

**T.R.
SAKARYA UNIVERSITY
GRADUATE SCHOOL OF NATURAL AND APPLIED SCIENCES**

**QUINONE BASED FLUORESCENT COMPOUNDS: SYNTHESIS,
CHARACTERIZATION, AND INVESTIGATION OF
PHOTOPHYSICAL/ELECTROCHEMICAL PROPERTIES**

PhD THESIS

Yavuz DERİN

**Department of Chemistry
Organic Chemistry Program**

AUGUST 2024

**T.R.
SAKARYA UNIVERSITY
GRADUATE SCHOOL OF NATURAL AND APPLIED SCIENCES**

**QUINONE BASED FLUORESCENT COMPOUNDS: SYNTHESIS,
CHARACTERIZATION, AND INVESTIGATION OF
PHOTOPHYSICAL/ELECTROCHEMICAL PROPERTIES**

PhD THESIS

Yavuz DERİN

Department of Chemistry

Organic Chemistry Program

Thesis Advisor: Prof. Dr. Ahmet TUTAR

AUGUST 2024

The thesis work titled “QUINONE BASED FLUORESCENT COMPOUNDS: SYNTHESIS, CHARACTERIZATION, AND INVESTIGATION OF PHOTOPHYSICAL/ELECTROCHEMICAL PROPERTIES” prepared by Yavuz DERİN was accepted by the following jury on **15/08/2024** by unanimously/majority of votes as a PhD THESIS in Sakarya University Graduate School of Natural and Applied Sciences, Chemistry Department, Organic Chemistry Programme.

Thesis Jury

Head of Jury : **Prof. Dr. Cavit UYANIK**
Kocaeli University

Jury Member : **Prof. Dr. Ahmet TUTAR** (Advisor)
Sakarya University

Jury Member : **Prof. Dr. Mustafa ARSLAN**
Sakarya University

Jury Member : **Prof. Dr. Fatih SÖNMEZ**
Sakarya University of Applied Sciences

Jury Member : **Prof. Dr. Kudret YILDIRIM**
Sakarya University



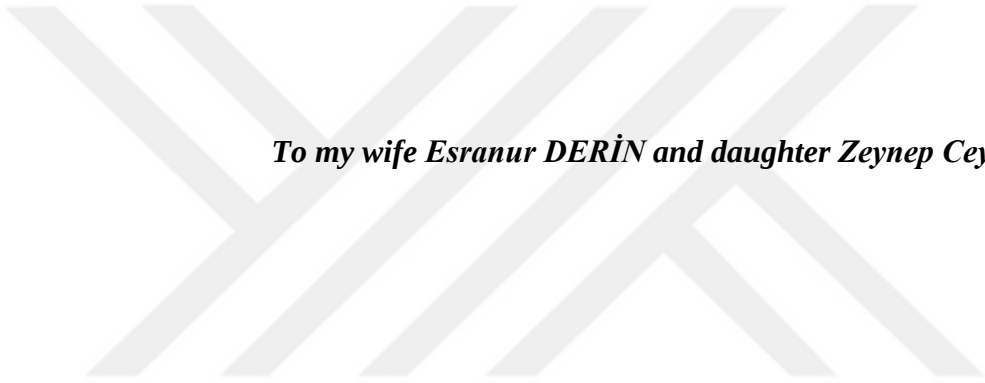
STATEMENT OF COMPLIANCE WITH THE ETHICAL PRINCIPLES AND RULES

I declare that the thesis work titled "QUINONE BASED FLUORESCENT COMPOUNDS: SYNTHESIS, CHARACTERIZATION, AND INVESTIGATION OF PHOTOPHYSICAL/ELECTROCHEMICAL PROPERTIES", which I have prepared in accordance with Sakarya University Graduate School of Natural and Applied Sciences regulations and Higher Education Institutions Scientific Research and Publication Ethics Directive, belongs to me, is an original work, I have acted in accordance with the regulations and directives mentioned above at all stages of my study, I did not get the innovations and results contained in the thesis from anywhere else, I duly cited the references for the works I used in my thesis, I did not submit this thesis to another scientific committee for academic purposes and to obtain a title, in accordance with the articles 9/2 and 22/2 of the Sakarya University Graduate Education and Training Regulation published in the Official Gazette dated 20.04.2016, a report was received in accordance with the criteria determined by the graduate school using the plagiarism software program to which Sakarya University is a subscriber, I accept all kinds of legal responsibility that may arise in case of a situation contrary to this statement.

15/08/2024

Yavuz DERİN





To my wife Esranur DERİN and daughter Zeynep Ceyda DERİN



ACKNOWLEDGEMENTS

Firstly, I would like to express my deepest gratitude to Prof. Dr. Ahmet TUTAR for being my mentor and supervisor. Besides his support, patience, and encouragement during my thesis work, I am very grateful to him for the experiences I gained from his advice as a person and professor.

Next, I would like to thank each of my thesis committee individually, Prof. Dr. Mustafa ARSLAN, Prof. Dr. Fatih SÖNMEZ, Prof. Dr. Kudret YILDIRIM, and Prof. Dr. Cavit UYANIK for their evaluation of my thesis and valuable feedback. I genuinely appreciate the assistance, support, and fruitful scientific talks from Özcan GÜLEÇ and Dr. Öğr. Üyesi Barış Seçkin ARSLAN.

I thank Haşim GÜL, Büşra Nur TOK, Nagihan ÖZTÜRK, Ömer Faruk TUTAR, Arş. Gör. Büşra ALBAYRAK MISIR, Zahidul ISLAM, Dr. Raşit Fikret YILMAZ, Dr. Yadigar ADİLOĞLU, Doç. Dr. Salih ÖKTEN and whoever we worked together in the past.

I pay special thanks to Tuğçe DUMAN and Sena YILDIZ, who are studying for a Bachelor of Chemistry at Sakarya University, and I wish them success in their education and life.

I am sincerely grateful to Prof. Dr. İlkey ŞİŞMAN, the dean of the Faculty of Science at Sakarya University, Prof. Dr. Mehmet NEBİOĞLU, Head of the Department of Chemistry at Sakarya University, Prof. Dr. Abdil ÖZDEMİR and each member of my department.

I appreciate Mustafa Mahmut SİNGİL, who took the time to characterize my compounds by HPLC-MS.

I am beyond grateful to Dr. Dilek ÜNLÜER and Cabir ÇOBANOĞLU from CBR Unique Fragrances who donated my starting material at the beginning of the study.

Finally, and most importantly, I am indebted to my special thanks all my family members and all my teachers in my life, especially my mother-and-in-law, Safiye MUTLU and Necla CEYLAN, my father-and-in-law Halit DERİN and Rüştü CEYLAN for their unconditional love, endless support, understanding, and patience.

I acknowledged that the study was financially supported by the scientific research projects unit of Sakarya University (Project number: 2021-7-25-5).

Yavuz DERİN



TABLE OF CONTENTS

Sayfa

ACKNOWLEDGEMENTS	ix
TABLE OF CONTENTS	xi
ABBREVIATIONS	xiii
SYMBOLS	xv
LIST OF TABLES	xvii
LIST OF FIGURES	xix
SUMMARY	xxvii
ÖZET	xxix
1. INTRODUCTION	1
1.1. Preface on Quinone and Related Structures.....	1
2. RESEARCH BACKGROUNDS	5
2.1. The Synthesis of 1,4-naphthoquinone and 2-hydroxy-1,4-naphthoquinone (Lawsone)	5
2.2. The Synthesis of Halogenated 1,4- naphthoquinone Derivatives.....	8
2.3. Synthetical Approaches to Obtain New 1,4-naphthoquinone Derivatives ..	10
2.3.1. Nucleophilic addition to Lawsone, 1,4-naphthoquinone and its halogenated derivatives	10
2.3.2. The synthesis of various 2-hydroxy 1,4-naphthoquinone derivatives.....	16
2.3.3. The synthesis of 1,4-naphthoquinones with heterocyclic ring.....	18
2.3.4. The Mannich reaction of 2-hydroxy-1,4-naphthoquinone	21
2.3.5. Multi-component reactions of 2-Hydroxy-1,4-naphthoquinone	27
2.4. Miscellaneous Reactions of 2-hydroxy-1,4-naphthoquinone	36
3. MATERIALS AND METHODS	41
3.1. Solvents and Chemicals	41
3.2. Devices and Instrumentation.....	41
3.3. Purification of Solvents.....	44
3.4. Column Chromatography.....	44
3.5. Crystallization	45
3.6. The Aim of the Study.....	45
4. EXPERIMENTAL STUDIES	47
4.1. The Bromination of 1,4-naphthoquinone.....	47
4.2. The Synthesis of Compound 4-2.....	47
4.3. The Synthesis of Compound 4-3.....	48
4.4. The Synthesis of Compound 4-4.....	48
4.5. The Synthesis of Compound 4-5.....	49
4.6. The Synthesis of Compound 4-6.....	49
4.7. The Synthesis of Compound 4-7.....	50
4.8. The Synthesis of Compound 4-8.....	50
4.9. The Synthesis of Compound 4-9.....	51
4.10. The Synthesis of Compound 4-10.....	51
4.11. The Synthesis of Compound 4-11.....	52

4.12. The Synthesis of Compound 4-12.....	52
4.13. The Synthesis of Compound 4-13.....	53
4.14. The Synthesis of Compound 4-14.....	54
4.15. The Synthesis of Compound 4-15.....	54
4.16. The Synthesis of Compound 4-16.....	55
4.17. The Synthesis of Compound 4-17.....	55
4.18. The Synthesis of Compound 4-18.....	56
4.19. The Synthesis of Compound 4-19.....	56
4.20. The Synthesis of Compound 4-20.....	57
4.21. The Synthesis of Compound 4-21.....	58
4.22. The Synthesis of Compound 4-22.....	58
4.23. The Synthesis of Compound 4-23.....	59
4.24. The Synthesis of Compound 4-24.....	59
4.25. The Synthesis of Compound 4-25.....	60
4.26. The Synthesis of Compound 4-26.....	60
4.27. The synthesis of Compound 4-27	61
4.28. The Synthesis of Compound 4-28.....	62
4.29. The Synthesis of Compound 4-29.....	62
4.30. The Synthesis of Compound 4-30.....	63
4.31. The Synthesis of Compound 4-31.....	64
4.32. The Synthesis of Compound 4-32.....	64
4.33. The Synthesis of Compound 4-33.....	65
4.34. The Synthesis of BODIPY	65
4.35. The Synthesis of Compound 4-35.....	66
4.36. The Synthesis of Compound 4-36.....	67
4.37. The Synthesis of Compound 4-37.....	67
4.38. The Synthesis of Compound 4-38.....	68
4.39. The Synthesis of Compound 4-39.....	69
4.40. The Synthesis of Compound 4-40.....	69
4.41. The Synthesis of Compound 4-41.....	70
4.42. The Synthesis of Compound 4-42.....	71
4.43. The Synthesis of Compound 4-43.....	71
4.44. The Photophysical Study	72
4.45. The Electrochemical Study	72
5. RESULTS AND DISCUSSION.....	73
5.1. Characterization of the Compounds by ^1H , ^{13}C , and ^{19}F NMR Methods	73
5.2. The Results of the Photophysical Study	113
5.3. The General Remarks on Electrochemical Features of the Compounds ...	121
REFERENCES.....	123
APPENDICES	143
CURRICULUM VITAE	201

ABBREVIATIONS

Ac₂O	: Acetic anhydride
AcOH	: Acetic acid
aq.	: Aqueous
a.u.	: Arbitrary unite
ATR	: Attenuated total reflectance
BF₃.OEt₂	: Boron trifluoro diethyl etherate
BODIPY	: Boron-dipyrromethene
br	: Broad singlet
CAN	: Cerium ammonium nitrate
CTAB	: Cetyltrimethylammonium bromide
d	: Doublet
dd	: Doublet of doublet
DMSO-d₆	: Deuterated dimethyl sulfoxide
DBU	: 1,8-Diazabicyclo[5.4.0]undec-7-ene
DDQ	: 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone
DMF	: <i>N, N</i> -Dimethylformamide
DMSO	: Dimethyl sulfoxide
DNA	: Deoxyribonucleic acid
Et₃N	: Triethylamine
EtOAc	: Ethyl acetate
EtOH	: Ethanol
eq.	: Equivalent(s)
F	: Faraday
FT-IR	: Fourier transform infrared spectroscopy
g	: Gram
GSH	: Glutathione
h.	: Hour(s)
J	: Spin-spin coupling
M	: Molar
m	: Multiplet

MHz	: Mega hertz
Me	: Methyl
MeOH	: Methanol
mL	: Millilitre
mmol	: Milimol
mp	: Melting point
min.	: Minute
m/z	: Mass to charge ratio
NBS	: <i>N</i> -Bromosuccinimide
NCS	: <i>N</i> -Chlorosuccinimide
nd	: Not determined
NH₄OAc	: Ammonium acetate
NIS	: <i>N</i> -Iodosuccinimide
nm	: nanometre
NMP	: <i>N</i> -Methylpyrrolidone
NMR	: Nuclear Magnetic Resonance Spectroscopy
OTf	: Triflate
ppm	: Parts per million
<i>p</i>-TSA	: Para toluene sulfonic acid
RNA	: Ribonucleic acid
rt.	: Room temperature
t	: Triplate
TBAB	: Tetrabutylammonium bromide
<i>t</i>-BuOK	: Potassium <i>tert</i> -butoxide
TFA	: trifluoroacetic acid
THF	: tetrahydrofuran
TLC	: thin layer chromatography

SYMBOLS

$^{\circ}\text{C}$	: Celcius degree
δ	: Chemical shift
ϵ	: Molar absorption coefficient
λ	: Wavelength
μL	: Microliter





LIST OF TABLES

	<u>Page</u>
Table 3.1. The instruments used in the study	42
Table 5.1. The photophysical properties of the compounds.	120





LIST OF FIGURES

	<u>Page</u>
Figure 1.1. Simple chemical structures of quinone-bearing molecules	1
Figure 1.2. The chemical structure of naphthalene, 1,2- and 1,4- naphthoquinone.	2
Figure 1.3. Henna plant and Lawsone (2-hydroxy-1,4-naphthoquinone) compound.	2
Figure 1.4. Naturally important naphthoquinones.	3
Figure 2.1. The synthesis of 1,4- naphthoquinone by oxidation of naphthalene.	5
Figure 2.2. The synthesis of 1,4-naphthoquinones by oxidation with NBS.....	6
Figure 2.3. The synthesis of 1,4-naphthoquinone by electrochemical oxidation.....	6
Figure 2.4. The synthesis of 2-hydroxy-1,4-naphthoquinone from 1,4-naphthoquinone.....	6
Figure 2.5. The synthesis of 2-hydroxy-1,4-naphthoquinone from 2-naphthol.	7
Figure 2.6. Oxidation of tetralone to 2-hydroxy-1,4-naphthoquinone.	7
Figure 2.7. Transformation of ammonium 1,2-naphthoquinone-4-sulfonate.....	8
Figure 2.8. The synthesis of dichlone.	8
Figure 2.9. The synthesis of 2-chloro-1,4-naphthoquinone	8
Figure 2.10. The Synthesis of 1,4-naphthoquinone with bromo and chloro atom at 2 position.....	9
Figure 2.11. The synthesis of 2-bromo-1,4-naphthoquinone by molecular bromine..	9
Figure 2.12. The synthesis of 2-bromo-1,4-naphthoquinone from 1-naphthol.....	9
Figure 2.13. The synthesis of 2,3-dibromo-1,4-naphthoquinone by molecular bromine	9
Figure 2.14. The synthesis of 2,3-diiodo-1,4-naphthoquinone	9
Figure 2.15. The asymmetric nucleophilic addition of nitrostyrene derivatives to Lawsone.	11
Figure 2.16. The nucleophilic substitution reaction of 1,4-naphthoquinone with 4-aminophenol.....	11
Figure 2.17. The nucleophilic substitution reaction of 1,4-naphthoquinone with 2-ethanolamine its functionalization with triazole ring.	12
Figure 2.18. The amination of 1,4-naphthoquinone with several amine derivatives.	12
Figure 2.19. The amination of 1,4-naphthoquinone with several alkyl amines.	12
Figure 2.20. The amination reaction of 1,4-naphthoquinone with aromatic amines by blue light.	13
Figure 2.21. The amination reaction of 1,4-naphthoquinone with aromatic nitro compounds by zinc-mediated reduction reaction	13
Figure 2.22. The synthesis of amino acid bearing 1,4-naphthoquinone	14

Figure 2.23. The synthesis of 1,4-naphthoquinones with amino acid and its modification with boronic ester and acid group.....	14
Figure 2.24. The nucleophilic substitution reaction and the formation of 2-amino-3-(substituted phenylamino)naphthalene-1,4-diones or phenazine derivatives.	14
Figure 2.25. The synthesis of 2-chloro-3-[(thiazol-2-yl)amino]-1,4-naphthoquinones.	15
Figure 2.26. The nucleophilic substitution reaction of 4-aminobenzeneselenolate anion with 2,3-dibromo-1,4-naphthoquinone	15
Figure 2.27. The nucleophilic substitution reaction of phenols and alcohols with 2,3-dichloro-1,4-naphthoquinone.....	16
Figure 2.28. The nucleophilic substitution reaction of thiols and thiophenols with 2,3-dichloro-1,4-naphthoquinone	16
Figure 2.29. The synthesis of 2-hydroxy-3-iodonaphthalene-1,4-dione.	16
Figure 2.30. The bromination of 1,4-naphthoquinone	16
Figure 2.31. Synthesis of 2-hydroxy-1,4-naphthoquinone with chlor or brom atom at 3-position.	17
Figure 2.32. The modification of Lawsone by the cross-coupling reaction.....	17
Figure 2.33. Palladium-catalyzed C-C bond formation of 1,4-naphthoquinone.	17
Figure 2.34. The formation of Lawsone-enaminone compounds.	17
Figure 2.35. The epoxidation of 1,4-naphthoquinone and its ring opening reaction with amin derivatives.	18
Figure 2.36. The synthesis of 2-allyl-3-hydroxynaphthalene-1,4-dione by Claisen rearrangement reaction.....	18
Figure 2.37. Diazotization reaction of 2-hydroxy-1,4-naphthoquinone.....	18
Figure 2.38. The synthesis of enantiomerically pure 1,4-pyranonaphthoquinones...	19
Figure 2.39. The synthesis of dehydro- α -lapachone.	19
Figure 2.40. The synthesis of 1,4-naphthoquinone fused furan derivatives.....	19
Figure 2.41. The synthesis of 1,4-naphthoquinone fused furan structures.....	20
Figure 2.42. The synthesis of naphtho[2,3- <i>b</i>]furan-4,9-dione derivatives.	20
Figure 2.43. Synthesis of 3-substituted 2-aminonaphtho[2,3- <i>b</i>]furan-4,9-dione derivatives.	20
Figure 2.44. The synthesis of furano1,4-naphthoquinones.	21
Figure 2.45. The synthesis of 2,3-dihydronaphtho[2,3- <i>b</i>]furan-4,9-dione derivatives.	21
Figure 2.46. Representative Mannich reaction.....	21
Figure 2.47. The proposed reaction mechanisms of Mannich base formation.....	22
Figure 2.48. The Mannich reaction and selected examples by Leffler and Hathaway.	23
Figure 2.49. Mannich bases reported in reference [101].....	23
Figure 2.50. Mannich bases reported by Paengsri et all.....	23
Figure 2.51. Mannich bases reported in reference [102].....	24
Figure 2.52. Three-component Mannich bases reported in reference [103].	25
Figure 2.53. Mannich bases derived from 5,5'-methylenebis(thiazol-2-amine).	25
Figure 2.54. Mannich bases obtained from heterocyclic amine derivatives.	26
Figure 2.55. The Mannich bases obtained from the reaction, which was catalyzed with InCl_3	26
Figure 2.56. The synthesis of 2-hydroxy-1,4-naphthoquinone with isoindoline moiety.	27

Figure 2.57. The multi-component reaction between indole and Lawsone with different aldehydes.....	28
Figure 2.58. The multi-component reaction between Lawsone, thiophenol, and aldehyde derivatives.	28
Figure 2.59. The synthesis of <i>para</i> - and <i>ortho</i> - naphthoxanthenes linked by thiol groups.....	29
Figure 2.60. The synthesis of 4 <i>H</i> -pyran-2-amino-3-carbonitrile derivatives with 1,4-naphthoquinone unite.....	29
Figure 2.61. 4 <i>H</i> -pyran-2-amino-3-carboxylate with naphthoquinone moiety.	29
Figure 2.62. The multi-component reaction between 1 <i>H</i> -pyrazole-4-carbaldehyde malononitrile, and Lawsone.....	30
Figure 2.63. The reaction between malononitrile, 2-hydroxy-1,4-naphthoquinone, and glyoxal compounds.	30
Figure 2.64. The preparation of 1,4-naphthoquinone fused chromene derivatives...	31
Figure 2.65. The synthesis of spirooxindole with naphthoquinone structure.	31
Figure 2.66. The synthesis of spiro[benzo[<i>g</i>]-furo[3,4- <i>b</i>]quinoline-indoline]-tetraones.	31
Figure 2.67. The synthesis of xanthene derivatives bearing naphthoquinone structure.	32
Figure 2.68. The synthesis of dibenzoxanthenetetraone compounds.....	33
Figure 2.69. The synthesis of benzoindenchromenetrione.....	33
Figure 2.70. The synthesis of benzo[<i>b</i>]xanthene-triones derivatives.....	34
Figure 2.71. The synthesis of 3-benzoyl-4 <i>H</i> -benzo[<i>g</i>]chromene-5,10-diones.....	34
Figure 2.72. The multi-step synthesis for benzo[<i>a</i>]benzo[6,7]chromeno[2,3- <i>c</i>]phenazine	34
Figure 2.73. The synthesis of benzylpyrazolyl naphthoquinone derivatives.	35
Figure 2.74. The synthesis of indazolophthalazine derivatives.	35
Figure 2.75. The synthesis of benzoindenoquinolinetriene	35
Figure 2.76. The construction of benzo[<i>g</i>]quinoline-5,10-dione skeleton.....	36
Figure 2.77. The synthesis of pyrimidine-fused tetrahydropyridines.	36
Figure 2.78. The synthesis of oxazine derivatives with naphthoquinone structure. .	36
Figure 2.79. The synthesis of benzo[<i>a</i>]phenazin-5-ol	37
Figure 2.80. The four-component reaction for the synthesis of benzo[<i>a</i>]pyrano[2,3- <i>c</i>]phenazine derivatives.....	37
Figure 2.81. The synthesis of 1 <i>H</i> -benzo[<i>a</i>]pyrano[2,3- <i>c</i>]phenazin-3-amine derivatives with methyl or phenyl sulfonyl groups	38
Figure 2.82. The synthesis of 5 <i>H</i> -benzo[<i>a</i>]phenoxazin-5-one.....	38
Figure 2.83. The synthesis of pyrimidophenazine derivatives.....	39
Figure 2.84. The synthesis of benzo[<i>h</i>]pyrazolo[3,4- <i>b</i>]quinoline-5,6(10 <i>H</i>)-diones with styryl group.....	39
Figure 2.85. The synthesis of 7-arylbenzo[<i>c</i>]acridine-5,6-diones derivatives.	40
Figure 2.86. The synthesis of 7-(aryl)-8-methyl-10-phenyl-5 <i>H</i> -benzo[<i>h</i>]pyrazolo[3,4- <i>b</i>]quinoline-5,6(10 <i>H</i>)-diones.	40
Figure 3.1. The synthetic pathway of aromatic, aliphatic amine, and ether group bearing 1,4-naphthoquinone derivatives in the study.	45
Figure 3.2. The synthetic pathway of Mannich bases.	46
Figure 4.1. The synthesis of compound 4-1.	47
Figure 4.2. The synthesis of compound 4-2	47
Figure 4.3. The synthesis of compound 4-3.	48
Figure 4.4. The synthesis of compound 4-4.	48

Figure 4.5.	The synthesis of compound 4-5.	49
Figure 4.6.	The synthesis of compound 4-6.	49
Figure 4.7.	The synthesis of compound 4-7.	50
Figure 4.8.	The synthesis of compound 4-8.	50
Figure 4.9.	The synthesis of compound 4-9.	51
Figure 4.10.	The synthesis of compound 4-10.	51
Figure 4.11.	The synthesis of compound 4-11.	52
Figure 4.12.	The synthesis of compound 4-12.	52
Figure 4.13.	The synthesis of compound 4-13.	53
Figure 4.14.	The synthesis of compound 4-14.	54
Figure 4.15.	The synthesis of compound 4-15.	54
Figure 4.16.	The synthesis of compound 4-16.	55
Figure 4.17.	The synthesis of compounds 4-17.	55
Figure 4.18.	The synthesis of compound 4-18.	56
Figure 4.19.	The synthesis of compound 4-19.	56
Figure 4.20.	The synthesis of compound 4-20.	57
Figure 4.21.	The synthesis of compound 4-21.	58
Figure 4.22.	The synthesis of compound 4-22.	58
Figure 4.23.	The synthesis of compound 4-23.	59
Figure 4.24.	The synthesis of compound 4-24.	59
Figure 4.25.	The synthesis of compound 4-25.	60
Figure 4.26.	The synthesis of compound 4-26.	60
Figure 4.27.	The synthesis of compound 4-27.	61
Figure 4.28.	The synthesis of compound 4-28.	62
Figure 4.29.	The synthesis of compound 4-29.	62
Figure 4.30.	The synthesis of compound 4-30.	63
Figure 4.31.	The synthesis of compounds 4-31.	64
Figure 4.32.	The synthesis of compound 4-32.	64
Figure 4.33.	The synthesis of compound 4-33.	65
Figure 4.34.	The synthesis of BODIPY.	65
Figure 4.35.	The synthesis of compound 4-35.	66
Figure 4.36.	The synthesis of compound 4-36.	67
Figure 4.37.	The synthesis of compound 4-37.	67
Figure 4.38.	The synthesis of compound 4-38.	68
Figure 4.39.	The synthesis of compound 4-39.	69
Figure 4.40.	The synthesis of compound 4-40.	69
Figure 4.41.	The synthesis of compound 4-41.	70
Figure 4.42.	The synthesis of compound 4-42.	71
Figure 4.43.	The synthesis of compound 4-43.	71
Figure 5.1.	¹ H NMR spectrum of compound 4-1.	73
Figure 5.2.	¹³ C NMR spectrum of compound 4-1.	73
Figure 5.3.	¹ H NMR spectrum of compound 4-2.	73
Figure 5.4.	¹³ C NMR spectrum of compound 4-2.	74
Figure 5.5.	¹ H NMR spectrum of compound 4-3.	74
Figure 5.6.	¹³ C NMR spectrum of compound 4-3.	74
Figure 5.7.	¹ H NMR spectrum of compound 4-4.	75
Figure 5.8.	¹³ C NMR spectrum of compound 4-4.	75
Figure 5.9.	¹ H NMR spectrum of compound 4-5.	75
Figure 5.10.	¹³ C NMR spectrum of compound 4-5.	76
Figure 5.11.	¹ H NMR spectrum of compound 4-6.	76

Figure 5.12.	^{13}C NMR spectrum of compound 4-6.....	77
Figure 5.13.	^1H NMR spectrum of compound 4-7.....	77
Figure 5.14.	^{13}C NMR spectrum of compound 4-7.....	77
Figure 5.15.	^1H NMR spectrum of compound 4-8.....	78
Figure 5.16.	^{13}C NMR spectrum of compound 4-8.....	78
Figure 5.17.	^1H NMR spectrum of compound 4-9.....	79
Figure 5.18.	^{13}C NMR spectrum of compound 4-9.....	79
Figure 5.19.	^1H NMR spectrum of compound 4-10.....	79
Figure 5.20.	^{13}C NMR spectrum of compound 4-10.....	80
Figure 5.21.	^1H NMR spectrum of compound 4-11.....	80
Figure 5.22.	^{13}C NMR spectrum of compound 4-11.....	80
Figure 5.23.	^1H NMR spectrum of compound 4-12.....	81
Figure 5.24.	^{13}C NMR spectrum of compound 4-12.....	81
Figure 5.25.	^1H NMR spectrum of compound 4-13.....	81
Figure 5.26.	^{13}C NMR spectrum of compound 4-13.....	81
Figure 5.27.	^1H NMR spectrum of compound 4-14.....	82
Figure 5.28.	^{13}C NMR spectrum of compound 4-14.....	82
Figure 5.29.	^1H NMR spectrum of compound 4-15.....	83
Figure 5.30.	^{13}C NMR spectrum of compound 4-15.....	83
Figure 5.31.	^1H NMR spectrum of compound 4-16.....	83
Figure 5.32.	^{13}C NMR spectrum of compound 4-16.....	84
Figure 5.33.	^1H NMR spectrum of compound 4-17.....	84
Figure 5.34.	^{13}C NMR spectrum of compound 4-17.....	85
Figure 5.35.	^1H NMR spectrum of compound 4-18.....	85
Figure 5.36.	^{13}C NMR spectrum of compound 4-18.....	85
Figure 5.37.	^1H NMR spectrum of compound 4-19.....	86
Figure 5.38.	^{13}C NMR spectrum of compound 4-19.....	86
Figure 5.39.	^1H NMR spectrum of compound 4-20.....	87
Figure 5.40.	^{13}C NMR spectrum of compound 4-20.....	87
Figure 5.41.	^1H NMR spectrum of compound 4-21.....	88
Figure 5.42.	^{13}C NMR spectrum of compound 4-21.....	88
Figure 5.43.	^1H NMR spectrum of compound 4-22.....	89
Figure 5.44.	^{13}C NMR spectrum of compound 4-22.....	89
Figure 5.45.	^1H NMR spectrum of compound 4-23.....	90
Figure 5.46.	^{13}C NMR spectrum of compound 4-23.....	90
Figure 5.47.	^1H NMR spectrum of compound 4-24.....	91
Figure 5.48.	^{13}C NMR spectrum of compound 4-24.....	91
Figure 5.49.	^1H NMR spectrum of compound 4-25.....	92
Figure 5.50.	^{13}C NMR spectrum of compound 4-25.....	92
Figure 5.51.	^1H NMR spectrum of compound 4-26.....	92
Figure 5.52.	^{13}C NMR spectrum of compound 4-26.....	92
Figure 5.53.	^1H NMR spectrum of compound 4-27.....	93
Figure 5.54.	^{13}C NMR spectrum of compound 4-27.....	93
Figure 5.55.	^1H NMR spectrum of compound 4-28.....	94
Figure 5.56.	^{13}C NMR spectrum of compound 4-28.....	94
Figure 5.57.	^1H NMR spectrum of compound 4-29.....	95
Figure 5.58.	^{13}C NMR spectrum of compound 4-29.....	95
Figure 5.59.	^1H NMR spectrum of compound 4-30.....	95
Figure 5.60.	^{13}C NMR spectrum of compound 4-30.....	96
Figure 5.61.	^1H NMR spectrum of compound 4-31.....	96

Figure 5.62.	^{13}C NMR spectrum of compound 4-31.	96
Figure 5.63.	^1H NMR spectrum of compound 4-32.	97
Figure 5.64.	^{13}C NMR spectrum of compound 4-32.	97
Figure 5.65.	^1H NMR spectrum of compound 4-33.	98
Figure 5.66.	^{13}C NMR spectrum of compound 4-33.	98
Figure 5.67.	^1H NMR spectrum of compound 4-34.	99
Figure 5.68.	^{13}C NMR spectrum of compound 4-34.	99
Figure 5.69.	^1H NMR spectrum of compound 4-35.	100
Figure 5.70.	^{13}C NMR spectrum of compound 4-35.	100
Figure 5.71.	^{19}F NMR spectrum of compound 4-35.	100
Figure 5.72.	^1H NMR spectrum of compound 4-36.	101
Figure 5.73.	^{13}C NMR spectrum of compound 4-36.	101
Figure 5.74.	^1H NMR spectrum of compound 4-37.	102
Figure 5.75.	^{13}C NMR spectrum of compound 4-37.	103
Figure 5.76.	^1H NMR spectrum of compound 4-38.	104
Figure 5.77.	^{13}C NMR spectrum of compound 4-38.	104
Figure 5.78.	^1H NMR spectrum of compound 4-39.	105
Figure 5.79.	^{13}C NMR spectrum of compound 4-39.	106
Figure 5.80.	^1H NMR spectrum of compound 4-40.	107
Figure 5.81.	^{13}C NMR spectrum of compound 4-40.	107
Figure 5.82.	^1H NMR spectrum of compound 4-41.	108
Figure 5.83.	^{13}C NMR spectrum of compound 4-41.	109
Figure 5.84.	^1H NMR spectrum of compound 4-42.	110
Figure 5.85.	^{13}C NMR spectrum of compound 4-42.	110
Figure 5.86.	^1H NMR spectrum of compound 4-43.	111
Figure 5.87.	^{13}C NMR spectrum of compound 4-43.	112
Figure 5.88.	The physical appearance of all compounds between 4-2 and 4-9 in the solution.	113
Figure 5.89.	The absorption spectra of the compounds between 4-1 and 4-9.	114
Figure 5.90.	The emission spectra of the compounds between 4-1 and 4-9.	114
Figure 5.91.	The physical appearance of the compounds between 4-10 and 4-14.	115
Figure 5.92.	The absorption spectra of the compounds between 4-10 and 4-14.	115
Figure 5.93.	The emission spectra of the compounds between 4-10 and 4-14.	116
Figure 5.94.	The physical appearance of 1,4-naphthoquinone derivatives between 4-15 and 4-30.	116
Figure 5.95.	The absorption spectra of 1,4-naphthoquinone derivatives between 4-15 and 4-30.	117
Figure 5.96.	The physical appearance of 1,4-naphthoquinone derivatives between 4-31 and 4-33.	117
Figure 5.97.	The absorption spectra of 1,4-naphthoquinone derivatives between 4-31 and 4-33.	118
Figure 5.98.	The emission spectra of 1,4-naphthoquinone derivatives between 4-15 and 4-30.	118
Figure 5.99.	The absorption and emission spectra of the compound 4-35 and its physical appearance in the solution.	119
Figure 5.100.	The physical appearance of Mannich bases between 4-36 and 4-43 in solution.	119
Figure 5.101.	The absorption spectra of Mannich bases.	120

Figure 5.102. The emission spectra of Mannich bases.	120
Figure 5.103. The redox process of 1,4-naphthoquinone derivatives.	122





QUINONE BASED FLUORESCENT COMPOUNDS: SYNTHESIS, CHARACTERIZATION, AND INVESTIGATION OF PHOTOPHYSICAL/ELECTROCHEMICAL PROPERTIES

SUMMARY

This study focuses on quinones and their derivatives, particularly 1,4-naphthoquinone and its derivatives. Quinones are aromatic compounds widely found in nature and can be obtained from fungi, algae, bacteria, and various plants. These compounds are present in some cancer treatment drugs and exhibit cytotoxic properties through DNA topoisomerase inhibition. 1,4-naphthoquinone is used as a raw material in the production of pharmaceuticals, agrochemicals, and other valuable compounds. The synthesis of 1,4-naphthoquinone is achieved through various oxidation methods of naphthalene. For example, the oxidation of naphthalene with chromic trioxide in acetic acid or the oxidation of 4-Amino-1-naphthol with potassium dichromate yields this product. Additionally, electrochemical oxidation methods are also used.

2-hydroxy-1,4-naphthoquinone (Lawsone) is a natural compound found in the *Lawsonia inermis* plant and is traditionally used as a dye for skin and hair. Its synthesis involves various chemical reactions, such as the Thiele-Winter reaction. The synthesis of halogenated 1,4-naphthoquinone derivatives is also examined in this study. For example, 2,3-dichloro-1,4-naphthoquinone is obtained by chlorination of 1,4-naphthoquinone with potassium perchlorate and hydrochloric acid. Similarly, 2-bromo-1,4-naphthoquinone is synthesized using NBS in the presence of CuBr₂.

1,4-naphthoquinone derivatives undergo nucleophilic substitution reactions with electron-rich nucleophiles. These reactions are used to synthesize new biologically active molecules. This study also obtained 2-hydroxy-1,4-naphthoquinone derivatives through the Mannich reaction. Mannich bases are used in the synthesis of biologically important drug candidates and are obtained by reacting with various amine compounds and aldehydes.

In this thesis study, Mannich reactions were performed with 2-hydroxy-1,4-naphthoquinone, hexylamine, and eight different benzaldehyde derivatives. Additionally, 1,4-naphthoquinone was brominated in acetic acid to yield 2,3-dibromo-1,4-naphthoquinone with high efficiency. This dibromo-1,4-naphthoquinone was subjected to nucleophilic substitution reactions with various nitrogen and oxygen-containing nucleophiles. These compounds, together with 1,4-naphthoquinone, contain pharmaceutically important structures such as carbazole, thiadiazole, tacrine, and BODIPY. The structures of all compounds were determined by ¹H, ¹³C, and ¹⁹F NMR methods. The structures of the final products were characterized by HPLC-MS and FT-IR in addition to these methods, and their melting points were determined. The photophysical properties of all 1,4-naphthoquinone derivatives were determined by UV-vis and fluorescence spectroscopy. Their electrochemical properties were investigated using cyclic voltammetry.



KİNÖN TEMELLİ FLORESANS BİLEŞİKLERİN SENTEZİ KARAKTERİZASYONU FOTOFİZİKSEL/ELEKTROKİMYASAL ÖZELLİKLERİNİN ARAŞTIRILMASI

ÖZET

Bu çalışmada, kinonlar ve türevleri, özellikle 1,4-naftokinon ve türevleri üzerine yoğunlaşmaktadır. Kinonlar, doğada yaygın olarak bulunan aromatik bileşiklerdir ve mantarlar, algler, bakteriler ve çeşitli bitkilerden elde edilebilirler. Bu kinon yapısı, kanser tedavisinde kullanılan anthracyclin, doxorubicin, daunorubicin, mitomycine, mitoxantron, ve saintopin ilaçlarının yapısında bulunur. DNA topoizomeraaz inhibisyonu yoluyla sitotoksik özellik gösterirler. 1,4-naftokinon, ilaç, tarım kimyasalları ve diğer değerli bileşiklerin üretiminde ham madde olarak kullanılır.

1,4-naftokinon eldesi, naftalinin çeşitli yöntemlerle oksidasyonu ile gerçekleştirilir. Örneğin, naftalinin krom trioksit ile asetik asit içinde oksidasyonu veya 4-Amino-1-naftolun potasyum dikromat ile oksidasyonu bu ürünü verir. Ayrıca, elektro-kimyasal oksidasyon gibi çeşitli yöntemler de kullanılmaktadır. 2-hidroksi-1,4-naftokinon (Lawson), *Lawsonia inermis* bitkisinde bulunan doğal bir bileşiktir ve geleneksel olarak cilt ve saç boyası olarak kullanılır. Sentezi için, Thiele-Winter reaksiyonu gibi çeşitli kimyasal reaksiyonlar kullanılır. Halojenlenmiş 1,4-naftokinon türevlerinin sentezi de bu çalışmada incelenmiştir. Örneğin, 2,3-diklor-1,4-naftokinon, 1,4-naftokinonun potasyum perklorat ve hidroklorik asit ile klorlanmasıyla elde edilir. Benzer şekilde, 2-bromo-1,4-naftokinon, NBS varlığında CuBr_2 kullanılarak sentezlenir. Lawson ve 1,4-naftakinon bir çok farklı reaksiyon ile çeşitli heterosiklik halka ve kinon grubu içeren tıbbi ve endüstriyel öneme sahip yeni bileşikler elde edilir.

1,4-naftakinon türevleri, elektron bakımından zengin nükleofiller ile nükleofilik yer değiştirme reaksiyonları verir. Bu reaksiyonlar, biyolojik olarak aktif yeni moleküllerin sentezinde kullanılmaktadır.

Bu çalışmada ayrıca, Mannich reaksiyonu ile 2-hidroksi-1,4-naftokinon türevleri elde edilmiştir. Mannich bazları, biyolojik olarak önemli ilaç adaylarının sentezinde kullanılır ve çeşitli amin bileşikleri ve aldehitlerle reaksiyona sokularak elde edilir.

Bu tez çalışmasında 2-hidroksi-1,4-naftokinon, hegzil amin ve sekiz farklı benzaldehit türevi ile Mannich reaksiyonu gerçekleştirilmiştir. Ayrıca 1,4-naftakinon brom ile asetik asit içerisinde bromlanarak yüksek verimle 2,3-dibrom-1,4-naftakinon elde edilmiştir. Bu dibrom-1,4-naftakinon çeşitli azot ve oksijen içeren nükleofillerle nükleofilik yer değiştirme reaksiyonuna tabi tutulmuştur. Elde edilen bileşiklerin IUPAC isimleri şöyledir; 2,3-dibromo-1,4-naftakinon, 2-amino-3-bromonaftalen-1,4-dion, 2-bromo-3-(metilamino)naftalen-1,4-dion, 2-bromo-3-(etilamino)naftalen-1,4-dion, 2-bromo-3-(butilamino)naftalen-1,4-dione, 2-bromo-3-(tert-bütilamino)naftalen-1,4-dion, 2-bromo-3-(hegzilamino)naftalen-1,4-dion, 2-bromo-3-(siklohegzilamino)naftalen-1,4-dion, 2-bromo-3-(oktilamino)naftalen-1,4-dion, 2-bromo-3-(pirolidin-1-il)naftalen-1,4-dion, 2-bromo-3-(piperidin-1-il)naftalen-1,4-dion, 2-bromo-3-morfolinonaftalen-1,4-dion, 2-bromo-3-(4-metilpiperazin-1-

il)naftalen-1,4-dion, 2-bromo-3-(3,4-dihidroisokinolin-2(1*H*)-il)naftalen-1,4-dion, 2-bromo-3-(fenilamino)naftalen-1,4-dion, 2-bromo-3-((4-metoksifenil)amino)naftalen-1,4-dion, 2-bromo-3-((2,3-dihidro-1*H*-inden-5-il)amino)naftalen-1,4-dion, 2-nitro-9*H*-fluoren, 2-amino-9*H*-fluoren, 2-((9*H*-fluoren-2-il)amino)-3-bromonaftalen-1,4-dion, 2-bromo-3-((4-metoksifenil)amino)naftalen-1,4-dion, 2-bromo-3-((3-kloro-4-metoksifenil)amino)naftalen-1,4-dion, 2-bromo-3-((3,4,5-trimetoksifenil)amino)naftalene-1,4-dion, 2-bromo-3-((4-dimetilamino)fenil)amino)naftalene-1,4-dion, 2-(4-metoksibenziliden)hidrazin-1-karbotiyoamid, 5-(4-metoksifenil)-1,3,4-tiyadiazol-2-amine, 2-bromo-3-((5-(4-metoksifenil)-1,3,4-tiyadiazol-2-il)amino)naftalen-1,4-dion, 2-bromo-3-((9-etil-9*H*-karbazol-3-il)amino)naftalen-1,4-dion, 1,2,3,4-tetrahidroakridin-9-amin, 2-bromo-3-((1,2,3,4-tetrahidroakridin-9-il)amino)naftalen-1,4-dion, 4-((3-bromo-1,4-diokso-1,4-dihidronaftalen-2-il)oksi)benzaldehit, 4-((3-bromo-1,4-diokso-1,4-dihironaftalen-2-il)okso)-3-metoksibenzaldehit, 2-((3-bromo-1,4-diokso-1,4-dihidronaftalen-2-il)okso)benzaldehit, 4-(5,5-difluoro-1,3,7,9-tetramethyl-5*H*-4 λ^4 ,5 λ^4 -dipirolo[1,2-*c*:2',1'-*f*][1,3,2]diazaborinin-10-il)fenol, 2-bromo-3-(4-(5,5-difluoro-1,3,7,9-tetrametil-5*H*-4 λ^4 ,5 λ^4 -dipirolo[1,2-*c*:2',1'-*f*][1,3,2]diazaborinin-10-il)fenoksi)naftalen-1,4-dion, 2-((hegzilamino)(4-metoksifenil)metil)-3-hidroksinaftalen-1,4-dion, 2-((hegzilamino)(*p*-tolil)metil)-3-hidroksinaftalen-1,4-dion, 2-((hegzilamino)(fenil)metil)-3-hidroksinaftalen-1,4-dion, 2-((4-(tert-butil)fenil)(hegzilamino)metil)-3-hidroksinaftalen-1,4-dion, 2-((hegzilamino)(4-nitrofenil)metil)-3-hidroksinaftalen-1,4-dion, 2-((4-klorofenil)(hegzilamino)metil)-3-hidroksinaftalen-1,4-dion, 2-((4-bromofenil)(hegzilamino)metil)-3-hidroksinaftalen-1,4-dion, 2-((3,5-dimetoksifenil)(hegzilamino)metil)-3-hidroksinaftalen-1,4-dion.

Bu bileşikler 1,4-naftakinon ile birlikte, karbazol, tiyadiazol, takrin ve BODIPY gibi farmasötik olarak önemli olan yapılar içerir. Tüm bileşiklerin yapıları ^1H , ^{13}C ve ^{19}F NMR spektroskopik teknikleri ile tayin edilmiştir. Ürünlerinin yapıları bu yöntemlere ek olarak HPLC-MS ve FT-IR ile karakterize edilmiş. Tüm 1,4-naftakinon türevlerinin fotofiziksel özellikleri UV-vis ve floresans spektroskopisi ile elektrokimyasal özellikleri ise dönüşümlü voltametre yöntemi ile araştırılmıştır. Bu spektrumlar incelendiğinde, nükleofilik yerdeğiştirme ürünlerinden azot grubu içerenler UV bölgedeki piklere ek olarak 336-523 nm arasında, BODIPY grubu içeren ise 499 nm'de maksimum absorpsiyon piki sergilediği görülmüştür. Ancak BODIPY haricindeki oksijen grubu içeren 1,4-naftokinonlar UV bölgede 271-284 nm aralığında absorpsiyon yaptığı gözlemlenmiştir. Bu 1,4-naftakinon bileşiklerinin 530-603 nm aralığında oldukça zayıf emisyon yaptığı kaydedilmiştir. Ancak aromatik anilin gruplarından elde edilen bileşikler için herhangi bir emisyon piki gözlemlenmemiştir. 1,4-naftakinon içeren Mannich bazlarının absorpsiyon spektrumları incelendiğinde bu bileşikler UV bölgedeki piklere ek olarak görünür bölgede 474-504 nm aralığında absorpsiyon yaptığı gözlemlenmiştir. Bu bileşiklerin 596-603 nm arasında emisyon yaptığı gözlemlenmiştir. Bu spektrumlardan görünür bölgedeki piklerin $n-\pi^*$ geçişlerinden, UV bölgedeki piklerin ise $\pi-\pi^*$ geçişlerinde kaynaklandığı sonucuna varılmıştır.

Bu tezdeki 1,4-naftakinon bileşiklerin elektrokimyasal özellikleri, DMSO içinde dönüşümlü voltametri yöntemi kullanılarak incelenmiştir. Voltammogramlarda genellikle katodik bölgede iki geri dönüşümlü pik gözlemlenmiştir. Bu pikler, naftokinonun indirgenerek seminaftokinon radikaline ve ardından dianyon katekole dönüşümünü göstermektedir. Anodik bölgede gözlemlenen pikler ise Mannich

bazlarındaki kinon halkasının veya bağı yan grupların oksidasyon sürecinden kaynaklanmaktadır.





1. INTRODUCTION

1.1. Preface on Quinone and Related Structures

Quinones are widely dispersed aromatic compounds that are ubiquitous in all of nature. They can be extracted from fungi, algae, bacteria, and different plant groups. Based on their chemical composition, quinones are divided into benzoquinones, anthraquinones, naphthoquinones, and phenanthrenequinones (Figure 1.1).

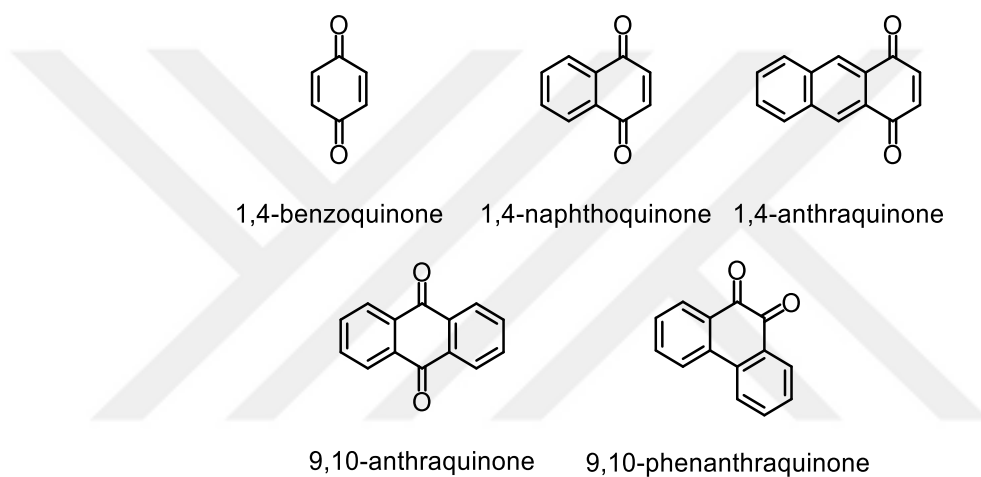


Figure 1.1. Simple chemical structures of quinone-bearing molecules.

Quinones are extremely prevalent substances in nature. They appear in cancer treatment medications such as anthracyclin, doxorubicin, daunorubicin, mitomycin, mitoxantron, and saintopin. The inhibition of DNA topoisomerase is what causes quinones to be cytotoxic. 1,4-naphthoquinones are used as raw materials in the production of pharmaceuticals, agrochemicals, and other valuable compounds. As they contain two ketone groups, 1,4-naphthoquinones have a very high potential for receiving electrons. An essential subclass of the quinone family is naphthoquinones. Naphthoquinones have two carbonyl groups at the 1,4-positions and share a structural resemblance with naphthalene. They are referred to as 1,4-naphthoquinone for this reason. On the other hand, carbonyl groups can be located at 1,2-position, but they are much less abundant than in 1,4-naphthoquinones (Figure 1.2).

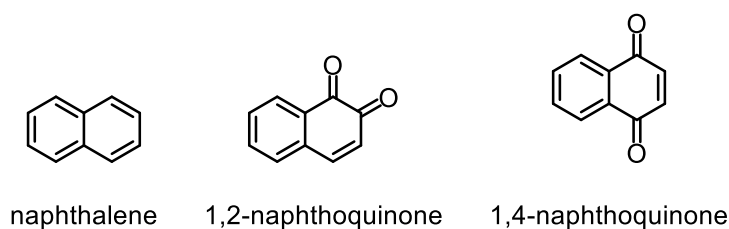


Figure 1.2. The chemical structure of naphthalene, 1,2- and 1,4- naphthoquinone.

Naphthoquinones are highly reactive organic compounds. These compounds are used as natural and synthetic dyes whose colours are in the yellow-red range. 1,4-naphthoquinones have intense colours due to conjugation between carbonyl groups and double bonds.

Since ancient times, naphthoquinones have been used as a dye. Henna is a dye prepared from grounding the leaves of *Lawsonia inermis* and has traditionally been used as a skin and hair colouring reagent for more than 5,000 years. Lawsone (2-hydroxy-1,4-naphthoquinone), one of the best-known naphthoquinones, is the main component of henna, which is responsible for colouring. In history, it has been used to colour wool and silk since ancient times (Figure 1. 3).

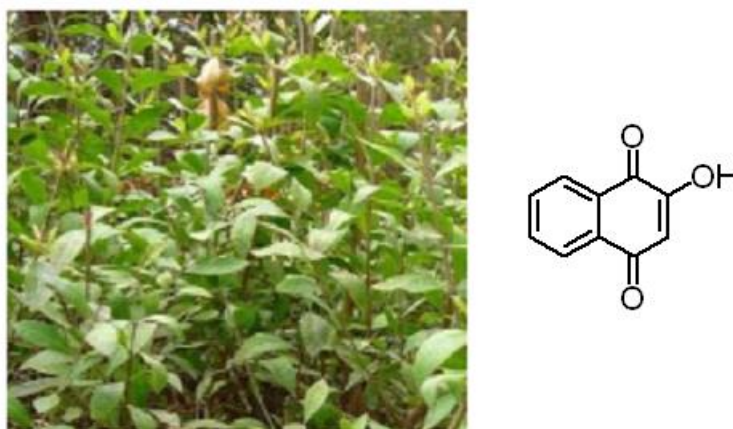


Figure 1.3. Henna plant and Lawsone (2-hydroxy-1,4-naphthoquinone) compound.

Lapachol (2-hydroxy-3-(3-methyl-2-butenyl)-1,4-naphthoquinone) and its cyclic derivatives (α - and β -lapachone) were isolated from tropical plants of the family Bignoniaceae. These are used in traditional Brazilian medicine. Juglone (5-hydroxy-1,4-naphthoquinone) was extracted from the nuts and leaves of several plants from the Juglandaceae family. 7-methyljuglone and its dimer diospyrin are active components of root extracts of *Euclea natalensis* and have antitubercular properties. 7-methyljuglone and its dimer diospyrin, structurally related to Juglone, are the main antitubercular components of *Euclea natalensis* root extracts (Figure 1.4).

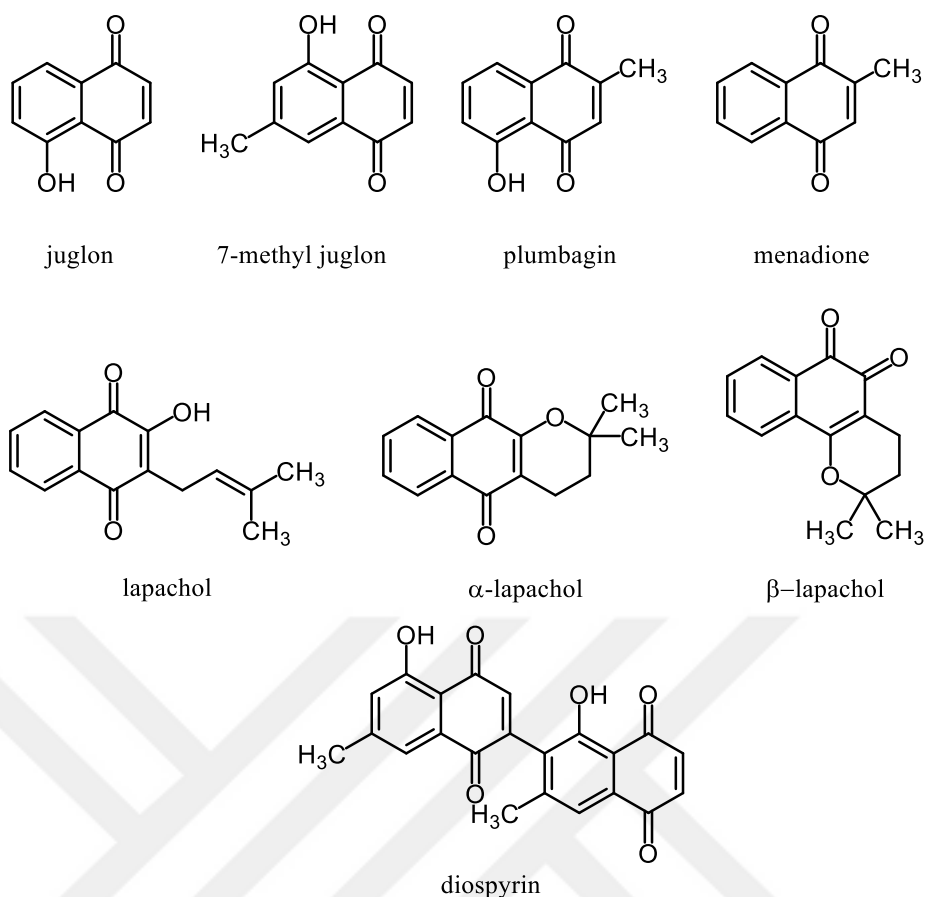


Figure 1.4. Naturally important naphthoquinones.

Due to their unique structural characteristics and biological properties, naphthoquinones hold a special place in medicinal chemistry. They play a key role in the electron transport chain by taking part in a variety of biological oxidative processes. Ease of reduction is a key feature of quinone chemistry, so it acts as an oxidizing or dehydrogenating agent. The basis of this redox property is the construction of a fully aromatic system. Plants that contain naphthoquinones are frequently used in folk medicine to treat a variety of illnesses. The anticancer activity of naphthoquinone derivatives isolated from traditionally used medicinal plants has been investigated [1].

Quinone compounds have an electrophilic and oxidative nature. The chemical core structure of quinones and their substituents have an impact on these characteristics. Moreover, the relative contribution of these features has a great effect on the toxic and therapeutic actions of these substances. Quinone and naphthoquinone derivatives, as aforementioned, are widely distributed in nature and possess various biological properties.



2. RESEARCH BACKGROUNDS

2.1. The Synthesis of 1,4-naphthoquinone and 2-hydroxy-1,4-naphthoquinone (Lawsone)

1,4-naphthoquinone is a crucial precursor used in the production of numerous industrially valuable products, including medicines, pigments, and dyes. Naphthalene can be oxidized to 1,4-naphthoquinone by chrome trioxide in acetic acid [2], and oxidation of 4-amino-1-naphthol by potassium dichromate yields the same product (Figure 2.1) [3].

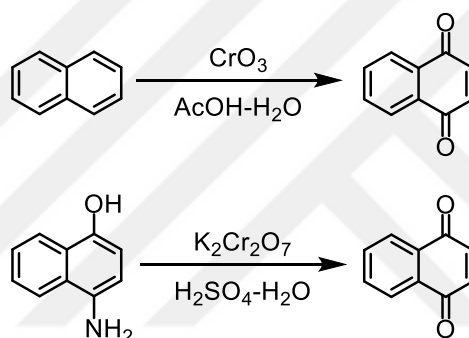


Figure 2.1. The synthesis of 1,4- naphthoquinone by oxidation of naphthalene.

Due to the significance of 1,4-naphthoquinone, a variety of methods, catalytic systems and oxidation reagents have been developed to oxidize naphthalene and related compounds to 1,4-naphthoquinone such as H_2O_2 -perfluorinated polymer with sulfonic acid supported on silica [4], Mn^{IV} bis(hydroxo) complex with acid [5], sodium ferrate- Pd(II)/Au(III) [6], ruthenium-based phase-transfer catalyst system [7], H_2O_2 -Ruthenium(2,2',6':2"-terpyridine)(2,6-pyridinedicarboxylate) system [8], iron (III) octakis (perfluorophenyl)tetraazaporphyrin μ -oxodimer complex[9], Iron complex of 5,10,15,20-tetrakis-pentafluoro phenylporphyrin [10]. Moreover, 1,4-naphthoquinone can be obtained by oxidation of naphthalene derivatives such as 1-naphthonitrile, 1-naphthoic acid, 1-naphthamide, and 1-naphthaldehyde using NBS in the DMF-water mixture at a mild temperature (Figure 2.2) [11]. It is also reported that it can be synthesized by the electrolysis of 3,0 M aqueous KBr solution in the presence of several naphthalene derivatives with Pt anode (Figure 2.3) [12].

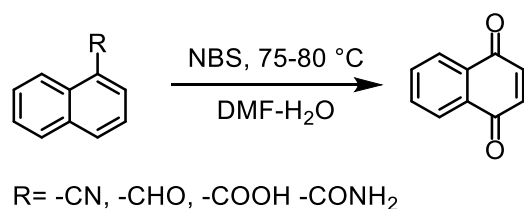


Figure 2.2. The synthesis of 1,4-naphthoquinones by oxidation with NBS.

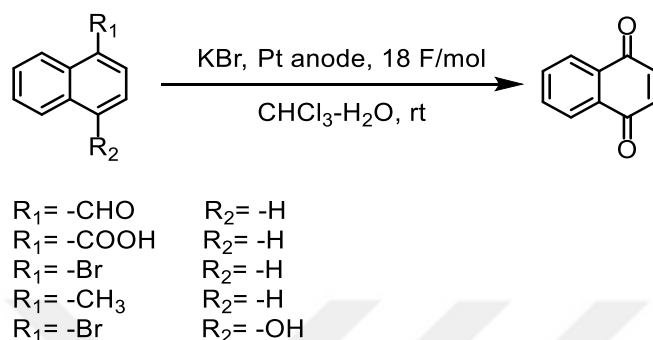


Figure 2.3. The synthesis of 1,4-naphthoquinone by electrochemical oxidation.

As mentioned in the previous section, 2-hydroxy-1,4-naphthoquinone, known as Lawsone or hennotannic acid, is present in the henna plant (*Lawsonia inermis*). The compound can be obtained from 1,4-naphthoquinone by Thiele-Winter reaction depicted in Figure 2.4. It involves acetylation of 1, 4-naphthoquinone into triacetoxy naphthalene in the presence of an H₂SO₄ catalyst, then it is hydrolyzed to the corresponding naphthalene-1,2,4-triol derivative with concentrated HCl. Finally, it is oxidized to the desired compound, namely 2-hydroxy- 1,4-naphthoquinone. The oxidation also proceeds with atmospheric oxygen [13,14].

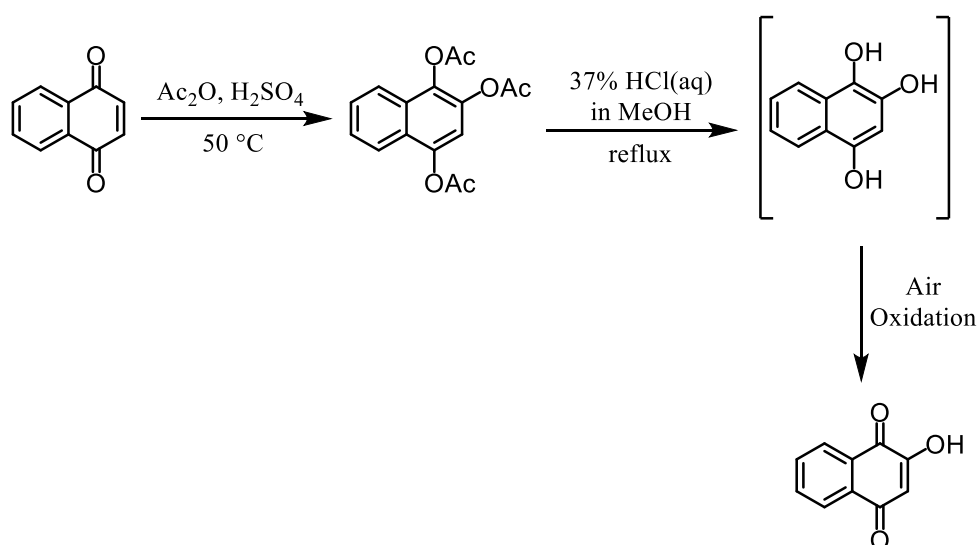


Figure 2.4. The synthesis of 2-hydroxy-1,4-naphthoquinone from 1,4-naphthoquinone

Another study reports the synthesis of 2-hydroxy-1,4-naphthoquinone starting from 2-naphthol. The method is outlined in Figure 2.5. Firstly, 2-methoxynaphthalene is obtained by methylation of 2-naphthol; then it was subsequently formylated to corresponding aldehyde by Vilsmeier-Haack formylation with DMF-POCl₃. Oxidation of aldehyde using NBS in aqueous DMF is carried out to get 2-methoxy-1,4-naphthoquinone. Finally, it is demethylated by AlCl₃ to the final compound [15].

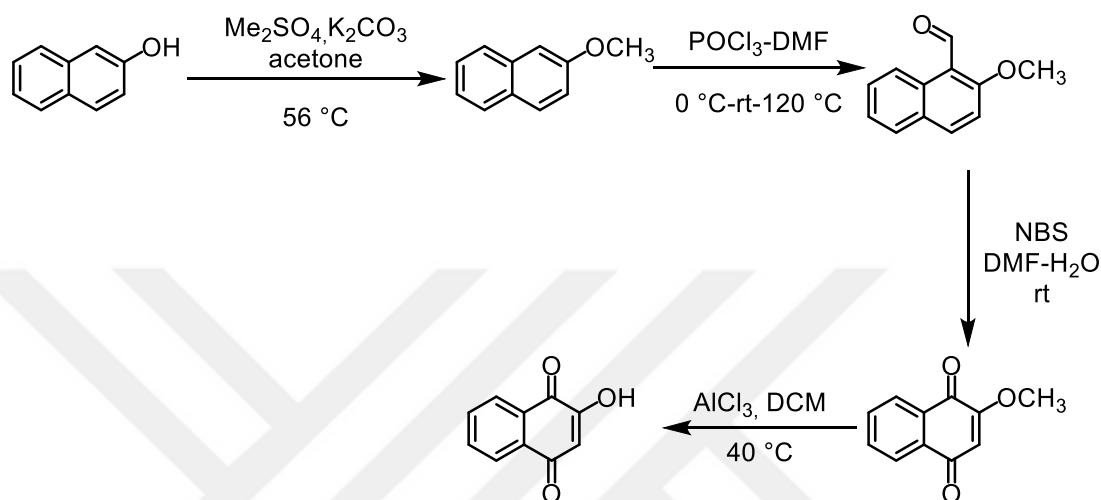


Figure 2.5. The synthesis of 2-hydroxy-1,4-naphthoquinone from 2-naphthol.

Moreover, 2-hydroxy-1,4-naphthoquinone can be obtained from the oxidation of tetralone in the presence of potassium *tert*-butoxide in *tert*-butanol with oxygen (Figure 2.6) [16,17].

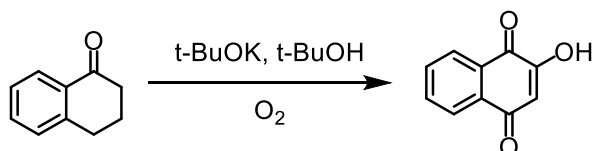


Figure 2.6. Oxidation of tetralone to 2-hydroxy-1,4-naphthoquinone.

The synthesis of 2-hydroxy-1,4-naphthoquinone was efficiently carried out by the transformation of ammonium-1,2-naphthoquinone-4-sulfonate in concentrated sulphuric acid into 2-methoxy-1,4-naphthoquinone, followed by demethoxylation with aqueous NaOH (Figure 2.7) [18].

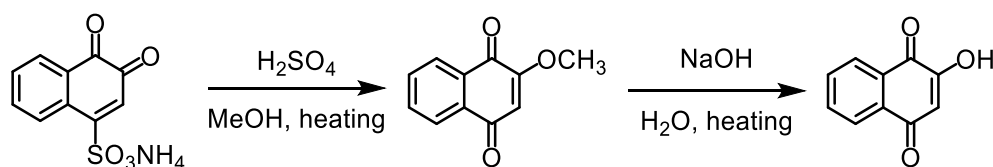


Figure 2.7. Transformation of ammonium 1,2-naphthoquinone-4-sulfonate.

2.2. The Synthesis of Halogenated 1,4- naphthoquinone Derivatives

Halogenated compounds have a special place in synthetic organic chemistry as these compounds are modified to obtain important compounds by various smart synthetic methodologies such as substitution reactions and metal-catalyzed coupling reactions. Because of the significance of the naphthoquinone core in a variety of areas, new derivatives of the naphthoquinones are derivatized utilizing the halogenated 1,4-naphthoquinones.

2,3-dichloro-1,4-naphthoquinone, dichlone, is a very important starting compound to achieve a wide variety of 1,4-naphthoquinone with different functionalities. It was reported that dichlone was obtained from chlorination of 1,4-naphthoquinone with potassium perchlorate in the presence of hydrochloric acid (Figure 2.8) [19].

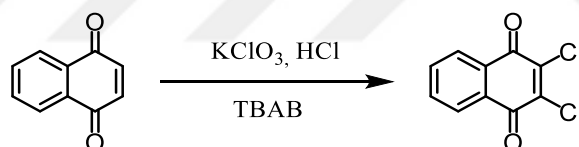


Figure 2.8. The synthesis of dichlone.

2-chloro-1,4-naphthoquinone was attained from the reaction of Lawsone with SOCl_2 [20, 21] and it was also obtained from chlorination of 1,4-naphthoquinone with NCS in the presence of CuCl_2 (Figure 2.9.) [22].

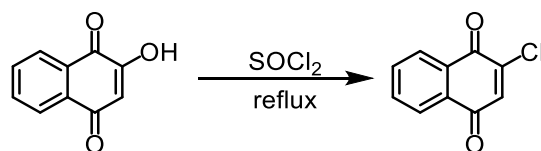


Figure 2.9. The synthesis of 2-chloro-1,4-naphthoquinone.

2-bromo-1,4-naphthoquinone was synthesized, as in chlorination, from bromination with NBS in the presence of CuBr_2 (Figure 2.10) [22]. It was also obtained from bromination with bromine in chloroform at 0°C later, refluxing in EtOH (Figure 2.11)

[23]. Another way to get 2-bromo-1,4-naphthoquinone was the reaction of 1-naphthol with NBS in an acetic acid-water mixture at a mild temperature (Figure 2.12) [24, 25].

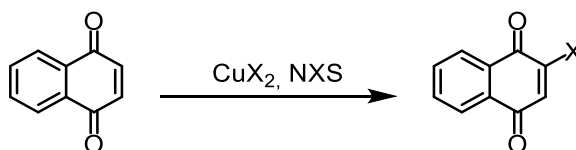


Figure 2.10. The Synthesis of 1,4-naphthoquinone with bromo and chloro atom at 2 position.

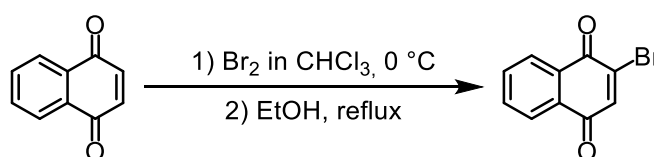


Figure 2.11. The synthesis of 2-bromo-1,4-naphthoquinone by molecular bromine.

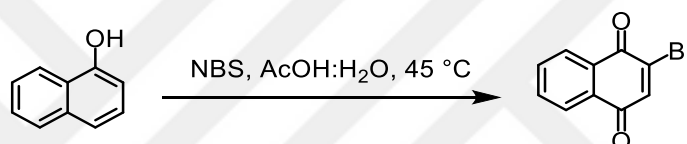


Figure 2.12. The synthesis of 2-bromo-1,4-naphthoquinone from 1-naphthol.

2,3-dibromo-1,4-naphthoquinone is another important molecule with similar reactivity to dichlone. It was synthesized from the bromination of 1,4-naphthoquinone in acetic acid at $110\text{ }^\circ\text{C}$ (Figure 2.13) [26, 27].

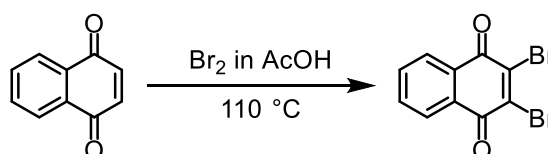


Figure 2.13. The synthesis of 2,3-dibromo-1,4-naphthoquinone by molecular bromine

Another study demonstrated that dichlone was converted to 2,3-diiodo-1,4-naphthoquinone by sodium iodide in a 1,4-dioxane-DMF mixture (Figure 2.14) [28].

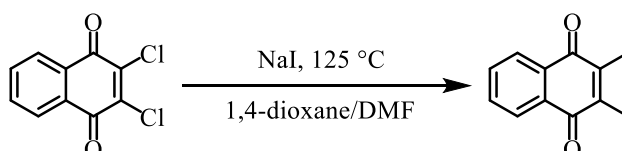


Figure 2.14. The synthesis of 2,3-diiodo-1,4-naphthoquinone

2.3. Synthetical Approaches to Obtain New 1,4-naphthoquinone Derivatives

Naphthoquinones are regarded as privileged structures in medicinal chemistry owing to their biological activity and structural characteristics. Plants that contain naphthoquinones are frequently used in folk medicine to cure various diseases. Several quinonoids obtained from traditional medicinal plants are being investigated for their anticancer properties [29]. Inspired by nature, 1,4-naphthoquinones are modified by numerous synthetic methods to attain new molecules with promising medicinal properties. The structure of naphthoquinone can easily be functionalized from the quinone ring, starting from bare naphthoquinone or naphthoquinones with halogen, amino, and hydroxy groups. The addition of functional groups on the benzene ring of the structure is more complicated than the quinone moiety.

2.3.1. Nucleophilic addition to Lawsone, 1,4-naphthoquinone and its Halogenated derivatives

Due to the electrophilic nature of quinone derivatives, they are prone to nucleophilic attack by electron-rich nucleophiles such as amino ($R-NH_2$), hydroxyl ($R-OH$), and thiol ($R-SH$) groups, as in Michael addition [30]. The Michael addition, named after Arthur Michael, is a versatile reaction occurring between nucleophiles and activated alkenes and alkynes in which the nucleophile is added to a carbon-carbon multiple bond. The extent of this reaction has considerably expanded over time to encompass a variety of acceptors and non-carbon donors [31]. Moreover, the Micheal-type reaction of quinone derivatives has a significant role in their biological activity. They interact with cellular nucleophiles like GSH, DNA, RNA, and proteins, leading to depletion in the cell [32, 33].

The asymmetric Michael addition of nitroalkenes to the compounds having enol part is an important way of C-C bond forming reaction. The addition of nitroalkenes as Michael acceptor to 2-hydroxy-1,4-naphthoquinones is particularly attractive as it provides 1,4-naphthoquinones with nitroalkyl group which are very useful precursors to get a variety of compounds with potential biological properties. Therefore, recent studies were focused on the synthesis of nitroalkyl group bearing 1,4-naphthoquinones with enantiopure by using various organocatalysts such as thiourea with the sugar-cinchona conjugate [34], thiourea with CF_3 group and trans *N,N*-dimethyl-1,2-diaminocyclohexane group [35], BINOL-quinine-squaramides [36], thiourea with

hydrophobic anchor and chiral moiety [37], binaphthyl-modified chiral bifunctional organocatalysts (Figure 2.6) [38].

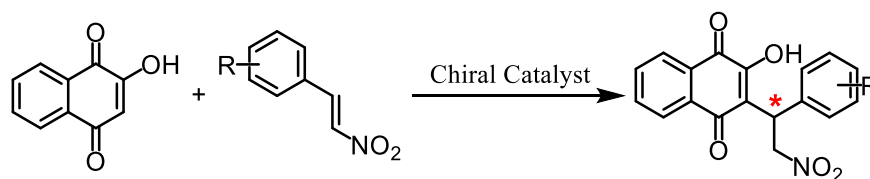


Figure 2.15. The asymmetric nucleophilic addition of nitrostyrene derivatives to Lawsone.

In the search for a new anticancer drug, 2-((4-hydroxyphenyl)amino)naphthalene-1,4-dione was synthesized by nucleophilic substitution reaction, and the key compound was further functionalized from the hydroxy group to obtain the compounds with anticancer activity against MCF-7, HL-60, and U937 cell lines (Figure 2.16) [39].

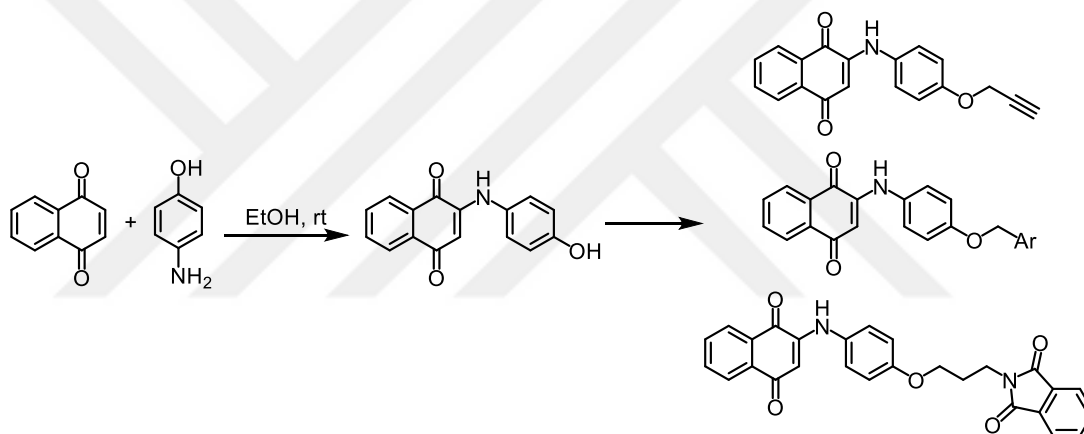


Figure 2.16. The nucleophilic substitution reaction of 1,4-naphthoquinone with 4-aminophenol.

It was reported that the synthesis of 2-hydroxyethylamino-1,4-naphthoquinone by the nucleophilic reaction between 1,4-naphthoquinone with ethanolamine in acetonitrile at room temperature, then the compound was converted to azido group bearing 1,4-naphthoquinone derivative which was modified with various alkyne derivatives by click reaction. The products were evaluated for their anti-malarial activity (Figure 2.17) [40, 41].

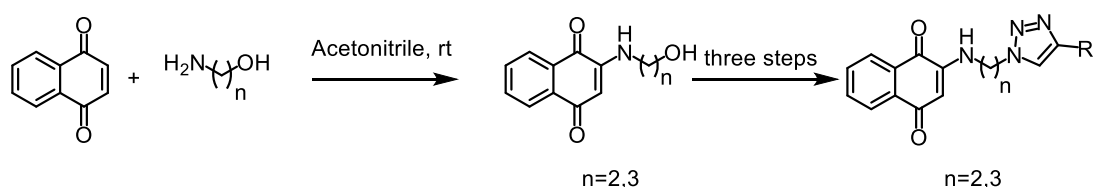


Figure 2.17. The nucleophilic substitution reaction of 1,4-naphthoquinone with 2-ethanolamine its functionalization with triazole ring.

Amination of naphthoquinone was carried out with several aniline derivatives, 2-aminopyridine, aromatic, and aliphatic amines, by *t*-BuOK as a base to access biologically and synthetically important derivatives. Moreover, several 3-indolynaphthoquinones were also aminated via the same methodology (Figure 2.18) [42].

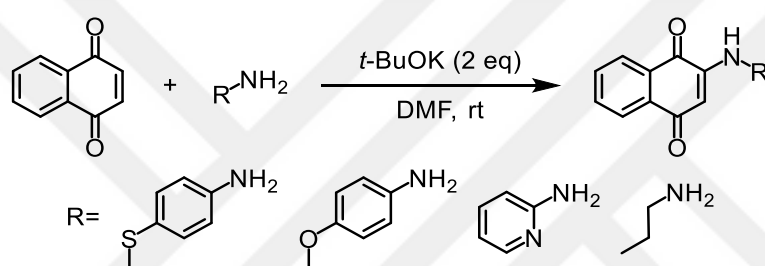


Figure 2.18. The amination of 1,4-naphthoquinone with several amine derivatives.

1,4-naphthoquinone was reacted with alkylamines in dichloromethane at room temperature. The final products were characterized by spectroscopic techniques (Figure 2.19) [43].

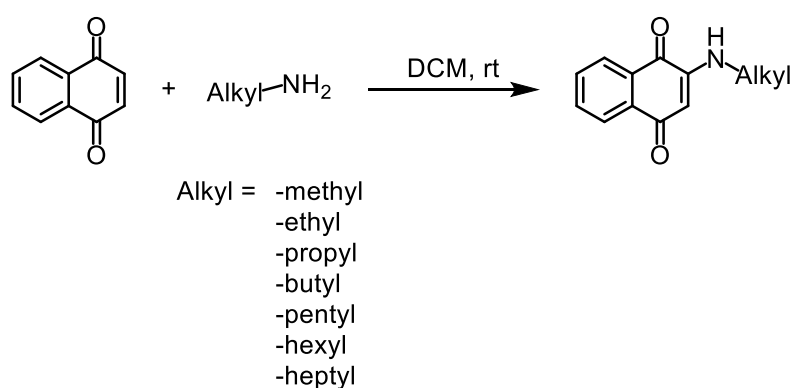


Figure 2.19. The amination of 1,4-naphthoquinone with several alkyl amines.

1,4-naphthoquinones and various anilines with electron-donating and accepting groups were coupled in various solvents by blue light irradiation without any additional reagents (Figure 2.20) [44].

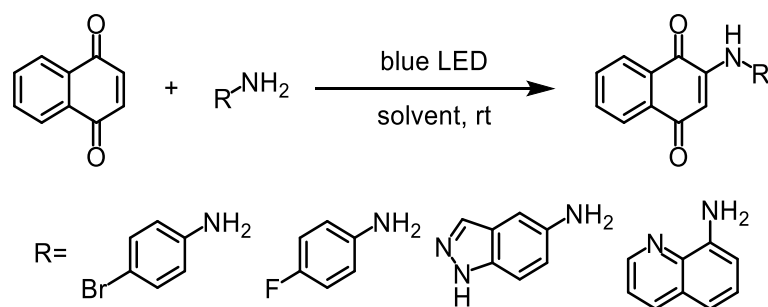


Figure 2.20. The amination reaction of 1,4-naphthoquinone with aromatic amines by blue light.

1,4-naphthoquinones with electron withdrawing group bearing aniline derivatives generally give low yield or no product. Therefore, several catalysts, such as cerium (III) chloride [45,46], iron (III) chloride [45], copper (II) acetate [47], and gold [48] were employed to overcome these problems. Moreover, the reactions were carried out with bentonite clay as a catalyst and ultrasonic treatment. The preparation of 2-amino-1,4-naphthoquinones was reported in the water medium by following the green chemistry rules [49]. Furthermore, it was also reported that 2-aminonaphthoquinones can be obtained by the reaction between nitro group bearing compounds and 1,4-naphthoquinone in the presence of reducing reagent such as zinc (Figure 2.21) [50].

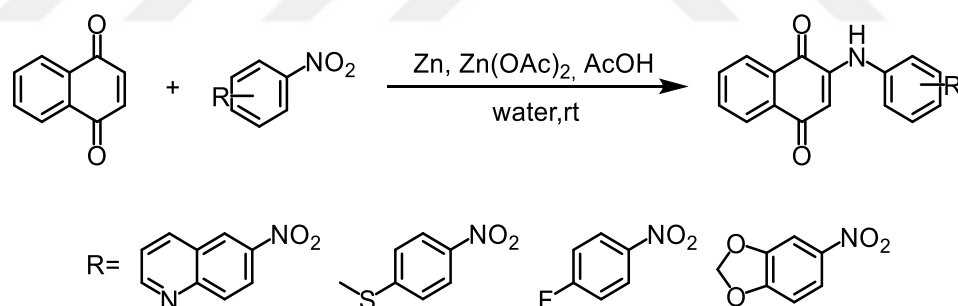


Figure 2.21. The amination reaction of 1,4-naphthoquinone with aromatic nitro compounds by zinc-mediated reduction reaction

Several studies reported the synthesis of 1,4-naphthoquinone with the amino acid moiety (

Figure 2.22) [50, 51]. In another study, 1,4 naphthoquinone-bearing amino acid group was synthesized, and they were further decorated with boronic acid and boronic acid ester groups for their proteasome activity (Figure 2.23) [52].

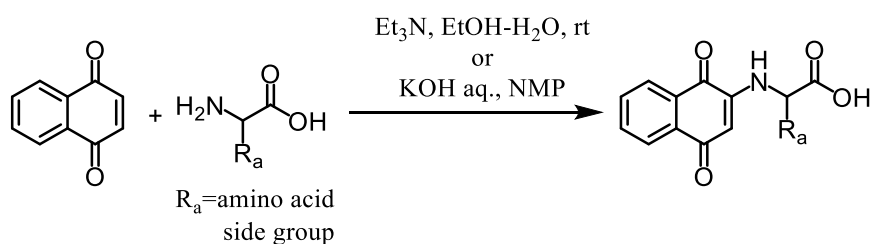


Figure 2.22. The synthesis of amino acid bearing 1,4-naphthoquinone.

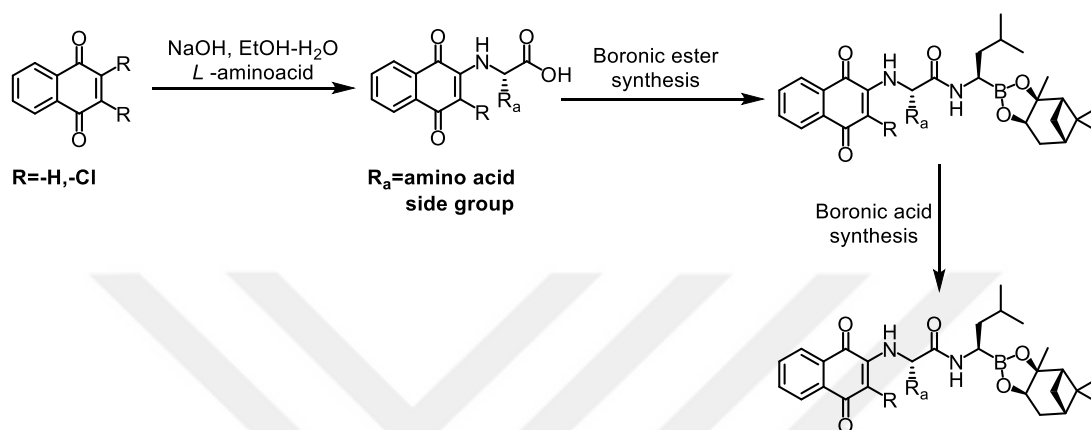


Figure 2.23. The synthesis of 1,4-naphthoquinones with amino acid and its modification with boronic ester and acid group.

2,3-dichloro-1,4-naphthoquinone was reacted with substituted anilines in EtOH with the presence of CeCl_3 to obtain 2-chloro-3-(substituted phenylamino)naphthalene-1,4-diones. As the products were refluxed with sodium azide in DMF, it yielded whether 2-amino-3-(substituted phenylamino)naphthalene-1,4-diones or phenazine by a thermolysis reaction, the latter one was obtained if the R was an electron-donating group (Figure 2.24) [52, 53].

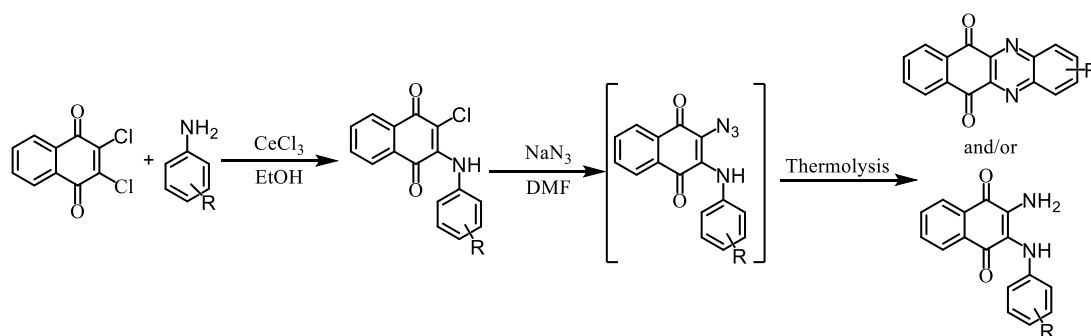


Figure 2.24. The nucleophilic substitution reaction and the formation of 2-amino-3-(substituted phenylamino)naphthalene-1,4-diones or phenazine derivatives.

2-chloro-3-[(thiazol-2-yl)amino]-1,4-naphthoquinones were prepared from the nucleophilic reaction of 2-aminothiazole precursors with 2,3-dichloro-1,4-naphthoquinone (Figure 2.25) [54].

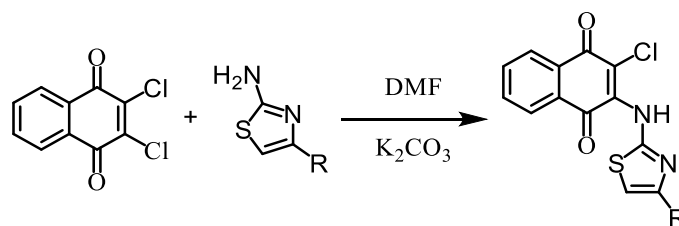


Figure 2.25. The synthesis of 2-chloro-3-[(thiazol-2-yl)amino]-1,4-naphthoquinones.

A study reported a method to obtain selenoaniline decorated 1,4-naphthoquinone. The method comprised a nucleophilic substitution reaction of 4-aminobenzeneselenolate anion formed *in situ* from 4-(2-(4-aminophenyl)diselanyl)benzenamin with 2,3-dibrom-1,4-naphthoquinone in EtOH (Figure 2.26) [55].

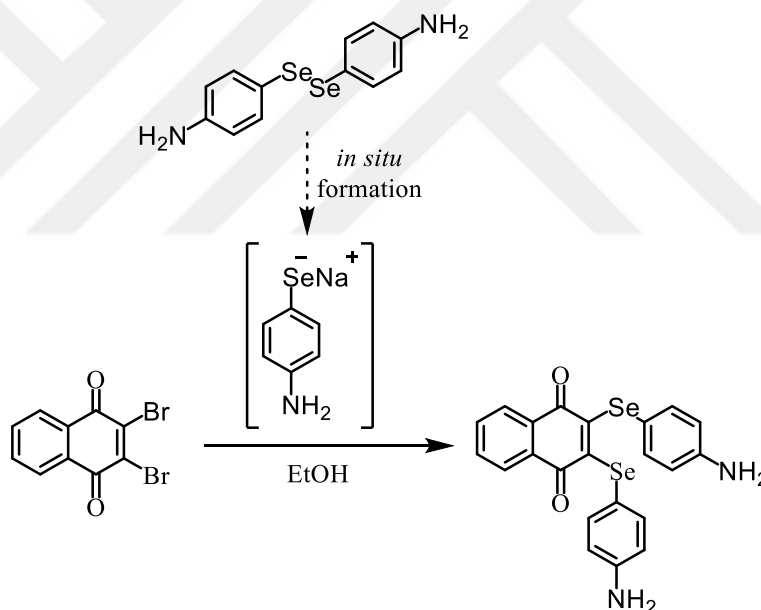


Figure 2.26. The nucleophilic substitution reaction of 4-aminobenzeneselenolate anion with 2,3-dibromo-1,4-naphthoquinone

The nucleophilic substitution reaction of phenols and alcohols with 2,3-dichloro-1,4-naphthoquinone in the presence of a base such as NEt_3 or K_2CO_3 at room temperature yielded aryl or alkoxy-1,4-naphthoquinones [56]. The reaction was also carried out in green conditions, such as in water media with surfactant (Figure 2.27) [57, 58].

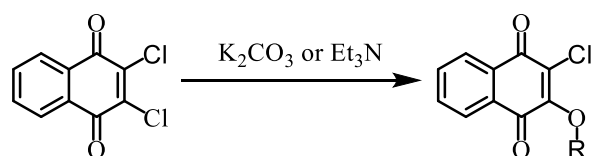


Figure 2.27. The nucleophilic substitution reaction of phenols and alcohols with 2,3-dichloro-1,4-naphthoquinone.

thiol or thiophenol substituted 1,4-naphthoquinone derivatives are obtained by the nucleophilic substitution reaction of thiols and thiophenols with 2,3-dichloro-1,4-naphthoquinone in the presence of a base such as NEt_3 or K_2CO_3 (Figure 2.28) [59-61].

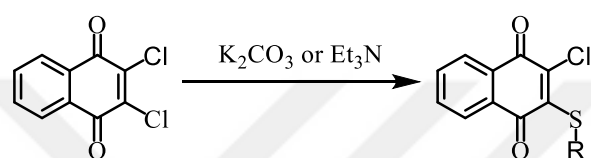


Figure 2.28. The nucleophilic substitution reaction of thiols and thiophenols with 2,3-dichloro-1,4-naphthoquinone.

2.3.2. The synthesis of various 2-hydroxy 1,4-naphthoquinone derivatives

Halogenation reaction is a versatile tool to attain intermediate molecules being able to transform into numerous molecules with various interests by metal-catalyzed cross-coupling reactions [62, 63]. 2-hydroxy 1,4-naphthoquinone was iodinated using iodine-morpholine complex[64] and NH_4I /Oxone[®] [65] that resulted in the formation of 2-hydroxy-3-iodonaphthalene-1,4-dione (

Figure 2.29. The synthesis of 2-hydroxy-3-iodonaphthalene-1,4-dione.

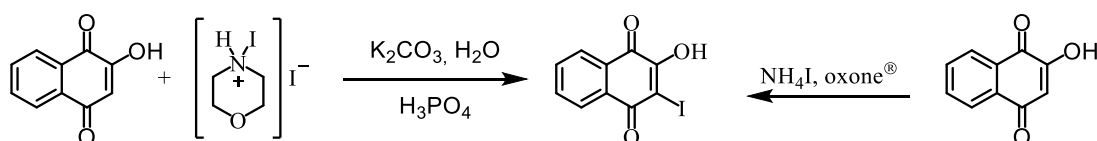


Figure 2.29. The synthesis of 2-hydroxy-3-iodonaphthalene-1,4-dione.

When Lawsone was brominated in acetonitrile, 2-hydroxy-3-bromonaphthalene-1,4-dione was produced (Figure 2.30) [64]. Moreover, the treatment of 2,3-dibromo or 2,3-dichloro-1,4-naphthoquinone with KOH led to 2-hydroxy-3-bromo or chloronaphthalene-1,4-dione compounds, respectively (Figure 2.31) [66, 67].

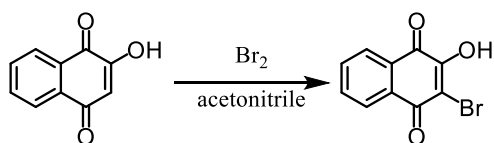


Figure 2.30. The bromination of 1,4-naphthoquinone.

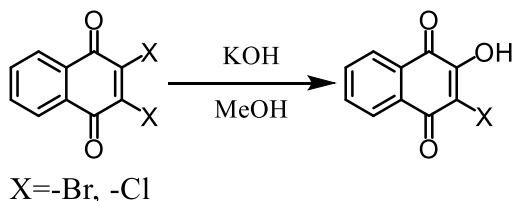


Figure 2.31. Synthesis of 2-hydroxy-1,4-naphthoquinone with chlor or brom atom at 3-position.

Suzuki Miyaura or Heck cross-coupling reaction of 2-hydroxy 3-bromo or iodo 1,4 naphthoquinone produced aryl or alkene group bearing Lawsone derivatives (Figure 2.32) [68-70].

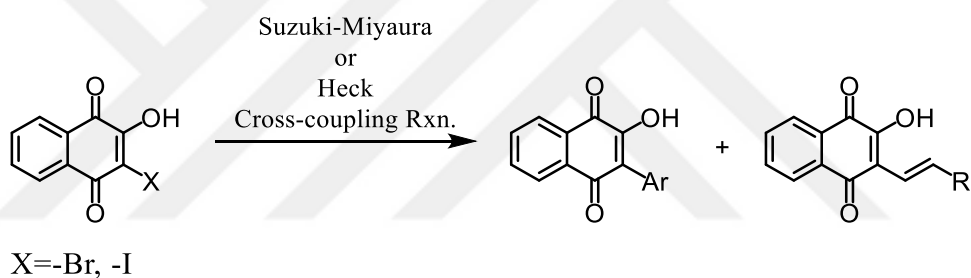


Figure 2.32. The modification of Lawsone by the cross-coupling reaction.

The synthesis of various 2-hydroxy 1,4-naphthoquinone derivatives was carried out through palladium-catalyzed hydroxy-involved enolate type C-C bond formation (Figure 2.33) [71].

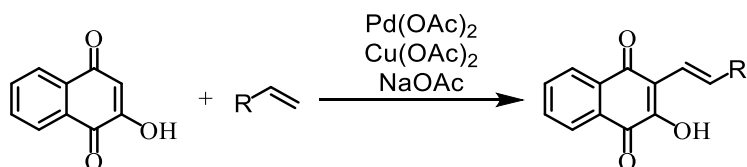


Figure 2.33. Palladium-catalyzed C-C bond formation of 1,4-naphthoquinone.

2-hydroxy-1,4-naphthoquinone, triorthoformate, and (hetero)aromatic amine derivatives led to the formation of Lawsone-enaminone compound in the presence of guanidium chloride without solvent (Figure 2.34) [72,73].

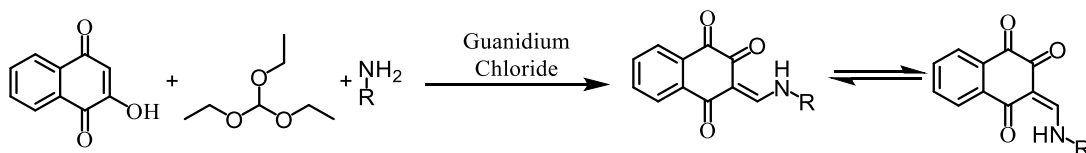


Figure 2.34. The formation of Lawsone-enaminone compounds.

2-hydroxy-1,4-naphthoquinone derivatives with aryl amine moiety were synthesized by a two-step process. In the first step, 1,4-naphthoquinone was reacted with hydrogen peroxide in the presence of Na_2CO_3 , which yielded an epoxy naphthoquinone, namely, 1*a*,7*a*-dihydronaphtho[2,3-*b*]oxirene-2,7-dione. Then, it was subjected to ring opening reaction by aniline or amine derivatives with ZnCl_2 catalyst producing the arylamine unite bearing 1,4-naphthoquinone (Figure 2.35) [74,75].

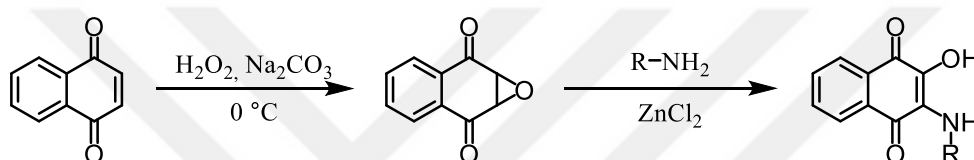


Figure 2.35. The epoxidation of 1,4-naphthoquinone and its ring opening reaction with amin derivatives.

The treatment of 2-hydroxy-1,4-naphthoquinone with allyl bromide, which is rearranged to 2-allyl-3-hydroxynaphthalene-1,4-dione by Claisen rearrangement reaction (Figure 2.36) [76-78].

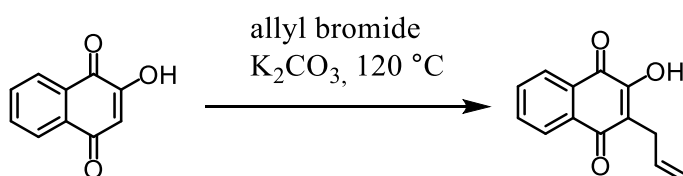


Figure 2.36. The synthesis of 2-allyl-3-hydroxynaphthalene-1,4-dione by Claisen rearrangement reaction.

2-hydroxy-1,4-naphthoquinone was coupled with aryldiazonium chlorides by diazotization reaction forming azo-appended Lawsone dyes (Figure 2.37) [79-82]

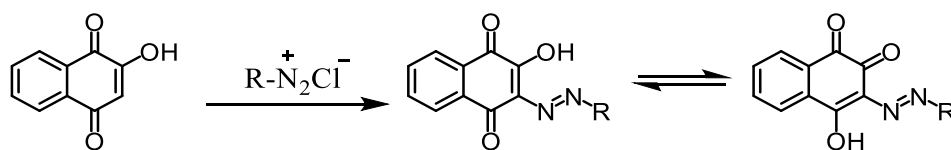


Figure 2.37. Diazotization reaction of 2-hydroxy-1,4-naphthoquinone.

2.3.3. The synthesis of 1,4-naphthoquinones with heterocyclic ring

1,4-pyranonaphthoquinones were synthesized from Lawsone and α,β -unsaturated aldehyde. The reaction was carried out in the presence of the chiral catalysts, namely diaryl prolinol ether derivatives, so the product had highly enantiomeric purity. It was reported that the reaction mechanism proceeded via the formation of an intermediate iminium ion from the catalyst and aldehyde. The resultant intermediate was added to 2-hydroxy-1,4-naphthoquinone with 1,4 addition reaction (Figure 2.38) [83].

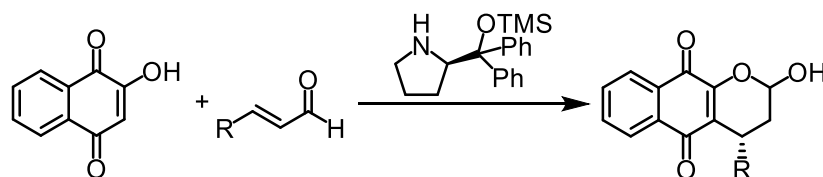


Figure 2.38. The synthesis of enantiomerically pure 1,4-pyranonaphthoquinones.

Dehydro- α -lapachone, a pyran ring bearing 1,4-naphthoquinone derivative, was synthesized from a cyclization reaction between 2-hydroxy-1,4-naphthoquinone and 3-methyl-2-butenal. The reaction was carried out by several routes, such as ethylenediamine diacetate in methanol [84], in aqueous media without catalyst [85], with microwave-irradiation [86], with triethylamine in benzene [87] (Figure 2.39).

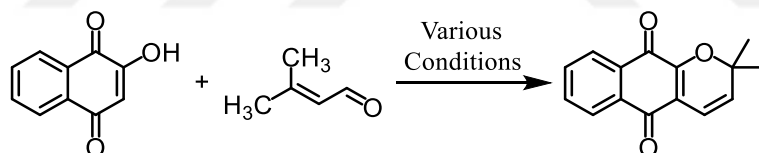


Figure 2.39. The synthesis of dehydro- α -lapachone.

Naphthoquinone fused furan derivatives, naphtho[2,3-*b*]furan-4,9-dione, were synthesized from Pd catalyzed the reaction of 2-hydroxy-1,4-naphthoquinones with chalcone derivatives [16] or NIS induced reaction [88] (Figure 2.40).

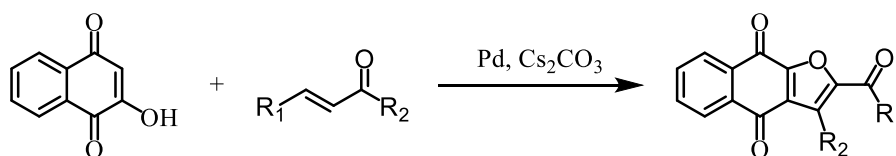


Figure 2.40. The synthesis of 1,4-naphthoquinone fused furan derivatives.

The reaction of 2-hydroxy-1,4-naphthoquinone, benzaldehyde, and 1-(2-oxo-2-phenylethyl)pyridinium bromide derivatives in the presence of ammonium acetate yielded 1,4-naphthoquinone fused furan structures similar to Figure 2.41. The reaction

was carried out in water media by conventional heating and microwave irradiation [89].

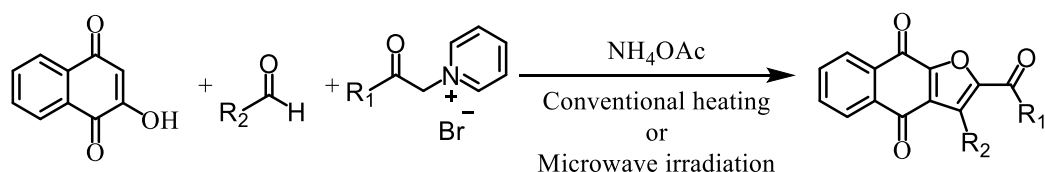


Figure 2.41. The synthesis of 1,4-naphthoquinone fused furan structures.

The similar compounds, naphtho[2,3-*b*]furan-4,9-dione derivatives, were obtained from α -bromonitroalkenes and 2-hydroxynaphthalene-1,4-dione using NaOAc and TBAB under aqueous conditions (Figure 2.42) [90, 91].

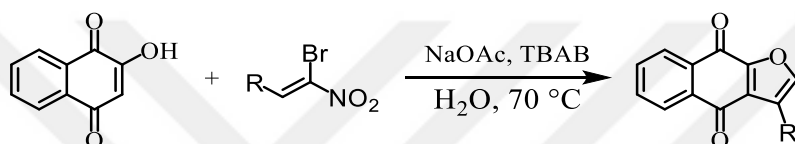


Figure 2.42. The synthesis of naphtho[2,3-*b*]furan-4,9-dione derivatives.

The synthesis of 3-substituted 2-aminonaphtho[2,3-*b*]furan-4,9-dione compounds was carried out in water [92] and deep eutectic solvent prepared from sorbitol and metformin.HCl (Figure 2.43) [93].

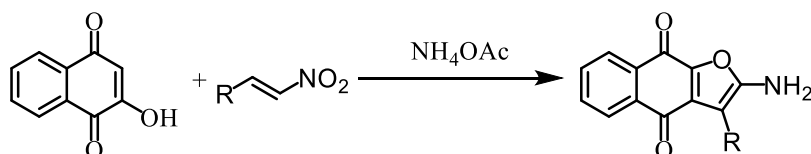


Figure 2.43. Synthesis of 3-substituted 2-aminonaphtho[2,3-*b*]furan-4,9-dione derivatives.

In another study, 2-hydroxy-1,4-naphthoquinone derivatives were fused with alkyne derivatives to form substituted furano1,4-naphthoquinones by blue light irradiation and CAN (Figure 2.44) [94]. Moreover, Similar oxidative cyclization reactions were conducted between alkene derivatives and 2-hydroxy-1,4-naphthoquinones forming 2,3-dihydronaphtho[2,3-*b*]furan-4,9-dione derivatives (Figure 2.45) [95, 96].

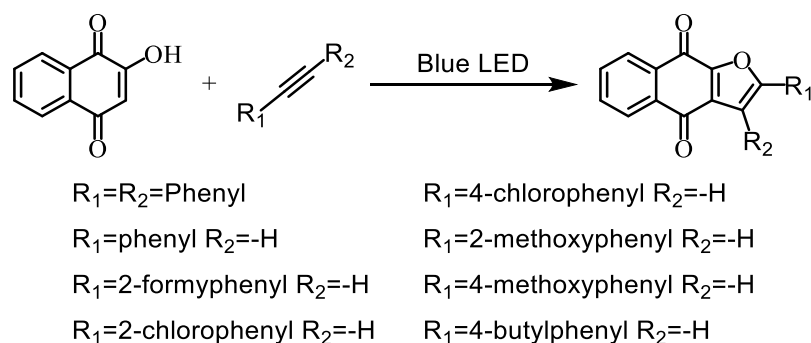


Figure 2.44. The synthesis of furano-1,4-naphthoquinones.

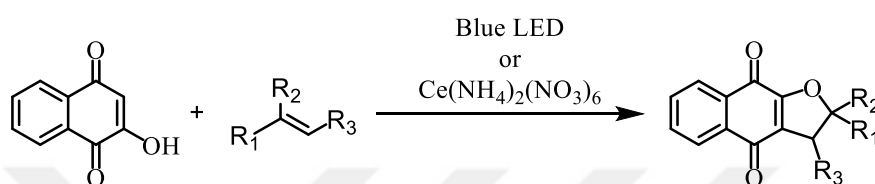


Figure 2.45. The synthesis of 2,3-dihydronaphtho[2,3-*b*]furan-4,9-dione derivatives.

2.3.4. The Mannich reaction of 2-hydroxy-1,4-naphthoquinone

Mannich reaction, also known as aminoalkylation, is one of the most important carbon-carbon bond-forming reactions in organic chemistry; the atom economy is the main advantage of the reaction to create biologically useful drug candidates. Three components, namely varied substrates with acidic hydrogen, an aldehyde derivative, and an amine group, combine to form a single molecule called Mannich bases. The reaction takes place in two steps. The first step is the formation of a Schiff base in which an amine group is added to a carbonyl group, followed by dehydration. In the next step, the Schiff base product is reacted with nucleophiles like enol or enone. Figure 2.46 represents Mannich reaction [97].

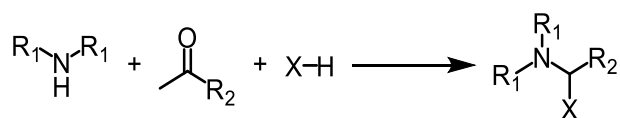


Figure 2.46. Representative Mannich reaction.

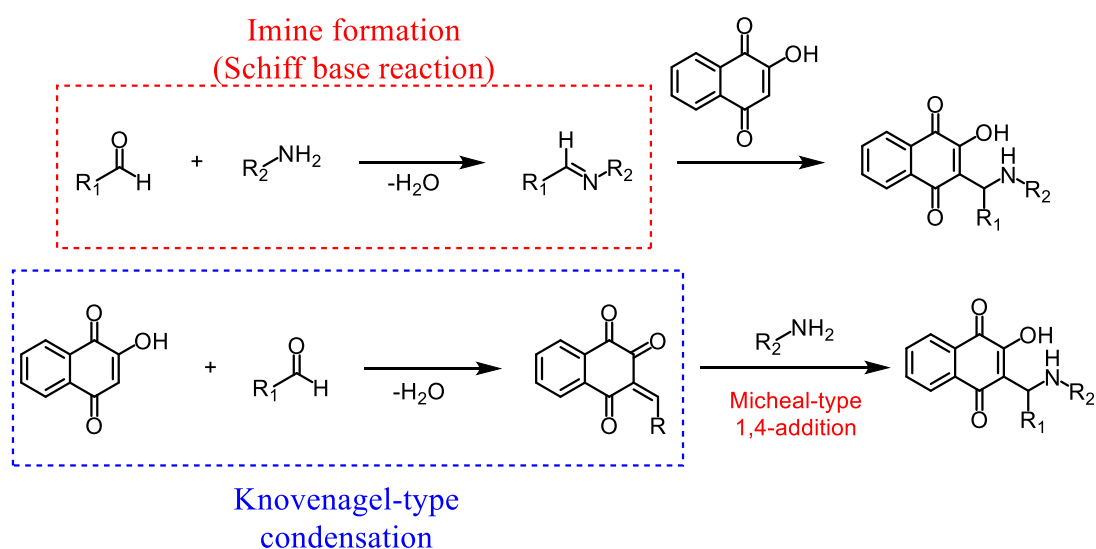


Figure 2.47. The proposed reaction mechanisms of Mannich base formation.

Mannich bases formed from 2-hydroxy-1,4-naphthoquinone and their metal complexes are of interesting biological activities like anticancer, antifungal, anti-parasitic, leishmanicidal, choline esterase inhibitors, antiviral, antibacterial, anti molluscicidal activities. Due to their widespread applications, new methods have been investigated to synthesize unique aminonaphthoquinone derivatives and metal complexes [98]. Two reaction mechanisms are proposed for the synthesis of Mannich bases derived from 2-hydroxy-1,4-naphthoquinone, as shown in Figure 2.47. The first mechanism is the nucleophilic attack of 2-hydroxy-1,4-naphthoquinone to imine formed by the reaction of amine and aldehyde. The second mechanism is 1,4 Micheal addition to α,β conjugated carbonyl species formed by Knoevenagel-type condensation between an aldehyde and 2-hydroxy-1,4-naphthoquinone. While the first mechanism occurs in transformations without catalysts, the second one probably requires some kind of catalyst [99].

Mannich reaction of 2-hydroxy-1,4-naphthoquinone was first studied in 1948 (Figure 2.48). The reaction in alcoholic solution at room or mild temperatures was carried out to screen the biological activities of Mannich bases [100].

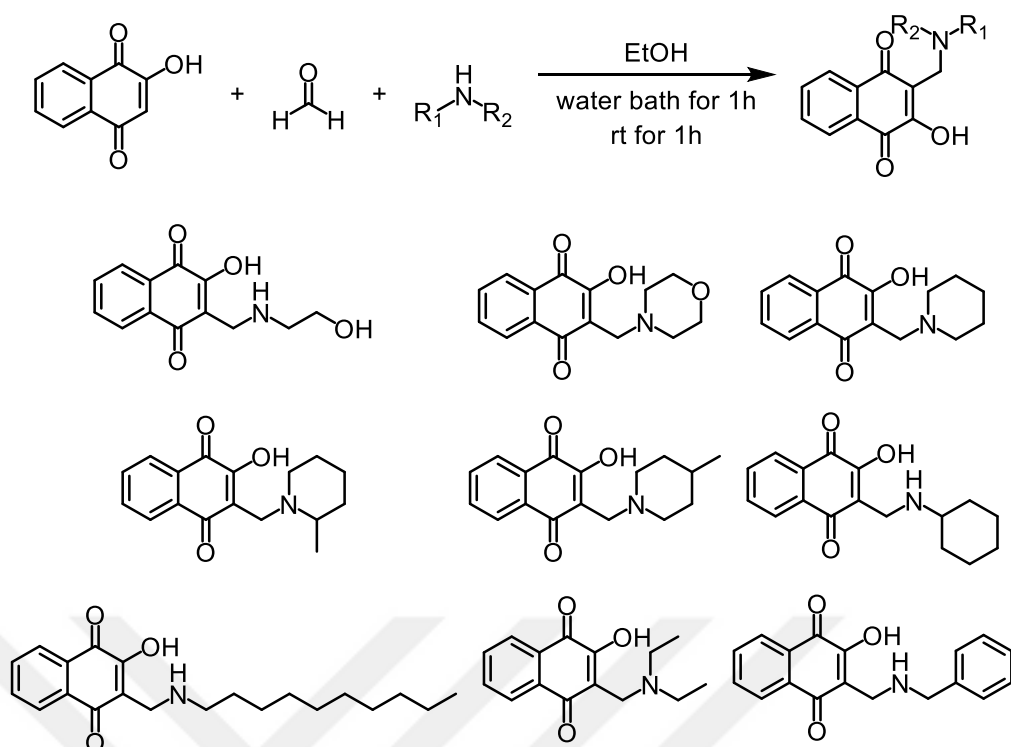


Figure 2.48. The Mannich reaction and selected examples by Leffler and Hathaway.

It is reported that the Mannich bases derived from Lawsone, aromatic aldehydes, and several amine compounds like aliphatic or (hetero)aromatic amines and their copper complexes were synthesized for their microbial activity evaluation (Figure 2.49) [101].

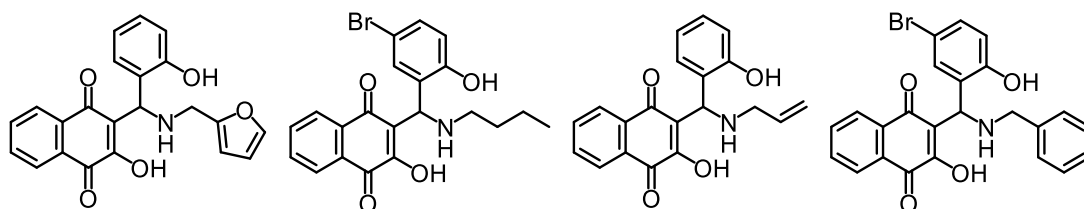


Figure 2.49. Mannich bases reported in reference [101].

A series of Mannich bases derived from 2-aminopyridine/butylamine and alkyl/aryl aldehydes were evaluated for their antibacterial activity against *Mycobacterium tuberculosis*. The compounds given in Figure 2.50 showed the highest activity [102].

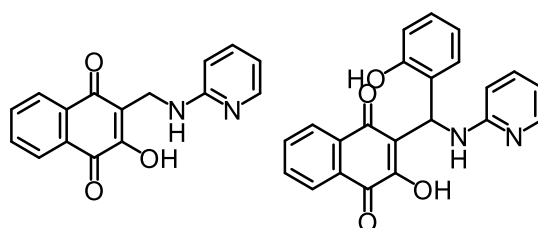


Figure 2.50. Mannich bases reported in [102].

Several Mannich bases were synthesized in ethanol at room temperature. It was found that the compounds had anti-cancer activity and anti-trypanosomal activities against parasitic *Trypanosoma brucei* cells with sub-micromolar levels Figure 2.51 [102].

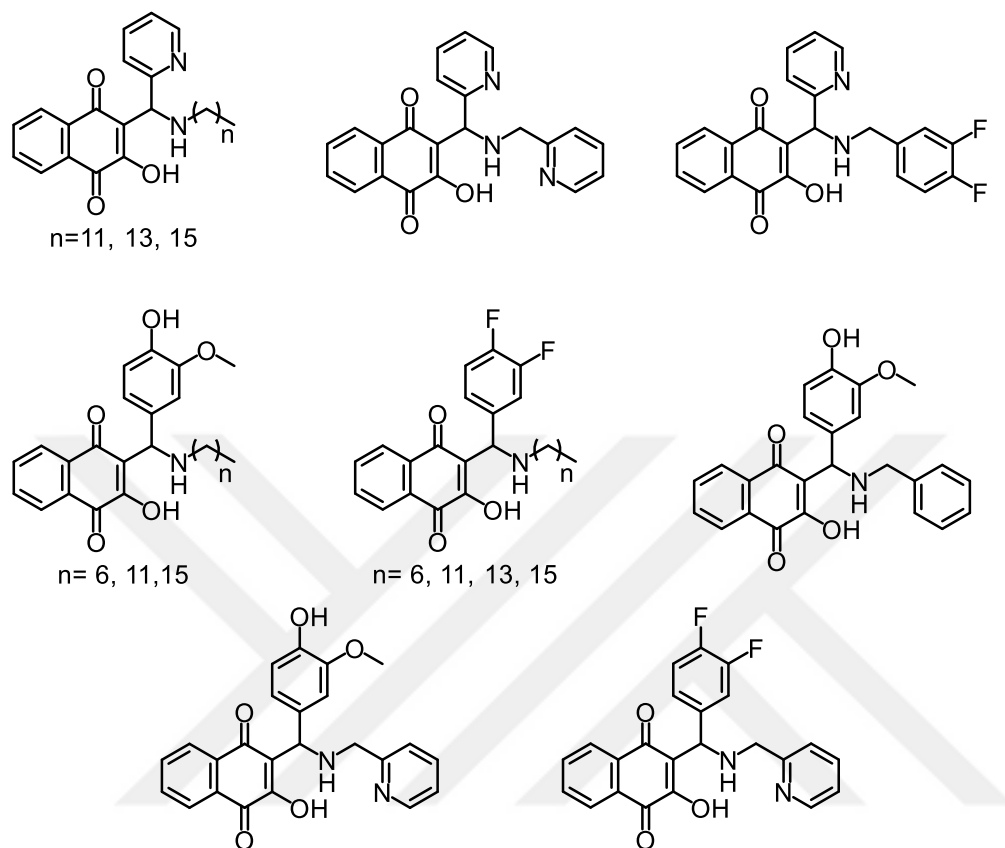


Figure 2.51. Mannich bases reported in reference [102].

The synthesis of aminonaphthoquinone compounds derived from Mannich reaction of 2-hydroxy-1,4-naphthoquinone with low reactivity aldehyde and amine derivatives was carried out using different catalytic systems and green protocols due to the biological interest.

In a study, a three-component Mannich reaction in the presence of *p*-TSA as a catalyst in acetonitrile at room temperature was reported. The reaction was carried out with a cheap catalyst and improved yields within a very short time (Figure 2.52) [103].

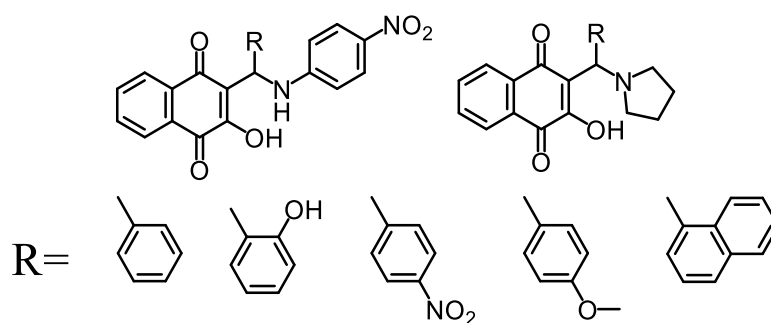


Figure 2.52. Three-component Mannich bases reported in reference [103].

The condensation reaction of 5,5'-methylenebis(thiazol-2-amine), 2-hydroxy-1,4-naphthoquinone and various aromatic aldehydes in one-pot was performed in ethanol by formic acid catalyst to get bishetero arylamino methylnaphthoquinone derivatives. Their antimicrobial activity was screened against several gram-positive and negative bacterial species [103].

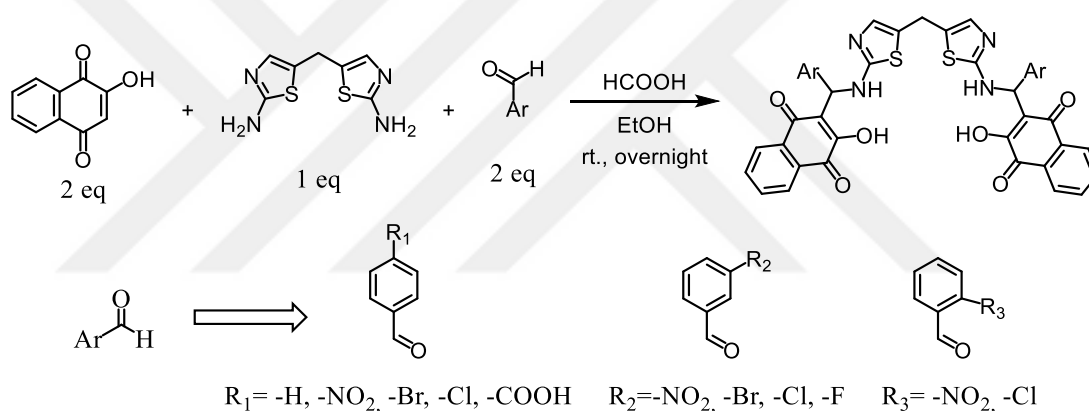


Figure 2.53. Mannich bases derived from 5,5'-methylenebis(thiazol-2-amine).

Bis-heteroarylaminomethylnaphthoquinone Mannich bases were obtained from terephthalaldehyde, aniline, or heterocyclic amine compounds in the presence of *p*-TSA in acetonitrile at room temperature. The study emphasized that the reaction had various advantages such as easy workup, purification of the compound without chromatographic separation, and high atom economical strategy (Figure 2.54) [104].

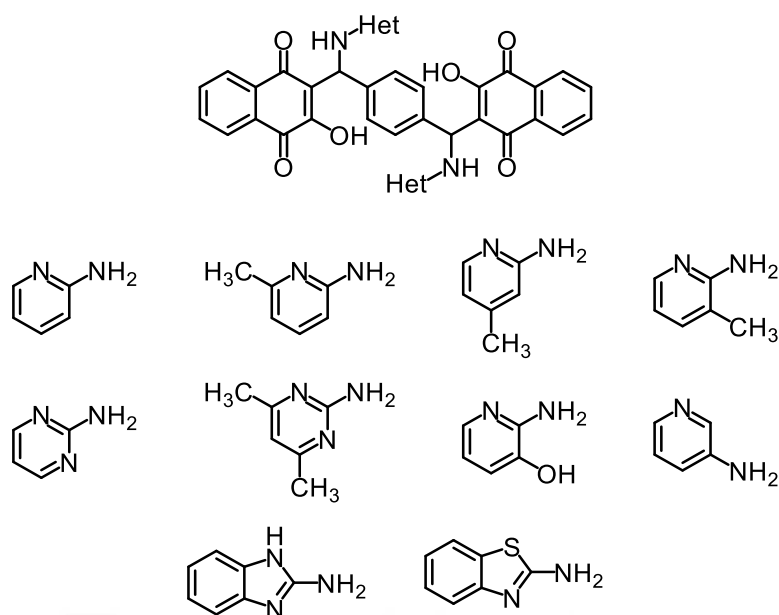


Figure 2.54. Mannich bases obtained from heterocyclic amine derivatives.

The Mannich bases with similar structures given in Figure 2. 54. were accomplished in one-pot and environmentally friendly conditions. In this reaction, dodecyl benzenesulfonic acid was used as a catalyst in aqueous media at room temperature [105].

Phenylphosphoric acid was also applied to catalyze the Mannich reaction at room temperature in water [106].

Moreover, various metal and Lewis acid catalysts were researched to carry out this reaction in a greener way. The synthesis of fluorescent Lawsone derivatives by a simple and multicomponent reaction using an InCl_3 catalyst in refluxing aqueous media was reported. The compounds in the study included Mannich bases derived from heterocyclic amines such as 2-amino-pyridine, 2-amino-benzimidazole, and amino-triazole (Figure 2.55) [107].

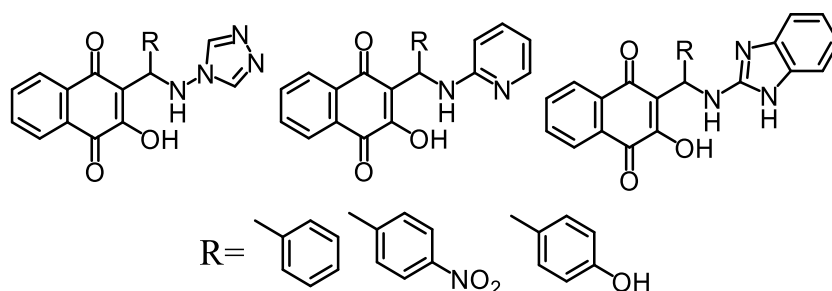


Figure 2.55. The Mannich bases obtained from the reaction, which was catalyzed with InCl_3 .

Ionic liquids like *N*-methylimidazolium formate, pyrrolidinium acetate, 1,8-diazabicyclo[5.4.0]-undec-7-en-8-ium acetate, piperidinium acetate, pyrrolidinium formate, piperidinium formate, and 3-hydroxypropanaminium acetate were utilized to obtain 2-hydroxy-naphthaphthalene-1,4-dione derivatives through Mannich reaction in solventless and ambient conditions [108].

In another methodology to obtain aminonaphthoquinones, a one-pot three-component reaction was designed, which was catalyzed under solventless conditions by immobilized Cu (II) on hyperbranched polyglycerol modified graphene oxide [109].

It was reported that bismuth was immobilized on triazine dendrimer stabilized Fe₃O₄ magnetic nanoparticle and used as an environmentally benign, highly efficient, and reusable catalyst. It was substantially highlighted that this magnetic nanoparticle displayed highly efficient catalytic conversion of symmetric and non-symmetric bis-aminonaphthoquinones starting from dialdehyde and/or diamine besides Lawsone-based Mannich bases derived from aniline derivatives [110]

Montmorillonite K-10 was reported to access new aminonaphthoquinone derivatives starting with 2-hydroxy-1,4-naphthoquinone, aldehyde, and aromatic/heterocyclic amines. It was noted that the synthesis of the Mannich bases with 2-aminobenzothiazol group was obtained. The main advantages of this protocol are time efficiency, easiness, and improved yields [111].

Another study reported that Lawsone with isoindoline structures was obtained from 2-hydroxy-1,4-naphthoquinone, 2-formyl benzoic acid, and several amin derivatives at room temperature using metal-free, environmentally benign methodology (Figure 2.56) [112].

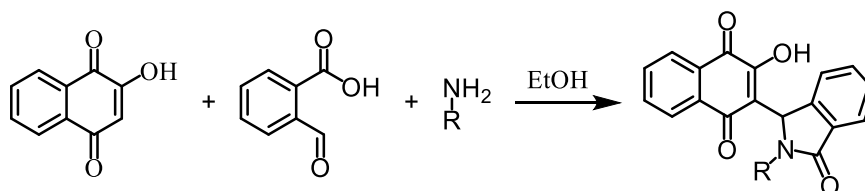


Figure 2.56. The synthesis of 2-hydroxy-1,4-naphthoquinone with isoindoline moiety.

2.3.5. Multi-component reactions of 2-Hydroxy-1,4-naphthoquinone

The reactions where three or more compounds are reacted in a single vessel to form a final product bearing most of the atoms of the starting compounds are called multi-component reactions. These chemical transformations are very useful for preparing

chemical libraries with high atom economy, in good yields. Furthermore, this method saves time, resources, and energy. It minimizes the waste, labour, and effort for the purification steps compared to conventional organic synthesis, offering the vast possibility of molecular diversity and complexity in a minimum number of steps within less time [113, 114]. 2-hydroxy-1,4-naphthoquinone has been highly utilized in multicomponent reactions to access new naphthoquinone derivatives as well as new heterocyclic scaffolds with potent bioactivities.

The three-component reaction of 2-hydroxy-1,4-naphthoquinone, indole, and aldehyde derivatives in the presence of CeCl_3 catalyst resulted in the formation of indole-bearing Lawsone derivatives [115]. On the other hand, when the same reaction was carried out using salicylaldehyde compounds with $\text{In}(\text{OTf})_3$ in solvent-free conditions led to 1,4-naphthoquinones-fused indoles (Figure 2.57) [116].

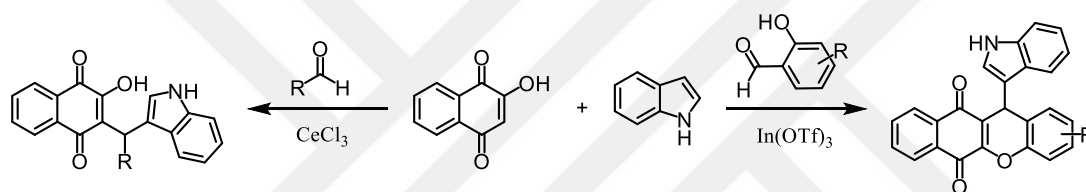


Figure 2.57. The multi-component reaction between indole and Lawsone with different aldehydes.

The multi-component reaction of 2-hydroxy-1,4-naphthoquinone, thiophenol, and aldehyde derivatives yielded 2-hydroxy-3-phenylsulfanylmethyl-1,4-naphthoquinones by microwave radiation (Figure 2.58) [117-119].

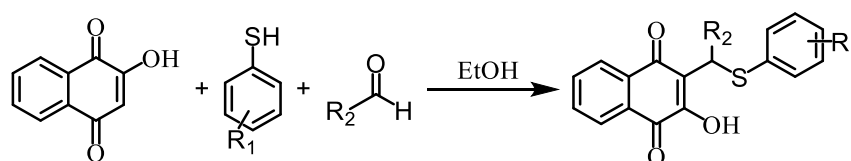


Figure 2.58. The multi-component reaction between Lawsone, thiophenol, and aldehyde derivatives.

para- and *ortho*- naphthoxanthenes linked by thiol groups were formed using urea as a catalyst when the same reaction as above was set up with salicylaldehyde derivatives (Figure 2.59) [120].

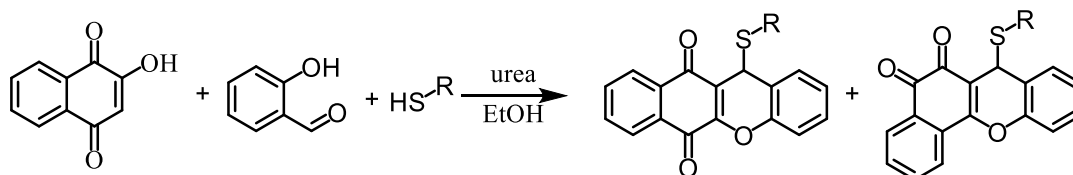


Figure 2.59. The synthesis of *para*- and *ortho*- naphthoxanthenes linked by thiol groups.

4*H*-pyran-2-amino-3-carbonitrile derivatives with 1,4-naphthoquinone unite were classically synthesized by a three-component reaction in the presence of piperidine in alcoholic solution (Figure 2.60) [121-124].

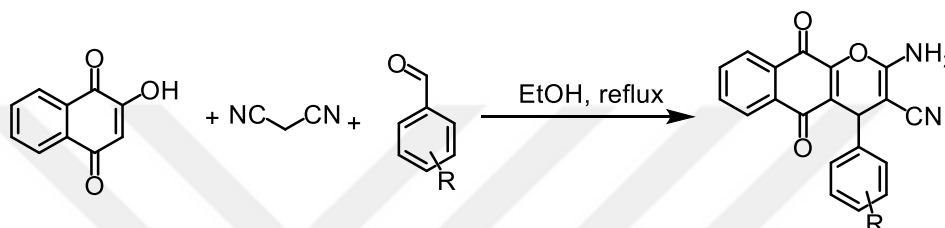


Figure 2.60. The synthesis of 4*H*-pyran-2-amino-3-carbonitrile derivatives with 1,4-naphthoquinone unite.

4*H*-pyran-2-amino-3-carboxylate with naphthoquinone moiety was synthesized by multicomponent reaction of ethyl-2-cyanoacetate, 2-hydroxy-1,4-naphthoquinone, and aldehyde derivatives with several catalytic systems such as potassium phthalimide-*N*-oxyl [125], DBU [126], dysprosium and balsalazide trapped between the functionalized g-C₃N₄ and halloysite [127], an amino-functionalized CeO₂/CuO@ nitrogen graphene quantum dot nanocomposite [128]. The same reaction was carried out by methyl-2-cyanoacetate and isopropyl-2-cyanoacetate using ammonium acetate in a water-ethanol mixture (Figure 2.61) [129].

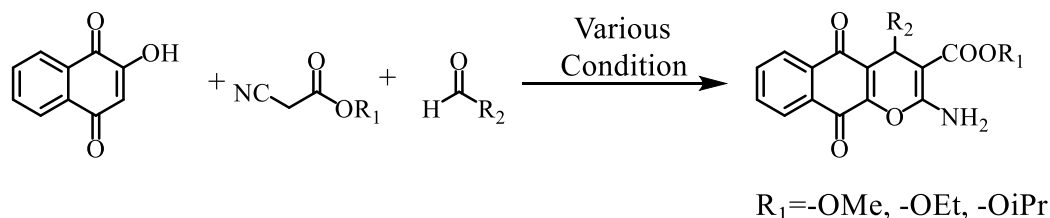


Figure 2.61. 4*H*-pyran-2-amino-3-carboxylate with naphthoquinone moiety.

New methodologies have been improved to obtain structurally alike products providing several advantages such as greener and mild conditions, cost-effective, environmentally benign, and time-saving by using a wide variety of catalytic systems

such as ionic liquids [130], silica-bonded propylpiperazine-*N*-sulfamic acid [131], DBU in water [126], CTAB in water [132], urea in water [133], triethanolamine [134], Mn-Schiff base complex@Hercynite [135], imidazole [136], nanostructured cobalt phthalocyanine [137], Zn(*L*-proline)₂ [138], NH₄OAc in EtOH-water mixture with ultrasonic treatment [129]. In another study, a similar reaction was performed with 1*H*-pyrazole-4-carbaldehyde as an aldehyde derivative under microwave conditions in the presence of an acetic acid-pyrrolidine bifunctional catalyst (Figure 2.62) [139].

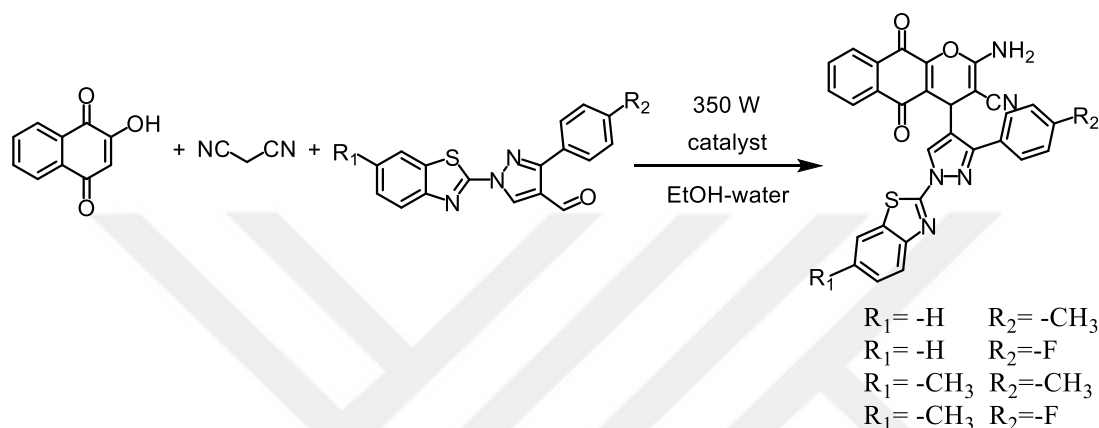


Figure 2.62. The multi-component reaction between 1*H*-pyrazole-4-carbaldehyde malononitrile, and Lawsone

The synthesis of 2-amino-4*H*-benzo[*g*]chromenes containing acyl group on the 4*H*-chromene ring was carried out by starting from malononitrile, 2-hydroxy-1,4-naphthoquinone and glyoxal compounds by catalyst-free, microwave irradiation in EtOH [140] or poly(*N*-vinylimidazole) catalyst [141], or without catalyst in reflux condition (Figure 2.63) [142].

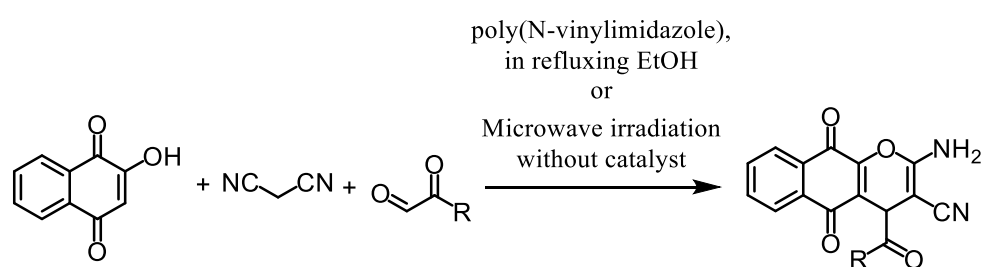


Figure 2.63. The reaction between malononitrile, 2-hydroxy-1,4-naphthoquinone, and glyoxal compounds.

The preparation of 1,4-naphthoquinone fused chromene derivatives from 2-hydroxy-1,4-naphthoquinone, 4-hydroxy-coumarin, and substituted aldehydes was carried out

in one pot and various conditions by several magnetic Fe₃O₄-based catalysts (Figure 2.64) [143–145].

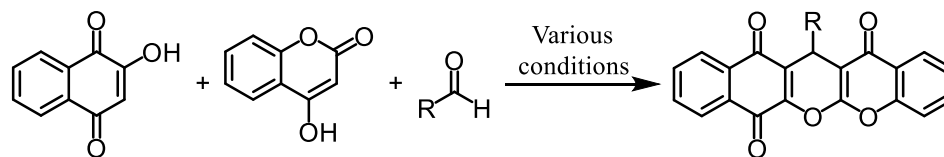


Figure 2.64. The preparation of 1,4-naphthoquinone fused chromene derivatives.

Spirooxindole compounds with quinone moiety were synthesized by three component reaction 2-hydroxy-1,4-naphthoquinone, malononitrile, and isatine derivatives by using several catalyst and reaction conditions such as phosphomolybdic acid on pre-synthesized *N*-doped graphene oxide (NGO/PMA) [146], graphene oxide-supported dicationic ionic liquid [147], cinchona-thiourea organocatalyst for asymmetric spirooxindole derivatives [148], *p*-toluenesulfonic acid in water media [149], 4-piperidine carboxylic acid tethered on Fe₃O₄ [150], copper ferrite nanoparticle in water [151], TBAB in aqueous media (Figure 2.65) [152].

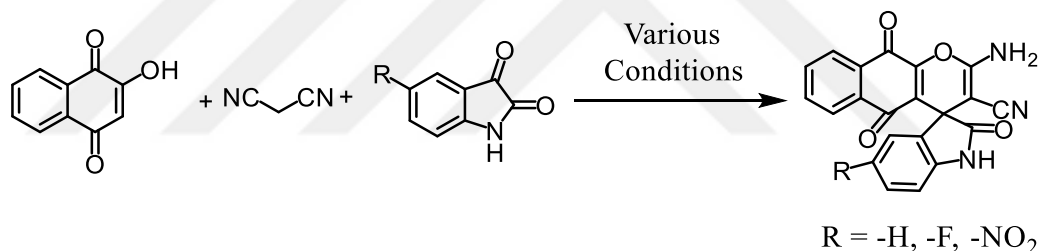


Figure 2.65. The synthesis of spirooxindole with naphthoquinone structure.

The synthesis of spiro[benzo[*g*]-furo[3,4-*b*]quinoline-indoline]-tetraones was accomplished by a multi-component method starting with tetrone acid, isatine, ammonium acetate, and 2-hydroxy-1,4-naphthoquinone in the presence of *p*-TSA catalyst with ultrasonic treatment (Figure 2.66) [153].

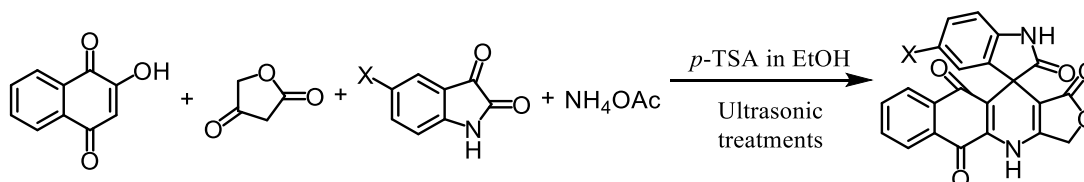


Figure 2.66. The synthesis of spiro[benzo[*g*]-furo[3,4-*b*]quinoline-indoline]-tetraones.

Xanthenes have been widely researched for the visualization of biologically important molecules, such as leuco-dyes, potential applications in laser technologies, and photodynamic therapy reagent. Its biological activity studies also have gathered great attention. Their significance captures the interest in synthesizing these structures, so intensive efforts to design diverse functional homogeneous and heterogeneous catalysts were made to improve parameters such as reaction yield and time in greener conditions with easy workup.

Xanthene derivatives bearing quinone structure were synthesized through multicomponent reaction by using various catalysts and mild reaction conditions in the presence of wide possibility of catalysts such as AcOH [154], nickel oxide supported on silica core-shell nanoparticles [155], silica-supported perchloric acid [156], nano $\text{Fe}_3\text{O}_4@\text{SiO}_2$ modified with sulfonic acid groups [157], silica chloride without solvent [158], poly(4-vinylpyridinium)hydrogen sulfate [159], 1-butyl-3-methylimidazolium hydrogen sulfate ([bmim]HSO₄) ionic liquid [160], *p*-TSA in water media [161], $\text{GaCl}_3@\text{Polystyrene}$ [162], Phosphoric acid appended on alumina ($\text{H}_3\text{PO}_4/\text{Al}_2\text{O}_3$) [163], basic ionic liquid prepared from ethan-1,2-diyl-bis (hydrogen sulfate) and DBU [164], ionic liquids 2-pyrrolidonium hydrogen sulfate and (4-sulfobutyl)tris(4-sulfophenyl) phosphonium hydrogen sulfate (Figure 2.67) [165].

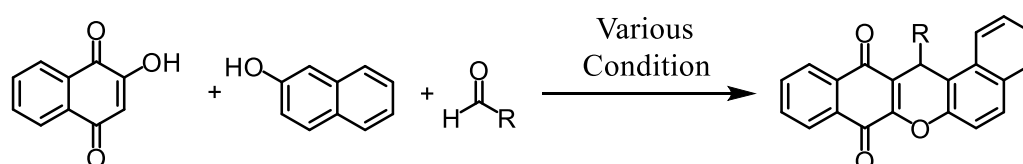


Figure 2.67. The synthesis of xanthene derivatives bearing naphthoquinone structure.

Two equivalents of 2-hydroxy-1,4-naphthoquinone with one equivalent of aldehyde derivatives led to the formation of the pyran ring. These products, dibenzoxanthenetetrone compounds, were obtained by using several catalytic reaction conditions such as Brønsted acidic ionic liquids [165], $\text{H}_3\text{PO}_4/\text{Al}_2\text{O}_3$ [163], $\text{NiFe}_2\text{O}_4@\text{Cu}$ immobilized at acid-activated montmorillonite [166], choline chloride and itaconic acid-based deep eutectic solvent [167], acidic ionic liquid 1-butyl-3-methylimidazolium hydrogen sulphate [168], solvent-free condition with graphene oxide/strontium as a nanocatalyst [169], $\text{Fe}_3\text{O}_4@\text{SiO}_2@(\text{CH}_2)_3\text{-Im-SO}_3\text{H}$ and trityl bromide [170], $\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$ [171], *p*-TSA in varied solvents [172], AcOH in ethylene glycol [173], *N*-sulfonic acid poly(4-vinylpyridinium) hydrogen sulfate with ultrasonic

treatment [174], graphene oxide/strontium nanocatalyst without solvent (Figure 2.68) [169].

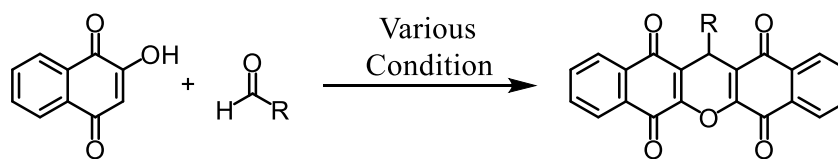


Figure 2.68. The synthesis of dibenzoxanthenetetraone compounds.

2-hydroxy-1,4-naphthoquinone, 1,3-indandione, and aldehyde derivatives were annulated to benzoindeno chromenetrione compounds following several methodologies such as solvent-free conditions with solid catalyst (poly(4-vinylpyridinium) hydrogensulfate) [175], ionic liquid catalyst [176], *N*-sulfonic acid poly(4-vinylpyridinium) hydrogen sulfate with ultrasonic treatment at room temperatures (Figure 2.69) [174].

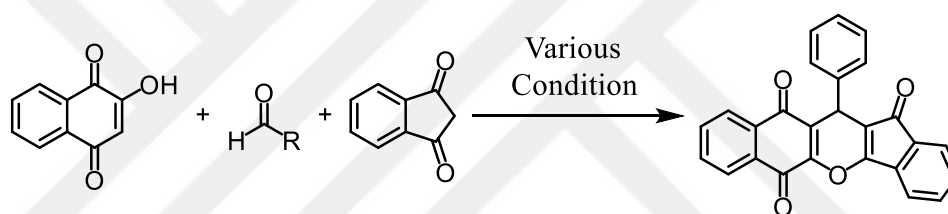


Figure 2.69. The synthesis of benzoindeno chromenetrione.

Multi-component cyclization reaction of 2-hydroxy-1,4-naphthoquinone and 1,3-diketone derivatives with aldehydes led to the formation of benzo[*b*]xanthene-triones. The new catalyst systems have been developed to prepare the compounds in eco-friendly conditions in higher yields with easy purification procedures such as SiO₂-supported tungstic acid with ultrasonic treatment [177], H₂SO₄ in water, ionic liquid 1-butyl-3-methylimidazolium hydrogen sulfate (bmim[HSO₄]) [178], poly(2-ethyl-2-oxazoline) immobilized on Fe₃O₄ nanoparticles (Fe₃O₄@SiO₂/PEtOx) [179], *L*-proline in aqueous media [180], 1-Butyl-3-methylimidazolium bromide [181], CAN under solvent-free media with microwave irradiation (Figure 2.70) [182].

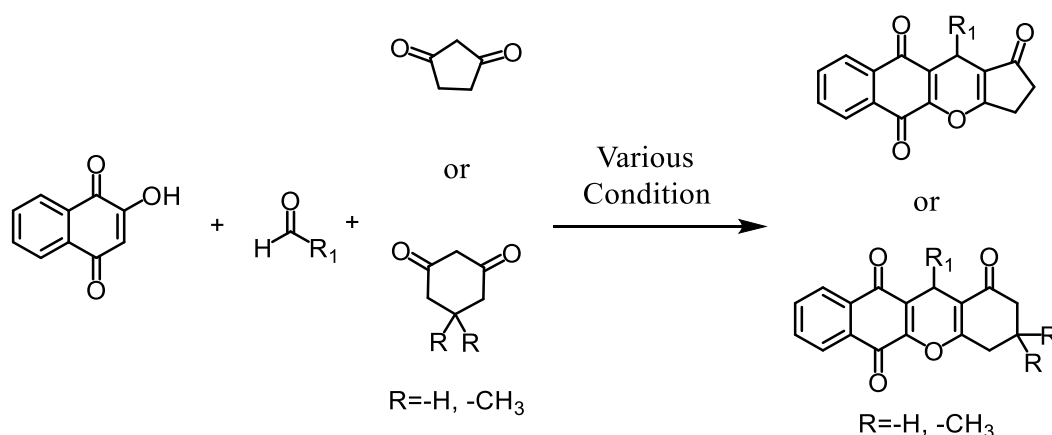


Figure 2.70. The synthesis of benzo[*b*]xanthene-triones derivatives.

The synthesis of 3-benzoyl-4*H*-benzo[*g*]chromene-5,10-diones was accomplished by multicomponent reactions of 2-hydroxy-1,4-naphthoquinone, aromatic aldehydes, and arylenaminones with acetic acid by microwave irradiation (Figure 2.71) [183].

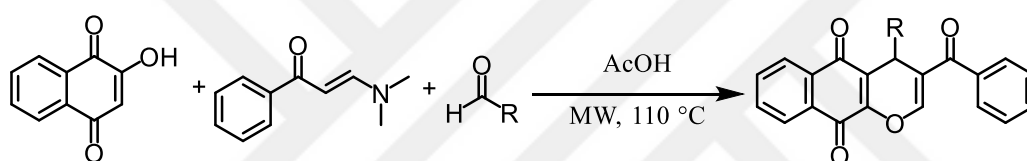


Figure 2.71. The synthesis of 3-benzoyl-4*H*-benzo[*g*]chromene-5,10-diones.

Benzo[*a*]benzo[6,7]chromeno[2,3-*c*]phenazine was synthesized from *o*-phenyldiamine, aldehyde derivatives, and two equivalents of 2-hydroxy-1,4-naphthoquinone in the presence of Ni-Gly-isatin@boehmite (Figure 2.72). The reported mechanism proceeded through the formation of benzo[*a*]phenazin-5-ol which was given in Figure 2.79 [184].

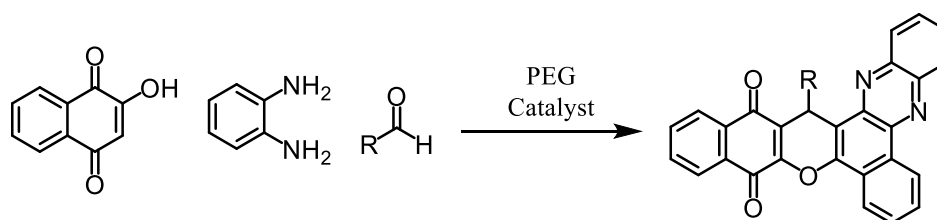


Figure 2.72. The multi-step synthesis for benzo[*a*]benzo[6,7]chromeno[2,3-*c*]phenazine.

Benzylpyrazolyl naphthoquinone derivatives were synthesized by a four-component reaction approach. The reaction of 2-hydroxy-1,4-naphthoquinone, aldehyde derivatives, various phenyl hydrazines, and ethylaceto acetate was yielded to the titled

compound by utilizing various catalytic systems like MgCl_2 in ethylene glycol [185], *p*-TSA [186], $[\text{nano-Fe}_3\text{O}_4@\text{BenzImi}]\text{SO}_3\text{H}$ (Figure 2.73) [187].

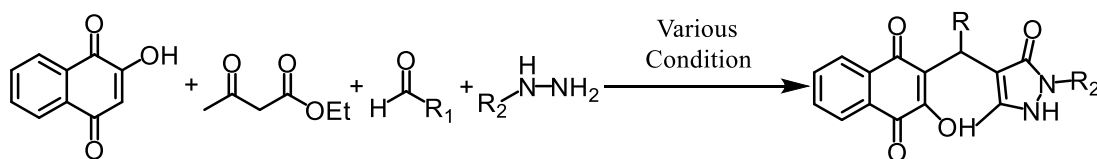


Figure 2.73. The synthesis of benzylpyrazolyl naphthoquinone derivatives.

The multi-component reaction of 2-hydroxy 1,4-naphthoquinone, phthalhydrazide, and various aldehydes in one pot led to the synthesis of various indazolophthalazine derivatives by conventional heating or ultrasonic treatment (Figure 2.74) [188].

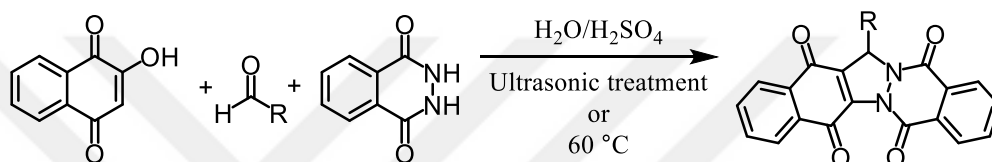


Figure 2.74. The synthesis of indazolophthalazine derivatives.

Benzoindenoquinolinetriene was obtained from four-component reactions of 2-hydroxy-1,4-naphthoquinone, ammonium acetate, 1,3-indandione, and aldehyde derivatives in one-pot using poly(4-vinyl pyridinium) hydrogen sulfate as a catalyst (Figure 2.75) [189].

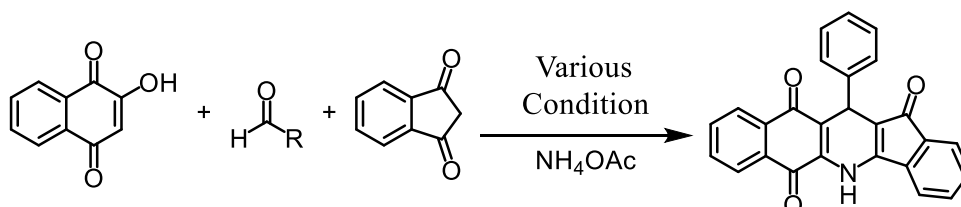


Figure 2.75. The synthesis of benzoindenoquinolinetriene.

Benzo[*g*]quinoline-5,10-dione skeleton is a substantial motif widely distributed in nature and is of diverse biological properties. It was reported that 2-hydroxy-1,4-naphthoquinone, methyl/ethyl acetoacetate, aldehyde derivatives, and NH_4OAc were annulated in refluxing ethanol by multicomponent reaction [190]. Another study reported that this reaction was carried out in the presence of a heterogeneous catalyst of the amino group bearing $\text{Fe}_3\text{O}_4@\text{SiO}_2$, which is a reusable and eco-friendly catalyst (Figure 2.76) [191].

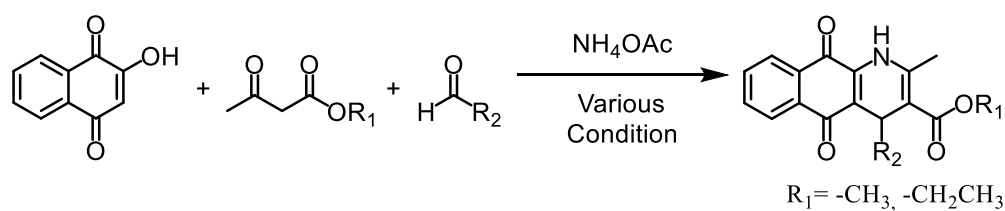


Figure 2.76. The construction of benzo[g]quinoline-5,10-dione skeleton.

Pyrimidine-fused tetrahydropyridines were obtained efficiently from microwave-assisted reaction of α,β -unsaturated aldehydes, 6-aminouracil, and 2-hydroxy-1,4-naphthoquinone using FeCl_3 catalyst (Figure 2.77) [192].

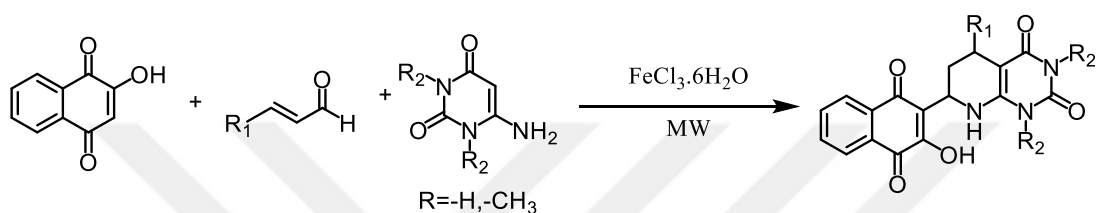


Figure 2.77. The synthesis of pyrimidine-fused tetrahydropyridines.

Oxazine derivatives were synthesized by three components reaction in one pot using new methodologies, including several catalytic systems like reduced graphene oxide [193], ionic liquid $[\text{bmim}]\text{BF}_4$ [194], catalyst-free in water with ultrasonic irradiation [195], Graphene oxide-supported ionic liquid phase catalyst (Figure 2.78) [196].

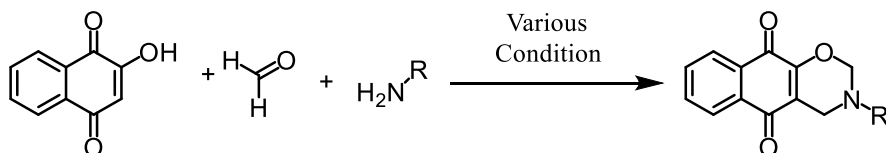


Figure 2.78. The synthesis of oxazine derivatives with naphthoquinone structure.

2.4. Miscellaneous Reactions of 2-hydroxy-1,4-naphthoquinone

Lawsone, 2-hydroxy-1,4-naphthoquinone, is also a good starting material to obtain unique structures without quinone moiety. The condensation of 2-hydroxy-1,4-naphthoquinone with *o*-phenylenediamine or its diamine derivatives yielded benzo[*a*]phenazin-5-ol compounds. This reaction was accomplished by several synthetic strategies. Moreover, the product was also quite interesting in accessing new heterocyclic compounds (Figure 2.79) [197].

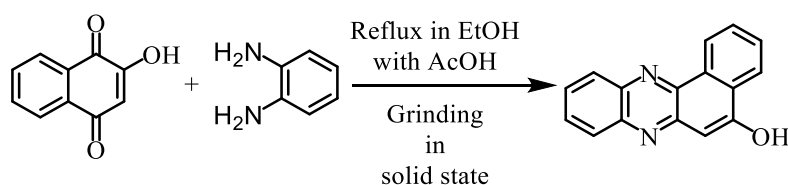


Figure 2.79. The synthesis of benzo[*a*]phenazin-5-ol.

Benzo[*a*]pyrano[2,3-*c*]phenazine compounds were synthesized through a four-component reaction. It was also reported that the formation of benzo[*a*]phenazin-5-ol, which was given in Figure 2.67, was the first step of the four-component reaction. A great deal of effort was made to improve the reaction in various respects using new catalysts like CoFe_2O_4 nanostructure modified by cerium 1*H*-pyrazole-3,5-dicarboxylic acid structure [198], nanostructured cobalt phthalocyanine [137], β -cyclodextrin in $\text{H}_2\text{O}:\text{EtOH}$ mixture [199], CuO quantum dot-modified magnetic silica mesoporous nanoparticles (Figure 2.80) [200].

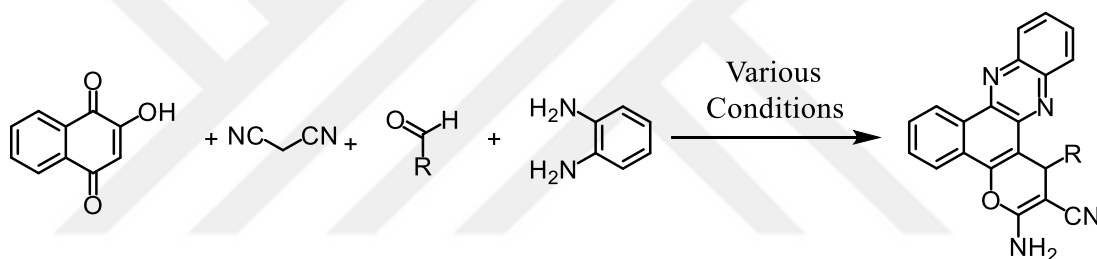


Figure 2.80. The four-component reaction for the synthesis of benzo[*a*]pyrano[2,3-*c*]phenazine derivatives.

The condensation of 1,2-phenylenediamine, 2-hydroxy-1,4-naphthoquinone, aryl aldehydes, and methyl or phenyl sulfonyl acetonitrile yielded 1*H*-benzo[*a*]pyrano[2,3-*c*]phenazin-3-amine derivatives with methyl or phenyl sulfonyl groups. The reaction, which was carried out with methylsulfonyl acetonitrile, was catalyzed by magnetic $\text{Fe}_3\text{O}_4@\text{SiO}_2$ modified with ionic liquid [201]. On the other hand, the one with phenyl sulfonyl group was obtained without solvent and in the presence of 2-hydroxyethylammonium formate as a green catalyst (Figure 2.81) [202].

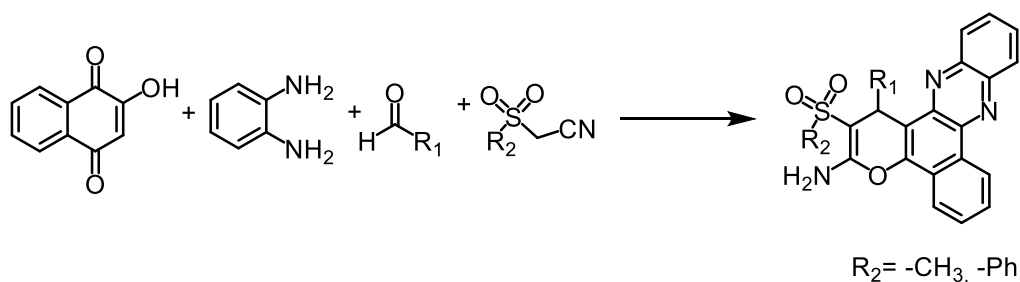


Figure 2.81. The synthesis of 1*H*-benzo[*a*]pyrano[2,3-*c*]phenazin-3-amine derivatives with methyl or phenyl sulfonyl groups.

5*H*-benzo[*a*]phenoxazin-5-one was obtained from the reaction of 2-aminophenol and 2-hydroxy-1,4-naphthoquinone as pictured in Figure 2.82 as a minor product. The major one was a non-cyclized product, which was generated from Micheal addition [203, 204].

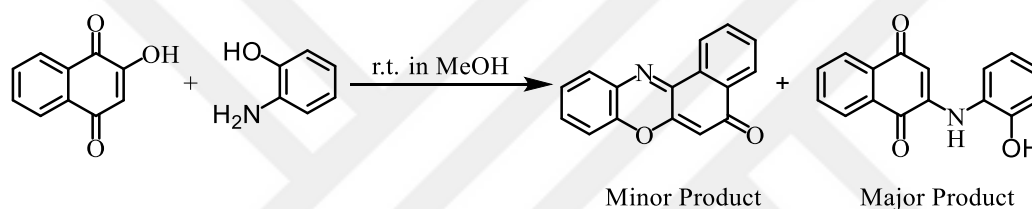


Figure 2.82. The synthesis of 5*H*-benzo[*a*]phenoxazin-5-one.

The synthesis of spiro-annulated pyrimidophenazine compounds was accomplished by a protocol involving a four-component reaction of 2-hydroxy-1,4-naphthoquinone, *o*-phenylenediamine, heterocyclic amines, and cyclic ketones. Several catalyst systems were studied to improve the reaction, such as $InCl_3$, $FeCl_3$, ZrO , ZnO , TiO_2 , and erbium-doped nanoparticles. It was concluded that the last one was the most promising catalyst for this four-component reaction (Figure 2.83) [205].

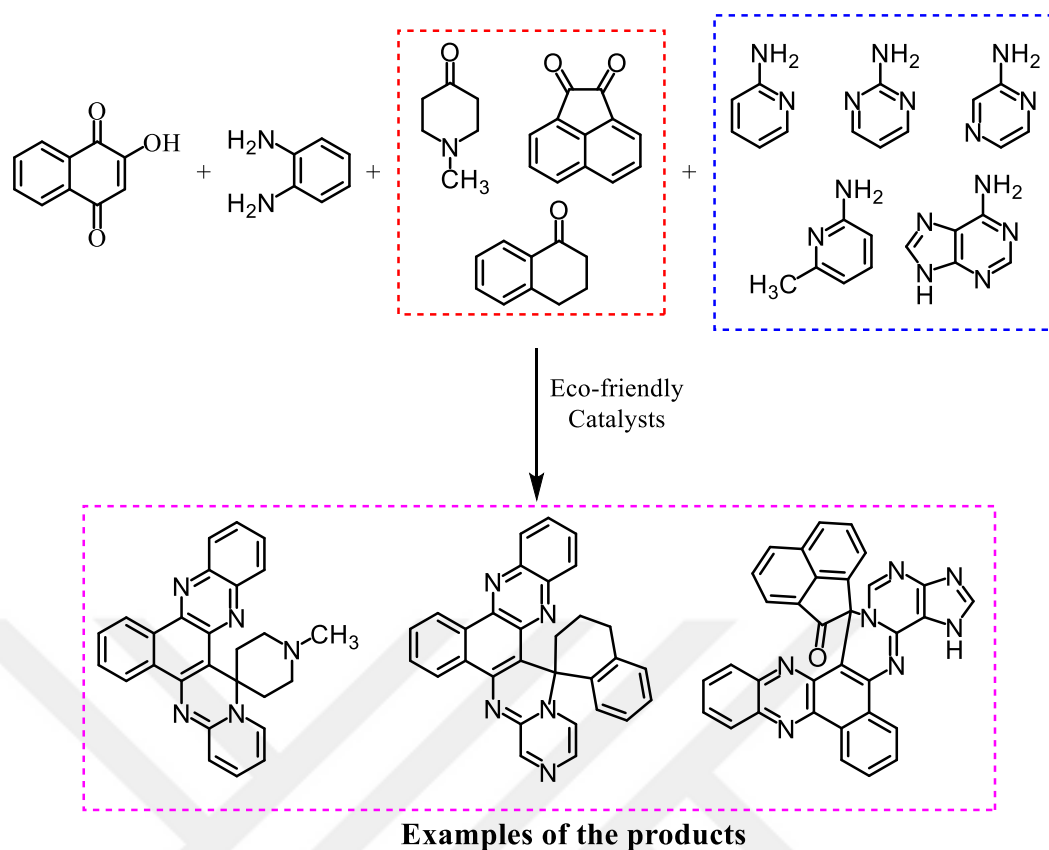


Figure 2.83. The synthesis of pyrimidophenazine derivatives.

It was reported that grinding of α,β -unsaturated aldehydes, 2-hydroxy-1,4-naphthoquinone, and 5-aminopyrazoles with low quantity of water in a mortar yielded benzo[*h*]pyrazolo[3,4-*b*]quinoline-5,6(10*H*)-diones with styryl group (Figure 2.84) [206].

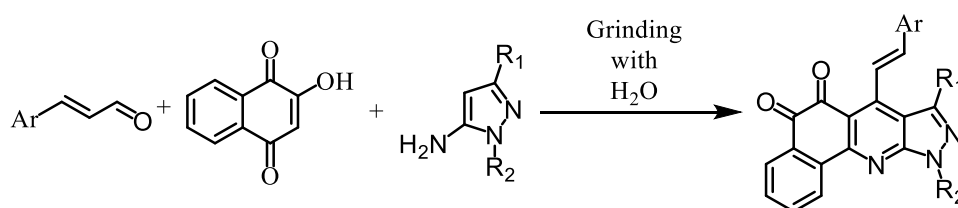


Figure 2.84. The synthesis of benzo[*h*]pyrazolo[3,4-*b*]quinoline-5,6(10*H*)-diones with styryl group.

The synthesis of 7-arylbenzo[*c*]acridine-5,6-diones derivatives by a domino reaction was reported. The reaction comprised three components: 2-hydroxy-1,4-naphthoquinone, aromatic amine, and aldehyde derivatives. Interestingly, when the same reaction was set up in water media with the same conditions (Figure 2.85), the product was different, which is a Mannich base, as reported in section 2.3.4. [207].

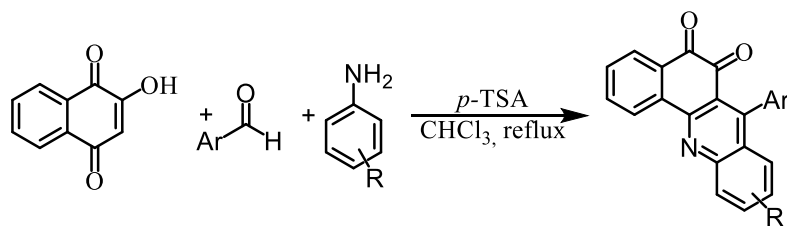


Figure 2.85. The synthesis of 7-arylbenzo[*c*]acridine-5,6-diones derivatives.

The four-component reaction of 2-hydroxy-1,4-naphthoquinone, phenylhydrazine, 3-aminocrotononitrile and various benzaldehydes derivatives yielded 7-(aryl)-8-methyl-10-phenyl-5*H*-benzo[*h*]pyrazolo[3,4-*b*]quinoline-5,6(10*H*)-diones. The reaction was catalyzed by *L*-proline in aqueous media (Figure 2.86) [208].

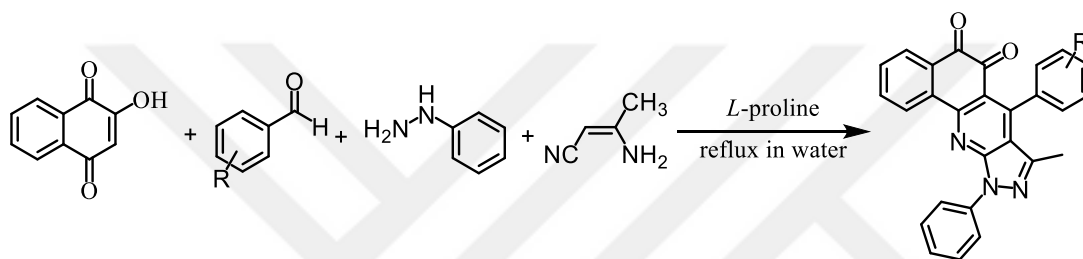


Figure 2.86. The synthesis of 7-(aryl)-8-methyl-10-phenyl-5*H*-benzo[*h*]pyrazolo[3,4-*b*]quinoline-5,6(10*H*)-diones.

3. MATERIALS AND METHODS

3.1. Solvents and Chemicals

The chemicals and solvents utilized in this study are given below, along with their CAS number in parentheses.

Ethanol (64-17-5), methanol (67-56-1), acetone (67-64-1), toluene (108-88-3), acetic acid (64-19-7), chloroform (67-66-3), hexane (110-54-3), and ethyl acetate (141-78-6) were used as solvents in the reaction and purification steps. The solvents of CDCl₃ (865-49-6) and DMSO-d₆ (2206-27-1) were used for NMR analysis of the compounds.

1,4-naphthoquinone (130-15-4), *p*-Anisidine (104-94-9), liquid bromine (7726-95-6), cyclohexylamine (108-91-8), pyrrolidine (123-75-1), hexylamine (111-26-2), morpholine (110-91-8), 1,2,3,4-tetrahydroisoquinoline (91-21-4), piperidine (110-89-4), octylamine (111-86-4), thiosemicarbazide (79-19-6), butylamine (109-73-9), *tert*-butylamine (75-64-9) 1-methylpiperazine (109-01-3), fluorene (86-73-7), 3-amino-9-ethylcarbazole (132-32-1), 3-chloro-4-methoxyaniline (5345-54-0), aniline (62-53-3), ethylamine (75-04-7), methylamine (74-89-5), 4-hydroxybenzaldehyde (123-08-0), vaniline (121-33-5), salicylaldehyde (90-02-8), *N,N*-dimethyl-*p*-phenylenediamine (99-98-9), 2,4-dimethylpyrrole (625-82-1), 3,4,5-trimethoxyaniline (24313-88-0), 2-aminobenzonitrile (1885-29-6), cyclohexanone (108-94-1), 5-aminoindan (24425-40-9) compounds are the chemicals used as reagents in the reactions.

3.2. Devices and Instrumentation

Various instruments were utilized in this study. The glasswares were dried in the laboratory oven after cleaning. The reagents to set up the reactions and the crude and pure products resulting from the reactions were weighed by analytical balance with high precision. The reactions were carried out by several magnetic stirrers with temperature controllers or without heating facilities. Some reactions were set up in the N₂ atmosphere supplied by the N₂ gas cylinder. The organic volatiles obtained after the reaction, extraction, and column chromatography processes were evaporated by rotary evaporators. NMR spectrometer, FT-IR spectrophotometer with ATR unite, and

HPLC-MS were used to determine the structure of the final and intermediate compounds. The photophysical properties of the compounds were studied by using a UV/visible spectrophotometer and fluorescence spectrofluorometer. Cyclic voltammograms of the compounds were recorded by potentiostat to study their electrochemical properties. All devices and instruments pronounced are listed in Table 3.1.

Table 3.1. The instruments used in the study

Instruments	The photo	The reason for the use	Brand Name
Rotary evaporator		The evaporation of the volatiles	Heidolph Laborota 4003-Digital
Magnetic stirrer with the hot plate		To carry out the reaction at higher temperatures with constant stirring	Heidolph-MR Hei-Standard
Precision balance		The mass measurement of the pure and crude products and compounds	Precisa

Table 3.1. (continued) The instruments used in the study

Instruments	The photo	The reason for the use	Brand Name
HPLC-MS		Determination of the mass-to-charge ratio of the pure final compounds	Shimadzu LCMS-9030
Spectrofluorometer		To record the fluorescence spectra of the final compounds	Hitachi F7000
UV/Vis Spectrophotometer		To record the UV/vis spectra of the final compounds	Shimadzu UV-2600
Oven		To dry the glassware	Thermo, Heraeus
NMR spectrometer		Determination of the structure of the compounds	Varian Infinity Plus 300 MHz

Table 3.1. (continued) The instruments used in the study

Instruments	The photo	The reason for the use	Brand Name
FT-IR spectrophotometer with ATR unite		To determine the functional groups of the compounds	Perkin Elmer Spectrum two

3.3. Purification of Solvents

Chloroform, hexane, and ethyl acetate were dried over anhydrous CaCl_2 and purified by fractional distillation. Deuterated solvents such as CDCl_3 and $\text{DMSO}-d_6$ were used for all NMR analyses as procured from Merck. The technical grade of Na_2SO_4 was dried in an oven at $100\text{ }^\circ\text{C}$ to obtain anhydrous Na_2SO_4 , then it was used to get rid of the remaining water residue in extraction steps. The solvents in which the reactions were performed were of high purity ($> 99\%$) and were used as purchased from the companies, but the solvents that were dried as described above were used as mobile phase in column chromatography.

3.4. Column Chromatography

The desired compounds in the reaction mixtures were purified by the silica gel column chromatography. Silica gel 60 (60-230 mesh) purchased from Merck was a stationary phase. Dried solvents such as hexane, chloroform, and ethyl acetate were used for the mobile phase. Silica gel was slurred with hexane. It was filled into the glass column. The crude mixture was loaded on the column with silica gel. The process began with hexane, and the polarity was gradually increased with chloroform or ethylacetate. The collected fractions from column chromatography were evaluated by TLC under a UV lamp (254 nm), and the ones with similar spots were combined. The solvents of the combined fractions were evaporated, and the obtained liquid or solid mass was characterized by spectroscopic techniques.

3.5. Crystallization

Crystallization is one of the crucial techniques for obtaining pure compounds. Dissolution of isolated products was carried out in the suitable solvent or solvent system by heating it, and the mixture was cooled down to room temperature. the mixture was observed by certain time intervals, and as the formation of crystals was started, it was then cooled in the refrigerator. The separated crystals were dried at room temperature.

3.6. The Aim of the Study

1,4-naphthoquinone derivatives, together with other heterocyclic counterparts, have gathered intense attention due to their various biological, pharmacological, and electrochemical features. In the first part of this study, 1,4-naphthoquinone was brominated to 2,3-dibromo-1,4-naphthoquinone. These starting compounds were reacted with nitrogen and phenolic nucleophiles such as aromatic primer, aliphatic primer, seconder amine, phenolic aldehydes, and BODIPY (Figure 3.1).

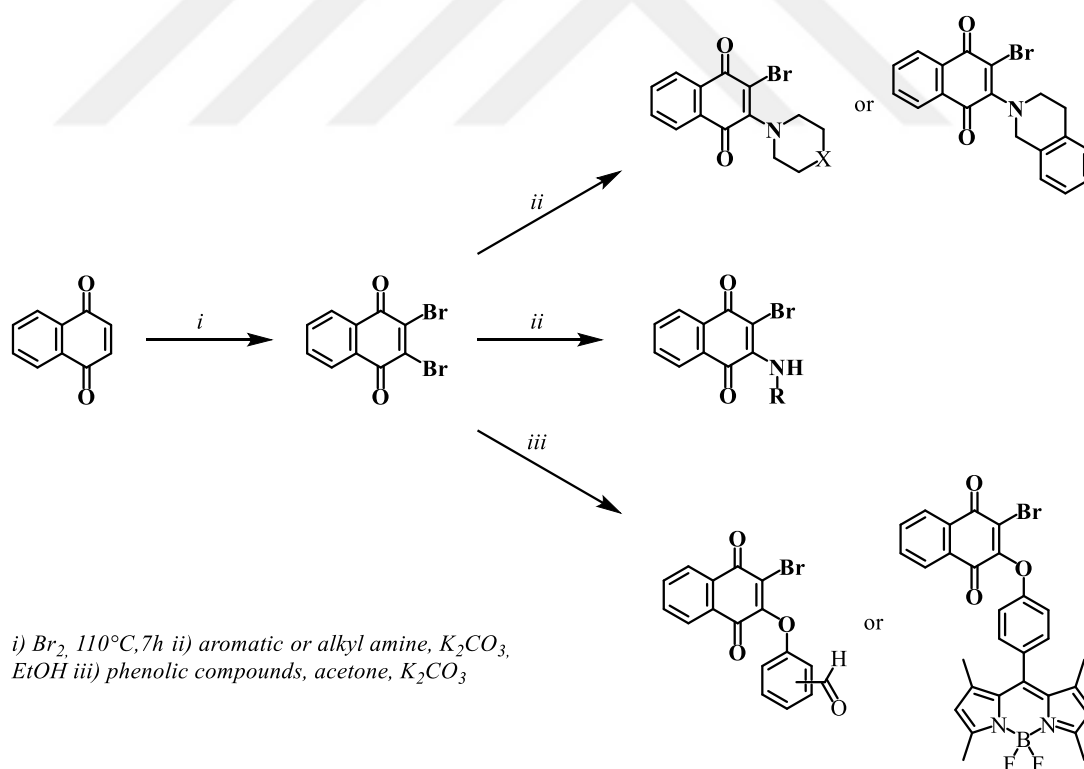


Figure 3.1. The synthetic pathway of aromatic, aliphatic amine, and ether group bearing 1,4-naphthoquinone derivatives in the study.

In the second part, Mannich bases were obtained from Lawsone, 2-hydroxy-1,4-naphthoquinone, hexylamine, and aldehyde derivatives in EtOH at room temperature (Figure 3.2).

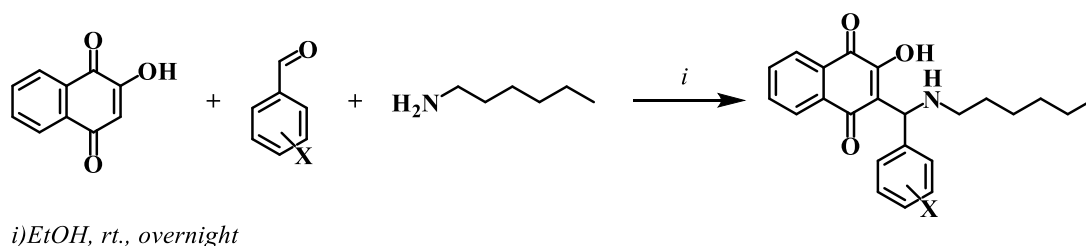


Figure 3.2. The synthetic pathway of Mannich bases.

All synthetic compounds were characterized by ^1H , ^{13}C , ^{19}F NMR, FT-IR, and HPLC-MS techniques. UV-vis and fluorescence spectra of the final compounds were recorded. Their electrochemical features were evaluated by cyclic voltammetry. The compounds obtained in the scope of the thesis contained medicinally important heterocyclic parts in addition to 1,4-naphthoquinone, such as thiadiazole, tacrine, and carbazole. In the light of the scientific literature, these compounds would have several biological activities. 1,4-naphthoquinone with the aldehyde groups are substantial key compounds to access new promising molecules. The incorporation of an intriguing structure like BODIPY into 1,4-naphthoquinone will enable the synthesis of a wide range of new compounds with diverse applications. These promising activity studies and synthetic works will be carried out soon.

4. EXPERIMENTAL STUDIES

4.1. The Bromination of 1,4-naphthoquinone

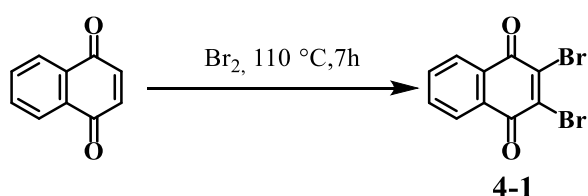


Figure 4.1. The synthesis of compound 4-1.

To a solution of naphthalene-1,4-dione (1.00 g, 6.32 mmol, 1 eq.) in glacial acetic acid, liquid bromine (2.02 g, 0.65 mL 12.64 mmol, 2 eq.) was dropwisely added. After the mixture was stirred at room temperature for 1 hour, it was heated to 110 °C for 7 hours. The mixture was poured into ice water, forming a solid precipitate. It was filtered, washed with plenty of water, and dried in an air atmosphere (Figure 4.1). It was pure enough to carry out the next steps [27]. ¹H NMR (300 MHz, CDCl₃) δ 8.19 (dd, *J* = 5.6, 3.4 Hz, 2H), 7.79 (dd, *J* = 5.6, 3.3 Hz, 2H). ¹³C NMR (75 MHz, CDCl₃) δ 176.05, 142.80, 134.77, 131.01, 128.46 HRMS (ESI) *m/z*: calculated for C₁₀H₄Br₂O₂ [M]⁺: 315.85576, found: 315.85568

4.2. The Synthesis of Compound 4-2

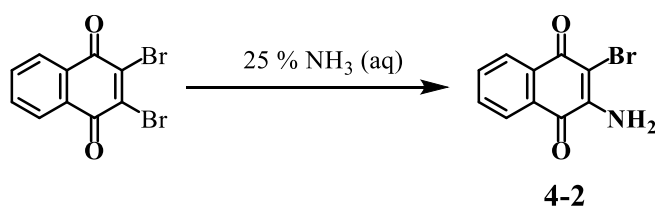


Figure 4.2. The synthesis of compound 4-2

To a solution of 2,3-dibromonaphthalene-1,4-dione (1.00 g, 3.17 mmol) in 30 mL of dioxane, 25% aqueous NH₃ (16 mL) was dropwisely added. The mixture was stirred at 25-30 °C. After 2.5 h, the reaction ceased with the addition of water. The formed solid was filtered off, washed with water, and dried in air (Figure 4.2). ¹H NMR (300 MHz, CDCl₃) δ 8.16 (d, *J* = 7.5 Hz, 1H), 8.06 (d, *J* = 7.5 Hz, 1H), 7.82 – 7.52 (m, 2H),

5.66 (bs, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ 178.74, 176.55, 147.39, 135.12, 132.94, 132.82, 129.93, 127.46, 126.98, 105.39. HRMS (ESI) m/z : calculated for $\text{C}_{10}\text{H}_6\text{BrNNaO}_2$ $[\text{M}+\text{Na}]^+$: 273.94796, found: 273.94665.

4.3. The Synthesis of Compound 4-3

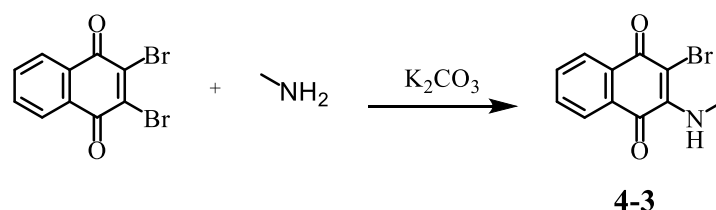


Figure 4.3. The synthesis of compound 4-3.

To 5 min. pre-stirred mixture of 80 μL of 40 % aqueous methylamine and K_2CO_3 (0.11g, 0.79 mmol) in EtOH, 2,3-dibromo-1,4-naphthoquinone (0.25g, 0.79 mmol) was added. The reaction was carried out at room temperature. After 24 hours, the reaction ceased with the addition of water. The obtained solid was filtered (Figure 4.3). It was crystallized from ethanol. Orange-red solid (0.18 g, 85 %). ^1H NMR (300 MHz, CDCl_3) δ 8.14 (d, $J = 7.4$ Hz, 1H), 8.01 (d, $J = 7.0$ Hz, 1H), 7.84 - 7.44 (m, 2H), 6.17 (s, 1H), 3.44 (d, $J = 5.8$ Hz, 3H). ^{13}C NMR (75 MHz, $\text{CDCl}_3 + \text{DMSO}-d_6$) δ 180.44, 175.75, 148.37, 135.15, 132.79, 132.55, 130.34, 127.00, 126.67, 99.71, 33.33. HRMS (ESI) m/z : calculated for $\text{C}_{11}\text{H}_8\text{BrNNaO}_2$ $[\text{M}+\text{Na}]^+$: 287.96361, found: 287.96257.

4.4. The Synthesis of Compound 4-4

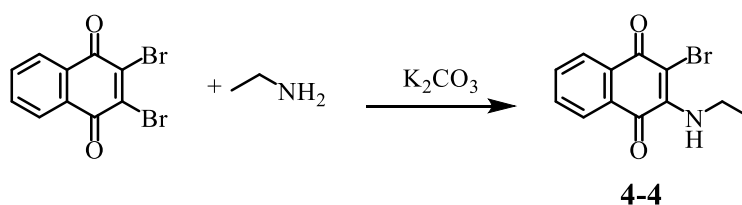


Figure 4.4. The synthesis of compound 4-4.

To 5 min. pre-stirred mixture of 75 μL of 66 % aqueous methylamine and K_2CO_3 (0.11g, 0.79 mmol) in EtOH, 2,3-dibromo-1,4-naphthoquinone (0.25g, 0.79 mmol) was added. The reaction was carried out at room temperature. After 24 hours, the reaction ceased with the addition of water. The obtained solid was filtered (Figure 4.4). It was crystallized from ethanol. Orange solid (0.22 g, 99 %). ^1H NMR (300 MHz, CDCl_3): δ 8.12 (d, $J = 7.7$ Hz, 1H), 7.99 (d, $J = 7.6$ Hz, 1H), 7.79 - 7.45 (m, 2H), 4.55

- 2.95 (m, 2H), 1.32 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3): δ 179.92, 176.08, 146.57, 134.76, 132.34, 129.71, 126.79, 126.67, 101.69, 16.26. HRMS (ESI) m/z : calculated for $\text{C}_{12}\text{H}_{10}\text{BrNNaO}_2$ $[\text{M}+\text{Na}]^+$: 301.97852, found: 301.97852.

4.5. The Synthesis of Compound 4-5

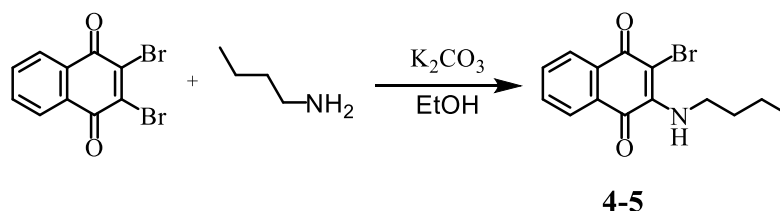


Figure 4.5. The synthesis of compound 4-5.

To 5 min. pre-stirred mixture of butylamine (0.06 g, 0.79 mmol) and K_2CO_3 (0.11g, 0.79 mmol) in EtOH, 2,3-dibromo-1,4-naphthoquinone (0.25g, 0.79 mmol) was added. The reaction was carried out at room temperature. After 24 hours, the reaction ceased with the addition of water. The obtained solid was filtered (Figure 4.5). It was crystallized from ethanol. Orange-red solid (0.22 g, 99 %). ^1H NMR (300 MHz, CDCl_3): δ 8.12 (d, $J = 8.6$ Hz, 1H), 8.00 (d, $J = 7.6$ Hz, 1H), 7.82 - 7.34 (m, 2H), 6.05 (s, 1H), 3.86 (q, $J = 7.0$ Hz, 2H), 1.80 - 1.58 (m, 2H), 1.56 - 1.25 (m, 2H), 0.96 (t, $J = 7.3$ Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3): δ 180.37, 176.65, 146.68, 135.06, 132.70, 132.54, 129.98, 127.29, 127.08, 102.94, 45.29, 33.12, 20.06, 13.99. HRMS (ESI) m/z : calculated for $\text{C}_{14}\text{H}_{14}\text{BrNNaO}_2$ $[\text{M}+\text{Na}]^+$: 330.01056, found: 330.01040.

4.6. The Synthesis of Compound 4-6

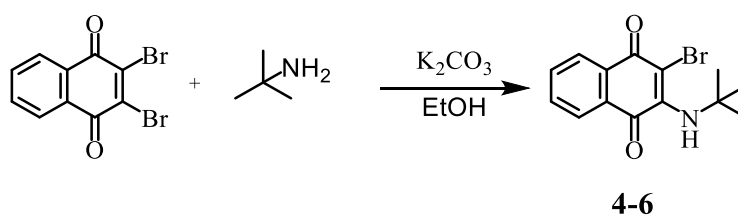


Figure 4.6. The synthesis of compound 4-6.

To 5 min. pre-stirred mixture of *t*-butylamine (0.06 g, 0.79 mmol) and K_2CO_3 (0.11g, 0.79 mmol) in EtOH, 2,3-dibromo-1,4-naphthoquinone (0.25g, 0.79 mmol) was added. The reaction was carried out at room temperature. After 24 hours, the reaction ceased with the addition of water. The obtained solid was filtered (Figure 4.6). It was crystallized from ethanol. Orange solid (0.22 g, 99 %). ^1H NMR (300 MHz, CDCl_3) δ

8.11 (d, $J = 6.9$ Hz, 1H), 8.00 (s, 1H), 7.82 - 7.55 (m, 2H), 5.81 (s, 1H), 1.54 (s, 9H). ^{13}C NMR (75 MHz, $\text{CDCl}_3 + \text{DMSO-d}_6$) δ 179.92, 175.85, 149.67, 134.31, 132.63, 131.54, 130.79, 126.81, 126.31, 109.06, 56.09, 31.13. HRMS (ESI) m/z : calculated for $\text{C}_{14}\text{H}_{14}\text{BrNNaO}_2$ $[\text{M}+\text{Na}]^+$: 330.01056, found: 330.01055.

4.7. The Synthesis of Compound 4-7

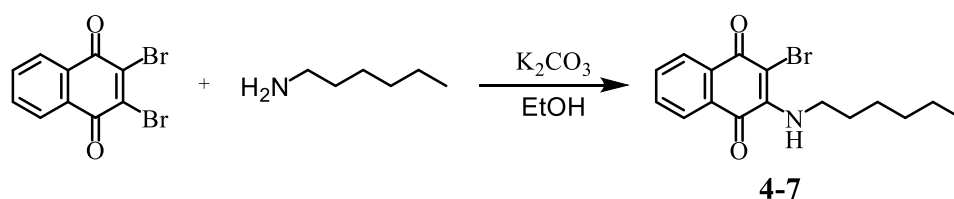


Figure 4.7. The synthesis of compound 4-7.

To 5 min. pre-stirred mixture of hexylamine (0.08 g, 0.79 mmol) and K_2CO_3 (0.11g, 0.79 mmol) in EtOH, 2,3-dibromo-1,4-naphthoquinone (0.25g, 0.79 mmol) was added. The reaction was carried out at room temperature. After 24 hours, the reaction ceased with the addition of water. The obtained solid was filtered (Figure 4.7). It was crystallized from ethanol. Orange solid (0.21 g, 79 %). ^1H NMR (300 MHz, CDCl_3) δ 8.12 (d, $J = 7.6$ Hz, 1H), 8.00 (d, $J = 7.6$ Hz, 1H), 7.81 - 7.51 (m, 2H), 6.08 (bs, 1H), 3.84 (q, $J = 7.2, 6.8$ Hz, 3H), 1.85 - 1.55 (m, 2H), 1.52 - 1.15 (m, 6H), 0.89 (t, $J = 6.4$ Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 180.35, 176.62, 146.65, 135.04, 132.70, 132.52, 129.97, 127.27, 127.06, 102.83, 45.58, 31.64, 31.05, 26.53, 22.76, 14.21. HRMS (ESI) m/z : calculated for $\text{C}_{16}\text{H}_{18}\text{BrNNaO}_2$ $[\text{M}+\text{Na}]^+$: 358.04186, found: 358.04108.

4.8. The Synthesis of Compound 4-8

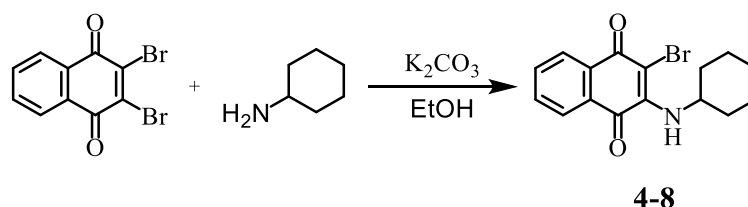


Figure 4.8. The synthesis of compound 4-8.

To pre-stirred mixture of hexylamine (0.08 g, 0.79 mmol) and K_2CO_3 (0.11g, 0.79 mmol) in EtOH for 5 min., 2,3-dibromo-1,4-naphthoquinone (0.25g, 0.79 mmol) was added. The reaction was carried out at room temperature. After 24 hours, the reaction

ceased with the addition of water. The obtained solid was filtered (Figure 4.8). It was crystallized from ethanol. Orange solid (0.21 g, 79 %). ^1H NMR (300 MHz, CDCl_3) δ 8.10 (d, J = 8.2 Hz, 1H), 7.98 (d, J = 7.6 Hz, 1H), 7.78 - 7.39 (m, 2H), 6.05 (s, 1H), 4.69 - 4.39 (m, 1H), 2.24 - 1.90 (m, 2H), 1.90 - 1.59 (m, 3H), 1.54 - 1.13 (m, 5H). ^{13}C NMR (75 MHz, CDCl_3) δ 180.40, 176.60, 145.83, 135.03, 132.72, 132.50, 129.98, 127.28, 127.10, 102.45, 52.73, 34.70, 25.55, 24.71. HRMS (ESI) m/z : calculated for $\text{C}_{16}\text{H}_{16}\text{BrNNaO}_2$ $[\text{M}+\text{Na}]^+$: 356.02621, found 356.02561.

4.9. The Synthesis of Compound 4-9

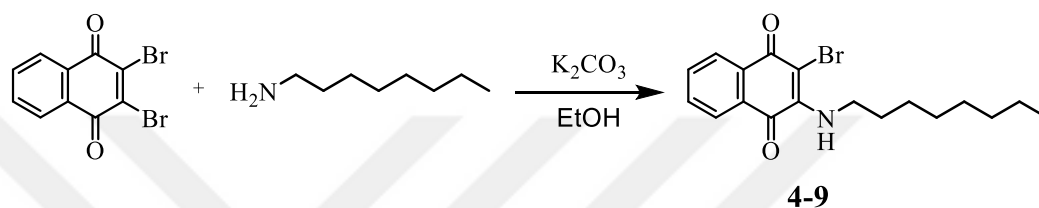


Figure 4.9. The synthesis of compound 4-9.

To 5 min. pre-stirred mixture of octylamine (0.10 g, 0.79 mmol) and K_2CO_3 (0.11g, 0.79 mmol) in EtOH, 2,3-dibromo-1,4-naphthoquinone (0.25g, 0.79 mmol) was added. The reaction was carried out at room temperature. After 24 hours, the reaction ceased with the addition of water. The obtained solid was filtered (Figure 4.9). It was crystallized from ethanol. Orange solid (0.26 g, 90 %). ^1H NMR (300 MHz, CDCl_3) δ 8.12 (d, J = 8.0 Hz, 1H), 8.00 (d, J = 7.7 Hz, 2H), 7.84 - 7.42 (m, 2H), 6.00 (bs, 1H), 4.04 - 3.73 (m, 2H), 1.85 - 1.54 (m, 2H), 1.54 - 1.09 (m, 10H), 0.87 (t, J = 6.6 Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 180.38, 176.64, 146.72, 135.06, 132.72, 132.54, 129.99, 127.30, 127.08, 102.97, 45.58, 31.98, 31.09, 29.44, 29.39, 26.86, 22.86, 14.32. HRMS (ESI) m/z : calculated for $\text{C}_{18}\text{H}_{22}\text{BrNO}_2$ $[\text{M}+\text{Na}]^+$: 386.07316, found: 386.07258.

4.10. The Synthesis of Compound 4-10

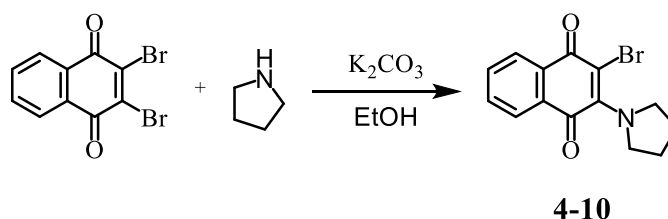


Figure 4.10. The synthesis of compound 4-10.

To 5 min. pre-stirred mixture of pyrrolidine (0.06 g, 0.79 mmol) and K_2CO_3 (0.11g, 0.79 mmol) in EtOH, 2,3-dibromo-1,4-naphthoquinone (0.25 g, 0.79 mmol) was added. The reaction was carried out at room temperature. After 24 hours, the reaction ceased with the addition of water. The obtained solid was filtered (Figure 4.10). It was crystallized from ethanol. Orange solid (0.19 g, 78 %). ^1H NMR (300 MHz, $CDCl_3$) δ 8.08 (d, J = 7.6 Hz, 1H), 7.89 (d, J = 7.5 Hz, 1H), 7.80 - 7.39 (m, 2H), 4.21 - 3.48 (m, 4H), 2.32 - 1.66 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 183.30, 177.12, 152.61, 134.26, 132.23, 131.48, 126.67, 126.48, 125.61, 102.31, 54.64, 25.96. HRMS (ESI) m/z : calculated for $C_{14}H_{12}BrNO_2$ $[M]^-$: 305.00514, found: 304.68004.

4.11. The Synthesis of Compound 4-11

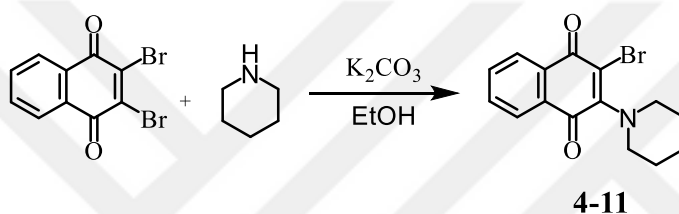


Figure 4.11. The synthesis of compound 4-11.

To 5 min. pre-stirred mixture of piperidine (0.07 g, 0.79 mmol) and K_2CO_3 (0.11g, 0.79 mmol) in EtOH, 2,3-dibromo-1,4-naphthoquinone (0.25 g, 0.79 mmol) was added. The reaction was carried out at room temperature. After 24 hours, the reaction ceased with the addition of water. The obtained solid was filtered (Figure 4.11). It was crystallized from ethanol. Orange solid (0.13 g, 51 %). ^1H NMR (300 MHz, $CDCl_3$) δ 8.12 (d, J = 7.4 Hz, 1H), 8.01 (d, J = 7.5 Hz, 1H), 7.76 - 7.58 (m, 2H), 4.60 - 3.14 (m, 4H), 2.41 - 0.95 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 182.05, 178.41, 153.75, 134.13, 133.11, 131.80, 131.70, 127.12, 127.05, 116.31, 53.63, 27.05, 24.33. HRMS (ESI) m/z : calculated for $C_{15}H_{14}BrNO_2$ $[M+Na]^+$: 342.01056, found 342.00999.

4.12. The Synthesis of Compound 4-12

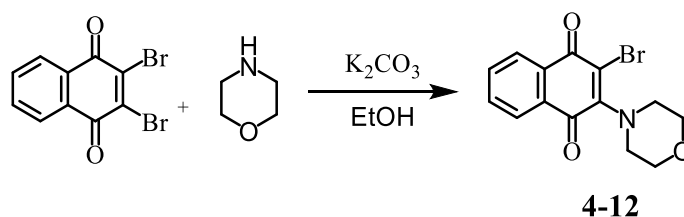


Figure 4.12. The synthesis of compound 4-12.

To 5 min. pre-stirred mixture of morpholine (0.07 g, 0.79 mmol) and K_2CO_3 (0.11g, 0.79 mmol) in EtOH, 2,3-dibromo-1,4-naphthoquinone (0.25 g, 0.79 mmol) was added. The reaction was carried out at room temperature. After 24 hours, the reaction ceased with the addition of water. The obtained solid was filtered (Figure 4.12). It was crystallized from ethanol. Orange solid (0.18 g, 51 %). ^1H NMR (300 MHz, $CDCl_3$) δ 8.36 - 8.06 (m, 1H), 8.06 - 7.93 (m, 1H), 7.81 - 7.51 (m, 2H), 4.02 - 3.81 (m, 4H), 3.75 - 3.50 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 181.76, 178.38, 152.58, 134.38, 133.44, 131.56, 131.48, 127.24, 127.20, 117.71, 67.76, 52.39. HRMS (ESI) m/z: calculated for $C_{14}H_{12}BrNO_3$ $[M+Na]^+$: 343.98983, found 343.98889.

4.13. The Synthesis of Compound 4-13

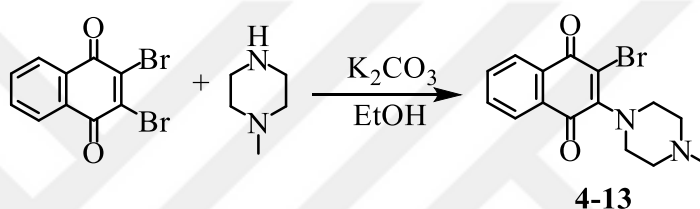


Figure 4.13. The synthesis of compound 4-13.

To 5 min. pre-stirred mixture of 1-Methylpiperazine (0.09 g, 0.79 mmol) and K_2CO_3 (0.11g, 0.79 mmol) in EtOH, 2,3-dibromo-1,4-naphthoquinone (0.25 g, 0.79 mmol) was added. The reaction was carried out at room temperature. After 24 hours, the reaction ceased with the addition of water. The obtained solid was filtered (Figure 4.13). It was crystallized from ethanol. Orange solid (0.27 g, quantitative). ^1H NMR (300 MHz, $CDCl_3$) δ 8.24 - 7.99 (m, 1H), 7.97 - 7.81 (m, 1H), 7.79 - 7.44 (m, 2H), 3.61 (t, 4H), 2.59 (t, 4H), 2.33 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 181.74, 178.29, 152.84, 134.25, 133.29, 131.58, 131.47, 127.15, 127.07, 117.23, 55.77, 51.77, 46.30. HRMS (ESI) m/z: calculated for $C_{15}H_{15}BrN_2O_2$ $[M+Na]^+$: 335.03952, found 335.03778.

4.14. The Synthesis of Compound 4-14

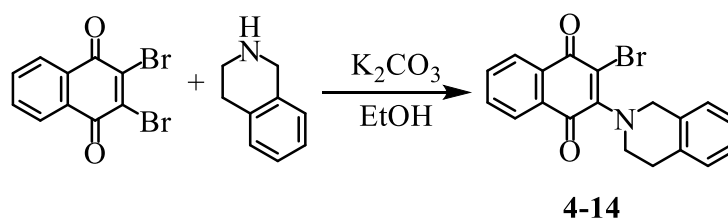


Figure 4.14. The synthesis of compound 4-14.

To 5 min. pre-stirred mixture of 1,2,3,4-tetrahydroisoquinoline (0.09 g, 0.79 mmol) and K_2CO_3 (0.11g, 0.79 mmol) in EtOH, 2,3-dibromo-1,4-naphthoquinone (0.25 g, 0.79 mmol) was added. The reaction was carried out at room temperature. After 24 hours, the reaction ceased with the addition of water. The obtained solid was filtered (Figure 4.14). It was crystallized from ethanol. Orange solid (0.11 g, 38 %). ^1H NMR (300 MHz, $CDCl_3$): δ 8.16 - 8.08 (m, 1H), 8.06 - 7.97 (m, 1H), 7.70 - 7.62 (m, 2H), 7.20 - 7.16 (m, 3H), 7.10 - 7.04 (m, 1H), 4.81 (s, 2H), 3.87 (t, J = 5.8 Hz, 2H), 3.18 (t, J = 5.7 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 182.03, 178.35, 153.04, 134.30, 134.08, 133.81, 133.29, 131.66, 131.52, 129.35, 127.22, 127.12, 126.91, 126.35, 126.27, 116.32, 54.51, 49.85, 29.72. HRMS (ESI) m/z : calculated for $C_{19}H_{14}BrNO_2$ $[M+Na]^+$: 368.02862, found 368.01052.

4.15. The Synthesis of Compound 4-15

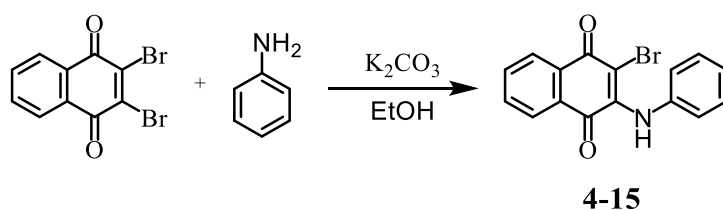


Figure 4.15. The synthesis of compound 4-15.

Anilin (0.15 g, 1.58 mmol) and K_2CO_3 (0.22 g, 1.58 mmol) in a round bottom flask were stirred in 20 mL EtOH for 10 min., and 2,3-dibromonaphthalene-1,4-dione (0.50 g, 1.58 mmol) was then added to the mixture. It was refluxed overnight. The reaction mixture was poured into water and extracted with EtOAc (3x50 mL) (Figure 4.15). The solvents were evaporated under vacuum. The crude product was purified by SiO_2 column chromatography with EtOAc:Hexane (10:90) red solid (0.44 g, 85 %). ^1H NMR (300 MHz, $CDCl_3$) δ 8.18 (dd, J = 7.7, 1.5 Hz, 1H), 8.09 (dd, J = 7.4, 1.6 Hz,

1H), 7.83 - 7.59 (m, 3H), 7.43 - 7.30 (m, 2H), 7.29 - 7.17 (m, 1H), 7.16 - 7.06 (m, 2H). ¹³C NMR (75 MHz, CDCl₃) δ 180.29, 177.57, 144.42, 137.68, 135.19, 133.15, 132.62, 130.09, 128.74, 127.66, 127.30, 126.02, 124.98, 107.89. HRMS (ESI) m/z: calculated for C₁₆H₁₀BrNO₂ [M+Na]⁺: 349.97926, found 349.97862.

4.16. The Synthesis of Compound 4-16

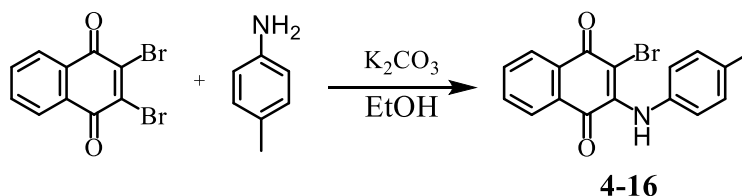


Figure 4.16. The synthesis of compound 4-16.

p-Toluidine (0.09 g, 0.79 mmol) and K₂CO₃ (0.11 g, 0.79 mmol) in a round bottom flask were stirred in 10 mL EtOH for 10 min., and 2,3-dibromonaphthalene-1,4-dione (0.25 g, 0.79 mmol) was then added to the mixture. It was refluxed overnight. The reaction mixture was poured into water and extracted with EtOAc (3x50 mL) (Figure 4.16). The solvents were evaporated under vacuum. The crude product was purified by SiO₂ column chromatography with EtOAc:Hexane (10:90) red solid (0.22 g, 81 %). ¹H NMR (300 MHz, CDCl₃) δ 8.19 (dd, *J* = 7.6, 1.4 Hz, 1H), 8.10 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.91 - 7.59 (m, 3H), 7.15 (d, *J* = 8.1 Hz, 2H), 7.00 (d, *J* = 8.2 Hz, 2H), 2.36 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 180.32, 177.52, 144.49, 136.04, 135.17, 135.07, 133.05, 132.68, 130.06, 129.32, 127.61, 127.26, 125.06, 107.05, 21.32. HRMS (ESI) m/z: calculated for C₁₇H₁₂BrNO₂ [M+Na]⁺: 363.99491, found 363.99439.

4.17. The Synthesis of Compound 4-17

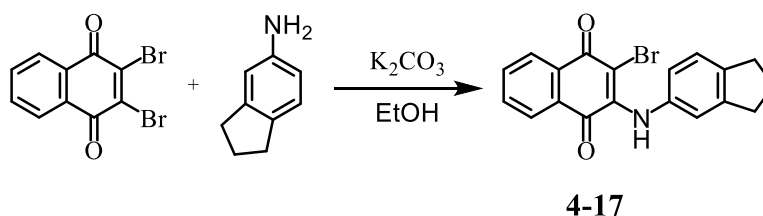


Figure 4.17. The synthesis of compounds 4-17.

5-aminoindan (0.12 g, 0.79 mmol) and K₂CO₃ (0.11 g, 0.79 mmol) in a round bottom flask were stirred in 10 mL EtOH for 10 min., and 2,3-dibromonaphthalene-1,4-dione (0.25 g, 0.79 mmol) was then added to the mixture. It was refluxed overnight. The

reaction mixture was poured into water and extracted with EtOAc (3x50 mL) (Figure 4.17). The solvents were evaporated under vacuum. The crude product was purified by SiO₂ column chromatography with EtOAc:Hexane (10:90) dark red solid (0.26 g, 89 %). ¹H NMR (300 MHz, CDCl₃): δ 8.24 - 8.17 (m, 1H), 8.15 - 8.06 (m, 1H), 7.81 - 7.63 (m, 3H), 7.18 (d, *J* = 7.9 Hz, 1H), 6.96 (d, *J* = 2.1 Hz, 1H), 6.88 (dd, *J* = 7.8, 2.2 Hz, 1H), 2.91 (t, *J* = 7.4 Hz, 6H), 2.11 (p, *J* = 7.5 Hz, 2H). ¹³C NMR (75 MHz, CDCl₃): δ 180.40, 177.56, 145.01, 144.57, 142.40, 135.70, 135.17, 133.02, 132.74, 130.09, 127.61, 127.26, 124.25, 123.06, 121.17, 106.91, 33.15, 32.71, 25.79. HRMS (ESI) *m/z*: calculated for C₁₉H₁₄BrNO₂ [M+Na]⁺: 390.01056, found 390.00971.

4.18. The Synthesis of Compound 4-18

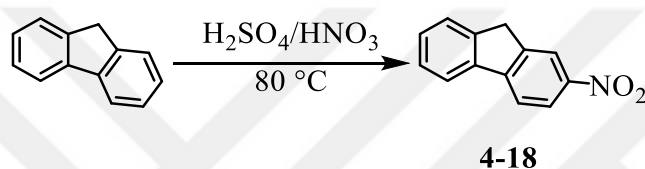


Figure 4.18. The synthesis of compound 4-18.

Into the solution of 9H-fluorene (4.9 g, 30 mmol) in 45 mL of glacial acetic acid at 60 °C, 7 mL of 65 % HNO₃ was dropped for 15 min with vigorous stirring. During the addition, the colour turned yellow, and some solids started to precipitate. The reaction mixture was allowed to stir at 80 °C. After completion of the reaction (Figure 4.18), the mixture was poured into plenty of water, and then, the solid was filtered off, washed with water, and recrystallized from ethanol to afford the product 2-nitro-9H-fluorene (6.12 g, 98 %). ¹H NMR (300 MHz, CDCl₃) δ 8.40 (s, 1H), 8.30 (d, *J* = 9.5 Hz, 1H), 7.87 (d, *J* = 8.3 Hz, 2H), 7.62 (d, *J* = 8.3 Hz, 1H), 7.53 - 7.38 (m, 2H), 4.01 (s, 2H). ¹³C NMR (75 MHz, CDCl₃) δ 148.31, 147.01, 145.04, 144.15, 139.71, 129.09, 127.67, 125.65, 123.36, 121.56, 120.71, 120.10, 37.20.

4.19. The Synthesis of Compound 4-19

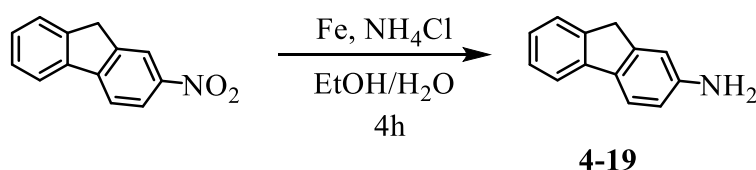


Figure 4.19. The synthesis of compound 4-19.

2-nitro-9*H*-fluorene 1 (2.0 g, 9.5 mmol), iron powder (1.60 g, 28.51 mmol), and NH₄Cl (1.11 g, 19 mmol) were stirred under an inert atmosphere at reflux for 5h. After completion of the reaction (Figure 4.19), saturated aqueous NaHCO₃ was added, and the resultant was filtered. All volatiles were evaporated. The resultant mixture was filtrated off to obtain 2-amino-9*H*-fluorene. ¹H NMR (300 MHz, CDCl₃): δ 7.64 (d, *J* = 7.5 Hz, 1H), 7.57 (d, *J* = 8.0 Hz, 1H), 7.47 (d, *J* = 8.3 Hz, 1H), 7.37 - 7.28 (m, 1H), 7.24 - 7.13 (m, 1H), 6.88 (d, *J* = 1.6 Hz, 1H), 6.71 (dd, *J* = 8.0, 2.2 Hz, 1H), 3.81 (s, 2H), 3.74 (s, 2H). ¹³C NMR (75 MHz, CDCl₃): δ 145.95, 145.39, 142.49, 142.35, 133.23, 126.86, 125.32, 124.99, 120.90, 118.82, 114.20, 112.05, 37.06.

4.20. The Synthesis of Compound 4-20

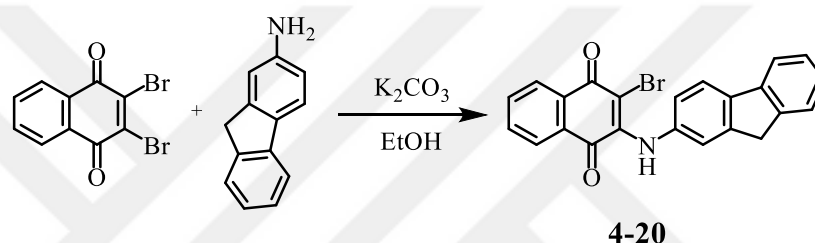


Figure 4.20. The synthesis of compound 4-20.

9*H*-fluoren-2-amine (0.16 g, 0.79 mmol) and K₂CO₃ (0.11 g, 0.79 mmol) in a round bottom flask were stirred in 10 mL EtOH for 10 min., and 2,3-dibromonaphthalene-1,4-dione (0.25 g, 0.79 mmol) was then added to the mixture. It was refluxed overnight. The reaction mixture was poured into water and extracted with EtOAc (3x50 mL) (Figure 4.20). The solvents were evaporated under vacuum. The crude product was purified by SiO₂ column chromatography with EtOAc:Hexane (10:90) maroon solid (0.32 g, 97 %). ¹H NMR (300 MHz, CDCl₃) δ 8.21 (dd, *J* = 7.5, 1.3 Hz, 1H), 8.11 (dd, *J* = 7.5, 1.3 Hz, 1H), 7.86 (bs, 1H), 7.82 - 7.61 (m, 4H), 7.54 (d, *J* = 7.9 Hz, 1H), 7.47 - 7.23 (m, 3H), 7.12 (dd, *J* = 8.1, 2.1 Hz, 1H), 3.90 (s, 2H). ¹³C NMR (75 MHz, CDCl₃) δ 180.38, 177.61, 144.38, 143.84, 143.52, 141.21, 139.86, 136.21, 135.25, 133.13, 132.70, 130.04, 127.67, 127.31, 127.19, 127.05, 125.31, 123.80, 121.74, 120.12, 119.83, 107.45, 37.20. HRMS (ESI) *m/z*: calculated for C₂₃H₁₄BrNO₂ [M+Na]⁺: 438.01056, found 438.01053.

4.21. The Synthesis of Compound 4-21

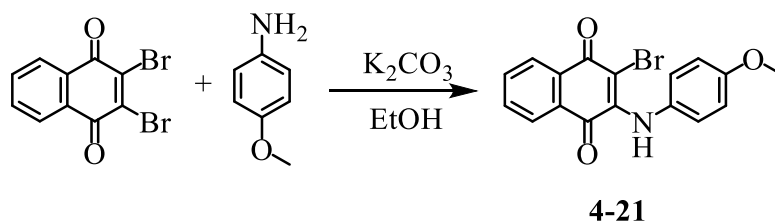


Figure 4.21. The synthesis of compound 4-21.

p-Anisidine (0.11 g, 0.79 mmol) and K_2CO_3 (0.11 g, 0.79 mmol) in a round bottom flask were stirred in 10 mL EtOH for 10 min., and 2,3-dibromonaphthalene-1,4-dione (0.25 g, 0.79 mmol) was then added to the mixture. It was refluxed overnight. The reaction mixture was poured into water and extracted with EtOAc (3x50 mL) (Figure 4.21). The solvents were evaporated under vacuum. The crude product was purified by SiO_2 column chromatography with EtOAc:Hexane (10:90) purple solid (0.26 g, 92 %). ^1H NMR (300 MHz, $CDCl_3$) δ 8.19 - 7.79 (m, 3H), 7.69 - 7.43 (m, 2H), 6.88 (d, J = 8.8 Hz, 2H), 6.68 (d, J = 8.7 Hz, 2H), 3.63 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO- d_6) δ 180.13, 177.27, 157.89, 144.80, 135.00, 132.88, 132.52, 130.62, 129.92, 127.21, 127.09, 126.92, 113.67, 105.52, 55.55. HRMS (ESI) m/z : calculated for $C_{17}H_{12}BrNO_3$ $[M+Na]^+$: 379.95085, found 379.99091.

4.22. The Synthesis of Compound 4-22

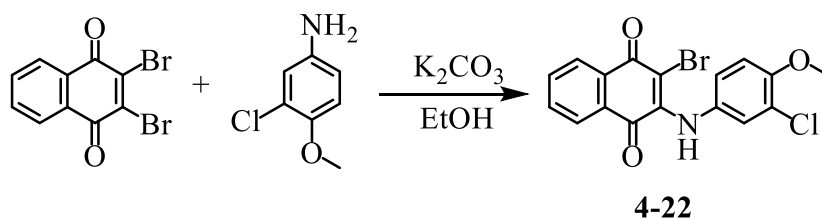


Figure 4.22. The synthesis of compound 4-22.

3-chloro-4-methoxyaniline (0.12 g, 0.79 mmol) and K_2CO_3 (0.11 g, 0.79 mmol) in a round bottom flask was stirred in 10 mL EtOH for 10 min., 2,3-dibromonaphthalene-1,4-dione (0.25 g, 0.79 mmol) was added to the mixture. It was refluxed overnight. The reaction mixture was poured into water and extracted with EtOAc (3x50 mL) (Figure 4.22). The solvents were evaporated under vacuum. The crude product was purified by SiO_2 column chromatography with EtOAc:Hexane (10:90) maroon solid (0.21 g, 68 %). ^1H NMR (300 MHz, $CDCl_3$) δ 8.03 (bs, 1H), 7.90 (dd, J = 14.5, 7.7

Hz, 2H), 7.58 - 7.43 (m, 2H), 6.96 (d, $J = 2.5$ Hz, 1H), 6.82 (d, $J = 8.9$ Hz, 1H), 6.70 (d, $J = 8.8$ Hz, 1H), 3.70 (s, 1H). ^{13}C NMR (75 MHz, $\text{DMSO-}d_6$) δ 180.36, 177.40, 152.50, 146.46, 135.45, 133.81, 133.01, 132.51, 130.83, 127.30, 127.03, 126.89, 125.35, 120.74, 112.61, 107.27, 56.93. HRMS (ESI) m/z : calculated for $\text{C}_{17}\text{H}_{11}\text{BrClNO}_3$ $[\text{M}+\text{Na}]^+$: 413.95085, found 413.95072.

4.23. The Synthesis of Compound 4-23

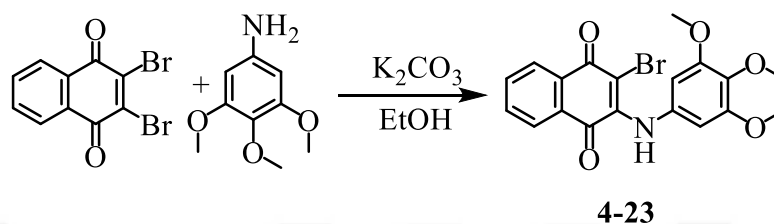


Figure 4.23. The synthesis of compound 4-23.

3,4,5-trimethoxyaniline (0.14 g, 0.79 mmol) and K_2CO_3 (0.11 g, 0.79 mmol) in a round bottom flask were stirred in 10 mL EtOH for 10 min., 2,3-dibromonaphthalene-1,4-dione (0.25 g, 0.79 mmol) was added to the mixture. It was refluxed overnight. The reaction mixture was poured into water and extracted with EtOAc (3x50 mL) (Figure 4.23). The solvents were evaporated under vacuum. The crude product was purified by SiO_2 column chromatography with EtOAc:Hexane (10:90) maroon solid (0.24 g, 73 %). ^1H NMR (300 MHz, CDCl_3) δ 8.19 (d, $J = 7.6$ Hz, 1H), 8.11 (d, $J = 7.5$ Hz, 1H), 7.93 - 7.61 (m, 3H), 6.34 (s, 2H), 3.86 (s, 3H), 3.84 (s, 6H). ^{13}C NMR (75 MHz, CDCl_3) δ 180.30, 177.61, 153.18, 144.28, 136.51, 135.28, 133.20, 132.68, 129.98, 127.69, 127.30, 125.09, 107.31, 103.16, 61.31, 56.45. HRMS (ESI) m/z : calculated for $\text{C}_{19}\text{H}_{16}\text{BrNO}_5$ $[\text{M}+\text{Na}]^+$: 440.01095, found 440.01168.

4.24. The Synthesis of Compound 4-24

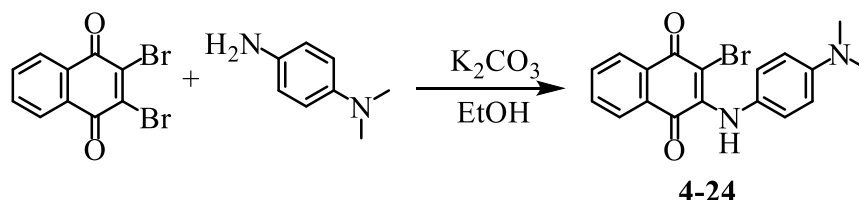


Figure 4.24. The synthesis of compound 4-24.

N,N-Dimethyl-*p*-phenylenediamine (0.11 g, 0.79 mmol) and K_2CO_3 (0.11 g, 0.79 mmol) in round bottom flask was stirred in 10 mL EtOH for 10 min., 2,3-

dibromonaphthalene-1,4-dione (0.25 g, 0.79 mmol) was added to the mixture. It was refluxed overnight. The reaction mixture was poured into water and extracted with EtOAc (3x50 mL) (Figure 4.24). The solvents were evaporated under vacuum. The crude product was purified by SiO₂ column chromatography with EtOAc:Hexane (10:90) maroon solid (0.24 g, 82 %). ¹H NMR (300 MHz, CDCl₃) δ 8.17 (d, *J* = 7.6 Hz, 1H), 8.08 (d, *J* = 7.5 Hz, 1H), 7.86 - 7.60 (m, 3H), 7.00 (d, *J* = 8.7 Hz, 2H), 6.66 (d, *J* = 8.9 Hz, 2H), 2.97 (s, 6H). ¹³C NMR (75 MHz, CDCl₃) δ 180.49, 177.40, 149.15, 144.51, 135.16, 132.93, 132.80, 130.00, 127.54, 127.20, 126.80, 126.47, 111.95, 104.98, 40.82. HRMS (ESI) *m/z*: calculated for C₁₈H₁₅BrN₂O₂ [M+H]⁺: 371.03952, found: 371.03947.

4.25. The Synthesis of Compound 4-25

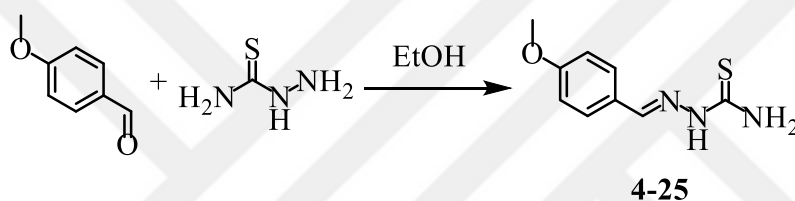


Figure 4.25. The synthesis of compound 4-25.

4-methoxybenzaldehyde (1 g, 7.34 mmol) and thiosemicarbazide (0.74 g, 8.07 mmol) were stirred in anhydrous alcohol (15 mL). The mixture was kept at rt. overnight. The formed solid was separated by filtration (Figure 4.25). The product was dried at room temperature and was used in the next reaction (1.50 g, 89 %). ¹H NMR (300 MHz, DMSO-*d*₆): δ 11.30 (s, 1H), 8.09 (s, 1H), 7.98 (s, 1H), 7.89 (s, 1H), 7.71 (d, *J* = 8.7 Hz, 2H), 6.94 (d, *J* = 8.7 Hz, 2H), 3.77 (s, 3H). ¹³C NMR (75 MHz, DMSO-*d*₆): δ 178.28, 161.37, 142.94, 129.61, 127.42, 114.85, 55.97.

4.26. The Synthesis of Compound 4-26

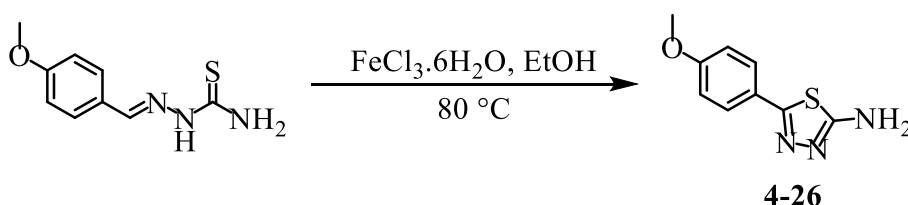


Figure 4.26. The synthesis of compound 4-26.

(*E*)-2-benzylidenehydrazine-1-carbothioamide (0.50 g, 2.39 mmol) was suspended in 15 mL of ethanol, to the stirring mixture of this suspension, solid FeCl₃·6H₂O (1.94 g, 7.17 mmol) was added with small portions, then was heated at 80 °C for 1.5 h. The reaction was cooled to room temperature and quenched by adding citric acid (5.51 g). The resultant was neutralized with an ammonia solution, which led to solid formation (Figure 4.26). The solid was separated by filtration to afford a white solid (0.25g, 51 %). ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.66 (d, *J* = 8.5 Hz, 2H), 7.28 (s, 2H), 7.00 (d, *J* = 8.5 Hz, 2H), 3.78 (s, 3H). ¹³C NMR (75 MHz, DMSO-*d*₆) δ 168.58, 160.96, 156.98, 128.50, 124.32, 115.20, 56.01.

4.27. The synthesis of Compound 4-27

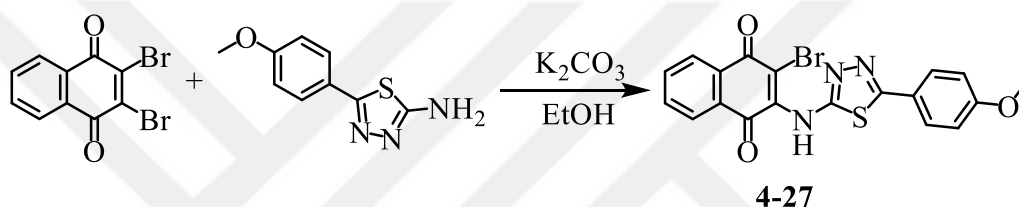


Figure 4.27. The synthesis of compound 4-27.

5-(4-methoxyphenyl)-1,3,4-thiadiazol-2-amine (0.17 g, 0.79 mmol) and K₂CO₃ (0.11 g, 0.79 mmol) in a round bottom flask were stirred in 10 mL EtOH for 10 min., 2,3-dibromonaphthalene-1,4-dione (0.25 g, 0.79 mmol) was added to the mixture. It was refluxed overnight. The reaction mixture was poured into water and extracted with EtOAc (3x50 mL) (Figure 4.27). The solvents were evaporated under vacuum. The crude product was purified by SiO₂ column chromatography with EtOAc:Hexane (10:90) shining orange-red solid (0.21 g, 60 %). ¹H NMR (300 MHz, CDCl₃) δ 8.27 - 8.17 (m, 1H), 8.16 - 8.03 (m, 1H), 7.83 (d, *J* = 8.8 Hz, 2H), 7.80 - 7.68 (m, 2H), 6.98 (d, *J* = 8.9 Hz, 2H), 3.87 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 178.80, 177.52, 165.70, 162.19, 160.75, 144.86, 135.28, 134.01, 131.79, 130.23, 129.24, 127.90, 127.61, 122.91, 117.28, 114.80, 55.75. HRMS (ESI) *m/z*: calculated for C₁₉H₁₂BrN₃O₃S [M+Na]⁺: 463.96804, found 463.96704.

4.28. The Synthesis of Compound 4-28

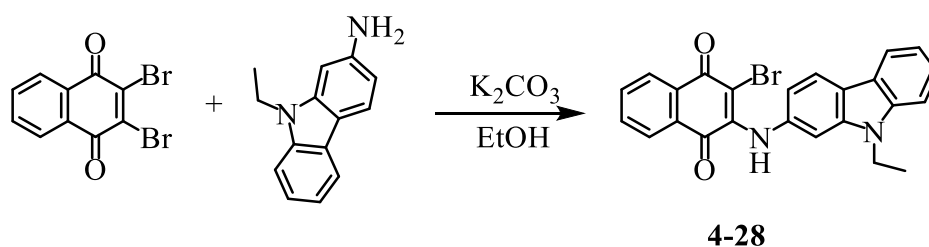


Figure 4.28. The synthesis of compound 4-28.

9-ethyl-9H-carbazol-3-amine (0.16 g, 0.79 mmol) and K_2CO_3 (0.11 g, 0.79 mmol) in a round bottom flask was stirred in 10 mL EtOH for 10 min., 2,3-dibromonaphthalene-1,4-dione (0.25 g, 0.79 mmol) was added to the mixture. It was refluxed overnight. The reaction mixture was poured into water and extracted with EtOAc (3x50 mL) (Figure 4.28). The solvents were evaporated under vacuum. The crude product was purified by SiO_2 column chromatography with EtOAc:Hexane (10:90) dark blue solid (0.32 g, 91 %). mp. 215 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 8.21 (d, J = 7.6 Hz, 1H), 8.12 (d, J = 7.5 Hz, 1H), 8.04 (d, J = 8.1 Hz, 2H), 7.85 (bs, 1H), 7.82 - 7.63 (m, 2H), 7.58 - 7.33 (m, 3H), 7.30 - 7.16 (m, 2H), 4.38 (q, J = 7.0 Hz, 2H), 1.47 (t, J = 6.9 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 180.54, 177.59, 144.71, 140.85, 138.52, 135.20, 132.92, 130.08, 129.18, 128.43, 127.61, 127.26, 126.45, 124.03, 122.87, 122.79, 120.90, 119.38, 117.83, 109.00, 108.23, 105.57, 38.02, 14.12. HRMS (ESI) m/z : calculated for $C_{16}H_{10}BrNO_2$ $[M+Na]^+$: 467.03711, found 467.03702.

4.29. The Synthesis of Compound 4-29

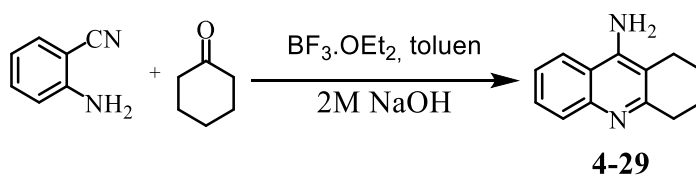


Figure 4.29. The synthesis of compound 4-29.

To a mixture of 2-aminobenzonitrile (1.18 g, 10.0 mmol) and cyclohexanone (1.08 g, 11.0 mmol) in toluene (12 mL) placed in a round bottom flask connected to a reflux condenser was added $BF_3 \cdot OEt_2$ (1.48 mL, 12.0 mmol). The mixture was refluxed for 24 h under stirring. After cooling to room temperature, the remaining solids were treated with 15 mL 2M NaOH solution, and this mixture was heated at reflux for 24 h. On cooling to room temperature, the reaction mixture was extracted with $CHCl_3$ (3x25

mL), and the organic layers were combined and dried over Na₂SO₄. The solvent was evaporated under reduced pressure to give the desired product (1.78g, 90 %) (Figure 4.29). ¹H NMR (300 MHz, DMSO-*d*₆) δ 8.12 (d, *J* = 8.4 Hz, 1H), 7.60 (d, *J* = 8.4 Hz, 1H), 7.46 (t, 1H), 7.26 (t, 1H), 6.36(bs, 2H), 2.80 (t, *J* = 5.5 Hz, 2H), 2.53 (t, *J* = 5.8 Hz, 2H), 2.12 - 1.50 (m, 4H). ¹³C NMR (75 MHz, DMSO-*d*₆) δ 157.93, 148.97, 146.71, 128.72, 128.26, 123.33, 122.57, 117.62, 109.53, 34.04, 24.32, 23.25, 23.18. [209].

4.30. The Synthesis of Compound 4-30

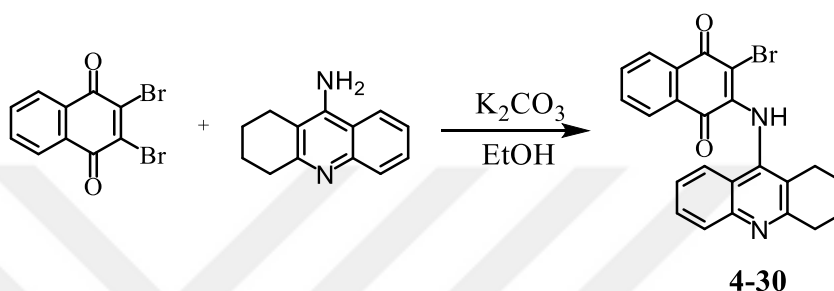


Figure 4.30. The synthesis of compound 4-30.

9-amino-1,2,3,4-tetrahydroacridine, tacrine (0.11 g, 0.55 mmol) and K₂CO₃ (0.08 g, 0.55 mmol) in the round bottom flask were stirred in 10 mL EtOH for 10 min., 2,3-dibromonaphthalene-1,4-dione (0.18 g, 0.55 mmol) was added to the mixture. It was refluxed overnight. The reaction mixture was poured into water and extracted with EtOAc (3x50 mL) (Figure 4.30). The solvents were evaporated under vacuum. The crude product was purified by SiO₂ column chromatography with EtOAc:Hexane (10:90) red solid (0.21 g, 87 %). ¹H NMR (300 MHz, DMSO-*d*₆) δ 8.41 (d, *J*=8.5 Hz, 1H), 7.98-7.26 (m, 7H), 2.94-2.90 (m, 2H), 2.69-2.34 (m, 2H), 2.05-1.40 (m, 4H) ¹³C NMR (75 MHz, DMSO-*d*₆) δ 184.23, 174.25, 168.34, 156.07, 151.99, 137.62, 135.73, 134.24, 133.65, 131.15, 126.24, 126.13, 123.89, 119.73, 115.38, 109.84, 106.30, 28.46, 23.20, 21.68, 21.19. HRMS (ESI) *m/z*: calculated for C₂₃H₁₇BrN₂O₂ [M+H+HCOOH]⁺: 479.06064, found 479.16322.

4.31. The Synthesis of Compound 4-31

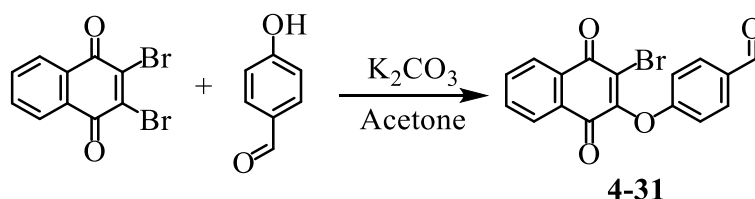


Figure 4.31. The synthesis of compounds 4-31.

4-hydroxybenzaldehyde (0.39 g, 3.16 mmol) and K_2CO_3 (0.22 g, 3.16 mmol) in a round bottom flask were stirred in 30 mL acetone for 10 min., 2,3-dibromonaphthalene-1,4-dione (1.00 g, 3.16 mmol) were added to the mixture. The reaction ceased after 2 days. The mixture was poured into water, and the obtained solid was applied to SiO_2 column chromatography with hexane: $CHCl_3$ (90:10) Yellow solid (1.11 g, 97 %) (Figure 4.31). ^1H NMR (300 MHz, $CDCl_3$) δ 9.95 (s, 1H), 8.23 (dd, J = 7.0, 2.0 Hz, 1H), 8.06 (dd, J = 6.6, 2.5 Hz, 1H), 7.89 (d, J = 8.8 Hz, 2H), 7.80 (dd, J = 6.4, 2.9 Hz, 2H), 7.13 (d, J = 8.7 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 190.71, 178.31, 177.17, 160.83, 155.45, 135.03, 134.85, 132.71, 132.22, 131.32, 130.67, 129.05, 128.09, 127.65, 117.11. HRMS (ESI) m/z : calculated for $C_{17}H_9BrO_4$ $[M+H+HCOONa]^+$: 424.96367, found 424.99944.

4.32. The Synthesis of Compound 4-32

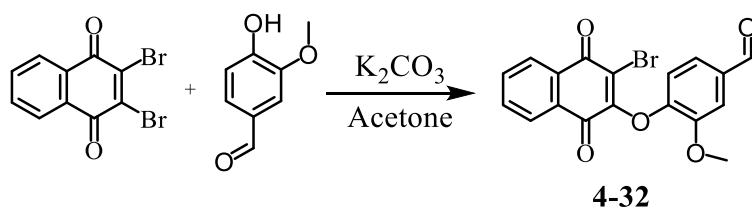


Figure 4.32. The synthesis of compound 4-32.

Vanillin (0.24 g, 1.58 mmol) and K_2CO_3 (0.22 g, 1.58 mmol) in a round bottom flask were stirred in 20 mL acetone for 10 min., 2,3-dibromonaphthalene-1,4-dione (0.50 g, 1.58 mmol) was added to the mixture. The reaction was ceased after 2 days. The mixture was poured into water, and the obtained solid was applied to SiO_2 column chromatography with hexane: $CHCl_3$ (90:10). Yellow solid (0.47 g, 77 %) (Figure 4.32). ^1H NMR (300 MHz, $CDCl_3$) δ 9.92 (s, 1H), 8.21 (d, J = 8.8 Hz, 1H), 8.00 (d, J = 8.8 Hz, 1H), 7.88 - 7.71 (m, 2H), 7.57 - 7.43 (m, 2H), 7.33 - 7.18 (m, 1H), 3.81 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 190.98, 178.63, 176.85, 157.07, 150.67, 149.80,

134.89, 134.57, 133.58, 131.30, 130.46, 127.90, 127.37, 126.07, 123.05, 118.63, 111.41, 56.67. HRMS (ESI) m/z : calculated for $C_{18}H_{11}BrO_5$ $[M+H+HCOONa]^+$: 454.97424, found 455.01045.

4.33. The Synthesis of Compound 4-33

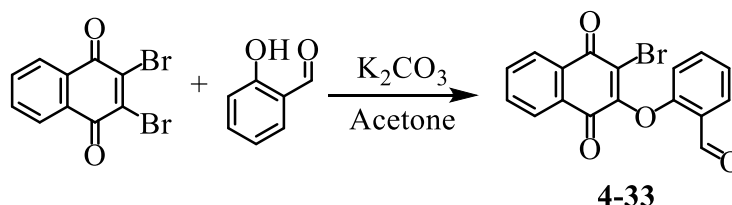


Figure 4.33. The synthesis of compound 4-33.

Salicylaldehyde (0.24 g, 1.58 mmol) and K_2CO_3 (0.22 g, 1.58 mmol) in a round bottom flask were stirred in 20 mL acetone for 10 min., 2,3-dibromonaphthalene-1,4-dione (0.50 g, 1.58 mmol) was added to the mixture. The reaction ceased after 2 days. The mixture was poured into water, and the obtained solid was applied to SiO_2 column chromatography with hexane: $CHCl_3$ (90:10). Yellow solid (0.48 g, 85 %). (Figure 4.33). ^1H NMR (300 MHz, $CDCl_3$): δ 10.58 (s, 1H), 8.23 (d, $J = 8.9$ Hz, 1H), 8.11 - 7.94 (m, 2H), 7.86 - 7.70 (m, 2H), 7.49 (t, $J = 7.5$ Hz, 1H), 7.27 (t, $J = 7.5$ Hz, 1H), 6.83 (d, $J = 8.3$ Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 188.86, 178.37, 177.48, 158.43, 155.86, 135.76, 135.05, 134.83, 131.29, 130.57, 129.57, 128.60, 128.08, 127.60, 125.93, 124.80, 116.64. HRMS (ESI) m/z : calculated for $C_{17}H_9BrO_4$ $[M+H+HCOONa]^+$: 424.96367, found 424.99954.

4.34. The Synthesis of BODIPY

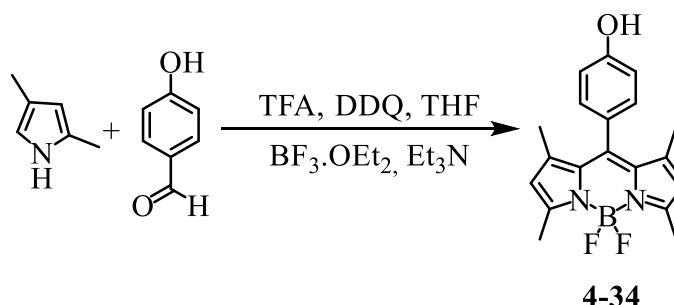


Figure 4.34. The synthesis of BODIPY.

In a round balloon, 2,4-dimethylpyrrole (0.78, 8.18 mmol) and 4-hydroxy benzaldehyde (0.5 g, 4.09 mmol) were mixed in 50 mL THF under nitrogen

atmosphere, and then after adding a few drops of TFA. The resultant mixture was stirred overnight. DDQ in 50 mL THF was dropped into this solution by the dropping funnel over 30 min, and the reaction was carried out for 2 hours. 6.4 mL Et₃N was added to the reaction balloon placed in an ice bath, and the stirring continued for 30 min. Finally, After the addition of 7 mL BF₃.OEt₂ dropwisely, it was stirred for 12h. After the evaporation of the solvent, the semi-solid residue was purified through SiO₂ column chromatography by eluation of EtOAc: Hexane (20:80). 0.8 g pure product was obtained with % 57 yields as an orange-red solid (Figure 4.34). ¹H NMR (300MHz, CDCl₃) δ 7.12 (d, *J* = 8.7 Hz, 2H), 6.96 (d, *J* = 8.7 Hz, 2H), 6.00 (s, 2 H), 5.30 (br. s., 1H), 2.58 (s, 6H), 1.46 (s, 6H). ¹³C NMR (75 MHz, CDCl₃) δ 156.27, 155.32, 143.21, 141.74, 131.82, 129.40, 127.20, 121.18, 116.12, 14.59.

4.35. The Synthesis of Compound 4-35

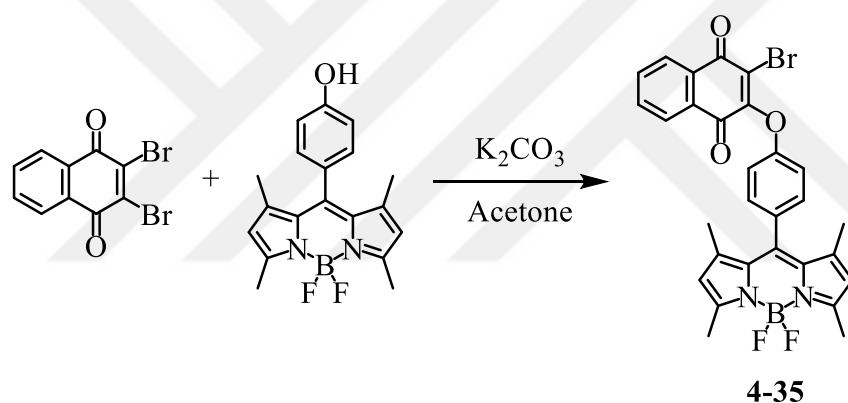


Figure 4.35. The synthesis of compound 4-35.

BODIPY (0.39 g, 1.14 mmol) and K₂CO₃ (0.16 g, 1.14 mmol) in a round bottom flask were stirred in 20 mL acetone for 10 min., 2,3-dibromonaphthalene-1,4-dione (0.36 g, 1.14 mmol) was added to the mixture. The reaction ceased after 2 days. The mixture was poured into water, and it was extracted with EtOAc (3x75 mL). All solvents were evaporated, and the solid left was loaded into SiO₂. 0.51 g pure solid was gained as a shining green solid with a yield of % 78 by column chromatography with an EtOAc-hexane gradient (Figure 4.35). ¹H NMR (300 MHz, CDCl₃) δ 8.23 (d, *J* = 9.0 Hz, 1H), 8.07 (d, *J* = 9.0 Hz, 1H), 7.95 - 7.64 (m, 2H), 7.25 (d, *J* = 8.7 Hz, 2H), 7.14 (d, *J* = 8.7 Hz, 2H), 5.99 (s, 2H), 2.54 (s, 6H), 1.48 (s, 6H). ¹³C NMR (75 MHz, CDCl₃) δ 178.55, 177.47, 157.04, 156.14, 155.87, 143.39, 140.84, 134.90, 134.72, 131.75, 131.24, 130.83, 130.79, 129.83, 128.04, 127.98, 127.52, 121.62, 117.93, 14.95, 14.84. ¹⁹F

NMR (282 MHz, CDCl₃) δ -146.63 (q, $J_{\text{BF}} = 31.2$ Hz). HRMS (ESI) m/z : calculated for C₂₉H₂₃BF₂N₂O₄ [M+Na]⁺: 597.07726, found 597.07806.

4.36. The Synthesis of Compound 4-36

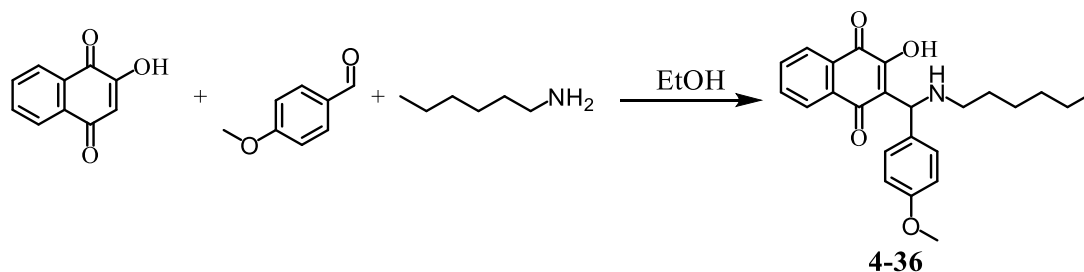


Figure 4.36. The synthesis of compound 4-36.

To 2-hydroxy-1,4-naphthoquinone (0.25 g, 1.44 mmol) suspended in ethanol (10 mL), hexylamine (0.15g, 1.44 mmol) was added. The mixture turned red after the addition of amine. After 5 min. *p*-anisaldehyde (0.20 g, 1.44 mmol) was added to the solution. The mixture was stirred overnight and filtered (Figure 4.36). The compounds were recrystallized from ethanol. Orange solid (0.45 g, 80 %). ¹H NMR (CDCl₃ + DMSO-*d*₆): δ 0.50 (t, $J = 6.5$ Hz, 3H), 0.90 (m, 6H), 1.34 (m, 2H), 2.54 (m, 2H), 3.40 (s, 3H), 5.12 (s, 1H), 6.46 (d, $J = 8.5$ Hz, 2H), 7.13-7.28 (m, 4H), 7.59 (t, $J = 6.9$ Hz, 2H), 8.70 (bs, 1H), 10.31 (bs, 1H). ¹³C NMR (CDCl₃ + DMSO-*d*₆): δ 13.9, 22.3, 26.1, 26.42, 31.1, 46.5, 55.2, 60.2, 112.0, 114.0, 125.4, 125.8, 129.4, 130.4, 130.9, 131.7, 133.6, 134.4, 159.6, 170.6, 180.4, 184.8. HRMS (ESI) m/z : calculated for C₂₄H₂₇NO₄ [M+H]⁺: 394.20183, found 394.20165.

4.37. The Synthesis of Compound 4-37

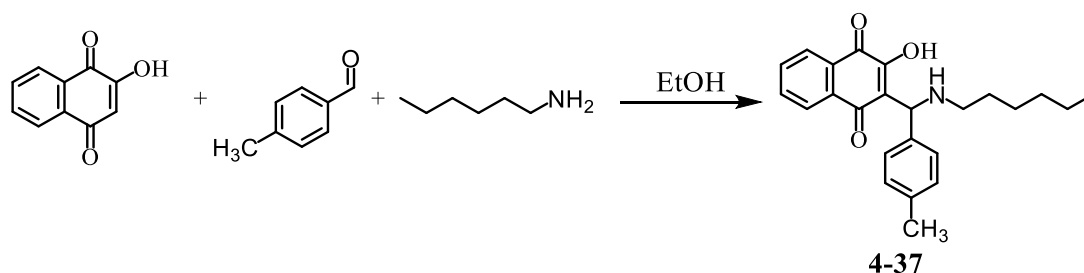


Figure 4.37. The synthesis of compound 4-37.

To 2-hydroxy-1,4-naphthoquinone (0.25 g, 1.44 mmol) suspended in ethanol (10 mL), hexylamine (0.15g, 1.44 mmol) was added. The mixture turned red after the addition

of amine. After 5 min. *p*-tolualdehyde (0.20 g, 1.44 mmol) was added to the solution. The mixture was stirred overnight and filtered (Figure 4.37). The compounds were recrystallized from ethanol. Orange solid (0.17 g, 31 %). ^1H NMR ($\text{CDCl}_3 + \text{DMSO}-d_6$): 0.14 (t, $J = 6.4$ Hz, 3H), 0.77 - 0.38 (m, 6H), 1.20 - 0.79 (m, 3H), 1.56 (s, 3H), 4.80 (s, 1H), 6.38 (d, $J = 7.7$ Hz, 2H), 6.77-6.19 (m, 4H), 7.22 (t, $J = 8.1$ Hz, 2H), 8.53 (bs, 1H), 9.90 (bs, 1H). ^{13}C NMR ($\text{CDCl}_3 + \text{DMSO}-d_6$): 14.0, 21.1, 22.3, 26.2, 26.4, 31.1, 46.5, 60.3, 112.0, 125.5, 126.0, 127.9, 129.3, 131.0, 131.6, 133.7, 134.4, 135.3, 138.2, 170.5, 180.6, 184.8. HRMS (ESI) m/z : calculated for $\text{C}_{24}\text{H}_{27}\text{NO}_3$ $[\text{M}+\text{H}]^+$: 378.20692, found 378.20712.

4.38. The Synthesis of Compound 4-38

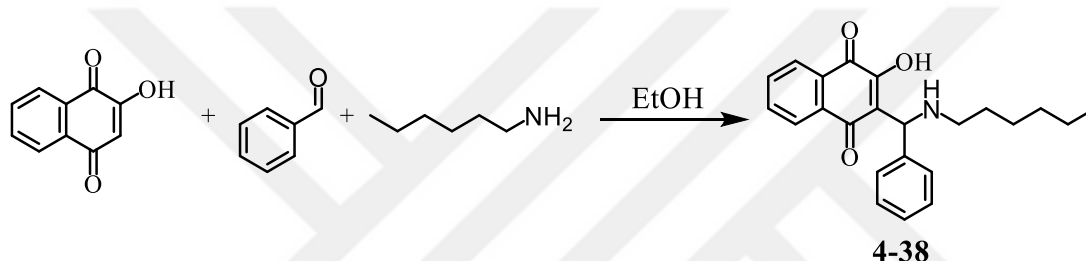


Figure 4.38. The synthesis of compound 4-38.

To 2-hydroxy-1,4-naphthoquinone (0.25 g, 1.44 mmol) suspended in ethanol (10 mL), hexylamine (0.15g, 1.44 mmol) was added. The mixture turned red after the addition of amine. After 5 min. benzaldehyde (0.20 g, 1.44 mmol) was added to the solution. The mixture was stirred overnight and filtered (Figure 4.38). The compounds were recrystallized from ethanol. Orange solid (0.41 g, 78 %). ^1H NMR ($\text{CDCl}_3 + \text{DMSO}-d_6$): 0.02 (t, $J = 5.9$ Hz, 3H), 0.69 - 0.30 (m, 6H), 1.06 - 0.70 (m, 2H), 2.43 (s, 2H), 4.70 (s, 1H), 6.49-6.43 (m, 3H), 6.93-6.57 (m, 4H), 7.15-7.08 (m, 2H), 8.42 (s, 1H), 9.82 (s, 1H). ^{13}C NMR ($\text{CDCl}_3 + \text{DMSO}-d_6$): 13.9, 22.1, 26.2, 31.0, 46.5, 60.2, 111.5, 125.3, 125.7, 127.8, 128.3, 128.6, 130.9, 131.5, 133.6, 134.3, 138.4, 170.5, 180.3, 184.6. HRMS (ESI) m/z : calculated for $\text{C}_{23}\text{H}_{25}\text{NO}_3$ $[\text{M}+\text{H}]^+$: 364.19127, found 364.19147.

4.39. The Synthesis of Compound 4-39

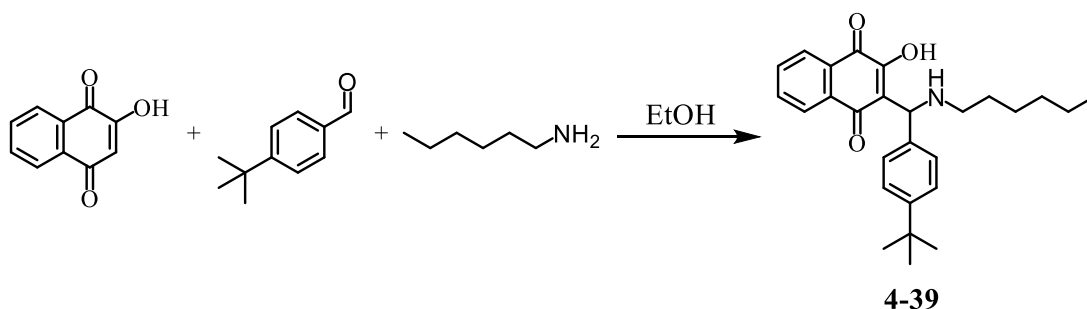


Figure 4.39. The synthesis of compound 4-39.

To 2-hydroxy-1,4-naphthoquinone (0.25 g, 1.44 mmol) suspended in ethanol (10 mL), hexylamine (0.15g, 1.44 mmol) was added. The mixture turned red after the addition of amine. After 5 min. t-butylbenzaldehyde (0.23 g, 1.44 mmol) was added to the solution. The mixture was stirred overnight and filtered (Figure 4.39). The compounds were recrystallized from ethanol. Orange solid (0.35 g, 58 %). ^1H NMR (CDCl_3 + DMSO-d_6): 0.69 (t, J = 6.5 Hz, 3H), 1.31 - 0.85 (m, 15H), 1.90 - 1.33 (m, 2H), 3.06 - 2.56 (m, 2H), 5.35 (s, 1H), 7.10 (d, J = 8.4 Hz, 2H), 7.47 - 7.22 (m, 4H), 7.73 (t, J = 6.9 Hz, 2H), 9.04 (bs, 1H), 10.53 (bs, 1H). ^{13}C NMR (CDCl_3 + DMSO-d_6): 22.4, 26.4, 26.7, 31.3, 31.3, 34.6, 112.4, 125.6, 125.8, 126.1, 127.8, 131.1, 131.6, 133.8, 134.5, 135.1, 151.5, 170.4, 181.0, 185.0. HRMS (ESI) m/z : calculated for $\text{C}_{24}\text{H}_{27}\text{NO}_4$ $[\text{M}+\text{H}]^+$: 420.25387, found 420.25376.

4.40. The Synthesis of Compound 4-40

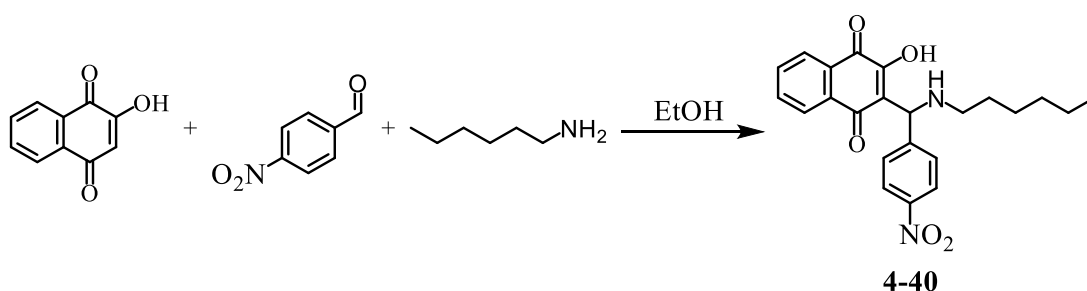


Figure 4.40. The synthesis of compound 4-40.

To 2-hydroxy-1,4-naphthoquinone (0.25 g, 1.44 mmol) suspended in ethanol (10 mL), hexylamine (0.15g, 1.44 mmol) was added. The mixture turned red after the addition of amine. After 5 min. 4-nitrobenzaldehyde (0.21 g, 1.44 mmol) was added to the solution. The mixture was stirred overnight and filtered (Figure 4.40). The compounds

were recrystallized from ethanol. Yellow solid (0.51 g, 58 %). ^1H NMR ($\text{CDCl}_3 + \text{DMSO-d}_6$): 0.09 (t, $J = 6.4$ Hz, 3H), 0.74 - 0.40 (m, 6H), 1.25 - 0.80 (m, 2H), 2.39 (s, 2H), 5.04 (s, 1H), 6.91-6.75 (m, 4H), 7.46 - 7.07 (m, 2H), 9.06 (bs, 1H), 9.66 (bs, 1H). ^{13}C NMR ($\text{CDCl}_3 + \text{DMSO-d}_6$): 13.9, 22.3, 26.2, 26.4, 31.1, 46.7, 59.0, 110.7, 123.5, 125.6, 126.1, 128.6, 131.2, 131.5, 133.9, 134.3, 145.3, 147.2, 170.6, 180.6, 184.6. HRMS (ESI) m/z : calculated for $\text{C}_{23}\text{H}_{24}\text{N}_2\text{O}_5$ $[\text{M}+\text{H}]^+$: 409.17635, found 409.17596.

4.41. The Synthesis of Compound 4-41

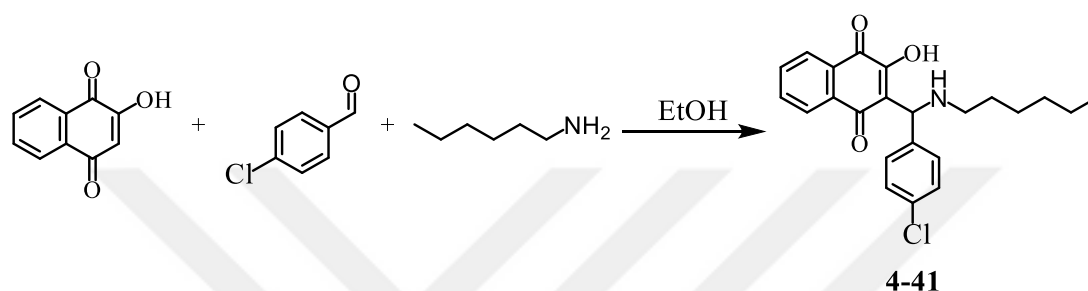


Figure 4.41. The synthesis of compound 4-41.

To 2-hydroxy-1,4-naphthoquinone (0.25 g, 1.44 mmol) suspended in ethanol (10 mL), hexylamine (0.15g, 1.44 mmol) was added. The mixture turned red after the addition of amine. After 5 min. 4-chlorobenzaldehyde (0.20 g, 1.44 mmol) was added to the solution. The mixture was stirred overnight and filtered (Figure 4.41). The compounds were recrystallized from ethanol. Orange solid (0.50 g, 88 %). ^1H NMR ($\text{CDCl}_3 + \text{DMSO-d}_6$): 0.63 (t, $J = 6.6$ Hz, 3H), 1.30 - 0.74 (m, 6H), 1.74 - 1.24 (m, 2H), 2.79 - 2.59 (m, 2H), 5.35 (s, 1H), 7.02 (d, $J = 8.4$ Hz, 2H), 7.42-7.28 (m, 4H), 7.73 (t, $J = 7.8$ Hz, 1H), 9.22 (bs, 1H), 10.35 (bs, 1H). ^{13}C NMR ($\text{CDCl}_3 + \text{DMSO-d}_6$): 14.0, 22.4, 26.3, 26.6, 31.2, 46.7, 59.9, 111.6, 125.6, 126.1, 128.8, 129.5, 131.2, 131.6, 133.9, 134.1, 134.4, 136.8, 170.6, 180.9, 184.9. HRMS (ESI) m/z : calculated for $\text{C}_{23}\text{H}_{24}\text{ClNO}_3$ $[\text{M}+\text{H}]^+$: 398.15239, found 398.15217.

4.42. The Synthesis of Compound 4-42

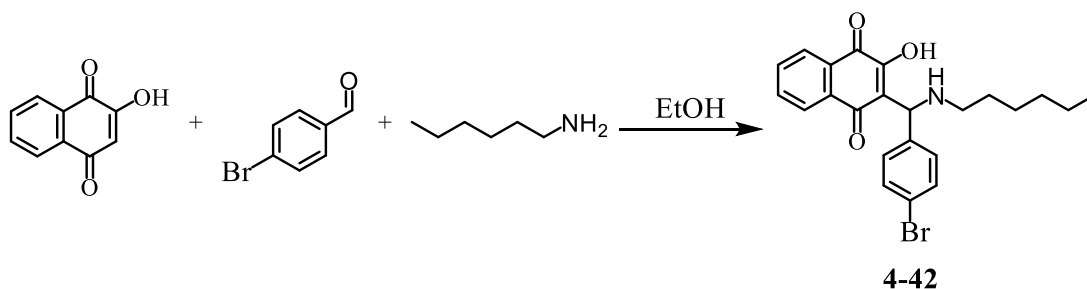


Figure 4.42. The synthesis of compound 4-42.

To 2-hydroxy-1,4-naphthoquinone (0.25 g, 1.44 mmol) suspended in ethanol (10 mL), hexylamine (0.15g, 1.44 mmol) was added. The mixture turned red after the addition of amine. After 5 min. 4-bromobenzaldehyde (0.26 g, 1.44 mmol) were added to the solution (Figure 4.42). The mixture was stirred overnight and filtered. The compounds were recrystallized from ethanol. Yellow solid (0.57 g, 90 %). ^1H NMR ($\text{CDCl}_3 + \text{DMSO-d}_6$): 0.19 (t, $J = 6.5$ Hz, 3H), 0.83 - 0.41 (m, 6H), 1.10-0.99 (m, 2H), 2.45 - 2.12 (m, 2H), 4.92 (s, 1H), 6.72 (d, $J = 8.5$ Hz, 2H), 7.05 - 6.82 (m, 4H), 7.51 - 7.17 (m, 2H), 8.96 (bs, 1H), 9.84 (bs, 1H). ^{13}C NMR ($\text{CDCl}_3 + \text{DMSO-d}_6$): 14.0, 22.4, 26.2, 26.5, 31.2, 46.7, 59.8, 111.6, 122.3, 125.6, 126.1, 129.8, 131.2, 131.6, 131.7, 133.9, 134.4, 137.3, 170.4, 180.9, 184.8. HRMS (ESI) m/z : calculated for $\text{C}_{23}\text{H}_{24}\text{BrNO}_3$ $[\text{M}+\text{H}]^+$: 442.10178, found 442.10192.

4.43. The Synthesis of Compound 4-43

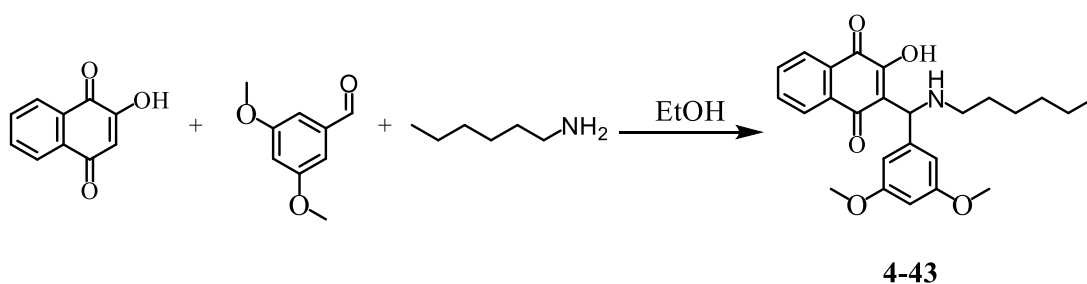


Figure 4.43. The synthesis of compound 4-43.

To 2-hydroxy-1,4-naphthoquinone (0.25 g, 1.44 mmol) suspended in ethanol (10 mL), hexylamine (0.15g, 1.44 mmol) was added. The mixture turned red after the addition of amine. After 5 min. 3,5-dimethoxybenzaldehyde (0.37 g, 1.44 mmol) was added to the solution. The mixture was stirred overnight and filtered (Figure 4.43). The compounds were recrystallized from ethanol. Yellow solid (0.51 g, 84 %). ^1H NMR

(CDCl₃+ DMSO-d₆): 0.44 (t, *J* = 6.6 Hz, 3H), 1.09 - 0.73 (m, 6H), 1.60 - 1.18 (m, 2H), 2.84 (s, 2H), 3.32 (s, 6H), 5.10 (s, 1H), 5.92 (s, 1H), 6.40 (s, 2H), 7.10 (t, *J* = 7.5 Hz, 1H), 7.21 (t, *J* = 7.5 Hz, 1H), 7.53 (dd, *J* = 16.6, 7.6 Hz, 2H), 8.93 (bs, 1H), 10.07 (bs, 1H). ¹³C NMR (CDCl₃ + DMSO-d₆): 13.9, 22.2, 26.1, 26.3, 31.0, 46.4, 60.3, 99.8, 106.0, 111.4, 125.4, 125.4, 125.8, 130.9, 131.6, 133.6, 134.4, 140.2, 160.8, 170.7, 180.5, 184.7. HRMS (ESI) *m/z*: calculated for C₂₅H₂₉NO₅ [M+H]⁺: 424.21240, found 424.21387.

4.44. The Photophysical Study

Photophysical features of all 1,4-naphthoquinone derivatives were evaluated by UV/vis spectroscopy and fluorescence spectroscopy methods. The solutions of 2-bromo-1,4-naphthoquinone derivatives were prepared in EtOAc. The solutions of Mannich base derivatives were prepared in DMSO. The concentration of the stock solutions was adjusted between 1x10⁻² and 5.6x10⁻³ M in the mentioned solvents. These solutions were diluted to 1x10⁻⁵ M with the solvent of the stock solution. The UV/vis spectra of the diluted solution of the compounds were recorded by using UV/vis spectrophotometry. The emission spectra of stock solutions of the compounds were recorded by using spectrofluorometry.

4.45. The Electrochemical Study

The electrochemical properties of the final compounds were studied by Cyclic voltammetry method. A three-electrode configuration consisting of a glacial carbon electrode, platinum wire electrode, and a silver/silver chloride electrode as the working electrode, a counter electrode, and the reference electrode were set up. The electrochemical behaviours of the dyes were investigated in DMSO containing TBAPF₆ as a supporting electrolyte at a 100 mV/s scan rate.

5. RESULTS AND DISCUSSION

5.1. Characterization of the Compounds by ^1H , ^{13}C , and ^{19}F NMR Methods

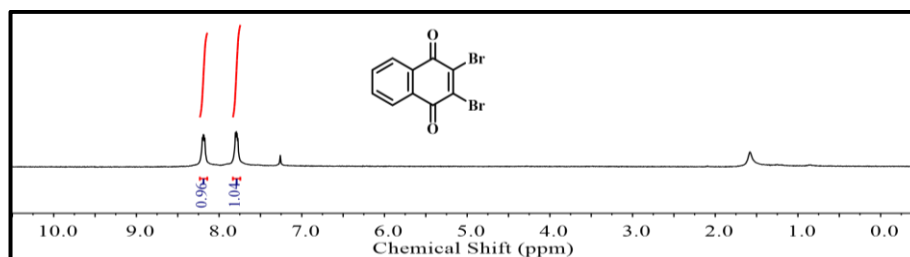


Figure 5.1. ^1H NMR spectrum of compound 4-1.

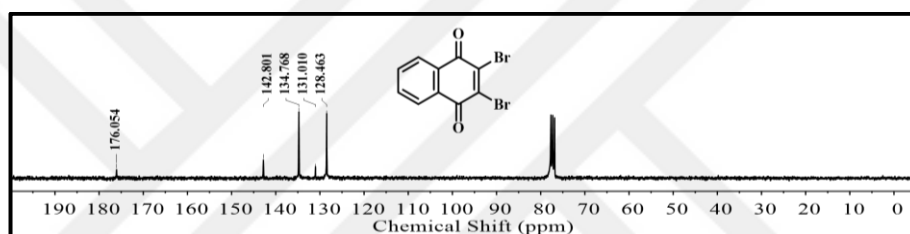


Figure 5.2. ^{13}C NMR spectrum of compound 4-1.

The compound has 4 protons, but it has chemically inequivalent 2 protons as it is a symmetrical molecule. The first proton, which is closer to the carbonyl carbon, resonated at 7.79 ppm, and another one resonated at 8.19 ppm as doublets of the doublet in the ^1H NMR spectrum (Figure 5.1). Similarly, the compound has five carbon atoms that are chemically inequivalent. ^{13}C NMR spectrum of the compound (Figure 5.2) was in agreement with its structure. The carbons at the benzene ring appeared at 142.8, 134.8, and 131.0 ppm. The alkene carbon and the carbonyl carbon were observed at 128.5 and 176.0 ppm, respectively.

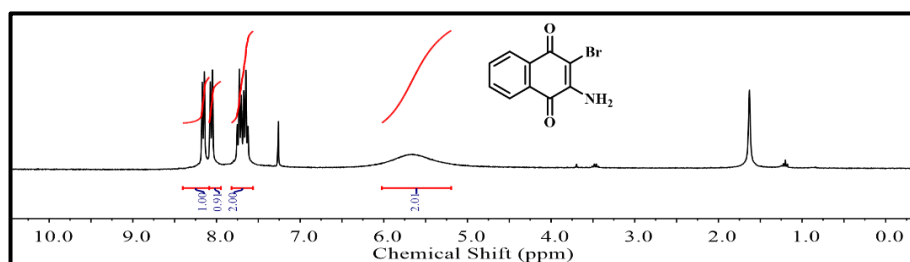


Figure 5.3. ^1H NMR spectrum of compound 4-2.

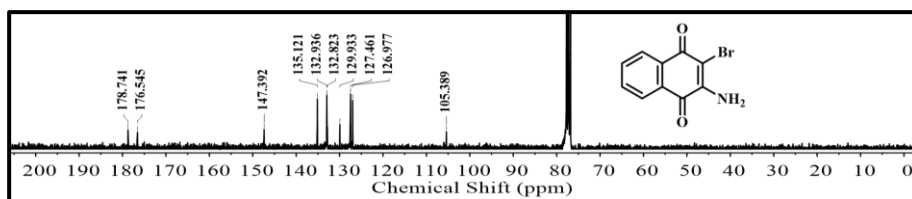


Figure 5.4. ^{13}C NMR spectrum of compound 4-2.

The peaks corresponding to the protons at the benzene ring of the compound were observed at 8.16, 8.06 ppm as doublets, 7.82 - 7.52 ppm as a multiplet in proton NMR (Figure 5.3). The amine group ($-\text{NH}_2$) protons appeared at 5.66 ppm as a broad singlet. The compound has 10 chemically inequivalent carbon atoms, so the structure and ^{13}C NMR spectrum (Figure 5.4) are matched. The carbonyl carbon was observed at 178.7 and 176.6 ppm.

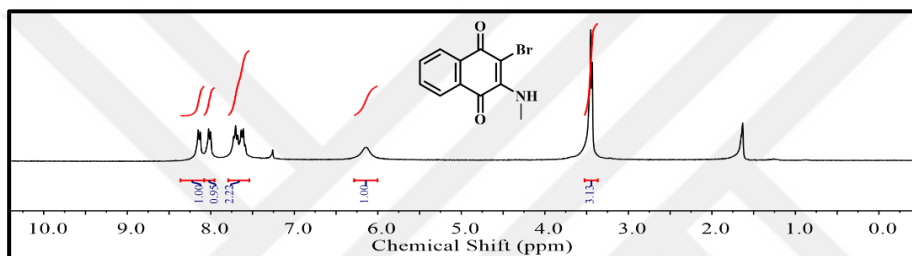


Figure 5.5. ^1H NMR spectrum of compound 4-3.

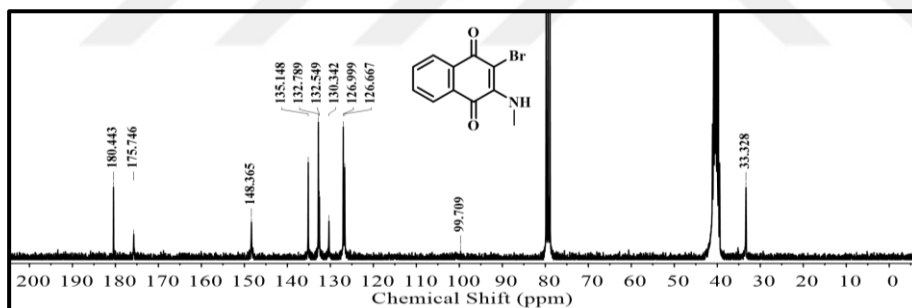


Figure 5.6. ^{13}C NMR spectrum of compound 4-3.

The peaks corresponding to the protons at the benzene ring of the compound were observed at 8.14, 8.01 ppm as doublets, 7.84 - 7.44 ppm as multiplet in proton NMR (Figure 5.5). The amine proton ($-\text{NH}-$) protons appeared at 6.17 ppm as a broad singlet. The methyl group appeared at 3.44 ppm. The compound has 11 chemically inequivalent carbon atoms, so the structure and ^{13}C NMR spectrum (Figure 5.6) were matched. The carbonyl carbon was observed at 178.7 and 176.6 ppm and the methyl carbon signaled at 33.3 ppm.

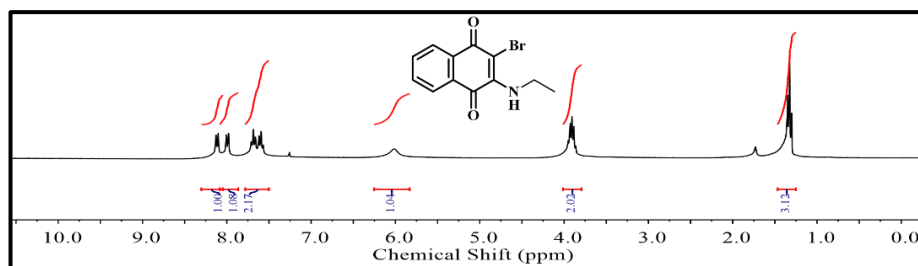


Figure 5.7. ^1H NMR spectrum of compound 4-4.

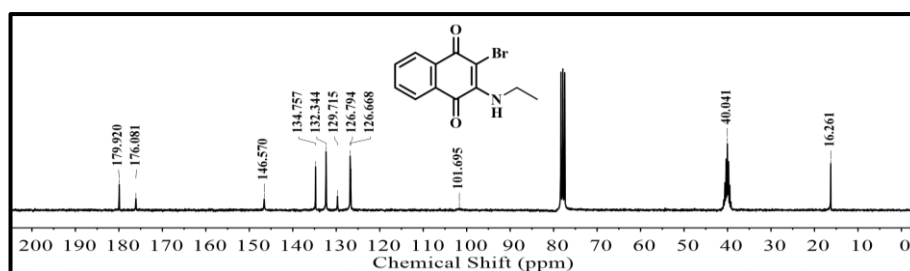


Figure 5.8. ^{13}C NMR spectrum of compound 4-4.

The peaks corresponding to the protons at the benzene ring of the compound were observed at 8.12, 7.99 ppm as doublets, 7.79 - 7.45 ppm as multiplet in proton NMR (Figure 5.7). The amine proton (-NH-) protons appeared at 6.02 ppm as a broad singlet. The ethyl group appeared at 4.55 - 2.95 ppm as multiplet and 1.32 ppm as triplet, corresponding to $-\text{CH}_2-$ and methyl moiety, respectively. The compound has 12 chemically inequivalent carbon atoms, so the structure and ^{13}C NMR spectrum (Figure 5.8) were matched. The carbonyl carbon was observed at 179.9 and 176.1 ppm, and the ethyl carbon signaled at 40.0 and 16.3 ppm, corresponding to $-\text{CH}_2-$ and methyl moiety, respectively.

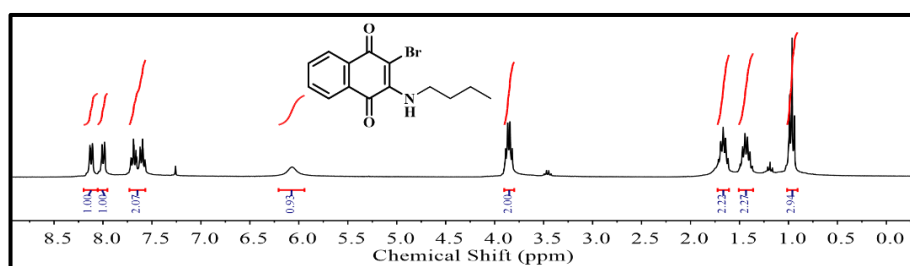


Figure 5.9. ^1H NMR spectrum of compound 4-5.

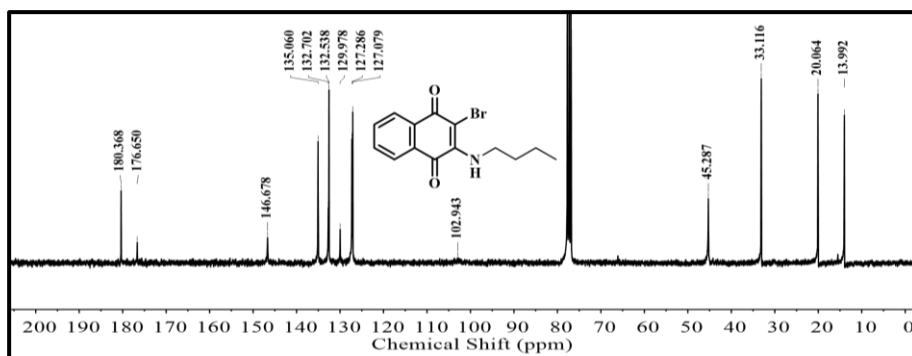


Figure 5.10. ^{13}C NMR spectrum of compound 4-5.

The peaks corresponding to the protons at the benzene ring of the compound were observed at 8.12, 8.00 ppm as doublets, 7.82 - 7.34 ppm as multiplet in proton NMR (Figure 5.9). The amine proton (-NH-) protons appeared at 6.05 ppm as a broad singlet. The peaks that appeared at 3.86 ppm as a quartet, 1.80 - 1.58 as a multiplet, 1.56 - 1.25 ppm as a multiplet, and 0.96 ppm as a triplet corresponded to $-\text{CH}_2-$ groups and $-\text{CH}_3$ group butyl amine moiety. The compound has 14 chemically inequivalent carbon atoms, so the structure was in agreement with the ^{13}C NMR spectrum (Figure 5.10). The carbonyl carbon was observed at 180.4 and 176.6 ppm, and the butyl carbon signaled at 45.29, 33.12, 20.06, and 13.99 ppm.

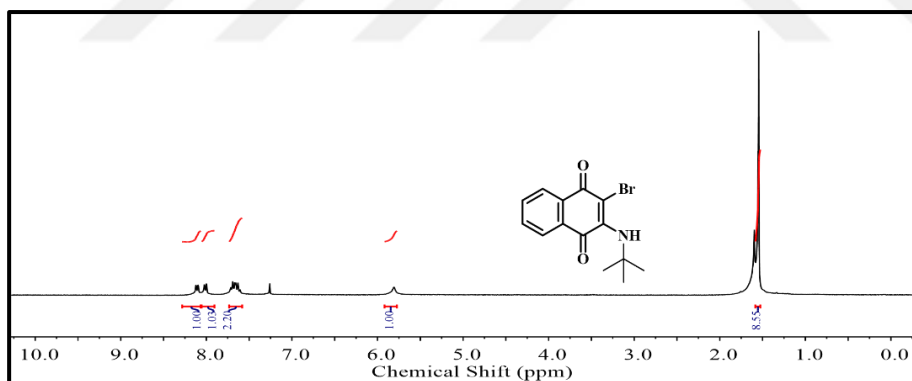


Figure 5.11. ^1H NMR spectrum of compound 4-6.

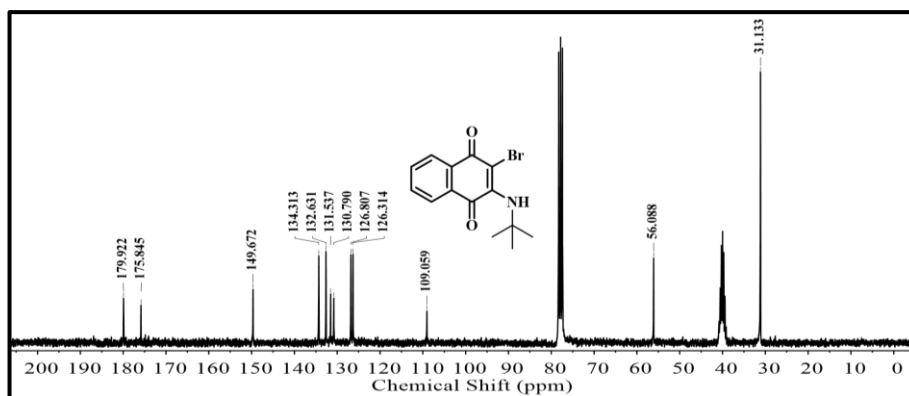


Figure 5.12. ^{13}C NMR spectrum of compound 4-6.

The peaks corresponding to the protons at the benzene ring of the compound were observed at 8.11, 8.00 ppm as doublets, 7.82 - 7.34 ppm as multiplet in proton NMR (Figure 5.11). The amine proton (-NH-) protons appeared at 5.81 ppm as a broad singlet. The peaks that appeared at 1.54 ppm resulted from the methyl moiety of the *tert* butyl amine group. The compound has 12 chemically inequivalent carbon atoms, so the structure was in agreement with the ^{13}C NMR spectrum (Figure 5.12). The carbonyl carbons were observed at 179.9 and 175.8 ppm, and the signals at 56.09 and 31.13 ppm corresponded to methyl and quarter carbon of the *tert* butyl amine moiety.

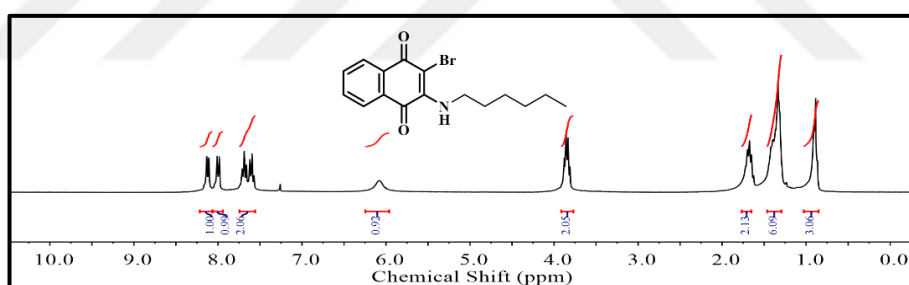


Figure 5.13. ^1H NMR spectrum of compound 4-7.

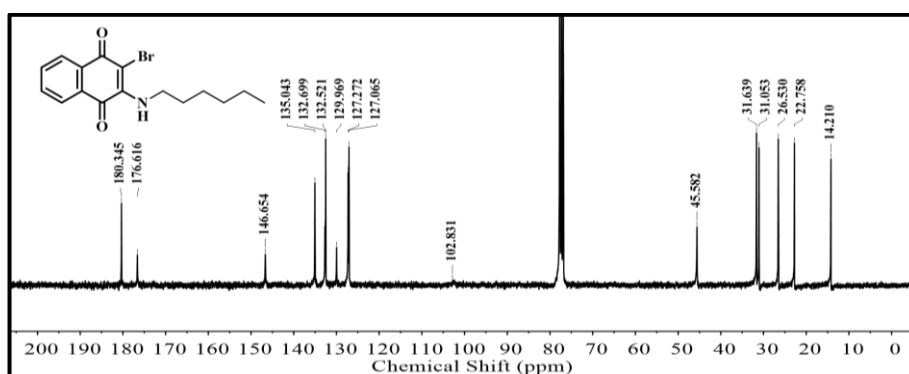


Figure 5.14. ^{13}C NMR spectrum of compound 4-7.

The peaks corresponding to the protons at the benzene ring of the compound were observed at 8.12, 8.00 ppm as doublets, and 7.81 - 7.51 ppm as multiplet in proton

NMR (Figure 5.13). The amine proton (-NH-) protons appeared at 6.08 ppm as a broad singlet. The peaks that appeared at 3.84 ppm as a quartet, 1.85 - 1.55 as a multiplet, 1.52-1.15 ppm as a multiplet, and 0.89 ppm as a triplet corresponded to aliphatic protons of hexylamine moiety. The compound has 16 chemically inequivalent carbon atoms, so the structure was in agreement with the ^{13}C NMR spectrum (Figure 5.14). The carbonyl carbon was observed at 180.4 and 176.6 ppm, and the hexyl carbons signaled at 45.58, 31.64, 31.05, 26.53, 22.76, and 14.21 ppm.

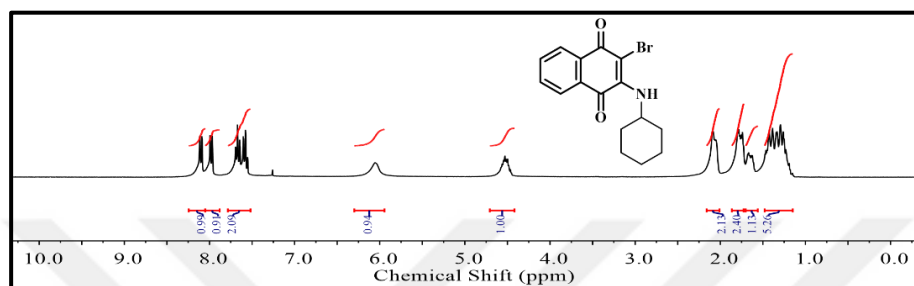


Figure 5.15. ^1H NMR spectrum of compound 4-8.

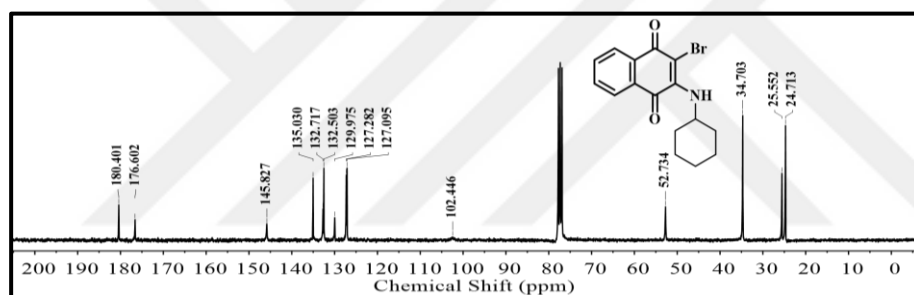


Figure 5.16. ^{13}C NMR spectrum of compound 4-8.

The peaks corresponding to the protons at the benzene ring of the compound were observed at 8.10, 7.98 ppm as doublets, and 7.78 - 7.39 ppm as multiplet in proton NMR (Figure 5.15). The amine proton (-NH-) protons appeared at 6.05 ppm as a broad singlet. The peaks that appeared at 4.69 - 4.39 ppm, 2.24 - 1.90, 1.90 - 1.59, 1.54 - 1.13 ppm as multiplets corresponded to the protons of cyclohexylamine moiety. The compound has 14 chemically inequivalent carbon atoms, so the structure was in agreement with the ^{13}C NMR spectrum (Figure 5.16). The carbonyl carbon was observed at 180.4 and 176.6 ppm, and the butyl carbon signaled at 52.73, 34.70, 25.55, and 24.71 ppm.

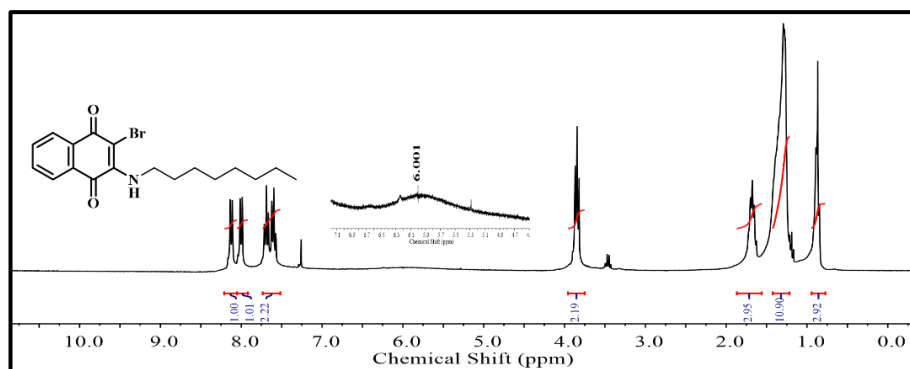


Figure 5.17. ^1H NMR spectrum of compound 4-9.

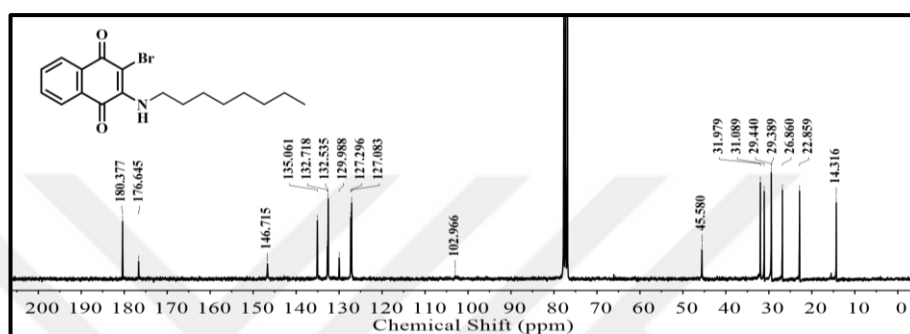


Figure 5.18. ^{13}C NMR spectrum of compound 4-9.

The peaks corresponding to the protons at the benzene ring of the compound were observed at 8.12, 8.00 ppm as doublets, and 7.84 - 7.42 ppm as multiplet in proton NMR (Figure 5.17). The amine proton (-NH-) protons appeared at 6.00 ppm as a broad singlet. The peaks that appeared at 4.04 - 3.73, 1.85 - 1.54, 1.54 - 1.09 ppm as multiplets, and 0.87 ppm as triplet corresponded to the protons of octylamine moiety. The compound has 18 chemically inequivalent carbon atoms, so the structure was in agreement with the ^{13}C NMR spectrum (Figure 5.18). The carbonyl carbon was observed at 180.4 and 176.6 ppm, and the hexyl carbons signaled at 45.58, 31.98, 31.09, 29.44, 29.39, 26.86, 22.86, and 14.32 ppm.

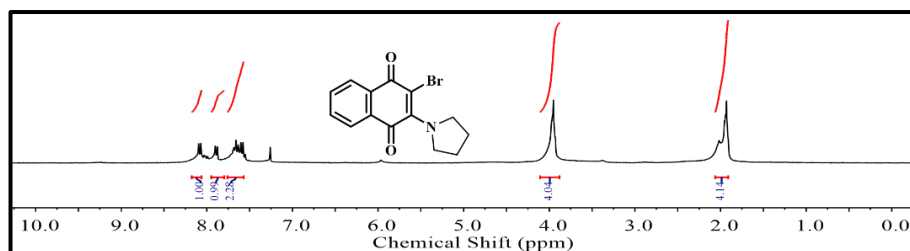


Figure 5.19. ^1H NMR spectrum of compound 4-10.

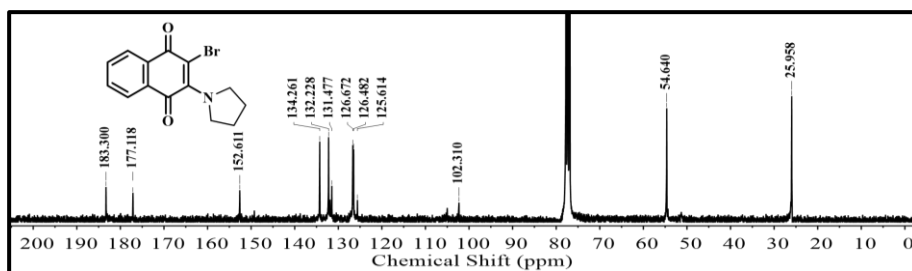


Figure 5.20. ^{13}C NMR spectrum of compound 4-10.

The peaks corresponding to the protons at the benzene ring of the compound were observed at 8.08, 7.89 ppm as doublets, and 7.80 - 7.39 ppm as multiplet in proton NMR (Figure 5.19). The peaks that appeared at 4.21 - 3.48 ppm and 2.32 - 1.66 ppm as multiplets corresponded to the protons of pyrrolidine moiety. The compound has 12 chemically inequivalent carbon atoms, so the structure was in agreement with the ^{13}C NMR spectrum (Figure 5.20). The carbonyl carbon was observed at 183.3 and 177.1 ppm, and the pyrrolidine carbons signaled at 54.6 and 26.0 ppm.

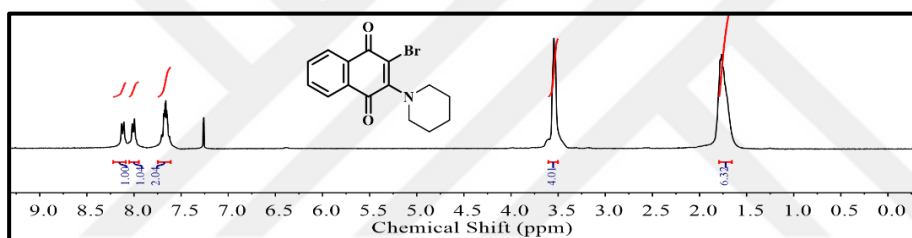


Figure 5.21. ^1H NMR spectrum of compound 4-11.

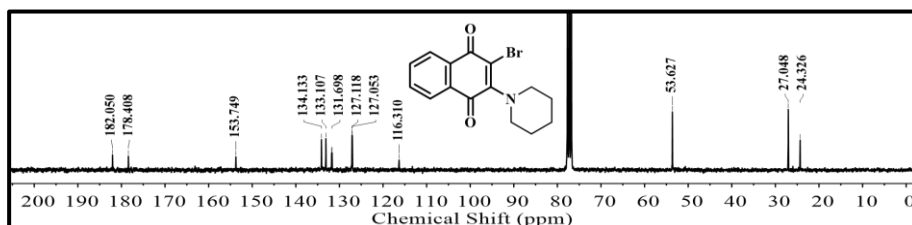


Figure 5.22. ^{13}C NMR spectrum of compound 4-11.

The peaks corresponding to the protons at the benzene ring of the compound were observed at 8.12, 8.01 ppm as doublets, and 7.76 - 7.58 ppm as multiplet in proton NMR (Figure 5.21). The peaks that appeared at 4.60 - 3.14 ppm and 2.41 - 0.95 ppm as multiplets corresponded to the protons of piperidine moiety. The compound has 13 chemically inequivalent carbon atoms, so the structure was in agreement with the ^{13}C NMR spectrum (Figure 5.22). The carbonyl carbon was observed at 182.0 and 178.4 ppm, and the piperidine carbons signalled at 53.6, 27.0, and 24.3 ppm.

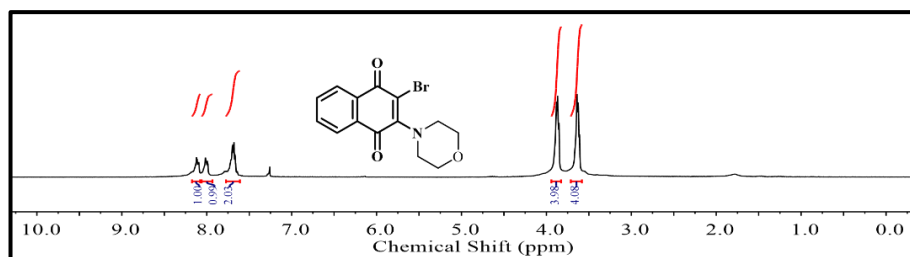


Figure 5.23. ^1H NMR spectrum of compound 4-12.

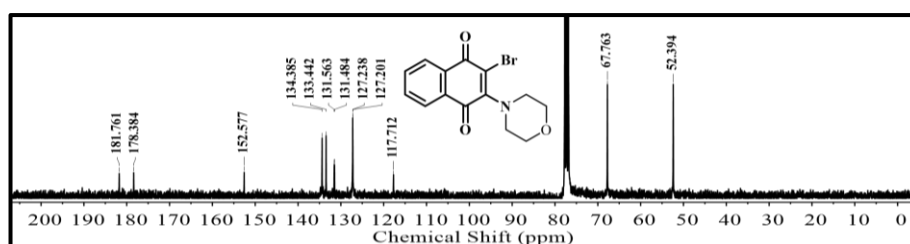


Figure 5.24. ^{13}C NMR spectrum of compound 4-12.

The peaks corresponding to the protons at the benzene ring of the compound were observed at 8.36 - 8.06 ppm, 8.06 - 7.93 ppm, and 7.81 - 7.51 as multiplets in proton NMR (Figure 5.23). The peaks that appeared at 4.02 - 3.81 ppm and 3.75 - 3.50 ppm as multiplets corresponded to the protons of morpholine moiety. The compound has 12 chemically inequivalent carbon atoms, so the structure was in agreement with the ^{13}C NMR spectrum (Figure 5.24). The carbonyl carbon was observed at 181.8 and 178.4 ppm, and the morpholine carbons signaled at 67.76 and 52.39 ppm.

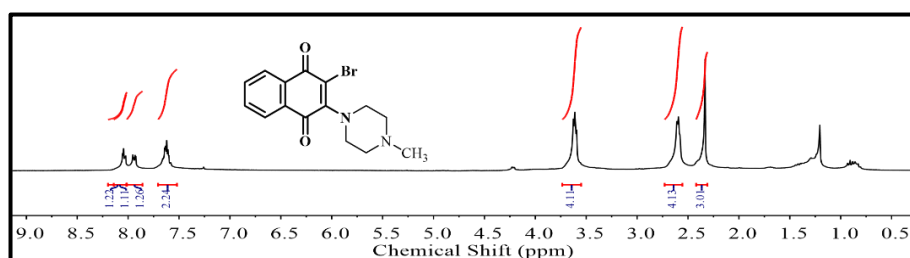


Figure 5.25. ^1H NMR spectrum of compound 4-13.

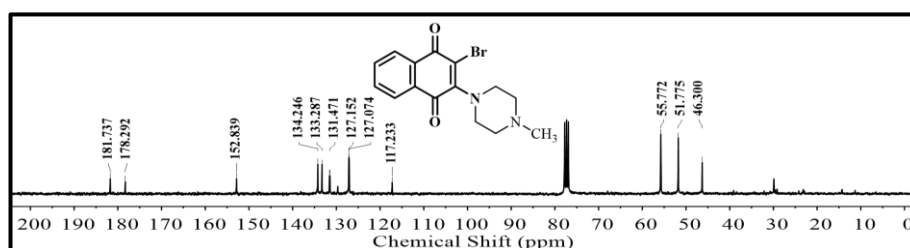


Figure 5.26. ^{13}C NMR spectrum of compound 4-13.

The peaks corresponding to the protons at the benzene ring of the compound were observed at 8.24 - 7.99 ppm, 7.97 - 7.81 ppm, and 7.79 - 7.44 ppm as multiplets in proton NMR (Figure 5.25). The peaks that appeared at 3.61 and 2.59 ppm as triplet corresponded to the protons of piperazine ring moiety. The protons of the methyl group located at the nitrogen atom of piperazine were seen at 2.33 as singlet. The compound has 13 chemically inequivalent carbon atoms, so the structure was in agreement with the ^{13}C NMR spectrum (Figure 5.26). The carbonyl carbon was observed at 181.7 and 178.3 ppm, and the piperazine ring carbons signalled at 55.77 and 51.77 ppm. The carbon of the methyl group, which is located at the nitrogen atom of piperazine, resonated at 46.3 ppm.

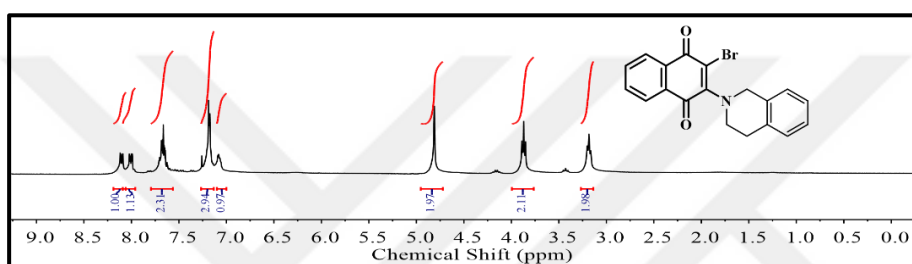


Figure 5.27. ^1H NMR spectrum of compound 4-14.

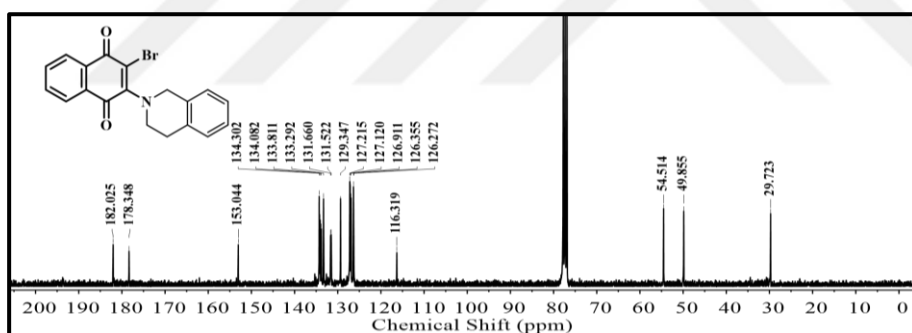


Figure 5.28. ^{13}C NMR spectrum of compound 4-14.

The peaks corresponding to the protons at the benzene ring of 1,4-naphthoquinone moiety were observed at 8.16 - 8.08 ppm, 8.06 - 7.97 ppm, and 7.70 - 7.62 ppm as multiplets in proton NMR (Figure 5.27). The protons at the nitrogen-bearing ring of the tetrahydroisoquinoline structure resonated at 4.81 ppm, 3.87 ppm, and 3.18 ppm as singlet, triplet, and triplet, respectively. As for the protons at the benzene ring of tetrahydroisoquinoline, the peaks of their protons appeared at 7.20 - 7.16 and 7.10 - 7.04 ppm as multiplets. The compound has 19 chemically inequivalent carbon atoms, so the structure was in agreement with the ^{13}C NMR spectrum (Figure 5.28). The carbonyl carbon was observed at 182.0 and 178.4 ppm. The peaks at 54.5, 49.8, and 29.7 ppm resulted from the carbons at the aliphatic ring with a nitrogen atom.

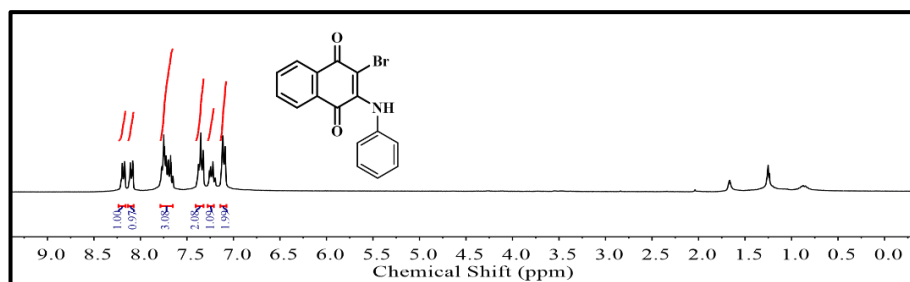


Figure 5.29. ^1H NMR spectrum of compound 4-15.

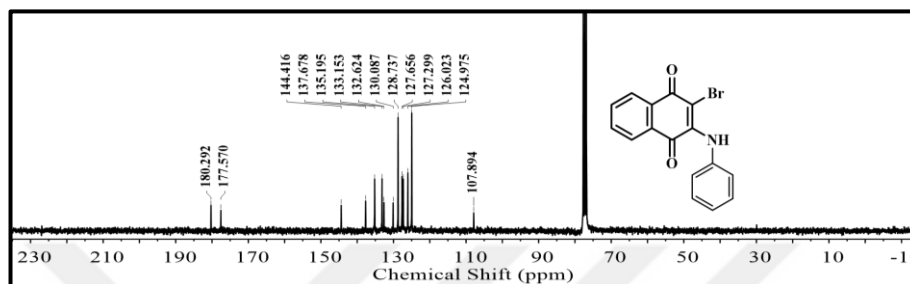


Figure 5.30. ^{13}C NMR spectrum of compound 4-15.

^1H NMR spectrum of 2-bromo-3-(phenylamino)naphthalene-1,4-dione is given in Figure 5.29. The peaks corresponding to the protons at the benzene ring of naphthoquinone structure were observed at 8.18, 8.09 ppm as doublets of the doublet and 7.83 - 7.59 ppm as multiplet in proton NMR. The peak of the -NH proton overlapped with the peaks of benzene ring protons of the naphthoquinone at 7.83 - 7.59 ppm. The protons of the aniline moiety were observed at 7.43 - 7.30, 7.29 - 7.17, and 7.16 - 7.06 ppm as multiplet peaks. ^{13}C NMR spectrum () of the compound is given in Figure 5.30. The carbonyl carbons were observed at 180.29 and 177.57 ppm. The compound has 14 chemically inequivalent carbon atoms, so the structure was in agreement with the ^{13}C NMR spectrum.

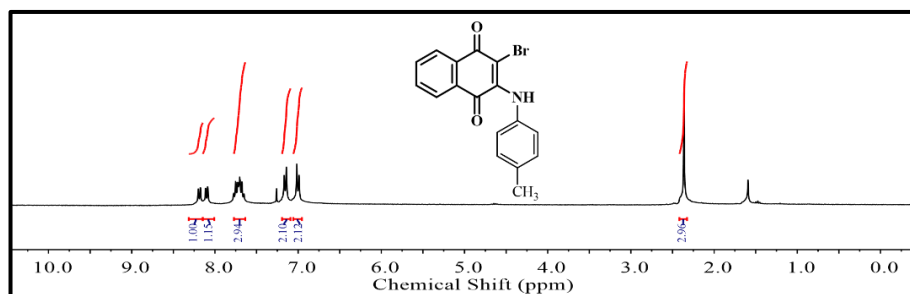


Figure 5.31. ^1H NMR spectrum of compound 4-16.

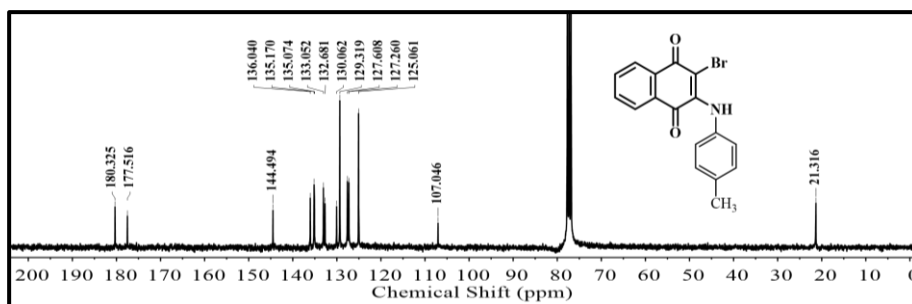


Figure 5.32. ^{13}C NMR spectrum of compound 4-16.

^1H NMR spectrum of 2-bromo-3-(*p*-tolylamino)naphthalene-1,4-dione is given in Figure 5.31. The peaks corresponding to the protons at the benzene ring of the naphthoquinone structure were observed at 8.19, 8.10 ppm as doublets of the doublet, and 7.91 - 7.59 ppm as multiplet in proton NMR. The peak of the -NH proton overlapped with the peaks of benzene ring protons of the naphthoquinone at 7.91 - 7.59 ppm. The aromatic protons of the *p*-tolylaniline moiety were observed at 7.15 and 7.00 ppm as doublet peaks. Moreover, the methyl group at *p*-tolylaniline moiety was observed at 2.36 ppm. ^{13}C NMR spectrum of the compound is given in Figure 5.32. The carbonyl carbons were observed at 180.32 and 177.52 ppm. The methyl group at *p*-tolylaniline moiety was observed at 21.32 ppm. The compound has 15 chemically inequivalent carbon atoms, so the structure was in agreement with the ^{13}C NMR spectrum.

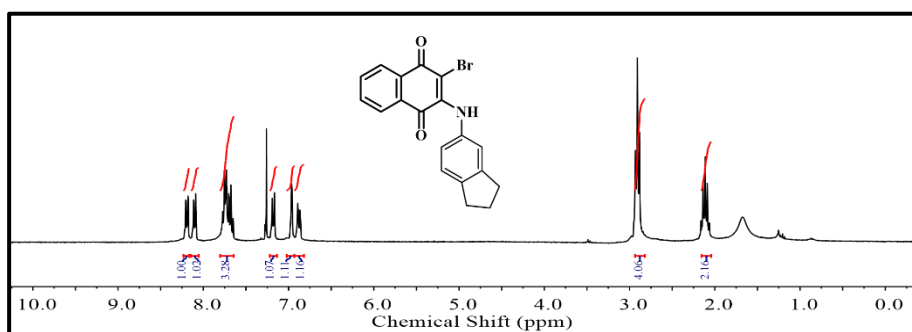


Figure 5.33. ^1H NMR spectrum of compound 4-17.

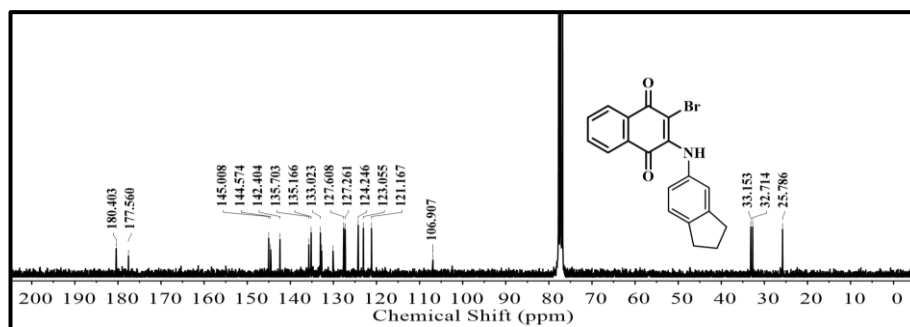


Figure 5.34. ^{13}C NMR spectrum of compound 4-17.

^1H NMR spectrum of 2-bromo-3-((2,3-dihydro-1*H*-inden-5-yl)amino)naphthalene-1,4-dione is given in Figure 5.33. The peaks corresponding to the protons at the benzene ring of naphthoquinone structure were observed at 8.24 - 8.17, 8.15 - 8.06 and 7.81 - 7.63 as multiplet in proton NMR. The peak of the -NH proton overlapped with the peaks of benzene ring protons of the naphthoquinone at 7.81 - 7.63 ppm. The aromatic protons of the 5-aminoindan moiety were observed at 7.18 as a doublet, 6.96 as a doublet, and 6.88 as a doublet of the doublets. Moreover, the aliphatic ring protons of 5-aminoindan moiety were observed at 2.91 and 2.11 ppm as triplet and pentet, respectively. ^{13}C NMR spectrum of the compound is given in Figure 5.34. The carbonyl carbons were observed at 180.40 and 177.56 ppm. The aliphatic ring carbons of 5-aminoindan moiety were observed at 33.15, 32.71, and 25.79 ppm. The compound has 19 chemically inequivalent carbon atoms, so the structure was in agreement with the ^{13}C NMR spectrum.

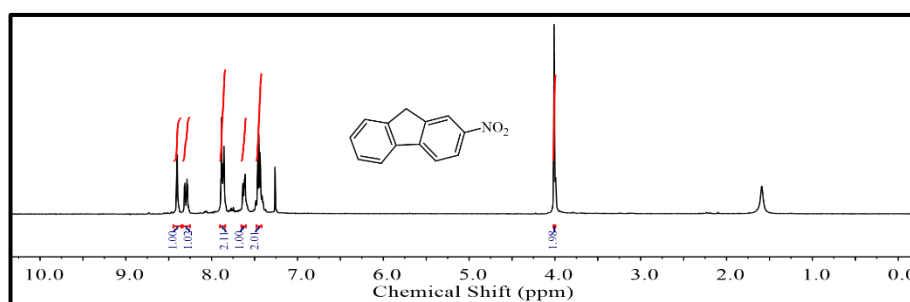


Figure 5.35. ^1H NMR spectrum of compound 4-18.

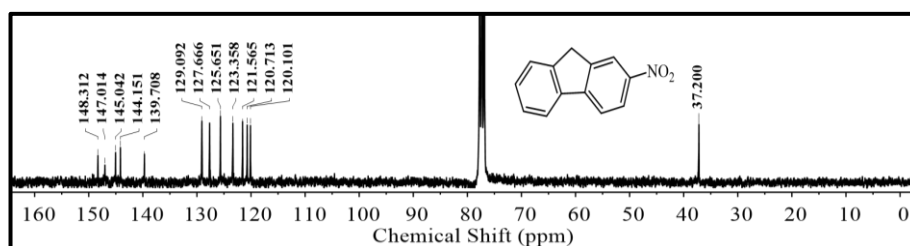


Figure 5.36. ^{13}C NMR spectrum of compound 4-18.

^1H NMR spectrum of 2-nitro-9*H*-fluorene was given in Figure 5.35. The $-\text{CH}_2-$ bridge of fluorene appeared at 4.01 ppm. The aromatic peaks were displayed at 8.40 as a singlet, 8.30 as a doublet, 7.87 as a doublet, 7.62 as a doublet, and 7.53 - 7.38 ppm as a multiplet. It was worth mentioning that nitration distorted the symmetry of the molecule. As a result, five different peaks or peak groups were observed. Most importantly, it is evident from the successful nitration reaction that the singlet peak at 8.40 ppm belonged to the single proton next to the nitro group. ^{13}C NMR spectrum of 2-nitro-9*H*-fluorene was given in Figure 5.36. The $-\text{CH}_2-$ bridge of fluorene appeared at 37.20 ppm. The peaks of the aromatic carbons at 148.31, 147.01, 145.04, 144.15, 139.71, 129.09, 127.67, 125.65, 123.36, 121.56, 120.71 and 120.10 ppm were in accordance with the structure.

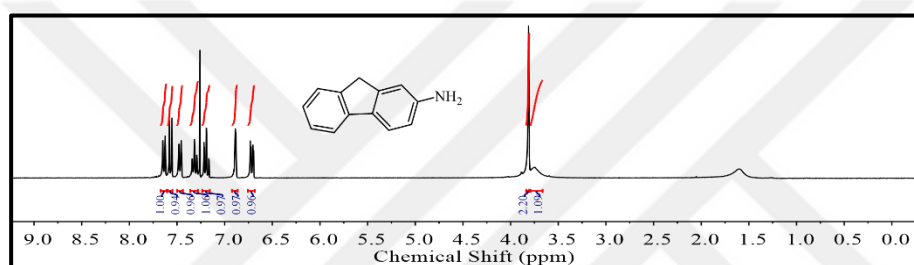


Figure 5.37. ^1H NMR spectrum of compound 4-19.

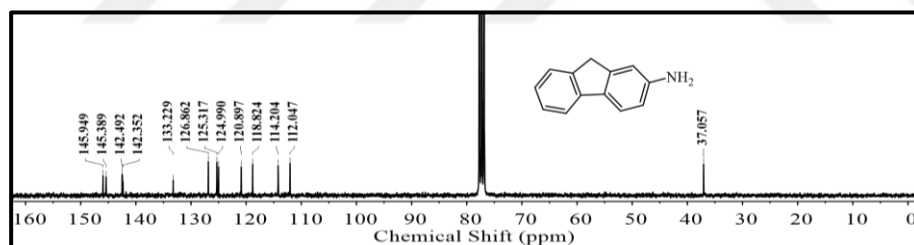


Figure 5.38. ^{13}C NMR spectrum of compound 4-19.

^1H NMR spectrum of 2-amino-9*H*-fluorene was given in Figure 5.37. The $-\text{CH}_2-$ bridge and amino group ($-\text{NH}_2$) of fluorene appeared at 3.81 and 3.74 ppm, respectively. The aromatic peaks were displayed at 7.64 as a doublet, 7.57 as a doublet, 7.47 as a doublet, 7.37 - 7.28 as a multiplet, 7.24 - 7.13 as a multiplet, 6.88 as a doublet, and 6.71 as a doublet of the doublet. ^{13}C NMR spectrum of 2-amino-9*H*-fluorene was given in Figure 5.38. The $-\text{CH}_2-$ bridge of fluorene appeared at 37.06 ppm. The peaks of the aromatic carbons at 145.95, 145.39, 142.49, 142.35, 133.23, 126.86, 125.32, 124.99, 120.90, 118.82, 114.20 and 112.05 ppm were in accordance with the structure. As compared to the nitro derivative, the peaks of the compound were up fielded by the reduction of the nitro group.

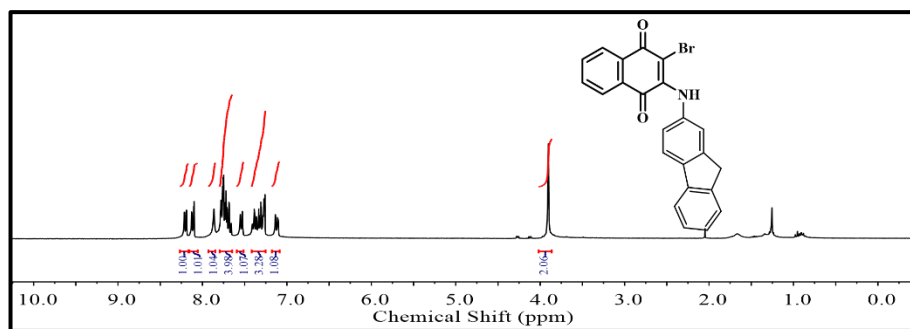


Figure 5.39. ^1H NMR spectrum of compound 4-20.

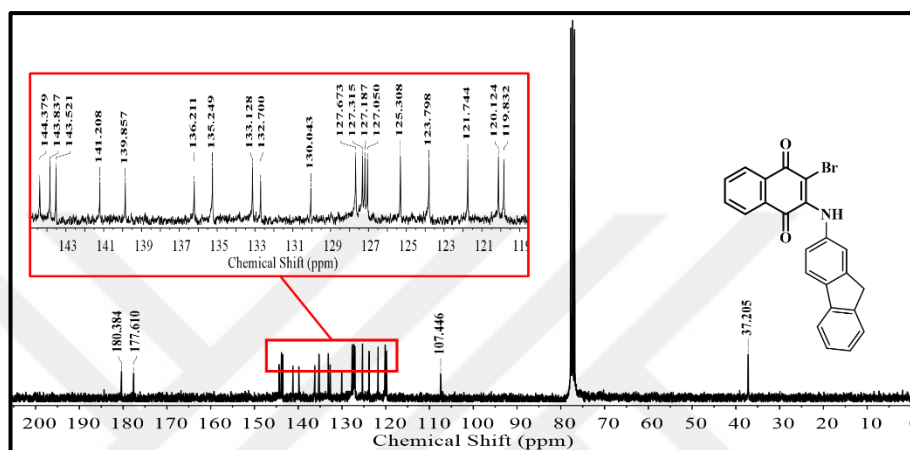


Figure 5.40. ^{13}C NMR spectrum of compound 4-20.

^1H NMR spectrum of 2-((9*H*-fluoren-2-yl)amino)-3-bromonaphthalene-1,4-dione is given in Figure 5.39. The peaks corresponding to the protons at the benzene ring of naphthoquinone structure were observed at 8.21 and 8.11 ppm as a doublet of the doublets and 7.82 - 7.61 ppm as a multiplet peak in proton NMR. The peak of the -NH proton was seen at 7.86 ppm as a broad singlet. The aromatic protons of 9*H*-fluoren-2-amine moiety were observed at 7.54 ppm as a doublet, 7.47 - 7.23 as a multiplet peak, and 7.12 ppm as a doublet of the doublet. Moreover, the aliphatic proton peak belonging to the -CH₂- bridge of fluorene appeared at 3.90 ppm as a singlet. ^{13}C NMR spectrum of the compound is given in Figure 5.40. The carbonyl carbons were observed at 180.38 and 177.61 ppm. The -CH₂- bridge of fluorene was observed at 37.20 ppm. The compound has 23 chemically inequivalent carbon atoms, so the structure was in agreement with the ^{13}C NMR spectrum.

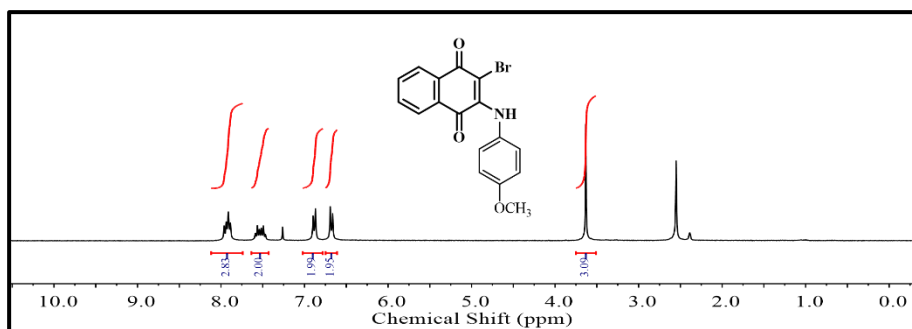


Figure 5.41. ¹H NMR spectrum of compound 4-21.

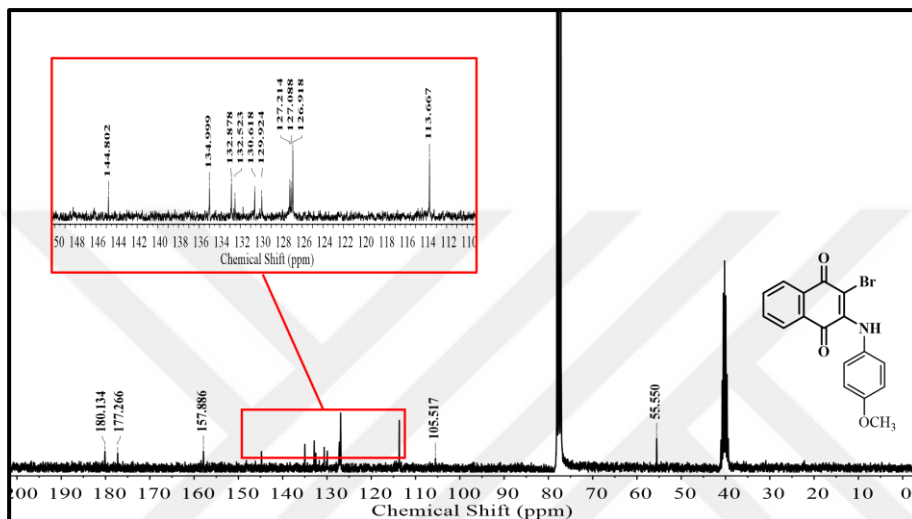


Figure 5.42. ¹³C NMR spectrum of compound 4-21.

¹H NMR spectrum of 2-bromo-3-((4-methoxyphenyl)amino)naphthalene-1,4-dione is given in Figure 5.41. The peaks corresponding to the protons at the benzene ring of naphthoquinone structure were observed at 8.19 - 7.79 and 7.69 - 7.43 ppm as multiplet peaks in proton NMR. The aromatic protons of *p*-anisidine moiety were observed at 6.88 and 6.68 ppm as doublets. Moreover, the methoxy group protons at *p*-anisidine moiety appeared at 3.63 ppm as a singlet. ¹³C NMR spectrum of the compound is given in Figure 5.42. The carbonyl carbons were observed at 180.13 and 177.27 ppm. The methoxy group carbons at *p*-anisidine moiety resonated at 55.55 ppm. The compound has 15 chemically inequivalent carbon atoms, so the structure was in agreement with the ¹³C NMR spectrum.

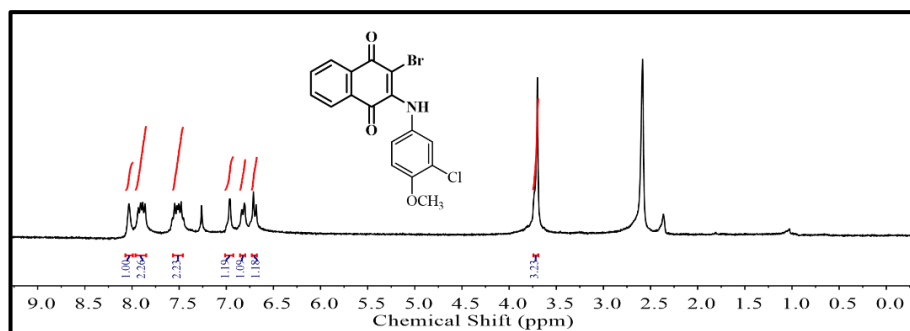


Figure 5.43. ¹H NMR spectrum of compound 4-22.

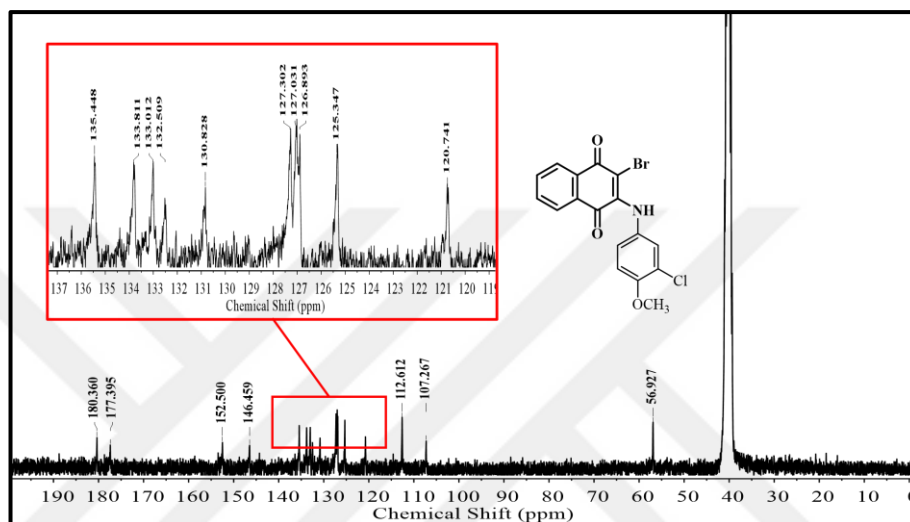


Figure 5.44. ¹³C NMR spectrum of compound 4-22.

¹H NMR spectrum of 2-bromo-3-((3-chloro-4-methoxyphenyl)amino)naphthalene-1,4-dione is given in Figure 5.43. The peaks corresponding to the protons at the benzene ring of the naphthoquinone structure were observed at 7.90 as a doublet of doublet and 7.58 - 7.43 as multiplet peaks in proton NMR. The aromatic protons of 3-chloro-4-methoxyaniline moiety were observed at 6.96, 6.82, and 6.70 ppm as doublets. Moreover, the methoxy group protons at 3-chloro-4-methoxyaniline moiety appeared at 3.70 ppm as a singlet. ¹³C NMR spectrum of the compound is given in Figure 5.44. The carbonyl carbons were observed at 180.36 and 177.40 ppm. The methoxy group carbons at 3-chloro-4-methoxyaniline moiety resonated at 56.93 ppm. The compound has 17 chemically inequivalent carbon atoms, so the structure was in agreement with the ¹³C NMR spectrum.

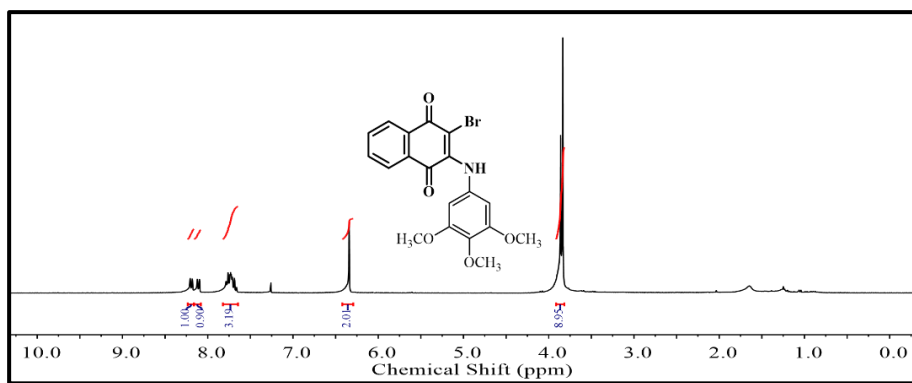


Figure 5.45. ^1H NMR spectrum of compound 4-23.

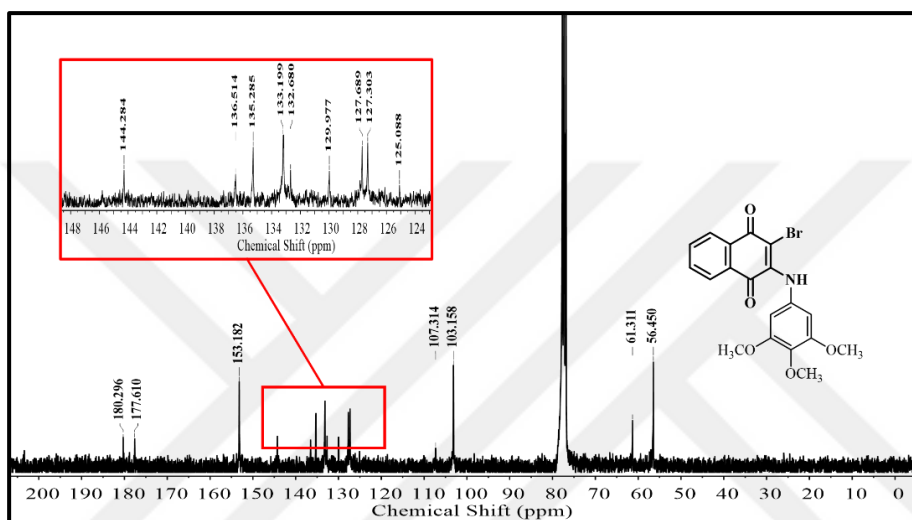


Figure 5.46. ^{13}C NMR spectrum of compound 4-23.

^1H NMR spectrum of 2-bromo-3-((3,4,5-trimethoxyphenyl)amino)naphthalene-1,4-dione is given in Figure 5.45. The peaks corresponding to the protons at the benzene ring of the naphthoquinone structure were observed at 8.19 and 8.11 ppm as doublet peaks in proton NMR. The aromatic protons of 3,4,5-trimethoxy aniline moiety were observed at 6.34 ppm as a singlet peak. The compound had three methoxy groups, and two of them were symmetrical, so the proton NMR spectrum displayed two peaks at 3.86 and 3.84 ppm, which correspond to a single methoxy group and two symmetrical methoxy, respectively. ^{13}C NMR spectrum of the compound is given in Figure 5.46. The carbonyl carbons were observed at 180.30 and 177.61 ppm. ^{13}C NMR spectrum displayed two peaks at 61.31 and 56.45 ppm, which correspond to a single methoxy group and two symmetrical methoxy, respectively. The compound has 16 chemically inequivalent carbon atoms, so the structure was in agreement with the ^{13}C NMR spectrum.

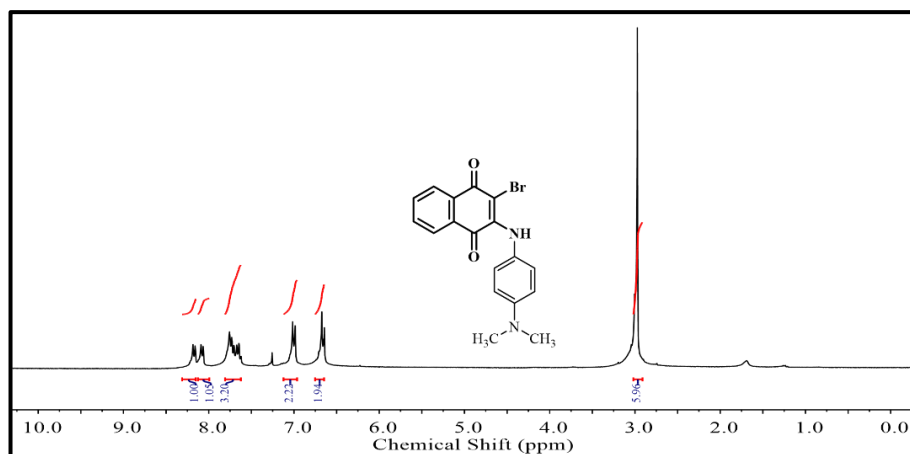


Figure 5.47. ¹H NMR spectrum of compound 4-24.

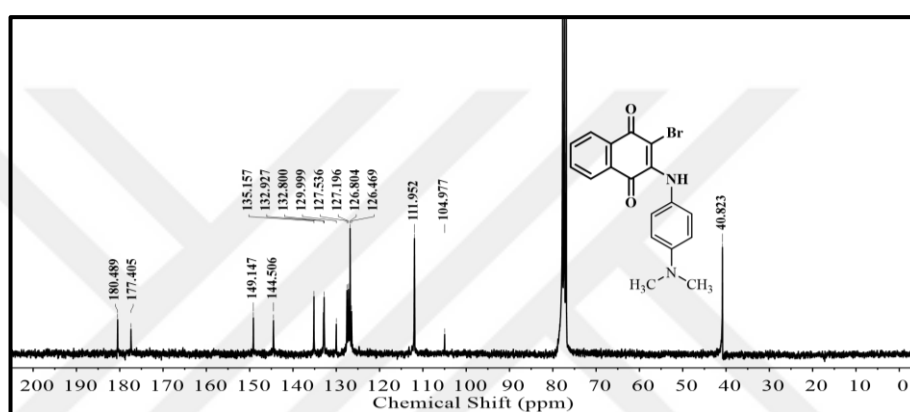


Figure 5.48. ¹³C NMR spectrum of compound 4-24.

¹H NMR spectrum of 2-bromo-3-((4-(dimethylamino)phenyl)amino)naphthalene-1,4-dione is given in Figure 5.47. The peaks corresponding to the protons at the benzene ring of naphthoquinone structure were observed at 8.17 as doublet, 8.08 ppm as doublet and 7.86 - 7.60 ppm as multiplet peaks in proton NMR. The aromatic protons of *N,N*-dimethyl-*p*-phenylenediamine moiety were observed at 7.00 and 6.66 as doublets. The peak of the -NH proton overlapped with the peaks of benzene ring protons of the naphthoquinone at 7.86 - 7.60 ppm. The methyl groups at *N,N*-dimethyl-*p*-phenylenediamine moiety were observed at 2.97 as a singlet peak. ¹³C NMR spectrum of the compound is given in Figure 5.48. The carbonyl carbons were observed at 180.49 and 177.40 ppm. ¹³C NMR spectrum displayed a peak at 40.82 ppm, which corresponds to the methyl group at *N,N*-dimethyl-*p*-phenylenediamine moiety. The compound has 15 chemically inequivalent carbon atoms, so the structure was in agreement with the ¹³C NMR spectrum.

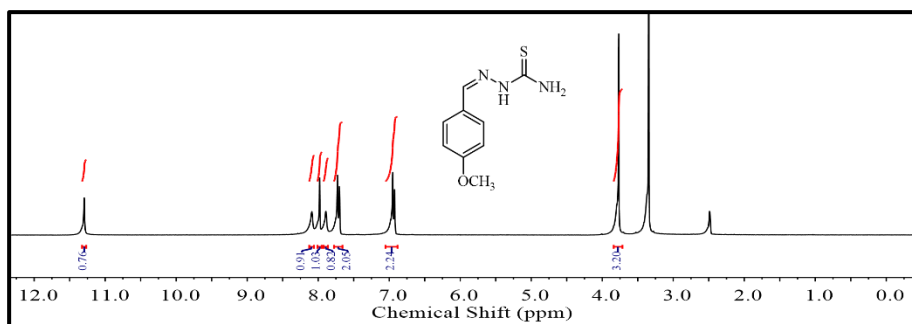


Figure 5.49. ^1H NMR spectrum of compound 4-25.

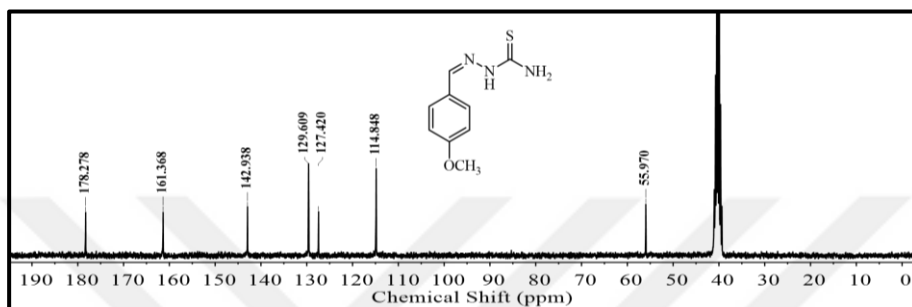


Figure 5.50. ^{13}C NMR spectrum of compound 4-25.

^1H NMR spectrum of the (*E*)-2-(4-methoxybenzylidene)hydrazine-1-carbothioamide was given in Figure 5.49. The protons at the amine groups (-NH- and -NH₂) were observed at 11.30, 8.09, and 7.89 as broad singlets. The enamine peak was observed at 7.98 ppm as a sharp singlet. The aromatic protons were signaled at 7.71 and 6.94 ppm as doublets. The methoxy group was seen at 3.77 ppm as a singlet. ^{13}C NMR spectrum of the compound was given in Figure 5.50. The thiocarbonyl group carbon resonated at 178.28 ppm, and the methoxy group resonated at 55.97 ppm.

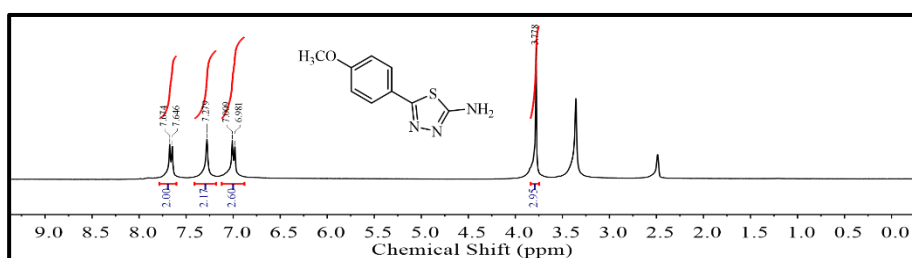


Figure 5.51. ^1H NMR spectrum of compound 4-26.

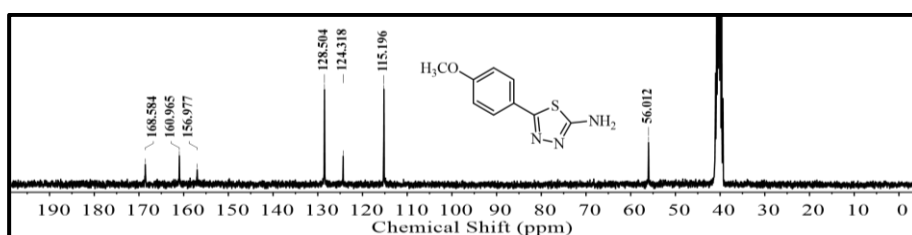


Figure 5.52. ^{13}C NMR spectrum of compound 4-26.

^1H NMR spectrum of 5-(4-methoxyphenyl)-1,3,4-thiadiazol-2-amine was given in Figure 5.51. The aromatic protons resonated at 7.66 and 7.00 ppm as doublets. The amine group was seen at 7.28 ppm as a broad singlet. The protons of the methoxy group were observed at 3.78 ppm. ^{13}C NMR spectrum of the compound was given in Figure 5.52. The peak seen at 56.01 ppm belonged to the methoxy group carbon. The aromatic carbons resonated at 168.58, 160.96, 156.98, 128.50, 124.32, and 115.20 ppm, which were in accordance with the structure.

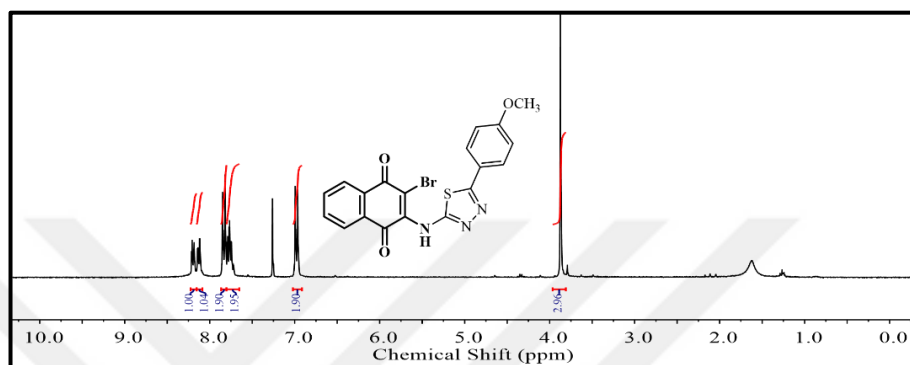


Figure 5.53. ^1H NMR spectrum of compound 4-27.

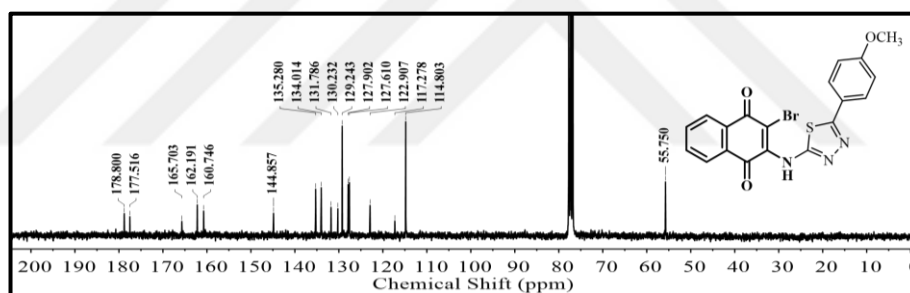


Figure 5.54. ^{13}C NMR spectrum of compound 4-27.

^1H NMR spectrum of 2-bromo-3-((5-(4-methoxyphenyl)-1,3,4-thiadiazol-2-yl)amino)naphthalene-1,4-dione is given in Figure 5.53. The peaks corresponding to the protons at the benzene ring of naphthoquinone structure were observed at 8.27 - 8.17, 8.16 - 8.03 and 7.80 - 7.68 as a multiplet peaks in proton NMR. The aromatic protons of 5-(4-methoxyphenyl)-1,3,4-thiadiazol-2-amine moiety were observed at 7.83 and 6.98 ppm as doublets. Moreover, the methoxy group protons at 5-(4-methoxyphenyl)-1,3,4-thiadiazol-2-amine moiety appeared at 3.87 ppm as a singlet. ^{13}C NMR spectrum of the compound is given in Figure 5.54. The carbonyl carbons were observed at 178.80 and 177.52 ppm. The methoxy group carbons at 5-(4-methoxyphenyl)-1,3,4-thiadiazol-2-amine moiety resonated at 55.75 ppm. The compound has 17 chemically inequivalent carbon atoms, so the structure was in agreement with the ^{13}C NMR spectrum.

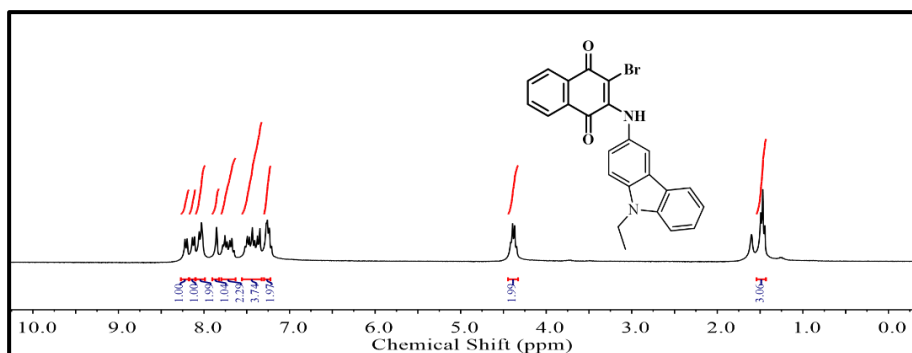


Figure 5.55. ¹H NMR spectrum of compound 4-28.

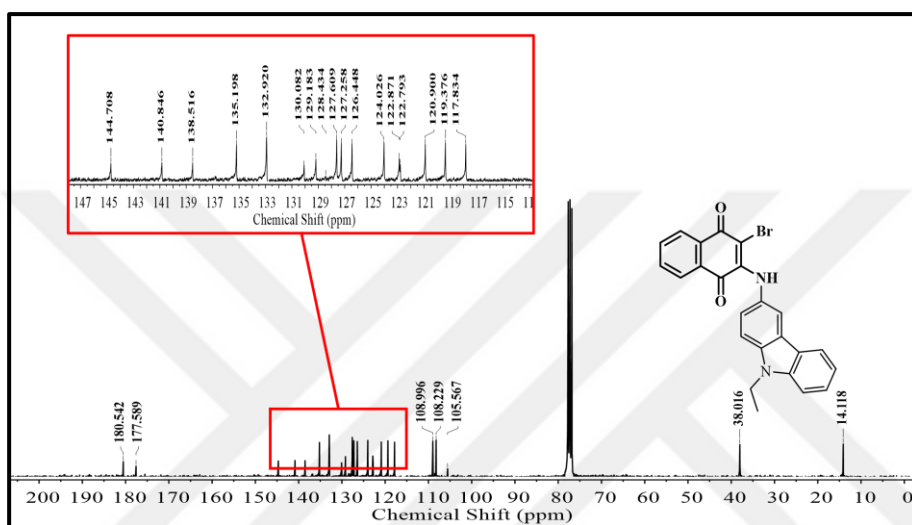


Figure 5.56. ¹³C NMR spectrum of compound 4-28.

¹H NMR spectrum of 2-bromo-3-((9-ethyl-9H-carbazol-3-yl)amino)naphthalene-1,4-dione is given in Figure 5.55. The peaks corresponding to the protons at the benzene ring of naphthoquinone structure were observed at 8.21, 8.12 and 8.04 ppm as doublet peaks in proton NMR. The aromatic protons of 9-ethyl-9H-carbazol-3-amine moiety were observed at 7.82 - 7.63, 7.58 - 7.33, and 7.30 - 7.16 ppm as multiplets. The peak of the -NH proton was seen at 7.85 ppm as a broad singlet. The ethyl groups at the nitrogen atom of carbazole moiety were observed at 4.38 as a quartet and 1.47 as a triplet peak. ¹³C NMR spectrum of the compound is given in Figure 5.56. The carbonyl carbons were observed at 180.54 and 177.59 ppm. ¹³C NMR spectrum displayed a peak at 38.02 and 14.12 ppm, which correspond to the ethyl group at the nitrogen atom of carbazole moiety. The compound has 24 chemically inequivalent carbon atoms, so the structure was in agreement with the ¹³C NMR spectrum.

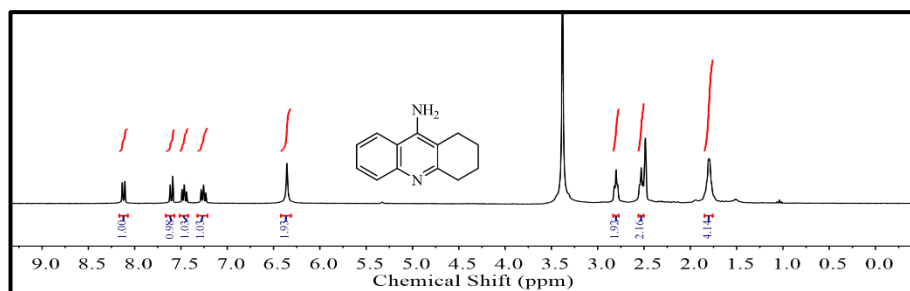


Figure 5.57. ^1H NMR spectrum of compound 4-29.

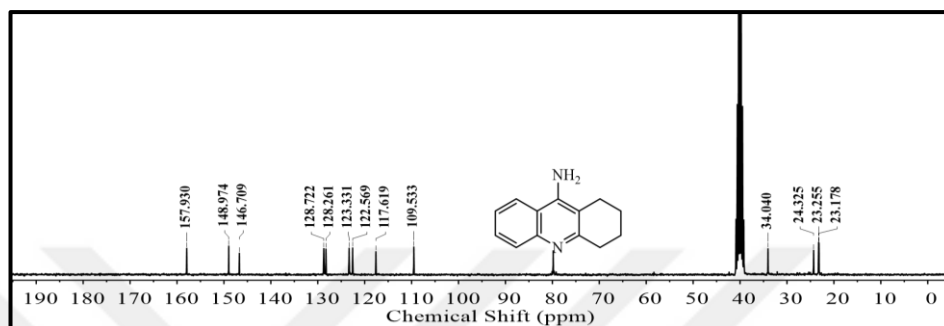


Figure 5.58. ^{13}C NMR spectrum of compound 4-29.

^1H NMR spectrum of 9-Amino-1,2,3,4-tetrahydroacridine, shortly tacrine, is given in Figure 5.57. The peaks at 8.12 as a doublet, 7.60 as a doublet, 7.46 as a triplet, and 7.26 ppm as a triplet belonged to the aromatic proton of tacrine. The protons of the cyclohexane ring resonated at 2.80 ppm as a triplet, 2.53 as a triplet, and 2.12 - 1.50 as a multiplet. The amine group was observed at 6.36 ppm as a broad singlet. ^{13}C NMR spectrum of the compound is given in Figure 5.58. The spectrum displayed 9 peaks at the aromatic region and 4 peaks at the aliphatic region of the spectrum, which are in accordance with the structure of the compound.

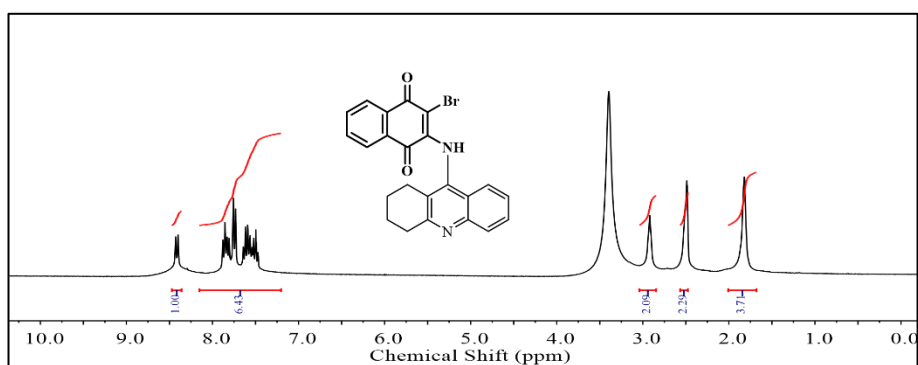


Figure 5.59. ^1H NMR spectrum of compound 4-30.

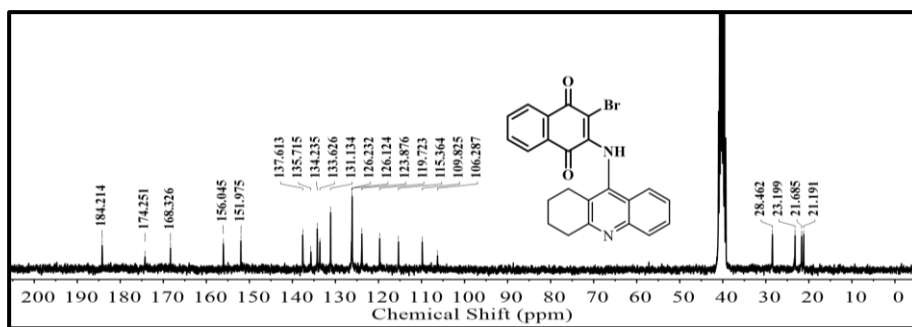


Figure 5.60. ^{13}C NMR spectrum of compound 4-30.

^1H NMR spectrum of 1,4-naphthoquinone with tacrine structure is given in Figure 5.59. The peaks corresponding to aromatic protons of the compound were observed at 8.41 as a doublet and 7.98-7.26 ppm as a multiplet peak in proton NMR. The protons of the cyclohexyl ring of the tacrine ring were seen at 2.94-2.90, 2.69-2.34, and 2.05-1.40 ppm as multiplets. ^{13}C NMR spectrum of the compound is given in Figure 5.60. The non-symmetrical carbonyl carbons were observed at 184.23 as one peak. The cyclohexyl ring carbons of the compound were signaled at 28.46, 23.20, 21.68, and 21.19 ppm. All other carbon peaks resulted from the aromatic carbons of the compounds.

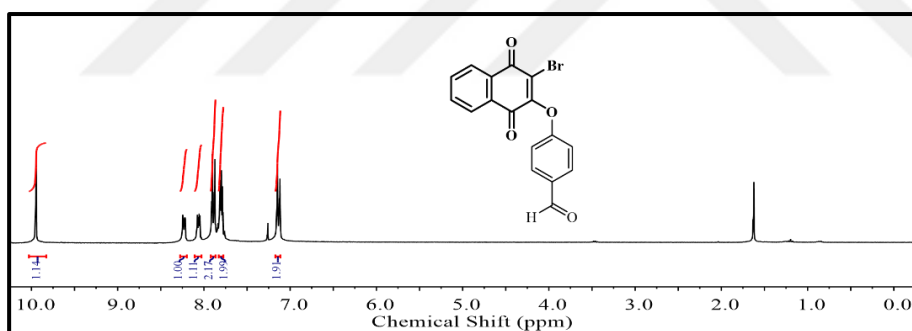


Figure 5.61. ^1H NMR spectrum of compound 4-31.

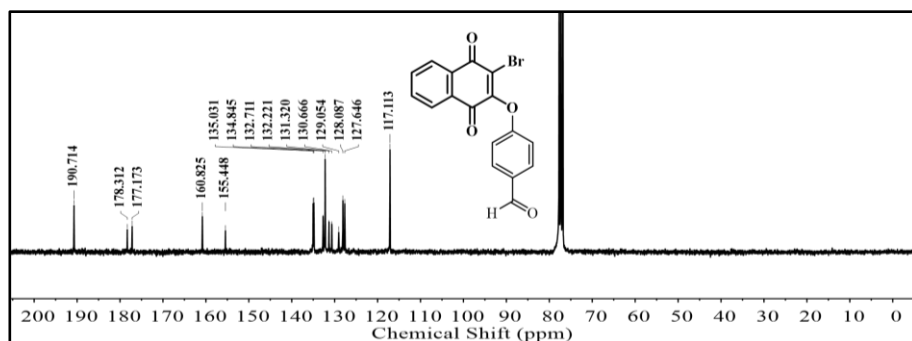


Figure 5.62. ^{13}C NMR spectrum of compound 4-31.

^1H NMR spectrum of 4-((3-bromo-1,4-dioxo-1,4-dihydronaphthalen-2-yl)oxy)benzaldehyde is given in Figure 5.61. The peaks corresponding to the protons

at the benzene ring of the naphthoquinone structure were observed at 8.23 ppm as a doublet of the doublet, 8.06 ppm as a doublet of the doublet, and 7.89 ppm as a doublet peak in proton NMR. The aromatic protons of 4-hydroxybenzaldehyde moiety were observed at 7.80 and 7.13 ppm as doublets. Moreover, the aldehyde proton at 4-hydroxybenzaldehyde moiety appeared at 9.95 ppm as a singlet. ^{13}C NMR spectrum of the compound is given in Figure 5.62. The carbonyl carbons were observed at 178.31 and 177.17 ppm. the aldehyde carbon at 4-hydroxybenzaldehyde moiety resonated at 190.71 ppm. The compound has 15 chemically inequivalent carbon atoms, so the structure was in agreement with the ^{13}C NMR spectrum.

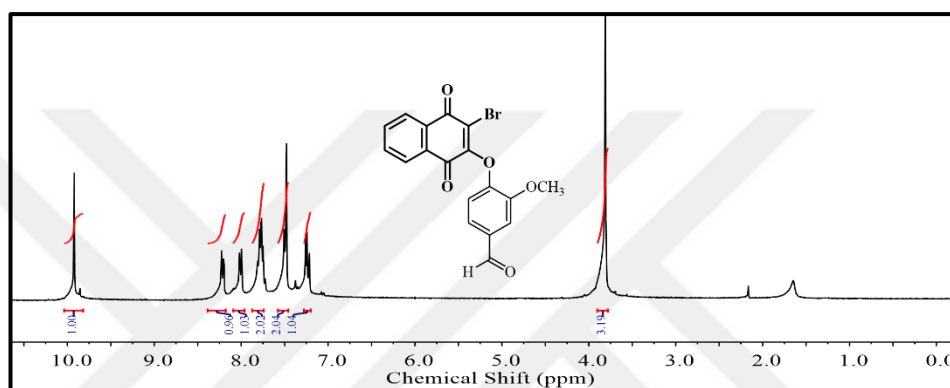


Figure 5.63. ^1H NMR spectrum of compound 4-32.

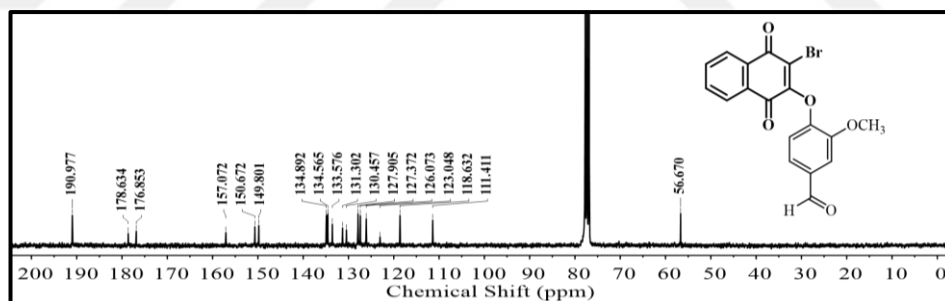


Figure 5.64. ^{13}C NMR spectrum of compound 4-32.

^1H NMR spectrum of 4-((3-bromo-1,4-dioxo-1,4-dihydronaphthalen-2-yl)oxy)-3-methoxybenzaldehyde is given in Figure 5.63. The peaks corresponding to the protons at the benzene ring of the naphthoquinone structure were observed at 8.21 as a doublet, 8.00 as a doublet, 7.88 - 7.71 as a multiplet peak in proton NMR. The aromatic protons of vanillin moiety were observed at 7.57 - 7.43 ppm and 7.33 - 7.18 ppm as multiples. Moreover, the methoxy group and the aldehyde protons at vanillin moiety appeared at 3.81 and 9.92 ppm as singlets. ^{13}C NMR spectrum of the compound is given in Figure 5.64. The carbonyl carbons were observed at 178.63 and 176.85 ppm. The methoxy group and the aldehyde carbons at vanillin moiety resonated at 56.67 and 190.98 ppm.

The compound has 18 chemically inequivalent carbon atoms, so the structure was in agreement with the ^{13}C NMR spectrum.

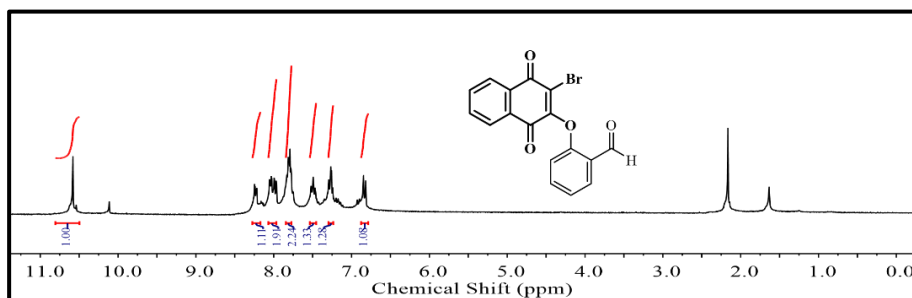


Figure 5.65. ^1H NMR spectrum of compound 4-33.

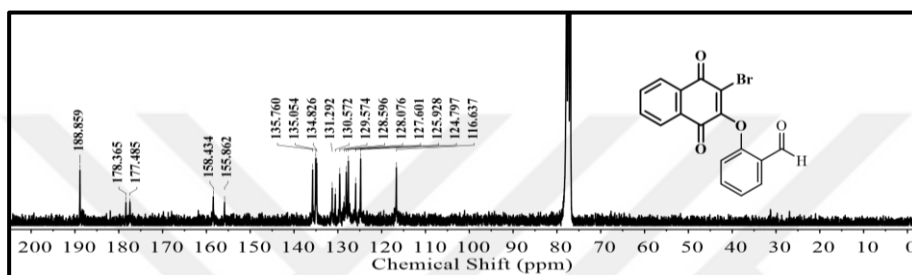


Figure 5.66. ^{13}C NMR spectrum of compound 4-33.

^1H NMR spectrum of 2-((3-bromo-1,4-dioxo-1,4-dihydronaphthalen-2-yl)oxy)benzaldehyde is given in Figure 5.65. The peaks corresponding to the protons at the benzene ring of naphthoquinone structure were observed at 8.23 ppm as a doublet, 8.11 - 7.94 ppm as a multiplet, and 7.86 - 7.70 ppm as a multiplet peak in proton NMR. The aromatic protons of salicylaldehyde moiety were observed at 7.49 ppm and 7.27 ppm as a triplet, 6.83 ppm as a doublet peak. Moreover, one of the peaks, which belonged to the salicylaldehyde moiety overlapped with the multiplet peak of 1,4-naphthoquinone proton at 8.11 - 7.94 ppm. The aldehyde proton at salicylaldehyde moiety appeared at 10.58 ppm as a singlet. ^{13}C NMR spectrum of the compound is given in Figure 5.66. The carbonyl carbons were observed at 178.37 and 177.48 ppm. The aldehyde carbon at salicylaldehyde moiety resonated at 188.86 ppm. The compound has 17 chemically inequivalent carbon atoms, so the structure was in agreement with the ^{13}C NMR spectrum.

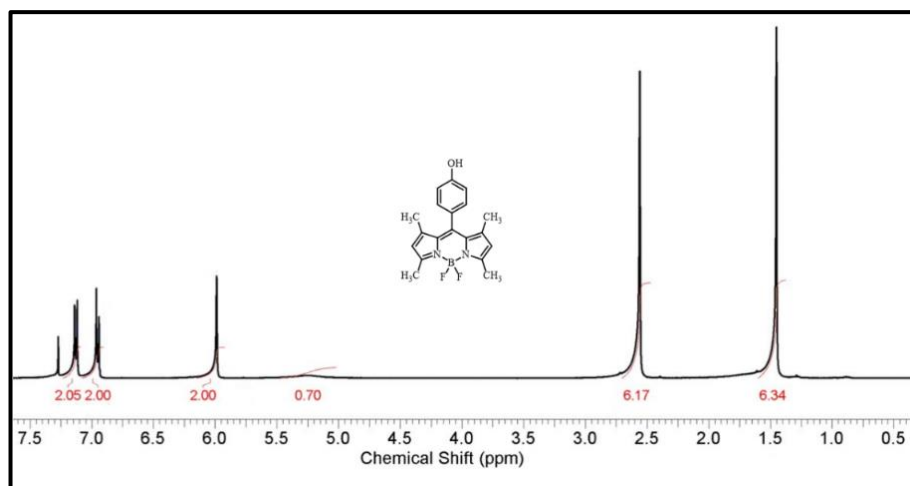


Figure 5.67. ^1H NMR spectrum of compound 4-34.

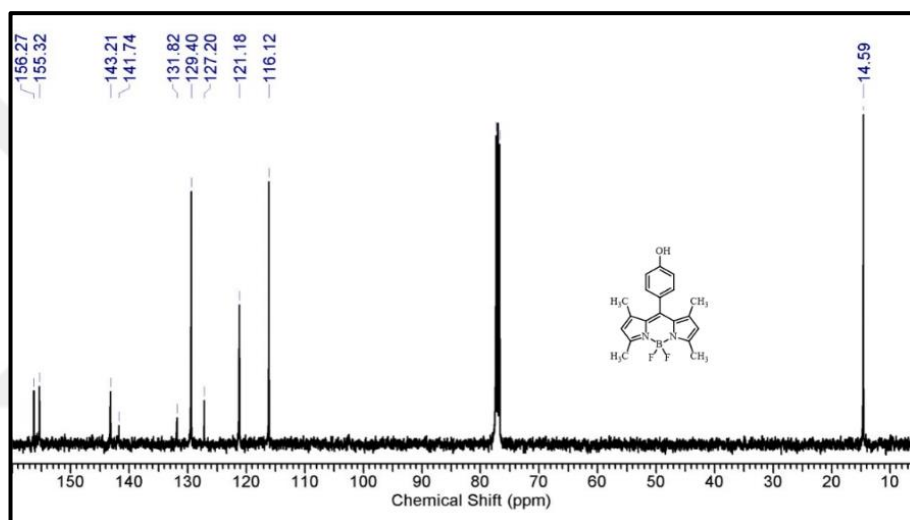


Figure 5.68. ^{13}C NMR spectrum of compound 4-34.

^1H NMR spectrum of BODIPY is given in Figure 5.67. The peaks corresponding to the protons at the phenol ring at the *meso* position of BODIPY were observed at 7.12 and 6.69 ppm as doublets. The protons at the BODIPY core resonated at 6.00 ppm. The phenolic proton was observed at 5.30 ppm as a broad singlet. The methyl protons appeared at 2.58 and 1.46 ppm. ^{13}C NMR spectrum of the compound is given in Figure 5.68. The compound has 11 chemically inequivalent carbon atoms, so the structure was in agreement with the ^{13}C NMR spectrum.

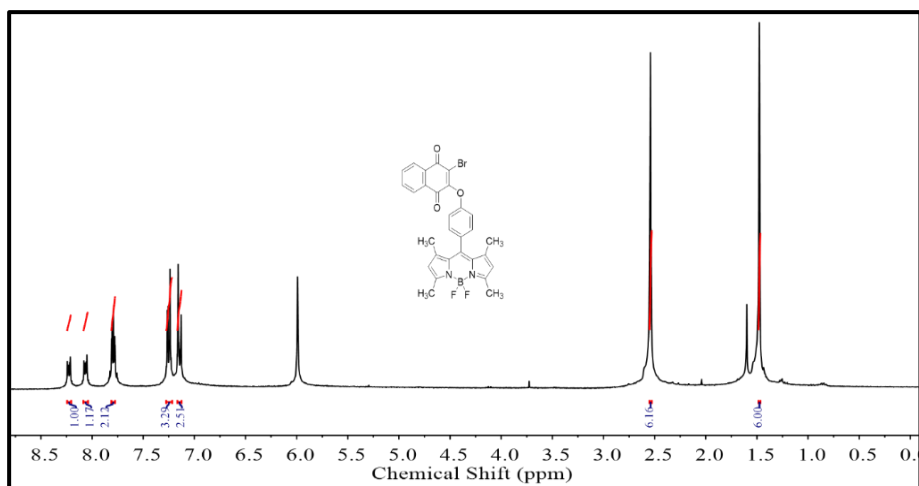


Figure 5.69. ^1H NMR spectrum of compound 4-35.

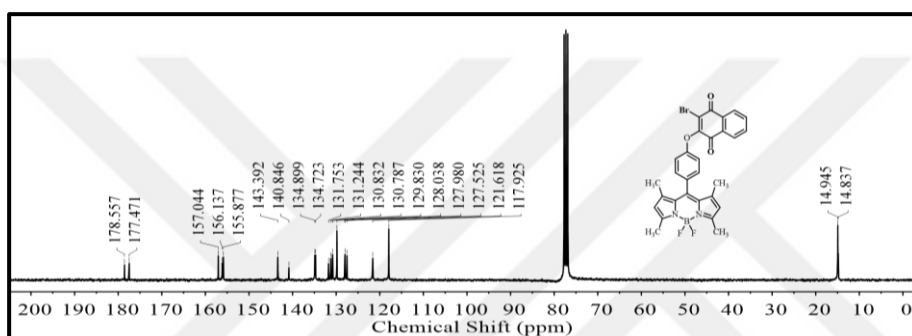


Figure 5.70. ^{13}C NMR spectrum of compound 4-35.

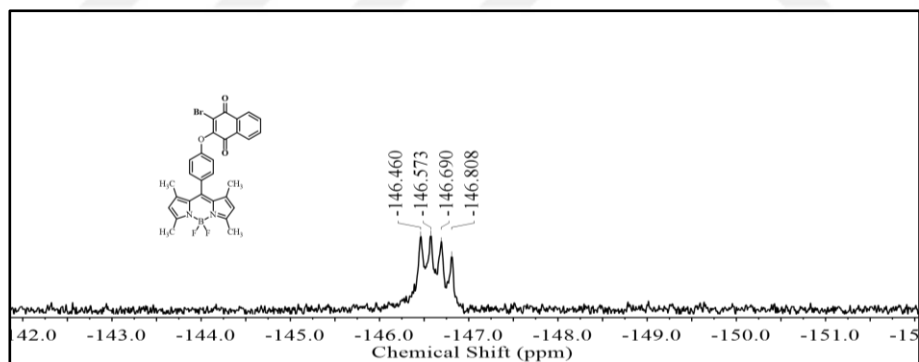


Figure 5.71. ^{19}F NMR spectrum of compound 4-35.

^1H NMR spectrum of 2-bromo-3-(4-(5,5-difluoro-1,3,7,9-tetramethyl-5H-4,5λ⁴-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-10-yl)phenoxy)naphthalene-1,4-dione is given in Figure 5.69. The peaks corresponding to the protons at the benzene ring of naphthoquinone structure were observed at 8.23, 8.07 ppm as doublets and 7.95 - 7.64 ppm as multiplet in proton NMR. The aromatic protons of phenylene spacer between 1,4-naphthoquinone and BODIPY core were observed at 7.25 and 7.14 ppm as doublets. Moreover, the protons of the BODIPY core resonated at 5.99 ppm as a

singlet, and the methyl protons were observed at 2.54 and 1.48 ppm as singlets. ^{13}C NMR spectrum of the compound is given in Figure 5.70. The carbonyl carbons were observed at 178.55 and 177.47 ppm. The peaks resulting from the methyl carbons were obtained at 14.95 and 14.84 ppm. The compound has 21 chemically inequivalent carbon atoms, so the structure was in agreement with the ^{13}C NMR spectrum. ^{19}F NMR spectrum of the compound is given in Figure 5.71. The fluorine atom was seen at -146.63 ppm as a quartet, which was split by a boron atom in fluorine NMR spectrum.

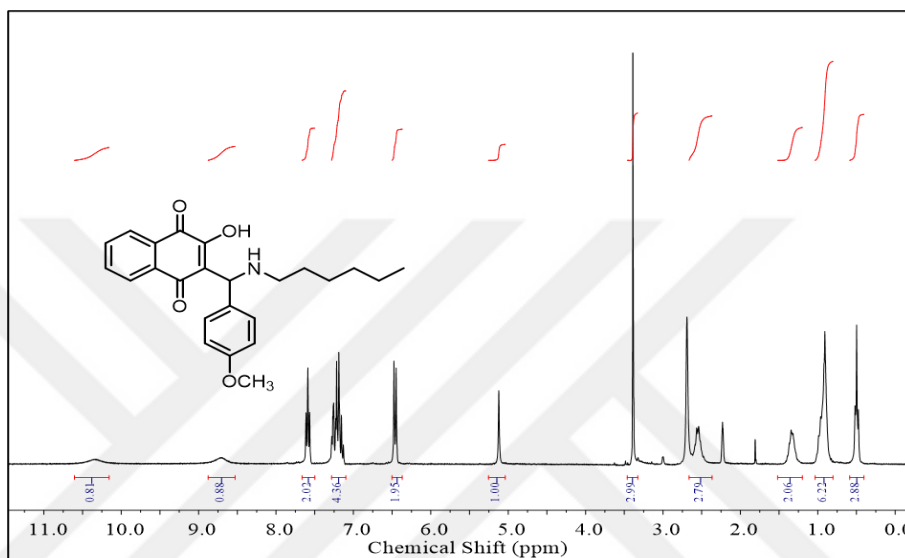


Figure 5.72. ^1H NMR spectrum of compound 4-36.

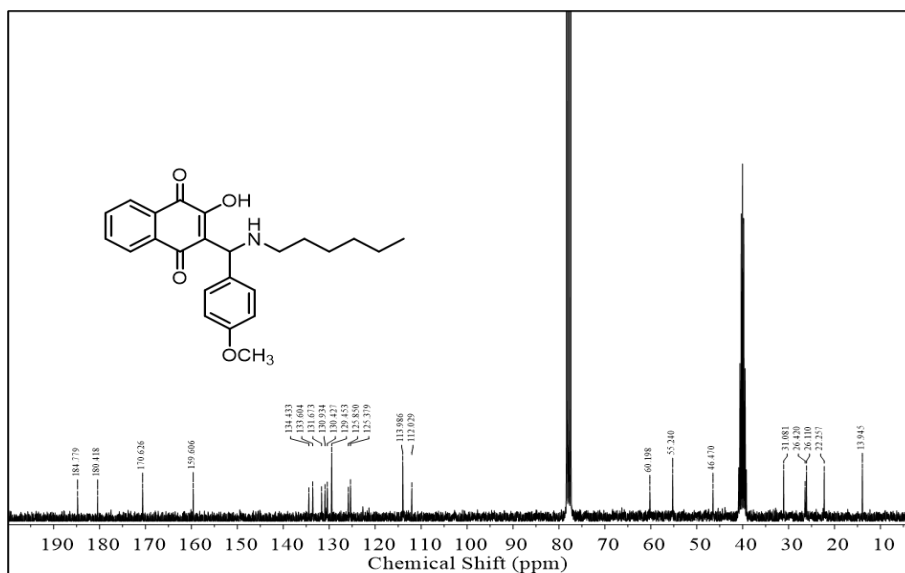


Figure 5.73. ^{13}C NMR spectrum of compound 4-36.

^1H NMR spectrum of 2-((hexylamino)(4-methoxyphenyl)methyl)-3-hydroxynaphthalene-1,4-dione is given in Figure 5.72. The compound has two

aromatic rings bearing hydrogen atoms. Those hydrogens were observed at the aromatic region of ^1H NMR spectrum, namely 6.46 ppm, 7.13-7.28 ppm and 7.59 ppm, as doublet, multiplet, and triplet peaks, respectively. The aliphatic hydrogens of the hexyl group were seen at the aliphatic region of NMR spectrum. The triplet at 0.50 ppm and multiplets at 0.90 ppm, 1.34 ppm, and 2.54 ppm belong to the aliphatic hydrogens of the hexyl group. The singlet peak at 3.40 ppm belongs to the methoxy group at the phenyl ring. More importantly, the singlet peak at 5.12 ppm is quite evident in the formation of our target product and belonged to the CH group formed at the junction of aldehyde, naphthoquinone and amine. The OH and NH groups' protons appeared at 10.31 and 8.70 ppm as broad singlets, respectively.

The compound has 22 chemically inequivalent carbon atoms, so ^{13}C NMR spectrum (Figure 5.73) have 22 peaks corresponding to these carbons. Two carbonyl carbons appeared at 180.4 ppm and 184.8 ppm. The peaks of the carbons belonging to the hexyl group were at 13.9, 22.3, 26.1, 26.42, 31.1 and 46.5 ppm. The methoxy group was observed at 55.2 ppm. The carbon signal belonging to the CH group was observed at 60.2 ppm. The remaining peaks resulting from aromatic and alkene carbons appeared between 110-175 ppm.

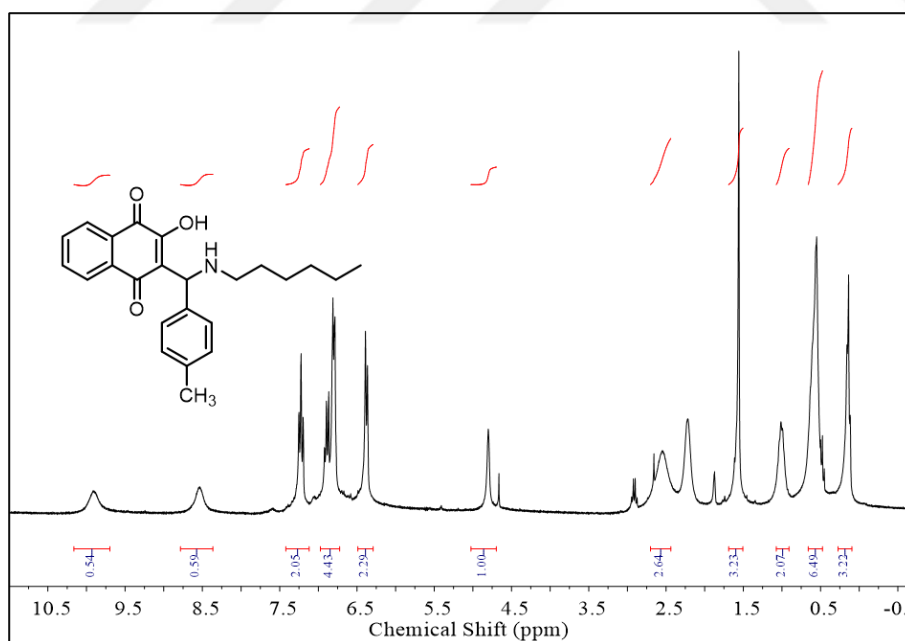


Figure 5.74. ^1H NMR spectrum of compound 4-37.

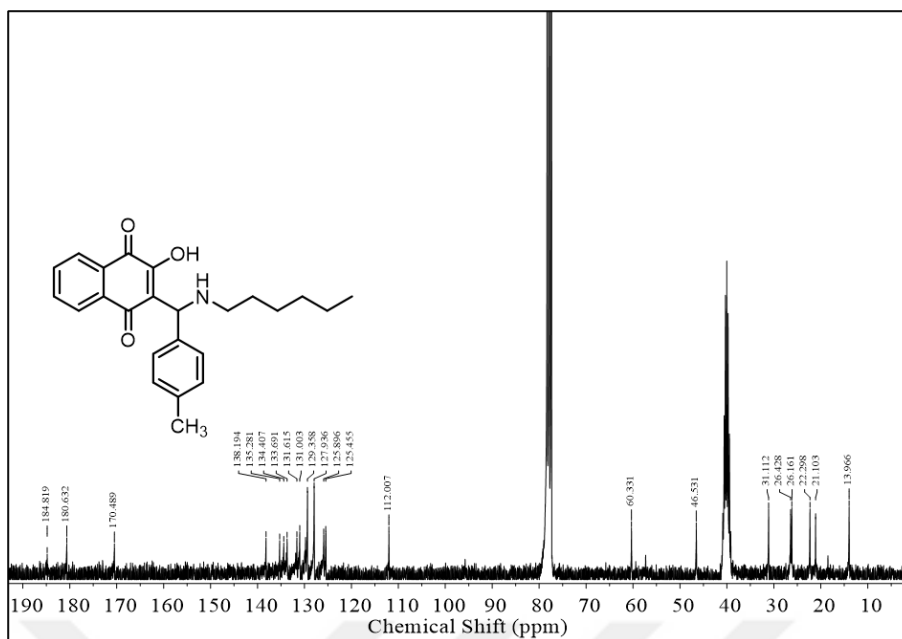


Figure 5.75. ^{13}C NMR spectrum of compound 4-37.

^1H NMR spectrum of 2-((hexylamino)(p-tolyl)methyl)-3-hydroxynaphthalene-1,4-dione is given in Figure 5.74. The compound has two aromatic rings bearing hydrogen atoms. Those hydrogens were observed at the aromatic region of ^1H NMR spectrum, namely 6.38, 6.77-6.19, and 7.22, as doublet, multiplet, and triplet peaks, respectively. The aliphatic hydrogens of the hexyl group were seen at the aliphatic region of NMR spectrum. The triplet at 0.14 ppm and multiplets at 0.77 - 0.38 ppm, 1.20 - 0.79 ppm, and singlet at 2.53 ppm belonged to the aliphatic hydrogens of the hexyl group. The singlet peak at 1.56 ppm belongs to the methyl group at the phenyl ring. More importantly, the singlet peak at 4.80 ppm is quite evident in the formation of our target product and belonged to the CH group formed at the junction of aldehyde, 1,4-naphthoquinone and amine. The OH and NH groups' protons appeared at 9.90 and 8.53 ppm as broad singlets, respectively.

The compound has 22 chemically inequivalent carbon atoms, so ^{13}C NMR spectrum (Figure 5.75) have 22 peaks corresponding to these carbons. Two carbonyl carbons appeared at 180.6 ppm and 184.8 ppm. The peaks of the carbons belonging to the hexyl group were at 14.0, 21.1, 26.2, 26.4, 31.1 and 46.5 ppm. The methyl group was observed at 22.3 ppm. The carbon signal belonging to the CH group was observed at 60.3 ppm. The remaining peaks resulting from aromatic and alkene carbons appeared between 110-175 ppm.

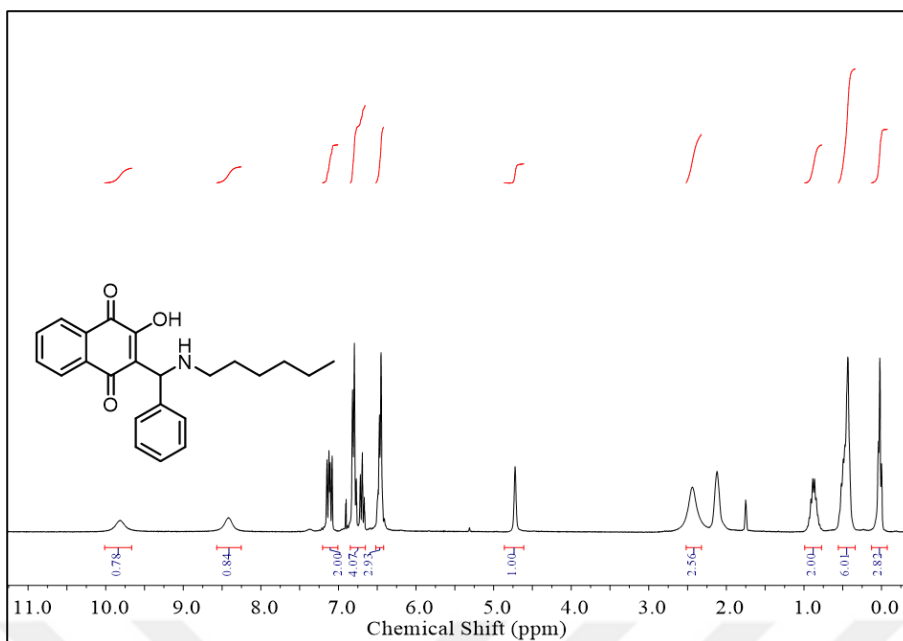


Figure 5.76. ^1H NMR spectrum of compound 4-38.

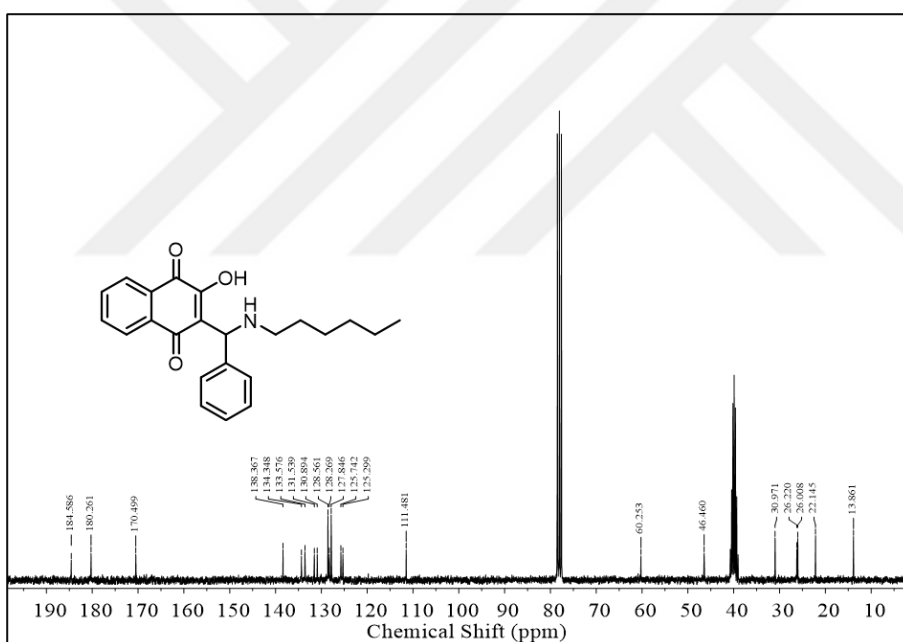


Figure 5.77. ^{13}C NMR spectrum of compound 4-38.

^1H NMR spectra of 2-((hexylamino)(phenyl)methyl)-3-hydroxynaphthalene-1,4-dione is given in Figure 5.76. The compound has two aromatic rings bearing hydrogen atoms. Those hydrogens were observed at the aromatic region of ^1H NMR spectrum, namely 6.49-6.43, 6.93-6.57, and 7.15-7.08 as multiplet peaks. The aliphatic hydrogens of the hexyl group were seen at the aliphatic region of NMR spectrum. The triplet at 0.02 ppm and multiplets at 0.69 - 0.30 ppm, 1.06 - 0.70 ppm, and singlet at 2.43 ppm belonged to the aliphatic hydrogens of the hexyl group. More importantly, the singlet

peak at 4.70 ppm is quite evident in the formation of our target product and belonged to the CH group formed at the junction of aldehyde, 1,4-naphthoquinone, and amine. The OH and NH groups' protons appeared at 9.82 and 8.42 ppm as broad singlets, respectively.

The compound has 21 chemically inequivalent carbon atoms, so ^{13}C NMR spectrum (Figure 5.77) have 21 peaks corresponding to these carbons. Two carbonyl carbons appeared at 180.3 ppm and 184.6 ppm. The peaks of the carbons belonging to the hexyl group were at 13.9, 22.1, 26.1, 26.2, 31.0, and 46.5 ppm. The carbon signal belonging to the CH group was observed at 60.2 ppm. The remaining peaks resulting from aromatic and alkene carbons appeared between 110-175 ppm.

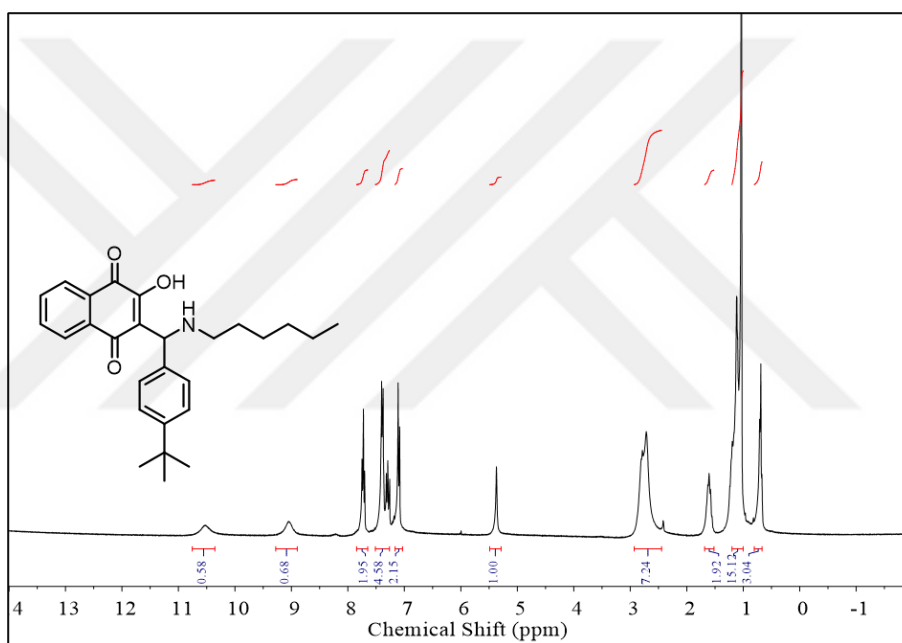


Figure 5.78. ^1H NMR spectrum of compound 4-39.

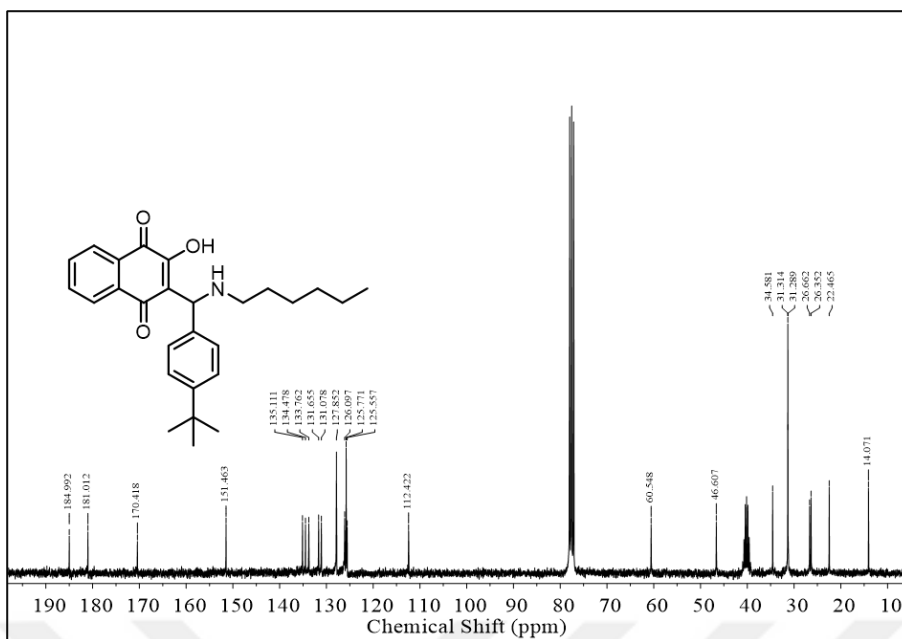


Figure 5.79. ^{13}C NMR spectrum of compound 4-39.

^1H NMR spectrum of 2-((4-(*tert*-butyl)phenyl)(hexylamino)methyl)-3-hydroxynaphthalene-1,4-dione is given in Figure 5.78. The compound has two aromatic rings bearing hydrogen atoms. Those hydrogens were observed at the aromatic region of ^1H NMR spectrum, namely 7.10, 7.47 - 7.22, and 7.73 ppm as doublet, multiplet and triplet peaks. The aliphatic hydrogens of the hexyl group were seen at the aliphatic region of NMR spectrum. The triplet at 0.69 ppm and multiplets at 1.31-0.85, 1.90 - 1.33 ppm, 3.06 - 2.56 ppm belonged to the aliphatic hydrogens of the hexyl group and *tert*-butyl group at the phenyl ring. It is worth mentioning that aliphatic protons of *tert* butyl and hexyl groups overlapped between 1.90 - 1.33 ppm. More importantly, the singlet peak at 5.35 ppm is quite evident in the formation of our target product and belonged to the CH group formed at the junction of aldehyde, 1,4-naphthoquinone, and amine. The OH and NH groups' protons appeared at 10.53 and 9.04 ppm as broad singlets, respectively.

The compound has 22 chemically inequivalent carbon atoms, so ^{13}C NMR spectrum (Figure 5.79) have 22 peaks corresponding to these carbons. Two carbonyl carbons appeared at 181.0 ppm and 185.0 ppm. The peaks of the carbons belonging to the hexyl group were at 14.1, 22.5, 26.34, 26.7, 31.2 and 46.6 ppm. The carbon signal belonging to the CH group was observed at 60.5 ppm. The remaining peaks resulting from aromatic and alkene carbons appeared between 110-175 ppm.

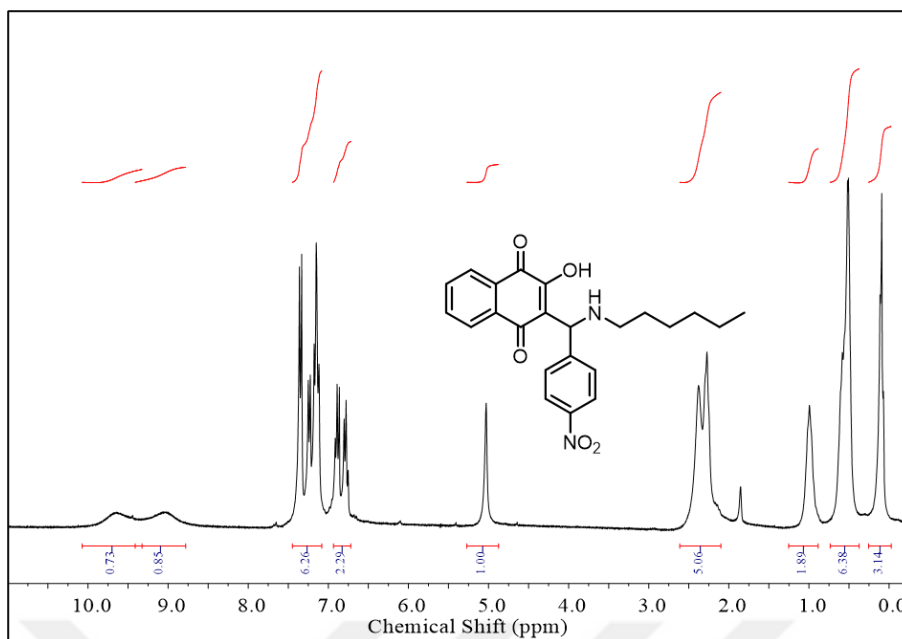


Figure 5.80. ¹H NMR spectrum of compound 4-40.

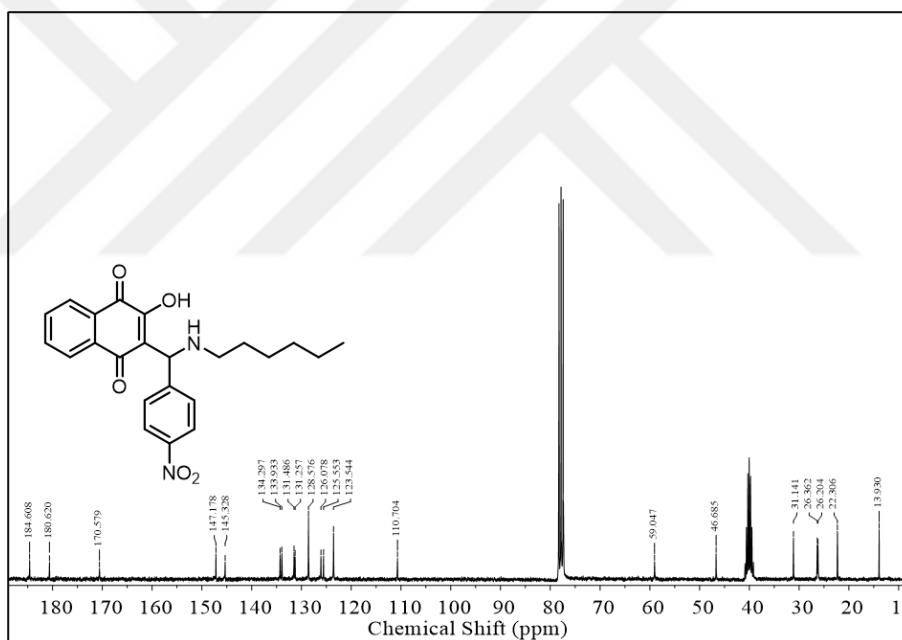


Figure 5.81. ¹³C NMR spectrum of compound 4-40.

¹H NMR spectrum of 2-((hexylamino)(4-nitrophenyl)methyl)-3-hydroxynaphthalene-1,4-dione is given in Figure 5.80. The compound has two aromatic rings bearing hydrogen atoms. Those hydrogens were observed at the aromatic region of ¹H NMR spectrum, namely between 6.91-6.75 and 7.46 - 7.07 ppm as multiplet peaks. The aliphatic hydrogens of the hexyl group were seen at the aliphatic region of NMR spectrum. The triplet at 0.09 ppm, multiplets at 0.74 - 0.40, 1.25 - 0.80 ppm, 3.06 - 2.56 ppm and singlet at 2.39 ppm belonged to the aliphatic hydrogens of the hexyl

group and tert butyl group at the phenyl ring. More importantly, the singlet peak at 5.04 ppm is quite evident in the formation of our target product and belonged to the CH group formed at the junction of aldehyde, 1,4-naphthoquinone and amine. The OH and NH groups' protons appeared at 9.66 and 9.06 ppm as broad singlets, respectively. The compound has 20 chemically inequivalent carbon atoms, so ^{13}C NMR spectrum (Figure 5.81) have 22 peaks corresponding to these carbons. Two carbonyl carbons appeared at 180.6 ppm and 184.6 ppm. The peaks of the carbons belonging to the hexyl group were at 13.9, 22.3, 26.2, 26.4, 31.1 and 46.7 ppm. The carbon signal belonging to the CH group was observed at 59.0 ppm. The remaining peaks resulting from aromatic and alkene carbons appeared between 110-175 ppm.

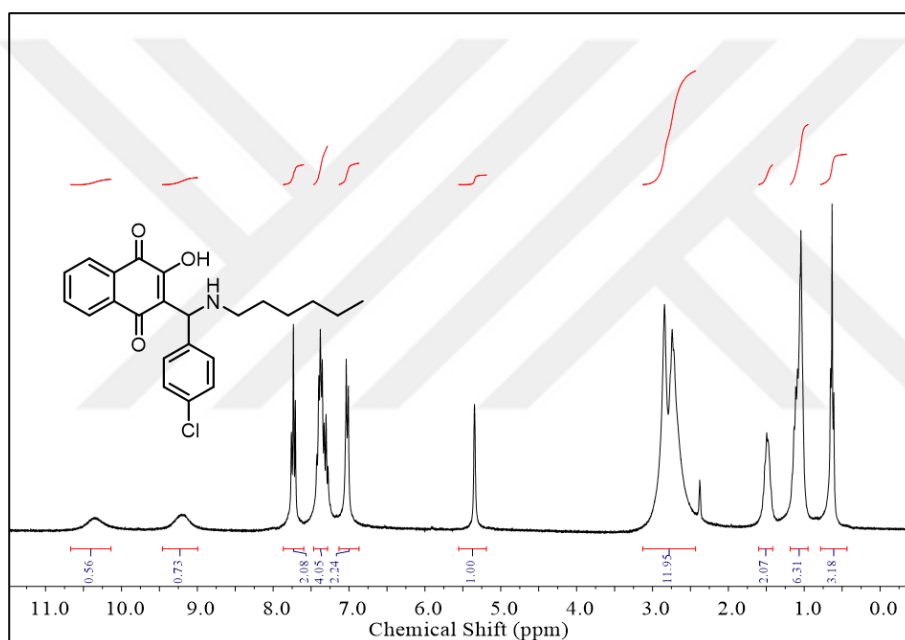


Figure 5.82. ^1H NMR spectrum of compound 4-41.

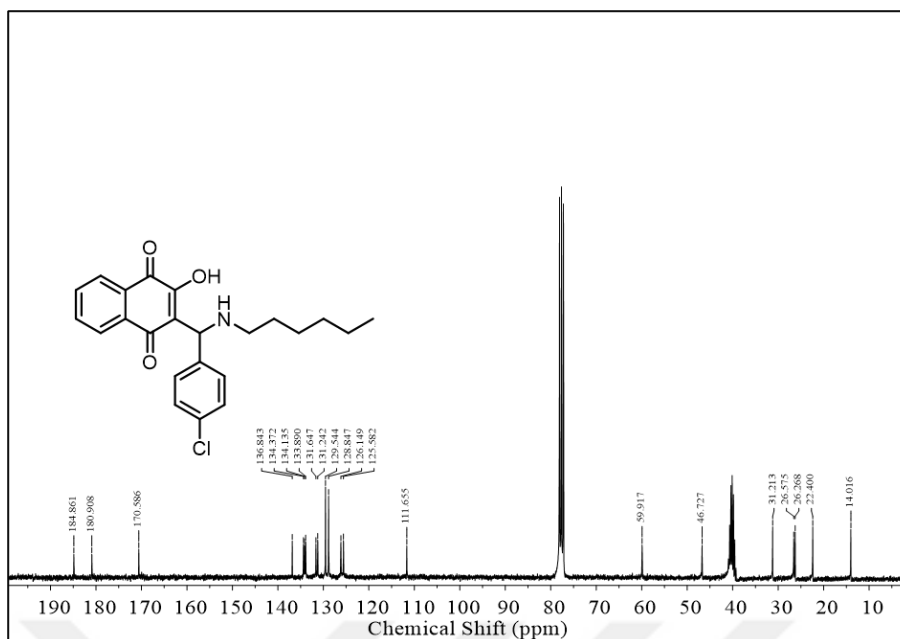


Figure 5.83. ^{13}C NMR spectrum of compound 4-41.

^1H NMR spectrum of 2-((4-chlorophenyl)(hexylamino)methyl)-3-hydroxynaphthalene-1,4-dione is given in Figure 5.82. The compound has two aromatic rings bearing hydrogen atoms. Those hydrogens were observed at the aromatic region of ^1H NMR spectrum, namely doublet at 7.02 ppm, multiplet at 7.42-7.28 ppm, and triplet at 7.73 ppm. The aliphatic hydrogens of the hexyl group were seen at the aliphatic region of NMR spectrum. The triplet at 0.63 ppm, multiplets at 1.30 - 0.74, 1.74 - 1.24 ppm, and 2.79 - 2.59 ppm belonged to the aliphatic hydrogens of the hexyl group. More importantly, the singlet peak at 5.35 ppm is quite evident in the formation of our target product and belonged to the CH group formed at the junction of aldehyde, 1,4-naphthoquinone and amine. The OH and NH groups' protons appeared at 10.35 and 9.22 ppm as broad singlets, respectively.

The compound has 20 chemically inequivalent carbon atoms, so ^{13}C NMR spectrum (Figure 5.83) have 22 peaks corresponding to these carbons. Two carbonyl carbons appeared at 180.6 ppm and 184.6 ppm. The peaks of the carbons belonging to the hexyl group were at 14.0, 22.4, 26.3, 26.6, 31.2, and 46.7 ppm. The carbon signal belonging to the CH group was observed at 59.9 ppm. The remaining peaks resulting from aromatic and alkene carbons appeared between 110-175 ppm.

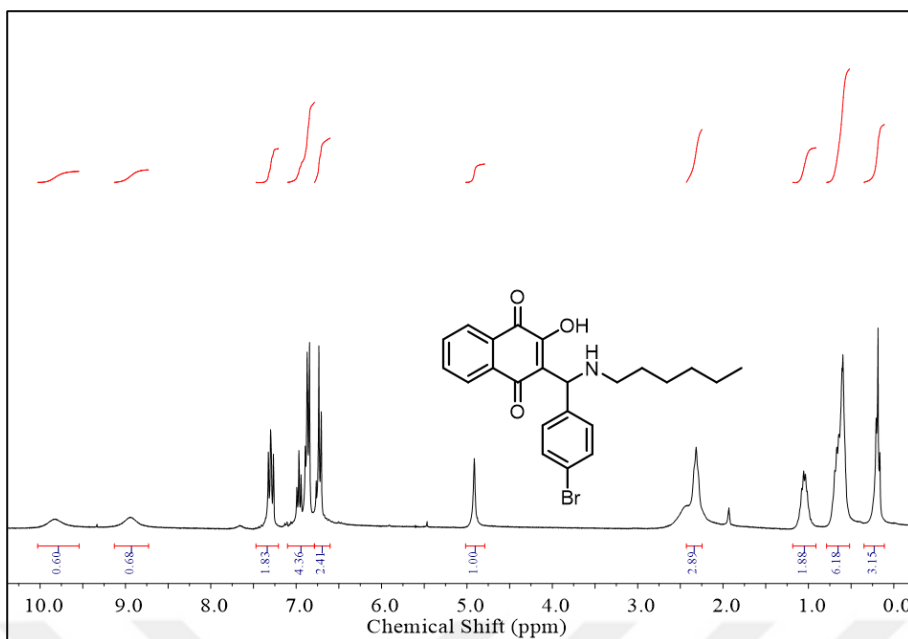


Figure 5.84. ¹H NMR spectrum of compound 4-42.

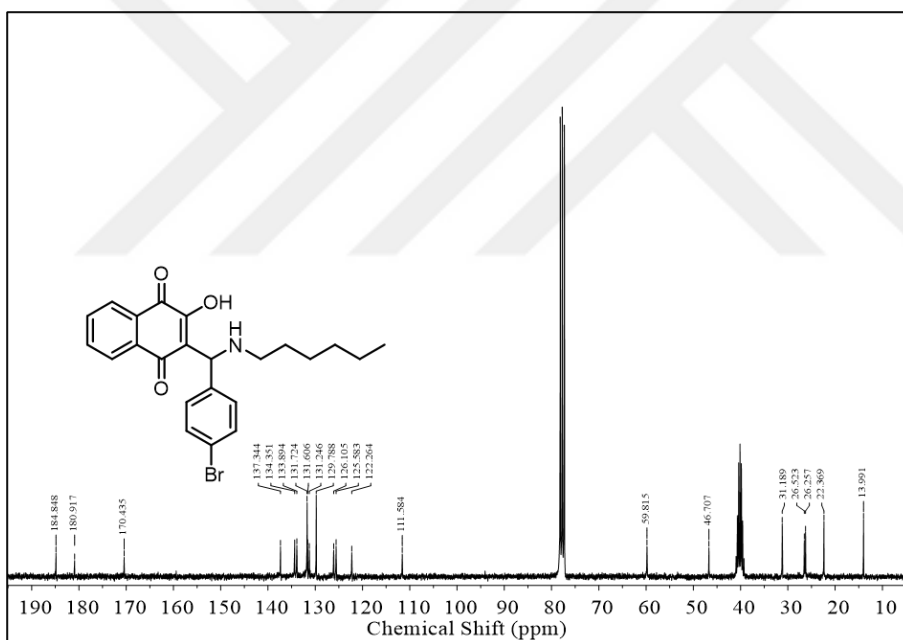


Figure 5.85. ¹³C NMR spectrum of compound 4-42.

¹H NMR spectrum of 2-((4-bromophenyl)(hexylamino)methyl)-3-hydroxynaphthalene-1,4-dione is given in Figure 5.84. The compound has two aromatic rings bearing hydrogen atoms. Those hydrogens were observed at the aromatic region of ¹H NMR spectrum, namely doublet at 6.72 ppm, multiplet at 7.05 - 6.82 ppm, and 7.51 - 7.17 ppm. The aliphatic hydrogens of the hexyl group were seen at the aliphatic region of NMR spectrum. The triplet at 0.19 ppm, multiplets at 0.83 - 0.41, 1.10-0.99 ppm, and 2.45 - 2.12 ppm belonged to the aliphatic hydrogens of the

hexyl group. More importantly, the singlet peak at 4.92 ppm is quite evident in the formation of our target product and belonged to the CH group formed at the junction of aldehyde, 1,4-naphthoquinone, and amine. The OH and NH groups' protons appeared at 9.84 and 8.96 ppm as broad singlets, respectively.

The compound has 20 chemically inequivalent carbon atoms, so ^{13}C NMR spectrum (Figure 5.85) have 22 peaks corresponding to these carbons. Two carbonyl carbons appeared at 180.9 ppm and 184.8 ppm. The peaks of the carbons belonging to the hexyl group were at 14.0, 22.4, 26.2, 26.5, 31.2, and 46.7 ppm. The carbon signal belonging to the CH group was observed at 59.8 ppm. The remaining peaks resulting from aromatic and alkene carbons appeared between 110-175 ppm.

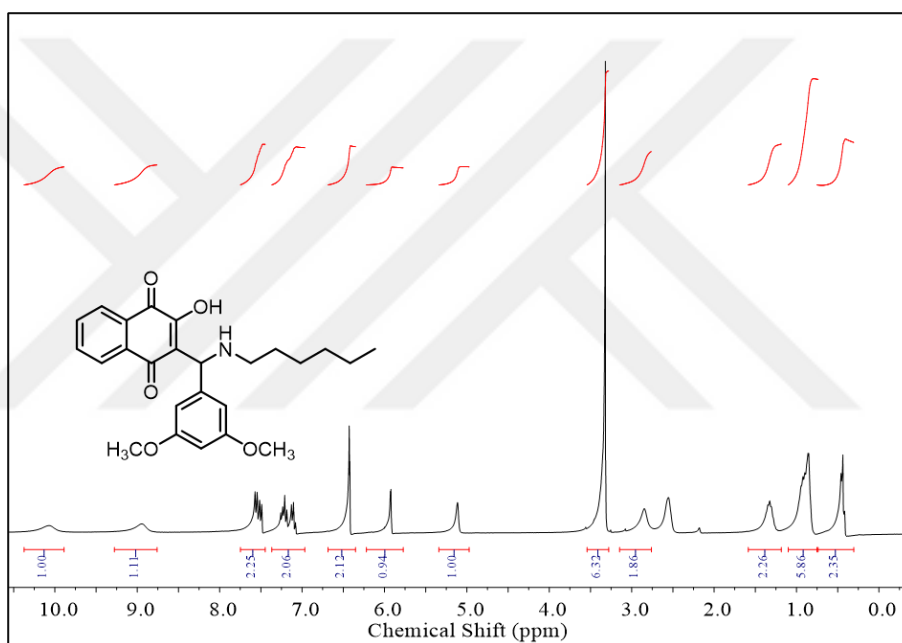


Figure 5.86. ^1H NMR spectrum of compound 4-43.

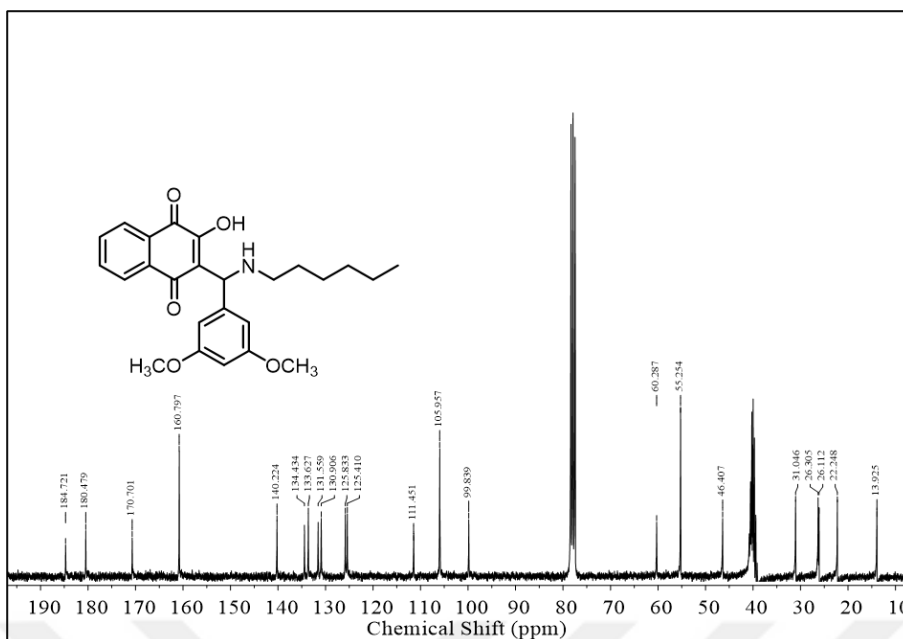


Figure 5.87. ^{13}C NMR spectrum of compound 4-43.

^1H NMR spectrum of 2-((3,5-dimethoxyphenyl)(hexylamino)methyl)-3-hydroxynaphthalene-1,4-dione is given in Figure 5.86. The compound has two aromatic rings bearing hydrogen atoms. Those hydrogens were observed at the aromatic region of ^1H NMR spectrum, namely 6.46 ppm, 7.13-7.28 ppm, and 7.59 ppm, as doublet, multiplet, and triplet peaks, respectively. The aliphatic hydrogens of the hexyl group were seen at the aliphatic region of NMR spectrum. The triplet at 0.44 ppm and multiplets between 1.09 - 0.73 ppm and 1.60 - 1.18 ppm 2.84 ppm belong to the aliphatic hydrogens of the hexyl group. The singlet peak at 3.32 ppm belongs to two methoxy groups at the phenyl ring. More importantly, the singlet peak at 5.10 ppm is quite evident in the formation of our target product and belonged to the CH group formed at the junction of aldehyde, naphthoquinone, and amine. The OH and NH groups' protons appeared at 10.31 and 8.70 ppm as broad singlets, respectively.

The compound has 22 chemically inequivalent carbon atoms, so ^{13}C NMR spectrum (Figure 5.87) have 22 peaks corresponding to these carbons. Two carbonyl carbons appeared at 180.5 ppm and 184.7 ppm. The peaks of the carbons belonging to the hexyl group were at 13.9, 22.2, 26.1, 26.3, 31.0, and 46.4 ppm. The methoxy group was observed at 55.2 ppm. The carbon signal belonging to the CH group was observed at 60.3 ppm. The remaining peaks resulting from aromatic and alkene carbons appeared between 100-175 ppm.

5.2. The Results of the Photophysical Study

Figure 5.88 showed the physical appearance of the compounds with the -NH_2 group (4-2) and -NHR groups (between 4-3 and 4-9) in the solution. Figure 5.89 displayed the absorption spectrum of the compounds. Their absorption bands appeared at the range of 429-470 nm in the visible region because of $\text{n-}\pi^*$ transition, and the peaks at 250-300 nm resulted from $\pi\text{-}\pi^*$ transitions. They displayed red-shifted spectrum compared to the compound 4-1 ($\lambda_{\text{abs}} = 336 \text{ nm}$). Their molar absorption coefficients are between $3700\text{--}6400 \text{ M}^{-1}\cdot\text{cm}^{-1}$. Figure 5.90 showed the emission spectrum of the compounds. The emission band was observed at 562 nm for the compound 4-2 with the -NH_2 group. The emission peaks were observed at the region of 581-592 nm for the compounds between 4-3 and 4-9. It has been seen that the addition of alkyl groups led to a *ca.* 20 nm red shift, but the alkyl groups' size and length didn't affect much the intensity and position of the peaks.



Figure 5.88. The physical appearance of all compounds between 4-2 and 4-9 in the solution.

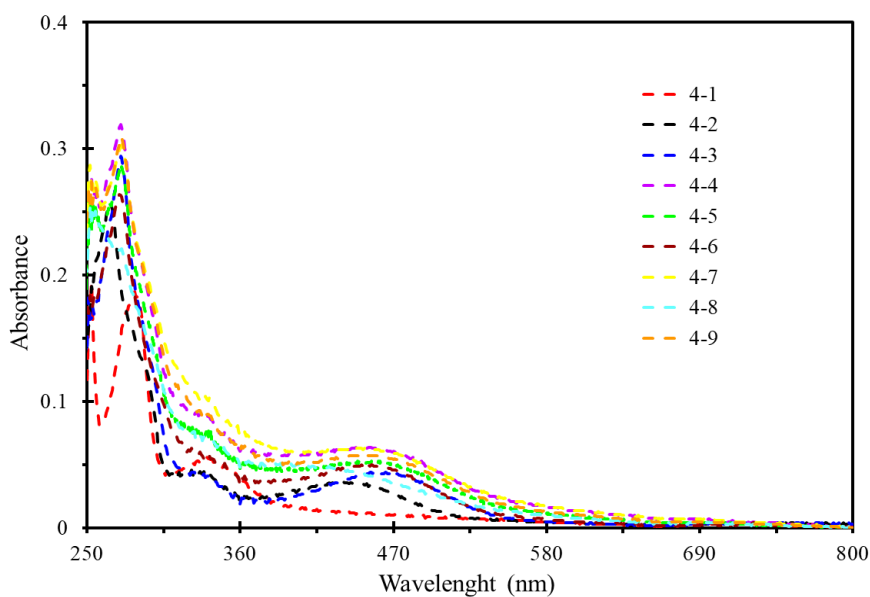


Figure 5.89. The absorption spectra of the compounds between 4-1 and 4-9

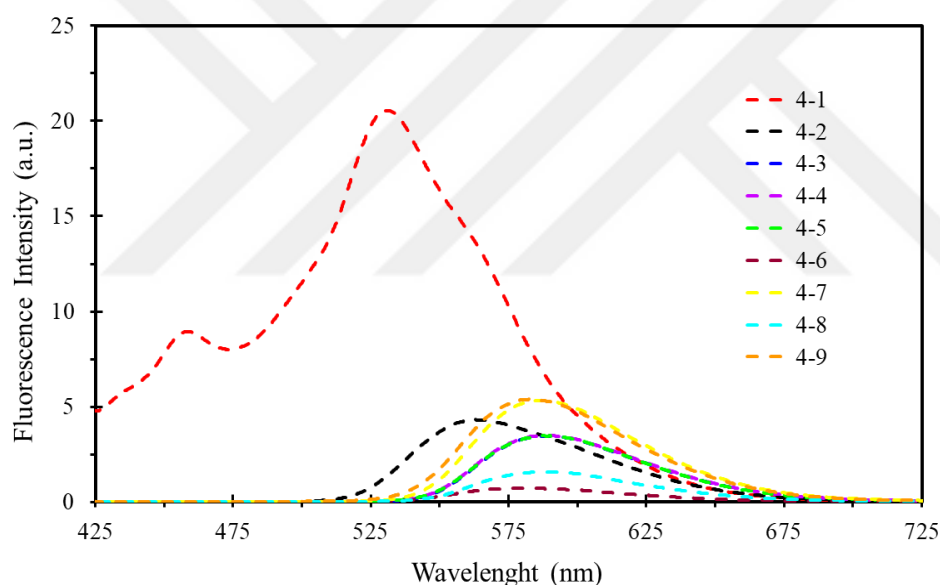


Figure 5.90. The emission spectra of the compounds between 4-1 and 4-9.

Figure 5.91 shows the physical appearance of the compounds produced from secondary cyclic amines and 2,3-dibrom-1,4-naphthoquinone in the solution. Figure 5.92 displays the absorption spectra of the compounds. Their absorption bands appeared at the range of 436-466 nm in the visible region because of $n\text{-}\pi^*$ transition, and the peaks at 250-300 nm resulted from $\pi\text{-}\pi^*$ transitions.

They displayed red-shifted spectra compared to the compound 4-1 ($\lambda_{\text{abs}} = 336 \text{ nm}$). Their molar absorption coefficients are between 3600-9200 $\text{M}^{-1}\cdot\text{cm}^{-1}$. Figure 5.93

shows the emission spectra of the compounds. The emission peaks were observed at the region of 574-602 nm.



Figure 5.91. The physical appearance of the compounds between 4-10 and 4-14.

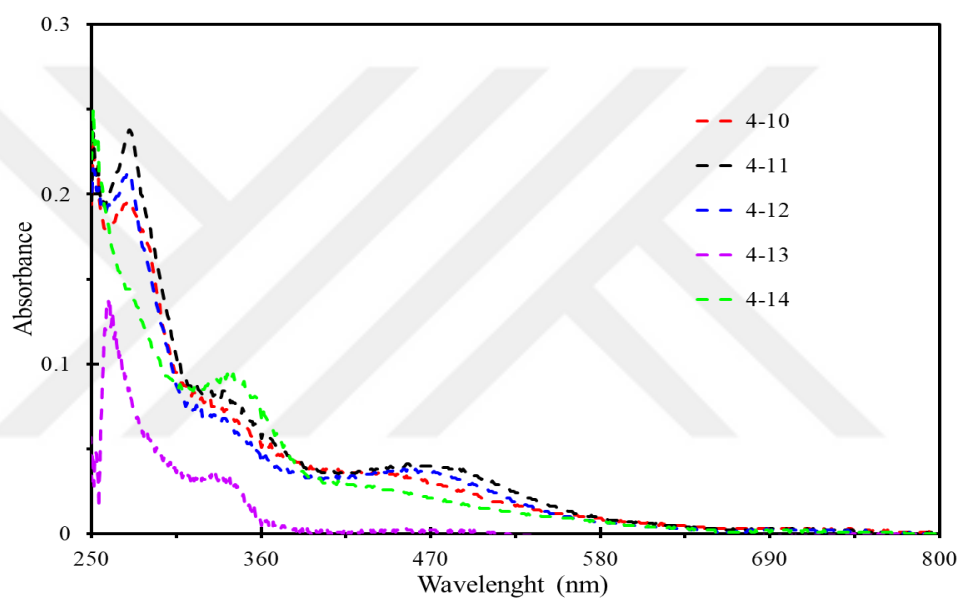


Figure 5.92. The absorption spectra of the compounds between 4-10 and 4-14.

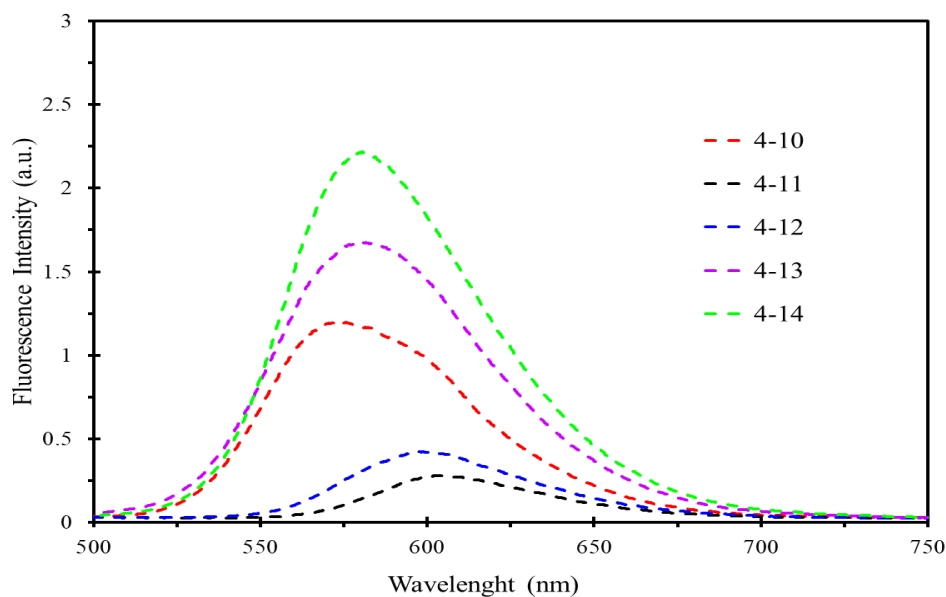


Figure 5.93. The emission spectra of the compounds between 4-10 and 4-14.

Figure 5.94 shows the physical appearance of 1,4-naphthoquinone with aromatic or hetero-aromatic amine groups in the solution state. Figure 5.95 displays the absorption spectra of the compounds. Their absorption bands appeared at the range of 440-523 nm in the visible region because of $n\text{-}\pi^*$ transition, and the peaks at 250-300 nm resulted from $\pi\text{-}\pi^*$ transitions. They displayed red-shifted spectra compared to their counterparts bearing the alkyl amine. Their molar absorption coefficients are between $2100\text{-}6400\text{ M}^{-1}\cdot\text{cm}^{-1}$. These compounds didn't produce any emission spectra.



Figure 5.94. The physical appearance of 1,4-naphthoquinone derivatives between 4-15 and 4-30.

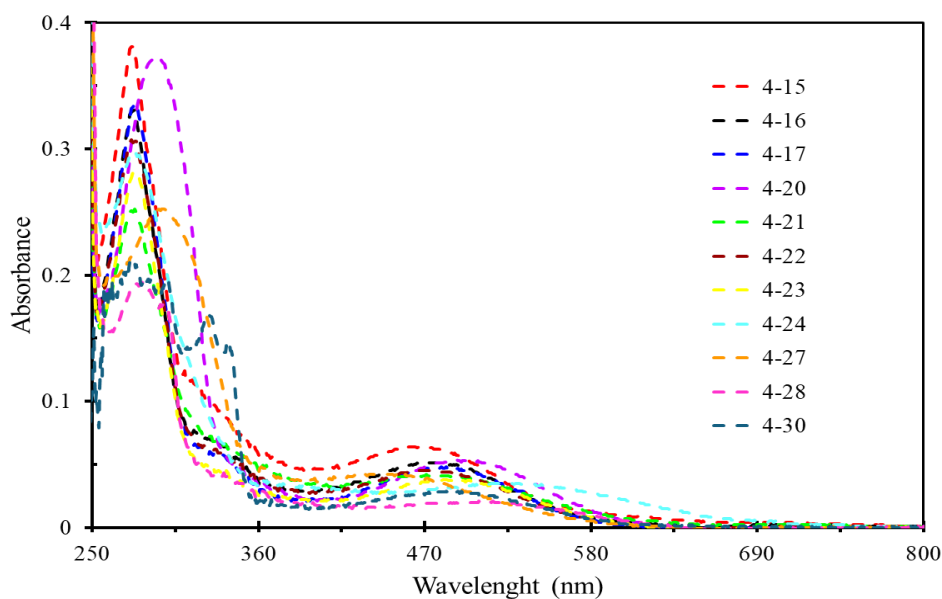


Figure 5.95. The absorption spectra of 1,4-naphthoquinone derivatives between 4-15 and 4-30.

Figure 5.96 shows the physical appearance of 1,4-naphthoquinone with phenolic aldehydes in the solution state. Figure 5.97 displays the absorption spectra of the compounds. Their absorption bands appeared at the range of 276-284 nm in the UV region because of π - π^* transition. Figure 5.97 shows the emission spectra of the compounds. The emission peaks were observed at the region of 522-532 nm.



Figure 5.96. The physical appearance of 1,4-naphthoquinone derivatives between 4-31 and 4-33.

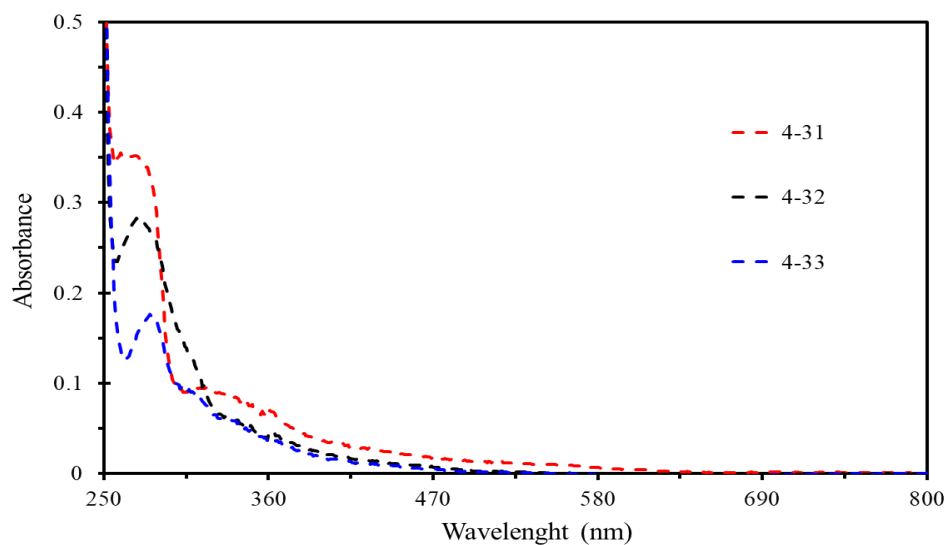


Figure 5.97. The absorption spectra of 1,4-naphthoquinone derivatives between 4-31 and 4-33.

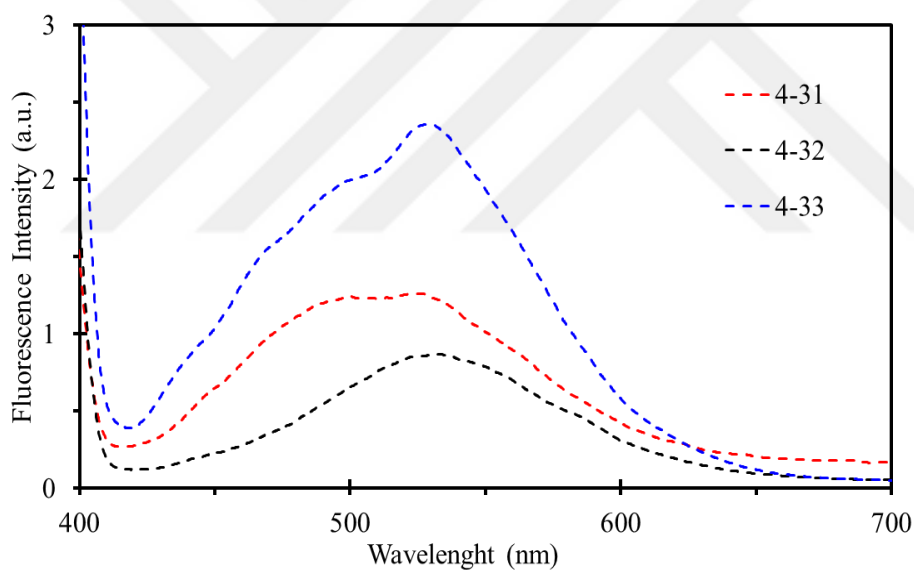


Figure 5.98. The emission spectra of 1,4-naphthoquinone derivatives between 4-15 and 4-30.

The emission and absorption spectra of the compound with its physical appearance in the solution are shown in Figure 5.99. The absorption band and emission spectra appeared at 449 and 552 nm, respectively. The absorption peak at the visible region of the spectra resulted from $n\text{-}\pi^*$ transitions. The one seen at the higher energy side of the spectrum resulted from $\pi\text{-}\pi^*$ transitions. The highest molar absorption coefficient ($71700\text{ M}^{-1}\cdot\text{cm}^{-1}$) obtained in all the compounds stemmed from the BODIPY core of the 1,4-naphthoquinone (4-35).

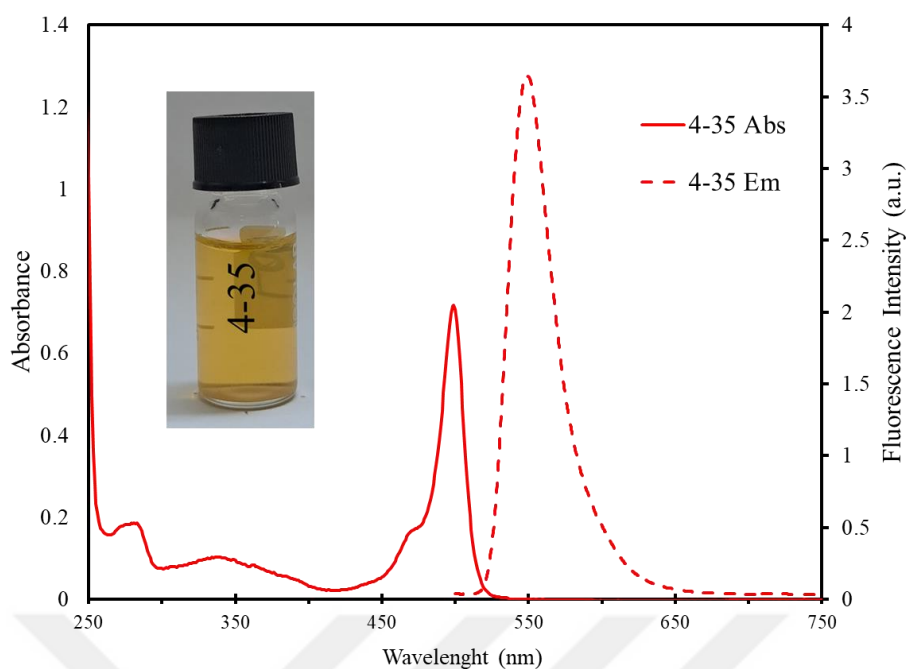


Figure 5.99. The absorption and emission spectra of the compound 4-35 and its physical appearance in the solution.

The Mannich base compounds in the solution state were given in Figure 5.100. Figure 5.101 displays the absorption spectra of the Mannich bases. Their absorption bands appeared at the range of 474-504 nm in the visible region because of $n-\pi^*$ transition, and the peaks at 250-300 nm resulted from $\pi-\pi^*$ transitions. Their molar absorption coefficients are between $2100-4500 \text{ M}^{-1}\cdot\text{cm}^{-1}$. Figure 5.102 shows the emission spectra of the compounds. The emission peaks were observed at the region of 595-603 nm.



Figure 5.100. The physical appearance of Mannich bases between 4-36 and 4-43 in solution.

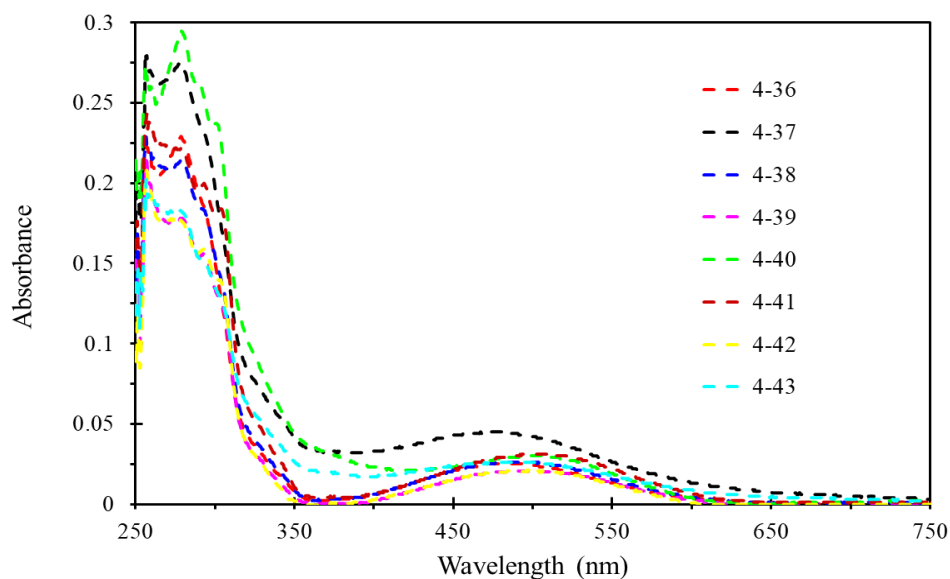


Figure 5.101. The absorption spectra of Mannich bases.

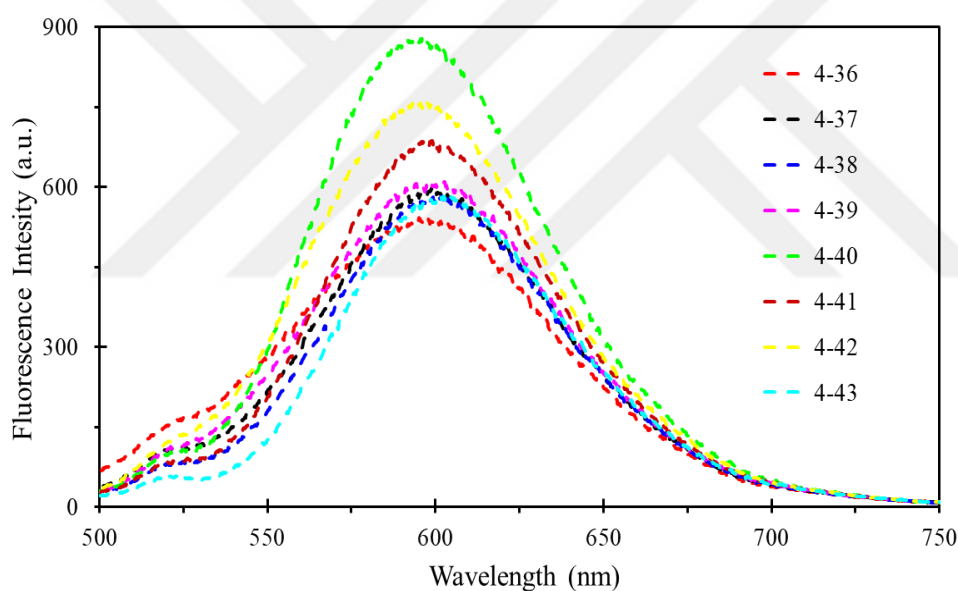


Figure 5.102. The emission spectra of Mannich bases.

The photophysical parameters of the final compounds were tabulated in Table 5.1 and discussed above.

Table 5.1. The photophysical properties of the compounds.

The compound	λ_{abs} (nm)	λ_{em} (nm)	ϵ ($\text{L}\cdot\text{mol}^{-1}\text{cm}^{-1}$)
4-1	336	530	5600
4-2	434	562	3700
4-3	470	590	4400
4-4	447	589	6400
4-5	454	590	5300

Table 5.1. (continued) The photophysical properties of the compounds.

The compound	λ_{abs} (nm)	λ_{em} (nm)	ϵ (L.mol ⁻¹ cm ⁻¹)
4-6	450	581	5000
4-7	446	587	6300
4-8	429	592	4800
4-9	451	583	5800
4-10	436	574	3600
4-11	456	602	4100
4-12	453	597	3800
4-13	336	580	9500
4-14	340	580	9200
4-15	466	<i>nd</i>	6400
4-16	472	<i>nd</i>	5200
4-17	484	<i>nd</i>	4800
4-20	500	<i>nd</i>	5300
4-21	470	<i>nd</i>	4200
4-22	473	<i>nd</i>	4500
4-23	486	<i>nd</i>	3800
4-24	523	<i>nd</i>	3500
4-27	440	<i>nd</i>	4200
4-28	510	<i>nd</i>	2100
4-30	492	<i>nd</i>	2900
4-31	276	522	35400
4-32	271	532	28400
4-33	284	530	17800
4-35	499	552	71700
4-36	480	595	2500
4-37	474	599	4500
4-38	490	602	2600
4-39	504	603	2100
4-40	500	596	3000
4-41	503	599	3100
4-42	502	595	2100
4-43	486	601	2600

5.3. The General Remarks on Electrochemical Features of the Compounds

The electrochemical properties of the compounds were investigated in DMSO by the cyclic voltammetry method. The recorded voltammograms were presented in Appendix A. The voltammograms generally exhibited two reversible peaks in the cathodic region. Those peaks corresponded to the transformation of naphthoquinone to seminaaphthoquinone radical and seminaaphthoquinone to dianion catechol by the reduction process. The reduction steps were depicted in Figure 5.103. The peak observed at the anodic side resulted from the oxidation process of the quinone ring of the naphthoquinone ring in the case of the Mannich bases or the attached side groups.

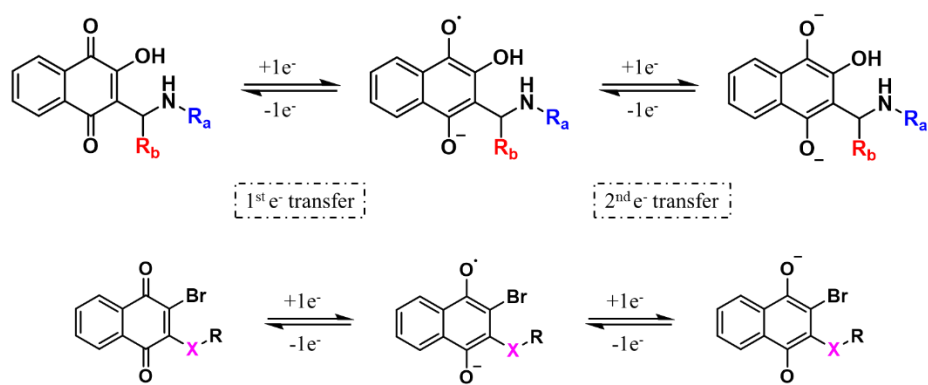


Figure 5.103. The redox process of 1,4-naphthoquinone derivatives.

REFERENCES

- [1] Aminin D, Polonik S. 1,4-Naphthoquinones: Some Biological Properties and Application. *Chem Pharm Bull (Tokyo)* 2020;68:46–57. <https://doi.org/10.1248/cpb.c19-00911>.
- [2] 1,4-NAPHTHOQUINONE. *Organic Syntheses* 1953;33:50. <https://doi.org/10.15227/orgsyn.033.0050>.
- [3] 1,4-NAPHTHOQUINONE. *Organic Syntheses* 1925;5:79. <https://doi.org/10.15227/orgsyn.005.0079>.
- [4] Pancrazzi F, Maestri G, Maggi R, Viscardi R. Oxidative Dearomatization of Phenols and Polycyclic Aromatics with Hydrogen Peroxide Triggered by Heterogeneous Sulfonic Acids. *European J Org Chem* 2021;2021:5407–14. <https://doi.org/https://doi.org/10.1002/ejoc.202100861>.
- [5] Jeong D, Yan JJ, Noh H, Hedman B, Hodgson KO, Solomon EI, et al. Oxidation of Naphthalene with a Manganese(IV) Bis(hydroxo) Complex in the Presence of Acid. *Angewandte Chemie International Edition* 2018;57:7764–8. <https://doi.org/https://doi.org/10.1002/anie.201802641>.
- [6] Srivastava M, Srivastava A, Goyal A, Mishra A, Tomer P, Dwivedi J, et al. One-pot oxidation of aromatic and cyclic hydrocarbons using the Au (III) and Pd (II) catalyst under microwave irradiation. *J Phys Org Chem* 2017;30:e3602. <https://doi.org/https://doi.org/10.1002/poc.3602>.
- [7] Shi F, Tse MK, Beller M. A Novel and Convenient Process for the Selective Oxidation of Naphthalenes with Hydrogen Peroxide. *Adv Synth Catal* 2007;349:303–8. <https://doi.org/https://doi.org/10.1002/adsc.200600395>.
- [8] Wienhöfer G, Schröder K, Möller K, Junge K, Beller M. A Novel Process for Selective Ruthenium-Catalyzed Oxidation of Naphthalenes and Phenols. *Adv Synth Catal* 2010;352:1615–20. <https://doi.org/https://doi.org/10.1002/adsc.201000137>.
- [9] Yusubov MS, Celik C, Geraskina MR, Yoshimura A, Zhdankin V V., Nemykin VN. Binuclear iron(III) octakis(perfluorophenyl)tetraazaporphyrin μ -oxodimer: a highly efficient catalyst for biomimetic oxygenation reactions. *Tetrahedron Lett* 2014;55:5687–90. <https://doi.org/10.1016/J.TETLET.2014.08.070>.
- [10] Rebelo SLH, Silva AMN, Medforth CJ, Freire C. Iron(III) Fluorinated Porphyrins: Greener Chemistry from Synthesis to Oxidative Catalysis Reactions. *Molecules* 2016;21. <https://doi.org/10.3390/molecules21040481>.
- [11] Natarajan P, Vagicherla VD, Vijayan MT. A mild oxidation of deactivated naphthalenes and anthracenes to corresponding para-quinones by N-bromosuccinimide. *Tetrahedron Lett* 2014;55:3511–5. <https://doi.org/10.1016/J.TETLET.2014.04.088>.

- [12] Natarajan P, Vagicherla VD, Vijayan MT. Indirect electrochemical oxidation of substituted polycyclic aromatic hydrocarbons to corresponding para-quinones with potassium bromide in water–chloroform medium. *Tetrahedron Lett* 2014;55:5817–21. <https://doi.org/10.1016/J.TETLET.2014.08.121>.
- [13] Zhou Q, Peng C, Du F, Zhou L, Shi Y, Du Y, et al. Design, synthesis and activity of BBI608 derivatives targeting on stem cells. *Eur J Med Chem* 2018;151:39–50. <https://doi.org/10.1016/J.EJMECH.2018.03.054>.
- [14] Spyroudis S. Hydroxyquinones: Synthesis and Reactivity. *Molecules* 2000;5:1291–330. <https://doi.org/10.3390/51201291>.
- [15] Kumar BS, Ravi K, Verma AK, Fatima K, Hasanain M, Singh A, et al. Synthesis of pharmacologically important naphthoquinones and anticancer activity of 2-benzyllawsone through DNA topoisomerase-II inhibition. *Bioorg Med Chem* 2017;25:1364–73. <https://doi.org/10.1016/J.BMC.2016.12.043>.
- [16] Li J, Zhang J, Li M, Zhang C, Yuan Y, Liu R. Naphtho[2,3-b]furan-4,9-dione synthesis via palladium-catalyzed reverse hydrogenolysis. *Chemical Communications* 2019;55:2348–51. <https://doi.org/10.1039/C8CC09369E>.
- [17] Wu L, Ma X, Yang X, Zhang C. Synthesis and biological evaluation of β -lapachone-monastrol hybrids as potential anticancer agents. *Eur J Med Chem* 2020;203:112594. <https://doi.org/10.1016/J.EJMECH.2020.112594>.
- [18] 2-HYDROXY-1,4-NAPHTHOQUINONE. *Organic Syntheses* 1941;21:56. <https://doi.org/10.15227/orgsyn.021.0056>.
- [19] Cheng Y, An LK, Wu N, Wang XD, Bu XZ, Huang ZS, et al. Synthesis, cytotoxic activities and structure-activity relationships of topoisomerase I inhibitors: Indolizinoquinoline-5,12-dione derivatives. *Bioorg Med Chem* 2008;16:4617–25. <https://doi.org/10.1016/j.bmc.2008.02.036>.
- [20] Calil FA, David JS, Chiappetta ERC, Fumagalli F, Mello RB, Leite FHA, et al. Ligand-based design, synthesis and biochemical evaluation of potent and selective inhibitors of *Schistosoma mansoni* dihydroorotate dehydrogenase. *Eur J Med Chem* 2019;167:357–66. <https://doi.org/10.1016/j.ejmech.2019.02.018>.
- [21] Neufeind S, Hülsken N, Neudörfl J-M, Schlörer N, Schmalz H-G. Total Synthesis of cyclo-Mumbaistatin Analogues through Anionic Homo-Fries Rearrangement. *Chemistry – A European Journal* 2011;17:2633–41. <https://doi.org/https://doi.org/10.1002/chem.201003166>.
- [22] Su J, Zhang Y, Chen M, Li W, Qin X, Xie Y, et al. A Copper Halide Promoted Regioselective Halogenation of Coumarins Using N-Halosuccinimide as Halide Source. *Synlett* 2019;30:630–4. <https://doi.org/10.1055/s-0037-1612080>.
- [23] Krishnan A, Kamaraj S. Direct Access to Quinone-Fused 5-Substituted-1,4-Benzodiazepine Scaffolds from Azidoquinones with/without [1,2]-Azide-Nitrogen Migration: Mechanistic Insights. *J Org Chem* 2023;88:16315–29. <https://doi.org/10.1021/acs.joc.3c01810>.
- [24] Brimble MA, Bachu P, Sperry J. Enantioselective synthesis of an analogue of nanaomycin A. *Synthesis (Stuttg)* 2007:2887–93. <https://doi.org/10.1055/s-2007-983848>.

- [25] Kalt MM, Schuehly W, Saf R, Ochensberger S, Solnier J, Bucar F, et al. Palladium-catalysed synthesis of aryl naphthoquinones as antiprotozoal and antimycobacterial agents. *Eur J Med Chem* 2020;207. <https://doi.org/10.1016/j.ejmech.2020.112837>.
- [26] Anuratha M, Jawahar A, Umadevi M, Sathe VG, Vanelle P, Terme T, et al. SERS investigations of 2,3-dibromo-1,4-naphthoquinone on silver nanoparticles. *Spectrochim Acta A Mol Biomol Spectrosc* 2013;105:218–22. <https://doi.org/10.1016/j.saa.2012.12.028>.
- [27] Jia Y, Xu Y, Nie R, Chen F, Zhu Z, Wang J, et al. Artificial photosynthesis of methanol from carbon dioxide and water via a Nile red-embedded TiO₂ photocathode. *J Mater Chem A Mater* 2017;5:5495–501. <https://doi.org/10.1039/C6TA10231J>.
- [28] Migulin VA. A New Synthetic Pathway to Symmetric Bisubstituted Naphthoquinones. *Synthesis* (Germany) 2020;52:60–8. <https://doi.org/10.1055/s-0039-1690725>.
- [29] Ventura Pinto A, de Castro S. The Trypanocidal Activity of Naphthoquinones: A Review. *Molecules* 2009;14:4570–90. <https://doi.org/10.3390/molecules14114570>.
- [30] Ilangovan A, Palayullaparambil Adarsh Krishna T. C—H Activation Strategies for Heterofunctionalization and Heterocyclization on Quinones: Application in the Synthesis of Bioactive Compounds. *Organic Synthesis - A Nascent Relook [Working Title]*, IntechOpen; 2020. <https://doi.org/10.5772/intechopen.90930>.
- [31] Mather BD, Viswanathan K, Miller KM, Long TE. Michael addition reactions in macromolecular design for emerging technologies. *Progress in Polymer Science* (Oxford) 2006;31:487–531. <https://doi.org/10.1016/j.progpolymsci.2006.03.001>.
- [32] Klotz L-O, Hou X, Jacob C. 1,4-Naphthoquinones: From Oxidative Damage to Cellular and Inter-Cellular Signaling. *Molecules* 2014;19:14902–18. <https://doi.org/10.3390/molecules190914902>.
- [33] Buffinton GD, Ollinger K, Brunmark A, Cadenas E. DT-diaphorase-catalysed reduction of 1,4-naphthoquinone derivatives and glutathionyl-quinone conjugates Effect of substituents on autoxidation rates. vol. 257. 1989.
- [34] Reddy BVS, Reddy SM, Swain M. Sugar thiourea catalyzed highly enantioselective Michael addition of 2-hydroxy-1,4-naphthoquinone to β -nitroalkenes. *RSC Adv* 2013;3:930–6. <https://doi.org/10.1039/C2RA22270A>.
- [35] Jiménez EI, Vallejo Narváez WE, Román-Chavarría CA, Vazquez-Chavez J, Rocha-Rinza T, Hernández-Rodríguez M. Bifunctional Thioureas with α -Trifluoromethyl or Methyl Groups: Comparison of Catalytic Performance in Michael Additions. *J Org Chem* 2016;81:7419–31. <https://doi.org/10.1021/acs.joc.6b01063>.
- [36] Zhou E, Liu B, Dong C. BINOL–quinine–squaramides as efficient organocatalysts for the asymmetric Michael addition of 2-hydroxy-1,4-naphthoquinone to nitroalkenes. *Tetrahedron Asymmetry* 2014;25:181–6. <https://doi.org/10.1016/J.TETASY.2013.11.019>.

- [37] Jichu T, Inokuma T, Aihara K, Kohiki T, Nishida K, Shigenaga A, et al. A Recyclable Hydrophobic Anchor-Tagged Asymmetric Amino Thiourea Catalyst. *ChemCatChem* 2018;10:3402–5. <https://doi.org/https://doi.org/10.1002/cctc.201800714>.
- [38] Woo SB, Kim DY. Enantioselective Michael addition of 2-hydroxy-1,4-naphthoquinones to nitroalkenes catalyzed by binaphthyl-derived organocatalysts. *Beilstein Journal of Organic Chemistry* 2012;8:699–704. <https://doi.org/10.3762/bjoc.8.78>.
- [39] Gholampour M, Seradj H, Pirhadi S, Khoshneviszadeh M. Novel 2-amino-1,4-naphthoquinone hybrids: Design, synthesis, cytotoxicity evaluation and in silico studies. *Bioorg Med Chem* 2020;28:115718. <https://doi.org/10.1016/J.BMC.2020.115718>.
- [40] De Oliveira RN, Da Silva MG, Da Silva MT, Melo VN, Valença WO, Da Paz JA, et al. New strategies for molecular diversification of 2-[Aminoalkyl-(1H-1,2,3-Triazol-1-yl)]-1,4-naphthoquinones using click chemistry. *J Braz Chem Soc* 2017;28:681–8. <https://doi.org/10.21577/0103-5053.20160207>.
- [41] Costa Souza RM, Montenegro Pimentel LML, Ferreira LKM, Pereira VRA, Santos ACDS, Dantas WM, et al. Biological activity of 1,2,3-triazole-2-amino-1,4-naphthoquinone derivatives and their evaluation as therapeutic strategy for malaria control. *Eur J Med Chem* 2023;255:115400. <https://doi.org/10.1016/J.EJMECH.2023.115400>.
- [42] Dong Y, Mei T, Luo QQ, Feng Q, Chang B, Yang F, et al. t-BuOK mediated oxidative coupling amination of 1,4-naphthoquinone and related 3-indolynaphthoquinones with amines. *RSC Adv* 2021;11:6776–80. <https://doi.org/10.1039/d1ra00193k>.
- [43] Patil R, Chadar D, Chaudhari D, Peter J, Nikalje M, Weyhermüller T, et al. Synthesis and characterization of 2-(n-alkylamino)-1,4-naphthoquinone: Molecular structures of ethyl and hexyl derivatives. *J Mol Struct* 2014;1075:345–51. <https://doi.org/10.1016/j.molstruc.2014.06.094>.
- [44] Jha RK, Batabyal M, Kumar S. Blue Light Irradiated Metal-, Oxidant-, and Base-Free Cross-Dehydrogenative Coupling of C(sp²)-H and N-H Bonds: Amination of Naphthoquinones with Amines. *J Org Chem* 2023;88:7401–24. <https://doi.org/10.1021/acs.joc.3c00666>.
- [45] Leyva E, López LI, Loredó-Carrillo SE, Rodríguez-Kessler M, Montes-Rojas A. Synthesis, spectral and electrochemical characterization of novel 2-(fluoroanilino)-1,4-naphthoquinones. *J Fluor Chem* 2011;132:94–101. <https://doi.org/10.1016/j.jfluchem.2010.12.001>.
- [46] Benites J, Valderrama JA, Bettega K, Pedrosa RC, Calderon PB, Verrax J. Biological evaluation of donor-acceptor aminonaphthoquinones as antitumor agents. *Eur J Med Chem* 2010;45:6052–7. <https://doi.org/10.1016/J.EJMECH.2010.10.006>.
- [47] Lisboa C da S, Santos VG, Vaz BG, de Lucas NC, Eberlin MN, Garden SJ. C–H Functionalization of 1,4-Naphthoquinone by Oxidative Coupling with Anilines in the Presence of a Catalytic Quantity of Copper(II) Acetate. *J Org Chem* 2011;76:5264–73. <https://doi.org/10.1021/jo200354u>.

- [48] Jiang C, Wang S. Gold(III)-catalyzed 1,4-nucleophilic addition: Facile approach to prepare 2-amino-1,4-naphthalenedione and 6-amino-5,8-quinolinedione derivatives. *Synlett* 2009;1099–102. <https://doi.org/10.1055/s-0028-1088116>.
- [49] Leyva E, López LI, Moctezuma E, De Lasa H. A bentonitic clay assisted method for the preparation of 2-(R-anilino)-1, 4-naphthoquinones. *Top Catal*, vol. 49, 2008, p. 281–7. <https://doi.org/10.1007/s11244-008-9088-x>.
- [50] Chen XL, Dong Y, He S, Zhang R, Zhang H, Tang L, et al. A One-Pot Approach to 2-(N-Substituted Amino)-1,4-naphthoquinones with Use of Nitro Compounds and 1,4-Naphthoquinones in Water. *Synlett* 2019;30:615–9. <https://doi.org/10.1055/s-0037-1610689>.
- [51] Katritzky AR, Huang L, Sakhuja R. Efficient syntheses of naphthoquinone-dipeptides. *Synthesis (Stuttg)* 2010;2011–6. <https://doi.org/10.1055/s-0029-1220012>.
- [52] Ge Y, Li A, Wu J, Feng H, Wang L, Liu H, et al. Design, synthesis and biological evaluation of novel non-peptide boronic acid derivatives as proteasome inhibitors. *Eur J Med Chem* 2017;128:180–91. <https://doi.org/10.1016/J.EJMECH.2017.01.034>.
- [53] Loredó-Carrillo SE, Leyva E, Platz MS, Cárdenas-Chaparro A, Martínez-Richa A. Thermolysis of 2-azido-3-(R-anilino)-1,4-naphthoquinones. Nitrene insertion versus hydrogen abstraction. *Tetrahedron Lett* 2020;61. <https://doi.org/10.1016/j.tetlet.2020.151731>.
- [54] Olawode EO, Tandlich R, Prinsloo E, Isaacs M, Hoppe H, Seldon R, et al. Synthesis and biological evaluation of 2-chloro-3-[(thiazol-2-yl)amino]-1,4-naphthoquinones. *Bioorg Med Chem Lett* 2019;29:1572–5. <https://doi.org/10.1016/j.bmcl.2019.05.001>.
- [55] Shaaban S, Ashmawy AM, Negm A, Wessjohann LA. Synthesis and biochemical studies of novel organic selenides with increased selectivity for hepatocellular carcinoma and breast adenocarcinoma. *Eur J Med Chem* 2019;179:515–26. <https://doi.org/10.1016/j.ejmech.2019.06.075>.
- [56] Espinosa-Bustos C, Vázquez K, Varela J, Cerecetto H, Paulino M, Segura R, et al. New aryloxy-quinone derivatives with promising activity on *Trypanosoma cruzi*. *Arch Pharm (Weinheim)* 2020;353:1900213. <https://doi.org/https://doi.org/10.1002/ardp.201900213>.
- [57] Tandon VK, Maurya HK. Water-promoted unprecedented chemoselective nucleophilic substitution reactions of 1,4-quinones with oxygen nucleophiles in aqueous micelles. *Tetrahedron Lett* 2010;51:3843–7. <https://doi.org/10.1016/j.tetlet.2010.05.071>.
- [58] Tandon VK, Maurya HK, Mishra NN, Shukla PK. Micelles catalyzed chemoselective synthesis “in water” and biological evaluation of oxygen containing hetero-1,4-naphthoquinones as potential antifungal agents. *Bioorg Med Chem Lett* 2011;21:6398–403. <https://doi.org/10.1016/j.bmcl.2011.08.095>.

- [59] Ibis C, Tuyun AF, Ozsoy-Gunes Z, Bahar H, Stasevych M V., Musyanovych RY, et al. Synthesis and biological evaluation of novel nitrogen- and sulfur-containing hetero-1,4-naphthoquinones as potent antifungal and antibacterial agents. *Eur J Med Chem* 2011;46:5861–7. <https://doi.org/10.1016/j.ejmech.2011.09.048>.
- [60] Deniz NG, Sayil C, Akyüz D, Koca A. Synthesis, electrochemistry, in-situ spectroelectrochemistry and molecular structures of 1,4-naphthoquinone derivatives. *J Mol Struct* 2021;1224. <https://doi.org/10.1016/j.molstruc.2020.129145>.
- [61] Ibis C, Tuyun AF, Ozsoy-Gunes Z, Bahar H, Stasevych M V., Musyanovych RY, et al. Synthesis and biological evaluation of novel nitrogen- and sulfur-containing hetero-1,4-naphthoquinones as potent antifungal and antibacterial agents. *Eur J Med Chem* 2011;46:5861–7. <https://doi.org/10.1016/j.ejmech.2011.09.048>.
- [62] Mısır BA, Derin Y, Ökten S, Aydın A, Koçyiğit ÜM, Şahin H, et al. Novel diarylated tacrine derivatives: Synthesis, characterization, anticancer, antiepileptic, antibacterial, and antifungal activities. *J Biochem Mol Toxicol* 2024;38:e23706. <https://doi.org/https://doi.org/10.1002/jbt.23706>.
- [63] Yilmaz RF, Derin Y, Misir BA, Atalay VE, Tutar ÖF, Ökten S, et al. Synthesis and spectral properties of symmetrically arylated BODIPY dyes: Experimental and computational approach. *J Mol Struct* 2023;1291. <https://doi.org/10.1016/j.molstruc.2023.135962>.
- [64] Louvis A da R, Silva NAA, Semaan FS, da Silva F de C, Saramago G, de Souza LCS V, et al. Synthesis, characterization and biological activities of 3-aryl-1,4-naphthoquinones – green palladium-catalysed Suzuki cross coupling. *New Journal of Chemistry* 2016;40:7643–56. <https://doi.org/10.1039/C6NJ00872K>.
- [65] Marri MR, MacHarla AK, Peraka S, Nama N. Oxidative iodination of carbonyl compounds using ammonium iodide and oxone®. *Tetrahedron Lett* 2011;52:6554–9. <https://doi.org/10.1016/j.tetlet.2011.09.106>.
- [66] Dar UA, Bhand S, Lande DN, Rao SS, Patil YP, Gejji SP, et al. Molecular structures of 2-hydroxy-1,4-naphthoquinone derivatives and their zinc(II) complexes: Combining experiment and density functional theory. *Polyhedron* 2016;113:61–72. <https://doi.org/10.1016/j.poly.2016.04.002>.
- [67] Egleton JE, Thinnes CC, Seden PT, Laurieri N, Lee SP, Hadavizadeh KS, et al. Structure-activity relationships and colorimetric properties of specific probes for the putative cancer biomarker human arylamine N-acetyltransferase 1. *Bioorg Med Chem* 2014;22:3030–54. <https://doi.org/10.1016/j.bmc.2014.03.015>.
- [68] Louvis A da R, Silva NAA, Semaan FS, da Silva F de C, Saramago G, de Souza LCS V, et al. Synthesis, characterization and biological activities of 3-aryl-1,4-naphthoquinones – green palladium-catalysed Suzuki cross coupling. *New Journal of Chemistry* 2016;40:7643–56. <https://doi.org/10.1039/C6NJ00872K>.
- [69] Faria RX, Oliveira FH, Salles JP, Oliveira AS, von Ranke NL, Bello ML, et al. 1,4-Naphthoquinones potently inhibiting P2X7 receptor activity. *Eur J Med Chem* 2018;143:1361–72. <https://doi.org/10.1016/j.ejmech.2017.10.033>.

- [70] Pasha SPBS, Sishtla K, Sulaiman RS, Park B, Shetty T, Shah F, et al. Ref-1/APE1 inhibition with novel small molecules blocks ocular neovascularizations. *Journal of Pharmacology and Experimental Therapeutics* 2018;367:108–18. <https://doi.org/10.1124/jpet.118.248088>.
- [71] Wang N, Wu X, Qin T, Zhou J, You Q, Zhang X. Palladium(ii)-catalyzed hydroxy-involved enolate-type efficient C–C functionalization of hydroxynaphthoquinones at room temperature. *RSC Adv* 2016;6:104126–30. <https://doi.org/10.1039/C6RA21652H>.
- [72] Olyaei A, Mohamadi A, Rahmani N. Green synthesis of new lawsone enaminones and their Z/E(C=C)-isomerization induced by organic solvent. *RSC Adv* 2021;11:12990–4. <https://doi.org/10.1039/D1RA01858B>.
- [73] Hosseini SO, Sadeghpour M, Zanjanchi F. Theoretical Study of Effective Factors on the Synthesis of Novel Lawsone Enaminones and Their Z/E(C = C)-Isomerization. *Iranian Journal of Science* 2023;47:1531–40. <https://doi.org/10.1007/s40995-023-01547-y>.
- [74] Rezende LCD De, Fumagalli F, Bortolin MS, Oliveira MG De, Paula MH De, Andrade-Neto VF De, et al. In vivo antimalarial activity of novel 2-hydroxy-3-anilino-1,4-naphthoquinones obtained by epoxide ring-opening reaction. *Bioorg Med Chem Lett* 2013;23:4583–6. <https://doi.org/10.1016/j.bmcl.2013.06.033>.
- [75] Calil FA, David JS, Chiappetta ERC, Fumagalli F, Mello RB, Leite FHA, et al. Ligand-based design, synthesis and biochemical evaluation of potent and selective inhibitors of *Schistosoma mansoni* dihydroorotate dehydrogenase. *Eur J Med Chem* 2019;167:357–66. <https://doi.org/10.1016/J.EJMECH.2019.02.018>.
- [76] Kongkathip N, Kongkathip B, Siripong P, Sangma C, Luangkamin S, Niyomdecha M, et al. Potent antitumor activity of synthetic 1,2-naphthoquinones and 1,4-naphthoquinones. *Bioorg Med Chem* 2003;11:3179–91. [https://doi.org/10.1016/S0968-0896\(03\)00226-8](https://doi.org/10.1016/S0968-0896(03)00226-8).
- [77] Kilic-Kurt Z, Ozmen N, Bakar-Ates F. Synthesis and anticancer activity of some pyrimidine derivatives with aryl urea moieties as apoptosis-inducing agents. *Bioorg Chem* 2020;101. <https://doi.org/10.1016/j.bioorg.2020.104028>.
- [78] Li S-Y, Sun Z-K, Zeng X-Y, Zhang Y, Wang M-L, Hu S-C, et al. Potent Cytotoxicity of Novel L-Shaped Ortho-Quinone Analogs through Inducing Apoptosis. *Molecules* 2019;24. <https://doi.org/10.3390/molecules24224138>.
- [79] Arya Y, Kumar Bera S, Kumar Lahiri G. Azo Appended Modified Lawsone Derived Ru-Systems with Multi-Redox Entities. Competitive Electronic Form and the Question of Azo Reduction. *Chemistry – A European Journal* 2023;29:e202204049. <https://doi.org/https://doi.org/10.1002/chem.202204049>.
- [80] Romanyuk AL, Polishchuk OP, Litvin BL, Ganushchak NI. Synthesis and Transformations of 2-Hydroxy-3-arylazo-1,4-naphthoquinones. vol. 72. 2002.
- [81] Shoaib AGF. Catalytic activity of some new copper(II) azo-complexes. *J Coord Chem* 2012;65:3511–8. <https://doi.org/10.1080/00958972.2012.719079>.

- [82] Choudhari AS, Patil SR, Sekar N. Solvatochromism, halochromism, and azo-hydrazone tautomerism in novel V-shaped azo-azine colorants – consolidated experimental and computational approach. *Coloration Technology* 2016;132:387–98. <https://doi.org/https://doi.org/10.1111/cote.12226>.
- [83] Rueping M, Sugiono E, Merino E. Asymmetric Iminium Ion Catalysis: An Efficient Enantioselective Synthesis of Pyranonaphthoquinones and β -Lapachones. *Angewandte Chemie International Edition* 2008;47:3046–9. <https://doi.org/https://doi.org/10.1002/anie.200705110>.
- [84] Yong RL, Won KL. Efficient synthesis of biologically interesting dehydro- α -lapachone and α -lapachone. *Synth Commun* 2004;34:4537–43. <https://doi.org/10.1081/SCC-200043216>.
- [85] Jung EJ, Park BH, Lee YR. Environmentally benign, one-pot synthesis of pyrans by domino Knoevenagel/ 6π -electrocyclization in water and application to natural products. *Green Chemistry* 2010;12:2003–11. <https://doi.org/10.1039/C0GC00265H>.
- [86] Edayadulla N, Lee YR. Microwave-assisted solvent and catalyst free synthesis of 2H-Pyrans. *Bull Korean Chem Soc* 2013;34:2963–7. <https://doi.org/10.5012/bkcs.2013.34.10.2963>.
- [87] Da Rocha DR, Mota K, Da Silva IMCB, Ferreira VF, Ferreira SB, Da Silva FDC. Synthesis of fused chromene-1,4-naphthoquinones via ring-closing metathesis and Knoevenagel-electrocyclization under acid catalysis and microwave irradiation. *Tetrahedron*, vol. 70, Elsevier Ltd; 2014, p. 3266–70. <https://doi.org/10.1016/j.tet.2013.11.068>.
- [88] Liu Y, Ge W-H, Zhu Y-Q, Hu H-Y, Fan H, Shi Y-H, et al. NIS-Induced Enone Difunctionalization for the Synthesis of Naphtho[2,3-b]furan-4,9-diones. *European J Org Chem* 2017;2017:551–9. <https://doi.org/https://doi.org/10.1002/ejoc.201601291>.
- [89] Prasanna P, Balamurugan K, Perumal S, Menéndez JC. A facile, three-component domino protocol for the microwave-assisted synthesis of functionalized naphtho[2,3-b]furan-4,9-diones in water. *Green Chemistry* 2011;13:2123–9. <https://doi.org/10.1039/C0GC00952K>.
- [90] Baiju T V., Almeida RG, Sivanandan ST, de Simone CA, Brito LM, Cavalcanti BC, et al. Quinonoid compounds via reactions of lawsone and 2-aminonaphthoquinone with α -bromonitroalkenes and nitroallylic acetates: Structural diversity by C-ring modification and cytotoxic evaluation against cancer cells. *Eur J Med Chem* 2018;151:686–704. <https://doi.org/10.1016/j.ejmech.2018.03.079>.
- [91] Zhang R, Xu D, Xie J. Efficient Synthesis of 3-Phenylnaphtho[2,3-b]furan-4,9-diones in Water and Their Fluorimetric Study in Solutions. *Chin J Chem* 2012;30:1690–4. <https://doi.org/https://doi.org/10.1002/cjoc.201200499>.
- [92] Zanzwar MR, Kavala V, Gawande SD, Kuo C-W, Kuo T-S, Chen M-L, et al. Synthesis of 3-Substituted 2-Aminonaphtho[2,3-b]furan-4,9-diones from 2-Hydroxy-1,4-Naphthoquinone and Nitroalkenes. *European J Org Chem* 2013;2013:8288–98. <https://doi.org/https://doi.org/10.1002/ejoc.201300996>.

- [93] Rad-Moghadam K, Mousazadeh Hassani SAR, Toorchi Roudsari S. The deep eutectic melt of sorbitol and metformin hydrochloride: synthesis of 3-substituted 2-aminonaphtho[2,3-b]furan-4,9-diones and their photophysical properties. *RSC Adv* 2016;6:13152–9. <https://doi.org/10.1039/C5RA19619A>.
- [94] Acuña J, Piermattey J, Caro D, Bannwitz S, Barrios L, López J, et al. Synthesis, Anti-Proliferative Activity Evaluation and 3D-QSAR Study of Naphthoquinone Derivatives as Potential Anti-Colorectal Cancer Agents. *Molecules* 2018;23. <https://doi.org/10.3390/molecules23010186>.
- [95] Costa DCS, Francisco AS, Matuck BVA, Furtado PS, de Oliveira AASC, Rabelo VWH, et al. Diacetate Naphthoquinone Derivatives Tethered to 1,2,3-Triazoles: Synthesis and Cytotoxicity Evaluation in Caco-2 Cells. *J Braz Chem Soc* 2022;33:48–59. <https://doi.org/10.21577/0103-5053.20210123>.
- [96] Costa DCS, de Almeida GS, Rabelo VWH, Cabral LM, Sathler PC, Alvarez Abreu P, et al. Synthesis and evaluation of the cytotoxic activity of Furanaphthoquinones tethered to 1H-1,2,3-triazoles in Caco-2, Calu-3, MDA-MB231 cells. *Eur J Med Chem* 2018;156:524–33. <https://doi.org/10.1016/j.ejmech.2018.07.018>.
- [97] Roman G. Mannich bases in medicinal chemistry and drug design. *Eur J Med Chem* 2015;89:743–816. <https://doi.org/10.1016/j.ejmech.2014.10.076>.
- [98] Olyaei A, Sadeghpour M, Khalaj M. Mannich bases derived from lawsone and their metal complexes: synthetic strategies and biological properties. *RSC Adv* 2020;10:30265–81. <https://doi.org/10.1039/D0RA05717G>.
- [99] Jordão AK, Vargas MD, Pinto AC, da Silva F de C, Ferreira VF. Lawsone in organic synthesis. *RSC Adv* 2015;5:67909–43. <https://doi.org/10.1039/C5RA12785H>.
- [100] Leffler MT, Hathaway RJ. Naphthoquinone Antimalarials. XIII. 2-Hydroxy-3-substituted-aminomethyl Derivatives by the Mannich Reaction. *J Am Chem Soc* 1948;70:3222–3. <https://doi.org/10.1021/ja01190a006>.
- [101] Neves AP, Barbosa CC, Greco SJ, Vargas MD, Visentin LC, Pinheiro CB, et al. Novel Aminonaphthoquinone Mannich Bases Derived from Lawsone and their Copper(II) Complexes: Synthesis, Characterization and Antibacterial Activity. vol. 20. 2009.
- [102] Paengsri W, Lee VS, Chong WL, Wahab HA, Baramée A. Synthesis, antituberculosis activity and molecular docking studies for novel naphthoquinone derivatives. *International Journal of Biological Chemistry* 2012;6:69–88. <https://doi.org/10.3923/ijbc.2012.69.88>.
- [103] Fiorot RG, Allochio Filho JF, Pereira TMC, Lacerda V, Dos Santos RB, Romão W, et al. A simple and convenient method for synthesis of new aminonaphthoquinones derived from lawsone by catalytic multicomponent Mannich reaction. *Tetrahedron Lett* 2014;55:4373–7. <https://doi.org/10.1016/j.tetlet.2014.06.031>.
- [104] Khodabakhshi MR, Adl A, Olyaei A. Design, synthesis and antimicrobial activities of novel bis-Mannich bases derived from lawsone. *Research on Chemical Intermediates* 2023;49:4759–70. <https://doi.org/10.1007/s11164-023-05103-6>.

- [105] Allochio Filho JF, Fiorot RG, Lacerda V, dos Santos RB, Vanini G, Romão W, et al. First synthesis of aminonaphthoquinones derived from lawsone in a colloidal dispersion system created by a Brønsted acid-surfactant-combined catalyst in water: An environmentally friendly protocol. *Colloids and Interface Science Communications* 2015;4:14–8. <https://doi.org/10.1016/j.colcom.2015.03.002>.
- [106] Liu D, Zhou S, Gao J. Roomerature synthesis of hydroxynaphthalene-1,4-dione derivative catalyzed by phenylphosphinic acid. *Synth Commun* 2014;44:1286–90. <https://doi.org/10.1080/00397911.2013.853314>.
- [107] Dabiri M, Tisseh ZN, Bazgir A. Synthesis of fluorescent hydroxyl naphthalene-1,4-dione derivatives by a three-component reaction in water. *Dyes and Pigments* 2011;89:63–9. <https://doi.org/10.1016/j.dyepig.2010.09.004>.
- [108] Shaterian HR, Mohammadnia M. Effective preparation of 2-amino-3-cyano-4-aryl-5,10-dioxo-5,10-dihydro-4H- benzo[g]chromene and hydroxyl naphthalene-1,4-dione derivatives under ambient and solvent-free conditions. *J Mol Liq* 2013;177:353–60. <https://doi.org/10.1016/j.molliq.2012.10.012>.
- [109] Naeimi H, Zarabi MF. One pot synthesis of aminonaphthoquinone derivatives using Cu(II) immobilized on hyperbranched polyglycerol functionalized graphene oxide as a reusable catalyst under solvent-free conditions. *Tetrahedron* 2018;74:2314–23. <https://doi.org/10.1016/j.tet.2018.03.047>.
- [110] Asadi B, Mohammadpoor-Baltork I, Tangestaninejad S, Moghadam M, Mirkhani V, Landarani-Isfahani A. Synthesis and characterization of Bi(iii) immobilized on triazine dendrimer-stabilized magnetic nanoparticles: a reusable catalyst for the synthesis of aminonaphthoquinones and bis-aminonaphthoquinones. *New Journal of Chemistry* 2016;40:6171–84. <https://doi.org/10.1039/C5NJ03050A>.
- [111] Jayashree S, Shivashankar K. Montmorillonite K-10 catalyzed Mannich reaction: Synthesis of aminonaphthoquinone derivatives from Lawsone. *Synth Commun* 2018;48:1805–15. <https://doi.org/10.1080/00397911.2018.1466334>.
- [112] Nariya P, Kumar S, Seshadri S, Patel M, Thakore S. Novel substituted isoindolinones derived from lawsone: synthesis, characterization, theoretical, biological activity and docking studies. *J Mol Struct* 2022;1267. <https://doi.org/10.1016/j.molstruc.2022.133601>.
- [113] Graziano G, Stefanachi A, Contino M, Prieto-Díaz R, Ligresti A, Kumar P, et al. Multicomponent Reaction-Assisted Drug Discovery: A Time- and Cost-Effective Green Approach Speeding Up Identification and Optimization of Anticancer Drugs. *Int J Mol Sci* 2023;24. <https://doi.org/10.3390/ijms24076581>.
- [114] Dömling A, Wang W, Wang K. Chemistry and Biology Of Multicomponent Reactions. *Chem Rev* 2012;112:3083–135. <https://doi.org/10.1021/cr100233r>.
- [115] Zhang C, Qu Y, Niu B. Design, synthesis and biological evaluation of lapachol derivatives possessing indole scaffolds as topoisomerase I inhibitors. *Bioorg Med Chem* 2016;24:5781–6. <https://doi.org/10.1016/j.bmc.2016.09.034>.

- [116] Yang X, Wu L. Synthesis of Novel 1,4-Naphthoquinones Possessing Indole Scaffolds Using In(OTf)₃ in Solvent-Free Conditions. *Molecules* 2018;23. <https://doi.org/10.3390/molecules23081954>.
- [117] Lara LS, Lechuga GC, Moreira C dos S, Santos TB, Ferreira VF, da Rocha DR, et al. Optimization of 1,4-Naphthoquinone Hit Compound: A Computational, Phenotypic, and In Vivo Screening against *Trypanosoma cruzi*. *Molecules* 2021;26. <https://doi.org/10.3390/molecules26020423>.
- [118] Sharma A, Santos IO, Gaur P, Ferreira VF, Garcia CRS, Da Rocha DR. Addition of thiols to o-quinone methide: New 2-hydroxy-3-phenylsulfanylmethyl[1,4]naphthoquinones and their activity against the human malaria parasite *Plasmodium falciparum* (3D7). *Eur J Med Chem* 2013;59:48–53. <https://doi.org/10.1016/j.ejmech.2012.10.052>.
- [119] Novais JS, Moreira CS, Silva ACJA, Loureiro RS, Sá Figueiredo AM, Ferreira VF, et al. Antibacterial naphthoquinone derivatives targeting resistant strain Gram-negative bacteria in biofilms. *Microb Pathog* 2018;118:105–14. <https://doi.org/10.1016/j.micpath.2018.03.024>.
- [120] Cardoso MFC, Forezi LSM, Cavalcante VGS, Juliani CSR, Resende JALC, Da Rocha DR, et al. Synthesis of new xanthenes based on lawsone and coumarin via a tandem three-component reaction. *J Braz Chem Soc* 2017;28:1926–36. <https://doi.org/10.21577/0103-5053.20170032>.
- [121] Kangani M, Hazeri N, Yazdani-Elah-Abadi A, Maghsoodlou M-T. Piperidine-Promoted Three-Component Condensation: Synthesis of Chromene Heterocycles and Pyrazolotriazoles. *Journal of the Chinese Chemical Society* 2017;64:1259–69. <https://doi.org/https://doi.org/10.1002/jccs.201700074>.
- [122] Abdelaziz AAS, Nawaz M, Izzeldin I, Abubshait HA, Alsadig A, Gomaa MS, et al. Molecular docking and Anticancer Activity of Some Synthesized 1,4-naphthoquinone Derivatives against Human Cancer Cell Line. *J Mol Struct* 2023;1275. <https://doi.org/10.1016/j.molstruc.2022.134702>.
- [123] Mahdavi M, Hariri R, Mirfazli SS, Lotfian H, Rastergari A, Firuzi O, et al. Synthesis and Biological Activity of Some Benzochromenoquinolinones: Tacrine Analogs as Potent Anti-Alzheimer's Agents. *Chem Biodivers* 2019;16:e1800488. <https://doi.org/https://doi.org/10.1002/cbdv.201800488>.
- [124] Feliciano A, Gómez-García O, Escalante CH, Rodríguez-Hernández MA, Vargas-Fuentes M, Andrade-Pavón D, et al. Three-Component Synthesis of 2-Amino-3-cyano-4H-chromenes, In Silico Analysis of Their Pharmacological Profile, and In Vitro Anticancer and Antifungal Testing. *Pharmaceuticals* 2021;14. <https://doi.org/10.3390/ph14111110>.
- [125] Dekamin MG, Eslami M, Maleki A. Potassium phthalimide-N-oxyl: A novel, efficient, and simple organocatalyst for the one-pot three-component synthesis of various 2-amino-4H-chromene derivatives in water. *Tetrahedron* 2013;69:1074–85. <https://doi.org/10.1016/j.tet.2012.11.068>.
- [126] Khurana JM, Nand B, Saluja P. DBU: A highly efficient catalyst for one-pot synthesis of substituted 3, 4- dihydropyrano[3, 2-c]chromenes, dihydropyrano[4, 3-b]pyranes, 2-amino-4H- benzo[h]chromenes and 2-amino-4H benzo[g]chromenes in aqueous medium. *Tetrahedron* 2010;66:5637–41. <https://doi.org/10.1016/j.tet.2010.05.082>.

- [127] Rahimzadeh G, Tajbakhsh M, Daraie M, Mohammadi M. Dysprosium–balsalazide complex trapped between the functionalized halloysite and g-C₃N₄: A novel heterogeneous catalyst for the synthesis of annulated chromenes in water. *Appl Organomet Chem* 2022;36:e6829. <https://doi.org/https://doi.org/10.1002/aoc.6829>.
- [128] Safaei-Ghomi J, Bateni F-S, Babaei P. CeO₂/CuO@N-GQDs@NH₂ nanocomposite as a high-performance catalyst for the synthesis of benzo[g]chromenes. *Appl Organomet Chem* 2020;34:e5657. <https://doi.org/https://doi.org/10.1002/aoc.5657>.
- [129] Gracious SN, Kerru N, Maddila S, van Zyl WE, Jonnalagadda SB. Facile one-pot green synthesis of 2-amino-4H-benzo[g]chromenes in aqueous ethanol under ultrasound irradiation. *Synth Commun* 2020;50:1960–71. <https://doi.org/10.1080/00397911.2020.1761393>.
- [130] Shaterian HR, Mohammadnia M. Effective preparation of 2-amino-3-cyano-4-aryl-5,10-dioxo-5,10-dihydro-4H- benzo[g]chromene and hydroxyl naphthalene-1,4-dione derivatives under ambient and solvent-free conditions. *J Mol Liq* 2013;177:353–60. <https://doi.org/10.1016/j.molliq.2012.10.012>.
- [131] Khorami F, Shaterian HR. Silica-bonded propylpiperazine-N-sulfamic acid as recyclable solid acid catalyst for preparation of 2-amino-3-cyano-4-aryl-5, 10-dioxo-5, 10-dihydro-4H-benzo[g]chromenes and hydroxy-substituted naphthalene-1, 4-dione derivatives. *Cuihua Xuebao/Chinese Journal of Catalysis* 2014;35:242–6. [https://doi.org/10.1016/s1872-2067\(12\)60761-x](https://doi.org/10.1016/s1872-2067(12)60761-x).
- [132] Khurana JM, Magoo D, Chaudhary A. Efficient and green approaches for the synthesis of 4 H-benzo[g]chromenes in water, under neat conditions, and using task-specific ionic liquid. *Synth Commun* 2012;42:3211–9. <https://doi.org/10.1080/00397911.2011.580069>.
- [133] Brahmachari G, Banerjee B. Facile and One-Pot Access to Diverse and Densely Functionalized 2-Amino-3-cyano-4H-pyrans and Pyran-Annulated Heterocyclic Scaffolds via an Eco-Friendly Multicomponent Reaction at Room Temperature Using Urea as a Novel Organo-Catalyst. *ACS Sustain Chem Eng* 2014;2:411–22. <https://doi.org/10.1021/sc400312n>.
- [134] Maleki B, Baghayeri M, Sheikh S, Babaee S, Farhadi S. One-pot synthesis of some 2-amino-4H-chromene derivatives using triethanolamine as a novel reusable organocatalyst under solvent-free conditions and its application in electrosynthesis of silver nanoparticles. *Russ J Gen Chem* 2017;87:1064–72. <https://doi.org/10.1134/S1070363217050280>.
- [135] Mohammadi M, Ghorbani-Choghamarani A. A novel Hercynite-supported tetradentate Schiff base complex of manganese catalyzed one-pot annulation reactions. *Appl Organomet Chem* 2022;36:e6905. <https://doi.org/https://doi.org/10.1002/aoc.6905>.
- [136] Khan MdN, Pal S, Karamthulla S, Choudhury LH. Imidazole as organocatalyst for multicomponent reactions: diversity oriented synthesis of functionalized hetero- and carbocycles using in situ-generated benzylidenemalononitrile derivatives. *RSC Adv* 2014;4:3732–41. <https://doi.org/10.1039/C3RA45252B>.

- [137] Dashteh M, Safaiee M, Bagheri S, Zolfigol MA. Application of cobalt phthalocyanine as a nanostructured catalyst in the synthesis of biological henna-based compounds. *Appl Organomet Chem* 2019;33. <https://doi.org/10.1002/aoc.4690>.
- [138] Maleki B, Babaei S, Tayebee R. Zn(L-proline)₂ as a powerful and reusable organometallic catalyst for the very fast synthesis of 2-amino-4H-benzo[g]chromene derivatives under solvent-free conditions. *Appl Organomet Chem* 2015;29:408–11. <https://doi.org/10.1002/aoc.3306>.
- [139] Patel HB, Gohil JD, Patel MP. Microwave-assisted, solvent-free, one-pot, three-component synthesis of fused pyran derivatives containing benzothiazole nucleus catalyzed by pyrrolidine-acetic acid and their biological evaluation. *Monatsh Chem* 2017;148:1057–67. <https://doi.org/10.1007/s00706-016-1875-7>.
- [140] Mishra R, Choudhury LH. Catalyst-free microwave-assisted arylglyoxal-based multicomponent reactions for the synthesis of fused pyrans. *RSC Adv* 2016;6:24464–9. <https://doi.org/10.1039/C5RA25536H>.
- [141] Khaligh NG. Synthesis and characterization of some novel 4-arylglyoxal-chromene derivatives in the presence of a polymeric catalyst and biological evaluation against *Escherichia coli*. *Monatsh Chem* 2018;149:33–8. <https://doi.org/10.1007/s00706-017-2059-9>.
- [142] Nasri S, Bayat M. One pot synthesis of new heterocyclic systems: Polysubstituted pyrano[3,2-c]chromene and benzo[g]chromene derivatives. *J Mol Struct* 2018;1164:77–83. <https://doi.org/10.1016/j.molstruc.2018.03.055>.
- [143] Abdollahi-Basir MH, Shirini F, Tajik H, Ghasemzadeh MA. One-pot synthesis of chromenes in the presence of magnetic nanocomposite based on NH₂-UiO-66(Zr), graphene oxide and Fe₃O₄. *J Mol Struct* 2022;1263. <https://doi.org/10.1016/j.molstruc.2022.133022>.
- [144] Safaei-Ghomi J, Eshteghal F, Shahbazi-Alavi H. L-phenyl alanine-attached Fe₃O₄@SiO₂ nanoparticles as an efficient catalyst for the synthesis of chromenes. *Journal of the Iranian Chemical Society* 2018;15:661–9. <https://doi.org/10.1007/s13738-017-1266-y>.
- [145] Safaei-Ghomi J, Eshteghal F, Shahbazi-Alavi H. Novel ionic liquid supported on Fe₃O₄ nanoparticles as an efficient catalyst for the synthesis of new chromenes. *Appl Organomet Chem* 2018;32:e3987. <https://doi.org/10.1002/aoc.3987>.
- [146] Palizi N, Moradi L. Green pathway to the synthesis of some spirooxindole derivatives using NGO/PMA as a new and effective solid acid catalyst. *Appl Organomet Chem* 2023;37:e7196. <https://doi.org/10.1002/aoc.7196>.
- [147] Patel N, Patel U, Dadhania A. Highly efficient and green synthesis of spiro[indoline-3,9'-xanthene]trione and spiro[chromene-4,3'-indoline]-3-carbonitrile derivatives in water catalyzed by graphene oxide-supported dicationic ionic liquid. *Research on Chemical Intermediates* 2021;47:2189–206. <https://doi.org/10.1007/s11164-021-04405-x>.

- [148] Zhao H-W, Li B, Tian T, Meng W, Yang Z, Song X-Q, et al. Highly Enantioselective Synthesis of Chiral Pyranonaphthoquinone-Fused Spirooxindoles through Organocatalytic Three-Component Cascade Reactions. *European J Org Chem* 2015;2015:3320–6. <https://doi.org/https://doi.org/10.1002/ejoc.201500152>.
- [149] Ghahremanzadeh R, Amanpour T, Bazgir A. An efficient, three-component synthesis of spiro[benzo[g]chromene-4,3'-indoline]-3-carbonitrile and spiro[indoline-3,5'-pyrano[2,3-d]pyrimidine]-6'-carbonitrile derivatives. *J Heterocycl Chem* 2009;46:1266–70. <https://doi.org/https://doi.org/10.1002/jhet.240>.
- [150] Thongni A, Phanrang PT, Pandya C, Diengdoh DF, Gannon PM, Kaminsky W, et al. Ultrasound assisted synthesis of spirooxindole analogs catalyzed by Fe₃O₄@PPCA NPs: Experimental, theoretical and in vitro biological studies. *J Mol Struct* 2023;1284. <https://doi.org/10.1016/j.molstruc.2023.135363>.
- [151] Bazgir A, Hosseini G, Ghahremanzadeh R. Copper Ferrite Nanoparticles: An Efficient and Reusable Nanocatalyst for a Green One-Pot, Three-component Synthesis of Spirooxindoles in Water. *ACS Comb Sci* 2013;15:530–4. <https://doi.org/10.1021/co400057h>.
- [152] Mobinikhaledi A, Foroughifar N, Fard MAB. Simple and efficient method for three-component synthesis of spirooxindoles in aqueous and solvent-free media. *Synth Commun* 2011;41:441–50. <https://doi.org/10.1080/00397911003587507>.
- [153] Dabiri M, Tisseh ZN, Bahramnejad M, Bazgir A. Sonochemical multi-component synthesis of spirooxindoles. *Ultrason Sonochem* 2011;18:1153–9. <https://doi.org/10.1016/j.ultsonch.2010.12.004>.
- [154] Srinivas V, Rao VR. Facile, ONE-POT, THREE-component synthesis of benzo[a]NAPHTHACENE-8,13- DIONES. *Synth Commun* 2012;42:388–93. <https://doi.org/10.1080/00397911.2010.524961>.
- [155] Thanaraj C, Alagesan M, Velladurai R. Reusable SiO₂@NiO core-shell nanoparticles catalyzed efficient synthesis of 14-aryl-14H-dibenzo[a,i]xanthene-8, 13-dione derivatives. *Synth Commun* 2023;53:2002–17. <https://doi.org/10.1080/00397911.2023.2261571>.
- [156] Qiang Wu L, Fang Wu Y, Guang Yang C, Min Yang L, Juan Yang L. Silica Supported Perchloric Acid: An Efficient Catalyst for the Synthesis of 14-Aryl-14H-dibenzo[a,i]xanthene-8,13-diones. vol. 221. 2010.
- [157] Ghasemzadeh MA, Azimi-Nasrabad M. Nano-Fe₃O₄ -encapsulated silica particles bearing sulfonic acid groups as a magnetically separable catalyst for the green and efficient synthesis of 14-aryl-14H-dibenzo[a,i]xanthene-8,13-dione derivatives. *Research on Chemical Intermediates* 2016;42:1057–69. <https://doi.org/10.1007/s11164-015-2073-7>.
- [158] Wu L, Zhang J, Fang L, Yang C, Yan F. Silica chloride catalyzed synthesis of 14-aryl-14H-dibenzo[a,i]xanthene-8,13-diones. *Dyes and Pigments* 2010;86:93–6. <https://doi.org/10.1016/j.dyepig.2009.12.008>.

- [159] Ghaffari Khaligh N. Poly(4-vinylpyridinium) hydrogen sulfate: an efficient catalyst for the synthesis of xanthene derivatives under solvent-free conditions. *Catal Sci Technol* 2012;2:2211–5. <https://doi.org/10.1039/C2CY20276J>.
- [160] Khurana JM, Chaudhary A, Lumb A, Nand B. Efficient one-pot syntheses of dibenzo[a, i]xanthene-diones and evaluation of their antioxidant activity. *Can J Chem* 2012;90:739–46. <https://doi.org/10.1139/v2012-033>.
- [161] Dabiri M, Tisseh ZN, Bazgir A. An efficient three-component synthesis of benzoxanthenes in water. *J Heterocycl Chem* 2010;47:1062–5. <https://doi.org/https://doi.org/10.1002/jhet.420>.
- [162] Rahmatpour A. Polystyrene-supported GaCl₃ as a highly efficient and reusable heterogeneous Lewis acid catalyst for the three-component synthesis of benzoxanthene derivatives. *Monatsh Chem* 2013;144:1205–12. <https://doi.org/10.1007/s00706-013-0931-9>.
- [163] Shaterian HR, Azizi K, Fahimi N. Phosphoric acid supported on alumina (H₃PO₄/Al₂O₃) as an efficient and reusable catalyst for the one-pot synthesis of benzoxanthene pigments. *Research on Chemical Intermediates* 2014;40:1403–14. <https://doi.org/10.1007/s11164-013-1047-x>.
- [164] Maleki B, Akbarzadeh E, Babaei S. New basic ionic liquid from ethan-1,2-diyl bis (hydrogen sulfate) and DBU (1,8-diazobicyclo[5.4.0]undec-7-ene) as an efficient catalyst for one-pot synthesis of xanthene derivatives. *Dyes and Pigments* 2015;123:222–34. <https://doi.org/10.1016/j.dyepig.2015.08.009>.
- [165] Shaterian HR, Ranjbar M, Azizi K. Synthesis of benzoxanthene derivatives using Brønsted acidic ionic liquids (BAILs), 2-pyrrolidonium hydrogen sulfate and (4-sulfobutyl)tris(4- sulfophenyl)phosphonium hydrogen sulfate. *J Mol Liq* 2011;162:95–9. <https://doi.org/10.1016/j.molliq.2011.06.013>.
- [166] Zeynizadeh B, Rahmani S. Immobilized copper-layered nickel ferrite on acid-activated montmorillonite, [(NiFe₂O₄@Cu)(H⁺-Mont)], as a superior magnetic nanocatalyst for the green synthesis of xanthene derivatives. *RSC Adv* 2019;9:28038–52. <https://doi.org/10.1039/c9ra04320a>.
- [167] Liu P, Hao JW, Liang SJ, Liang GL, Wang JY, Zhang ZH. Choline chloride and itaconic acid-based deep eutectic solvent as an efficient and reusable medium for the preparation of 13-aryl-5H-dibenzo[b,i]xanthene-5,7,12,14(13H)-tetraones. *Monatsh Chem* 2016;147:801–8. <https://doi.org/10.1007/s00706-015-1571-z>.
- [168] Khurana JM, Lumb A, Chaudhary A, Nand B. Acid Catalyzed Efficient Syntheses of Aryl-5H-dibenzo[b,i]xanthene-5,7,12,14-(13H)-tetraones and 3,3-(Arylmethylene)bis(2-hydroxynaphthalene-1,4-diones) and In Vitro Evaluation of their Antioxidant Activity. *J Heterocycl Chem* 2014;51:1747–51. <https://doi.org/https://doi.org/10.1002/jhet.1871>.
- [169] Mousavi SR, Rashidi Nodeh H, Zamiri Afshari E, Foroumadi A. Graphene Oxide Incorporated Strontium Nanoparticles as a Highly Efficient and Green Acid Catalyst for One-Pot Synthesis of Tetramethyl-9-aryl-hexahydroxanthenes and 13-Aryl-5H-dibenzo[b,i]xanthene-5,7,12,14(13H)-tetraones Under Solvent-Free Conditions. *Catal Letters* 2019;149:1075–86. <https://doi.org/10.1007/s10562-019-02675-0>.

- [170] Zarei M, Zolfigol MA, Moosavi-Zare AR, Noroozizadeh E. Trityl bromide versus nano-magnetic catalyst in the synthesis of henna-based xanthenes and bis-coumarins. *Journal of the Iranian Chemical Society* 2017;14:2187–98. <https://doi.org/10.1007/s13738-017-1155-4>.
- [171] Tavakoli HR, Moosavi SM, Bazgir A. $\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$ as an efficient catalyst for the synthesis of dibenzo [b,i]xanthene-tetraones and fluorescent hydroxyl naphthalene-1,4-diones. *Research on Chemical Intermediates* 2015;41:3041–6. <https://doi.org/10.1007/s11164-013-1413-8>.
- [172] Bazgir A, Tisseh ZN, Mirzaei P. An efficient synthesis of spiro[dibenzo[b,i]xanthene-13,3'-indoline]-pentaones and 5H-dibenzo[b,i]xanthene-tetraones. *Tetrahedron Lett* 2008;49:5165–8. <https://doi.org/10.1016/j.tetlet.2008.06.077>.
- [173] Chen Y, Wu S, Tu S, Li C, Shi F. A simple procedure for the synthesis of benzoxanthene derivatives under microwave irradiation conditions. *J Heterocycl Chem* 2008;45:931–4. <https://doi.org/10.1002/jhet.5570450345>.
- [174] Khaligh NG, Shirini F. N-Sulfonic acid poly(4-vinylpyridinium) hydrogen sulfate as an efficient and reusable solid acid catalyst for one-pot synthesis of xanthene derivatives in dry media under ultrasound irradiation. *Ultrason Sonochem* 2015;22:397–403. <https://doi.org/10.1016/j.ultsonch.2014.06.020>.
- [175] Khaligh NG. Poly(4-vinylpyridinium) hydrogensulfate catalyzed synthesis of 12-aryl-12H-indeno[1,2-b]naphtho[3,2-e]pyran-5,11,13-triones. *Tetrahedron Lett* 2012;53:1637–40. <https://doi.org/10.1016/j.tetlet.2012.01.092>.
- [176] Shaterian HR, Mohammadnia M, Moradi F. Acidic ionic liquids catalyzed three-component synthesis of 12-aryl-12H-indeno[1,2-b]naphtho[3,2-e]pyran-5,11,13-trione and 13-aryl-indeno[1,2-b]naphtho[1,2-e]pyran-12(13H)-one derivatives. *J Mol Liq* 2012;172:88–92. <https://doi.org/10.1016/j.molliq.2012.05.018>.
- [177] Reddy AVS, Reddy MV, Jeong YT. Silica tungstic acid (STA) as a highly efficient and reusable catalyst for the synthesis of benzoxanthenes under solvent-free conditions in ultrasonication. *Research on Chemical Intermediates* 2016;42:5209–18. <https://doi.org/10.1007/s11164-015-2350-5>.
- [178] Khurana JM, Lumb A, Chaudhary A, Nand B. Efficient and green syntheses of 12-aryl-2,3,4,12-tetrahydrobenzo[b] xanthene-1,6,11-triones in water and task-specific ionic liquid. *Synth Commun* 2013;43:2147–54. <https://doi.org/10.1080/00397911.2012.688230>.
- [179] Rahnamafar R, Moradi L, Khoobi M. Synthesis of benzo[b]xanthene-triones and tetrahydrochromeno[2,3-b]xanthene tetraones via three- or pseudo-five-component reactions using $\text{Fe}_3\text{O}_4 @ \text{SiO}_2 / \text{PEtOx}$ as a novel, magnetically recyclable, and eco-friendly nanocatalyst. *J Heterocycl Chem* 2020;57:1825–37. <https://doi.org/10.1002/jhet.3911>.
- [180] Mofakham H, Ghadari R, Shaabani A, Pedarpour M, Ghasemi S. “on-water” organic synthesis: L-proline catalyzed synthesis of pyrimidine-2,4-dione-, benzo[g]- and dihydropyrano[2,3-g]chromene derivatives in aqueous media. *Journal of the Iranian Chemical Society* 2013;10:307–17. <https://doi.org/10.1007/s13738-012-0160-x>.

- [181] Du B, Cai G, Zhao B, Meng X, Wang X, Li Y. Efficient one-pot three-component synthesis of 3,4-dihydro-12-phenyl-2H-benzo[b]xanthene-1,6,11(12H)-trione derivatives in ionic liquid. *Research on Chemical Intermediates* 2013;39:1323–33. <https://doi.org/10.1007/s11164-012-0688-5>.
- [182] Jardosh HH, Patel MP. Microwave-induced CAN promoted atom-economic synthesis of 1H-benzo[b]xanthene and 4H-benzo[g]chromene derivatives of N-allyl quinolone and their antimicrobial activity. *Medicinal Chemistry Research* 2013;22:2954–63. <https://doi.org/10.1007/s00044-012-0301-x>.
- [183] Le-Nhat-Thuy G, Dang Thi TA, Hoang Thi P, Nguyen Thi QG, Nguyen HT, Vu Ngoc D, et al. Multicomponent synthesis of novel 3-benzoyl-4H-benzo[g]chromene-5,10-dione derivatives. *Tetrahedron Lett* 2021;75. <https://doi.org/10.1016/j.tetlet.2021.153215>.
- [184] Ghorbani-Choghamarani A, Sahraei R, Taherinia Z. Ni(II) immobilized on modified boehmite nanostructures: a novel, inexpensive, and highly efficient heterogeneous nanocatalyst for multicomponent domino reactions. *Research on Chemical Intermediates* 2019. <https://doi.org/10.1007/s11164-019-03787-3>.
- [185] Fu Z, Qian K, Li S, Shen T, Song Q. MgCl₂ catalyzed one-pot synthesis of 2-hydroxy-3-((5-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)(phenyl)methyl)naphthalene-1,4-dione derivatives in EG. *Tetrahedron Lett* 2016;57:1104–8. <https://doi.org/10.1016/j.tetlet.2016.01.089>.
- [186] Lakshmanan S, Ramalakshmi N. One-pot, four-component synthesis of benzylpyrazolyl naphthoquinone derivatives and molecular docking studies. *Synth Commun* 2016;46:2045–52. <https://doi.org/10.1080/00397911.2016.1244693>.
- [187] Chandane W, Gajare S, Patil A, Rashinkar G, Tamhankar B. Nanoparticle Supported Bronsted Acidic Ionic Liquid Catalyzed Synthesis of Dihydro-1H-pyrazolynaphthalene-1,4-diones. *Catal Letters* 2023;153:3357–70. <https://doi.org/10.1007/s10562-022-04243-5>.
- [188] Vajargahy MP, Dabiri M, MaGee D, Bazgir A. Ultrasound-assisted multi-component synthesis of indazolophthalazine derivatives. *Journal of the Iranian Chemical Society* 2015;12:1613–21. <https://doi.org/10.1007/s13738-015-0634-8>.
- [189] Khaligh NG, Mihankhah T. Poly(4-vinylpyridinium) hydrogen sulfate catalyzed synthesis of 12-aryl-12-hydro-5H-benzo[g]indeno[2,1-b]quinoline-6,11,13-trione derivatives. *Research on Chemical Intermediates* 2015;41:4569–79. <https://doi.org/10.1007/s11164-014-1552-6>.
- [190] Devi Bala B, Balamurugan K, Perumal S. Facile, four-component, domino reactions for the regioselective synthesis of tetrahydrobenzo[g]quinolines. *Tetrahedron Lett* 2011;52:4562–6. <https://doi.org/10.1016/j.tetlet.2011.06.102>.
- [191] Ghasemzadeh MA, Elyasi Z, Azimi-Nasrabad M, Mirhosseini-Eshkevari B. Magnetite Nanoparticles-Supported APTES as a Powerful and Recoverable Nanocatalyst for the Preparation of 2-Amino-5,10-dihydro-5,10-dioxo-4H-benzo[g]chromenes and Tetrahydrobenzo[g]quinoline-5,10-diones. *Combinatorial Chemistry & High Throughput Screening*, 2017;20:64–76. <https://doi.org/10.2174/1386207319666161>.

- [192] Kumari P, Yadav R, Bharti R, Parvin T. Regioselective synthesis of pyrimidine-fused tetrahydropyridines and pyridines by microwave-assisted one-pot reaction. *Mol Divers* 2020;24:107–17. <https://doi.org/10.1007/s11030-019-09929-4>.
- [193] Khurana I, Gupta S, Khurana JM, Rai PK. An efficient protocol for the synthesis of oxazine derivatives using a carbocatalyst in aqueous medium. *Synth Commun* 2020;50:3592–602. <https://doi.org/10.1080/00397911.2020.1806327>.
- [194] Khanna G, Aggarwal K, Khurana JM. An efficient and confluent approach for the synthesis of novel 3,4-dihydro-2H-naphtho[2,3-e][1,3]oxazine-5,10-dione derivatives by a three component reaction in ionic liquid. *RSC Adv* 2015;5:46448–54. <https://doi.org/10.1039/C5RA06169E>.
- [195] Cao YQ, Li XR, Wu W, Zhang D, Zhang ZH, Mo LP. A green approach for synthesis of naphthoquinone-fused oxazine derivatives in water under ultrasonic irradiation. *Research on Chemical Intermediates* 2017;43:3745–55. <https://doi.org/10.1007/s11164-016-2854-7>.
- [196] Gajare S, Patil A, Kale D, Bansode P, Patil P, Rashinkar G. Graphene Oxide-Supported Ionic Liquid Phase Catalyzed Synthesis of 3,4-Dihydro-2H-naphtho[2,3-e][1,3]oxazine-5,10-diones. *Catal Letters* 2020;150:243–55. <https://doi.org/10.1007/s10562-019-02934-0>.
- [197] Olyaei A, Sadeghpour M. A review on lawsone-based benzo[a]phenazin-5-ol: synthetic approaches and reactions. *RSC Adv* 2022;12:13837–95. <https://doi.org/10.1039/D2RA02139K>.
- [198] Daraie M, Tamoradi T, Heravi MM, Karmakar B. Ce immobilized 1H-pyrazole-3,5-dicarboxylic acid (PDA) modified CoFe₂O₄: A potential magnetic nanocomposite catalyst towards the synthesis of diverse benzo[a]pyrano[2,3-c]phenazine derivatives. *J Mol Struct* 2021;1245. <https://doi.org/10.1016/j.molstruc.2021.131089>.
- [199] Mishra A, Pandey YK, Tufail F, Singh J, Singh J. A Convenient and Green Synthetic Approach for Benzo[a]pyrano[2,3-c]phenazines via Supramolecular Catalysis. *Catal Letters* 2020;150:1659–68. <https://doi.org/10.1007/s10562-019-03057-2>.
- [200] Dehnavian M, Dehghani A, Moradi L. Introducing a green nanocatalytic process toward the synthesis of benzo[a]pyrano-[2,3-c]phenazines utilizing copper oxide quantum dot-modified core-shell magnetic mesoporous silica nanoparticles as high throughput and reusable nanocatalysts. *RSC Adv* 2022;12:25194–203. <https://doi.org/10.1039/d2ra03887k>.
- [201] Shirzaei F, Shaterian HR. Fe₃O₄@SiO₂[(CH₂)₃N+H₃HCOO]⁻ Nanoparticles: A Novel and Heterogeneous Nanocatalyst for Preparation of New (Methylsulfonyl)Benzopyranophenazin-3-Amine Derivatives. *Polycycl Aromat Compd* 2023. <https://doi.org/10.1080/10406638.2023.2254897>.
- [202] Shirzaei F, Shaterian HR. Basic ionic liquid, 2-hydroxyethylammonium formate, catalyzed one-pot synthesis of novel 2-(phenylsulfonyl)-1H-benzo[a]pyrano[2,3-c]phenazin-3-amine derivatives. *Research on Chemical Intermediates* 2022;48:751–70. <https://doi.org/10.1007/s11164-021-04627-z>.

- [203] Pal S, Konkimalla VB, Kathawate L, Rao SS, Gejji SP, Puranik VG, et al. Targeting a chemorefractory COLO205 (BRAF V600E) cell line using substituted benzo[α]phenoxazines. *RSC Adv* 2015;5:82549–63. <https://doi.org/10.1039/C5RA14949E>.
- [204] Kathawate L, Joshi P V., Dash TK, Pal S, Nikalje M, Weyhermüller T, et al. Reaction between lawsone and aminophenol derivatives: Synthesis, characterization, molecular structures and antiproliferative activity. *J Mol Struct* 2014;1075:397–405. <https://doi.org/10.1016/j.molstruc.2014.07.007>.
- [205] Verma K, Tailor YK, Khandelwal S, Agarwal M, Rushell E, Kumari Y, et al. An efficient and environmentally sustainable domino protocol for the synthesis of structurally diverse spiroannulated pyrimidophenazines using erbium doped TiO₂ nanoparticles as a recyclable and reusable heterogeneous acid catalyst. *RSC Adv* 2018;8:30430–40. <https://doi.org/10.1039/C8RA04919J>.
- [206] Yadav R, Parvin T. Multicomponent synthesis of styryl linked benzo[h]pyrazolo[3,4-b]quinoline-5,6(10H)-diones by liquid assisted grinding. *New Journal of Chemistry* 2021;45:10388–95. <https://doi.org/10.1039/D1NJ00770J>.
- [207] Mahajan S, Khullar S, Mandal SK, Singh IP. A one-pot, three-component reaction for the synthesis of novel 7-arylbenzo[c]acridine-5,6-diones. *Chemical Communications* 2014;50:10078–81. <https://doi.org/10.1039/C4CC03079F>.
- [208] Michael Rajesh S, Bala BD, Perumal S, Menéndez JC. l-Proline-catalysed sequential four-component “on water” protocol for the synthesis of structurally complex heterocyclic ortho-quinones. *Green Chemistry* 2011;13:3248–54. <https://doi.org/10.1039/C1GC15794A>.
- [209] Ekiz M, Tutar A, Ökten S. Convenient synthesis of disubstituted tacrine derivatives via electrophilic and copper induced reactions. *Tetrahedron* 2016;72:5323–30. <https://doi.org/10.1016/j.tet.2016.07.012>.



APPENDICES

APPENDIX A. Figures The cyclic voltammograms of the substituted 1,4-naphthoquinone derivatives.

APPENDIX B. FT-IR spectra of the substituted 1,4-naphthoquinone derivatives.

APPENDIX C. The mass spectra of the substituted 1,4-naphthoquinone derivatives.



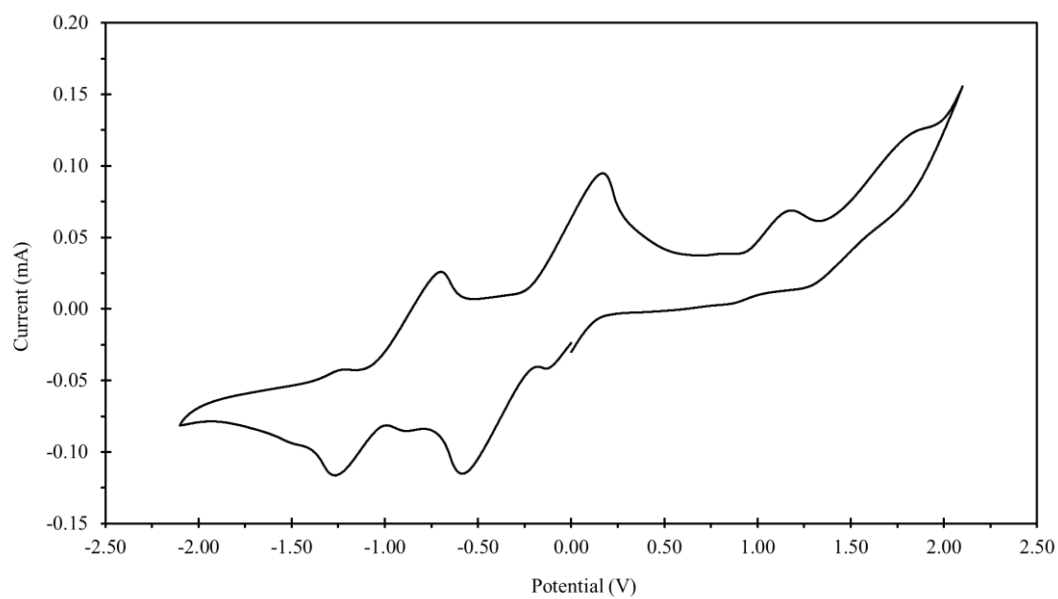


Figure A.1. The cyclic voltammogram of compound 4-1.

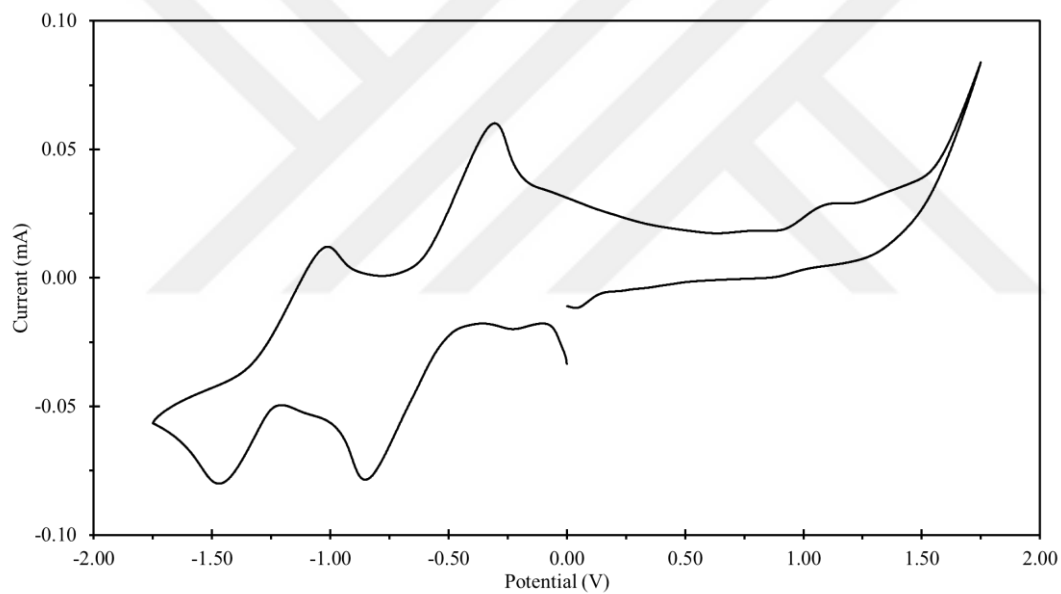


Figure A.2. The cyclic voltammogram of compound 4-2.

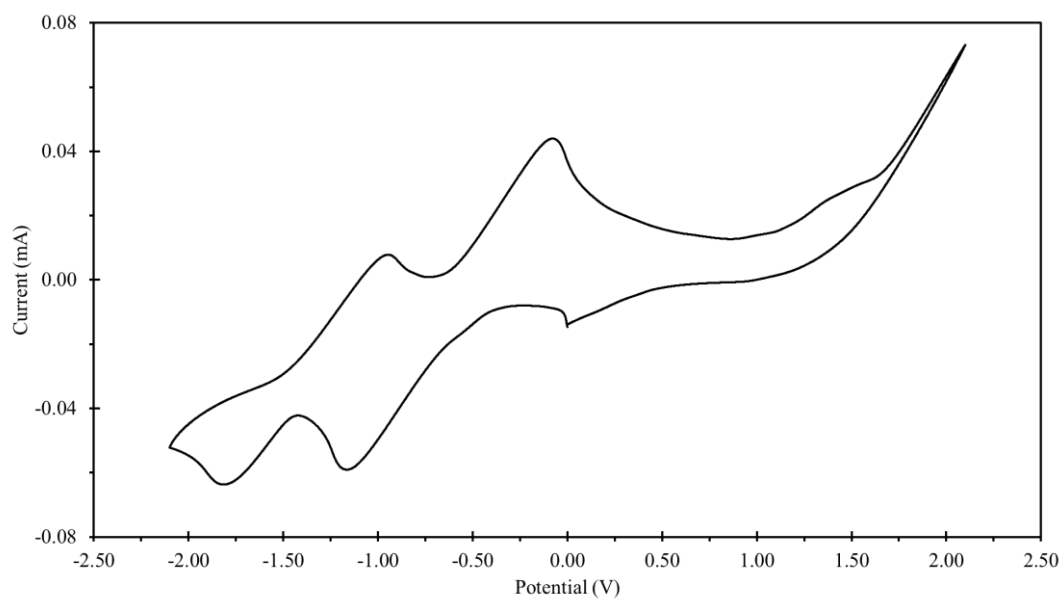


Figure A.3. The cyclic voltammogram of compound 4-3.

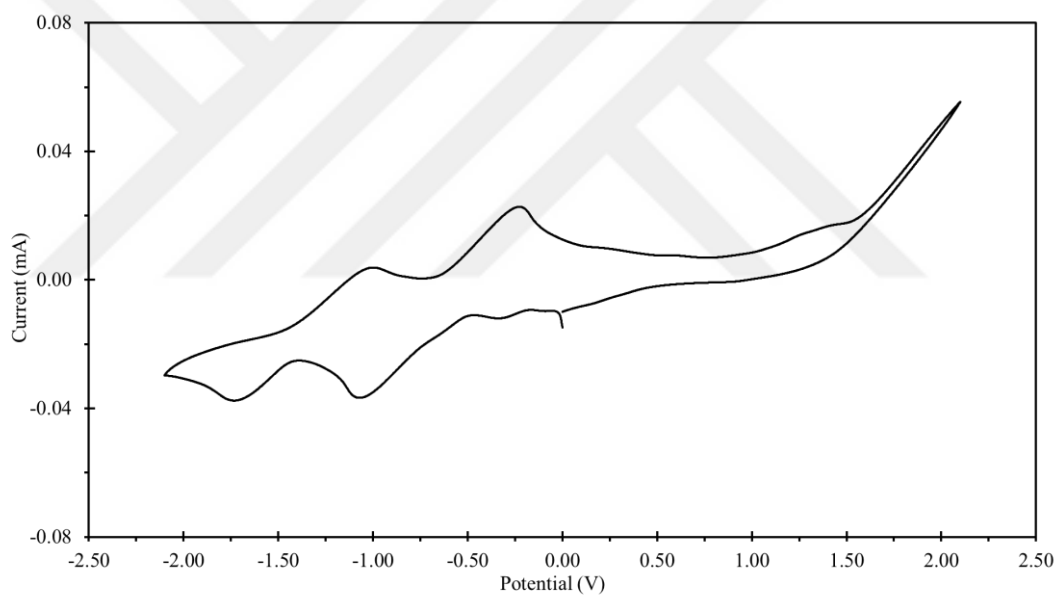


Figure A.4. The cyclic voltammogram of compound 4-4.

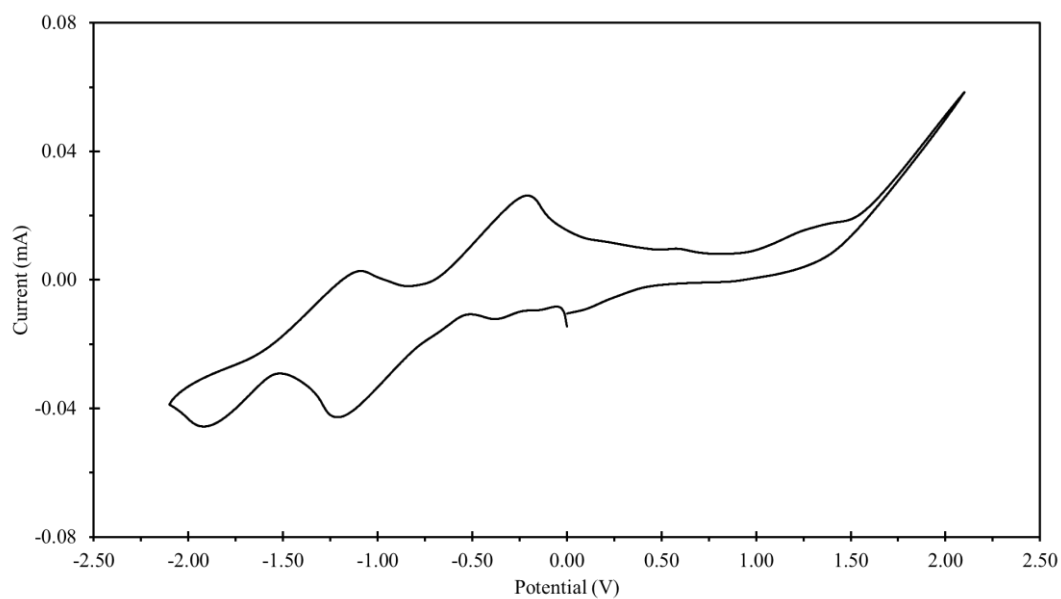


Figure A.5. The cyclic voltammogram of compound 4-5.

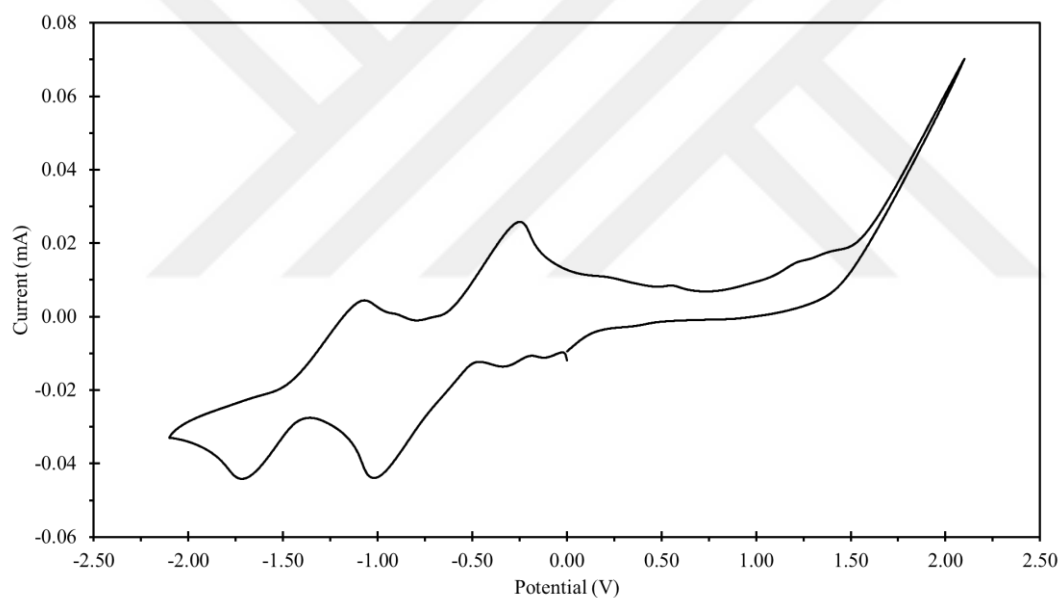


Figure A.6. The cyclic voltammogram of compound 4-6.

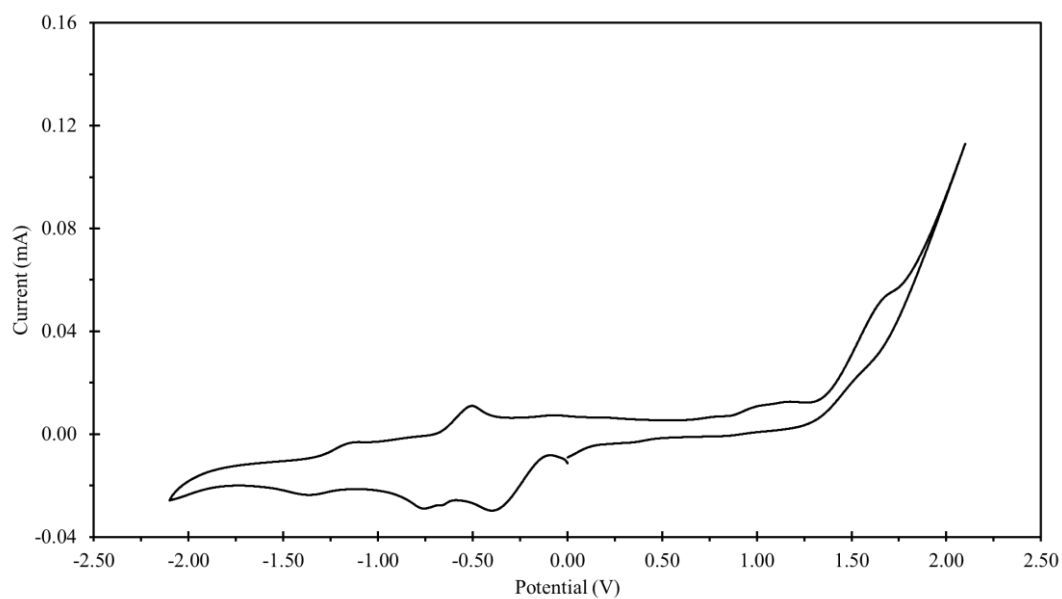


Figure A.7. The cyclic voltammogram of compound 4-7.

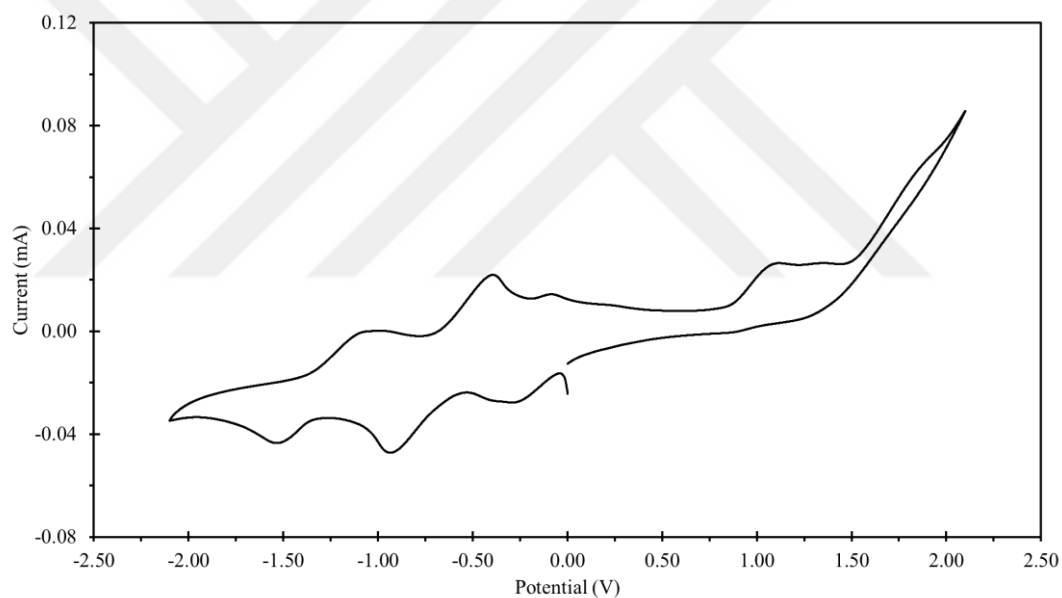


Figure A.8. The cyclic voltammogram of compound 4-8.

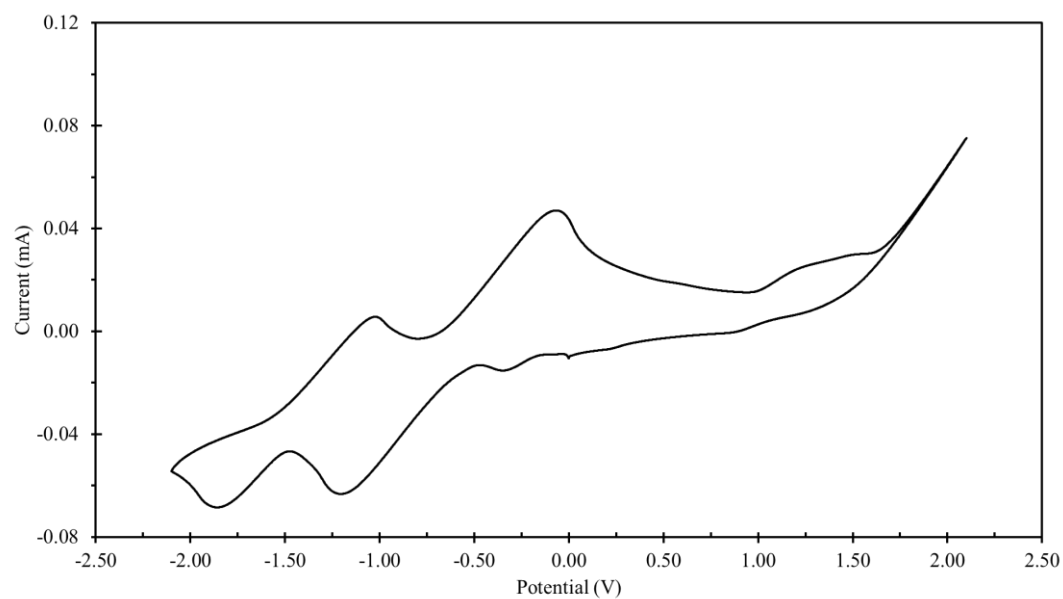


Figure A.9. The cyclic voltammogram of compound 4-9.

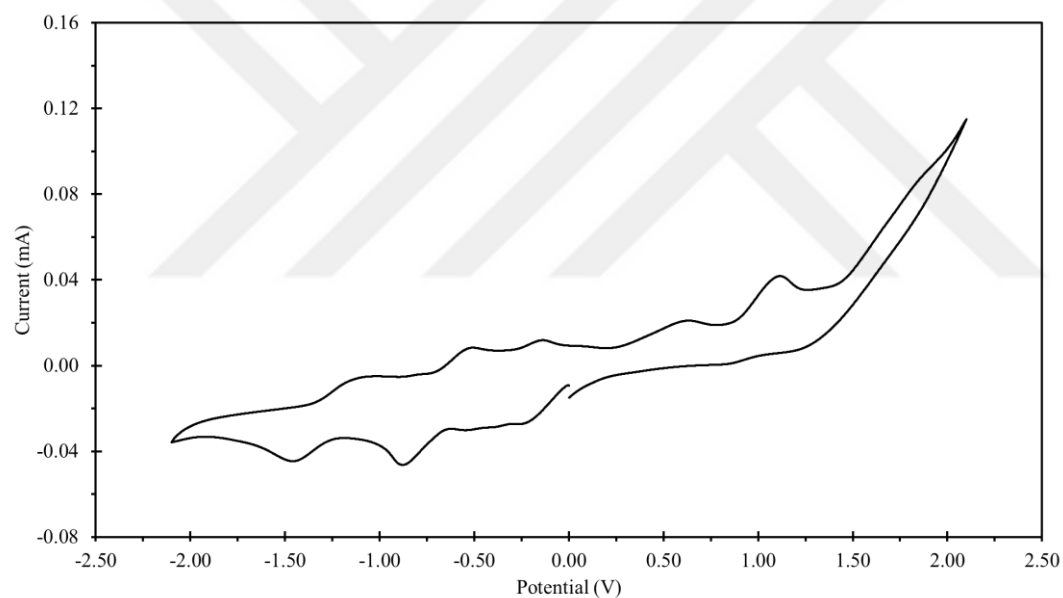


Figure A.10. The cyclic voltammogram of compound 4-10.

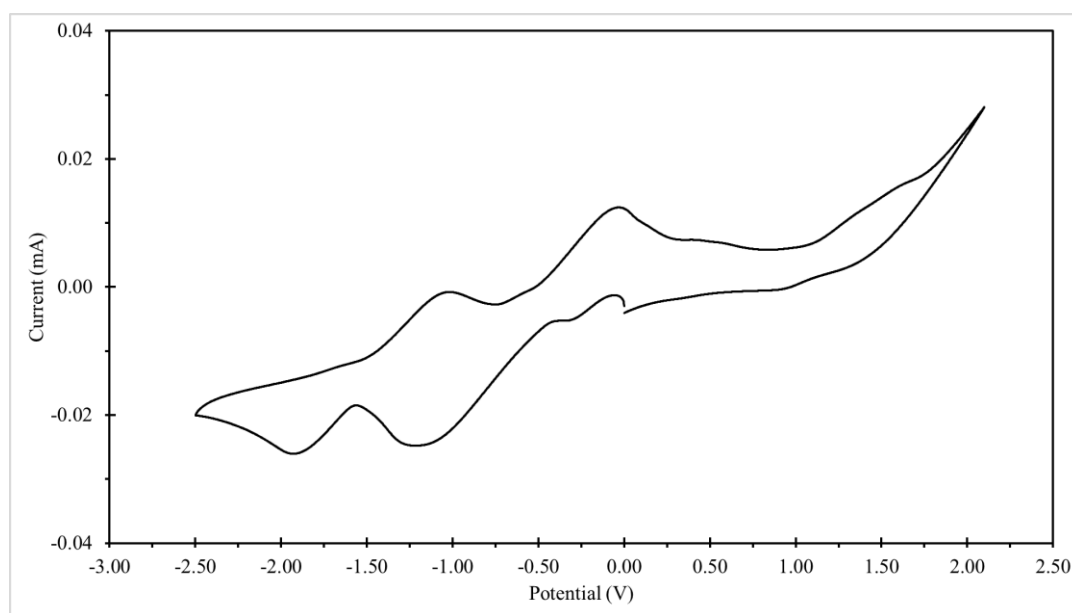


Figure A.11. The cyclic voltammogram of compound 4-11.

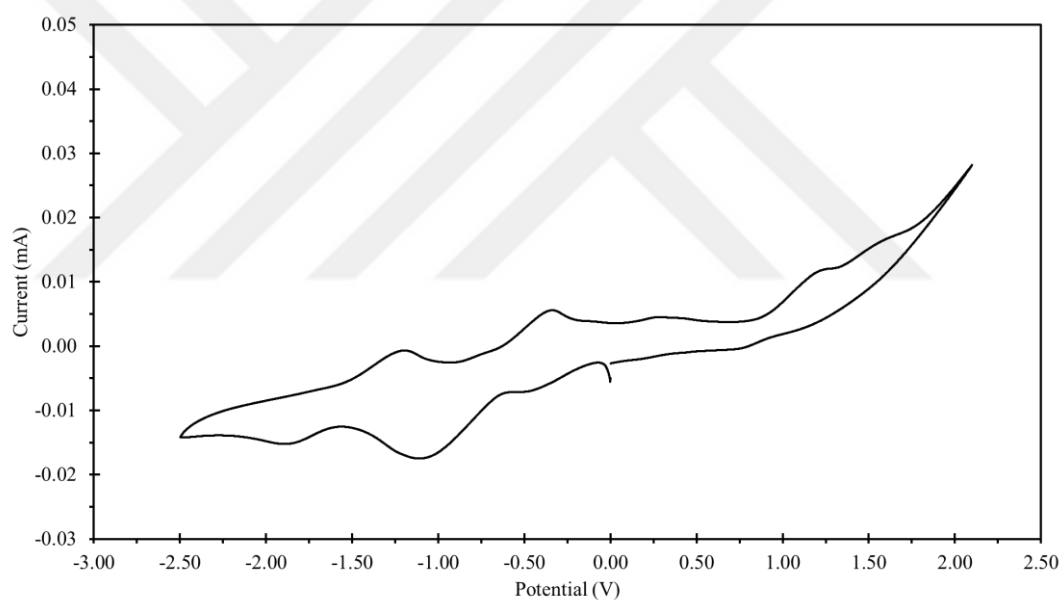


Figure A.12. The cyclic voltammogram of compound 4-12.

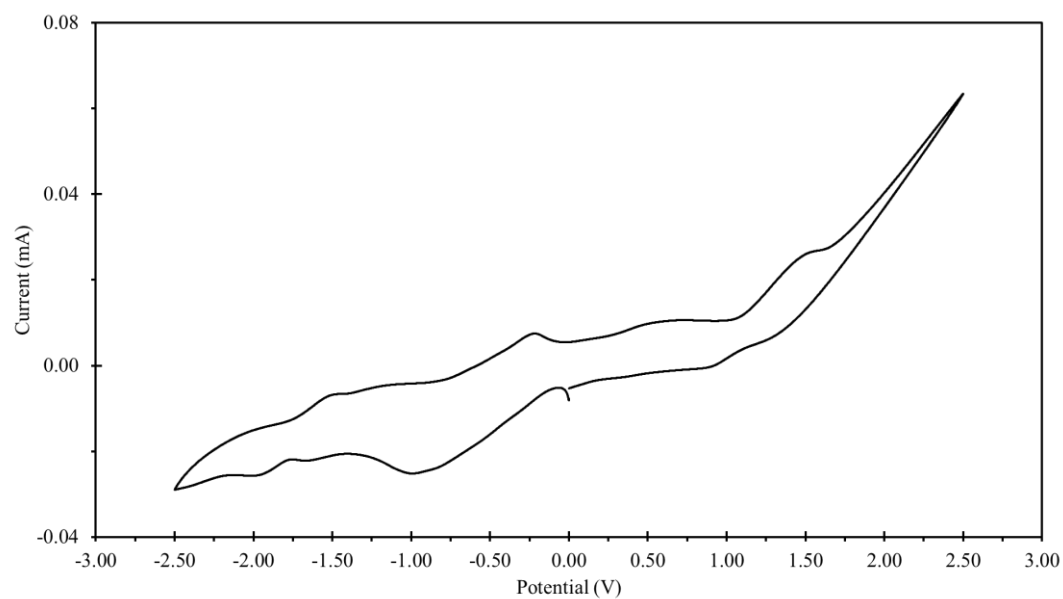


Figure A.13. The cyclic voltammogram of compound 4-13.

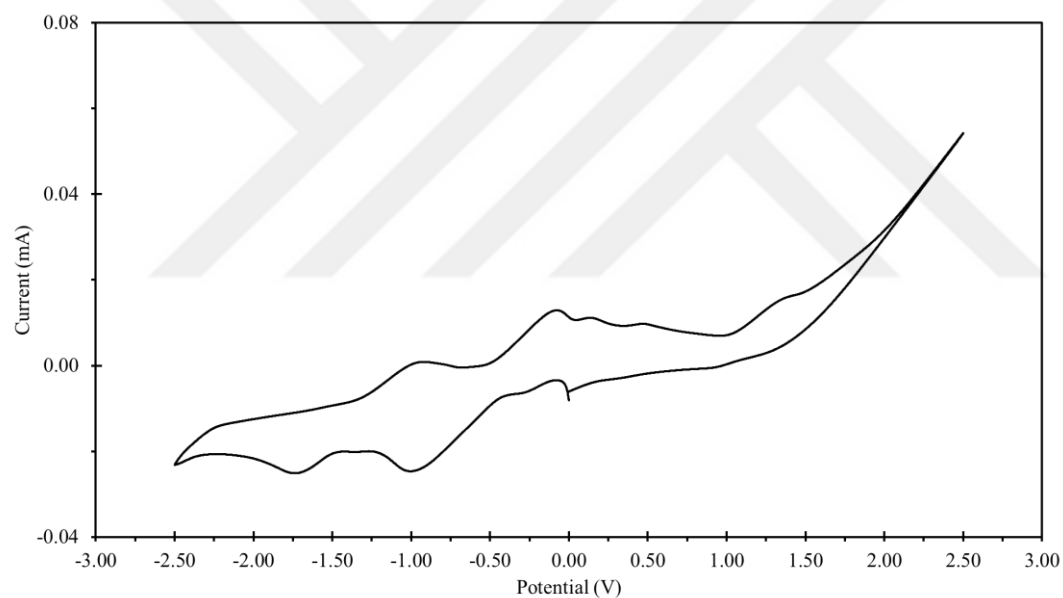


Figure A.14. The cyclic voltammogram of compound 4-14.

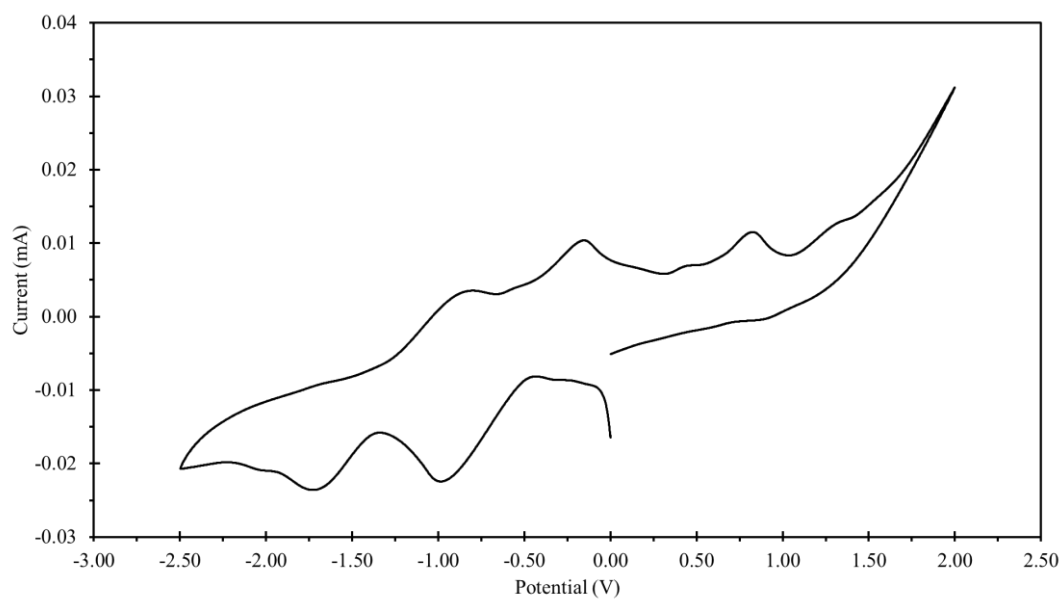


Figure A.15. The cyclic voltammogram of compound 4-15.

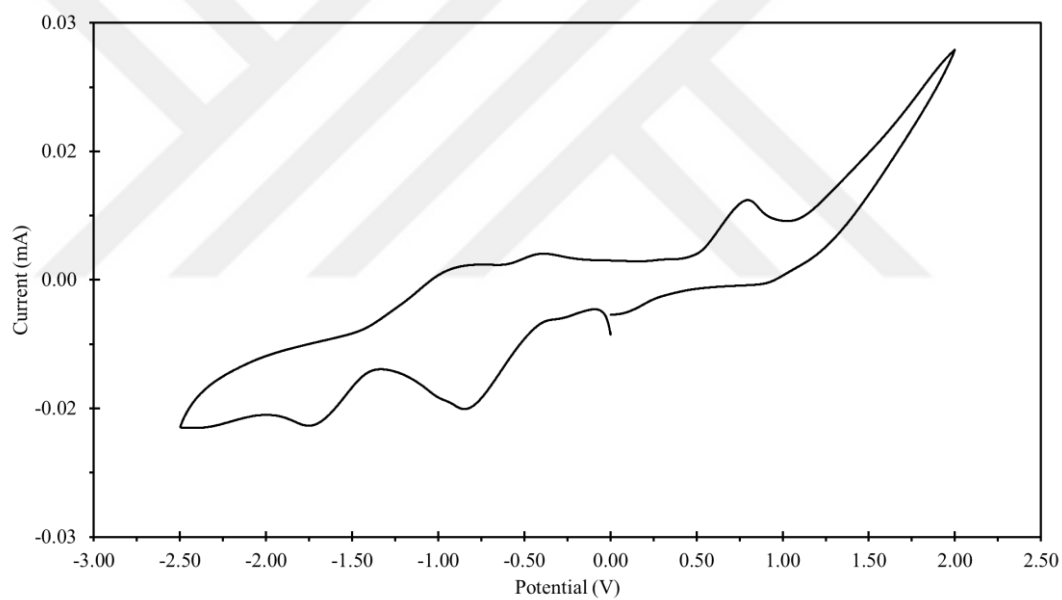


Figure A.16. The cyclic voltammogram of compound 4-16.

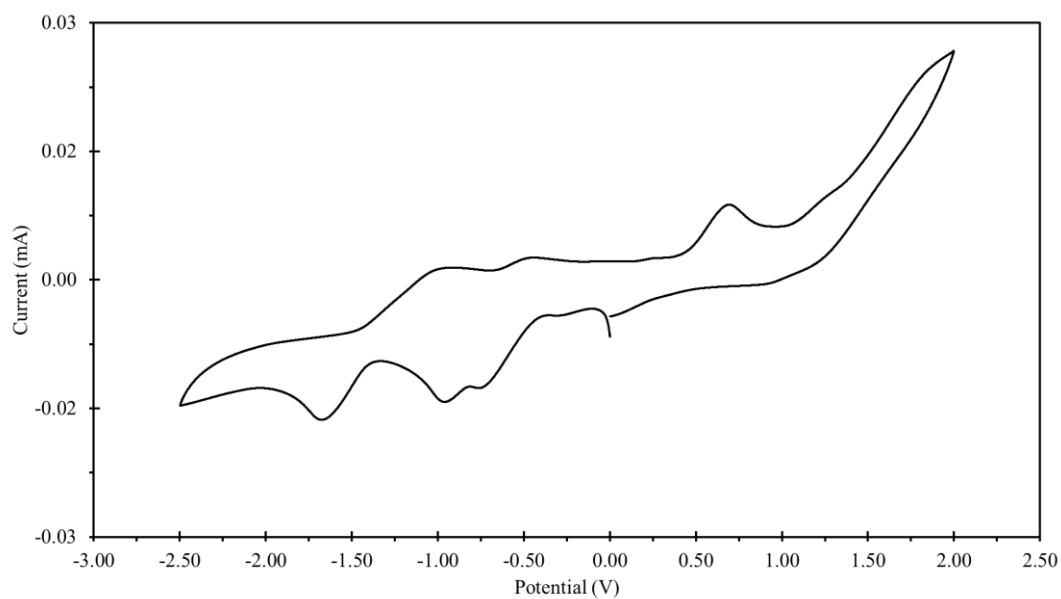


Figure A.17. The cyclic voltammogram of compound 4-17.

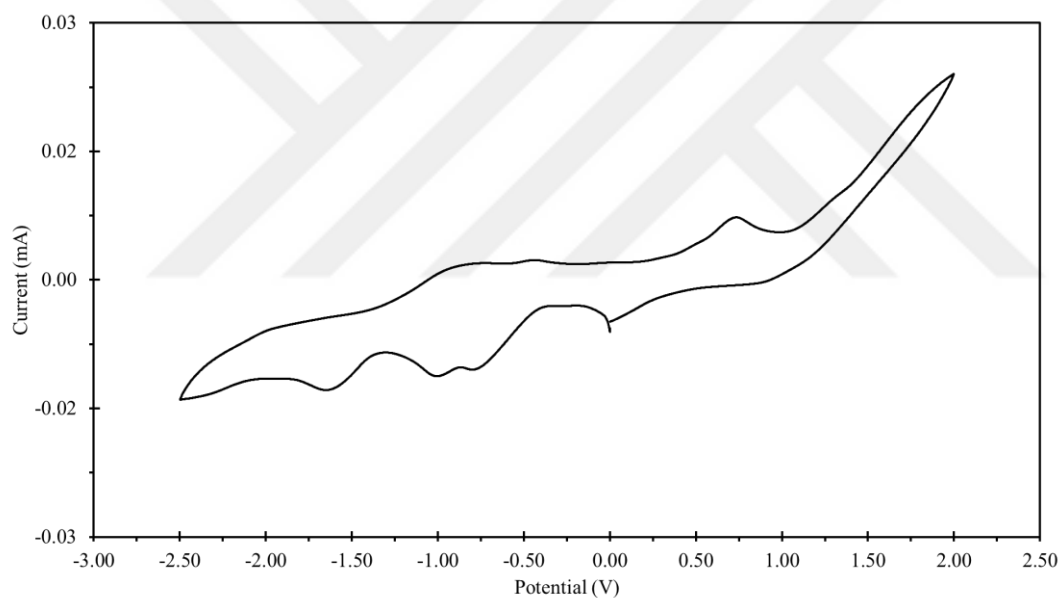


Figure A.18. The cyclic voltammogram of compound 4-20.

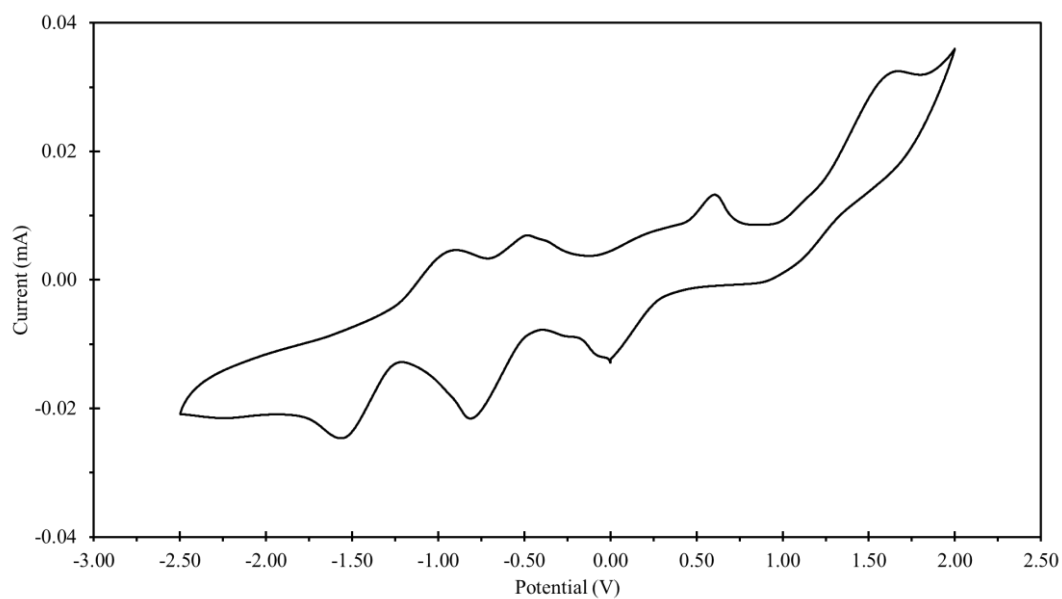


Figure A.19. The cyclic voltammogram of compound 4-21.

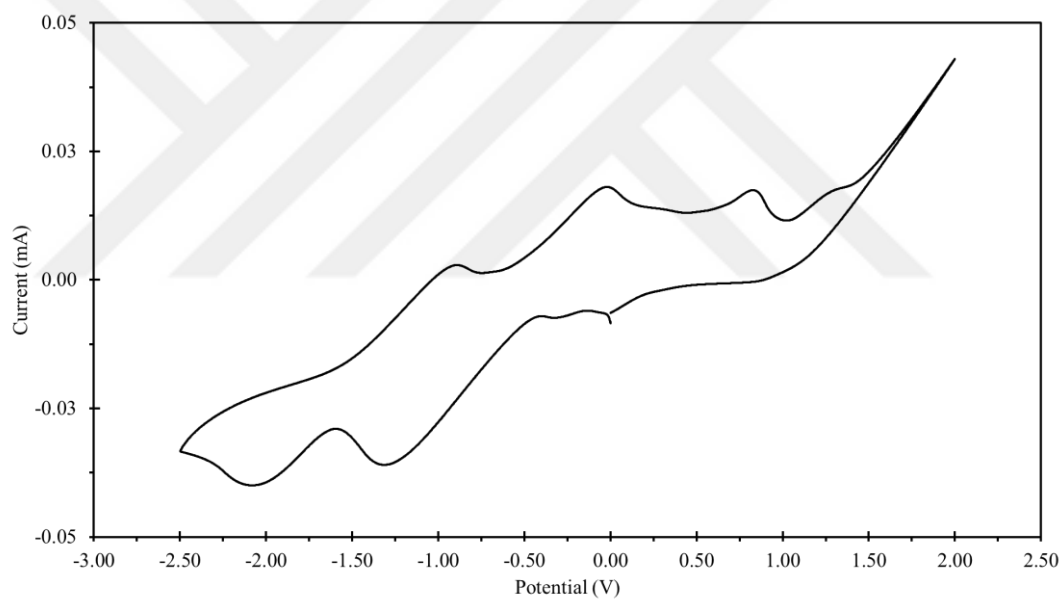


Figure A.20. The cyclic voltammogram of compound 4-22.

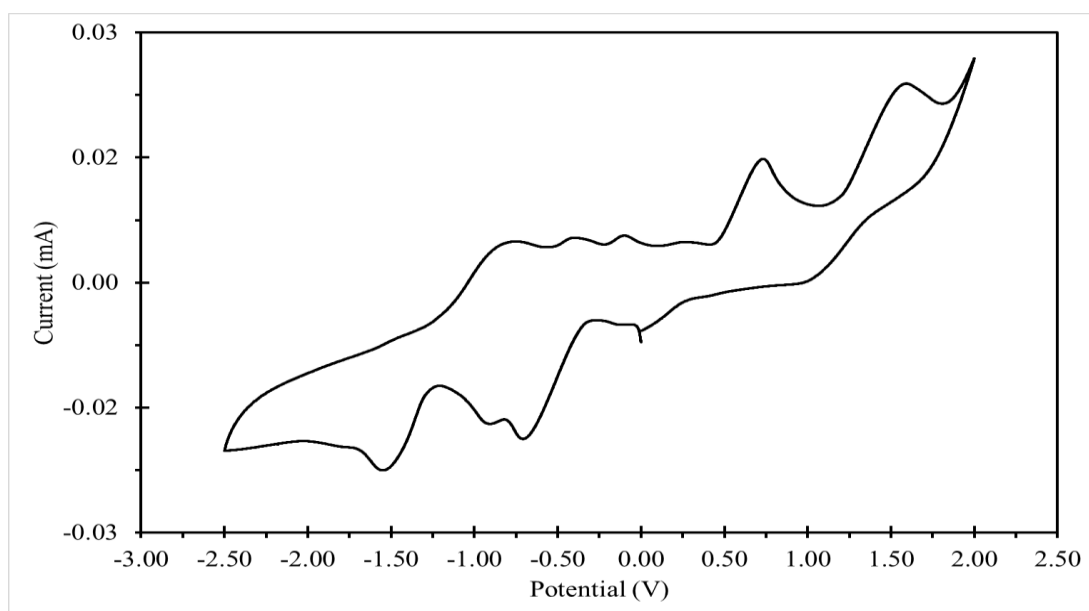


Figure A.21. The cyclic voltammogram of compound 4-23.

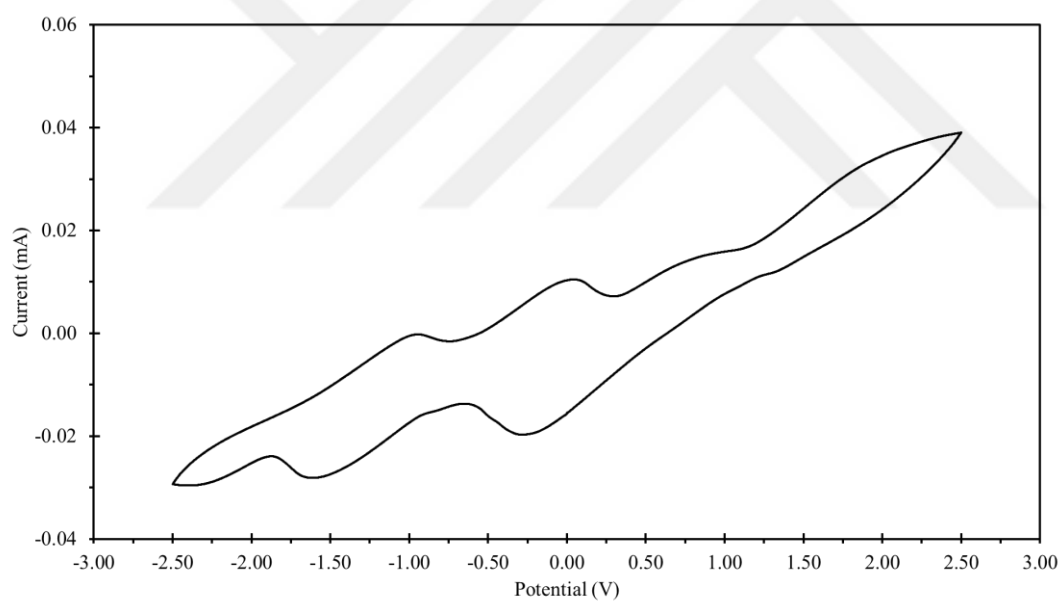


Figure A.22. The cyclic voltammogram of compound 4-24.

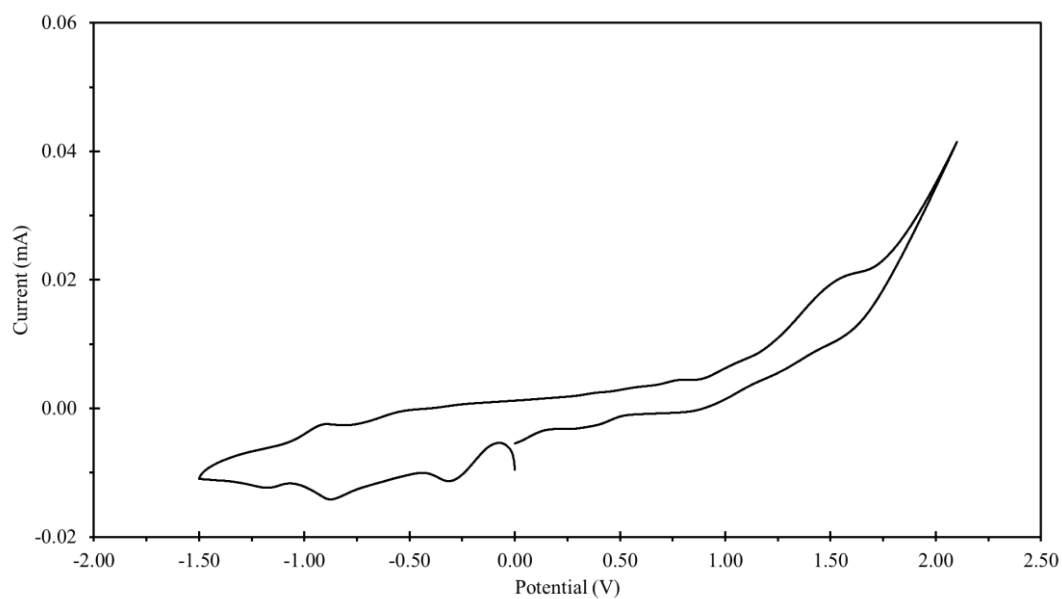


Figure A.23. The cyclic voltammogram of compound 4-27.

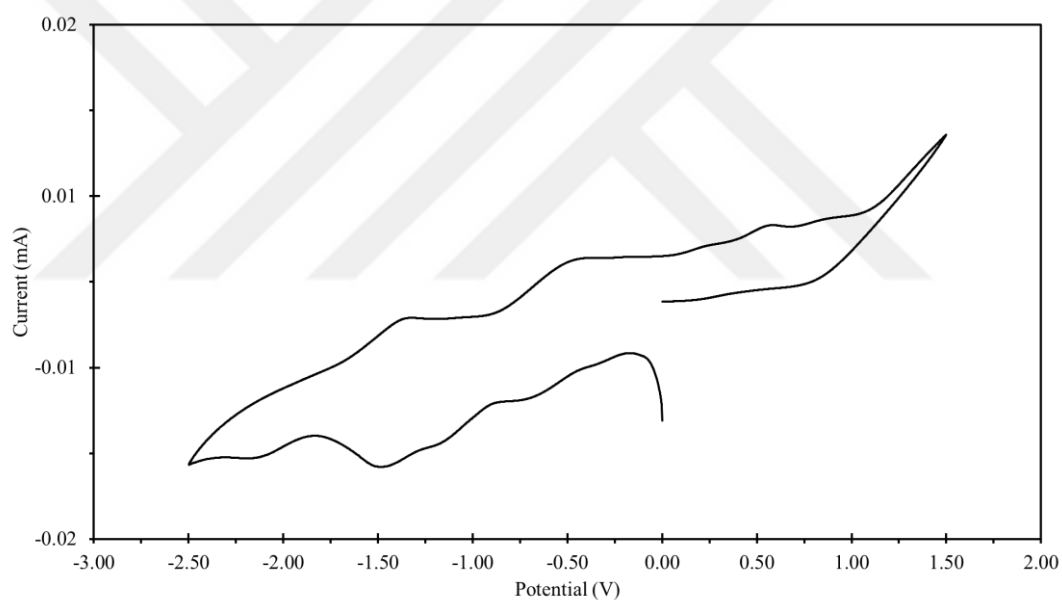


Figure A.24. The cyclic voltammogram of compound 4-28.

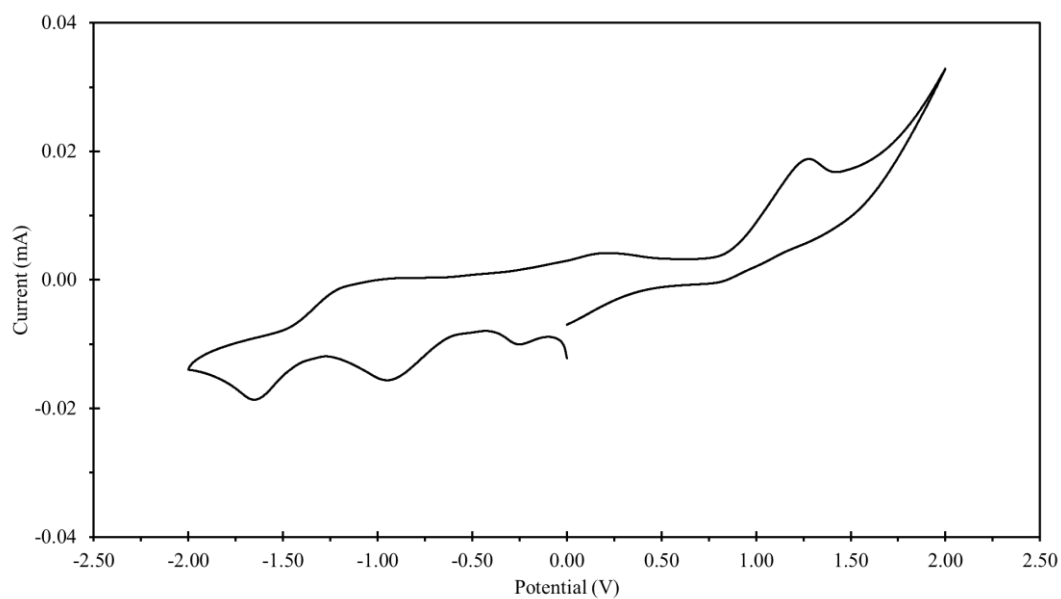


Figure A.25. The cyclic voltammogram of compound 4-30.

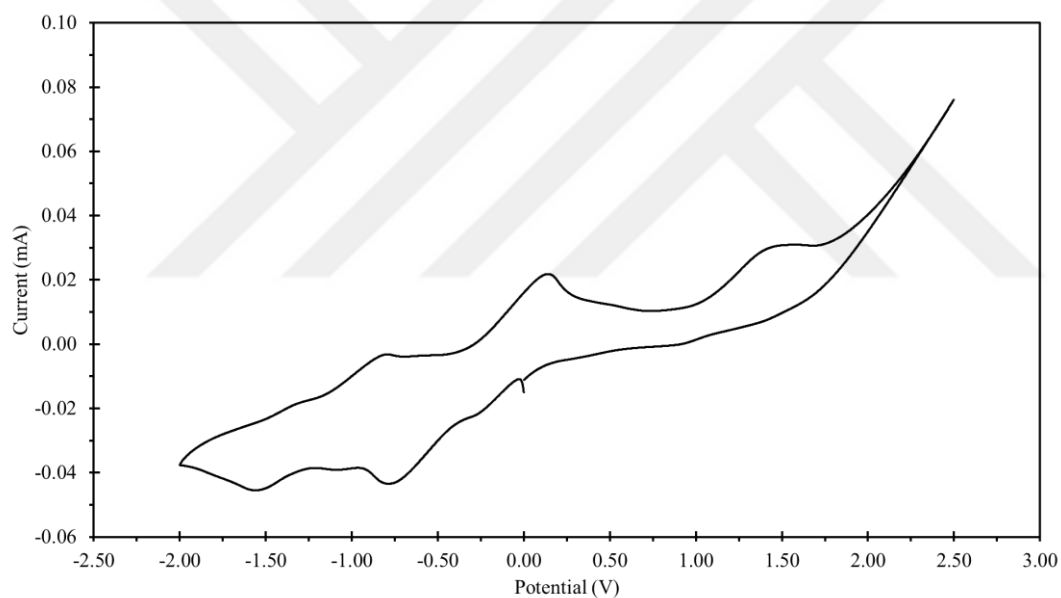


Figure A.26. The cyclic voltammogram of compound 4-31.

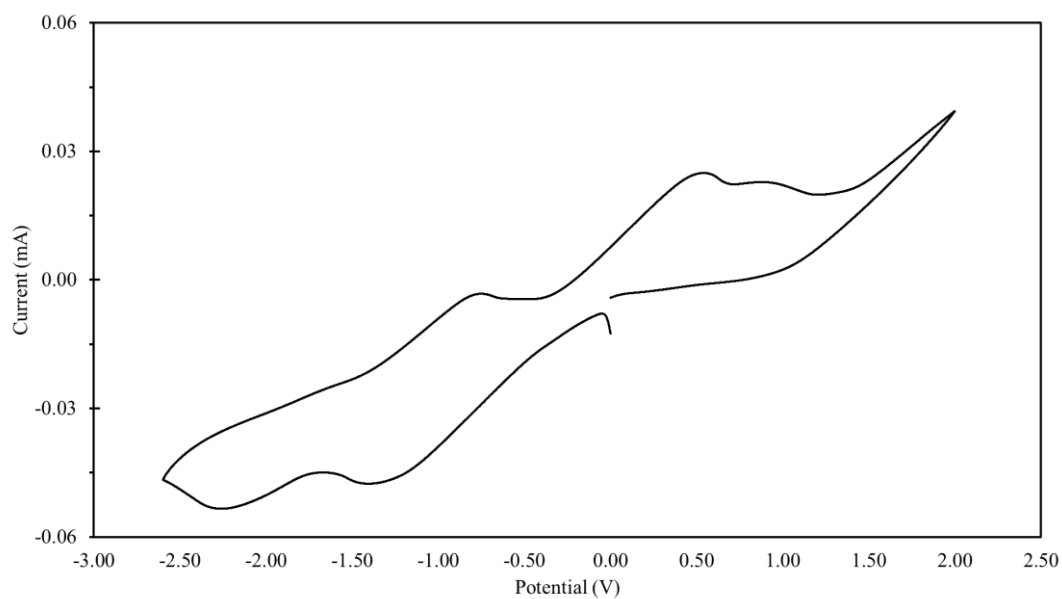


Figure A.27. The cyclic voltammogram of compound 4-32.

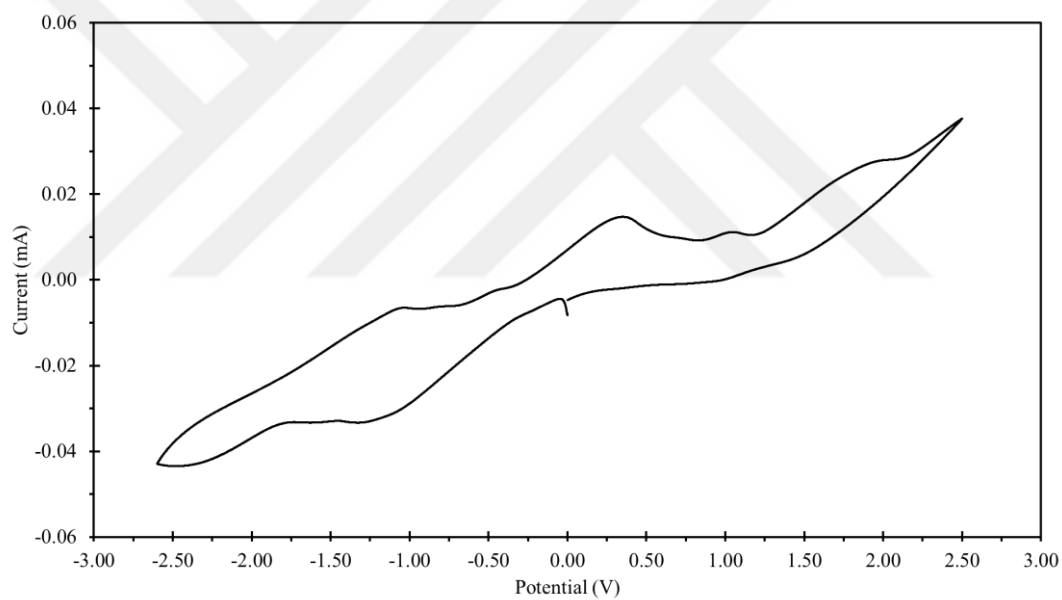


Figure A.28. The cyclic voltammogram of compound 4-33.

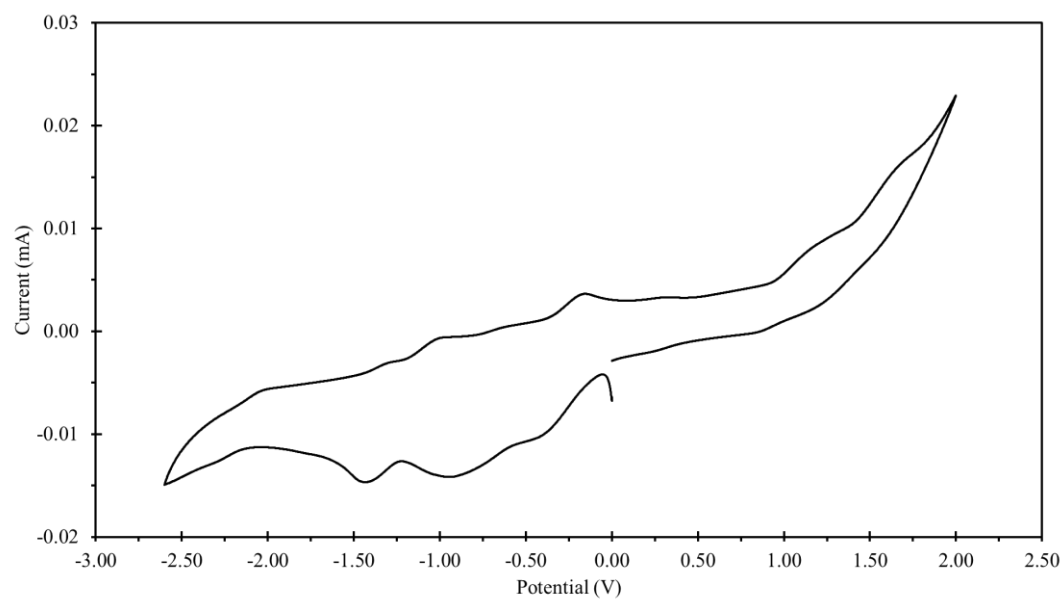


Figure A.29. The cyclic voltammogram of compound 4-35.

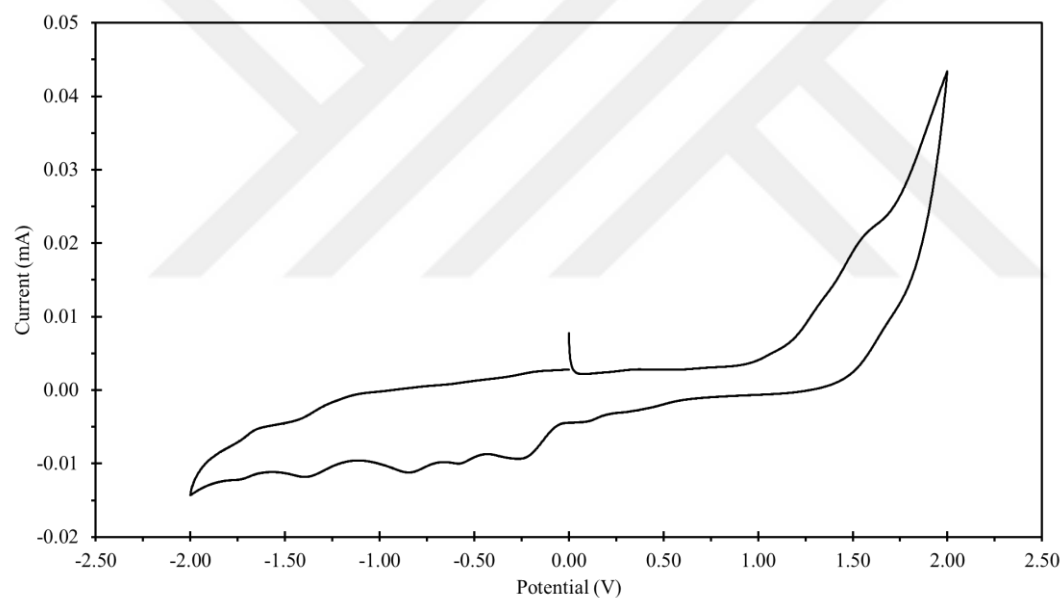


Figure A.30. The cyclic voltammogram of compound 4-36.

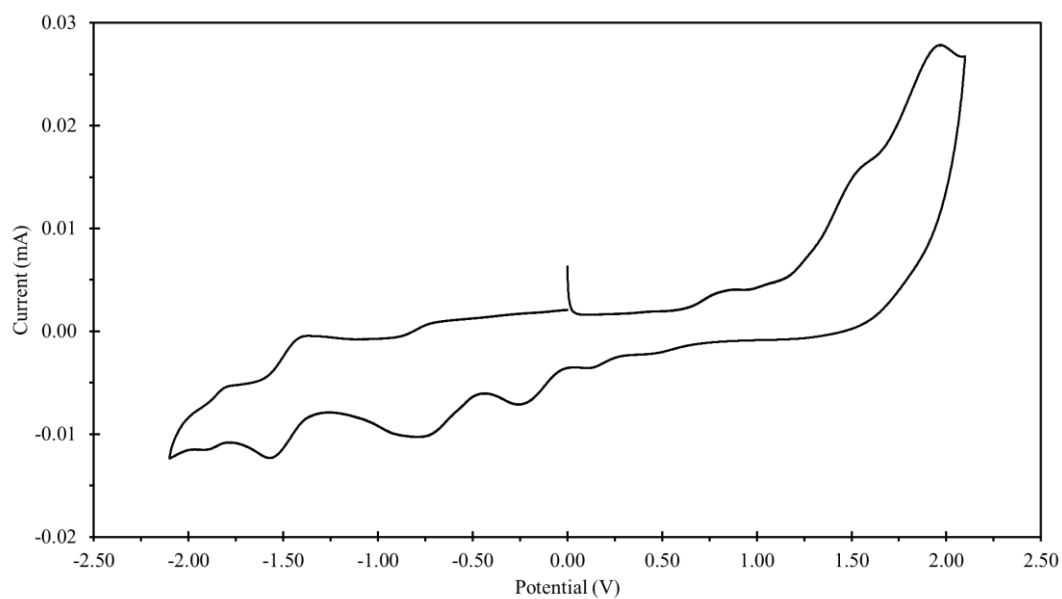


Figure A.31. The cyclic voltammogram of compound 4-37.

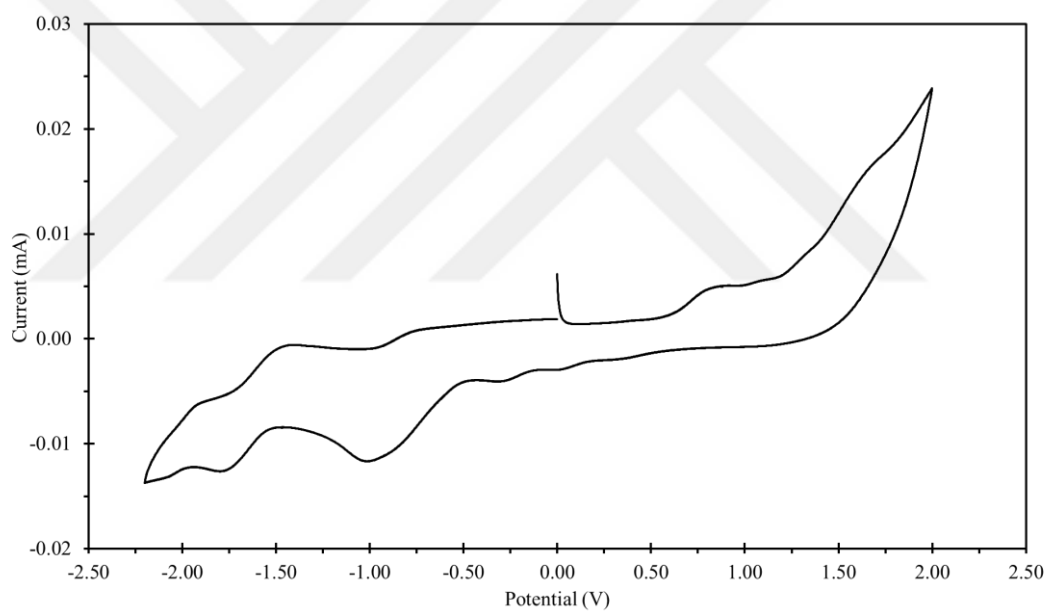


Figure A.32. The cyclic voltammogram of compound 4-38.

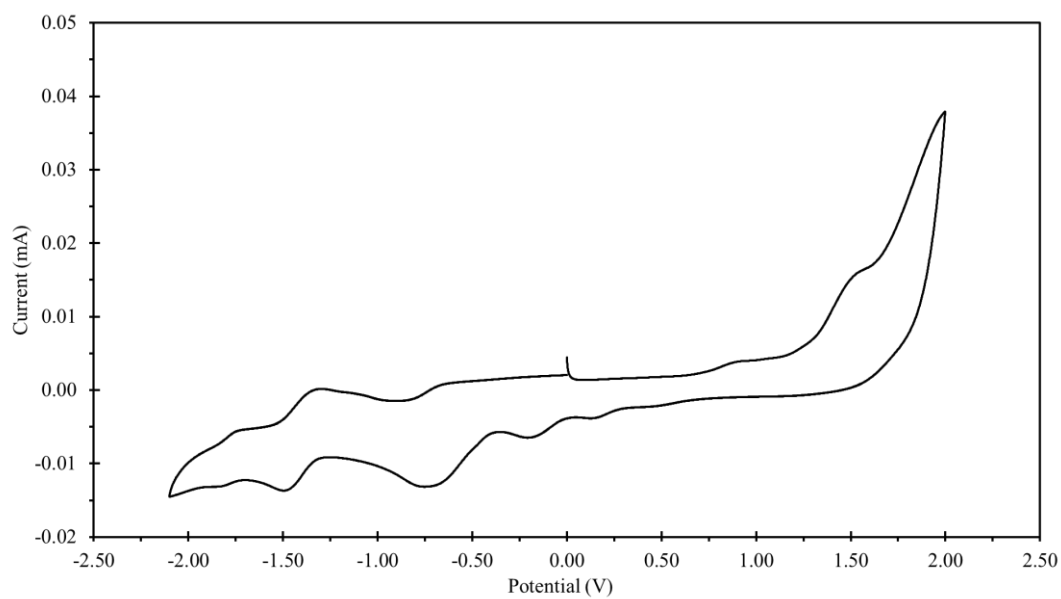


Figure A.33. The cyclic voltammogram of compound 4-39.

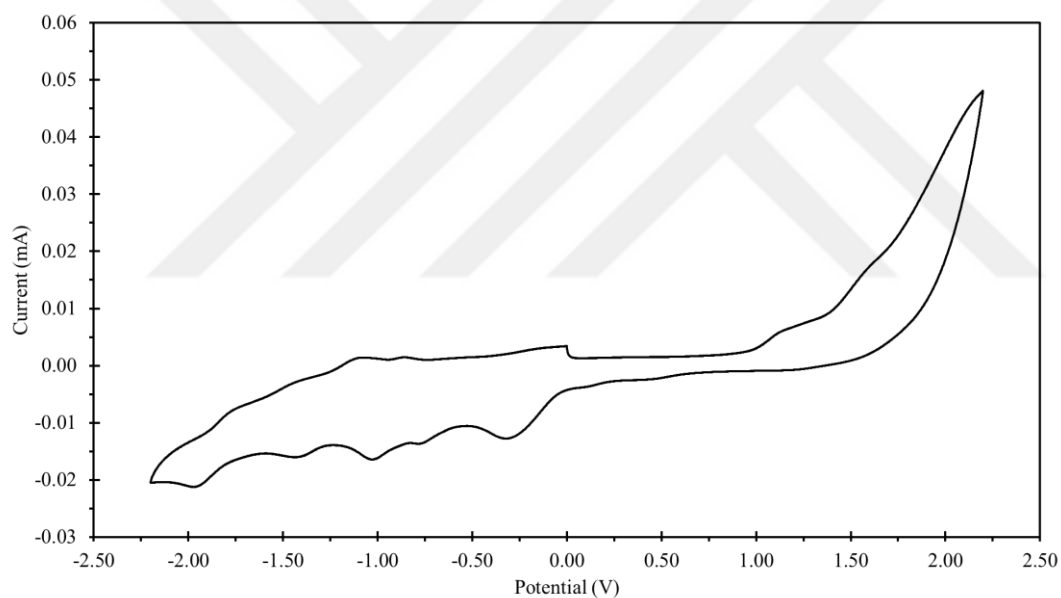


Figure A.34. The cyclic voltammogram of compound 4-40.

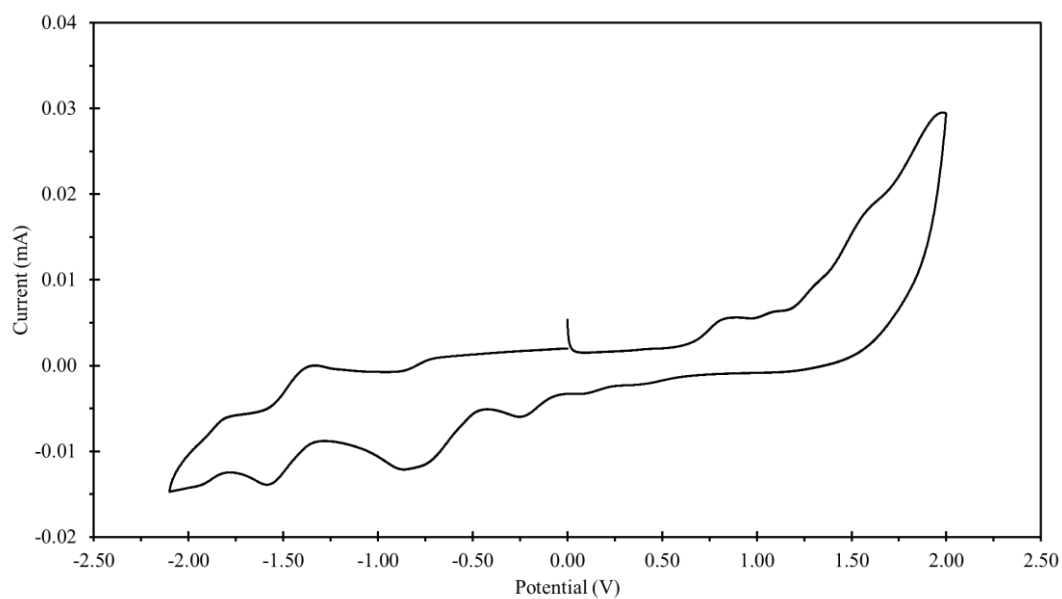


Figure A.35. The cyclic voltammogram of compound 4-41.

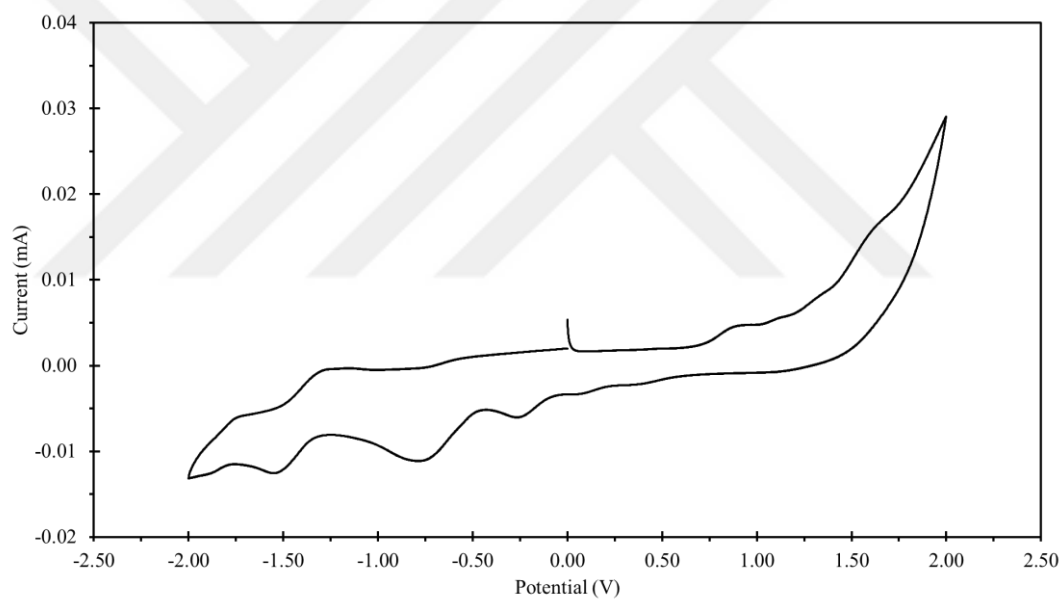


Figure A.36. The cyclic voltammogram of compound 4-42.

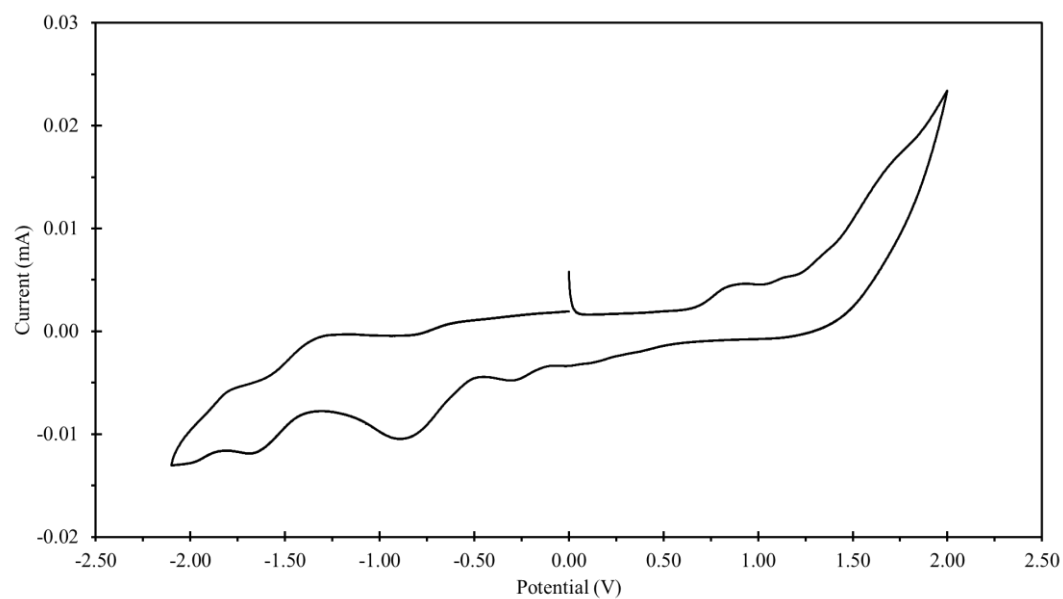


Figure A.37. The cyclic voltammogram of compound 4-43.

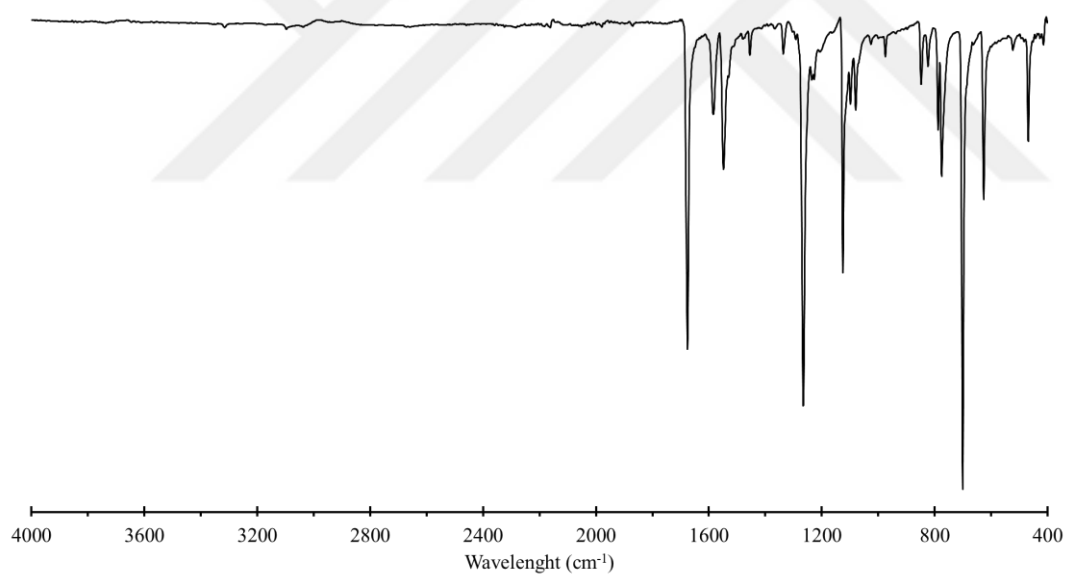


Figure B.1. FT-IR spectrum of the compound 4-1.

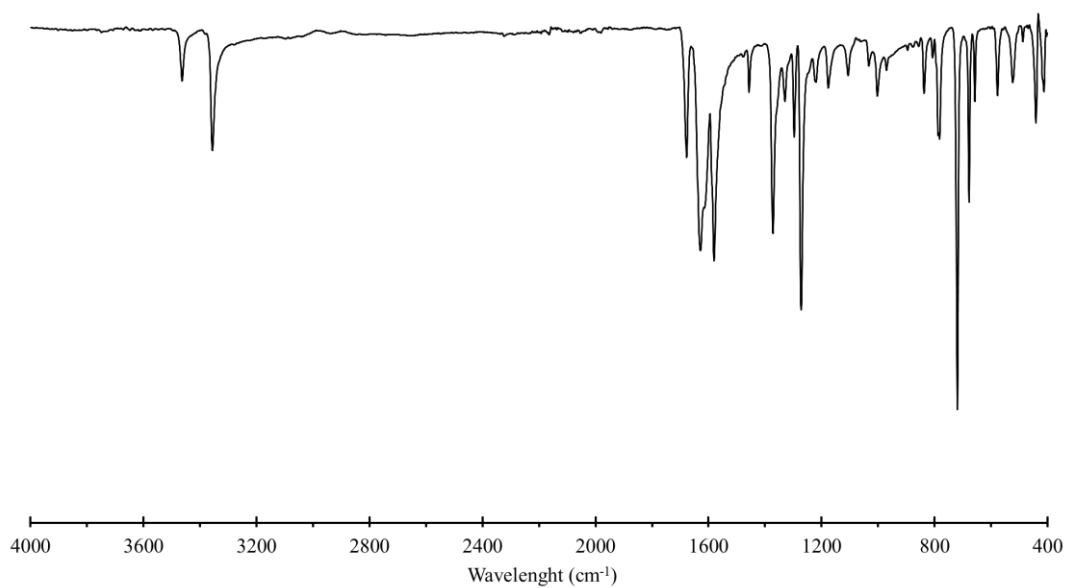


Figure B.2. FT-IR spectrum of the compound 4-2.

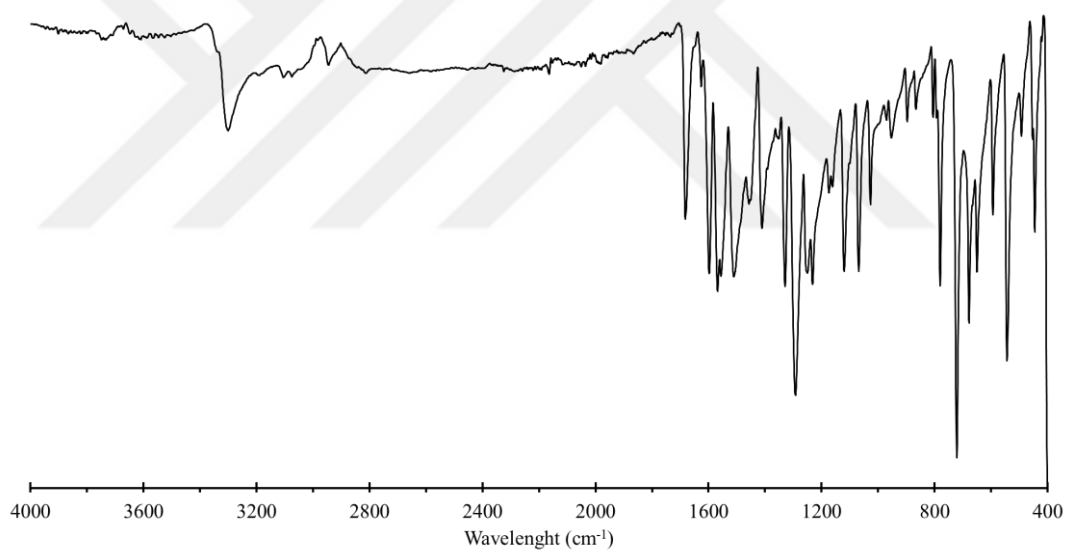


Figure B.3. FT-IR spectrum of the compound 4-3.

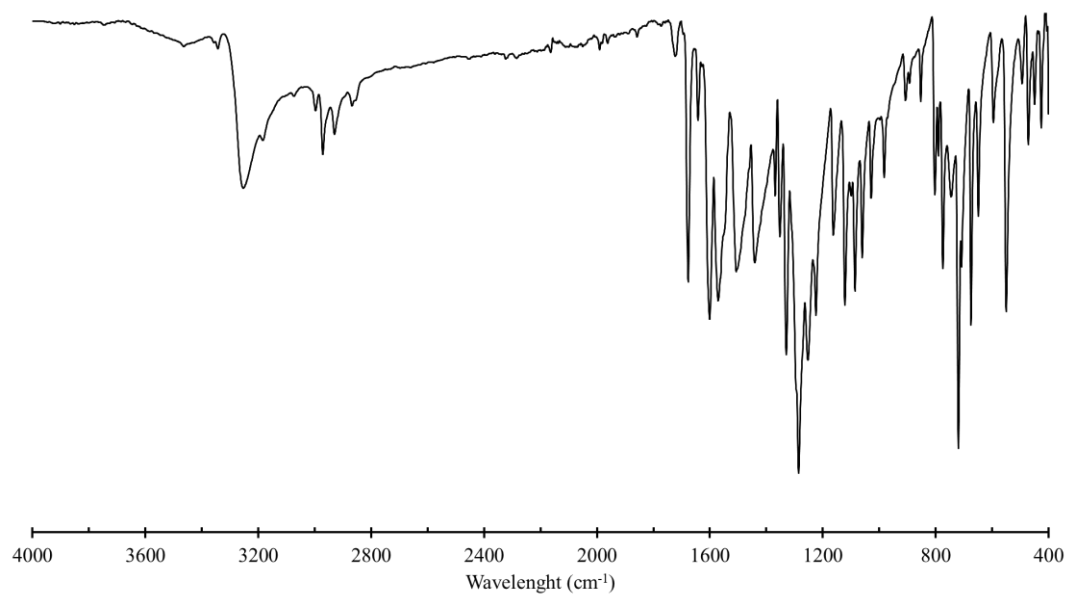


Figure B.4. FT-IR spectrum of the compound 4-4.

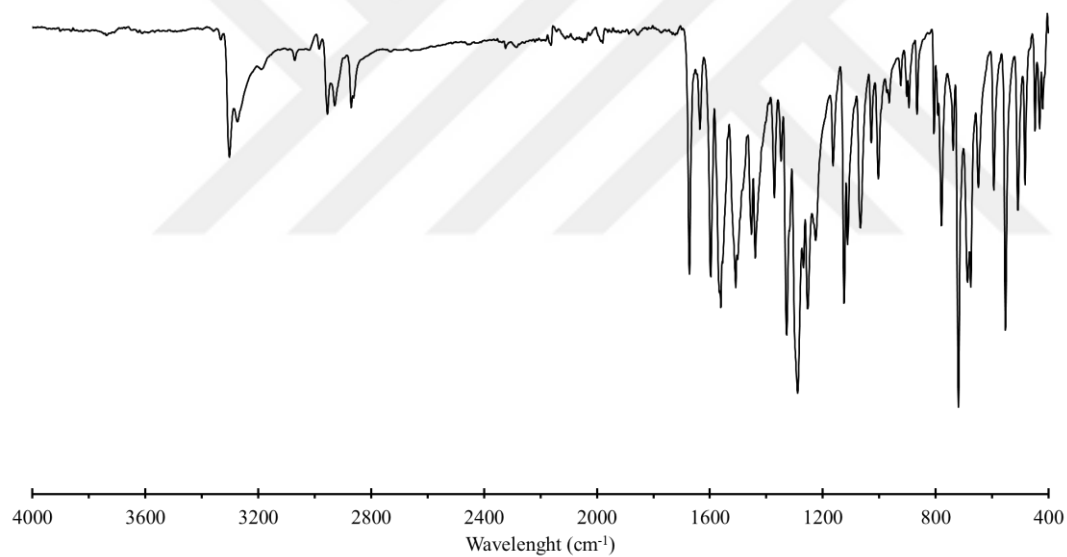


Figure B.5. FT-IR spectrum of the compound 4-5.

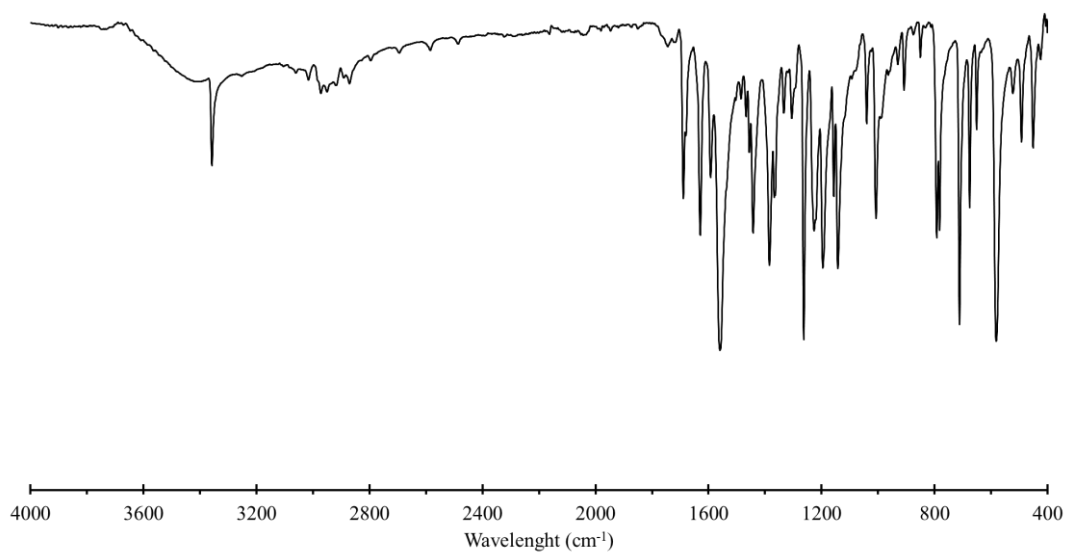


Figure B.6. FT-IR spectrum of the compound 4-6.

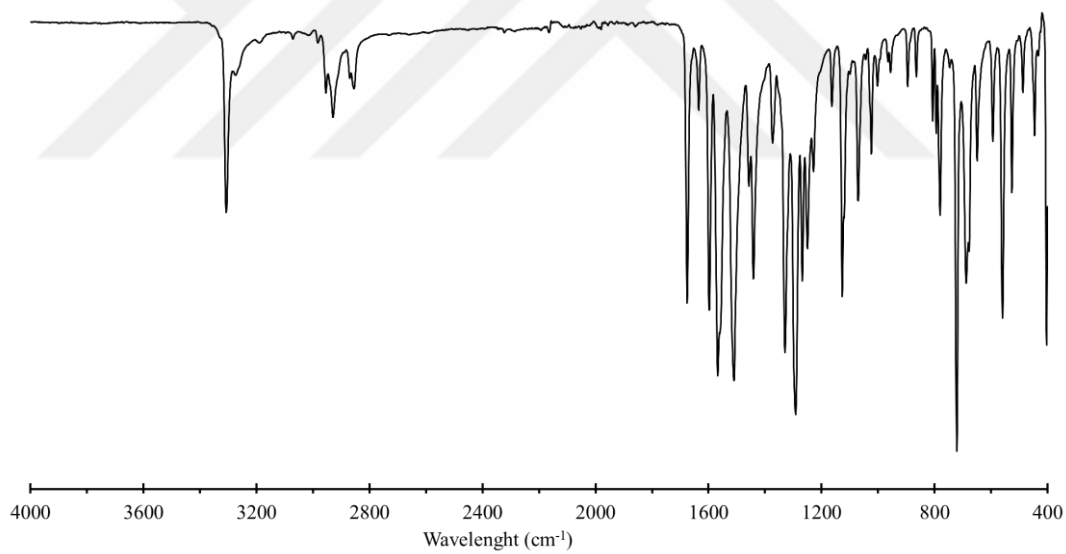


Figure B.7. FT-IR spectrum of the compound 4-7.

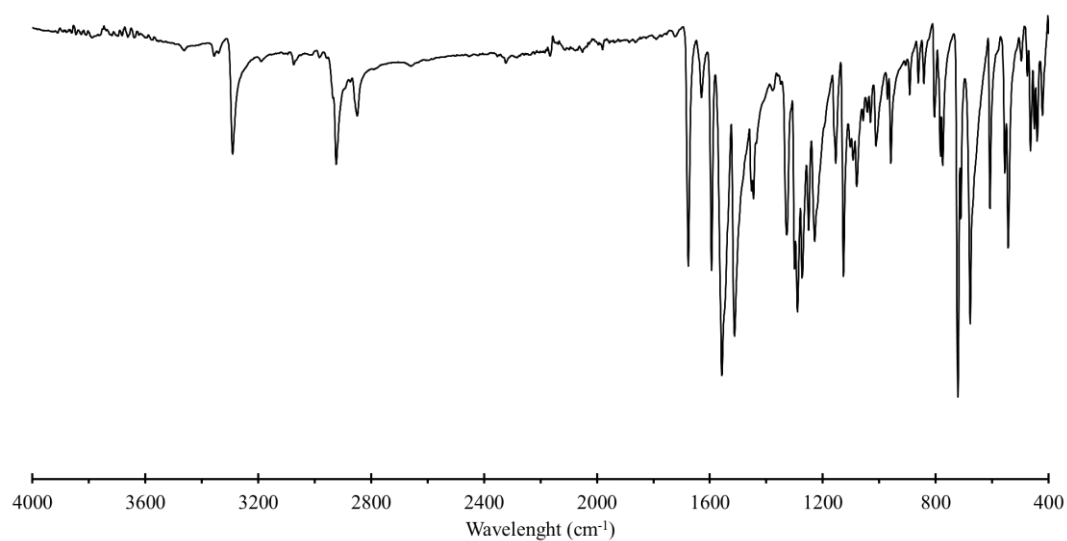


Figure B.8. FT-IR spectrum of the compound 4-8.

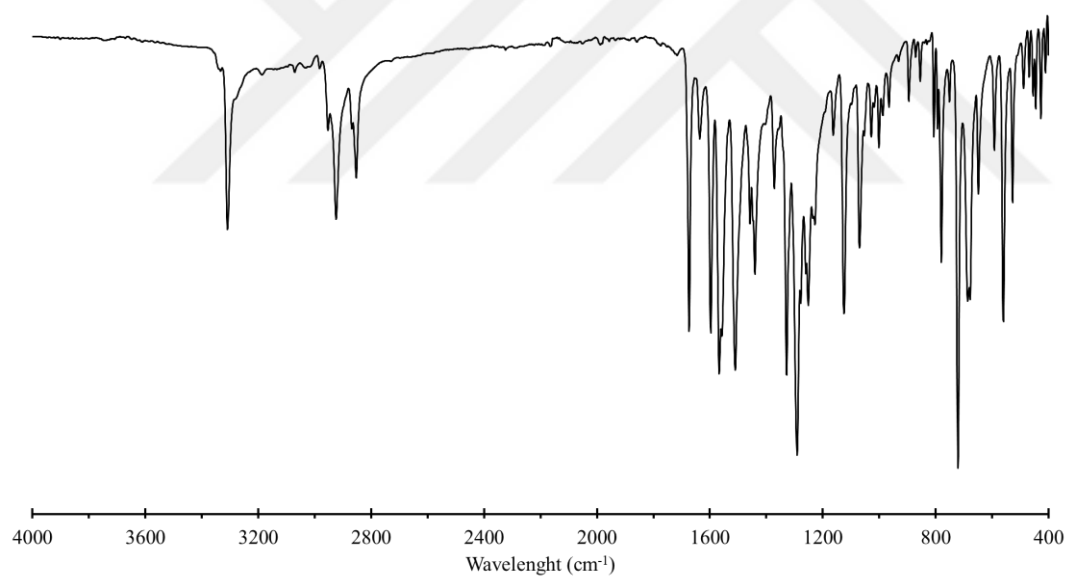


Figure B.9. FT-IR spectrum of the compound 4-9.

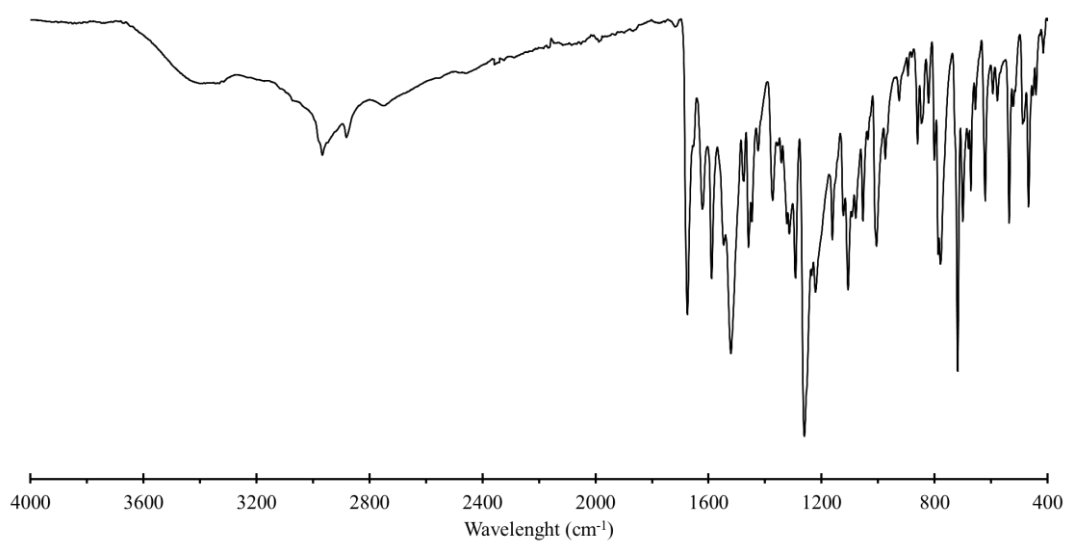


Figure B.10. FT-IR spectrum of the compound 4-10.

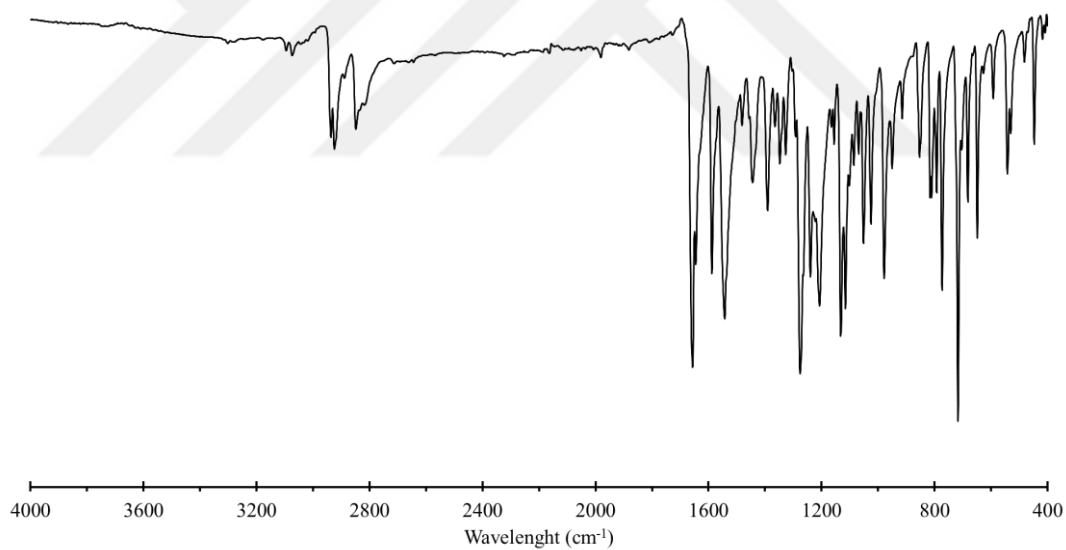


Figure B.11. FT-IR spectrum of the compound 4-11.

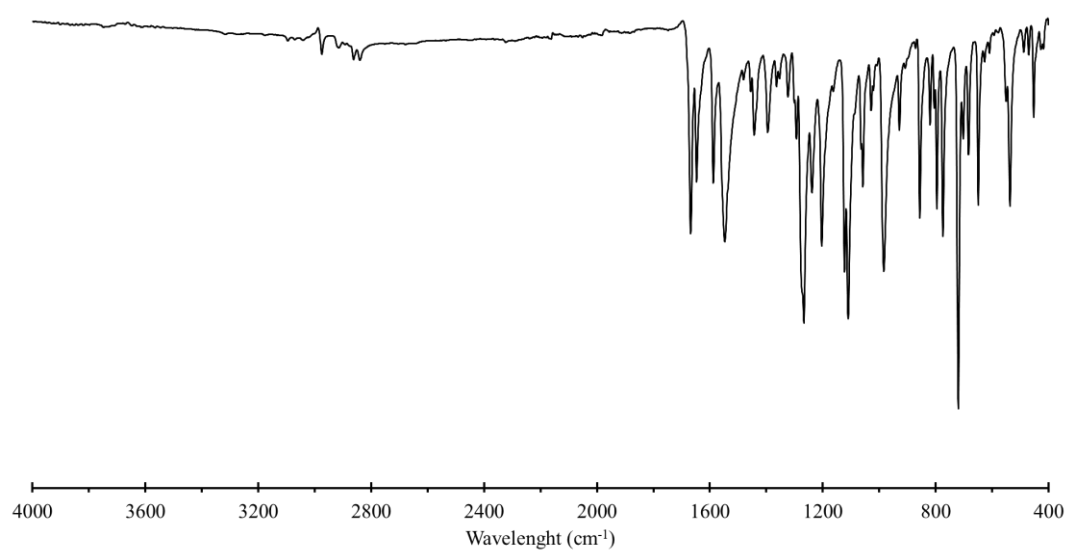


Figure B.12. FT-IR spectrum of the compound 4-12.

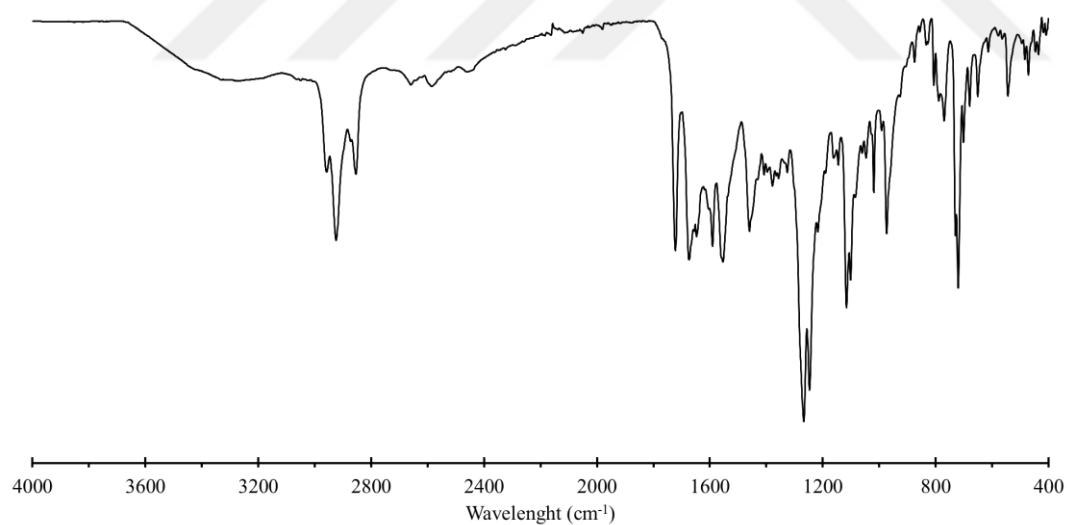


Figure B.13. FT-IR spectrum of the compound 4-13.

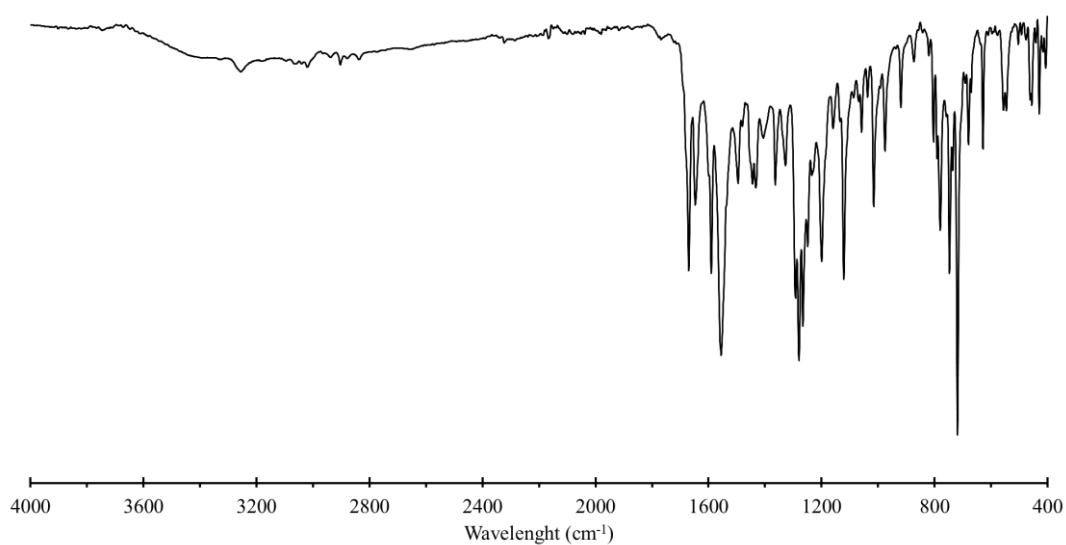


Figure B.14. FT-IR spectrum of the compound 4-14.

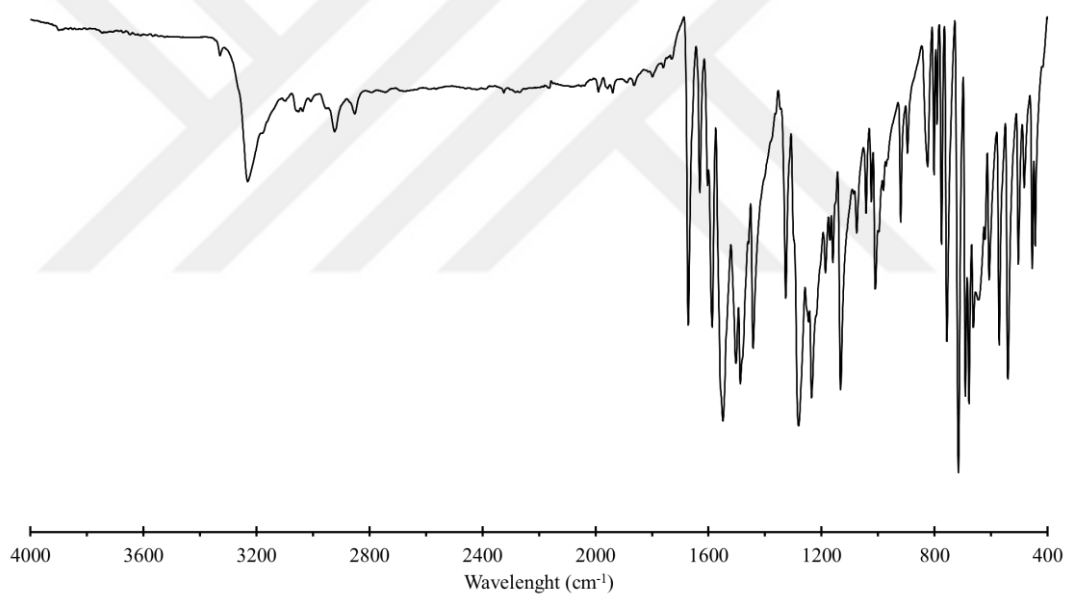


Figure B.15. FT-IR spectrum of the compound 4-15.

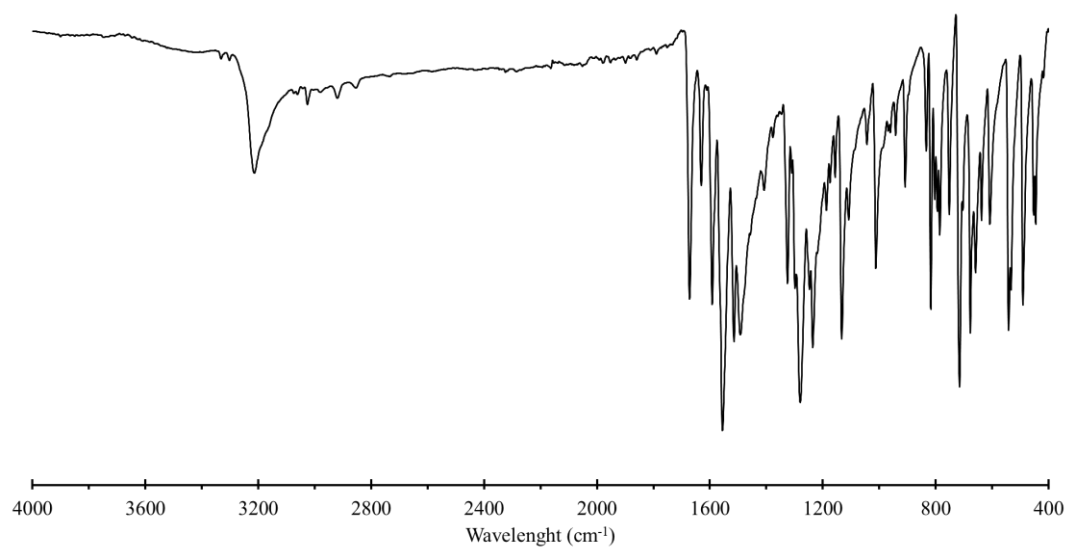


Figure B.16. FT-IR spectrum of the compound 4-16.

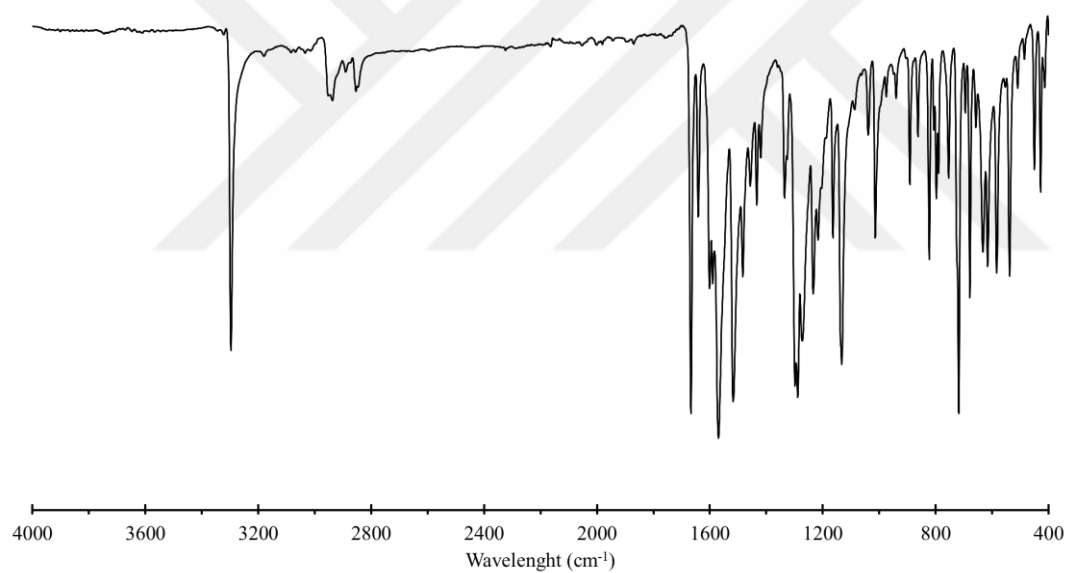


Figure B.17. FT-IR spectrum of the compound 4-17.

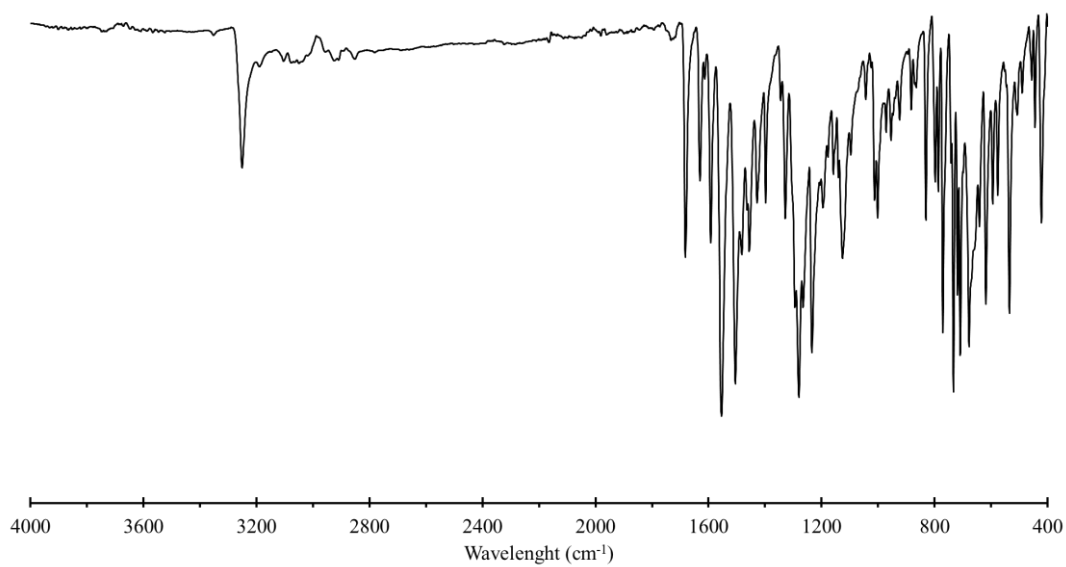


Figure B.18. FT-IR spectrum of the compound 4-20.

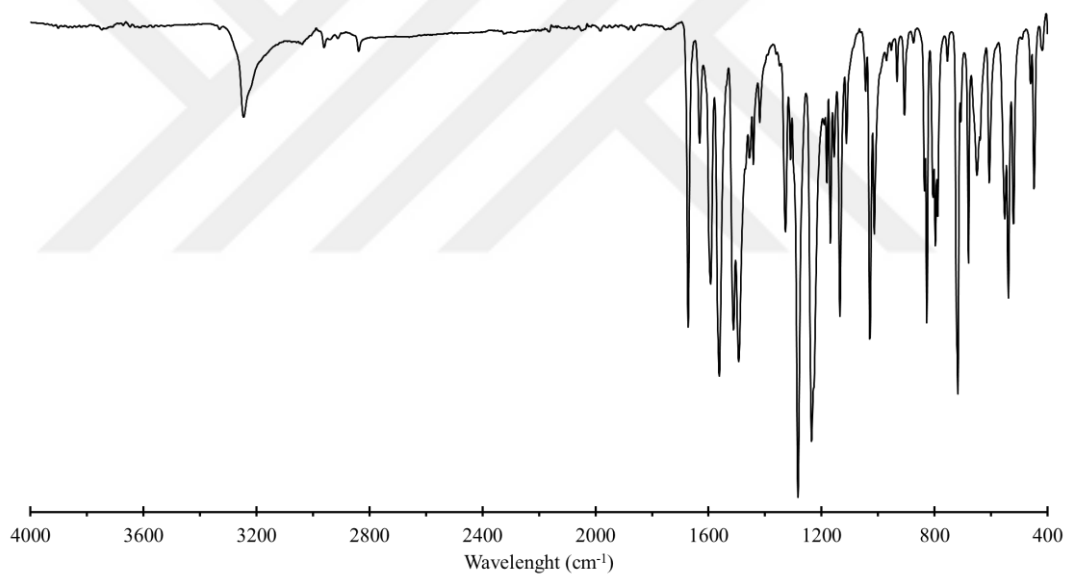


Figure B.19. FT-IR spectrum of the compound 4-21.

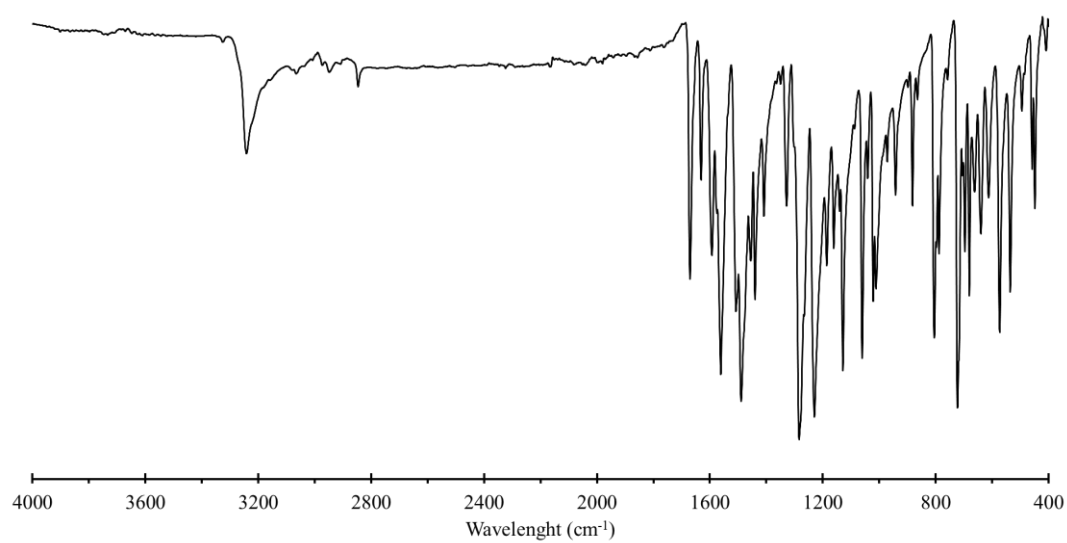


Figure B.20. FT-IR spectrum of the compound 4-22.

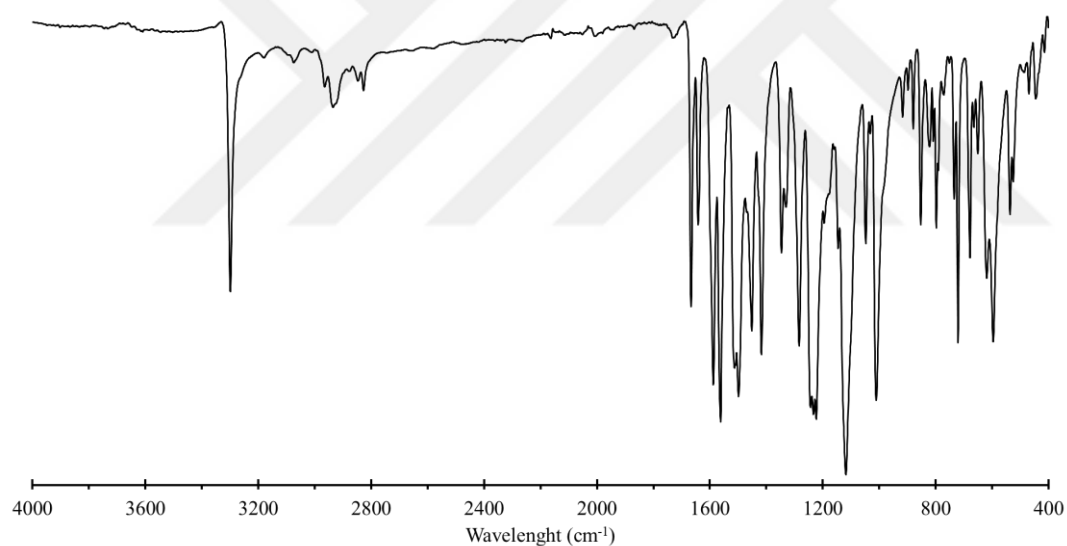


Figure B.21. FT-IR spectrum of the compound 4-23.

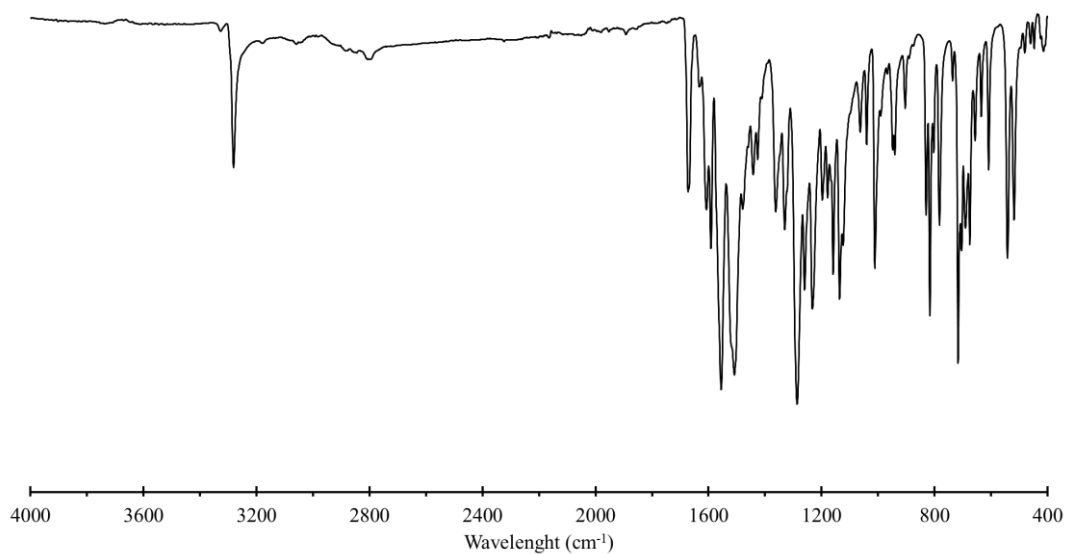


Figure B.22. FT-IR spectrum of the compound 4-24.

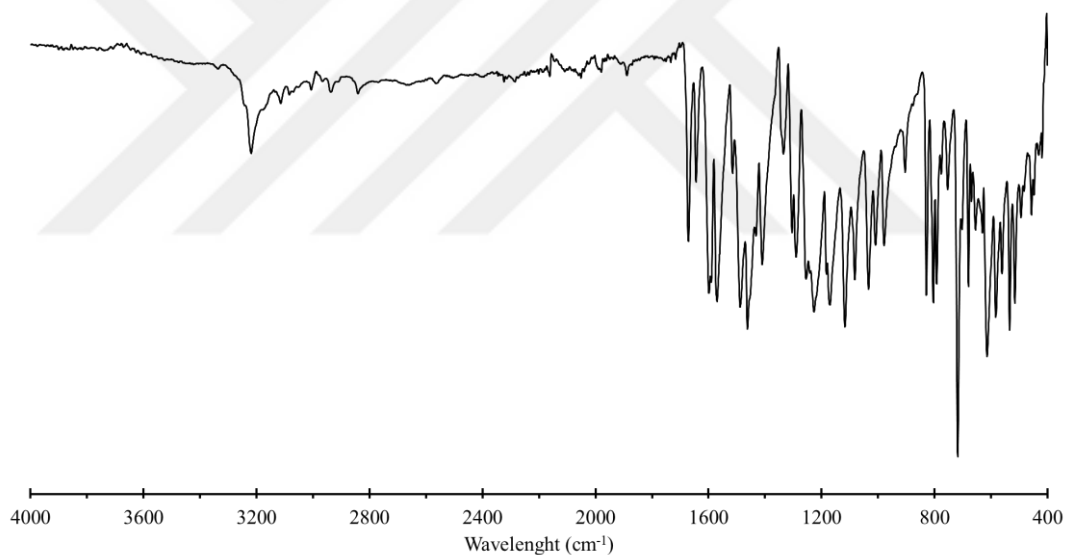


Figure B.23. FT-IR spectrum of the compound 4-27.

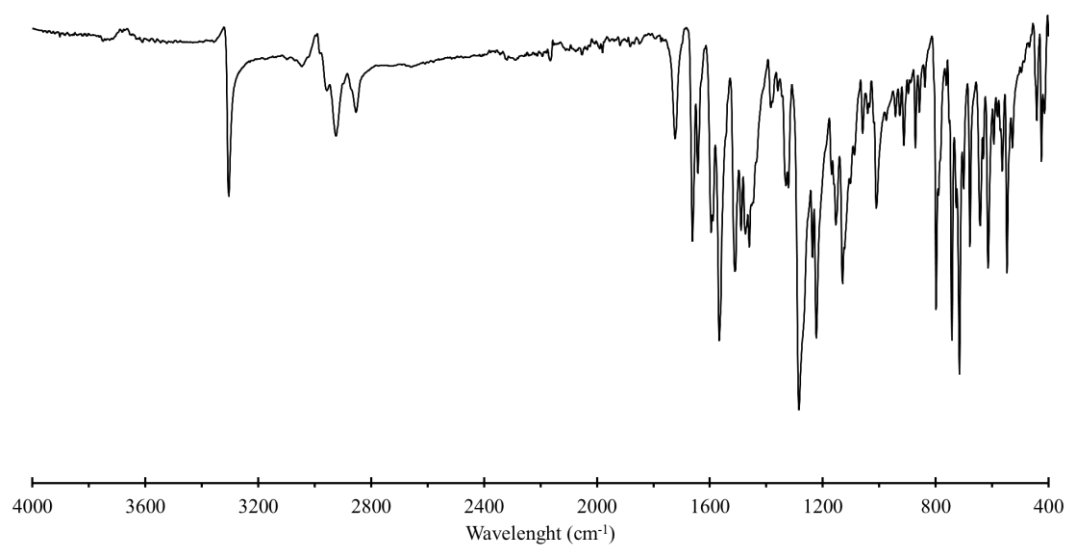


Figure B.24. FT-IR spectrum of the compound 4-28.

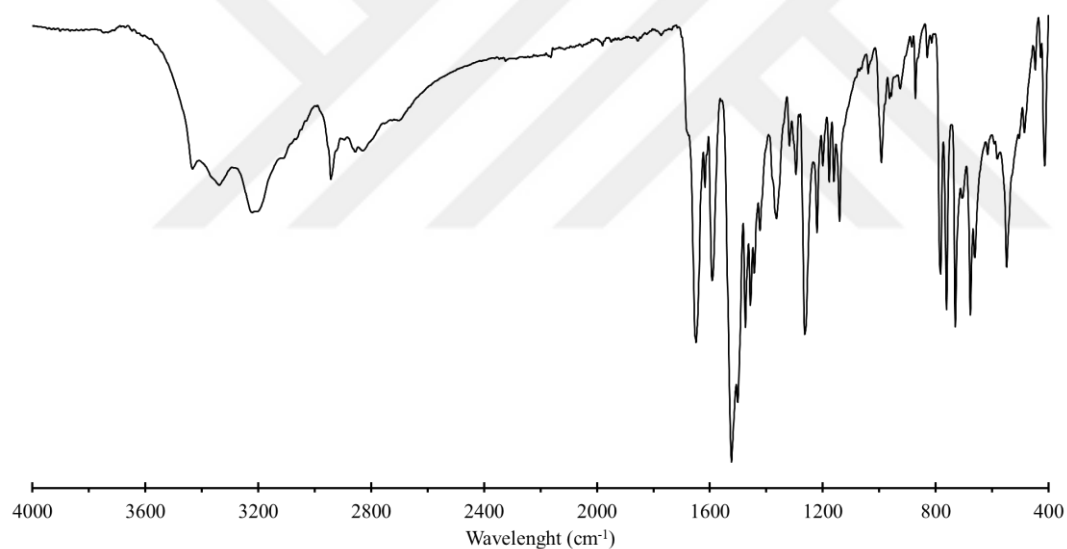


Figure B.25. FT-IR spectrum of the compound 4-30.

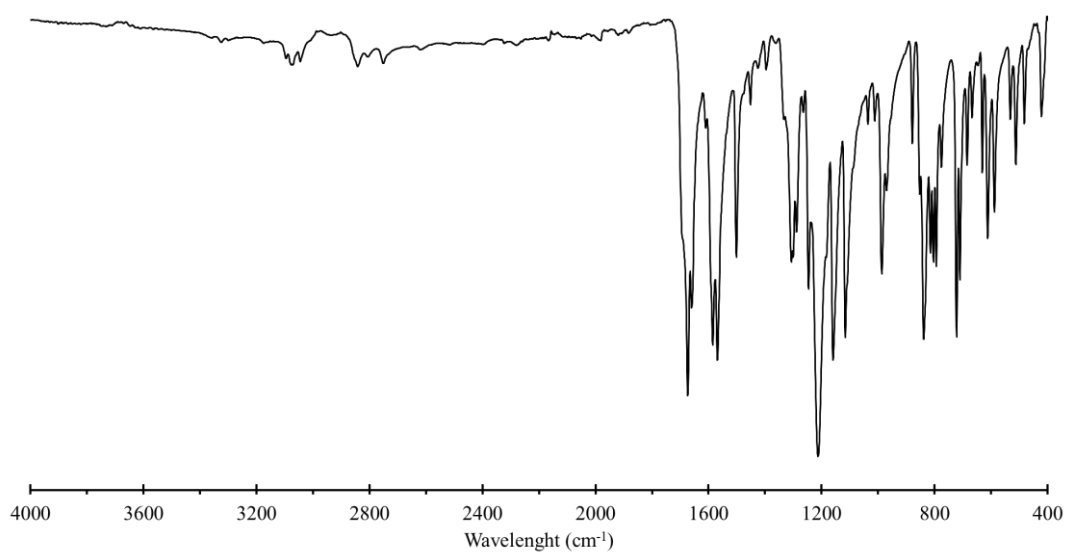


Figure B.26. FT-IR spectrum of the compound 4-31.

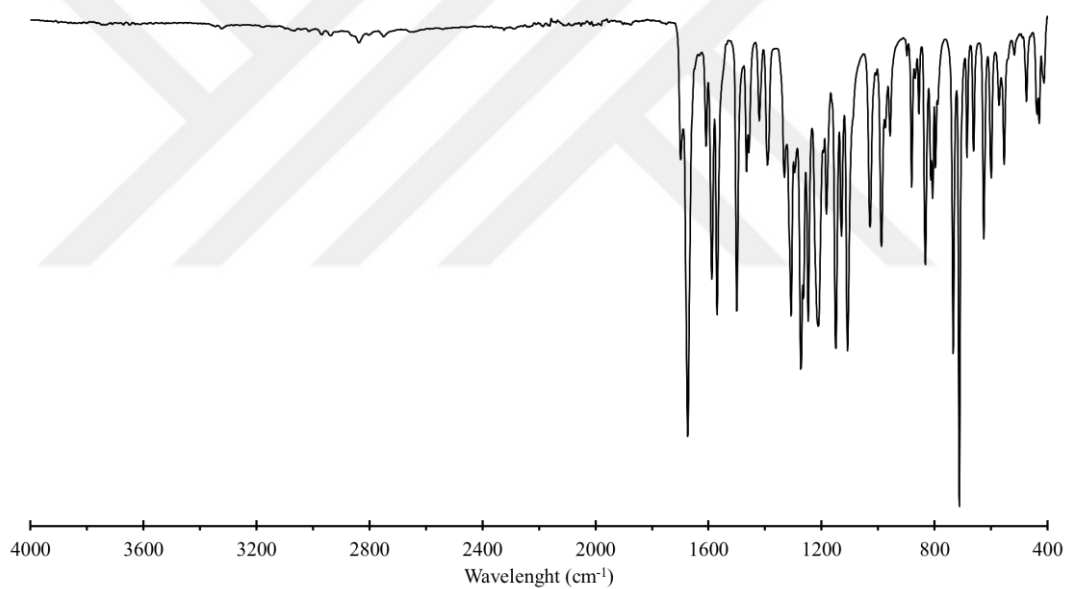


Figure B.27. FT-IR spectrum of the compound 4-32.

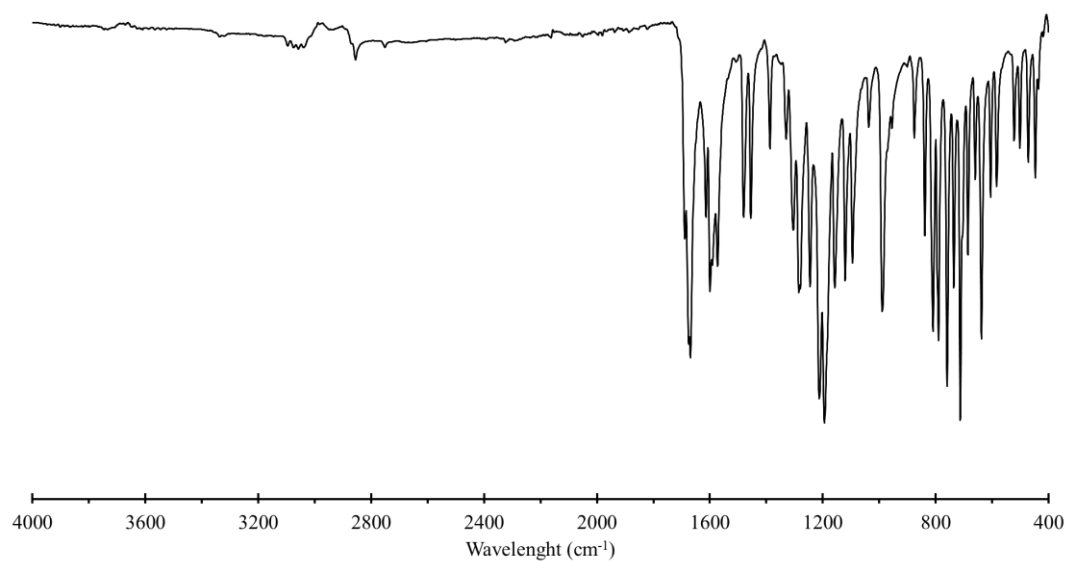


Figure B.28. FT-IR spectrum of the compound 4-33.

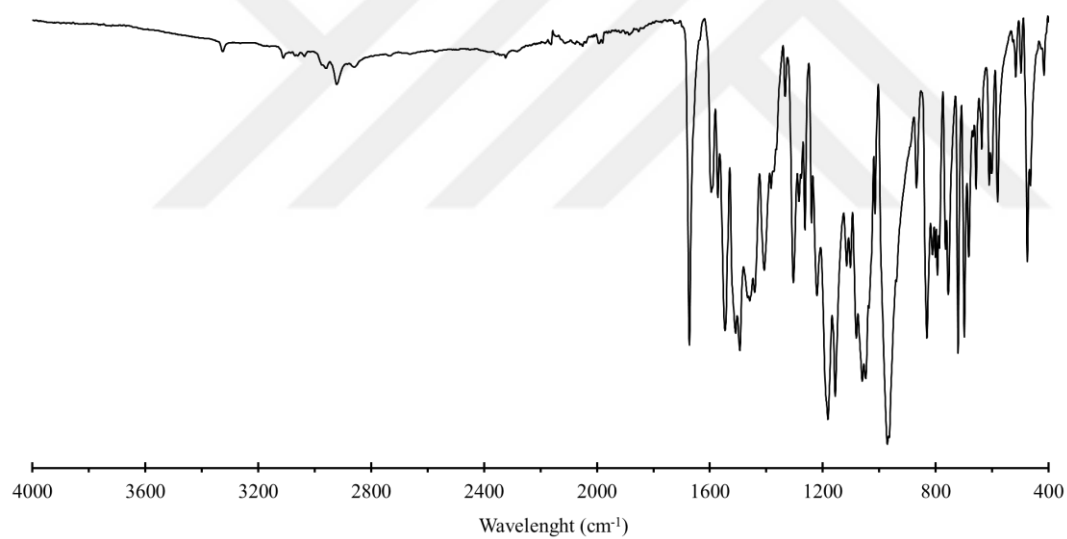


Figure B.29. FT-IR spectrum of the compound 4-35.

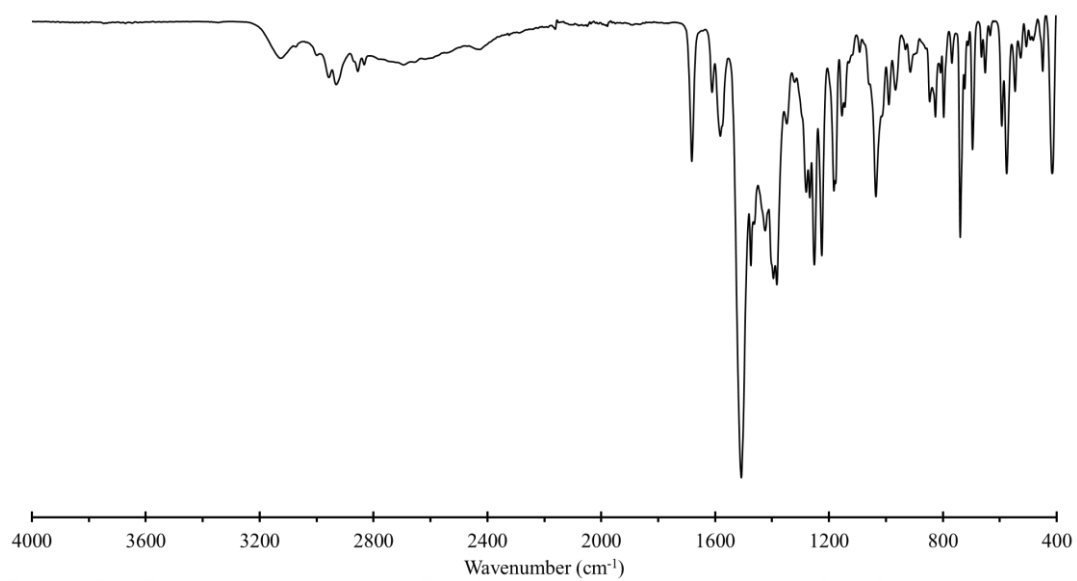


Figure B.30. FT-IR spectrum of the compound 4-36.

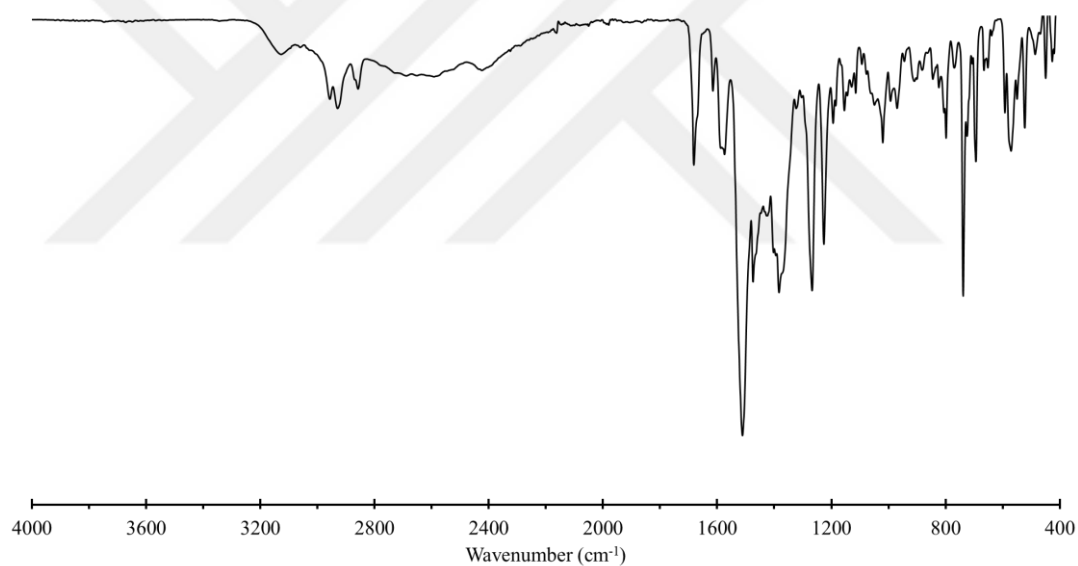


Figure B.31. FT-IR spectrum of the compound 4-37.

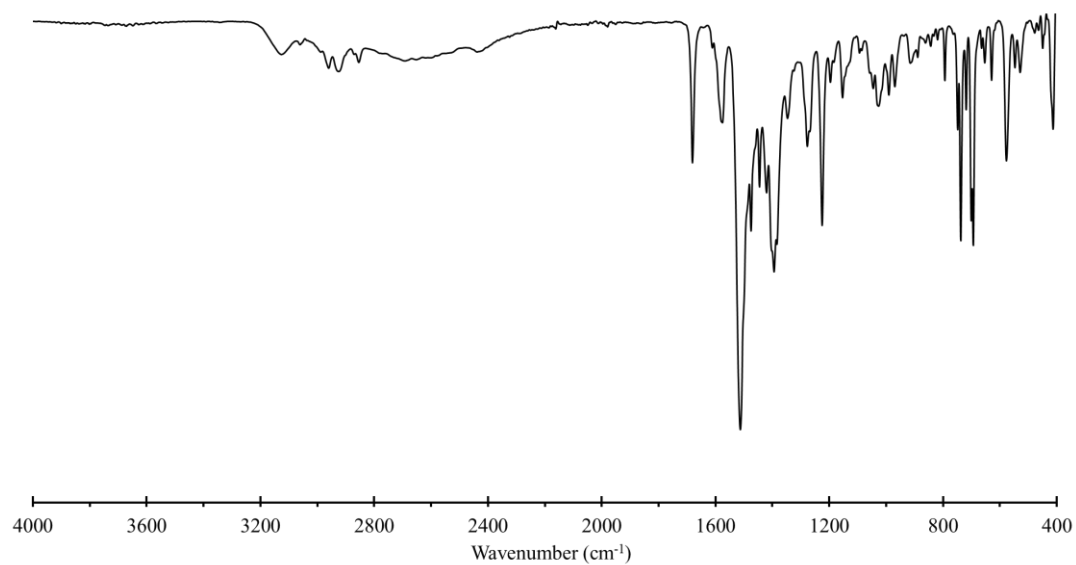


Figure B.32. FT-IR spectrum of the compound 4-38.

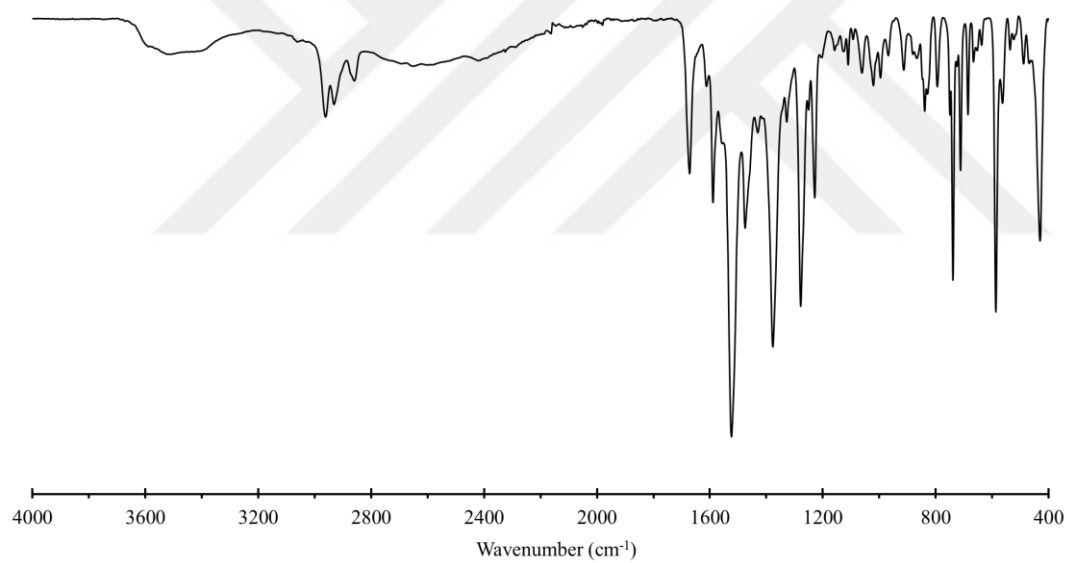


Figure B.33. FT-IR spectrum of the compound 4-39.

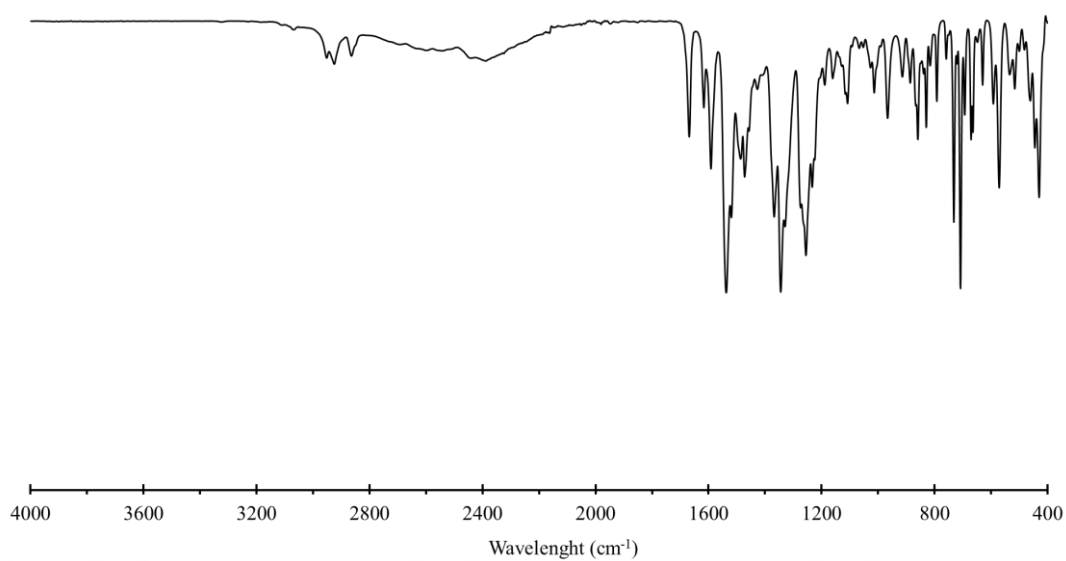


Figure B.34. FT-IR spectrum of the compound 4-40.

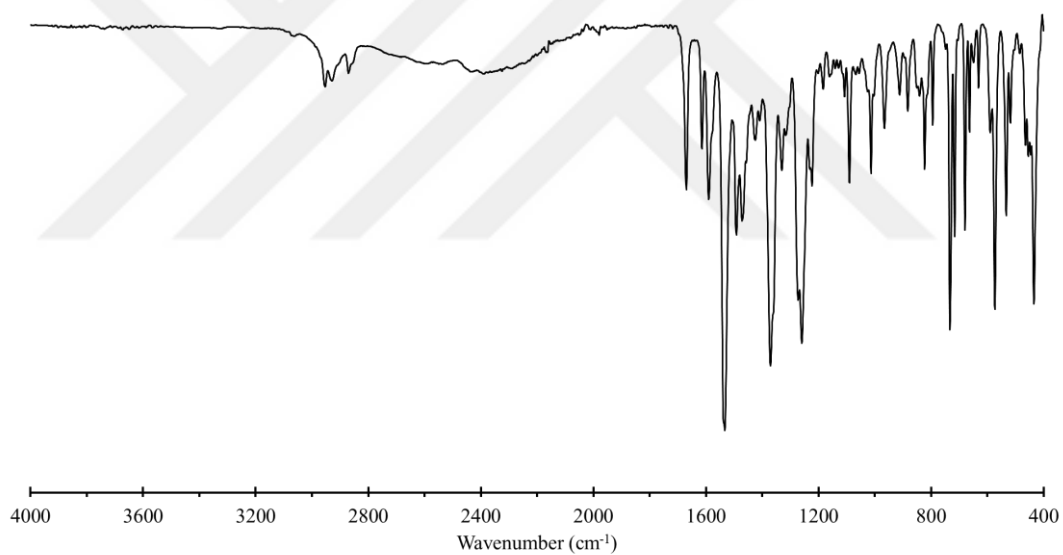


Figure B.35. FT-IR spectrum of the compound 4-41.

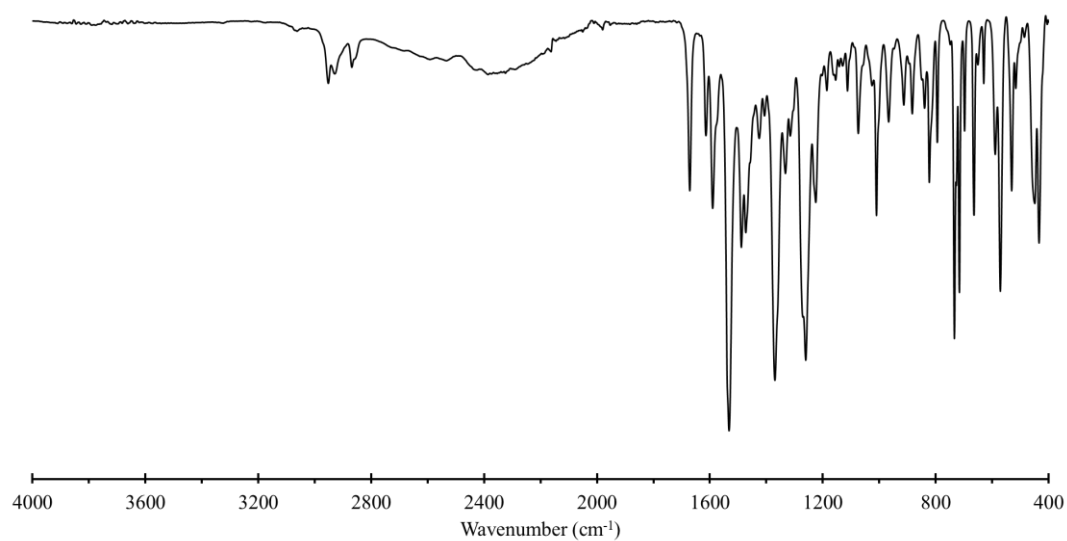


Figure B.36. FT-IR spectrum of the compound 4-42.

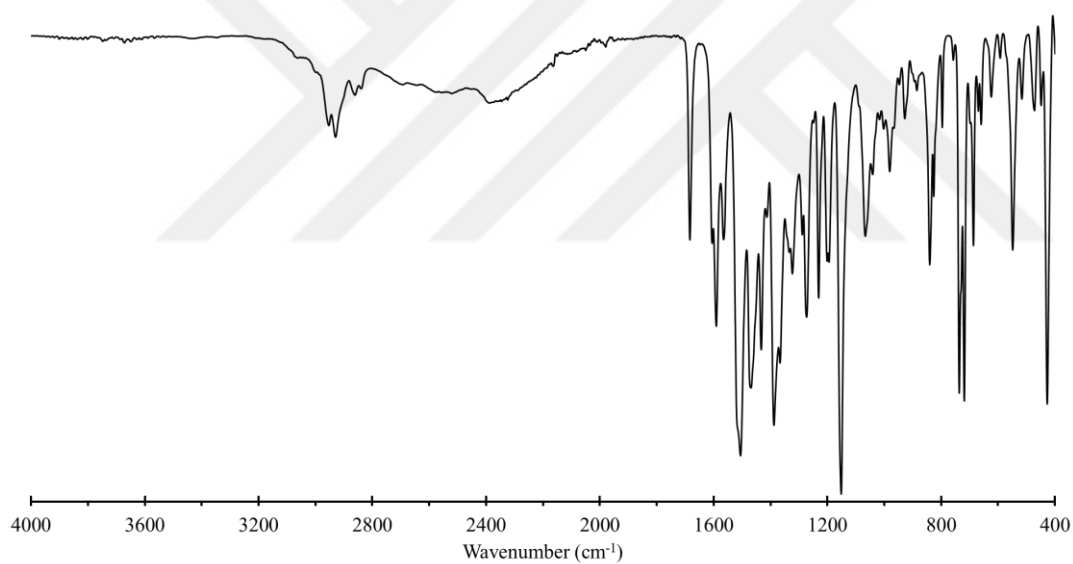


Figure B.37. FT-IR spectrum of the compound 4-43.

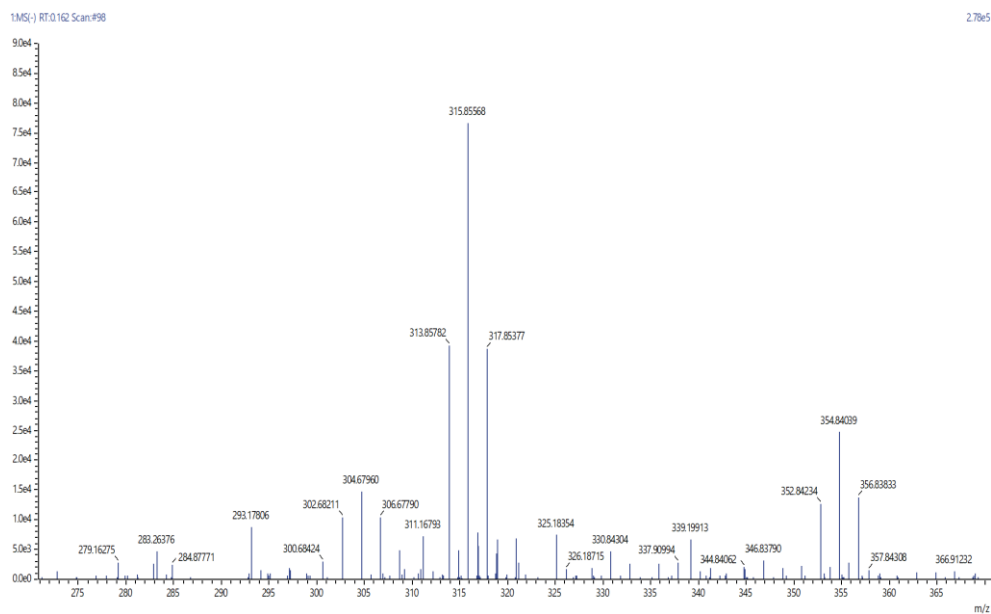


Figure C.1. Mass spectrum of the compound 4-1.

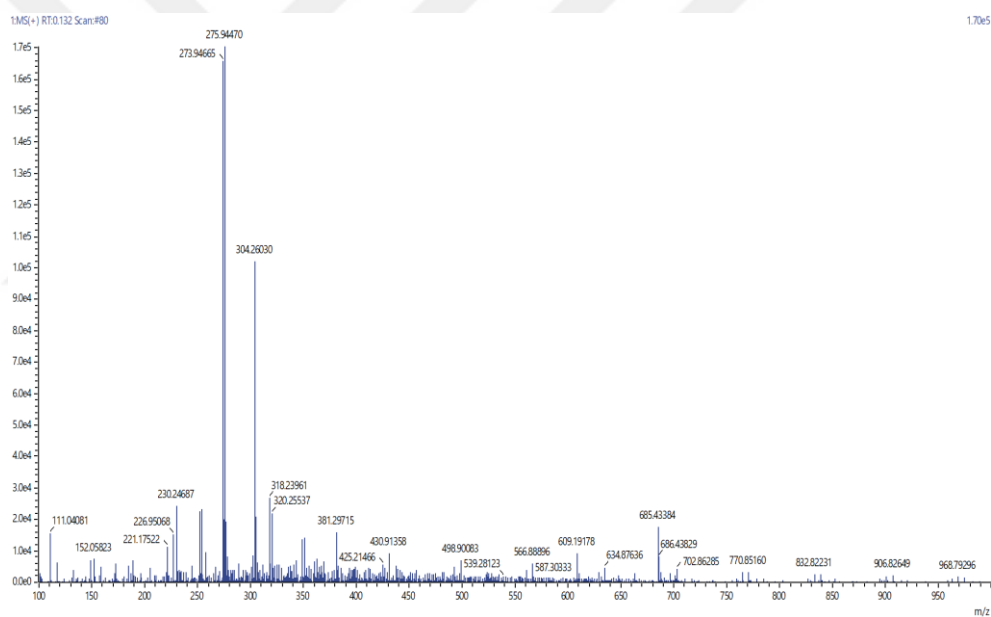


Figure C.2. Mass spectrum of the compound 4-2.

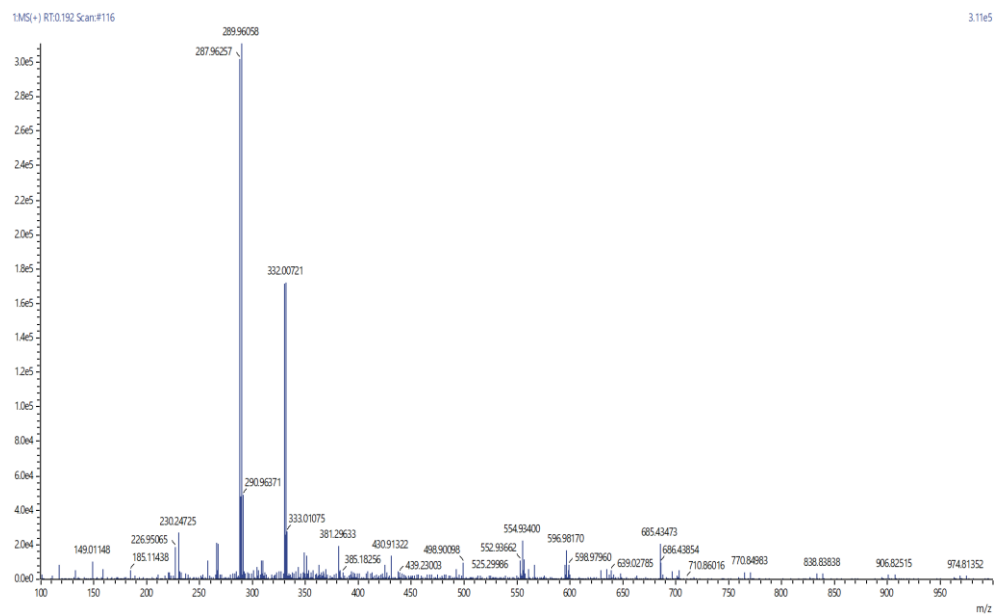


Figure C.3. Mass spectrum of the compound 4-3.

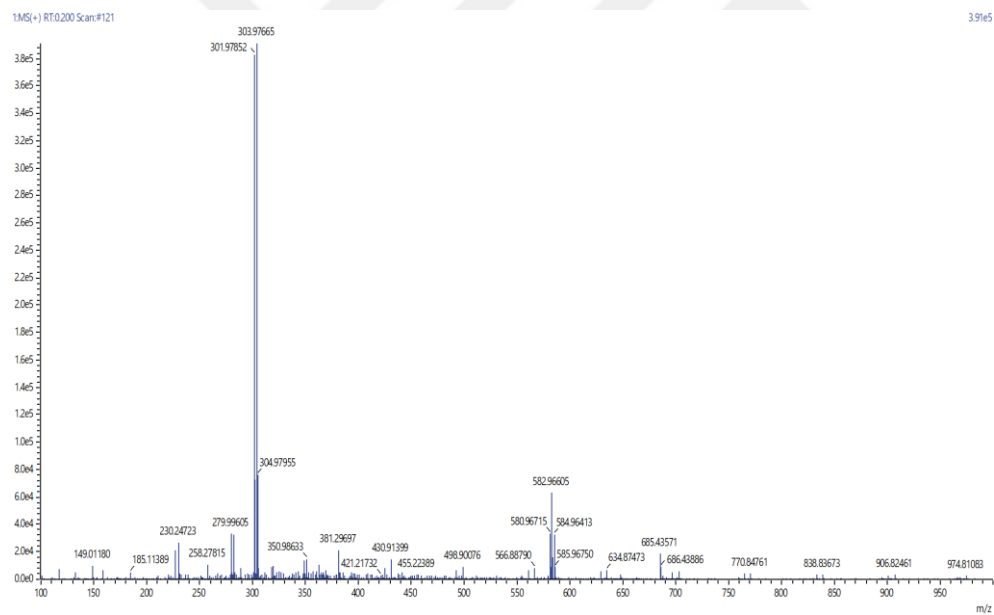


Figure C.4. Mass spectrum of the compound 4-4.

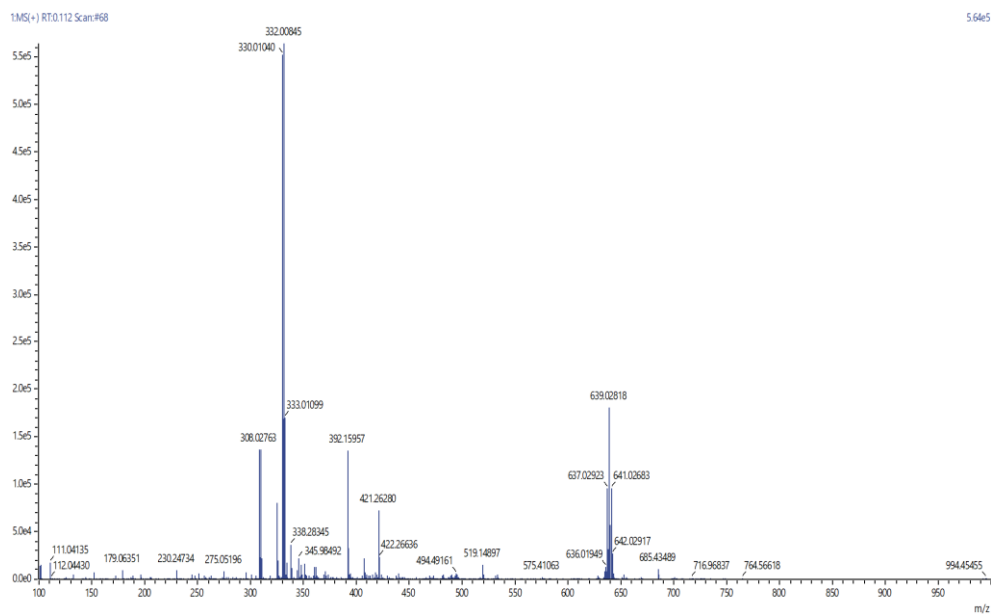


Figure C.5. Mass spectrum of the compound 4-5.

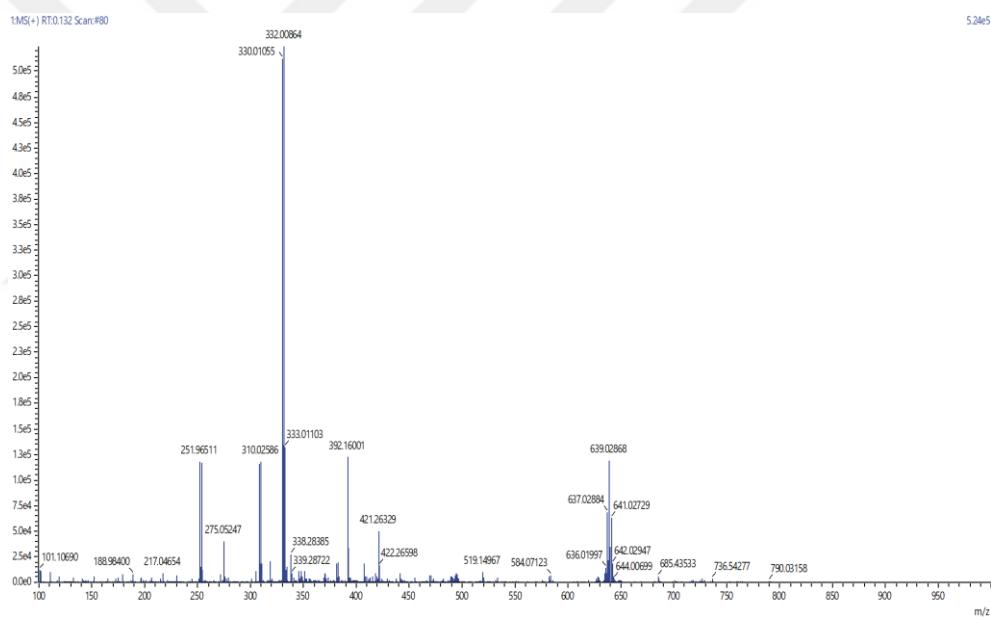


Figure C.6. Mass spectrum of the compound 4-6.

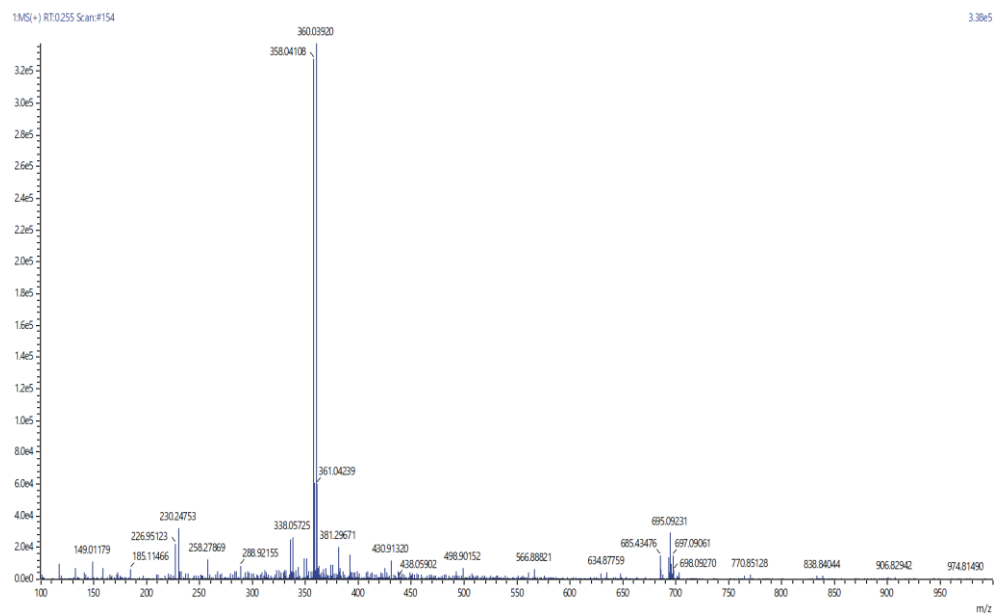


Figure C.7. Mass spectrum of the compound 4-7.

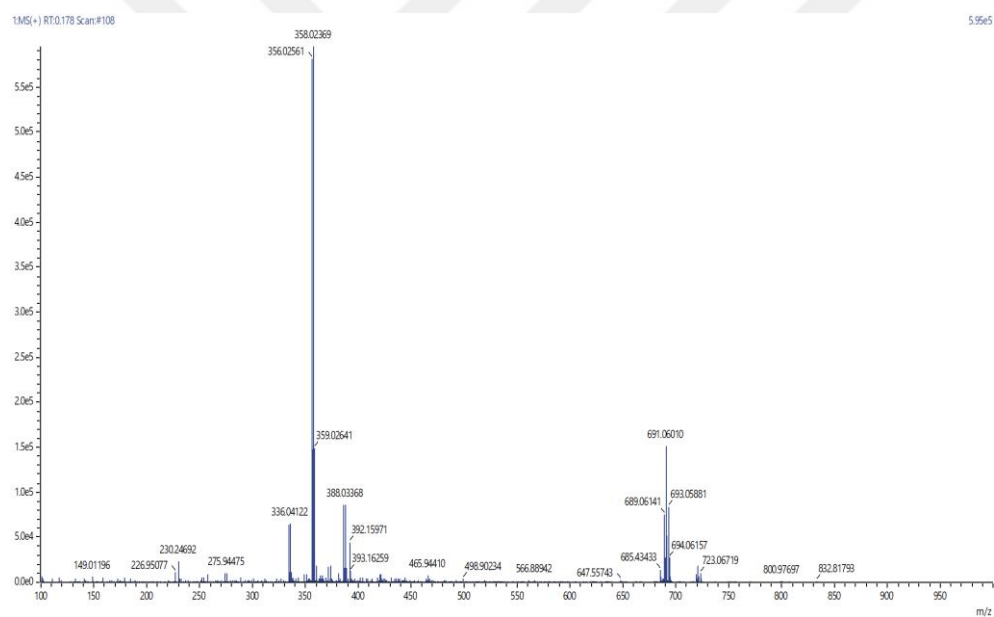


Figure C.8. Mass spectrum of the compound 4-8.

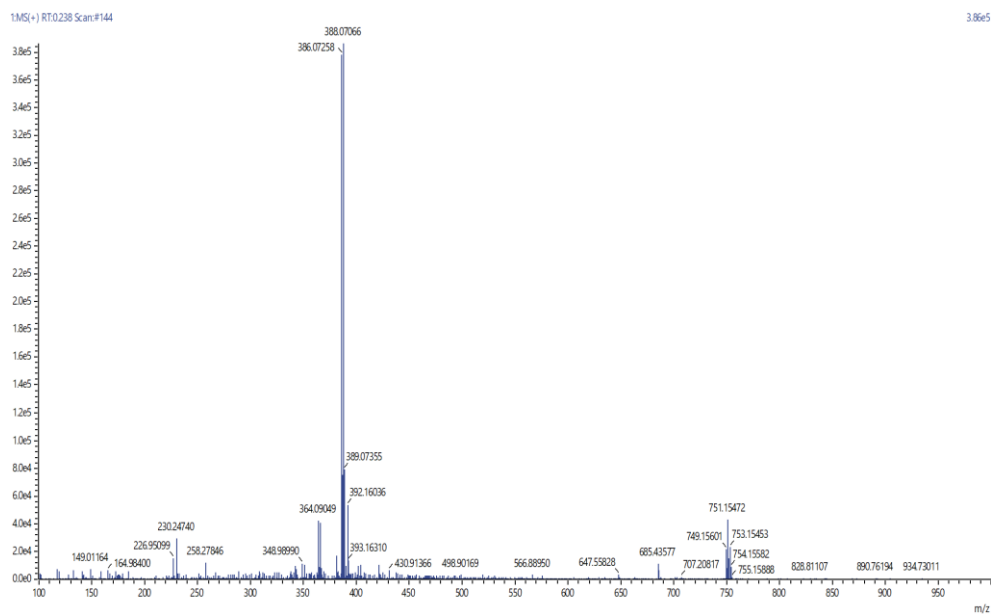


Figure C.9. Mass spectrum of the compound 4-9.

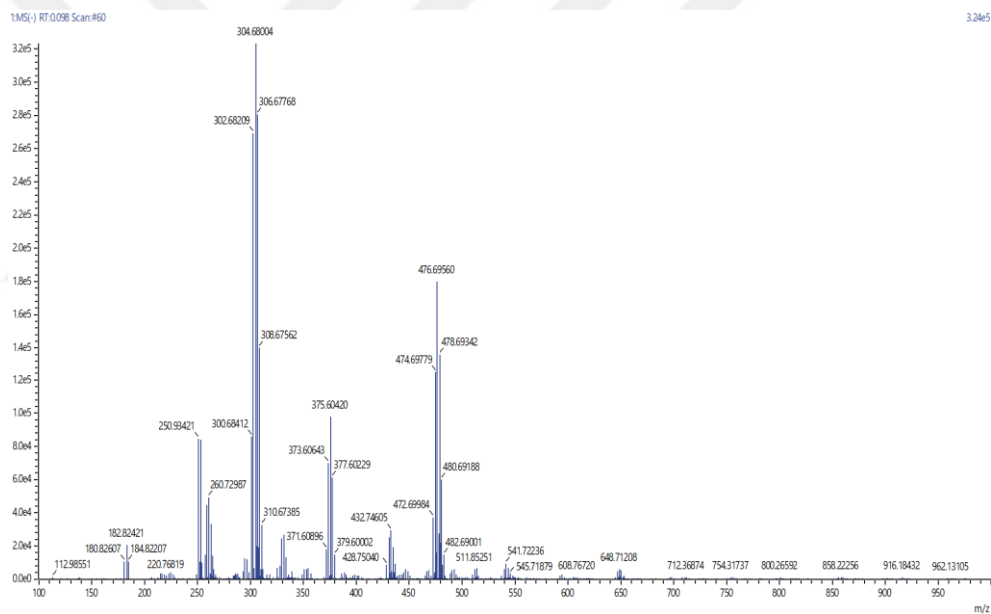


Figure C.10. Mass spectrum of the compound 4-10.

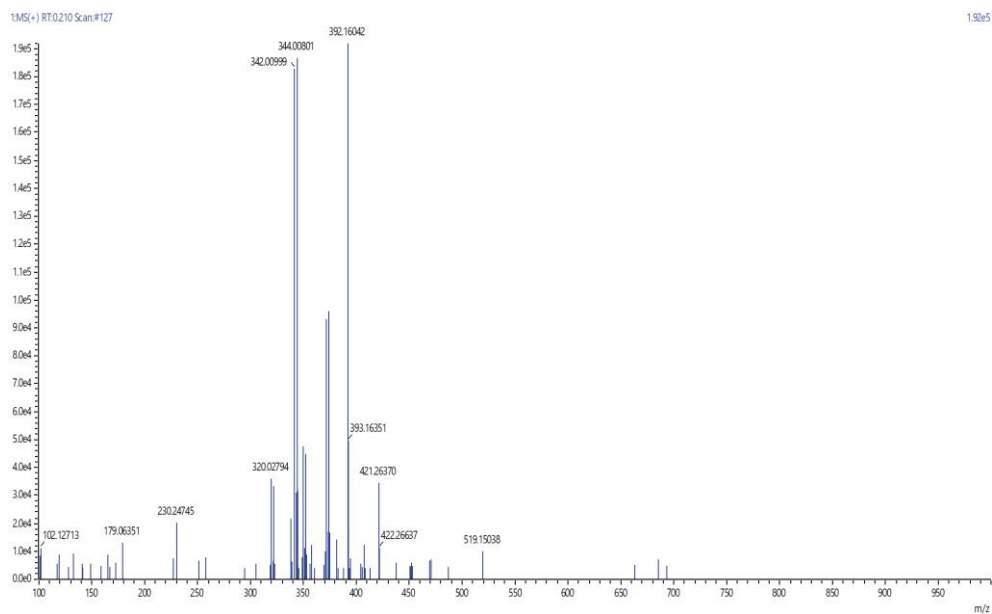


Figure C.11. Mass spectrum of the compound 4-11.

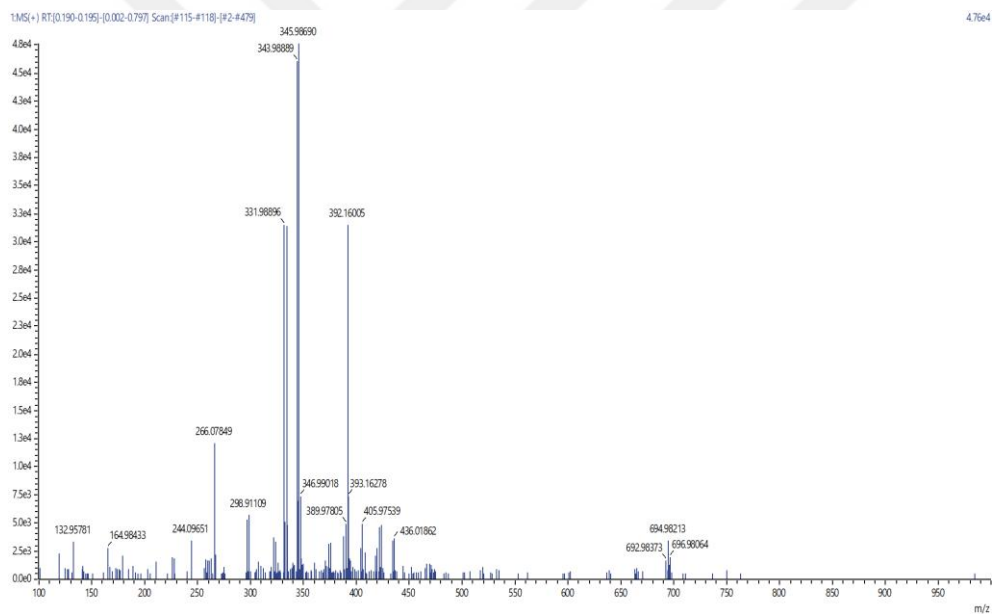


Figure C.12. Mass spectrum of the compound 4-12.

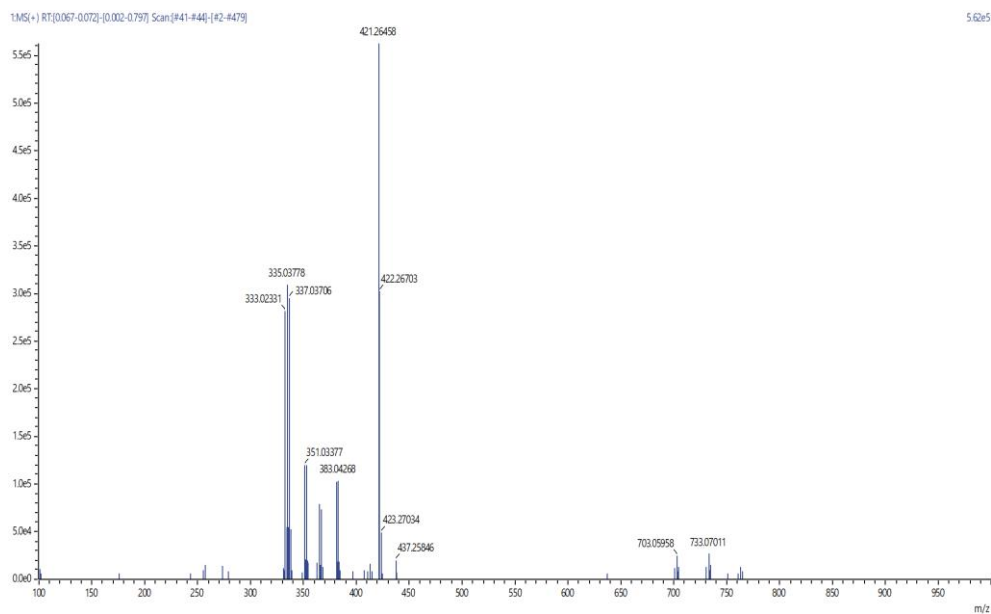


Figure C.13. Mass spectrum of the compound 4-13.

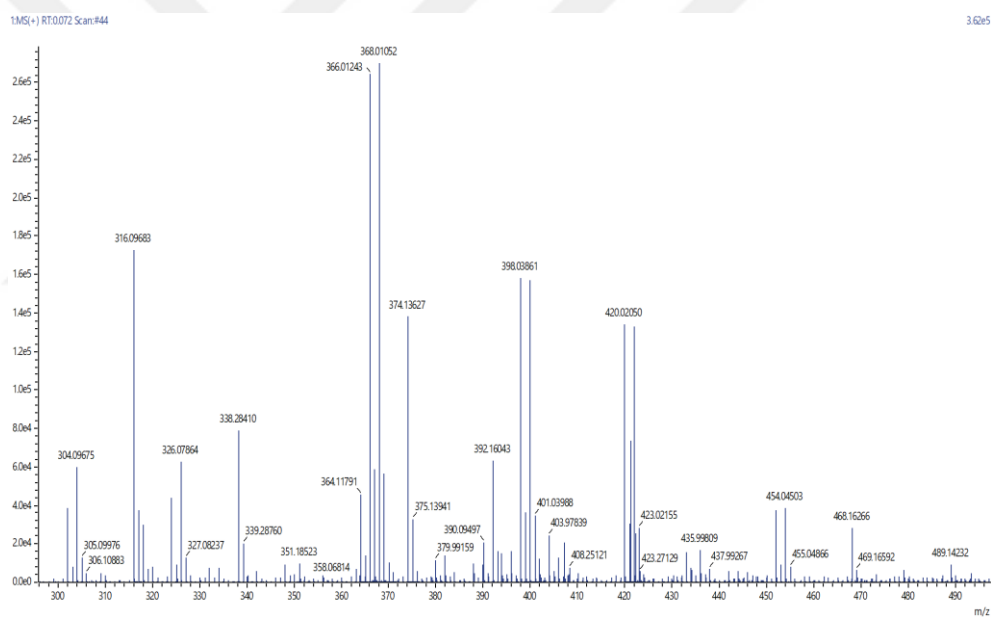


Figure C.14. Mass spectrum of the compound 4-14.

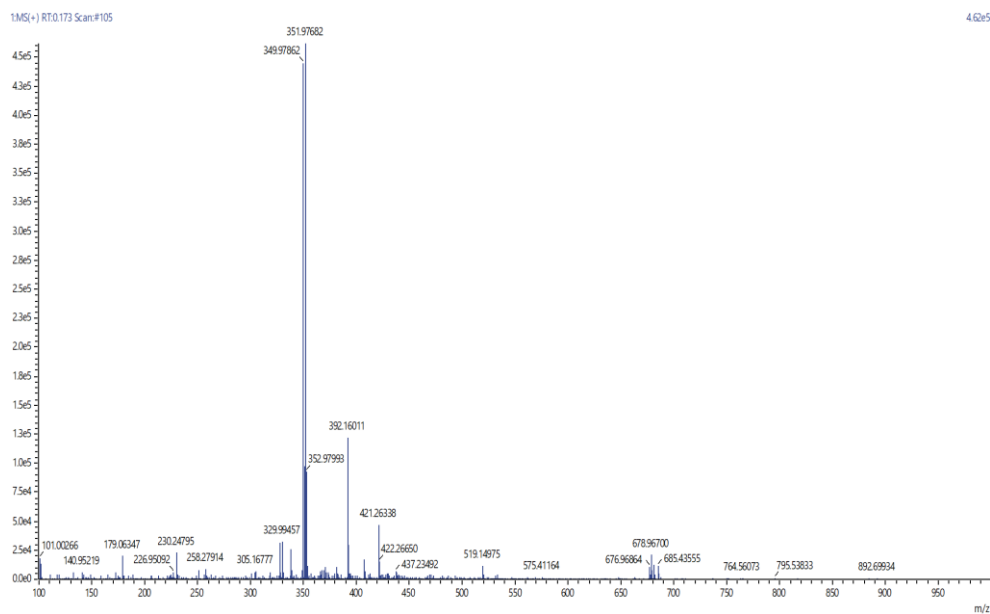


Figure C.15. Mass spectrum of the compound 4-15.

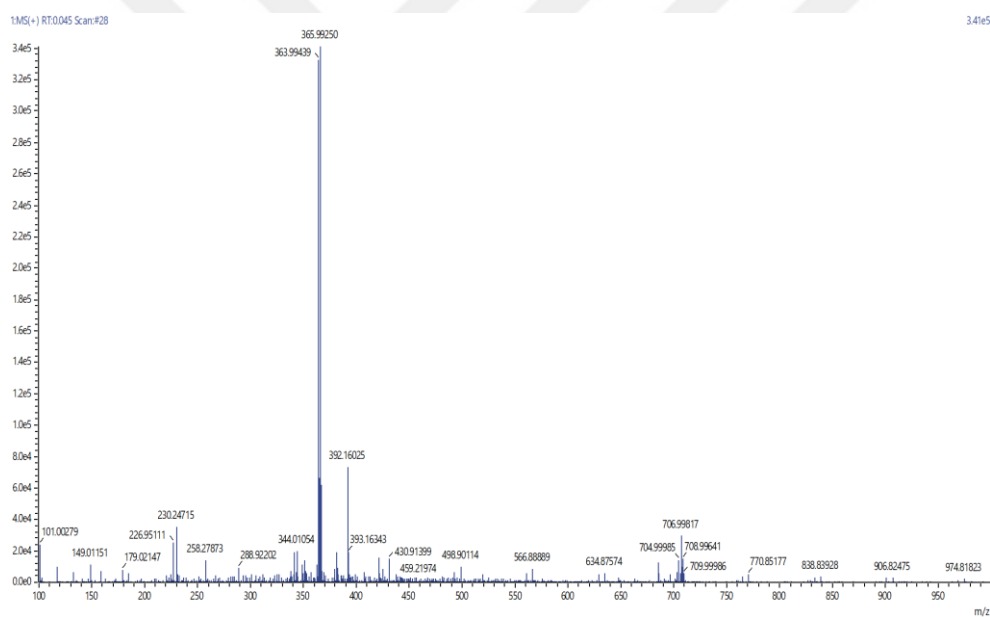


Figure C.16. Mass spectrum of the compound 4-16.

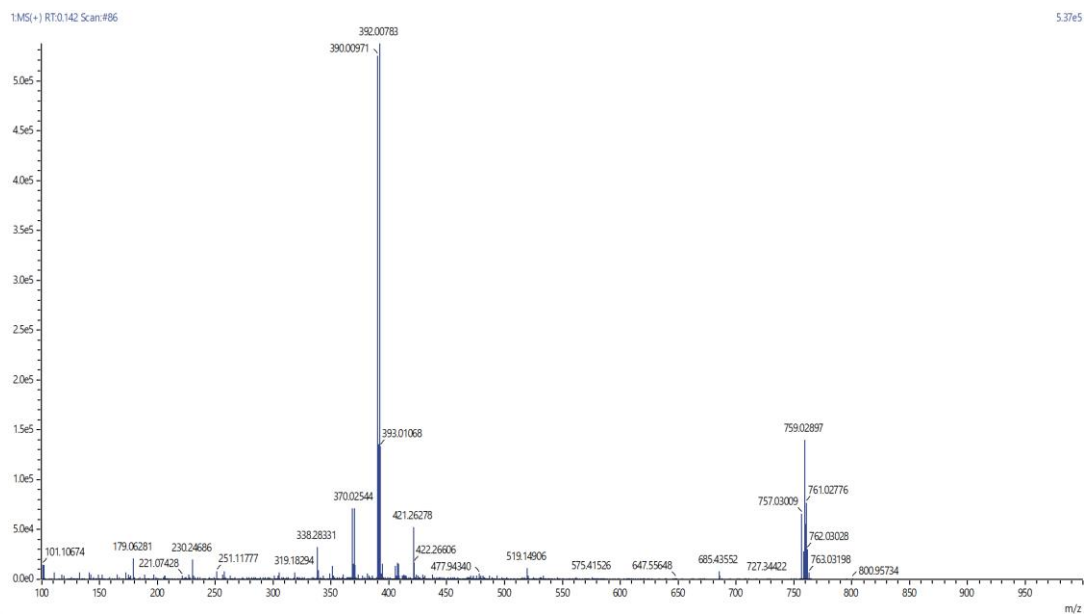


Figure C.17. Mass spectrum of the compound 4-17.

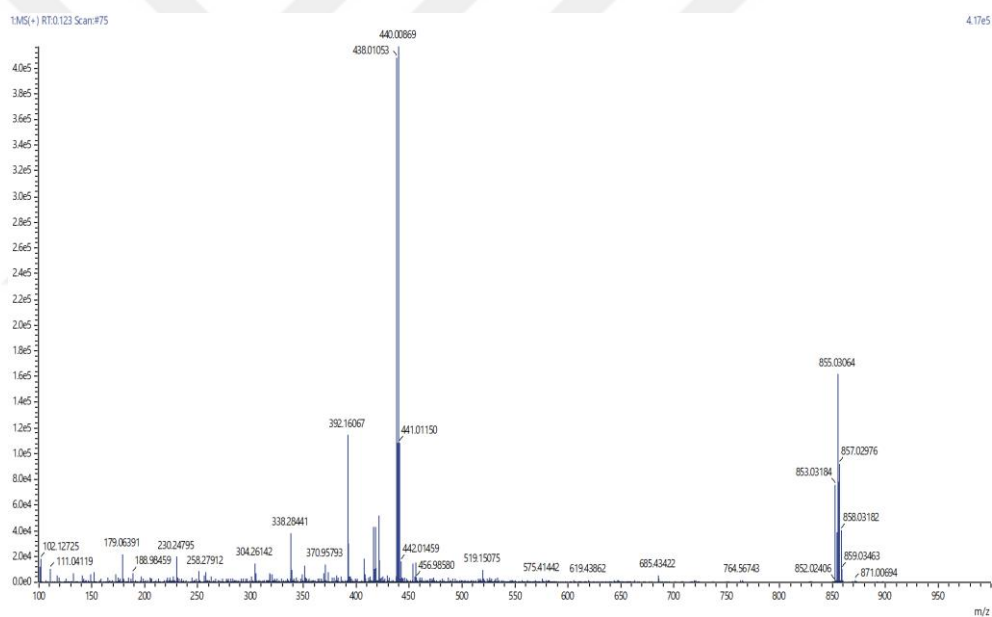


Figure C.18. Mass spectrum of the compound 4-20.

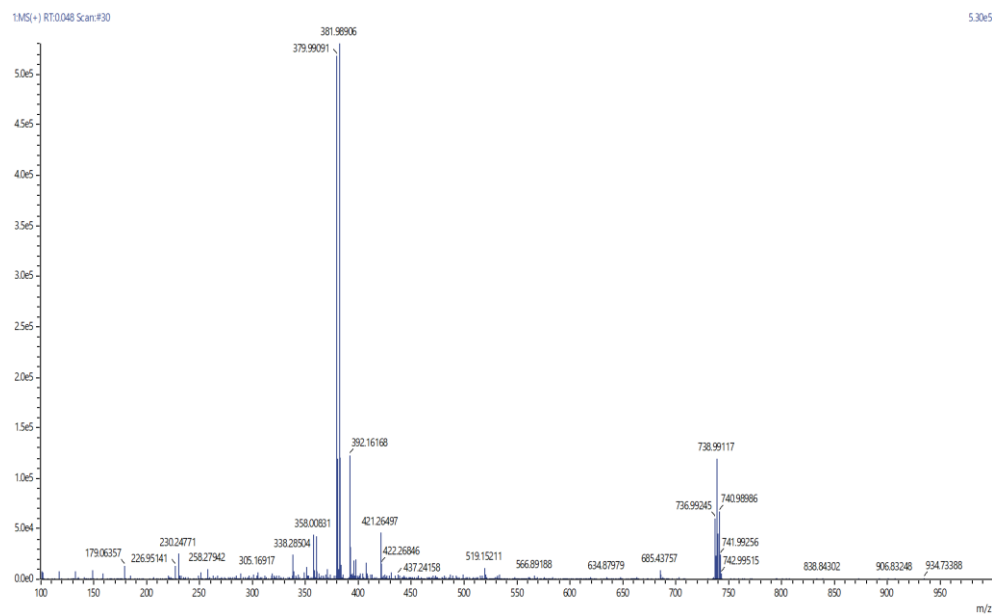


Figure C.19. Mass spectrum of the compound 4-21.

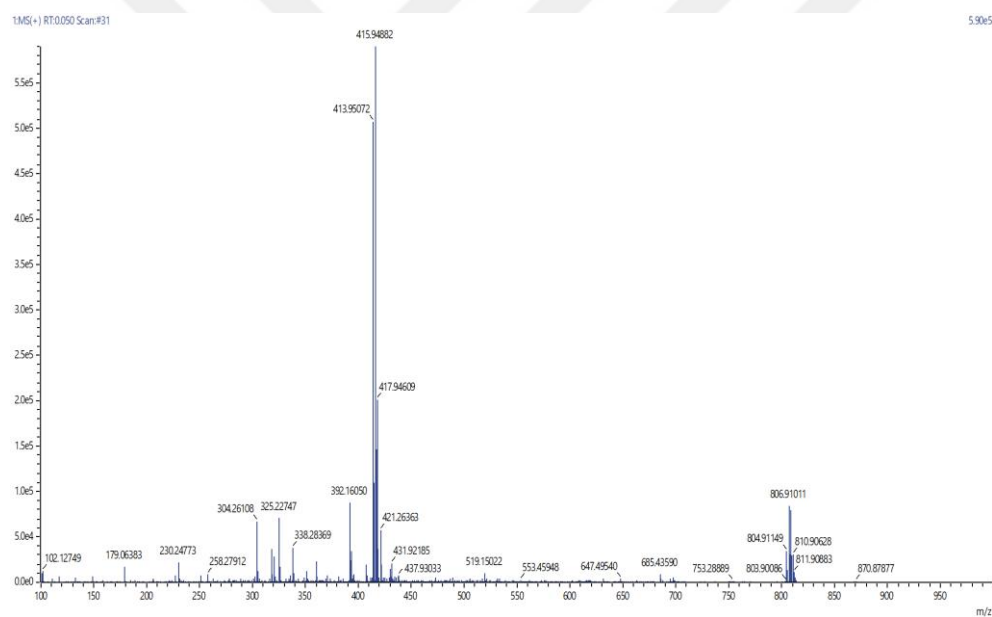


Figure C.20. Mass spectrum of the compound 4-22.

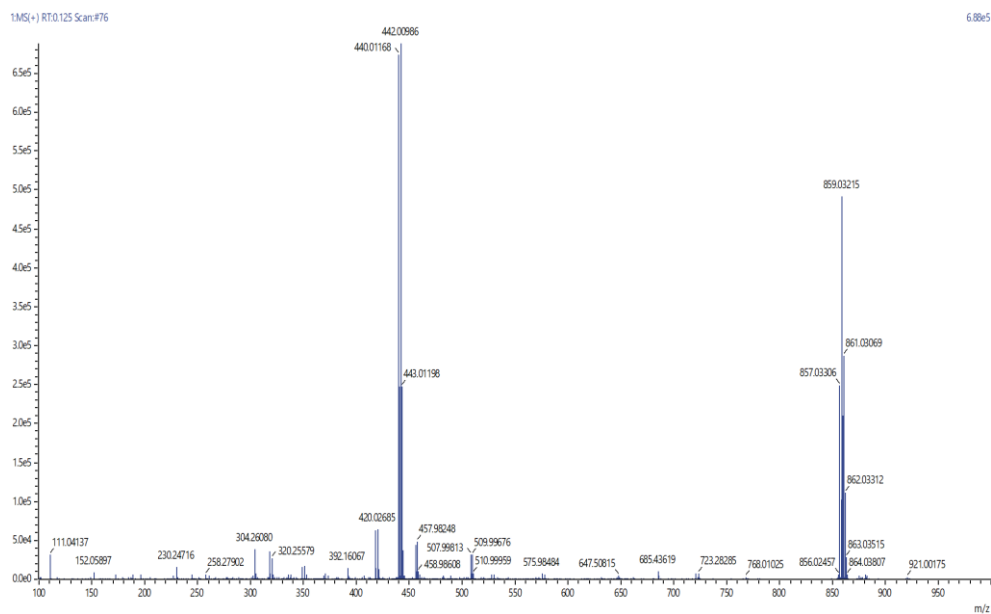


Figure C.21. Mass spectrum of the compound 4-23.

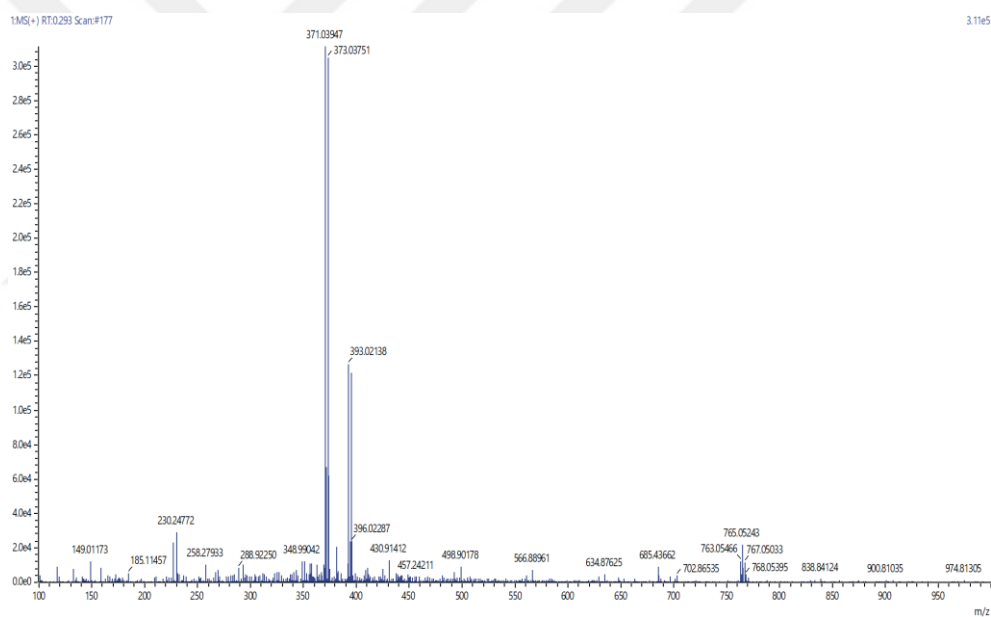


Figure C.22. Mass spectrum of the compound 4-24.

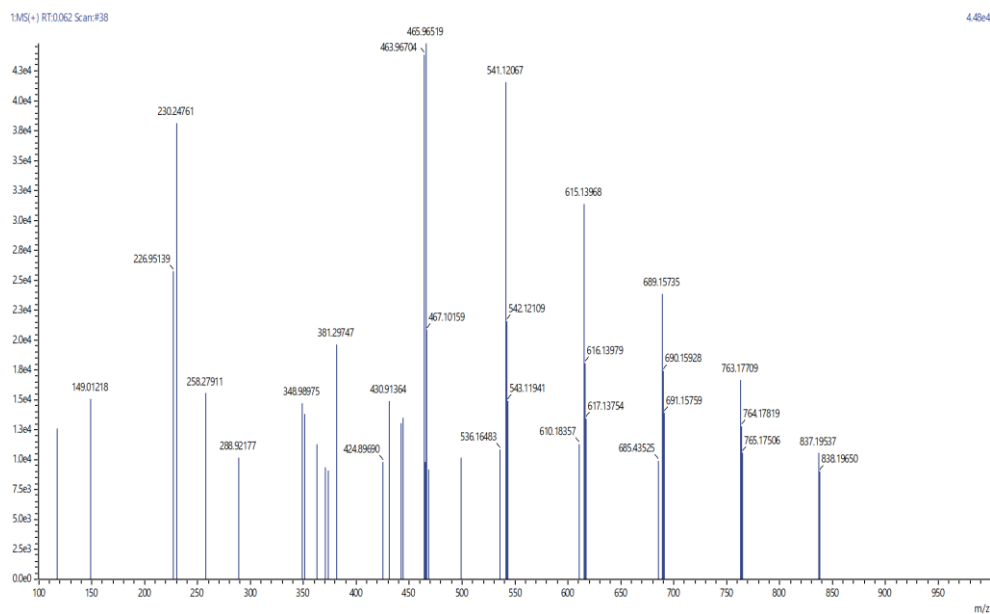


Figure C.23. Mass spectrum of the compound 4-27.

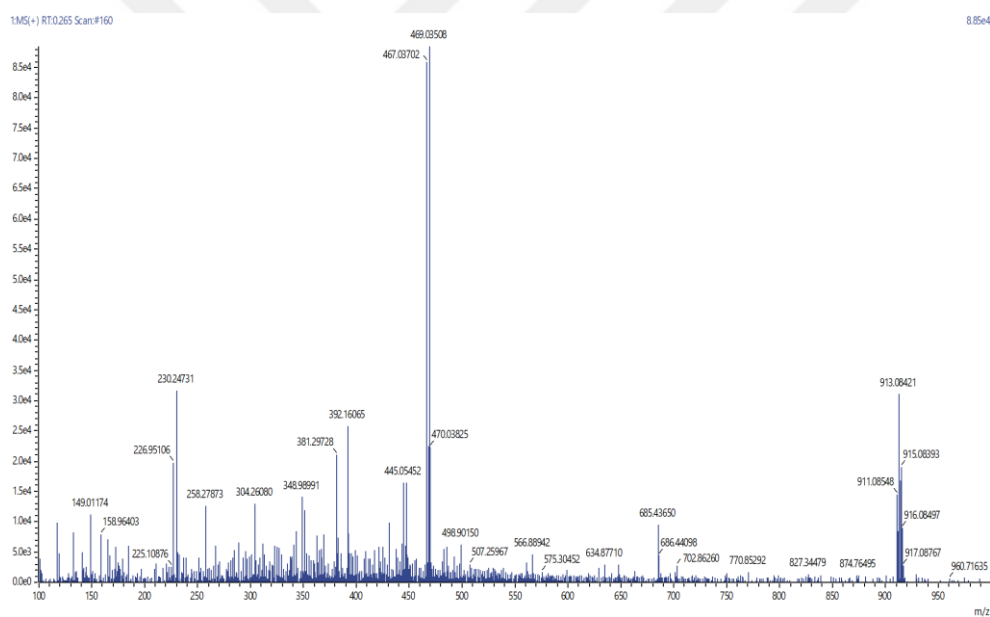


Figure C.24. Mass spectrum of the compound 4-28.

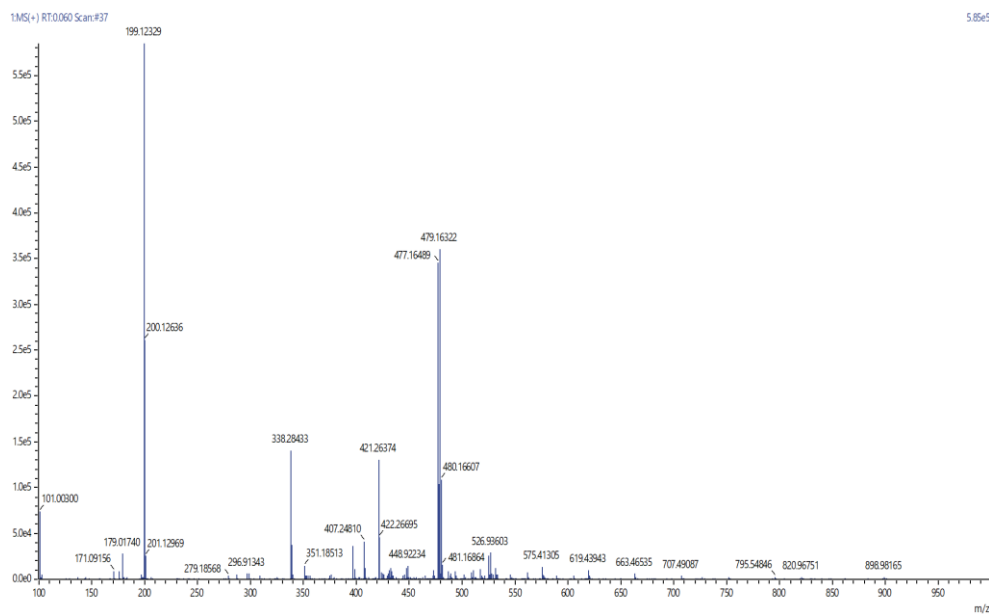


Figure C.25. Mass spectrum of the compound 4-30.

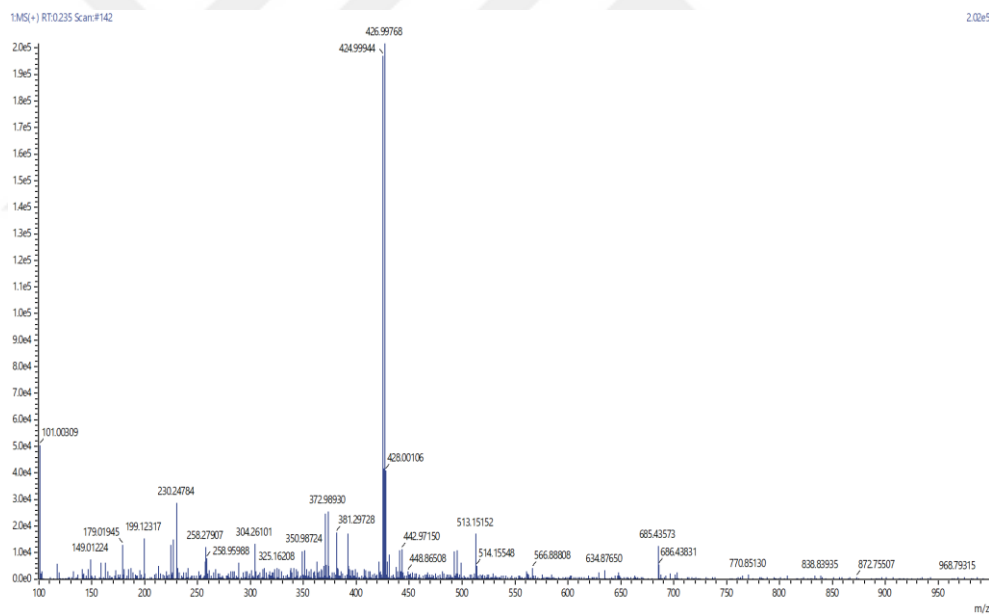


Figure C.26. Mass spectrum of the compound 4-31.

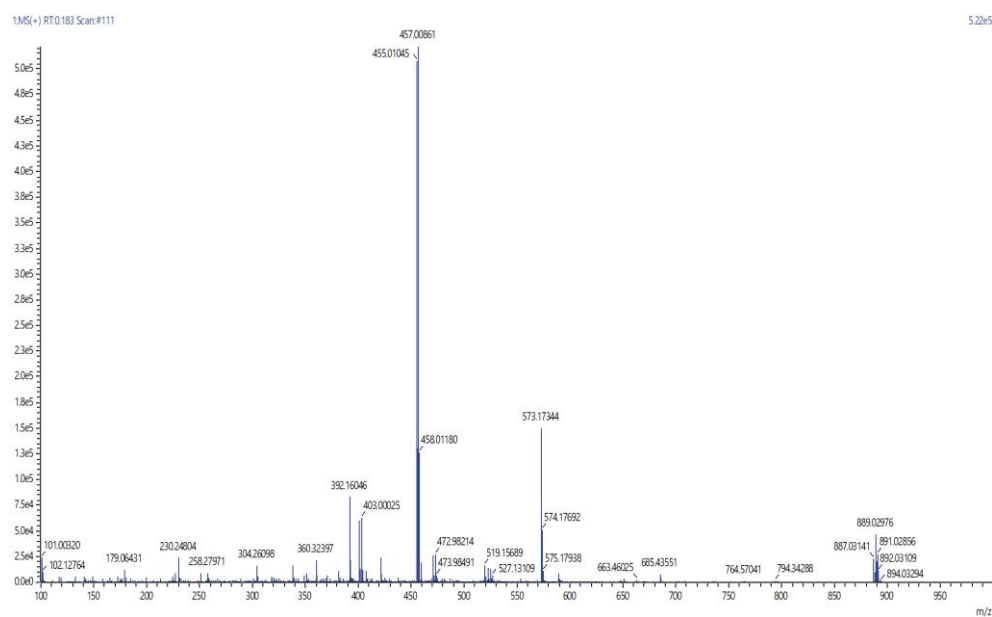


Figure C.27. Mass spectrum of the compound 4-32.

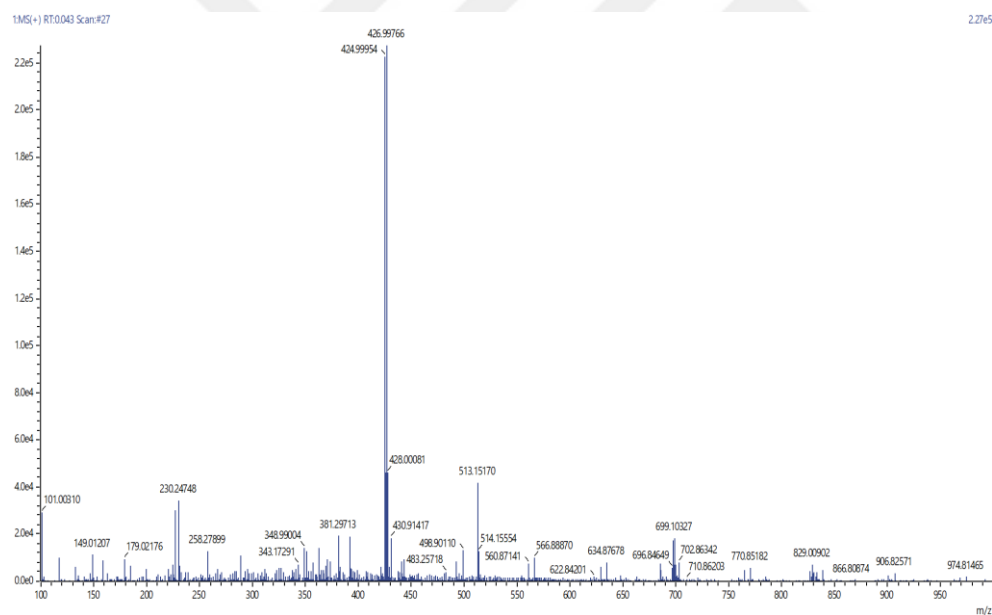


Figure C.28. Mass spectrum of the compound 4-33.

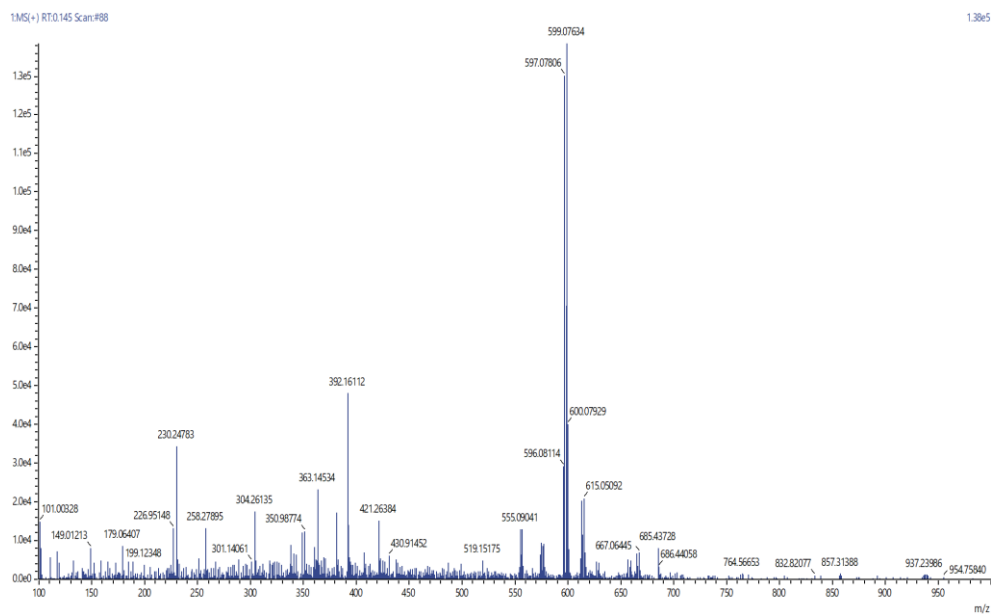


Figure C.29. Mass spectrum of the compound 4-35.

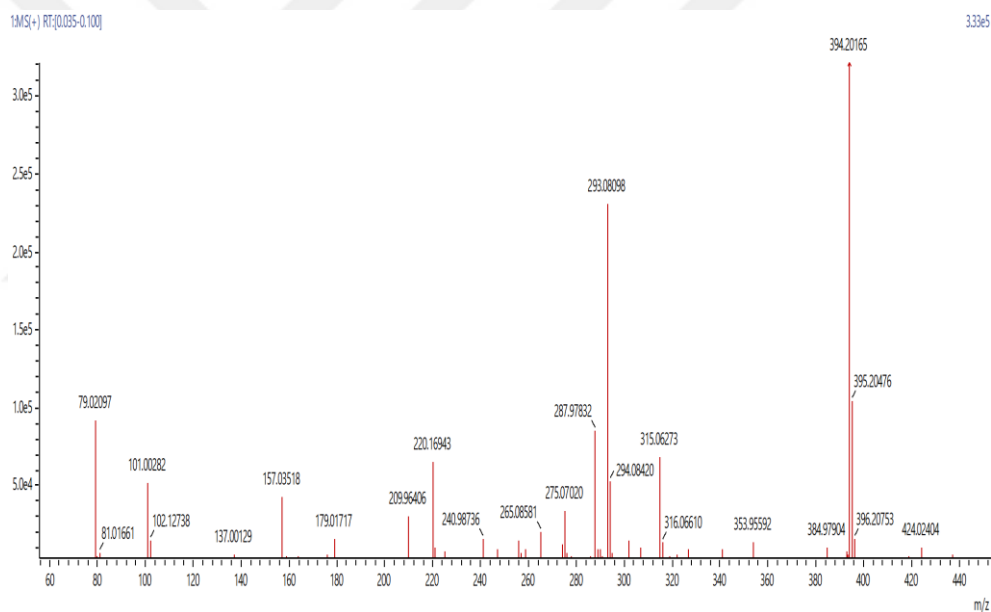


Figure C.30. Mass spectrum of the compound 4-36.

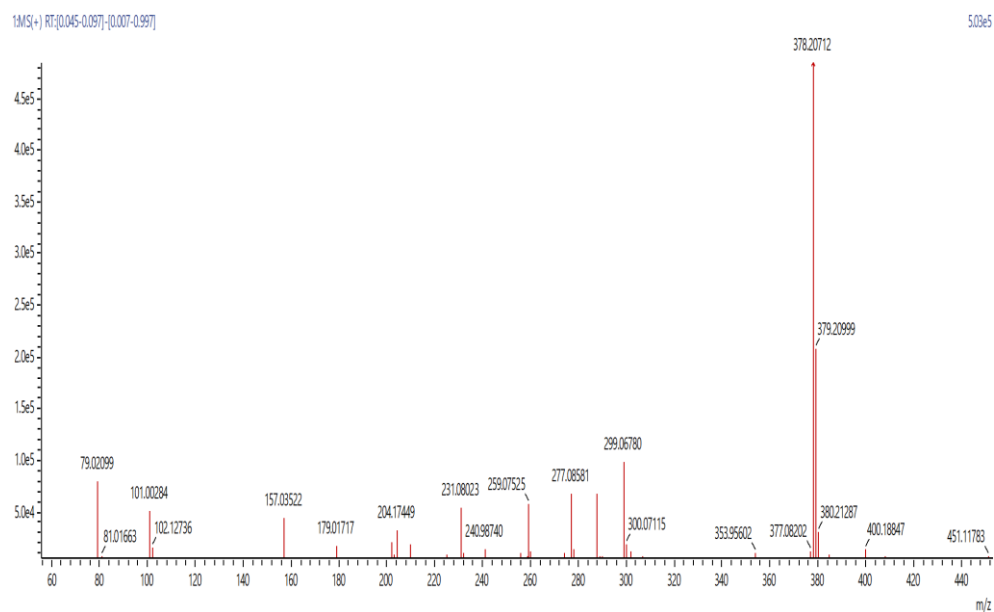


Figure C.31. Mass spectrum of the compound 4-37.

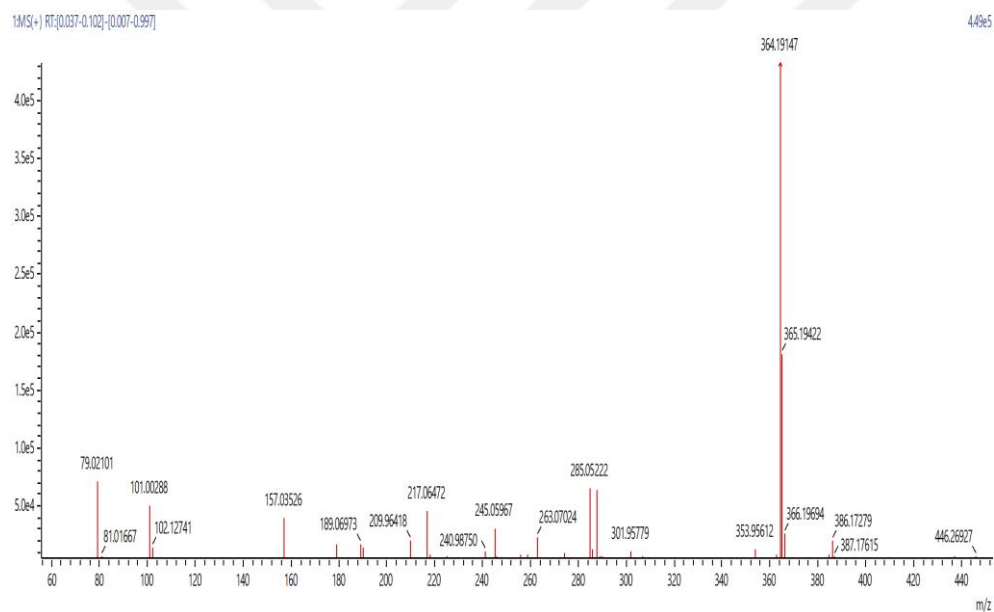


Figure C.32. Mass spectrum of the compound 4-38.

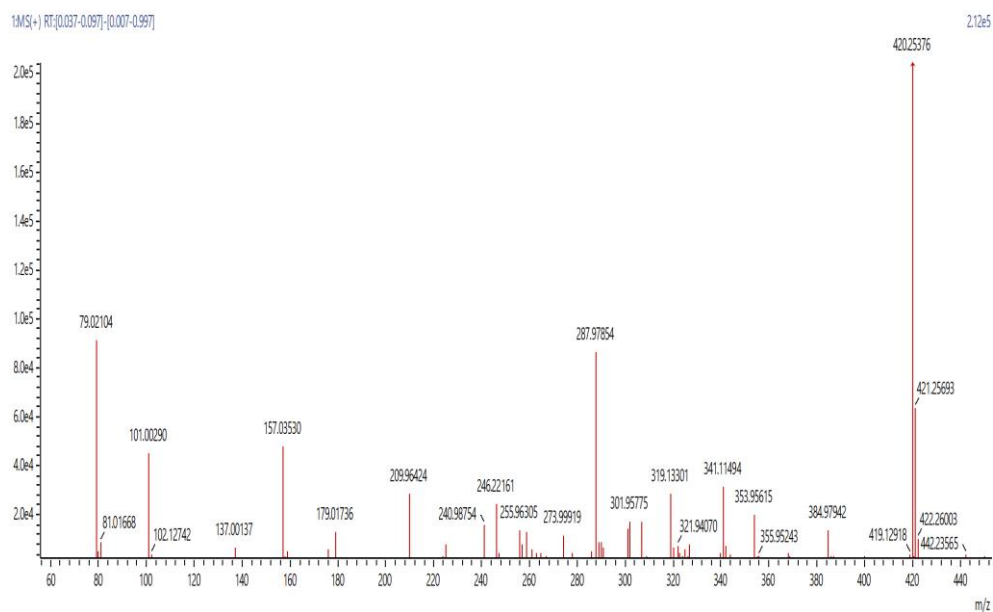


Figure C.33. Mass spectrum of the compound 4-39.

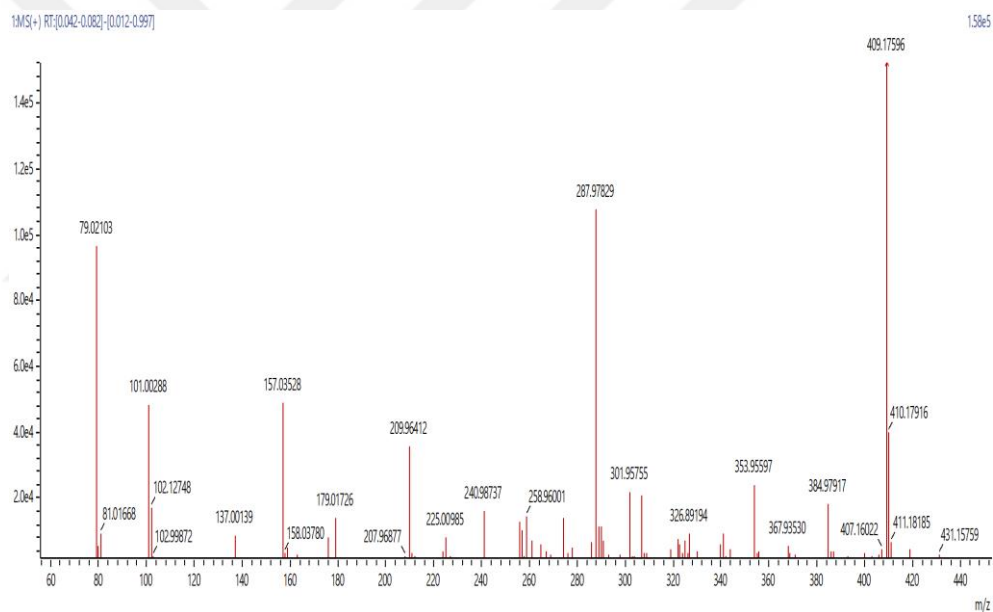


Figure C.34. Mass spectrum of the compound 4-40.

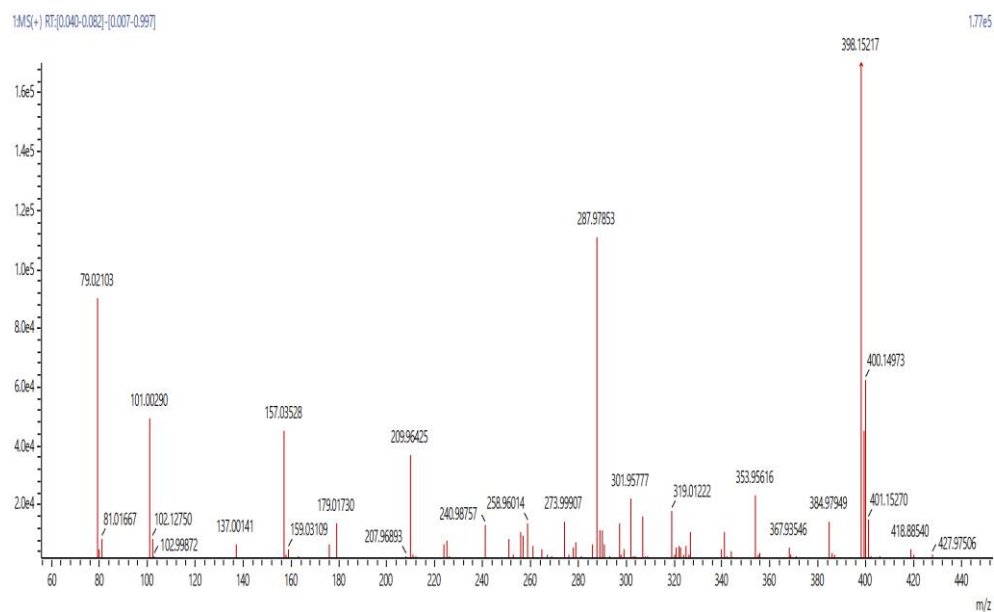


Figure C.35. Mass spectrum of the compound 4-41.

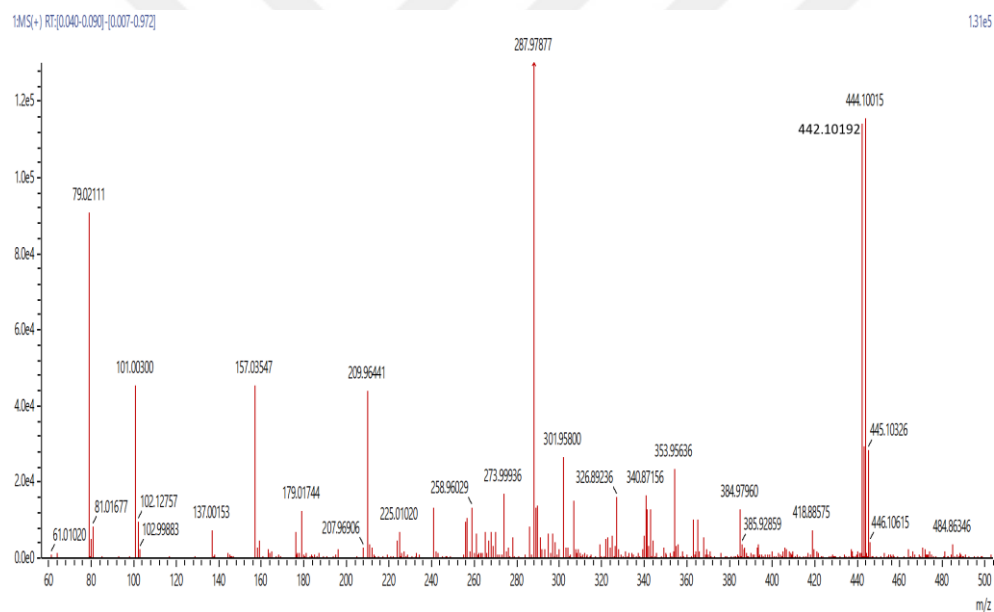


Figure C.36. Mass spectrum of the compound 4-42.

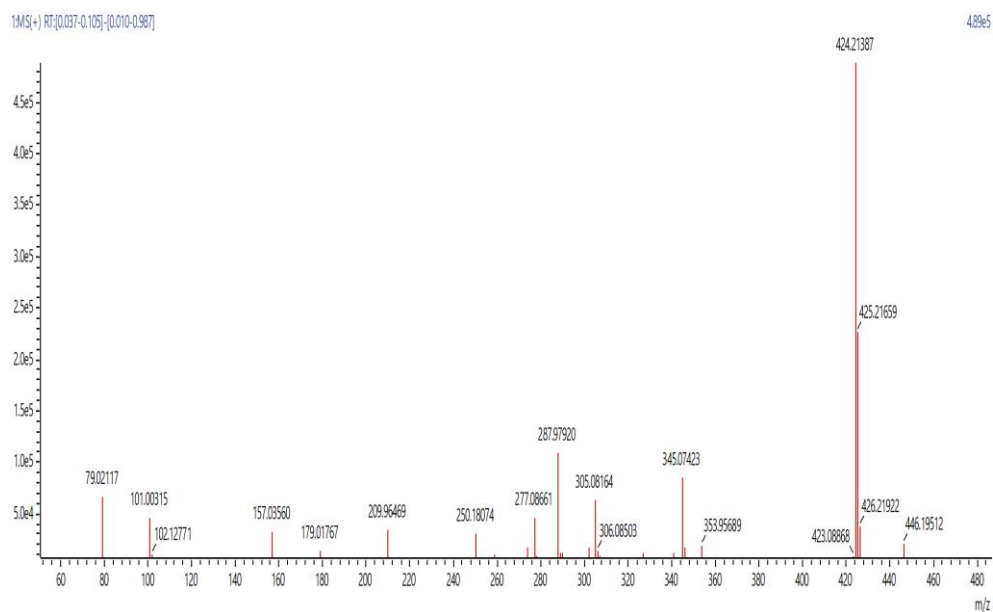


Figure C.37. Mass spectrum of the compound 4-43.



CURRICULUM VITAE

Name Surname :Yavuz DERİN

EDUCATION:

- **Undergraduate** : 2011, Sivas Cumhuriyet University, Faculty of Science, Department of Chemistry
- **Graduate** : 2017, Sakarya University, Institute of Natural Sciences Department, Department of Chemistry, Organic Chemistry
- **Doctor of Philosophy** : 2024, Sakarya University, Institute of Natural Sciences Department, Department of Chemistry, Organic Chemistry

PROFESSIONAL EXPERIENCE AND AWARDS:

- He worked as an NMR technical staff in 2015
- He has been working as a research assistant at Sakarya University, Faculty of Science, Department of Chemistry since 2015.
- He was awarded as a Scholarship Holder of the TUBITAK-1001 and TUBITAK 1002 (2018-2021) Projects Accepted by the Scientific and Technological Research Council of Turkey.

PUBLICATIONS, PRESENTATIONS AND PATENTS ON THE THESIS:

- New 3-(aminomethyl)Naphthoquinone Compounds Obtained from 2-Hydroxy1,4-Naphthoquinone by Mannich Reaction: Synthesis and Characterization Yavuz DERİN, Büşra ALBAYRAK, Gülhan KÖKLÜ, Ahmet TUTAR.

OTHER PUBLICATIONS, PRESENTATIONS AND PATENTS::

- Y. Derin, B. S. Arslan, B. A. Mısır, İ. Şişman, M. Nebioğlu, and A. Tutar, "Synthesis and photophysical investigation of AIEgen dyes bearing quinoline and BODIPY scaffolds," Chem Heterocycl Compd (N Y), vol. 56, no. 12, pp. 1542–1547, Dec. 2020, doi: 10.1007/s10593-020-02847-6.
- T. Rohand et al., "Design, synthesis, DFT calculations, molecular docking and antimicrobial activities of novel cobalt, chromium metal complexes of heterocyclic

- moiety-based 1,3,4-oxadiazole derivatives,” *J Biomol Struct Dyn*, vol. 40, no. 22, pp. 11837–11850, 2022, doi: 10.1080/07391102.2021.1965031.
- M. Z. Islam et al., “An efficient technique for the purification of fulvic acid extracted from leonardite,” *Chem Eng Commun*, vol. 210, no. 7, pp. 1223–1233, 2023, doi: 10.1080/00986445.2023.2185516.
 - S. Şimşek et al., “High-Performance Material for the Effective Removal of Uranyl Ion from Solution: Computationally Supported Experimental Studies,” *Langmuir*, vol. 38, no. 33, pp. 10098–10113, Aug. 2022, doi: 10.1021/acs.langmuir.2c00978.
 - B. S. Arslan et al., “Effect of electron donors on the photophysical and theoretical properties of BODIPY dyes based on tetrazolo[1,5-a]quinoline,” *J Mol Struct*, vol. 1267, Nov. 2022, doi: 10.1016/j.molstruc.2022.133608.
 - B. A. Mısırlı et al., “Novel diarylated tacrine derivatives: Synthesis, characterization, anticancer, antiepileptic, antibacterial, and antifungal activities,” *J Biochem Mol Toxicol*, vol. 38, no. 4, p. e23706, Apr. 2024, doi: <https://doi.org/10.1002/jbt.23706>.
 - B. S. Arslan et al., “The improvement of photovoltaic performance of quinoline-based dye-sensitized solar cells by modification of the auxiliary acceptors,” *J Photochem Photobiol A Chem*, vol. 404, Jan. 2021, doi: 10.1016/j.jphotochem.2020.112936.
 - R. F. Yılmaz et al., “Synthesis and spectral properties of symmetrically arylated BODIPY dyes: Experimental and computational approach,” *J Mol Struct*, vol. 1291, Nov. 2023, doi: 10.1016/j.molstruc.2023.135962.