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SYNTHESIS OF NOVEL 8-HYDROXY QUNOILINE DERIVATIVES AND INVESTIGATION OF THEIR BIOLOGICAL ACTIVITY

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May 2023

We certify that we have read this thesis and that in our opinion it is fully adequate, in scope and in quality, as a thesis for the degree of Master of Science

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ABSTRACT

SYNTHESIS OF NOVEL 8-HYDROXY QUNOILINE DERIVATIVES AND INVESTIGATION OF THEIR BIOLOGICAL ACTIVITY

Bahaa Safaa Tawfeeq ALRUDINI

Master of Science in Chemistry

Advisor: Prof. Dr. Zeynep GÜLTEKİN

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May 2023

Quinoline is a very important class of heterocyclic compound that exhibits unique biological and pharmacological properties, as well as pyrazoles and imines. The aim of this master thesis is: Synthesis and characterization of some novel quinoline-containing Pyrazole and imine derivatives and investigation of their biological activities. For this purpose, Compound (51) was obtained in 89% yield using 8-hydroxy quinoline (2) and 2-bromopropanoate in the presence of base. The reaction of (51) with hydrazine hydrate, the targeted compound (52) was obtained in 77% yield. Cyclization of compound (52) with acetyl acetone or benzoyl acetone yielded compounds (55) and (57) in good yields. In addition, the synthesis of imine (53a-f) was performed as a result of the condensation of compound (52) with various aromatic aldehydes. The synthesized compounds were investigated for *antimicrobial* activity test against two types of bacteria. These species are *Bacillus* and *Staphylococcus aureus.*

2023, 67 pages

Keywords: Schiff bases, Quinoline, Antibacterial activity, Cyclization

ÖZET

YENİ 8-HİDROKSİ KİNOLİN TÜREVLERİNİN SENTEZİ VE BİYOLOJİK AKTİVİTELERİNİN İNCELENMESİ

Bahaa Safaa Tawfeeq ALRUDINI
Kimya, Yüksek Lisans
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Eş Danışman: Dr. Muhannad Al-SAEDY
Mayıs 2023

Kinolin, pirazol ve iminlerin yanısıra biyolojik ve farmakolojik özellikler gösteren çok önemli bir heterosiklik bileşik sınıfıdır. Bu Yüksek Lisans tezinin amacı: Bazı yeni kinolin içeren pirazol ve imin türevlerinin sentezi, karekterizasyonu ve biyolojik aktivitelerinin araştırılmasıdır. Bu amaç için 8-hidroksi kinolin (2) nin 2-bromopropanoat ve baz eşliğinde reaksiyonu sonucu %89 verimle (51) nolu ürün ele geçti. Bu ürünün hidrazin hidrat ile reaksiyonu sonucu hedeflenen (52) nolu bileşik % 77 verimle ele geçti. Bileşik (52) nin asetil aseton veya benzoil aseton ile halkalaşması sonucu pirazol (55) ve (57) nolu ürünler iyi verimle ele geçti. Ek olarak, 52 nolu bileşiğin çeşitli aromatik aldehitlerle kondenzasyon sonucu imin (53a-f) nin sentezi yapıldı. Sentezlenen bileşikler iki tür bakteriye karşı *anti bakteriyel* aktivite testi araştırıldı. Bu türler *Bacillus* ve *Staphylococcus aureus* dir.

2023, 67 sayfa

Anahtar Kelimeler: Schiff bazları, Kinolin, Antibakteriyel aktivite, Halkalaşma

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Çankırı-2023

CONTENTS

ABSTRACT ..... **i**
ÖZET ..... **ii**
PREFACE AND ACKNOWLEDGEMENTS ..... **iii**
CONTENTS ..... **iv**
LIST OF SYMBOLS ..... **vi**
LIST OF ABBREVIATIONS ..... **vii**
LIST OF FIGURES ..... **viii**
LIST OF TABLES ..... **x**
1. INTRODUCTION **1**
1.1 Quinoline **2**
1.2. 8-Hydroxy quinoline **2**
1.3 Synthesis of 8-Hydroxyquinoline and Derivatives **3**
1.4 Applications of 8-Hydroxyquinoline Derivatives **4**
1.4.1 Anti-bacterial **5**
1.4.2 Antifungal Agents **5**
1.4.3 Anti-cancer and Anti HIV **7**
1.5 Hydrazide Derivative **8**
1.5.1 Anti-bacterial Activity **9**
1.5.2 Anti-cancer Activity: **10**
1.6 Schiff Bases **10**
1.6.1 Uses of Schiff bases **13**
1.7 Pyrazole **13**
1.7.1 Some biologically active molecules containing pyrazole (or 1H pyrazole) ring **14**
2. LITERATURE REVIEW **16**
2.1 Synthesis of Ester Derivatives **16**
2.2 Synthesis of Hydrazide Dervatives **16**
2.3 Synthesis of Schiff's Bases **17**
2.4 Synthesis of Payrzole **18**
3. MATERIALS AND METHODS **19**
3.1 Chemicals Used in Material Synthesis **19**

3.2 General procedure for synthesis of schiff's bases and pyrazole 19

3.2.1 Ethyl 2-(quinolin-8-yloxy) propanoate (51) 19

3.2.2 2-(quinolin-8-yloxy) propanehydrazide (52) 20

3.2.3 General procedure for the synthesis of (E)-N'-benzylidene-2-(quinolin-8-yloxy) propanehydrazide (53a-f) 21

3.2.4 1-(3,5-dimethyl-1H-pyrazol-1-yl)-2-(quinolin-8-yloxy) propan-1-one 55 24

3.2.5 1-(3-methyl-5-phenyl-1H-pyrazol-1-yl)-2-(quinolin-8-yloxy)propan-1-one....24

4. RESULTS AND DISCUSSION 26

5. THE STUDY OF ANTIBACTERIAL ACTIVITY 41

5.1 Antibacterial Studies 41

6. CONCLUSIONS AND RECOMMENDATION 45

REFERENCES 46

APPENDICES 54

CURRICULUM VITAE 67

LIST OF SYMBOLS

^{o}C	Celsius Temperature
D	Doublet
DD	Double doublet
G	Gram
HR	Hour
M	Multiplet
MMOL	Milimol
MP	Melting point
Q	Quartet
T	Triplet
S	Singlet

LIST OF ABBREVIATIONS

8HQ	8-Hydroxy quinoline
AR	Aryl
AC	Acetyl
CHHD	Coumarin hydrazide-hydrazone derivatives
COSY	Correlation spectroscopy
ET.OH	Ethanol
IR	Infrared spectroscopy
ME	Methyl
NMR	Nuclear magnetic resonance
NU	Nucleophile
NAASC	Sodium ascorbate
PH	Phenyl

LIST OF FIGURES

Figure 1.1 Types of heterocyclic compounds 1
Figure 1.2 Quinoline ring system 2
Figure 1.3 Structure 8-Hydroxy quinoline (8HQ) 3
Figure 1.4 Four- and six-covalent metal complexes of 8-HQ 3
Figure 1.5 Skraup, Doebner-von miller and friedlander methods 4
Figure 1.6 Synthetic routes for the preparation of 8-hydroxyquinoline derivatives 5
Figure 1.7 8-HQ and halogens derivatives that can act as anti-fungal agents 6
Figure 1.8 Anti-fungicide agent 10a-d 6
Figure 1.9 General routes for synthesis of compound 13 7
Figure 1.10 Derivative of 8-HQ that show antitumor activities 8
Figure 1.11 Derivative of 8-HQ that show anti HIV activities 8
Figure 1.12 Keto enol form of hydrazide (hydrazone) structure 9
Figure 1.13 Benzimidazoles containing hydrazone with antibacterial properties 9
Figure 1.14 The most potent HHD's as anticancer agent 10
Figure 1.15 General structure of a Schiff base ..... .11
Figure 1.16 Reaction of aldehyde or ketone with amine to form Schiff base 11
Figure 1.17 Synthesis of [1-((3-(4-fluorophenyl)-1-isopropyl-1H-indol-2-yl) methylene) hydrazine] ligand 12
Figure 1.18 Synthesis of metal complexes 12
Figure 1.19 Synthesis of (NZ,N'Z)-4,4'-methylenebis(N-(4-methoxybenzylidene) aniline sensor L (32) 12
Figure 1.20 Diels-Alder reaction 13
Figure 1.21 Structure of Pyrazole 14
Figure 1.22 (E)-N-((5-(4-chlorophenyl) -1-phenyl-3-(trifluoromethyl)-1H-pyrazol-4-yl) methylene)-3.5-bis (trifluoromethyl) aniline 14
Figure 1.23 Synthesis of pyrazoline analogs 15
Figure 1.24 Synthesis of pyrazole quinolone pyridine hybrids 15
Figure 2.1 Preparation ethyl 2-(quinolin-8-yloxy) acetate 16
Figure 2.2 Preparation of 2-(quinolin-8-yloxy) acetohydrazide 17
Figure 2.3 Preparation of N'- arylidene -2-(quinolin- 8 -yloxy) aceto hydrazide 17
Figure 2.4 Preparation synthesis of pyrazole ring 18
Figure 2.5 Preparation of pyrazole ring 18
Figure 3.1 Preparation Ethyl 2-(quinolin-8-yloxy) propanoate (51) 19
Figure 3.2 Preparation 2-(quinolin-8-yloxy) propanehydrazide (52) 20
Figure 3.3 Preparation general for the synthesis of Schiff bases (53a-f) 21
Figure 3.4 Preparation 1-(3.5-dimethyl-1H-pyrazol-yl)-2-(quinoline-8-yloxy) propan-1- one (55) 24
Figure 3.5 1-(3-methyl-5-phenyl-1H-pyrazol-1-yl)-2-(quinolin-8-yloxy) propan-1-one (57) 25
Figure 4.1 Synthetic route for the prepared compounds 26

Figure 4.2 Preparation ethyl 2-(quinolin-8-yloxy) propanoate 51 27
Figure 4.3 Mechanism steps for preparation of ethyl 2- (quinolin-8-yloxy) propanoate 51 27
Figure 4.4 IR spectrum for compound 51 28
Figure 4.5 Ethyl 2-(quinolin-8-yloxy)propanoate 28
Figure 4.6 ^{1}H NMR Spectra of Compound 51 29
Figure 4.7 ^{13}C NMR spectrum Compound 51 30
Figure 4.8 Preparation 2-(quinoline-8-yloxy) acetohydrazide compound 52 30
Figure 4.9 Mechanism steps for preparation of 2-(quinoline-8-yloxy)acetohydrazide 31
Figure 4.10 IR spectrum for compound 52 31
Figure 4.11 2-(quinolin-8-yloxy) propanehydrazide 32
Figure 4.12 ^{1}H NMR spectrum Compound of 52 32
Figure 4.13 ^{13}C NMR spectrum Compound of 52 33
Figure 4.14 Preparation (E)-N'-benzylidene-2-(quinolin-8-yloxy) propane-hydrazide (53a-f) 34
Figure 4.15 Mechanism steps for preparation of schiff bases (53a-f) 35
Figure 4.16 (E)-N'-(3-nitrobenzylidene)-2-(quinolin-8-yloxy) propanehydrazide 35
Figure 4.17 ^{1}H NMR spectrum Compound of 53-a 36
Figure 4.18 ^{13}C NMR spectrum Compound of 53-a 37
Figure 4.19 Preparation of pyrazol compound 57 37
Figure 4.20 Mechanism steps for preparation of pyrazole 55 38
Figure 4.21 1-(3-methyl-5-phenyl-1H-pyrazol-1-yl)-2-(quinolin-8-yloxy) propan-1-one 39
Figure 4.22 Compound 57 ^{1}H NMR spectrum 39
Figure 4.23 Compound 57 ^{13}C NMR spectrum 40
Figure 5.1 Anti-bacterial test of compounds 52, 55, 57 43
Figure 5.2 Anti-bacterial test of compounds 53-a and 8-hydroxy quinoline 44

LIST OF TABLES

Table 3.1 Physicochemical and spectral data of the compounds (52a-f)..... 21
Table 3.2 ^{1}H NMR, ^{13}C NMR of compounds (52a-f)..... 22
Table 4.1 The approximately purity of these compounds (52a-f)..... 34
Table 5.1 In vitro anti-bacterial (Gram Positive) data 42

1. INTRODUCTION

Heterocyclic compounds are cyclic compounds with at least one carbon atom and contains one other additional element. Monocyclic compounds are those that include exclusively heteroatoms in their rings. Heterocyclic compounds are created by replacing a carbon atom in an organic ring structure with an atom of oxygen, nitrogen, suphlur, or another similar element (Figure 1.1) (Kaur *et al.* 2013).

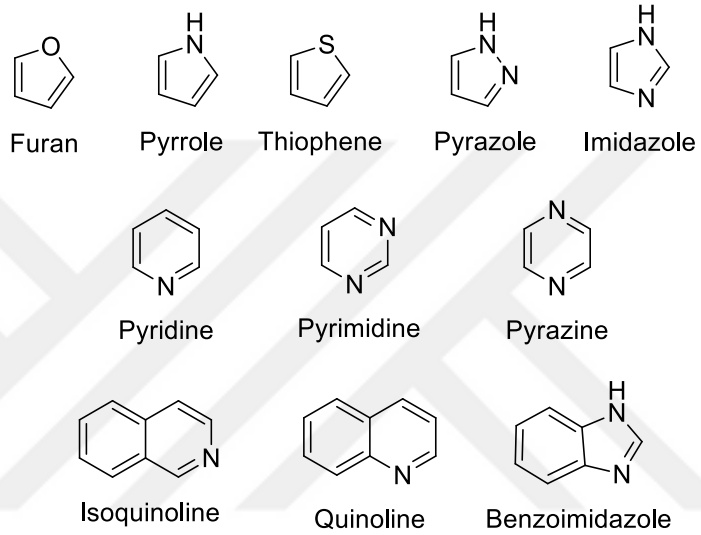
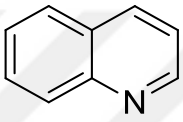


Figure 1.1 Types of heterocyclic compounds

It is known that heterocyclic compounds with an azole nucleus play a significant role in biochemical processes, are widely present in a variety of medicinal medicines, and exhibit a wide spectrum of pharmacological activity (Qadir *et al.* 2022, Al-Masoudi *et al.* 2006, Ravindra *et al.* 2006). Their extensive clinical use as well as industries as various as agriculture (Arunkumar 2015), photochemistry (Lefebvre *et al.* 2020), anticancer activity (Ardestani *et al.* 2022), and polymer science (Hassan 2014), anti-inflammatory (Sondhi *et al.* 2007).

1.1 Quinoline

Quinoline is a nitrogen-containing heterocyclic aromatic compound also known as 1-aza-napthalene or benzo[b]pyridine. Its general formula of quinoline as shown down in (Figure 1.2). Quinoline ring is weak base and can produce salt with acids. Most natural compounds contain a quinoline ring and they are pharmacologically active drugs with a wide range of biological activity. Quinoline containing molecules has been effective against anti-malarial, antibacterial, anti-fungal, anthelmintic, cardio tonic, anticonvulsant, anti-inflammatory, and analgesic properties (Figure 1.2) (Marella *et al*. 2013).



1

Figure 1.2 Quinoline ring system

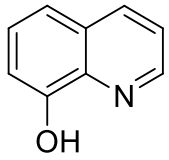
1.2 8-Hydroxy quinoline

One of the most well-known and useful organic compounds is 8-Hydroxquinoline (8-HQ). 8-Hydroxquinoline is a bicyclic compound and consists of two rings system, carbocyclic ring and pyridine ring with hydroxyl group substituted at position-8as shown in (Figure 1.3).

8-Hydroxyquinoline and its derivatives are used in a wide range of products, including pharmaceuticals, organic light-emitting diodes (OLED) electron carriers (Tang *et al.* 1987) and fluorescent chemo sensors for metal ions (Zheng *et al.* 2005).

8-Hydroxyquinoline derivatives have potential applications in medicine as antimicrobial, antibacterial, antifungal, anti-inflammatory, anti-leukemic and anticancer (Basavanna *et al.* 2022, Saadeh *et al.* 2020).

Additionally, derivatives of 8-HQ have found many uses in fluorescence sensing of biologically and environmentally significant metal ions including Fe^{3+}, Zn^{2+} and Al^{3+} due to their ability to chelate toward a wide variety of metal cations (Paul and Luxami 2020).



2

Figure 1.3 Structure 8-hydroxy quinoline (8HQ)

8-HQ shows a good ligand property. The metal in 8-HQ is attached to both the oxygen and the nitrogen, and the hydrogen of the hydroxyl group is displaced. Therefore, for each metal atom in a four covalent metal complex, two molecules of 8-HQ are needed, and for a six covalent metal complex, three molecules of 8-HQ are needed (Figure 1.4) (Al-Busafi *et al.* 2014, Shoji *et al*. 2003).

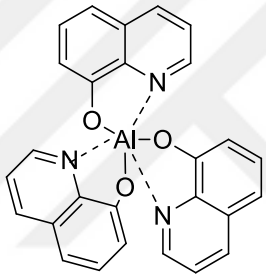


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Figure 1.4 Four- and six-covalent metal complexes of 8-HQ

1.3 Synthesis of 8-Hydroxyquinoline and Derivatives

The most convenient method for preparation of quinoline and its derivatives are Skraupor Friedlander methods. In 1880, Skraup was reported synthesis of quinoline by heating aniline and glycerol in the presence of acid and oxidizing reagent (Skraup, 1880). Doebner-Miller and Friedlander modified this method by using α,β-unsaturated aldehyde or condensation of substituted o-aminobenzaldehyde or o-aminoacetophenone with suitable aldehyde or ketone (Figure 1.5) (Cheng & Yan, 2004, Manske and kulka 1953, Matsugi *et al.* 2000, Weyesa and Mulugeta 2020).

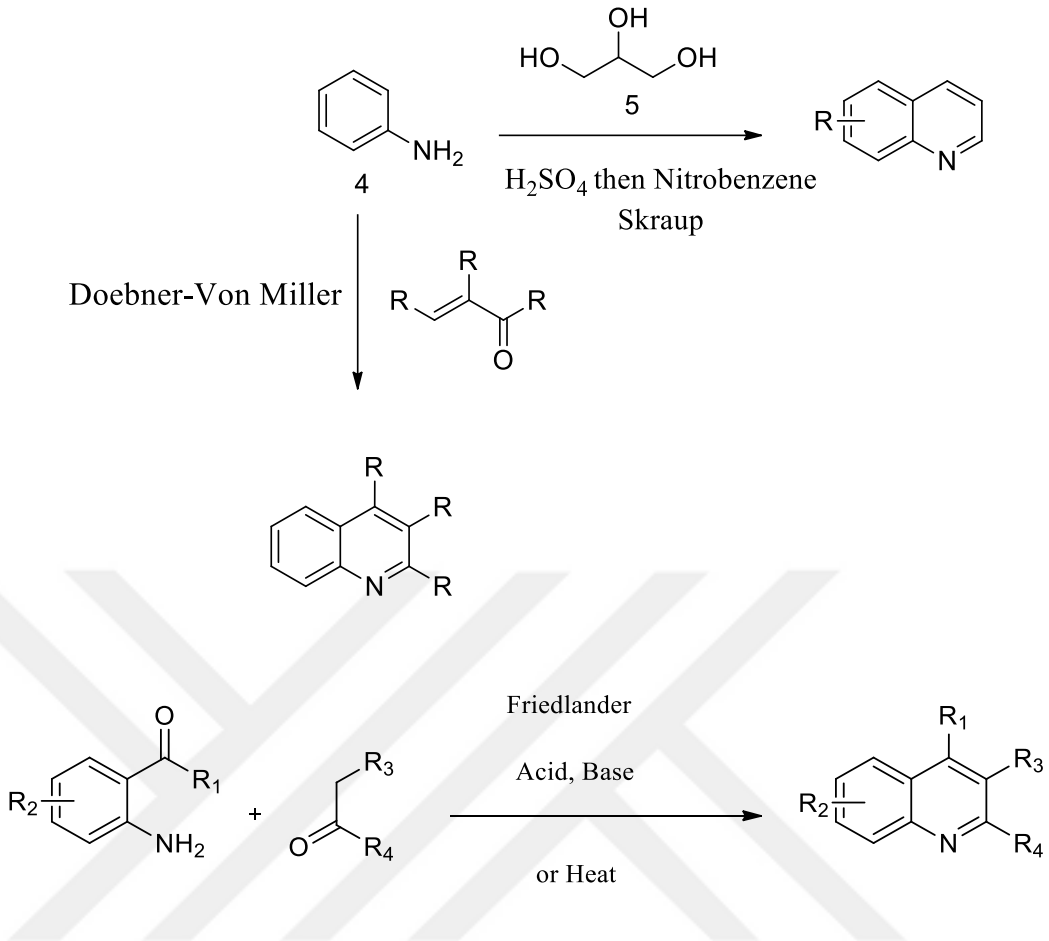


Figure 1.5 Skraup, Doebner-von miller and friedlander methods

1.4 Applications of 8-Hydroxyquinoline Derivatives:

8-Hydroxyquinoline and its derivatives were investigated against the three species of plant hopper by Lee. Isoquinoline and 6-methoxyquinoline were found the most effective against the three species based on 48 h LD50 values. In their research, it was found that high levels of 8-hydroxyquinoline, 4-methylquinoline, 6-methylquinoline, and 8-hydroxy-2-methylquinoline showed high levels of insecticidal activity (Lee *et al.* 2010). The activity test of 8-Hydroxyquinoline and its derivatives has been tested by manyl authors, for example:

1.4.1 Anti-bacterial:

8-hydroxyquinoline derivatives were prepared by Rbaa and their antimicrobial activity was tested. The antibacterial activity of all the prepared compounds has been assessed "in vitro" using the bacterial strains E. coli, S. aureus, V. parahaemolyticus, and P. aeruginosa. In their research, 8-hydroxyquinoline 7 was shown high antibacterial activity compare to penicillin (Figure 1.6) (Rbaa *et al.* 2019).

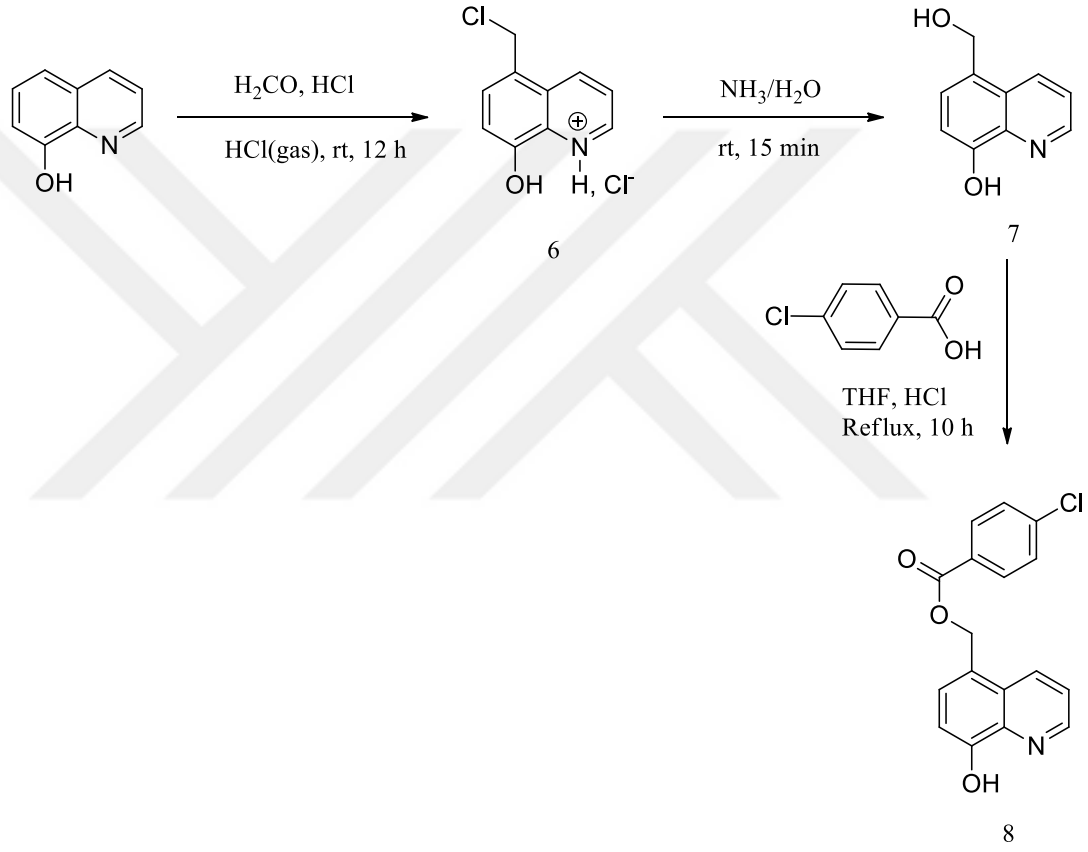
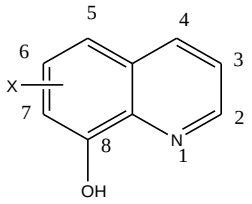


Figure 1.6 Synthetic routes for the preparation of 8-hydroxyquinoline derivatives

1.4.2 Antifungal Agents:

8-HQ is widely used as a fungicide in many countries to control freckle, scab, and black spot diseases in cucumber, grape, wax apple, pear, and citrus (Al-Busafi *et al*. 2014). Antifungal activity of several derivative of 8-hydroxyquinoline such as 2-, 3-, 4-, 5-, 6- and 7 chloro and bromo were tested against aspergillus niger, aspergillus oryzae,

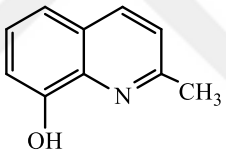
myrothecium verrucaria, trichoderma viride and trichophyton mentagrophytes by Gershon (Figure 1.7) (Gershon *et al.* 1994).



X: Br and Cl

Figure 1.7 8-HQ and halogens derivatives that can act as anti-fungal agents

Antifungal activity of 8-hydroxy quinoline derivatives (10a-10d) have been investigated against A niger, A.oryzae, M.verrucaria, T.viride, M.cirinelloides and T.mentagrophytes by Gershon (Gershon *et al.* 2001). The 5-bromo-7-sulfonic acids (10c) have been observed to inhibit fungal growth to an extent of 8-quinolinol (Figure 1.8).



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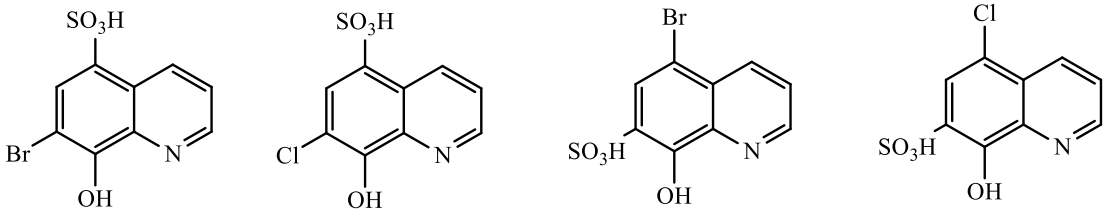


10a 10b 10c 10d

Figure 1.8 Anti-fungicide agent 10a-d

1.4.3 Anti-cancer and Anti HIV:

8-Hydroxyquinoline have been reported in the literature and important in medicinal chemistry (Gupta *et al.* 2021).

1,2,3-Triazole containing novel 8-hydroxyquinoline derivatives were reported by Freitas using the Click reaction with compound 11 and D-galactopyranose derivative 12 in the presence of $CuSO_4$ catalysis. This compound was shown the most active potent anti-proliferative and was found to show high selectivity against cancer cells (Figure 1.9) (Freitas *et al.* 2014).

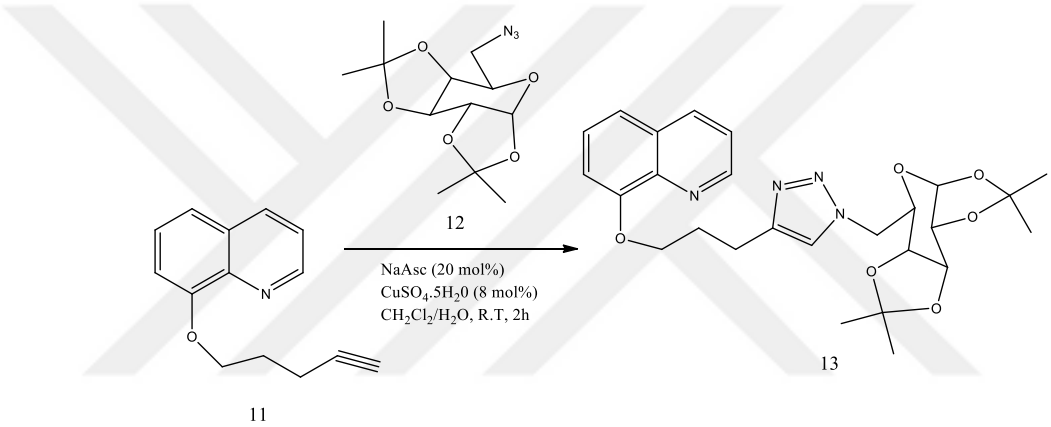


Figure 1.9 General routes for synthesis of compound 13

The synthesis of iron chelates 8-Quinolinamine 14 was prepared by Corcé and it was found to show highly effective anti-proliferative activity in the micro molar range (Corcé *et al.* 2012).

Also, compounds 15 and 16 were published by Oliveri and found to show anti-proliferative activity against different tumor cell lines in the presence of copper (II) ions (Figure 1.10) (Oliveri *et al.* 2012).

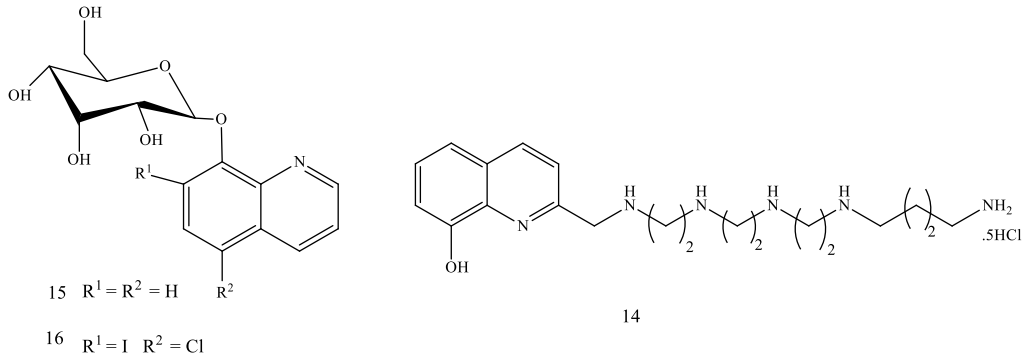


Figure 1.10 Derivative of 8-HQ that show antitumor activities

Polanski and co-worker were reported synthesis of quinolic acid derivatives and they investigated anti HIV test of these compounds; among them 5-hydroxy-8-nitro-6-quinolic acid 17 was found to be the most effective in inhibiting HIV-1 integrates in vitro as shown in (Figure 1.10) (Polanski *et al.* 2006).

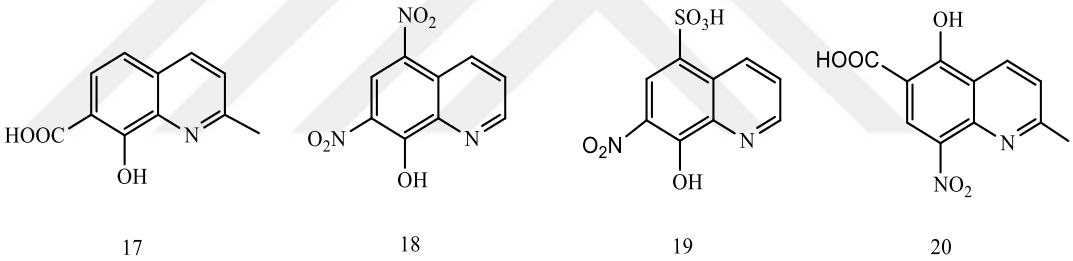


Figure 1.11 Derivative of 8-HQ that show anti HIV activities

1.5 Hydrazide Derivatives

A large class of organic hydrazine derivatives, known as organic hydrazine, include the functional group (-C=O) $NHNH_2$. Important bidentate ligands and form keto-enol (amido-iminol) tautomerism (Figure 1.11) (Mali *et al.* 2021).

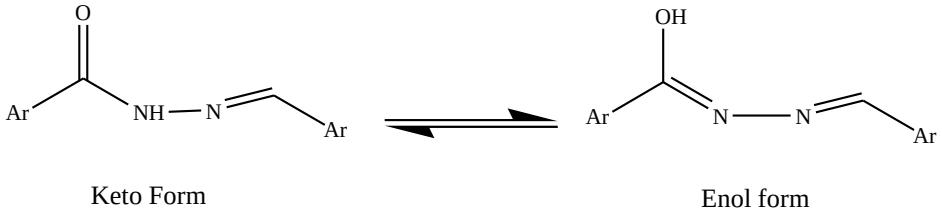


Figure 1.12 Keto enol form of hydrazide (hydrazone) structure

Hydrazine can be prepared using substituted hydrazine with corresponding aldehydes or ketones (Hajipour *et al.* 1999).

Variety of hydrazide derivatives are biologically active compounds. Their antiviral, anti-inflammatory, antiplatelet, vasodilator, antidepressant, analgesic, anticonvulsant, anticancer and antimicrobial activities have been reported (Narang *et al.* 2012, Popiołek 2017, Rollas and Küçükgüzel 2007).

1.5.1 Anti-bacterial Activity

Numerous hydrazones and their derivatives were prepared in the literature and their antibacterial activity was tested. Özkay and co-worker were synthesized hydrazone derivatives containing Benzimidazole ring and they investigated their antibacterial activity. Compound 21 and 22 were found to have an effective antibacterial activity against salmonella thyhimurium (Figure 1.12) (Özkay *et al.* 2010).

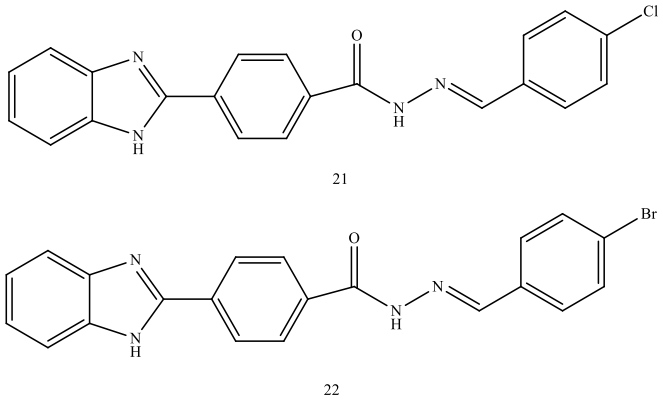


Figure 1.13 Benzimidazole containing hydrazone with antibacterial properties

1.5.2 Anti-cancer Activity:

The hydrazide-hydrazone moiety plays a substantial significance as an anticancer agent, according to a literature review (Vicini *et al.* 2006, Terzioglu and Gürsoy 2003, Abadi *et al.* 2003, Kumar *et al.* 2012).

Nasr *et al* reported derivatives of hydrazone containing furan; thiophene, pyrrole, and oxoindolin have potent anticancer activity against resistant Panc-1-cells. Compound 25 and 26 were found to have the most potent anti-proliferative activity (Figure 1.14) (Nasr *et al.* 2014).

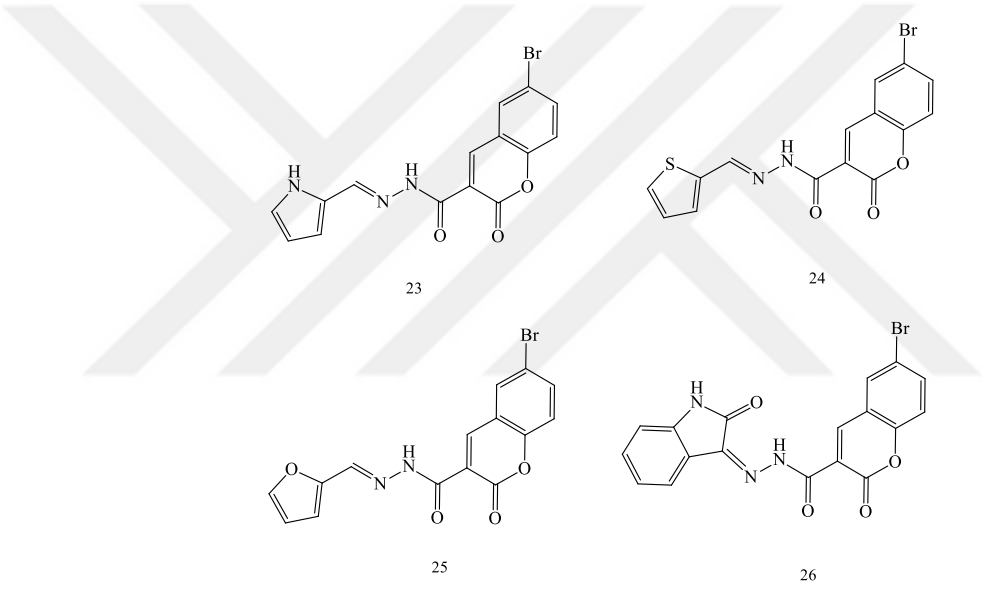
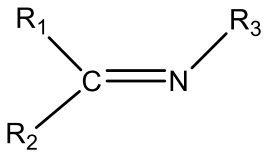


Figure 1.14 The most potent CHHD's as anticancer agents

1.6 Schiff Bases

Schiff bases were first reported by Hugo Schiff in 1864 (Schiff, 1864). General formula of Schiff base as shown in (Figure 1.13), R and R1 can be any of several different substituted alkyl, aryl, cycloalkyl, or heterocyclic groups. These substances may alternatively be referred to as anils, imines, or azomethines.



R_1, $R_{2,}$ and/or R_3 = alkyl or aryl

Figure 1.15 General structure of a Schiff base

Most convenient method for synthesis of Schiff bases is condensation of aldehydes or ketones with amines under acid or base catalyst (Figure 1.14) (Dalia *et al.* 2018).

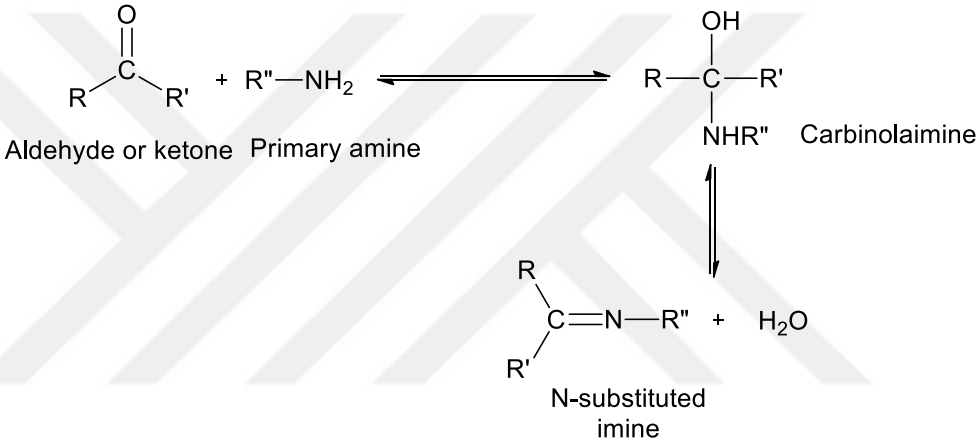


Figure 1.16 Reaction of aldehyde or ketone with amine to form Schiff base

Since then, numerous imine (Schiff base) synthesis techniques have been described by several authors (Zheng *et al.* 2009, Dalia *et al.* 2018).

Joshi *et al.* reported synthesis of a new (1-((3-(4-fluorophenyl)-1-isopropyl-1H-indol-2-yl) methylene) hydrazine) Schiff base. This compound was used as a ligand with various metals. Antimicrobial and anti-tubercular activity of synthesized metal complexes was tested by Joshi. Cu (II) and Cd (II) metal complexes were found to have the best antimicrobial and anti-tubercular activity as shown (Figure 1.17) and (Figure 1.18) (Joshi *et al.* 2022).

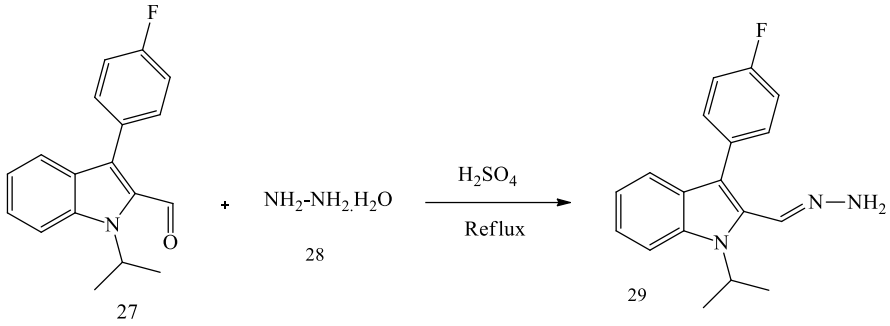


Figure 1.17 Synthesis of [1-((3-(4-fluorophenyl)-1-isopropyl-1H-indol-2-yl)methylene) hydrazine] ligand

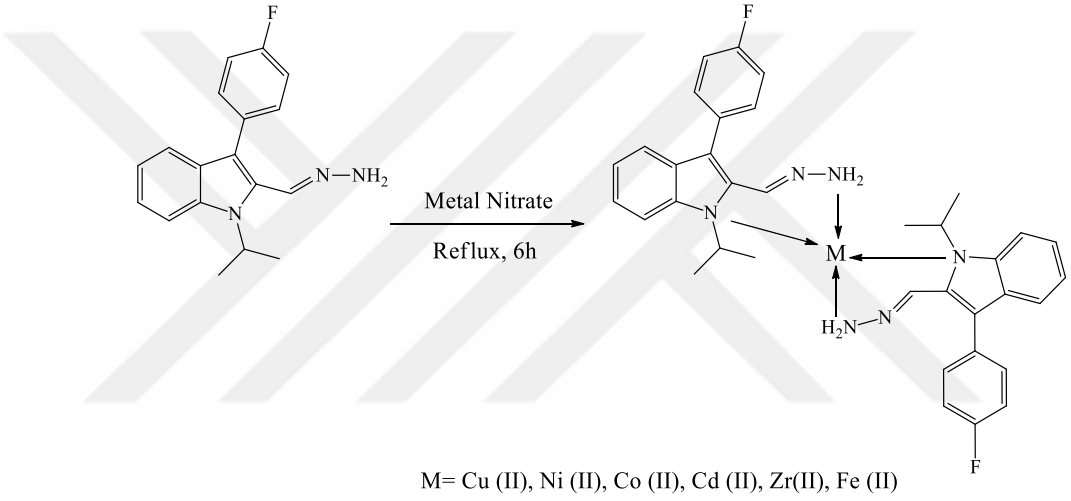


Figure 1.18 Synthesis of metal complexes

Das *et al.* reported synthesis of the sensor (L) 32. Reaction of 4, 4′-methylenedianiline 30 with 4-methoxybenzaldehyde 31 in ethanol at room temperature after 15 min. compound L30 was obtained in 74% yield as shown (Figure 1.19) (Das *et al*. 2019).

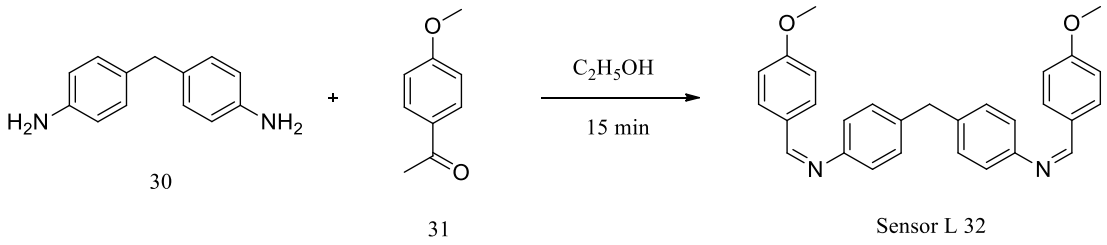


Figure 1.19 Synthesis of (NZ,N'Z) - 4,4'- methylenebis (N-(4-methoxybenzylidene) aniline sensor L (32)

1.6.1 Uses of Schiff bases

Schiff bases are well-known for being chemically active substances with a variety of uses as potent antimicrobial agents (Rani *et al.* 2015), and important in medicinal chemistry (Hameed *et al.* 2017).

They are also used as a ligands in coordination chemistry (Yousif *et al.* 2017). Metal ion complexes of Schiff bases shown biological activity such as antimicrobial, anti-fungal, antitumor activities (Uddin *et al.* 2019).

Schiff bases are widely used in the literature in aza-Diels-Alder reactions for the preparation of nitrogen-containing heterocyclic compounds (Masson *et al.* 2013).

Pégot *et al* reported asymmetric Diels-Alder reaction between Danishefsky's diene 34 and imines 33 in chiral organic liquids. High di stereo selectivity (60%) was obtained using chiral ionic liquid IL4 (Pégot *et al.* 2006) at 30°C (Figure 1.20).

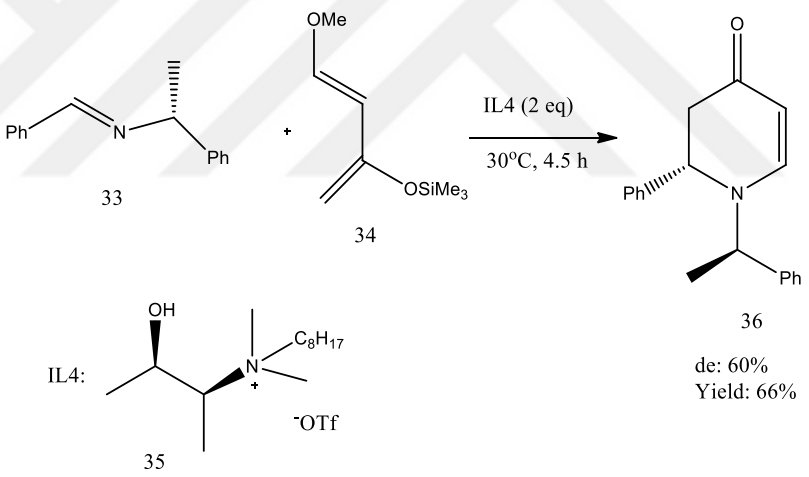
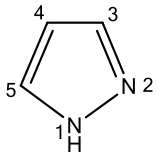


Figure 1.20 Diels-Alder reaction

1.7 Pyrazole

Pyrazole was first reported by Ludwig Knorr in 1883 (Knorr 1883). The Pyrazole family of simple aromatic ring organic compounds has a five-membered ring structure with three carbon atoms and two nitrogen atoms near together. Structure of pyrazole as shown in (Figure 1.21).



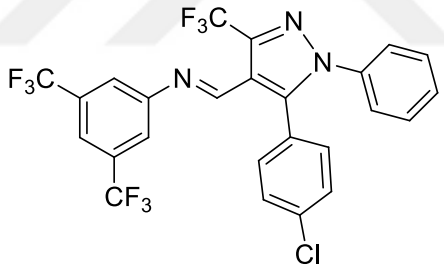
37

Figure 1.21 Structure of pyrazole.

Compounds containing a pyrazole ring have been synthesized by many researcher because of their biological activity properties such as anticancer (Li *et al.* 2012), anti-inflammatory and analgesic (Gokulan *et al.* 2012), anti-diabetic (Faidallah *et al.* 2011), antimicrobial (Vijesh *et al.* 2013), anticonvulsant (Abdel-Aziz *et al.* 2009).

1.7.1 Some biologically active molecules containing Pyrazole (or 1H pyrazole) ring

Various pyrazole derivatives were prepared by El-Sayed among them, which compound 38, was found to have anti-inflammatory activity (Figure 1.22) (El-Sayed *et al*. 2012).



38

Figure 1.22 (E)-N-((5-(4-chlorophenyl)-1-phenyl-3-(trifluoromethyl)-1H-pyrazol-4-yl) methylene)-3,5-bis(trifluoromethyl) aniline

Ahsan et al reported synthesis of compound 39. Condensation of 4-aminoacetophenone 40 and p-anisidine 36 in methanolic sodium hydroxide solution, followed by the cyclization of intermediate chaconne 41 with the proper semicarbazide / thiosemicarbazide in glacial acetic acid have designed and synthesized a series of thiocetazone-based Pyrazoline analogs (Figure 1.23). Compound 42 was shown moderate anti-tubercular activity (Ahsan & Saini 2015)

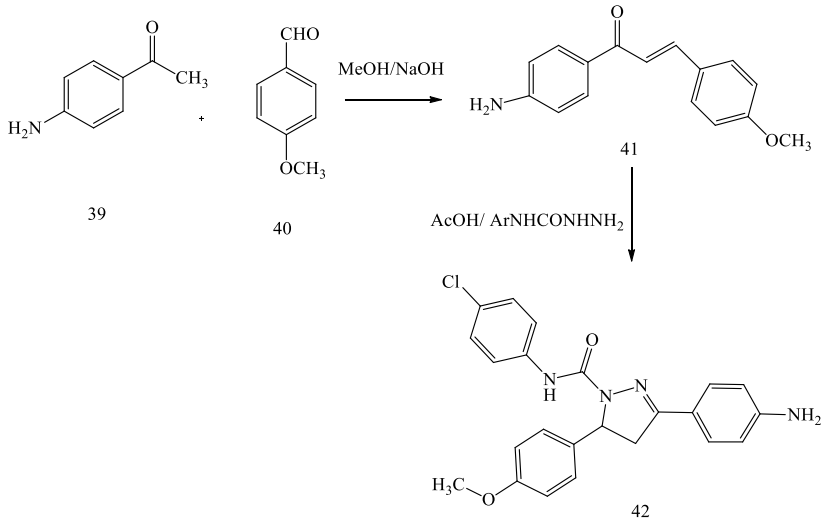


Figure 1.23 Synthesis of pyrazoline analogs

Sangani group have been prepared pyrazole quinolone-pyridine hybrid derivatives using a one-pot multi component reaction. All substances were examined by Sangani for their in vitro antibacterial and anticancer effects, and 46 was found most effective against epidermal growth factor receptor (Figure 1.24) (Sangani *et al.* 2014).

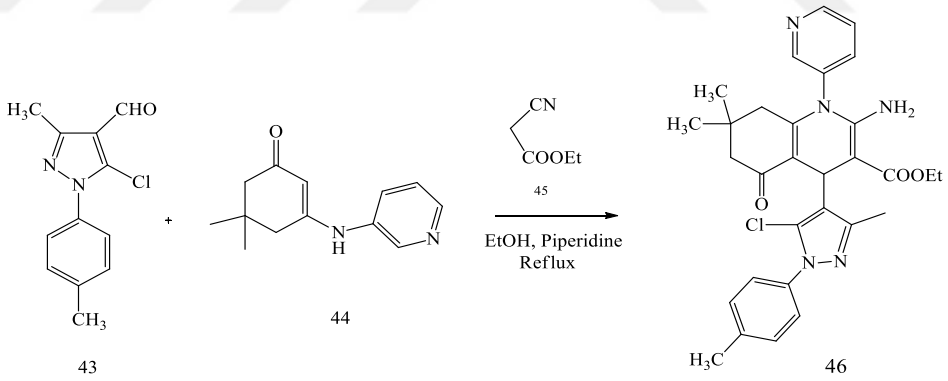


Figure 1.24 Synthesis of pyrazole quinolone pyridine hybrids

2. LITERATURE REVIEW

Due to the importance of heterocyclic compounds containing pyrazole ring and their ester, hydrazides, Schiff base derivatives in medicine, industry and agriculture, In this chapter, we will review the scientific studies about this area.

2.1 Synthesis of Ester Derivatives

Ethyl 2-(quinolin-8-yloxy) acetate 44 was prepared by several authors (Ahmed *et al.* 2006, Althobiti and Zabin 2020, Boukabcha *et al.* 2019, Hayat *et al*. 2010, Mohammed and Subrahmanyam 2009). Kumar and co-workers reported the preparation of compound 44 starting from 8-hydroxy quinoline and ethyl chloro acetate 43 in the presence of anhydrous potassium carbonate under refluxing for 8 hr. in 90%yield as shown in (Figure 2.1) (Kumar *et al*. 2013).

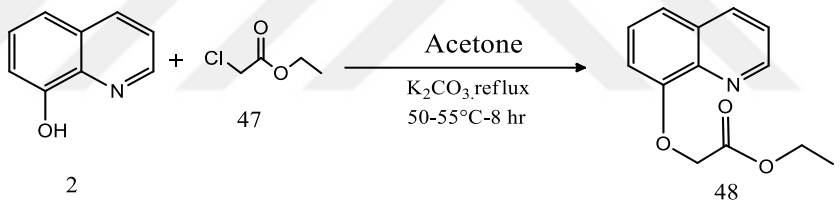


Figure 2.1 Preparation ethyl 2-(quinolin-8-yloxy) acetate

2.2 Synthesis of Hydrazide Derivatives

In the literature, 2-(quinolin-8-yloxy) acetohydrazide 45 was synthesized from 2-(quinolin-8-yloxy) acetate 44 and hydrazine hydrate 25 in ethanol after 15 hr. in 80% yield (Figure 2.2) (Mohammed and Subrahmanyam 2009, Hayat *et al.* 2010, Boukabcha *et al*. 2019, Althobiti and Zabin 2020).

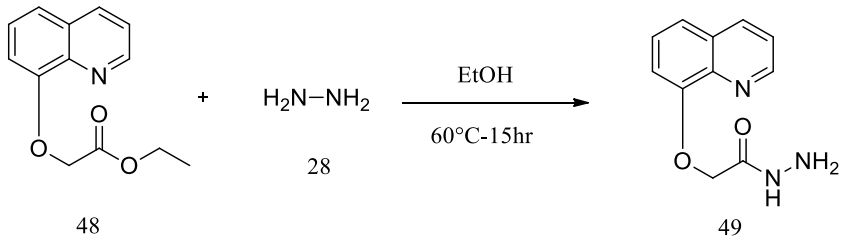


Figure 2.2 Preparation of 2-(quinolin-8-yloxy) acetohydrazide

2.3 Synthesis of Schiff bases

Literature survey shows that many Schiff bases exhibit biological activities such as antifungal (Jarrahpour *et al.* 2007), antibacterial (Mohammed & Subrahmanyam, 2009), antineoplastic (Islam *et al.* 2002), anti-inflammatory (Vazzana *et al.* 2004), and Anticonvulsant (Verma *et al.* 2004).

Compound 49 was used as a starting material for synthesis of Schiff bases using various aromatic aldehydes in the literature (Ahmed *et al*. 2006, Mohammed and Subrahmanyam 2009, Boukabcha *et al*. 2019, Althobiti and Zabin 2020).

Mohammed and Subrahmanyam wasreported synthesized of N'- arylidene -2-(quinolin-8-yloxy) aceto hydrazide from2-(quinolin-8-yloxy) acetohydrazide 45 and aromatic aldehydes in ethanol for 4-8 hr. (Figure 2.3) (Mohammed & Subrahmanyam, 2009).

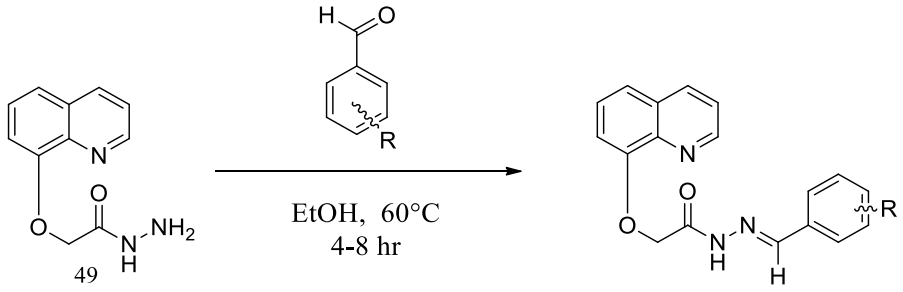


Figure 2.3 Preparation of N'- arylidene -2-(quinolin- 8 -yloxy) aceto hydrazide

2.4 Synthesis of Pyrazole

Pyrazoles were prepared by Heller using hydrazine and 1, 3-diketones. This method allows a fast and general synthesis of previously inaccessible Pyrazole and synthetically demanding Pyrazole containing fused ring (Figure 2.4) (Heller & Natarajan, 2006).

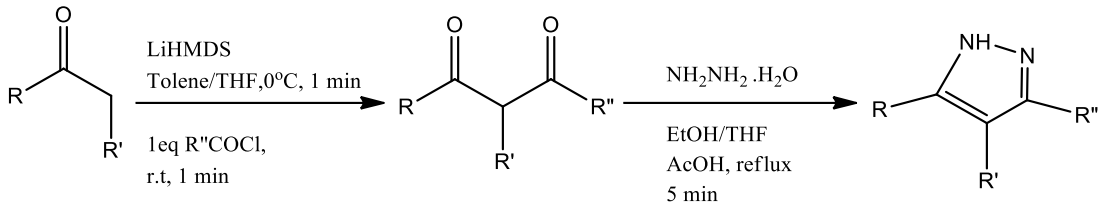


Figure 2.4 Preparation synthesis of pyrazole ring

Highly regioselective routes for synthesis of unsymmetrically substituted Pyrazole were reported by Kumar using active methylene ketones and aryl hydrazine. Substituted 1-aryl-3,5-bisarylpyrazoles was reported in high regioselectivity using easily accessible 1,3-bis aryl - monothio - 1,3 - diketone or 3-(methylthio) - 1,3 – bis aryl - 2 - propenones with aryl hydrazine in ethanol (Figure 2.5) (Kumar SV*et al*. 2013).

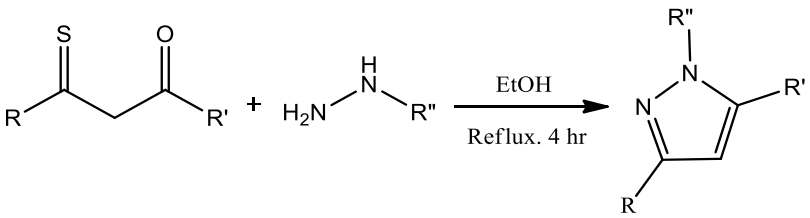


Figure 2.5 Preparation of pyrazole ring

3. MATERIALS AND METHODS

3.1 Chemical Used in Material Synthesis

All chemicals were used directly from Merck, Rhawn (China), Sigma-Aldrich suppliers, without further purification. The spectra (NMR) was measured on an Agilent 600 MHz spectrometer in DMSO, The multiplicities are defined as s = singlet, d = doublet, m = multiplet, dd = double doublet, q = quartet. The chemical shifts were recorded on the δ scale. All coupling constants are measured in Hertz.Infra-red spectra were recorded on a Shimadzu FTIR spectrophotometer. The melting points were recorded by means of Gallen Kamp's melting point tool, hot stage; also, they have been in corrected.

The synthesis of compounds (51-57) was achieved using a modified procedure for the conversion of ester to acid hydrazide (or condensation of acid hydrazide with aldehydes) (or for the cyclisation of acid hydrazide to Pyrazole) (Ahmed *et al*. 2006, Mohammed and Subrahmanyam 2009, Hayat *et al*, 2010, Kumar *et al*. 2013, Boukabcha *et al*. 2019, Althobiti and Zabin 2020).

3.2 General Procedure for Synthesis of Ester and Hydrazide and Schiff's bases and Pyrazole

3.2.1 Ethyl 2-(quinolin-8-yloxy) propanoate (51)

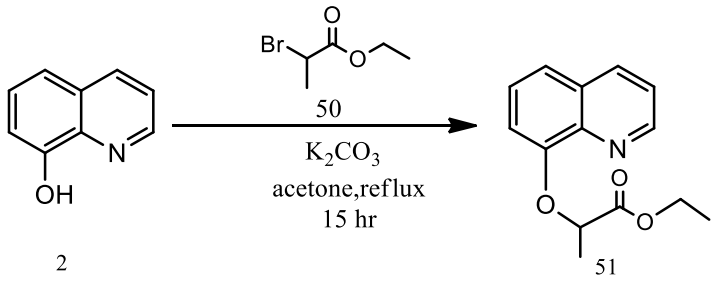


Figure 3.1 Preparation Ethyl 2-(quinolin-8-yloxy) propanoate (51)

A mixture of 8- hydroxy quinoline (0,04 mmol,7g) DL-ethyl 2-bromopropinoate (0,04 mmol,6,28 ml) and anhydrous potassium carbonate (0,06 mol, 9,9g) in dry acetone (60 ml) was refluxed on a water bath for 15 hr. The crude mixture was directly filtered to remove potassium carbonate, and then the filtrate was cooled, concentrated and then washed with methanol to provide a desired product a brown oil. (Yield 89%), IR (KBr) ν_{max} /cm^{-1}:3059 (Aromatic C-H stretch), 2937 (C-H stretch in CH_3/CH_2), 1746(C=O stretch), 1258, 1016 (sp^2 /sp^3 C-O stretch);^{1}H NMR (600 MHz, DMSO) δ 8.85 (1H ,dd, J = 4.0, 1.3 Hz,Ar*H*), 8.29 (1H ,dd, J = 8.2, 1.2 Hz,Ar*H*), 7.58 – 7.36 (**3**H,m,Ar*H*), 7.03 (1H ,d, J = 7.6 Hz,Ar*H*), 5.18 (1H ,q, J = 6.7 Hz,O-C*H*), 4.12 (2H ,q, J = 7.1 Hz,O-CH_2), 1.61 (3H ,d, J = 6.8 Hz,CH-CH_3), 1.13 (3H ,t, J = 7.1 Hz,O-CH_2-CH_3).;^{13}C NMR (151 MHz, DMSO) δ 176.68(C=O), 158.20 (ArC-O), 154.25 (C=N), 144.95 (ArC), 141.13 (ArC), 134.39 (ArCH), 131.73 (ArCH), 127.06 (ArCH), 125.95 (ArCH), 116.60 (ArCH), 78.09 (O-CH), 65.90 (O-CH_2), 23.61 (O-CH-CH_3), 19.16 (O-CH_2-CH_3).

3.2.2 2-(quinolin-8-yloxy) propanehydrazide (52)

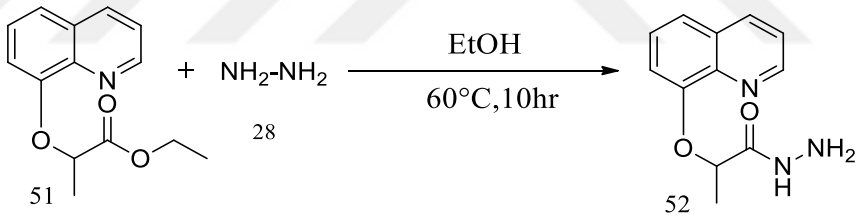


Figure 3.2 Preparation 2-(quinolin-8-yloxy) propanehydrazide (52**)**

Equimolar quantity of (51) (0.016 mol.4g) in absolute ethanol (50 ml), hydrazine hydrate (99%, 0.016 mol, 0,5 ml) was added and the reaction mixture was refluxed for 10 hrs. The solution was concentrated and allowed to cool overnight. The resulting solid obtained was filtered, washed with cold water, and recrystallized from ethanol. The compound was separated as white crystals (Yield 77%, m.p. 120–125°C).IR (KBr)ν_{max} : 3330, 3245 (N-H stretch), 3092 (C-H stretch in aromatics), 1427 (C-H stretch in CH_3/CH_2), 1650 (C=O stretch), 1260, 1038 (sp^2 /sp^3 C-O stretch) cm^{-1}; ^{1}H NMR (600 MHz, DMSO) δ 9.63 (1H ,s, NH-), 8.88 (1H ,dd, *J* = 4.1, 1.6 Hz, Ar-H), 8.33 (1H ,dd, J = 8.3, 1.6 Hz, Ar-H), 7.67 – 7.40 (3H ,m, Ar-H), 7.24 (1H ,d, J = 7.2 Hz, Ar-H), 4.92

(1H ,q, J = 6.6 Hz, O-CH), 4.28 (2H ,s,-NH_2), 1.56 (3H ,d, J = 6.7 Hz,CH_3) ; ^{13}C NMR (151 MHz, DMSO) δ 175.41 (C=O), 158.65 (ArC-O), 154.55 (C=N), 145.38 (ArC), 141.40 (ArC), 134.41 (ArCH), 131.96 (ArCH), 127.15 (ArCH), 126.41 (ArCH), 118.50 (ArCH), 80.96 (O-CH), 24.27 (CH_3).

3.2.3 General procedure for the synthesis of (E)-N'-benzylidene-2-(quinolin-8-yloxy) propanehydrazide (53a-f)

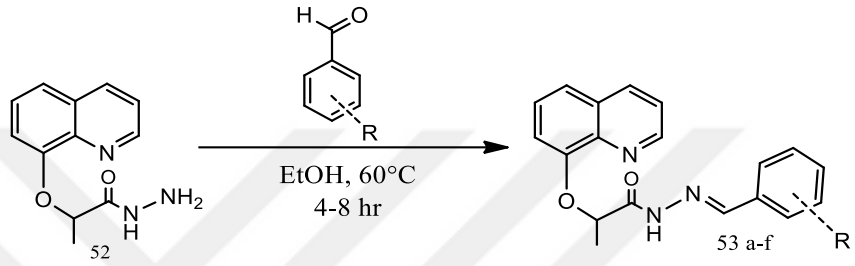


Figure 3.3 Preparation general for the synthesis of Schiff bases (53a-f)

Equimolar quantity of the hydrazide compound (52) (0.002mol, 0.5g) and aromatic aldehydes (0.002mol) in ethanol (25 ml) were heated on a water bath for 6-8 hrs. The resulting Schiff's bases (53a-f) were cooled and poured into crushed ice. The precipitate that obtained was filtered washed with cold water and purified by recrystallized from ethanol, Table (3.1) Table (3.2).

Table 3.1 Physicochemical and spectral data of the compounds (53a-f)

NO.	R	Molecular formula	Yield %[a]	Color
53-a	3-NO_2	$C_{19}H_{16}N_4O_4$	80	White
53-b	4-NO_2	$C_{19}H_{16}N_4O_4$	77	Pale-yellow
53-c	4-Br	$C_{19}H_{16}BrN_3O_2$	68	White
53-d	4-Cl	$C_{19}H_{16}ClN_3O_2$	65	White
53-e	4-OH	$C_{19}H_{17}N_3O_3$	70	Yellow
53-f	Furfural	$C_{17}H_{15}N_3O_3$	60	Off white

a: Yield was determined by Proton ^{1}H NMR spectrum of crude mixture

Table 3.2 ^{1}H NMR, ^{13}C NMR of compounds (53a-f)

NO.	^{1}H NMR (600 MHz, DMSO)δ	^{13}C NMR (151 MHz, DMSO)δ
53-a	9.03 (1H, dd, *J* = 4.2, 1.7 Hz, ArH), 8.53 (1H ,s, CONH), 8.46 (1H, s, N=CH), 8.38 (3H , dd, *J* = 8.3, 1.7 Hz, ArH), 7.75 – 7.40 (5H ,m, ArH), 6.96 (1H ,dd, *J* = 6.9, Hz, ArH), 5.94 (1H , q, *J* = 6.6 Hz, OCH), 1.67 (3H , dd, *J* = 9.1, 6.6 Hz, CH_3).	168.66(C=O), 153.92(ArC-O), 150.06(ArC), 148.63(ArC=N), 146.01(N-C=N), 140.68(ArC), 136.85(ArC), 136.42(ArCH), 133.71(ArCH), 130.85(ArCH), 129.66(ArC), 127.33(ArCH), 124.82(ArCH), 122.55(ArCH), 122.36(ArCH), 121.71(ArCH), 114.98(ArCH), 77.36(OCH), 19.38(CH_3).
53-b	9.01 (1H, dd, *J* = 4.2, 1.7 Hz, ArH), 8.44 (1H , s, CONH), 8.38 (1H , dd, *J* = 8.4, 1.7 Hz, ArH), 8.29 – 8.25 (1H ,m, ArH), 8.23 – 8.19 (1H ,m, ArH), 8.11 (1H ,s, N=CH), 7.98 – 7.85(2H ,m, ArH), 7.65 – 7.42 (3H, m, ArH), 6.95 (1H, dd, *J* =7.8, 1.3 Hz, ArH), 5.93 (1H ,q, *J* = 6.6 Hz, OCH), 1.67 (3H, t, *J* = 6.9, Hz,CH_3)	168.74(C=O), 153.88(ArC-O), 150.00(ArC), 149.43(ArC=N), 148.48(N-C=N), 146.00(ArC), 142.17(ArC), 140.83(ArCH), 136.83(ArCH), 128.56(**2x**ArCH), 127.32(ArC), 124.45(**2x**ArCH), 122.55(ArCH), 122.33(ArCH), 114.84(ArCH), 77.23(OCH), 19.5(CH_3)
53-c	9.00 (1H, dd, *J* = 4.2, 1.7 Hz, ArH), 8.37(1H ,dd, *J*=8.4, 1.7, Ar*H*), 8.31 (1H, s, CONH), 7.99 (1H, s, N=CH), 7.68 – 7.38 (6H ,m, Ar*H*), 7.31 (1H ,d, *J* = 7.6 Hz, Ar*H*), 6.92 (1H ,d, *J* = 7.6, 1.3, Hz, Ar*H*), 5.88 (1H ,q, *J* = 6.6 Hz, OCH), 1.66 (3H ,dd, *J*= 10.7, 6,6, CH_3).	168.36(C=O), 153.91(ArC-O), 149.95(ArC=N), 147.16(N-C=N), 143.34(ArC), 140.64(ArC), 136.80(ArCH), 133.79(ArCH), 132.23(**2x**ArCH), 129.47(**2x**ArCH), 129.20(ArC), 127.32(ArC), 122.54(ArCH), 122.23(ArCH), 114.69(ArCH), 77.21(O-CH), 19.43(CH_3).

53-d	8.99 (1H, dd, *J* = 4.2, 1.7 Hz, ArH), 8.36 (1H , dd, *J* = 8.3, 1.7 Hz, Ar*H*), 8.32 (1H, s, CONH), 8.01 (1H, s, N=CH), 7.74-7.40, (6H ,m,Ar*H*), 7.31 (1H ,dd, *J* = 7.7 Hz,Ar*H*), 6.92 (1H, d, *J* = 7.6 Hz,ArH), 5.88 (1H ,q, *J* = 6.6 Hz,OCH), 1.66 (3H , dd, *J* = 10.1, 6.6 Hz, CH_3).	168.34(C=O), 153.92(ArC-O), 149.97(ArC=N), 147.07(N-C=N), 143.23(ArC), 140.64(ArC) 136.80(ArC), 135.06(ArCH), 133.45(ArCH), 129.33(**2x**ArCH), 129.24(2xArCH), 128.98(ArC), 127.32(ArCH), 122.54(ArCH), 114.70(ArCH), 77.36(OCH), 19.43(CH_3).
53-e	9.91 (1H, s, OH), 8.98 (1H , dd, *J* = 4.2, 1.7 Hz, ArH), 8.36 (1H, dd, *J* = 8.3, 1.7 Hz,ArH), 8.20 (1H, s, CONH), 7.93 (1H, s, N=CH), 7.64-7.56 (2H, m, ArH), 7.54 – 7.40 (4H, m,ArH), 7.31 (1H, m,ArH), 6.83 – 6.75 (2H , m, ArH), 5.83 (1H ,q, *J* = 6.6 Hz,OCH), 1.65 (3H ,dd, *J* = 9.6, 6.6 Hz,CH_3).	167.81(C=O), 159.92(ArC), 153.97(ArC-O), 149.91(ArC=N), 148.59(N-C=N), 136.78(ArC), 129.72(ArC), 129.39(2xArCH), 129.05(ArCH), 127.33(ArCH), 125.43(ArC), 122.53(ArCH), 122.13(ArCH), 116.12(2xArCH), 114.66(ArCH), 77.24(OCH), 19.53(CH_3).
53-f	9.00 (1H ,dd, *J* = 4.2, 1.7 Hz, ArH), 8.33 (1H, s, CONH), 8.03 (1H, s, N=CH), 7.70 – 7.68 (1H ,m, Ar*H*), 7.64-7.58 (2H ,m, Ar*H*), 7.53 – 7.50 (1H, m, ArH), 7.44 – 7.29 (4H , m, ArH), 5.88 (1H,q, *J* = 6.6 Hz, OCH), 1.67 (3H ,t, *J* = 6.8 Hz, CH_3).	168.23(C=O), 153.94(ArC-O), 149.95(ArC=N), 149.32(ArC), 148.37(N-C=N), 144.49(ArCH), 140.66(ArC), 136.80(ArCH), 129.23(ArC), 127.61(2xArCH), 127.32(ArCH), 122.54(ArCH), 122.11(ArCH) 114.68(ArCH), 77.22(OCH), 19.46(CH_3)

3.2.4 1-(3,5-dimethyl-1H-pyrazol-1-yl)-2-(quinolin-8-yloxy) propan-1-one (55)

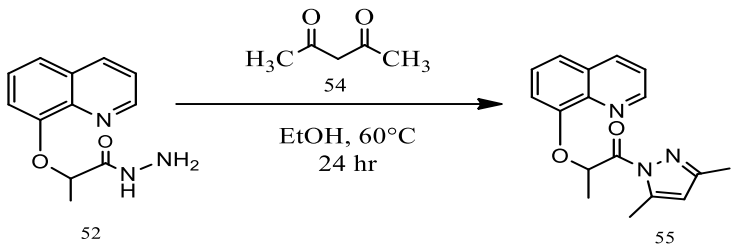


Figure 3.4 Preparation 1-(3.5-dimethyl-1H-pyrazol-yl)-2-(quinoline-8-yloxy) propan-1-one (55)

Equimolar quantity of the acid hydrazide (52) (0.002mol, 0.5g) and acetyl acetone (54) (0.002mol, 0.21 ml) in ethanol (25 ml) were heated on a water bath for 24 hrs. The resulting mixture was cooled and poured into crushed ice. The precipitate that obtained was filtered washed with cold water and purified by recrystallized from ethanol to provide the product as a white solid (yield 80% m.p167-144**ºC**); ^{1}H NMR (600 MHz, DMSO) δ 8.85-8.86 (1H, m, ArC*H*), 8.39 – 8.14 (1H ,m, ArC*H*), 7.60 – 7.29 (3H ,m, ArC*H*), 6.91- 6.66 (1H ,m, ArC*H*), 6.44 (1H ,s, NC=CH), 5.72 – 5.45 (1H ,m,O-CH), 1.99-2.00 (3H ,d, *J* = 6.2 Hz, N=C-CH_3), 1.70-1.73 (3H ,d, *J* = 1.58 Hz,N-C-CH_3), 1.58-1.55(3H, dd, *J*=6,3 9.5 H_Z, O-CH-C$\underline{H_3}$); ^{13}C NMR (151 MHz, DMSO) δ 168.73 (C=O), 156.36 (ArC-O), 153.82 (ArC=N), 149.38 ($CH_3\underline{C}$=C), 149.35 (CH_3-C=$\underline{C}$), 139.97 (ArC), 136.21 (ArCH), 129.50 (ArC), 127.08 (ArCH), 122.26 (ArCH), 120.21 (ArCH), 110.04 (ArCH), 91.05, (CH_3-C=$\underline{CH}$), 72.15 (OCH), 18.49 (C=C-$\underline{C}H_3$), 17.84 (N=C-CH_3), 16.43 (O-CH-CH_3).

3.2.5 1-(3-methyl-5-phenyl-1H-pyrazol-1-yl)-2-(quinolin-8-yloxy)propan-1-one (57)

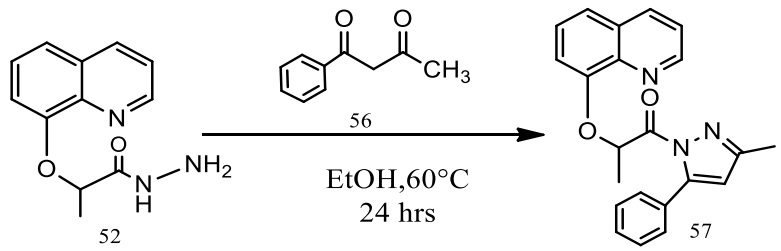


Figure 3.5 1-(3-methyl-5-phenyl-1H-pyrazol-1-yl)-2-(quinolin-8-yloxy)propan-1-one (57)

Equimolar quantity of the acid hydrazide (52) (0.002mol, 0.5g) and benzoyl acetone (56) (0.002mol, 0.21 ml) in ethanol (25 ml) were heated on a water bath for 24 hrs. The resulting mixture were cooled and poured into crushed ice. The precipitate that obtained was filtered washed with cold water and purified by recrystallized from ethanol to provide the product as a yellow solid (yield 80% m.p175-155°C). ^{1}H NMR (600 MHz, DMSO) δ 8.80 (1H , dd, *J* = 4.4, 2.0 Hz, ArC*H*), 8.28-8.21 (1H ,m, ArC*H*), 7.51 – 7.17 (9H ,m, Ar*H*), 6.91 (1H ,br s, NC=CH), 5.66 (1H , q, *J* = 6.5 Hz, O-CH), 2.06 (3H ,s, N=C-CH_3), 1.60 (3H ,t, *J* = 6.6 Hz,CH_3); ^{13}C NMR (151 MHz, DMSO) δ 167.56 (C=O), 155.83 (ArCO), 153.67 (ArC=N), 149.31 (Ph<u>C</u>=C), 144.11 (CH_3C=C), 139.93 (ArC), 136.11(2xArC), 129.51(ArC), 128.16 (2xArCH), 126.92 (ArCH), 124.78 (3xArCH), 122.24 (ArCH), 120.28 (ArCH), 110.28 (ArCH), 92.51(C=<u>C</u>H), 71.90 (O-CH), 17.92 (N=C-<u>C</u>H_3), (16.33) (O-CH-<u>C</u>H_3)

4. RESULTS AND DISCUSSIONS

This work includes the synthesis of new heterocyclic compounds from the preparation of ester, hydrazide, and its condensation with a different of aldehydes and the preparation of new Pyrazole compounds from the reaction of hydrazide with two types of acetyl acetone, benzoyl acetone (Figure 4.1).

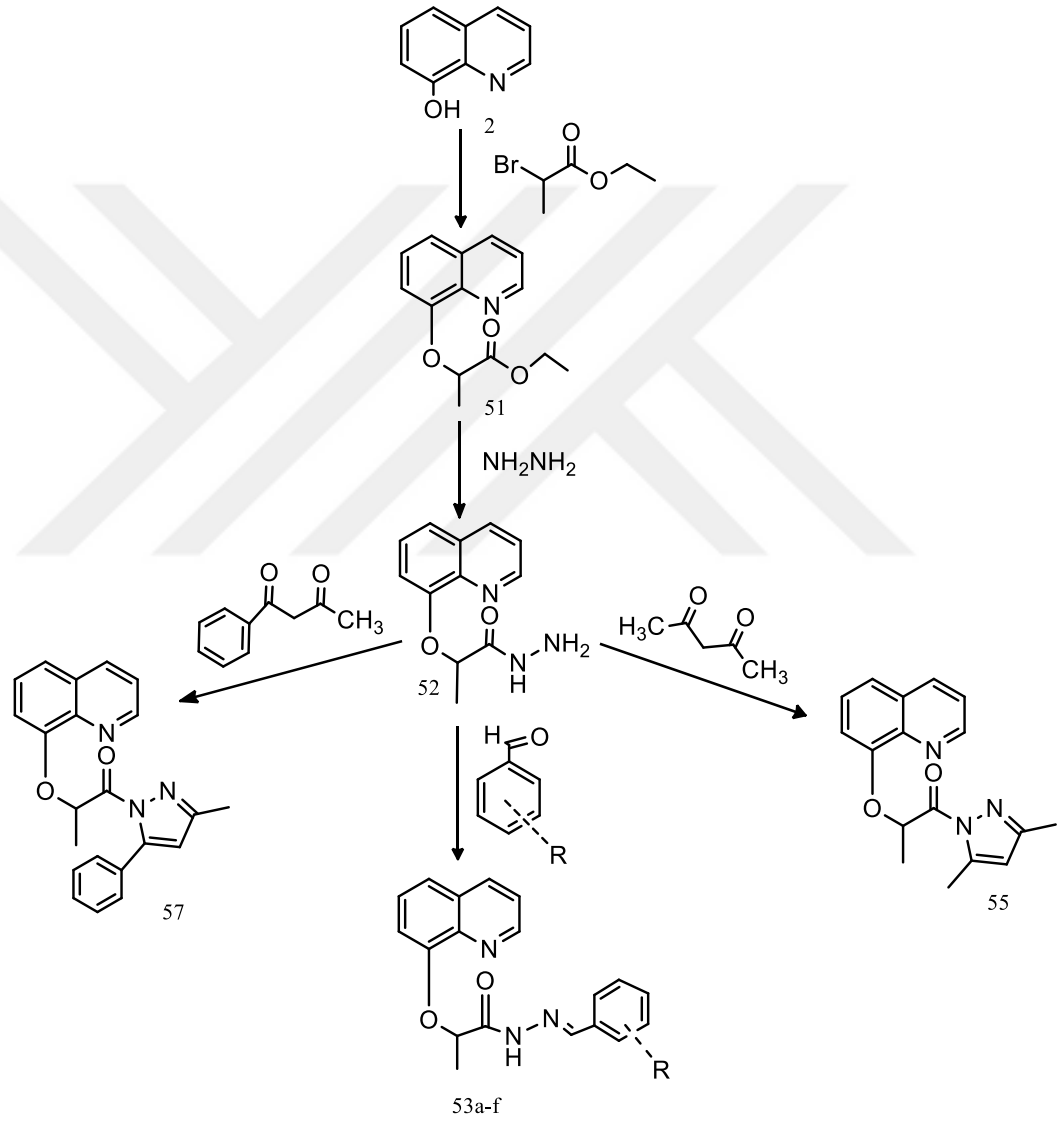


Figure 4.1 synthetic routes for the prepared compounds

We prepared the compound (51) by mixing 8HQ, and DL-ethyl 2-bromopropinoate, potassium carbonate, via S_N2 attack. As shown below (Figure 4.2) (Figure 4.3)

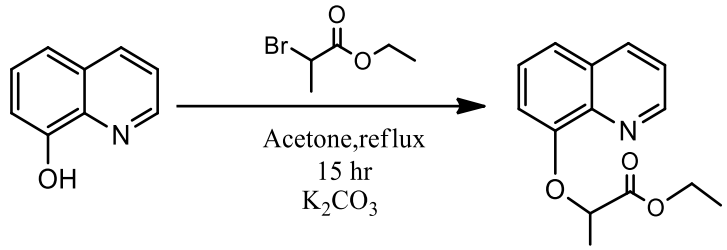


Figure 4.2 Preparation ethyl 2-(quinolin-8-yloxy) propanoate 51

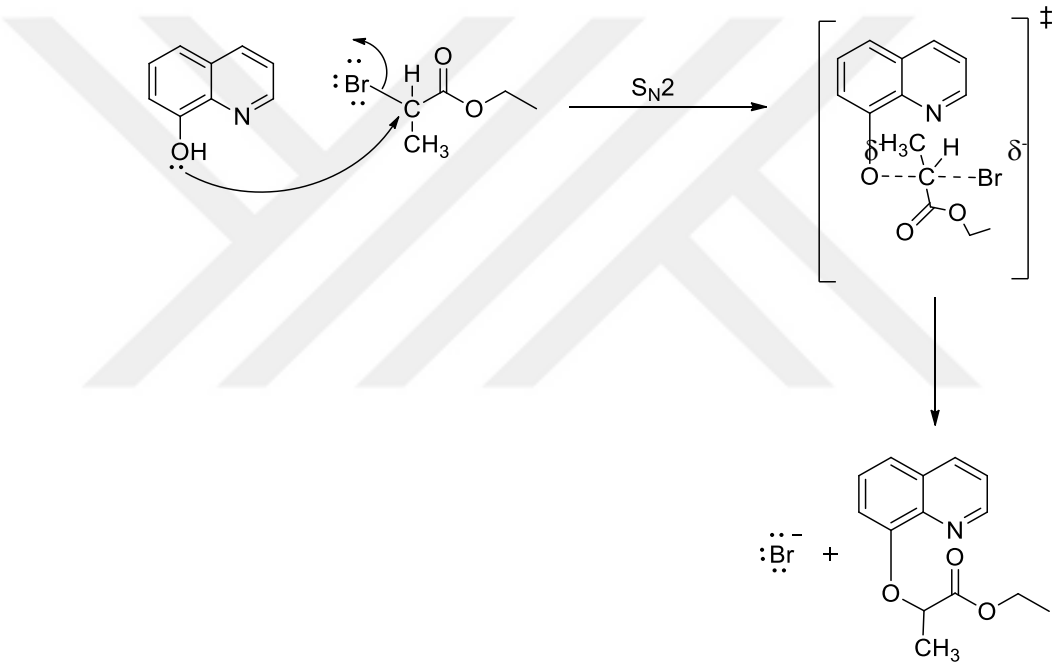


Figure 4.3 Mechanism steps for preparation of ethyl 2-(quinolin-8-yloxy) propanoate 51

The FTIR spectra of compound (51) showed the new peak was appeared at (1746) cm^{-1} which is attributed to a new (C=O) group and the appearance of 3040 (C-H stretch in CH_3/CH_2) as shown in (Figure 4.4).

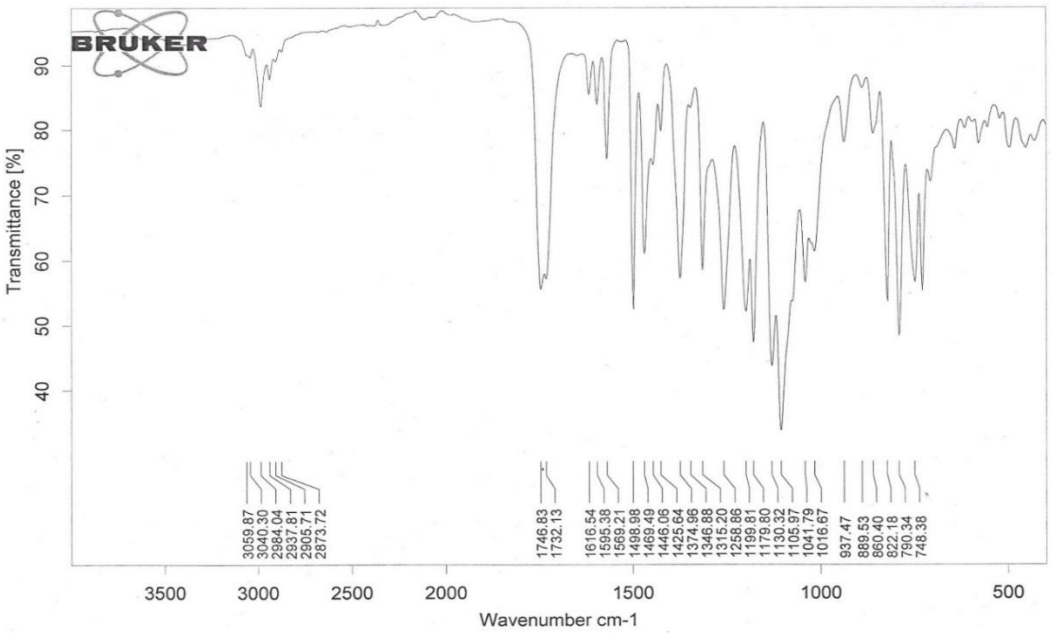


Figure 4.4 IR spectrums for compound 51

Determination of compound 51 by ^{1}H NMR spectra:

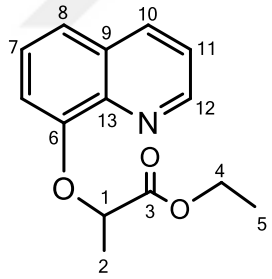


Figure 4.5 Ethyl 2-(quinolin-8-yloxy) propanoate (51)

The structure of (51) was determined by the use of ^{1}H NMR spectra. It was found that one protonate C-1 appears as quartet at 5.18 ppm (O-CH), two protons at C-4appears as quartet at 4.12 ppm (O-CH_2), three protons at C-2 appear as a doubled at 1.61 ppm (O-CH-*CH_3*), three protons at C-5 appears as triplet at 1.13 ppm (O-CH_2-*CH_3*) (Figure 4.6).

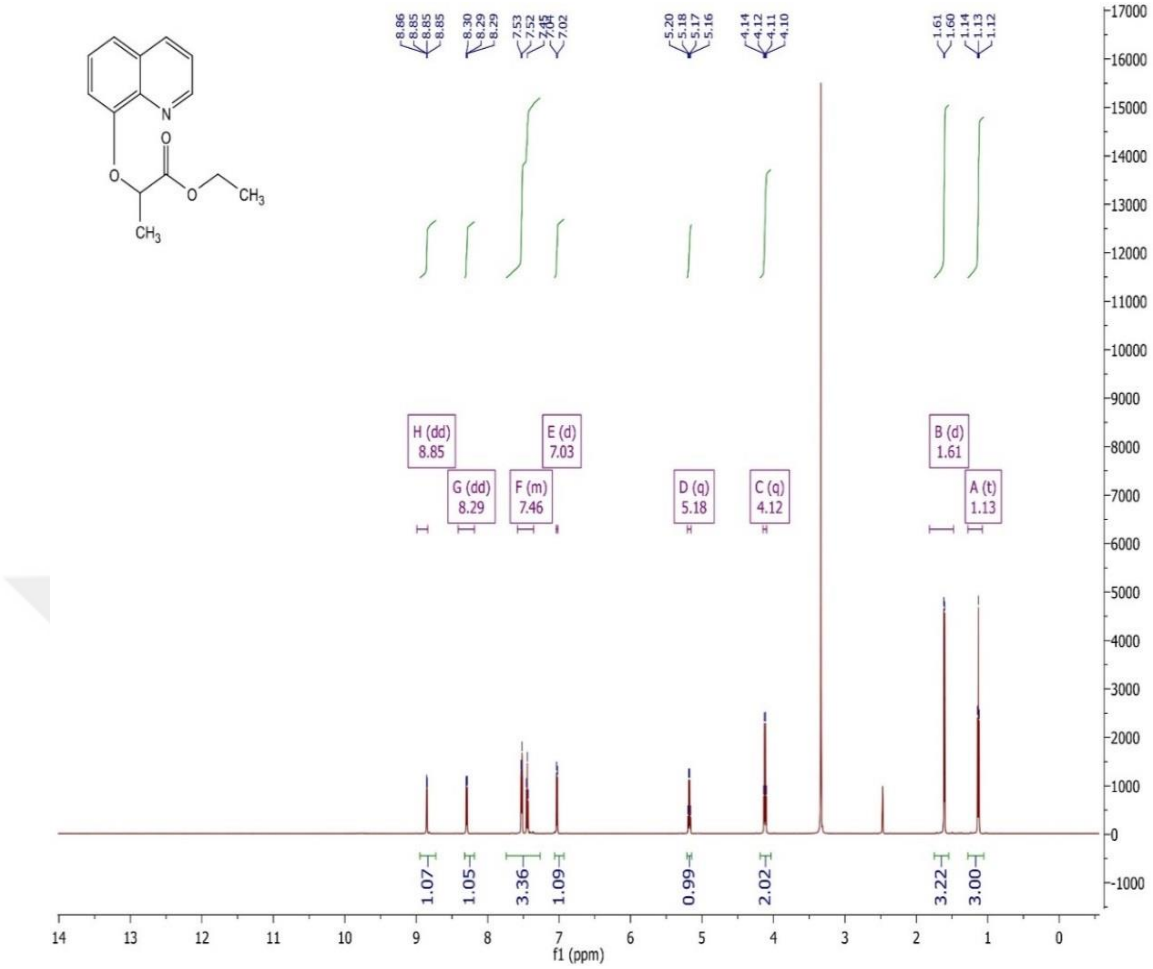


Figure 4.6 ^{1}H NMR spectra of compound 51

^{13}C NMR spectra of compound 51 showed these results measured by ppm: 176.68 (C=O), 158.20(ArC-O), 154.25(C=N), 144.95(ArC), 141.13(ArC), 134.39(ArCH), 131.73 (ArCH), 127.06(ArCH), 125.95(ArCH), 116.60(ArCH), 78.09(O-CH), 65.90(O-CH_2), 23.61(CH-$\underline{CH_3}$), 19.16(CH_2-$\underline{CH_3}$) (Figure 4.7).

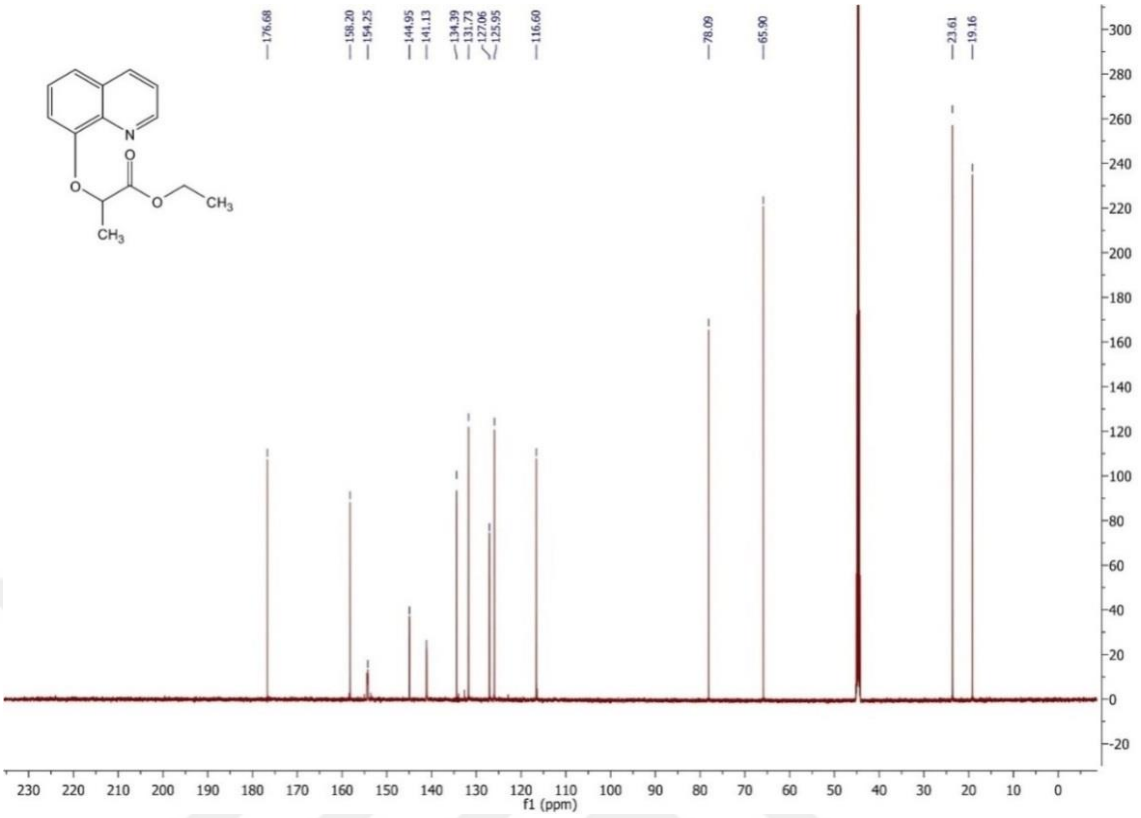


Figure 4.7 ^{13}C NMR spectra compound 51

Compound (52) was prepared starting from compound (51) and hydrazine. The treatment of compound (51) with hydrazine in ethanol at 60ºC, afforded the desired compound (52) in good yield as shown in (Figure 4.8).

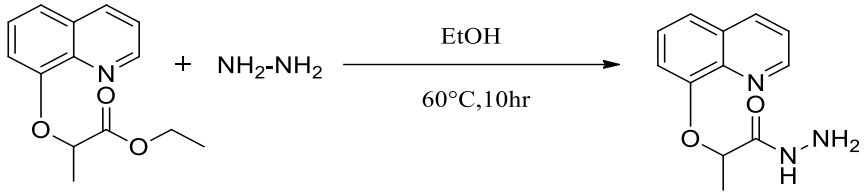


Figure 4.8 Preparation 2-(quinoline-8-yloxy) acetohydrazide compound 52

A probable mechanism for the formation of 2-(quinoline-8-yloxy) acetohydrazide 52. The mechanism is similarly like Wolff-Kishner reduction. First hydrazine attack on the carbonyl carbon of ester followed by elimination of ethoxide base then removal of proton to form hydrazide as shown (Figure 4.9).

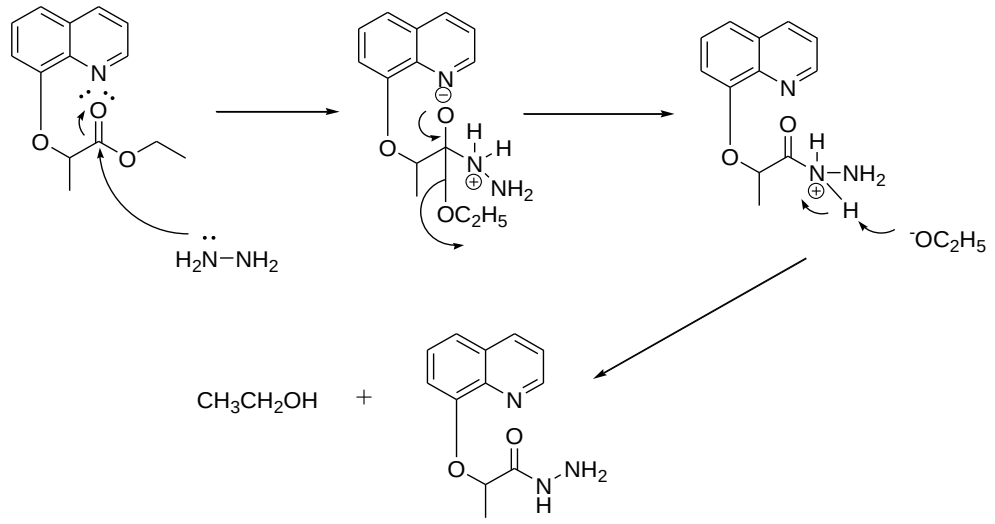


Figure 4.9 Mechanism steps for preparation of 2-(quinoline-8-yloxy) acetohydrazide 52

The FTIR spectra of compound (52) which show the following characteristic absorption bands. The C=O stretching 1650 $cm^{-1}$and N-H stretching 3330, 3245 cm^{-1} was assigned in the infrared spectra as show below (Figure 4.10)

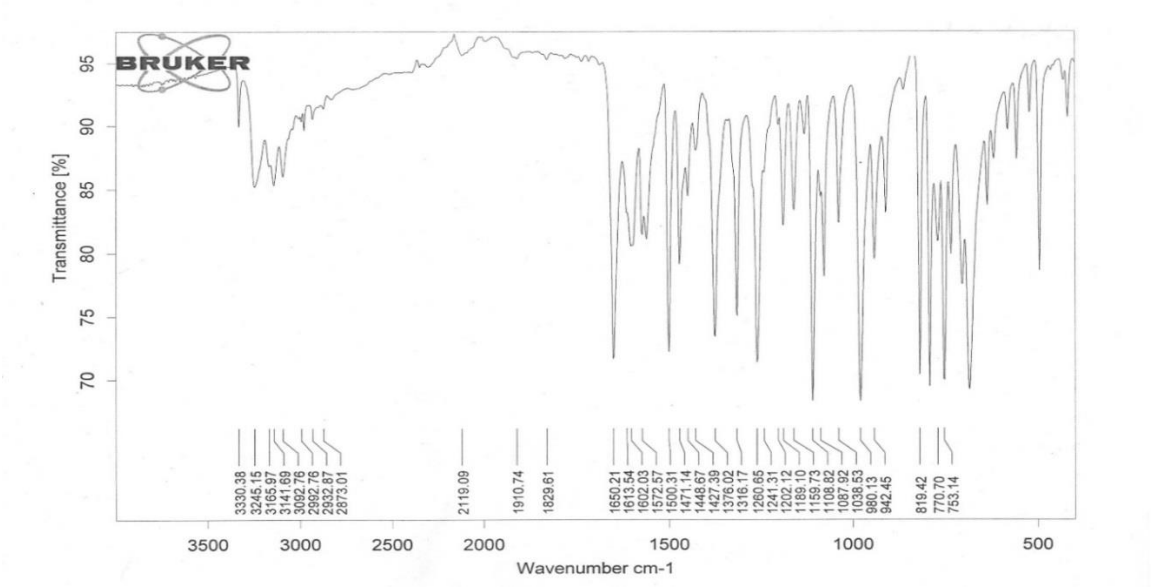


Figure 4.10 FTIR spectra of compound 52

Determination of compound 52 by ^{1}H NMR spectra:

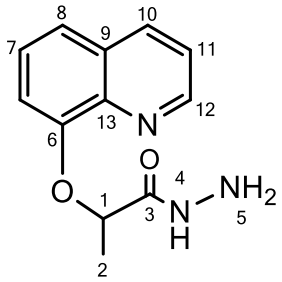


Figure 4.11 2-(quinolin-8-yloxy) propanehydrazide (52)

The structure of (52) was determined by $^{1}HNMR$ spectra. It was found that NH proton appears as singlet at 9.63 ppm, H at C-1appear as quartet at 4.92 ppm (O-CH), two NH_2 protons appears as singlet at 4.28 ppm, three protons at C-2 appears as doublet at 1.56 ppm (CH_3) as shown below in (Figure 4.12).

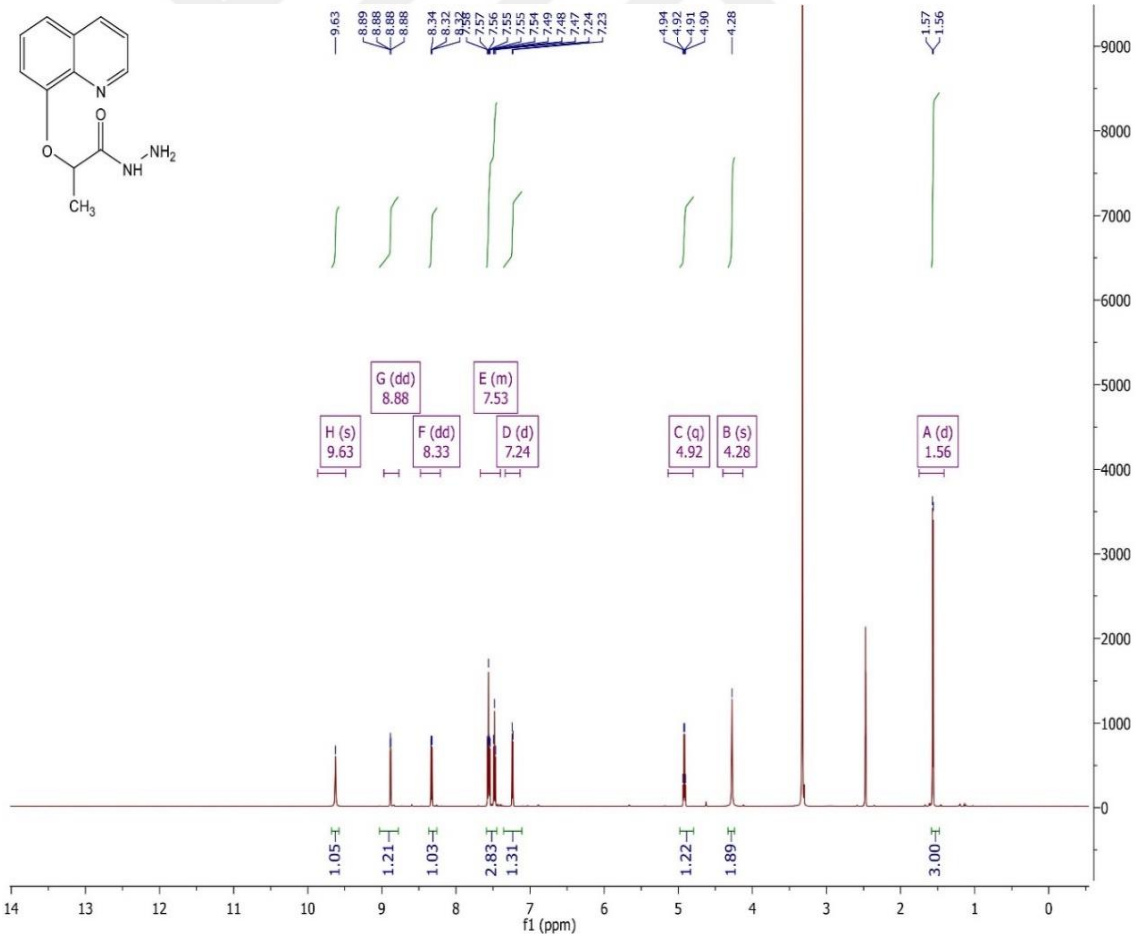


Figure 4.12 ^{1}H NMR spectra of compound 52

^{13}C NMR spectra of compound (52) showed these results measured by ppm: 175.41 (C=O), 158.65 (ArC-O), 154.55 (C=N), 145.38 (ArC), 141.40 (ArC), 134.41 (ArCH), 131.96 (ArCH), 127.51 (ArCH), 126.41 (ArCH), 118.50 (ArCH), 80.96 (O-CH), 24.27 (CH_3) (Figure 4.13).

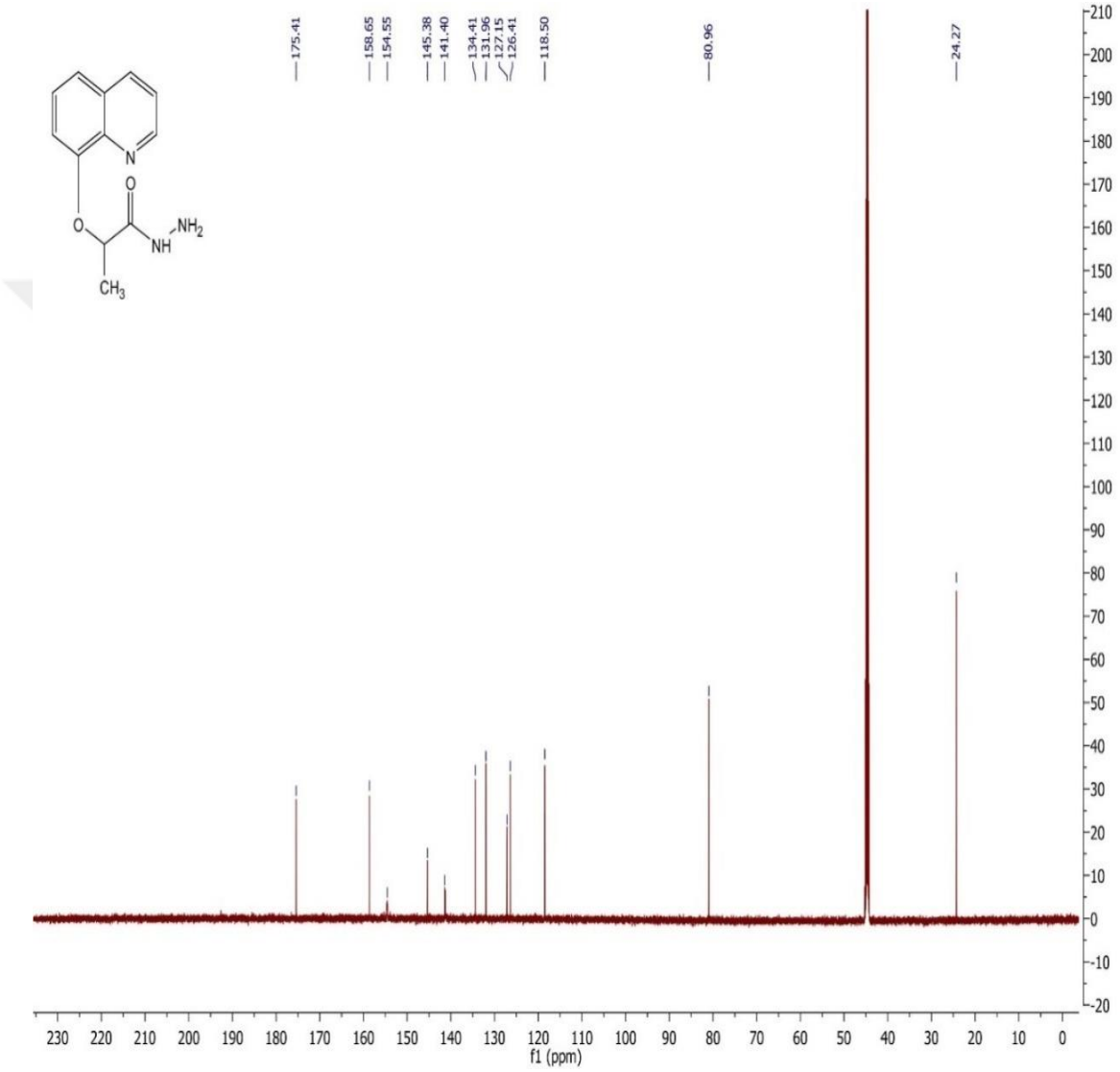


Figure 4.13 ^{13}C NMR spectra of compound 52

NOTE:

It was found that purification of imines derivatives (53a-f) was tricky because of retardation factors of both the desired compound and the impurities (the excess of aldehyde or hydrazide) are very close which causes difficulties to purify the desired compounds via crystallization or column chromatography. Table (4.1) shows the approximately purity of these compounds depends on ^{1}H-NMR.

Table 4.1 the approximately purity of these compounds (53a-f)

Compounds NO.	The desired compound %[a]	The impurities (aldehyde or acidhydrazide)
53-a	80%	20%
53-b	77%	23%
53-c	68%	32%
53-d	65%	35%
53-e	70%	30%
53-f	60%	40%

a: Yield was determined by Proton 1H NMR spectrum of crude mixture

Compound 52 reacted with an equal amount of various aldehydes in ethanol after 4 to 8 hr. at 60°C Schiff's bases (53a-f) were obtained as shown in (Figure 4.14).and (Figure 4.15).

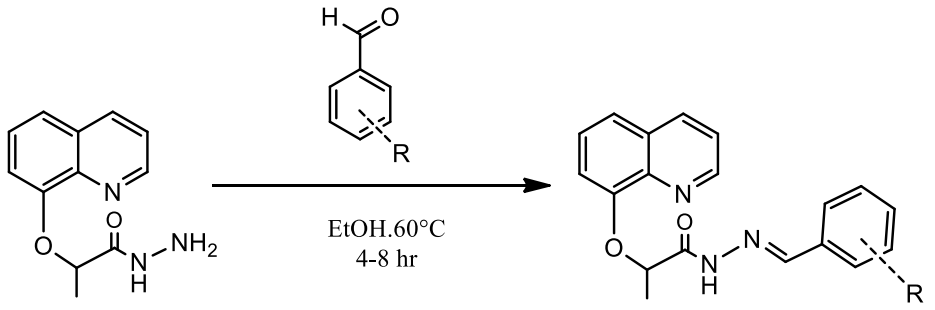


Figure 4.14 Preparation (E)-N'-benzylidene-2-(quinolin-8-yloxy) propane-hydrazide (53a-f)

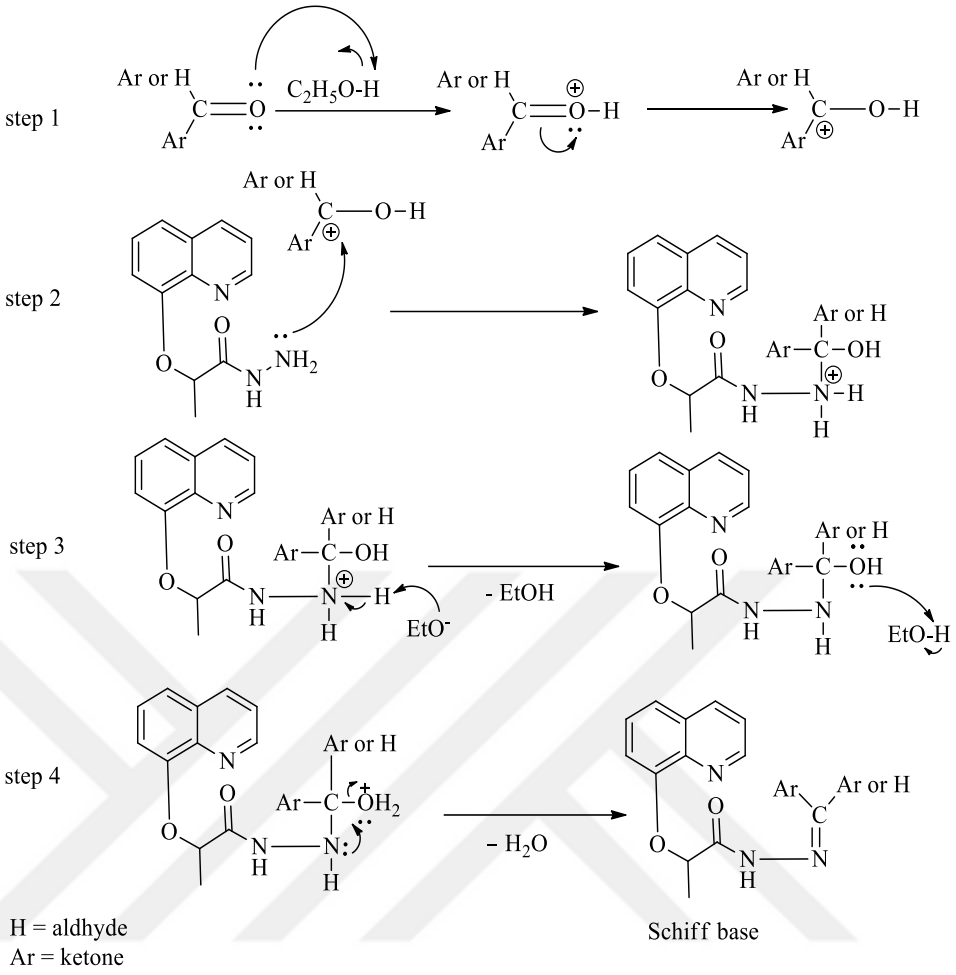


Figure 4.15 Mechanism steps for preparation of schiff bases (53a-f)

Determination of compound (53- a) by ^{1}H NMR:

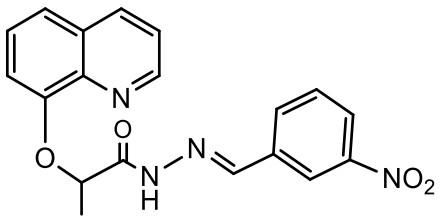


Figure 4.16 (E)-N'-(3-nitrobenzylidene)-2-(quinolin-8-yloxy) propanehydrazide (53- a)

The structure of (53-a) was determined by the use of ^{1}H NMR spectra. It was found that H at N-1 appears as singlet at 8.53 ppm (CONH) and (N=CH) appears as singlet at 8.46 ppm, H at C-1 appears as quartet at 5.94 ppm (-OCH), three protons at C-2 appears as multiplet at 1.67 (CH_3) ppm (Figure 4.17).

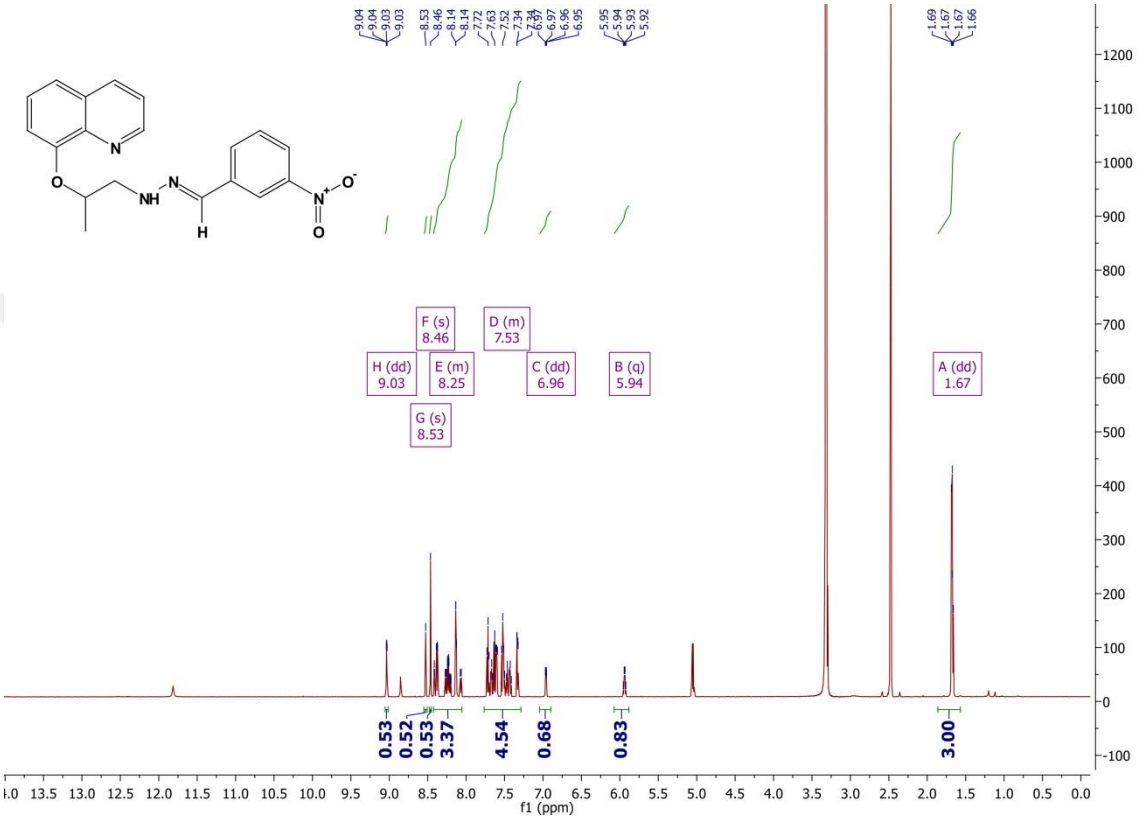


Figure 4.17 ^{1}H NMR spectra compound of 53-a

^{13}C NMR of this compound showed these results measured by ppm: 168.66 (C=O), 153.92 (ArC-O), 150.06 (ArC), 148.63 (ArC=N), 146.01 (N-C=N), 140.68 (ArC), 136.85 (ArC), 133.71 (ArCH), 130.85 (ArCH), 129.75 (ArC), 127.33 (ArCH), 124.82 (ArCH), 122.55 (ArCH), 122.36 (ArCH), 121.71 (ArCH), 114.98 (ArCH), 77,36 (-OCH), 19,38 (CH_3) (Figure 4.18).

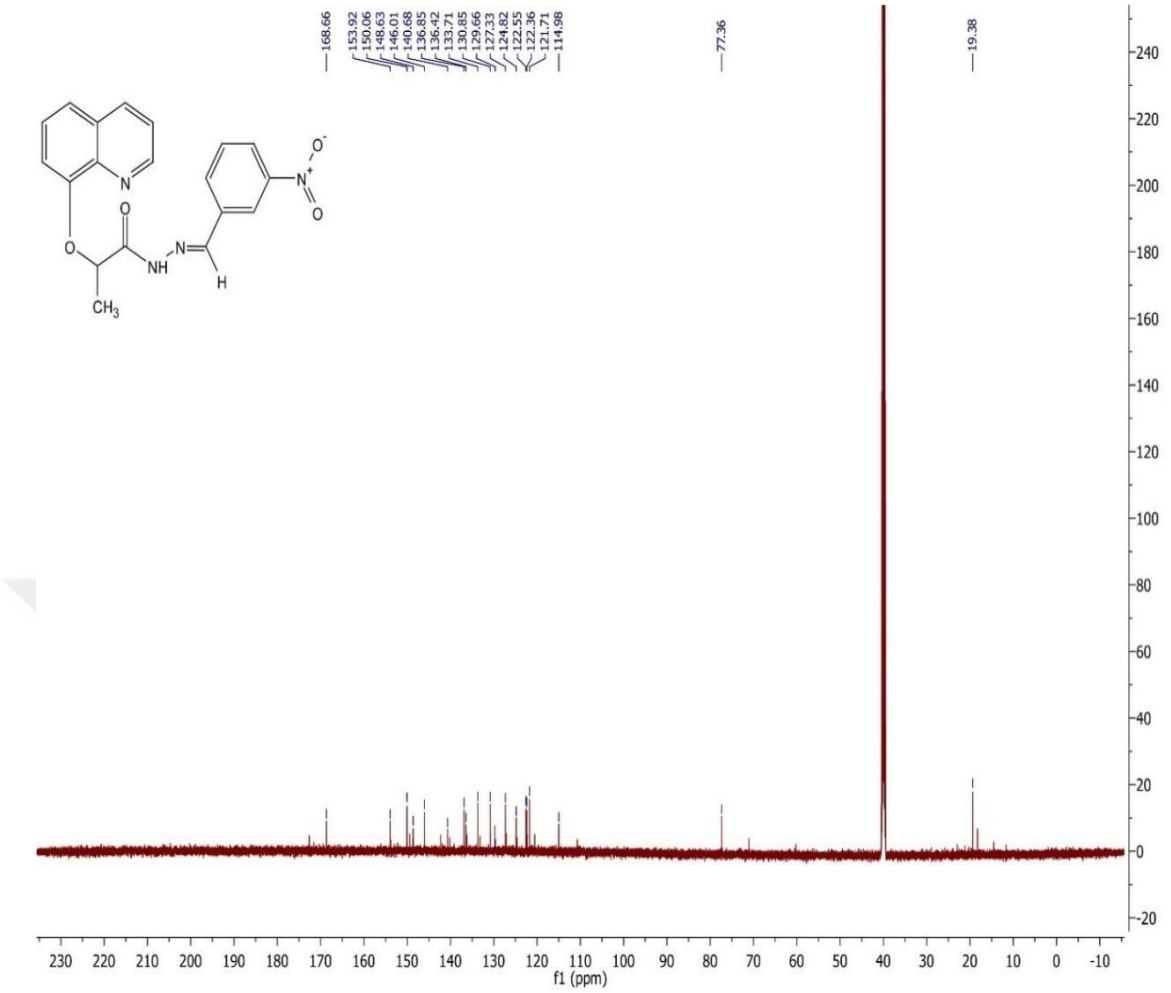


Figure 4.18 ^{13}C NMR spectra compound of 53-a

The Pyrazole compound 57 was synthesized in the final step of our work by mixing equal quantities of compound 52 and benzoyl acetone 56 with ethanol for 24 hours at 60 °C, the desired compound obtained in 80% yield as shown in (Figure 4.19).

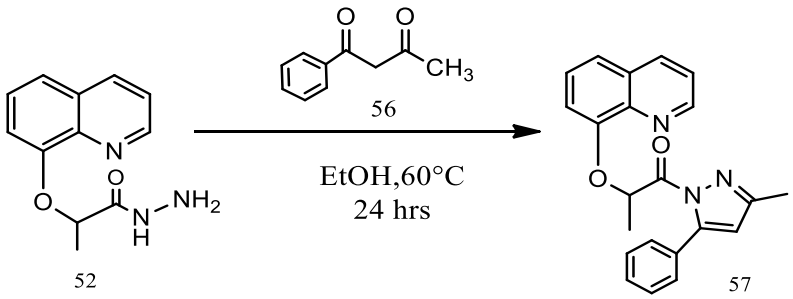


Figure 4.19 Preparation of pyrazol compound 57

Reasonable mechanism for formation of pyrazole (55) shown in (Figure 4.20) (Amaranth *et al*. 1991, Flood *et al.* 2018).

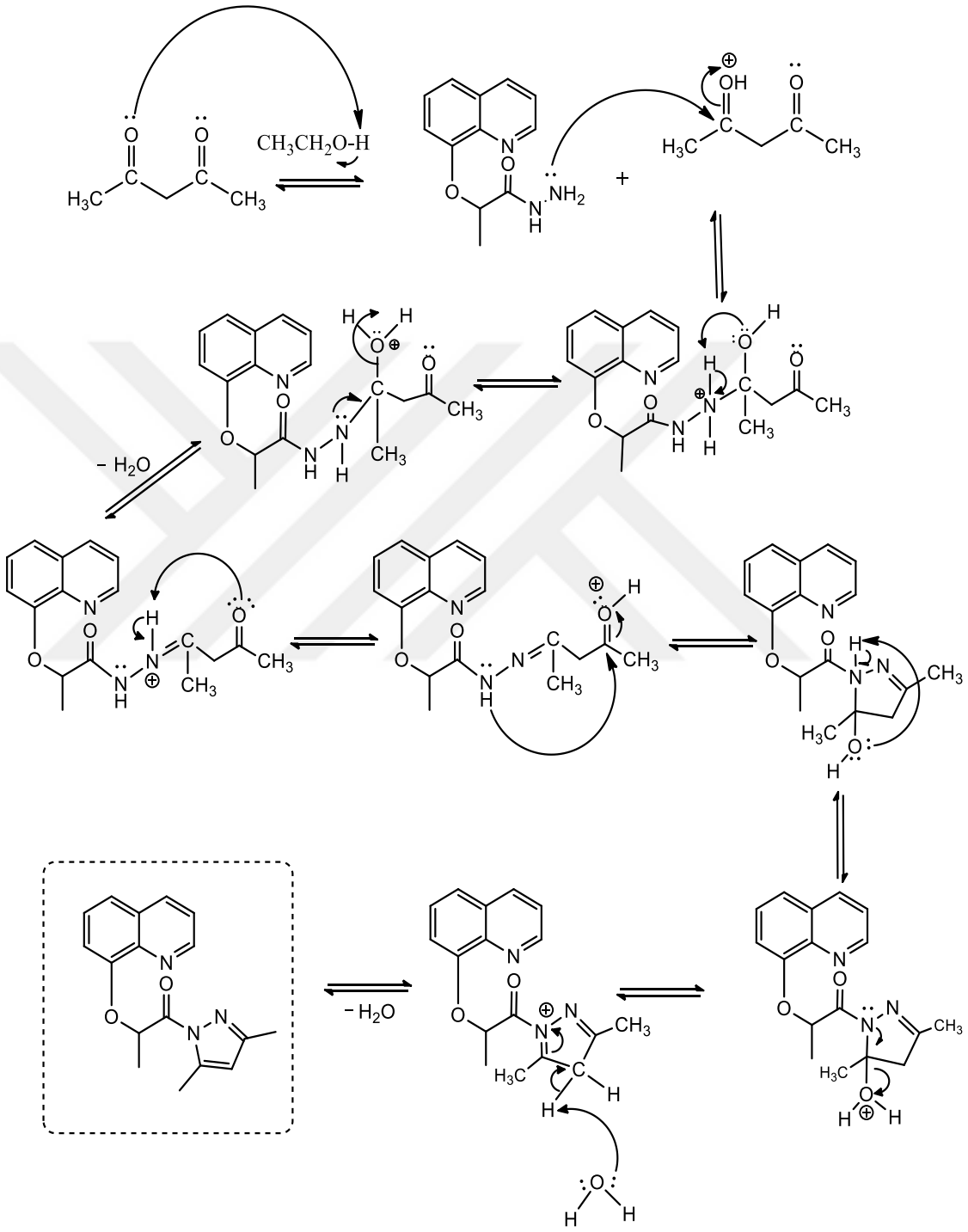


Figure 4.20 Mechanism steps for preparation of pyrazole (55)

Determination of compound 57 by ^{1}H NMR:

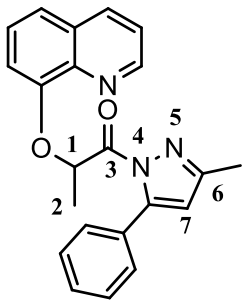


Figure 4.21 1-(3-methyl-5-phenyl-1H-pyrazol-1-yl)-2-(quinolin-8-yloxy) propan-1-one 57

The structure of 57 was determined by the use of $^{1}HNMR$ spectra. It was found that H at C-7 appears as singlet at 6.9 (NC=CH) ppm, C-1 appears as quartet at 5.64 (-OCH) ppm, three protons at C-6 appear as singlet at 2.07 ppm, three protons at C-2 appears as doublet at 1.60 ppm (Figure 4.22).

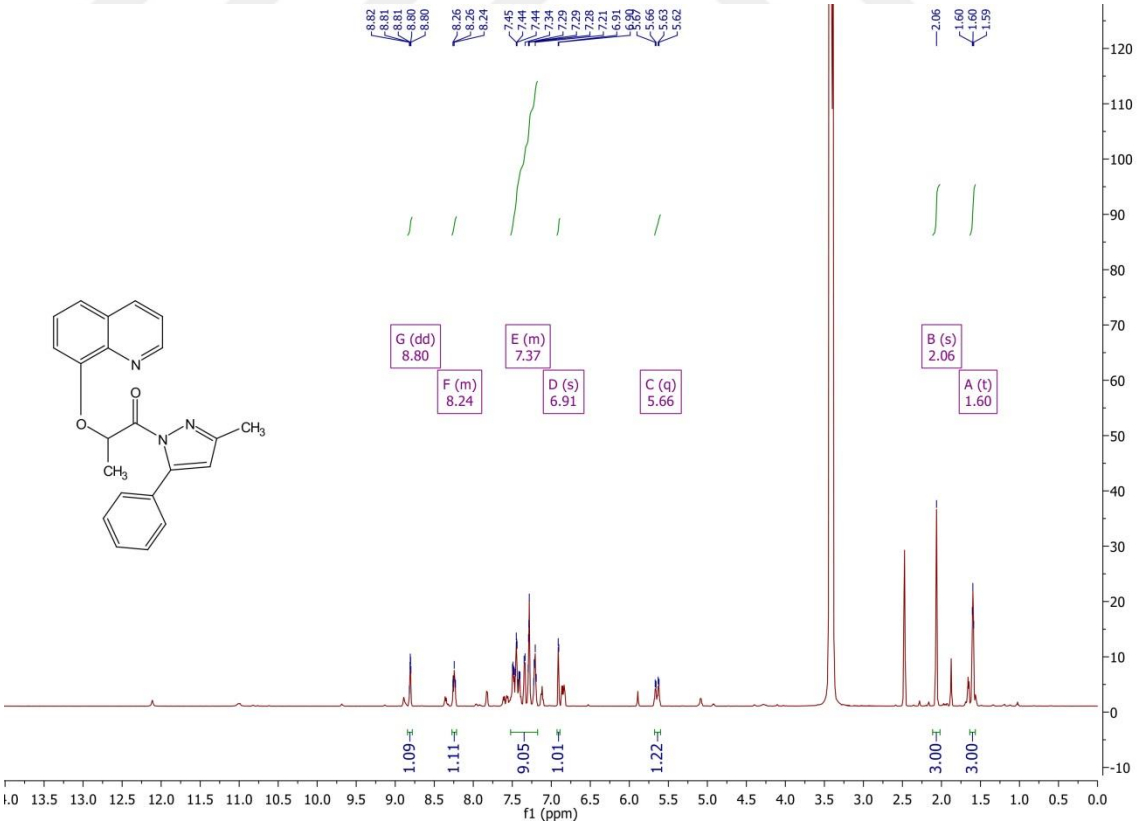


Figure 4.22 ^{1}H NMR spectra compound 57

^{13}C NMR of this compound 57 showed these results measured by ppm: 167.56 (C=O), 155.83 (ArC-O), 153.67 (C=N), 149.31 (ArC), 144.11 (ArC), 139.93 (ArC), 136.11 (ArCH), 129.51 (ArC), 128.16 (3xArCH), 126.92 (ArCH), 124.93 (2xArCH), 122.24 (ArCH), 120.28 (ArCH), 110.28 (ArCH), 92.51 (C=C), 71.90 (O-CH), 17.92 (N=C-<u>C</u>H$_3$), 16.33 (O-CH-<u>C</u>H$_3$) (Figure 4.23).

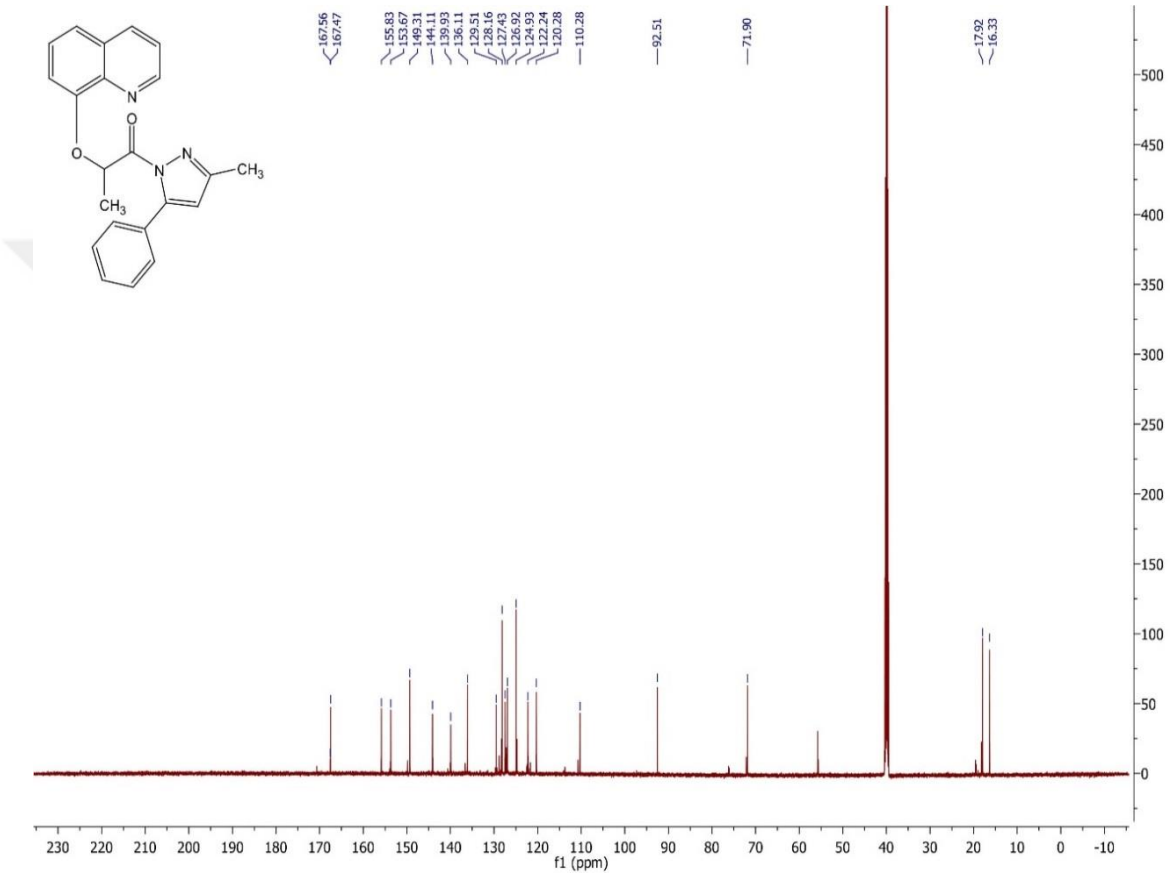


Figure 4.23 ^{13}C NMR spectra compound 57

5. THE STUDY OF ANTIBACTERIAL ACTIVITY

The synthesized compounds were tested for their biological activity against two type of gram-positive bacteria; Staphylococcus aureus and Bacillus in vitro with four different concentrations using agar diffusion method. A sterile cotton swab is dipped into the suspension prepared and then swabbed evenly across the surface of a Muller-Hinton agar plate; 4-5 holes with 4 mm diameter cut in the agar gel, 20 mm apart from one to another. After that 100 µL from each prepared diluted concentration (10, 25, 50, 100, µg/mL) were added to each of the wells. DMSO was used as a solvent. The plates were incubated for 24 h at 37ºC, under aerobic conditions in candle jar. After incubation, growth was observed and the inhibition of the growth was measured in mm. The results were compared antibacterial ciprofloxacin by concentration 100 µg/mL which was used as a reference drugs. (Balouiri *et al*, 2016).

5.1 Antibacterial Studies

The results of antibacterial activity are shown in table (5.2) and selected photographs of growth inhibition zones are listed below.

Generally, all prepared compounds showed acceptable to good biological activity against these types of bacteria, more effectively than the substrate 8-hydroxy quinoline as shown in (Figure 5.1) and (Figure 5.2). This ability of inhibition increased with the increasing the concentration of tested compounds. More specifically, compounds (55 and 57) exhibited the highest reactivity against the both bacteria at 100 µg/mL concentration entry (24 and 28), which was significantly better than other concentrations. The biological effectiveness of these compounds is approximately close to the effectiveness of ciprofloxacin antibiotic entry (34), which could be due to the existence of the pyrazole five-membered ring. In addition, ester (51) and hydrazide (52) displayed a good reactivity in comparison with a reference drug entry (4 and 8). However, Schiff bases (53-a, 53-b, 53-c) presented a fluctuated range of biological activity entry (9-20) and the best inhibition was (19mm and 20mm) by compound (53-a) against (Staphylococcus aureus) and (Bacillus) respectively, entry (12).

Table 5.1 In vitro anti-bacterial (gram positive) data

Entry	Compound No.	Concentration (µg/mL)	Inhibition Zone in (mm)	
			(Staphylococcus aureus)	(Bacillus)
1	51	10	10	9
2		25	13	12
3		50	14	13
4		100	17	16
5	52	10	10	10
6		25	14	13
7		50	14	14
8		100	18	19
9	53-a	10	9	10
10		25	13	14
11		50	17	16
12		100	19	20
13	53-b	10	10	7
14		20	13	8
15		25	14	10
16		100	15	12
17	53-c	10	7	8
18		25	10	10
19		50	13	14
20		100	18	17
21	55	10	9	9
22		25	12	14
23		50	18	16
24		100	20	20
25	57	10	8	10
26		25	13	12
27		50	17	15
28		100	20	19
29	8-Hydroxy quinoline	10	0	0
31		25	6	9
31		50	7	10
32		100	10	12
33	DMSO	-	0	0
34	Ciprofloxacin	100	22	22

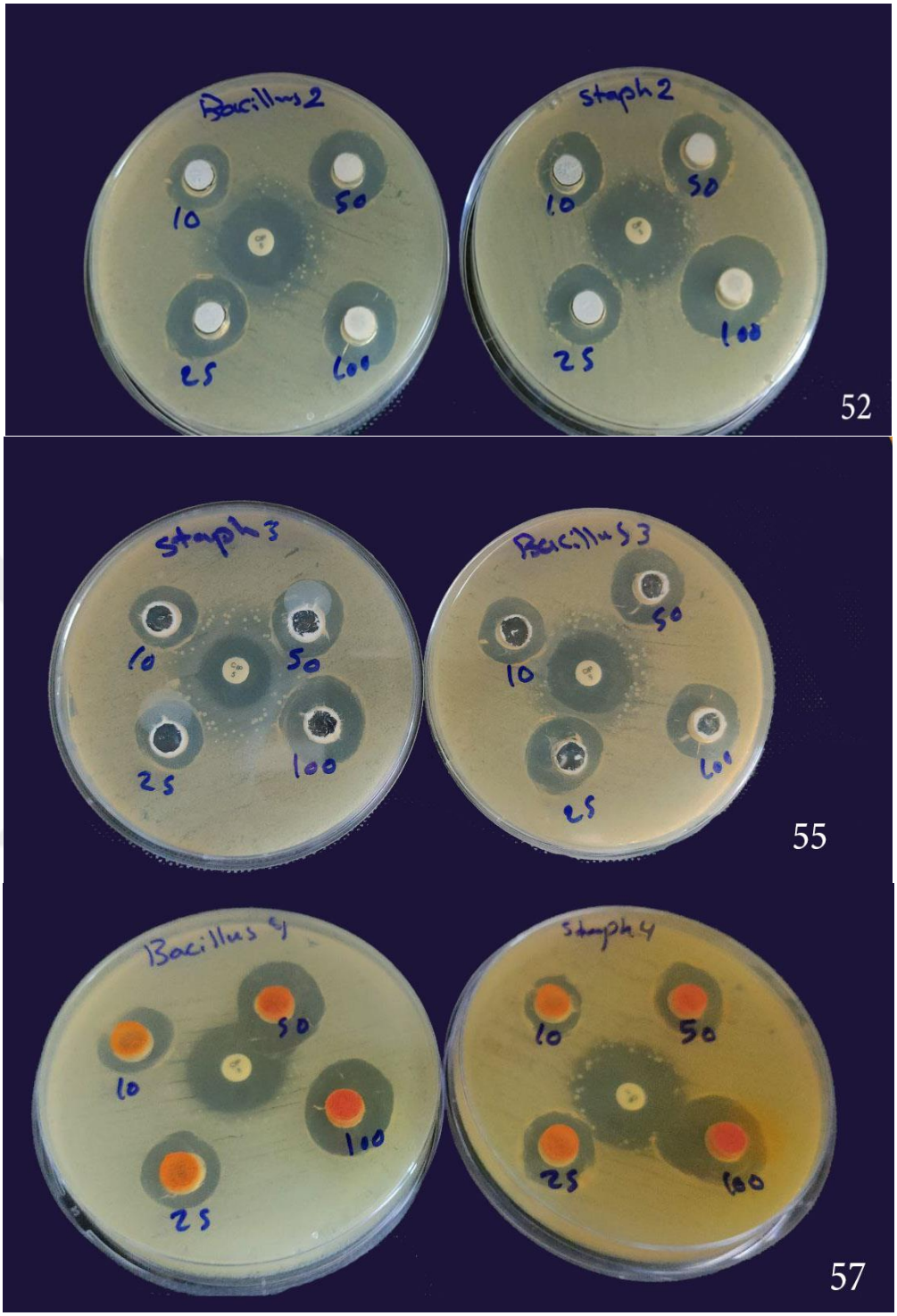


Figure 5.1 Anti-bacterial test of compounds 52, 55, 57

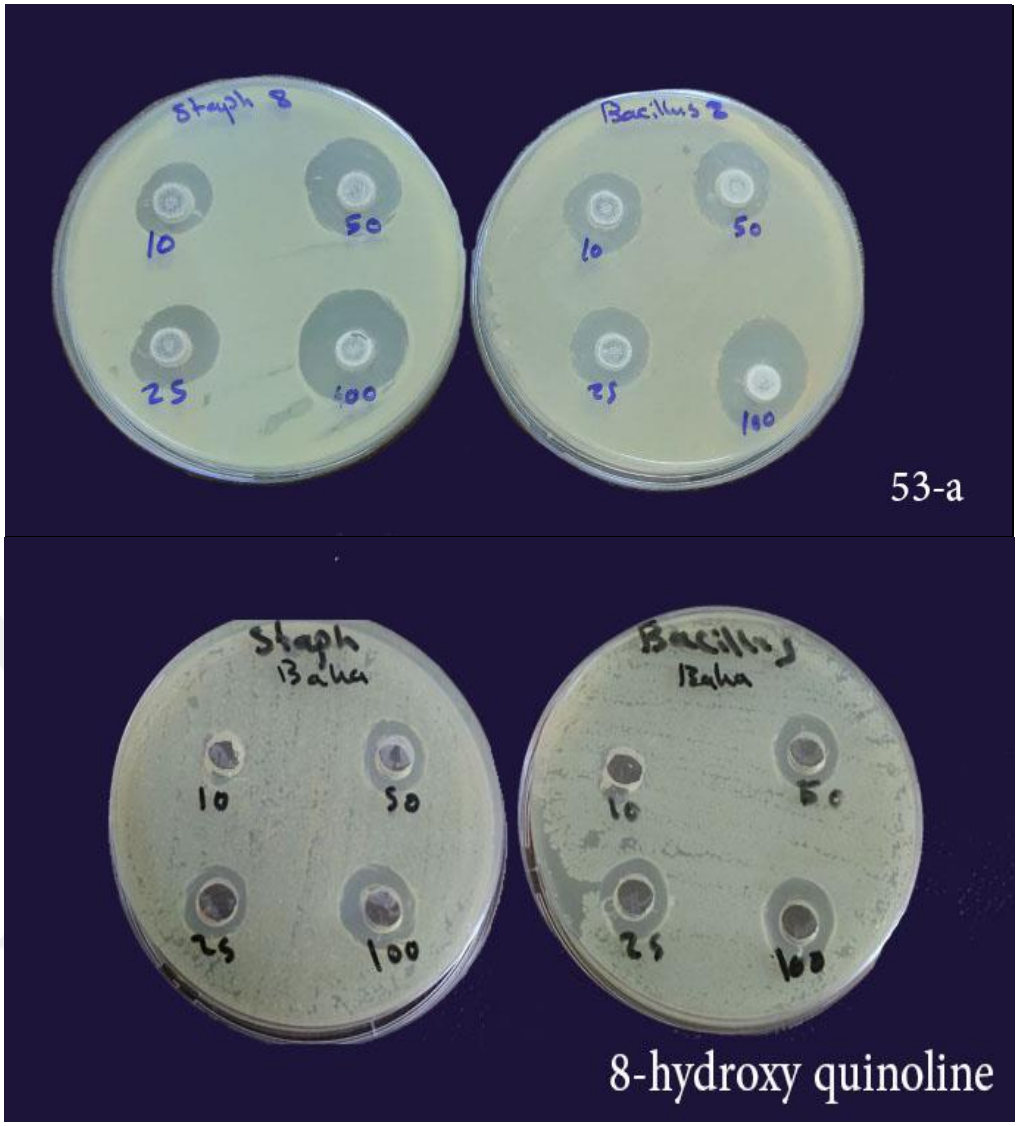


Figure 5.2 Anti-bacterial test of compounds 53-a and 8-hydroxy quinoline

6. CONCLUSIONS AND RECOMMENDATION

A number of new derivatives of 8-hydroxyquinoline have been prepared, including the derivative of ester, hydrazide, and a range of Schiff bases (imines) as well as five-membered ring containing heterocyclic derivatives. The Biological activities of these new derivatives have been investigated against some bacteria such as Bacillus and Staphylococcus aureus (staph.au.)

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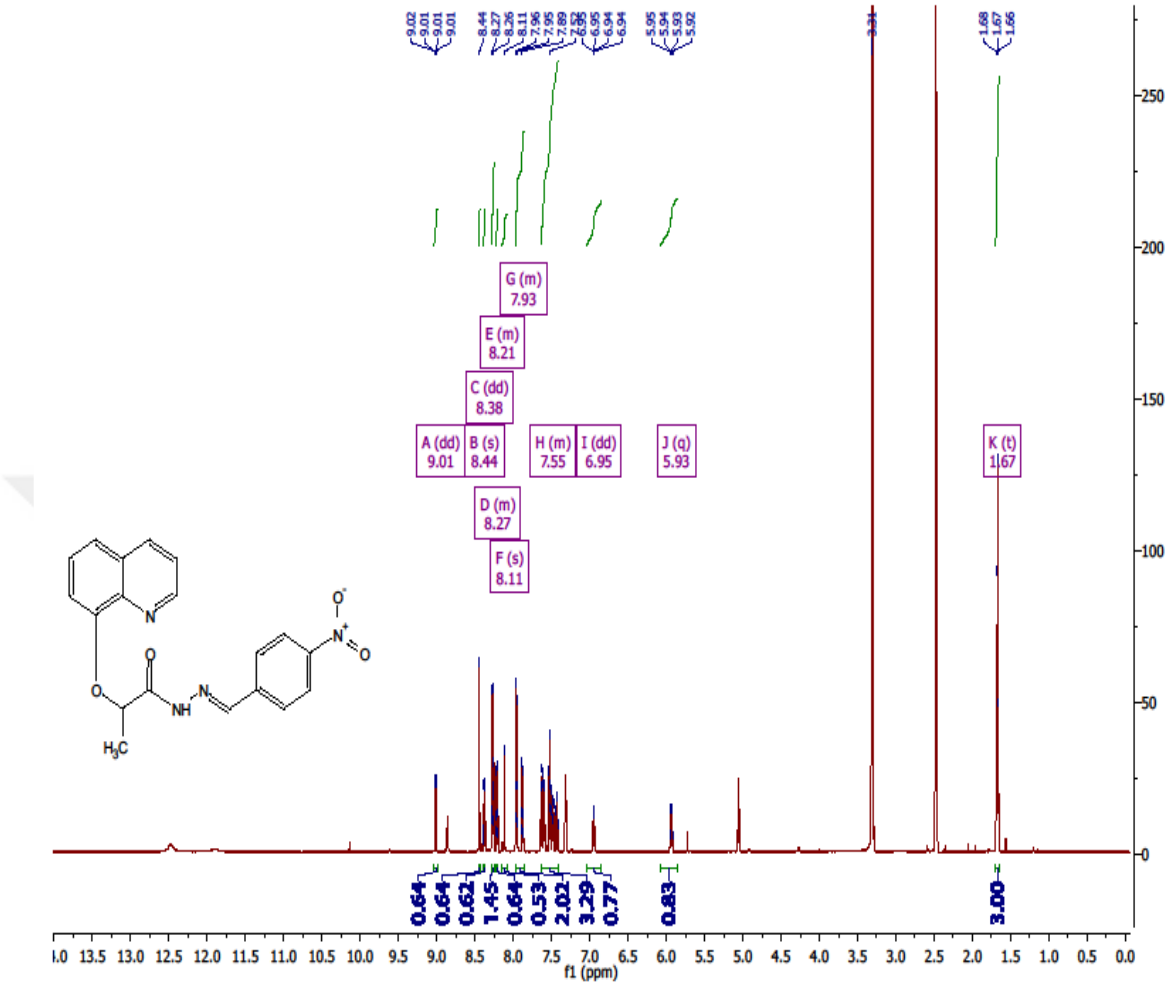
APPENDICES

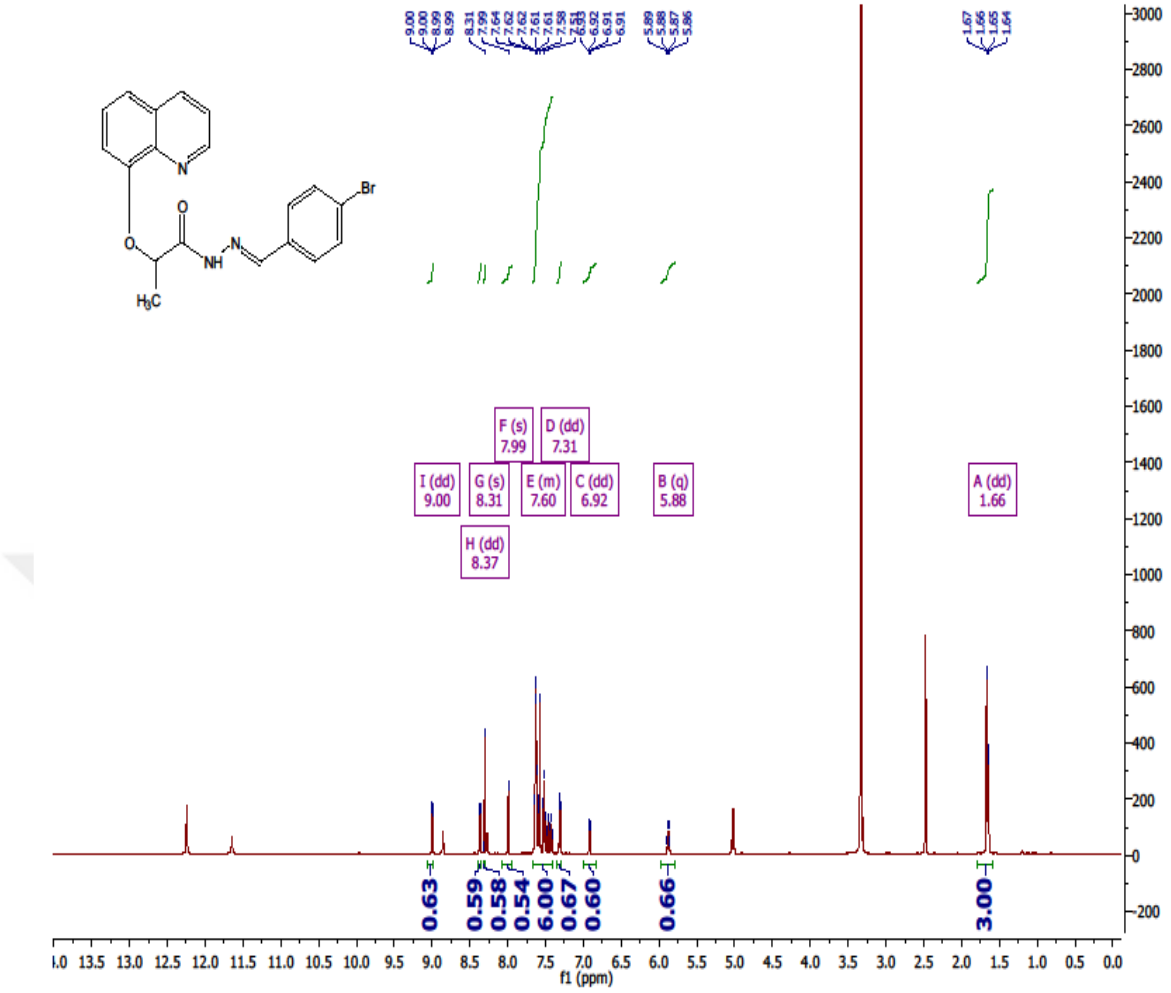
1. APPENDIX ^{1}H NMR Spectra for the compounds 53 (b, c, d, e, f) and 55.

2. APPENDIX ^{13}C NMR Spectra for the compounds 53 (b, c, d, e, f) and 55

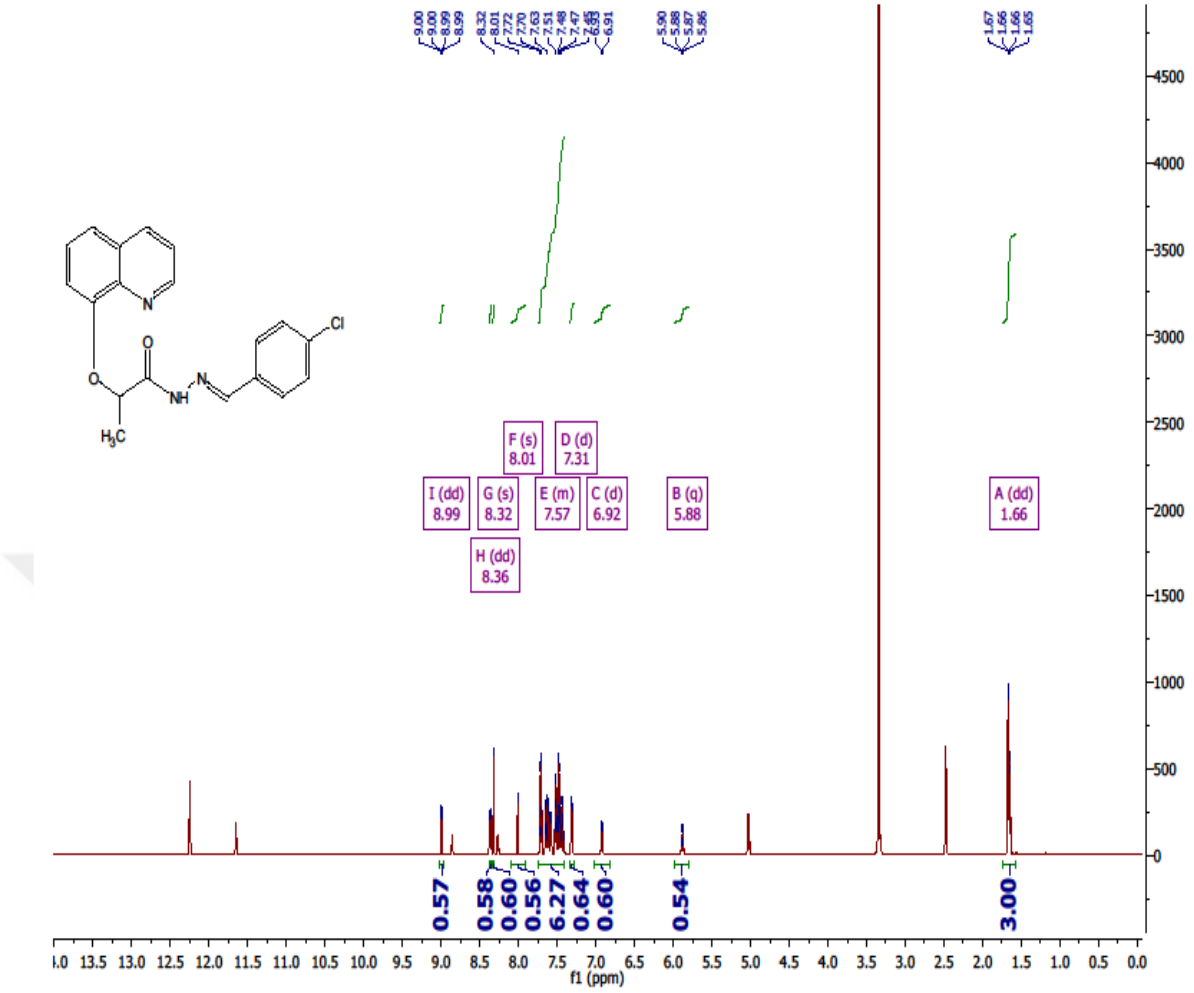
1. APPENDIX ^{1}H NMR Spectra for the compounds 53 (b, c, d, e, f) and 55.



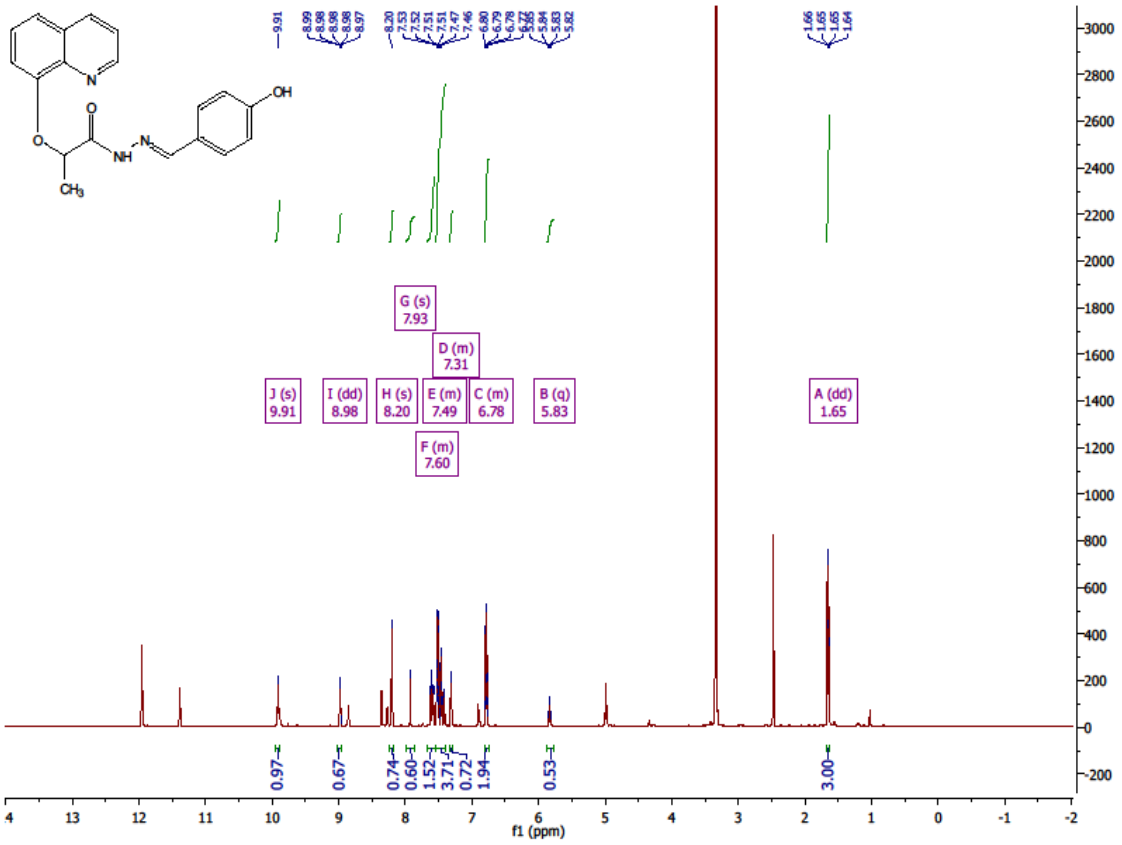
^{1}H NMR spectrum for the compound 53b



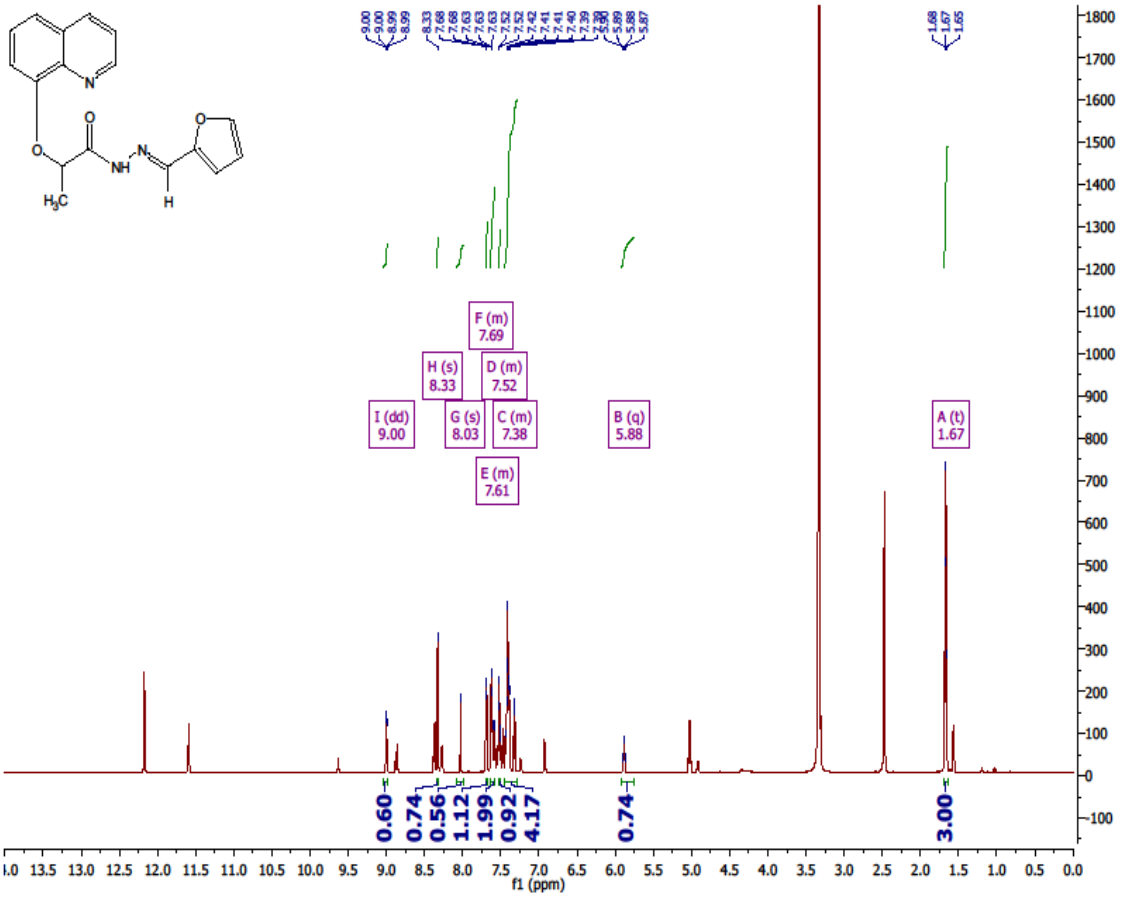
^{1}H NMR spectrum for the compound 53c



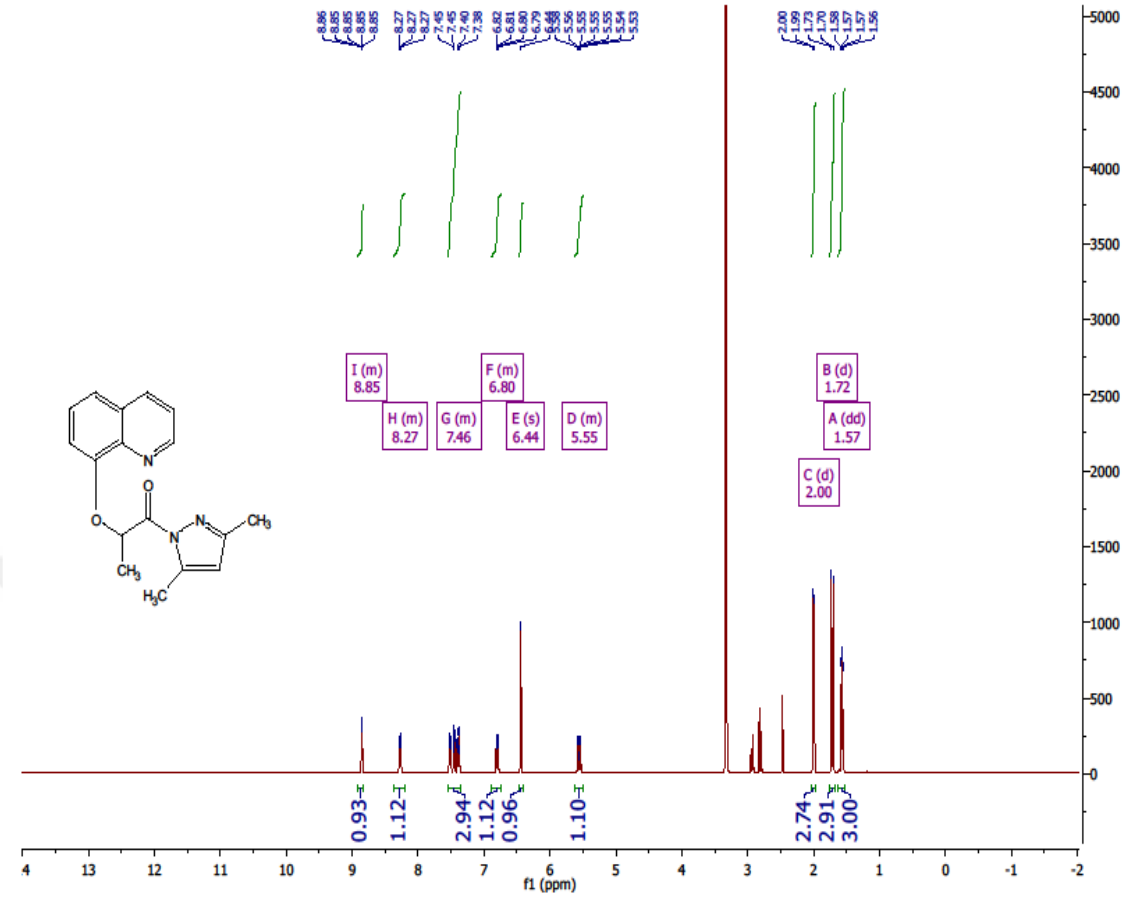
[1]H NMR spectrum for the compound 53d



^{1}H NMR spectrum for the compound 53e

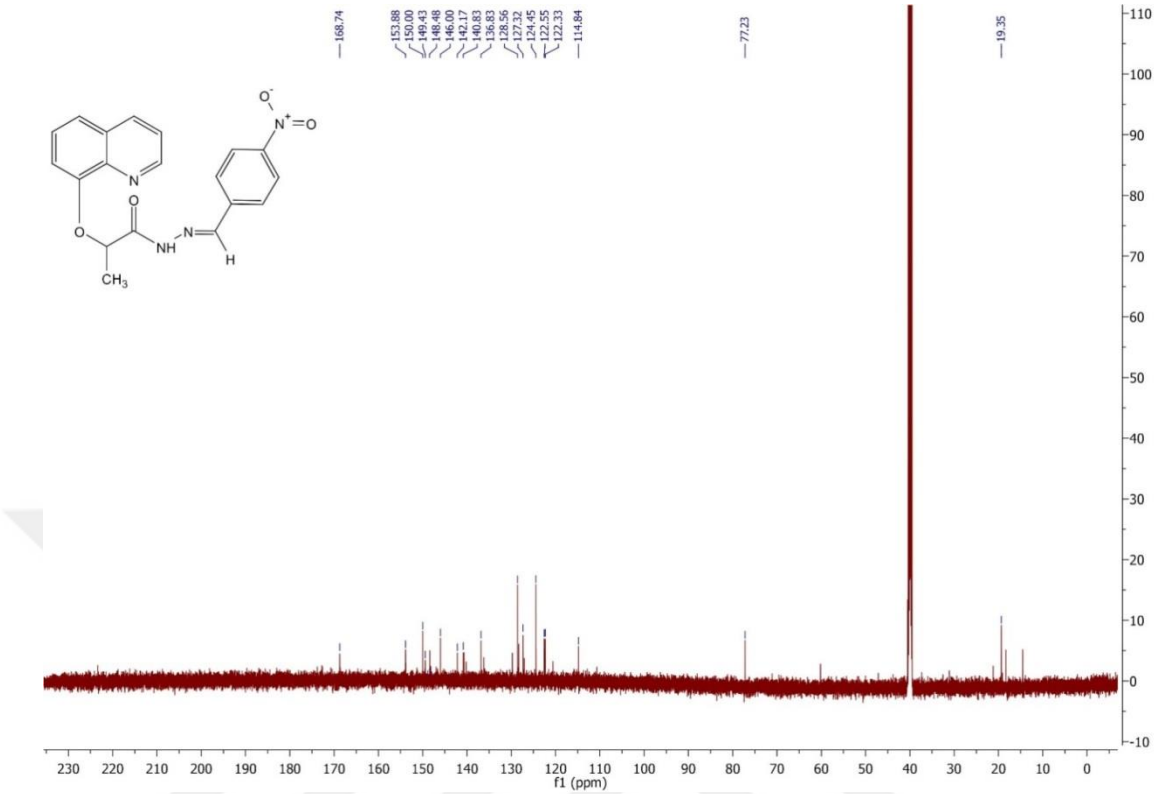


^{1}H NMR spectrum for the compound 53f

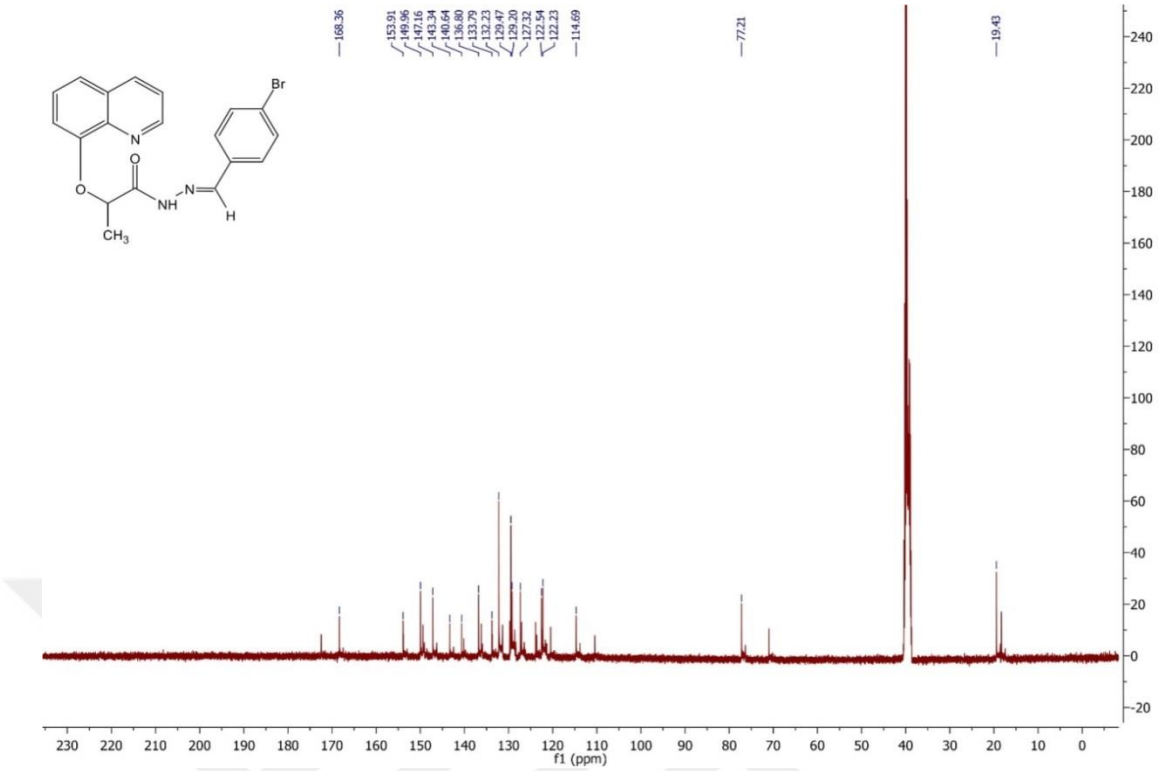


^{1}H NMR spectrum for the compound 55

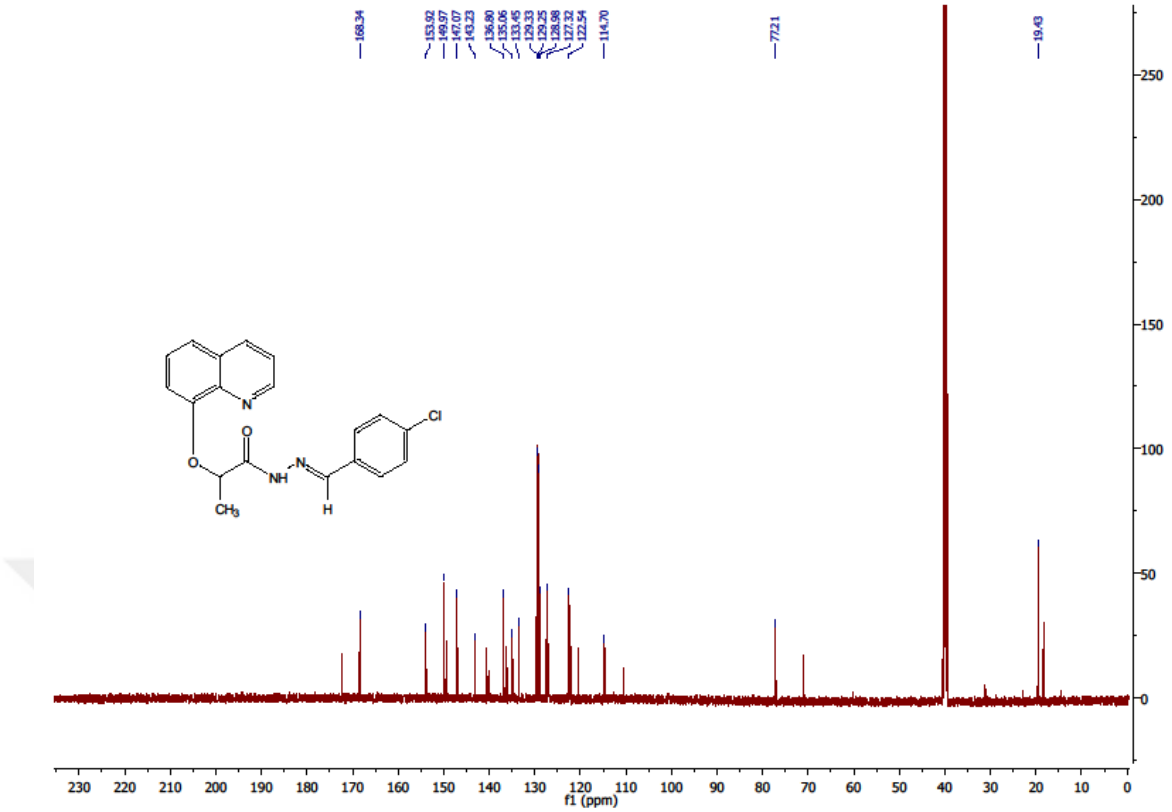
2. APPENDIX ^{13}C NMR Spectra for the compounds 53 (b, c, d, e, f) and 55



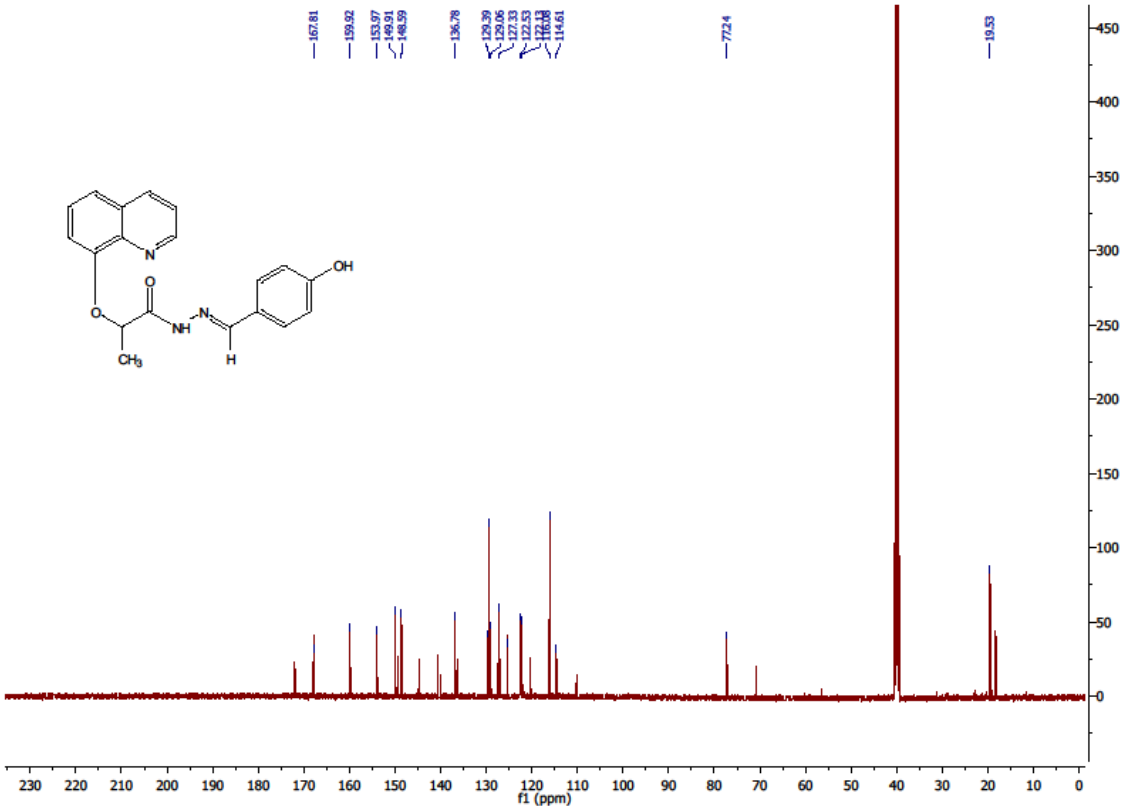
^{13}C NMR spectrum for the compound 53b



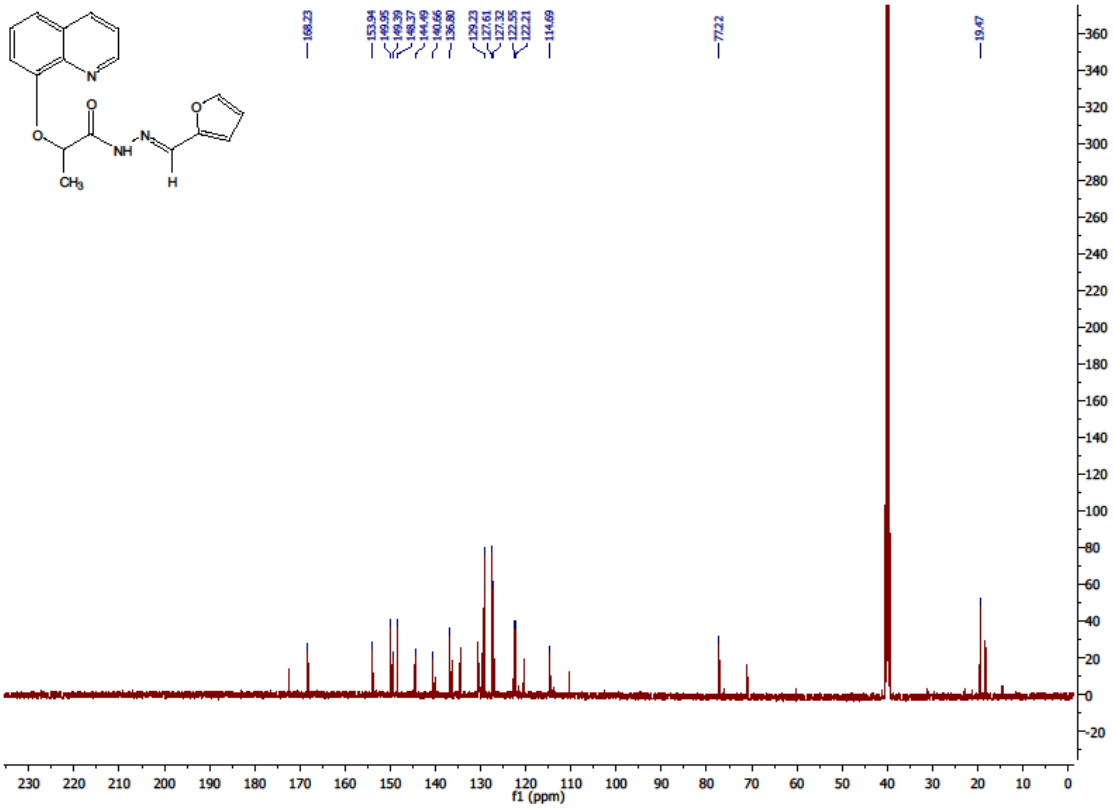
^{13}C NMR spectrum for the compound 53c



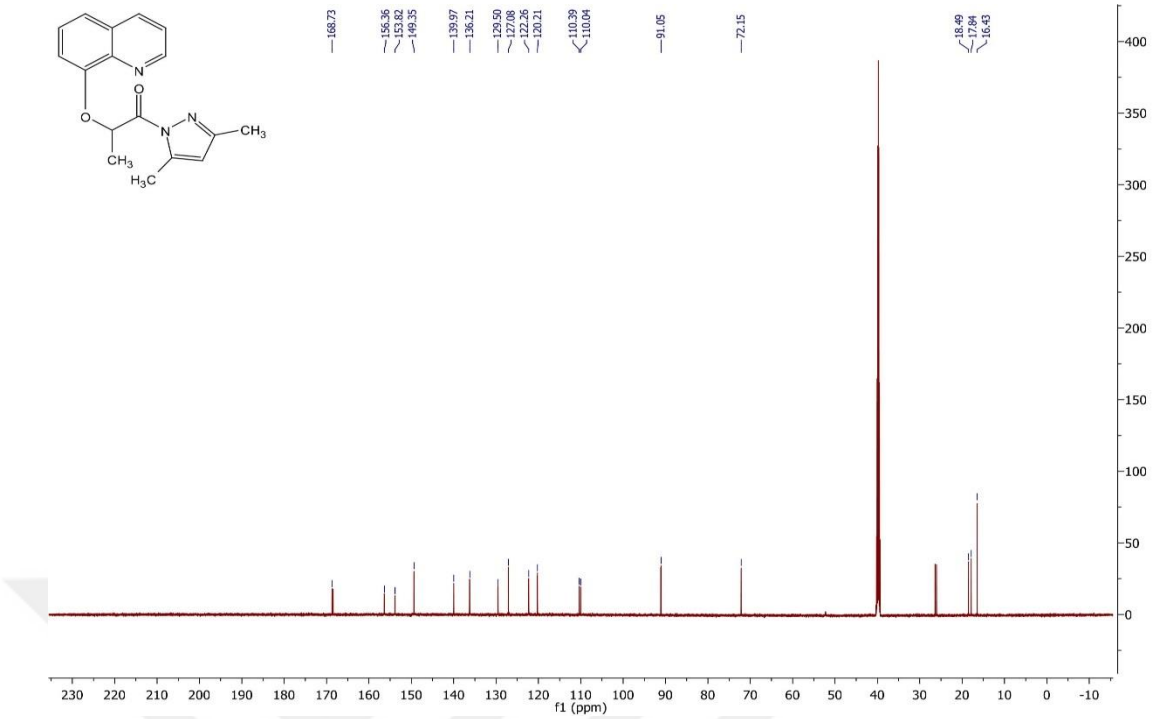
^{13}C NMR spectrum for the compound 53d



^{13}C NMR spectrum for the compound 53e



^{13}C NMR spectrum for the compound 53f



^{13}C NMR spectrum for the compound 55

CURRICULUM VITAE

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Education

Undergraduate	Mustansiriyah University College of Science Department of Chemistry	2006-2007

Work Experience

Year	Institution	Position
2011- Present	Ministry of Higher Education, Iraq	Employee

Academic Activities

Not currently available