SYNTHESIS, CHARACTERIZATION AND DERIVATIZATIONS OF QUINAZOLIN-3-OXIDES

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GRADUATE SCHOOL OF NATURAL AND APPLIED SCIENCES

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THESIS APPROVAL

This thesis titled "SYNTHESIS, CHARACTERIZATION AND DERIVATIZATIONS OF QUINAZOLIN-3-OXIDES" and prepared by Rashinikumar SINGH SAMANDRAM has been accepted as a **PhD THESIS** in Bursa Uludağ University Graduate School of Natural and Applied Sciences, Department of Chemistry following a unanimous vote of the jury below.

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Rashinikumar SINGH SAMANDRAM

ÖZET

Doktora Tezi

KİNAZOLİN-3-OKSİTLERİN SENTEZLERİ, KARAKTERİZASYONLARI VE TÜREVLENDİRİLMELERİ

Rashinikumar SINGH SAMANDRAM

Bursa Uludağ Üniversitesi
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Kimya Anabilim Dalı

Danışman: Prof. Dr. Necdet COŞKUN

2-Aminobenzaldehit, 1-(2-aminofenil)etanon ve 2-aminofenil fenil metanon oksimler **1,** karşılık gelen 1,2-dihidrokinazolin-3-oksitleri vermek üzere aromatik aldehitlerle reaksiyona sokuldu. Oda sıcaklığında çevreye zarar vermeyen H_2O_2-tungstat oksidan sistemi kullanılarak yüksek verimlerle bir dizi kinazolin-3-oksit **3**'e dönüştürüldü. Bileşik **3**'ün sentezi için yüksek verimli tek kap prosedürü de geliştirilmiştir. 2-Aril-kinazolin 3-oksitlerin arilboronik asitlerle C-4 arilasyonlarında oksidan bileşen olarak manganez triasetatın kullanımı rapor edilmiştir. Yeni yöntem, iyi ila yüksek verimlerde yeni 2,4-diarillenmiş kinazolin 3-oksitler hazırlamak için uygulanmıştır. Yöntemin, her iki aromatik halka üzerinde çeşitli sübstitüentleri tolere ettiği, oksijensizleşme ve kinazolin-4(3H)-one'ye yeniden düzenleme gibi dezavantajları olmadığı gösterilmiştir. Kinazolin-3-oksitler **3**'ün, karşılık gelen N-(2-(((hidroksiimino)metil)fenil)-benzamidler **9**'u vermek üzere $ZrOCl_2$ varlığında hidrolitik halka açılmasına maruz kaldıkları gösterilmiştir. **9** bileşikleri, katalitik miktarlarda bir asit beraberinde DMSO içinde tekrar halkalaştırılmıştır.

Anahtar Kelimeler: 1,2-dihidrokinazolin-3-oksit, H_2O_2 oksidasyonu, N-oksitler, Kinazolin, Kinazolin-3-oksit, Kinazolin-4(3H)-on, C-H aktivasyonu, $Mn(OAc)_3$

ABSTRACT

PhD Thesis

SYNTHESIS, CHARACTERIZATION AND DERIVATIZATIONS OF QUINAZOLIN-3-OXIDES

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Department of Chemistry

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2-Aminobenzaldehyde, 1-(2-aminophenyl)ethanone and 2-aminophenyl phenyl methanone oximes **1** were reacted with aromatic aldehydes to give the corresponding 1,2-dihydroquinazoline-3-oxides **2**. The latter were converted in high yields to a series of quinazoline-3-oxides **3** using environmentally benign H_2O_2-tungstate oxidant system at room temperature. High yielding one-pot procedure was also developed for the synthesis of compounds **3**. The use of manganese triacetate as an oxidant component in the C-4 arylations of 2-aryl-quinazoline 3-oxides with arylboronic acids is reported. The new protocol was applied to prepare new 2,4-diarylated quinazoline 3-oxides in good to high yields. The method was shown to tolerate variety of substituents on both aromatic rings and no complications as deoxygenation and rearrangement to quinazolin-4(3*H*)-one were observed. Quinazoline-3-oxides **3** were shown to undergo hydrolytic ring opening in the presence of $ZrOCl_2$ to give the corresponding N-(2-((hydroxyimino)methyl)phenyl)-benzamides **9**. The latter can be recyclized in DMSO using catalytic amounts of an acid.

Key words: 1,2-dihydroquinazoline-3-oxide, H_2O_2 oxidation; N-oxides, Quinazoline, Quinazoline-3-oxide, Quinazolin-4(3*H*)-one, C-H activation, $Mn(OAc)_3$

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First and foremost, I want to express my gratitude to God, without whom nothing is possible. Research is a never-ending process that involves a group of people working together to reach new heights in research. Without the encouragement and cooperation of my teachers, parents, friends, well-wishers, and relatives, this thesis would not have been accomplished. I would like to take this opportunity to express my heartfelt gratitude to everyone.

I would also like to express my gratitude to Prof. Dr. Necdet Coşkun my supervisor, for his invaluable assistance, patience, and unwavering guidance. I owe him a debt of gratitude for his valuable advice and unwavering support during my studies. I am confident that the ethics and moral ideals that I learned from him would help me become a better human being.

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Finally, I am at a loss for words when it comes to praising the person I admire the most, my girlfriend, Dr. Puja Sorokhaibam, who could only have witnessed all of my ups and downs, complaints, and disappointments while pursuing my PhD. This thesis would not have been possible without her care, love, and unwavering support.

Rashinikumar SINGH SAMANDRAM
21/09/2021

CONTENTS

SYMBOLS and ABBREVIATIONS

Symbols	Definition
DMSO	Dimethyl sulfoxide
DCM	Dichloromethane
DMF	N,N'-Dimethyl formamide
NMP	N-Methylpyrrolidone (N-methyl-2-pyrrolidone)
TBHP	Tetra butyl hydrogen peroxide
HPLC	High Performance Liquid Chromatography
NMR	Nuclear Magnetic Resonance
FTIR	Fourier-Transform Infrared Spectroscopy
THF	Tetrahydrofuran
TLC	Thin Layer Chromatography
DCE	1,2-Dichloroethane
HRMS	High Resolution Mass Spectrometry
TsCl	4-Toluenesulfonyl chloride
HMDS	Hexamethyldisilazane
TMSOTf	Trimethylsilyl trifluoromethanesulfonate
TBPB	tert-Butyl peroxybenzoate
CAN	Ceric ammonium nitrate

FIGURES

Page

SCHEMES

TABLES

Pages

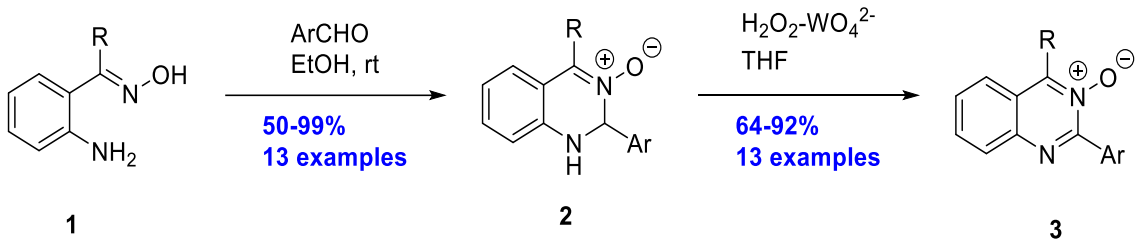
1. INTRODUCTION

The quinazoline skeleton can be found in both natural and synthetic organic compounds. Quinazoline alkaloids and their analogues have piqued researchers interest worldwide since the 19th century, showing their numerous bioactivities (Shang et al. 2018). Anti-cancer, anti-microbial, anti-convulsant, and anti-hyperlipidemic properties of quinazoline-based scaffolds have been discovered (Auti et al. 2020, Hameed et al. 2018, Bhatia et al. 2020, Shagufta and Ahmad 2017). To produce synthetic medications and to make more effective medicines, a large variety of quinazoline derivatives have been manufactured (gefitinib, erlotinib, raltitrexed, prazosin, doxazosin etc.) Recent advances in eco-friendly, green, and efficient (in most cases) synthesis methods for obtaining quinazoline and quinazolinone derivatives from inexpensive and widely available commercial feedstocks are discussed (Khan et al. 2015).

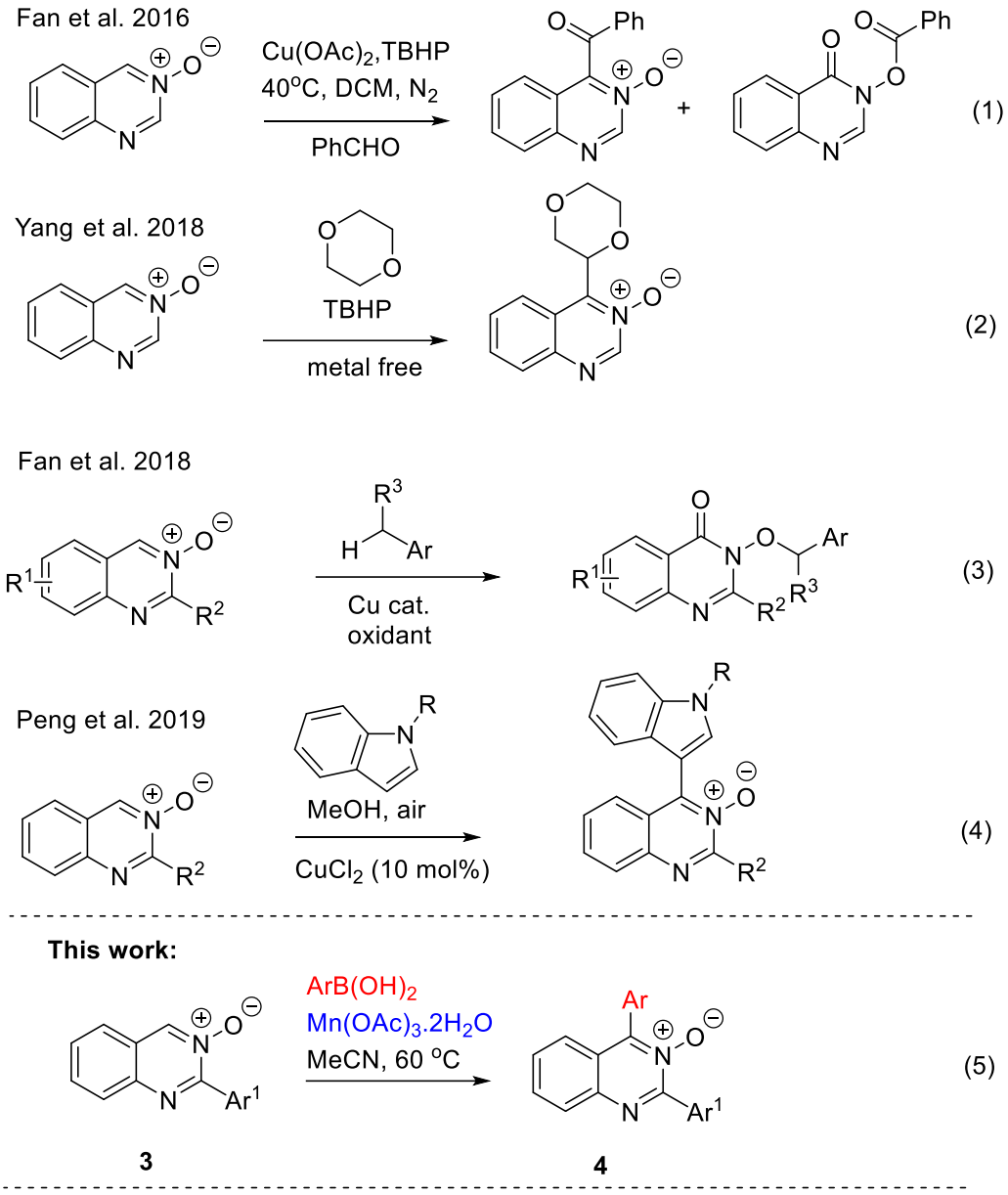
C-H activation has become a useful technique in molecular sciences, material sciences, crop protection, drug discovery, and the pharmaceutical industries are just a few of the areas where it can be used. The discovery of less toxic, low-cost 3d metal catalysts for C-H activation has gotten a lot of attention (Gandeepan et al. 2019, Ackermann 2020, Zhao et al. 2020, Chen et al. 2015, Asensio et al. 2020, Ackermann et al. 2016). Approaches to functionalize N-heterocyclic N-oxides using C-H activation (e.g. pyridine and quinoline N-oxides) have been reported in the literature (Shen et al. 2014, Yuan and Qu 2017, Bering and Antonchick 2015, Mai et al. 2012). The oxidative coupling of quinazoline 3-oxides and unactivated aldehydes was reported using a copper catalyst (Scheme. 1.2; (1)), (Fan et al. 2016). In the presence of TBHP, the C-4 position of quinazoline 3-oxides was alkylated with ethers. The reaction is carried out in a metal-free environment and gives moderate to good yield. (Scheme. 1.2; (2)) (Yang et al. 2018). Highly effective copper-catalyzed oxidative functionalization of benzylic C(sp^3)–H bonds using quinazoline 3-oxides was also described (Scheme. 1.2; (3)) (Fan et al. 2018). This method provides a wide range of quinazolin-4(3*H*)-one derivative in good to excellent yields. It has also been reported that 4-(indole-3-yl)quinazolines can be synthesized via cross-dehydrogenative coupling of quinazoline 3-oxides and indoles in an air atmosphere (Scheme. 1.2; (4)) (Yang et al. 2019). A number of biheteroaryl compounds were produced in good yields. Manganese is an excellent contender for long-term C-H

activation catalysis. Manganese catalysis is particularly cost-effective because it is the twelfth most prevalent element in the earth crust and the third most abundant transition metal after iron and titanium (Gandeepan et al. 2019). A review of the literature found that Mn(III) acetate is only occasionally used in C-H activation methods. Through an oxidative cross-coupling of arylboronic acids with quinoxalin-2-ones, it gives 3-aryl quinoxalin-2-one derivatives (Ramesh et al. 2018). A reaction of arylboronic acids and arylpropiolic acids by using Mn(III) acetate give diaryl 1,2-diketones via radical pathway in moderate to good yields (Lv et al. 2015).

In a previous investigation, the product of quinazoline-1-ols and their ring expansion upon carbamoylation with aryl isocyanates have been described (Coşkun and Çetin 2004). Then, the H_2O_2-tungstate system was used to oxidize 2-substituted-1,2,3,4-tetrahydroquinazolines. It gives regioselectively the appropriate quinazoline-1-oxides (Coşkun and Çetin 2007). In the same report, photochemical and thermal properties were thoroughly examined. In this work, the synthesis of 1,2-dihydroquinazoline-3-oxides and their eco-friendly transformation into quinazoline-3-oxides using H_2O_2-tungstate oxidant system is reported (Scheme 1.1).

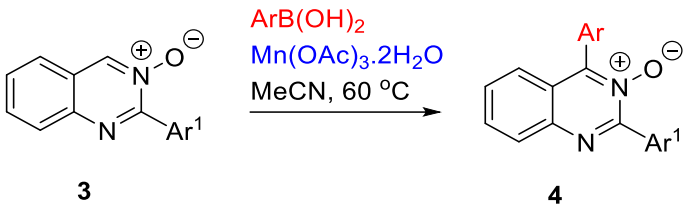


Scheme 1.1. The synthesis of 1,2-dihydroquinazoline- and quinazoline-3-oxides.



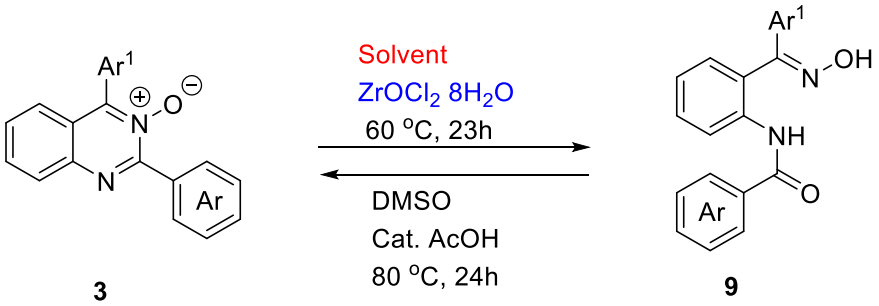
Scheme 1.2. C–H bond activation reaction of quinazoline 3-oxides.

Then under mild reaction conditions, we describe high yielding wide substrate scope C-4 arylations of 2-arylquinazoline 3-oxides with arylboronic acids in the presence of Mn(III) acetate dihydrate (Scheme 1.3).



Scheme 1.3. C–H bond activation reaction of quinazoline 3-oxides.

Further we report on the hydrolytic ring-opening of quinazoline-3-oxides **3** in the presence of $ZrOCl_2$ to give the corresponding N-(2-((hydroxyimino)methyl)phenyl)-benzamides **9**. The latter can be recyclized in DMSO using catalytic amounts of an acid (Scheme 1.4).



Scheme 1.4. Hydrolysis of compound **3** and recyclization of compound **9**.

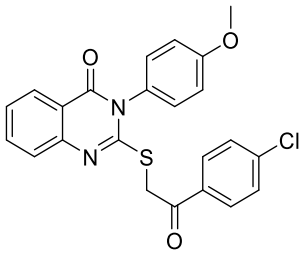
2. LITERATURE REVIEW

2.1. Biologically active natural and synthetic quinazoline derivatives

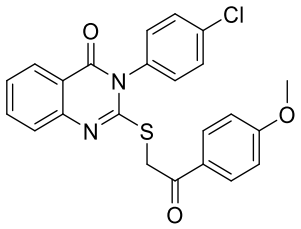
The major biological activity of quinazoline and quinazolinone skeletons in diverse disciplines is dependent mainly on the substituents of quinazoline compounds, as previously stated. Different substituted quinazoline compounds have been shown to have antihypertensive, antineoplastic, depressive, and antipsychotic properties, while others have analgesic, antipsychotic, antiarrhythmic, and cancer-fighting properties (Heba 2020, Pati and Banerjee 2013, Rajput and Mishra 2012, Vijayakumar et al. 2013, Auti et al. 2020).

2.1.1. Anticancer activity of quinazoline derivatives.

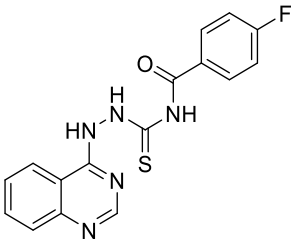
Gawad et al. (2010) reported that **(1)** 2- ((2-(4-chlorophenyl) -2-oxoethyl)thio)-3-(4-methoxyphenyl)quinazolin-4(3*H*)-one and **(2)** 3-(4-chlorophenyl)-2-((2-(4-methoxyphenyl)-2-oxoethyl)thio)quinazolin-4(3*H*)-one have been shown to have extensive anticancer activity against many cell types. And antitumor activity has been shown in many quinazoline derivatives containing the thiosemicarbazide moiety (He et al. 2012). Compounds are **(3)** 4-fluoro-N-(2-(quinazolin-4-yl)hydrazine-1-carbonothioyl)benzamide, **(4)** N-(2-(quinazolin-4-yl)hydrazine-1-carbonothioyl)benzamide and **(5)** 4-chloro-N-(2-(quinazolin-4-yl)hydrazine-1-carbonothioyl).



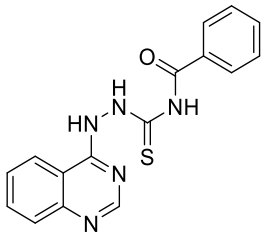
(1) 2-((2-(4-chlorophenyl)-2-oxoethyl)thio)-3-(4-methoxyphenyl)quinazolin-4(3*H*)-one



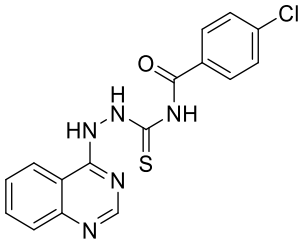
(2) 3-(4-chlorophenyl)-2-((2-(4-methoxyphenyl)-2-oxoethyl)thio)quinazolin-4(3*H*)-one



(3) 4-fluoro-*N*-(2-(quinazolin-4-yl)hydrazine-1-carbonothioyl)benzamide



(4) *N*-(2-(quinazolin-4-yl)hydrazine-1-carbonothioyl)benzamide

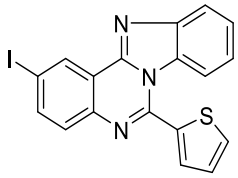


(5) 4-chloro-*N*-(2-(quinazolin-4-yl)hydrazine-1-carbonothioyl)benzamide

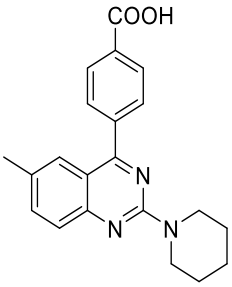
Figure 2.1. Structure of quinazoline (**3,4,5**) and quinazolinone (**1,2**) derivatives showing anticancer activity.

2.1.2. Antibacterial activity of quinazoline derivatives.

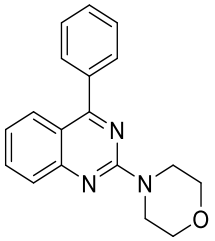
Alafeefy et al. (2011) reported that **(6)** 2-iodo-6-(thiophen-2-yl) benzo[4,5] imidazo[1,2-c]quinazoline, **(7)** 4-(6-methyl-2-(piperidin-1-yl)quinazolin-4-yl)benzoic acid, **(8)** 4-(4-phenylquinazolin-2-yl)morpholine and **(9)** N,N-dimethyl-4-(6-methyl-2-morpholinoquinazolin-4-yl)aniline possess remarkable activity toward Gram-negative bacteria E. Coli.



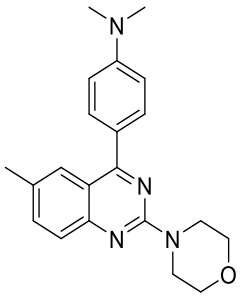
(6) 2-iodo-6-(thiophen-2-yl)benzo[4,5]imidazo[1,2-*c*]quinazoline



(7) 4-(6-methyl-2-(piperidin-1-yl)quinazolin-4-yl)benzoic acid



(8) 4-(4-phenylquinazolin-2-yl)morpholine

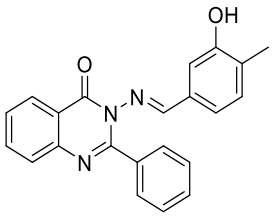


(9) *N*,*N*-dimethyl-4-(6-methyl-2-morpholinoquinazolin-4-yl)aniline

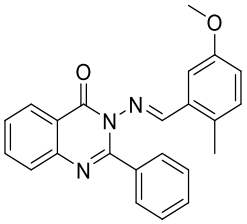
Figure 2.2. Structure of quinazolines (**6 to 9**) having antibacterial activity.

2.1.3. Antiviral activity of quinazoline derivatives.

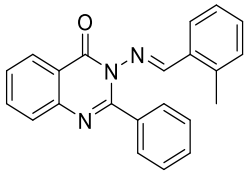
Kumar et al. (2010) reported that a collection of Schiff bases of various 2-phenyl quinazoline-4(3)*H*-one derivatives posses antiviral activity.



(10) (*E*)-3-((3-hydroxy-4-methylbenzylidene)amino)-2-phenylquinazolin-4(3*H*)-one



(11) (*E*)-3-((5-methoxy-2-methylbenzylidene)amino)-2-phenyl quinazolin-4(3*H*)-one

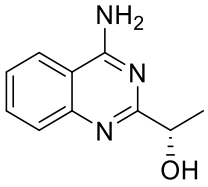


(12) (*E*)-3-((2-methylbenzylidene)amino)-2-phenylquinazolin-4(3*H*)-one

Figure 2.3. Structure of quinazolines (**10 to 12**) having antiviral activity.

2.1.4. Antimutagenic activity of quinazoline derivatives.

Sharma and Singh (2009) reported that (**13**) (S)-1-(4-aminoquinazolin-2-yl)ethan-1-ol possess great antimutagenic activity when tested by using E. coli and Salmonella typhimurium and WP2uvrA teste strains.

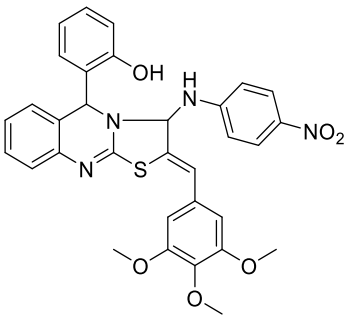


(13) (*S*)-1-(4-aminoquinazolin-2-yl)ethan-1-ol

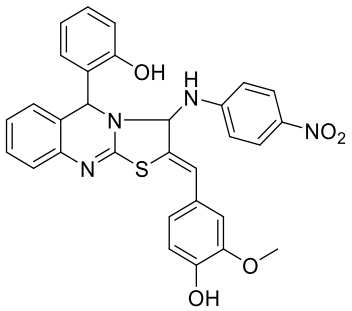
Figure 2.4. Structure of quinazolines (**13**) having antimutagenic activity.

2.1.5. Antioxidant activity of quinazoline derivatives.

Selvam et al. (2010) reported the DPPH test, hydrogen peroxide scavenging activity and nitric oxide scavenging activity were used to investigate the antioxidant activity of various new thiazoloquinazoline derivatives, and they were found to exhibit high potent antioxidant activity.



(14) (*Z*)-2-(3-((4-nitrophenyl)amino)-2-(3,4,5-trimethoxybenzylidene)-2,3-dihydro-5*H*-thiazolo[2,3-*b*]quinazolin-5-yl)phenol



(15) (*Z*)-4-((5-(2-hydroxyphenyl)-3-((4-nitrophenyl)amino)-5*H*-thiazolo[2,3-*b*]quinazolin-2(3*H*)-ylidene)methyl)-2-methoxyphenol

Figure 2.5. Structure of quinazolines (**14,15**) having antioxidant activity.

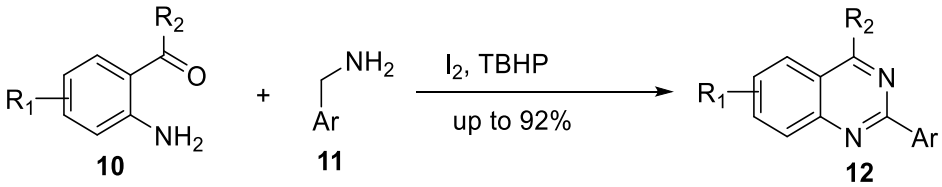
2.1.6. Industrial uses of quinazoline derivatives.

Armarego (1963) review reported that quinazolines in drug manufacture, certain quinazoline derivatives condensed with aminoanthraquinones could be used as a dye-stuff. Nitrosubstituted 4-hydroxyquinazolines suppress colour stains or use as a coating in photography.

2.2. Synthesis of Quinazolines.

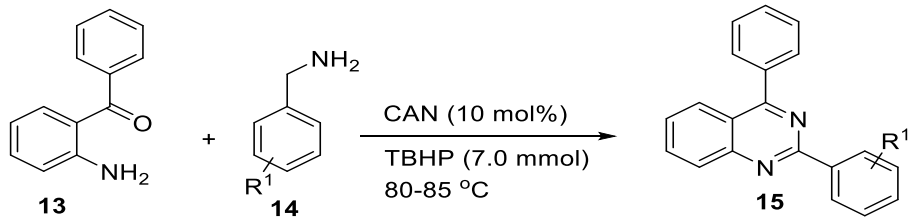
2.2.1. Methods based on *o*-aminoarylketone as starting material

Zhang et al. (2010) reported a reaction between 2-aminobenzophenones **10** and benzylic amines **11** following sp^3 C-H functionalization was used to establish a simple and new approach to the synthesis of 2-phenylquinazolines **12**.



Scheme 2.1. Synthesis of quinazolines from 2-aminobenzophenone with benzylic amine as starting material

Karnakar et al. (2011) described a method based on the reaction between 2-aminobenzophenones **13** and benzylamines **14** using a catalytic amount of ceric ammonium nitrate (CAN)–TBHP in acetonitrile to give 2-phenylquinazolines **15** in good yields.

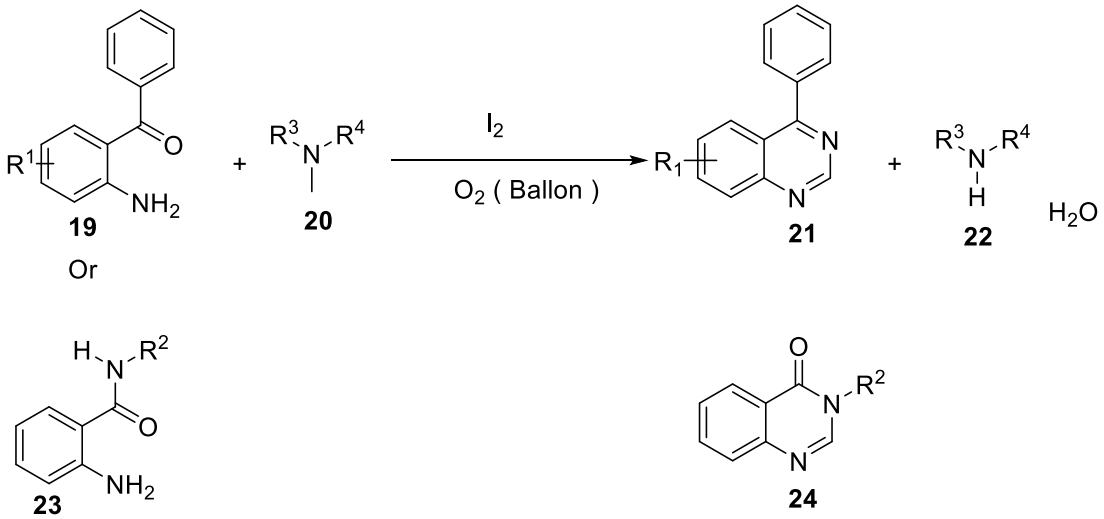


Scheme 2.2. Synthesis of quinazolines from 2-aminobenzophenone with benzylamine as starting material

Anand et al. (2012) reported the synthesis of 2-phenylquinazolines **18** from 2-aminoarylketones **16** and benzyl amines **17** in the presence of (MRIONC) catalyst with TBHP. It was discovered that MRIONC is a new and highly efficient green catalyst.

Scheme 2.3. Synthesis of quinazolines from 2-aminoarylketone with benzylamine as starting material

Yan et al. (2015) described a method based on a reaction between *o*-aminoarylketone **19 or 23** and tertiary amines **20** performed under an oxygen atmosphere in the presence of iodine-catalyst to develop quinazolines **21** and quinazolinones **24** in excellent yields. This method is metal-free, peroxide-free and simple to apply with various substrates and represents a new avenue for multiple C-N bond formations.



Scheme 2.4. Synthesis of quinazoline and quinazolinones from *o*-aminoarylketone as starting material

Yan et al. (2016) reported a method based on the reaction of arylacetic acids with 2-aminoarylketones **25** and ammonium acetate **26** in the presence of an effective copper-catalyst under an oxygen atmosphere. This reaction opens up a new way to developed 2-arylquinazolines **27** with good yields by forming numerous C–N bonds. This technique

uses a low-cost copper catalyst, molecular oxygen as an oxidant, H_2O and CO_2 as wastes, and a wide range of substrates.

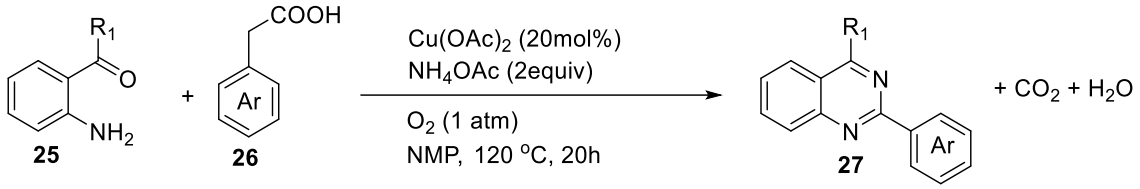
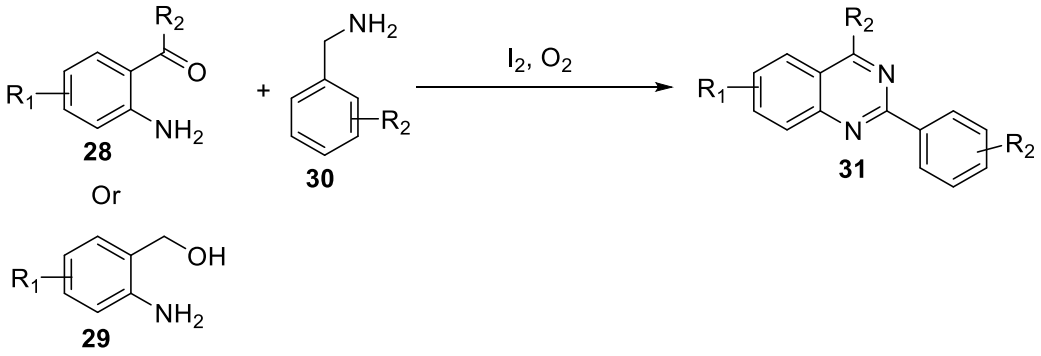


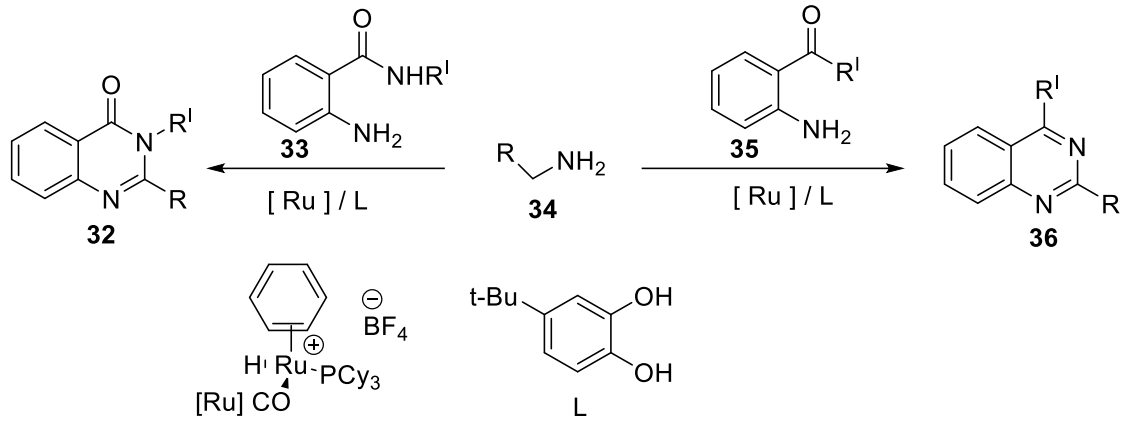
Figure 2.5. Synthesis of quinazolines from 2-aminoarylketones with arylacetic acids starting material

Deshmukh and Bhanage (2018) reported the cost-effective and eco-friendly synthesis of quinazolines **31** from 2-aminobenzaldehydes **28** and 2-aminobenzophenones **29** with benzylamines **30** in the presence of molecular iodine catalyst under oxygen atmosphere.



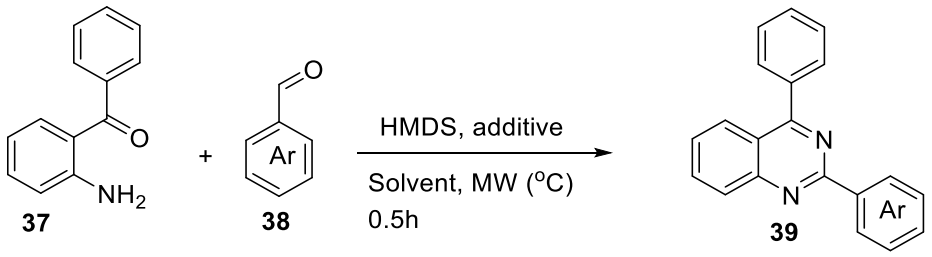
Scheme 2.6. Synthesis of quinazolines from 2-aminobenzophenone and 2-aminobenzylalcohol as starting material

Kirinde and Yi (2019) reported the dehydrogenative coupling of 2-aminophenyl ketones **35** and 2-aminophenylamides **33** with amines **34** to give quinazoline **36** and quinazolinone **32** products in the presence of ruthenium ([Ru]/L) catalyst. Without using reactive reagents or the formation of any toxic byproducts, quinazoline and quinazolinone derivatives can be synthesized.



Scheme 2.7. Synthesis of quinazoline and quinazolinones from 2-aminophenylketones and 2-aminophenylamides as starting materials

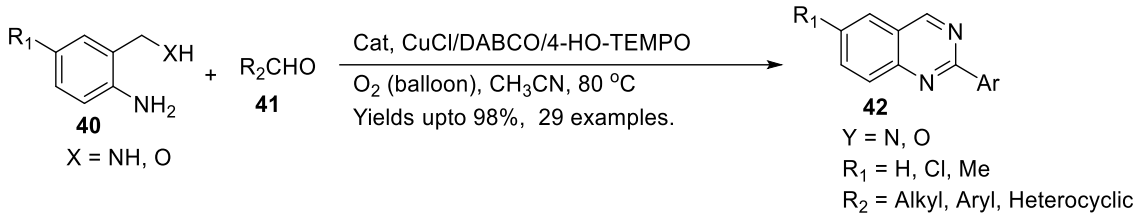
Chan et al. (2020) reported the formation of substituted quinazolines **39** from functionalized 2-aminobenzophenones **37** with different benzaldehydes **38** in the presence of TMSOTf catalyst and hexamethyldisilazane (HMDS) under neat, metal-free, and microwave irradiation conditions gives gaseous ammonia.



Scheme 2.8. Synthesis of quinazolines from 2-aminobenzophenone with benzaldehyde as starting material

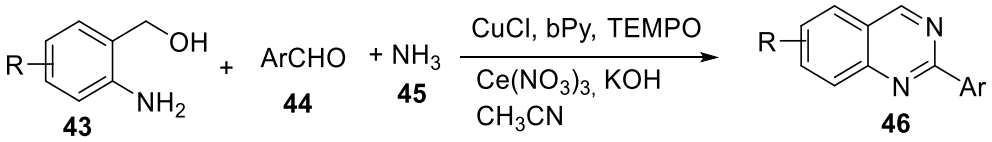
2.2.2. Methods based on *o*-aminobenzylalcohol and *o*-aminobenzylamine as starting material

Han et al. (2012) reported a method based on the reaction of aldehydes with 2-aminobenzylamines in the presence of CuCl/DABCO/4-HO-TEMPO catalysts under O_2 atm. to develop 2-substituted quinazolines.



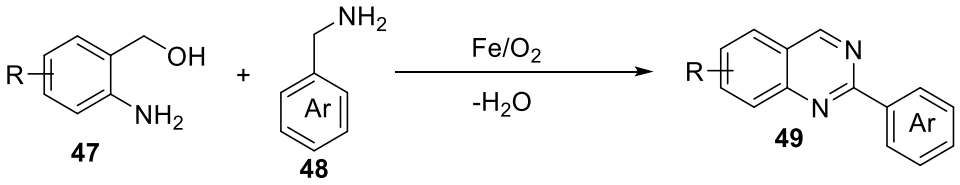
Scheme 2.9. Synthesis of quinazolines from 2-aminobenzylalcohol with aldehydes as starting material

Chen et al. (2013) reported the reaction of 2-aminobenzylalcohol **43** with aldehydes **44** using cerium nitrate hexahydrate and ammonia **45** in the presence of copper-catalyst.



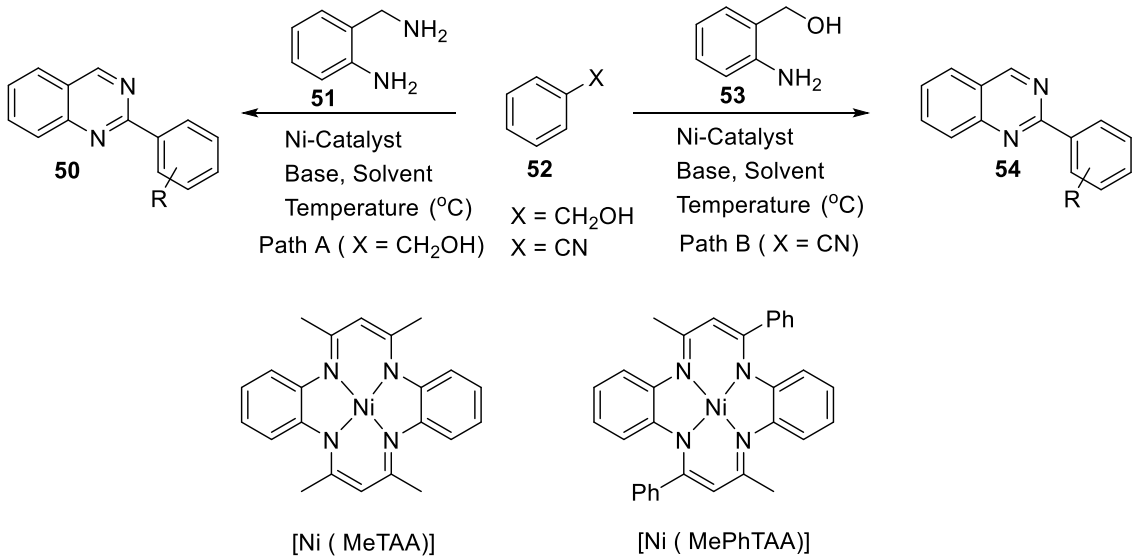
Scheme 2.10. Synthesis of quinazolines from 2-aminobenzylalcohol, aldehydes and ammonia as starting material

Gopalaiah et al. (2017) reported a method based on the reaction of 2-aminobenzyl alcohols **47** with benzylamines **48** in the presence of iron catalyst to give 2-aryl/heteroaryl quinazolines **49**.



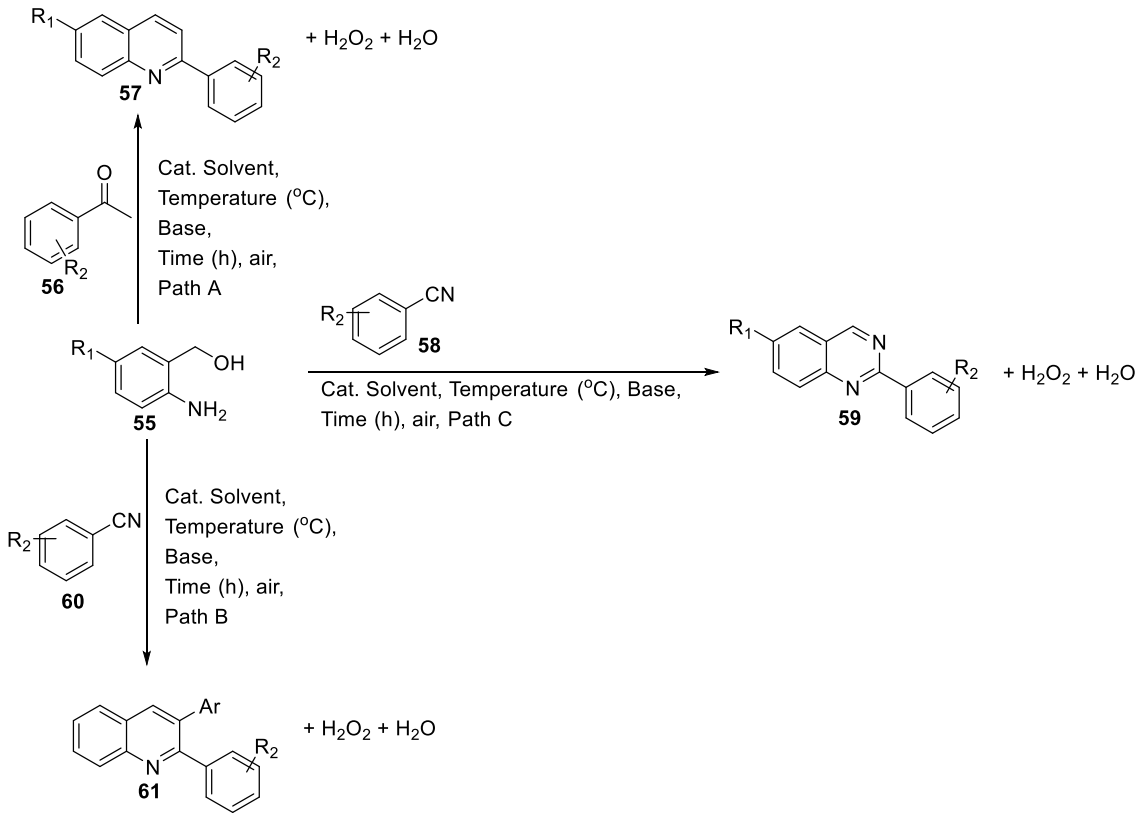
Scheme 2.11. Synthesis of quinazolines from 2-aminobenzylalcohol with benzylamine as starting material

Parua et al. (2018) described eco-friendly ways for the synthesis of quinazolines **54** by dehydrogenative coupling of 2-aminobenzylamine **51** with benzyl alcohol **53** (Path A) and 2-aminobenzylalcohol **53** with benzonitrile **52** (Path B), both catalyzed by Ni catalyst. Tetraaza macrocyclic ligands are used to make nickel catalysts. Ligands like 6,15-dimethyl-8,17-diphenyltetraaza[14]annulene (MeTAA) or tetramethyltetraaza[14]annulene (MeTAA) (MePhTAA)) have been used to make the corresponding Ni catalyst.



Scheme 2.12. Synthesis of quinazolines from 2-aminobenzylalcohol and 2-aminobenzylamine as starting material

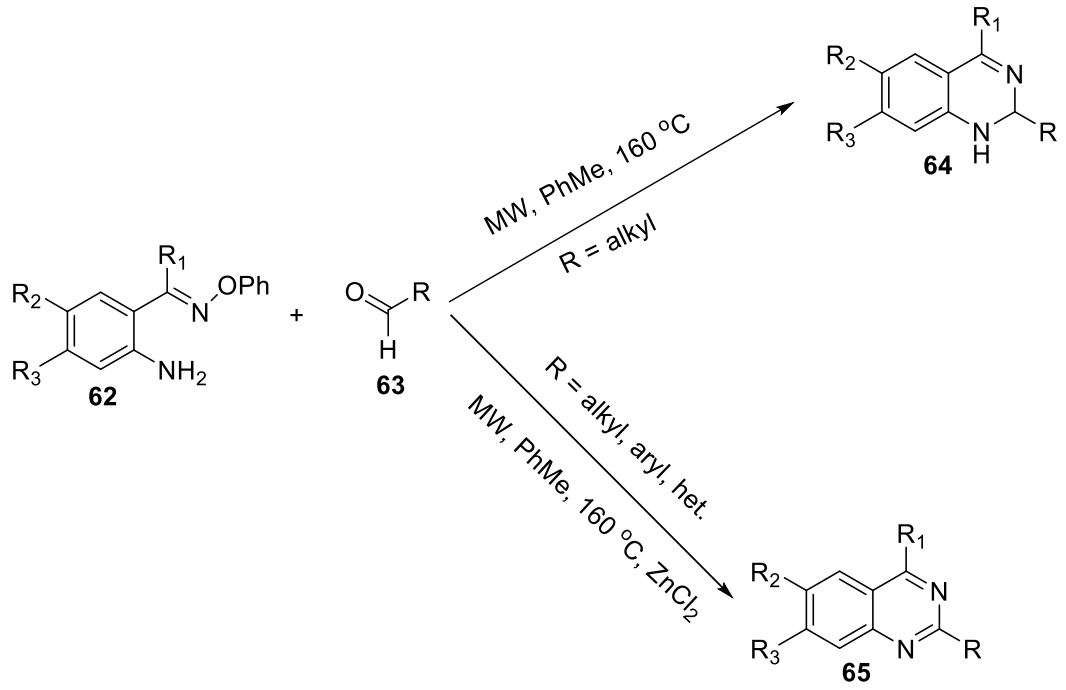
Chakraborty et al. (2019) described the synthesis of quinolines **57**, 2-aminoquinolines **61** and quinazolines **59** by coupling reaction of 2-aminobenzylalcohol **55** with acetophenone **56** (Path A) and 2-aminobenzylalcohol **55** with benzonitrile **58** (Path B) & (Path C), in the presence of Ni(II) catalyst.



Scheme 2.13. Synthesis of quinoline, 2-aminoquinoline and quinazolines from 2-aminobenzylalcohol as starting material and Ni as catalyst.

2.2.3. Methods based on 2-aminoarylalkanone O-phenyl oximes as starting material

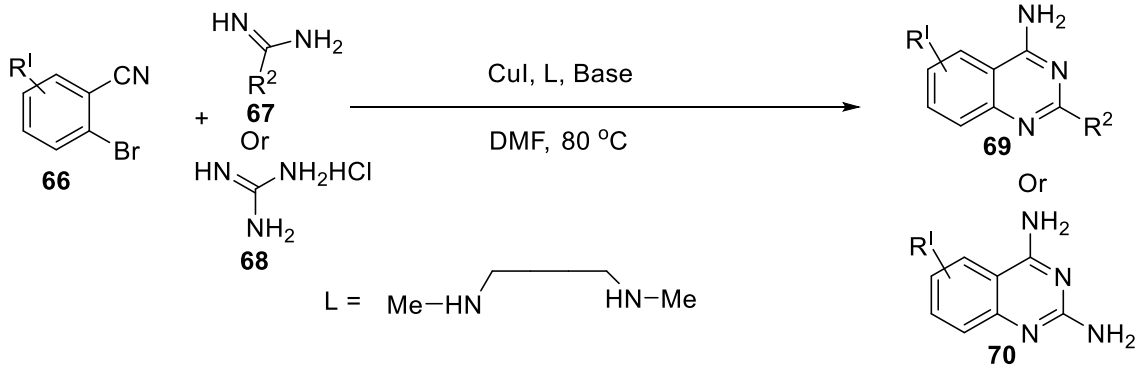
Cubillo et al. (2009) described the preparation of quinazolines **65** by a reaction of 2-aminoarylalkanone O-phenyl oximes **62** and aldehydes **63** in the presence of $ZnCl_2$ catalyst under microwave irradiation, in the absence of $ZnCl_2$ catalyst, it gives dihydroquinazolines **64**.



Scheme 2.14. Synthesis of dihydroquinazoline and quinazolines from 2-aminoarylalkanone O-phenyl oximes as starting material

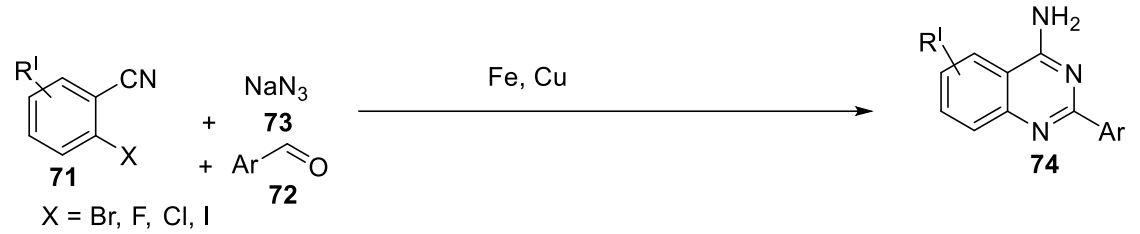
2.2.4. Methods based on ortho-halogenated benzonitriles as starting material

Yang et al. (2009) reported a method based on a reaction of substituted 2-bromobenzonitriles **66** with amidines **67** or guanidine **68** in the presence of copper-catalyst to give 4-aminoquinazoline **69** and 2,4-diaminoquinazolines **70** derivatives.



Scheme 2.15. Synthesis of quinazolines from ortho-bromo benzonitriles as starting material

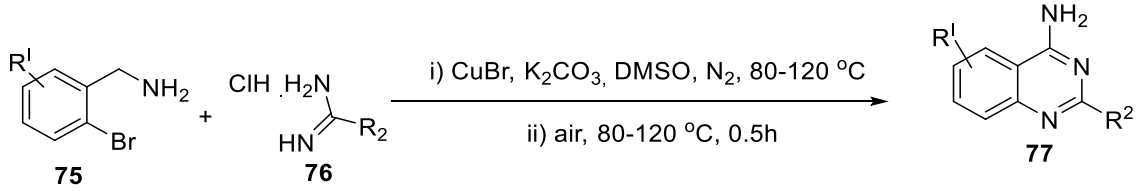
Jia et al. (2015) reported the synthesis of 2-phenylquinazolin-4-amines **74** from commercially available ortho-halogenated benzonitriles **71**, aldehydes **72**, and sodium azide **73** in the presence of Fe/Cu based catalyst.



Scheme 2.16. Synthesis of quinazolines from ortho-halogenated benzonitriles as starting material

2.2.5. Methods based on (2-bromophenyl)methylamine as starting material

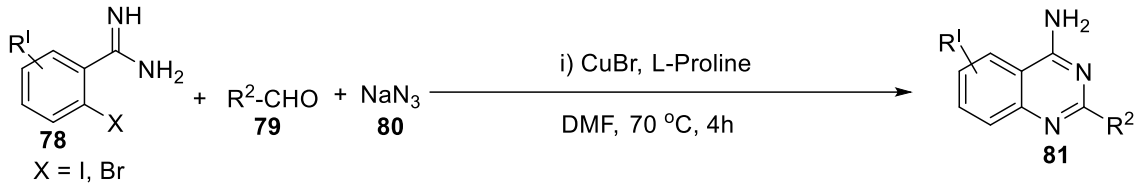
Liu et al. (2013) reported a method based on the reaction of (2-bromophenyl)methylamines **75** and amidine hydrochlorides **76** in the presence of CuBr catalyst under air atm to give quinazoline **77** derivatives in excellent yield.



Scheme 2.17. Synthesis of quinazolines from (2-bromophenyl)methylamine as starting material

2.2.6. Methods based on 2-iodo- or 2-bromobenzimidamides as starting material

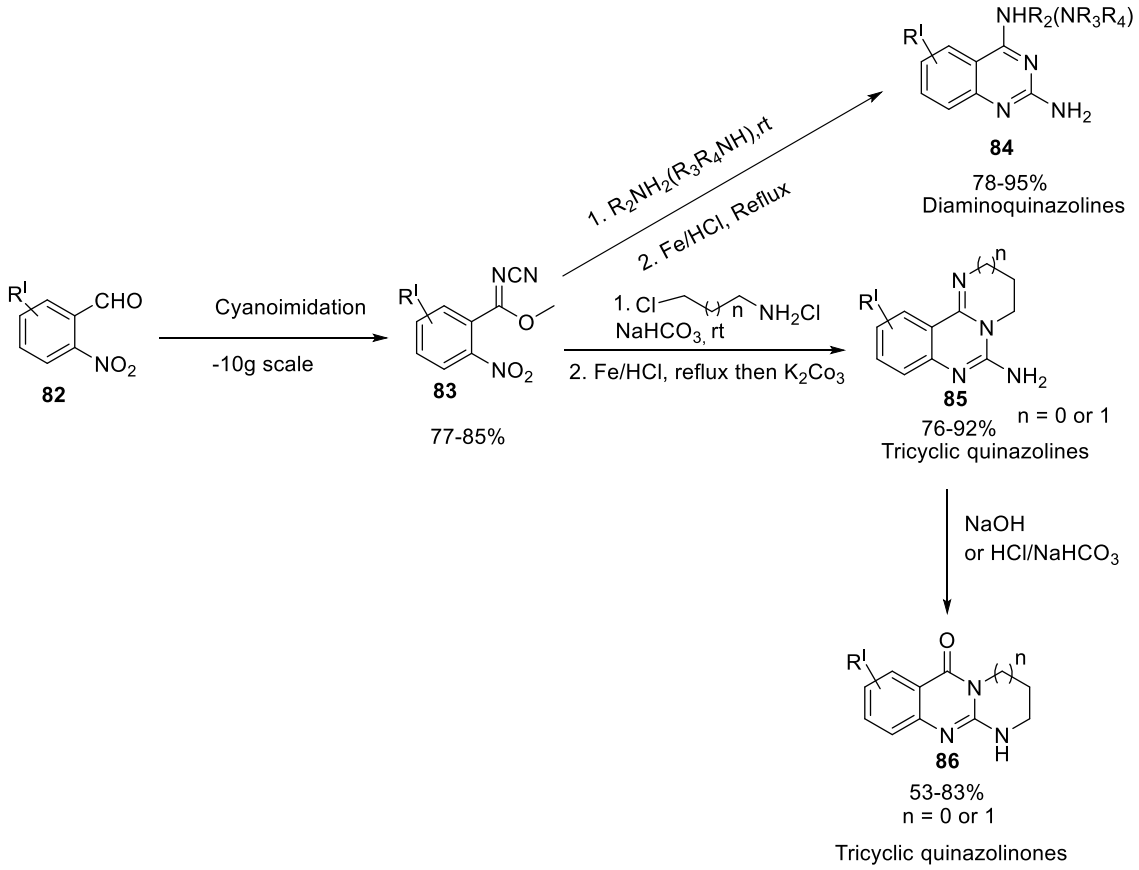
Yang et al. (2017) reported a method based on the reaction of 2-iodo- or 2-bromobenzimidamides **78**, aldehydes **79**, and sodium azide **80** in the presence of copper-catalyst to give 4-aminoquinazolines **81**. It gives 50–90% yield.



Scheme 2.18. Synthesis of quinazolines from 2-iodo- or 2-bromobenzimidamides as starting material

2.2.7. Methods based on 2-nitrobenzaldehyde as starting material

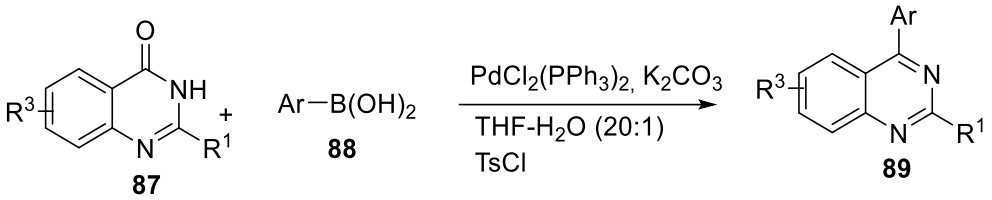
Yin et al. (2012) reported a route to the synthesis of diaminoquinazolines **84** had been developed by condensation of cyanoimidate−amine reductive cyclization in the presence of the iron−HCl system. It shows a two-step synthesis of tricyclic quinazolines **85**, which is affected by cyanoimidation and reductive cyclization from 2-nitrobenzaldehydes **82.** It shows that the synthesis of tricyclic quinazolinones **86** in good yields relies on the selective hydrolysis of tricyclic quinazolines **85** in the base or acid system.



Scheme 2.19. Synthesis of quinazolines based on 2-nitrobenzaldehyde as starting material

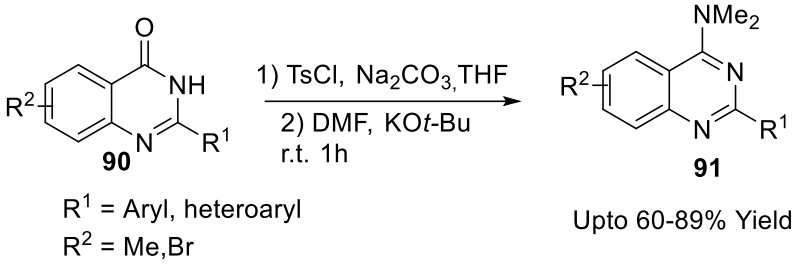
2.2.8. Methods based on quinazolin-4-ones as starting material

Qiu et al. (2013) reported a method based on the reaction of quinazolin-4-ones **87** and arylboronic acid **88** in the presence of palladium catalyst and TsCl to give 4-arylquinazolines **89** in high yield.



Scheme 2.20. Synthesis of quinazolines based on arylation of quinazolin-4-ones as starting material

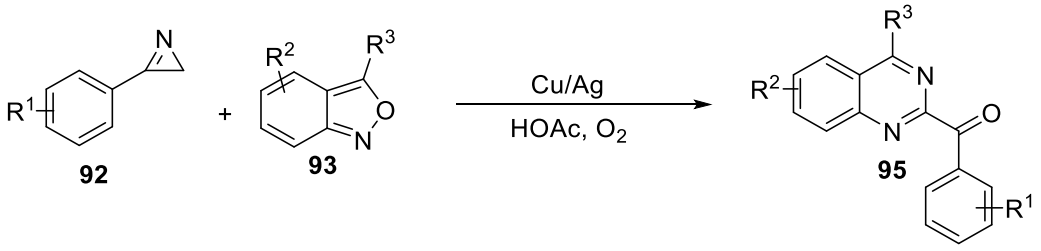
Chen et al. (2015) reported a method based on synthesising 4-(dimethylamino)quinazolines **91** via direct amination of quinazolin-4(3H)-ones **90**. Using N, N-dimethylformamide as a nitrogen source, the C–OH bond is activated by 4-toluenesulfonyl chloride at room temperature.



Scheme 2.21. Synthesis of quinazolines based on amination of quinazolin-4-ones as starting material

2.2.9. Methods based on azirines with anthranils as starting material

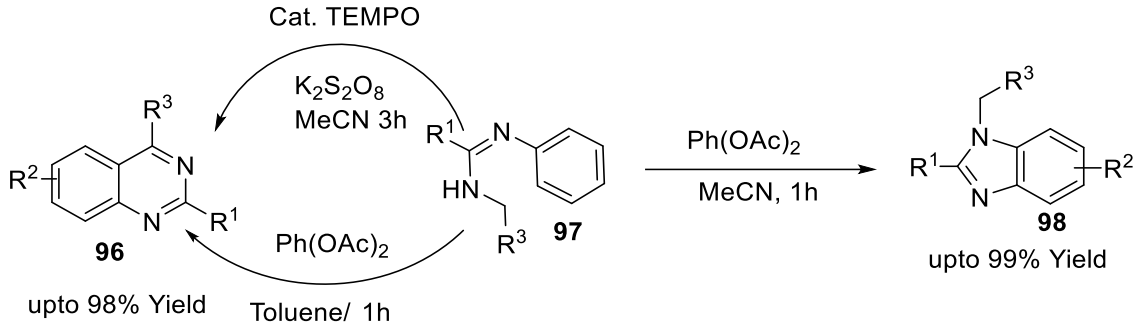
Sun et al. (2020) reported a reaction of 3-aryl-2*H*-azirines **92** with anthranils **93** in the presence of Cu/Ag-catalyst and AcOH under oxygen atm to give (quinazolin2-yl)methanone **95** derivatives.



Scheme 2.22. Synthesis of quinazolines based on azirines with anthranils as starting material

2.2.10. Methods based on arylamidines as starting material

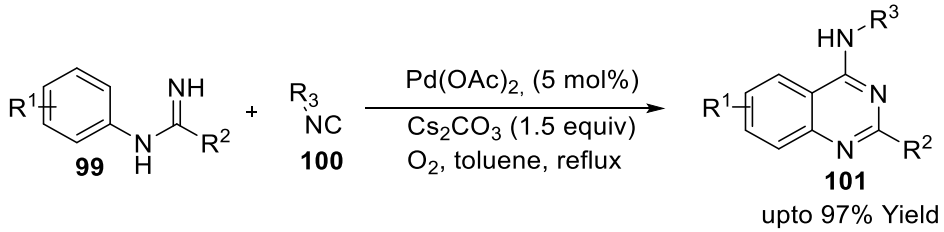
Lin et al. (2014) reported a synthesis of quinazolines **96** and benzimidazoles **98** from amidines **97** via iodine(III) oxidative C−C and C−N bond formation in nonpolar and polar solvents, respectively. Further synthesis of quinazolines **96** in polar solvent was developed by TEMPO as catalyst, and $K_2S_2O_8$ as an oxidant.



Scheme 2.23. Synthesis of quinazolines and benzimidazoles based on arylamidines as starting material

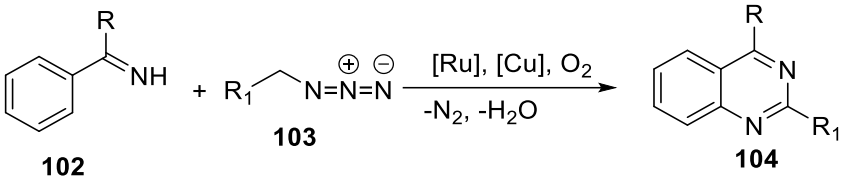
2.2.11. Methods based on C-H functionalization

Wang et al. (2011) reported a method based on the reaction of N-arylamidines **99** and isonitriles **100** in the presence of Pd catalyst with a base to give 4-amino-2-aryl(alkyl)quinazolines **101**.



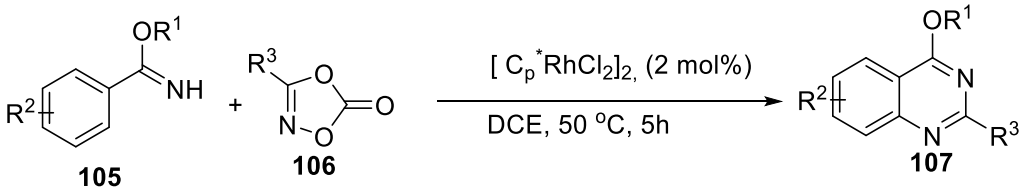
Scheme 2.24. Synthesis of quinazolines based on N-arylamidines with isonitriles as starting material

Wang and Jiao (2016) reported a method based on the reaction of imidate ester **102** with alkyl azides **103** in the presence of rhodium- and copper-co-catalyst under oxygen atm to give the multisubstituted quinazoline **104.**



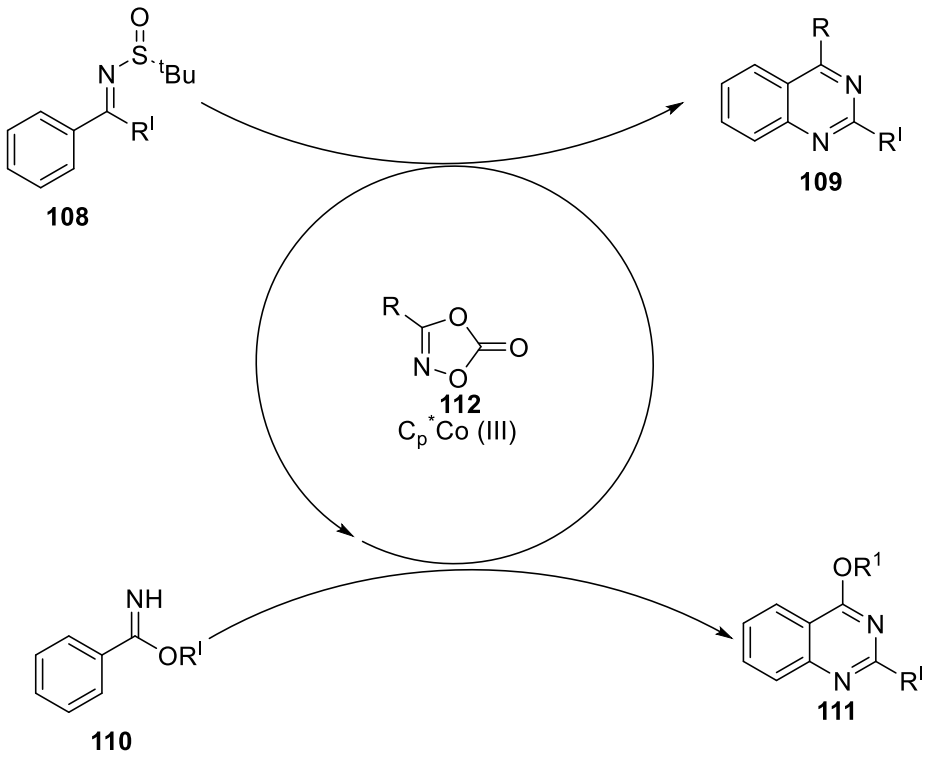
Scheme 2.25. Synthesis of quinazolines based on C−H annulation with alkyl azides as starting material

Wang et al. (2016) reported a method based on the reaction of benzimidates **105** and dioxazolones **106** in the presence of $[Cp^*RhCl_2]_2/AgBF_4$ catalyst to give highly substituted quinazoline **107**.



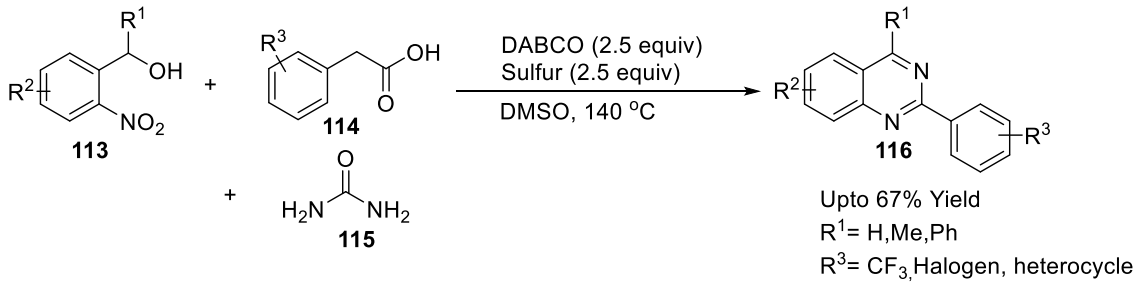
Scheme 2.26. Synthesis of quinazolines based on N-arylamidines with dioxazolones as starting material

Wang et al. (2016) reported the synthesis of quinazolines **109,111,** in the presence of Co(III)-catalyst via activation of benzimidates **110** and N-sulfinylimines **108**. Under Co(III) catalysis, dioxazolones **112** were used as a nitrile synthon, and subsequent coupling with arenes such as N-sulfinylimines **108** and benzimidates **110** bearing a functionalizable directing group provided easy access to two classes of quinazolines **109** & **111**.



Scheme 2.27. Synthesis of quinazolines based on N-sulfinylimines and benzimidates as starting material

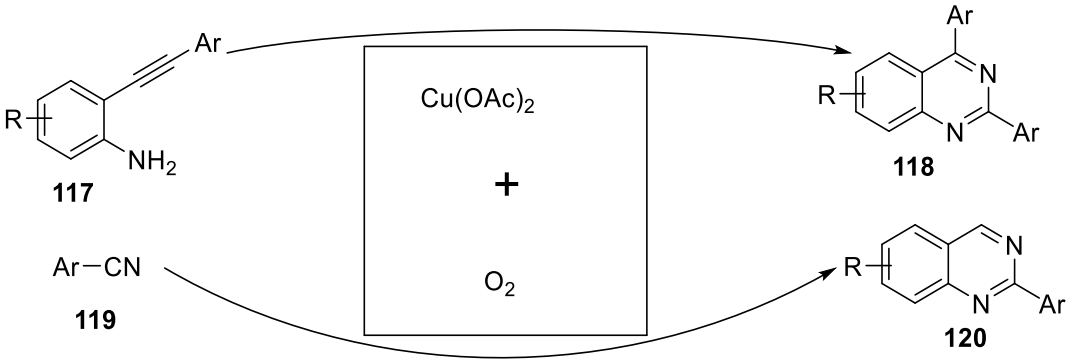
Nguyen et al. (2020) reported the condensation of 2-nitrobenzyl alcohols **113** with arylacetic acids **114** for producing substituted quinazolines **116**. Urea **115** is used as a nitrogen supply, elemental sulfur as a promoter, DABCO as a base, and DMSO as a solvent in this transformation. The reaction conditions were compatible with functionalities such as chloro, fluoro, trifluoromethyl, thienyl and indolyl groups.



Scheme 2.28. Synthesis of quinazolines based on 2-nitrobenzylalcohol as starting material

2.2.12. Methods based on benzonitriles and 2-ethynylanilines as starting material

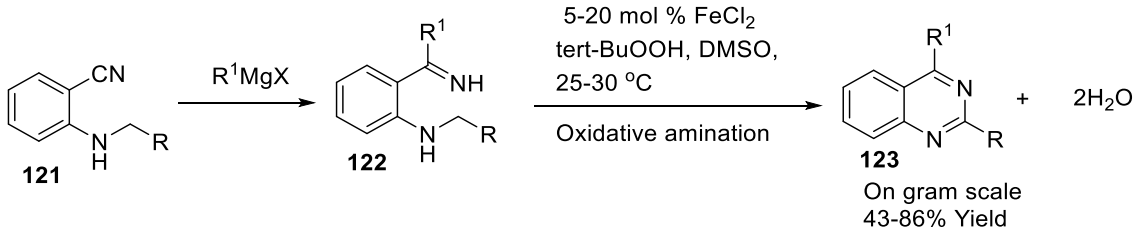
Wang et al. (2018) reported the synthesis of substituted quinazolines **118,120,** from benzonitriles **119** and 2-ethynylanilines **117** using molecular oxygen (O_2) as the only oxidant in the presence of a copper-catalyst. In this method, the mild catalytic system enabled the effective cleavage of the C-C triple bond, as well as new C-N and C-C bonds is constructed.



Scheme 2.29. Synthesis of quinazolines based on benzonitriles and 2-ethynylanilines as starting material

2.2.13. Methods based on oxidative amination of N-H ketimines as starting material

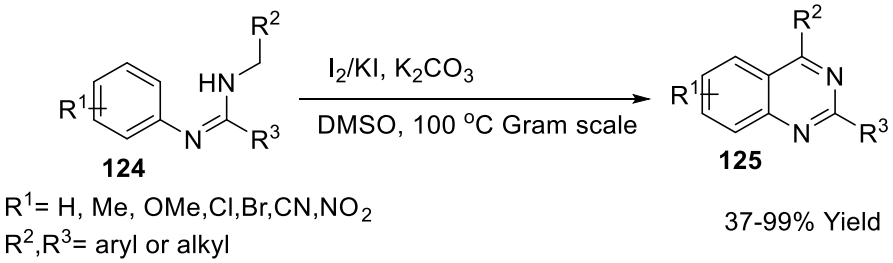
Chen et al. (2018) reported the reaction of commercially available 2-alkylamino benzonitriles **121** with various Grignard reagents led to 2-alkylamino N-H ketimine **122** species. Following oxidation with tert-BuOOH in the presence of iron-catalyst allows the formation of quinazolines **123** in good yield.



Scheme 2.30. Synthesis of quinazolines based on oxidative amination of N-H ketimines as starting material

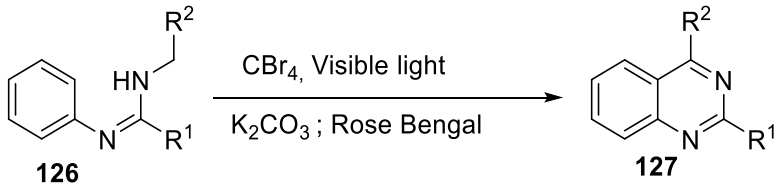
2.2.14. Methods based on N,N'-disubstituted amidines as starting material

Lv et al. (2016) reported an I_2/KI oxidative bond formation reaction in DMSO to produce quinazolines **125** from N,N'-disubstituted amidines **124** in the presence of K_2CO_3.



Scheme 2.31. Synthesis of quinazolines based on N,N'-disubstituted amidines as starting material

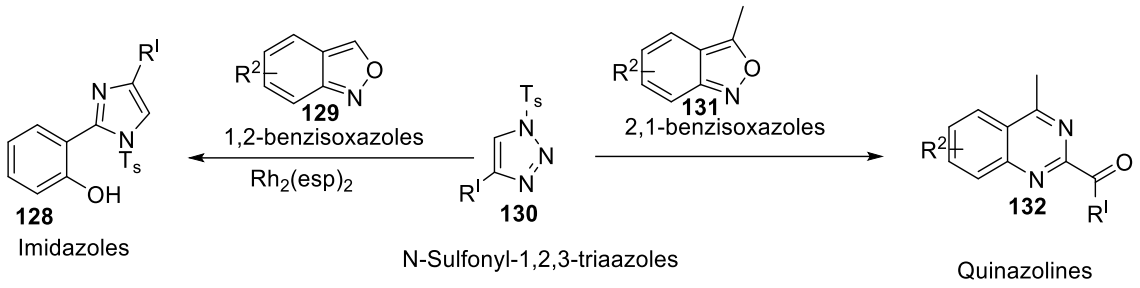
Shen et al. (2016) reported the synthesis of disubstituted quinazolines **127** from commercially available amidines **126** in the presence of photoredox organocatalyst via visible light-mediated oxidative C-C bond formation.



Scheme 2.32. Synthesis of quinazolines based on amidines as starting material

2.2.15. Methods based on N-sulfonyl -1,2,3 -triazoles as starting material

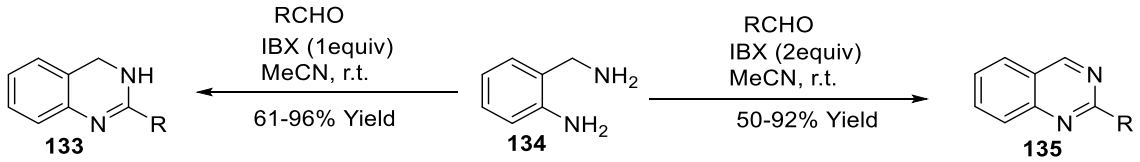
Lei et al. (2016) reported a method based on the synthesis of quinazoline **132** derivatives by annulation of N-sulfonyl-1,2,3-triazoles **130** with 2,1-benzisoxazoles **131** in the presence of Rh(II)-catalyst. N-sulfonyl-1,2,3-triazole **130** has been used as an aza-[2C]-component in cycloadditions. In the meantime, a Rh(II)-catalyzed formal [3+2] cycloaddition of N-sulfonyl -1,2,3-triazoles **130** with 2,1-benzisoxazoles **131** is described allowing the synthesis of functionalized imidazole **128** derivatives.



Scheme 2.33. Synthesis of quinazoline and imidazoles based on N-sulfonyl-1,2,3-triazoles as starting material

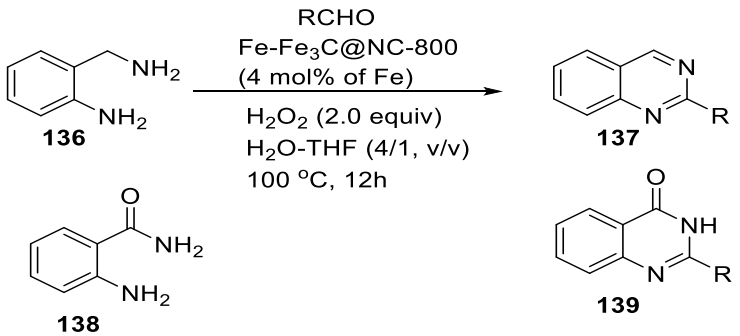
2.2.16. Methods based on *o*-aminobenzylamine as starting material

Hati and Sen (2016) reported that *o*-iodoxybenzoic acid (IBX) mediated tandem reaction of commercially available *o*-aminobenzylamine **134** and aldehydes resulted in the simple synthesis of diversely substituted quinazolines **135** and 3,4-dihydroquinazolines **133**. The reactions yielded between 50-96%.



Scheme 2.34. Synthesis of quinazoline and 3,4-dihydroquinazolines based on *o*-aminobenzylamine as starting material

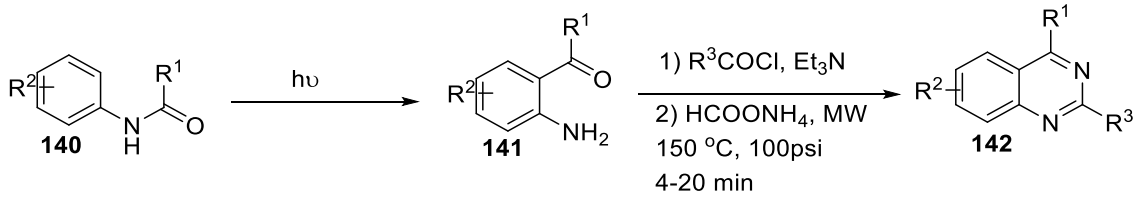
Ma et al. (2019) reported the synthesis of quinazoline **137** and quinazolinones **139** via oxidative coupling reaction of amines **136** and aldehydes in aqueous solution under mild conditions using H_2O_2 as the oxidant in the presence of Fe-Fe_3C@NC-800 catalyst.



Scheme 2.35. Synthesis of quinazoline and quinazolinones based on *o*-aminobenzylamine as starting material

2.2.17. Methods based on anilides as starting material

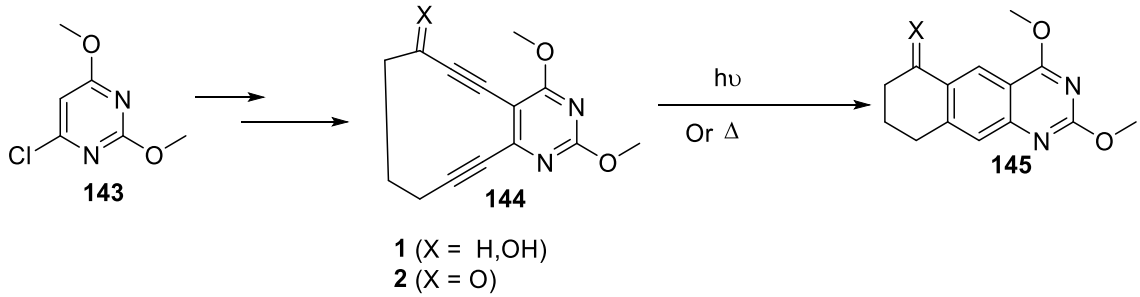
Ferrini et al. (2007) reported the synthesis of 2,4-dialkyl or aryl quinazolines **142** in three steps starting from commercially available anilides **140**. Initially, a photochemically induced Fries rearrangement of the anilides resulted in numerous *o*-aminoacylbenzene **141** derivatives. They are acylated to give the corresponding acilamides which underwent fast reaction under MW activation in the presence of ammonium formate.



Scheme 2.36. Synthesis of quinazolines based on anilides as starting material

2.2.18. Methods based on 4-chloro-2,6-dimethoxypyrimidine as starting material

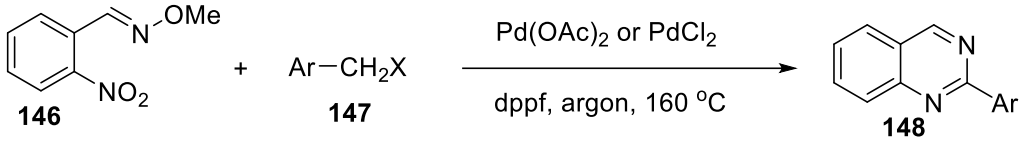
Choy et al. (2000) described the synthesis of novel 10-membered pyrimidine enediynes **145** (**1** & **2**) in seven to eight steps. The ability of these compounds to undergo Bergman cyclization both thermally and photochemically were studied. In *i*-PrOH, alcohol **1** cyclized both thermally and photochemically, but ketone **2** exclusively cyclized thermally. Under the right conditions, both chemicals were also found to cleave dsDNA.



Scheme 2.37. Synthesis of quinazolines based on 4-chloro-2,6-dimethoxypyrimidine as starting material

2.2.19. Methods based on (E)-2-nitrobenzaldehyde O-methyl oximes as starting material

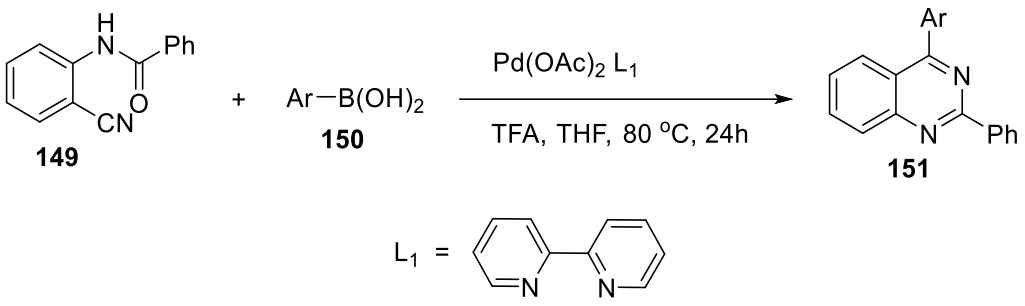
Wang et al. (2014) reported the synthesis of 2-arylquinazoline **148** via various (E)-2-nitrobenzaldehyde O-methyl oximes **146** interacted readily with alcohols or benzyl amines **147** in the presence of Pd catalyst. Similarly, 1-(2-nitrophenyl)ethanone, urea, and benzyl alcohols could be used to make heterocyclic compounds.



Scheme 2.38. Synthesis of quinazolines based on (E)-2-nitrobenzaldehyde O-methyl oximes as starting material

2.2.20. Methods based on N-(2-cyanoaryl) benzamides as starting material

Zhu et al. (2018) reported the synthesis of 2,4-disubstituted quinazolines **151** from the reaction of arylboronic acids **150** with N-(2-cyanoaryl)benzamides **149** in the presence of Pd-L_1 catalyst. Halogen and hydroxyl substituents, in particular, are well tolerated and are open to future synthetic elaborations.

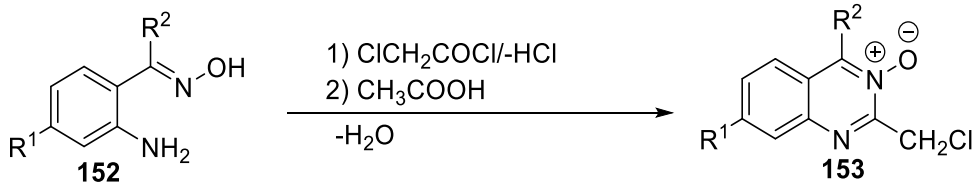


Scheme 2.39. Synthesis of quinazolines based on N-(2-cyanoaryl) benzamides as starting material.

2.3. Methods for the synthesis of quinazoline-3-oxide derivatives.

2.3.1. Methods based on chloroacetyl chloride as starting material

Jürgen (1994) reported a reaction of 1-(2-aminophenyl) ethanone oxime **152** with chloroacetyl chloride in glacial acetic acid, at 50°C. It gives quinazoline-3-oxide **153** derivatives after 10 minutes of stirring.



Scheme 2.40. Synthesis of quinazoline-3-oxide derivatives from 2-aminoaryl oxime derivatives.

2.3.2. Methods based on 1,2-dihydro-4-(2-flourophenyl)quinazoline-3-oxide as starting material

Walser and Flynn (1974) reported 2-fluorophenylquinazoline-3-oxide **156** derivatives are produced by oxidizing 1,2-dihydro-4-(2-fluorophenyl)quinazoline-3-oxide **154** with MnO_2 in methylene chloride. 2-Fluorophenylquinazoline **155** is obtained by treating acetic anhydride with 1,2-dihydro-4-(2-fluorophenyl)quinazoline-3-oxide **154**.

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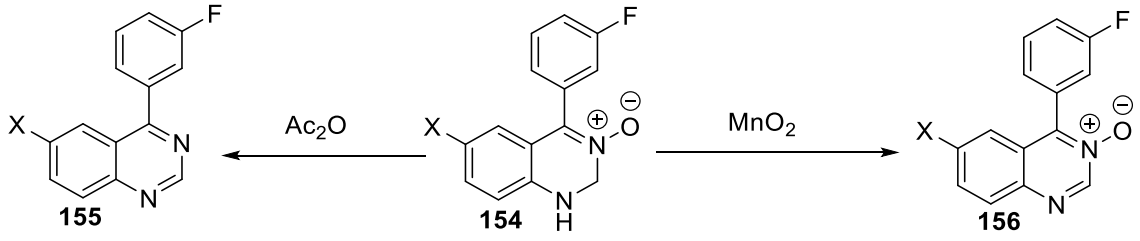
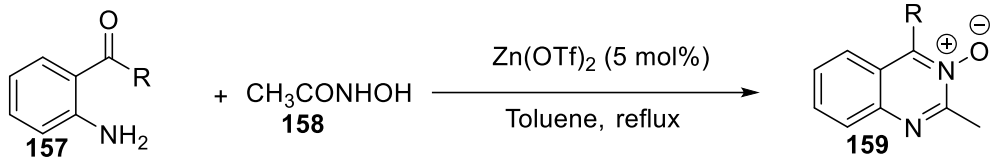


Scheme 2.41. Synthesis of 2-fluorophenylquinazoline-3-oxides and 2-fluorophenylquinazolines from 1,2-dihydro-4-(2-fluorophenyl)quinazoline-3-oxides.

2.3.3. Methods based on 2-aminoaryl ketones as starting material

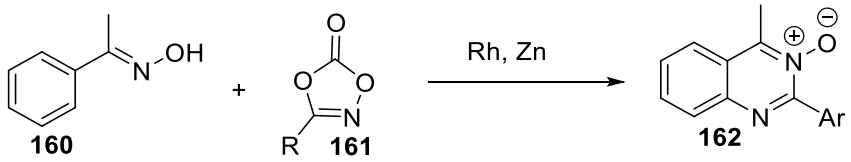
Madabhushi et al. (2014) reported the reaction of a hydroxamic acid **158** with 2-aminoaryl ketones **157** in the presence of zinc(II) triflate catalyst under reflux. It gives disubstituted quinazoline 3-oxides **159** with 62-95% yield.



Scheme 2.42. Synthesis of disubstituted quinazoline-3-oxides from 2-aminoaryl ketones.

2.3.4 Methods based on ketoximes and 1,4,2-dioxazol-5-ones as starting material

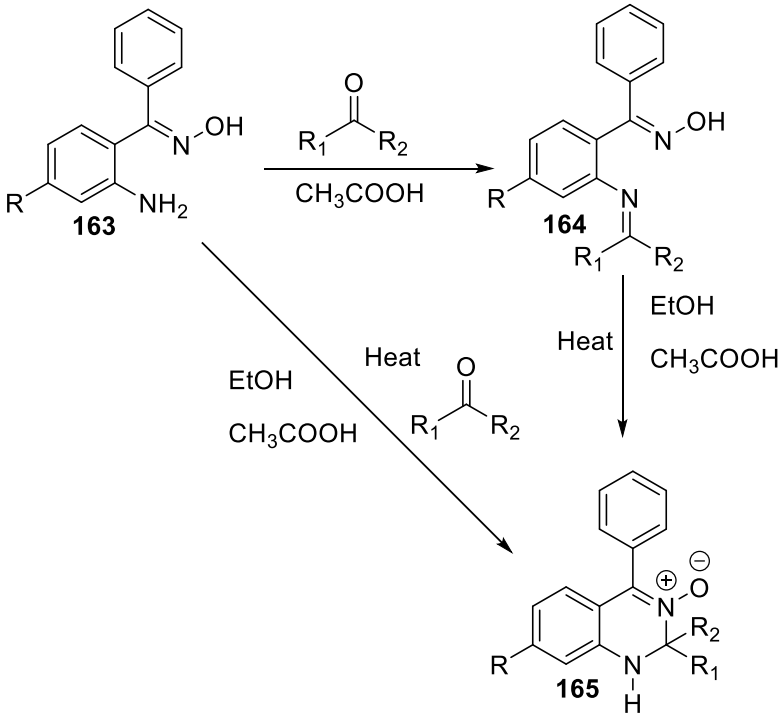
Wang et al. (2016) reported a method based on the reaction of ketoximes **160** and 1,4,2-dioxazol-5-ones **161** in the presence of Rh(III) and Zn(II) as catalysts to give quinazoline N-oxides **162**.



Scheme 2.43. Synthesis of disubstituted quinazoline-3-oxides from ketoximes and 1,4,2-dioxazol-5-ones as starting material.

2.3.5. Methods based on 2-amino-5-chlorobenzophenone E-oxime and 2-(N-methylideneamine)benzophenone oxime as starting material

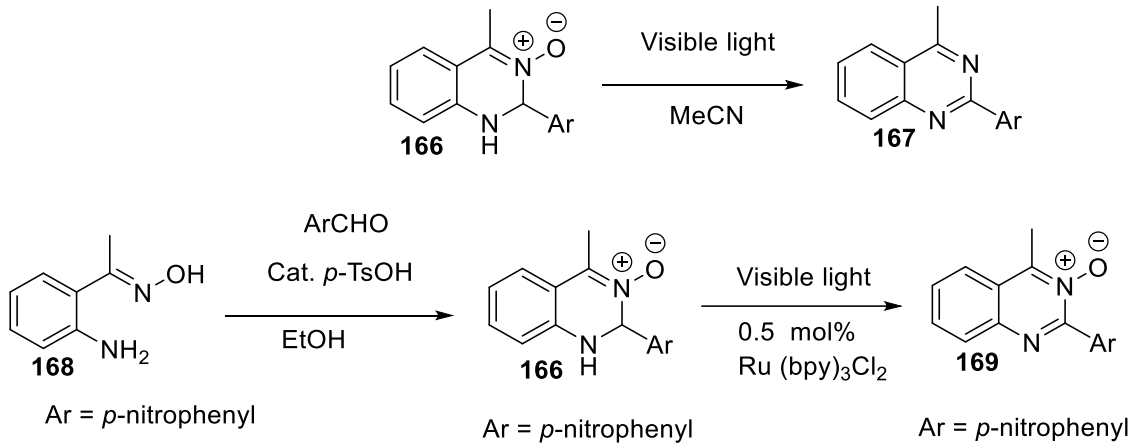
Olasik et al. (2004) reported 2-(N-methylideneamine)benzophenone oxime **164** is produced by combining 2-amino-5-benzophenone E-oxime **163** with suitable aldehydes or ketones. The 1,2-dihydroquinazoline-3-oxides **165** were generated by cyclo-condensation of oxime in acetic acid.



Scheme 2.44. Synthesis of 1,2-dihydroquinazoline -3-oxides derivatives from oxime.

2.3.6. Methods based on (E)-1-(2-aminophenyl)ethan-1-one oxime as starting material

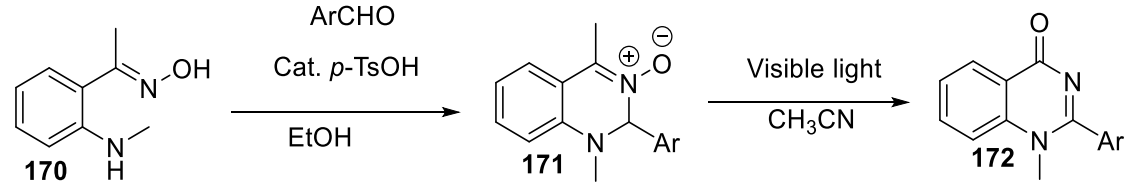
Chen and Yang (2013) reported the synthesis of 1,2-dihydroquinazoline-3-oxides **166** in the presence of a *p*-TsOH catalyst, from a condensation reaction of (E)-1-(2-aminophenyl)ethan-1-one oxime **168** and aldehydes. Without using any external sensitizers, 1,2-dihydroquinazoline 3-oxides **166** were exposed to visible light in acetonitrile, a variety of quinazolines **167** with good to excellent yields were generated. Except for 2-(p-nitrophenyl) substituted substrate, 2-(p-nitrophenyl) substituted substrate is transformed into quinazoline 3-oxide **169** in the presence of ruthenium photoredox catalyst.



Scheme 2.45. Synthesis of 1,2-dihydroquinazoline-3-oxides, quinazoline-3-oxides and quinazolines based on (E)-1-(2-aminophenyl)ethan-1-one oxime as starting material.

2.3.7. Methods based on 1-(2-(methylamino)phenyl)ethanone oxime as starting material

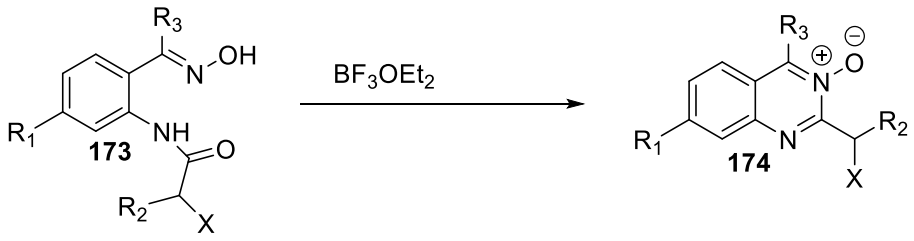
Wu and Yang (2016) described a condensation reaction of arylaldehyde and 1-(2-(methylamino)phenyl)ethanone oxime **170** in ethanol in the presence of *p*-TsOH. It gives 1,4-dimethyl-2-phenyl-1,2-dihydroquinazoline 3-oxides or 1-methyl-2-phenyl-1,2-dihydroquinazoline 3-oxides **171** as a product. In the absence of any photosensitizers from outside sources, 1-methyl-2-phenylquinazolin-4(1*H*)-ones **172** were produced in good yield by exposing 1,4-dimethyl-2-phenyl-1,2-dihydroquinazoline 3-oxides or 1-methyl-2-phenyl-1,2-dihydroquinazoline 3-oxides **171** to visible light in acetonitrile.



Scheme 2.46. Synthesis of 1,2-dihydroquinazoline 3-oxides, and quinazolinones based on 1-(2-(methylamino)phenyl)ethanone oxime as starting material.

2.3.8. Methods based on amidoxime as starting material

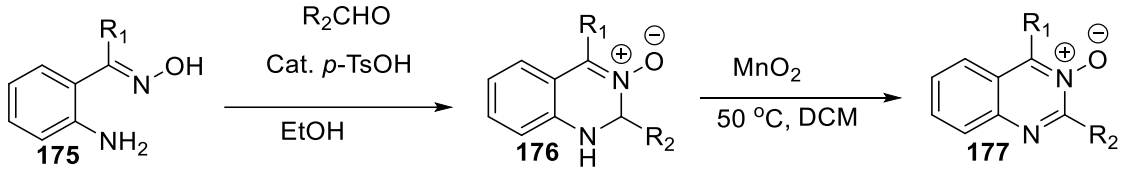
Heilig (1994) reported a reaction of amidoxime **173** and boron trifluoride etherate gives corresponding substituted quinazoline-3-oxides **174**.



Scheme 2.47. Synthesis of quinazoline-3-oxides based on amido oxime as starting material.

2.3.9. Methods based on (E)-1-(2-aminophenyl)ethan-1-one oxime as starting material

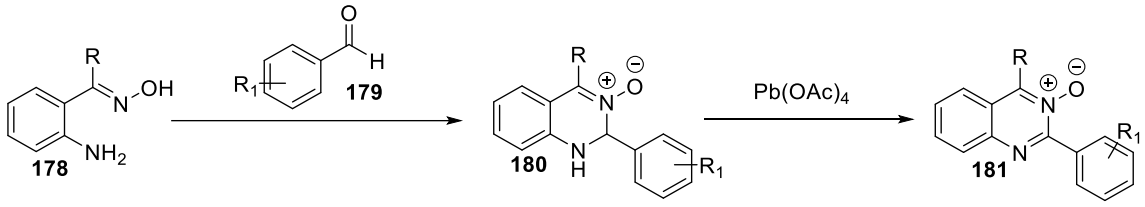
Ye et al. (2019) reported a condensation reaction of oxime **175** and aldehydes in the presence of *p*-TsOH catalyst to give 1,2-dihydroquinazoline-3-oxides **176**. The corresponding 1,2-dihydroquinazoline-3-oxides **176** converted into quinazoline-3-oxides **177** by using active MnO_2.



Scheme 2.48. Synthesis of 1,2-dihydroquinazoline-3-oxides and quinazoline-3-oxides starting from (E)-1-(2-aminophenyl)ethan-1-one oxime.

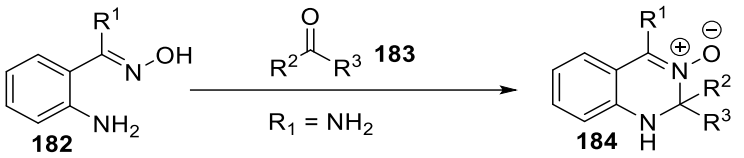
2.3.10. Methods based on *o*-amino-ketoximes as starting material

Atmaram et al. (1982) reported dihydro-quinazoline N-oxides **180** from the condensation reaction of *o*-aminoketoximes **178** and arylaldehydes **179**. Later, they were converted into quinazoline-3-oxide **181** in the presence of lead tetracetate as oxidant.



Scheme 2.49. Synthesis of 1,2-dihydroquinazoline-3-oxides, quinazoline-3-oxides starting from *o*-amino-ketoximes.

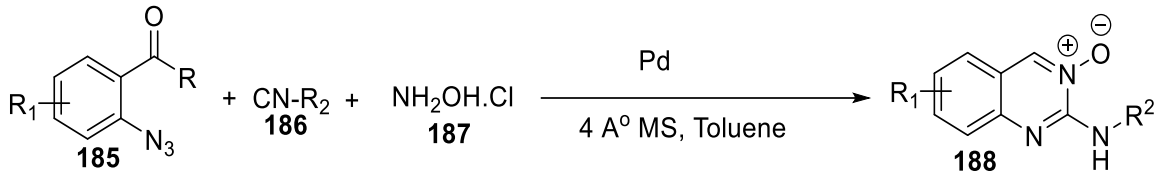
Lessel (1995) reported the cyclocondensation of *o*-aminophenyl-substituted keto-oximes **182** and amidoximes (R^1=NH_2) with carbonyl compounds **183** to give 1,2-dihydroquinazoline-3-oxides **184**.



Scheme 2.50. Synthesis of 1,2-dihydroquinazoline-3-oxides based on *o*-amino keto-oxime and amido-oximes as starting material.

2.3.11. Methods based on 2-azidobenzaldehyde as starting material

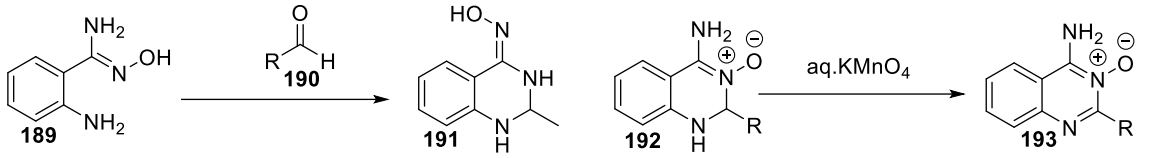
Pathare et al. (2019) reported the three-component reaction of 2-azidobenzaldehyde **185**, isonitrile **186** and hydroxylamine hydrochloride **187** in the presence of palladium catalyst to give quinazoline-3-oxides **188**.



Scheme 2.51. Synthesis of quinazoline-3-oxides based on 2-azidobenzaldehyde as starting material

2.3.12. Methods based on *o*-aminobenzamide oxime as starting material

Korbonits and Kolonits (1986) reported a condensation reaction of (Z)-2-amino-N'-hydroxybenzimidamide **189** with aldehydes **190** gives (E)-2-alkyl-2,3-dihydroquinazolin-4(1*H*)-one oxime **191**. Contrary to previous statements, the reaction between aldehydes and *o*-aminobenzamide oxime gives 4-amino-1,2-dihydroquinazoline 3-oxides.

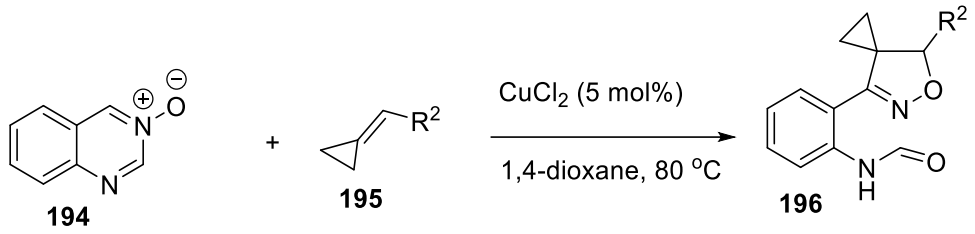


Scheme 2.52. Synthesis of (E)-2-alkyl-2,3-dihydroquinazolin-4(1H)-one oxime, 1,2-dihydro quinazoline-3-oxide and quinazoline-3-oxides.

2.4. C–H bond activation reaction of quinazoline 3-oxides.

2.4.1. Coupling reaction of quinazoline-3-oxide with alkylidenecyclopropane.

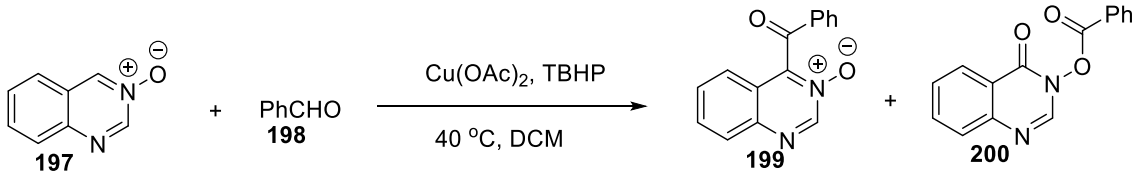
An et al. (2014) reported three-component reaction of quinazoline-3-oxide **194**, alkylidenecyclopropanes **195** and water under mild conditions in the presence of copper catalyst. This reaction involved [3+2] cycloaddition and intramolecular rearrangement to N-(2-(5-oxa-6-azaspiro[2.4]hept-6-en-7-yl)phenyl)formamides **196**.



Scheme 2.53. A reaction of quinazoline 3-oxides with alkylidene- cyclopropane.

2.4.2. Coupling reaction of quinazoline-3-oxide with unactivated aldehydes.

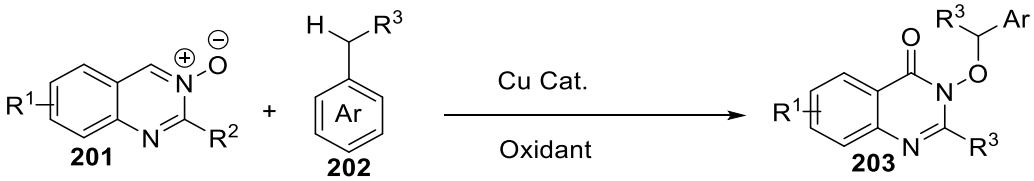
Fan et al. (2016) described the oxidative coupling reaction of quinazoline 3-oxides **197** and unactivated aldehydes **198** in the presence of copper catalyst and TBHP as an oxidant. To give a mixture of quinazoline ketones **199** and quinazolinone esters **200**.



Scheme 2.54. A reaction of quinazoline-3-oxides with various aldehydes.

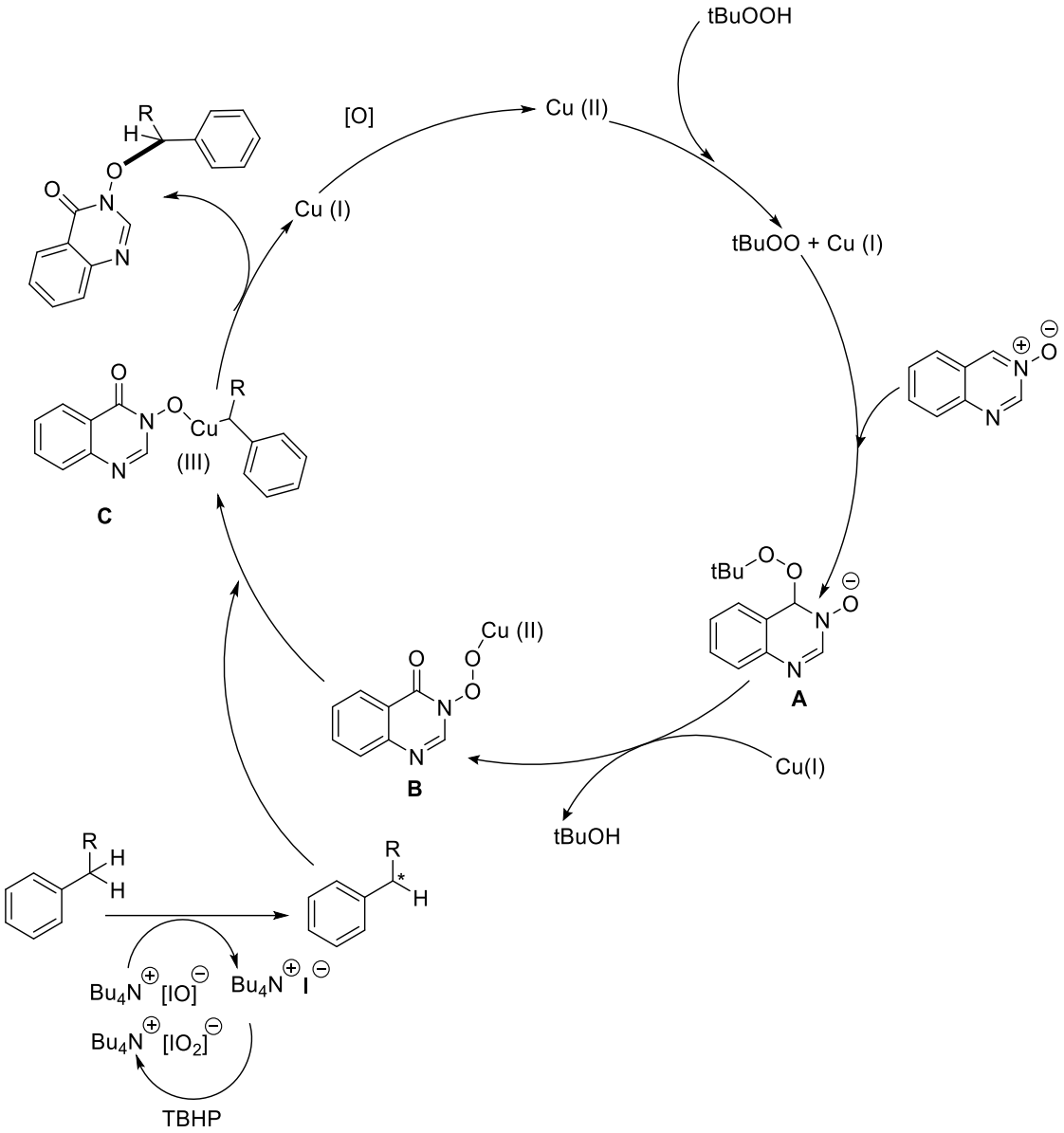
2.4.3. Coupling reaction of quinazoline-3-oxide with benzylic C(sp^3)–H bonds.

Fan et al. (2018) reported functionalization of benzylic C–H bonds **202** with quinazoline 3-oxides **201** in the presence of copper-catalyst. Using TBHP as an oxidant, this approach produces a broad range of quinazolin-4(3*H*)-one derivatives **203** with good yields.



Scheme 2.55. A reaction of quinazoline 3-oxides with benzylic C–H bond.

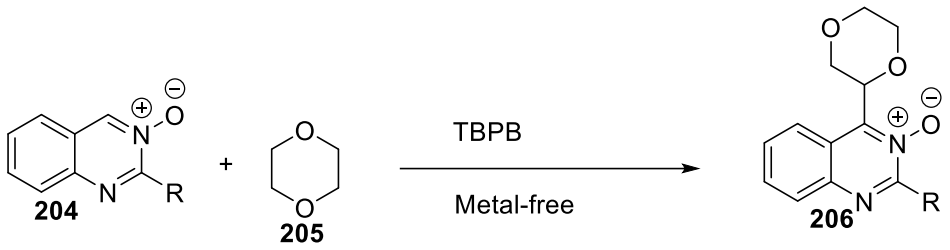
A possible reaction mechanism was proposed for this reaction, as shown in (Fig.2.61) The Cu(II) catalyst reacts with TBHP to give the tert-butylperoxy radical and a Cu(I) species. Following that, when the tert-butylperoxy radical is added to quinazoline 3-oxide give O-centered radical **A**, which interacts with Cu(I) to give an organocopper(II) species **B** while simultaneously eliminating t-BuOH. TBHP, on the other hand, *n*-Bu_4NI is oxidised by TBHP to provide the ammonium hypoiodite $[Bu_4N]^+[IO]^-$ or $[Bu_4N]^+[IO2]^-$. The benzyl radical was then formed when the ammonium hypoiodite interacted with the benzyl C–H bond. Organocopper(II) species **B** captured the benzyl radical, resulting in Cu(III) species **C**. The reductive elimination produces a Cu(I) species by completing the C–O bond. The catalytic cycle was finished when Cu(I) was oxidized to generate the Cu(II) catalyst.



Scheme 2.56. A plausible reaction mechanism of benzylic C–H bonds with quinazoline 3-oxides.

2.4.4. Coupling reaction of quinazoline-3-oxide with ethers.

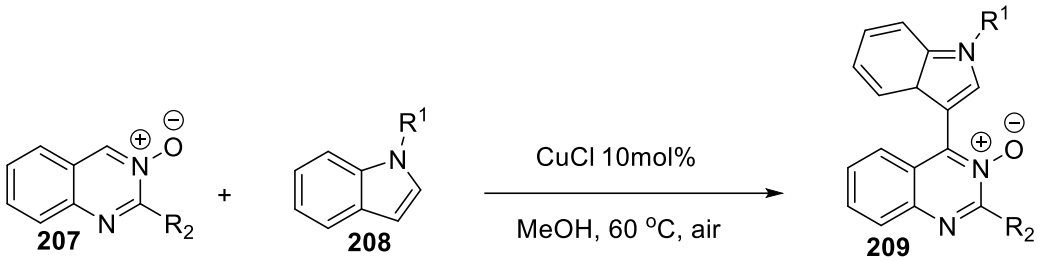
Yang et al. (2018) described cross-coupling reaction of quinazoline 3-oxide **204** with 1,4-dioxane **205**, in the presence of TBPB as an oxidant component. New quinazoline-containing heterocyclic compounds **206** were prepared with good yields under metal-free conditions.



Scheme 2.57. A reaction of quinazoline 3-oxide with 1,4-dioxane.

2.4.5. Coupling reaction of quinazoline-3-oxide with 1-methylindole.

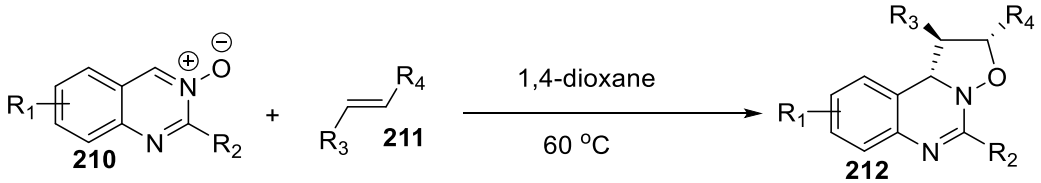
Yang et al. (2019) reported the cross-dehydrogenative coupling of quinazoline-3-oxides **207** with indoles **208** in the presence of a Cu catalyst in an air atmosphere to produce 4-(indole-3-yl)quinazolines **209**. It gives moderate to good yields, and several biheteroaryl compounds were produced.



Scheme 2.58. A reaction of quinazoline-3-oxides with 1-methylindole.

2.4.6. Cycloaddition of quinazoline-3-oxide with acrylates.

Yin et al. (2020) reported [3+2] cycloaddition of quinazoline-3-oxides **210** with acrylates **211** to make a range of isoxazolo[2,3-c] quinazolines **212**. In 1,4-dioxane, the corresponding isoxazolo[2,3-c] quinazolines **212** can be produced in good yields.

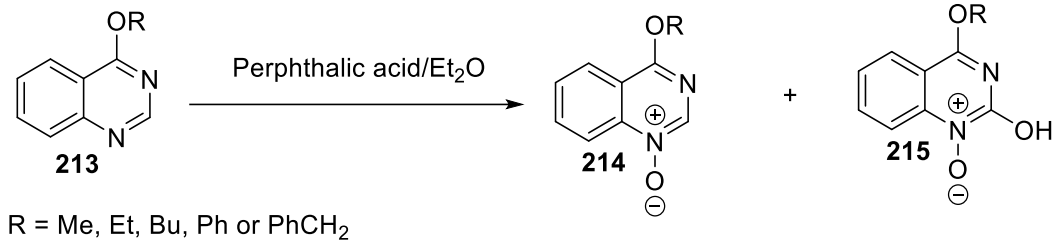


Scheme 2.59. Cycloaddition of quinazoline-3-oxides with acrylates.

2.5. Synthetic methods for quinazoline-1-oxide derivatives.

2.5.1. Methods based on quinazoline as a starting material.

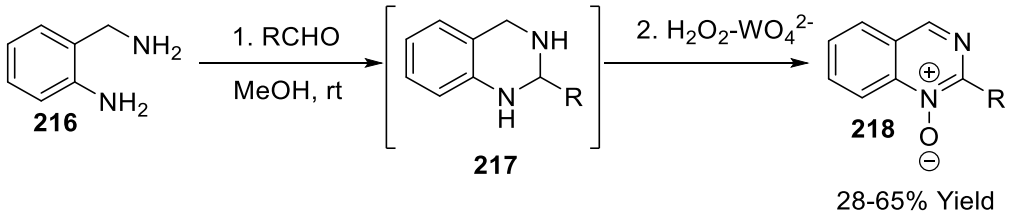
Hayashi and Higashino (1964) reported the oxidation of quinazoline **213** with perphthalic acid and ether to give quinazolines-1-oxides **214,215**. A little amount of the alkali soluble 2-hydroxy compound was also produced after the oxidation with perphthalic acid.



Scheme 2.60. Synthesis of quinazoline-1-oxides based on quinazoline as a starting material.

2.5.2. Methods based on 2-aminobenzylamine as a starting material.

Coşkun and Çetin (2007) reported quinazolin-1-oxides **218** were synthesis by the oxidation of tetrahydroquinazolines **217** with H_2O_2–tungstate, and their ambient light photochemistry were studied. In this protocol, Substituent effects on their photochemical cyclization were also studied with its solvent effect.

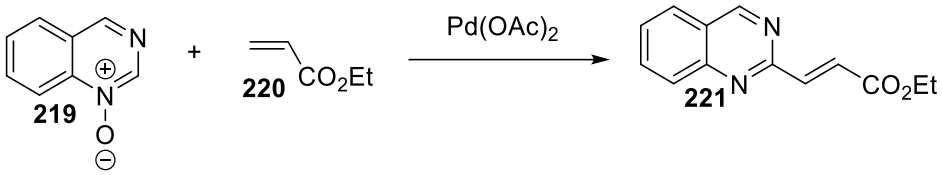


Scheme 2.61. Synthesis of quinazoline-1-oxide based on 2-aminobenzylamine as a starting material.

2.6. C-H functionalization of quinazoline-1-oxide.

2.6.1. Methods based on Alkenylation of Quinazoline-1-oxides.

Wu et al. (2009) reported a reaction of quinazoline-1-oxide **219** with ethylacrylate **220** in the presence of Pd catalyst under external-Oxidant-Free to give alkenylation of quinazoline **221**.



Scheme 2.62. C-H functionalization of quinazoline-1-oxide with ethylacrylate.

3. MATERIALS and METHODS

3.1. Instrument used in this study.

Melting points

An electrothermal digital melting point equipment was used to record melting points.

Nuclear Magnetic Resonance.

Bruker 600, Jeol 500, and Agilent 400 MHz spectrometers were used to record ^{1}H and ^{13}C NMR spectra.

Elemental analysis.

The elemental analyses were performed on a TruSpec and EuroEA 3000 CHNS analysers, the exact mass of some of the compounds were detected using waters SYNAPT G1 HRMS,

Infrared spectroscopy.

IR spectrum were recorded on a Jasco FT/IR 6600.

3.2. Chemicals used in this study.

The compounds were dried at room temperature in a vacuum oven. using technical grade solvents, column chromatography was done using 70-230 mesh (0,063-0,200 mm) silica gel and preparative TLC with silica gel 60 HF254 (90% <45 m). all of the reagents used in this study came from commercial sources and were utilized without further purification.

3.2.1. Chemicals of analytical purity.

PRODUCT CODE	NAME
A9628 ALDRICH	2-Aminobenzaldehyde
210250 SIGMA-ALDRICH	Hydroxylamine sulfate
324930 ALDRICH	Zinc powder
N10845 ALDRICH	3-Nitrobenzaldehyde
D130605 ALDRICH	2,5-Dimethoxybenzaldehyde
N10802 ALDRICH	2-Nitrobenzaldehyde
T35602 ALDRICH	*p*-Tolualdehyde
185914 SIGMA-ALDRICH	Furfural
124974 ALDRICH	2-Chlorobenzaldehyde
117552 ALDRICH	*o*-Tolualdehyde
P5833 SIGMA-ALDRICH	Potassium carbonate
12310 ALDRICH	Iron
A88107 ALDRICH	*p*-Anisaldehyde
112216 ALDRICH	4-Chlorobenzaldehyde
B57400 ALDRICH	4-Bromobenzaldehyde
B1334 SIGMA-ALDRICH	Benzaldehyde
202126 ALDRICH	Cesium carbonate
320331 SIGMA-ALDRICH	Hydrochloric acid
239313 SIGMA-ALDRICH	Sodium sulfate
06858 SIGMA-ALDRICH	Celite® S
499145 SIGMA-ALDRICH	Ammonia solution
483052 ALDRICH	Silver tetrafluoroborate
A6283 SIGMA-ALDRICH	Acetic acid
225657 ALDRICH	Zirconiumoxychloride octahydride
216763 SIGMA-ALDRICH	Hydrogen peroxide solution
223336 SIGMA-ALDRICH	Manganese triacetate dihydrate
P20009 ALDRICH	Phenylboronic acid
417599 ALDRICH	4-Methoxyphenylboronic acid
393614 ALDRICH	*m*-Tolylboronic acid

417548 ALDRICH	4-Chlorophenylboronic acid
1.06008 EMD MILLIPORE	Methanol
32205 SIGMA-ALDRICH	Ethanol
1.00668 EMD MILLIPORE	Dichloromethane
676764 SIGMA-ALDRICH	Tetrahydrofuran
208752 SIGMA-ALDRICH	Hexane
1.00003 EMD MILLIPORE	Acetonitrile
D4540 SIGMA	Dimethyl sulfoxide
32299 SIGMA-ALDRICH	Petroleum ether
1.09646 EMD MILLIPORE	Benzene
494488 SIGMA-ALDRICH	N,N-Dimethylformamide
1.00014 EMD MILLIPORE	Acetone
319929 SIGMA-ALDRICH	1,2-Dichloroethane
1.00849 EMD MILLIPORE	Toluene
1.02432 EMD MILLIPORE	Chloroform
613339 SIGMA-ALDRICH	Formamide solution
01870 SIGMA-ALDRICH	Silica gel 60 ADAMANT™ on TLC plates
1.07734 EMD MILLIPORE	Silica gel 60 (0.06-0.20 mm)
S7795 SIGMA-ALDRICH	Sodium carbonate

3.3. Experimental Procedures and Spectral data of the compounds

3.3.1. Synthesis of Oximes 1:

General procedure: The amino carbonyl (2-aminobenzaldehyde, 1-(2-aminophenyl)ethanone and 2-aminophenyl phenyl methanone) (33 mmol) and hydroxylamine sulfate (4.92 g, 30 mmol) were dissolved in MeOH/H_2O (35 mL, 6/1) and the reaction mixture stirred at ambient temperature and the reaction was monitored by TLC. After completion of the reaction the unreacted hydroxylamine sulfate was filtered off. Water was added to the mixture (20 mL) and extracted with chloroform (4X25 mL). The combined organic phases were dried over anhydrous Na_2SO_4, filtered and the solvent evaporated under reduced pressure. The residue was purified by flash column chromatography (Hexane and ethyl acetate) or recrystallization from CH_2Cl_2: Hexane. The NMR spectra of the starting oximes **1** were identical with those reported in the literature (Bella et al. 2004, Counceller et al. 2008).

3.3.2. Preparation of compounds 2a-m

General procedure: To a solution of amino oxime (1 mmol) in EtOH (20 mL) aldehyde (1 mmol) was added at room temperature and stirred for 24 h (for compounds **2k-m**, 47 h). The precipitating product was isolated by filtration trough a sintered glass funnel and washed with warm hexane. In the case of **2f** the solvent was evaporated and the crude was treated with warm hexane. Recrystallization from acetonitrile provided yellow coloured crystals.

2-(*p*-Nitrophenyl)-1,2-dihydroquinazoline 3-oxide 2a. Yield 97% (0.261 g). Yellow crystals, mp 196-197 ^oC. IR; ν_{N-H} 3213 cm^{-1}; ^1H NMR (600 MHz, DMSO-d_6) δ 8.23 (d, *J* = 8.8 Hz, 2H), 7.96 (s, 1H), 7.78 – 7.72 (m, 3H), 7.17 – 7.09 (m, 2H), 6.86 (d, *J* = 8.0 Hz, 1H), 6.74 (t, *J* = 7.5 Hz, 1H), 6.28 (d, *J* = 3.1 Hz, 1H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 148.2, 145.9, 139.3, 131.2, 130.8, 128.5, 126.0, 124.1, 119.6, 116.4, 114.4, 78.9. *Anal Calcd* for $C_{14}H_{11}N_3O_3$ (269.26): C, 62.45, H, 4.12, N, 15.61. *Found* C, 62.51, H, 4.14, N, 15.54.

2-(*p*-Chlorophenyl)-1,2-dihydroquinazoline 3-oxide 2b. Yield 96% (0.248 g). Yellow crystals, mp 187-188 ºC. IR; ν_{N-H} 3228 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.89 (s, 1H), 7.59 (d, *J* = 2.9 Hz, 1H), 752 – 7.48 (m, 2H), 7.46 – 7.41 (m, 2H), 7.19 – 7.06 (m, 2H), 6.83 (d, *J* = 8.0 Hz, 1H), 6.72 (td, *J* = 7.5, 1.1 Hz, 1H), 6.10 (d, *J* = 2.8 Hz, 1H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 139.6, 138.2, 132.5, 131.8, 130.8, 130.6, 129.3, 125.8, 119.3, 116.4, 114.2, 79.2. *Anal Calcd* for $C_{14}H_{11}ClN_2O$ (258.71); C, 65.00; H, 4.29; N, 10.83; *Found* C, 65.07; H, 4.30; N, 10.80.

2-(3-Bromophenyl)-1,2-dihydroquinazoline 3-oxide 2c. Yield 99% (0.300 g). Yellow crystals, mp 176-177 ºC. IR; ν_{N-H} 3215 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.93 (s, 1H), 7.69 – 7.61 (m, 2H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.46 (d, *J* = 7.8 Hz, 1H), 7.33 (t, *J* = 7.9 Hz, 1H), 7.17 – 7.07 (m, 2H), 6.84 (d, *J* = 8.0 Hz, 1H), 6.73 (t, *J* = 7.5 Hz, 1H), 6.12 (d, *J* = 2.8 Hz, 1H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 141.3, 139.5, 132.1, 131.2, 131.1, 130.8, 129.8, 126.0, 125.9, 122.0, 119.4, 116.2, 114.2, 78.9. *Anal Calcd* for $C_{14}H_{11}BrN_2O$ (303.15); C, 55.47, H, 3.66, N, 9.24, *Found* C, 55.59, H,3.65, N, 9.26.

2-(3-Chlorophenyl)-1,2-dihydroquinazoline 3-oxide 2d. Yield 94% (0.243 g). Yellow crystals, mp 169-170 ºC. IR; ν_{N-H} 3226 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.93 (s, 1H), 7.64 (d, *J* = 2.7 Hz, 1H), 7.52 (s, 1H), 7.41 (dt, *J* = 9.8, 7.3 Hz, 3H), 7.16 – 7.09 (m, 2H), 6.84 (d, *J* = 8.0 Hz, 1H), 6.76 – 6.71 (m, 1H), 6.12 (d, *J* = 2.8 Hz, 1H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 141.1, 139.5, 133.5, 131.2, 130.9, 130.8, 129.2, 126.9, 126.0, 125.6, 119.4, 116.2, 114.2, 78.9. *Anal Calcd* for $C_{14}H_{11}ClN_2O$ (258.71); C, 65.00, H, 4.29, N, 10.83, *Found* C, 64.97, H, 4.30, N, 10.81.

2-(*p*-Methoxyphenyl)-1,2-dihydroquinazoline 3-oxide 2e. Yield 53% (0.135 g). Yellow crystals, mp 174-175 ºC. IR; ν_{N-H} 3185 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (s, 1H), 7.52 (d, *J* = 8.6 Hz, 2H), 7.23 (t, *J* = 7.7 Hz, 1H), 7.08 (d, *J* = 7.6 Hz, 1H), 6.90 (t, *J* = 7.9 Hz, 3H), 6.80 (d, *J* = 7.9 Hz, 1H), 6.10 (d, *J* = 2.2 Hz, 1H), 4.82 (s, 1H), 3.82 (s, 3H). 13C NMR (101 MHz, $CDCl_3$) δ 153.2, 138.5, 131.6, 130.7, 129.3, 128.6, 125.8, 122.8, 120.5, 114.2, 114.1, 80.2, 55.3. *Anal Calcd* for $C_{15}H_{14}N_2O_2$ (254.28); C, 70.85, H, 5.55, N, 11.02, *Found* C, 70.76, H, 5.57, N,11.00.

2-Phenyl-1,2-dihydroquinazoline 3-oxide (2f). Yield 94% 0.211 g. Yellow crystals, mp 139-140 °C. IR; ν_{N-H} 3152 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (s, 1H), 7.60 – 7.48 (m, 1H), 7.41 (dt, J = 8.7, 4.6 Hz, 2H), 7.35 – 7.25 (m, 3H), 7.08 – 7.00 (m, 2H), 6.75 (d, J = 7.9 Hz, 1H), 6.65 (td, J = 7.5, 0.8 Hz, 1H), 6.00 (d, J = 2.6 Hz, 1H). ^{13}C NMR (126 MHz) δ 139.9, 139.0, 130.6, 130.5, 129.3, 128.8, 127.0, 125.8, 119.1, 116.4, 114.0, 79.8; *Anal Calcd* for $C_{14}H_{12}N_2O$ (224.26), C, 74.98, H, 5.39, N, 12.49. *Found* C, 74.72, H, 5.40, N, 12.48.

2-(*p*-Bromophenyl)-1,2-dihydroquinazoline 3-oxide 2g. Yield 96% (0.291 g). Yellow crystals, mp 198-199 °C. IR; ν_{N-H} 3232 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.89 (s, 1H), 7.64 – 7.54 (m, 3H), 7.43 (d, *J* = 8.1 Hz, 2H), 7.16 – 7.07 (m, 2H), 6.82 (d, *J* = 8.0 Hz, 1H), 6.72 (t, *J* = 7.5 Hz, 1H), 6.08 (d, *J* = 2.9 Hz, 1H). ^{13}C NMR (151 MHz, DMSO) δ 139.6, 138.2, 132.5, 131.8, 130.8, 130.6, 129.3, 125.8, 119.3, 116.4, 114.2, 79.2. *Anal Calcd* for $C_{14}H_{11}BrN_2O$ (303.15); C, 55.47, H, 3.66, N, 9.24. *Found* C, 55.63, H, 3.65, N, 9.20.

2-(3,4-Dimethoxyphenyl)-1,2-dihydroquinazoline 3-oxide 2h. Yield 96% (0.273 g). Yellow crystals, mp 141-142 °C. IR; ν_{N-H} 3221 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.84 (s, 1H), 7.53 (d, *J* = 2.7 Hz, 1H), 7.15 – 7.08 (m, 2H), 7.07 (dd, *J* = 7.8,1.5 Hz, 1H), 6.95 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.90 (d, *J* = 8.4 Hz, 1H), 6.82 (d, *J* = 7.8 Hz, 1H), 6.70 (td, *J* = 7.5,1.1 Hz, 1H), 5.97 (d, *J* = 2.5 Hz, 1H), 3.70 (d, *J* = 17.5 Hz, 6H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 149.6, 148.9, 140.0, 131.1, 130.4, 130.3, 125.6, 119.3**,** 119.0, 116.5, 114.0, 111.8, 110.9, 79.7, 56.0, 55.9. *Anal Calcd* for $C_{16}H_{16}N_2O_3$ (284.31), C, 67.59, H, 5.67, N, 9.85. *Found* C, 67.64, H, 5.69, N, 9.86.

2-(4-Methylphenyl)-1,2-dihydroquinazoline 3-oxide 2i. Yield 68% (0.162 g). Yellow crystals, mp 157-158 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (s, 1H), 7.41 (d, *J* = 8.1 Hz, 2H), 7.20 – 7.08 (m, 3H), 7.01 (d, *J* = 7.6 Hz, 1H), 6.82 (dd, *J* = 11.0, 4.0 Hz, 1H), 6.77 – 6.69 (m, 1H), 6.05 (d, *J* = 2.6 Hz, 1H), 4.94 (s, 1H), 2.30 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.6, 138.6, 134.2, 131.8, 130.7, 129.4, 126.9, 125.8, 120.3, 116.4, 114.3, 80.0, 21.0. *Anal Calcd* for $C_{15}H_{14}N_2O$ (238.29), C, 75.61; H, 5.92; N, 11.76. *Found* C, 75.50; H, 5.92; N, 11.71.

2-(Furan-2-yl)-1,2-dihydroquinazoline 3-oxide 2j. Yield 50% (0.107 g). Yellow crystals, mp 118-119 ºC. IR; ν_{N-H} 3125 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (s, 1H), 7.39 (d, *J* = 1.4 Hz, 1H), 7.21 (td, *J* = 7.9, 1.3 Hz, 1H), 7.08 (d, *J* = 7.5 Hz, 1H), 6.89 (t, *J* = 7.5 Hz, 1H), 6.78 (d, *J* = 8.0 Hz, 1H), 6.45 (d, *J* = 3.3 Hz, 1H), 6.33 (dd, *J* = 3.3, 1.8 Hz, 1H), 6.13 (d, *J* = 2.9 Hz, 1H), 4.91 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.7, 138.1, 131.9, 130.9, 125.9, 120.7, 116.2, 114.5, 110.6, 109.8, 74.60. *Anal Calcd* for $C_{12}H_{10}N_2O_2$ (214.22), C, 67.28, H, 4.71, N, 13.08, *Found* C, 67.10, H, 4.70, N, 13.10.

4-Methyl-2-(4-nitrophenyl)-1,2-dihydroquinazoline 3-oxide 2k. Yield 79% (0.224 g). Yellow crystals, mp 167-168 ºC; Lit mp 166-167 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.7 Hz, 2H), 7.75 (d, *J* = 8.7 Hz, 2H), 7.27 – 7.20 (m, 2H), 7.01 – 6.88 (m, 2H), 6.25 (d, *J* = 4.2 Hz, 1H), 5.28 (d, *J* = 3.9 Hz, 1H), 2.46 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.3, 144.2, 140.7, 137.7, 130.6, 127.9, 124.9, 123.8, 121.6, 118.6, 116.3, 78.6, 12.5 (Y.-C. Chen and Yang 2013).

2-(4-Methoxyphenyl)-4-methyl-1,2-dihydroquinazoline 3-oxide 2l. Yield 84% (0.225 g). Yellow crystals, mp 160-161 ºC; Lit mp 164-165 ºC.^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, *J* = 8.1 Hz, 2H), 7.24 – 7.13 (m, 2H), 6.88 (t, *J* = 7.5 Hz, 1H), 6.85-6.75 (m, 3H), 6.05 (d, *J* = 2.2 Hz, 1H), 5.08 (s, 1H), 3.76 (s, 3H), 2.42 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.2, 140.0, 139.1, 130.1, 129.8, 128.2, 124.6, 120.2, 117.9, 114.8, 113.9, 79.2, 55.3, 12.4.

2-(4-Nitrophenyl)-4-phenyl-1,2-dihydroquinazoline 3-oxide 2m. Yield 73% (0.242 g). Yellow crystals, mp 191-192 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 – 8.17 (m, 2H), 7.88 (d, *J* = 8.7 Hz, 2H), 7.53 – 7.43 (m, 5H), 7.25 – 7.20 (m, 1H), 6.95 (d, *J* = 7.9 Hz, 1H), 6.87 – 6.79 (m, 2H), 6.30 (d, *J* = 4.9 Hz, 1H), 5.37 (d, *J* = 4.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.1, 143.7, 140.7, 138.1, 130.2, 129.9, 129.6 (2C), 128.3, 127.7, 127.0, 123.6, 121.5, 119.6, 117.0, 79.5. *Anal Calcd* for $C_{20}H_{15}N_3O_3$ (345.36), C, 69.56; H, 4.38; N, 12.17; *Found* C, 69.40, H, 4.39, N, 12.12.

3.3.3. General procedure of preparation of compounds 3a-m.

To a solution of substrate **2a-m** (1 mmol) in THF (4 mL), H_2O_2 (4 mmol, 35%, 0.389 g) and $Na_2WO_4.2H_2O$ (0.05 mmol, 0.017 g) were added and the mixture was stirred at room temperature for compounds **3a-j** (20-24 h). For the compounds **3k-m** the reaction was performed at 60 ^oC (47 h). After evaporation of the solvent water was added (15 mL) and the mixture basified with 10% NaOH, the mixture was extracted with chloroform (3x15 mL) and the combined extracts were dried over anhydrous Na_2SO_4, filtered. The residue after evaporation of the solvent was subjected to flash column chromatography using silica gel as an adsorbent and ethyl acetate–petroleum ether as eluent mixture. The isolated products were recrystallized from acetonitrile.

2-(*p*-Nitrophenyl) quinazoline 3-oxide 3a. Yield 92% (0.246 g). Yellow crystals, mp 233-234 ^oC. ^1H NMR (600 MHz, DMSO-d_6) δ 9.47 (s, 1H), 8.50 (d, J = 9.0 Hz, 2H), 8.39 (d, J = 9.0 Hz, 2H), 8.06 (d, J =8.3 Hz, 1H), 7.99 (d, J = 8.0 Hz, 1H), 7.88 (t, J = 8.4 Hz, 1H), 7.79 (t, J = 8.1 Hz, 1H); ^{13}C NMR (151 MHz, DMSO) δ 153.3, 148.8, 142.6, 140.3, 138.7, 132.4, 132.0, 130.8, 128.4, 125.4, 125.0, 123.3. *Anal Calcd* for $C_{14}H_9N_3O_3$ (267.24); C, 62.92, H, 3.39, N, 15.72. *Found* C, 62.94, H, 3.39, N,15.69.

2-(*p*-Chlorophenyl) quinazoline 3-oxide 3b. Yield 70% (0.180 g), (78% from one-pot). Yellow crystals, mp 160-162 ^oC; Lit. mp.161-162 ^oC. ^1H NMR (600 MHz, $CDCl_3$) δ 9.04 (s, 1H), 8.43 (d, J = 8.2 Hz, 2H), 8.06 (d, J = 8.4 Hz, 1H), 7.80 (t, J =7.7 Hz, 1H), 7.75 (d, J = 8.1 Hz, 1H), 7.69 (t, J = 7.6 Hz, 1H), 7.53 (d, J = 8.0 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 154.2, 142.3, 141.4, 137.5, 132.1, 131.9, 130.2, 129.9, 128.6, 128.4, 124.2, 121.3. (Necdet Coşkun and Çetin 2007)

2-(3-Bromophenyl) quinazoline 3-oxide 3c. Yield 64% (0.193 g), (77% from one-pot). Yellow crystals, mp 189-190 ^oC. ^1H NMR (600 MHz, $CDCl_3$) δ 9.11 (s, 1H), 8.57 (s, 1H), 8.41 (d, J = 7.9 Hz, 1H), 8.10 (d, J = 8.5 Hz 1H), 7.84 (t, J = 7.7 Hz, 1H), 7.78 (d, J = 8.2 Hz, 1H), 7.72 (t, J = 8.2 Hz, 2H), 7.43 (t, J = 7.8 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 140.6, 134.2, 133.4, 133.3, 132.4, 130.5, 130.2, 129.6, 129.1, 128.7, 124.4,

122.3, 122.1, 120.5. *Anal Calcd* for $C_{14}H_9BrN_2O$ (301.14); C, 55.84, H, 3.01, N, 9.30. *Found* C, 55.77, H, 3.02, N, 9.33.

2-(3-Chlorophenyl) quinazoline 3-oxide 3d. Yield 73% (0.187 g). Yellow crystals, mp 176-177 ºC. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.06 (s, 1H), 8.40 (t, *J* = 1.9 Hz, 1H), 8.33 (dt, *J* = 7.8, 1.4 Hz, 1H), 8.05 (d, *J* = 8.5 Hz, 1H), 7.80 (ddd, *J* = 8.4, 6.8, 1.4 Hz, 1H), 7.74 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.68 – 7.63 (m, 1H), 7.52 (ddd, *J* = 8.0, 2.2, 1.1 Hz, 1H), 7.46 (t, *J* = 7.9 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 142.3, 141.4, 134.2, 134.1, 133.3, 132.2, 131.2, 130.4, 130.1, 129.5, 129.3, 128.6, 124.2, 124.0. *Anal. Calcd* for $C_{14}H_9ClN_2O$ (256.69), C, 65.51, H, 3.53, N, 10.91. *Found* C, 65.60, H, 3.52, N,10.85.

2-(*p*-Methoxyphenyl) quinazoline-3-oxide 3e. Yield 68% (0.171 g), (75% from one-pot). Yellow crystals, mp 136-137 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.96 (s, 1H), 8.45 (d, *J* = 8.6 Hz, 1H), 7.98 (d, *J* = 8.4 Hz, 1H), 7.76 – 7.63 (m, 2H), 7.57 (ddd, *J* = 8.1, 6.9, 1.1 Hz, 1H), 7.00 (d, *J* = 8.6 Hz, 3H), 3.86 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.6, 132.4, 131.7, 130.3, 128.9, 128.3, 124.1, 116.8, 116.3, 116.1, 113.4, 113.4, 55.4. *Anal. Calcd* for $C_{15}H_{12}N_2O_2$ (252.27); C, 71.42, H, 4.79, N, 11.10. *Found* C, 71.22, H, 4.75, N, 11.08.

2-Phenylquinazoline 3-oxide 3f. Yield 65% (0.144 g) (69% from one-pot). Yellow crystals, mp 126-127 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.98 (s, 1H), 8.38 – 8.28 (m, 2H), 8.02 (d, *J* = 8.4 Hz, 1H), 7.77 – 7.58 (m, 3H), 7.57 – 7.44 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.3, 141.8, 141.2, 131.8, 131.7, 131.1, 130.3, 129.6, 128.5, 128.1, 124.0, 123.9. *Anal. Calcd* for $C_{14}H_{10}N_2O$ (222.24); C, 75.66, H, 4.54, N, 12.60. *Found* C, 75.58, H, 4.56, N, 12.59.

2-(4-Bromophenyl)quinazoline 3-oxide 3g. Yield 66% (0.199 g), (70% from one-pot). Yellow crystals, mp 173-174 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.00 (s, 1H), 8.39 – 8.25 (m, 2H), 8.03 (d, *J* = 8.4 Hz, 1H), 7.78 (ddd, *J* = 8.4, 6.8, 1.6 Hz, 1H), 7.74 – 7.69 (m, 1H), 7.69 – 7.63 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.0, 132.0, 131.3, 131.3, 130.6, 130.6, 130.2, 129.8, 128.5, 125.9, 124.1, 120.6. *Anal Calcd* for $C_{14}H_9BrN_2O$ (301,14) C, 55.84; H, 3.01; N, 9.30. *Found* C, 55.64; H, 3.00; N, 9.25.

2-(3,4-Dimethoxyphenyl)quinazoline 3-oxide 3h. Yield 73% (0.206 g). Yellow crystals, mp 151-152 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.99 (s, 1H), 8.21 (dd, *J* = 8.5, 2.0 Hz, 1H), 8.13 (d, *J* = 2.0 Hz, 1H), 8.04 (d, *J* = 8.4 Hz, 1H), 7.76 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H), 7.70 (d, *J* = 7.3 Hz, 1H), 7.66 – 7.59 (m, 1H), 7.04 – 6.99 (m, 1H), 4.01 (s, 3H), 3.99 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.5, 151.6, 148.2, 142.1, 141.4, 131.7, 129.3, 128.3, 124.5, 124.2, 124.0, 123.5, 113.3, 110.3, 56.1, 56.0. *Anal Calcd* for $C_{16}H_{14}N_2O_3$ (282,30) C, 68.08; H, 5.00; N, 9.92. *Found* C, 68.00; H, 4.99; N, 9.90.

2-(*p*-Tolyl)quinazoline-3-oxide 3i. Yield 79% (0.187 g), (81% from one-pot). Yellow crystals, mp 126-127 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.01 (s, 1H), 8.31 (d, *J* = 4.6 Hz, 2H), 8.05 (d, *J* = 8.4 Hz, 1H), 7.84 – 7.56 (m, 3H), 7.35 (d, *J* = 4.4 Hz, 2H), 2.47 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.3, 141.2, 130.8, 130.6, 130.0, 129.5, 129.4, 129.0, 128.7, 128.6, 125.0, 123.8, 21.6. *Anal. Calcd* for $C_{15}H_{12}N_2O$ (236.27) C, 76.25; H, 5.12; N, 11.86. *Found* C, 76.15; H, 5.11; N, 11.90.

2-(Furan-2-yl)quinazoline 3-oxide 3j. Yield 67% (0.142 g). Yellow crystals, mp 158-159 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.02 (s, 1H), 8.31 (d, *J* = 3.4 Hz, 1H), 8.14 (d, *J* = 8.5 Hz, 1H), 7.84 – 7.76 (m, 2H), 7.71 (d, *J* = 7.9 Hz, 1H), 7.63 (t, *J* = 6.8 Hz, 1H), 6.71 (dd, *J* = 3.5, 1.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.5, 144.6, 141.9, 141.4, 132.2, 129.3, 128.4, 124.2, 121.5, 120.5, 112.7, 108.6. *Anal Calcd* for $C_{12}H_8N_2O_2$ (212.21) C, 67.92; H, 3.80; N, 13.20. *Found* C, 67.90; H, 3.82; N, 13.18.

4-Methyl-2-(4-nitrophenyl)quinazoline 3-oxide 3k. Yield 72% (0.202 g). Yellow crystals, mp 167-168 °C; Lit mp 167-168 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (d, *J* = 8.8 Hz, 2H), 8.36 (d, *J* = 8.8 Hz, 2H), 8.07 (d, *J* = 8.2 Hz, 1H), 7.95 (d, *J* = 8.3 Hz, 1H), 7.81 (t, *J* = 7.1 Hz, 1H), 7.74 (t, *J* = 7.2 Hz, 1H), 2.96 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.4, 152.1, 148.8, 140.3, 138.6, 131.6, 130.1, 129.7, 129.5, 123.9, 123.4, 123.0, 13.4. (Y.-C. Chen and Yang 2013)

2-(4-methoxyphenyl)-4-methylquinazoline 3-oxide 3l. Yield 84% (0.224 g). Yellow crystals, mp 157-158 °C; Lit mp 158-159 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (d, *J* = 8.6 Hz, 2H), 8.03 (d, *J* = 8.3 Hz, 1H), 7.90 (d, *J* = 8.2 Hz, 1H), 7.75 (t, *J* = 7.5 Hz, 1H),

7.70 – 7.60 (m, 1H), 7.04 (d, *J* = 8.6 Hz, 2H), 3.88 (d, *J* = 26.7 Hz, 3H), 2.95 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.7, 154.2, 152.6, 140.6, 132.4, 130.2, 129.6, 128.8, 124.9, 123.2, 113.3, 100.9, 55.5, 13.4. (Ye et al. 2019)

2-(4-Nitrophenyl)-4-phenylquinazoline 3-oxide 3m. Yield 73% (0.251 g). Yellow crystals, mp 179-180 ^oC. ^1H NMR (400 MHz, $CDCl_3$) δ 8.64 (d, *J* = 8.9 Hz, 2H), 8.35 (d, *J* = 8.9 Hz, 2H), 8.12 (d, *J* = 8.4 Hz, 1H), 7.84 – 7.77 (m, 1H), 7.68 – 7.59 (m, 6H), 7.55 (d, *J* = 8.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.2, 152.1, 148.8, 141.2, 138.4, 131.8, 131.5, 130.4, 130.1, 129.9, 129.1, 128.9, 128.7, 125.2, 124.2, 122.9. *Anal. Calcd* for $C_{20}H_{13}N_3O_3$ (343.34) C, 69.97; H, 3.82; N, 12.24, *Found* C, 69.81; H, 3.80; N, 12.25.

2-(3-methoxyphenyl)-1,2-dihydroquinazoline 3-oxide 3n. Yield 68% (0.171 g), Yellow crystals, mp 179-180 ^oC. ^1H NMR (400 MHz, $cdcl_3$) δ 7.68 (s, 1H), 7.30 – 7.22 (m, 1H), 7.18 (td, *J* = 7.7, 1.5 Hz, 1H), 7.13 (dd, *J* = 7.4, 1.5 Hz, 2H), 7.03 (dd, *J* = 7.7, 1.4 Hz, 1H), 6.92 – 6.81 (m, 2H), 6.77 (d, *J* = 8.0 Hz, 1H), 6.07 (d, *J* = 3.0 Hz, 1H), 5.03 (d, *J* = 3.3 Hz, 1H), 3.76 (s, 3H). ^{13}C NMR (101 MHz, $cdcl_3$) δ 159.8, 138.6, 138.4, 131.8, 130.8, 129.8, 125.8, 120.4, 119.1, 116.4, 115.1, 114.4, 112.4, 80.2, 55.2.

3.3.4. One-pot procedure for the preparation of compounds 3b,c,e-g,i.

To a solution of amino oxime **1** (1 mmol) in THF (4 mL) aldehyde (1 mmol) was added at room temperature and after an hour H_2O_2 (4 mmol, 35%, 0.389 g) and $Na_2WO_4.2H_2O$ (0.05 mmol, 0.017 g) were added and the mixture was stirred for 24 h. The isolation procedure is the same for compounds **3** obtained according to the general procedure starting from isolated **2**.

3.3.5. Synthesis of compounds 4.

General Procedure: To a suspension of quinazoline 3-oxides **3** (0.2 mmol) in MeCN (1 mL), arylboronic acids (0.6 mmol), and $Mn(OAc)_3 2H_2O$ (0.6 mmol, 0.160 g) were added, and the mixture was stirred at 60 °C for 44 h. The reaction mixture was diluted with CH_2Cl_2, then washed with water for three times. The resulting organic phase was dried over anhydrous Na_2SO_4 and concentrated under vacuum. The crude product was purified by silica gel column chromatography using ethyl acetate/petroleum ether (1:2) as eluent to obtain the desired products.

2-(4-Nitrophenyl)-4-phenylquinazoline-3-oxide 4a. Yield 71% (0.049 g). Yellow solid, mp 184-185 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (d, *J* = 8.9 Hz, 2H), 8.35 (d, *J* = 8.9 Hz, 2H), 8.12 (d, *J* = 8.4 Hz, 1H), 7.84 – 7.77 (m, 1H), 7.68 – 7.59 (m, 6H), 7.55 (d, *J* = 8.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.2, 152.1, 148.8, 141.2, 138.4, 131.8, 131.5, 130.4, 130.1, 129.9, 129.1, 128.9, 128.7, 125.2, 124.2, 122.9. HRMS (ESI-TOF-MS) *Calcd* for $[C_{20}H_{14}N_3O_3]^+$ m/z = 344.1035 *Found* 344.1035.

2-(4-Chlorophenyl)-4-phenylquinazoline-3-oxide 4b. Yield 72% (0.048 g). Yellow solid, mp 183-184 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 – 8.38 (m, 2H), 8.07 (d, *J* = 8.4 Hz, 1H), 7.74 (ddd, *J* = 8.4, 6.8, 1.5 Hz, 1H), 7.65 – 7.52 (m, 6H), 7.51 – 7.44 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.8, 141.1, 137.0, 132.1, 131.5, 131.1, 130.8, 130.2, 129.9, 129.3, 129.1, 128.7, 128.0, 126.7, 125.0, 121.4. HRMS (ESI-TOF-MS) *Calcd* for $[C_{20}H_{14}N_2OCl]^+$ m/z = 333.0795 *Found* 333.0795.

2-(3-Bromophenyl)-4-phenylquinazoline 3-oxide 4c. Yield 74% (0.056 g). Yellow solid, mp 161-162 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 – 8.59 (m, 1H), 8.37 (d, *J* = 7.9 Hz, 1H), 8.09 (d, *J* = 8.4 Hz, 1H), 7.81 – 7.72 (m, 1H), 7.69 – 7.47 (m, 8H), 7.38 (t, *J* = 8.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$,) δ 143.8, 141.0, 134.2, 133.8, 133.4, 131.1, 130.2, 129.9, 129.5, 129.3, 129.0, 128.9, 128.8, 128.7, 125.0, 124.3, 123.9, 121.8. HRMS (ESI-TOF-MS) *Calcd* for $[C_{20}H_{14}N_2OBr]^+$ m/z = 377.0289 *Found* 377.0289.

2-(3-Nitrophenyl)-4-phenylquinazoline 3-oxide 4d. Yield 70% (0.048 g). Yellow solid, mp 165-166 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.39 – 9.28 (m, 1H), 8.86 (d, *J* = 7.9 Hz, 1H), 8.38 (dd, *J* = 8.2, 1.2 Hz, 1H), 8.12 (d, *J* = 8.4 Hz, 1H), 7.86 – 7.75 (m, 1H), 7.71 – 7.45 (m, 8H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.8, 152.0, 147.9, 141.1, 136.5, 134.0, 131.5, 130.4, 130.0, 129.9, 129.0, 128.9, 128.8, 128.7, 126.0, 125.4, 125.2, 124.1. HRMS (ESI-TOF-MS) *Calcd* for $[C_{20}H_{14}N_3O_3]^+$ m/z = 344.1035 *Found* 344.1035.

2-(4-Methoxyphenyl)-4-phenylquinazoline 3-oxide 4e. Yield 83% (0.055 g). Yellow solid, mp 201-202 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 – 8.45 (m, 2H), 8.06 (d, *J* = 8.4 Hz, 1H), 7.78 – 7.69 (m, 1H), 7.62 (dd, *J* = 11.8, 4.1 Hz, 5H), 7.55 – 7.42 (m, 2H), 7.07 – 6.97 (m, 2H), 3.90 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.7, 145.5, 141.2, 135.2, 132.7, 130.8, 130.0, 129.9, 129.5, 128.7, 128.6, 124.9, 124.7, 123.5, 113.6, 113.2, 55.4. HRMS (ESI-TOF-MS) *Calcd* for $[C_{21}H_{17}N_2O_2]^+$ m/z = 329.1290 *Found* 329.1290.

2,4-Diphenylquinazoline 3-oxide 4f. Yield 75% (0.045 g). Yellow solid, mp 159-160 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 – 8.34 (m, 2H), 8.09 (d, *J* = 8.4 Hz, 1H), 7.74 (ddd, *J* = 8.4, 6.6, 1.7 Hz, 1H), 7.68 – 7.48 (m, 10H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.5, 151.4, 141.1, 132.4, 130.9, 130.8, 130.5, 130.3, 130.1, 130.0, 129.2, 128.8, 128.7, 127.8, 125.0, 123.8. HRMS (ESI-TOF-MS) *Calcd* for $[C_{20}H_{15}N_2O]^+$ m/z = 299.1184 *Found* 299.1184.

2-(4-Bromophenyl)-4-phenylquinazoline 3-oxide 4g. Yield 71% (0.054 g). Yellow solid, mp 178-179 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 – 8.30 (m, 2H), 8.07 (d, *J* = 8.4 Hz, 1H), 7.74 (ddd, *J* = 8.3, 6.9, 1.4 Hz, 1H), 7.69 – 7.45 (m, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.4, 151.7, 141.1, 132.3, 131.3, 131.1(2C), 131.0, 130.2, 129.9, 129.4, 129.1, 128.7, 125.6, 125.1, 123.8, HRMS (ESI-TOF-MS) *Calcd* for $[C_{20}H_{14}N_2OBr]^+$ m/z = 377.0289 *Found* 377.0289.

2-(3,4-Dimethoxyphenyl)-4-phenylquinazoline 3-oxide 4h. Yield 76% (0.055 g). Yellow solid, mp 153-154 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (dd, *J* = 11.1, 2.6 Hz, 2H), 8.08 (d, *J* = 8.4 Hz, 1H), 7.73 (dd, *J* = 11.1, 4.1 Hz, 1H), 7.68 – 7.55 (m, 5H), 7.56 – 7.48 (m, 1H), 7.45 (d, *J* = 7.9 Hz, 1H), 7.00 (d, *J* = 8.5 Hz, 1H), 3.98 (d, *J* = 2.4 Hz,

6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.3, 154.7, 151.4, 148.0, 141.2, 130.9, 130.0, 129.9, 129.5, 128.8, 128.6, 125.0, 123.5, 120.4, 117.2, 115.5, 113.7, 110.2, 56.1, 56.0. HRMS (ESI-TOF-MS) *Calcd* for $[C_{22}H_{19}N_2O_3]^+$ m/z = 359.1396 *Found* 359.1396.

4-Phenyl-2-(p-tolyl)quinazoline 3-oxide 4i. Yield 83% (0.052 g). Yellow solid, mp 149-150 ºC; Lit(Ye et al. 2019) mp 182–183°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (d, *J* = 8.2 Hz, 2H), 8.08 (d, *J* = 8.4 Hz, 1H), 7.73 (ddd, *J* = 8.3, 6.7, 1.6 Hz, 1H), 7.68 – 7.56 (m, 5H), 7.56 – 7.45 (m, 2H), 7.32 (d, *J* = 8.2 Hz, 2H), 2.44 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.5, 151.4, 141.3, 141.2, 131.6, 131.3, 130.8, 130.6, 130.0, 129.5, 129.4, 128.9, 128.7, 128.5, 125.0, 123.7, 21.6.

2-(Furan-2-yl)-4-phenylquinazoline 3-oxide 4j. Yield 78% (0.045 g). Yellow solid, mp 226-227 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, *J* = 3.5 Hz, 1H), 8.17 (d, *J* = 8.5 Hz, 1H), 7.82 (d, *J* = 1.8 Hz, 1H), 7.76 (t, *J* = 7.6 Hz, 1H), 7.62 (q, *J* = 6.4 Hz, 5H), 7.55 – 7.42 (m, 2H), 6.67 (dd, *J* = 3.6, 1.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.5, 145.3, 141.4, 139.1, 131.6, 130.4, 130.1, 129.9, 129.4, 129.1, 128.7, 125.2, 122.8, 122.4, 112.8, 109.9. HRMS (ESI-TOF-MS) *Calcd* for $[C_{18}H_{13}N_2O_2]^+$ m/z = 289.0977 *Found* 289.0977.

2-(4-Nitrophenyl)-4-(m-tolyl)quinazoline 3-oxide 4k. Yield 78% (0.056 g). Yellow solid, mp 170-171ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 – 8.59 (m, 2H), 8.34 (dd, *J* = 9.1, 2.1 Hz, 2H), 8.13 – 8.06 (m, 1H), 7.83 – 7.74 (m, 1H), 7.60 (dd, *J* = 9.1, 5.0 Hz, 1H), 7.52 (dd, *J* = 9.5, 6.0 Hz, 2H), 7.41 (dd, *J* = 14.9, 6.4 Hz, 3H), 2.47 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.3, 131.8, 131.4, 131.2, 130.8, 130.4, 130.1, 130.0, 129.4, 129.0, 128.9, 128.8, 128.7, 126.9, 126.8, 125.3, 124.1, 122.9, 29.7. HRMS (ESI-TOF-MS) *Calcd* for $[C_{21}H_{16}N_3O_3]^+$ m/z = 358.1192 *Found* 358.1192.

4-(4-Bromophenyl)-2-(4-nitrophenyl)quinazoline 3-oxide 4l. Yield 74% (0.063 g). Yellow solid, mp 149-150 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 – 8.57 (m, 2H), 8.35 (dd, *J* = 9.1, 2.0 Hz, 2H), 8.14 – 8.07 (m, 1H), 7.83 – 7.73 (m, 3H), 7.67 – 7.58 (m, 1H), 7.57 – 7.49 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.9, 147.6, 132.2, 132.1, 132.0, 131.8, 131.7, 131.6, 130.4, 130.3, 129.5, 129.4, 129.2, 124.8, 123.8, 122.9. HRMS (ESI-TOF-MS) *Calcd* for $[C_{20}H_{13}N_3O_3Br]^+$ m/z = 422.0140 *Found* 422.0140.

4-(4-Chlorophenyl)-2-(4-nitrophenyl)quinazoline 3-oxide 4m. Yield 72% (0.055 g). Yellow solid, mp 171-172 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (d, *J* = 8.8 Hz, 2H), 8.35 (d, *J* = 8.8 Hz, 2H), 8.11 (d, *J* = 8.4 Hz, 1H), 7.81 (dd, *J* = 8.6, 6.8 Hz, 1H), 7.67 – 7.57 (m, 5H), 7.53 (d, *J* = 8.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ δ 149.0, 141.2, 138.4, 136.9, 131.8, 131.7, 131.6, 130.5, 129.5, 129.4, 129.3, 127.1, 124.9, 123.9, 123.1, 109.9. HRMS (ESI-TOF-MS) *Calcd* for $[C_{20}H_{13}N_3O_3Cl]^+$ m/z = 378.0645 *Found* 378.0645.

4-(4-Formylphenyl)-2-phenylquinazoline 3-oxide 4n. Yield 75% (0.049 g). Yellow solid, mp 110-111 ^{o}C;^{1}H NMR (400 MHz, $CDCl_3$) δ 10.15 (s, 1H), 8.35 (dd, *J* = 7.8, 2.0 Hz, 2H), 8.12 (dd, *J* = 10.4, 8.2 Hz, 3H), 7.83 (d, *J* = 8.1 Hz, 2H), 7.81 – 7.72 (m, 1H), 7.62 – 7.46 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.8, 141.4, 137.4, 135.8, 135.4, 133.5, 132.2, 131.5, 131.3, 131.2, 130.7, 130.1, 129.8, 129.3, 128.2, 124.5, 123.5. HRMS (ESI-TOF-MS) *Calcd* for $[C_{21}H_{15}N_2O_2]^+$ m/z = 327.1134 *Found* 327.1134.

4-(4-Methoxyphenyl)-2-(4-nitrophenyl)quinazoline 3-oxide 4o. Yield 76% (0.057 g). Yellow solid, mp 166-167 ^{o}C;^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (d, *J* = 8.9 Hz, 2H), 8.32 (d, *J* = 8.9 Hz, 2H), 8.08 (d, *J* = 8.4 Hz, 1H), 7.77 (ddd, *J* = 8.3, 6.5, 1.8 Hz, 1H), 7.60 (dd, *J* = 18.1, 8.6 Hz, 4H), 7.13 (d, *J* = 8.7 Hz, 2H), 3.91 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.1, 152.0, 148.7, 141.2, 138.6, 136.1, 131.9, 131.7, 131.4, 129.9, 129.0, 125.5, 124.2, 122.9, 120.4, 114.2, 55.5. HRMS (ESI-TOF-MS) *Calcd* for $[C_{21}H_{16}N_3O_4]^+$ m/z = 374.1141 *Found* 374.1140.

4-(4-Chlorophenyl)-2-phenylquinazoline 3-oxide 4p. Yield 71% (0.048 g). Yellow solid, mp 213-214 ^{o}C;^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 – 8.38 (m, 2H), 8.07 (d, *J* = 8.4 Hz, 1H), 7.74 (ddd, *J* = 8.4, 6.8, 1.5 Hz, 1H), 7.65 – 7.52 (m, 6H), 7.51 – 7.44 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.5, 150.2, 141.1, 136.3, 132.2, 131.6, 131.1, 131.0, 129.4, 129.1, 129.0, 127.9, 127.6, 124.6, 123.6, 122.0. HRMS (ESI-TOF-MS) *Calcd* for $[C_{20}H_{14}ClN_2O]^+$ m/z = 333.0795 *Found* 333.0795.

4-(4-Bromophenyl)-2-phenylquinazoline 3-oxide 4q. Yield 73% (0.056 g). Yellow solid, mp 181-182 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 – 8.30 (m, 2H), 8.09 (d, *J* = 8.4

Hz, 1H), 7.75 (dd, *J* = 7.9, 6.0 Hz, 3H), 7.61 – 7.45 (m, 7H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.0, 135.0, 132.2, 132.0, 131.8, 131.2, 131.0, 130.5, 129.5, 129.0, 128.0, 127.9, 124.7, 124.7, 123.5, 122.9. HRMS (ESI-TOF-MS) *Calcd* for $[C_{20}H_{14}N_2OBr]^+$ m/z = 377.0289 *Found* 377.0289.

4-(4-Formylphenyl)-2-(4-methoxyphenyl)quinazoline 3-oxide 4r. Yield 76% (0.055 g). Yellow solid, mp 175-176 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.25 (s, 1H), 8.58 (d, *J* = 8.5 Hz, 2H), 8.20 (dd, *J* = 23.8, 8.1 Hz, 3H), 7.87 (dd, *J* = 33.3, 7.9 Hz, 3H), 7.62 (t, *J* = 7.8 Hz, 1H), 7.47 (d, *J* = 8.4 Hz, 1H), 7.10 (d, *J* = 8.5 Hz, 2H), 3.98 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.7, 162.1, 155.0, 151.0, 141.9, 137.3, 135.4, 132.9, 131.8, 131.1, 130.1, 129.4, 129.0, 124.7, 124.2, 123.1, 113.5, 55.6. HRMS (ESI-TOF-MS) *Calcd* for $[C_{22}H_{17}N_2O_3]^+$ m/z = 357.1239 *Found* 357.1239.

4-(m-Tolyl)-2-(p-tolyl)quinazoline 3-oxide 4s. Yield 76% (0.050 g). Yellow solid, mp 123-124 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, *J* = 8.1 Hz, 2H), 8.06 (d, *J* = 8.4 Hz, 1H), 7.72 (t, *J* = 6.9 Hz, 1H), 7.62 – 7.13 (m, 8H), 2.46 (s, 3H), 2.43 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.5, 151.7, 145.4, 141.3, 141.2, 138.5, 130.8, 130.6, 130.3, 129.6, 129.3, 128.9, 128.7, 128.6, 127.0, 125.1, 124.5, 123.8, 21.6, 21.6. HRMS (ESI-TOF-MS) *Calcd* for $[C_{22}H_{19}N_2O]^+$ m/z = 327.1497 *Found* 327.1497.

2-(2-Chlorophenyl)-4-phenylquinazoline 3-oxide 4t. Yield 73% (0.049 g). Yellow solid, mp 127-128 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, *J* = 8.4 Hz, 1H), 7.79 (dd, *J* = 10.7, 4.0 Hz, 1H), 7.73 – 7.56 (m, 8H), 7.56 – 7.50 (m, 1H), 7.50 – 7.40 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.7, 151.1, 140.9, 133.7, 133.1, 131.2, 131.1, 130.7, 130.5, 130.4, 129.9, 129.6, 129.1, 128.7, 128.6, 127.0, 125.4, 124.3. HRMS (ESI-TOF-MS) *Calcd* for $[C_{20}H_{14}N_2OCl]^+$ m/z=333.0795 *Found* 333.0795.

2-(4-Nitrophenyl)quinazoline 5. Yellow solid, mp 200-201 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.53 (s, 1H), 8.83 (d, *J* = 8.9 Hz, 2H), 8.39 (d, *J* = 8.9 Hz, 2H), 8.15 (d, *J* = 8.4 Hz, 1H), 8.00 (d, *J* = 8.1 Hz, 2H), 7.71 (t, *J* = 7.5 Hz, 1H).” The spectrum is identical with those in the literature.(Liu et al. 2013)

2-(4-Nitrophenyl)-4-phenylquinazoline 6. Yellow solid, mp 207-208 °C; Lit (Jianghe Zhu, Yinlin Shao, Kun Hu, Linjun Qi 2018) mp 207-209 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.93 – 8.84 (m, 2H), 8.42 – 8.33 (m, 2H), 8.25 – 8.14 (m, 2H), 7.96 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H), 7.94 – 7.85 (m, 2H), 7.69 – 7.55 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.5, 157.8, 151.4, 149.2, 137.1, 135.4, 134.2, 130.2, 130.1, 129.6, 129.5, 128.6, 128.1, 127.2, 123.7, 121.9.

2-(4-Nitrophenyl)quinazolin-4(3*H*)-one 7a. Yellow solid, mp 285-286 °C; Lit(Shabber Mohammed 2015) mp >300°C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.86 (s, 1H), 8.33 (d, *J* = 8.4 Hz, 2H), 8.17 (d, *J* = 7.9 Hz, 1H), 8.05 (d, *J* = 8.3 Hz, 2H), 7.84 (t, *J* = 7.5 Hz, 1H), 7.74 (d, *J* = 8.1 Hz, 1H), 7.57 (t, *J* = 7.5 Hz, 1H).

2-(4-Bromophenyl)quinazolin-4(3*H*)-one 7b. Yellow solid, mp 289-290 °C; Lit(Shabber Mohammed 2015) mp 292- 295°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.14 (s, 1H), 8.32 (d, *J* = 8.0 Hz, 1H), 8.03 – 7.96 (m, 2H), 7.85 – 7.80 (m, 2H), 7.74 – 7.68 (m, 2H), 7.53 (dt, *J* = 8.1, 4.4 Hz, 1H).

[1,1'-Biphenyl]-4,4'-dicarbaldehyde 8. Yellow solid, mp 128-129 °C; Lit(Seema Dwivedi, Soumik Bardhan 2014) mp 146-148 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.18 – 10.07 (m, 2H), 8.02 (dt, *J* = 8.3, 2.0 Hz, 4H), 7.91 – 7.72 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.9, 145.7, 136.1, 130.5, 128.2.

3.3.6. Synthesis of compounds 9.

General Procedure: $ZrOCl_2.8H_2O$ (0.4 mmol, 0.128 g) was added to a suspension of quinazoline 3-oxides **3** (0.2 mmol) in MeOH (1 mL), and the mixture was stirred at 60 ºC for 44 h. The reaction mixture was diluted with CH_2Cl_2 and then rinsed three times with water. The organic phase that resulted was dried over anhydrous Na_2SO_4 and vacuum concentrated. The crude product was purified using silica gel column chromatography with ethyl acetate/petroleum ether (1:2) as the eluent to achieve the desired products.

N-(2-((Hydroxyimino)methyl)phenyl)-4-nitrobenzamide 9a. Yield 76% (0.048 g). Yellow solid, mp 210-211 ºC ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.72 (s, 1H), 11.58 (s, 1H), 8.53 – 8.34 (m, 4H), 8.31 – 8.10 (m, 2H), 7.61 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.44 (ddd, *J* = 8.5, 7.5, 1.6 Hz, 1H), 7.24 (td, *J* = 7.6, 1.2 Hz, 1H).
^{13}C NMR (101 MHz, DMSO-d_6) δ 163.8, 150.6, 149.8, 140.1, 137.0, 131.0, 130.4, 129.4, 125.0, 124.5, 122.3, 121.7. HRMS (ESI-TOF-MS) *Calcd* for $[C_{14}H_{12}N_3O_4]^+$ m/z=286. 0822 *Found* 286.0828.

4-Chloro-N-(2-((hydroxyimino)methyl)phenyl)benzamide 9b. Yield 78% (0.043 g). White solid, mp 184-185 ºC.^{1}H NMR (400 MHz, dmso) δ 11.69 (s, 1H), 11.41 (s, 1H), 8.41 (d, *J* = 7.5 Hz, 1H), 8.34 (s, 1H), 7.97 (d, *J* = 8.6 Hz, 2H), 7.59 (t, *J* = 8.6 Hz, 3H), 7.41 (t, *J* = 7.8 Hz, 1H), 7.26 – 7.13 (m, 1H).^{13}C NMR (101 MHz, dmso) δ 164.7, 151.0, 137.5, 133.6, 131.3, 130.5, 130.0, 129.6, 129.8, 124.8, 122.2, 121.6.

N-(2-((Hydroxyimino)methyl)phenyl)-4-methylbenzamide 9c. Yield 82% (0.042 g). Yellow solid, mp 155-156ºC. ^{1}H NMR (400 MHz, dmso) δ 11.70 (s, 1H), 11.38 (s, 1H), 8.50 (dd, *J* = 8.4, 1.2 Hz, 1H), 8.35 (s, 1H), 7.87 (d, *J* = 8.2 Hz, 2H), 7.55 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.49 – 7.31 (m, 3H), 7.17 (td, *J* = 7.5, 1.2 Hz, 1H), 2.38 (s, 3H).^{13}C NMR (101 MHz, dmso) δ 165.4, 151.2, 142.6, 137.7, 131.8, 131.4, 130.3, 129.9, 127.9, 124.1, 121.4, 121.0, 21.5

N-(2-((Hydroxyimino)methyl)phenyl)-4-methoxybenzamide 9d. Yield 86% (0.47 g). Yellow solid, mp 143-144 ºC. ^{1}H NMR (400 MHz, dmso) δ 11.71 (s, 1H), 11.36 (s, 1H), 8.51 (dd, *J* = 8.3, 1.2 Hz, 1H), 8.36 (s, 1H), 8.00 – 7.89 (m, 2H), 7.55 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.40 (ddd, *J* = 8.6, 7.4, 1.6 Hz, 1H), 7.17 (td, *J* = 7.5, 1.2 Hz, 1H), 7.10 – 7.02 (m, 2H), 3.84 (s, 3H).^{13}C NMR (101 MHz, dmso) δ 165.0, 162.6, 151.3, 137.8, 131.4, 130.3, 129.8, 126.7, 123.9, 121.3, 120.9, 114.6, 55.9.

N-(2-((Hydroxyimino)methyl)phenyl)-3,4-dimethoxybenzamide 9e. Yield 81% (0.049 g). Yellow solid, mp 155-156ºC. ^{1}H NMR (400 MHz, dmso) δ 11.53 (s, 1H), 11.16 (s, 1H), 8.33 (d,1H), 8.25 (s, 1H), 7.70 (t, *J* = 7.7 Hz, 1H), 7.59 (t, *J* = 7.6 Hz, 1H), 7.47 (ddd, *J* = 7.6, 5.6, 1.8 Hz, 1H), 7.40 (d, *J* = 2.1 Hz, 1H), 7.08 (t, *J* = 7.5 Hz, 1H), 6.99 (dd, *J* = 15.6, 8.5 Hz, 1H), 3.75 (d, *J* = 3.8 Hz, 6H). ^{13}C NMR (101 MHz,) δ 164.7, 153.1, 151.0, 142.4, 132.0, 131.0, 130.2, 129.6, 124.5, 124.0, 122.5, 121.1, 120.7, 113.9, 111.0, 55.9, 55.8.

4-Bromo-N-(2-((hydroxyimino)methyl)phenyl)benzamide 9f. Yield 80% (0.052 g). White solid, mp 181-182 ºC. ^{1}H NMR (400 MHz, dmso) δ 11.72 (s, 1H), 11.44 (s, 1H), 8.50 – 8.32 (m, 2H), 8.00 – 7.87 (m, 2H), 7.82 – 7.71 (m, 2H), 7.66 – 7.56 (m, 1H), 7.43 (d, *J* = 9.2 Hz, 1H), 7.23 (d, *J* = 6.5 Hz, 1H). ^{13}C NMR (101 MHz, dmso) δ 164.9, 151.0, 137.6, 134.0, 132.6, 131.3, 130.6, 130.2, 126.5, 124.8, 122.2, 121.6.

2-Chloro-N-(2-((hydroxyimino)(phenyl)methyl)phenyl)benzamide 9g. Yield 76% (0.054 g). Yellow solid, mp 79-80 ºC.^{1}H NMR (400 MHz, dmso) δ 11.62 (s, 1H), 11.50 (s, 1H), 7.91 – 6.82 (m, 13H). ^{13}C NMR (101 MHz, dmso) δ 165.3, 154.0, 137.0, 136.9, 136.1, 130.6, 130.5, 130.4, 130.2, 129.8, 129.6, 129.4, 128.8, 128.6, 127.6, 127.5, 126.0, 125.9.

N-(2-((Hydroxyimino)methyl)phenyl)benzamide 9h. Yield 83% (0.040 g). Yellow solid, mp 167-168 ºC. ^{1}H NMR (400 MHz, dmso) δ 11.73 (s, 1H), 11.44 (s, 1H), 8.50 (dd, *J* = 8.4, 1.2 Hz, 1H), 8.37 (s, 1H), 8.05 – 7.95 (m, 2H), 7.67 – 7.54 (m, 4H), 7.42 (ddd, *J* = 8.6, 7.4, 1.6 Hz, 1H), 7.20 (td, *J* = 7.5, 1.2 Hz, 1H). ^{13}C NMR (101 MHz, dmso) δ 165.7, 151.3, 137.8, 134.7, 132.7, 131.5, 130.5, 129.6, 128.0, 124.5, 121.9, 121.4.

3.3.7. Recyclization procedure for the compound 9a-b.

To a suspension of N-(2-((hydroxyimino)methyl)phenyl)-4-benzamide **9** (0.2 mmol) in DMSO (0.5 mL) in the presence of AcOH (20 mol%) catalyst and the mixture was stirred at 80 ^{o}C for 24 h. The reaction mixture was diluted with CH_2Cl_2 and then rinsed three times with water. The organic phase that resulted was dried over anhydrous Na_2SO_4 and vacuum concentrated. To achieve the desired products **3a-b**, the crude product was purified using silica gel column chromatography with ethyl acetate/petroleum ether (1:2) as the eluent.

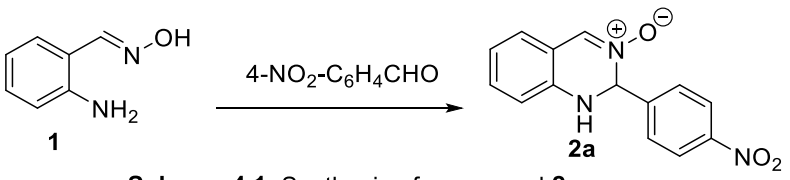
4. RESULTS and DISCUSSION

4.1. Eco-friendly H_2O_2 oxidation of 1,2-dihydroquinazoline-3-oxides to quinazoline-3-oxides.

4.1.1. Optimization reaction conditions for the synthesis of compounds 2.

As a continuation of our investigations on the reactions of cyclic nitrones like 3,4-dihydroisoquinoline-2-oxides (Coşkun and Tunçman 2006) and 2,5-dihydro-1*H*-imidazole-3-oxides (Coşkun and Ay 1998, Coşkun and Çetin 2010) and photochemical conversions of quinazoline-1-oxides (Coşkun and Çetin 2007) we needed a series of 4-unsubstituted-quinazoline-3-oxides **3a-j** to investigate their photochemical as well as thermal behaviours. To begin with, we have prepared first compounds **2a-j** from the reaction of amino oximes **1** with the corresponding aldehydes (Chen and Din 2013, Rasouli et al. 2017) (Scheme 4.1). The optimization (Table 1) of the reaction conditions was conducted in the case of aminobenzaldehyde oxime and *p*-nitrobenzaldehyde (Table 4.1).

Table 4.1. Optimization of the reaction conditions for the synthesis of compounds **2**.



Scheme 4.1. Synthesis of compound **2a**

Entry[a]	**Solvent (cat)**	**Yield (%)**
1	CH_2Cl_2 (AgOTf)	94
2	CH_2Cl_2	96
3	$CHCl_3$	96
4	Benzene	93
5	Toluene	94
6	MeOH / H_2O[b]	91
7	EtOH	97

[a]All reactions were performed in 20 mL of solvent using equivalent amounts of oxime **1** (1 mmol) and the corresponding aldehyde. at room temperature the reaction mixtures were stirred for 24 h. In the case of entry 1, 0.02 mol% AgOTf was used as a catalyst.[b]The solvent ratio is 1/1.

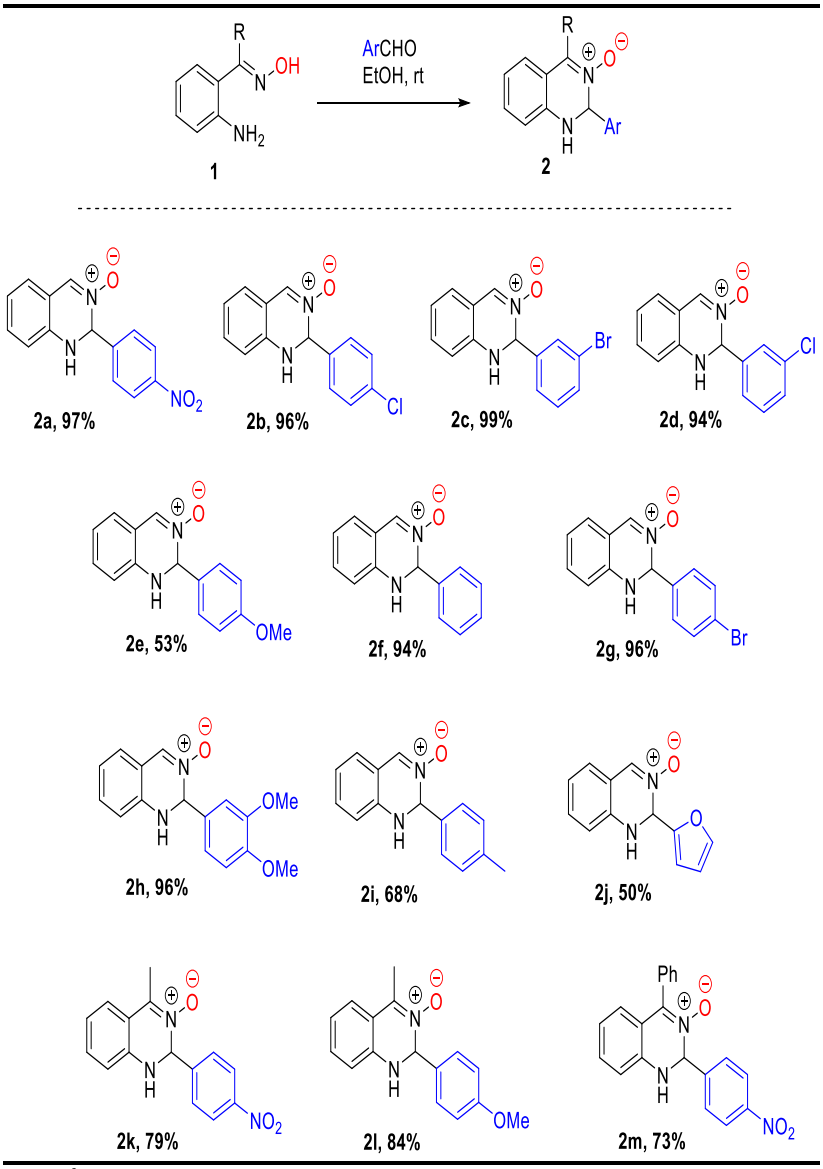
The reaction was first performed in CH_2Cl_2 at room temperature using AgOTf as a catalyst and the corresponding **2a** was obtained in 94% yield. The yield of the reaction in the same solvent was 96% when it was performed in the absence of the catalyst. Chloroform, benzene and toluene were also good media for the conversion of **1** into **2a**. However, ethanol proved to be the best solvent for the reaction at room temperature.

4.1.2. Synthesis of 1,2-dihydroquinazoline-3-oxides from the oxime.

Equimolar amounts of amino oxime **1** and aromatic aldehydes were dissolved in ethanol and stirred at room temperature for *ca* 24 h. In all cases except **2f** the products are precipitating and easily isolated by filtration. The precipitates were washed several times with warm hexane then dried under vacuum. The structures and the yields of compounds **2a-m** are presented in Table 4.2.

Compounds **2k-l** and **3k-l** are known, (Chen and Yang 2013, Ye et al. 2019) however to the best of our knowledge a method for the synthesis and characterization data for **2a-j** and **3a-j** are not available in the literature. Therefore, we propose a simple high yielding procedures for the synthesis of compounds **2a-m** and their oxidation with H_2O_2-tungstate in THF to the synthetically important quinazoline-3-oxides **3a-m**. The newly prepared compounds were characterized by spectral as well as analytical methods.

Table 4.2. Structures and yields[a,b] of 1,2-dihydroquinazoline-3-oxides **2a-m.**

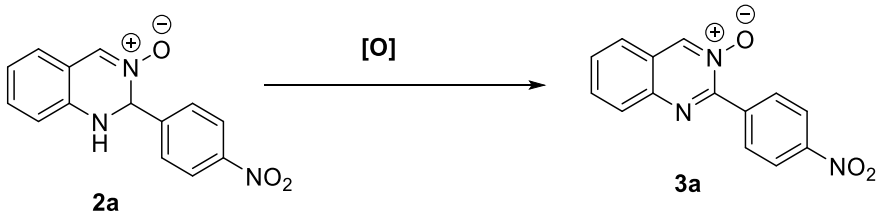


[a]Isolated yields: [b]*Reaction conditions*: amino oxime 1 and aldehyde each 1 mmol, dissolved in EtOH (20 mL) were stirred at room temperature for 24 h (for compounds 2k-m, 47 h).

4.1.3. Optimization of the reaction conditions for the synthesis of compounds 3.

Compound **2a** was subjected to oxidation with AgOTf, MnO_2 and $KMnO_4$ (Table 4.3, entries 1-3) in DMSO and the reaction product **3a** was formed only in the cases of entries 2-3 in low yields. No product formation was observed in the case of AgOTf (Table 4.3, entry 1). The use of MnO_2 and $KMnO_4$ without solvent did not produce the expected **3a** (Table 4.3, entries 4-5). The use of $KMnO_4/MnO_2$ mixtures in DMSO and DMF or without solvent produced the quinazoline-3-oxide in moderate yields (Table 4.3, entries 6-8). The oxidation of **2a** with the H_2O_2-Na_2WO_4 in THF-H_2O and THF provided the formation of product **3a** in high yields at room temperature (Table 4.3, entries 9-10). The use of dry THF proved to be the better choice as a reaction solvent.

Table 4.3. Optimization of the reaction conditions for the synthesis of compounds **3.**



2a **3a**

Scheme 4.2. Synthesis of compound **3a**

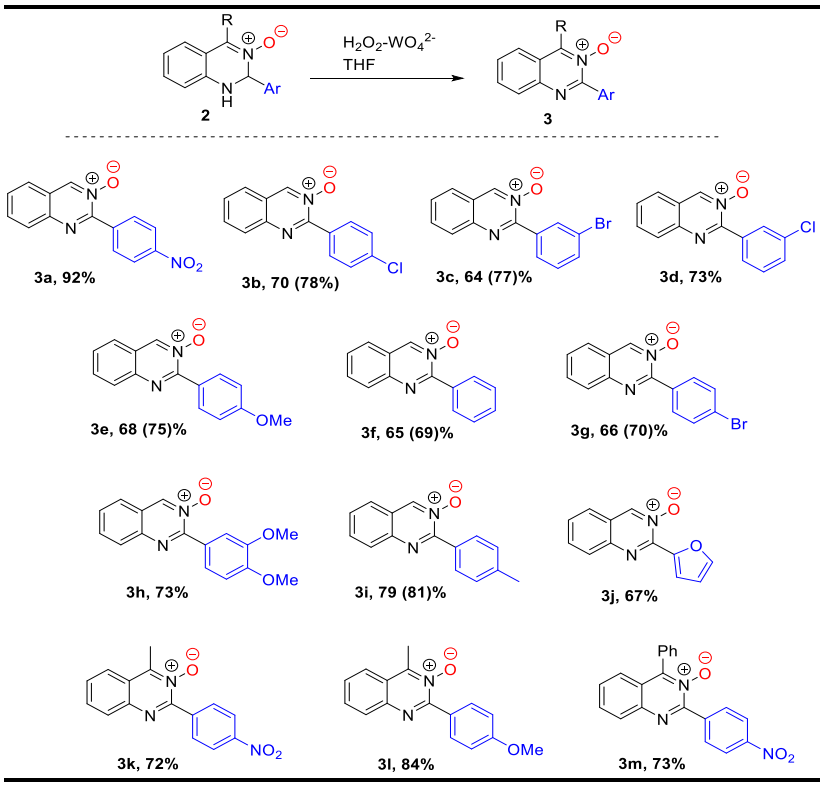
Entry	Solvent	Oxidizing agent	Time (h)	Temp (°C)	Yield (%)[a]
1	DMSO[b]	AgOTf[c]	8	90	-
2	DMSO[b]	MnO_2[c]	23	130	52
3	DMSO[b]	$KMnO_4$[c]	22	130	43
4	-	MnO_2[c]	8	rt	-
5	-	$KMnO_4$[c]	5	rt	-
6	DMSO[b]	$KMnO_4$/ MnO_2[d]	23	100	49
7	DMF[b]	$KMnO_4$/ MnO_2[d]	20	100	47
8	-	$KMnO_4$/ MnO_2[d]	21	rt	52
9	THF/H_2O[f]	H_2O_2-Na_2WO_4[e]	24	rt	74
10	THF[b]	H_2O_2-Na_2WO_4[e]	24	rt	92

[a]Isolated yields; [b]The reactions were performed in 4 mL of solvent with 1 mmol of **2a**; [c]1 mmol of the oxidizer was used; [d]The ratio is 0.3 / 0.7; [e] 4 / 0.05; [f]4 mL (1/1).

4.1.4. Synthesis of quinazoline-3-oxides 3 from the 1,2-quinazoline-3-oxides 2.

Compounds **2a-m** were subjected to H_2O_2-tungstate in THF under the optimized conditions to give compounds **3a-m** in good to high yields (Table 4.4). The structures of compounds **3** were elucidated by elemental analysis, ^{1}H and ^{13}C NMR data. 4-Methyl-2-(4-nitrophenyl)-1,2-dihydroquinazoline-3-oxide **2k** was identical with the one obtained by irradiation of **1k** in acetonitrile in the presence of $Ru(bpy)_3Cl_2$. (Chen and Yang 2013) The first 4-unsubstituted quinazoline-3-oxide **3b** was obtained in our lab as a by-product from the oxidation of corresponding tetrahydroquinazoline. (Coşkun and Çetin 2007) The physical and spectral data for **3b** obtained by oxidation of **2b** with H_2O_2-tungstate were the same as for our previously reported one.

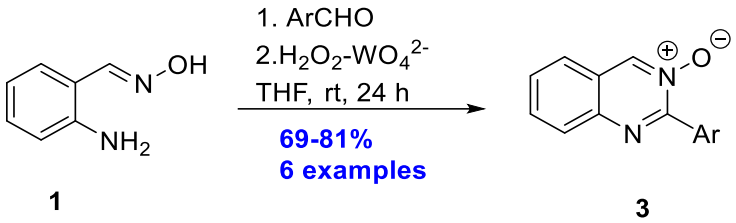
Table 4.4. Oxidation of 1,2-dihydroquinazoline-3-oxides[a,b] 2a-m with H_2O_2-Na_2WO_4 in THF at rt.



[a]Isolated yields; The yields in the parenthesis are according to the one-pot procedure. [b]*Reaction conditions*: To the solution of compound **2** (1 mmol) in THF (4 mL), H_2O_2 (4 mmol, 35%, 0.389 g) and $Na_2WO_4.2H_2O$ (0.05 mmol, 0.017 g) were added and at room temperature the mixture was stirred (for compounds **3a-j** 20-24 h). For the compounds **3k-m** the reaction was performed at 60 ^{o}C (47 h).

4.1.5. Synthesis of quinazoline-3-oxides 3 from Oxime in one pot procedure.

One-pot procedure involving the short time stirring of the amino oxime and aldehyde mixture in THF and addition of the oxidizing system provided compounds **3b, c,e-g,i** with improved overall yields (Scheme 4.3, Table 4.4).



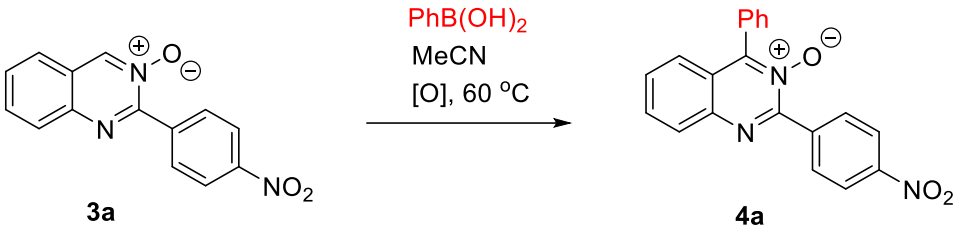
Scheme 4.3. One-pot synthesis of compounds **3b,c,e-g,i**

4.2. $Mn(OAc)_3$ Induced C-4 Arylations of quinazoline 3-oxides with arylboronic acids

4.2.1. Search for oxidant in the direct arylation of compounds 3.

The reaction between 2-(4-nitrophenyl)quinazoline 3-oxide **3a** and phenylboronic acid was used as a model to find an oxidant in the C-4 arylation of quinazoline 3-oxides with arylboronic acids. The reactions were performed in MeCN at 60 ^{o}C (Table 1). C-H arylation product **4a** is forming in trace amounts in the case of MnO_2 (Table 1, entry 1). The work up of the reaction mixture after 23 h and column chromatography provided 2-(4-nitrophenyl)-4-phenylquinazoline (Jianghe et al. 2018, Yizhe et al. 2016) and the 2-(4-nitrophenyl)quinazoline (Liu et al. 2013) in 70 and 25% yields respectively.

Table 4.5. Search for oxidant in the direct arylation of compounds **3**.

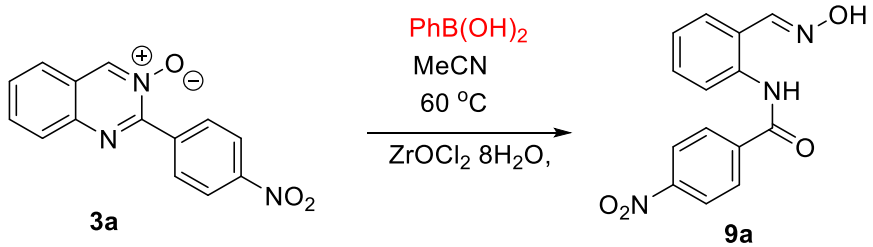


Scheme 4.4. Synthesis of compound **4a**

Entry	**Oxidant**[a]	**Yield** (%)
1	MnO_2	trace
2	$Mn(OAc)_3.\ 2H_2O$	42
3	$KMnO_4$	11
4	$ZrOCl_2.\ 8H_2O$	0[b]
5	CeO_2	0
6	H_2O_2	0

[a] For 23 hours, 0.2 mmol of 4a was exposed to equivalent amounts of the oxidants and 1.5 eqv of $PhB(OH)_2$.[b]The product was N-(2-((hydroxyimino)methyl)phenyl)-4-nitrobenzamide

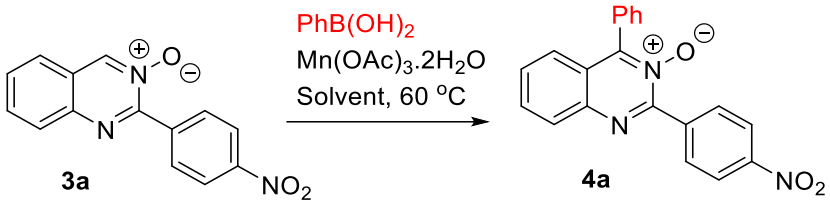
The isolated yields of the product in the cases of $Mn(OAc)_3.\ 2H_2O$ and $KMnO_4$ were 42 and 11%, respectively (Table 4.5, entries 2-3). $ZrOCl_2.\ 8H_2O$, CeO_2 and H_2O_2 proved to be inefficient oxidants in the C-H arylation of quinazoline 3-oxides (Table 4.5, 4-6). The reaction without oxidant did not produce any product after 44 h heating in acetonitrile. To our surprise, the reaction in the presence of $ZrOCl_2.\ 8H_2O$ lead to a compound that was proved to be N-(2-((hydroxyimino)methyl)phenyl)-4-nitrobenzamide **9a** (Scheme 4.5).



Scheme 4.5. Synthesis of compound **9a**

4.2.2. Optimization of the arylation of quinazoline 3-oxide reaction conditions.

Table 4.6. Optimization of the arylation of quinazoline 3-oxide reaction conditions.



Scheme 4.6. Synthesis of compound **4a** from compound **3a** as a starting material.

Entry [a]	**$Mn(OAc)_3.2H_2O$** (eqv)	**Solvent**	**Time** (h)	**Phenylboronic acid** (eqv)	**Yield** (%)[b]
1	(1)	MeCN	23	1.5	42
2	(1)	AcOH	23	1.5	0
3	(1)	Dioxane	23	1.5	34
4	(1)	DMSO	23	1.5	trace
5	(1)	Toluene	23	1.5	30
6	(1)	EtOH	23	1.5	0
7	(1)	MeOH	23	1.5	trace
8	(1)	MeCN	44	1.5	45
9	(2.5)	MeCN	44	3	63
10	(3)	MeCN	44	3	71

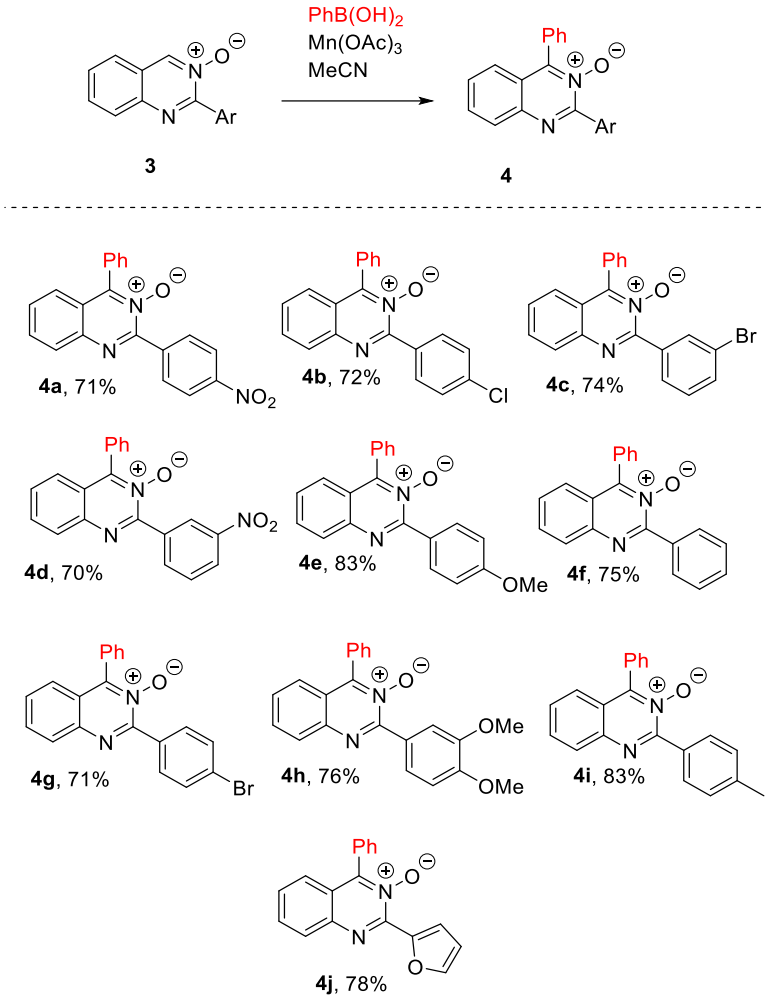
[a]The reactions were carried out at 60 °C using 3a (0.2 mmol), 1.0 mL of solvent, and **3a** (0.2 mmol).[b]After column chromatography, yields are given for separated products.

The use of AcOH, DMSO, EtOH and MeOH did not produce any arylation product (Table 4.6, entries 2,4,6-7). The yield in MeCN, dioxane and toluene were 42, 34 and 30%, respectively (Table 4.6, entries 1,3,5). Prolonging the reaction time slightly increased the yield (entry 8). Increasing the amount of the oxidant and the phenylboronic acid improved the yields (Table 4.6, entries 9-10). Under the optimized conditions, we have screened a series of bases like Cs_2CO_3, K_2CO_3, Na_2CO_3, $NaHCO_3$ and NaOAc each 2 eqvs. TLC analysis of the reaction mixtures revealed that in the presence of Cs_2CO_3 **4a** was almost undetectable. The results in the cases of Na_2CO_3 and $NaHCO_3$ were similar. Only in the cases of K_2CO_3 and NaOAc **2a** was isolated in 66 and 67%, respectively. In the cases of Cs_2CO_3, Na_2CO_3 and $NaHCO_3$, the products isolated were proved to be the 2-(4-nitrophenyl)quinazolin-4(3H)-one (yield, 49, 45 and 59% respectively). Under the same conditions, **3b** produced 2-(4-bromophenyl)quinazolin-4(3H)-one (yield, 42, 46 and 52% respectively). The mps and NMR characteristics of the corresponding quinazolin-4(3H)-ones were the same as reported in the literature (Mohammed 2015). The use of 20 mol% of copper salts like $Cu(OAc)_2$ and CuCl diminished the reaction yields (62 and 64%, respectively).

4.2.3. C-4 Phenylation of 2-arylquinazoline 3-oxides.

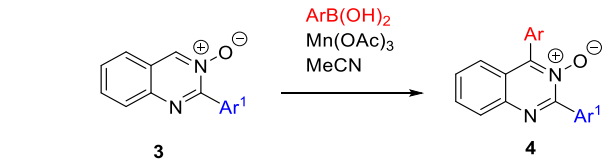
C-2 Aryl(hetaryl) substituted compounds **3** were treated with phenylboronic acid under the optimized conditions to give the corresponding **4a-j** in good to high (71-83%) yields (Table 4.7). It is seen that the developed method tolerates well all types of substituents on the aromatic rings at C-2 of the quinazoline 3-oxide ring. The second series of compounds **4k-t** was synthesized by combining compounds **3** and differently substituted arylboronic acids. Compounds **4** were isolated in 71-78% yields (Table 4.8) and characterized by ^{1}H and ^{13}C NMR analysis. The elemental composition of the newly prepared **4** was determined by HRMS analysis.

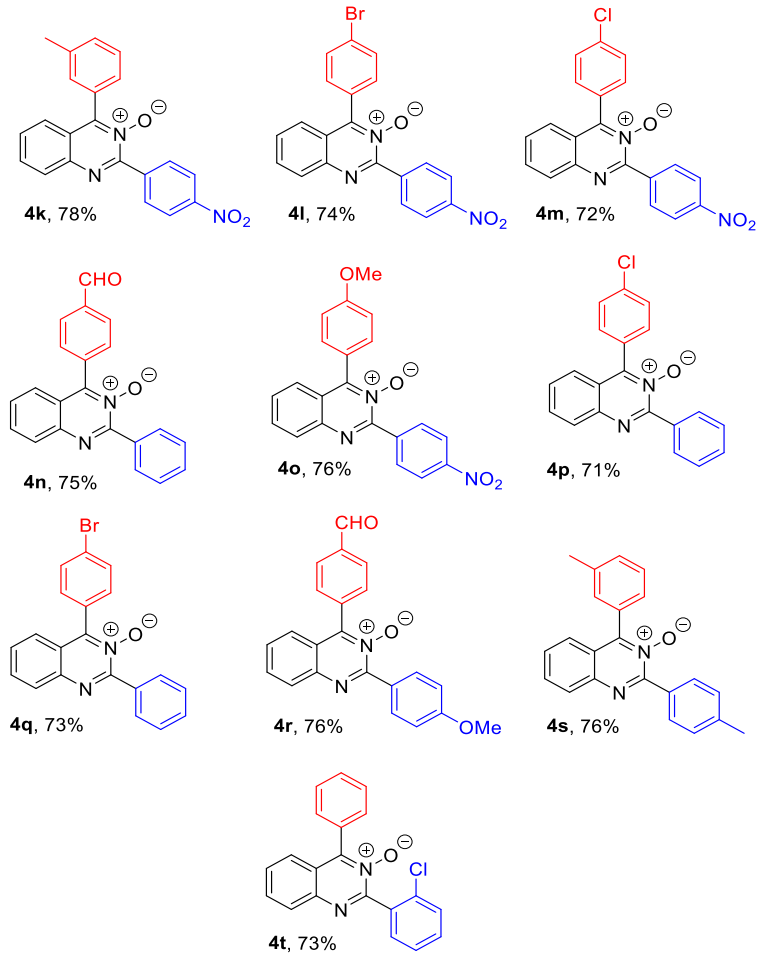
Table 4.7. C-4 Phenylation of 2-arylquinazoline 3-oxides.[a,b]



[a]Reaction conditions: (44 h), $Mn(OAc)_3.2H_2O$ (0.6 mmol, 0.160 g), 60 °C, **1** (0.2 mmol), arylboronic acid (0.6 mmol), solvent (1.0 mL), [b]After column chromatography, yields are given for separated products.

Table 4.8. C-4 Arylation of 2-arylquinazoline 3-oxides.[a,b]

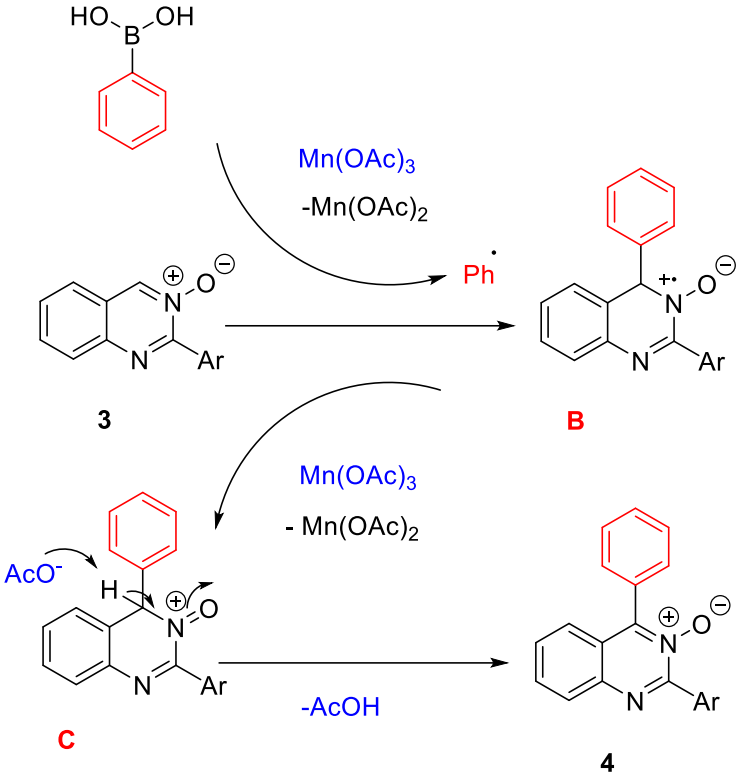




[a]Reaction conditions: (44 h), $Mn(OAc)_3.2H_2O$ (0.6 mmol, 0.160 g), 60 °C, **1** (0.2 mmol), arylboronic acid (0.6 mmol), solvent (1.0 mL), [b]After column chromatography, yields are given for separated products.

4.2.4. A plausible mechanism for the Phenylation of 2-arylquinazoline 3-oxides.

Mn(III) induced carbon-boron bond homolysis provides phenyl radical (Ramesh et al. 2018) **A** which attack the C-4 position of quinazoline 3-oxide **3** is producing intermediate **B**. One more electron transfer from **B** to Mn(III) could provide **C**, and its deprotonation facilitated by the acetate anion is giving rise to the formation of **4**.

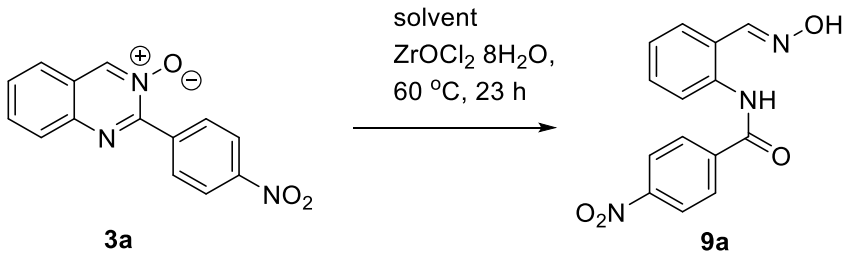


Scheme 4.7. A possible process for the arylation of compounds **3** with arylboronic acids by $Mn(OAc)_3$

A byproduct from the reactions of (4-formylphenyl)boronic acid and the corresponding quinazoline 3-oxides was isolated as a yellow solid and characterized to be the corresponding [1,1'-Biphenyl]-4,4'-dicarbaldehyde. The formation of the latter is in good agreement with the proposed free radical pathway in the formation of compounds **4**.

4.3. $ZrOCl_2$ ring-opening of quinazoline-3-oxides and recyclization in DMSO using catalytic amounts of an acid

Table 4.9. Optimization of the reaction conditions for the synthesis of compounds **9**



Scheme 4.8. Synthesis of compound **9a** from compound **3a** as a starting material

Entry	$ZrOCl_2$. $8H_2O$(eqv)	Solvent	Yield of **9** (%)
1	(1)	MeCN	25
2	(1)	DMSO	22
3	(1)	DMF	24
4	(1)	NMP	28
5	(1)	MeOH	42
6	(1)	MeOH	46
7	(1)	MeOH	38
8	(1)	MeOH	58
9	(1.5)	MeOH	62
10	(2)	MeOH	76
11	(2.5)	MeOH	44

[a]Reaction conditions: (23 h), the solvent (1.0 mL) and at 60 °C, **3a** (0.2 mmol), $ZrOCl_2$ (0.4 mmol) [b]After column chromatography, yields are given for separated products.

The reaction between 2-(4-nitrophenyl)quinazoline 3-oxide 3a and $ZrOCl_2.8H_2O$ was utilized as a model to discover optimum reaction conditions for obtaining the desired ring-opening product **9**. Initially, the reactions were carried out in MeCN at 80°C. shows the desired product **9a** in 25% yield (Table 4.9, entry 1). Like such examined, The yield in MeCN, DMSO, DMF, NMP and MeOH were 22, 24,28 and 42%, respectively (Table

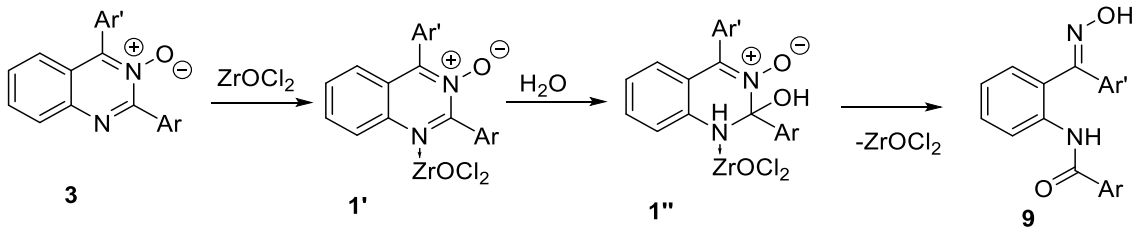
4.9, entries 2,3,4,5). The amount of $ZrOCl_2.8H_2O$ was also examined. Increasing the amount of the $ZrOCl_2.8H_2O$ from 1 to 2 equiv. Improved the yields, and product **9a** obtained the highest yield (76%) (Table 4.9, entries 6-10). Further, increasing in the quantity of $ZrOCl_2.8H_2O$ to 2.5 equiv. had no improvement on the yield (Table 4.9, entry 11).

4.3.1. $ZrOCl_2$ ring-opening of quinazoline-3-oxides.

Under optimal condition, quinazoline-3-oxides **3** were treated with $ZrOCl_2.8H_2O$ to generate the corresponding **9a-h** in good to high yields (76-86%) (Table 10). This method appears to tolerate all forms of substituents on the aromatic rings at C-2 of the quinazoline 3-oxide ring quite well. ^1H and ^{13}C NMR studies were used to describe the substance. HRMS analysis was used to identify the elemental makeup of the newly produced **9**.

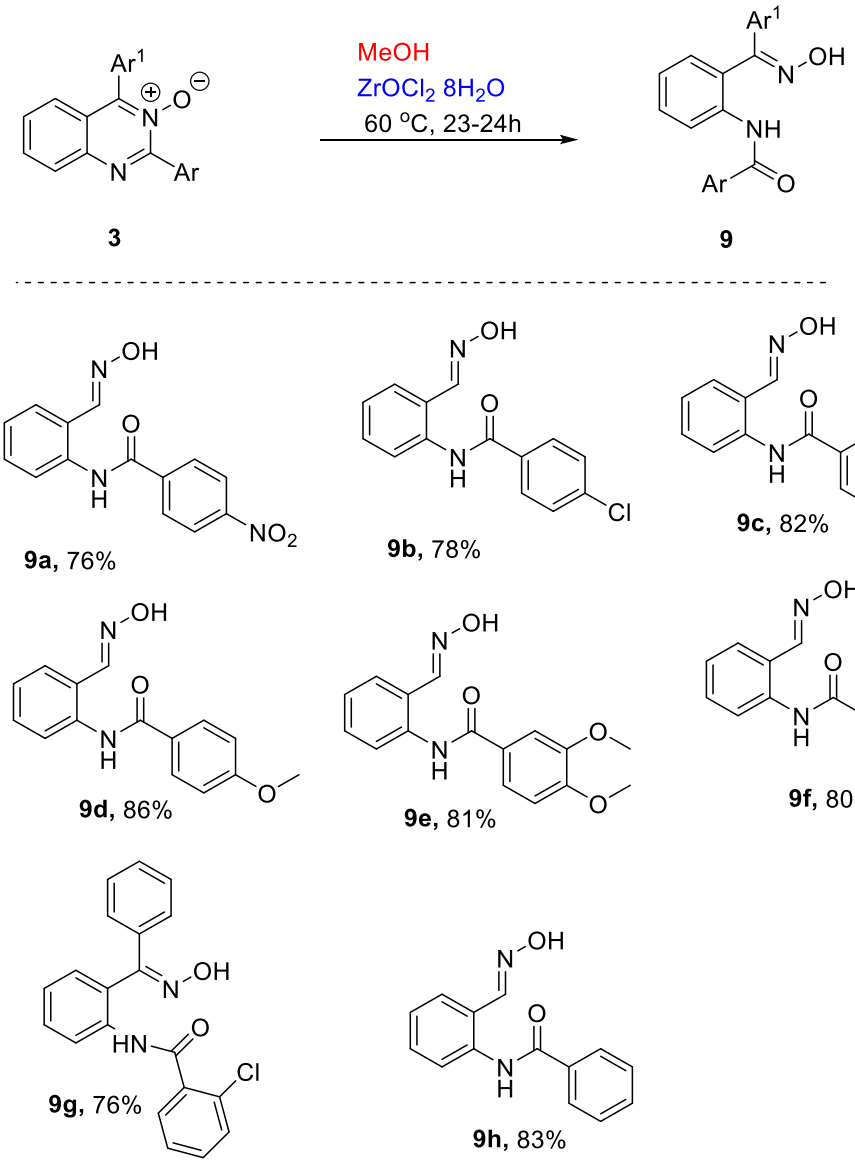
4.3.2. A plausible mechanism for the $ZrOCl_2$ induced ring-opening of quinazoline-3-oxides.

As indicated in (Scheme 4.9.) proposes a probable mechanism for this reaction. $ZrOCl_2$ reacts with quinazoline-3-oxide **3** via $ZrOCl_2$ is co-ordinated into the N1-position and activated C2 position to attacked by the nucleophile of compound **3** to give intermediate **1**'. Then hydrolysis occurs when the H_2O molecule nucleophile attacked to c2 position with intermediate **1**' to provide intermediate **1**". Then release $ZrOCl_2$ from intermediate **1**" to give the desired product **9.**



Scheme 4.9. Probable mechanism for the $ZrOCl_2$ induced ring-opening of quinazoline-3-oxides.

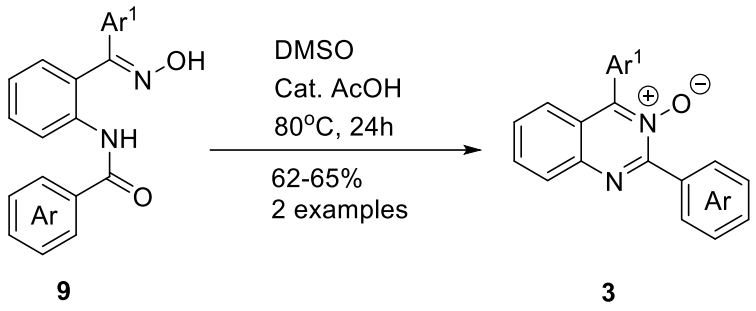
Table 4.10. $ZrOCl_2$ ring-opening of quinazoline-3-oxides **3.**[a-b]



[a]Reaction conditions: (23-24 h), the solvent (1.0 mL) and at 60 °C, **3a** (0.2 mmol), $ZrOCl_2$ (0.4 mmol) [b]after column chromatography, [b]yields are given for separated products.

4.3.3. Recyclization of compound 9

N-(2-((hydroxyimino)methyl)phenyl)-4-benzamide **9a-b** (0.2 mmol) in DMSO (0.5 mL) in the presence of AcOH (20 mol%) catalyst and at 80 ^{o}C, the mixture was stirred for 24 h. to give the desire product **3a-b** as 62% & 65% yield (Scheme 4.10, Table 4.10).



9 **3**

Scheme 4.10. Synthesis of quinazoline-3-oxides **3** from N-(2-((hydroxyimino)methyl) phenyl)-4-benzamide **9.**

5. CONCLUSION

5.1. Eco-friendly H_2O_2 oxidation of 1,2-dihydroquinazoline-3-oxides to quinazoline-3-oxides

Thus the developed methods provide the synthesis of 1,2-dihydroquinazoline- **2a-m** and quinazoline-3-oxides **3a-m** in high yields at room temperature. The method for the synthesis of compounds **2** involves the none photochemical, expensive metal complexes free condensation of compounds **1** with the corresponding aldehydes. The ease of the product isolation, simply filtering the formed precipitate, is another advantage to worth mentioning. Compounds **3** were prepared by oxidation of isolated **2** in high yields at room temperature using H_2O_2-tungstate system. Compounds **3** can also be obtained in improved overall yields and for shorter reaction times when the mixture of **1** and the aromatic aldehyde in THF is treated with the above mentioned oxidizing system.

5.2. $Mn(OAc)_3$ Induced C-4 Arylations of quinazoline 3-oxides with arylboronic acids.

A novel method for the synthesis of 2,4-diarylated quinazoline 3-oxides **4a-t** was developed. The starting 2-aryl-quinazoline 3-oxides **3**, available according to our previously reported procedure, were arylated in good to high yields using arylboronic acids. An easily removable solvent like acetonitrile was proved to be the best among the screened solvent series. Manganese triacetate was demonstrated to be the best oxidant in comparison with MnO_2, $KMnO_4$, $ZrOCl_2$ $8H_2O$, CeO_2 and H_2O_2. A variety of substituents on the C2-Ar group and on the arylboronic acid were well tolerated under the optimized reaction conditions. A plausible free radical reaction mechanism involving the aryl radical addition to C-4 and the single-electron oxidation of the latter was discussed. The reaction of 2-(*p*-nitrophenyl)-1,2-dihydroquinazoline 3-oxide with $ZrOCl_2.8H_2O$ in MeOH lead to the formation of hydrolytic ring-opening product (E)-N-(2-((hydroxyimino)methyl)phenyl)-4-nitrobenzamide.

5.3. $ZrOCl_2$ ring-opening of quinazoline-3-oxides and recyclization in DMSO using catalytic amounts of an acid

N-(2-((hydroxyimino)methyl)phenyl)-4-benzamide **9a-h** was synthesized using a new technique. The starting quinazoline 3-oxides **3**, available according to our previously reported procedure, were ring opening in good to high yields by using $ZrOCl_2.8H_2O$. Methanol, a readily removable solvent, was found to be the best of the screening solvent series. Under the optimized reaction conditions, a variety of substituents on the C2-Ar group and on the arylboronic acid were well tolerated. It can be recycled in DMSO with catalytic quantities of acid to produce quinazoline-3-oxides **3**.

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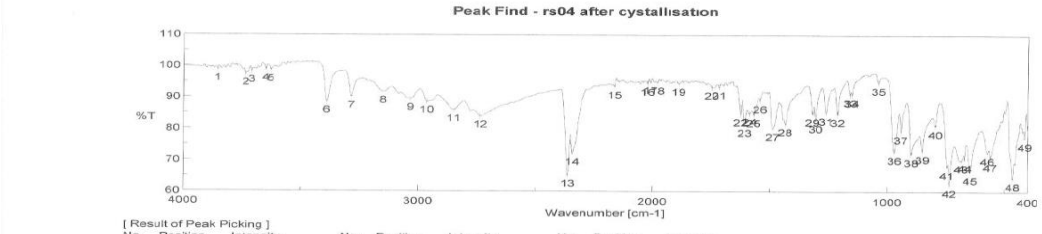
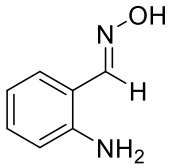
APPENDIX

APPX 1 IR and NMR spectra of compound **1**

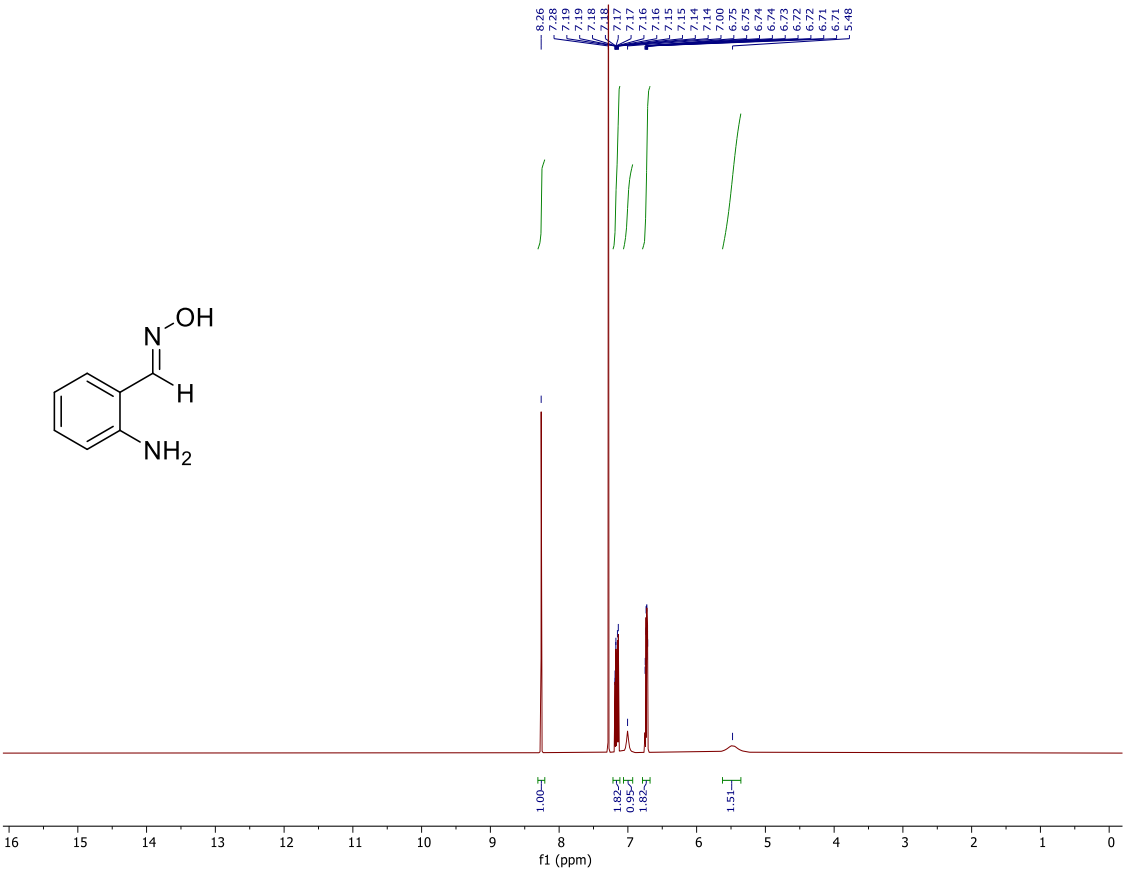


[Result of Peak Picking]

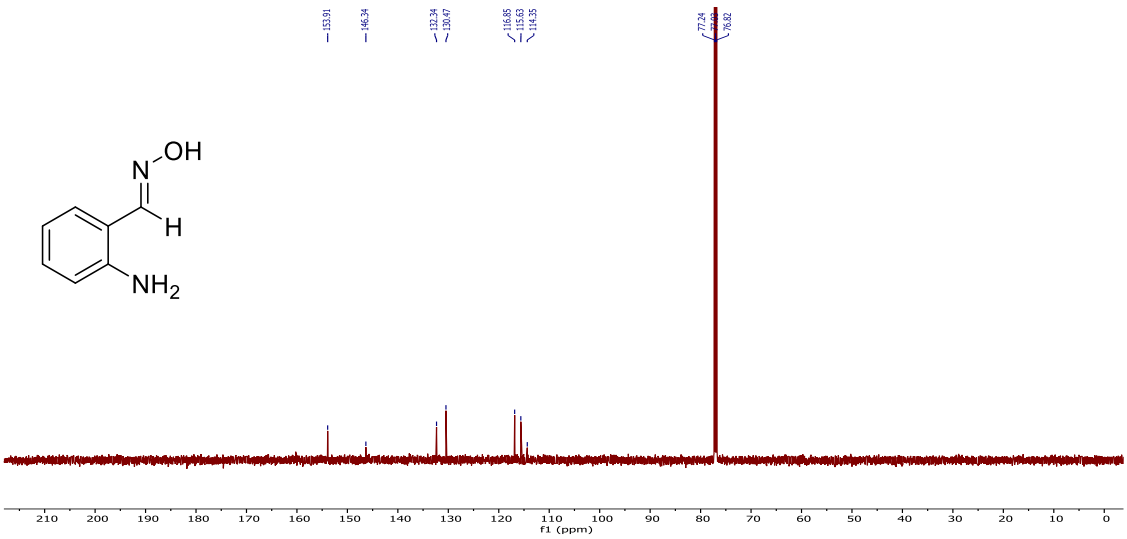
No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity
1	3853.08	9.87E+001	2	3733.51	9.73E+001	3	3709.41	9.82E+001
4	3648.66	9.87E+001	5	3628.41	9.85E+001	6	3390.24	8.84E+001
7	3284.18	9.00E+001	8	3149.19	9.17E+001	9	3032.51	8.94E+001
10	2963.09	8.85E+001	11	2849.31	8.59E+001	12	2734.57	8.39E+001
13	2360.44	6.51E+001	14	2341.16	7.21E+001	15	2161.81	9.33E+001
16	2021.03	9.43E+001	17	2009.46	9.48E+001	18	1979.57	9.47E+001
19	1888.93	9.43E+001	20	1748.16	9.31E+001	21	1717.3	9.32E+001
22	1625.7	8.47E+001	23	1607.38	8.13E+001	24	1587.13	8.48E+001
25	1568.81	8.44E+001	26	1541.81	8.88E+001	27	1487.81	8.01E+001
28	1434.78	8.16E+001	29	1318.11	8.47E+001	30	1304.61	8.25E+001
31	1261.22	8.50E+001	32	1211.08	8.46E+001	33	1158.04	9.08E+001
34	1150.33	9.08E+001	35	1037.52	9.46E+001	36	969.055	7.25E+001
37	942.055	7.91E+001	38	897.701	7.19E+001	39	849.49	7.29E+001
40	794.528	8.09E+001	41	745.352	6.79E+001	42	734.746	6.21E+001
43	684.508	7.00E+001	44	669.178	7.02E+001	45	647.001	6.63E+001
46	572.755	7.25E+001	47	560.22	7.05E+001	48	464.761	6.43E+001
49	413.656	7.71E+001						



APPX 1.1 IR spectra of compound **1**

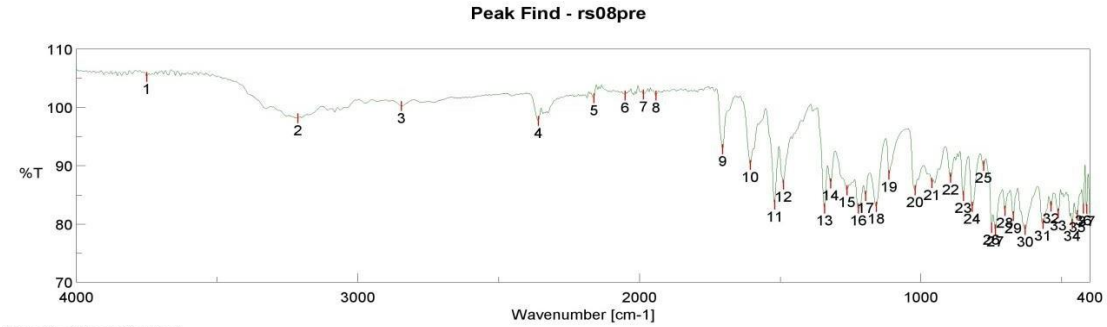


APPX 1.2 ^{1}H NMR (600 MHz, Chloroform-d) of compound **1**



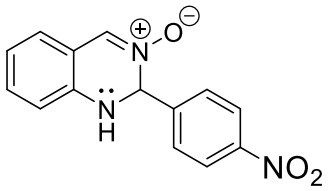
APPX 1.3 ^{13}C NMR (151 MHz, Chloroform-d) of compound **1**

APPX 2 IR and NMR Spectra of compound **2**

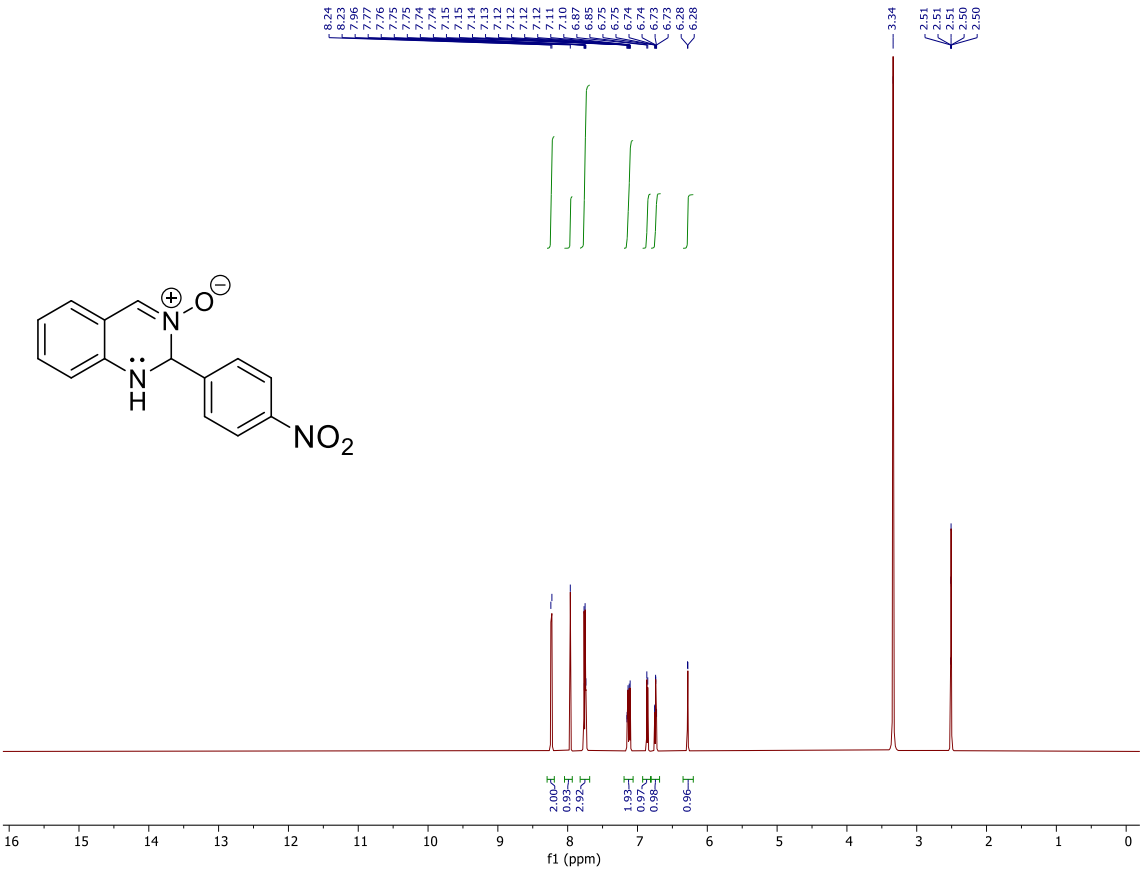


[Result of Peak Picking]

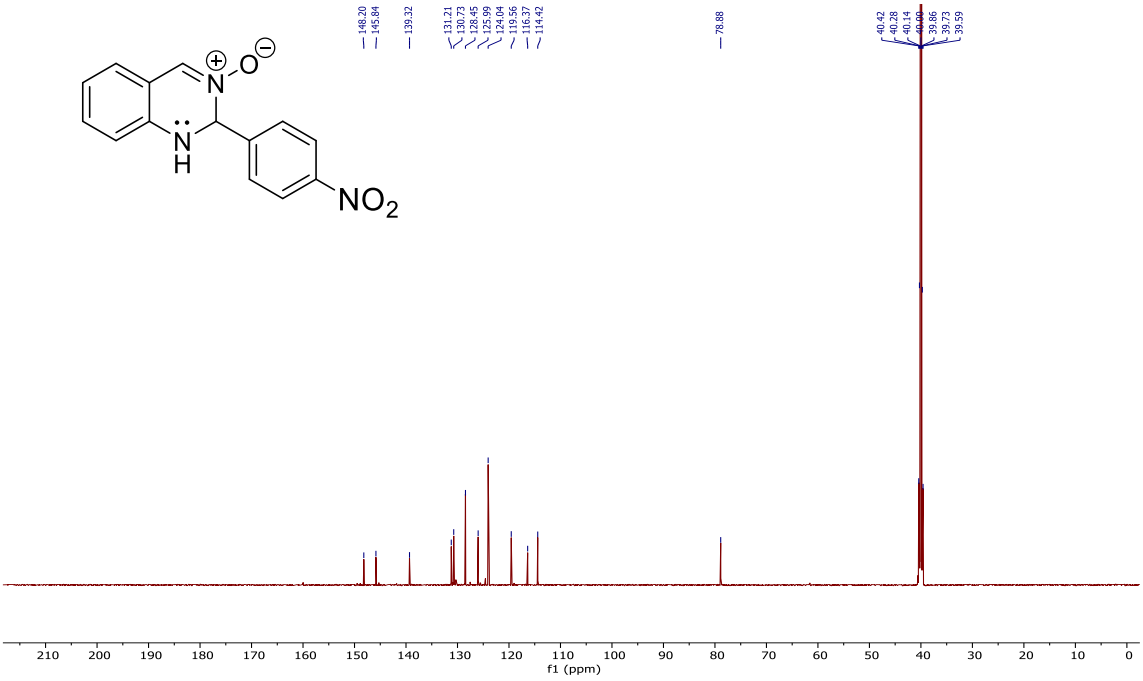
No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity
1	3749.9	1.05E+002	2	3213.79	9.81E+001	3	2845.45	1.00E+002
4	2359.48	9.77E+001	5	2161.81	1.02E+002	6	2050.92	1.02E+002
7	1986.32	1.02E+002	8	1941.97	1.02E+002	9	1704.76	9.28E+001
10	1606.41	9.01E+001	11	1519.63	8.33E+001	12	1488.78	8.68E+001
13	1342.21	8.27E+001	14	1321	8.70E+001	15	1263.15	8.58E+001
16	1221.68	8.27E+001	17	1196.61	8.48E+001	18	1159.01	8.30E+001
19	1113.69	8.85E+001	20	1021.12	8.58E+001	21	961.341	8.70E+001
22	894.809	8.79E+001	23	849.49	8.48E+001	24	818.634	8.29E+001
25	778.136	9.00E+001	26	749.209	7.93E+001	27	735.71	7.91E+001
28	701.962	8.23E+001	29	672.071	8.14E+001	30	629.644	7.90E+001
31	566.969	8.01E+001	32	538.042	8.30E+001	33	512.008	8.18E+001
34	462.832	8.00E+001	35	444.512	8.15E+001	36	423.298	8.27E+001
37	411.728	8.26E+001						



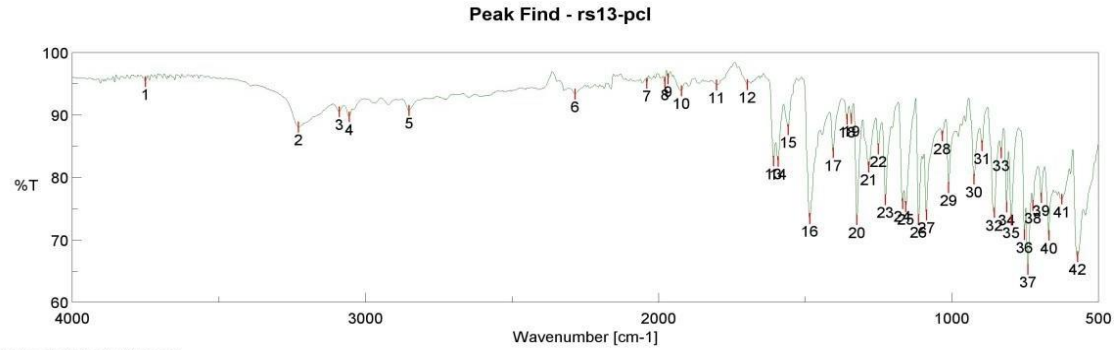
APPX 2.1 IR Spectra of compound **2a**



APPX 2.2 ^{1}H NMR (600 MHz, DMSO-d6) of compound **2a**

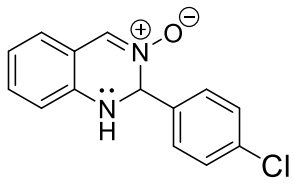


APPX 2.3^{13}C NMR (151 MHz, DMSO-d6) of compound **2a**

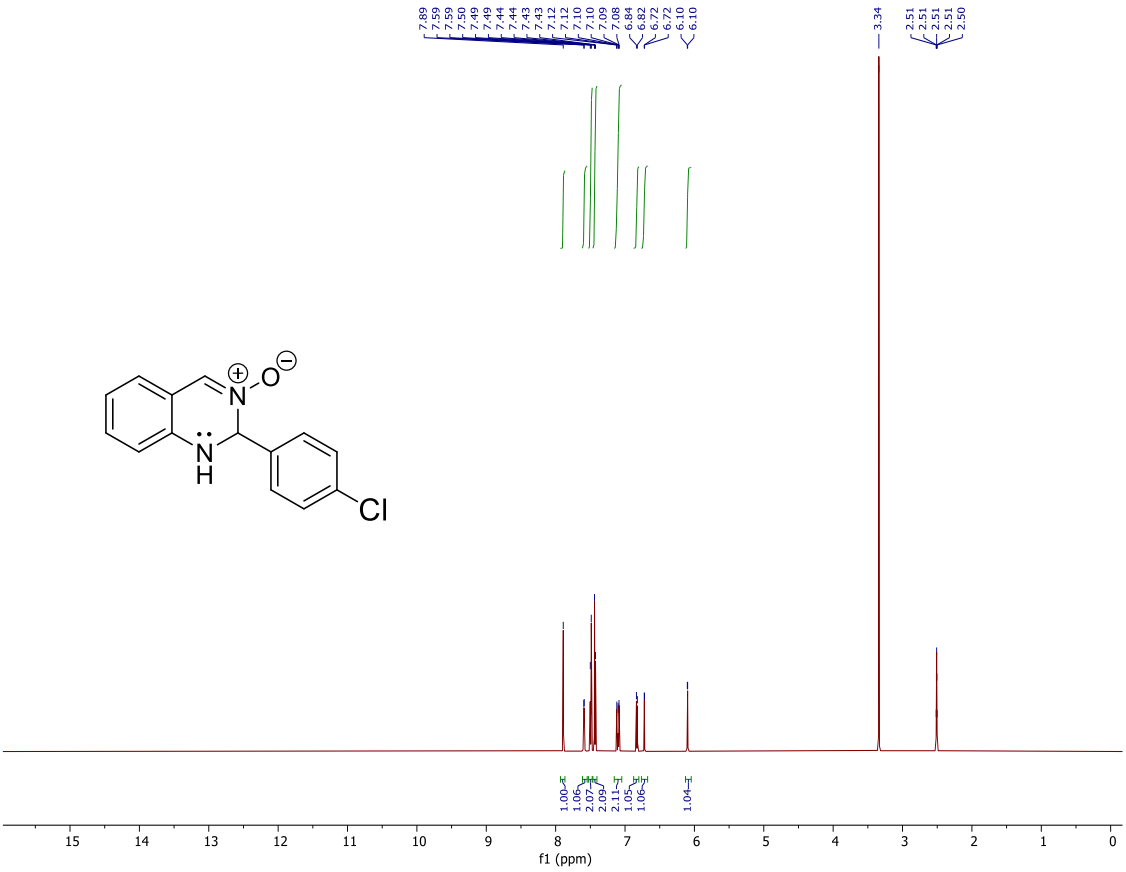


[Result of Peak Picking]

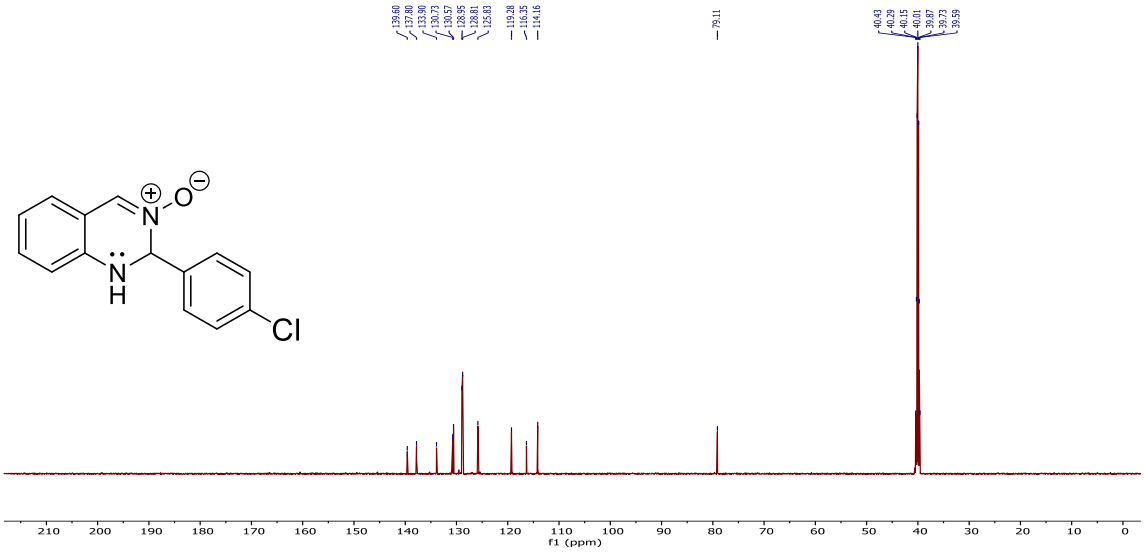
No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity
1	3750.87	9.53E+001	2	3228.25	8.81E+001	3	3089.4	9.05E+001
4	3055.66	8.97E+001	5	2852.2	9.07E+001	6	2285.23	9.34E+001
7	2040.32	9.51E+001	8	1979.57	9.53E+001	9	1968	9.58E+001
10	1922.68	9.39E+001	11	1802.15	9.48E+001	12	1698.02	9.49E+001
13	1608.34	8.26E+001	14	1592.91	8.26E+001	15	1558.2	8.77E+001
16	1484.92	7.34E+001	17	1404.89	8.40E+001	18	1357.64	8.93E+001
19	1343.18	8.94E+001	20	1323.89	7.32E+001	21	1283.39	8.17E+001
22	1250.61	8.46E+001	23	1226.5	7.64E+001	24	1168.65	7.58E+001
25	1157.08	7.53E+001	26	1113.69	7.33E+001	27	1086.69	7.40E+001
28	1032.69	8.66E+001	29	1011.48	7.84E+001	30	924.7	7.97E+001
31	896.737	8.51E+001	32	855.275	7.44E+001	33	832.133	8.39E+001
34	812.849	7.52E+001	35	797.421	7.32E+001	36	752.102	7.08E+001
37	740.531	6.53E+001	38	723.175	7.55E+001	39	695.212	7.68E+001
40	669.178	7.07E+001	41	624.823	7.65E+001	42	571.79	6.73E+001



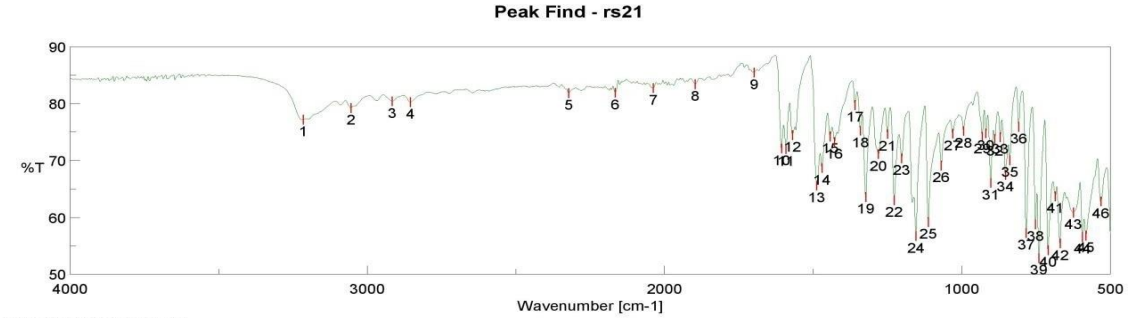
APPX 2.4 IR Spectra of compound **2b**



APPX 2.5 ^{1}H NMR (600 MHz, DMSO-d_6) of compound **2b**

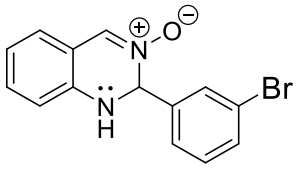


APPX 2.6 ^{13}C NMR (151 MHz, DMSO) of compound **2b**

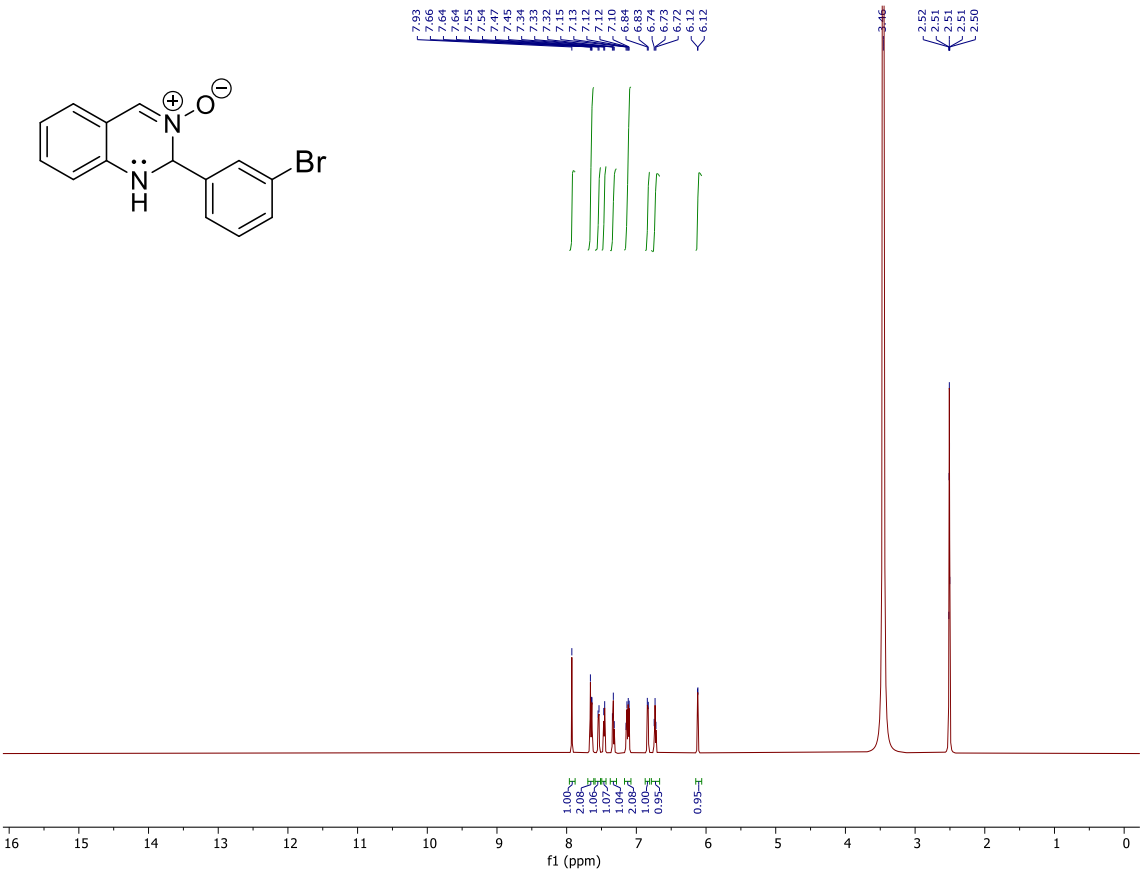


[Result of Peak Picking]

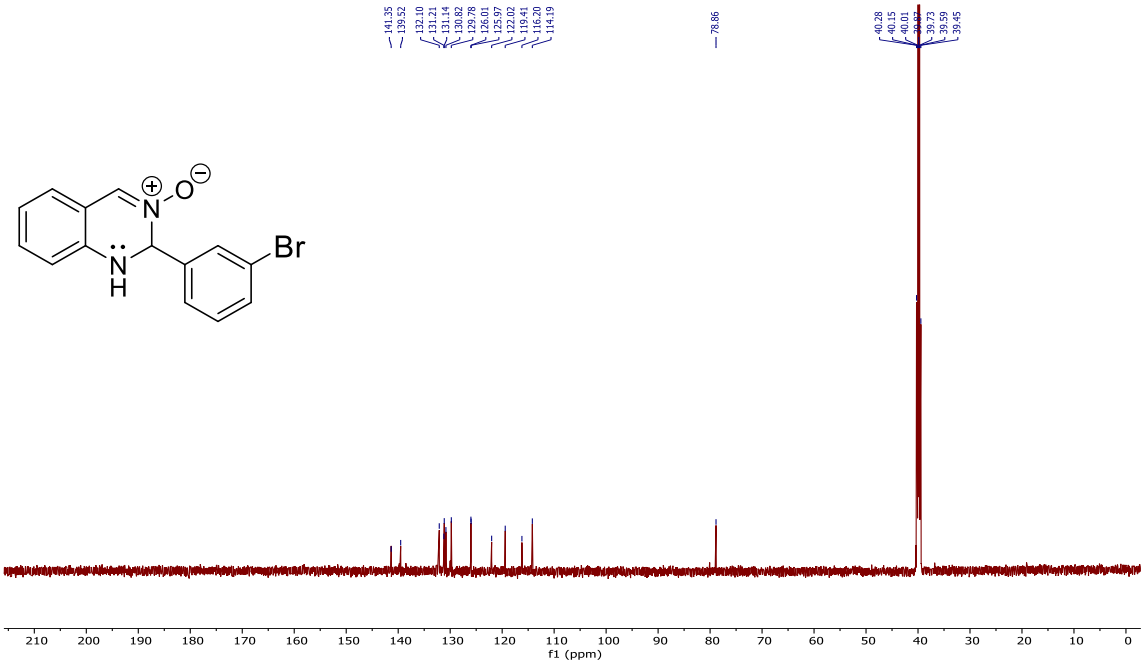
No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity
1	3215.72	7.72E+001	2	3054.69	7.92E+001	3	2915.84	8.04E+001
4	2855.1	8.03E+001	5	2321.87	8.18E+001	6	2165.67	8.19E+001
7	2037.43	8.27E+001	8	1896.65	8.34E+001	9	1698.02	8.55E+001
10	1606.41	7.21E+001	11	1590.99	7.20E+001	12	1568.81	7.45E+001
13	1487.81	6.56E+001	14	1470.46	6.87E+001	15	1442.49	7.42E+001
16	1428.03	7.32E+001	17	1358.6	7.97E+001	18	1340.28	7.53E+001
19	1322.93	6.36E+001	20	1280.5	7.11E+001	21	1249.65	7.47E+001
22	1227.47	6.30E+001	23	1202.4	7.04E+001	24	1154.19	5.67E+001
25	1112.73	5.92E+001	26	1069.33	6.91E+001	27	1030.77	7.47E+001
28	994.125	7.52E+001	29	930.485	7.42E+001	30	918.914	7.48E+001
31	902.523	6.61E+001	32	889.023	7.38E+001	33	870.703	7.41E+001
34	853.347	6.75E+001	35	837.919	7.00E+001	36	808.028	7.59E+001
37	782.958	5.73E+001	38	752.102	5.88E+001	39	740.531	5.29E+001
40	709.676	5.42E+001	41	685.57	6.37E+001	42	669.178	5.54E+001
43	624.823	6.09E+001	44	593.968	5.66E+001	45	582.397	5.68E+001
46	532.257	6.28E+001						



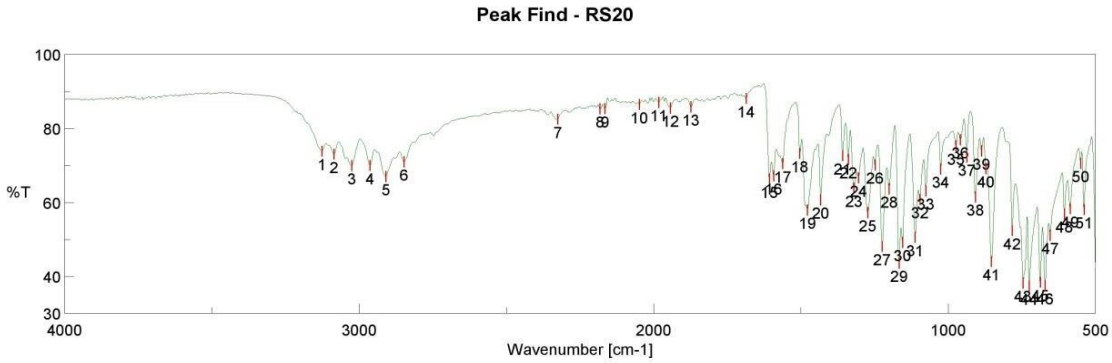
APPX 2.7 IR spectra of compound **2c**



APPX 2.8 ^{1}H NMR (600 MHz, DMSO-d_6) of compound **2c**

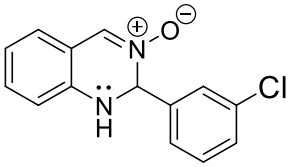


APPX 2.9 ^{13}C NMR (151 MHz, DMSO-d_6) of compound **2c**

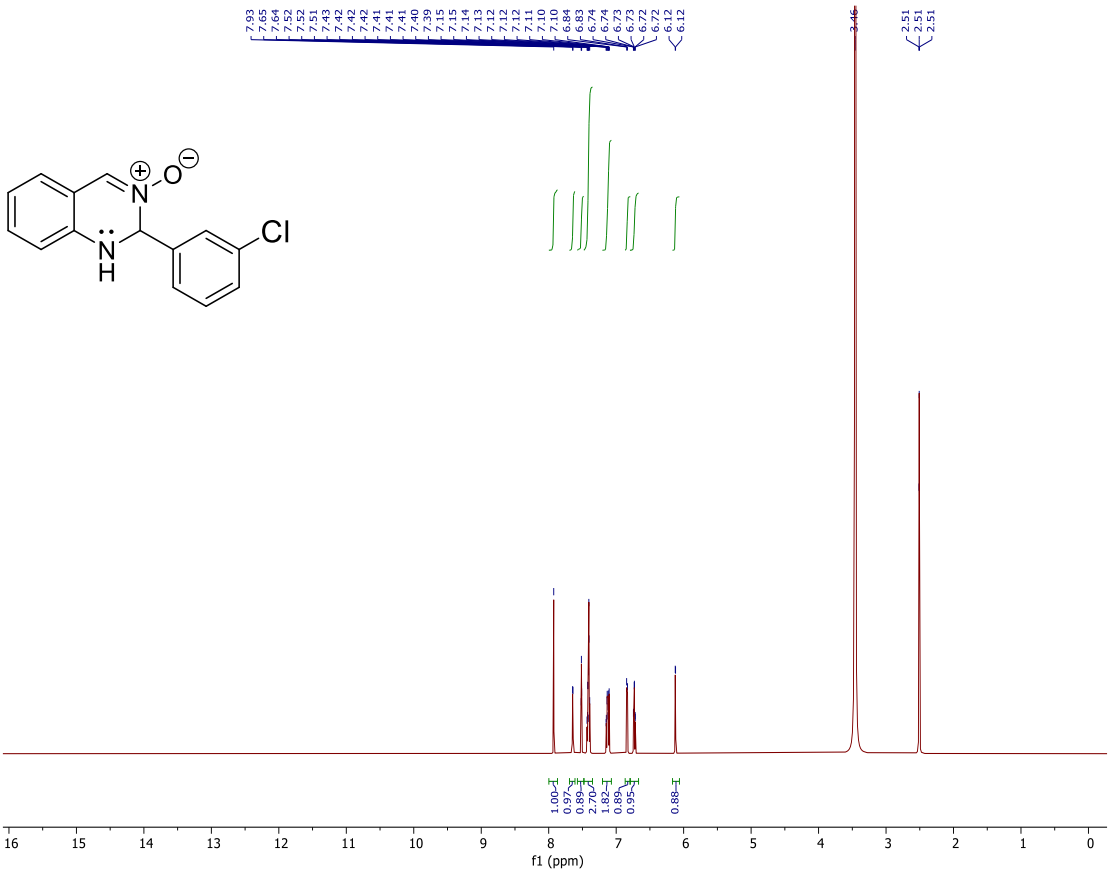


[Result of Peak Picking]

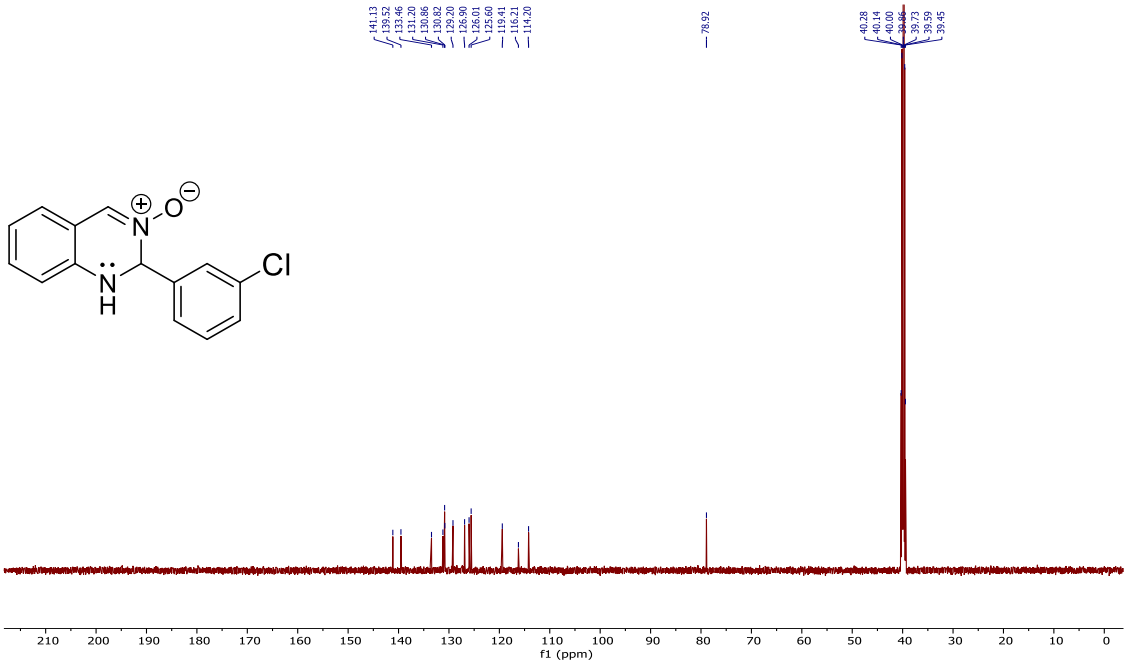
No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity
1	3126.04	7.39E+001	2	3085.55	7.30E+001	3	3025.76	7.00E+001
4	2963.09	7.00E+001	5	2910.06	6.70E+001	6	2847.38	7.10E+001
7	2325.73	8.25E+001	8	2182.06	8.53E+001	9	2165.67	8.54E+001
10	2049	8.65E+001	11	1982.46	8.70E+001	12	1942.93	8.55E+001
13	1873.51	8.58E+001	14	1686.44	8.81E+001	15	1607.38	6.63E+001
16	1592.91	6.72E+001	17	1562.06	7.05E+001	18	1504.2	7.33E+001
19	1478.17	5.80E+001	20	1432.85	6.07E+001	21	1358.6	7.26E+001
22	1339.32	7.16E+001	23	1320.04	6.39E+001	24	1304.61	6.67E+001
25	1273.75	5.72E+001	26	1248.68	7.02E+001	27	1224.58	4.81E+001
28	1200.47	6.37E+001	29	1166.72	4.36E+001	30	1155.15	4.92E+001
31	1112.73	5.06E+001	32	1096.33	6.08E+001	33	1076.08	6.31E+001
34	1025.94	6.90E+001	35	973.876	7.52E+001	36	958.448	7.70E+001
37	937.235	7.23E+001	38	908.308	6.15E+001	39	887.095	7.39E+001
40	871.667	6.91E+001	41	853.347	4.41E+001	42	782.958	5.24E+001
43	746.317	3.82E+001	44	725.104	3.75E+001	45	687.498	3.85E+001
46	671.106	3.76E+001	47	653.75	5.11E+001	48	605.539	5.69E+001
49	586.254	5.83E+001	50	550.577	7.05E+001	51	539.007	5.81E+001



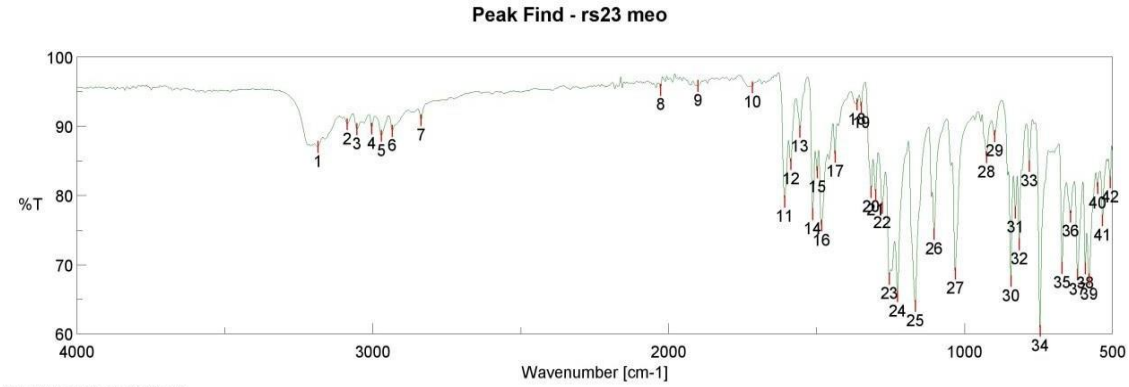
APPX 2.10 IR spectra of compound **2d**



APPX 2.11 ^{1}H NMR (600 MHz, DMSO-d_6) of compound **2d**

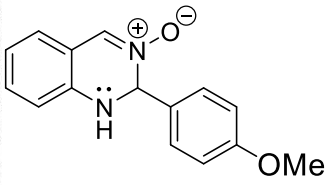


APPX 2.12 ^{13}C NMR (151 MHz, DMSO) of compound **2d**

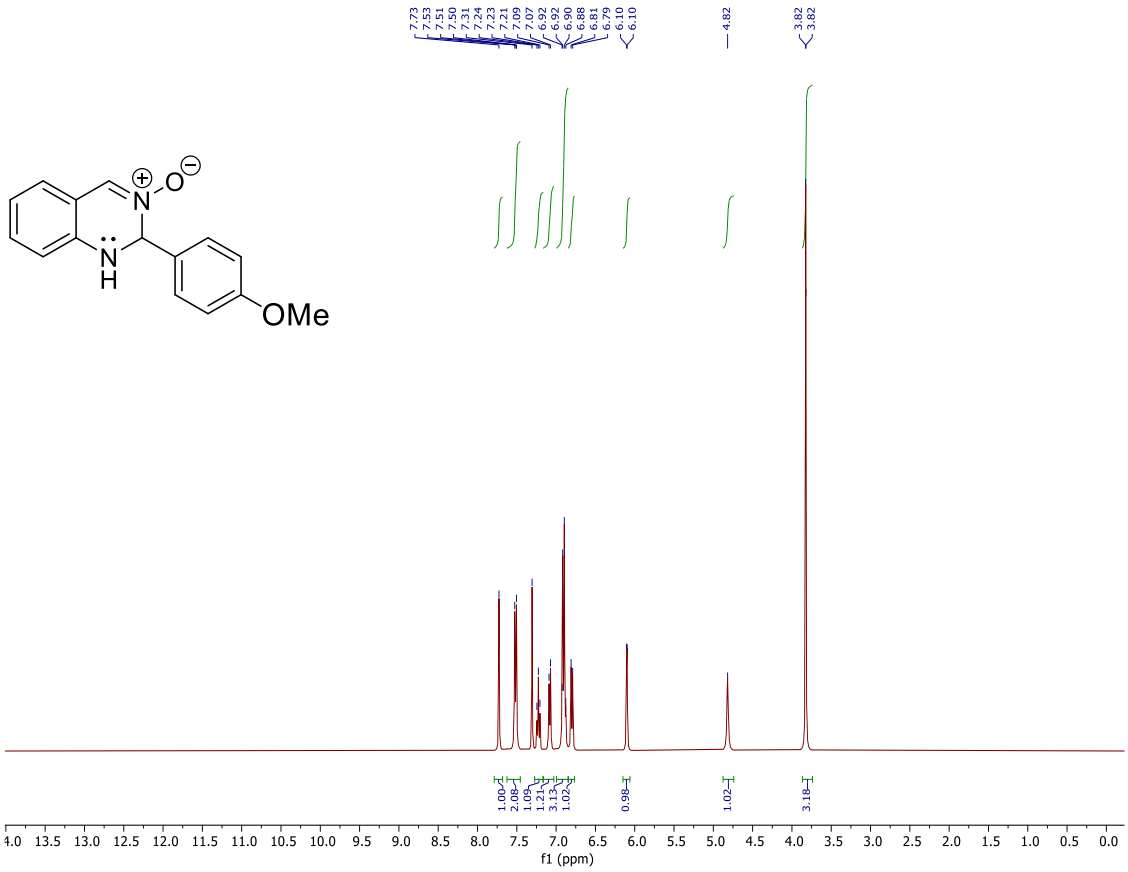


[Result of Peak Picking]

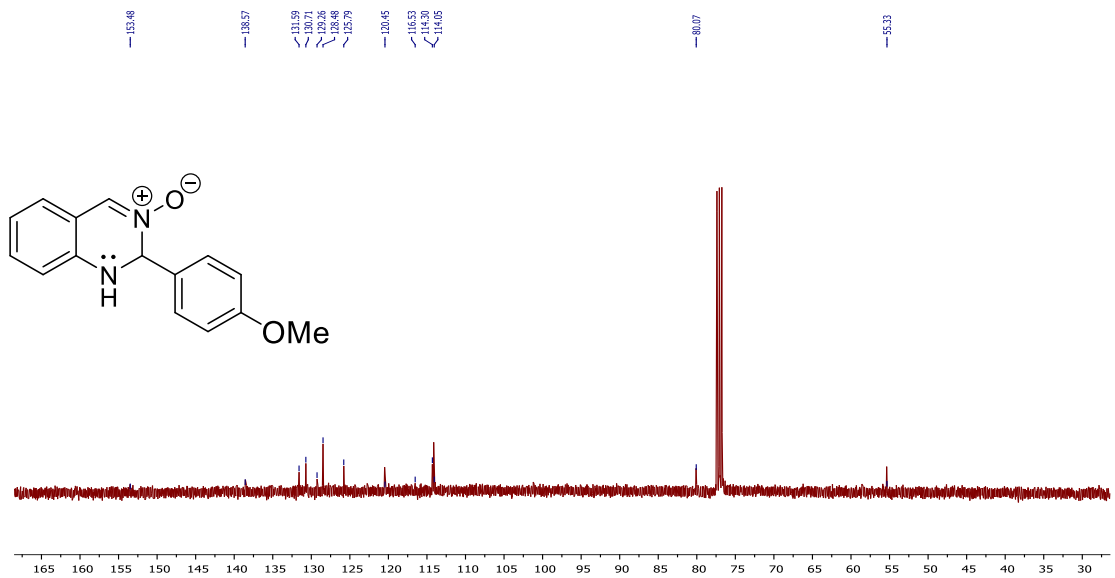
No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity
1	3185.83	8.70E+001	2	3086.51	9.03E+001	3	3053.73	8.96E+001
4	3003.59	8.97E+001	5	2970.8	8.86E+001	6	2934.16	8.93E+001
7	2836.77	9.09E+001	8	2027.78	9.53E+001	9	1901.47	9.59E+001
10	1717.3	9.56E+001	11	1608.34	7.91E+001	12	1587.13	8.45E+001
13	1557.24	8.92E+001	14	1513.85	7.73E+001	15	1498.42	8.34E+001
16	1483.96	7.57E+001	17	1437.67	8.56E+001	18	1364.39	9.31E+001
19	1348.96	9.27E+001	20	1316.18	8.05E+001	21	1300.75	8.01E+001
22	1278.57	7.82E+001	23	1254.47	6.80E+001	24	1226.5	6.54E+001
25	1166.72	6.40E+001	26	1103.08	7.44E+001	27	1031.73	6.87E+001
28	926.628	8.55E+001	29	898.666	8.86E+001	30	843.704	6.76E+001
31	828.277	7.75E+001	32	815.742	7.30E+001	33	781.029	8.42E+001
34	745.352	6.04E+001	35	671.106	6.95E+001	36	642.179	7.70E+001
37	618.074	6.86E+001	38	592.039	6.95E+001	39	579.504	6.79E+001
40	550.577	8.11E+001	41	534.185	7.64E+001	42	508.151	8.19E+001



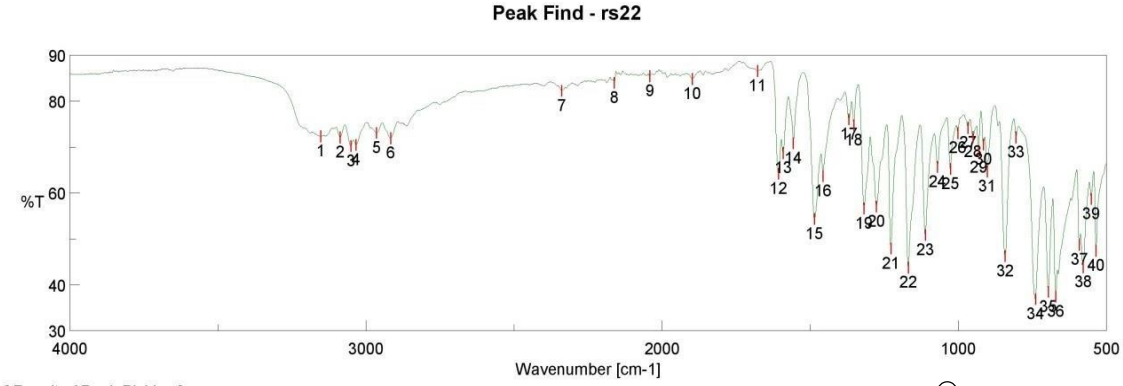
APPX 2.13 IR spectra of compound **2e**



APPX 2.14 ^{1}H NMR (400 MHz, $CDCl_3$) of compound **2e**

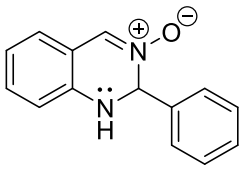


APPX 2.15 ^{13}C NMR (101 MHz, $CDCl_3$) of compound **2e**

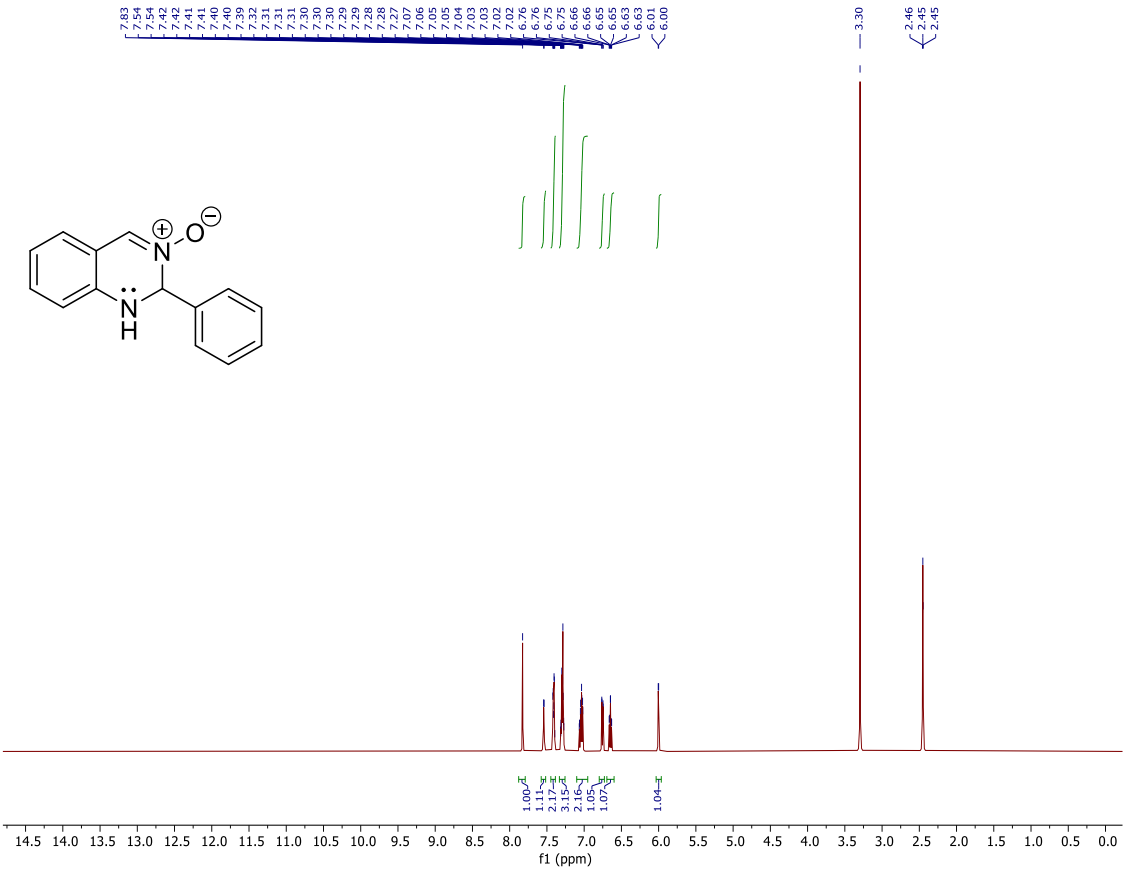


[Result of Peak Picking]

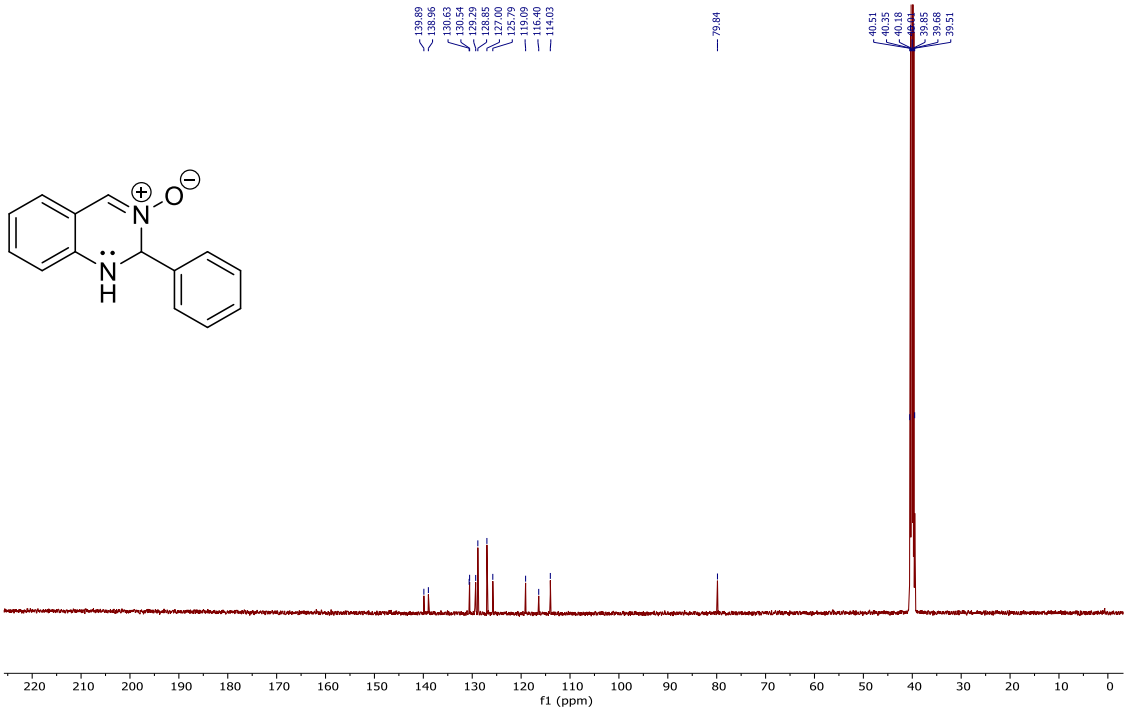
No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity
1	3152.08	7.23E+001	2	3087.48	7.21E+001	3	3050.83	7.02E+001
4	3033.48	7.05E+001	5	2964.05	7.31E+001	6	2916.81	7.19E+001
7	2339.23	8.23E+001	8	2161.81	8.40E+001	9	2042.25	8.54E+001
10	1898.58	8.48E+001	11	1677.77	8.66E+001	12	1607.38	6.42E+001
13	1590.99	6.87E+001	14	1557.24	7.08E+001	15	1485.88	5.44E+001
16	1456.96	6.37E+001	17	1369.21	7.60E+001	18	1352.82	7.48E+001
19	1318.11	5.66E+001	20	1276.65	5.70E+001	21	1227.47	4.79E+001
22	1168.65	4.38E+001	23	1111.76	5.09E+001	24	1070.3	6.57E+001
25	1026.91	6.52E+001	26	1001.84	7.31E+001	27	967.126	7.42E+001
28	950.734	7.22E+001	29	931.45	6.88E+001	30	915.058	7.06E+001
31	902.523	6.47E+001	32	841.776	4.63E+001	33	805.135	7.21E+001
34	739.567	3.69E+001	35	696.177	3.85E+001	36	671.106	3.75E+001
37	591.075	4.87E+001	38	578.54	4.39E+001	39	551.542	5.87E+001
40	535.15	4.74E+001						



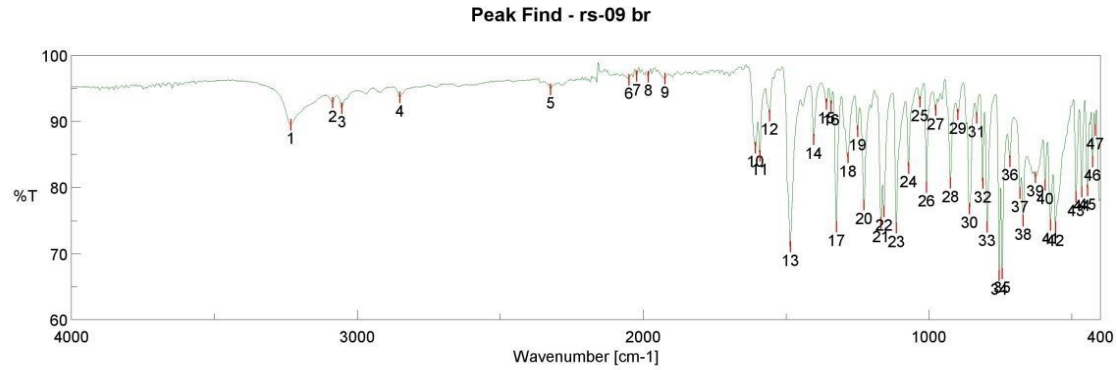
APPX 2.16 IR spectra of compound **2f**



APPX 2.17 ^{1}H NMR (500 MHz, DMSO-d6) of compound **2f**

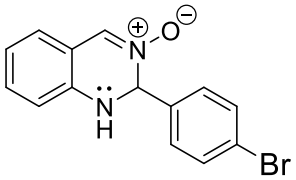


APPX 2.18 ^{13}C NMR (126 MHz, DMSO-d6) of compound **2f**

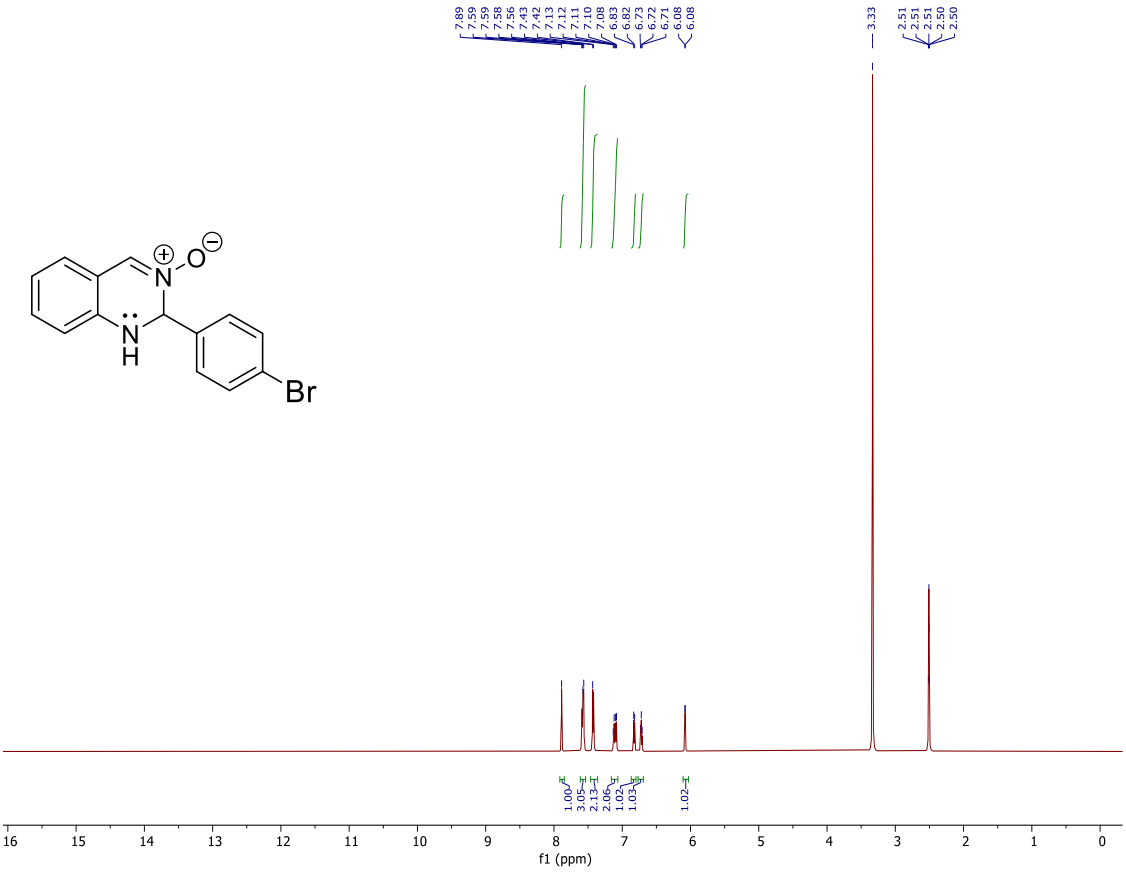


[Result of Peak Picking]

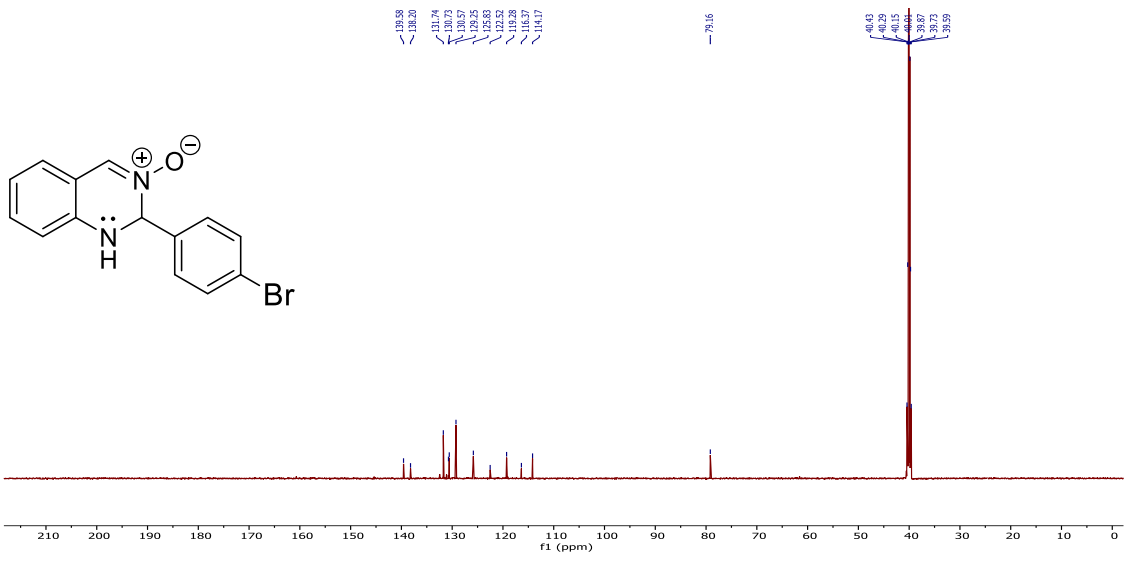
No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity
1	3232.11	8.95E+001	2	3086.51	9.28E+001	3	3054.69	9.20E+001
4	2851.24	9.36E+001	5	2323.8	9.49E+001	6	2049.96	9.63E+001
7	2022	9.68E+001	8	1982.46	9.68E+001	9	1923.65	9.65E+001
10	1607.38	8.60E+001	11	1591.95	8.48E+001	12	1558.2	9.09E+001
13	1484.92	7.11E+001	14	1402.96	8.73E+001	15	1358.6	9.26E+001
16	1342.21	9.23E+001	17	1323.89	7.41E+001	18	1283.39	8.46E+001
19	1249.65	8.85E+001	20	1227.47	7.74E+001	21	1167.69	7.46E+001
22	1157.08	7.64E+001	23	1113.69	7.39E+001	24	1071.26	8.29E+001
25	1031.73	9.30E+001	26	1008.59	8.01E+001	27	976.769	9.17E+001
28	924.7	8.07E+001	29	898.666	9.10E+001	30	858.168	7.68E+001
31	833.098	9.05E+001	32	811.885	8.07E+001	33	796.457	7.41E+001
34	754.031	6.67E+001	35	743.424	6.70E+001	36	716.425	8.40E+001
37	681.713	7.92E+001	38	670.142	7.50E+001	39	627.716	8.15E+001
40	593.004	8.04E+001	41	574.683	7.44E+001	42	557.327	7.41E+001
43	485.009	7.86E+001	44	464.761	7.94E+001	45	445.476	7.96E+001
46	427.155	8.39E+001	47	418.477	8.87E+001			



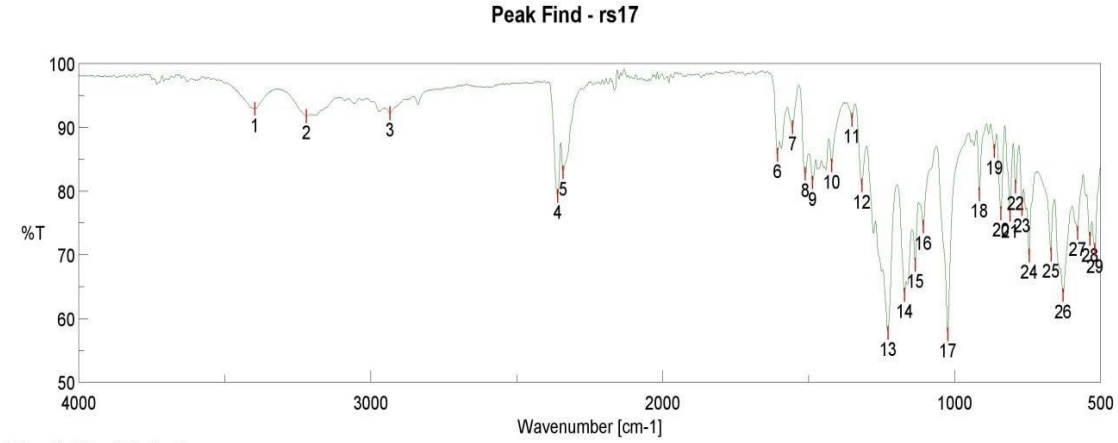
APPX 2.19 IR spectra of compound **2g**



APPX 2.20 ^{1}H NMR (600 MHz, DMSO-d6) of compound **2g**

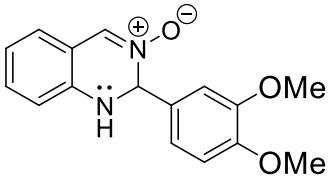


APPX 2.21 ^{13}C NMR (151 MHz, DMSO) of compound **2g**

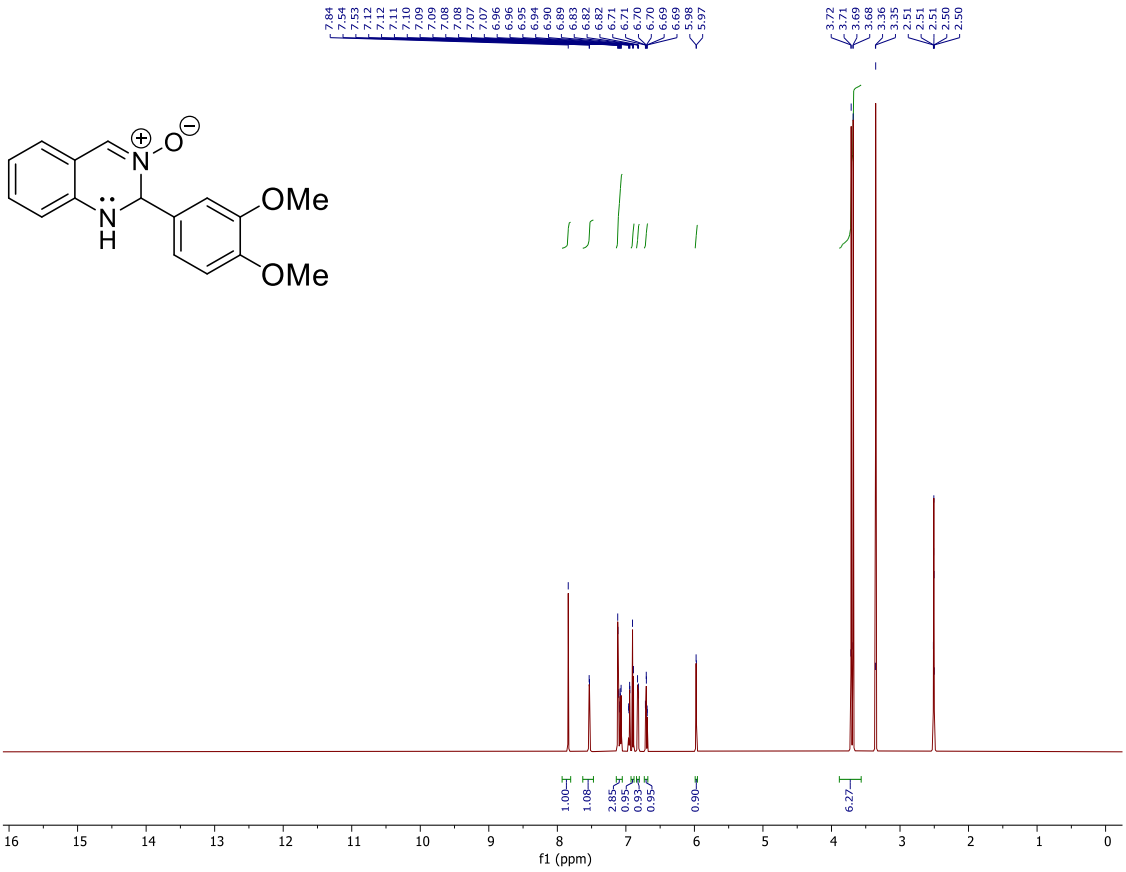


[Result of Peak Picking]

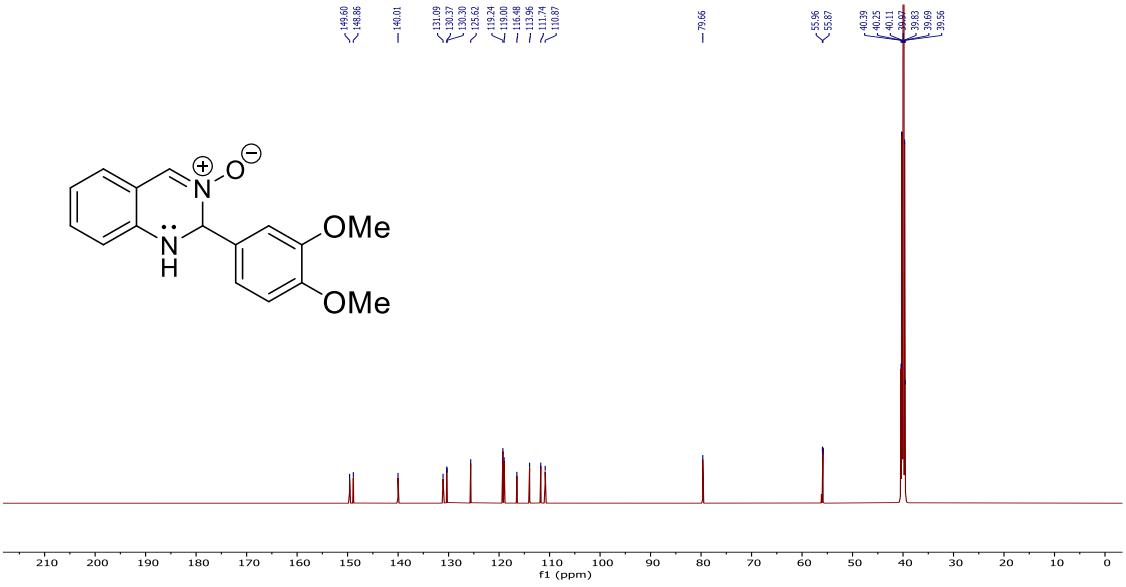
No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity
1	3396.99	9.29E+001	2	3221.5	9.17E+001	3	2934.16	9.22E+001
4	2359.48	7.93E+001	5	2341.16	8.29E+001	6	1607.38	8.56E+001
7	1556.27	9.00E+001	8	1511.92	8.27E+001	9	1486.85	8.13E+001
10	1421.28	8.40E+001	11	1351.86	9.12E+001	12	1318.11	8.09E+001
13	1228.43	5.78E+001	14	1171.54	6.37E+001	15	1134.9	6.84E+001
16	1107.9	7.44E+001	17	1024.02	5.76E+001	18	916.022	7.95E+001
19	863.953	8.63E+001	20	841.776	7.65E+001	21	810.92	7.63E+001
22	791.636	8.07E+001	23	769.458	7.72E+001	24	745.352	6.99E+001
25	670.142	7.00E+001	26	628.68	6.37E+001	27	579.504	7.34E+001
28	537.078	7.25E+001	29	519.722	7.08E+001			



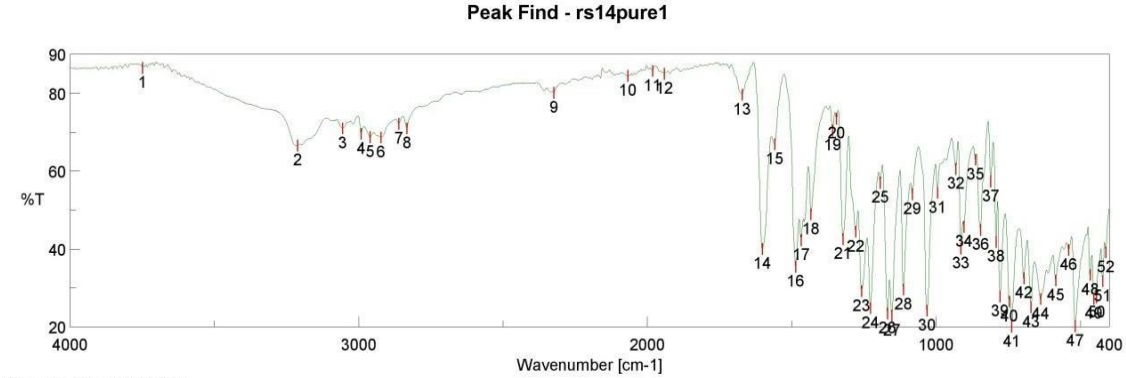
APPX 2.22 IR spectra of compound **2h**



APPX 2.23 ^{1}H NMR (600 MHz, DMSO-d_6) of compound **2h**

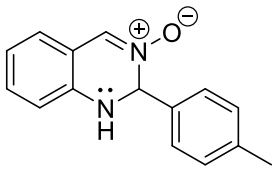


APPX 2.24 ^{13}C NMR (151 MHz, DMSO-d_6) of compound **2h**

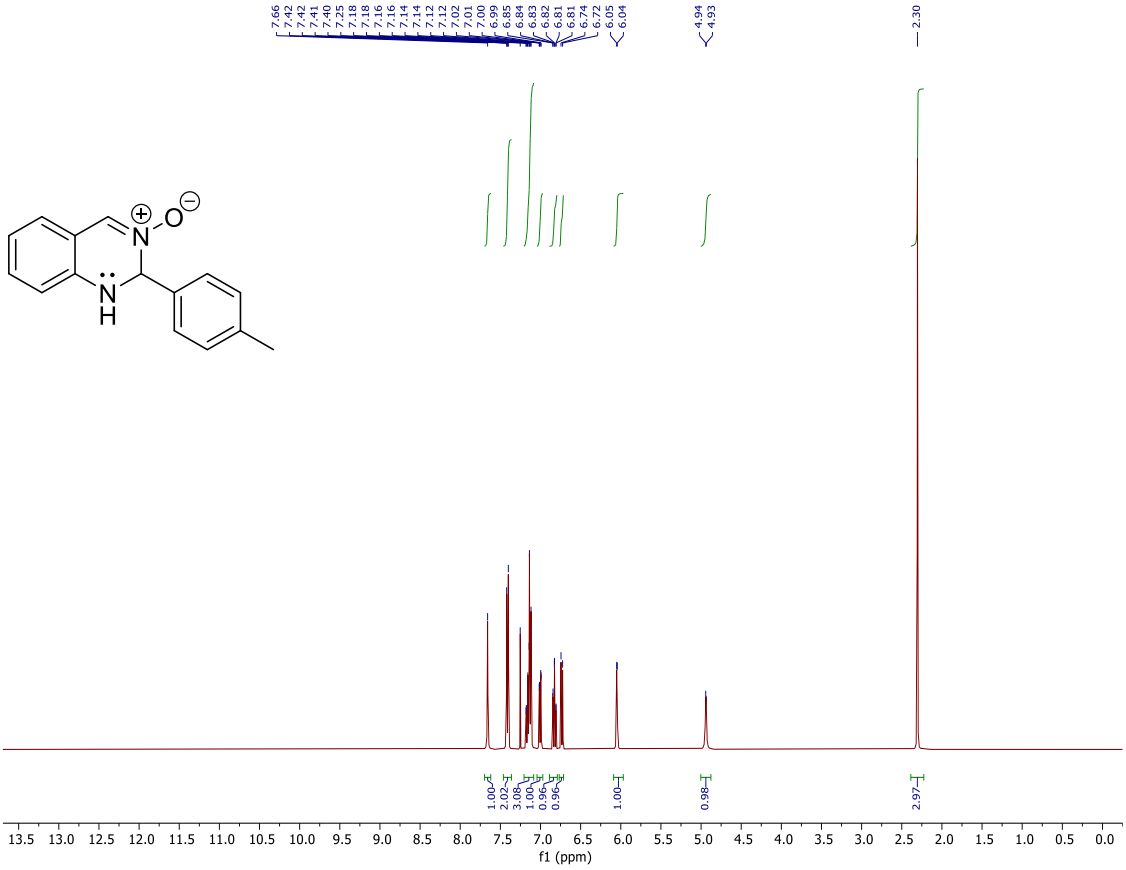


[Result of Peak Picking]

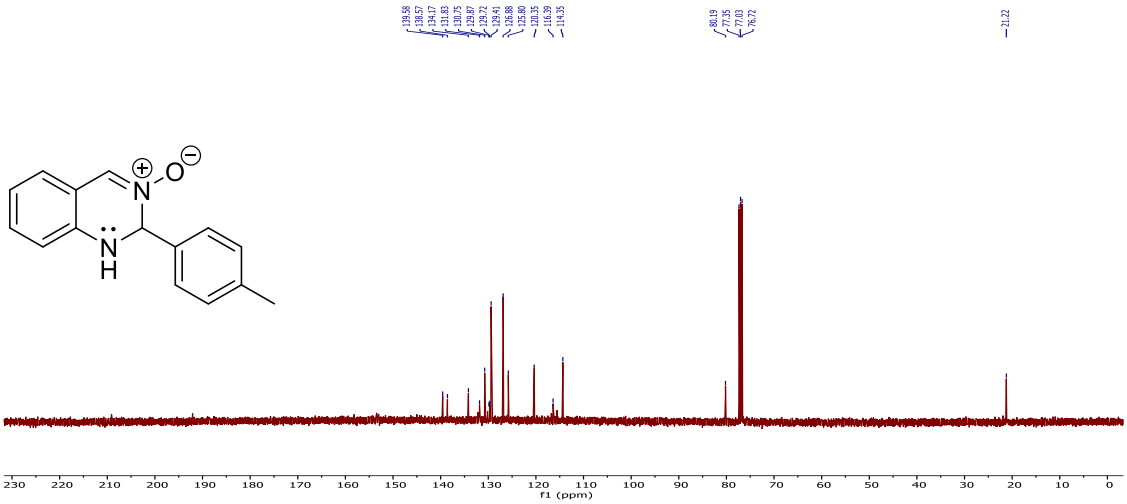
No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity
1	3748.94	8.65E+001	2	3211.86	6.66E+001	3	3055.66	7.10E+001
4	2991.05	6.95E+001	5	2960.2	6.87E+001	6	2923.56	6.87E+001
7	2860.88	7.22E+001	8	2832.92	7.10E+001	9	2323.8	8.01E+001
10	2068.28	8.45E+001	11	1982.46	8.57E+001	12	1941	8.50E+001
13	1671.98	7.96E+001	14	1602.56	4.00E+001	15	1559.17	6.69E+001
16	1486.85	3.55E+001	17	1467.56	4.23E+001	18	1433.82	4.89E+001
19	1358.6	7.04E+001	20	1345.11	7.35E+001	21	1322.93	4.26E+001
22	1278.57	4.45E+001	23	1258.32	2.92E+001	24	1227.47	2.48E+001
25	1193.72	5.70E+001	26	1168.65	2.35E+001	27	1153.22	2.29E+001
28	1113.69	2.96E+001	29	1082.83	5.41E+001	30	1031.73	2.42E+001
31	995.089	5.44E+001	32	931.45	6.06E+001	33	914.093	4.01E+001
34	903.487	4.57E+001	35	863.953	6.29E+001	36	845.633	4.49E+001
37	810.92	5.73E+001	38	792.6	4.19E+001	39	779.101	2.78E+001
40	747.281	2.66E+001	41	738.603	2.00E+001	42	696.177	3.25E+001
43	671.106	2.50E+001	44	638.323	2.72E+001	45	586.254	3.19E+001
46	540.935	3.98E+001	47	518.758	2.02E+001	48	466.689	3.34E+001
49	454.154	2.72E+001	50	444.512	2.76E+001	51	423.298	3.17E+001



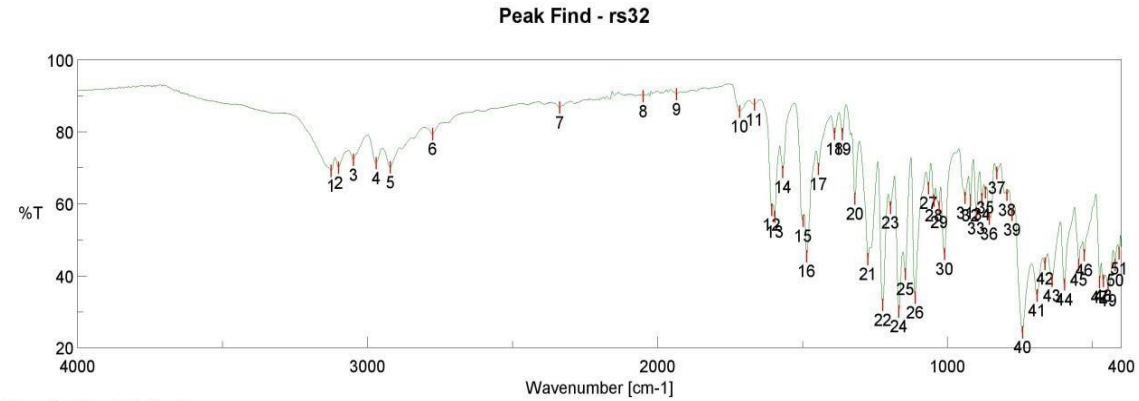
APPX 2.25 IR spectra of compound **2i**



APPX 2.26 ^{1}H NMR (400 MHz, Chloroform-*d*) of compound **2i**

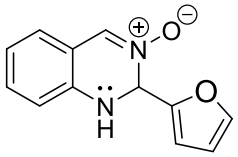


APPX 2.27 ^{13}C NMR (101 MHz, Chloroform-*d*) of compound **2i**

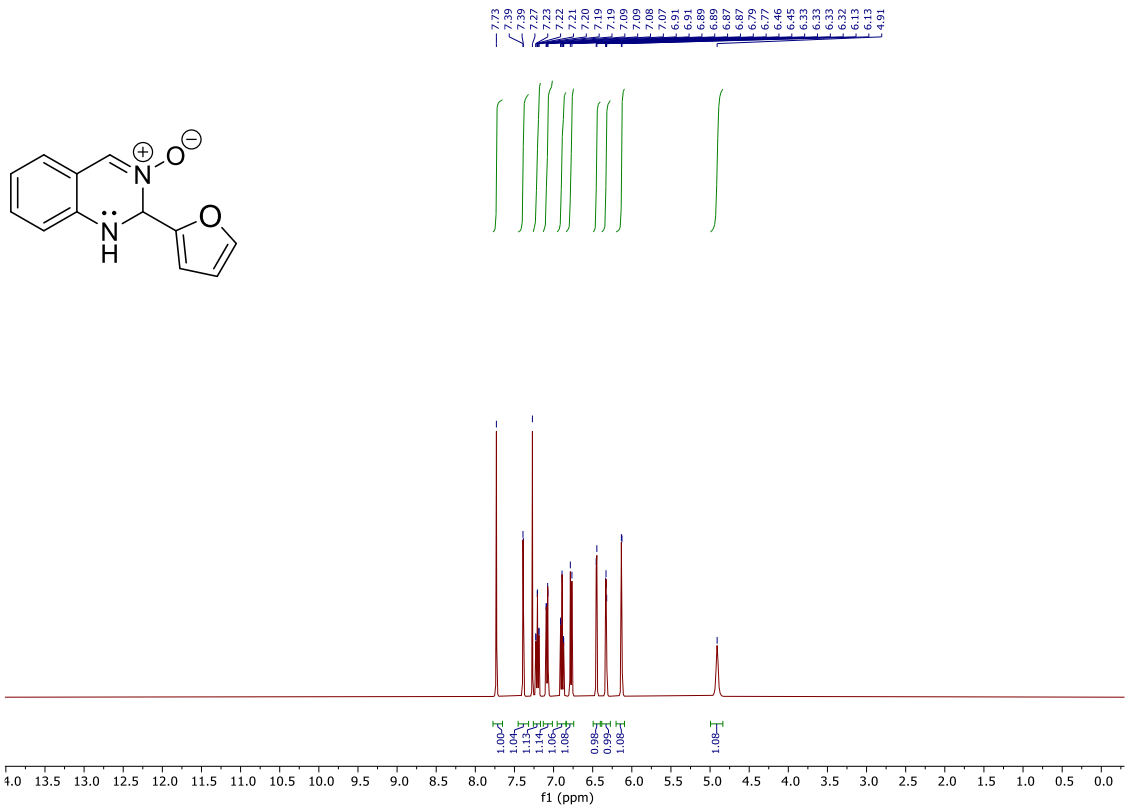


[Result of Peak Picking]

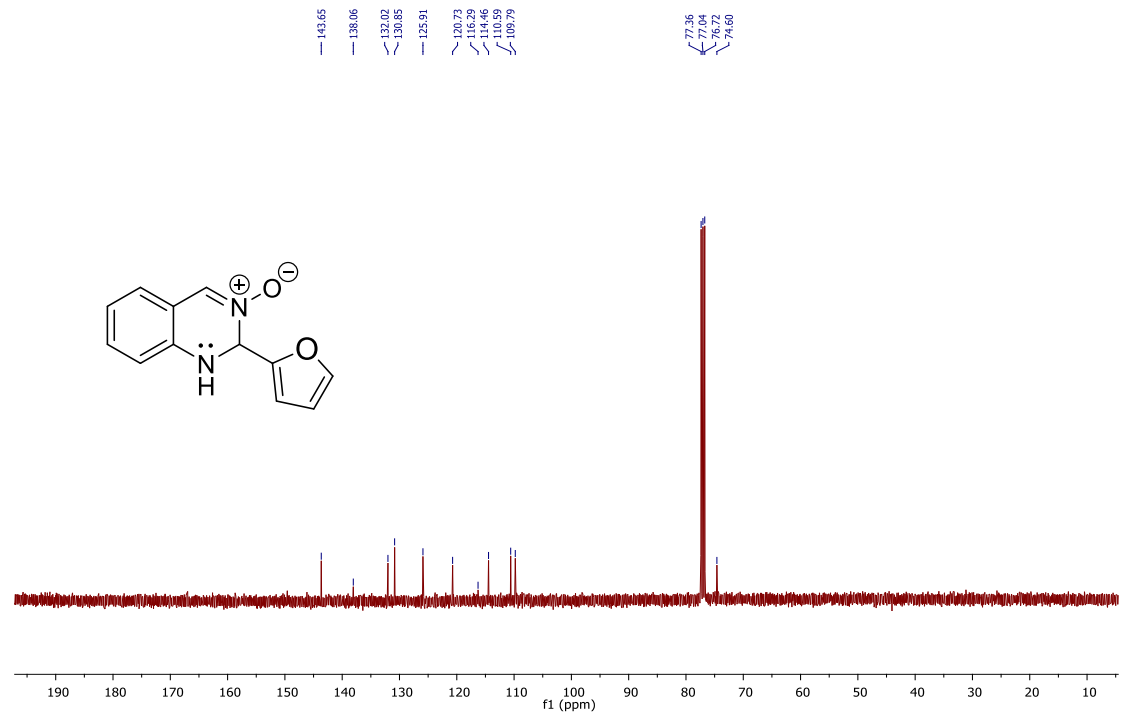
No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity
1	3125.08	6.92E+001	2	3100.01	7.00E+001	3	3048.91	7.22E+001
4	2970.8	7.13E+001	5	2921.63	7.01E+001	6	2776.03	7.94E+001
7	2337.3	8.68E+001	8	2049	8.99E+001	9	1935.22	9.05E+001
10	1717.3	8.56E+001	11	1665.23	8.76E+001	12	1606.41	5.84E+001
13	1595.81	5.64E+001	14	1567.84	6.89E+001	15	1498.42	5.53E+001
16	1485.88	4.55E+001	17	1445.39	6.97E+001	18	1389.46	7.94E+001
19	1362.46	7.94E+001	20	1319.07	6.14E+001	21	1274.72	4.46E+001
22	1223.61	3.19E+001	23	1196.61	5.89E+001	24	1167.69	3.01E+001
25	1145.51	4.05E+001	26	1111.76	3.39E+001	27	1065.48	6.44E+001
28	1047.16	6.09E+001	29	1028.84	5.91E+001	30	1010.52	4.61E+001
31	939.163	6.16E+001	32	920.843	6.10E+001	33	900.594	5.73E+001
34	881.309	6.13E+001	35	868.774	6.32E+001	36	856.239	5.59E+001
37	830.205	6.86E+001	38	794.528	6.25E+001	39	777.172	5.69E+001
40	741.496	2.43E+001	41	691.355	3.45E+001	42	663.393	4.34E+001
43	640.251	3.86E+001	44	596.861	3.76E+001	45	547.685	4.30E+001
46	528.4	4.58E+001	47	475.367	3.83E+001	48	462.832	3.86E+001
49	446.44	3.73E+001	50	421.37	4.30E+001	51	407.871	4.62E+001



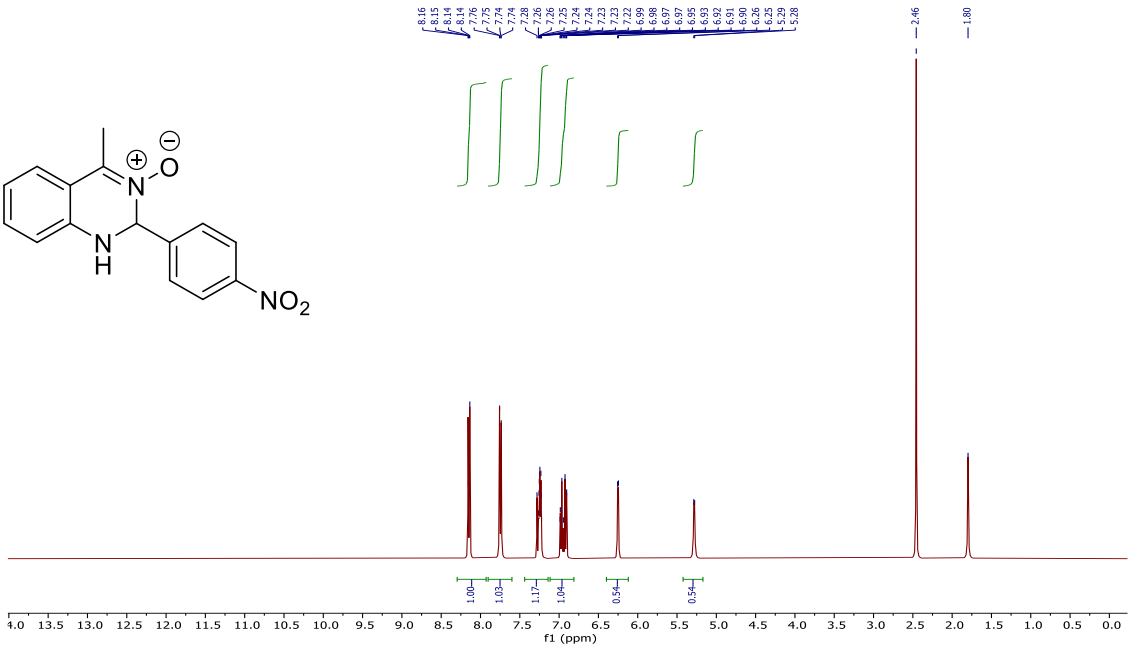
APPX 2.28 IR spectra of compound **2j**



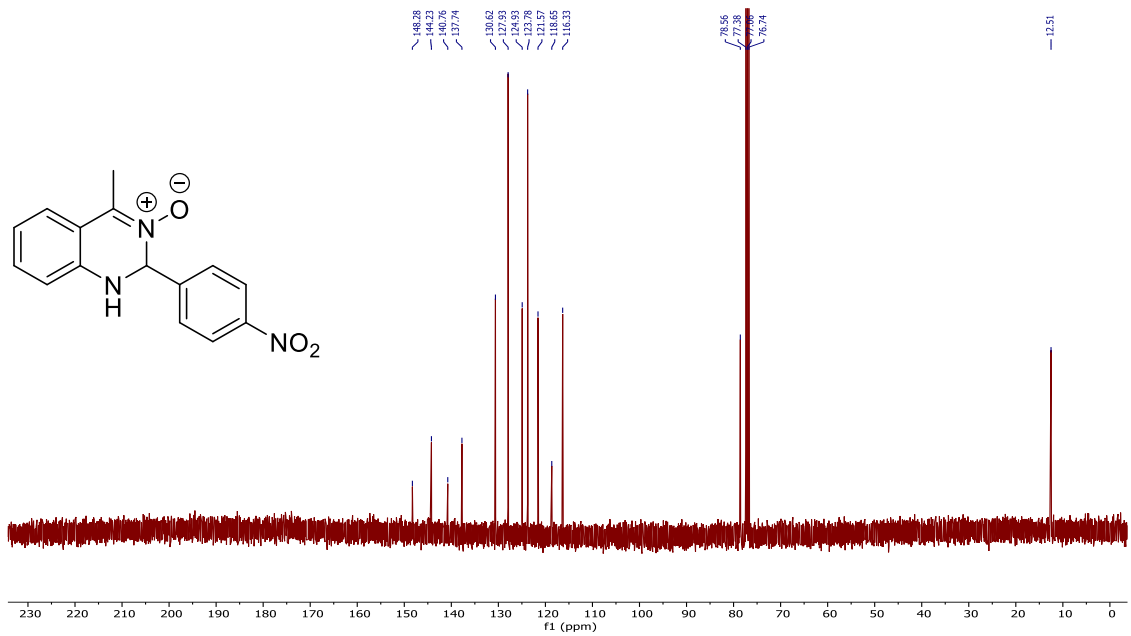
APPX 2.29 ^{1}H NMR (400 MHz, Chloroform-*d*) of compound **2j**



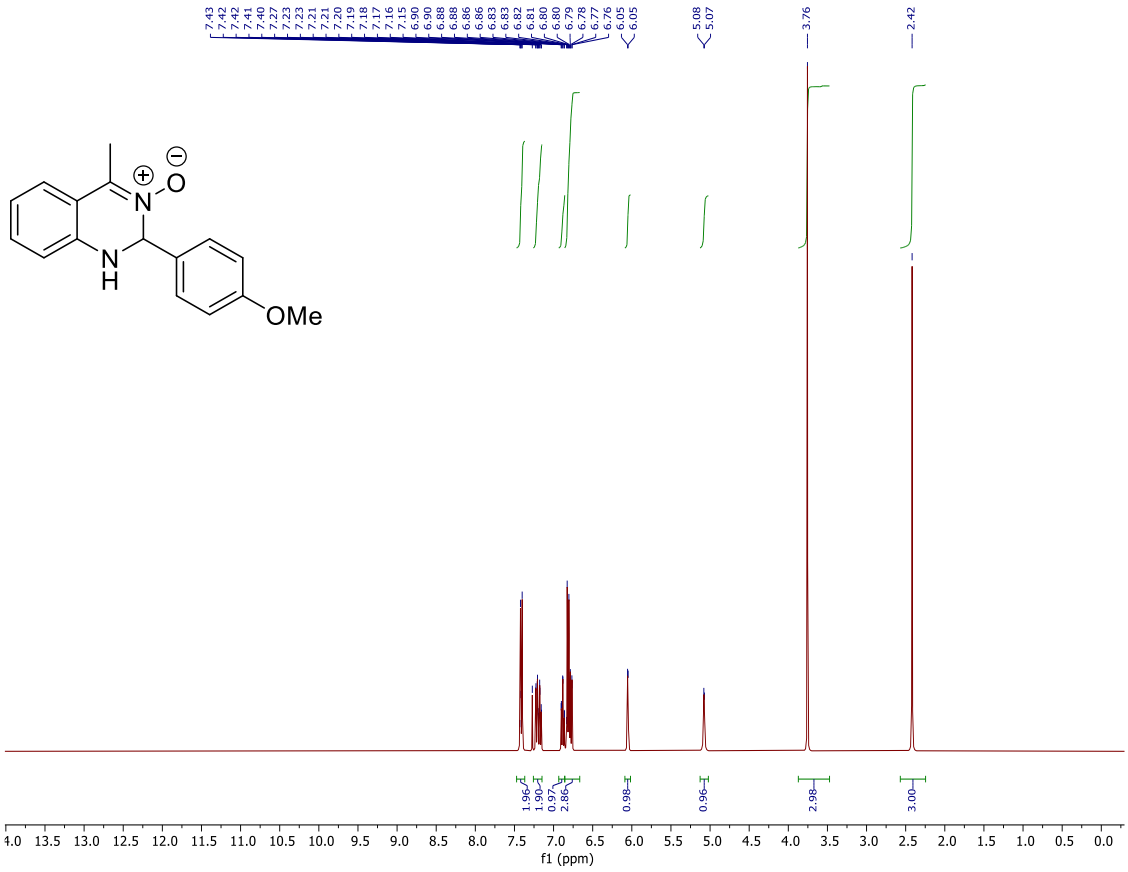
APPX 2.30 ^{13}C NMR (101 MHz, $CDCl_3$) of compound **2j**



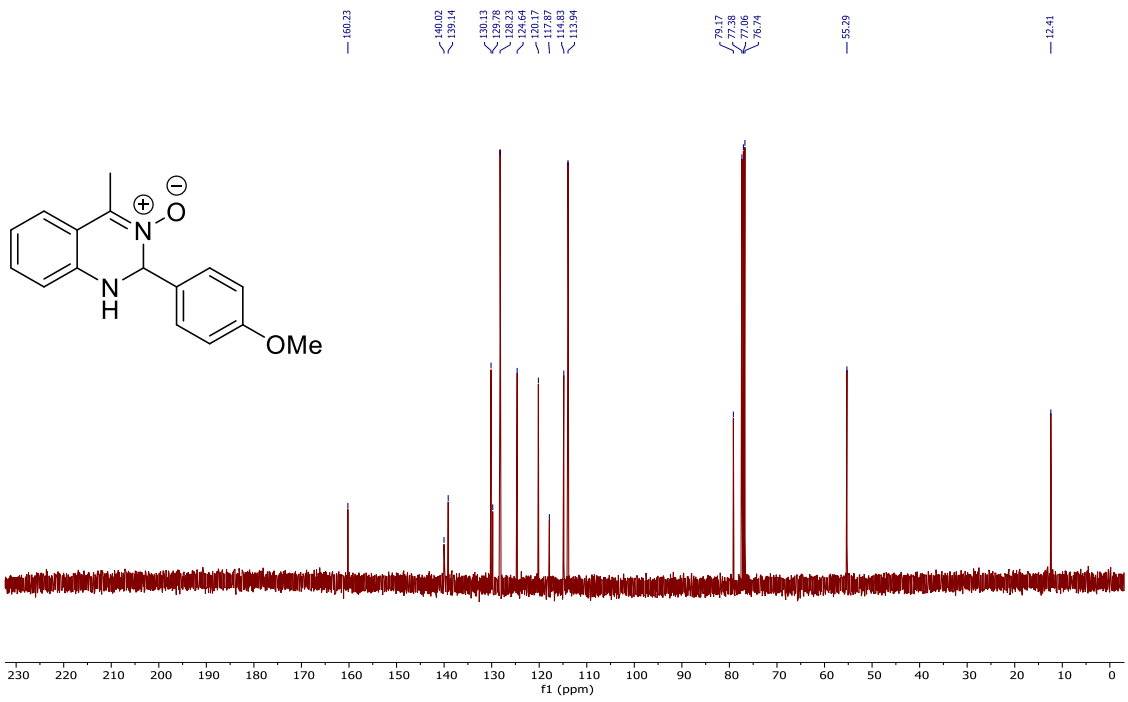
APPX 2.31 ^{1}H NMR (400 MHz, Chloroform-*d*) of compound **2k**



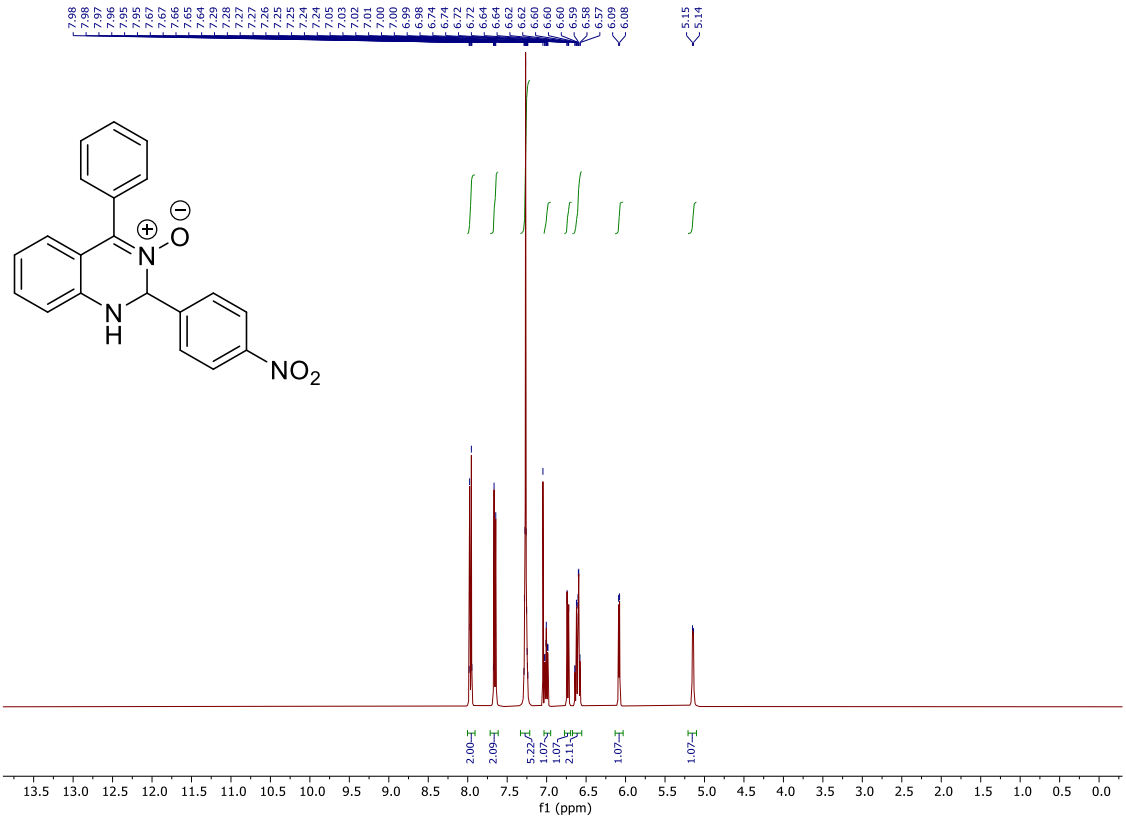
APPX 2.32 ^{13}C NMR (101 MHz, $CDCl_3$) of compound **2k**



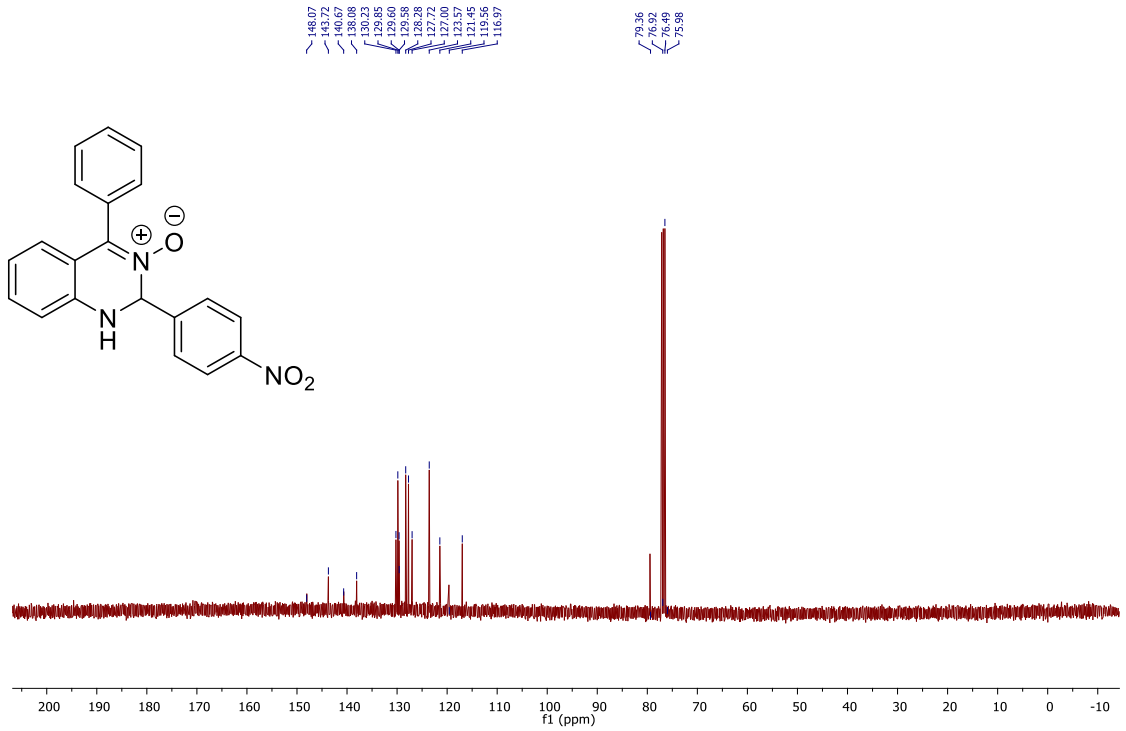
APPX 2.33 ^{1}H NMR (400 MHz, Chloroform-*d*) of compound **2l**



APPX 2.34 ^{13}C NMR (101 MHz, $CDCl_3$) of compound **2l**

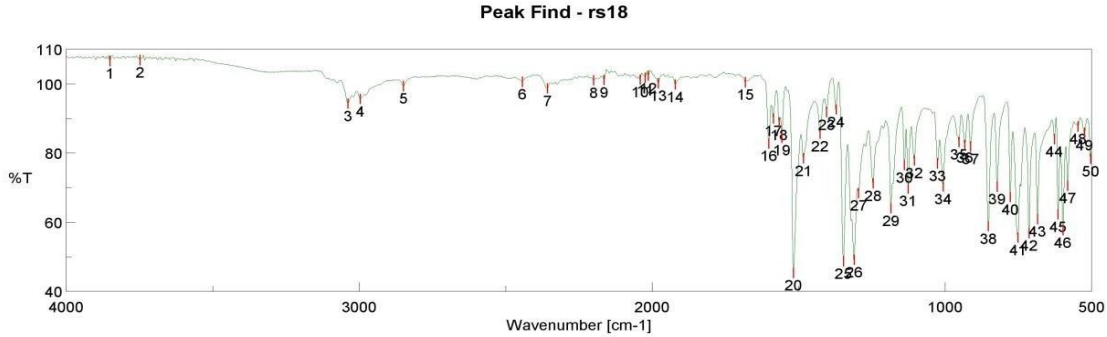


APPX 2.35 ^{1}H NMR (400 MHz, Chloroform-*d*) of compound **2m**



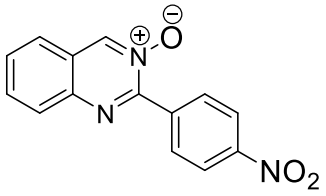
APPX 2.36 ^{13}C NMR (101 MHz, $CDCl_3$) of compound **2m**

APPX 3 IR and NMR Spectra of compound **3**

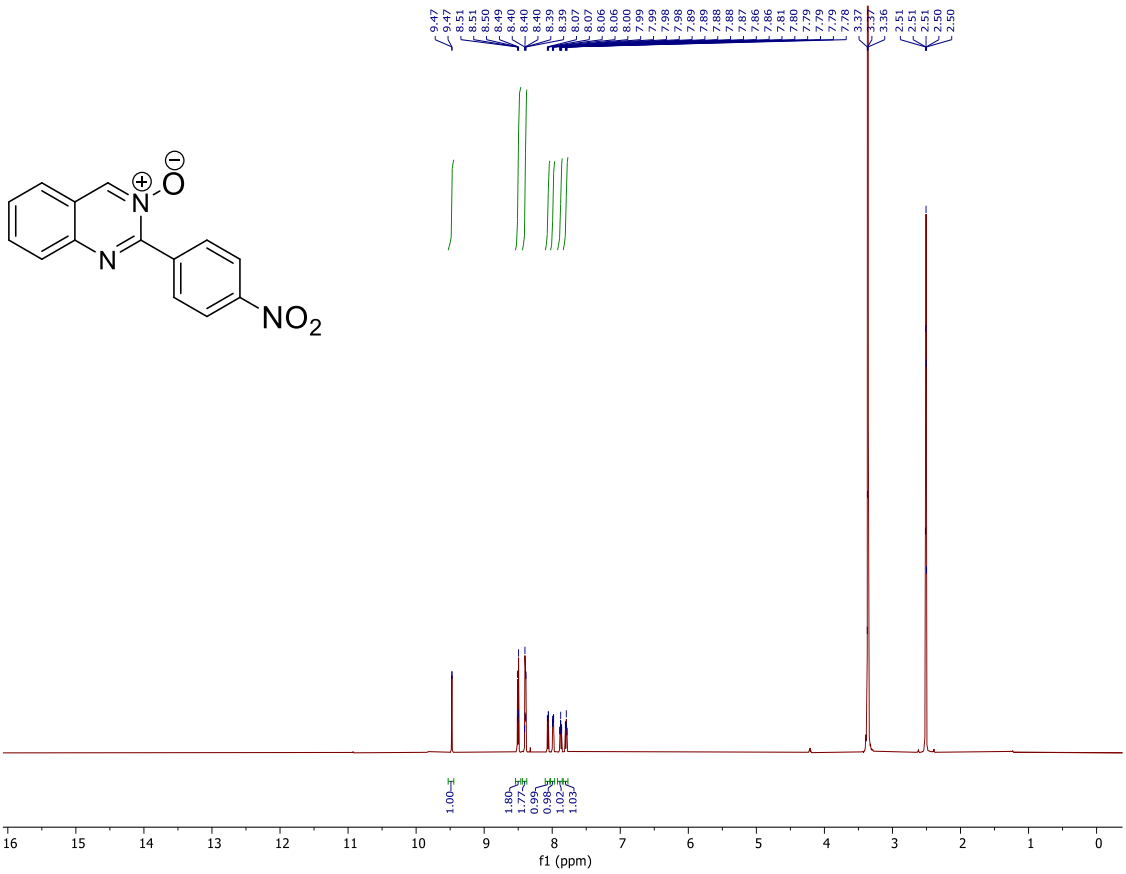


[Result of Peak Picking]

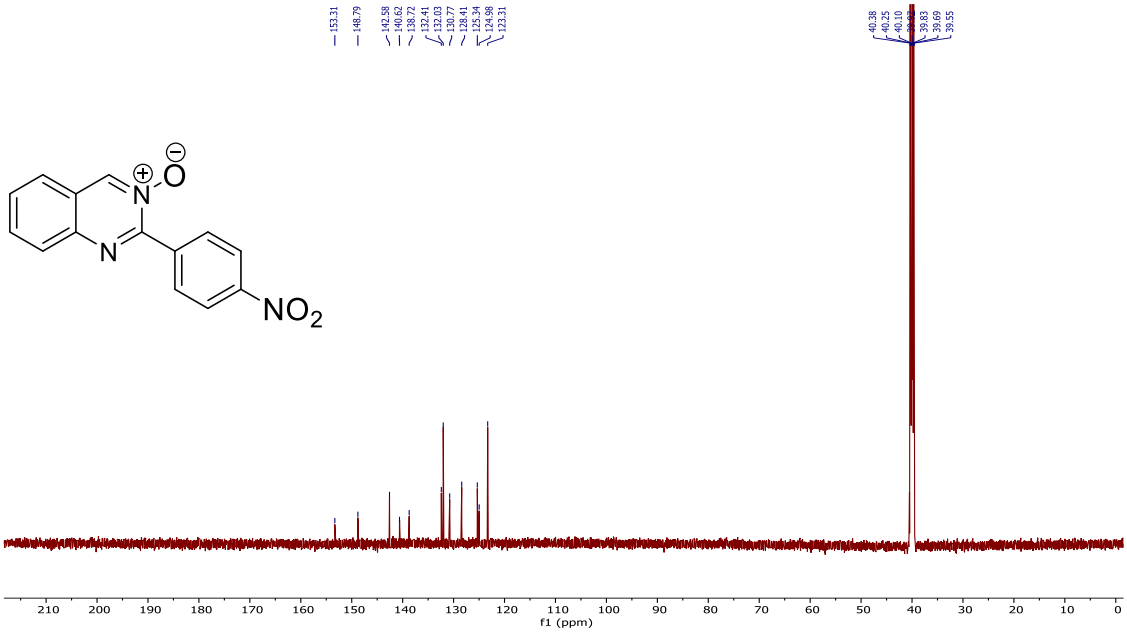
No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity
1	3851.15	1.07E+002	2	3747.98	1.07E+002	3	3038.3	9.44E+001
4	2995.87	9.57E+001	5	2848.35	9.94E+001	6	2443.37	1.01E+002
7	2357.55	9.87E+001	8	2199.42	1.01E+002	9	2163.74	1.01E+002
10	2041.28	1.01E+002	11	2022.96	1.02E+002	12	2013.32	1.02E+002
13	1978.61	1.00E+002	14	1920.75	9.98E+001	15	1681.62	1.01E+002
16	1601.59	8.28E+001	17	1586.16	9.00E+001	18	1566.88	8.88E+001
19	1557.24	8.44E+001	20	1517.7	4.54E+001	21	1482.99	7.85E+001
22	1427.07	8.56E+001	23	1403.92	9.18E+001	24	1372.1	9.26E+001
25	1347.03	4.88E+001	26	1310.39	4.92E+001	27	1294.97	6.85E+001
28	1245.79	7.12E+001	29	1185.04	6.41E+001	30	1138.76	7.66E+001
31	1126.22	6.98E+001	32	1105.01	7.79E+001	33	1025.94	7.70E+001
34	1006.66	7.03E+001	35	952.663	8.32E+001	36	932.414	8.23E+001
37	913.129	8.19E+001	38	852.382	5.89E+001	39	822.491	7.03E+001
40	777.172	6.73E+001	41	751.138	5.56E+001	42	713.533	5.69E+001
43	684.606	6.09E+001	44	626.752	8.40E+001	45	614.217	6.23E+001
46	597.825	5.77E+001	47	581.433	7.06E+001	48	545.756	8.77E+001
49	524.543	8.58E+001	50	503.33	7.84E+001			



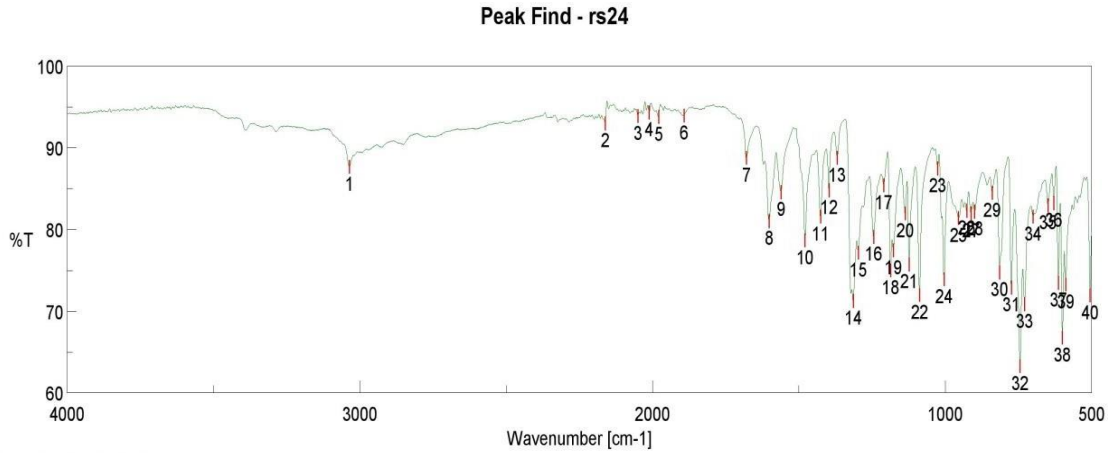
APPX 3.1 IR spectra of compound **3a**



APPX 3.2 ^{1}H NMR (600 MHz, DMSO-d_6) of compound **3a**

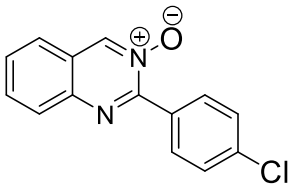


APPX 3.3 ^{13}C NMR (151 MHz, DMSO) of compound **3a**

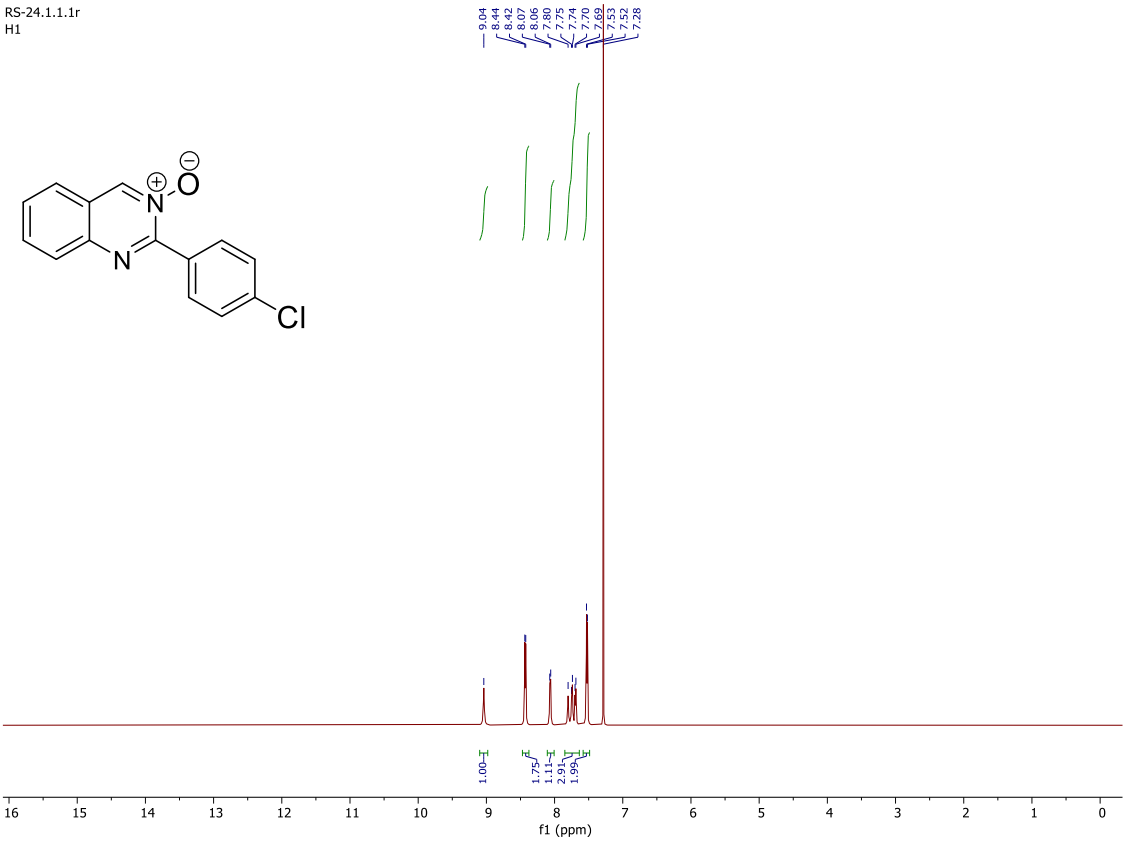


[Result of Peak Picking]

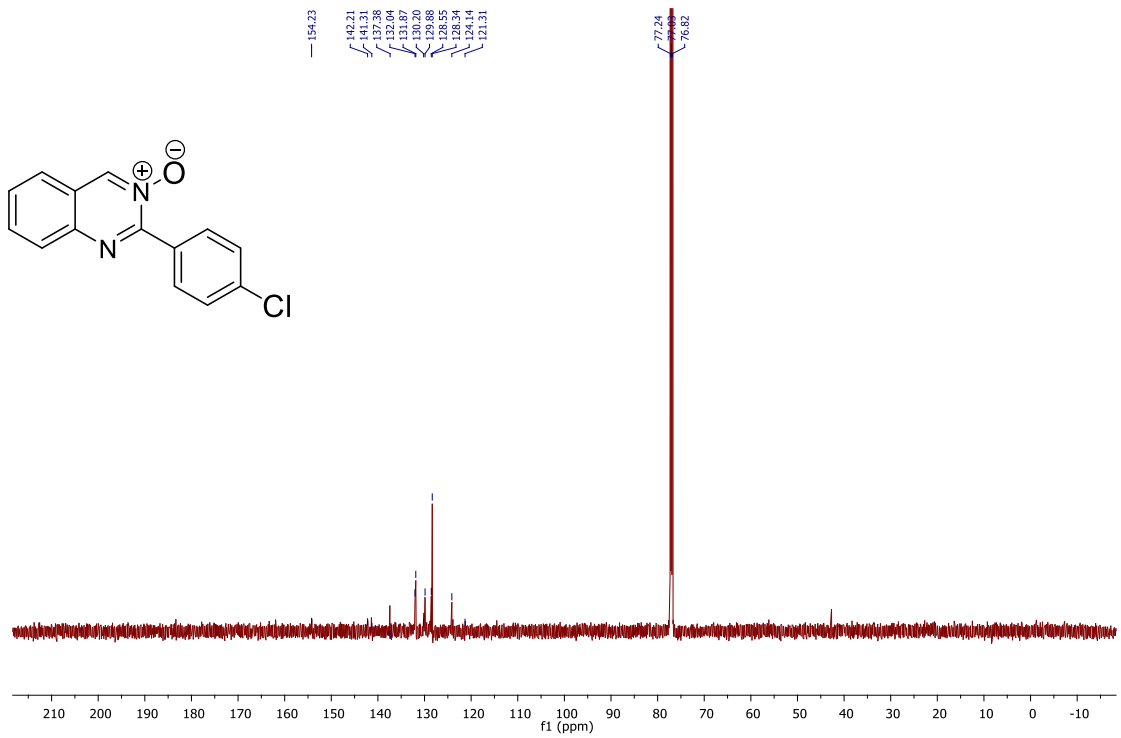
No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity
1	3035.41	8.77E+001	2	2161.81	9.30E+001	3	2049.96	9.39E+001
4	2011.39	9.43E+001	5	1979.57	9.38E+001	6	1892.79	9.40E+001
7	1679.69	8.88E+001	8	1601.59	8.10E+001	9	1561.09	8.46E+001
10	1479.13	7.87E+001	11	1426.1	8.16E+001	12	1397.17	8.48E+001
13	1369.21	8.88E+001	14	1314.25	7.13E+001	15	1296.89	7.72E+001
16	1244.83	7.91E+001	17	1210.11	8.54E+001	18	1186.97	7.50E+001
19	1177.33	7.75E+001	20	1136.83	8.20E+001	21	1123.33	7.57E+001
22	1087.66	7.20E+001	23	1025.94	8.75E+001	24	1003.77	7.39E+001
25	954.591	8.14E+001	26	926.628	8.23E+001	27	912.165	8.20E+001
28	899.63	8.22E+001	29	839.847	8.45E+001	30	814.777	7.48E+001
31	774.279	7.29E+001	32	744.388	6.33E+001	33	728.961	7.09E+001
34	700.034	8.16E+001	35	648.929	8.30E+001	36	628.68	8.32E+001
37	613.252	7.35E+001	38	599.753	6.68E+001	39	588.182	7.33E+001
40	505.258	7.19E+001						



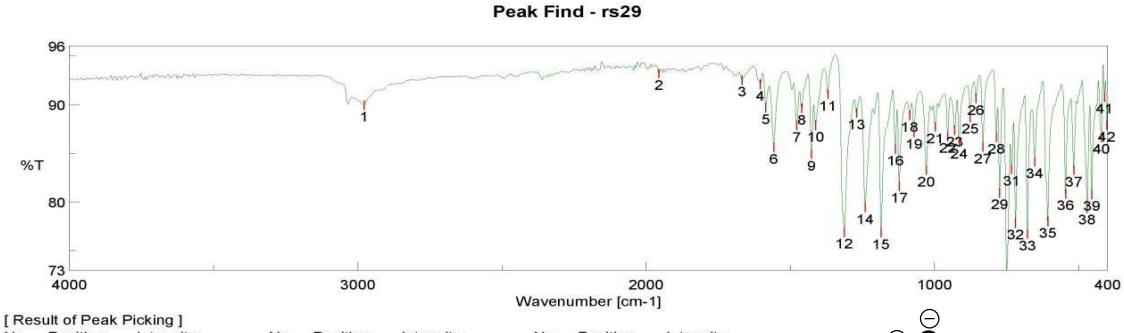
APPX 3.4 IR spectra of compound **3b**



APPX 3.5 ^{1}H NMR (600 MHz, Chloroform-*d*) of compound **3b**

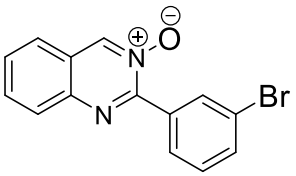


APPX 3.6 ^{13}C NMR (151 MHz, $CDCl_3$) of compound **3b**

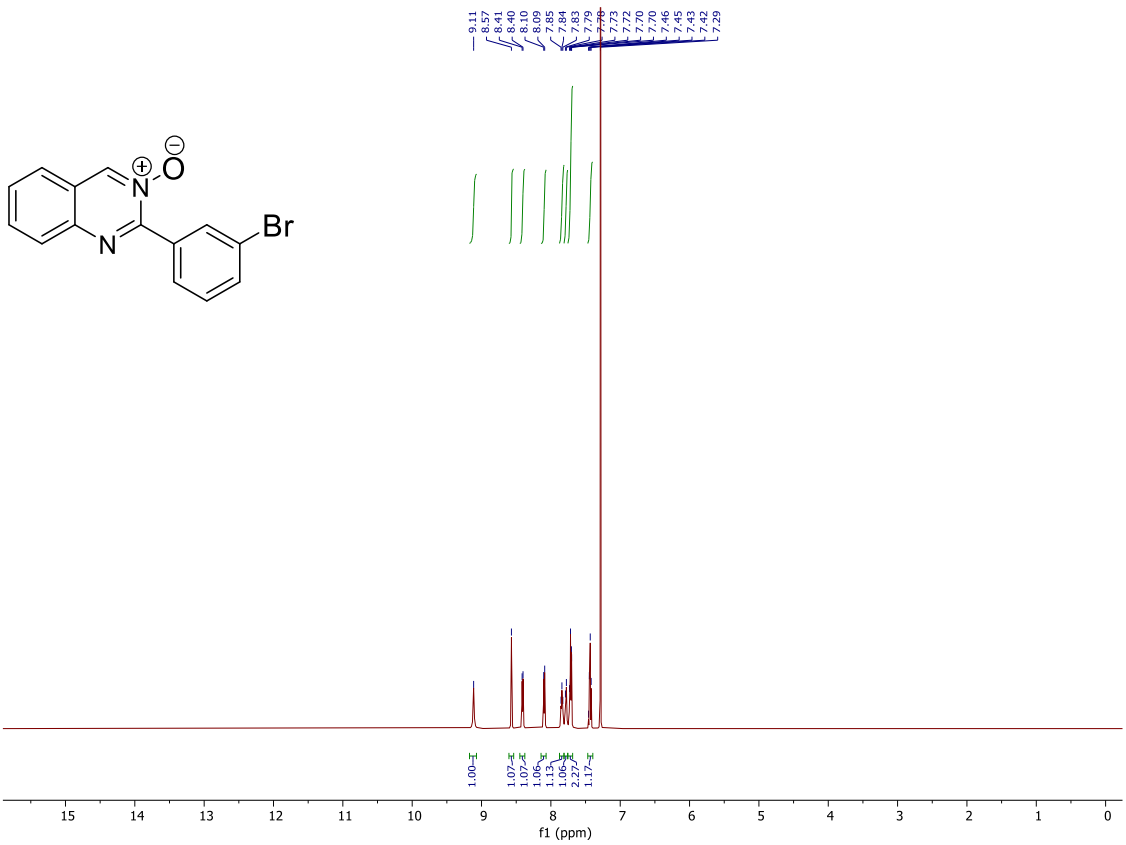


[Result of Peak Picking]

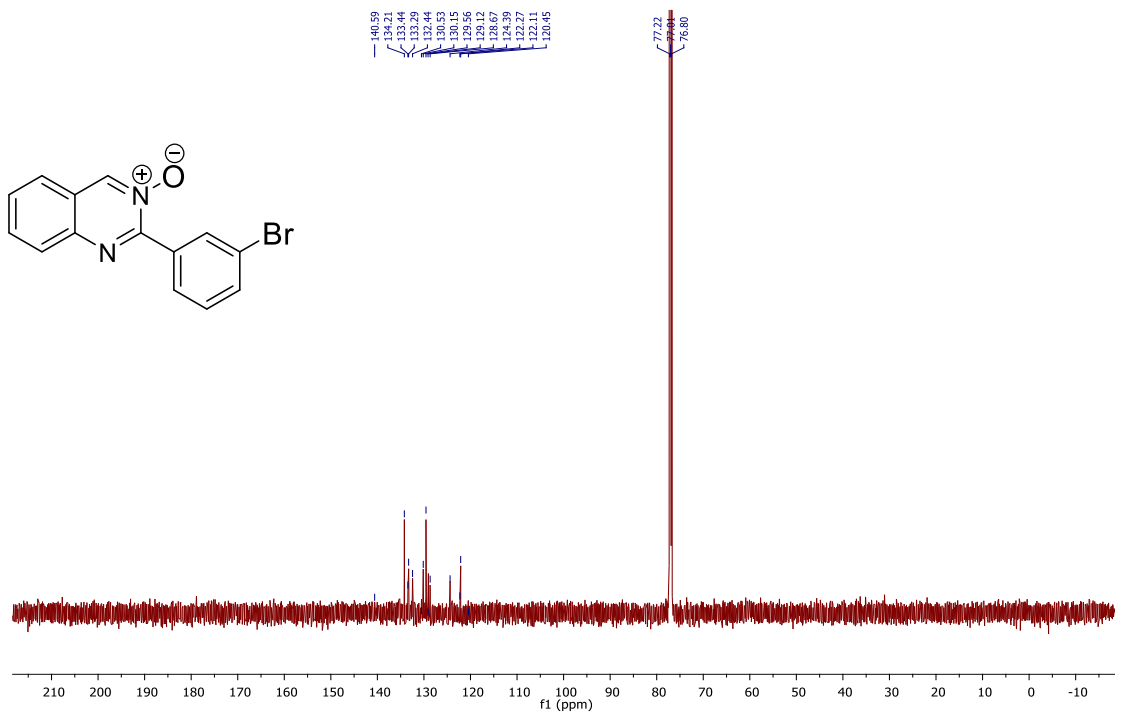
No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity
1	2978.52	8.99E+001	2	1956.43	9.32E+001	3	1668.12	9.25E+001
4	1604.48	9.21E+001	5	1585.2	8.97E+001	6	1558.2	8.56E+001
7	1478.17	8.79E+001	8	1460.81	8.96E+001	9	1427.07	8.49E+001
10	1412.6	8.79E+001	11	1370.18	9.11E+001	12	1313.29	7.69E+001
13	1270.86	8.91E+001	14	1240.97	7.94E+001	15	1186.01	7.69E+001
16	1135.87	8.54E+001	17	1122.37	8.16E+001	18	1086.69	8.89E+001
19	1071.26	8.71E+001	20	1028.84	8.33E+001	21	997.982	8.77E+001
22	954.591	8.67E+001	23	930.485	8.74E+001	24	915.058	8.61E+001
25	876.488	8.87E+001	26	856.239	9.06E+001	27	833.098	8.56E+001
28	785.85	8.66E+001	29	774.279	8.10E+001	30	749.209	7.30E+001
31	732.817	8.34E+001	32	719.318	7.78E+001	33	677.856	7.67E+001
34	652.786	8.41E+001	35	607.467	7.80E+001	36	545.756	8.08E+001
37	517.793	8.33E+001	38	471.51	7.94E+001	39	455.118	8.08E+001
40	421.37	8.66E+001	41	410.763	9.08E+001	42	403.05	8.79E+001



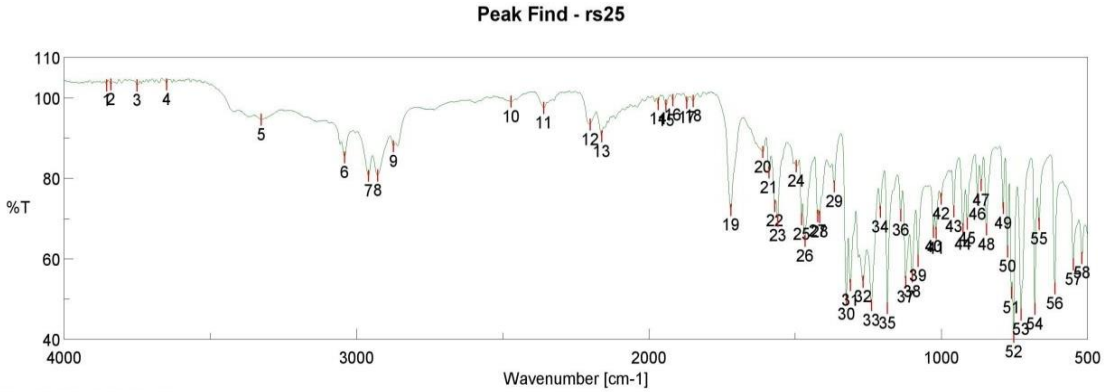
APPX 3.7 IR spectra of compound **3c**



APPX 3.8[1]H NMR (600 MHz, Chloroform-*d*) of compound **3c**

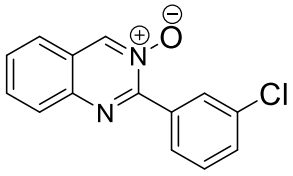


APPX 3.9 [13]C NMR (151 MHz, Chloroform-*d*) of compound **3c**

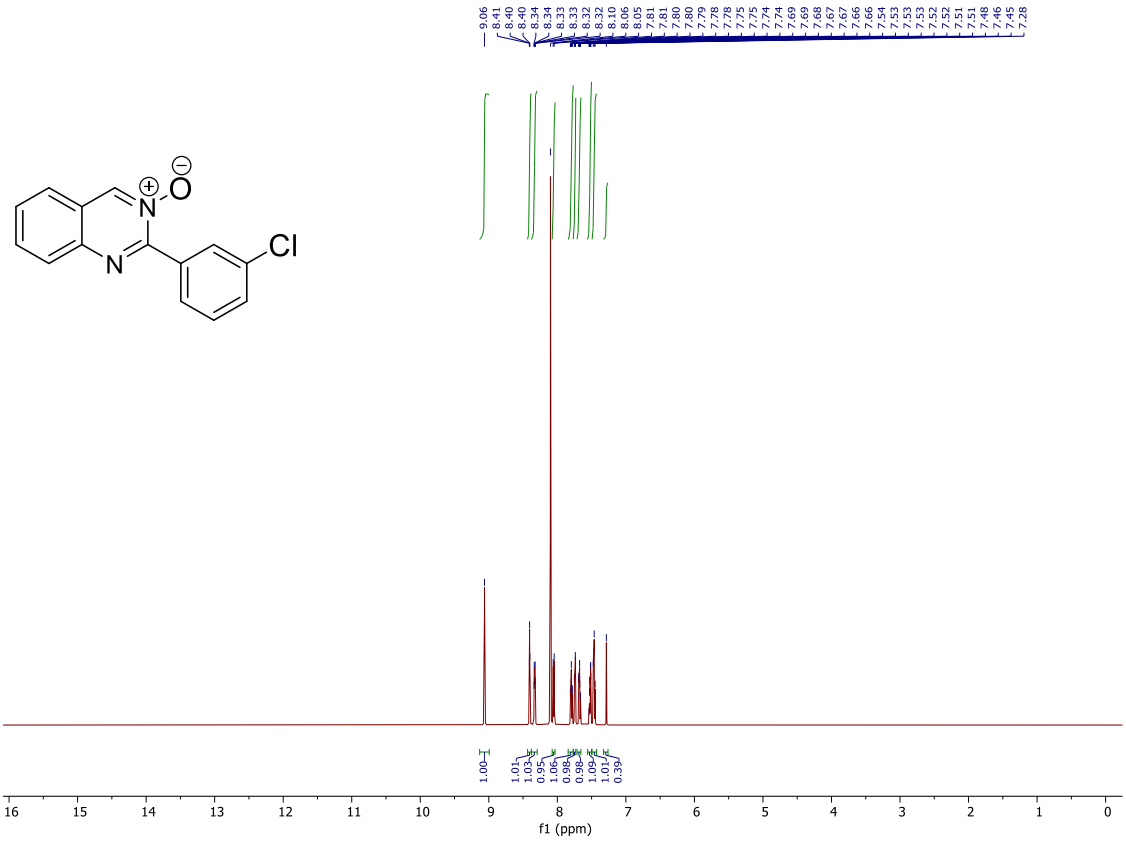


[Result of Peak Picking]

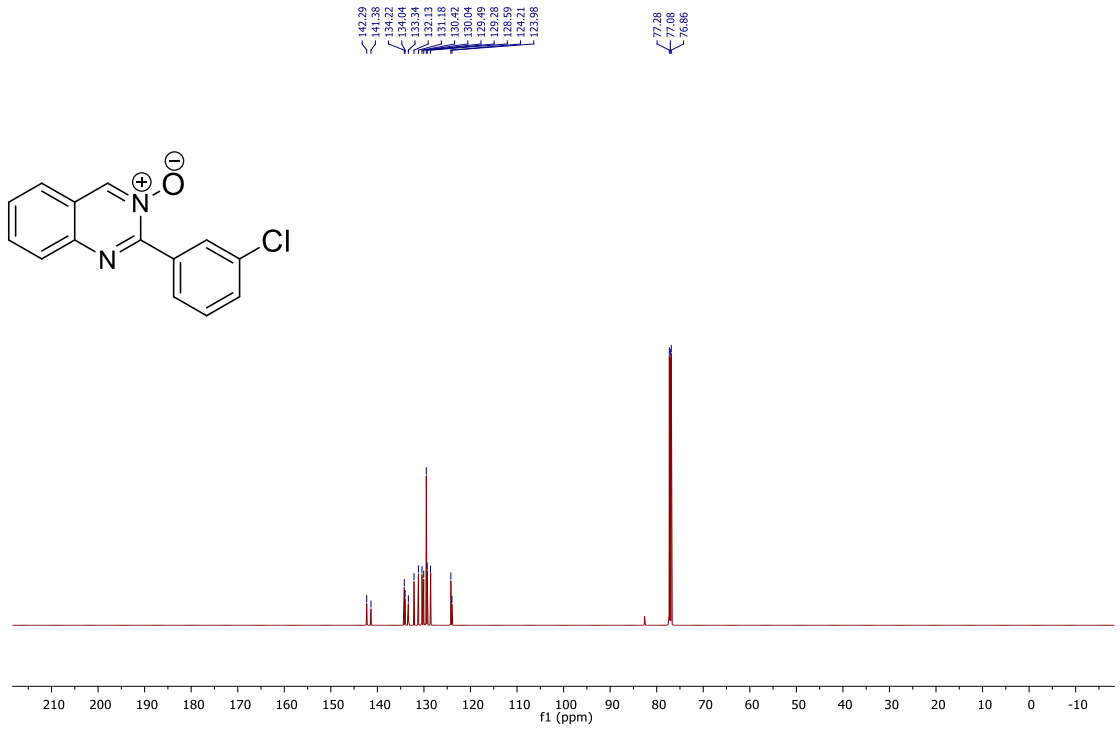
No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity
1	3854.04	1.03E+002	2	3839.58	1.03E+002	3	3750.87	1.03E+002
4	3649.62	1.03E+002	5	3325.64	9.45E+001	6	3040.23	8.52E+001
7	2959.23	8.06E+001	8	2928.38	8.07E+001	9	2873.42	8.79E+001
10	2471.33	9.90E+001	11	2359.48	9.74E+001	12	2201.35	9.33E+001
13	2161.81	9.04E+001	14	1968.96	9.85E+001	15	1941.97	9.81E+001
16	1917.86	9.94E+001	17	1870.61	9.88E+001	18	1848.44	9.92E+001
19	1720.19	7.22E+001	20	1610.27	8.65E+001	21	1590.02	8.14E+001
22	1569.77	7.31E+001	23	1559.17	6.95E+001	24	1496.49	8.30E+001
25	1478.17	6.99E+001	26	1466.6	6.45E+001	27	1423.21	7.06E+001
28	1416.46	7.04E+001	29	1366.32	7.80E+001	30	1324.86	4.99E+001
31	1311.36	5.35E+001	32	1267.97	5.43E+001	33	1239.04	4.85E+001
34	1209.15	7.17E+001	35	1185.04	4.78E+001	36	1138.76	7.08E+001
37	1122.37	5.43E+001	38	1100.19	5.56E+001	39	1079.94	5.95E+001
40	1026.91	6.67E+001	41	1018.23	6.64E+001	42	1000.87	7.49E+001
43	957.484	7.18E+001	44	925.664	6.73E+001	45	911.201	6.88E+001
46	876.488	7.48E+001	47	863.953	7.83E+001	48	845.633	6.73E+001
49	788.743	7.26E+001	50	774.279	6.19E+001	51	760.78	5.16E+001



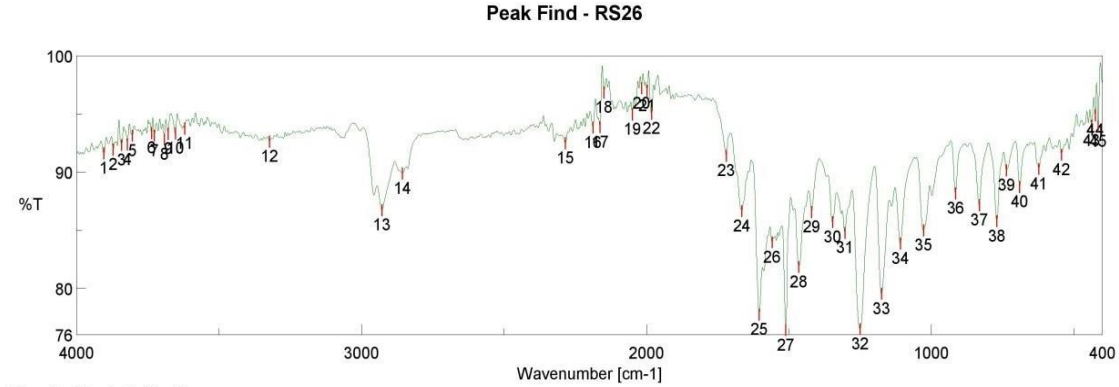
APPX 3.10 IR spectra of compound **3d**



APPX 3.11 ^{1}H NMR (600 MHz, Chloroform-*d*) of compound **3d**

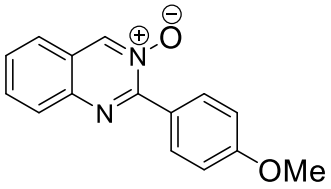


APPX 3.12 ^{13}C NMR (151 MHz, Chloroform-*d*) of compound **3d**

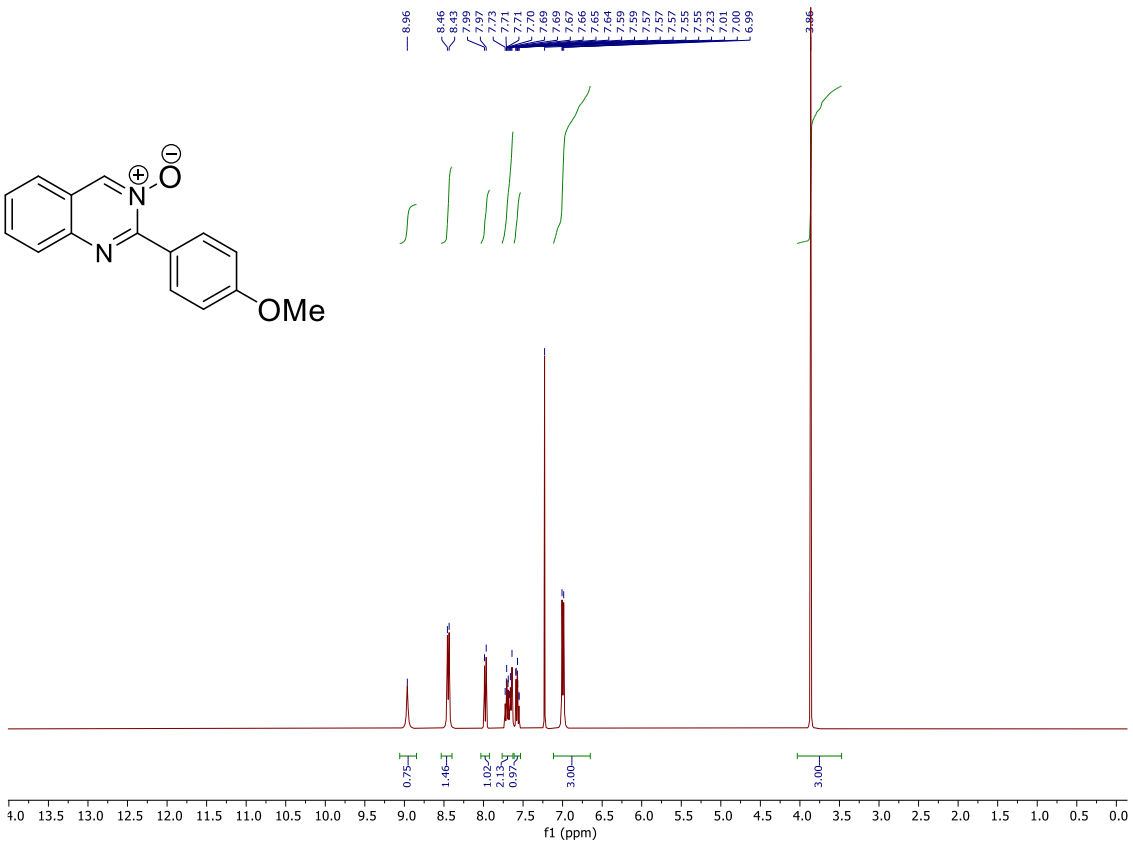


[Result of Peak Picking]

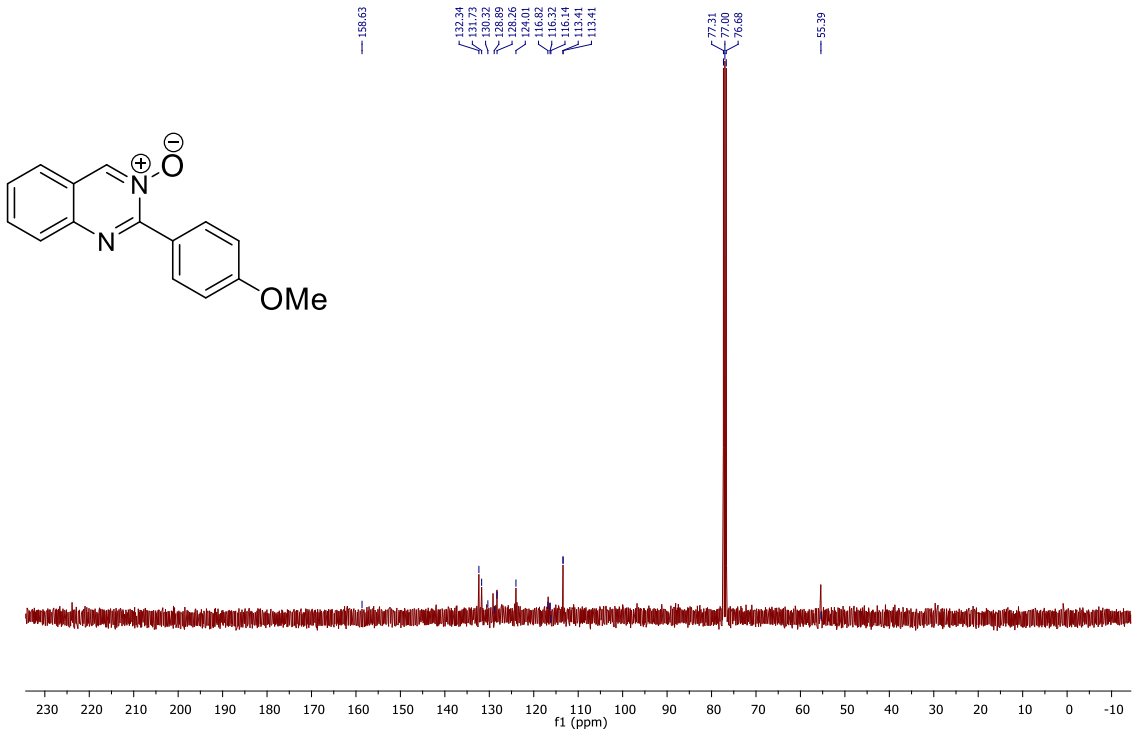
No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity
1	3904.18	9.16E+001	2	3871.4	9.19E+001	3	3841.51	9.23E+001
4	3821.26	9.24E+001	5	3803.9	9.31E+001	6	3737.37	9.34E+001
7	3726.76	9.31E+001	8	3692.05	9.28E+001	9	3678.55	9.33E+001
10	3653.48	9.33E+001	11	3620.7	9.37E+001	12	3322.75	9.26E+001
13	2928.38	8.67E+001	14	2856.06	8.99E+001	15	2284.27	9.25E+001
16	2187.85	9.38E+001	17	2162.78	9.39E+001	18	2149.28	9.68E+001
19	2049	9.50E+001	20	2017.18	9.72E+001	21	1997.89	9.70E+001
22	1982.46	9.50E+001	23	1720.19	9.14E+001	24	1665.23	8.66E+001
25	1604.48	7.77E+001	26	1559.17	8.40E+001	27	1510.95	7.64E+001
28	1465.63	8.18E+001	29	1420.32	8.66E+001	30	1347.03	8.57E+001
31	1303.64	8.48E+001	32	1250.61	7.65E+001	33	1175.4	7.95E+001
34	1108.87	8.39E+001	35	1027.87	8.50E+001	36	915.058	8.82E+001
37	832.133	8.71E+001	38	770.423	8.58E+001	39	736.674	9.01E+001
40	690.391	8.87E+001	41	622.895	9.03E+001	42	543.828	9.15E+001
43	437.762	9.40E+001	44	425.227	9.49E+001	45	414.62	9.39E+001



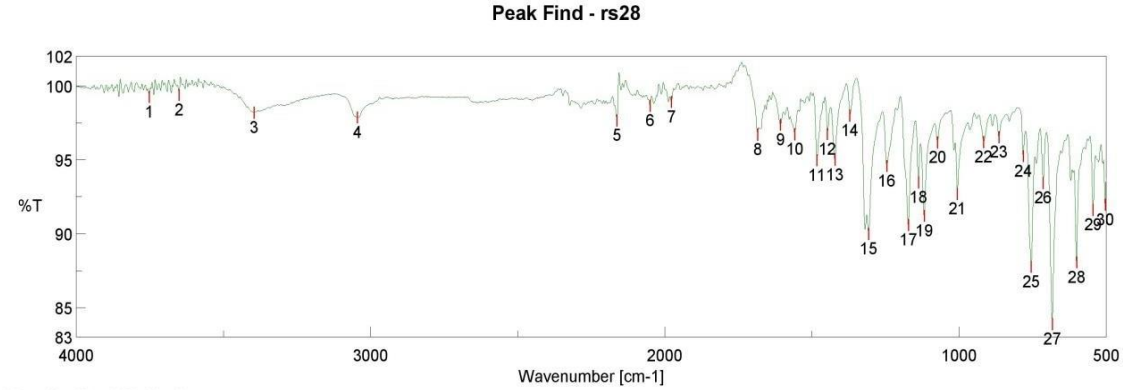
APPX 3.13 IR spectra of compound **3e**



APPX 3.14 ^{1}H NMR (400 MHz, Chloroform-*d*) of compound **3e**

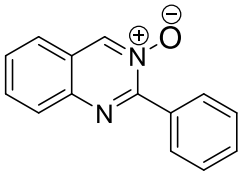


APPX 3.15 ^{13}C NMR (101 MHz, Chloroform-*d*) of compound **3e**

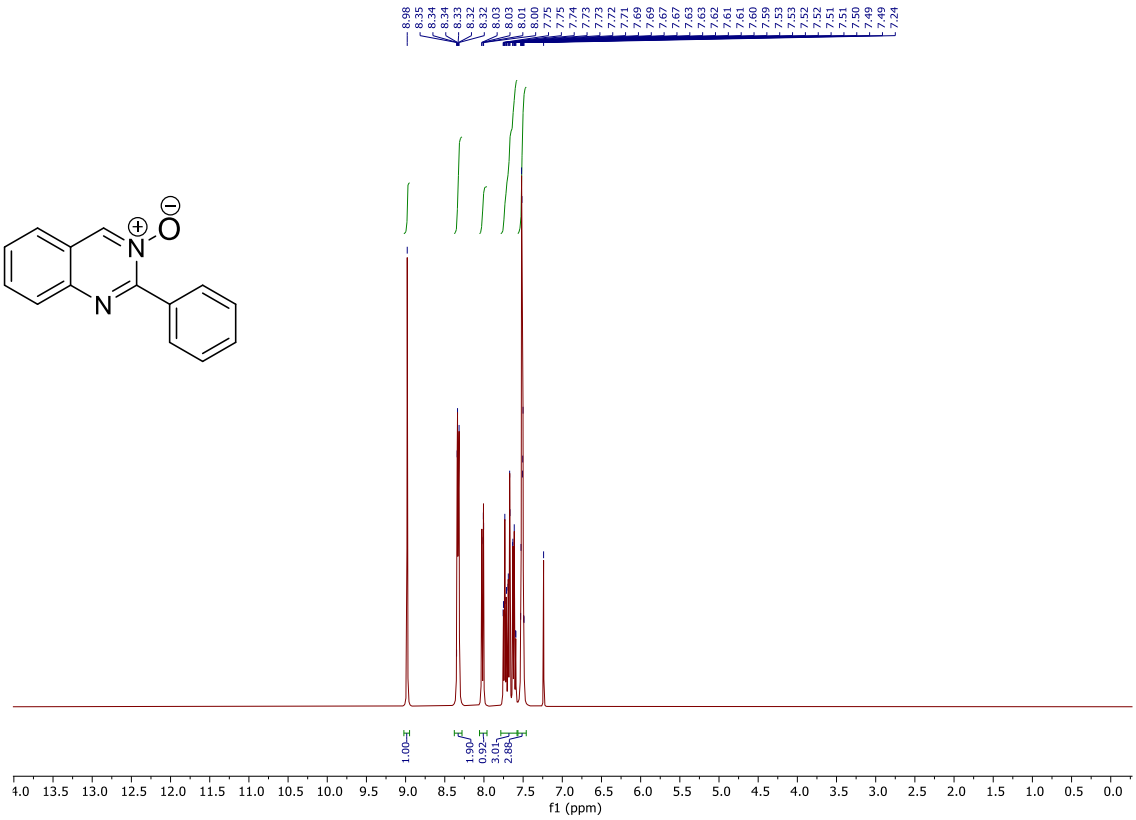


[Result of Peak Picking]

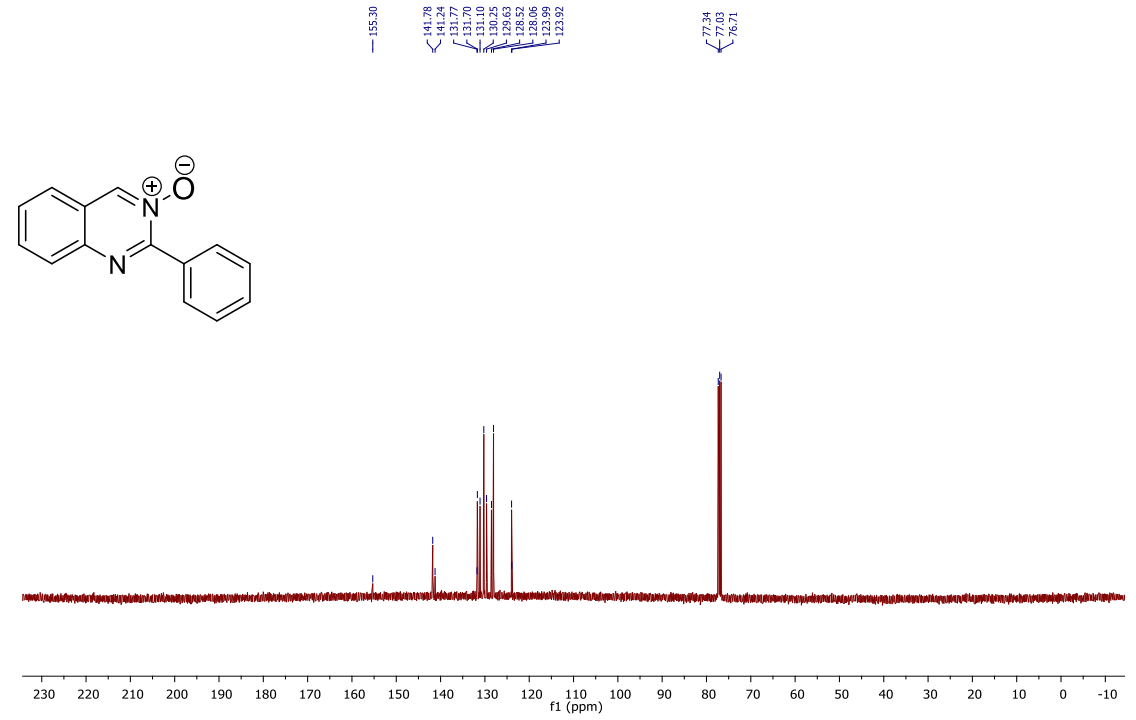
No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity
1	3751.83	9.92E+001	2	3650.59	9.94E+001	3	3396.03	9.82E+001
4	3045.05	9.79E+001	5	2162.78	9.77E+001	6	2049.96	9.86E+001
7	1977.64	9.89E+001	8	1684.52	9.67E+001	9	1607.38	9.74E+001
10	1558.2	9.67E+001	11	1482.99	9.50E+001	12	1447.31	9.67E+001
13	1422.24	9.50E+001	14	1371.14	9.80E+001	15	1307.5	9.00E+001
16	1245.79	9.46E+001	17	1172.51	9.06E+001	18	1137.8	9.35E+001
19	1118.51	9.12E+001	20	1073.19	9.62E+001	21	1005.7	9.27E+001
22	916.986	9.62E+001	23	864.917	9.65E+001	24	781.993	9.52E+001
25	754.995	8.78E+001	26	714.497	9.34E+001	27	683.642	8.39E+001
28	600.717	8.81E+001	29	544.792	9.16E+001	30	503.33	9.20E+001



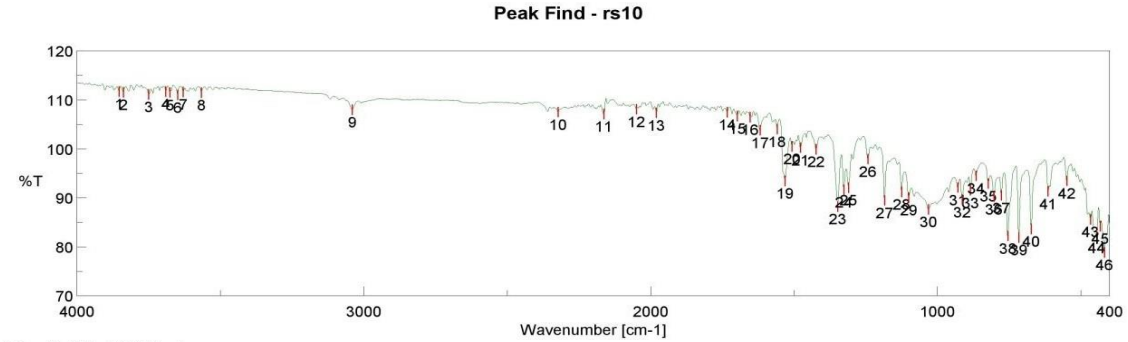
APPX 3.16 IR spectra of compound **3f**



APPX 3.17 ^{1}H NMR (400 MHz, Chloroform-*d*) of compound **3f**

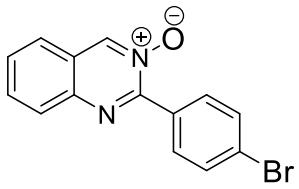


APPX 3.18 ^{13}C NMR (101 MHz, Chloroform-*d*) of compound **3f**

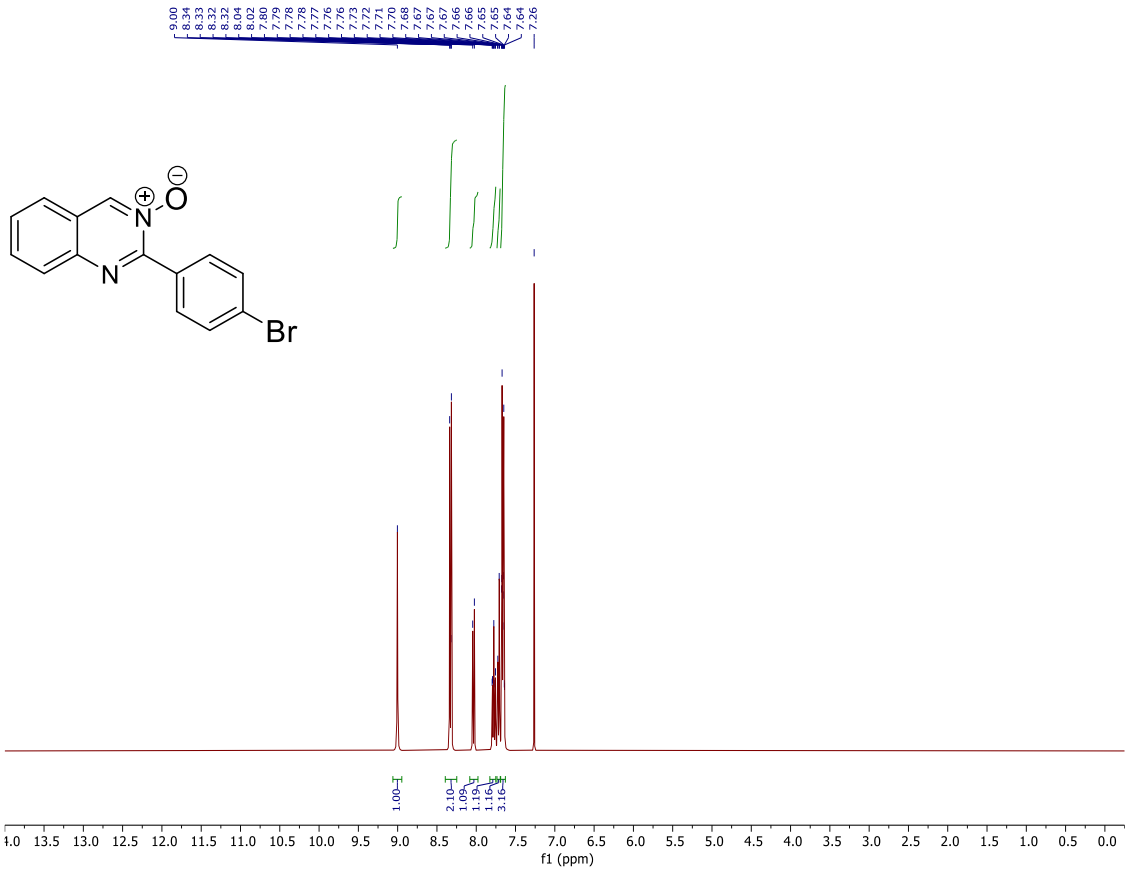


[Result of Peak Picking]

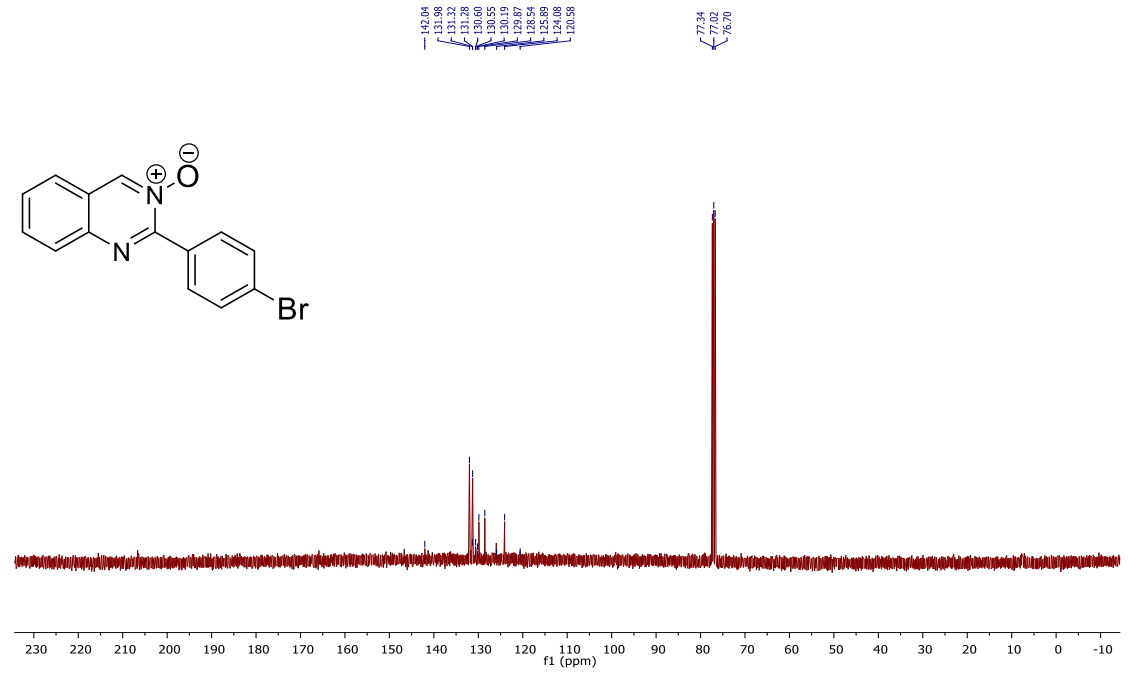
No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity
1	3853.08	1.12E+002	2	3838.61	1.12E+002	3	3749.9	1.11E+002
4	3690.12	1.12E+002	5	3675.66	1.12E+002	6	3648.66	1.11E+002
7	3629.37	1.12E+002	8	3565.74	1.11E+002	9	3041.19	1.08E+002
10	2322.84	1.08E+002	11	2163.74	1.07E+002	12	2049.96	1.08E+002
13	1980.54	1.07E+002	14	1732.73	1.07E+002	15	1698.02	1.07E+002
16	1653.66	1.06E+002	17	1618.95	1.04E+002	18	1559.17	1.04E+002
19	1531.2	9.34E+001	20	1507.1	1.01E+002	21	1478.17	1.00E+002
22	1423.21	9.99E+001	23	1348	8.82E+001	24	1326.79	9.17E+001
25	1310.39	9.21E+001	26	1242.9	9.79E+001	27	1185.04	8.95E+001
28	1125.26	9.12E+001	29	1100.19	9.01E+001	30	1031.73	8.76E+001
31	929.521	9.21E+001	32	914.093	8.96E+001	33	885.166	9.15E+001
34	865.882	9.45E+001	35	823.455	9.29E+001	36	803.206	9.02E+001
37	778.136	9.05E+001	38	754.995	8.22E+001	39	716.425	8.19E+001
40	673.999	8.37E+001	41	615.181	9.13E+001	42	549.613	9.35E+001
43	466.689	8.56E+001	44	445.476	8.24E+001	45	432.941	8.42E+001
46	418.477	7.88E+001						



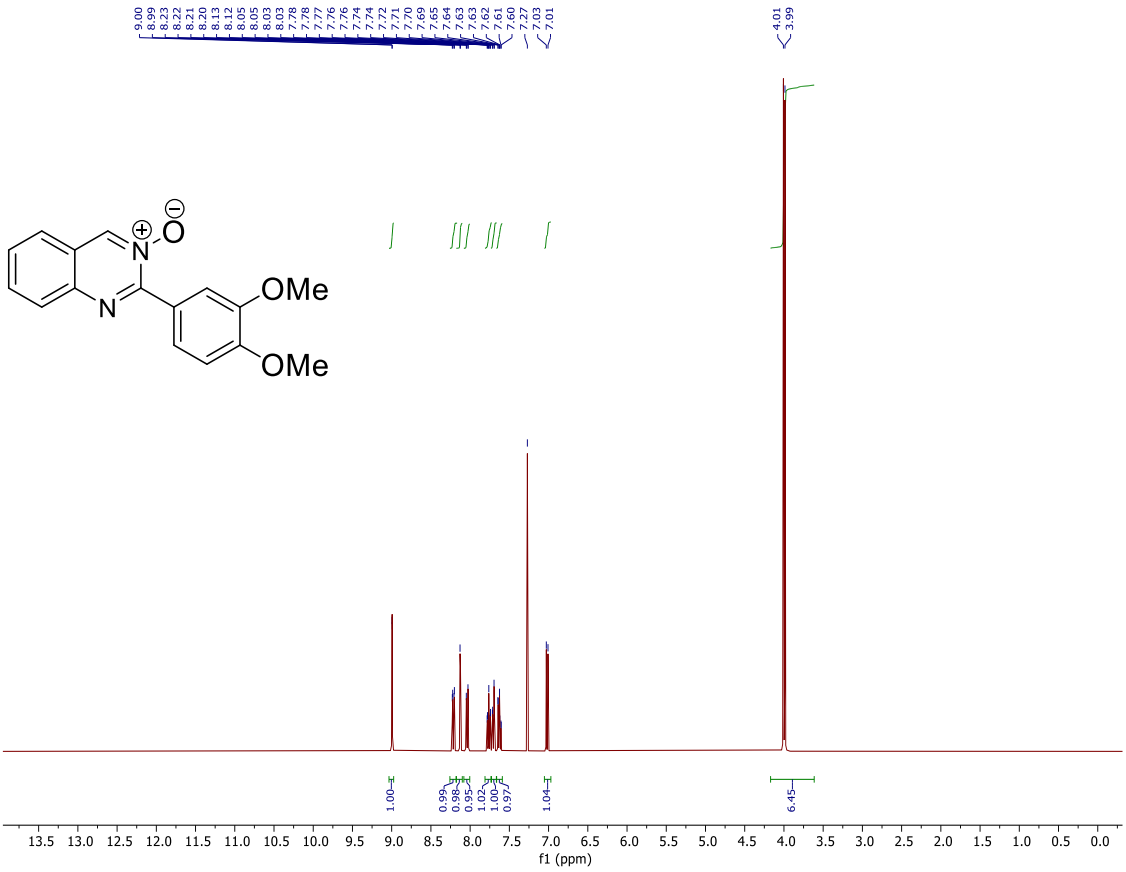
APPX 3.19 IR spectra of compound **3g**



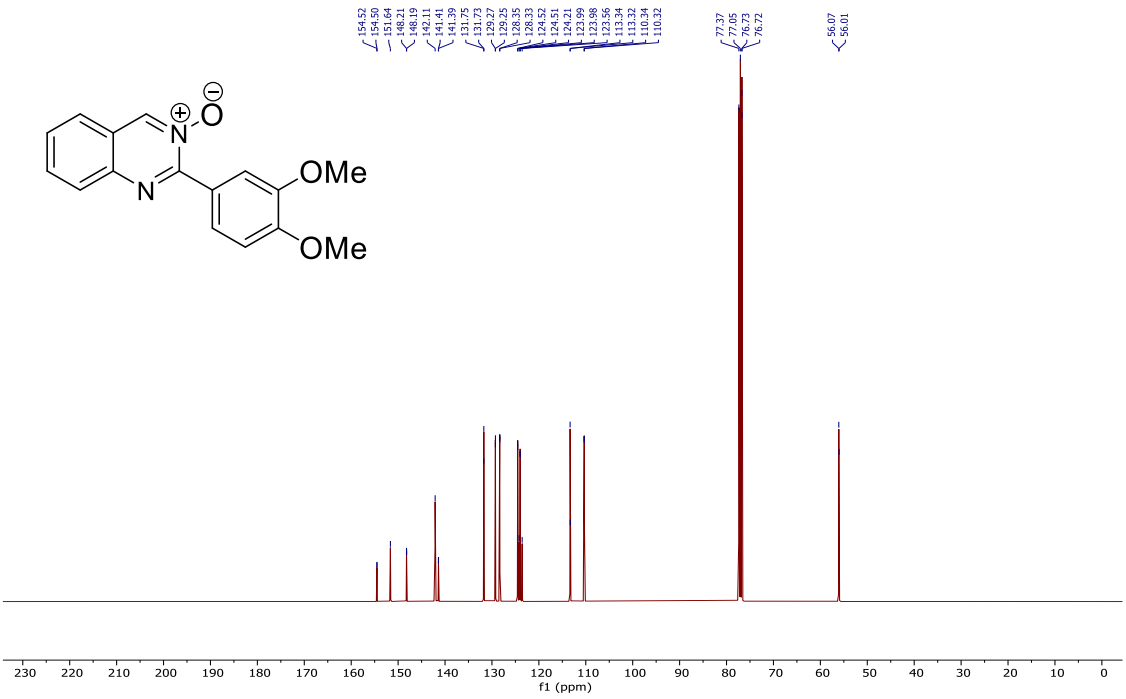
APPX 3.20 ^{1}H NMR (400 MHz, Chloroform-*d*) of compound **3g**



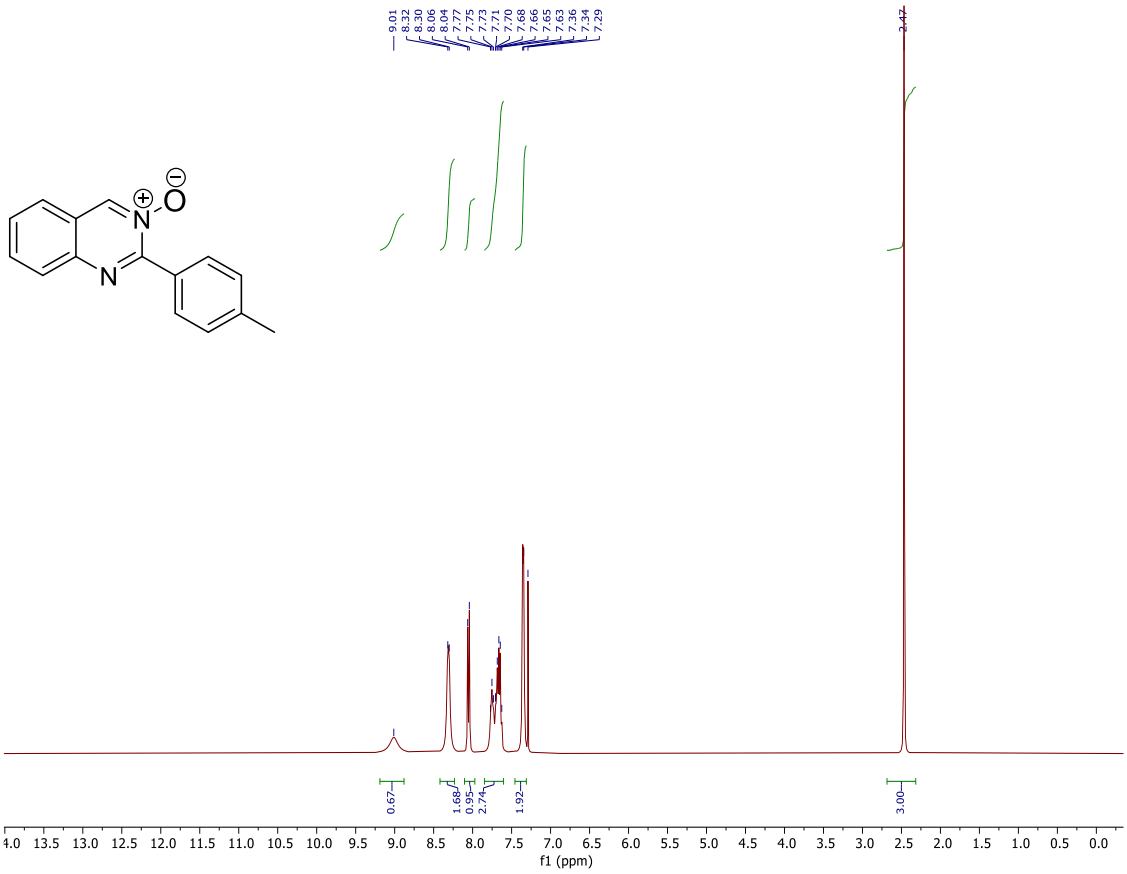
APPX 3.21 ^{13}C NMR (101 MHz, Chloroform-*d*) of compound **3g**



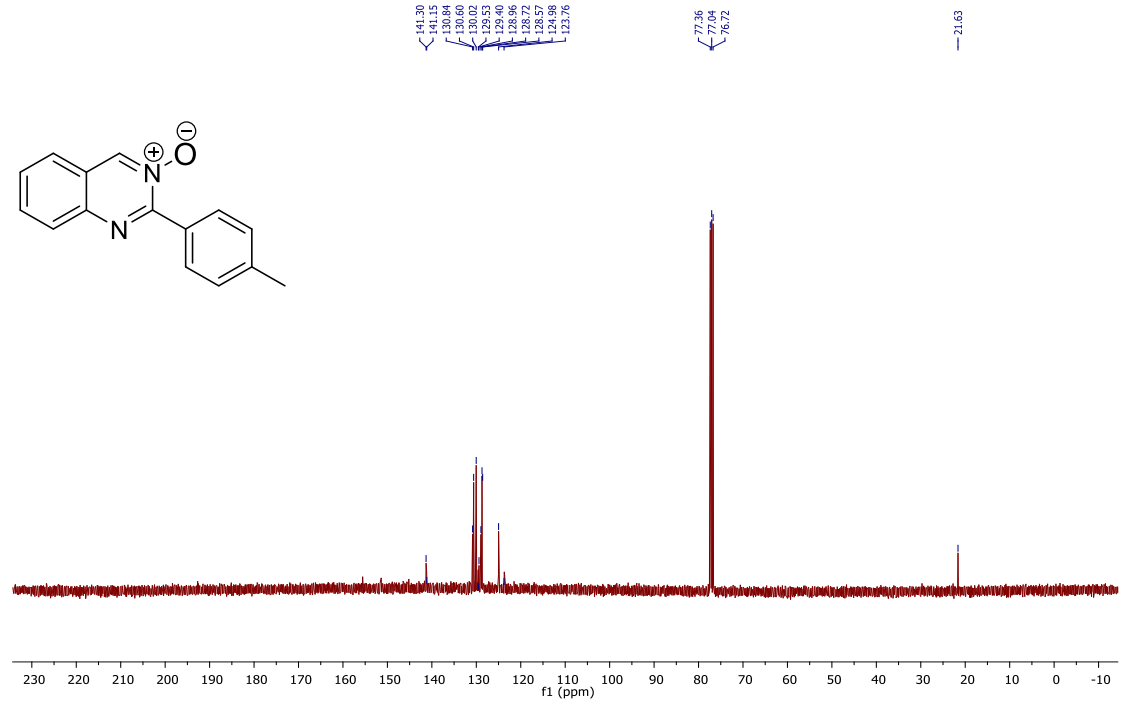
APPX 3.22 ^{1}H NMR (400 MHz, Chloroform-*d*) of compound **3h**



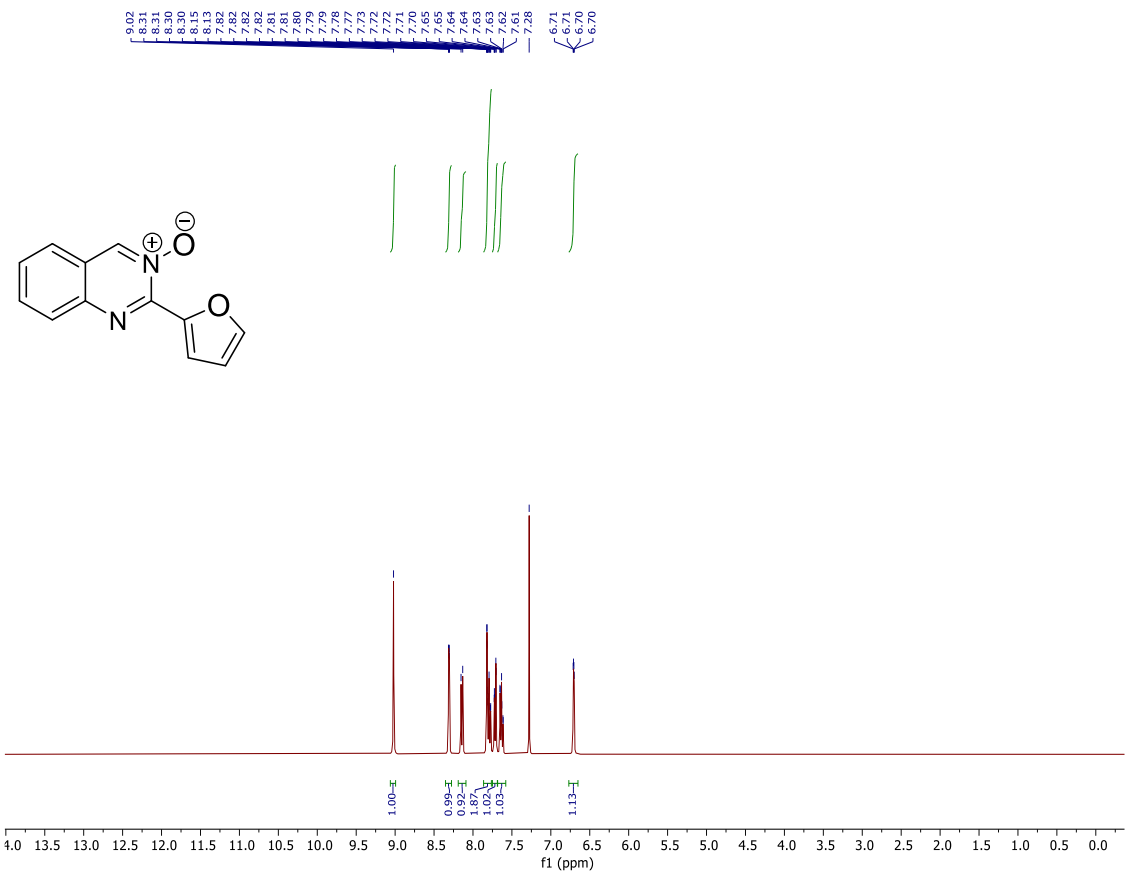
APPX 3.23 ^{13}C NMR (101 MHz, Chloroform-*d*) of compound **3h**



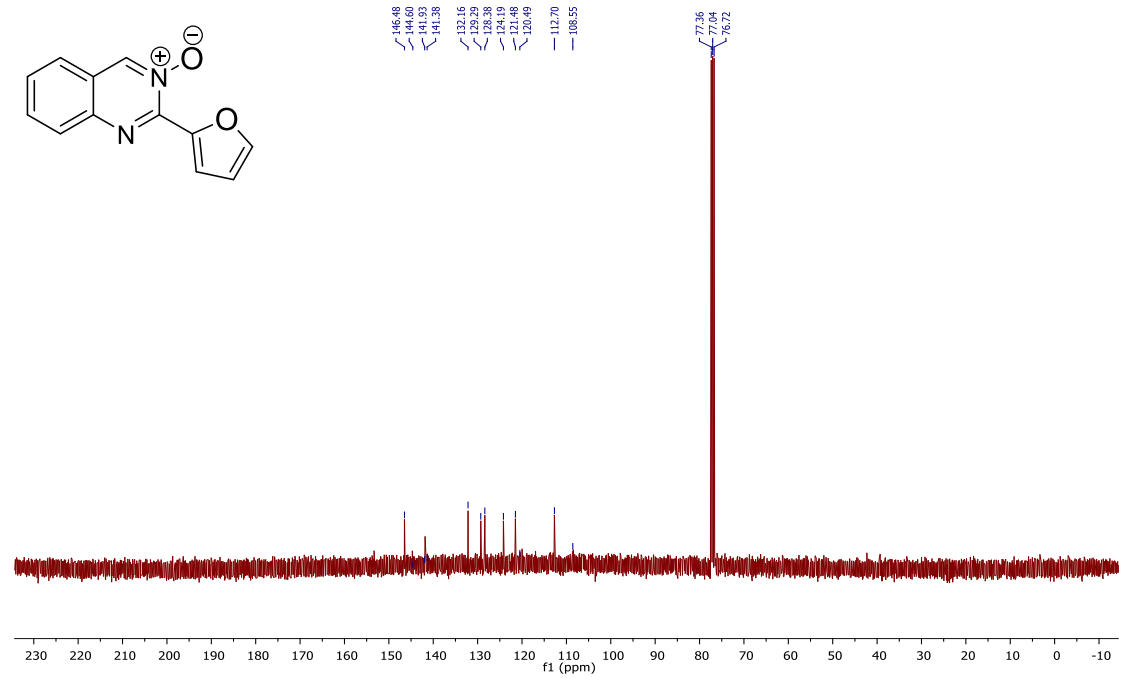
APPX 3.24 ^{1}H NMR (400 MHz, Chloroform-*d*) of compound **3i**



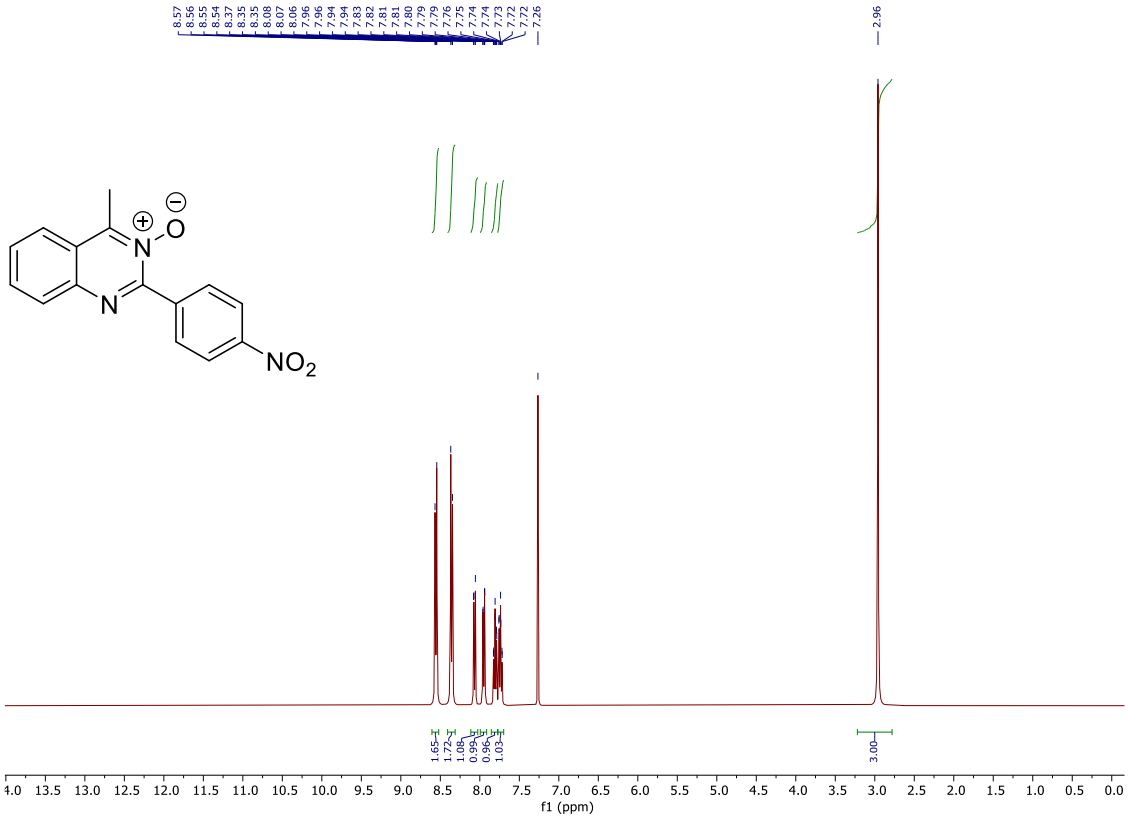
APPX 3.25 ^{13}C NMR (101 MHz, Chloroform-*d*) of compound **3i**



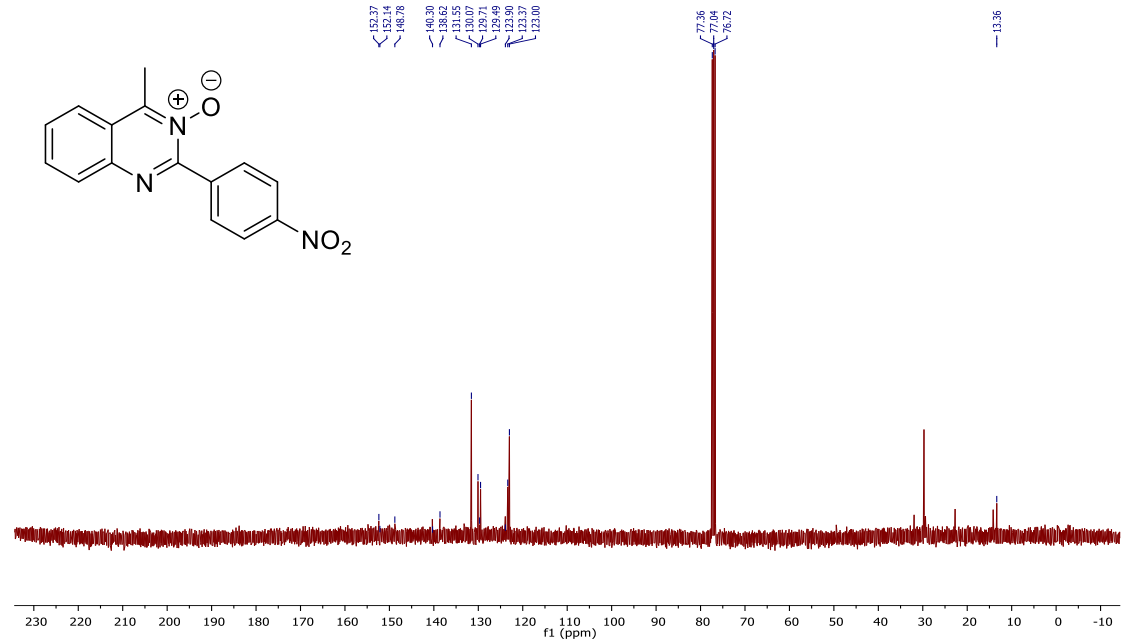
APPX 3.26 ^{1}H NMR (400 MHz, Chloroform-*d*) of compound **3j**



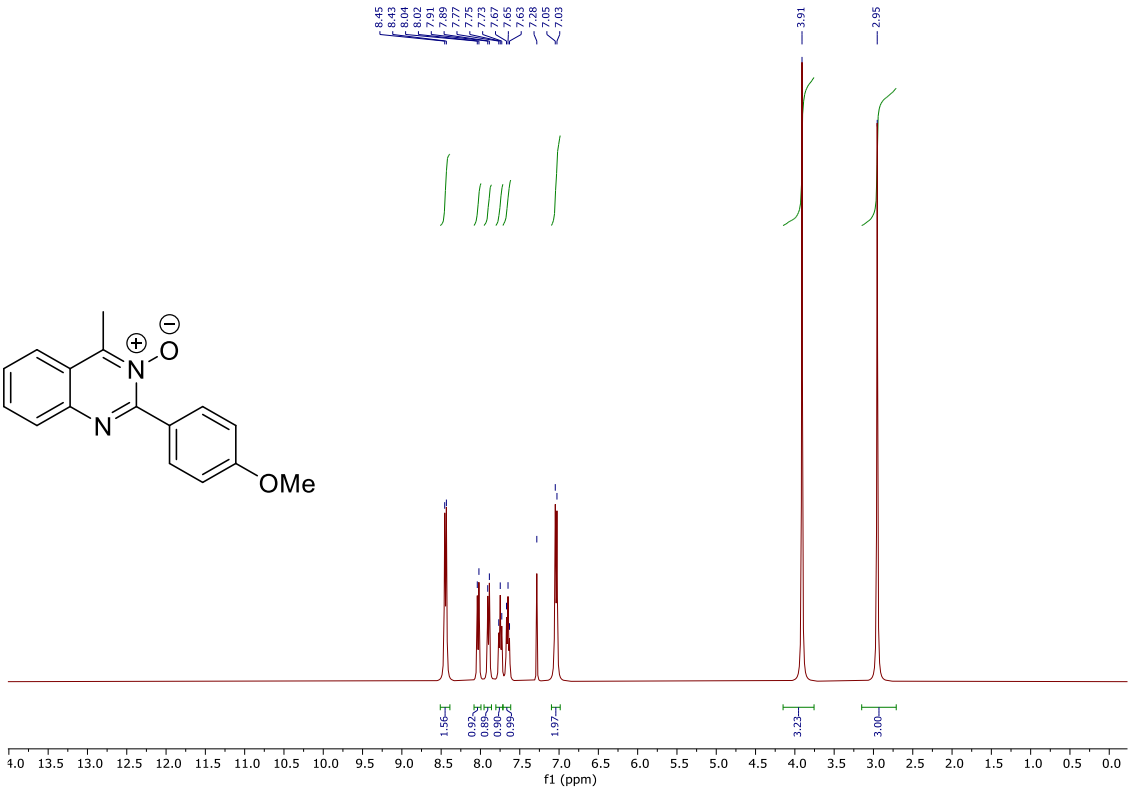
APPX 3.27 ^{13}C NMR (101 MHz, Chloroform-*d*) of compound **3j**



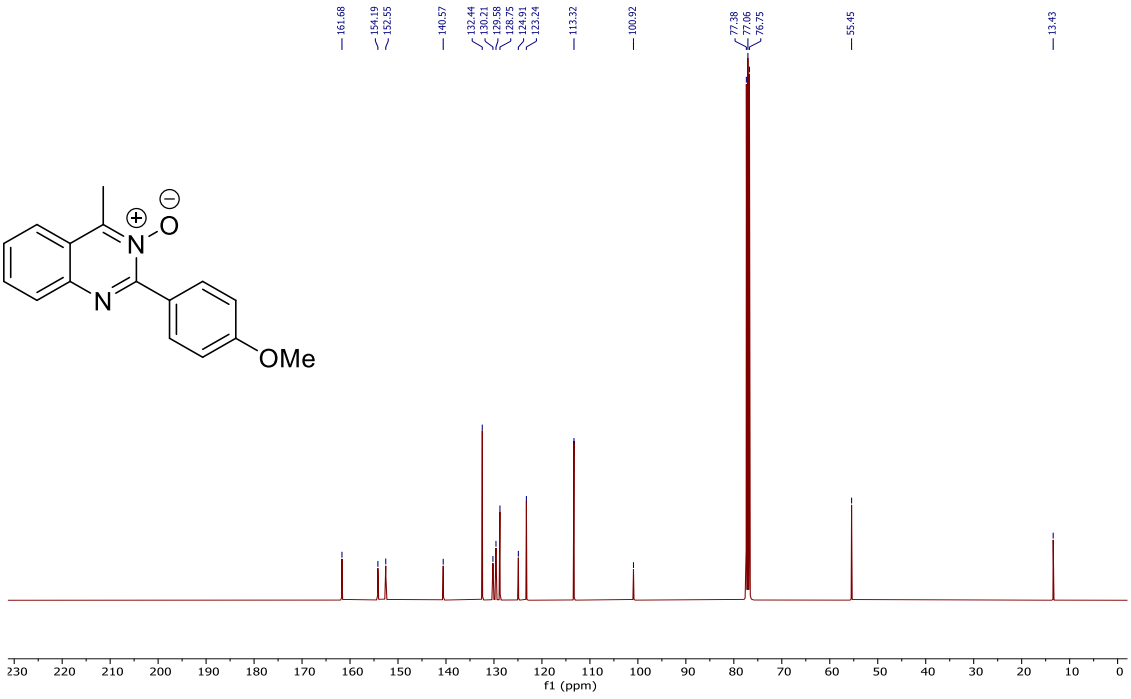
APPX 3.28 ^{1}H NMR (400 MHz, Chloroform-*d*) of compound **3k**



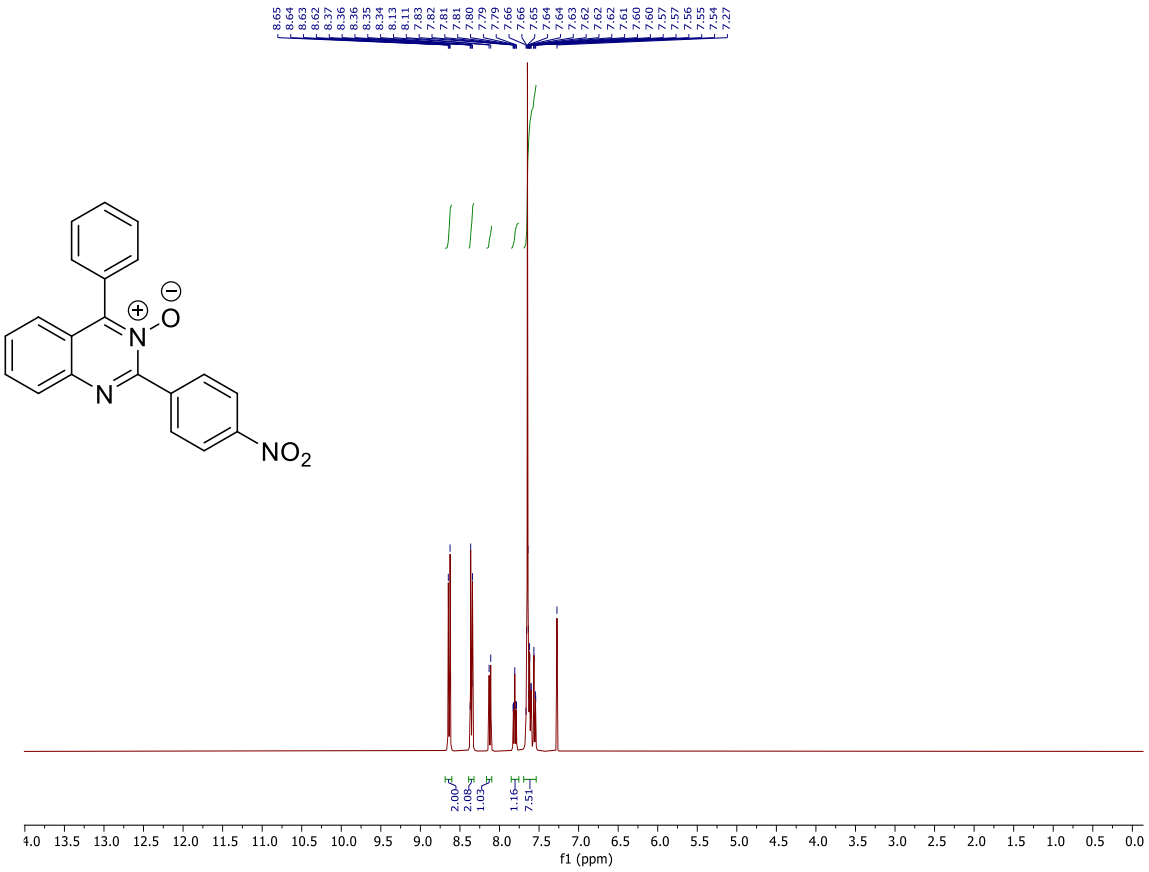
APPX 3.29 ^{13}C NMR (101 MHz, Chloroform-*d*) of compound **3k**



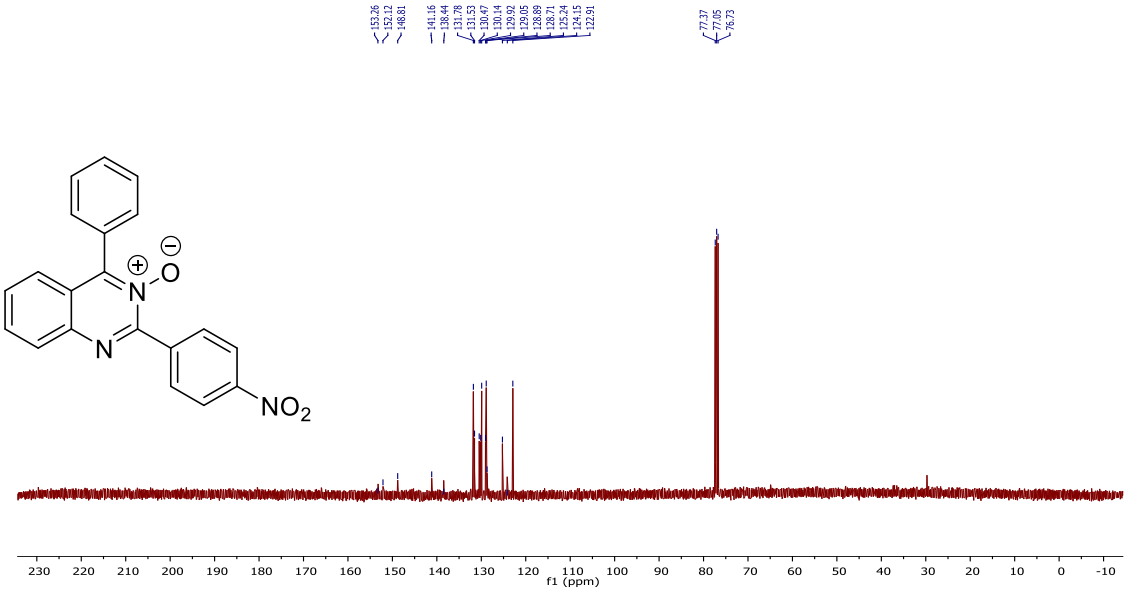
APPX 3.30 [1]H NMR (400 MHz, Chloroform-*d*) of compound **3l**



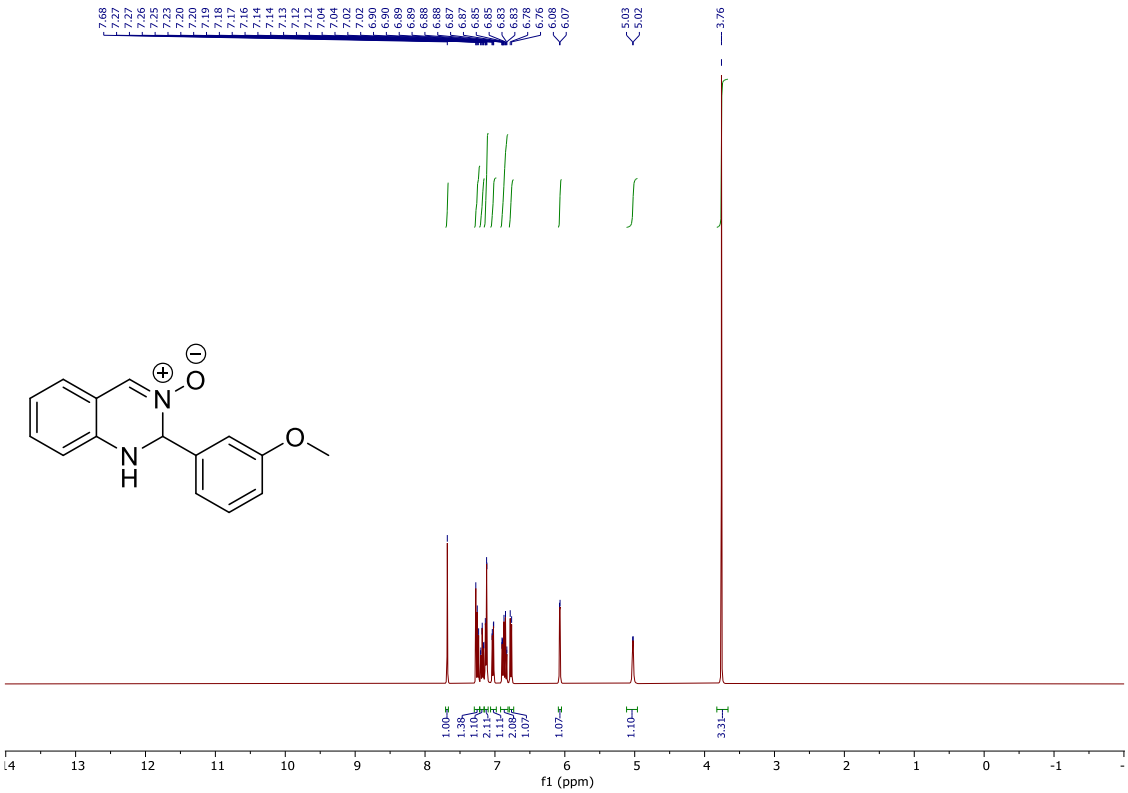
APPX 3.31 [13]C NMR (101 MHz, Chloroform-*d*) of compound **3l**



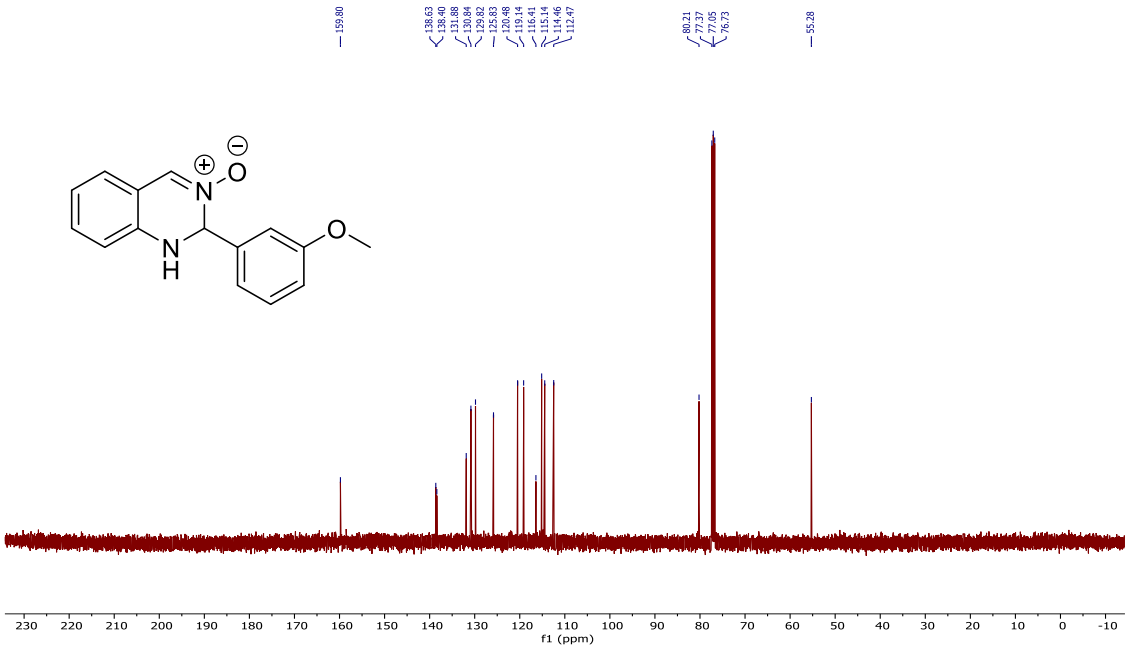
APPX 3.32 ^{1}H NMR (400 MHz, Chloroform-*d*) of compound **3m**



APPX 3.33 ^{13}C NMR (101 MHz, Chloroform-*d*) of compound **3m**

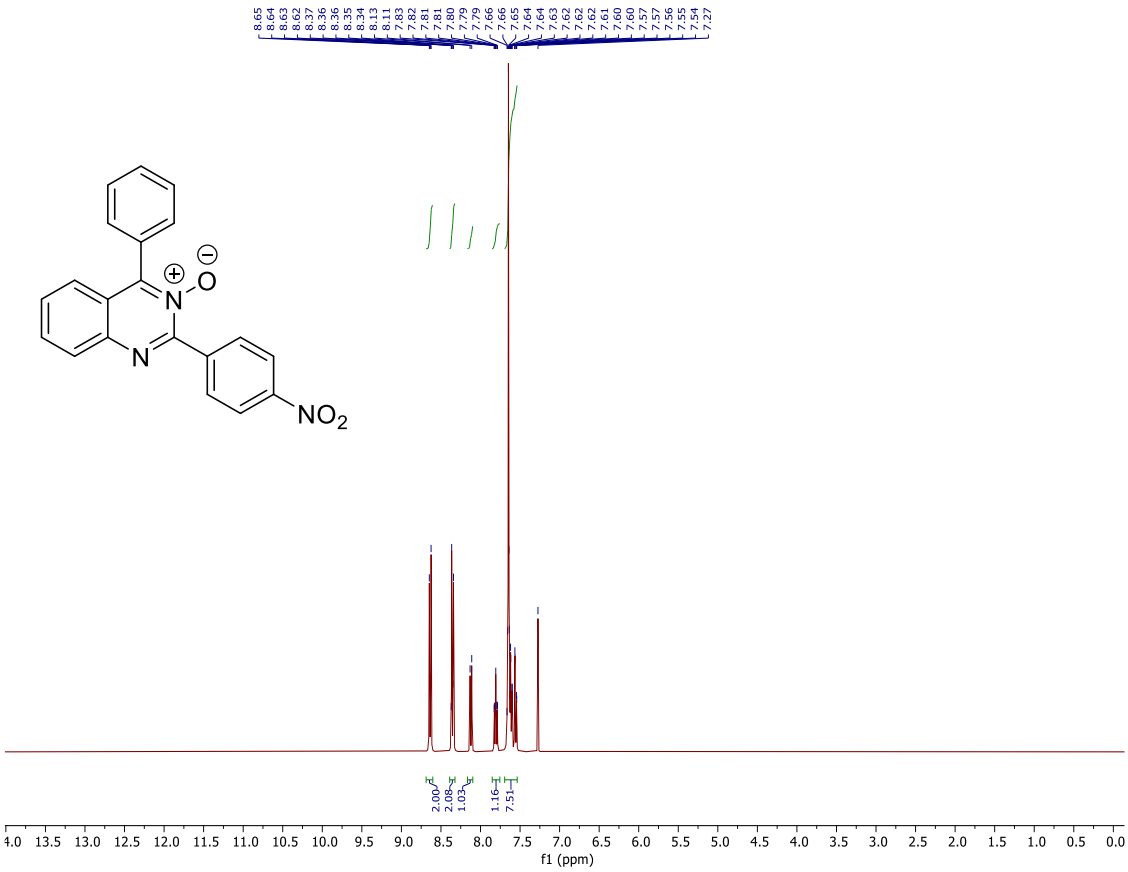


APPX 3.34 ^{1}H NMR (400 MHz, Chloroform-*d*) of compound **3n**

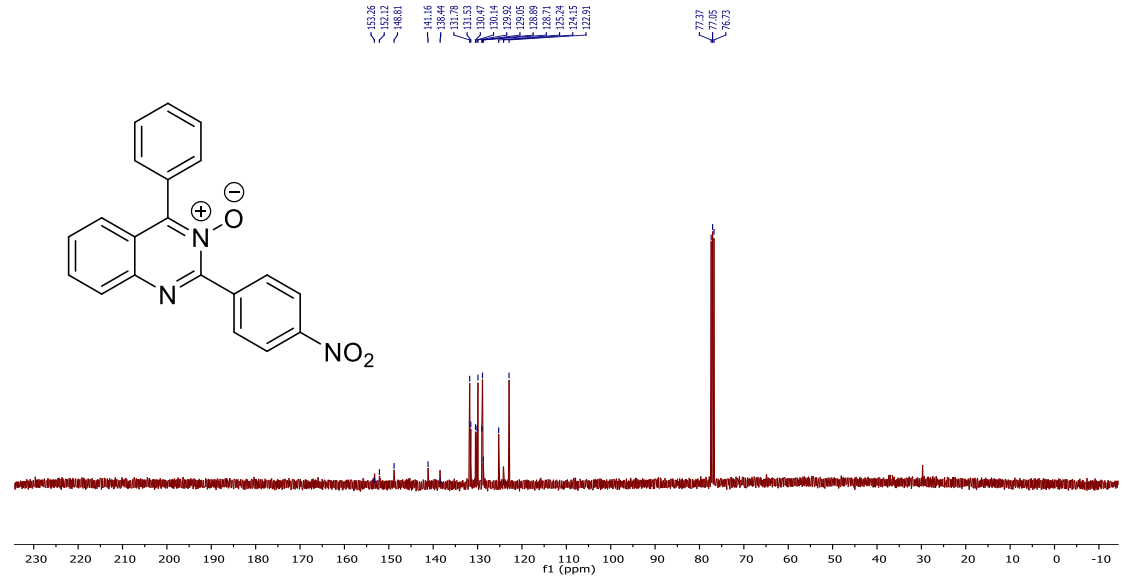


APPX 3.35 ^{13}C NMR (101 MHz, Chloroform-*d*) of compound **3n**

APPX 4 NMR and HRMS Spectra of compound **4**



APPX 4.1 ^{1}H NMR (400 MHz, Chloroform-*d*) of compound **4a**



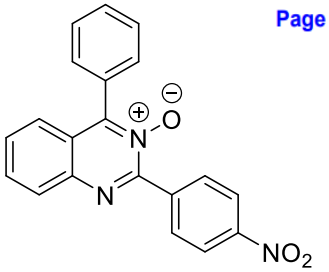
APPX 4.2 ^{13}C NMR (101 MHz, Chloroform-*d*) of compound **4a**

Elemental Composition Report **Page 1**

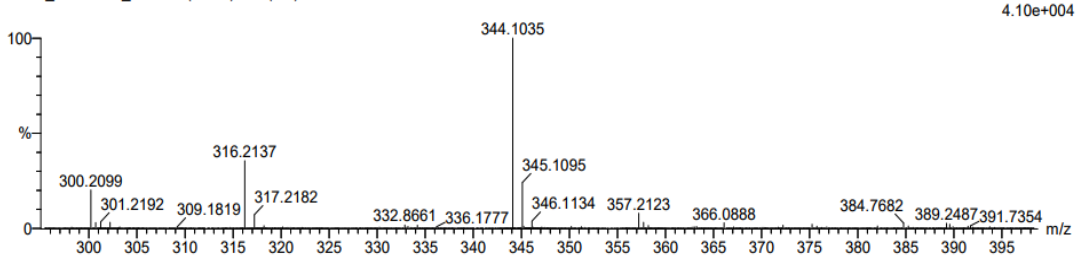
Single Mass Analysis
Tolerance = 1000.0 PPM / DBE: min = -5.5, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Odd and Even Electron Ions
1 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 20-20 H: 13-14 N: 3-3 O: 3-3

Necdet Coskun
32440_20210428_01-04 8 (0.328) Cm (1:8)

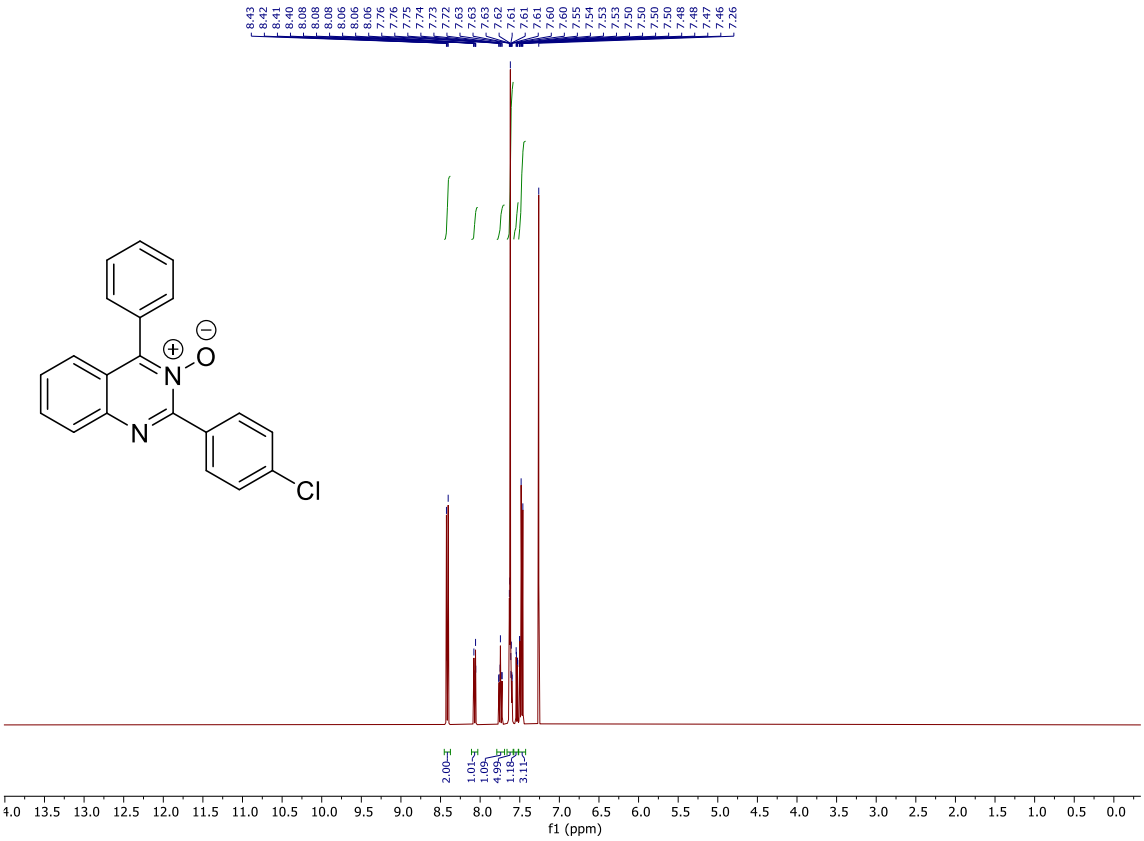


1: TOF MS ES+
4.10e+004

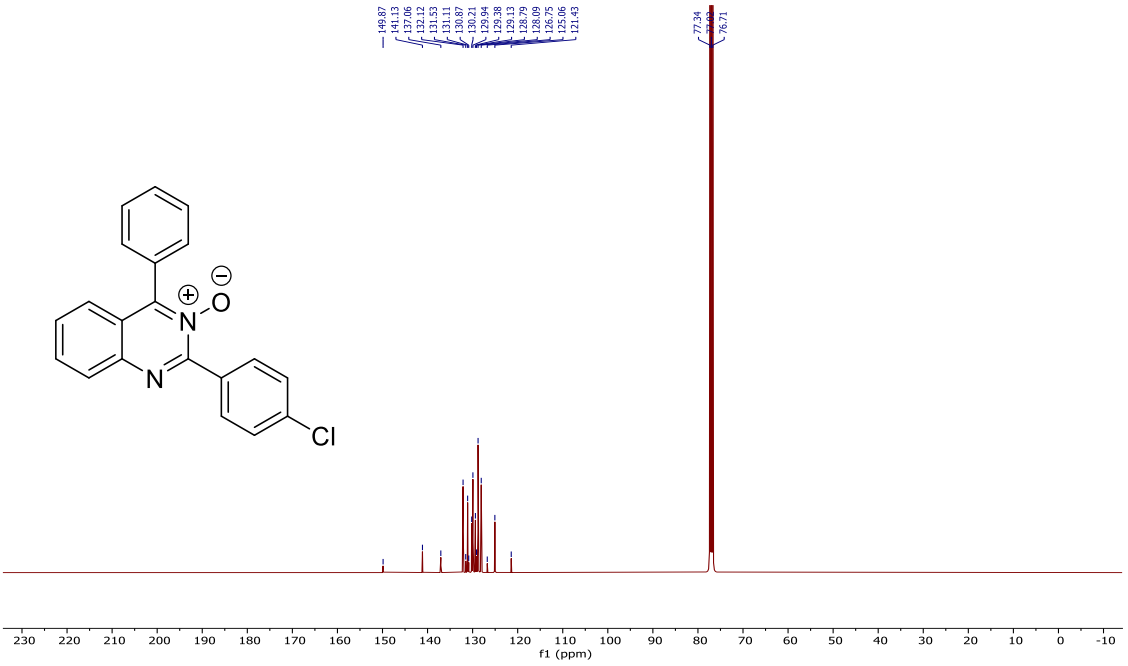


Minimum:				-5.5			
Maximum:		1000.0	1000.0	1000.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
344.1035	344.1035	0.0	0.0	15.5	387.5	0.0	C20 H14 N3 O3

APPX 4.3 HRMS (ESI-TOF-MS) of compound **4a**



APPX 4.4 ^{1}H NMR (400 MHz, Chloroform-*d*) of compound **4b**

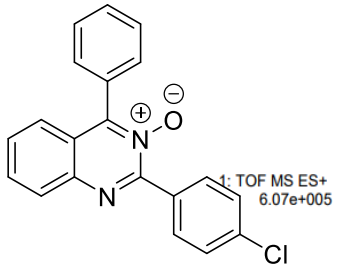


APPX 4.5 ^{13}C NMR (101 MHz, Chloroform-*d*) of compound **4b**

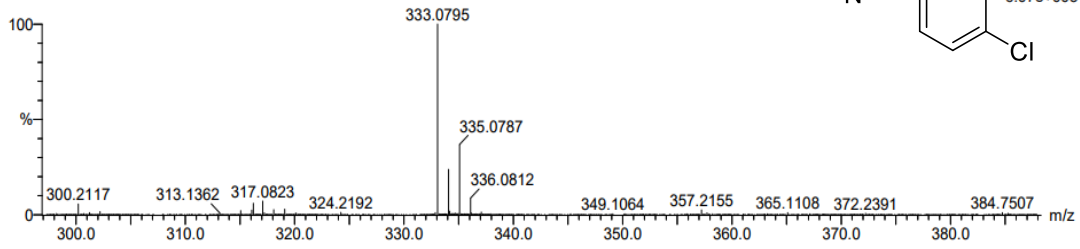
Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 1000.0 PPM / DBE: min = -5.5, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Odd and Even Electron Ions
6 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 20-21 H: 13-17 N: 2-3 O: 1-4 Cl: 1-1
Necdet Coskun
32440_20210428_18-02 9 (0.362) Cm (7:12)

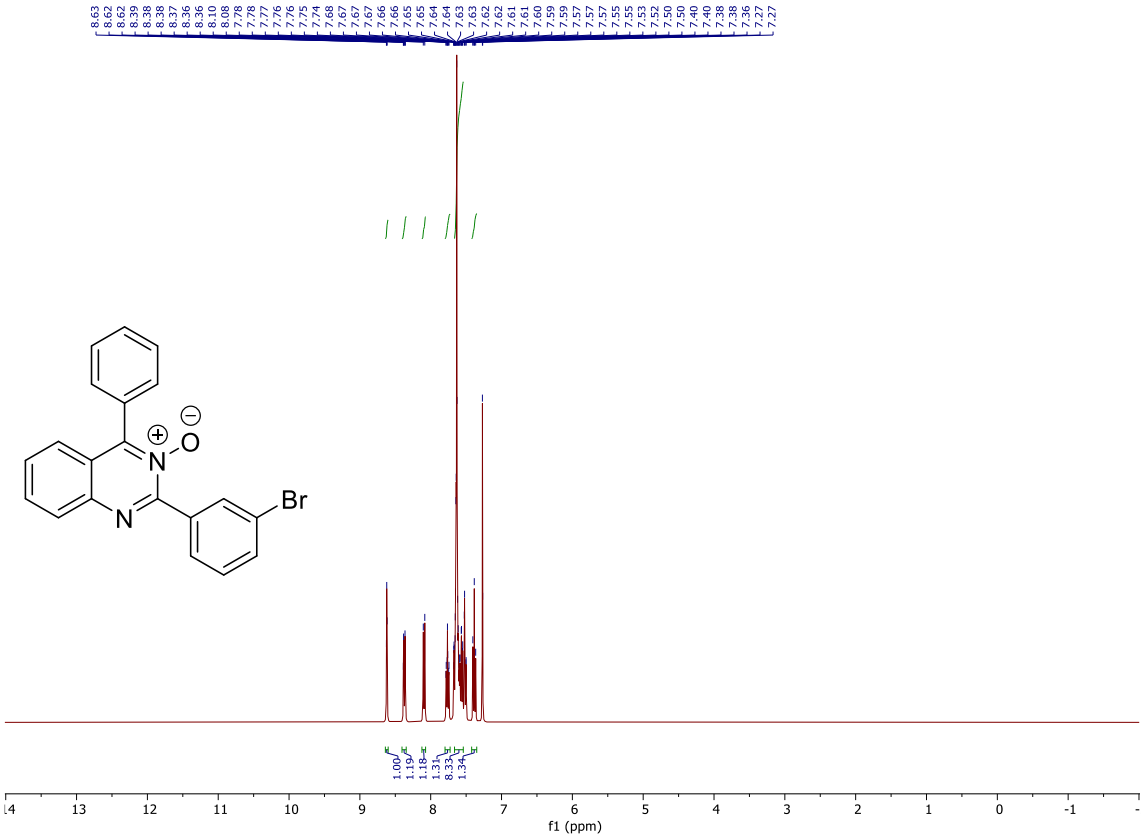


1: TOF MS ES+
6.07e+005

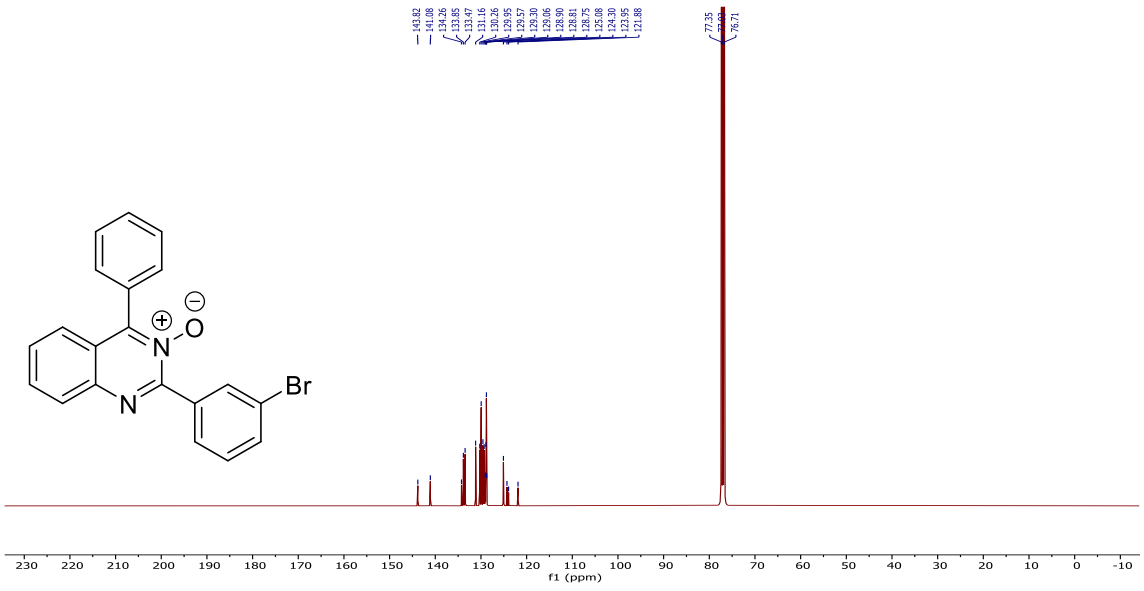


Minimum:				-5.5			
Maximum:		1000.0	1000.0	1000.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
333.0795	333.0795	0.0	0.0	14.5	634.7	0.0	C20 H14 N2 O Cl

APPX 4.6 HRMS (ESI-TOF-MS) of compound **4b**



APPX 4.7 ^{1}H NMR (400 MHz, Chloroform-*d*) of compound **4c**



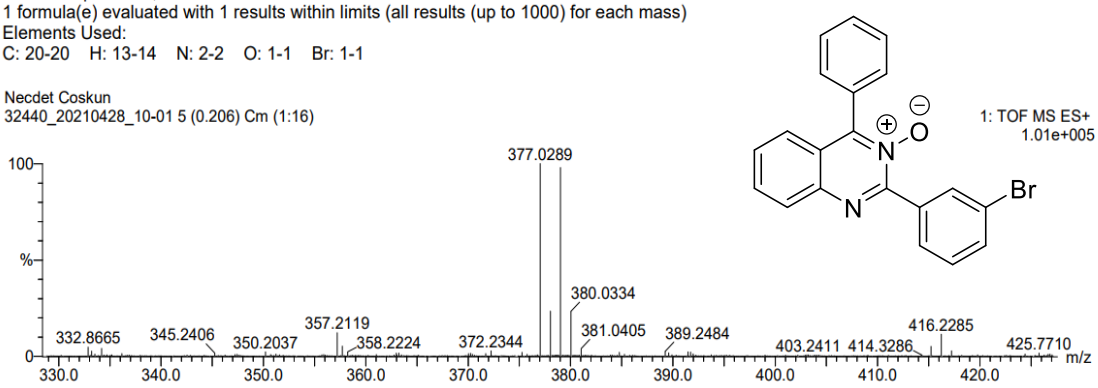
APPX 4.8^{13}C NMR (101 MHz, Chloroform-*d*) of compound **4c**

Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 1000.0 PPM / DBE: min = -5.5, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

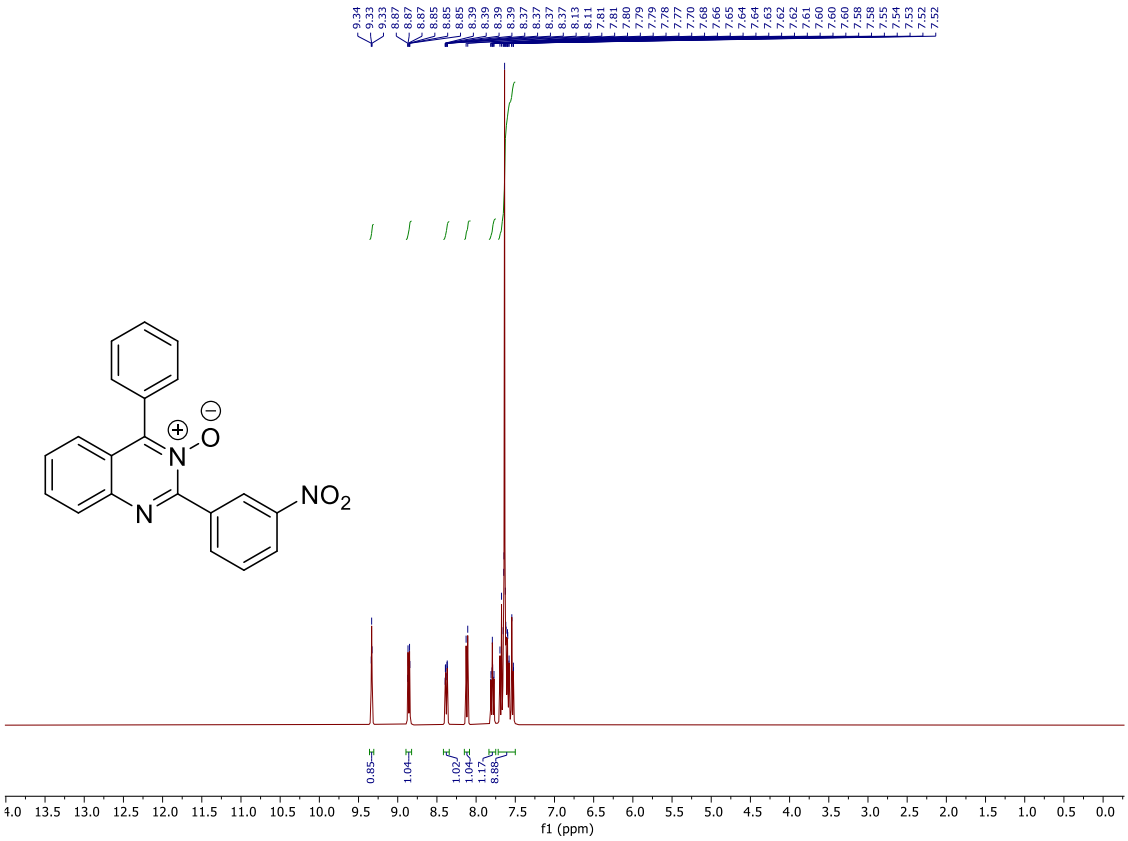
Monoisotopic Mass, Even Electron Ions
1 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 20-20 H: 13-14 N: 2-2 O: 1-1 Br: 1-1

Necdet Coskun
32440_20210428_10-01 5 (0.206) Cm (1:16)

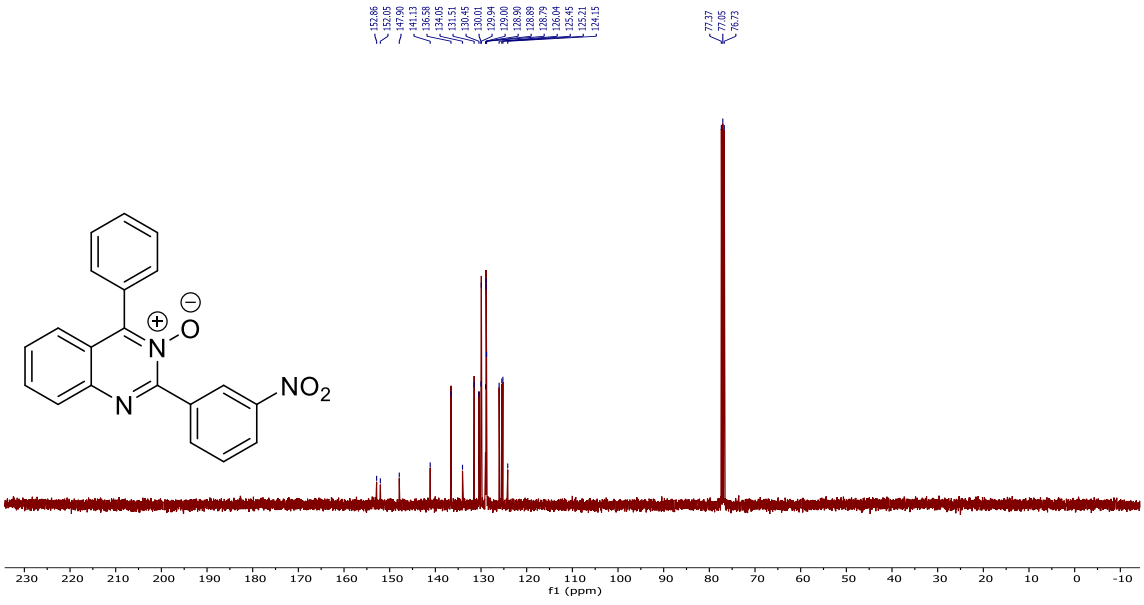


Minimum:				-5.5			
Maximum:		1000.0	1000.0	1000.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
377.0289	377.0289	0.0	0.0	14.5	426.3	0.0	C20 H14 N2 O Br

APPX 4.9 HRMS (ESI-TOF-MS) of compound **4c**



APPX 4.10 ^{1}H NMR (400 MHz, Chloroform-*d*) of compound **4d**

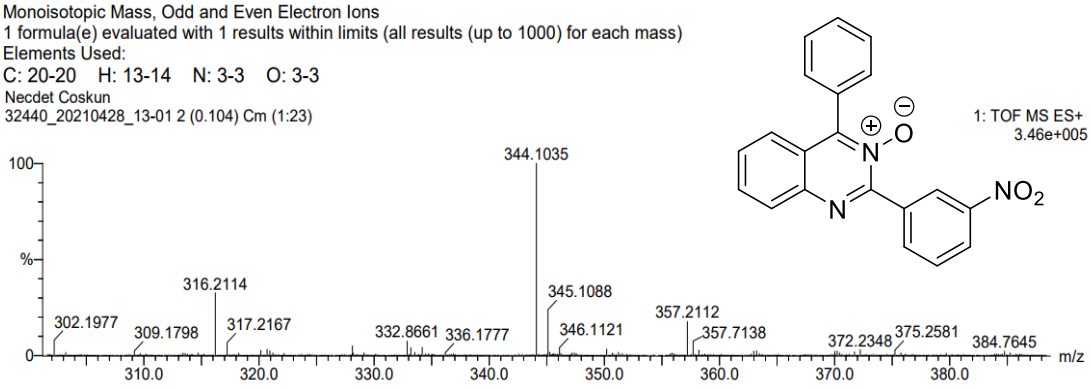


APPX 4.11 ^{13}C NMR (101 MHz, Chloroform-*d*) of compound **4d**

Elemental Composition Report **Page 1**

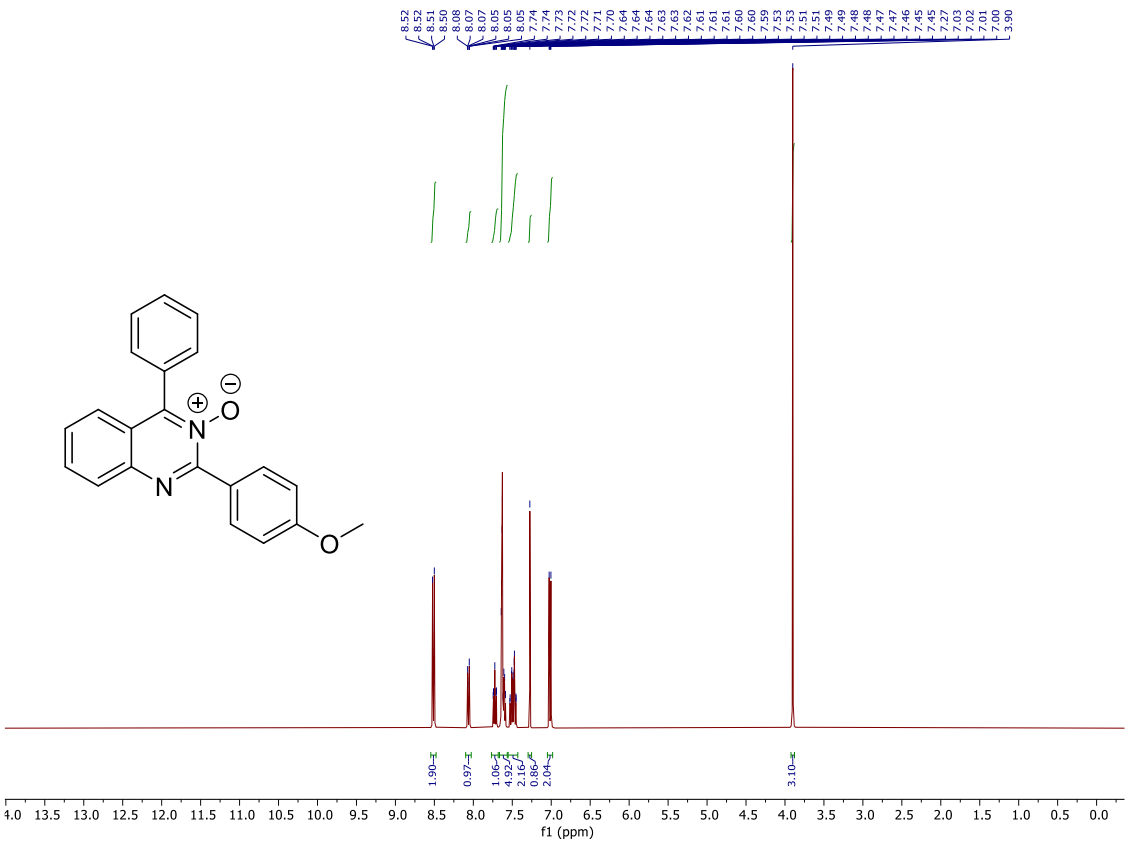
Single Mass Analysis
Tolerance = 1000.0 PPM / DBE: min = -5.5, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Odd and Even Electron Ions
1 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 20-20 H: 13-14 N: 3-3 O: 3-3
Necdet Coskun
32440_20210428_13-01 2 (0.104) Cm (1:23)

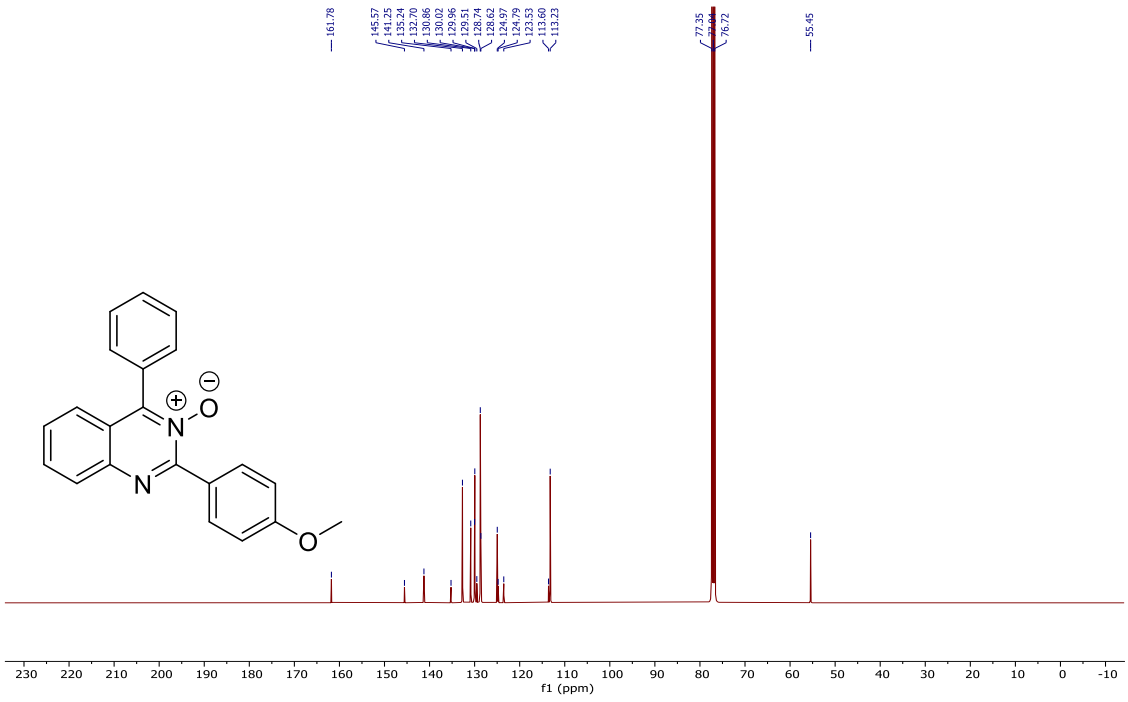


Minimum:				-5.5			
Maximum:		1000.0	1000.0	1000.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
344.1035	344.1035	0.0	0.0	15.5	625.4	0.0	C20 H14 N3 O3

APPX 4.12 HRMS (ESI-TOF-MS) of compound **4d**



APPX 4.13 ^{1}H NMR (400 MHz, Chloroform-*d*) of compound **4e**

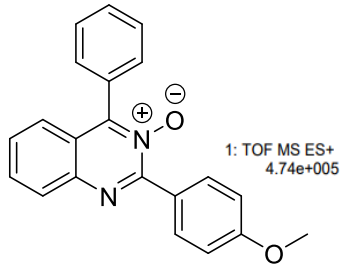


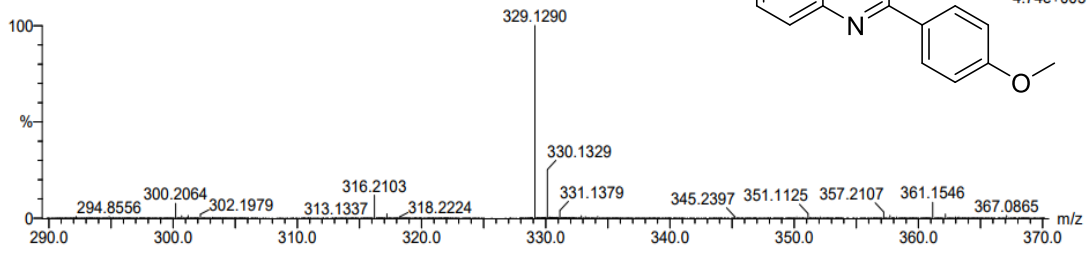
APPX 4.14 ^{13}C NMR (101 MHz, Chloroform-*d*) of compound **4e**

Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 1000.0 PPM / DBE: min = -5.5, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

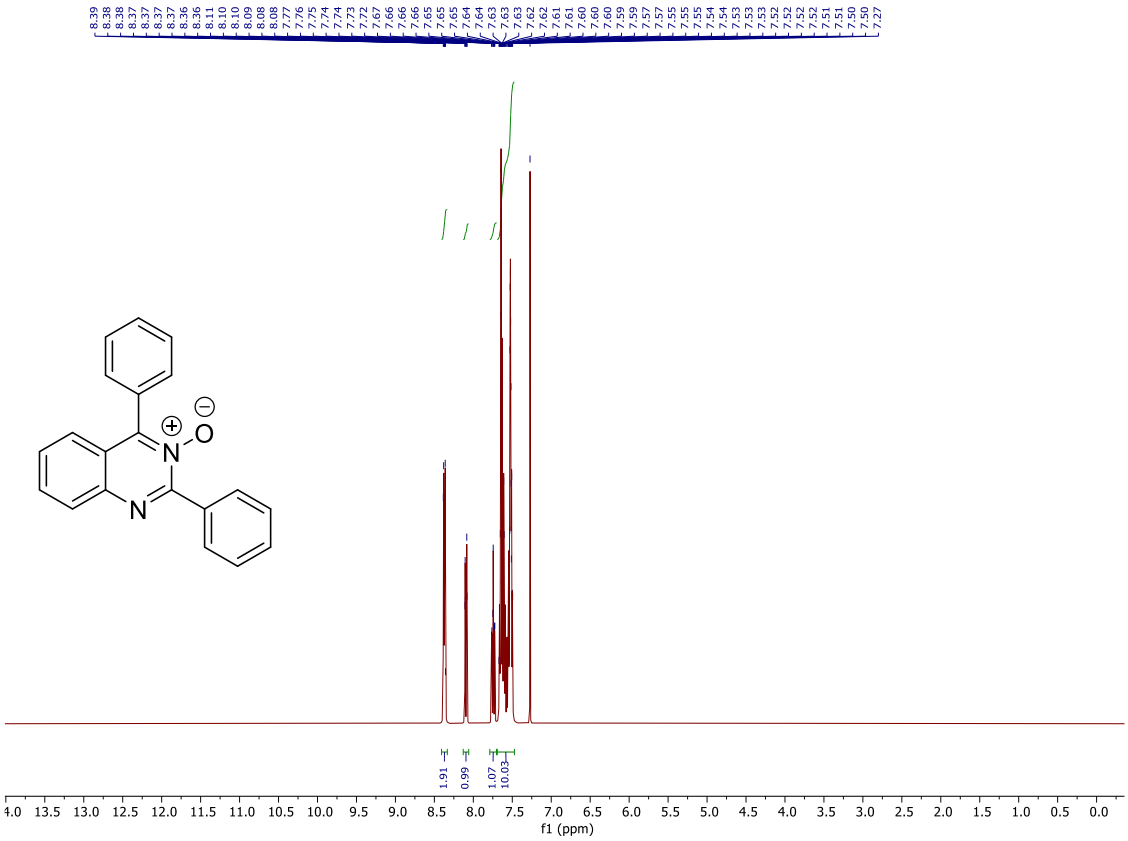
Monoisotopic Mass, Odd and Even Electron Ions
1 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 21-21 H: 16-17 N: 2-2 O: 2-2
Necdet Coskun
32440_20210428_03-02 20 (0.775) Cm (16:25)



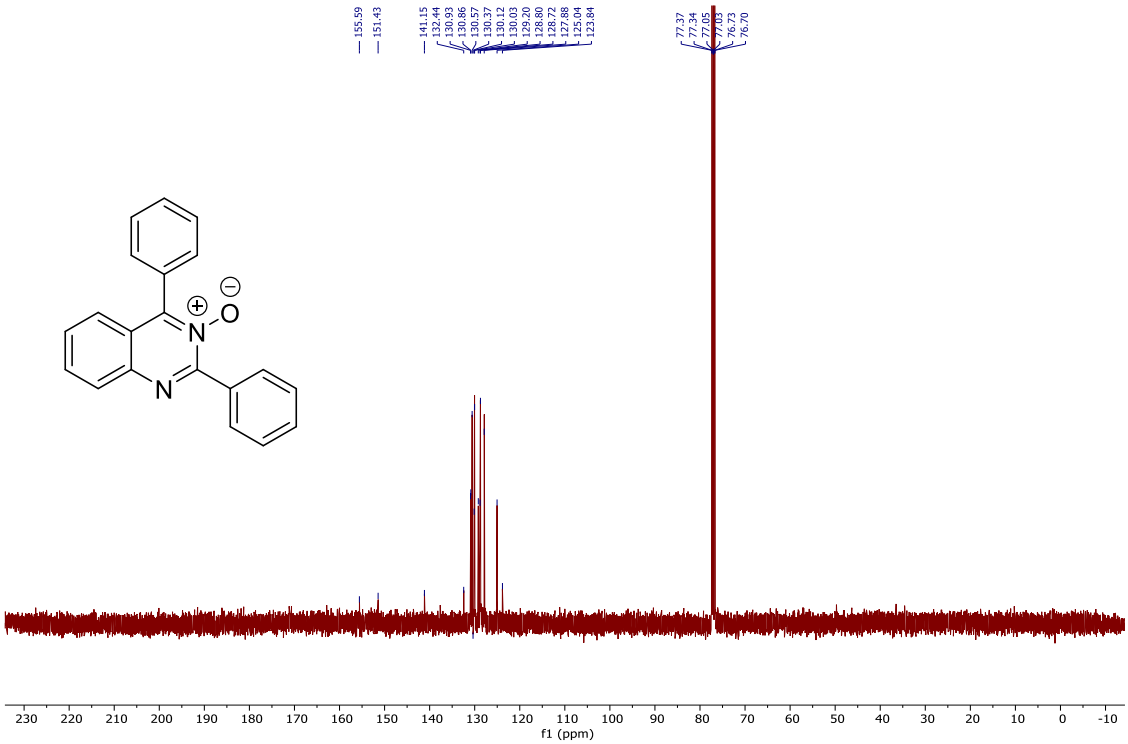


Minimum:				-5.5			
Maximum:		1000.0	1000.0	1000.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
329.1290	329.1290	0.0	0.0	14.5	674.5	0.0	C21 H17 N2 O2

APPX 4.15 HRMS (ESI-TOF-MS) of compound **4e**



APPX 4.16 ^{1}H NMR (400 MHz, Chloroform-*d*) of compound **4f**

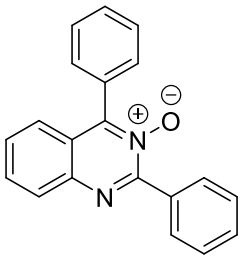


APPX 4.17 ^{13}C NMR (101 MHz, Chloroform-*d*) of compound **4f**

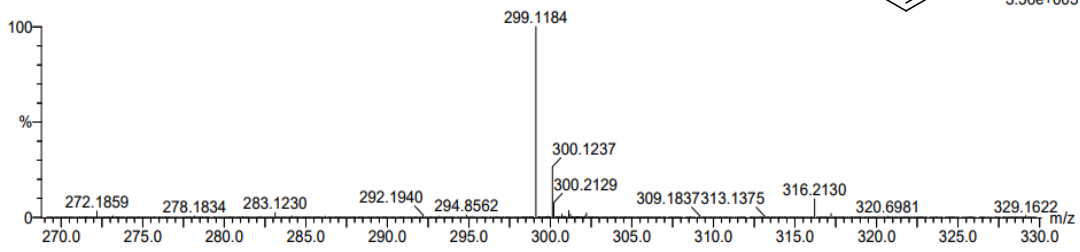
Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 1000.0 PPM / DBE: min = -5.5, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Odd and Even Electron Ions
1 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 20-20 H: 13-15 N: 2-2 O: 1-1
Necdet Coskun
32440_20210428_14-01 11 (0.450) Cm (5:22)

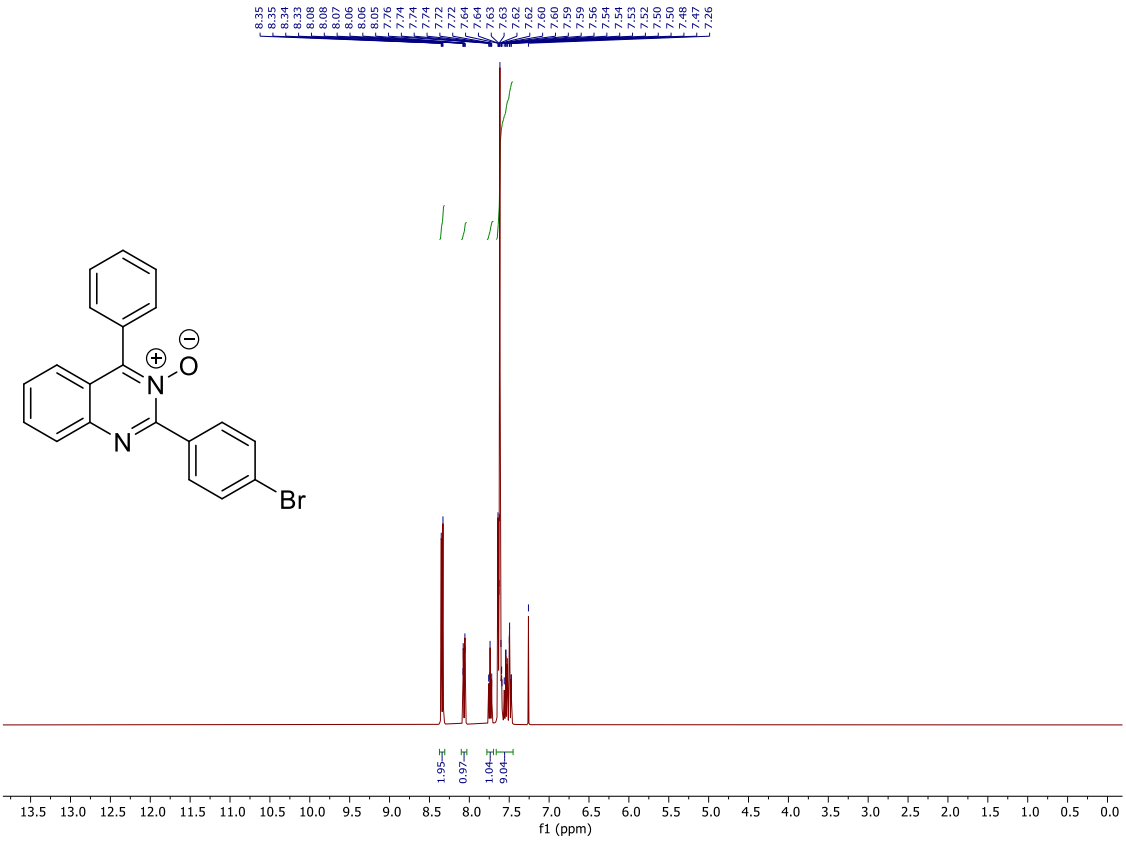


1: TOF MS ES+
3.56e+005

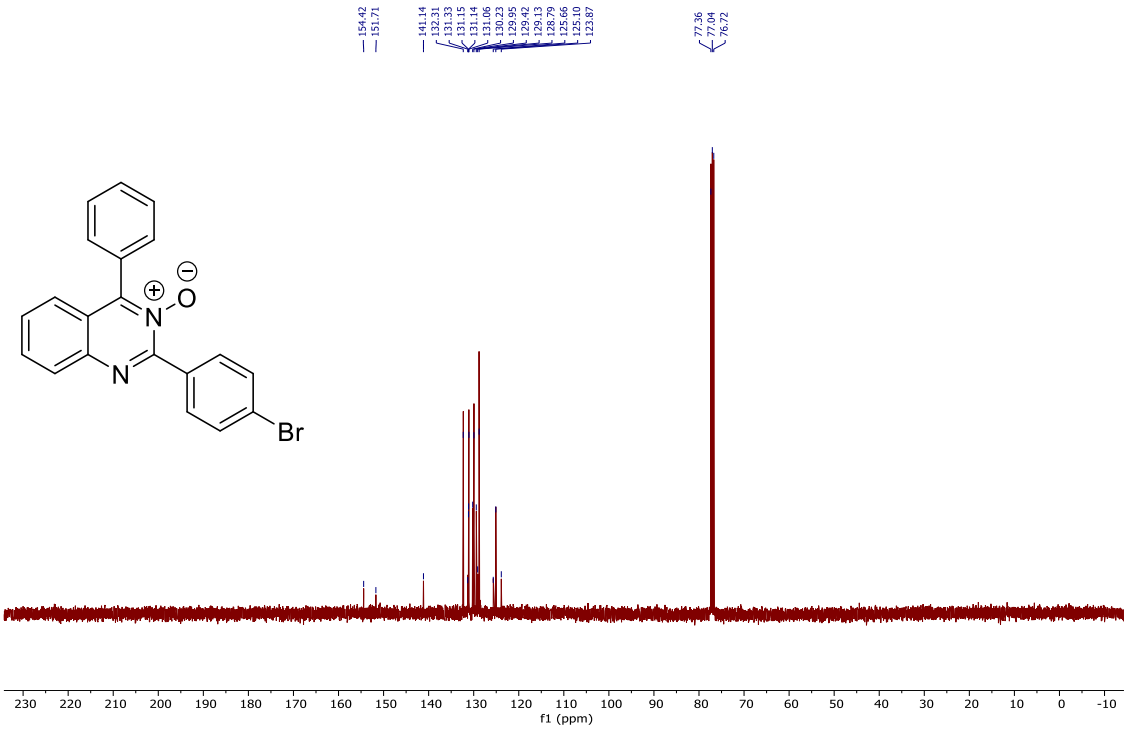


Minimum:				-5.5			
Maximum:		1000.0	1000.0	1000.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
299.1184	299.1184	0.0	0.0	14.5	642.0	0.0	C20 H15 N2 O

APPX 4.18 HRMS (ESI-TOF-MS) of compound **4f**



APPX 4.19 ^{1}H NMR (400 MHz, Chloroform-*d*) of compound **4g**

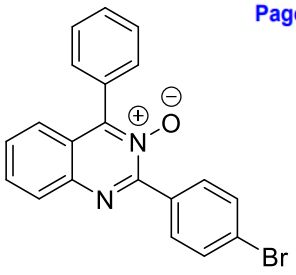


APPX 4.20 ^{13}C NMR (101 MHz, Chloroform-*d*) of compound **4g**

Elemental Composition Report **Page 1**

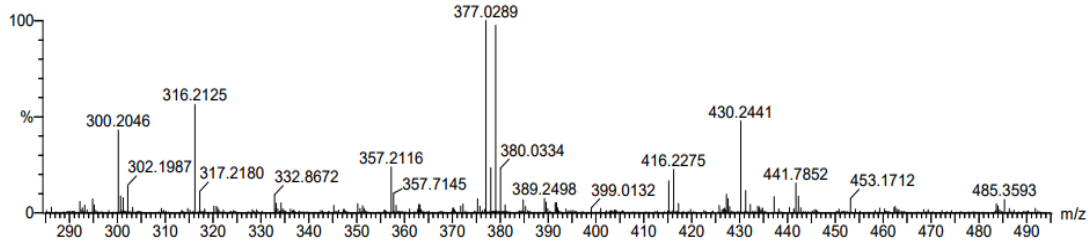
Single Mass Analysis
Tolerance = 1000.0 PPM / DBE: min = -5.5, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
1 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 20-21 H: 13-17 N: 2-2 O: 1-2 Br: 1-1



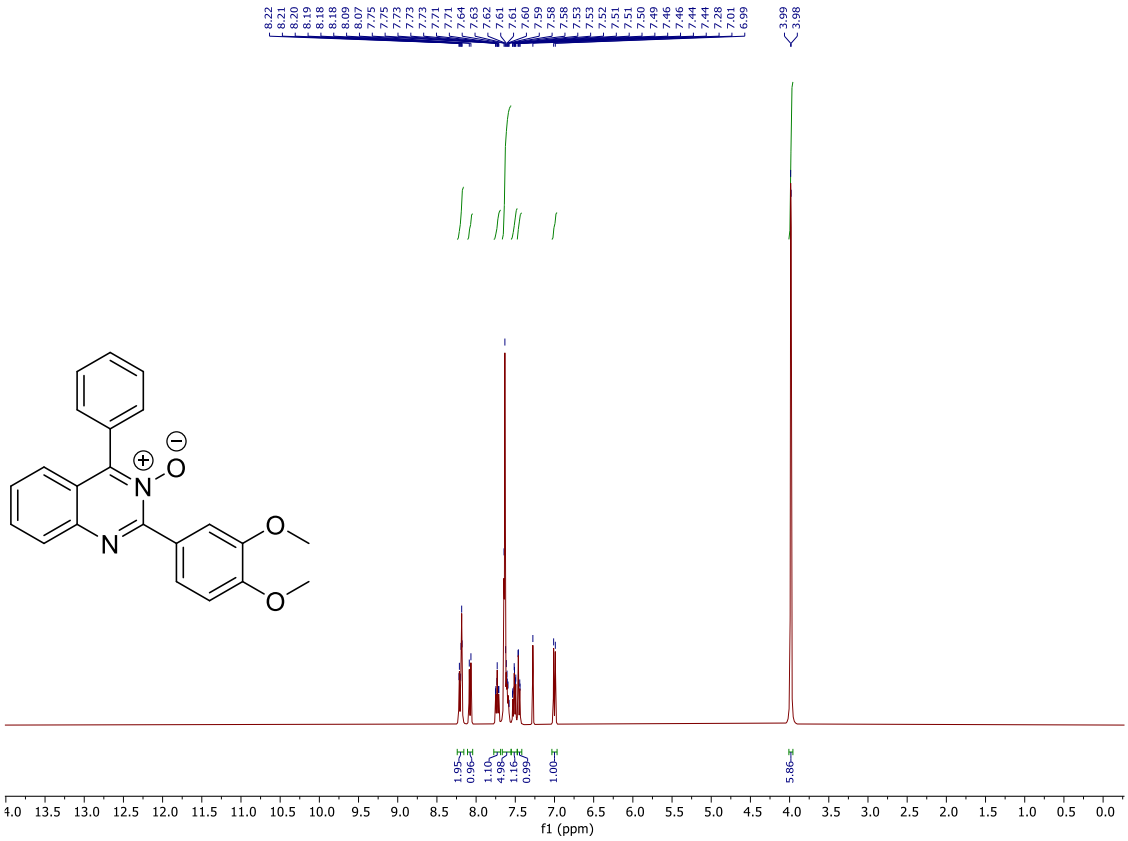
Necdet Coskun
32440_20210428_04-01 13 (0.518) Cm (2:25)

1: TOF MS ES+
2.31e+005

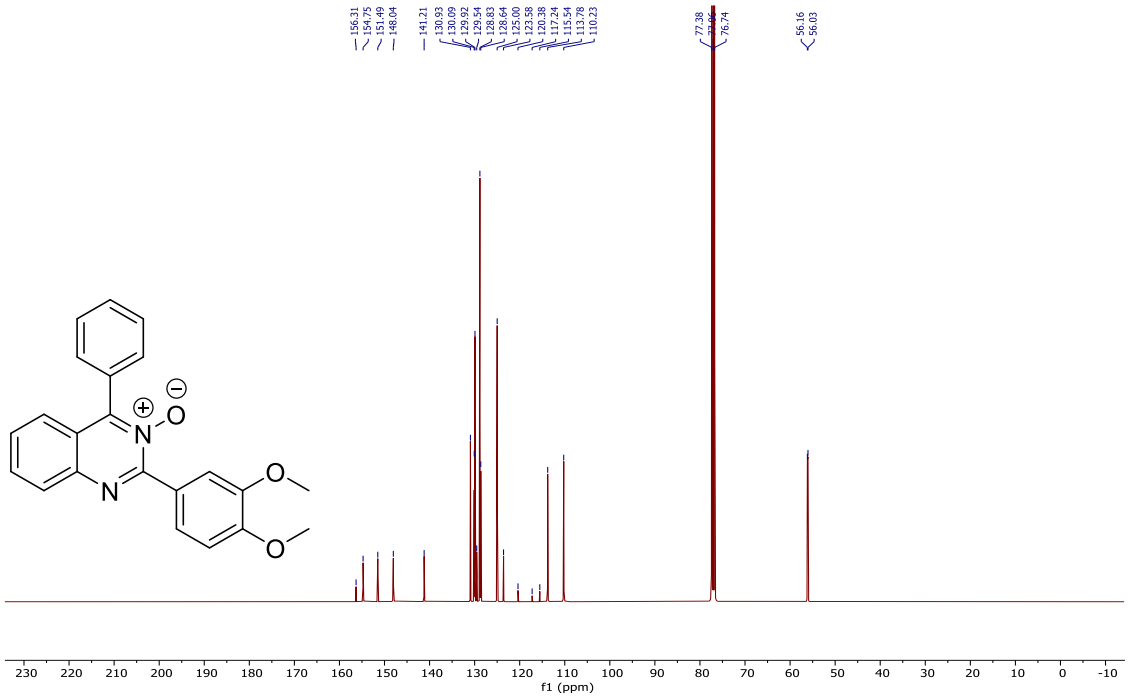


Minimum:				-5.5			
Maximum:		1000.0	1000.0	1000.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
377.0289	377.0289	0.0	0.0	14.5	524.1	0.0	C20 H14 N2 O Br

APPX 4.21 HRMS (ESI-TOF-MS) of compound **4g**



APPX 4.22 ^{1}H NMR (400 MHz, Chloroform-*d*) of compound **4h**



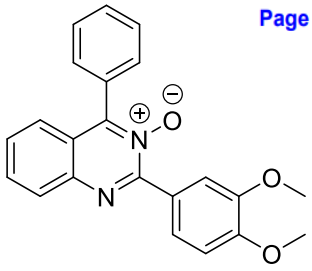
APPX 4.23 ^{13}C NMR (101 MHz, Chloroform-*d*) of compound **4h**

Elemental Composition Report **Page 1**

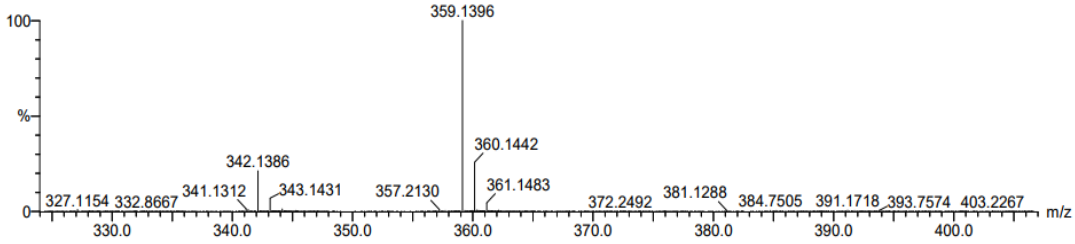
Single Mass Analysis
Tolerance = 1000.0 PPM / DBE: min = -5.5, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Odd and Even Electron Ions
2 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 22-22 H: 13-19 N: 2-3 O: 1-4

Necdet Coskun
32440_20210428_19-01 19 (0.741) Cm (18:25)

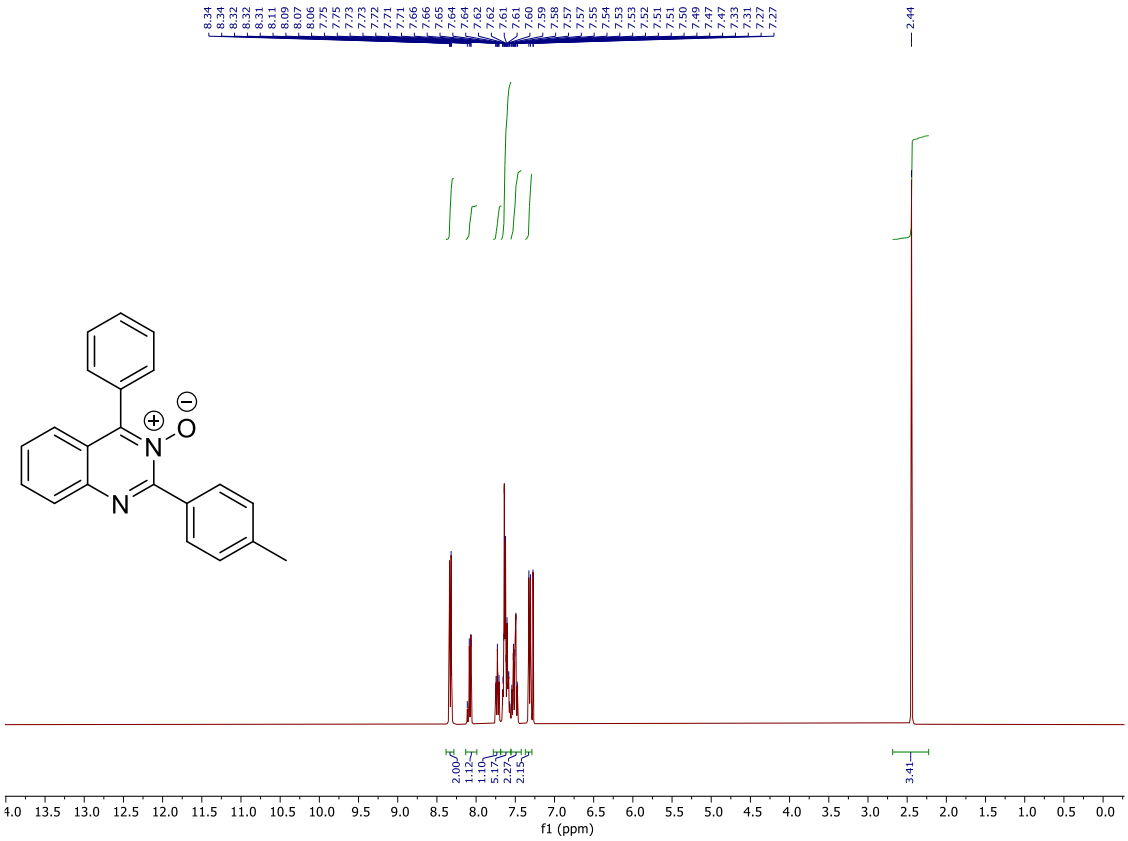


1: TOF MS ES+
1.59e+006

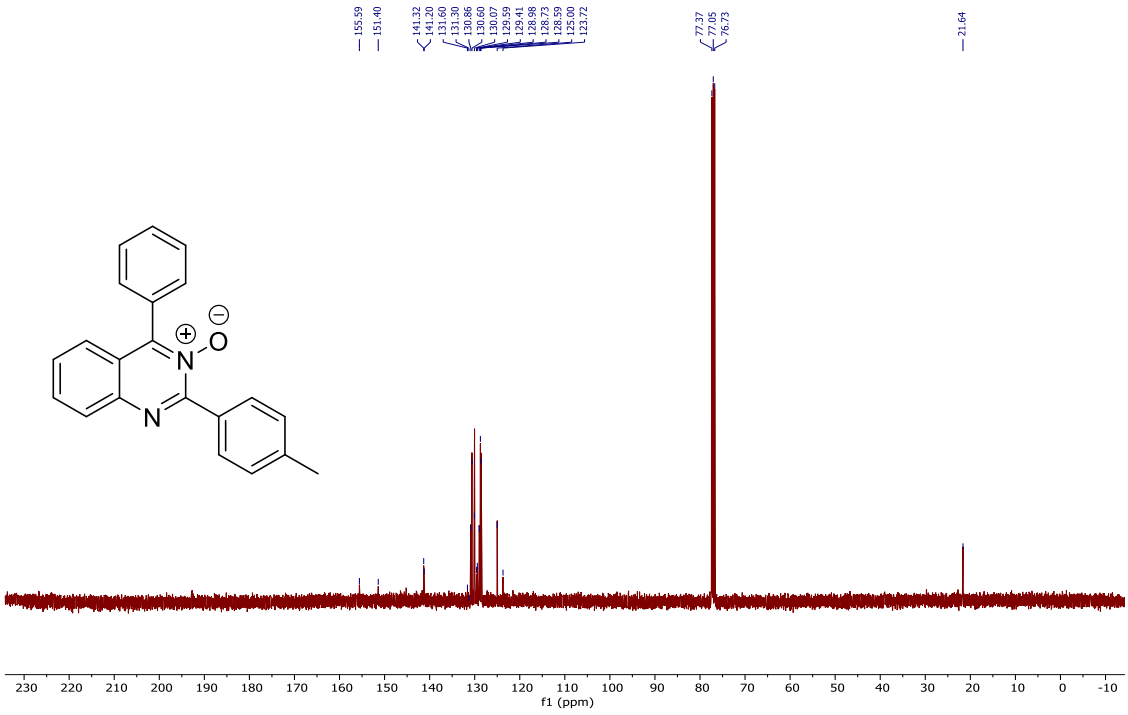


Minimum:				-5.5			
Maximum:		1000.0	1000.0	1000.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
359.1396	359.1396	0.0	0.0	14.5	637.3	0.0	C22 H19 N2 O3

APPX 4.24 HRMS (ESI-TOF-MS) of compound **4h**



APPX 4.25 ^{1}H NMR (400 MHz, Chloroform-*d*) of compound **4i**



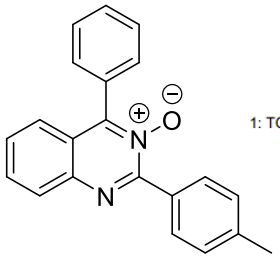
APPX 4.26 ^{13}C NMR (101 MHz, Chloroform-*d*) of compound **4i**

Elemental Composition Report **Page 1**

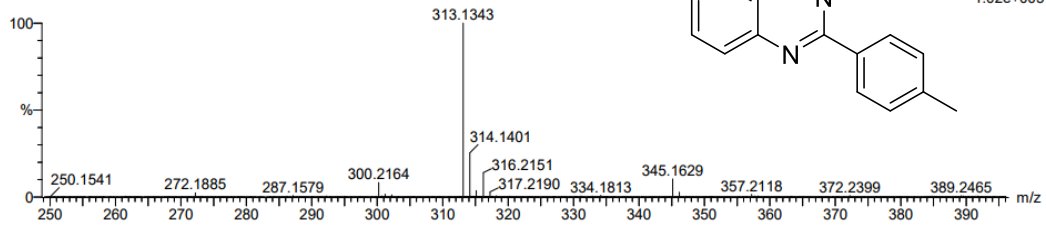
Single Mass Analysis
Tolerance = 1000.0 PPM / DBE: min = -5.5, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
1 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 21-21 H: 15-17 N: 2-2 O: 1-2

Nejdet Coskun
32810_20210615_02-04 23 (0.897) Cm (1:25)

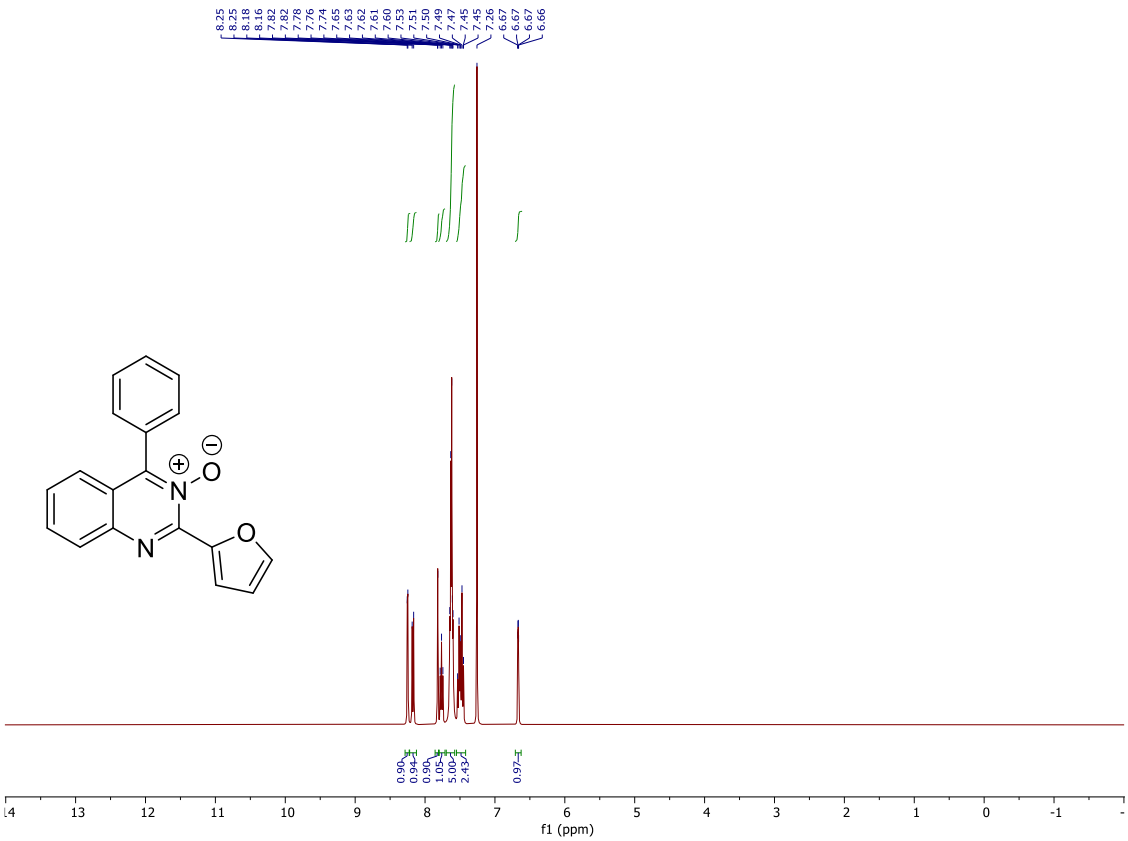


1: TOF MS ES+
1.02e+005

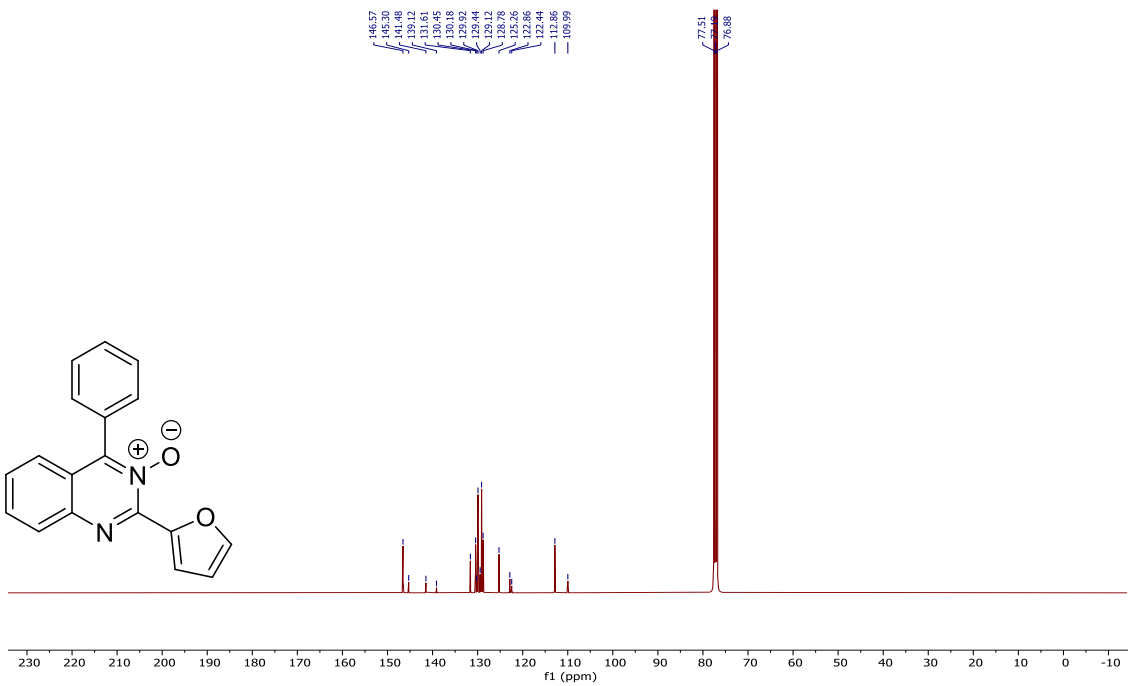


Minimum:				-5.5			
Maximum:		1000.0	1000.0	1000.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
313.1343	313.1341	0.2	0.6	14.5	507.6	0.0	C21 H17 N2 O

APPX 4.27 HRMS (ESI-TOF-MS) of compound **4i**



APPX 4.28 ^{1}H NMR (400 MHz, Chloroform-*d*) of compound **4j**



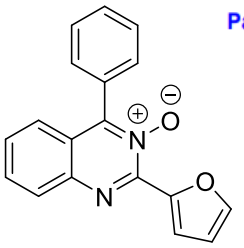
APPX 4.29 ^{13}C NMR (101 MHz, Chloroform-*d*) of compound **4j**

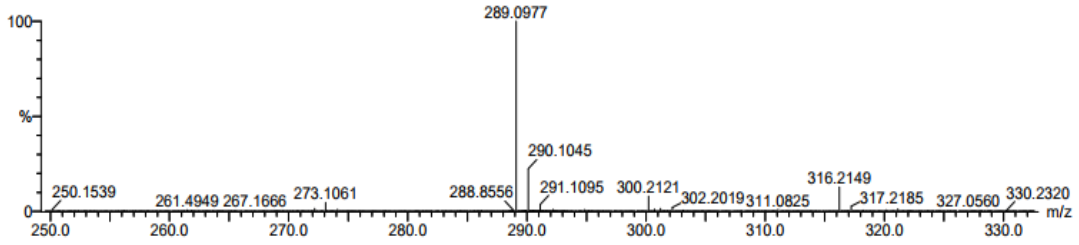
Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 1000.0 PPM / DBE: min = -5.5, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Odd and Even Electron Ions
1 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 18-18 H: 12-13 N: 2-2 O: 2-2

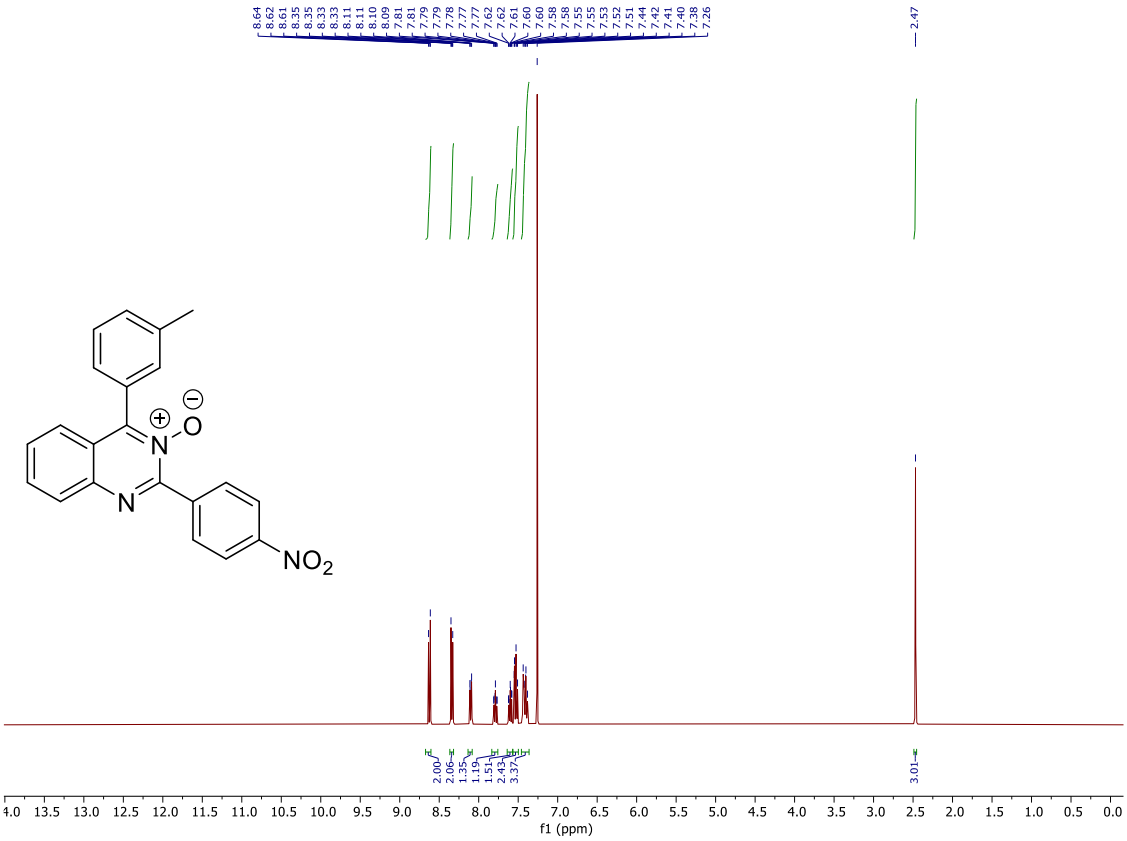
Necdet Coskun
32440_20210428_09-01 4 (0.172) Cm (1:25)



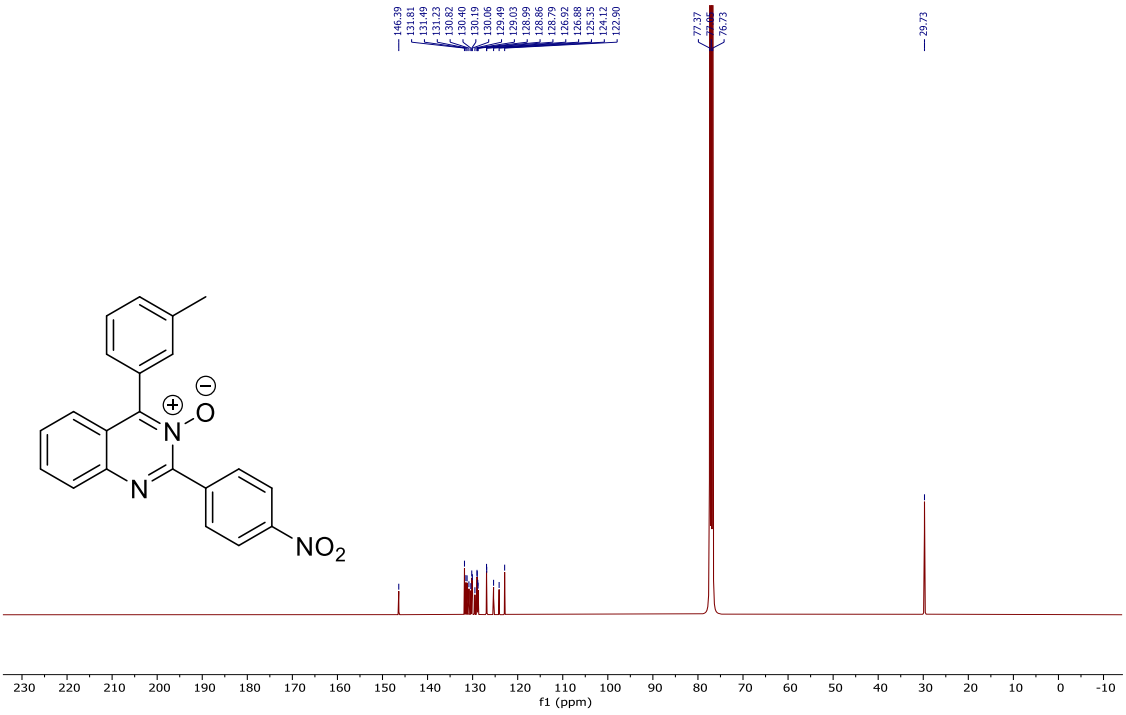


Minimum:				-5.5			
Maximum:		1000.0	1000.0	1000.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
289.0977	289.0977	0.0	0.0	13.5	609.0	0.0	C18 H13 N2 O2

APPX 4.30 HRMS (ESI-TOF-MS) of compound **4j**



APPX 4.31 ^{1}H NMR (400 MHz, Chloroform-*d*) of compound **4k**

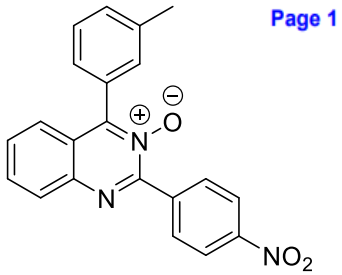


APPX 4.32 ^{13}C NMR (101 MHz, Chloroform-*d*) of compound **4k**

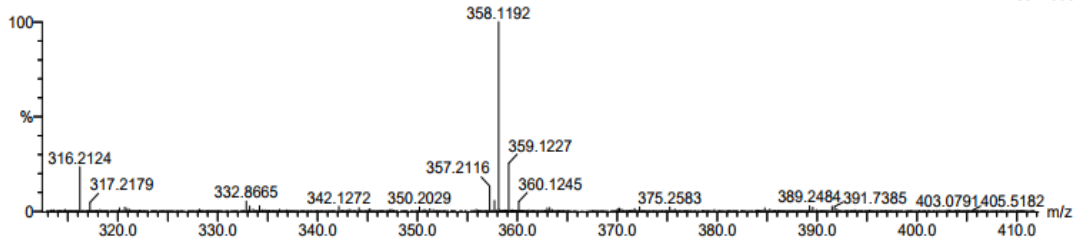
Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 1000.0 PPM / DBE: min = -5.5, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Odd and Even Electron Ions
1 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 21-21 H: 15-16 N: 3-3 O: 3-3
Necdet Coskun
32440_20210428_08-01 25 (0.965) Cm (14:25)

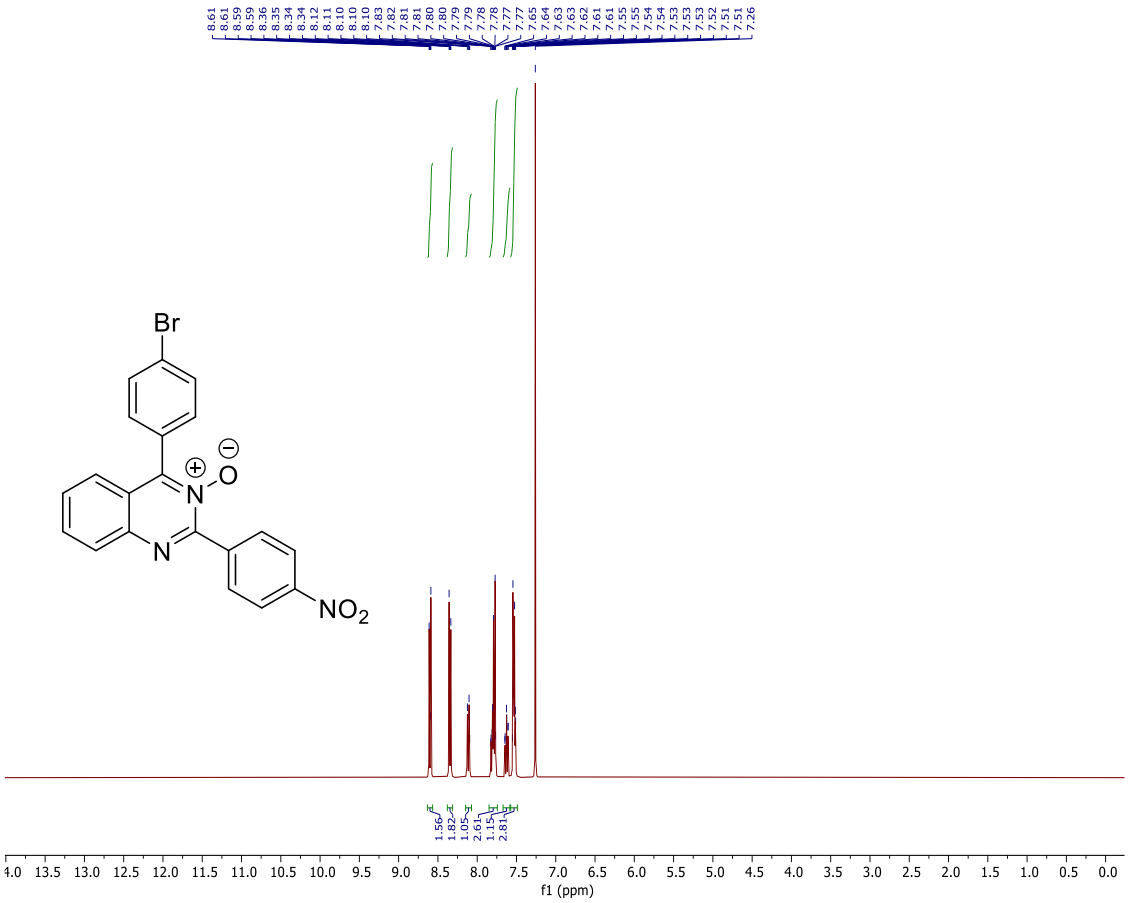


1: TOF MS ES+
1.83e+005

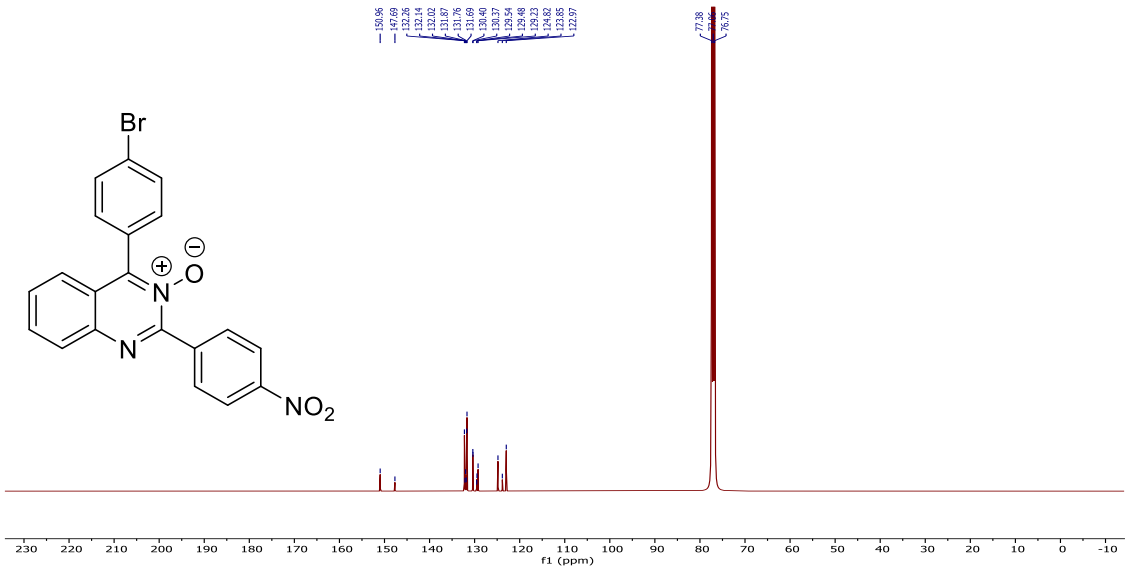


Minimum:				-5.5			
Maximum:		1000.0	1000.0	1000.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
358.1192	358.1192	0.0	0.0	15.5	558.2	0.0	C21 H16 N3 O3

APPX 4.33 HRMS (ESI-TOF-MS) of compound **4k**



APPX 4.34 ^{1}H NMR (400 MHz, Chloroform-*d*) of compound **4l**

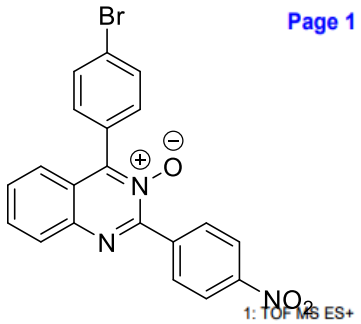


APPX 4.35 ^{13}C NMR (101 MHz, Chloroform-*d*) of compound **4l**

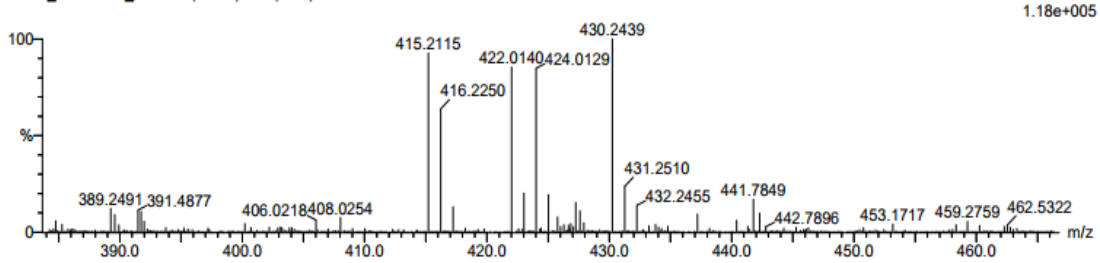
Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 1000.0 PPM / DBE: min = -5.5, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
1 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 20-20 H: 12-13 N: 3-3 O: 3-3 Br: 1-1

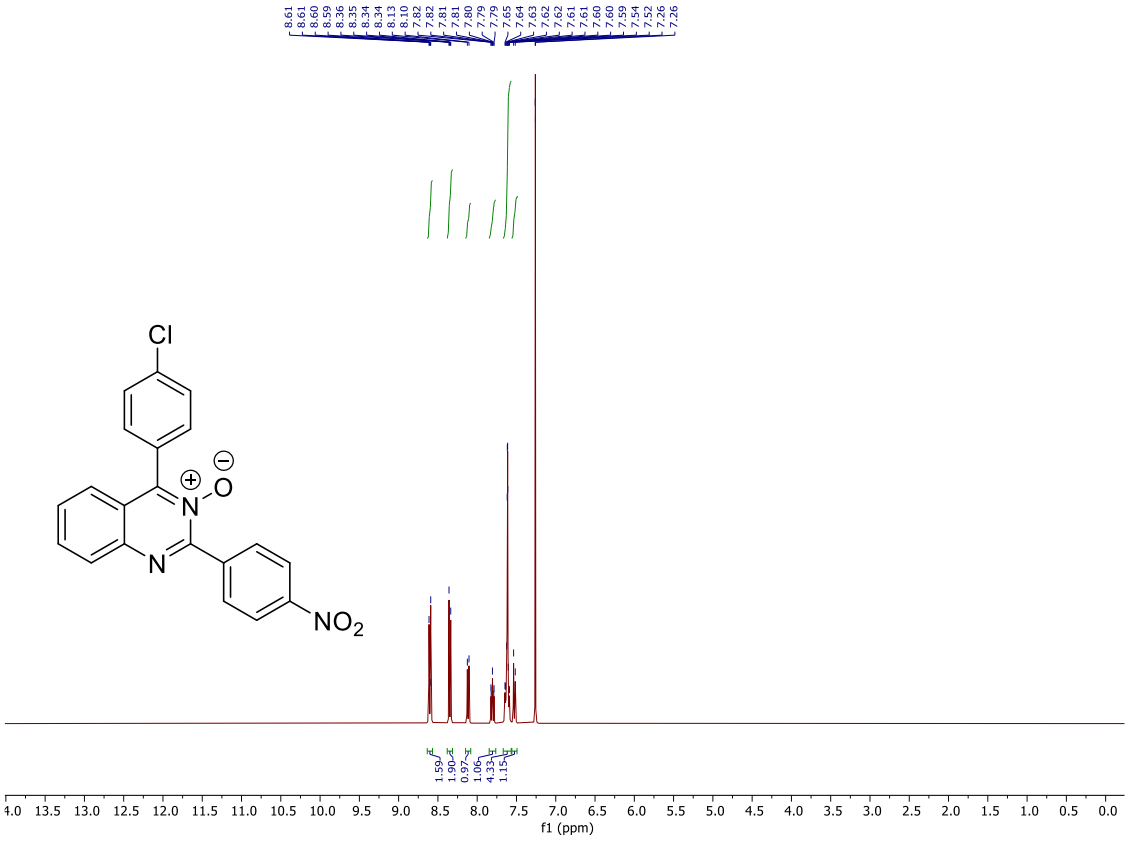


Necdet Coskun
32440_20210428_06-02 9 (0.362) Cm (9:25)

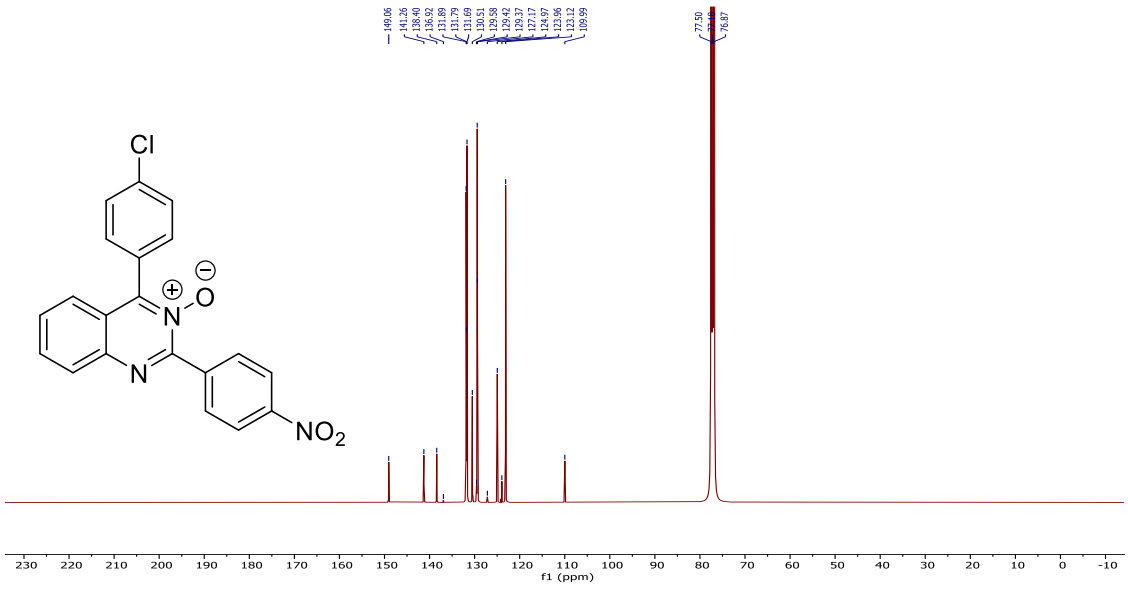


Minimum:				-5.5			
Maximum:		1000.0	1000.0	1000.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
422.0140	422.0140	0.0	0.0	15.5	271.8	0.0	C20 H13 N3 O3 Br

APPX 4.36 HRMS (ESI-TOF-MS) of compound **4l**



APPX 4.37 ^{1}H NMR (400 MHz, Chloroform-*d*) of compound **4m**

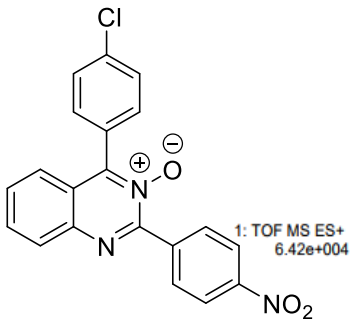


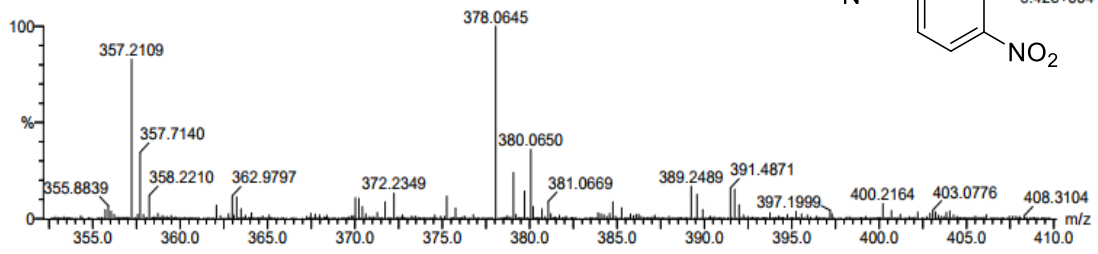
APPX 4.38 ^{13}C NMR (101 MHz, Chloroform-*d*) of compound **4m**

Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 1000.0 PPM / DBE: min = -5.5, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

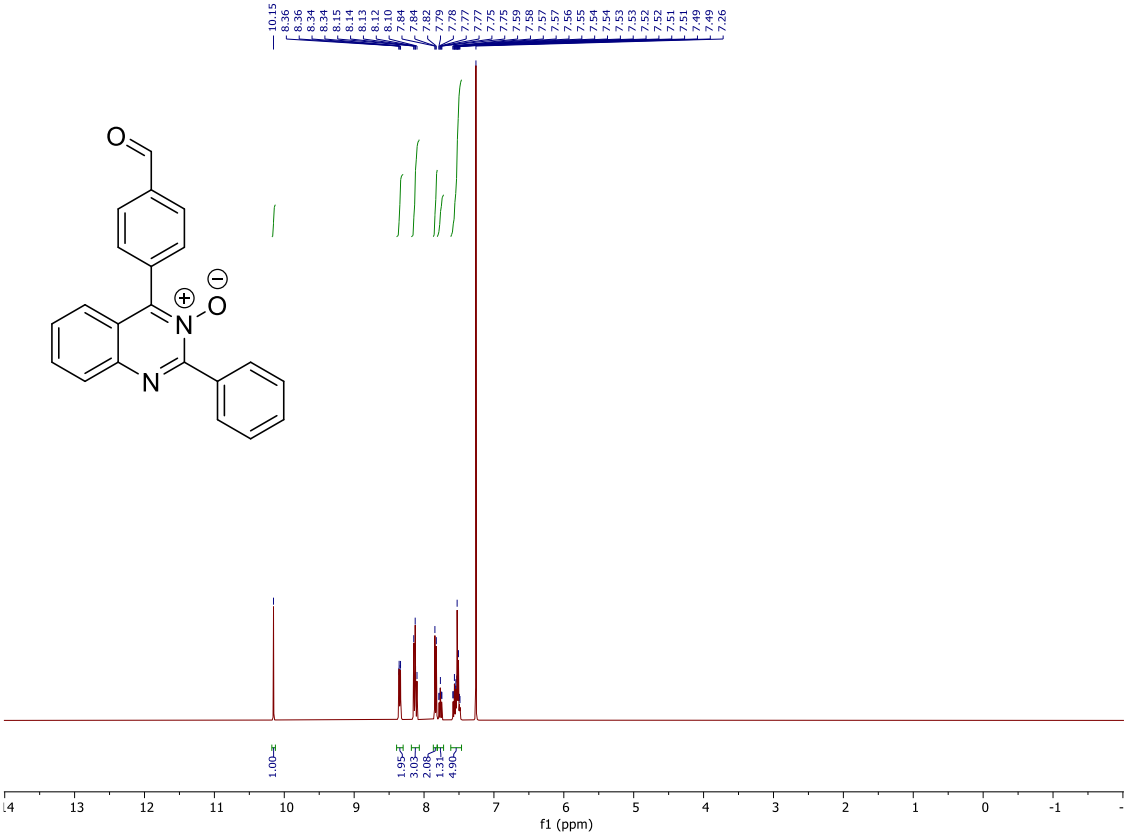
Monoisotopic Mass, Odd and Even Electron Ions
1 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 20-20 H: 12-13 N: 3-3 O: 3-3 Cl: 1-1
Necdet Coskun
32440_20210428_07-01 25 (0.965) Cm (12:25)



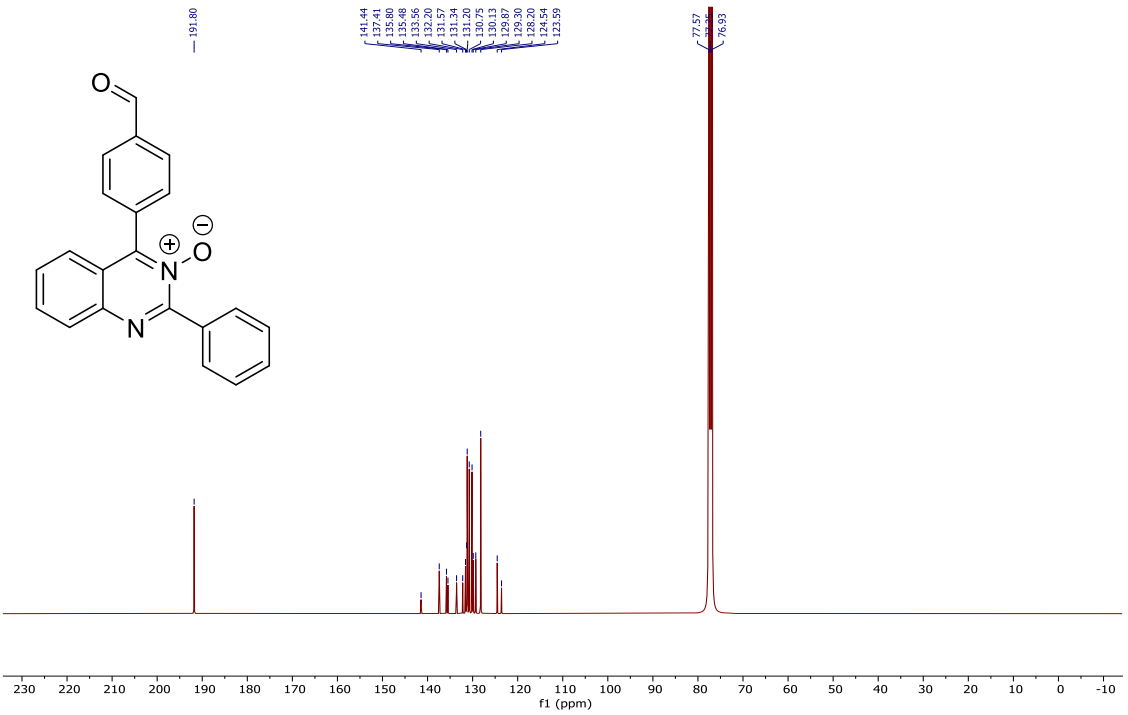


Minimum:				-5.5			
Maximum:		1000.0	1000.0	1000.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
378.0645	378.0645	0.0	0.0	15.5	318.0	0.0	C20 H13 N3 O3 Cl

APPX 4.39 HRMS (ESI-TOF-MS) of compound **4m**



APPX 4.40 ^{1}H NMR (400 MHz, Chloroform-d) of compound **4n**

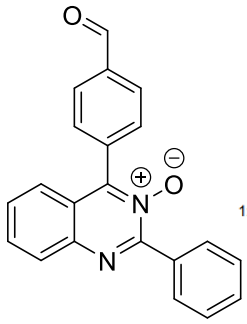


APPX 4.41 ^{13}C NMR (101 MHz, Chloroform-d) of compound **4n**

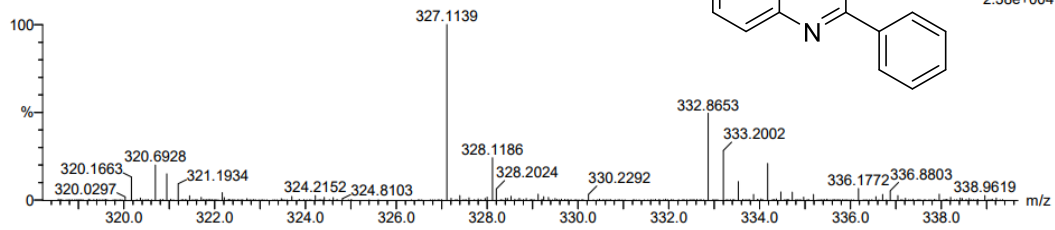
Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 1000.0 PPM / DBE: min = -5.5, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Odd and Even Electron Ions
1 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 21-21 H: 15-16 N: 2-2 O: 2-2
Nejdet Coskun
32810_20210615_01-01 9 (0.362) Cm (1:10)

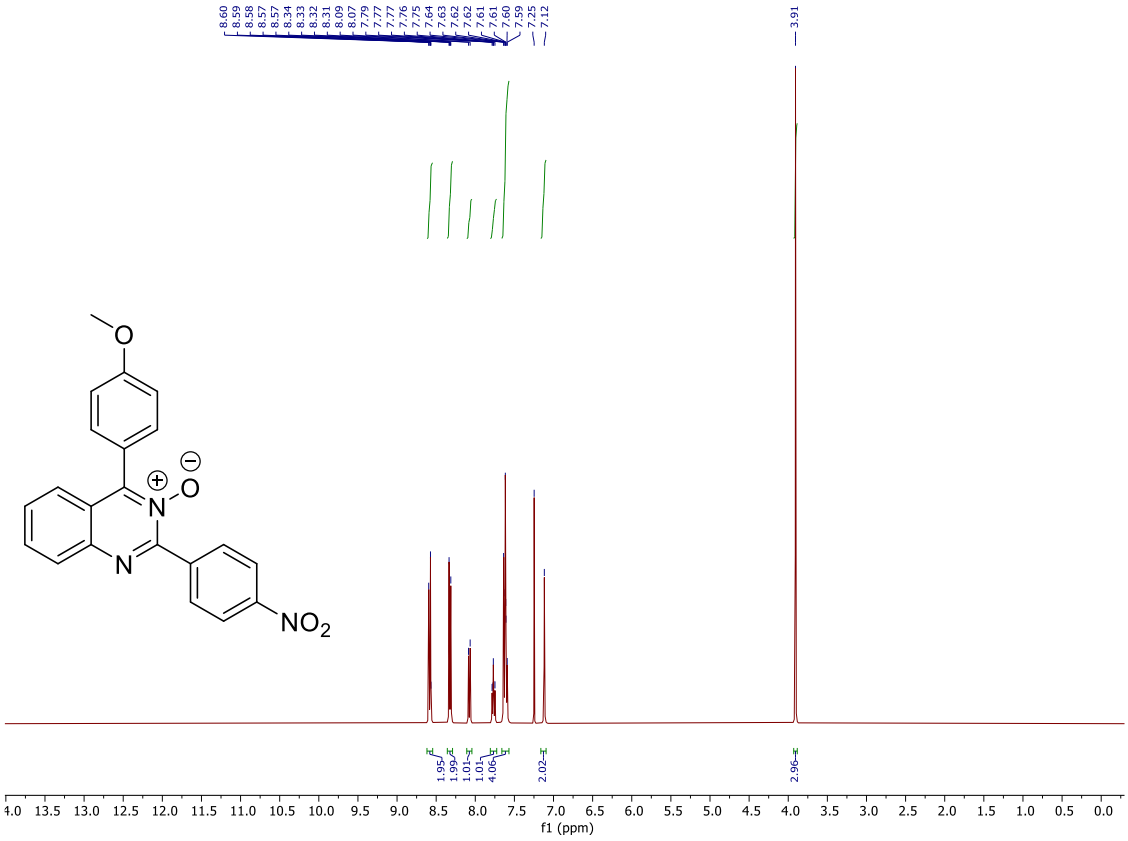


1: TOF MS ES+
2.38e+004

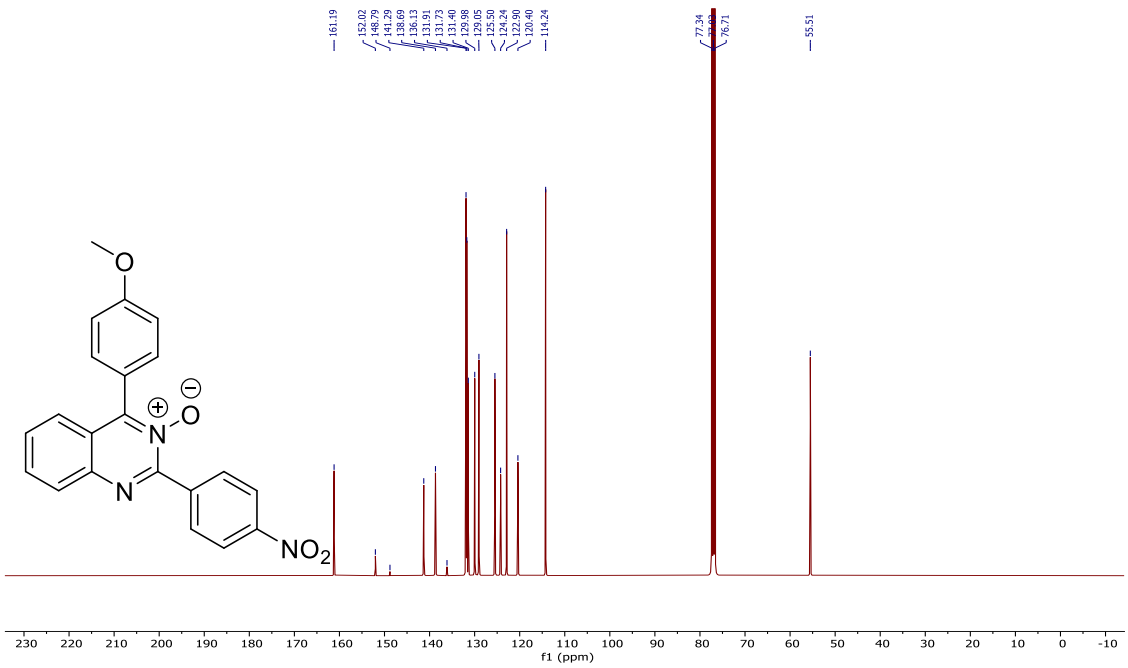


Minimum:				-5.5						
Maximum:		1000.0	1000.0	1000.0						
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula			
327.1139	327.1134	0.5	1.5	15.5	297.8	0.0	C21	H15	N2	O2

APPX 4.42 HRMS (ESI-TOF-MS) of compound **4n**



APPX 4.43 ^{1}H NMR (400 MHz, Chloroform-*d*) of compound **4o**

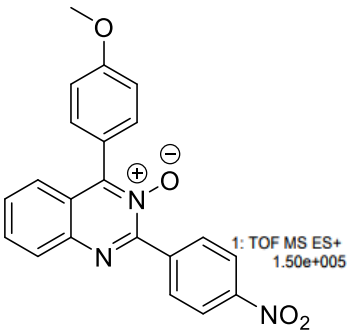


APPX 4.44 ^{13}C NMR (101 MHz, Chloroform-*d*) of compound **4o**

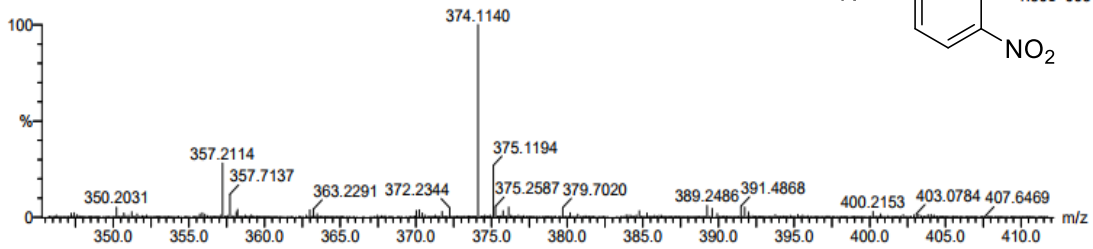
Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 1000.0 PPM / DBE: min = -5.5, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
1 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 20-21 H: 15-16 N: 3-3 O: 4-4
Necdet Coskun
32440_20210428_11-02 19 (0.741) Cm (10:23)

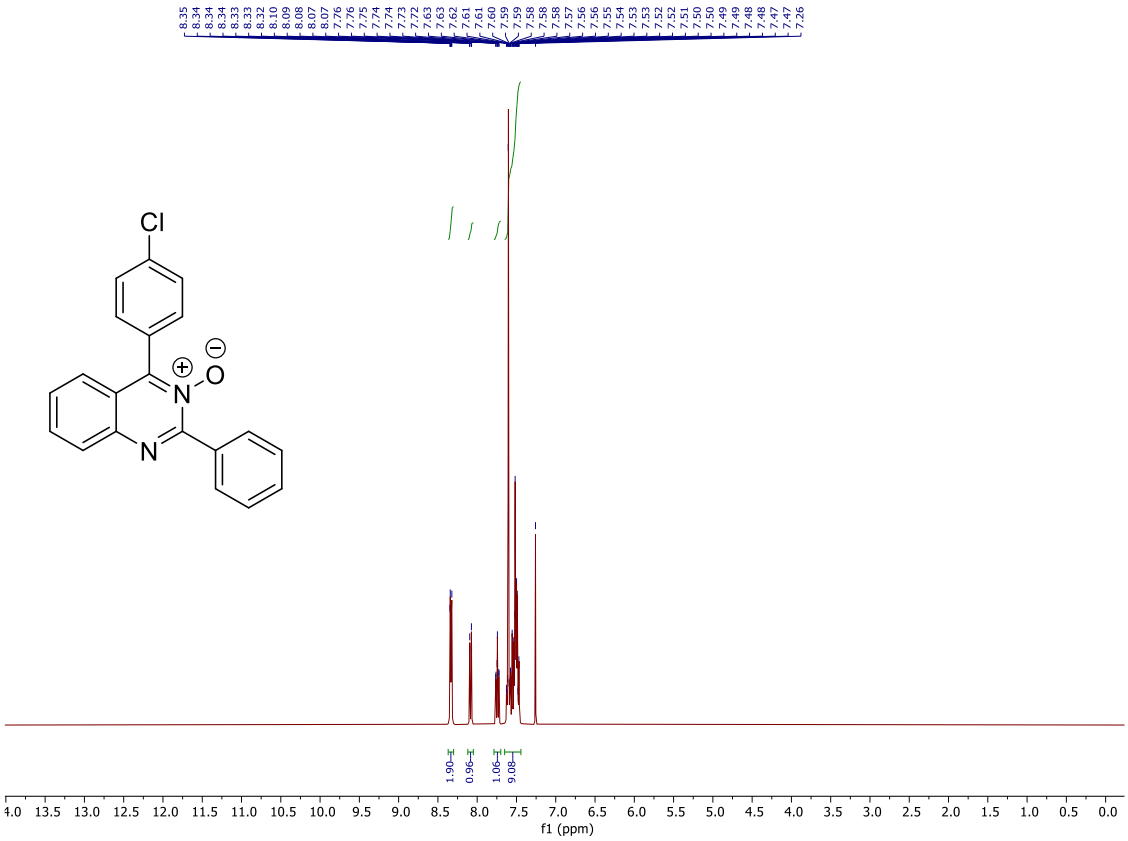


1: TOF MS ES+
1.50e+005

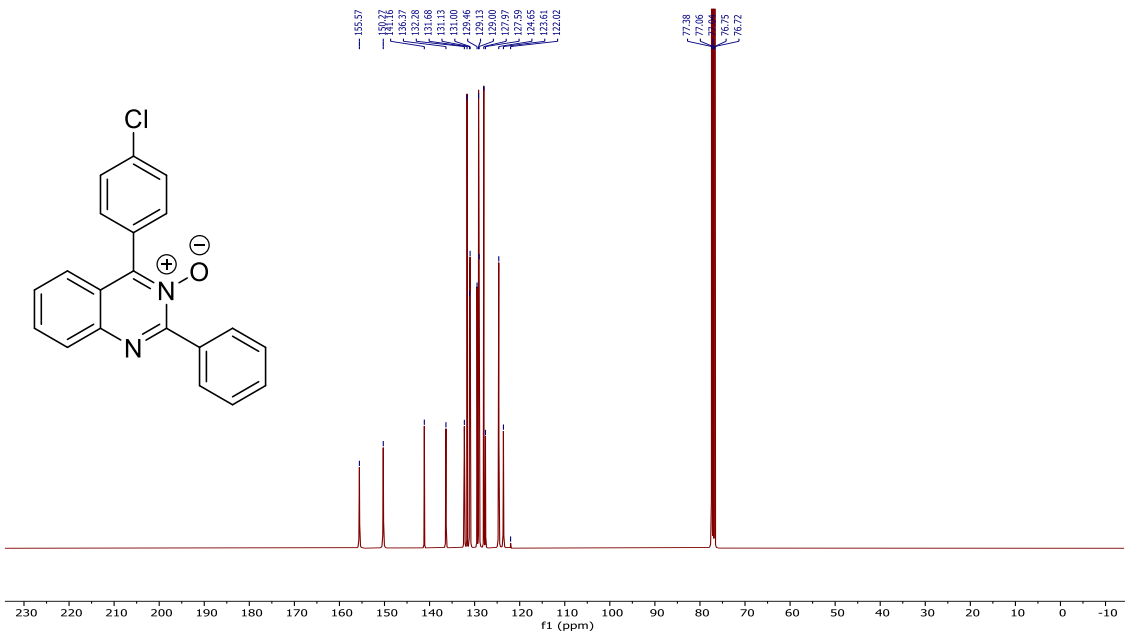


Minimum:				-5.5			
Maximum:		1000.0	1000.0	1000.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
374.1140	374.1141	-0.1	-0.3	15.5	445.8	0.0	C21 H16 N3 O4

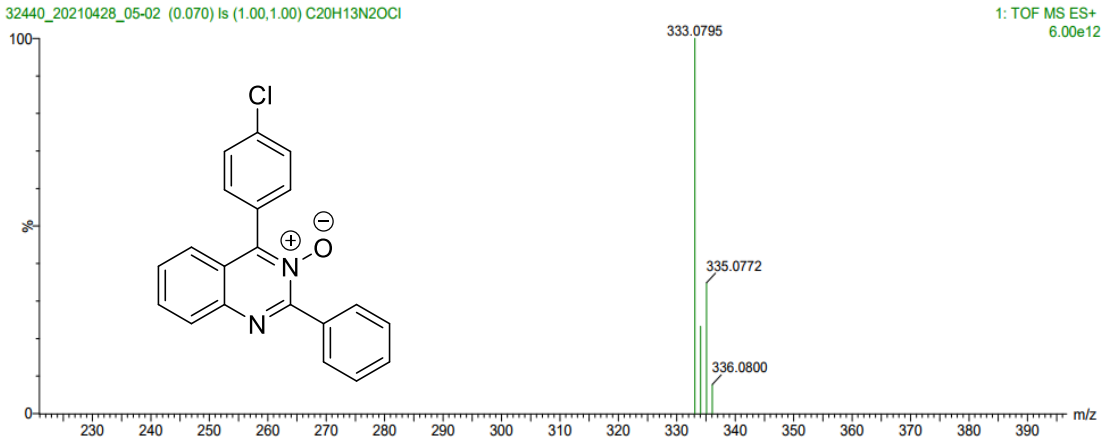
APPX 4.45 HRMS (ESI-TOF-MS) of compound **4o**



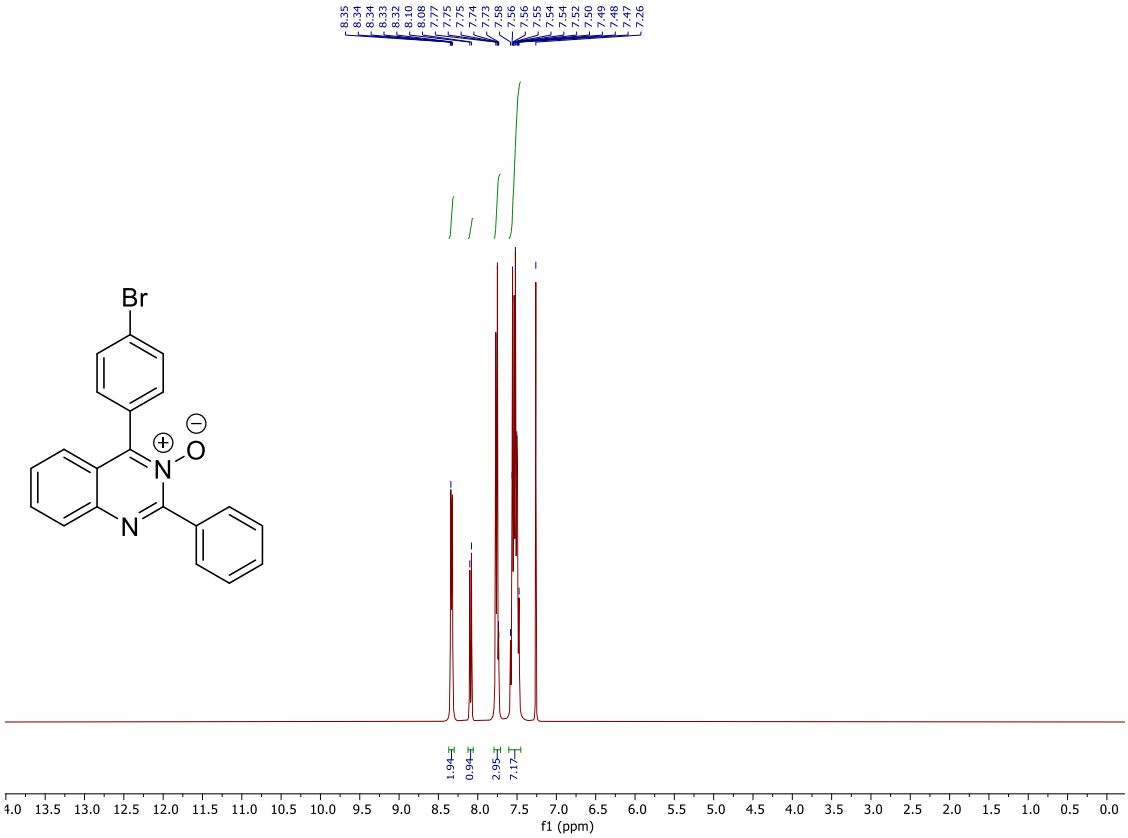
APPX 4.46 ^{1}H NMR (400 MHz, Chloroform-*d*) of compound **4p**



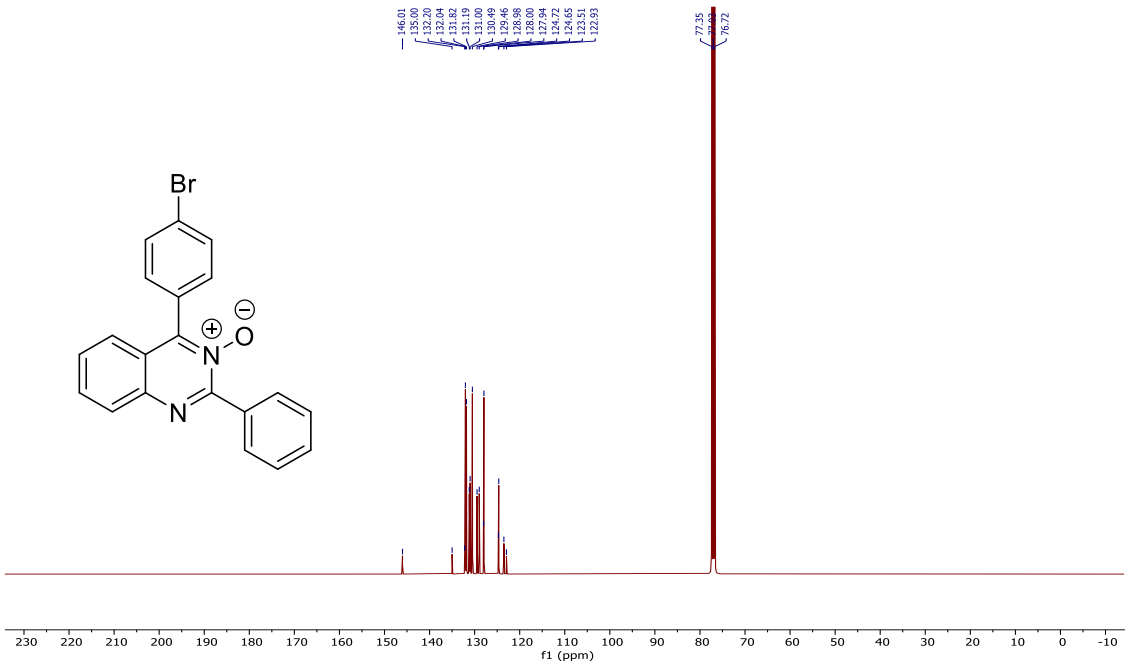
APPX 4.47 ^{13}C NMR (101 MHz, Chloroform-*d*) of compound **4p**



APPX 4.48 HRMS (ESI-TOF-MS) of compound **4p**



APPX 4.49 ^{1}H NMR (400 MHz, Chloroform-*d*) of compound **4q**

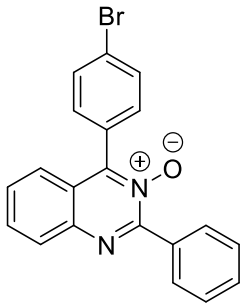


APPX 4.50 ^{13}C NMR (101 MHz, Chloroform-*d*) of compound **4q**

Elemental Composition Report **Page 1**

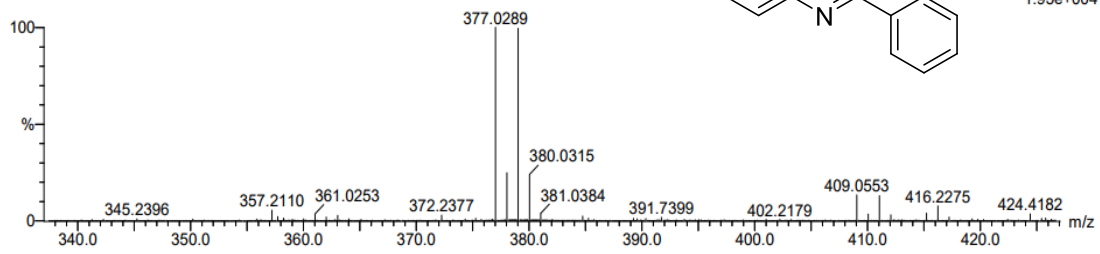
Single Mass Analysis
Tolerance = 1000.0 PPM / DBE: min = -5.5, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
6 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 20-21 H: 13-17 N: 2-3 O: 1-4 Br: 1-1



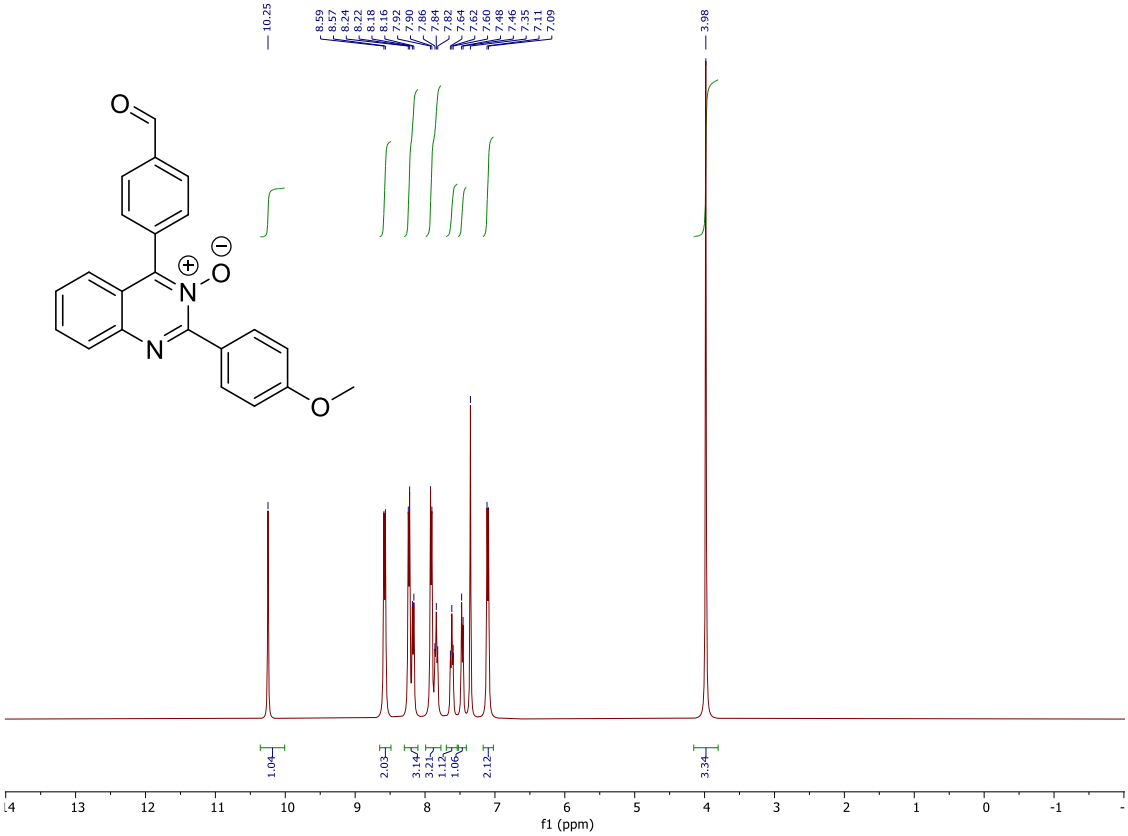
Necdet Coskun
32440_20210428_17-04 6 (0.260) Cm (1:8)

1: TOF MS ES+
1.95e+004

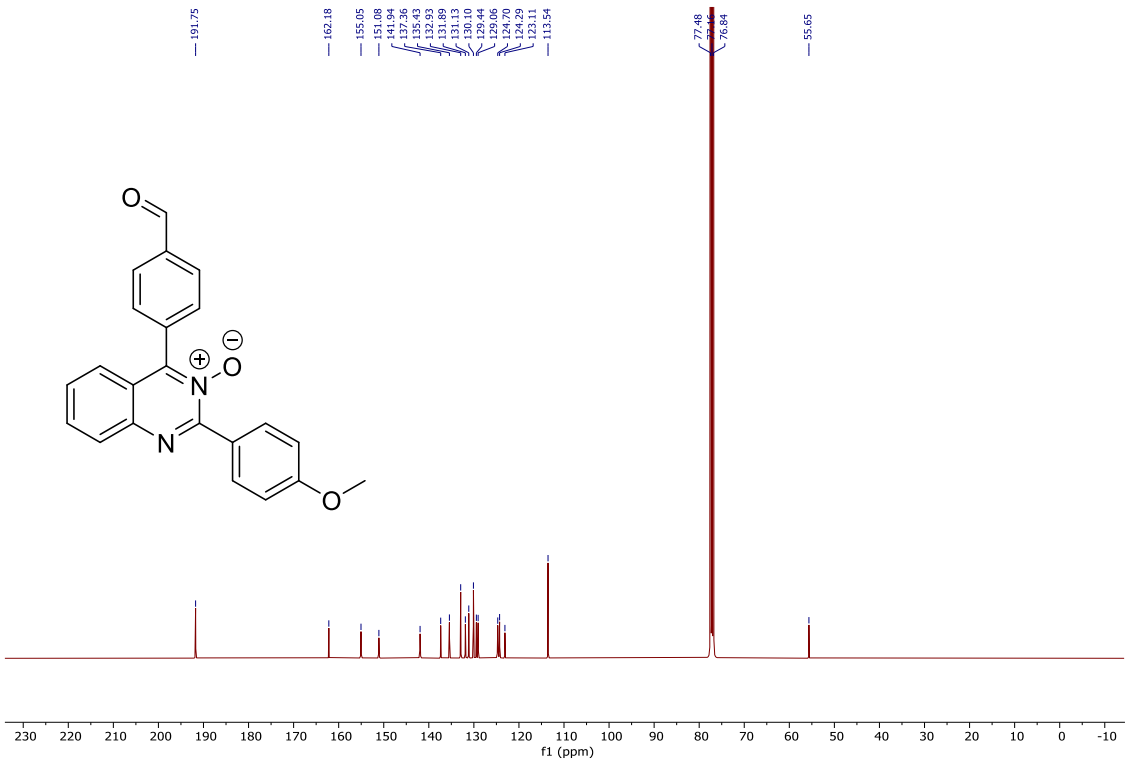


Minimum:				-5.5			
Maximum:		1000.0	1000.0	1000.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
377.0289	377.0289	0.0	0.0	14.5	284.9	0.0	C20 H14 N2 O Br

APPX 4.51 HRMS (ESI-TOF-MS) of compound **4q**



APPX 4.52 ^{1}H NMR (400 MHz, Chloroform-d) of compound **4r**

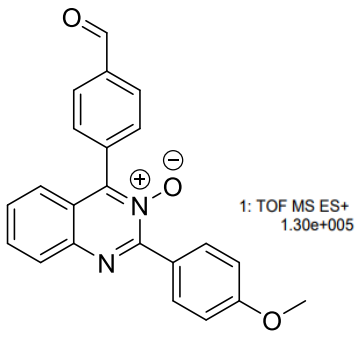


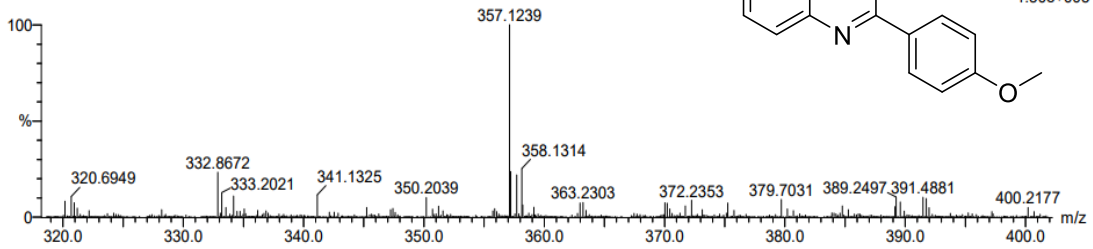
APPX 4.53 ^{13}C NMR (101 MHz, Chloroform-*d*) of compound **4r**

Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 1000.0 PPM / DBE: min = -5.5, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

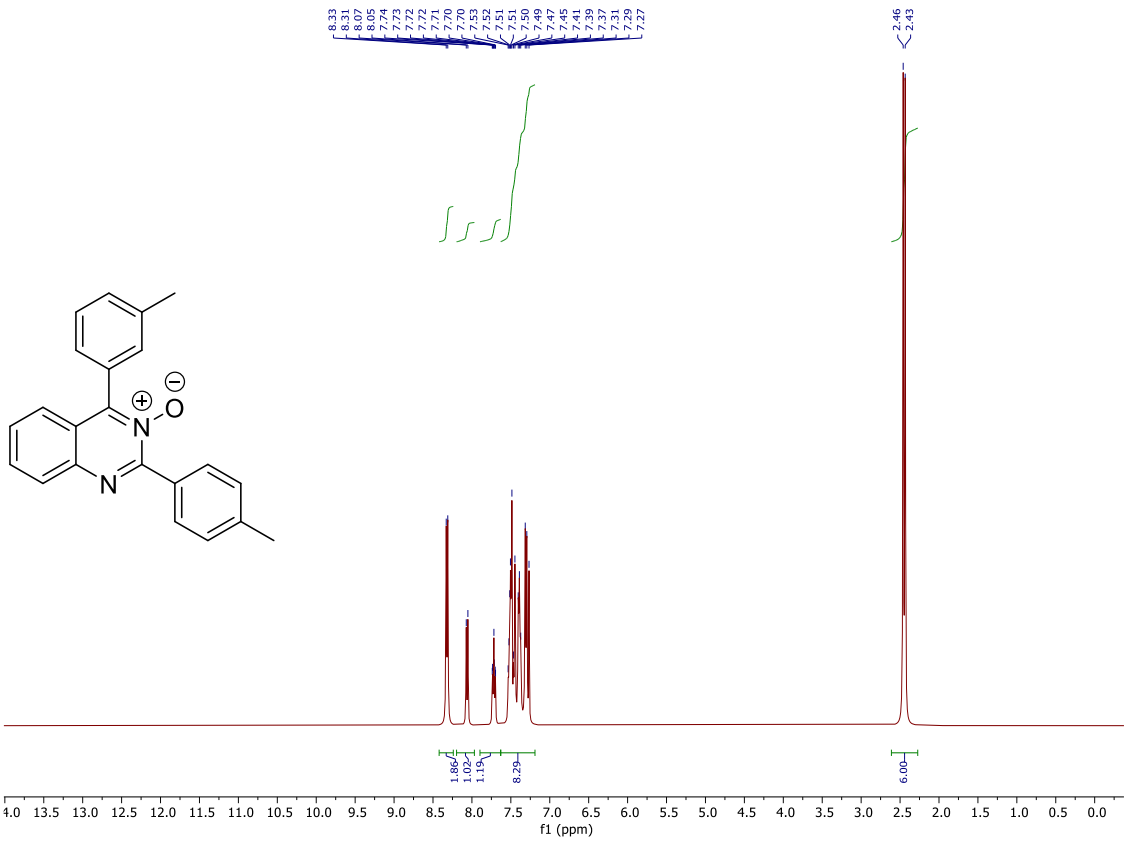
Monoisotopic Mass, Odd and Even Electron Ions
1 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 22-22 H: 13-17 N: 2-2 O: 3-3
Necdet Coskun
32440_20210428_15-01 10 (0.396) Cm (1:15)



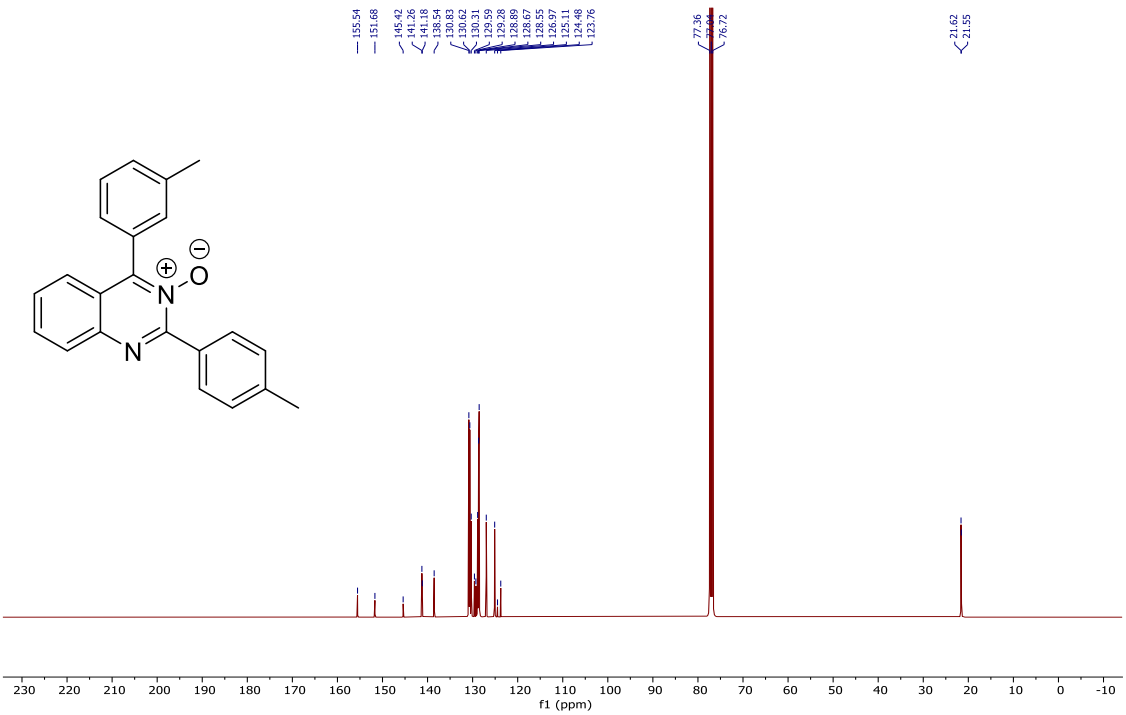


Minimum:				-5.5			
Maximum:		1000.0	1000.0	1000.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
357.1239	357.1239	0.0	0.0	15.5	422.1	0.0	C22 H17 N2 O3

APPX 4.54 HRMS (ESI-TOF-MS) of compound **4r**



APPX 4.55 ^{1}H NMR (400 MHz, Chloroform-*d*) of compound **4s**

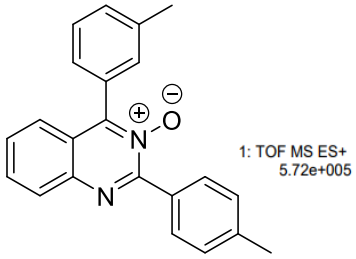


APPX 4.56 ^{13}C NMR (101 MHz, Chloroform-*d*) of compound **4s**

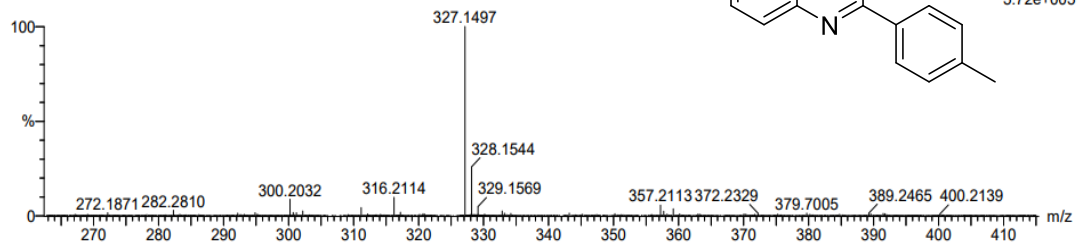
Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 1000.0 PPM / DBE: min = -5.5, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Odd and Even Electron Ions
1 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 20-28 H: 15-19 N: 2-2 O: 1-1
Necdet Coskun
32440_20210428_12-02 10 (0.396) Cm (1:10)

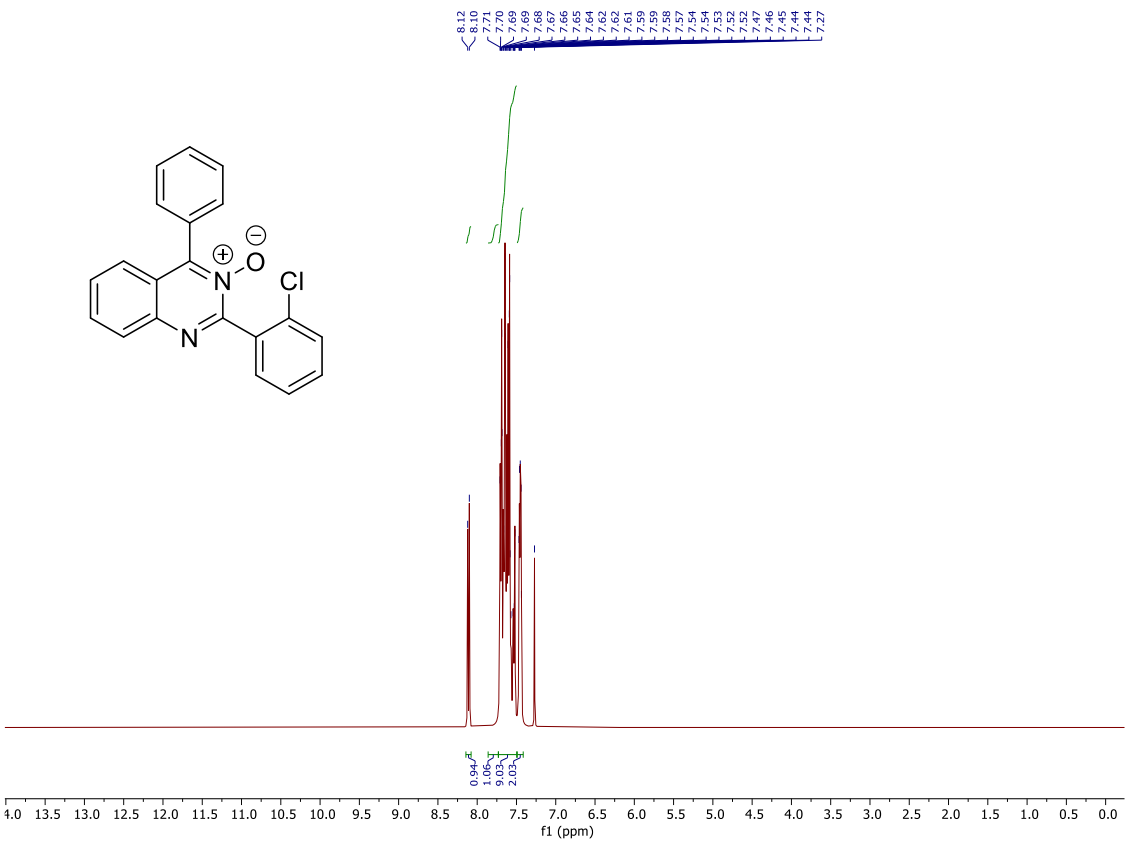


1: TOF MS ES+
5.72e+005

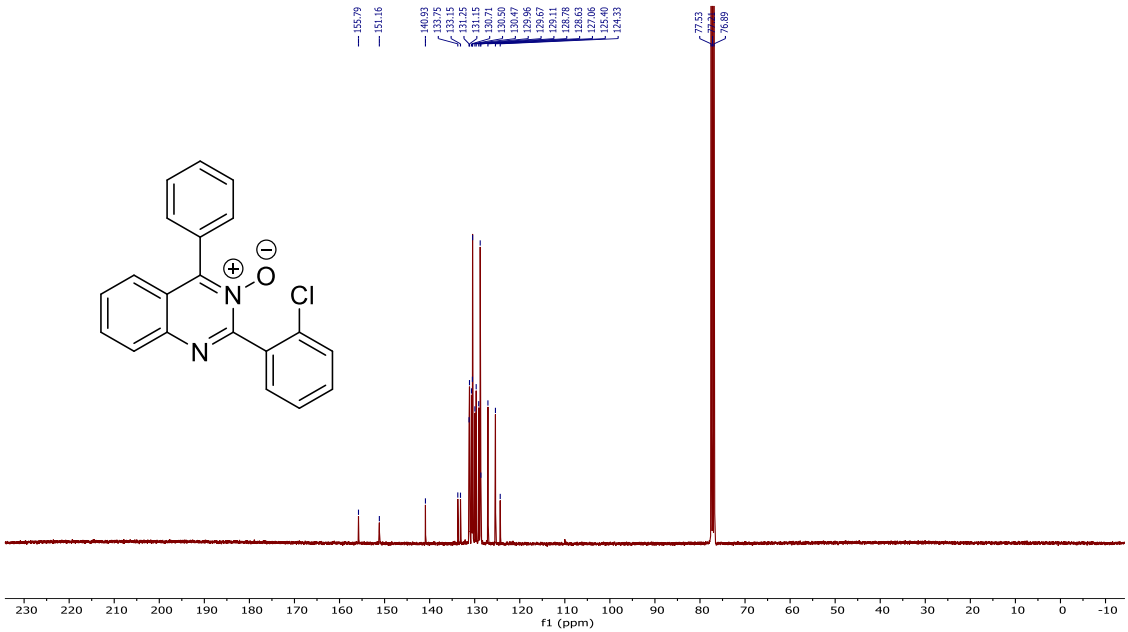


Minimum:				-5.5			
Maximum:		1000.0	1000.0	1000.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
327.1497	327.1497	0.0	0.0	14.5	664.0	0.0	C22 H19 N2 O

APPX 4.57 HRMS (ESI-TOF-MS) of compound **4s**



APPX 4.58 ^{1}H NMR (400 MHz, Chloroform-*d*) of compound **4t**

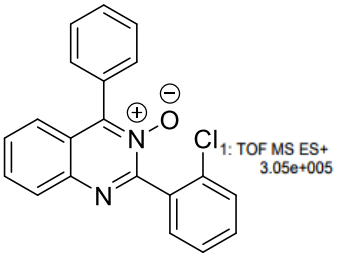


APPX 4.59 ^{13}C NMR (101 MHz, Chloroform-d) of compound **4t**

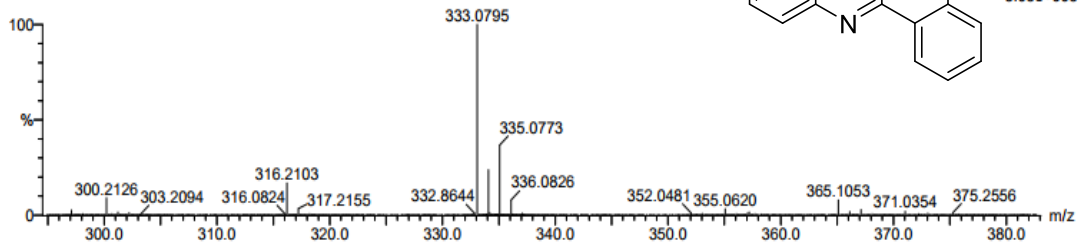
Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 1000.0 PPM / DBE: min = -5.5, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Odd and Even Electron Ions
1 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 20-20 H: 13-14 N: 2-2 O: 1-1 Cl: 1-1
Necdet Coskun
32440_20210428_20-02 5 (0.206) Cm (1:11)



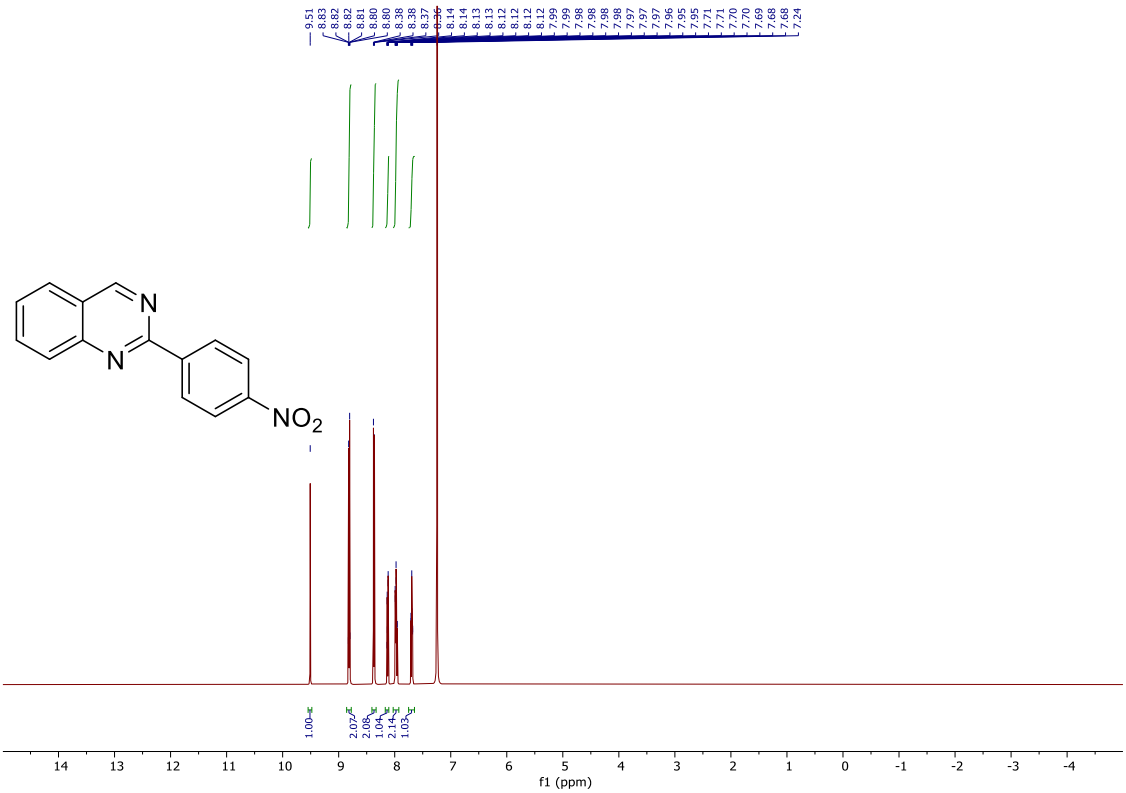
1: TOF MS ES+
3.05e+005



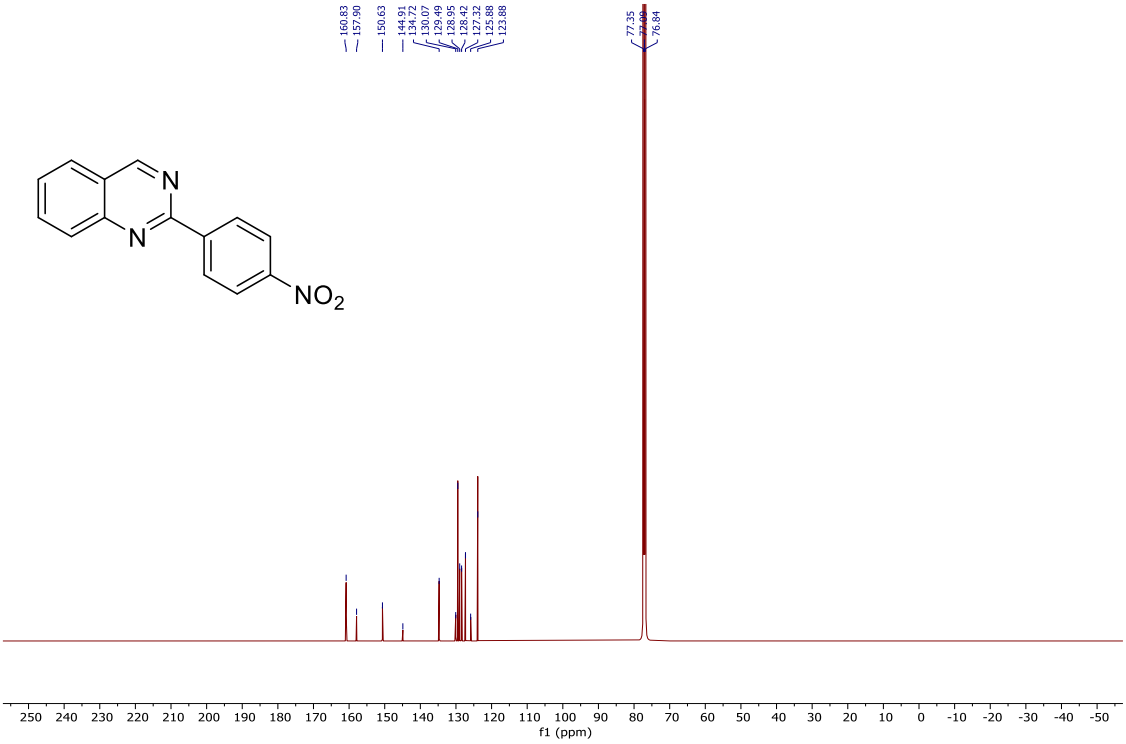
Minimum:				-5.5			
Maximum:		1000.0	1000.0	1000.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
333.0795	333.0795	0.0	0.0	14.5	621.1	0.0	C20 H14 N2 O Cl

APPX 4.60 HRMS (ESI-TOF-MS) of compound **4t**

APPX 5 NMR Spectra of compound **5**

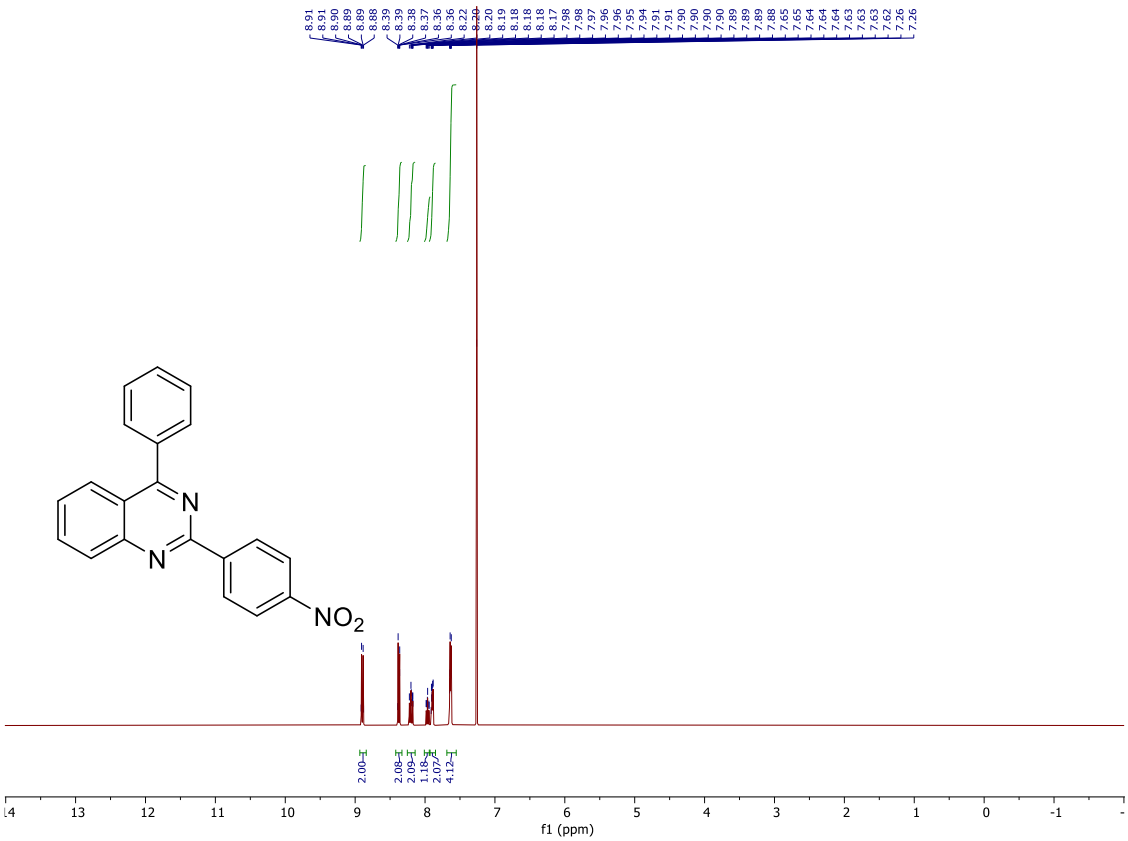


APPX 5.1 ^{1}H NMR (500 MHz, Chloroform-*d*) of Compound **5**

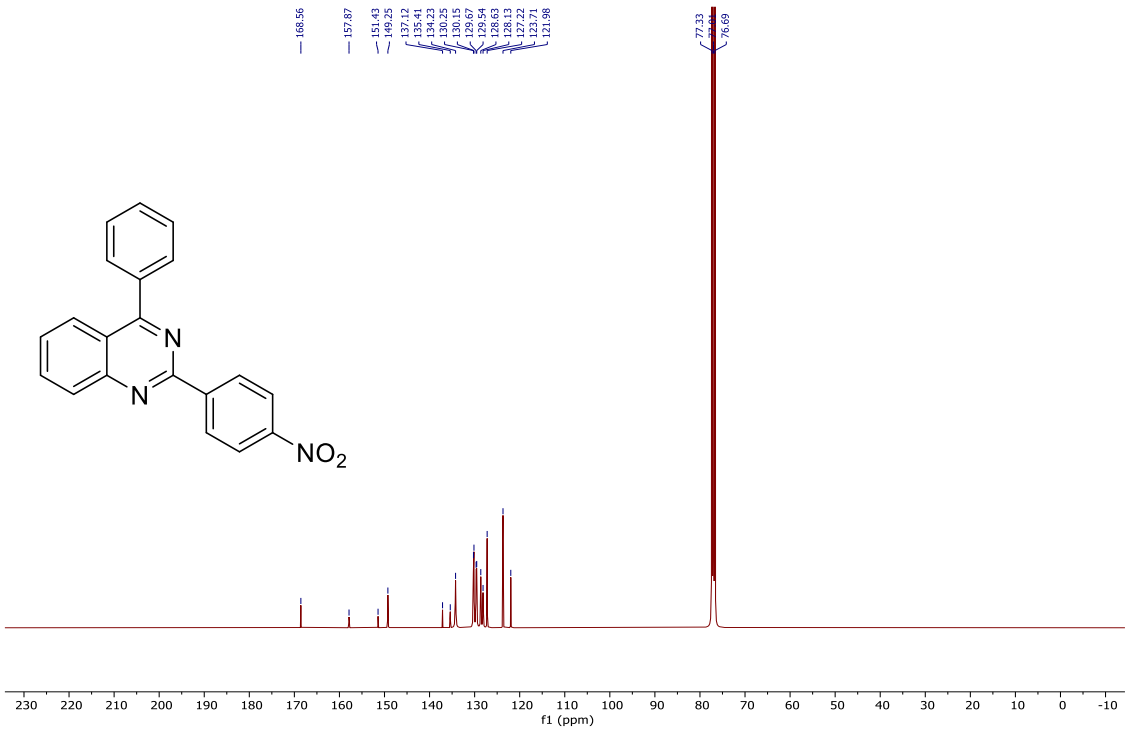


APPX 5.2 ^{13}C NMR (125 MHz, Chloroform-d) of compound **5**

APPX 6 NMR Spectra of compound **6**

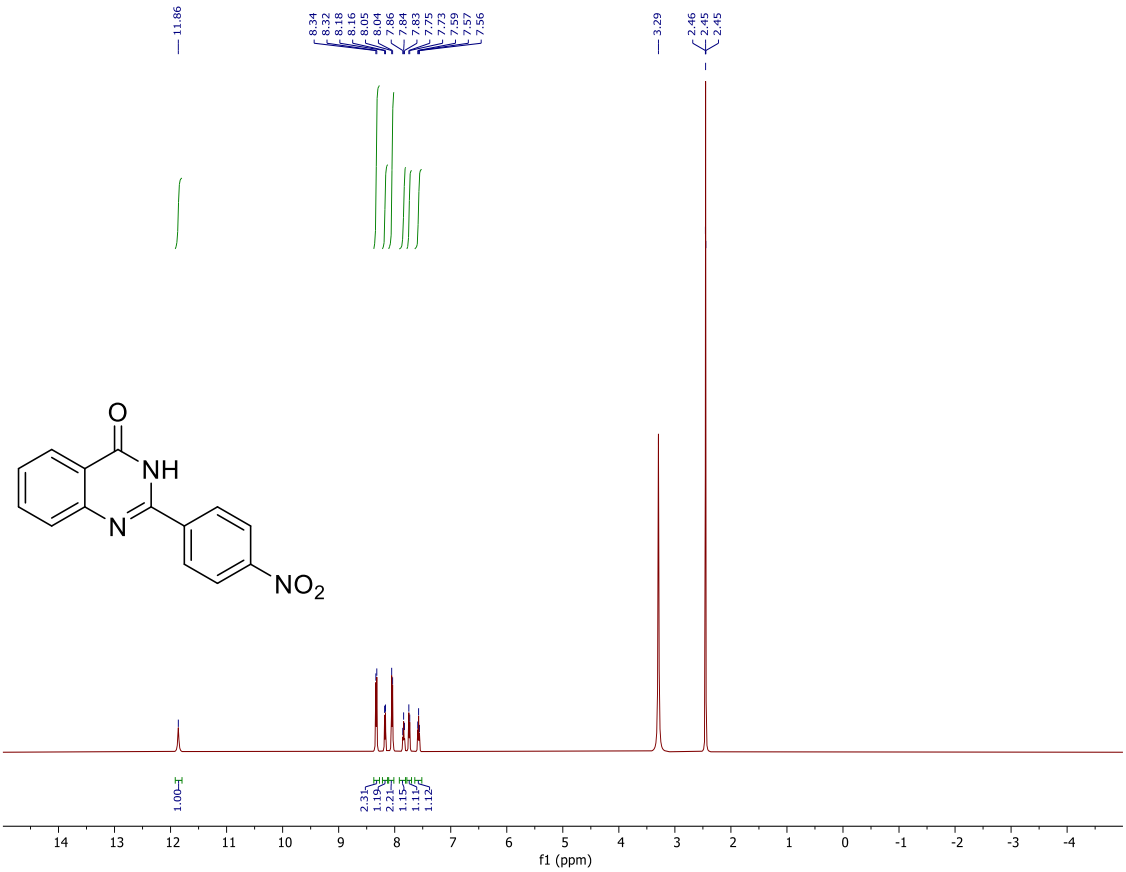


APPX 6.1 ^{1}H NMR (400 MHz, Chloroform-*d*) of compound **6**

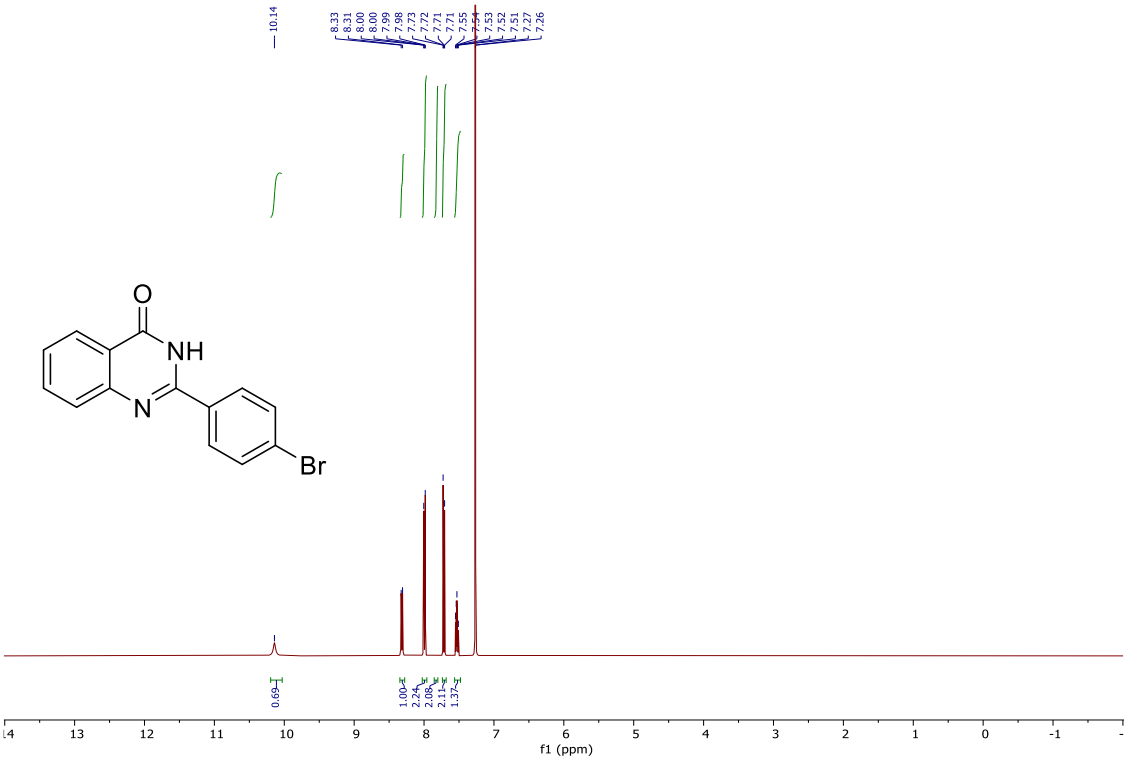


APPX 6.2 ^{13}C NMR (101 MHz, Chloroform-d) of compound **6**

APPX 7 NMR Spectra of compound **7**

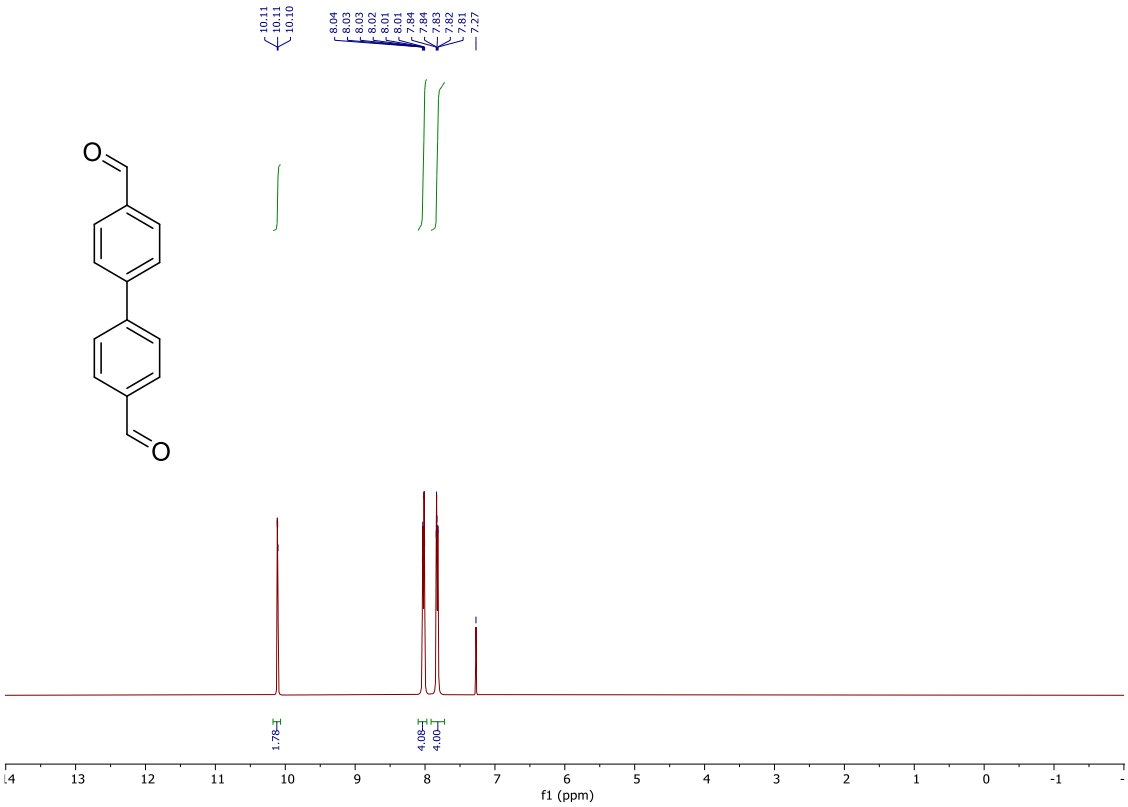


APPX 7.1 ^{1}H NMR (500 MHz, DMSO-d_6) of compound **7a**

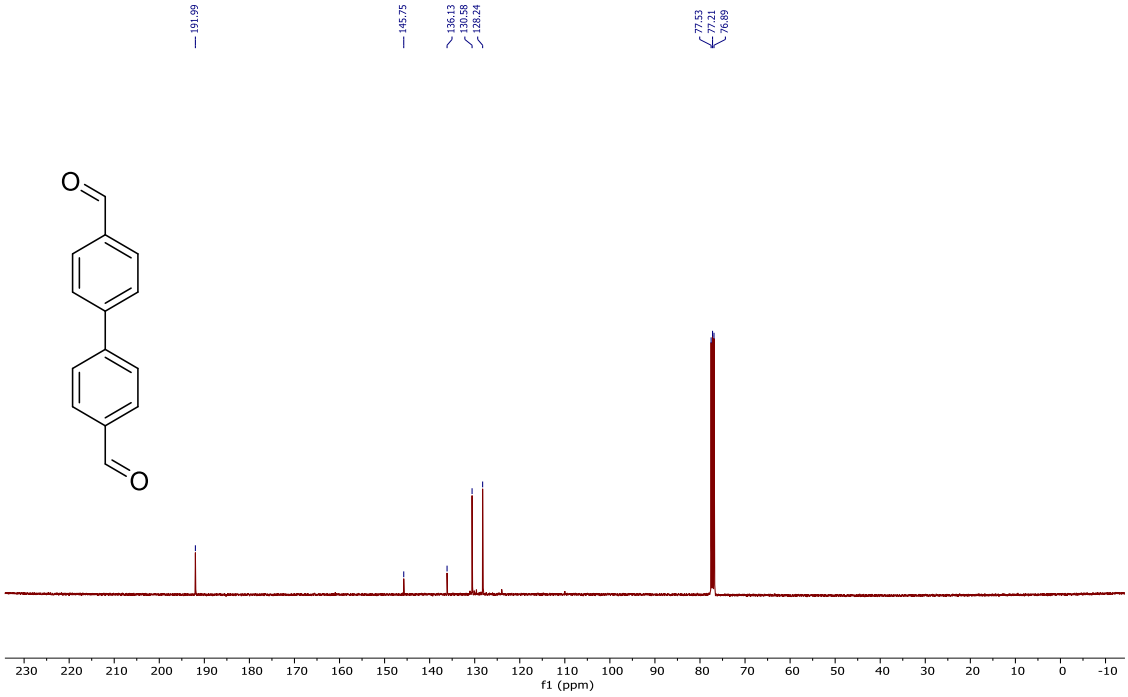


APPX 7.2[1]H NMR (400 MHz, Chloroform-d_6) of compound **7b**

APPX 8 NMR Spectra of compound **8**

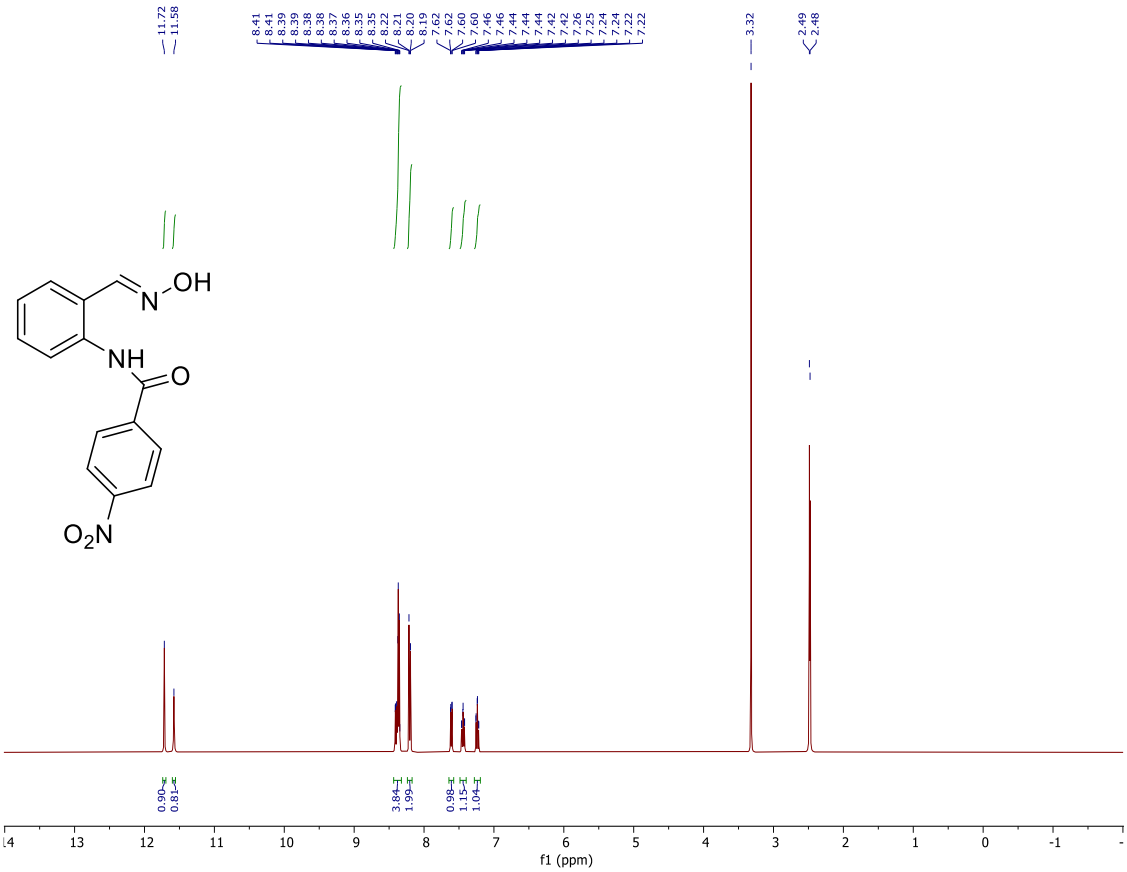


APPX 8.1 ^{1}H NMR (400 MHz, Chloroform-*d*) of compound **8**

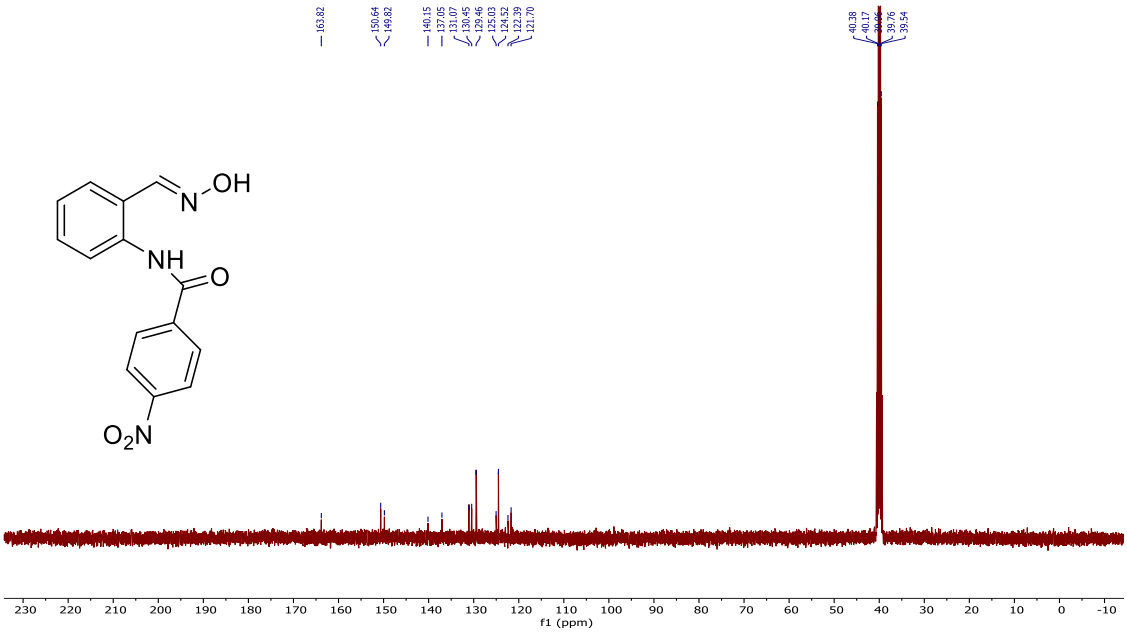


APPX 8.2 ^{13}C NMR (101 MHz, Chloroform-d) of compound **8**

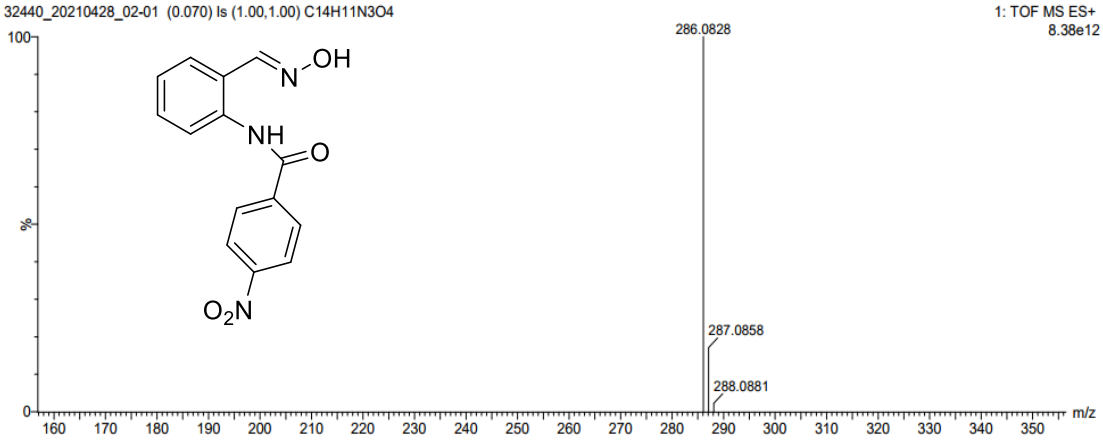
APPX 9 NMR and HRMS Spectra of compound **9**



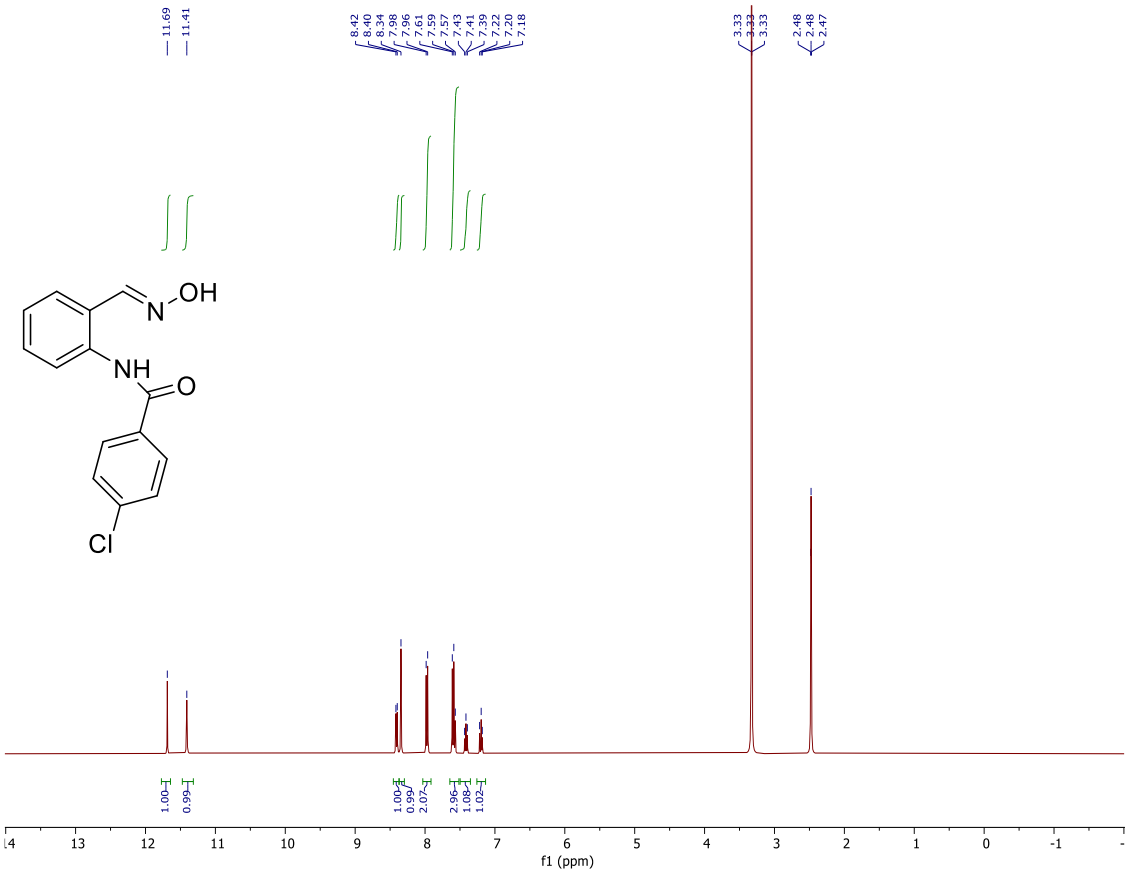
APPX 9.1 ^{1}H NMR (400 MHz, DMSO-d_6) of compound **9a**



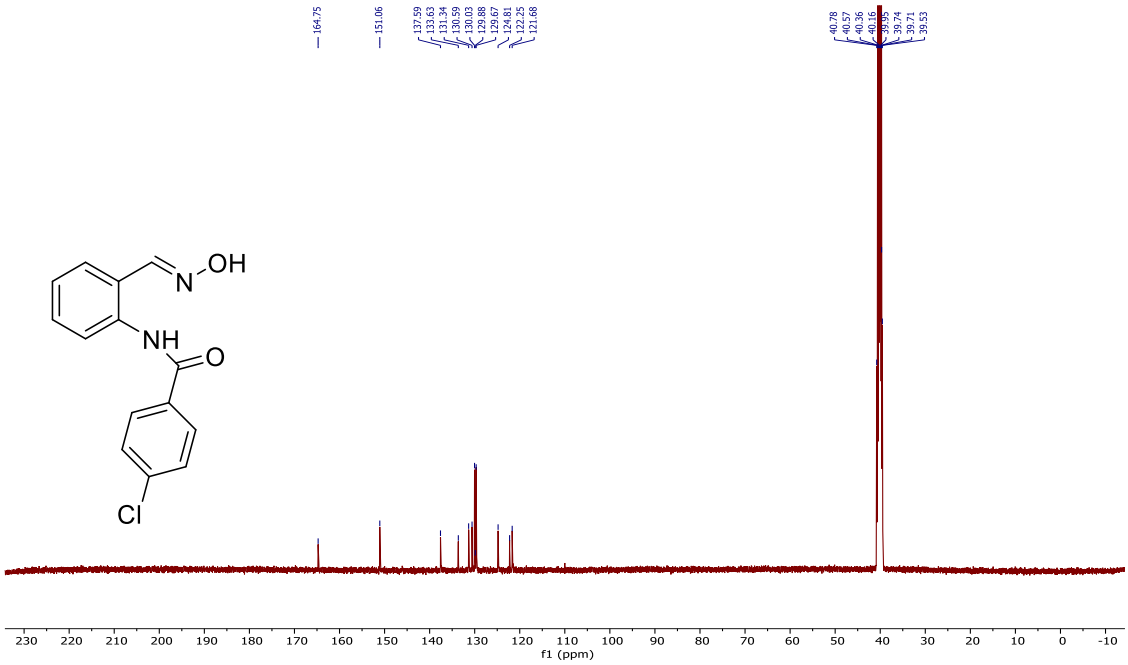
APPX 9.2 ^{13}C NMR (101 MHz, DMSO-d_6) of compound **9a**



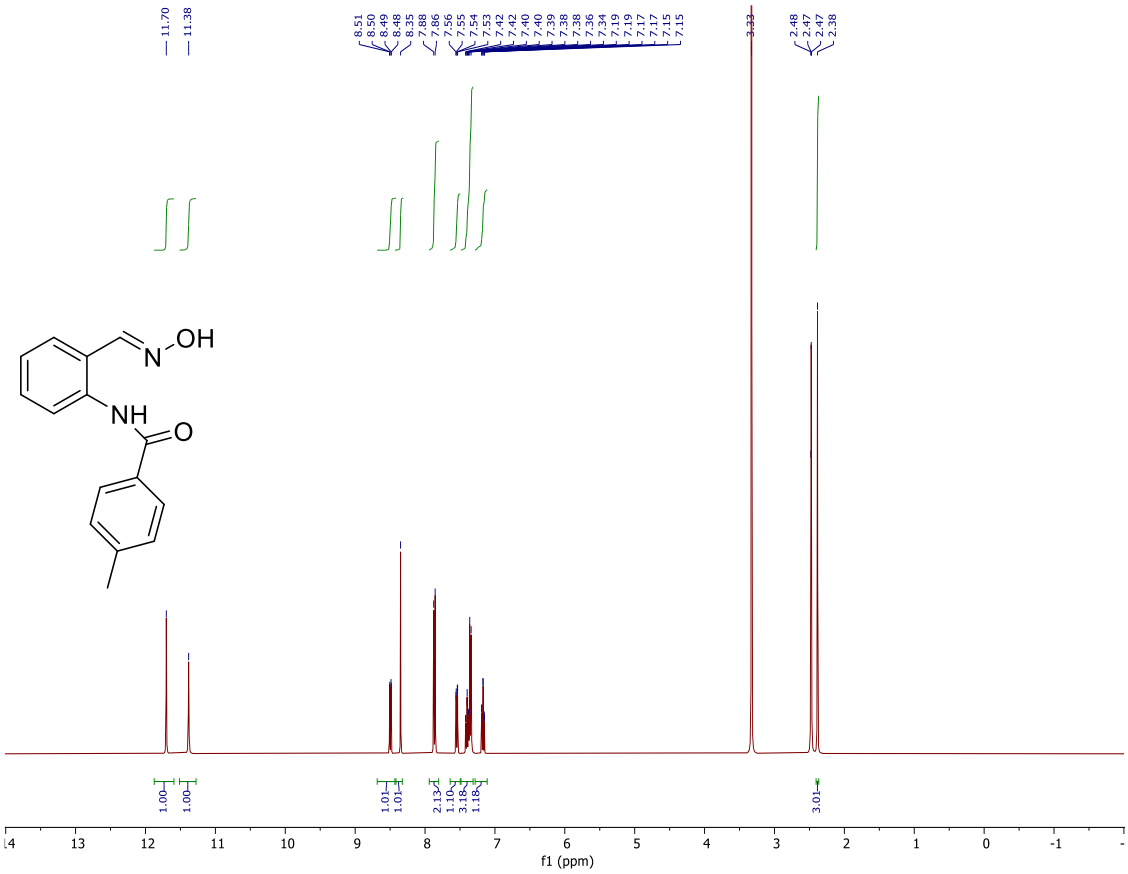
APPX 9.3 Supporting file-1HRMS (ESI-TOF-MS) of compound **9a**



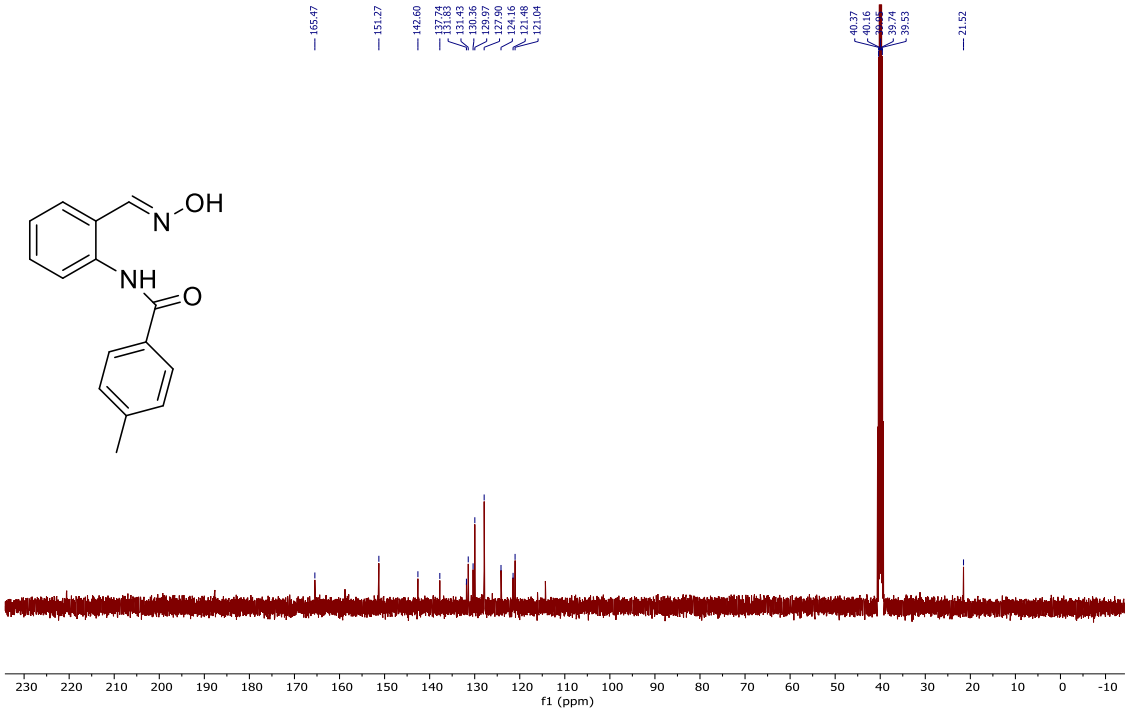
APPX 9.4 ^{1}H NMR (400 MHz, DMSO-d_6) of compound **9b**



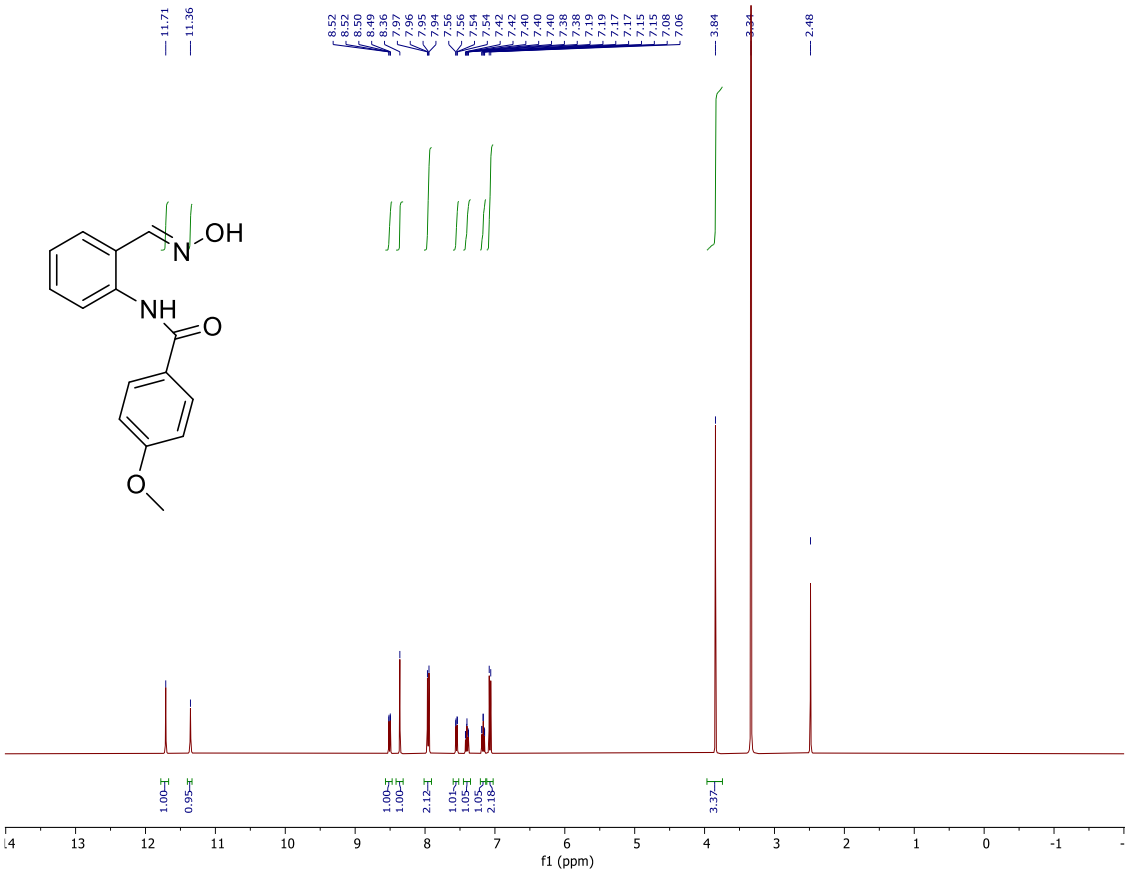
APPX 9.5 ^{13}C NMR (101 MHz, DMSO-d$_6$) of compound **9b**



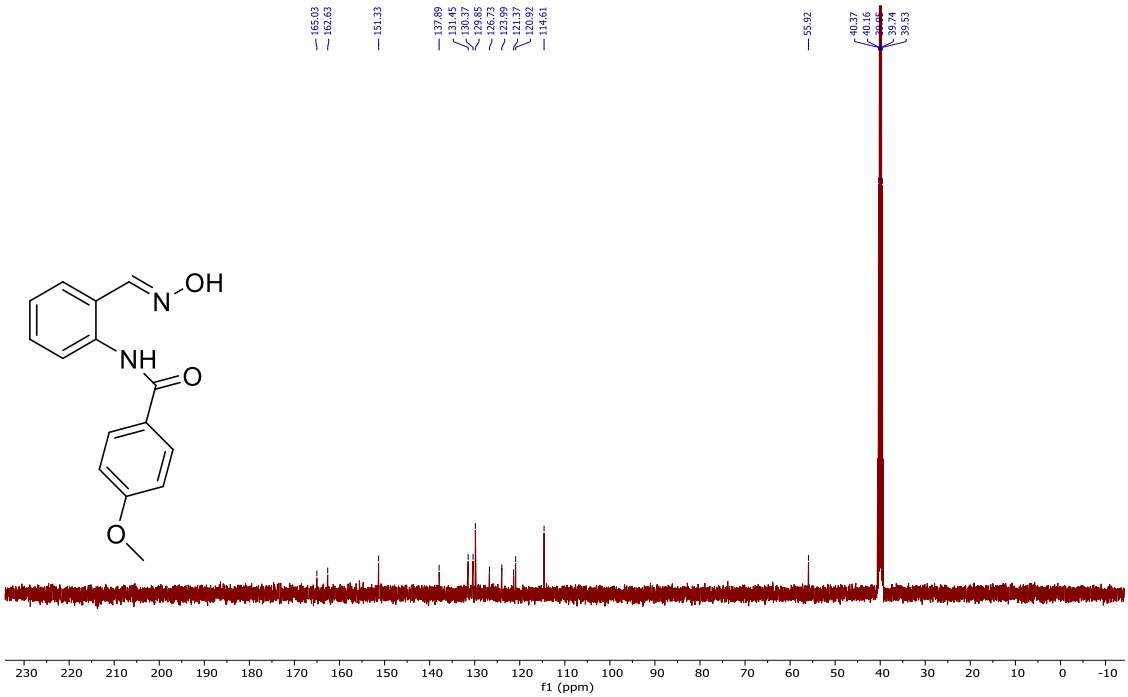
APPX 9.6 ^{1}H NMR (400 MHz, DMSO-d_6) of compound **9c**



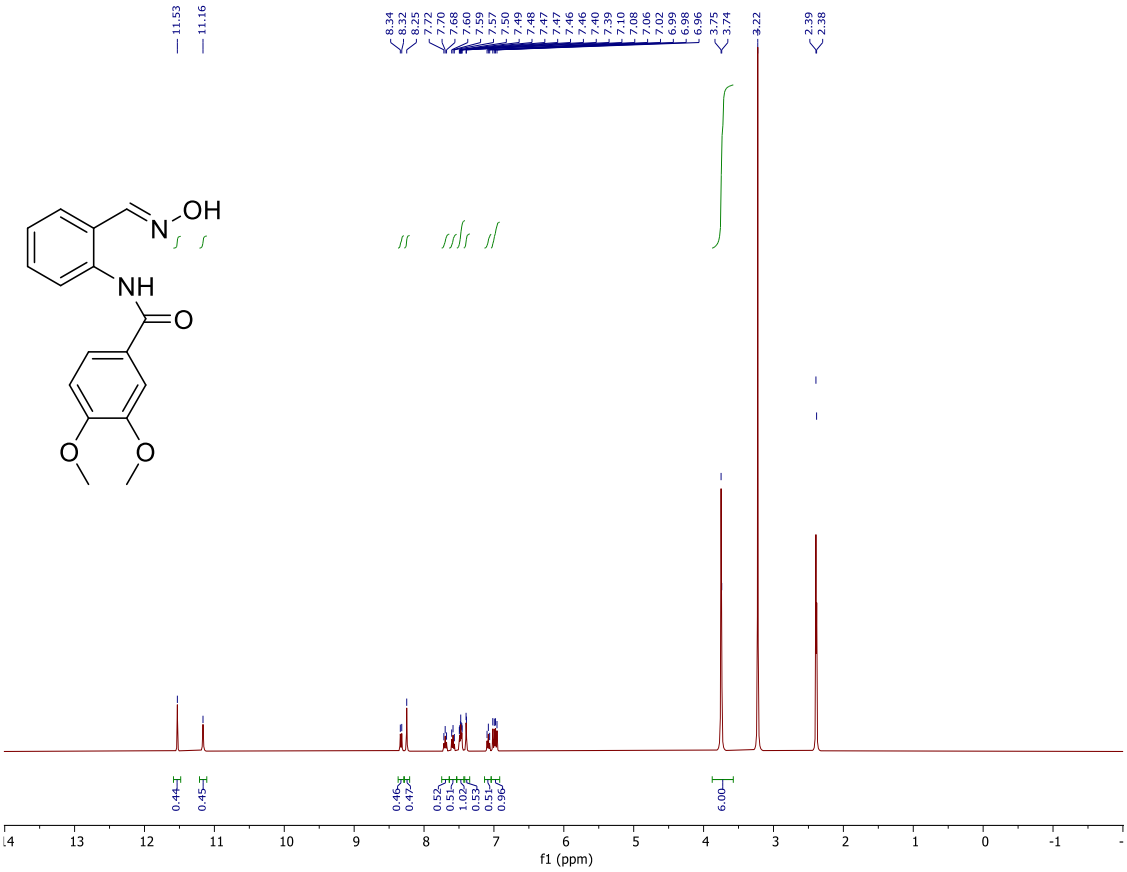
APPX 9.7 ^{13}C NMR (101 MHz, DMSO-d$_6$) of compound **9c**



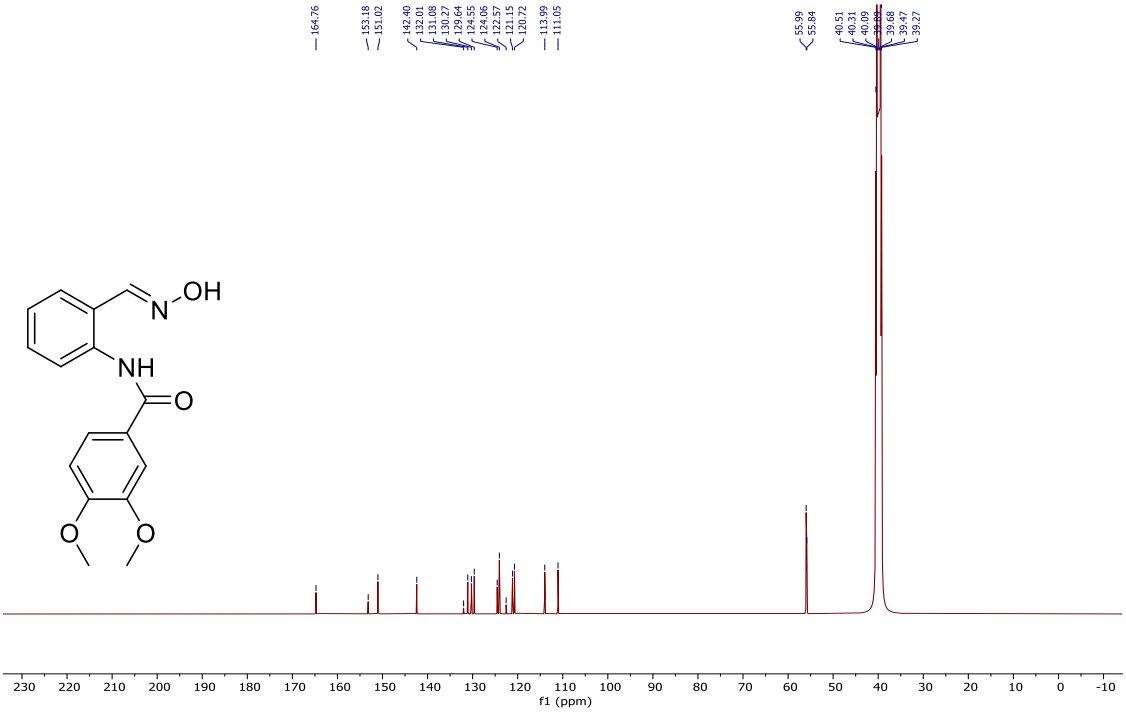
APPX 9.8 ^{1}H NMR (400 MHz, DMSO-d_6) of compound **9d**



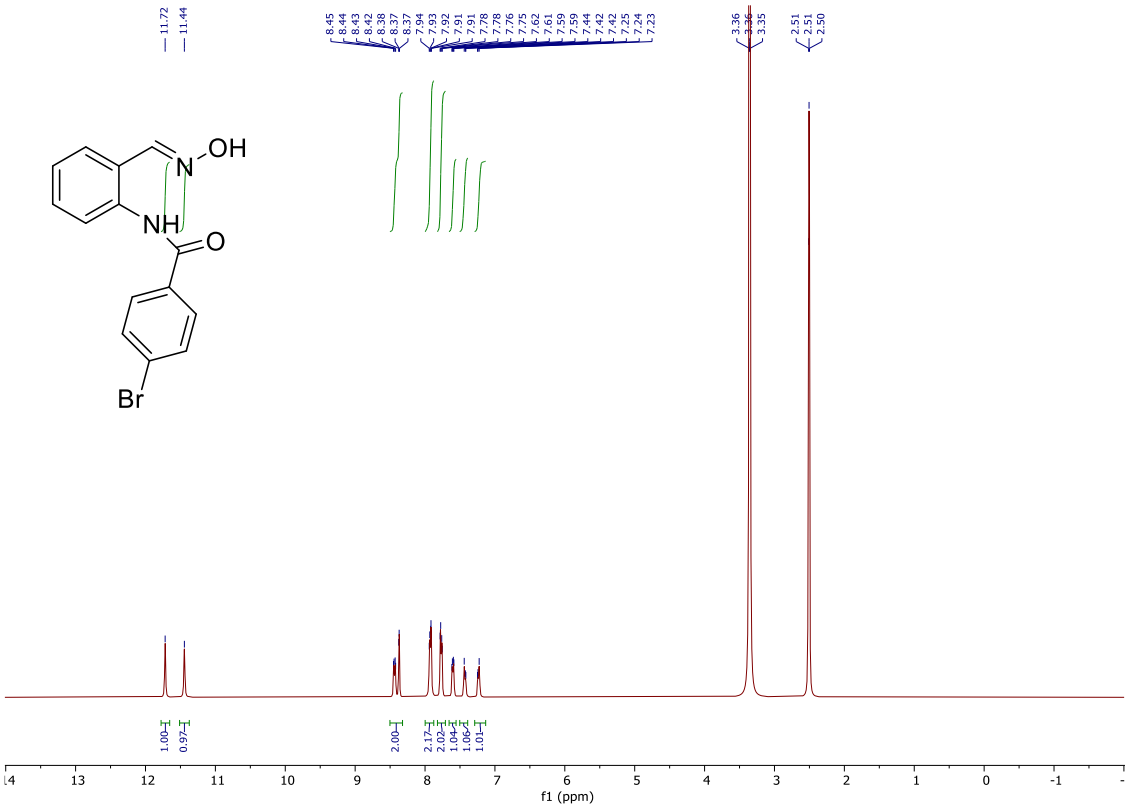
APPX 9.9 ^{13}C NMR (101 MHz, DMSO-d_6) of compound **9d**



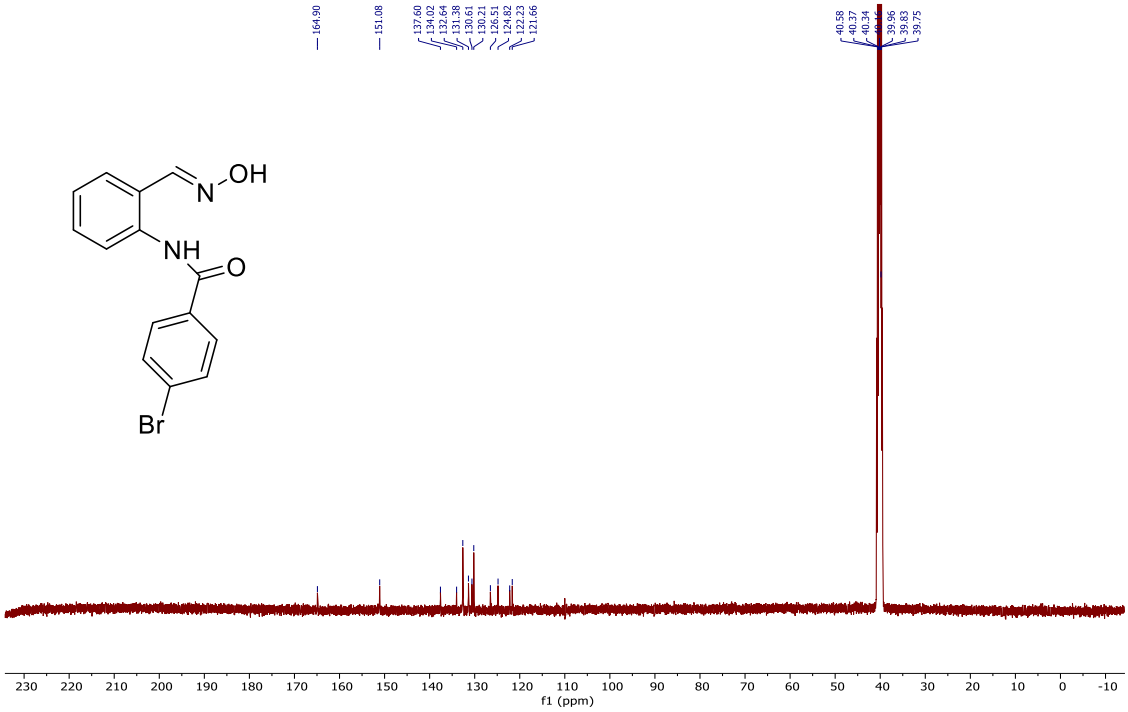
APPX 9.10 ^{1}H NMR (400 MHz, DMSO-d_6) of compound **9e**



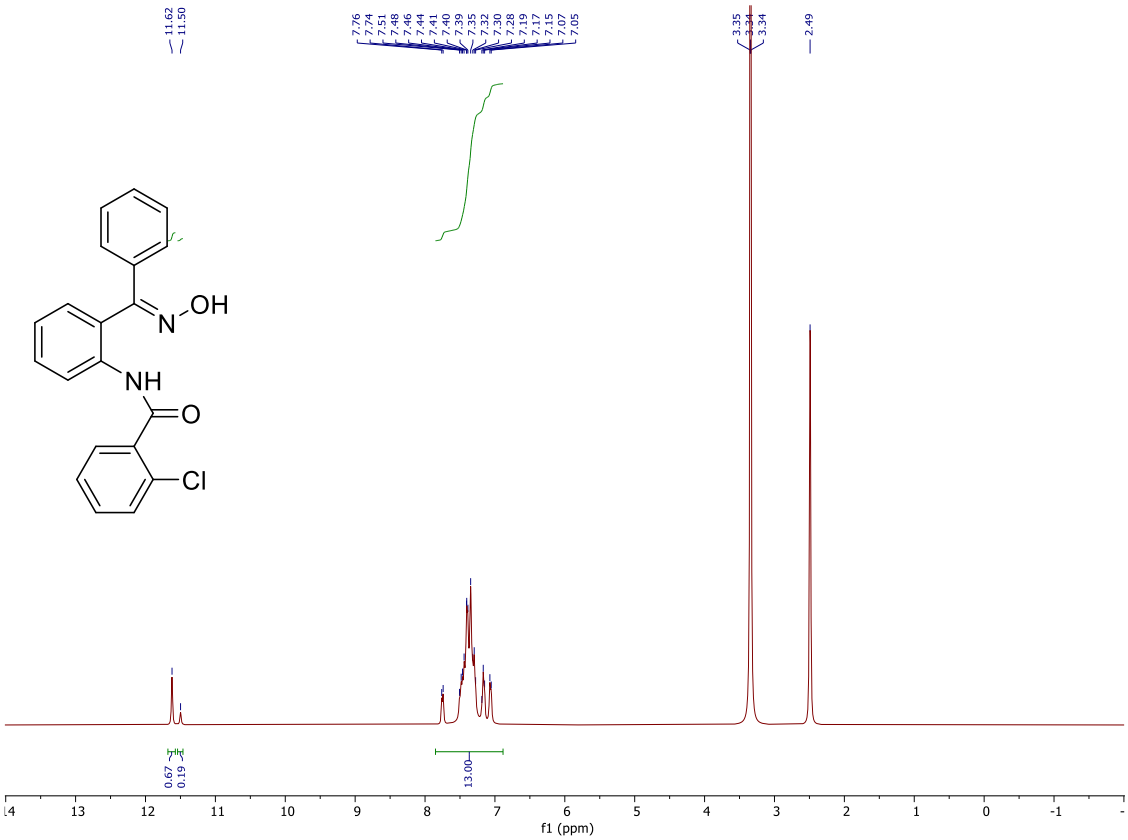
APPX 9.11 ^{13}C NMR (101 MHz, DMSO-d_6) of compound **9e**



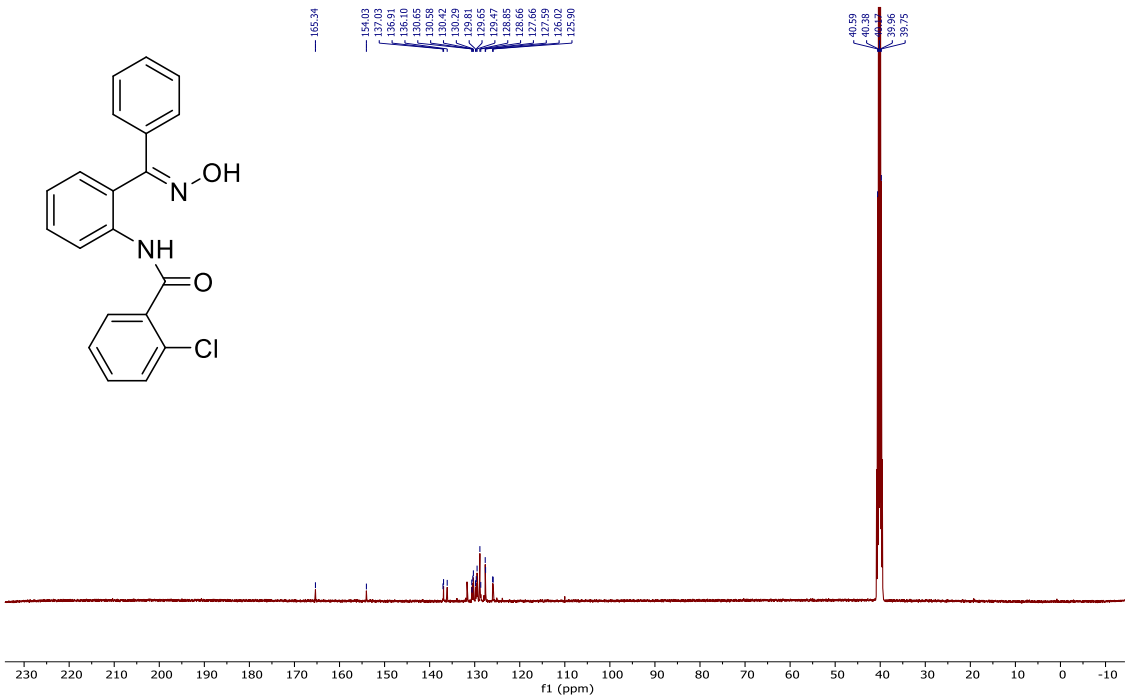
APPX 9.12 ^{1}H NMR (400 MHz, DMSO-d_6) of compound **9f**



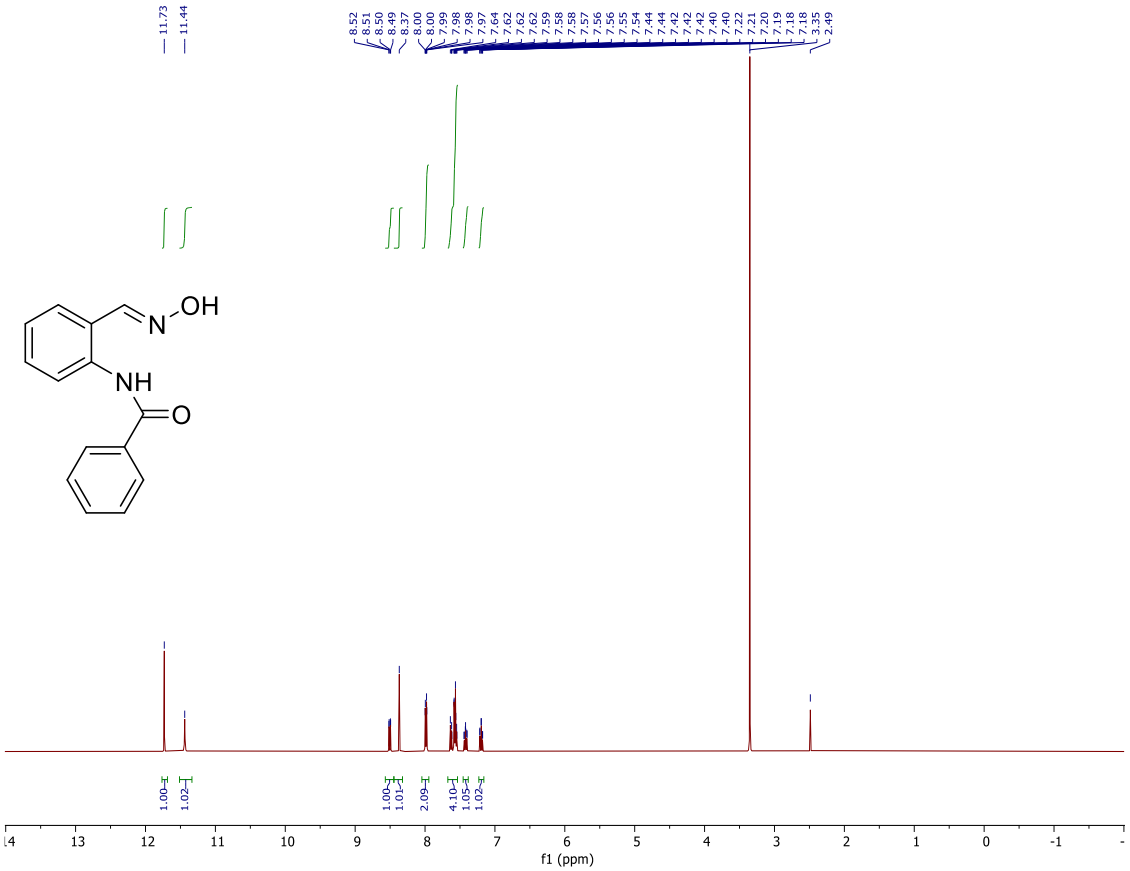
APPX 9.13 ^{13}C NMR (101 MHz, DMSO-d_6) of compound **9f**



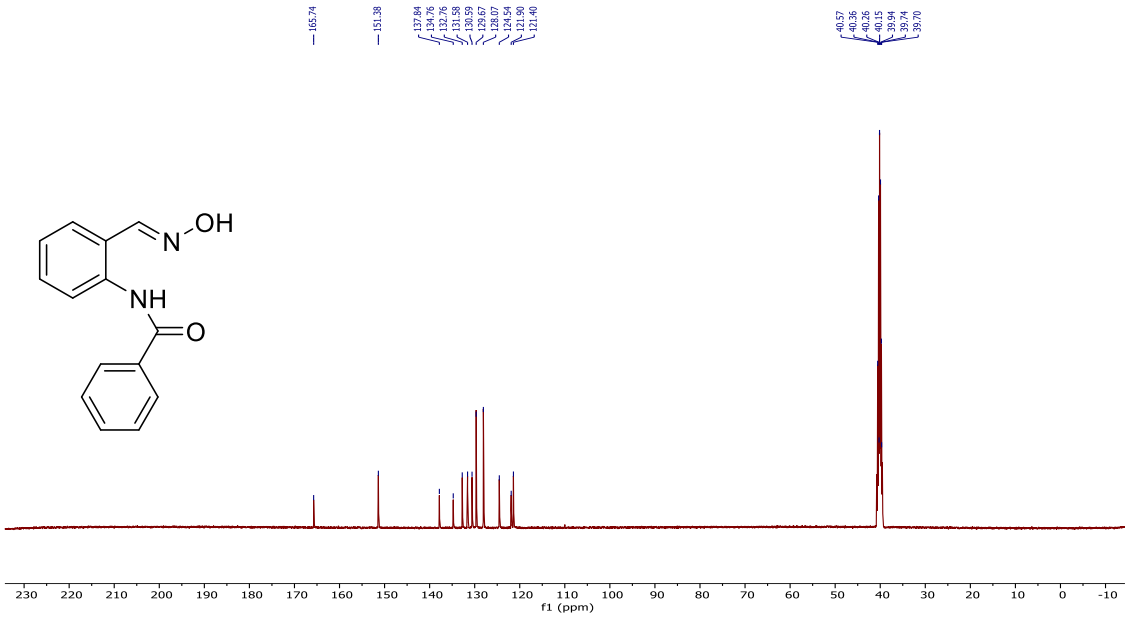
APPX 9.14 ^{1}H NMR (400 MHz, DMSO-d_6) of compound **9g**



APPX 9.15 ^{13}C NMR (101 MHz, DMSO-d_6) of compound **9g**



APPX 9.16 ^{1}H NMR (400 MHz, DMSO-d_6) of compound **9h**



APPX 9.17 ^{13}C NMR (101 MHz, DMSO-d$_6$) of compound **9h**

RESUME

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Publications:

1) **Samandram, R., Coskun, N., Çetin, M. 2021**. $Mn(OAc)_3$ induced C-4 arylations of quinazoline 3-oxides with arylboronic acids. *Synthesis*, 53: 10.1055/a-1577-6344.

2) **Samandram, R., Coşkun, N., Çetin, M. 2021.** Eco-friendly H_2O_2 oxidation of 1,2-dihydroquinazoline-3-oxides to quinazoline-3-oxides, *Synthetic Communications*, 51(15): 2349-2356.