Visible light mediated C-H functionalization of heteroaromatic compounds *via* photoredox catalysis

A Dissertation Submitted

to

Sikkim University

In Partial Fulfilment of the Requirement for the

Degree of Master of Philosophy

By

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DECLARATION

I hereby declare that the work embodied in this dissertation entitled "**Visible light mediated C-H functionalization of heteroaromatic compounds *via* photoredox catalysis.**" to be submitted for the Degree of Master of Philosophy in Chemistry of Sikkim University is my original work and the content of this dissertation is based on the experiments which I have performed myself. This dissertation has not been submitted to any other University or Institution for the award of any degree or diploma.

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CERTIFICATE

This is to certify that the thesis titled "**Visible light mediated C-H functionalization of hetero-aromatic compounds *via* photoredox catalysis.**" submitted to **Sikkim University** in partial fulfilment of the requirement for the degree of **Master of Philosophy (Chemistry)** is a result of original research work carried out by **Mr. Joneswar Basumatary** under my guidance and supervision. The date and results presented in this dissertation are original and have been obtained in this laboratory.

All the assistance and help received during the course of the investigation have been acknowledged by him.

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List of Abbreviations

ACN	Acetonitrile
TFA	Trifluoroacetic acid
NaOH	Sodium hydroxide
EtOAc	Ethylacetate
$Na_2S_2O_8$	Sodiumperoxodisulphate
SET	Single electron transfer
PET	Photo induced electron transfer
LED	Light emitting diode
CPY	Cytochrome
HAT	Hydrogen atom transfer
NMR	Nuclear magnetic resonance
FTIR	Fourier transformed infrared spectroscopy
UV	Ultraviolet
$CsPbX_3$	Cesium lead halide
Et_3CN	Triethyl amine
DCM	Dichloromethane
THF	Tetrahydrofuran
TLC	Thin layer chromatography
BDE	Bond dissociation energy
DMSO	Dimethyl sulfoxide
TEMPO	(2, 2, 6, 6-Tetramethylpiperidin-1-yl)oxyl

RB	Round bottom flask
PC	Photocatalyst
DMF	Dimethylformamide
IRPC	Iridium photocatalyst
DIPEA	*N*, *N*-Diisopropyethylamine

List of figures, tables and schemes

Chapter-1: Introduction, literature review and objectives

1.1: Introduction:

Light is an abundant and renewable sources of energy, and nature have been using this energy for various chemical reactions. One of the best example is the phenomenon called "photosynthesis"[1] in which plants and some other organism use solar energy and covert it to chemical energy to produce food from carbon dioxide and water. Nature's this ability to utilize light energy to perform various chemical reactions have inspired researchers to develop new methods that would allow the use of light energy for various chemical transformations. Hence, studies have been going on, in an effort to mimic this natural phenomenon.[2-5] About a century ago Ciamician first realized that light is an abundant and renewable sources of energy for performing chemical reactions that would be green and sustainable in nature.[6] Since then photochemistry,[7] photocatalysis[8] and photoredoxcatalysis[9] have found great importance in the field of organic synthesis.[10-12] Over the recent years, a plethora of new systems have been developed which focus on the utilization of light as the source of energy for various chemical reactions. Among these the "Visible light mediated photoredoxcatalysis"[12, 13] have gathered increasing attention.

Since the beginning of the 20th century photochemistry has attracted organic chemists because of the milder condition required and their potential for greener reactions. Over the recent years, classical photochemical methodologies have found great application in synthetic chemistry[10] and can be considered to be an already highly developed field of research.[14] However, despite the large popularity and advantages of photochemical

reactions, the simple fact that most organic molecules are incapable of absorbing light in the visible range has significantly limited the application of photochemical transformation. Thus, to address this major drawback, a new strategy has been developed which is known as "Photoredox catalysis"[9] (that uses photocatalysts to absorb light in the visible range and utilize their property to transfer electron/energy for sensitizing organic molecules and carry out the desired reactions).[15, 16] Visible light-mediated photoredox catalysis[17] in recent years has developed into a very important tool in the field of organic synthesis. This is mostly due to their ability to mediate various complex reactions with very high efficiency and minimum by-product formation compared to the conventional methods. Photoredox catalysis generally relies upon the visible light absorbing ability and redox behaviour of the light active photocatalyst. By understanding the process that governs this redox behaviour of the photocatalysts, suitable reaction methodologies/schemes can be developed and applied by organic chemists.

All the reactions *via* photoredox catalysis begin with absorption of light/photon by the light active photocatalyst (PC) which in turn goes to a higher energy photo-excited state (PC*) (Fig: 1.1).[9] This gain in energy by the photocatalysts enables the various redox processes involved in photoredox catalysis, because it is the excited state (PC*) which can undergo either reduction or oxidation more readily compared to its corresponding ground state (PC). The PC* may undergo various minor deactivation pathways like fluorosence,[18]

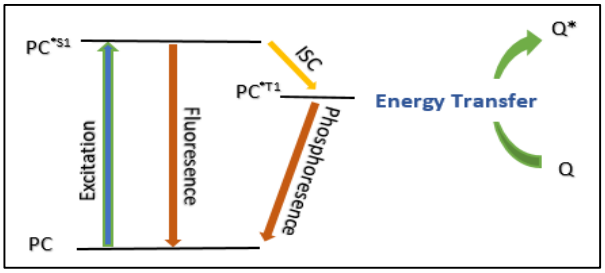

Fig: 1.1 General Jablongski diagram of photocatalyst

internal conversion[19] and bimolecular quenching reactions.[20] But the most important pathways are the electron transfer and the energy transfer reactions.[21]

Photoredox catalysis generally depends on the property of the excited state (PC*) to undergo either oxidation or reduction. Hence, the photocatalyst can serve as either an electron donor or an electron acceptor. The photocatalyst generally undergo two electron transfer steps, first is the quenching (which may be either oxidative or reductive) and the regeneration step to give back the catalyst in the catalytic cycle (Fig:1.2).[13]

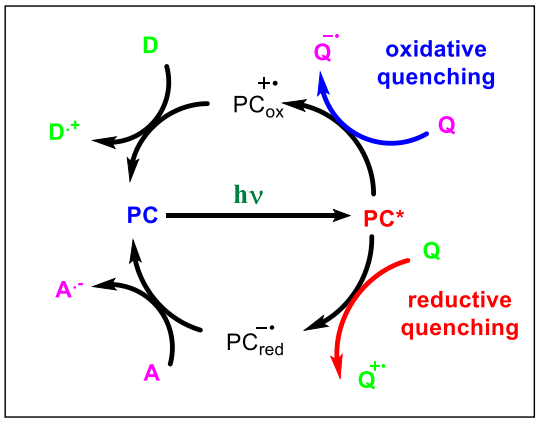

Fig: 1.2 General catalytic cycle of photoredox catalysis

This general methodology allows various single-electron transfer (SET) processes with organic substrate[22] that facilitates the formation of bonds that are often difficult or even impossible *via* the classical two-electron pathways. This property of the photocatalytic methodologies is because of the fact that the intermediate species (photcatalyst) formed during the reaction, in the photoexcited state have high efficiency to donate or accept an electron from a compound *via* a photo induced electron transfer (PET) mechanism.[23] And the photo-excited states are sufficiently long lived (e.g. 1100 ns for $Ru(bpy)_3^2$)[24, 25] to assure that these electrons can compete with fluorescence, phosphorescence and other deactivation pathways[26] and are transported to the catalytic site where the reactions takes place. The first ever reaction that demonstrated the use of visible light mediated photoredox catalysis in the field of organic synthesis were the reduction

reactions in which electron donors were required as reductants.[27] Since then a plethora of reactions have been reported using visible light photoredox catalysis; like The Pschorr Reaction,[28] various oxidation reactions,[29,30] reduction reactions,[31-33] and cycloaddition reaction.[34]

Among the various complex reactions, the visible light mediated sp^3 C-H fuctionalisation[35] of organic molecules through various single-electron transfer mechanism[12] has recently emerged as a very important area for research in the field of photocatalysis. Usually the sp^3 C-H bonds are unreactive and its functionalization under the conventional organic methods is rather difficult. This makes the visible light mediated photoredox catalysis (which allows activation of such unreactive bond) a very useful method for such organic synthesis. So far numerous methodologies for the formation of C-C, C-O and C-N bonds *via* C-H activation have been developed, which uses organic catalyst,[36] transition-metal catalyst[37] and inorganic semiconductors as the photoredox catalyst.[38] Given the recent advancement in the visible light-mediated photoredox catalysis of C-H bond, and their widespread application in organic synthesis, we in our work look to develop a photoredox catalytic protocol for direct C-H functionalization of various hetero-arenes under visible light (blue LED), to produce hetero-aromatic adducts which are among the most important and extensively utilized pharmacophore in development of drugs.[39] Over the recent years, the direct C-H functionalization of hetero-arenes have emerged as a very important and efficient transformation, with their broad scale application in both drug development programs and process chemistry.

According to the studies done by Neubig and group in the year 2006[40] it was found that drugs containing heteroarens show higher therapeutic potency i.e. maximum effect with

minimum dosage. It has also been found that the drug molecules that contain heteroaromatic compounds in their structures are known to reduce the lipophilicity of drugs. According to the studies done by Odberg J.M., Kufmann P et. al. in 2003,[41] hetero-aromatic compounds are also found to increase the aqueous solubility of the drug molecules. In addition to this, drug molecules with hetero-aromatic rings are also known to reduce the inhibition of Cytochrome P450,[42, 43] an important enzyme that plays a very important role in synthesis of hormones and their breakdown and also functions to metabolize various potentially toxic compounds in our body, and facilitates their excreation from the body.[44] Given below are some of the commercially available drug molecules that possess hetero-aromatic ring in their structure.

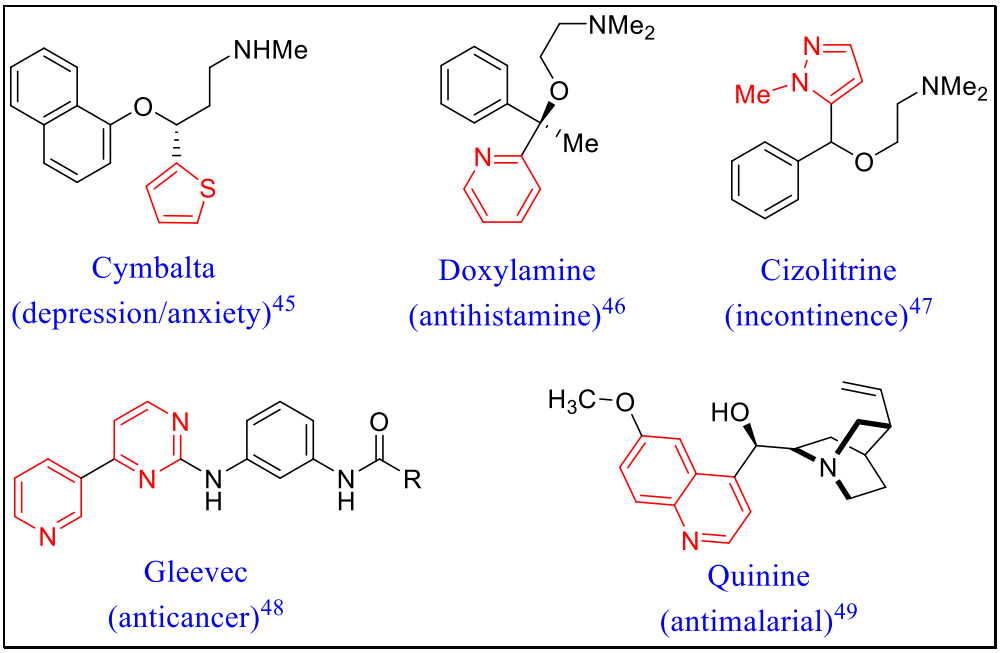

Fig: 1.3 Commercially available heteroarene containing drug molecules[45-49]

Thus, keeping in mind the recent development in photocatalysis and the importance of hetero-arenes in medicinal chemistry, we in our work have looked for photocatalytic C-H functionalisation of hetero-arenes to form C-C bonds with various organic molecules like cyclic ethers, acyclic ethers, aliphatic and aromatic alcohols to form new

hetero-aromatic moieties which would be of high pharmacological importance. In other words, we sought to develop synthetic methodologies that will allow us to convert feedstock hetero-aromatic compounds into a high-value pharmacophore adducts *via* a visible light-mediated C-H functionalization using organo photocatalyst and cesium lead halide perovskites as photocatalyst.

1.2: An update on visible light mediate C-H functionalizations:

Since its discovery, visible light mediated C-H functionalization has developed into a fundamental tool in the field of organic synthesis. Over the last decade, visible light-mediated photoredox catalysis has gained tremendous importance in the field of organic synthesis. Given below are the descriptions of the previous works related to visible light- mediated photocatalytic C-H functionalisation of various organic molecules.

1.2.a: C-C bond formation *via* C-H functionalization: R. Aleyda Garza-Sanchez. et al. in 2017 reported a synthetic protocol for direct visible light-mediated C-H alkylation of hetero-arenes using carboxylic acids.[50] The author demonstrated the use of acyl radicals[51] generated from cyclic and acyclic primary, secondary and tertiary carboxylic acids to perform acylation of various electron-deficient hetero-aromatic compounds like quinoline, isoquinoline, pyridine, phthalazine, benothiazole and other heterocyclic compounds under standard conditions at room temperature (Fig: 1.4). The functionalization were carried out under blue LED irradiation *via* the generation of carbon cantered radicals followed by a Minisci-type reaction using commercially available Iridium catalyst $[Ir(Df(CF_3)ppy)_2(dtbbpy)]PF_6$ along with ammonium persulfate as oxidants.

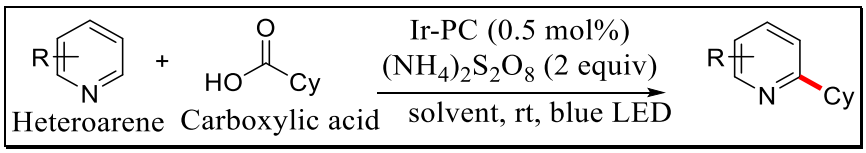

Fig: 1.4 Visible light-mediated C-H alkylation of heteroarene using carboxylic acid.

Over the past few years, great deal of progress has been made in the field of photoredox catalysis. However, most of the methodologies involve the use of organo catalyst,[36] transition metal catalyst[52] and inorganic semiconductor catalysts,[53, 54] which requires; inert condition, complicated synthetic method and even costly metals. Thus, making them less desirable for photocatalytic application. Thus there is a need for development of a material that is easy to produce, cost-efficient and effective for photoredox catalysis. Lead-halide perovskites[55] have been well known for its application in photovoltices.[56] Owing to this property of the perovskite nanocrystals to absorb and store solar energy makes them a very good candidate for photoredox catalysis. Xiaolin Zhu. et al. in 2019 illustrated the use of lead halide perovskites as a photocatalyst for an organic reaction that enabled the C-C bond formation under visible light[57]. The C-C bond formation was carried out between α, β-unsaturated ketone and quinoline derivative *via* C-H activation under blue light (Fig: 1.5).

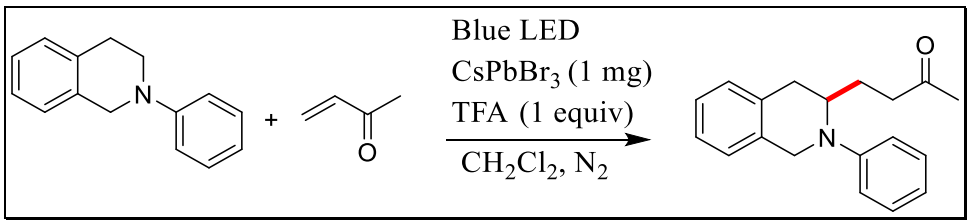

Fig: 1.5 Visible light-mediated C-C bond formation using Lead halide perovskite.

The authors also discussed the effect of the size of the perovskites on the rate of the reaction; they suggested that smaller size nanocrystal promoted faster rate of reaction

but gave lower overall yield, whereas the larger sized nanocrystal promoted slower reaction but had higher overall yield.

1.2.b: C-N bond formation *via* C-H functionalization: One of the major aim in organic syntheses is the development of methodologies for enantioselective formation of C-N bonds. Guiseppe Cecere. et al. developed a method to enatioselectively build C-N bond between amines and aldehydes. Direct α-amination of aldehydes was achieved *via* the combination of photoredox and organo catalysis (Fig: 1.6).[58] Cecere. et al. suggested that, photo generated nitrogen-centred radicals undergo enantioselective α-addition to catalytically formed chiral enamines to directly produce α-amino aldehyde adducts. The authors also presented a detailed catalytic cycle of their proposed mechanism and postulated that an electrophilic nitrogen-centred radical was generated from an amine substrate through the course of the reaction. They suggested that such open-shell reaction pattern was best accomplished using sub-units like dinitrophenysulfonyloxy (ODNs).

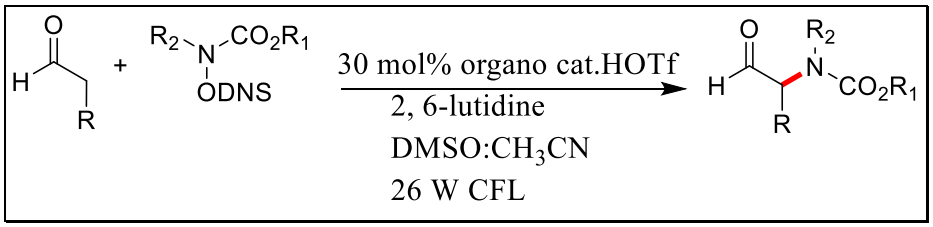

Fig: 1.6 C-N bond formation via photoredox catalysis.

Qixue Qin and Shouyun YU in the year 2014 established a methodology for direct C-H amidation of hetero-arenes using hydroxylamine. The authors suggested that photo-generated N-centred radicals[59] (in which hydroxylamine derivatives were used as the nitrogen source)[60-62] could react with the hetero-arene to produce a C-N bond and also

generate a carbon centred radical. These reactions were carried out under visible light *via* single electron transfer pathway. The amidation was carried out with various hetero-arenes like, indoles, pyrroles and furans (Fig: 1.7).

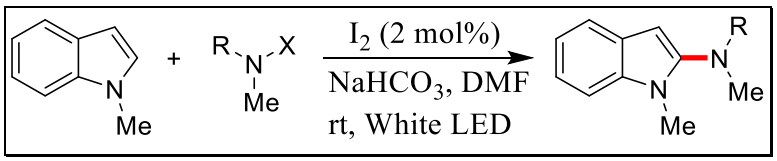

Fig: 1.7 C-H amidation of hetero-arenes using hydroxylamine as nitrogen source under visible light.

The authors also conducted some experiments to understand the mechanism of the reaction and found out that, reaction was completely terminated when TEMPO was used. Suggesting that the reaction proceeded through single-electron pathway. They also found out that with 1,2-dimethylindoles the reaction was not feasible, this indicated that it is the N-centred radicals that attacks the indole.

Catalytically functionalizing the unactivated C(sp^3)-H bond in an efficient and selective way is considered to be exciting as well as challenging in modern day organic synthesis.[63] Over the past few years, functionalization of such unactivated bonds *via* photoredox catalysis is emerging as an important strategy in the field of organic synthesis.[64] Ganesh Pandey. et. al in the year 2016 developed a photocatalytic protocol for C-H functionalization of benzylic position to produce C-N bonds (Fig: 1.8).[65] This coupling reaction was used to incorporate hetero-aromatic compounds to benzylic position. The methodology involved the use of iridium photocatalyst and blue light irradiation. They further extended the methodology for selective benzylic oxidation to produce compounds that are important for industrial and academic purposes.

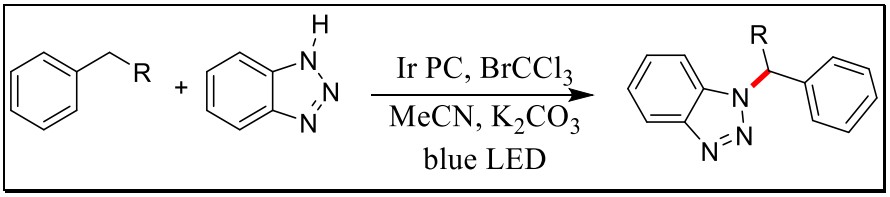

Fig: 1.8 C-H functionalization of benzylic position to produce C-N bond via photocatalysis under blue Light

1.2.c: Fluorination *via* C-H functionalization: Drug discovery in modern day depends on the development of synthetic methods that would address the difficulties associated with designing new pharmaceutical agents.[66] One such difficulty arises from the drug enzymatic metabolism, *in vivo* by CP450 oxidase, that use single-electron oxidation mechanism to modify small molecules and facilitate their excretion.[67] A common synthetic strategy utilised to overcome this challenge is, the introduction of electron withdrawing functional group like fluorine into the drug moieties.[68] The CF_3 moiety in this regard has found great importance, moreover incorporation of the CF_3 moiety into the potential pharmacophores have resulted to enhanced bioactivity of the drug moieties.[69-71] The CF_3 group was generally incorporated by means of transition metal catalysed cross-coupling methodologies which are limited to few organic moeties.[72]

David A. Nagib and David W.C. MacMillan developed a methodology for direct trifluoromethylation of heteroarenes and arenes using photoredox catalysis.[73] The trifluoromethyl moiety was installed by means of cross-coupling using trifluoromethyl sulfonyl chloride and transition metal photocatalyst under blue light (Fig: 1.9). This photocatalytic methodology facilitated the trifluoromethylation of aromatic as well as

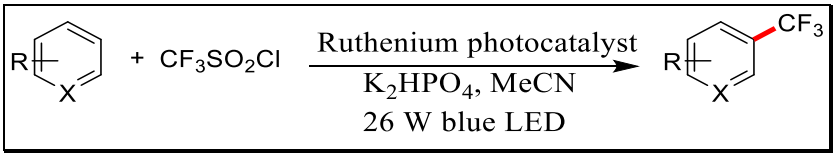

Fig: 1.9 Trifluoromethylation of arenses and heteroarenes.

Hetero-aromatic compounds without the requirement for the pre-activation of the aryl system. Further, the importance of this methodology have been demonstrated by incorporating CF_3 groups to biologically active molecules.

David W.C. MacMillan. et.al in the year 2015 reported a methodology for direct conversion of aliphatic carboxylic acids to alkyl fluorides *via* visible-light mediated photocatalysis (Fig: 2.0).[74] The fluorination of the carboxylic acids was achieved using selectofluoro as the fluorinating agent.

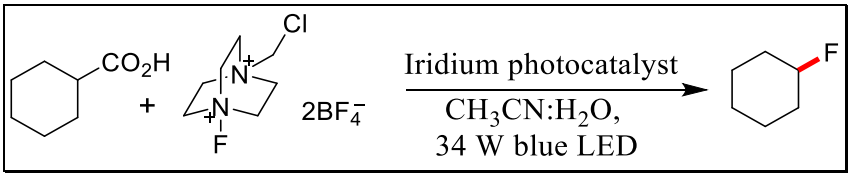

Fig: 2.0 Direct fluorination of aliphatic carboxylic acids to give corresponding alkyl fluoride

In this work the authors examined the range of the photocatalyst for the methodology and found out that a combination of disodium hydrogen phosphate and $Ir[dF(CF_3)ppy]_2(dtbbpy)^{2+}$ gave higher yield. While the use of more oxidising catalyst like $Ru(phen)_3^{2+}$ resulted into slower or no reaction. The authors also demonstrated the importance of using water: acetonitrile mixture as solvent, in which they reported that in the absence of any of the solvent the reaction was not feasible. The authors suggested that the reaction proceeds through the formation electrophilic alkyl radical that can rapidly react with enamines.

1.3: Aims and objectives:

Primary aims and objectives of our research work would comprise of the following features -

1. Development of new methodology for visible light-induced C-H activation of hetero-aromatic compounds using photo-catalysts.
2. Development of new photocatalytic method for the C-C bond formation between hetero-aromatic compounds and ethers.
3. Development of new photocatalytic method for formation of hetero-aromatic alkyl/aryl ketones through oxidative C-C bond formation.
4. In-depth study of the mechanism and substrate scope of the newly developed methodologies and determination of structures of the newly synthesized compounds.

References

(1) Bryant, D. A.; Frigaard, N.-U. Prokaryotic Photosynthesis and Phototrophy Illuminated. *Trends Microbiol.* **2006**, *14* (11), 488–496.

(2) Gust, D.; Moore, T. A. Mimicking Photosynthesis. *Science* **1989**, *244* (4900), 35–41.

(3) Tseng, H.-W.; Zong, R.; Muckerman, J. T.; Thummel, R. Mononuclear Ruthenium(II) Complexes That Catalyze Water Oxidation. *Inorg. Chem.* **2008**, *47* (24), 11763–11773.

(4) Gust, D.; Moore, T.; Moore, A. Molecular Mimicry of Photosynthetic Energy and Electron Transfer. *Acc. Chem. Res.* **1993**, *26* (4), 198–205.

(5) Balzani, V.; Credi, A.; Venturi, M. Photochemical Conversion of Solar Energy. *ChemSusChem 1* (1–2), 26–58.

(6) Ciamician, G. The Photochemistry of the Future. *Science* **1912**, *36* (926), 385–394.

(7) Glusac, K. What Has Light Ever Done for Chemistry? *Nat. Chem.* **2016**, *8* (8), 734–735.

(8) Ameta, R.; Solanki, M. S.; Benjamin, S.; Ameta, S. C. Chapter 6 - Photocatalysis. In *Advanced Oxidation Processes for Waste Water Treatment*; Ameta, S. C., Ameta, R., Eds.; Academic Press, 2018; pp 135–175.

(9) Tucker, J. W.; Stephenson, C. R. J. Shining Light on Photoredox Catalysis: Theory and Synthetic Applications. *J. Org. Chem.* **2012**, *77* (4), 1617–1622.

(10) Hoffmann, N. Photochemical Reactions as Key Steps in Organic Synthesis. *Chem. Rev.* **2008**, *108* (3), 1052–1103.

(11) Fagnoni, M.; Dondi, D.; Ravelli, D.; Albini, A. Photocatalysis for the Formation of the C−C Bond. *Chem. Rev.* **2007**, *107* (6), 2725–2756.

(12) Xuan, J.; Xiao, W.-J. Visible-Light Photoredox Catalysis. *Angew. Chem. Int. Ed.* **2012**, *51* (28), 6828–6838.

(13) Zeitler, K. Photoredox Catalysis with Visible Light. *Angew. Chem. Int. Ed.* **2009**, *48* (52), 9785–9789.

(14) Esswein, A. J.; Nocera, D. G. Hydrogen Production by Molecular Photocatalysis. *Chem. Rev.* **2007**, *107* (10), 4022–4047.

(15) Sagir, M.; Tahir, M. B.; Waheed, U. Role of Photocatalysts in Organic Pollutants Degradation. In *Reference Module in Materials Science and Materials Engineering*; Elsevier, 2020.

(16) Gómez Alvarez, E.; Wortham, H.; Strekowski, R.; Zetzsch, C.; Gligorovski, S. Atmospheric Photosensitized Heterogeneous and Multiphase Reactions: From Outdoors to Indoors. *Environ. Sci. Technol.* **2012**, *46* (4), 1955–1963.

(17) Narayanam, J. M. R.; Stephenson, C. R. J. Visible Light Photoredox Catalysis: Applications in Organic Synthesis. *Chem. Soc. Rev.* **2010**, *40* (1), 102–113.

(18) Lakowicz, J. R. *Principles of Fluorescence Spectroscopy*; Springer Science & Business Media, 2007.

(19) M, H. K. Atkins' Physical Chemistry (8th Edition) - Peter Atkins & Julio de Paula.

(20) Heitele, H. Fundamentals of Photoinduced Electron Transfer. Von G. J. Kavarnos. VCH Verlagsgesellschaft, Weinheim/VCH Publishers, New York, 1993. 359 S., Geb. 105.00 DM/75.00 $. – ISBN 3-527-27856-1/0-89573-751-5. *Angew. Chem.* **1995**, *107* (4), 540–541.

(21) Proctor, R. S. J.; Colgan, A. C.; Phipps, R. J. Exploiting Attractive Non-Covalent Interactions for the Enantioselective Catalysis of Reactions Involving Radical Intermediates. *Nat. Chem.* **2020**, *12* (11), 990–1004.

(22) Schultz, D. M.; Yoon, T. P. Solar Synthesis: Prospects in Visible Light Photocatalysis. *Science* **2014**, *343* (6174).

(23) Ramamurthy, V. *Organic and Inorganic Photochemistry*; CRC Press, 1998.

(24) Batsanov, S. S.; Batsanov, A. S. Crystal Structure – Idealised. *Introd. Struct. Chem.* **2012**, 275–328.

(25) Balzani, V.; Bergamini, G.; Campagna, S.; Puntoriero, F. Photochemistry and Photophysics of Coordination Compounds: Overview and GeneralConcepts. In

Photochemistry and Photophysics of Coordination Compounds I; Balzani, V., Campagna, S., Eds.; Topics in Current Chemistry; Springer: Berlin, Heidelberg, 2007; pp 1–36.

(26) Guillet, J. Polymer Photophysics and Photochemistry: An Introduction to the Study of Photoprocesses in Macromolecules. **1987**.

(27) Pac, C.; Ihama, M.; Yasuda, M.; Miyauchi, Y.; Sakurai, H. Tris(2,2'-Bipyridine)Ruthenium(2+)-Mediated Photoreduction of Olefins with 1-Benzyl-1,4-Dihydronicotinamide: A Mechanistic Probe for Electron-Transfer Reactions of NAD(P)H-Model Compounds. *J. Am. Chem. Soc.* **1981**, *103* (21), 6495–6497.

(28) Cano-Yelo, H.; Deronzier, A. Photocatalysis of the Pschorr Reaction by Tris-(2,2′-Bipyridyl)Ruthenium(II) in the Phenanthrene Series. *J. Chem. Soc. Perkin Trans. 2* **1984**, No. 6, 1093–1098.

(29) Cano-Yelo, H.; Deronzier, A. Photo-Oxidation of Some Carbinols by the Ru(II) Polypyridyl Complex-Aryl Diazonium Salt System. *Tetrahedron Lett.* **1984**, *25* (48), 5517–5520.

(30) Ding, W.; Zhou, Q.-Q.; Xuan, J.; Li, T.-R.; Lu, L.-Q.; Xiao, W.-J. Photocatalytic Aerobic Oxidation/Semipinacol Rearrangement Sequence: A Concise Route to the Core of Pseudoindoxyl Alkaloids. *Tetrahedron Lett.* **2014**, *55* (33), 4648–4652.

(31) Fukuzumi, Shunichi.; Mochizuki, Seiji.; Tanaka, Toshio. Photocatalytic Reduction of Phenacyl Halides by 9,10-Dihydro-10-Methylacridine: Control between the Reductive and Oxidative Quenching Pathways of Tris(Bipyridine)Ruthenium Complex Utilizing an Acid Catalysis. *J. Phys. Chem.* **1990**, *94* (2), 722–726.

(32) Okada, K.; Okubo, K.; Morita, N.; Oda, M. Reductive Decarboxylation of N-(Acyloxy)Phthalimides via Redox-Initiated Radical Chain Mechanism. *Tetrahedron Lett.* **1992**, *33* (48), 7377–7380.

(33) Hasegawa, E.; Mori, K.; Tsuji, S.; Nemoto, K.; Ohta, T.; Iwamoto, H. Visible Light-Promoted Metal-Free Reduction of Organohalides by 2-Naphthyl or 2-Hydroxynaphthyl-Substituted 1,3-Dimethylbenzimidazolines. *Aust. J. Chem.* **2015**, *68* (11), 1648.

(34) Du, J.; Yoon, T. P. Crossed Intermolecular [2+2] Cycloadditions of Acyclic Enones via Visible Light Photocatalysis. *J. Am. Chem. Soc.* **2009**, *131* (41), 14604–14605.

(35) McNally, A.; Prier, C. K.; MacMillan, D. W. C. Discovery of an α-Amino C–H Arylation Reaction Using the Strategy of Accelerated Serendipity. *Science* **2011**, *334* (6059), 1114–1117.

(36) Romero, N. A.; Nicewicz, D. A. Organic Photoredox Catalysis. *Chem. Rev.* **2016**, *116* (17), 10075–10166.

(37) Prier, C. K.; Rankic, D. A.; MacMillan, D. W. C. Visible Light Photoredox Catalysis with Transition Metal Complexes: Applications in Organic Synthesis. *Chem. Rev.* **2013**, *113* (7), 5322–5363.

(38) Wu, K.; Wu, L.-Z. Semiconductor Nanoparticles Photocatalyze Precise Organic Cycloaddition. *Chem* **2021**, *7* (4), 842–844.

(39) Anthonsen, T. Strategies for Organic Drug Synthesis and Design. By Daniel Lednicer. *ChemMedChem* **2009**, *4* (8), 1377–1377.

(40) Neubig, R. R.; Spedding, M.; Kenakin, T.; Christopoulos, A.; International Union of Pharmacology Committee on Receptor Nomenclature and Drug Classification. International Union of Pharmacology Committee on Receptor Nomenclature and Drug Classification. XXXVIII. Update on Terms and Symbols in Quantitative Pharmacology. *Pharmacol. Rev.* **2003**, *55* (4), 597–606.

(41) Tambosi, G.; Coelho, P. F.; Luciano, S.; Lenschow, I. C. S.; Zétola, M.; Stulzer, H. K.; Pezzini, B. R. Challenges to Improve the Biopharmaceutical Properties of Poorly Water-Soluble Drugs and the Application of the Solid Dispersion Technology. *Matér. Rio Jan.* **2018**, *23*.

(42) Zhou, S.; Chan, S. Y.; Goh, B. C.; Chan, E.; Duan, W.; Huang, M.; McLeod, H. L. Mechanism-Based Inhibition of Cytochrome P450 3A4 by Therapeutic Drugs. *Clin. Pharmacokinet.* **2005**, *44* (3), 279–304.

(43) Anttila, S.; Vainio, H.; Hietanen, E.; Camus, A. M.; Malaveille, C.; Brun, G.; Husgafvel-Pursiainen, K.; Heikkilä, L.; Karjalainen, A.; Bartsch, H. Immunohistochemical Detection of Pulmonary Cytochrome P450IA and Metabolic Activities Associated with P450IA1 and P450IA2 Isozymes in Lung Cancer Patients. *Environ. Health Perspect.* **1992**, *98*, 179–182.

(44) Lee, J.; Braun, G.; Henneberger, L.; König, M.; Schlichting, R.; Scholz, S.; Escher, B. I. Critical Membrane Concentration and Mass-Balance Model to Identify Baseline Cytotoxicity of Hydrophobic and Ionizable Organic Chemicals in Mammalian Cell Lines. *Chem. Res. Toxicol.* **2021**.

(45) Gupta, S.; Nihalani, N.; Masand, P. Duloxetine: Review of Its Pharmacology, and Therapeutic Use in Depression and Other Psychiatric Disorders. *Ann. Clin. Psychiatry* **2007**, *19* (2), 125–132.

(46) Pelser, A.; Müller, D. G.; du Plessis, J.; du Preez, J. L.; Goosen, C. Comparative Pharmacokinetics of Single Doses of Doxylamine Succinate Following Intranasal, Oral and Intravenous Administration in Rats. *Biopharm. Drug Dispos.* **2002**, *23* (6), 239–244.

(47) Zát'ura, F.; Všetiča, J.; Abadías, M.; Pavlík, I.; Schraml, P.; Brod'ák, M.; Villoria, J.; Sust, M. Cizolirtine Citrate Is Safe and Effective for Treating Urinary Incontinence Secondary to Overactive Bladder: A Phase 2 Proof-of-Concept Study. *Eur. Urol.* **2010**, *57* (1), 145–153.

(48) Lachowicz, J. L.; Post, G. S.; Brodsky, E. A Phase I Clinical Trial Evaluating Imatinib Mesylate (Gleevec) in Tumor-Bearing Cats. *J. Vet. Intern. Med.* **2005**, *19* (6), 860–864.

(49) Achan, J.; Talisuna, A. O.; Erhart, A.; Yeka, A.; Tibenderana, J. K.; Baliraine, F. N.; Rosenthal, P. J.; D'Alessandro, U. Quinine, an Old Anti-Malarial Drug in a Modern World: Role in the Treatment of Malaria. *Malar. J.* **2011**, *10* (1), 144.

(50) Manna, S.; Prabhu, K. R. Visible-Light-Mediated Direct Decarboxylative Acylation of Electron-Deficient Heteroarenes Using α-Ketoacids. *J. Org. Chem.* **2019**, *84* (9), 5067–5077.

(51) Fontana, F.; Minisci, F.; Nogueira Barbosa, M. C.; Vismara, E. Homolytic Acylation of Protonated Pyridines and Pyrazines with .Alpha.-Keto Acids: The Problem of Monoacylation. *J. Org. Chem.* **1991**, *56* (8), 2866–2869.

(52) Prier, C. K.; Rankic, D. A.; MacMillan, D. W. C. Visible Light Photoredox Catalysis with Transition Metal Complexes: Applications in Organic Synthesis. *Chem. Rev.* **2013**, *113* (7), 5322–5363.

(53) Wu, K.; Wu, L.-Z. Semiconductor Nanoparticles Photocatalyze Precise Organic Cycloaddition. *Chem* **2021**, *7* (4), 842–844.

(54) Cherevatskaya, M.; Neumann, M.; Füldner, S.; Harlander, C.; Kümmel, S.; Dankesreiter, S.; Pfitzner, A.; Zeitler, K.; König, B. Visible-Light-Promoted Stereoselective Alkylation by Combining Heterogeneous Photocatalysis with Organocatalysis. *Angew. Chem. Int. Ed.* **2012**, *51* (17), 4062–4066.

(55) Saparov, B.; Mitzi, D. B. Organic–Inorganic Perovskites: Structural Versatility for Functional Materials Design. *Chem. Rev.* **2016**, *116* (7), 4558–4596.

(56) Burschka, J.; Pellet, N.; Moon, S.-J.; Humphry-Baker, R.; Gao, P.; Nazeeruddin, M. K.; Grätzel, M. Sequential Deposition as a Route to High-Performance Perovskite-Sensitized Solar Cells. *Nature* **2013**, *499* (7458), 316–319.

(57) Zhu, X.; Lin, Y.; San Martin, J.; Sun, Y.; Zhu, D.; Yan, Y. Lead Halide Perovskites for Photocatalytic Organic Synthesis. *Nat. Commun.* **2019**, *10* (1), 2843.

(58) Cecere, G.; König, C. M.; Alleva, J. L.; MacMillan, D. W. C. Enantioselective Direct α-Amination of Aldehydes via a Photoredox Mechanism: A Strategy for Asymmetric Amine Fragment Coupling. *J. Am. Chem. Soc.* **2013**, *135* (31), 11521–11524.

(59) Minozzi, M.; Nanni, D.; Spagnolo, P. From Azides to Nitrogen-Centered Radicals: Applications of Azide Radical Chemistry to Organic Synthesis. *Chem. – Eur. J.* **2009**, *15* (32), 7830–7840.

(60) Allen, L. J.; Cabrera, P. J.; Lee, M.; Sanford, M. S. N-Acyloxyphthalimides as Nitrogen Radical Precursors in the Visible Light Photocatalyzed Room Temperature C–H Amination of Arenes and Heteroarenes. *J. Am. Chem. Soc.* **2014**, *136* (15), 5607–5610.

(61) Foo, K.; Sella, E.; Thomé, I.; Eastgate, M. D.; Baran, P. S. A Mild, Ferrocene-Catalyzed C–H Imidation of (Hetero)Arenes. *J. Am. Chem. Soc.* **2014**, *136* (14), 5279–5282.

(62) Qin, Q.; Yu, S. Visible-Light-Promoted Redox Neutral C–H Amidation of Heteroarenes with Hydroxylamine Derivatives. *Org. Lett.* **2014**, *16* (13), 3504–3507.

(63) Handbook of C−H Transformations: Applications in Organic Synthesis, Volumes 1−2 Edited by Gerald Dyker (Bochum University, Germany). Wiley-VCH Verlag GmbH & Co. KGaA: Weinheim. 2005. Xxvi + Xxvi + 662 Pp. $385. ISBN 3-527-31074-6. *J. Am. Chem. Soc.* **2006**, *128* (17), 5982–5982.

(64) Yoon, T. P.; Ischay, M. A.; Du, J. Visible Light Photocatalysis as a Greener Approach to Photochemical Synthesis. *Nat. Chem.* **2010**, *2* (7), 527–532.

(65) Pandey, G.; Laha, R.; Singh, D. Benzylic C(Sp3)–H Functionalization for C–N and C–O Bond Formation via Visible Light Photoredox Catalysis. *J. Org. Chem.* **2016**, *81* (16), 7161–7171.

(66) *Modern Drug Synthesis: Li/Modern*; Li, J. J., Johnson, D. S., Eds.; John Wiley & Sons, Inc.: Hoboken, NJ, USA, 2010.

(67) *Cytochrome P450: Structure, Mechanism, and Biochemistry*, 3rd ed.; Montellano, P. R. O. de, Ed.; Springer US, 2005.

(68) Filler, R.; 1923-; Kobayashi, Y.; 1924-; Yagupolskii, L. M. *Organofluorine Compounds in Medicinal Chemistry and Biomedical Applications*; Elsevier, 1993.

(69) Müller, K.; Faeh, C.; Diederich, F. Fluorine in Pharmaceuticals: Looking Beyond Intuition. *Science* **2007**, *317* (5846), 1881–1886.

(70) Purser, S.; Moore, P. R.; Swallow, S.; Gouverneur, V. Fluorine in Medicinal Chemistry. *Chem. Soc. Rev.* **2008**, *37* (2), 320–330..

(71) Hagmann, W. K. The Many Roles for Fluorine in Medicinal Chemistry. *J. Med. Chem.* **2008**, *51* (15), 4359–4369.

(72) Tomashenko, O. A.; Grushin, V. V. Aromatic Trifluoromethylation with Metal Complexes. *Chem. Rev.* **2011**, *111* (8), 4475–4521.

(73) Nagib, D. A.; MacMillan, D. W. C. Trifluoromethylation of Arenes and Heteroarenes by Means of Photoredox Catalysis. *Nature* **2011**, *480* (7376), 224–228.

(74) Ventre, S.; Petronijevic, F. R.; MacMillan, D. W. C. Decarboxylative Fluorination of Aliphatic Carboxylic Acids via Photoredox Catalysis. *J. Am. Chem. Soc.* **2015**, *137* (17), 5654–5657.

Chapter-2 Photocatalytic C-C bond formation between heteroarenes and ethers *via* C-H functionalization

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2.1: Introduction:

Over the past decade a great deal of interest has developed among the chemists for the effective and efficient functionalization of the unactivated C-H bond.[1] With the ever expanding arrays of new C-H functionalization methods, there is a realization among the community of medicinal chemistry for the use of this simple transformation for exploration of the chemical space more effectively. The availability of this new simple yet powerful functionalization method have created possibility for synthetic chemists to resort to new synthetic strategies rather than depending only on the conventional synthetic methods.[2] Among the various types of structures, hetero-aromatic moieties are among the ones considered to be the privileged structures to be used most commonly in medicinal chemistry.[3] Hetero-aromatic adducts are in fact considered to be one of the most important components of pharmaceutical compounds.[39] Unfortunately the synthesis of such privileged structures is limited to the conventional methods that depends on the cyclization of simple starting materials.[4] These methods are no doubt effective for synthesizing the target molecules, but are ineffective when trying to access the library of structurally rich and diverse hetero-arenes. Thus, to overcome these challenges new synthetic strategies are required for diversification of common hetero-arenes.

Over the recent years the C-H functionalization of hetero-aromatic compounds have become a very important and effective transformation, which is mainly because of their

broad-scale application in medicinal chemistry as well as process chemistry[5]. The direct α-addition of the alkyl groups to heteo-aromatic compounds, a reaction known as the Minisci reaction[6] has become very important for the C-H functionalization of hetero-arenes. Over the last decade, various synthetic protocols were developed in which, photoredox catalysis were coupled with Minisci reaction which allowed hetero-arylation of ethers through selective C-H functionalization of ethers.

It has been well established that the α-oxoalkyl radicals are highly stable yet nucleophilic species and can readily react with various electron deficient moieties like, hetero-arenes, carbonyls or imines. So far many photocatalyzed C-H functionalization processes have been developed that enable the functionalization of hetero-arenes with various α-alkyl, ethers and alcohols. And most of these methodologies uses transition-metal catalyst[37] and inorganic semiconductors as the photoredox catalyst.[38] However, most of these catalysts require: costly transition-metals; dry (air-free) reaction conditions; complicated synthetic procedure; or may even show toxicity and therefore, are not preferred. Thus, there is a need for a photo-catalyst that is easy to synthesize, economical, effective and highly-tolerant for a broad scope of chemical bond formations. Among the various potential photoactive materials, cesium lead halide perovskites[7] have been found to be a very important candidate. Cesium lead halide perovskites have shown promise for low cost photovoltices and are known to have strong light absorption,[8] long excited-state lifetime,[9] and efficient separation and transport of opposite charge carriers.[57] These photo-physical properties of cesium lead halide perovskites demonstrated for photovoltaic application are of great importance and can be utilized in photocatalytic organic synthesis. In fact, it was since the early 1970's, that the photocatalytic activities of perovskites have been reported; in which oxidation and reduction reactions were carried out using perovskites as a

photocatalyst.[10] Due to the strong absorption of light and the emission properties of perovskites, researchers have in fact started to anticipate that perovskites material are the next alternative photocatalyst for the existing one. Scientific community has now started to use perovskites as the next generation photo-catalyst owing to their photo-physical and structural variation properties. Perovskites have the ability to alter their band gap by modifying their shape and size.[11] As a result, the photo-physical properties of perovskite materials can be easily controlled by simple size and shape modification, making perovskites more versatile and advantageous over the existing photo-catalyst.

Among the various types of perovskite materials, lead halide perovskites are the ones that has attracted most attention in the field of photocatalysis. Halide perovskite have a general formula -ABX_3, consisting of a monovalent A^+ ion, a divalent B^+ ion and X^- halide ion. The A^+ monovalent ion can be any material like; Cs^+, Rb^+, methylammonium (MA) ion or formamidine (FA) ions. The divalent B^+ ion can be metals like Pb, Ge, Sn *etc.* whereas the halide ions can chloro, bromo or iodo ions. The structure of mono-halide perovskite is generally octahedral; with monovalent A^+ ion situated in the centre, which is surrounded by $[BX_6]^{4-}$ ion (Fig :2.1).[12] However, it can also form cubic, orthorhombic or cubic structures. Halide perovskites have the ability to absorb energy in the wavelength rage of visible-light, and recent studies have revealed that several C-C, C-O and C-N bond formation have been successfully carried out using perovskite nanocrystals as the photocatalyst under visible light.[13]

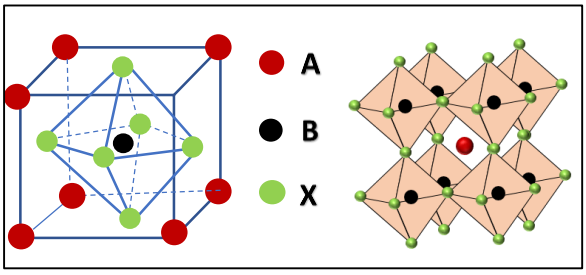


Fig: 2.1 General structure of monohalide perovskite

Thus, herein we developed a photoredox catalytic C-H functionalization protocol that would enable direct α-alkylation of hetero-aromatic compounds using various cyclic and acyclic ethers using cesium lead halide perovskite as our photocalyst. This methodology will thus allow us to convert feedstock hetero-arenes and ethers into high value pharmacophore adducts.

2.2: Literature review:

Photocatalytic C-C functionalization in last decade have emerged as one of the most important tools in the field of synthetic chemistry. Jian Jin and David W.C. MacMillian[14] in 2015 reported a methodology for the direct α-arylation of cyclic and acyclic ethers with hetero-arenes through the design a photoredox-mediated C-H Functionalization pathway (Fig: 2.2). The methodology describes conversion of feedstock substrates into valuable pharmacophore by generating α-oxyalkyl radical from a variety of ethers followed by an Minisci-type reaction[15] with hetero-arenes using Iridium photocatalyst - $[Ir(Df(CF_3)ppy)_2(dtbbpy)]PF_6$.

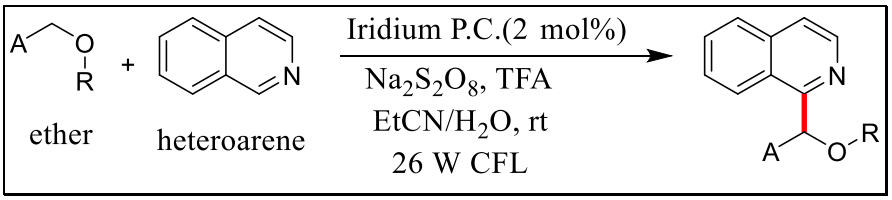


Fig: 2.2 C-H functionalization of hetero-aromatic compounds using ether as an alkylating agent

In 2017 R. Aleyda Garza-Sanchez. et al reported a synthetic protocol for direct visible light-mediated C-H alkylation of hetero-arenes using carboxylic acids (Fig: 2.3).[16] Functionalization of quinoline, isoquinoline, pyridine, phthalazine, benothiazole and other heterocyclic derivatives were carried out with cyclic and acyclic primary, secondary and tertiary carboxylic acids under standard conditions at room temperature. The functionalization were carried out under blue LED irradiation *via* the generation of

carbon centred radicals followed by a Minisci-type reaction using commercially available Iridium catalyst $[Ir(Df(CF_3)ppy)_2(dtbbpy)]PF_6$ along with ammonium persulfate as oxidants.

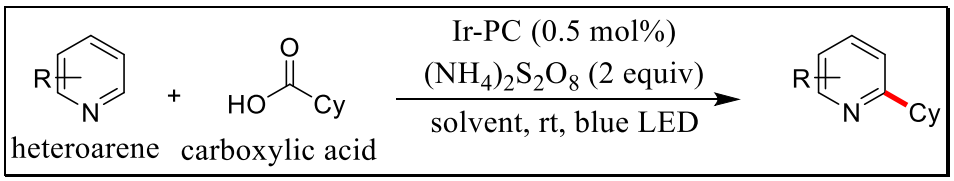


Fig: 2.3 Visible light-mediated direct decarboxylative C-H functionalization of heteroarenes.

Lead halide perovskites have also been widely known to be used as a photocatalyst. Xiaolin Zhu. et al. in 2019 illustrated the use of lead halide perovskites as a photocatalyst for several fundamental organic reactions like C-C, C-N and C-O bond formation under visible light (Fig: 2.4).[17]

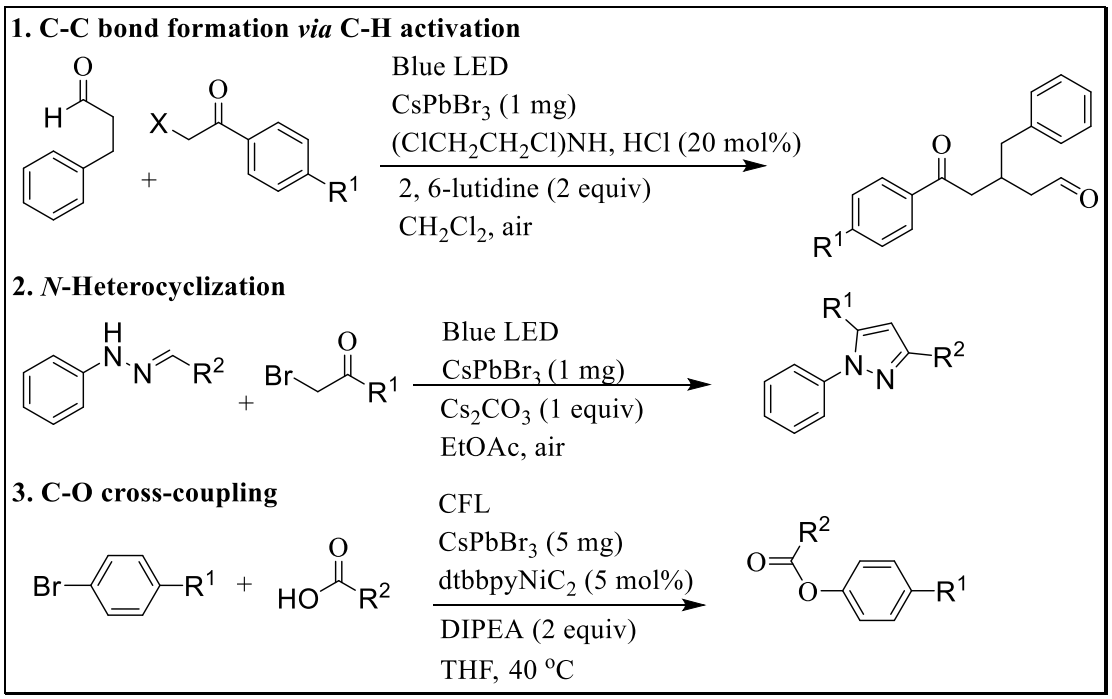


Fig: 2.4 Library of C-C, C-O and C-N bond formation reactions using perovskites under visible-light.

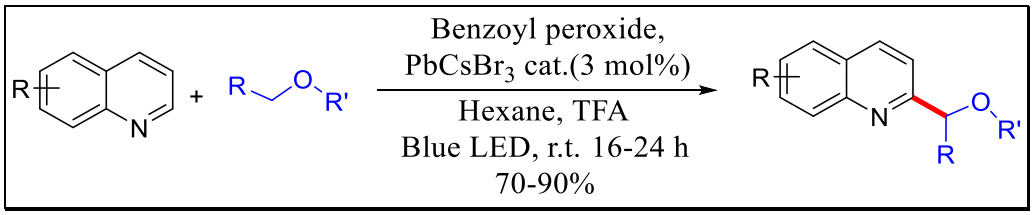
The C-C bond formation was carried out via C-H activation, while the C-N and C-O bond formations were achieved *via N*-heterocyclization and aryl-esterification

respectively.

From the study of the previous works in the field of C-H functionalization we see that various methodologies have already been established for the C-H functionalization of hetero-arenes. However, most of these methodologies are found to use Iridium based photocatalyst which is very costly and difficult to synthesize. Hence, there is a need for a methodology which requires the use of such costly catalyst. Also, we found out that cesium lead halide perovskites are beginning to gain importance for photocatalysis. We therefore, in our work have developed a visible light-mediated photocatalytic protocol for C-H functionalization of hetero-arenes using cesium lead halide perovskites as our photocatalyst.

2.3: Synthetic scheme:

In this chapter we have described a methodology that deals with C-C bond formation between aromatic aza-heterocycles and ethers through photocatalytic C-H functionalization (Scheme: 1).



Scheme: 1 Schematic representations for photocatalytic C-C bond formation between ethers and hetero-aromatic compounds.

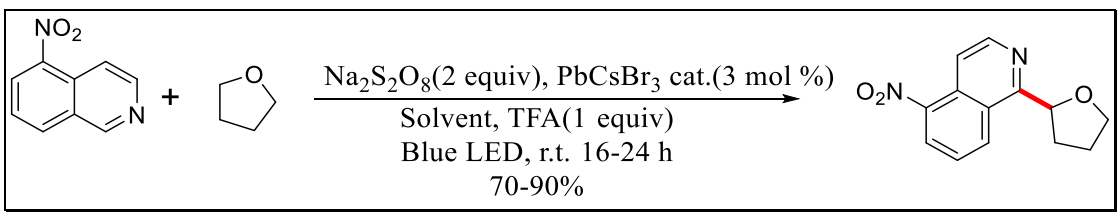
The reactions were carried out under blue light using $CsPbBr_3$ perovskites as the photocatalyst and Benzoyl peroxide (BPO) as the radical initiator as well as an oxidant. While hexane was used as a solvent and trifluoroacetic acid was used for the protonation of the nitrogen containing hetero-arenes.

2.4: Results and discussion:

Keeping in mind the recent advancement of photocatalysis and the significance of hetero-aromatic compounds, we developed a general methodology for the photocatalytic C-H functionalization of hetero-aromatic compounds, which was used for direct C-H functionalization of aromatic aza-heterocyclic compounds to establish a C-C bond with cyclic and acyclic ethers, resulting into the formation of various hetero-aromatic adducts which might be important pharmacological precursors. In this methodology we carried out our reactions using $CsPbBr_3$ perovskites as the photocatalyst and blue light as the source of energy. Blue light has a wavelength range between 400–525 nm. While the $CsPbBr_3$ that was used was found to absorb energy in the wavelength range of 520 nm. Hence, it is possible for the photocatalyst to absorb energy from the blue light and then transfer its energy to the reaction process; acting as the driving force for our desired reactions.

To optimize the reaction condition of our methodology we performed some preliminary experiments using 5-nitroisoquinoline and THF as our starting materials. In which we first carried out our reaction under blue light using a mixture of acetonitrile and water in the ratio of 1:1 as solvent, sodium peroxodisulfate as oxidant and $CsPbBr_3$ as the photocatalyst (Table: 1, serial no. 1) and obtained a percentage yield of 90% for the product. Then to study the effect of solvent over our developed methodology, we

(Table: 1).



Sl.No.	Photocatalyst	Oxidant	Solvent	Light	Yield %
1	$PbCsBr_3$	$Na_2S_2O_8$	ACN:H_2O	Blue LED	90 %
2	$PbCsBr_3$	$Na_2S_2O_8$	DCM	Blue LED	—
3	$PbCsBr_3$	—	ACN:H_2O	Blue LED	—
4	$PbCsBr_3$	H_2O_2	ACN:H_2O	Blue LED	—
5	$PbCsBr_3$	Triisopropylsilane	ACN:H_2O	Blue LED	—
6	$PbCsBr_3$	$Na_2S_2O_8$	EtOAc	Blue LED	—
7	$PbCsBr_3$	$Na_2S_2O_8$	ACN	Blue LED	60 %
8	—	$Na_2S_2O_8$	ACN:H_2O	Blue LED	—
9	$PbCsBr_3$	$Na_2S_2O_8$	ACN:H_2O	—	—
10	$PbCsBr_3$	Benzoylperoxide	Hexane	Blue LED	92%

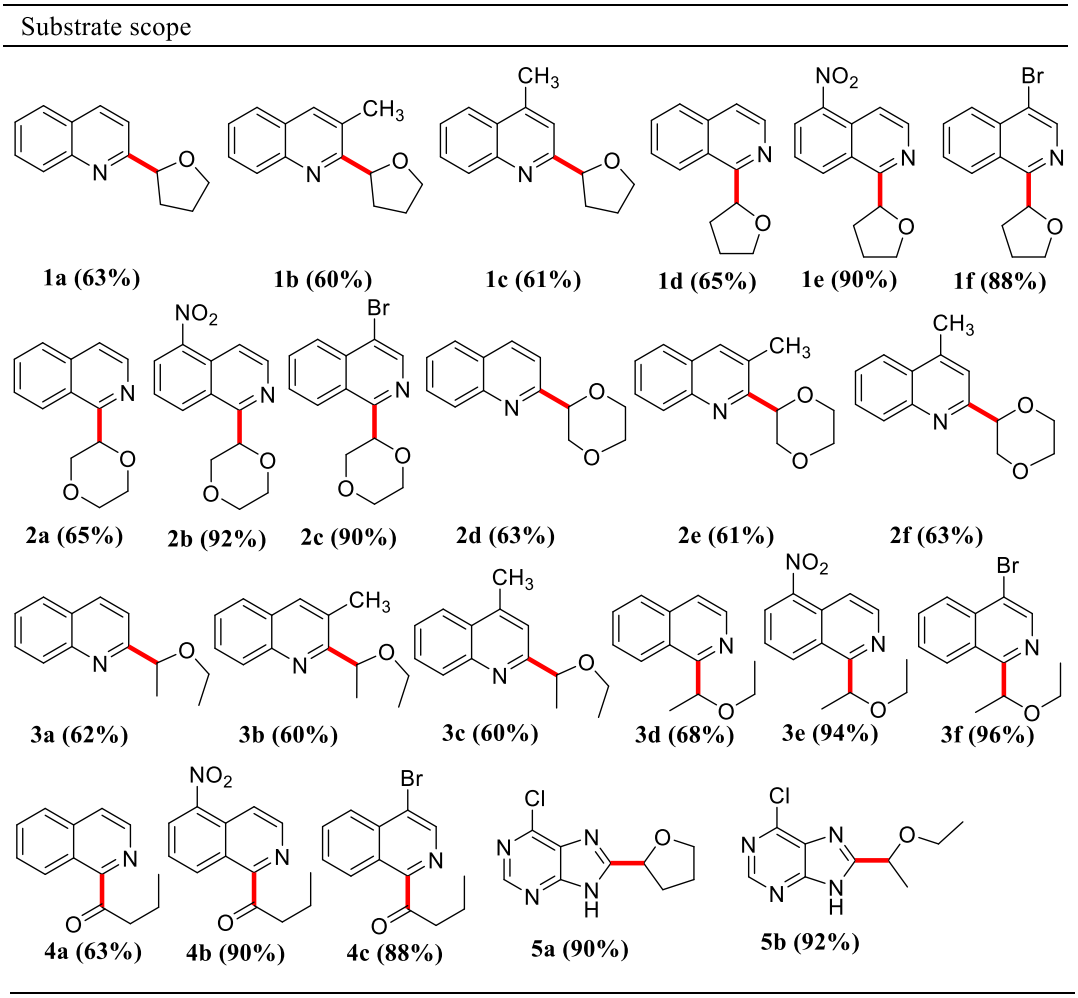
Table: 1 Optimization table for photocatalytic C-C bond forming reaction of hetero-arenes.

performed the same reaction using dichloromethane as the solvent, in which no product was formed. The probable reason for this might be due to the fact that the sodium peroxodisulphate oxidant was insoluble in dichloromethane as we know that sodium peroxodisulphate is an ionic compound and requires a polar solvent like water solubilize. To further confirm this observation, we performed the reaction in the absence of sodium peroxodisulphate (Table: 1, serial no. 3) and we observed that no reaction occurred; this confirmed the significance of the oxidant in the methodology and justified the use of acetonitrile water mixture as the solvent medium. Further, the reaction was carried out using other oxidants like hydrogen peroxide and triisopropylsilane (Table: 1, serial no. 4, 5), but no reaction occurred, thus further confirming the importance of the sodium peroxodisulfate oxidant in the methodology. Then to confirm the role of the photocatalyst, we performed the reaction in the absence of the photocatalyst, where it was observed that no reaction occurred (Table: 1, serial no. 8). This is because of the fact that, in the absence of the photocatalyst there is no any system in the reaction mixture that can absorb energy (from the light irradiated) that is required for our reaction to proceed. This suggested that the photocatalyst plays

a very important role in our methodology and in its absence the methodology would fail, justifying the significance of the photcatalyst in the reaction. Further, the reaction was carried out in dark condition and we observed that no reaction took place (Table: 1, serial no. 9). This confirmed that the methodology that we have developed is a visible light mediated photocatalytic process, and the optimized condition for this reaction is we carried out the reaction under blue light using cesium lead halide perovskite as photocatalyst, mixture of acetonitrile and water in the ratio of 1:1 as the solvent, and $Na_2S_2O_8$ as the oxidant (Table: 1, serial no. 1). However, lead halide perovskites are highly unstable in polar solvent like acetonitrile or water. This simple but undeniable fact makes our methodology unfavourable for larger scale reaction. Thus, to solve this issues we soughed for a system that would not require the use of such polar solvents. Hence, we change our oxidant from sodium peroxodisulphate to benzoyl peroxide which is soluble in non-polar solvent like hexane (Table: 1, serial no. 10). And we observed that reaction was successful with 92% yield. Thus, with this we were able to solve the stability issue of our photocatalyst and used this optimized reaction condition for synthesis of various heteroaromatic adducts.

Using this methodology, we carried out our reactions with quinolone, isoquinole and their derivatives as heteroarenes and THF, 1,4-dioxane, diethyl ether and n-butyl methyl ether as the ethers; with THF, 1,4-dioxane and diethyl ether we obtained heteroaromatic alkyl ethers as our product (Scheme: 2). While, with unsymmetrical n-butyl methyl ether a heteroaromatic alkyl ketone was obtained (Scheme: 2, **4a, 4b, 4c**). To study the effect of different substituents over our developed methodology we tried our reactions with different substituents on the heteroarenes. We observed that On varying the heteroarenes with electron withdrawing groups like $–NO_2$ and Br in their rings which makes the heteroarenes electron deficient, higher yields was obtained (88-

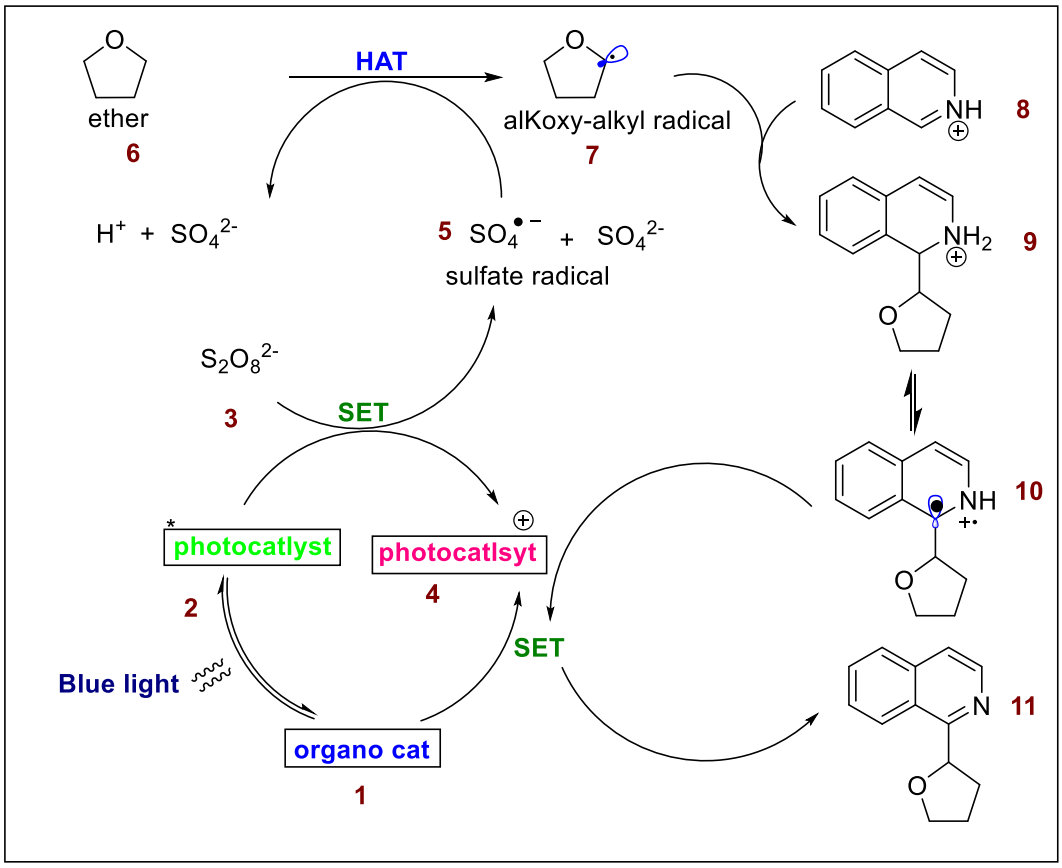
90%), while the heteroarenes with electron donating groups like –CH_3 which makes the hetroarenes electron rich showed lower yield (60-65%).



Scheme:2 Substrate scope for the C-C bond formation between ethers and hetero-arenes via photocatalytic C-H functionalization.

The reason for this trend in the yields of the product might be because of the fact that the reaction proceeds *via* the formation a radical intermediate α-ethoxyalkyl radical, which is nucleophilic in nature and would prefer to attack the electron deficient ring compared to the electron rich ring leading to the above observed trend of the yields. This brings us to the mechanism of our reaction.

The probable mechanism for our reaction involves irradiation of the reaction mixture with blue light (Scheme: 3). As a consequence, the photocatalyst absorbs energy from the light and goes into a higher energy excited state. The excited photocatalyst **2** then transfers its energy to the Sodium peroxodisulphate oxidant, which undergoes a single electron transfer (SET) reaction to form sulphate radical **5**. This radical then reacts with the ether to undergo a hydrogen atom transfer (HAT) reaction



Scheme: 3 Proposed mechanism for photocatalytic alkylative C-H functionalization of hetero-arenes.

forming an alkoxy-alkyl radical **7**. The alkoxy-alkyl radical attacks the protonated hetero-arene **8** (protonation of the hetero-arene was done by trifluroacetic acid) to give intermediate **9.** The intermediate **9** then undergoes resonance stabilization to form intermediate **10** which then undergoes a single electron transfer reaction (SET) to

finally form the alkylated hetero-arene **11**. Formation of the final product **11** can be confirmed from the proton ^{1}HNMR values of our compounds. In which we observed that peak in the range of 9 ppm which is a characteristic peak for hydrogen next to the nitrogen atom in the aromatic ring of the aza-heteroarene is absent. Disappearance of this peak indicates that the proton at that position has been replaced by a substituent. And the attachment of the ether group to that position can be confirmed by the appearance of peaks in the range of 5-5.5 ppm and 4-4.5 ppm which are the characteristic peaks of benzylic proton and proton attached to the carbon next to oxygen of an ether respectively.

2.5: General procedures:

Preparation of 0.04 M Cs-oleate stock solution: Cesium carbonate (0.056 g) (0.2 mmol) was taken in a two neck RB. To this, 1 ml of oleic acid and 9 ml of octadecene were added. The solution was then air fluxed and heated to 130-150 ^{o}C until a clear solution was obtained. This solution was then stored in a deaerated argon-filled container.

Synthesis of lead halide perovskite: $PbBr_2$ (0.0367 g) (0.1 mmol) was taken in a three neck RB. Then oleic acid (0.5 ml,) oleylamine (0.5 ml) and 5 ml of octadecene were added. The solution was the deaerated and nitrogen fluxed, followed by heating to 165-170 ^{0}C. At that temperature 1 ml of the 0.04 M cesium-oleate stock was injected. Just after the injection, the reaction flask was quickly kept in an ice bath. The crude product was dissolved in acetone and centrifuged for 10 mins at 6000 rpm to obtain the pure lead halide perovskite.

Photocatalytic C-H functionalization of heteroarnes: 5-nitroisoquinoline (50 mg) was taken in a 5 ml vile. To this vile 4 ml of solvent (hexane) was added. To this sodium

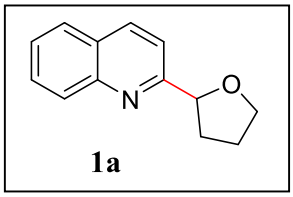
peroxodisulphate (100 mg) was added. Then Tetrahydrofuran (THF) (30 µl) (1.2 equivalents) was added to the reaction mixture. Then 50 µl (2 equivalents) of Trifluoroacetic acid (TFA) was added, followed by addition of $CsPbBr_3$ perovskites (5 mg) (3 mmol) to the reaction mixture. The reaction mixture was then kept under blue light at room temperature with continuous stirring for 16 h. After completion of the reaction, which confirmed by TLC (thin layer chromatography), the reaction mixture was neutralized using 1% aqueous NaOH solution. The organic compound was then extracted with 3 × 20 ml dichloromethane using a separating funnel. The crude organic compound was then purified by column chromatography to obtain compound **1a.**

2.6: Conclusion:

In this work we have developed a photocatalytic methodology for direct alkylation of aza-heteroarenes using ethers as the alkylating agent and lead halide perovskites as the phtotocatalyst. Using this mild and general methodology we are able to alkylate various derivatives of quinoline, isoquinolines and purine, to produce high value pharmacophores. In the beginning we carried out our reaction in a mixture of acetonitrile and water (1:1) as solvent. However, we realised that such a solvent system would not be suitable for large scale reaction as perovskites are unstable in polar solvents. Hence, we optimized our reaction condition and used non-polar hexane as the solvent, in which perovskites are most stable. We further plan on using this general methodology to functionalize various natural products that contains such functional groups. We believe that this mild visible light mediated methodology for C-H functionalization of hetero-arenes using lead halide perovskites will find good application in the field of organic synthesis as well as pharmaceutical chemistry.

2.7: Spectral data of newly synthesized compounds:

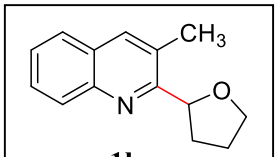
2-(tetrahydrofuran-2-yl)quinoline



1a

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.18 (d, *J* = 8.5 Hz, 1H), 8.08 (d, *J* = 8.5 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.72 (t, *J* = 7.2 Hz, 1H), 7.63 (d, *J* = 8.5 Hz, 1H), 7.53 (t, *J* = 7.5 Hz, 1H), 5.21 (t, *J* = 6.8 Hz, 1H), 4.20 (q, *J* = 7.1, 6.5 Hz, 1H), 4.07 (q, *J* = 7.1 Hz, 1H), 2.59 – 2.50 (m, 1H), 2.11 – 2.00 (m, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 163.63, 136.81, 129.51, 129.00, 127.64, 127.44, 126.11, 118.01, 82.07, 77.26, 69.34, 33.48, 25.97.

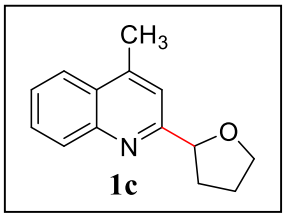
3-methyl-2-(tetrahydrofuran-2-yl)quinoline



1b

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.11 (d, *J* = 8.4 Hz, 1H), 7.89 (s, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.64 (t, *J* = 7.1 Hz, 1H), 7.49 (t, *J* = 7.5 Hz, 1H), 5.34 (t, *J* = 7.1 Hz, 1H), 4.23 (q, *J* = 7.5 Hz, 1H), 4.06 – 3.99 (m, 1H), 2.58 (s, 3H), 2.43 – 2.31 (m, 2H), 2.20 (td, *J* = 13.8, 13.0, 6.1 Hz, 1H), 2.13 – 2.03 (m, 1H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 160.06, 136.56, 129.40, 129.23, 128.32, 127.76, 126.59, 126.24, 79.56, 68.92, 30.27, 29.73, 19.00.

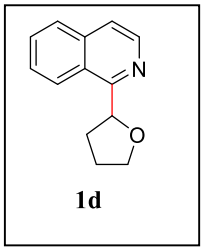
4-methyl-2-(tetrahydrofuran-2-yl)quinoline



1c

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.09 (d, *J* = 8.5 Hz, 1H), 7.97 (d, *J* = 8.5 Hz, 1H), 7.59 (s, 1H), 7.56 (d, *J* = 3.3 Hz, 1H), 7.54 (d, *J* = 1.7 Hz, 1H), 5.19 (t, *J* = 6.8 Hz, 1H), 4.19 (q, *J* = 7.0, 6.4 Hz, 1H), 4.06 (q, *J* = 7.6, 7.1 Hz, 1H), 2.56 (d, *J* = 7.8 Hz, 4H), 2.11 – 2.03 (m, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 162.59, 136.11, 135.88, 131.75, 129.11, 128.67, 127.48, 126.49, 118.01, 82.10, 69.28, 33.42, 25.97, 21.55.

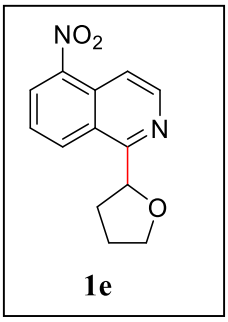
1-(tetrahydrofuran-2-yl)isoquinoline



1d

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.52 (d, *J* = 5.7 Hz, 1H), 8.35 (d, *J* = 8.4 Hz, 1H), 7.86 (d, *J* = 8.2 Hz, 1H), 7.70 (t, *J* = 7.5 Hz, 1H), 7.64 (d, *J* = 7.3 Hz, 1H), 7.60 (d, *J* = 5.7 Hz, 1H), 5.75 (t, *J* = 7.1 Hz, 1H), 4.22 (q, *J* = 7.4 Hz, 1H), 4.07 (q, *J* = 7.8 Hz, 1H), 2.49 (ddd, *J* = 29.2, 12.7, 7.8 Hz, 2H), 2.17 (ddq, *J* = 19.7, 12.2, 6.9, 6.5 Hz, 2H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 159.62, 141.58, 136.53, 129.83, 127.32, 127.11, 126.60, 125.28, 120.51, 79.11, 69.00, 30.78, 26.16.

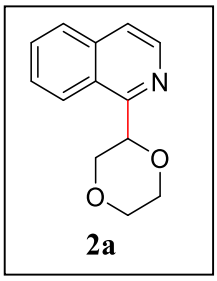
5-nitro-1-(tetrahydrofuran-2-yl)isoquinoline



1e

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.83 (d, *J* = 4.5 Hz, 1H), 8.13 (dd, *J* = 9.2, 5.7 Hz, 1H), 7.56 (d, *J* = 4.4 Hz, 1H), 7.54 – 7.44 (m, 2H), 5.47 (t, *J* = 7.1 Hz, 1H), 4.24 – 4.18 (m, 1H), 4.04 (q, *J* = 7.2 Hz, 1H), 2.66 – 2.53 (m, 1H), 2.05 (dtd, *J* = 26.7, 12.5, 6.1 Hz, 2H), 1.90 – 1.80 (m, 1H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 161.44, 149.63, 148.93, 145.18, 132.67, 132.58, 119.25, 118.99, 117.20, 107.11, 106.89, 76.78, 68.97, 33.61, 25.91.

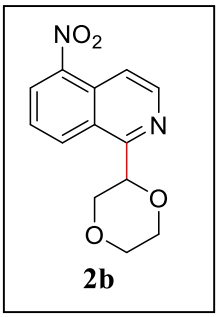
1-(1, 4-dioxan-2-yl)isoquinoline



2a

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.54 (d, *J* = 5.4 Hz, 1H), 8.32 (d, *J* = 8.3 Hz, 1H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.72 – 7.67 (m, 1H), 7.67 – 7.63 (m, 1H), 7.62 (d, *J* = 5.9 Hz, 1H), 5.48 (dd, *J* = 9.8, 2.9 Hz, 1H), 4.19 (dd, *J* = 12.2, 2.9 Hz, 1H), 4.16 – 4.09 (m, 2H), 4.08 (d, *J* = 2.0 Hz, 1H), 3.93 – 3.87 (m, 2H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 141.84, 136.46, 130.05, 127.49, 126.47, 124.68, 121.08, 75.83, 70.30, 67.59, 66.52.

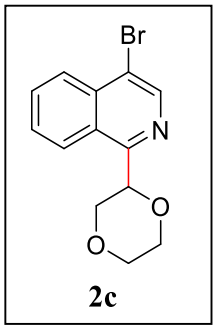
1-(1, 4-dioxan-2-yl)-5-nitroisoquinoline



2b

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.72 (s, 1H), 8.33 (d, *J* = 8.3 Hz, 1H), 8.21 (d, *J* = 8.4 Hz, 1H), 7.81 (t, *J* = 7.8 Hz, 1H), 7.70 (t, *J* = 7.8 Hz, 1H), 5.42 (dd, *J* = 9.3, 2.9 Hz, 1H), 4.21 – 4.10 (m, 2H), 4.08 (d, *J* = 6.8 Hz, 2H), 3.89 (dd, *J* = 7.4, 3.0 Hz, 2H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 155.54, 143.52, 135.11, 131.33, 128.40, 127.74, 126.82, 125.13, 120.09, 75.54, 70.08, 67.57, 66.49.

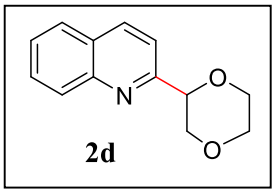
4-bromo-1-(1, 4-dioxan-2-yl)isoquinoline



2c

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.72 (s, 1H), 8.33 (d, *J* = 8.3 Hz, 1H), 8.21 (d, *J* = 8.4 Hz, 1H), 7.81 (t, *J* = 7.8 Hz, 1H), 7.70 (t, *J* = 7.8 Hz, 1H), 5.42 (dd, *J* = 9.3, 2.9 Hz, 1H), 4.21 – 4.10 (m, 2H), 4.08 (d, *J* = 6.8 Hz, 2H), 3.89 (dd, *J* = 7.4, 3.0 Hz, 2H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 155.54, 143.52, 135.11, 131.33, 128.40, 127.74, 126.82, 125.13, 120.09, 75.54, 70.08, 67.57, 66.49.

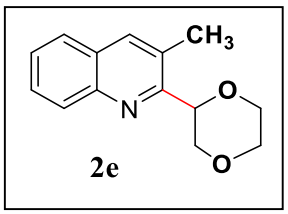
2-(1, 4-dioxan-2-yl)quinoline



2d

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.22 (d, *J* = 8.3 Hz, 1H), 8.10 (d, *J* = 8.3 Hz, 1H), 7.84 (d, *J* = 8.3 Hz, 1H), 7.74 (t, *J* = 7.6 Hz, 1H), 7.64 (d, *J* = 8.8 Hz, 1H), 7.56 (t, *J* = 7.3 Hz, 1H), 4.96 (d, *J* = 9.8 Hz, 1H), 4.27 (d, *J* = 11.7 Hz, 1H), 4.04 (d, *J* = 10.3 Hz, 2H), 3.91 – 3.79 (m, 2H), 3.66 (t, *J* = 11.0 Hz, 1H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 136.90, 129.67, 129.26, 127.64, 126.52, 118.53, 78.71, 71.12, 67.08, 66.45.

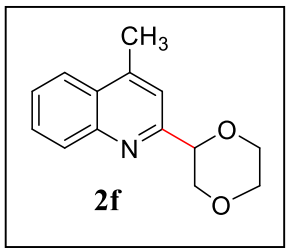
2-(1, 4-dioxan-2-yl)-3-methylquinoline



2e

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.73 (s, 1H), 8.67 (d, *J* = 8.8 Hz, 1H), 8.09 (d, *J* = 8.6 Hz, 1H), 7.65 (d, *J* = 7.3 Hz, 1H), 7.55 (d, *J* = 1.5 Hz, 1H), 5.44 (dd, *J* = 10.3, 2.9 Hz, 1H), 4.12 (d, *J* = 9.8 Hz, 1H), 4.03 – 4.00 (m, 2H), 3.98 – 3.90 (m, 2H), 3.80 (dd, *J* = 12.0, 3.2 Hz, 1H), 2.62 (s, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 153.23, 147.78, 138.96, 130.58, 130.19, 128.40, 128.27, 126.40, 126.20, 125.15, 76.53, 76.43, 69.80, 68.68, 68.58, 67.65, 67.57, 66.51, 66.42, 17.86.

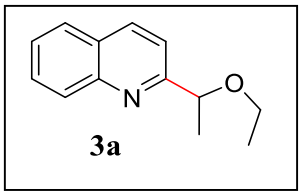
2-(1, 4-dioxan-2-yl)-4-methylquinoline



2f

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.09 (d, *J* = 8.3 Hz, 1H), 7.99 (d, *J* = 8.3 Hz, 1H), 7.74 – 7.68 (m, 1H), 7.56 (t, *J* = 7.8 Hz, 1H), 7.48 (s, 1H), 4.91 (dd, *J* = 9.8, 2.9 Hz, 1H), 4.25 (dd, *J* = 11.7, 2.9 Hz, 1H), 4.02 (dd, *J* = 9.8, 2.9 Hz, 2H), 3.87 – 3.77 (m, 2H), 3.65 (dd, *J* = 11.7, 9.8 Hz, 1H), 2.73 (s, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 157.81, 147.28, 145.23, 129.78, 129.32, 127.62, 126.24, 123.70, 119.12, 78.79, 71.12, 67.09, 66.44, 18.88.

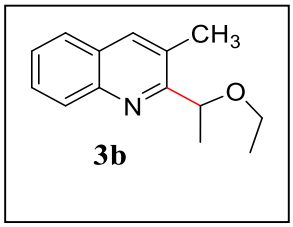
2-(1-ethoxyethyl)quinoline



3a

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.21 (d, *J* = 8.3 Hz, 1H), 8.09 (d, *J* = 8.8 Hz, 1H), 7.84 (d, *J* = 8.3 Hz, 1H), 7.77 – 7.69 (m, 1H), 7.64 (d, *J* = 8.3 Hz, 1H), 7.55 (t, *J* = 7.3 Hz, 1H), 4.75 (q, *J* = 6.8 Hz, 1H), 3.55 (dq, *J* = 9.3, 6.8 Hz, 1H), 3.44 (dq, *J* = 9.3, 6.8 Hz, 1H), 1.57 (d, *J* = 6.8 Hz, 3H), 1.25 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 164.46, 137.03, 129.48, 129.01, 127.60, 126.21, 117.81, 79.68, 77.20, 64.67, 29.69, 22.66, 15.44.

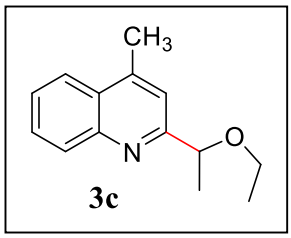
2-(1-ethoxyethyl)-3-methylquinoline



3b

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.11 (d, *J* = 8.3 Hz, 1H), 7.91 (s, 1H), 7.75 (d, *J* = 8.3 Hz, 1H), 7.66 (t, *J* = 7.8 Hz, 1H), 7.51 (t, *J* = 7.6 Hz, 1H), 4.97 (q, *J* = 6.8 Hz, 1H), 3.53 (dq, *J* = 9.3, 7.1 Hz, 1H), 3.44 (dq, *J* = 9.3, 6.8 Hz, 1H), 2.63 (s, 3H), 1.63 (s, 3H), 1.26 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 161.32, 137.29, 129.02, 128.51, 126.59, 126.31, 78.77, 77.20, 64.38, 29.69, 19.95, 18.69, 15.46.

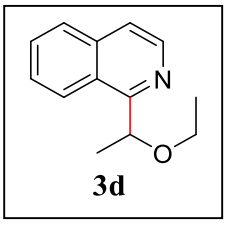
2-(1-ethoxyethyl)-4-methylquinoline



3c

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.11 (d, *J* = 8.3 Hz, 1H), 8.01 (d, *J* = 8.3 Hz, 1H), 7.72 (dd, *J* = 8.8, 6.8 Hz, 1H), 7.57 (t, *J* = 7.6 Hz, 1H), 7.47 (s, 1H), 4.72 (q, *J* = 6.8 Hz, 1H), 3.59 – 3.49 (m, 1H), 3.49 – 3.39 (m, 1H), 2.76 (s, 3H), 1.56 (d, *J* = 6.8 Hz, 3H), 1.25 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 163.94, 147.00, 145.44, 129.40, 129.24, 127.67, 126.04, 123.69, 118.35, 79.53, 64.66, 22.59, 18.96, 15.44.

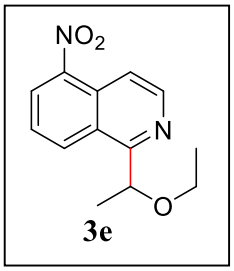
1-(1-ethoxyethyl)isoquinoline



3d

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.71 (d, *J* = 8.3 Hz, 1H), 8.47 (d, *J* = 5.4 Hz, 1H), 7.84 (d, *J* = 7.8 Hz, 1H), 7.68 (t, *J* = 7.6 Hz, 1H), 7.59 (dd, *J* = 9.0, 6.6 Hz, 2H), 5.20 (q, *J* = 6.6 Hz, 1H), 3.53 (dq, *J* = 9.8, 6.8 Hz, 1H), 3.41 (dq, *J* = 9.3, 7.1 Hz, 1H), 2.45 (s, 1H), 1.72 (d, *J* = 6.8 Hz, 3H), 1.20 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 161.81, 141.39, 129.94, 127.41, 126.90, 125.63, 120.55, 79.98, 64.50, 21.61, 15.44.

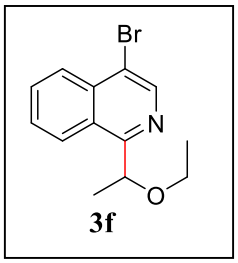
1-(1-ethoxyethyl)-5-nitroisoquinoline



3e

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.19 (d, *J* = 8.3 Hz, 1H), 8.67 (d, *J* = 5.9 Hz, 1H), 8.48 (d, *J* = 7.8 Hz, 1H), 8.35 (d, *J* = 6.4 Hz, 1H), 7.71 (t, *J* = 8.1 Hz, 1H), 5.19 (q, *J* = 6.6 Hz, 1H), 3.56 (dq, *J* = 9.3, 6.8 Hz, 1H), 3.40 (dq, *J* = 9.3, 7.1 Hz, 1H), 1.73 (d, *J* = 6.8 Hz, 3H), 1.20 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 162.80, 145.85, 144.72, 132.61, 129.35, 127.57, 126.60, 125.25, 115.21, 80.99, 64.73, 21.74, 15.41.

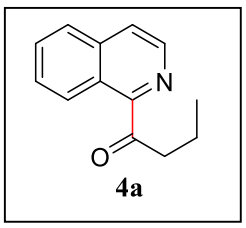
4-bromo-1-(1-ethoxyethyl)isoquinoline



3f

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.73 (d, *J* = 8.8 Hz, 1H), 8.68 (s, 1H), 8.23 (d, *J* = 8.4 Hz, 1H), 7.85 – 7.77 (m, 1H), 7.67 (dd, *J* = 8.6, 6.6 Hz, 1H), 5.16 (q, *J* = 6.8 Hz, 1H), 3.53 (dq, *J* = 9.3, 6.8 Hz, 1H), 3.42 (dq, *J* = 9.3, 6.8 Hz, 1H), 1.71 (d, *J* = 6.8 Hz, 3H), 1.21 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 161.44, 143.30, 131.14, 127.77, 127.43, 126.73, 125.90, 119.28, 79.66, 64.55, 21.54, 15.41.

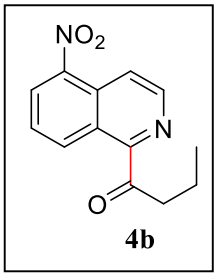
1-(isoquinolin-1-yl)butan-1-one



4a

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.87 (d, *J* = 8.3 Hz, 1H), 8.59 (d, *J* = 5.4 Hz, 1H), 7.93 – 7.85 (m, 1H), 7.82 (d, *J* = 5.9 Hz, 1H), 7.78 – 7.65 (m, 2H), 3.32 (t, *J* = 7.3 Hz, 2H), 1.84 (q, *J* = 7.3 Hz, 2H), 1.07 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 204.23, 142.97, 131.59, 129.78, 127.19, 126.87, 126.30, 123.51, 42.33, 17.66, 13.88.

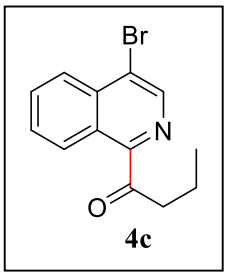
1-(5-nitroisoquinolin-1-yl)butan-1-one



4b

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.22 (d, *J* = 8.3 Hz, 1H), 8.81 (d, *J* = 6.4 Hz, 1H), 8.62 (d, *J* = 5.9 Hz, 1H), 8.54 (d, *J* = 7.8 Hz, 1H), 7.80 (t, *J* = 8.1 Hz, 1H), 3.35 (t, *J* = 7.3 Hz, 2H), 1.84 (q, *J* = 7.3 Hz, 2H), 1.08 (t, *J* = 7.6 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.14, 154.05, 144.29, 133.73, 128.05, 127.13, 118.93, 77.33, 77.01, 76.70, 42.36, 17.58, 13.84, 204.14.

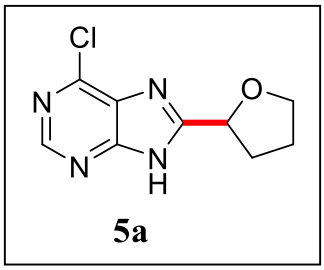
1-(4-bromoisoquinolin-1-yl)butan-1-one



4c

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.91 – 8.86 (m, 1H), 8.78 (s, 1H), 8.26 (dd, *J* = 8.3, 1.0 Hz, 1H), 7.85 (ddd, *J* = 8.8, 6.8, 1.7 Hz, 1H), 7.75 (ddd, *J* = 8.3, 6.9, 1.5 Hz, 1H), 3.29 (t, *J* = 7.3 Hz, 2H), 1.82 (q, *J* = 7.6 Hz, 2H), 1.06 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 204.23, 142.97, 131.59, 129.78, 127.19, 126.87, 126.30, 123.51, 42.33, 17.66, 13.88.

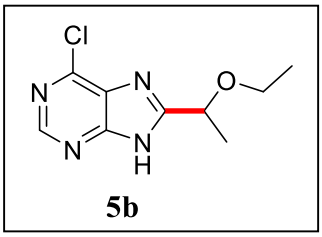
6-chloro-8-(tetrahydrofuran-2-yl)-9H-purine



5a

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84 (s, 1H), 5.35 (dd, *J* = 7.9, 5.9 Hz, 1H), 4.11 (td, *J* = 6.8, 4.7 Hz, 2H), 2.68 – 2.58 (m, 1H), 2.41 (d, *J* = 6.3 Hz, 1H), 2.13 (dt, *J* = 7.8, 6.3 Hz, 1H), 2.05 – 1.98 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.34, 152.62, 150.87, 150.10, 132.66, 69.56, 32.14, 25.85.

6-chloro-8-(1-ethoxyethyl)-9H-purine



5b

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.85 (s, 1H), 4.92 (d, *J* = 6.5 Hz, 1H), 3.80 – 3.66 (m, 1H), 3.64 – 3.52 (m, 1H), 1.67 (d, *J* = 6.7 Hz, 3H), 1.26 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 160.68, 152.99, 151.30, 150.54, 132.29, 72.94, 65.86, 21.45, 15.56.

References

(1) Martín Romo, R. C□H Activation. Topics in Current Chemistry, Volume 292. Edited by Jin-Quan Yu and Zhangjie Shi. *Angew. Chem. Int. Ed.* **2011**, *50* (11), 2433–2433.

(2) Cernak, T.; Dykstra, K. D.; Tyagarajan, S.; Vachal, P.; Krska, S. W. The Medicinal Chemist's Toolbox for Late Stage Functionalization of Drug-like Molecules. *Chem. Soc. Rev.* **2016**, *45* (3), 546–576.

(3) Schneider, P.; Schneider, G. Privileged Structures Revisited. *Angew. Chem. Int. Ed.* **2017**, *56* (27), 7971–7974. h

(4) Yang, D.; Burugupalli, S.; Daniel, D.; Chen, Y. Microwave-Assisted One-Pot Synthesis of Isoquinolines, Furopyridines, and Thienopyridines by Palladium-Catalyzed Sequential Coupling–Imination–Annulation of 2-Bromoarylaldehydes with Terminal Acetylenes and Ammonium Acetate. *J. Org. Chem.* **2012**, *77* (9), 4466–4472.

(5) Wang, W.; Zhao, X.; Tong, L.; Chen, J.; Zhang, X.; Yan, M. Direct Inter- and Intramolecular Addition of Amides to Arylalkenes Promoted by KOt-Bu/DMF. *J. Org. Chem.* **2014**, *79* (18), 8557–8565.

(6) Nagib, D. A.; MacMillan, D. W. C. Trifluoromethylation of Arenes and Heteroarenes by Means of Photoredox Catalysis. *Nature* **2011**, *480* (7376), 224–228.

(7) Saparov, B.; Mitzi, D. B. Organic-Inorganic Perovskites: Structural Versatility for Functional Materials Design. *Chem. Rev.* **2016**, *116* (7), 4558–4596.

(8) Yang, Y.; Yang, M.; Moore, D. T.; Yan, Y.; Miller, E. M.; Zhu, K.; Beard, M. C. Top and Bottom Surfaces Limit Carrier Lifetime in Lead Iodide Perovskite Films. *Nat. Energy* **2017**, *2* (2), 1–7.

(9) Dong, Q.; Fang, Y.; Shao, Y.; Mulligan, P.; Qiu, J.; Cao, L.; Huang, J. Electron-Hole Diffusion Lengths > 175 Mm in Solution-Grown CH3NH3PbI3 Single Crystals. *Science* **2015**, *347* (6225), 967–970.

(10) Royer, S.; Duprez, D.; Can, F.; Courtois, X.; Batiot-Dupeyrat, C.; Laassiri, S.; Alamdari, H. Perovskites as Substitutes of Noble Metals for Heterogeneous Catalysis: Dream or Reality. *Chem. Rev.* **2014**, *114* (20), 10292–10368.

(11) Qaid, S. M. H.; Al Sobaie, Mohammed. S.; Majeed Khan, M. A.; Bedja, I. M.; Alharbi, Fahhad. H.; Nazeeruddin, M. K.; Aldwayyan, A. S. Band-Gap Tuning of Lead Halide Perovskite Using a Single Step Spin-Coating Deposition Process. *Mater. Lett.* **2016**, *164*, 498–501.

(12) Chen, H.; Li, M.; Wang, B.; Ming, S.; Su, J. Structure, Electronic and Optical Properties of CsPbX3 Halide Perovskite: A First-Principles Study. *J. Alloys Compd.* **2021**, *862*, 158442.

(13) Kanhere, P.; Chen, Z. A Review on Visible Light Active Perovskite-Based Photocatalysts. *Molecules* **2014**, *19* (12), 19995–20022.

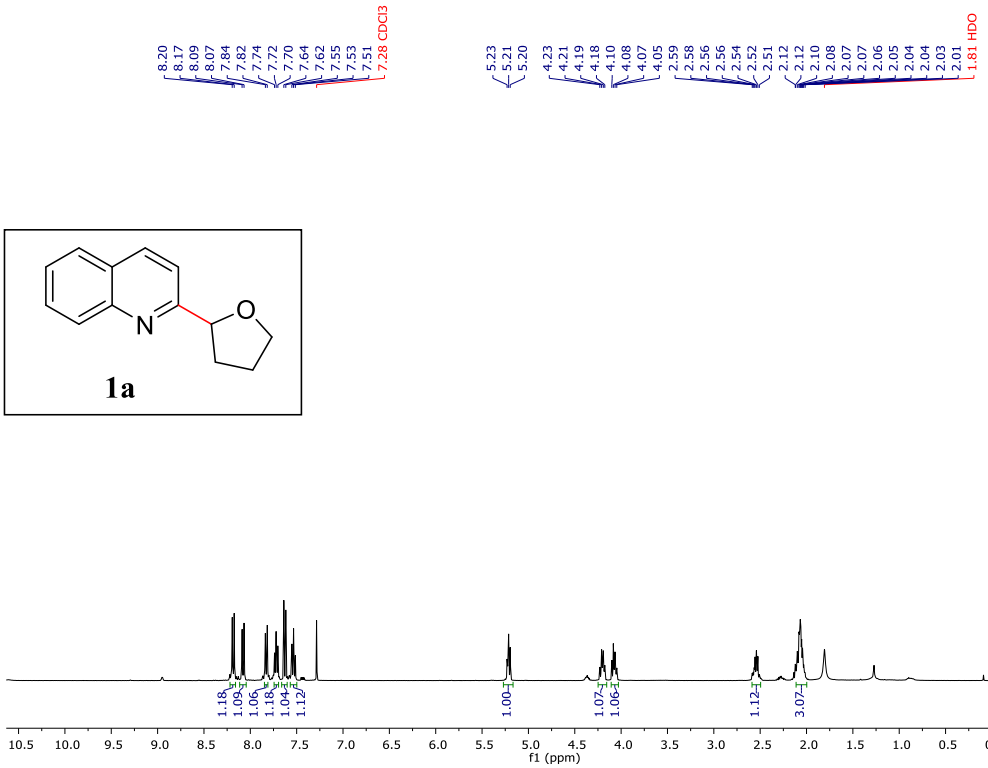
(14) Jin, J.; MacMillan, D. W. C. Direct α-Arylation of Ethers through the Combination of Photoredox-Mediated C□H Functionalization and the Minisci Reaction. *Angew. Chem. Int. Ed.* **2015**, *54* (5), 1565–1569.

(15) J. Duncton, M. A. Minisci Reactions: Versatile CH-Functionalizations for Medicinal Chemists. *MedChemComm* **2011**, *2* (12), 1135–1161.

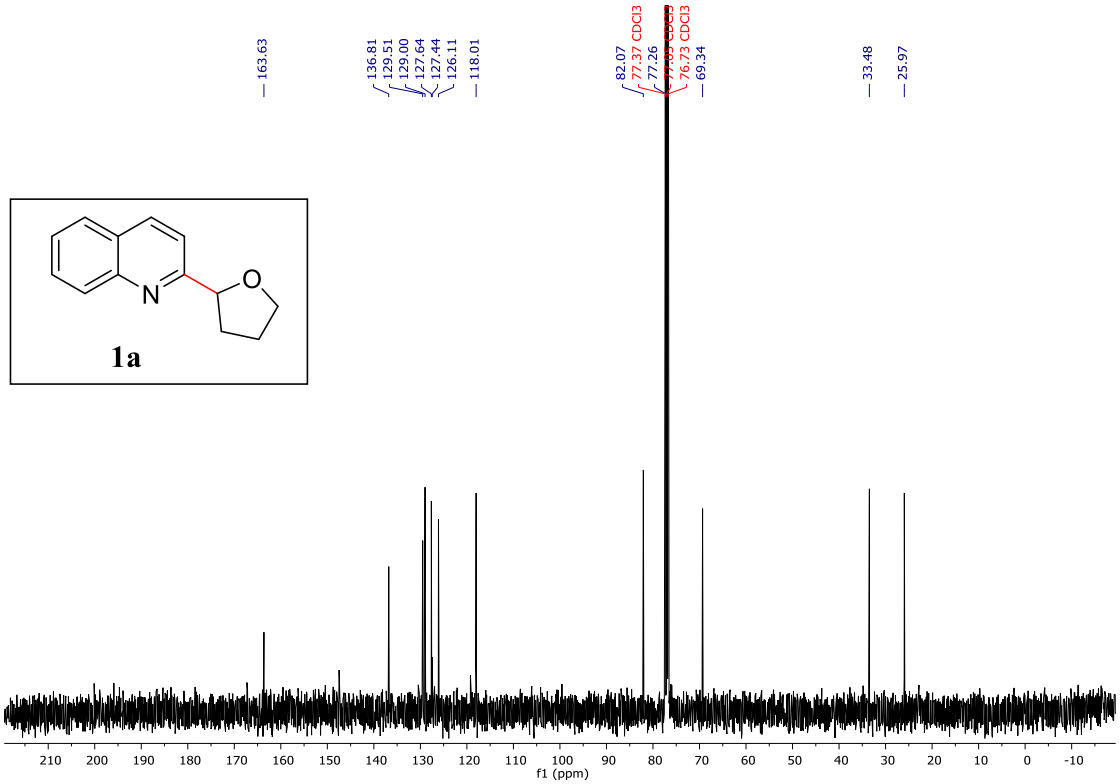
(16) Matsui, J. K.; Molander, G. A. Organocatalyzed, Photoredox Heteroarylation of 2-Trifluoroboratochromanones via C–H Functionalization. *Org. Lett.* **2017**, *19* (4), 950–953.

(17) Zhu, X.; Lin, Y.; San Martin, J.; Sun, Y.; Zhu, D.; Yan, Y. Lead Halide Perovskites for Photocatalytic Organic Synthesis. *Nat. Commun.* **2019**, *10* (1), 2843.

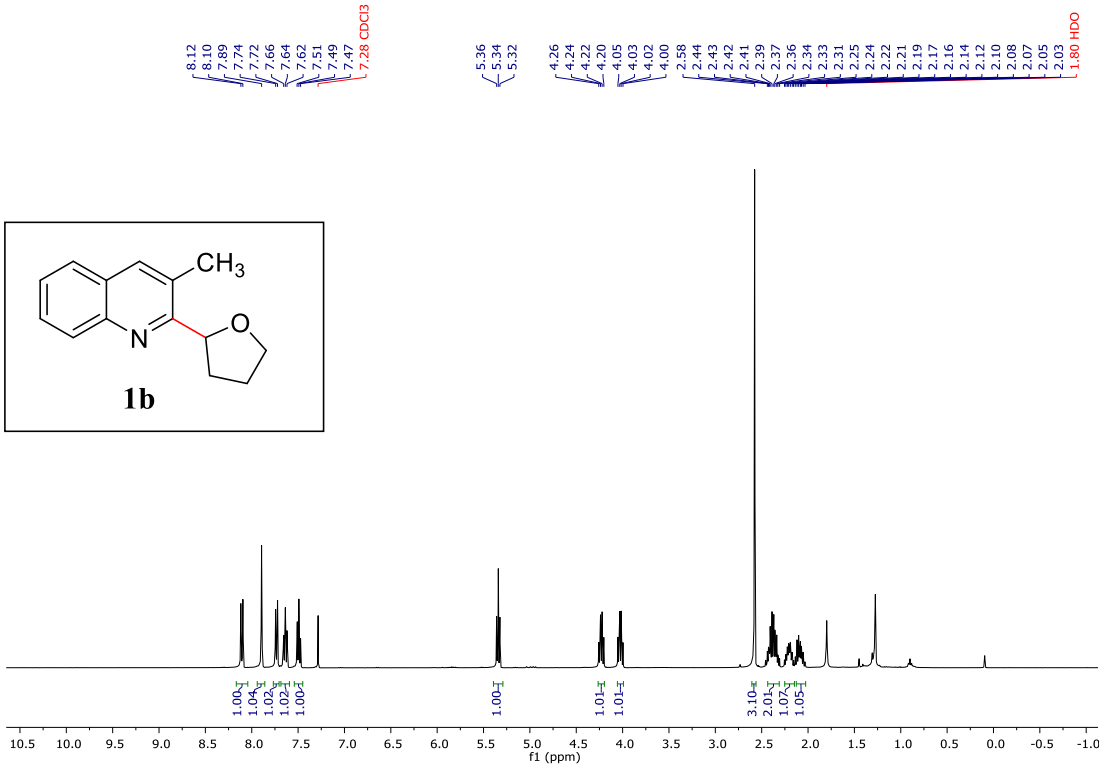
2.8: NMR spectra of newly synthesized compounds:



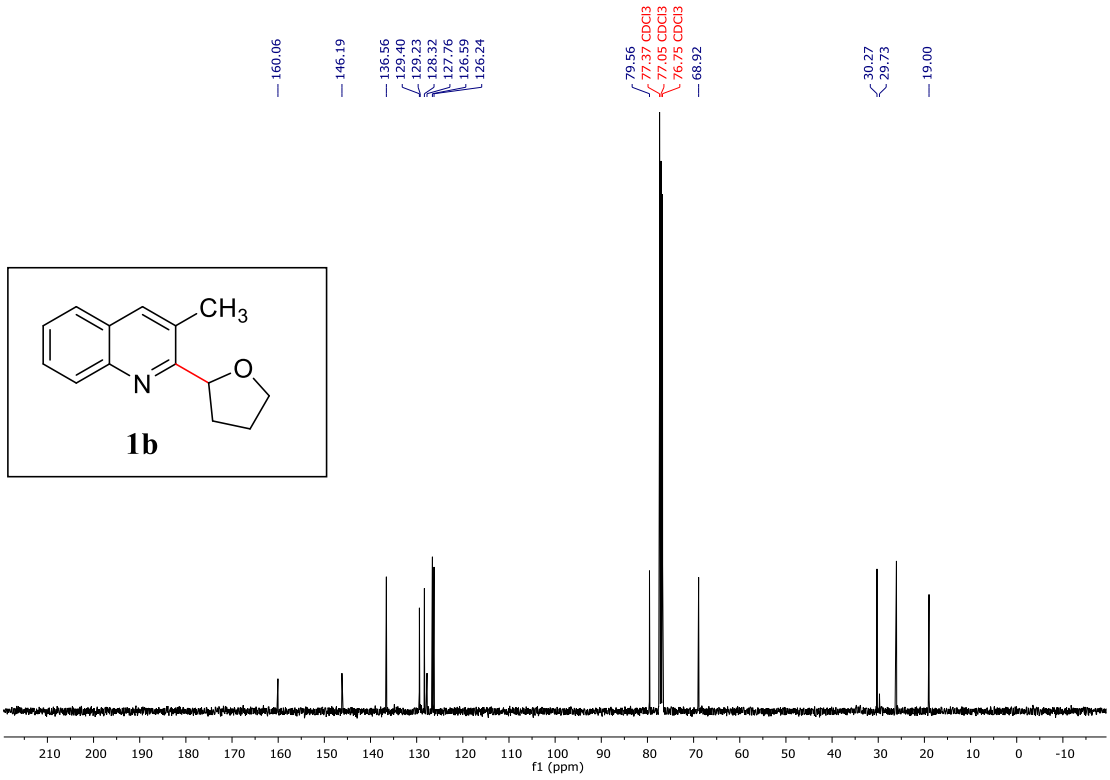
^{1}H NMR ($CDCl_3$, 400 MHz) Spectrum of 2-(tetrahydrofuran-2-yl)quinoline



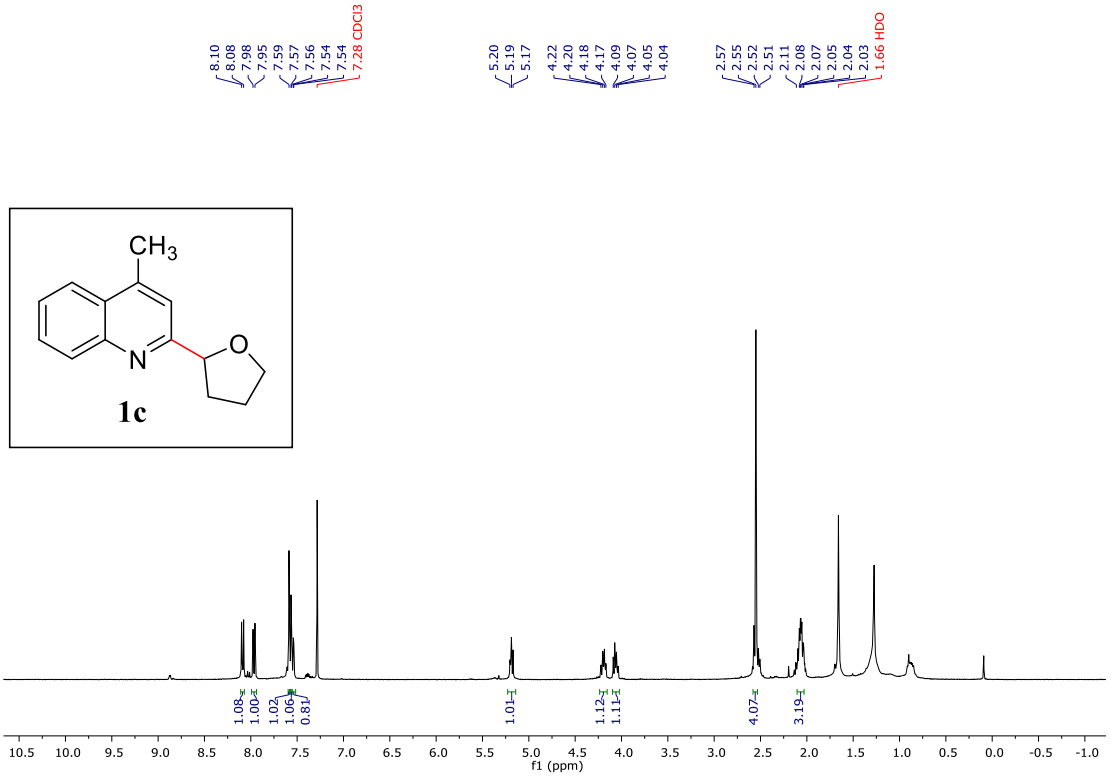
^{13}C NMR ($CDCl_3$, 100 MHz) Spectrum of 2-(tetrahydrofuran-2-yl)quinoline



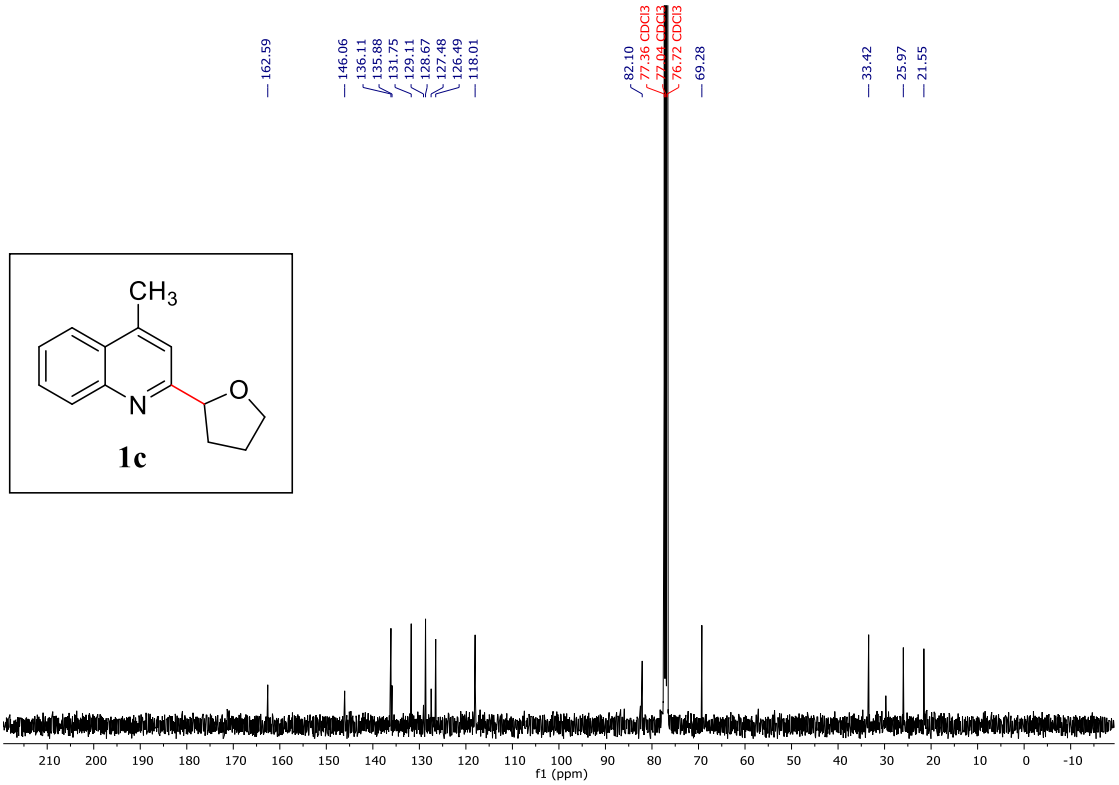
^{1}H NMR ($CDCl_3$, 400 MHz) Spectrum of 3-methyl-2-(tetrahydrofuran-2-yl)quinoline



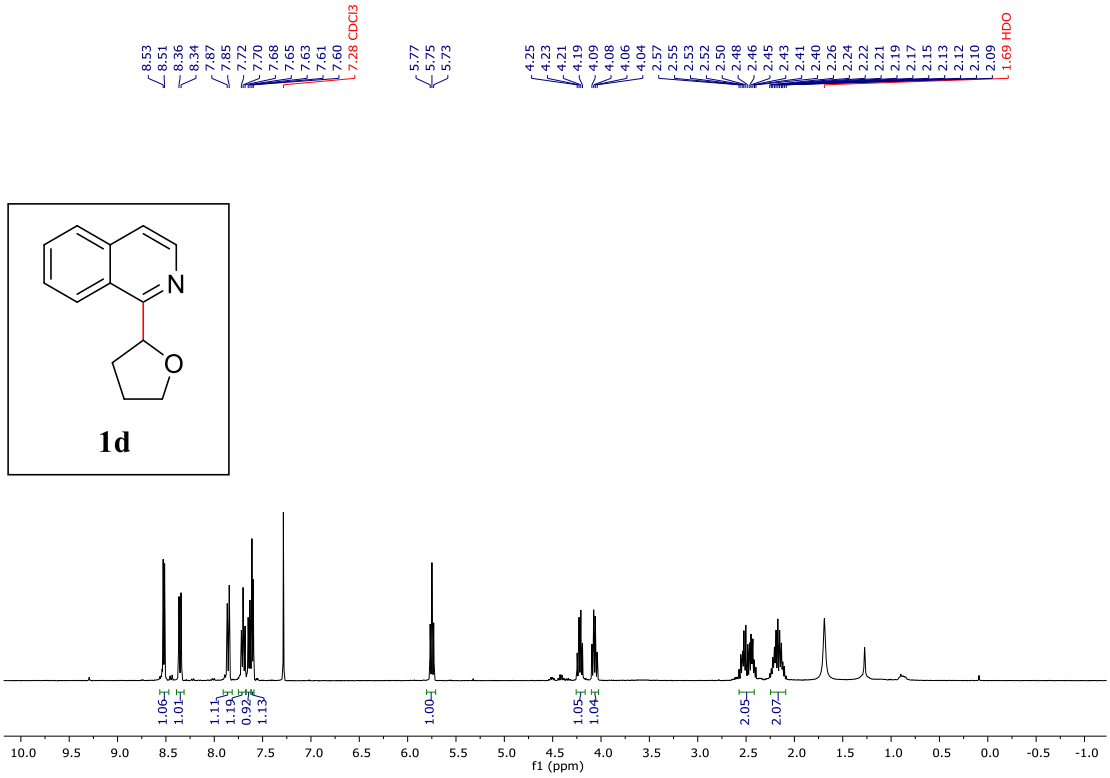
^{13}C NMR ($CDCl_3$, 100 MHz) Spectrum of 3-methyl-2-(tetrahydrofuran-2-yl)quinoline



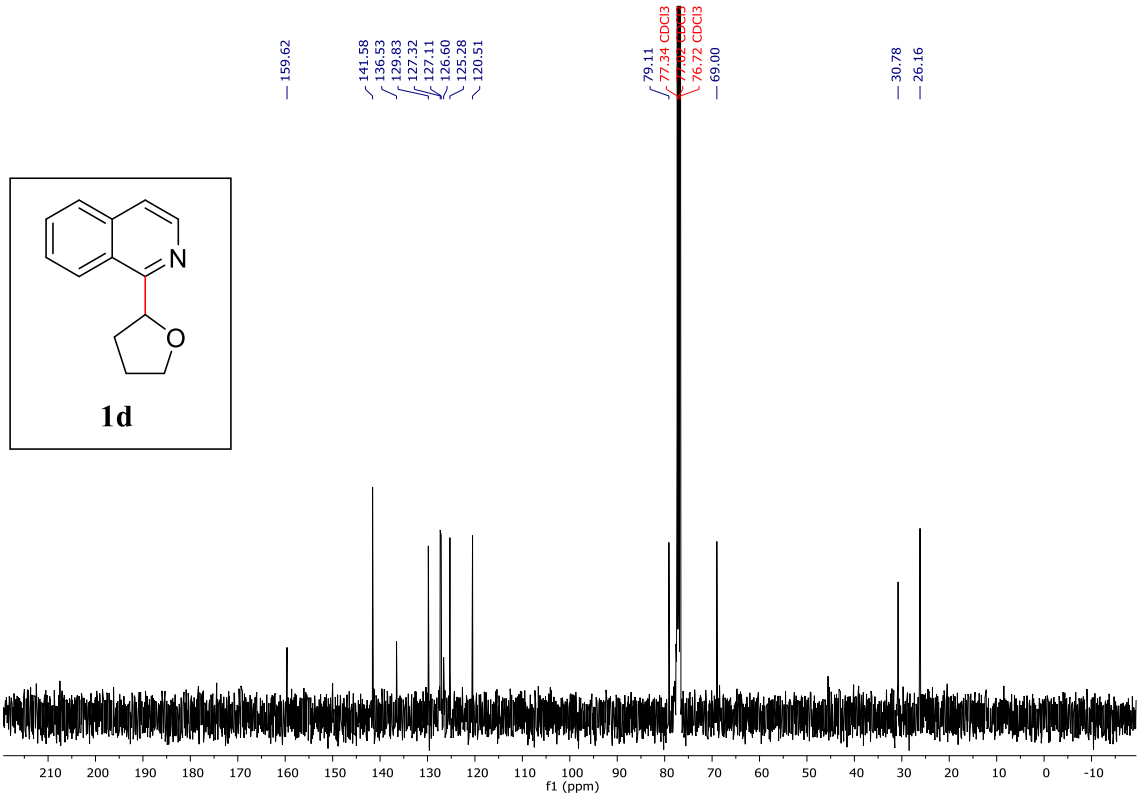
^{1}H NMR ($CDCl_3$, 400 MHz) Spectrum of 4-methyl-2-(tetrahydrofuran-2-yl)quinoline



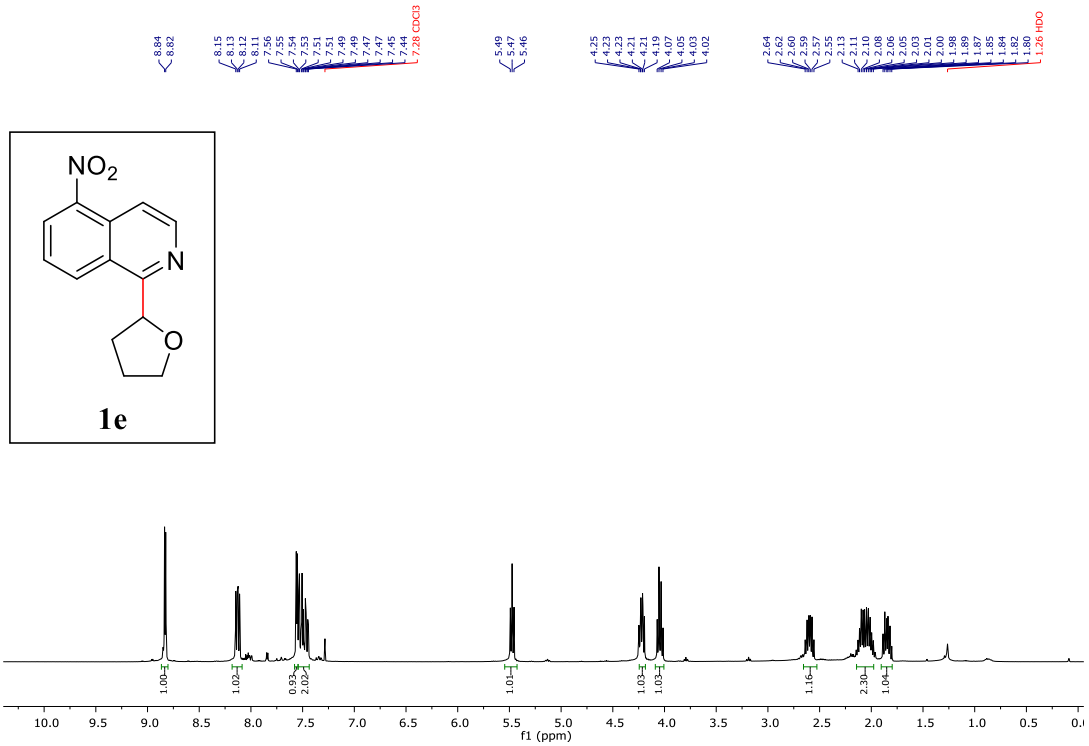
^{13}C NMR ($CDCl_3$, 100 MHz) Spectrum of 4-methyl-2-(tetrahydrofuran-2-yl)quinoline



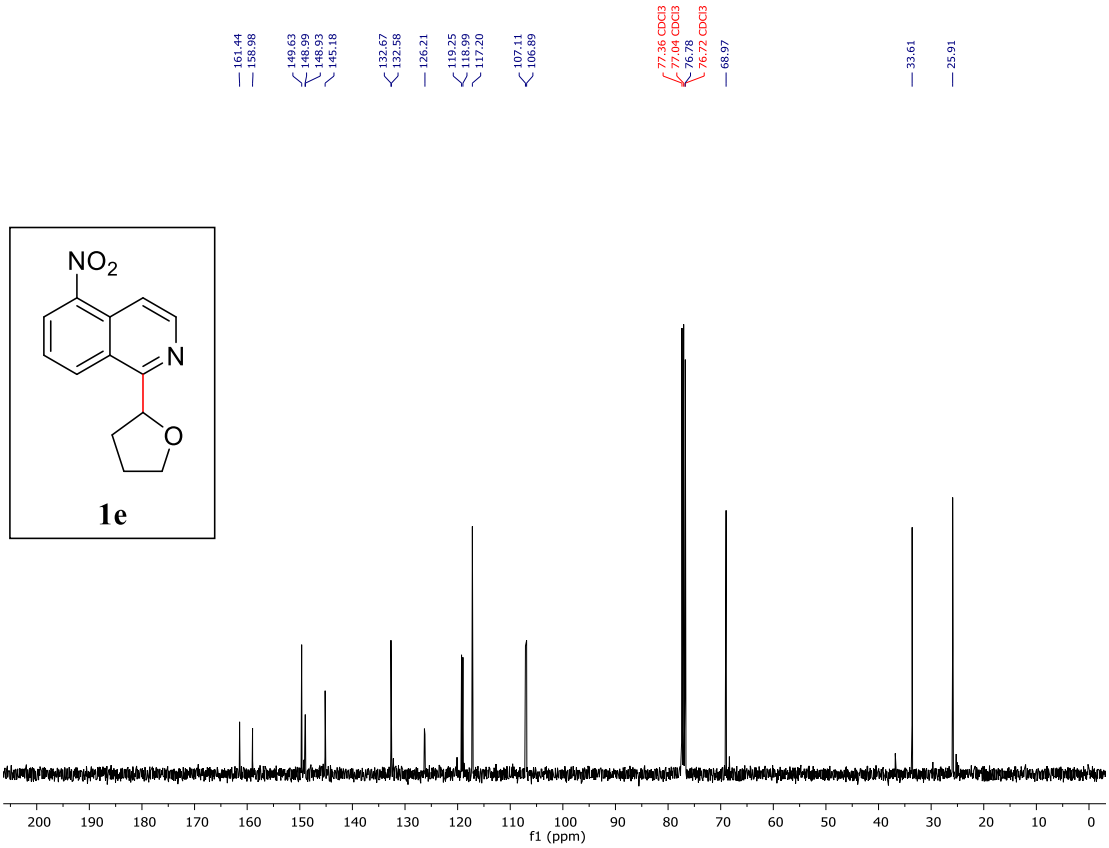
^{1}H NMR ($CDCl_3$, 400 MHz) Spectrum of 1-(tetrahydrofuran-2-yl)isoquinoline



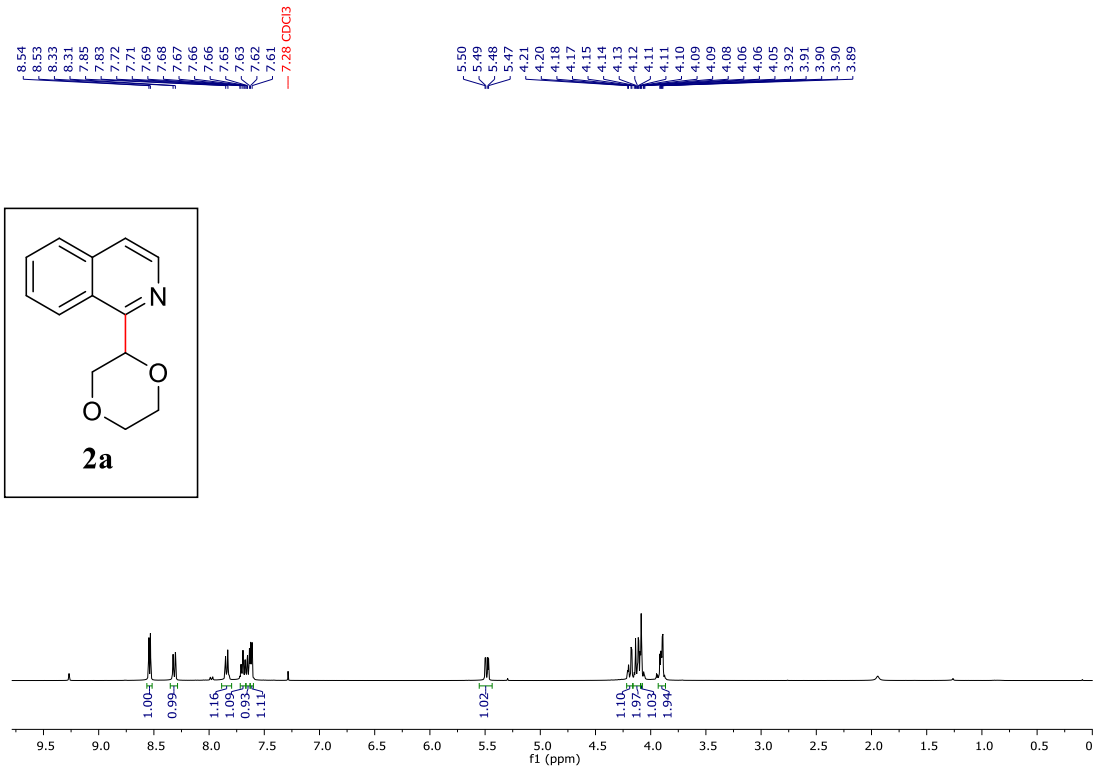
^{13}C NMR ($CDCl_3$, 100 MHz) Spectrum of 1-(tetrahydrofuran-2-yl)isoquinoline



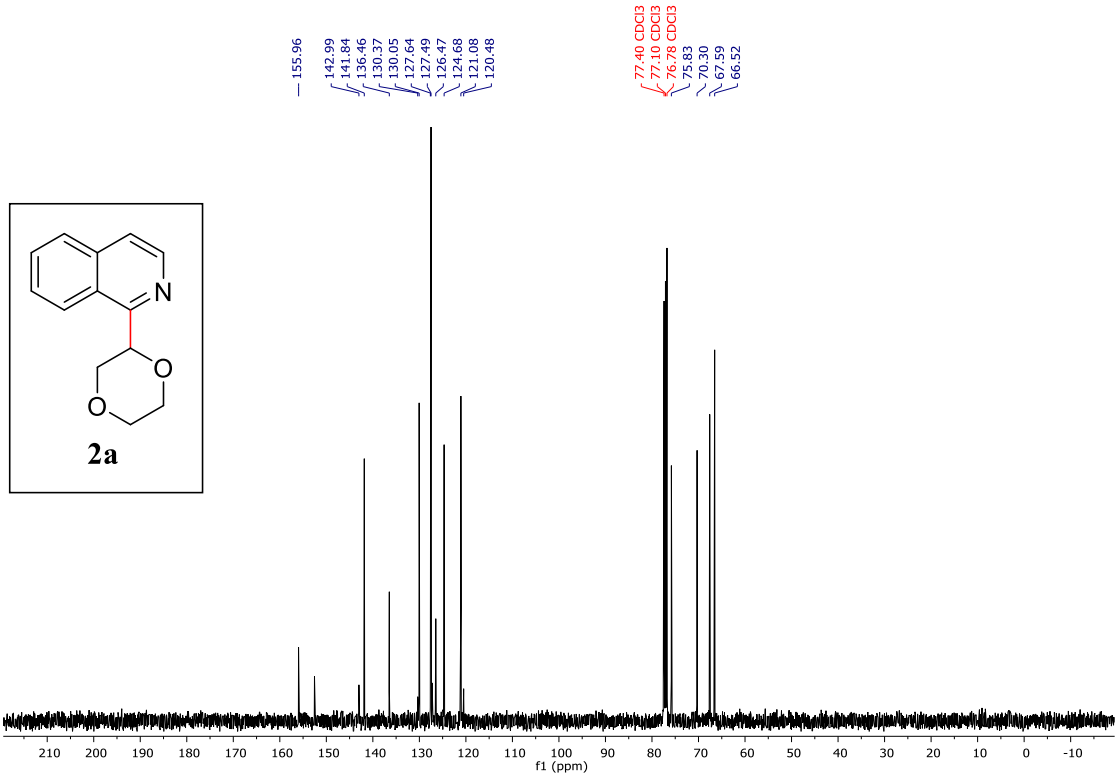
^{1}H NMR ($CDCl_3$, 400 MHz) Spectrum of 5-nitro-1-(tetrahydrofuran-2-yl)isoquinoline



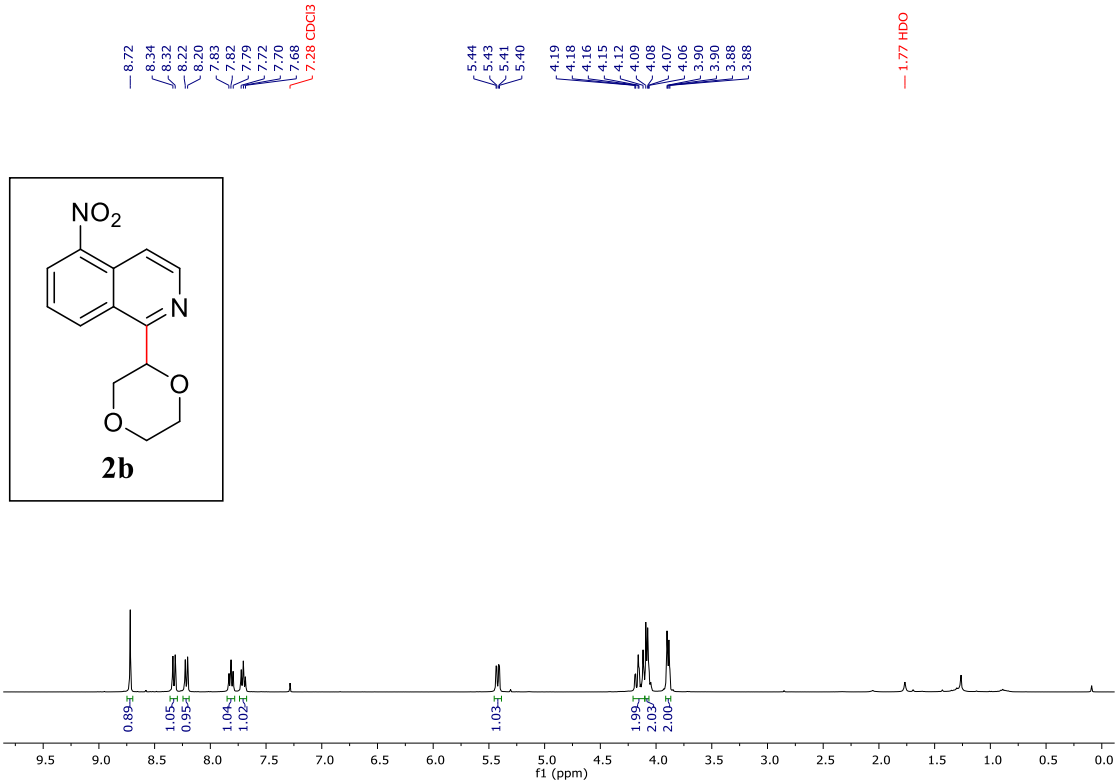
^{13}CNMR ($CDCl_3$, 100 MHz) Spectrum of 5-nitro-1-(tetrahydrofuran-2-yl)isoquinoline



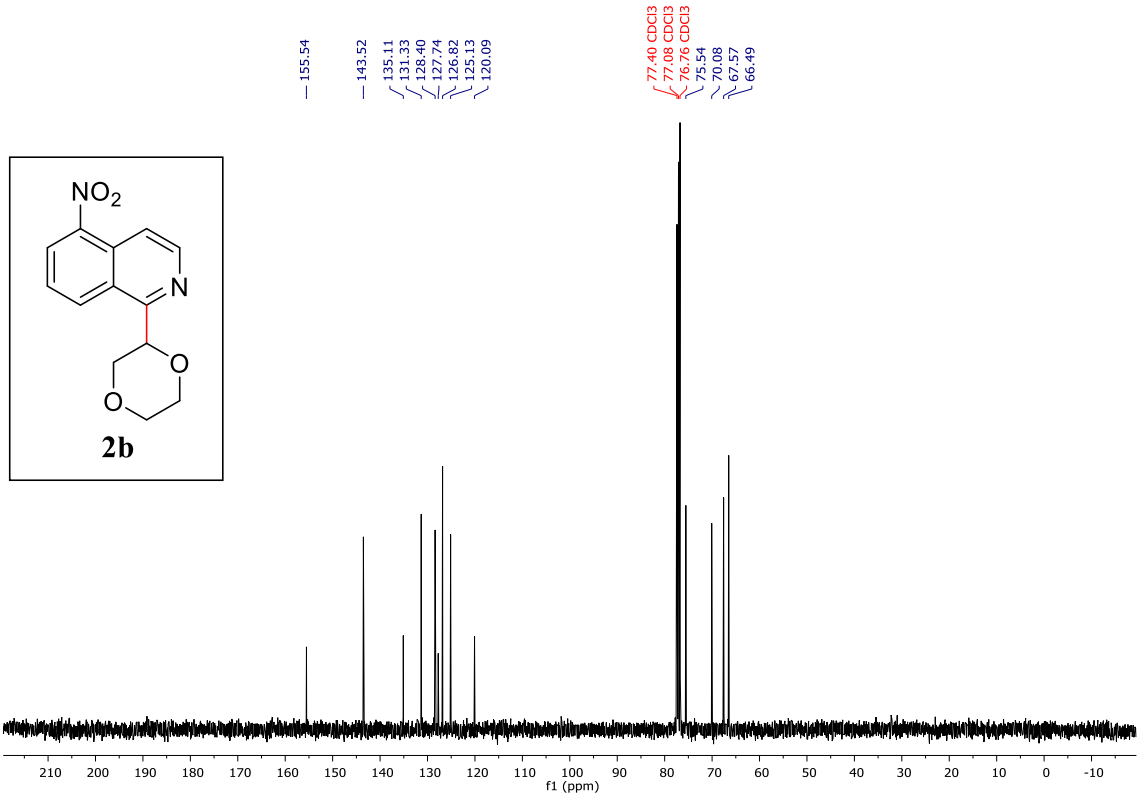
^{1}H NMR ($CDCl_3$, 400 MHz) Spectrum of 1-(1, 4-dioxan-2-yl)isoquinoline



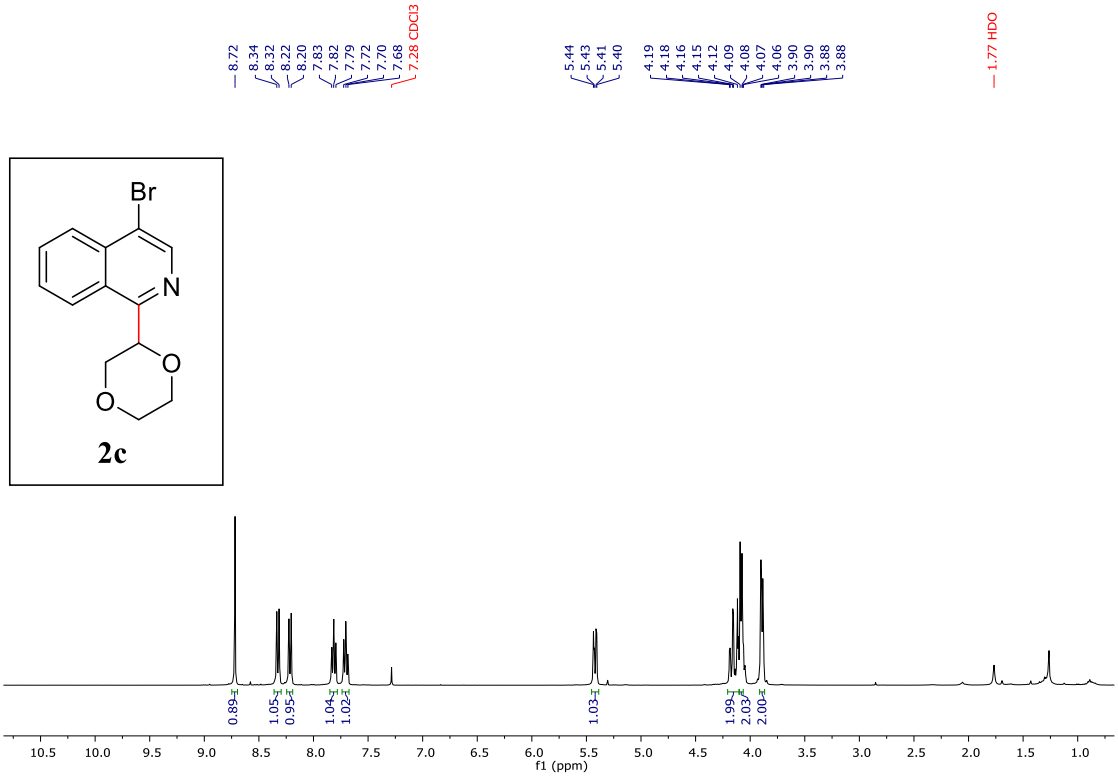
^{13}C NMR ($CDCl_3$, 100 MHz) Spectrum of 1-(1, 4-dioxan-2-yl)isoquinoline



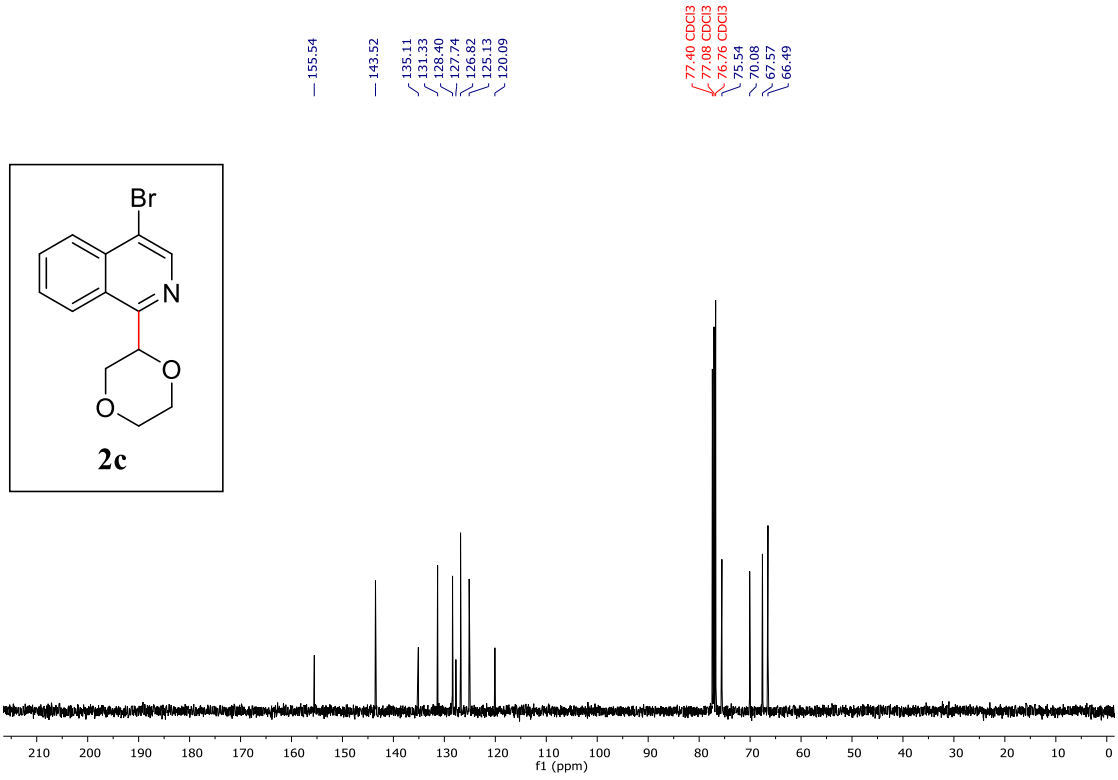
^{1}H NMR ($CDCl_3$, 400 MHz) Spectrum of 1-(1, 4-dioxan-2-yl)-5-nitroisoquinoline



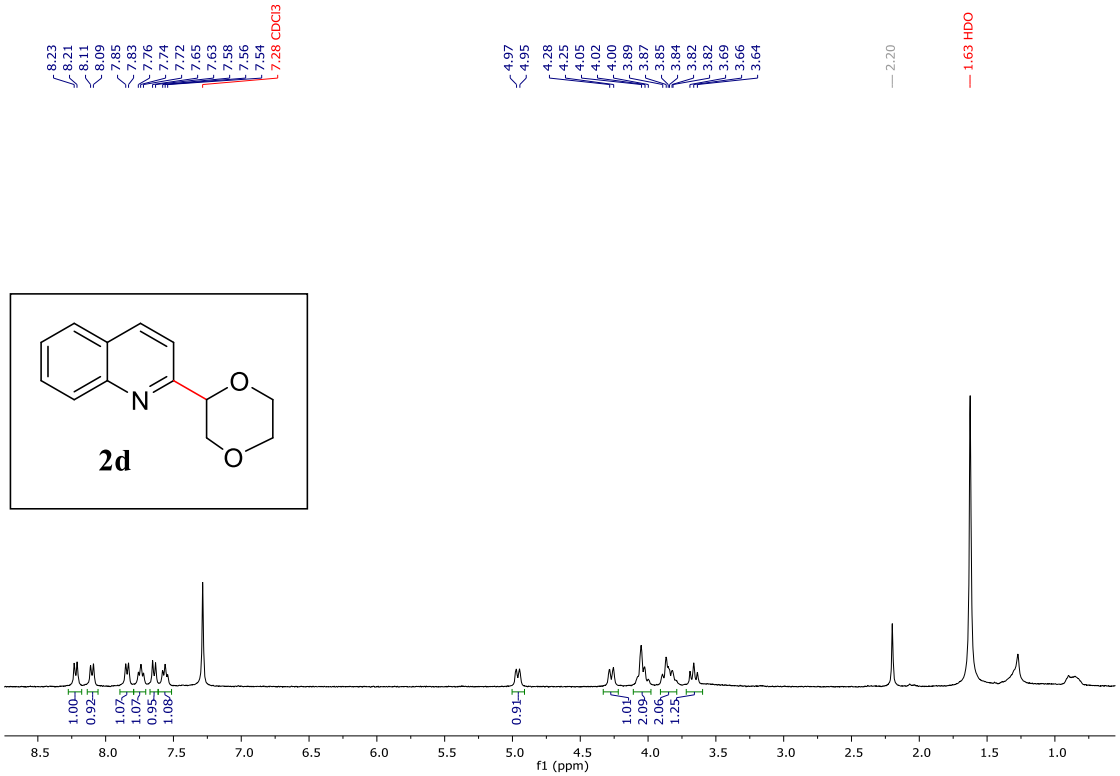
^{13}C NMR ($CDCl_3$, 100 MHz) Spectrum of 1-(1, 4-dioxan-2-yl)-5-nitroisoquinoline



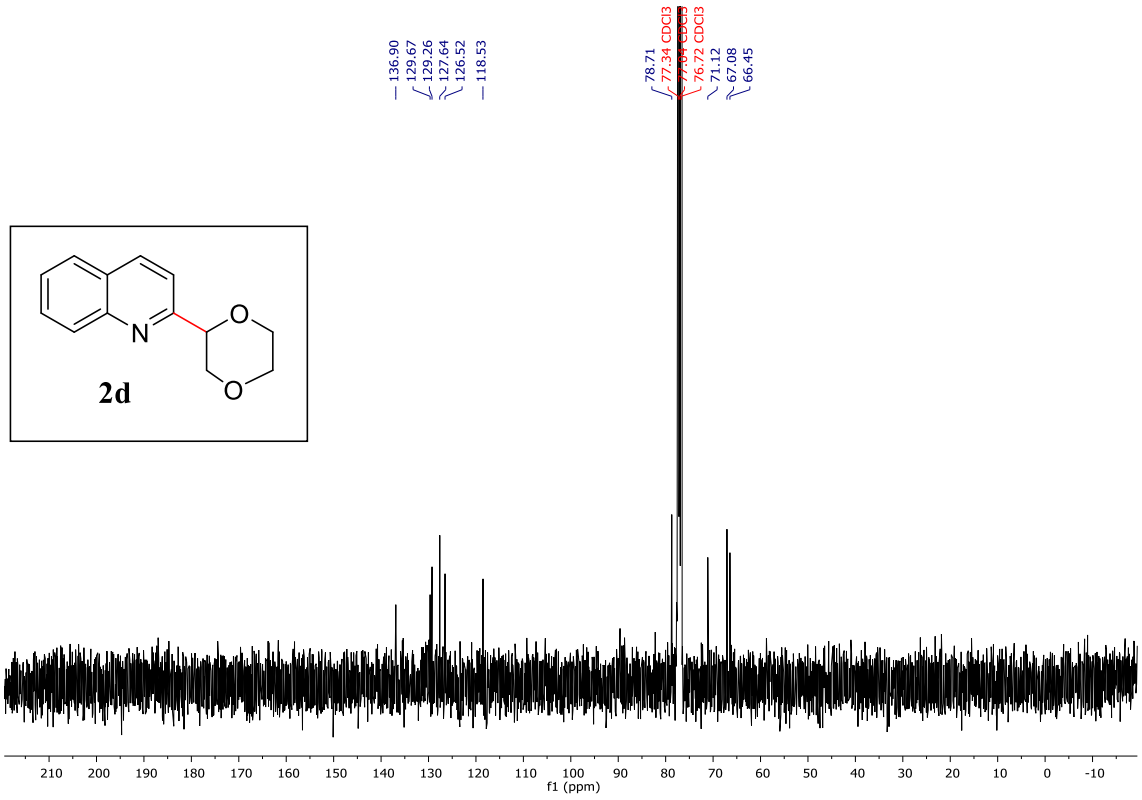
^{1}H NMR ($CDCl_3$, 400 MHz) Spectrum of 4-bromo-1-(1, 4-dioxan-2-yl)isoquinoline



^{13}C NMR ($CDCl_3$, 100 MHz) Spectrum of 4-bromo-1-(1, 4-dioxan-2-yl)isoquinoline



^{1}H NMR ($CDCl_3$, 400 MHz) Spectrum of 2-(1, 4-dioxan-2-yl)quinoline



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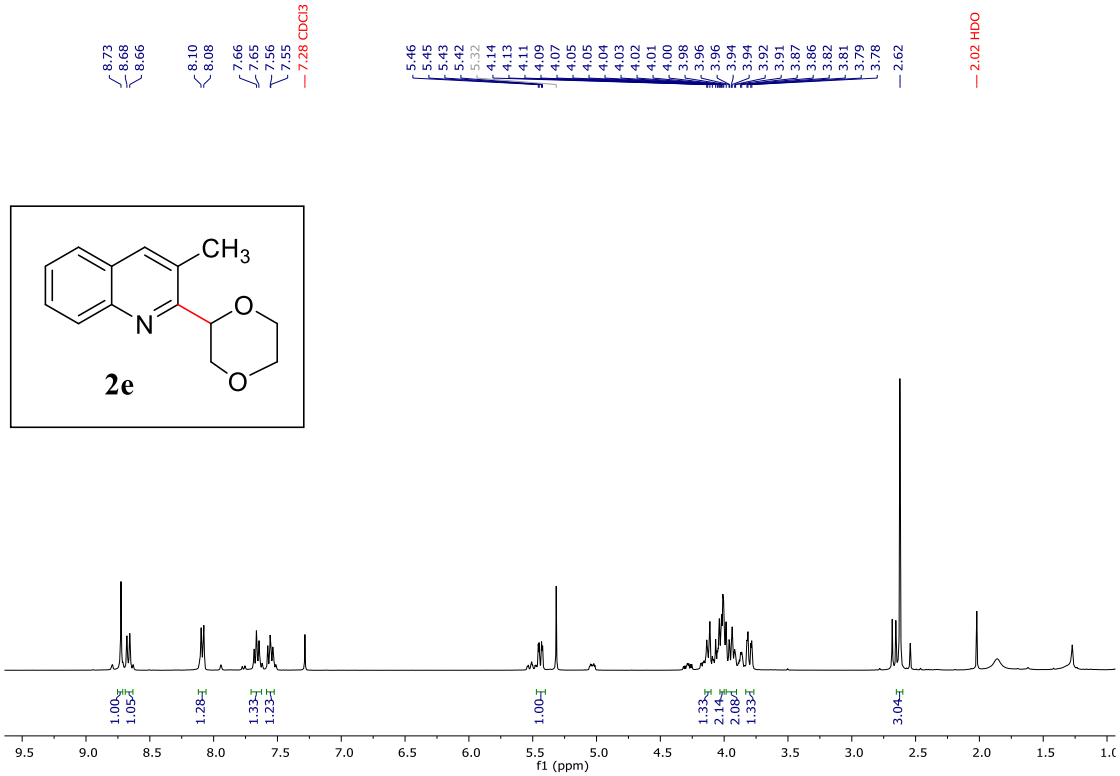

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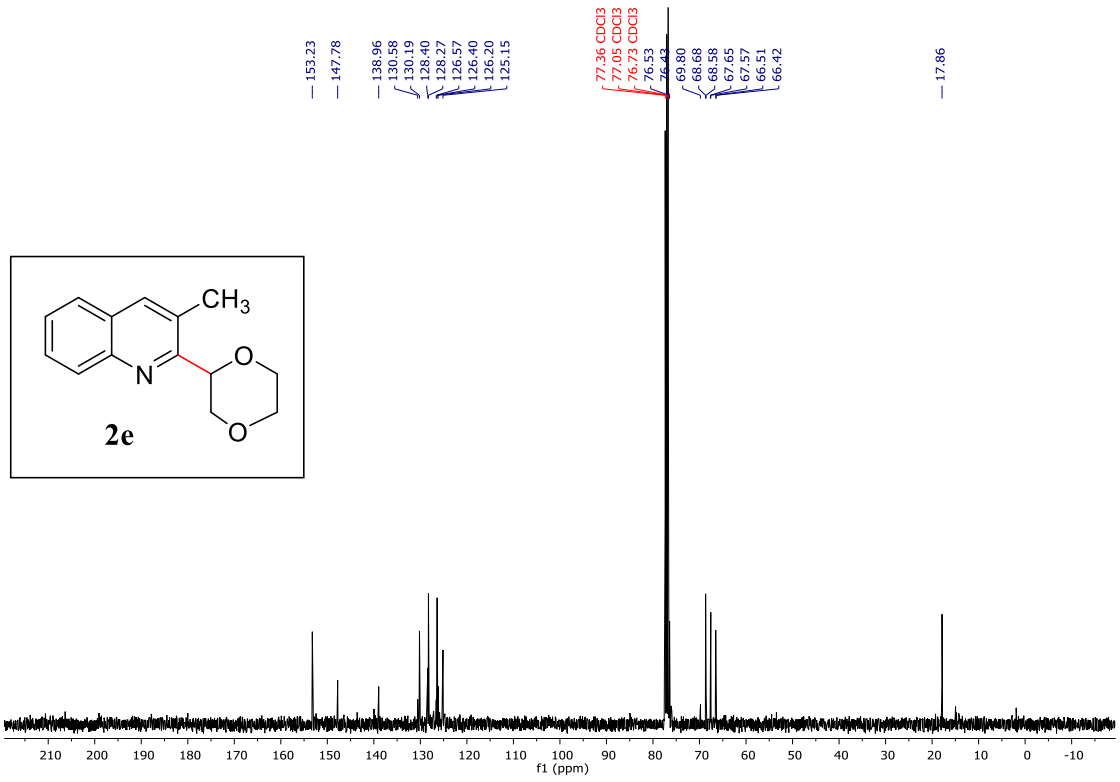

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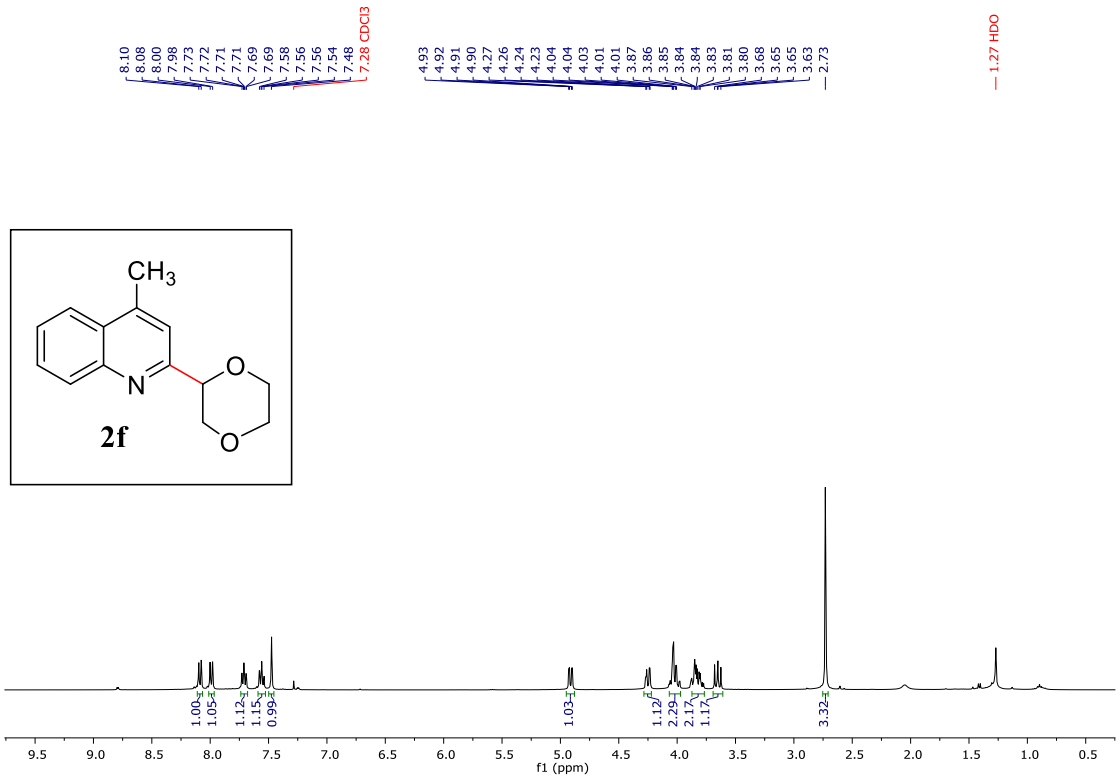

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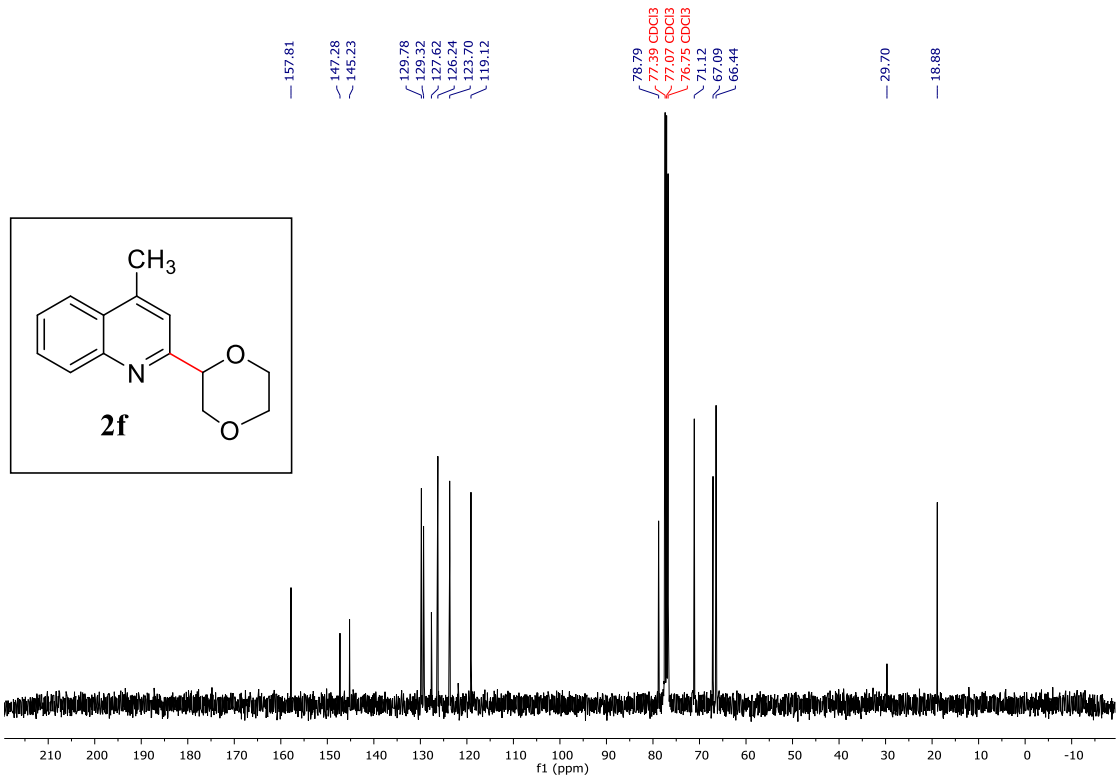

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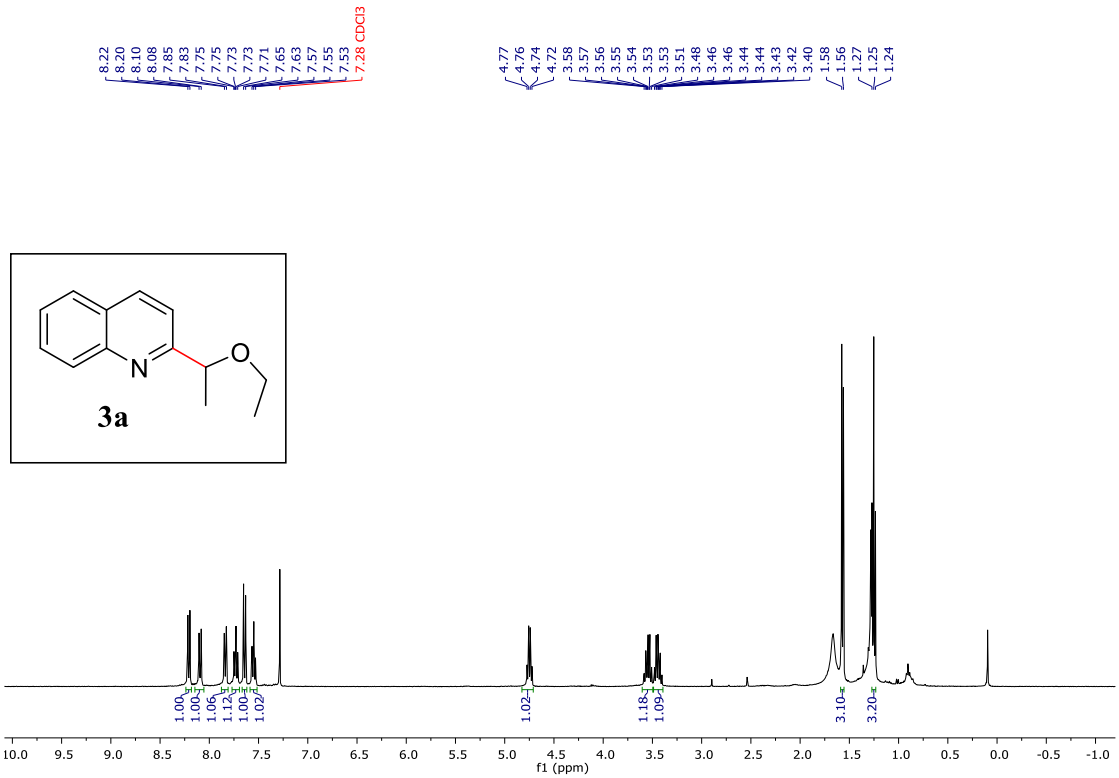

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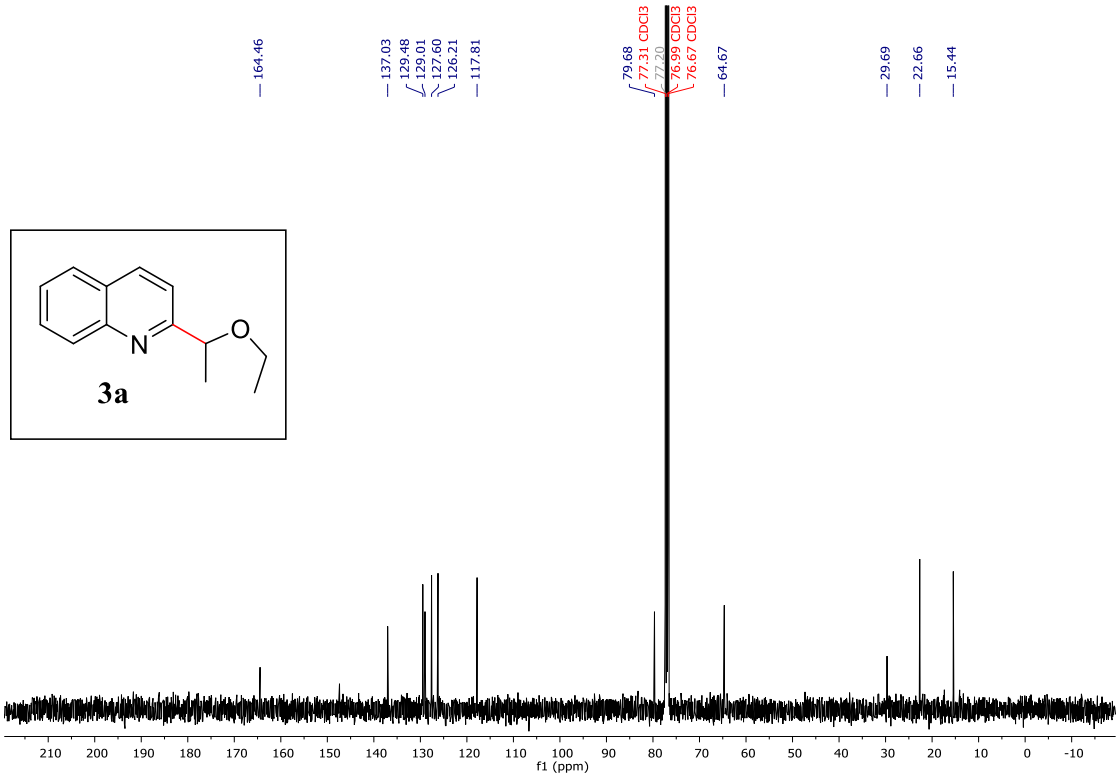

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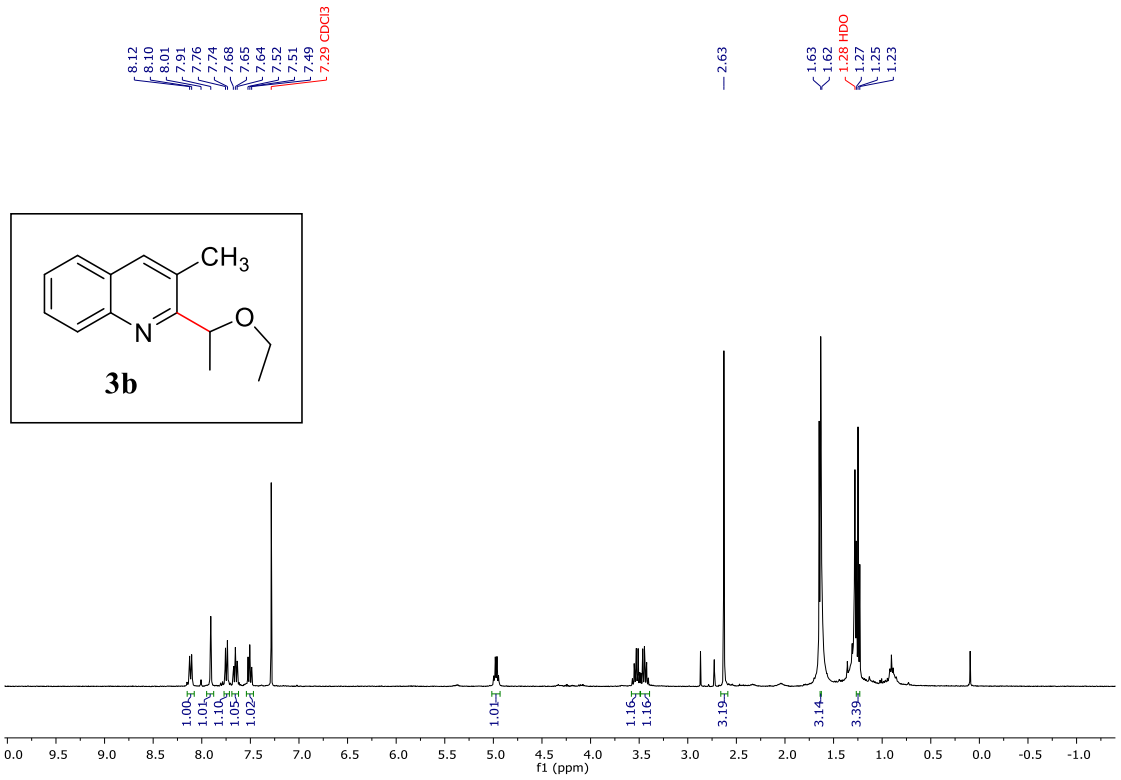

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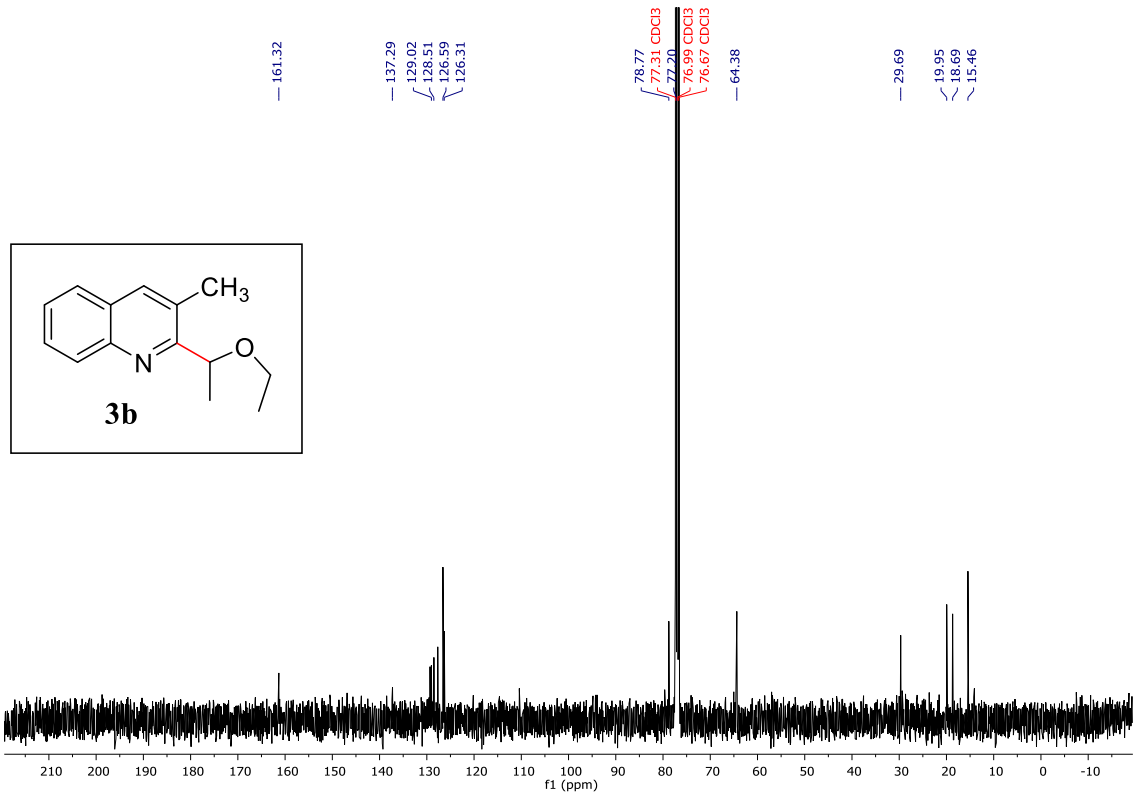

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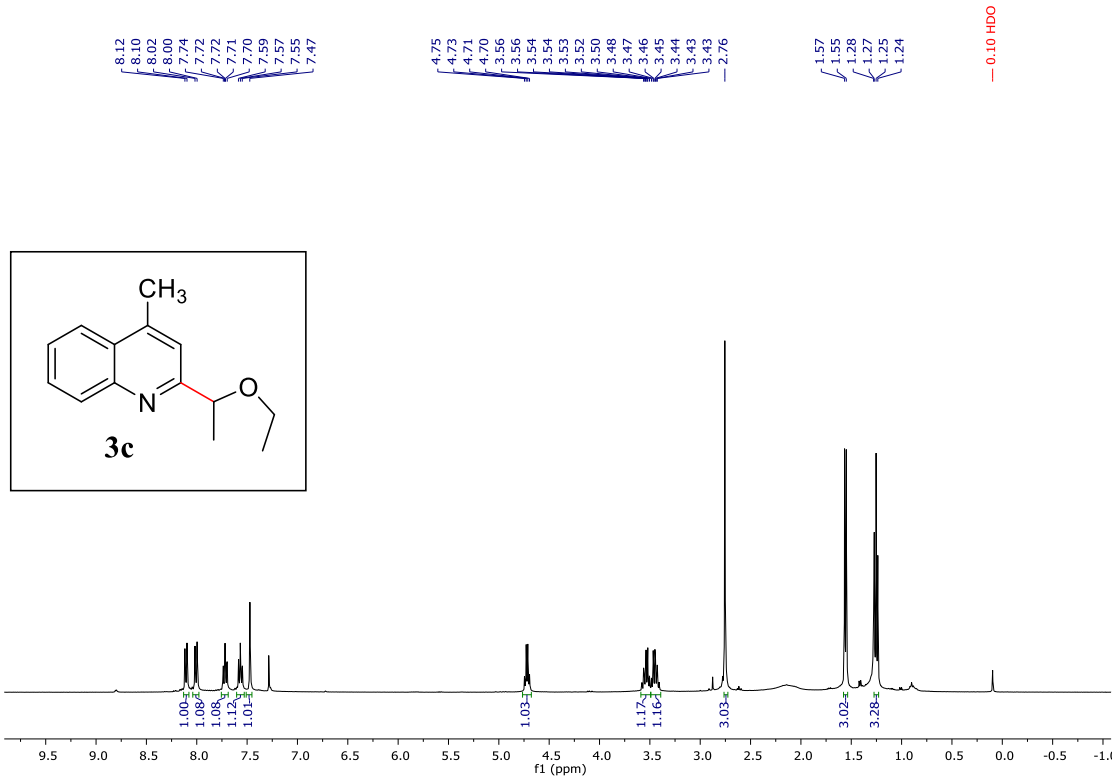

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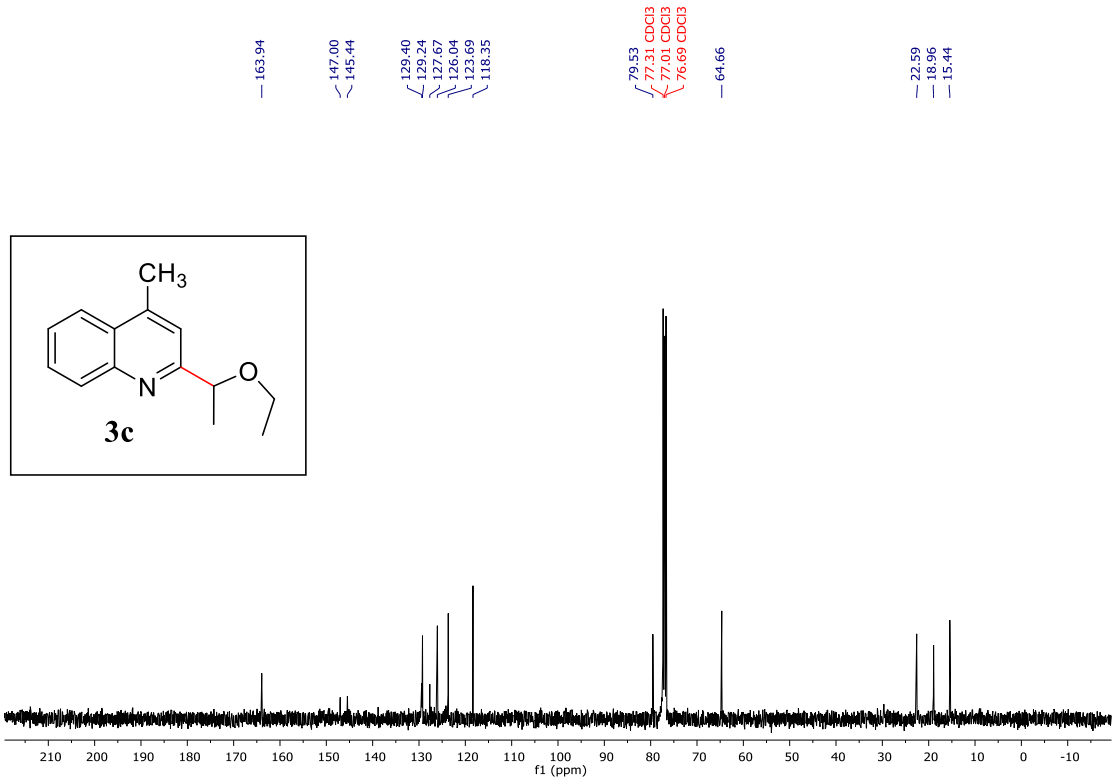

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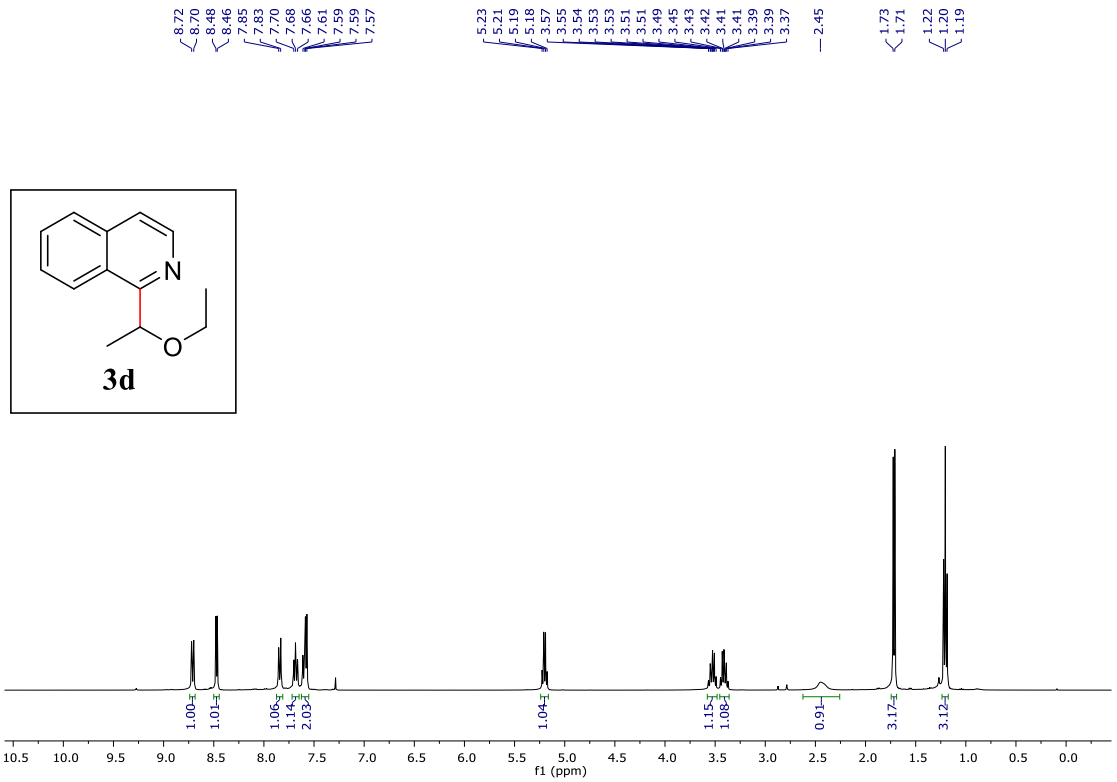
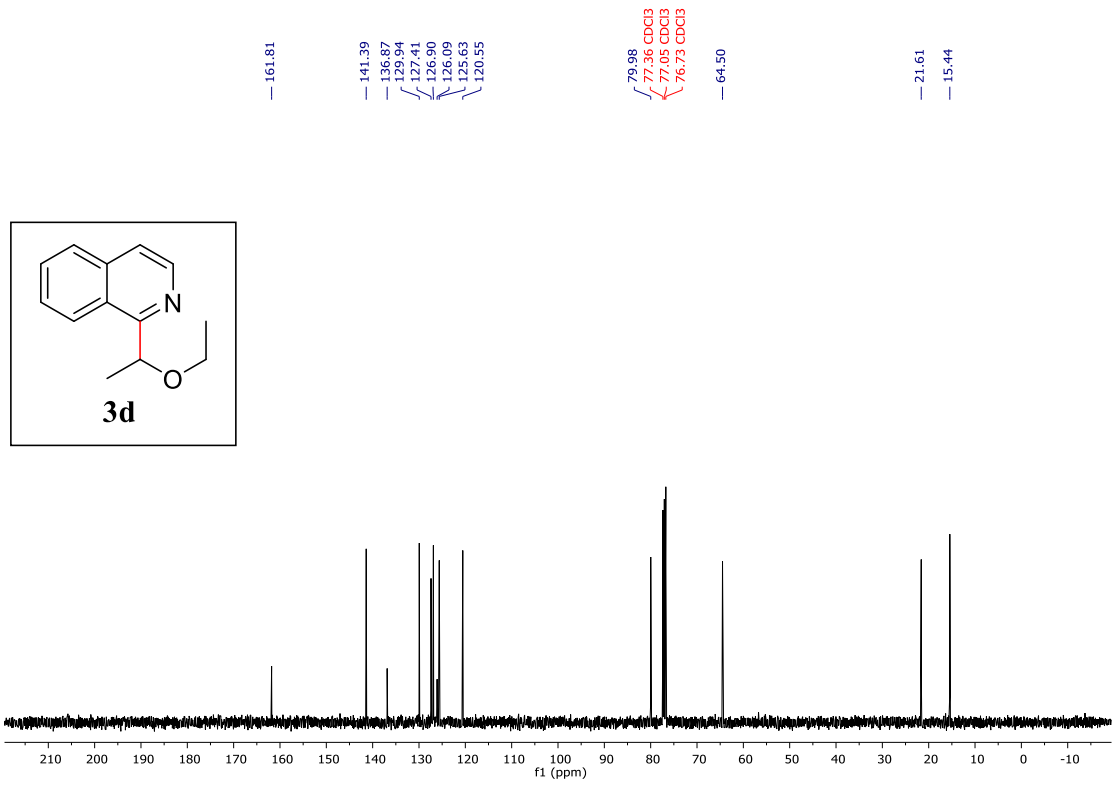
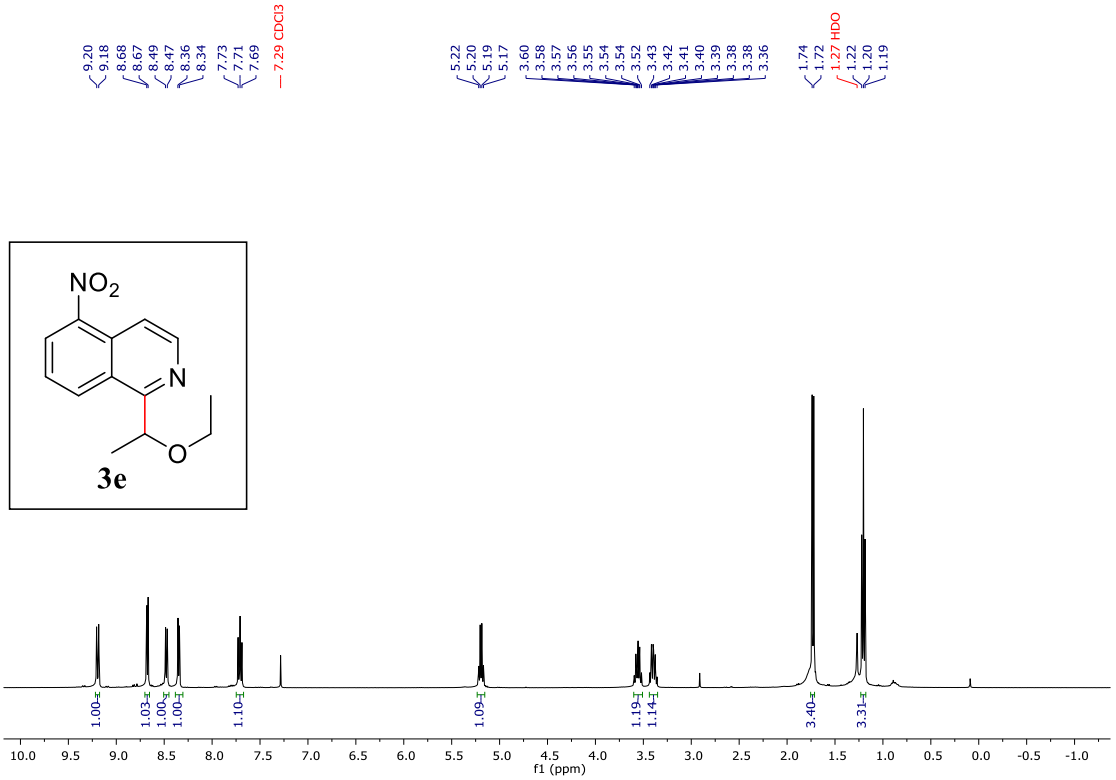


^{1}H NMR ($CDCl_3$, 400 MHz) Spectrum of 1-(1-ethoxyethyl)isoquinoline



^{13}C NMR ($CDCl_3$, 100 MHz) Spectrum of 1-(1-ethoxyethyl)isoquinoline



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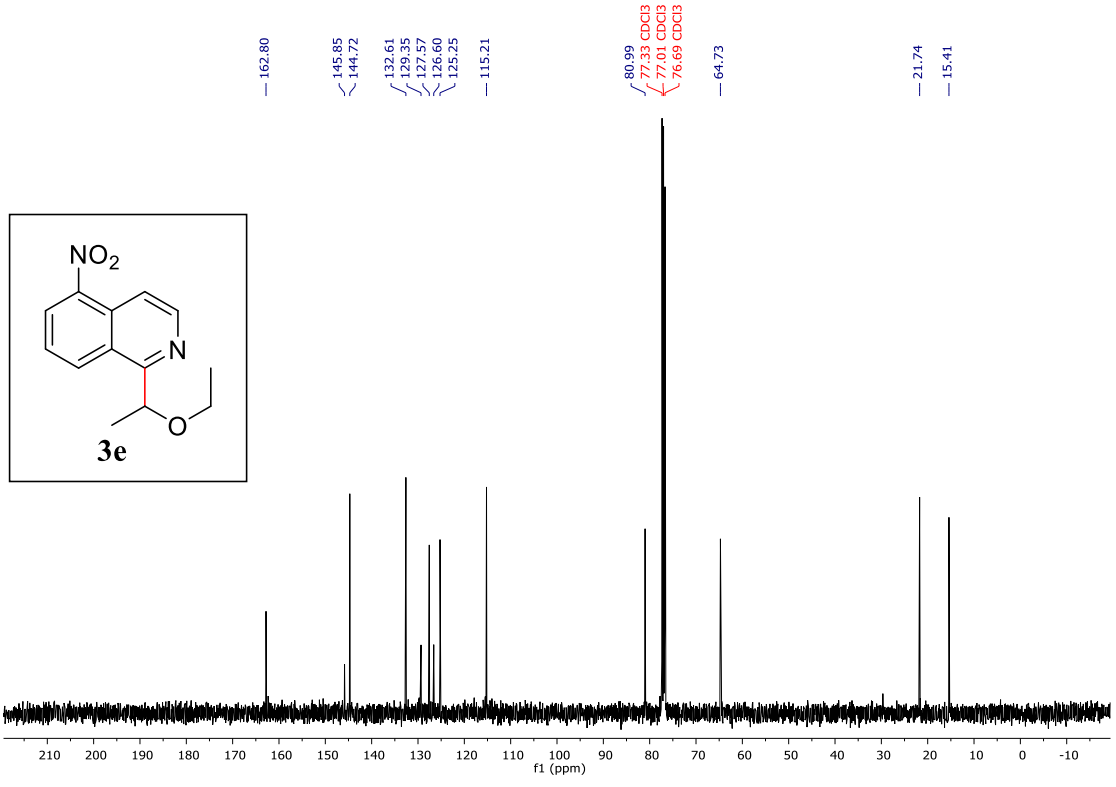

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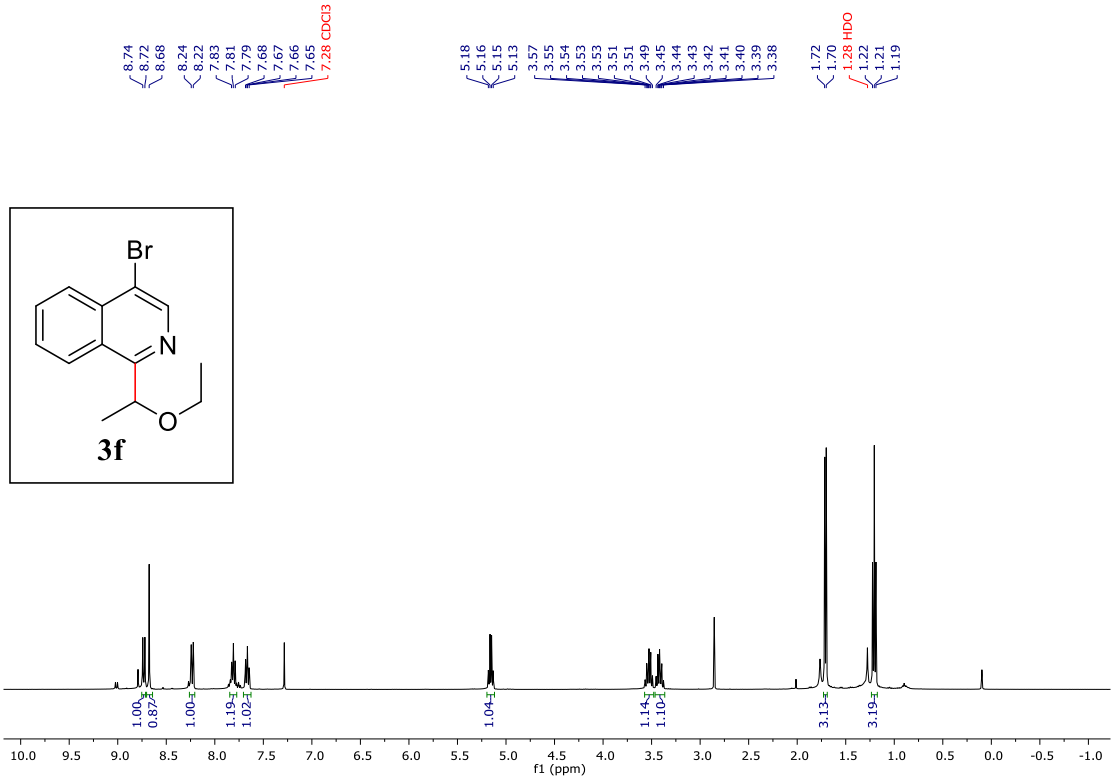
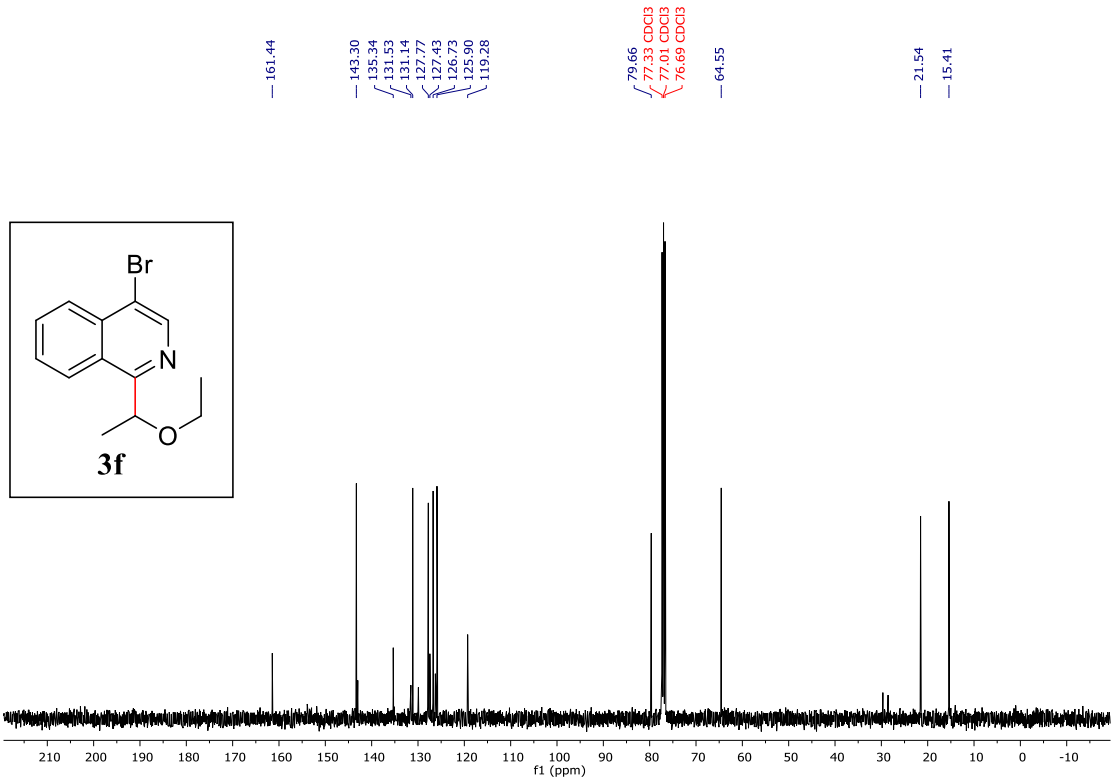


^{1}H NMR ($CDCl_3$, 400 MHz) Spectrum of 4-bromo-1-(1-ethoxyethyl)isoquinoline



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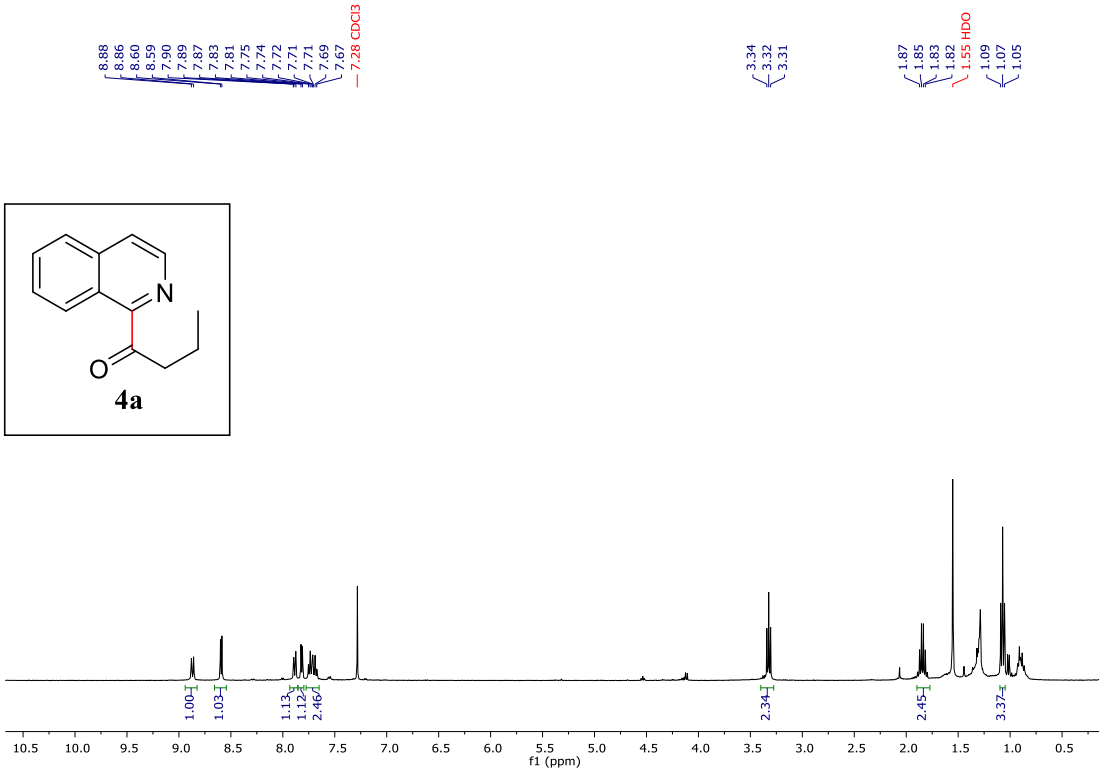
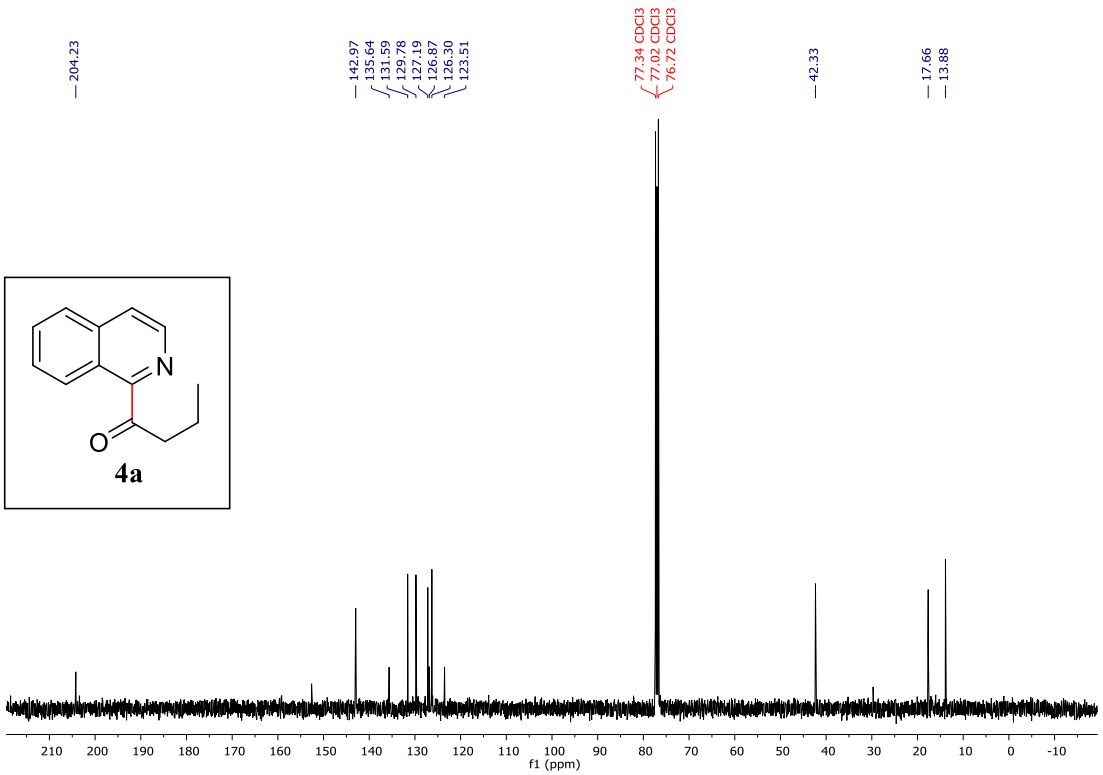


^{1}H NMR ($CDCl_3$, 400 MHz) Spectrum of 1-(isoquinolin-1-yl)butan-1-one



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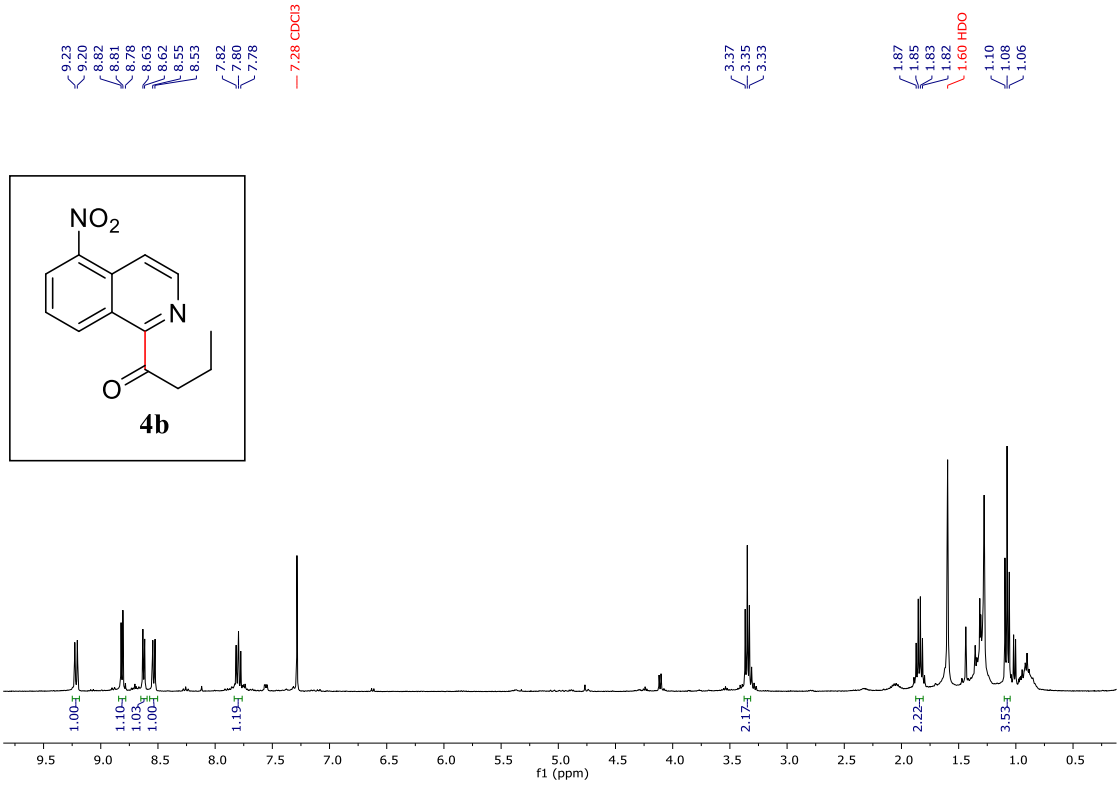

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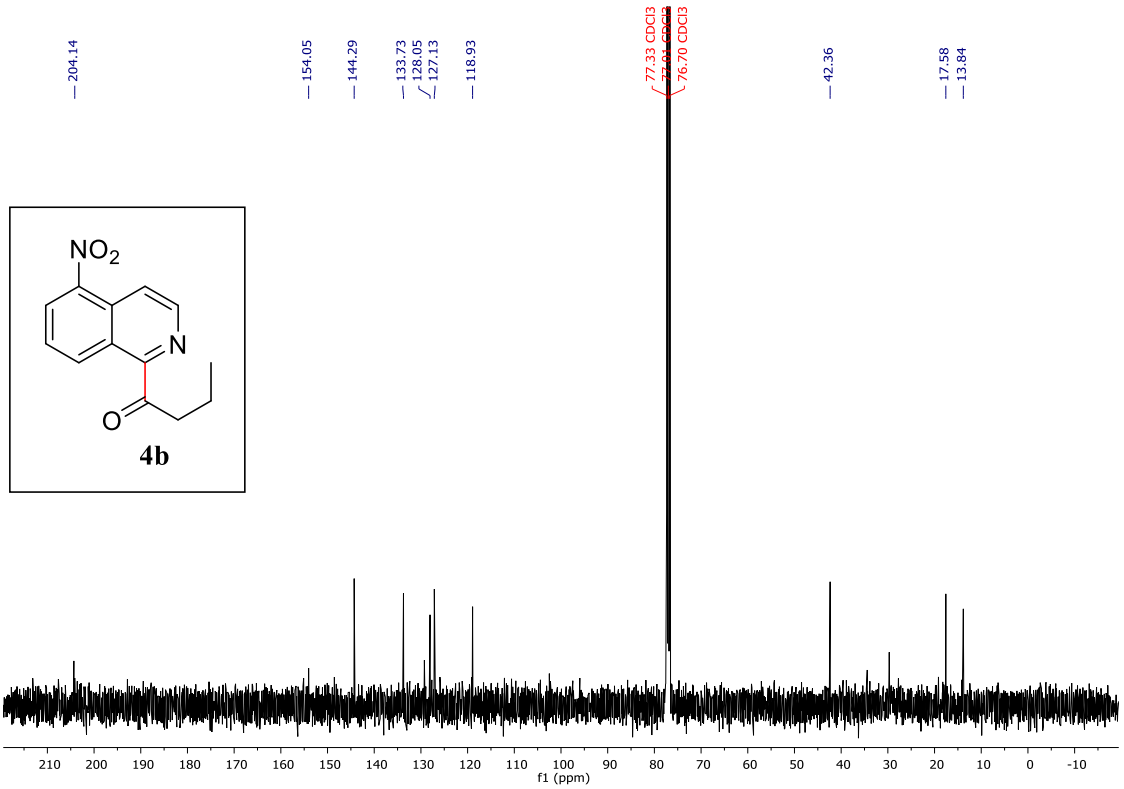

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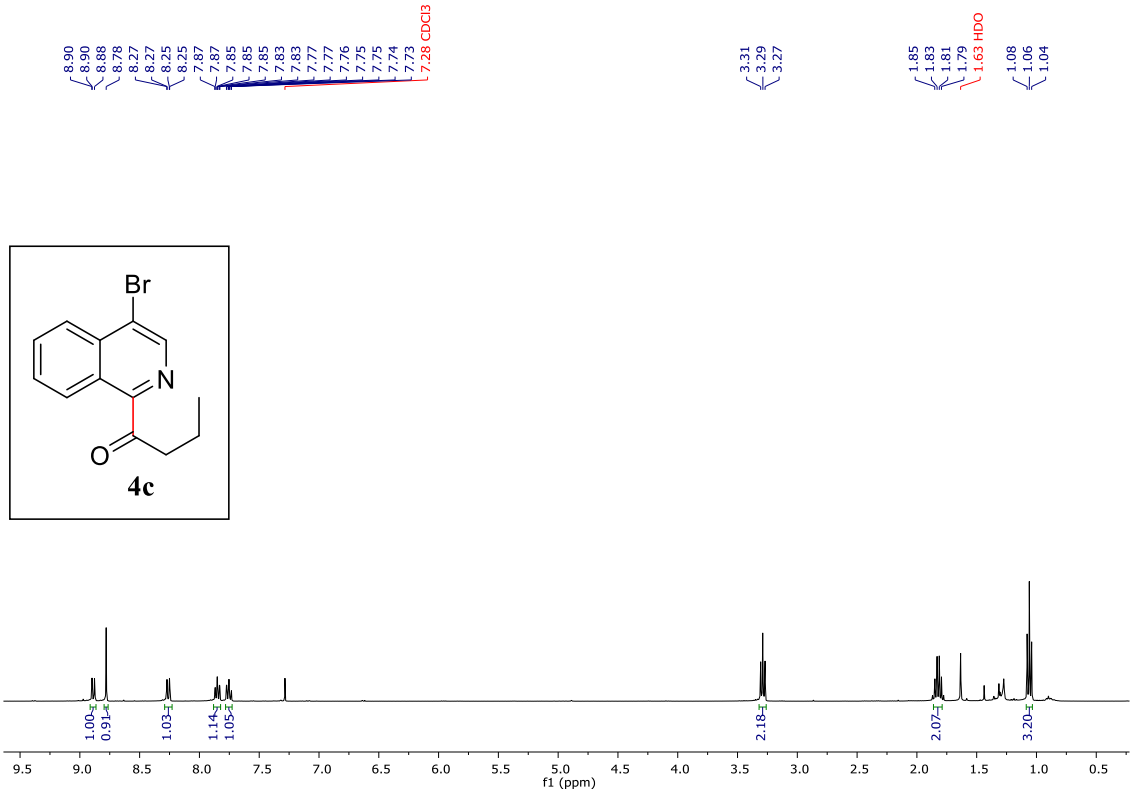

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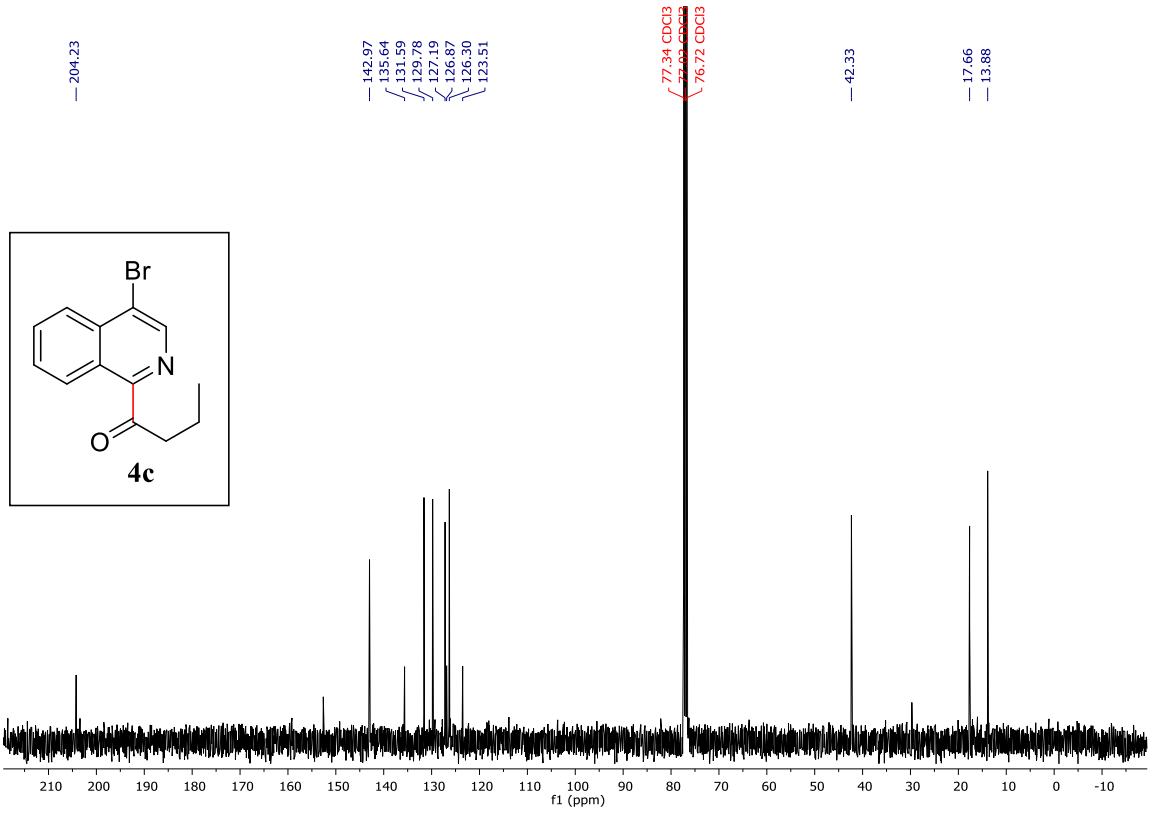

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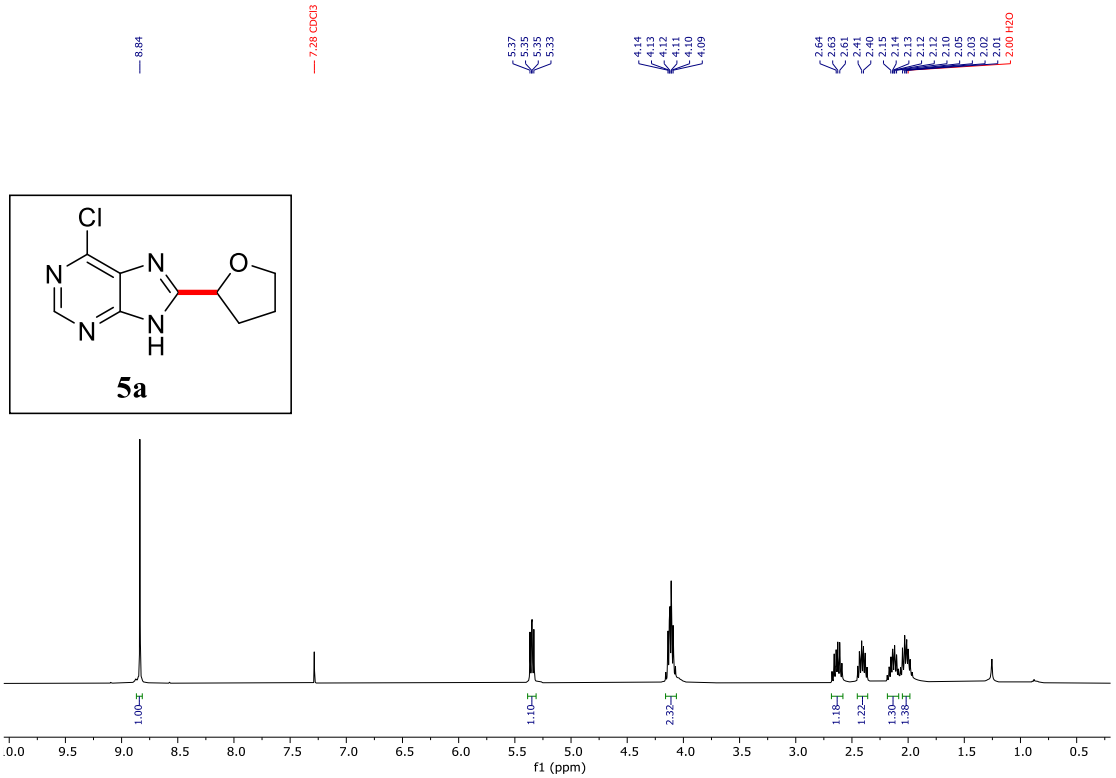
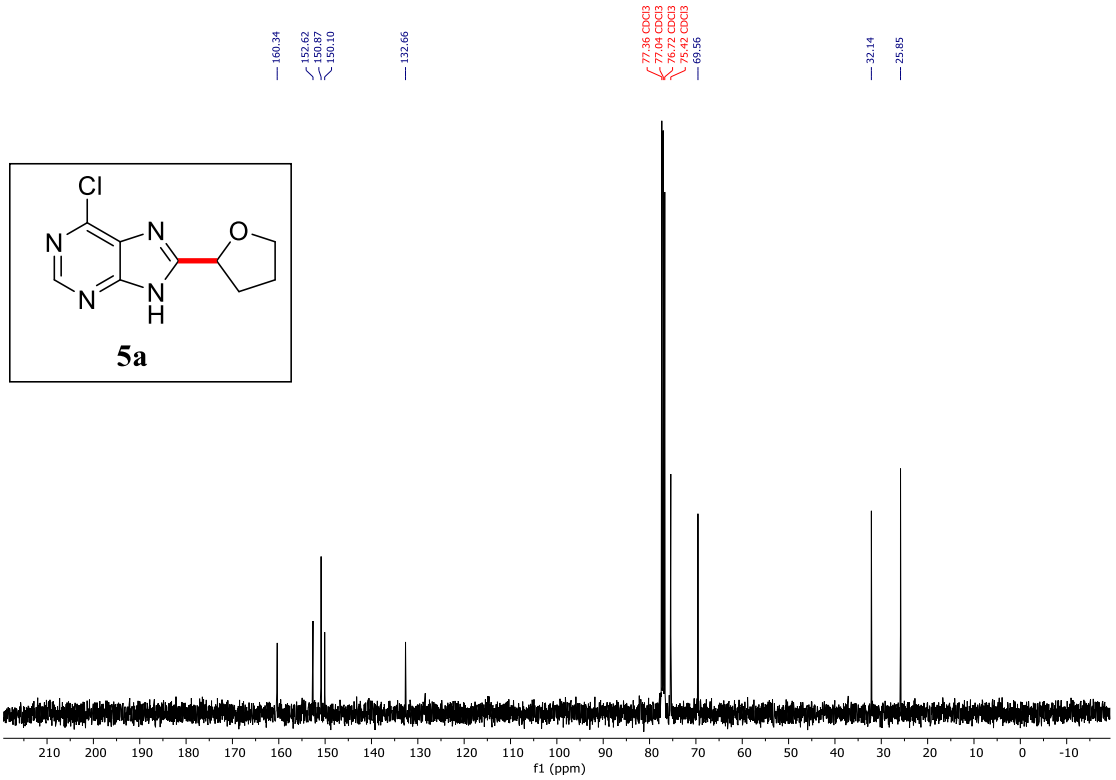
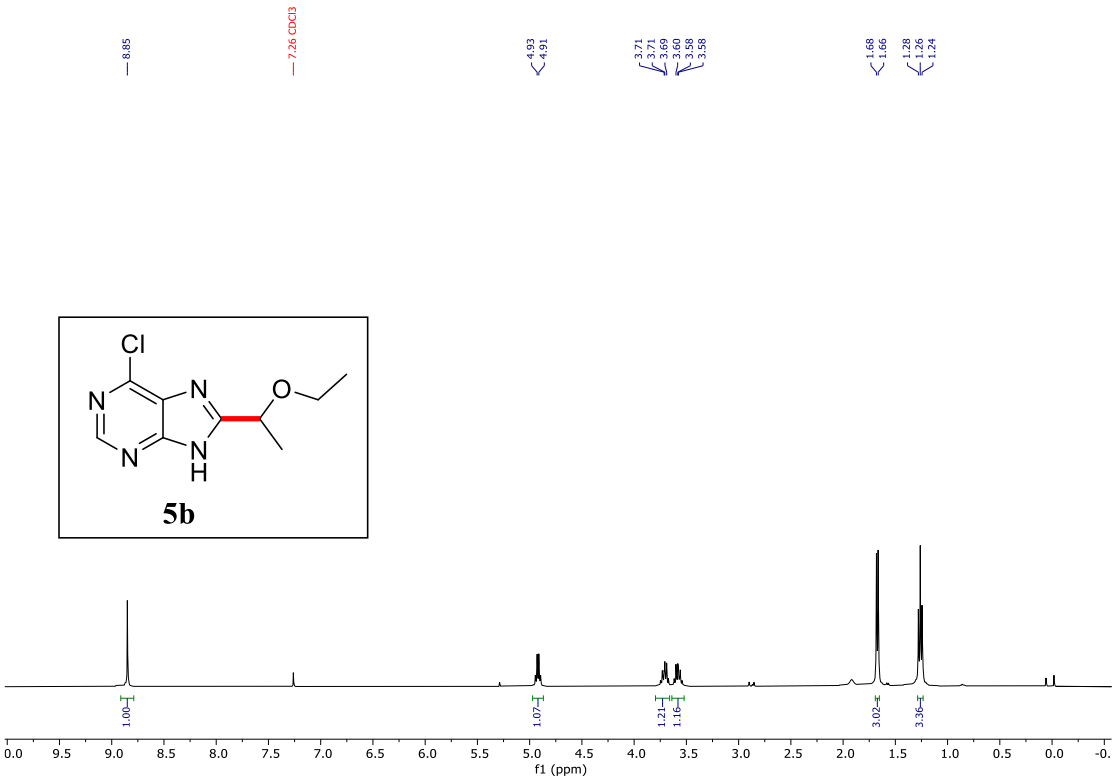


^{1}H NMR ($CDCl_3$, 400 MHz) Spectrum of 6-chloro-8-(tetrahydrofuran-2-yl)-9H-purine



^{13}C NMR ($CDCl_3$, 100 MHz) Spectrum of 6-chloro-8-(tetrahydrofuran-2-yl)-9H-purine



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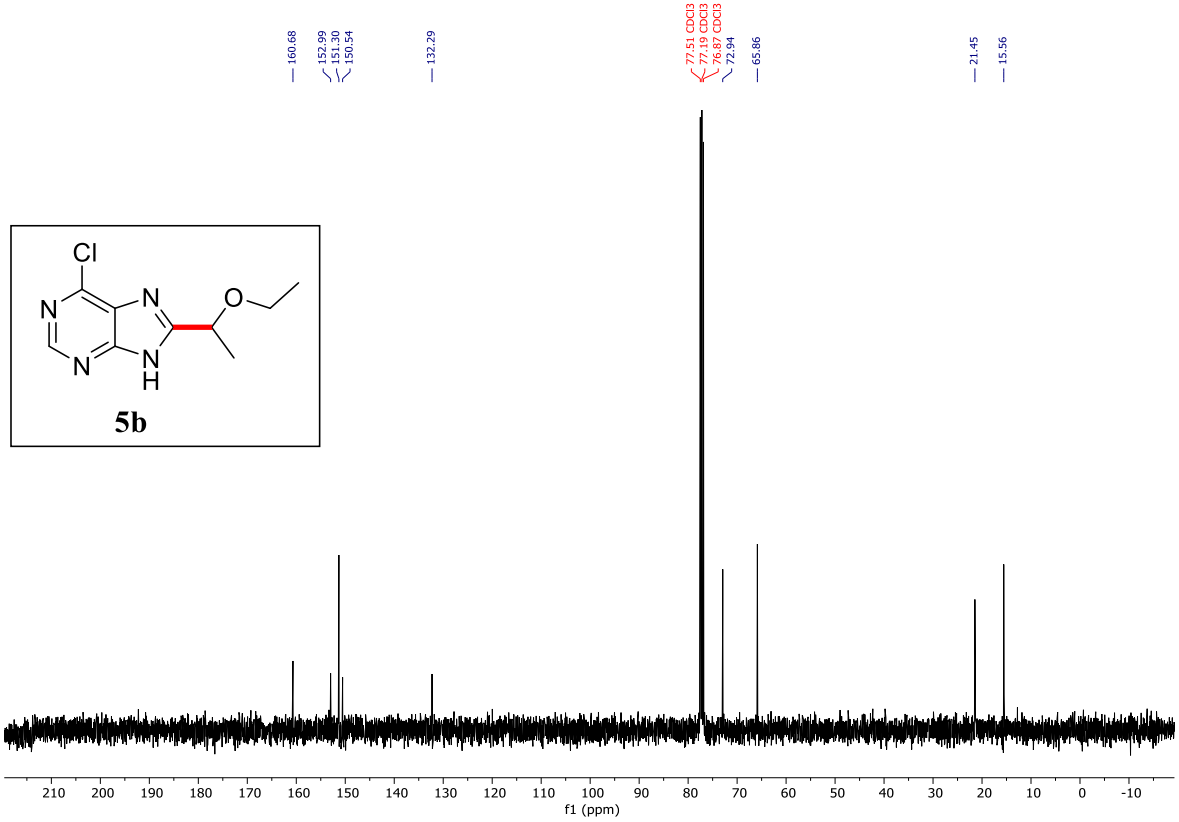

^{13}C NMR ($CDCl_3$, 100 MHz) Spectrum of 6-chloro-8-(1-ethoxyethyl)-9H-purine

Chapter-3 Formation of heteroaromatic alkyl/aryl ketones *via* oxidative C-C bond formation

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3.1: Introduction:

Visible light-mediated photoredox catalysis in the past few years have developed as a very important technique in the field of organic synthesis. This technique facilitates various single electron transfer events with organic substrates and allow the formation of bonds that are not possible *via* conventional two electron pathway.[1] Among the various transformations using visible light mediated photoredox catalysis, C-H activation of the unactivated *(sp^3)* C-H bonds is one the most important reaction. An organic molecule often consists of multiple C-H bonds that have different BDE (bond dissociation energies) and different inherent reactivity. This difference in the properties of different C-H bonds depends on various factors like, inductive effect, steric effect and polarization effect. In the recent studies it has been found that the C-H bonds α to alcohol functional group has a bond energy of 92.0 kcal/mol[2] which is lesser compared to the C-H bonds of alkanes (102.0 kcal/mol).[3] This difference in energy arises from the polarisation caused by the hydrogen bonding formed by Oxygen in an alcohol. Thus, this makes the C-H bonds α to oxygen atom to undergo various single-electron transfer (SET)[4] and hydrogen atom transfer (HAT)[5] events which would allow the formation of α-oxyalkyl radicals.[6] It has been well established that α-oxyalkyl radicals are very stable yet highly reactive nucleophilic species that can easily attack electron deficient centres. This property of the C-H bonds α to alcohols functional groups to form nucleophilic radical intermediates have been known to be used for formation of C-C bonds through

a radical-radical coupling reactions *via* C-H functionalizatioin. There are several reports for direct C-H alkylation of hetero-aromatic compopunds using commercially available alcohols to form various hetero-aromatic alkanes. However, a photocatalytic oxidative alkylation has been rather elusive. Thus, herein we have developed a visible light-mediated photocatalytic reaction for the formation of hetero-aromatic alkyl/aryl ketones through oxidative C-C coupling *via* C-H functionalization through the formation of α-oxoalkyl radical. In this methodology we have used metal-free acridinium base organo-photocatalyst[7] which was developed by our research group itself (Fig: 2.5). The advantage of using this photocatalyst lies in the greener aspect of our methodology. Most of the photocatalyst, be it transition metal based-photocatalyst or perovskites, all of them requires the use of metal which are very costly or even toxic. Thus, using a photocatalyst which is free of metal easily making our methodology environment friendly and more sustainable, as there is minimum risk of toxicity and also reduces the cost of preparing the catalyst. The photoctalytic properties of our phtocatalyst has also been well established by our research group through various photocatalytic reaction; our research group have reported the synthesis quinolone-2-(1*H*)-ones from quinolone N-oxides using this phtotcatalyst,[8] also aromatization of aza-heteroarenes was also achieved by our reaseach group using the same phtotcatalyst.[9] This methodology will thus allow us to convert feedstock hetero-arenes and alcohols into high value pharmacophores under a green and more sustainable condition.

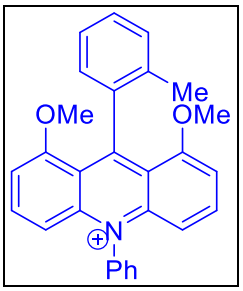


Fig: 2.5 Acridinium based metal free organophotocatalyst

3.2: Literature review:

The selective C-H activation of alcohol α-C-H bonds in the presence of wide range of other C-H bonds have found to be achieved over the past few years. David W. C. MacMillian in the year 2015 reported a synthetic protocol for selective activation alcohol of α C-H bonds *via* photo-catalyzed, H-bond assisted bond activation strategies.[10] This methodology allowed the selective C-H activation alcohol C-H bonds in presence of allylic, benzylic α-oxy and α-acyl C-H bonds by using Iridium based photo-redox catalyst.

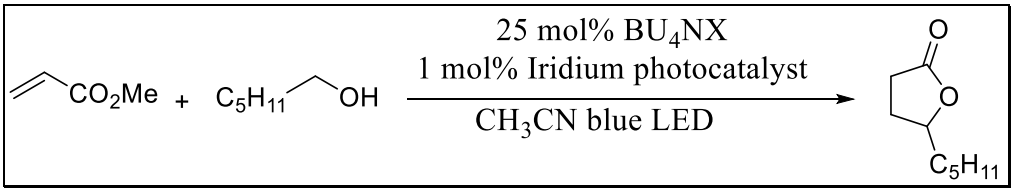


Fig: 2.6 Photocatalytic selective C-H activation of alcohol α C-H bonds.

In the year 2015 Jian Jin and David W. C. MacMillian developed a photocatalytic method for the C-H functionalization hetero-arenes using alcohlos as an alkylating agent.[11] The methodology used Iridium photocatalyst and visiblelight to form a C-C bond between hetero-arenes and alcohols.

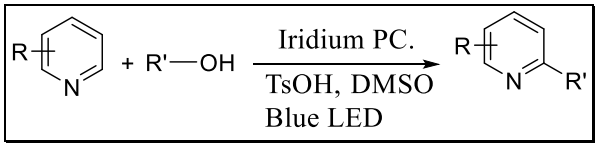


Fig: 2.7 C-H functionalization of hetero-arenes using alcohol as an alkylating agent.

E. Kianmerh et.al. in the year 2016 developed a methodology for the acylation of pyridine derivative with alcohols.[12] The methodology showcased the acylation of

pyridine derivatives with aliphatic and aromatic alcohols using sodium peoxodisulphate as oxidant and water as the solvent (Fig:3.1).

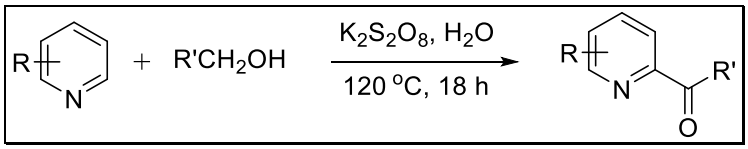
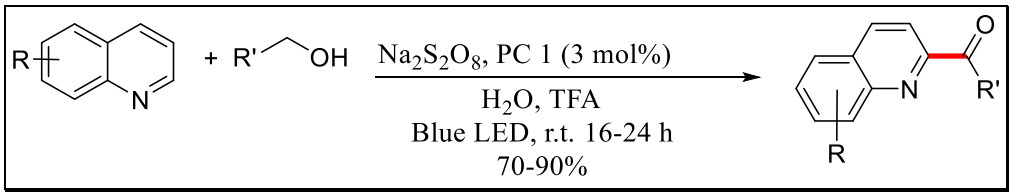


Fig: 2.8 Metal free acylation of pyridine derivatives using alcohols.

One of the major drawback of this methodology was that it was limited to only pyridine derivatives and requires application of heat (120 ^{o}C), which is a harsh condition. Thus, making the methodology less sustainable and less desirable. Thus, there is a need for development of a methodology that is more versatile and sustainable compared to existing ones.

3.3: Synthetic scheme:

Herein we have developed a visible light mediated metal free general methodology for C-H functionalization of hetero-aromatic compounds using water as the solvent. This methodology enabled the formation of hetero-aromatic alkyl/aryl ketones through oxidative C-C bond formation between aliphatic and aromatic alcohols and hetero-arenes *via* the formation of a α-oxoalkyl radical, using metal free acridinium based organo catalyst **1**, and water as the solvent (Scheme: 4).

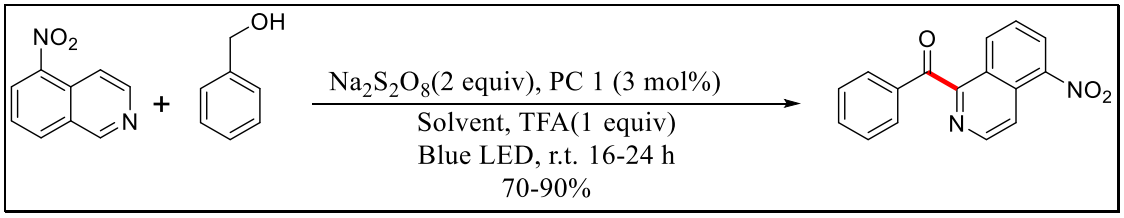


Scheme: 4 Schematic representation for the formation of hetero-aromatic alkyl/aryl ethers through oxidative C-C bond formation

3.4: Results and discussion:

In this chapter we have described a photocatalytic methodology for C-H functionalization of hetero-aromatic compounds which we have developed. This methodology allowed the formation of hetero-aromatic alkyl/aryl ketones through oxidative C-C bond formation between ketones and hetero-arenes *via* photoredox catalysis. This methodology involves the use of organo photocatalyst **1** as the phtocatalyst which absorbs light in the wavelength range of 400-500 nm, making it suitable for use as a catalyst under blue light.

To study the effect of different conditions over our developed methodology, we performed some optimization reactions for the oxidative methodology using 5-nitroisoquinole and benzyl alcohol as our starting reagents (Table: 2).

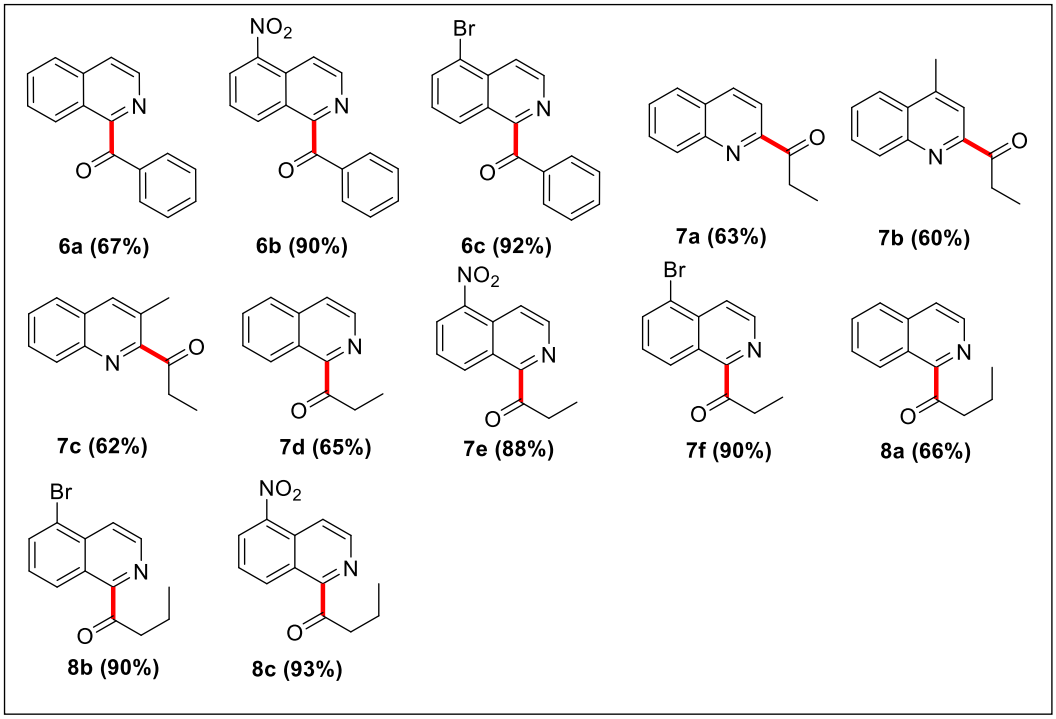


Entry	Photocatalyst	Oxidant	Solvent	Light	Yield %
1	Organophotocat.1	$Na_2S_2O_8$	ACN:H_2O	Blue LED	90 %
2	Organophotocat.1	$Na_2S_2O_8$	DCM	Blue LED	—
3	Organophotocat.1	—	ACN:H_2O	Blue LED	—
4	Organophotocat.1	H_2O_2	ACN:H_2O	Blue LED	—
5	Organophotocat.1	Triisopropylsilane	ACN:H_2O	Blue LED	—
6	Organophotocat.1	$Na_2S_2O_8$	EtOAc	Blue LED	—
7	Organophotocat.1	$Na_2S_2O_8$	ACN	Blue LED	62 %
8	—	$Na_2S_2O_8$	ACN:H_2O	Blue LED	—
9	Organophotocat.1	$Na_2S_2O_8$	ACN:H_2O	—	—
10	Organophotocat.1	$Na_2S_2O_8$	H_2O	Blue LED	91%

Table: 2 Optimization table for formation of hetero-aromatic alkyl/aryl ketones

In the optimization reactions we observed that when the above mentioned reaction was carried out under blue light using a mixture of acetonitrile and water as solvent, sodium peroxodisulphate as oxidant and organo photocatalyst as the photocatalyst, the percentage yield of the product was 90% (Table:2, serial no.1). Whereas, when the same reaction was carried out using dichloromethane as the solvent (Table:2, serial no 2), no reaction occurred. The reason for this might have been due to the fact that the sodium peroxodisulphte oxidant did not dissolve in DCM as it is an ionic compound and requires a polar solvent to solublize. Hence, we used a mixture of acetonitrile and water. To further understand this observation, we carried out the same reaction without using any oxidant (Table:2, serial no 3), and it was observed that the reaction did not take place. From this result we can say that the reaction in absence of the oxidant is not feasible. Then to confirm the role of the photocatalyst in the methodology, the reaction was carried out in the absence of the photocatalyst, where it was observed that no reaction occurred. This is because of the fact that, in this methodology the organo-photocatalyst function as a photosensitizer, which absorbs energy from the blue light and transfers that energy to our system which is required for activation of our desired bonds. This justifies the use and significance of the organo-photocatalyst **1** in our methodology. Further, the reaction was carried out in dark condition. It was observed that no reaction took place. This confirmed that our developed methodology allowed the C-H functionalization of the hetero-aromatic compounds *via* visible light-mediated photocatalysis. We then carried our reaction using only water as the solvent, and we found out that the reaction was feasible even with water as the solvent. Thus, making our methodology more sustainable and greener.

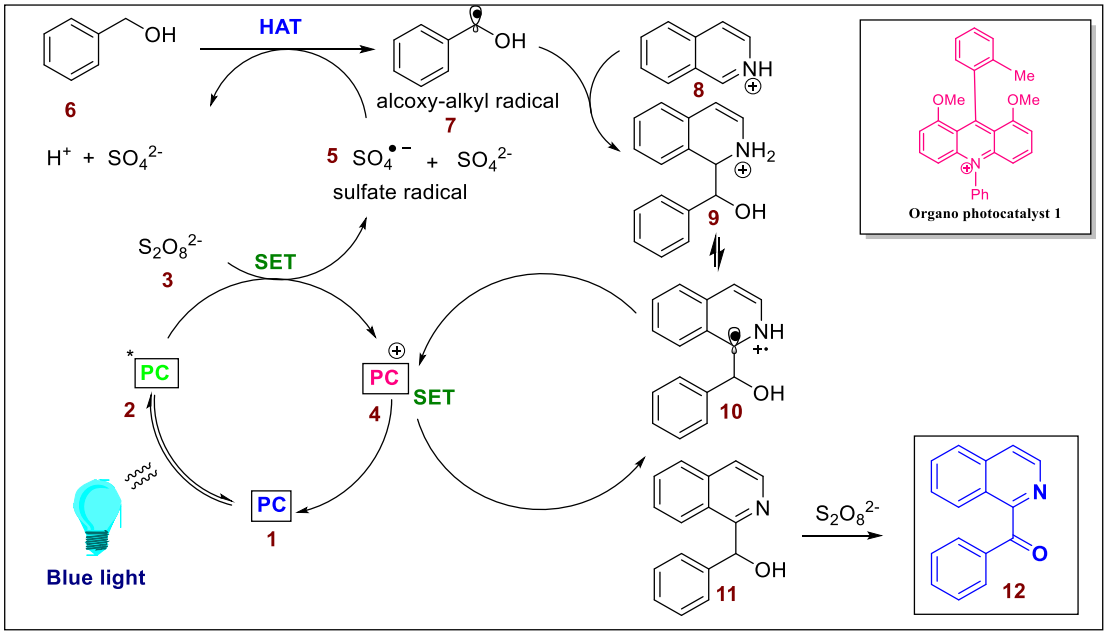
To explore the substrate scope of this methodology, we performed the reaction with various quinoline, isoquinoline and their derivatives to give a large number of hetero-aromatic adducts (Scheme: 5). Similar to the ether methodology this methodology also showed trend of higher yield (88%-93%) for hetero-arenes with electron withdrawing groups like $–NO_2$ and Br which makes the hetero-arenes electron deficient. While for hetero-arenes with electron donating groups like $–CH_3$ which makes the hetero-arenes electron rich, lower yields (60%-65%) were observed.



Scheme: 5 Substrate scope for oxidative C-H functionalization of hetero-aromatic compounds.

The reason for this was due the formation of the nucleophilic alkoxyalkyl radical intermediate which prefers to attack electron deficient centres rather than an electron rich centre. This brings us to the mechanism of the reaction (Scheme: 6) The mechanism for this reaction involves irradiation of the photocatalyst **1** with blue light, causing it to go into a higher energy excited state **2.** The excited photocatalyst **2** then transfers its energy to the Sodium peroxodisulphate oxidant, which undergoes a single electron

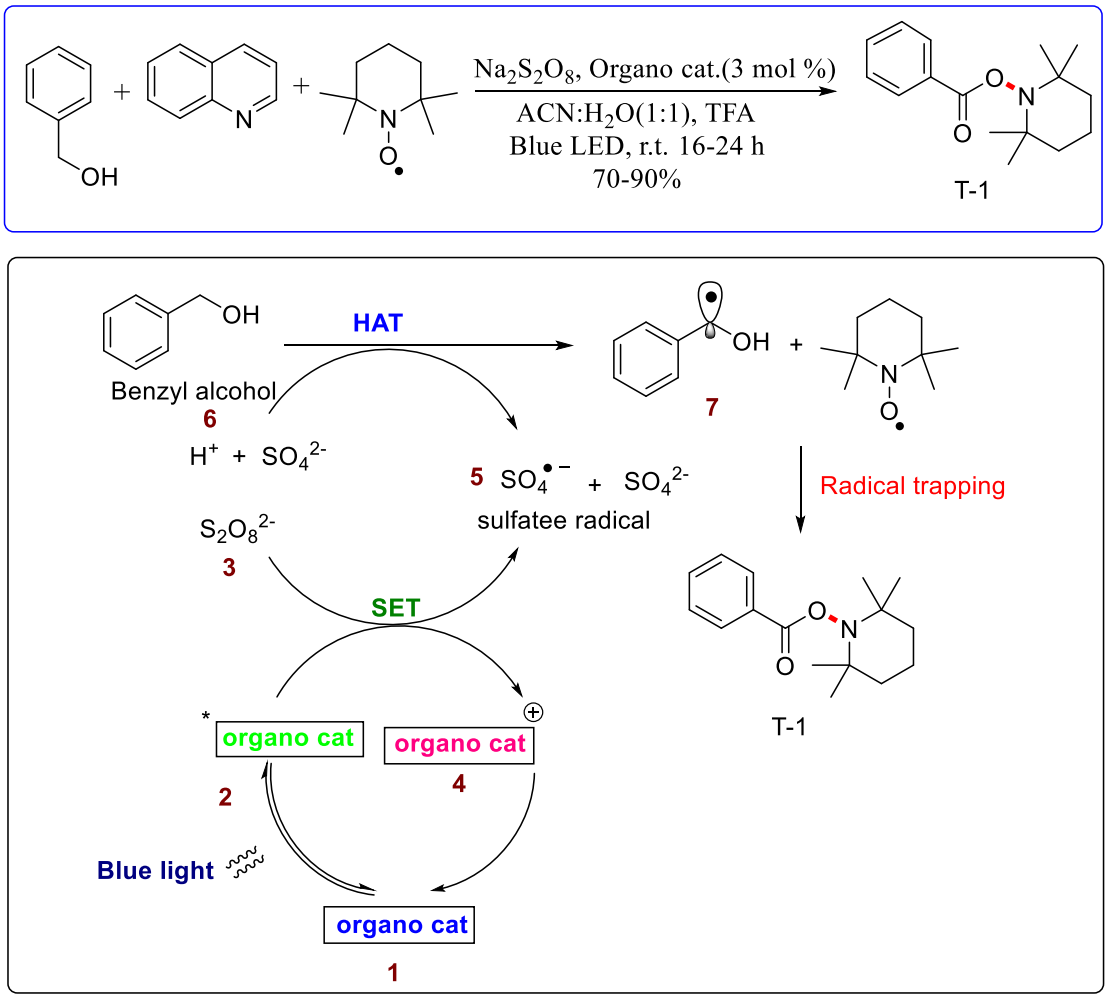
transfer (SET) reaction to form sulphate radical **5**. This radical intermediate then reacts with the ether to undergo a hydrogen atom transfer reaction (HAT) forming an alkoxyalkyl radical **7.**



Scheme:6 Proposed mechanism for the formation of heteroaromatic alkyl/aryl ketones.

To confirm the formation of the alkoxy-alkyl radical, we performed a radical trapping experiment (Scheme: 7) in which we were able to trap the α-oxoalkyl radical using a trapping agent TEMPO {2, 2, 6, 6-Tetramethylpiperidin-1-yl)oxyl} as the trapping agent, which is a highly reactive species and binds to any radical centre formed in the reaction. In this experiment we irradiated benzyl alcohol with blue light in presence of organo photocatalyst and the sodium peroxodisulfate oxidatnt. This resulted into the formation of α-oxoalkyl which further react with the trapping agent TEMPO to form compound **T-1.** And the formation of compound **T-1** confirms the formation of the alkoxyalkyl radical. We confirmed the formation of compound **T-1** by NMR spectroscopy. Where singlet peak at 1.41 ppm for 12 H are for 12 protons of the four -

CH_3 groups. While a multiplet at 1.85 ppm for 6 H are for the six proton of the three – CH_2 groups of the piperidine and the peaks at 7.41 ppm and 8.10 ppm are for the proton of the benzene ring. Furthermore, the peak at 172.97 ppm in the ^{13}CNMR spectra confirms the formation of ester like group in the compound **T-1.**



Scheme:7 Radical trapping experiment using TEMPO as the radical trapping agent.

The alkoxyalkyl radical in our reaction reacts with the protonated hetero-arene **8** (protonation of the hetero-arene was done by trifluroacetic acid) to give intermediate **9.** The intermediate **9** then undergoes resonance stabilization to form intermediate **10** which then undergoes a single electron transfer reaction (SET) to finally form the hetero-arene substituted alcohol **11.** Formation of this alcohol was confirmed from the

proton NMR values in which peak at 4.79 is for the benzylic proton, peaks in the range of 9-7 ppm are for the eleven proton of the aromatic rings. This alcohol **11** undergoes further oxidation to give a ketone **12** which is the final product. Formation of ketone **12** was confirmed by NMR spectroscopy. The absence of the peak in the range of 5 ppm in the ^{1}HNMR spectra of **12** indicates the absence of the benzylic proton which infers that the alcohol group is not present **and** peak at 203.34 ppm in the carbon NMR confirms the formation of the ketone.

3.5: General procedures:

5-nitroisoquinoline (0.05 g) was taken in a 5 ml vile. To this vile, 4 ml of solvent (water) was added. To this sodium peroxodisulphate (0.24 gm) was added. Then benzyl alcohol (1.2 equivalents) (0.043 ml) was added to the reaction mixture. Then Trifluoroacetic acid (TFA) (0.053 ml) (2 equivalents) was added, followed by addition of organo photocatalyst (3 mmol) to the reaction mixture. The reaction mixture was then kept under blue light at room temperature with continuous stirring for 14 h. After completion of the reaction, which confirmed by TLC (thin layer chromatography), the reaction mixture was neutralized using 1% aqueous NaOH solution. The organic compound was then extracted with 3 X 20 ml dichloromethane using a separating funnel. The crude organic compound was then purified by column chromatography to obtain compound **6a**

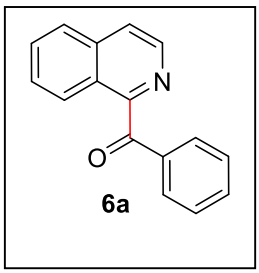
3.6: Conclusion:

In summary, we have developed a mild and metal-free visible light mediated phtotocatalylic protocol for C-H functionalization of hetero-arenes. The methodology involves metal-free acridinium based organo-photocatalyst, and water as solvent.

Making our methodology green and sustainable. This efficient methodology was used for the acylation of various derivatives of quinoline and isoquinolines using alcohols like propanol, butanol, and benzyl alcohol as the acylating agent. We also carried out a detailed study of the mechanism involved in our methodology and found out that the reaction involves the formation of an alkoxy radical which attack the electron deficient heteroarenes to form hetero-aromatic alcohols which further oxidises to form hetero-aromatic ketones. Using this general methodology, we are able to synthesise various hetero-aromatic aryl/alkyl ketones which may be of great pharmacophoric importance. We also aim for further application of our methodology with natural products. We anticipate that this new mild and efficient methodology will find broad application in the modern day organic synthesis as well as drug development programs.

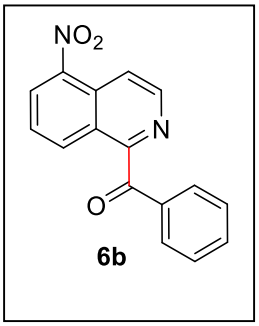
3.7: Spectral data of newly synthesized compounds:

isoquinolin-1-yl(phenyl)methanone



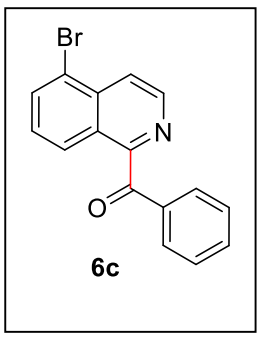
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.63 (d, *J* = 5.4 Hz, 1H), 8.25 (d, *J* = 8.8 Hz, 1H), 7.97 (t, *J* = 8.6 Hz, 3H), 7.84 (d, *J* = 5.4 Hz, 1H), 7.78 (t, *J* = 7.6 Hz, 1H), 7.69 – 7.61 (m, 2H), 7.51 (t, *J* = 7.8 Hz, 2H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 194.78, 141.19, 136.73, 133.69, 130.77, 128.48, 128.34, 127.11, 126.21, 122.60.

(5-nitroisoquinolin-1-yl)(phenyl)methanone



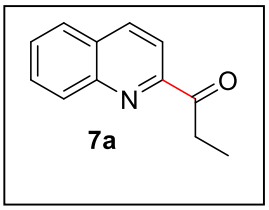
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.83 (s, 1H), 8.32 (d, *J* = 8.3 Hz, 1H), 8.26 (d, *J* = 8.8 Hz, 1H), 8.00 – 7.95 (m, 2H), 7.93 – 7.87 (m, 1H), 7.72 (t, *J* = 7.8 Hz, 1H), 7.64 (d, *J* = 7.8 Hz, 1H), 7.51 (t, *J* = 7.8 Hz, 2H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 193.98, 155.73, 142.95, 136.42, 135.54, 133.88, 132.01, 130.75, 129.23, 128.54, 127.58, 126.66, 126.50, 121.76.

(5-bromoisoquinolin-1-yl)(phenyl)methanone



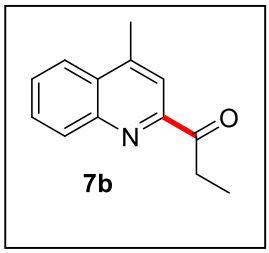
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.83 (s, 1H), 8.32 (d, *J* = 8.3 Hz, 1H), 8.26 (d, *J* = 8.8 Hz, 1H), 8.00 – 7.94 (m, 2H), 7.93 – 7.86 (m, 1H), 7.72 (t, *J* = 7.8 Hz, 1H), 7.65 (t, *J* = 7.3 Hz, 1H), 7.51 (t, *J* = 7.8 Hz, 2H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 193.98, 181.11, 155.73, 148.45, 142.95, 136.42, 135.54, 133.88, 132.01, 130.75, 129.23, 128.54, 127.58, 126.50, 121.77.

1-(quinolin-2-yl)propan-1-one



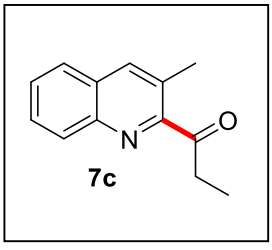
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.88 (d, *J* = 8.3 Hz, 1H), 8.59 (d, *J* = 5.9 Hz, 1H), 7.89 (d, *J* = 8.3 Hz, 1H), 7.83 (d, *J* = 5.4 Hz, 1H), 7.78 – 7.66 (m, 2H), 3.37 (q, *J* = 7.3 Hz, 2H), 1.30 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 205.32, 153.44, 141.06, 137.00, 130.34, 128.94, 126.97, 126.75, 124.24, 33.63, 8.14.

1-(4-methylquinolin-2-yl)propan-1-one



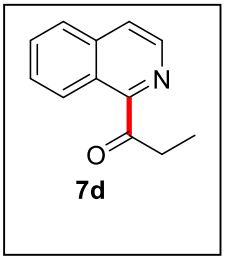
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.21 (d, *J* = 8.8 Hz, 1H), 8.06 (d, *J* = 8.3 Hz, 1H), 7.99 (s, 1H), 7.79 (s, 1H), 7.69 (d, *J* = 7.8 Hz, 1H), 3.44 (q, *J* = 7.3 Hz, 2H), 2.78 (s, 3H), 1.30 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 203.58, 152.72, 147.09, 145.27, 131.12, 129.56, 128.16, 123.80, 118.70, 30.81, 29.67, 22.09, 22.09, 18.91.

1-(3-methylquinolin-2-yl)propan-1-one



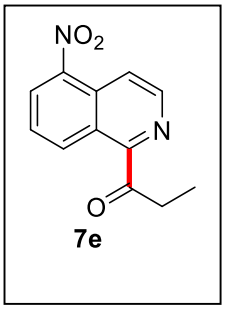
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.21 (d, *J* = 8.8 Hz, 1H), 8.06 (d, *J* = 8.3 Hz, 1H), 7.99 (s, 1H), 7.79 (s, 1H), 7.69 (d, *J* = 7.8 Hz, 1H), 3.44 (q, *J* = 7.3 Hz, 2H), 2.78 (s, 3H), 1.30 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 203.58, 152.72, 147.09, 145.27, 131.12, 129.56, 128.16, 123.80, 118.70, 30.81, 22.09, 22.09, 18.91.

1-(isoquinolin-1-yl)propan-1-one



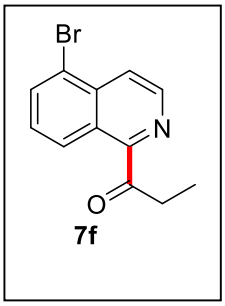
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.88 (d, *J* = 8.3 Hz, 1H), 8.59 (d, *J* = 5.9 Hz, 1H), 7.89 (d, *J* = 8.3 Hz, 1H), 7.83 (d, *J* = 5.4 Hz, 1H), 7.78 – 7.66 (m, 2H), 3.37 (q, *J* = 7.3 Hz, 2H), 1.30 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 205.32, 153.44, 141.06, 137.00, 130.34, 128.94, 126.97, 126.75, 124.24, 33.63, 8.14.

1-(5-nitroisoquinolin-1-yl)propan-1-one



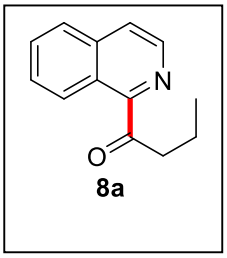
^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.23 (d, *J* = 8.6 Hz, 1H), 8.81 (d, *J* = 6.0 Hz, 1H), 8.62 (d, *J* = 6.0 Hz, 1H), 8.54 (d, *J* = 7.7 Hz, 1H), 7.80 (t, *J* = 8.3 Hz, 1H), 3.40 (q, *J* = 7.3 Hz, 2H), 1.32 (d, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 153.87, 145.28, 144.29, 133.76, 129.24, 128.03, 127.14, 125.93, 118.96, 33.77, 29.70, 8.05.

1-(5-bromoisoquinolin-1-yl)propan-1-one



^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.90 (d, *J* = 8.3 Hz, 1H), 8.78 (s, 1H), 8.26 (d, *J* = 8.4 Hz, 1H), 7.85 (dd, *J* = 8.9, 6.4 Hz, 1H), 7.75 (dd, *J* = 8.8, 6.8 Hz, 1H), 3.34 (q, *J* = 7.3 Hz, 2H), 1.28 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 204.63, 142.97, 135.63, 131.58, 129.78, 127.20, 126.87, 126.27, 123.56, 33.71, 8.12.

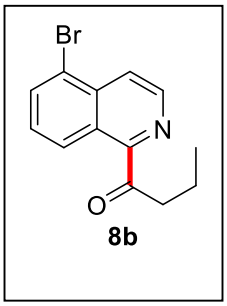
1-(isoquinolin-1-yl)butan-1-one



8a

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.87 (d, *J* = 8.3 Hz, 1H), 8.59 (d, *J* = 5.4 Hz, 1H), 7.93 – 7.85 (m, 1H), 7.82 (d, *J* = 5.9 Hz, 1H), 7.78 – 7.65 (m, 2H), 3.32 (t, *J* = 7.3 Hz, 2H), 1.84 (q, *J* = 7.3 Hz, 2H), 1.07 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 204.23, 142.97, 131.59, 129.78, 127.19, 126.87, 126.30, 123.51, 42.33, 17.66, 13.88.

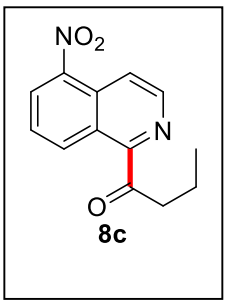
1-(5-nitroisoquinolin-1-yl)butan-1-one



8b

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.22 (d, *J* = 8.3 Hz, 1H), 8.81 (d, *J* = 6.4 Hz, 1H), 8.62 (d, *J* = 5.9 Hz, 1H), 8.54 (d, *J* = 7.8 Hz, 1H), 7.80 (t, *J* = 8.1 Hz, 1H), 3.35 (t, *J* = 7.3 Hz, 2H), 1.84 (q, *J* = 7.3 Hz, 2H), 1.08 (t, *J* = 7.6 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.14, 154.05, 144.29, 133.73, 128.05, 127.13, 118.93, 77.33, 77.01, 76.70, 42.36, 17.58, 13.84, 204.14.

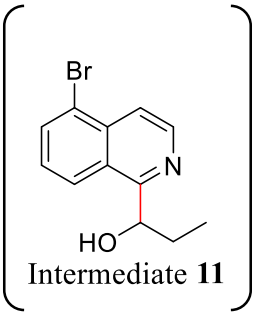
1-(4-bromoisoquinolin-1-yl)butan-1-one



8c

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.91 – 8.86 (m, 1H), 8.78 (s, 1H), 8.26 (dd, *J* = 8.3, 1.0 Hz, 1H), 7.85 (ddd, *J* = 8.8, 6.8, 1.7 Hz, 1H), 7.75 (ddd, *J* = 8.3, 6.9, 1.5 Hz, 1H), 3.29 (t, *J* = 7.3 Hz, 2H), 1.82 (q, *J* = 7.6 Hz, 2H), 1.06 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 204.23, 142.97, 131.59, 129.78, 127.19, 126.87, 126.30, 123.51, 42.33, 17.66, 13.88.

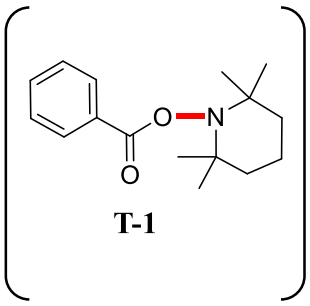
1-(5-bromoisoquinolin-1-yl)propan-1-ol



Intermediate **11**

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.66 (s, 1H), 8.25 (d, *J* = 8.8 Hz, 1H), 8.07 (d, *J* = 8.3 Hz, 1H), 7.85 (t, *J* = 7.6 Hz, 1H), 7.72 (t, *J* = 7.6 Hz, 1H), 5.47 (q, *J* = 4.2 Hz, 1H), 4.79 (d, *J* = 7.3 Hz, 1H), 1.93 (d, *J* = 2.9 Hz, 1H), 1.77 – 1.59 (m, 3H), 1.54 – 1.46 (m, 1H), 0.98 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 161.25, 142.19, 134.97, 131.52, 128.25, 126.97, 125.95, 124.46, 118.86, 69.43, 41.44, 18.81, 14.00.

Phenyl(2,2,6,6-tetramethylpiperidin-1-yloxy)methanol



T-1

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, *J* = 7.6 Hz, 2H), 7.50 (d, *J* = 7.1 Hz, 1H), 7.44 (t, *J* = 7.5 Hz, 2H), 2.16 – 1.17 (m, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.97, 133.85, 131.64, 129.81, 128.00, 127.83, 65.53, 37.18, 27.77, 20.25, 16.01.

References

(1) Narayanam, J. M. R.; Stephenson, C. R. J. Visible Light Photoredox Catalysis: Applications in Organic Synthesis. *Chem. Soc. Rev.* **2010**, *40* (1), 102–113.

(2) Cheng, J.-P.; Zhao, Y. Homolytic Bond Cleavage Energies of the Acidic N□H Bonds in Dimethyl Sulfoxide Solution and Properties of the Corresponding Radicals and Radical Cations. *Tetrahedron* **1993**, *49* (24), 5267–5276.

(3) Blanksby, S. J.; Ellison, G. B. Bond Dissociation Energies of Organic Molecules. *Acc. Chem. Res.* **2003**, *36* (4), 255–263.

(4) Lebeau, E. L.; Binstead, R. A.; Meyer, T. J. Mechanistic Implications of Proton Transfer Coupled to Electron Transfer. *J. Am. Chem. Soc.* **2001**, *123* (43), 10535–10544.

(5) Capaldo, L.; Ravelli, D. Hydrogen Atom Transfer (HAT): A Versatile Strategy for Substrate Activation in Photocatalyzed Organic Synthesis. *Eur. J. Org. Chem.* **2017**, *2017* (15), 2056–2071.

(6) Anglada, J. M.; Martins-Costa, M. T. C.; Francisco, J. S.; Ruiz-López, M. F. Triplet State Promoted Reaction of SO2 with H2O by Competition between Proton Coupled Electron Transfer (Pcet) and Hydrogen Atom Transfer (Hat) Processes. *Phys. Chem. Chem. Phys.* **2019**, *21* (19), 9779–9784.

(7) Mandal, S.; Chhetri, K.; Bhuyan, S.; Roy, B. G. Efficient Iron Catalyzed Ligand-Free Access to Acridines and Acridinium Ions. *Green Chem.* **2020**, *22* (10), 3178–3185.

(8) Mandal, S.; Bhuyan, S.; Jana, S.; Hossain, J.; Chhetri, K.; Roy, B. G. Efficient Visible Light Mediated Synthesis of Quinolin-2(1H)-Ones from Quinoline N-Oxides. *Green Chem.* **2021**, *23* (14), 5049–5055.

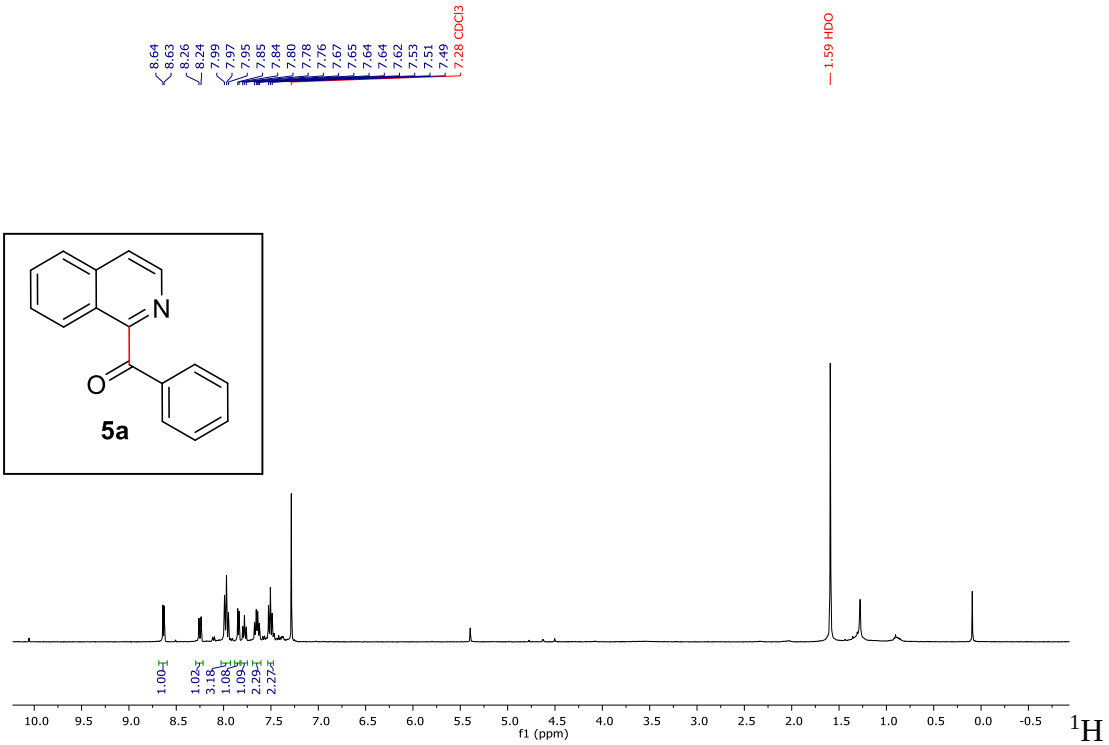
(9) Chhetri, K.; Bhuyan, S.; Mandal, S.; Chhetri, S.; Lepcha, P. T.; Lepcha, S. W.; Basumatary, J.; Roy, B. G. Efficient Metal-Free Visible Light Photocatalytic Aromatization of Azaheterocyles. *Curr. Res. Green Sustain. Chem.* **2021**, *4*, 100135.

(10) Jeffrey, J. L.; Terrett, J. A.; MacMillan, D. W. C. O-H Hydrogen Bonding Promotes H-Atom Transfer from α C-H Bonds for C-Alkylation of Alcohols. *Science* **2015**, *349* (6255), 1532–1536.

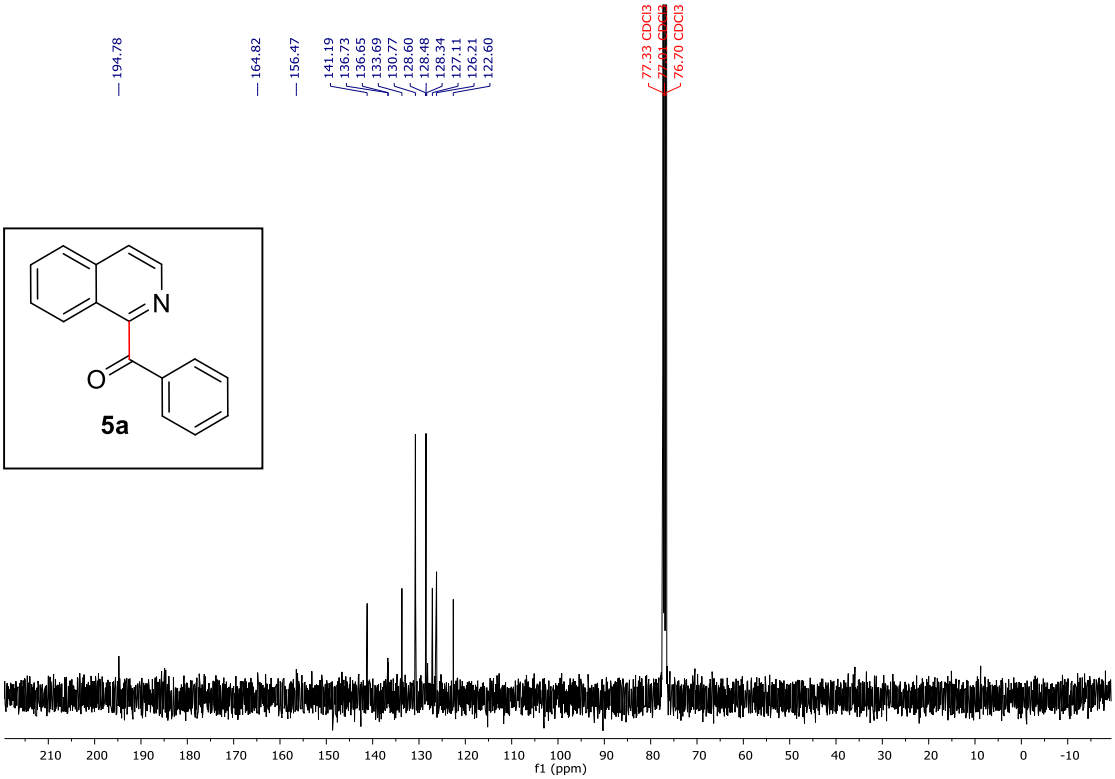
(11) Jin, J.; MacMillan, D. W. C. Alcohols as Alkylating Agents in Heteroarene C–H Functionalization. *Nature* **2015**, *525* (7567), 87–90.

(12) Kianmehr, E.; Pakbaznia, A.; Faghih, N.; Foroumadi, A. Metal-Free Chemo- and Regioselective Acylation of Pyridine Derivatives with Alcohols in Water. *Tetrahedron* **2017**, *73* (11), 1407–1412.

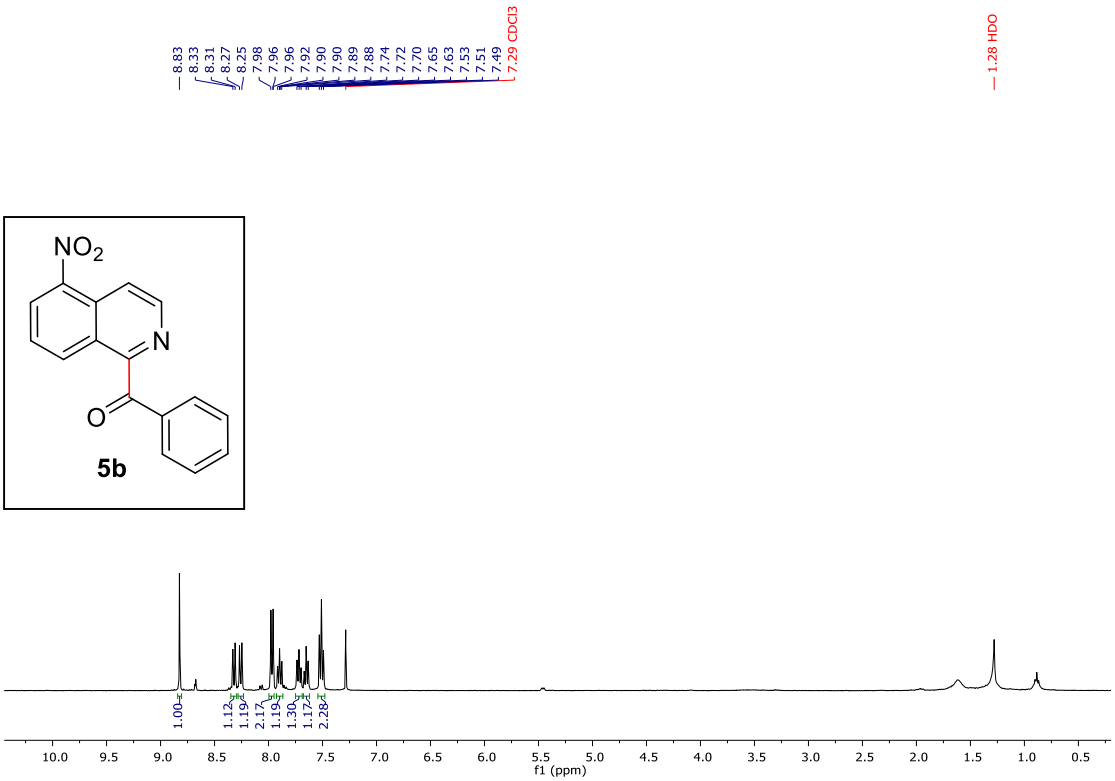
3.8: NMR Spectra of newly synthesized compounds:



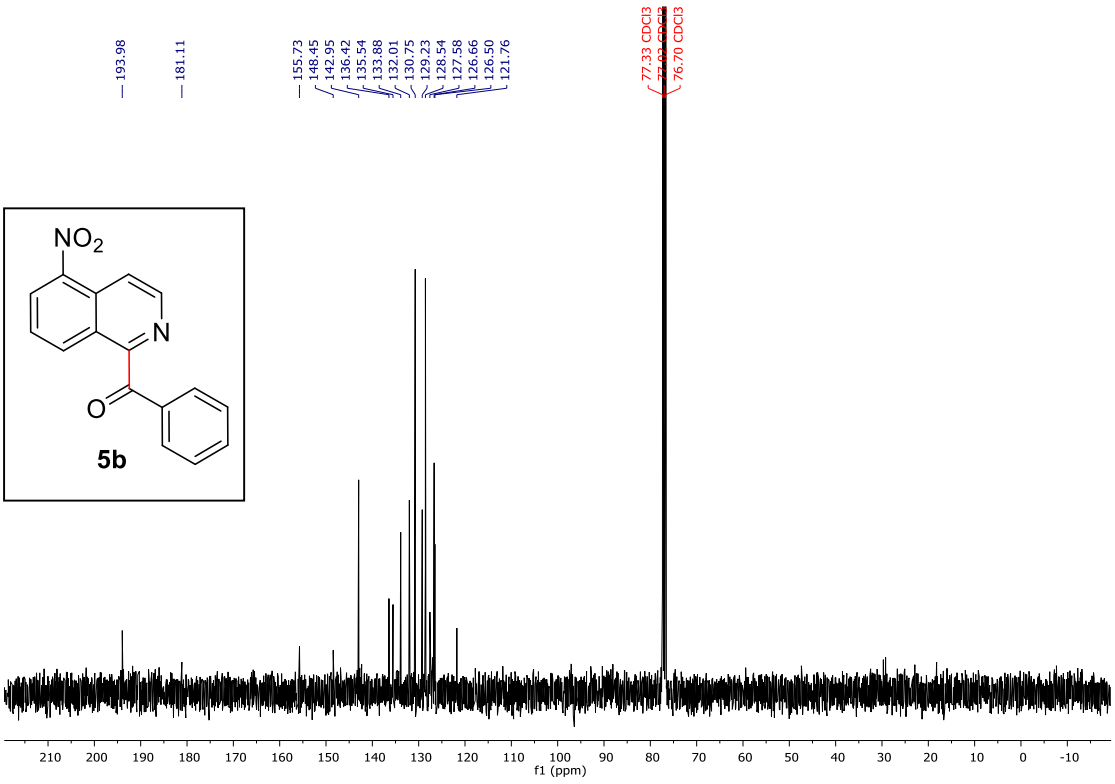
^{1}H NMR ($CDCl_3$, 400 MHz) Spectrum of **i**soquinolin-1-yl(phenyl)methanone



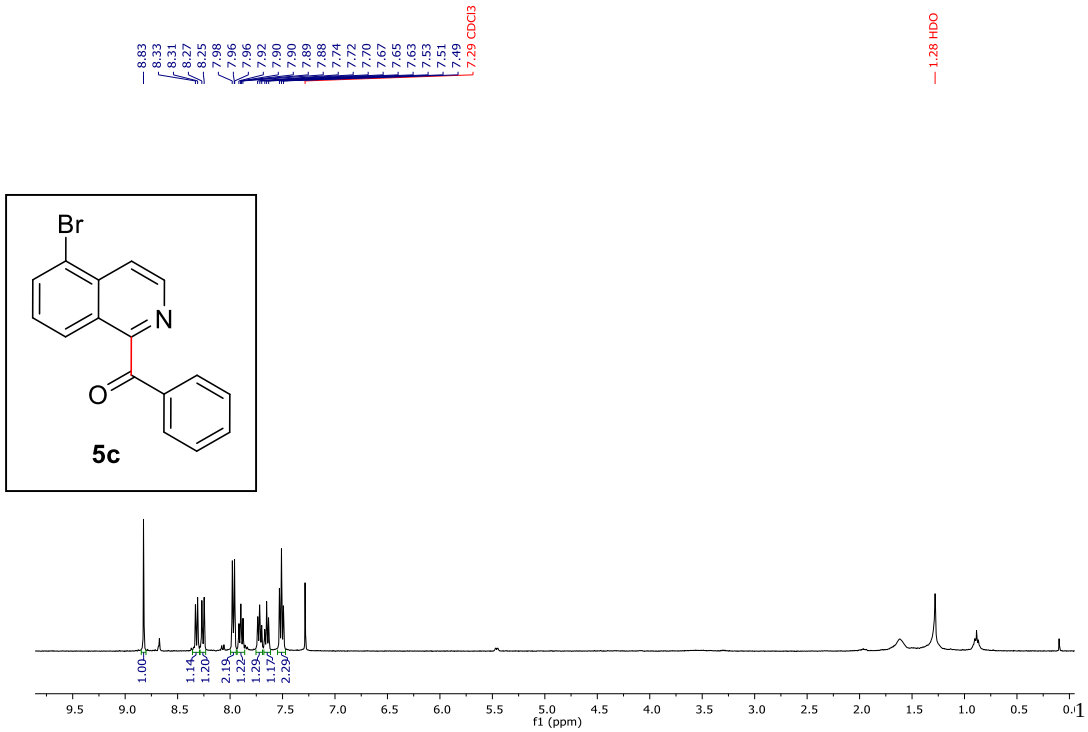
^{13}C NMR ($CDCl_3$, 100 MHz) Spectrum of **i**soquinolin-1-yl(phenyl)methanone



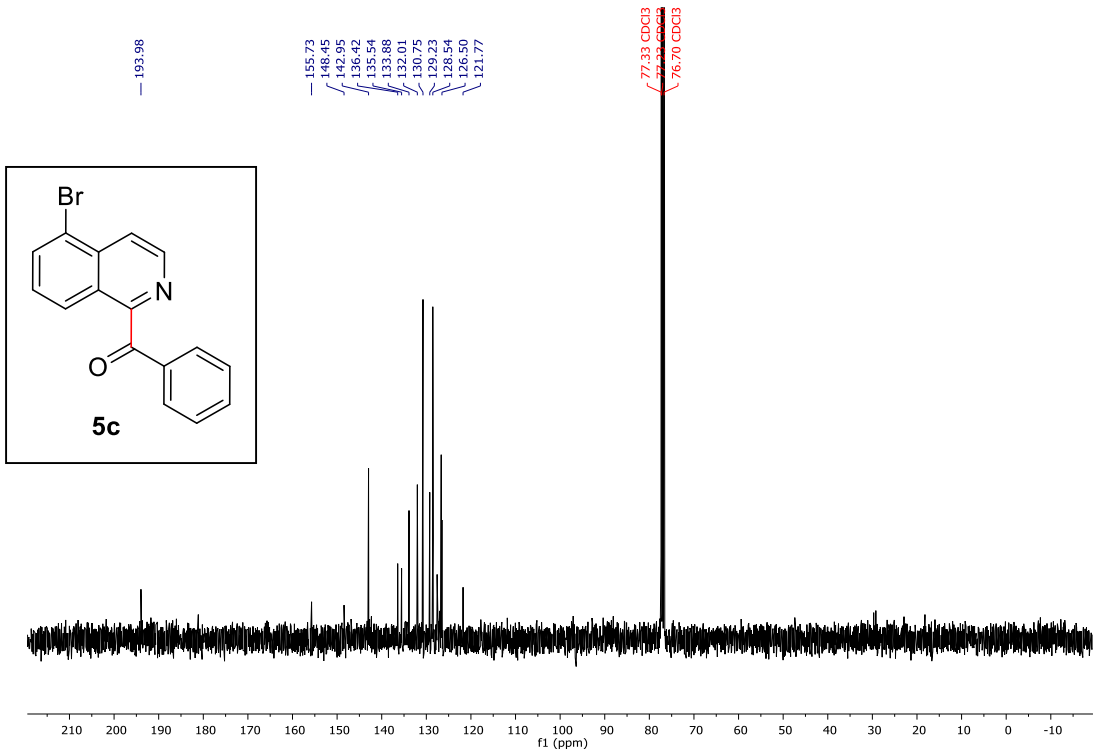
^{1}H NMR ($CDCl_3$, 400 MHz) Spectrum of (5-nitroisoquinolin-1-yl)(phenyl)methanone



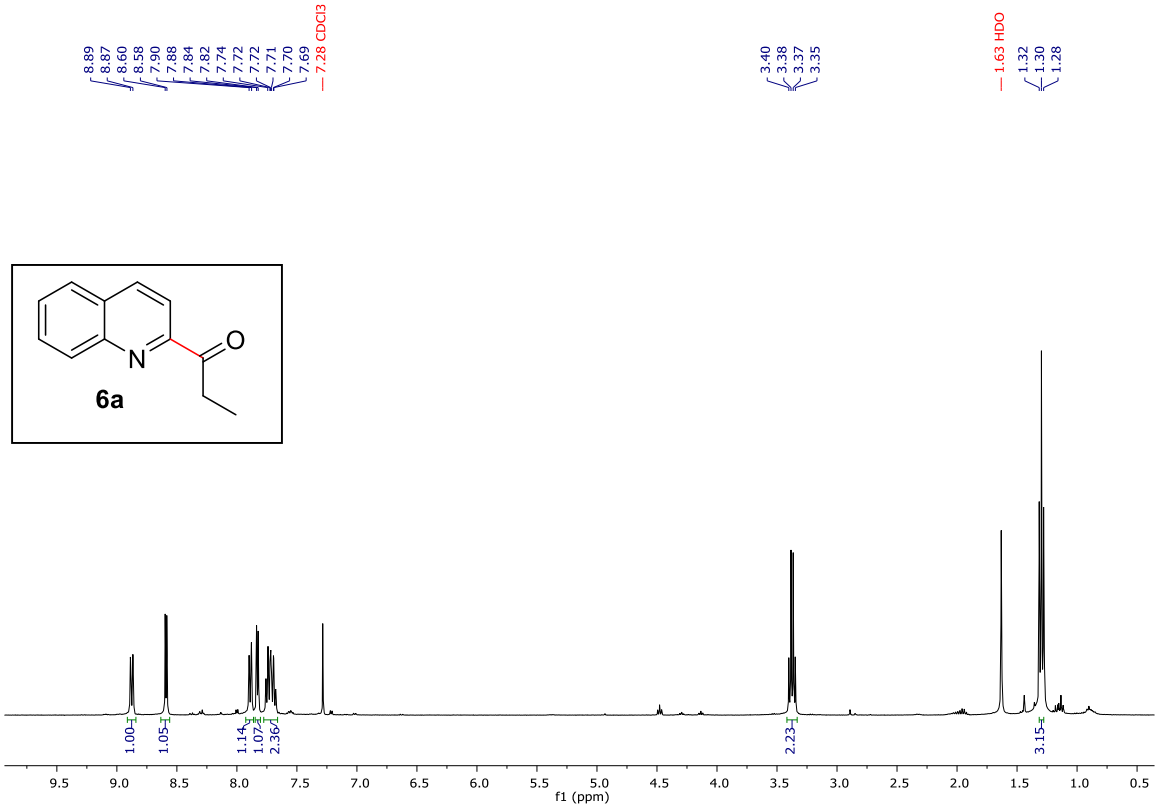
^{13}C NMR ($CDCl_3$, 100 MHz) spectrum of (5-nitroisoquinolin-1-yl)(phenyl)methanone



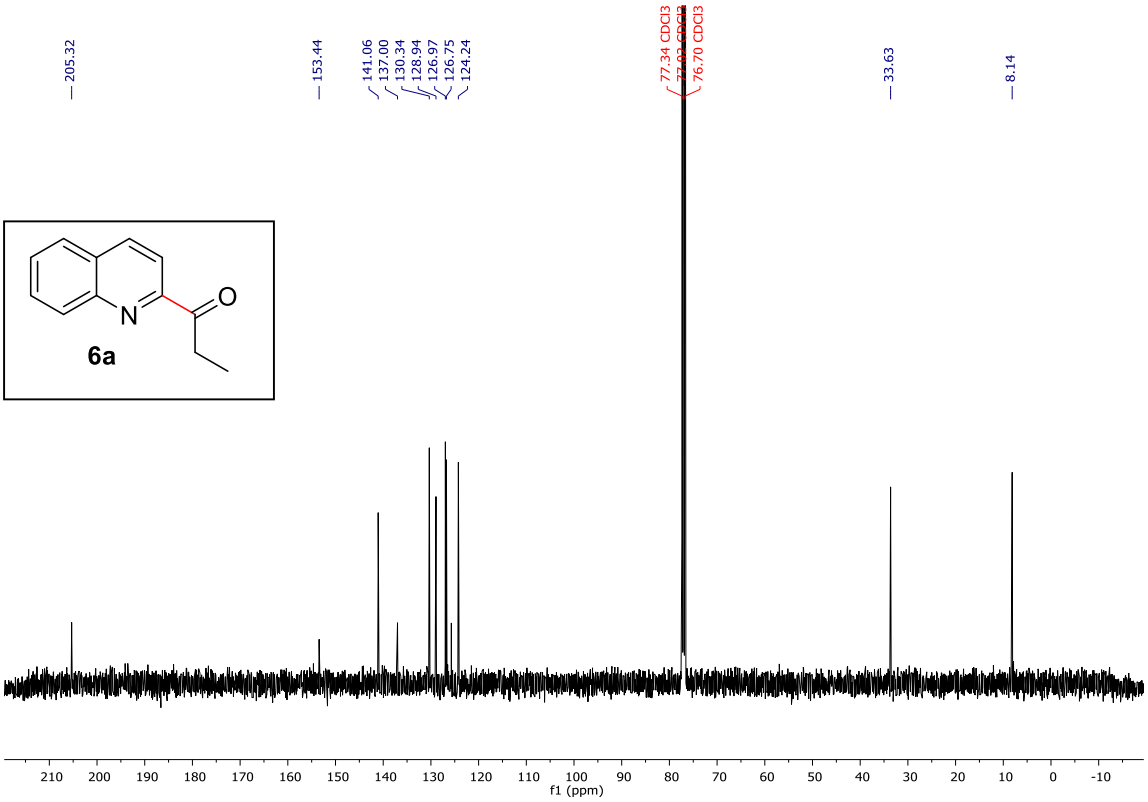
H NMR ($CDCl_3$, 400 MHz) Spectrum of (5-bromoisoquinolin-1-yl)(phenyl)methanone



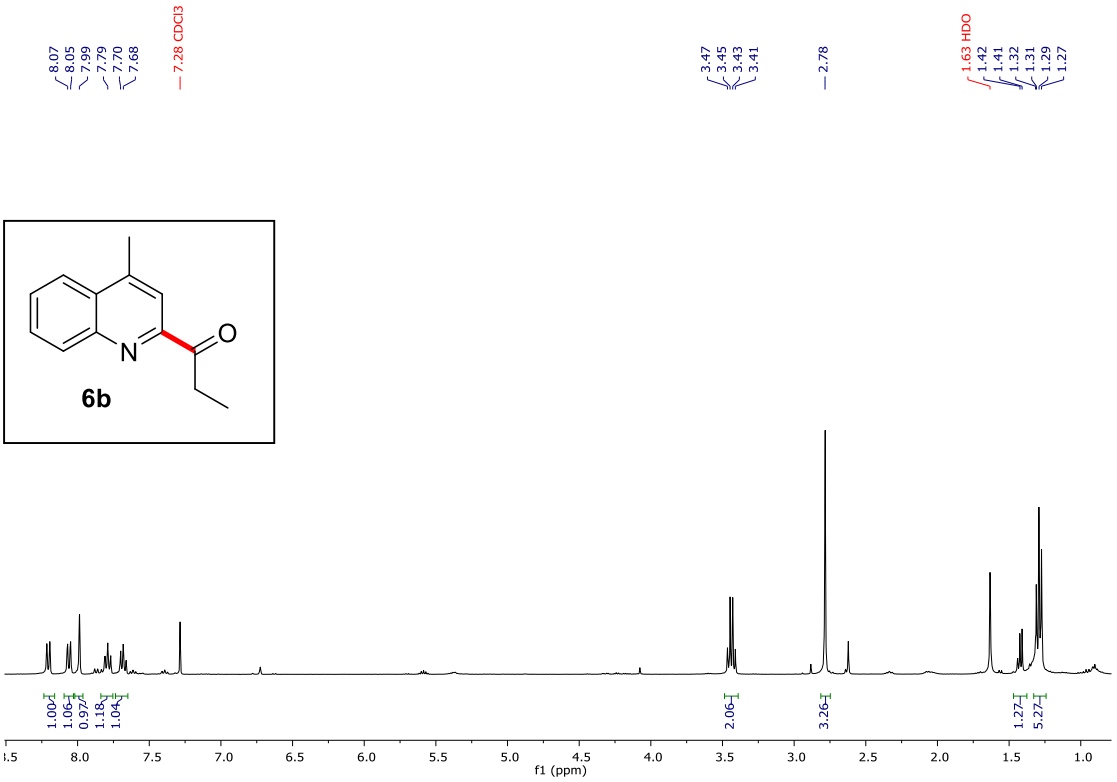
^{13}C NMR ($CDCl_3$, 100 MHz) Spectrum of (5-bromoisoquinolin-1-yl)(phenyl)methanone



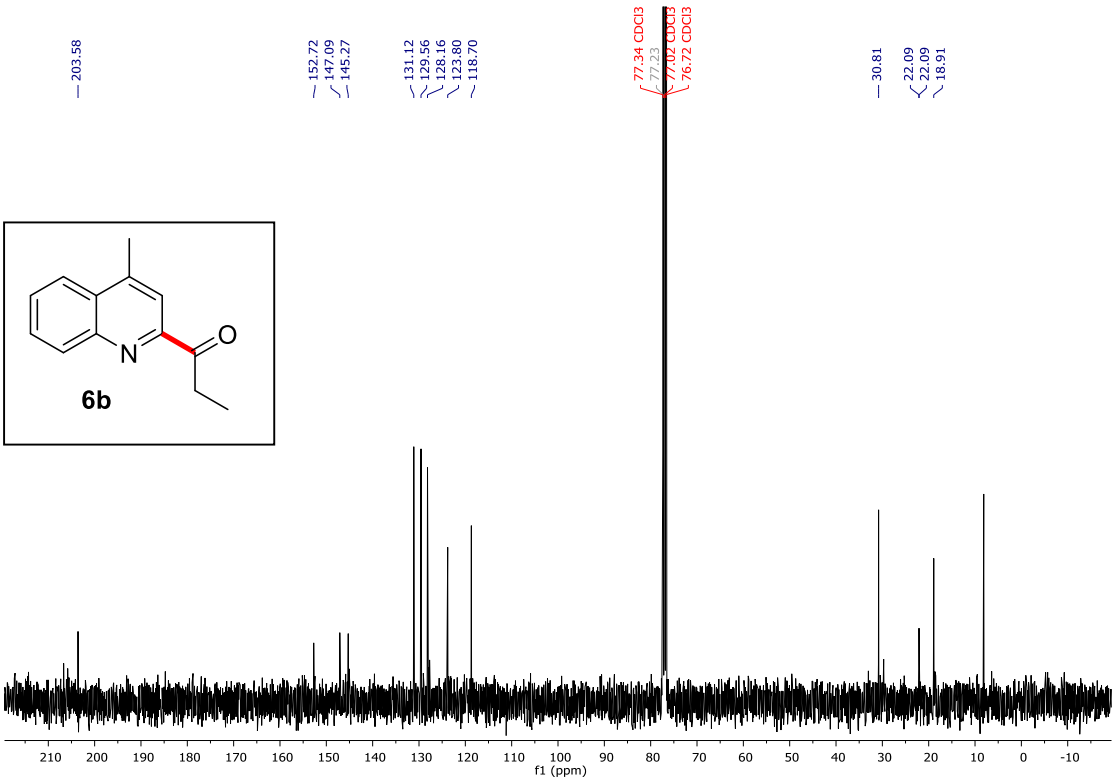
^{1}H NMR ($CDCl_3$, 400 MHz) Spectrum of 1-(quinolin-2-yl)propan-1-one



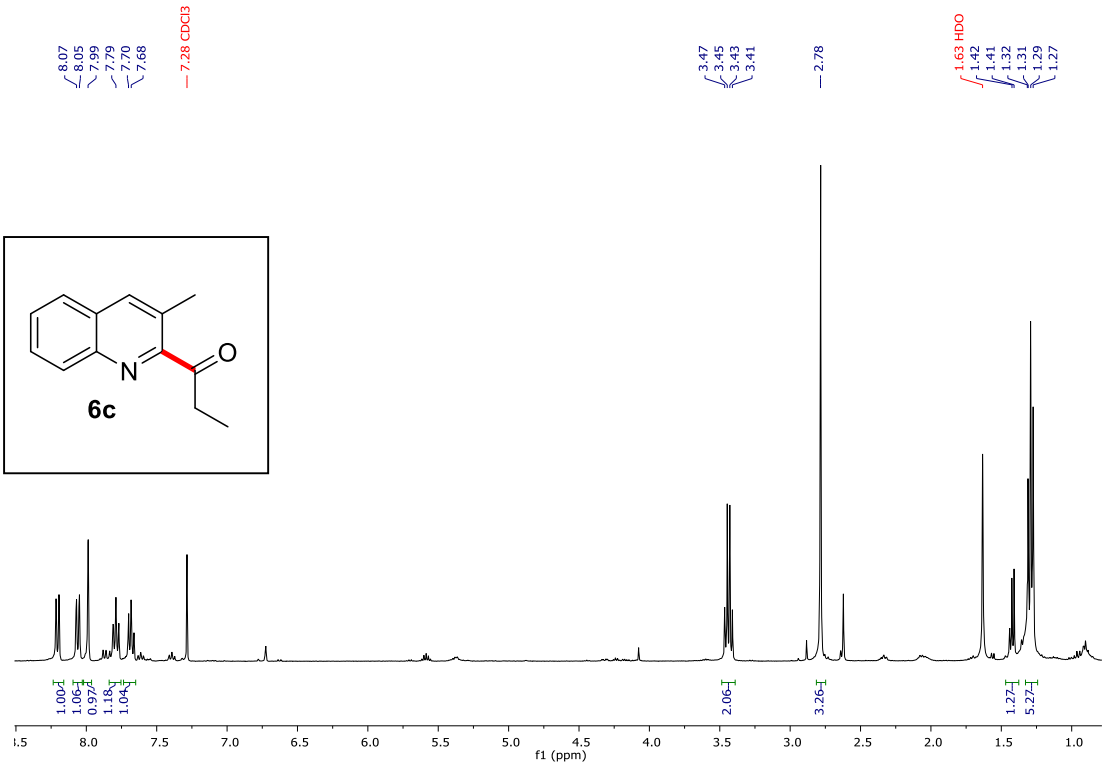
^{13}C NMR ($CDCl_3$, 100 MHz) Spectrum of 1-(quinolin-2-yl)propan-1-one



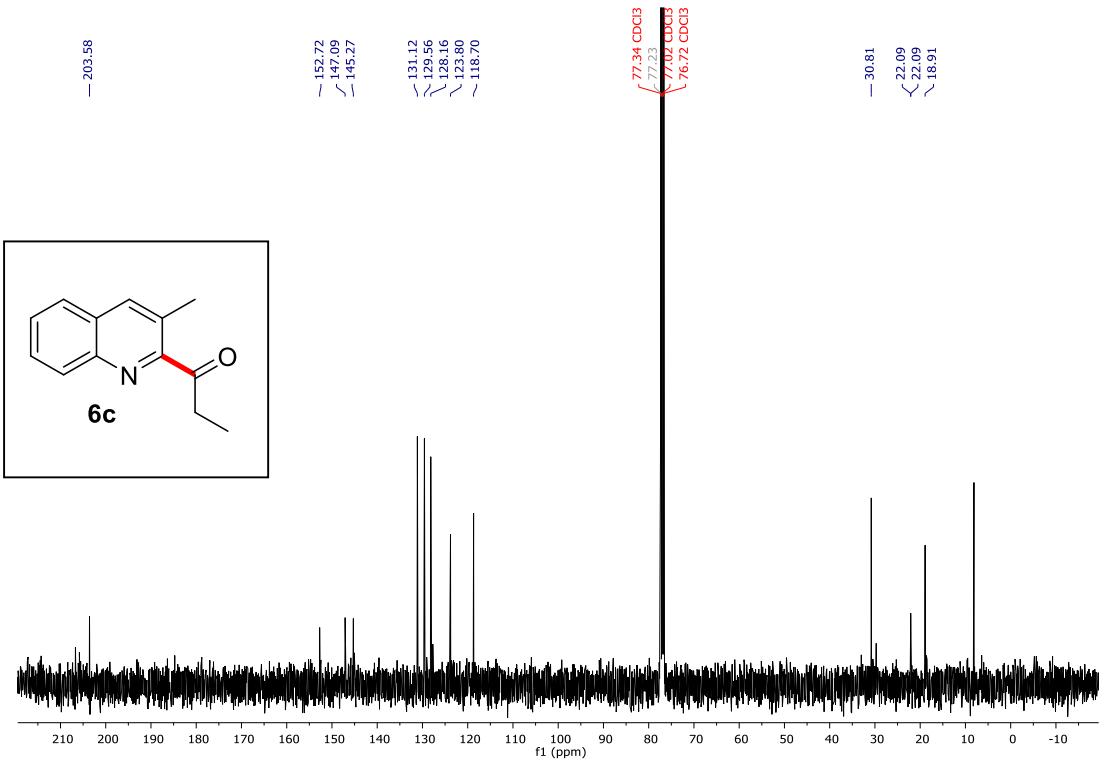
^{1}H NMR ($CDCl_3$, 400 MHz) Spectrum of 1-(4-methylquinolin-2-yl)propan-1-one



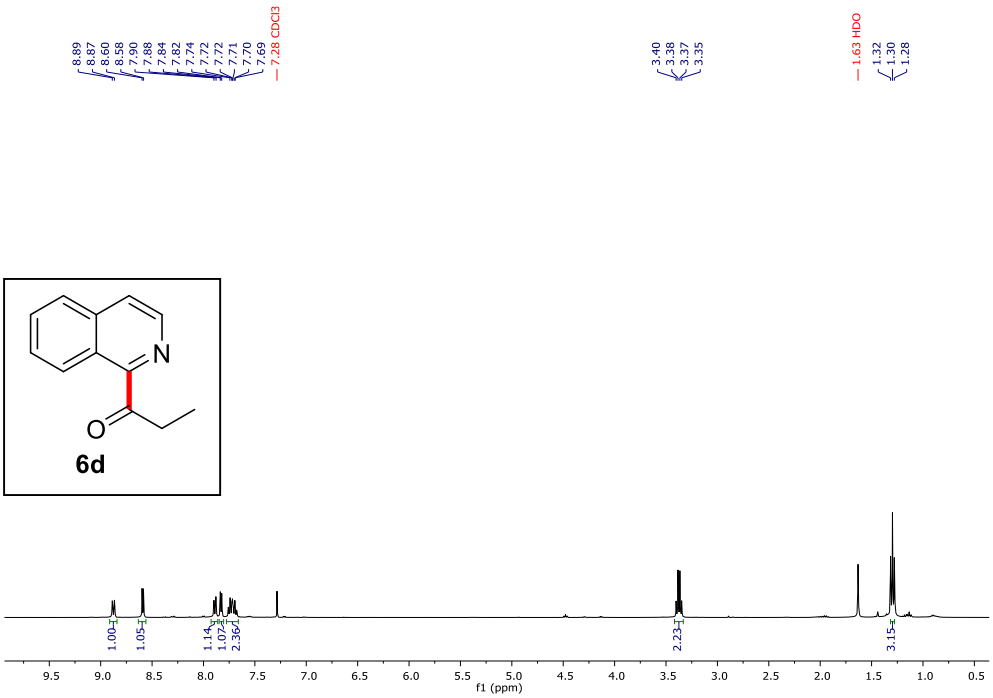
^{13}C NMR ($CDCl_3$, 100 MHz) Spectrum of 1-(4-methylquinolin-2-yl)propan-1-one



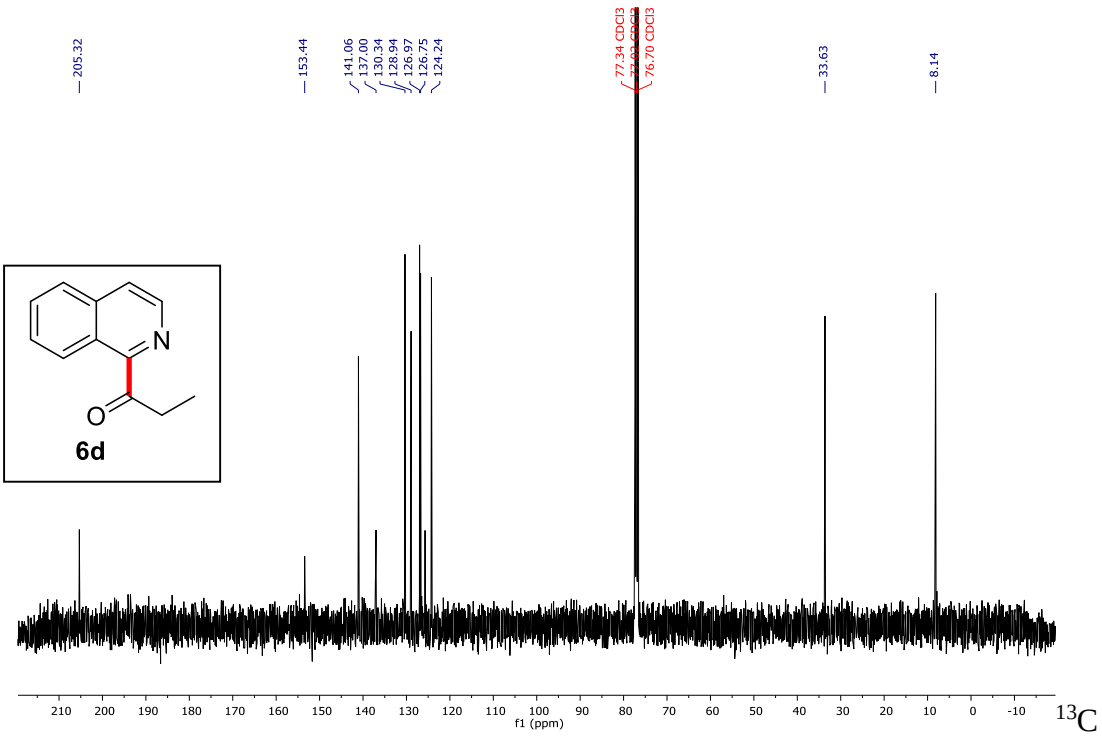
^{1}H NMR ($CDCl_3$, 400 MHz) Spectrum of 1-(3-methylquinolin-2-yl)propan-1-one



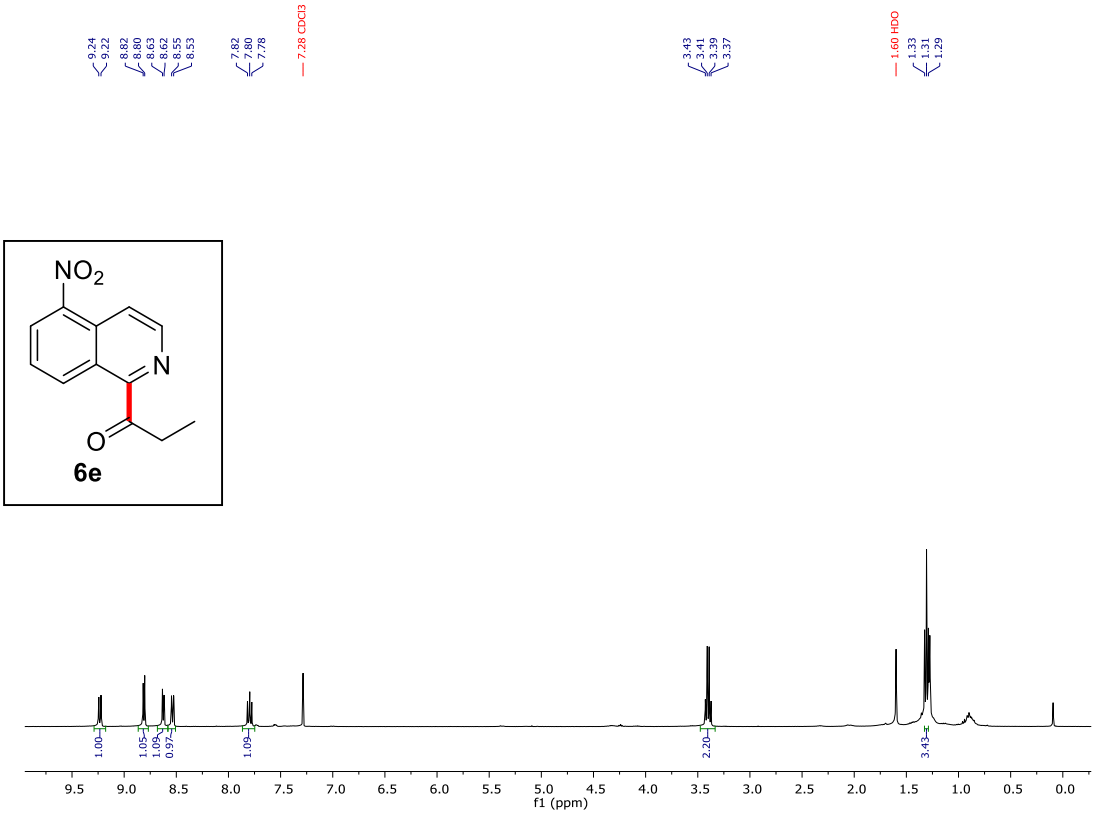
^{13}C NMR ($CDCl_3$, 100 MHz) Spectrum of 1-(3-methylquinolin-2-yl)propan-1-one



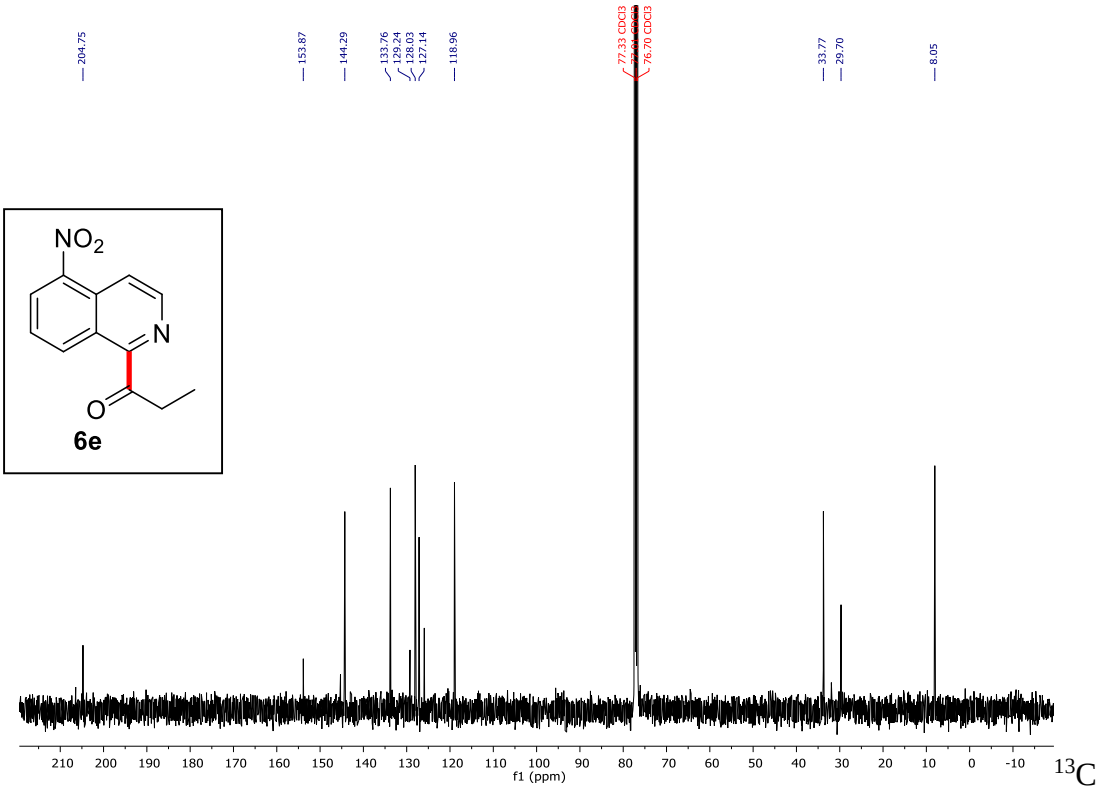
^{1}H NMR ($CDCl_3$, 400 MHz) Spectrum of 1-(isoquinolin-1-yl)propan-1-one



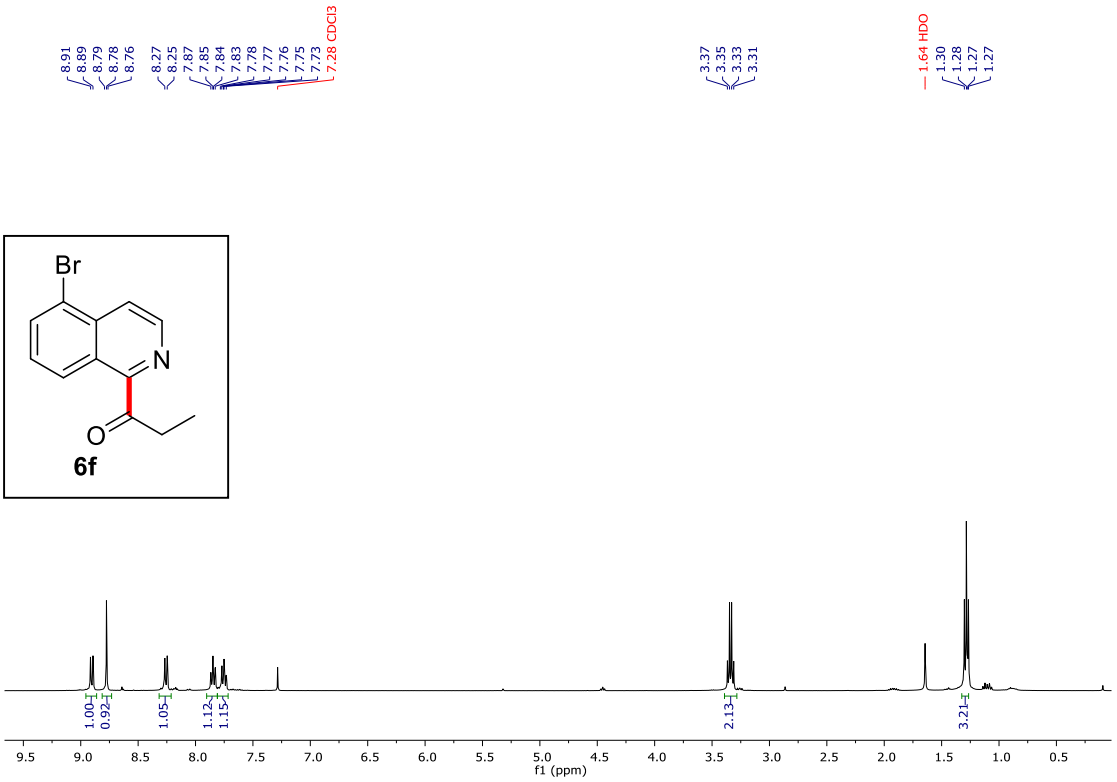
^{13}C NMR ($CDCl_3$, 100 MHz) Spectrum of 1-(isoquinolin-1-yl)propan-1-one



^{1}H NMR ($CDCl_3$, 400 MHz) Spectrum of 1-(5-nitroisoquinolin-1-yl)propan-1-one



^{13}C NMR ($CDCl_3$, 100 MHz) Spectrum of 1-(5-nitroisoquinolin-1-yl)propan-1-one



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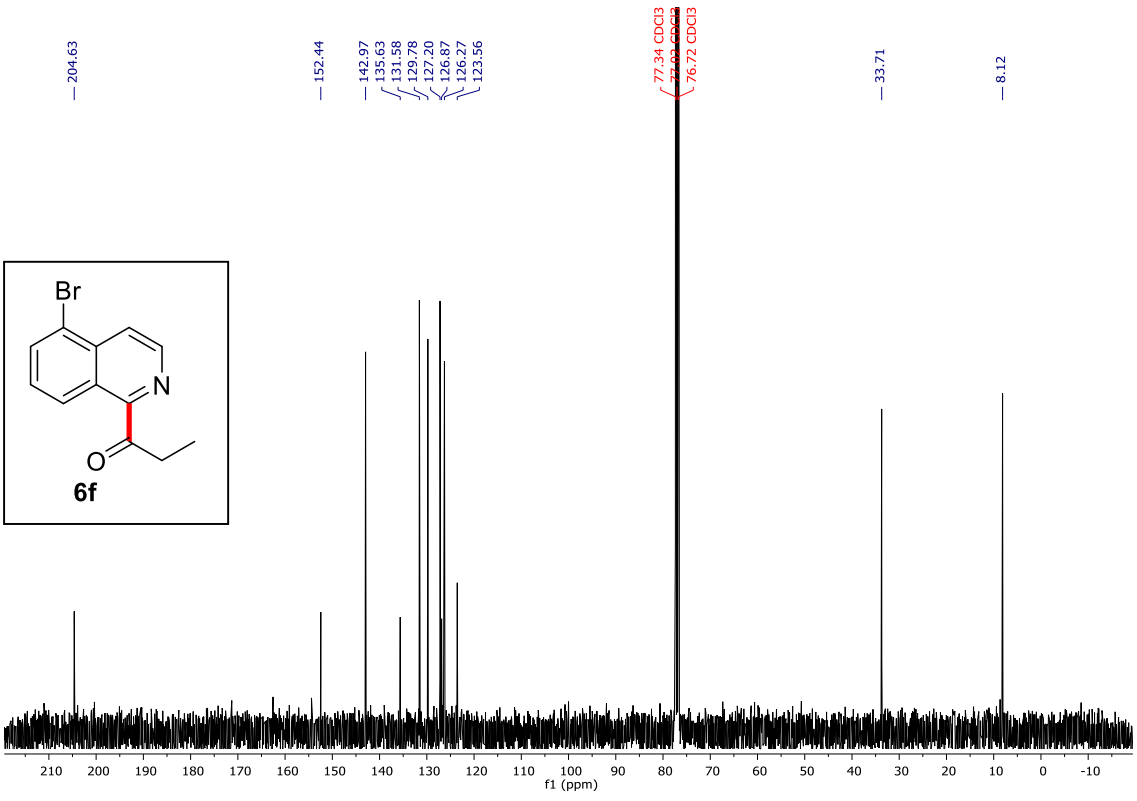
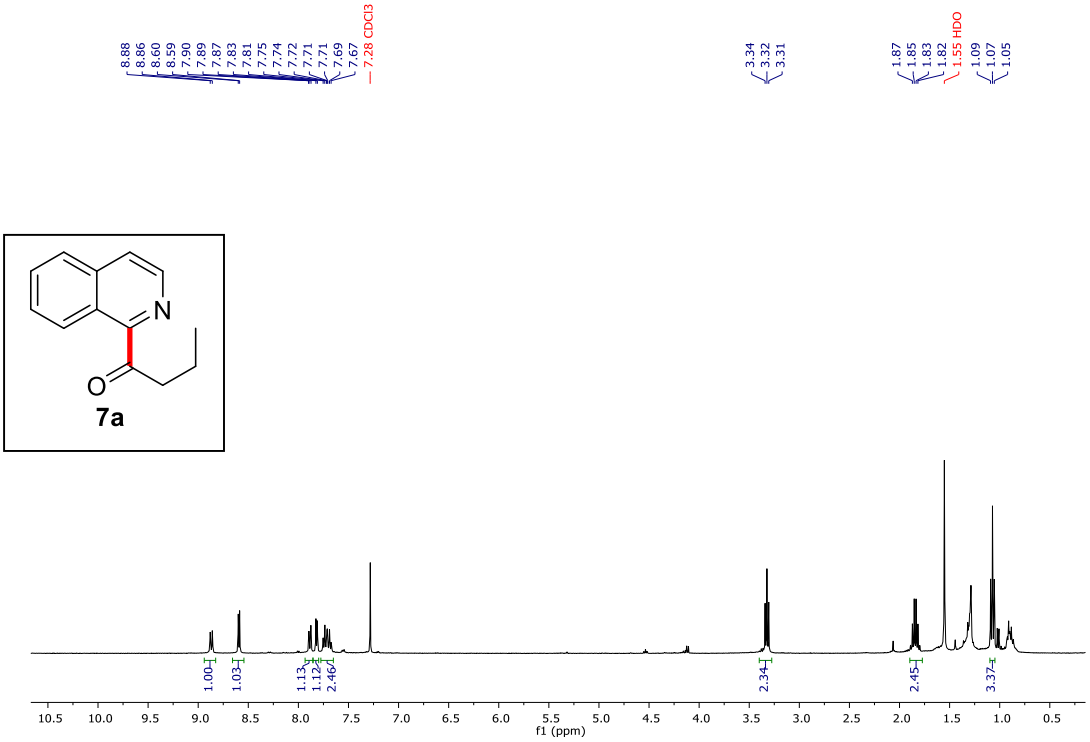
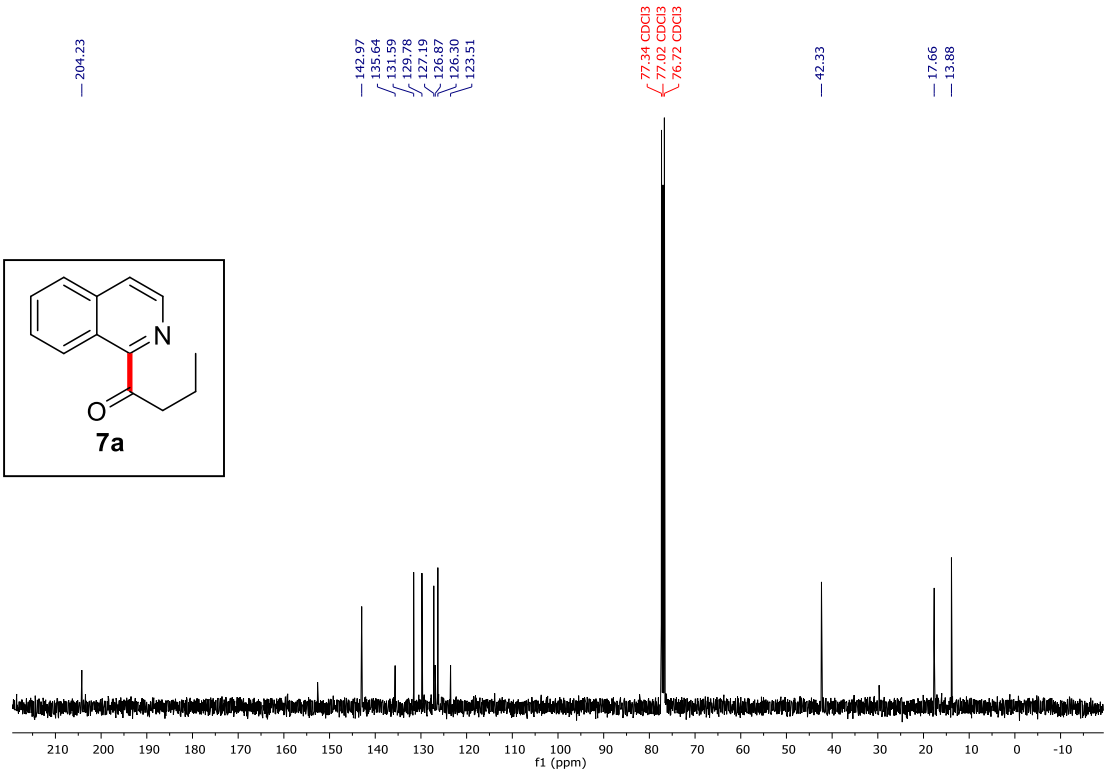


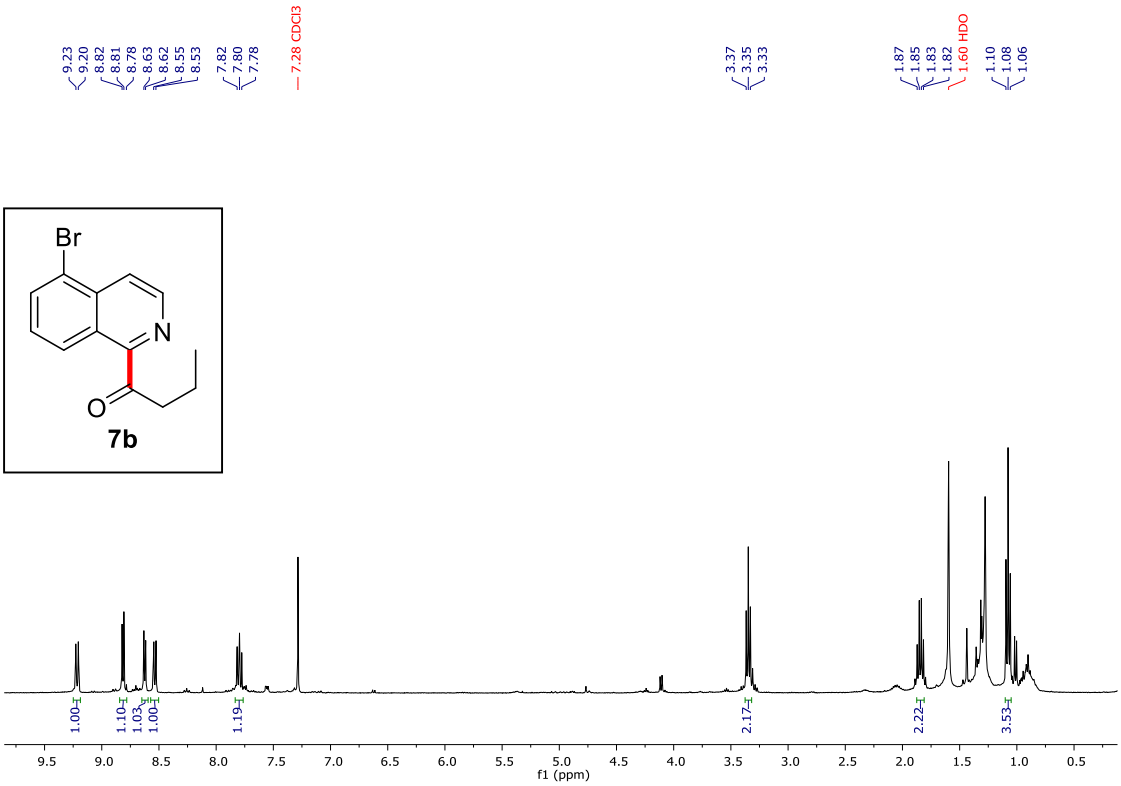
^{13}C NMR ($CDCl_3$, 100 MHz) Spectrum of 1-(5-bromoisoquinolin-1-yl)propan-1-one



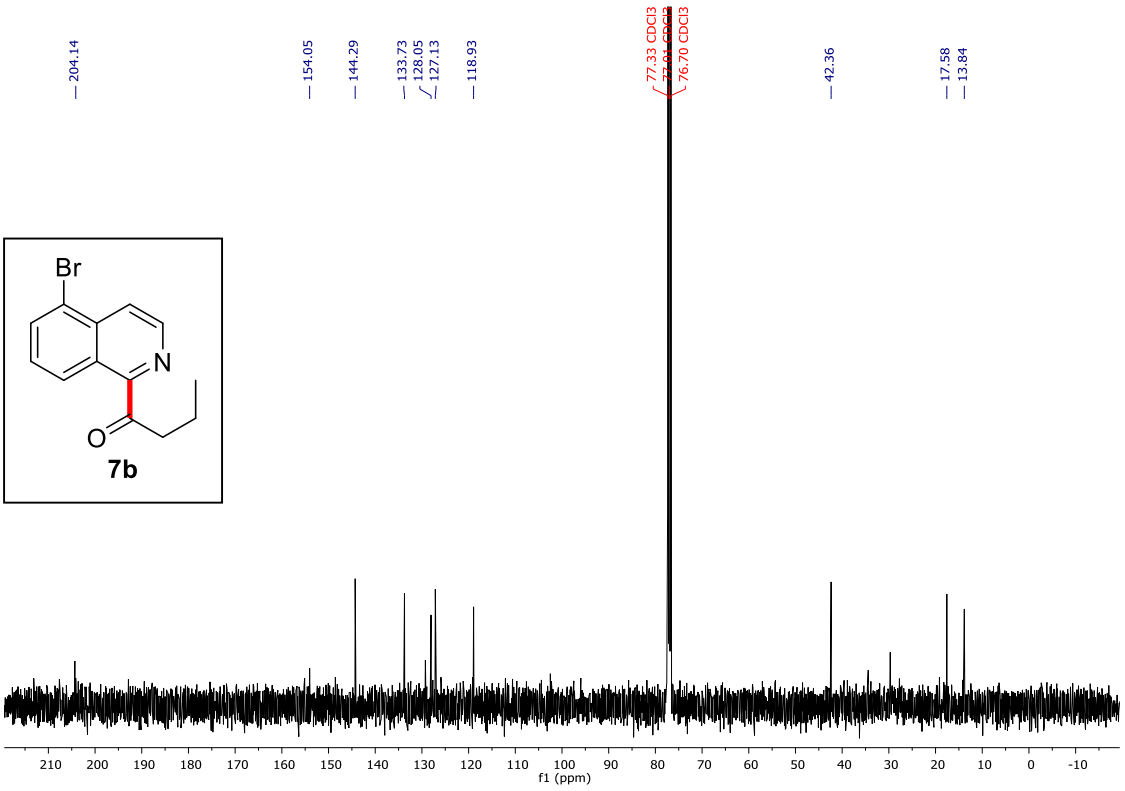
^{1}H NMR ($CDCl_3$, 400 MHz) Spectrum of 1-(isoquinolin-1-yl)butan-1-one



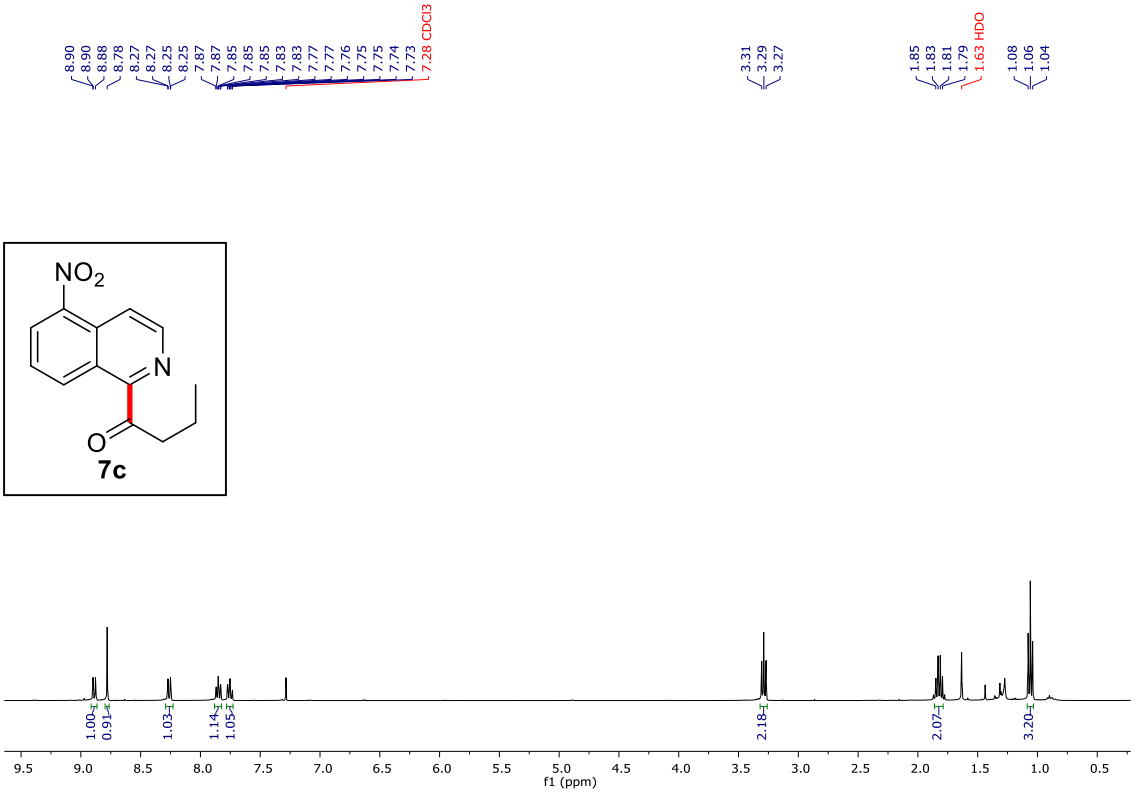
^{13}C NMR ($CDCl_3$, 100 MHz) Spectrum of 1-(isoquinolin-1-yl)butan-1-one



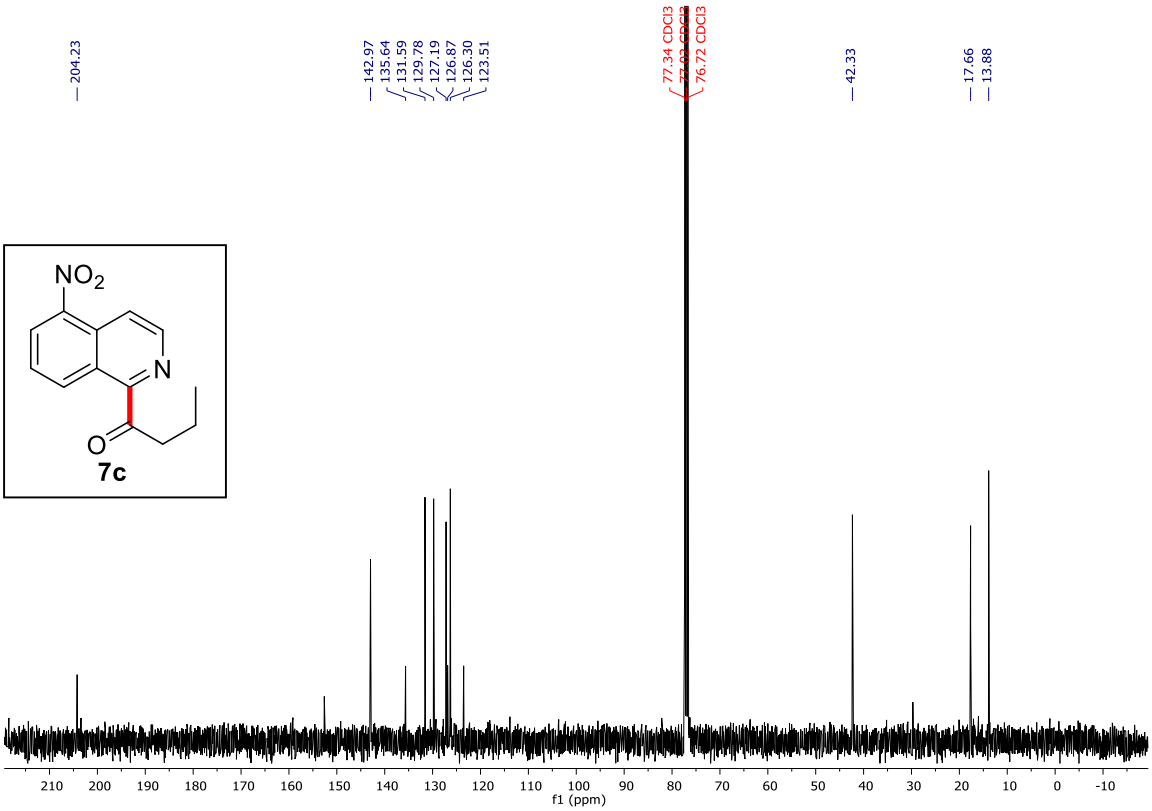
^{1}H NMR ($CDCl_3$, 400 MHz) Spectrum of 1-(5-nitroisoquinolin-1-yl)butan-1-one



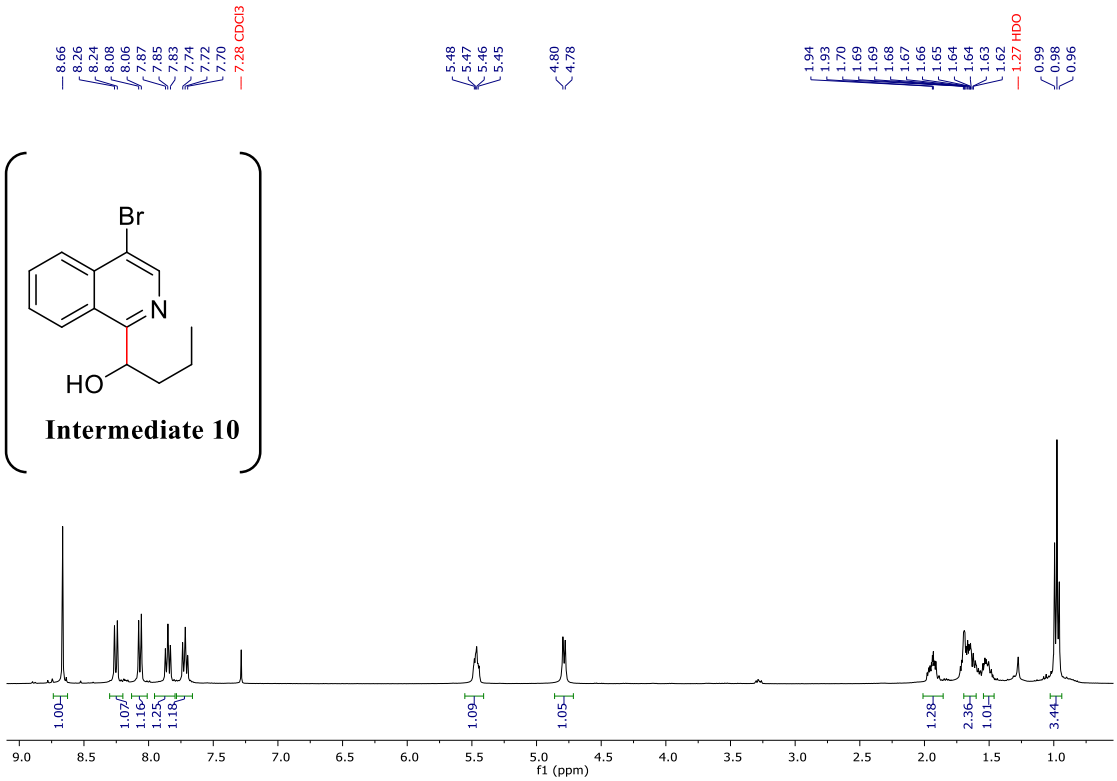
^{13}C NMR ($CDCl_3$, 100 MHz) Spectrum of 1-(5-nitroisoquinolin-1-yl)butan-1-one



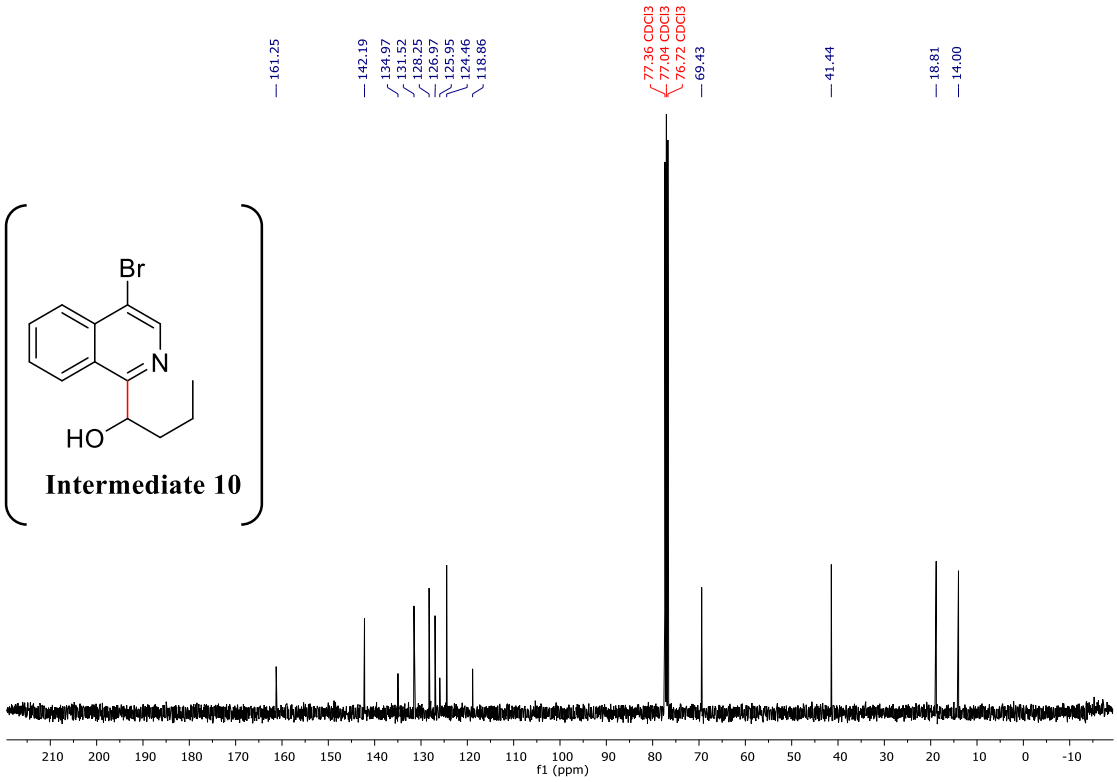
^{1}H NMR ($CDCl_3$, 400 MHz) Spectrum of 1-(4-bromoisoquinolin-1-yl)butan-1-one



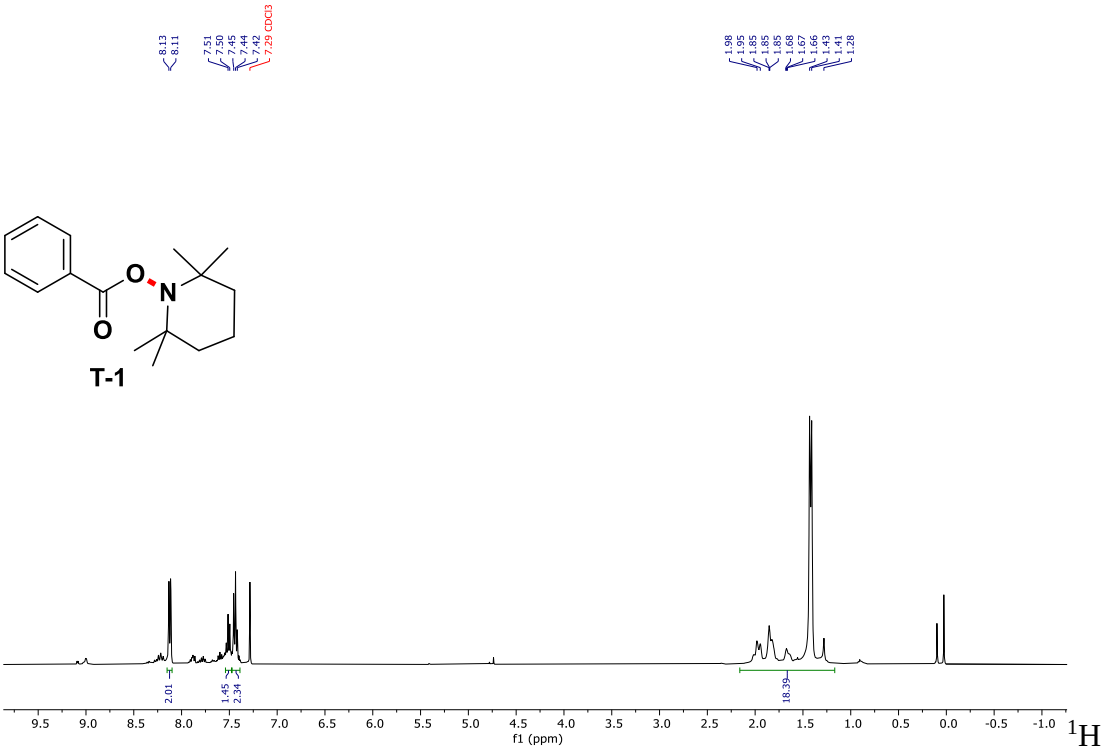
^{13}C NMR ($CDCl_3$, 100 MHz) Spectrum of 1-(4-bromoisoquinolin-1-yl)butan-1-one



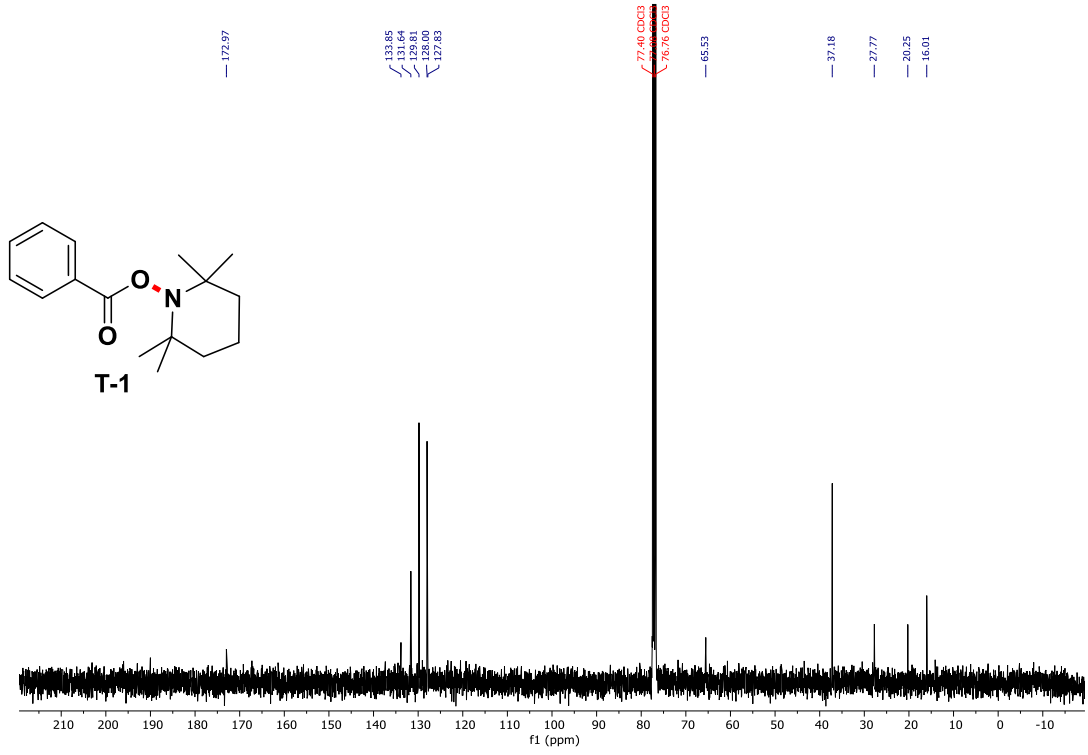
^{1}H NMR ($CDCl_3$, 400 MHz) Spectrum of 1-(4-bromoisoquinolin-1-yl)butan-1-ol



^{13}C NMR ($CDCl_3$, 100 MHz) Spectrum of 1-(4-bromoisoquinolin-1-yl)butan-1-ol



^{1}H NMR ($CDCl_3$, 400 MHz) Spectrum of phenyl((2,2,6,6-tetramethylpiperidin-1-yl)oxy)methanol



^{13}C NMR ($CDCl_3$, 100 MHz) Spectrum of phenyl((2,2,6,6-tetramethylpiperidin-1-yl)oxy)methane