Convenient strategies to C–N bond formation: Synthesis of β-Heteroarylated Ketones, Scorpionate Ligands *E*-Allyl-*gem*-Dipyrazoles (ADPs) and *ortho*-Amido Aryl Ketones

A Thesis
Submitted for the degree of
DOCTOR OF PHILOSOPHY

By

M. Bhanuchandra

School of Chemistry
University of Hyderabad
Hyderabad 500 046
Andhra Pradesh
India

August, 2013

To Well-Wishers

TABLE OF CONTENTS

STATEMENT

I hereby declare that the matter embodied in the thesis is the result of investigation carried out by me in the School of Chemistry, University of Hyderabad, Hyderabad, India, under the supervision of **Dr. Akhila Kumar Sahoo**.

In keeping with the general practice of reporting scientific observations, due acknowledgements have been made wherever the work described is based on the findings of other investigators. Any omission, which might have occurred by oversight or error, is regretted.

M. Bhanuchandra

University of Hyderabad

August, 2013

Dr. A. K. Sahoo
Associate Professor
Work: +91-40-23134822
Fax: +91-40-23012460
e-mail: akssc@uohyd.ernet.in/
akhilkumar_s@yahoo.com

School of Chemistry
University of Hyderabad
Prof. C. R. Rao Road, Gachi Bowli
Hyderabad – 500 046
INDIA

CERTIFICATE

Certified that the work contained in the thesis entitled "*Convenient Strategies to C–N Bond Formation: Synthesis of β-Heteroarylated Ketones, Scorpionate Ligands E-Allyl-gem-Dipyrazoles (ADPs) and ortho-Amido Aryl Ketones*" has been carried out by *Mr. M. Bhanuchandra* under my supervision and the same has not been submitted elsewhere for a degree.

Dr. Akhila Kumar Sahoo

(Supervisor)

Dean

School of Chemistry

Acknowledgements

I Thank Lord Jesus Christ for his Agape Love on Me.

I express my deep sense of gratitude and profound thanks to my supervisor **Dr. Akhila Kumar Sahoo** for his excellent guidance, encouragement, and for the freedom he gave to me in carrying out various research projects. His optimistic approach and patience towards every aspect was admirable and inspiring. Throughout my Ph.D tenure, he is always approachable, helpful, friendly and in every situation he is extremely tolerant. I am fortunate enough to join in his research group. He considered me as a one the family member.

I take this opportunity to thank Prof. M. V. Rajasekharan, Dean, School of Chemistry for providing us the facilities needed for our research. I extend my sincere thank to former Deans Prof. D. Basavaiah and Prof. M. Periasamy, and all the faculty members, School of Chemistry for their co-operation on various aspects.

I sincerely thank all the non-teaching staff of the School of Chemistry for their assistance on various occasions. I would like to acknowledge DST and UGC for providing the basic requirements and CSIR and DST for the financial support.

My sincere thank to Prof. Kalidas Sen for his generous in providing DST- JC Bose fellowship to me.

I am indebted to Prof. A. Samanta for his suggestions and allowing me to perform studies using the fluorescence spectroscopy facilities for my research work.

I feel fortunate to have friends Balaji (Gvk Bio), Seshadri, Dr. Balaji (SVU), who has inspired me to join in research program.

From the bottom of my heart I thank to my co-worker Mallesh and my labmates Ramu, Nayan, Nagarjuna, Sudheer, Sanatan, Raja for their helpful discussion, pleasant company, and cooperation during my Ph.D. tenure. Without their help and encouragement it is not possible to complete the work. I wish to thank the recently joined co-workers in our lab Koushik, Sankar, Prabhagar for their support, help and creating cheerful work atmosphere. I thank to M.Sc and UGC networking project students Naveen, Deepak (ugc), Mahesh, Ms. Priyanka (ugc) for their help during my thesis work.

I am fortunate to have a family friends Smt. Rashmita Sahoo and cute Amlesh (sonu) for their love and affection on my family. My special thanks to Madam for her patience in preparing a many variety of dishes, when our lab members are gathered in home.

It is my pleasure to thank Prof. D. Gunasekar, Prof. C. Suresh Reddy, Prof. Y. Prabhakar Reddy, Dr. Balaji, Dr. Rasheed, Dr. Lavanya, and Dr. Prathima for their valuable suggestions during my stay at S.V. University, Tirupati.

I take this opportunity to thank my school and college teachers, Chenchaiah (Science teacher), Manohar (Maths), Rammurthi (Telugu), college lecturers Rajendra Prasad, Karunakar (Chemistry), Dhayalan (Maths), and B.Sc lecturers Chenchu Krishnaiah, Dr. Kandha Swamy (Chemistry), and Subba Reddy, Dr. Nagarajulu Naidu (Physics), and Prof. Jaya Prakash (Jagruti-coaching center).

I am lucky enough to have the support of School of Chemistry friends and colleagues Seshadri, Venu, Sudha Rani, Ramakrishna, Madhu, Dhinesh, Dr. Suresh (PRS), Chandrasekhar, Supartim, Pramiti, Ajay, Narayana, Krishna, Dr. Bharath, Dr. Kishore, Sridevi, Dr. Vijji, Ramesh, Rama Raju, Anand, Prabhu, Kishore, Dr. Hanumantha Rao, Dr. Sekhar, Vignesh, Ganesh, Praveen, Naidu, Srinivas, Vikas, Malkappa, Krishna Charry, Dr. Karuna, Ritwik, Anup, Nandha, Obaiah, Sathish (PKP), Vikranth, Sreenu, Ganesh, Raveendra, Vanaja, Naveen, Manoj, Saktivelu, Venkaiah, Madhavachary, Mallikarjuna, Santhosh (DB), Dr. Ram Suresh, Ramesh, Seshi, Tirupati, Pavan, Hari, Gupta, Kesav, Srujana, Santhosh (AS), Madhileti, Sudalai, Geetha, Rajagopal, Naga Prasad, Venkatash (acrhem), Anil and sreenivasulu (sest, uoh).

I am indeed fortunate to have friends like Vijay-Macha, Seshadri, Venu, Vigenesh who have been good friends over the years, and make my moments with them as a bunch of joyful memories throughout my life. I would like to acknowledge Vignesh's father and Mother (Smt. Gayathri) for their love and affection. I specially thank to my M.Sc. classmates Balaji (Gvk), Venkatesh (Gvk), Kondaiah, Subba Reddy (IICT), Dr. Jagadeesh (IITM), Jagan (Gvk), Janardhan (IICT), Anil (IICT), Sankar Rao, Umapathi, Sivasankar, Srinath, Surya for their help and happy movements during my post graduation.

. I would like to thank my school and college friends D. Haribabu, Sivaiah, Karuna, Dhamu, Dhoravelu, Prabhakar, Kataiah, Eswaraiah, Chandra, Raghavaiah, Rajasekhar.

My heartfelt thanks to my Church members, Dr. Ravi (acrhem), Bro. Syam, Mastan, Syambabu, Chandra, Samuel for their prayers and kind loving nature during my stay in the campus.

It is great pleasure to thank my family members Amma, Nanna, Sister, Brother, my cute sons (Jaswin and Aswin), uncles, brother-in-laws and sister-in-laws for their support, love and affection. I take this opportunity to thank my wife Janaki Devi for her extreme co-operation in our journey.

M. Bhanuchandra

University of Hyderabad
August, 2013

SYNOPSIS

The thesis work entitled with **"Convenient strategies to C–N bond formation: Synthesis of β-Heteroarylated Ketones, Scorpionate Ligands *E*-Allyl-*gem*-Dipyrazoles (ADPs) and *ortho*-Amido Aryl Ketones"** consists of three chapters: (**1**) A Convenient Approach to β-Heteroarylated (C–N bond) Ketones from Cs_2CO_3 Promoted Reaction between Propargyl Alcohols and Nitrogen-Heterocycles, (**2**) Silver(I)-Catalyzed Reaction between Pyrazole and Propargyl Acetates: Stereoselective Synthesis of Scorpionate Ligands *E*-Allyl-*gem*-Dipyrazoles (ADPs), (**3**) Ru(II)-Catalyzed Intermolecular *Ortho*-C–H Amidation of Aromatic Ketones with Sulfonyl Azides.

In this thesis, each chapter is subdivided into three parts: (a) Introduction (literature survey), (b) Results and Discussion (including future work) and (c) Experimental Section. The compounds obtained in the present study are generally characterized by ^{1}H NMR, ^{13}C NMR, IR, MS, and HRMS spectral techniques followed by elemental analyses. Some of the representative compounds are unambiguously characterized by X-ray crystallography.

Chapter 1

A Convenient Approach to β-Heteroarylated (C–N bond) Ketones from Cs_2CO_3 Promoted Reaction between Propargyl Alcohols and Nitrogen-Heterocycles

In this chapter, an efficient and direct approach to β-heteroarylated (C–N bond) ketones is demonstrated. Base promoted redox isomerization of propargyl alcohol to α,β-unsaturated ketones followed by conjugate addition to NH-heteroarenes affords a wide range of β-heteroarylated ketones in good to excellent yields.

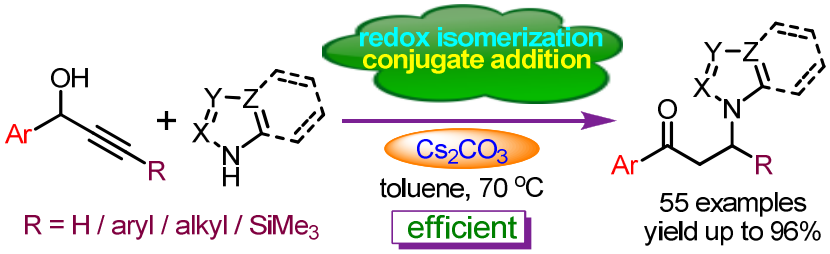
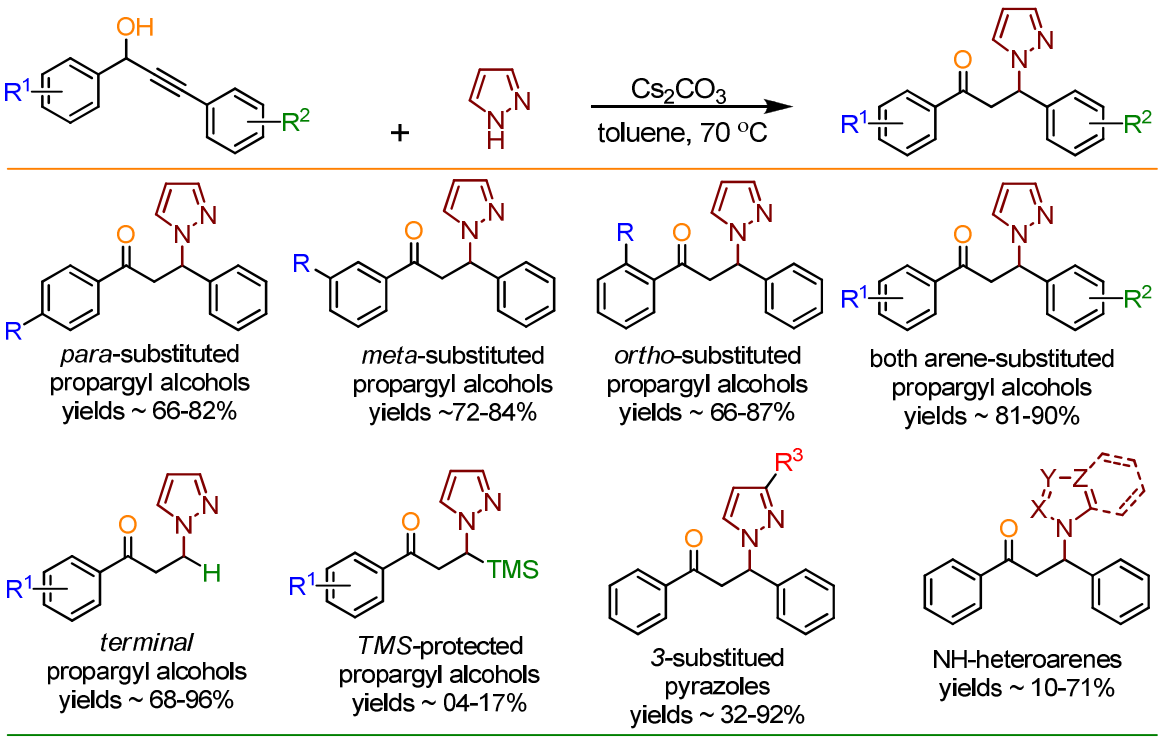


Figure 1. Schematic Representation of Synthesis of β-Heteroarylated Ketones from Propargyl Alcohols and Nitrogen-Heterocycles

This chapter starts with the pharmaceutical importance of azole-bearing compounds and a brief overview of conventional synthetic methods for the preparation of β-heteroarylated (C–N bond) ketones. Highly stable, easily accessible propargyl alcohols and commercially available NH-heteroarenes are employed in this strategy. Electron rich, electron poor and sterically congested propargyl alcohols are effectively participated under the reaction condition.



Scheme 1: Substrate Scope for the Synthesis of β-Heteroarylated (C–N bond) Ketones.

The furyl- and thienyl-2-substituted propargyl alcohols afforded the corresponding β-pyrazolyl ketones in good yields. The reaction of 3-substituted-pyrazole with the propargyl alcohol provided exclusively single regioisomer. A wide range of NH-bearing compounds such as: 1,2,4-triazole, 1,2,3-triazole, imidazole, pyrrole, indoles and aniline are successfully delivered the desired β-heteroarylated ketones.

Chapter 2

Silver(I)-Catalyzed Reaction between Pyrazole and Propargyl Acetates: Stereoselective Synthesis of Scorpionate Ligands *E*-Allyl-*gem*-Dipyrazoles (ADPs)

Chapter 2 describes the silver(I)-catalyzed reaction between commercially available pyrazole and easily accessible propargyl acetates for the synthesis of scorpionate ligands *E*-allyl-*gem*-dipyrazoles (ADPs). The reaction also affords 1,2-disubstituted allyl acetates and 1,3-dipyrazolyl-3-aryl propenes.

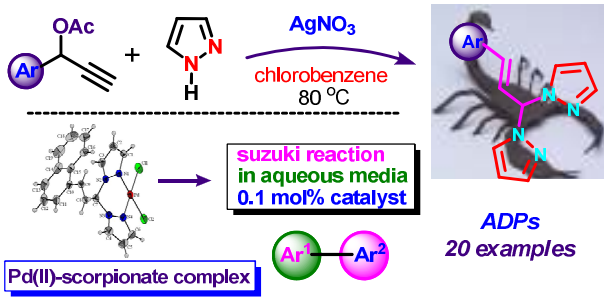
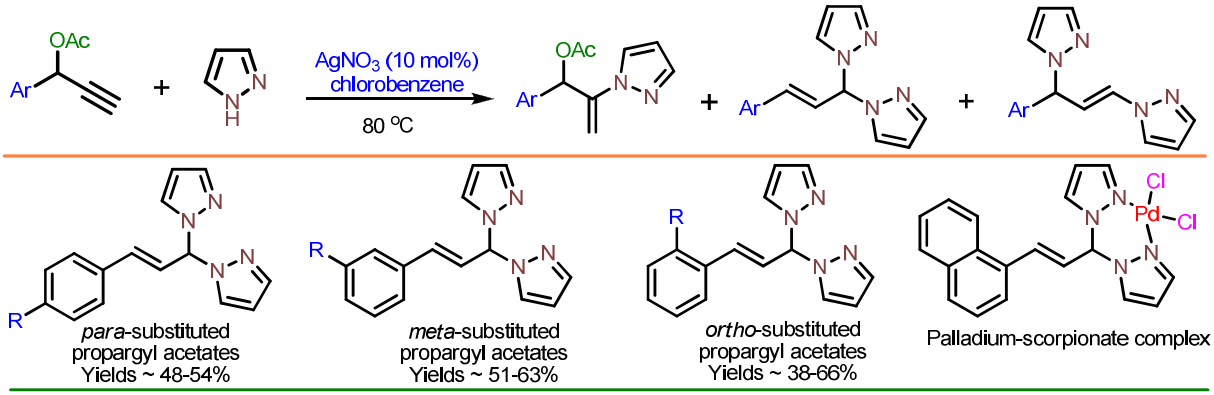


Figure 2. Schematic Representation of the Ag(I)-Catalyzed Synthesis of ADPs from Propargyl Acetates and Pyrazole.

Interestingly, the *gem*-dipyrazolyl derivatives are biologically important compounds. This chapter begins with the previous reports on nucleophilic substitution of propargyl alcohols; continued with propargyl substitution and cyclization cascade reactions for the synthesis of functionalized heteroarenes. The results and discussion part begins with the optimization of the reaction conditions for the synthesis of ADPs from propargyl acetate and pyrazole.



Scheme 2: Substrate Scope for the Synthesis of ADPs.

In the presence of $AgNO_3$ catalyst, the desired ADPs is obtained in good yields. The reaction showed broad substrate scope, and various functional and protecting groups were tolerated under the reaction conditions. The scorpionate ligands *E*-allyl-*gem*-dipyrazoles easily coordinated with $PdCl_2$ in acetonitrile at room temperature. The $PdCl_2$-chelated complex of ADPs was successfully employed in Suzuki reactions for biaryl synthesis in water.

Chapter 3

Ru(II)-Catalyzed Intermolecular *Ortho*-C–H Amidation of Aromatic Ketones with Sulfonyl Azides

Chapter **3** describes the direct intermolecular *o*-C(aryl)–H amidation of weakly coordinating aromatic ketones with sulfonyl azides. In this study, the inexpensive, easy-to-prepare and air-stable Ru(II)-catalysts is employed for direct intermolecular *o*-C–H amidation.

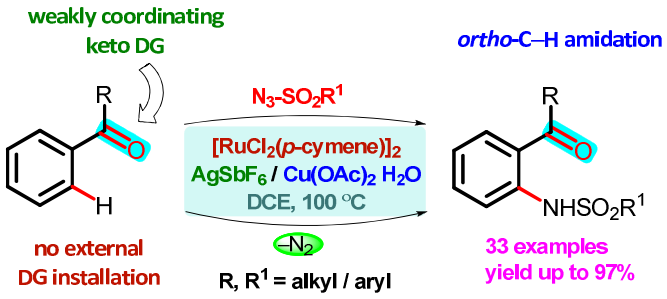
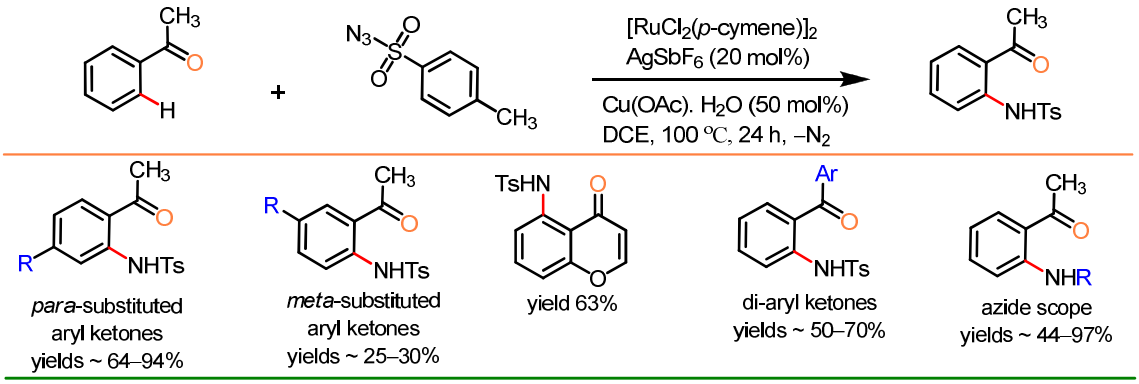


Figure 3. Schematic Representation of Ru(II)-Catalyzed *o*-C–H Amidation of Aromatic Ketones with Sulfonyl Azides

This chapter starts with the synthetic potential of *ortho*-amido aryl ketones in the synthesis of pharmaceutically important nitrogen-bearing drugs. Next the representative examples of DG assisted *o*-C–H amidation are depicted. We have employed the previously developed catalytic conditions of *o*-C–H amidations on aryl-sulfoximines in this study. The *o*-amido aryl ketones are obtained by changing the base from KOAc to $Cu(OAc)_2 \cdot H_2O$ under the influence of Ru-catalyst. The reaction proceeds with the broad scope of arylketones and sulfonyl azides in good yields. Various functional and protecting groups are survived under the reaction conditions. Quantitative formation of *o*-amino aryl ketones are achieved by the simple hydrolysis of the *ortho*-amidated aromatic ketone with H_2SO_4.

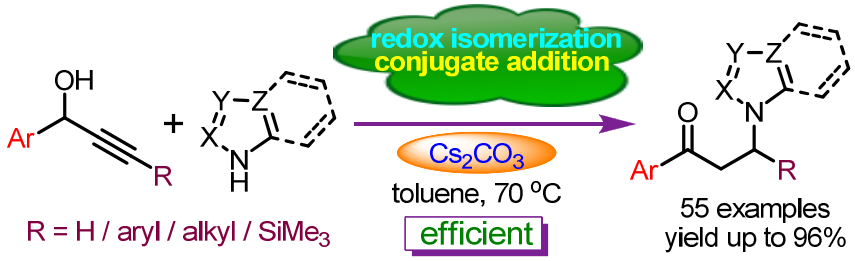


Scheme 3: Substrate Scope for the Synthesis of *ortho*-Amido Aryl Ketones.

A Convenient Approach to β-Heteroarylated (C–N bond) Ketones from Cs_2CO_3 Promoted Reaction between Propargyl Alcohols and Nitrogen-Heterocycles

1 Chapter

Abstract



An efficient and direct approach to β-heteroarylated (C–N bond) ketones is demonstrated. Base promoted redox isomerization of propargyl alcohol to α,β-unsaturated ketones followed by conjugate addition to NH-heteroarenes affords a wide range of β-heteroarylated ketones in good to excellent yields. Aryl, heteroaryl, alkyl C(sp), and terminal alkynes containing unactivated propargyl alcohols effectively undergo redox-isomerization conjugate addition (RICA) with NH-heteroarenes. Reaction of 3-substituted pyrazoles or indazole with propargyl alcohols enables highly regioselective products. A diverse range of NH-bearing nucleophiles such as: pyrazoles, imidazole, triazoles, pyrrole, indoles and aniline participate in this reaction and deliver the corresponding β-heteroarylated ketones.

Reference:

M. Bhanuchandra, M. R. Kuram and A. K. Sahoo, *Org. Biomol. Chem.*, 2012, **10**, 3538

1.1. Introduction

The nitrogen-containing heteroarenes are often found in various natural products, materials and biologically active compounds of pharmaceutical interest.[1] The azole-bearing compounds econazole, miconazole, voriconazole, fluconazole, fluoxetine, ravuconazole, ketoconazole, posaconazole are the potential antifungal agents and are already in the market (Figure 1.1).[3]

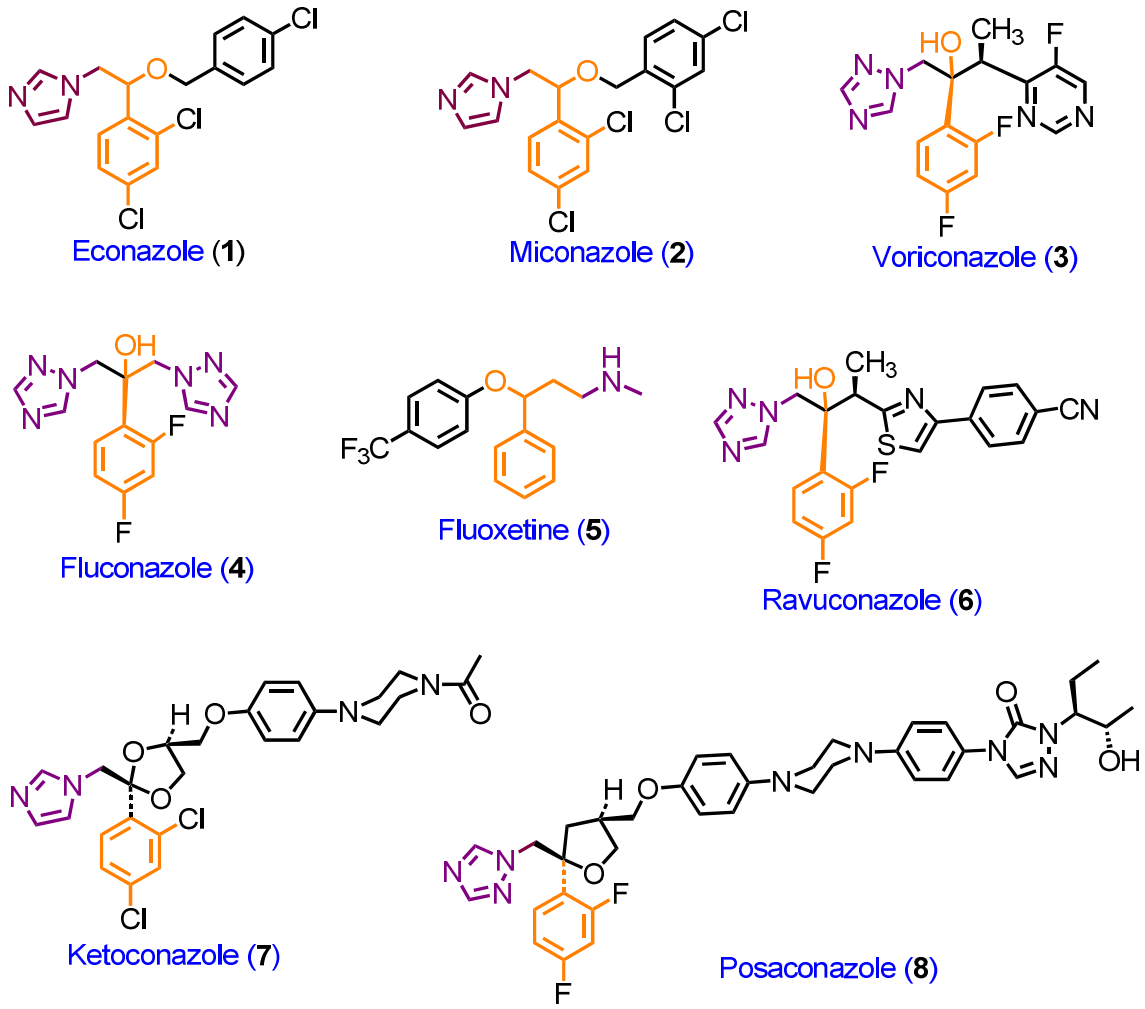
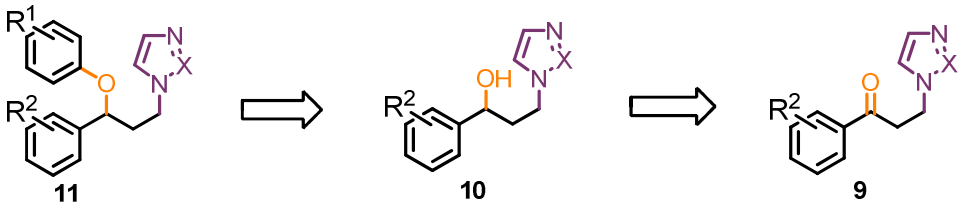


Figure 1.1: Azole Antifungal Agents

The imidazole bearing econozole (**1**) and miconazole (**2**) showed antifungal properties useful in treating tinea pedis, tinea cruris, athlete's foot and tinea corporis. The voriconazole (**3**) and fluconazole (**4**) are the triazole containing heterocycles applied for the treatment of serious invasive fungal infection. In 1970 Bryan Molloy and Robert Rathbun from Eli Lilly discovered the fluoxetine (**5**). It is an antidepressant of the

selective serotonin reuptake inhibitor (SSRI).[1d] Ravuconazole (**6**) is a potential triazole antifungal drug developed by Bristol-Myers Squibb; this molecule is in phase I and II clinical trials. The ketoconazole (**7**) especially used for the treatment of fungal infections of skin or nails. It blocks the growth of the infected fungi. Posaconazole (**8**) is another class of antifungal agent, employed successfully for the treatment of prophylaxis and invasive fungal infections. It disrupts the close packing of acyl chains of phospholipids, and impairing the functions of certain membrane-bound enzyme systems such as ATPase and enzymes of the electron transport system. From these discussions, it appears that the β-heteroaryl-α-aryl-ethanol skeleton bearing molecules possibly useful as antifungal agents. Recently, the structure–activity relationship (SARs) studies reveal that the 1-[3-aryloxy-3-aryl)propyl]-1*H*-imidazoles (**11**) are lead structural units, showing potent activity against *Candida albicans* and *dermatophytes*.[3] Compounds of type **11** can be easily prepared from β-heteroarylated ketones **9** via the reduction of the carbonyl group followed by O-arylation (Scheme 1.1).[5a]



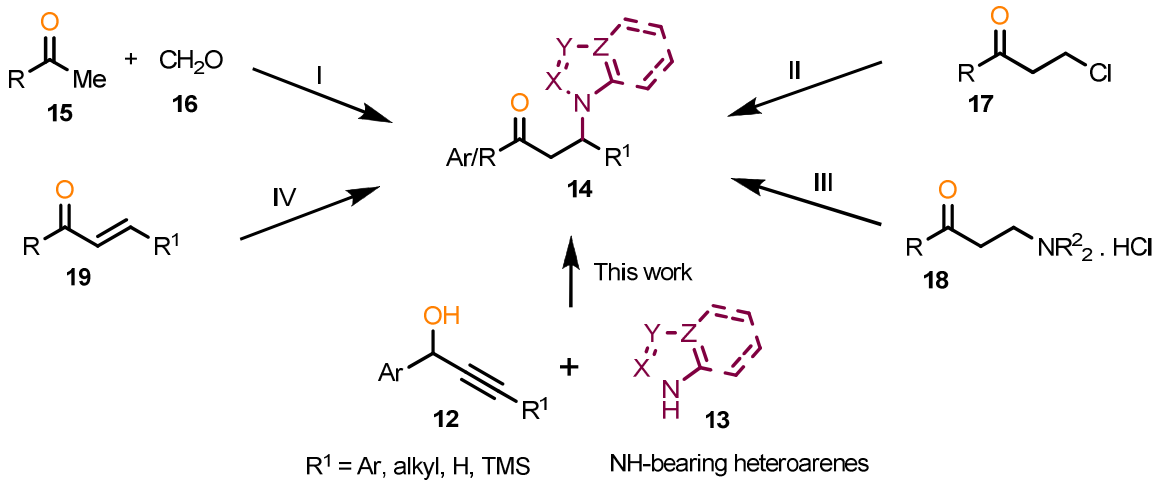
Scheme 1.1: Synthetic Strategy to Azole Derivatives **11**.

Therefore, development of simple and efficient processes to β-heteroarylated ketones (C–N bond) has always been attracted considerable attention.[2]

1.1.1. Conventional Strategies for β-Heteroarylated (C–N bond) Ketone Synthesis

The β-heteroarylated ketones could be prepared using conventional methods. However, synthesis of these desired molecules by efficient atom-economical approaches is always desirable.

A brief overview of synthetic methods for the preparation of β-heteroarylated (C–N bond) ketones (**14**) is shown in Scheme 1.2.



Scheme 1.2: Overview of β-Heteroarylated Ketone Synthesis.

The classical Mannich reaction is used for the preparation of β-amino carbonyls. The condensation of an enolizable carbonyl compound (**15**) with a non enolizable aldehyde (**16**) and ammonia / primary / secondary amine (**13**) furnishes β-aminocarbonyl compounds. However, this transformation has limited substrate scope; the formation of undesired side products are observed in many cases (Path I).[4]

The nucleophilic substitution of nitrogen heterocycles **13** to the β-chloro ketones (**17**) deliverd the desired product **14** (Path II).[5] The nucleophilic replacement of nitrogen heterocycles to the hydrochloride salts of the β-aminocarbonyl compounds (**18**) produces the β-heteroarylated ketones **14** (Path III). These processes produce hazardous wastes such as acids and quaternary amines.[6]

The most preferred and atom-efficient strategy is the aza-Michael conjugate addition of NH-bearing nucleophiles **13** to the activated α,β-unsaturated ketones **19** (Path IV), however, multiple steps are invariably required for the preparation of starting materials **19**.[7] The necessity of the strong bases and acids in aza-Michael additions allow in the formation of other side reactions.[7d,e,g] The Lewis acid catalysts such as $Sc(OTf)_3$,[7a] KF-Al_2O_3, $Bi(NO_3)_3 \cdot 5H_2O$,[7b] $HfCl_4$, $ScCl_3$,[7f] (S,S)-(salen)Al,[7h] $Bi(NO)_3$[7i] have successfully been used for this process.[8]

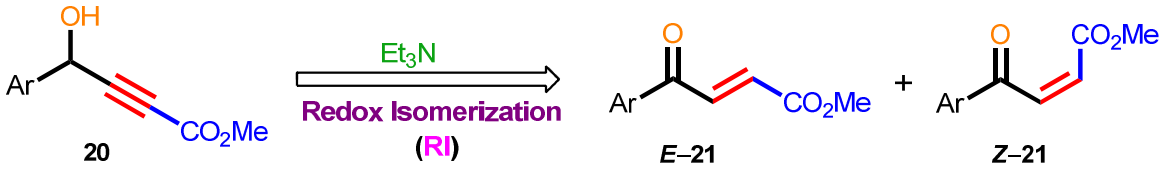
The detailed survey of the literature reveal that most of the strategies lack generality and have a narrow reaction-scope.[4,6] Therefore, discovering a practicable, and efficient method

for the construction of β-heteroarylated (C–N bond) ketones (**14**) from readily available starting materials is always desirable.[9]

1.1.2. Background for Redox-Isomerization Conjugate Addition (RICA) Reactions

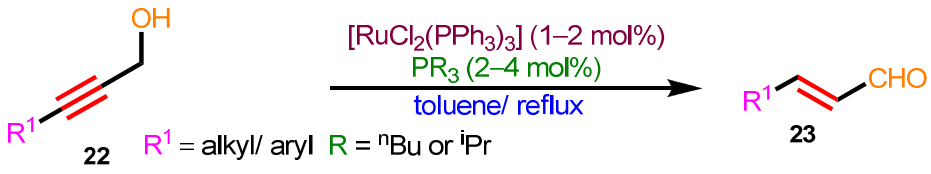
Redox isomerization is a process that creates two new functional groups in the product; the conversion of propargylic alcohols to conjugated enones is a suitable example justifying the redox isomerization process. The propargylic alcohols undergo internal redox type process by oxidizing the alcohol unit to carbonyl group and reducing the triple bond to olefin simultaneously.

In 1949, the first example of redox-isomerization of propargyl alcohol to enones was reported by Nineham and Raphael. The α,β-unsaturated ketone *E*-**21** was obtained, when *activated propargyl alcohol* **20** distilled in the presenc of excess of NEt_3 (Scheme 1.3). Presumably isomerization of *Z*-**21** to *E*-**21** occurs in the presence of NEt_3 at an elevated temperature, enabling the *E*-selective product.[21h]



Scheme 1.3: Nineham-Raphael Reaction

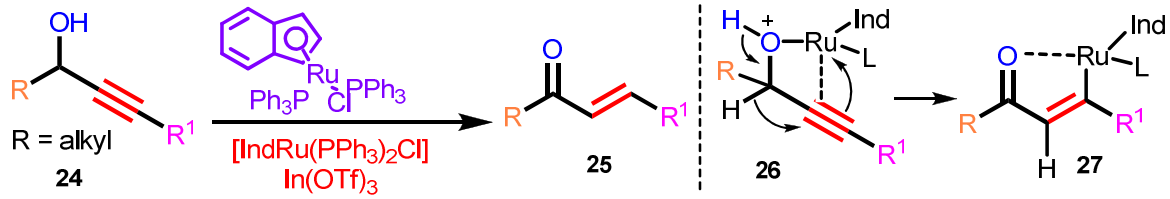
Lu and co-workers reported the first Ru-catalyzed stereoselective isomerization of unactivated primary alkynols **22** to the corresponding *E*-enals (**23**) in good yields (Scheme 1.4).[10h]



Scheme 1.4: Redox-Isomerization of Primary Alkynols

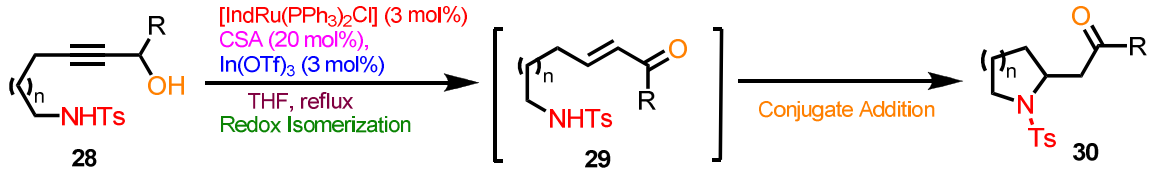
An elegant method for the Ru-catalyzed redox-isomerization of alkyl substituted propargyl alcohols (**24**) to α,β-unsaturated carbonyl compounds (**25**) has been demonstrated by Trost and Livingston (Scheme 1.5).[10f] The reaction begins with the coordination of the active ruthenium catalyst to the triple bond and alcoholic oxygen forming complex **26**.

Subsequently, the [1,2]-hydrogen shift provides the vinyl metal species **27**. Finally, protonolysis of **27** delivers the desired enone **25**.

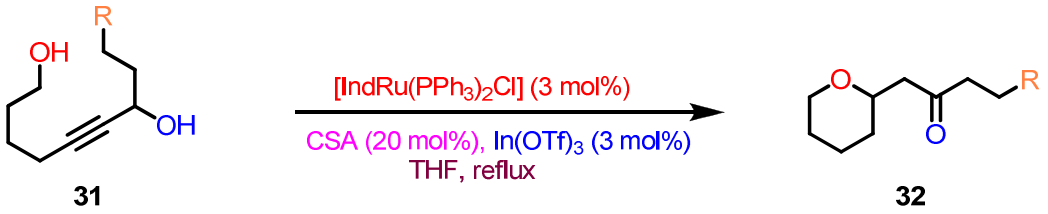


Scheme 1.5: Redox-Isomerization of Propargyl Alcohols

Exploration of this strategy to nitrogen and oxygen bearing heterocycles **30** and **32** involves intramolecular conjugate addition of the heteroatom to the in situ generated α,β-unsaturated carbonyls (**29**) from the propargyl alcohols. The isomerization of the propargyl alcohol (**28** and **31**) moiety to the enone occurs in the presence of co-operative mixture of catalysts Ru and In. Next, Michael attack of the hetero-atom moiety to enone led to produce the N- and O-bearing heterocycles (Schemes 1.6 and 1.7).[10c,d]



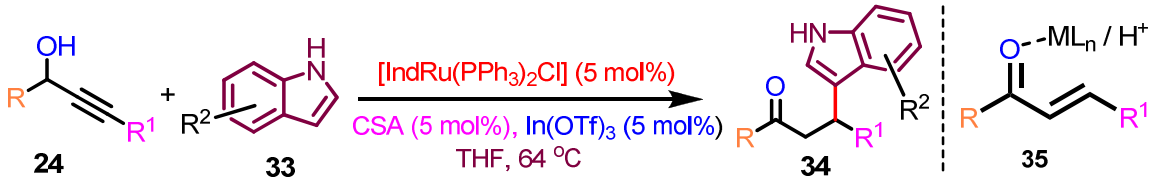
Scheme 1.6: Redox-Isomerization Intramolecular Conjugate Addition of Nitrogen Nucleophiles



Scheme 1.7: Redox-Isomerization Intramolecular Conjugate Addition of Oxygen Nucleophiles

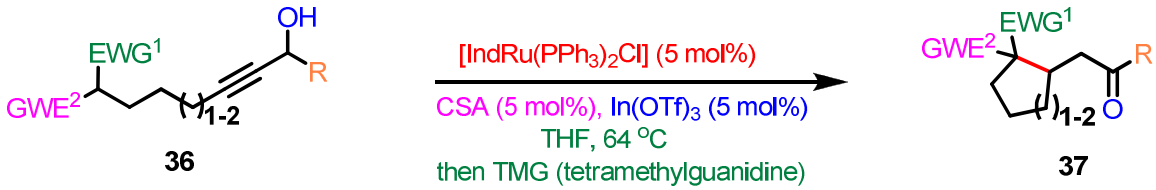
A direct chemoselective synthesis of β-heteroarylated (C–C) ketones (**34**) proceeds through the addition of indoles (**33**) to propargyl alcohols (**24**) *via* a Ru/In catalyzed tandem redox-isomerization conjugate addition (RICA) sequence.[10a,e] In the course of the reaction sequence, propargyl alcohol moiety chemoselectively isomerized to the desired

electrophile α,β-unsaturated carbonyl compound. The transiently formed enone coordinates to the metal to give **35**. Finally, Friedel-Crafts/conjugate addition reaction with electron rich C3-carbon of indole produce the chemoselective β-heteroarylated ketone **34** (Scheme 1.8).



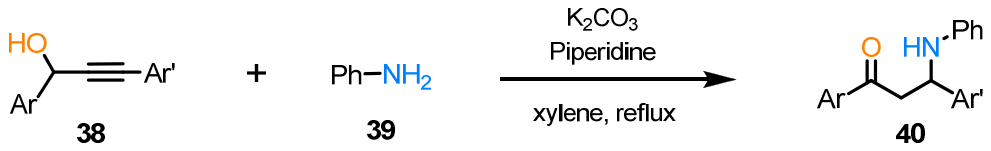
Scheme 1.8: Redox-Isomerization Intermolecular Conjugate Addition of Indole Nucleophiles

Recently, Trost and coworkers demonstrated an atom-economical and one-pot synthesis of functionalized cycloalkanes **37**. The Ru-catalyzed redox isomerization of ynols **36** to enones followed by an intramolecular Michael addition of carbon nucleophiles delivers carbocycles in good yields (Scheme 1.9). [10g]



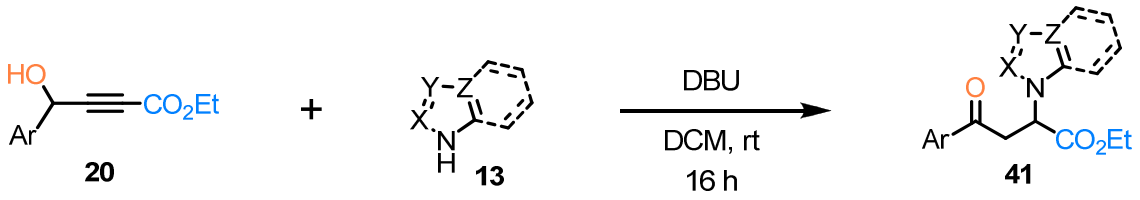
Scheme 1.9: Redox-Isomerization Intramolecular Conjugate Addition of Carbon Nucleophiles

Reisch has shown the effective addition of aniline (**39**) to propargyl alcohols (**38**) in the presence of K_2CO_3 and piperidine, when refluxed in xylene (Scheme 1.10).[12c]



Scheme 1.10: Sythesis of β-Aminoketones from Propargyl Alcohol

The DBU catalyzed redox isomerization of *activated propargyl alcohol* **20** followed by aza-Michael attack of the nitrogen heterocycle (**13**) is a mild method to β-heteroarylated ketone synthesis (**41**) (Scheme 1.11).[12b]

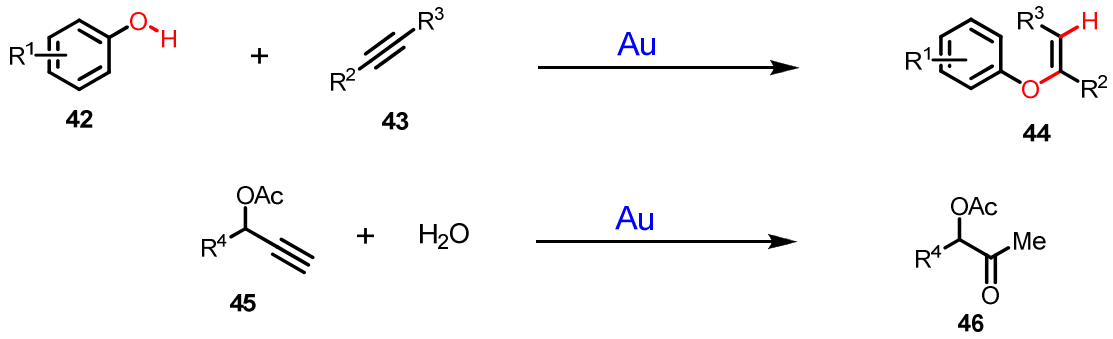


Scheme 1.11: Practical Method to β-Heteroketones from Propargyl Alcohol

These results reveal the effective use of the transiently formed α,β-unsaturated carbonyl compounds from propargyl alcohols through redox-isomerization.[10] Moreover, propargyl alcohols are highly-stable and easily fabricated by the addition of terminal alkynes into the carbonyl compounds in a single step.[21e]

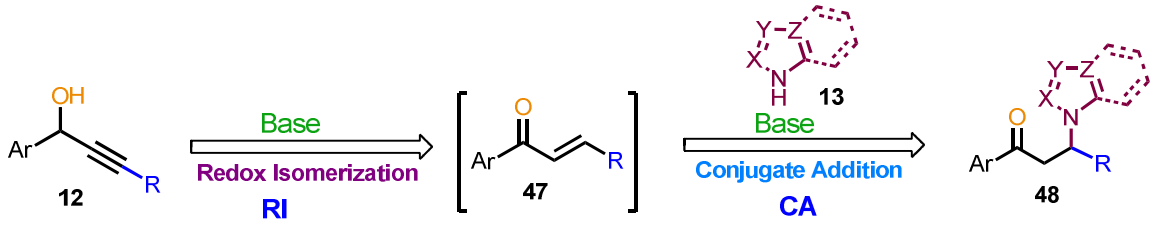
1.1.3. Motivation and Design Plan

Recently, we have demonstrated gold-catalyzed addition of phenols (**42**) to unactivated internal alkynes (**43**) for the atom-efficient syntheses of arylvinyl ethers (**44**) and the hydration of propargyl acetates (**45**) to the preparation of α-acyloxy methyl ketones (**46**) (Scheme 1.12).[11]



Scheme 1.12: Syntheses of Arylvinyl Ethers and α-Acyloxy Methyl Ketones

The current interest in finding new atom-economical transformations inspired us exploring a direct and efficient approach to the synthesis of β-heteroarylated ketones. We envison that the conjugate addition of NH-heteroarenes **13** to transiently formed α,β-unsaturated carbonyls **47** derived from propargyl alcohols **12** through redox-isomerization sequence would create β-heteroarylated ketones **48** directly as shown in Scheme 1.13. Furthermore, the detailed examinations in the intermolecular addition of various NH-heteroarenes to aryl, alkyl, TMS substituted and terminal alkynes containing *unactivated propargyl alcohols* needs to be investigated.[12a]



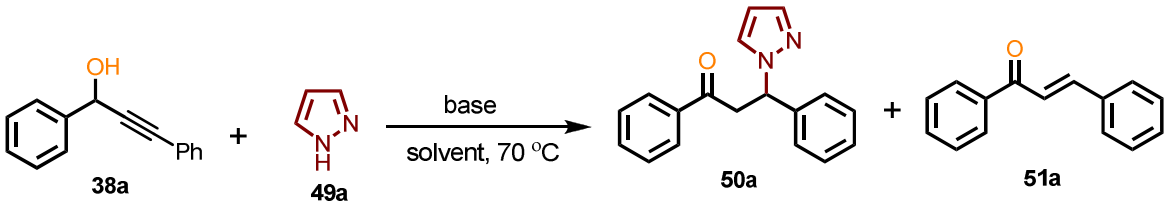
Scheme 1.13: Tentative Approach to β-Heteroketones from Propargyl Alcohol

1.2. Results and Discussion

1.2.1. Reaction Optimization

To probe the viability of the intermolecular addition of NH-heteroarenes to propargyl alcohols, the reaction between 1,3-diphenylprop-2-yn-1-ol (**38a**) and pyrazole (**49a**) in the presence of different bases was investigated at first. Table 1.1 summarizes the results of the optimization studies. The reaction proceeds sluggishly at temperatures below 70 °C. Progress of the reaction was monitored after stirring overnight (12 h) at 70 °C.

Table 1.1: **Optimization of Reaction Conditions.**[a]



entry	**49a** (equiv)	base	solvent	time (h)	yield (%)[b] **50a**	**51a**
1	2.0	K_2CO_3	toluene	12	00	17
2	2.0	*i*-Pr_2NEt	toluene	12	00	08
3	2.0	K_3PO_4	toluene	12	68	09
4	2.0	Cs_2CO_3	toluene	12	95	05
5	2.0	Cs_2CO_3	THF	12	88	12
6	2.0	Cs_2CO_3	dioxane	12	81	19
7	2.0	Cs_2CO_3	CH_3CN	12	81	19
8	2.0	Cs_2CO_3	DMF	12	74	26
9	2.0	DBU	CH_2Cl_2	12	49	16
10	**2.0**	**Cs_2CO_3**	**toluene**	**01**	**95**	**05**
11	1.5	Cs_2CO_3	toluene	01	92	08
12	1.2	Cs_2CO_3	toluene	01	88	12
13	1.0	Cs_2CO_3	toluene	01	85	15

[a]Reactions were carried out using **38a** (0.5 mmol), base (0.5 mmol) in solvent (1.0 mL). [b]NMR yield.

Redox isomerization of **38a** to α,β-unsaturated ketone **51a** was exclusively observed albeit in poor yield, when the reaction was performed in K_2CO_3 in toluene (entry 1). Organic base *i*-Pr_2NEt proved futile, producing only a negligible amount of **51a** (entry 2). Gratifyingly, reaction of **38a** in the presence of K_3PO_4 delivered the desired 1,3-diphenyl-3-(1*H*-pyrazol-1-yl)propan-1-one (**50a**) and **51a** in 68% and 9% yields, respectively (entry 3). To our delight, Cs_2CO_3 base gave the best results and the yield of the desired redox isomerization conjugate addition (RICA) product **50a** was calculated 95% by NMR (entry 4). With a selective base in hand, the effect of solvent on this reaction was then examined. Polar-aprotic solvents did not affect the progress of the reaction; however, undesired **51a** was detected in a substantial amount (entries 5–8). For example: use of the solvents such as: THF, dioxane, CH_3CN and DMF led to the formation of **51a** in 12%, 19%, 19% and 26% yields, respectively (entries 5–8). Among various solvents screened, toluene was found to be the best (entry 4). In Han report, the reaction between activated 4-aryl-4-hydroxy-2,3-alkynyl esters (**20**) and NH-heterocycles in the presence of DBU in CH_2Cl_2 provides 2-heterocycle-(C–N bond)-substituted-4-oxo-4- arylbutanoates (**41**) efficiently;[12b] however, a moderate yield of **50a** was noticed under this reaction condition (entry 9). To our delight, quantitative formation of **50a** and complete consumption of **38a** was observed even within 1h, when the reaction was performed in Cs_2CO_3 in toluene at 70 °C (entry 10). This demonstrates the efficiency of the optimized condition. Next, the amount of pyrazole (**49a**) required for this RICA transformation was pursued. Loading of reduced amounts of pyrazole resulted in producing the more of the redox isomerized product **51a** (entries 11–13). Moreover, the use of 2.0 equiv of pyrazole was found to be optimum (entry 10).

1.2.2. Detailed Optimization of Reaction Conditions

Table 1.2: Screening of Bases[a,b]

entry	**49a** (equiv)	Base (1.0 equiv)	solvent	time (h)	yield (%) **50a**	**51a**
1	2.0	Na_2CO_3	toluene	12	00	17
2	2.0	Li_2CO_3	toluene	12	00	27
3	2.0	$NaHCO_3$	toluene	12	00	36
4	2.0	pyridine	toluene	12	00	22
5	2.0	2,6-lutidine	toluene	12	00	07
6	2.0	CsOPiv	toluene	12	02	28
7	2.0	DBU	toluene	12	85	15

[a]Reactions were carried out using **38a** (50 mg, 0.25 mmol) in solvent (0.5 mL) at 70 °C. [b]NMR yield.

Examination of various bases in the RICA reaction was then investigated. The results are shown in Table 1.2. The use of Na_2CO_3, Li_2CO_3, $NaHCO_3$, pyridine, and 2,6-lutidine bases did not produce the desired **50a**, in stead **51a** was obtained albeit in moderate amount (entries 1–5). The base CsOPiv is ineffective (entry 6). Organic base such as DBU gave the desired β-heteroketone (**50a**) in 85% yield after 12 h at 70 °C (entry 7).

Table 1.3: Screening of Solvents[a,b]

entry	**49a** (equiv)	Base (1.0 equiv)	solvent	time (h)	yield (%) **50a**	yield (%) **51a**
1	2.0	K_2CO_3	THF	12	00	02
2	2.0	DBU	THF	12	76	19
3	2.0	*i*-Pr_2NEt	THF	12	00	00
4	2.0	pyridine	THF	12	00	00
5	2.0	K_2CO_3	dioxane	12	00	02
6	2.0	DBU	dioxane	12	82	16
7	2.0	*i*-Pr_2NEt	dioxane	12	00	00
8	2.0	pyridine	dioxane	12	00	03
9	2.0	K_2CO_3	CH_3CN	12	88	05
10	2.0	DBU	CH_3CN	12	83	17
11	2.0	*i*-Pr_2NEt	CH_3CN	12	00	00
12	2.0	pyridine	CH_3CN	12	00	00
13	2.0	Cs_2CO_3	CH_3CN	01	74	26
14	2.0	Cs_2CO_3	dioxane	01	50	23
15	2.0	Cs_2CO_3	THF	01	92	08
16	2.0	Cs_2CO_3	DCE	01	18	16
17	2.0	Cs_2CO_3	MeOH	01	34	10

[a]Reactions were carried out using **38a** (50 mg, 0.25 mmol) in solvent (0.5 mL) at 70 °C. [b]NMR yield.

Next we investigated various combinations of solvents and bases. The results are shown in Table 1.3. The use of DBU base in THF, dioxane and CH_3CN solvent furnished the **50a** in 76%, 82% and 83% yield, respectively (entries 2, 6 and 10). Unfortunately, *i*-Pr_2NEt and pyridine bases are totally ineffective (entries 3, 4, 7, 8, 11, and 12). The base K_2CO_3 in THF or dioxane did not produce **50a** (entries 1and 5); while K_2CO_3 in CH_3CN gave the **50a** in 88% yield (entry 9). Moderate yield of **50a** was obtained when the reaction was carried out with Cs_2CO_3 in dioxane, DCE and MeOH (entry 14, 16 and 17); whereas good yield of **50a** was noticed in CH_3CN and THF in 1 h (entry 13 and 15).

Table 1.4: Effect of Temperature[a,b]

entry	**49a** (equiv)	Base (1.0 equiv)	solvent	temp (°C)	time (h)	yield (%) **50a**	**51a**
1	2.0	Cs_2CO_3	toluene	rt	12	34	13
2	2.0	Cs_2CO_3	toluene	60	05	94	06
3	2.0	Cs_2CO_3	toluene	70	01	95	05

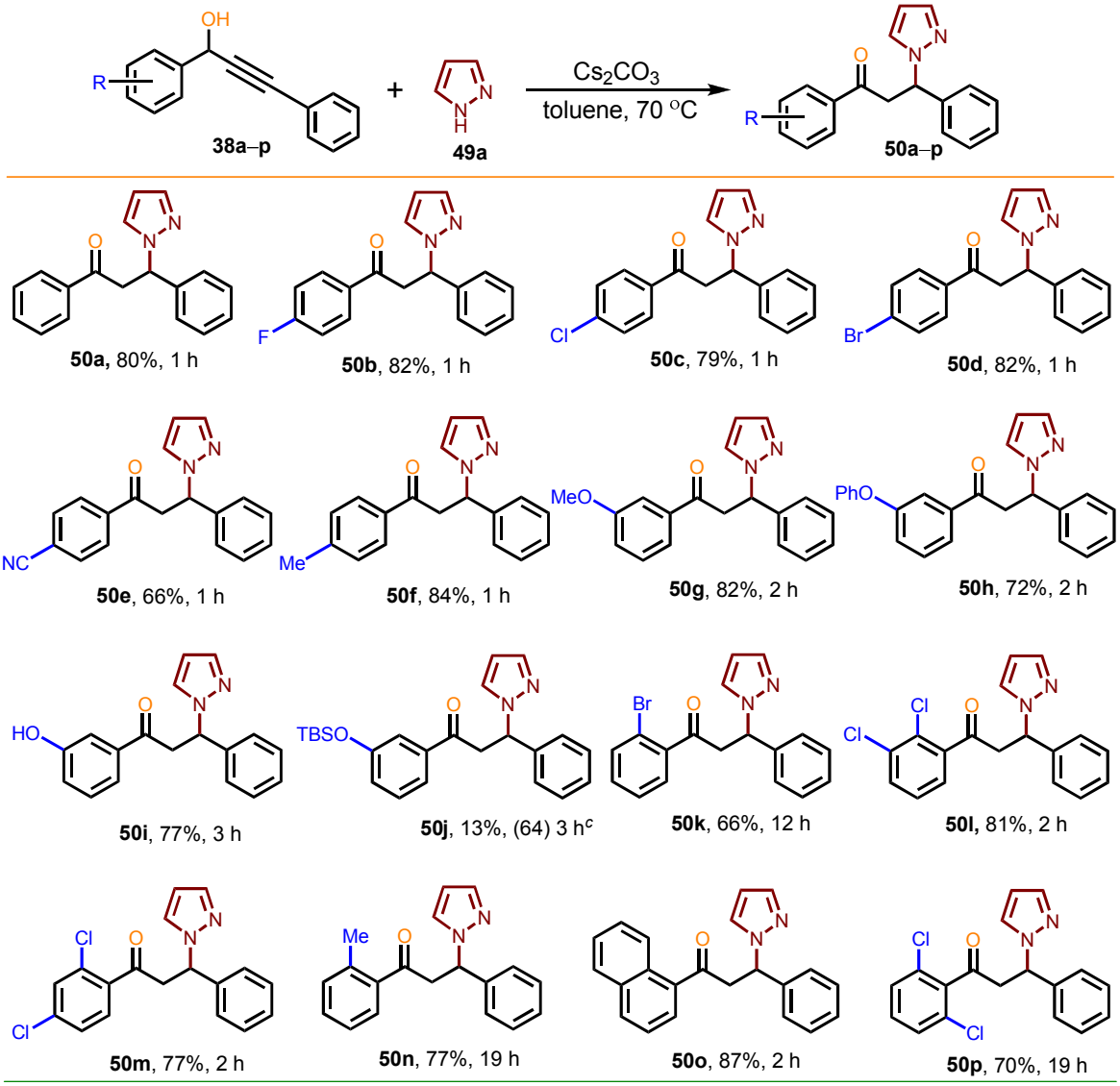
[a]Reactions were carried out using **38a** (50 mg, 0.25 mmol) in solvent (0.5 mL). [b]NMR yield.

Finally, the effect of temperature in RICA reaction was investigated. Incomplete convertion of starting material was noticed even though the reaction was continued for 12 h at room temperature (Table 1.4, entry 1). Increase of temperature from RT to 60 °C resulted forming the desired product **50a** was obtained in 94% yield in 5 h (entry 2). Excellent yield of **50a** in 1 h when the reaction conducted at 70 °C (entry 3).

1.2.3. Scope of the Reaction

To explore the generality of the reaction and the synthesis of new RICA products **50**, reactions between a variety of propargyl alcohols and pyrazole (**49a**) were investigated under the optimized conditions (1 equiv of Cs_2CO_3 in toluene at 70 °C). The effect of substitution on the aryl-moiety at the propargyl position of the propargyl alcohol, 1-aryl-3 -phenylprop-2-yn-1-ol (**38**), on the RICA with **49a** was examined at first (Table 1.5). As observed in the optimization studies, electronically neutral substrate **38a** reacted efficiently with **49a** to give **50a** in 80% isolated yield.[12d] The Cu-assisted or the base-mediated replacement of aromatic halo-groups by pyrazole is a well-established phenomenon.[14] Surprisingly fluoro, chloro and bromo groups survived to this reaction condition and the corresponding products **50b**–**d** were isolated in good yields. Transition-metal catalyzed functionalization of the halo groups would generate new heteroaryl-bearing valuable substrates. Interestingly, cyano group is survived; however, trace of moisture in the system hydrolyses the cyano group partially, producing **50e** in moderate yield.[15] Propargyl alcohols having the electron-donating substitutions methyl, methoxy or phenoxy groups at the 3- and/or 4-position on aromatic ring reacted efficiently with **49a** and the corresponding products **50f**–**h** are produced in excellent yields. Next, we examined the RICA of propargyl alcohol containing free phenol-OH moiety with **49a**.

Table 1.5: Effect of Arenes at the Propargyl Position of Propargyl Alcohols to the RICA with **49a**[a,b]



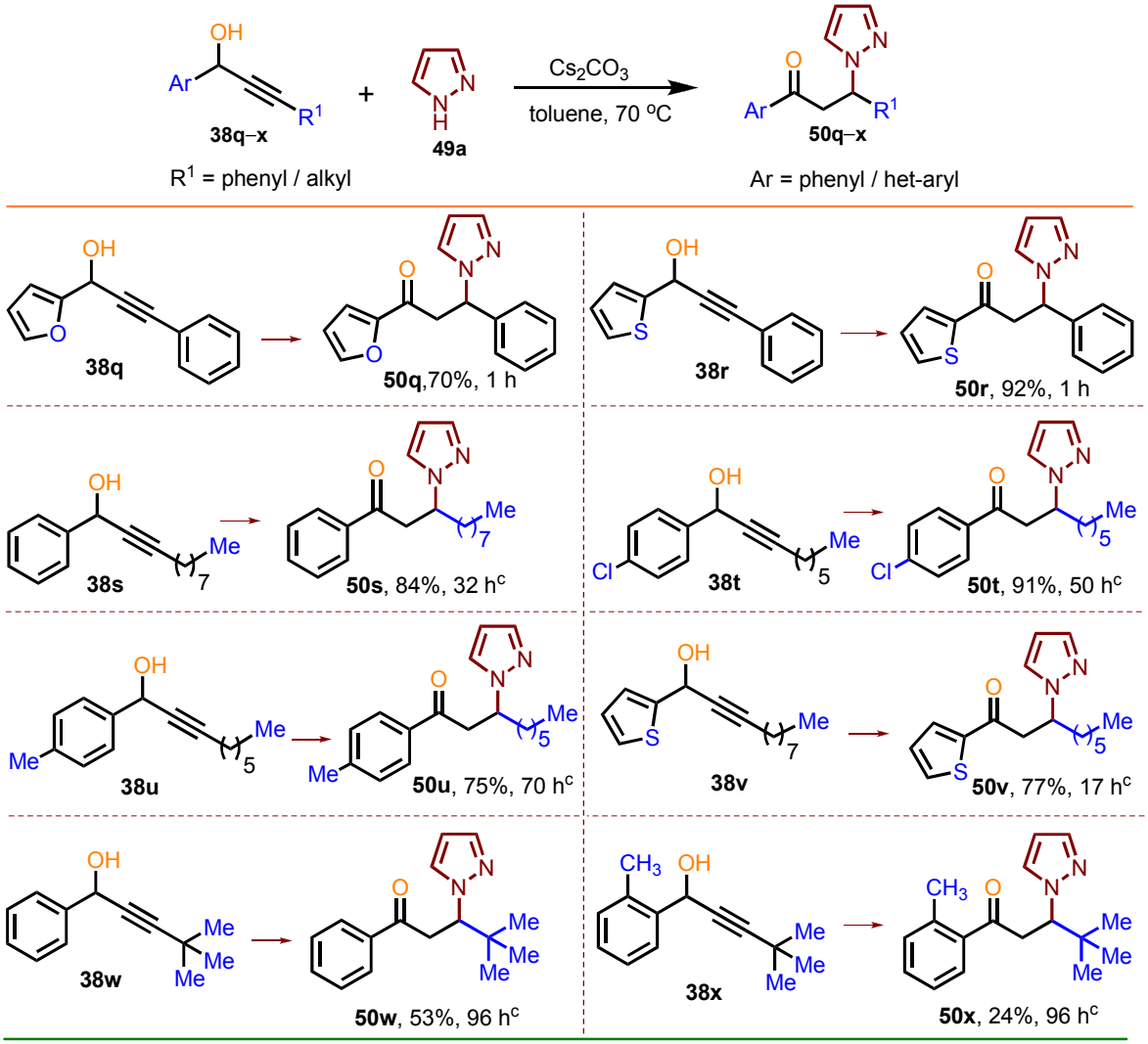
[a]Reactions were carried out using **38** (1.0 mmol), **49a** (2.0 mmol), Cs_2CO_3 (1.0 mmol) in toluene (2.0 mL) at 70 °C. [b]Isolated yield. [c]Cleavage of O–TBDMS protecting group was observed; the corresponding –OH bearing product **50i** was obtained in 64% yield.

A report of the Liu group describes the synthesis of benzofurans from Lewis-acid assisted annulation of phenols with propargyl alcohols.[16] The phenoxide ion generated in situ with the aid of the base is expected to undergo conjugate addition to the α,β-unsaturated ketones.[10c] Gratifyingly, we did not observe the participation of the free phenol-OH group in the reaction and **50i** was exclusively obtained in 77% yield in 3 h. Generally, silyl protected hydroxyl groups are sensitive to acidic and basic reagents.[15] To assess the

relative stability of the silyl-protecting groups; the –OTBDMS containing precursor **38j** was subjected to the reaction condition. As anticipated, the TBDMS group was partial survived and the corresponding silicon protected and deprotected products **50j** and **50i** were isolated in 13%, 64% yields, respectively. The optimized procedure was subsequently applied to a range of propargyl alcohols having *ortho*-substituted arenes, to assess the steric effect in this RICA reaction sequence. The *ortho*-halo groups on the aryl moiety are inert to the reaction condition, displaying good reactivity and appreciable yields (**50k**–**m**). Incomplete conversion of **38n** was observed to the synthesis of **50n** (77% yield) even with prolonged reaction time. 1-Naphthyl substituted propargyl alcohol underwent RICA with **49a** efficiently and **50o** obtained in 87% yield. The more sterically demanding propargyl alcohol **38p** having two *ortho*-substitutions on aryl group did not affect the product-formation, although the reaction requires longer time for completion, producing **50p** in slightly lower yield. These experimental results reveal that the electronic as well as steric effect on the aryl group at the propargyl position in propargyl alcohol did not influence much to the reaction outcome.

Next, the RICA reactions of **49a** with heteroaryl bearing propargyl alcohols were surveyed (Table 1.6). The nucleophilic β-carbon and the acidic α-hydrogen of furan and thiophene would lead to C-alkylation product with propargyl alcohols.[17] Fortunately, the furyl- and thienyl-2-substituted propargyl alcohols (**38q** and **38r**) reacted efficiently with **49a** and afforded the corresponding β-pyrazolyl ketones **50q** and **50r** in 70% and 92% yields, respectively. We then turned our attention to examine the effect of alkyl-substitution at the C(sp)-center of the propargyl alcohols on the RICA with **49a**. The results are shown in Table 1.6. It is obvious that the inductively donating alkyl group enhances the electron density on the alkynes. As a consequence, slow redox-iosmerization of the propargyl alcohol to the α,β-conjugated ketone is expected. To overcome this problem, we therefore performed the reactions at a higher temperature and a relatively longer time. Gratifyingly, product **50s** was isolated in 84% yield, when the reaction between C(sp)-octyl substituted propargyl alcohol **38s** and **49a** was conducted at 80 °C for 32 h. Even though the reaction took 50 h at 80 °C, an excellent yield of the desired **50t** was isolated with the survival of the chloro group.

Table 1.6: RICA of Heteroarenes/Arenes and/or C(sp)-Alkyls Containing Propargyl Alcohols with **49a**[a,b]

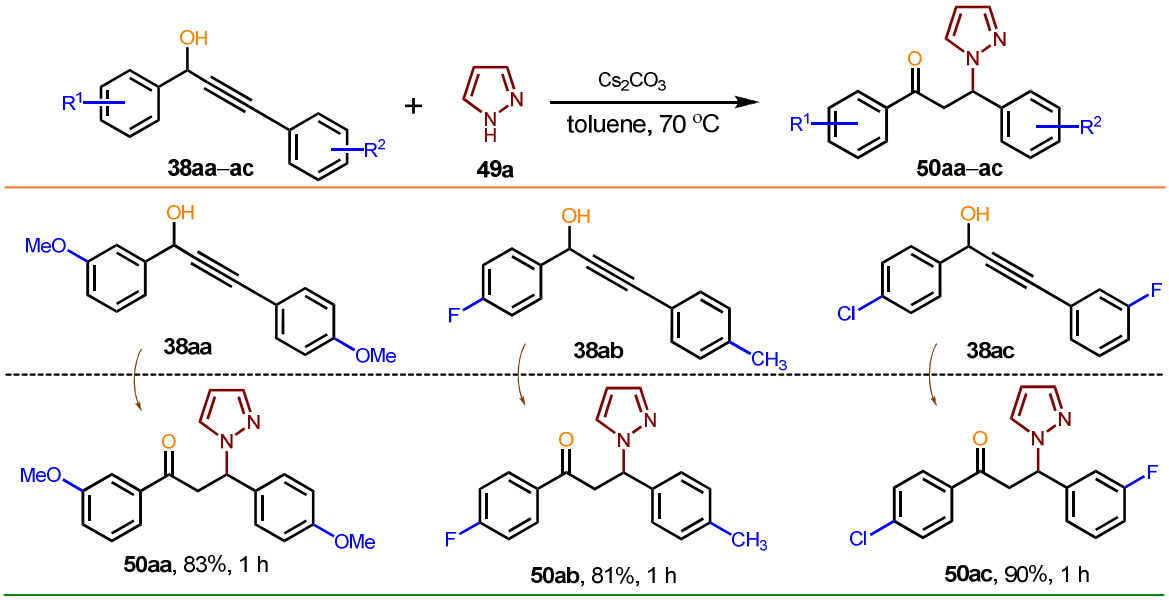


[a]Reactions were carried out using **38** (1.0 mmol), **49a** (2.0 mmol), Cs_2CO_3 (1.0 mmol) in toluene (2.0 mL) at 70 °C. [b]Isolated yield. [c]at 80 °C

The electron-rich propargyl alcohol **38u** smoothly participated in the RICA reaction and furnished the ketone **50u** in good yield. Similarly, the propargyl alcohol having thienyl and C(sp)-alkyl moieties reacted with **49a** and produced **50v** in 77% yield. Importantly, the sterically encumbered C(sp)-*t*-butyl containing propargyl alcohol underwent RICA with **49a**. Incomplete conversion of **38w** was noticed and the corresponding β-pyrazolyl ketone **50w** was isolated in 53% yield, even though the reaction was continued for 4 days. The more sterically congested product **50x** was obtained albeit in poor yield from the RICA between **38x** and **49a** under the optimized condition.

Encouraged by the excellent performance of the RICA between **38** and pyrazole (**49a**), the effect of electronic groups on both the arene-moieties attached at the propargyl and C(sp) positions in propargyl alcohols was next investigated, and the results are shown in Table 1.7.

Table 1.7: Electronic Effect of Aryl-Groups of Propargyl Alcohols to the RICA with **49a**[a,b]

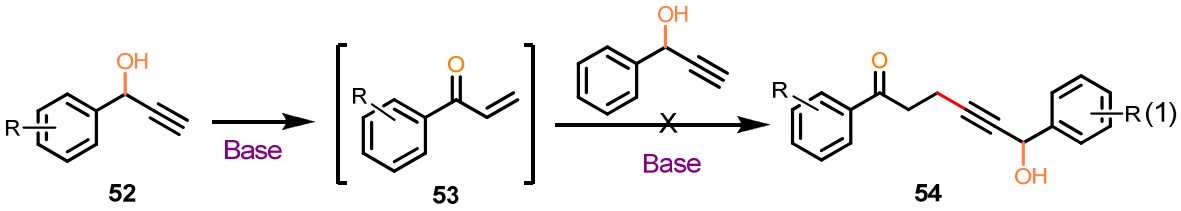


[a]Reactions were carried out using **38** (1.0 mmol), **49a** (2.0 mmol), Cs_2CO_3 (1.0 mmol) in toluene (2.0 mL) at 70 °C. [b]Isolated yield.

The presence of electron donating methoxy substituents on both arenes did not affect the reaction efficiency, and the desired RICA product **50aa** was isolated in 83% yield. Propargyl alcohol bearing an electron-withdrawing (–F) and electron donating (–Me) group at *para*-position on both the aryl moieties reacted with **49a**, affording **50ab** in 81% yield. Efficient reaction and excellent yield of the corresponding β-pyrazolyl ketone **50ac** was obtained from the RICA between the electrondeficient **38ac** and **49a**. These results show that the electronic variation of the propargyl alcohol did not display a pronounced effect on the reaction efficiency.

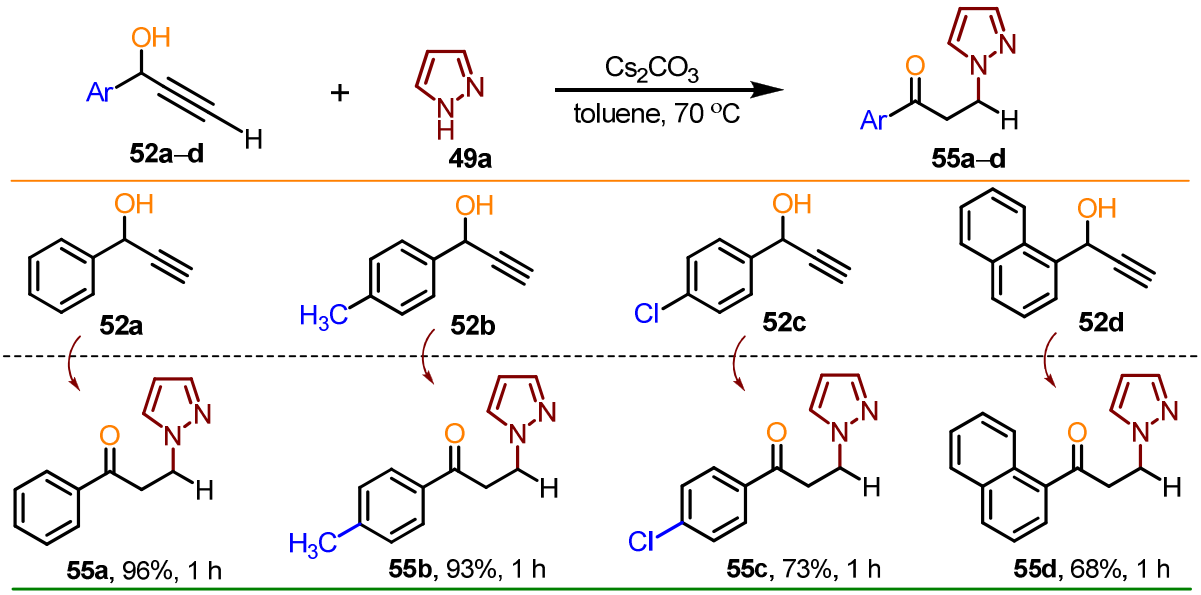
Next, exploration of terminal and alkynyl-C-TMS protected propargyl alcohols in the RICA with **49a** was pursued and the results are detailed in Table 1.8. Generally, base promotes the generation of the acetylides from terminal alkynes.[18] We speculate that the formation of the corresponding ketones **54** will occur through the conjugate addition of the C-nucleophile (acetylide) to α,β-unsaturated ketones (**53**), obtained from the base induced

redox isomerization of propargyl alcohol **52** (Eq. 1).[19] This would inhibit the formation of the desired β-heteroarylated ketones.



To probe this assumption, the terminal propargyl alcohol **52a** and **49a** were exposed to the optimized conditions. To our surprise, the β-pyrazolyl ketone **55a** was exclusively obtained in 96% yield. Similarly, an excellent yield of product **55b** was isolated from the reaction of electron-rich propargyl alcohol **52b** with **49a**. An electron withdrawing group at the *p*-position in the alcohol **52c** underwent RICA with **49a** efficiently. Reaction of **49a** with naphthalene-containing propargyl alcohol **52d** was performed and **55d** was isolated in reasonable yield.

Table 1.8: RICA of Terminal Substituted Propargyl Alcohols with **49a**[a,b]

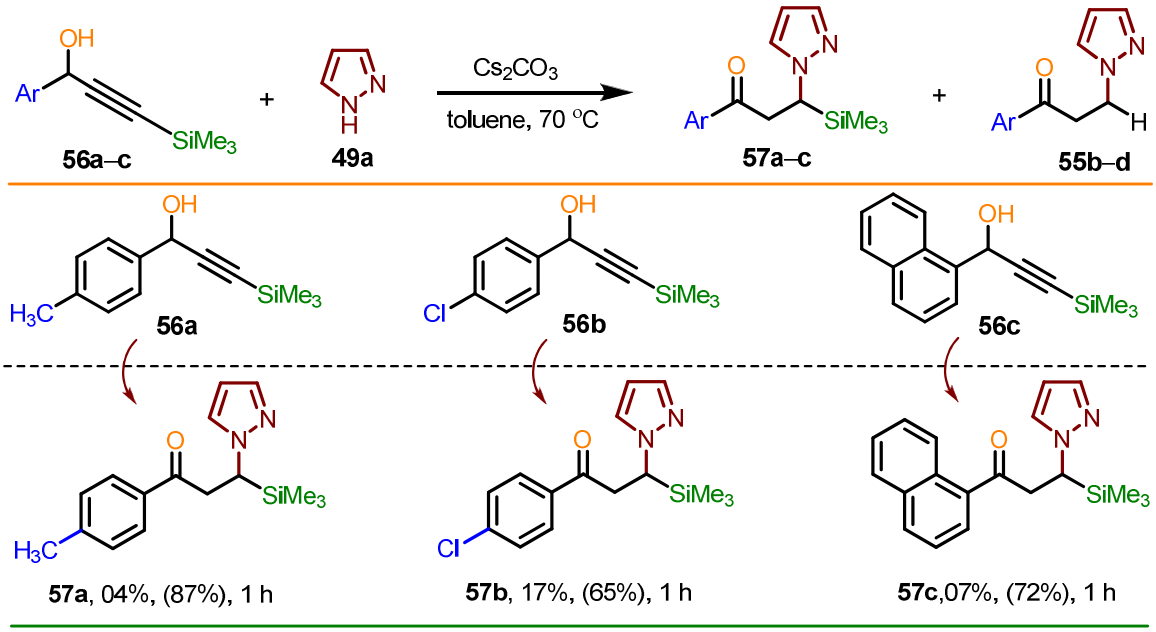


[a]Reactions were carried out using **52** (1.0 mmol), **49a** (2.0 mmol), Cs_2CO_3 (1.0 mmol) in toluene (2.0 mL) at 70 °C. [b]Isolated yield.

Generally, deprotection of the silyl protecting groups occurs under basic media at an ambient temperature.[15] With this fact in mind, we intend to test the reaction condition for the alkynyl-TMS protected propargyl alcohols and the results are summarized in Table 1.9.

Although the reaction between **56a** and **49a** proceeded efficiently, the corresponding C-TMS containing β-heteroarylated ketone **57a** was obtained in poor yield (4%) and the silyl-deprotected product **55b** isolated in 87% yield. Similar trends of the product-selectivity were also noticed in case of RICA of 4-chlorophenyl and 1-naphthyl substituted alkynyl-TMS containing propargyl alcohols (**56b** and **56c**) and the corresponding silyl tethered compounds **57b** and **57c** are obtained in 17% and 7% yields, respectively. We therefore conclude that this optimized reaction condition did not tolerate the C-TMS group up to our expectations.

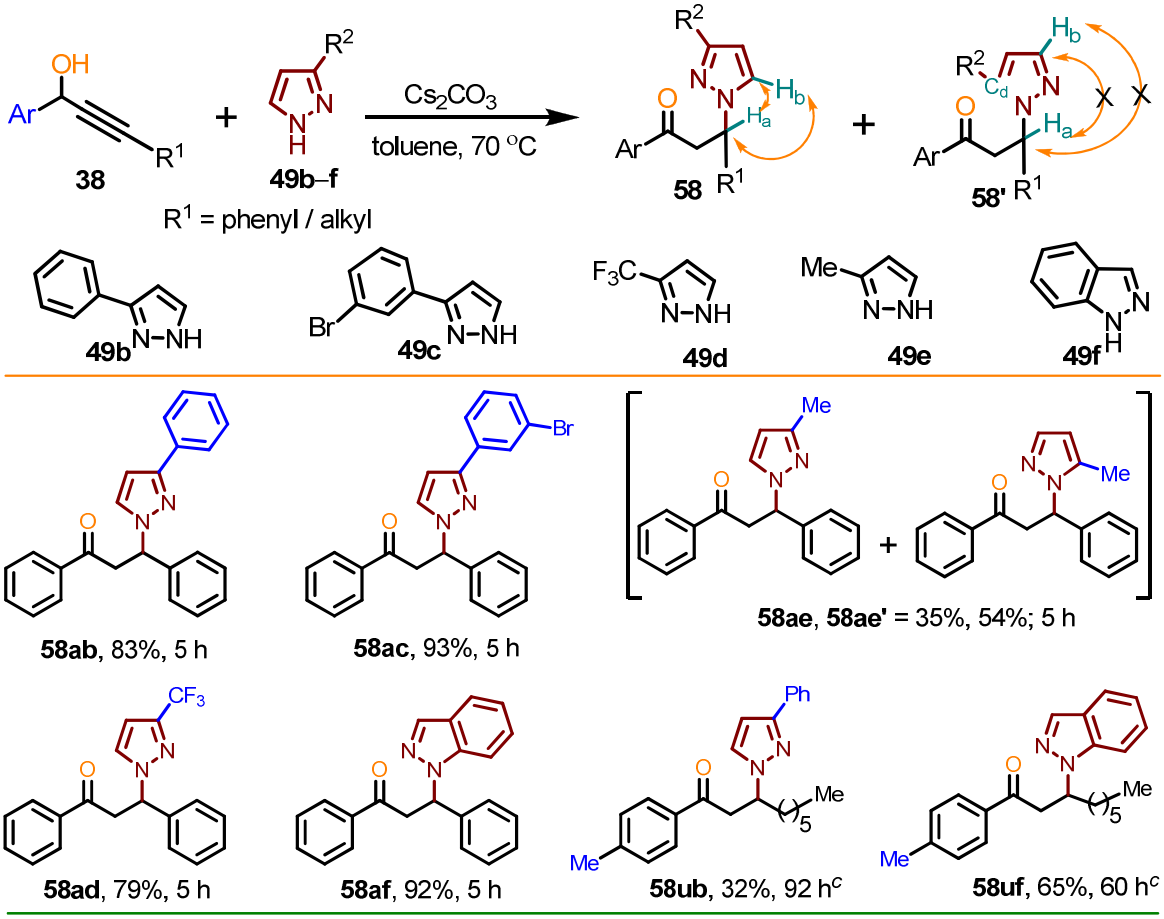
Table 1.9: RICA of TMS Substituted Propargyl Alcohols with **49a**[a,b]



[a]Reactions were carried out using **56** (1.0 mmol), **49a** (2.0 mmol), Cs_2CO_3 (1.0 mmol) in toluene (2.0 mL) at 70 °C. [b]Isolated yield. Yield of desilylated product shown in parentheses.

To broaden the reaction scope, we then investigated the RICA between various substituted pyrazoles and propargyl alcohols. Table 1.10 summarizes the results of this study. The reaction of 3-substituted-pyrazole (**49b-e**) with the propargyl alcohol (**38**) usually provides a mixture of two regioisomers. For example, addition of 3-substituted pyrazole or indazole to 4-aryl-4-hydroxy-2,3-alkynyl esters (**20**) in the presence of DBU in CH_2Cl_2 gave two non-separable regioisomers of the corresponding β-heteroarylated ketones.[12b] To examine the amount of regioselective product formation in the reaction, RICA between 3-phenyl pyrazole (**49b**) and **38a** was performed in the presence of Cs_2CO_3 (1.0 equiv) in toluene at 70 °C. To our surprise, single regioisomer **58ab** (83%) was exclusively produced.

Table 1.10: RICA between Propargyl Alcohols and Pyrazole Derivatives (**13**)[a,b]



[a]Reactions were carried out using **38** (1.0 mmol), **49** (2.0 mmol), Cs_2CO_3 (1.0 mmol) in toluene (2.0 mL) at 70 °C. [b]Isolated yield. [c]at 80 °C.

The structure of **58ab** was confirmed based on X-ray crystallographic analysis (Figure 1.8). Similarly, reaction of 3-(3-bromophenyl)-1*H*-pyrazole (**49c**) with **38a** led to only **58ac** in excellent yield.

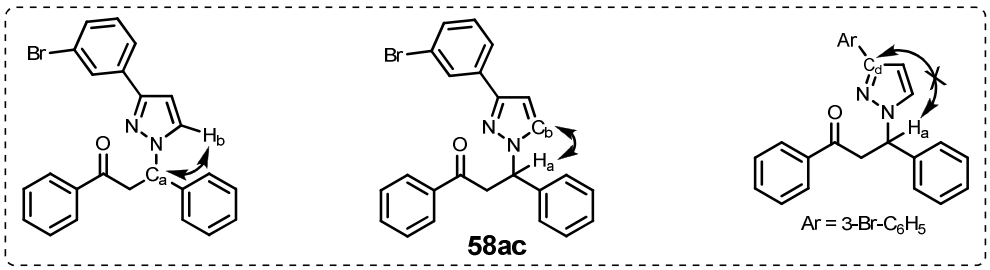


Figure 1.2: HMBC studies of **58ac**

The structure of **58ac** is established based on the heteronuclear multiple bond correlation (HMBC) studies (Figure 1.2); correlation between C_a (61.3 ppm) and H_b (7.04 ppm), H_a

(6.20 ppm) and C_b (131.1 ppm) are quite significant whereas the correlation between H_a and C_d (149.3 ppm) are not seen. Furthermore, the X-ray crystallographic analysis data supports the structure of **58ac** (Figure 1.8). We assume that the steric nature of the substituent and the relatively milder reaction conditions are detrimental to this high regioselectivity. Electron-poor and relatively small 3-CF_3-substituted pyrazole (**49d**) reacted efficiently with **38a** at 80 °C, affording the desired β-heteroarylated ketone **58ad** in 79% yield; a trace of the other regioisomer (ca. ~3% by GC) was also noticed.

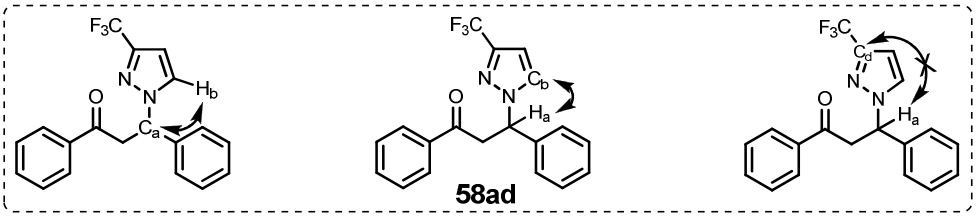


Figure 1.3: HMBC studies of **58ad**

The structure of **58ad** is established based on the HMBC studies (Figure 1.3); correlation between C_a (61.8 ppm) and H_b (7.50 ppm), H_a (6.11 ppm) and C_b (131.1 ppm) are quite significant whereas the correlation between H_a and C_d (142.3 ppm) are not seen. However, RICA between 3-methyl pyrazole (**49e**) and **38a** gave a mixture of regioisomers; both the isomers are separated by flash chromatography resulting **58ae** and **58ae′** in 35% and 54% yields, respectively. Once again, the structures of **58ae** and **58ae′** are confirmed through detailed HMBC studies.

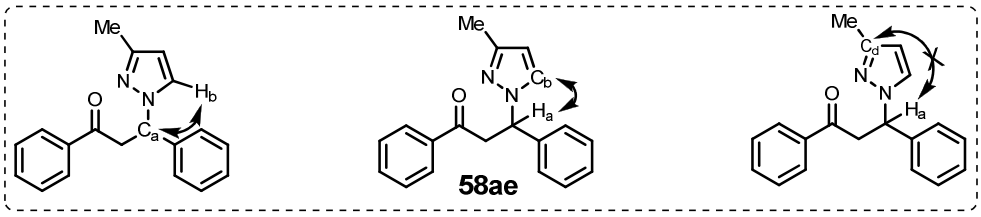


Figure 1.4: HMBC studies of **58ae**

The observed correlation between C_a (60.7 ppm) and H_b (7.38 ppm), H_a (6.05 ppm) and C_b (130.4 ppm) and the absence of correlation between H_a and C_d (148.5 ppm) establish the structure of **58ae** (Figure 1.4).

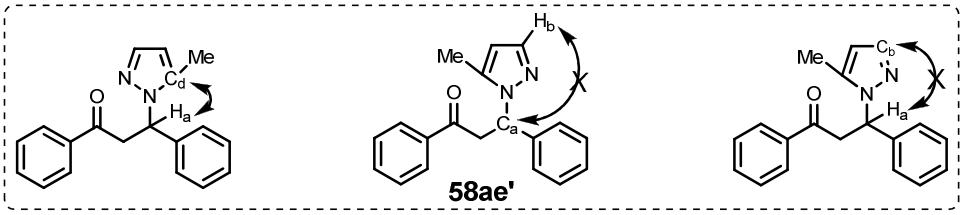


Figure 1.5: HMBC studies of **58ae'**

Similarly, the structure of **58ae'** is established based on the HMBC studies (Figure 1.5); significant correlation between C_d (138.8 ppm) and H_a (6.08 ppm) are observed whereas the correlation between C_a (57.0 ppm) and H_b (7.42 ppm), H_a and C_b (138.1 ppm) are not seen. Divergence in the behaviour of the observed regioselectivity is interesting; however, the factors responsible for this effect are unclear. It appears that the steric and electronic nature of the C-3-substitution in pyrazole contribute to the regioselectivity. Gratifyingly, a single isomer **58af** in excellent yield was obtained from the RICA between **38a** and indazole (**49f**). The structure of **58af** was confirmed based on X-ray crystallographic analysis (Figure 1.8). Similarly, **49b** and **49f** were independently reacted with 1-*p*-tolylnon-2-yn-1-ol (**38u**) and the corresponding β-heteroarylated ketones **58ub** and **58uf** are isolated in 32% and 65% yields, respectively; incomplete conversion of **38u** was observed even with the extended reaction time. Poor reactivity and the moderate product yields are the consequences of the alkyl-substitution of the propargyl alcohols. The structure of **58ub** and **58uf** are confirmed through detailed HMBC studies.

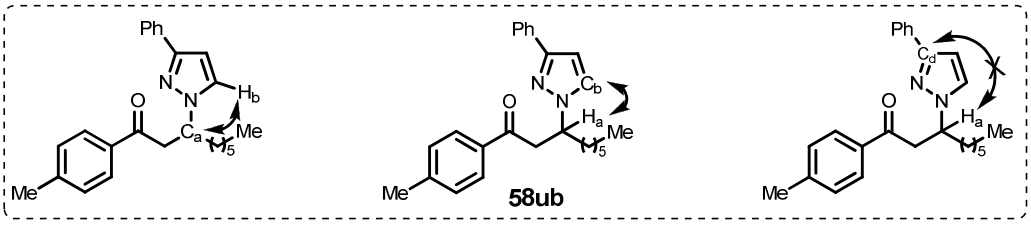


Figure 1.6: HMBC studies of **58ub**

The structure of **58ub** is established based on the HMBC studies (Figure 1.6); correlation between C_a (58.5 ppm) and H_b (7.51 ppm), H_a (4.83 ppm) and C_b (131.1 ppm) are quite significant whereas the correlation between H_a and C_d (151.4 ppm) are not seen. The structure of **58uf** is established based on the HMBC studies (Figure 1.7); correlation between C_b (140.2 ppm) and H_a (5.31 ppm) are quite significant whereas the correlation between C_a (54.1 ppm) and H_d (8.01 ppm), C_d (133.3 ppm) and H_a are not seen.

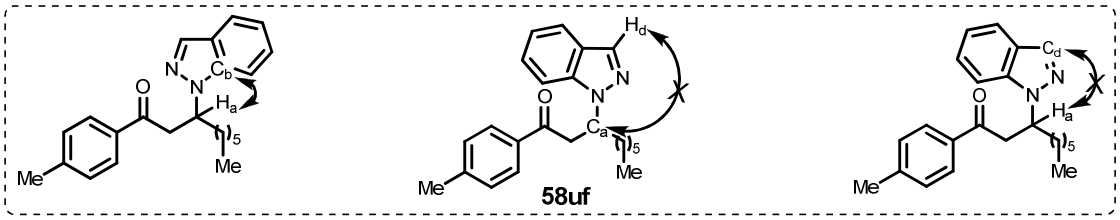


Figure 1.7: HMBC studies of **58uf**

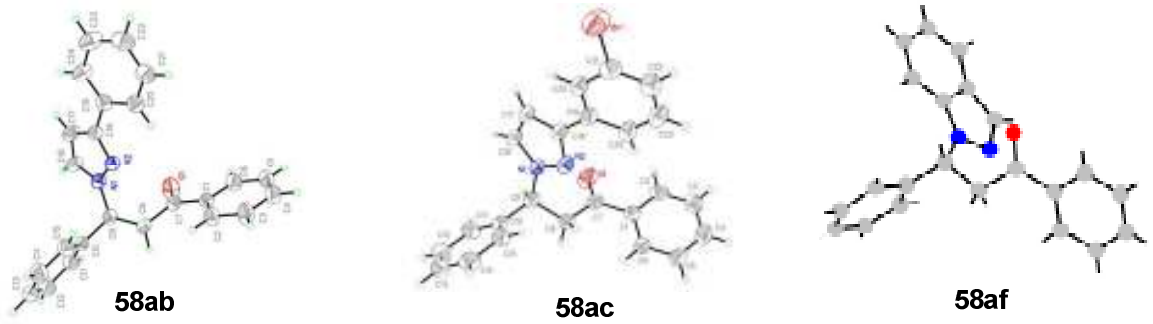
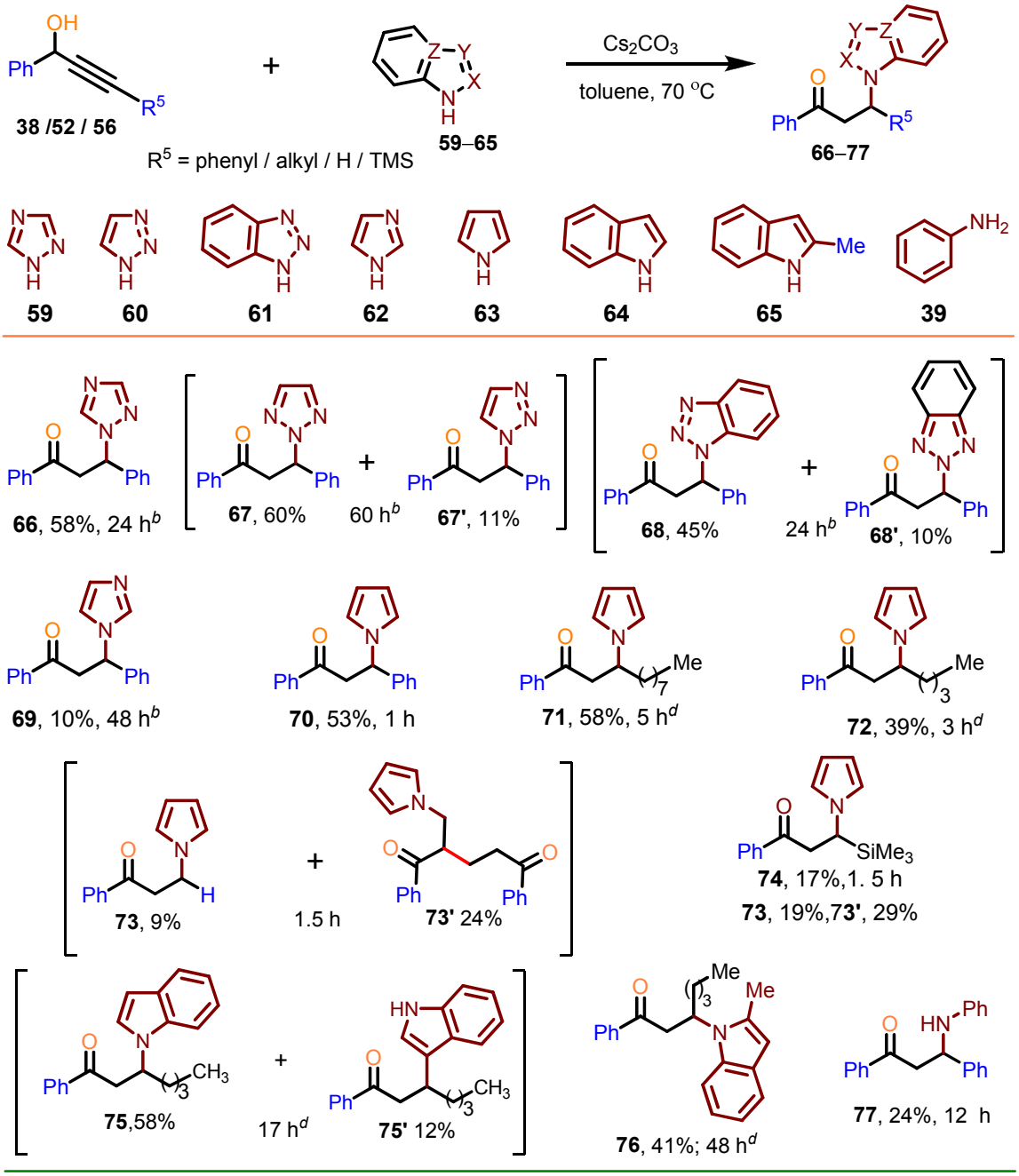


Figure 1.8: ORTEP Diagrams of **58ab**, **58ac** and **58af**

To widen the synthetic utility of this methodology, various NH-bearing heterocycles such as triazoles, imidazole, pyrrole, indole, aniline and its derivatives were tested in the RICA reaction with propargyl alcohols. The results of this survey are detailed in Table 1.11. *Conjugate addition of triazole to the propargyl alcohol in the presence of DBU was unsuccessful*.[12b] Under the optimized conditions, addition of triazoles with **38a** led to little conversion of **38a** even though the reaction continued for 4 days. This failure led us to find a suitable condition for this transformation. In order to improve the product yield and reaction efficiency, we at first surveyed mixtures of different solvents for this RICA reaction. Interestingly, complete conversion of **38a** has been observed, when a toluene (1.5 mL) and DMF (0.5 mL) mixture was employed and the reaction was heated at 80 °C. Thus, a moderate yield of **66** was obtained from the RICA between 1,2,4-triazole (**59**) and **38a** under the modified reaction conditions. Although reaction of 1,2,3-triazole (**60**) with **38a** was sluggish, the corresponding regioisomers **67** and **67′** (6 : 1) were isolated in satisfactory overall yields.[7d,12b] However, in case of the benzotriazole (**61**), a reverse trend of the regioisomer selectivity **68** and **68′** (1 : 4.5; 55% yield) was noticed.[7c] The reaction between imidazole (**62**) and **38a** was complex, however, the product **69** was obtained in only 10% yield.

Table 1.11: RICA between Propargyl Alcohols and other NH-Heteroarenes[a,c]

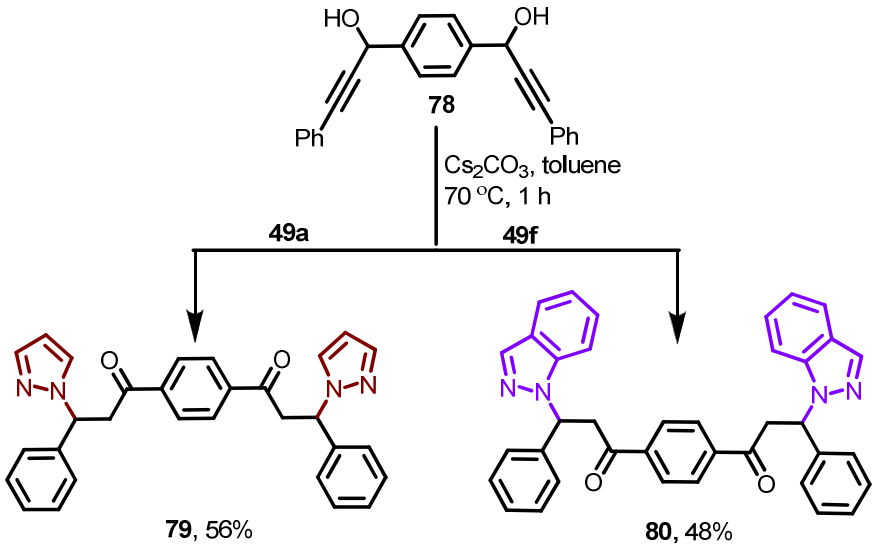


[a]Reactions were carried out using **12** (1.0 mmol), **59–65** (2.0 mmol), Cs_2CO_3 (1.0 mmol) in toluene (2.0 mL) at 70 °C, [b]Reactions were carried out using toluene (1.5 mL) + DMF (0.5 mL) at 80 °C, [c]Isolated yields. [d]at 80 °C.

The pyrrole-building block has been widely found in biologically active molecules.[20a,b] However, owing to the better reactivity, pyrrole intend to polymerize at an elevated temperature.[20c,d] Therefore, we are interested in examining the reactivity of pyrrole (**63**)

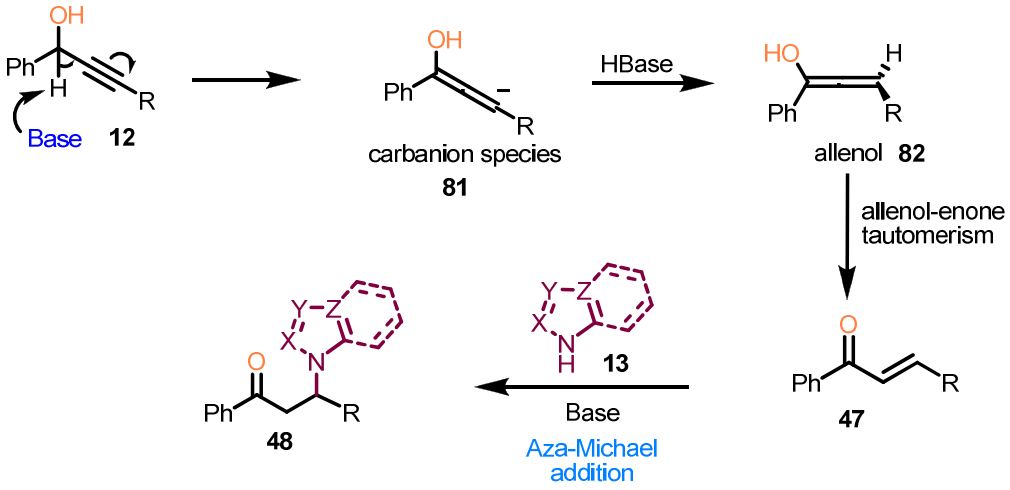
with various propargyl alcohols. Interestingly, pyrrole reacted with **38a** sluggishly under the optimized reaction conditions and a moderate amount of product **70** was produced in 53% yield. Relatively poor-reactive C(sp)-alkyl substituted propargyl alcohols **38s** and 1-phenylhept-2-yn-1-ol (**38y**) successfully underwent RICA with pyrrole at 80 °C and delivered the corresponding β-pyrrolyl ketones **71** and **72** albeit in moderate yields. Surprisingly, a fast reaction between **63** and terminal propargyl alcohol **52a** has been observed, the addition product 1-phenyl-3-(1*H*-pyrrol-1-yl)propan-1-one (**73**) was obtained in only 9% yield. Interestingly, a Michael adduct **73′**, obtained through the conjugate addition of the carbanion (α-to carbonyl) of **73** to the α,β-unsaturated ketone, was isolated in 24% yield. The products **74**, **73**, **73′** has been isolated in overall good yield, when **63** reacted with 1-phenyl-3-(trimethylsilyl)prop-2-yn-1-ol (**56d**). Because of the nucleophilic character of NH– and the C-3 center of indole, C–C and C–N bond formations with the redox isomerized product of the propargyl alcohol are possible.[10a,12b] Thus, RICA between indole (**64**) and **38y** was performed; the β-indolyl-(C–N bond)-ketone (**75**) and C-3 functionalized β-indolyl-(C–C bond)-ketone (**75′**) (5 : 1) are obtained in overall good yields. However, 2-methyl indole (**65**) underwent RICA with **38y** and exclusively produced the β-indolyl-(C–N bond)-ketone **76**; the ^{1}H spectrum of crude reaction mixture did not show any trace of the corresponding β-indolyl-(C–C bond)-ketone. A recent report from the Trost group describes the synthesis of β-indolyl-(C–C bond)-ketones from RICA between substituted indole derivatives and propargyl alcohols.[10a] Therefore, RICA between propargyl alcohols and indoles under different reaction conditions can generate two distinct products. Importantly, the –NH_2 group of aniline (**39**) participated in this RICA to **38a** and the product **77** was generated in only 24% yield. Unfortunately, the electron-rich indole or aniline failed to react with ethyl 4-hydroxy-4- phenylbut-2-ynoate (**20**).[12b] Therefore, we believe that our optimized reaction conditions are better because they show a broader reaction scope.

To enlarge the molecular diversity by incorporating more heteroarenes in the molecule, compound **78** having two propargyl alcohol units was prepared. The pyrazole (**49a**) and indazole (**49f**) were independently exposed to **78** under the optimized conditions and the desired β-heteroarylated ketone **79** and **80** resulted albeit in reasonable yields (Scheme 1.14).



Scheme 1.14 RICA of Bis-Propargyl Alcohol (**78**) with **49a**/**49f**.

Based on the precedence, the reaction is likely to proceed through the following mechanism, as shown in Scheme 1.15.[21] The first step is the formation of the carbanion *via* the abstraction of the acidic benzylic C–H proton in the presence of base.[21e,f] Stabilization of carbanion through delocalization with triple bond furnishes the allenyl carbanion **81**. Protonation of **81** with the conjugate acid delivers the corresponding allenol **82**. Allenol–enone tautomerism gives the reactive α,β-unsaturated carbonyl compound **47**. Finally, base mediated conjugate addition of NH-heteroarenes with enones produces the desired β-heteroarylated ketones.[7b,d,e,g]



Scheme 1.15 Plausible Mechanism

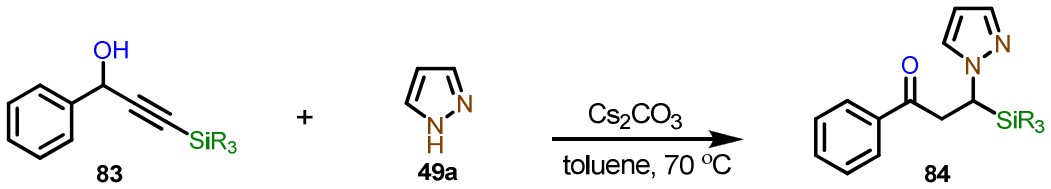
1.3. Conclusion

In conclusion, a direct, practicable and efficient approach to β-heteroarylated ketones is demonstrated. The reaction proceeds through the base induced redox-isomerization of easily accessible propargyl alcohols followed by conjugate addition of NH-heteroarenes in one-step. This reaction displays broad scope and tolerates a variety of reactive functional groups. Aryl, heteroaryl, alkyl C(sp), and terminal alkynes containing unactivated propargyl alcohols undergo RICA with the pyrazole efficiently. Notably, the RICA of 3-substituted pyrazoles or indazole with propargyl alcohols delivers the products with a better level of regioselectivity. RICA between propargyl alcohols and a range of NH-bearing compounds such as: 1,2,4-triazole, 1,2,3-triazole, imidazole, pyrrole, indoles and aniline are successfully demonstrated. The antifungal activities for these molecules are yet to examined. We are belive that some of these new molecular entities would be useful as antifungal agents.

1.4. Future Work

We have developed a reliable approach to β-heteroarylated ketones from easily accessible propargyl alcohols and NH-heteroarenes in one-step. The β-heteroarylated ketones architecture closely resemble to the azole-bearing antifungal agents. We are therefore interested studying the antifungal activities of the newly synthesized molecules.

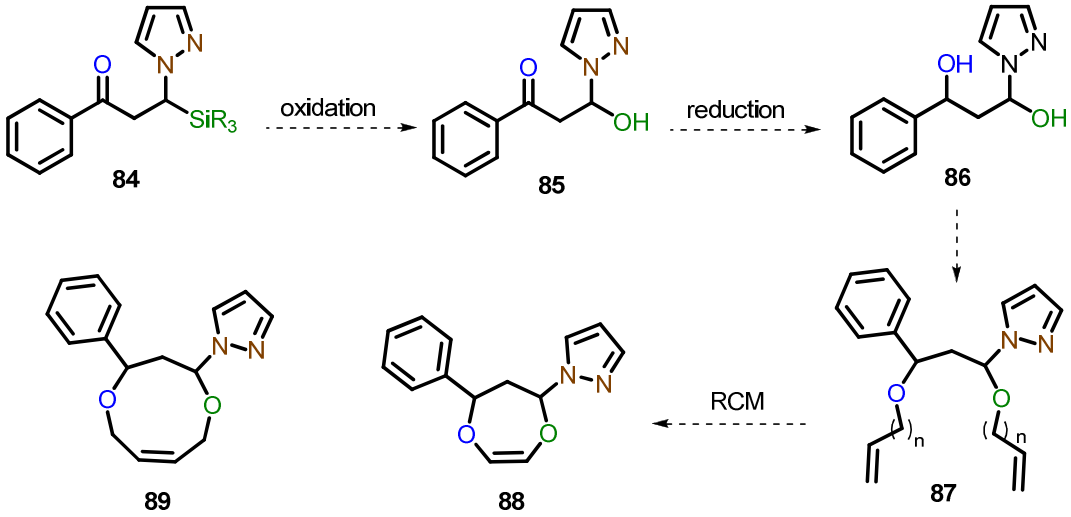
The stability as well as the ease modifiable nature of the silyl-moiety allows in applying the sily-group in this study. Furthermore, the partial survivel of TMS (trimethylsilyl) group inspires us to study the relative stability of other silyl protecting groups under the optimized condition (Scheme 1.16).



Scheme 1.16: Relative Stability of Silyl Protecting Groups

The successful incorporation of the modifiable sily-group in the product **84**, would allow examining the Tamao-Flemming oxidations. This would enable installing –OH functionality. Furthermore, reduction of carbonyl group would deliver the di-hydroxy

compound **86**. Sequential O-allylation / vinylation and ring closing metathesis (RCM) could furnish a varietyof azole containg macrocycles **88** and **89** (Scheme 1.17).



Scheme 1.17: Synthesis of Azole Containing Macrocycles

1.5. Experimetal

1.5.1. General Experimental Information for all the work in this Thesis

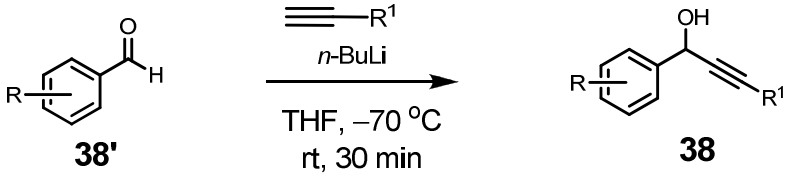
All the reactions were performed in an oven-dried Schlenk flask/ pressure tubes under an argon atmosphere or in open air conditions. Commercial grade solvents were distilled prior to use. Column chromatography was performed using silica gel procured from Merck (100-200 Mesh) eluting with hexanes and ethyl acetate mixture. Flash column chromatography was performed using silica gel procured from Acme's (230-400 Mesh) eluting with hexanes and ethyl acetate mixture. Thin layer chromatography (TLC) was performed on silica gel GF254 (Merck) plates. Visualization of spots on TLC plate was accomplished with UV light (254 nm) and staining over I_2 chamber.

Proton and carbon nuclear magnetic resonance spectra (^{1}H NMR, ^{13}C NMR and ^{19}F NMR) were recorded on a Bruker Avance 400 (^{1}H NMR, 400 MHz; ^{13}C NMR, 101 MHz; ^{19}F NMR, 376 MHz) spectrometer, Bruker Avance 500 (^{1}H NMR, 500 MHz; ^{13}C NMR, 126 MHz; ^{19}F NMR, 470 MHz) spectrometer having solvent resonance as internal standard (^{1}H NMR, $CHCl_3$ at 7.26 ppm; ^{13}C NMR, $CDCl_3$ at 77.0 ppm). Few cases tetramethylsilane (TMS) at 0.00 ppm was used as reference standard. Data for ^{1}H NMR are reported as follows: chemical shift (ppm), multiplicity (s = singlet; bs = broad singlet; d = doublet; bd = broad doublet, t = triplet; bt = broad triplet; q = quartet; m = multiplet), coupling

constants, *J*, in (Hz), and integration. Data for ^{13}C NMR, ^{19}F NMR were reported in terms of chemical shift (ppm). GC analysis was performed on a Shimadzu GCMS QP2010 equipped with an ZB-1 column (30 m × 0.25 mm, pressure = 20.0 kPa, detector = EI, 300 °C) with helium gas as carrier. IR spectra were recorded on JASCO FT/IR-5300 spectrometer and reported in cm^{-1}. LC-MS spectra were obtained with a Shimadzu 2010A (EI-positive/ negative mode) with ionization voltage of 70eV; data was reported in the form of m/z (intensity relative to base peak = 100). Elemental (C, H, N) analysis were carried out using THERMO FINNIGAN FLASH EA 1112 analyzer. High resolution mass spectrum (HRMS) was recorded on a Bruker maxis mass spectrometer using ESI (electrospray ionization). Melting points were determined on electro-thermal melting point apparatus and are uncorrected. X-Ray data was collected at 298K on a Bruker-Nonius SMART APEX CCD single crystal diffractometer using graphite monochromated Mo-Kα radiation (0.71073 Å).

1.5.2. Materials: Unless otherwise noted, all the reagents and intermediates were obtained commercially and used without purification. According to the standard procedures solvents were dried and stored under molecular sieves.[29] Cesium carbonate, terminal alkynes, pyrazole and pyrazole derivatives were purchased from Sigma Aldrich Ltd. and used as received. Analytical and spectral data of all those known compounds are exactly matching with the reported values.

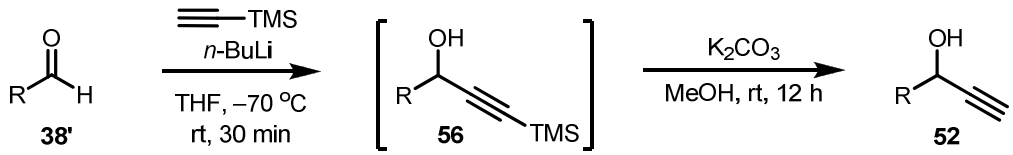
1.5.3. General Procedure for the Preparation of 38 from Aldehydes (38') (GP-1)



A solution of terminal-alkyne (1.2 equiv) in THF (50 mL) was stirred in a 100 mL oven-dried two-necked round bottom flask under an argon atmosphere at −70 °C. n-Butyllithium (1.2 equiv, 1.60 M in THF) was introduced over 30 minutes at −70 °C. After an additional 1 h stirring, a solution of aldehyde (**38'**, 1.0 equiv) in THF (5.0 mL) was added at −70 °C. The resulting mixture was stirred for 1 h and warmed to room temperature slowly and stirring continued for 30 minutes. The reaction mixture was quenched with saturated NH_4Cl aqueous solution (20 mL) at 0 °C. The organic layer was

separated; the aqueous layer was extracted with Et_2O (2 × 20 mL). The combined extracts were washed with water (2 × 20 mL), brine (25 mL) and dried over Na_2SO_4. Solvent was filtered and evaporated under reduced pressure. The crude residue was purified using column chromatography on silica gel. The desired propargyl alcohols are obtained in good yields. Physical characterization data is exactly matching with the reported values for the respective compounds **1a**–**h**,[22] **1k**–**s**,[22,23] **1u**–**w**,[24] **1ab**,[25] **1y**[26] and **29**,[27] whereas **1i**–**j**, **1t**, **1x**, **1aa** and **1ac** are new.

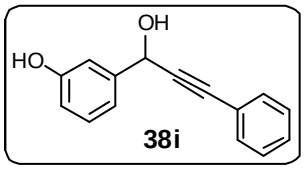
1.5.4. General Procedure for the Synthesis of 52 and 56 from 38' (GP-2)



A solution of trimethylsilylacetylene (1.2 equiv) in THF (50 mL) was stirred in a 100 mL oven-dried two-necked round bottom flask under an argon atmosphere at −70 °C. *n*-Butyllithium (1.2 equiv, 1.60 M in THF) was introduced over 30 minutes at −70 °C. After an additional 1 h stirring, a solution of aldehyde (**38'**, 1.0 equiv) in THF (5 mL) was added at −70 °C. The resulting mixture was stirred for 1 h and warmed to room temperature slowly and stirring continued for 30 minutes. The reaction mixture was quenched with saturated NH_4Cl aqueous solution (20 mL) at 0 °C. The organic layer was separated; the aqueous layer was extracted with Et_2O (2 × 20 mL). The combined extracts were washed with water (2 × 20 mL), brine (25 mL) and dried over Na_2SO_4. Solvent was filtered and evaporated under reduced pressure to give **56**. The crude residue was subsequently used for the desilylation reaction to give **52**. Methanol (15 mL) and K_2CO_3 (2.5 equiv) was introduced to the crude residue obtained in the above reaction and the heterogeneous mixture was stirred under an argon atmosphere at ambient temperature overnight. The reaction mixture was diluted with ethyl acetate (50 mL) and washed with water (2 × 20 mL) and brine (10 mL). The organic layer was separated, dried over Na_2SO_4, filtered, and concentrated under vacuum. The crude residue was purified using column chromatography on silica gel. Physical characterization data is exactly matching with the reported values for the respective compounds **52a**–**d** and **56a**–**c**.[29–34]

1.5.5. Spectral and Analytical Data of the Compounds:

3-(1-Hydroxy-3-phenylprop-2-ynyl)phenol (38i):

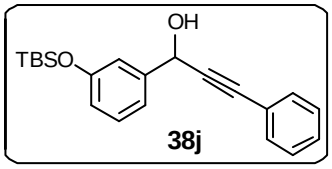


38i

Following the literature procedure,[28] $LiOAc \cdot 2H_2O$ (52 mg, 10 mol%) was added to a solution of 1-(3-(*tert*-butyldimethylsilyloxy)phenyl)- 3-phenylprop-2-yn-1-ol (**38j**, 2.7 g, 8.0 mmol) in DMF–H_2O. The resulting mixture was heated at 70 °C under an inert atmosphere. Upon complete consumption of starting material, the reaction mixture was extracted with ethyl acetate. After usual work up, the crude material was purified using silica gel column chromatography. The product **38i** was isolated 1.43 g in 80% yield as pale yellow thick oil.

R_f = 0.28 (4 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.52–7.43 (m, 2H), 7.38–7.23 (m, 4H), 7.19–7.10 (m, 2H), 6.86–6.81 (m, 1H), 5.72 (bs, 1H), 5.64 (s, 1H), 2.34 (bs, 1H); **^{13}C NMR (101 MHz, DMSO-d6)** δ 157.8, 143.9, 131.7 (2C), 129.7, 129.1 (2C), 129.0, 122.8, 117.6, 115.0, 113.8, 91.9, 84.7, 63.3; **IR (Neat)** ν_{max} 3337, 3155, 2220, 1602, 1466, 1311, 1259, 1163, 1020, 902, 752 cm^{-1}; **MS (EI)** *m/z* (%) 225 (M^+ + 1, 100), 207 (2), 174 (2); **Elemental analysis** calcd for $C_{15}H_{12}O_2$: C, 80.34; H, 5.39. Found: C, 80.15; H, 5.31.

1-(3-(*tert*-Butyldimethylsilyloxy)phenyl)-3-phenylprop-2-yn-1-ol (38j):

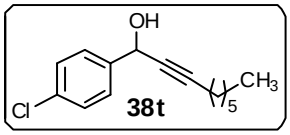


38j

Following the general procedure (GP-1), reaction of 3-(*tert* butyldimethylsilyloxy)benzaldehyde (**38'j**; 1.89 g,8.00 mmol), phenyl acetylene (980 mg, 9.60 mmol) and *n*-BuLi (6.0 mL, 1.6 M in THF, 9.60 mmol) gave **38j** (1.63 g, 60% yield) as a light yellow thick oil.

R_f = 0.42 (4 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.52□7.48 (m, 2H), 7.38–7.20 (m, 5H), 7.13 (s, 1H), 6.83 (d, *J* = 8.0 Hz, 1H), 5.64 (s, 1H), 2.32 (bs, 1H), 1.00 (s, 9H), 0.22 (s, 6H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 155.9, 142.2, 131.8 (2C), 129.7, 128.6, 128.3 (2C), 122.4, 120.1, 119.6, 118.5, 88.7, 86.6, 64.9, 25.7 (3C), 18.2, −4.4 (2C); **IR (Neat)** ν_{max} 3441, 3065, 2932, 2887, 2197, 1643, 1599, 1485, 1439, 1286, 939, 839 cm^{-1}; **MS (EI)** *m/z* (%) 339 (M^+ + 1, 10), 321 (100), 229 (2); **Elemental analysis** calcd for $C_{21}H_{26}O_2Si$: C, 74.51; H, 7.74. Found: C, 74.45; H, 7.71.

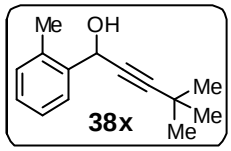
1-(4-Chlorophenyl)non-2-yn-1-ol (38t):



Following the general procedure (GP-1), reaction of 4-chlorobenzaldehyde (**38't**; 1.40 g, 10.0 mmol), 1-octyne (1.32 g, 12.0 mmol) and *n*-BuLi (7.5 mL, 1.6 M in THF, 12.0 mmol) gave **38t** (2.18 g, 87% yield) as a colorless oil.

R_f = 0.45 (9 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.48 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.8 Hz, 2H), 5.43 (d, *J* = 5.6 Hz, 1H), 2.27 (td, *J* = 1.6, 6.8 Hz, 2H), 2.12 (d, *J* = 6.0 Hz, 1H), 1.57–1.50 (m, 2H), 1.43–1.32 (m, 2H), 1.32–1.23 (m, 4H), 0.89 (t, *J* = 6.8 Hz, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 139.8, 133.9, 128.6 (2C), 128.0 (2C), 88.1, 79.6, 64.0, 31.2, 28.6, 28.5, 22.5, 18.8, 14.0; **IR (Neat)** ν_{max} 3368, 2930, 2858, 1489, 1091, 1014, 779 cm^{-1}; **MS (EI)** *m/z* (%) 203 (M^+ + 1, 100), 167 (8), 139 (27), 91 (8); **Elemental analysis** calcd for $C_{15}H_{19}ClO$: C, 71.84; H, 7.64. Found: C, 71.94; H, 7.69.

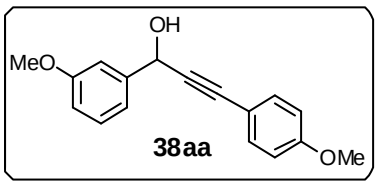
4,4-Dimethyl-1-*o*-tolylpent-2-yn-1-ol (38x):



Following the general procedure (GP-1), reaction of 2-methylbenzaldehyde (**38'x**; 960 mg, 8.0 mmol), 3,3-dimethylbut-1-yne (788 mg, 9.6 mmol) and *n*-BuLi (6.0 mL, 1.6 M in THF, 9.6 mmol) gave **38x** (389 mg, 72% yield) as a colorless oil.

R_f = 0.40 (32 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.65 (t, *J* = 4.0 Hz, 1H), 7.26–7.20 (m, 2H), 7.20–7.16 (m, 1H), 5.60 (d, *J* = 5.6 Hz, 1H), 2.45 (s, 3H), 1.99 (d, *J* = 5.6 Hz, 1H), 1.26 (s, 9H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 139.1, 136.1, 130.7, 128.2, 126.5, 126.1, 95.1, 78.3, 62.6, 31.0 (3C), 27.5, 19.0; **IR (Neat)** ν_{max} 3368, 2968, 1460, 983, 750 cm^{-1}; **MS (EI)** *m/z* (%) 203 (M^+ + 1, 100), 167 (8), 139 (27), 91 (8); **Elemental analysis** calcd for $C_{14}H_{18}O$: C, 83.12; H, 8.97. Found: C, 83.21; H, 8.92.

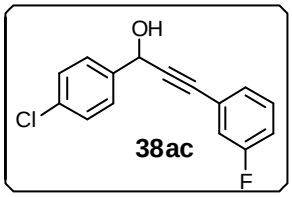
1-(3-Methoxyphenyl)-3-(4-methoxyphenyl)prop-2-yn-1-ol (38aa):



Following the general procedure (GP-1), reaction of 3-methoxybenzaldehyde (**38'g**; 500 mg, 3.78 mmol), 1-ethynyl-4-methoxybenzene (599 mg, 4.53 mmol) and *n*-BuLi (2.8 mL, 1.6 M in THF, 4.53 mmol) gave **38aa** (730 mg, 72% yield) as a yellow thick oil.

R_f = 0.28 (9 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.51–7.26 (m, 3H), 7.25–7.12 (m, 2H), 6.95–6.75 (m, 3H), 5.65 (s, 1H), 3.83 (s, 3H), 3.78 (s, 3H), 2.60 (bs, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 159.8 (2C), 142.5, 133.3 (2C), 129.7, 119.0, 114.5, 114.0, 113.9 (2C), 112.2, 87.4, 86.6, 65.1, 55.3 (2C); **IR (Neat)** ν_{max} 3385, 3011, 2968, 2930, 2843, 1606, 1510, 1248, 1170, 1030, 831 cm^{-1}; **MS (EI)** *m/z* (%) 269 (M^+ + 1, 100), 186 (13), 137 (23); **Elemental analysis** calcd for $C_{17}H_{16}O_3$: C, 76.10; H, 6.01. Found: C, 76.23; H, 6.10.

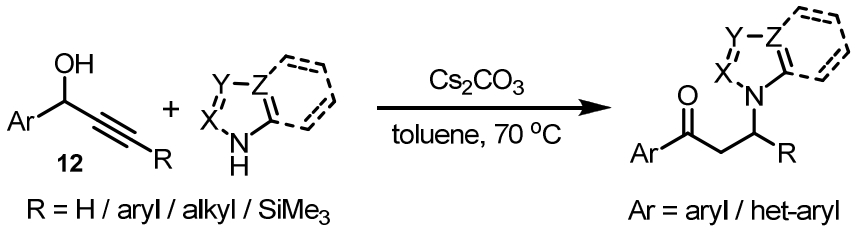
1-(4-Chlorophenyl)-3-(3-fluorophenyl)prop-2-yn-1-ol (38ac):



Following the general procedure (GP-1), reaction of 4-chlorobenzaldehyde (**38'c**; 1.00 g, 7.14 mmol), 1-ethynyl-3-fluorobenzene (1.03 g, 8.56 mmol) and *n*-BuLi (5.0 mL, 1.6 M in THF, 8.56 mmol) gave **38ac** (1.40 g, 75% yield) as a colorless solid.

mp = 59–60 °C; R_f = 0.45 (6 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.54 (d, *J* = 8.0 Hz, 2H), 7.38 (d, *J* = 8.4 Hz, 2H), 7.33–7.23 (m, 2H), 7.16 (d, *J* = 9.6 Hz, 1H), 7.06 (t, *J* = 8.8 Hz, 1H), 5.67 (d, *J* = 6.0 Hz, 1H), 2.36 (d, *J* = 6.0 Hz, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 162.2 (d, *J* = 248 Hz), 138.7, 134.2, 129.9 (d, *J* = 8.7 Hz), 128.7 (2C), 128.0 (2C), 127.5 (d, *J* = 3.2 Hz), 123.8 (d, *J* = 9.4 Hz), 118.4 (d, *J* = 23.1 Hz), 116.1(d, *J* = 21.2 Hz), 89.1, 85.5 (d, *J* = 3.3 Hz), 64.1; **IR (KBr)** ν_{max} 3341, 2874, 1571, 1487, 1168, 1016, 785, 680 cm^{-1}; **MS (EI)** *m/z* (%) 203 (M^+ + 1, 100), 167 (8), 139 (27), 91 (8); **Elemental analysis** calcd for $C_{15}H_{10}ClFO$: C, 69.11; H, 3.87. Found: C, 69.25; H, 3.83.

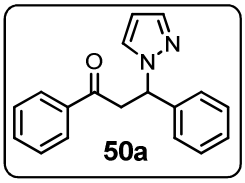
1.5.6. General Procedure for the RICA between Propargyl Alcohols and NH-Heteroarenes (GP-3)



Propargyl alcohol **12** (1.0 mmol), NH-heteroarene (2.0 mmol) and cesium carbonate (326 mg, 1.0 mmol) were taken in an oven-dried Schlenk flask under an argon atmosphere. Toluene (2.0 mL) was added to this mixture. The resulting solution was stirred at 70 °C as per the time shown in the representative tables. Upon complete consumption of **12**, the

reaction mixture was diluted with dichloromethane (10 mL), and filtered over a small pad of Celite. The solvent was evaporated under the reduced pressure and the crude reaction mixture was purified using column chromatography on silica gel.

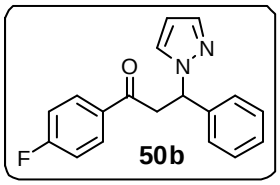
1,3-Diphenyl-3-(1*H*-pyrazol-1-yl)propan-1-one (50a):



Following the general procedure (GP-3); 1,3-diphenyl-2-yn-1-ol (**38a**; 208 mg, 1.0 mmol), pyrazole (**49a**; 136 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 70 °C for 1 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (9:1) to afford **50a** (220 mg) in 80% yield as light yellow solid.

mp = 79–80 °C; R_f = 0.31 (9 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.98 (d, *J* = 7.2 Hz, 2H), 7.60–7.50 (m, 3H), 7.45 (t, *J* = 7.6 Hz, 2H), 7.37–7.32 (m, 4H), 7.31–7.26 (m, 1H), 6.24 (s, 1H), 6.13 (dd, *J* = 5.6, 8.4 Hz, 1H), 4.50 (dd, *J* = 8.4, 17.6 Hz, 1H), 3.65 (dd, *J* = 5.2, 17.6 Hz, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 196.6, 140.8, 139.3, 136.5, 133.4, 129.8, 128.8 (2C), 128.6 (2C), 128.2 (2C), 128.0, 126.7 (2C), 105.6, 60.8, 44.2; **IR (KBr)** ν_{max} 3032, 2925, 1682, 758, 563 cm^{-1}; **MS (EI)** *m/z* (%) 278 (M^+ + 2, 54), 241 (27), 209 (100), 105 (8), 69 (8); **Elemental analysis** calcd for $C_{18}H_{16}N_2O$: C, 78.24; H, 5.84; N, 10.14. Found: C, 78.09; H, 5.76; N, 10.25.

1-(4-Fluorophenyl)-3-phenyl-3-(1*H*-pyrazol-1-yl)propan-1-one (50b):

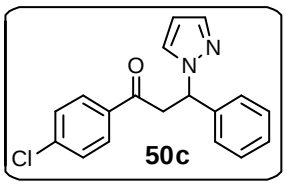


Following the general procedure (GP-3); 1-(4-fluorophenyl)-3-phenylprop-2-yn-1-ol (**38b**; 226 mg, 1.0 mmol), pyrazole (**49a**; 136 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 70 °C for 1 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (9:1) to afford **50b** (241 mg) in 82% yield as colorless solid.

mp = 42–43 °C; R_f = 0.38 (9 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.04–7.94 (m, 2H), 7.53 (s, 1H), 7.50 (d, *J* = 1.6 Hz, 1H), 7.37–7.25 (m, 5H), 7.08 (t, *J* = 8.4 Hz, 2H), 6.24 (t, *J* = 2.0 Hz, 1H), 6.12 (dd, *J* = 5.2, 8.4 Hz, 1H), 4.50 (dd, *J* = 8.8,17.6 Hz, 1H), 3.58 (dd, *J* = 4.8, 17.6 Hz, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 194.8, 165.6 (d, *J* = 255 Hz), 140.5, 139.0, 132.7, 130.7 (d, *J* = 10.1 Hz, 2C), 129.6, 128.6 (2C), 127.8, 126.4 (2C), 115.5 (d, *J* = 21.2 Hz, 2C), 105.5, 60.6,

43.8; **^{19}F NMR (376 MHz, $CDCl_3$)** δ −104.58 to −104.66 (m); **IR (KBr)** ν_{max} 3111, 3034, 2920, 1682, 1599, 1157, 991, 756, 628 cm^{-1}; **MS (EI)** *m/z* (%) 296 (M^+ + 2, 51), 295 (M^+ + 1, 100), 259 (24), 227 (70), 123 (11), 101 (11), 69 (14); **Elemental analysis** calcd for $C_{18}H_{15}FN_2O$: C, 73.45; H, 5.14; N, 9.52. Found: C, 73.35; H, 5.21; N, 9.66.

1-(4-Chlorophenyl)-3-phenyl-3-(1*H*-pyrazol-1-yl)propan-1-one (50c):

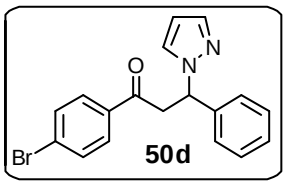


50c

Following the general procedure (GP-3); 1-(4-chlorophenyl)-3-phenylprop-2-yn-1-ol (**38c**; 243 mg, 1.0 mmol), pyrazole (**49a**; 136 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 70 °C for 1 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (9:1) to afford **50c** (246 mg) in 79% yield as colorless solid.

mp = 74–75 °C; R_f = 0.25 (9 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.90 (d, *J* = 8.0 Hz, 2H), 7.48 (d, *J* = 10.8 Hz, 2H), 7.40 (d, *J* = 8.4 Hz, 2H), 7.39–7.23 (m, 5H), 6.22 (s, 1H), 6.08 (dd, *J* = 4.8, 8.0 Hz, 1H), 4.49 (dd, *J* = 8.8, 17.6 Hz, 1H), 3.57 (dd, *J* = 4.8, 17.2 Hz, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 195.5, 140.6, 139.9, 139.3, 134.9, 129.8, 129.7 (2C), 128.9 (2C), 128.8 (2C), 128.1, 126.6 (2C), 105.7, 60.8, 44.1; **IR (KBr)** ν_{max} 3042, 2924, 1684, 1087, 750 cm^{-1}; **MS (EI)** *m/z* (%) 313 (M^+ + 2, 54), 312 (M^+ + 1, 54), 311 (M^+, 100), 139 (19), 107 (3); **Elemental analysis** calcd for $C_{18}H_{15}ClN_2O$: C, 69.57; H, 4.86; N, 9.01. Found: C, 69.37; H, 4.81; N, 9.12.

1-(4-Bromophenyl)-3-phenyl-3-(1*H*-pyrazol-1-yl)propan-1-one (50d):



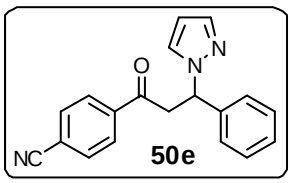
50d

Following the general procedure (GP-3); 1-(4-bromophenyl)-3-phenylprop-2-yn-1-ol (**38d**; 287 mg, 1.0 mmol), pyrazole (**49a**; 136 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 70 °C for 1 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (9:1) to afford **50d** (291 mg) in 82% yield as pale yellow solid.

mp = 81–82 °C; R_f = 0.40 (9 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.80 (d, *J* = 8.4 Hz, 2H), 7.54 (d, *J* = 8.8 Hz, 2H), 7.47 (dd, *J* = 1.6, 12.8 Hz, 2H), 7.36–7.22 (m, 5H), 6.21 (s, 1H), 6.07 (dd, *J* = 4.8, 8.4 Hz, 1H), 4.45 (dd, *J* = 8.8, 17.6 Hz, 1H), 3.53 (dd, *J* = 4.8, 17.6 Hz, 1H); **^{13}C**

NMR (101 MHz, $CDCl_3$) δ 195.4, 140.4, 139.0, 135.0, 131.7 (2C), 129.6, 129.5 (2C), 128.6 (2C), 128.3, 127.9, 126.4 (2C), 105.5, 60.5, 43.9; **IR (KBr)** ν_{max} 3108, 1684, 1585, 1070, 752, 702 cm^{-1}; **MS (EI)** *m/z* (%) 357 (M^+ + 2, 97), 355 (M^+, 100), 287 (32), 209 (30), 101 (20), 69 (16); **Elemental analysis** calcd for $C_{18}H_{15}BrN_2O$: C, 60.86; H, 4.26; N, 7.89. Found: C, 60.75; H, 4.31; N, 7.79.

4-(3-Phenyl-3-(1*H*-pyrazol-1-yl)propanoyl)benzonitrile (50e):

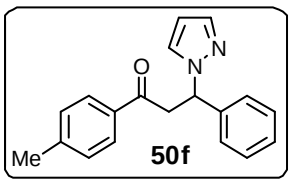


50e

Following the general procedure (GP-3); 4-(1-hydroxy-3-phenylprop-2-ynyl)benzonitrile (**38e**; 233 mg, 1.0 mmol), pyrazole (**49a**; 136 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 70 °C for 1 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (3:1) to afford **50e** (198 mg) in 66% yield as yellow solid.

mp = 117–118 °C; R_f = 0.50 (3 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.03 (d, *J* = 8.0 Hz, 2H), 7.72 (d, *J* = 8.4 Hz, 2H), 7.46 (d, *J* = 7.6 Hz, 2H), 7.39–7.22 (m, 5H), 6.22 (s, 1H), 6.07 (dd, *J* = 4.8, 8.8 Hz, 1H), 4.55 (dd, *J* = 8.8, 17.6 Hz, 1H), 3.53 (dd, *J* = 4.8, 17.6 Hz, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 195.5, 140.3, 139.4, 139.1, 132.4 (2C), 129.7, 128.8 (2C), 128.5 (2C), 128.1, 126.5 (2C), 117.8, 116.4, 105.8, 60.6, 44.3; **IR (KBr)** ν_{max} 3074, 2922, 2227, 1687, 754, 696, 625 cm^{-1}; **MS (EI)** *m/z* (%) 303 (M^+ + 2, 41), 302 (100), 130 (5), 69 (16); **Elemental analysis** calcd for $C_{19}H_{15}N_3O$: C, 75.73; H, 5.02; N, 13.94. Found: C, 75.61; H, 5.10; N, 13.86.

3-Phenyl-3-(1*H*-pyrazol-1-yl)-1-p-tolylpropan-1-one (50f):



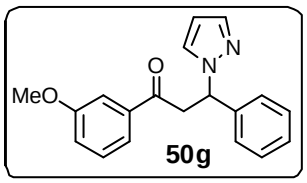
50f

Following the general procedure (GP-3); 3-phenyl-1-p-tolylprop-2-yn-1-ol (**38f**; 222 mg, 1.0 mmol), pyrazole (**49a**; 136 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 70 °C for 1 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (6:1) to afford **50f** (244 mg) in 84% yield as colorless solid.

mp = 41–42 °C; R_f = 0.37 (6 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.83 (d, *J* = 8.0 Hz, 2H), 7.47 (d, *J* = 12.8 Hz, 2H), 7.33–7.24 (m, 4H), 7.24–7.19 (m, 1H), 7.17 (d, *J* = 8.0 Hz, 2H), 6.18 (s, 1H), 6.10 (dd, *J* = 5.2, 8.0 Hz, 1H), 4.42 (dd, *J* = 8.4, 17.2 Hz, 1H), 3.58 (dd, *J* = 5.2,

17.6 Hz, 1H), 2.32 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 195.9, 143.9, 140.6, 139.0, 133.8, 129.5, 129.0 (2C), 128.5 (2C), 128.1 (2C), 127.7, 126.5 (2C), 105.3, 60.6, 43.8, 21.4; **IR (KBr)** ν_{max} 3032, 2920, 1682, 1454, 817, 752, 628 cm^{-1}; **MS (EI)** *m/z* (%) 292 (M^+ + 2, 59), 291 (M^+ + 1, 100), 255 (14), 223 (59), 119 (14), 91 (8); **Elemental analysis** calcd for $C_{19}H_{18}N_2O$: C, 78.59; H, 6.25; N, 9.65. Found: C, 78.47; H, 6.32; N, 9.55.

1-(3-Methoxyphenyl)-3-phenyl-3-(1*H*-pyrazol-1-yl)propan-1-one (50g):

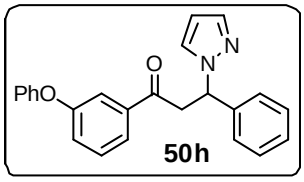


50g

Following the general procedure (GP-3); 1-(3-methoxyphenyl)-3-phenylprop-2-yn-1-ol (**38g**; 238 mg, 1.0 mmol), pyrazole (**49a**; 136 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 70 °C for 2 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (6:1) to afford **50g** (251 mg) in 82% yield as light yellow thick liquid.

R_f = 0.36 (6 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.55 (d, *J* = 7.6 Hz, 1H), 7.50 (s, 1H), 7.47 (bd, *J* = 5.6 Hz, 2H), 7.35–7.21 (m, 6H), 7.07 (dd, *J* = 2.0, 8.0 Hz, 1H), 6.21 (s, 1H), 6.09 (dd, *J* = 5.2, 8.0 Hz, 1H), 4.45 (dd, *J* = 8.8, 18.0 Hz, 1H), 3.78 (s, 3H), 3.64 (dd, *J* = 5.2, 17.6 Hz, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 196.0, 159.5, 140.5, 138.9, 137.5, 129.4, 129.3, 128.5 (2C), 127.7, 126.4 (2C), 120.6, 119.7, 111.9, 105.3, 60.5, 55.0, 43.9; **IR (Neat)** ν_{max} 3065, 2939, 1682, 1454, 1045, 754, 626 cm^{-1}; **MS (EI)** *m/z* (%) 308 (M^+ + 2, 80), 271 (39), 239 (100), 135 (19), 101 (16), 69 (14); **Elemental analysis** calcd for $C_{19}H_{18}N_2O_2$: C, 74.49; H, 5.92; N, 9.14. Found: C, 74.36; H, 5.98; N, 9.25.

1-(3-Phenoxyphenyl)-3-phenyl-3-(1*H*-pyrazol-1-yl)propan-1-one (50h):



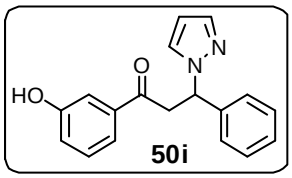
50h

Following the general procedure (GP-3); 1-(3-phenoxyphenyl)-3-phenylprop-2-yn-1-ol (**38h**; 300 mg, 1.0 mmol), pyrazole (**49a**; 136 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 70 °C for 2 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (6:1) to afford **50h** (265 mg) in 72% yield as yellow solid.

R_f = 0.68 (6 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.67 (d, *J* = 7.6 Hz, 1H), 7.58 (s, 1H) 7.49 (s, 1H), 7.46 (s, 1H), 7.41–7.22 (m, 8H), 7.18 (dd, *J* = 1.6, 8.0 Hz, 1H), 7.11 (t, *J* = 7.6

Hz, 1H), 6.98 (d, *J* = 8.4 Hz, 2H), 6.21 (s, 1H), 6.07 (dd, *J* = 5.2, 8.0 Hz, 1H), 4.44 (dd, *J* = 8.8, 18.0 Hz, 1H), 3.58 (dd, *J* = 5.2, 17.6 Hz, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 195.7, 157.5, 156.3, 140.5, 139.0, 138.1, 129.8, 129.7 (2C), 129.5, 128.6 (2C), 127.8, 126.4 (2C), 123.6, 123.3, 122.8, 118.9 (2C), 117.7, 105.4, 60.5, 44.1; **IR (KBr)** ν_{max} 3032, 2916, 1687, 1581, 1240, 752, 696 cm^{-1}; **MS (EI)** *m/z* (%) 370 (M^+ + 2, 51), 369 (M^+ + 1, 100), 333 (35), 301 (76), 197 (11), 101 (11), 69 (8); **Elemental analysis** calcd for $C_{24}H_{20}N_2O_2$: C, 78.24; H, 5.47; N, 7.60. Found: C, 78.32; H, 5.43; N, 7.52.

1-(3-Hydroxyphenyl)-3-phenyl-3-(1*H*-pyrazol-1-yl)propan-1-one (50i):

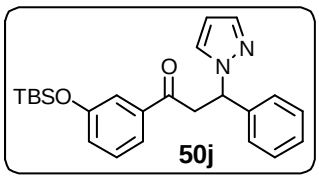


50i

Following the general procedure (GP-3); 3-(1-hydroxy-3-phenylprop-2-ynyl)phenol (**38i**; 224 mg, 1.0 mmol), pyrazole (**49a**; 136 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 70 °C for 3 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (2:1) to afford **50i** (225 mg) in 77% yield as colorless solid.

mp = 129–130 °C; R_f = 0.53 (2 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.70–8.00 (bs, –OH, 1H), 7.55 (dd, *J* = 2.0, 16.4 Hz, 2H), 7.40–7.36 (m, 1H), 7.35 (bt, *J* = 2.4 Hz, 1H), 7.31–7.24 (m, 5H), 7.14 (t, *J* = 8.0 Hz, 1H), 6.91 (dd, *J* = 2.4, 8.0 Hz, 1H), 6.27 (t, *J* = 2.4 Hz, 1H), 6.10 (dd, *J* = 5.2, 8.4 Hz, 1H), 4.42 (dd, *J* = 8.8, 18.0 Hz, 1H), 3.63 (dd, *J* = 5.2, 18.0 Hz, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 196.4, 156.7, 140.1, 139.3, 137.5, 130.5, 129.6, 128.8 (2C), 128.1, 126.6 (2C), 120.8, 119.9, 115.1, 105.9, 60.9, 43.8; **IR (KBr)** ν_{max} 3112, 1684, 1587, 1280, 750, 698, 625 cm^{-1}; **MS (EI)** *m/z* (%) 294 (M^+ + 2, 100), 257 (5), 225 (27), 121 (11), 101 (19), 69 (27); Anal. calcd for $C_{18}H_{16}N_2O_2$: C, 73.95; H, 5.52; N, 9.58. Found: C, 73.85; H, 5.48; N, 9.68.

1-(3-(*tert*-Butyldimethylsilyloxy)phenyl)-3-phenyl-3-(1*H*-pyrazol-1-yl)propan-1-one (50j):



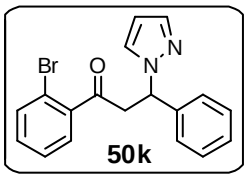
50j

Following the general procedure (GP-3); 1-(3-(*tert*-butyldimethylsilyloxy)phenyl)-3-phenylprop-2-yn-1-ol (**38j**; 339 mg, 1.0 mmol), pyrazole (**49a**; 136 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 70 °C for 3 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (9:1) to

afford **50j** (53 mg) in 13% yield as brown color thick liquid along with **50i** (188 mg) in 64% yield.

R_f = 0.55 (9 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.58 (d, *J* = 8.0 Hz, 1H), 7.51 (d, *J* = 10.8 Hz, 2H), 7.42 (s, 1H), 7.38–7.23 (m, 6H), 7.03 (d, *J* = 8.0 Hz, 1H), 6.24 (bd, *J* = 1.2 Hz, 1H), 6.10 (t, *J* = 7.6 Hz, 1H), 4.45 (dd, *J* = 8.0, 17.6 Hz, 1H), 6.63 (dd, *J* = 4.8, 17.6 Hz, 1H), 0.99 (s, 9H), 0.21 (s, 6H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 196.4, 160.0, 140.7, 139.3, 138.0, 129.7, 129.6, 128.8 (2C), 128.0, 126.7 (2C), 125.2, 121.3, 119.4, 105.5, 60.8, 44.3, 25.6 (3C), 18.1, −4.4 (2C); **IR (Neat)** ν_{max} 3065, 2957, 1687, 1581, 1280, 931, 837, 625 cm^{-1}; **MS (EI)** *m/z* (%) 408 (M^+ + 1, 35), 390 (23), 376 (100), 344 (100), 316 (8), 288 (8), 79 (10), 65 (6); **Elemental analysis** Calcd for $C_{24}H_{30}N_2O_2Si$: C, 70.90; H, 7.44; N, 6.89. Found: C, 71.21; H, 7.48; N, 6.75.

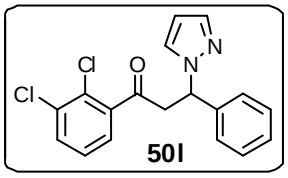
1-(2-Bromophenyl)-3-phenyl-3-(1*H*-pyrazol-1-yl)propan-1-one (50k):



Following the general procedure (GP-3); 1-(2-bromophenyl)-3-phenylprop-2-yn-1-ol (**38k**; 287 mg, 1.0 mmol), pyrazole (**49a**; 136 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 70 °C for 12 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (12:1) to afford **50k** (234 mg) in 66% yield as yellow thick liquid.

R_f = 0.31 (12 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.60–7.54 (m, 2H), 7.47 (d, *J* = 2.0 Hz, 1H), 7.39–7.20 (m, 8H), 6.26 (t, *J* = 2.0 Hz, 1H), 6.08 (dd, *J* = 5.2, 9.6 Hz, 1H), 4.38 (dd, *J* = 9.2, 17.2 Hz, 1H), 3.63 (dd, *J* = 4.8, 17.2 Hz, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 200.1, 140.7, 140.0, 139.0, 133.4, 131.7, 129.6, 129.0 (2C), 128.7, 128.0, 127.2, 126.5 (2C), 118.5, 105.6, 60.9, 47.9; **IR (Neat)** ν_{max} 3030, 2918, 1699, 1284, 875 cm^{-1}; **MS (EI)** *m/z* (%) 358 (M^+ + 3, 30), 357 (M^+ + 2, 100), 356 (M^+ + 1, 30), 355 (M^+, 100), 321 (8), 319 (8), 289 (30), 287 (30), 185 (14), 183 (14), 101 (8); **Elemental analysis** calcd for $C_{18}H_{15}BrN_2O$: C, 60.86; H, 4.26; N, 7.89. Found: C, 60.75; H, 4.32; N, 7.68.

1-(2,3-Dichlorophenyl)-3-phenyl-3-(1*H*-pyrazol-1-yl)propan-1-one (50l):

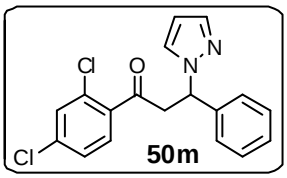


Following the general procedure (GP-3); 1-(2,3-dichlorophenyl)-3-phenylprop-2-yn-1-ol (**38l**; 277 mg, 1.0 mmol), pyrazole (**49a**; 136 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in

toluene (2.0 mL) was heated at 70 °C for 2 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (9:1) to afford **50l** (279 mg) in 81% yield as pale yellow thick liquid.

R_f = 0.30 (9 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.53 (s, 1H), 7.48 (dd, *J* = 1.2, 8.0 Hz, 1H), 7.44 (s, 1H), 7.38–7.22 (m, 6H), 7.17 (t, *J* = 7.6 Hz, 1H), 6.24 (s, 1H), 6.06 (dd, *J* = 4.8, 9.2 Hz, 1H), 4.35 (dd, *J* = 10.0, 17.6 Hz, 1H), 3.57 (dd, *J* = 4.4, 17.2 Hz, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 198.9, 141.0, 139.8, 138.9, 133.6, 132.0, 129.5, 128.6 (2C), 128.5, 127.9, 127.4, 126.8, 126.4 (2C), 105.6, 60.9, 48.2; **IR (Neat)** ν_{max} 3065, 2924, 1701, 1410, 736, 625 cm^{-1}; **MS (EI)** *m/z* (%) 347 (M^+ + 2, 84), 346 (M^+ + 1, 38), 345 (M^+, 100), 277 (14), 173 (22), 69 (11); **Elemental analysis** calcd for $C_{18}H_{14}Cl_2N_2O$: C, 62.62; H, 4.09; N, 8.11. Found: C, 62.48; H, 4.15; N, 8.25.

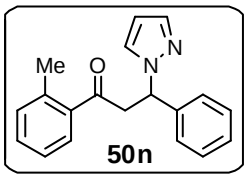
1-(2,4-Dichlorophenyl)-3-phenyl-3-(1*H*-pyrazol-1-yl)propan-1-one (50m):



Following the general procedure (GP-3); Following the general procedure (GP-3); 1-(2,4-dichlorophenyl)-3-phenylprop-2-yn-1-ol (**38m**; 277 mg, 1.0 mmol), pyrazole (**49a**; 136 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 70 °C for 2 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (9:1) to afford **50m** (265 mg) in 77% yield as yellow thick liquid.

R_f = 0.33 (9 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.47 (bd, *J* = 1.2 Hz, 1H), 7.38 (dd, *J* = 2.8, 11.6 Hz, 3H), 7.34–7.19 (m, 6H), 6.21 (t, *J* = 2.0 Hz, 1H), 6.02 (dd, *J* = 4.8, 9.6 Hz, 1H), 4.35 (dd, *J* = 9.6, 17.2 Hz, 1H), 3.53 (dd, *J* = 4.8, 17.2 Hz, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 198.2, 140.0, 138.9, 137.4, 136.8, 131.9, 130.6, 130.1, 129.6, 128.7 (2C), 128.0, 127.1, 126.4 (2C), 105.7, 61.0, 48.1; **IR (Neat)** ν_{max} 3063, 2926, 1697, 1375, 750, 625 cm^{-1}; **MS (EI)** *m/z* (%) 347 (M^+ + 2, 84), 346 (M^+ + 1, 41), 345 (M^+, 100), 277 (11), 173 (24), 147 (8), 69 (8); **Elemental analysis** calcd for $C_{18}H_{14}Cl_2N_2O$: C, 62.62; H, 4.09; N, 8.11. Found: C, 62.71; H, 4.03; N, 8.07.

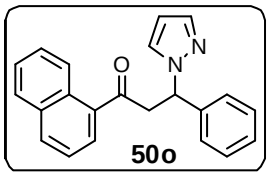
3-Phenyl-3-(1*H*-pyrazol-1-yl)-1-*o*-tolylpropan-1-one (50n):



Following the general procedure (GP-3); 3-phenyl-1-*o*-tolylprop-2-yn-1-ol (**38n**; 222 mg, 1.0 mmol), pyrazole (**49a**; 136 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 70 °C for 19 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (9:1) to afford **50n** (223 mg) in 77% yield as pale yellow thick liquid.

R_f = 0.43 (9 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.68 (d, *J* = 7.6 Hz, 1H), 7.51 (s, 1H), 7.46 (s, 1H), 7.37–7.16 (m, 8H), 6.22 (s, 1H), 6.06 (dd, *J* = 5.2, 8.8 Hz, 1H), 4.36 (dd, *J* = 9.2, 17.6 Hz, 1H), 3.51 (dd, *J* = 5.2, 17.2 Hz, 1H), 2.34 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 200.2, 140.4, 139.0, 137.9, 137.5, 131.7, 131.3, 129.5, 128.6 (2C), 128.4, 127.8, 126.5 (2C), 125.5, 105.4, 60.9, 46.8, 20.8; **IR (Neat)** ν_{max} 3063, 2966, 1689, 1494, 1089, 750, 625 cm^{-1}; **MS (EI)** *m/z* (%) 292 (M^+ + 2, 75), 255 (59), 223 (100), 119 (16), 91 (12), 69 (10); **Elemental analysis** calcd for $C_{19}H_{18}N_2O$: C, 78.59; H, 6.25; N, 9.65. Found: C, 78.66; H, 6.21; N, 9.58.

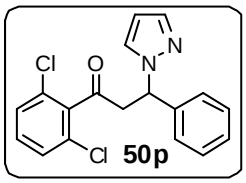
1-(Naphthalen-1-yl)-3-phenyl-3-(1*H*-pyrazol-1-yl)propan-1-one (50o):



Following the general procedure (GP-3); 1-(naphthalen-1-yl)-3-phenylprop-2-yn-1-ol (**38o**; 258 mg, 1.0 mmol), pyrazole (**49a**; 136 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 70 °C for 2 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (9:1) to afford **50o** (283 mg) in 87% yield as pale yellow solid.

mp = 77–78 °C; R_f = 0.21 (9 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.39 (d, *J* = 8.0 Hz, 1H), 7.87 (d, *J* = 7.2 Hz, 2H), 7.76 (d, *J* = 7.2 Hz, 1H), 7.49 (s, 1H), 7.48–7.40 (m, 3H), 7.36 (t, *J* = 8.0 Hz, 1H), 7.33–7.17 (m, 5H), 6.19 (s, 1H), 6.15 (dd, *J* = 5.2, 8.8 Hz, 1H), 4.50 (dd, *J* = 9.2, 17.2 Hz, 1H), 3.61 (dd, *J* = 4.8, 17.2 Hz, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 200.2, 140.4, 139.1, 135.3, 133.6, 132.7, 129.9, 129.6, 128.6 (2C), 128.2, 127.9, 127.8, 127.7, 126.5 (2C), 126.3, 125.5, 124.2, 105.5, 61.1, 47.3; **IR (KBr)** ν_{max} 3036, 1743, 1682, 1396, 752 cm^{-1}; **MS (EI)** *m/z* (%) 328 (M^+ + 2, 100), 291 (27), 259 (95), 155 (49), 144 (11), 69 (3); **Elemental analysis** calcd for $C_{22}H_{18}N_2O$: C, 80.96; H, 5.56; N, 8.58. Found: C, 80.75; H, 5.51; N, 8.49.

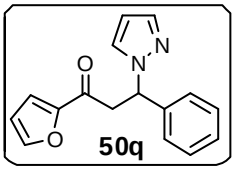
1-(2,6-Dichlorophenyl)-3-phenyl-3-(1*H*-pyrazol-1-yl)propan-1-one (50p):



Following the general procedure (GP-3); 1-(2,6-dichlorophenyl)-3-phenylprop-2-yn-1-ol (**38p**; 277 mg, 1.0 mmol), pyrazole (**49a**; 136 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 70 °C for 19 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (9:1) to afford **50p** (241 mg) in 70% yield as pale yellow liquid.

R_f = 0.33 (9 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.55 (d, *J* = 6.8 Hz, 2H), 7.45–7.36 (m, 3H), 7.36–7.19 (m, 5H), 6.25 (s, 1H), 6.11 (t, *J* = 7.2 Hz, 1H), 4.27 (dd, *J* = 8.0, 18.8 Hz, 1H), 3.72 (dd, *J* = 5.2, 18.8 Hz, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 198.4, 139.6, 139.3, 138.5, 130.6, 130.3, 129.5 (2C), 128.5 (2C), 128.1 (2C), 127.9, 126.8 (2C), 105.3, 59.8, 48.9; **IR (Neat)** ν_{max} 3067, 2916, 1712, 1431, 779, 625 cm^{-1}; **MS (EI)** *m/z* (%) 347 (M^+ + 2, 86), 345 (M^+, 100), 309 (49), 277 (22), 173 (22), 69 (16); **Elemental analysis** calcd for $C_{18}H_{14}Cl_2N_2O$: C, 62.62; H, 4.09; N, 8.11. Found: C, 62.51; H, 4.15; N, 8.21.

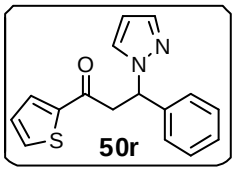
1-(Furan-2-yl)-3-phenyl-3-(1*H*-pyrazol-1-yl)propan-1-one (50q):



Following the general procedure (GP-3); 1-(furan-2-yl)-3-phenylprop-2-yn-1-ol (**38q**; 198 mg, 1.0 mmol), pyrazole (**49a**; 136 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 70 °C for 1 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (6:1) to afford **50q** (187 mg) in 70% yield as light brown solid.

mp = 98–99 °C; R_f = 0.28 (6 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.58 (s, 1H), 7.50 (d, *J* = 16.8 Hz, 2H), 7.32 (bs, 4H), 7.31–7.25 (m, 1H), 7.22 (bd, *J* = 3.2 Hz, 1H), 6.52 (bt, *J* = 1.6 Hz, 1H), 6.22 (s, 1H), 6.07 (dd, *J* = 5.6, 8.4 Hz, 1H), 4.30 (dd, *J* = 8.8, 16.8 Hz, 1H), 3.53 (dd, *J* = 5.2, 17.2 Hz, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 185.1, 152.0, 146.6, 140.2, 139.1, 129.5, 128.6 (2C), 127.8, 126.5 (2C), 117.7, 112.2, 105.4, 60.2, 43.6; **IR (KBr)** ν_{max} 3115, 2922, 1653, 756, 698, 625 cm^{-1}; **MS (EI)** *m/z* (%) 268 (M^+ + 2, 86), 231 (7), 199 (100), 157 (9), 101 (3), 69 (14); **Elemental analysis** calcd for $C_{16}H_{14}N_2O_2$: C, 72.16; H, 5.30; N, 10.52. Found: C, 72.28; H, 5.36; N, 10.

3-Phenyl-3-(1*H*-pyrazol-1-yl)-1-(thiophen-2-yl)propan-1-one (50r):

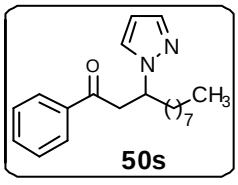


50r

Following the general procedure (GP-3); 3-phenyl-1-(thiophen-2-yl)prop-2-yn-1-ol (**38r**; 214 mg, 1.0 mmol), pyrazole (**49a**; 136 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 70 °C for 1 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (9:1) to afford **50r** (259 mg) in 92% yield as brown solid.

mp = 42–43 °C; R_f = 0.18 (9 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.76 (bd, *J* = 3.6 Hz, 1H), 7.58 (bd, *J* = 4.8 Hz, 1H), 7.48 (dd, *J* = 1.2, 17.6 Hz, 2H), 7.35–7.22 (m, 5H), 7.07 (bt, *J* = 3.6 Hz, 1H), 6.21 (s, 1H), 6.07 (dd, *J* = 5.6, 8.4 Hz, 1H), 4.38 (dd, *J* = 8.4, 16.8 Hz, 1H), 3.59 (dd, *J* = 5.2, 17.2 Hz, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 189.3, 143.5, 140.3, 139.3, 134.1, 132.4, 129.7, 128.7 (2C), 128.1, 127.9, 126.6 (2C), 105.5, 60.6, 44.6; **IR (KBr)** ν_{max} 3103, 2924, 1662, 1053, 750, 625 cm^{-1}; **MS (EI)** *m/z* (%) 284 (M^+ + 2, 35), 283 (100), 247 (5), 215 (35), 111 (3); **Elemental analysis** Calcd for $C_{16}H_{14}N_2OS$: C, 68.06; H, 5.00; N, 9.92. Found: C, 68.15; H, 5.12; N, 9.86.

1-Phenyl-3-(1*H*-pyrazol-1-yl)undecan-1-one (50s):

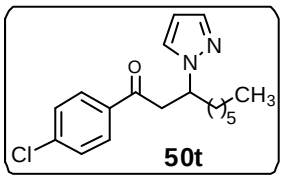


50s

Following the general procedure (GP-3); 1-phenylundec-2-yn-1-ol (**38s**; 244 mg, 1.0 mmol), pyrazole (**49a**; 136 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 80 °C for 32 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (19:1) to afford **50s** (262 mg) in 84% yield as colorless solid.

mp = 43–44 °C; R_f = 0.52 (19 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.91 (d, *J* = 8.4 Hz, 2H), 7.54 (bt, *J* = 7.2 Hz, 1H), 7.48 (d, *J* = 13.6 Hz, 2H), 7.42 (t, *J* = 7.6 Hz, 2H), 6.15 (bt, *J* = 2.0 Hz, 1H), 4.91–4.79 (m, 1H), 3.80 (dd, *J* = 7.2, 17.2 Hz, 1H), 3.32 (dd, *J* = 5.2, 17.6 Hz, 1H), 2.12–2.01 (m, 1H), 1.87–1.74 (m, 1H), 1.29–1.18 (m, 11 H), 1.12–0.97 (m, 1H), 0.86 (t, *J* = 6.8 Hz, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 197.6, 139.5, 136.6, 133.3, 130.0, 128.5 (2C), 128.0 (2C), 104.2, 58.0, 44.0, 35.3, 31.7, 29.3, 29.1, 29.0, 26.1, 22.6, 14.0; **IR (KBr)** ν_{max} 3102, 2918, 1674, 1446, 1095, 760, 625 cm^{-1}; **MS (EI)** *m/z* (%) 314 (M^+ + 2, 49), 313 (M^+ + 1, 100), 277 (11), 245 (19), 101 (3), 69 (6); **Elemental analysis** calcd for $C_{20}H_{28}N_2O$: C, 76.88; H, 9.03; N, 8.97. Found: C, 76.81; H, 9.08; N, 8.85.

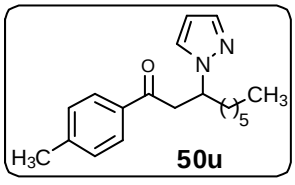
1-(4-Chlorophenyl)-3-(1*H*-pyrazol-1-yl)nonan-1-one (50t):



Following the general procedure (GP-3); 1-(4-chlorophenyl)non-2-yn-1-ol (**38t**; 251 mg, 1.0 mmol), pyrazole (**49a**; 136 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 80 °C for 50 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (9:1) to afford **50t** (290 mg) in 91% yield as colorless liquid.

R_f = 0.45 (9 : 1 hexane–EtOAc); **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.82 (d, *J* = 8.5 Hz, 2H), 7.46 (dd, *J* = 1.5, 22 Hz, 2H), 7.37 (d, *J* = 8.5 Hz, 2H), 6.13 (bt, *J* = 2.0 Hz, 1H), 4.84–4.80 (m, 1H), 3.78 (dd, *J* = 7.5, 17.0 Hz, 1H), 3.24 (dd, *J* = 5.0, 17.5 Hz, 1H), 2.13–1.99 (m, 1H), 1.87–1.73 (m, 1H), 1.33–1.13 (m, 7H), 1.09–0.98 (m, 1H), 0.84 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR (125 MHz, $CDCl_3$)** δ 196.4, 139.7, 139.5, 134.8, 130.0, 129.4 (2C), 128.8 (2C), 104.3, 58.0, 43.8, 35.3, 31.5, 28.6, 25.9, 22.4, 13.9; **IR (Neat)** ν_{max} 2926, 1687, 1589, 1091, 831, 750 cm^{-1}; **MS (EI)** *m/z* (%) 322 (M^+ + 3, 11), 321 (M^+ + 2, 51), 320 (M^+ + 1, 38), 319 (M^+, 100), 146 (5), 69 (3); **Elemental analysis** calcd for $C_{18}H_{23}ClN_2O$: C, 67.81; H, 7.27; N, 8.79. Found: C, 67.71; H, 7.21; N, 8.68.

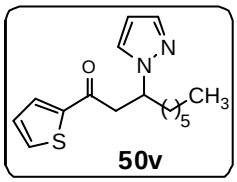
3-(1*H*-Pyrazol-1-yl)-1-*p*-tolylnonan-1-one (50u):



Following the general procedure (GP-3); 1-*p*-tolylnon-2-yn-1-ol (**38u**; 230 mg, 1.0 mmol), pyrazole (**49a**; 136 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 80 °C for 77 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (12:1) to afford **50u** (223 mg) in 75% yield as pale yellow thick liquid.

R_f = 0.41 (12 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.82 (d, *J* = 8.0 Hz, 2H), 7.50 (dd, *J* = 1.2, 15.6 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 6.16 (bs, 1H), 4.92–4.78 (m, 1H), 3.77 (dd, *J* = 7.6, 17.2 Hz, 1H), 3.32 (dd, *J* = 5.2, 17.2 Hz, 1H), 2.39 (s, 3H), 2.13–2.02 (m, 1H), 1.89–1.78 (m, 1H), 1.35–1.13 (m, 7H), 1.11–0.96 (m, 1H), 0.84 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 197.2, 144.1, 139.5, 134.2, 130.0, 129.2 (2C), 128.2 (2C), 104.2, 58.2, 44.0, 35.4, 31.6, 28.8, 26.1, 22.5, 21.6, 14.0; **IR (Neat)** ν_{max} 3103, 2928, 1682, 1574, 1043, 812, 748, 625 cm^{-1}; **MS (EI)** *m/z* (%) 300 (M^+ + 2, 62), 299 (M^+ + 1, 100), 263 (8), 231 (27), 179 (3), 91 (3); **Elemental analysis** calcd for $C_{19}H_{26}N_2O$: C, 76.47; H, 8.78; N, 9.39. Found: C, 76.58; H, 8.68; N, 9.21.

3-(1*H*-Pyrazol-1-yl)-1-(thiophen-2-yl)nonan-1-one (50v):

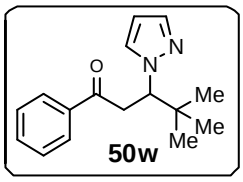


50v

Following the general procedure (GP-3); 1-(thiophen-2-yl)non-2-yn-1-ol (**38v**; 222 mg, 1.0 mmol), pyrazole (**49a**; 136 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 80 °C for 17 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (9:1) to afford **50v** (223 mg) in 77% yield as pale yellow thick liquid.

R_f = 0.38 (9 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.65 (dt, *J* = 1.2, 22 Hz, 2H), 7.51 (d, *J* = 1.2 Hz, 1H), 7.44 (d, *J* = 2.4 Hz, 1H), 7.10–7.06 (m, 1H), 6.14 (dd, *J* = 1.6, 3.2 Hz, 1H), 4.87–4.73 (m, 1H), 3.71 (dd, *J* = 7.6, 16.4 Hz, 1H), 3.27 (dd, *J* = 5.2, 16.4 Hz, 1H), 2.15–2.00 (m, 1H), 1.86–1.74 (m, 1H), 1.35–1.08 (m, 7H), 1.08–0.93 (m, 1H), 0.85 (t, *J* = 6.8 Hz, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 190.4, 144.0, 139.6, 134.1, 132.5, 130.1, 128.2, 104.3, 58.3, 44.8, 35.3, 31.6, 28.7, 26.0, 22.5, 14.0; **IR (Neat)** ν_{max} 3103, 2926, 1660, 1516, 1047, 748, 625 cm^{-1}; **MS (EI)** *m/z* (%) 292 (M^+ + 2, 51), 291 (M^+ + 1, 100), 255 (8), 223 (35), 101 (5), 69 (8); **Elemental analysis** calcd for $C_{16}H_{22}N_2OS$: C, 66.17; H, 7.64; N, 9.65. Found: C, 66.32; H, 7.61; N, 9.59.

4,4-Dimethyl-1-phenyl-3-(1*H*-pyrazol-1-yl)pentan-1-one (50w):

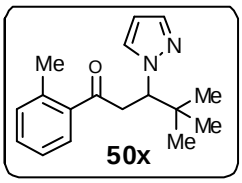


50w

Following the general procedure (GP-3); 4,4-dimethyl-1-phenylpent-2-yn-1-ol (**38w**; 188 mg, 1.0 mmol), pyrazole (**49a**; 136 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 80 °C for 96 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (9:1) to afford **50w** (136 mg) in 53% yield as colorless solid.

mp = 37–38 °C; R_f = 0.43 (9 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.94 (d, *J* = 6.4 Hz, 2H), 7.59–7.50 (m, 1H), 7.50–7.40 (m, 4H), 6.14 (bt, *J* = 1.6 Hz, 1H), 4.68 (dd, J = 2.0, 8.0 Hz, 1H), 4.23 (dd, *J* = 8.0, 14.0 Hz, 1H), 3.20 (dd, *J* = 2.0, 14.0 Hz, 1H), 1.03 (s, 9H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 197.9, 138.8, 136.9, 133.1, 131.7, 128.5 (2C), 128.1 (2C), 103.8, 66.0, 38.3, 35.4, 27.2 (3C); **IR (KBr)** ν_{max} 3109, 2959, 1684, 1402, 754, 626 cm^{-1}; **MS (EI)** *m/z* (%) 258 (M^+ + 2, 43), 257 (M^+ + 1, 100), 221 (16), 189 (43), 101 (11), 69 (8); **Elemental analysis** calcd for $C_{16}H_{20}N_2O$: C, 74.97; H, 7.86; N, 10.93. Found: C, 74.85; H, 7.95; N, 11.07.

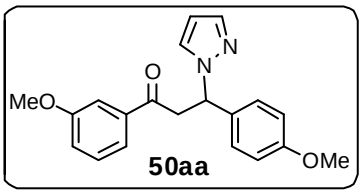
4,4-Dimethyl-3-(1*H*-pyrazol-1-yl)-1-*o*-tolylpentan-1-one (50x):



Following the general procedure (GP-3); 4,4-dimethyl-1-*o*-tolylpent-2-yn-1-ol (**38x**; 202 mg, 1.0 mmol), pyrazole (**49a**; 136 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 80 °C for 96 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (32:1) to afford **50x** (65 mg) in 24% yield as colorless oil.

R_f = 0.40 (32 : 1 hexane–EtOAc); **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.62 (d, *J* = 6.0 Hz, 1H), 7.46 (dd, *J* = 2.0, 11 Hz, 2H), 7.34 (td, *J* = 1.0, 7.5 Hz, 1H), 7.24 (t, *J* = 7.5 Hz, 1H), 7.18 (d, *J* = 7.5 Hz, 1H), 6.16 (bt, *J* = 2.0 Hz, 1H), 4.36 (dd, *J* = 8.0, 11 Hz, 1H), 4.10 (dd, *J* = 11, 17 Hz, 1H), 3.12 (dd, *J* = 3.0, 17 Hz, 1H), 2.28 (s, 3H), 1.01 (s, 9H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 202.2, 138.8, 138.3, 137.7, 131.7 (2C), 131.2, 128.3, 125.6, 103.9, 66.5, 41.2, 35.3, 27.1 (3C), 20.7; **IR (Neat)** ν_{max} 2962, 1687, 1093, 750, 625 cm^{-1}; **MS (EI)** *m/z* (%) 272 (M^+ + 2, 22), 271 (M^+ + 1, 100), 228 (3), 186 (11), 141 (5), 109 (11); **Elemental analysis** calcd for $C_{17}H_{22}N_2O$: C, 75.52; H, 8.20; N, 10.36. Found: C, 75.39; H, 8.26; N, 10.45.

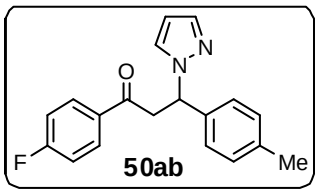
1-(3-Methoxyphenyl)-3-(4-methoxyphenyl)-3-(1*H*-pyrazol-1-yl)propan-1-one (50aa):



Following the general procedure (GP-3); 1-(3-methoxyphenyl)-3-(4-methoxyphenyl)prop-2-yn-1-ol (**38aa**; 268 mg, 0.5 mmol), pyrazole (**49a**; 68 mg, 1.0 mmol), and cesium carbonate (163 mg, 0.5 mmol) in toluene (1.0 mL) was heated at 70 °C for 1 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (3:1) to afford **50aa** (278 mg) in 83% yield as pale yellow solid.

mp = 62–63 °C; R_f = 0.42 (3 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.56 (d, *J* = 7.6 Hz, 1H), 7.50 (s, 1H), 7.46 (s, 2H), 7.33 (t, *J* = 8.0 Hz, 1H), 7.30–7.23 (m, 2H), 7.09 (dd, *J* = 1.6, 8.0 Hz, 1H), 6.85 (d, *J* = 8.4 Hz, 2H), 6.21 (s, 1H), 6.04 (bt, *J* = 7.2 Hz. 1H), 4.40 (dd, *J* = 8.0, 17.6 Hz, 1H), 3.81 (s, 3H), 3.76 (s, 3H), 3.64 (dd, *J* = 5.6, 17.6 Hz, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 196.5, 159.7, 159.2, 139.2, 137.8, 132.5, 129.5, 129.4, 128.0 (2C), 120.8, 120.0, 114.0 (2C), 112.1, 105.4, 60.3, 59.3, 55.2, 44.2; **IR (KBr)** ν_{max} 3057, 2939, 1682, 1612, 739 cm^{-1}; **MS (EI)** *m/z* (%) 338 (M^+ + 2, 57), 337 (M^+ + 1, 100); **Elemental analysis** calcd for $C_{20}H_{20}N_2O_3$: C, 71.41; H, 5.99; N, 8.33. Found: C, 71.56; H, 6.12; N, 8.21.

1-(4-Fluorophenyl)-3-(1*H*-pyrazol-1-yl)-3-*p*-tolylpropan-1-one (50ab):

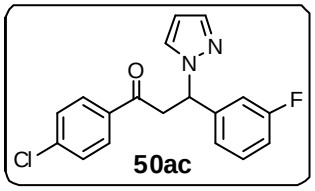


50ab

Following the general procedure (GP-3); 1-(4-fluorophenyl)-3-*p*-tolylprop-2-yn-1-ol (**38ab**; 240 mg, 1.0 mmol), pyrazole (**49a**; 136 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 70 °C for 1 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (6:1) to afford **50ab** (249 mg) in 81% yield as yellow thick liquid.

R_f = 0.52 (6 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.99 (dd, *J* = 4.8, 10.4 Hz, 2H), 7.47 (dd, *J* = 1.6, 12.8 Hz, 2H), 7.17 (dd, *J* = 8.0, 26 Hz, 4H), 7.08 (t, *J* = 4.8 Hz, 2H), 6.21 (t, *J* = 2.0 Hz, 1H), 6.05 (dd, *J* = 5.2, 8.4 Hz, 1H), 4.40 (dd, *J* = 8.4, 17.2 Hz, 1H), 3.57 (dd, *J* = 5.2, 17.6 Hz, 1H), 2.31 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 195.1, 165.8 (d, *J* = 256 Hz), 139.2, 137.8, 137.5, 133.0 (d, *J* = 3.0 Hz), 130.8 (d, *J* = 9.5 Hz, 2C), 129.6, 129.4 (2C), 126.6 (2C), 115.6 (d, *J* = 22.0 Hz, 2C), 105.5, 60.6, 44.0, 21.0; **^{19}F NMR (376 MHz, $CDCl_3$)** δ −104.63 to −104.70 (m); **IR (Neat)** ν_{max} 3105, 2922, 1684, 1599, 1508, 841, 752 cm^{-1}; **MS (EI)** *m/z* (%) 311 (M^+ + 3, 89), 309 (M^+ + 1, 100), 299 (57), 277 (73), 243 (5), 209 (14), 173 (3); **Elemental analysis** Calcd for $C_{19}H_{17}FN_2O$: C, 74.01; H, 5.56; N, 9.08. Found: C, 74.16; H, 5.49; N, 9.15.

1-(4-Chlorophenyl)-3-(3-fluorophenyl)-3-(1*H*-pyrazol-1-yl)propan-1-one (50ac):



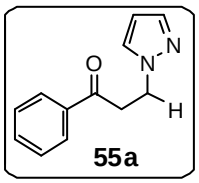
50ac

Following the general procedure (GP-3); 1-(4-chlorophenyl)-3-(3-fluorophenyl)prop-2-yn-1-ol (**38ac**; 260 mg, 1.0 mmol), pyrazole (**49a**; 136 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 70 °C for 1 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (6:1) to afford **50ac** (296 mg) in 90% yield as colorless solid.

mp = 108–109 °C; R_f = 0.55 (6 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.90 (d, *J* = 8.4 Hz, 2H), 7.50 (d, *J* = 7.6 Hz, 2H), 7.41 (d, *J* = 8.4 Hz, 2H), 7.34–7.24 (m, 1H), 7.05 (dd, *J* = 8.0, 20 Hz, 2H), 6.97 (t, *J* = 8.4 Hz, 1H), 6.24 (s, 1H), 6.08 (dd, *J* = 5.2, 8.8 Hz, 1H), 4.46 (dd, *J* = 8.8, 17.6 Hz, 1H), 3.55 (dd, *J* = 5.2, 17.6 Hz, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 195.2, 162.9 (d, *J* = 247 Hz), 143.1 (d, *J* = 6.1 Hz), 140.0, 139.5, 134.6, 130.3 (d, *J* = 8.1 Hz), 129.9, 129.6 (2C), 128.9 (2C), 122.2, 115.0 (d, *J* = 21.2 Hz), 113.7 (d, *J* = 22.2 Hz), 105.9, 60.2, 44.0; **^{19}F NMR (376**

MHz, $CDCl_3$) δ −111.80 to −111.86 (m); **IR (KBr)** ν_{max} 3061, 2968, 1680, 1589, 1400, 758, 522 cm^{-1}; MS (EI) *m/z* (%) 332 (M^+ + 3, 41), 331 (M^+ + 2, 76), 330 (M^+ + 1, 100), 264 (11), 258 (11); **Elemental analysis** calcd for $C_{18}H_{14}ClFN_2O$: C, 65.76; H, 4.29; N, 8.52. Found: C, 65.81; H, 4.23; N, 8.45.

1-Phenyl-3-(1*H*-pyrazol-1-yl)propan-1-one (55a):[35]

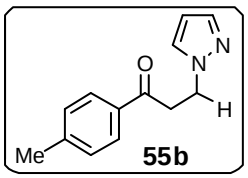


55a

Following the general procedure (GP-3); 1-phenylprop-2-yn-1-ol (**52a**; 132 mg, 1.0 mmol), pyrazole (**49a**; 136 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 70 °C for 1 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (3:1) to afford **55a** (192 mg) in 96% yield as pale yellow solid.

mp = 45–46 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.96 (d, *J* = 7.6 Hz, 2H), 7.59 (t, *J* = 7.2 Hz, 1H), 7.52 (s, 2H), 7.48 (t, *J* = 7.6 Hz, 2H), 6.23 (s, 1H), 4.63 (t, *J* = 6.4 Hz, 2H), 3.62 (t, *J* = 6.4 Hz, 2H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 197.3, 139.5, 136.3, 133.4, 130.0, 128.6 (2C), 128.0 (2C), 105.2, 46.5, 38.8; **IR (KBr)** ν_{max} 3111, 3063, 2953, 1682, 1448, 1217, 750, 619 cm^{-1}; **MS (EI)** *m/z* (%) 202 (M^+ + 2, 8), 201 (48), 157 (100), 143 (6), 69 (8).

3-(1*H*-Pyrazol-1-yl)-1-*p*-tolylpropan-1-one (55b):

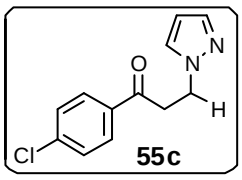


55b

Following the general procedure (GP-3); 1-*p*-tolylprop-2-yn-1-ol (**52b**; 146 mg, 1.0 mmol), pyrazole (**49a**; 136 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 70 °C for 1 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (4:1) to afford **55b** (199 mg) in 93% yield as pale yellow thick liquid.

R_f = 0.23 (4 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.83 (d, *J* = 8.0 Hz, 2H), 7.50 (d, *J* = 2.0 Hz, 2H), 7.23 (d, *J* = 8.0 Hz, 2H), 6.20 (bt, *J* = 2.0 Hz, 1H), 4.58 (t, *J* = 6.4 Hz, 2H), 3.56 (t, *J* = 6.4 Hz, 2H), 2.39 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 196.9, 144.3, 139.4, 133.8, 130.0, 129.2 (2C), 128.0 (2C), 105.1, 46.6, 38.6, 21.6; **IR (Neat)** ν_{max} 3032, 2951, 1682, 1398, 1089, 978, 752 cm^{-1}; **MS (EI)** *m/z* (%) 216 (M^+ + 2, 35), 215 (M^+ + 1, 100), 147 (8), 101 (3), 91 (3), 69 (6); **Elemental analysis** calcd for $C_{13}H_{14}N_2O$: C, 72.87; H, 6.59; N, 13.07. Found: C, 72.91; H, 6.51; N, 13.15.

1-(4-Chlorophenyl)-3-(1*H*-pyrazol-1-yl)propan-1-one (55c):

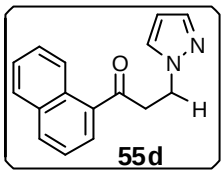


55c

Following the general procedure (GP-3); 1-(4-chlorophenyl)prop-2-yn-1-ol (**52c**; 166 mg, 1.0 mmol), pyrazole (**49a**; 136 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 70 °C for 1 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (6:1) to afford **55c** (171 mg) in 73% yield as colorless solid.

mp = 76–77 ^{o}C; R_f = 0.14 (6 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.87 (d, *J* = 8.4 Hz, 2H), 7.50 (s, 2H), 7.42 (d, *J* = 8.4 Hz, 2H), 6.21 (s, 1H), 4.59 (t, *J* = 6.8 Hz, 2H), 3.56 (t, *J* = 6.4 Hz, 2H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 196.2, 139.9, 139.6, 134.6, 130.0, 129.4 (2C), 128.9 (2C), 105.2, 46.4, 38.7; **IR (KBr)** ν_{max} 3103, 2924, 1689, 1589, 1400, 754, 617 cm^{-1}; **MS (EI)** *m/z* (%) 238 (M^+ + 3, 11), 237 (M^+ + 2, 65), 236 (M^+ + 1, 30), 235 (M^+, 100), 167 (3), 101 (12), 69 (19); **Elemental analysis** calcd for $C_{12}H_{11}ClN_2O$: C, 61.41; H, 4.72; N, 11.94. Found: C, 61.52; H, 4.66; N, 11.85.

1-(Naphthalen-1-yl)-3-(1*H*-pyrazol-1-yl)propan-1-one (55d):

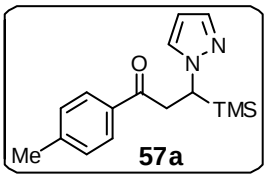


55d

Following the general procedure (GP-3); 1-(naphthalen-1-yl)prop-2-yn-1-ol (**52d**; 182 mg, 1.0 mmol), pyrazole (**49a**; 136 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 70 °C for 2 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (6:1) to afford **55d** (171 mg) in 68% yield as pale yellow thick liquid.

R_f = 0.14 (6 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.62 (d, *J* = 8.8 Hz, 1H), 7.99 (d, *J* = 8.0 Hz, 1H), 7.86 (dd, *J* = 7.6, 12.8 Hz, 2H), 7.60 (dtd, *J* = 1.6, 1.2, 8.2 Hz, 1H), 7.57–7.52 (m, 3H), 7.47 (t, *J* = 7.2 Hz, 1H), 6.24 (t, *J* = 2.0 Hz, 1H), 4.68 (t, *J* = 6.4 Hz, 2H), 3.68 (t, *J* = 6.4 Hz, 2H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 201.1, 139.6, 134.8, 133.8, 133.1, 130.0, 129.9, 128.4, 128.1, 128.0, 126.4, 125.6, 124.3, 105.2, 46.9, 41.8; **IR (Neat)** ν_{max} 3049, 2951, 1678, 1510, 777, 619 cm^{-1}; **MS (EI)** *m/z* (%) 252 (M^+ + 2, 38), 251 (M^+ + 1, 100), 215 (19), 183 (19), 165 (16), 101 (11), 69 (11); **Elemental analysis** calcd for $C_{16}H_{14}N_2O$: C, 76.78; H, 5.64; N, 11.19. Found: C, 76.62; H, 5.58; N, 11.25.

3-(1*H*-Pyrazol-1-yl)-1-*p*-tolyl-3-(trimethylsilyl)propan-1-one (57a):

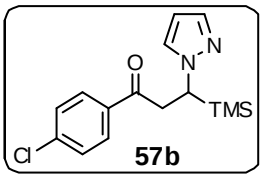


57a

Following the general procedure (GP-3); 1-*p*-tolyl-3-(trimethylsilyl)prop-2-yn-1-ol (**56a**; 218 mg, 1.0 mmol), pyrazole (**49a**; 136 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 70 °C for 1 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (6:1) to afford **57a** (11 mg) in 4% yield as pale yellow liquid along with **55b** (186 mg) in 87% yield.

R_f = 0.74 (6 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.80 (d, *J* = 8.4 Hz, 2H), 7.40 (d, *J* = 12.8 Hz, 2H), 7.21 (d, *J* = 8.0 Hz, 2H), 6.09 (t, *J* = 2.0 Hz, 1H), 4.51 (dd, *J* = 3.2, 10.0 Hz, 1H), 3.92 (dd, *J* = 10.0, 17.6 Hz, 1H), 3.10 (dd, *J* = 3.2, 17.6 Hz, 1H), 2.39 (s, 3H), 0.10 (s, 9H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 198.1, 144.1, 138.9, 134.3, 130.5, 129.2 (2C), 128.2 (2C), 104.2, 49.4, 39.2, 21.6, −2.9 (3C); **IR (Neat)** νmax 2951, 1684, 1506, 1182, 844, 748 cm^{-1}; **MS (EI)** *m/z* (%) 288 (M^+ + 2, 51), 287 (M^+ + 1, 100), 251 (19), 219 (32), 101 (5), 69 (5); **Elemental analysis** calcd for $C_{16}H_{22}N_2OSi$: C, 67.09; H, 7.74; N, 9.78. Found: C, 67.22; H, 7.69; N, 9.71.

1-(4-Chlorophenyl)-3-(1*H*-pyrazol-1-yl)-3-(trimethylsilyl)propan-1-one (57b):

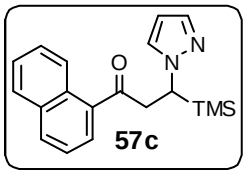


57b

Following the general procedure (GP-3); 1-(4-chlorophenyl)-3-(trimethylsilyl)prop-2-yn-1-ol (**56b**; 239 mg, 1.0 mmol), pyrazole (**49a**; 136 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 70 °C for 1 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (6:1) to afford **57b** (52 mg) in 17% yield as colorless liquid along with **55c** (153 mg) in 65% yield.

R_f = 0.66 (6 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.81 (d, *J* = 8.4 Hz, 2H), 7.41 (bd, *J* = 1.6 Hz, 1H), 7.39–7.33 (m, 3H), 6.08 (bt, *J* = 2.2 Hz, 1H), 4.47 (dd, *J* = 2.8, 10.4 Hz, 1H), 3.93 (dd, *J* = 10.4, 17.2 Hz, 1H), 3.04 (dd, *J* = 2.8, 17.2 Hz, 1H), 0.09 (s, 9H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 197.5, 139.6, 139.0, 135.0, 130.5, 129.5 (2C), 128.8 (2C), 104.3, 49.5, 39.2, −3.0 (3C); **IR (Neat)** ν_{max} 3103, 2955, 1689, 1589, 1091, 845, 696 cm^{-1}; **MS (EI)** *m/z* (%) 310 (M^+ + 3, 24), 309 (M^+ + 2, 76), 308 (M^+ + 2, 59), 307 (M^+, 100), 239 (5), 223 (110, 101 (3), 69 (11); **Elemental analysis** calcd for $C_{15}H_{19}ClN_2OSi$: C, 58.71; H, 6.24; N, 9.13. Found: C, 58.62; H, 6.21; N, 9.21.

1-(Naphthalen-1-yl)-3-(1*H*-pyrazol-1-yl)-3-(trimethylsilyl)propan-1-one (57c):

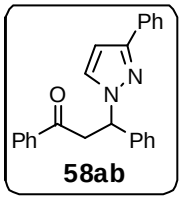


57c

Following the general procedure (GP-3); 1-(naphthalen-1-yl)-3-(trimethylsilyl)prop-2-yn-1-ol (**56c**; 254 mg, 1.0 mmol), pyrazole (**49a**; 136 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 70 °C for 1 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (6:1) to afford **57c** (23 mg) in 7% yield as pale yellow liquid along with **55d** (180 mg) in 72% yield.

R_f = 0.62 (6 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.34 (d, *J* = 8.0 Hz, 1H), 7.95 (d, *J* = 8.0 Hz, 1H), 7.84 (d, *J* = 7.2 Hz, 1H), 7.73 (d, *J* = 7.2 Hz, 1H), 7.59–7.42 (m, 4H), 7.40 (bd, *J* = 1.6 Hz, 1H), 6.13 (bt, *J* = 1.6 Hz, 1H), 4.60 (dd, *J* = 3.2, 11.2 Hz, 1H), 4.06 (dd, *J* = 10.8, 16.8 Hz, 1H), 3.14 (dd, *J* = 3.2, 16.8 Hz, 1H), 0.13 (s, 9H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 202.8, 139.0, 136.0, 133.8, 132.6, 130.6, 129.9, 128.3, 127.8, 127.6, 126.4, 125.5, 124.3, 104.3, 50.1, 42.9, −3.0 (3C); **IR (Neat)** ν_{max} 3051, 2955, 1682, 1249, 844, 750, 623 cm^{-1}; **MS (EI)** *m/z* (%) 325 (M^+ + 2, 32), 324 (100), 288 (5), 255 (27), 165 (27), 101 (5), 69 (14); **Elemental analysis** calcd for $C_{19}H_{22}N_2OSi$: C, 70.77; H, 6.88; N, 8.69. Found: C, 70.65; H, 6.91; N, 8.61.

1,3-Diphenyl-3-(3-phenyl-1*H*-pyrazol-1-yl)propan-1-one (58ab):



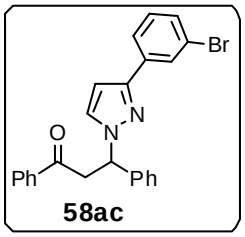
58ab

Following the general procedure (GP-3); 1,3-diphenylprop-2-yn-1-ol (**38a**; 208 mg, 1.0 mmol), 3-phenyl-1*H*-pyrazole (**49b**; 288 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 70 °C for 5 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (6:1) to afford **58ab** (293 mg) in 83% yield as colorless solid.

mp = 110–111 °C; R_f = 0.51 (6 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.02 (d, *J* = 8.0 Hz, 2H), 7.72 (d, *J* = 8.0 Hz, 2H), 7.56 (t, *J* = 7.2 Hz, 1H), 7.49–7.42 (m, 3H), 7.42–7.37 (m, 2H), 7.34 (td, *J* = 1.6, 6.4 Hz, 4H), 7.29–7.22 (m, 2H), 6.52 (bd, *J* = 2.0 Hz, 1H), 6.11 (dd, *J* = 5.2, 8.8 Hz, 1H), 4.61 (dd, *J* = 8.4, 17.2 Hz, 1H), 3.56 (dd, *J* = 5.2, 17.6 Hz, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 196.7, 150.8, 140.7, 136.6, 133.7, 133.2, 130.9, 128.7 (2C), 128.5 (2C), 128.3 (2C), 128.1 (2C), 127.9, 127.3, 126.7 (2C), 125.5 (2C), 102.9, 61.2, 44.2; **IR (KBr)** ν_{max} 3063, 2920, 1684, 1454, 750, 694 cm^{-1}; **MS (EI)** *m/z* (%) 354 (M^+ + 2, 51), 353 (M^+ + 1, 100), 263 (5);

Elemental analysis calcd for $C_{24}H_{20}N_2O$: C, 81.79; H, 5.72; N, 7.59. Found: C, 81.65; H, 5.76; N, 7.88. X-Ray crystallographic analysis confirms the structure of **58ab**.

3-(3-(3-Bromophenyl)-1*H*-pyrazol-1-yl)-1,3-diphenylpropan-1-one (58ac):

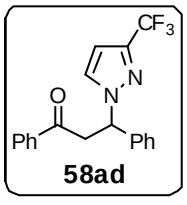


58ac

Following the general procedure (GP-3); 1,3-diphenylprop-2-yn-1-ol (**38a**; 208 mg, 1.0 mmol), 3-(3-bromophenyl)-1*H*-pyrazole (**49c**; 446 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 70 °C for 5 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (6:1) to afford **58ac** (401 mg) in 93% yield as colorless solid.

mp = 105–106 °C; R_f = 0.42 (6 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.01 (d, *J* = 7.6 Hz, 2H), 7.87 (d, *J* = 1.2 Hz, 1H), 1.57 (dd, *J* = 8.0, 17.2 Hz, 2H), 7.51–7.41 (m, 3H), 7.41–7.25 (m, 6H), 7.17 (t, *J* = 8.0 Hz, 1H), 6.49 (d, *J* = 2.4 Hz, 1H), 6.10 (dd, *J* = 4.8, 8.8 Hz, 1H), 4.58 (dd, *J* = 8.8, 17.6 Hz, 1H), 3.52 (dd, *J* = 4.8, 17.2 Hz, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 196.7, 149.3, 140.4, 136.5, 135.7, 133.2, 131.1, 130.1, 129.9, 128.7 (2C), 128.5 (2C), 128.3, 128.1 (2C), 128.0, 126.6 (2C), 124.0, 122.5, 103.1, 61.3, 44.1; **IR (KBr)** ν_{max} 3063, 2918, 1684, 1452, 995, 752, 688 cm^{-1}; **MS (EI)** *m/z* (%) 434 (M^+ + 2, 30), 433 (M^+ + 1, 100), 431 (M^+, 100), 257 (8), 255 (8), 209 (67), 145 (16); **Elemental analysis** calcd for $C_{24}H_{19}BrN_2O$: C, 66.83; H, 4.44; N, 6.49. Found: C, 66.75; H, 4.51; N, 6.41. X-Ray crystallographic analysis confirms the structure of **58ac**.

1,3-Diphenyl-3-(3-(trifluoromethyl)-1*H*-pyrazol-1-yl)propan-1-one (58ad):



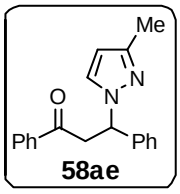
58ad

Following the general procedure (GP-3); 1,3-diphenylprop-2-yn-1-ol (**38a**; 208 mg, 1.0 mmol), 3-(trifluoromethyl)-1*H*-pyrazole (**49d**; 272 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 80 °C for 5 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (6:1) to afford **58ad** (272 mg) in 79% yield as colorless solid.

mp = 80–81 °C; R_f = 0.38 (6 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.96 (dd, *J* = 0.8, 6.4 Hz, 2H), 7.56 (tt, *J* = 1.2, 6.8 Hz, 1H), 7.50 (bd, *J* = 1.6 Hz, 1H), 7.45 (bt, *J* = 8.0 Hz, 2H), 7.36–7.27 (m, 5H), 6.47 (bd, *J* = 2.0, 1H), 6.11 (dd, *J* = 5.2, 8.4 Hz, 1H), 4.49 (dd, *J* = 8.4, 17.6 Hz, 1H), 3.61 (dd, *J* = 4.8, 17.6 Hz, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 196.3, 142.2 (q, *J* = 58.3 Hz), 139.5, 136.3, 133.5, 131.1, 128.9 (2C), 128.6 (2C), 128.4, 128.1 (2C), 126.7 (2C), 121.3 (d, *J*

= 270 Hz), 104.4, 61.8, 44.0; **^{19}F NMR (376 MHz, $CDCl_3$)** δ −66.54; **IR (KBr)** ν_{max} 3151, 2947, 1693, 1242, 773, 688 cm−1; **MS (EI)** *m/z* (%) 346 (M^+ + 2, 41), 345 (M^+ + 1, 100), 195 (11), 165 (5), 91 (3); **Elemental analysis** calcd for $C_{19}H_{15}F_3N_2O$: C, 66.27; H, 4.39; N, 8.14. Found: C, 66.15; H, 4.46; N, 8.21.

3-(3-Methyl-1*H*-pyrazol-1-yl)-1,3-diphenylpropan-1-one (58ae):

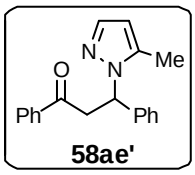


58ae

Following the general procedure (GP-3); 1,3-diphenylprop-2-yn-1-ol (**38a**; 208 mg, 1.0 mmol), 3-methyl-1*H*-pyrazole (**49e**; 164 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 70 °C for 5 h. Upon filtration over Celite and evaporation, the crude mixture was purified by flash column chromatography eluting with hexane: ethyl acetate (12:1) to afford **58ae** (101 mg) in 35% yield and **58ae'** (157 mg) in 54% yield as pale yellow thick liquids.

R_f = 0.35 (12 : 1 hexane–EtOAc); **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.98 (d, *J* = 8.0 Hz, 2H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.44 (t, *J* = 5.5 Hz, 2H), 7.35 (d, *J* = 2.5 Hz, 1H), 7.31 (d, *J* = 4.5 Hz, 4H), 7.28–7.24 (m, 1H), 6.02 (dd, *J* = 5.5, 8.0 Hz, 1H), 5.98 (d, *J* = 2.0 Hz, 1H), 4.41 (dd, *J* = 8.0, 17.5 Hz, 1H), 3.65 (dd, *J* = 5.5, 17.5 Hz, 1H), 2.24 (s, 3H); **^{13}C NMR (125 MHz, $CDCl_3$)** δ 196.8, 148.5, 140.9, 136.7, 133.3, 130.4, 128.7 (2C), 128.6 (2C), 128.3 (2C), 127.9, 126.7 (2C), 105.1, 60.7, 44.3, 13.8; **IR (Neat)** ν_{max} 2926, 1685, 1450, 1203, 752 cm^{-1}; **MS (EI)** *m/z* (%) 292 (M^+ + 2, 20), 291 (M^+ + 1, 100), 219 (3), 97 (3); **Elemental analysis** calcd for $C_{19}H_{18}N_2O$: C, 78.59; H, 6.25; N, 9.65. Found: C, 78.45; H, 6.31; N, 9.58.

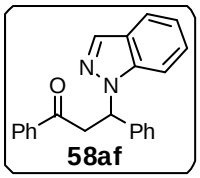
3-(5-Methyl-1*H*-pyrazol-1-yl)-1,3-diphenylpropan-1-one (58ae'):



58ae'

R_f = 0.35 (12 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.01 (d, *J* = 7.2 Hz, 2H), 7.57 (t, *J* = 7.2 Hz, 1H), 7.46 (t, *J* = 8.0 Hz, 2H), 7.42 (d, *J* = 1.6 Hz, 1H), 7.37–7.31 (m, 2H), 7.31–7.25 (m, 3H), 6.08 (dd, *J* = 4.4, 8.8 Hz, 1H), 6.03 (s, 1H), 4.66 (dd, *J* = 9.2, 17.6 Hz, 1H), 3.57 (dd, *J* = 4.4, 17.6 Hz, 1H), 2.35 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 196.9, 141.0, 138.8, 138.1, 136.6, 133.2, 128.7 (2C), 128.5 (2C), 128.2 (2C), 127.6, 126.5 (2C), 105.5, 57.0, 44.7, 11.0; **IR (Neat)** ν_{max} 3030, 2922, 1685, 1448, 752, 698 cm^{-1}; **MS (EI)** *m/z* (%) 292 (M^+ + 2, 35), 291 (M^+ + 1, 100), 241 (22), 209 (81), 115 (22), 83 (22); **Elemental analysis** Calcd for $C_{19}H_{18}N_2O$: C, 78.59; H, 6.25; N, 9.65. Found: C, 78.49; H, 6.21; N, 9.76.

3-(1*H*-Indazol-1-yl)-1,3-diphenylpropan-1-one (58af):

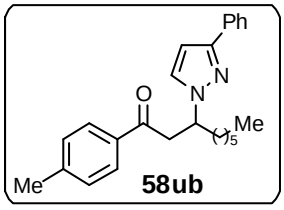


58af

Following the general procedure (GP-3); 1,3-diphenylprop-2-yn-1-ol (**38a**; 208 mg, 1.0 mmol), 1*H*-indazole (**49f**; 236 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 70 °C for 5 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (6:1) to afford **58af** (301 mg) in 92% yield as colorless solid.

mp = 92–93 °C; R_f = 0.42 (6 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.00 (s, 1H), 7.98 (s, 2H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.52 (t, *J* = 7.6 Hz, 2H), 7.43 (t, *J* = 8.0 Hz, 2H), 7.37–7.20 (m, 6H), 7.10 (t, *J* = 8.0 Hz, 1H), 6.46 (dd, *J* = 5.2, 8.8 Hz, 1H), 4.67 (dd, *J* = 8.8, 18.0 Hz, 1H), 3.74 (dd, *J* = 4.8, 17.6 Hz, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 196.4, 140.7, 139.5, 136.4, 133.1, 132.9, 128.6 (2C), 128.4 (2C), 128.0 (2C), 127.6, 126.5 (2C), 126.2, 124.1, 120.8, 120.7, 109.4, 57.3, 44.2; **IR (KBr)** ν_{max} 3061, 2916, 1682, 1018, 750, 696 cm^{-1}; **MS (EI)** *m/z* (%) 328 (M^+ + 2, 41), 327 (M^+ + 1, 100), 241 (5), 209 (67), 151 (3), 119 (14); **Elemental analysis** calcd for $C_{22}H_{18}N_2O$: C, 80.96; H, 5.56; N, 8.58. Found: C, 80.85; H, 5.51; N, 8.65. X-Ray crystallographic analysis elucidates the structure of **58af**.

3-(3-Phenyl-1*H*-pyrazol-1-yl)-1-*p*-tolylnonan-1-one (58ub):



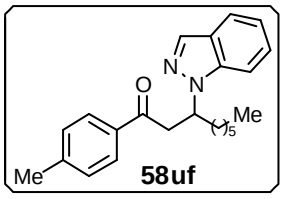
58ub

Following the general procedure (GP-3); 1-p-tolylnon-2-yn-1-ol (**38u**; 230 mg, 1.0 mmol), 3-phenyl-1*H*-pyrazole (**49b**; 288 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 80 °C for 92 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (9:1) to afford **58ub** (120 mg) in 32% yield as pale yellow thick liquid.

R_f = 0.63 (9 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.82 (d, *J* = 8.0 Hz, 2H), 7.76 (dd, *J* = 1.2, 8.4 Hz, 2H), 7.46 (d, *J* = 2.0 Hz, 1H), 7.35 (t, *J* = 7.2 Hz, 2H), 7.24 (tt, *J* = 1.2, 7.2 Hz, 1H), 7.18 (d, *J* = 8.0 Hz, 2H), 6.42 (d, *J* = 2.0 Hz, 1H), 4.86–4.80 (m, 1H), 3.83 (dd, *J* = 7.2, 17.2 Hz, 1H), 3.30 (dd, *J* = 5.2, 17.2 Hz, 1H), 2.34 (s, 3H), 2.18–2.07 (m, 1H), 1.88–1.78 (m, 1H), 1.37–1.18 (m, 7H), 1.17–1.07 (m, 1H), 0.84 (t, *J* = 6.8 Hz, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 197.4, 151.4, 144.0, 134.3, 134.0, 131.1, 129.2 (2C), 128.4 (2C), 128.2 (2C), 127.2, 125.6 (2C), 101.6, 58.5, 43.9, 35.2, 31.6, 28.7, 26.1, 22.5, 21.5, 14.0; **IR (Neat)** ν_{max} 3034, 2928, 1682, 1606,

1458, 750, 694 cm^{-1}; **MS (EI)** *m/z* (%) 376 (M^+ + 2, 54), 375 (M^+ + 1, 100), 263 (3), 231 (19), 177 (11), 145 (19), 91 (3); **Elemental analysis** calcd for $C_{25}H_{30}N_2O$: C, 80.17; H, 8.07; N, 7.48. Found: C, 80.06; H, 8.12; N, 7.56.

3-(1*H*-Indazol-1-yl)-1-*p*-tolylnonan-1-one (58uf):

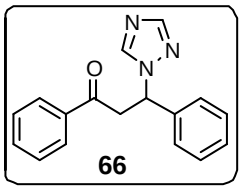


58uf

Following the general procedure (GP-3); 1-*p*-tolylnon-2-yn-1-ol (**38u**; 230 mg, 1.0 mmol), 1*H*-indazole (**49f**; 236 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 80 °C for 60 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (9:1) to afford **58uf** (226 mg) in 65% yield as pale yellow thick liquid.

R_f = 0.47 (9 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.01 (s, 1H), 7.81 (d, *J* = 8.4 Hz, 2H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.61 (d, *J* = 8.8 Hz, 1H), 7.39 (td, *J* = 0.8, 6.8 Hz, 1H), 7.20 (d, *J* = 8.0 Hz, 2H), 7.12 (t, *J* = 7.6 Hz, 1H), 5.23–5.32 (m, 1H), 3.85 (dd, *J* = 7.2, 17.6 Hz, 1H), 3.46 (dd, *J* = 5.6, 17.2 Hz, 1H), 2.38 (s, 3H), 2.24–2.13 (m, 1H), 2.00–1.87 (m, 1H), 1.30–1.13 (m, 7H), 1.05–0.93 (m, 1H), 0.82 (t, *J* = 6.8 Hz, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 197.3, 144.1, 140.2, 134.2, 133.3, 129.2 (2C), 128.2 (2C), 126.1, 123.4, 120.8, 120.4, 109.4, 54.1, 43.8, 35.5, 31.5, 28.8, 26.1, 22.5, 21.6, 13.9; **IR (Neat)** ν_{max} 3059, 2928, 1682, 1608, 1014, 740 cm^{-1}; **MS (EI)** *m/z* (%) 350 (M^+ + 2, 62), 349 (M^+ + 1, 100), 263 (14), 231 (57), 151 (11), 119 (19); **Elemental analysis** calcd for $C_{23}H_{28}N_2O$: C, 79.27; H, 8.10; N, 8.04. Found: C, 79.45; H, 8.06; N, 8.12.

1,3-Diphenyl-3-(1*H*-1,2,4-triazol-1-yl)propan-1-one (66):[36]



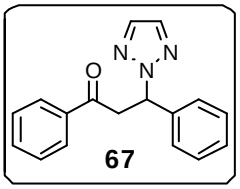
66

Following the general procedure (GP-3); 1,3-diphenylprop-2-yn-1-ol (**38a**; 208 mg, 1.0 mmol), 1*H*-1,2,4-triazole (**59**; 138 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (1.5 mL) + DMF (0.5 mL) was heated at 80 °C for 24 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (1.5:1) to afford **66** (162 mg) in 58% yield as pale yellow solid.

mp = 77–78 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.20 (s, 1H), 7.96 (d, *J* = 8.0 Hz, 2H), 7.92 (s, 1H), 7.56 (t, *J* = 7.6 Hz, 1H), 7.50–7.32 (m, 7H), 6.20 (dd, J = 4.8, 9.2 Hz, 1H), 4.44 (dd, *J* = 8.8,

17.6 Hz, 1H), 3.63 (dd, *J* = 4.4, 17.6 Hz, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 195.8, 151.6, 143.5, 138.7, 136.0, 133.7, 129.0 (2C), 128.7 (2C), 128.6, 128.1 (2C), 126.9 (2C), 58.9, 43.7; **IR (KBr)** ν_{max} 2922, 1685, 1502, 1006, 754, 690 cm^{-1}; **MS (EI)** *m/z* (%) 279 (M^+ + 2, 30), 278 (M^+ + 1, 100), 241 (16), 209 (57), 105 (8), 70 (8).

1,3-Diphenyl-3-(2*H*-1,2,3-triazol-2-yl)propan-1-one (67):[7d]

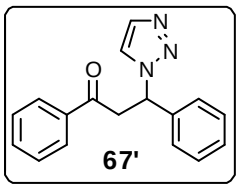


67

Following the general procedure (GP-3); 1,3-diphenylprop-2-yn-1-ol (**38a**; 208 mg, 1.0 mmol), 1*H*-1,2,3-triazole (**60**; 138 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (1.5 mL) + DMF (0.5 mL) was heated at 80 °C for 60 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (6:1) to afford **67** (166 mg) in 60% yield and **67'** (31mg) in 11% yields as colorless solids.

mp = 90–91 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.95 (d, *J* = 7.6 Hz, 2H), 7.59–7.49 (m, 3H), 7.41 (t, *J* = 8.0 Hz, 2H), 7.35–7.22 (m, 5H), 6.51 (dd, *J* = 5.2, 9.2 Hz, 1H), 4.51 (dd, *J* = 9.2, 18.0 Hz, 1H), 3.69 (dd, *J* = 5.2, 18.0 Hz, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 195.6, 139.3, 136.2, 134.0 (2C), 133.3, 128.7 (2C), 128.5 (2C), 128.1, 128.0 (2C), 126.5 (2C), 63.8, 43.8; **IR (KBr)** ν_{max} 3063, 2908, 1682, 1332, 960, 750, 687 cm^{-1}; **MS (EI)** *m/z* (%) 279 (M^+ + 2, 15), 278 (M^+ + 1, 52), 241 (6), 209 (100), 79 (5), 68 (5).

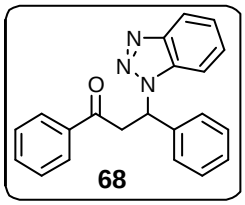
1,3-Diphenyl-3-(1*H*-1,2,3-triazol-1-yl)propan-1-one (67'):[7d]



67'

mp = 147–148 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.96 (d, *J* = 8.0 Hz, 2H), 7.68 (s, 1H), 7.61 (s, 1H), 7.57 (t, *J* = 7.6 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 2H), 7.39–7.29 (m, 5H), 6.32 (dd, *J* = 4.8, 8.4 Hz, 1H), 4.65 (dd, *J* = 8.4, 17.6 Hz, 1H), 3.74 (dd, *J* = 5.2, 18.0 Hz, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 195.7, 139.0, 136.1, 133.8, 133.6, 129.0 (2C), 128.7 (2C), 128.1 (2C), 127.1, 126.8 (2C), 124.2, 60.3, 44.2; **IR (KBr)** ν_{max} 3097, 1682, 1213, 752, 690, 549 cm^{-1}; **MS (EI)** *m/z* (%) 280 (M^+ + 3, 14), 279 (M^+ + 2, 35), 278 (M^+ + 1, 100), 156 (3), 123 (5).

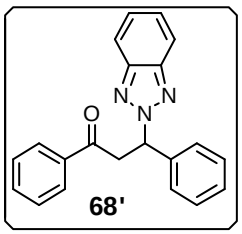
3-(1*H*-Benzo[*d*][1,2,3]triazol-1-yl)-1,3-diphenylpropan-1-one (68):



Following the general procedure (GP-3); 1,3-diphenylprop-2-yn-1-ol (**38a**; 208 mg, 1.0 mmol), 1*H*-benzotriazole (**61**; 238 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (1.5 mL) + DMF (0.5 mL) was heated at 80 °C for 24 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (4:1) to afford **68** (147 mg) in 45% yield as light yellow solid and **68'** (33 mg) in 10% yield as yellow thick liquid.

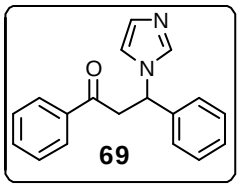
mp = 85–86 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.01 (d, *J* = 8.4 Hz, 1H), 7.97 (d, *J* = 7.2 Hz, 2H), 7.53 (s, 1H), 7.51 (t, *J* = 3.6 Hz, 1H), 7.45–7.35 (m, 5H), 7.35–7.22 (m, 4H), 6.60 (dd, *J* = 4.8, 8.8 Hz, 1H), 4.86 (dd, *J* = 8.8, 18 Hz, 1H), 3.89 (dd, *J* = 4.8, 17.6 Hz, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 195.7, 145.9, 138.9, 135.9, 133.4, 132.8, 128.8 (2C), 128.5 (2C), 128.3, 128.0 (2C), 127.1, 126.5 (2C), 123.9, 119.6, 109.8, 58.1, 44.2; **IR (KBr)** ν_{max} 3061, 2924, 1687, 1267, 920, 746 cm^{-1}; **MS (EI)** *m/z* (%) 228 (M^+ + 1, 100), 196 (46), 183 (14), 100 (6).

3-(2*H*-Benzo[*d*][1,2,3]triazol-2-yl)-1,3-diphenylpropan-1-one (68'):



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02–7.30 (m, 14 H), 6.78 (dd, *J* = 5.0, 9.0 Hz, 1H), 4.73 (dd, *J* = 9.0, 18.0 Hz, 1H), 3.89 (dd, *J* = 5.0, 18.0 Hz, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 195.5, 144.1 (2C), 138.8, 136.2, 133.5, 130.9, 128.9 (2C), 128.7 (2C), 128.2 (2C), 126.8 (2C), 126.2 (2C), 118.2 (2C), 65.7, 44.1; **IR (KBr)** ν_{max} 3063, 2930, 1582, 1332, 960, 700, 687 cm^{-1}; **MS (EI)** *m/z* (%) 328 (M^+ + 1, 100), 277 (14), 191 (22), 108 (6), 67 (6).

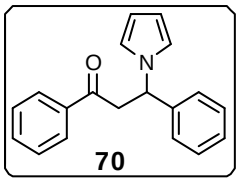
3-(1*H*-Imidazol-1-yl)-1,3-diphenylpropan-1-one (69):[37]



Following the general procedure (GP-3); 1,3-diphenylprop-2-yn-1-ol (**38a**; 208 mg, 1.0 mmol), imidazole (**62**; 136 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (1.5 mL) + DMF (0.5 mL) was heated at 80 °C for 48 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (1:1) to afford **69** (28 mg) in 10% yield as pale yellow solid.

mp = 147–148 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.92 (d, J = 7.2 Hz, 2H), 7.52 (t, *J* = 7.2 Hz, 1H), 7.39 (t, *J* = 8.0 Hz, 3H), 7.35–7.23 (m, 4H), 7.23–7.16 (m, 1H), 6.90 (s, 2H), 4.84 (t, *J* = 6.8 Hz, 1H), 4.22 (dd, *J* = 7.6, 18.0 Hz, 1H), 3.58 (dd, *J* = 6.0, 18.0 Hz, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 198.2, 149.4, 141.6, 136.6, 133.2 (2C), 128.8 (2C), 128.5 (2C), 128.1 (2C), 128.0 (2C), 127.1 (2C), 44.1, 40.0; **IR (KBr)** ν_{max} 3040, 1682, 1462, 752, 688, 553 cm^{-1}; **MS (EI)** *m/z* (%) 278 (M^+ + 2, 46), 277 (M^+ + 1, 100), 209 (3), 157 (5), 69 (2).

1,3-Diphenyl-3-(1*H*-pyrrol-1-yl)propan-1-one (70):

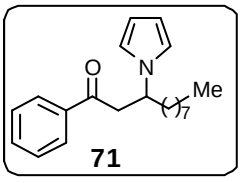


70

Following the general procedure (GP-3); 1,3-diphenylprop-2-yn-1-ol (**38a**; 208 mg, 1.0 mmol), pyrrole (**63**; 134 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 70 °C for 1 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (6:1) to afford **70** (146 mg) in 53% yield as pale yellow solid.

mp = 89–90 °C; R_f = 0.57 (6 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.95 (d, *J* = 7.6 Hz, 2H), 7.59 (t, *J* = 8.2 Hz, 1H), 7.48 (t, *J* = 7.8 Hz, 2H), 7.37–7.25 (m, 3H), 7.22 (d, *J* = 7.2 Hz, 2H), 6.79 (s, 2H), 6.17 (s, 2H), 5.99 (t, *J* = 6.8 Hz, 1H), 3.96 (dd, *J* = 7.2, 17.2 Hz, 1H), 3.80 (dd, *J* = 6.4, 17.2 Hz, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 196.2, 141.1, 136.5, 133.5, 128.8 (2C), 128.7 (2C), 128.0 (2C), 127.8, 126.4 (2C), 119.7 (2C), 108.4 (2C), 58.2, 44.6; **IR (KBr)** ν_{max} 3059, 2924, 1680, 1269, 723, 634 cm^{-1}; **MS (EI)** *m/z* (%) 277 (M^+ + 2, 5), 276 (M^+ + 1, 24), 156 (100), 129 (13), 105 (15), 97 (33); **Elemental analysis** calcd for $C_{19}H_{17}NO$: C, 82.88; H, 6.22; N, 5.09. Found: C, 82.75; H, 6.28; N, 5.15.

1-Phenyl-3-(1*H*-pyrrol-1-yl)undecan-1-one (71):



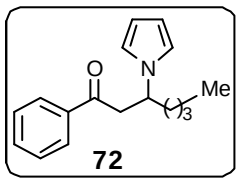
71

Following the general procedure (GP-3); 1-phenylundec-2-yn-1-ol (**38s**; 244 mg, 1.0 mmol), pyrrole (**63**; 134 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 80 °C for 5 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (19:1) to afford **71** (180 mg) in 58% yield as brown color solid.

mp = 41–42 °C; R_f = 0.52 (19 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.88 (d, *J* = 7.2 Hz, 2H), 7.56 (bt, *J* = 7.6 Hz, 1H), 7.44 (bt, *J* = 7.6 Hz, 2H), 6.72 (s, 2H), 6.11 (s, 2H), 4.63 (bt, *J*

= 7.2 Hz, 1H), 3.46 (dd, *J* = 6.4, 17.2 Hz, 1H), 3.32 (dd, *J* = 6.8, 17.2 Hz, 1H), 1.81 (bd, *J* = 6.4 Hz, 2H), 1.35–1.15 (m, 12 H), 0.86 (t, *J* = 6.4 Hz, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 197.4, 136.7, 133.2, 128.6 (2C), 128.0 (2C), 118.9 (2C), 107.8 (2C), 55.7, 45.7, 36.2, 31.8, 29.3, 29.2 (2C), 26.1, 22.6, 14.1; **IR (KBr)** ν_{max} 3130, 2922, 1680, 758 cm^{-1}; **MS (EI)** *m/z* (%) 312 (M^+ + 1, 49), 311 (100), 269 (8), 210 (3); **Elemental analysis** calcd for $C_{21}H_{29}NO$: C, 80.98; H, 9.38; N, 4.50. Found: C, 80.78; H, 9.41; N, 4.61.

1-Phenyl-3-(1*H*-pyrrol-1-yl)heptan-1-one (72):

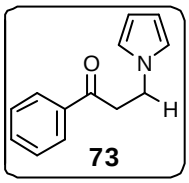


72

Following the general procedure (GP-3); 1-phenylhept-2-yn-1-ol (**38y**; 188 mg, 1.0 mmol), pyrrole (**63**; 134 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 80 °C for 3 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (19:1) to afford **72** (99 mg) in 39% yield as brown color solid.

mp = 47–48 °C; R_f = 0.47 (19 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.90 (d, *J* = 7.2 Hz, 2H), 7.57 (t, *J* = 7.2 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 2H), 6.75 (t, *J* = 2.4 Hz, 2H), 6.14 (t, *J* = 2.0 Hz, 2H), 4.72–4.59 (m, 1H), 3.49 (dd, *J* = 6.4, 17.2 Hz, 1H), 3.34 (dd, *J* = 6.8, 17.2 Hz, 1H), 1.93–1.76 (m, 2H), 1.43–1.19 (m, 3H), 1.19–1.05 (m, 1H), 0.87 (t, *J* = 6.8 Hz, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 197.4, 136.7, 133.3, 128.6 (2C), 127.9 (2C), 118.9 (2C), 107.8 (2C), 55.7, 45.7, 35.9, 28.3, 22.2, 13.9; **IR (KBr)** ν_{max} 3059, 2957, 1682, 1448, 725, 690 cm^{-1}; **MS (EI)** *m/z* (%) 257 (M^+ + 2, 35), 256 (100), 238 (51), 189 (5), 136 (11), 80 (8); **Elemental analysis** calcd for $C_{17}H_{21}NO$: C, 79.96; H, 8.29; N, 5.49. Found: C, 79.85; H, 8.32; N, 5.41.

1-Phenyl-3-(1*H*-pyrrol-1-yl)propan-1-one (73):[38]

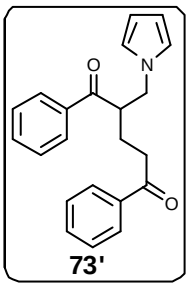


73

Following the general procedure (GP-3); 1-phenylprop-2-yn-1-ol (**52a**; 132 mg, 1.0 mmol), pyrrole (**63**; 134 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 70 °C for 1.5 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (12:1) to afford **73** (18 mg) in 9% yield as brown color semi-solid and **73'** (39 mg) in 24% yield as brown thick liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.0 Hz, 2H), 7.59 (t, *J* = 8.0 Hz, 1H), 7.47 (t, *J* = 8.0 Hz, 2H), 6.73 (s, 2H), 6.16 (s, 2H), 4.39 (t, *J* = 6.8 Hz, 2H), 3.46 (t, *J* = 6.8 Hz, 2H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 197.4, 136.4, 133.4, 128.7 (2C), 127.9 (2C), 120.7 (2C), 108.3 (2C), 44.2, 40.5; **IR (Neat)** ν_{max} 3057, 2935, 1678, 1498, 1284, 1089, 748, 621 cm^{-1}; **MS (EI)** *m/z* (%) 201 (M^+ + 2, 24), 200 (M^+ + 1, 100), 182 (5), 156 (3), 80 (8).

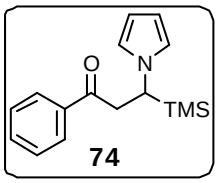
2-((1*H*-Pyrrol-1-yl)methyl)-1,5-diphenylpentane-1,5-dione (73'):



73'

R_f = 0.34 (12 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.91–7.82 (m, 4H), 7.54 (t, *J* = 7.2 Hz, 2H), 7.42 (t, *J* = 7.6 Hz, 4H), 6.63 (t, *J* = 1.6 Hz, 2H), 6.06 (t, *J* = 2.0 Hz, 2H), 4.38 (q, *J* = 9.6 Hz, 1H), 4.15–4.04 (m, 2H), 3.01–2.89 (m, 1H), 2.89–2.76 (m, 1H), 2.29–2.18 (m, 1H), 2.10–2.00 (m, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 202.2, 199.1, 136.7, 136.5, 133.5, 133.1, 128.7 (2C), 128.5 (2C), 128.1 (2C), 127.9 (2C), 120.9 (2C), 108.5 (2C), 51.2, 47.3, 35.0, 25.1; **IR (Neat)** ν_{max} 3061, 2928, 1680, 1448, 1089, 727, 690 cm^{-1}; **MS (EI)** *m/z* (%) 332 (M^+ + 1, 50), 314 (100), 265 (40), 212 (16), 200 (20), 194 (25); **Elemental analysis** calcd for $C_{22}H_{21}NO_2$: C, 79.73; H, 6.39; N, 4.23. Found: C, 79.65; H, 6.31; N, 4.35.

1-Phenyl-3-(1*H*-pyrrol-1-yl)-3-(trimethylsilyl)propan-1-one (74):

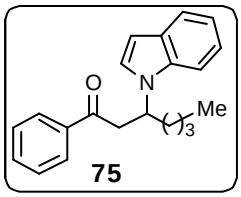


74

Following the general procedure (GP-3); 1-phenyl-3-(trimethylsilyl)prop-2-yn-1-ol (**56a**; 204 mg, 1.0 mmol), pyrrole (**63**; 134 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 70 °C for 1.5 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (12:1) to afford **74** (47 mg) in 17% yield as light brown liquid and **73** (39 mg) in 19% yield and **73'** (49 mg) in 29% yield.

R_f = 0.66 (12 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.89 (d, *J* = 3.6 Hz, 2H), 7.56 (t, *J* = 7.2 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 2H), 6.63 (s, 2H), 6.08 (s, 2H), 4.34 (dd, *J* = 4.4, 9.6 Hz, 1H), 3.63 (dd, *J* = 9.6, 17.2 Hz, 1H), 3.21 (dd, *J* = 4.4, 17.2 Hz, 1H), 0.10 (s, 9H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 197.9, 136.7, 133.1, 128.6 (2C), 128.0 (2C), 120.4 (2C), 107.5 (2C), 46.9, 40.4, −3.0 (3C); **IR (Neat)** ν_{max} 2957, 1687, 1251, 979, 842, 721, 628 cm^{-1}; **MS (EI)** *m/z* (%) 274 (M^+ + 3, 16), 273 (M^+ + 2, 51), 272 (M^+ + 1, 100), 254 (11), 237 (110, 205 (14), 152 (110, 93 (3); **Elemental analysis** Calcd for $C_{16}H_{21}NOSi$: C, 70.80; H, 7.80; N, 5.16. Found: C, 70.58; H, 7.76; N, 5.21.

3-(1*H*-Indol-1-yl)-1-phenylheptan-1-one (75):

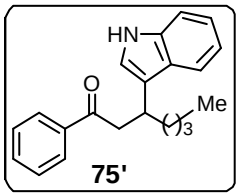


75

Following the general procedure (GP-3); 1-phenylhept-2-yn-1-ol (**38y**; 188 mg, 1.0 mmol), indole (**64**; 234 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 80 °C for 17 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (19:1) to afford **75** (177 mg) in 58% yield as pale yellow thick liquid and **75'** (36 mg) in 12% yield as brown color thick liquid.

R_f = 0.43 (19 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.85 (d, *J* = 7.6 Hz, 2H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.54–7.44 (m, 2H), 7.39 (bt, *J* = 7.6 Hz, 2H), 7.23–7.16 (m, 2H), 7.08 (t, *J* = 7.2 Hz, 1H), 6.52 (d, *J* = 2.4 Hz, 1H), 5.15–5.05 (m, 1H), 3.55–3.40 (m, 2H), 2.04–1.90 (m, 2H), 1.36–1.18 (m, 3H), 1.13–1.01 (m, 1H), 0.80 (t, *J* = 6.4 Hz, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 197.3, 136.5, 135.9, 133.3, 128.6 (2C), 128.5, 127.9 (2C), 124.7, 121.4, 120.9, 119.3, 109.8, 101.9, 52.2, 44.7, 34.9, 28.3, 22.3, 13.8; **IR (Neat)** ν_{max} 3055, 2957, 1658, 1460, 1307, 740, 690 cm^{-1}; **MS (EI)** *m/z* (%) 307 (M^+ + 2, 46), 306 (M^+ + 1, 100), 236 (5), 209 (8), 91 (10); **Elemental analysis** calcd for $C_{21}H_{23}NO$: C, 82.58; H, 7.59; N, 4.59. Found: C, 82.45; H, 7.65; N, 4.51.

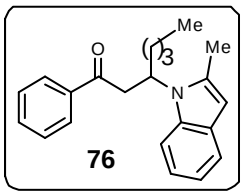
3-(1*H*-Indol-3-yl)-1-phenylheptan-1-one (75'):



75'

R_f = 0.13 (19 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.99–7.93 (bs, 1H), 7.90 (d, *J* = 8.0 Hz, 2H), 7.69 (d, *J* = 8.0 Hz, 1H), 7.51 (t, *J* = 7.6 Hz, 1H), 7.40 (t, *J* = 7.6 Hz, 2H), 7.33 (t, *J* = 8.0 Hz, 1H), 7.18 (t, *J* = 7.6 Hz, 1H), 7.10 (t, *J* = 7.6 Hz, 1H), 7.01 (s, 1H), 3.72–3.61 (m, 1H), 3.42 (dd, *J* = 6.4, 16.0 Hz, 1H), 3.34 (dd, *J* = 7.2, 16.4 Hz, 1H), 1.91–1.77 (m, 2H), 1.33–1.23 (m, 4H), 0.82 (t, *J* = 6.8 Hz, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 199.9, 137.3, 136.5, 132.8, 128.4 (2C), 128.0 (2C), 126.6, 121.8, 121.2, 119.5, 119.4, 119.1, 111.2, 45.3, 35.2, 32.9, 29.9, 22.7, 14.0; **IR (Neat)** ν_{max} 3416, 3057, 2928, 1682, 1454, 740 cm^{-1}; **MS (EI)** *m/z* (%) 307 (M^+ + 2, 46), 306 (100), 236 (5), 209 (8), 91 (10); **Elemental analysis** calcd for $C_{21}H_{23}NO$: C, 82.58; H, 7.59; N, 4.59. Found: C, 82.71; H, 7.52; N, 4.65.

3-(2-Methyl-1*H*-indol-1-yl)-1-phenylheptan-1-one (76):

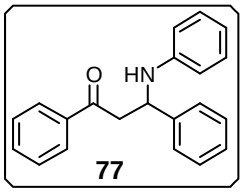


76

Following the general procedure (GP-3); 1-phenylhept-2-yn-1-ol (**38y**; 188 mg, 1.0 mmol), 2-methyl-1*H*-indole (**65**; 262 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 80 °C for 48 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (12:1) to afford **76** (132 mg) in 41% yield as brown color thick liquid.

R_f = 0.27 (12 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.99 (bs, 1H), 7.93 (d, *J* = 7.6 Hz, 2H), 7.81–7.73 (m, 1H), 7.53 (t, *J* = 7.2 Hz, 1H), 7.41 (t, *J* = 8.0 Hz, 2H), 7.31–7.23 (m, 1H), 7.21–7.13 (m, 2H), 3.73–3.60 (m, 2H), 3.46 (dd, *J* = 8.8, 18.4 Hz, 1H), 2.37 (s, 3H), 2.15–2.02 (m, 1H), 1.98–1.85 (m, 1H), 1.45–1.20 (m, 4H), 0.89 (t, *J* = 6.4 Hz, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 200.4, 137.2, 135.5, 132.6, 131.4, 128.3 (2C), 127.9 (2C), 127.0, 120.3, 118.8, 118.6, 113.4, 110.5, 44.6, 34.7, 32.8, 30.2, 22.5, 13.9, 11.8; **IR (Neat)** ν_{max} 3055, 2928, 1680, 1462, 742, 690 cm^{-1}; **MS (EI)** *m/z* (%)320 (M^+ + 1, 100), 232 (38), 199 (65), 200 (100), 144 (65), 132 (5); **Elemental analysis** calcd for $C_{22}H_{25}NO$: C, 82.72; H, 7.89; N, 4.38. Found: C, 82.59; H, 7.81; N, 4.43.

1,3-Diphenyl-3-(phenylamino)propan-1-one (77):[39]

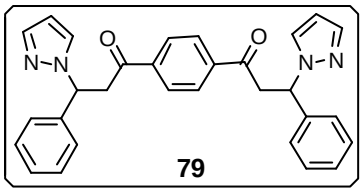


77

Following the general procedure (GP-3); 1,3-diphenylprop-2-yn-1-ol (**38a**; 208 mg, 1.0 mmol), aniline (**39**; 186 mg, 2.0 mmol), and cesium carbonate (326 mg, 1.0 mmol) in toluene (2.0 mL) was heated at 70 °C for 12 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (9:1) to afford **77** (72 mg) in 24% yield as colorless solid.

mp = 165–166 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.96–7.87 (m, 2H), 7.57 (tt, *J* = 1.2, 7.2 Hz, 1H), 7.51–7.41 (m, 4H), 7.34 (t, *J* = 8.0 Hz, 2H), 7.29–7.22 (m, 1H), 7.15–7.05 (m, 2H), 6.68 (t, *J* = 7.2 Hz, 1H), 6.57 (dd, *J* = 0.8, 8.4 Hz, 2H), 5.02 (dd, *J* = 5.2, 7.6 Hz, 1H), 4.57 (bs, 1H), 3.52 (dd, *J* = 5.2, 16.0 Hz, 1H), 3.43 (dd, *J* = 7.6, 16.0 Hz, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 198.2, 147.0, 142.9, 136.7, 133.4, 129.1 (2C), 128.8 (2C), 128.7 (2C), 128.2 (2C), 127.3, 126.3 (2C), 117.7, 113.8 (2C), 54.8, 46.3; **IR (KBr)** ν_{max} 3385, 3024, 2918, 1670, 1599, 1290, 744, 686 cm^{-1}; **MS (EI)** *m/z* (%) 300 (M^+ − 1, 100), 284 (5).

1,1'-(1,4-Phenylene)bis(3-phenyl-3-(1*H*-pyrazol-1-yl)propan-1-one) (79):

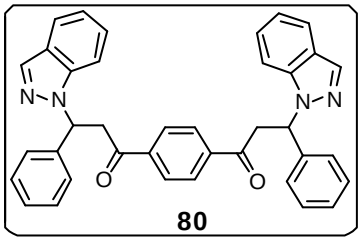


79

Following the general procedure (GP-3); 1,1'-(1,4-phenylene)bis(3-phenylprop-2-yn-1-ol) (**78**; 338 mg, 1.0 mmol), pyrazole (**49a**; 272 mg, 4.0 mmol), and cesium carbonate (652 mg, 2.0 mmol) in toluene (4.0 mL) was heated at 70 °C for 1 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (3:1) to afford **79** (265 mg) in 56% yield as light brown solid.

mp = 173–174 °C; R_f = 0.28 (3 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.01 (s, 4H), 7.47 (dd, *J* = 1.6, 10.0 Hz, 4H), 7.42–7.30 (m, 10H), 6.22 (t, *J* = 2.0 Hz, 2H), 6.08 (dd, *J* = 4.8, 8.4 Hz, 2H), 4.52 (dd, *J* = 8.8, 17.6 Hz, 2H), 3.58 (dd, *J* = 5.2, 17.6 Hz, 2H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 196.2 (2C), 140.4 (2C), 139.8 (2C), 139.2 (2C), 129.7 (2C), 128.8 (4C), 128.4 (4C), 128.1 (2C), 126.6 (4C), 105.7 (2C), 60.7 (2C), 44.5 (2C); **IR (KBr)** ν_{max} 3063, 2918, 1687, 1398, 754, 626 cm^{-1}; **MS (EI)** *m/z* (%) 476 (M^+ + 2, 16), 474 (M^+, 61), 473 (41), 406 (51), 353 (51), 338 (100), 238 (3), 96 (3); **Elemental analysis** calcd for $C_{30}H_{26}N_4O_2$: C, 75.93; H, 5.52; N, 11.81. Found: C, 75.86; H, 5.49; N, 11.68.

1,1'-(1,4-Phenylene)bis(3-(1*H*-indazol-1-yl)-3-phenylpropan-1-one) (80):



80

Following the general procedure (GP-3); 1,1'-(1,4-phenylene)bis(3-phenylprop-2-yn-1-ol) (**78**; 338 mg, 1.0 mmol), 1*H*-indazole (**49f**; 472 mg, 4.0 mmol), and cesium carbonate (652 mg, 2.0 mmol) in toluene (4.0 mL) was heated at 70 °C for 1 h. Upon filtration over Celite and evaporation, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (3:1) to afford **80** (276 mg) in 48% yield as yellow thick liquid.

R_f = 0.50 (3 : 1 hexane–EtOAc); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.07–8.02 (m, 6H), 7.72 (d, *J* = 8.0 Hz, 2H), 7.53 (d, *J* = 8.8 Hz, 2H), 7.41–7.25 (m, 12 H), 7.15 (t, *J* = 7.6 Hz, 2H), 6.49 (dd, *J* = 4.4, 8.8 Hz, 2H), 4.75 (dd, *J* = 8.8, 17.6 Hz, 2H), 3.74 (dd, *J* = 4.4, 17.6 Hz, 2H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 196.2 (2C), 140.5 (2C), 139.7 (2C), 139.5 (2C), 133.0 (2C), 128.7 (4C), 128.3 (4C), 127.8 (2C), 126.5 (4C), 126.3 (2C), 124.2 (2C), 120.9 (2C), 120.8 (2C), 109.4 (2C), 57.4 (2C), 44.6 (2C); **IR (Neat)** ν_{max} 3061, 2924, 1687, 1498, 1024, 740 cm^{-1}; **MS (EI)** *m/z* (%) 576

(M^+ + 1, 14), 575 (M^+, 35), 457 (20), 339 (100), 151 (51), 119 (82); **Elemental analysis** calcd for $C_{38}H_{30}N_4O_2$: C, 79.42; H, 5.26; N, 9.75. Found: C, 79.52; H, 5.21; N, 9.68.

1.5.7. X-Ray Crystallography: Single crystal X-Ray data for the compound **58ab**, **58ac** and **58af** were collected using the detector system [λ(Mo-Kα) = 0.71073 Å] at 298K, graphite monochromator with a ω scan width of 0.3°, crystal-detector distance 60 mm, collimator 0.5 mm. The SMART software[40] was used for the intensity data acquisition and the SAINTPLUS Software[1] was used for the data extraction. In each case, absorption correction was performed with the help of SADABS program,[40] an empirical absorption correction using equivalent reflections was performed with the program. The structure was solved using SHELXS-97,[41] and full-matrix least-squares refinement against F^2 was carried out using SHELXL-97.[41] All non-hydrogen atoms were refined anisotropically. Aromatic and methyl hydrogens were introduced on calculated positions and included in the refinement riding on their respective parent atoms.

Table 1.12. Crystal Data.

	Compound1	**Compound2**	**Compound3**
Identification code	**58ab**	**58ac**	**58af**
Formula	$C_{24}H_{20}N_2O$	$C_{24}H_{19}BrN_2O$	$C_{22}H_{18}N_2O$
F_w	352.42	431.31	326.38
T (K)	298(2)	298(2)	298(2)
λ (Å)	0.71073	0.71073	0.71073
Crystal system	Monoclinic	Triclinic	orthorhombic
Space group	P21/c	*P-1*	Pca2(1)
a (Å)	10.9862(9)	8.4392(16)	19.7487(16)
b (Å)	19.4309(13)	9.3575(16)	9.7599(8)
c (Å)	9.9118(9)	13.599(3)	18.4670(12)
α (^{o})	90.00	103.140(16)	90.00
β (^{o})	115.173(10)	91.434(16)	90.00
γ (^{o})	90.00	104.756(15)	90.00
V (Å^3)	1914.9(3)	1007.4(3)	3559.4(5)
Z	4	2	8
ρ_{calcd} (Mg m^{-3})	1.222	1.422	1.218
μ (mm^{-1})	0.075	2.057	0.076
F (000)	744.0	440.0	1376.0
Crystal Size (mm)	0.20 × 0.18 × 0.16	0.22 × 0.18 × 0.12	0.24 × 0.22 × 0.18
2θ range/deg	3.09 / 24.68	2.83 / 28.95	2.93 / 29.15
Reflections collected	3254	4434	6639
Unique reflections	2181	1946	3376
Completeness to 2θ (%)	24.68 (100)	28.95 (100.0)	29.15 (100)
T_{max}, T_{min}	1.00000, 0.91047	1.00000, 0.66383	0.9865, 0.9821
Parameters	248	253	460
GOF (F^2)	1.068	0.983	1.040
R1, *wR2 [I>2σ(I)]*	0.0962, 0.1026	0.1253, 0.1669	0.0918, 0.1178
R1, *wR2* (all data)	0.0371, 0.0620	0.0634, 0.1573	0.0554, 0.1286
Largest diff. Peak	0.118and -0.114	0.288 and -0.514	0.097 and -0.104

1.6. References

1) See, for example: (a) P. M. Dewick, *Medicinal Natural Products: A Biosynthetic Approach*, 3rd ed.; John Wiley & Sons Ltd: Chichester, 2009. (b) A. R. Katritzky and Pozharskii, *Handbook of Heterocyclic Chemistry*, 2nd ed.; Oxford: Pergamon, 2002. (c) *The Alkaloids: Chemistry and Biology*; G. A. Cordell, Ed.; Academic Press: San Diego, CA, 2000; Vol. 54; (d) D. T. Wang, J. S. Horng, F. P. Bymaster, K. L. Hauser and B. B. Molloy, *Life Sciences*, 1974, **15**, 471.
2) (a) T. B. Poulsen and K. A. Jørgensen, *Chem. Rev*., 2008, **108**, 2903. (b) A. Kleemann, J. Engel, B. Kutscher and D. Reichert, *Pharmaceutical Substences: Synthesis, Patents, Applications*, 4th ed.; George Thieme: Stuttgart, 2001. (c) A. K. Lawrence and K. Gademann, *Synthesis*, 2008, 331. (d) M. D. Lopez, J. Cobo and M. Nogueras, *Curr. Org. Chem*., 2008, **12**, 718. (e) J. P. Michael, *Nat. Prod. Rep*. 2008, **25**, 139.
3) G. L. Regina, F. D. D'Auria, A. Tafi, F. Piscitelli, S. Olla, F. Caporuscio, L. Nencioni, R. Cirilli, F. L. Torre, N. R. De Melo, S. L. Kelly, D. C. Lamb, M. Artico, M. Botta, A. T. Palamara and R. Silvestri, *J. Med. Chem.*, 2008, **51**, 3841.
4) (a) V. K. Marrapu, M. Mittal, R. Shivahare, S. Gupta and K. Bhandari, *Eur. J. Med. Chem.*, 2011, **46**, 1694. (b) K. Bhandari, N. Srinivas, V. K. Marrapu, A. Verma, S. Srivastava and S. Gupta, *Bioorg. Med. Chem. Lett.*, 2010, **20**, 291. (c) R. I. Ishmetova, V. G. Kitaeva and G. L. Rusinov, *Zh. Org. Khim*., 1995, **31**, 431.
5) (a) L. Kumar, A. Sarswat, N. Lal, A. Jain, S. Kumar, S. T. V. S. K. Kumar, J. P. Maikhuri, A. K. Pandey, P. K. Shukla, G. Gupta and V. L. Sharma, *Bioorg. Med. Chem. Lett.*, 2011, **21**, 176. (b) B. K. Pchelka, A. Loupy and A. Petit, *Tetrahedron: Asymmetry*, 2006, **17**, 2516. (c) A. R. Katritzky, B. Galuszka, S. Rachwal and M. Black *J. Heterocycl. Chem.*, 1994, **31**, 917. (d) A. Popov, Z. P. Piskunova, V. N. Matvienko, G. P. Kondratenko and Y. I. Nikolenko, *Khim.–Farm. Zh.*, 1989, **23**, 1232.
6) (a) N. Srinivas and K. Bhandari, *Tetrahedron Lett.*, 2008, **49**, 7070. (b) G. Roman, E. E. Comanita and B. Comanita, *Tetrahedron*, 2002, **58**, 1617. (c) G. Roman, E. Comanita and B. Comanita**,** *Chem. Heterocycl. Compd*, 2002, **38**, 1072. (d) F. Andreani, R. Andrisano, C. D. Casa and M.Tramontini, *Tetrahedron Lett*., 1968, **9**, 1059.
7) (a) J. Wang, W. Wang, X. Liu, Z. Hou, L. Lin and X. Feng, *Eur. J. Org. Chem.*, 2011, 2039. (b) S. Bayindir, E. Erdogen, H. Kilic and N. Saracoglu, *Synlett*, 2010, **10**, 1455.

(c) J. Lv, H. Wu and Y. Wang, *Eur. J. Org. Chem.*, 2010, 2073 and references cited there in. (d) S. W. Kwok, J. E. Hein, V. V. Fokin and K. B. Sharpless, *Heterocycles*, 2008, **76**, 1141. (e) C.-E. Yeom, M. J. Kim and B. M. Kim, *Tetrahedron,* 2007, **63**, 904. (f) M. Kawatsura, S. Aburatani and J. Uenishi, *Tetrahedron,* 2007, **63**, 4172. (g) M. Bandini, A. Eichholzer, M. Monari, F. Piccinelli and A. Umani-Ronchi, *Eur. J. Org. Chem.*, 2007, 2917. (h) M. Gandelman and E. N. Jacobsen, *Angew. Chem. Int. Ed.*, 2005, **44**, 2393. (i) N. Srivastava and B. K. Banik, *J. Org. Chem.*, 2003, **68**, 2109.

8) (a) I. Gosney and A. G. Rowley, *Org. Synth*., 1979, **1**, 5. (b) B. E. Maryanoff and A. B. Reitz, *Chem. Rev*., 1989, **89**, 863.

9) (a) B. M. Trost, *Acc. Chem. Res*., 2002, **35**, 695. (b) P. T. Anastas and J. C. Warner, *Green Chemistry: Theory and Practice*; Oxford University Press: New York, 1998. (c) B. M. Trost, *Science*, 1991, **254**, 1471.

10) (a) B. M. Trost and A. Breder, *Org. Lett.*, 2011, **13**, 398. (b) V. Cadierno, P. Crochet, S. E. García-Garrido and J. Gimeno, *Dalton Trans.*, 2010, **39**, 4015. (c) B. M. Trost, A. C. Gutierrez and R. C. Livingston, *Org. Lett.*, 2009, **11**, 2539. (d) B. M. Trost, N. Maulide and R. C. Livingston, *J. Am. Chem. Soc.*, 2008, **130**, 16502. (e) Y. Miyake, S. Endo, Y. Nomaguchi, M. Yuki and Y. Nishibayashi, *Organometallics*, 2008, **27**, 4017. (f) B. M. Trost and R. C. Livingston, *J. Am. Chem. Soc.*, 1995, **117**, 9586; (g) B. M. Trost, A. Breder and B. Kai, *Org. Lett.*, 2012, **14**, 1708. (h) D. Ma and X. Lu, *J. Chem. Soc., Chem. Commun.*, 1989, 890.

11) (a) N. Ghosh, S. Nayak and A. K. Sahoo, *J. Org. Chem*., 2011, **76**, 500. (b) M. R. Kuram, M. Bhanuchandra and A. K. Sahoo, *J. Org. Chem*., 2010, **75**, 2247.

12) (a) E. Haak, *Eur. J. Org. Chem.*, 2007, 2815. (b) X. Han, *Tetrahedron Lett.*, 2007, **48**, 2845. (c) J. Reisch, *Arch. Pharm*., 1965, **298**, 588. (d) Reaction of **2a** (2.0 mmol) with **4a** (1.0 mmol) in the presence of Cs_2CO_3 in toluene produced **3a** in 81% yield in 1 h at 70 °C.

13) See the Experimental Section.

14) (a) T. W. Green and P. G. M. Wuts, *Protective Groups in Organic Synthesis*, 4th ed.; Wiley: New York, 2007. (b) P. J. Kocienski, *Protecting Group*, 3rd ed.; Thieme: Stuttgart, Germany, 2005.

15) (a) K. W. Hunt, D. A. Moreno, N. Suiter, C. T. Clark and G. Kim, *Org. Lett.*, 2009, **11**, 5054. (b) H. Kaddouri, V. Vicente, A. Ouali, F. Ouazzani and M. Taillefer, *Angew. Chem. Int. Ed.*, 2009, **48**, 333.

16) M. P. Kumar and R.-S. Liu, *J. Org. Chem.*, 2006, **71**, 4951.

17) (a) V. Cadierno, J. Gimeno and N. Nebra, *Adv. Synth. Catal.*, 2007, **349**, 382. (b) V. Cadierno, J. Gimeno and N. Nebra, *Chem.–Eur. J.*, 2007, **13**, 9973. (c) Z.-P. Zhan, J.-L. Yu, H.-J. Liu, Y.-Y. Cui, R.-F. Yang, W.-Z. Yang and J.-P. Li, *J. Org. Chem.*, 2006, **71**, 8298 and references cited therein.

18) (a) X. Zhang, W.-Z. Zhang, X. Ren, L.-L. Zhang and X.-B. Lu, *Org. Lett.*, 2011, **13**, 2402. (b) M. Carril, A. Correa and C. Bolm, *Angew. Chem. Int. Ed.*, 2008, **47**, 4862.

19) T. Nishimura, X.-X. Guo, N. Uchiyama, T. Katoh and T. Hayashi, *J. Am. Chem. Soc.*, 2008, **130**, 1576.

20) (a) B. M. Trost, M. Osipov and G. Dong, *J. Am. Chem. Soc.*, 2010, **132**, 15800. (b) F. Bellina and R. Rossi, *Tetrahedron*, 2006, **62**, 7213. (c) J. S. Yadav, S. Abraham, B. V. S. Reddy and G. Sabitha, *Tetrahedron Lett.*, 2001, **42**, 8063. (d) J. M. Patterson and S. Soedigdo, *J. Org. Chem.*, 1968, **33**, 2057.

21) (a) J. P. Sonye and K. Koide, *J. Org. Chem.*, 2007, **72**, 1846. (b) J. P. Sonye and K. Koide, *Org. Lett.*, 2006, **8**, 199. (c) J. P. Sonye and K. Koide, *J. Org. Chem.*, 2006, **71**, 6254. (d) J. P. Sonye and K. Koide, *Synth. Commun.*, 2006, **36**, 599. (e) T. Ishikawa, T. Mizuta, K. Hagiwara, T. Aikawa, T. Kudo and S. Saito, *J. Org. Chem.*, 2003, **68**, 3702. (f) A. Coelho, E. Sotelo and E. Raviña, *Tetrahedron*, 2003, **59**, 2477. (g) T. J. J. Müller, M. Ansorge and D. Aktah, *Angew. Chem. Int. Ed.*, 2000, **39**, 1253. (h) A. W. Nineham and R. A. Raphael. *J. Chem. Commun.*, 1949, 118.

22) (a) J.-L. Niu, M.-C. Wang, L.-J. Lu, G.-L. Ding, H.-J. Lu, Q.-T. Chen and M.-P. Song, *Tetrahedron: Asymmetry*, 2009, **20**, 2616. (b) J. Mao, Z. Bao, J. Guo and S. Ji, *Tetrahedron*, 2008, **64**, 9901. (c) K. Yoshizawa and T. Shioiri, *Tetrahedron*, 2007, **63**, 6259. (d) L. Liu and L. Pu, *Tetrahedron*, 2004, **60**, 7427. (e) J. H. Ahn, M. J. Joung and N. M. Yoon, *J. Org. Chem.*, 1995, **60**, 6173.

23) (a) S. K. Sharma, S. Gupta, M. Saifuddin, A. K. Mandadapu, P. K. Agarwal, H. M. Gauniyal and B. Kundu, *Tetrahedron Lett.*, 2011, **52**, 65. (b) C. Li, X. Li, X. Meng, T. Wang, J. Li and B. Chen, *Synth. Commun.*, 2011, **41**, 1208. (c) D.-W. Chen and M. Ochiai, *J. Org. Chem.*, 1999, **64**, 6804.

24) (a) X. Du, Q. Wnag, X. He, R.-G. Peng, X. Zhang and X.-Q. Yu, *Tetrahedron: Asymmetry*, 2011, **22**, 1142. (b) C. Morrill and R. H. Grubbs, *J. Am. Chem. Soc.*, 2005, **127**, 2842. (c) W. C. Agosta, R. A. Caldwell, J. Jay, L. J. Johnston, B. R. Venepalli, J. C. Scaiano, M. Singh and S. Wolff, *J. Am. Chem. Soc.*, 1987, **109**, 3050.

25) D. Kashinath, S. Tisserand, N. Puli, J. R. Falck and R. Baati, *Eur. J. Org. Chem.*, 2010, 1869.

26) W. Yan, Q. Wang, Y. Chen, J. L. Petersen and X. Shi, *Org. Lett*., 2010, **12**, 3308.

27) L. I. Vereshchagin, L. P. Kirillova and S. I. Demina, *Zh. Org. Khim.*,1973, **9**, 300.

28) B. Wang, H.-X. Sun and Z.-H. Sun, *J. Org. Chem*., 2009, **74**, 1781.

29) V. Maraval, C. Duhayon, Y. Coppel and R. Chauvin, *Eur. J. Org. Chem.*, 2008, 5144.

30) U. Kazmaier, S. Lucas and M. Klein, *J. Org. Chem*., 2006, **71**, 2429.

31) A. Yoshida, M. Ikeda, G. Hattori, Y. Miyake and Y. Nishibayashi, *Org. Lett.*, 2011, **13**, 592.

32) G. Blay, L. Cardona, I. Fernández, A. Marco-Aleixandre, M. C. Muñoz and J. R. Pedro, *Org. Biomol. Chem.*, 2009, **7**, 4301.

33) Y. Yue, M. Turlington, X.-Q. Yu and L. Pu, *J. Org. Chem.*, 2009, **74**, 8681.

34) H. Yamabe, A. Mizuno, H. Kusama and N. Iwasawa, *J. Am. Chem. Soc.*, 2005, **127**, 3248.

35) F. Andreani, R. Andrisano, C. Della Casa and M. Tramontini, *J. Chem. Soc. (C)*, 1970, 1157.

36) A. R. Katritzky, A. Pastor and M. Voronkov, *Org. Lett.*, 2000, **2**, 249.

37) A. L. Patel, H. R. Talele, H. S. Rama and A. V. Bedekar, *Synth. Commun.*, 2009, **39**, 3016.

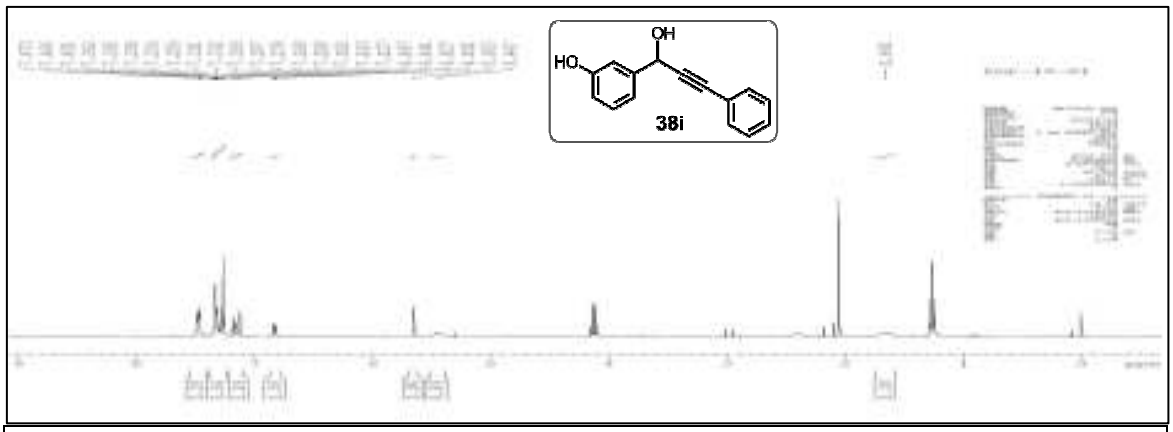
38) C. C. Llopart and J. Joule, *Arch. Org. Chem.*, 2004, **10**, 20.

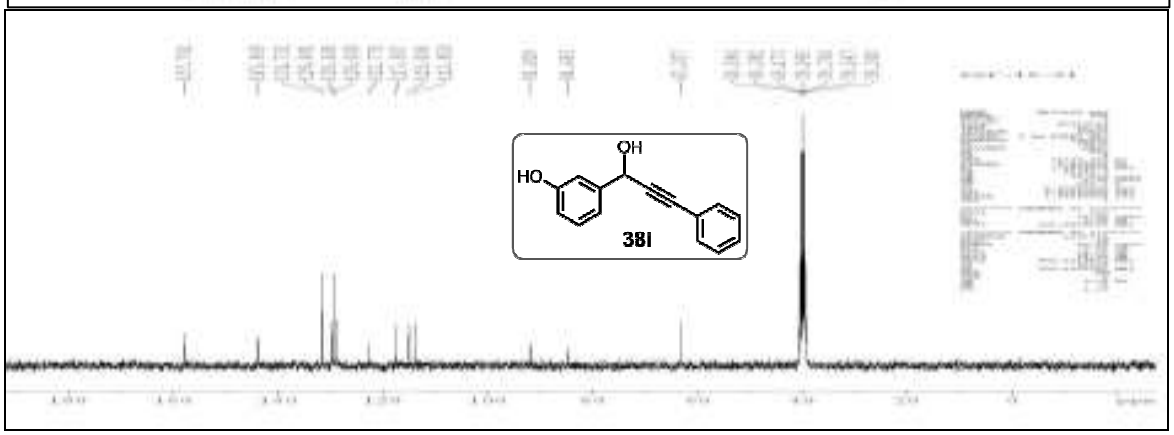
39) S. R. Roy and A. K. Chakraborti, *Org. Lett.*, 2010, **12**, 3866.

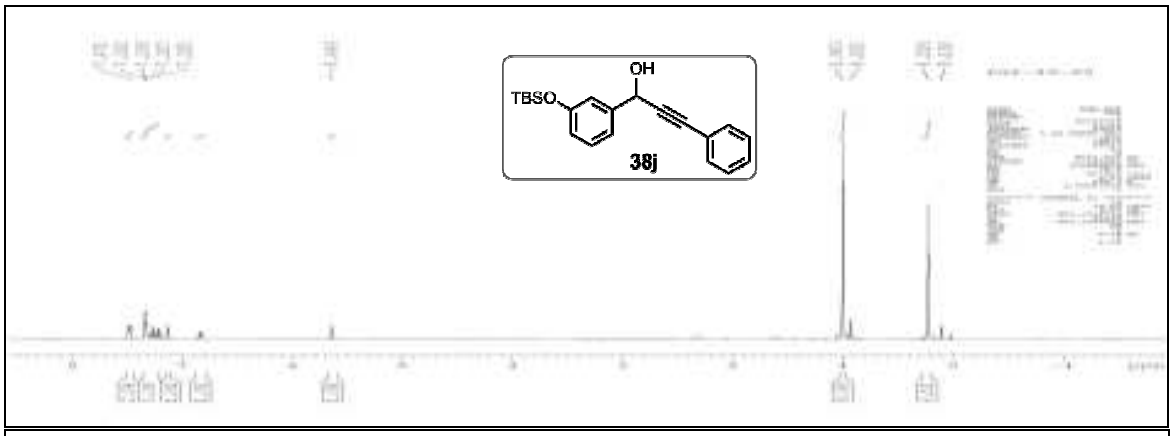
40) Bruker SMART V5.630 and SAINT-PLUS V6.45, Bruker-Nonius Analytical X-ray Systems Inc.: Madison, Wisconsin, USA 2003. SADABS, Empirical absorption correction program, Bruker AXS Inc., Madison, Wisconsin, USA 1997.

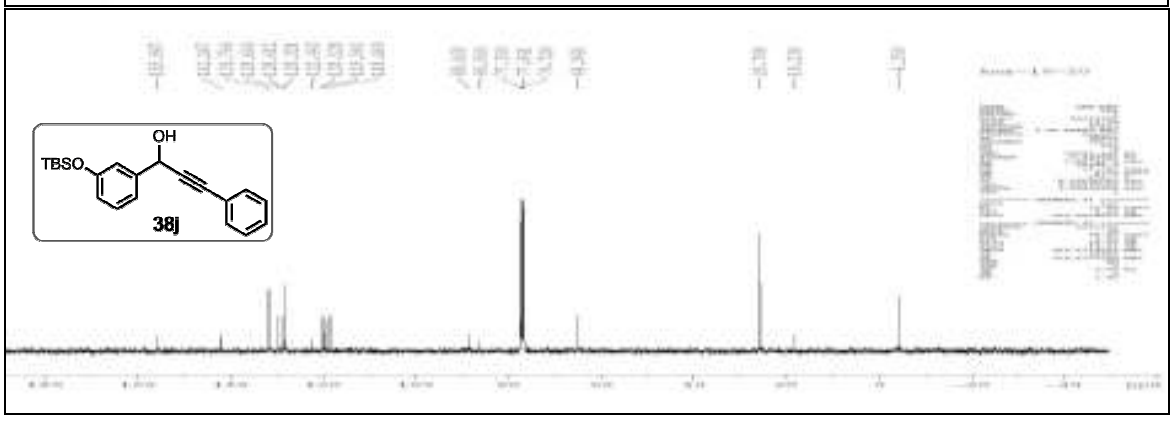
41) Sheldrick, G. M. *Acta Crystallogr. Sect. A* 2008, **64**, 112.

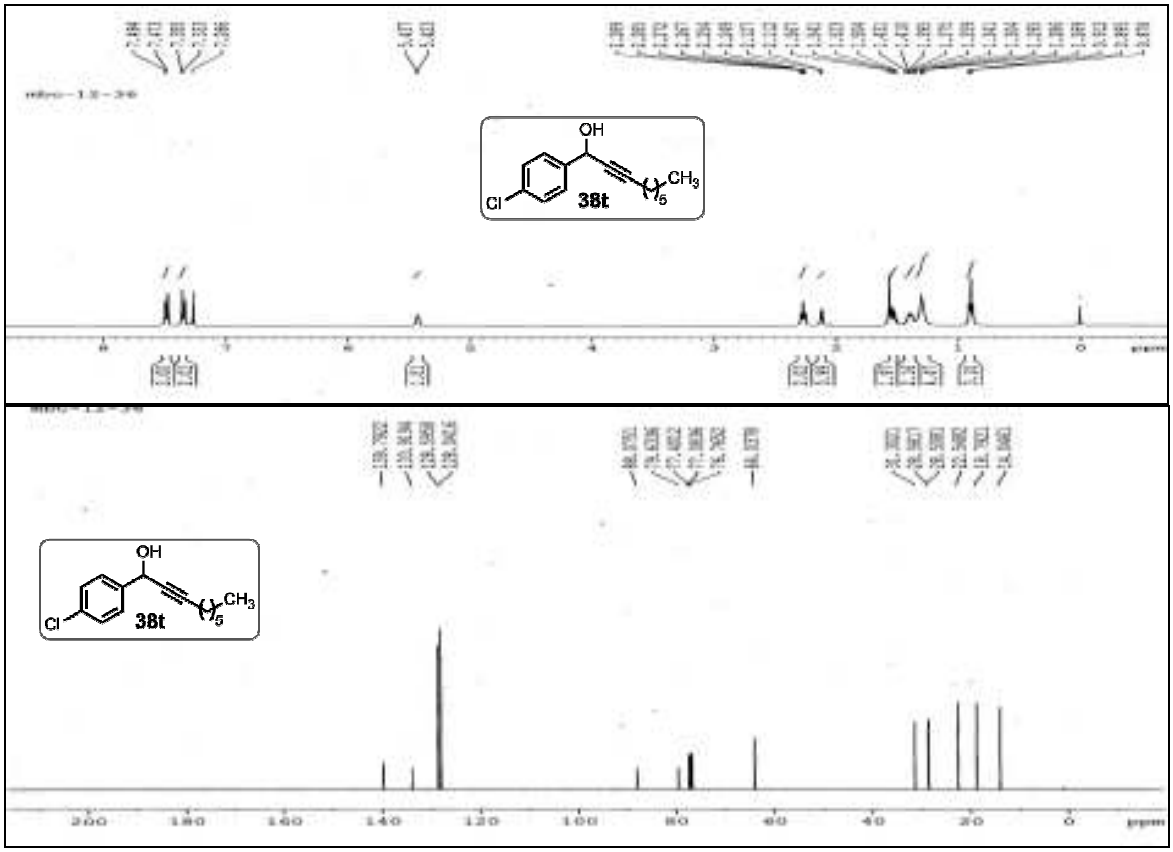
1.7. Spectra

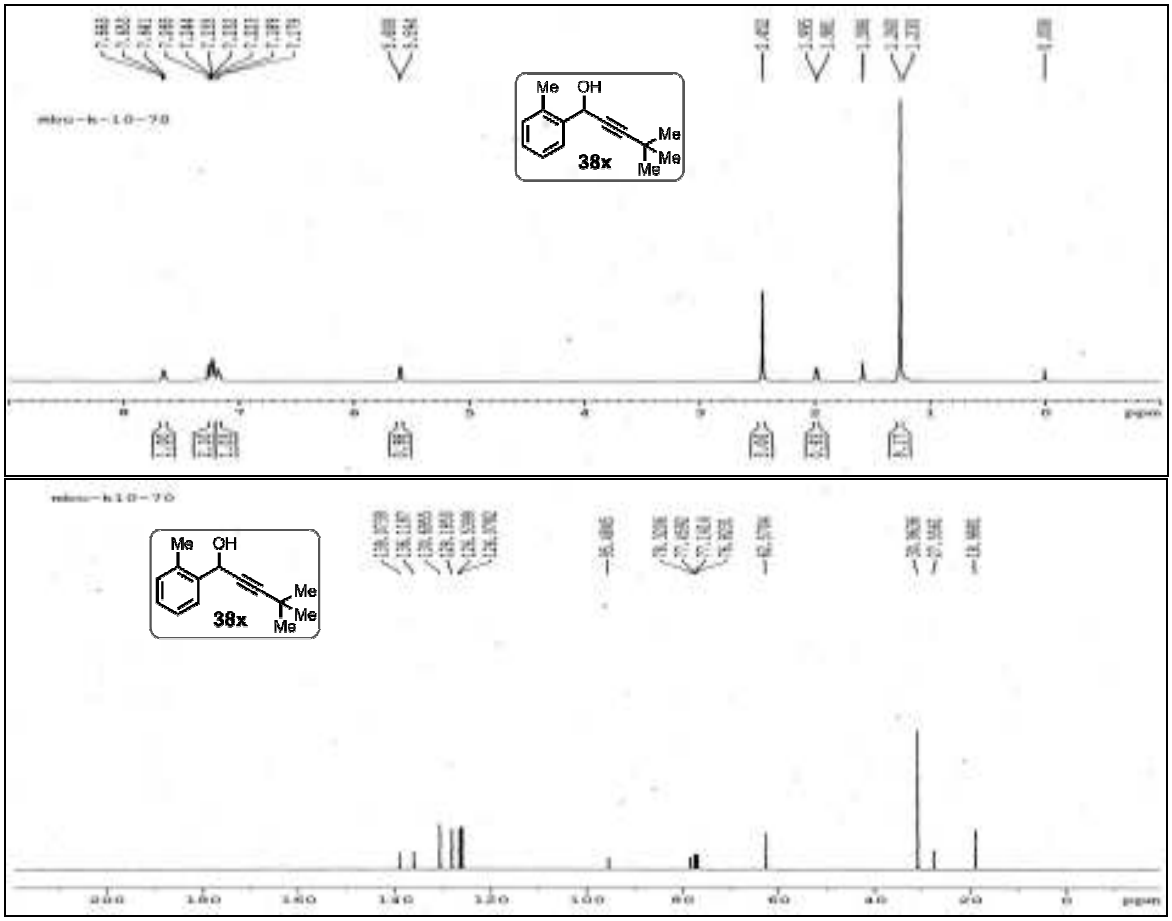


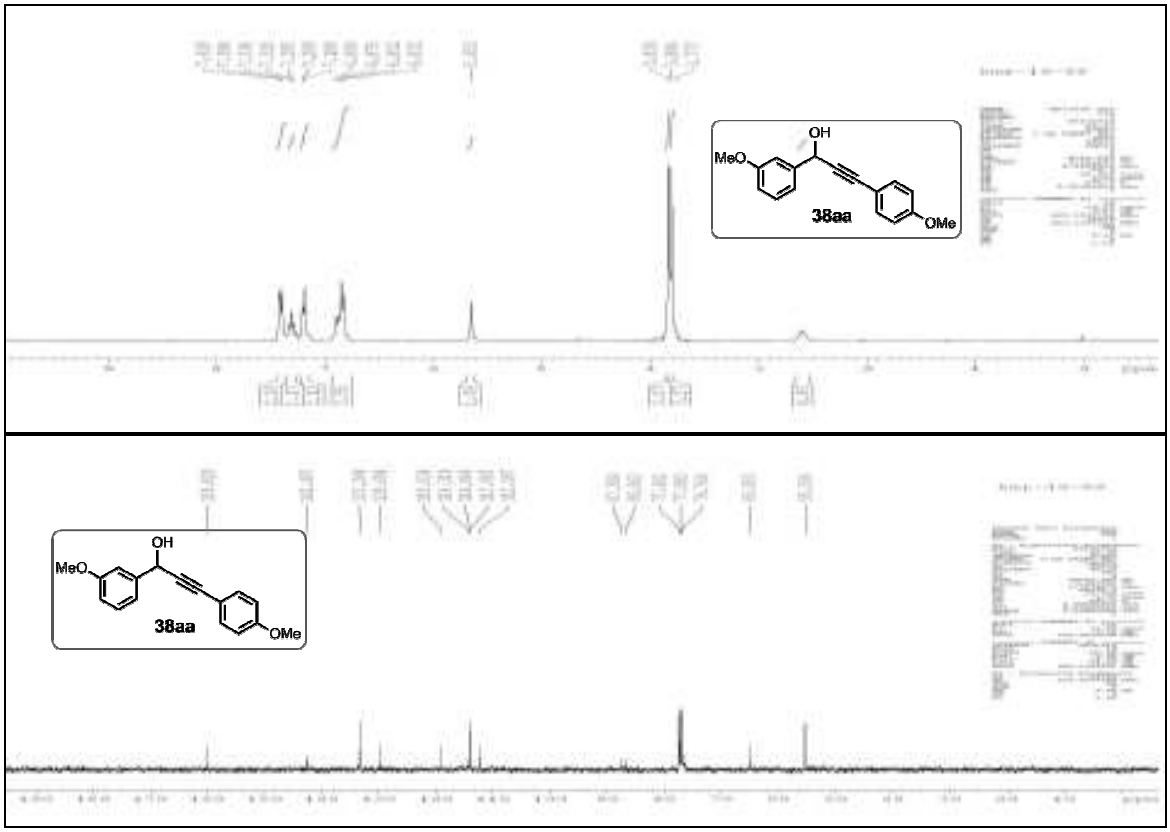


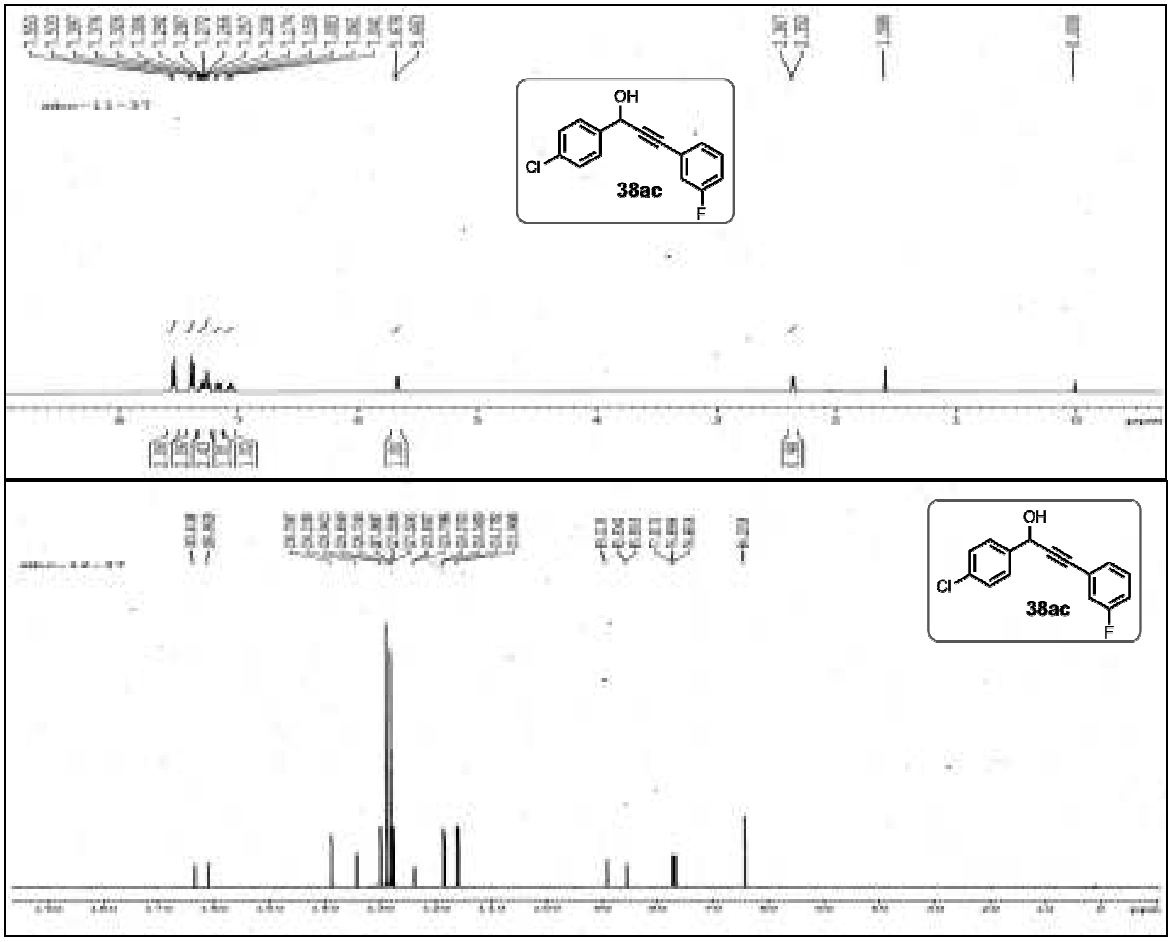


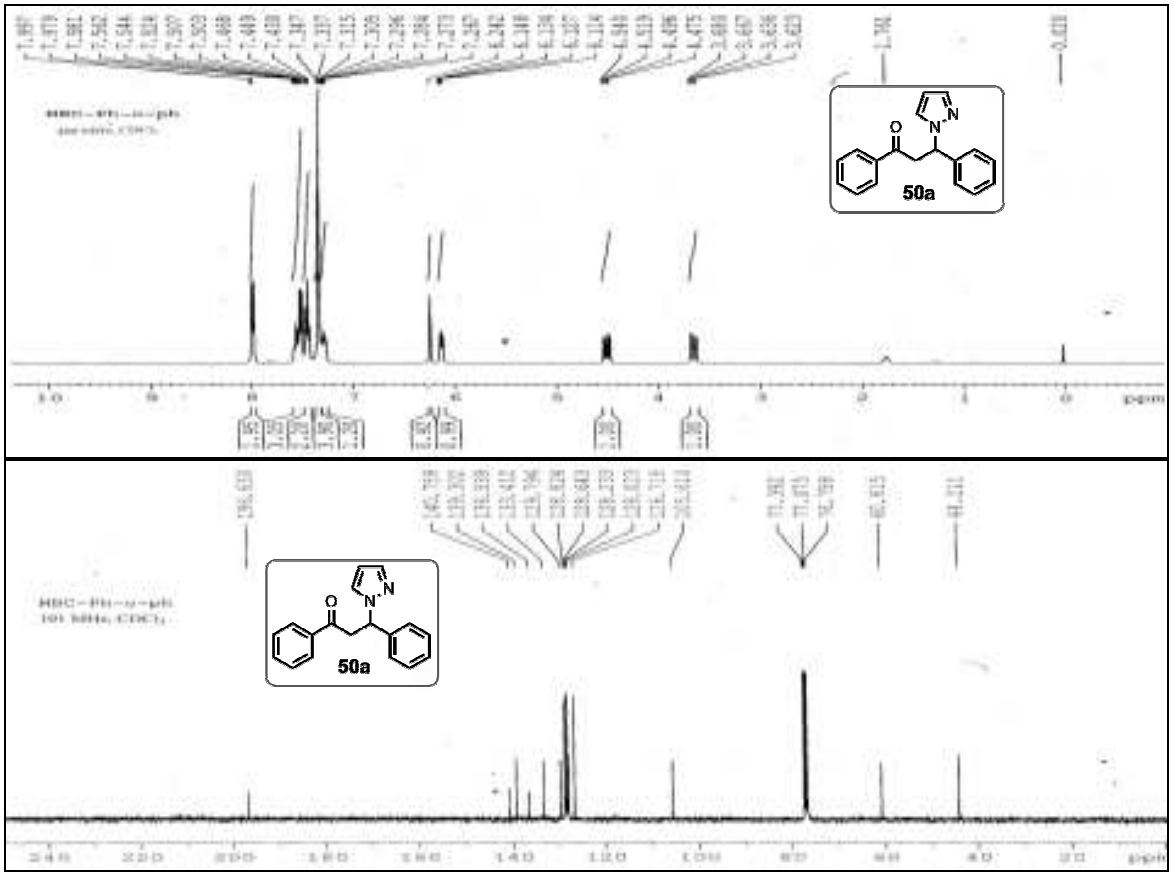


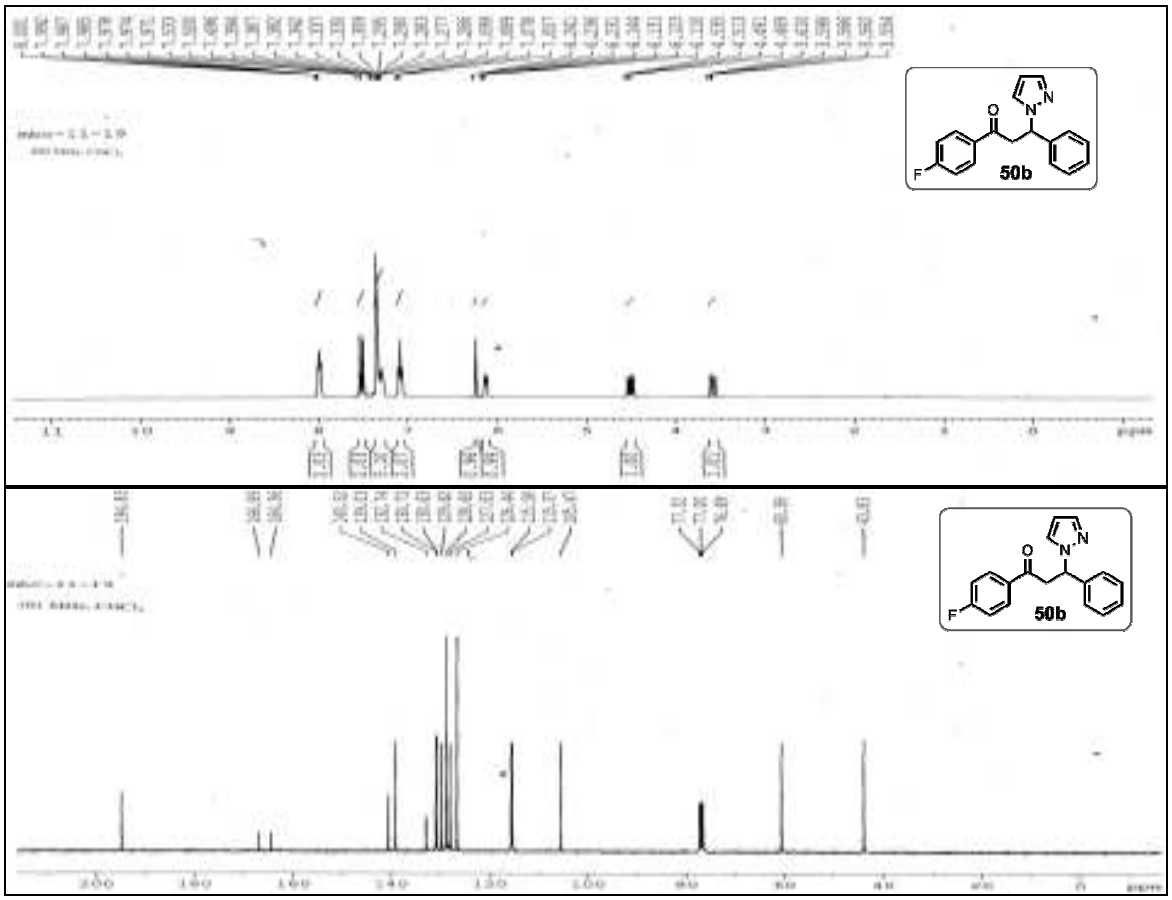

OH
Cl
38t
CH3
5

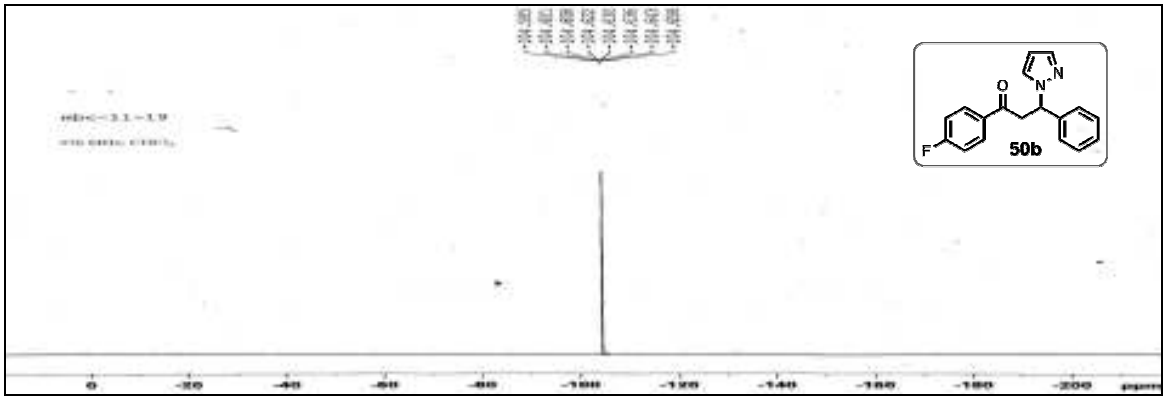

Me
OH
Me
Me
38x

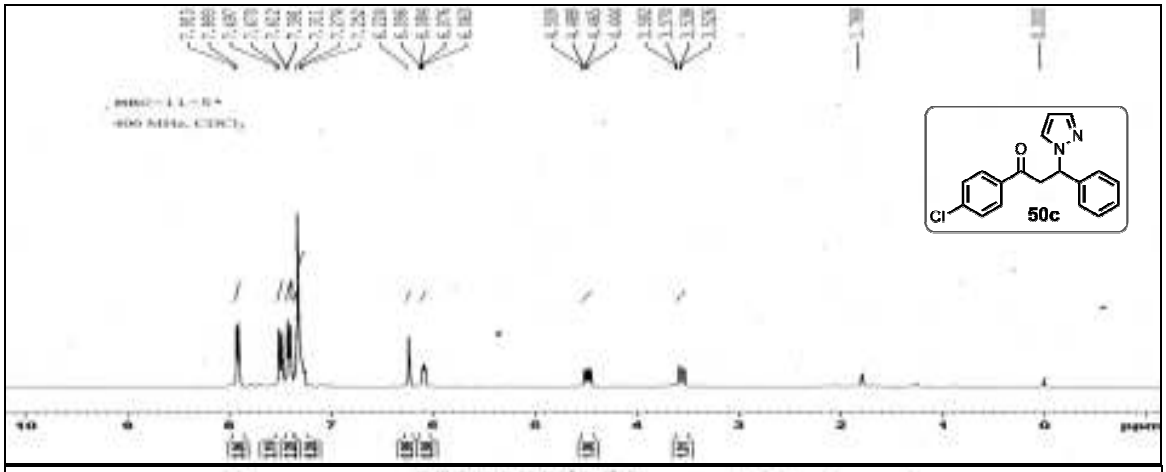

OH
MeO
38aa
OMe
OH
MeO
38aa
OMe

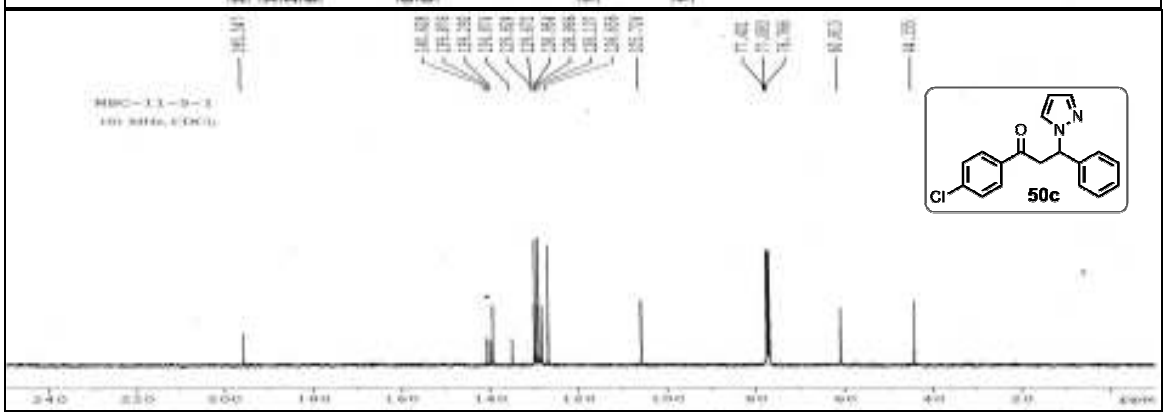

OH
Cl
38ac
F
OH
Cl
38ac
F

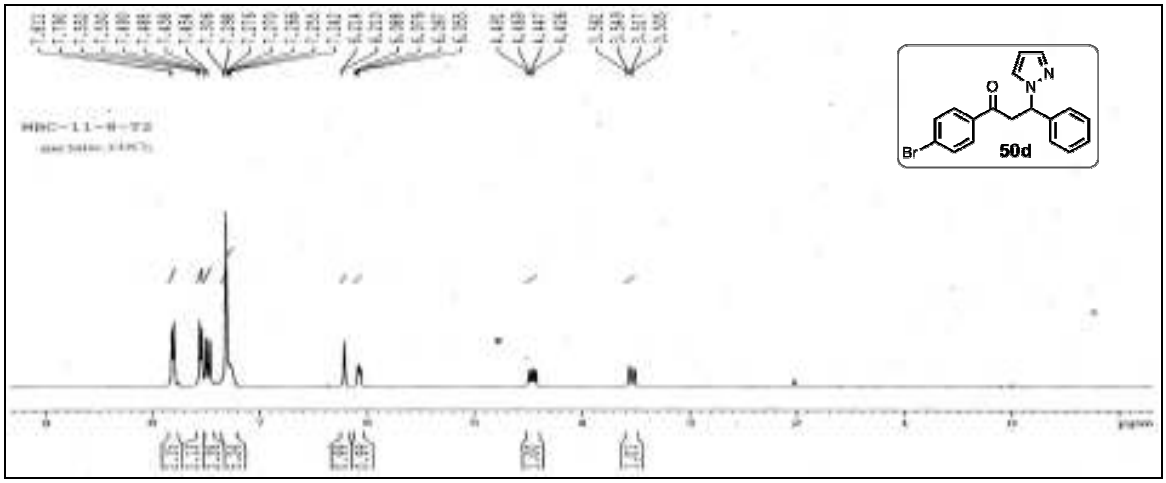

50a
50a

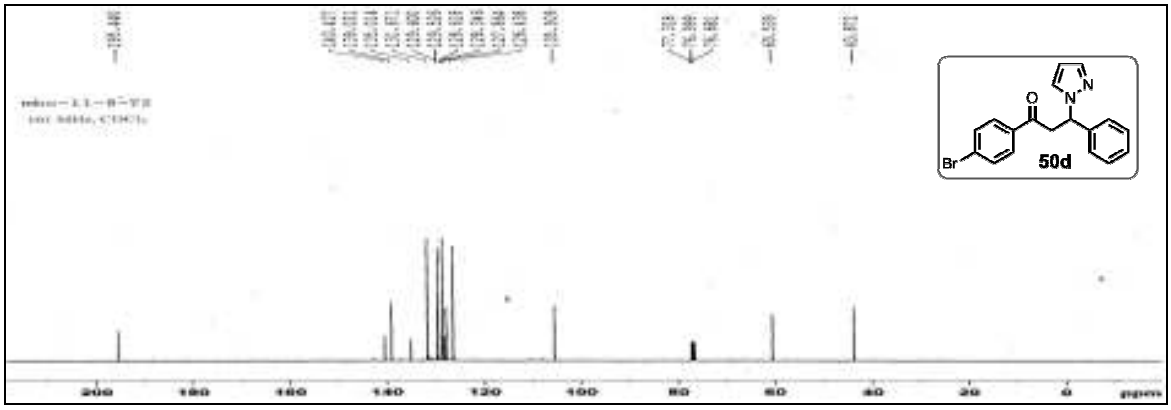

50b
50b

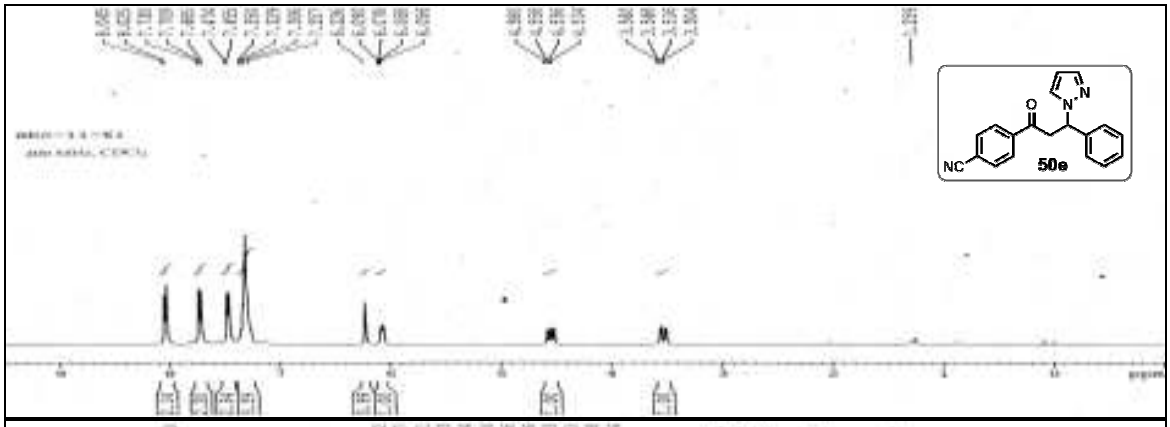

50b

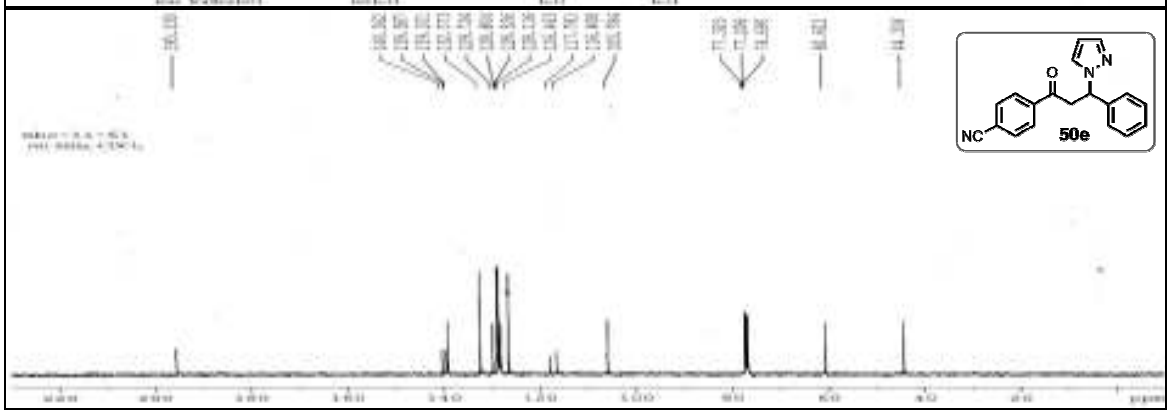

50c

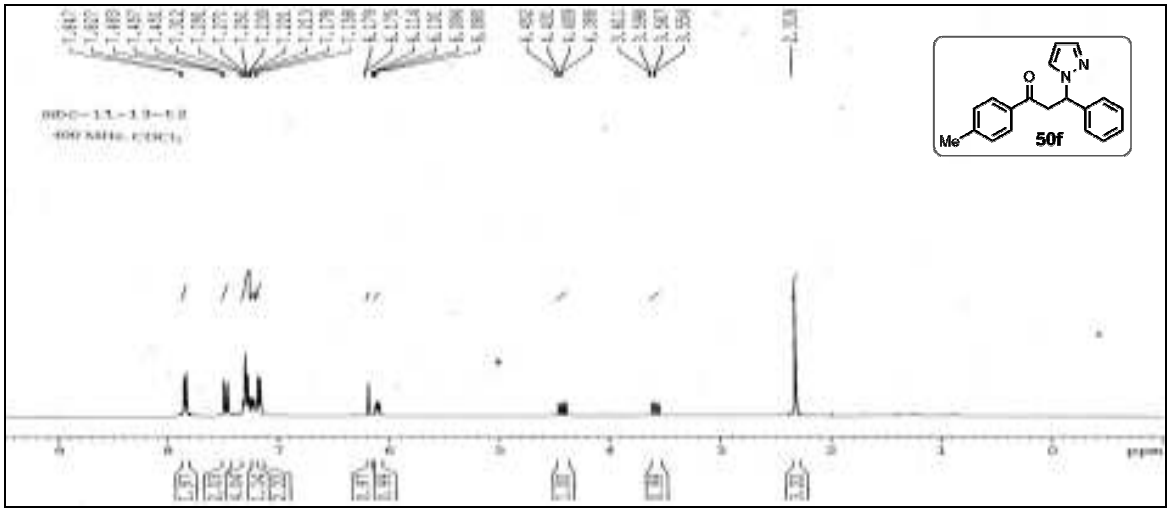

50c

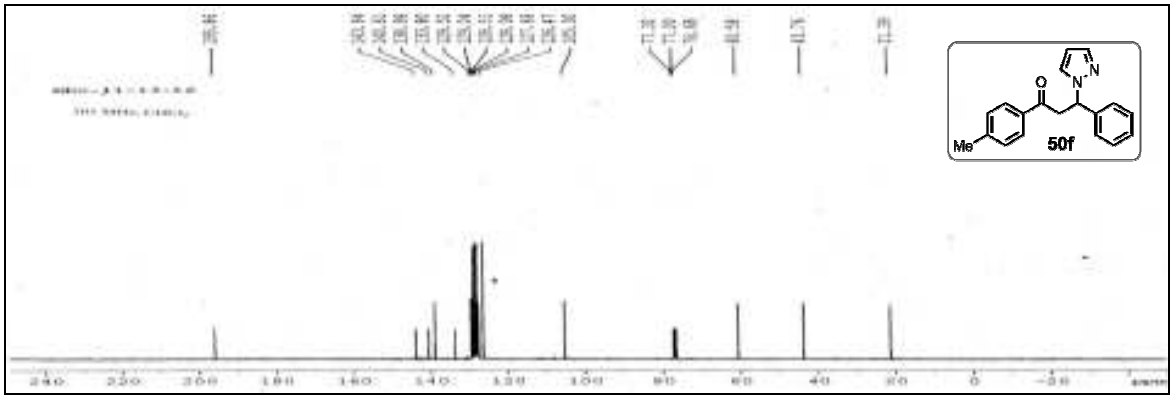

50d

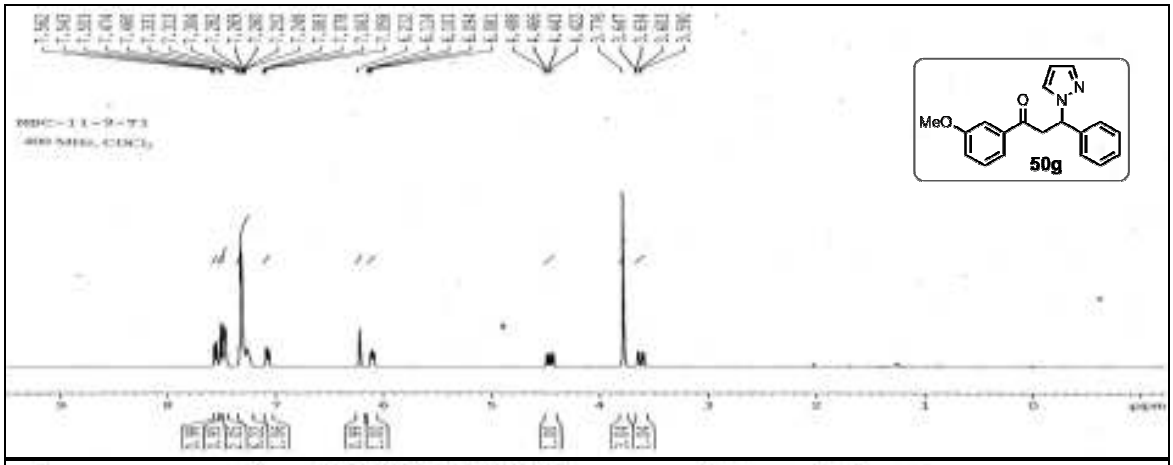

Br
50d

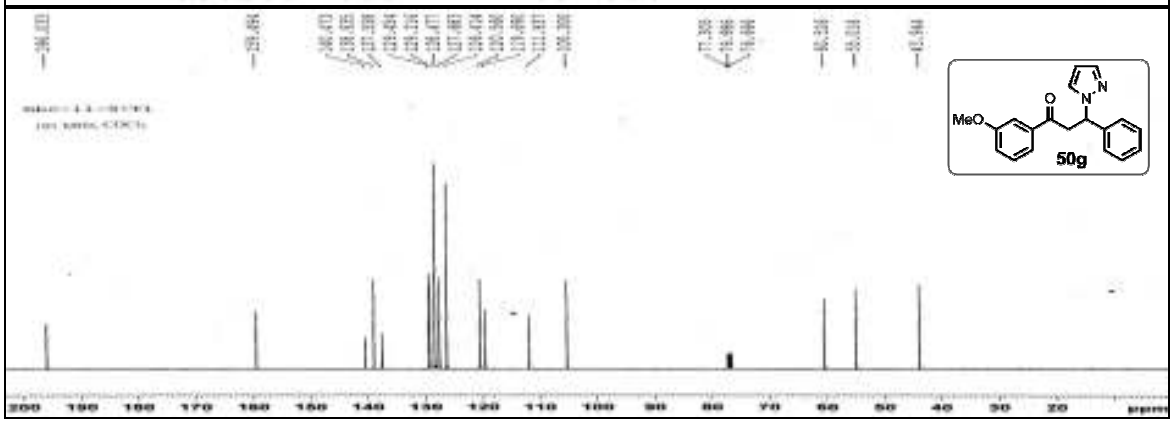

NC
50e

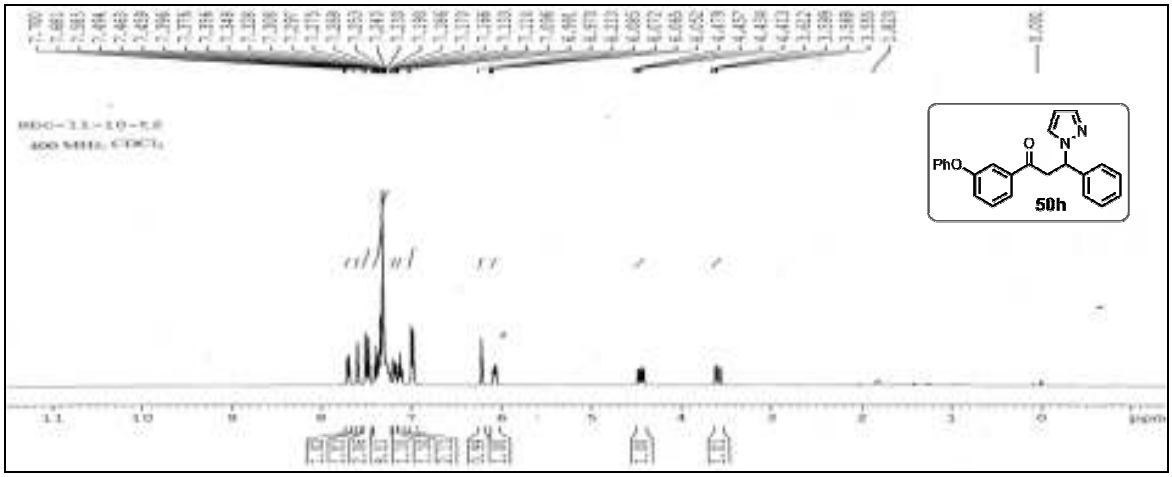

NC
50e

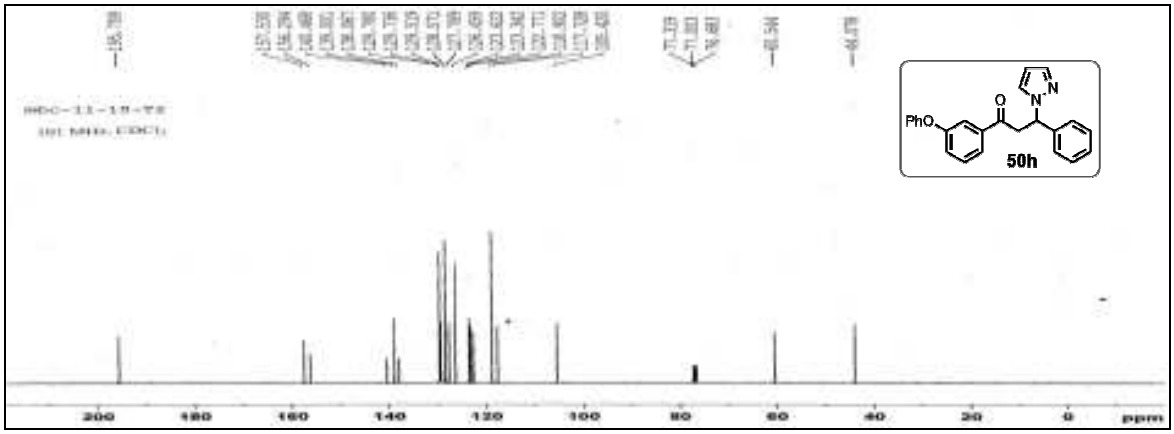

Me
50f

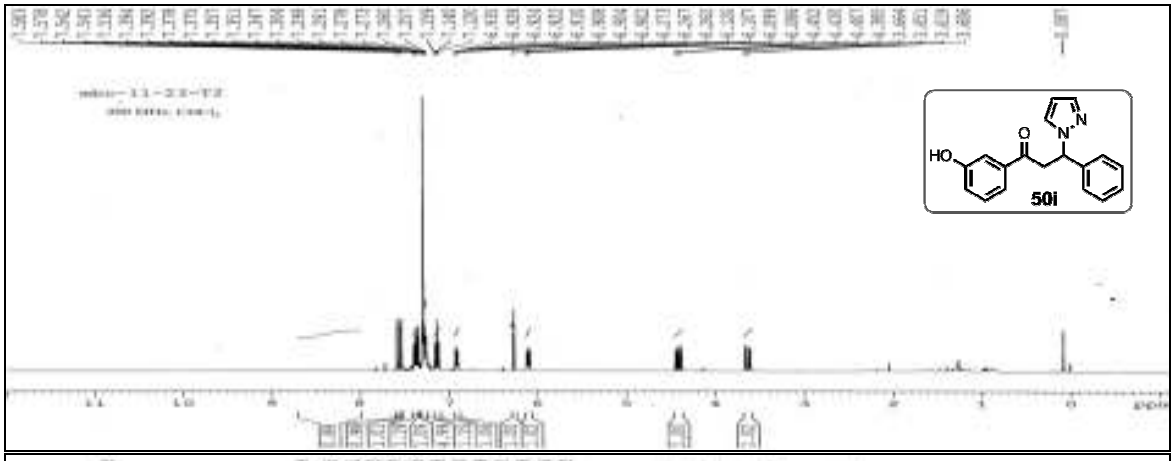

Me
50f

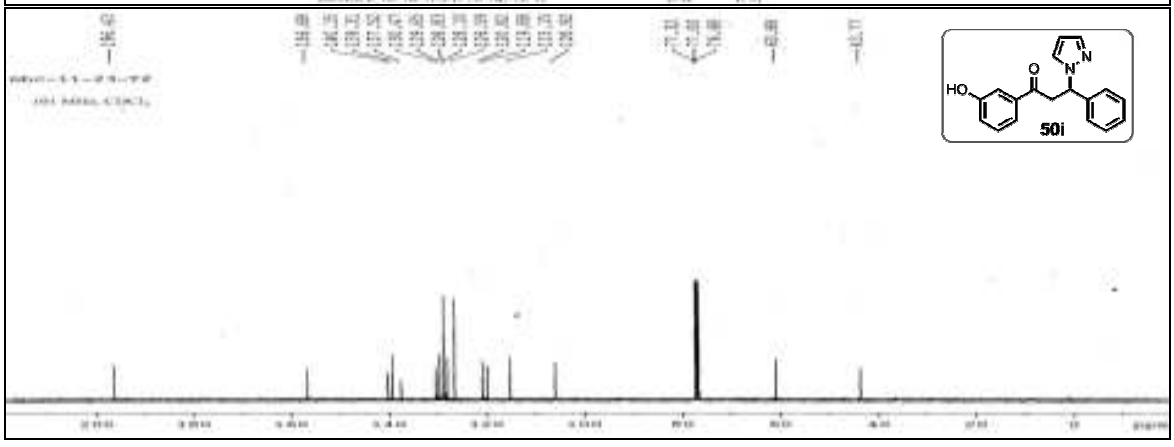

MeO
50g

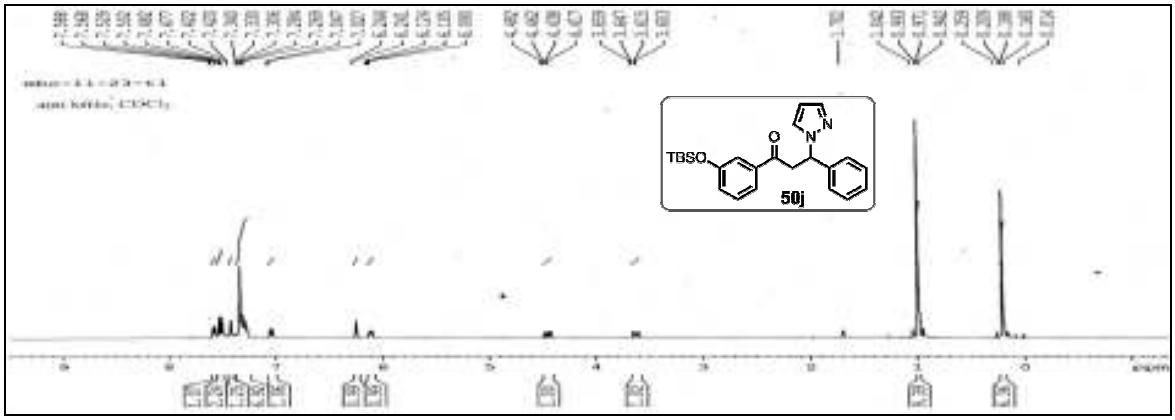

MeO
50g

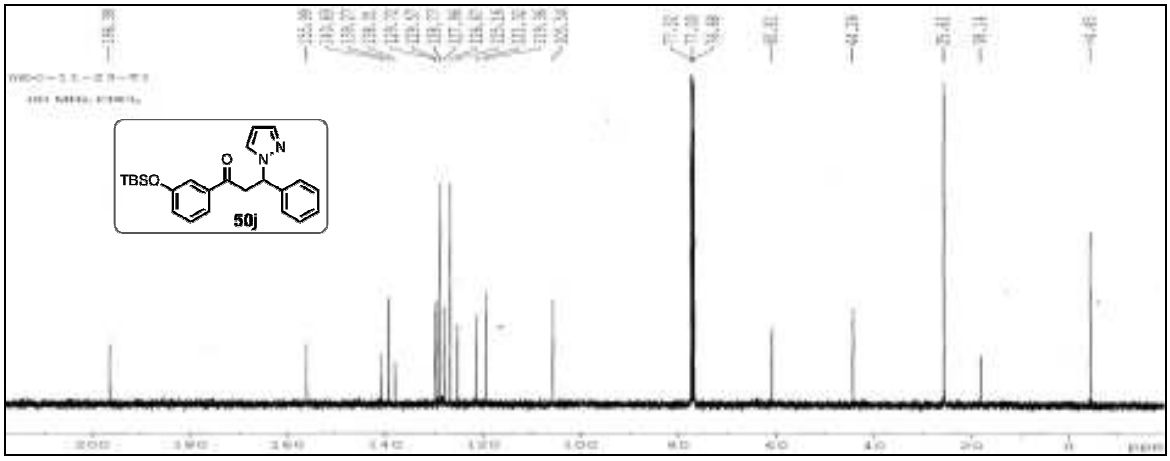

PhO
50h

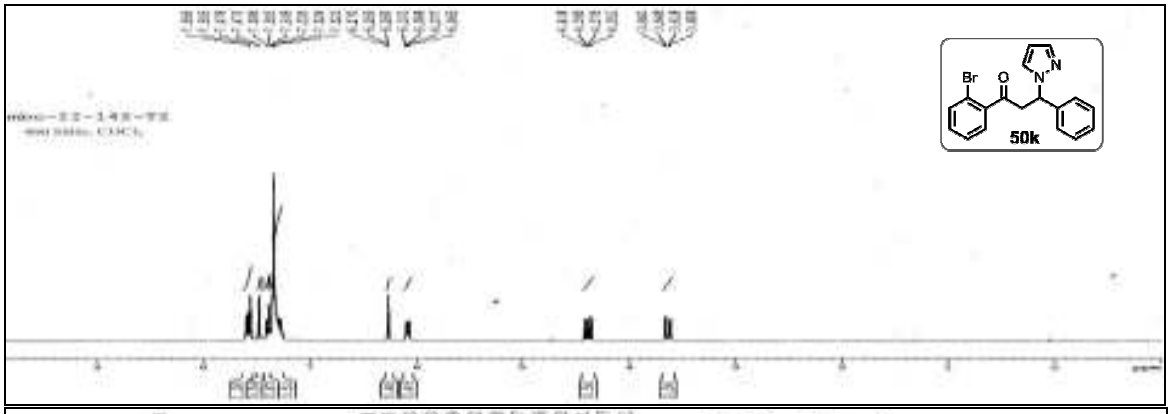

PhO
50h

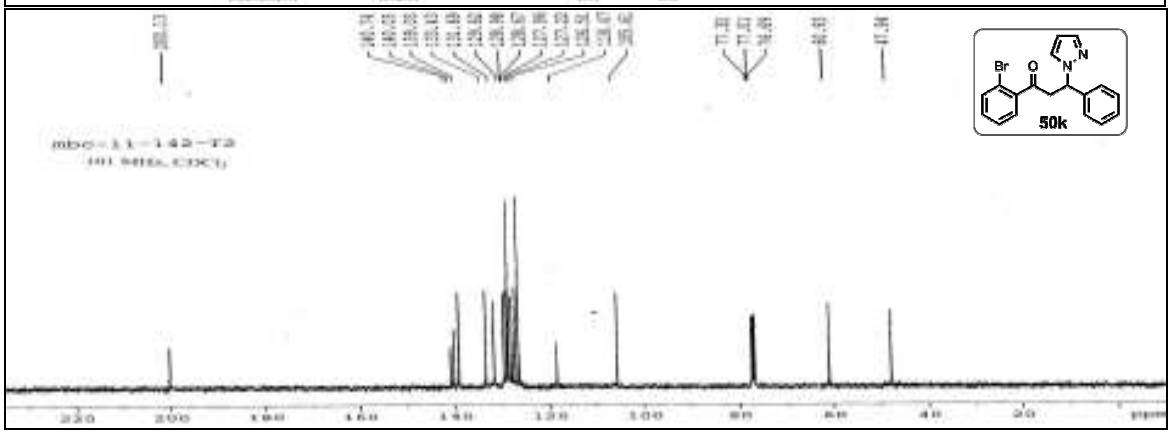

HO
50i

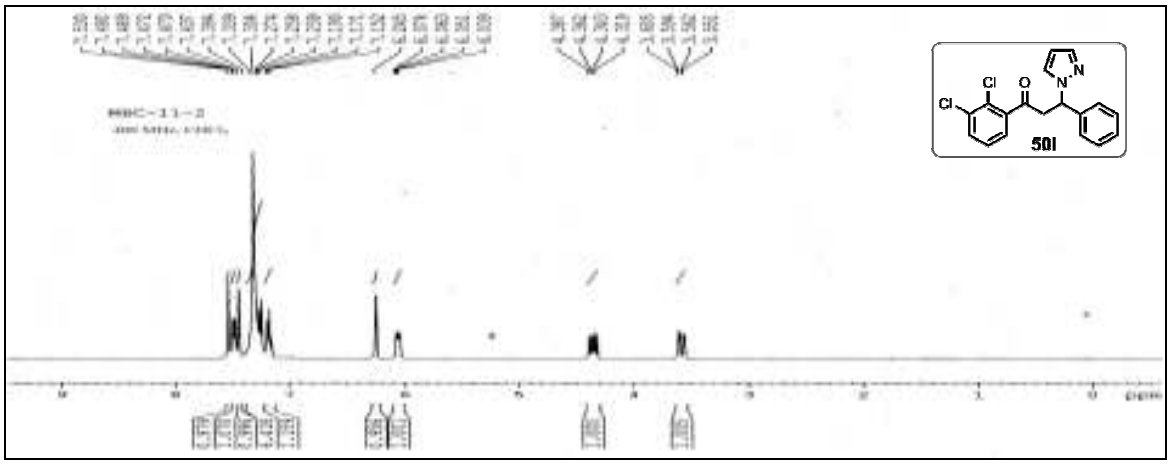

HO
50i

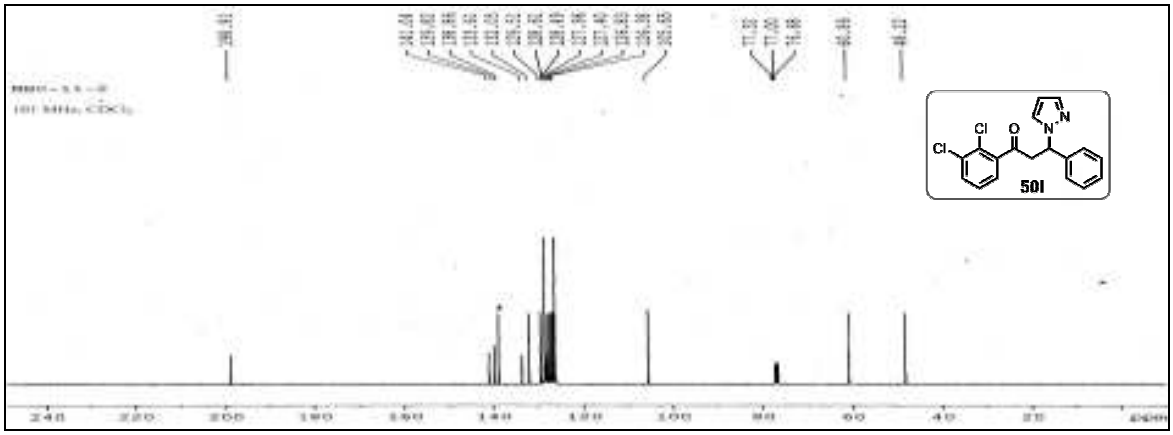

TBSO
50j

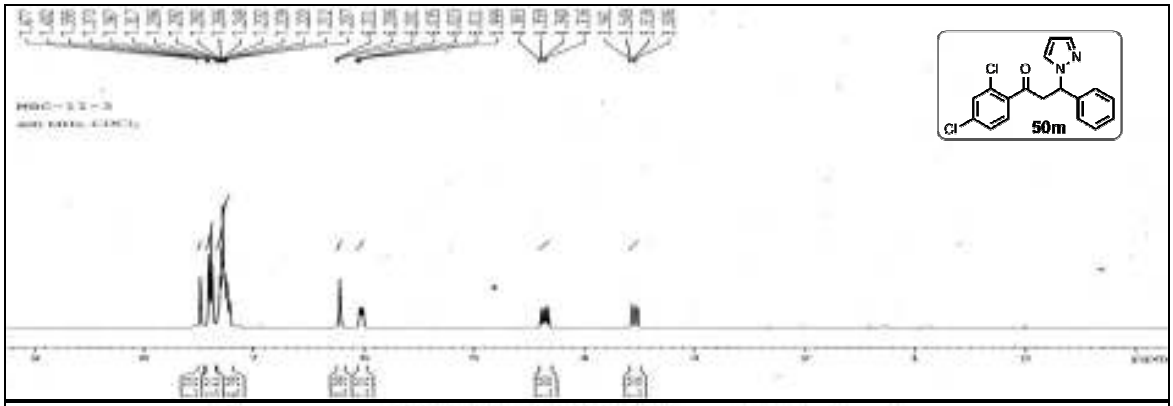

TBSO
O
N
N
50j

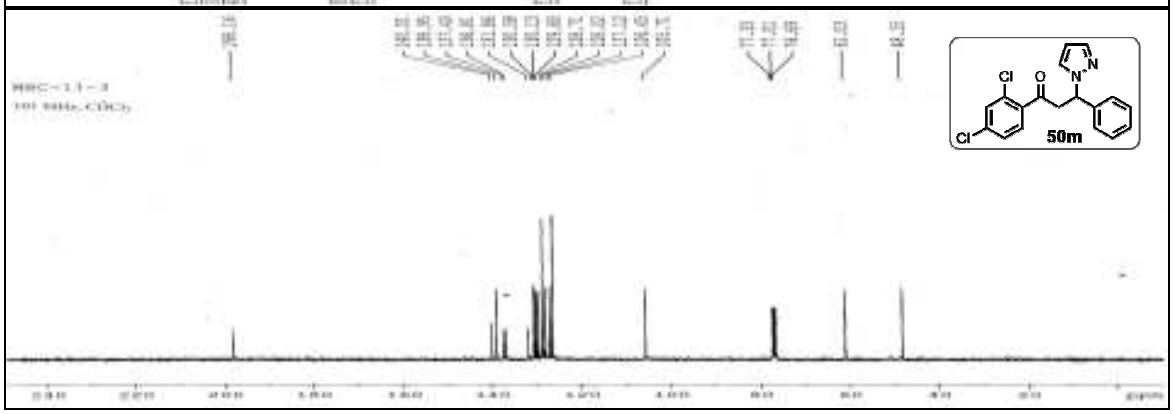

Br
O
N
N
50k

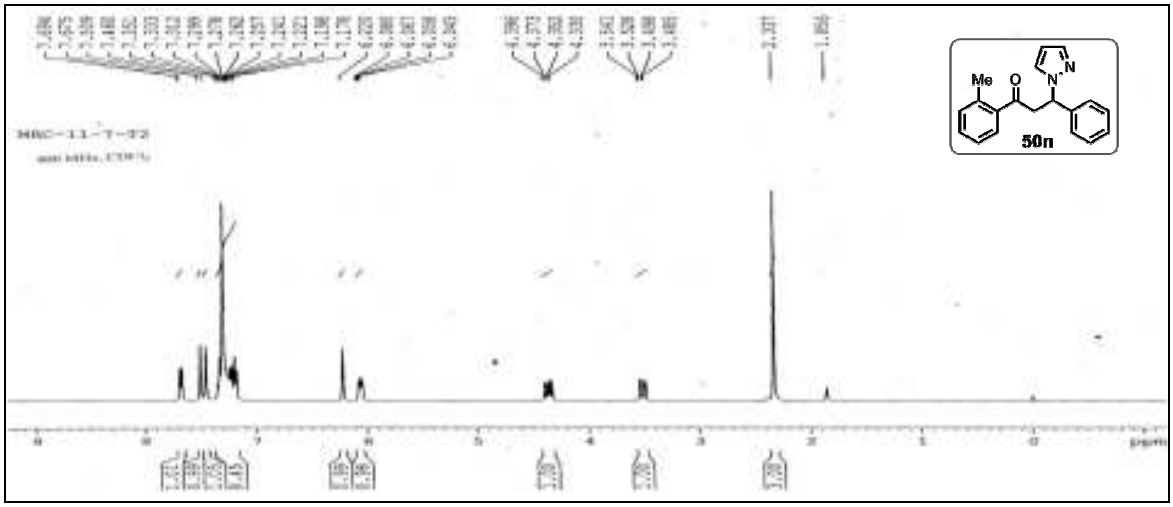

Br
O
N
N
50k

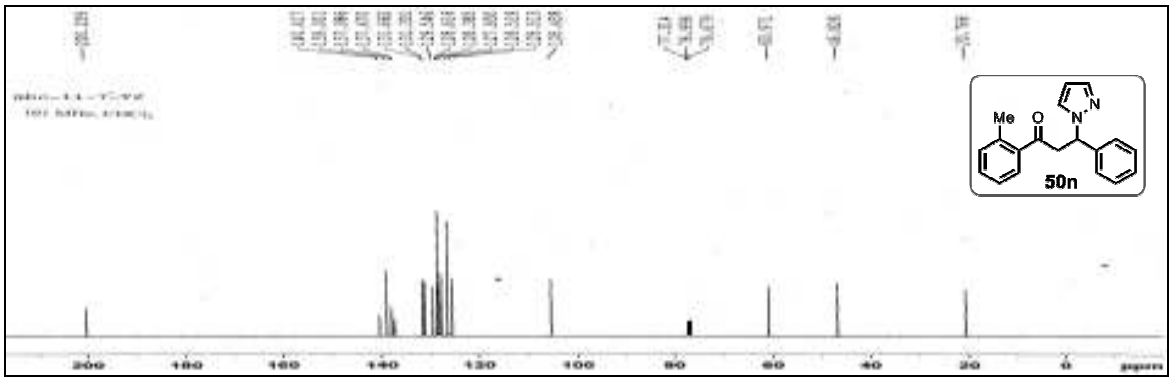

Cl
Cl
O
N
N
50l

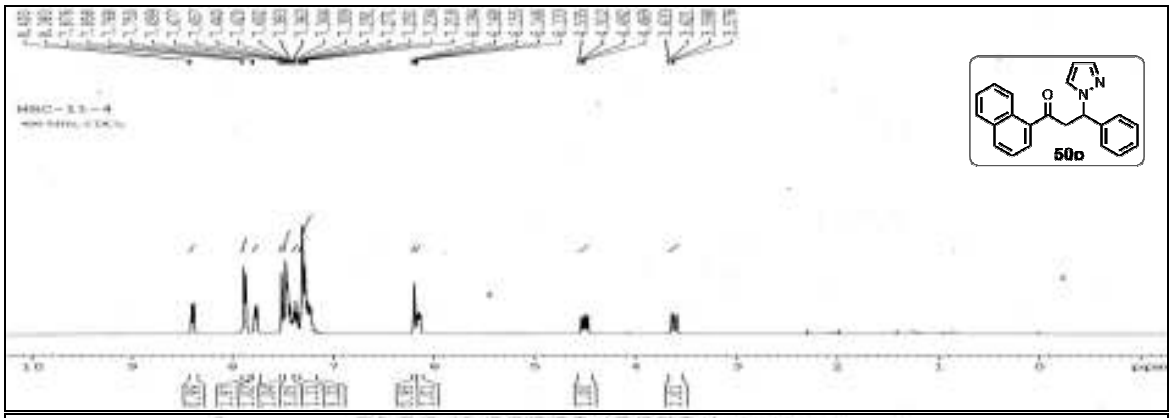

50l

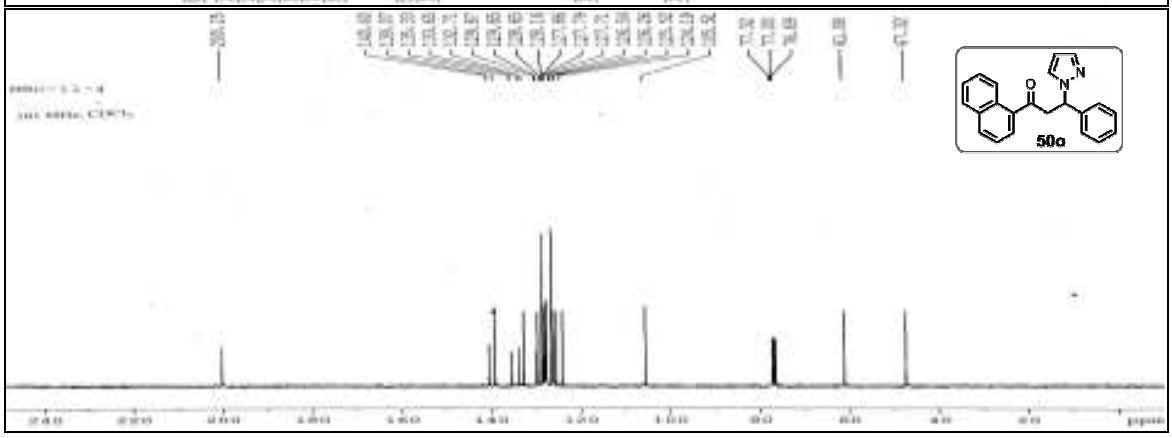

50m

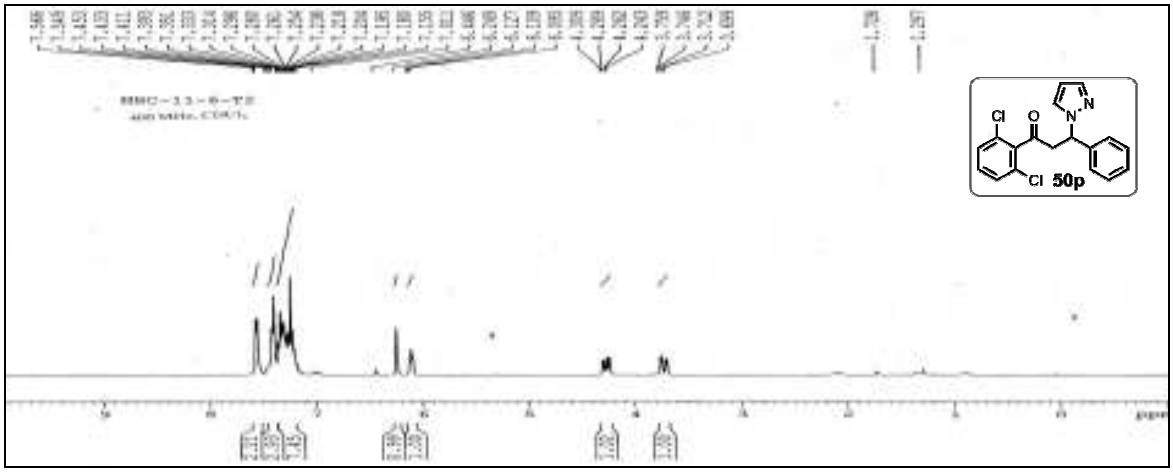

50m

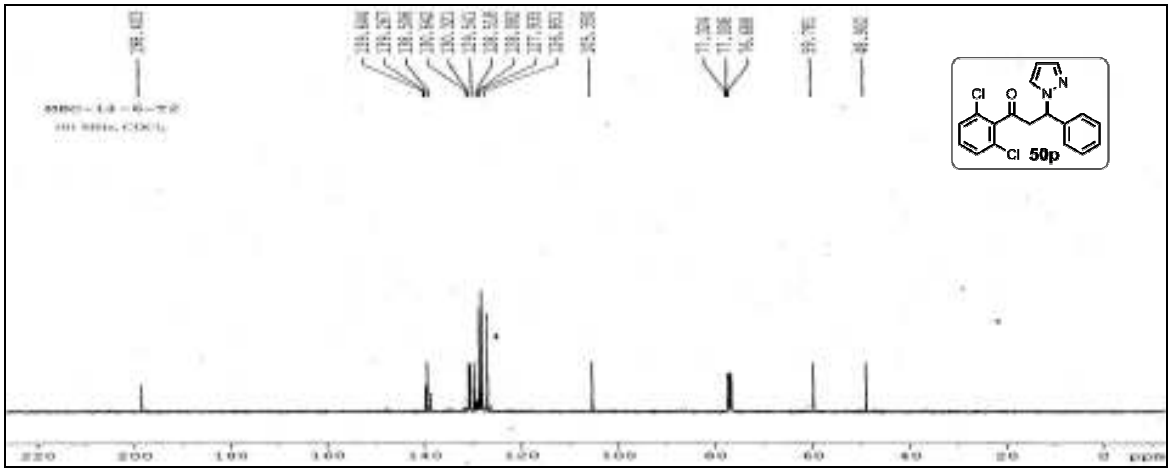

Me
50n

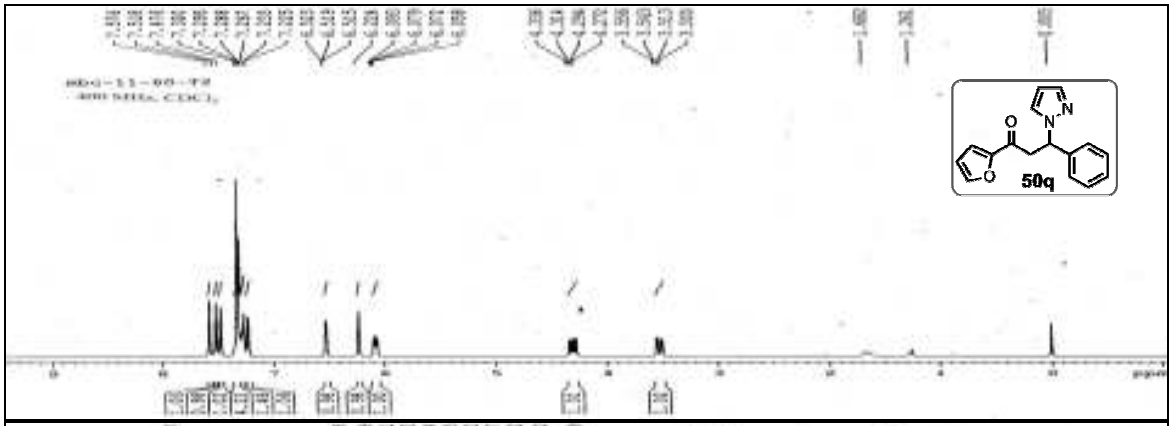

Me
O
N
N
50n

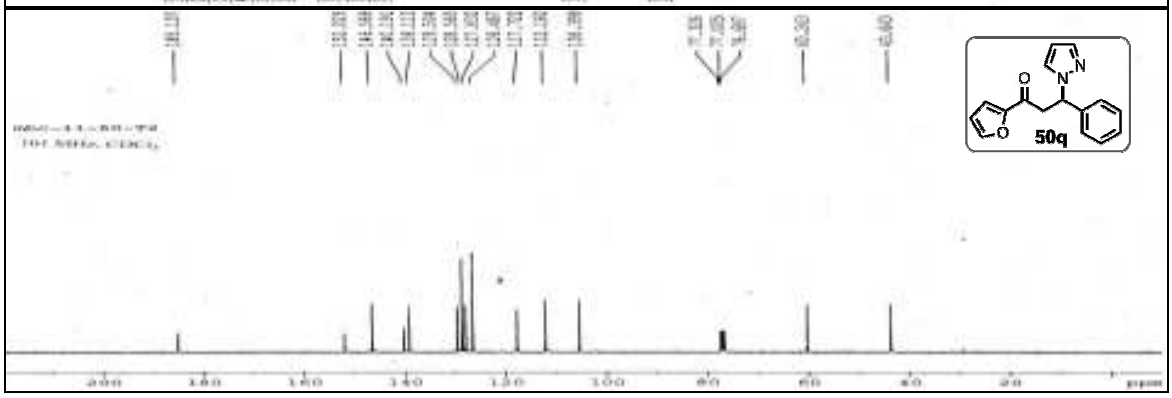

O
N
N
50o

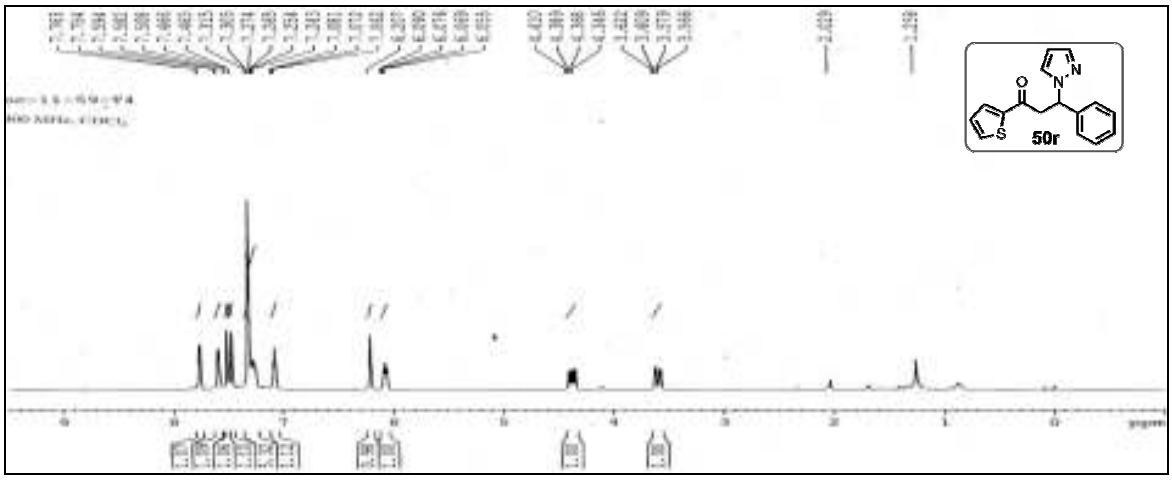

O
N
N
50a

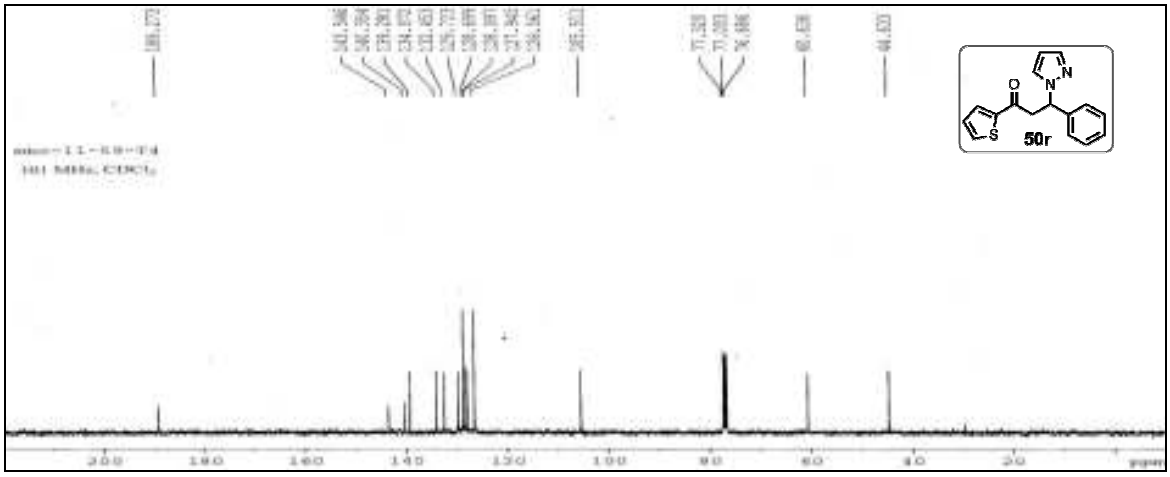

Cl
O
N
Cl
50p

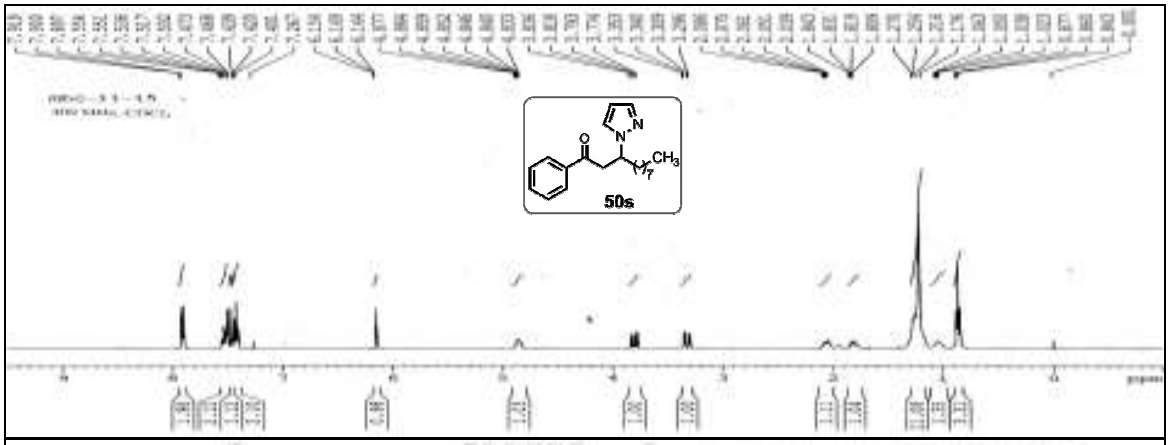

Cl
O
N
N
Cl
50p

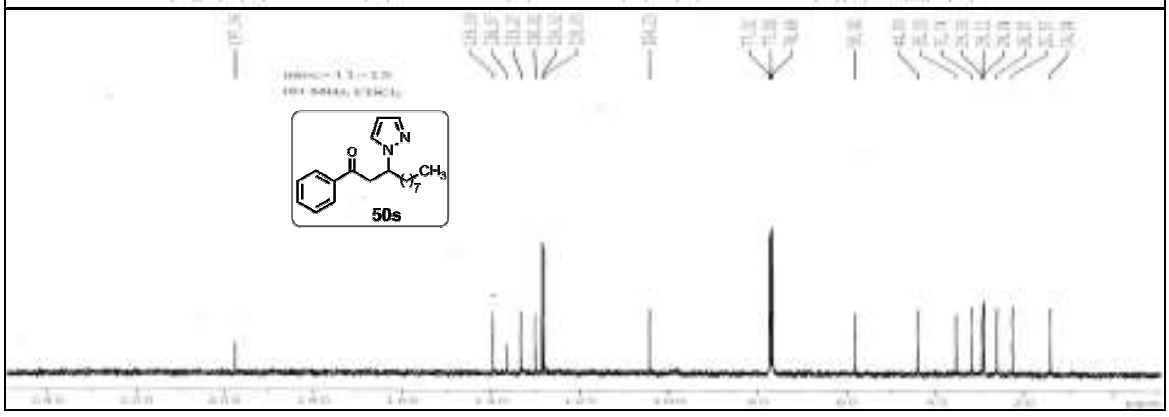

O
N
N
O
50q

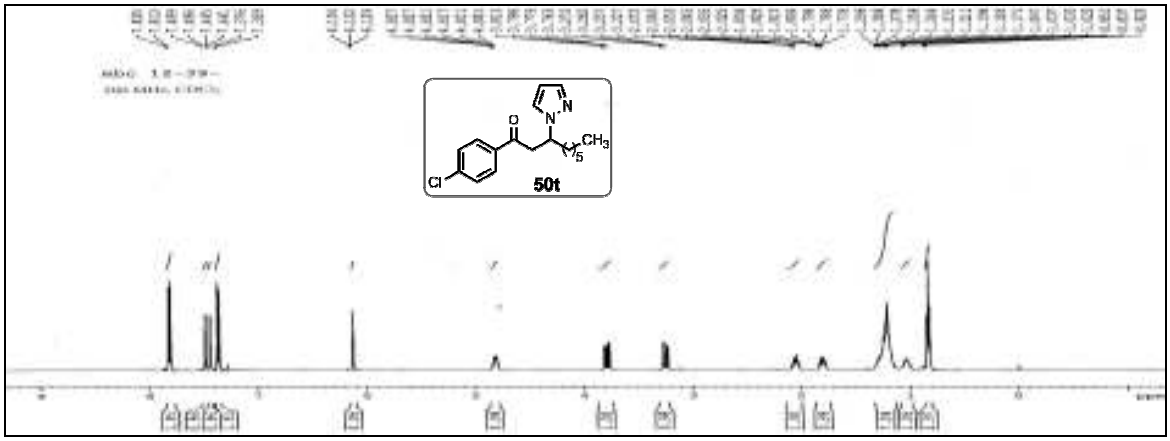

O
N
N
O
50q

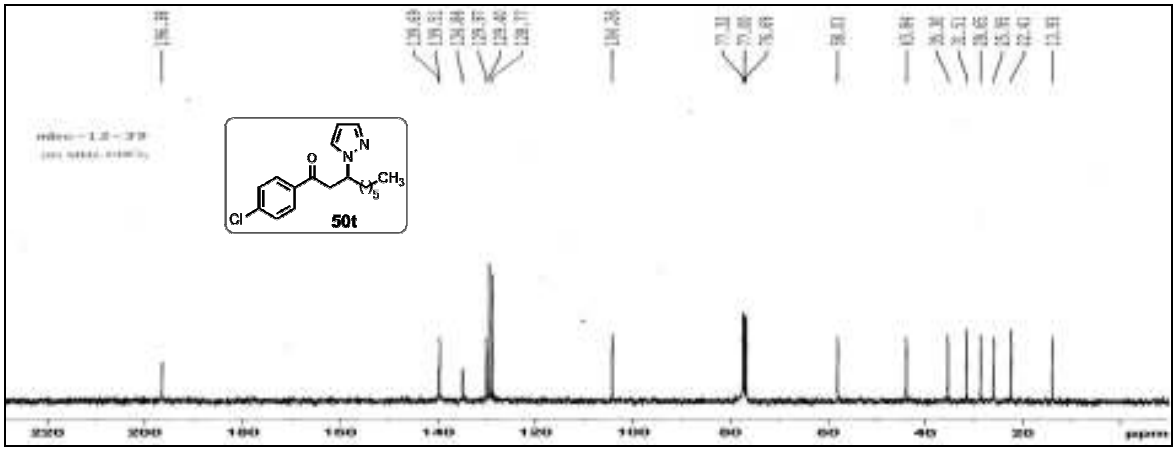

O
N
N
S
50r

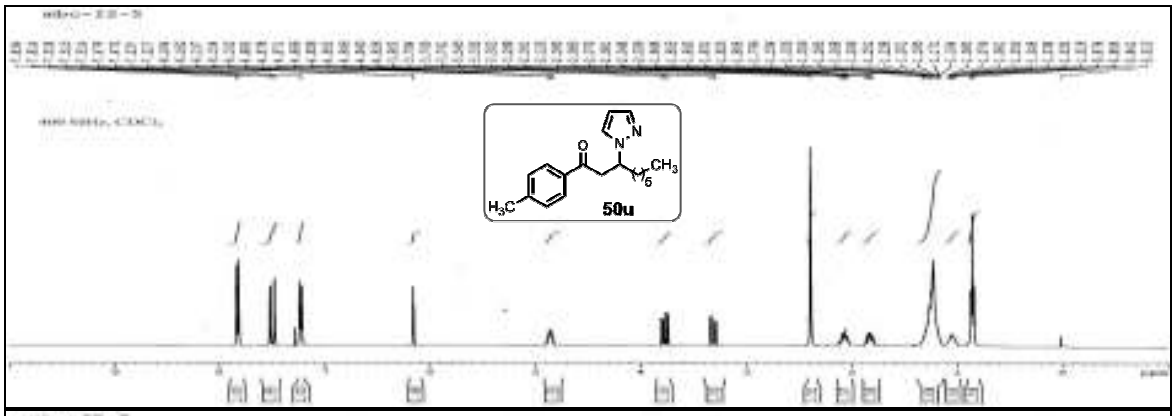

50r

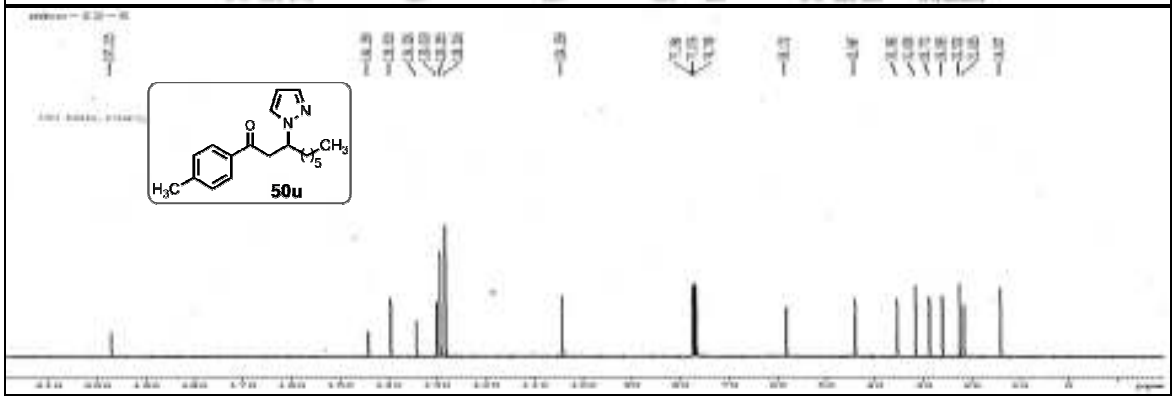

50s

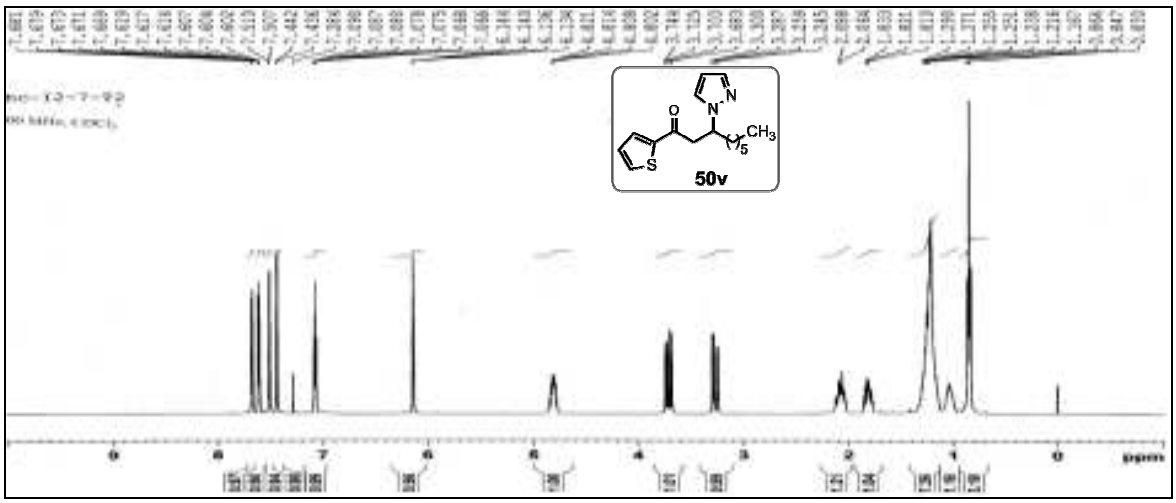

50s

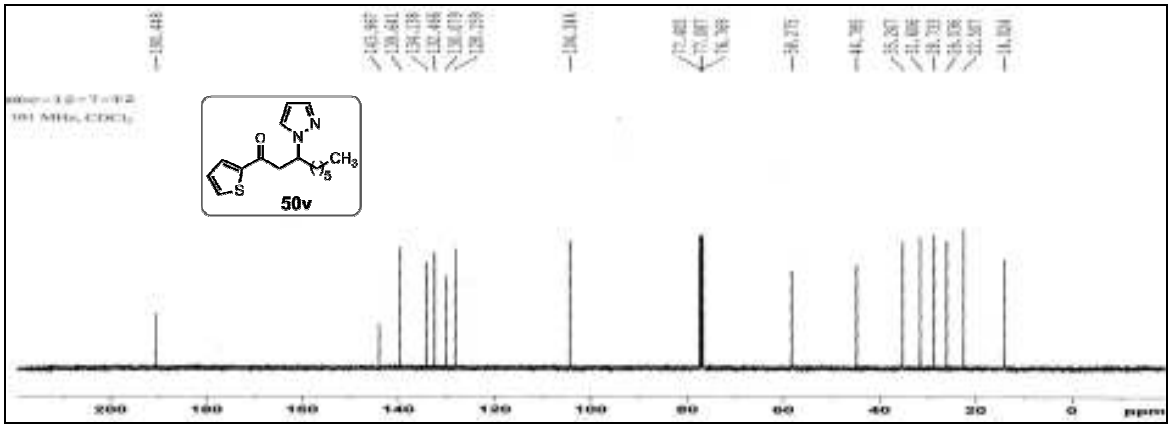

50t

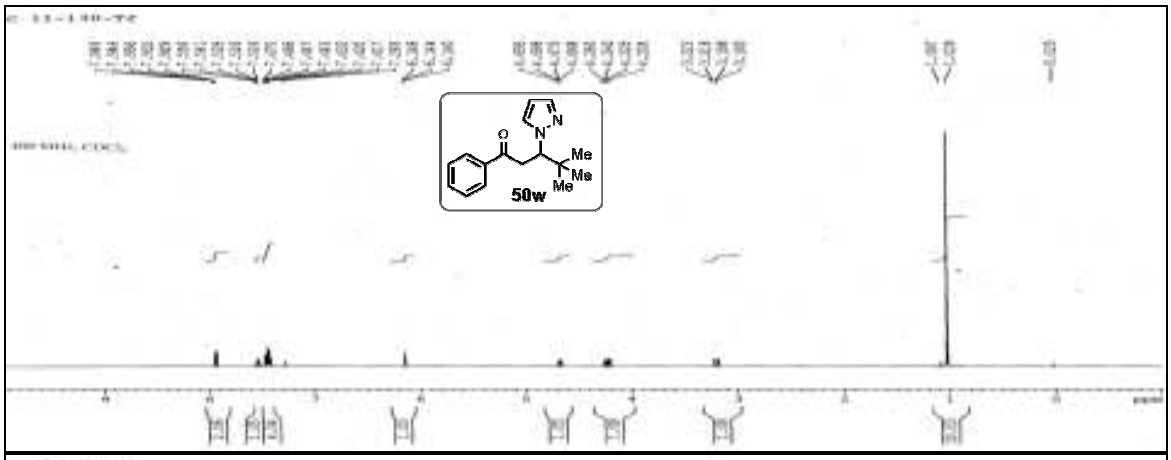

50t
ppm

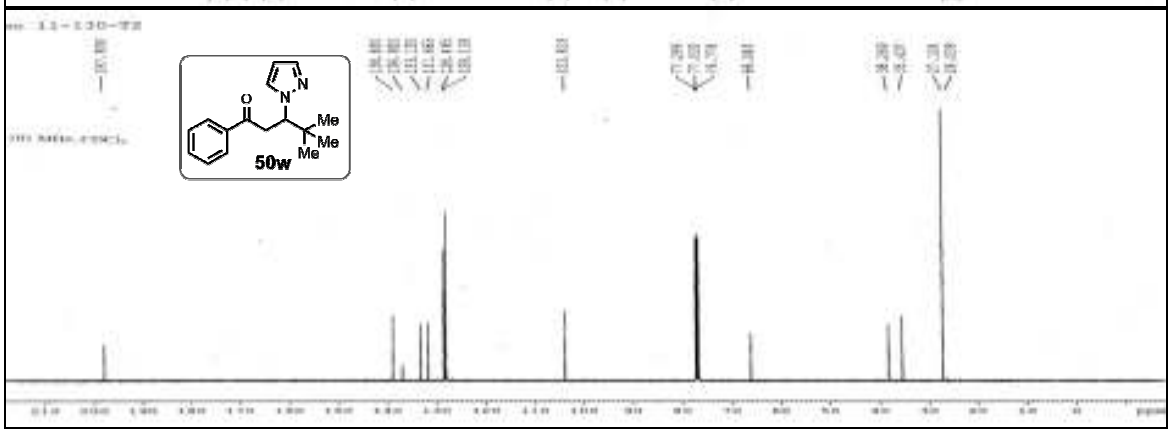

50u

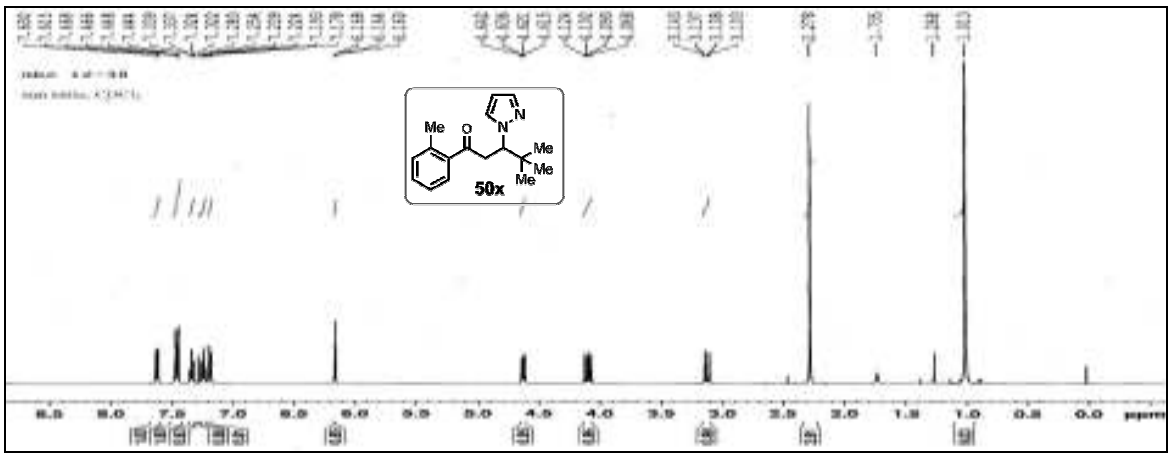

50u

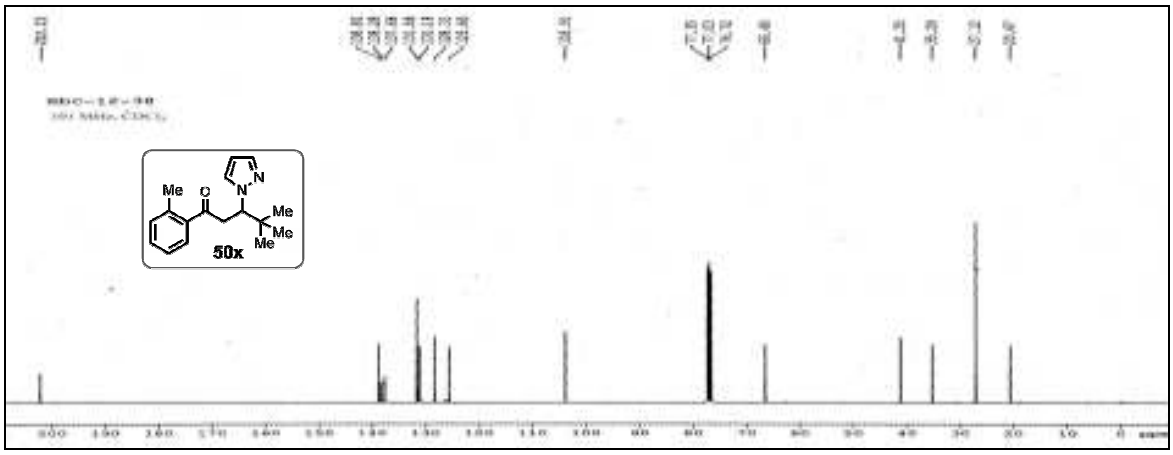

50v
ppm

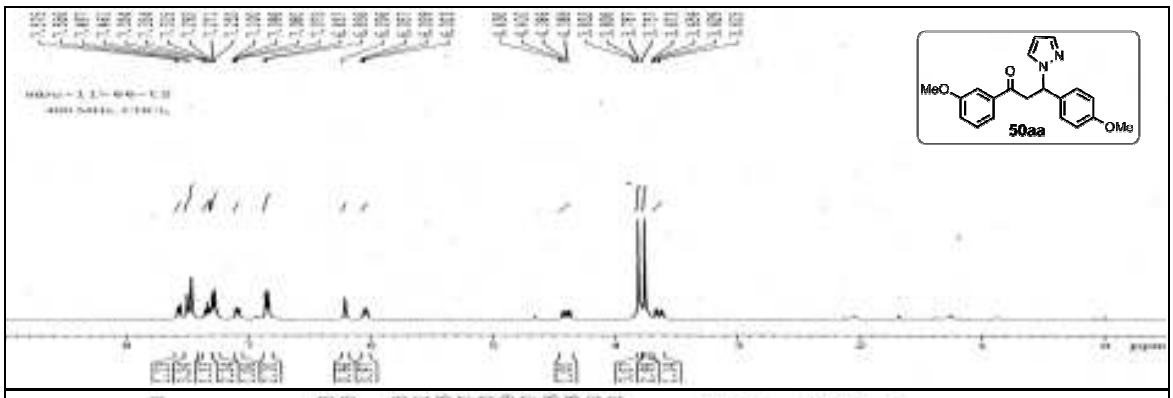

50v

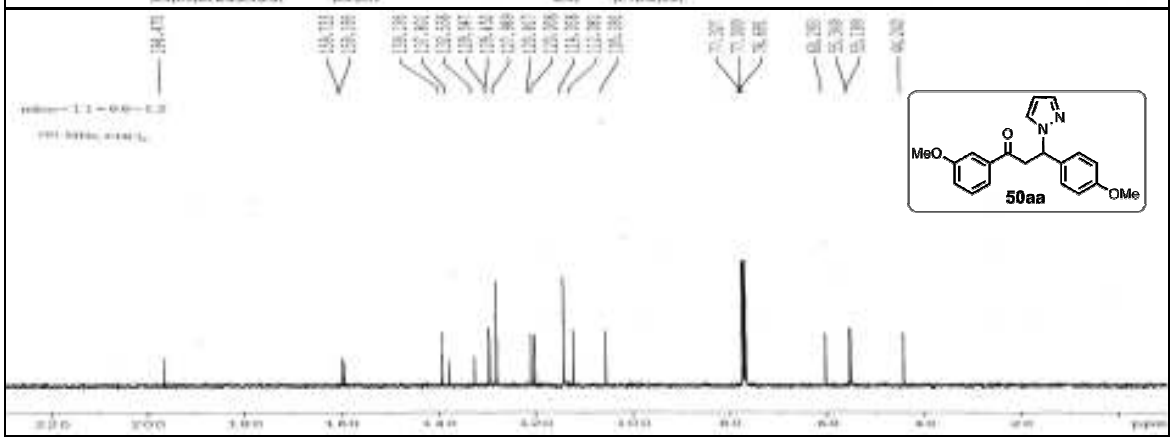

50w

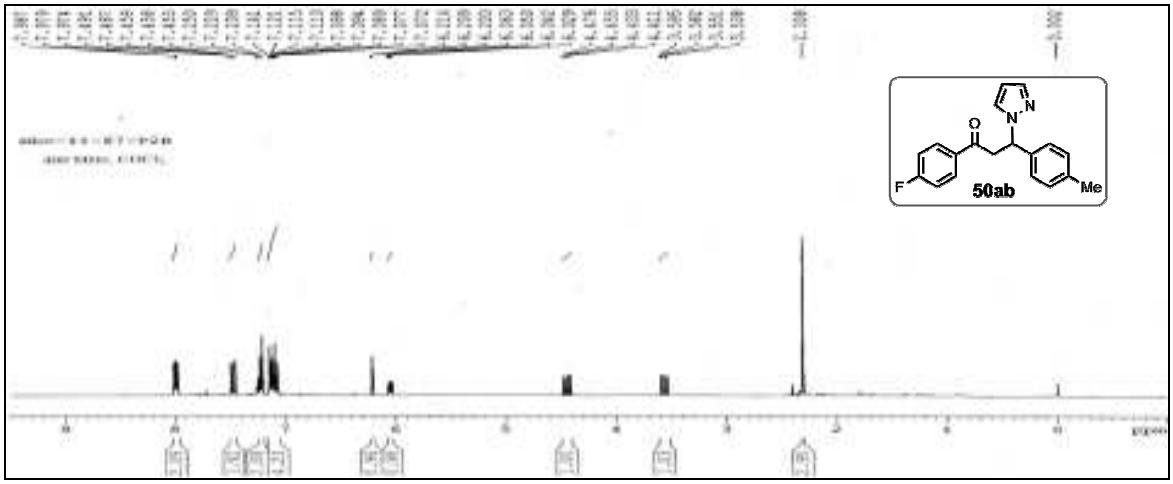

50w

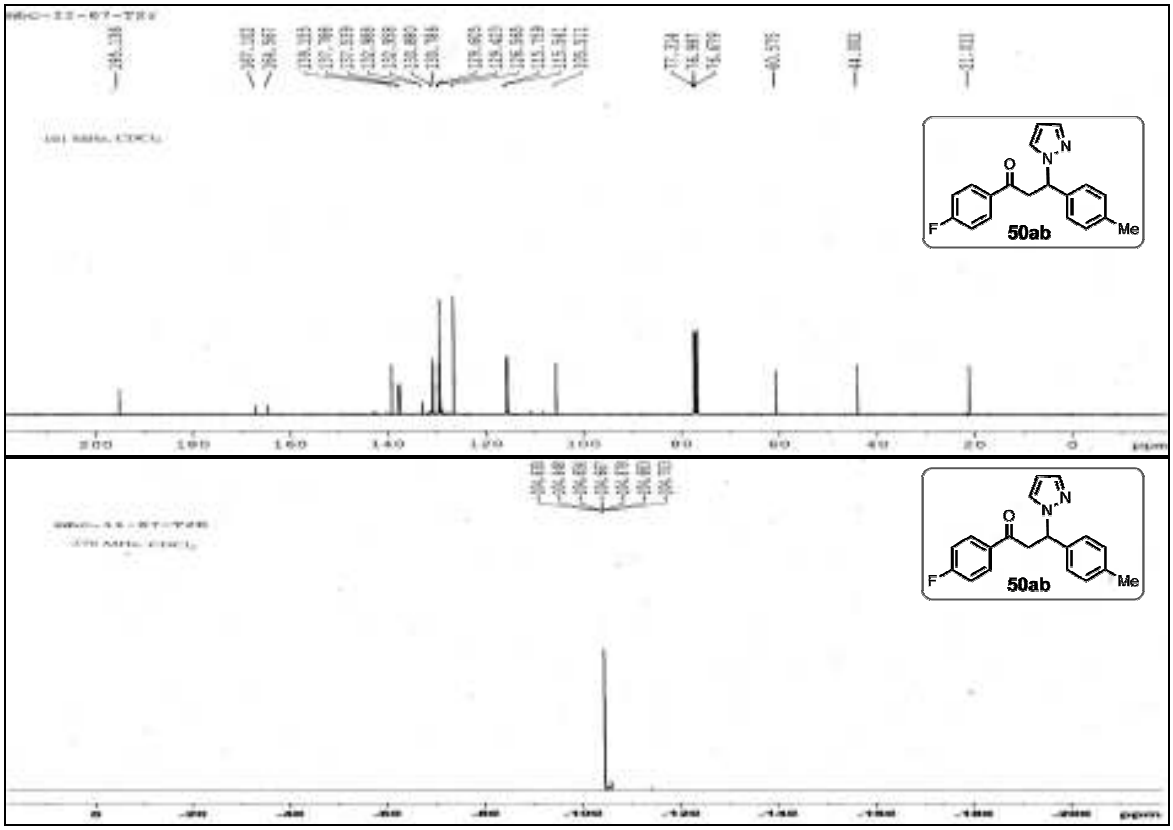

50x

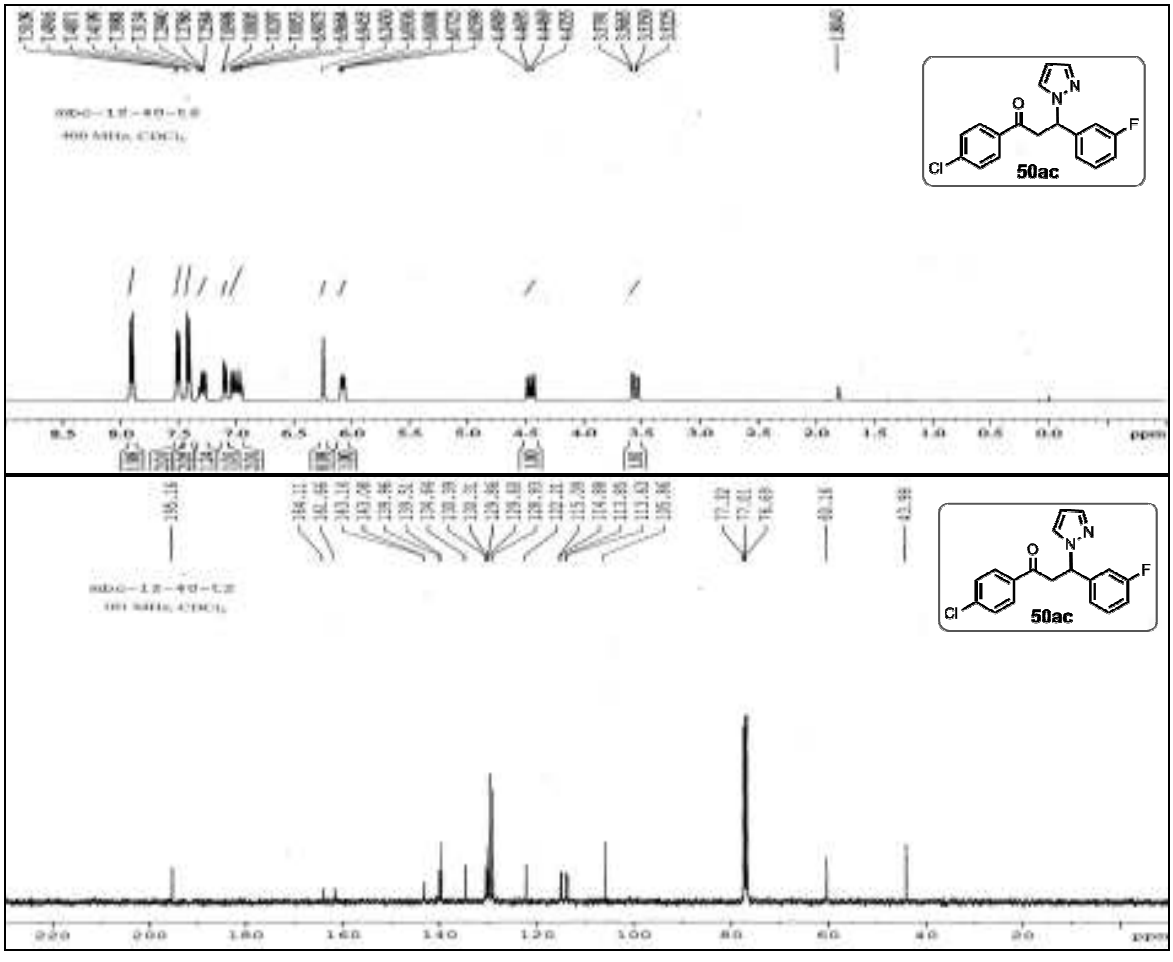

Me
O
N
N
Me
Me
Me
50x

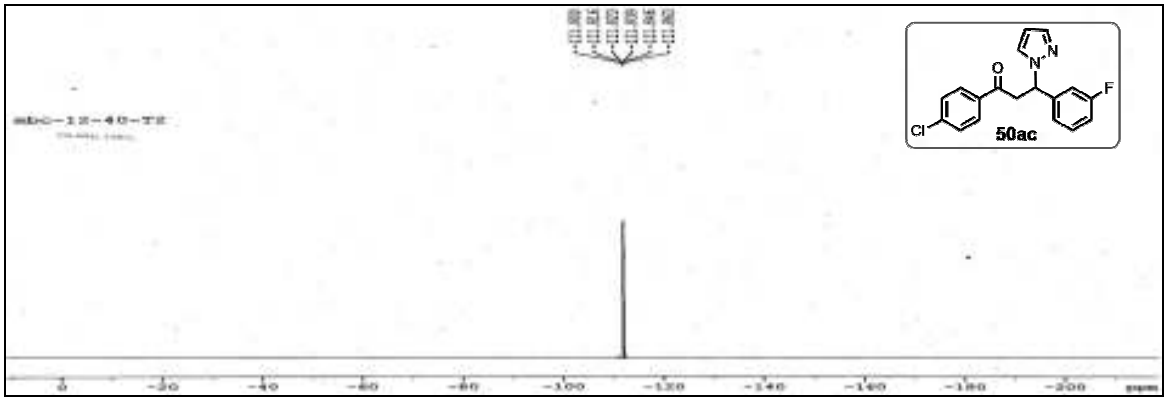

MeO
O
N
N
OMe
50aa

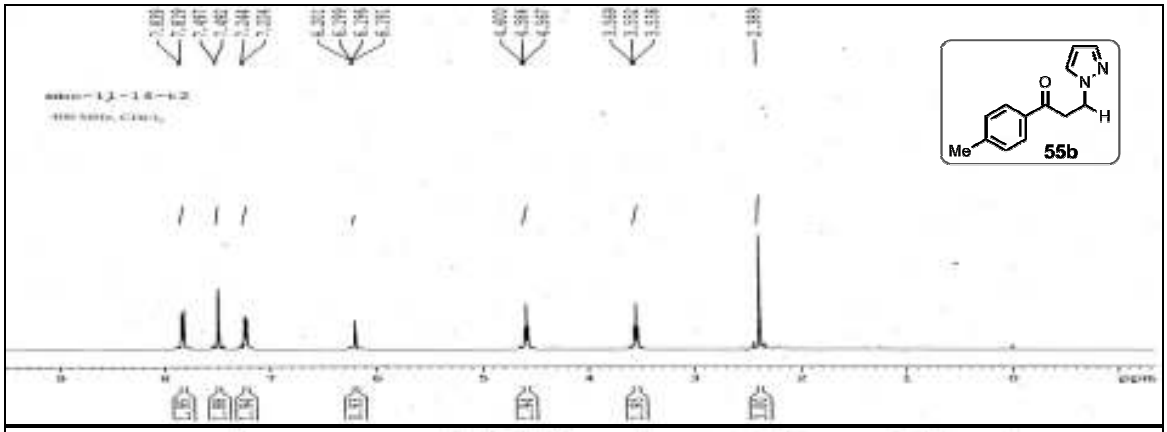

MeO
O
N
N
OMe
50aa

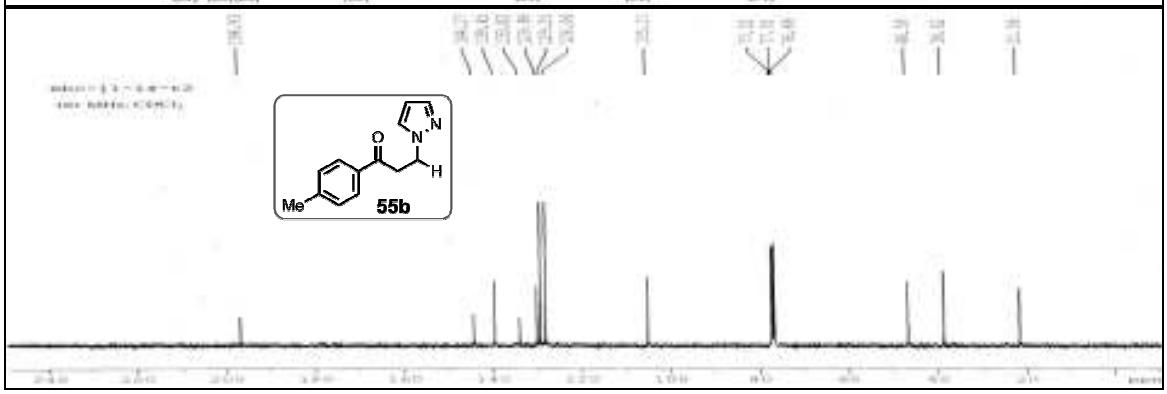

O
N
N
F
Me
50ab

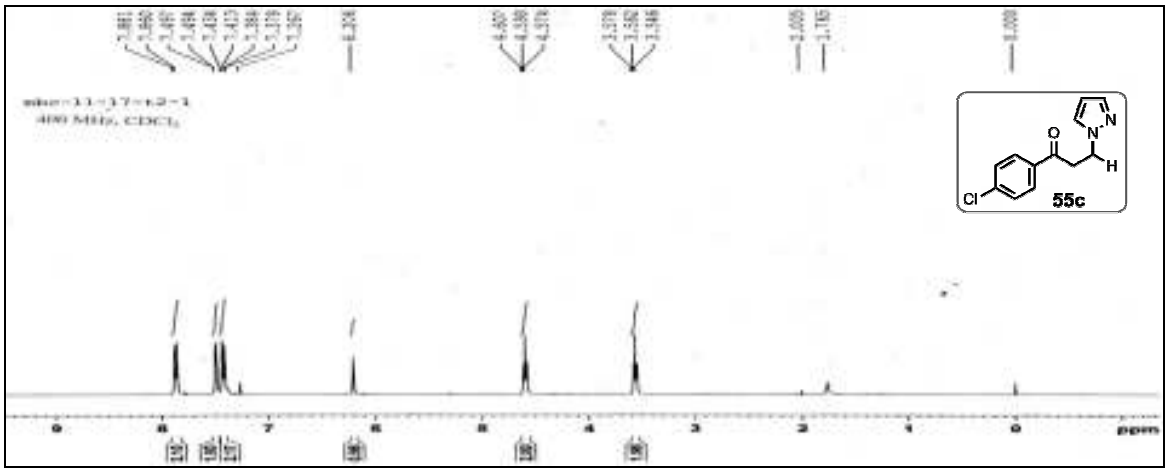

50ab
50ab

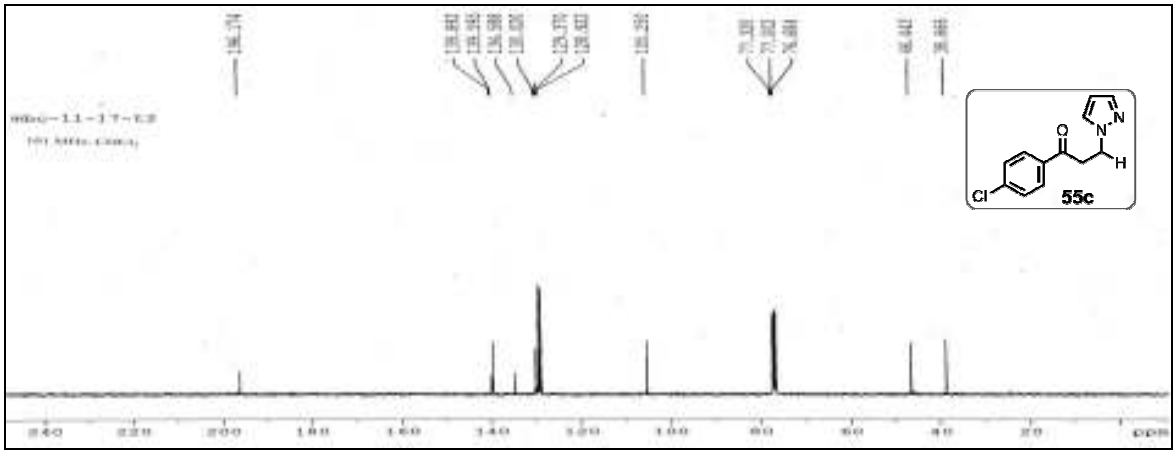

50ac
50ac

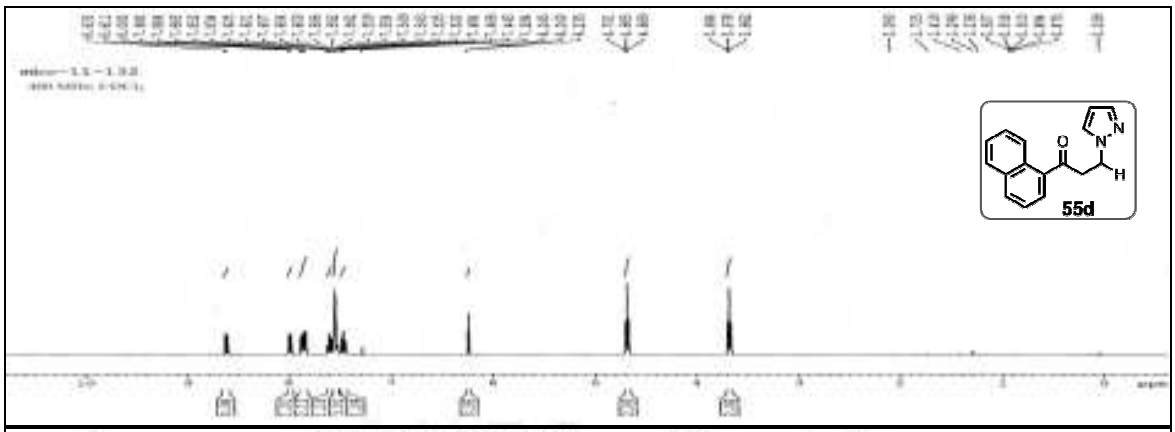

50ac

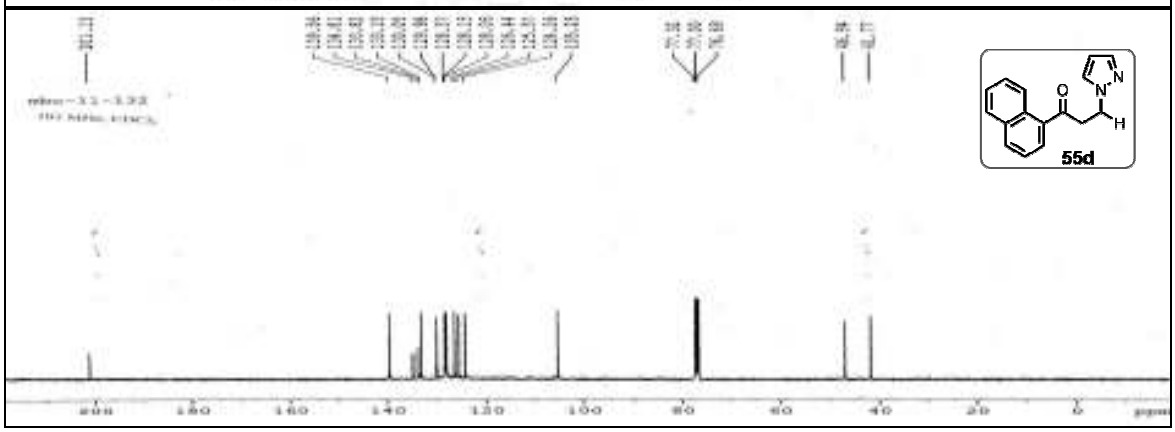

55b

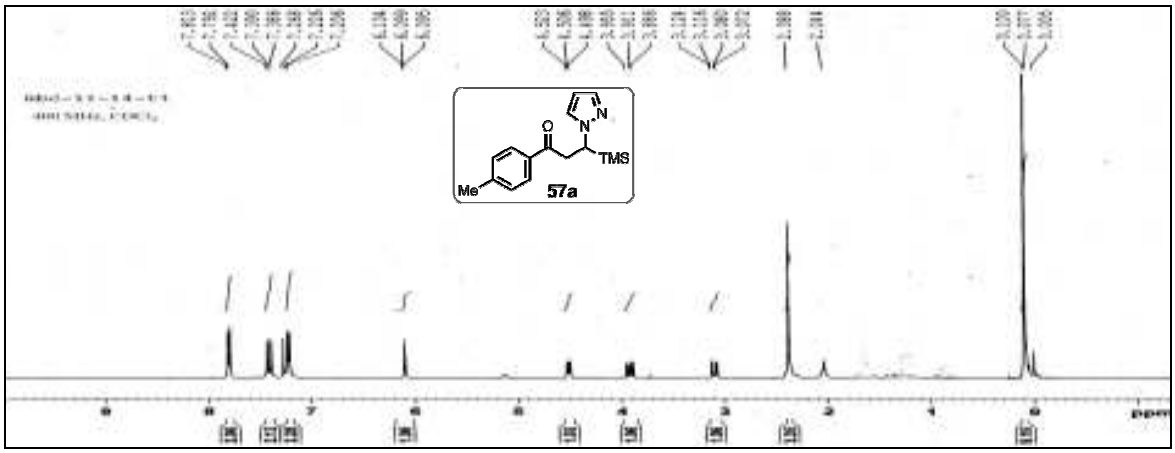

55b

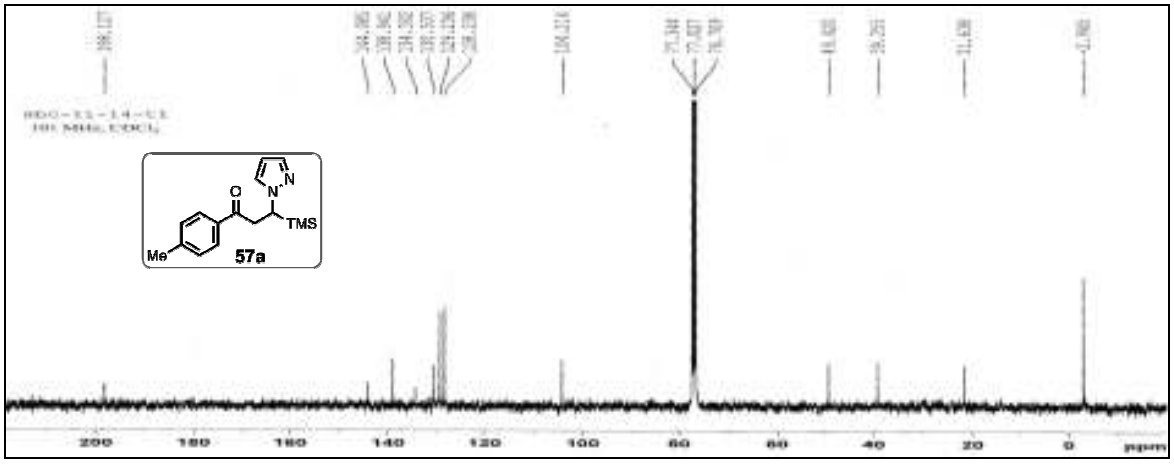

55c

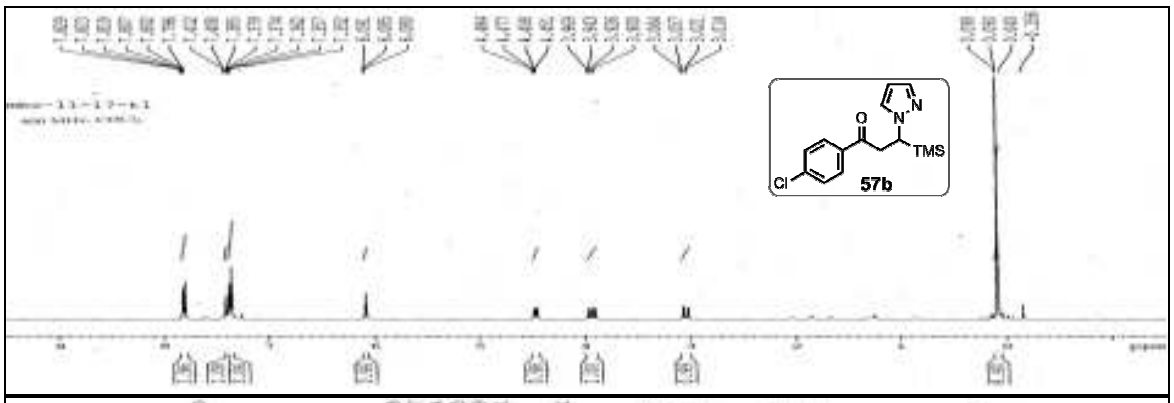

55c

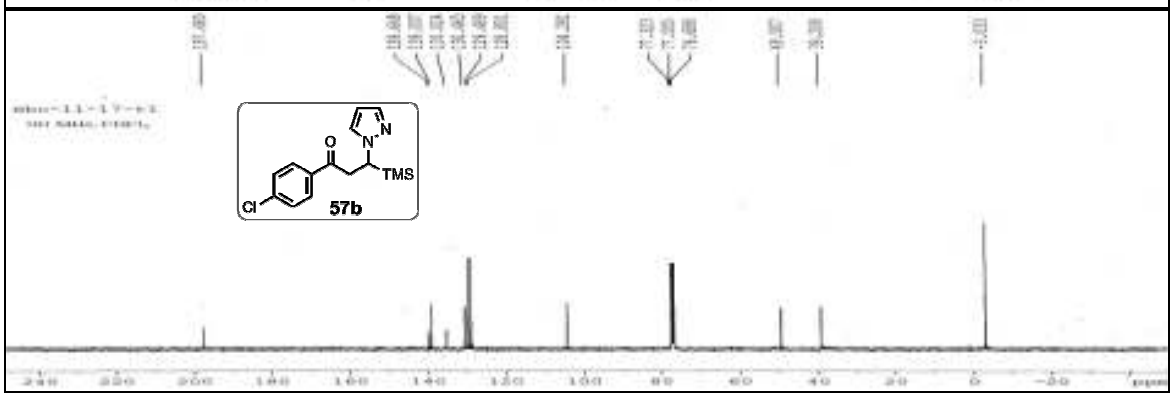

55d

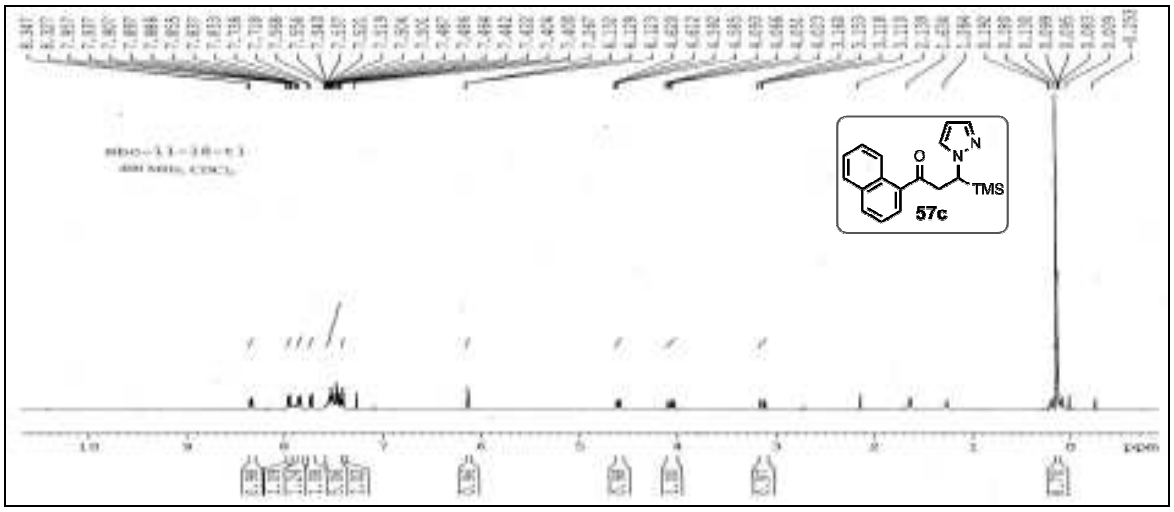

55d

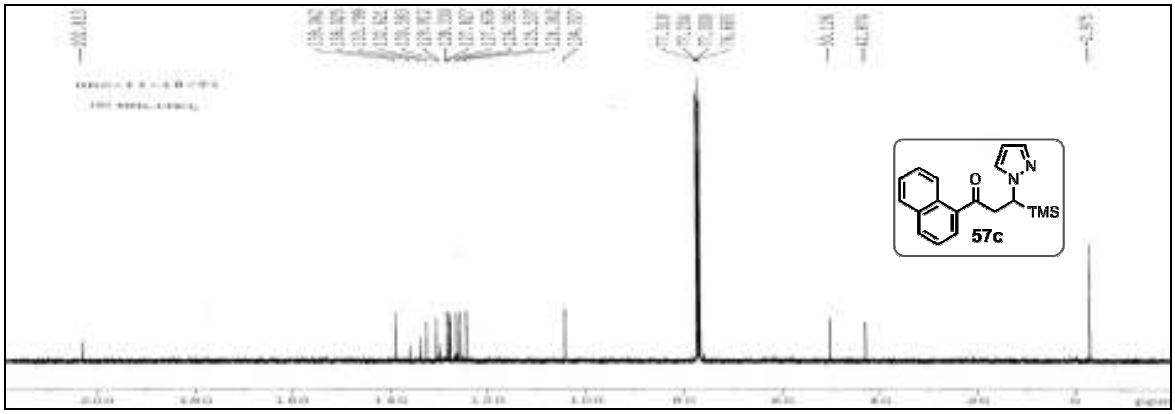

TMS
Me
57a

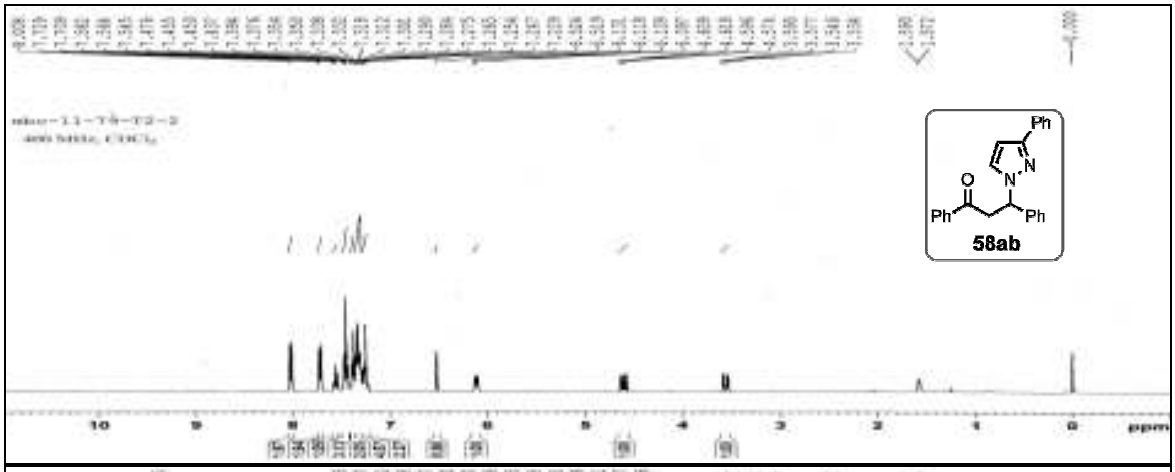

TMS
Me
57a

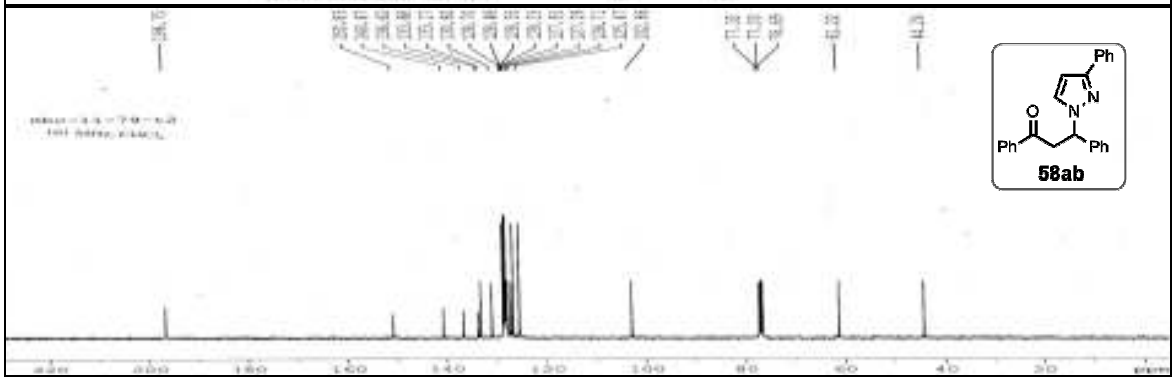

TMS
Cl
57b

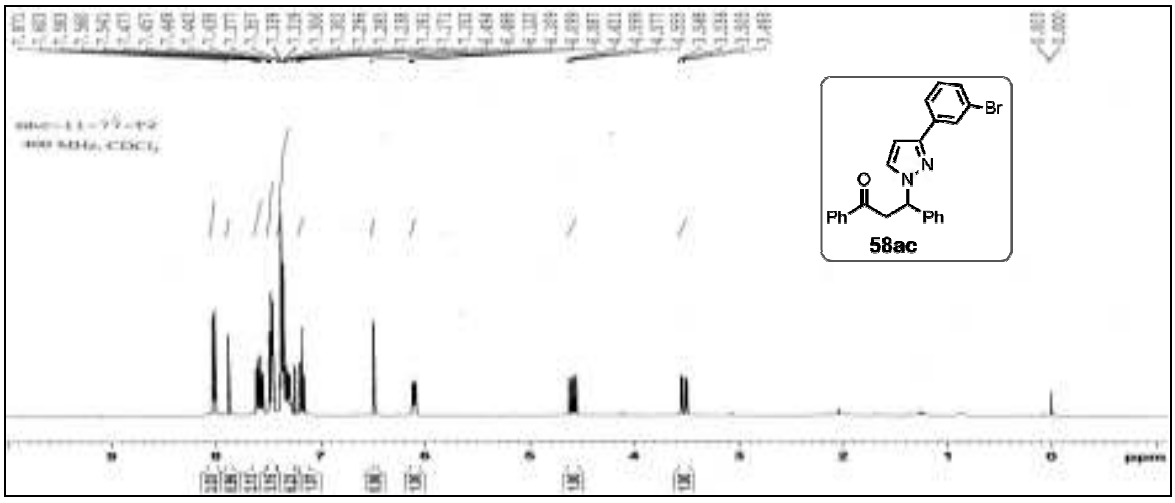

TMS
Cl
57b

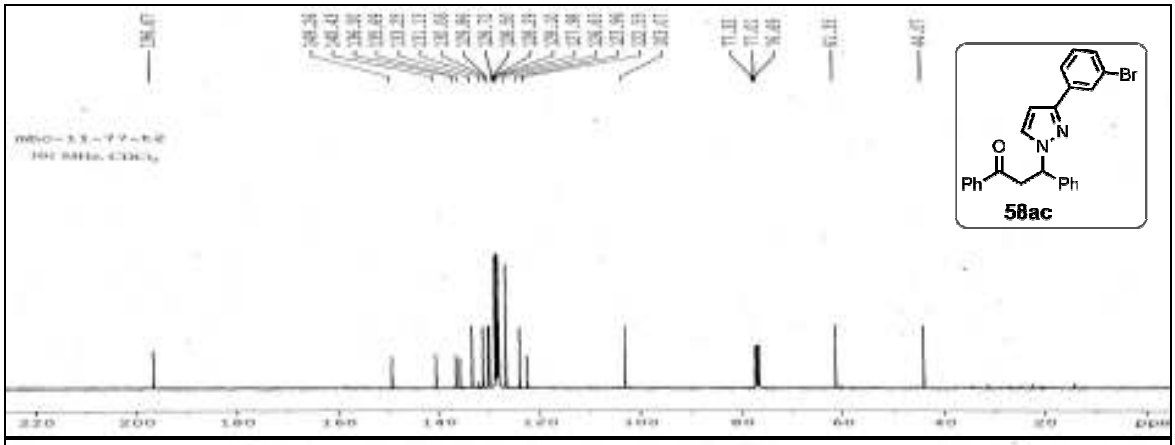

TMS
57c

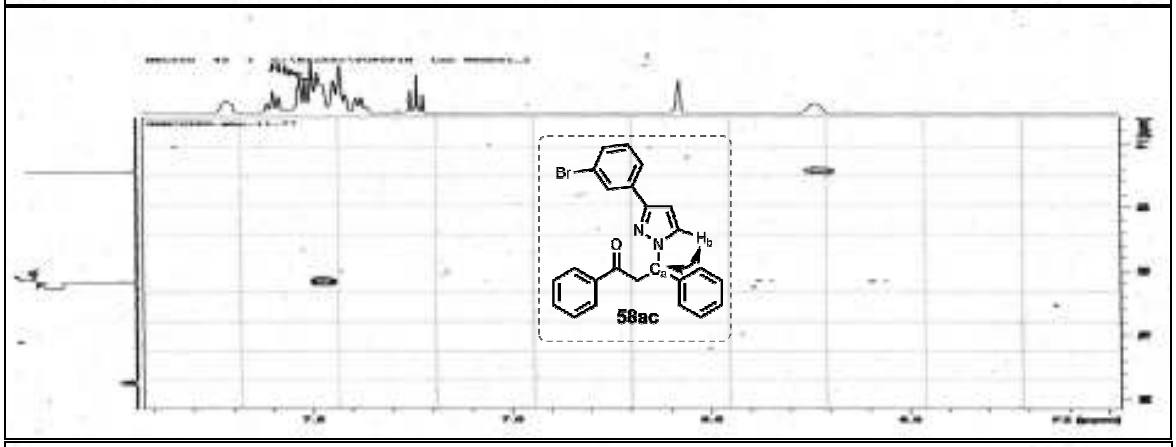

TMS
57c

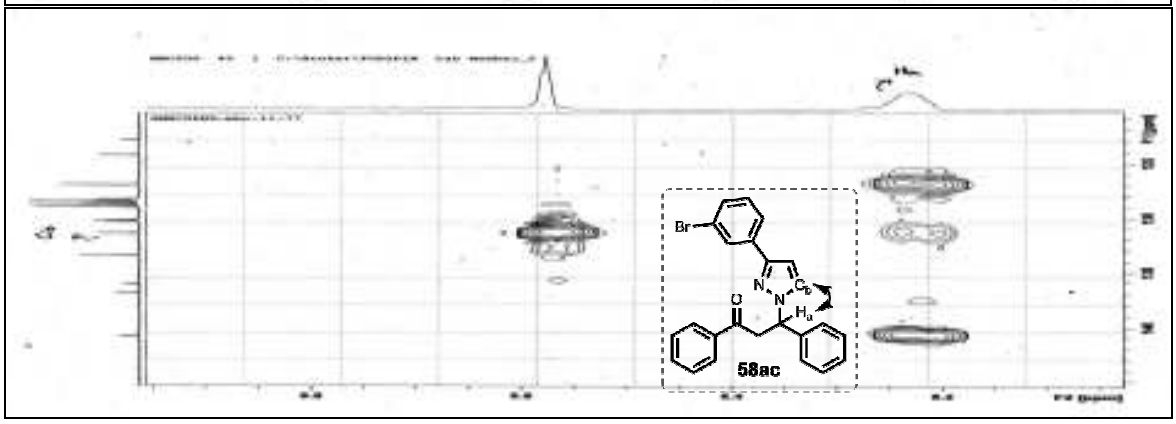

Ph
Ph
Ph
58ab

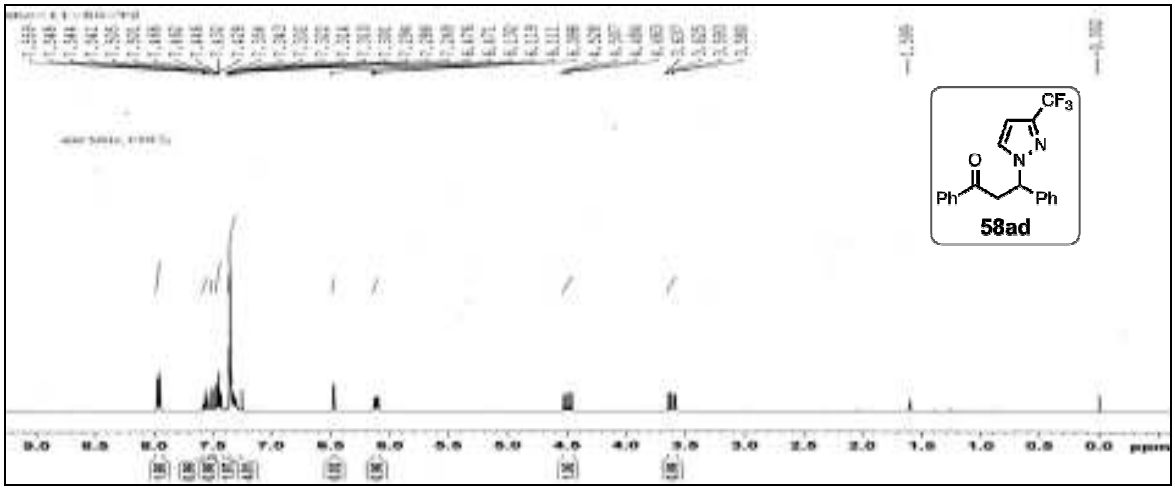

Ph
Ph
Ph
58ab

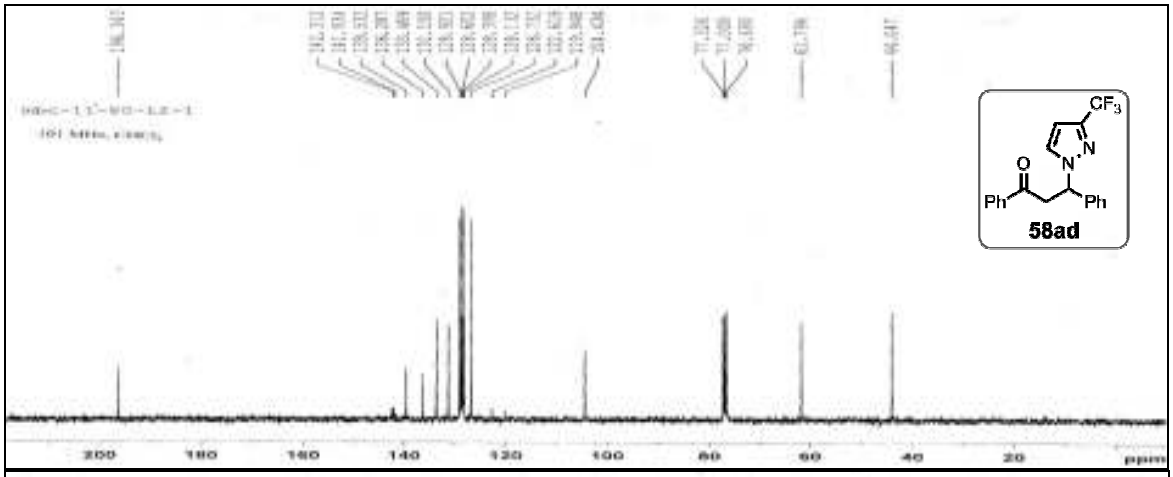

Br
Ph
Ph
58ac

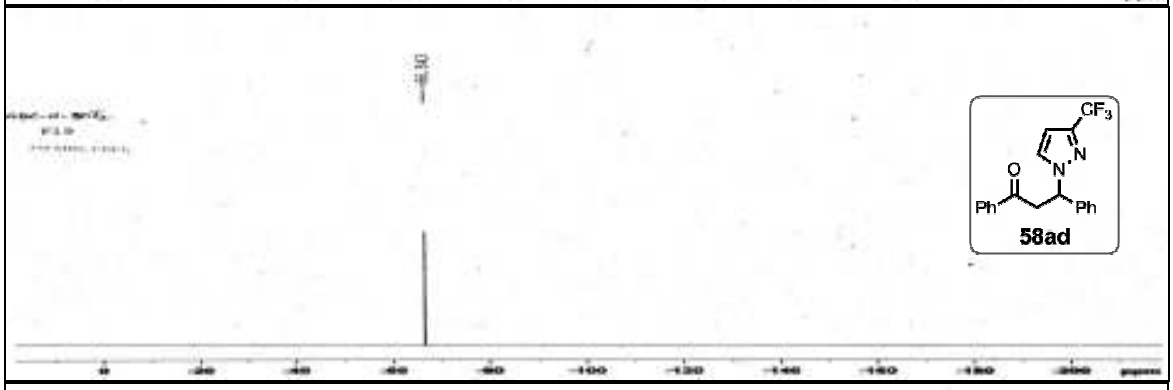

Br
N
N
O
Ph
Ph
58ac

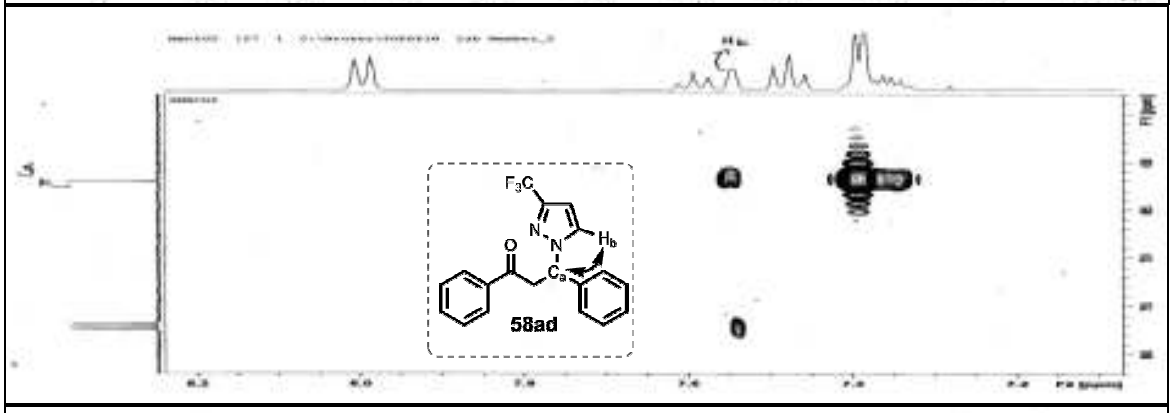

Br
N
N
O
H_b
C_a
58ac

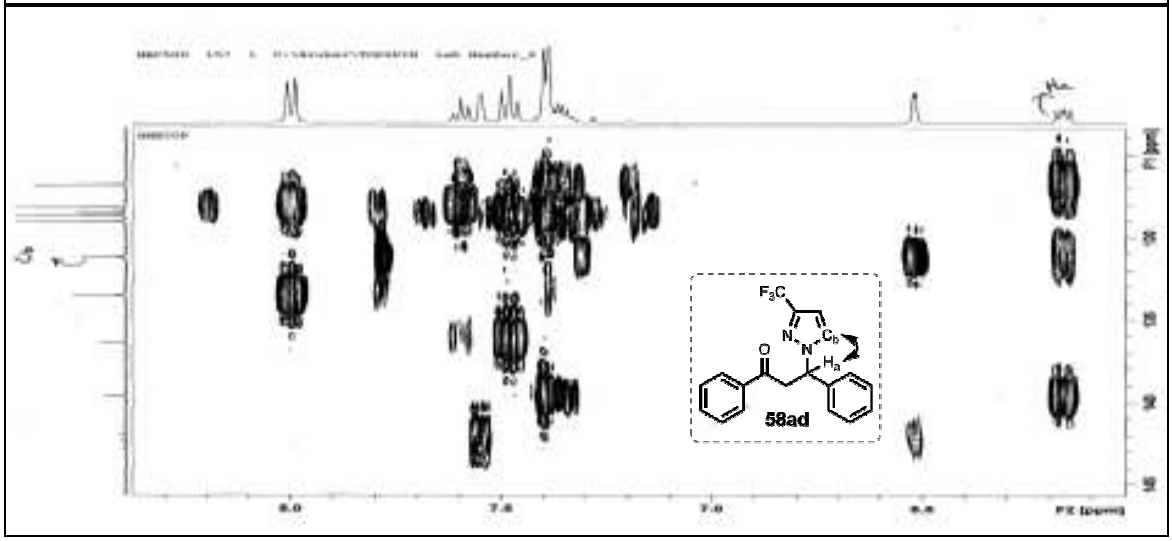

Br
N
N
O
C_b
H_a
58ac

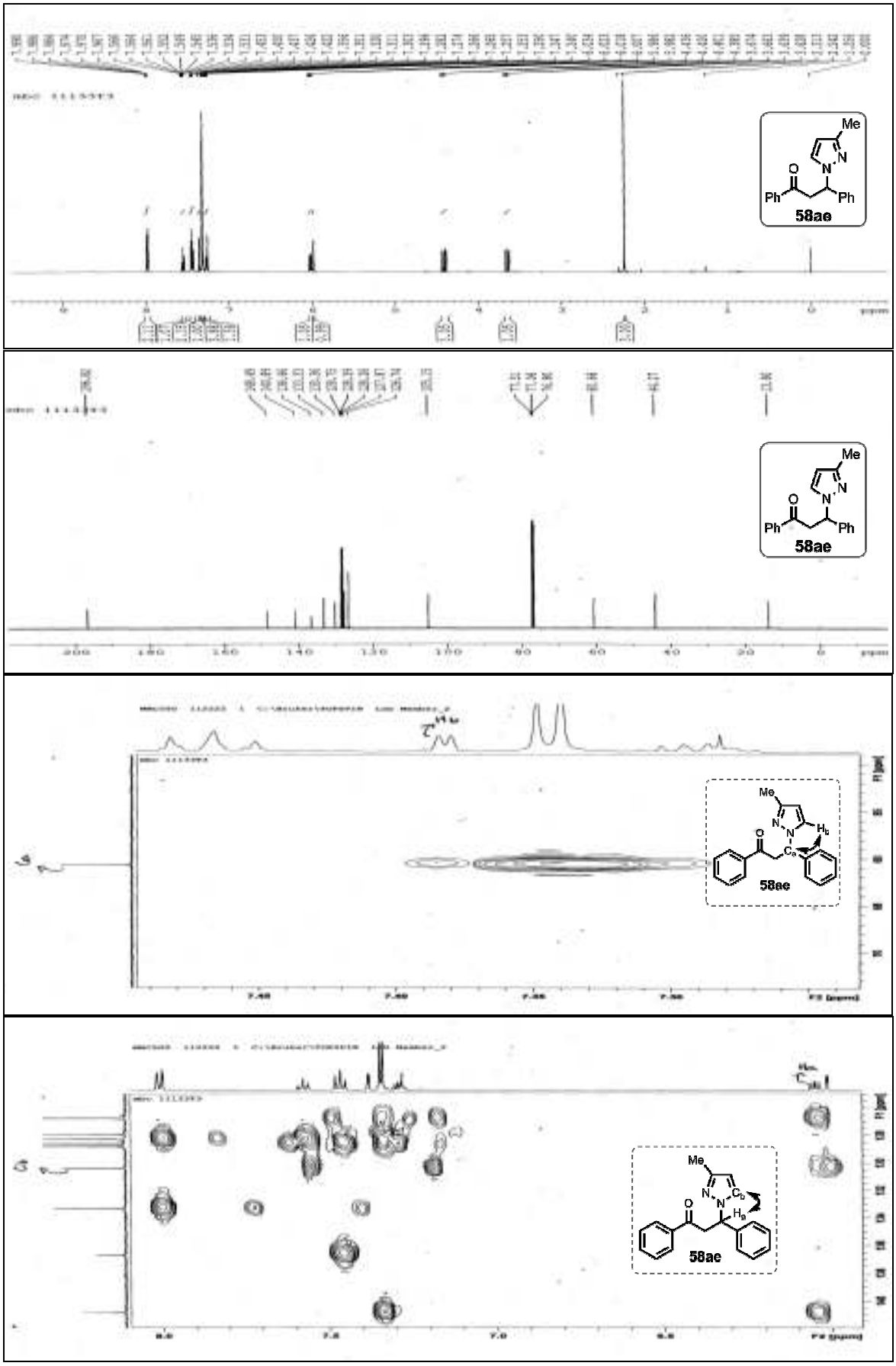

CF_3
N
N
O
Ph
Ph
58ad

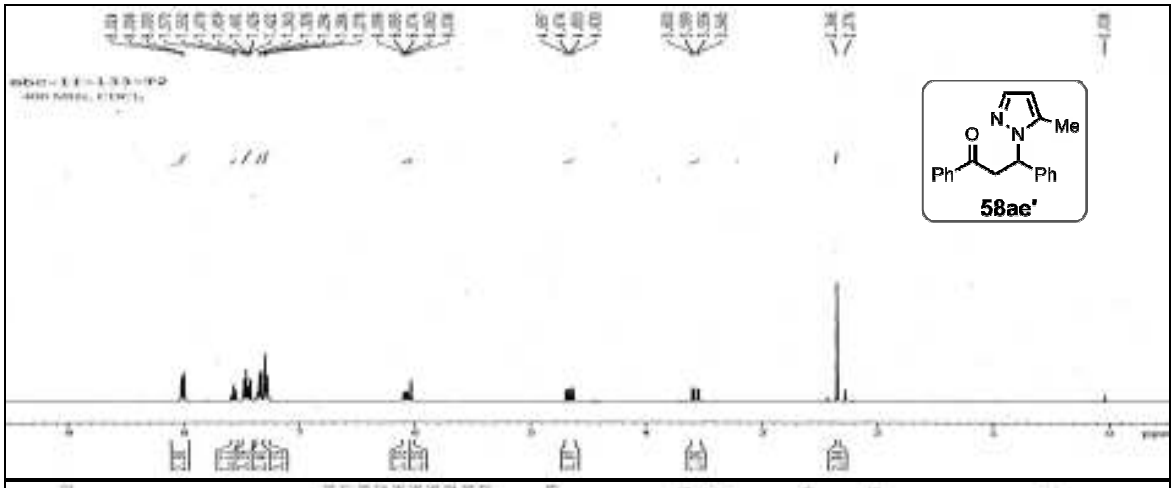

CF3
Ph
Ph
58ad

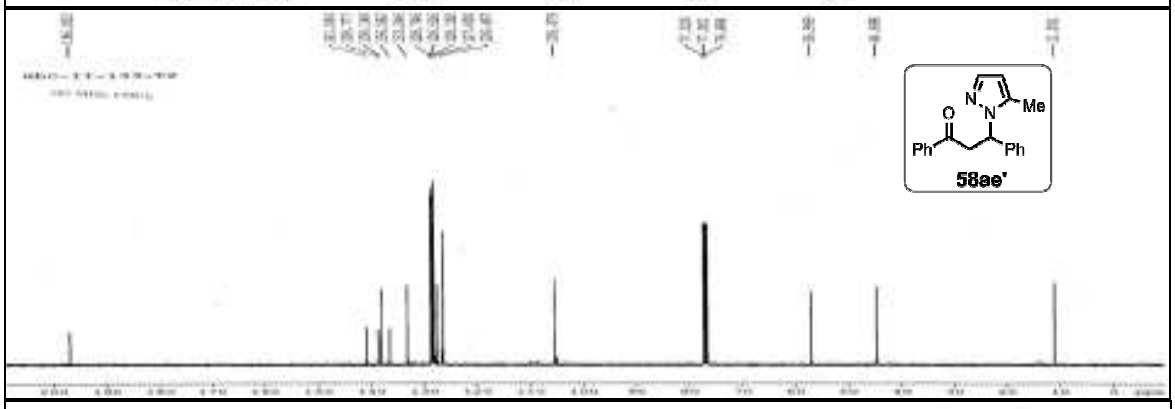

CF3
Ph
Ph
58ad

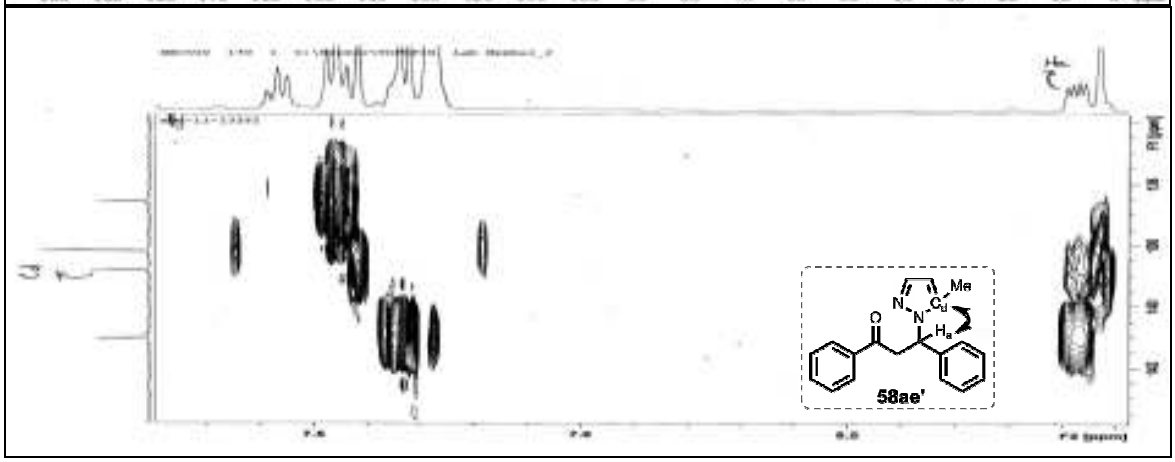

F3C
Hb
Ca
58ad

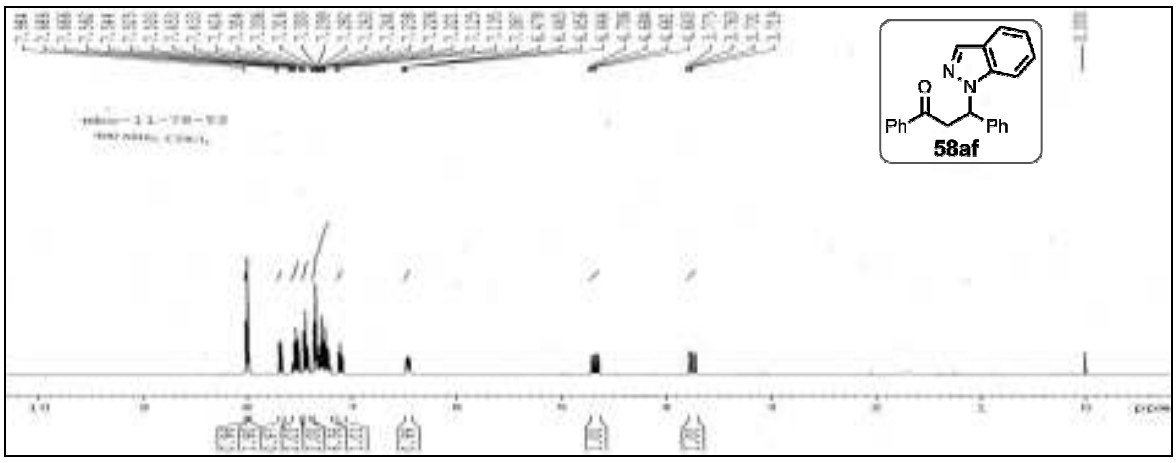

F3C
Cb
Ha
58ad

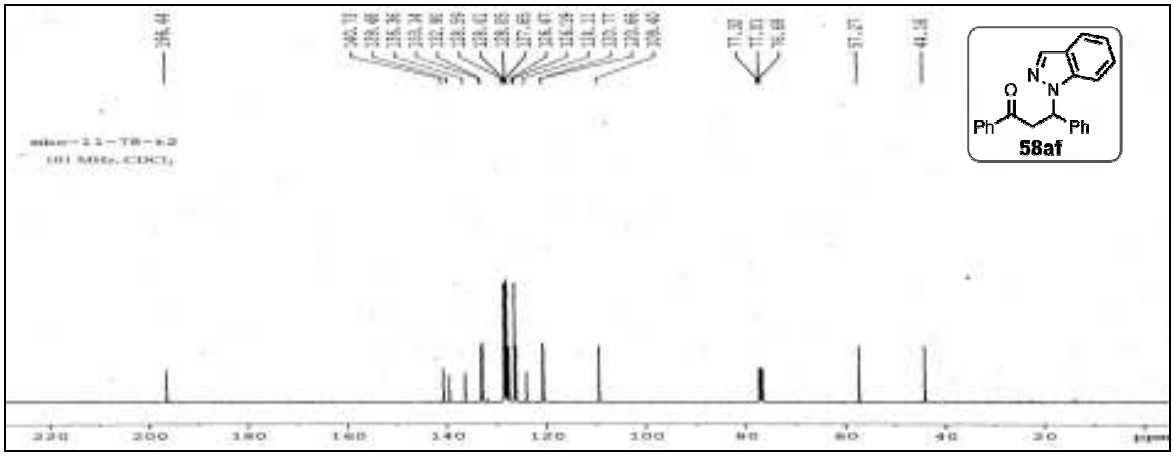

Me
N
N
O
Ph
Ph
58ae
Me
N
N
O
Ph
Ph
58ae
Me
N
N
O
Ph
58ae
Me
N
N
O
58ae

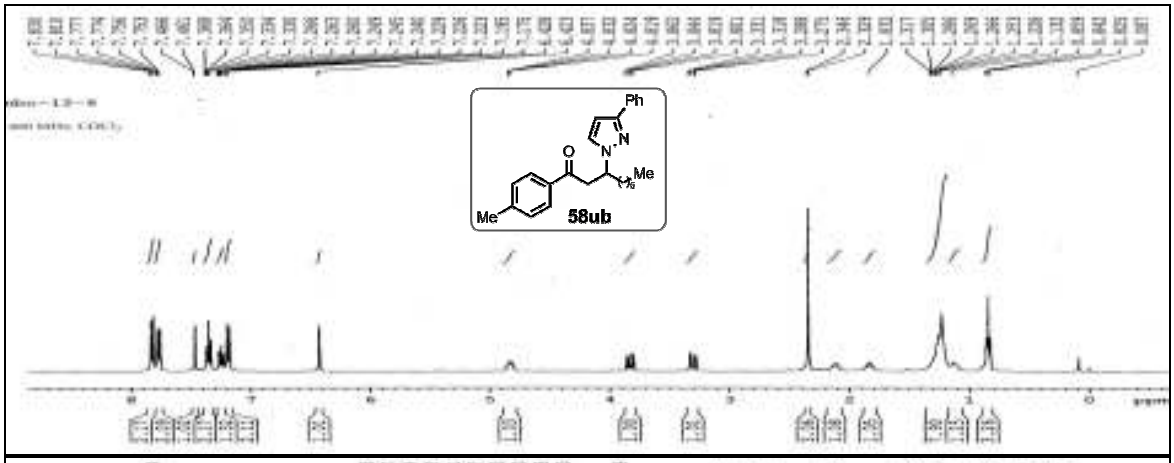

Me
O
Ph
Ph
58ae'

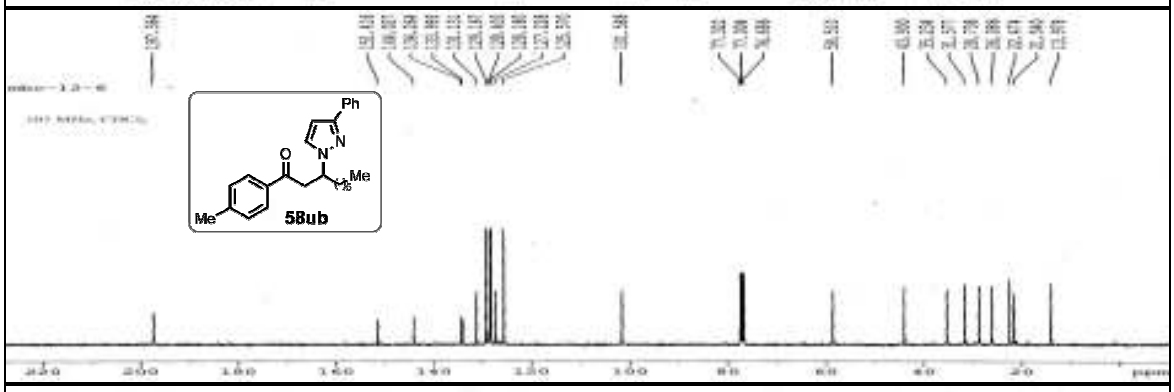

Me
O
Ph
Ph
58ae'

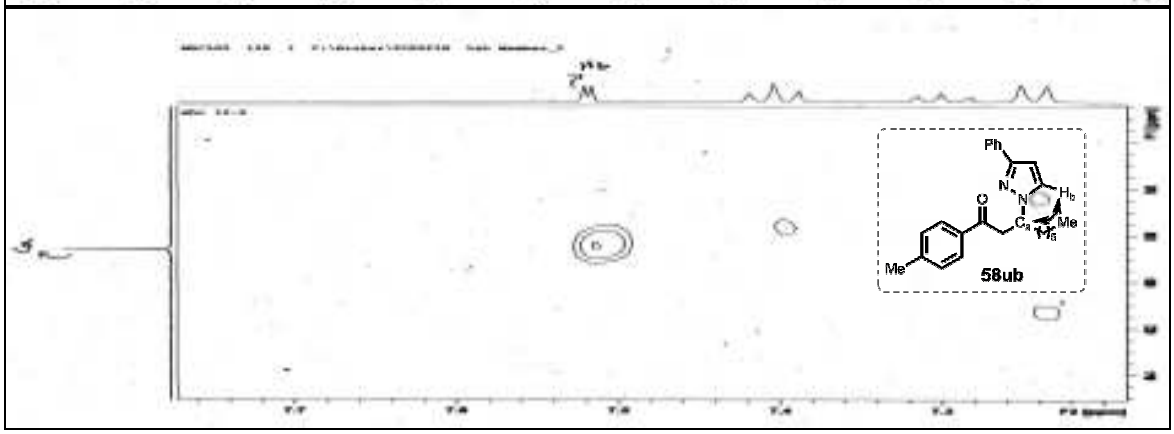

Me
Cu
O
Ha
58ae'

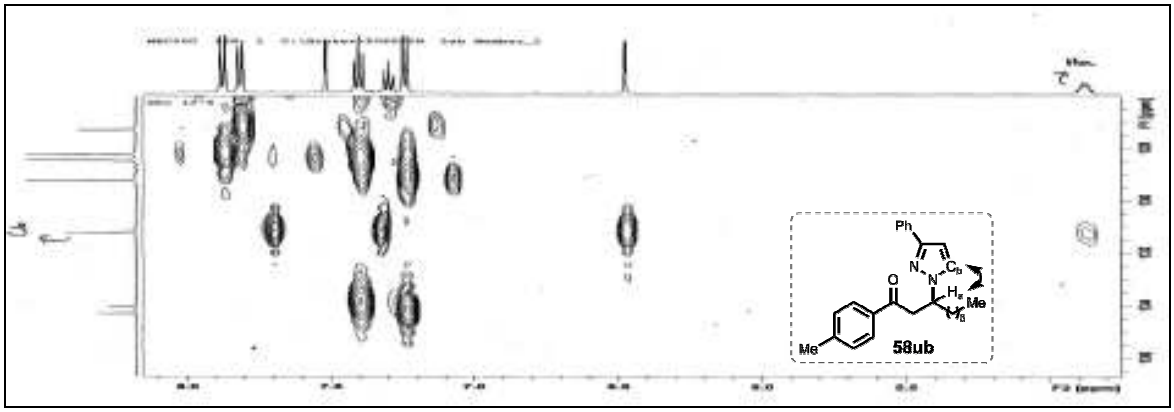

O
Ph
Ph
58af

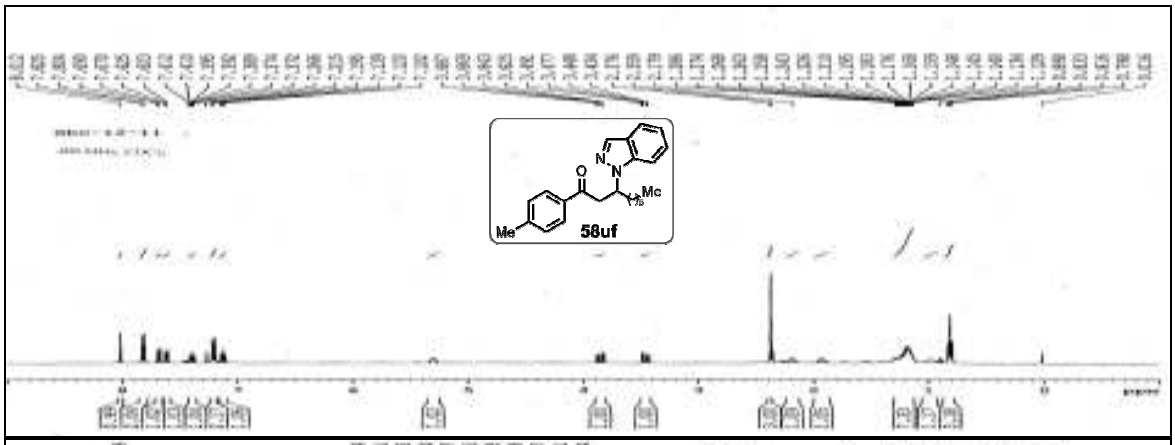

58af

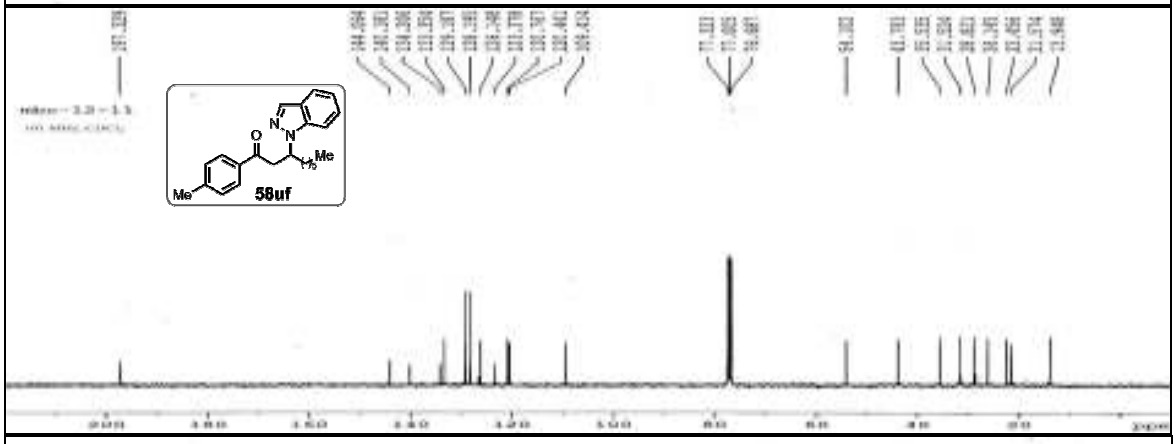

58ub

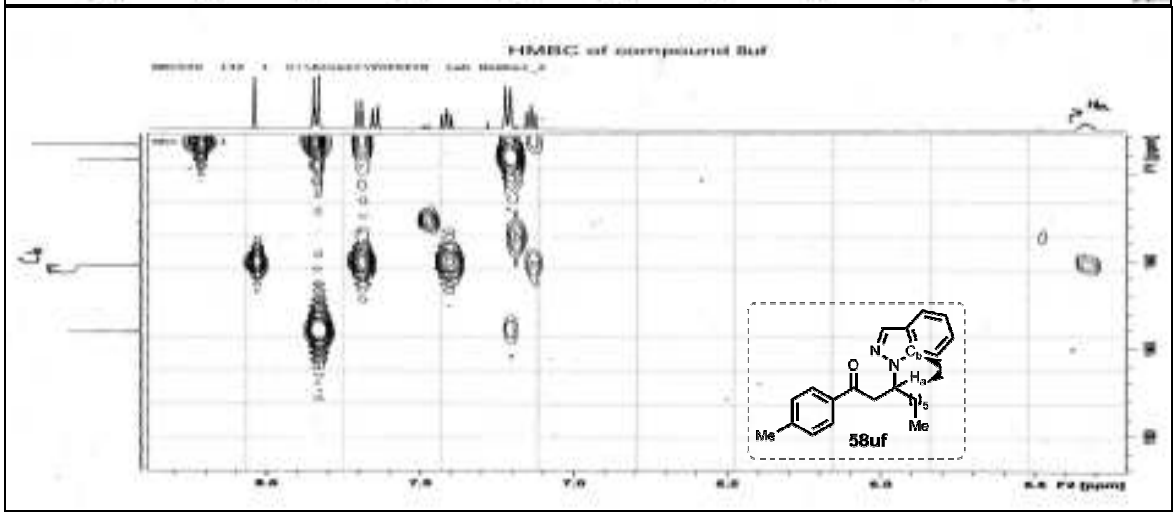

58ub

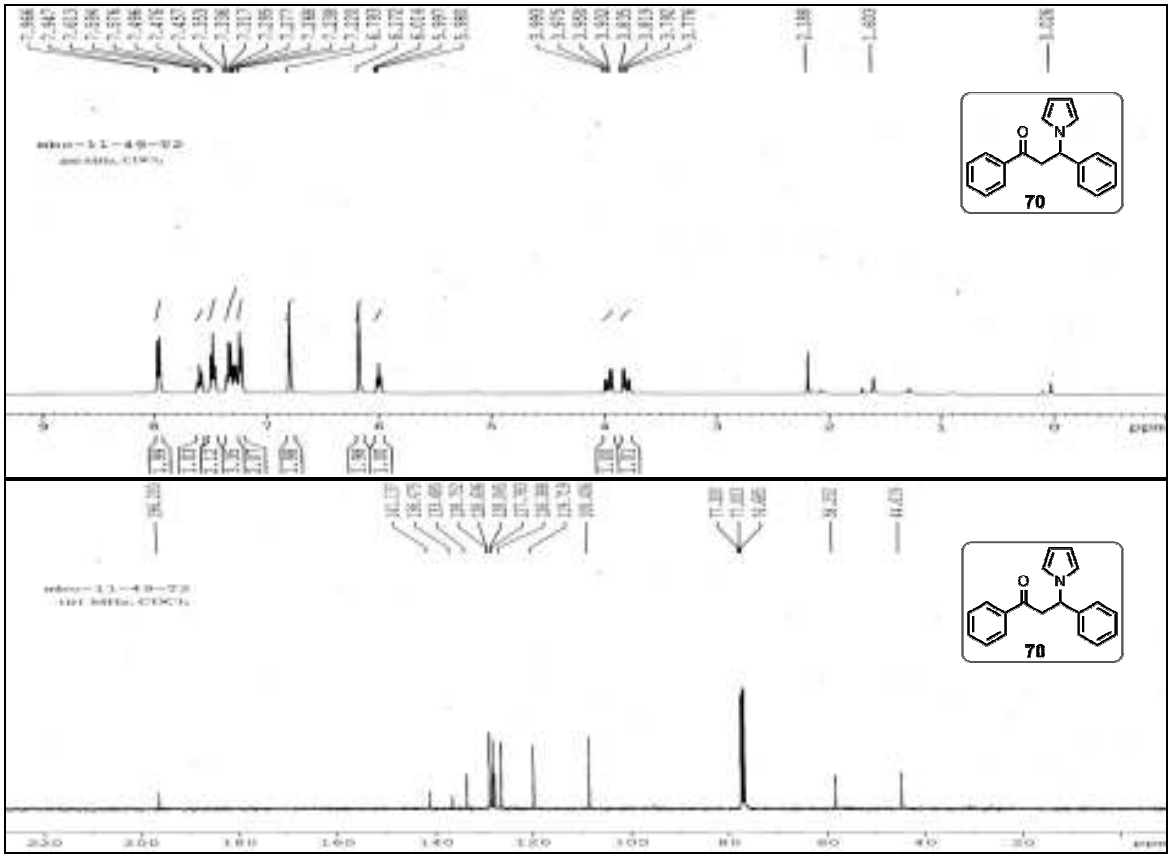

58ub

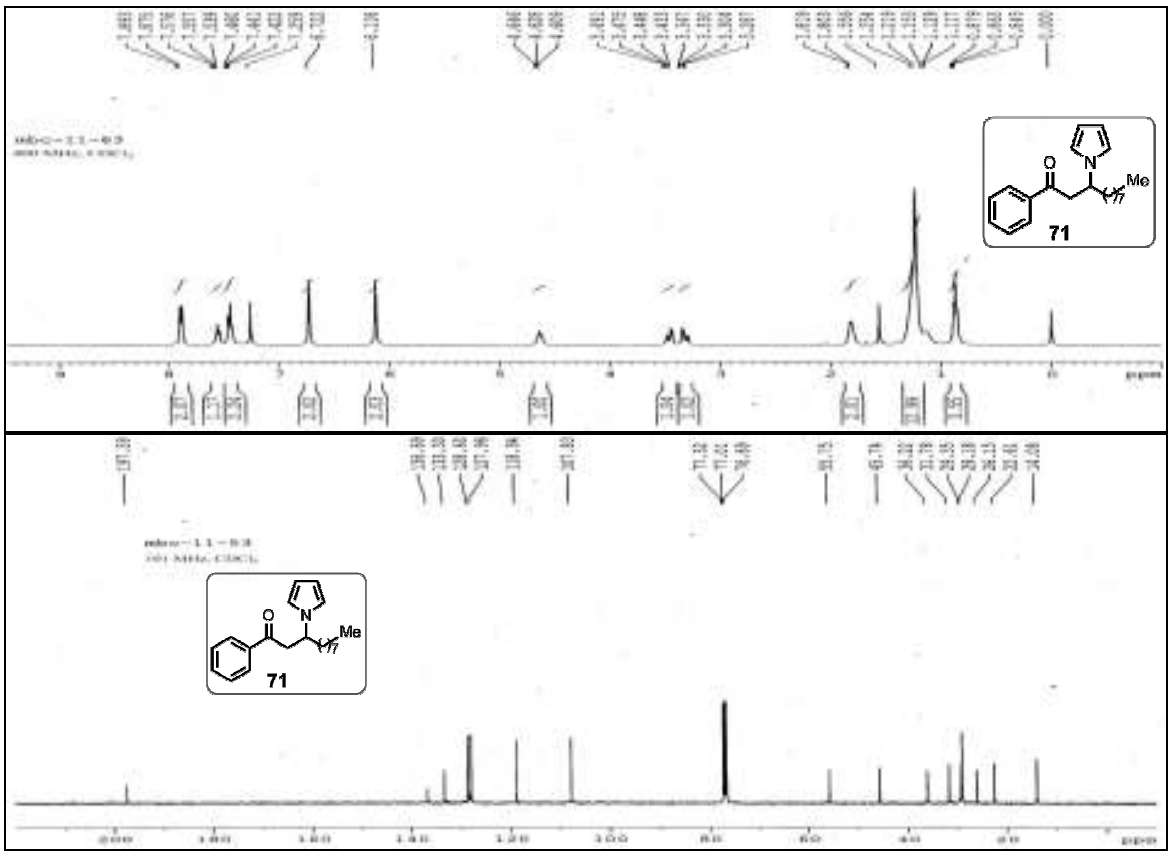

Ph
Me
58ub

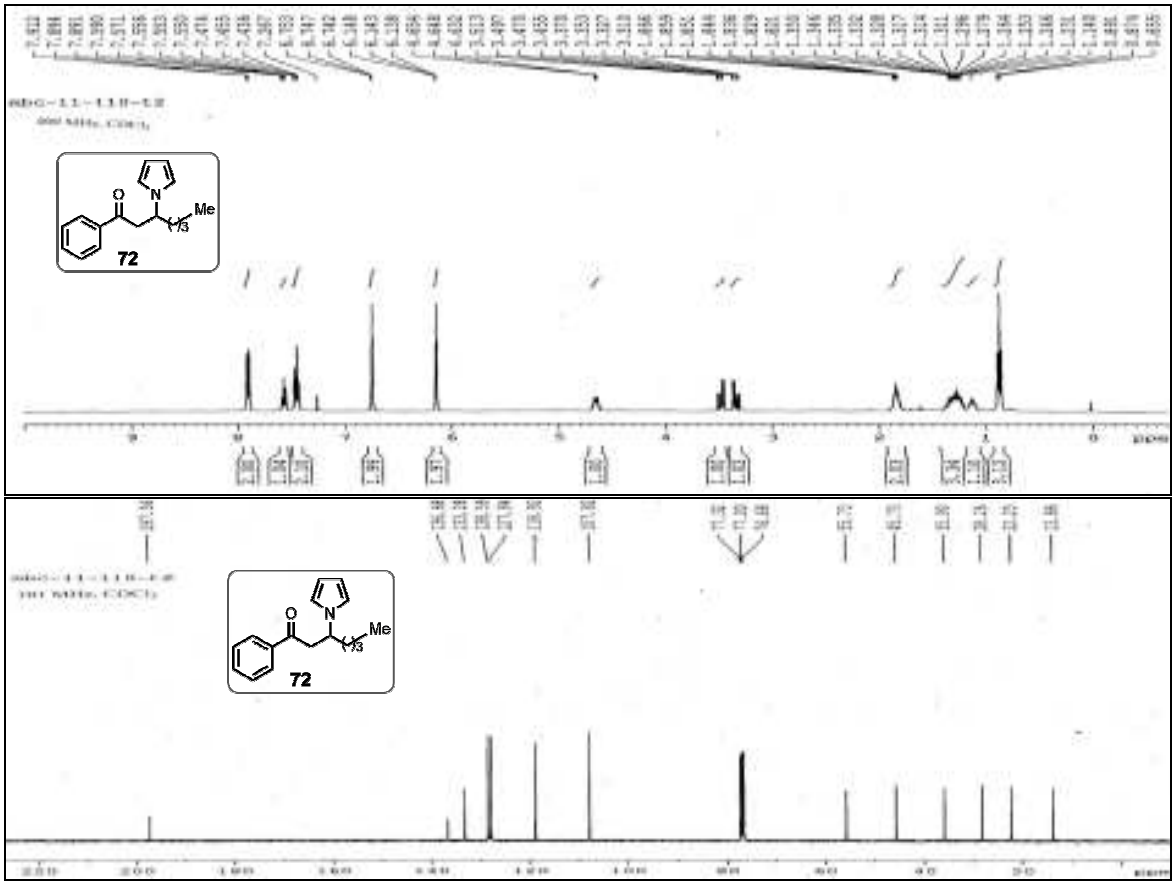

Me
58uf

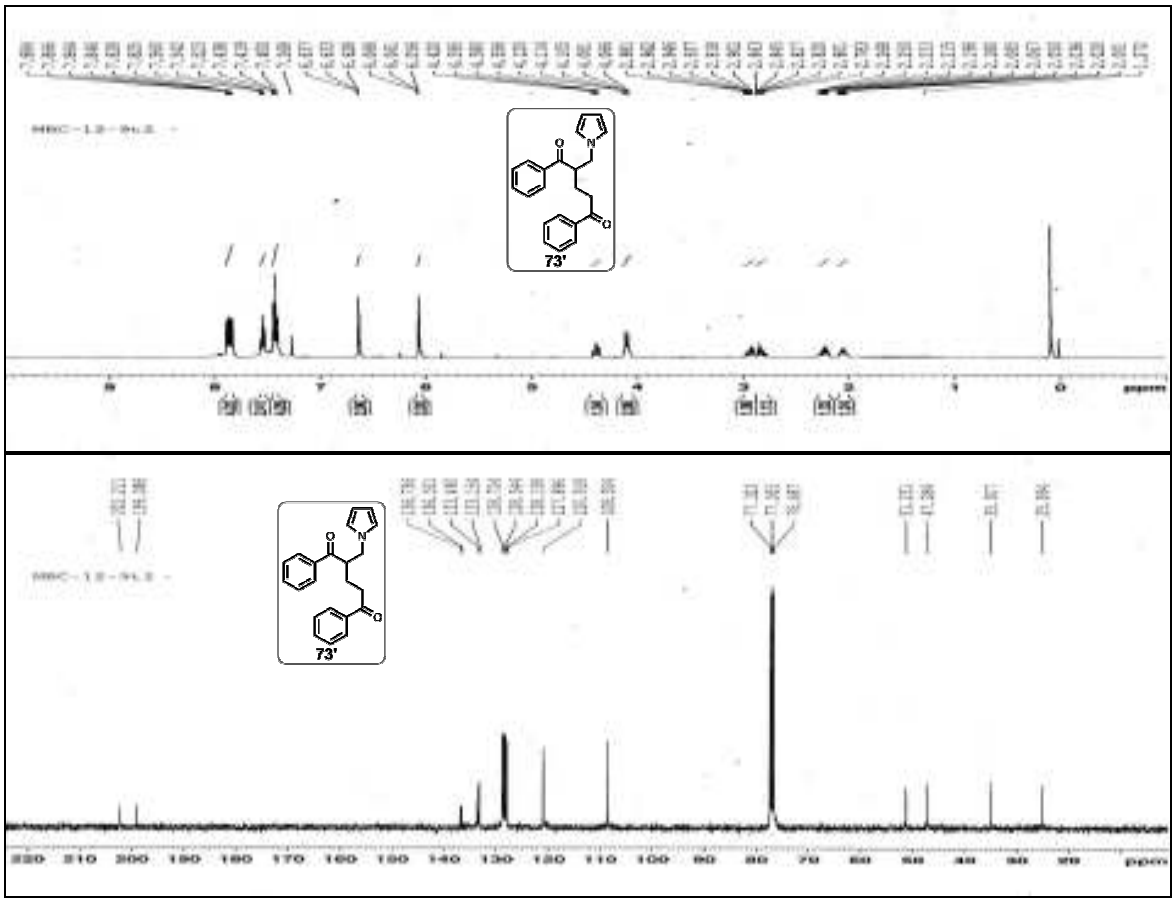

Me
58uf

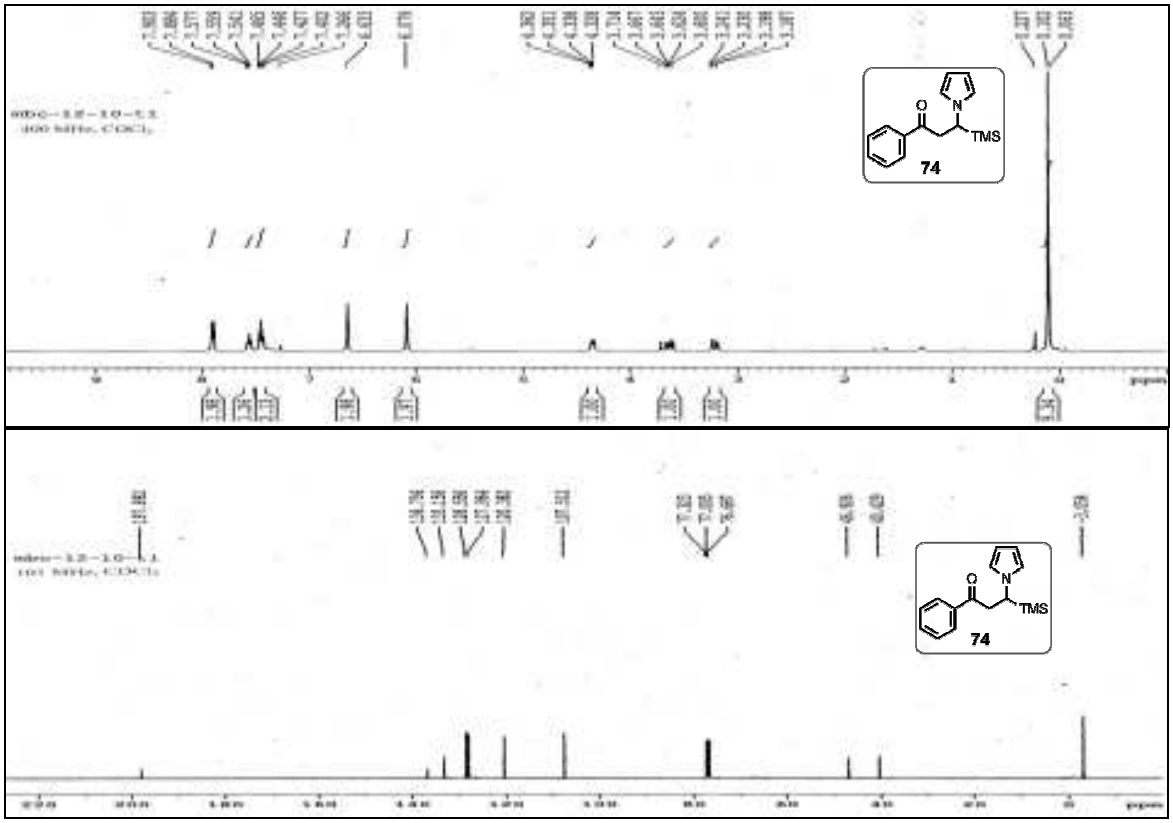

HMBC of compound 8uf
Me
58uf

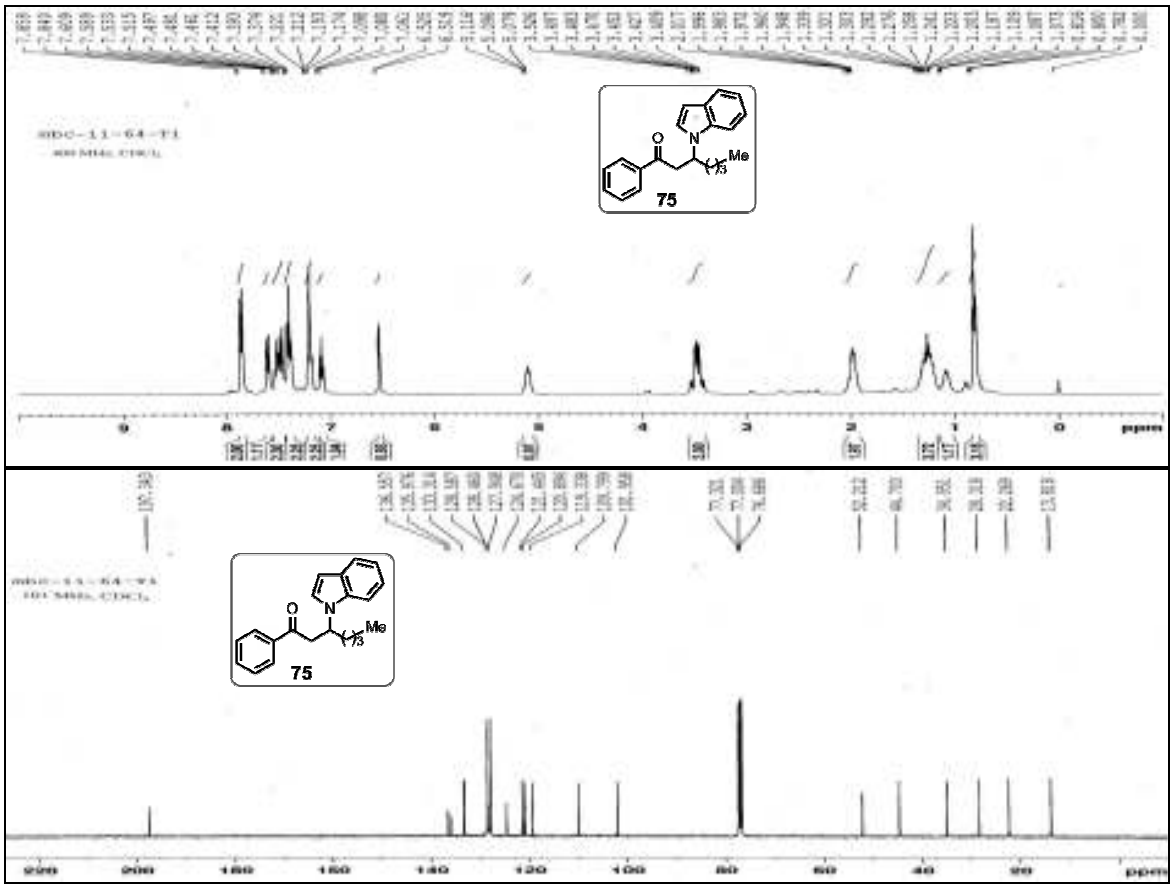

70
70

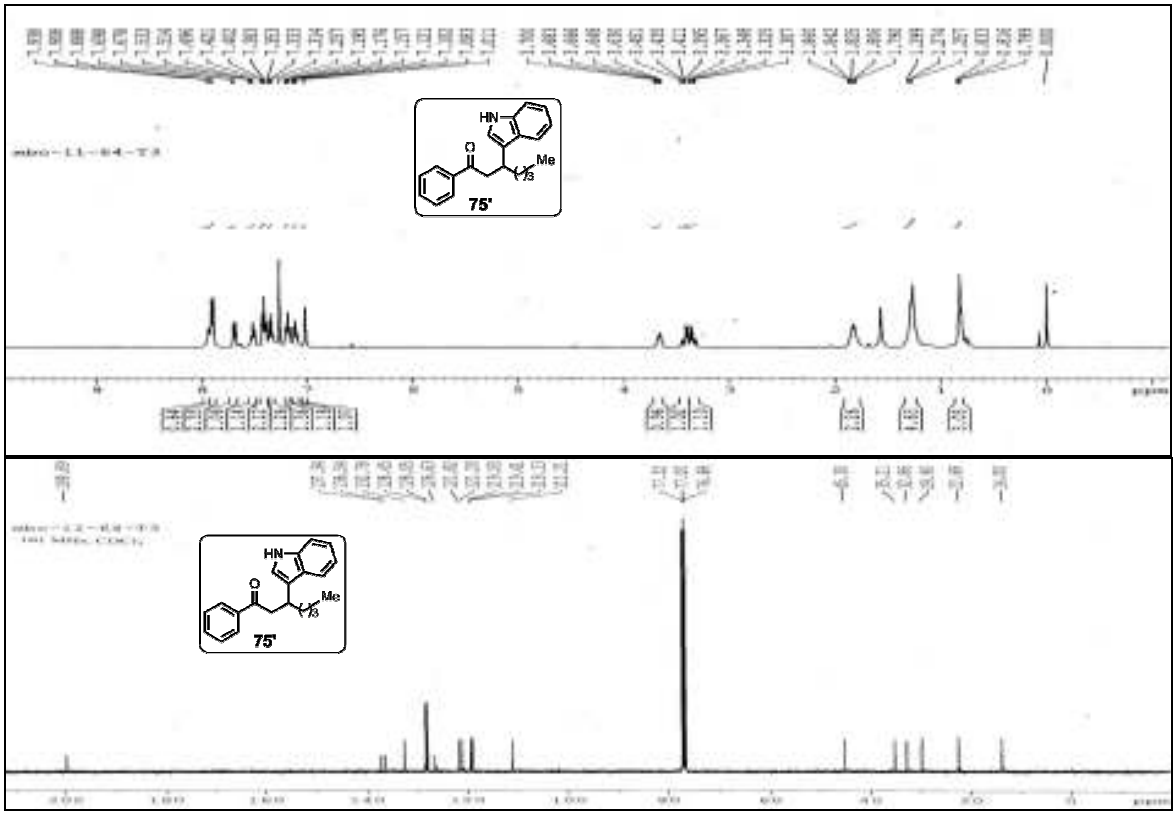

71
71

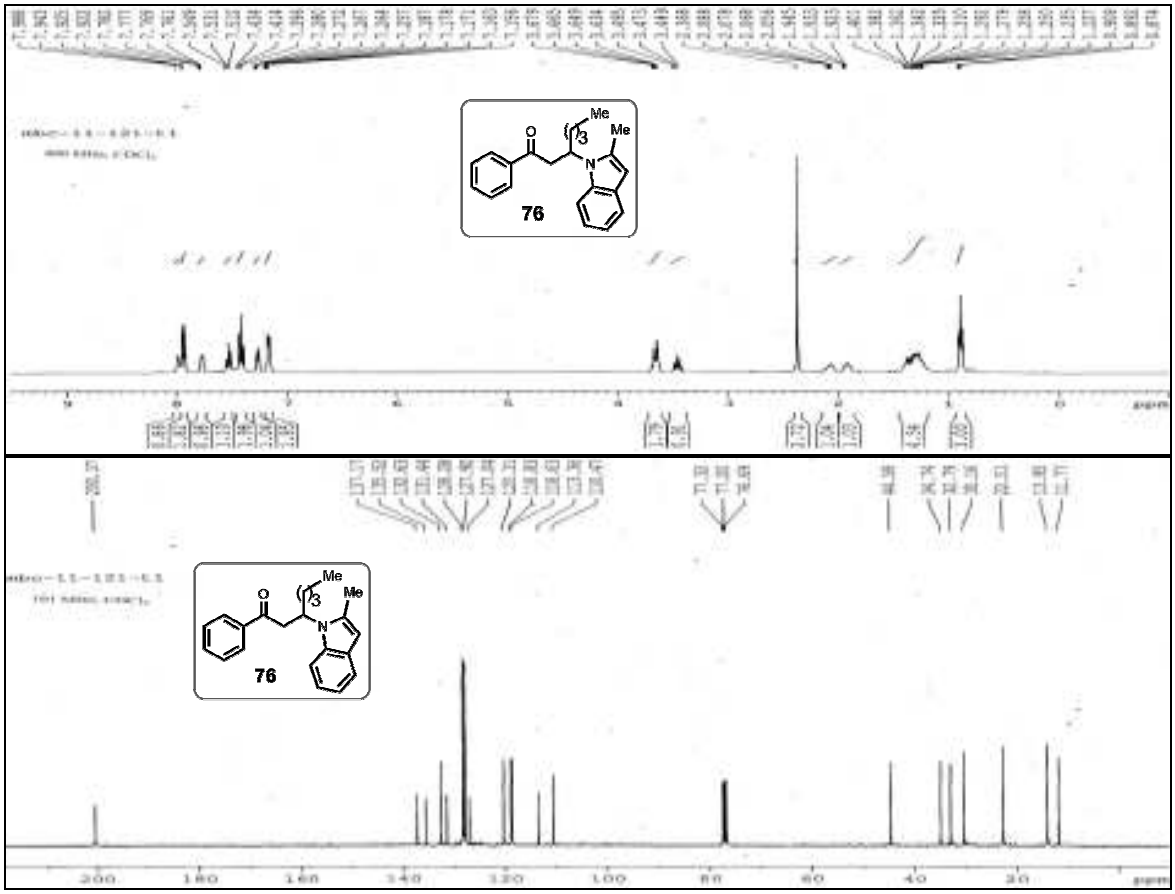

72
72

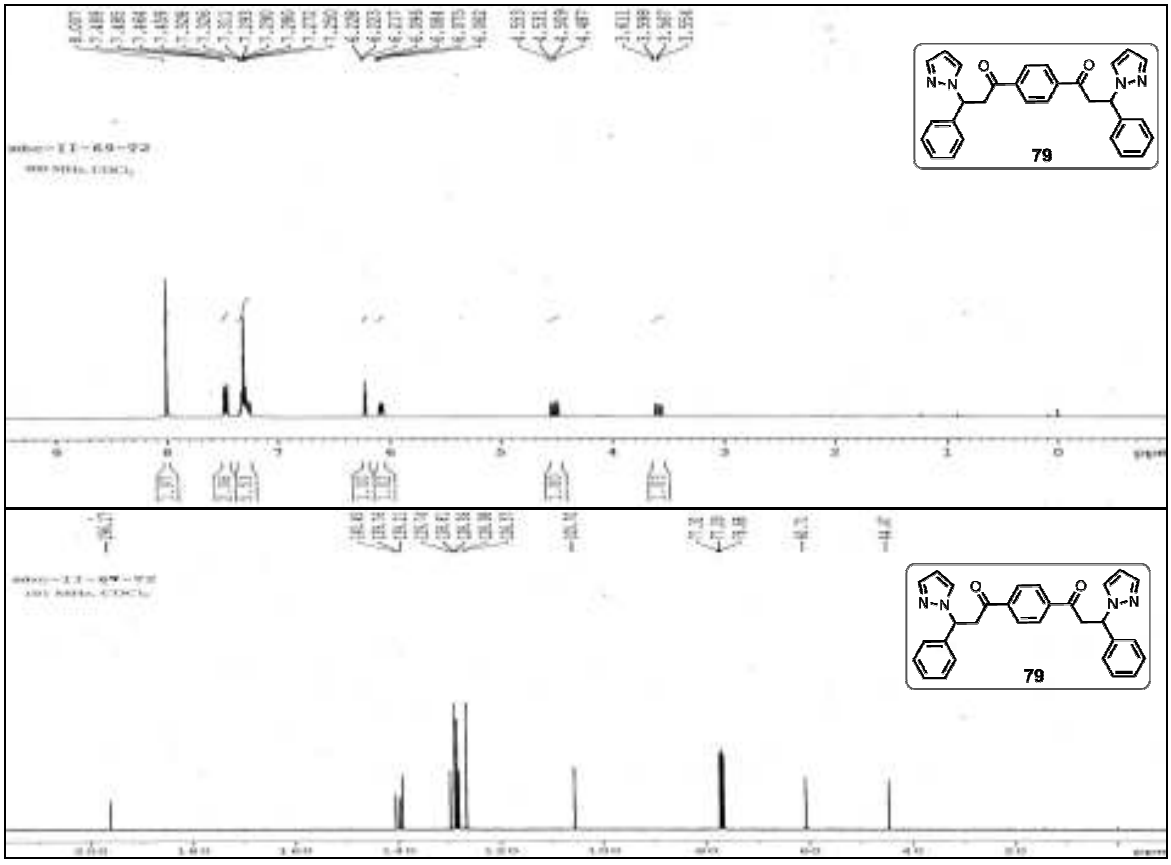

73'
73'

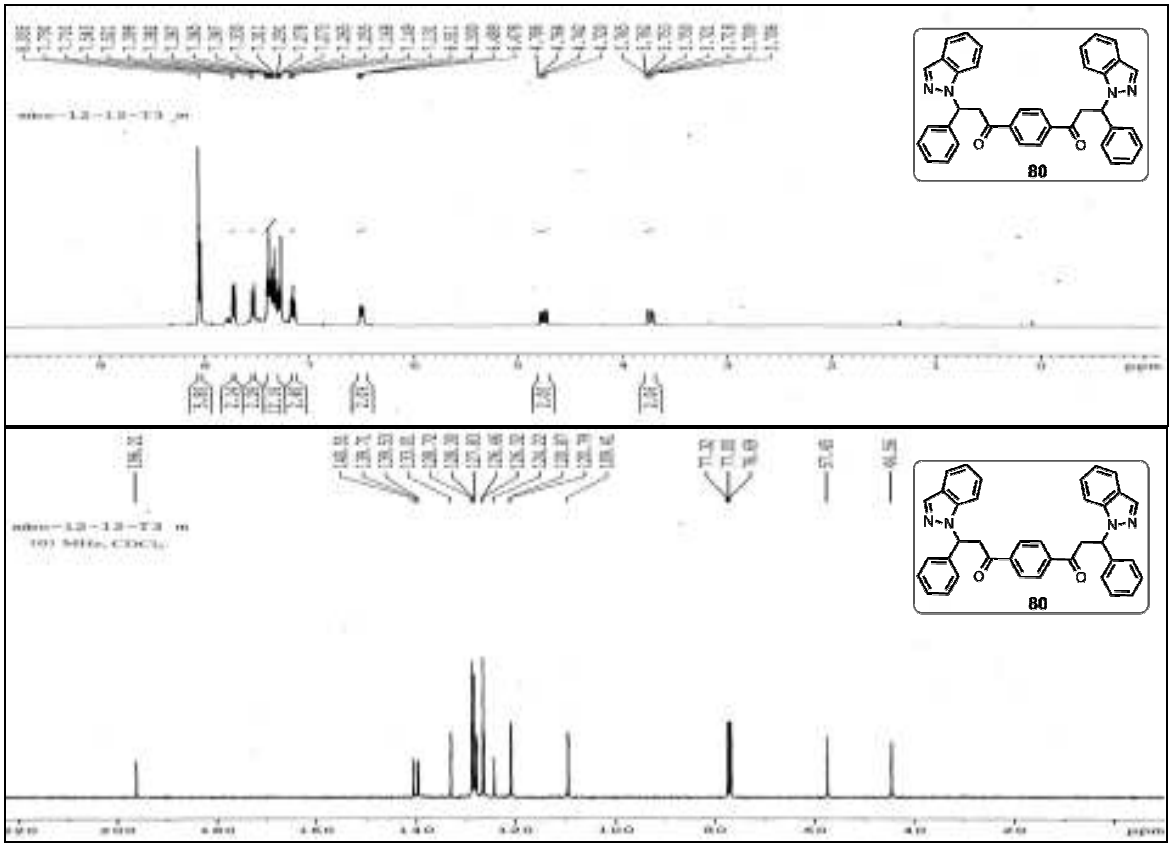

TMS
74
TMS
74


Me
75
Me
75


HN
O
Me
75'
HN
O
Me
75'


Me
Me
O
N
76
Me
Me
O
N
76

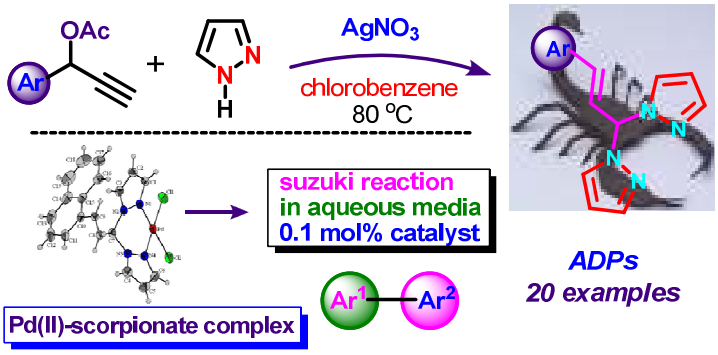

79
79


80
80

Silver(I)-Catalyzed Reaction between Pyrazole and Propargyl Acetates: Stereoselective Synthesis of Scorpionate Ligands *E*-Allyl-*gem*-Dipyrazoles (ADPs)

2 Chapter

Abstract



The reaction between readily accessible pyrazole and propargyl acetates in the presence of Ag(I) catalyst yielded a new class of *E*-allyl-*gem*-dipyrazole scorpionate ligands, 1-aryl-2-*N*-pyrazolyl allyl acetates and 1,3-dipyrazolyl-3-aryl propene. The reaction showed broad substrate scope, and various functional and protecting groups are tolerated under the reaction conditions. The palladium(II) scorpionate complex could thus be easily prepared and successfully employed in Suzuki-Miyaura cross-couplings in water.

Reference:

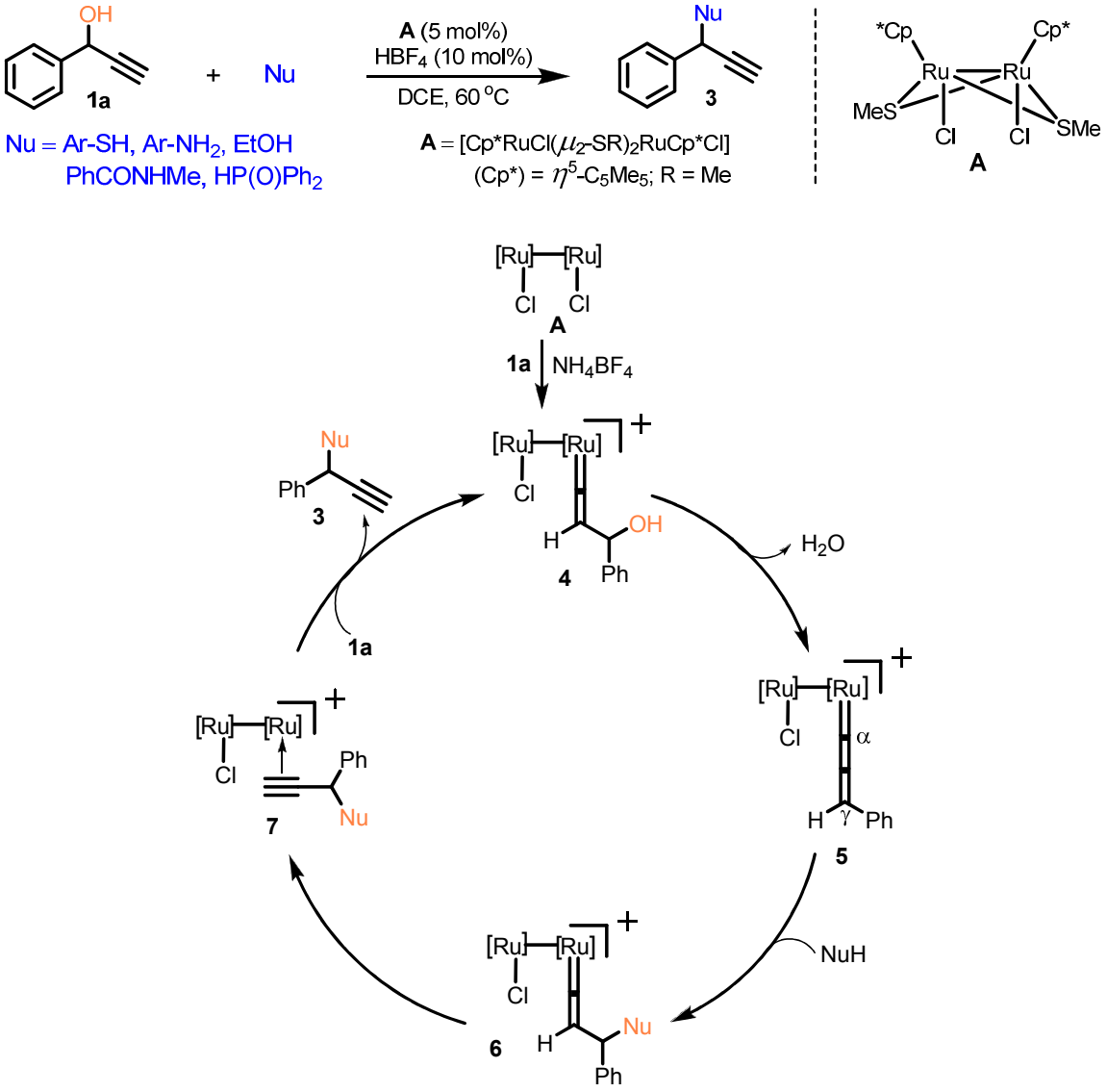
M. Bhanuchandra, Malleswara Rao Kuram and Akhila K. Sahoo

(Manuscript Submitted)

2.1. Introduction

Propargyl alcohols readily undergo nucleophilic substitution because of the presence of hydroxyl and alkyne functionalities and hence can be used for the facile construction of complex molecular frameworks.[1]

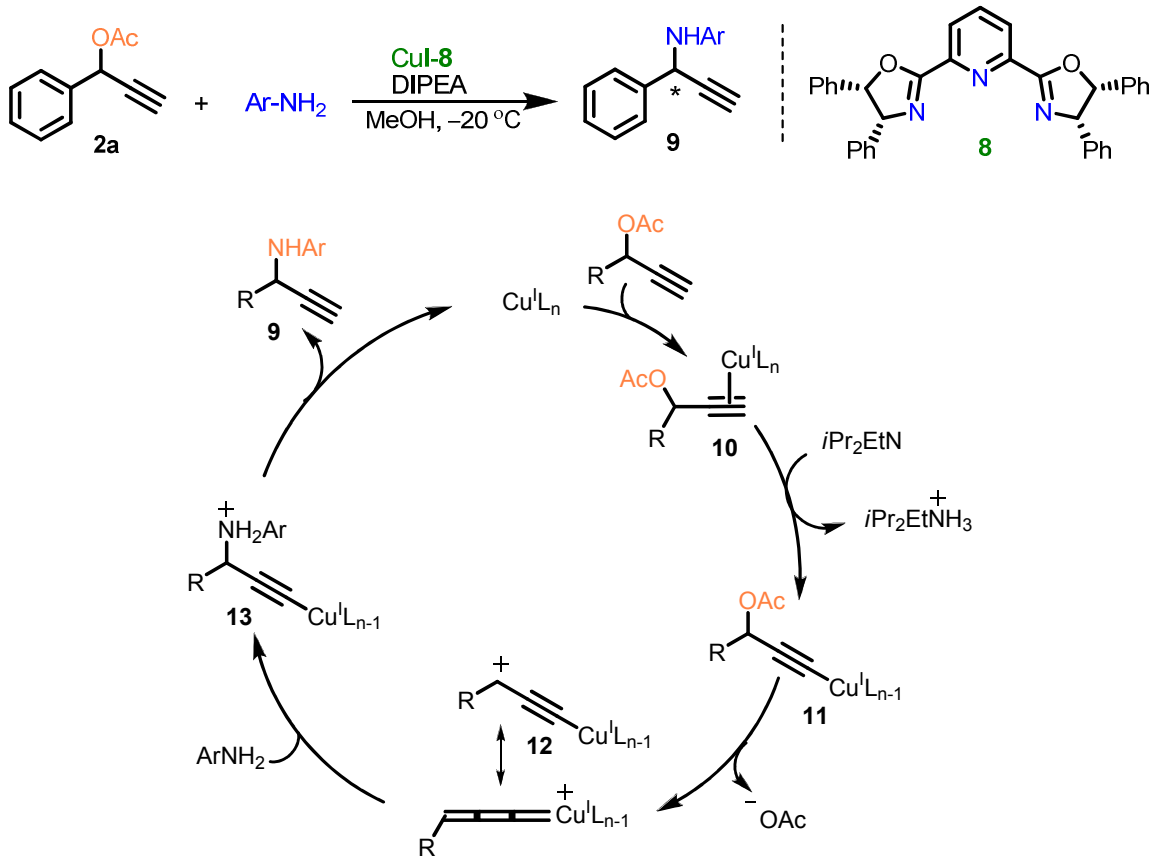
The Nishibayashi group reported the propargylic substitution reaction using the thiolate-bridged diruthenium complex (**A**). The reaction between propargyl alcohol (**1a**) and amide, amine, thiol or diphenylphosphine oxide in the presence of catalyst-A furnishes the propargylic substitution product **3** in good to excellent yields (Scheme 2.1).[1a]



Scheme 2.1: Propargylic Substitution Reaction Catalyzed by Diruthenium Complex.

The reaction initiates with the formation of vinylidene complex **4** from diruthenium complex **A** and propargyl alcohol **1a** in the presence of NH_4BF_4. The elimination of H_2O from **4** generates allenylidene complex **5**. The attack of nucleophile at the C-γ-atom in **5** resulted another vinylidene complex **6**. Complex **6** is then transformed to η^2-coordinated propargylic tautomer **7.** Finally, propargylic substituted product **3** is liberated with the generation of Ru-complex for the next catalytic cycle (Scheme 2.1).

The copper-catalyzed enantioselective propargylic amination of propargyl acetates **2a** is reported by Maarseveen and co-workers.[1j] The nitrogen containing chiral tridentate ligand **8** is employed in this strategy.

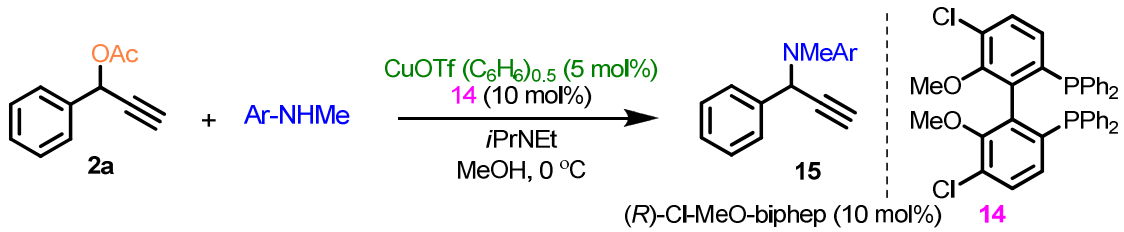


Scheme 2.2: Enantioselective Copper-Catalyzed Propargylic Amination.

In the first step, the ligated copper complex coordinates to the triple bond of propargyl acetates forming π-complex **10**. The copper coordination lowers the pK_a value of the acetylenic hydrogen atom, allowing facile deprotonation of **10** with base and forms the copper acetylide **11**. The loss of acetate moiety from **11** delivers electrophilic intermediate **12**. The attack of amine nucleophile to **12** generates **13**. The facial blockage of copper-

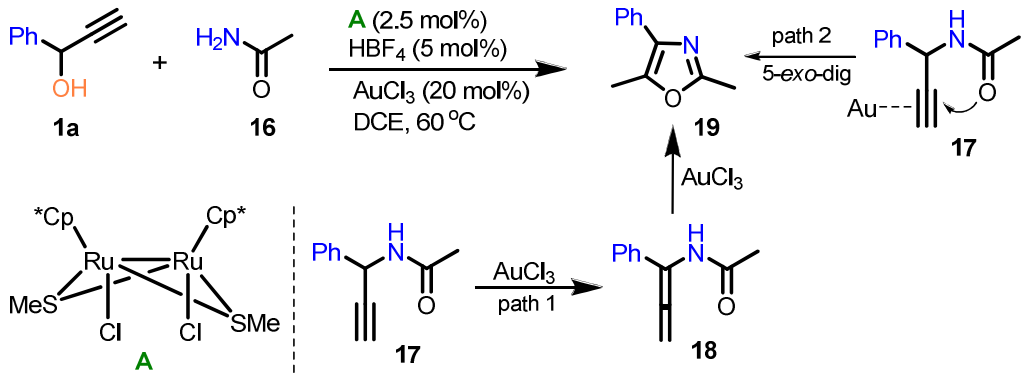
pybox complex in **12** determines the outcome of the regio- and enantioselectivity. Protodemetalation of **13** produces desired compound **9** and regenerates the catalyst for the next cycle (Scheme 2.2).

A similar report from the Nishibayashi group demonstrates the copper-catalyzed asymmetric propargylic substitution reaction of propargylic acetates **2a** with amines. Chiral ligand (*R*)-Cl-MeO-biphep (**14**) is used in this asymmetric reaction (Scheme 2.3).[1k]



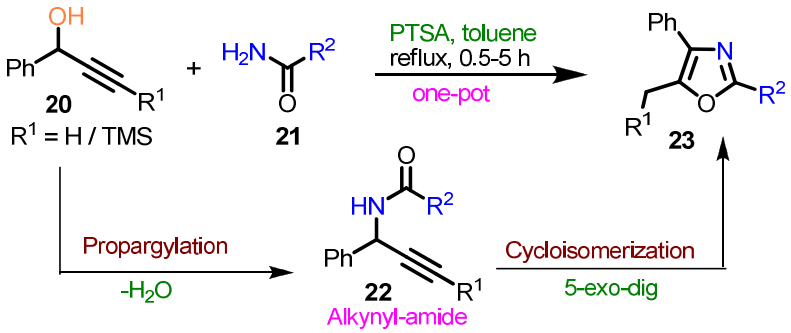
Scheme 2.3: Copper-Catalyzed Enantioselective Propargylic Amination.

In 2004, the Uemura group demonstrated an elegant approach for the synthesis of a variety of substituted oxazoles by using Ru- and Au- catalyzed sequential reaction between propargyl alcohol **1a** and amides **16**.[1b] The reaction begins with the Ru-catalyzed propargylic substitution of acetamide (**16**) with **1a** to give propargylic amide **17**. Next, the $AuCl_3$ assists in the isomerization of **17** to the allene intermediate **18**. Finally, gold-catalyzed intramolecular cyclization of **18** furnishes the oxazole derivatives **19** (Scheme 2.4). An alternate pathway involves the intramolecular 5-*exo*-dig cyclization of amide carbonyl to Au-coordinated triple bond of **17** followed by protodemetalation and tautomerisation to yield **19** (path 2; Scheme 2.4).



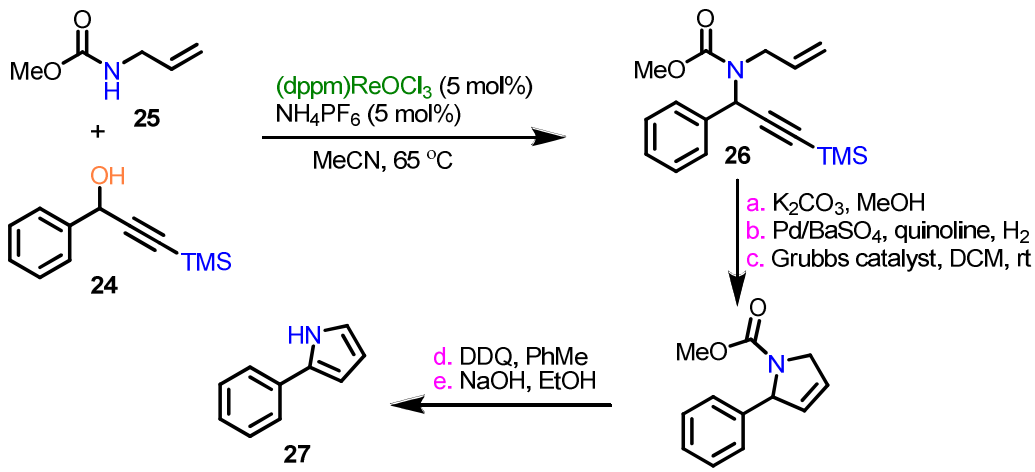
Scheme 2.4: Synthesis of Substituted Oxazoles from Propargylic Alcohols and Amides.

Zhan et al. reported an efficient one-pot strategy for the synthesis of substituted oxazole derivatives **23** from propargyl alcohols **20** and amides **21** with the influence of *p*-toluenesulfonic acid monohydrate as bifunctional catalyst.[1m] The PTSA successfully catalyzes the tandem propargylation/cycloisomerisation reactions; the reaction proceeds with the participation of intermediate **22** (Scheme 2.5).

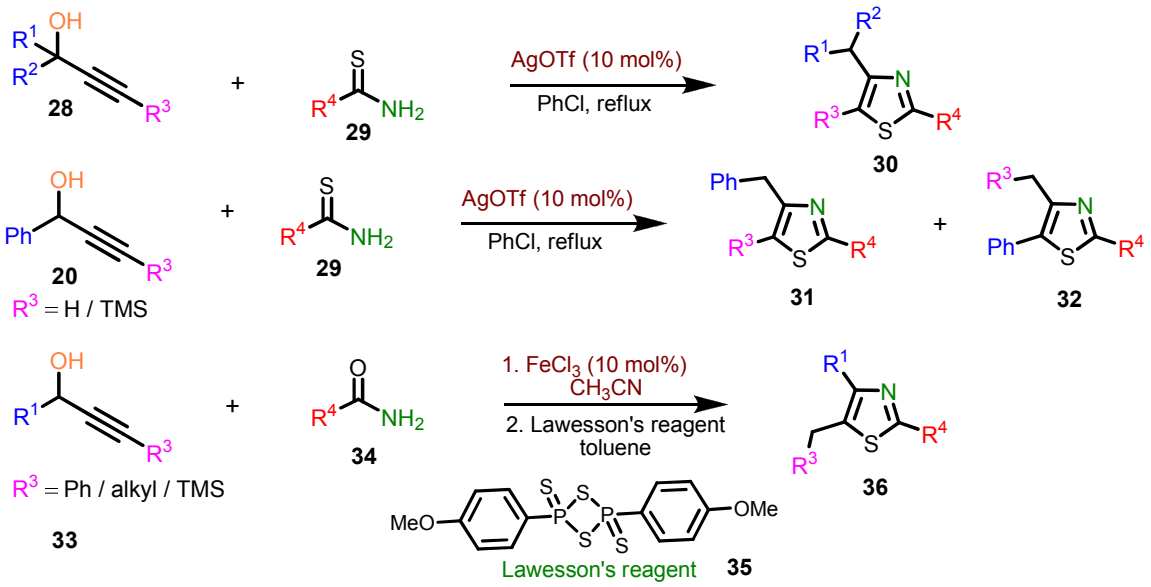


Scheme 2.5: PTSA-Catalyzed Propargylation/ Cycloisomerization Tandem Reaction.

A regioselective propargylamines **26** is obtained from propargyl alcohol **24** and tosylamine or carbamates under the influence of air and moisture stable rhenium-oxo complex.[1c] Following this strategy, a series of 2-phenyl pyrrole (**27**) derivatives, structurely related to Lipoxygenase Inhibitors, are easily synthesized.[1c] For instance: rhenium-catalyzed reaction of *N*-allyl methyl carbamate (**25**) with propargyl alcohol **24** furnishes **26**. The desilylation, reduction of triple bond to olefin by Lindlar's catalyst, and finally ring-closing metathesis followed by oxidative aromatization with DDQ allows the synthesis of the desired pyrrole derivative **27** (Scheme 2.6).

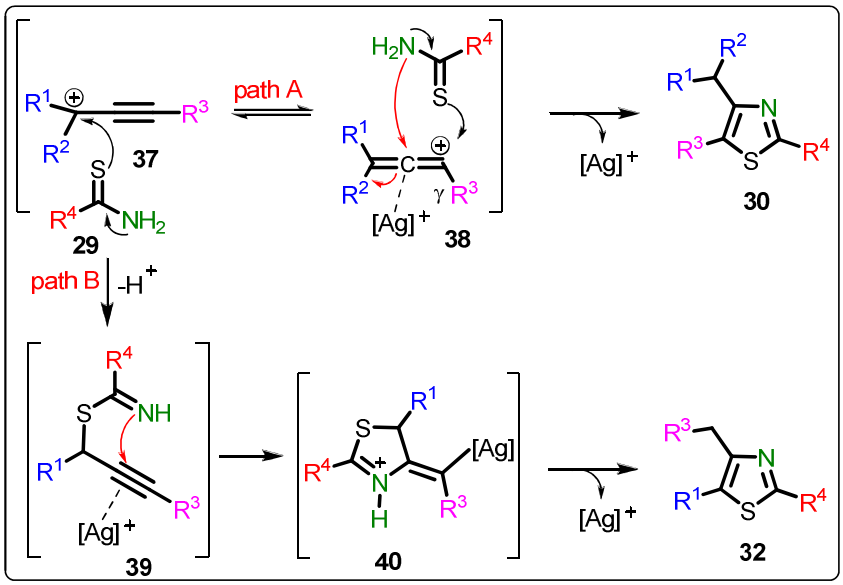


Scheme 2.6: Re(V)-Catalyzed Propargyl Substitution with Carbamates.



Scheme 2.7: One-pot Synthesis of Substituted Thiazoles from Propargyl Alcohols.

The silvertriflate catalyzed reaction of propargyl alcohols with thioamides (**29**) offers one-pot synthesis of various substituted thiazoles (**30**–**32** and **36**) (Scheme 2.7).[1o]

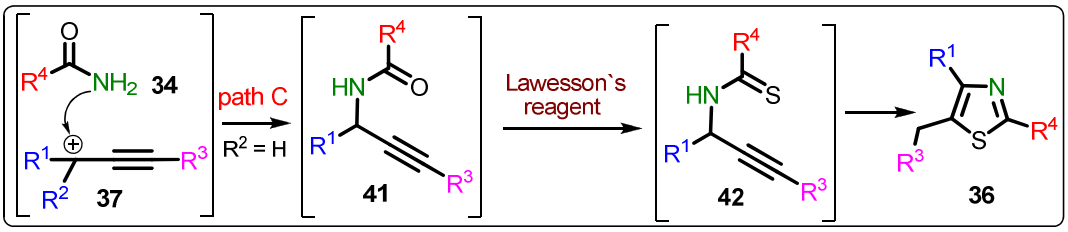


Scheme 2.8: Proposed Mechanism (path A and path B) for the Synthesis of Thiazole.

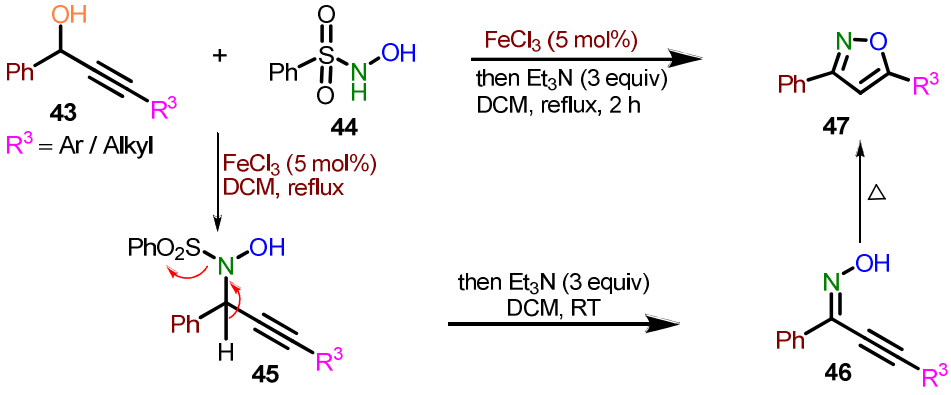
The reaction initiates with the formation of propargyl cation **37** from the corresponding propargyl alcohol under the influence of cationic Ag(I). In Path A: propargyl cation **37** isomerizes to allenyl cation **38**. The attack of sulfur atom of thioamide **29** to the γ–position of **38** followed by the 5-*exo-dig* mode cyclization –NH_2 of thioamide gives the thiazole **30**.

In path B, the sulfur atom in thioamide attacks directly to the propargyl cation **37**. Subsequently, 5-*exo-dig* mode cyclization of amido group to the silver (I) coordinated alkyne complex **39** delivers **40**. Finally, protodemetalation followed by isomerization of **40** furnishes thiazole **32**. The reaction of secondary propargyl alcohols (R^3 = alkyl or aryl) or tertiary propargyl alcohols with Ag-catalyst mainly adopts the Path A (Scheme 2.8). Because of the involvement of either the non-stabilized allenyl cation intermediate **38** (R^3 = H) or the hindrance posed due to the steric nature of the trimethylsilane group at the γ-position of intermediate **38** (R^3 = TMS), the secondary propargyl alcohols having the R^3 = TMS or H follows the Path B (Scheme 2.8).

The Path C involves the reaction of amide **34** with propargyl cation **37** giving the alkynyl-amide **41**. In the presence of Lawesson`s reagent, **41** readily converted to alkynyl-thioamide **42**. Subsequently, cycloisomerisation of **42** delivers the final product **36** (Scheme 2.9).



Scheme 2.9: Proposed Mechanism (path C) for the Synthesis of Thiazole.

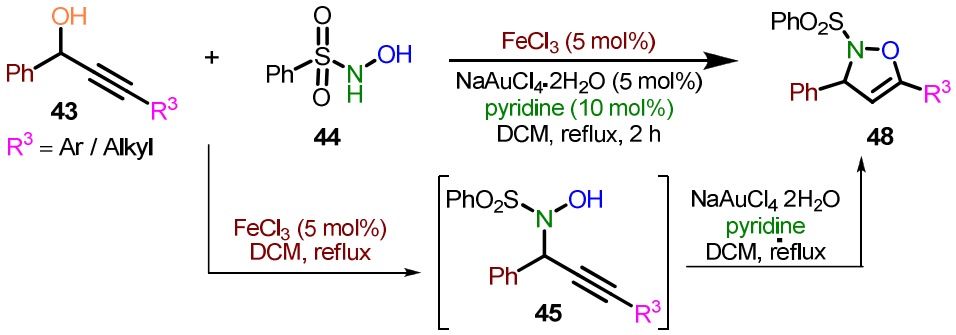


Scheme 2.10: One-pot Synthesis of Isoxazoles from Propargyl Alcohols.

The base induced β-elimination of the sulfone moiety of propargyl hydroxylamines (**45**) affords propargyl oximes **46**, which subsequently undergo 5-*endo-dig* cyclization to give the isoxazole **47** (Scheme 2.10). The compound **45** obtained through iron-catalyzed

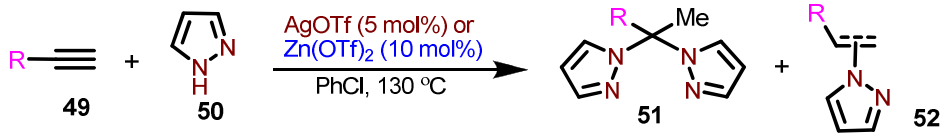
propargylic substitution of bi-nucleophile *N*-sulfonyl-protected hydroxylamine **44** with propargyl alcohol **43** (Scheme 2.10).[1p]

The isoxazolines **48** are obtained in good yields when **43** and **44** reacted with $FeCl_3$ followed by $NaAuCl_4 \cdot 2H_2O$ in the presence of pyridine instead of Et_3N base (Scheme 2.11).



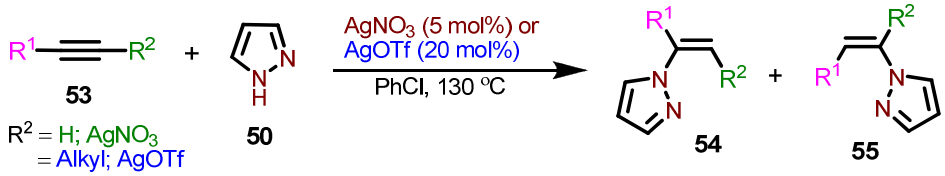
Scheme 2.11: One-pot Synthesis of Isoxazolines from Propargyl Alcohols.

Tsuchimoto group reportd the AgOTf or $Zn(OTf)_2$ catalyzed addition of pyrazole (**50**) to terminal-alkyne **49** for the synthesis of *gem*-dipyrazolylalkanes **51** *via* double addition of pyrazole to alkynes.[2a] The mono-addition products **52** is also obtained in poor yield (Scheme 2.12).



Scheme 2.12: Lewis Acid Catalyzed Double Addition of Pyrazole to Alkynes.

In the presence of $AgNO_3$ (terminal alkynes) or AgOTf (internal alkynes), the Markovnikov's and anti-Markovnikov's hydroamination products **54** and **55** were obtained when pyrazole reacted with the corresponding alkynes, respectively (Scheme 2.13).

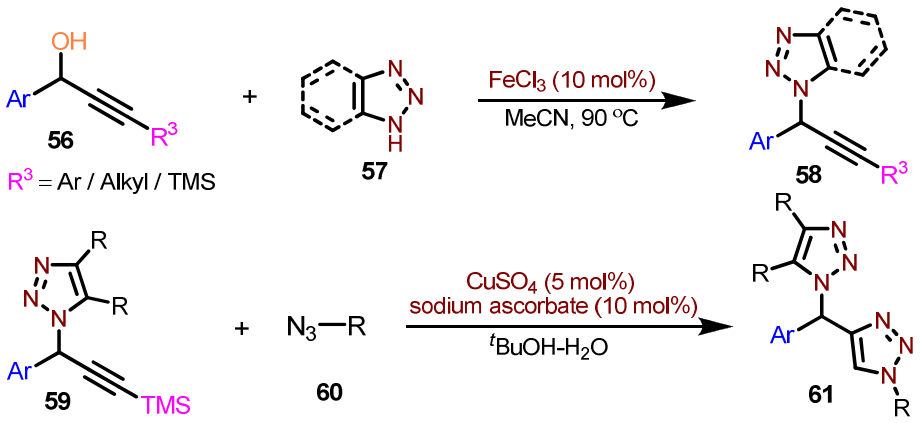


Scheme 2.13: Lewis Acid Catalyzed Mono Addition of Pyrazole to Alkynes.

The above reports demonstrate the efficient synthesis of functionalized heteroarenes *via* sequential propargyl substitution and cyclization cascade. In principle, the reaction between propargyl acetate and NH-heteroarenes offers the formation of 1) propargyl heteroarenes through substitution of the alcohol-group by the NH-heteroarene; 2) 1,2-disubstituted allyl acetates via hydroamination of the NH moiety with the alkyne; 3) 1,3-di-substituted allenes via attack of the heteroaryls at the terminal position of the alkyne; and 4) allyl-*gem*-diheteroaryl- and 1,3-diheteroaryl-substituted propenes through attack of the NH heteroarene on the *in situ* generated allene. Thus, various functionalized heteroarenes can be practically realized via a single-step reaction between propargyl acetates and NH-heteroarenes as sketched in Scheme 2.16.[2]

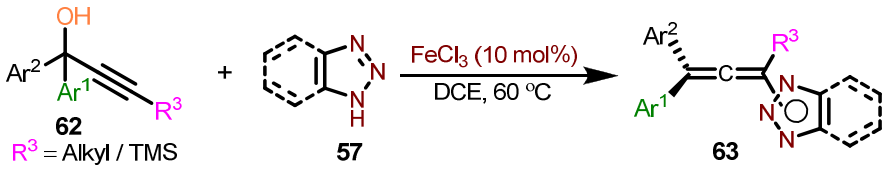
2.1.1. Precedents for Reaction between Propargyl Alcohol and NH-Heteroarenes

Recently, Shi and co-workers demonstrated the synthesis of propargyl-1,2,3-triazole (**58**) using iron-catalyzed C–O bond activation of propargylic alcohols **56**. [2b] Furthermore, the Cu-catalyzed [3+2]-click reaction between the alkyne moiety in **58** and the azide installs another triazole skeleton producing **61** (Scheme 2.14).



Scheme 2.14: $FeCl_3$-Catalyzed 1,2,3-Triazole Propargylation.

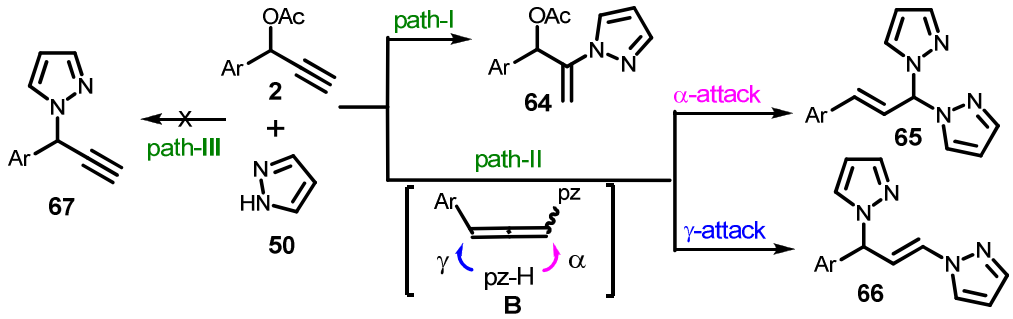
Allene triazole derivatives are successfully synthesized by Shi's group through iron catalyzed regioselective addition of triazole (**57**) to tertiary propargyl alcohols **62**.[2c] The di-substitution at the propargylic position increases the steric hindrance and thus allows the preferential attack of triazole to the terminal position of alkyne furnishing the desired allene triazole derivatives **63** (Scheme 2.15).



Scheme 2.15: Synthesis of Allene Triazoles from Propargylic Alcohols.

2.1.2. Design Plan

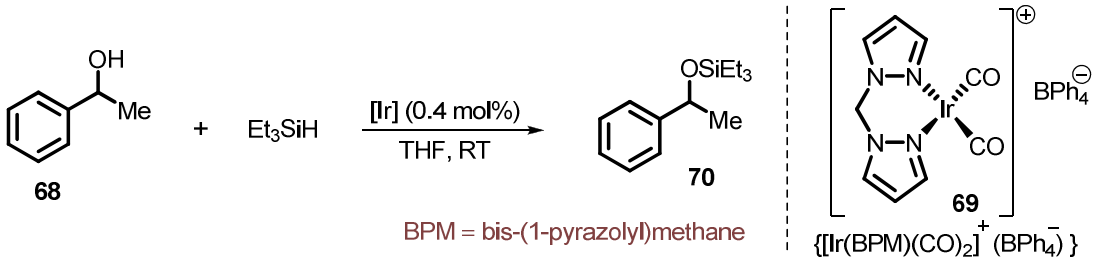
Our recent work in the development of novel reactions of propargyl alcohols inspired us to explore the Lewis acid catalyzed reaction between propargyl acetate and pyrazole.[3] We anticipated the formation of the rarely observed hydroamination compound 1-aryl-2-pyrazolyl allyl acetate **64** (path I), 1-aryl-3-pyrazolyl allene (**B**, path II), and propargyl-*N*-pyrazole (**67**, path III) (Scheme 2.16). Furthermore, α-attack of pyrazole on the transiently formed allene pyrazole **B** could afford (*E*)-allyl-*gem*-dipyrazoles (**65**) (ADPs), a new class of *scorpionate-type ligands*, whereas γ-attack of pyrazole could afford (*E*)-1,1'-(3-arylprop-1-ene-1,3-diyl)bis(1*H*-pyrazole) (**66**) (Scheme 2.16).



Scheme 2.16: Reaction between Propargyl Acetate and Pyrazole.

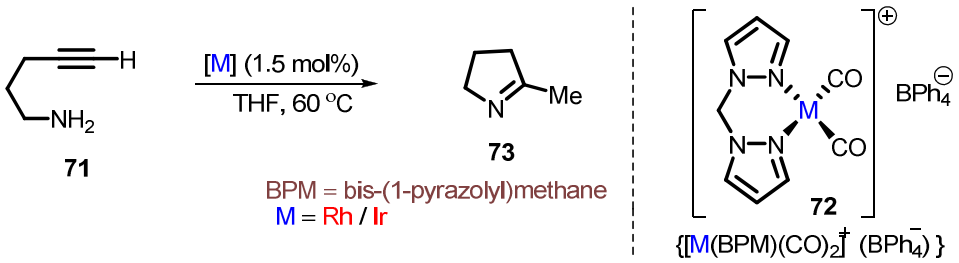
2.1.3. Applications of Scorpionate-type Ligands

Interestingly, the *gem*-dipyrazolyl derivatives exhibited analgesic and anti-inflammatory activities.[4] The two adjacent nitrogen atoms in **65** give strong chelation ability to the metal, and the complexes are useful in accomplishing various catalytic organic transformations.[5,6] For example, scorpionate ligand bis-(1-pyrazolyl)methane (bpm) coordinated cationic iridium complex (**69**) is successfully employed for protecting the hydroxyl group with Et_3SiH (Scheme 2.17).[6a]



Scheme 2.17: Protection of -OH group with Et_3SiH

Cationic rhodium and iridium complexes 7**2** chelated by bis-(1-pyrazolyl)methane (bpm), are efficiently used for the hydroamination. For instance: the intramolecular hydroamination of the $–NH_2$ group in 4-pentyn-1-amine (**71**) with alkyne-moiety under the cationic complexes $[Rh(bpm)(CO)_2]^+[BPh_4]^-$ or $[Ir(bpm)(CO)_2]^+[BPh_4]^-$ yielded 2-methyl-1-pyrroline (**73**) (Scheme 2.18).[6b]



Scheme 2.18: Intramolecular Hydroamination

Importantly, some of the Pt-coordinated complexes showed anticancer activities (Figure 2.1).[7]

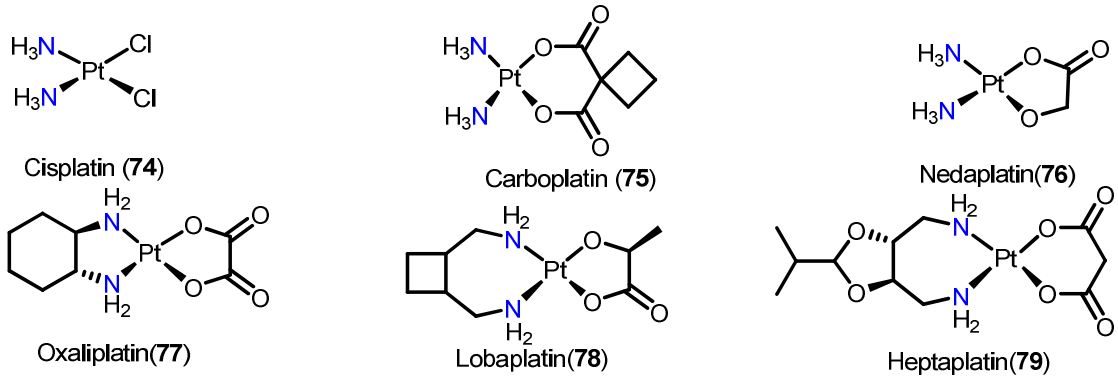


Figure 2.1: Anticancer Platinium (II) Complexes

In 1969, Rosenberg et al discovered the antitumor drug c*isplatin* (**74**) [(*cis*-dichlorodiamino platinum(II)]. This anticancer drug is widely used against testicular, ovarian cancers and other human solid tumors. However, the poor solubility of cisplatin in water appeals for the development of alternate water soluble platinum complexes.

Carboplatin (**75**) [*cis*-diamino(1,1'-cyclobutanedicarboxylato)paltinum (II)] is the second generation cisplatin analogous of antitumor platinum compound. Interestingly, the carboplatin have the better solubility in water than cisplatin showing strong antitumor effect.

The *nedaplatin* (**76**) [*cis*-diamino(glycolato)platinum (II)] is in the preclinical studies. Owing to the high cytotoxicity nature, the clinically approved nedaplatin is used for the treatment of non-small cell lung cancer, uterus cancer, neck, and head cancers etc. The c*arboplatin* and *nedaplatin* are the second generation antitumor drugs.

Oxaliplatin (**77**) [(1,2-diaminecyclohexane)oxalate platinum (II)] is the third generation platinum drug with lower myelo- and nephrotoxicity compared to cisplatin and carboplatin, however, it is highly neurotoxic.

Lobaplatin (**78**) [1,2-diaminomethyl-cyclobutane-platinum(II)-lactate] shows remarkable cytotoxicity against animal tumor test systems. It is used for the treatment of chronic myeloid leukemia and lungs cancers.

Heptaplatin (**79**) {*cis*-malonato[(*4R,5R*)-4,5-bis(aminomethyl)-2-isopropyl-1,3-dioxolane]platinum(II)} is a newly developed platinum derivative, reported to be less toxic than cisplatin.

Looking into the utility of the various Pt-complexes shown in Figure 2.1, it reveals that the replacement of monodentate ammonia ligand by alkyl-bridged nitrogen bidentate ligands and chloride anions by aliphatic or alicyclic dicarboxylate anions in *cisplatin* enhances the activity of the platinum anticancer drugs.

As discussed in Scheme 2.16, the synthesis of novel ADPs (**65**), 1-aryl-2-*N*-pyrazolyl-allyl acetate (**64**), and 1,3-dipyrazolyl-3-aryl propene (**66**) from propargyl acetates and pyrazoles in the presence of $AgNO_3$ is reported herein.

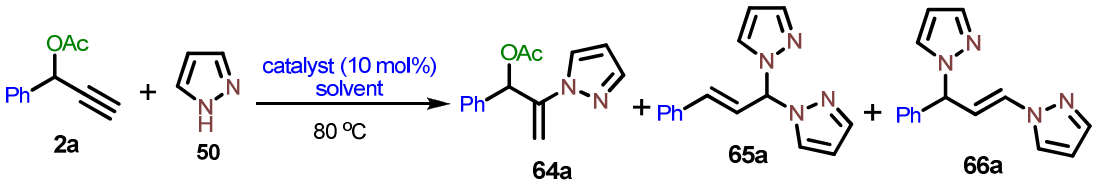
2.2. Results and Discussion

2.2.1. Reaction Optimization:

To start with 1-phenylprop-2-ynyl acetate (**2a**) and pyrazole (**50**) were independently reacted in the presence of various Lewis acids at 80 °C for 24 h. The details of the optimization studies are shown in Table 2.1. The reaction between **2a** (1.0 equiv) and **50** (5.0 equiv) with 10 mol% AgOTf in chlorobenzene produced (*E*)-allyl-*gem*-dipyrazoles (ADPs) **65a** in 41% yield, 1-phenyl-2-*N*-pyrazolyl allyl acetate **64a** (18%), and 1,3-dipyrazolyl-3-phenyl propene **66a** (20%) with incomplete consumption of **2a** (entry 1). Gratifyingly, **65a**, **64a**, **66a**, and unreacted **2a** were easily isolated through flash column chromatography in pure form. Incomplete conversion of **2a** and poor overall yield of the products **64**–**66a** were noticed, when $Cu(OTf)_2$, $In(OTf)_3$, and $CuNO_3.H_2O$ were independently employed (entries 2–4). To our delight, reaction with $AgNO_3$ delivered an improved yield of **65a** (58%), though **64a** and **66a** were also isolated in 21% and 11% yields, respectively (entry 5). A trace amount of products **64**–**66a** were noticed in GC-MS, when the reaction conducted with AgCl (entry 6); whereas Ag_2CO_3 or $AgBF_4$ influenced moderately (entries 7 and 8). Of various Ag-salts examined, $AgNO_3$ was found to be effective (entry 5). Worthy mentioning that, we did not observe even a trace of propargyl-*N*-pyrazole **67**. We next explored the effect of solvents. Incomplete conversion of **2a** with the formation of moderate amount of **65a** was observed, when polar aprotic solvents such as THF, CH_3CN and DMF were used (entries 9–11). The reaction in DCE was poor (entry

12). The use of different amount of pyrazole was further investigated. The loading of lower amount of pyrazole, from 5.0 to 2.0 or 4.0 equiv, led to **65a** with slightly decreased yield (entries 13 and 14). An enhanced yield of **66a** was observed, when 6.0/8.0 equiv of **50** was employed (entries 15 and 16). We therefore used 5.0 equiv of pyrazole in this transformation. The reaction of propargyl-O-pivolate with pyrazole produced **64** (47%), **65a** (39%) and **66a** (6%), on the basis of GC-MS analysis. A reverse trend of product selectivity was observed when O-Boc protected propargyl alcohol reacted with pyrazole; **64** (16%), **65a** (21%) and **66a** (52%).

Table 2.1: Optimization of Reaction Conditions[a]



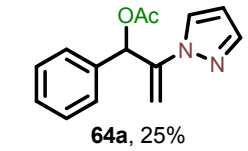
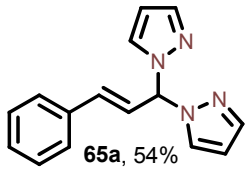
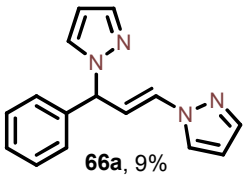
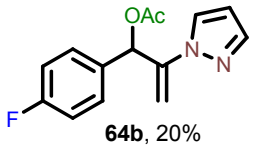
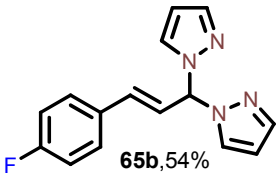
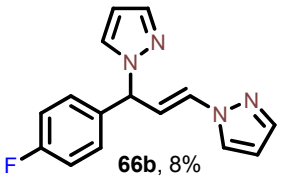
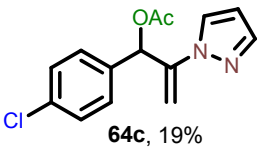
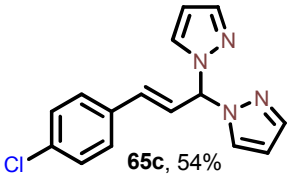
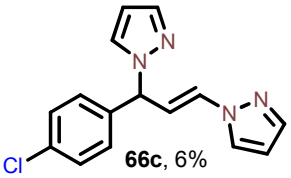
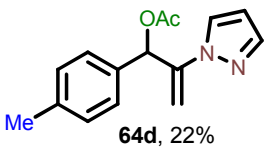
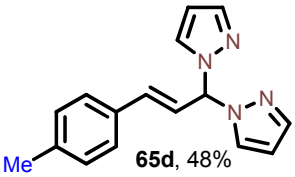
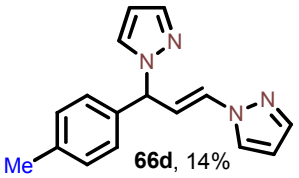
entry	**50** equiv	catalyst	solvent	yield (%)[b] **64a**	**65a**	**66a**
1	5.0	AgOTf	chlorobenzene	18	41	20
2	5.0	$Cu(OTf)_2$	chlorobenzene	<1	<5	<2
3	5.0	$In(OTf)_3$	chlorobenzene	<1	<6	<3
4	5.0	$CuNO_3.H_2O$	chlorobenzene	<2	<8	<7
5	**5.0**	**$AgNO_3$**	**chlorobenzene**	**21**	**58**	**11**
6	5.0	AgCl	chlorobenzene	<2	<9	<6
7	5.0	Ag_2CO_3	chlorobenzene	13	25	12
8	5.0	$AgBF_4$	chlorobenzene	17	35	18
9	5.0	$AgNO_3$	THF	18	36	16
10	5.0	$AgNO_3$	CH_3CN	10	37	29
11	5.0	$AgNO_3$	DMF	22	38	17
12	5.0	$AgNO_3$	1,2-DCE	08	20	12
13	2.0	$AgNO_3$	chlorobenzene	25	43	08
14	4.0	$AgNO_3$	chlorobenzene	21	55	10
15	6.0	$AgNO_3$	chlorobenzene	20	53	18
16	8.0	$AgNO_3$	chlorobenzene	21	51	19

[a]Reactions were carried out using **2a** (0.5 mmol), catalyst (10 mol%) in solvent (0.5 mL) at 80 °C for 24 h. [b]isolated yields.

2.2.2. Scope of the Reaction

The optimized catalytic condition shown in entry 5, Table 2.1 (10 mol% $AgNO_3$ in chlorobenzene at 80 °C) was finally selected in screening the reaction between a series of propargyl acetates (**2**) and pyrazole (**50**). The effect of *para*-substitution on the aryl-moiety in propargyl acetate on $AgNO_3$ catalyzed reaction with **50** was examined at first. The results are summarized in Table 2.2. The electron-neutral 1-phenylprop-2-ynyl acetate (**2a**) reacted with **50** to give **64**–**66a** in overall good yields, with the isolation of 54% of **65a**. The electon withdrawing substituents such as F/Cl groups at the *p*-position on aryl moiety in **2b**/**2c** reacted effectively with **50** and the corresponding allyl acetates **64b–c** and di-pyrazolyl bearing compounds (**65b–c** and **66b–c**) were obtained in good overall yields. The electron rich 4-methyl-propargyl acetate reacted with **50** under the catalytic condition to furnish **65d** in 48% yield.

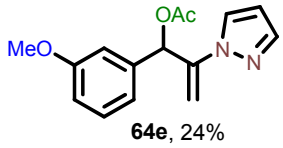
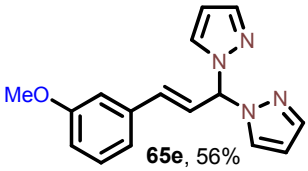
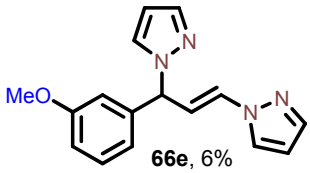
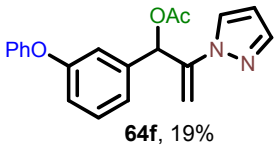
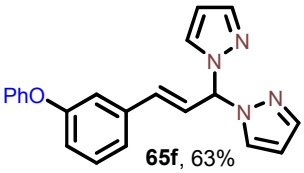
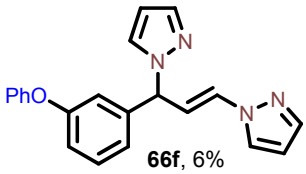
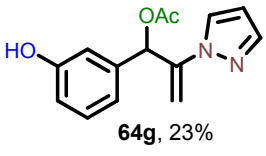
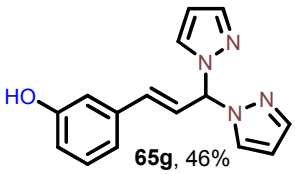
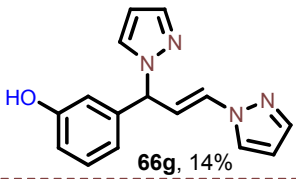
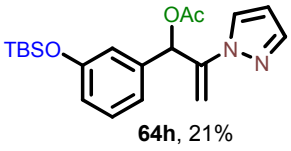
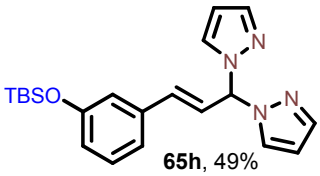
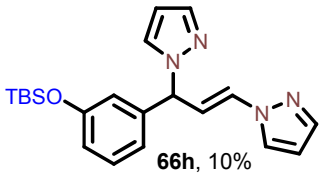
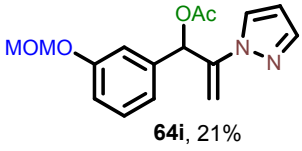
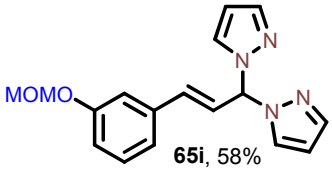
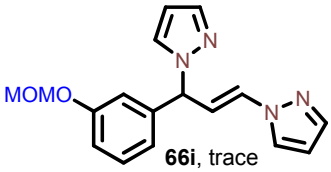
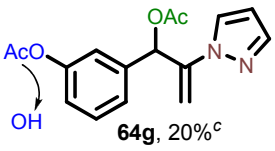
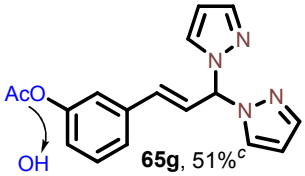
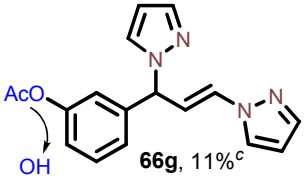
Table 2.2: $AgNO_3$ Catalyzed Reaction between *para*-Substituted Propargyl Acetates and Pyrazole[a,b]

 **64a**, 25%	 **65a**, 54%	 **66a**, 9%
 **64b**, 20%	 **65b**,54%	 **66b**, 8%
 **64c**, 19%	 **65c**, 54%	 **66c**, 6%
 **64d**, 22%	 **65d**, 48%	 **66d**, 14%

[a] Reactions were carried out using **2** (1.0 mmol), **50** (5.0 mmol), $AgNO_3$ (10 mol%) in chlorobenzene (1.0 mL) at 80 °C for 24 h. [b]Isolated yield.

Next, we examined the effect of *meta*-groups on aryl moiety in propargyl acetate to the synthesis of desired ADPs products (Table 2.3). The reaction of propargyl acetates having electron donating methoxy or phenoxy groups at the 3-position on aryl ring with **50** gave the corresponding ADPs **65e**, and **65f** in 56%, and 63% yields, respectively. The free phenol –OH moiety did not affect the reaction outcome, and the corresponding phenol products **64–66g** were isolated in 83% overall yield.

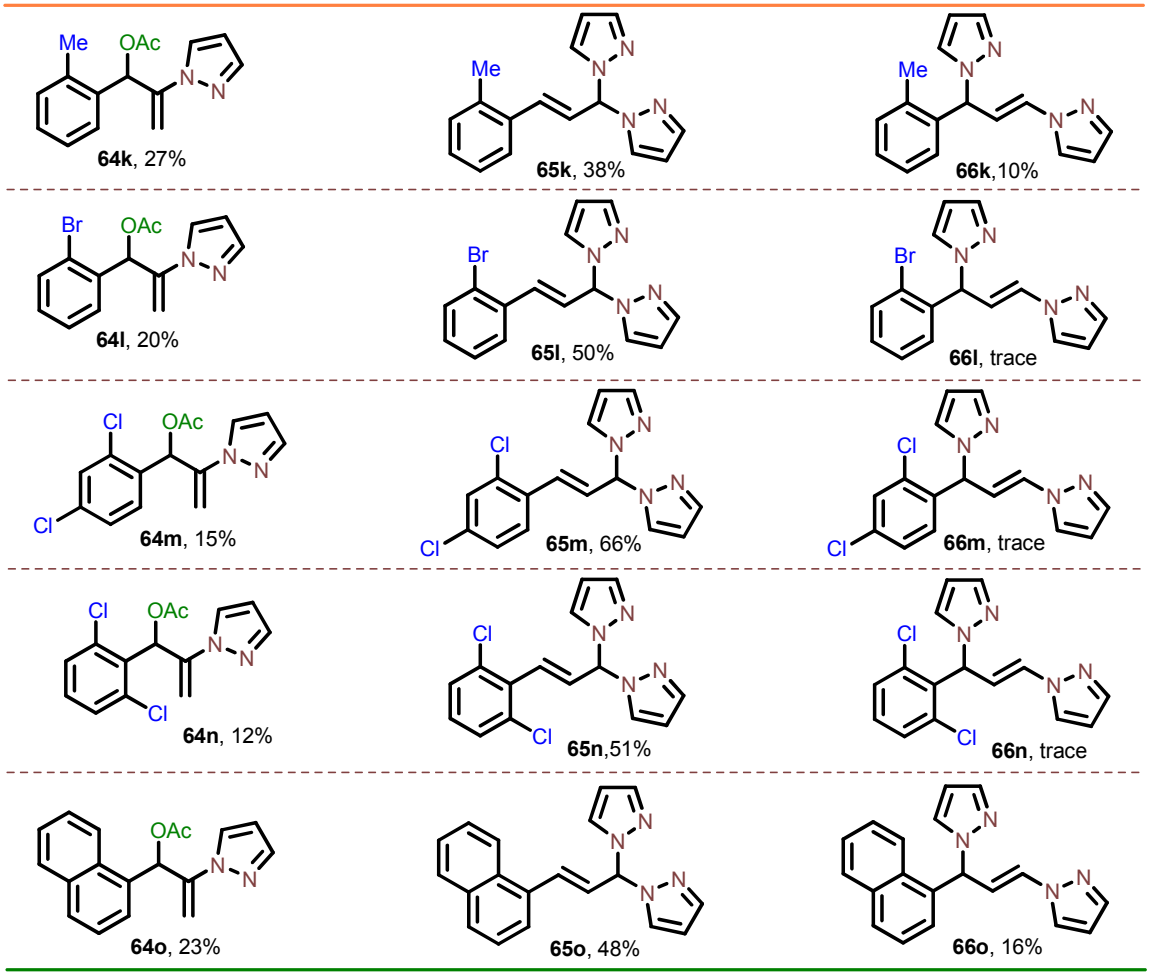
Table 2.3: $AgNO_3$ Catalyzed Reaction between *meta*-Substituted Propargyl Acetates and Pyrazole[a,b]

 **64e**, 24%	 **65e**, 56%	 **66e**, 6%
 **64f**, 19%	 **65f**, 63%	 **66f**, 6%
 **64g**, 23%	 **65g**, 46%	 **66g**, 14%
 **64h**, 21%	 **65h**, 49%	 **66h**, 10%
 **64i**, 21%	 **65i**, 58%	 **66i**, trace
 **64g**, 20%[c]	 **65g**, 51%[c]	 **66g**, 11%[c]

[a]Reactions were carried out using **2** (1.0 mmol), **50** (5.0 mmol), $AgNO_3$ (10 mol%) in chlorobenzene (1.0 mL) at 80 °C for 24 h. [b]Isolated yield. [c]Deprotection of acetyl group was observed.

Although annulation between phenols and propargyl alcohols in the presence of a Lewis acid is known to furnish benzofurans,[8] not even a trace amount of benzofuran was formed under the optimized reaction condition. Gratifyingly, the hydroxyl protected groups O-TBDMS and O-MOM were survived during the reaction and the corresponding products **64**–**66h** and **64**–**66i** were obtained in good yields. Since phenolic esters are more labile than the esters obtained from the alcohols,[9] we expect cleavage of the phenol-*O*-acetate group in this Ag-catalyzed transformation.

Table 2.4: $AgNO_3$ Catalyzed Reaction between *ortho*-Substituted Propargyl Acetates and Pyrazole[a,b]



[a]Reactions were carried out using **2** (1.0 mmol), **50** (5.0 mmol), $AgNO_3$ (10 mol%) in chlorobenzene (1.0 mL) at 80 °C for 24 h. [b]Isolated yield.

As anticipated, the acyl group was cleaved under the reaction conditions to afford **64–66g**. To investigate the effect of *ortho*-substitution, the optimized reaction condition was

subsequently applied to a range of propargyl acetates having *ortho*-substituted arenes (Table 2.4). The ADPs **65k** containing electron donating methyl groups at 2-position of aryl moiety was obtained albeit in moderate yield. The electron withdrawing *o*-bromo and *o,p*-dichloro groups on aryl moiety in the propargyl acetates were reacted individually with **50** and the corresponding products **64**–**66l** and **64**–**66m** were isolated in 70% and 81% overall yields, respectively. Moreover, the reaction between sterically demanding 1-(2,6-dichlorophenyl)-prop-2-ynyl acetate (**2n)** and **50** enabled **64n** (12%) and **65n** (51%) in overall moderate amount. X–ray crystallographic analysis unambiguously elucidated the structure of **65n**. The 1-naphthyl substituted ADPs **65o** was obtained in 48% yield. The structure of **64o** and **66o** was confirmed based on X–ray crystallographic analysis (Figure 2.2).

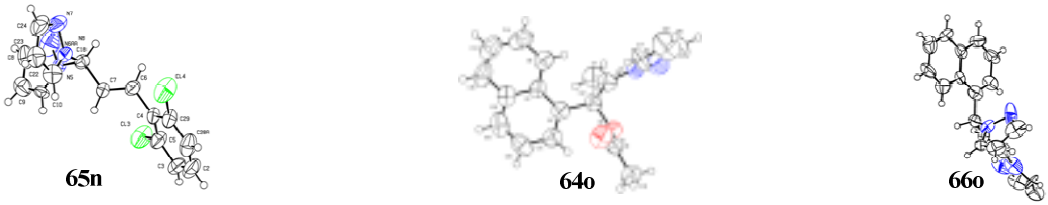
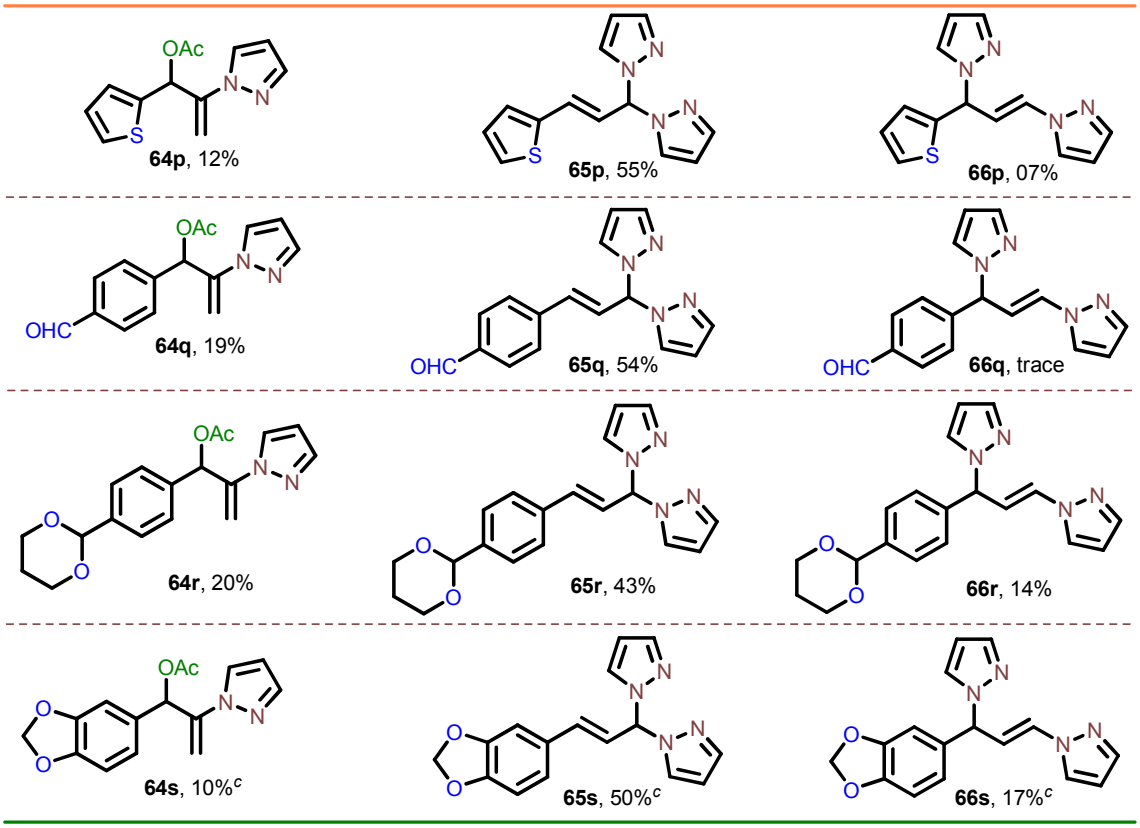


Figure 2.2: ORTEP Diagrams of **65n**, **64o** and **66o**

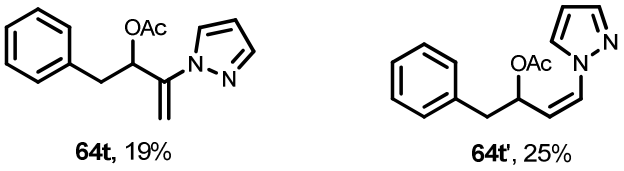
Next, the reactions of heteroaryl and labile-functional group-substituted propargyl acetates with **50** under the optimized catalytic conditions are pursued and the results are detailed in Table 2.5. Generally, coordination of the *S*-heteroatom to the Lewis acid has a negative impact on the reaction outcome.[10] Gratifyingly, thienyl-2-substituted propargyl acetate **2p** reacted with **50** under the optimized conditions to afford **64p**, **65p**, and **66p**, albeit in relatively good yields 12%, 55%, and 7%, respectively. The formyl group did not affect the reaction and the corresponding products **64**–**65q** are obtained in 73% isolated yield. The optimized condition tolerates the labile 1,3-dioxolane protecting group, furnishing **64**–**66r** in 77% overall yield. The electron-rich methylenedioxy substituted propargyl acetate **2s** reacted sluggishly with **50**, delivering 10%, 50%, and 17% of **64s**, **65s**, and **66s**, respectively. These experimental results reveal that the electronic as well as steric effect on the aryl group in propargyl acetates did not influence much to the reaction outcome.

Table 2.5: $AgNO_3$ Catalyzed Reaction between Heteroaryl/ Functional group-Substituted Propargyl Acetates and Pyrazole[a,b]



[a]Reactions were carried out using **2** (1.0 mmol), **50** (5.0 mmol), $AgNO_3$ (10 mol%) in chlorobenzene (1.0 mL) at 80 °C for 24 h. [b]Isolated yield. [c]Reaction continued for 53 h

However, the reaction of alkyl-propargyl acetate with **50** gave the Markovnikov's and anti-Markovnikov's hydroamination products **64t** and **64t'**, respectively (scheme 2.19).[2a]

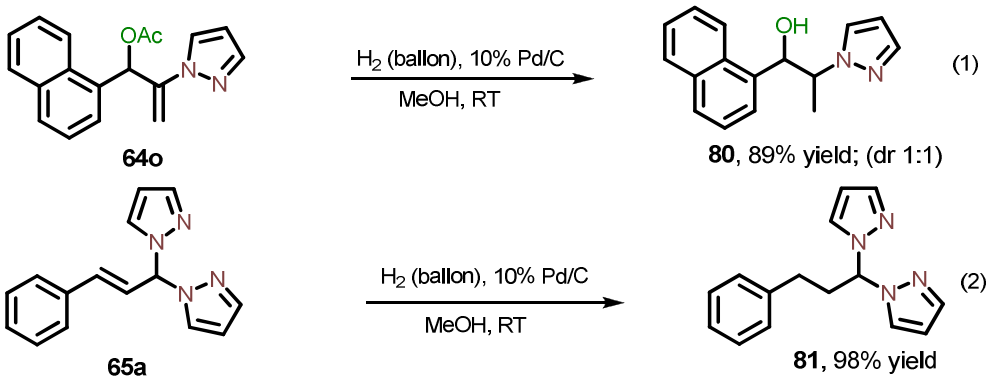


Scheme 2.19: Reaction with Alkyl Propargyl Acetates

2.2.3. Synthetic Applications

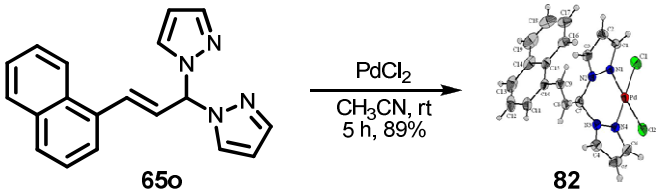
With the isolation of the products **64** and ADPs **65**, the hydrogenation of the double bond in **64** and **65** is next investigated. For example: hydrogenation of 1-(naphthalen-1-yl)-2-(1*H*-pyrazol-1-yl)allyl acetate (**64o)** with Pd/C, in the presence of H_2 balloon in MeOH

furnished a mixture of equal amount of diastereomers of α-heteroarylated alcohol **80**, a key skeletons found in various azole bearing anti-fungal agents.[11] (Eq. 1, Scheme 2.20). Similarly **65a** was hydrogenated under the identical conditions, producing gem-dipyrazolyl alkane **81** in 98% yield (Eq. 2, Scheme 2.20). The gem-dipyrazolyl alkanes exhibit anti-inflammatory actions.[4]



Scheme 2.20: Hydrogenation Reactions.

Thus, the reaction between propargyl acetates and pyrazole offered a wide array of stereoselective scorpionate ligands *E*-allyl-*gem*-dipyrazoles (ADPs) in moderate to good yields (Tables 2.2–2.5). The presence of double bond and two adjacent *N*-atoms in ADPs offers the structural rigidity of these newly synthesized scorpionate ligands. We therefore envisioned examining the chelation ability of ADPs to the transition-metal. Gratifyingly, the reaction of **65o** with $PdCl_2$ in CH_3CN at room temperature readily delivered the palladium complex **82** as a pale yellow solid, in quantitative yield (Scheme 2.21). The structure of **82** was confirmed based on X–ray crystallographic analysis.

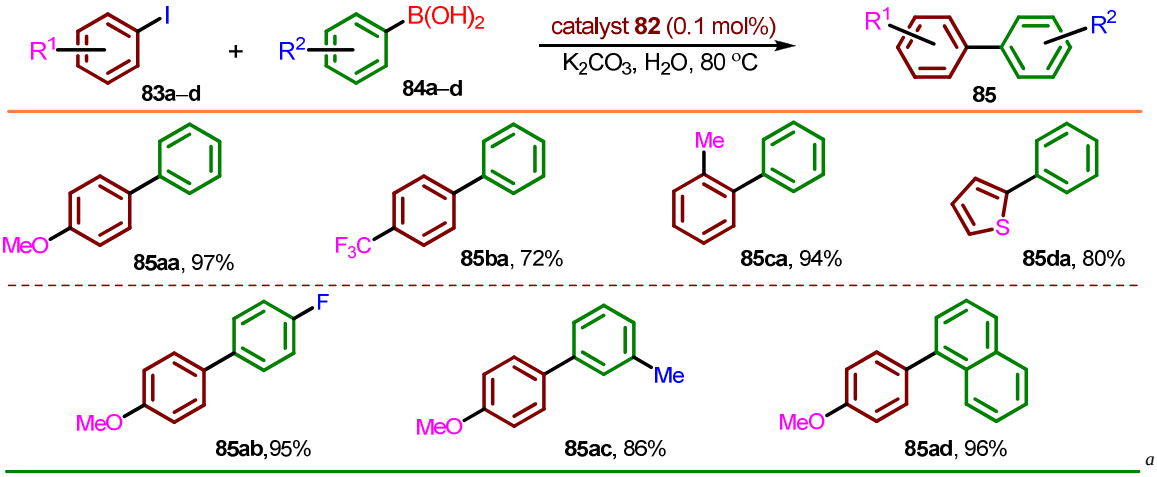


Scheme 2.21: Complexation with $PdCl_2$.

To demonstrate the utility of the newly synthesized complex, we explored examining this scorpionate-ligand-bearing Pd–complex **82** to the well known Suzuki-Miyaura biaryl cross-couplings (Table 2.6).[12] Gratifyingly, the coupling reactions proceeded in the

presence of 0.1 mol% of catalyst **82** in aqueous K_2CO_3 at 80 °C. To investigate the catalytic activity of complex **82** in H_2O system, at first the coupling between the phenylboronic acid (**84a**) and substituted aryliodides (**83**) is examined. The electron-rich 4-iodoanisole (**83a**) coupled with **84a** to afford the cross-coupled product **85aa** in excellent yield. The electronically poor trifluoromethyl group at *para*-position on aryliodide **83b** and **84a** underwent Suzuki reaction efficiently, and the corresponding product **85ba** is isolated in good yield. Interesteingly, the sterically congested bi-aryl product **85ca** is isolated in excellent yields, when the reaction carried out between 2-iodotoluene (**83c**) and **84a** under the influence of **82**. It is reported that heteroaryl halides show a slower reaction rate due to the potential binding nature of heteroatom to the metal center resulting in the formation of inactive substrate-metal complex.[13] Interestingly, the 2-iodothiophene (**83d**) cross-coupled with **84a**, and the corresponding heterobiaryl compound **85da** afforded in 80% yield. These results show that the electron-rich, -poor, sterically hindered, and heteroaryl iodides **83** were effectively coupled with **84a** under the reaction condition. We next studied the effect of substituents on aromatic ring in arylboronic acids with 4-iodoanisole (**83a**) (Table 2.6).

Table 2.6: Suzuki Coupling between various Aryliodides and Arylboronic Acids.[a,b]



[a] Reactions were carried out using **83** (3.0 mmol), **84** (6.0 mmol), catalyst **82** (0.1 mol%), K_2CO_3 (6.0 mmol) in H_2O (10.0 mL) at 80 °C for 24 h. [b]Isolated yield.

Arylboronic acids containing electron withdrawing fluoro and electron donating methyl at 3-position on aryl moiety in **84b** and **84c** was independently coupled with **83a** and provided the corresponding biaryl products in 95% and 86% yields, respectively. The

reaction of 1-naphthylboranic acid (**84d**) with **83a** afforded the desired biaryl in excellent yield. These results show that the efficiency of catalyst **82** in the Suzuki reaction in aqueous medium.

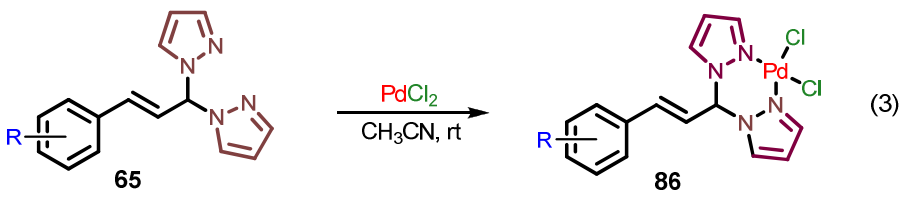
On the basis of precedence and the observation, the plausible reaction pathway is shown in Scheme 2.16.[1s,2,14] Markovnikov's hydroamination of pyrazole to the Lewis acid activated triple bond of propargyl acetate provides the 1-aryl-2-pyrazolyl allyl acetate (Path I).[14b] The attack of pyrazole to terminal side of alkyne in the propargyl-acetate generates the allene intermediate **B** with the cleavage of the acetate moiety (Path II**)**. Subsequently, addition of pyrazole at α or γ-position of allene delivers ADPs **65** (major) and 1,3-dipyrazolyl-3-aryl propene **64** (minor) products.

2.3. Conclusion

In conclusion, we have demonstrated the Ag-catalyzed reaction between propargyl acetate and pyrazole for the synthesis of novel ADPs. The reaction also affords 1,2-disubstituted allyl acetates **64** (10–25% yield) and 1,3-dipyrazolyl-3-aryl propenes **66** (6–17% yield). The reaction condition showed a broad substrate scope, and tolerates various O-bearing labile protecting groups. The $PdCl_2$-chelated complex of ADPs was successfully employed in Suzuki reactions for biaryl synthesis. As this method deliver various functionalized pyrazoles in a single-step reaction between propargyl acetates and pyrazole, we therefore believe these molecules and the metal complexes would find widespread use in synthetic chemistry.

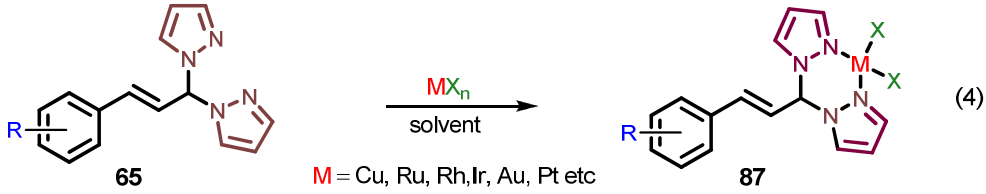
2.4. Future Work

The scorpionate ligands *E*-allyl-*gem*-dipyrazoles easily coordinated with $PdCl_2$ in acetonitrile at room temperature. This result demonstrated the strong chelating ability of ADPs to form a complex with $PdCl_2$. Therefore, we are interested in the synthesis of a wide variety of ADPs-$PdCl_2$ complexes **86** (Eq. 3)



(3)

In addition, our interest is directed in studying the synthesis and utility of the other metal chelated ADPs-complex such as ADPs-Cu, -Ru, -Rh, -Au, and -Pt etc (Eq. 4).



(4)

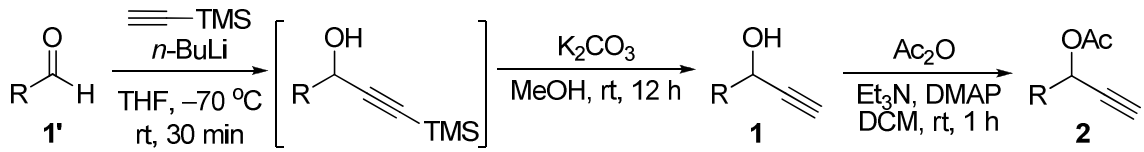
After successful preparation of ADPs-metal complexes, we would like to examine the catalytic activity of **86/87** in various organic transformations such as Suzuki, Heck, Sonagashira, and C–H activations.

2.5. Experimental

2.5.1. General Experimental Information for this Chapter is same as mentioned in Chapter 1.

2.5.2. Materials: Unless otherwise noted, all the reagents and intermediates were obtained commercially and used without purification. Dichloromethane (DCM) and chlorobenzene were distilled over $CaCl_2$. THF was freshly distilled over sodium/benzophenone ketyl under dry nitrogen. Methanol was dried over magnesium cake. $AgNO_3$, terminal alkynes and pyrazole were purchased from Sigma Aldrich Ltd. and used as received. Analytical and spectral data of all those known compounds are exactly matching with the reported values.

2.5.3. General Procedure for the Synthesis of Propargyl Acetate:



Scheme 2.22: Synthesis of Propargyl Acetates

Preparation of 1 from 1′; General Procedure (GP-1):

A solution of trimethylsilylacetylene (1.2 equiv) in THF (50 mL) was stirred in a 100 mL oven-dried two-necked round bottom flask under an argon atmosphere at –70 °C. *n*-Butyllithium (1.2 equiv, 1.60 M in THF) was introduced over 30 minutes at –70 °C. After an additional 1 h stirring, a solution of aldehyde (**1′**, 1.0 g, 1.0 equiv) in THF (5 mL) was

added at −70 °C. The resulting mixture was stirred for 1 h and warmed to room temperature slowly and continued for 30 minutes. The reaction mixture was quenched with saturated NH_4Cl aqueous solution (20 mL) at 0 °C. The organic layer was separated; the aqueous layer was extracted with Et_2O (2 × 20 mL). The combined extracts were washed with water (2 × 20 mL), brine (25 mL) and dried over Na_2SO_4. Solvent was filtered and evaporated under the reduced pressure. The crude residue was subsequently used for the desilylation reaction.

Methanol (15 mL) and K_2CO_3 (2.5 equiv) was introduced to the crude residue obtained in the above reaction and the heterogeneous mixture was stirred under an argon atmosphere at an ambient temperature overnight. The reaction mixture was diluted with ethyl acetate (50 mL) and washed with water (2 × 20 mL) and brine (10 mL). The organic layer was separated, dried over Na_2SO_4, filtered, and concentrated under vacuum. Most of the cases the crude residue was used for the acetylation reaction without purification, following the general procedure (GP 2).

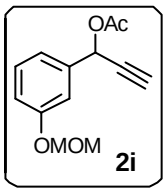
Synthesis of 2 from 1 through Acylation of –OH Moiety; General Procedure (GP-2):

To a solution of **1** (1.0 equiv) and DMAP (0.1 equiv) in dichloromethane (15 mL) was added Et_3N (3.0 equiv), acetic anhydride (1.3 equiv) under an argon atmosphere at an ambient temperature. The resulting reaction mixture was stirred for 1 h at an ambient temperature. Water (20 mL) was added to the reaction mixture. The organic layer was separated; the aqueous layer was extracted with CH_2Cl_2 (2 × 20 mL). The combined extracts were washed with water (2 × 20 mL), brine (25 mL) and dried over Na_2SO_4. Solvent was filtered and evaporated under the reduced pressure. The crude residue was purified using column chromatography on silica gel.

Physical characterization data is exactly matching with the reported values for the respective compounds 2a–h, 2k–q, 2s–t;[1] whereas 2i–j, 2r are new.

2.5.4. Spectral and Analytical Data of the Compounds:

1-(3-(Methoxymethoxy)phenyl)prop-2-ynyl acetate (2i):

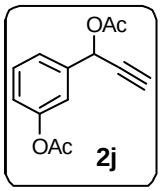


Following the general procedure (GP-1 and GP-2); reaction of 3-(methoxymethoxy)benzaldehyde (**1'i**; 1.0 g, 6.02 mmol), trimethylsilylacetylene (0.71 g, 7.22 mmol) and *n*-BuLi (4.6 mL, 1.6 M in THF, 7.22 mmol) followed by desilylation gave crude product **1i**.

Acetylation of the –OH moiety of the crude **1i** afforded 1-(3-(methoxymethoxy)phenyl)prop-2-ynyl acetate (**2i**; 775 mg) in overall 55% yield as pale yellow liquid.

R_f = 0.71 (4:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.31 (t, *J* = 8.0 Hz, 1H), 7.21 (bt, *J* = 2.0 Hz, 1H), 7.17 (d, *J* = 7.6 Hz, 1H), 7.06 (ddd, *J* = 8.4, 2.4, 0.8 Hz, 1H), 6.42 (bd, *J* = 2.0 Hz, 1H), 5.20 (bs, 2H), 3.49 (s, 3H), 2.66 (bd, *J* = 2.0 Hz, 1H), 2.13 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 169.5, 157.3, 137.8, 129.7, 121.0, 116.6, 115.6, 94.3, 80.0, 75.4, 64.9, 55.9, 20.9; **IR (Neat)** ν_{max} 3287, 2957, 2125, 1743, 1601, 1226, 696 cm^{-1}; **MS (EI)** *m/z* (%) 235 (M^+ + 1, 100), 220 (3); **Elemental analysis** calcd for $C_{13}H_{14}O_4$: C, 66.66; H, 6.02. Found: C, 66.72; H, 6.15.

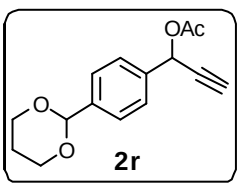
1-(3-Acetoxyphenyl)prop-2-ynyl acetate (2j):



Following the general procedure (GP-1 and GP-2); reaction of 3-(*tert*-butyldimethylsilyloxy)benzaldehyde (**1'j**; 1.0 g, 4.24 mmol), trimethylsilyl acetylene (498 mg, 5.07 mmol) and *n*-BuLi (3.2 mL, 1.6 M in THF, 5.08 mmol) gave crude propargylic alcohol. Desilylation and acetylation of both the –OH moieties afforded 1-(3-acetoxyphenyl)prop-2-ynyl acetate (**2j**; 462 mg) in 47% overall yield as pale yellow oil.

R_f = 0.11 (9:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.43–7.36 (m, 2H), 7.27 (s, 1H), 7.10 (bd, *J* = 2.8 Hz, 1H), 6.44 (s, 1H), 2.67 (bs, 1H), 2.28 (s, 3H), 2.09 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 169.4, 169.1, 150.6, 137.8, 129.5, 124.9, 122.2, 120.8, 79.6, 75.6, 64.4, 20.9, 20.8; **IR (Neat)** ν_{max} 3288, 2935, 1739, 1201, 1016, 800 cm^{-1}; **MS (EI)** *m/z* (%) 255 (M^+ + Na, 100), 232 (M^+, 4), 173 (8); **Elemental analysis** calcd for $C_{13}H_{12}O_4$: C, 67.23; H, 5.21. Found: C, 67.35; H, 5.18.

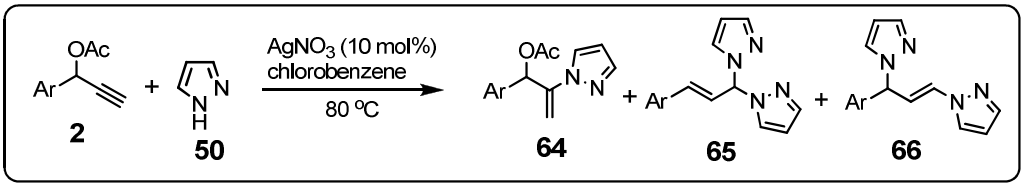
1-(4-(1,3-Dioxan-2-yl)phenyl)prop-2-ynyl acetate (2r):



Following the general procedure (GP-1 and GP-2); reaction of 4-(1,3-dioxan-2-yl)benzaldehyde (**1'r**; 1.0 g, 5.21 mmol), trimethylsilylacetylene (0.61 g, 6.25 mmol) and *n*-BuLi (4.0 mL, 1.6 M in THF, 6.25 mmol) followed by desilylation gave crude product **1r**. Acetylation of the –OH moiety of the crude **1r** afforded 1-(4-(1,3-dioxan-2-yl)phenyl)prop-2-ynyl acetate (**2r**; 840 mg) in 62% overall yield as colorless liquid.

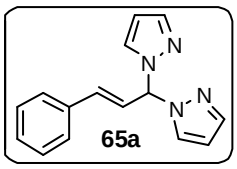
R_f = 0.69 (3:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.59–7.49 (m, 4H), 6.45 (bd, *J* = 2.4 Hz, 1H), 5.51 (s, 1H), 4.27 (dd, *J* = 11.2, 5.2 Hz, 2H), 3.99 (td, *J* = 12.0, 2.4 Hz, 2H), 2.64 (bd, *J* = 2.0 Hz, 1H), 2.30–2.15 (m, 1H), 2.09 (s, 3H), 1.46 (dd, *J* = 13.6, 1.2 Hz, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 169.5, 139.5, 136.8, 127.5, 126.3, 100.9, 80.0, 75.4, 67.2, 64.9, 25.6, 20.9; **IR (Neat)** ν_{max} 3287, 2966, 1741, 1377, 1016, 642 cm^{-1}; **MS (EI)** *m/z* (%) 261 (M^+ + 1, 100), 247 (5), 245 (5); **Elemental analysis** calcd for $C_{15}H_{16}O_4$: C, 69.22; H, 6.20. Found: C, 69.06; H, 6.27.

2.5.5. Silver(I)-Catalyzed Reaction between Pyrazole (50) and Propargyl Acetates 2; General Procedure (GP-3):



Propargyl acetate **2** (1.0 mmol), pyrazole (5.0 mmol) and $AgNO_3$ (16.9 mg, 0.1 mmol) were taken in an oven-dried Schlenk flask under an argon atmosphere. Chlorobenzene (1.0 mL) was added to this mixture. The resulting solution was stirred at 80 °C for 24 h. Upon complete consumption of **2**, the crude reaction mixture was purified using column chromatography on silica gel.

(*E*)-1,1'-(3-Phenylprop-2-ene-1,1-diyl)bis(1*H*-pyrazole) (65a):

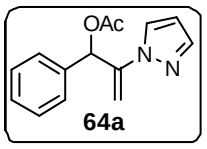


Following the general procedure (GP-3); 1-phenylprop-2-ynyl acetate (**2a**; 174 mg, 1.0 mmol), pyrazole (**50**; 340 mg, 5.0 mmol), and $AgNO_3$ (16.9 mg, 0.1 mmol) in chlorobenzene (1.0 mL) was heated at 80 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (4:1) to afford **64a** (61 mg) in 25% yield as pale yellow oil, **65a** (135 mg) in 54% yield as colorless solid, and **66a** (23 mg) in 9% yield as yellow oil.

mp = 94–95 °C; R_f = 0.30 (4:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.69 (bd, *J* = 2.4 Hz, 2H), 7.63 (bd, *J* = 1.6 Hz, 2H), 7.43 (d, *J* = 7.6 Hz, 2H), 7.36–7.27 (m, 3H), 7.23 (d, *J* = 6.4 Hz, 1H), 6.95 (dd, *J* = 15.6, 6.0 Hz, 1H), 6.60 (d, *J* = 16.0 Hz, 1H), 6.33 (bt, *J* = 1.6 Hz, 2H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 140.3, 135.5, 134.9, 128.6, 128.5, 128.4, 126.9, 122.4, 106.5, 76.0; **IR (KBr)** ν_{max} 3109, 1392, 1296, 970, 754, 628 cm^{-1}; **MS (EI)** *m/z* (%) 249

($M^+ - 1$, 100), 229 (54), 211 (35), 171 (35), 134 (19), 113 (27); **Elemental analysis** calcd for $C_{15}H_{14}N_4$: C, 71.98; H, 5.64; N, 22.38. Found: C, 72.05; H, 5.71; N, 22.31.

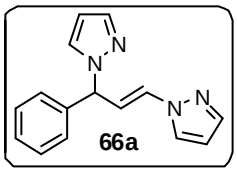
1-Phenyl-2-(1*H*-pyrazol-1-yl)allyl acetate (64a):



64a

R_f = 0.53 (4:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.60 (dd, J = 5.6, 2.4 Hz, 2H), 7.44 (dd, J = 8.0, 1.6 Hz, 2H), 7.37–7.29 (m, 3H), 7.12 (s, 1H), 6.27 (t, J = 2.0 Hz, 1H), 5.58 (bd, J = 0.8 Hz, 1H), 5.11 (s, 1H), 2.14 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 169.3, 144.0, 140.5, 136.8, 128.5, 127.8, 127.2, 106.8, 103.3, 73.1, 21.0; **IR (Neat)** ν_{max} 3474, 2932, 1745, 1226, 949, 752 cm^{-1}; **MS (EI)** *m/z* (%) 243 (M^+ + 1, 100), 159 (3), 137 (3), 81 (3); **Elemental analysis** calcd for $C_{14}H_{14}N_2O_2$: C, 69.41; H, 5.82; N, 11.56. Found: C, 69.75; H, 6.12; N, 11.15.

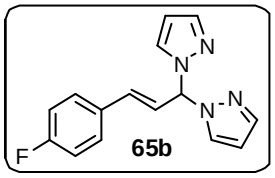
(E)-1,1'-(3-Phenylprop-1-ene-1,3-diyl)bis(1*H*-pyrazole) (66a):



66a

R_f = 0.23 (4:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.62 (dd, J = 4.8, 1.6 Hz, 2H), 7.56 (d, J = 2.4 Hz, 1H), 7.50 (d, J = 2.4 Hz,1H), 7.41–7.27 (m, 5H), 6.85 (dd, J = 14.0, 0.8 Hz, 1H), 6.69 (dd, J = 14.0, 7.2, Hz, 1H), 6.36 (t, J = 2.0 Hz, 1H), 6.33 (t, J = 2.0 Hz, 1H), 6.22 (d, J = 7.2 Hz, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 141.3, 139.7, 138.8, 130.5, 128.9, 128.5, 128.34, 128.31, 127.3, 114.9, 107.4, 105.8, 65.1; **IR (Neat)** ν_{max} 3433, 3113, 2924, 1680, 1394, 1091, 750 cm^{-1}; MS (EI) *m/z* (%) 249 ($M^+ - 1$, 100), 237 (14), 209 (4); **Elemental analysis** calcd for $C_{15}H_{14}N_4$: C, 71.98; H, 5.64; N, 22.38. Found: C, 71.86; H, 5.61; N, 22.45.

(*E*)-1,1'-(3-(4-Fluorophenyl)prop-2-ene-1,1-diyl)bis(1*H*-pyrazole) (65b):



65b

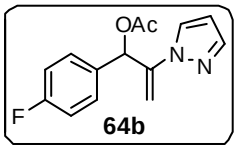
Following the general procedure (GP-3); 1-(4-fluorophenyl)prop-2-ynyl acetate (**2b**; 192 mg, 1.0 mmol), pyrazole (**50**; 340 mg, 5.0 mmol), and $AgNO_3$ (16.9 mg, 0.1 mmol) in chlorobenzene (1.0 mL) was heated at 80 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (3:1) to afford **64b** (52 mg) in 20% yield as pale yellow semi-solid, **65b** (145 mg) in 54% yield as pale yellow solid and **66b** (21 mg) in 8% yield as yellow oil.

mp = 60–61 °C; R_f = 0.44 (3:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.65 (bd, J = 2.0 Hz, 2H), 7.59 (bd, J = 1.6 Hz, 2H), 7.34 (dd, J = 8.8, 5.6 Hz, 2H), 7.18 (d, J = 6.0, 1H), 6.97 (t, J = 8.8 Hz, 2H), 6.84 (dd, J = 16.0, 6.4 Hz, 1H), 6.51 (d, J = 16.0 Hz, 1H), 6.29

(t, *J* = 2.0 Hz, 2H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 162.7 (d, *J*= 250 Hz), 140.3, 134.2, 131.0, 128.6, 128.5, 122.2, 115.4 (d, *J* = 21.7 Hz), 106.5, 75.9.

^{19}F NMR (376 MHz, $CDCl_3$) δ −112.26 to −112.34 (m); **IR (KBr)** ν_{max} 3115, 2924, 1678, 1510, 1394, 1226, 752 cm^{-1}; **MS (EI)** *m/z* (%) 269 (M^+ + 1, 100), 186 (11), 137 (19), 91 (4); **Elemental analysis** calcd for $C_{15}H_{13}FN_4$: C, 67.15; H, 4.88; N, 20.88. Found: C, 67.22; H, 4.81; N, 20.75.

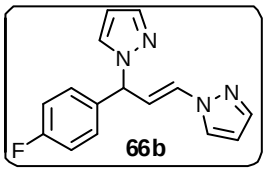
1-(4-Fluorophenyl)-2-(1*H*-pyrazol-1-yl)allyl acetate (64b):



64b

R_f = 0.66 (3:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.58 (d, *J* = 2.4 Hz, 1H), 7.56 (bd, *J* = 1.2 Hz, 1H), 7.46–7.37 (m, 2H), 7.09 (s, 1H), 7.00 (t, *J* = 8.8 Hz, 2H), 6.26 (bt, *J* = 2.0 Hz, 1H), 5.52 (s, 1H), 5.11 (s, 1H), 2.13 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 169.3, 162.7 (d, *J* = 248 Hz), 144.2, 140.7, 132.9, 129.3 (d, *J* = 8.4 Hz), 127.8, 115.5 (d, *J* = 21.6 Hz) 107.0, 102.9, 72.4, 21.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ −113.07 to −113.14 (m); **IR (Neat)** ν_{max} 3128, 1747, 1510, 1224, 752 cm^{-1}; **MS (EI)** *m/z* (%) 261 (M^+ + 1, 100), 233 (54), 219 (14), 201(16), 113 (9); **Elemental analysis** calcd for $C_{14}H_{13}FN_2O_2$: C, 64.61; H, 5.03; N, 10.76. Found: C, 64.48; H, 5.10; N, 10.85.

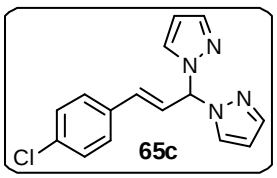
(*E*)-1,1'-(3-(4-Fluorophenyl)prop-1-ene-1,3-diyl)bis(1*H*-pyrazole) (66b):



66b

R_f = 0.31 (3:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.63 (bd, *J* = 2.0 Hz, 1H), 7.61 (bd, *J* = 2.0 Hz, 1H), 7.56 (d, *J* = 2.4 Hz, 1H), 7.49 (d, *J* = 2.4 Hz, 1H), 7.26–7.17 (m, 2H), 7.10–7.03 (m, 2H), 6.82 (dd, *J* = 14.0, 0.8 Hz, 1H), 6.66 (dd, *J* = 14.0, 6.8 Hz, 1H), 6.37 (t, *J* = 2.0 Hz, 1H), 6.33 (t, *J* = 2.4 Hz, 1H), 6.19 (d, *J* = 6.8 Hz, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 162.5 (d, *J* = 248 Hz), 141.5, 139.9, 134.7 (d, *J* = 3.2 Hz), 130.6, 129.1 (d, *J* = 8.5 Hz), 128.4 (2c), 115.8 (d, *J* = 21.9 Hz), 114.7, 107.5, 106.0, 64.4; **^{19}F NMR (376 MHz, $CDCl_3$)** δ −113.53 to −113.60 (m); **IR (Neat)** ν_{max} 2924, 1678, 1510, 1394, 1226, 752 cm^{-1}; **MS (EI)** *m/z* (%) 269 (M^+ + 1, 19), 201 (100), 113 (14); **Elemental analysis** calcd for $C_{15}H_{13}FN_4$: C, 67.15; H, 4.88; N, 20.88. Found: C, 67.06; H, 4.91; N, 20.95.

(*E*)-1,1'-(3-(4-Chlorophenyl)prop-2-ene-1,1-diyl)bis(1*H*-pyrazole) (65c):



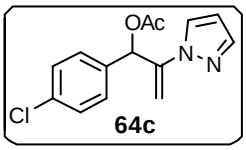
65c

Following the general procedure (GP-3); 1-(4-chlorophenyl)prop-2-ynyl acetate (**2c**; 208 mg, 1.0 mmol), pyrazole (**50**; 340 mg, 5.0 mmol), and $AgNO_3$ (16.9 mg, 0.1 mmol) in chlorobenzene (1.0 mL) was heated at 80 °C for 24 h. Finally, the crude mixture was

purified by silica gel column chromatography eluting with hexane: ethyl acetate (3:1) to afford **64c** (52 mg) in 19% yield as yellow oil, **65c** (153 mg) in 54% yield as pale yellow solid and **66c** (17 mg) in 6% yield as yellow oil.

mp = 111–112 °C; R_f = 0.44 (3:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.64 (bd, *J* = 2.4 Hz, 2H), 7.59 (bd, *J* = 2.0 Hz, 2H), 7.28 (q, *J* = 8.4 Hz, 4H), 7.18 (dd, *J* = 6.0, 0.8 Hz, 1H), 6.89 (dd, *J* = 16.0, 6.0 Hz, 1H), 6.49 (d, *J* = 16.0 Hz, 1H), 6.30 (bt, *J* = 2.0 Hz, 2H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 140.4, 134.3, 134.1, 133.4, 128.7, 128.5, 128.1, 123.2, 106.6, 75.9; **IR (KBr)** ν_{max} 3099, 1390, 1089, 750 cm^{-1}; **MS (EI)** *m/z* (%) 286 (M^+ + 1, 100), 230 (21), 208 (4), 190 (6); **Elemental analysis** calcd for $C_{15}H_{13}ClN_4$: C, 63.27; H, 4.60; N, 19.68. Found: C, 63.41; H, 4.53; N, 19.58.

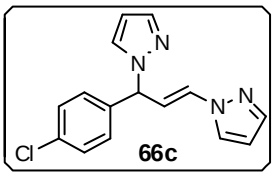
1-(4-Chlorophenyl)-2-(1*H*-pyrazol-1-yl)allyl acetate (64c):



64c

R_f = 0.66 (3:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ7.59 (d, *J* = 2.4 Hz, 1H), 7.57 (d, *J* = 1.6 Hz, 1H), 7.37 (dt, *J* = 8.8, 2.0 Hz, 2H), 7.29 (dt, *J* = 8.4, 2.0 Hz, 2H), 7.08 (s, 1H), 6.27 (bt, *J* = 2.4 Hz, 1H), 5.51 (bd, *J* = 1.2 Hz,. 1H), 5.11 (s, 1H), 2.13 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ169.2, 143.9, 140.6, 135.5, 134.4, 128.8, 128.7, 127.7, 107.0, 102.9, 72.4, 20.9; **IR (Neat)** ν_{max} 3128, 2928, 1745, 1651, 1228, 752 cm^{-1}; **MS (EI)** *m/z* (%) 277 (M^+, 94), 249 (49), 217 (100), 183 (29), 149 (6); **Elemental analysis** calcd for $C_{14}H_{13}ClN_2O_2$: C, 60.77; H, 4.74; N, 10.12. Found: C, 60.61; H, 4.71; N, 10.18.

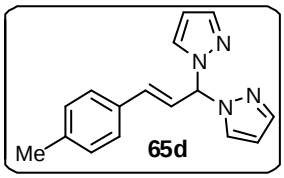
(*E*)-1,1'-(3-(4-Chlorophenyl)prop-1-ene-1,3-diyl)bis(1*H*-pyrazole) (66c):



66c

R_f = 0.31 (3:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.62 (d, *J* = 1.6 Hz, 1H), 7.60 (d, *J* = 1.6 Hz, 1H), 7.55 (d, *J* = 2.4 Hz, 1H), 7.49 (d, *J* = 2.4 Hz, 1H), 7.34 (dt, *J* = 8.4, 2.0 Hz, 2H), 7.17 (dt, *J* = 8.4, 1.6 Hz, 2H), 6.83 (d, *J* = 14.4 Hz, 1H), 6.64 (dd, *J* = 14.0, 7.2 Hz, 1H), 6.36 (t, *J* = 2.0 Hz, 1H), 6.32 (t, *J* = 2.4 Hz, 1H), 6.17 (d, *J* = 6.8 Hz, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 141.5, 140.6, 140.0, 137.4, 134.3, 130.8, 129.1, 128.6, 128.5, 114.4, 107.5, 106.0, 64.5; **IR (Neat)** ν_{max} 3113, 2924, 1678, 1394, 1091, 752 cm^{-1}; **MS (EI)** *m/z* (%) 286 (M^+ + 1, 20), 285 (M^+, 40), 233 (40), 217 (100), 181 (40), 149 (35); **Elemental analysis** calcd for $C_{15}H_{13}ClN_4$: C, 63.27; H, 4.60; N, 19.68. Found: C, 63.35; H, 4.65; N, 19.55.

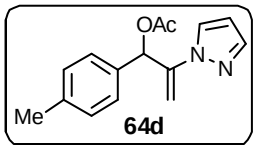
(*E*)-1,1'-(3-*p*-Tolylprop-2-ene-1,1-diyl)bis(1*H*-pyrazole) (65d):



Following the general procedure (GP-3); 1-*p*-tolylprop-2-ynyl acetate (**2d**; 188 mg, 1.0 mmol), pyrazole (**50**; 340 mg, 5.0 mmol), and $AgNO_3$ (16.9 mg, 0.1 mmol) in chlorobenzene (1.0 mL) was heated at 80 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (4:1) to afford **64d** (56 mg) in 22% yield as pale yellow solid, **65d** (127 mg) in 48% yield as pale yellow solid and **66d** (37 mg) in 14% yield as yellow oil.

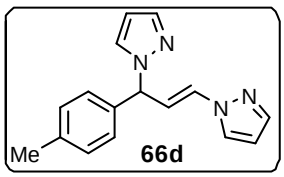
mp = 79–80 °C; R_f = 0.44 (4:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.67 (bd, *J* = 2.4 Hz, 2H), 7.61 (bd, *J* = 2.0 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.19 (dd, *J* = 6.0, 1.2 Hz, 1H), 7.14 (d, *J* = 8.0 Hz, 2H), 6.88 (dd, *J* = 16.0, 6.4 Hz, 1H), 6.58 (d, *J* = 16.4 Hz, 1H), 6.31 (bt, *J* = 2.4 Hz, 2H), 2.34 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 140.4, 138.7, 135.6, 132.2, 129.3, 128.5, 126.9, 121.4, 106.5, 76.2, 21.1; **IR (KBr)** ν_{max} 2916, 1512, 1388, 972, 758 cm^{-1}; **MS (EI)** *m/z* (%) 265 (M^+ + 1, 100), 251 (11); **Elemental analysis** calcd for $C_{16}H_{16}N_4$: C, 72.70; H, 6.10; N, 21.20. Found: C, 72.58; H, 6.15; N, 21.07.

2-(1*H*-Pyrazol-1-yl)-1-*p*-tolylallyl acetate (64d):



mp = 60–61 °C; R_f = 0.62 (4:1 hexane/EtOAc); [Silica, UV and I_2] **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.60–7.56 (m, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.13 (d, *J* = 8.0 Hz, 2H), 7.04 (s, 1H), 6.26 (bt, *J* = 2.4 Hz, 1H), 5.58 (s, 1H), 5.10 (s, 1H), 2.32 (s, 3H), 2.13 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 169.4, 144.1, 140.5, 138.4, 133.8, 129.2, 127.8, 127.3, 106.8, 103.1, 73.0, 21.1, 21.0; **IR (KBr)** ν_{max} 3026, 2924, 1745, 1228, 1028, 752 cm^{-1}; **MS (EI)** *m/z* (%) 257 (M^+ + 1, 100), 239 (8), 157 (16), 133 (16), 85 (8); **Elemental analysis** calcd for $C_{15}H_{16}N_2O_2$: C, 70.29; H, 6.29; N, 10.93. Found: C, 70.38; H, 6.21; N, 10.85.

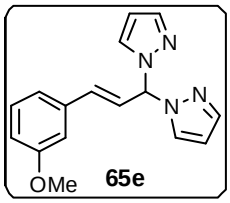
(*E*)-1,1'-(3-*p*-Tolylprop-1-ene-1,3-diyl)bis(1*H*-pyrazole) (66d):



R_f = 0.29 (4:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.60 (bd, *J* = 6.4 Hz, 2H), 7.53 (bd, *J* = 2.0 Hz, 1H), 7.45 (bd, *J* = 2.0 Hz, 1H), 7.16 (bd, *J* = 2.0 Hz, 4H), 6.82 (d, *J* = 14.0 Hz, 1H), 6.66 (dd, *J* = 14.0, 6.8 Hz, 1H), 6.32 (d, *J* = 17.2 Hz, 2H), 6.16 (d, *J* = 6.8 Hz, 1H), 2.34 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 141.2, 139.6, 138.1, 135.7, 130.3, 129.5, 128.4, 128.2, 127.2, 115.1, 107.3, 105.7, 64.8, 21.0; **IR (Neat)** ν_{max} 3111, 2922, 1678, 1514,

1089, 754 cm^{-1}; MS (EI) *m/z* (%) 265 (M^+ + 1, 100), 197 (3), 147 (3); **Elemental analysis** calcd for $C_{16}H_{16}N_4$: C, 72.70; H, 6.10; N, 21.20. Found: C, 72.85; H, 6.03; N, 21.28.

(*E*)-1,1'-(3-(3-Methoxyphenyl)prop-2-ene-1,1-diyl)bis(1*H*-pyrazole) (65e):

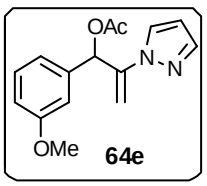


65e

Following the general procedure (GP-3); 1-(3-methoxyphenyl)prop-2-ynyl acetate (**2e**; 204 mg, 1.0 mmol), pyrazole (**50**; 340 mg, 5.0 mmol), and $AgNO_3$ (16.9 mg, 0.1 mmol) in chlorobenzene (1.0 mL) was heated at 80 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (4:1) to afford **64e** (65 mg) in 24% yield as colorless oil, **65e** (157 mg) in 56% yield as pale yellow solid and **66e** (17 mg) in 6% yield as yellow oil.

mp = 97–98 °C; R_f = 0.24 (4:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.68 (bd, *J* = 2.4 Hz, 2H), 7.61 (bd, *J* = 1.6 Hz, 2H), 7.29 –7.19 (m, 2H), 7.02 (d, *J* = 7.6 Hz, 1H), 6.99–6.90 (m, 2H), 6.85 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.58 (d, *J* = 16.0 Hz, 1H), 6.32 (bt, *J* = 2.4 Hz, 2H), 3.79 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 159.7, 140.4, 136.3, 135.5, 129.5, 128.6, 122.7, 119.6, 114.5, 112.0, 106.5, 76.0, 55.1; **IR (KBr)** ν_{max} 3111, 2957, 1599, 1390, 1043, 754 cm^{-1}; **MS (EI)** *m/z* (%) 281 (M^+ + 1, 100), 265 (14), 163 (4), 137 (14); **Elemental analysis** calcd for $C_{16}H_{16}N_4O$: C, 68.55; H, 5.75; N, 19.99. Found: C, 68.47; H, 5.82; N, 19.85.

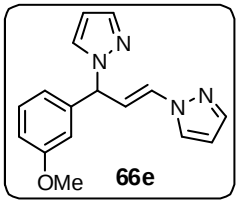
1-(3-Methoxyphenyl)-2-(1H-pyrazol-1-yl)allyl acetate (64e):



64e

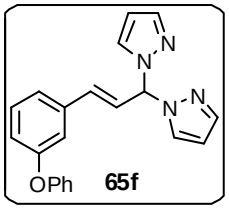
R_f = 0.43 (4:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.62–7.58 (m, 2H), 7.25 (t, *J* = 8.0 Hz, 1H), 7.08 (s, 1H), 7.02 (d, *J* = 7.6 Hz, 1H), 6.97 (bt, *J* = 2.0 Hz, 1H), 6.84 (ddd, *J* = 8.0, 2.4, 0.8 Hz, 1H), 6.27 (t, *J* = 2.0 Hz, 1H), 5.57 (d, *J* = 0.8 Hz, 1H), 5.11 (s, 1H), 3.78 (s, 3H), 2.15 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 169.3, 159.6, 144.0, 140.5, 138.4, 129.5, 127.8, 119.4, 113.8, 112.9, 106.8, 103.4, 72.9, 55.1, 21.0; **IR (Neat)** ν_{max} 3130, 2939, 1747, 1602, 1228, 1030, 754 cm^{-1}; **MS (EI)** *m/z* (%) 273 (M^+ + 1, 82), 245 (36), 229 (54), 213 (100), 145 (7), 102 (5); **Elemental analysis** calcd for $C_{15}H_{16}N_2O_3$: C, 66.16; H, 5.92; N, 10.29. Found: C, 66.32; H, 5.86; N, 10.15.

(*E*)-1,1'-(3-(3-Methoxyphenyl)prop-1-ene-1,3-diyl)bis(1*H*-pyrazole) (66e):



R_f = 0.14 (4:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.63 (bd, *J* = 1.2 Hz, 1H), 7.62 (bd, *J* = 1.6 Hz, 1H), 7.57 (d, *J* = 2.0 Hz, 1H), 7.51 (d, *J* = 2.0 Hz, 1H), 7.32–7.27 (m, 1H), 6.89–6.84 (m, 3H), 6.78 (bt, *J* = 1.6 Hz, 1H), 6.67 (dd, *J* = 11.2, 5.6 Hz, 1H), 6.37 (t, *J* = 1.6 Hz, 1H), 6.33 (t, *J* = 1.6 Hz, 1H), 6.18 (d, *J* = 5.6 Hz, 1H), 3.79 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 160.0, 141.3, 140.4, 139.7, 130.7, 129.9, 128.5, 128.3, 119.6, 114.8, 113.7, 113.2, 107.4, 105.9, 65.1, 55.3; **IR (Neat)** ν_{max} 3117, 2932, 1678, 1601, 1261, 1043, 754 cm^{-1}; **MS (EI)** *m/z* (%) 281 (M^+ + 1, 100), 249 (8), 171 (4); **Elemental analysis** calcd for $C_{16}H_{16}N_4O$: C, 68.55; H, 5.75; N, 19.99. Found: C, 68.41; H, 5.71; N, 19.85.

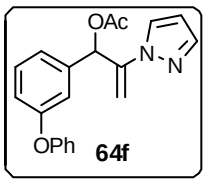
(*E*)-1,1'-(3-(3-Phenoxyphenyl)prop-2-ene-1,1-diyl)bis(1*H*-pyrazole) (65f):



Following the general procedure (GP-3); 1-(3-phenoxyphenyl)prop-2-ynyl acetate (**2f**; 266 mg, 1.0 mmol), pyrazole (**50**; 340 mg, 5.0 mmol), and $AgNO_3$ (16.9 mg, 0.1 mmol) in chlorobenzene (1.0 mL) was heated at 80 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (6:1) to afford **64f** (63 mg) in 19% yield as pale yellow oil, **65f** (215 mg) in 63% yield as pale yellow solid and **66f** (21 mg) in 6% yield as yellow oil.

mp = 75–76 °C; R_f = 0.35 (6:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.66 (bd, *J* = 2.8 Hz, 2H), 7.61 (bd, *J* = 1.2 Hz, 2H), 7.38–7.25 (m, 3H), 7.19 (dd, *J* = 12.8, 6.0 Hz, 2H), 7.14–7.08 (m, 2H), 7.02 (d, *J* = 8.8 Hz, 2H), 6.96 (d, *J* = 7.2 Hz, 1H), 6.91 (dd, *J* = 16.0, 6.0 Hz, 1H), 6.54 (d, *J* = 16.0 Hz, 1H), 6.31 (s, 2H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 157.3, 156.8, 140.4, 136.8, 134.8, 129.8, 129.6, 128.5, 123.3, 123.2, 121.9, 119.1, 118.6, 117.2, 106.6, 75.9; **IR (KBr)** ν_{max} 3109, 1577, 1388, 1271, 750 cm^{-1}; **MS (EI)** *m/z* (%) 343 (M^+ + 1, 3), 275 (38), 243 (100), 242 (27), 207 (14), 130 (8); **Elemental analysis** calcd for $C_{21}H_{18}N_4O$: C, 73.67; H, 5.30; N, 16.36. Found: C, 73.57; H, 5.36; N, 16.25.

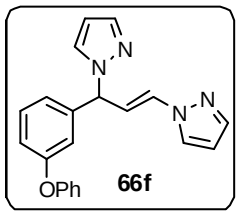
1-(3-Phenoxyphenyl)-2-(1*H*-pyrazol-1-yl)allyl acetate (64f):



R_f = 0.56 (6:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.61 (d, *J* = 2.0 Hz, 1H), 7.60 (bd, *J* = 0.8 Hz, 1H), 7.38–7.33 (m, 2H), 7.30 (t, *J* = 6.4 Hz, 1H), 7.18 (d, *J* = 6.4 Hz, 1H), 7.15–7.09 (m, 3H), 6.98

(bt, *J* = 0.8 Hz, 1H), 6.97 (bt, *J* = 0.8 Hz, 1H), 6.96–6.92 (m, 1H), 6.30 (t, *J* = 1.6 Hz, 1H), 5.55 (bd, *J* = 0.8 Hz, 1H), 5.11 (s, 1H), 2.15 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 169.3, 157.4, 156.9, 144.1, 140.6, 139.0, 129.9, 129.8, 127.9, 123.4, 122.1, 118.9, 118.7, 117.7, 106.9, 103.5, 72.8, 21.0; **IR (Neat)** ν_{max} 3065, 2930, 1747, 1585, 1234, 1024, 754 cm^{-1}; **MS (EI)** *m/z* (%) 336 (M^+ + 2, 51), 335 (M^++1, 100), 263 (11); **Elemental analysis** calcd for $C_{20}H_{18}N_2O_3$: C, 71.84; H, 5.43; N, 8.38. Found: C, 71.68; H, 5.52; N, 8.31.

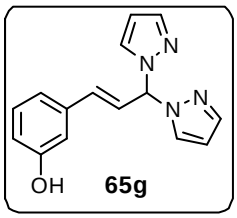
(*E*)-1,1'-(3-(3-Phenoxyphenyl)prop-1-ene-1,3-diyl)bis(1*H*-pyrazole) (66f):



66f

R_f = 0.20 (6:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.62 (bs, 1H), 7.60 (bd, *J* = 1.6 Hz, 1H), 7.56 (bd, *J* = 2.4 Hz, 1H), 7.51 (bd, *J* = 2.4 Hz, 1H), 7.37–7.28 (m, 3H), 7.11 (td, *J* = 7.6, 1.6 Hz, 1H), 7.01–6.86 (m, 6H), 6.64 (dd, *J* = 14.0, 7.2 Hz, 1H), 6.36 (bt, *J* = 2.4 Hz, 1H), 6.32 (bt, *J* = 2.4 Hz, 1H), 6.17 (d, *J* = 7.2 Hz, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 157.8, 156.7, 141.4, 141.0, 139.8, 130.8, 130.2, 129.8, 128.5, 128.3, 123.6, 121.8, 119.1, 118.2, 117.7, 114.5, 107.5, 105.9, 64.9; **IR (Neat)** ν_{max} 2922, 1678, 1583, 1487, 1248, 752 cm^{-1}; **MS (EI)** *m/z* (%) 343 (M^+ + 1, 100), 209 (6), 135 (3); **Elemental analysis** calcd for $C_{21}H_{18}N_4O$: C, 73.67; H, 5.30; N, 16.36. Found: C, 73.56; H, 5.38; N, 16.21.

(*E*)-3-(3,3-Di(1*H*-pyrazol-1-yl)prop-1-enyl)phenol (65g):



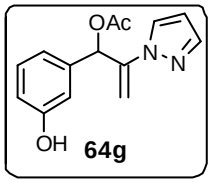
65g

Following the general procedure (GP-3); 1-(3-hydroxyphenyl)prop-2-ynyl acetate (**2g**; 190 mg, 1.0 mmol), pyrazole (**50**; 340 mg, 5.0 mmol), and $AgNO_3$ (16.9 mg, 0.1 mmol) in chlorobenzene (1.0 mL) was heated at 80 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (2:1) to afford **64g** (59 mg) in 23% yield as brown color oil, **65g** (122 mg) in 46% yield as light brown solid and **66g** (37 mg) in 14% yield as brown color oil.

mp = 100–101 °C; R_f = 0.34 (2:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.64 (bd, *J* = 2.0 Hz, 2H), 7.61 (bd, *J* = 1.2 Hz, 2H), 7.12 (dd, *J* = 5.2, 0.8 Hz, 1H), 7.09 (d, *J* = 6.4 Hz, 1H), 6.86 (d, *J* = 6.4 Hz, 1H), 6.83–6.79 (m, 1H), 6.78 (d, *J* = 4.8 Hz, 1H), 6.77–6.73 (m, 1H), 6.43 (d, *J* = 12.8 Hz, 1H), 6.31 (t, *J* = 2.0 Hz, 2H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 156.6, 140.6, 136.4, 136.0, 129.8, 129.0, 122.2, 119.2, 116.3, 114.0, 106.8, 76.1; **IR (KBr)** ν_{max} 3142, 2729, 1595, 1392, 1089, 756 cm^{-1}

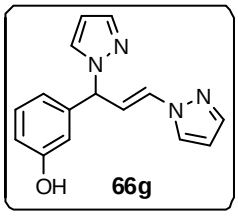
MS (EI) *m/z* (%) 268 (M^+ + 2, 100), 156 (14); **Elemental analysis** calcd for $C_{15}H_{14}N_4O$: C, 67.65; H, 5.30; N, 21.04. Found: C, 67.49; H, 5.26; N, 21.15.

1-(3-Hydroxyphenyl)-2-(1*H*-pyrazol-1-yl)allyl acetate (64g):



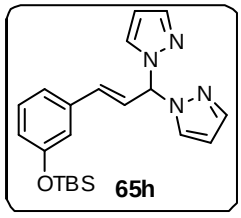
R_f = 0.53 (2:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.59 (bd, *J* = 2.0 Hz, 1H), 7.58 (bd, *J* = 1.2 Hz, 1H), 7.18 (t, *J* = 6.0 Hz, 1H), 6.98 (s, 1H), 6.95 (d, *J* = 6.4 Hz, 1H), 6.88 (bt, *J* = 1.6 Hz, 1H), 6.79–6.74 (m, 1H), 6.27 (t, *J* = 1.6 Hz, 1H), 5.57 (bd, *J* = 0.8 Hz, 1H), 5.12 (s, 1H), 2.12 (s, 3H), 1.90–1.70 (bs, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 169.6, 156.1, 143.7, 140.6, 138.3, 129.8, 128.2, 119.2, 115.8, 114.3, 106.9, 104.4, 73.0, 21.0; **IR (Neat)** ν_{max} 3333, 2926, 1747, 1593, 1228, 760 cm^{-1}; MS **(EI)** *m/z* (%) 260 (M^+ + 2, 100), 163 (6); **Elemental analysis** calcd for $C_{14}H_{14}N_2O_3$: C, 65.11; H, 5.46; N, 10.85. Found: C, 65.21; H, 5.41; N, 10.76.

(*E*)-3-(1,3-Di(1*H*-pyrazol-1-yl)allyl)phenol (66g):



R_f = 0.22 (2:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.35–8.35 (bs, 1H), 7.61 (bd, *J* = 1.6 Hz, 1H), 7.54 (bd, *J* = 1.6 Hz, 1H), 7.51 (bd, *J* = 2.4 Hz, 1H), 7.49 (bd, *J* = 2.4 Hz, 1H), 7.09 (t, *J* = 8.0 Hz, 1H), 6.79 (d, *J* = 14.0 Hz, 1H), 6.66 (t, *J* = 8.0 Hz, 2H), 6.57 (dd, *J* = 14.0, 7.2 Hz, 1H), 6.48 (s, 1H), 6.34 (bt, *J* = 2.0 Hz, 1H), 6.28 (bt, *J* = 2.0 Hz, 1H), 6.07 (d, *J* = 7.2 Hz, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 157.2, 141.3, 139.8, 139.5, 130.8, 129.9, 129.0, 128.7, 118.4, 115.8, 114.6, 114.1, 107.5, 105.9, 64.8; **IR (Neat)** ν_{max} 3146, 2928, 1678, 1601, 1282, 945, 653 cm^{-1}; **MS (EI)** *m/z* (%) 268 (M^+ + 2, 30), 267 (M^+ + 1, 100), 235 (81); **Elemental analysis** calcd for $C_{15}H_{14}N_4O$: C, 67.65; H, 5.30; N, 21.04. Found: C, 67.48; H, 5.21; N, 21.15.

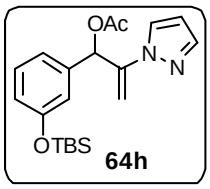
(*E*)-1,1'-(3-(3-(*tert*-Butyldimethylsilyloxy)phenyl)prop-2-ene-1,1-diyl)bis(1*H*-pyrazole) (65h):



Following the general procedure (GP-3); 1-(3-(*tert*-butyldimethylsilyloxy)phenyl)prop-2-ynyl acetate (**2h**; 304 mg, 1.0 mmol), pyrazole (**50**; 340 mg, 5.0 mmol), and $AgNO_3$ (16.9 mg, 0.1 mmol) in chlorobenzene (1.0 mL) was heated at 80 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (4:1) to afford **64h** (78 mg) in 21% yield as pale yellow oil, **65h** (186 mg) in 49% yield as colorless solid and **66h** (38 mg) in 10% yield as yellow oil.

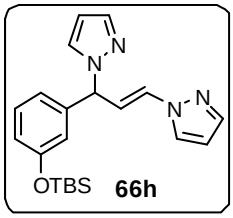
mp = 62–63 °C; R_f = 0.53 (4:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.67 (bd, *J* = 2.4 Hz, 2H), 7.60 (bd, *J* = 1.6 Hz, 2H), 7.19 (t, *J* = 7.6 Hz, 2H), 7.03 (d, *J* = 7.6 Hz, 1H), 6.94–6.86 (m, 2H), 6.79 (dd, *J* = 8.0, 2.4 Hz, 1H), 6.54 (d, *J* = 15.6 Hz, 1H), 6.31 (bd, *J* = 1.6 Hz, 2H), 1.00 (s, 9H), 0.20 (s, 6H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 155.7, 140.4, 136.4, 135.4, 129.4, 128.5, 122.5, 120.3, 120.1, 118.6, 106.5, 76.0, 25.5, 18.0, –4.5; **IR (KBr)** ν_{max} 3109, 1595, 1280, 966, 621 cm^{-1}; **MS (EI)** *m/z* (%) 381 (M^+ + 1, 100), 203 (3), 106 (6); **Elemental analysis** calcd for $C_{21}H_{28}N_4OSi$: C, 66.28; H, 7.42; N, 14.72. Found: C, 66.42; H, 7.35; N, 14.61.

1-(3-(*tert*-Butyldimethylsilyloxy)phenyl)-2-(1H-pyrazol-1-yl)allyl acetate (64h):



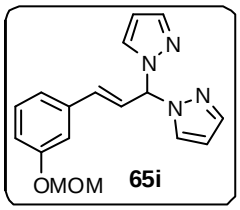
R_f = 0.70 (4:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.58 (t, *J* = 2.4 Hz, 2H), 7.18 (t, *J* = 7.6 Hz, 1H), 7.06–6.99 (m, 2H), 6.88 (bt, *J* = 2.4 Hz, 1H), 6.77 (ddd, *J* = 8.4, 2.4, 0.8 Hz, 1H), 6.26 (t, *J* = 2.4 Hz, 1H), 5.56 (bd, *J* = 0.8 Hz, 1H), 5.07 (s, 1H), 2.14 (s, 3H), 0.96 (s, 9H), 0.15 (s, 6H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 169.4, 155.7, 144.0, 140.6, 138.3, 129.5, 127.9, 120.3, 120.1, 119.0, 106.8, 103.5, 72.9, 25.6, 21.0, 18.2, –4.5; **IR (Neat)** ν_{max} 2957, 1751, 1602, 1226,750 cm^{-1}; **MS (EI)** *m/z* (%) 373 (M^+ + 1, 100), 235 (9), 203 (9), 171 (3); **Elemental analysis** calcd for $C_{20}H_{28}N_2O_3Si$: C, 64.48; H, 7.58; N, 7.52. Found: C, 64.32; H, 7.63; N, 7.45.

(*E*)-1,1'-(3-(3-(*tert*-Butyldimethylsilyloxy)phenyl)prop-1-ene-1,3-diyl)bis(1*H*-pyrazole) (66h):



R_f = 0.38 (4:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.61 (bd, *J* = 1.6 Hz, 1H), 7.60 (bd, *J* = 1.6 Hz, 1H), 7.54 (d, *J* = 2.4 Hz, 1H), 7.48 (d, *J* = 2.4 Hz, 1H), 7.22 (t, *J* = 8.0 Hz, 1H), 6.87–6.82 (m, 2H), 6.82–6.78 (m, 1H), 6.68–6.61 (m, 2H), 6.35 (t, *J* = 2.0 Hz, 1H), 6.31 (t, *J* = 2.0 Hz, 1H), 6.15 (d, *J* = 6.8 Hz, 1H), 0.95 (s, 9H), 0.15 (s, 6H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 156.1, 141.3, 140.3, 139.7, 130.6, 129.8, 128.5, 128.3, 120.1, 119.9, 118.9, 114.7, 107.4, 105.8, 64.9, 25.6, 18.1, –4.5; **IR (Neat)** ν_{max} 2929, 1676, 1485, 1278, 748 cm^{-1}; **MS (EI)** *m/z* (%) 381 (M^+ + 1, 100), 201 (9), 145 (9), 105 (9); **Elemental analysis** calcd for $C_{21}H_{28}N_4OSi$: C, 66.28; H, 7.42; N, 14.72. Found: C, 66.32; H, 7.51; N, 14.86.

(*E*)-1,1'-(3-(3-(Methoxymethoxy)phenyl)prop-2-ene-1,1-diyl)bis(1*H*-pyrazole) (65i):

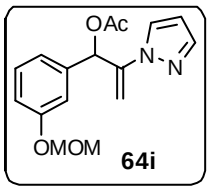


65i

Following the general procedure (GP-3); 1-(3-(methoxymethoxy)phenyl)prop-2-ynyl acetate (**2i**; 234 mg, 1.0 mmol), pyrazole (**50**; 340 mg, 5.0 mmol), and $AgNO_3$ (16.9 mg, 0.1 mmol) in chlorobenzene (1.0 mL) was heated at 80 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (4:1) to afford **64i** (63 mg) in 21% yield as yellow oil and **65i** (180 mg) in 58% yield as pale yallow solid.

mp = 57–58 °C; R_f = 0.23 (4:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.66 (d, *J* = 2.4 Hz, 2H), 7.60 (bd, *J* = 1.6 Hz, 2H), 7.25 (t, *J* = 8.0 Hz, 1H), 7.17 (dd, *J* = 6.4, 1.6 Hz, 1H), 7.10 (bt, *J* = 2.4 Hz, 1H), 7.07 (d, *J* = 7.6 Hz, 1H), 6.98 (ddd, *J* = 8.0, 2.4, 0.8 Hz, 1H), 6.91 (dd, *J* = 15.6, 6.0 Hz, 1H), 6.56 (dd, *J* = 16.0, 0.8 Hz, 1H), 6.32 (t, *J* = 2.0 Hz, 2H), 5.17 (s, 2H), 3.47 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 157.4, 140.5, 136.5, 135.4, 129.6, 128.6, 123.0, 120.8, 116.7, 114.6, 106.6, 94.3, 76.1, 55.9; **IR (KBr)** ν_{max} 2955, 1745, 1585, 1018, 756 cm^{-1}; **MS (EI)** *m/z* (%) 311 (M^+ + 1, 100), 269 (6), 227 (3); **Elemental analysis** calcd for $C_{17}H_{18}N_4O_2$: C, 65.79; H, 5.85; N, 18.05. Found: C, 65.58; H, 5.76; N, 18.21.

1-(3-(Methoxymethoxy)phenyl)-2-(1*H*-pyrazol-1-yl)allyl acetate (64i):



64i

R_f = 0.41 (4:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.59 (bd, *J* = 2.4 Hz, 1H), 7.58 (bd, *J* = 1.6 Hz, 1H), 7.28–7.20 (m, 1H), 7.08 (bt, *J* = 2.0 Hz, 1H), 7.07–7.03 (m, 2H), 6.98 (ddd, *J* = 8.4, 2.4, 1.2 Hz, 1H), 6.26 (t, *J* = 2.0 Hz, 1H), 5.56 (bd, *J* = 1.2 Hz, 1H), 5.13 (s, 2H), 5.09 (s, 1H), 3.45 (s, 3H), 2.13 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 169.3, 157.3, 143.9, 140.5, 138.4, 129.5, 127.8, 120.7, 116.0, 115.3, 106.8, 103.6, 94.4, 72.8, 55.9, 21.0; **IR (Neat)** ν_{max} 2925, 1747, 1588, 1221, 767 cm^{-1}; **MS (EI)** *m/z* (%) 303 (M^+ + 1, 100), 282 (11), 215 (8), 79 (24); **Elemental analysis** calcd for $C_{16}H_{18}N_2O_4$: C, 63.56; H, 6.00; N, 9.27. Found: C, 63.42; H, 6.15; N, 9.31.

1-(3-Hydroxyphenyl)-2-(1*H*-pyrazol-1-yl)allyl acetate (64g):

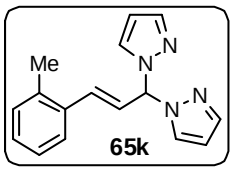
(*E*)-3-(3,3-Di(1*H*-pyrazol-1-yl)prop-1-enyl)phenol (65g):

(*E*)-3-(1,3-Di(1*H*-pyrazol-1-yl)allyl)phenol (66g):

Following the general procedure (GP-3); 1-(3-Acetoxyphenyl)prop-2-ynyl acetate (**2j**; 232 mg, 1.0 mmol), pyrazole (**50**; 340 mg, 5.0 mmol), and $AgNO_3$ (16.9 mg, 0.1 mmol) in

chlorobenzene (1.0 mL) was heated at 80 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (2:1) to afford acetyl deprotected compounds **64g** (52 mg) in 20% yield as brown color oil, **65g** (135 mg) in 51% yield as light brown solid and **66g** (29 mg) in 11% yield as brown color oil.

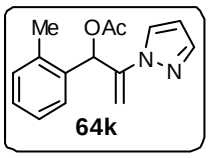
(*E*)-1,1'-(3-*o*-Tolylprop-2-ene-1,1-diyl)bis(1*H*-pyrazole) (65k):



Following the general procedure (GP-3); 1-*o*-tolylprop-2-ynyl acetate (**2k**; 188 mg, 1.0 mmol), pyrazole (**50**; 340 mg, 5.0 mmol), and $AgNO_3$ (16.9 mg, 0.1 mmol) in chlorobenzene (1.0 mL) was heated at 80 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (4:1) to afford **64k** (69 mg) in 27% yield as yellow oil, **65k** (100 mg) in 38% yield as colorless solid and **66k** (27 mg) in 10% yield as yellow oil.

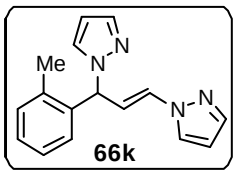
mp = 73–74 °C; R_f = 0.33 (4:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.69 (d, *J* = 2.4 Hz, 2H), 7.62 (bd, *J* = 1.6 Hz, 2H), 7.53 (dd, *J* = 6.8, 2.4 Hz, 1H), 7.25–7.09 (m, 4H), 6.83 (bd, *J* = 2.8 Hz, 2H), 6.33 (t, *J* = 2.0 Hz, 2H), 2.29 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 140.4, 135.9, 134.0, 133.4, 130.3, 128.5, 126.1, 125.9, 123.6, 106.5, 76.2, 19.5; **IR (KBr)** ν_{max} 3109, 2986, 1510, 1392, 754 cm^{-1}; **MS (EI)** *m/z* (%) 265 (M^+ + 1, 100), 251 (12); **Elemental analysis** calcd for $C_{16}H_{16}N_4$: C, 72.70; H, 6.10; N, 21.20. Found: C, 72.59; H, 6.18; N, 21.32.

2-(1*H*-Pyrazol-1-yl)-1-*o*-tolylallyl acetate (64k):



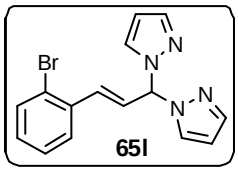
R_f = 0.57 (4:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.63 (d, *J* = 2.4 Hz, 1H), 7.59 (bd, *J* = 1.6 Hz, 1H), 7.42 (dd, *J* = 6.8, 2.0 Hz, 1H), 7.27 (s, 1H), 7.24–7.16 (m, 3H), 6.31 (t, *J* = 2.0 Hz, 1H), 5.54 (s, 1H), 4.90 (s, 1H), 2.43 (s, 3H), 2.10 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 169.4, 144.0, 140.5, 136.6, 135.0, 130.5, 128.4, 127.4, 126.6, 126.0, 106.8, 104.1, 70.1, 20.8, 19.0; **IR (Neat)** ν_{max} 3128, 3024, 1745, 1232, 756 cm^{-1}; **MS (EI)** *m/z* (%) 257 (M^+ + 1, 90), 229 (34), 215 (21), 197 (100), 182 (5); **Elemental analysis** calcd for $C_{15}H_{16}N_2O_2$: C, 70.29; H, 6.29; N, 10.93. Found: C, 70.18; H, 6.21; N, 10.85.

(*E*)-1,1'-(3-*o*-Tolylprop-1-ene-1,3-diyl)bis(1*H*-pyrazole) (66k):



R_f = 0.27 (4:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.61 (bd, *J* = 1.6 Hz, 1H), 7.60 (bd, *J* = 1.6 Hz, 1H), 7.51 (d, *J* = 2.4 Hz, 1H), 7.37 (d, *J* = 2.0 Hz, 1H), 7.29–7.18 (m, 3H), 7.17–7.08 (m, 1H), 6.66–6.62 (m, 2H), 6.42 (d, *J* = 4.8 Hz, 1H), 6.34 (t, *J* = 2.4 Hz, 1H), 6.29 (t, *J* = 2.0 Hz, 1H), 2.29 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 141.3, 139.7, 136.5, 136.3, 130.9, 130.1, 128.6, 128.5, 128.4, 127.2, 126.5, 114.8, 107.3, 105.7, 61.9, 19.0; **IR (Neat)** ν_{max} 3024, 2924, 1678,1394, 960, 752 cm^{-1}; **MS (EI)** *m/z* (%) 265 (M^+ + 1, 100), 243 (4), 219 (12), 163 (12), 145 (8); **Elemental analysis** calcd for $C_{16}H_{16}N_4$: C, 72.70; H, 6.10; N, 21.20. Found: C, 72.85; H, 6.04; N, 21.13.

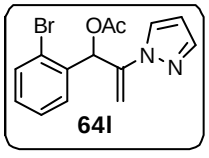
(*E*)-1,1'-(3-(2-Bromophenyl)prop-2-ene-1,1-diyl)bis(1*H*-pyrazole) (65l):



Following the general procedure (GP-3); 1-(2-bromophenyl)prop-2-ynyl acetate (**2l**; 253 mg, 1.0 mmol), pyrazole (**50**; 340 mg, 5.0 mmol), and $AgNO_3$ (16.9 mg, 0.1 mmol) in chlorobenzene (1.0 mL) was heated at 80 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (4:1) to afford **64l** (64 mg) in 20% yield as pale yellow semi-solid and **65l** (165 mg) in 50% yield as pale yellow solid.

mp = 74–75 °C; R_f = 0.33 (4:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.68 (bd, *J* = 2.4 Hz, 2H), 7.60 (bd, *J* = 1.6 Hz, 2H), 7.57 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.51 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.26 (d, *J* = 4.4 Hz, 1H), 7.23 (d, *J* = 6.0 Hz, 1H), 7.10 (td, *J* = 7.6, 1.6 Hz, 1H), 7.00–6.84 (m, 2H), 6.31 (t, *J* = 2.0 Hz, 2H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 140.4, 134.9, 134.2, 132.8, 129.8, 128.6, 127.4, 127.3, 125.3, 123.9, 106.6, 75.7; **IR (KBr)** ν_{max} 3022, 2968, 1514, 1087, 968, 754 cm^{-1}; **MS (EI)** *m/z* (%) 331 (M^++2, 78), 330 (M^+ + 1, 100), 264 (11), 262 (11); **Elemental analysis** calcd for $C_{15}H_{13}BrN_4$: C, 54.73; H, 3.98; N, 17.02. Found: C, 54.85; H, 3.91; N, 17.15.

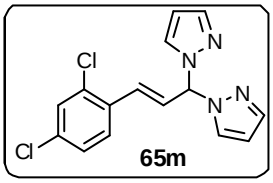
1-(2-Bromophenyl)-2-(1*H*-pyrazol-1-yl)allyl acetate (64l):



R_f = 0.45 (4:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.69 (d, *J* = 2.4 Hz, 1H), 7.60 (bs, 1H), 7.58 (d, *J* = 1.2 Hz, 1H), 7.48 (dd, *J* = 6.8, 1.6 Hz, 1H), 7.35–7.29 (m, 2H), 7.21 (td, *J* = 6.8, 1.6 Hz,

1H), 6.33 (t, *J* = 2.0 Hz, 1H), 5.65 (bd, *J* = 1.2 Hz, 1H), 4.82 (bt, *J* = 1.2 Hz, 1H), 2.12 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 169.2, 142.8, 140.7, 136.1, 133.1, 130.1, 128.4, 127.6, 127.2, 123.9, 107.0, 104.6, 72.3, 20.7; **IR (Neat)** ν_{max} 3063, 2928, 1747, 1224, 756 cm^{-1}; **MS (EI)** *m/z* (%) 323 (M^+ + 2, 28), 321 (M^+, 28), 208 (17), 151 (100), 108 (34), 76 (38); **Elemental analysis** calcd for $C_{14}H_{13}BrN_2O_2$: C, 52.36; H, 4.08; N, 8.72. Found: C, 52.25; H, 4.12; N, 8.65.

(*E*)-1,1'-(3-(2,4-Dichlorophenyl)prop-2-ene-1,1-diyl)bis(1*H*-pyrazole) (65m):

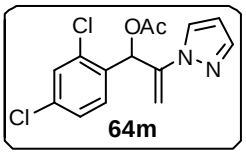


65m

Following the general procedure (GP-3); 1-(2,4-dichlorophenyl)prop-2-ynyl acetate (**2m**; 242 mg, 1.0 mmol), pyrazole (**50**; 340 mg, 5.0 mmol), and $AgNO_3$ (16.9 mg, 0.1 mmol) in chlorobenzene (1.0 mL) was heated at 80 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (6:1) to afford **64m** (47 mg) in 15% yield as pale yellow solid and **65m** (210 mg) in 66% yield as colorless solid.

mp = 107–108 °C; R_f = 0.54 (6:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.65 (d, *J* = 2.4 Hz, 2H), 7.60 (bd, *J* = 1.6 Hz, 2H), 7.50 (dd, *J* = 8.4, 2.8 Hz, 1H), 7.33 (bt, *J* = 2.4 Hz, 1H), 7.22 (d, *J* = 3.2 Hz, 1H), 7.18 (dt, *J* = 8.4, 2.4 Hz, 1H), 6.94–6.91 (m, 2H), 6.31 (bt, *J* = 2.0 Hz, 2H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 140.5, 134.7, 134.0, 131.8, 130.5, 129.4, 128.6, 127.9, 127.2, 125.8, 106.7, 75.8; **IR (KBr)** ν_{max} 3109, 2962, 1585, 1388, 754 cm^{-1}; **MS (EI)** *m/z* (%) 320 (M^+ + 1, 8), 290 (13), 251 (100), 215 (21), 183 (11), 102 (8); **Elemental analysis** calcd for $C_{15}H_{12}Cl_2N_4$: C, 56.44; H, 3.79; N, 17.55. Found: C, 56.32; H, 3.83; N, 17.41.

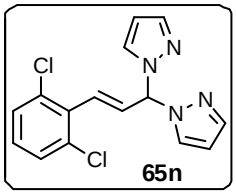
1-(2,4-Dichlorophenyl)-2-(1*H*-pyrazol-1-yl)allyl acetate (64m):



64m

mp = 57–58 °C; R_f = 0.57 (6:1 hexane/EtOAc); [Silica, UV and I_2]
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 2.4 Hz, 1H), 7.58 (bd, *J* = 1.6 Hz, 1H), 7.41 (d, *J* = 11.2 Hz, 1H), 7.42 (s, 1H), 7.34 (s, 1H), 7.25 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.32 (bt, *J* = 2.0 Hz, 1H), 5.60 (bd, *J* = 1.6 Hz, 1H), 4.88 (bt, *J* = 1.2 Hz, 1H), 2.12 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 169.1, 142.6, 140.8, 135.1, 134.6, 133.3, 129.7, 129.3, 127.34, 127.28, 107.2, 104.2, 69.6, 20.7; **IR (KBr)** ν_{max} 3128, 2932, 1751, 1222, 1026, 754 cm^{-1}; **MS (EI)** *m/z* (%) 313 (M^+ + 2, 67), 311 (M^+, 100), 289 (41), 253 (41), 251 (61), 216 (14), 102 (14); **Elemental analysis** calcd for $C_{14}H_{12}Cl_2N_2O_2$: C, 54.04; H, 3.89; N, 9.00. Found: C, 54.15; H, 3.81; N, 8.86.

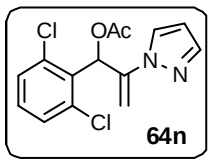
(*E*)-1,1'-(3-(2,6-Dichlorophenyl)prop-2-ene-1,1-diyl)bis(1*H*-pyrazole) (65n):



Following the general procedure (GP-3); 1-(2,6-dichlorophenyl)prop-2-ynyl acetate (**2n**; 242 mg, 1.0 mmol), pyrazole (**50**; 340 mg, 5.0 mmol), and $AgNO_3$ (16.9 mg, 0.1 mmol) in chlorobenzene (1.0 mL) was heated at 80 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (6:1) to afford **64n** (37 mg) in 12% yield as colorless solid and **65n** (162 mg) in 51% yield as colorless solid.

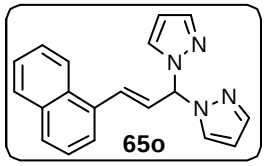
mp = 105–106 °C; R_f = 0.64 (4:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.73 (s, 2H), 7.60 (s, 2H), 7.33–7.25 (m, 3H), 7.10 (t, *J* = 7.6 Hz, 1H), 6.96 (dd, *J* = 16.4, 4.4 Hz, 1H), 6.55 (d, *J* = 16.0 Hz, 1H), 6.32 (bd, *J* = 1.2 Hz, 2H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 140.6, 134.4, 132.5, 131.2, 129.4, 129.0, 128.8, 128.4, 106.6, 75.8; **IR (KBr)** ν_{max} 3109, 2962, 1582, 1388, 1041, 754 cm^{-1}; **MS (EI)** *m/z* (%) 320 (M^+ + 1, 37), 319 (M^+, 100), 146 (4), 110 (4); **Elemental analysis** calcd for $C_{15}H_{12}Cl_2N_4$: C, 56.44; H, 3.79; N, 17.55. Found: C, 56.51; H, 3.72; N, 17.41.

1-(2,6-Dichlorophenyl)-2-(1*H*-pyrazol-1-yl)allyl acetate (64n):



mp = 86–87 °C; R_f = 0.57 (6:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.83 (bdd, *J* = 8.4, 1.6 Hz, 1H), 7.65 (bs, 1H), 7.60 (bd, *J* = 2.0 Hz, 1H), 7.30 (s, 1H), 7.28 (s, 1H), 7.13 (t, *J* = 8.0 Hz, 1H), 6.88 (d, *J* = 9.6 Hz, 1H), 6.34 (bt, *J* = 2.0 Hz, 1H), 5.74 (t, *J* = 8.8 Hz, 1H), 2.09 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 170.0, 141.6, 135.4, 134.7, 130.5, 129.5, 129.2, 128.0, 113.3, 106.9, 68.8, 20.9; **IR (KBr)** ν_{max} 2924, 1730, 1244, 761 cm^{-1}; **MS (EI)** *m/z* (%) 313 (M^+ + 2, 20), 311 (M^+, 35), 289 (17), 251 (100), 203 (100), 183 (41), 130 (17), 102 (100); **Elemental analysis** calcd for $C_{14}H_{12}Cl_2N_2O_2$: C, 54.04; H, 3.89; N, 9.00. Found: C, 53.95; H, 3.94; N, 9.12.

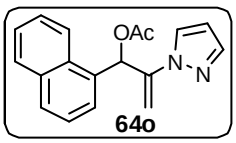
(*E*)-1,1'-(3-(Naphthalen-1-yl)prop-2-ene-1,1-diyl)bis(1*H*-pyrazole) (65o):



Following the general procedure (GP-3); 1-(naphthalen-1-yl)prop-2-ynyl acetate (**2o**; 224 mg, 1.0 mmol), pyrazole (**50**; 340 mg, 5.0 mmol), and $AgNO_3$ (16.9 mg, 0.1 mmol) in chlorobenzene (1.0 mL) was heated at 80 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (4:1) to afford **64o** (67 mg) in 23% yield as colorless solid, **65o** (144 mg) in 48% yield as colorless solid and **66o** (48 mg) in 16% yield as pale yellow solid.

mp = 85–86 °C; R_f = 0.38 (4:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.01–7.94 (m, 1H), 7.89–7.81 (m, 2H), 7.75 (bd, *J* = 2.4 Hz, 2H), 7.72–7.65 (m, 3H), 7.54–7.44 (m, 3H), 7.35 (dd, *J* = 10.4, 4.4 Hz, 2H), 6.97 (dd, *J* = 16.0, 5.6 Hz, 1H), 6.37 (bt, *J* = 2.0 Hz, 2H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 140.5, 133.4, 132.9, 132.6, 130.9, 129.0, 128.6, 128.5, 126.3, 125.9, 125.6, 125.4, 124.4, 123.3, 106.7, 76.1; **IR (KBr)** ν_{max} 3117, 3057, 1512, 1390, 966, 754 cm^{-1}; **MS (EI)** *m/z* (%) 301 (M^+ + 1, 100), 287 (6), 255 (4); **Elemental analysis** calcd for $C_{19}H_{16}N_4$: C, 75.98; H, 5.37; N, 18.65. Found: C, 75.86; H, 5.31; N, 18.56.

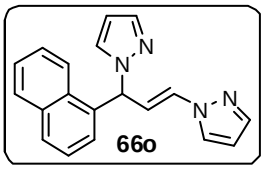
1-(Naphthalen-1-yl)-2-(1*H*-pyrazol-1-yl)allyl acetate (64o):



64o

mp = 92–93 °C; R_f = 0.56 (4:1 hexane/EtOAc); [Silica, UV and I_2] **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.16 (d, *J* = 8.4 Hz, 1H), 7.93 (s, 1H), 7.87 (dd, *J* = 11.6, 8.4 Hz, 2H), 7.71–7.64 (m, 2H), 7.62 (bd, *J* = 1.6 Hz, 1H), 7.59–7.49 (m, 2H), 6.47 (t, *J* = 7.6 Hz,. 1H), 6.31 (bt, *J* = 1.6 Hz,. 1H), 5.62 (bd, *J* = 1.2 Hz, 1H), 4.95 (s, 1H), 2.14 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 169.5, 143.9, 140.7, 133.7, 132.4, 130.9, 129.4, 128.7, 127.4, 126.7, 125.9, 125.1, 123.4, 107.0, 104.6, 70.0, 20.9; **IR (KBr)** ν_{max} 3065, 2930, 1736, 1224, 773 cm^{-1}; **MS (EI)** *m/z* (%) 293 (M^+ + 1, 100); **Elemental analysis** calcd for $C_{18}H_{16}N_2O_2$: C, 73.95; H, 5.52; N, 9.58. Found: C, 74.05; H, 5.48; N, 9.51.

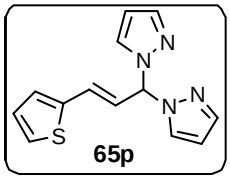
(*E*)-1,1'-(3-(Naphthalen-1-yl)prop-1-ene-1,3-diyl)bis(1*H*-pyrazole) (66o):



66o

mp = 95–96 °C; R_f = 0.29 (4:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.00–7.93 (m, 1H), 7.92–7.83 (m, 2H), 7.63 (d, *J* = 12.8 Hz, 2H), 7.53–7.41 (m, 5H), 7.33 (bd, *J* = 2.0 Hz, 1H), 7.02 (d, *J* = 5.6 Hz, 1H), 6.82 (dd, *J* = 14.0, 6.0 Hz, 1H), 6.63 (d, *J* = 14.0 Hz, 1H), 6.32 (bt, *J* = 2.0 Hz, 1H), 6.26 (bt, *J* = 2.0 Hz, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 141.3, 139.7, 133.9, 133.8, 130.9, 130.2, 129.5, 128.84, 128.77,128.5, 126.9, 126.0, 125.7, 125.2, 122.9, 115.0, 107.2, 105.9, 61.7; **IR (KBr)** ν_{max} 3051, 2924, 1678, 1394, 958, 754 cm^{-1}; **MS (EI)** *m/z* (%) 301 (M^+ + 1, 100), 282 (11); **Elemental analysis** calcd for $C_{19}H_{16}N_4$: C, 75.98; H, 5.37; N, 18.65. Found: C, 75.85; H, 5.32; N, 18.71.

(*E*)-1,1'-(3-(Thiophen-2-yl)prop-2-ene-1,1-diyl)bis(1*H*-pyrazole) (65p):

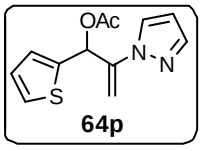


65p

Following the general procedure (GP-3); 1-(thiophen-2-yl)prop-2-ynyl acetate (**2p**; 180 mg, 1.0 mmol), pyrazole (**50**; 340 mg, 5.0 mmol), and $AgNO_3$ (16.9 mg, 0.1 mmol) in chlorobenzene (1.0 mL) was heated at 80 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (6:1) to afford **64p** (30 mg) in 12% yield as brown oil, **65p** (141 mg) in 55% yield as brown solid and **66p** (18 mg) in 7% yield as brown oil.

mp = 63–64 °C; R_f = 0.35 (6:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.64 (bd, J = 2.4 Hz, 2H), 7.59 (bd, J = 1.6 Hz, 2H), 7.18 (dd, J = 11.2, 4.8 Hz, 2H), 6.99 (d, J = 3.6 Hz, 1H), 6.93 (t, J = 4.4 Hz, 1H), 6.69 (d, J = 5.2 Hz, 1H), 6.67 (s, 1H), 6.29 (bt, J = 2.4 Hz, 2H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 140.3, 139.6, 128.5, 128.4, 127.7, 127.3, 125.8, 121.4, 106.5, 75.6; **IR (KBr)** ν_{max} 3107, 1649, 1514, 1390, 1087, 960, 754 cm^{-1}; **MS (EI)** *m/z* (%) 257 (M^+ + 1, 100), 243 (3), 211 (30), 167 (16), 97 (6); **Elemental analysis** calcd for $C_{13}H_{12}N_4S$: C, 60.91; H, 4.72; N, 21.86. Found: C, 60.75; H, 4.81; N, 21.75.

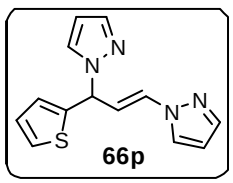
2-(1*H*-Pyrazol-1-yl)-1-(thiophen-2-yl)allyl acetate (64p):



64p

R_f = 0.56 (6:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.66 (bd, J = 2.0 Hz, 1H), 7.61 (s, 1H), 7.34 (s, 1H), 7.27 (bd, J = 3.2 Hz, 1H), 7.09 (bd, J = 3.2 Hz, 1H), 6.93 (t, J = 4.0 Hz, 1H), 6.31 (bs, 1H), 5.57 (s, 1H), 5.27 (s, 1H), 2.15 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 169.2, 143.8, 140.7, 139.9, 128.0, 127.3, 126.8, 126.3, 107.0, 102.9, 68.8, 21.0; **IR (Neat)** ν_{max} 2926, 1747, 1653, 1224, 1024, 754 cm^{-1}; **MS (EI)** *m/z* (%) 247 (M^+ – 1, 100), 244 (54), 220 (30), 186 (6), 136 (3); **Elemental analysis** calcd for $C_{12}H_{12}N_2O_2S$: C, 58.05; H, 4.87; N, 11.28. Found: C, 58.12; H, 4.81; N, 11.35.

(*E*)-1,1'-(3-(Thiophen-2-yl)prop-1-ene-1,3-diyl)bis(1*H*-pyrazole) (66p):

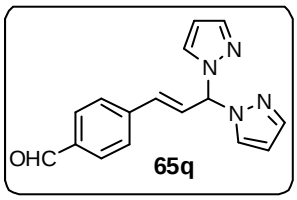


66p

R_f = 0.20 (6:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.62 (bd, J = 1.6 Hz, 1H), 7.60 (bd, J = 1.6 Hz, 1H), 7.55 (d, J = 2.4 Hz, 1H), 7.50 (d, J = 2.4 Hz, 1H), 7.32 (dd, J = 5.2, 1.2 Hz, 1H), 7.06 (bd, J = 3.6 Hz, 1H), 7.01 (dd, J = 5.2, 3.6 Hz, 1H), 6.92 (d, J = 13.6 Hz, 1H), 6.67 (dd, J = 14.0, 6.8 Hz, 1H), 6.43 (d, J = 7.2 Hz, 1H), 6.36 (bt, J = 2.0 Hz, 1H), 6.31 (bt, J = 2.4 Hz, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 141.7, 141.5, 139.8, 130.3, 128.5, 128.1, 127.0,

126.5, 126.3, 114.7, 107.5, 106.1, 60.7; **IR (Neat)** ν_{max} 3107, 2924, 1678, 1520, 1394, 1089, 752 cm^{-1}; **MS (EI)** *m/z* (%) 257 (M^+ + 1, 100), 239 (6), 215 (6), 181 (9), 157 (12), 133 (12); **Elemental analysis** calcd for $C_{13}H_{12}N_4S$: C, 60.91; H, 4.72; N, 21.86. Found: C, 61.06; H, 4.68; N, 21.95.

(*E*)-4-(3,3-Di(1*H*-pyrazol-1-yl)prop-1-enyl)benzaldehyde (65q):

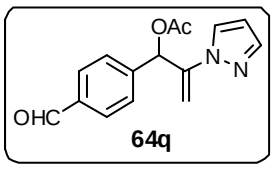


65q

Following the general procedure (GP-3); 1-(4-formylphenyl)prop-2-ynyl acetate (**2q**; 202 mg, 1.0 mmol), pyrazole (**50**; 340 mg, 5.0 mmol), and $AgNO_3$ (16.9 mg, 0.1 mmol) in chlorobenzene (1.0 mL) was heated at 80 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (3:1) to afford **64q** (51 mg) in 19% yield as pale yellow oil and **65q** (150 mg) in 54% yield as pale yellow solid.

mp = 104–105 °C; R_f = 0.29 (3:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.99 (s, 1H), 7.84 (d, *J* = 8.0 Hz, 2H), 7.65 (d, *J* = 2.4 Hz, 2H), 7.61 (bd, *J* = 1.6 Hz, 2H), 7.57 (d, *J* = 8.0 Hz, 2H), 7.21 (dd, *J* = 5.6, 1.2 Hz, 1H), 7.06 (dd, *J* = 16.0, 6.0 Hz, 1H), 6.61 (d, *J* = 16.0 Hz, 1H), 6.34 (bd, *J* = 2.0 Hz, 2H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 191.4, 140.7, 140.5, 136.0, 134.0, 129.9, 128.6, 127.4, 126.1, 106.8, 75.7; **IR (KBr)** ν_{max} 2926, 1691, 1390, 1209, 1089, 765, 625 cm^{-1}; **MS (EI)** *m/z* (%) 279 (M^+ + 1, 100), 233 (3), 212 (5); **Elemental analysis** calcd for $C_{16}H_{14}N_4O$: C, 69.05; H, 5.07; N, 20.13. Found: C, 69.18; H, 5.15; N, 20.06.

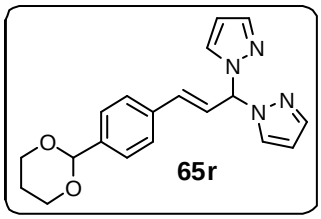
1-(4-Formylphenyl)-2-(1*H*-pyrazol-1-yl)allyl acetate (64q):



64q

R_f = 0.61 (3:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.96 (s, 1H), 7.82 (d, *J* = 8.0 Hz, 2H), 7.63–7.55 (m, 4H), 7.17 (s, 1H), 6.26 (bt, *J* = 2.0 Hz, 1H), 5.51 (bd, *J* = 1.2 Hz, 1H), 5.12 (s, 1H), 2.15 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 191.6, 169.1, 143.6, 140.7, 136.2, 129.8, 127.8, 127.7, 107.1, 103.1, 72.5, 20.9; **IR (Neat)** ν_{max} 2928, 1741, 1608, 1226, 1032, 758 cm^{-1}; **MS (EI)** *m/z* (%) 271 (M^+ + 1, 100), 240 (5); **Elemental analysis** calcd for $C_{15}H_{14}N_2O_3$: C, 66.66; H, 5.22; N, 10.36. Found: C, 66.48; H, 5.32; N, 10.25.

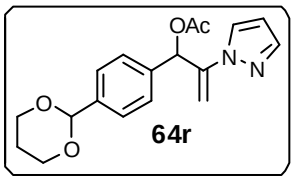
(*E*)-1,1'-(3-(4-(1,3-Dioxan-2-yl)phenyl)prop-2-ene-1,1-diyl)bis(1*H*-pyrazole) (65r):



Following the general procedure (GP-3); 1-(4-(1,3-dioxan-2-yl)phenyl)prop-2-ynyl acetate (**2s**; 260 mg, 1.0 mmol), pyrazole (**50**; 340 mg, 5.0 mmol), and $AgNO_3$ (16.9 mg, 0.1 mmol) in chlorobenzene (1.0 mL) was heated at 80 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (3:1) to afford **64r** (66 mg) in 20% yield as colorless solid, **65r** (145 mg) in 43% yield as colorless solid and **66r** (47 mg) in 14% yield as pale yellow solid.

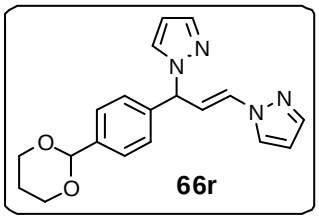
mp = 120–121 °C; R_f = 0.25 (3:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.65 (bd, *J* = 1.6 Hz, 2H), 7.59 (bs, 2H), 7.46 (bd, *J* = 6.8 Hz, 2H), 7.41 (bd, *J* = 6.4 Hz, 2H), 7.20 (dd, *J* = 5.2, 1.2 Hz, 1H), 6.91 (dd, *J* = 12.8, 4.8 Hz, 1H), 6.56 (d, *J* = 12.8 Hz, 1H), 6.29 (bd, *J* = 1.6 Hz, 2H), 5.47 (s, 1H), 4.23 (bdd, *J* = 8.8, 3.6 Hz, 2H), 3.94 (t, *J* = 10.0 Hz, 2H), 2.25–2.12 (m, 1H), 1.40 (bd, *J* = 10.0 Hz, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 140.2, 139.0, 135.2, 135.0, 128.5, 126.7, 126.1, 122.7, 106.4, 100.8, 75.8, 67.0, 25.4; **IR (KBr)** ν_{max} 3101, 2962, 1392, 1105, 758 cm^{-1}; **MS (EI)** *m/z* (%) 337 (M^+ + 1, 100), 323 (3); **Elemental analysis** calcd for $C_{19}H_{20}N_4O_2$: C, 67.84; H, 5.99; N, 16.66. Found: C, 67.71; H, 5.91; N, 16.58.

1-(4-(1,3-Dioxan-2-yl)phenyl)-2-(1*H*-pyrazol-1-yl)allyl acetate (64r):



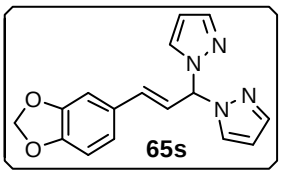
mp = 119–120 °C; R_f = 0.44 (3:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.56 (bt, *J* = 2.0 Hz, 2H), 7.49–7.42 (m, 4H), 7.11 (s, 1H), 6.24 (t, *J* = 2.0 Hz, 1H), 5.56 (s, 1H), 5.48 (s, 1H), 5.09 (s, 1H), 4.25 (dd, *J* = 8.8, 4.0 Hz, 2H), 3.97 (td, *J* = 9.6, 1.6 Hz, 2H), 2.26–2.16 (m, 1H), 2.12 (s, 3H), 1.44 (d, *J* = 10.8 Hz, 1H); **^{13}C NMR (125 MHz, $CDCl_3$)** δ 169.2, 143.9, 140.5, 138.9, 137.4, 127.8, 127.2, 126.2, 106.8, 103.3, 101.0, 72.8, 67.3, 25.6, 20.9; **IR (KBr)** ν_{max} 3130, 2974, 1738, 1244, 763 cm^{-1}; **MS (EI)** *m/z* (%) 329 (M^+ + 1, 100), 223 (11), 121 (3); **Elemental analysis** calcd for $C_{18}H_{20}N_2O_4$: C, 65.84; H, 6.14; N, 8.53. Found: C, 65.72; H, 6.21; N, 8.65.

(*E*)-1,1'-(3-(4-(1,3-Dioxan-2-yl)phenyl)prop-1-ene-1,3-diyl)bis(1*H*-pyrazole) (66r):



mp = 105–106 °C; R_f = 0.17 (3:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.61 (bd, *J* = 1.2 Hz, 1H), 7.59 (bd, *J* = 1.2 Hz, 1H), 7.53–7.48 (m, 3H), 7.43 (d, *J* = 1.6 Hz, 1H), 7.25 (d, *J* = 6.4 Hz, 2H), 6.77 (dd, *J* = 11.2, 0.4 Hz, 1H), 6.68 (dd, *J* = 11.2, 5.2 Hz, 1H), 6.34 (bt, *J* = 2.0 Hz, 1H), 6.29 (bt, *J* = 1.6 Hz, 1H)., 6.23 (d, *J* = 5.6 Hz, 1H), 5.51 (s, 1H), 4.26 (dd, *J* = 8.4, 3.6 Hz, 2H), 3.99 (td, *J* = 10.0, 2.0 Hz, 2H), 2.28–2.16 (m, 1H), 1.45 (d, *J* = 10.8 Hz, 1H); **^{13}C NMR (125 MHz, $CDCl_3$)** δ 141.3, 139.6, 139.1, 138.9, 130.5, 128.5, 128.4, 127.2, 126.5, 114.8, 107.3, 105.8, 100.9, 67.3, 64.8, 25.6; **IR (KBr)** ν_{max} 3111, 2924, 1676, 1392, 1103, 748 cm^{-1}; **MS (EI)** *m/z* (%) 337 (M^+ + 1, 100), 323 (3); **Elemental analysis** calcd for $C_{19}H_{20}N_4O_2$: C, 67.84; H, 5.99; N, 16.66. Found: C, 67.92; H, 6.08; N, 16.75.

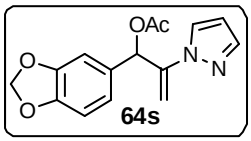
(*E*)-1,1'-(3-(Benzo[*d*][1,3]dioxol-5-yl)prop-2-ene-1,1-diyl)bis(1*H*-pyrazole) (65s):



Following the general procedure (GP-3); 1-(benzo[*d*][1,3]dioxol-5-yl)prop-2-ynyl acetate (**2r**; 218 mg, 1.0 mmol), pyrazole (**50**; 340 mg, 5.0 mmol), and $AgNO_3$ (16.9 mg, 0.1 mmol) in chlorobenzene (1.0 mL) was heated at 80 °C for 53 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (6:1) to afford **64s** (29 mg) in 10% yield as brown oil, **65s** (147 mg) in 50% yield as light brown solid and **66s** (50 mg) in 17% yield as brown oil.

mp = 115–116 °C; R_f = 0.43 (6:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.64 (bd, *J* = 2.0 Hz, 2H), 7.59 (bd, *J* = 1.6 Hz, 2H), 7.13 (d, *J* = 6.0 Hz, 1H), 6.98 (bd, *J* = 1.2 Hz, 1H), 6.84 (d, *J* = 8.0 Hz, 1H), 6.78–6.70 (m, 2H), 6.50 (d, *J* = 16.0 Hz, 1H), 6.31 (bt, *J* = 2.0 Hz, 2H), 5.95 (s, 2H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 148.2, 148.1, 140.4, 135.3, 129.5, 128.5, 122.3, 120.7, 108.3, 106.6, 106.1, 101.2, 76.3; **IR (KBr)** ν_{max} 3103, 2901, 1651, 1448, 1255, 1037, 761, 625 cm^{-1}; **MS (EI)** *m/z* (%) 294 (M^+, 24), 293 (M^+ – 1, 100); **Elemental analysis** calcd for $C_{16}H_{14}N_4O_2$: C, 65.30; H, 4.79; N, 19.04. Found: C, 65.21; H, 4.71; N, 19.15.

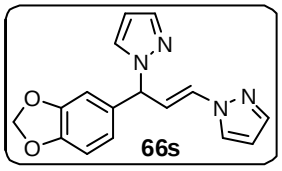
1-(Benzo[*d*][1,3]dioxol-5-yl)-2-(1*H*-pyrazol-1-yl)allyl acetate (64s):



R_f = 0.64 (6:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.58 (bd, *J* = 2.8 Hz, 1H), 7.57 (bd, *J* = 1.6 Hz, 1H), 6.99 (s, 1H), 6.96–6.90 (m, 2H), 6.73 (d, *J* = 8.4 Hz, 1H), 6.26 (bt, *J* = 2.0 Hz,

1H), 5.92 (s, 2H), 5.53 (s, 1H), 5.12 (s, 1H), 2.12 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 169.3, 147, 77, 147.76, 144.1, 140.5, 130.6, 127.7, 121.4, 108.2, 107.8, 106.8, 102.8, 101.2, 72.8, 21.0; **IR (Neat)** ν_{max} 2924, 1743, 1228, 756, 696 cm^{-1}; **MS (EI)** *m/z* (%) 287 (M^+ + 1, 100), 269 (6), 241 (9), 229 (14), 197 (8); **Elemental analysis** calcd for $C_{15}H_{14}N_2O_4$: C, 62.93; H, 4.93; N, 9.79. Found: C, 62.85; H, 4.88; N, 9.65.

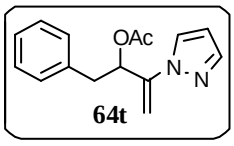
(*E*)-1,1'-(3-(Benzo[*d*][1,3]dioxol-5-yl)prop-1-ene-1,3-diyl)bis(1*H*-pyrazole) (66s):



66s

R_f = 0.18 (6:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.62 (bd, *J* = 1.6 Hz, 1H), 7.60 (bd, *J* = 1.2 Hz, 1H), 7.56 (bd, *J* = 2.0 Hz, 1H), 7.48 (bd, *J* = 2.0 Hz, 1H), 6.83 (d, *J* = 11.6 Hz, 1H), 6.81–6.75 (m, 2H), 6.74 (bd, *J* = 1.2 Hz, 1H), 6.64 (dd, *J* = 11.2, 5.6 Hz, 1H), 6.36 (bt, *J* = 1.6 Hz, 1H), 6.31 (bt, *J* = 1.6 Hz, 1H), 6.12 (d, *J* = 5.6 Hz, 1H), 5.97–5.95 (m, 2H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 148.1, 147.6, 141.3, 139.7, 132.6, 130.4, 128.4, 128.3, 120.9, 115.0, 108.4, 107.8, 107.4, 105.8, 101.3, 64.8; **IR (Neat)** ν_{max} 2924, 1678, 1248, 1039, 754 cm^{-1}; **MS (EI)** *m/z* (%) 295 (M^+ + 1, 100), 252 (41), 204 (14); **Elemental analysis** calcd for $C_{16}H_{14}N_4O_2$: C, 65.30; H, 4.79; N, 19.04. Found: C, 65.48; H, 4.85; N, 18.89.

1-Phenyl-3-(1*H*-pyrazol-1-yl)but-3-en-2-yl acetate (64t):

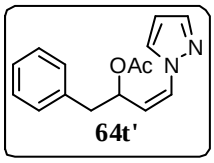


64t

Following the general procedure (GP-3); 1-phenylbut-3-yn-2-yl acetate (**2t**; 188 mg, 1.0 mmol), pyrazole (**50**; 340 mg, 5.0 mmol), and $AgNO_3$ (16.9 mg, 0.1 mmol) in chlorobenzene (1.0 mL) was heated at 80 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (19:1) to afford **64t** (49 mg) in 19% yield as colorless oil, **64t′** (65 mg) in 25% yield as colorless oil.

R_f = 0.57 (19:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.73 (s, 1H), 7.67 (s, 1H), 7.48–7.12 (m, 5H), 6.38 (s, 1H), 6.22 (s, 1H), 5.33 (s, 1H), 4.95 (s, 1H), 3.23–3.13 (m, 1H), 3.06–2.90 (m, 1H), 2.06 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 169.6, 144.2, 140.8, 136.7, 129.5, 128.2, 127.8, 126.7, 107.0, 102.3, 39.6, 21.0; **IR (Neat)** ν_{max} 3030, 2926, 1747, 1651, 1232, 1045, 754 cm^{-1}; **MS (EI)** *m/z* (%) 257 (M^+ + 1, 100), 199 (8), 167 (14), 139 (5); **Elemental analysis** calcd for $C_{15}H_{16}N_2O_2$: C, 70.29; H, 6.29; N, 10.93. Found: C, 70.18; H, 6.22; N, 10.88.

(*Z*)-1-Phenyl-4-(1*H*-pyrazol-1-yl)but-3-en-2-yl acetate (64t'):

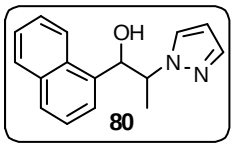


64t'

R_f = 0.45 (19:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.69 (s, 1H), 7.50 (s, 1H), 7.36–7.18 (m, 5H), 6.74 (d, J = 9.6 Hz, 1H), 6.56 (s, 1H), 6.34 (s, 1H), 5.14 (t, J = 8.8 Hz, 1H), 3.24–3.15 (m, 1H), 3.05–2.98 (m, 1H), 1.99 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 170.1, 141.4, 137.2, 130.3, 129.6, 128.1, 126.4, 125.7, 117.2, 106.6, 71.5, 40.4, 21.1.

IR (Neat) ν_{max} 3028, 2924, 1736, 1521, 1236, 738 cm^{-1}; **MS (EI)** *m/z* (%) 257 (M^+ + 1, 100), 223 (14), 211 (27), 167 (14), 97 (11), 91 (11); **Elemental analysis** calcd for $C_{15}H_{16}N_2O_2$: C, 70.29; H, 6.29; N, 10.93. Found: C, 70.35; H, 6.23; N, 10.99.

1-(Naphthalen-1-yl)-2-(1*H*-pyrazol-1-yl)propan-1-ol (80):

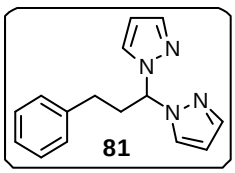


80

In an oven dried RB, **64o** (50 mg, 0.2 mmol) and 10% Pd/C in MeOH was taken. The reaction mixture was stirred at room temperature under H_2 (balloon) atmosphere for 1 h. The crude residue was diluted with CH_2Cl_2 and filtered through a small pad of Celite. The filtrate was concentrated under the reduced pressure. The crude residue was purified by column chromatography on silica gel eluting with hexane: ethyl acetate (4:1) to afford inseperable mixture of two diastereomers of **80** (1:1, 45 mg) in 89% yield as pale yellow oil.

R_f = 0.61 (4:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.02 (d, J = 8.4 Hz, 2H), 7.87 (d, J = 8.4 Hz, 2H), 7.74 (d, J = 8.0 Hz, 2H), 7.59 (bd, J = 1.6 Hz, 2H), 7.57–7.47 (m, 4H), 7.32 (t, J = 8.0 Hz, 2H), 7.13–7.06 (m, 4H), 6.12 (t, J = 2.4 Hz, 2H), 4.77–4.67 (m, 2H), 3.70 (dd, J = 14.0, 7.2 Hz, 2H), 3.46 (dd, J = 13.6, 6.8 Hz, 2H), 1.62 (s, 3H), 1.61 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 139.1, 134.0, 133.8, 131.8, 128.8, 127.8, 127.5, 127.4, 126.1, 125.5, 125.3, 123.4, 104.5, 58.6, 40.9, 20.6; **IR (Neat)** ν_{max} 3059, 2934, 1745, 1396, 1045, 750, 623 cm^{-1}; **MS (EI)** *m/z* (%) 253 (M^+ + 1, 100), 207 (3), 184 (3), 168 (3); **Elemental analysis** calcd for $C_{16}H_{16}N_2O$: C, 76.16; H, 6.39; N, 11.10. Found: C, 76.28; H, 6.31; N, 11.25.

1,1'-(3-Phenylpropane-1,1-diyl)bis(1*H*-pyrazole) (81):



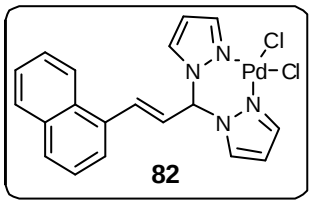
81

In an oven dried RB, **65a** (100 mg, 0.4 mmol) and 10% Pd/C in MeOH was taken. The reaction mixture was stirred at room temperature under H_2 (balloon) atmosphere for 1 h. The crude residue

was diluted with CH_2Cl_2 and filtered through a small pad of Celite. The filtrate was concentrated under the reduced pressure. The crude residue was purified by column chromatography on silica gel eluting with hexane: ethyl acetate (4:1) to afford **81** (99 mg) in 98% yield as colorless solid.

mp = 69–70 °C; R_f = 0.35 (4:1 hexane/EtOAc); [Silica, UV and I_2]; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.63 (bd, *J* = 2.4 Hz, 2H), 7.56 (bd, *J* = 1.6 Hz, 2H), 7.31 (bt, *J* = 7.6 Hz, 2H), 7.26–7.19 (m, 1H), 7.15 (bd, *J* = 1.6 Hz, 1H), 7.14 (s, 1H), 6.33 (t, *J* = 7.6 Hz, 1H), 6.28 (bt, *J* = 2.0 Hz, 2H), 2.95 (q, *J* = 7.2 Hz, 2H), 2.58 (t, *J* = 7.6 Hz, 2H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 140.0, 139.6, 128.6, 128.5, 128.4, 126.4, 106.4, 74.5, 35.1, 31.1. **IR (KBr)** ν_{max} 3109, 2928, 1514, 1390, 1091, 752, 623 cm^{-1}; **MS (EI)** *m/z* (%) 253 (M^+ + 1, 100), 209 (3), 146 (3); **Elemental analysis** calcd for $C_{15}H_{16}N_4$: C, 71.40; H, 6.39; N, 22.21. Found: C, 71.56; H, 6.31; N, 22.15.

Synthesis of Pd-Complex 82 from 65o:



82

In an oven dried schlenk tube, **65o** (90 mg, 0.3 mmol) and $PdCl_2$ (53 mg, 0.3 mmol) in CH_3CN (6.0 mL) was taken. The reaction mixture was stirred at room temperature for 5 h. The yellow precipitate was filtered off to afford **82** (127 mg) in 89% yield as pale yellow solid.

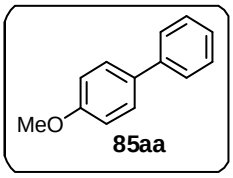
mp = 275–276 °C (decomposed); **^{1}H NMR (400 MHz, DMSO-D6)** δ 8.46 (bd, *J* = 2.4 Hz, 2H), 8.25 (bd, *J* = 4.0 Hz, 1H), 8.22 (d, *J* = 8.8 Hz, 1H), 8.08 (bd, *J* = 1.2 Hz, 2H), 8.03–7.89 (m, 3H), 7.67–7.45 (m, 4H), 7.10 (bs, 1H), 6.68 (s, 2H); **^{13}C NMR (101 MHz, DMSO-D6)** δ 144.4, 135.3, 133.6, 132.1, 131.1, 130.0, 129.0, 127.3, 126.7, 126.2, 125.3, 124.2, 108.1, 73.8; **IR (KBr)** ν_{max} 3145, 3123, 2931, 1408, 1282, 1205, 1086, 947, 860, 783, 613 cm^{-1}; **Elemental analysis** calcd for $C_{19}H_{16}Cl_2N_4Pd$: C, 47.77; H, 3.38; N, 11.73. Found: C, 47.86; H, 3.32; N, 11.65.

2.5.6: General Procedure for Suzuki-Miyaura Cross Coupling Reaction (GP-4):

A 25 mL Schlenk tube was charged with aryliodide (**83**; 1.0 equiv), arylboronic (**84**; 2.0 equiv), K_2CO_3 (2.0 equiv) and palladium complex **82** (0.1 mol%) in H_2O. The reaction micture was stirred at 80 °C for 24 h. After being cooled to room temperature, it was diluted with water, and extracted with EtOAc. The organic layer was separated, dried over Na_2SO_4 and concentrated under vacuum. The crude residue was purified using column

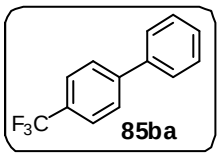
chromatography on silica gel. Analytical and spectral data of cross-coupled products **85** are exactly matching with the reported values.

4-Methoxybiphenyl (85aa):[15]



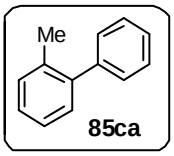
Following the general procedure (GP-4); 4-iodoanisole (**83a**; 702 mg, 3.0 mmol), phenylboronic acid (**84a**; 732 mg, 6.0 mmol), K_2CO_3 (828 mg, 6.0 mmol) and complex-**82** (1.5 mg, 0.3 mol%) in H_2O (10 mL) was heated at 80 °C for 24 h. After usual workup, the crude mixture was purified by silica gel column chromatography eluting with hexane to afford **85aa** (536 mg) in 97% yield. Analytical data ^1H and ^{13}C NMR are concurrently matching with the reported values.

4-(Trifluoromethyl)biphenyl (85ba):[16]



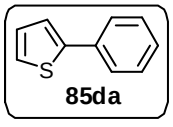
Following the general procedure (GP-4); 4-iodobenzotrifluoride (**83b**; 816 mg, 3.0 mmol), phenylboronic acid (**84a**; 732 mg, 6.0 mmol), K_2CO_3 (828 mg, 6.0 mmol) and complex-**82** (1.5 mg, 0.3 mol%) in H_2O (10 mL) was heated at 80 °C for 24 h. After usual workup, the crude mixture was purified by silica gel column chromatography eluting with hexane to afford **85ba** (480 mg) in 72% yield. Analytical data ^1H and ^{13}C NMR are concurrently matching with the reported values.

2-Methylbiphenyl (85ca):[17]



Following the general procedure (GP-4); 4-iodotoluene (**83c**; 654 mg, 3.0 mmol), phenylboronic acid (**84a**; 732 mg, 6.0 mmol), K_2CO_3 (828 mg, 6.0 mmol) and complex-**82** (1.5 mg, 0.3 mol%) in H_2O (10 mL) was heated at 80 °C for 24 h. After usual workup, the crude mixture was purified by silica gel column chromatography eluting with hexane to afford **85ca** (473 mg) in 94% yield. Analytical data ^1H and ^{13}C NMR are concurrently matching with the reported values.

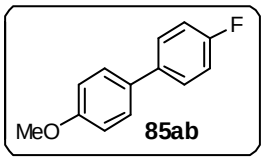
2-Phenylthiophene (85da):[15]



Following the general procedure (GP-4); 4-iodothiophene (**83d**; 630 mg, 3.0 mmol), phenylboronic acid (**84a**; 732 mg, 6.0 mmol), K_2CO_3 (828 mg,

6.0 mmol) and complex-**82** (1.5 mg, 0.3 mol%) in H_2O (10 mL) was heated at 80 °C for 24 h. After usual workup, the crude mixture was purified by silica gel column chromatography eluting with hexane to afford **85da** (385 mg) in 80% yield. Analytical data ^1H and ^{13}C NMR are concurrently matching with the reported values.

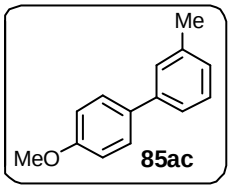
4-Fluoro-4'-methoxybiphenyl (85ab):[18]



85ab

Following the general procedure (GP-4); 4-iodoanisole (**83a**; 702 mg, 3.0 mmol), 4-fluorophenylboronic acid (**84b**; 840 mg, 6.0 mmol), K_2CO_3 (828 mg, 6.0 mmol) and complex-**82** (1.5 mg, 0.3 mol%) in H_2O (10 mL) was heated at 80 °C for 24 h. After usual workup, the crude mixture was purified by silica gel column chromatography eluting with hexane to afford **85ab** (577 mg) in 95% yield. Analytical data ^1H and ^{13}C NMR are concurrently matching with the reported values.

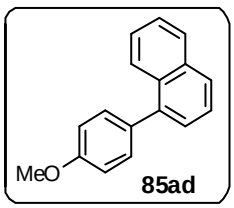
4'-Methoxy-3-methylbiphenyl (85ac):[16]



85ac

Following the general procedure (GP-4); 4-iodoanisole (**83a**; 702 mg, 3.0 mmol), *m*-tolylboronic acid (**84c**; 816 mg, 6.0 mmol), K_2CO_3 (828 mg, 6.0 mmol) and complex-**82** (1.5 mg, 0.3 mol%) in H_2O (10 mL) was heated at 80 °C for 24 h. After usual workup, the crude mixture was purified by silica gel column chromatography eluting with hexane to afford **85ac** (511 mg) in 86% yield. Analytical data ^1H and ^{13}C NMR are concurrently matching with the reported values.

1-(4-Methoxyphenyl)naphthalene (85ad):[19]



85ad

Following the general procedure (GP-4); 4-iodoanisole (**83a**; 702 mg, 3.0 mmol), naphthalene-1-boronic acid (**84d**; 1.0 g, 6.0 mmol), K_2CO_3 (828 mg, 6.0 mmol) and complex-**82** (1.5 mg, 0.3 mol%) in H_2O (10 mL) was heated at 80 °C for 24 h. After usual workup, the crude mixture was purified by silica gel column chromatography eluting with hexane to afford **85ad** (674 mg) in 96% yield. Analytical data ^1H and ^{13}C NMR are concurrently matching with the reported values.

2.5.7: X-Ray Crystallography: Single crystal X-ray data for the compounds **65n, 64o, 63o and 82.**

Table 2.7. Crystal Data

Compound	**65n**	**64o**	**66o**	**82**
formula	$C_{15}H_{12}Cl_2N_4$	$C_{18}H_{16}N_2O_2$	$C_{19}H_{16}N_4$	$C_{19}H_{16}Cl_2N_4Pd$
M_w	319.19	292.33	300.02	477.66
Crystal system	Triclinic	orthorhombic	Monoclinic	Monoclinic
Space group	P_1^-	$P2_12_12_1$	$P2_1/n$	$C2/c$
T [K]	293	293	293	298
a [Å]	8.4052(9)	7.6054(14)	16.904(4)	21.2570(19)
b [Å]	9.2279(9)	11.951(4)	17.000(4)	14.0225(13)
c [Å]	19.988(2)	17.019(6)	17.259(6)	13.2352(12)
α [°]	88.001(8)	90	90	90
β [°]	88.103(9)	90	109.76(3)	101.593(2)
γ [°]	81.877(9)	90	90	90
Z	4	4	4	8
V [Å^3]	1533.2(3)	1546.9(8)	4668(2)	3864.6(6)
D_{calc} [g cm^{-3}]	1.383	1.255	1.281	1.642
μ [mm^{-1}]	0.421	0.083	0.079	1.247
total reflns	8459	3168	12487	3415
unique reflns	6947	2973	10588	3412
Observed reflns	2011	1027	1088	2935
R_1 [$I > 2\sigma(I)$]	0.0794	0.0813	0.0937	0.0281
wR_2 [all]	0.1851	0.1049	0.2510	0.0708
GOF	0.951	0.986	0.830	0.975
Diffractometer	SMART APEX CCD	SMART APEX CCD	SMART APEX CCD	SMART APEX CCD

2.6. References

1) (a) Y. Nishibayashi, I. Wakiji and M. Hidai, *J. Am. Chem. Soc.*, 2000, **122**, 11019. (b) M. D. Milton, Y.Inada, Y. Nishibayashi and S. Uemura, *Chem. Commun.*, 2004, 2712. (c) R. V. Ohri, A. T. Radosevich, K. J. Hrovat, C. Musich, D. Huang, T. R. Holman and F. D. Toste, *Org. Lett.*, 2005, **7**, 2501; (d) L. Zhang, *J. Am. Chem. Soc.*, 2005, **127**, 16804; (e) J. P. Markham, S. T. Staben and F. D. Toste, *J. Am. Chem. Soc.*, 2005, **127**, 9708; (f) X. Shi, D. J. Gorin and F. D. Toste, *J. Am. Chem. Soc.*, 2005, **127**, 5802; (g) S. Wang and L. Zhang, *J. Am. Chem. Soc.*, 2006, **128**, 8414; (h) L. Zhang and S. Wang, *J. Am. Chem. Soc*., 2006, **128**, 1442; (i) G. Zhang, V. J. Catalano and L. Zhang, *J. Am. Chem. Soc*., 2007, **129**, 11358; (j) R. J. Detz, M. M. E. Delville, H. Hiemstra and J. H. van Maarseveen, *Angew. Chem. Int. Ed.*, 2008, **47**, 3777. (k) G.Hattori, H. Matsuzawa, Y. Miyake and Y. Nishibayashi, *Angew. Chem. Int. Ed.*, 2008, **47**, 3781. (l) N. D. Shapiro, Y. Shi and F. D. Toste, *J. Am. Chem. Soc.*, 2009, **131**, 11654; (m) Y.-M. Pan, F.-J. Zheng, H.-X. Lin and Z.-P. Zhan, *J. Org. Chem.*, 2009, **74**, 3148; (n) L. Ye, W. He and L. Zhang, *J. Am. Chem. Soc.*, 2010, **132**, 8550; (o) X. Gao, Y.-M. Pan, M. Lin, L. Chen and Z.-P. Zhan, *Org. Biomol. Chem.*, 2010, **8**, 3259; (p) O. Debleds, E. Gayon, E. Ostaszuk, E. Vrancken and J.-M. Champagne, *Chem.—Eur. J.*, 2010, **16**, 12207; (q) E. B. Bauer, *Synthesis* 2012, **44**, 1131; (r) W. Yan, X. Ye, N. G. Akhmedov, J. L. Petersen and X. Shi, *Org. Lett.*, 2012, **14**, 2358; (s) C.-F. Xu, M. Xu, L.-Q. Yang and C.-Y. Li, *J. Org. Chem.*, 2012, **77**, 3010.
2) (a) T. Tsuchimoto, K. Aoki, T. Wagatsuma and Y. Suzuki, *Eur. J. Org. Chem.*, 2008, 4035; (b) W. Yan, Q. Wang, Y. Chen, J. L. Petersen and X. Shi, *Org. Lett.*, 2010, **12**, 3308; (c) W. Yan, X. Ye, K. Weise, J. L. Petersen and X. Shi, *Chem. Commun.*, 2012, **48**, 3521.
3) (a) N. Ghosh, S. Nayak and A. K. Sahoo, *J. Org. Chem.*, 2011, **76**, 500; (b) M. Bhanuchandra, M. R. Kuram and A. K. Sahoo, *Org. Biomol. Chem.*, 2012, **10**, 3538.
4) (a) P. T. Pavlov, A. F. Goleneva, A. E. Lesnov and T. S. Prokhorova, *Khim. Farm. Zh.*, 1998, **32**, 28.
5) C. Pettinari and R. Pettinari, *Coord. Chem. Rev.*, 2005, **249**, 663.
6) As a catalysts in organic transformation: (a) L. D. Field, B. A. Messerle, M. Rehr, L. P. Soler and T. W. Hambley, *Organometallics*, 2003, **22**, 2387; (b) S. Burling, L. D. Field, B. A. Messerle and P. Turner, *Organometallics*, 2004, **23**, 1714; (c) A. Otero, J.

Fernández-Baeza, A. Antiñolo, J. Tejeda and A. Lara-Sánchez, *Dalton Trans.*, 2004, 1499; (d) M. C. Carrión, F. A. Jalón, B. R. Manzano, A. M. Rodríguez, F. Sepúlveda and M. Maestro, *Eur. J. Inorg. Chem.*, 2007, 3961; (e) S. Kealey, P. W. Miller, N. J. Long, C. Plisson, L. Martarello and A. D. Gee, *Chem. Commun.*, 2009, 3696.

7) (a) N. J. Wheate, B. J. Evison, A. J. Herlt, D. R. Phillips and J. G. Collins, *Dalton Trans.* 2003, 3486; (b) J. G. Collins and N. J. Wheate, *J. Inorg. Biochem.* 2004, **98**, 1578.
8) M. P. Kumar and R.-S. Liu, *J. Org. Chem.*, 2006, **71**, 4951.
9) (a) P. J. Kocienski, Protecting Group, Thieme, Stuttgart, Germany, 3rd edn, 2005; (b) T. W. Green and P. G. M. Wuts, Protective Groups in Organic Synthesis, Wiley, New York, 4th edn, 2007.
10) A. S. K. Hashmi, M. Rudolph, J. W. Bats, W. Frey, F. Rominger and T. Oeser, *Chem.—Eur. J.*, 2008, **14**, 6672.
11) (a) G. L. Regina, F. D. D'Auria, A. Tafi, F. Piscitelli, S. Olla, F. Caporuscio, L. Nencioni, R. Cirilli, F. L. Torre, N. R. De Melo, S. L. Kelly, D. C. Lamb, M. Artico, M. Botta, A. T. Palamara and R. Silvestri, *J. Med. Chem.*, 2008, **51**, 3841; (b) A. Bosak, I. G. Smilović, G. Šinko, V. Vinković and Z. Kovarik, *J. Med. Chem.*, 2012, **55**, 6716.
12) (a) C. Nájera, J. Gil-Moltó, S. Karlström and L. R. Falvello, *Org. Lett.*, 2003, **5**, 1451; (b) F. Bellina, A. Carpita and R. Rossi, *Synthesis*, 2004, 2419; (c) R. Franzén and Y. Xu, *Can. J. Chem.*, 2005, **83**, 266; (d) C. Liu, Q. Ni, P. Hu and J. Qiu, *Org. Biomol. Chem.*, 2011, **9**, 1054; (e) Q.-L. Luo, J.-P. Tan, Z.-F. Li, W.-H. Nan and D.-R. Xiao, *J. Org. Chem.*, 2012, **77**, 8332; (f) M. Mondal and U. Bora, *Green Chem.*, 2012, **14**, 1873; (g) J.-P. Wan, C. Wang, R. Zhoua and Y. Liu, *RSC Advances*, 2012, **2**, 8789; (h) G. Enderlin, G. Sartori, G. Herve and C. Len, *Tetrahedron Lett.*, 2013, **54**, 3374.
13) (a) M. Kertesz, C. H. Choi and S. Yang *Chem. Rev*. 2005**, 105**, 3448; (b) H.Tomori, J. M. Fox and S. L. Buchwald, *J. Org. chem.*, 2000, **65**, 5334.
14) (a) T. J. J. Müller, *Eur. J. Org. Chem.*, 2001, 2021; (b) R. S. Robinson, M. C. Dovey and D. Gravestock, *Eur. J. Org. Chem.*, 2005, 505; (c) N. Marion, P. Carlqvist, R. Gealageas, P. D. Frémont, F. Maseras and S. P. Nolan, *Chem.–Eur. J.*, 2007, **13**, 6437; (d) E. Gayon, M. Szymczyk, H. Gérard, E. Vrancken and J.-M. Campagne, *J. Org. Chem.*, 2012, **77**, 9205.

15) Nakao, Y.; Imanaka, H.; Sahoo, A. K.; Yada A.; Hiyama, T. *J. Am. Chem. Soc*. **2005**, *127*, 6952.

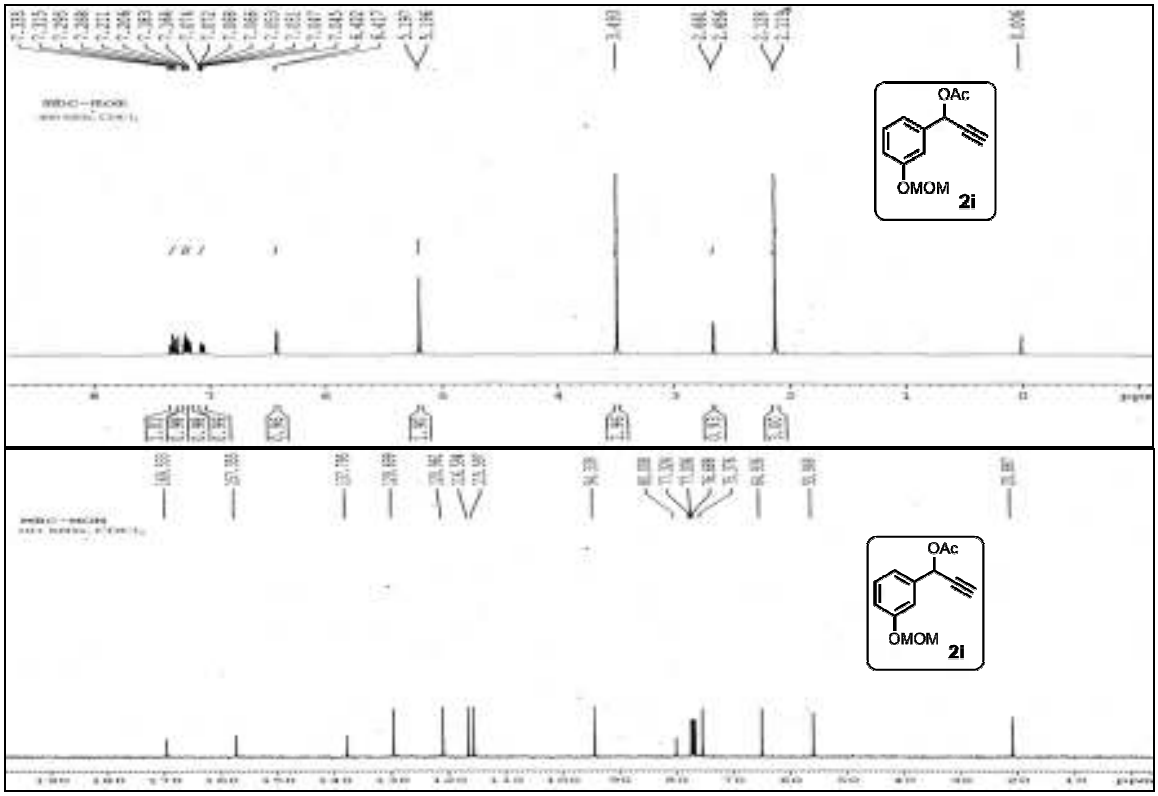
16) Ackermann, L.; Gschrei, C. J.; Althammer, A.; Riederer, M. *Chem. Commun.* **2006**, 1419.

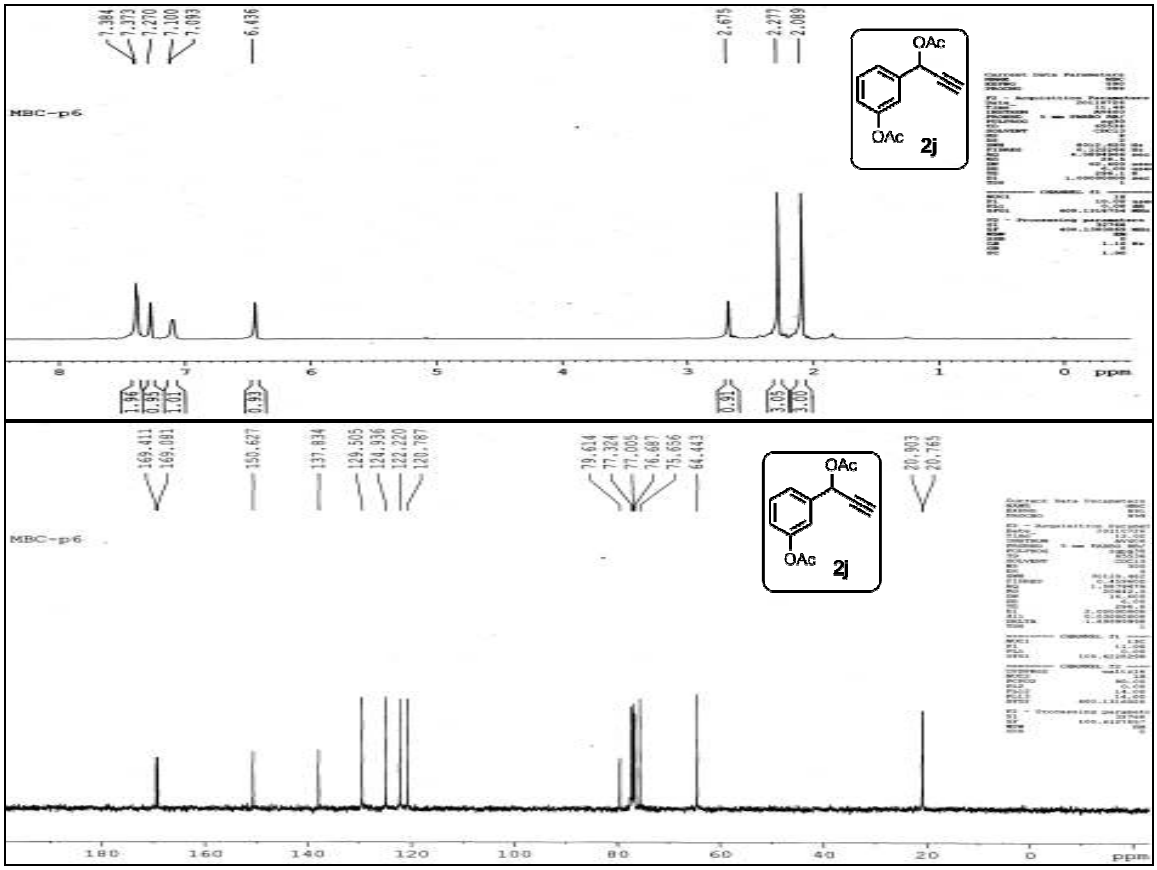
17) Kitamura, Y.; Sakurai, A.; Udzu, T.; Maegawa, T.; Monguchi, Y.; Sajiki, H. *Tetrahedron* **2007**, *63*, 10596.

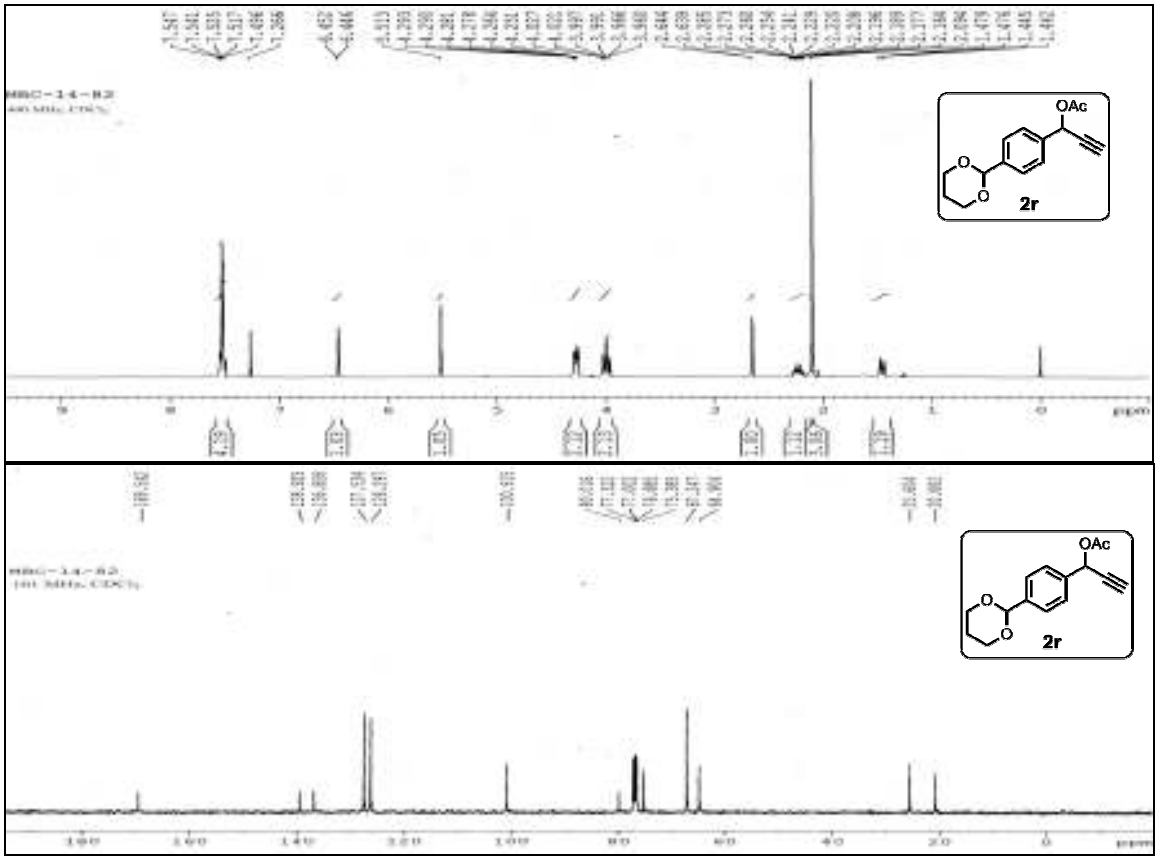
18) Moore, L. R.; Shaughnessy, K. H. *Org. Lett.* **2004**, *6*, 225.

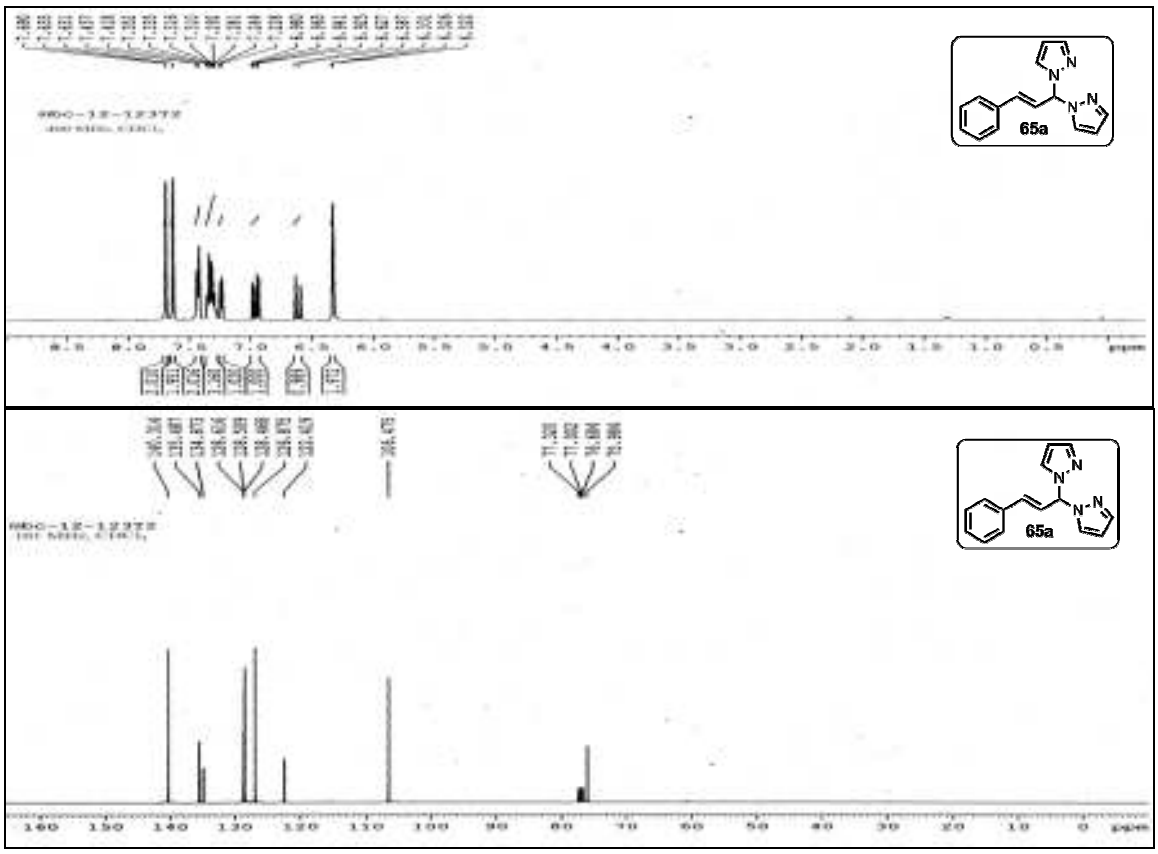
19) Molander, G. A.; Beaumard, F. *Org. Lett.* **2010**, *12*, 4022.

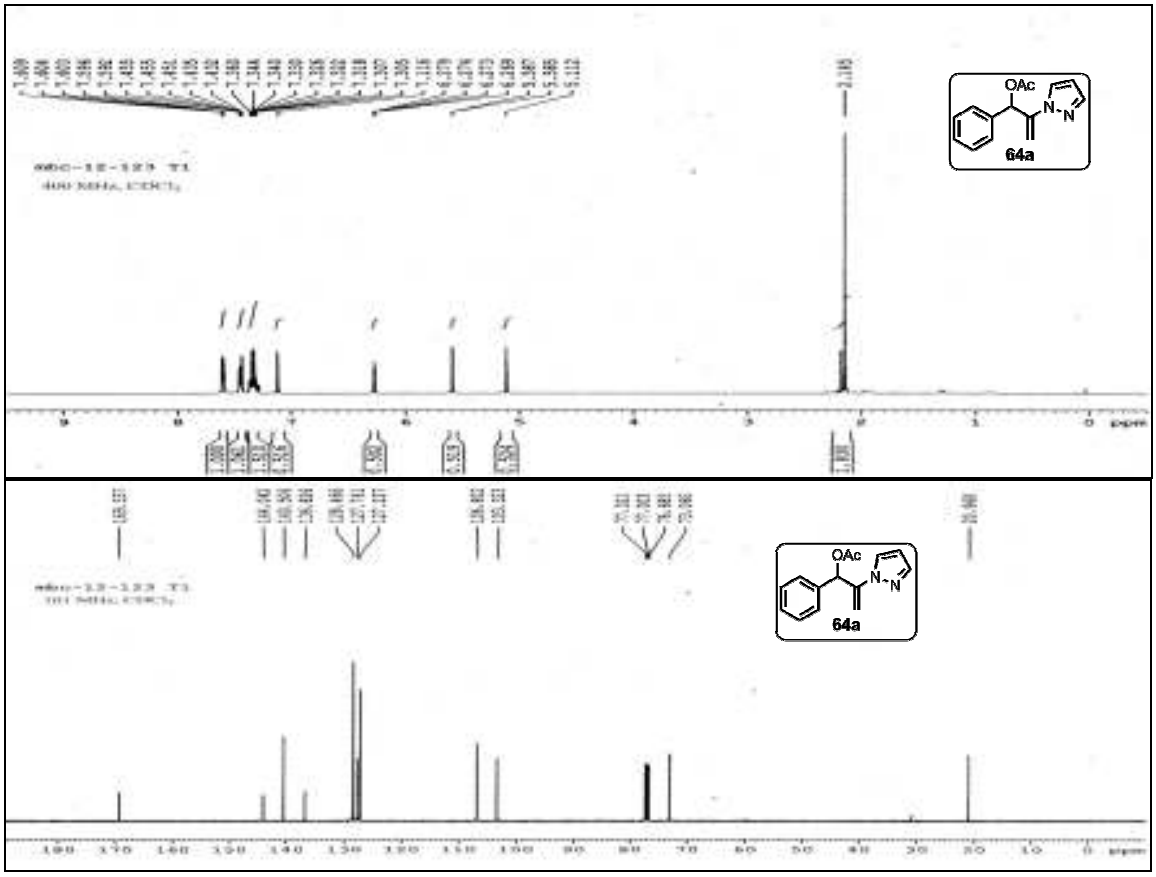
2.7. Spectra

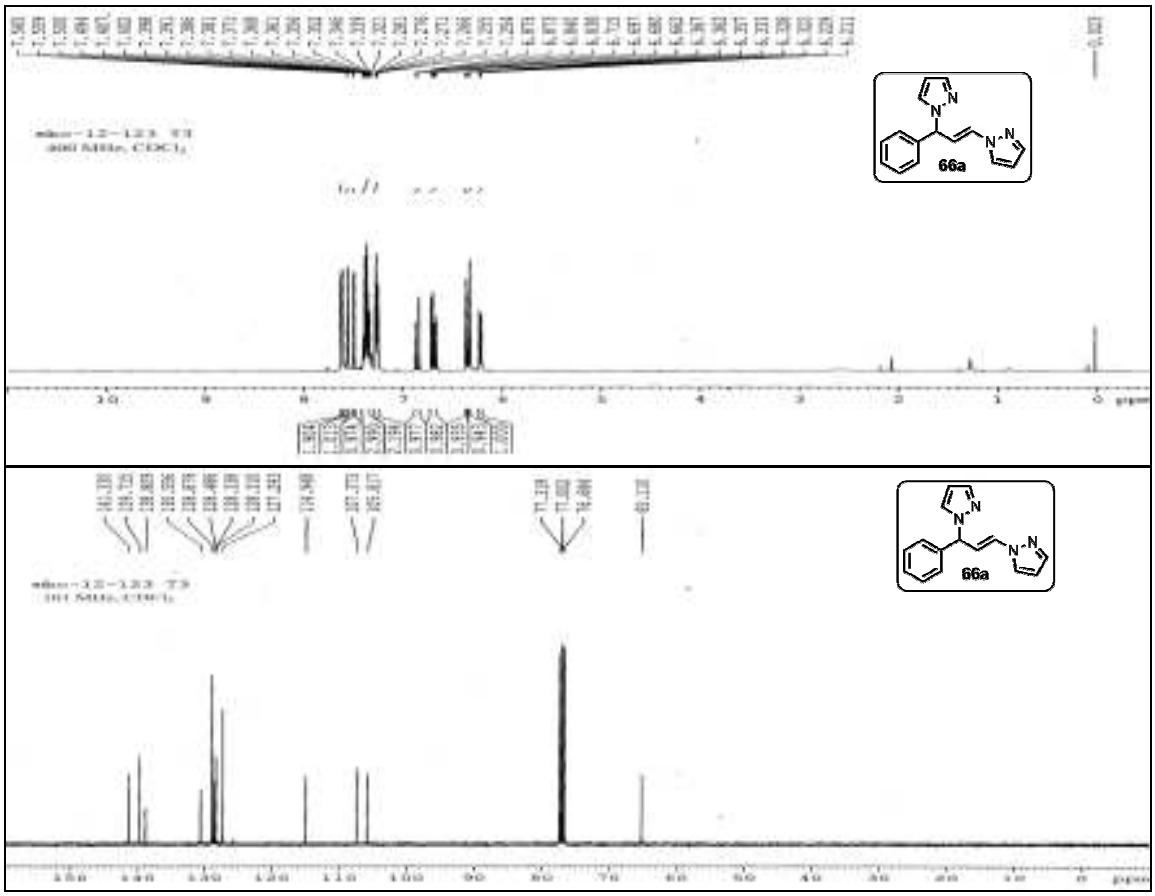


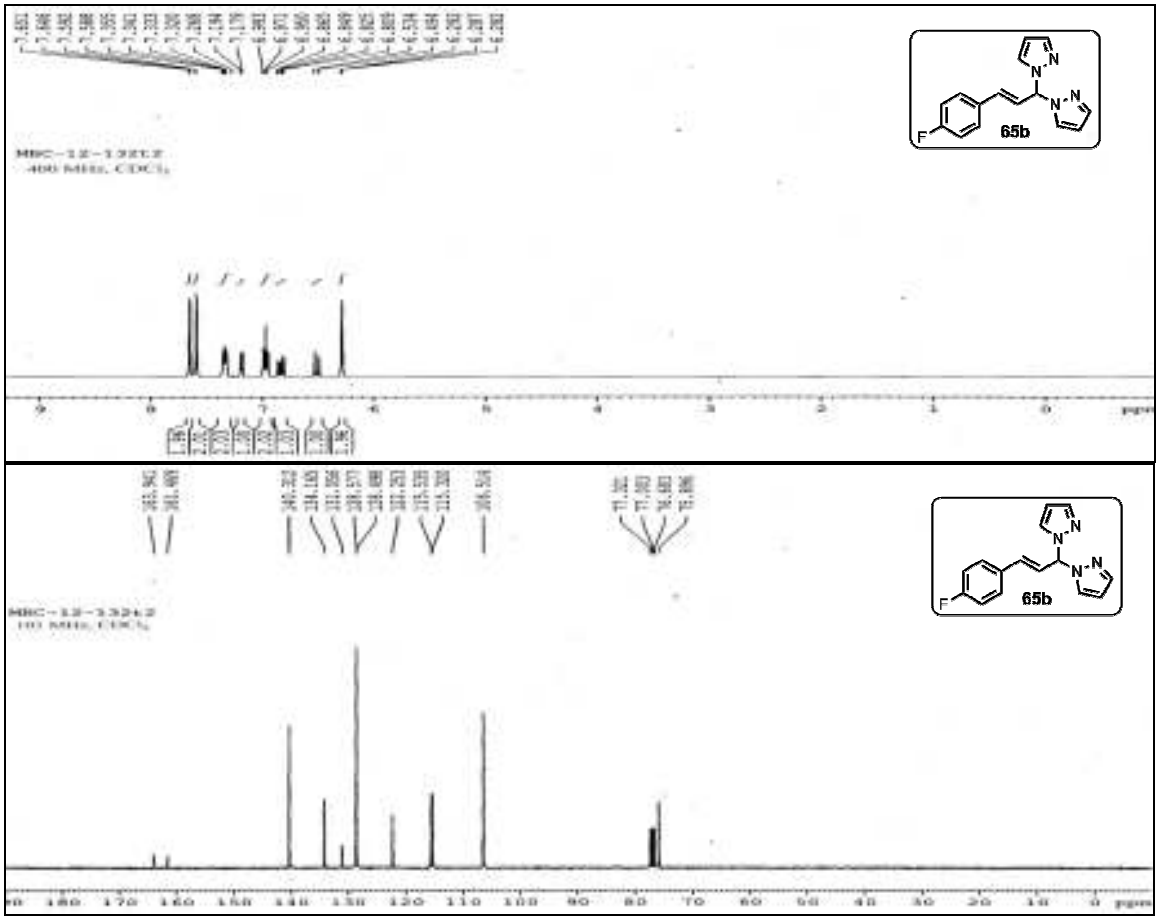


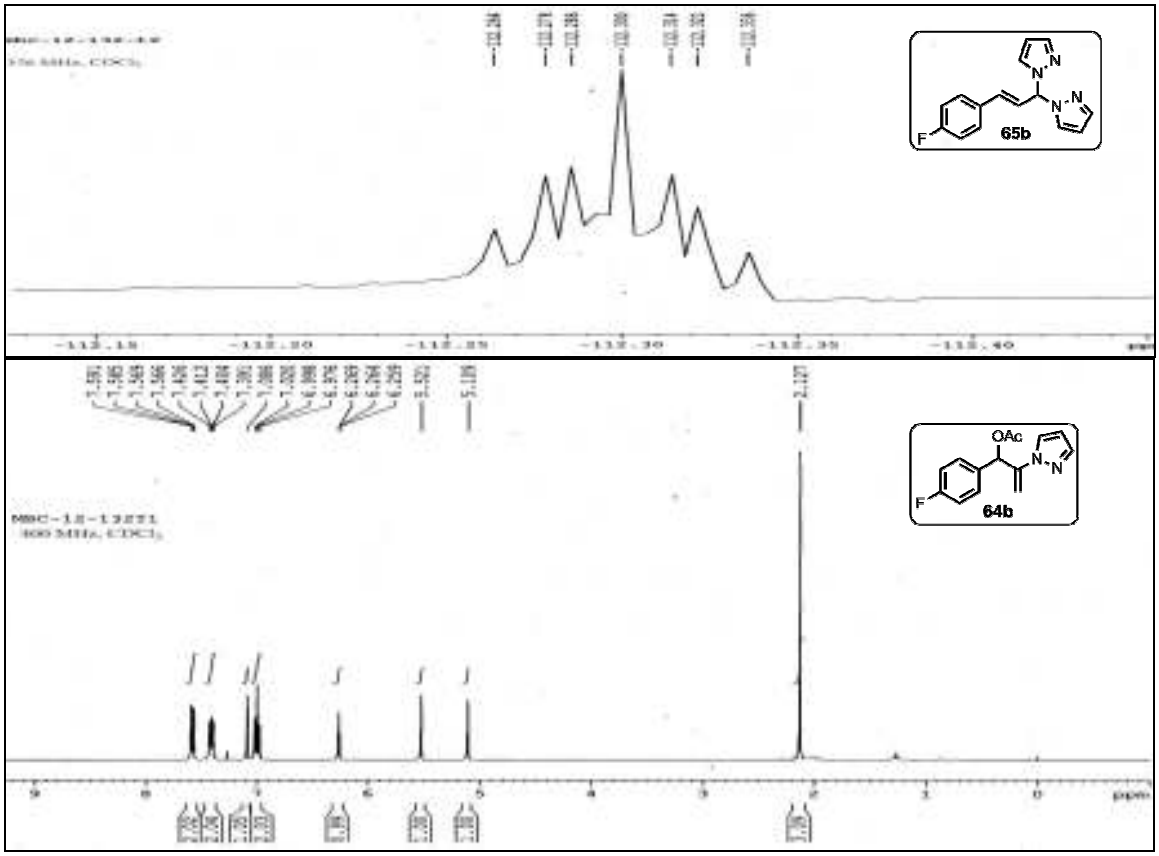

OAc
2r
OAc
2r

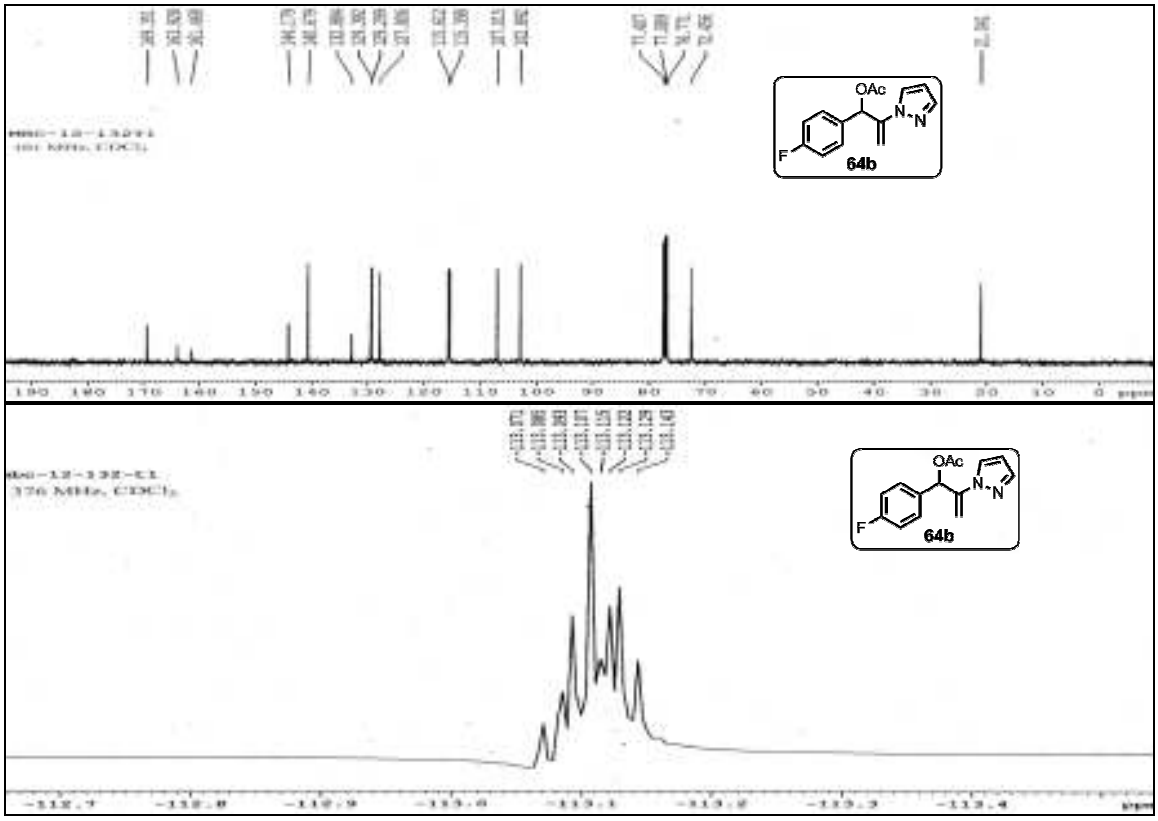

65a
65a

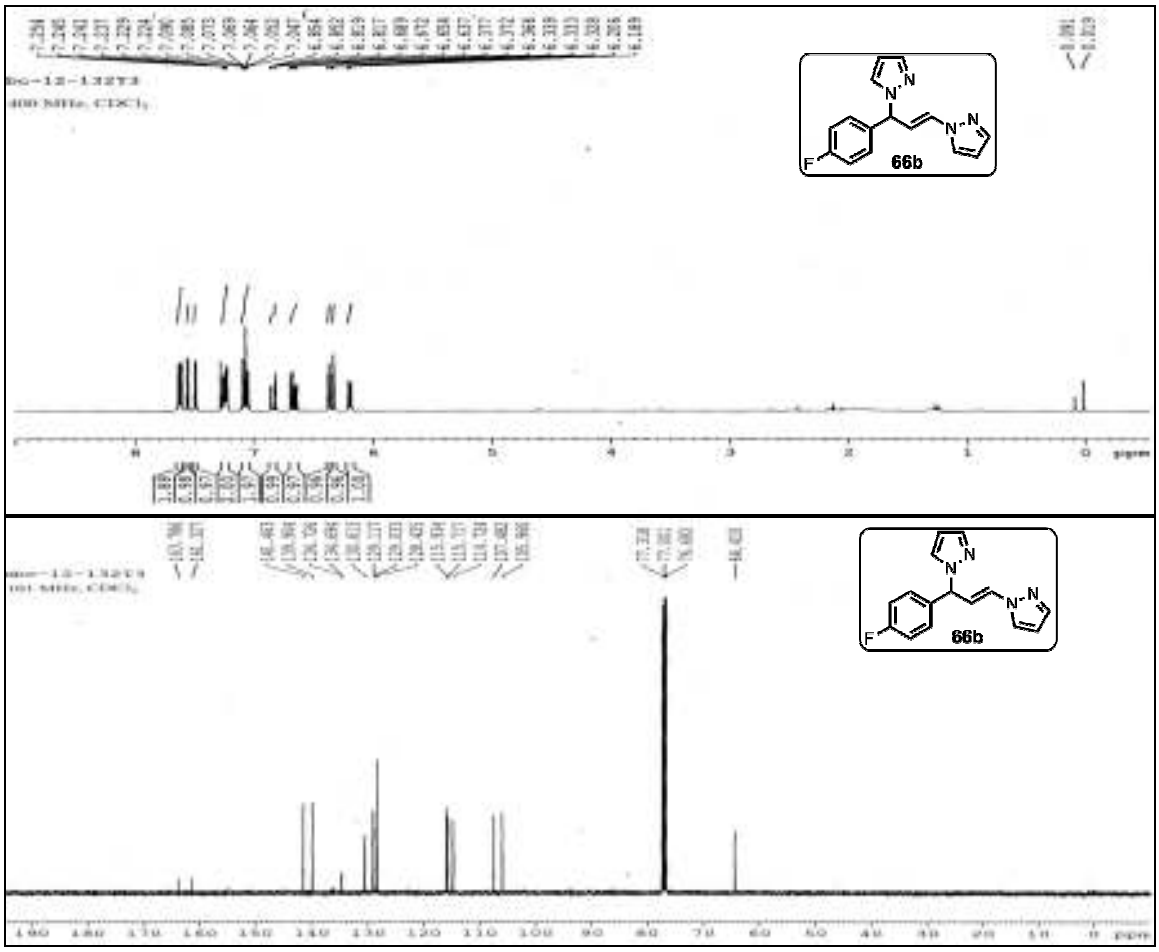

OAc
64a
OAc
64a

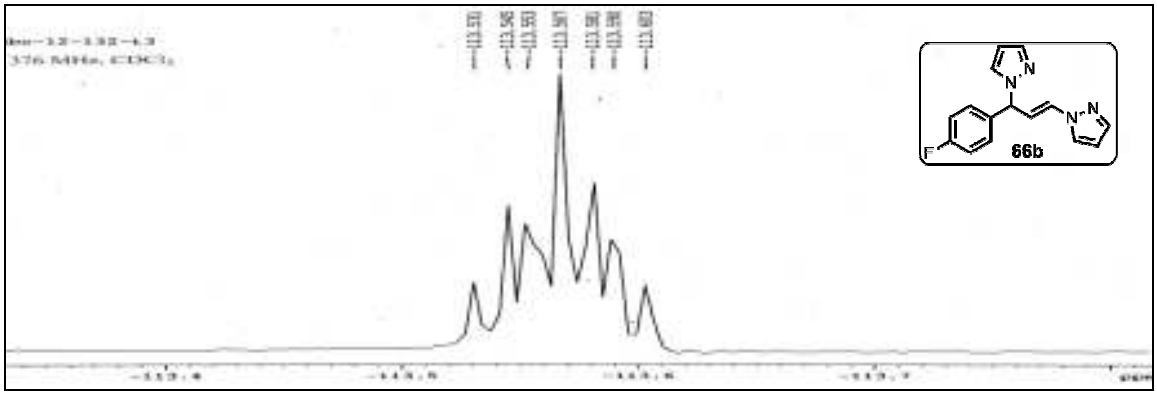

66a
66a

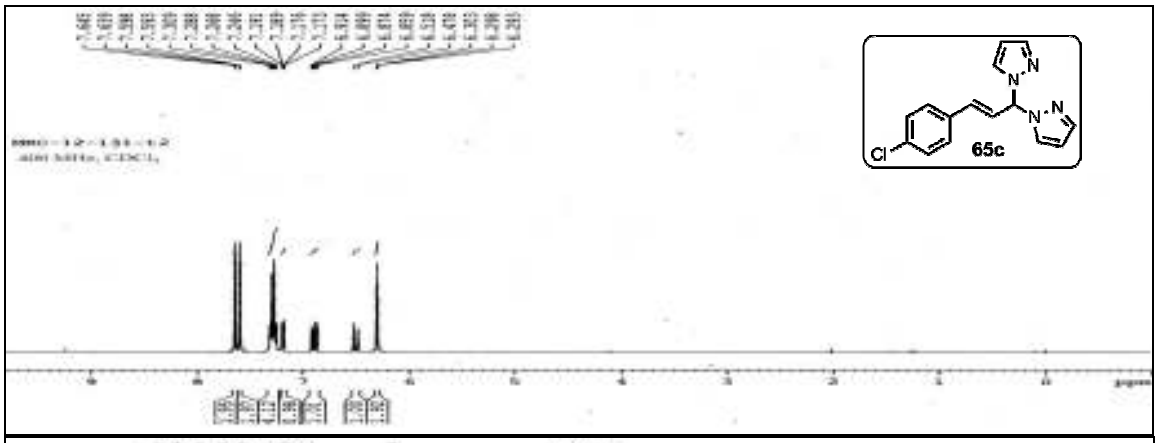

65b
65b

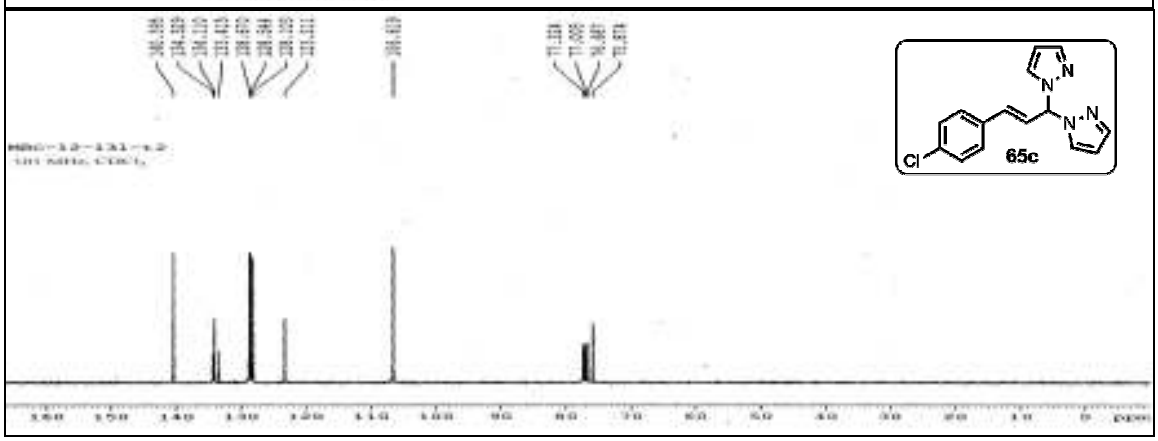

65b
64b
OAc

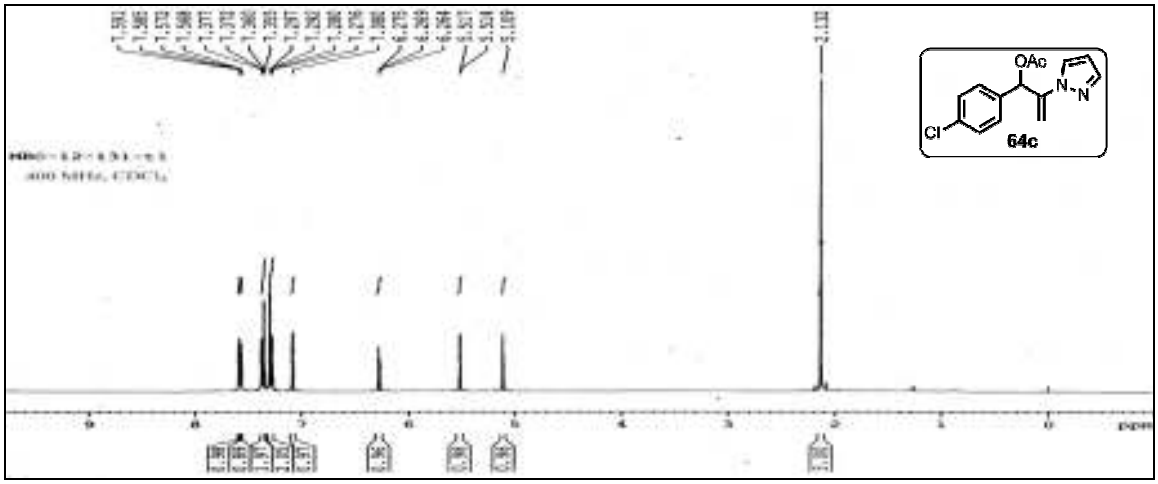

OAc
F
64b
OAc
F
64b

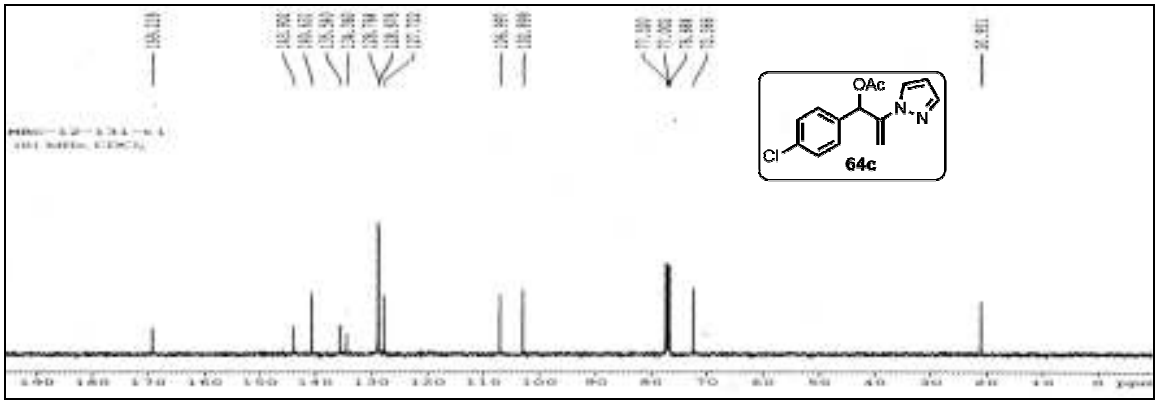

F
66b
F
66b

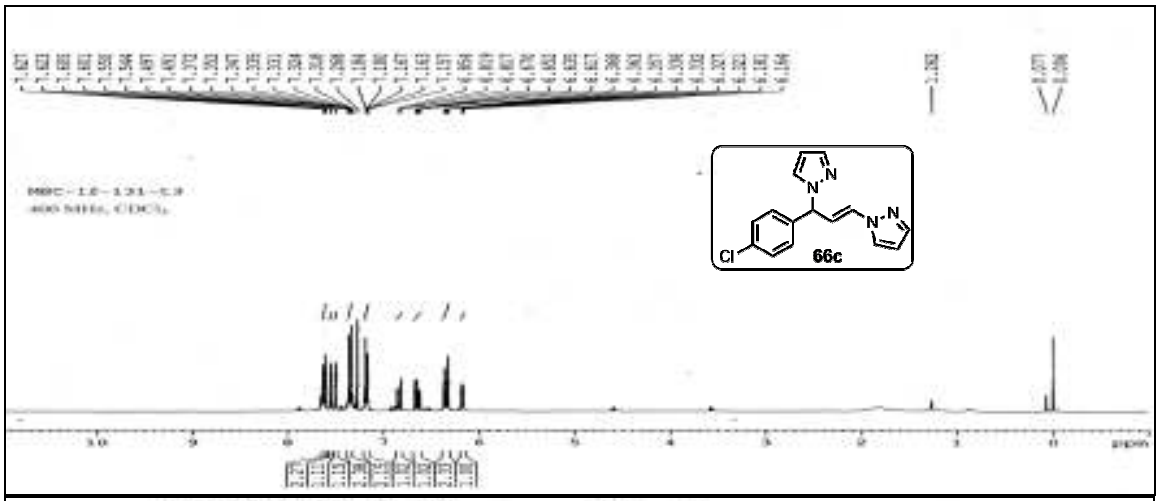

66b

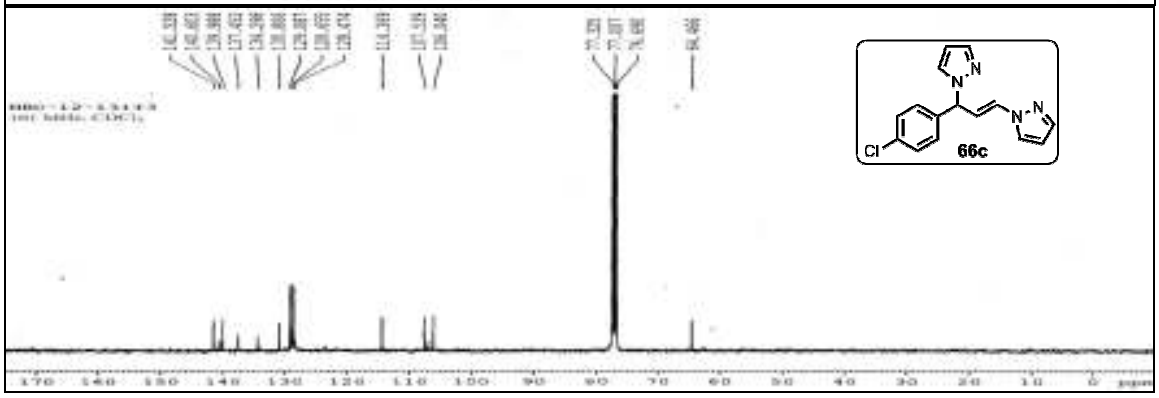

65c

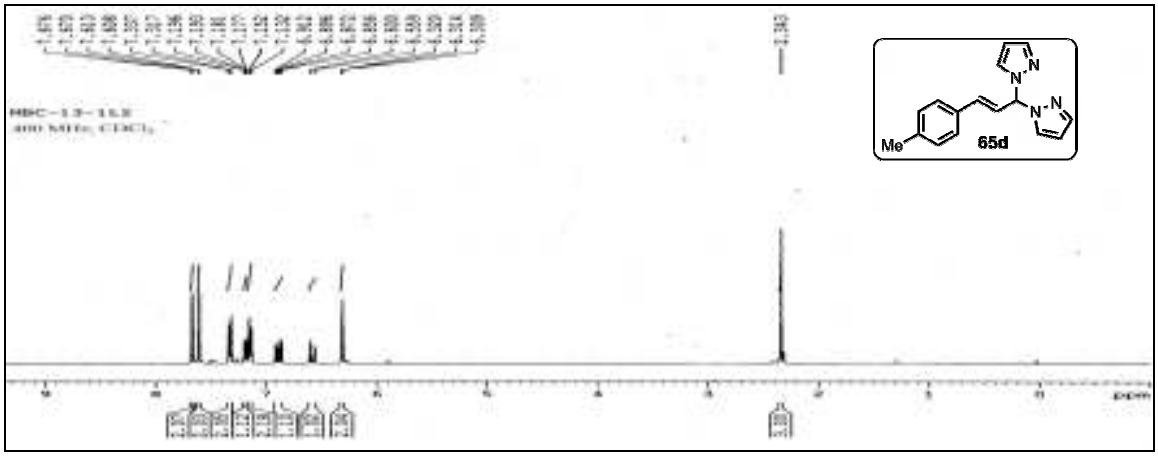

65c

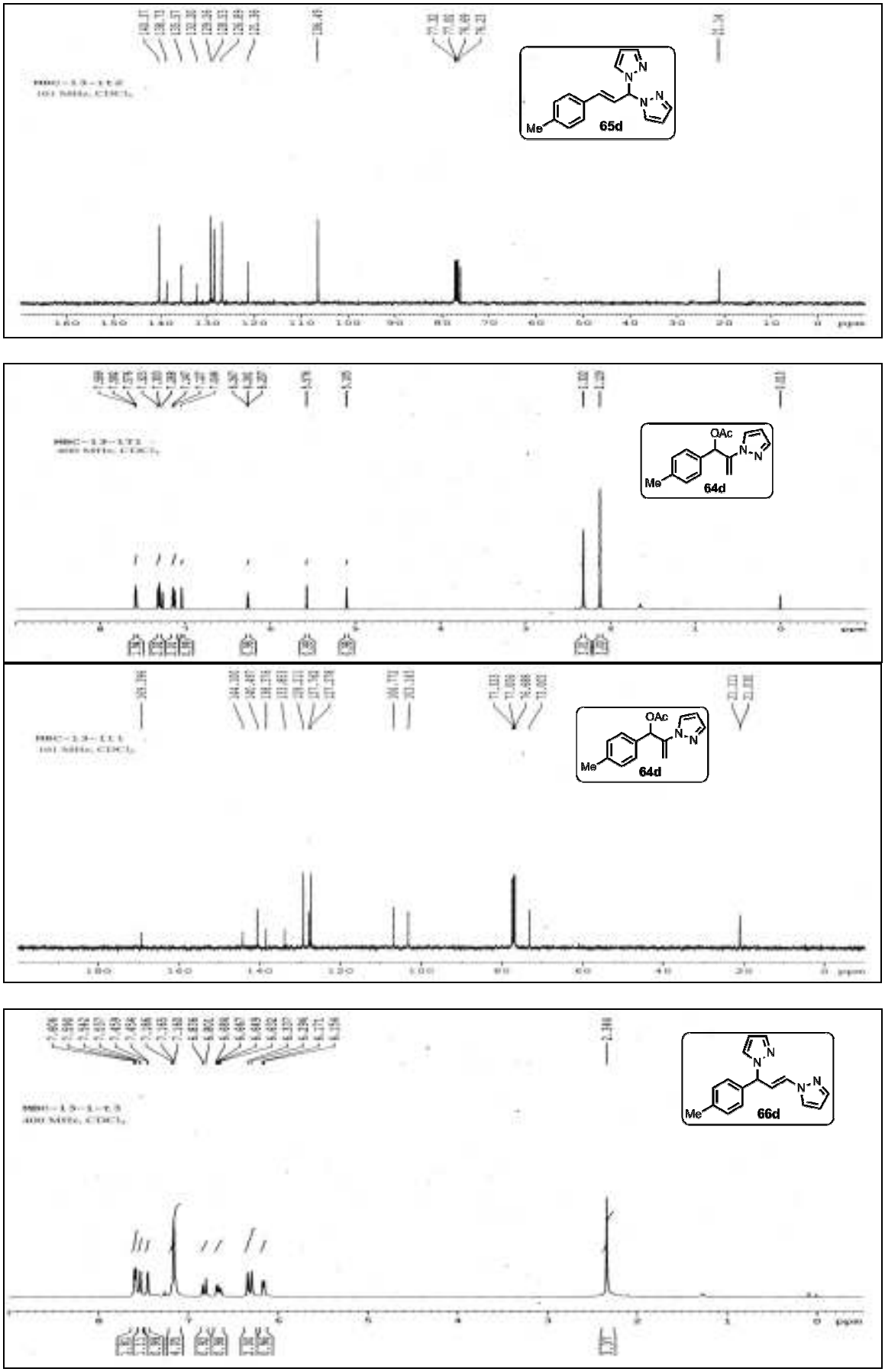

OAc
64c

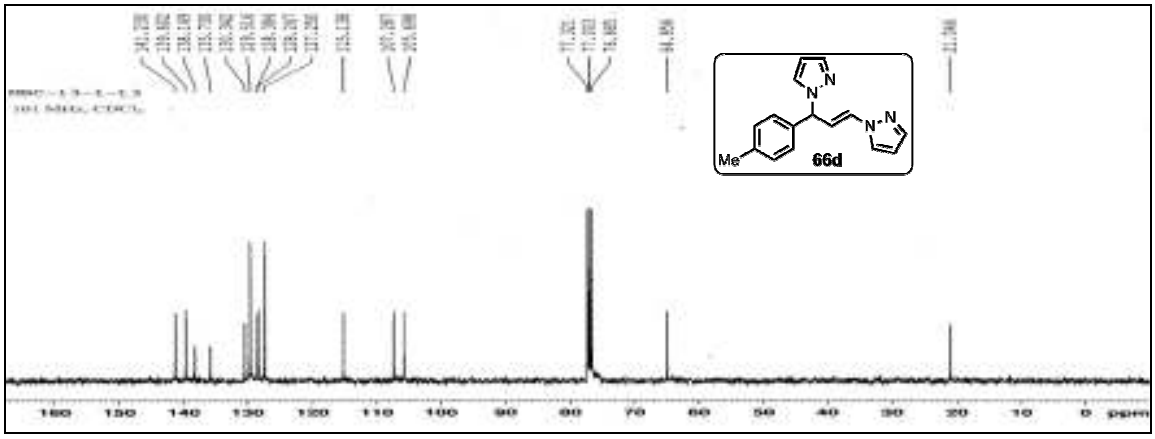

OAc
Cl
64c

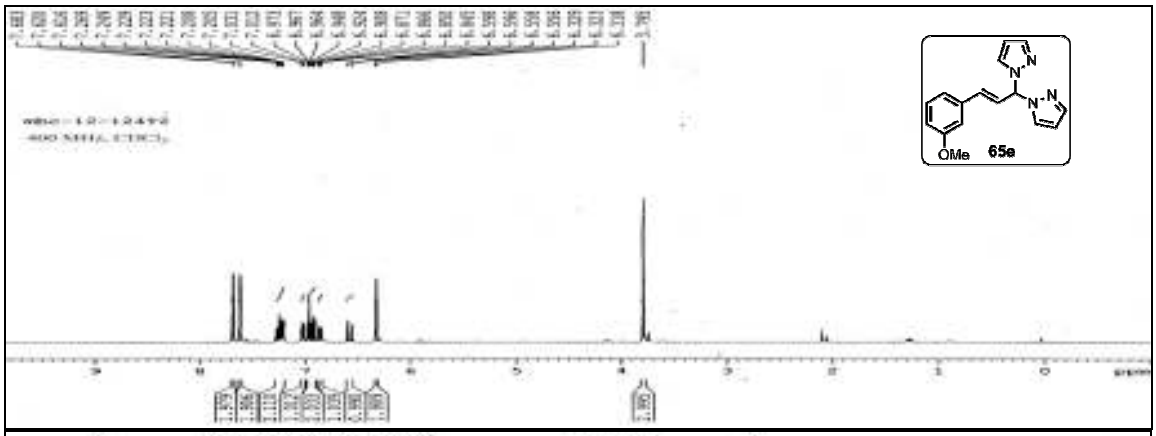

Cl
66c

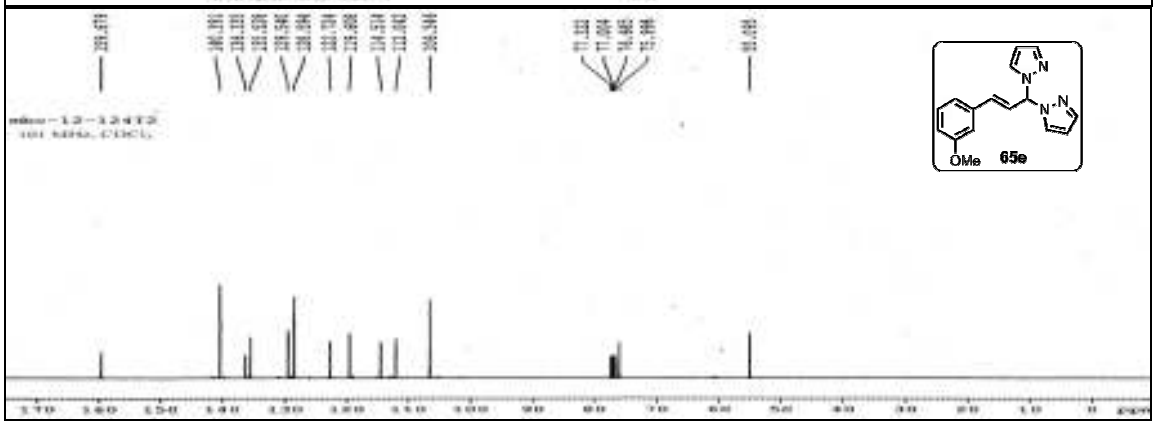

Cl
66c

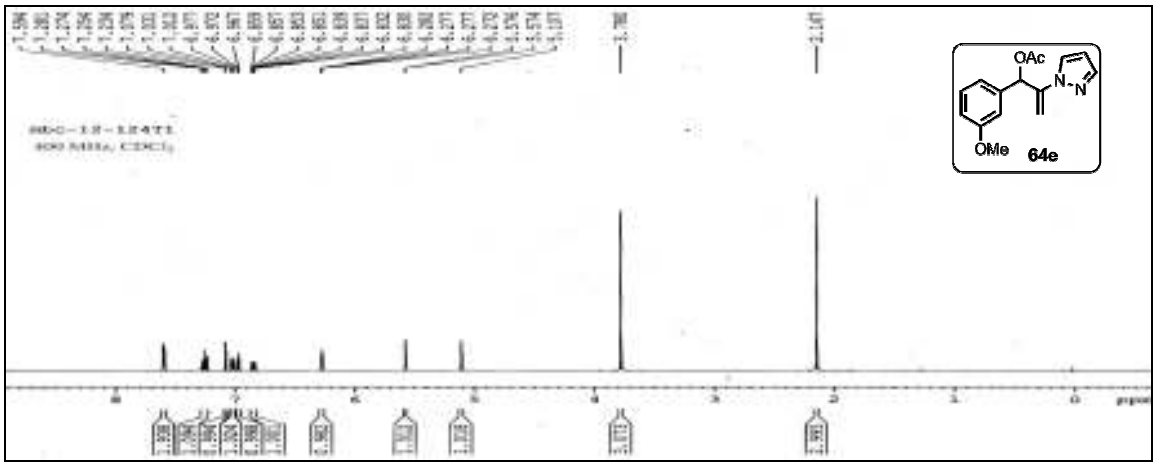

Me
65d

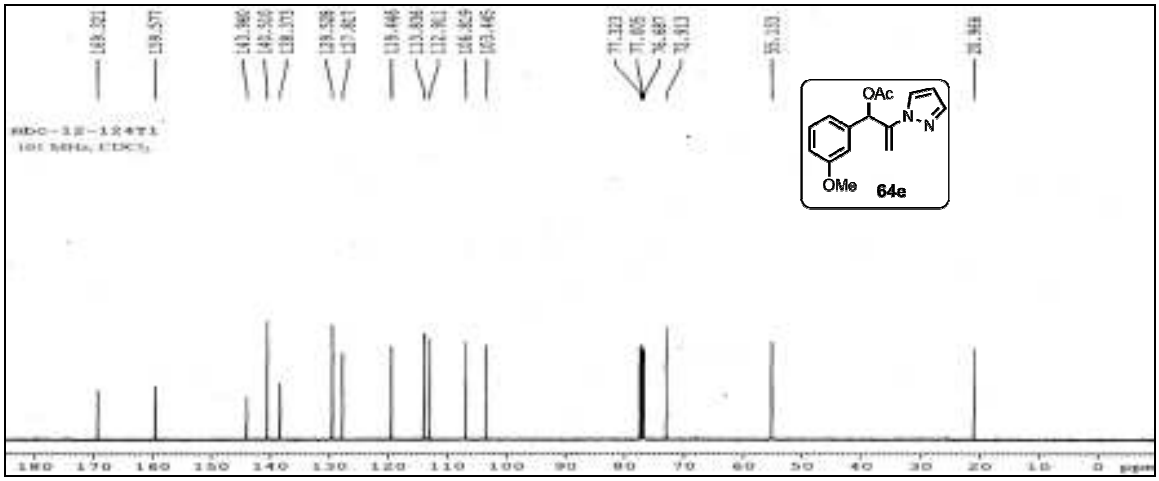

Me
65d
OAc
Me
64d
OAc
Me
64d
Me
66d

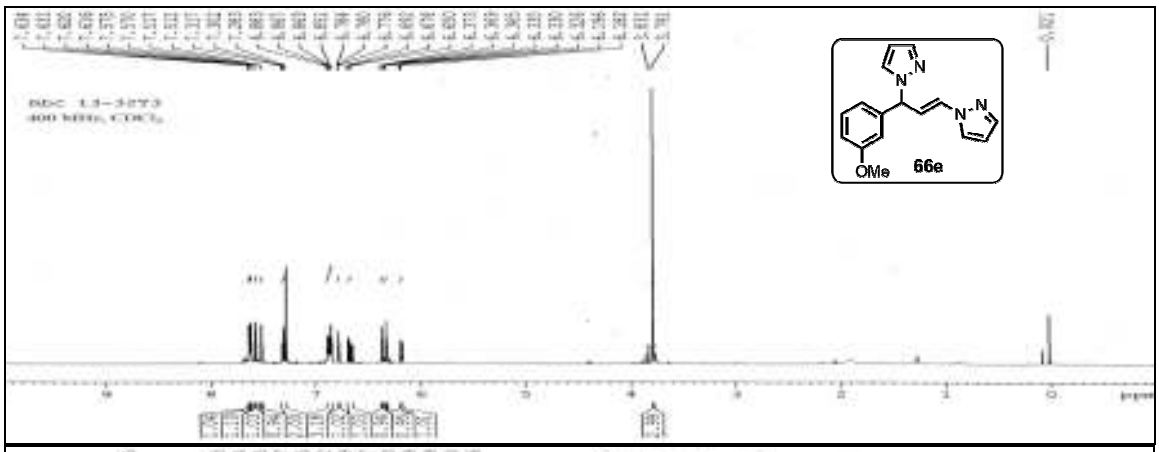

Me
66d

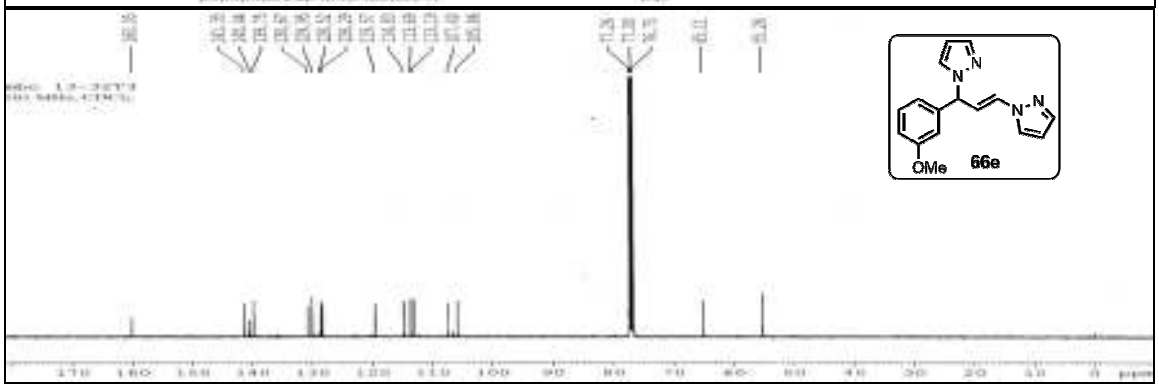

OMe
65e

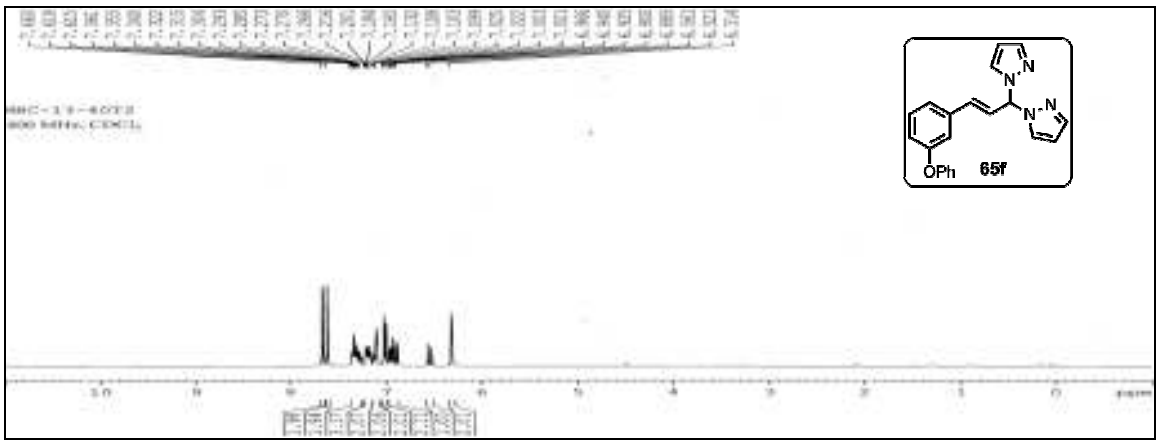

OMe
65e

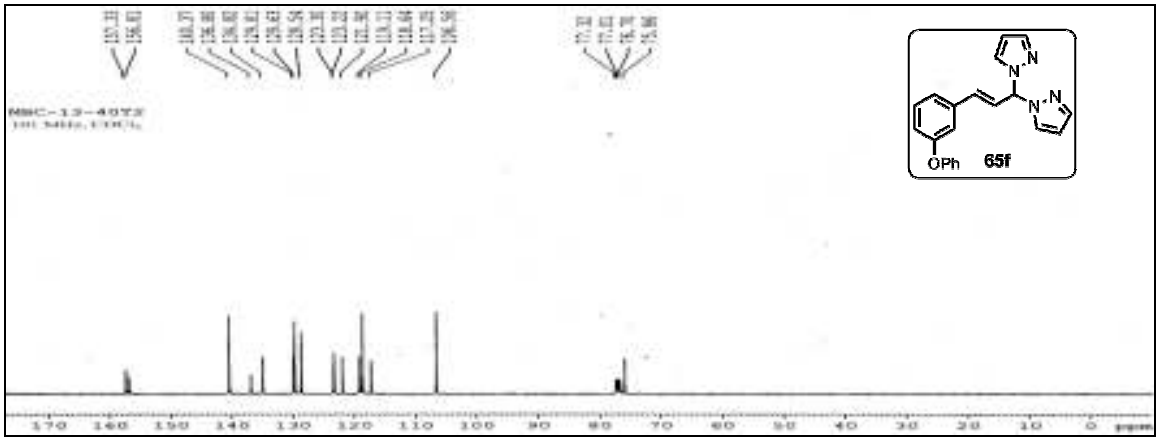

OAc
OMe
64e

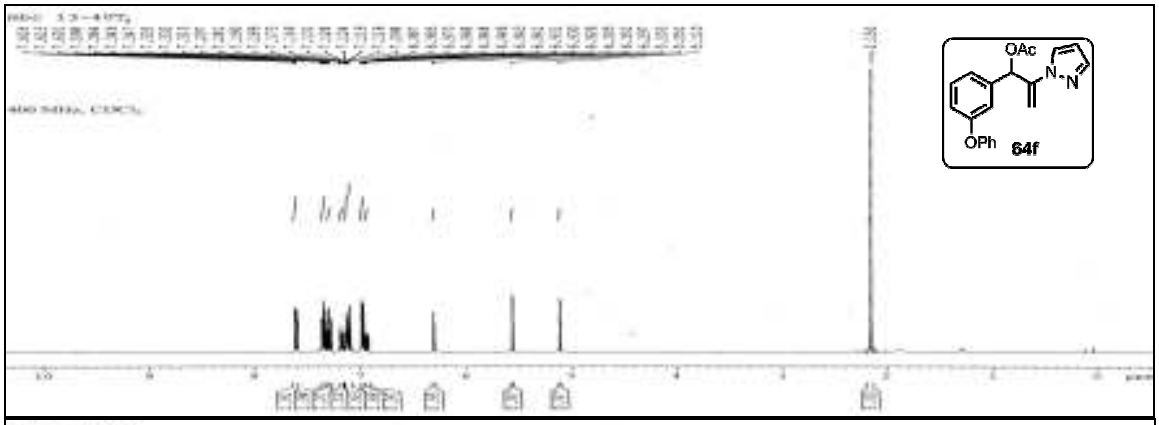

OAc
OMe
64e

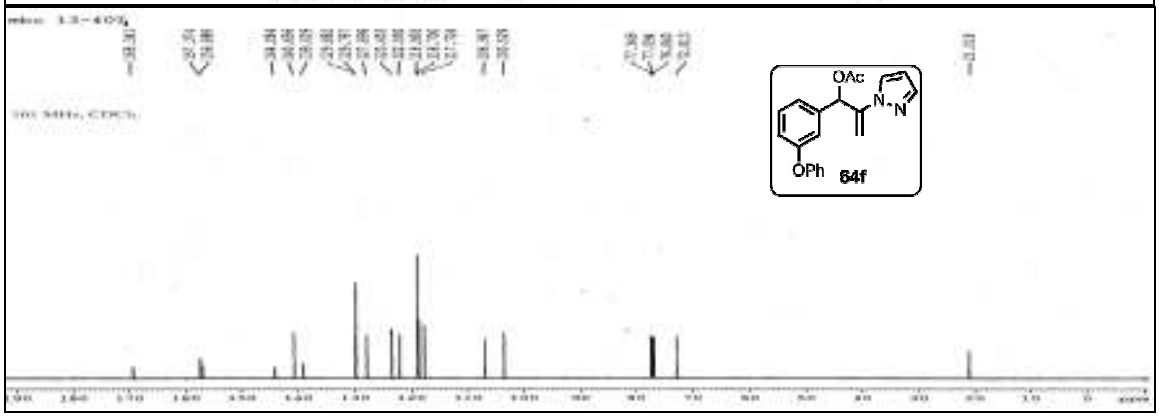

OMe
66e

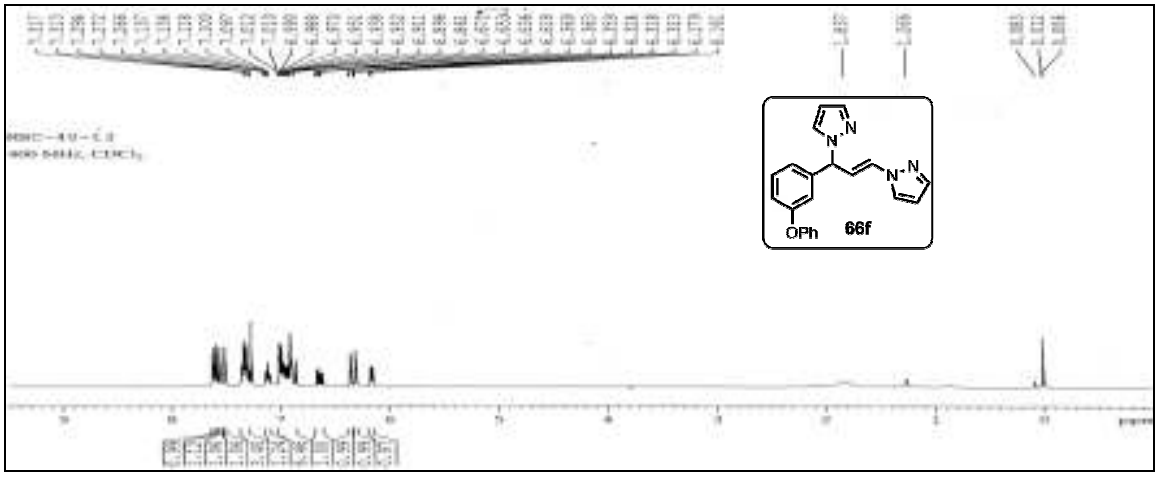

OMe
66e

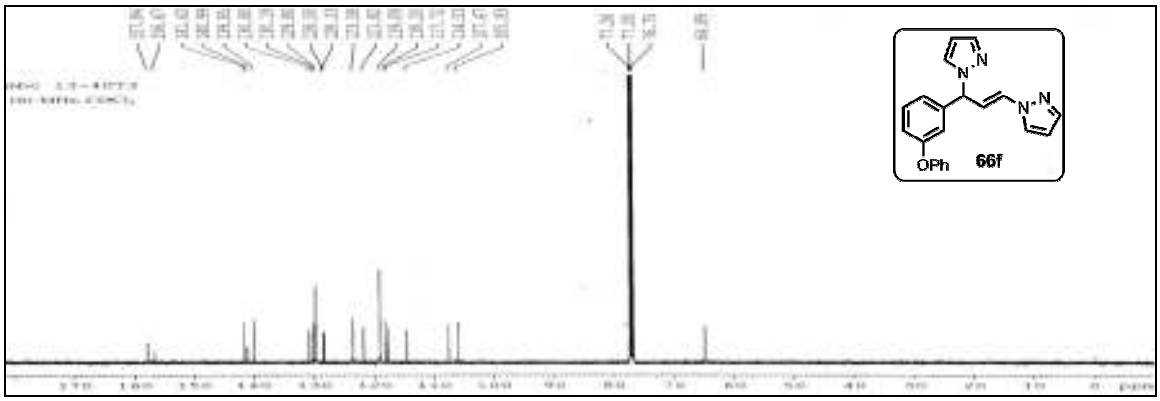

OPh
65f

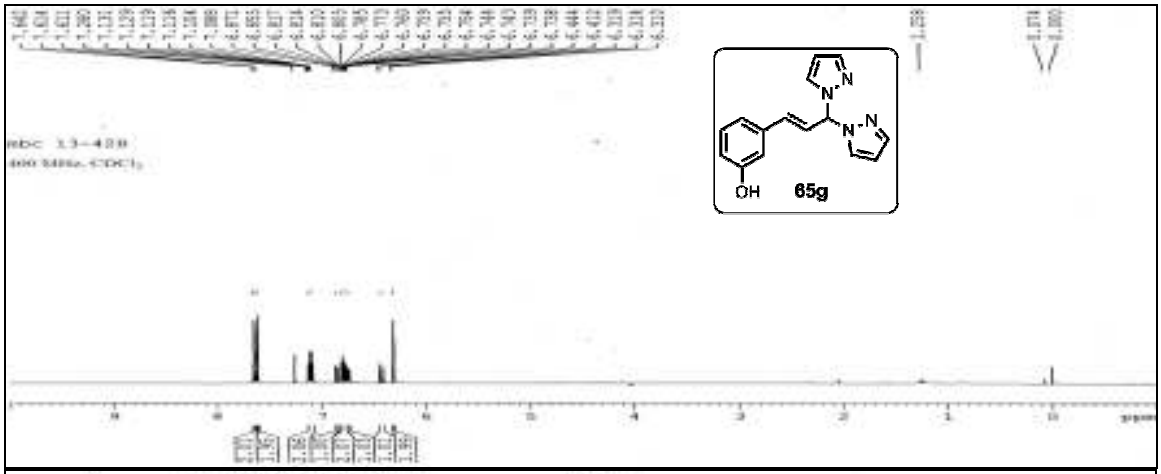

OPh
65f

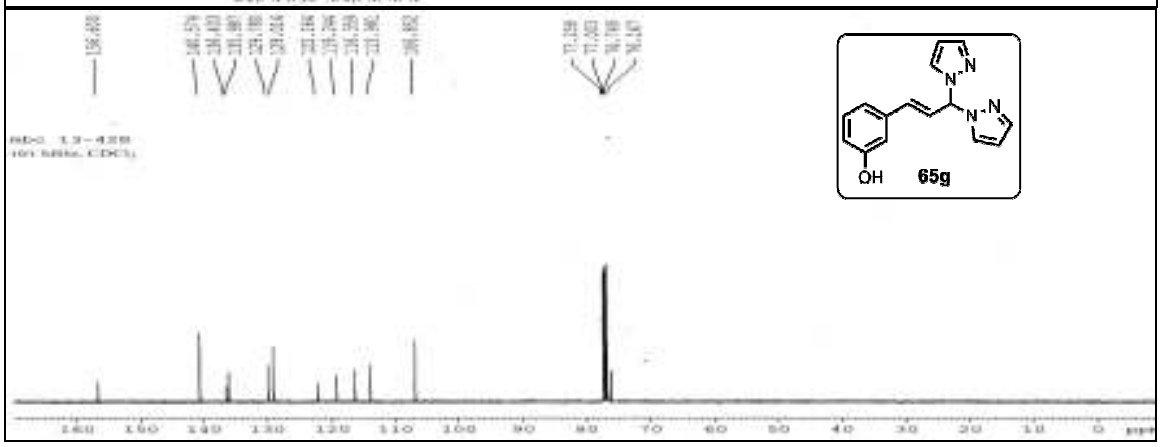

OAc
OPh
64f

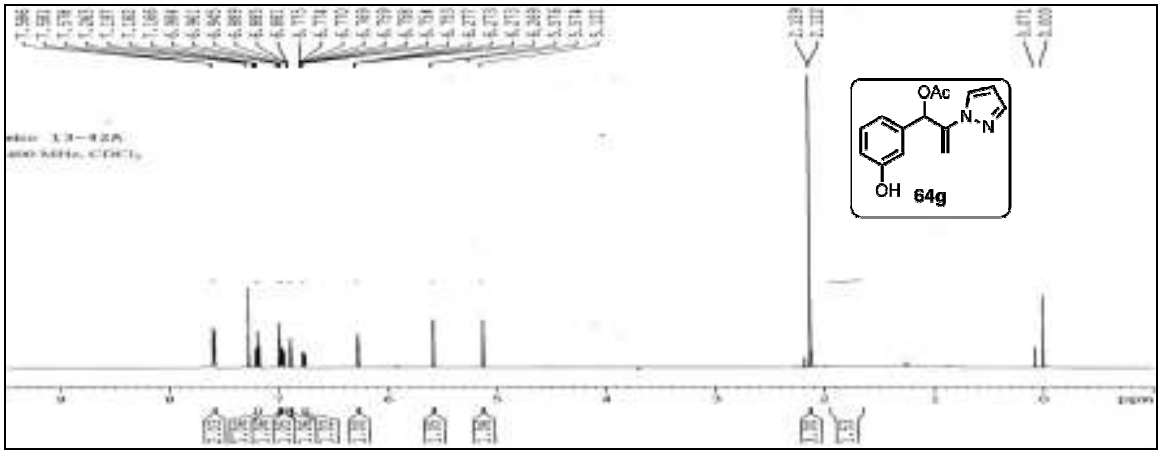

OAc
OPh
64f


OPh
66f

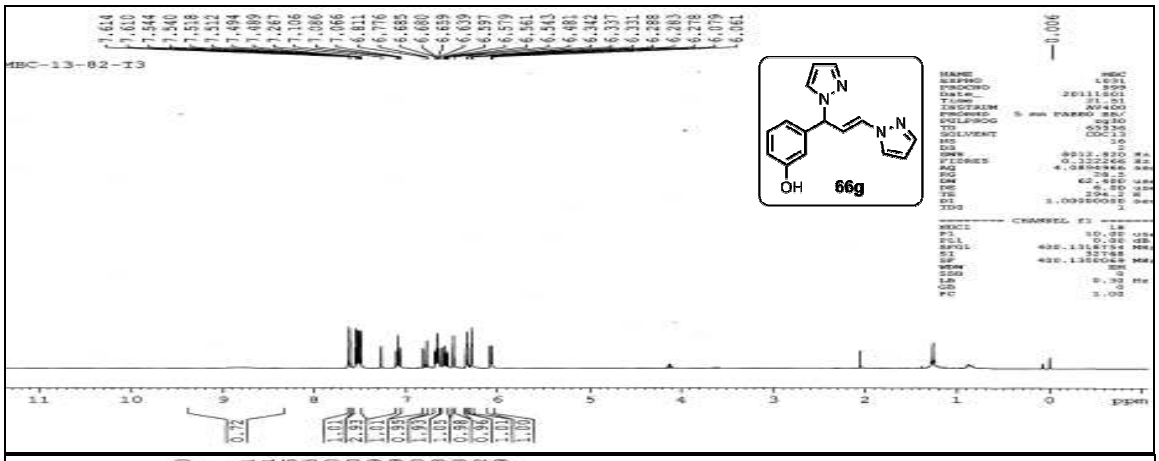

OPh
66f

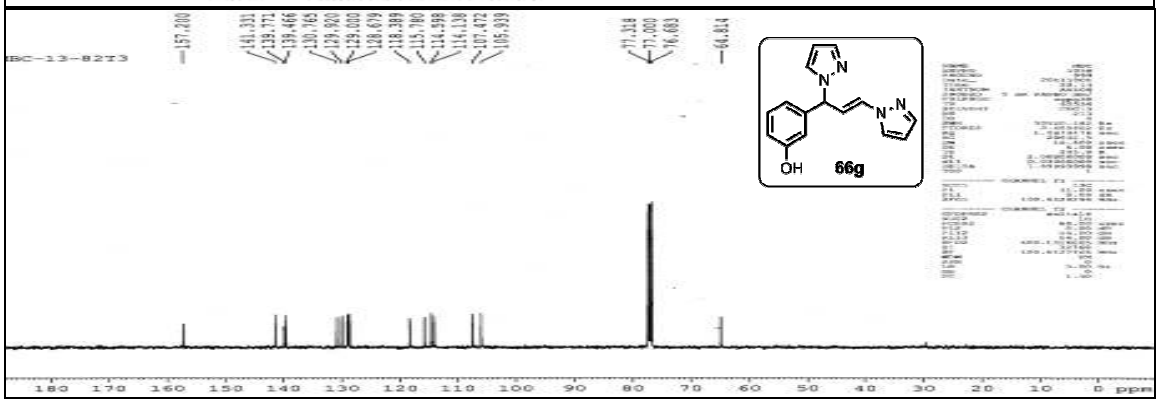

OH
65g

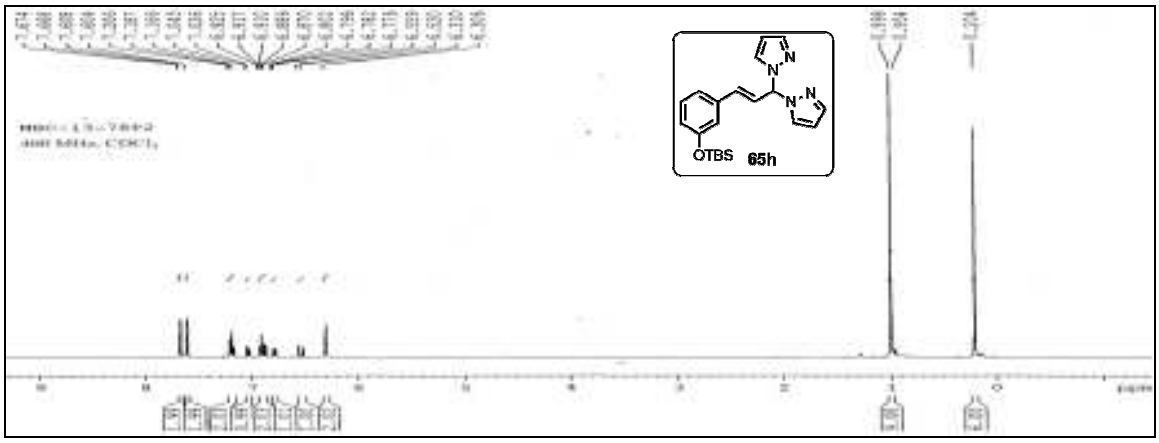

OH
65g

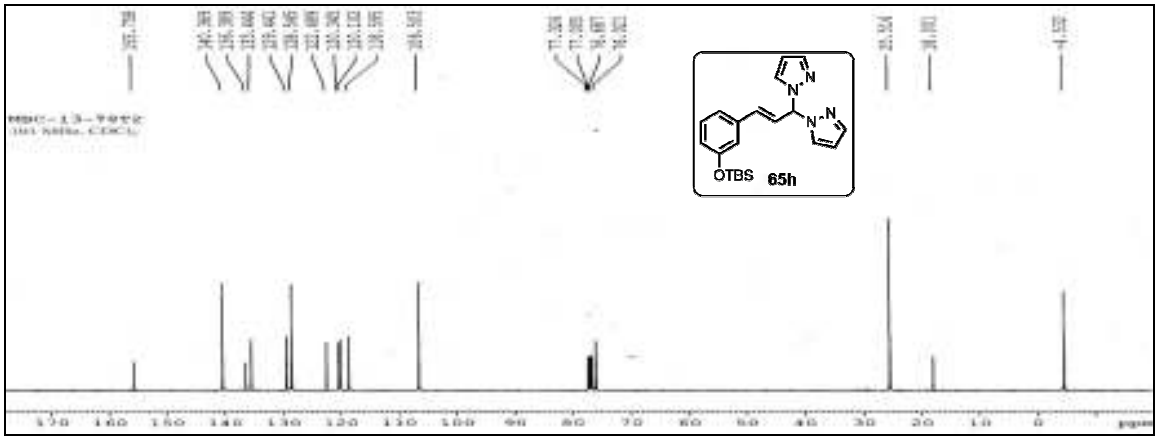

OAc
OH
64g

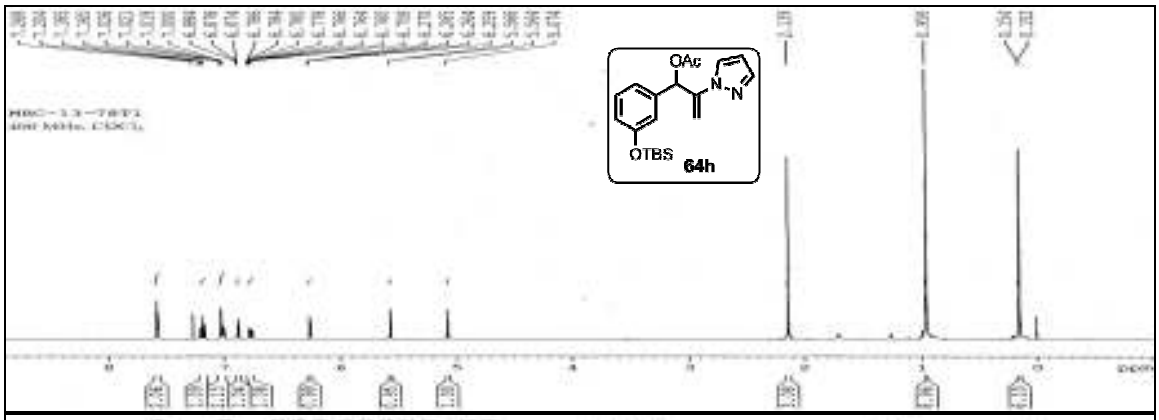

OAc
OH
64g

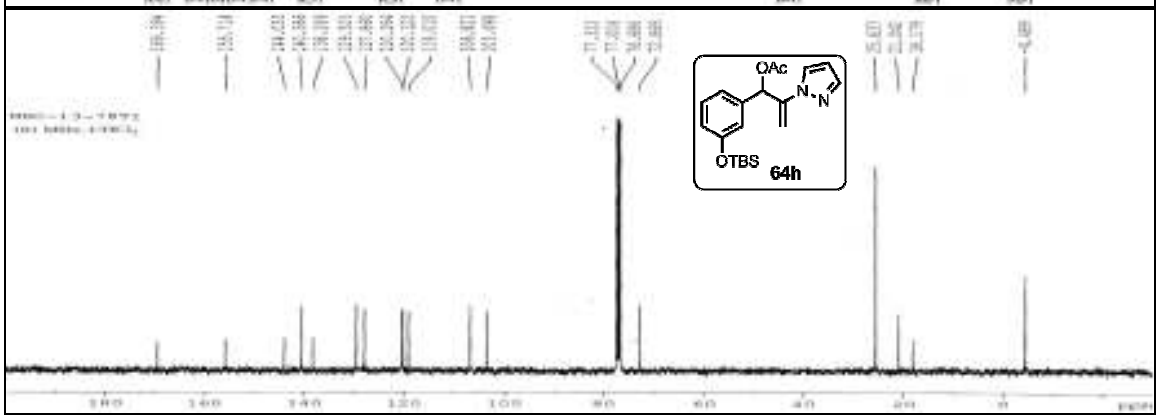

OH
66g

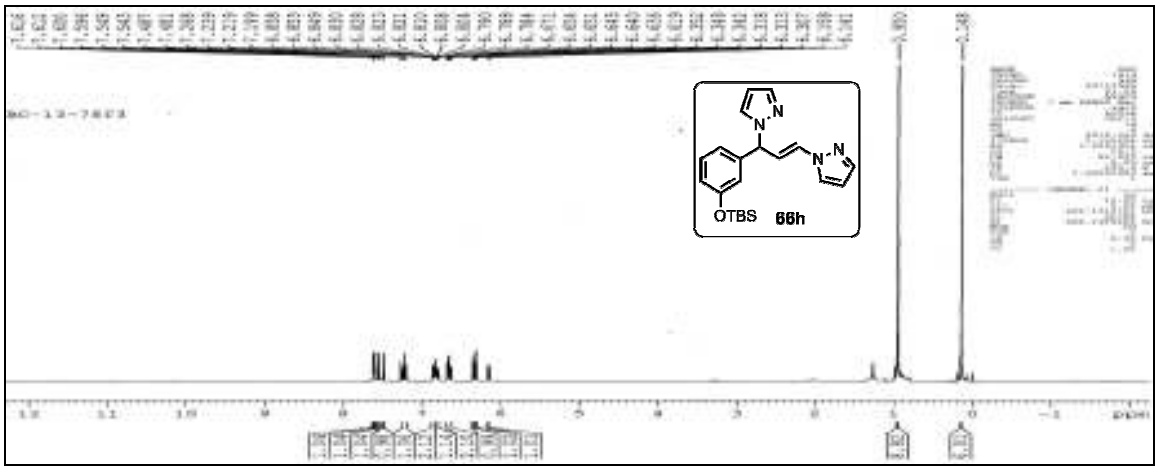

OH
66g

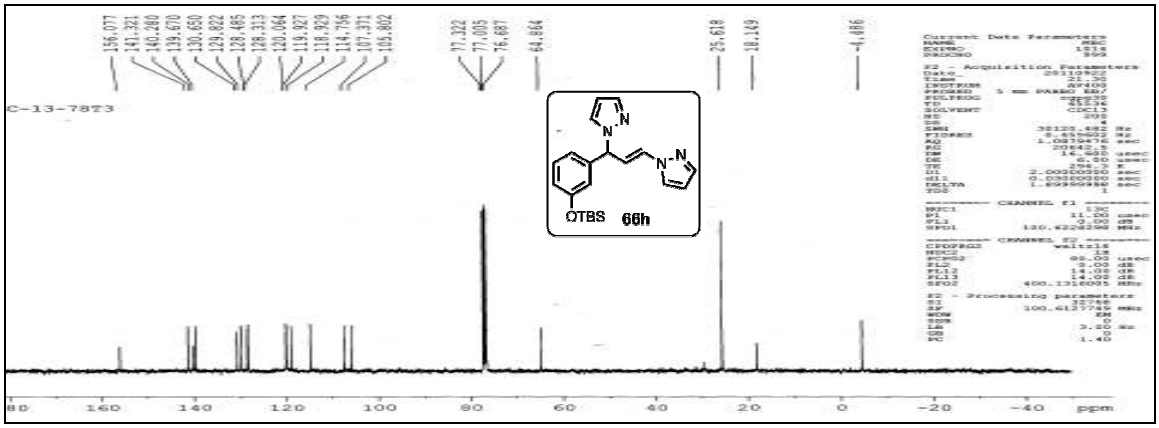

OTBS
65h

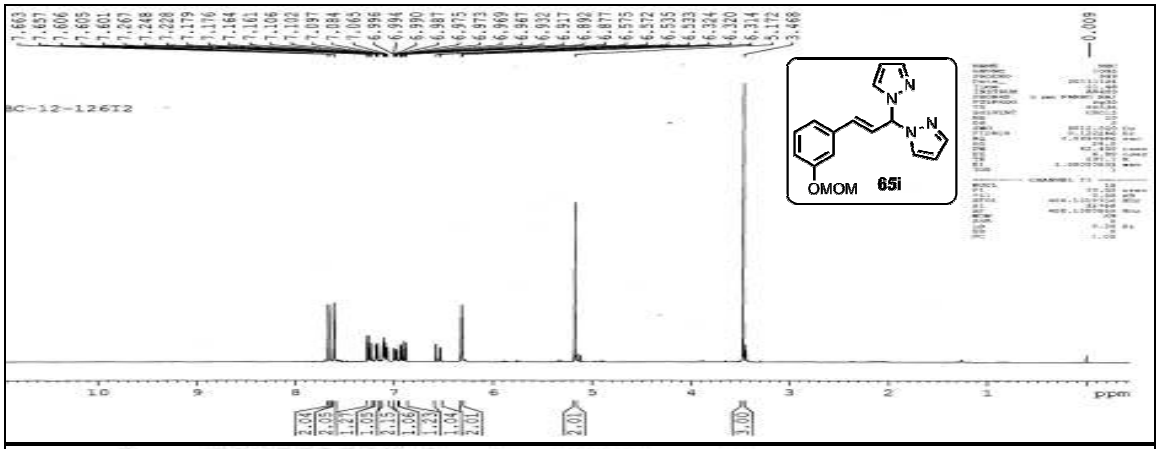

OTBS
65h

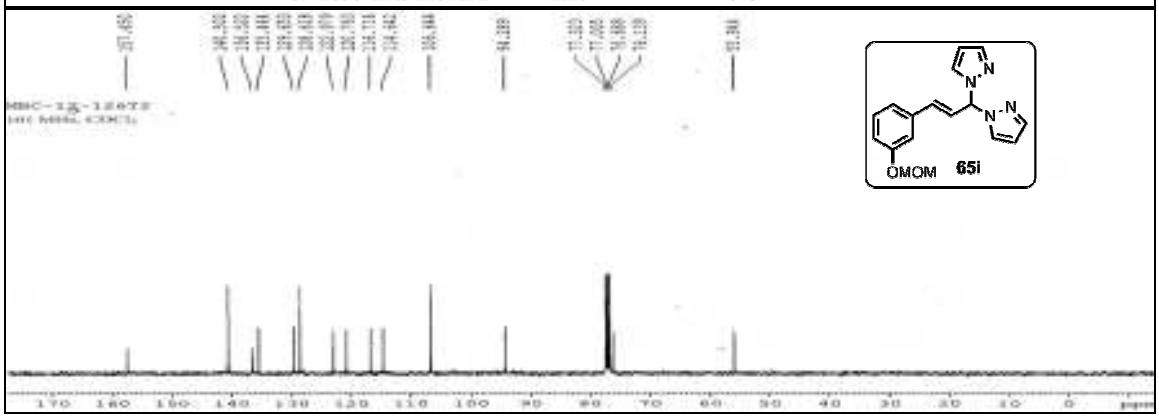

OAc
OTBS
64h

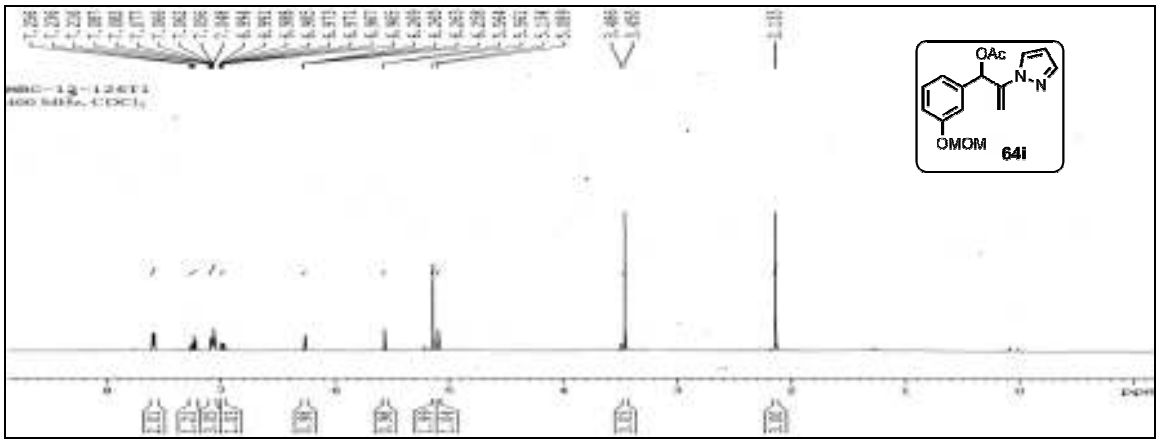

OAc
OTBS
64h

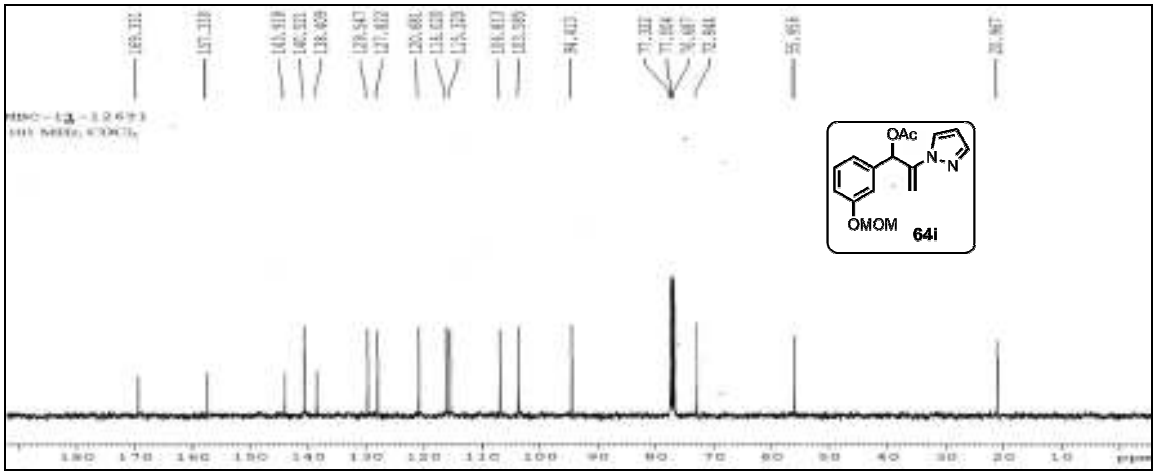

OTBS
66h

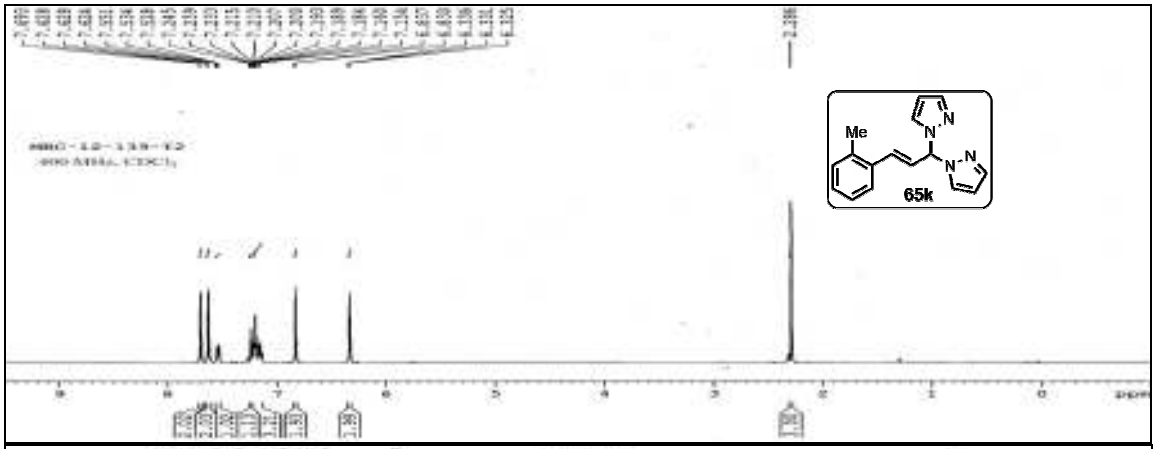

OTBS 66h

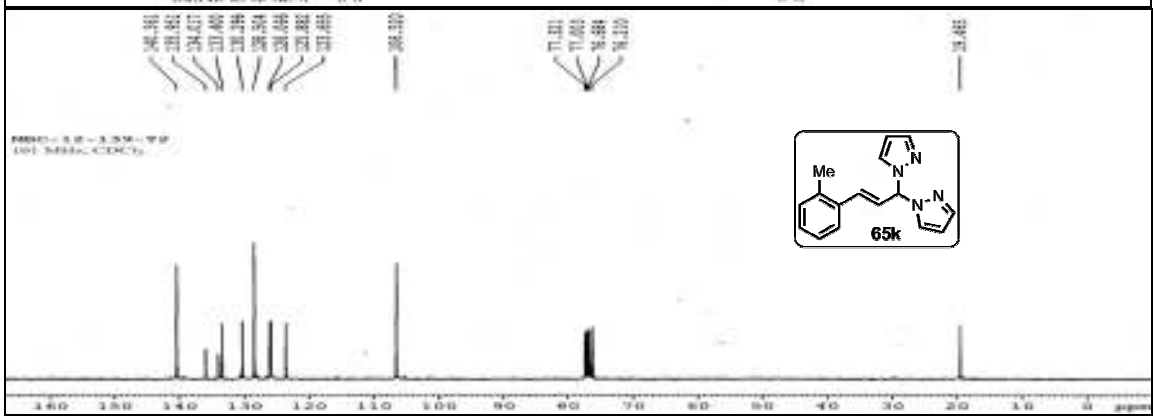

OMOM 65i

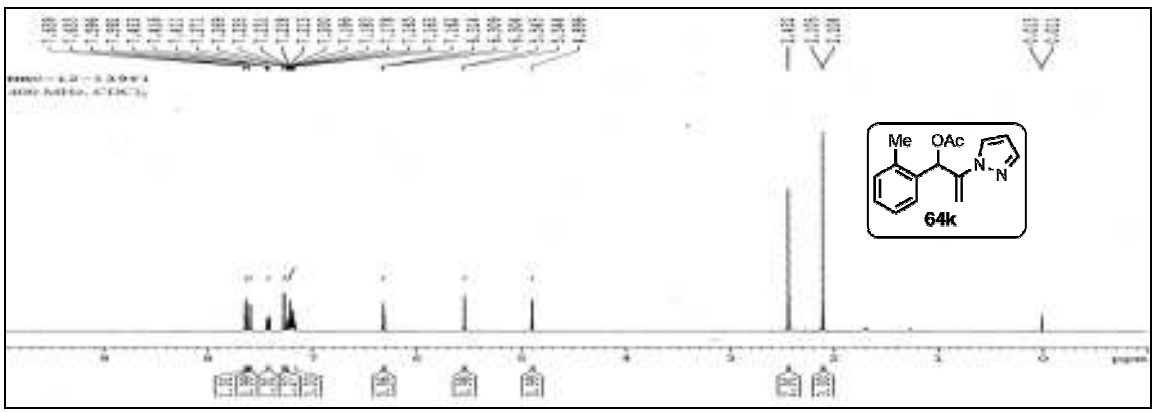

OMOM 65i

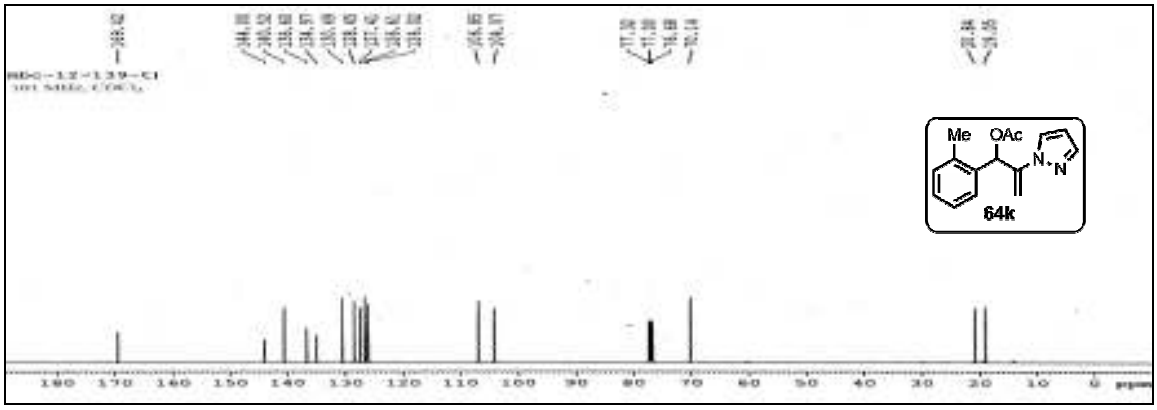

OAc
OMOM 64i

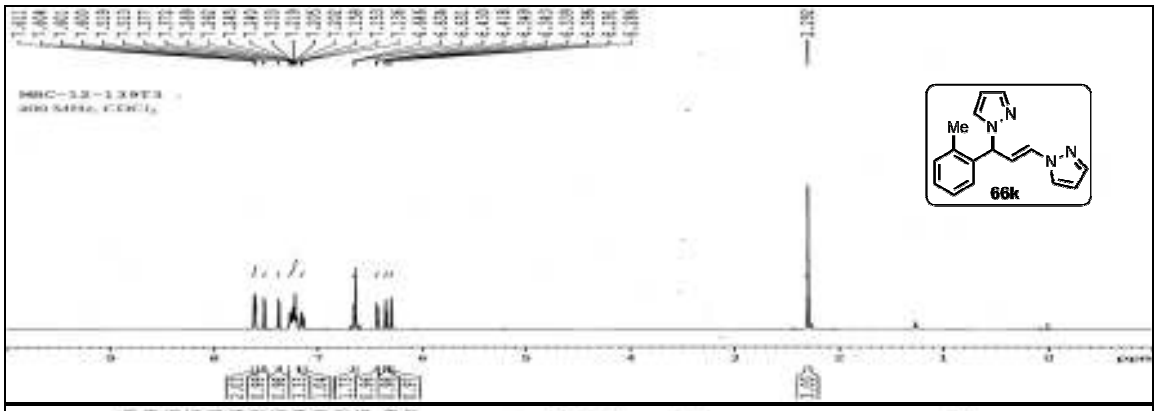

OAc
OMOM
64l

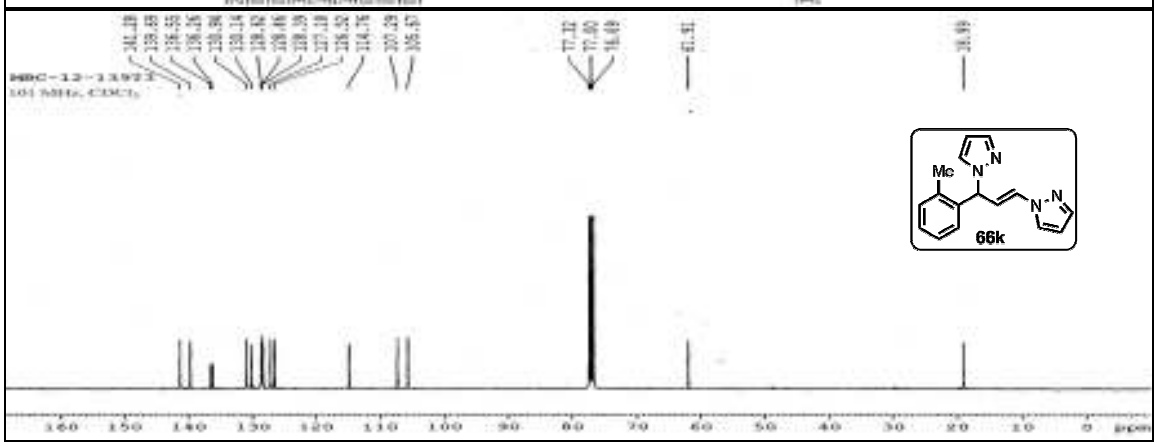

Me
65k

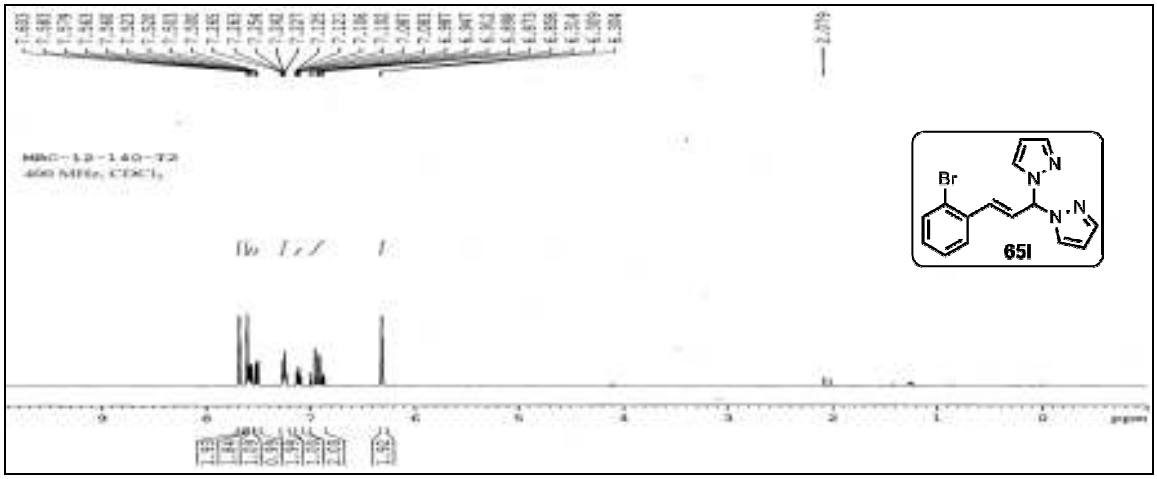

Me
65k

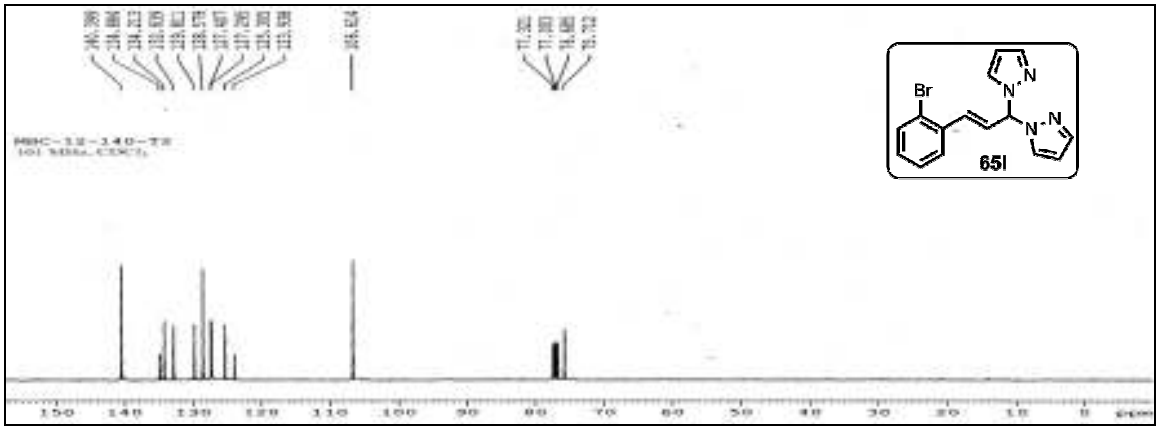

Me
OAc
64k

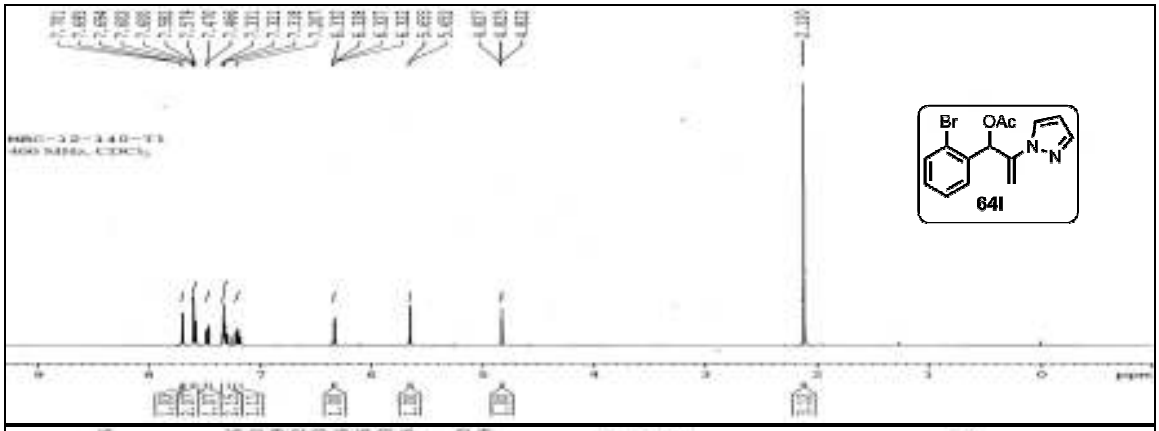

Me
OAc
64k

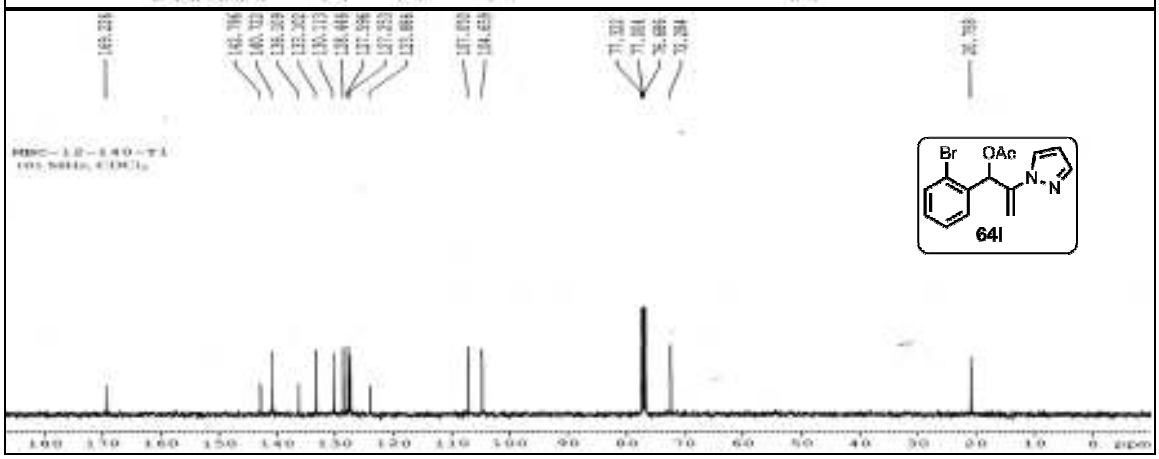

Me
66k

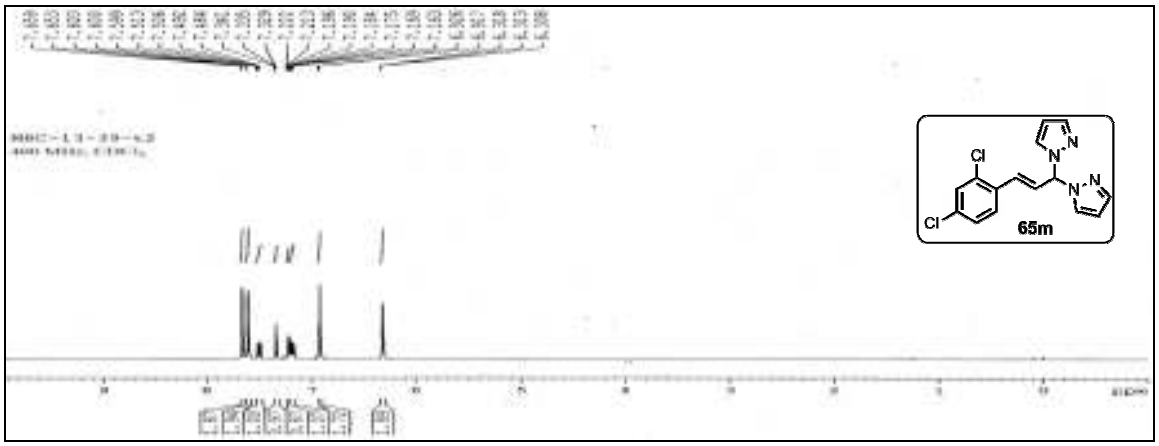

Me
66k

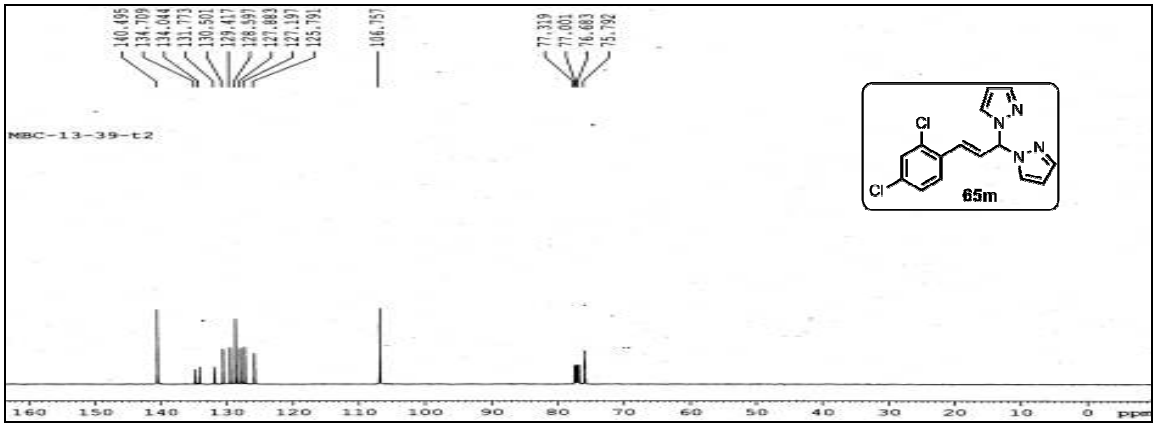

Br
65l

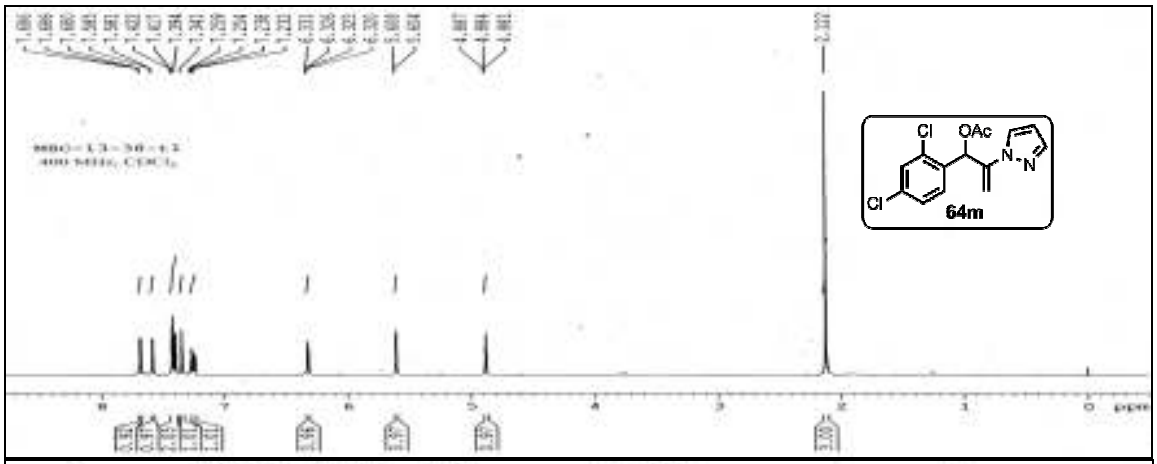

Br
N
N
N
N
65l

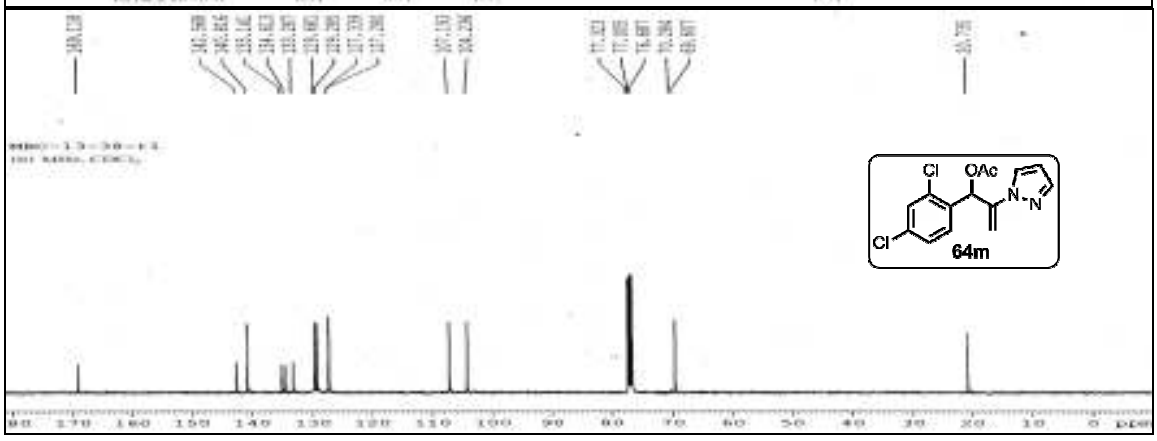

Br
OAc
N
N
64l

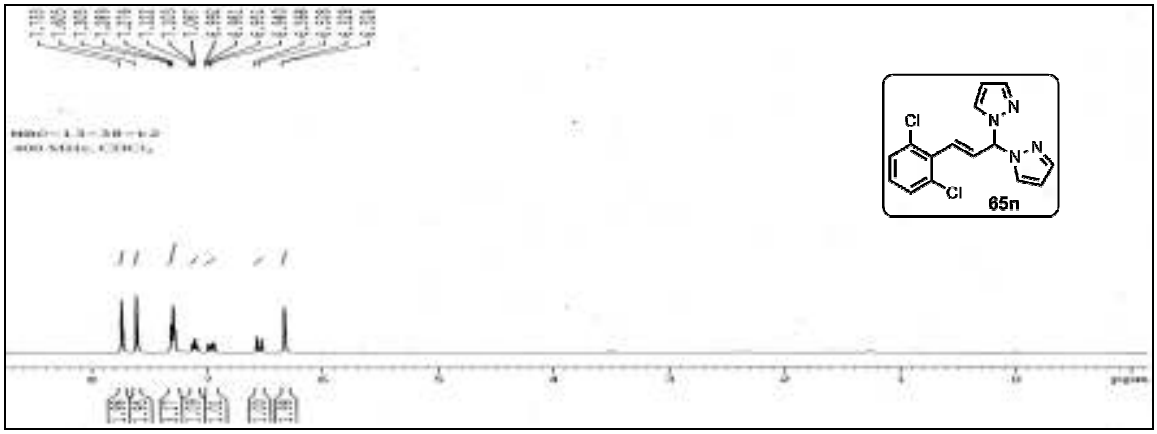

Br
OAc
N
N
64l

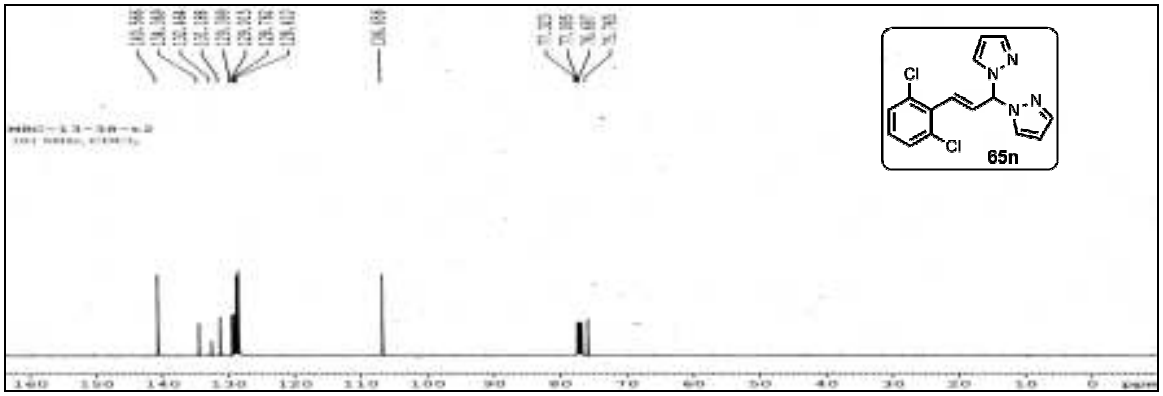

Cl
Cl
N
N
N
65m

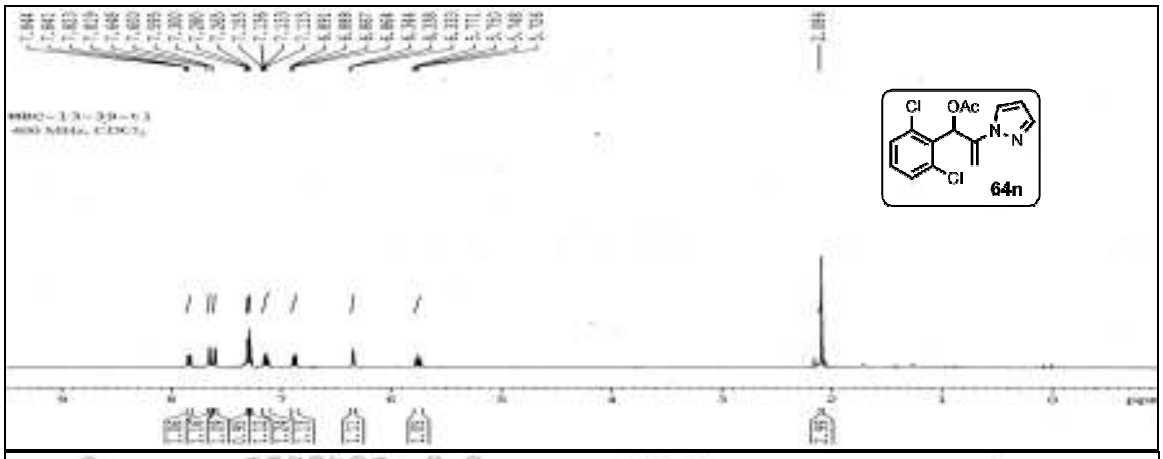

NBC-13-39-t2
65m

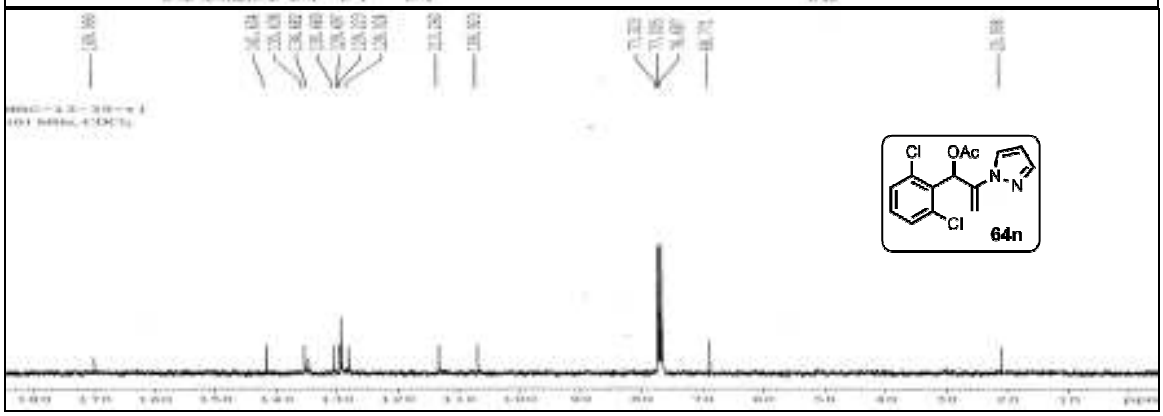

64m

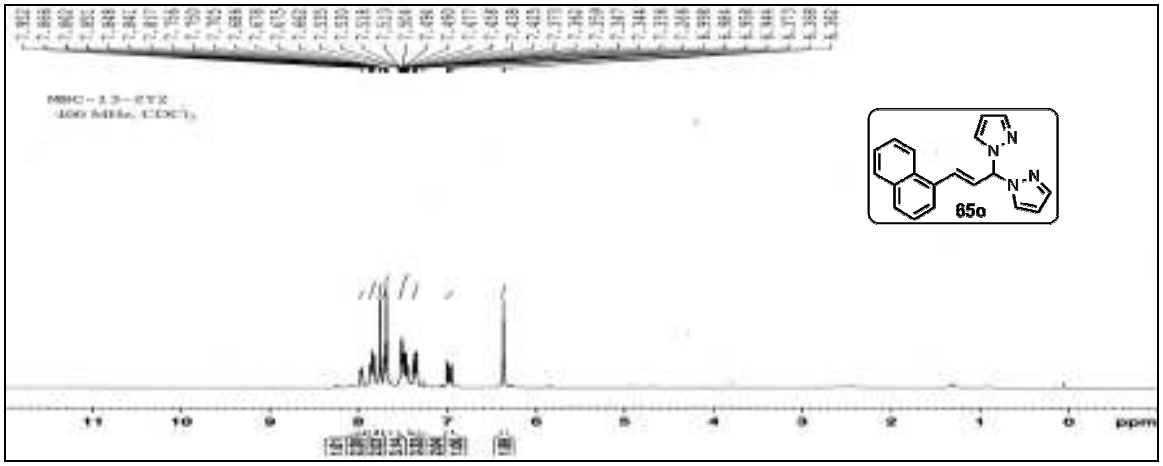

64m

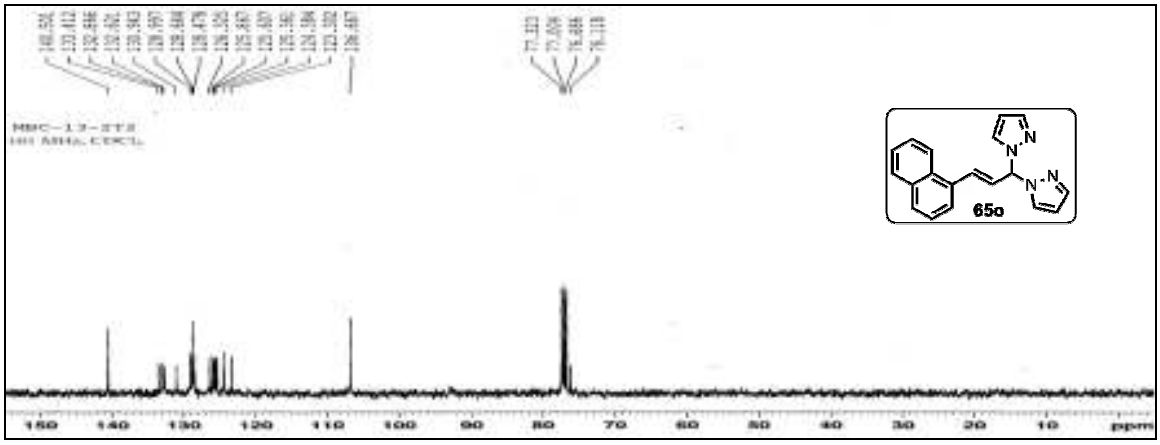

65n

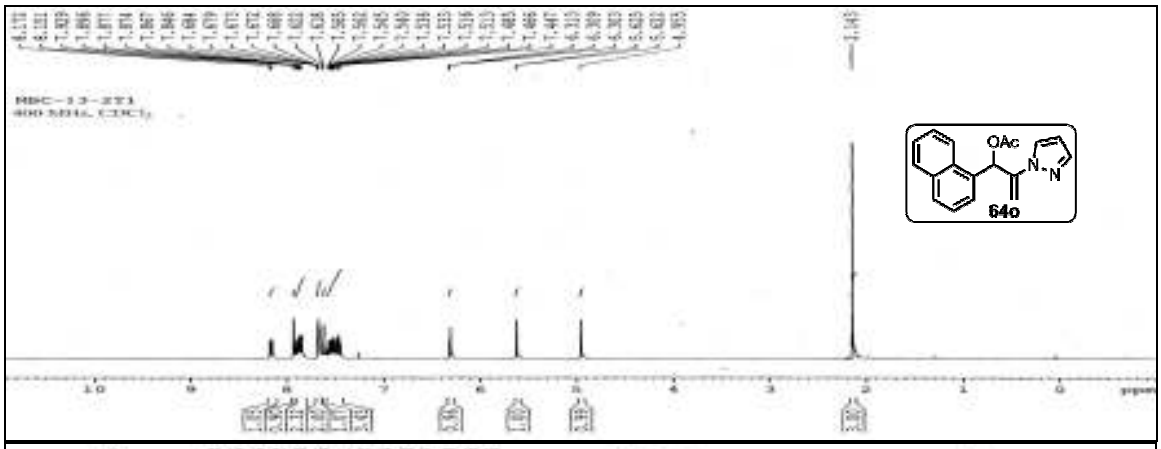

Cl
Cl
65n

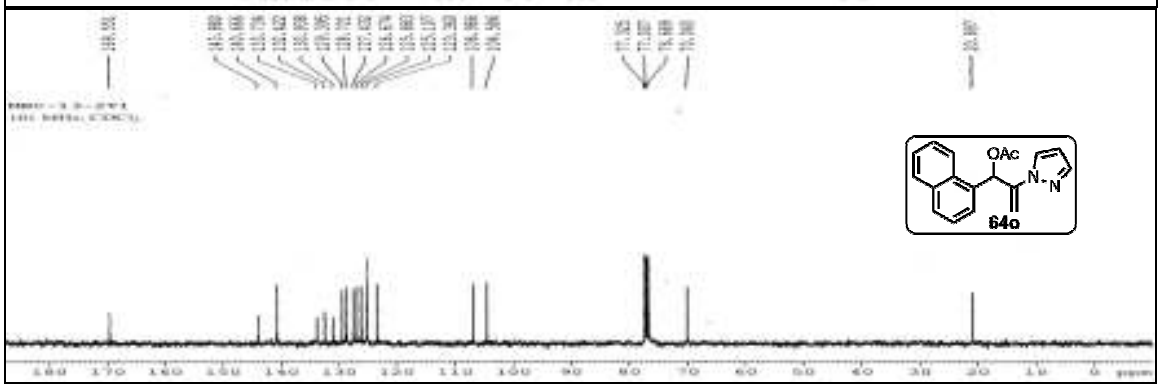

Cl
OAc
Cl
64n

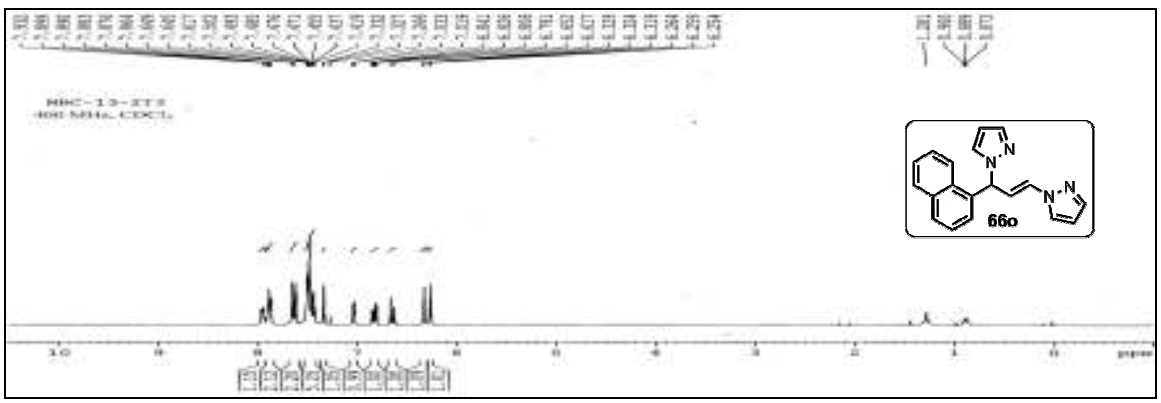

Cl
OAc
Cl
64n

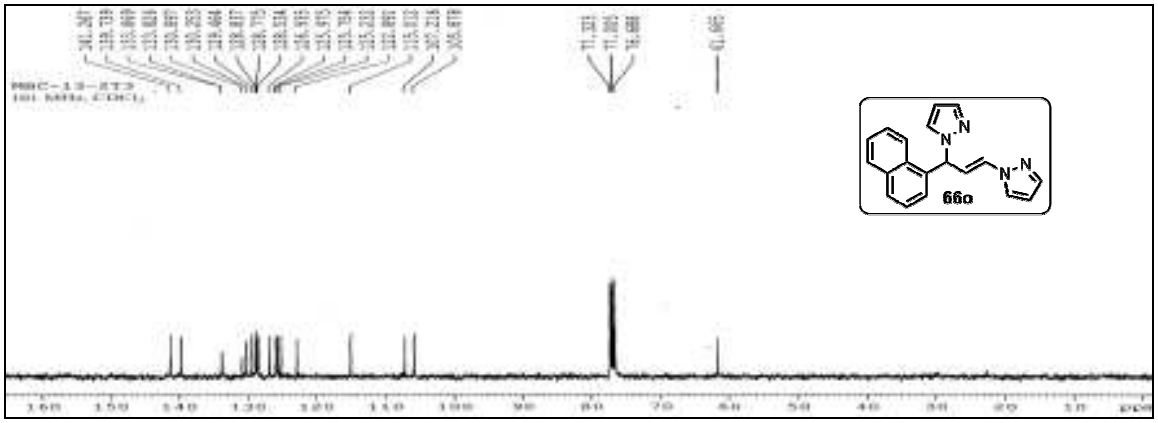

65o
ppm

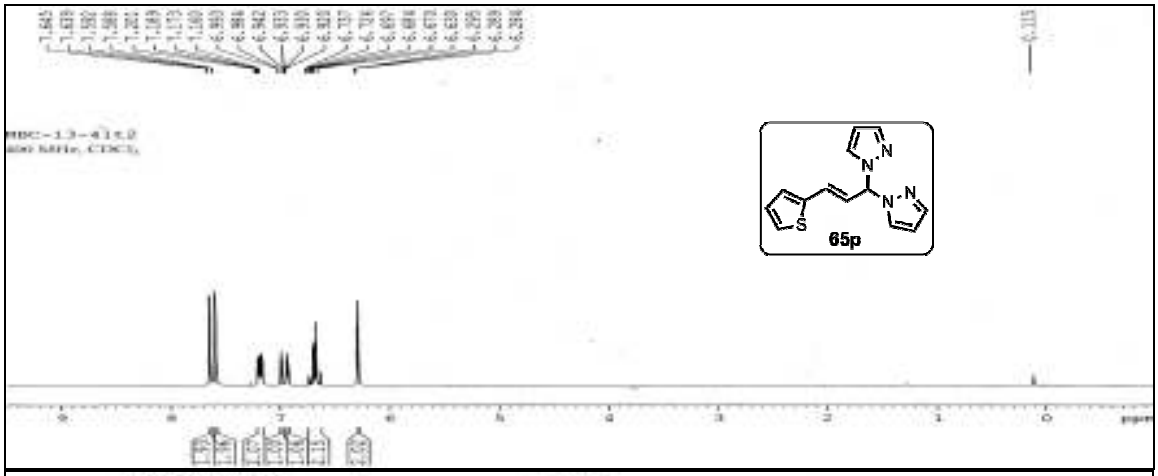

65o

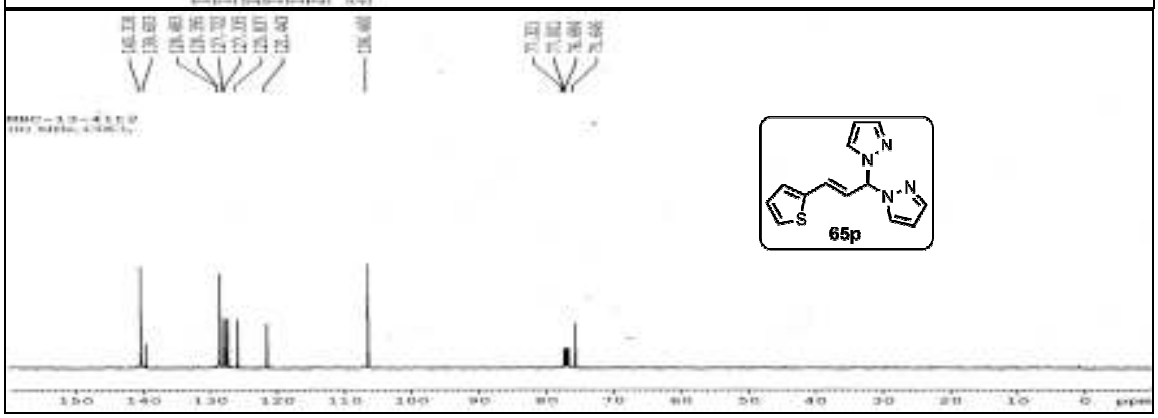

OAc
64o

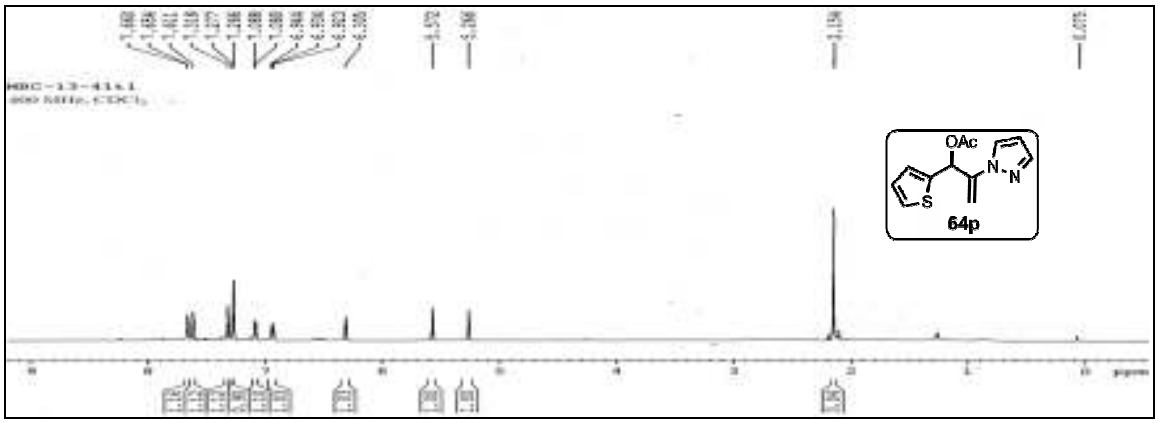

OAc
64o

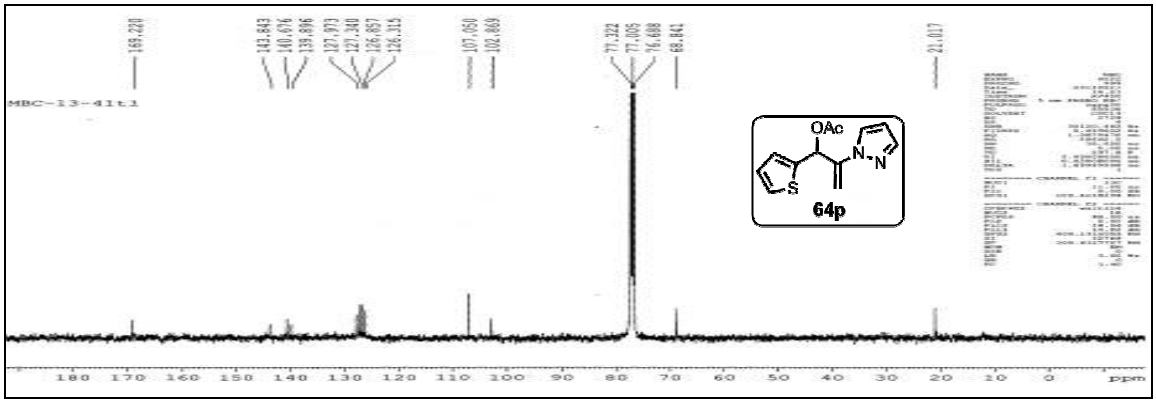

66o

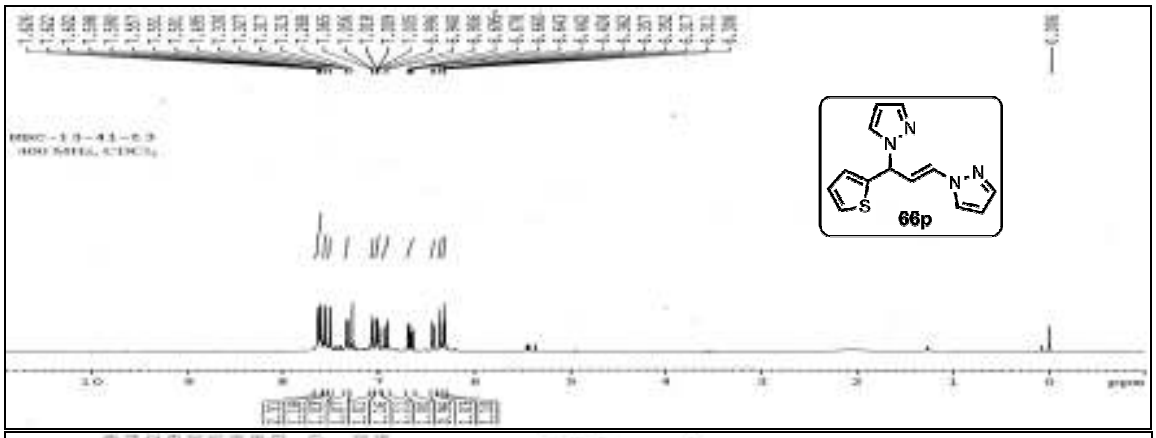

66o

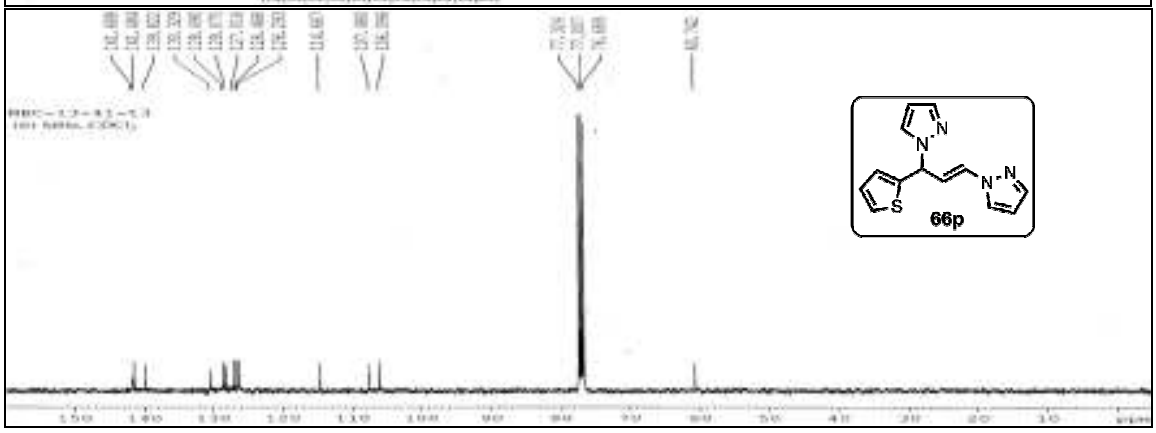

65p

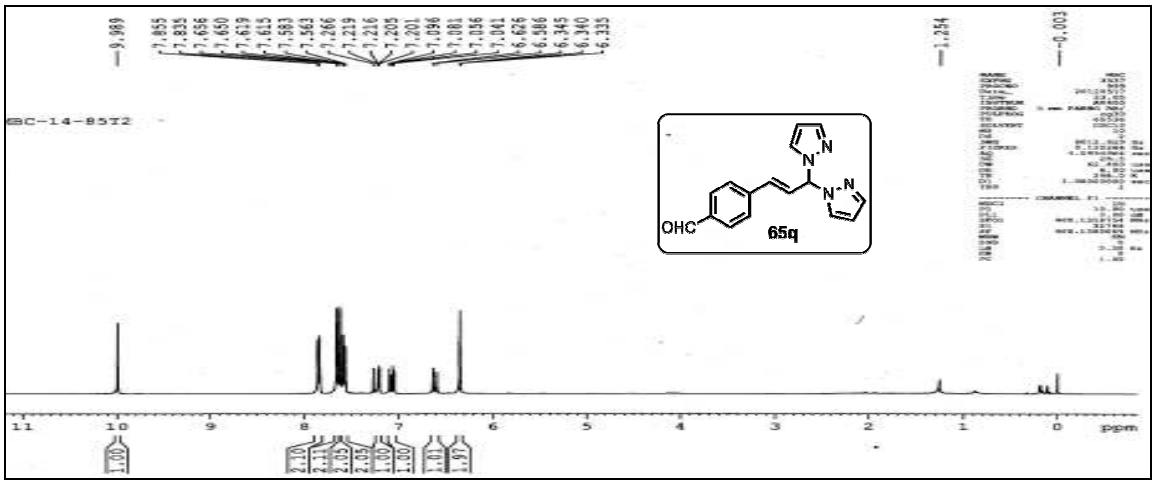

65p

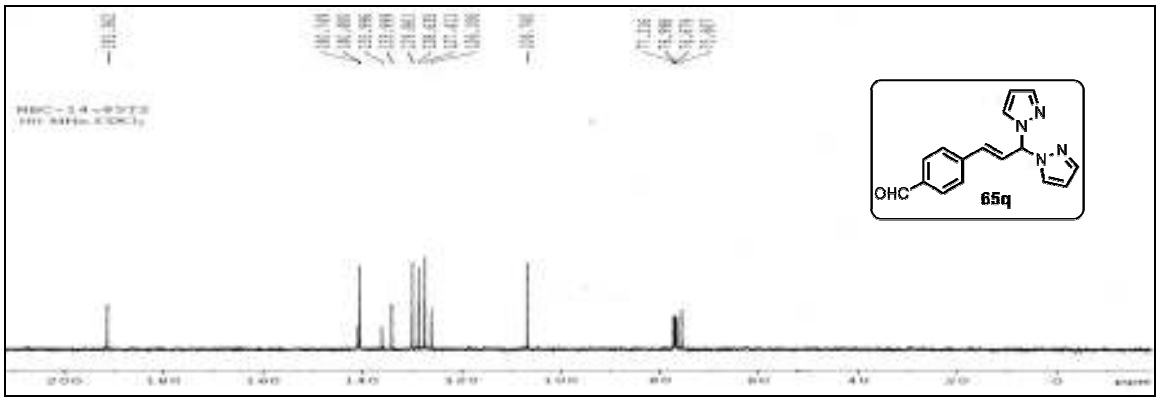

OAc
64p

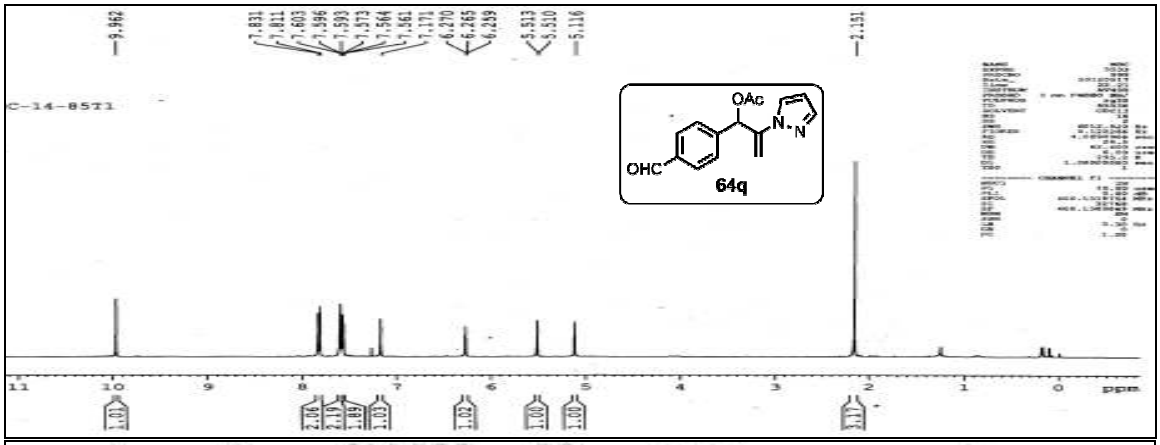

MBC-13-41t1
OAc
64p
ppm

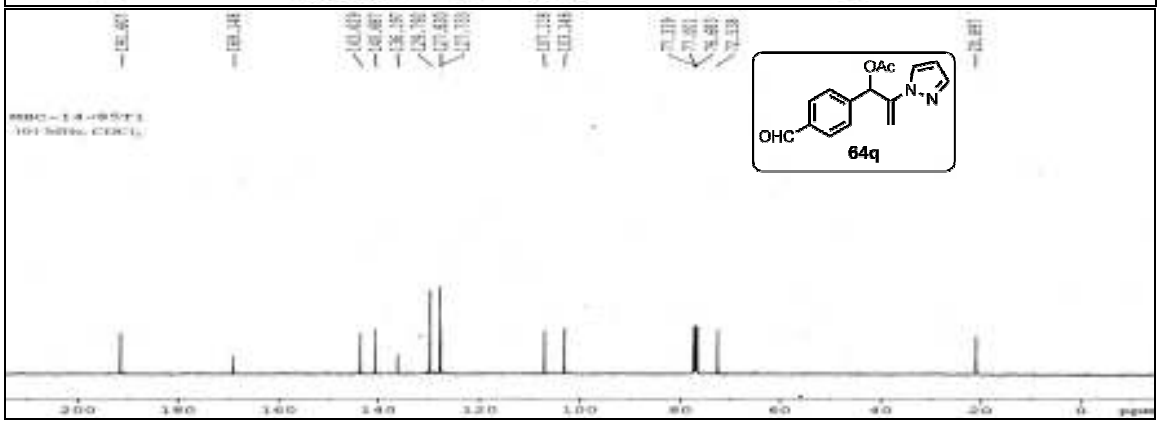

66p
ppm


66p

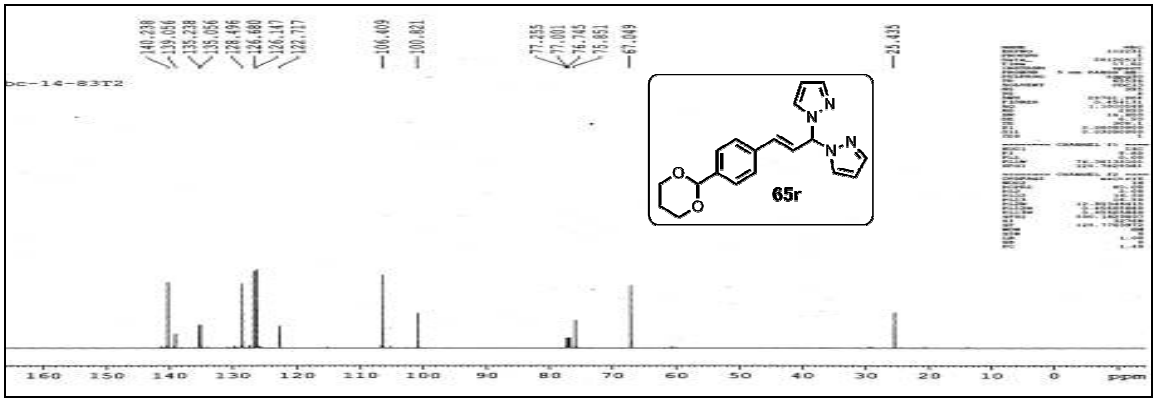

OHC
65q
ppm

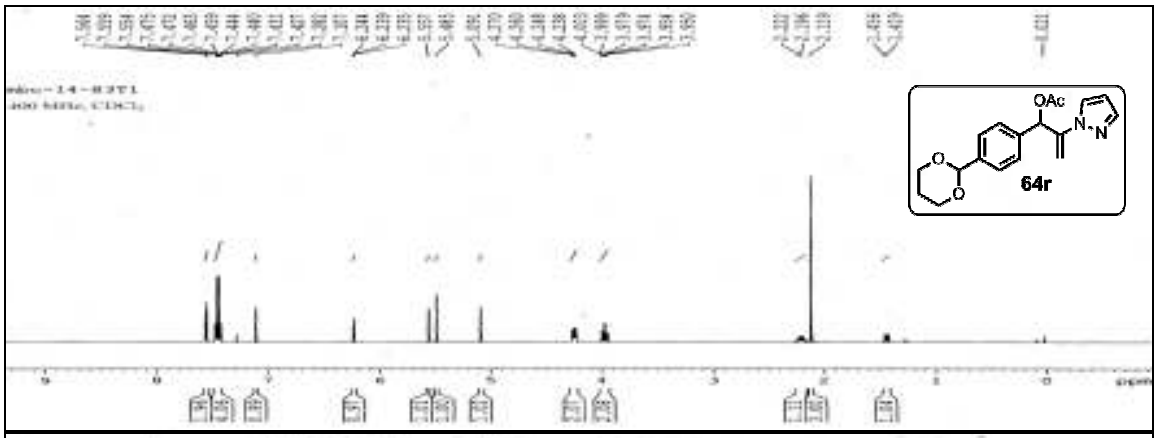

65q

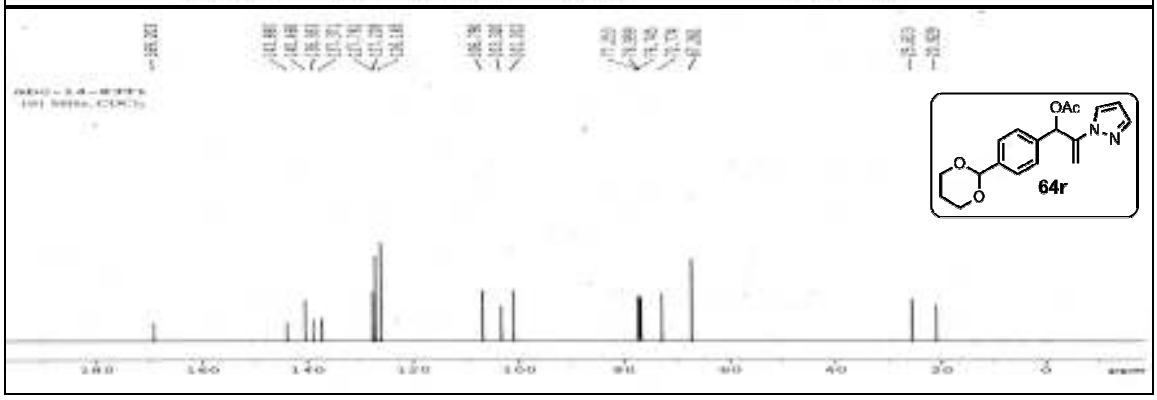

OAc
OHC
64q

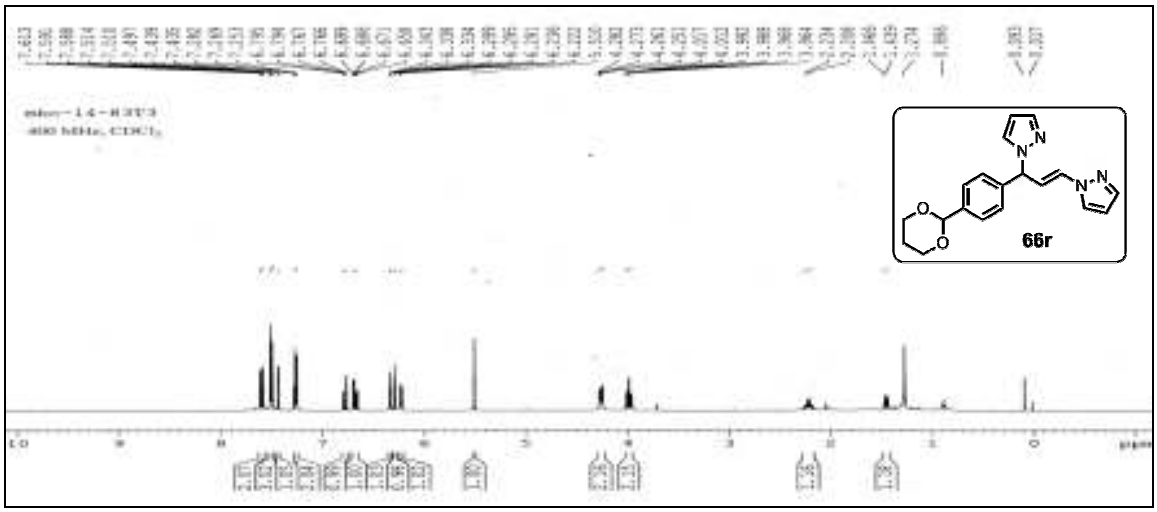

OAc
OHC
64q

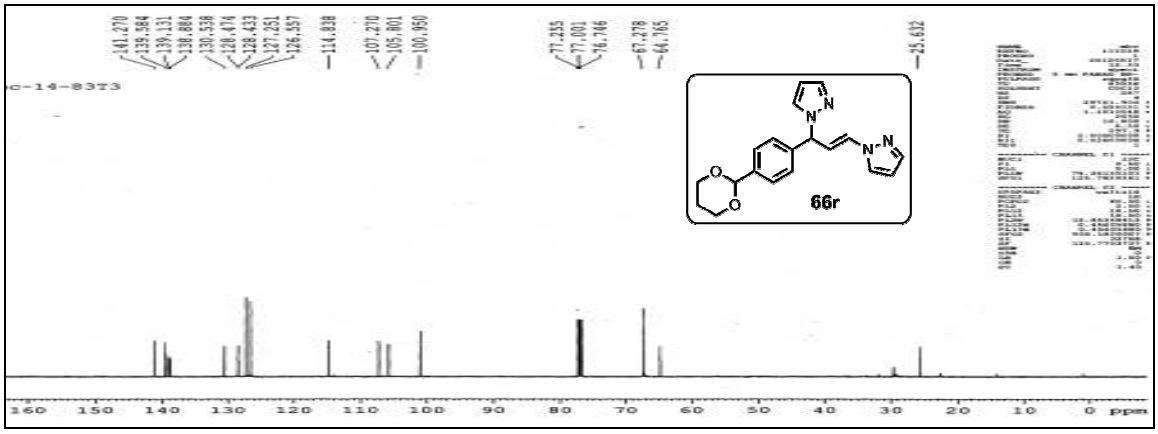

65r

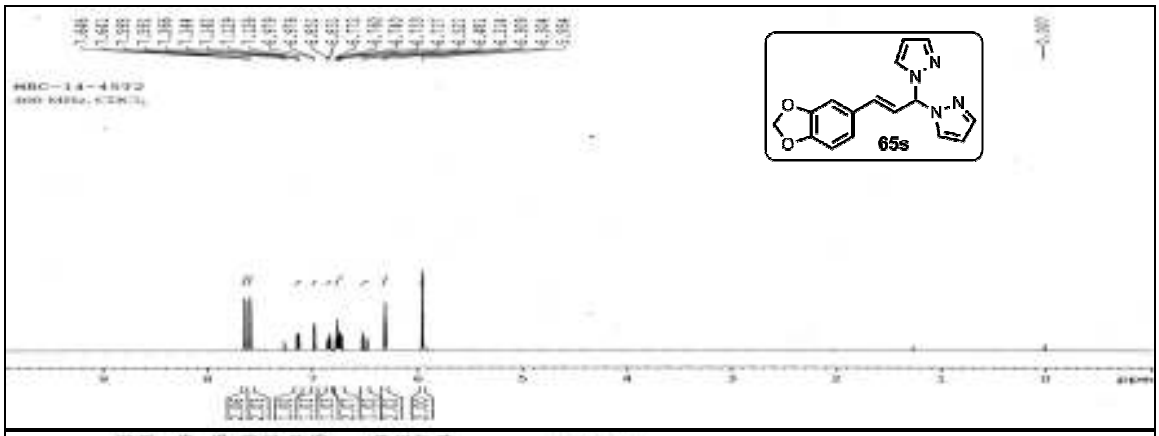

65r

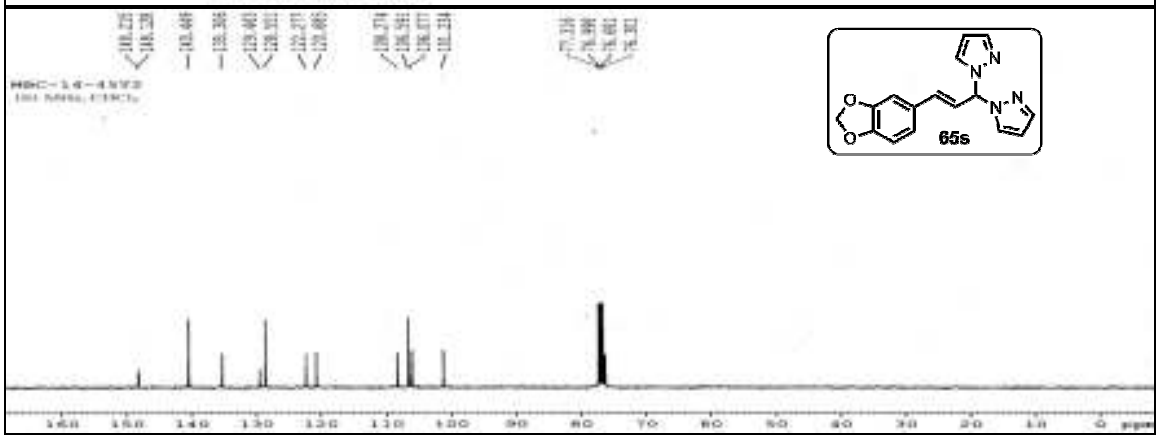

OAc
64r

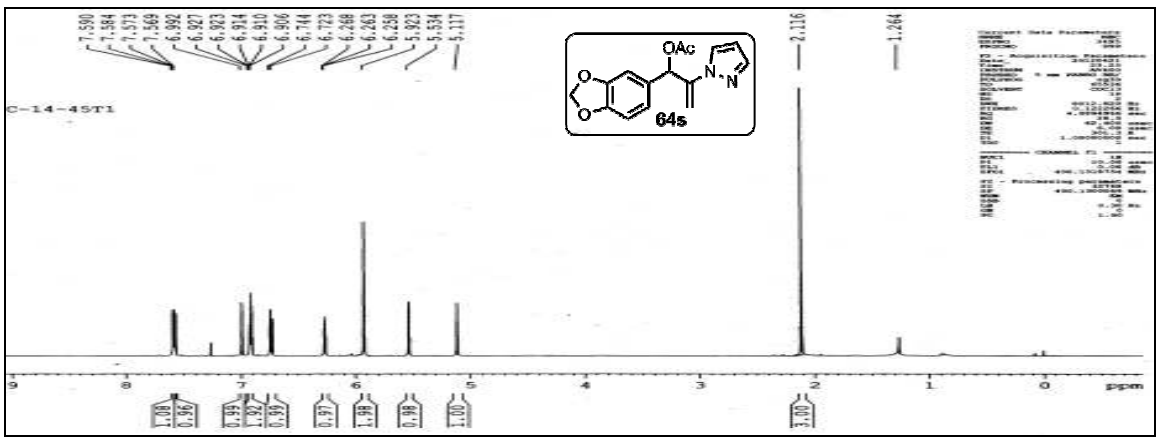

OAc
64r

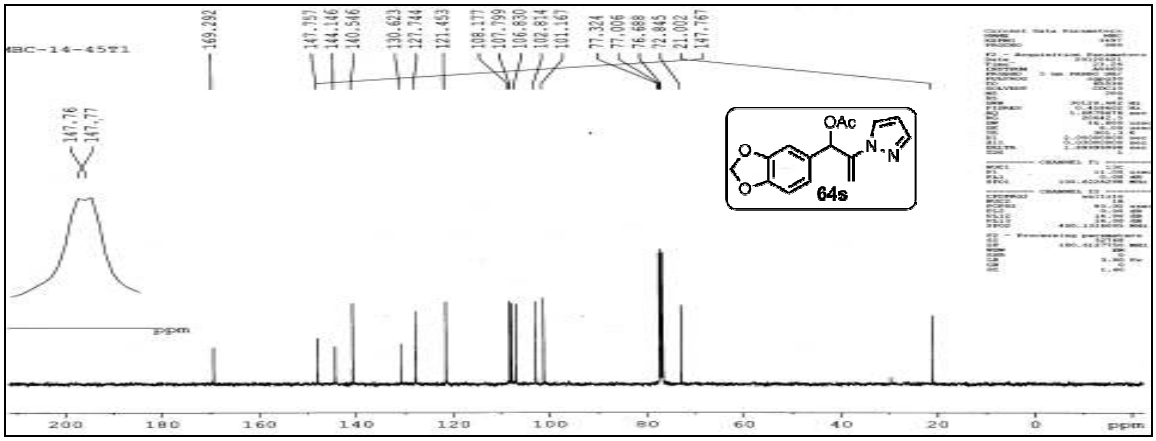

66r

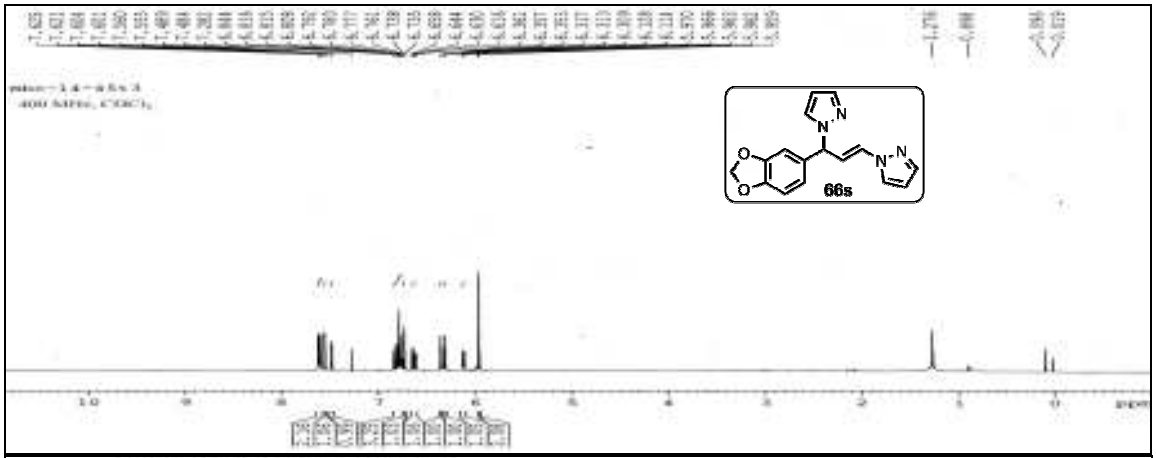

66r


65s

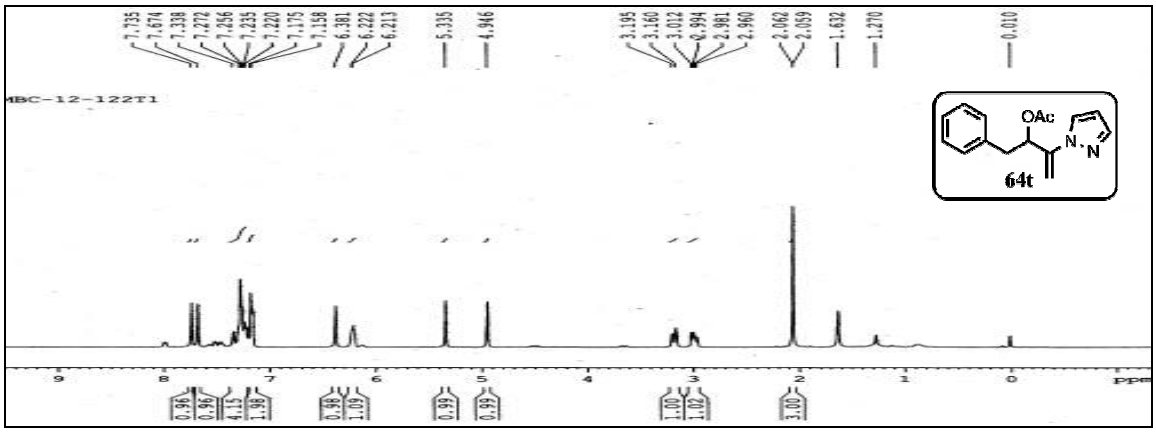

65s

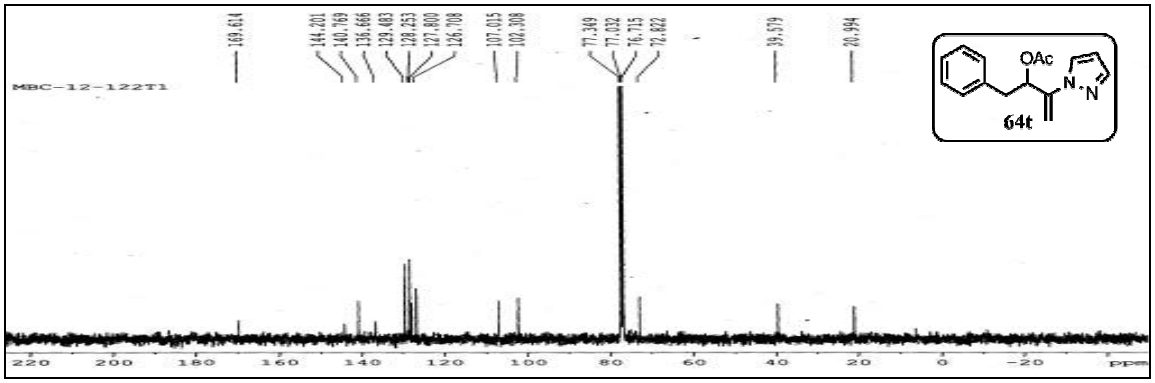

OAc
64s

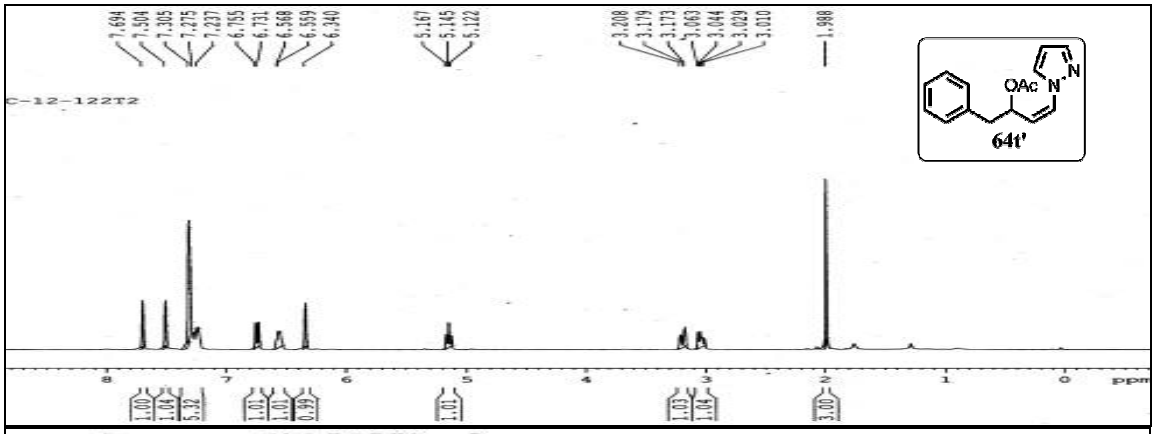

64s

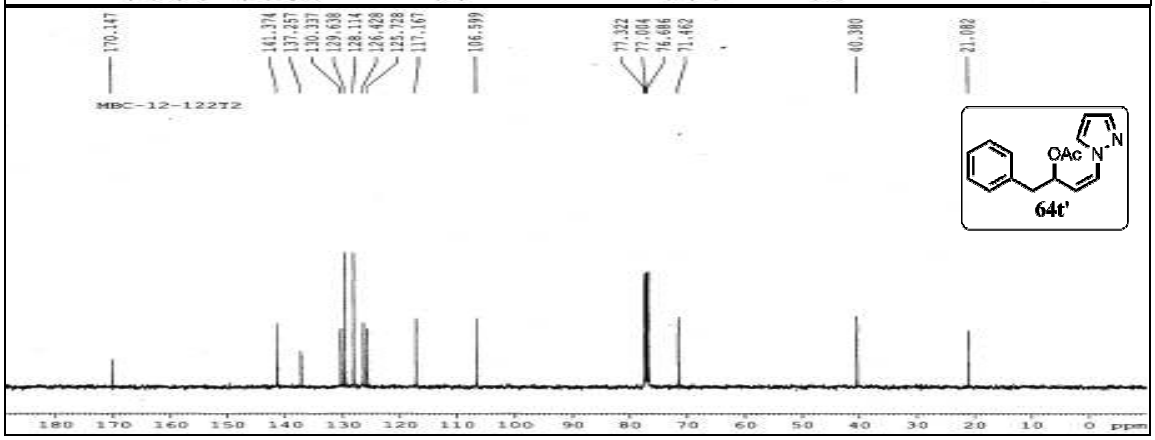

66s

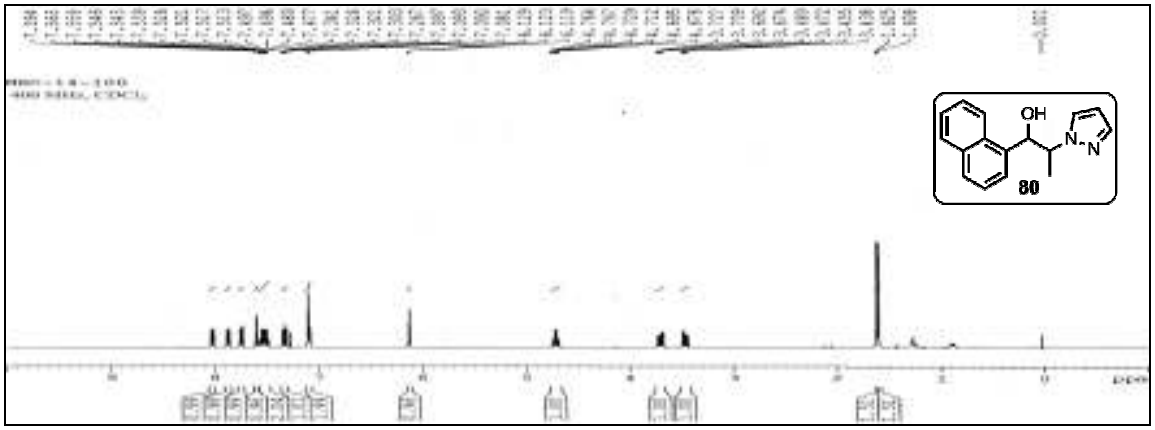

66s

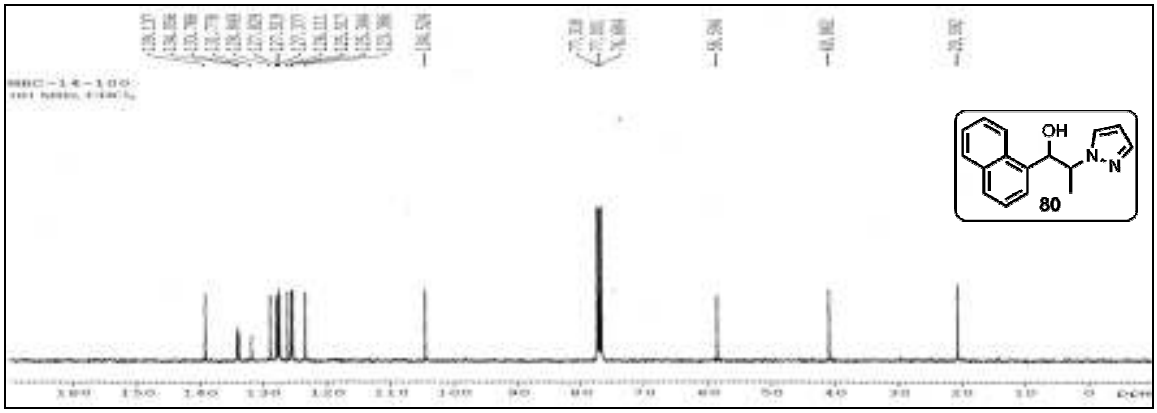

64t

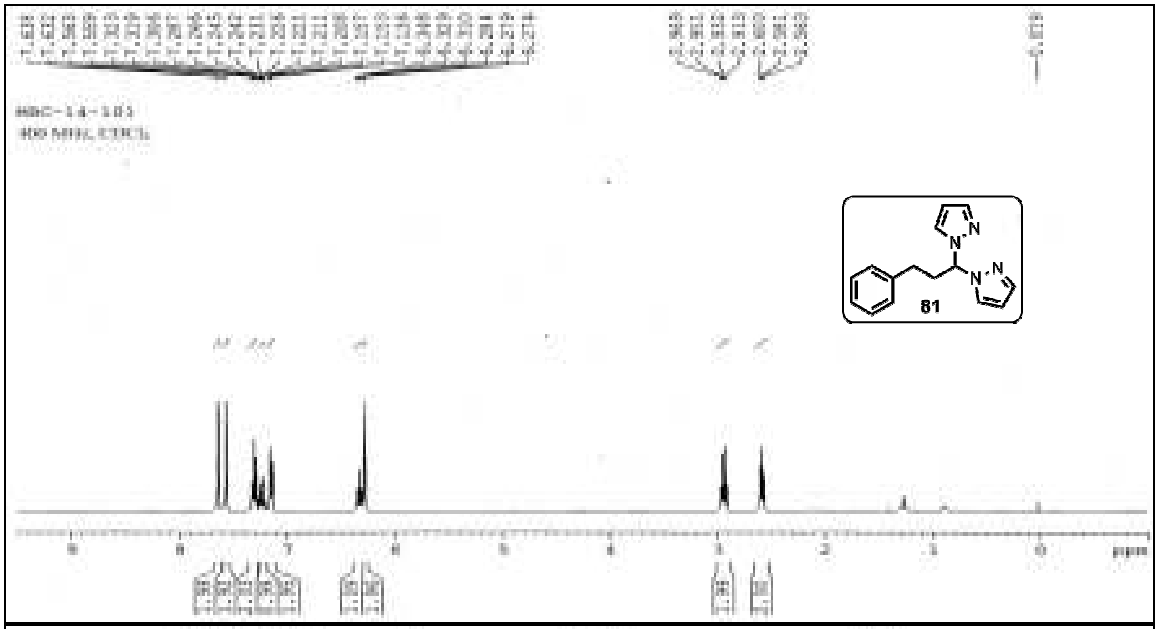

MBC-12-122T1
169.614
144.201
140.769
135.666
129.483
128.253
127.800
126.708
107.015
102.308
77.349
77.032
76.715
72.822
39.579
20.994
OAc
64t

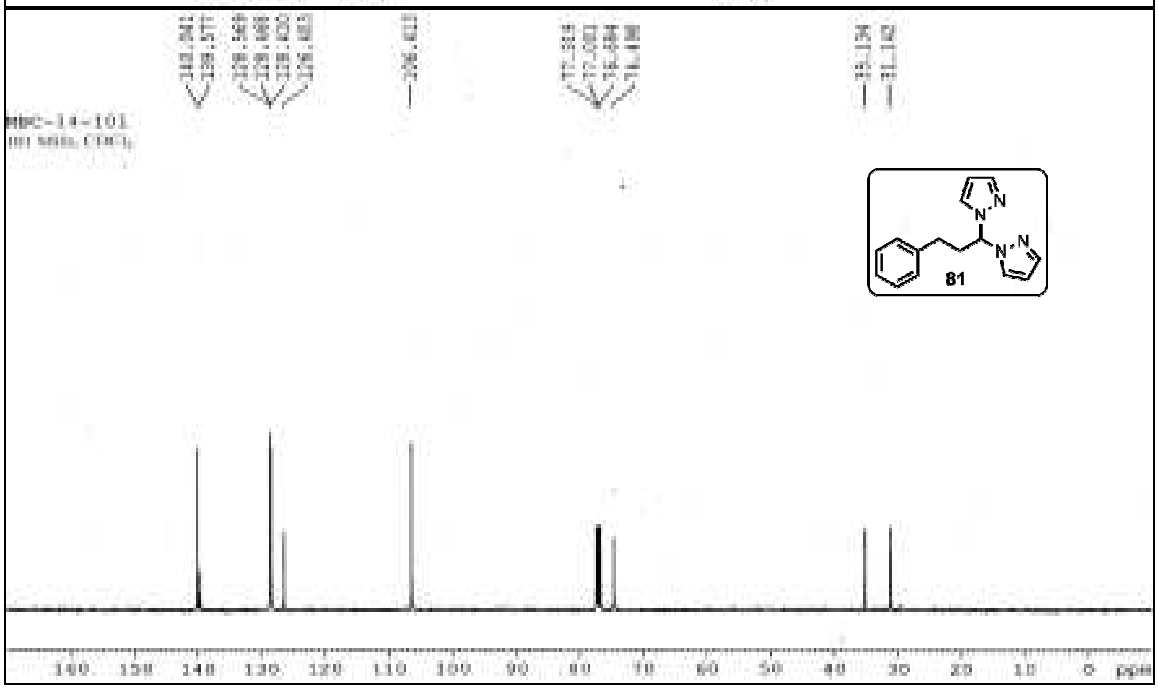

7.694
7.504
7.305
7.275
7.237
6.755
6.731
6.568
6.559
6.340
5.167
5.145
5.122
3.208
3.179
3.173
3.063
3.044
3.029
3.010
1.988
OAc
64t'

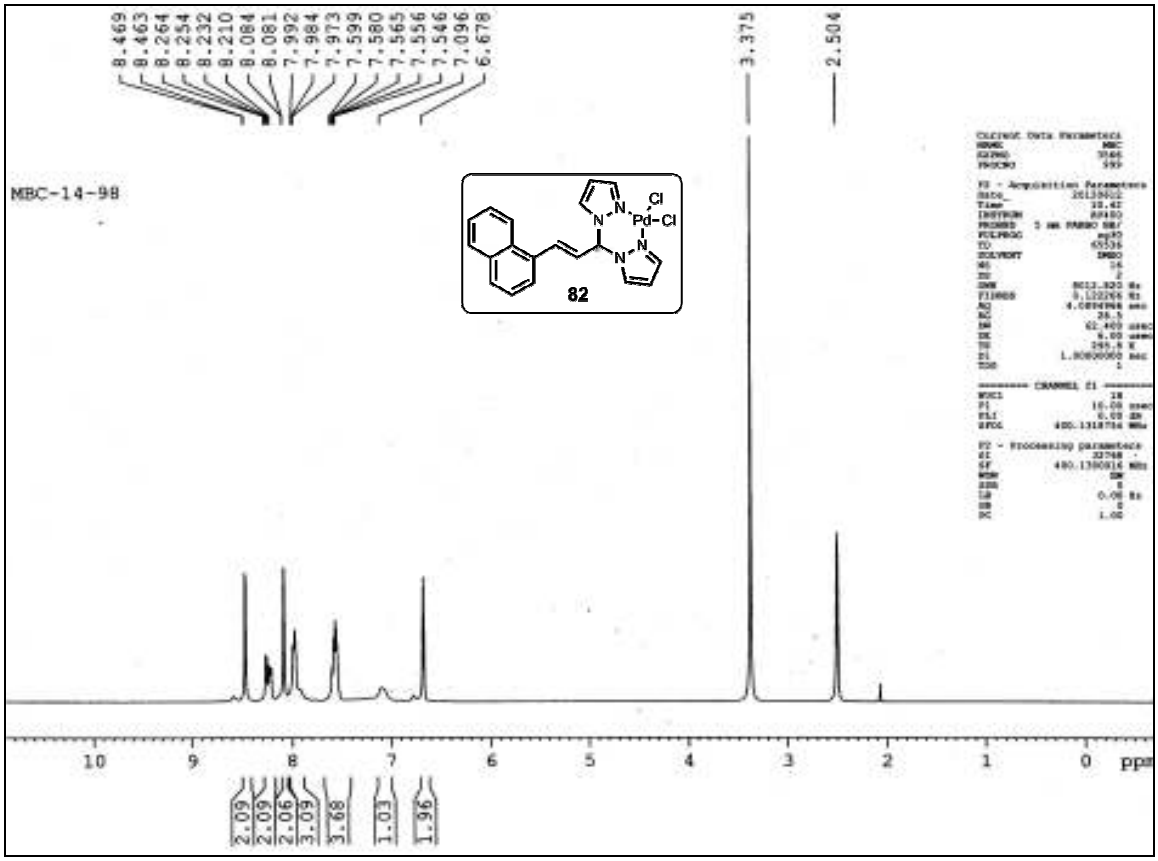

MBC-12-122T2
170.147
141.374
137.457
130.337
129.638
128.114
126.428
125.728
117.167
106.599
77.322
77.004
76.686
71.462
40.380
21.002
OAc
64t'

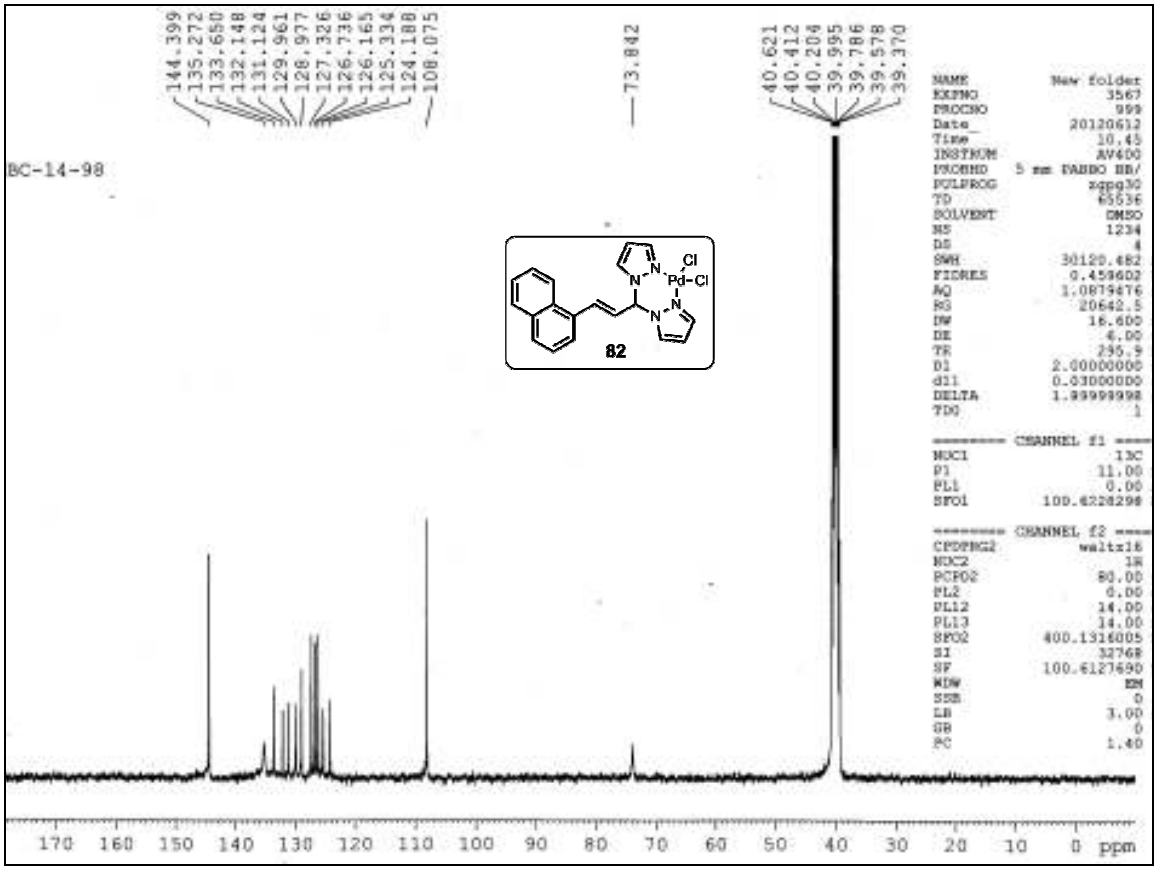

OH
80


OH
N
N
80


N
N
N
N
81
ppm


N
N
N
N
81
ppm

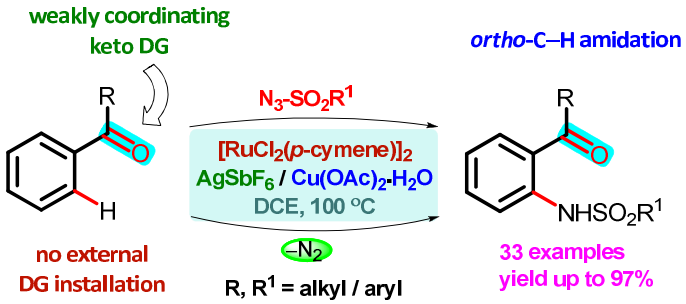

8.469
8.463
8.264
8.254
8.232
8.210
8.084
8.081
7.992
7.984
7.973
7.599
7.580
7.565
7.556
7.546
7.096
6.678
3.375
2.504
MBC-14-98
Cl
Pd-Cl
82
10
9
8
7
6
5
4
3
2
1
0
ppm
2.09
2.09
2.06
3.09
3.68
1.03
1.96


144.399
135.272
133.650
132.148
131.124
129.961
128.977
127.326
126.736
126.165
125.334
124.188
108.075
73.842
40.621
40.412
40.204
39.995
39.786
39.578
39.370
BC-14-98
Cl
Pd-Cl
82
NAME New folder
EXPNO 3567
PROCNO 999
Date_ 20120612
Time 10.45
INSTRUM AV400
PROBHD 5 mm PABBO BB/
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 1234
DS 4
SWH 30120.482
FIDRES 0.459602
AQ 1.0879476
RG 20642.5
DW 16.600
DE 6.00
TE 295.9
D1 2.00000000
d11 0.03000000
DELTA 1.99999998
TD0 1
CHANNEL f1
NUC1 13C
P1 11.00
PL1 0.00
SFO1 100.6228298
CHANNEL f2
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00
PL2 0.00
PL12 14.00
PL13 14.00
SFO2 400.1316005
SI 32768
SF 100.6127690
WDW EM
SSB 0
LB 3.00
GB 0
PC 1.40
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

Ru(II)-Catalyzed Intermolecular *ortho*-C–H Amidation of Aromatic Ketones with Sulfonyl Azides

3
Chapter

Abstract



The Ru(II)-catalyzed intermolecular *ortho*-C–H amidation of weakly coordinating aromatic ketones with sulfonyl azides is demonstrated. The developed reaction conditions comprising of [{$RuCl_2$(*p*-cymene)}$_2$, $AgSbF_6$, $Cu(OAc)_2 \cdot H_2O$ in dichloroethane at 100 °C] can be extended to various substituted aromatic ketones to afford wide range of the desired C–N bond formation products in good yields. A wide range of sulfonyl azides were successfully installed on arylketones.

Reference:

M. Bhanuchandra, M. Ramu Yadav, Raja K. Rit, Malleswara Rao Kuram and Akhila K. Sahoo, *Chem. Commun.*, 2013, **49**, 5225.

3.1. Introduction

Particular attention has been paid to C–N bond formation because of the broad synthetic potential of nitrogen-bearing compounds.[1] Pharmaceutically important nitrogen-bearing drugs could be synthesized from *o*-amidated arenes. Some of the representative molecules accessed from *o*-amino ketones are shown in Figure 3.1.

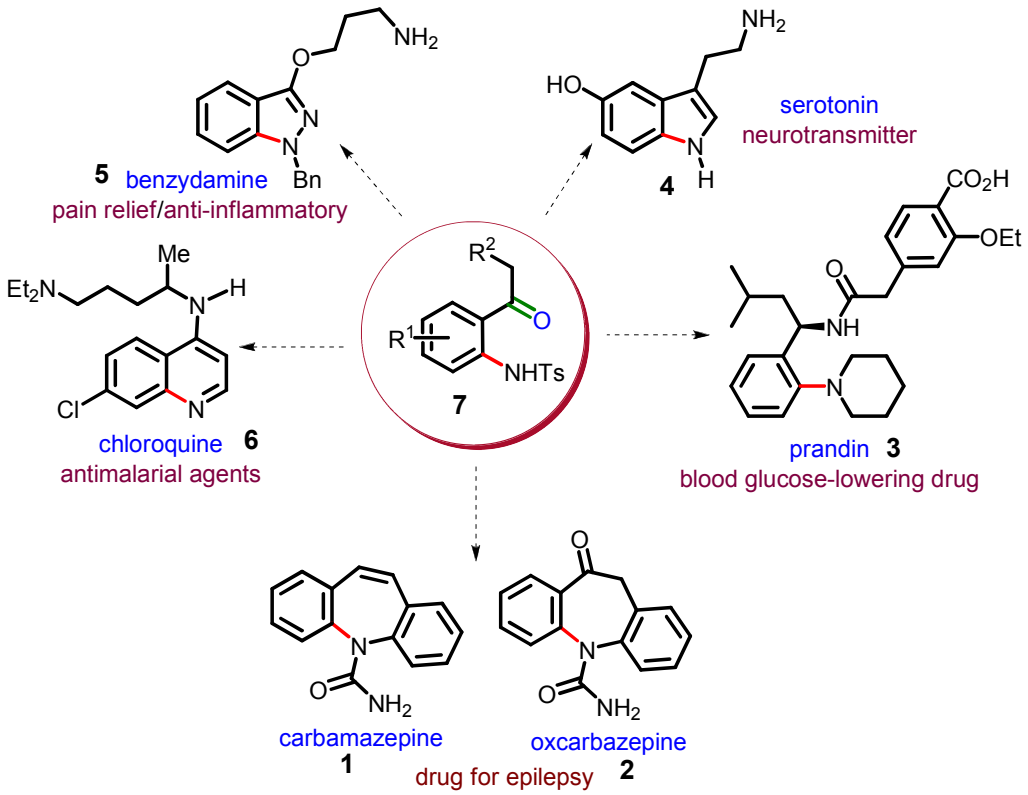
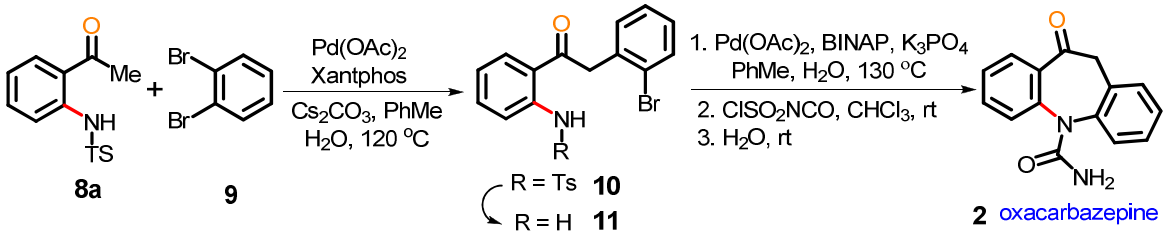


Figure 3.1: Synthetic Potential of *ortho*-Amidated Aryl Ketones

3.1.1 Synthetic Strategies of Pharmaceutically Important Nitrogen-bearing Drugs

Carbamazepine (**1**; Figure 3.1) is an anticonvulsant and mood-stabilizing drug used primarily in the treatment of epilepsy and bipolar disorder. Carbamazepine may cause life-threatening allergic reactions called Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN). These allergic reactions may cause severe damage to the skin and internal organs. Interestingly, the oxcarbazepine (**2**, marked as trileptal; Figure 3.1) a synthetic analogue of carbamazepine (**1**) showed better efficiency in treating the mood disorders; as a result trileptal is the widely prescribed drug for the treatment of epilepsy both in adults and children.[2]

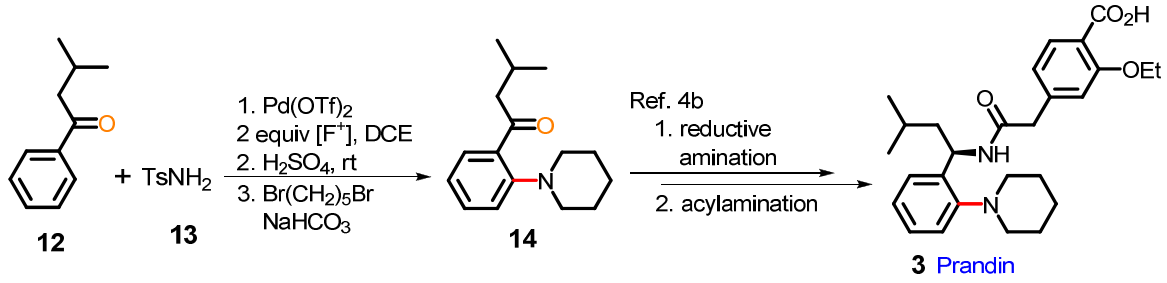
Oxcarbazepine (**2**) was readily prepared from *o*-amidated acetophenone **8a**. α-Arylation of acetophenone enolate with 1,2-dibromobenzene (**9**) in the presence of $Pd(OAc)_2$ provided the α-arylated acetophenone **11**. Palladium catalyzed intramolecular *N*-arylation followed by carbamoylation with chlorosulfonyl isocyanate furnished the target molecule oxcarbazepine **2** (Scheme 3.1).[3]



Scheme 3.1: Synthetic Strategy to Oxcarbazepine

Prandin (**3**; Figure 3.1) is an oral blood glucose-lowering drug of the meglitinide class and effectively used in the management of non-insulin dependent diabetes (type 2 diabetes) mellitus.

Liu and co-workers synthesized a key intermediate for prandin using palladium catalyzed *ortho*-C–H amidation of isovalerophenone (**12**) with tosylamine (**13**) followed by NH-detosylation and coupling with 1,5-dibromopentane. Reductive amination of carbonyl group with $HCONH_2$/$HCOONH_2$ and acylamination sequences yielded the prandin drug **3** (Scheme 3.2).[4]

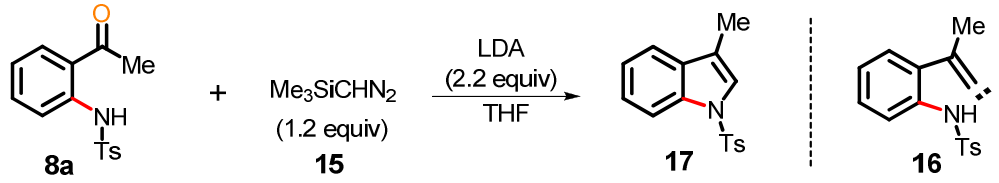


Scheme 3.2: Synthetic Strategy to Prandin

Serotonin (**4**; Figure 3.1) is an 3,5-disubstituted-indole derivative with free -NH_2 and -OH functional groups. It is primarily found in the gastrointestinal tract, platelets and in the central nervous system of animals and human. Serotonin functions as a neurotransmitter

and responsible for the growth of wound healing cells. Tryptamine, psilocybin, arbidol, ajmalicine etc are few examples of the indole-ring bearing biologically active molecules.

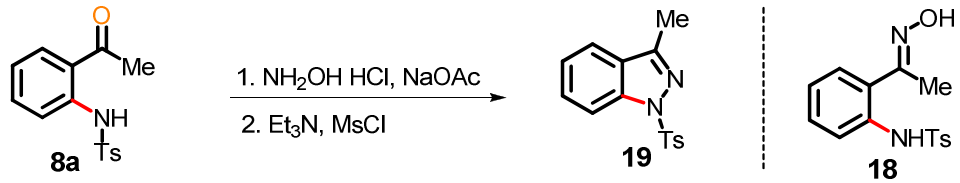
The reaction between *o*-acyl-*N*-tosylaniline (**8a**), trimethylsilyldiazomethane ($TMSCHN_2$, **15**) and lithium diisopropylamide (LDA) in THF allows one pot synthesis of 3-substituted *N*-tosylindole **17**.[5] The reaction begins with the in-situ formation of lithium salt of trimethylsilyldiazomethane ($TMSC(Li)N_2$) from $TMSCHN_2$ and LDA. The attack of $TMSC(Li)N_2$ to the carbonyl moiety generates the alkylidene carbenes **16**. Finally intramolecular insertion of N–H to alkylidene carbene delivers **17** (Scheme 3.3).



Scheme 3.3: Synthetic Strategy to Indole Derivatives

The 1*H*-indazole **19** containing molecules are useful as anti-cancer, anti-inflammatory, anti-HIV, and anti-microbial drugs. For instance, benzydamine (**5**; Figure 3.1) is highly effective drug that relieves pain and inflammation associated with a sore throat or mouth sores caused by radiation therapy; these molecules are sold with a brand name of tantum verde or difflam.

The 3-methyl-1*H*-indazoles (**19**) is readily obtained from *o*-amidated ketones **8a**. Reaction of **8a** with hydroxylamine hydrochloride furnishes ketoximes (**18**); intramolecular condensation of **18** in the presence of Et_3N and methanesulphonyl chloride deliver **19** (Scheme 3.4).[6]

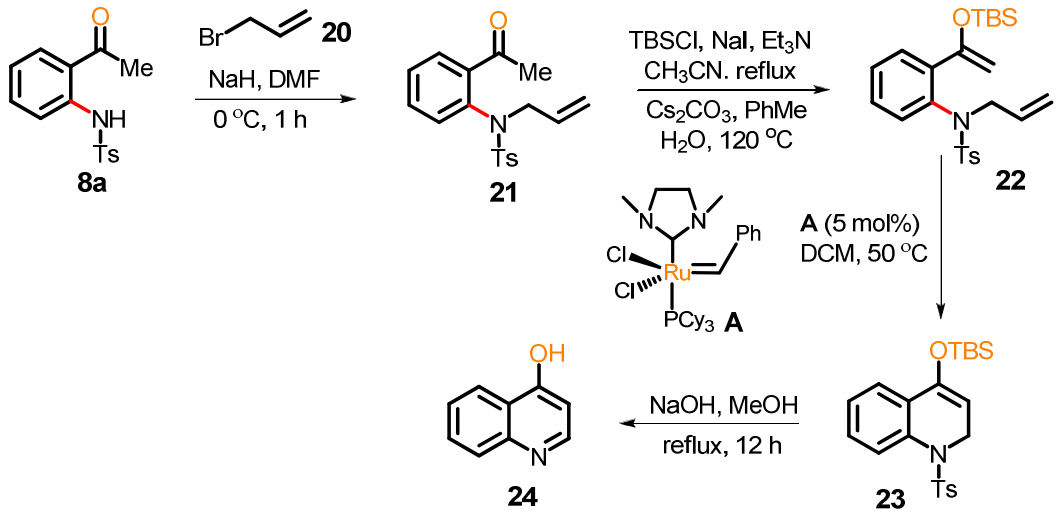


Scheme 3.4: Synthetic Strategy to 1*H*-Indazole Derivatives

Malaria is one of the world's most devastating infectious diseases. The quinoline motifs containing molecules quinine, chloroquine (**6**), mefloquine and premaquine are some of

the effective anti-malarial agents. In particular, chloroquine (**6**, Figure 3.1) discovered by Hans Andersag and coworkers at the Bayer laboratories in **1934** is found to be effective.

The Nakagawa group synthesized 4-hydroxy quinoline (**24**) from **8a** using ring closing metathesis (RCM) as key step. The *N*-allylation, and base assisted formation of silyl-enol ether of **8a** followed by RCM of **22** under the influence of Grubb's catalyst provides **23**. Finally, global deprotection of the O-silyl ether and N-tosyl groups in **23** affords **24** (Scheme 3.5)**,** which is a key intermediate for the synthesis of anti-malaria agents.[7]



Scheme 3.5: Synthetic Strategy to Quinolines Derivatives

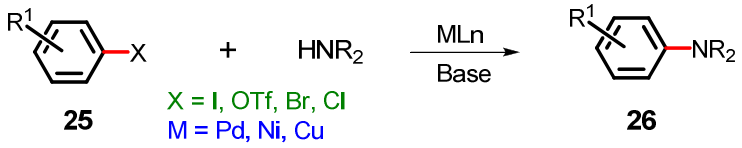
The precursor *o*-amidated arylketones **8a** has successfully been employed for the synthesis of pharmaceutically important molecules. The compound **8** can be obtained from the aryl ketones through conventional electrophilic nitration/reduction processes involving harsh reaction conditions. The Ullmann coupling or Buchwald–Hartwig amination on *pre-functionalized o*-haloarylketones also led to **8**.

Therefore, the development of novel methods for direct formation of C(aryl)–N bonds through the activation of C(aryl)–H bonds is highly desirable. This would enable accessing wide scope of substrates owing to the ready availability of the precursors.

3.1.2. Precedents and Strategies for C–H Amination/Amidation of Arenes

Buchwald–Hartwig amination, for instance, allows the induction of C–N bond in arenes from readily available pre-functionalized haloarenes **25** (Scheme 3.6).[8] However, multiple

steps are required to install the functional groups halogens or pseudo-halogens in the molecule that are subsequently used for the fabrication of complex molecule synthesis.

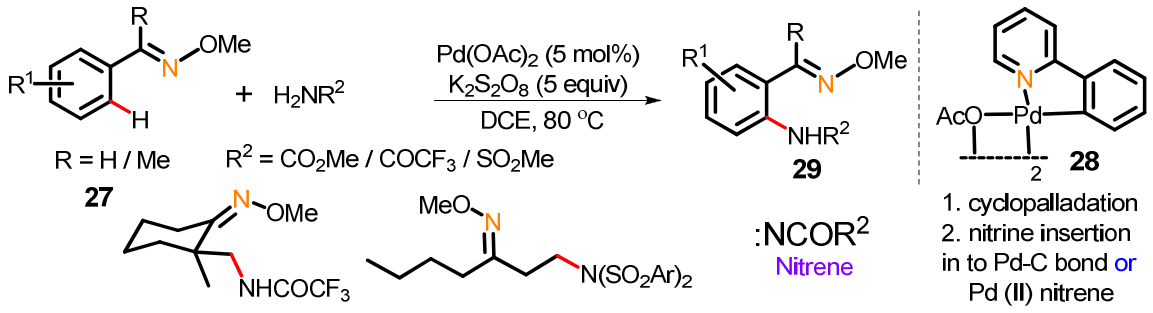


Scheme 3.6: Buchwald–Hartwig Coupling

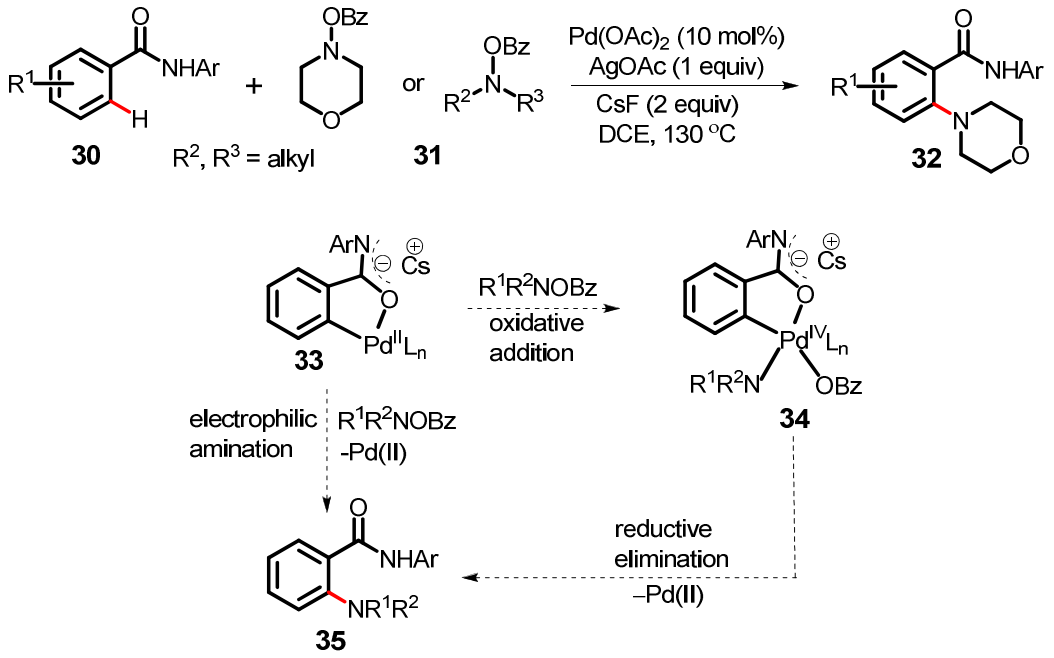
Interestingly, direct amination of the C–H bond of arenes presents the advantages of accessing broad scenario of substrate generality and minimal waste production.[9] However, this process requires a strongly coordinating, i.e., nitrogen-bearing, directing group (DG), which can be obtained from arene carbonyls/carboxylic acids through multiple synthetic manipulations.[10] Representative examples of DG assisted *o*-C–H amidation is shown in Scheme 3.7–3.23.[11,12]

3.1.2.1. Palladium Catalyzed *ortho*-C–H Amidation

The intermolecular amidation of unactivated sp^2 and sp^3 C–H bonds *via* palladium-catalyzed C–H activation was demonstrated by the Che group.[11d] The chelation ability of *N*-atom in oxime **27** to transition-metal triggers activating the *o*-C–H bond in the formation of cyclopalladation compound **28**. The nitrene insertion to the Pd–C bond of **28** delivers the *o*-amidated product **29** (Scheme 3.7). The carbamate, acetamide, and sulfonamide nucleophiles are successfully employed in this reaction.

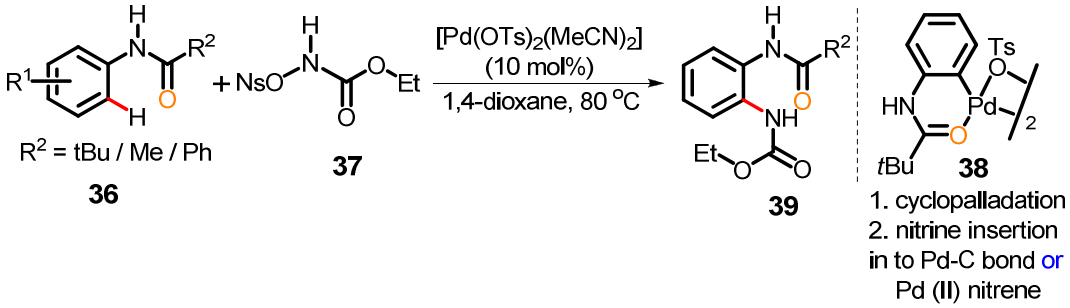


Scheme 3.7: Pd-Catalyzed Oxime Directed Amidation of Unactivated sp^2 and sp^3 C–H Bonds



Scheme 3.8: Pd-Catalyzed C–H Amination of *N*-Aryl Benzamides with Alkylamines

A notable strategy for the *ortho*-C–H amination reaction of *N*-aryl benzamides **30** with electrophilic O-benzoyl hydroxylamine (**31**) is reported by the Yu group.[11b] The reaction proceeds through the oxidative addition of O-benzoyl hydroxylamine **31** to the Pd(II) in palladacycle **33** in the generation of Pd(IV) intermediate **34**. Reductive elimination of **34** furnishes the desired *o*-amino benzamides **35**. The electrophilic substitution of **33** with aminating reagent is the other possible mechanism involved for the C–N bond formations (Scheme 3.8).

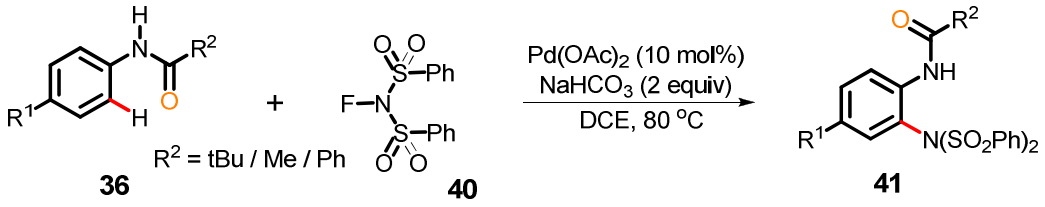


Scheme 3.9: Pd-Catalyzed *ortho*-C–H Amidation of Anilides by *N*-Nosyloxycarbamate

An interesting and facile approach to 2-aminoaniline derivatives **39** is reported from the Pd-catalyzed intermolecular *ortho*-C–H amidation of anilides (**36**) by *N*-nosyloxycarbamate (**37**).[11c] Nitrene generated from *N*-nosyloxycarbamate **37** undergoes

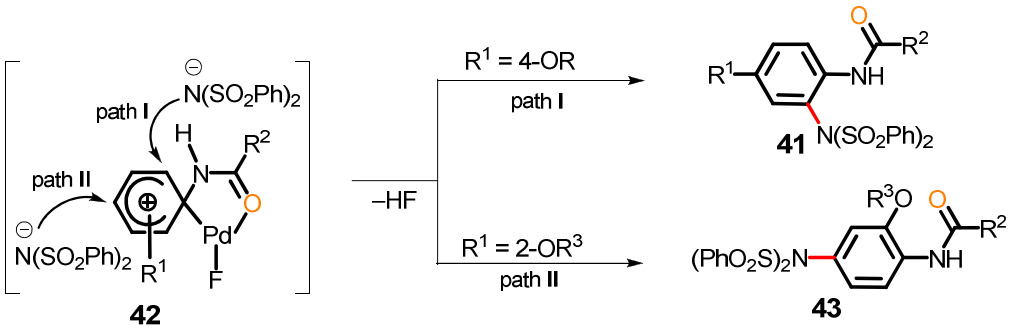
formal nitrene insertion to the cyclopalladated complex **38** *via* metal-nitrene pathway to furnish the *o*-aminoanilides **39** (Scheme 3.9).

The Zhang group demonstrated a highly selective intermolecular *o*-C–H amination of anilides **36** with non-nitrene based nitrogen source *N*-fluorobenzenesulfonamide (**40**).[11a] Interestingly, the presence of –OR group at *ortho*-position on arene moiety in **36** selectively provided the *para*-amidation product **43** in good yields; whereas *para*-OR-substituted **36** furnishes the *ortho*-amidation product **41** (Scheme 3.10 / 3.11).



Scheme 3.10: Pd-Catalyzed *ortho*-C–H Amidation of Anilides by *N*-Fluorobenzenesulfonimide

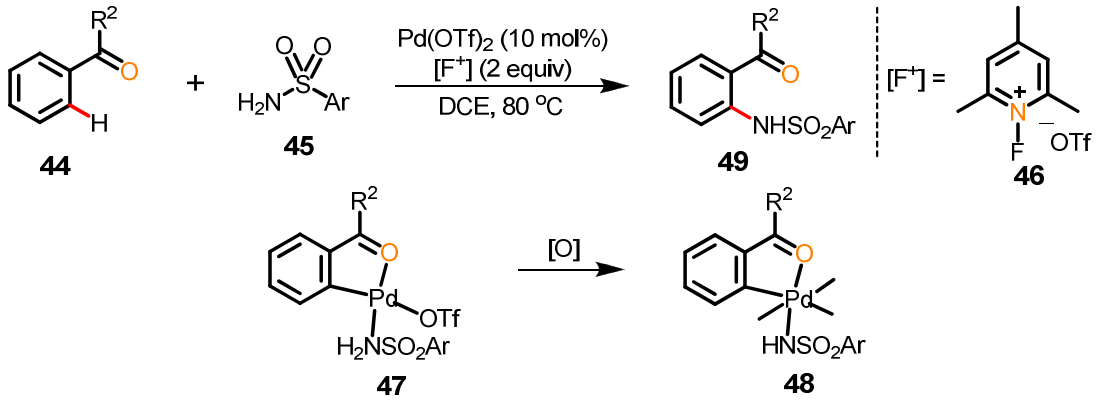
In mechanism, oxidative addition of Pd(0) to the N–F bond of NFSI **40** furnishes $FPdN(SO_2Ph)_2$ at first. Electrophilic palladation of anilide **36** with in situ-generated $FPdN(SO_2Ph)_2$ forms dearomatized spiro-palladacycle intermediate **42**, which could undergo nucleophilic amination with benzenesulfonimide followed by elimination of hydrogen provides *ortho*-amination **41** or *para*-amination **43** products depending on the electronic and steric effect of the arene substituent (Scheme 3.11).



Scheme 3.11: Proposed Mechanism for Nucleophilic Amidation

An elegant approach for Pd-catalyzed carbonyl-group directed amidation of arene C–H bonds with sulfonamides **45** reported by the Liu group (Scheme 3.12).[11e] *N*-Fluoro-2,4,6-

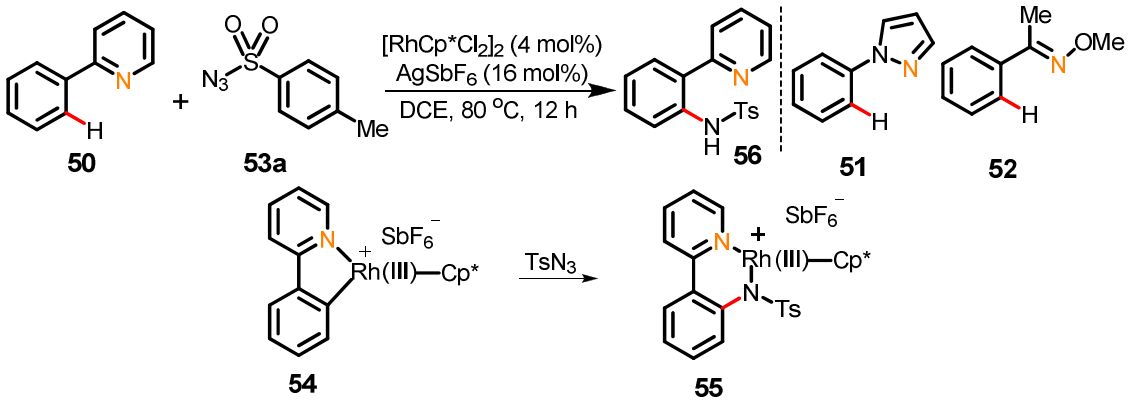
trimethyl-pyridinum triflate (**46**) was used as oxidant. The sulfonamide coordinated Pd(II) complex **47** was isolated and characterized by X-ray crystallographic analysis. Addition of oxidants such as $[F]^+$ or $N_2S_2O_8$ converted **47** to Pd(IV) imido complex **48**. Finally, reductive elimination of **48** produces the *o*-amidated aromatic ketones **49**.



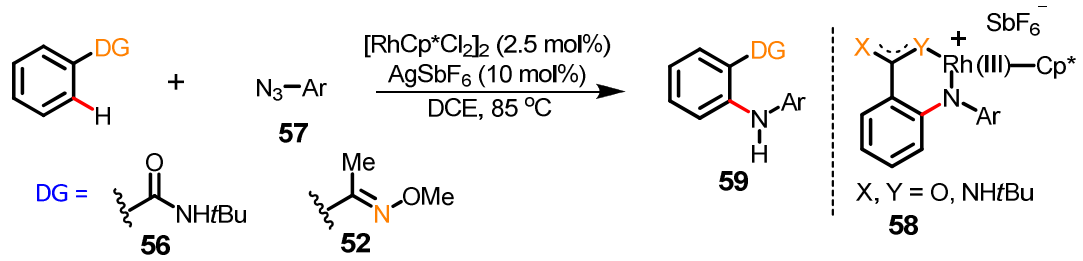
Scheme 3.12: Pd-Catalyzed Direct C–H Amidation of Aromatic Ketones

3.1.2.2. Rhodium Catalyzed *ortho*-C–H Amidation/Amination

The Rh(III)-catalyzed pyridyl (**50**), pyrazole (**51**), and/or oxime (**52**)-directed amidation of arene C–H bonds with sulfonyl azides (**53a**) has recently been reported by the Chang group;[12a] this process produces the benign N_2 gas byproduct. The C–H bond activation of 2-phenylpyridine (**50**) with cationic Rh(III) species affords a five-membered rhodacycle intermediate **54**. Coordination of azide to **54** and subsequent insertion of a sulfonamido moiety into the rhodacycle provides Rh(III) amido complex **55**. Finally, protonolysis of **55** delivers the desired product **56** (Scheme 3.13).

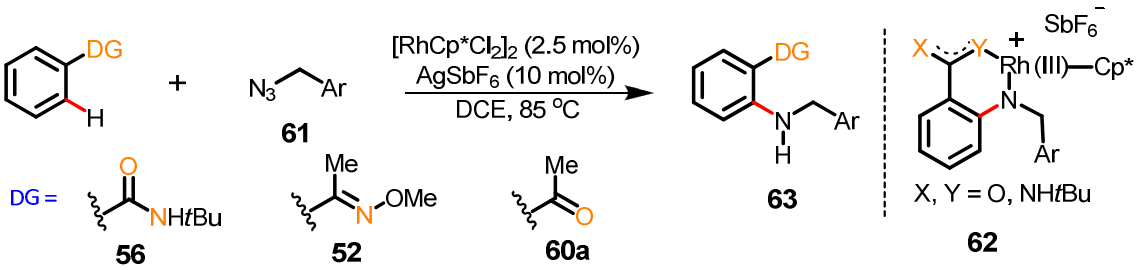


Scheme 3.13: Rh-Catalyzed *ortho*-C–H Amidation of Arenes with Sulfonyl Azides



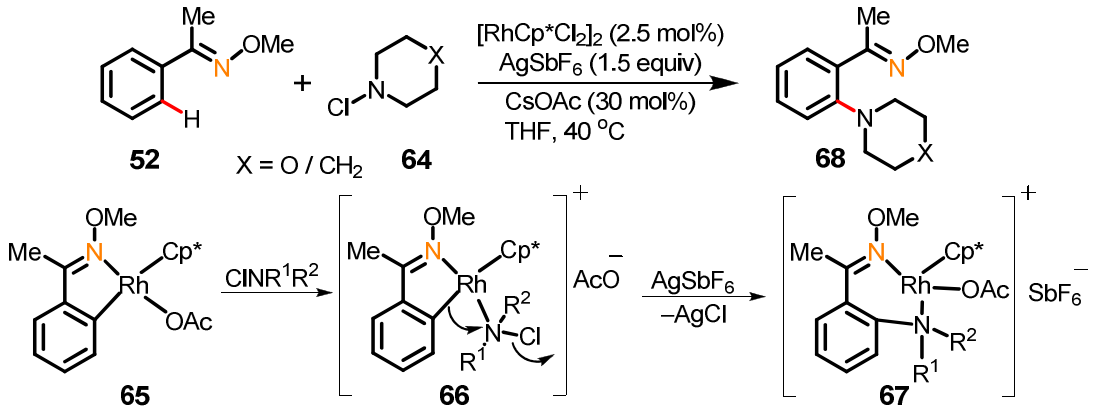
Scheme 3.14: Rh-Catalyzed Direct C–H Amination of Benzamides with Aryl Azides

Furthermore, the Chang group disclosed the rhodium-catalyzed direct C–H amination of benzamides (**56**) and aromatic ketoxime (**52**) *with aryl azides* (**57**).[12b] This reaction proceeds via Rh(III) amido intermediate **58** and produces the unsymmetrical diarylamines **59** (Scheme 3.14).



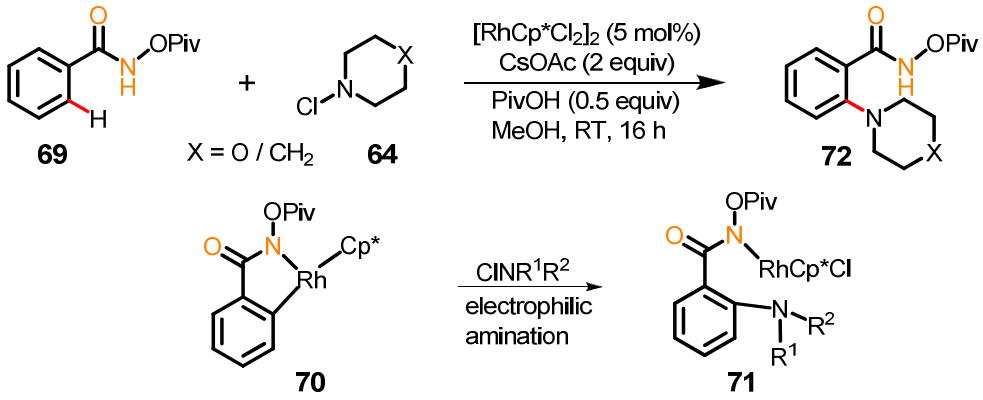
Scheme 3.15: Rh-Catalyzed Direct C–H Amination of Benzamides with Alkyl Azides

Benzamide (**56**), ketoximes (**52**) and aryl ketones (**60a**) directed Rh-catalyzed *o*-C–H amination of arenes *with alkyl azides* (**61**), recently been published by the Chang group (Scheme 3.15).[12c] As shown previously in Scheme 3.14, the reaction proceeds involving the Rh(III) amido intermediate **62**.



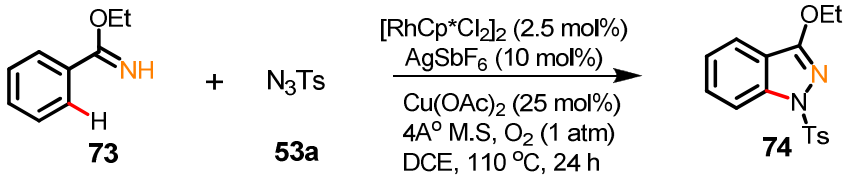
Scheme 3.16: Rh-Catalyzed Direct C–H Amination of Ketoxime with *N*-Chloroamines

The typical method for the synthesis of *o*-amino ketoxime **68** involves Rh(III)-catalyzed amination of aromatic C–H bonds with *N*-chloroamines **64** (Scheme 3.16).[12d] The reaction is likely to go through the cyclometalated aryl-Rh(III) complex **65**. Coordination of the *N*-chloroamine to rhodacycle **65** produces **66**. The silver promoted chloride abstraction allows the migration of the aryl group to nitrogen; finally, reductive removal of Rh-catalyst delivers the C–N bond forming product **68** (Scheme 3.16).



Scheme 3.17: Rh-Catalyzed *ortho*-C–H Amination of *N*-pivaloyloxy Benzamides with *N*-Chloroamines at Room Temperature

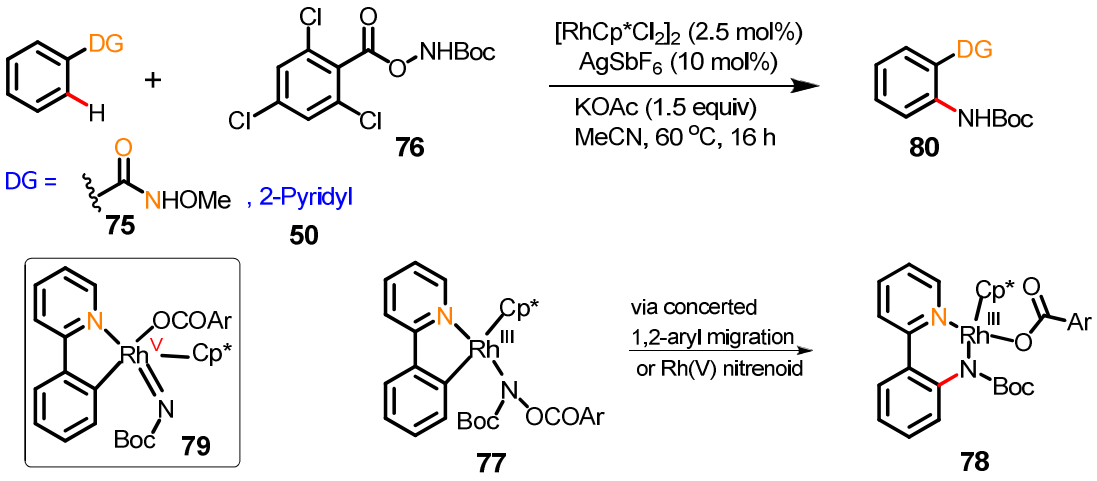
Recently, the Glorius group demonstrated an efficient and room temperature direct C–H amination of *N*-pivaloyloxy benzamides (**69**) with *N*-chloroamines (**64**).[12e] Electrophilic amination of rhodacycle **70** with *N*-chloroamine gives amide nitrogen coordinated rhodium species **71**, which upon protodemetalation affords the desired amination product **72** and Rh(III)-catalyst for next cycle (Scheme 3.17).



Scheme 3.18: Rh/Cu-Cocatalyzed Synthesis of 1*H*-Indazoles through C−H Amidation

An attractive strategy for the synthesis of 1*H*-indazole (**74**) was reported by Glorius and coworkers.[12f] Rh(III)/Cu(II) Co-catalyzed cascade *o*-C–H amidation and N–N bond formation of ethyl phenylimidate **73** with tosyl azide (**53a**) afforded the 1*H*-indazole **74**.

The *o*-C–H amidation of 2-phenylpyridine (**50**) and O-methylhydroxamic acids (**75**) with electrophilic amidation partner aryloxycarbamates (**76**) is reported by the Glorius group.[12g] The nitrogen atom in aroyloxycarbamate coordinates to the rhodacycle to afford **77**. The 1,2-aryl migration to the amide nitrogen with concomitant N–O cleavage delivers the complex **78**. Alternatively, reductive elimination of Rh(V) nitrenoid species **79** could generate **78**. Finally, proto-demetallation of **78** affords the desired product **80** (Scheme 3.19).

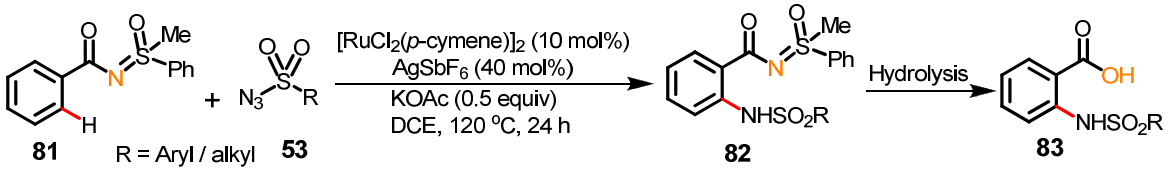


Scheme 3.19: Rh-Catalyzed *ortho*-C–H Amidation of Arenes with Aroyloxycarbamates

3.1.2.3. Ruthenium Catalyzed *ortho*-C–H Amidation

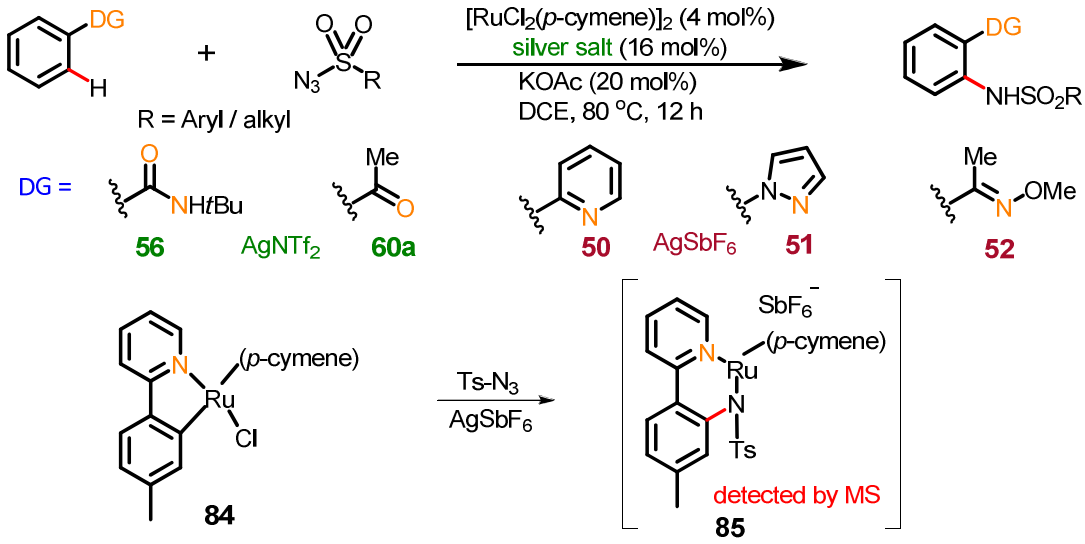
Ruthenium complexes have been widely employed as one of the most efficient and selective catalysts for the C–H bond activation. Following Murai's pioneering study on Ru-catalyzed C–H activation of arylketones,[13] there has been significant interest in the development of transition-metal-catalyzed carbonyl-directed aryl *ortho*-C(sp^2)–H functionalization for C–C and C–X (X = halogen, O, or N) bond formation. The ruthenium-catalyzed C–H bond activation strategy has been practiced almost exclusively for the introduction of alkyl, vinyl, or aryl groups.[14] However, to the best of our knowledge, the use of Ru-catalysts for the C–H amidation of arylketones is unprecedented.[15] Recently, our group demonstrated Ru-catalyzed reusable sulfoximine (**81**) assisted C(aryl)–N bond formation with sulfonyl azides (**53**) to produce anthranilic acid derivatives (**83**).[16] The preliminary results inspired us to examine the direct intermolecular *o*-C(aryl)–H amidation of weakly coordinating arylketones (**60**) with

tosylazides (**53a**). In this study, we focus on the use of inexpensive, easy-to-prepare and air-stable Ru(II) catalysts for direct intermolecular *o*-C–H amidation.



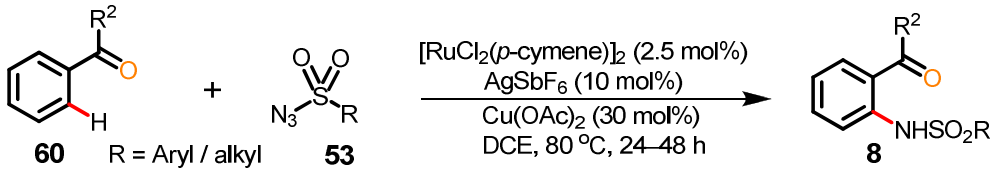
Scheme 3.20: Ru-Catalyzed *o*-C–H Amidation of Arenes in *N*-Benzoylated Sulfoximine with Sulfonyl Azides

A seminal report by the Chang group demonstrates the *o*-C–H amidation of arenes under the influence of the benzamides (**56**), pyridine (**50**), pyrazole (**51**), aromatic ketoxime (**52**), and aryl-ketones (**60**) directing groups.[17a] The reaction between 2-phenylpyridine (**50**) and stoichiometric amounts of $[RuCl_2(p\text{-cymene})]_2$ in the presence of KOAc in MeOH gave a ruthenacycle species **84** (Scheme 3.21). The structure of **84** was characterized by X-ray crystallographic analysis. Interestingly, the amido insertion ruthenium species **85** was detected by mass spectroscopy, when **84** and tosyl azide were reacted in the presence of $AgSbF_6$ (Scheme 3.21). Finally, protonolysis of **85** gave desired amidation product.



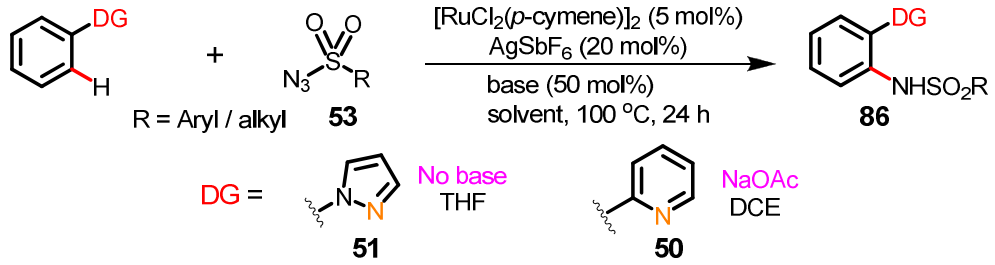
Scheme 3.21: Ru-Catalyzed Direct C–H Amidation of Arenes with Sulfonyl Azides

After our publication on Ru-catalyzed *ortho*-amidation of aromatic ketones, Jiao group reported the Ru(II)-catalyzed intermolecular amidation of weakly coordinating ketones (**60**) with sulfonyl azide (**53**) via C–H bond activation (Scheme 3.22).[17b]



Scheme 3.22: Ru-Catalyzed *o*-C–H Amidation of Weakly Coordinating Ketones with Sulfonyl Azides

A recent report of Ackermann group demonstrates the ruthenium-catalyzed heteroaryl-directed *o*-C–H amidation of arenes (**51**) with sulfonylazides (**53**) (Scheme 3.23).[17c]



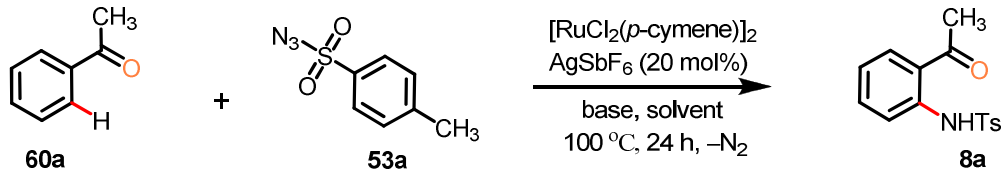
Scheme 3.23: Ru-Catalyzed *o*-C–H Amidation of Heteroaryl Arenes with Sulfonyl Azides

3.2. Results and Discussion

3.2.1. Reaction Optimization:

To find general conditions for the *ortho*-C(sp^2)–H amidation on aryl-ketones, reaction of acetophenone (**60a**) with tosylazide (**53a**) was conducted in the presence of the previously established catalytic conditions $[RuCl_2(p\text{-cymene})]_2$ (5 mol%), $AgSbF_6$ (20 mol%) and bases in 1,2-dichloroethane (1,2-DCE) at 100 °C for 24 h used for the *o*-C–H amidations on aryl-sulfoximines. The details of the optimization studies are shown in Table 3.1. The reaction did not proceed in the absence of base (entry 1). Interestingly, a trace amount of desired *ortho*-amidation product **8a** was noticed, when KOAc was employed in the reaction (entry 2). However, use of $Cu(OAc)_2 \cdot H_2O$ enhanced the product formation, affording **8a** in 65% yield (entry 3). The other acetate source CsOAc was ineffective, whereas LiOAc and AgOAc furnished moderate yield of **8a** (entries 4–6). Other solvents such as chlorobenzene yielded poor amount of **8a** (entry 7), whereas $CHCl_3$, CH_3CN, toluene and THF failed to produce even 10% of **8a** (entries 8–11). The less amount of $Cu(OAc)_2 \cdot H_2O$ (0.5 equiv) improved the yield of **8a** to 74% (entry 12).

Table 3.1: Optimization of the Reaction Conditions.[a]



entry	base	solvent	yield (%)[b]
1	---	$ClCH_2CH_2Cl$	NR
2	KOAc	$ClCH_2CH_2Cl$	< 5
3	$Cu(OAc)_2 \cdot H_2O$	$ClCH_2CH_2Cl$	65
4	LiOAc	$ClCH_2CH_2Cl$	42
5	CsOAc	$ClCH_2CH_2Cl$	08
6	AgOAc	$ClCH_2CH_2Cl$	56
7	$Cu(OAc)_2 \cdot H_2O$	chlorobenzene	28
8	$Cu(OAc)_2 \cdot H_2O$	$CHCl_3$	< 5
9	$Cu(OAc)_2 \cdot H_2O$	CH_3CN	< 5
10	$Cu(OAc)_2 \cdot H_2O$	toluene	< 5
11	$Cu(OAc)_2 \cdot H_2O$	THF	08
12	**$Cu(OAc)_2 \cdot H_2O$[c]**	**$ClCH_2CH_2Cl$**	**74**

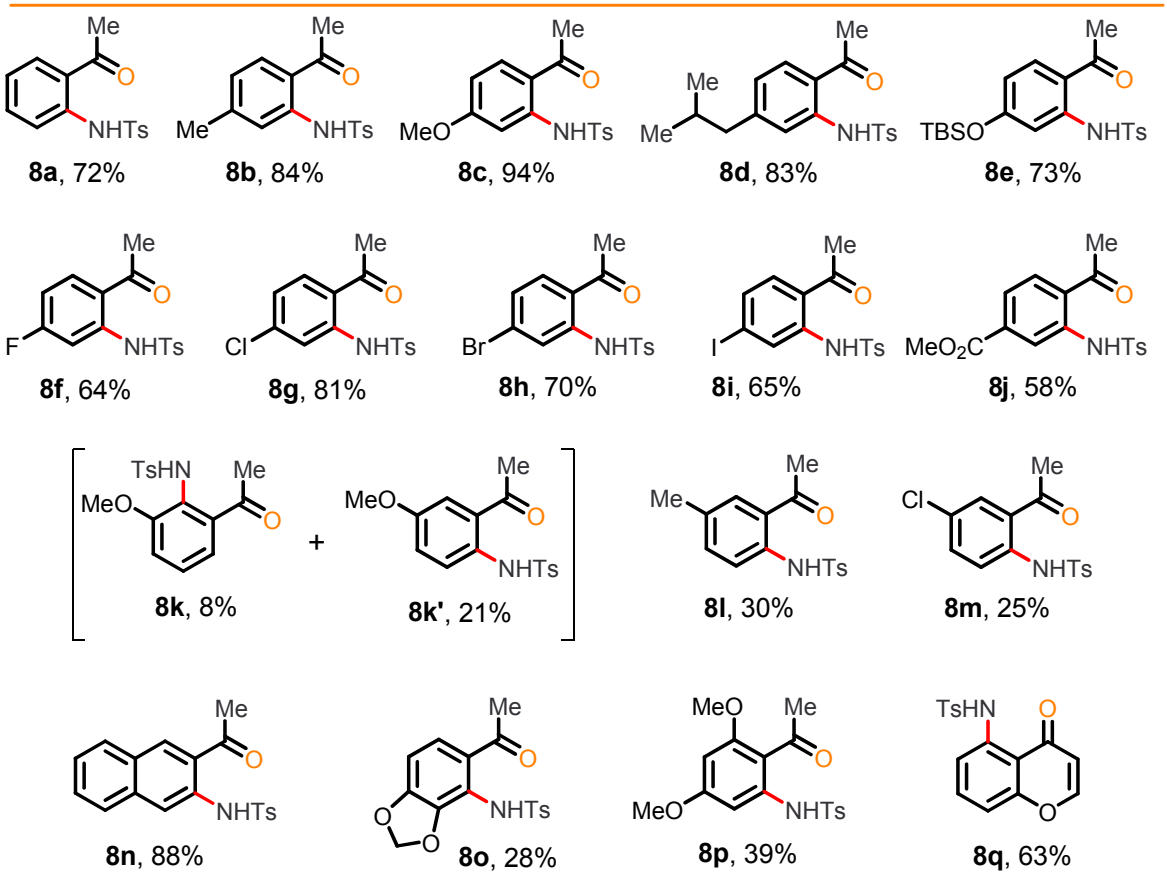
[a]Reaction conditions: **60a** (0.5 mmol), **53a** (0.75 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5 mol%), base (0.5 mmol), [b]Isolated yields, [c]$Cu(OAc)_2 \cdot H_2O$ (50 mol%). NR = no reaction.

3.2.2. Scope of the Reaction

The optimized conditions in entry 12, Table 3.1, were screened examining the scope and functional group tolerance of this transformation. Table 3.2 summarizes the results of *o*-C–H amidation on arylmethyl ketones with **53a**. The *o*-C–H amidation product **8a** was isolated in 72% yield from the acetophenone (**60a**). The *para*-substituted arylmethyl ketones possessing electron-donating methyl, methoxy, *i*-butyl substituents delivered the corresponding *ortho*-amidation products **8b**–**d** in good to excellent yields. Interestingly, the OTBS protecting group was well tolerated, yielding 73% of **8e**. Next we examined the effect of electron withdrawing groups at *para*-position of arylketones. Halo groups (F, Cl, Br and I) were inert under the present reaction conditions, furnishing the desired products **8f**–**i** in good yields. The tolerance of iodo groups under the catalytic conditions is notable. The optimized conditions did not affect the ester-group, producing **8j** in 58% yield. The amidations on *meta*-substituted arylketones were found to be inferior.[11e] The regioisomeric products **8k** and **8k'** were obtained in 8% and 21% yields, respectively, from the *m*-methoxyacetophenone **8k**. Similarly, the other *meta*-substituted compounds such as 3-methylacetophenones (**60l**) and 3-chloroacetophenone (**60m**) gave the corresponding less-

hindered *o*-C–H amidation products **8l** in 30% and **8m** in 25% yield, respectively. The reaction of 2-acetonaphthone (**60n**) with **53a** furnished a highly regioselective product **8n** in good yield. Notably, the hindered *o*-C–H was amidated, when 3',4'-(methylenedioxy)acetophenone (**60o**) reacted with **53a**; the 2-NHTs substituted **8o** was produced albeit in poor yield.[14h] The highly electron rich 2,4-dimethoxy substituted acetophenone (**60p**) afforded **8p** in 39% yield. Pleasingly, the reaction between chromone (**60q**) and **53a** gave good amount of **8q**, leaving the conjugated double bond unaffected.

Table 3.2: Substrate Scope of Aromatic Ketones. [a,b]

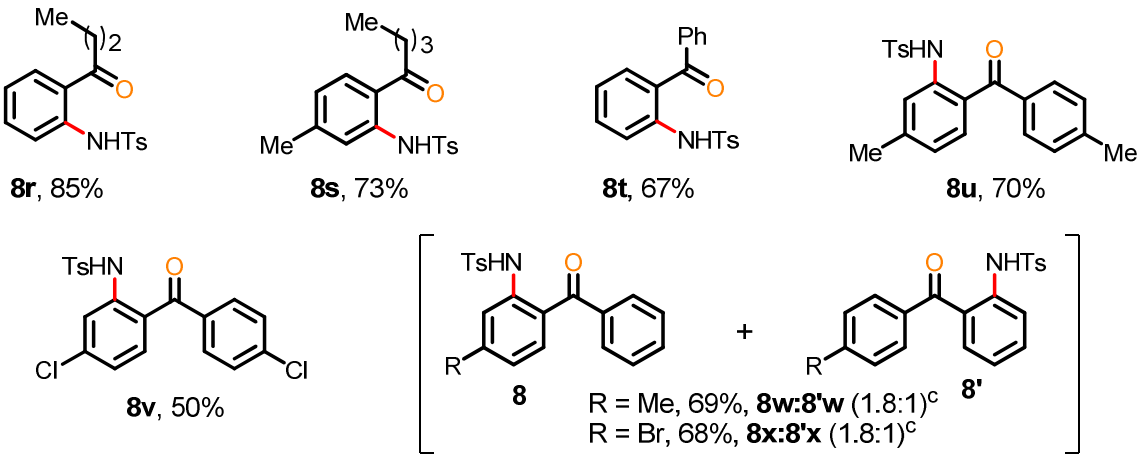


[a]Reaction conditions: Aryl ketone (**60**) (1.0 mmol), **53a** (1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5 mol%), $AgSbF_6$ (20 mol%), $Cu(OAc)_2 \cdot H_2O$ (50 mol%), 1,2-DCE (2.0 mL) at 100 °C for 24 h. [b]Isolated yields.

Next, we studied the *ortho*-amidation of various alkyl–aryl ketones and aryl–aryl ketones with tosyl azides and the results are shown in Table 3.3. Propyl and *n*-butyl substituted ketones, **60r** and **60s**, independently reacted with **53a** to deliver **8r** and **8s** in 85% and 73% yield, respectively. Aryl–aryl ketone amidation product **8t** was obtained from

benzophenone (**60t**) in good yield. Similarly, electron-rich symmetrical 4,4'-dimethyl-benzophenone (**60u**) gave 70% of **8u**; whereas electron deficient Cl-bearing **60v** yielded **8v** in moderate yield. We next investigated the reaction of unsymmetrical diarylketones bearing an electron donating (–Me) (**60w**) and electron-withdrawing (–Br) group (**60x**) at the *para*-position in one of the arylmoieties with **53a**. The inseparable regioisomeric mixtures of the corresponding amidation products **8w**/**8'w** and **8x**/**8'x** (1.8:1) are obtained in moderate yields. Interestingly, electron poor bromo-substituted phenyl ring in **60x** was participated effectively in the *o*-C-H amidation to give **8x** as a major product. The ^{1}H NMR analysis indicates that the product **8w** was formed in excess amount; in which electron rich aryl moiety of **60w** involved in the C–N bond formation effectively.

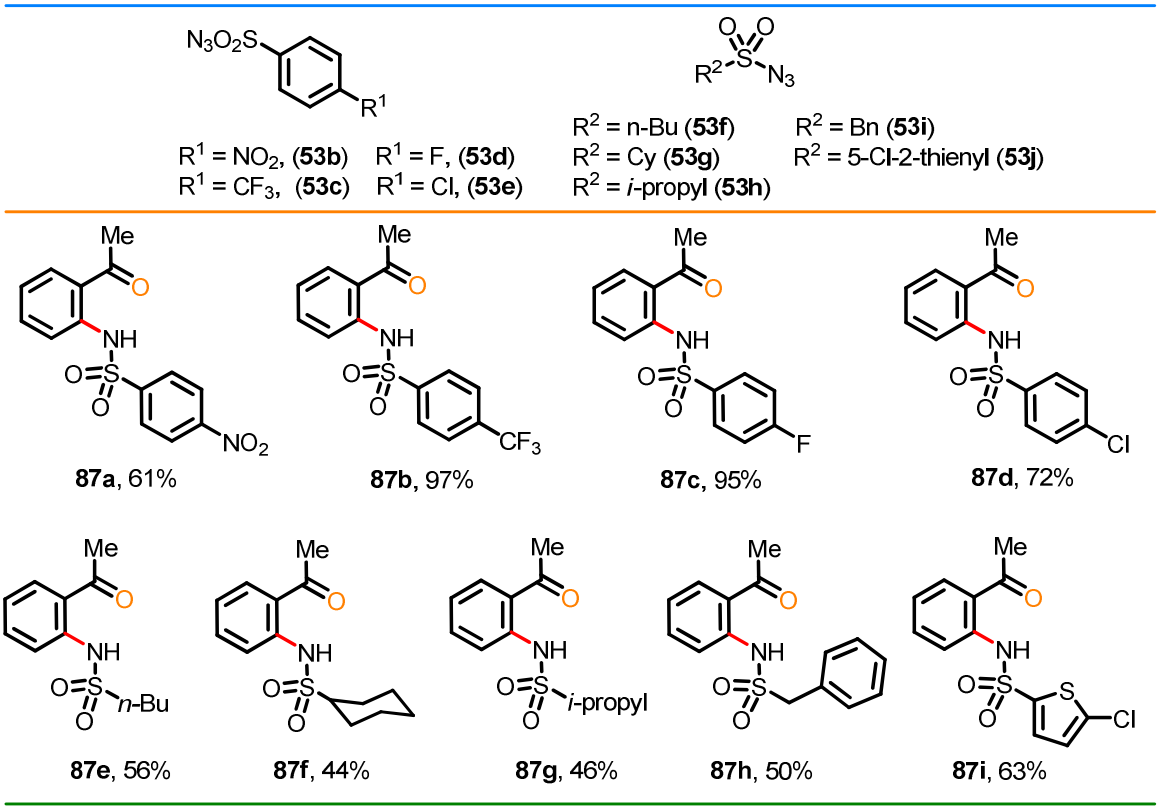
Table 3.3: Substrate Scope of Aryl/Alkyl and Aryl/Aryl Ketones. [a,b]



[a]Reaction conditions: Aryl ketone (**60**) (1.0 mmol), **53a** (1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5 mol%), $AgSbF_6$ (20 mol %), $Cu(OAc)_2 \cdot H_2O$ (50 mol %), 1,2-DCE (2.0 mL) at 100 °C for 24 h. [b]Isolated yields. [c]Mixture of two regioisomers.

We next turned our attention to the scope of different sulfonyl azides in the *ortho*-amidation on acetophenone (Table 3.4). Electron withdrawing arene-sulfonyl azides (**53b**–**e**), having NO_2, CF_3, F or Cl groups, successfully underwent amidation with **60a**, producing the corresponding *ortho*-C–N bearing products **87a**–**d** in good to excellent yields. The structure of **87a** was characterized by X-ray crystallographic analysis (Figure 3.2). Aliphatic sulfonyl azides **53f**–**i** are also viable, delivering the desired *o*-amido aryl ketones **87e**–**h** in moderate yields. The thienyl–sulfonyl amido bearing product **87i** was obtained in 63% yield, when 5-chlorothiophene-2-sulfonyl azide (**53j**) reacted with **60a**.

Table 3.4: Sulfonyl Azide Scope [a,b]



[a]Reaction conditions: **60a** (1.0 mmol), **53** (1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5 mol%), $AgSbF_6$ (20 mol%), $Cu(OAc)_2 \cdot H_2O$ (50 mol%), 1,2-DCE (2.0 mL). [b]Isolated yields.

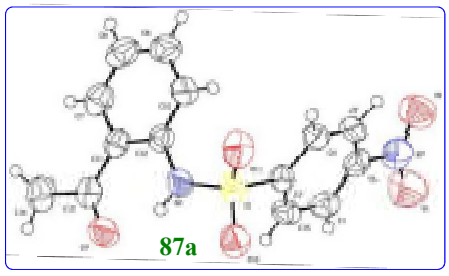
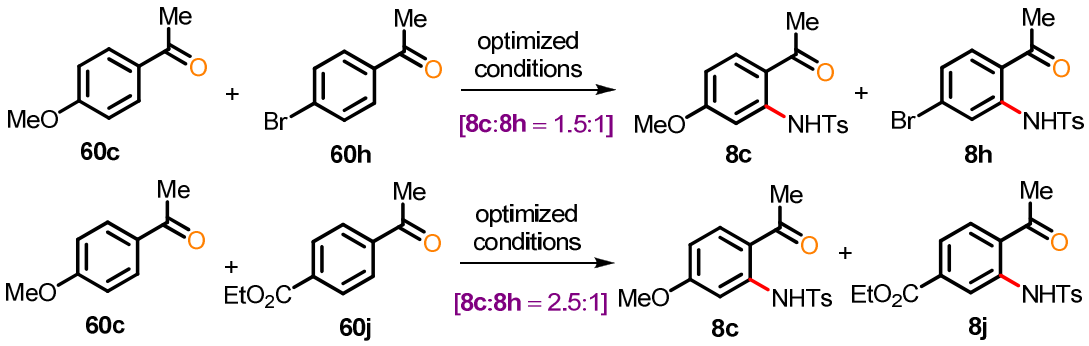


Figure 3.2: ORTEP Diagram of **87a**

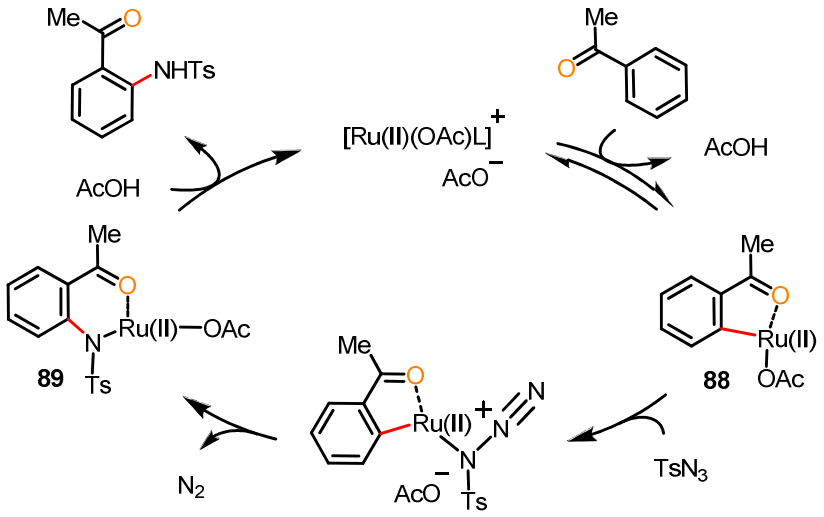
The intermolecular competitive amidation among electron rich 4'-methoxyacetophenone (**60c**) and electron poor 4'-bromoacetophenone (**60h**), also **60c** and highly electron deficient methyl 4-acetylbenzoate (**60j**) with **53a** was independently performed under the optimized conditions (Scheme 3.24). The ratios of products **8c**/**8h** and **8c**/**8j** were found to be 1.5/1.0 and 2.5/1.0, respectively, indicating better reactivity of the electron-rich over electron-poor arenes.



Scheme 3.24: Competitive Experiments

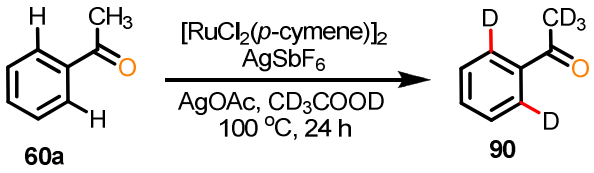
3.2.3. Mechanistic Studies

Although the detailed mechanism of Ru(II)-catalyzed C–H amidation of arenes is yet to be established, the proposed mechanism is outlined in Scheme 3.25.[18] The combination of $[RuCl_2(p\text{-cymene})]_2$, base, and $AgSbF_6$ generates the active Ru(II)-catalyst.



Scheme 3.25: Proposed Mechanistic Cycle

The coordination of carbonyl oxygen to the coordinatively unsaturated Ru-catalyst triggers activation of the *o*-C–H bond and delivers the metallacycle intermediate **88**;[10e] the deuterium scrambling experiment supports the reversible cleavage of C–H bonds (Scheme 3.26). Coordination of azide to **88** followed by migratory insertion of sulfonamido moieties with evolution of N_2 gas leads to the intermediate **89**. Finally, protonolysis of **89** provides the desired product and generates the active ruthenium-complex for the next catalytic cycle.



Scheme 3.26: Deuterium Experiment

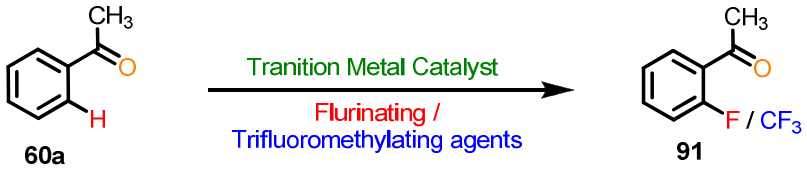
3.3. Conclusion

In summary, we have developed a ruthenium-catalyzed direct aryl *o*-C–H amidation on the readily available aryl–alkyl and aryl–aryl ketones with sulfonyl azides. The reaction proceeds with the broad scope of arylketones in good yields. The reaction condition tolerates O-bearing labile protecting group –OTBS and ester functionality. A wide range of sulfonyl azides were successfully installed on arylketones.

3.4. Future Work

The presence of halo-groups, mainly the fluoro functionality enhances the solubility of the molecules in biological system. Therefore, the fluoro-bearing compounds showed better pharmacological properties compare to the non-fluoro analogs. Therefore, the development of novel methods for the direct formation of carbon-fluorine (C–F) and carbon-trifluoromethyl (C–CF_3) bonds is essential.

To the best of our knowledge, the transition metal catalyzed *o*-C–H fluorination and trifluoromethylation on arenes in the weakly coordinating aromatic ketones remains elusive. We therefore envisioned investigating the transition-metal catalyzed fluorination and trifluoromethylation of *o*-C–H aromatic ketones using the readily available fluorinating/trifluoromethylating reagents (Scheme 3.27 and Figure 3.3).



Scheme 3.27: C–H Fluorination / Trifluoromethylation

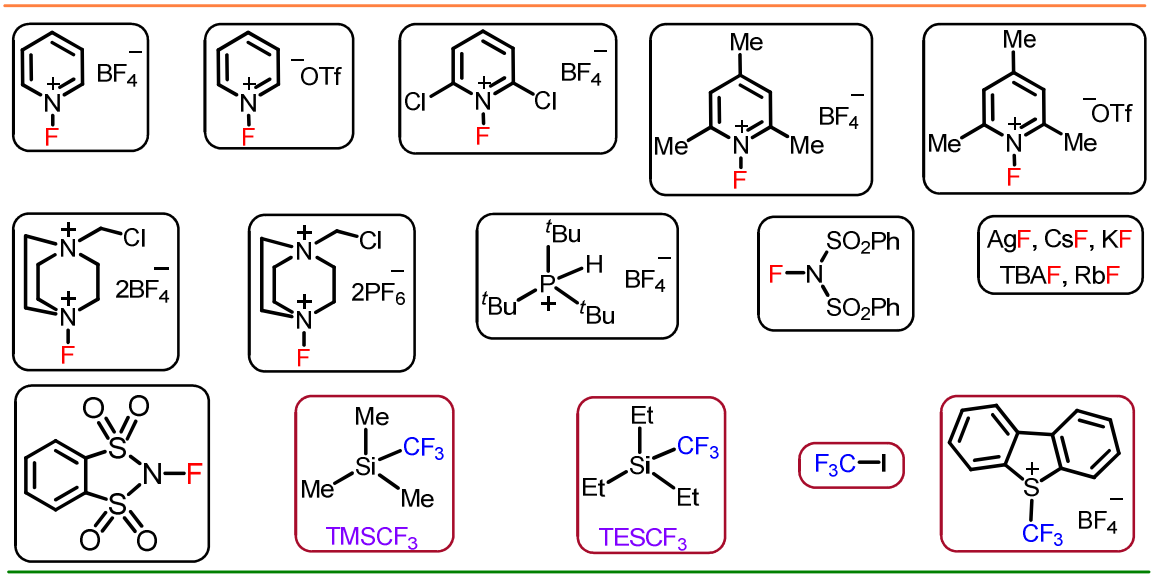


Figure 3. 3: Fluorinating / Trifluoromethylating Reagents

3.5. Experimetal

3.5.1. General Experimental Information for this Chapter is same as mentioned in Chapter 1.

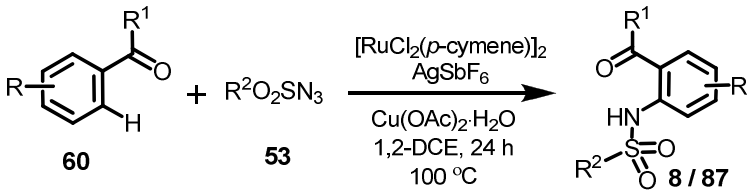
3.5.2. Materials: Unless otherwise noted, all the reagents were obtained commercially and used without purification. 1,2-Dichloroethane (DCE) are distilled over $CaCl_2$. Aryl ketones, $[RuCl_2(p\text{-cymene})]_2$, $Cu(OAc)_2 \cdot H_2O$ and $AgSbF_6$ were purchased from Sigma Aldrich Ltd. and used as received. Analytical and spectral data of all those known compounds are exactly matching with the reported values.

3.5.3. General Procedure for the Synthesis of Azides (GP-1): [19]

The azides are prepared following the known procedure.

To a solution of sodium azide (1.99 g, 30 mmol) in water (10 mL) was added a solution of *p*-toluenesulfonyl chloride (3.85 g, 20 mmol) in acetone (20 mL) dropwise at 0 °C. The reaction was warmed up to room temperature and stirred for overnight, the acetone was removed under reduced pressure and the reaction mixture was extracted with EtOAc (20 mL) for three times. The combined organic layers were washed with water and saturated Na_2CO_3 solution, dried over Na_2SO_4 and the solvent was removed under the reduced pressure. The crude product is subsequently used without further purification.

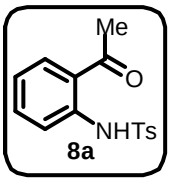
3.5.4. *Ortho*-C-H Amidation of Ketones with Sulfonyl Azides; General Procedure (GP-2):



Aryl ketones (**60**; 1.0 mmol), sulfonyl azides (**53**; 1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5 mol%), $Cu(OAc)_2 \cdot H_2O$ (50 mol%) and $AgSbF_6$ (20 mol%) were taken in an oven-dried Schlenk flask under an argon atmosphere. 1,2-Dichloroethane (DCE) (2.0 mL) was added to this mixture. The resulting solution was stirred at 100 °C for 24 h. The crude reaction mixture was diluted with dichloromethane and passed through a small pad of Celite. After evaporation of the solvent, the crude reaction mixture was purified using column chromatography on silica gel.

3.5.5. Spectral and Analytical Data of the Compounds:

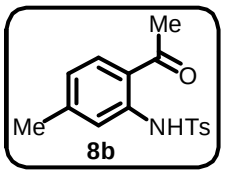
***N*-(2-Acetylphenyl)-4-methylbenzenesulfonamide (8a):**[20]



Following the general procedure (GP-2); acetophenone (**60a**; 120 mg, 1.0 mmol), tosyl azide (**53a**; 296 mg, 1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (31 mg, 5 mol%), $Cu(OAc)_2 \cdot H_2O$ (100 mg, 50 mol%) and $AgSbF_6$ (69 mg, 20 mol%) in 1,2-DCE (2.0 mL) was heated at 100 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (6:1) to afford **8a** (209 mg) in 72% yield as colorless solid.

mp = 150–151 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.48 (s, 1H), 7.79 (dd, J = 8.0, 1.2 Hz, 1H), 7.71 (d, J = 8.4 Hz, 2H), 7.66 (d, J = 8.4 Hz, 1H), 7.43 (t, J = 7.2 Hz, 1H), 7.20 (d, J = 8.0 Hz, 2H), 7.05 (t, J = 8.0 Hz, 1H), 2.54 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.4, 143.8, 139.8, 136.3, 134.8, 131.9, 129.5, 127.1, 122.5, 122.1, 118.8, 28.0, 21.4.

***N*-(2-Acetyl-5-methylphenyl)-4-methylbenzenesulfonamide (8b):**

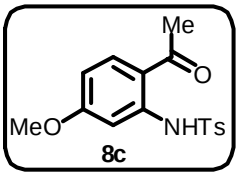


Following the general procedure (GP-2); 4'-methylacetophenone (**60b**; 134 mg, 1.0 mmol), tosyl azide (**53a**; 296 mg, 1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (31 mg, 5 mol%), $Cu(OAc)_2 \cdot H_2O$ (100 mg, 50 mol%) and

$AgSbF_6$ (69 mg, 20 mol%) in 1,2-DCE (2.0 mL) was heated at 100 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (4:1) to afford **8b** (255 mg) in 84% yield as colorless solid.

mp = 133–134 °C; R_f = 0.36 (4:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.54 (s, 1H), 7.74 (d, *J* = 8.0 Hz, 2H), 7.67 (d, *J* = 8.0 Hz, 1H), 7.50 (s, 1H), 7.23 (d, *J* = 8.0 Hz, 2H), 6.86 (d, *J* = 8.0 Hz, 1H), 2.53 (s, 3H), 2.37 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.9, 146.4, 143.8, 140.2, 136.6, 131.9, 129.6, 127.3, 123.5, 119.9, 119.3, 28.0, 22.1, 21.6; IR (KBr) ν_{max} 2926, 1649, 1567, 1161, 657, 536 cm^{-1}; HRMS–ESI (*m/z*): $[M+Na]^+$ Calcd for $C_{16}H_{17}NO_3SNa$, 326.0827; found, 326.0831.

***N*-(2-Acetyl-5-methoxyphenyl)-4-methylbenzenesulfonamide (8c):**

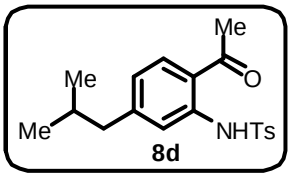


8c

Following the general procedure (GP-2); 4'-methoxyacetophenone (**60c**; 150 mg, 1.0 mmol), tosyl azide (**53a**; 296 mg, 1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (31 mg, 5 mol%), $Cu(OAc)_2 \cdot H_2O$ (100 mg, 50 mol%) and $AgSbF_6$ (69 mg, 20 mol%) in 1,2-DCE (2.0 mL) was heated at 100 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (4:1) to afford **8c** (299 mg) in 94% yield as colorless solid.

mp = 139–140 °C; R_f = 0.29 (4:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.92 (s, 1H), 7.85 –7.66 (m, 3H), 7.21 (d, *J* = 8.0 Hz, 2H), 7.14 (d, *J* = 2.0 Hz, 1H), 6.51 (dd, *J* = 9.2, 2.4 Hz, 1H), 3.79 (s, 3H), 2.39 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.8, 164.3, 143.9, 142.5, 136.3, 134.0, 129.6, 127.2, 115.3, 108.8, 102.6, 55.5, 27.7, 21.4; IR (KBr) ν_{max} 2947, 1632, 1265, 1161, 887, 663, 548 cm^{-1}; HRMS–ESI (*m/z*): $[M+Na]^+$ Calcd for $C_{16}H_{17}NO_4SNa$, 342.0776; found, 342.0777.

***N*-(2-Acetyl-5-*iso*-butylphenyl)-4-methylbenzenesulfonamide (8d):**



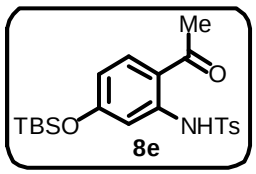
8d

Following the general procedure (GP-2); 1-(4-isobutylphenyl)ethanone (**60d**; 120 mg, 1.0 mmol), tosyl azide (**53a**; 296 mg, 1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (31 mg, 5 mol%), $Cu(OAc)_2 \cdot H_2O$ (100 mg, 50 mol%) and $AgSbF_6$ (69 mg, 20

mol%) in 1,2-DCE (2.0 mL) was heated at 100 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (4:1) to afford **8d** (286 mg) in 83% yield as brown color solid.

mp = 91–92 °C; R_f = 0.50 (4:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.53 (s, 1H), 7.69 (t, *J* = 8.4 Hz, 3H), 7.46 (bd, *J* = 1.6 Hz, 1H), 7.19 (d, *J* = 8.0 Hz, 2H), 6.82 (dd, *J* = 8.0, 1.6 Hz, 1H), 2.52 (s, 3H), 2.44 (d, *J* = 7.2 Hz, 2H), 2.34 (s, 3H), 1.89–1.75 (m, 1H), 0.82 (d, *J* = 6.8 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.9, 149.9, 143.7, 139.9, 136.3, 131.8, 129.5, 127.2, 123.5, 120.0, 119.3, 45.4, 29.9, 27.9, 22.1, 21.4; IR (KBr) ν_{max} 2964, 1643, 1429, 1160, 651 cm^{-1}; HRMS–ESI (*m/z*): $[M+Na]^+$ Calcd for $C_{19}H_{23}NO_3SNa$, 368.1296; found, 368.1297.

_N_-(2-Acetyl-5-(tert-butyldimethylsilyloxy)phenyl)-4-methylbenzenesulfonamide (8e):

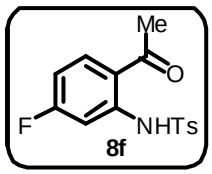


8e

Following the general procedure (GP-2); 1-(4-(*tert*-butyldimethylsilyloxy)phenyl)ethanone (**60e**; 250 mg, 1.0 mmol), tosyl azide (**53a**; 296 mg, 1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (31 mg, 5 mol%), $Cu(OAc)_2 \cdot H_2O$ (100 mg, 50 mol%) and $AgSbF_6$ (69 mg, 20 mol%) in 1,2-DCE (2.0 mL) was heated at 100 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (15:1) to afford **8e** (304 mg) in 73% yield as brown color semi-solid.

R_f = 0.28 (15:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.84 (s, 1H), 7.71 (d, *J* = 8.0 Hz, 2H), 7.68 (d, *J* = 8.4 Hz, 1H), 7.21 (d, *J* = 8.4 Hz, 2H), 7.08 (bd, *J* = 2.0 Hz, 1H), 6.46 (dd, *J* = 8.0, 1.2 Hz, 1H), 2.49 (s, 3H), 2.34 (s, 3H), 0.94 (s, 9H), 0.91 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.9, 161.3, 143.8, 142.3, 136.4, 134.0, 129.5, 127.1, 115.9, 114.5, 109.0, 27.7, 25.4, 21.4, 18.1, –4.6; IR (Neat) ν_{max} 2964, 1632, 1599, 1342, 1255, 1161, 915, 641 cm^{-1}; HRMS–ESI (*m/z*): $[M+H]^+$ Calcd for $C_{21}H_{30}NO_4SSi$, 420.1665; found, 420.1664.

_N_-(2-Acetyl-5-fluorophenyl)-4-methylbenzenesulfonamide (8f):



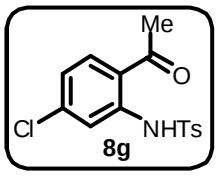
8f

Following the general procedure (GP-2); 4'-fluoroacetophenone (**60f**; 138 mg, 1.0 mmol), tosyl azide (**53a**; 296 mg, 1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (31 mg, 5 mol%), $Cu(OAc)_2 \cdot H_2O$ (100 mg, 50 mol%) and $AgSbF_6$ (69 mg, 20 mol%) in 1,2-DCE (2.0 mL) was heated at 100 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography

eluting with hexane: ethyl acetate (4:1) to afford **8f** (197 mg) in 64% yield as colorless solid.

mp = 150–151 °C; R_f = 0.30 (4:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.81 (s, 1H), 7.84 (bt, *J* = 4.0 Hz, 1H), 7.77 (bd, *J* = 1.6 Hz, 2H), 7.42 (d, *J* = 8.8 Hz, 1H), 7.27 (bd, *J* = 6.0 Hz, 2H), 6.74 (bt, *J* = 6.0 Hz, 1H), 2.57 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.1, 165.97 (d, *J* = 205.9 Hz), 144.2, 142.84 (d, *J* = 9.4 Hz), 136.2, 134.55 (d, *J* = 8.4 Hz), 129.8, 127.2, 118.3, 109.65 (d, *J* = 17.8 Hz), 105.46 (d, *J* = 21.6 Hz), 28.1, 21.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ –99.27 (quin); IR (KBr) ν_{max} 3090, 1659, 1593, 1429, 1171, 892, 662 cm^{-1}; HRMS–ESI (*m/z*): $[M+Na]^+$ Calcd for $C_{15}H_{14}FNO_3SNa$, 330.0576; found, 330.0570.

_N_-(2-Acetyl-5-chlorophenyl)-4-methylbenzenesulfonamide (8g):[21]

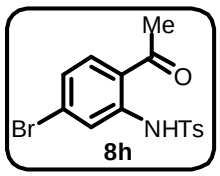


8g

Following the general procedure (GP-2); 4'-chloroacetophenone (**60g**; 155 mg, 1.0 mmol), tosyl azide (**53a**; 296 mg, 1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (31 mg, 5 mol%), $Cu(OAc)_2 \cdot H_2O$ (100 mg, 50 mol%) and $AgSbF_6$ (69 mg, 20 mol%) in 1,2-DCE (2.0 mL) was heated at 100 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (4:1) to afford **8g** (262 mg) in 81% yield as colorless solid.

mp = 162–163 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.60 (s, 1H), 7.76 (dd, *J* = 8.4, 2.0 Hz, 2H), 7.73 (d, *J* = 4.0 Hz, 1H), 7.71 (d, *J* = 2.4 Hz, 1H), 7.27 (d, *J* = 8.4 Hz, 2H), 7.00 (dd, *J* = 8.8, 2.0 Hz, 1H), 2.55 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.5, 144.2, 141.2, 141.1, 136.1, 133.0, 129.8, 127.2, 122.6, 120.1, 118.4, 28.1, 21.5.

_N_-(2-Acetyl-5-bromophenyl)-4-methylbenzenesulfonamide (8h):

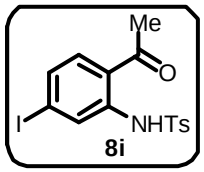


8h

Following the general procedure (GP-2); 4'-bromoacetophenone (**60h**; 198 mg, 1.0 mmol), tosyl azide (**53a**; 296 mg, 1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (31 mg, 0.5 mol%), $Cu(OAc)_2 \cdot H_2O$ (100 mg, 50 mol%) and $AgSbF_6$ (69 mg, 20 mol%) in 1,2-DCE (2.0 mL) was heated at 100 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (4:1) to afford **8h** (257 mg) in 70% yield as light brown color solid.

mp = 171–172 °C; R_f = 0.47 (4:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.56 (s, 1H), 7.85 (s, 1H), 7.72 (d, *J* = 8.0 Hz, 2H), 7.64 (d, *J* = 8.4 Hz, 1H), 7.24 (d, *J* = 8.0 Hz, 2H), 7.16 (d, *J* = 8.8 Hz, 1H), 2.54 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.7, 144.2, 140.9, 136.0, 133.0, 129.7, 127.1, 125.6, 121.4, 120.4, 28.1, 21.5; IR (KBr) ν_{max} 3063, 1649, 1561, 1161, 926, 657, 569 cm^{-1}; HRMS–ESI (*m/z*): $[M+H]^+$ Calcd for $C_{15}H_{15}BrNO_3S$, 367.9956; found, 367.9954.

_N_-(2-Acetyl-5-iodophenyl)-4-methylbenzenesulfonamide (8i):

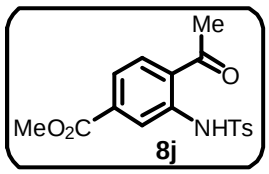


8i

Following the general procedure (GP-2); 4'-iodoacetophenone (**60i**; 246 mg, 1.0 mmol), tosyl azide (**53a**; 296 mg, 1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (31 mg, 5 mol%), $Cu(OAc)_2 \cdot H_2O$ (100 mg, 50 mol%) and $AgSbF_6$ (69 mg, 20 mol%) in 1,2-DCE (2.0 mL) was heated at 100 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (4:1) to afford **8i** (269 mg) in 65% yield as colorless solid.

mp = 167–168 °C; R_f = 0.38 (4:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.45 (s, 1H), 8.08 (bd, *J* = 0.8 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 2H), 7.49–7.37 (m, 2H), 7.27 (d, *J* = 8.0 Hz, 2H), 2.53 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.9, 144.2, 140.6, 136.2, 132.6, 131.7, 129.8, 127.7, 127.3, 121.0, 102.7, 28.0, 21.5; IR (KBr) ν_{max} 2925, 1659, 1588, 1484, 1160, 930, 662 cm^{-1}; HRMS–ESI (*m/z*): $[M+H]^+$ Calcd for $C_{15}H_{15}INO_3S$, 415.9817; found, 415.9819.

Methyl 4-acetyl-3-(4-methylphenylsulfonamido)benzoate (8j):



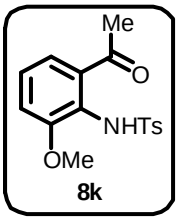
8j

Following the general procedure (GP-2); methyl 4-acetylbenzoate (**60j**; 178 mg, 1.0 mmol), tosyl azide (**53a**; 296 mg, 1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (31 mg, 5 mol%), $Cu(OAc)_2 \cdot H_2O$ (100 mg, 50 mol%) and $AgSbF_6$ (69 mg, 20 mol%) in 1,2-DCE (2.0 mL) was heated at 100 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (4:1) to afford **8j** (201 mg) in 58% yield as colorless solid.

mp = 152–153 °C; R_f = 0.25 (4:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.32 (s, 1H), 8.31 (bd, *J* = 0.8 Hz, 1H), 7.85 (d, *J* = 8.4 Hz, 1H), 7.76 (d, *J* = 8.4 Hz, 2H), 7.68

(dd, *J* = 8.4, 1.6 Hz, 1H), 7.24 (d, *J* = 8.0 Hz, 2H), 3.94 (s, 3H), 2.59 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.0, 165.4, 144.1, 140.0, 136.2, 135.3, 131.8, 129.7, 127.4, 124.7, 123.1, 119.9, 52.7, 28.4, 21.5; IR (KBr) ν_{max} 2953, 1720, 1649, 1419, 1156, 926, 663, 536 cm^{-1}; HRMS–ESI (*m/z*): $[M+H]^+$ Calcd for $C_{17}H_{18}NO_5S$, 348.0906; found, 348.0907.

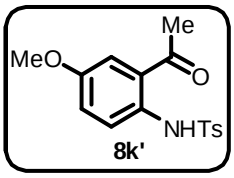
_N_-(2-Acetyl-6-methoxyphenyl)-4-methylbenzenesulfonamide (8k):



Following the general procedure (GP-2); 3'-methoxyacetophenone (**60k**; 150 mg, 1.0 mmol), tosyl azide (**53a**; 296 mg, 1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (31 mg, 5 mol%), $Cu(OAc)_2 \cdot H_2O$ (100 mg, 50 mol%) and $AgSbF_6$ (69 mg, 20 mol%) in 1,2-DCE (2.0 mL) was heated at 100 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (4:1) to afford **8k** (27 mg) in 8% yield as ash color solid and **8k′** (68 mg) in 21% yield as colorless solid.

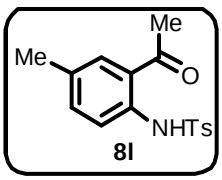
mp = 175–176 °C; R_f = 0.13 (4:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (bd, *J* = 1.6 Hz, 1H), 7.80 (d, *J* = 1.6 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.27 (s, 1H), 7.19 (bd, *J* = 2.0 Hz, 1H), 3.90 (s, 3H), 2.62 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.1, 147.2, 145.2, 143.6, 139.6, 129.8, 127.0, 125.8, 124.8, 115.7, 109.4, 56.1, 28.0, 21.5; IR (KBr) ν_{max} 3430, 3314, 2932, 1654, 1604, 1144, 668, 585 cm^{-1}; HRMS–ESI (*m/z*): $[M+H]^+$ Calcd for $C_{16}H_{18}NO_4S$, 320.0957; found, 320.0955.

_N_-(2-Acetyl-4-methoxyphenyl)-4-methylbenzenesulfonamide (8k′):[21]



mp = 119–120 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.67 (s, 1H), 7.63 (d, *J* = 9.2 Hz, 1H), 7.57 (d, *J* = 8.4 Hz, 2H), 7.19 (d, *J* = 2.8 Hz, 1H), 7.16 (d, *J* = 8.4 Hz, 2H), 7.02 (dd, *J* = 9.2, 3.2 Hz, 1H), 3.77 (s, 3H), 2.41 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.9, 155.2, 143.6, 136.0, 132.3, 129.4, 127.1, 124.7, 122.5, 119.8, 116.5, 55.6, 28.0, 21.4.

_N_-(2-Acetyl-4-methylphenyl)-4-methylbenzenesulfonamide (8l):

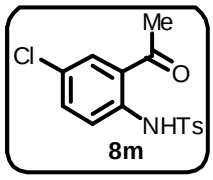


Following the general procedure (GP-2); 3'-methylacetophenone (**60l**; 134 mg, 1.0 mmol), tosyl azide (**53a**; 296 mg, 1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (31 mg, 5 mol%), $Cu(OAc)_2 \cdot H_2O$ (100 mg, 50 mol%) and $AgSbF_6$ (69 mg, 20 mol%) in 1,2-DCE (2.0 mL) was heated at 100 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography

eluting with hexane: ethyl acetate (4:1) to afford **8l** (90 mg) in 30% yield as colorless solid.

mp = 134–135 °C; R_f = 0.44 (4:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.23 (s, 1H), 7.69 (d, *J* = 8.0 Hz, 2H), 7.59 (d, *J* = 8.4 Hz, 1H), 7.56 (s, 1H), 7.30–7.24 (m, 1H), 7.20 (d, *J* = 8.4 Hz, 2H), 2.52 (s, 3H), 2.35 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.4, 143.7, 137.4, 136.5, 135.6, 132.3, 132.0, 129.5, 127.2, 122.6, 119.5, 28.1, 21.5, 20.6; IR (KBr) ν_{max} 3057, 1660, 1484, 1095, 646 cm^{-1}; HRMS–ESI (*m/z*): $[M+Na]^+$ Calcd for $C_{16}H_{17}NO_3SNa$, 326.0827; found, 326.0828.

_N_-(2-Acetyl-4-chlorophenyl)-4-methylbenzenesulfonamide (8m):

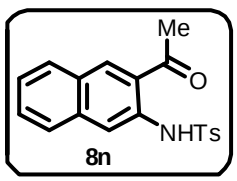


8m

Following the general procedure (GP-2); 3'-chloroacetophenone (**60m**; 154 mg, 1.0 mmol), tosyl azide (**53a**; 296 mg, 1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (31 mg, 5 mol%), $Cu(OAc)_2 \cdot H_2O$ (100 mg, 50 mol%) and $AgSbF_6$ (69 mg, 20 mol%) in 1,2-DCE (2.0 mL) was heated at 100 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (6:1) to afford **8m** (81 mg) in 25% yield as brown color solid.

mp = 135–136 °C; R_f = 0.48 (6:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.27 (s, 1H), 7.73 (d, *J* = 2.4 Hz, 1H), 7.70 (d, *J* = 8.4 Hz, 2H), 7.66 (d, *J* = 8.8 Hz, 1H), 7.39 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.22 (d, *J* = 8.0 Hz, 2H), 2.54 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.3, 144.1, 138.4, 136.1, 134.6, 131.3, 129.7, 127.8, 127.2, 123.2, 120.6, 28.1, 21.5; IR (KBr) ν_{max} 3073, 2931, 1649, 1588, 1249, 926, 657 cm^{-1}; HRMS–ESI (*m/z*): $[M+H]^+$ Calcd for $C_{15}H_{15}ClNO_3S$, 324.0461; found, 324.0464.

_N_-(3-Acetylnaphthalen-2-yl)-4-methylbenzenesulfonamide (8n):

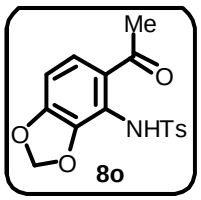


8n

Following the general procedure (GP-2); 2-acetonaphthone (**60n**; 170 mg, 1.0 mmol), tosyl azide (**53a**; 296 mg, 1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (31 mg, 5.0 mol%), $Cu(OAc)_2 \cdot H_2O$ (100 mg, 50 mol%) and $AgSbF_6$ (69 mg, 20 mol%) in 1,2-DCE (2.0 mL) was heated at 100 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (3:1) to afford **8n** (299 mg) in 88% yield as pale yellow solid.

mp = 154–155 °C; R_f = 0.48 (3:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.05 (s, 1H), 8.32 (s, 1H), 8.00 (s, 1H), 7.79 (d, *J* = 8.4 Hz, 1H), 7.71 (bt, *J* = 7.6 Hz, 3H), 7.55 (t, *J* = 7.2 Hz, 1H), 7.41 (t, *J* = 7.2 Hz, 1H), 7.14 (d, *J* = 8.0 Hz, 2H), 2.63 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.4, 143.6, 136.2, 135.8, 134.8, 134.4, 129.8, 129.4, 129.0, 128.4, 127.1, 127.0, 125.8, 123.1, 116.9, 28.0, 21.3; IR (KBr) ν_{max} 3095, 2926, 1649, 1506, 1160, 897, 673, 541 cm^{-1}; HRMS–ESI (*m/z*): $[M+Na]^+$ Calcd for $C_{19}H_{17}NO_3SNa$, 362.0827; found, 362.0827.

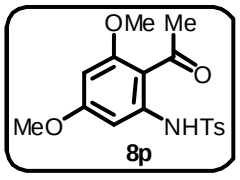
_N_-(6-Acetylbenzo[*d*][1,3]dioxol-5-yl)-4-methylbenzenesulfonamide (8o):



Following the general procedure (GP-2); 3',4'-(methylenedioxy)acetophenone (**60o**; 164 mg, 1.0 mmol), tosyl azide (**53a**; 296 mg, 1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (31 mg, 5.0 mol%), $Cu(OAc)_2 \cdot H_2O$ (100 mg, 50 mol%) and $AgSbF_6$ (69 mg, 20 mol%) in 1,2-DCE (2.0 mL) was heated at 100 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (3:1) to afford **8o** (95 mg) in 28% yield as pale yellow solid.

mp = 107–108 °C; R_f = 0.47 (3:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.15 (s, 1H), 7.64 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.4 Hz, 1H), 7.22 (d, *J* = 8.0 Hz, 2H), 6.65 (d, *J* = 8.4 Hz, 1H), 6.05 (s, 2H), 2.39 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.5, 153.0, 143.6, 142.2, 136.4, 129.1, 127.5, 127.0, 123.2, 121.7, 104.8, 102.4, 27.8, 21.5; IR (KBr) ν_{max} 2915, 1644, 1463, 1320, 1156, 909, 663, 542 cm^{-1}; HRMS–ESI (*m/z*): $[M+H]^+$ Calcd for $C_{16}H_{16}NO_5S$, 334.0749; found, 334.0752.

_N_-(2-Acetyl-3,5-dimethoxyphenyl)-4-methylbenzenesulfonamide (8p):

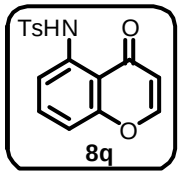


Following the general procedure (GP-2); 2',4'-dimethoxyacetophenone (**60p**; 180 mg, 1.0 mmol), tosyl azide (**53a**; 296 mg, 1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (31 mg, 5.0 mol%), $Cu(OAc)_2 \cdot H_2O$ (100 mg, 50 mol%) and $AgSbF_6$ (69 mg, 20 mol%) in 1,2-DCE (2.0 mL) was heated at 100 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (4:1) to afford **8p** (137 mg) in 39% yield as pale yellow solid.

mp = 144–145 °C; R_f = 0.27 (4:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.64 (s, 1H), 7.67 (d, *J* = 8.4 Hz, 2H), 7.21 (d, *J* = 8.0 Hz, 2H), 6.80 (bd, *J* = 2.4 Hz, 1H), 6.10

(bd, J = 2.0 Hz, 1H), 3.80 (s, 6H), 2.38 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.9, 164.1, 162.6, 143.7, 142.5, 136.3, 129.5, 127.2, 109.3, 96.3, 94.0, 55.5, 33.5, 21.4; IR (KBr) ν_{max} 3260, 2931, 1605, 1277, 1161, 674, 548 cm^{-1}; HRMS–ESI (*m/z*): $[M+H]^+$ Calcd for $C_{17}H_{20}NO_5S$, 350.1062; found, 350.1062.

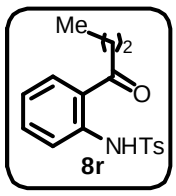
4-Methyl-*N*-(4-oxo-4*H*-chromen-5-yl)benzenesulfonamide (8q):



Following the general procedure (GP-2); chromone (**60q**; 146 mg, 1.0 mmol), tosyl azide (**53a**; 296 mg, 1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (31 mg, 5 mol%), $Cu(OAc)_2 \cdot H_2O$ (100 mg, 50 mol%) and $AgSbF_6$ (69 mg, 20 mol%) in 1,2-DCE (2.0 mL) was heated at 100 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (3:1) to afford **8q** (200 mg) in 63% yield as colorless solid.

mp = 176–177 °C; R_f = 0.37 (3:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.34 (s, 1H), 7.80 (d, J = 8.4 Hz, 2H), 7.76 (d, J = 5.6 Hz, 1H), 7.54–7.47 (m, 2H), 7.23 (d, J = 8.4 Hz, 2H), 7.02 (dd, J = 7.2, 6.4 Hz, 1H), 6.26 (d, J = 6.0 Hz, 1H), 2.35 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 181.2, 157.3, 155.2, 144.0, 140.1, 136.5, 134.7, 129.7, 127.4, 112.9, 112.5, 112.4, 111.6, 21.6; IR (KBr) ν_{max} 2915, 1633, 1484, 1150, 1008, 657, 542 cm^{-1}; HRMS–ESI (*m/z*): $[M+Na]^+$ Calcd for $C_{16}H_{13}NO_4SNa$, 338.0463; found, 338.0467.

***N*-(2-Butyrylphenyl)-4-methylbenzenesulfonamide (8r):**

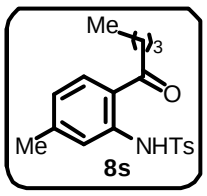


Following the general procedure (GP-2); butyrophenone (**60r**; 148 mg, 1.0 mmol), tosyl azide (**53a**; 296 mg, 1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (31 mg, 5.0 mol%), $Cu(OAc)_2 \cdot H_2O$ (100 mg, 50 mol%) and $AgSbF_6$ (69 mg, 20 mol%) in 1,2-DCE (2.0 mL) was heated at 100 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (4:1) to afford **8r** (270 mg) in 85% yield as colorless solid.

mp = 112–113 °C; R_f = 0.51 (4:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.46 (s, 1H), 7.80 (dd, J = 8.0, 1.2 Hz, 1H), 7.73–7.65 (m, 3H), 7.43 (t, J = 7.8 Hz, 1H), 7.20 (d, J = 8.0 Hz, 2H), 7.06 (t, J = 7.8 Hz, 1H), 2.85 (t, J = 7.4 Hz, 2H), 2.35 (s, 3H), 1.72–1.59 (m, 2H), 0.93 (t, J = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 204.6, 143.8, 139.8, 136.5, 134.5, 130.9, 129.5, 127.1, 122.7, 122.4, 119.5, 41.4, 21.4, 17.8, 13.6; IR (KBr) ν_{max} 2964, 2876, 1649,

1501, 1161, 931, 569 cm^{-1}; HRMS–ESI (*m/z*): $[M+Na]^+$ Calcd for $C_{17}H_{19}NO_3SNa$, 340.0983; found, 340.0988.

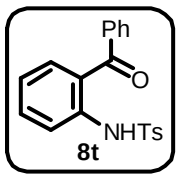
4-Methyl-*N*-(5-methyl-2-pentanoylphenyl)benzenesulfonamide (8s):



Following the general procedure (GP-2); 4'-methylvalerophenone (**60s**; 176 mg, 1.0 mmol), tosyl azide (**53a**; 296 mg, 1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (31 mg, 5.0 mol%), $Cu(OAc)_2 \cdot H_2O$ (100 mg, 50 mol%) and $AgSbF_6$ (69 mg, 20 mol%) in 1,2-DCE (2.0 mL) was heated at 100 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (15:1) to afford **8s** (253 mg) in 73% yield as pale yellow semi-solid.

R_f = 0.37 (15:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.52 (s, 1H), 7.67 (d, *J* = 8.0 Hz, 3H), 7.48 (s, 1H), 7.18 (d, *J* = 8.0 Hz, 2H), 6.84 (d, *J* = 8.0 Hz, 1H), 2.81 (t, *J* = 7.4 Hz, 2H), 2.32 (s, 3H), 2.30 (s, 3H), 1.62–1.49 (m, 2H), 1.38–1.23 (m, 2H), 0.89 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 204.3, 145.8, 143.6, 139.8, 136.4, 131.0, 129.4, 127.0, 123.7, 119.9, 119.7, 39.1, 26.5, 22.1, 21.8, 21.3, 13.8; IR (Neat) ν_{max} 2953, 1649, 1566, 1155, 662, 569 cm^{-1}; HRMS–ESI (*m/z*): $[M+H]^+$ Calcd for $C_{19}H_{24}NO_3S$, 346.1477; found, 346.1482.

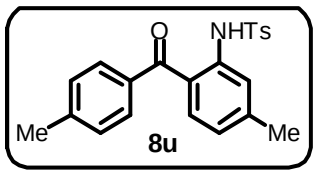
***N*-(2-Benzoylphenyl)-4-methylbenzenesulfonamide (8t):**[20]



Following the general procedure (GP-2); benzophenone (**60t**; 182 mg, 1.0 mmol), tosyl azide (**53a**; 296 mg, 1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (31 mg, 5.0 mol%), $Cu(OAc)_2 \cdot H_2O$ (100 mg, 50 mol%) and $AgSbF_6$ (69 mg, 20 mol%) in 1,2-DCE (2.0 mL) was heated at 100 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (9:1) to afford **8t** (236 mg) in 67% yield as colorless solid.

mp = 125–126 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.99 (s, 1H), 7.78 (d, *J* = 8.0 Hz, 1H), 7.63–7.46 (m, 4H), 7.44–7.29 (m, 5H), 7.10 (td, *J* = 7.7, 0.8 Hz, 1H), 7.02 (d, *J* = 8.0 Hz, 2H), 2.21 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.4, 143.7, 138.7, 137.3, 135.6, 133.7, 133.0, 132.6, 129.7, 129.5, 128.0, 127.1, 126.2, 123.5, 123.1, 21.3.

4-Methyl-*N*-(5-methyl-2-(4-methylbenzoyl)phenyl)benzenesulfonamide (8u):

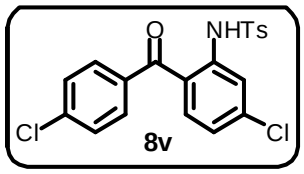


8u

Following the general procedure (GP-2); 4,4'-dimethylbenzophenone (**60u**; 210 mg, 1.0 mmol), tosyl azide (**53a**; 296 mg, 1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (31 mg, 5.0 mol%), $Cu(OAc)_2 \cdot H_2O$ (100 mg, 50 mol%) and $AgSbF_6$ (69 mg, 20 mol%) in 1,2-DCE (2.0 mL) was heated at 100 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (6:1) to afford **8u** (265 mg) in 70% yield as colorless solid.

mp = 161–162 °C; R_f = 0.61 (6:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.09 (s, 1H), 7.59 (s, 1H), 7.55 (d, J = 7.6 Hz, 2H), 7.30–7.23 (m, 3H), 7.18 (d, J = 7.6 Hz, 2H), 7.02 (d, J = 8.0 Hz, 2H), 6.89 (d, J = 8.0 Hz, 1H), 2.42 (s, 3H), 2.40 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.0, 144.8, 143.5, 143.3, 138.9, 135.8, 135.0, 133.0, 129.9, 129.4, 128.6, 127.1, 124.3, 123.9, 123.4, 21.9, 21.6, 21.3; IR (KBr) ν_{max} 3249, 2920, 1648, 1604, 1374, 1171, 541 cm^{-1}; HRMS–ESI (m/z): $[M+H]^+$ Calcd for $C_{22}H_{22}NO_3S$, 380.1320; found, 380.1319.

***N*-(5-Chloro-2-(4-chlorobenzoyl)phenyl)-4-methylbenzenesulfonamide (8v):**

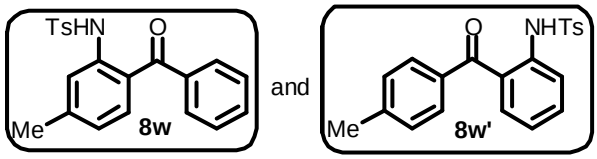


8v

Following the general procedure (GP-2); 4,4'-dichlorobenzophenone (**60v**; 251 mg, 1.0 mmol), tosyl azide (**53a**; 296 mg, 1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (31 mg, 5.0 mol%), $Cu(OAc)_2 \cdot H_2O$ (100 mg, 50 mol%) and $AgSbF_6$ (69 mg, 20 mol%) in 1,2-DCE (2.0 mL) was heated at 100 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (16:1) to afford **8v** (210 mg) in 50% yield as colorless solid.

mp = 111–112 °C; R_f = 0.37 (16:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.08 (s, 1H), 7.80 (bd, J = 2.0 Hz, 1H), 7.60 (d, J = 8.4 Hz, 2H), 7.44–7.29 (m, 5H), 7.11 (d, J = 8.4 Hz, 2H), 7.07 (dd, J = 8.4, 1.6 Hz, 1H), 2.28 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.4, 144.1, 140.3, 139.4, 135.6, 133.8, 131.0, 129.7, 128.6, 127.2, 123.5, 123.4, 122.3, 21.4; IR (KBr) ν_{max} 3243, 1649, 1588, 1166, 952 cm^{-1}; HRMS–ESI (m/z): $[M+H]^+$ Calcd for $C_{20}H_{16}Cl_2NO_3S$, 420.0228; found, 420.0223.

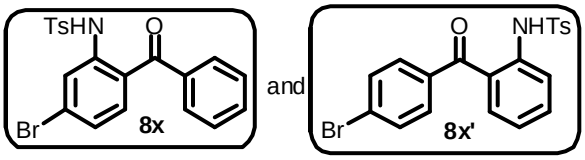
_N_-(2-Benzoyl-5-methylphenyl)-4-methylbenzenesulfonamide (8w):
4-Methyl-_N_-(2-(4-methylbenzoyl)phenyl)benzenesulfonamide (8w'):



Following the general procedure (GP-2); 4-methylbenzophenone (**60w**; 196 mg, 1.0 mmol), tosyl azide (**53a**; 296 mg, 1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (31 mg, 5.0 mol%), $Cu(OAc)_2 \cdot H_2O$ (100 mg, 50 mol%) and $AgSbF_6$ (69 mg, 20 mol%) in 1,2-DCE (2.0 mL) was heated at 100 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (15:1) to afford inseparable mixture **8w** and **8w′** (64:36; 251 mg) in 69% yield as yellow thick liquid.

R_f = 0.32 (15:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.18 (s, 1H), 9.88 (s, 0.56H), 7.77 (d, J = 8.4 Hz, 0.64H), 7.64–7.47 (m, 6H), 7.42–7.32 (m, 5H), 7.29–7.24 (m, 2H), 7.18 (d, J = 8.0 Hz, 1H), 7.10 (t, J = 7.6 Hz, 1H), 7.04 (d, J = 8.0 Hz, 2H), 6.99 (d, J = 8.0 Hz, 1H), 6.89 (d, J = 7.6 Hz, 1H), 2.42 (s, 1.8H), 2.39 (s, 3H), 2.23 (s, 3H), 2.20 (s, 1.7H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.4, 197.9, 145.1, 143.6, 139.1, 138.5, 137.7, 135.7, 135.6, 134.6, 133.4, 133.3, 132.7, 132.3, 130.0, 129.6, 129.4, 128.7, 127.9, 127.1, 126.8, 124.3, 123.5, 123.4, 123.3, 123.2, 21.9, 21.6, 21.3; IR (KBr) ν_{max} 3243, 2915, 1627, 1386, 1265, 1156, 1095, 909, 701 cm^{-1}; HRMS–ESI (m/z): $[M+H]^+$ Calcd for $C_{21}H_{20}NO_3S$, 366.1164; found, 366.1164.

_N_-(2-Benzoyl-5-bromophenyl)-4-methylbenzenesulfonamide (8x):
_N_-(2-(4-Bromobenzoyl)phenyl)-4-methylbenzenesulfonamide (8x'):

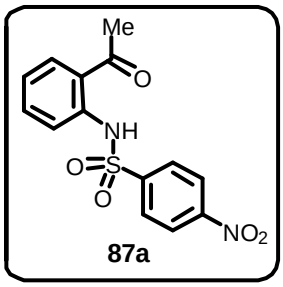


Following the general procedure (GP-2); 4-bromobenzophenone (**60x**; 261 mg, 1.0 mmol), tosyl azide (**53a**; 296 mg, 1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (31 mg, 5.0 mol%), $Cu(OAc)_2 \cdot H_2O$ (100 mg, 50 mol%) and $AgSbF_6$ (69 mg, 20 mol%) in 1,2-DCE (2.0 mL) was heated at 100 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (15:1) to afford inseparable mixture **8x** and **8x′** (64:36; 291 mg) in 68% yield as yellow thik liquid.

R_f = 0.32 (15:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.14 (s, 1H), 9.83 (s, 0.56H), 7.97 (bd, J = 1.6 Hz, 1H), 7.77 (d, J = 8.4 Hz, 1H), 7.59 (d, J = 8.0 Hz, 3H), 7.57–7.50 (m, 3H), 7.45–7.31 (m, 5H), 7.29–7.19 (m, 3H), 7.08 (d, J = 8.0 Hz, 3H), 7.08 (d, J =

8.0 Hz, 2H), 7.03 (d, *J* = 8.0 Hz, 1H), 2.26 (s, 3H), 2.24 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.8, 197.1, 144.0, 143.8, 140.2, 138.7, 137.2, 136.1, 135.6, 135.5, 134.2, 133.9, 132.8, 132.5, 131.3, 131.2, 129.7, 129.6, 129.5, 128.5, 128.2, 127.9, 127.8, 127.1, 126.4, 126.0, 125.2, 124.2, 123.6, 123.4, 21.4; IR (KBr) ν_{max} 3249, 2931, 1632, 1589, 1484, 1380, 1167, 1090, 942, 663 cm^{-1}; HRMS–ESI (*m/z*): $[M+Na]^+$ Calcd for $C_{20}H_{16}BrNO_3SNa$, 451.9932; found, 451.9935.

_N_-(2-Acetylphenyl)-4-nitrobenzenesulfonamide (87a):

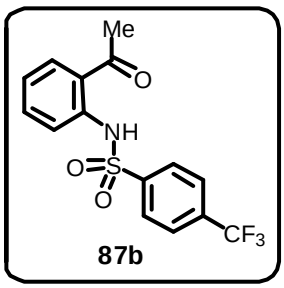


87a

Following the general procedure (GP-2); acetophenone (**60a**; 120 mg, 1.0 mmol), 4-nitrobenzenesulfonyl azide (**53b**; 342 mg, 1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (31 mg, 5.0 mol%), $Cu(OAc)_2 \cdot H_2O$ (100 mg, 50 mol%) and $AgSbF_6$ (69 mg, 20 mol%) in 1,2-DCE (2.0 mL) was heated at 100 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (4:1) to afford **87a** (196 mg) in 61% yield as colorless solid.

mp = 149–150 °C; R_f = 0.33 (4:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.04 (s, 1H), 8.61 (d, *J* = 8.8 Hz, 2H), 8.37 (d, *J* = 8.4 Hz, 2H), 8.18 (d, *J* = 7.6 Hz, 1H), 8.06 (d, *J* = 8.4 Hz, 1H), 7.85 (t, *J* = 7.6 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 1H), 2.93 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.8, 150.2, 145.2, 139.2, 135.3, 132.3, 128.5, 124.3, 123.6, 122.4, 119.2, 28.2; IR (KBr) ν_{max} 3106, 1643, 1539, 1353, 1161, 931, 608 cm^{-1}; HRMS–ESI (*m/z*): $[M+Na]^+$ Calcd for $C_{14}H_{12}N_2O_5SNa$, 343.0365; found, 343.0364.

_N_-(2-Acetylphenyl)-4-(trifluoromethyl)benzenesulfonamide (87b):



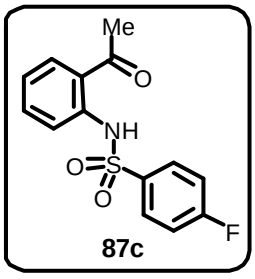
87b

Following the general procedure (GP-2); acetophenone (**60a**; 120 mg, 1.0 mmol), 4-(trifluoromethyl)benzenesulfonyl azide (**53c**; 376 mg, 1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (31 mg, 5.0 mol%), $Cu(OAc)_2 \cdot H_2O$ (100 mg, 50 mol%) and $AgSbF_6$ (69 mg, 20 mol%) in 1,2-DCE (2.0 mL) was heated at 100 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (4:1) to afford **87b** (334 mg) in 97% yield as colorless solid.

mp = 133–134 °C; R_f = 0.48 (4:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.63 (s, 1H), 7.97 (d, *J* = 8.0 Hz, 2H), 7.83 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.73–7.67 (m, 3H), 7.49

(td, *J* = 7.9, 1.2 Hz, 1H), 7.12 (td, *J* = 7.6, 1.2 Hz, 1H), 2.57 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.6, 143.0, 139.3, 135.1, 134.52 (q, *J* = 33.3 Hz), 132.1, 127.7, 126.2, 126.1, 123.3, 122.83 (q, *J* = 91.9 Hz), 119.1, 28.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ-63.21; IR (KBr) ν_{max} 3057, 1638, 1578, 1408, 1320, 1161, 1139, 608 cm^{-1}; HRMS–ESI (*m/z*): $[M+Na]^+$ Calcd for $C_{15}H_{12}F_3NO_3SNa$, 366.0388; found, 366.0388.

_N_-(2-Acetylphenyl)-4-fluorobenzenesulfonamide (87c):

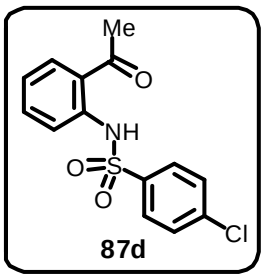


87c

Following the general procedure (GP-2); acetophenone (**60a**; 120 mg, 1.0 mmol), 4-fluorobenzenesulfonyl azide (**53d**; 302 mg, 1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (31 mg, 5.0 mol%), $Cu(OAc)_2 \cdot H_2O$ (100 mg, 50 mol%) and $AgSbF_6$ (69 mg, 20 mol%) in 1,2-DCE (2.0 mL) was heated at 100 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (4:1) to afford **87c** (278 mg) in 95% yield as colorless solid.

mp = 158–159 °C; R_f = 0.39 (4:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.50 (s, 1H), 7.90–7.84 (m, 2H), 7.82 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.69 (dd, *J* = 8.2, 0.6 Hz, 1H), 7.48 (td, *J* = 7.9, 1.3 Hz, 1H), 7.15–7.06 (m, 3H), 2.57 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.5, 165.17 (d, *J* = 256 Hz), 139.7, 135.5, 135.0, 132.0, 129.95 (d, *J* = 9.09 Hz), 123.0, 122.4, 119.2, 116.27 (d, *J* = 22.2 Hz), 28.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ–104.48; IR (KBr) ν_{max} 3101, 1649, 1490, 1172, 931, 558 cm^{-1}; HRMS–ESI (*m/z*): $[M+Na]^+$ Calcd for $C_{14}H_{12}FNO_3SNa$, 316.0420; found, 316.0416.

_N_-(2-Acetylphenyl)-4-chlorobenzenesulfonamide (87d):



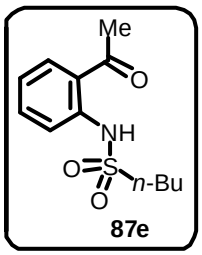
87d

Following the general procedure (GP-2); acetophenone (**60a**; 120 mg, 1.0 mmol), 4-chlorobenzenesulfonyl azide (**53e**; 326 mg, 1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (31 mg, 5.0 mol%), $Cu(OAc)_2 \cdot H_2O$ (100 mg, 50 mol%) and $AgSbF_6$ (69 mg, 20 mol%) in 1,2-DCE (2.0 mL) was heated at 100 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (4:1) to afford **87d** (224 mg) in 72% yield as colorless solid.

mp = 135–136 °C; R_f = 0.46 (4:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.54 (s, 1H), 7.82 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.79–7.73 (m, 2H), 7.67 (bd, *J* =8.0 Hz, 1H), 7.46

(td, *J* = 8.4, 1.2 Hz, 1H), 7.38 (dt, *J* = 8.8, 2.0 Hz, 2H), 7.09 (td, *J* = 8.0, 1.0 Hz, 1H), 2.57 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.6, 139.5, 139.4, 137.8, 135.0, 132.0, 129.2, 128.6, 123.0, 122.2, 119.0, 28.1; IR (KBr) ν_{max} 3090, 2926, 1649, 1495, 1249, 1167, 920, 756, 558 cm^{-1}; HRMS–ESI (*m/z*): $[M+Na]^+$ Calcd for $C_{14}H_{12}ClNO_3SNa$, 332.0124; found, 332.0125.

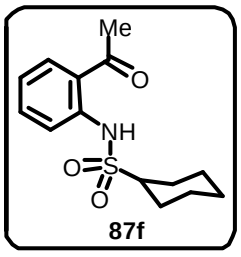
_N_-(2-Acetylphenyl)butane-1-sulfonamide (87e):



Following the general procedure (GP-2); acetophenone (**60a**; 120 mg, 1.0 mmol), butane-1-sulfonyl azide (**53f**; 244 mg, 1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (31 mg, 5.0 mol%), $Cu(OAc)_2 \cdot H_2O$ (100 mg, 50 mol%) and $AgSbF_6$ (69 mg, 20 mol%) in 1,2-DCE (2.0 mL) was heated at 100 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (16:1) to afford **87e** (143 mg) in 56% yield as pale yellow oil.

R_f = 0.19 (16:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.29 (s, 1H), 7.91 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.72 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.51 (td, *J* = 8.0, 1.2 Hz, 1H), 7.11 (td, *J* = 8.4, 1.2 Hz, 1H), 3.20–3.03 (m, 2H), 2.64 (s, 3H), 1.81–1.63 (m, 2H), 1.42–1.31 (m, 2H), 0.84 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.6, 140.6, 135.4, 132.5, 122.4, 121.4, 117.6, 51.9, 28.3, 25.3, 21.3, 13.5; IR (Neat) ν_{max} 3095, 2964, 1654, 1601, 1577, 1248, 1150, 930, 749, 629 cm^{-1}; HRMS–ESI (*m/z*): $[M+Na]^+$ Calcd for $C_{12}H_{17}NO_3SNa$, 278.0827; found, 278.0827.

_N_-(2-Acetylphenyl)cyclohexanesulfonamide (87f):

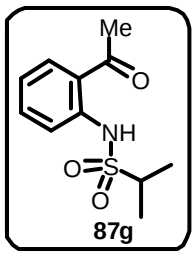


Following the general procedure (GP-2); acetophenone (**60a**; 120 mg, 1.0 mmol), cyclohexanesulfonyl azide (**53g**; 284 mg, 1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (31 mg, 5.0 mol%), $Cu(OAc)_2 \cdot H_2O$ (100 mg, 50 mol%) and $AgSbF_6$ (69 mg, 20 mol%) in 1,2-DCE (2.0 mL) was heated at 100 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (16:1) to afford **87f** (124 mg) in 44% yield as brown color semi-solid.

R_f = 0.19 (16:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.25 (s, 1H), 7.91 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.50 (td, *J* = 8.8, 1.6 Hz, 1H), 7.09 (td, *J* = 8.0, 1.0 Hz, 1H), 3.10–2.99 (m, 1H), 2.64 (s, 3H), 2.10–2.05 (m, 2H), 1.86–1.80 (m, 2H), 1.65–1.48 (m, 3H), 1.24–1.10 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.7, 141.2, 135.3, 132.4,

122.1, 121.1, 117.7, 61.0, 28.3, 26.2, 25.04, 24.98; IR (Neat) ν_{max} 3068, 2931, 2854, 1649, 1489, 1249, 925, 766, 634 cm^{-1}; HRMS–ESI (*m/z*): $[M+H]^+$ Calcd for $C_{14}H_{20}NO_3S$, 282.1164; found, 282.1164.

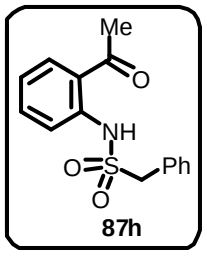
_N_-(2-Acetylphenyl)propane-2-sulfonamide (87g):



Following the general procedure (GP-2); acetophenone (**60a**; 120 mg, 1.0 mmol), propane-2-sulfonyl azide (**53h**; 223 mg, 1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (31 mg, 5.0 mol%), $Cu(OAc)_2 \cdot H_2O$ (100 mg, 50 mol%) and $AgSbF_6$ (69 mg, 20 mol%) in 1,2-DCE (2.0 mL) was heated at 100 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (16:1) to afford **87g** (110 mg) in 46% yield as pink color oil.

R_f = 0.19 (16:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.26 (s, 1H), 7.92 (bd, *J* = 7.2 Hz, 1H), 7.81 (bd, *J* = 8.4 Hz, 1H), 7.51 (bt, *J* = 7.0 Hz, 1H), 7.11 (bt, *J* = 7.4 Hz, 1H), 3.33 (bt, *J* = 6.8 Hz, 1H), 2.66 (s, 3H), 1.36 (d, *J* = 6.8 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.5, 141.0, 135.2, 132.3, 122.1, 121.2, 117.8, 53.0, 28.2, 16.3; IR (Neat) ν_{max} 3112, 2980, 1649, 1489, 1330, 1249, 1144, 925, 761 cm^{-1}; HRMS–ESI (*m/z*): $[M+Na]^+$ Calcd for $C_{11}H_{15}NO_3SNa$, 264.0671; found, 264.0673.

_N_-(2-Acetylphenyl)-1-phenylmethanesulfonamide (87h):

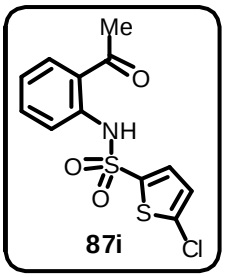


Following the general procedure (GP-2); acetophenone (**60a**; 120 mg, 1.0 mmol), phenylmethanesulfonyl azide (**53i**; 296 mg, 1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (31 mg, 5 mol%), $Cu(OAc)_2 \cdot H_2O$ (100 mg, 50 mol%) and $AgSbF_6$ (69 mg, 20 mol%) in 1,2-DCE (2.0 mL) was heated at 100 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (9:1) to afford **87h** (146 mg) in 50% yield as brown color solid.

mp = 119–120 °C; R_f = 0.44 (9:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.22 (s, 1H), 7.87 (d, *J* = 7.6 Hz, 1H), 7.68 (d, *J* = 8.4 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 1H), 7.35–7.23 (m, 3H), 7.21–7.09 (m, 3H), 4.40 (s, 2H), 2.58 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.0, 140.7, 135.1, 132.1, 130.5, 128.8, 128.6, 128.0, 122.4, 121.4, 117.8, 58.4, 28.1; IR (KBr)

ν_{max} 3041, 2936, 1654, 1495, 1254, 1134, 936, 601 cm^{-1}; HRMS–ESI (*m/z*): $[M+Na]^+$ Calcd for $C_{15}H_{15}NO_3SNa$, 312.0671; found, 312.0671.

***N*-(2-Acetylphenyl)-5-chlorothiophene-2-sulfonamide (87i):**



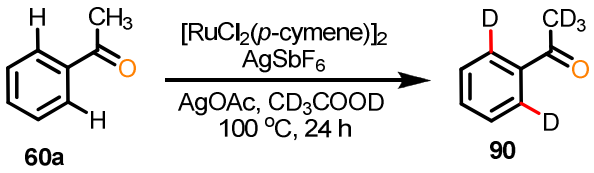
87i

Following the general procedure (GP-2); acetophenone (**60a**; 120 mg, 1.0 mmol), 5-chlorothiophene-2-sulfonyl azide (**53j**; 335 mg, 1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (31 mg, 5.0 mol%), $Cu(OAc)_2 \cdot H_2O$ (100 mg, 50 mol%) and $AgSbF_6$ (69 mg, 20 mol%) in 1,2-DCE (2.0 mL) was heated at 100 °C for 24 h. Finally, the crude mixture was purified by silica gel column chromatography eluting with hexane: ethyl acetate (6:1) to afford **87i** (200 mg) in 63% yield as light brown color solid.

mp = 107–108 °C; R_f = 0.28 (6:1 hexane/EtOAc); [Silica, UV and I_2]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.65 (s, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.75 (d, *J* = 8.4 Hz, 1H), 7.53 (bt, *J* = 7.6 Hz, 1H), 7.39 (d, *J* = 4.0 Hz, 1H), 7.16 (bt, *J* = 7.6 Hz, 1H), 6.83 (d, *J* = 4.0 Hz, 1H), 2.62 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.7, 139.3, 138.0, 137.8, 135.2, 132.24, 132.19, 126.7, 123.4, 122.4, 119.1, 28.2; IR (KBr) ν_{max} 3101, 1649, 1578, 1249, 1161, 920, 602 cm^{-1}; HRMS–ESI (*m/z*): $[M+Na]^+$ Calcd for $C_{12}H_{10}ClNO_3S_2Na$, 337.9688; found, 337.9689.

3.5.6. Deuterium Experiment:

Deuterium experiment was carried out in a 10 mL Schlenk tube with high pressure valve and side arm. The tube was charged with acetophenone (**60a,** 30 mg, 0.25 mmol), $[RuCl_2(p\text{-cymene})]_2$ (8.0 mg, 5 mol%), AgOAc (42.0 mg, 0.25mmol). Subsequently, $AgSbF_6$ (17 mg, 20 mol %) was introduced to the flask in a glovebox. CD_3CO_2D (0.5 mL) was added to the mixture and the resulting mixture was stirred at 100 °C for 24 h.

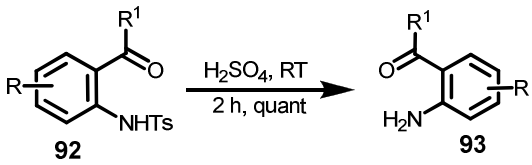


60a **90**

The reaction mixture was cooled to ambient temperature, filtered through a small plug of Celite and then washed with dichloromethane (3 × 10 mL). The solvents were evaporated under the reduced pressure. The ^{1}H NMR showed the 100% deuterium insertion on the *ortho*-C–H bonds of **60a**. This preliminary deuterium scrambling data suggests the

reversible cyclo-ruthenation step in the Ru(II)-catalyzed *o*-C–H bond functionalization of acetophenone.

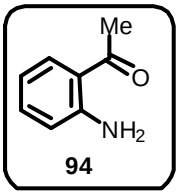
3.5.7. General Procedure for Deprotection of Tosylgroup (GP-3): [11e]



92 93

The *ortho*-amidated aromatic ketone (1.0 mmol) was added to the cold concentrated H_2SO_4 (6.0 mL) at 0 °C. The mixture was stirred at RT for 2 h. Upon completion, the reaction mixture was quenched with $NaHCO_3$ solution and the resulting mixture was extracted with EtOAc (2 × 10 mL). The organic layers were dried over Na_2SO_4, and concentrated in vacuum to give *ortho*-amino aromatic ketones.

2′-Aminoacetophenone (94):



94

Following the general procedure (GP-3); *N*-(2-acetylphenyl)-4-methylbenzenesulfonamide acetophenone (**8a**; 100 mg, 0.35 mmol) was added to cold concentrated H_2SO_4 (1.0 mL). The mixture was stirred at RT for 2 h. After usal work-up, the organic layer was dried over Na_2SO_4, and concentrated in vacuum to give 2-amino acetophenone (**94**) in quantitative yield as light brown liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (dd, J = 8.4, 1.2Hz, 1H), 7.26 (dt, J = 8.0, 0.8 Hz, 1H), 6.72–6.58 (m, 2H), 6.50–6.07 (bs, 1H), 2.57 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.7, 150.2, 134.3, 132.0, 118.1, 117.1, 115.6, 27.8.

3.5.8. X-Ray crystallography: Single crystal X-ray data for the compounds **87a**.

Table 3.5. Crystallographic Data and Structural Refinement for **87a.**

Compound	**87a**
formula	$C_{14}H_{12}N_2O_5S$
M_w	320.33
Crystal system	Triclinic
Space group	P_1^-
T [K]	293(2)
a [Å]	7.7099(16)
b [Å]	8.2501(17)
c [Å]	11.659(2)
α [°]	99.961(3)
β [°]	101.130(3)
γ [°]	92.491(3)
Z	2
V [Å^3]	714.4(2)
D_{calc} [g cm^{-3}]	1.489
μ [mm^{-1}]	0.253
total reflns	2777
unique reflns	2750
Observed reflns	2750
R_1 [$I > 2\sigma(I)$]	0.0424
wR_2 [all]	0.1146
GOF	1.053
Diffractometer	SHELXL-97

3.6. References

1) Amino Group Chemistry, From Synthesis to the Life Sciences; A. Ricci, Ed.; Wiley-VCH: Weinheim, 2007.
2) R. G. Lande, *Int. J. Psychiatry Clin. Pract.,* 2004, **8**, 37. (b) M. Hopwood and D. Manning, WO Patent Application 2004035041, 2004; *Chem. Abstr*., 2004, **140**, 363050.
3) M. Carril, R. SanMartin, F. Churruca, I. Tellitu and E. Domı´nguez, *Org. Lett.*, 2005, **7**, 4787.
4) (a) B. Xiao, T.-J. Gong, J. Xu, Z.-J. Liu and L. Liu *J. Am. Chem. Soc.*, 2011, **133**, 1466. (b) W. Grell, R. Hurnaus, G. Griss, R. Sauter, E. Rupprecht, M. Mark, P. Luger, H. Nar, H. Wittneben and P. Müller, *J. Med. Chem.* 1998, **41**, 5219.
5) T. Miyagi, Y. Hari and T. Aoyama, *Tetrahedron Lett.*, 2004, **45**, 6303.
6) C. M. Counceller, C. C. Eichman, B. C. Wray, E. R. Welin and J. P. Stambuli, *Org. Synth.*, 2011, **88**, 33.
7) C. Theeraladanon, M. Arisawa, A. Nishida and M. Nakagawa, *Tetrahedron*, 2004, **60**, 3017.
8) (a) J. W. Tye, Z. Weng, A. M. Johns, C. D. Incarvito and J. F. Hartwig, *J. Am. Chem. Soc.*, 2008, **130**, 9971; (b) J. F. Hartwig, *Acc. Chem. Res.*, 2008, **41**, 1534; (c) J. P. Wolfe, S. Wagam, J.-F. Marcoux and S. L. Buchwald, *Acc. Chem. Res.*, 1998, **31**, 805; (d) F. Paul, J. Patt and J. F. Hartwig, *J. Am. Chem. Soc.*, 1994, **116**, 5969; (e) A. S. Guram and S. L. Buchwald, *J. Am. Chem. Soc.*, 1994, **116**, 7901.
9) Reviews on direct C–H amination, see: (a) J. Wencel-Delord, T. Dröge, F. Liu and F. Glorius, *Chem. Soc. Rev.*, 2011, **40**, 4740; (b) S. H. Cho, J. Y. Kim, J. Kwak and S. Chang, *Chem. Soc. Rev.*, 2011, **40**, 5068.
10) For recent reviews on C–H activation, see: (a) L. Ackermann, A. R. Kapdi, H. K. Potukuchi and S. I. Kozhushkov "*Syntheses via C–H Bond Functionalizations"*, in *Handbook of Green Chemistry* (Volume-Eds.: C.-J. Li), Wiley-VCH, **2012**, Weinheim, 259-305; (b) S. R. Neufeldt and M. S. Sanford, *Acc. Chem. Res.*, 2012, **45**, 936; (c) D. A. Colby, A. S. Tsai, R. G. Bergman and J. A. Ellman, *Acc. Chem. Res.*, 2012, **45**, 814; (d) K. M. Engle, T.-S. Mei, M. Wasa and J.-Q. Yu, *Acc. Chem. Res.*, 2012, **45**, 788; (e) P. B. Arockiam, C. Bruneau and P. H. Dixneuf, *Chem. Rev.*, 2012, **112**, 5879; (f) L. Ackermann, *Chem. Rev.* 2011, **111**, 1315. (g) L.-M. Xu, B.-J. Li, Z. Yang and Z.-J. Shi, *Chem. Soc. Rev.*, 2010, **39**, 712.
11) (a) K. Sun, Y. Li, T. Xiong, J. Zhang and Q. Zhang, *J. Am. Chem. Soc.*, 2011, **133**, 1694; (b) E. J. Yoo, S. Ma, T.-S. Mei, K. S. L. Chan and J.-Q. Yu, *J. Am. Chem. Soc.*, 2011, **133**, 7652; (c) K.-H. Ng, A. S. C. Chan and W.-Y. Yu, *J. Am. Chem. Soc.*, 2010, **132**, 12862; (d) H.-Y. Thu, W.-Y. Yu and C.-M. Che, *J. Am. Chem. Soc*., 2006, **128**, 9048; (e) B. Xiao, T.-J. Gong, J. Xu, Z.-J. Liu and L. Liu *J. Am. Chem. Soc.*, 2011, **133**, 1466.
12) Rh(III)-catlayzed C–N bond with azide, see: (a) J. Y. Kim, S. H. Park, J. Ryu, S. H. Cho, S. H. Kim and S. Chang, *J. Am. Chem. Soc.*, 2012, **134**, 9110; (b) J. Ryu, K. Shin, S. H. Park, J. Y. Kim and S. Chang, *Angew. Chem. Int., Ed.*, 2012, **51**,

9904; (c) K. Shin, Y. Baek and S. Chang, *Angew. Chem. Int., Ed.*, 2013, **52**, 8031; (d) K.-H. Ng, Z. Zhou and W.-Y. Yu, *Org. Lett.*, 2012, **14**, 272; (e) C. Grohmann, H. Wang and F. Glorius, *Org. Lett.*, 2012, **14**, 656; (f) D.-G. Yu, M. Suri and F. Glorius, *J. Am. Chem. Soc.*, 2013, **135**, 8802; (g) C. Grohmann, H. Wang and F. Glorius, *Org. Lett.*, 2013, **15**, 3014; (h) J. Shi, B. Zhou, Y. Yang and Y. Li, *Org. Biomol. Chem.*, 2012, **10**, 8953.

13) S. Murai, F. Kakiuchi, S. Sekine, Y. Tanaka, A. Kamatani, M. Sonoda and N. Chatani, *Nature*, 1993, **366**, 529.

14) Selected examples, For keto-directed *o*-C–H bond alkylation, see: (a) F. Kakiuchi, T. Kochi, E. Mizushima and S. Murai, *J. Am. Chem. Soc*., 2010, **132**, 17741; (b) F. Kakiuchi, T. Sato, K. Igi, N. Chatani and S. Murai, *Chem. Lett.*, 2001, 386; (c) T. Sato, F. Kakiuchi, N. Chatani and S. Murai, *Chem. Lett.*, 1998, 893; For keto-directed *o*-C–H bond alkenylation, see: (d) K. muralirajan, K. Parthasarathy and C.-H. Cheng, *Angew. Chem., Int. Ed.*, 2011, **50**, 4169; (e) K. Padala and M. Jeganmoham, *Org. Lett.*, 2011, **13**, 6144; (f) F. Kakiuchi, T. Uetsuhara, Y. Tanaka, N. Chatani and S. Murai, *J. Mol. Catal. A*, 2002, 511; (g) F. Kakiuchi, Y. Yamamoto, N. Chatani and S. Murai, *Chem. Lett.*, 1995, 681; (h) M. Sonoda, F. Kakiuchi, N. Chatani and S. Murai, *Bull. Chem. Soc. Jpn.*, 1997, **70**, 3117; For keto-directed *o*-C–H bond arylation, see: (i) F. Kakiuchi, Y. Matsuura, S. Kan and N. Chatani, *J. Am. Chem. Soc*., 2005, **127**, 5936; (j) F. Kakiuchi, S. Kan, K. Igi, N. Chatani and S. Murai, *J. Am. Chem. Soc.*, 2003, **125**, 1698; For keto-directed *o*-C–H bond halogenation, see: (k) N. Schröder, J. Wencel-Delord and F. Glorius, *J. Am. Chem. Soc*., 2012, **134**, 8298; For keto-directed *o*-C**–**H bond oxygenation, see: (l) P. Y. choy and Y. Kwong, *Org. Lett.*, 2013, **15**, 270; (m) F. Mo, L. J. Trzepkowski and G. Dong, *Angew. Chem. Int., Ed.*, 2012, **51**, 13075**;** (n) V. S. Thirunavukkarasu and L. Ackermann *Org. Lett.*, 2012, **14**, 6206.

15) Ru-catalyzed C–N bond formation, see: (a) M.-L. Louillat and F. W. Patureau, *Org. Lett.*, 2013, **15**, 164 ; (b) J. Hu, S. Chen, Y. Sun, J. Yang and Y. Rao, *Org. Lett.*, 2012, **14**, 5030; (c) M. E. Harvey, D. G. Musaev and J. Du Bois, *J. Am. Chem. Soc*., 2011, **133**, 17207; (d) E. Milczek, N. Boudet and S. Blakey, *Angew. Chem., Int. Ed.*, 2008, **47**, 6825. (e) S. K.-Y. Leung, W.-M. Tsui, J.-S. Huang, C.-M. Che, J.-L. Liang and N. Zhu, *J. Am. Chem. Soc*., 2005, **127**, 16629; (f) L. He, P. W. H. Chan, W.-M. Tsui, W.-Y. Yu and C.-M. Che, *Org. Lett.*, 2004, **6**, 2405; (g) J.-L. Liang, S.-X. Yuan, J.-S. Huang, W.-Y. Yu and C.-M. Che, *Angew. Chem., Int. Ed.*, 2002, **41**, 3465.

16) M. R. Yadav, R. K. Rit and A. K. Sahoo, *Org. Lett.*, 2013, **15**, 1638.

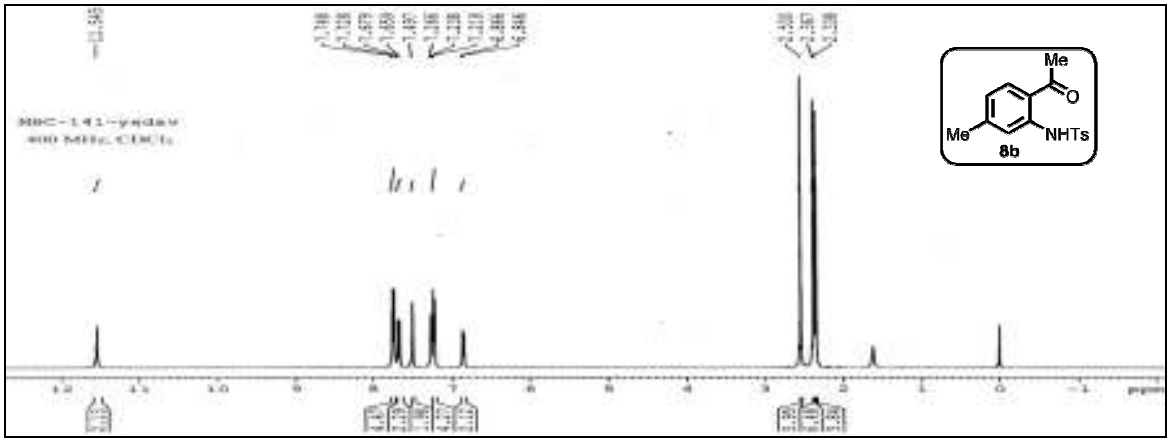
17) (a) J. Kim, J. Kim and S. Chang, *Chem.–Eur. J*., 2013, **19**, 7328; (b) Q.-Z. Zheng, Y.-F. Liang, C. Qin and N. Jiao, *Chem. Commun.*, 2013, **49**, 5654; (c) V. S. Thirunavukkarasu, K. Raghuvanshi and L. Ackermann, *Org. Lett.*, 2013, **15**, 3286.

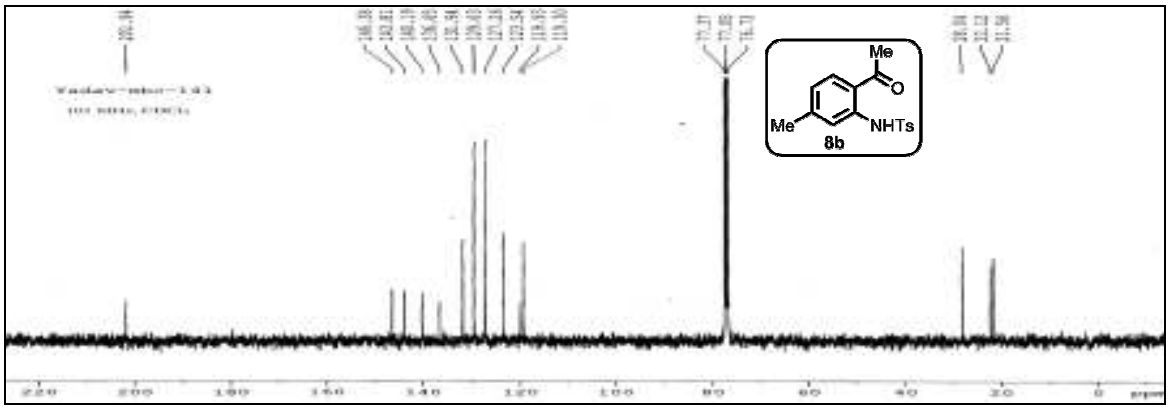
18) (a) K. Graczyk, W. Ma and L. Ackermann, *Org. Lett.*, 2012, **14**, 4110; (b) L. Ackermann, J. Pospech, K. Graczyk and K. Rauch, *Org. Lett.*, 2012, **14**, 930; (c) E.

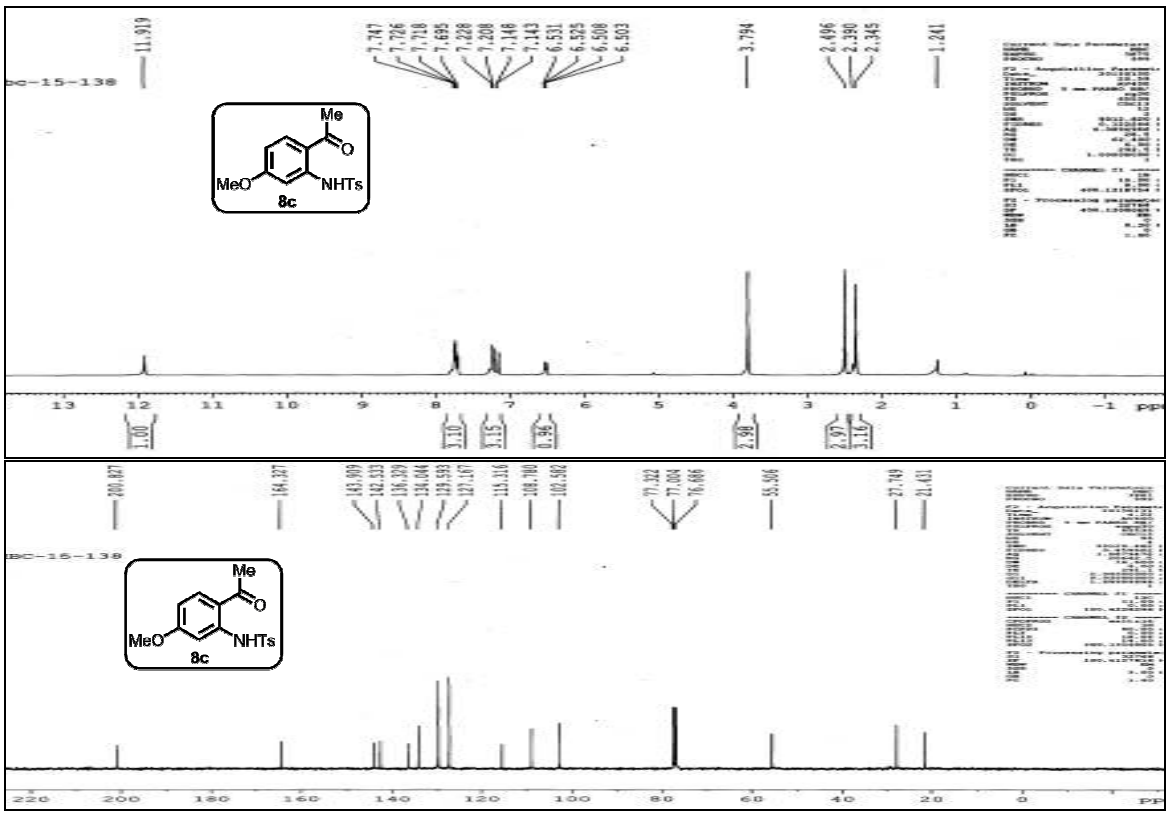
F. Flegeau, C. Bruneau, P. H. Dixneuf and A. Jutand, *J. Am. Chem. Soc.*, 2011, **133**, 10161.

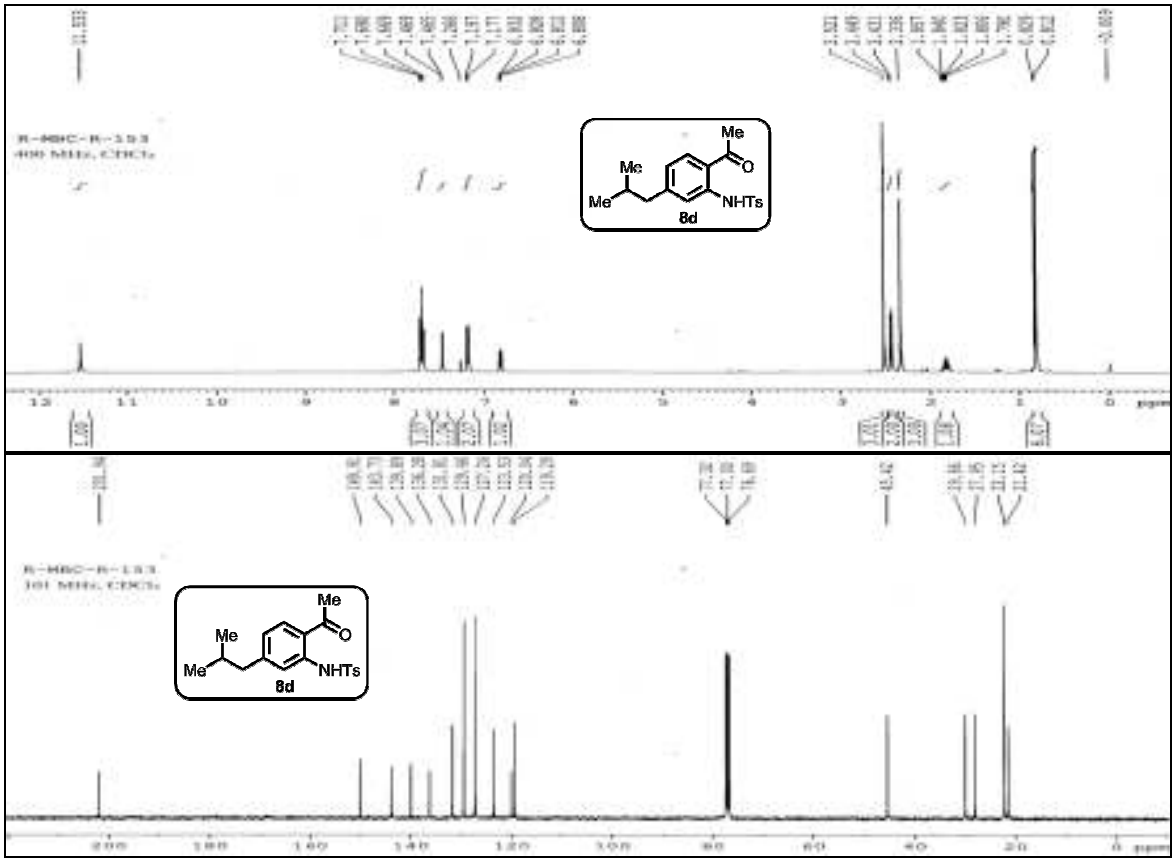
19) J. Waser, B. Gaspar, S. K. Richardson, E. M. Carreira, *J. Am. Chem. Soc.*, **2006**, *128*, 11693.
20) Y. Hari, T. Kanie, T. Miyagi and T. Aoyama, *Synthesis*, 2006, **8**, 1249.
21) C. Theeraladanon, M. Arisawa, A. Nishida and M. Nakagawa, *Tetrahedron*, 2004, **60**, 3017.

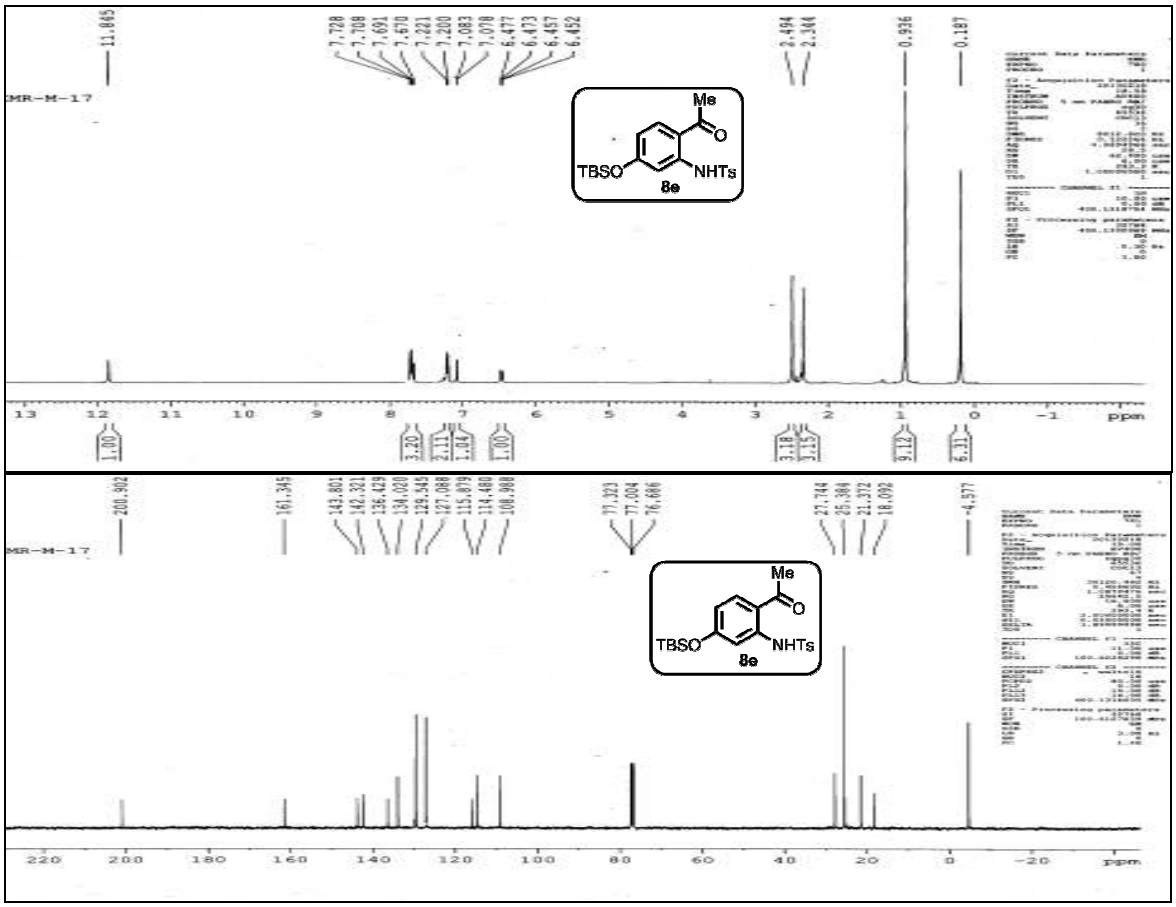
3.7. Spectra

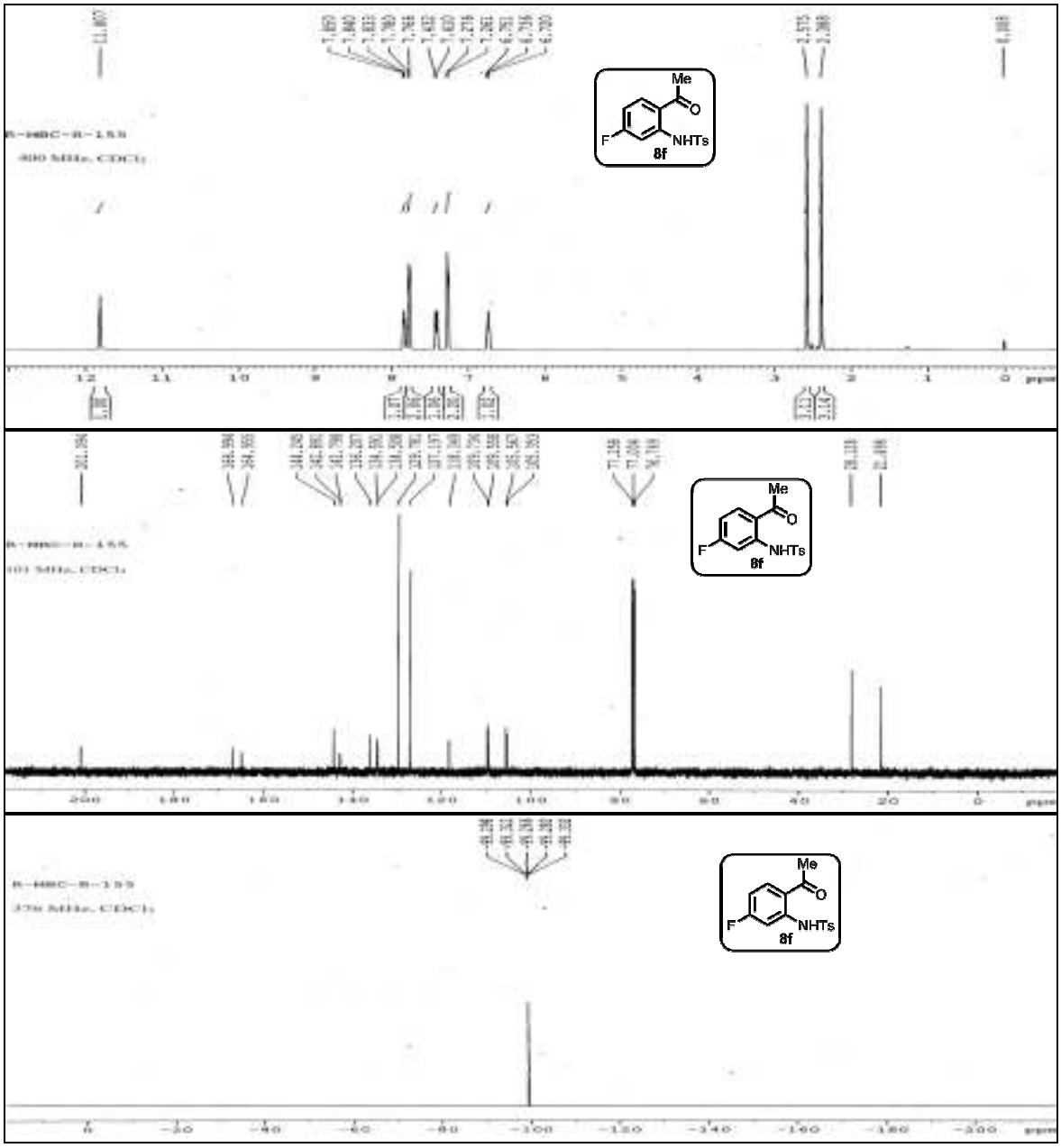


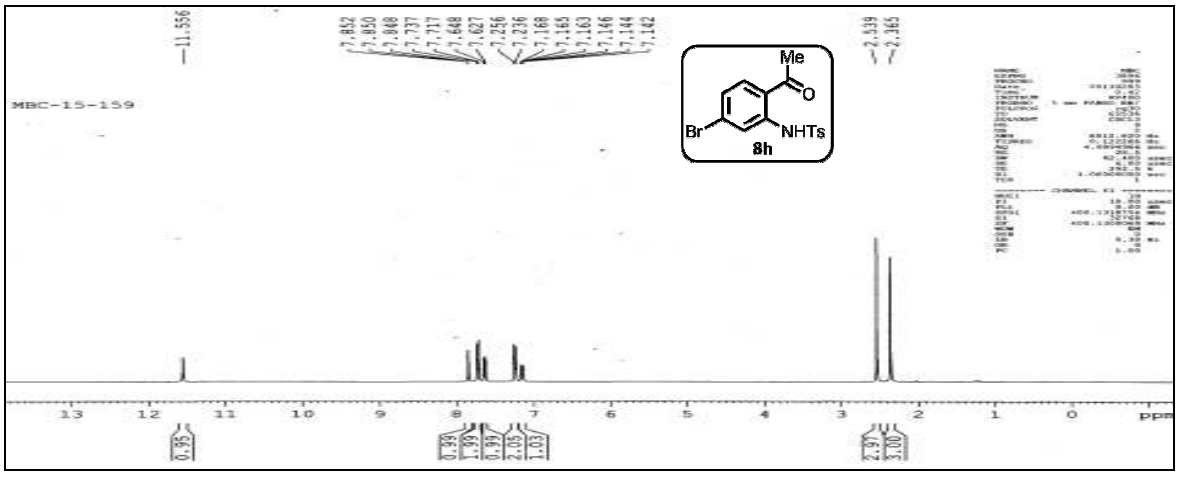


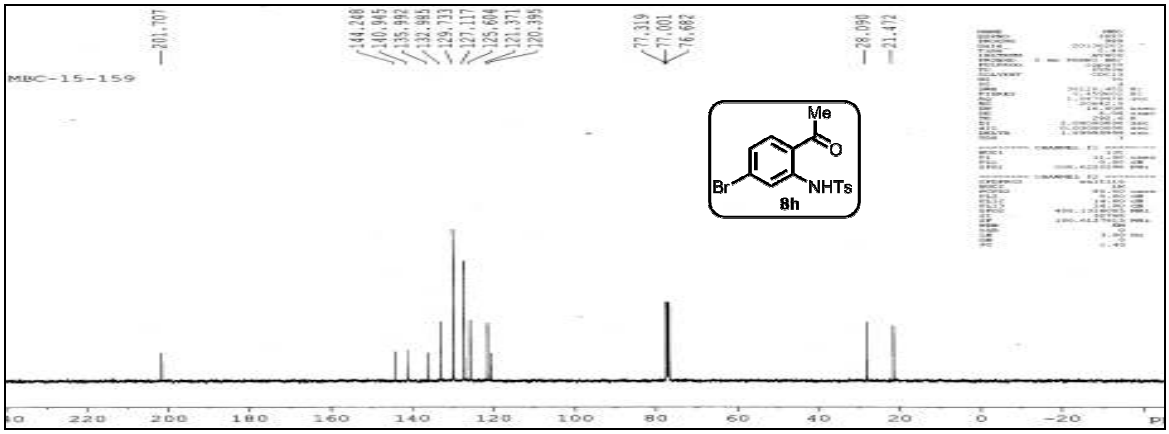


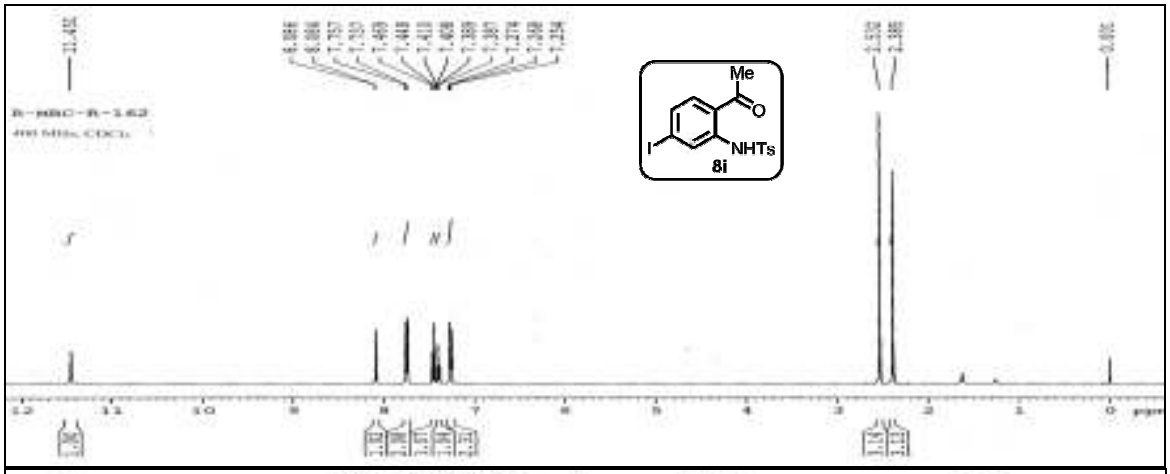

Me
Me
Me
O
NHTs
8d

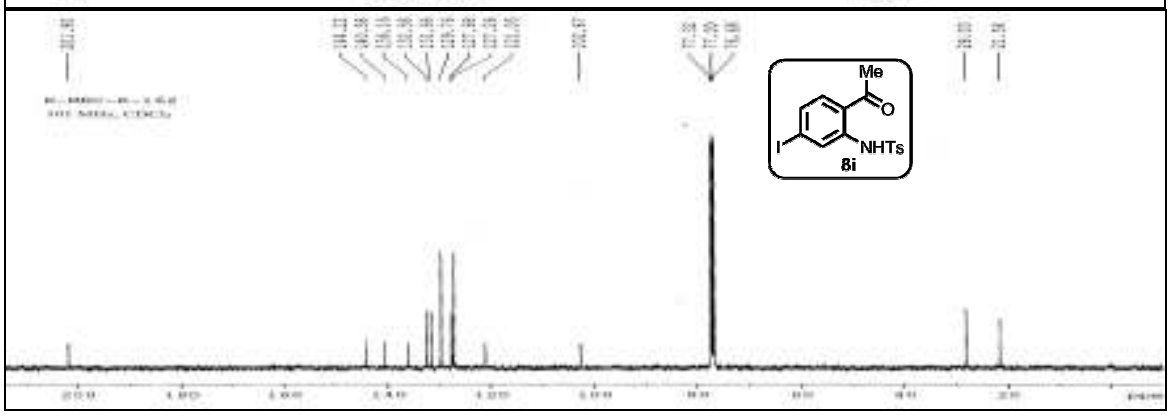

Me
TBSO
O
NHTs
8e

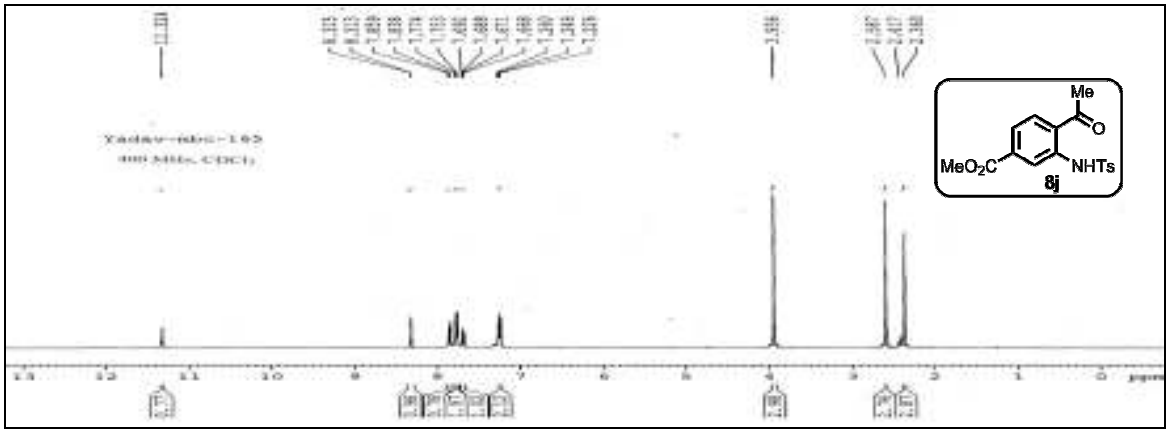

Me
O
F
NHTs
8f

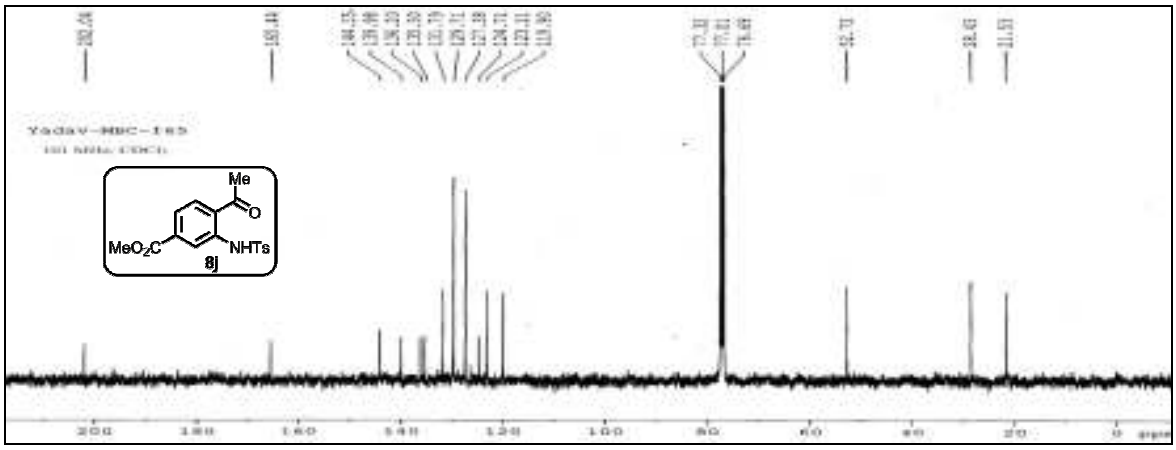

MBC-15-159
Me
O
Br
NHTs
8h

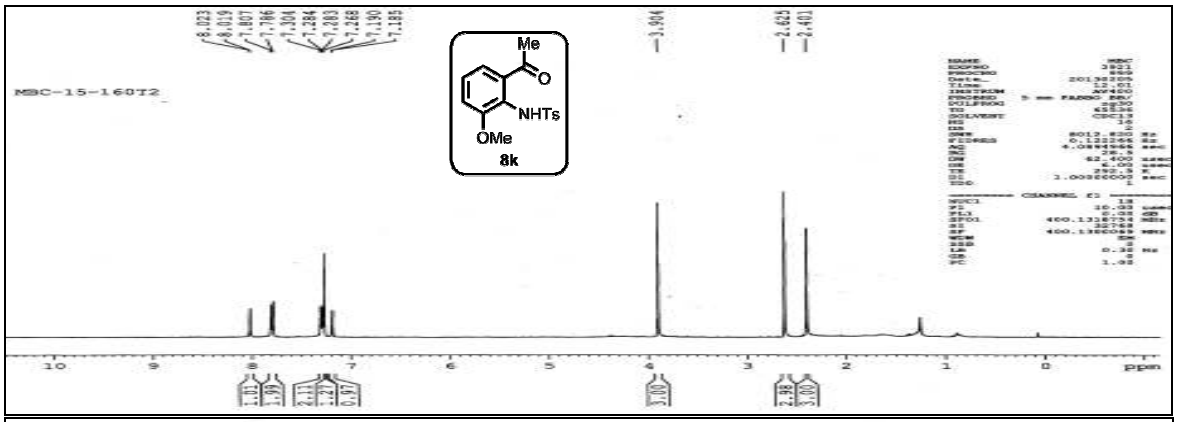

MBC-15-159
Me
O
Br
NHTs
8h

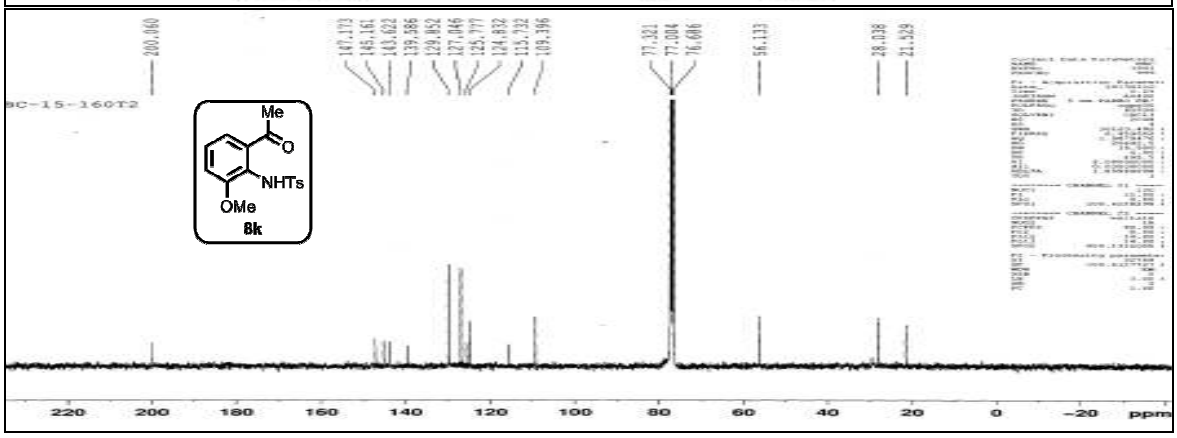

Me
O
I
NHTs
8i

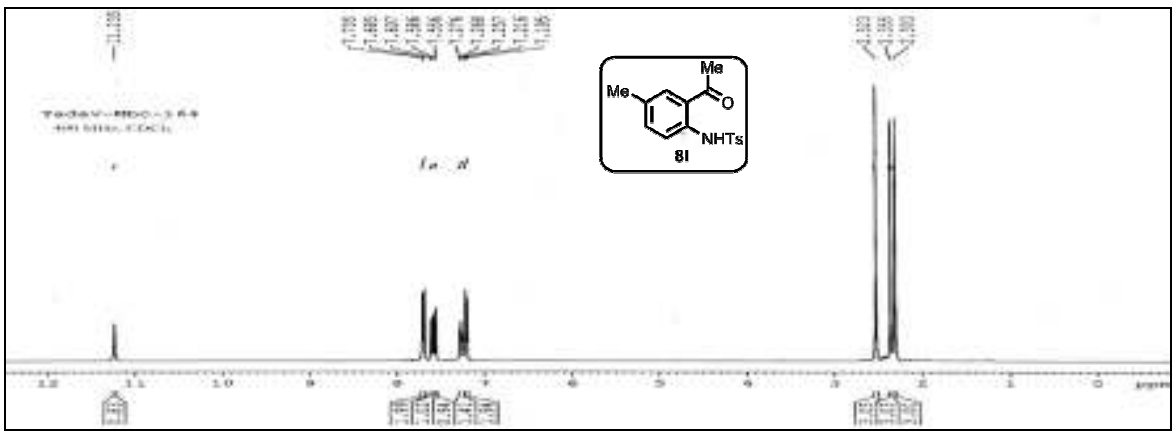

Me
O
I
NHTs
8i

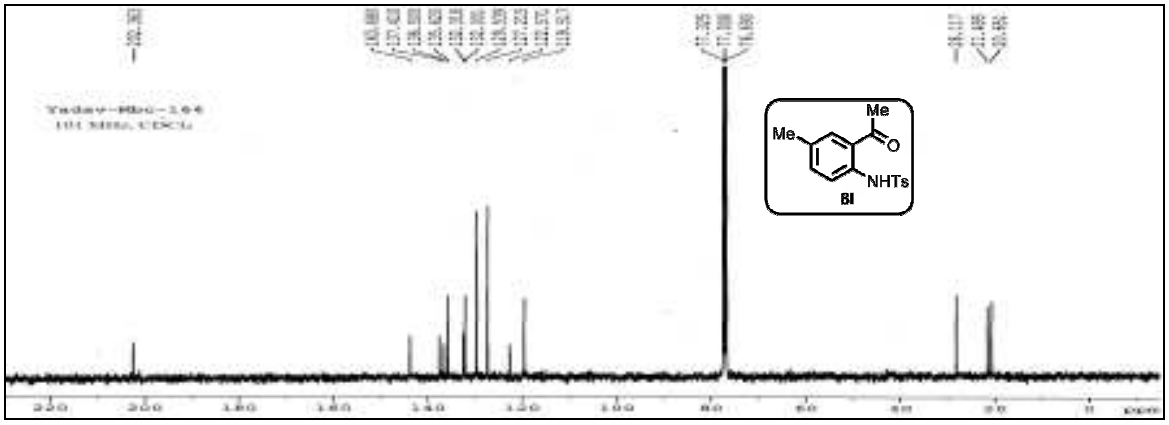

Yadav-mbc-165
Me
O
MeO2C
NHTs
8j

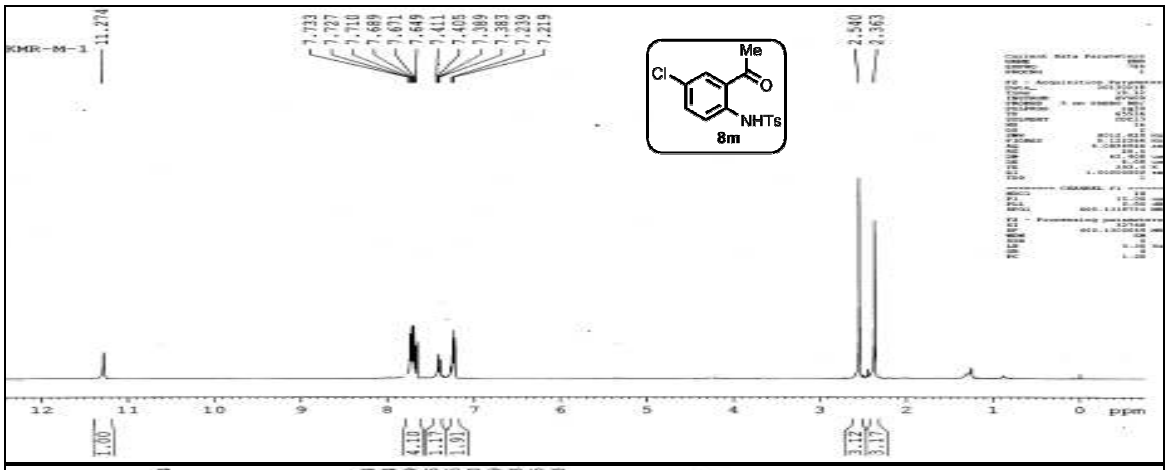

Me
O
MeO2C
NHTs
8j

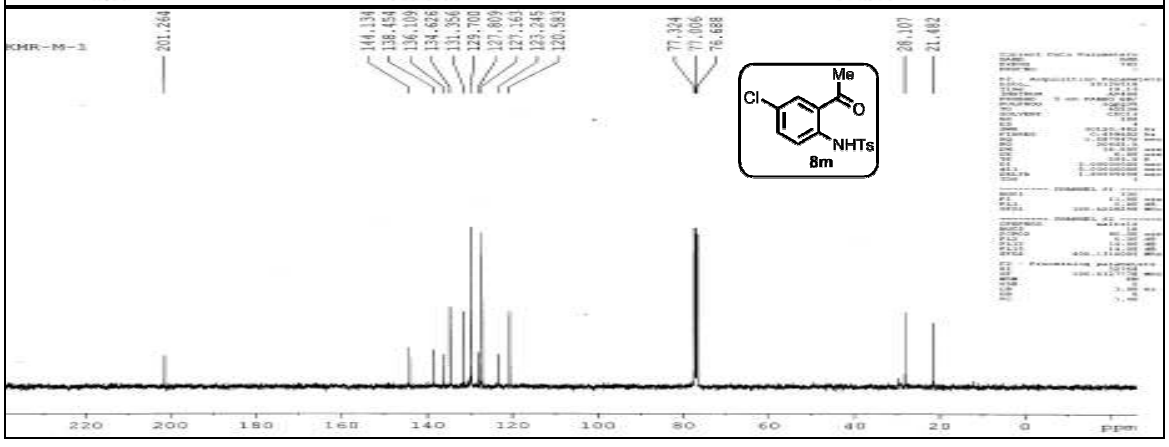

Me
O
NHTs
OMe
8k

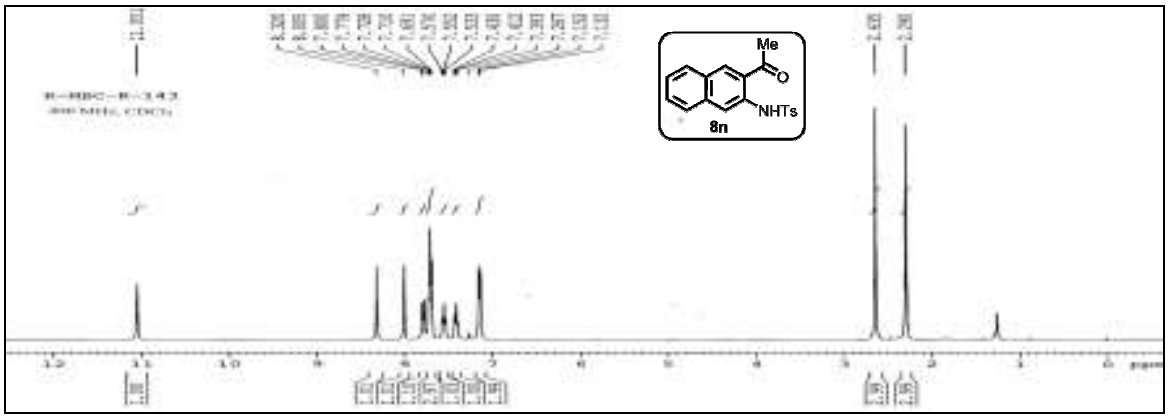

Me
O
NHTs
OMe
8k

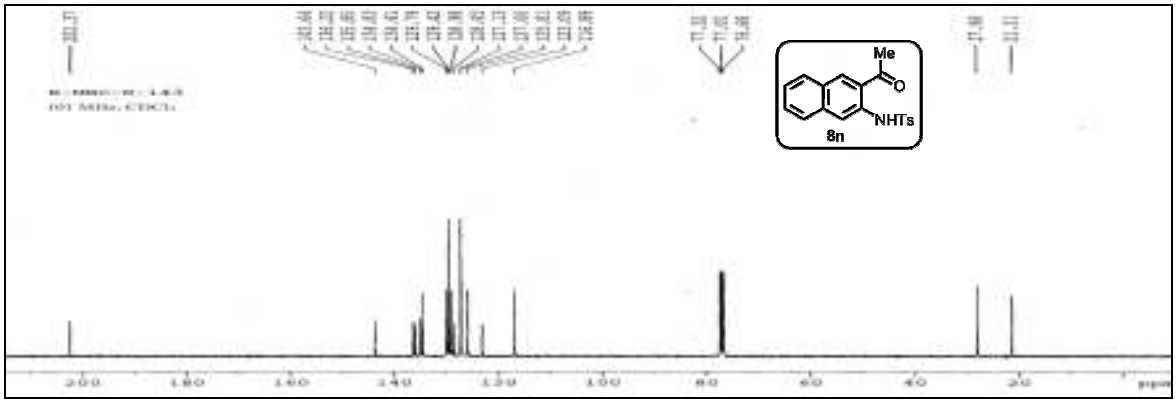

Me
Me
O
NHTs
8l

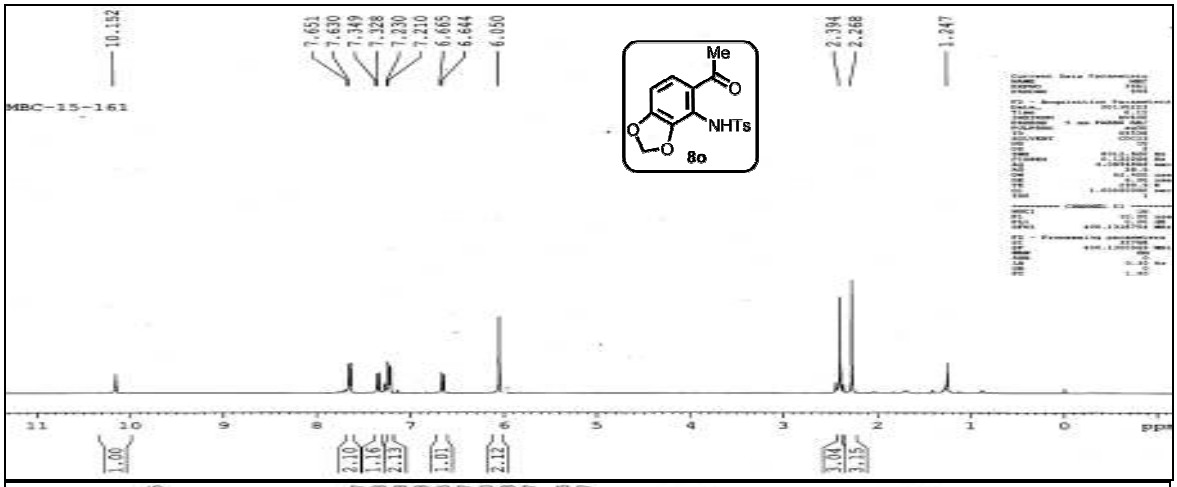

Me
Me
O
NHTs
8l

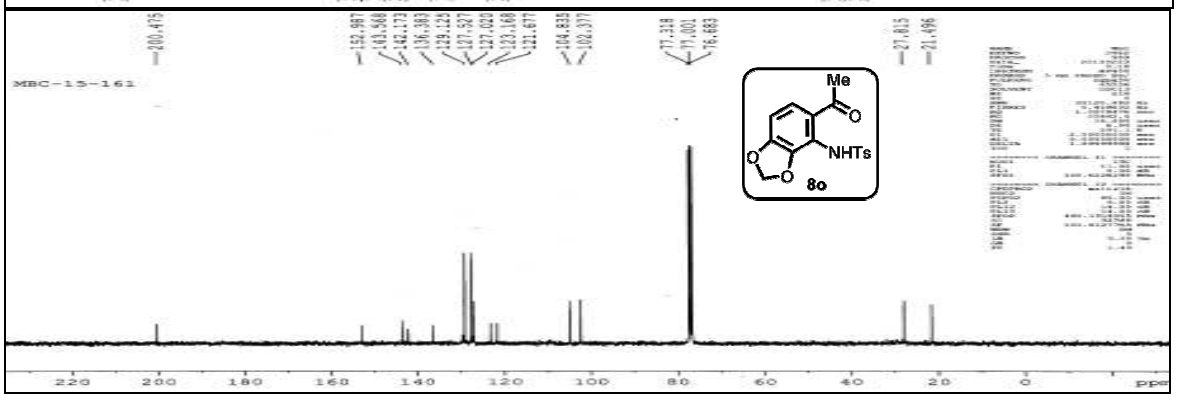

Me
Cl
O
NHTs
8m

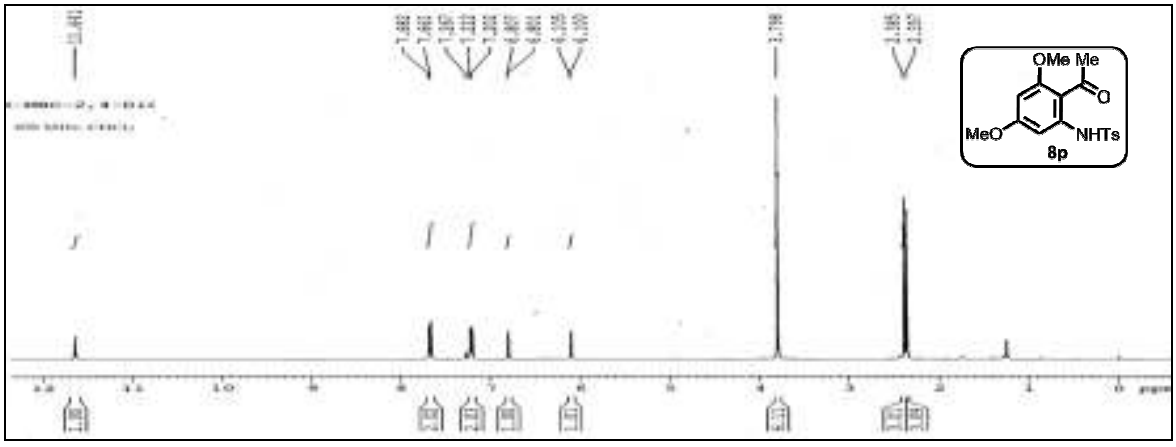

Me
Cl
O
NHTs
8m

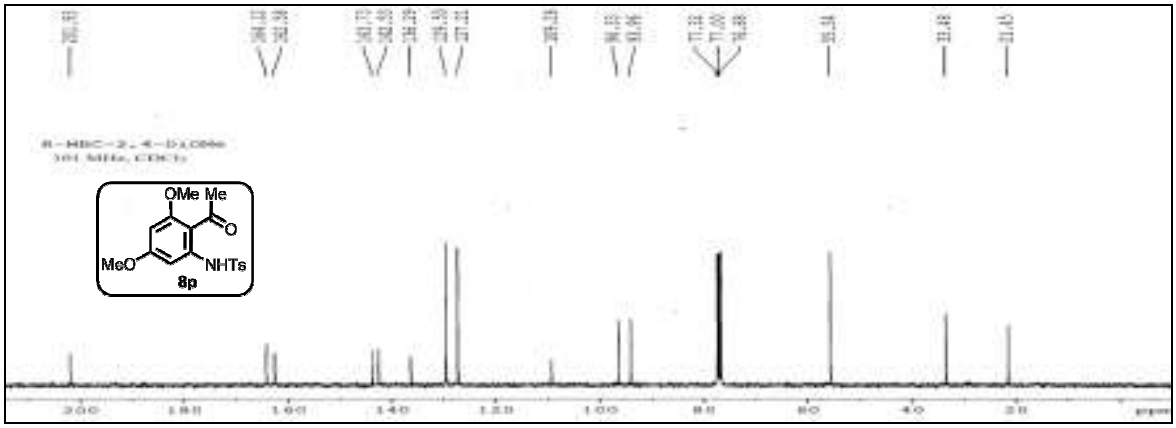

Me
O
NHTs
8n

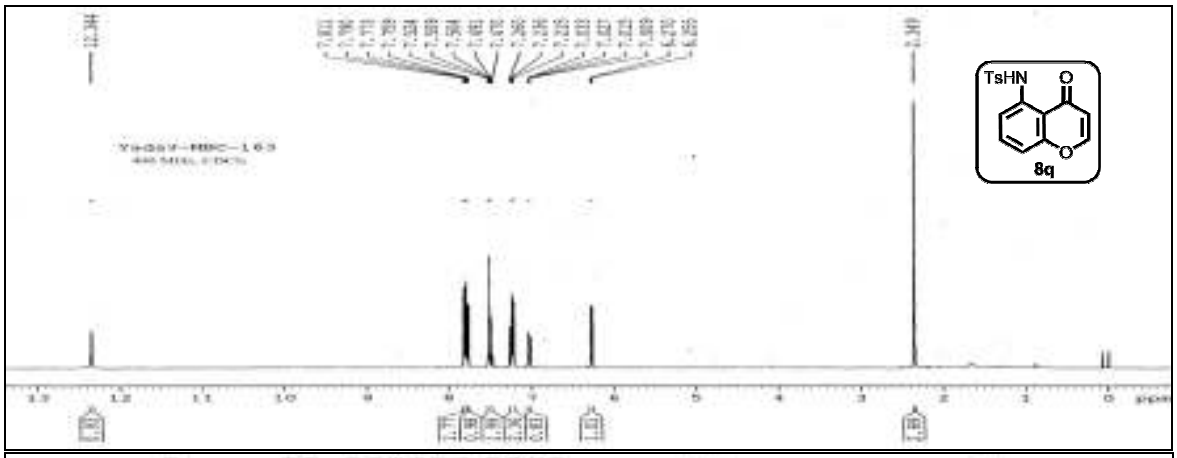

Me
O
NHTs
8n

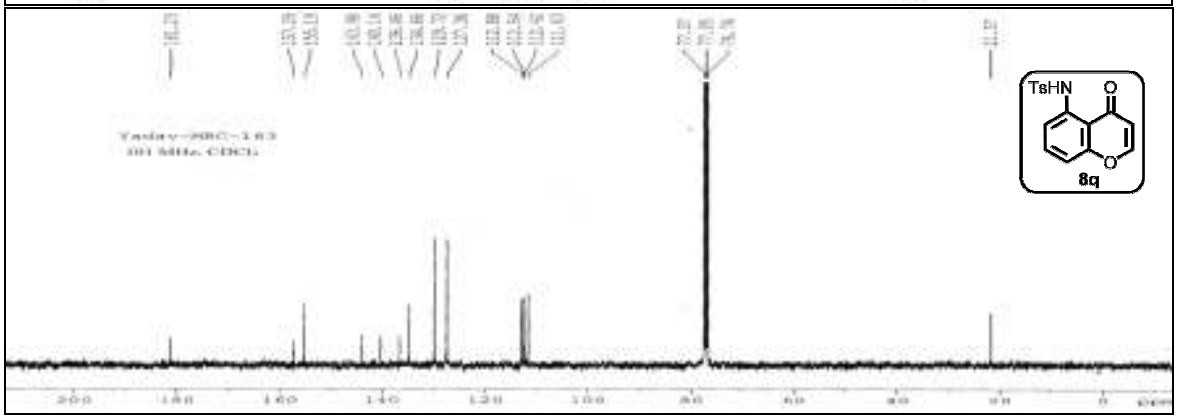

MBC-15-161
Me
O
NHTs
O
O
8o

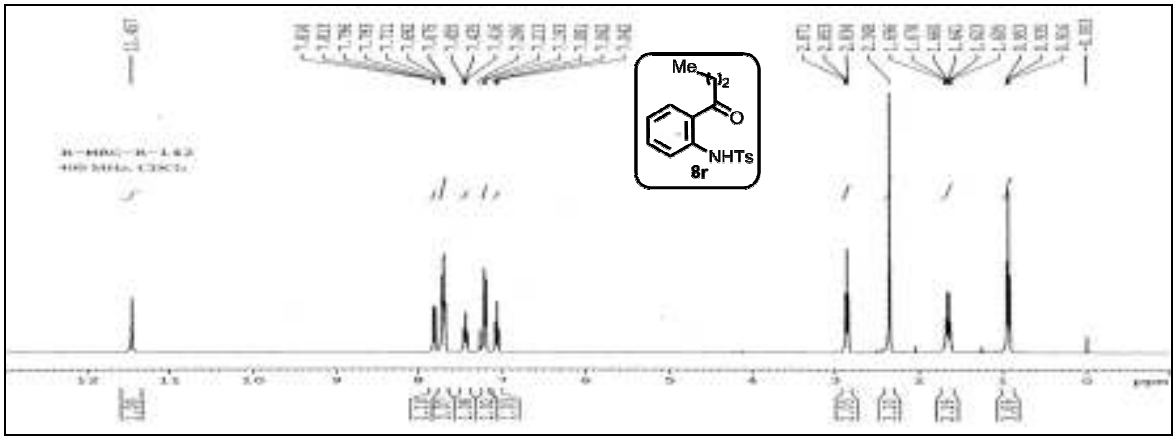

MBC-15-161
Me
O
NHTs
O
O
8o

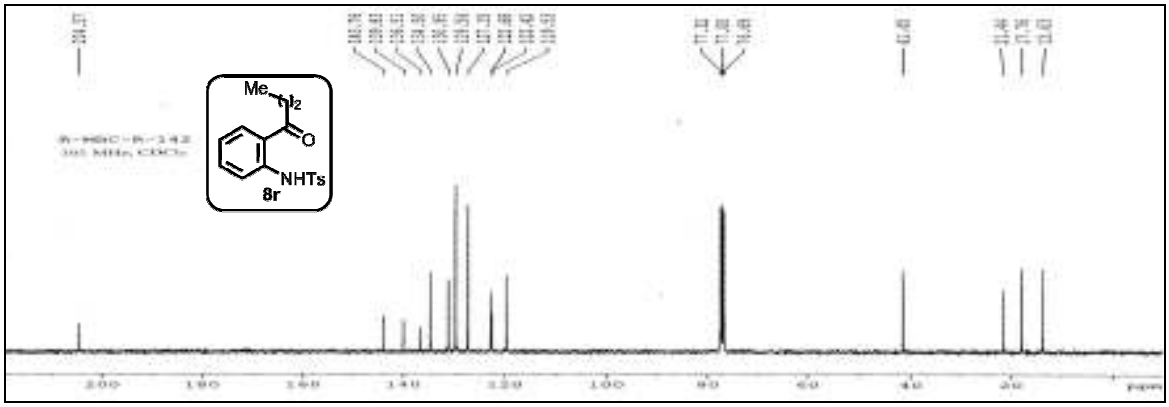

OMe Me
O
MeO
NHTs
8p

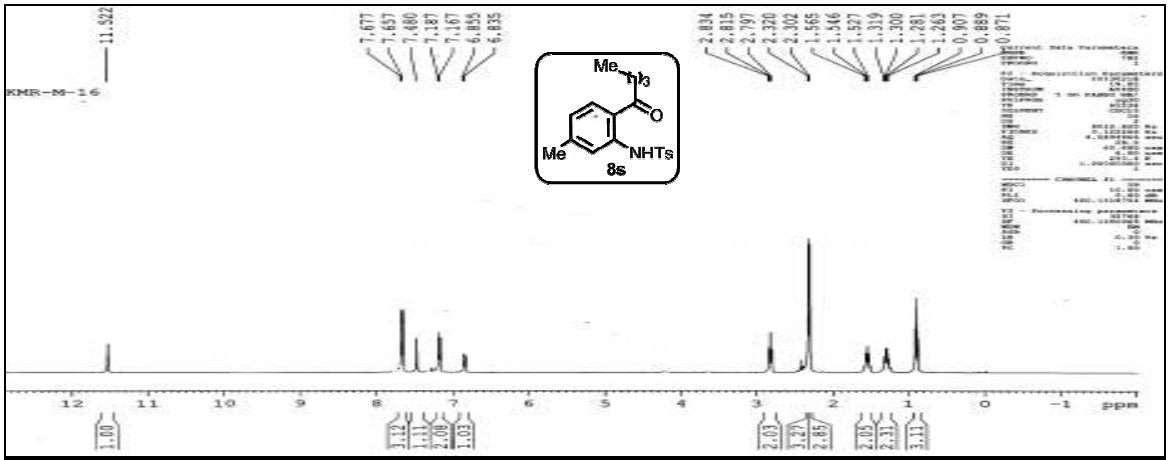

OMe Me
O
MeO
NHTs
8p

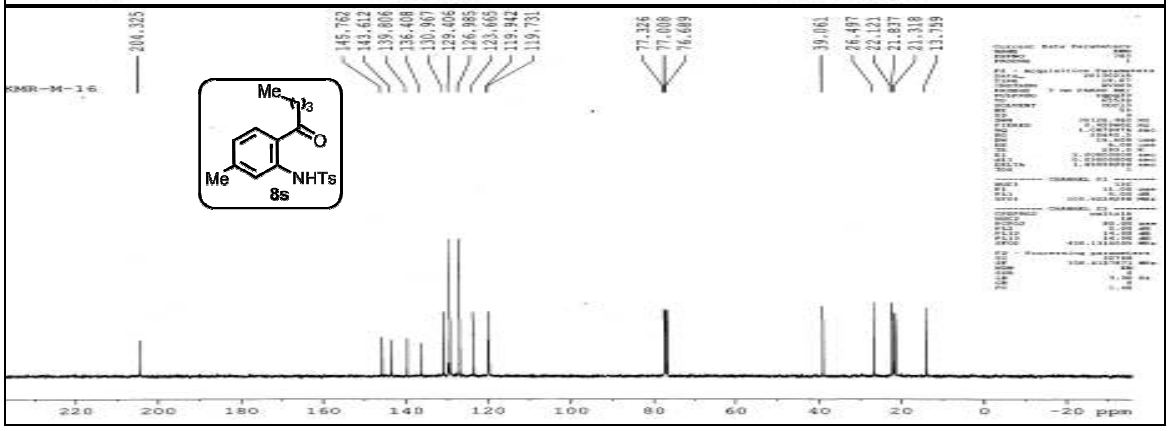

TsHN
O
O
8q

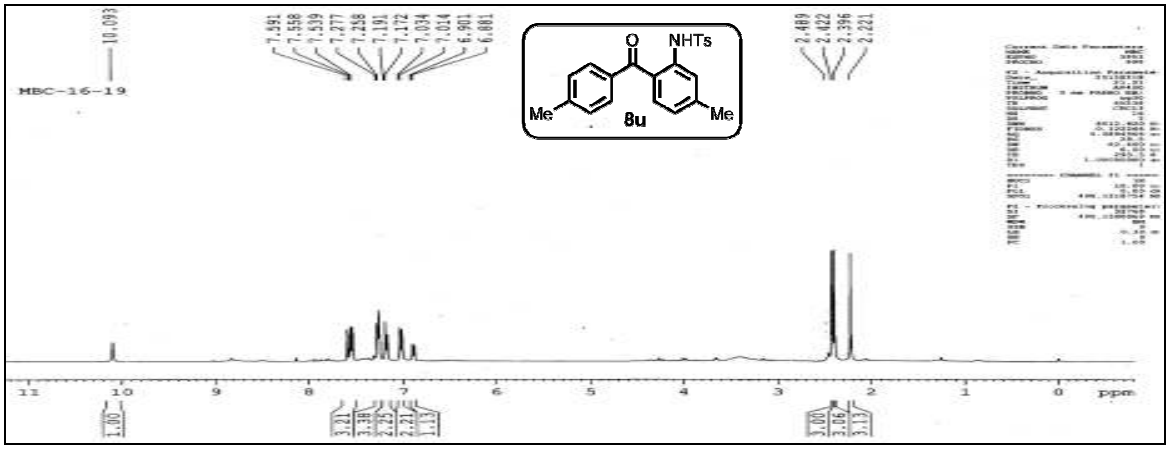

TsHN
O
O
8q

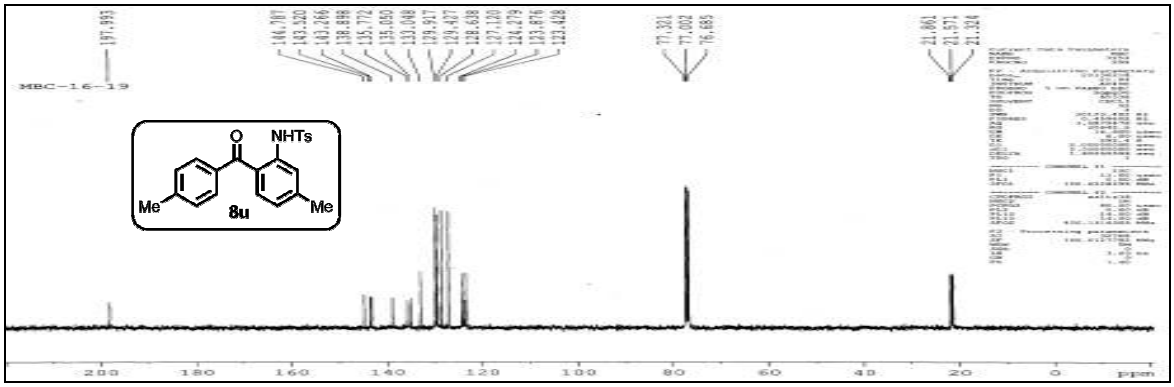

Me
O
NHTs
8r

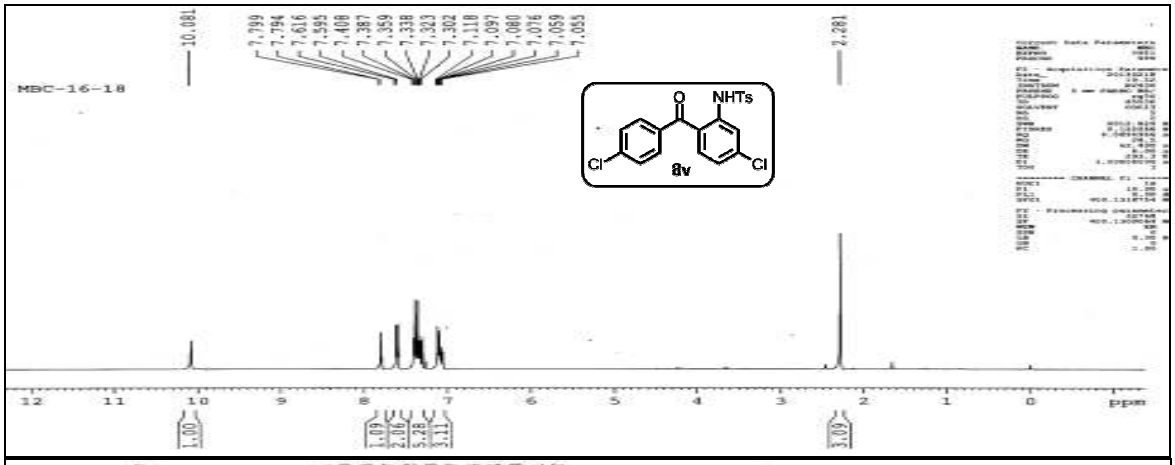

Me
NHTs
8r

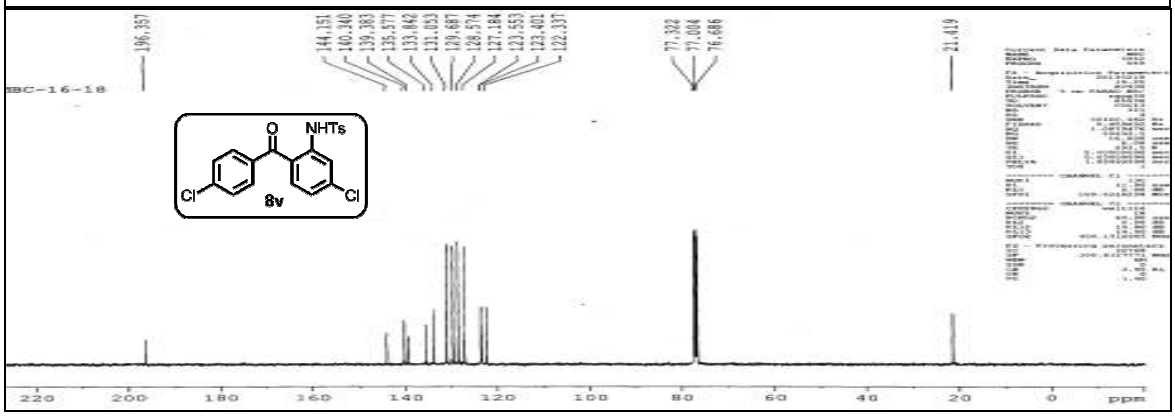

KMR-M-16
Me
NHTs
Me
8s

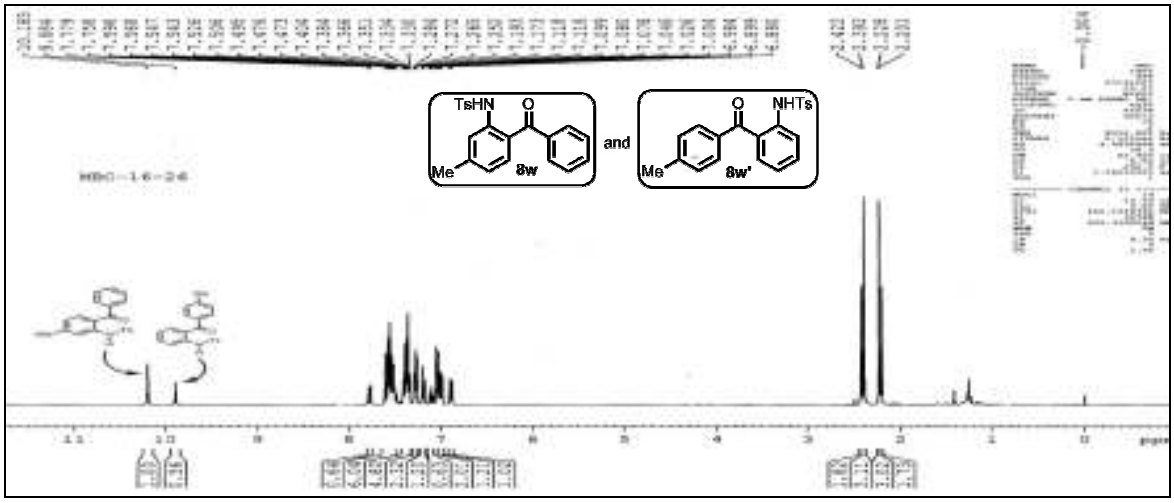

KMR-M-16
Me
NHTs
Me
8s

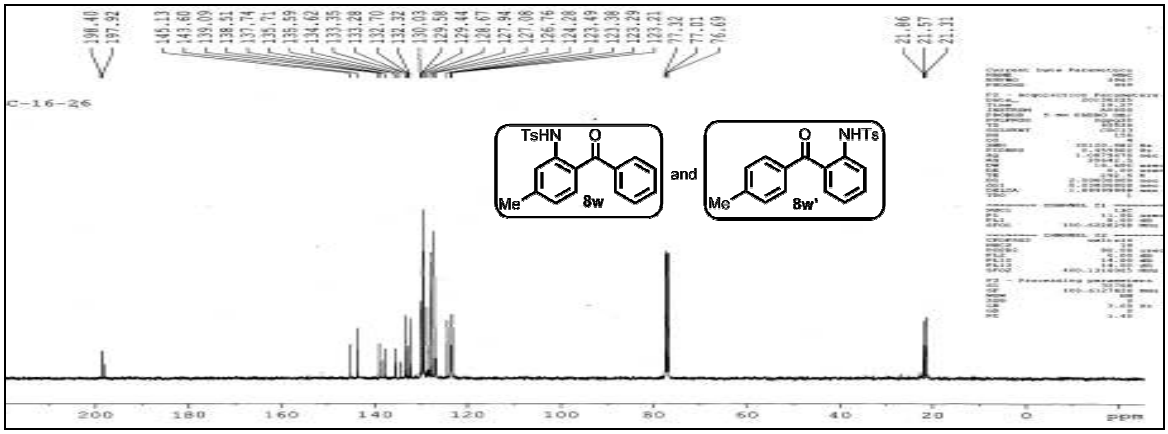

MBC-16-19
O
NHTs
Me
Me
8u

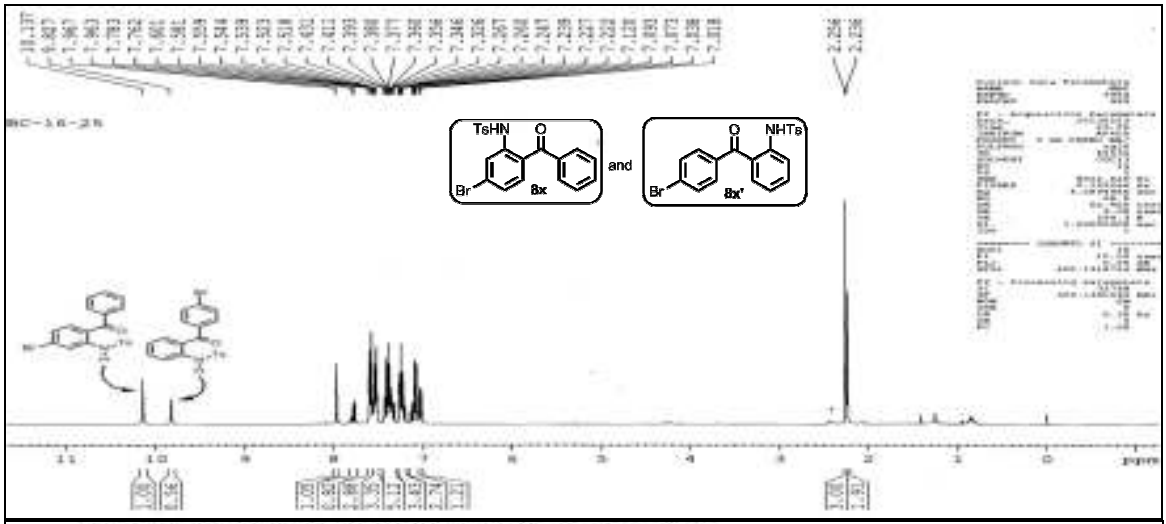

MBC-16-19
O
NHTs
Me
Me
8u

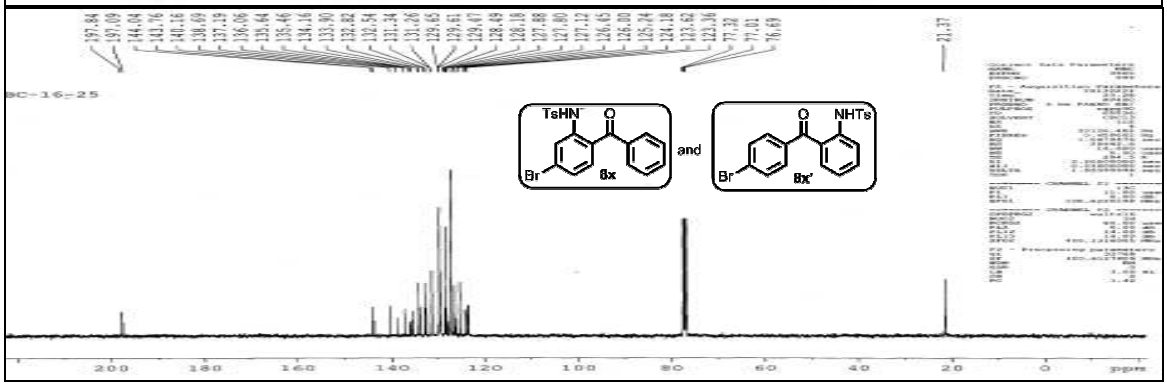

MBC-16-18
O
NHTs
Cl
Cl
8v

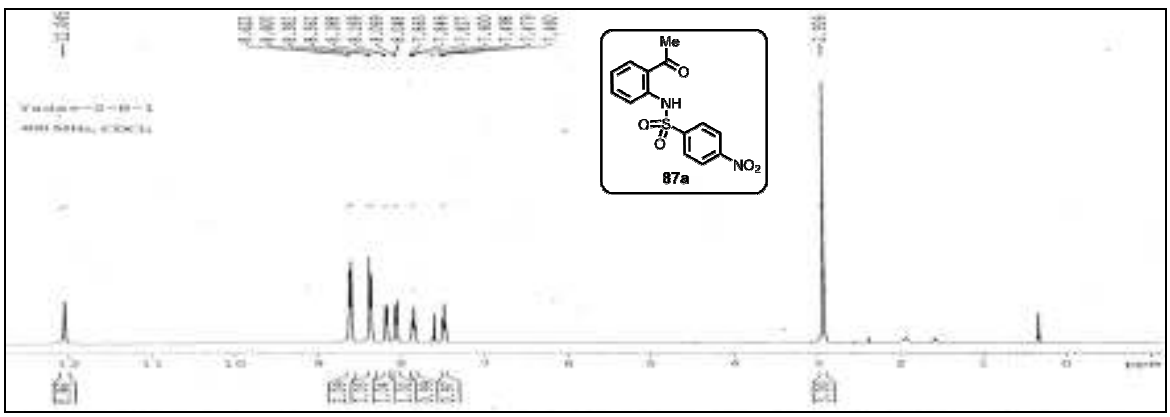

MBC-16-18
O
NHTs
Cl
Cl
8v

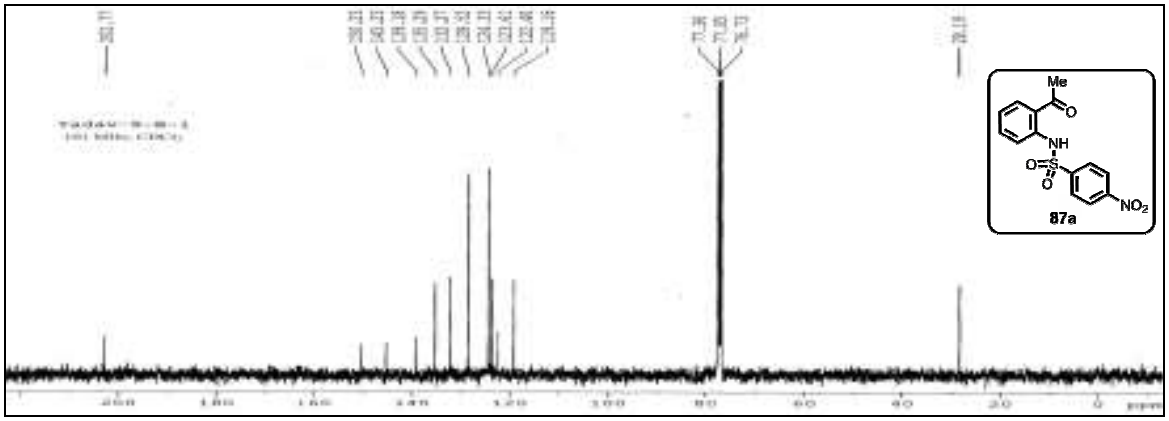

TsHN
O
Me
8w
and
O
NHTs
Me
8w'
MBC-16-24

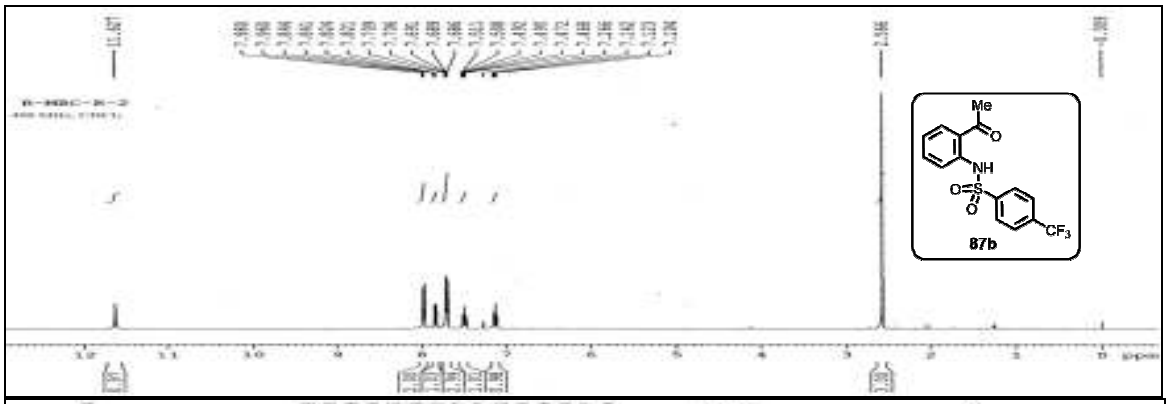

TsHN
O
Me
8w
and
O
NHTs
Me
8w'

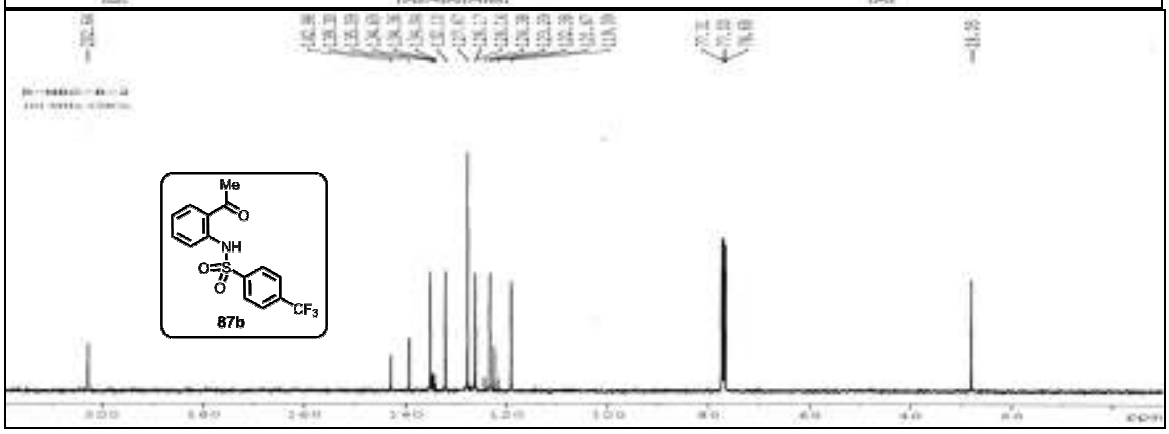

TsHN
O
Br
8x
and
O
NHTs
Br
8x'

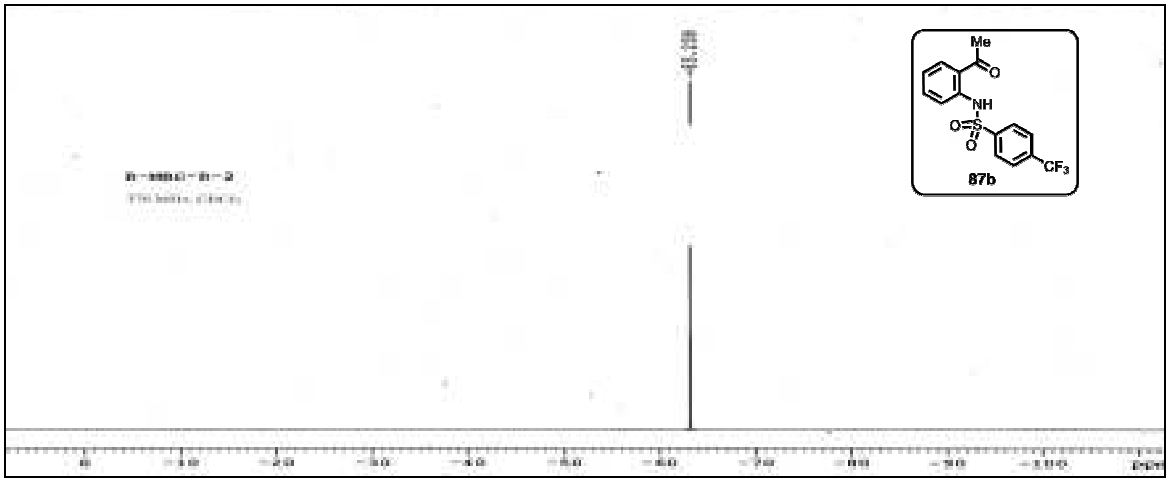

TsHN
O
Br
8x
and
O
NHTs
Br
8x'

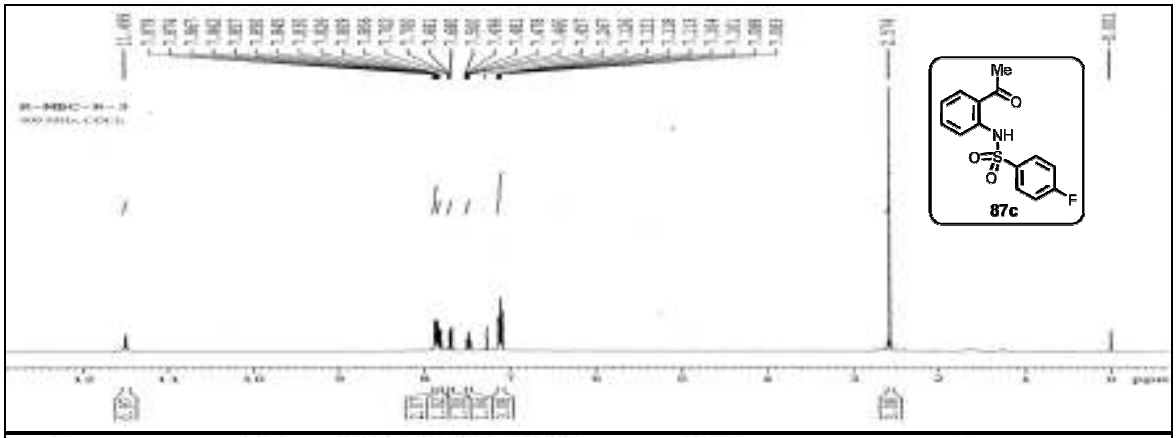

Me
O
NH
O=S=O
NO2
87a

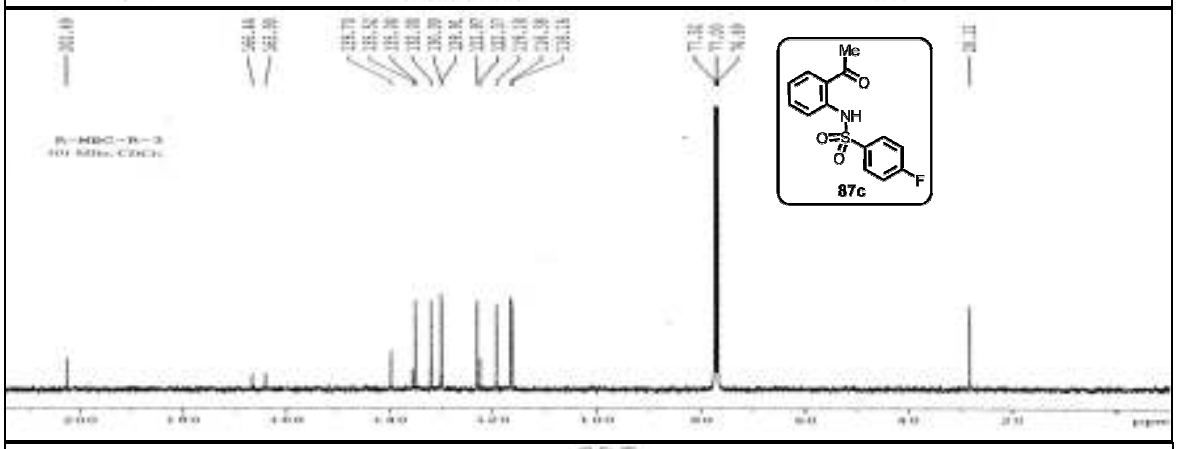

Me
O
NH
O=S=O
NO2
87a


Me
O
NH
O=S=O
CF3
87b

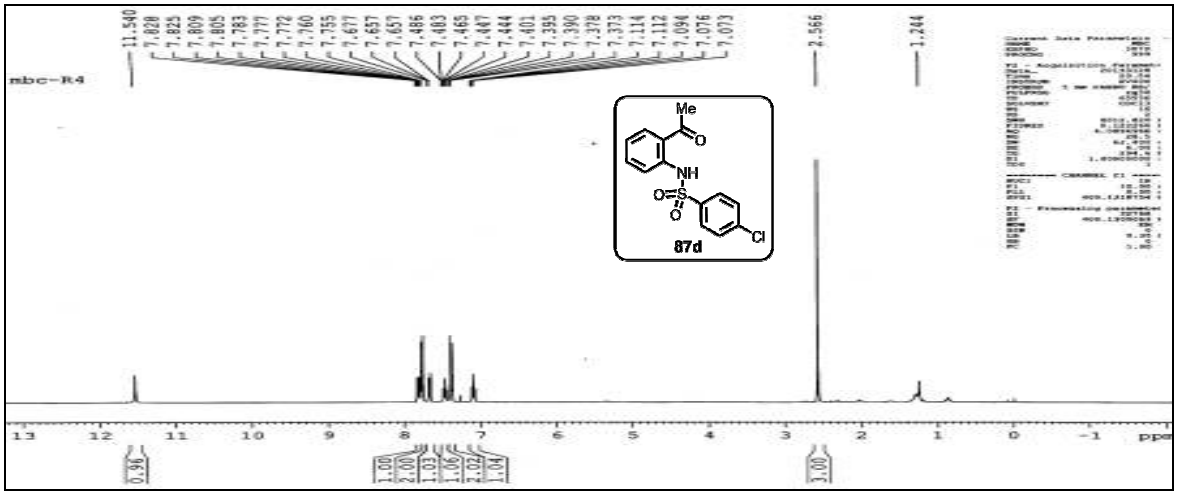

Me
O
NH
O=S=O
CF3
87b

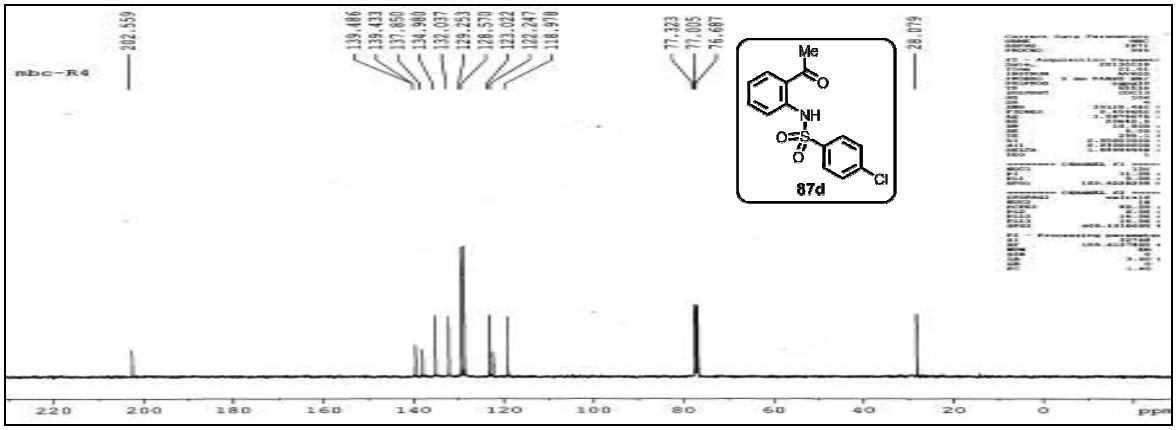

Me
O
NH
O=S=O
CF3
87b

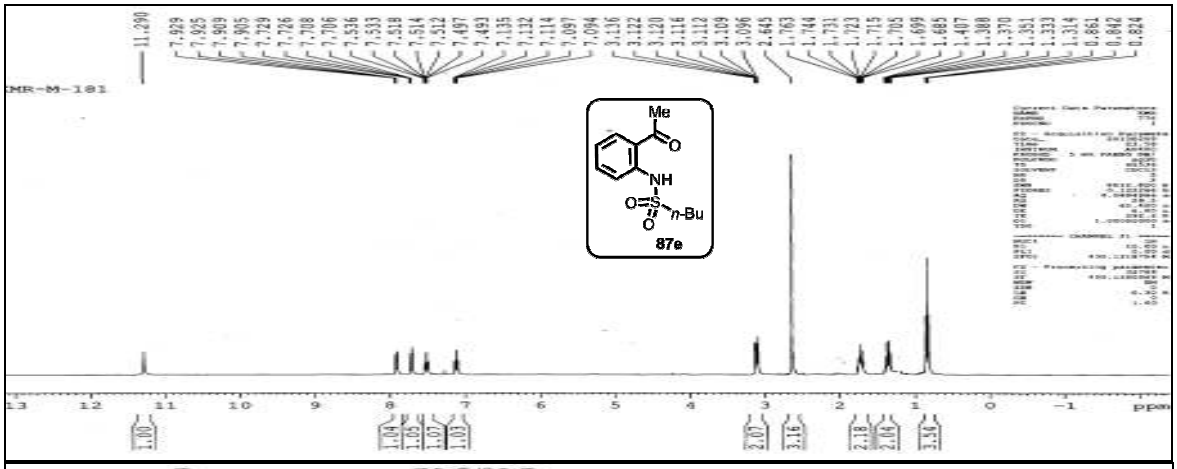

Me
O
NH
O
S
O
F
87c

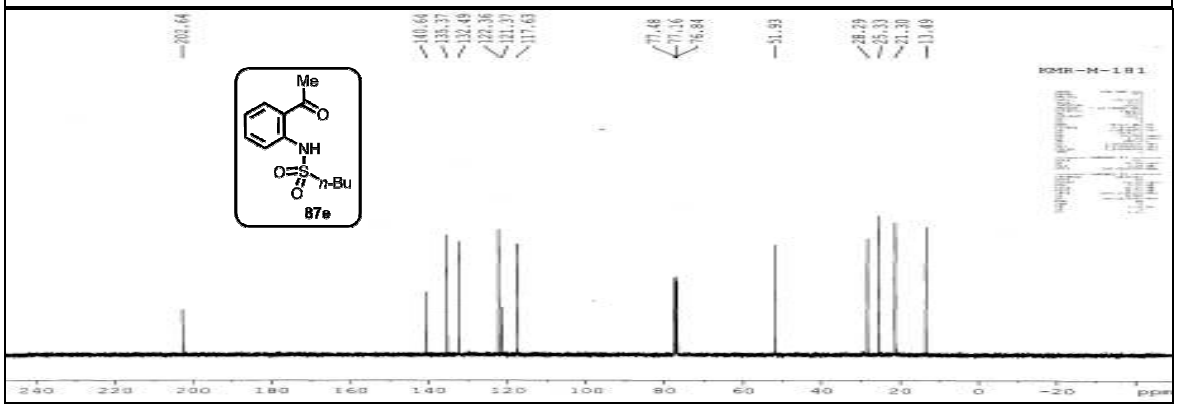

Me
O
NH
O
S
O
F
87c

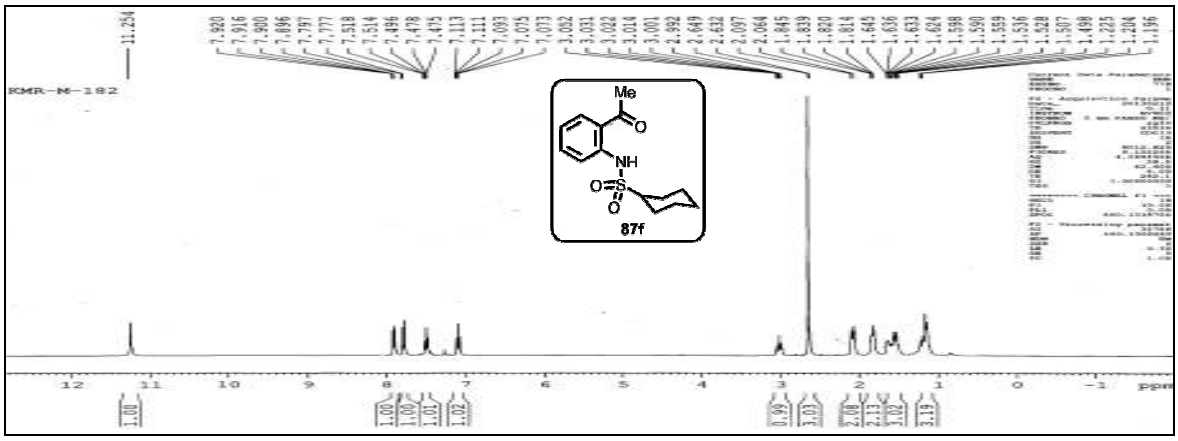

Me
O
NH
O
S
O
F
87c

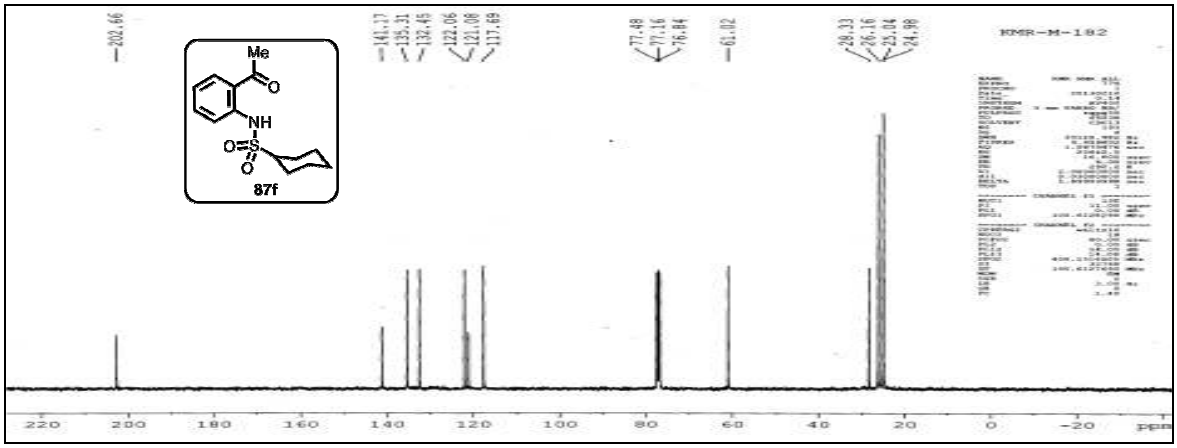

nbc-R4
Me
O
NH
O
S
O
Cl
87d

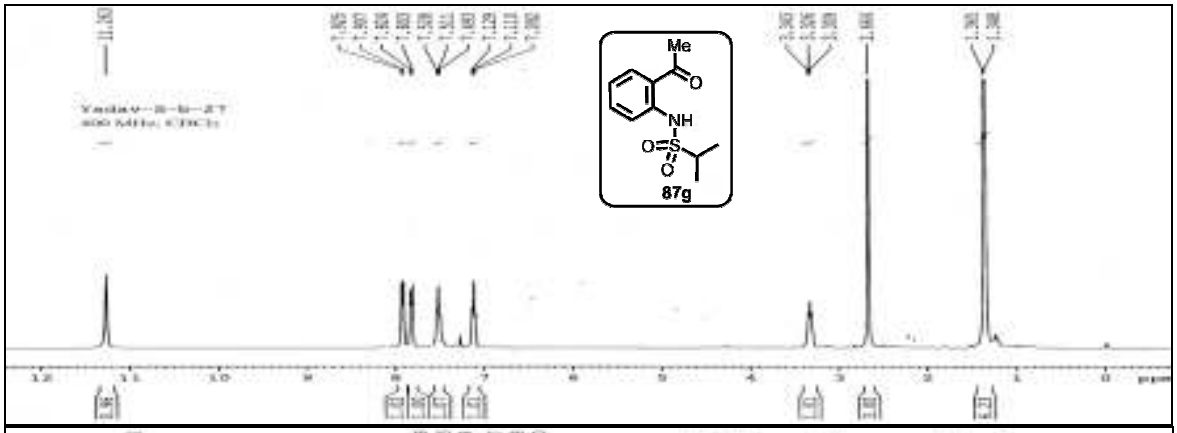

mbc-R4
Me
NH
O
O
S
O
87d
Cl

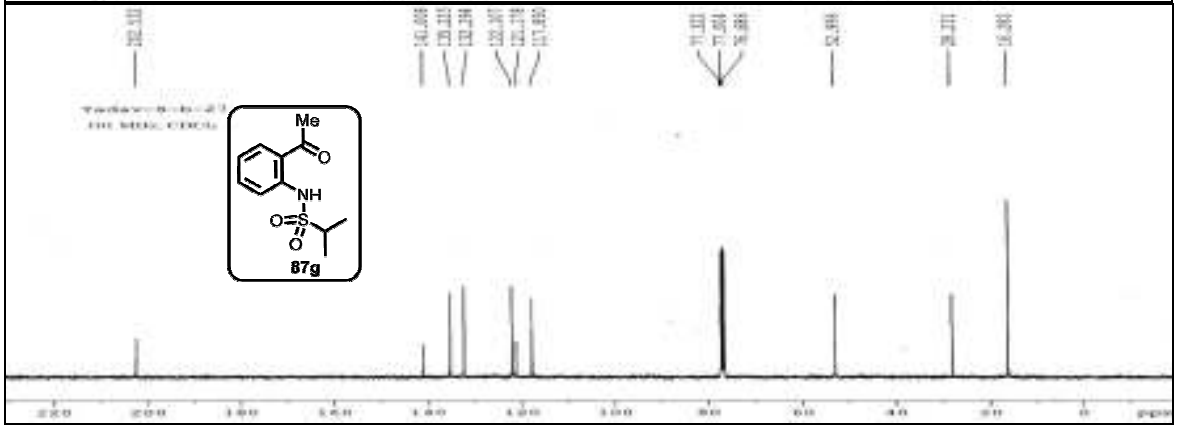

KMR-M-181
Me
NH
O
O
S
O
n-Bu
87e

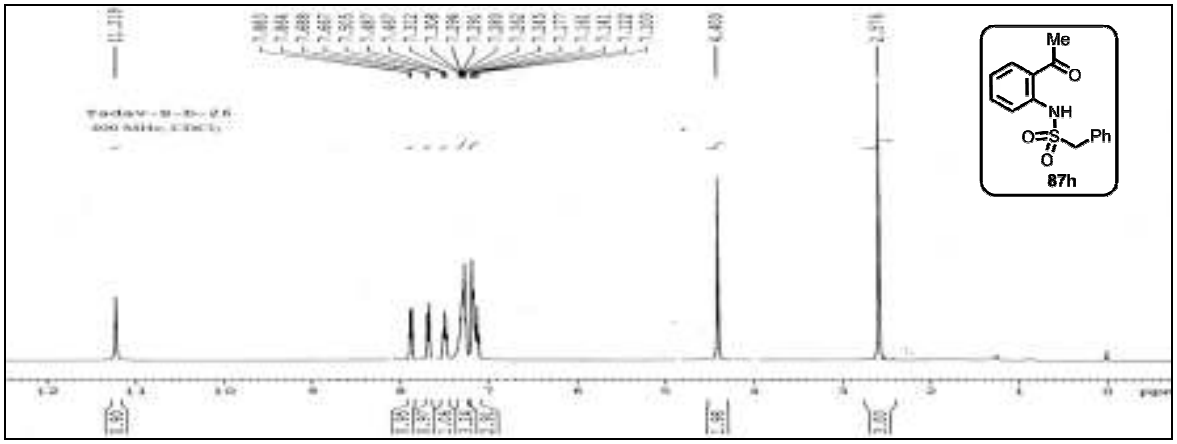

KMR-M-181
Me
NH
O
O
S
O
n-Bu
87e

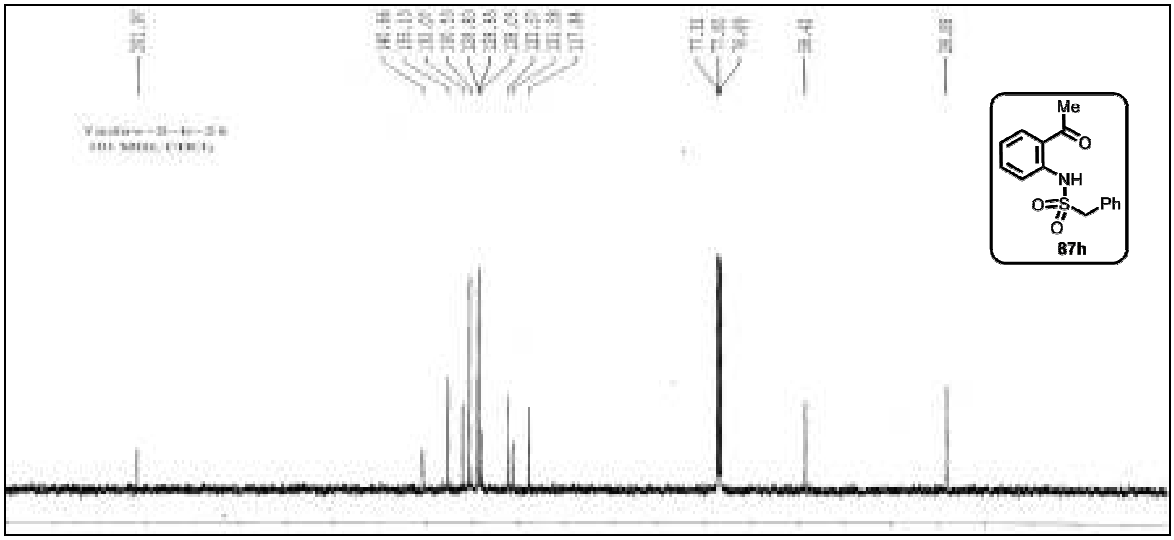

KMR-M-182
Me
NH
O
O
S
O
87f

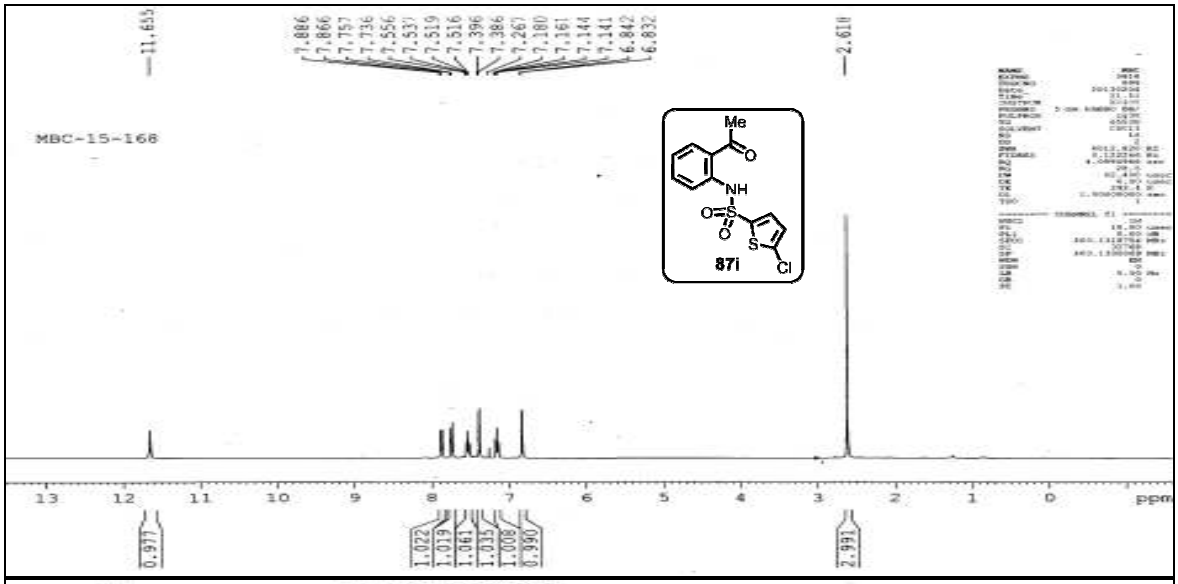

202.66
141.17
135.31
132.45
122.06
121.08
117.69
77.48
77.16
76.84
61.02
28.33
26.16
25.04
24.98
KMR-M-182
Me
O
NH
O=S=O
87f

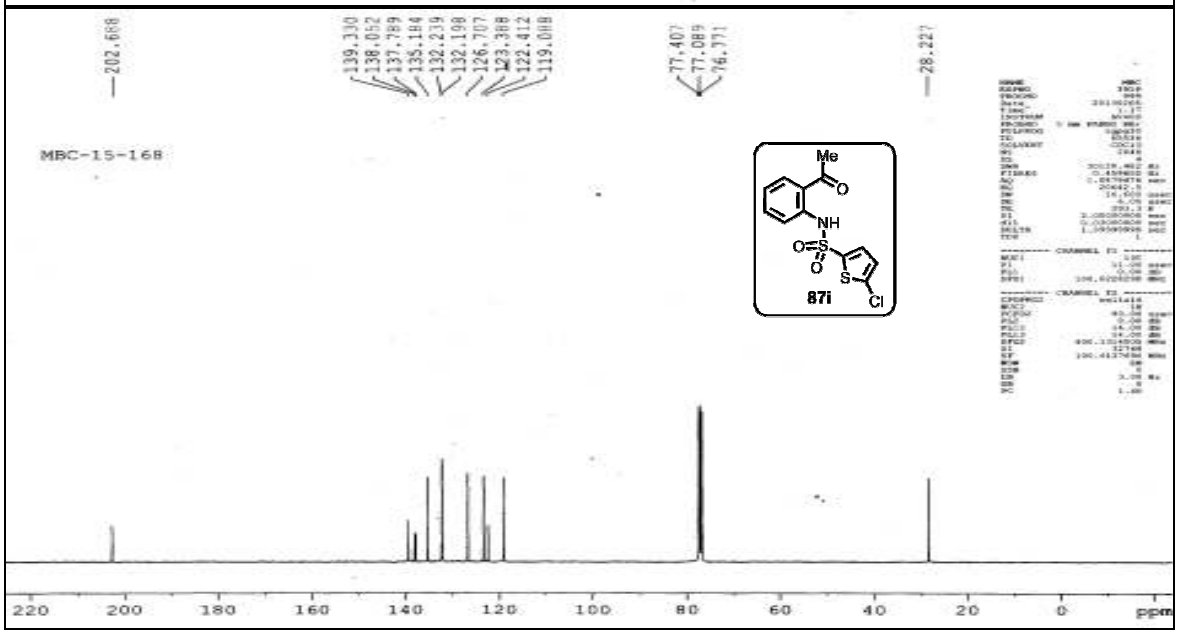

Me
O
NH
O=S=O
87g


Me
O
NH
O=S=O
87g


Me
O
NH
O=S=O
Ph
87h


Me
NH
Ph
87h


MBC-15-168
Me
NH
87i
Cl
ppm


MBC-15-168
Me
NH
87i
Cl
ppm

List of Publications

1. Gold-Catalyzed Intermolecular Hydrophenoxylation of Unactivated Internal Alkynes. Malleswara Rao Kuram, **M. Bhanuchandra**, and Akhila Kumar Sahoo, *J. Org. Chem.* 2010, **75**, 2247.

2. A Convenient Approach to β-Heteroarylated (C–N bond) Ketones from Cs_2CO_3 Promoted Reaction between Propargyl Alcohols and Nitrogen Heterocycles.
   M. Bhanuchandra, Malleswara Rao Kuram, and Akhila Kumar Sahoo, *Org. Biomol. Chem.* 2012, **10**, 3538.

3. Direct Access to Benzo[*b*]Furans through Palladium-Catalyzed Oxidative Annulations of Phenols and Unactivated Internal Alkynes.
   Malleswara Rao Kuram, **M. Bhanuchandra**, and Akhila Kumar Sahoo, *Angew. Chem. Int. Ed.* 2013, **52**, 4607.

4. Ru(II)-Catalyzed Intermolecular *ortho*-C–H Amidation of Aromatic Ketones with Sulfonyl Azides.
   M. Bhanuchandra, Muntha Ramu Yadav, Raja Kumar Rit, Malleswara Rao Kuram, and Akhila Kumar Sahoo, *Chem. Commun.* 2013, **49**, 5225.

5. Silver(I)-Catalyzed Reaction between Pyrazole and Propargyl Acetates: Stereoselective Synthesis of Scorpionate Ligands *E*-Allyl-*gem*-Dipyrazoles (ADPs).
   M. Bhanuchandra, Malleswara Rao Kuram, and Akhila Kumar Sahoo, (*manuscript submitted*)
6. Design, Synthesis and Optoelectronic Properties of Fused Furo-Indole Derivatives. Malleswara Rao Kuram, **M. Bhanuchandra**, and Akhila Kumar Sahoo, (*manuscript under preparation)*

Poster and Oral Presentations

1. **M. Bhanuchandra**, Malleswara Rao Kuram, and Akhila Kumar Sahoo*, A Convenient Approach to β-Heteroarylated (C–N bond) Ketones from Cs_2CO_3 Promoted Reaction between Propargyl Alcohols and Nitrogen Heterocycles.

   (i) Poster and Oral presentation at "**Chemfest-2012** (***In-house***)" which was held in School of Chemistry, *University of Hyderabad*, Hyderabad, India on February, **2012**.

   (ii) Poster presentation at "***7th J-NOST conference***" which was held in *Indian Institute of Science Education and Research Mohali*, Mohali, India on December, **2011**.