Copper Oxide Nanoparticles Assisted Synthesis of 1,4-Triazole Based New Organic Molecules And Facile Access to N-Heterocycles Using Multicomponent Reactions

A Dissertation Submitted to the
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As Partial Fulfillment for the Degree of

DOCTOR OF PHILOSOPHY

by

Prasanta Ray Bagdi
Roll No. 10612217

Department of Chemistry
Indian Institute of Technology Guwahati
Guwahati-781 039
October 2015

Dedicated to

My Late Father

INDIAN INSTITUTE OF TECHNOLOGY, GUWAHATI

Department of Chemistry

STATEMENT

I do hereby declare that the matter embodied in this thesis entitled "*Copper Oxide Nanoparticles Assisted Synthesis of 1,4-Triazole Based New Organic Molecules And Facile Access to N-Heterocycles Using Multicomponent Reactions*" is the result of investigations carried out by me under the supervision of Prof. Abu T. Khan in the Department of Chemistry, Indian Institute of Technology Guwahati, India.

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.

IIT Guwahati
October 16, 2015

Prasanta Ray Bagdi

Indian Institute of Technology Guwahati
Guwahati – 781039, India
Tel. No.: +91-361-2582305
Fax No.: +91-361-2582349
E-mail: atk@iitg.ernet.in

Dr. Abu T. Khan
Professor of Chemistry

CERTIFICATE

This is to certify that Mr. Prasanta Ray Bagdi has been working in my research group since July, 2010 as a regular registered Ph. D. student. I am forwarding his thesis entitled "*Copper Oxide Nanoparticles Assisted Synthesis of 1,4-Triazole Based New Organic Molecules And Facile Access to N-Heterocycles Using Multicomponent Reactions*" for submission for the Ph. D. (Science) Degree of this Institute. I certify that he has fulfilled all the requirements according to the rules of this Institute regarding the investigations embodied in his thesis and this work has not been submitted elsewhere for a degree.

IIT Guwahati
October 10, 2015

Prof. A. T. Khan
(Thesis Supervisor)

Indian Institute of Technology Guwahati
Guwahati – 781039, India
Tel. No.: +91-361-2582307
Fax No.: +91-361-2582349
E-mail: patel@iitg.ernet.in

Dr. Bhisma K. Patel
Professor and Head
Department of Chemistry

CERTIFICATE

This is to certify that Mr. Prasanta Ray Bagdi has completed his Ph. D. Thesis work from July, 2010 as a regular registered Ph. D. student under my colleague Prof. Abu T. Khan. I have been appointed as a Co-Supervisor when Prof. Khan joined as Vice-Chancellor of Aliah University in West Bengal on deputation from IIT Guwahati. I am forwarding his thesis as a Co-supervisor entitled "*Copper Oxide Nanoparticles Assisted Synthesis of 1,4-Triazole Based New Organic Molecules And Facile Access to N-Heterocycles Using Multicomponent Reactions*" for submission for the Ph. D. (Science) Degree of this Institute. I also certify that he has fulfilled all the requirements according to the rules of this Institute regarding the investigations embodied in his thesis and this work has not been submitted elsewhere for a degree.

IIT Guwahati
October 16, 2015

Prof. B. K. Patel
(Thesis Co-Supervisor)

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At last but not least, I thank God for being there for me in a way no one else can.

Prasanta Ray Bagdi

Contents of the Thesis

Part A

GENERAL REMARKS

The present investigations were carried out at the Department of Chemistry, Indian Institute of Technology Guwahati, Guwahati -781 039, Assam during the period from 23rd July, 2010 to 16th October, 2015 as a Ph.D. student under the supervision of Prof. Abu T. Khan.

The analytical samples were routinely dried *in vacuo* at 50 °C. In TLC experiments, silica gel G (SRL) or silica gel GF 254 (SRL) was employed as adsorbent were used. Column chromatography was carried out with silica gel (60-120 mesh, Merck, SRL or Qualigen), for purifications of reaction mixture. After purification, the solvent was usually removed in rotavapor using Büchi R-114V instrument. Melting points were determined on a Büchi melting point apparatus. IR spectra were recorded on Perkin-Elmer 281 IR spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on Varian 400 MHz, Bruker 600 MHz and Varian 100 MHz, Bruker 150 MHz spectrometer TMS as internal reference; chemical shifts (δ scale) are reported in parts per million (ppm). ^{1}H NMR Spectra are reported in the order: multiplicity, no of protons and coupling constant (*J* value) in hertz (Hz); signals were characterized as s (singlet), d (doublet), t (triplet), m (multiplet), br s (broad singlet), dq (doublet of quartet), dt (doublet of triplet) and ddt (doublet of doublet of triplet). HRMS spectra were recorded using ESI (TOF) mode. Elemental analyses were carried out using Perkin-Elmer 2400 Series II CHNS/O analyzer at the Department of Chemistry, Indian Institute of Technology, Guwahati. FESEM image were recorded on Field Emission Scanning Electron Microscope. Crystal data were collected with Bruker Smart Apex-II CCD diffractometer using graphite monochromated MoKα radiation (λ = 0.71073 Å) at 296 K.

ABBREVIATIONS

Ac	acetyl
Ac_2O	acetic anhydride
AcOH	acetic acid
BDMS	bromodimethylsulfonium bromide
BINAP	2,2'-Bis(diphenylphosphino)-1,1'-binaphthyl
BINOL	1,1'-Bi-2-naphthol
Bn	benzyl
Boc	*tert*-butoxycarbonyl
Bu	butyl
^{t}Bu	*tert*-Butyl
Bz	benzoyl
CAN	ceric ammonium nitrate
CCDC	cambridge crystallographic data centre
COSY	correlation spectroscopy
CSA	Camphorsulfonic acid
DCE	1,2-Dichloroethene
DCM	dichloromethane
DDQ	2,3-Dichloro-5,6-Dicyanobenzoquinone
DHF	2,3-dihydrofuran
DHP	3,4-dihydropyran
DMF	*N*,*N*-dimethylformamide
DMSO	dimethylsulfoxide
Et	ethyl
Et_3N	triethyl amine
g	gram
h	hour
HRMS	High-resolution Mass Spectrometry
IR	infrared
MCR	Multicomponent reaction

M.p	melting point
MS	molecular sieves
MW	microwave
NaOAs	Sodium ascorbate
NaN_3	Sodium azide
NMR	nuclear magnetic resonance
ORTEP	oak ridge thermal ellipsoid program
PCC	pyridinium Chlorochromate
Ph	phenyl
Pr	propyl
i-Pr	isopropyl
ppm	parts per million
Py	pyridine
p-TSA	*p*-toluenesulfonic acid
rt	room temperature
TBAB	Tetrabutylammonium bromide
TBATB	Tetrabutylammonium tribromide
TFA	Trifluoroacetic acid
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	trimethylsilyl
TfOH	Triflic acid
Tf_2O	Triflic anhydride
t-BHP	tert-Butyl hydroperoxide
w	weight
XRD	x-ray diffraction

Part A

Chapter I

General Introduction of CuAAC Click Reaction, 1,4-Triazoles and Imidazo[1,2-α]pyridines

Review

1.1 Introduction

'Click Chemistry' is a concept introduced by K. Barry Sharpless[1] in 2001 that describes chemistry which mimics nature to generate substances quickly and reliably. It enables a modular synthetic approach towards the assembly of new molecular entities utilizing a collection of reliable chemical reactions. The most straightforward amongst them is the Cu(I) catalyzed Huisgen 1,3-dipolar cycloaddition[2] reaction of azides and alkynes which proceeds easily under mild reaction conditions as shown in Figure 1. This simple and efficient process is termed as CuAAC (Copper-Catalyzed variant of Huisgen Azide Alkyne Cycloaddition) click reaction, which is one of the most popular and widely used reactions. The characteristics of Click Chemistry are high functional group tolerance, work in aqueous conditions, regiospecific, single reaction trajectory, high efficiency, simple product isolation, high yields and shorter reaction time.

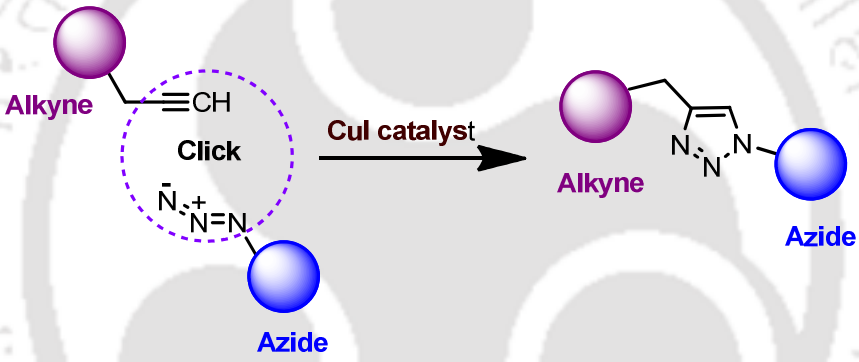


Figure 1. CuAAC Click Reaction

An extensive literature survey shows that Click reaction can be classified into four different categories. These are (i) cycloadditions, (ii) nucleophilic ring-opening reactions, (iii) addition to carbon-carbon multiple bonds and (iv) carbonyl chemistry of the non-aldol type which are represented in Figure 2. Among the four major classifications, cycloaddition reactions, particularly the Cu(I)-catalyzed Huisgen 1,3-dipolar cycloaddition reaction of azides and terminal alkynes that leads to the formation of 1,2,3-triazoles are most extensively studied. The design and synthesis of pharmacologically relevant triazole based new organic molecules by combinatorial techniques have proven to be a promising strategy for new pharmaceutical lead molecules. It has been found that, CuAAC reaction plays an important role in various fields such as pharmaceutical sciences, polymer sciences, modification of peptide or protein, combinatorial organic synthesis, chemo enzymatic functionalization, materials sciences and surface chemistry. In addition, CuAAC reactions are used for the synthesis of natural

products, macromolecules and multivalent carbohydrate vaccines.[3] It has emerged as one of the most powerful tools in chemical biology, drug discovery and proteomic applications.[4]

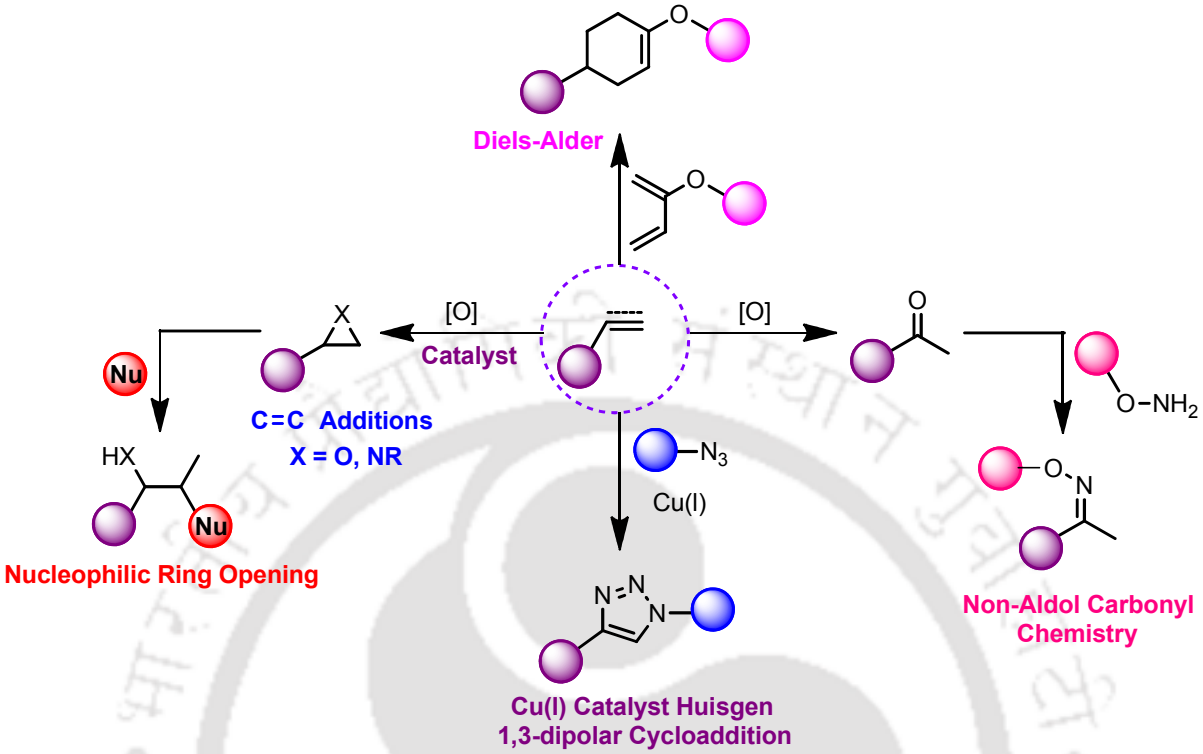


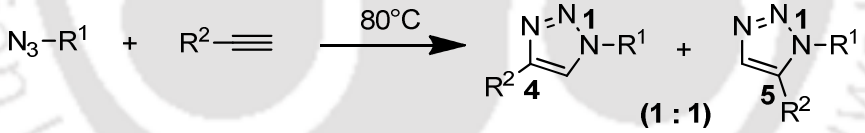
Figure 2

For CuAAC reaction, there exist numerous methods for the generation of the active catalyst. The most common of them is the reduction of Cu(II) salts i.e. $CuSO_4 \cdot 5H_2O$ *in situ* to form Cu(I) species using various reducing agents such as sodium ascorbate, hydrazine and tris(2-carboxyethyl)phosphine.[5] It has been found that *in situ* generated Cu(I) catalyst gives better results in terms of yield and reaction time as compared to Cu(I) salts such as CuI, CuCl, CuBr and $CuOTf \cdot C_6H_6$.[5a] Recently, there are reports which shows that the transitions metal salts such as $PtCl_2$, $PdCl_2$ and $NiCl_2$ may also act as a catalyst for Click reaction.[5c] In addition, pentamethyl cyclopentadienyl ruthenium (II) complexes (Cp*Ru) such as Cp*RuCl $(PPh_3)_2$, Cp*Ru(COD) and Cp*$[RuC_{l4}]$ have recently emerged as novel catalysts for Click Chemistry.[6] It has been found that Cp*Ru complexes afford selectively 1,5-substituted 1,2,3-triazoles as compared to all previously reported catalysts. In this context, as well as in continuation of our research objective to develop newer synthetic methodologies we envisaged the use of copper oxide nanoparticles as an efficient catalyst for the synthesis of traizole based new organic molecules involving Click Chemistry.

Nanoparticles are the colloidal particles ranging in the size from 1 to 1000 nm. Nanotechnology has emerged as 'Greener Technology' and it might resolve the challenging problem in environmental science. The use of nanocatalyst provides better selectivity and recyclability and moreover, they are eco-friendly. Transition metal based nanoparticle is found to be an efficient heterogeneous catalyst with distinct active sites[7] and creates its own space in the field of environment protection to overcome the problems of homogeneous catalysis. However, a considerable research effort has been devoted to develop transition metal based nanoparticle catalyst in organic synthesis.[8] The employment of heterogeneous copper oxide nanoparticles catalyst serves as an attractive candidate for the synthesis of new triazole based molecules that leads to the recovery as well as recyclability of the catalyst without any substantial loss of activity. From an industrial standpoint, these reactions are eye-catching since it brings down the cost and environmental impact of the process (E-factor). Thus, it is evident that the development of new methodology using Click Chemistry is an immense importance in synthetic organic chemistry.

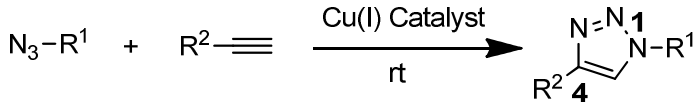
1.2 History and Synthetic Utility of CuAAC Reactions

In 1961, Huisgen *et al.* first reported[2a] the 1,3-dipolar cycloaddition reaction of azides and alkynes to afford a mixture of 1,4 and 1,5-substituted triazoles (1 : 1). The azide-alkyne Huisgen cycloaddition forms the backbone of CuAAC reaction as shown in Scheme 1.



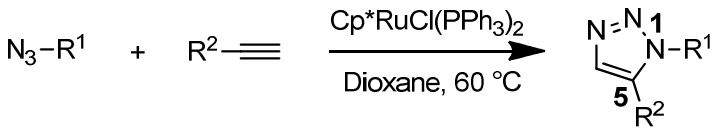
Scheme 1. Azide-Alkyne Huisgen cycloaddition Reaction

In 2002, Sharpless and Medal modified[5a,b] the Huisgen azide-alkyne cycloaddition reaction using Cu(I) catalyst to generate selectively 1,4-substituted triazole as shown in Scheme 2. Although the Cu(I) catalyzed modification gave rise to a 1,4-substituted triazole from a terminal alkyne and an azide, this reaction is not a 1,3-dipolar cycloaddition, it is better called as Copper(I)-catalyzed Azide-Alkyne Cycloaddition (CuAAC) or click reaction rather than Azide-Alkyne Huisgen cycloaddition Reaction.



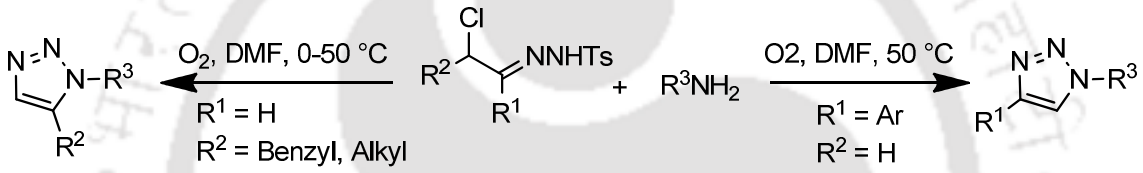
Scheme 2. CuAAC Reaction

Recently, Boren and his coworker[9] modified the Huisgen azide-alkyne cycloaddition reaction using Ru(II) catalyst to obtained selectively 1,5-substituted triazole. This reaction is often termed as Ruthenium-Catalyzed Azide-Alkyne Cycloaddition (RuAAC) reaction as shown in Scheme 3.



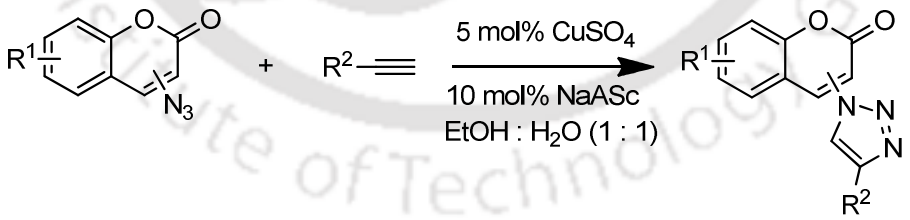
Scheme 3. RuAAC Reaction

Very recently, Ji and his coworker[10] demonstrated metal free and azide free, a novel synthetic approach for the synthesis of 1,5-disubstituted 1,2,3-triazoles and 1,4-disubstituted 1,2,3-triazoles by aerobic oxidative cycloaddition of α-chlorotosylhydrazone with primary aryl amine as shown in Scheme 4.



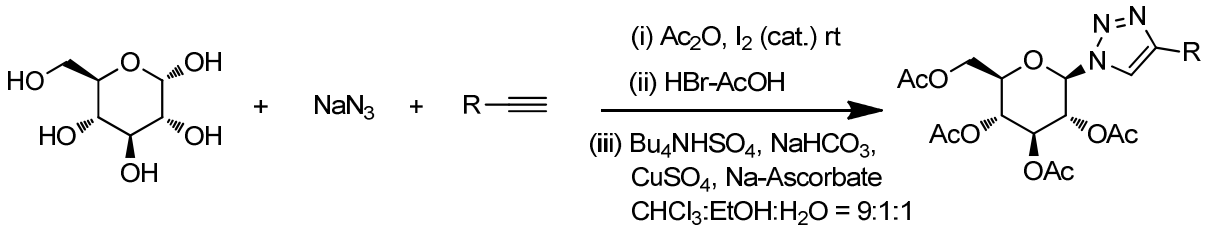
Scheme 4

Wang *et al.* reported[11] the synthesis of fluorescent coumarin dyes using copper(I)-catalyzed 1,3-dipolar cycloaddition reaction of nonfluorescent 3-azidocoumarins and terminal alkynes as shown in Scheme 5. This method is used to generate fluorescent DNA probes in the molecular biology.



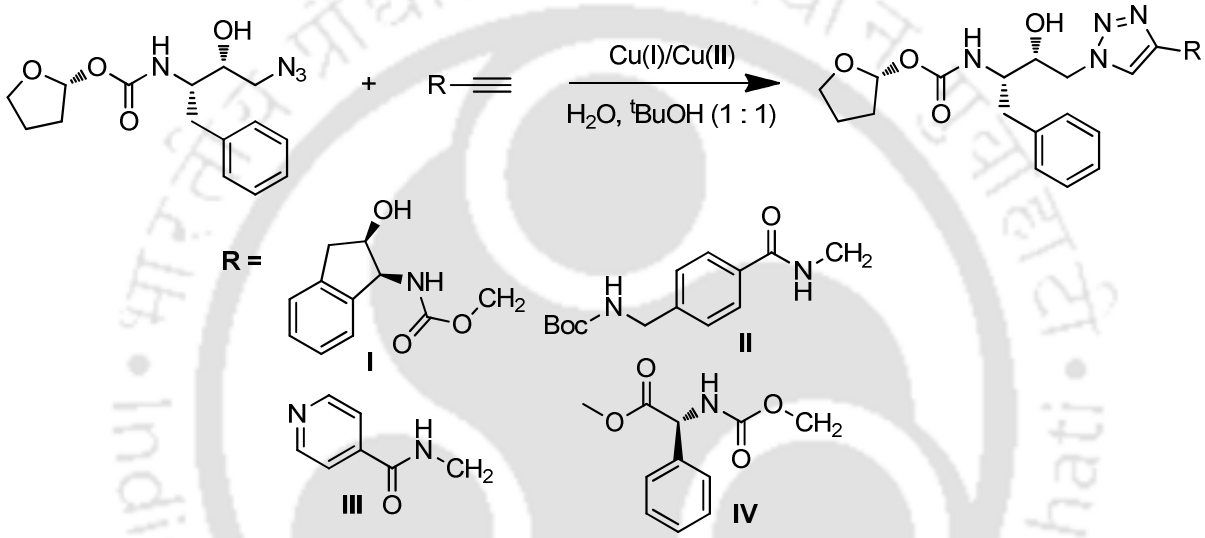
Scheme 5

Wang *et al*. have also demonstrated[12] an efficient one pot Huisgen azide-alkyne cycloaddition reaction for the synthesis of 1,4-substituted triazole linked glycoconjugates in the presence of *in situ* Cu(I) catalyst. This is one of the simplest strategies to prepare neoglycoconjugate derivatives from unprotected saccharides or per acetylated saccharides as shown in Scheme 6.



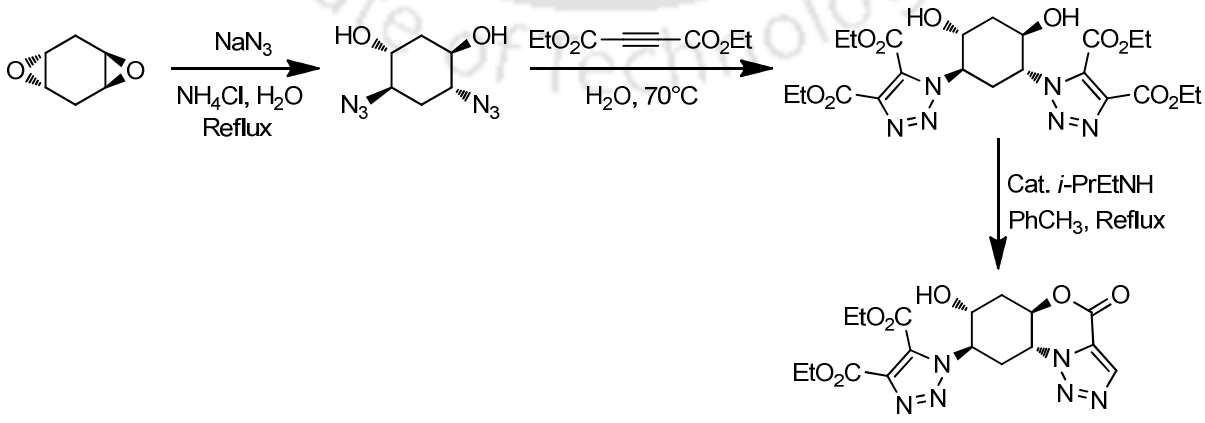
Scheme 6

Recently, Wong and his coworker[13] have utilized click chemistry for the synthesis of various biological inhibitors such as HIV protease, V82F, G48V and V82A from azide and terminal alkynes (I, II, III and IV) as shown in Scheme 7.



Scheme 7

Sharpless and coworkers have also demonstrated[1] an efficient method for the construction of steroid natural product through a one pot nucleophilic ring opening and 1,3-dipolar cycloaddition click reactions from diepoxides as shown in Scheme 8.



Scheme 8

The above literature highlights the importance of triazole based organic molecules in click chemistry. These are one of the most valuable building blocks for the synthesis of various pharmaceutical and natural products. Therefore, the development of click reactions is a great challenge in synthetic organic chemistry. Due to innumerable application of click reaction, we were interested to explore the novel method of preparation of triazole base new organic molecules. In this part of my thesis is aimed towards copper oxide nanoparticles assisted synthesis of triazole based new organic molecules. Therefore, I would like to address their importance as well as some recently developed synthetic methods as below.

1.3 1,4-triazoles and its importance

1,4-Disubstituted triazoles are important small organic molecules having numerous applications in industry, namely as dyestuffs, fluorescent whiteners, photo-stabilizers of corrosion inhibitors, polymers, optical brightening agents and as photographic photoreceptors.[14] Many of the 1,4-triazole derivatives finds extensive application in the field of material science, polymer chemistry, agrochemicals, biochemicals and the pharmaceutical sciences.[15] Triazole and its analogues are important class of pharmacophores, which are present in many pharmaceutical products. In particular, 1,4-disubstituted triazoles have been used as metal binding compounds, ligand linkers, and triazole-based monophosphine ligands.[16] The triazole unit is challenging to enzymatic degradation, hydrolysis and oxidation for the construction of biologically active molecules. The 1,4-substituted triazole scaffold containing organic molecules possess wide spectrum of biological activities such as antibacterial,[17] antitubercular,[18] anticancer,[19] antimicrobial,[20] analgesic,[21] antiallergic,[22] anti-inflammatory,[23] antioxidant,[24] antiviral,[25] anthelmintic antitumor and hypoglycaemic activities.[26] Some of the biologically active triazole based organic molecules are displayed in Figure 3. 1,4-Triazole derivatives are also associated with a wide range of biological properties such as magnetic resonance imaging and biomolecular sensors.[27] It has been found that, 1,4-triazole links has emerged as a popular bridging units in carbohydrate chemistry.[28] Furthermore, 1,4-triazoles has potential applications in bioconjugation and bioimaging in the field of molecular biology.[11] In addition, complex molecules having triazole unit act as cell imaging, glycosidase inhibitor, HIV protease inhibitor, and protein coupled receptors.[29]

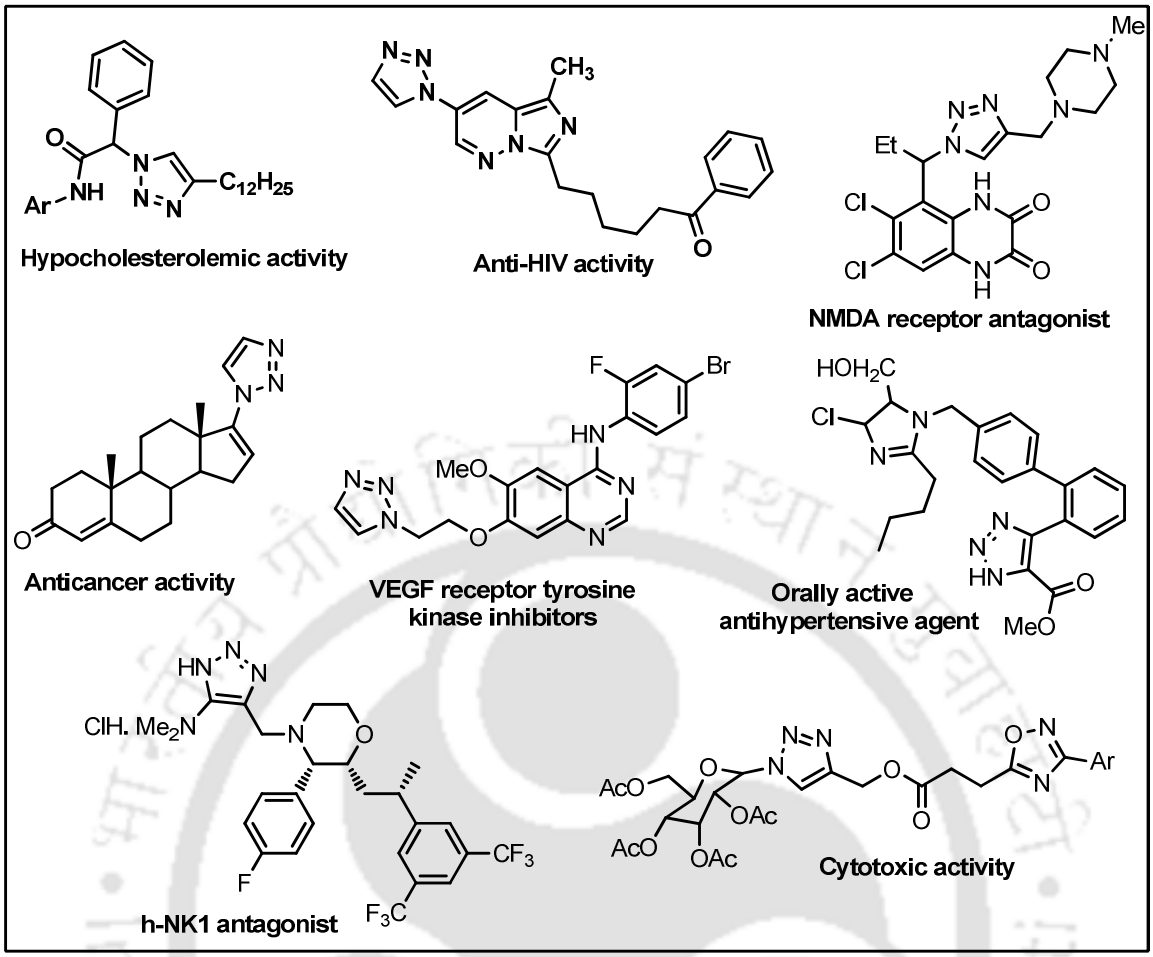
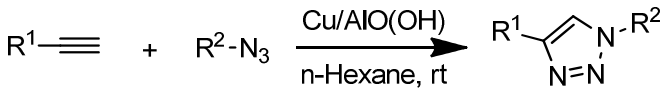


Figure 3

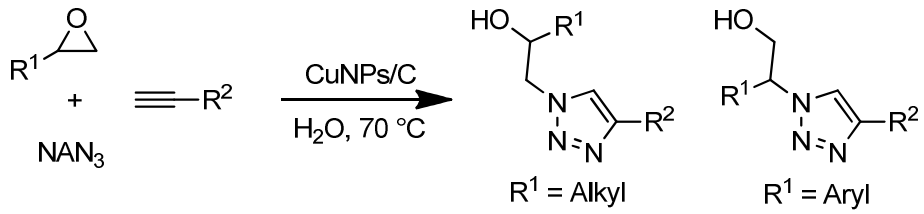
1.3a Synthetic methodology of 1,4-triazole derivatives

For the synthesis of 1,4-triazoles, most methods involves the employment of either the copper salts or different metal nanoparticles as a catalysts. In recent times, metal nanoparticle catalysts have been used in various organic transformations due to their high reactivity as well as recyclability of the catalyst. Therefore, the development of metal nanoparticles catalyzed click reaction finds its own way in the field of synthetic organic chemistry. Park *et al.* developed[30] a new copper-catalyzed azide-alkyne cycloaddition (CuAAC) reaction which involved immobilizing copper nanoparticles in aluminum oxyhydoxide fiber. The catalyst showed high catalytic activity for the synthesis of 1,4-triazoles from alkynes and various azides at room temperature as shown in Scheme 9.



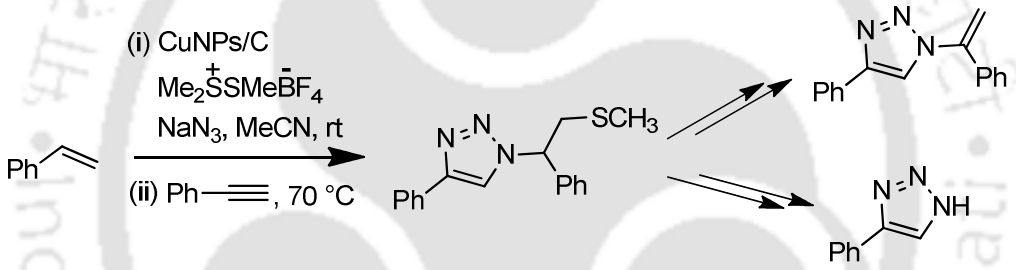
Scheme 9

Recently, Alonso and his coworker demonstrated[31] that copper nanoparticles on activated carbon acts as an efficient catalyst for the synthesis of β-hydroxy-1,2,3-triazoles from a variety of epoxides and alkynes in water as shown in Scheme 10.



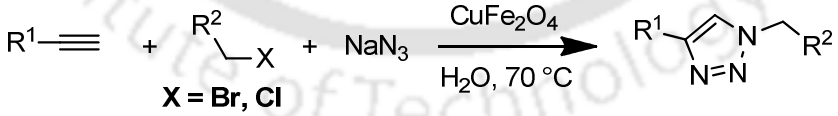
Scheme 10

Recently, Alonso and his coworker demonstrated[32] a one-pot method for the synthesis of 1,2,3-triazoles concerning two click reactions of inactivated alkenes: firstly, the azidosulfenylation reaction of the carbon-carbon double bond followed by the copper-catalyzed azide-alkyne cycloaddition (CuAAC) as shown in Scheme 11.



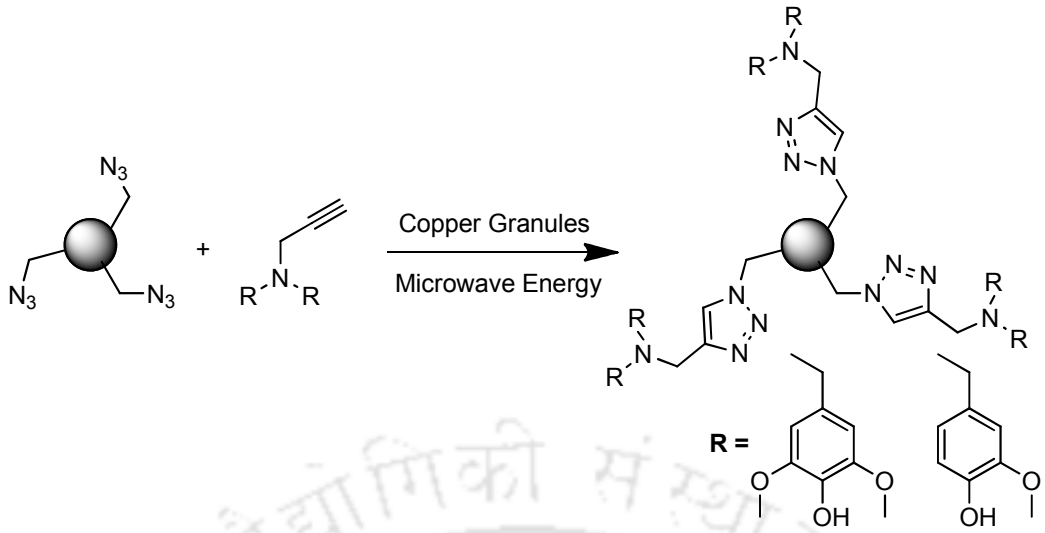
Scheme 11

Nageswar *et al.* reported[33] that magnetically separable $CuFe_2O_4$ nanoparticles catalyzed Huisgen azide-alkyne cycloaddition reaction for the synthesis of 1,4-disubstituted 1,2,3-triazoles from alkyl halides and terminal alkynes at 70 °C as shown in Scheme 12.



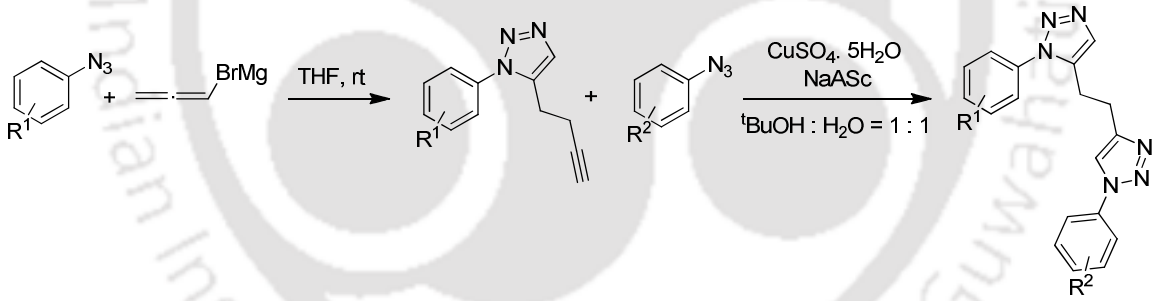
Scheme 12

Recently, Lee and his coworker developed[34] the microwave-assisted alkyne-azide 1,3-dipolar cycloaddition for the synthesis of syringaldehyde and vanillin based antioxidant dendrimers using copper granules as a catalyst as shown in Scheme 13.



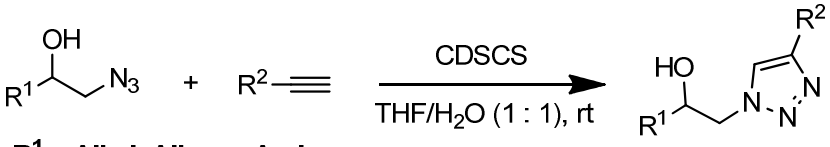
Scheme 13

In recent times, Banday and his coworker reported[35] the synthesis of unsymmetrical bis-1,2,3-triazoles involving copper-catalyzed azide-alkyne cycloaddition (CuAAC) reaction of aryl azides with allenylmagnesium bromide as shown in Scheme 14. These unsymmetrical bis-triazoles show antimicrobial activities against fungal strains and a panel of bacterial which leads to the emergence of bis-triazoles as potent antimicrobials.



Scheme 14

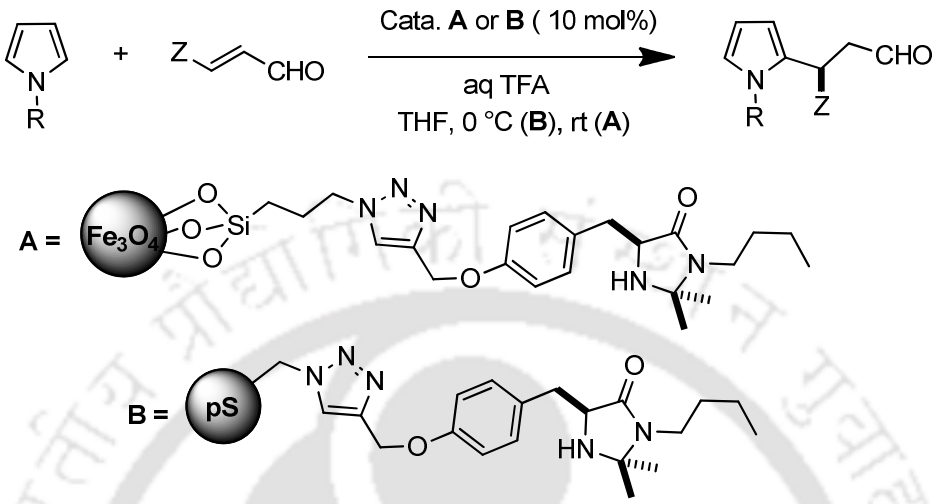
Recently, Rad *et al.*[36] demonstrated the use of copper-doped silica cuprous sulfate (CDSCS) as a highly efficient and new heterogeneous nano catalyst for Huisgen azide-alkyne cycloaddition reaction of organic azides with terminal alkynes to afford 1,4-triazoles as shown in Scheme 15.



R^1 = Alkyl, Alkoxy, Aryloxy
R^2 = $ArOCH_2$, Ph, $(Me)_2COH$

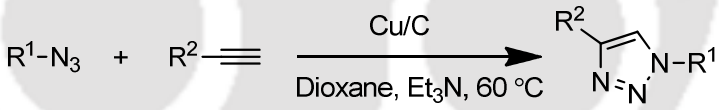
Scheme 15

Pericas *et al.*[37] recently, demonstrated the synthesis of first generation MacMillan catalyst through copper-catalyzed azide-alkyne cycloaddition (CuAAC) reaction. This catalyst is utilized in the Friedel Crafts alkylation reaction of N-substituted pyrroles with α, β-unsaturated aldehydes as shown in Scheme 16.



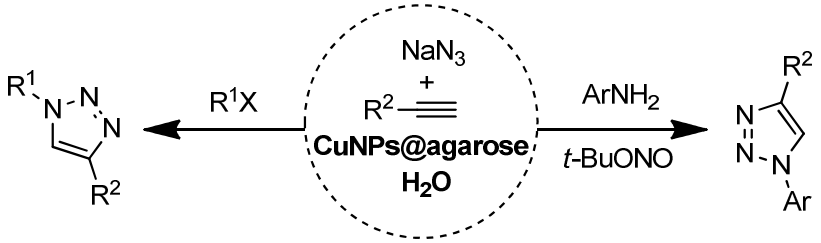
Scheme 16

Very recently, Buckley *et al.* outlined[38] the synthesis of 1,4-triazoles from organic azides and terminal alkynes at 60 °C using copper-in-charcoal as a heterogeneous catalyst as shown in Scheme 17.



Scheme 17

Very recently, Gholinejad and his coworker[39] promulgated agarose-supported copper nanoparticles (CuNPs@agarose) catalyzed Huisgen azide-alkyne cycloaddition reaction of benzyl halides with sodium azides and alkynes as well as arenediazonium salts with sodium azides and alkynes resulting in 1,4-triazoles as shown in Scheme 18.



Scheme 18

Over the years, various methods has been developed for the synthesis of 1,4-substituted 1,2,3-triazole based organic molecules involving copper-catalyzed azide-alkyne cycloaddition (CuAAC) reactions using a variety of copper catalysts such as CuI,[40] $CuSO_4$ along with different reducing agents,[41] polymeric imidazole-Cu(II),[42] Cu/SiO_2,[43] $CuBr(PPh_3)_3$,[44] polymer capped Cu/Cu_2O,[45] Cu(I)-modified zeolites[46] and various Cu-nanoparticles.[47] However, the above methods suffer from the several drawbacks such as harsh reaction conditions, need of expensive and usage of excess amount of catalyst and longer reaction time. Eventually, it creates a space for the development of a new methodology which might work better in terms of yield, reaction condition and substrate scope compatibility.

1.4 Imidazo[1,2-*a*]pyridines and its importance

Imidazo[1,2-*a*]pyridine a fused aza-heterocyclic compound,[48] is an important class of pharmacophore, has been widely exploited in manufacturing many synthetic pharmaceutical products. Molecules possessing imidazo[1,2-*a*]pyridine skeletons shows diverse biological activities such as antibacterial,[49] antiviral,[50] anti-inflammatory,[51] antihepatitis C,[52] anticonvulsant,[53] antipyretic,[54] antiulcer,[55] antianxiety,[56] hypnotic, cardiotonicagent,[57] and anticancer.[58] It is famed for its unique role in bioscience such as calcium channel blockers,[59] bradykinin B2 receptor antagonists,[60] cyclin-dependent kinase inhibitors[61] and amyloidinhibitors.[62] Further, it also act as dopamine D4 receptor agonists,[63] angiotensin II antagonists[64] and $5HT_3$ antagonists.[65] In addition, imidazo[1,2-*a*]pyridine also constitutes the core construction of several drugs. The most common drugs containing imidazo[1,2-*a*]pyridine scaffold are Olprinone, used for the treatment of heart failure,[66] Zolpidem used for the treatment of insomnia,[67] Zolimidine acts as an antiulcer agent[55] whereas Alpidem acts as an anxiolytic agent[68] etc, some of them are shown in Figure 4. Imidazo[1,2-*a*]pyridine also display an interesting application in material science.[69] In addition to that, imidazo[1,2-*a*]pyridines are widely used as microglial cell visualization and as probe for benzodiazepine receptors.[70]

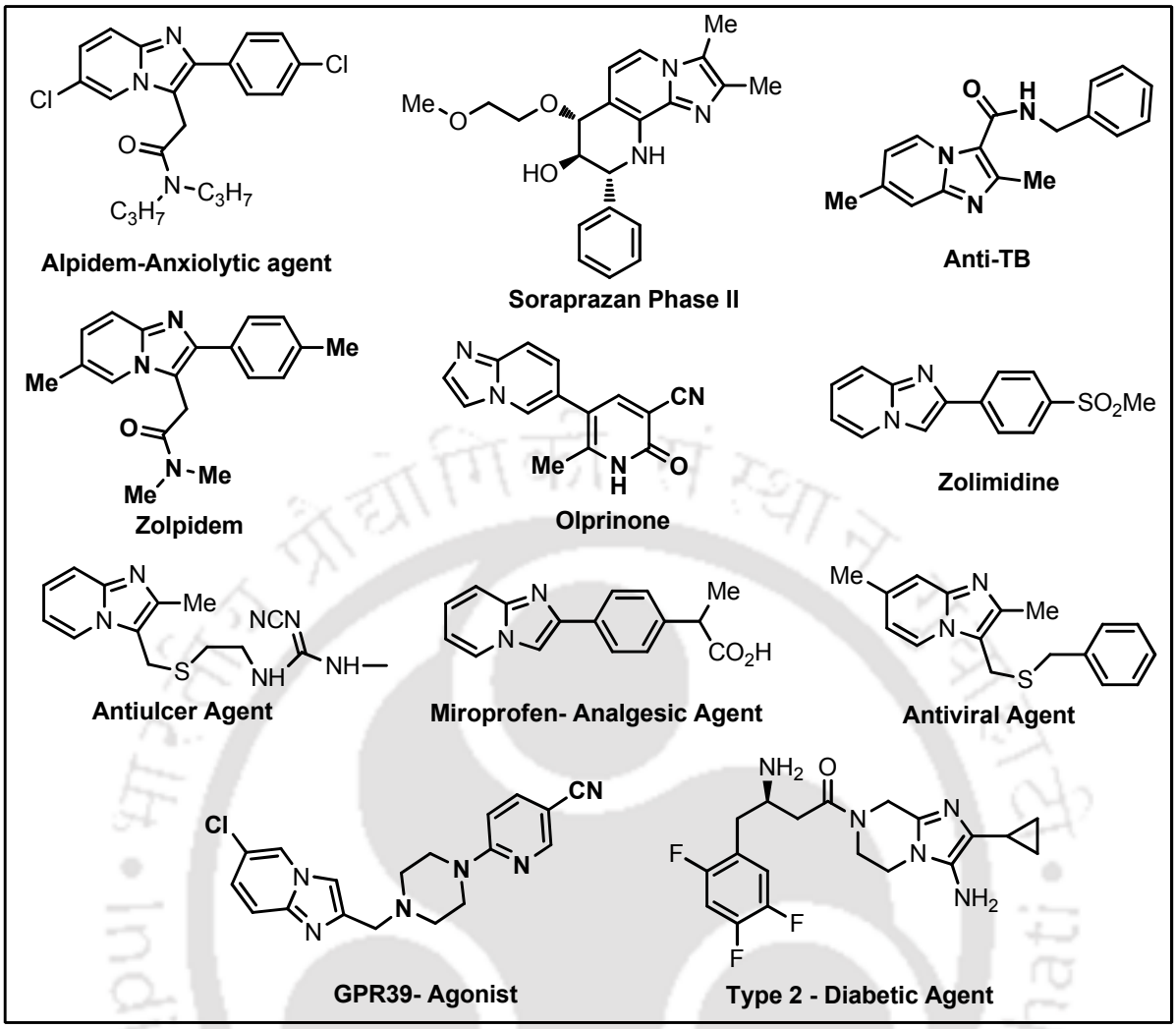
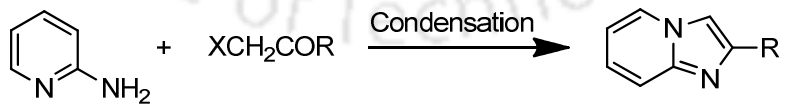


Figure 4

1.4a Synthetic utility of Imidazo[1,2-*α*]pyridines

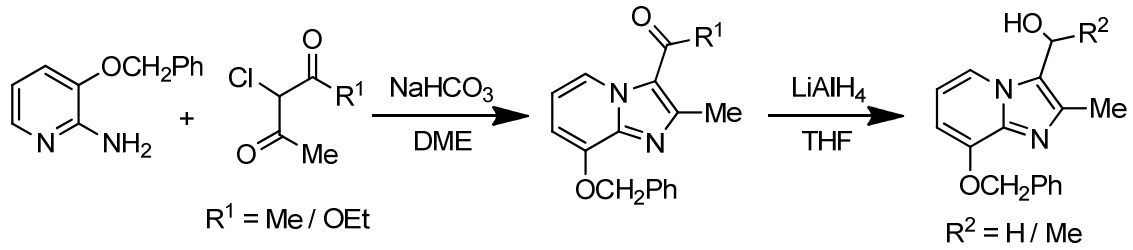
Fisher *et al.* demonstrated[71] a conventional methods for the synthesis of imidazo[1,2-a]pyridine derivatives by the condensation reaction of a-haloketones with 2-aminopyridines as shown in Scheme 19.



Scheme 19

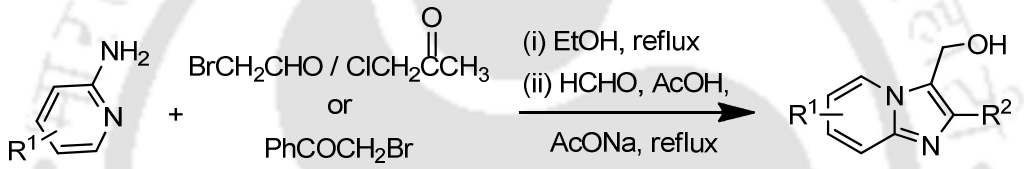
Starrett *et al.*[72] reported the condensation of 2-aminopyridines and α-chloro-1,3-dicarbonyl compound in the presence of sodium bicarbonate in DME solvent under refluxing conditions for the synthesis of C-3 carbonyl imidazo[1,2-*a*]pyridine derivatives. The obtained product on reduction with lithium aluminium hydride in THF afforded hydroxyl alkyl imidazo[1,2-

a]pyridine derivatives is shown in Scheme 20. Further, it was converted to functionalized primary amine derivative at C-3 position which acts as effective antiulcer agents.



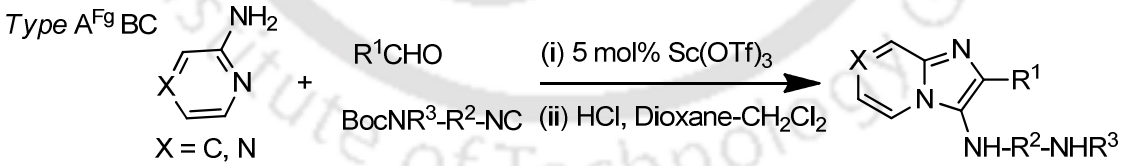
Scheme 20

Gueiffier *et al.*[73] outlined the direct synthesis of hydroxyl methylated imidazo[1,2-*a*]pyridine derivatives through one pot condensation reaction of 2-aminopyridines with α-halo-(acetaldehyde/acetone)/phenacyl bromide in ethanol under reflux condition, followed by reaction of formaldehyde and sodium acetate in acetic acid as shown in Scheme 21.



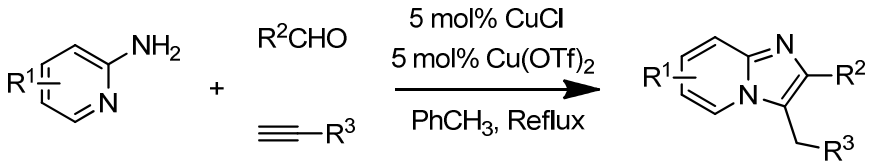
Scheme 21

Kercher *et al.*[74] reported a drug like library of A^{FG}BC type imidazo[1,2-*a*]pyridines by using amidines, aldehydes and Boc protected isocyanides in the presence of catalytic amount of scandium triflate. In the next step, deprotection of Boc in acidic condition afforded amino substituted imidazo[1,2-*a*]pyridines which is displayed in Scheme 22.



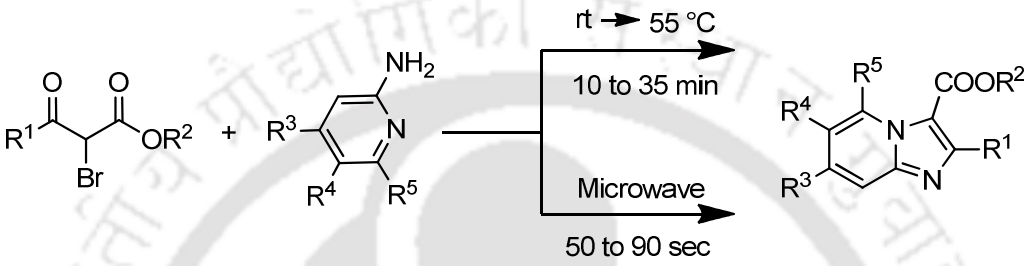
Scheme 22

Recently, Gevorgyan and his coworker[75] demonstrated one pot three-component coupling reaction for the synthesis of imidazo[1,2-*a*]pyridines by employing aldehydes, amidines and terminal alkynes in the presence of catalytic amount of CuCl and $Cu(OTf)_2$ in toluene under refluxing condition (Scheme 23). This method was utilized for the direct synthesis of Alpidem and Zolpidem drugs.



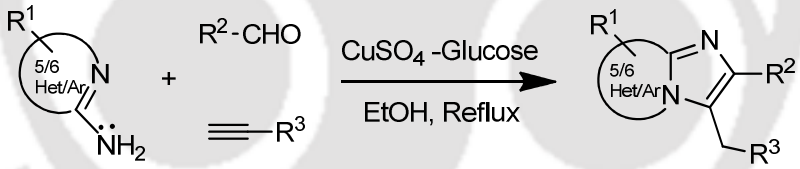
Scheme 23

Adimurthy and his coworker[76] established a solvent-free synthesis of highly substituted imidazo[1,2-*a*]pyridines through thermal and microwave irradiated method using α-bromo-β-keto esters and amino pyridines in a short reaction time as shown in Scheme 24.



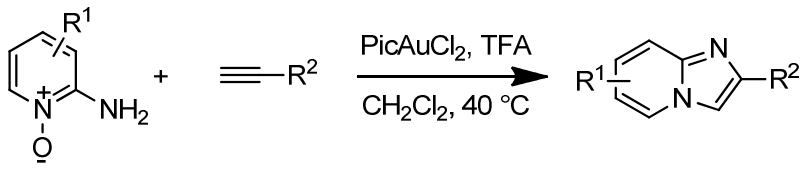
Scheme 24

Recently, Guchhait *et al.* reported[77] that, $CuSO_4$-glucose catalyzed three-component cascade reaction of A^3-coupling reaction of heterocyclic amidines with aldehydes and alkynes in ethanol under refluxing condition leads to imidazo[1,2-*a*]pyridines as shown in Scheme 25.



Scheme 25

Recently, Toste and his coworker[78] developed gold-catalyzed redox synthesis of Imidazo-[1,2-*a*]pyridines using pyridine N-oxide and alkynes with trifluoroacetic acid in dichloromethane at 40 °C as shown in Scheme 26.



Scheme 26

An extensive literature survey reveals that there are other various methods reported for the synthesis of Imidazo-[1,2-*a*]pyridines using different catalysts such as MNP@BiimCu,[79] $CuSO_4$/*p*-TsOH,[80] Cu-MnO,[81] Cu-MOFs,[82a] CuI/$NaHSO_4$-SiO_2,[82b] CuI/$Cu(OTf)_2$,[83] Fe_3O_4/NaHSO4–SiO_2,[84] and $InBr_3$/Et_3N.[85] However, these strategies are associated with certain limitations such as the use of expensive microwave equipment, requirement of expensive catalysts, involvement of longer reaction time and harsh reaction conditions. Although, these methods are quite useful but still chemists are on hot pursuit to look for alternatives that employs milder reaction conditions with high stereoselectivity.

From literature, it is worth mentioning that 1,4-triazole based organic molecules possess enormous potential for the synthesis of numerous natural product as well as pharmaceutical products. This facts always leaves the door open for the development of new and efficient catalytic methods for the synthesis of 1,4-triazole based new organic molecules in eco-friendly manner with good yields. Thus, the thesis work is designed to employ copper oxide nanoparticles as an efficient catalyst for the synthesis of 1,4-triazole based new orgnanic molecules i. e. triazolyl-allenyl-anthracenes, triazolyl-anthrones and 2-triazolyl-imidazo[1,2-*a*]pyridines which will be discussed in the successive chapters (Part A) of this thesis.

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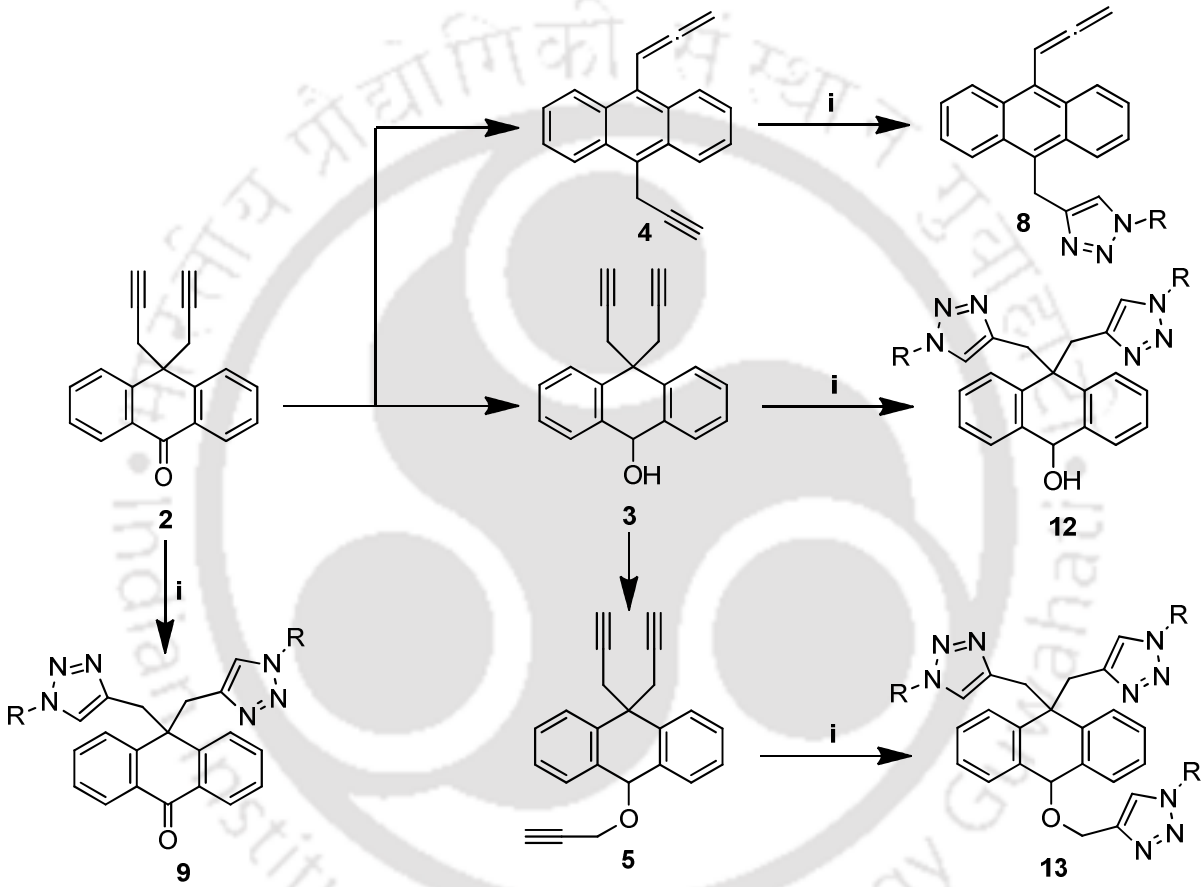
Chapter IIA

Copper oxide nanoparticle mediated 'Click Chemistry' for the synthesis of mono-, bis- and tris-triazole derivatives from 10,10-dipropargyl-9-anthrone as a key building block

Results and Discussion

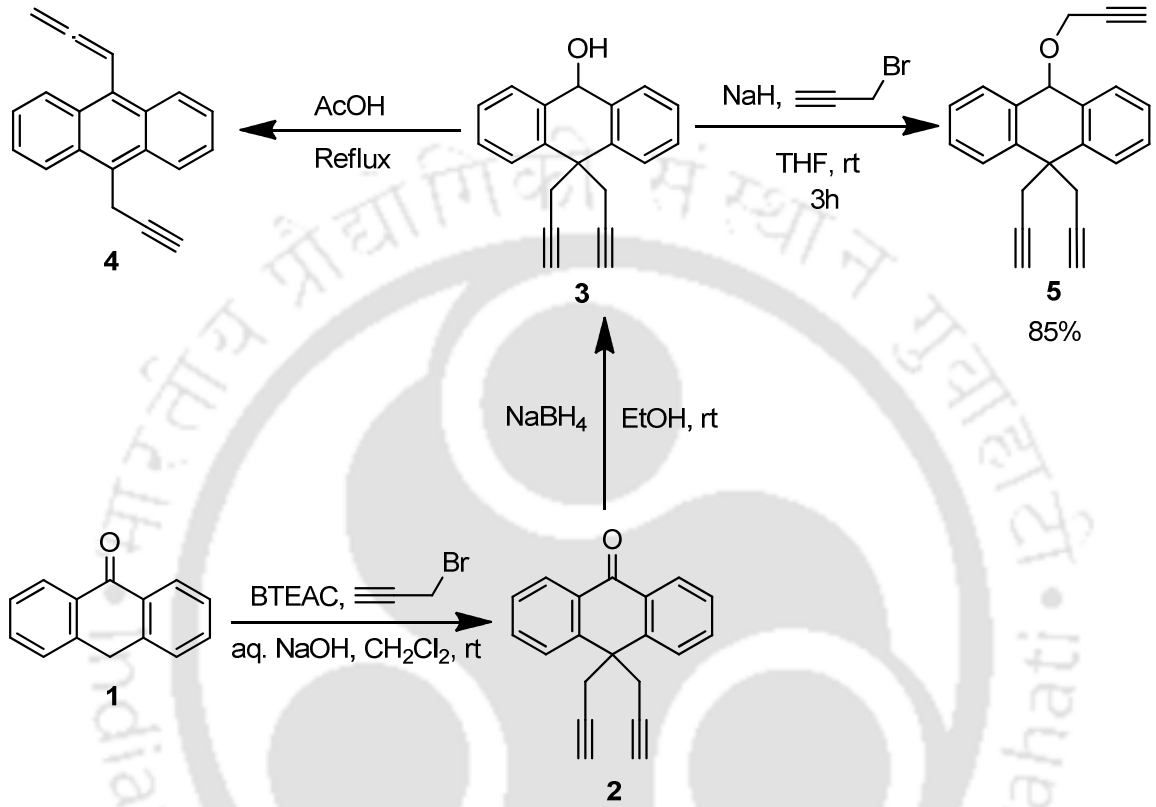
The importance of 1,4-triazole based organic molecules and the various methods of their synthesis have been discussed in Chapter 1. In this Chapter, we report the synthesis of mono-, bis- and tris- 1,4-triazole based new organic molecules by utilizing 10,10-dipropargyl-9-anthrone as well as other derivatives obtained from it, alkyl/benzyl bromides and sodium azide in the presence of 10 mol% of copper oxide nanoparticle along with 20 mol% sodium ascorbate in water as shown in Scheme 27.



Scheme 27. *Synthesis of mono-, bis- and tris-triazole derivatives, Reagents & condition: (i) RBr (1 mmol), NaN_3 (1 mmol), nano particle CuO (0.10 mmol), sodium ascorbate (0.20 mmol), water, 70 ^oC.*

For the present study, the catalyst copper oxide nano particle was purchased from Sigma-Aldrich. The key starting material, 10,10-diprop-2-ynylanthrone (**2**), was prepared by following literature procedure developed by Majumdar and co-workers[86] using phase-transfer catalyzed alkylation of anthrone (**1**) with propargyl bromide. Then **2** was converted into 9-allenyl-10-prop-2-ynyl-anthracene (**4**) in two steps, i.e. reduction with sodium borohydride in ethanol followed by [3,4] sigmatropic rearrangement in acetic acid. Subsequently, 10,10-

diprop-2-ynyl-9-(prop-2-yn-1-oxy)-9,10-dihydroanthracene (**5**) was obtained in 85 % yield from the reduced product **3** by deprotonation with sodium hydride followed by alkylation with propargyl bromide in THF at room temperature. The outline for the preparation of various building blocks essential for the synthesis of mono-, bis- and tris- triazole derivatives is shown in Scheme 28.



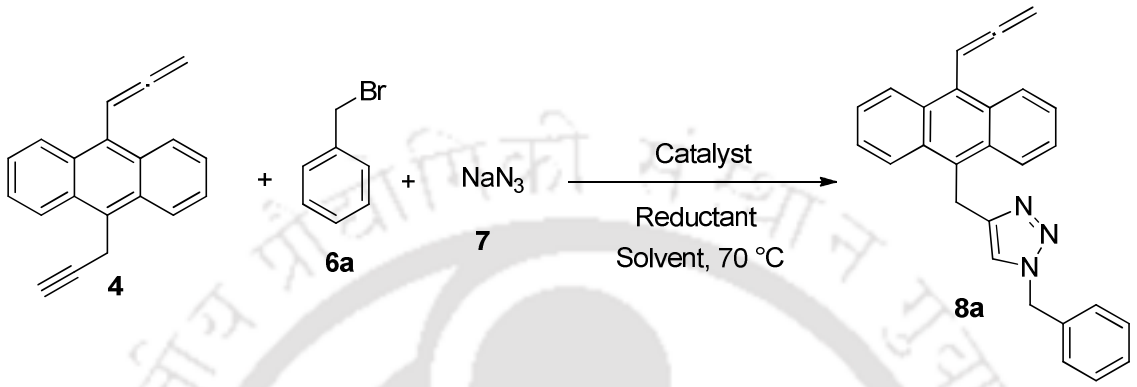
Scheme 28. *Synthesis of 10,10-diprop-2-ynylanthrone (**2**), 10,10-diprop-2-ynylanthran-9-ol (**3**), 9-allenyl-10-prop-2-ynyl-anthracene (**4**), and 10,10-diprop-2-ynyl-9-(prop-2-yn-1-oxy)-9,10-dihydroanthracene (**5**)*

At the outset, we have chosen 9-allenyl-10-prop-2-ynyl-anthracene (**4**), benzyl bromide (**6a**) and sodium azide (**7**) as the model substrates to find out the optimized reaction conditions for the synthesis of mono-1,2,3-triazole derivative (**8a**) and the successful results are summarized in Table 1. Moreover, the isolated product **8a** was characterized from ^{1}H and ^{13}C NMR spectra and elemental analysis. It gives the characteristic peaks at δ 6.66 as a singlet for H-5 in ^{1}H NMR spectrum and the requisite signal at δ 121.9 ppm for C-5 of triazole moiety in ^{13}C NMR spectrum, respectively.

It is worthy to mention that allene moiety remained unaffected during experimental conditions, which was confirmed from ^{1}H and ^{13}C NMR spectra. It was observed that 10 mol% of copper oxide nanoparticle along with 20 mol% sodium ascorbate in water at 70 ^{0}C

provided the best result in terms of reaction time and yield. The yield of mono-1,2,3-triazole derivative (**8a**) was reduced on increasing the catalyst load (Table 1, entry 11). In addition, using copper oxide nanoparticle in the absence of sodium ascorbate resulted in a much lower yield of the product **8a** (Table 1, entry 6).

Table 1. Optimization of the reaction conditions[a]



S.No	Catalyst	Reductant (20 mol%)	Solvent	Time (h)	Yield (%)[b]
01	10 mol% $CuSO_4 \cdot 5H_2O$	NaOAs	H_2O/PEG	2	72
02	10 mol% $CuSO_4 \cdot 5H_2O$	NaOAs	H_2O	6	55
03	10 mol% $CuSO_4 \cdot 5H_2O$	NaOAs	EtOH	3	60
04	10 mol% $CuSO_4 \cdot 5H_2O$	D-Glucose	H_2O/PEG	2.5	50
05	10 mol% $Cu(OAc)_2 \cdot 2H_2O$	NaOAs	H_2O/PEG	3.5	62
06	10 mol% CuONPs	-	H_2O	8	06
07	05 mol% CuONPs	NaOAs	H_2O	1.5	82
08	10 mol% CuONPs	NaOAs	EtOH	2	70
09	10 mol% CuONPs	D-Glucose	H_2O	3.5	55
10	10 mol% CuONPs	NaOAs	H_2O	0.5	90
11	15 mol% CuONPs	NaOAs	H_2O	2.5	85

[a]*The reactions were performed in 1 mmol scale using 9-allenyl 10-prop-2-ynyl-anthracene (**4**), benzyl bromide (**6a**), and sodium azide (**7**).* [b]*Isolated yield.*

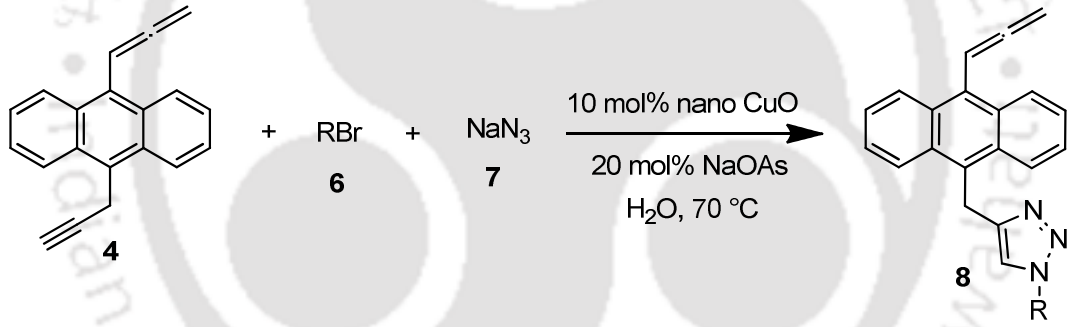
Moreover, various reactions were also screened using different Cu^{2+} ion source such as $CuSO_4.5H_2O$, $Cu(OAc)_2$ along with other reductant such as D-glucose and sodium ascorbate, which provided lower yield of the desired product **8a**. It was observed that water is the most

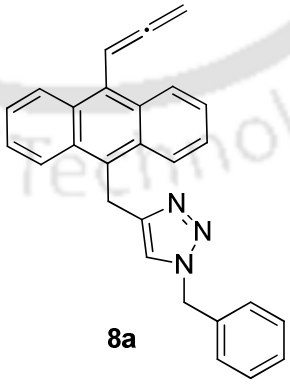
suitable solvent as compared to ethanol or a 1:1 mixture of polyethylene glycol and water as shown in Table 1.

After optimizing the reaction conditions, the scope of the reactions were conducted with 9-allenyl-10-prop-2-ynyl-anthracene (**4**), benzyl bromides (**6b** and **6c**) having electron-withdrawing (-NO_2) and electron-donating group (-OMe) substituent in the aromatic ring and sodium azide (**7**), respectively following identical reaction conditions. The desired products **8b** and **8c** were isolated in 87% and 85% yield (Table 2, entry 2 & 3).

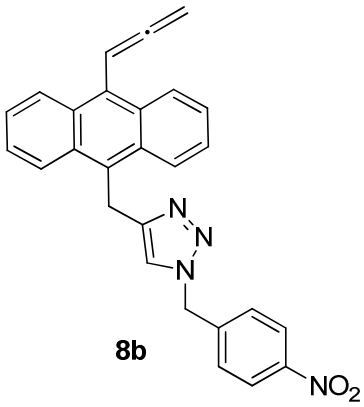
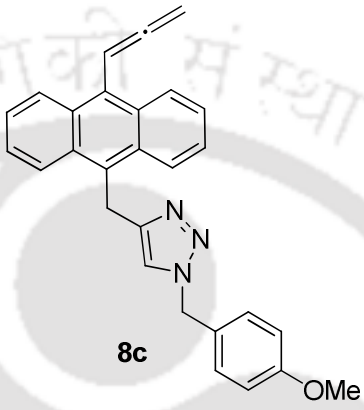
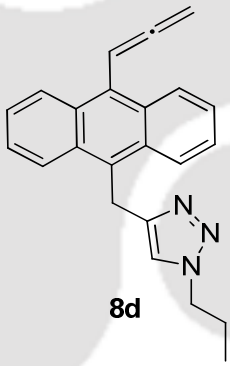
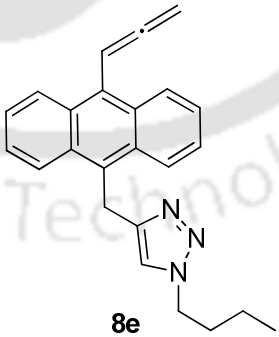
Encouraged by these results, the reactions were scrutinized with different aliphatic bromides such as n-propyl bromide (**6d**), n-butyl bromide (**6e**), sec-butyl bromide (**6f**), n-hexyl bromide (**6g**), with 9-allenyl-10-prop-2-ynyl-anthracene (**4**) and sodium azide (**7**) under identical reaction conditions and the expected products **8d-g** were obtained in good yields (Table 2, entries 4-7).

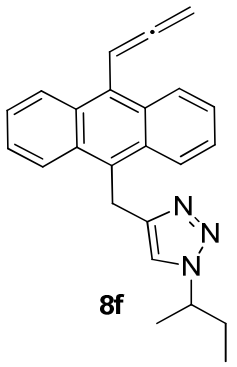
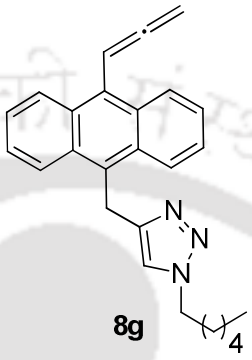
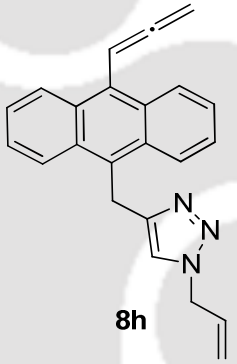
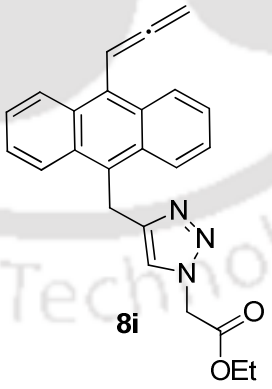
Table 2. Synthesis of mono-1,2,3-triazole derivatives (**8**) using CuO nanoparticle with sodium ascorbate as catalyst[a]

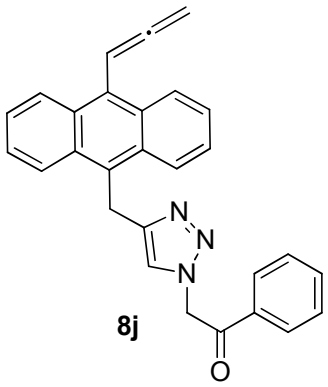


Entry	R (**6**)	Product (**8**)	Time (h)	% Yield[b]
1	Benzyl (**6a**)		0.5	90

8a

2	4-Nitrobenzyl (**6b**)	 **8b**	0.75	87
3	4-Methoxybenzyl (**6c**)	 **8c**	0.75	85
4	*n*-Propyl (**6d**)	 **8d**	1	76
5	*n*-Butyl (**6e**)	 **8e**	1	76

6	*Sec*-Butyl (**6f**)	 **8f**	1	80
7	*n*-Hexyl (**6g**)	 **8g**	1	76
8	Allyl (**6h**)	 **8h**	0.75	82
9	Ethoxycarbonylmethyl (**6i**)	 **8i**	1	78

10	Phenacyl (**6j**)	 **8j**	1	78

*[a]The reactions were performed in 1 mmol scale using 9-allenyl-10-prop-2-ynyl-anthracene (**4**), organic bromides (**6**), and sodium azide (**7**). [b]Isolated yield.*

The generality of this reaction was further examined using different functionalized aliphatic bromides such as allyl bromide (**6h**), ethyl bromoacetate (**6i**), phenacyl bromide (**6j**) using same amount of catalyst under identical reaction conditions and the required products **8h-j** were isolated in 78-82% yield (Table 2, entries 8-10). All of these products were fully characterized by ^{1}H & ^{13}C NMR spectra and elemental analyses.

Moreover, the structure of mono-1,2,3-triazole derivative **8b** was determined from single crystal X-ray crystallographic data (Figure 5A). The compound **8b** was crystallized from acetonitrile in monoclinic space group P21/n and its unit cell contains four molecules of **8b**.

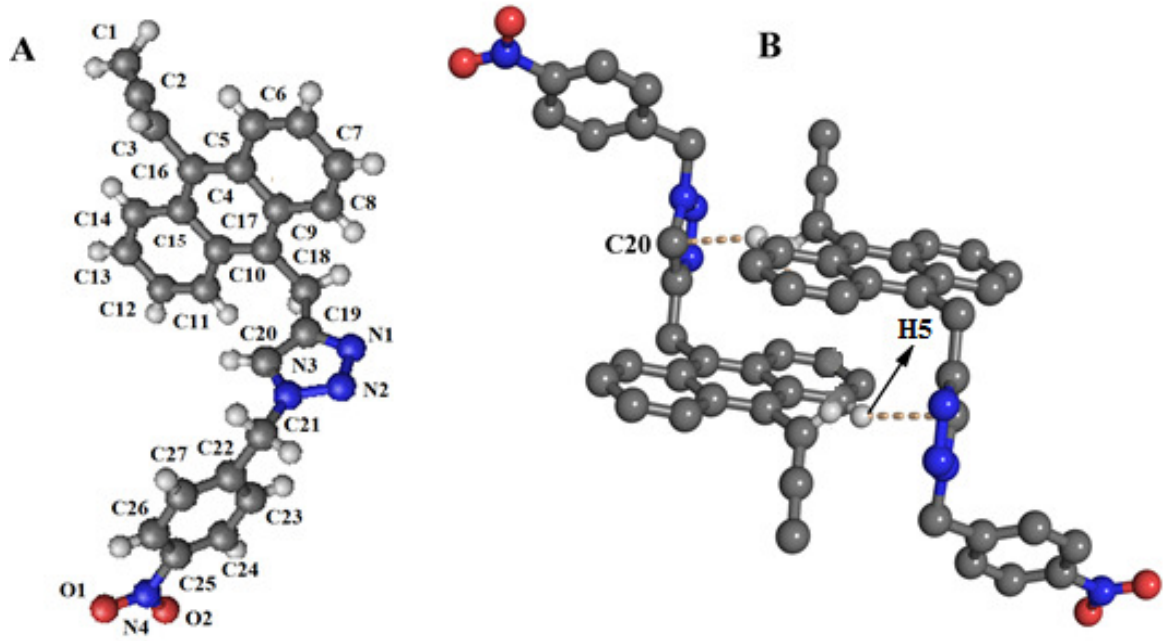


Figure 5. Single crystal X-ray structure of **8b** (A). Dimer formed by C–H···π interaction (B). Some hydrogen's are omitted for clarity

The molecule has electron rich anthracene ring and electron deficient nitro-benzene ring.

Investigation of the crystal structure reveals that it forms a dimer with C–H···π interactions involving H5 of anthracene ring and C20 of triazole ring (Figure 5B). It is reported in the literature that aromatic interactions are intermolecular forces and it offers a great potentiality in drug design, structural biology and asymmetric catalysis.

Crystal engineering *via* manipulation of hydrogen bonding has attracted much interest recently. Weak C–H···π,[87] π-stacking[88] and C–H···O interactions[89] have been found to generate different crystal engineering motifs. It was found that in solid state the nitro-benzene ring of one molecule undergoes π–π interaction (C10-C24) with anthracene ring of another molecule. In addition to this, the CH_2 group adjacent to nitro-benzene ring is involved in C–H···π interaction (C21-H21B···C5 of anthracene ring and C1-H1A···N1 of tetrazole ring). The combination of these π–π and C–H···π interactions allow the molecule to undergo extended assembly forming a *zig-zag* supramolecular structure (Figure 6B). These interactions also help to stabilize the dimers (Figure 5B) generating a very interesting supramolecular assembly in solid state (Figure 6A).

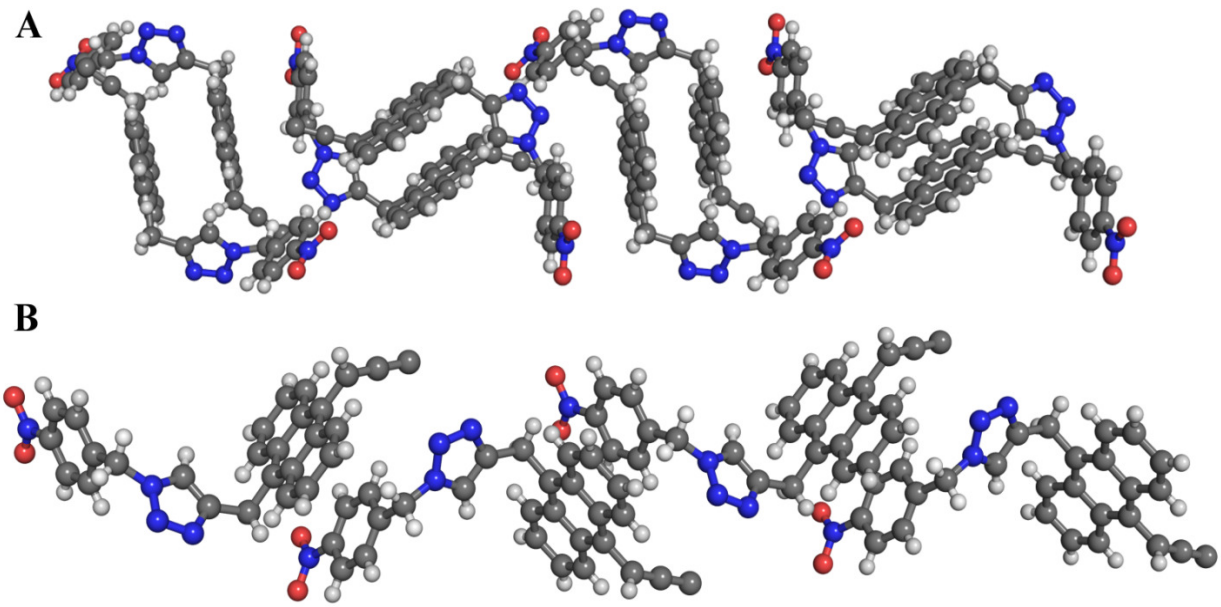


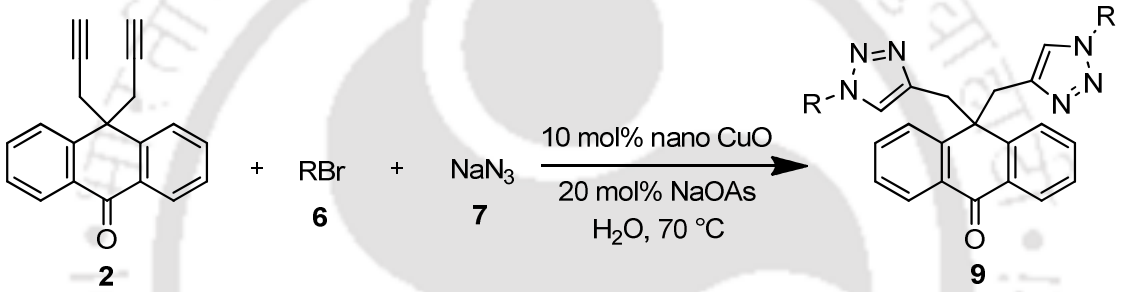
Figure 6. Supramolecular arrangement of **8b** in solid state

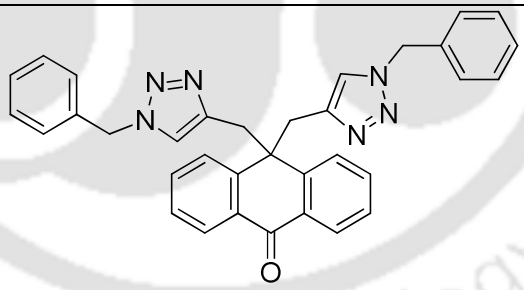
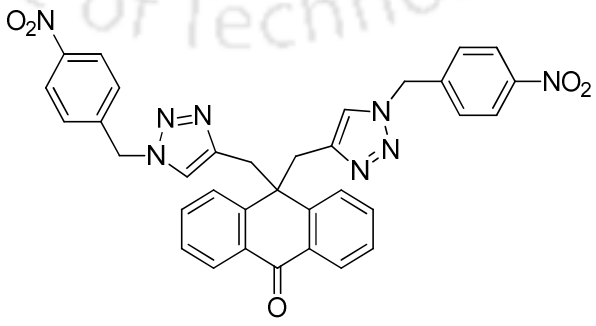
After accomplishing the synthesis mono-1,2,3-triazole derivatives (**8**), we planned to synthesize bis-1,2,3-triazole derivatives (**9**) from 10,10-dipropargyl-9-anthrone (**2**). The scope of the present protocol was examined with 10,10-dipropargyl-9-anthrone (**2**), different benzyl bromides (**6**) containing electron-withdrawing and electron-donating group on the aromatic ring and sodium azide (**7**) using 10 mol% of copper oxide nanoparticle along with 20 mol% sodium ascorbate in water at 70 ^{o}C. The desired products **9a-f** was obtained in 82-

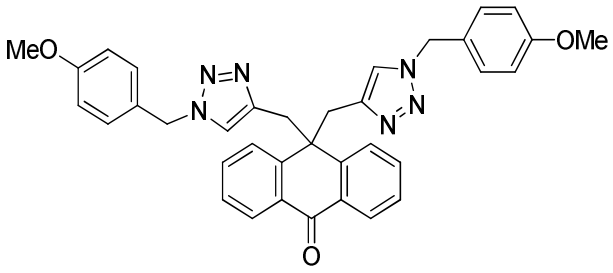
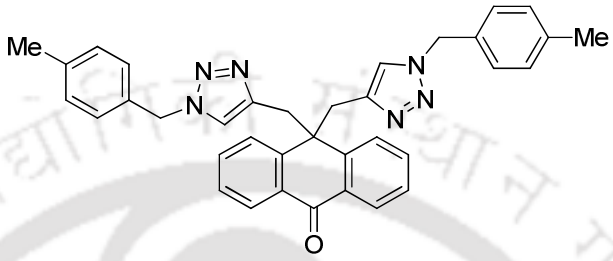
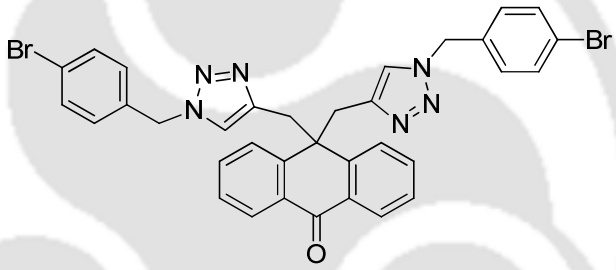
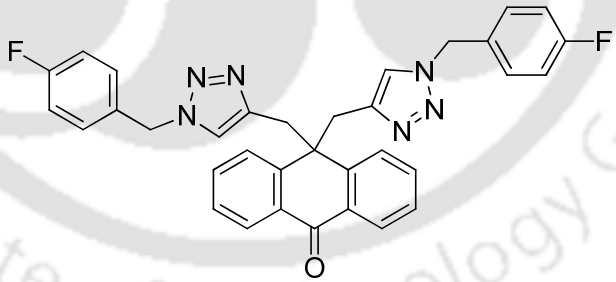
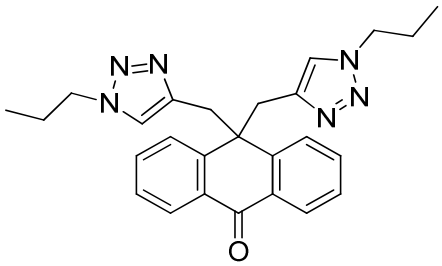
88% yields (Table 3, entries 1-6).

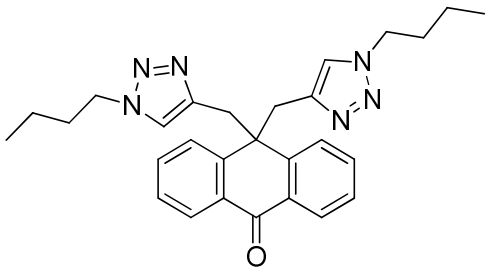
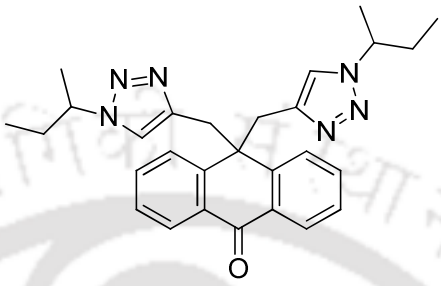
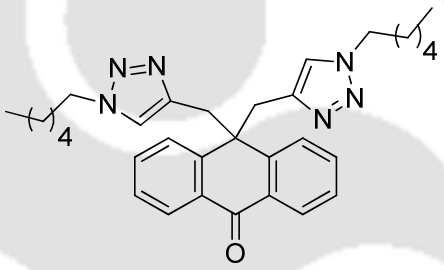
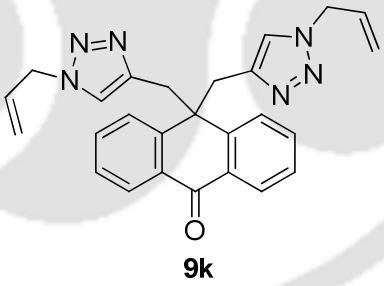
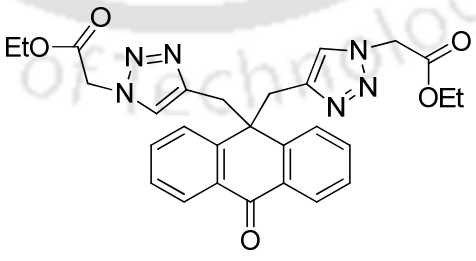
The present protocol was further executed with different aliphatic bromides such as *n*-propyl bromide (**6d**), *n*-butyl bromide (**6e**), s*ec*-butyl bromide (**6f**), and *n*-hexyl bromide (**6g**). Using these bromides, 10,10-dipropargyl-9-anthrone (**2**) and sodium azide (**7**), bis-1,2,3-triazole derivatives **9g-j** were obtained in good yields (Table 3, entries 7-10) by following similar reaction conditions. Likewise, bis-1,2,3-triazole derivatives **9k** and **9l** were synthesized from allyl bromide and ethyl bromoacetate (Table 3, entry 11 & 12). All these bis-1,2,3-triazole derivatives were fully characterized from ^{1}H & ^{13}C NMR spectra and elemental analyses.

Table 3. CuO nanoparticle with sodium ascorbate catalyzed synthesis of bis-1,2,3-triazole derivatives (**9**)[a]



Entry	R (**6**)	Product (**9**)	Time (h)	Yield (%)[b]
1	Benzyl (**6a**)	 **9a**	1	88
2	4-Nitrobenzyl (**6b**)	 **9b**	1.5	85

3	4-Methoxybenzyl (**6c**)	 **9c**	1.5	82
4	4-Methybenzyl (**6k**)	 **9d**	1	88
5	4-Bromobenzyl (**6l**)	 **9e**	1	85
6	4-Fluorobenzyl (**6m**)	 **9f**	0.75	86
7	*n*-Propyl (**6d**)	 **9g**	2	75

8	*n*-Butyl (**6e**)	 **9h**	2	75
9	*Sec*-Butyl (**6f**)	 **9i**	2	78
10	*n*-Hexyl (**6g**)	 **9j**	2	75
11	Allyl (**6h**)	 **9k**	1.5	80
12	Ethoxycarbonyl-methyl (**6i**)	 **9l**	2	80

[a]*The reactions were performed in 1 mmol scale using 10,10-diprop-2-ynylanthrone (**2**), organic bromide (**6**) and sodium azide (**7**).* [b]*Isolated yield.*

Moreover, the structure of **9b** was confirmed through single x-ray crystallographic data. The compound **9b** was crystallized from ethanol/water (95:5) in monoclinic space group $P2_1/c$.

The unit cell contains four **9b** molecules and four water molecules. The crystal structure of **9b** showed that two side chains are arranged above and below the plane of anthracenone ring (Figure 7A). Closer investigation of the crystal structure showed interesting self-assembly to form a duplex through C–H···O interaction [90] (Figure 7B). The non-conventional hydrogen bonds such as C–H···O interaction has also been proposed to have a significant influence on the transition states of certain catalytic asymmetric transformations.[91] Cα–H···O hydrogen bonds may add stability in diverse structural contexts of macromolecules in which the overall structures are determined by stronger interactions.[92] Recently Smith and coworkers have elegantly shown that C–H···O interaction can override the significant *trans*-planar conformational preferences of α-fluoroamide substituents.[93]

Wong and coworkers showed C–H···O interaction play important role in stabilizing the developing oxyanion for a cinchona alkaloid based organocatalyzed reactions.[94] This emphasizes that these interactions is important contributor in determining the overall structural picture. Herein we have shown that combination of four interactions can stabilize a ball shaped supramolecular self-assembled duplex in the solid state (Figure 7B). The O5 oxygen of **9bI** form C–H···O contact with H5 of **9bII** molecule. Moreover, the O3 oxygen of nitro group **9bI** forms intermolecular short contact with the C30 of **9bII** molecule. Two other identical contacts were seen from the nitro groups of **9bII** to **9bI**.

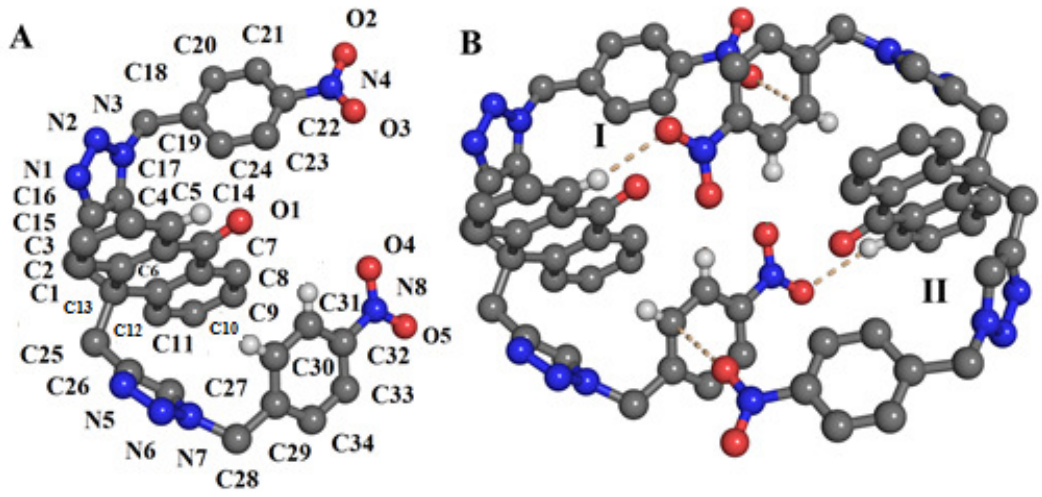


Figure 7. Crystal structure of **9b** (A) and self-assembly of **9b** through C–H···O interaction (B). For easier assignments the two **9b** molecules involved in duplex formation are labeled as **I** and **II**. Some hydrogen's are omitted for clarity

Further investigation of the crystal structure of **9b** revealed the presence of water molecules embedded in the crystal lattice. A detailed analysis revealed highly interesting features

(Figure 8). One of the triazole nitrogen N1 from the duplex forms short contact with the hydrogen atom of one water molecule. The same water molecule forms one C–H···Ow contact with the H3 of the anthracenone ring of another duplex. The oxygen of this water molecule is involved in bifurcated forming hydrogen bond with second water molecule which in turn forms similar N···H–Ow and C–H···Ow contact. This eventually led to the formation of a complex three-dimensional non-covalently bonded network. The water molecules are held together by strong Ow–H/Ow hydrogen bonding interactions.[95]

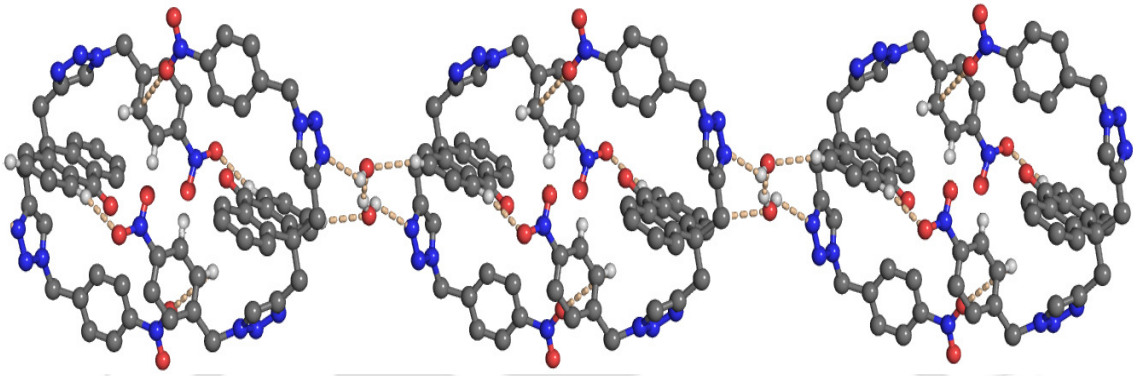


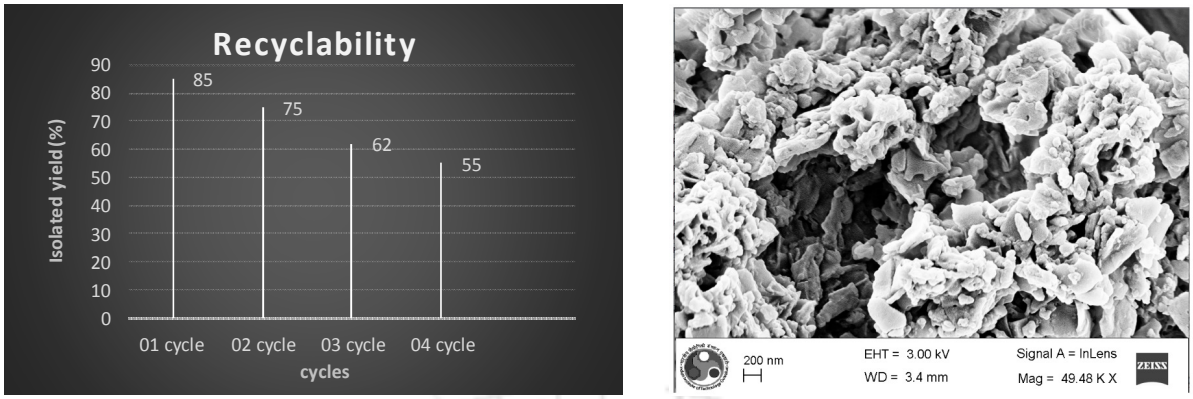
Figure 8. Crystal structure showing interaction of duplex of **9b** with water molecules

The recyclability of copper oxide nanoparticle was verified in the following way. The reactions were carried out with 4 mmol scale of 10,10-dipropargyl-9-anthrone (**2**), 4-nitrobenzyl bromide (**6b**), sodium azide (**7**) in the presence of 10 mol% of copper oxide nanoparticle along with 20 mol% sodium ascorbate in water. The yield of the product **9b** is shown (Table 4 and Figure 9A) after each cycle. Furthermore, the FESEM image of nano copper oxide catalyst after four times recycling as shown in Figure 9B.

Table 4. Recyclability of the catalyst[a] in **9b**

Entry	mmol scale	Amount of catalyst	Recovered catalyst	Time (h)	Yield (%)
01	04	32	28	1.5	85
02	3.5	28	24	2	75
03	3	24	20	2.5	62
04	2.5	20	15	3	55

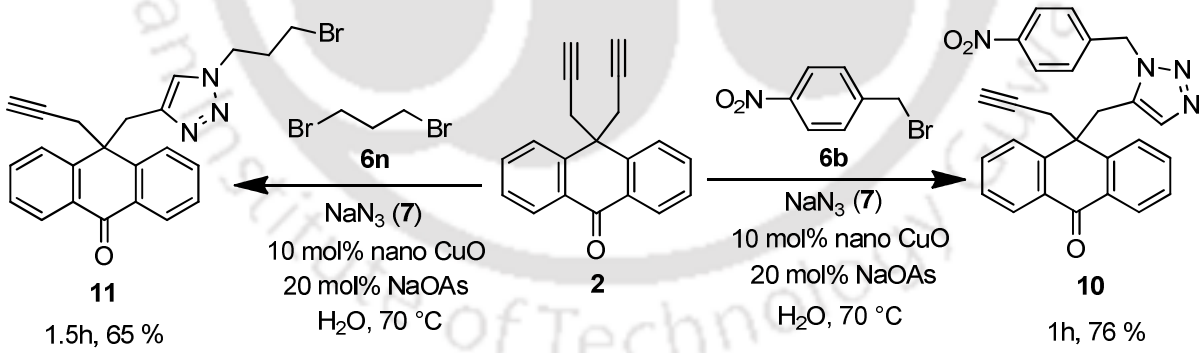
[a]*The copper oxide nanoparticle was reused as follows: it was filtered off, washed with dichloromethane and finally dried before use for next cycle.*



A **B**

Figure 9. (**A**) Recyclability of copper oxide nanoparticle of product **9b** and (**B**) FESEM image of CuO nanoparticle after four times recycling

It is noteworthy that mono-triazole derivative **10** could also be synthesized from 10,10-dipropargyl-9-anthrone (**2**) by tuning the reaction conditions using one equivalent of each starting materials. We have synthesized mono-triazole **10** in 76% yield from 10,10-dipropargyl-9-anthrone (**2**), 4-nitrobenzylbromide (**6b**) and sodium azide (**7**) by following identical reaction conditions. Likewise, on reaction with 10,10-dipropargyl-9-anthrone (**2**), 1,3-dibromopropane (**6n**) and sodium azide also provided the required mono-triazole **11** in 65% yield as shown in Scheme 29.

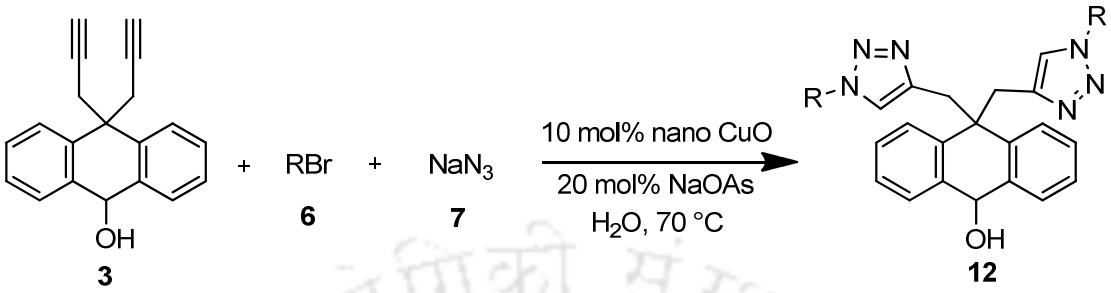


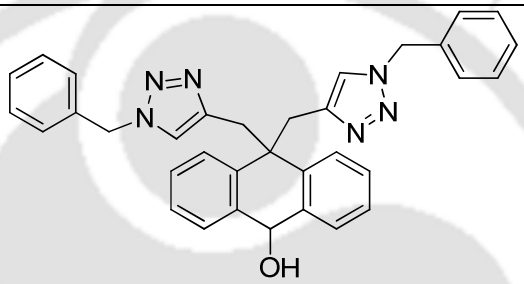
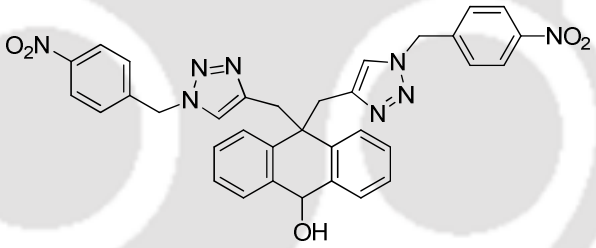
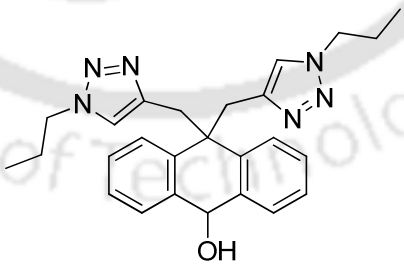
Scheme 29

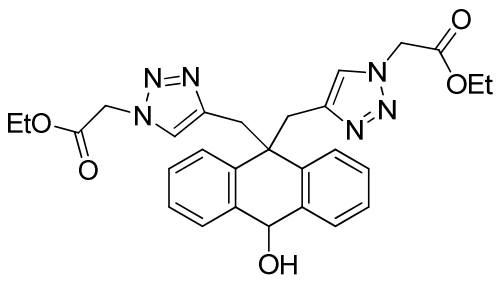
Next, we explored the possibility to synthesize the tris-triazole derivative from the bis-triazole precursor. Initially, we tried to reduce the substrate **9a** using $NaBH_4$ in ethanol. Interestingly, it takes much longer time (96 h) and also provides lower yield (65%). Therefore, 10,10-dipropargyl-9-anthrone (**2**) was reduced first to 10,10-diprop-2-ynylanthran-9-ol (**3**) using $NaBH_4$ in ethanol. Subsequently, it was explored for the synthesis of bis-1,2,3-triazole derivatives (**12**) by following similar synthetic strategy and the successful results are

given in Table 5 along their reaction time and yields. All the products were characterized using ^{1}H NMR, ^{13}C NMR spectra and elemental analyses.

Table 5. Synthesis of bis-1,2,3-triazole derivatives (**12**)[a]

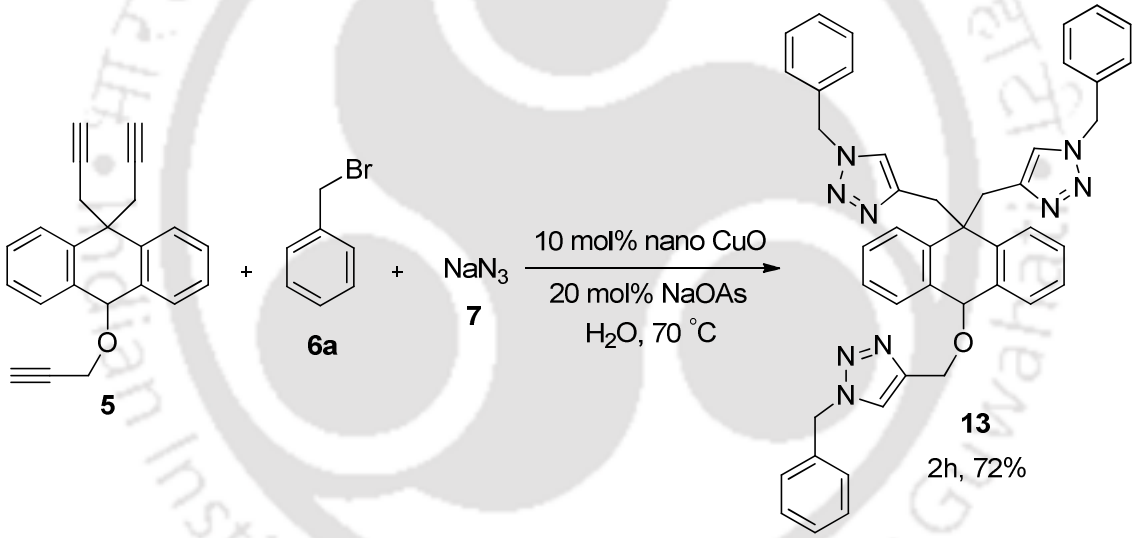


	R (**6**)	Product (**12**)	Time (h)	Yield (%)[b]
1	Benzyl (**6a**)	 **12a**	1.5	84
2	4-Nitrobenzyl (**6b**)	 **12b**	2	80
3	*n*-Propyl (**6d**)	 **12c**	2.5	72

4	Ethoxycarbonyl-methyl (**6i**)	 **12d**	2.5	78

[a]*The reactions were carried out in 1 mmol scale using 10,10-diprop-2-ynylanthran-9-ol (**3**), organic bromide (**6**), and sodium azide (**7**).* [b]*Isolated yield.*

Next, we put forward our efforts for the synthesis of tris-1,2,3-triazole derivatives from 10,10-diprop-2-ynyl-9-(prop-2-yn-1-oxy)-9,10-dihydroanthracene (**5**), benzyl bromide (**6a**) and sodium azide (**7**) using 10 mol% copper oxide nanoparticle and 20 mol% sodium ascorbate in water at 70 ^{0}C and it gave the corresponding expected product of tristriazole derivative **13** in 72% yield which is shown in Scheme 30.



Scheme 30. *Synthesis of tris-triazole **13***

In conclusion, we have developed a simple and efficient protocol for the synthesis of mono-, bis- and tris- triazole derivatives using 10 mol% of copper oxide nanoparticle, with 20 mol% sodium ascorbate in water using 10,10-dipropargyl-9-anthrone (**2**) as a primary building block. It's noteworthy to mention that allene moiety of the products **8** remain intact under the experimental conditions. The main features of the protocol are mild reaction conditions, easy reaction procedure, recyclability of the catalyst, environmentally benign and substrates scope compatibility. To the best of our knowledge, these triazole derivatives were reported first time in the literature using copper oxide nanoparticle along with sodium ascorbate as catalyst. The compound **8b** shows a combination of π–π and C–H···π interactions, which allows the

molecule to undergo extended assembly forming a *zig-zag* supramolecular architecture. We have further shown that combination of C–H···O interaction and hydrogen bonding between water molecules and bis-triazole **9b** gave rise to dazzling supramolecular architectures. It might be possible for self-assembled structure in some of the similar derivatives and their application in foldamer (conformationally constrained synthetic oligomer) synthesis.

Experimental

*General procedure for synthesis of compound **2**, **3** and 4*

The key starting materials 10,10-diprop-2-ynylanthrone (**2**), 10,10-diprop-2-ynylanthran-9-ol (**3**) and 9-allenyl-10-prop-2-ynyl-anthracene (**4**) were prepared by following earlier reported procedures.[86]

*General procedure for synthesis of 10,10-diprop-2-ynyl-9-(prop-2-yn-1-oxy)-9,10-dihydroanthracene (**5**)*

To a solution of 10,10-diprop-2-ynylanthran-9-ol (1 mmol) in THF solution was added NaH (60% purity, 100 mg, 2.5 mmol, washed with hexane). After stirring at rt for 15 min, propargyl bromide (111 µL, 1.3 mmol) was added slowly into it. After 3 h of additional stirring, the reaction mixture was quenched by adding 1 mL of MeOH and it was concentrated in a rotary evaporator. Then it was extracted with DCM (1 x 25 mL), dried over anhydrous Na_2SO_4. The organic layer was concentrated in a rotary evaporator and the crude residue was purified through silica gel column chromatography. The pure product **5** was obtained in 85 % yield as a pale yellow solid.

*General experimental protocol for mono-triazoles of allenyl-anthracene (**8**)*

To a mixture of sodium azide (1 mmol), alkyl/benzyl bromides (1 mmol) and 9-allenyl-10-prop-2-ynyl-anthracene (1 mmol) in 3 mL of water was added CuO nanoparticle (8 mg) sodium ascorbate (39.6 mg) successively. Then, the reaction mixture was kept with stirring in a pre-heated oil-bath at 70 ^oC. After completion of the reaction, it was extracted with DCM (1 x 25 mL). The organic extract was dried over anhydrous Na_2SO_4 and the solvent was removed in a rotary evaporator. Then the crude residue was subjected to column chromatography to obtain the pure product mono-triazoles of allenyl-anthracene.

*General procedure for preparation of mono-triazoles (**10** and **11**)*

To a mixture of 10,10-dipropargyl-9-anthrone (1 mmol), sodium azide (1 mmol) and alkyl/benzyl bromides (1 mmol) in 3 mL of water was added CuO nanoparticle and sodium ascorbate successively and the reaction mixture was heated with stirring at 70 ^oC. After completion of the reaction, it was extracted with DCM (1 x 25 mL) and dried over anhydrous Na_2SO_4 and evaporated in vacuo. Then the crude residue was purified by column chromatography to get the pure product mono-triazoles of anthrone.

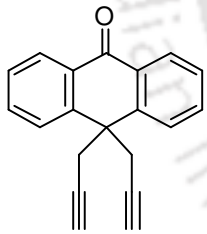
*General procedure for the synthesis of bis-triazoles (**9** and **12**)*

Into a 25 mL round bottomed flask was taken a mixture of 10,10-dipropargyl-9-anthrone (2, 1 mmol), alkyl/benzyl bromide (2 mmol), and sodium azide (2 mmol) in 3 mL of water. Then, CuO nanoparticle and sodium ascorbate were added into the above reaction mixture and it was kept for heating at 70 ˚C. After completion of the reaction, it was extracted with DCM (2 x 20 mL) and dried over anhydrous Na_2SO_4 and concentrated under reduced pressure, then the crude residue was passed through column chromatography and the pure product bis-triazoles **9** was obtained. The synthesis of bis-triazoles **12** were achieved by following identical reaction procedure.

*General experimental procedure for the synthesis of tris-triazole (**13**)*

CuO nanoparticle and sodium ascorbate were added one by one to a mixture of 10,10-diprop-2-ynyl-9-prop-2-ynyloxy-anthracene (1 mmol), benzyl bromide (3 mmol), sodium azide (3 mmol) in 3 mL of water and the reaction mixture was heated at 70 ˚C. After completion of the reaction, it was extracted with DCM and dried over anhydrous Na_2SO_4 and the solvent was evaporated in a rotary evaporator. Then the crude residue on silica gel column chromatography was purified and the pure product **13** was obtained.

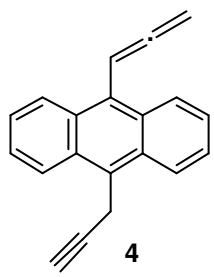
*10,10-dipropargyl-9-anthrone (**2**)*



2

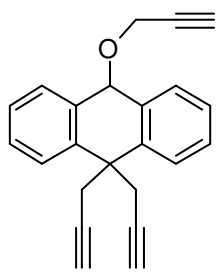
White solid, M.p 210-211 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.42-8.39 (m, 2H), 7.73-7.67 (m, 4H), 7.54-7.48 (m, 2H), 3.09 (d, *J* = 2.4 Hz, 4H), 1.66 (t, *J* = 2.4 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 183.8, 144.6, 133.7, 132.6, 127.8, 127.7, 126.0, 79.5, 71.7, 45.2, 33.5; **IR** (KBr)ν_{max} 3286, 3255, 3073, 2914, 2116, 1649, 1600, 1585, 1459, 1440, 1324, 1178 cm^{-1}; **Anal. calcd** for $C_{20}H_{14}O$: C, 88.86; H, 5.22. found C, 88.75; H, 5.15.

*9-allenyl-10-prop-2-ynyl-anthracene (**4**)*


4

Yellow solid, M.p 168-169 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.45 (d, *J* = 8.8 Hz, 2H), 8.33 (d, *J* = 8.8 Hz, 2H), 7.59-7.50 (m, 4H), 6.95 (t, *J* = 7.2 Hz, 1H), 5.05 (d, *J* = 7.2 Hz, 2H), 4.44 (d, *J* = 2.4 Hz, 2H), 2.07 (t, *J* = 2.8 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 211.2, 129.7, 129.6, 128.2, 127.8, 126.8, 126.2, 125.4, 124.6, 88.1, 82.4, 75.6, 69.8, 17.9; **IR** (KBr)ν_{max} 3284, 3043, 2972, 2109, 1945, 1622, 1442, 1374, 1314, 1180 cm^{-1}; **Anal. calcd** for $C_{20}H_{14}$: C, 94.45; H, 5.55. found C, 94.34; H, 5.49.

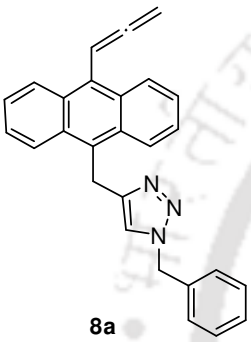
*10,10-diprop-2-ynyl-9-(prop-2-yn-1-oxy)-9,10-dihydroanthracene (**5**)*



5

Pale yellow solid, M.p 96-97 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.62 (d, *J* = 8.0 Hz, 2H), 7.53 (d, *J* = 7.2 Hz, 2H), 7.39 (t, *J* = 7.2 Hz, 2H), 7.33 (t, *J* = 7.2 Hz, 2H), 5.61 (s, 1H), 4.03 (d, *J* = 2.4 Hz, 2H), 3.34 (t, *J* = 2.8 Hz, 2H), 2.85 (d, *J* = 2.4 Hz, 2H), 2.49 (t, *J* = 2.4 Hz, 1H), 1.92 (t, *J* = 2.4 Hz, 1H), 1.59 (t, *J* = 2.4 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 141.3, 134.8, 130.0, 128.6, 127.2, 126.7, 126.0, 81.3, 81.0, 80.0, 75.7, 75.1, 71.9, 70.7, 54.3, 46.1, 35.9, 26.6; **IR** (KBr)ν_{max} 3286, 3066, 3028, 2923, 2853, 2116, 1649, 1599, 1484, 1446, 1323 cm^{-1}; **Anal. calcd** for $C_{23}H_{18}O$: C, 89.00; H, 5.85. found C, 88.88; H, 5.78.

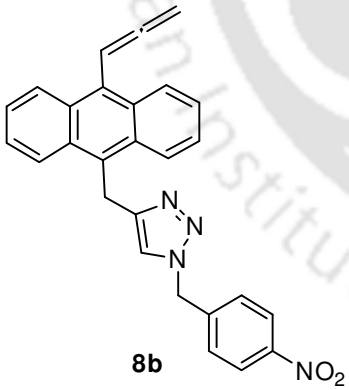
*1-benzyl-4-((9-(propa-1,2-dienyl)anthracen-10-yl)methyl)-1H-1,2,3-triazole (**8a**)*



8a

Yellow solid, M.p 177-178 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.38 (d, *J* = 9.6 Hz, 2H), 8.21 (d, *J* = 9.2 Hz, 2H), 7.44-7.41 (m, 4H), 7.18-7.16 (m, 3H), 7.01 (brs, 2H), 6.88 (t, *J* = 7.6 Hz, 1H), 6.66 (s, 1H), 5.22 (s, 2H), 4.99 (s, 2H), 4.98 (s, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 211.2, 134.9, 130.6, 129.9, 129.7, 129.1, 128.6, 127.9, 127.5, 126.7, 126.1, 125.9, 125.0, 121.9, 88.1, 75.7, 54.1, 25.3; **IR** (KBr)ν_{max} 3120, 3064, 2953, 1946, 1662, 1550, 1444, 1318, 1215 cm^{-1}; **Anal. calcd** for $C_{27}H_{21}N_3$: C, 83.69; H, 5.46; N, 10.84. found C, 83.56; H, 5.39; N, 10.78.

*1-(4-nitrobenzyl)-4-((9-(propa-1,2-dienyl)anthracen-10-yl)methyl)-1H-1,2,3-triazole (**8b**)*

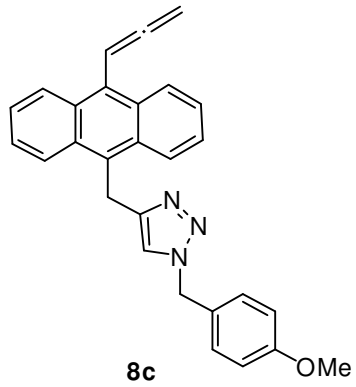


8b

Yellow solid, M.p 153-154˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.44 (d, *J* = 8.8 Hz, 2H), 8.25 (d, *J* = 8.8 Hz, 2H), 8.06 (d, *J* = 8.4 Hz, 2H), 7.50-7.48 (m, 4H), 7.18 (d, *J* = 8.4 Hz, 2H), 6.93 (t, *J* = 7.6 Hz, 1H), 6.74 (s, 1H), 5.35 (s, 2H), 5.06 (s, 2H), 5.03 (s, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 211.1, 148.5, 147.8, 141.7, 130.2, 129.7, 129.5, 128.3, 127.4 , 126.6, 126.1, 125.4, 124.7, 124.0, 122.1, 87.9, 75.6, 52.8, 25.0; **IR** (KBr)ν_{max} 3135, 3075, 3051, 2963, 1946, 1605, 1520, 1443, 1344, 1261, 1209 cm^{-1}; **Anal. calcd** for $C_{27}H_{20}N_4O_2$: C, 74.98; H, 4.66; N, 12.95. found C, 74.89; H, 4.59; N, 12.85.

*1-(4-methoxybenzyl)-4-((9-(propa-1,2-dienyl)anthracen-10-yl)methyl)-1H-1,2,3-triazole (**8c**)*

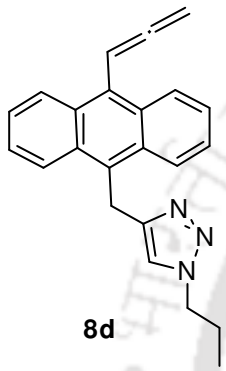
Yellow solid, M.p 161-162˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.45-8.42 (m, 2H), 8.28-8.26 (m, 2H), 7.51-7.45 (m, 4H), 7.02 (d, *J* = 8.4 Hz, 2H), 6.94 (t, *J* = 7.6 Hz, 1H), 6.74 (d, *J* = 7.6 Hz, 2H), 6.68 (s, 1H), 5.21 (s, 2H), 5.05 (s, 2H), 5.04 (d, *J* = 7.6 Hz, 2H), 3.72 (s, 3H); **^{13}C**



8c

NMR (100 MHz, $CDCl_3$): δ 211.1, 159.7, 147.9, 130.6, 129.8, 129.5, 129.3, 126.7, 126.5, 125.9, 125.3, 124.9, 121.5, 114.3, 87.9, 75.6, 55.2, 53.5, 25.2; **IR** (KBr)ν_{max} 3127, 3068, 2962, 2932, 2836, 1946, 1611, 1513, 1441, 1302, 1249, 1209 cm^{-1}; **Anal. calcd** for $C_{28}H_{23}N_3O$: C, 80.55; H, 5.55; N, 10.06. found C, 80.46; H, 5.46; N, 9.98.

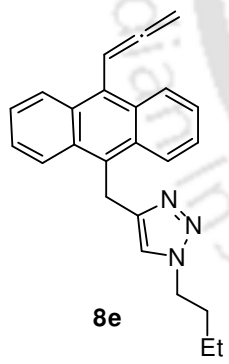
*4-((9-(propa-1,2-dienyl)anthracen-10-yl)methyl)-1-propyl-1H-1,2,3-triazole (**8d**)*



8d

Yellow solid, M.p 117-118˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.46-8.44 (m, 2H), 8.29-8.27 (m, 2H), 7.52-7.47 (m, 4H), 6.95 (t, *J* = 7.2 Hz, 1H), 6.68 (s, 1H), 5.06-5.04 (m, 4H), 4.04 (t, *J* = 7.6 Hz, 2H), 1.74-1.68 (m, 2H), 0.78 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 211.2, 147.7, 130.8, 129.9, 129.7, 127.4, 126.7, 126.1, 125.4, 125.0, 121.8, 88.1, 75.7, 51.9, 25.3, 23.7, 11.1; **IR** (KBr)ν_{max} 3119, 3068, 2966, 2931, 2875, 1950, 1620, 1550, 1443, 1383, 1262, 1218 cm^{-1}; **Anal. calcd** for $C_{23}H_{21}N_3$: C, 81.38; H, 6.24; N, 12.38. found C, 81.29; H, 6.15; N, 12.29.

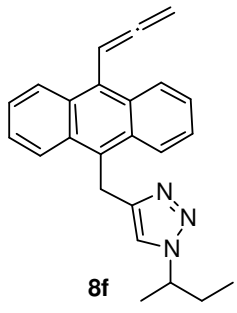
*1-butyl-4-((10-(propa-1,2-dien-1-yl)anthracen-9-yl)methyl)-1H-1,2,3-triazole (**8e**)*



8e

Yellow solid, M.p 120-121 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.47-8.44 (m, 2H), 8.31-8.28 (m, 2H), 7.52-7.48 (m, 4H), 6.66 (t, *J* = 7.2 Hz, 1H), 6.68 (s, 1H), 5.06-5.05 (m, 4H), 4.08 (t, *J* = 7.2 Hz, 2H), 1.69-1.64 (m, 2H), 1.23-1.14 (m, 2H), 0.81 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 211.2, 147.6, 130.7, 129.9, 129.6, 127.4, 126.6, 126.1, 125.4, 124.9, 121.7, 88.1, 75.6, 50.1, 32.2, 25.3, 19.8, 13.5; **IR** (KBr)ν_{max} 3120, 3070, 2962, 2929, 2871, 1951, 1599, 1460, 1385, 1261, 1217 cm^{-1}; **Anal. calcd** for $C_{24}H_{23}N_3$: C, 81.55; H, 6.56; N, 11.89. found C, 81.44; H, 6.45; N, 11.79.

*1-(sec-butyl)-4-((10-(propa-1,2-dien-1-yl)anthracen-9-yl)methyl)-1H-1,2,3-triazole (**8f**)*

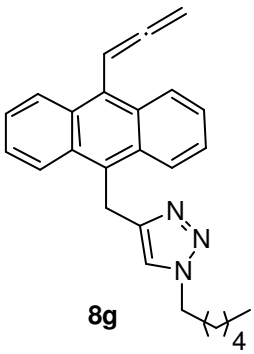


8f

Yellow solid, M.p 129-130 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.46-8.44 (m, 2H), 8.30-8.28 (m, 2H), 7.51-7.48 (m, 4H), 6.96 (t, *J* = 6.8 Hz, 1H), 6.68 (s, 1H), 5.08-5.05 (m, 4H), 4.33 (q, *J* = 7.2 Hz, 1H), 1.73-1.62 (m, 2H), 1.32 (d, *J* = 6.8 Hz, 3H), 0.68 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 211.2, 147.4, 130.9, 130.1, 129.7, 127.3, 126.6, 126.1, 125.4, 125.1, 119.7, 88.2, 75.7, 58.9, 30.3, 25.5, 20.8, 10.5; **IR**

(KBr)ν_{max} 3123, 3066, 2964, 2933, 2876, 1949, 1619, 1547, 1443, 1384, 1368, 1260, 1225 cm^{-1}; **Anal. calcd** for $C_{24}H_{23}N_3$: C, 81.55; H, 6.56; N, 11.89. found C, 81.45; H, 6.46; N, 11.80.

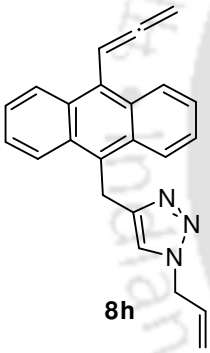
*1-hexyl-4-((10-(propa-1,2-dien-1-yl)anthracen-9-yl)methyl)-1H-1,2,3-triazole (**8g**)*



8g

Yellow solid, M.p 141-142 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.47-8.44 (m, 2H), 8.29-8.27 (m, 2H), 7.52-7.47 (m, 4H), 6.96 (t, *J* = 7.2 Hz, 1H), 6.67 (s, 1H), 5.06-5.04 (m, 4H), 4.07 (t, *J* = 7.2 Hz, 2H), 1.68-1.65 (m, 2H), 1.15-1.12 (m, 6H), 0.77 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 211.2, 147.7, 130.8, 129.9, 129.7, 127.4, 126.7, 126.1, 125.4, 125.0, 121.8, 88.1, 75.6, 50.3, 31.1, 30.2, 26.2, 25.3, 22.4, 13.9; **IR** (KBr)ν_{max} 3121, 3073, 2953, 2929, 2856, 1945, 1619, 1554, 1443, 1314, 1219 cm^{-1}; **Anal. calcd** for $C_{26}H_{27}N_3$: C, 81.85; H, 7.13; N, 11.01. found C, 81.74; H, 7.05; N, 10.94.

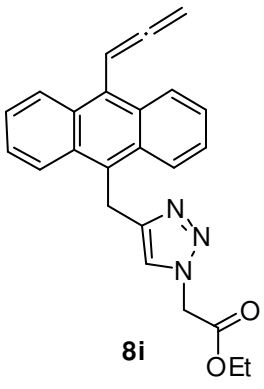
*1-allyl-4-((10-(propa-1,2-dien-1-yl)anthracen-9-yl)methyl)-1H-1,2,3-triazole (**8h**)*



8h

Yellow solid, M.p 164-165 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.46-8.44 (m, 2H), 8.30-8.27 (m, 2H), 7.51-7.44 (m, 4H), 6.95 (t, *J* = 7.2 Hz, 1H), 6.71 (s, 1H), 5.83-5.74 (m, 1H), 5.14 (d, *J* = 10.4 Hz, 2H), 5.06-5.02 (m, 4H), 4.72 (d, *J* = 6.0 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 211.2, 148.0, 131.3, 130.7, 129.9, 129.6, 127.4, 126.7, 126.1, 125.4, 124.9, 121.7, 120.1, 88.1, 75.6, 52.8, 25.3; **IR** (KBr)ν_{max} 3122, 3069, 2926, 2853, 1952, 1618, 1443, 1383, 1220, 1137 cm^{-1}; **Anal. calcd** for $C_{23}H_{19}N_3$: C, 81.87; H, 5.68; N, 12.45. found C, 81.76; H, 5.60; N, 12.36.

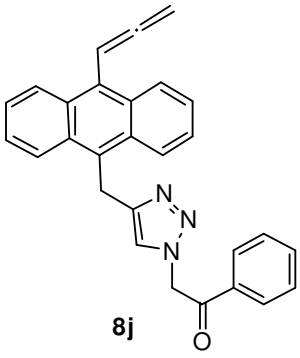
*Ethyl2-(4-((10-(propa-1,2-dien-1-yl)anthracen-9-yl)methyl)-1H-1,2,3-triazol-1-yl)acetate (**8i**)*



8i

Yellow solid, M.p 159-160 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.45-8.43 (m, 2H), 8.31-8.28 (m, 2H), 7.52-7.47 (m, 4H), 6.95 (t, *J* = 7.2 Hz, 1H), 6.85 (s, 1H), 5.09 (s, 2H), 5.05 (d, *J* = 6.8 Hz, 2H), 4.88 (s, 2H), 4.11 (q, *J* = 8.0 Hz, 2H), 1.14 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 211.2, 166.2, 148.1, 130.5, 129.9, 129.6, 127.4, 126.7, 126.1, 125.4, 124.9, 123.3, 88.1, 75.6, 62.3, 50.8, 25.1, 14.0; **IR** (KBr)ν_{max} 3132, 3080, 2990, 2961, 1938, 1756, 1620, 1546, 1445, 1375, 1217 cm^{-1}; **Anal. calcd** for $C_{24}H_{21}N_3O_2$: C, 75.18; H, 5.52; N, 10.96. found C, 75.05; H, 5.44; N, 10.87.

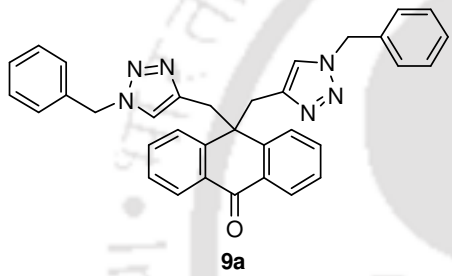
*1-phenyl-2-(4-((10-(propa-1,2-dien-1-yl)anthracen-9-yl)methyl)-1H-1,2,3-triazol-1-yl)ethanone (**8j**)*



8j

Yellow solid, M.p 181-182 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.38 (d, *J* = 8.8 Hz, 2H), 8.28 (d, *J* = 8.4 Hz, 2H), 7.76 (d, *J* = 8.0 Hz, 2H), 7.52 (t, *J* = 7.6 Hz, 2H), 7.48-7.40 (m, 3H), 7.37 (t, *J* = 7.2 Hz, 2H), 6.89-6.85 (m, 2H), 5.49 (s, 2H), 5.04 (s, 2H), 4.98 (d, *J* = 6.8 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 211.2, 190.4, 134.5, 133.9, 130.6, 129.9, 129.6, 129.2, 128.1, 127.4, 126.6, 126.2, 125.4, 124.9, 123.8, 88.1, 75.6, 55.4, 25.2; **IR** (KBr)ν_{max} 3134, 3067, 2963, 2923, 2853, 1948, 1705, 1597, 1448, 1412, 1349, 1261, 1226 cm^{-1}; **Anal. calcd** for $C_{28}H_{21}N_3O$: C, 80.94; H, 5.09; N, 10.11. found C, 80.82; H, 4.98; N, 10.04.

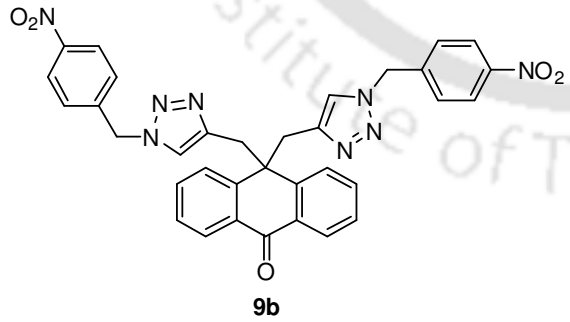
*10,10-bis((1-benzyl-1H-1,2,3-triazol-4-yl)methyl)anthracen-9(10H)-one (**9a**)*



9a

White solid, M.p 195-196 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.05 (d, *J* = 7.6 Hz, 2H), 7.88 (d, *J* = 8.0 Hz, 2H), 7.65 (d, *J* = 8.0 Hz, 2H), 7.34-7.25 (m, 8H), 6.76 (d, *J* = 6.0 Hz, 4H), 5.79 (s, 2H), 5.12 (s, 4H), 3.84 (s, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 182.6, 144.9, 143.2, 134.5, 133.9, 132.3, 129.0, 128.5, 127.4, 127.3, 127.2, 121.5, 53.6, 47.1, 40.8; **IR** (KBr)ν_{max} 3164, 3133, 3062, 3032, 2961, 1664, 1602, 1545, 1496, 1455, 1323, 1216 cm^{-1}; **Anal. calcd** for $C_{34}H_{28}N_6O$: C, 76.10; H, 5.26; N, 15.66. found C, 75.98; H, 5.18; N, 15.56.

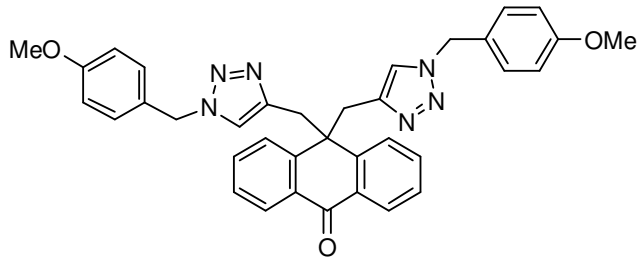
*10,10-bis((1-(4-nitrobenzyl)-1H-1,2,3-triazol-4-yl)methyl)anthracen-9(10H)-one (**9b**)*



9b

White solid, M.p 181-182 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.98 (d, *J* = 8.8 Hz, 4H), 7.90 (d, *J* = 8.0 Hz, 2H), 7.84 (d, *J* = 8.0 Hz, 2H), 7.62-7.58 (m, 2H), 7.26-7.22 (m, 2H), 6.71 (d, *J* = 8.8 Hz, 4H), 5.84 (s, 2H), 5.13 (s, 4H), 3.77 (s, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 181.3, 146.3, 144.1, 142.2, 141.7, 132.9, 130.9, 126.7, 126.2, 125.5, 122.7, 121.3, 50.9, 46.1, 39.4; **IR** (KBr)ν_{max} 3136, 3070, 2956, 2931, 2857, 1661, 1601, 1523, 1493, 1455, 1419, 1357, 1324, 1216 cm^{-1}.

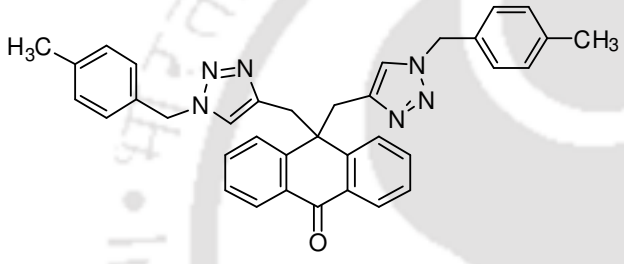
10,10-bis((1-(4-methoxybenzyl)-1H-1,2,3-triazol-4-yl)methyl)anthracen-9(10H)-one ***(9c)***



9c

White solid, M.p 167-168 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.01 (d, *J* = 7.6 Hz, 2H), 7.84 (d, *J* = 8.0 Hz, 2H), 7.61 (t, *J* = 8.0 Hz, 2H), 7.29 (t, *J* = 7.6 Hz, 2H), 6.77-6.69 (m, 8H), 5.70 (s, 2H), 5.01 (s, 4H), 3.80 (s, 6H), 3.78 (s, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 182.6, 159.8, 145.0, 143.1, 133.9, 132.4, 129.0, 127.4, 127.3, 126.6, 121.3, 114.4, 55.5, 53.3, 47.1, 40.9; **IR** (KBr)ν_{max} 3129, 3066, 2960, 2933, 2833, 1663, 1602, 1515, 1324, 1255, 1217 cm^{-1}; **Anal. calcd** for $C_{36}H_{32}N_6O_3$: C, 72.47; H, 5.41; N, 14.08. found C, 72.35; H, 5.30; N, 13.98.

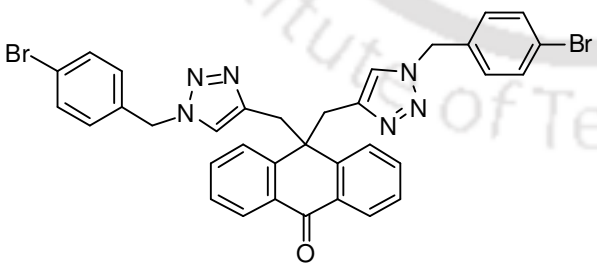
10,10-bis((1-(4-methylbenzyl)-1H-1,2,3-triazol-4-yl)methyl)anthracen-9(10H)-one ***(9d)***



9d

White solid, M.p 215-216 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.06 (d, *J* = 8.0 Hz, 2H), 7.87 (d, *J* = 8.0 Hz, 2H), 7.64 (t, *J* = 7.6 Hz, 2H), 7.32 (t, *J* = 7.6 Hz, 2H), 7.07 (d, *J* = 7.6 Hz, 4H), 6.68 (d, *J* = 7.6 Hz, 4H), 5.78 (s, 2H), 5.07 (s, 4H), 3.83 (s, 4H), 2.35 (s, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 182.6, 144.9, 143.1, 138.3, 133.9, 132.2, 131.5, 129.6, 127.4, 127.2, 121.4, 53.4, 47.0, 40.8, 21.2; **IR** (KBr)ν_{max} 3132, 3062, 3025, 2959, 2922, 1666, 1602, 1516, 1458, 1323, 1217 cm^{-1}; **Anal. calcd** for $C_{36}H_{32}N_6O$: C, 76.57; H, 5.71; N, 14.88. found C, 76.45; H, 5.60; N, 14.77.

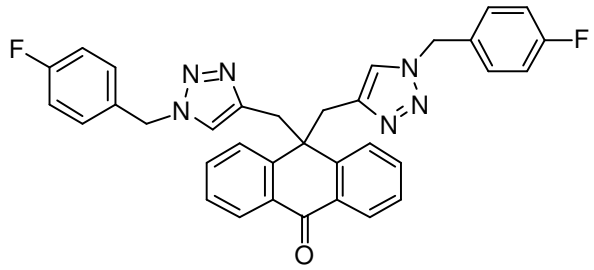
10,10-bis((1-(4-bromobenzyl)-1H-1,2,3-triazol-4-yl)methyl)anthracen-9(10H)-one ***(9e)***



9e

White solid, M.p 205-206 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.05 (d, *J* = 8.0 Hz, 2H), 7.92 (d, *J* = 8.0 Hz, 2H), 7.67 (t, *J* = 7.2 Hz, 2H), 7.41 (d, *J* = 8.4 Hz, 4H), 7.34 (t, *J* = 7.6 Hz, 2H), 6.63 (d, *J* = 8.4 Hz, 4H), 5.78 (s, 2H), 5.07 (s, 4H), 3.87 (s, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 182.6, 144.8, 134.1, 133.5, 132.2, 129.7, 128.9, 127.5, 127.3, 127.2, 122.6, 121.6, 52.9, 47.1, 40.7; **IR** (KBr)ν_{max} 3123, 3065, 2954, 2929, 1651, 1598, 1489, 1458, 1408, 1325, 1176 cm^{-1}; **Anal. calcd** for $C_{34}H_{26}Br_2N_6O$: C, 58.81; H, 3.77; N, 12.10. found C, 58.70; H, 3.69; N, 11.98.

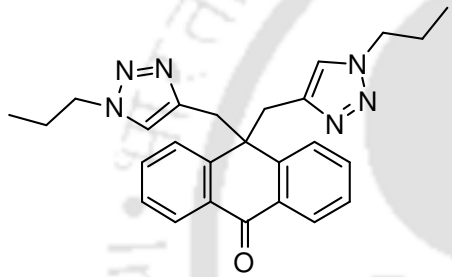
*10,10-bis((1-(4-fluorobenzyl)-1H-1,2,3-triazol-4-yl)methyl)anthracen-9(10H)-one (**9f**)*



9f

White solid, M.p 194-195 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.05 (d, *J* = 7.6 Hz, 2H), 7.89 (d, *J* = 8.0 Hz, 2H), 7.67 (t, *J* = 8.0 Hz, 2H), 7.34 (t, *J* = 7.2, Hz, 2H), 6.98-6.94 (m, 4H), 6.76-6.73 (m, 4H), 5.77 (s, 2H), 5.09 (s, 4H), 3.84 (s, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 182.5, 163.9, 144.9, 134.0, 132.2, 130.4, 129.2, 129.1, 127.5, 127.2, 127.1, 121.3, 116.1, 115.8, 52.8, 47.1, 40.8; **IR** (KBr)ν_{max} 3133, 3067, 2965, 1665, 1603, 1514, 1457, 1323, 1237, 1161 cm^{-1}; **Anal. calcd** for $C_{34}H_{26}F_2N_6O$: C, 71.32; H, 4.58; N, 14.68. found C, 71.22; H, 4.50; N, 14.59.

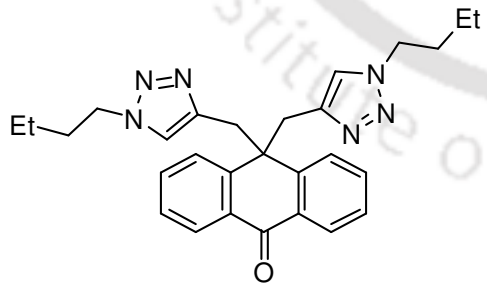
*10,10-bis((1-propyl-1H-1,2,3-triazol-4-yl)methyl)anthracen-9(10H)-one (**9g**)*



9g

White solid, M.p 188-189 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.14 (d, *J* = 8.0 Hz, 2H), 7.93 (d, *J* = 8.0 Hz, 2H), 7.72 (t, *J* = 7.6 Hz, 2H), 7.41 (t, *J* = 7.6 Hz, 2H), 5.86 (s, 2H), 3.91-3.82 (m, 8H), 1.53-1.46 (m, 4H), 0.57 (t, *J* = 7.2 Hz, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 182.9, 145.2, 142.8, 134.1, 132.5, 127.6, 127.3, 127.2, 121.1, 51.6, 46.9, 40.9, 23.5, 10.7; **IR** (KBr)ν_{max} 3133, 3063, 2965, 2934, 2876, 1666, 1602, 1457, 1385, 1352, 1323, 1215 cm^{-1}; **Anal. calcd** for $C_{26}H_{28}N_6O$: C, 70.89; H, 4.41; N, 19.08. found C, 70.77; H, 4.35; N, 18.97.

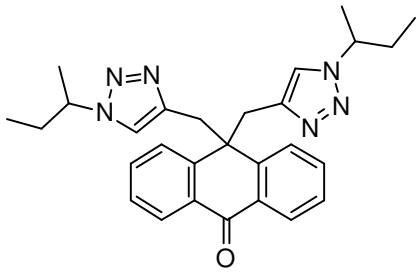
*10,10-bis((1-butyl-1H-1,2,3-triazol-4-yl)methyl)anthracen-9(10H)-one (**9h**)*



9h

White solid, M.p 176-177 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.18 (d, *J* = 8.0 Hz, 2H), 7.96 (d, *J* = 8.4 Hz, 2H), 7.76 (t, *J* = 8.4 Hz, 2H), 7.44 (t, *J* = 7.2 Hz, 2H), 5.89 (s, 2H), 3.94 (t, *J* = 7.2 Hz, 4H), 3.88 (s, 4H), 1.52-1.45 (m, 4H), 0.98-0.88 (m, 4H), 0.77 (t, *J* = 7.6 Hz, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 182.9, 145.2, 142.8, 134.1, 132.5, 127.6, 127.3, 127.2, 121.1, 49.7, 46.9, 40.9, 32.0, 19.4, 13.4; **IR** (KBr)ν_{max} 3129, 3071, 2957, 2928, 2856, 1666, 1603, 1461, 1324, 1215cm^{-1}; **Anal. calcd** for $C_{28}H_{32}N_6O$: C, 71.77; H, 6.88; N, 17.93. found C, 71.65; H, 6.79; N, 17.83.

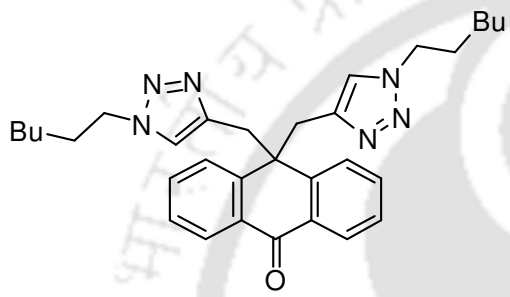
*10,10-bis((1-(sec-butyl)-1H-1,2,3-triazol-4-yl)methyl)anthracen-9(10H)-one (**9i**)*



9i

White solid, M.p 149-150 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.11 (d, *J* = 7.6 Hz, 2H), 7.92 (d, *J* = 8.4 Hz, 2H), 7.70 (t, *J* = 7.2 Hz, 2H), 7.38 (t, *J* = 7.6 Hz, 2H), 5.83 (s, 2H), 4.11 (q, *J* = 7.6 Hz, 2H), 3.84 (s, 4H), 1.49-1.36 (m, 4H), 1.14 (d, *J* = 6.8 Hz, 6H), 0.40 (t, *J* = 7.2 Hz, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 182.8, 145.3, 142.6, 134.0, 132.5, 127.5, 127.4, 127.1, 119.1, 58.4, 47.1, 40.8, 30.1, 20.6, 10.0; **IR** (KBr)ν_{max} 3137, 3067, 3036, 2963, 2935, 2875, 1666, 1603, 1479, 1459, 1351, 1326, 1217 cm^{-1}; **Anal. calcd** for $C_{28}H_{32}N_6O$: C, 71.77; H, 6.88; N, 17.93. found C, 71.64; H, 6.78; N, 17.82.

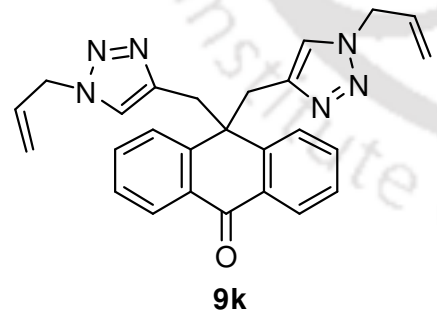
*10,10-bis((1-hexyl-1H-1,2,3-triazol-4-yl)methyl)anthracen-9(10H)-one (**9j**)*



9j

White solid, M.p 162-163 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.15 (d, *J* = 8.0 Hz, 2H), 7.92 (d, *J* = 7.6 Hz, 2H), 7.71 (t, *J* = 8.0 Hz, 2H), 7.41 (t, *J* = 8.0 Hz, 2H), 5.86 (s, 2H), 3.90 (t, *J* = 7.2 Hz, 4H), 3.85 (s, 4H), 1.50-1.43 (m, 4H), 1.19-1.06 (m, 8H), 0.94-0.86 (m, 4H), 0.81 (t, *J* = 7.2 Hz, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 182.9, 145.3, 142.8, 134.1, 132.6, 127.6, 127.3, 121.1, 50.0, 46.9, 41.1, 31.1, 30.1, 25.9, 22.5, 14.1; **IR** (KBr)ν_{max} 3132, 3061, 2953, 2931, 2860, 1668, 1603, 1459, 1383, 1323, 1213 cm^{-1}; **Anal. calcd** for $C_{32}H_{40}N_6O$: C, 70.25; H, 7.68; N, 16.02. found C, 70.11; H, 7.59; N, 15.91.

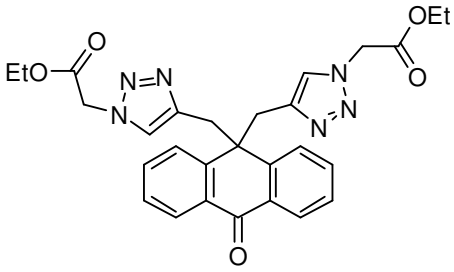
*10,10-bis((1-allyl-1H-1,2,3-triazol-4-yl)methyl)anthracen-9(10H)-one (**9k**)*



9k

White solid, M.p 179-180 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.17 (d, *J* = 8.0 Hz, 2H), 7.95 (d, *J* = 8.0 Hz, 2H), 7.75 (t, *J* = 8.0 Hz, 2H), 7.44 (t, *J* = 8.0 Hz, 2H), 5.92 (s, 2H), 5.69-5.62 (m, 2H), 5.11 (d, *J* = 10.4 Hz, 2H), 4.77 (d, *J* = 17.2 Hz, 2H), 4.57 (d, *J* = 6.0 Hz, 4H), 3.88 (s, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 182.9, 144.9, 142.9, 134.0, 132.4, 131.1, 127.5, 127.2, 121.3, 119.1, 52.1, 46.9, 40.8; **IR** (KBr)ν_{max} 3135, 3066, 2959, 2916, 2823, 1665, 1601, 1458, 1323, 1217 cm^{-1}; **Anal. calcd** for $C_{26}H_{24}N_6O$: C, 71.54; H, 5.54; N, 19.25. found C, 71.43; H, 5.45; N, 19.13.

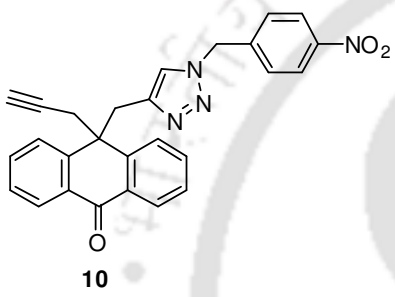
*diethyl2,2'-(4,4'-((10-oxo-9,10-dihydroanthracene-9,9-diyl)bis(methylene))bis(1H-1,2,3-triazole-4,1-diyl))diacetate (**9l**)*



9l

White solid, M.p 153-154 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.14 (d, *J* = 8.0 Hz, 2H), 7.94 (t, *J* = 8.0 Hz, 2H), 7.73 (t, *J* = 8.0 Hz, 2H), 7.40 (t, *J* = 7.6 Hz, 2H), 6.06 (s, 2H), 4.72 (s, 4H), 4.07 (q, *J* = 6.8 Hz, 4H), 3.88 (s, 4H), 1.13 (t, *J* = 7.2 Hz, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 182.8, 165.9, 144.9, 143.1, 133.9, 132.3, 127.5, 127.3, 122.7, 62.2, 50.6, 46.7, 40.7, 13.9; **IR** (KBr)ν_{max} 3170, 3138, 2987, 2939, 2845, 2861, 1755, 1666, 1603, 1459, 1354, 1324, 1263, 1231 cm^{-1}; **Anal. calcd** for $C_{28}H_{28}N_6O_5$ C, 63.63; H, 5.34; N, 15.90. found C, 63.50; H, 5.25; N, 15.78.

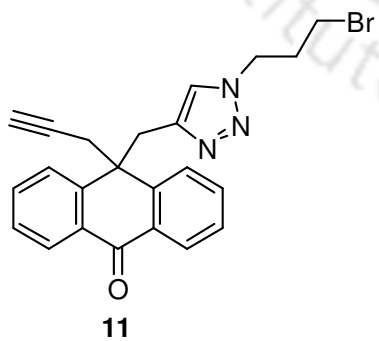
*10-((1-(4-nitrobenzyl)-1H-1,2,3-triazol-4-yl)methyl)-10-(prop-2-yn-1-yl)anthracen-9(10H)-one (**10**)*



10

White solid, M.p 183-184 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.23 (d, *J* = 8.4 Hz, 2H), 8.12 (d, *J* = 8.8 Hz, 2H), 7.79 (d, *J* = 8.0 Hz, 2H), 7.68 (t, *J* = 8.0 Hz, 2H), 7.43 (t, *J* = 8.0 Hz, 2H), 6.85 (d, *J* = 8.8 Hz, 2H), 5.87 (s, 1H), 5.23 (s, 2H), 3.73 (s, 2H), 3.21 (d, *J* = 2.4 Hz, 2H), 1.63 (t, *J* = 2.4 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 183.2, 148.0, 144.8, 143.9, 141.8, 134.0, 132.5, 127.9, 127.8, 127.5, 126.7, 124.3, 121.8, 79.4, 71.8, 52.7, 46.1, 39.9, 34.6; **IR** (KBr)ν_{max} 3287, 3139, 3073, 2926, 2852, 2301, 1657, 1602, 1517, 1460, 1348, 1324, 1224 cm^{-1}; **Anal. calcd** for $C_{27}H_{20}N_4O_3$: C, 72.31; H, 4.49; N, 12.49. found C, 72.18; H, 4.39; N, 12.37.

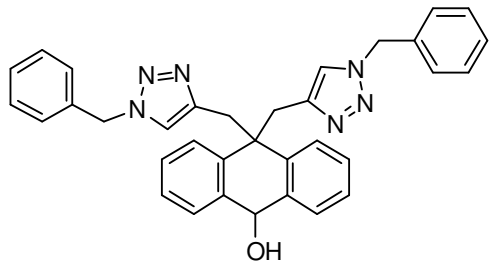
*10-((1-(3-bromopropyl)-1H-1,2,3-triazol-4-yl)methyl)-10-(prop-2-yn-1-yl)anthracen-9(10H)-one (**11**)*



11

Semi-solid, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.31 (d, *J* = 7.6 Hz, 2H), 7.82 (d, *J* = 8.0 Hz, 2H), 7.73 (t, *J* = 8.0 Hz, 2H), 7.49 (t, *J* = 7.6 Hz, 2H), 5.94 (s, 1H), 4.04 (t, *J* = 6.8 Hz, 2H), 3.73 (s, 2H), 3.23 (d, *J* = 2.8 Hz, 2H), 2.96 (t, *J* = 6.4 Hz, 2H), 1.84-1.77 (m, 2H), 1.65 (t, *J* = 2.4 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 183.3, 144.8, 142.9, 133.9, 132.5, 127.7, 127.5, 127.4, 126.5, 122.1, 121.7, 79.5, 71.6, 47.6, 46.7, 46.1, 39.7, 34.5, 32.3; **IR** (KBr)ν_{max} 3294, 3068, 2925, 2853, 2101, 1654, 1599, 1458, 1324, 1218, 1176 cm^{-1}; **Anal. calcd** for $C_{23}H_{20}BrN_3O$: C, 63.60; H, 4.64; N, 9.67. found C, 63.48; H, 4.55; N, 9.56.

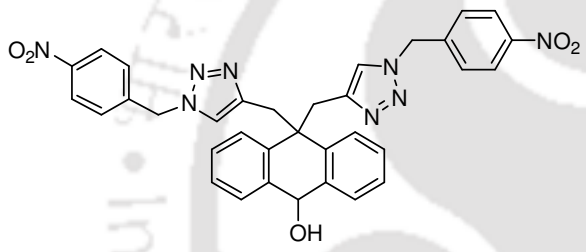
*10,10-bis((1-benzyl-1H-1,2,3-triazol-4-yl)methyl)-9,10-dihydroanthracen-9-ol (**12a**)*



12a

White solid, M.p 159-160 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.56 (d, *J* = 7.6 Hz, 2H), 7.34 (d, *J* = 7.6 Hz, 2H), 7.31-7.23 (m, 8H), 7.22-7.18 (m, 2H), 6.89 (d, *J* = 8.4 Hz, 2H), 6.79 (d, *J* = 6.8 Hz, 2H), 6.31 (s, 1H), 5.67 (s, 1H), 5.18 (s, 2H), 5.13 (s, 2H), 5.00 (s, 1H), 4.98 (s, 1H), 3.69 (s, 2H), 3.67 (s, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 144.6, 144.3, 138.4, 137.9, 135.0, 134.8, 129.0, 128.9, 128.8, 128.4, 127.7, 127.5, 127.1, 126.6, 122.6, 121.7, 67.8, 53.7, 53.6, 46.5, 40.4, 40.3; **IR** (KBr)ν_{max} 3532, 3146, 3061, 3035, 2924, 2825, 1601, 1543, 1490, 1415, 1352, 1325, 1220 cm^{-1}; **Anal. calcd** for $C_{34}H_{30}N_6O$: C, 75.81; H, 5.61; N, 15.60. found C, 75.65; H, 5.53; N, 15.48.

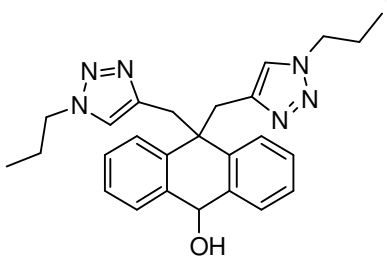
*10,10-bis((1-(4-nitrobenzyl)-1H-1,2,3-triazol-4-yl)methyl)-9,10-dihydroanthracen-9-ol (**12b**)*



12b

White solid, M.p 226-227 ˚C, **^{1}H NMR** (400 MHz, CD_2Cl_2): δ 8.10 (d, *J* = 8.4 Hz, 4H), 7.62 (d, *J* = 8.0 Hz, 2H), 7.42 (d, *J* = 7.6 Hz, 2H), 7.34 (t, *J* = 7.2 Hz, 2H), 7.27 (t, *J* = 7.2 Hz, 2H), 7.01 (d, *J* = 8.4 Hz, 2H), 6.89 (d, *J* = 8.4 Hz, 2H), 6.56 (s, 1H), 5.89 (s, 1H), 5.33 (s, 2H), 5.25 (s, 2H), 5.13 (s, 1H), 5.12 (s, 1H), 3.73 (s, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 145.8, 145.6, 141.8, 137.7, 136.6, 126.7, 126.6, 126.1, 125.6, 124.9, 124.8, 122.2, 122.1, 121.5, 64.3, 50.3, 44.9, 36.5; **IR** (KBr)ν_{max} 3543, 3132, 2962, 2927, 2855, 1603, 1517, 1487, 1421, 1754, 1261, 1218 cm^{-1}; **Anal. calcd** for $C_{34}H_{28}N_8O_5$: C, 63.96; H, 4.49; N, 17.82. found C, 63.83; H, 4.38; N, 18.70.

*10,10-bis((1-propyl-1H-1,2,3-triazol-4-yl)methyl)-9,10-dihydroanthracen-9-ol (**12c**)*

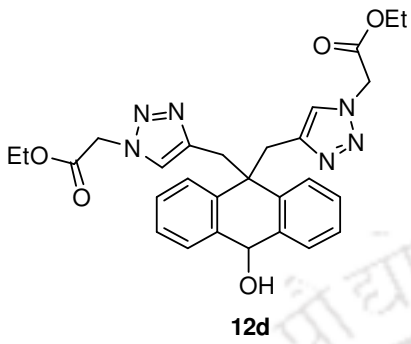


12c

White solid, M.p 141-142 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.57 (d, *J* = 7.6 Hz, 2H), 7.51 (d, *J* = 7.6 Hz, 2H), 7.35-7.31 (m, 2H), 7.28-7.26 (m, 2H), 6.40 (s, 1H), 5.79 (s, 1H), 5.32 (s, 1H), 3.96 (t, *J* = 7.2 Hz, 2H), 3.90-3.85 (m, 3H), 3.69-3.68 (m, 4H), 1.61 (q, *J* = 7.2 Hz, 2H), 1.53 (q, *J* = 7.2 Hz, 2H), 0.69 (t, *J* = 7.2 Hz, 3H), 0.59 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 144.1, 143.9, 138.9, 138.0, 129.0, 128.6, 127.3, 126.8, 122.5, 121.5, 111.9, 68.4, 51.7, 51.5, 46.6, 40.6, 39.8, 23.7; **IR** (KBr)ν_{max} 3537, 3132, 2964,

2927, 2875, 1602, 1542, 1490, 1457, 1328, 1261 cm^{-1}; **Anal. calcd** for $C_{26}H_{30}N_6O$: C, 70.56; H, 6.83; N, 18.99. found C, 70.45; H, 6.72; N, 18.88.

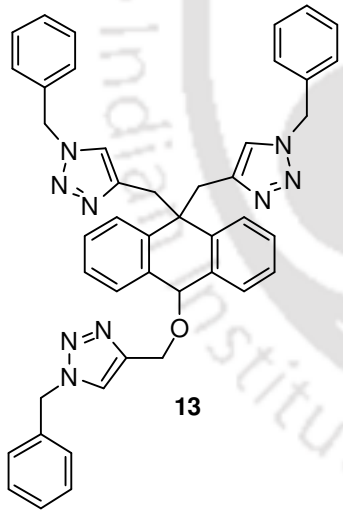
*diethyl 2,2'-(4,4'-((10-hydroxy-9,10-dihydroanthracene-9,9-diyl)bis(methylene))bis(1H-1,2,3-triazole-4,1-diyl))diacetate (**12d**)*



12d

White solid, M.p 145-146 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.65 (d, *J* = 8.0 Hz, 2H), 7.50 (d, *J* = 8.0 Hz, 2H), 7.33 (t, *J* = 7.6 Hz, 2H), 7.21 (t, *J* = 7.2 Hz, 2H), 6.17 (s, 1H), 5.95 (s, 1H), 5.20 (s, 1H), 4.72 (s, 2H), 4.70 (s, 2H), 4.68 (s, 1H), 4.08-4.02 (m, 4H), 3.74 (s, 2H), 3.66 (s, 2H), 1.15-1.11 (m, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 166.7, 166.1, 144.1, 138.3, 137.7, 128.7, 128.3, 127.6, 127.1, 126.5, 123.4, 122.9, 66.8, 62.4, 62.2, 50.6, 50.4, 46.6, 40.6, 40.3, 14.0, 13.9; **IR** (KBr)ν_{max} 3537, 3143, 2986, 2943, 1746, 1603, 1547, 1489, 1463, 1383, 1221 cm^{-1}; **Anal. calcd** for $C_{28}H_{30}N_6O_5$: C, 63.38; H, 5.70; N, 15.84. found C, 63.25; H, 5.59; N, 15.72.

*4,4'-((10-((1-benzyl-1H-1,2,3-triazol-4-yl)methoxy)-9,10-dihydroanthracene-9,9 diyl)bis(methylene))bis(1-benzyl-1H-1,2,3-triazole) (**13**)*



13

Semi-solid, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.50 (d, *J* = 8.0 Hz, 2H), 7.34-7.32 (m, 5H), 7.27-7.15 (m, 12H), 6.97-6.95 (m, 2H), 6.75 (d, *J* = 7.2 Hz, 2H), 6.28 (s, 1H), 5.71 (s, 1H), 5.42 (s, 2H), 5.11-5.09 (m, 4H), 5.07 (s, 2H), 3.81 (s, 2H), 3.71 (s, 2H), 3.64 (s, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 145.7, 144.4, 144.2, 140.2, 134.9, 134.7, 134.6, 129.0, 128.8, 128.7, 128.4, 128.3, 128.2, 128.1, 127.8, 127.2, 127.1, 126.8, 122.7, 122.5, 121.8, 74.5, 58.3, 53.9, 53.5, 53.3, 47.1, 40.7, 38.4; **IR** (KBr)ν_{max} 3135, 3061, 3031, 2925, 2847, 1603, 1544, 1496, 1453, 1325, 1217 cm^{-1}; **Anal. calcd** for $C_{44}H_{39}N_9O$: C, 74.45; H, 5.54; N, 17.76. found C, 74.32; H, 5.46; N, 17.64.

XRD for Compounds **8b** and **9b**

Complete crystallographic data of **8b** and **9b** for the structural analyses have been deposited with the Cambridge Crystallographic Data Centre, CCDC No. are 942856 and 921613 respectively. Copies of this information may be obtained free of charge from the Director,

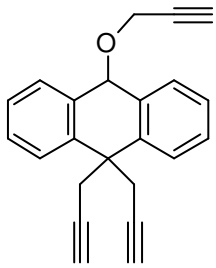
Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44-1223-336033, e-mail: deposit@ccdc.cam.ac.uk or via: www.ccdc.cam.ac.uk).

Table 6. Crystal data and structures refinement for the compounds **8b** and **9b**.

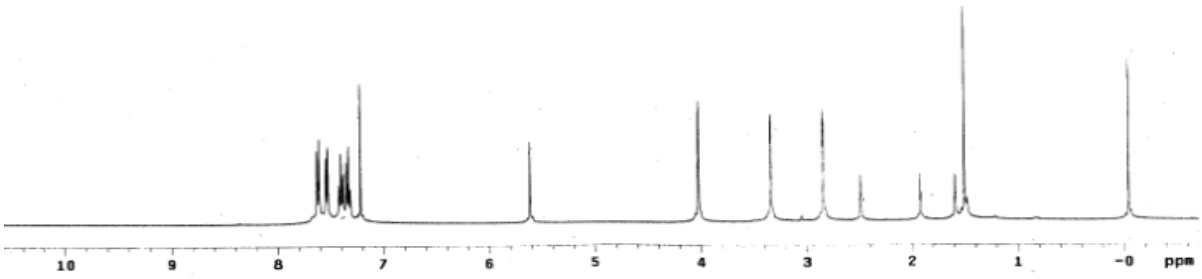
Entry	Identification code	Compound **8b**	Compound **9b**
01	Empirical formula	C_{27} H_{20} N_4 O_2	C_{34} $H_{27.05}$ N_8 $O_{5.53}$
02	Formula weight	432.47	636.09
03	Temperature	296(2) K	296(2) K
04	Wavelength	0.71073	0.71073
05	Radiation type	Mo K\a	Mo K\a
06	Radiation source	'fine-focus sealed tube'	fine-focus sealed tube
07	Crystal system	monoclinic	monoclinic
08	Space group	P 21/n	P 21/c
09	Cell length	a 12.4688(7) b 10.2492(6) c 16.9379(9)	a 17.5453(9) b 9.9306(6) c 18.5780(10)
10	Cell Angle	α 90.0 β 97.094(5)	α 90.0 β 108.562(2)
		δ 90.0	δ 90.0
11	Cell Volume	2148.0 (2)	3068.6(3)
12	Density	1.337	1.395
13	Completeness to theta	25.00° / 99.8%	25.25° / 96.9%
14	Absorption correction	multi-scan	multi-scan
15	Refinement method	Full-matrix least-squares on F2	Full-matrix least-squares on F2
16	Index ranges	-14<=h<=14, -12<=k<=6, -12<=l<=20	-20<=h<=19, -11<=k<=11, -22<=l<=22
17	Reflection number	3780	5375
18	Theta range	2.94-25.00	1.22-25.25
19	Cell formula units Z	4	4

20	CCDC no	942856	921613

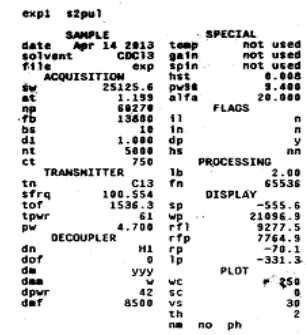
***^{1}H NMR (400 MHz, $CDCl_3$)**: 10,10-diprop-2-ynyl-9-(prop-2-yn-1-oxy)-9,10-dihydroanthracene (**5**)*

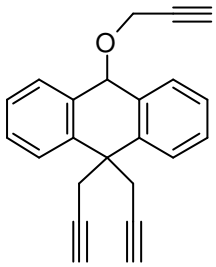


5



***^{13}C NMR (100 MHz, $CDCl_3$)**: 10,10-diprop-2-ynyl-9-(prop-2-yn-1-oxy)-9,10-dihydroanthracene (**5**)*





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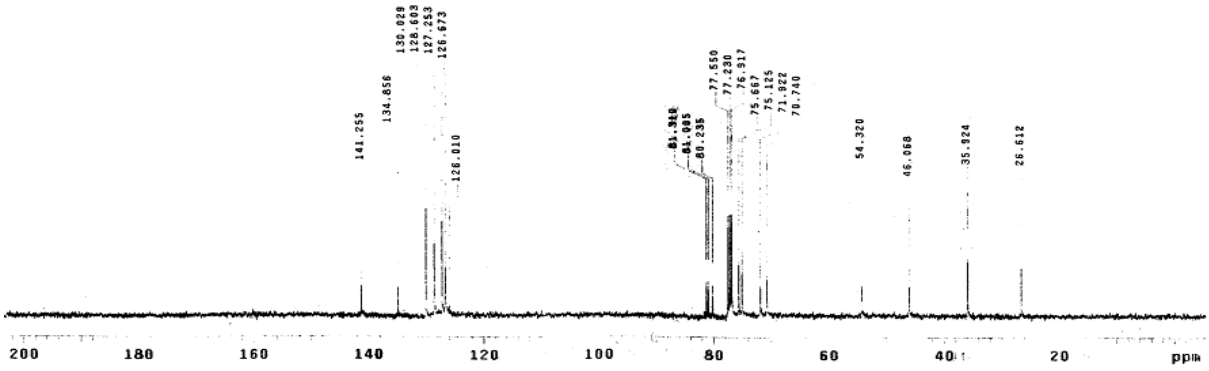
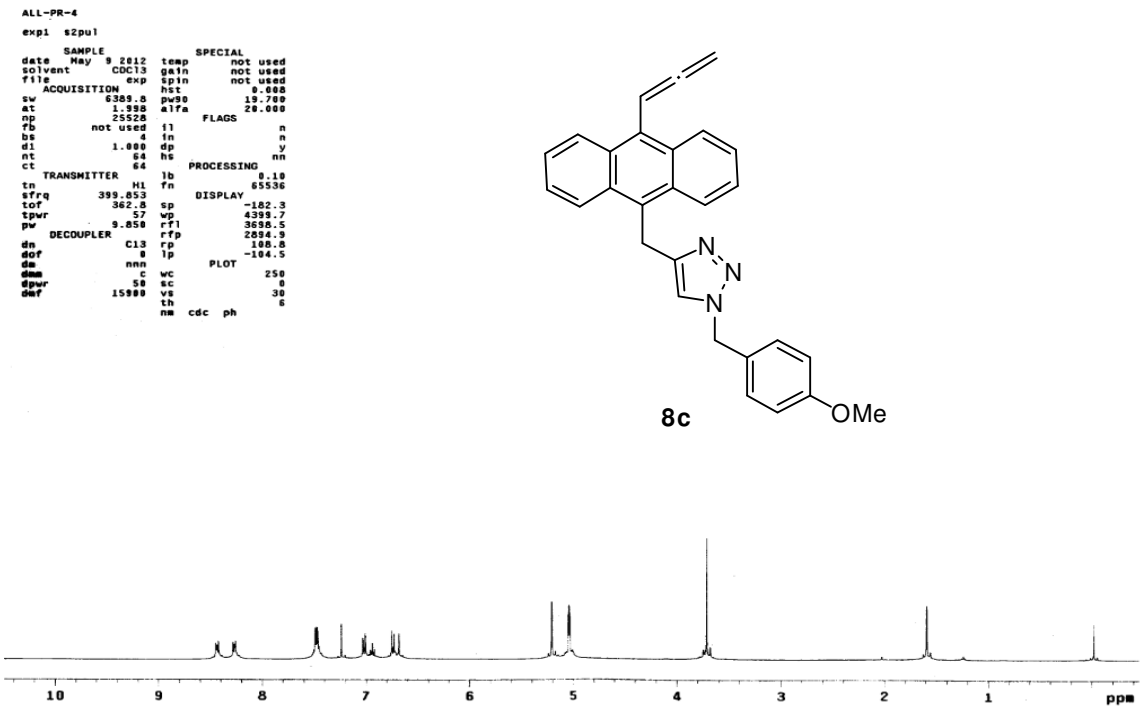
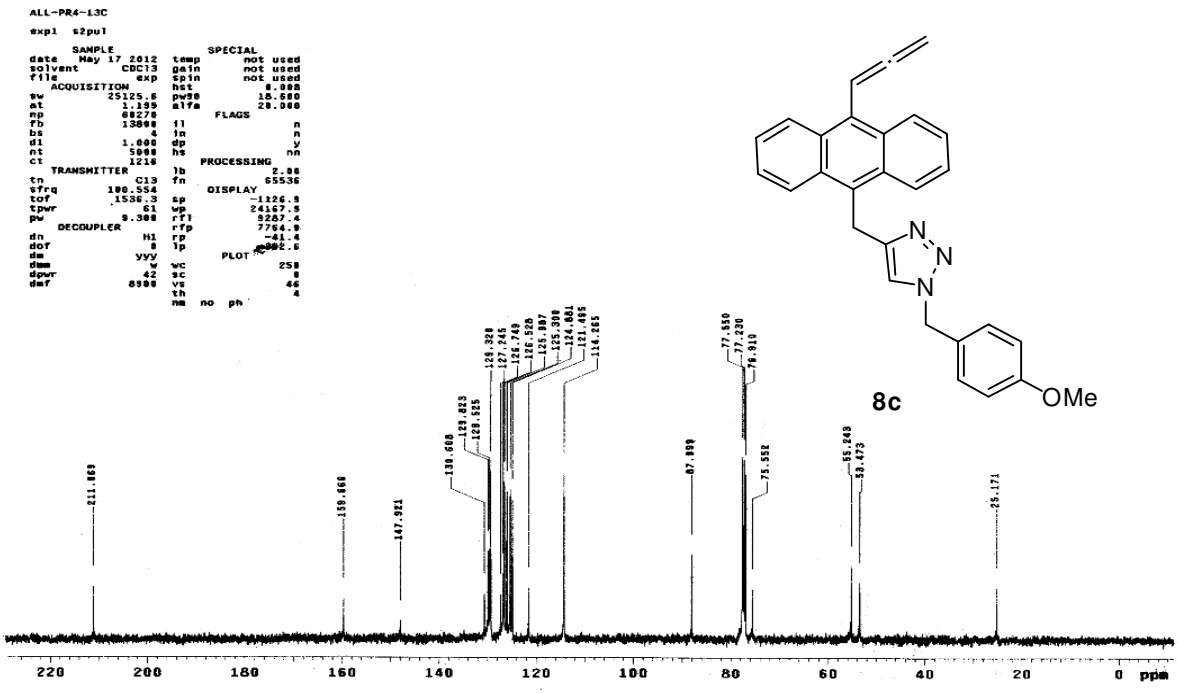


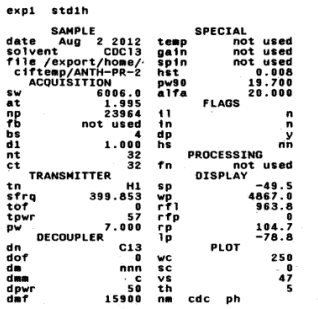
***^{1}H NMR (400 MHz, $CDCl_3$)**: 1-(4-methoxybenzyl)-4-((9-(propa-1,2-dienyl)anthracen-10-yl)methyl)-1H-1,2,3-triazole (**8c**)*

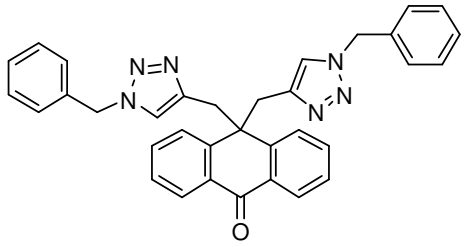


***^{13}C NMR (100 MHz, $CDCl_3$)**: 1-(4-methoxybenzyl)-4-((9-(propa-1,2-dienyl)anthracen-10-yl)methyl)-1H-1,2,3-triazole (**8c**)*

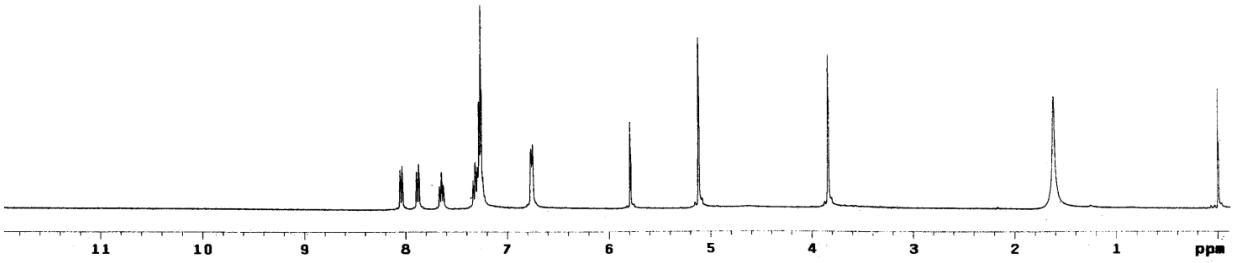


^{1}H NMR (400 MHz, $CDCl_3$): *10,10-bis((1-benzyl-1H-1,2,3-triazol-4-yl)methyl)anthracen-9(10H)-one (**9a**)*

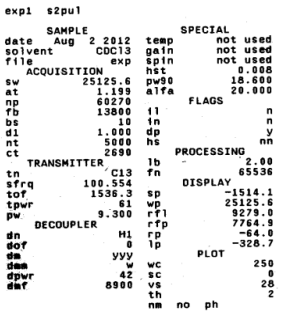


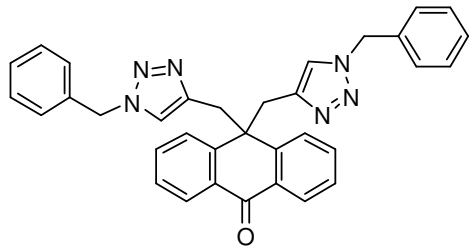


9a

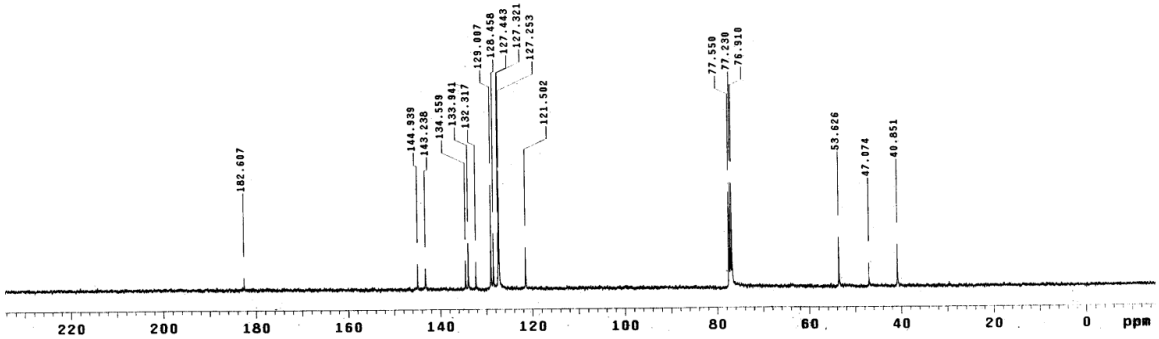


^{13}C NMR (100 MHz, $CDCl_3$): *10,10-bis((1-benzyl-1H-1,2,3-triazol-4-yl)methyl)anthracen-9(10H)-one (**9a**)*

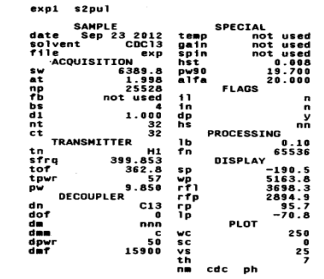


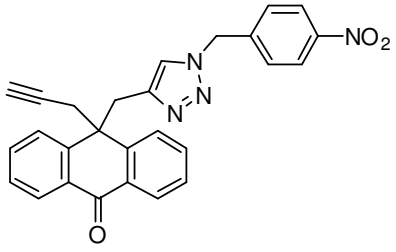


9a



^{1}H NMR (400 MHz, $CDCl_3$): *10-((1-(4-nitrobenzyl)-1H-1,2,3-triazol-4-yl)methyl)-10-(prop-2-yn-1-yl)anthracen-9(10H)-one (**10**)*





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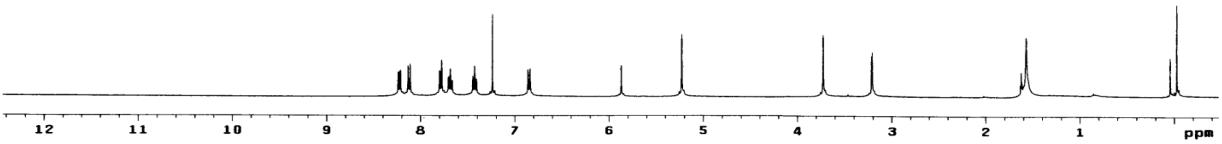
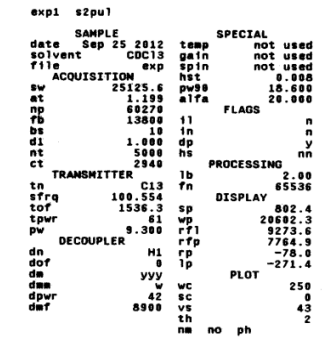
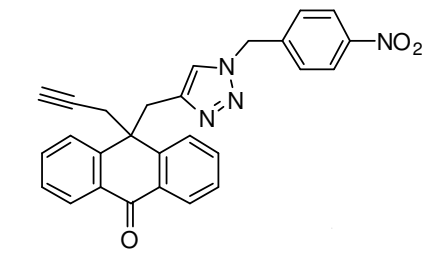


^{13}C NMR (100 MHz, $CDCl_3$): *10-((1-(4-nitrobenzyl)-1H-1,2,3-triazol-4-yl)methyl)-10-(prop-2-yn-1-yl)anthracen-9(10H)-one (**10**)*





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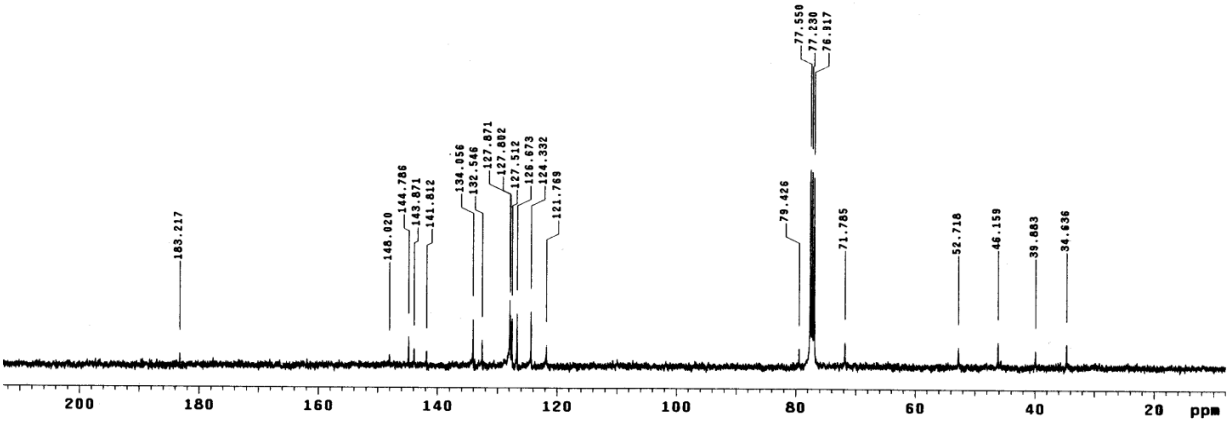
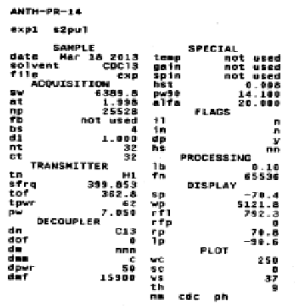
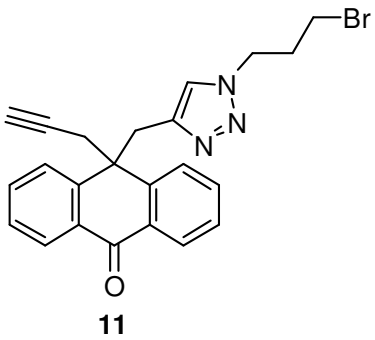
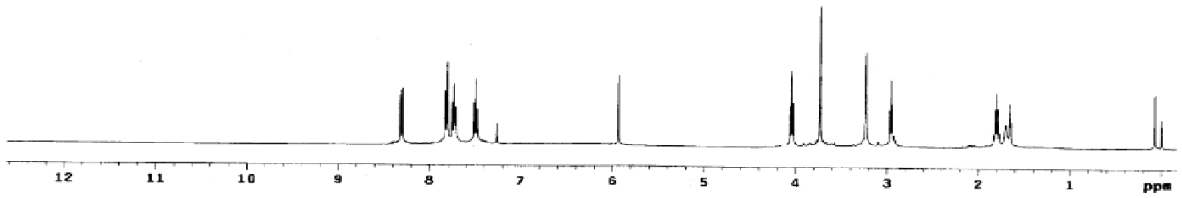


***^{1}H NMR (400 MHz, $CDCl_3$)**: 10-((1-(3-bromopropyl)-1H-1,2,3-triazol-4-yl)methyl)-10-(prop-2-yn-1-yl)anthracen-9(10H)-one (**11**)*

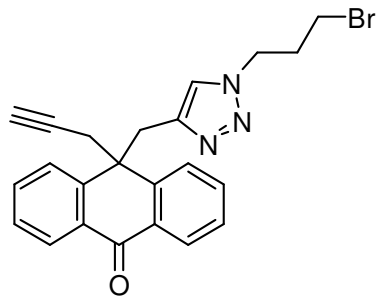




11



***^{13}C NMR (400 MHz, $CDCl_3$)**: 10-((1-(3-bromopropyl)-1H-1,2,3-triazol-4-yl)methyl)-10-(prop-2-yn-1-yl)anthracen-9(10H)-one (**11**)*



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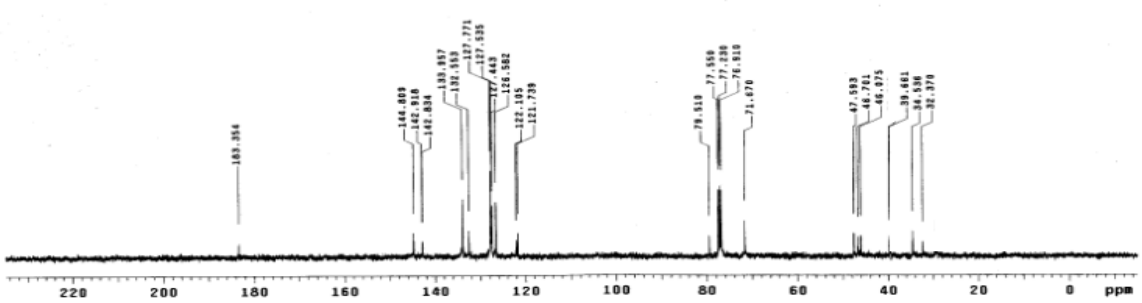
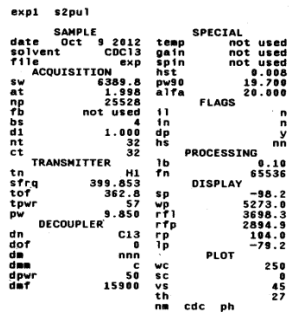
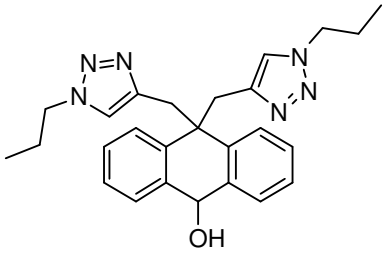
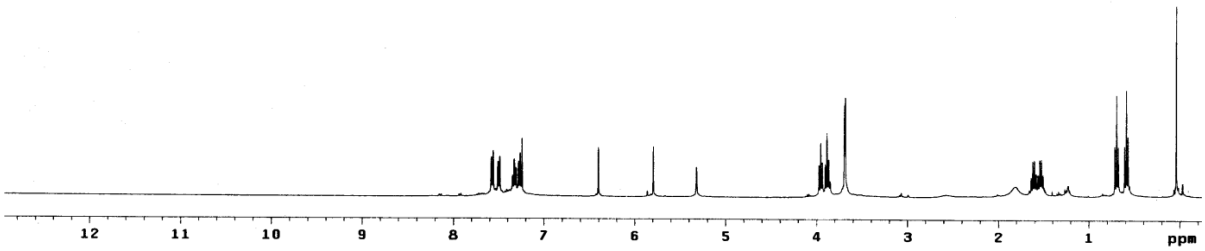


*^{1}H NMR (400 MHz, $CDCl_3$): 10,10-bis((1-propyl-1H-1,2,3-triazol-4-yl)methyl)-9,10-dihydroanthracen-9-ol (**12c**)*

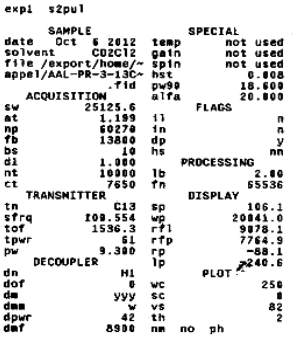


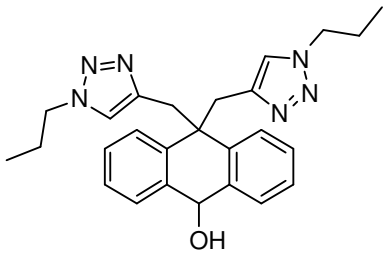


12c

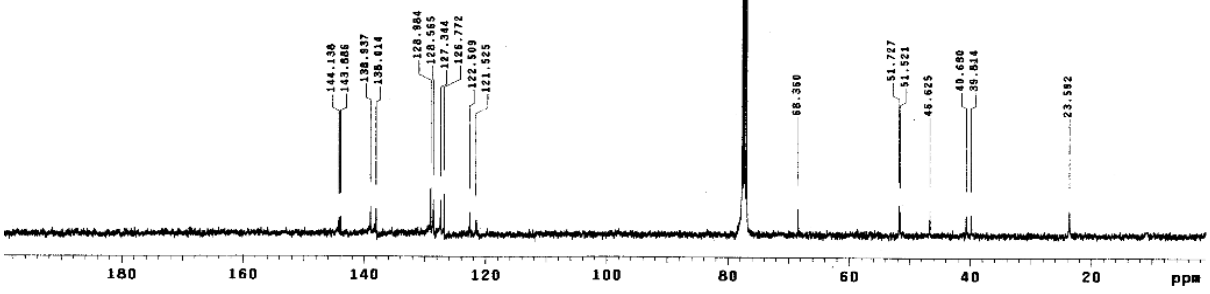


*^{13}C NMR (400 MHz, $CDCl_3$): 10,10-bis((1-propyl-1H-1,2,3-triazol-4-yl)methyl)-9,10-dihydroanthracen-9-ol (**12c**)*

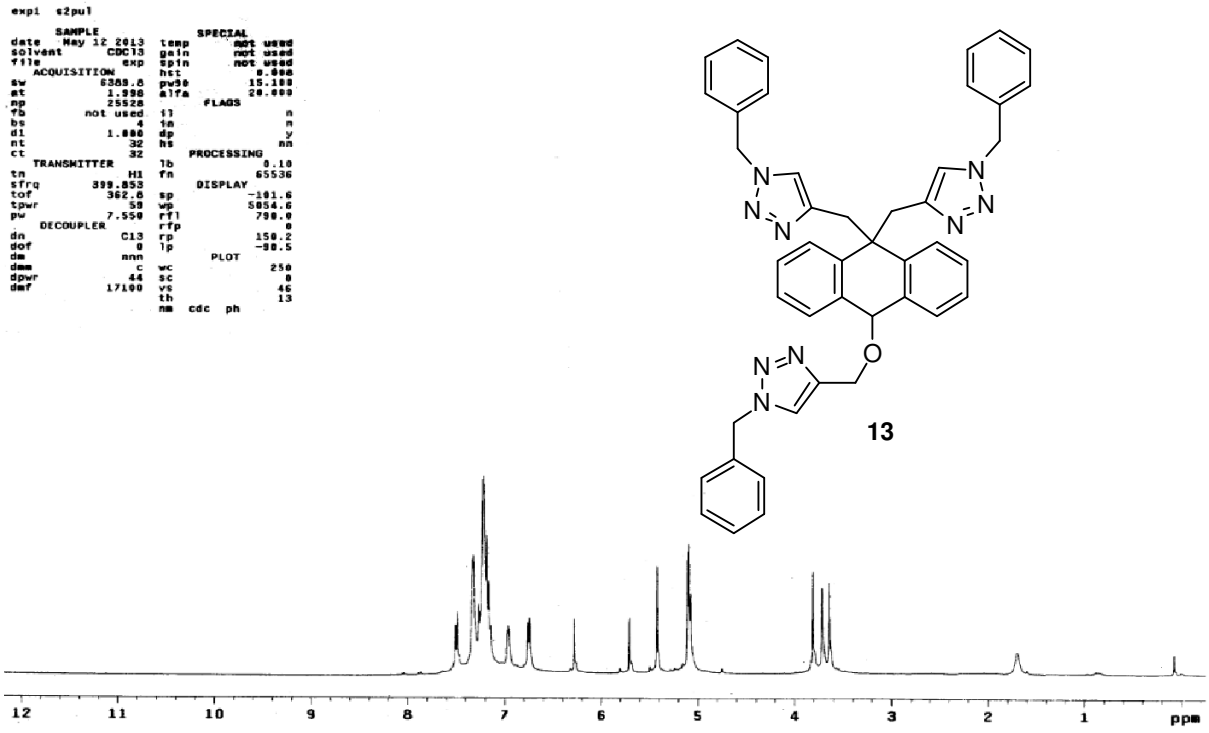




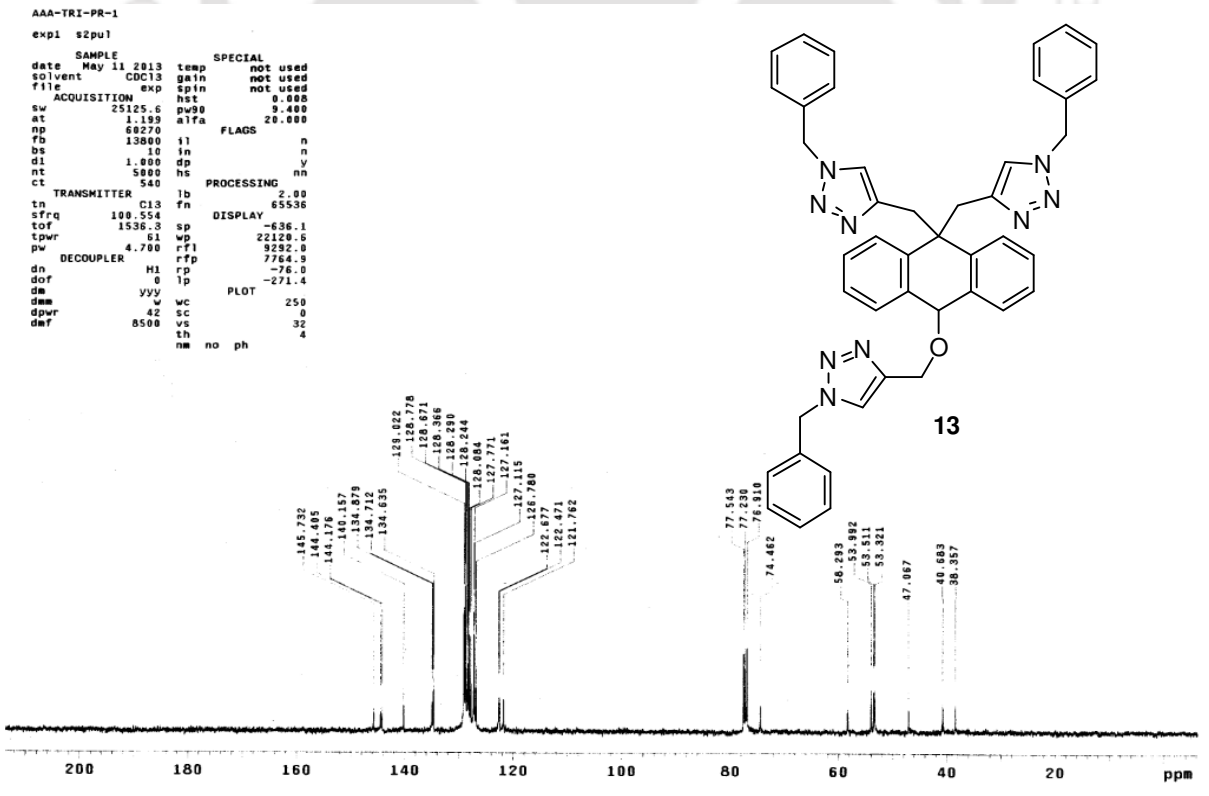
12c



*^{1}H NMR (400 MHz, $CDCl_3$): 4,4'-((10-((1-benzyl-1H-1,2,3-triazol-4-yl)methoxy)-9,10-dihydroanthracene-9,9 diyl)bis(methylene))bis(1-benzyl-1H-1,2,3-triazole) (**13**)*



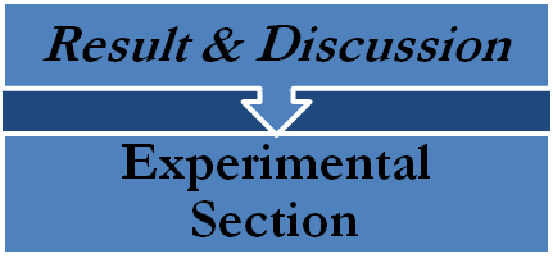
*^{13}C NMR (400 MHz, $CDCl_3$): 4,4'-((10-((1-benzyl-1H-1,2,3-triazol-4-yl)methoxy)-9,10-dihydroanthracene-9,9 diyl)bis(methylene))bis(1-benzyl-1H-1,2,3-triazole) (**13**)*



Part A

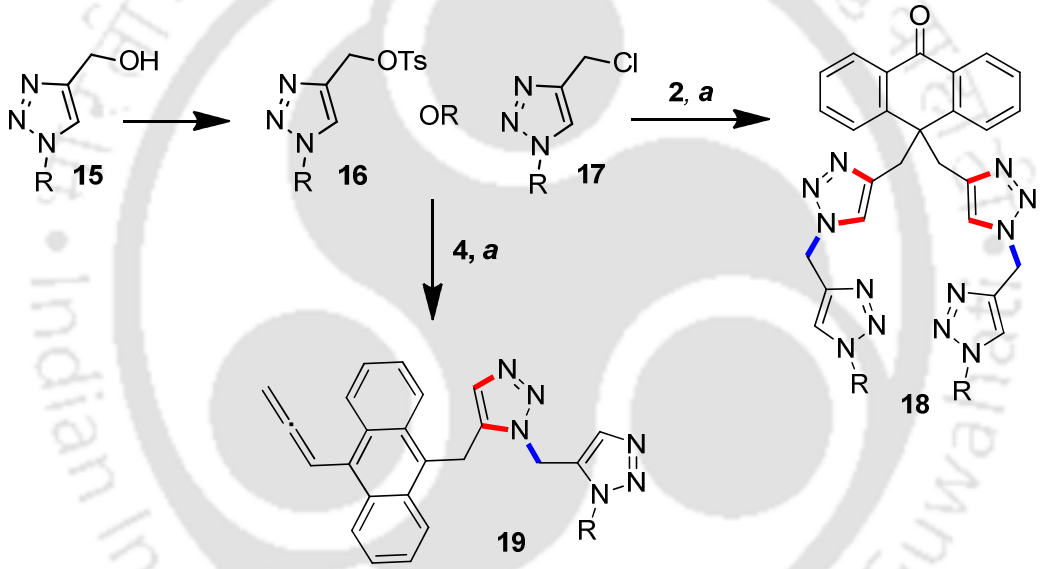
Chapter IIB

Click precursor in 'Click Chemistry' for the synthesis of bis-di-triazolyl-anthrone and di-triazolyl-allenyl-anthracene in one-pot three component reaction catalyzed by cuprous oxide nanoparticle in aqueous medium



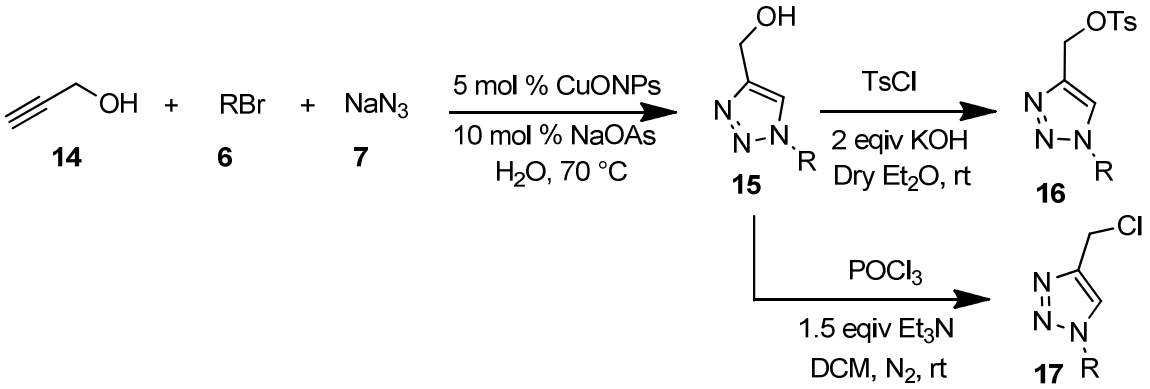
Results and Discussion

In the previous section of this Chapter IIA, we have developed a highly efficient method for the synthesis of various 1,4-triazole based new organic molecules i.e. mono-, bis- and tris-triazole derivatives by employing copper oxide nanoparticles along with sodium ascorbate as a catalyst. The use of excess amount of copper oxide nanoparticles along with the reductant sodium ascorbate brings some limitations to this method which prompted us to look for an alternative protocol which would be free from these short comings. The facts envisaged us that cuprous oxide nanoparticle might be an useful catalyst for the synthesis of 1,4-triazole based organic molecules. In this Chapter, we would like to report the synthesis of bis-di-triazolyl-anthrone and di-triazolyl-allenyl-anthracene derivatives using cuprous oxide nanoparticles as a catalyst which is depicted in Scheme 31.



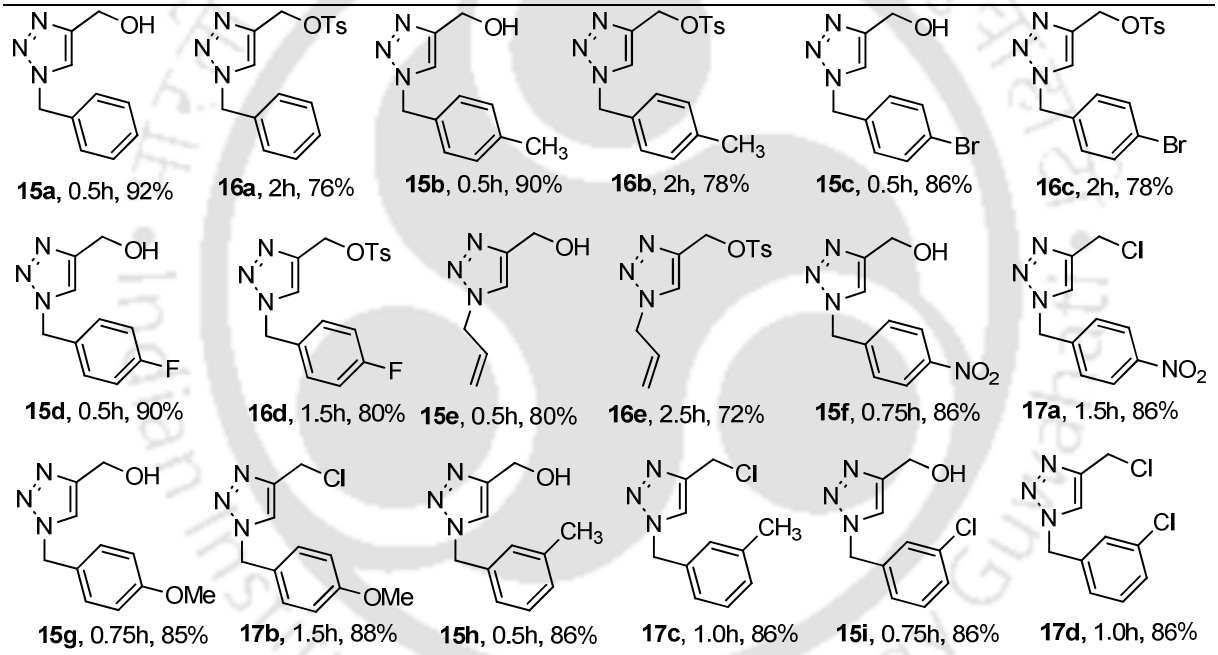
Scheme 31. *Synthesis of bis-di-triazolyl-anthrone and di-triazolyl-allenyl-anthracene derivatives, Reagents & condition: (**a**) NaN_3 (1 mmol), nano Cu_2O (0.05 mmol), water, 70 °C.*

The key starting material, (1-alkyl-1H-1,2,3-triazol-4-yl)methanol (**15**) was synthesized from sodium azide (**7**), alkyl bromide (**6**) and propargyl alcohol (**14**) in the presence of catalytic amount of copper oxide nanoparticle along with sodium ascorbate in water at 70 °C. Next, the product **15** on tosylation with tosyl chloride and potassium hydroxide in dry Et_2O at room temperature gave (1-alkyl-1H-1,2,3-triazol-4-yl)methyl 4-methylbenzenesulfonate (**16**) simultaneously it was also chlorinated to 4-(chloromethyl)-1-alkyl-1H-1,2,3-triazole (**17**) in the presence of $POCl_3$, tri-ethyl amine and DCM at room temperature. The outline for the present strategy is shown in Scheme 32.



Scheme 32. *Synthesis of (1-alkyl-1H-1,2,3-triazol-4-yl)methyl 4-methylbenzenesulfonate (**16**) and 4-(chloromethyl)-1-alkyl-1H-1,2,3-triazole (**17**) derivatives*

The representative examples for the required key starting material **15**, **16** and **17** are given below in terms of reaction time and percentage of yields.



[a]*All the reactions were carried out using 5 mmol scale.*[b]*Isolated yields.*

All the products **15**, **16** and **17** were characterized using IR, ^{1}H NMR and ^{13}C NMR spectra. In addition, the structure of compound **17a** was confirmed through single X-ray data as shown in Figure 10.

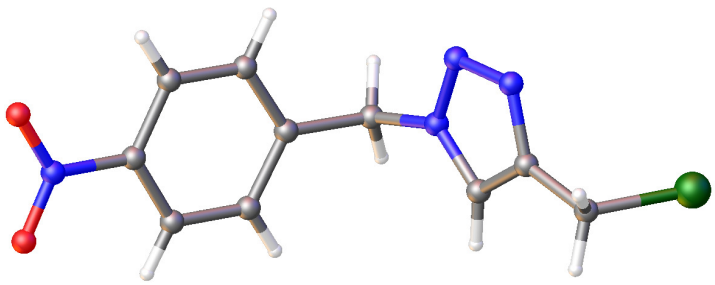
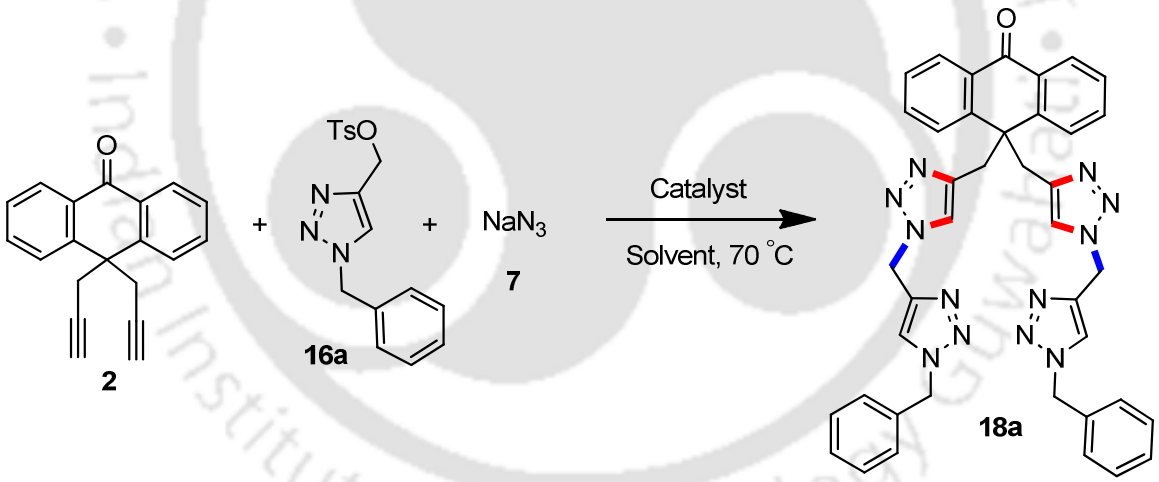


Figure 10. Single crystal X-ray structure of **17a**

Next, we examined the three-component one pot reaction of 10,10-dipropargyl-9-anthrone (**2**), the synthesized product **16a** and sodium azide (**7**) in the presence of 5 mol% of CuI under aqueous condition at 70 °C for 5 hour. To our delight the product **18a** was obtained in 52% yield (Table 7, entry 1). The isolated product **18a** was characterized by IR, ^{1}H and ^{13}C NMR spectra and HRMS. With an effort to improve the yield of the product the set of same reaction was again performed in the presence of other Cu(I) salts like CuBr, CuCl and also with different solvents such as ethanol, H_2O / PEG which proved futile (Table 7, entries 2-3) as the yield of the product was not increased satisfactorily (Table 7, entries 2-5). These results prompted us to look forward to cuprous oxide nanoparticles as catalyst with various solvents and the results are summarised in Table 7. Surprisingly, the yield of the product increased significantly to 84% when 5 mol% Cu_2ONPs was used as catalyst under aqueous condition and the time period was also reduced to 1 hour (Table 7, entry 11).

Table 7. Optimization of the reaction conditions for the synthesis of bis-di-triazolyl-9-anthrone[a]



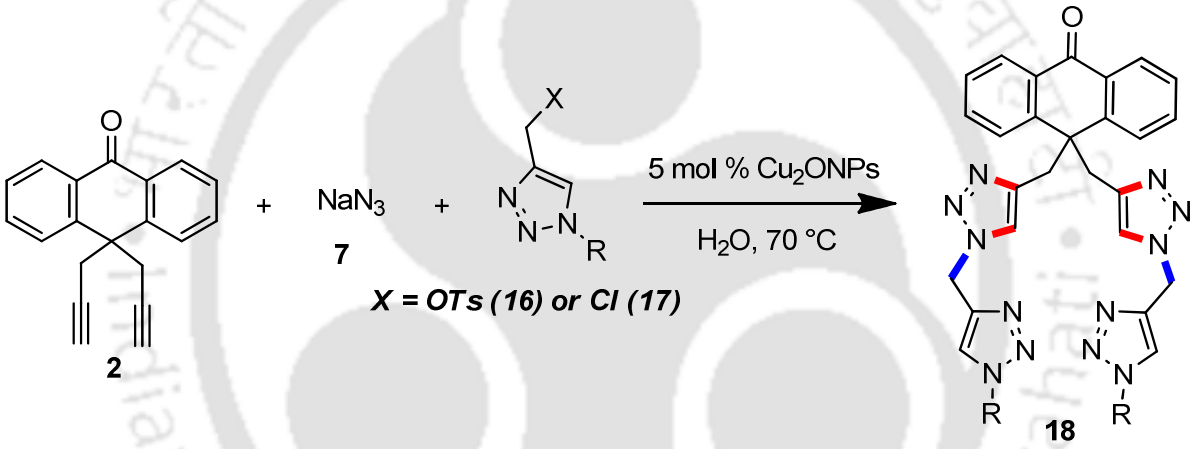
Entry	Catalyst (Mol%)	Solvent	Time (h)	Yield (%)[b]
1	CuI (5)	H_2O	5	52
2	CuBr (5)	H_2O	5	46
3	CuCl (5	H_2O	5	38
4	CuI (5)	EtOH	8	58
5	CuI (5)	H_2O/PEG	3	65
6	Cu_2ONPs (5)	EtOH	4	56
7	Cu_2ONPs (5)	DMSO	5	70
8	Cu_2ONPs (5)	DMF	5	62

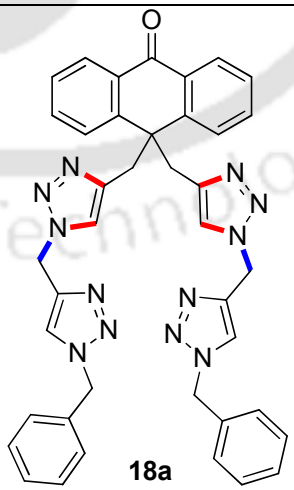
9	Cu_2ONPs (5)	H_2O/PEG	3	72
10	Cu_2ONPs (5)	THF	4	68
11	**Cu_2ONPs (5)**	**H_2O**	**1**	**84**
12	Cu_2ONPs (10)	H_2O	1.5	80

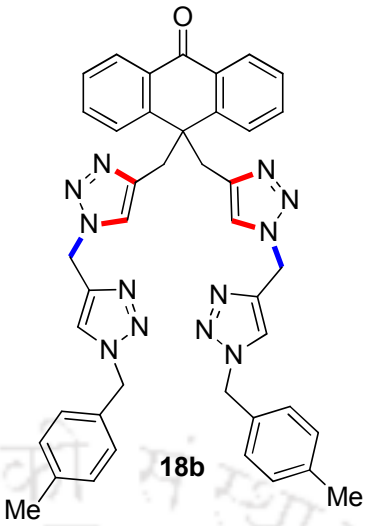
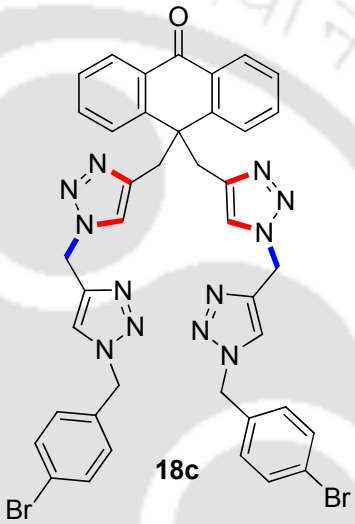
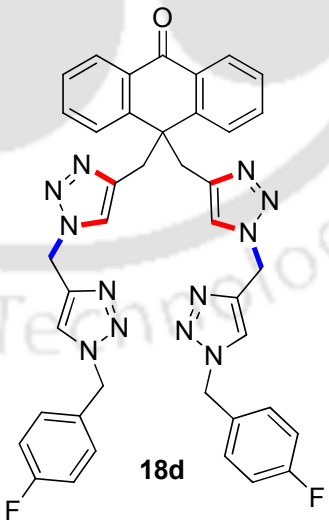
[a]*All the reaction were carried out using 0.5 mmol scale using 10,10-dipropargyl-9-anthrone (**2**), (1-(benzyl)-1,2,3-triazol-4-yl)methyl 4-methylbenzenesulfonate (**16a**) and sodium azide (**7**).* [b]*Isolated yield.*

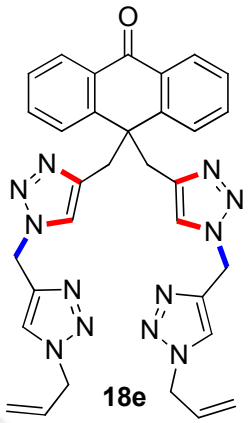
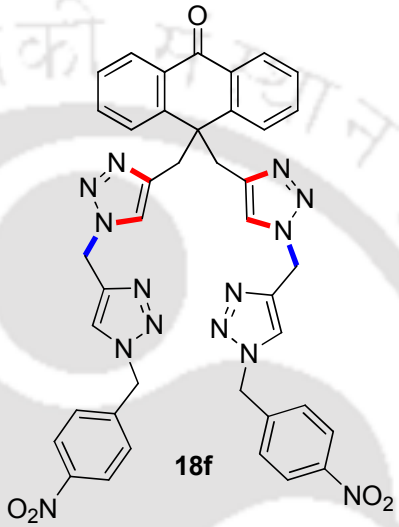
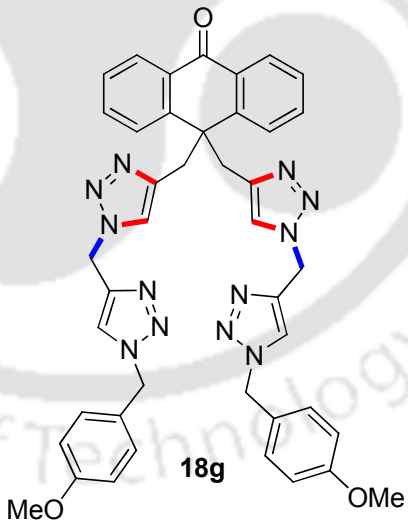
Increasing the catalyst load to 10 mol% didn't help much (Table 7, entry 12). Thus, the 5 mol% Cu_2ONPs under aqueous medium provided the optimum conditions for the synthesis bis-di-triazolyl-anthrone derivatives.

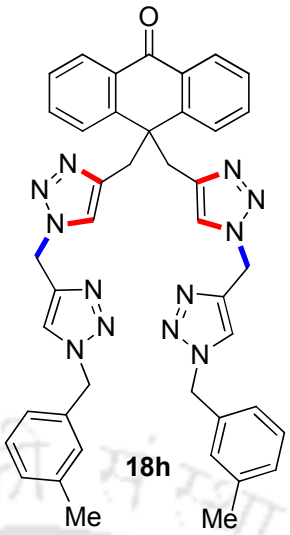
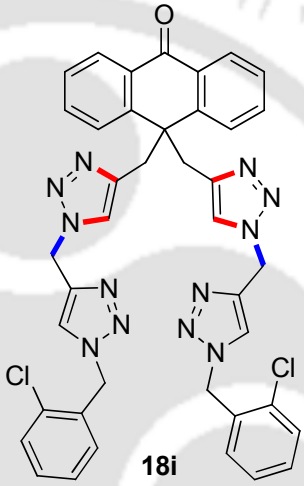
Table 8. Synthesis of bis-di-triazolyl-anthrone derivatives (**18**) using nano Cu_2O as catalyst[a]



Entry	X, R (**16 or 17**)	Product (**6**)	Time (h)	% Yield[b]
1	X = OTs, Benzyl (**16a**)	 **18a**	1	84

2	X = OTs, 4-Methybenzyl(**16b**)	 **18b**	1	86
3	X = OTs, 4-Bromobenzyl(**16c**)	 **18c**	1	82
4	X = OTs, 4-Fluorobenzyl (**16d**)	 **18d**	0.5	86

5	X = OTs, Allyl (**16e**)	 **18e**	1	75
6	X = Cl, 4-Nitrobenzyl (**17a**)	 **18f**	1.5	76
7	X = Cl, 4-Methoxybenzyl(**16c**)	 **18g**	1.5	78

8	X = Cl, 3-Methylbenzyl(**16c**)	 **18h**	1.5	76
9	X = Cl, 2-Chlorobenzyl(**16c**)	 **18i**	1.5	74

*[a]The reactions were performed in 0.5 mmol scale using 10,10-dipropargyl-9-anthrone (**2**), (1-(alkyl)-1,2,3-triazol-4-yl)methyl 4-methylbenzenesulfonate (**16**)/4-(chloromethyl)-1-alkyl-1H-1,2,3-triazole (**17**) and sodium azide (**5**). [b]Isolated yield.*

After optimization of the reaction conditions, the scope of the reaction was expanded with various synthesized product **16** or **17**. A mixture of 10,10-dipropargyl-9-anthrone (**2**), sodium azide (**7**) and the synthesized compound (**16b**) in the presence of 5 mol% of Cu_2ONPs under identical reaction conditions afforded the desired product **18b** in 86% yield (Table 8, entry 2). The synthesized tosylated products (**16c-d**) having para substituents such as Br and F in the aromatic ring lead to the isolation of the products **18c–d** in good yields (Table 8, entries 3–4) under the identical reaction conditions. Next the methodology was also extended with aliphatic tosylated product (**16e**) and the desired product **18e** was obtained in 75% yield (Table 8, entry 5).

The scope of the present protocol was further scrutinized with the other synthesized chlorinated products (**17a-d**), 10,10-dipropargyl-9-anthrone (**2**) and sodium azide (**7**) under

the identical reaction condition and the products **18f-i** were obtained in good yields (Table 8, entries 6-9). All of these products were fully characterized by ^{1}H NMR, ^{13}C NMR spectra and HRMS.

Moreover, the recyclability of catalyst was also tested in the following way. A reaction was carried out with 10,10-dipropargyl-9-anthrone (**2**), sodium azide (**7**) and the synthesized compound **16a** in 5 mmol scale in the presence of 5 mol% of cuprous oxide nanoparticle under aqueous condition. After complication of the reaction, catalyst was easily removed by filtration from the reaction mixture and recovered simply by washing with organic solvent (EtOAc) and dried under vacuum and then reused for at least five times without observation significant decrease in activity as shown in Figure 11.

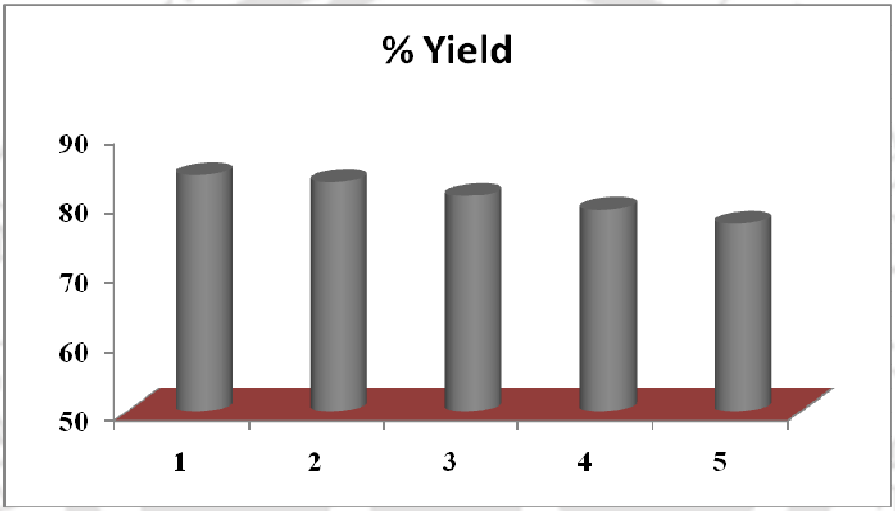
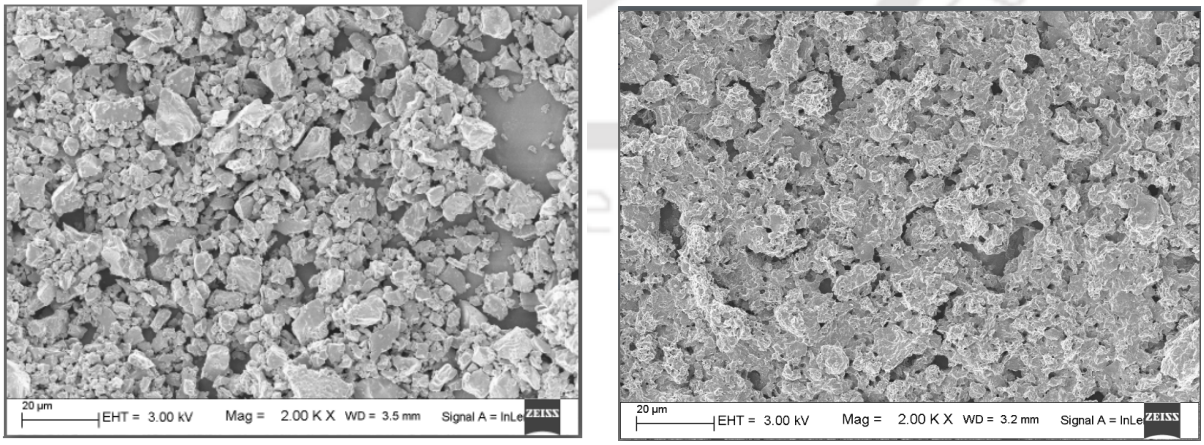


Figure 11. Recyclability of cuprous oxide nanoparticle of **18a**



(A) **(B)**

Figure 12. (**A**) FESEM image of Cu_2O nanoparticle before recycling and (**B**) FESEM image of Cu_2O nanoparticle after five times recycling.

In addition, the FESEM image and the powder X-ray data of catalyst after recycling did not show a significant change in the morphology (Figure 12B) and peak value of cuprous oxide nanoparticle (Figure 13) respectively. These successful results clearly indicates that the catalyst Cu_2O nanoparticle is recyclable and was not affected under the reaction conditions of this protocol.

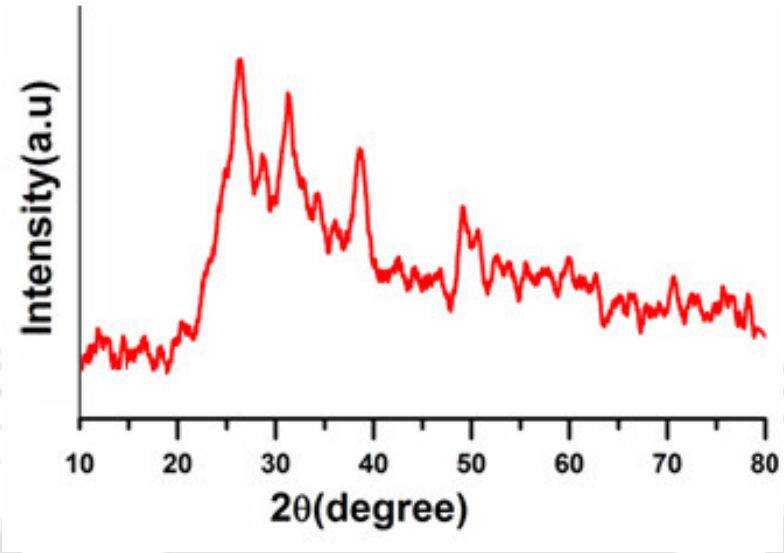
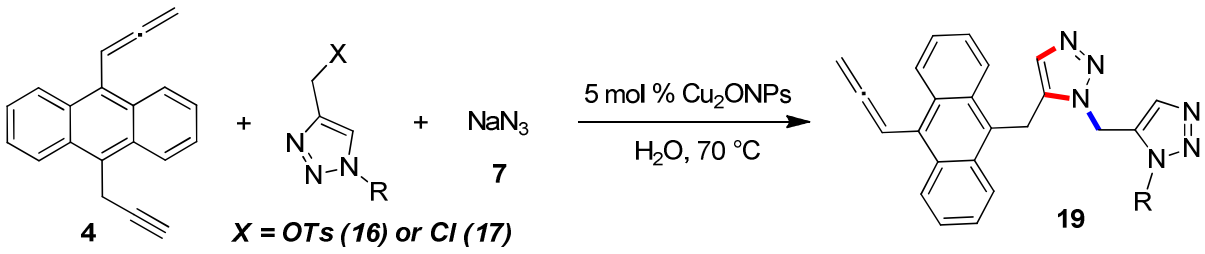
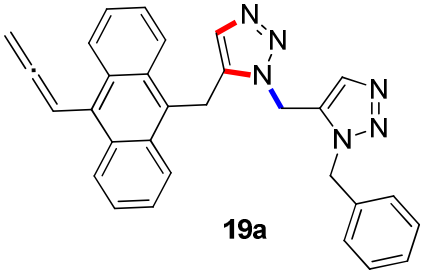
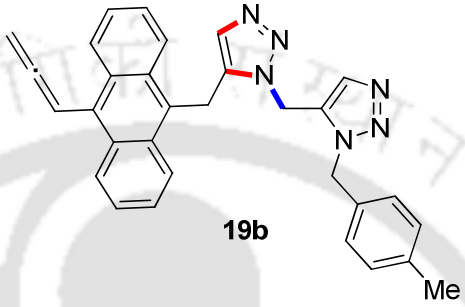
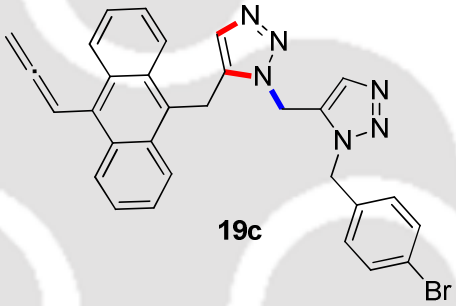
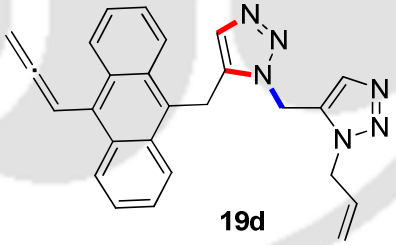
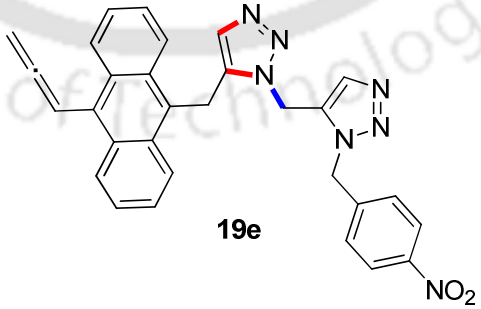


Figure 13. XRD patterns of Cu_2O nanoparticle after five times recycling

Inspired with the success of the above transformation, the generality of the reaction was further explored for the synthesis of di-triazolyl-9-allenyl-anthracene using 9-allenyl-10-prop-2-ynyl-anthracene (**4**) the synthesized compounds **16a-c** along with sodium azide (**7**) in the presence of **5** mol% cuprous oxide nanoparticles in water at 70 °C which lead to the isolation of products **19a-c** in good yield (Table 9, entries 1-3). Moreover, the present protocol was also scrutinized with aliphatic tosylated product (**16e**) and the desired product **19d** was obtained in 76% yield (Table 9, entry 4). Finally, the reaction with 9-allenyl-10-prop-2-ynyl-anthracene (**4**), the synthesized chlorinated product **17a** and sodium azide in a similar manner gave the product **19e** (Table 9, entry 5) in 78% yield.

Table 9. Synthesis of di-1,4-disubstituted-1,2,3-triazolyl-9-allenyl-anthracene **19**[a]



Entry	X, R (**16 or 17**)	Product (**19**)	Time (h)	% Yield[b]
1	X = OTs Benzyl (**16a**)	 **19a**	0.5	84
2	X = OTs 4-Methybenzyl(**16b**)	 **19b**	0.5	86
3	X = OTs 4-Bromobenzyl(**16d**)	 **19c**	0.5	80
4	X = OTs Allyl (**16e**)	 **19d**	1.0	76
5	X = Cl, 4-Nitrobenzyl (**17a**)	 **19e**	0.75	78

[a]*The reactions were performed in 0.5 mmol scale 9-allenyl-10-prop-2-ynyl-anthracene (**4**), (1-(alkyl)-1,2,3-triazol-4-yl)methyl 4-methylbenzenesulfonate (**16**)/4-(chloromethyl)-1-alkyl-1H-1,2,3-triazole (**17**) and sodium azide (**7**).*[b]*Isolated yield.*

All these di-triazolyl-allenyl-anthracene derivatives were fully characterized from ^{1}H & ^{13}C NMR spectra and HRMS.

In conclusion, we have demonstrated a simple and efficient strategy for the synthesis of bis-di-triazolyl-anthrone and di-triazolyl-9-allenyl-anthracene starting from the synthesized compounds **16** or **17**, sodium azide and 10,10-dipropargyl-9-anthrone (**2**) / 9-allenyl-10-prop-2-ynyl-anthracene (**4**) in the presence of 5 mol% cuprous oxide nanoparticle in water at 70 °C. The salient features of the present protocol are recyclability of the catalyst, environmentally benign, variety of substrate compatibility, simpler reaction procedure, shorter reaction time and good yields. Moreover, these triazole derivatives were reported first time in the literature using cuprous oxide nanoparticle as catalyst.

Experimental

*General experimental procedure for the Synthesis of (1-alkyl-1,2,3-triazol-4-yl)methanol (**15**)*

To a mixture of sodium azide (**7**, 10 mmol), alkyl/benzyl bromides (**6**, 10 mmol) and propargylic alcohol (**14**, 10 mmol) was added in 25 mL water followed by catalytic amount of CuO nanoparticle (39.7 mg) and sodium ascorbate (198 mg). Then the reaction mixture was kept for stirring at 70 °C till the completion of reaction as indicated by TLC. The reaction mixture was extracted with DCM (3 x 30 mL), dried over anhydrous Na_2SO_4, concentrated in vacco and finally purified by silica gel column chromatography to obtain the desired products **15**.

*General procedure for synthesis of (1-alkyl-1H-1,2,3-triazol-4-yl)methyl 4-methylbenzenesulfonates (**16**)*

Into a 50 mL two neck round bottomed flask was taken a mixture of KOH (6 mmol) and tosyl chloride (5 mmol) in dry Et_2O (10 mL). The suspension was cooled to 0 °C. The synthesized compound (1-alkyl-1H-1,2,3-triazol-4-yl)methanol (**15**, 5 mmol), was dissolved in 10 mL dry Et_2O and was added drop wise to the above suspension of reaction mixture. Then the mixture was stirred at room temperature. At the end of reaction, it was extracted with additional Et_2O, washed with brine solution and the organic phase obtained was dried over anhydrous Na_2SO_4 and the solvent was evaporated under vacuum. The crude product was purified by column chromatography using as eluent of a mixture of hexane/ethyl acetate and to get the pure product 16.

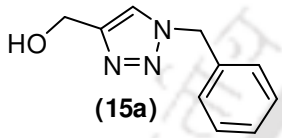
*General procedure for preparation of 4-(chloromethyl)-1-alkyl-1H-1,2,3-triazoles (**17**)*

In a 50 mL two neck flask under nitrogen atmosphere was added the synthesized (1-alkyl-1H-1,2,3-triazol-4-yl)methanol (**15**, 5 mmol) and Et_3N (6 mmol) in 15 mL dry DCM. After stirring the mixture at room temperature for 5 min, $POCl_3$ (0.51 mL, 5.5 mmol) was added drop wise into it. After completion of the reaction, it was extracted with DCM (2 x 15 mL) and the organic extract was dried over anhydrous Na_2SO_4 followed by the removal of solvent in a rotary evaporator. Then the crude residue was purified over a silica gel column chromatography using as an eluent mixture of hexane/ethyl acetate to obtain the pure products of 4-(chloromethyl)-1-alkyl-1H-1,2,3-triazoles **17**.

*General experimental protocol for synthesis of bis-di-triazolyl-anthrones (**18**) and di-triazolyl-allenyl-anthracenes (**19**)*

In a 25 mL round bottomed flask was added the starting material 10,10-dipropargyl-9-anthrone (**2**, 0.5 mmol), sodium azide (**7**, 0.5 mmol) and the synthesized products **16** or **17** in 3 mL of water. Then, Cu_2O nanoparticle (3.58 mg) was added into the above reaction mixture and was kept for heating at 70 ˚C. After completion of the reaction as indicated by TLC, it was extracted with DCM (2 x 15 mL) and the organic layer was dried over anhydrous Na_2SO_4 and evaporated in vacuo. Then the crude residue was purified on silica gel column chromatography affording the pure products of bis-di-triazolyl-anthrones **18**. The similar reaction procedure was followed for the synthesis of di-triazolyl-allenyl-anthracenes **19**.

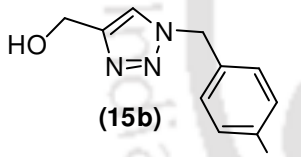
*(1-benzyl-1H-1,2,3-triazol-4-yl)methanol (**15a**)*



(15a)

White solid, M.p 78-79 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.51 (s, 1H), 7.32-7.31 (m, 3H), 7.23-7.21 (m, 2H), 5.44 (s, 2H), 4.69 (s, 2H), 4.23 (br s, 1H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 148.8, 134.6, 129.1, 128.8, 128.2, 122.4, 56.0, 54.2; **IR** (KBr)ν_{max} 3265, 3139, 3086, 3030, 2935, 2882, 1605, 1551, 1456, 1371, 1325, 1222, 1132, 1014 cm^{-1}.

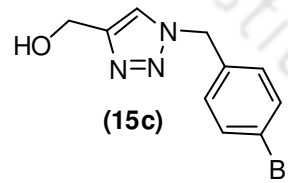
*(1-(4-methylbenzyl)-1H-1,2,3-triazol-4-yl)methanol (**15b**)*



(15b)

White solid, M.p 91-92 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.43 (s, 1H), 7.12 (br s, 4H), 5.39 (s, 2H), 4.67 (s, 2H), 3.89 (br s, 1H), 2.29 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 148.3, 138.5, 131.5, 129.6, 128.1, 122.2, 55.7, 53.9, 21.1; **IR** (KBr)ν_{max} 3252, 3140, 3086, 3050, 2945, 2917, 1612, 1553, 1515, 1446, 1375, 1330, 1223, 1134, 1013 cm^{-1}.

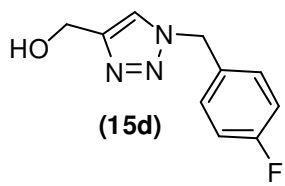
*(1-(4-bromobenzyl)-1H-1,2,3-triazol-4-yl)methanol (**15c**)*



(15c)

White solid, M.p 224-225 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.47 (d, *J* = 8.4 Hz, 2H), 7.44 (s, 1H), 7.12 (d, *J* = 8.4 Hz, 2H), 5.44 (s, 2H), 4.74 (s, 2H), 2.33 (br s, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 148.2, 133.6, 131.1, 129.1, 121.5, 121.5, 55.0, 52.2; **IR** (KBr)ν_{max} 3259, 3115, 3063, 2957, 2866, 1591, 1543, 1489, 1465, 1407, 1357, 1336, 1230, 1126, 1064, 1012 cm^{-1}.

*(1-(4-fluorobenzyl)-1H-1,2,3-triazol-4-yl)methanol (**15d**)*

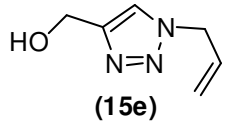


(15d)

White solid, M.p 68-69 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.53 (s, 1H), 725-7.21 (m, 2H), 7.02-6.97 (m, 2H), 5.42 (s, 2H), 4.82 (br s, 1H), 4.68 (s, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 163.8, 161.3, 148.3, 130.6, 130.5, 129.9, 129.8, 122.1, 115.9, 115.7, 55.6, 53.1;

IR (KBr)ν_{max} 3291, 3144, 3000, 2949, 2877, 1606, 1546, 1511, 1460, 1420, 1366, 1229, 1157, 1127, 1006 cm^{-1}.

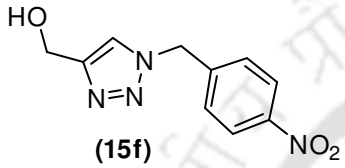
*(1-allyl-1H-1,2,3-triazol-4-yl)methanol (**15e**)*



(15e)

White solid, M.p 81-82 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.59 (s, 1H), 6.04-5.95 (m, 1H), 5.35 (d, *J* = 10.4 Hz, 1H), 5.30 (d, *J* = 17.2 Hz, 1H), 4.96 (d, *J* = 6.4 Hz, 2H), 4.75 (s, 2H), 3.48 (br s, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 148.2, 131.2, 122.1, 120.1, 55.8, 52.6; **IR** (KBr)ν_{max} 3266, 3147, 3092, 2933, 2877, 1646, 1553, 1457, 1435, 1420, 1336, 1225, 1141, 1056, 1011 cm^{-1}.

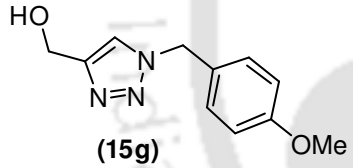
*(1-(4-nitrobenzyl)-1H-1,2,3-triazol-4-yl)methanol (**15f**)*



(15f)

White solid, M.p 129-130 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.24 (d, *J* = 8.8 Hz, 2H), 7.54 (s, 1H), 7.42 (d, *J* = 8.4 Hz, 2H), 5.65 (s, 2H), 4.82 (d, *J* = 5.2 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 148.0, 146.6, 141.8, 127.8, 122.9, 121.8, 54.7, 51.5; **IR** (KBr)ν_{max} 3263, 3114, 3066, 2973, 2944, 2860, 1611, 1537, 1494, 1470, 1351, 1229, 1128, 1014 cm^{-1}.

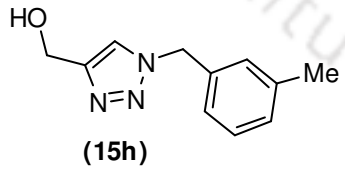
*(1-(4-methoxybenzyl)-1H-1,2,3-triazol-4-yl)methanol (**15g**)*



(15g)

White semi-solid, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.42 (s, 1H), 7.22 (d, *J* = 8.4 Hz, 2H), 6.88 (d, *J* = 8.4 Hz, 2H), 5.43 (s, 2H), 4.73 (s, 2H), 7.80 (s, 3H), 3.27 (br s, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 159.7, 148.2, 129.6, 126.6, 121.9, 114.3, 55.7, 55.2, 53.5; **IR** (KBr)ν_{max} 3107, 3062, 2942, 2841, 1611, 1514, 1452, 1438, 1359, 1298, 1249, 1220, 1180, 1057, 1006 cm^{-1}.

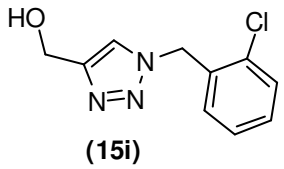
*(1-(3-methylbenzyl)-1H-1,2,3-triazol-4-yl)methanol (**15h**)*



(15h)

White solid, M.p 71-72 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.24-7.20 (m, 2H), 7.10 (s, 1H), 7.09 (s, 2H), 5.39 (s, 2H), 4.91 (s, 2H), 2.20 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 143.5, 139.0, 134.3, 129.7, 129.1, 125.5, 58.9, 55.3, 21.4; **IR** (KBr)ν_{max} 3116, 3068, 2949, 2847, 1609, 1519, 1455, 1439, 1357, 1296, 1244, 1222, 1185, 1054, 1009 cm^{-1}.

*(1-(2-chlorobenzyl)-1H-1,2,3-triazol-4-yl)methanol (**15i**)*

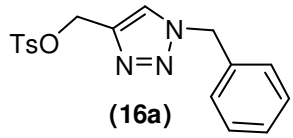


(15i)

White semi-solid, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.67 (s, 1H), 7.29-7.26 (m, 2H), 7.24 (s, 1H), 7.14-7.12 (m, 1H), 5.46 (s, 2H), 4.74 (s, 2H), 4.52 (br s, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 136.4, 134.9,

130.5, 129.1, 128.3, 126.4, 55.2, 53.8; **IR** (KBr)ν_{max} 3111, 3063, 2945, 2839, 1610, 1519, 1458, 1428, 1349, 1296, 1243, 1222, 1177, 1056, 1008 cm^{-1}.

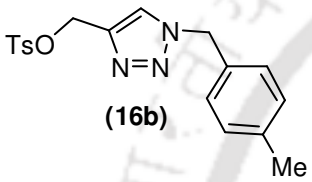
*(1-benzyl-1H-1,2,3-triazol-4-yl)methyl 4-methylbenzenesulfonate (**16a**)*



(16a)

White semi-solid, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.75 (d, *J* = 8.4 Hz, 2H), 7.49 (s, 1H), 7.36 (s, 3H), 7.29 (d, *J* = 8.4 Hz, 2H), 7.24 (s, 2H), 5.47 (s, 2H), 5.14 (s, 2H), 2.41 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 145.2, 141.4, 134.2, 132.9, 130.1, 129.3, 129.1, 128.3, 128.1, 124.1, 63.3, 54.4, 21.8; **IR** (KBr)ν_{max} 3107, 3062, 2941, 2851, 1637, 1608, 1557, 1497, 1451, 1373, 1251, 1179, 1125, 1035, 1011 cm^{-1}; HR**MS** (ESI) Calcd For $C_{17}H_{18}N_3O_3S$ 344.1064 ($M + H^+$); Found 344.1068.

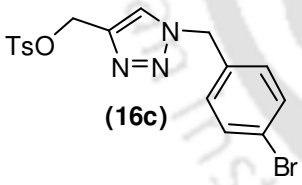
*(1-(4-methylbenzyl)-1H-1,2,3-triazol-4-yl)methyl 4-methylbenzenesulfonate (**16b**)*



(16b)

White semi-solid, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 7.76 (d, *J* = 8.4 Hz, 2H), 7.48 (s, 1H), 7.30 (d, *J* = 8.4 Hz, 2H), 7.18 (d, *J* = 7.8 Hz, 2H), 7.14 (d, *J* = 8.4 Hz, 2H), 5.43 (s, 2H), 5.14 (s, 2H), 2.43 (s, 3H), 2.35 (s, 3H);, **^{13}C NMR** (150 MHz $CDCl_3$): δ 145.1, 141.2, 138.9, 132.9, 130.0, 129.9, 128.9, 128.3, 128.0, 123.9, 63.8, 54.2, 21.7, 21.2; **IR** (KBr)ν_{max} 3115, 3069, 3009, 2953, 2845, 1641, 1610, 1561, 1499, 1459, 1377, 1247, 1181, 1128, 1039, 1015 cm^{-1}.

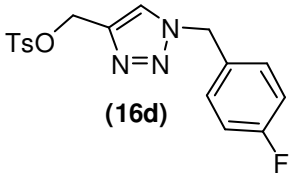
*(1-(4-bromobenzyl)-1H-1,2,3-triazol-4-yl)methyl 4-methylbenzenesulfonate (**16c**)*



(16c)

White semi-solid, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.77 (d, *J* = 7.6 Hz, 2H), 7.56 (s, 1H), 7.53-7.49 (m, 2H), 7.31 (d, *J* = 7.6 Hz, 2H), 7.12 (d, *J* = 7.6 Hz, 2H) 5.45 (s, 2H), 5.16 (s, 2H), 2.44 (s, 3H); **^{13}C NMR** (100 MHz $CDCl_3$): δ 145.3, 141.9, 140.4, 132.4, 132.2, 132.1, 130.1, 129.8, 128.0, 125.8, 63.5, 53.6, 21.8; **IR** (KBr)ν_{max} 3109, 3063, 2947, 2855, 1639, 1611, 1554, 1495, 1446, 1369, 1248, 1177, 1123, 1031, 1008 cm^{-1}.

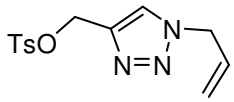
*(1-(4-fluorobenzyl)-1H-1,2,3-triazol-4-yl)methyl 4-methylbenzenesulfonate (**16d**)*



(16d)

White semi-solid, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 7.69 (d, *J* = 8.4 Hz, 2H), 7.49 (s, 1H), 7.24 (d, *J* = 7.8 Hz, 2H), 7.19-7.16 (m, 2H), 7.00-6.97 (m, 2H), 5.39 (s, 2H), 5.09 (s, 2H), 2.36 (s, 3H); **^{13}C NMR** (100 MHz $CDCl_3$): δ 164.1, 161.7, 145.3, 141.6, 140.6, 132.6, 130.2, 130.0, 129.0, 127.9, 125.9, 116.3, 116.1, 63.1, 53.6, 21.7; **IR** (KBr)ν_{max} 3119, 3068, 2937, 2859, 1643, 1609, 1554, 1498, 1449, 1379, 1238, 1187, 1129, 1039, 1005 cm^{-1}.

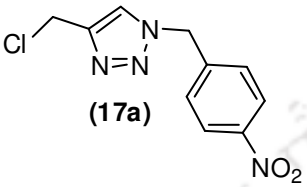
*(1-allyl-1H-1,2,3-triazol-4-yl)methyl 4-methylbenzenesulfonate (**16e**)*



(16e)

White semi-solid, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.74 (d, *J* = 8.4 Hz, 2H), 7.59 (s, 1H), 7.30 (d, *J* = 7.6 Hz, 2H), 5.92-5.90 (m, 1H), 5.30 (d, *J* = 10.0 Hz, 1H), 5.22 (d, *J* = 16.8 Hz, 1H), 5.14 (s, 2H), 4.90 (d, *J* = 6.4 Hz, 2H), 2.40 (s, 3H); **^{13}C NMR** (100 MHz $CDCl_3$): δ 145.5, 140.9, 140.0, 129.9, 127.9, 125.8, 123.9, 120.5, 63.2, 52.8, 21.6; **IR** (KBr)ν_{max} 3147, 3081, 2941, 2875, 1645, 1613, 1553, 1458, 1436, 1421, 1338, 1215, 1149, 1046, 1011 cm^{-1}.

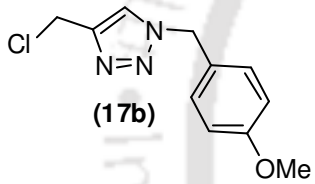
*4-(chloromethyl)-1-(4-nitrobenzyl)-1H-1,2,3-triazole (**17a**)*



(17a)

White solid, M.p 115-116 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.21 (d, *J* = 8.0 Hz, 2H), 7.61 (s, 1H), 7.41 (d, *J* = 7.6 Hz, 2H), 5.64 (s, 2H), 4.68 (s, 2H); **^{13}C NMR** (100 MHz $CDCl_3$): δ 145.8, 141.5, 128.8, 124.5, 124.4, 123.2, 53.4, 36.1; **IR** (KBr)ν_{max} 3153, 3110, 3075, 2964, 2850, 1609, 1520, 1477, 1343, 1260, 1169, 1158, 1105, 1041 cm^{-1}; HR**MS** (ESI) Calcd For $C_{10}H_{10}ClN_4O_2$ 253.0487 ($M + H^+$); Found 253.0495.

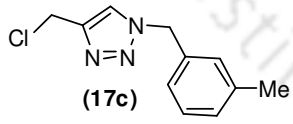
*4-(chloromethyl)-1-(4-methoxybenzyl)-1H-1,2,3-triazole (**17b**)*



(17b)

White solid, M.p 109-110 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.48 (s, 1H), 7.21 (d, *J* = 8.4 Hz, 2H), 6.88 (d, *J* = 8.4 Hz, 2H), 5.42 (s, 2H), 4.64 (s, 2H), 3.78 (s, 3H); **^{13}C NMR** (100 MHz $CDCl_3$): δ 160.1, 129.9, 126.3, 122.7, 114.6, 110.1, 55.4, 53.9, 36.3; **IR** (KBr)ν_{max} 3116, 3072, 3000, 2955, 2932, 2848, 1610, 1585, 1463, 1344, 1261, 1177, 1126, 1030 cm^{-1}; HR**MS** (ESI) Calcd For $C_{11}H_{13}ClN_3O$ 238.0742 ($M + H^+$); Found 238.0736.

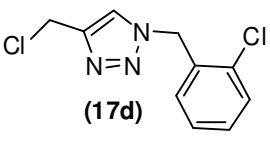
*4-(chloromethyl)-1-(3-methylbenzyl)-1H-1,2,3-triazole (**17c**)*



(17c)

White solid, M.p 93-94 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.49 (s, 1H), 7.25-7.15 (m, 2H), 7.08 (s, 2H), 5.47 (s, 2H), 4.67 (s, 2H), 2.33 (s, 3H); **^{13}C NMR** (100 MHz $CDCl_3$): δ 145.2, 139.3, 134.2, 129.9, 129.3, 129.1, 125.4, 122.9, 54.6, 36.3, 21.5; **IR** (KBr)ν_{max} 3135, 3075, 3023, 2955, 2919, 2856, 1611, 1573, 1439, 1340, 1262, 1219, 1124, 1077, 1051 cm^{-1}; HR**MS** (ESI) Calcd For $C_{11}H_{13}ClN_3$ 222.0793 ($M + H^+$); Found 22.0799.

*1-(2-chlorobenzyl)-4-(chloromethyl)-1H-1,2,3-triazole (**17d**)*

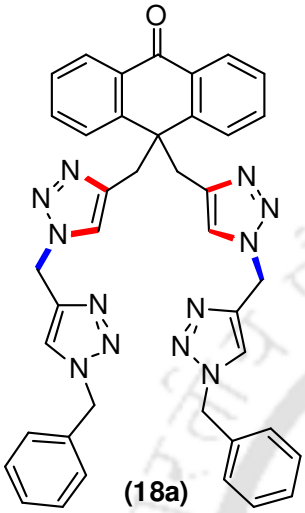


(17d)

White solid, M.p 77-78 ˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 7.55 (s, 1H), 7.22-7.20 (m, 2H), 7.16 (s, 1H), 7.05 (d, *J* = 8.4 Hz, 1H), 5.39 (s, 2H), 4.57 (s, 2H); **^{13}C NMR** (150 MHz $CDCl_3$): δ 144.9, 136.3, 134.8,

130.4, 130.2, 128.9, 126.2, 122.9, 53.4, 36.1; **IR** (KBr)ν_{max} 3130, 3077, 2953, 2851, 1600, 1577, 1435, 1342, 1266, 1220, 1123, 1078, 1053 cm^{-1}; **MS** (ESI) Calcd For $C_{10}H_{10}Cl_2N_3$ 242.0247 ($M + H^+$); Found 242.0296.

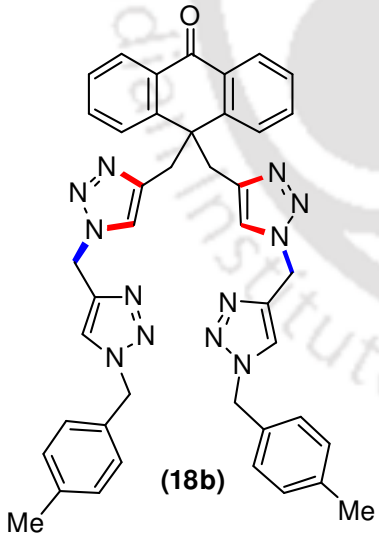
*10,10-bis((1-((1-benzyl-1H-1,2,3-triazol-4-yl)methyl)-1H-1,2,3-triazol-4-yl)methyl) anthracen-9(10H)-one (**18a**)*



(18a)

Colourless oily, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.92 (d, *J* = 8.0 Hz, 4H), 7.70 (t, *J* = 7.2 Hz, 2H), 7.39-7.37 (m, 4H), 7.34 (t, *J* = 7.2 Hz, 4H), 7.29-7.27 (m, 4H), 7.04 (s, 2H), 6.01 (s, 2H), 5.54 (s, 4H), 5.21 (s, 4H), 3.81 (s, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 182.9, 144.8, 143.2, 142.3, 134.4, 134.2, 132.2, 129.2, 128.9, 128.3, 127.7, 127.2, 126.8, 122.5, 121.5, 54.3, 47.2, 45.3, 40.6; **IR** (KBr)ν_{max} 3137, 3065, 2946, 1652, 1600, 1497, 1456, 1325, 1222, 1124, 1049 cm^{-1}; HR**MS** (ESI) Calcd For $C_{40}H_{35}N_{12}O$ 699.3052 ($M + H^+$); Found 699.3056.

*10,10-bis((1-((1-(4-methylbenzyl)-1H-1,2,3-triazol-4-yl)methyl)-1H-1,2,3-triazol-4-yl)methyl) anthracen-9(10H)-one (**18b**)*

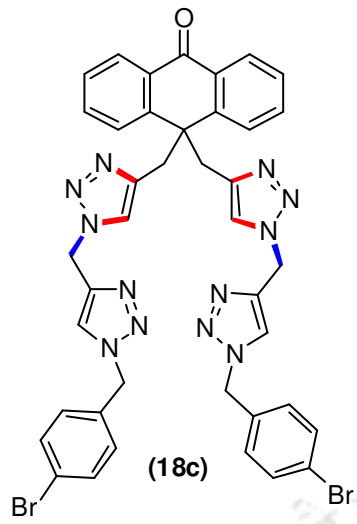


(18b)

Colourless oily, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.89 (dd, *J* = 11.2 Hz, 8.0 Hz, 4H), 7.66 (t, *J* = 7.6 Hz, 2H), 7.31 (t, *J* = 7.6 Hz, 2H), 7.16 (br s, 6H), 7.14 (s, 2H), 6.99 (s, 2H), 5.97 (s, 2H), 5.67 (s, 4H), 5.17 (s, 4H), 3.78 (s, 4H), 2.33 (s, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 183.0, 144.9, 143.3, 142.3, 139.0, 134.3, 132.3, 131.4, 129.9, 128.4, 127.8, 127.6, 127.3, 127.2, 127.0, 122.4, 121.5, 54.3, 47.3, 45.4, 40.8, 21.3; **IR** (KBr)ν_{max} 3142, 3053, 2916, 2848, 1653, 1601, 1463, 1324, 1264, 1218, 1128, 1049 cm^{-1}; **HRMS** (ESI) Calcd For $C_{42}H_{39}N_{12}O$ 727.3365 ($M + H^+$); Found 727.3370.

*10,10-bis((1-((1-(4-bromobenzyl)-1H-1,2,3-triazol-4-yl)methyl)-1H-1,2,3-triazol-4-yl)methyl) anthracen-9(10H)-one (**18c**)*

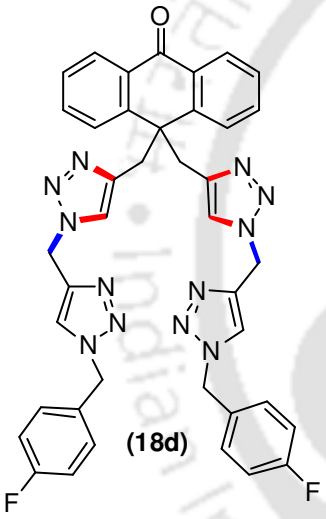
Colourless oily, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.90 (dd, *J* = 15.2 Hz, 8.0 Hz, 4H), 7.72 (t, *J* = 7.6 Hz, 2H), 7.50 (d, *J* = 8.0 Hz, 4H), 7.34 (t, *J* = 7.6 Hz, 2H), 7.15 (d, *J* = 8.0 Hz, 4H), 6.99 (s, 2H), 5.97 (s, 2H), 5.48 (s, 4H), 5.21 (s, 4H), 3.81 (s, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 183.1, 144.9, 143.3, 142.5, 134.3, 133.5, 132.4, 132.2, 129.9, 127.8, 127.3, 126.8,



(18c)

123.1, 122.5, 121.5, 53.6, 47.2, 45.3, 40.7; **IR** (KBr)ν_{max} 3137, 3065, 2929, 2853, 1653, 1600, 1546, 1489, 1459, 1325, 1267, 1222, 1125, 1050 cm^{-1}; **HRMS** (ESI) Calcd For $C_{40}H_{33}Br_2N_{12}O$ 855.1262 ($M + H^+$); Found 855.1275.

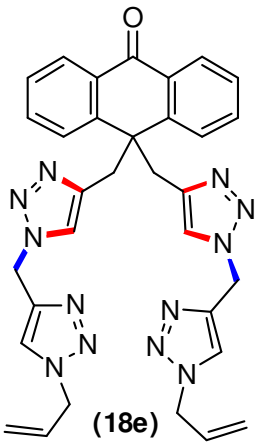
*10,10-bis((1-((1-(4-fluorobenzyl)-1H-1,2,3-triazol-4-yl)methyl)-1H-1,2,3-triazol-4-yl)methyl) anthracen-9(10H)-one (**18d**)*



(18d)

Colourless oily, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.93 (t, *J* = 8.0 Hz, 4H), 7.73 (t, *J* = 8.4 Hz, 2H), 7.36 (t, *J* = 7.6 Hz, 2H), 7.31-7.28 (m, 4H), 7.08 (t, *J* = 8.4 Hz, 4H), 7.03 (s, 2H), 6.01 (s, 2H), 5.52 (s, 4H), 5.23 (s, 4H), 3.83 (s, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 183.1, 164.3, 161.8, 144.9, 143.3, 142.5, 134.3, 132.2, 130.3, 130.2, 127.8, 127.3, 126.9, 122.4, 121.5, 116.4, 116.2, 53.6, 47.3, 45.3, 40.7; **IR** (KBr)ν_{max} 3138, 3070, 2950, 2846, 1652, 1601, 1547, 1511, 1459, 1325, 1267, 1223, 1125, 1050 cm^{-1}; **HRMS** (ESI) Calcd For $C_{40}H_{33}F_2N_{12}O$ 735.2863 ($M + H^+$); Found 735.2882.

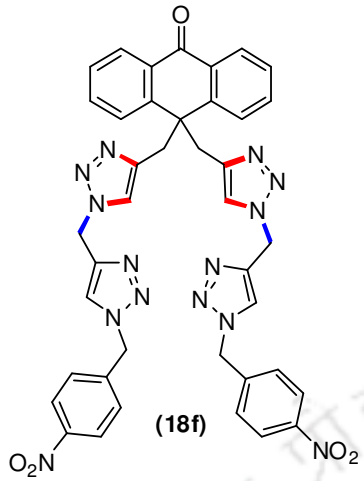
*10,10-bis((1-((1-allyl-1H-1,2,3-triazol-4-yl)methyl)-1H-1,2,3-triazol-4-yl)methyl)anthracen-9(10H)-one (**18e**)*



(18e)

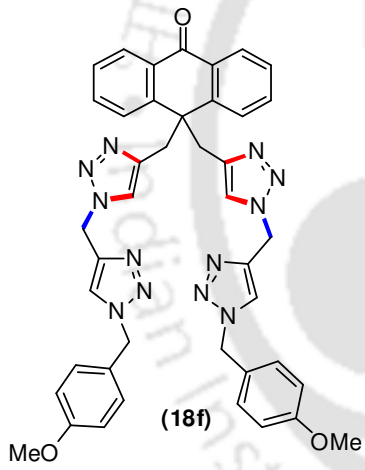
Colourless oily, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.92 (d, *J* = 7.6 Hz, 4H), 7.72 (t, *J* = 76. Hz, 2H), 7.37 (t, *J* = 7.6 Hz, 2H), 7.09 (s, 2H), 6.03-5.94 (m, 4H), 5.37-5.33 (m, 4H), 5.24 (s, 4H), 4.97 (d, *J* = 6.0 Hz, 4H), 3.82 (s, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 182.9, 144.8, 143.3, 142.1, 134.3, 132.2, 130.9, 127.8, 127.3, 126.9, 122.5, 121.6, 120.8, 53.0, 47.2, 45.3, 40.6; **IR** (KBr)ν_{max} 3137, 3068, 2955, 2912, 2828, 1655, 1600, 1558, 1448, 1323, 1255, 1217, 1131, 1048 cm^{-1}; **HRMS** (ESI) Calcd For $C_{32}H_{31}N_{12}O$ 599.2739 ($M + H^+$); Found 599.2747.

*10,10-bis((1-((1-(4-nitrobenzyl)-1H-1,2,3-triazol-4-yl)methyl)-1H-1,2,3-triazol-4-yl)methyl) anthracen-9(10H)-one (**18f**)*



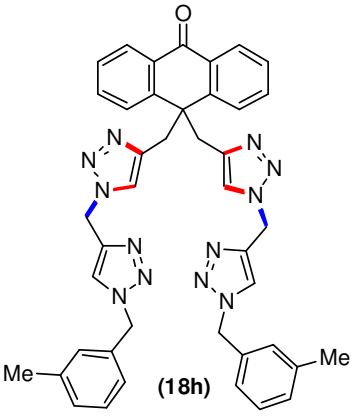
White semi-solid, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.16 (d, *J* = 9.2 Hz, 4H), 7.90 (d, *J* = 7.6 Hz, 2H), 7.81 (d, *J* = 7.6 Hz, 2H), 7.68-7.64 (m, 2H), 7.37 (d, *J* = 8.4 Hz, 4H), 7.28 (d, *J* = 8.0 Hz, 2H), 7.14 (s, 2H), 6.02 (s, 2H), 5.62 (s, 4H), 5.19 (s, 4H), 3.77 (s, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 182.9, 147.9, 144.7, 142.5, 141.5, 134.2, 131.9, 129.1, 128.8, 127.6, 127.3, 126.6, 124.2, 122.9, 121.5, 53.0, 47.1, 45.1, 40.8; **IR** (KBr)ν_{max} 3136, 3065, 2925, 2870, 2838, 1653, 1610, 1552, 1456, 1437, 1335, 1318, 1224, 1153, 1126, 1047 cm^{-1}; **HRMS** (ESI) Calcd For $C_{40}H_{33}N_{14}O_5$ 789.2753 ($M + H^+$); Found 789.2760.

*10,10-bis((1-((1-(4-methoxybenzyl)-1H-1,2,3-triazol-4-yl)methyl)-1H-1,2,3-triazol-4-yl) methyl)anthracen-9(10H)-one (**18g**)*



Colourless oily, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.96-7.91 (m, 4H), 7.71 (t, *J* = 7.6 Hz, 2H), 7.35 (t, *J* = 7.6 Hz, 2H), 7.25 (d, *J* = 8.4 Hz, 4H), 7.01 (s, 2H), 6.90 (d, *J* = 8.8 Hz, 4H), 5.99 (s, 2H), 5.48 (s, 4H), 5.21 (s, 4H), 3.81 (s, 10H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 182.9, 160.1, 144.8, 143.2, 142.2, 134.2, 132.2, 129.9, 127.9, 127.3, 127.0, 126.9, 126.4, 122.3, 121.5, 114.6, 55.4, 53.9, 47.2, 45.3, 40.6; **IR** (KBr)ν_{max} 3138, 3067, 2935, 2838, 1653, 1601, 1515, 1460, 1325, 1249, 1178, 1124, 1049 cm^{-1}; **HRMS** (ESI) Calcd For $C_{42}H_{39}N_{12}O_3$ 759.3263 ($M + H^+$); Found 759.3296.

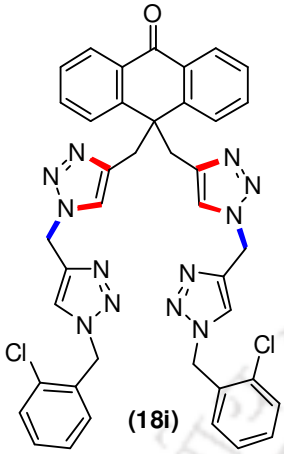
*10,10-bis((1-((1-(3-methylbenzyl)-1H-1,2,3-triazol-4-yl)methyl)-1H-1,2,3-triazol-4-yl)methyl) anthracen-9(10H)-one (**18h**)*



Colourless oily, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.94-9.93 (m, 4H), 7.72 (s, 2H), 7.34-7.27 (m, 4H), 7.18-7.11 (m, 6H), 7.03 (s, 2H), 6.01 (s, 2H), 5.51 (s, 4H), 5.22 (s, 4H), 3.82 (s, 4H), 2.35 (s, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 183.0, 144.9, 143.3, 142.4, 139.2, 134.4, 134.3, 132.3, 129.8, 129.2, 129.1, 127.8, 127.3, 126.9, 125.5, 122.5, 121.5, 54.5, 47.3, 45.4, 40.7, 21.7; **IR** (KBr)ν_{max} 3139, 3068, 2920, 2870, 2838, 1653, 1610,

1552, 1456, 1335, 1223, 1159, 1123, 1040 cm^{-1}; **HRMS** (ESI) Calcd For $C_{42}H_{39}N_{12}O$ 727.3365 ($M + H^+$); Found 727.3385.

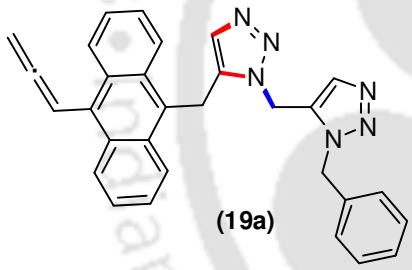
*10,10-bis((1-((1-(2-chlorobenzyl)-1H-1,2,3-triazol-4-yl)methyl)-1H-1,2,3-triazol-4-yl)methyl) anthracen-9(10H)-one (**18i**)*



(18i)

Colourless oily, **^{1}H NMR** (400 MHz, $CDCl_3$): δ ; **^{13}C NMR** (100 MHz, $CDCl_3$): δ 7.78-7.75 (m, 4H), 7.56 (s, 2H), 7.16 (s, 8H), 7.03 (s, 2H), 6.93 (s, 2H), 5.89 (s, 2H), 5.38 (s, 4H), 5.08 (s, 4H), 3.67 (s, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 183.1, 144.8, 136.4, 134.9, 134.3, 132.1, 130.5, 129.0, 128.3, 127.7, 127.3, 126.7, 126.4, 122.6, 53.5, 47.2, 45.9, 40.6; **IR** (KBr)ν_{max} 3137, 3066, 2932, 2833, 1654, 1606, 1549, 1459, 1339, 1225, 1155, 1122, 1045 cm^{-1}; **HRMS** (ESI) Calcd For $C_{40}H_{33}Cl_2N_{12}O$ 767.2272 ($M + H^+$); Found 767.2275.

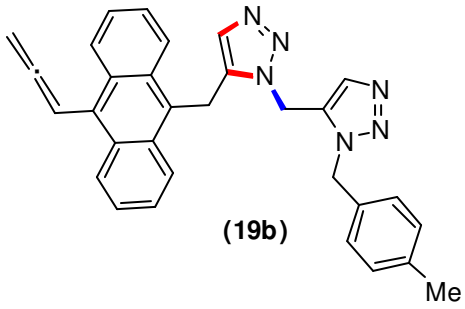
*1-benzyl-5-((5-((10-(propa-1,2-dien-1-yl)anthracen-9-yl)methyl)-1H-1,2,3-triazol-1-yl) methyl)-1H-1,2,3-triazole (**19a**)*



(19a)

Yellow solid, M.p 151-152 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.39 (d, *J* = 8.8 Hz, 2H), 8.20 (d, *J* = 8.0 Hz, 2H), 7.44-7.42 (m, 2H), 7.29-7.27 (m, 4H), 7.19 (s, 3H), 7.11 (s, 1H), 6.91-6.88 (m, 1H), 5.44 (s, 2H), 5.33 (s, 2H), 5.00 (s, 1H), 4.97 (s, 2H), 4.69 (s, 2H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 210.9, 147.7, 141.8, 130.3, 129.7, 129.4, 129.1, 129.0, 128.8, 128.0, 127.2, 126.5, 125.9, 125.2, 124.9, 123.0, 121.9, 87.8, 75.5, 54.2, 45.2, 29.9; **IR** (KBr)ν_{max} 3122, 3061, 2953, 2925, 2854, 1945, 1640, 1550, 1444, 1318, 1215, 1151, 1049 cm^{-1}; **HRMS** (ESI) Calcd For $C_{30}H_{25}N_6$ 469.2135 ($M + H^+$); Found 469.2117.

*1-(4-methylbenzyl)-5-((5-((10-(propa-1,2-dien-1-yl)anthracen-9-yl)methyl)-1H-1,2,3-triazol-1-yl)methyl)-1H-1,2,3-triazole (**19b**)*

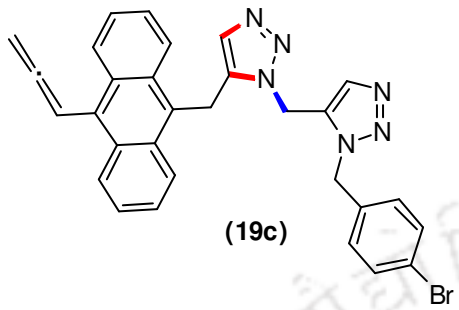


(19b)

Yellow solid, M.p 183-184 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.46-8.44 (m, 2H), 8.28-8.26 (m, 2H), 7.52-7.48 (m, 4H), 7.34 (s, 1H), 7.16 (br s, 1H), 7.14-7.11 (m, 2H), 7.08 (s, 1H), 6.97-6.93 (m, 1H), 5.44 (s, 2H), 5.38 (s, 2H), 5.35 (s, 2H), 5.06 (s, 1H), 5.04 (s, 2H), 2.33 (s, 3H); **^{13}C NMR** (100 MHz, CD_2Cl_2): δ 211.5, 148.1, 145.4, 142.4, 139.3, 130.2, 129.9, 128.6, 127.7, 127.0, 126.9, 126.7, 126.5, 125.9, 125.7, 125.4, 124.9, 123.3, 122.2, 120.6, 88.3, 75.7, 54.5, 45.8, 30.2, 21.4; **IR** (KBr)ν_{max}

3139, 3059, 2955, 2918, 2849, 1944, 1639, 1548, 1442, 1322, 1215, 1155, 1047 cm^{-1}; **HRMS** (ESI) Calcd For $C_{31}H_{27}N_6$ 483.2292 ($M + H^+$); Found 483.2291.

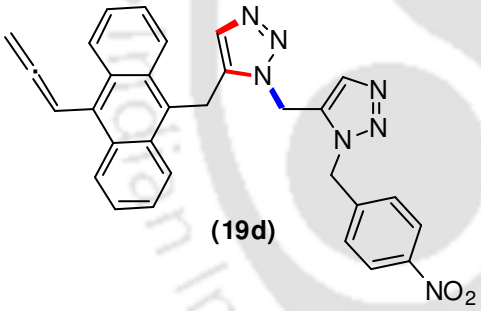
*1-(4-bromobenzyl)-5-((5-((10-(propa-1,2-dien-1-yl)anthracen-9-yl)methyl)-1H-1,2,3-triazol-1-yl)methyl)-1H-1,2,3-triazole (**19c**)*



(19c)

Yellow solid, M.p 175-176 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.48-8.46 (m, 2H), 8.28 (d, *J* = 9.2 Hz, 2H), 7.54-7.49 (m, 4H), 7.49 (d, *J* = 6.8 Hz, 2H), 7.39 (s, 1H), 7.04 (d, *J* = 8.0 Hz, 2H), 6.96-6.94 (m, 1H), 5.41 (s, 2H), 5.35 (s, 2H), 5.07 (s, 1H), 5.05 (s, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 211.2, 147.8, 142.4, 133.2, 132.5, 130.5, 129.9, 129.7, 127.6, 126.8, 126.2, 125.4, 124.9, 123.3, 123.1, 122.2, 88.1, 75.7, 53.7, 45.5, 29.9; **IR** (KBr)ν_{max} 3137, 3056, 2951, 2921, 2846, 1945, 1635, 1545, 1439, 1325, 1217, 1151, 1049 cm^{-1}; **HRMS** (ESI) Calcd For $C_{30}H_{24}BrN_6$ 547.1241 ($M + H^+$); Found 547.1251.

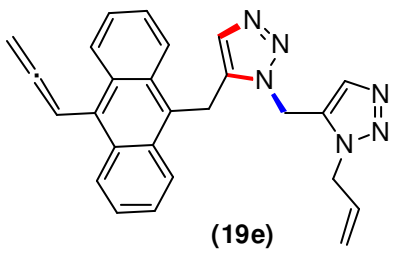
*1-(4-nitrobenzyl)-5-((5-((10-(propa-1,2-dien-1-yl)anthracen-9-yl)methyl)-1H-1,2,3-triazol-1-yl)methyl)-1H-1,2,3-triazole (**19d**)*



(19d)

Yellow solid, M.p 209-210 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.46 (d, *J* = 7.2 Hz, 2H), 8.28 (d, *J* = 8.8 Hz, 2H), 8.16 (d, *J* = 8.4 Hz, 2H), 7.51-7.49 (m, 4H), 7.47 (s, 1H), 7.29 (d, *J* = 8.0 Hz, 2H), 6.98-6.94 (m, 1H), 5.50 (s, 2H), 5.44 (s, 2H), 5.08 (s, 1H), 5.01 (s, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 211.2, 148.2, 142.8, 141.1, 139.5, 130.4, 129.9, 129.7, 128.9, 127.7, 126.8, 126.2, 125.5, 124.9, 124.5, 123.4, 122.2, 88.1, 75.8, 53.4, 45.4, 29.7; **IR** (KBr)ν_{max} 3136, 3067, 2925, 2870, 2838, 1947, 1640, 1552, 1457, 1439, 1333, 1321, 1227, 1154, 1121, 1048 cm^{-1}; **HRMS** (ESI) Calcd For $C_{30}H_{24}N_7O_2$ 514.1986 ($M + H^+$); Found 514.1986.

*1-allyl-5-((5-((10-(propa-1,2-dien-1-yl)anthracen-9-yl)methyl)-1H-1,2,3-triazol-1-yl)methyl)-1H-1,2,3-triazole (**19e**)*


(19e)

Yellow solid, M.p 148-149 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.47-8.46 (m, 2H), 8.30-8.28 (m, 2H), 7.51 (br s, 4H), 7.38 (s, 1H), 7.08 (s, 1H), 7.01-6.95 (m, 1H), 5.49 (s, 2H), 5.40 (s, 2H), 5.36 (m, 2H), 5.07 (s, 2H), 5.05 (s, 2H), 4.47 (s, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 211.2, 139.2,

134.0, 130.5, 130.0, 129.9, 129.8, 129.7, 129.2, 129.1, 129.0, 127.5, 126.7, 126.2, 125.4, 125.3, 124.9, 123.1, 122.2, 88.1, 75.7, 54.5, 45.5, 29.9; IR (KBr)ν_{max} 3131, 3061, 2956, 2833, 1950, 1635, 1552, 1447, 1429, 1336, 1221, 1118, 1050 cm^{-1}; **HRMS** (ESI) Calcd For $C_{26}H_{23}N_6$ 419.1979 ($M + H^+$); Found 419.1985.

XRD for Compounds **17a**

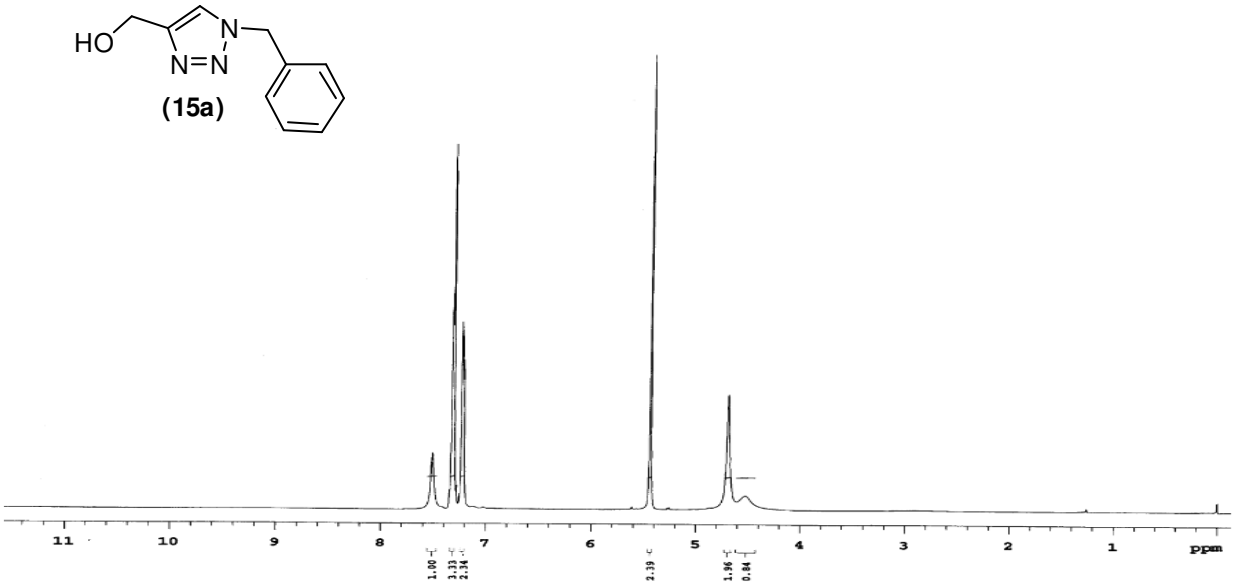
Complete crystallographic data of compound **17a** for the structural analyses have been deposited with the Cambridge Crystallographic Data Centre, CCDC No. is 1424488. Copies of this information may be obtained free of charge from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44-1223-336033, e-mail: deposit@ccdc.cam.ac.uk or via: www.ccdc.cam.ac.uk).

Table 10. Crystal Data and Structure Refinement for Compound **17a**

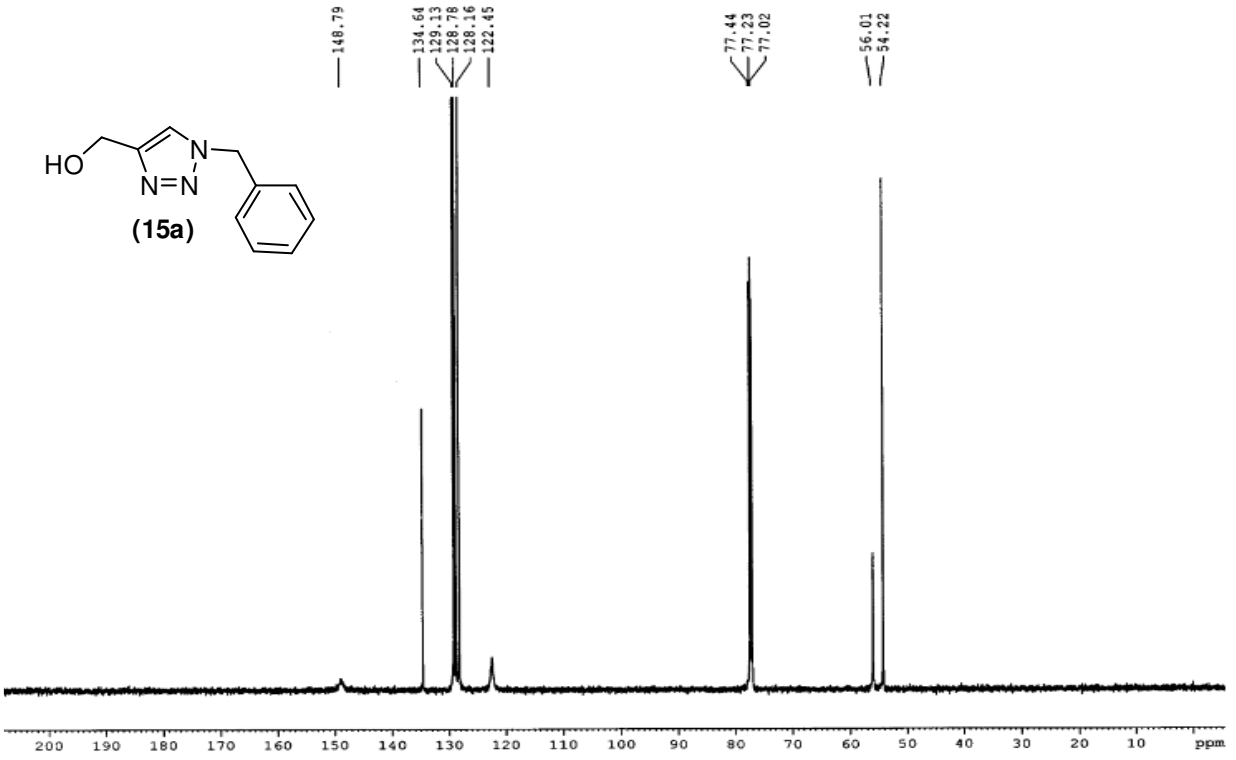
Entry	Identification code	Compound **17a**
01	Empirical formula	C_{10} H_9Cl N_4 O_2
02	Formula weight	252.66
03	Temperature	296(2) K
04	Wavelength	0.71073
05	Radiation type	Mo K\a
06	Radiation source	Fine-focus sealed tube
07	Crystal system	triclinic
08	Space group	P-1
09	Cell length	a 8.1461(4) b 8.5372(5) c 9.4139(5)
10	Cell Angle	α 87.801(4) β 74.734(3) δ 64.146(3)
11	Cell Volume	566.16(5)
12	Density	1.482
13	Completeness to theta	28.32° / 100%
14	Absorption correction	multi-scan
15	Refinement method	Full-matrix least-squares on F2
16	Index ranges	-8<=h<=10, -11<=k<=11, -12<=l<=12

17	Reflection number	2820
18	Theta range	4.51- 28.32
19	Cell formula units Z	2
20	CCDC no	1424488

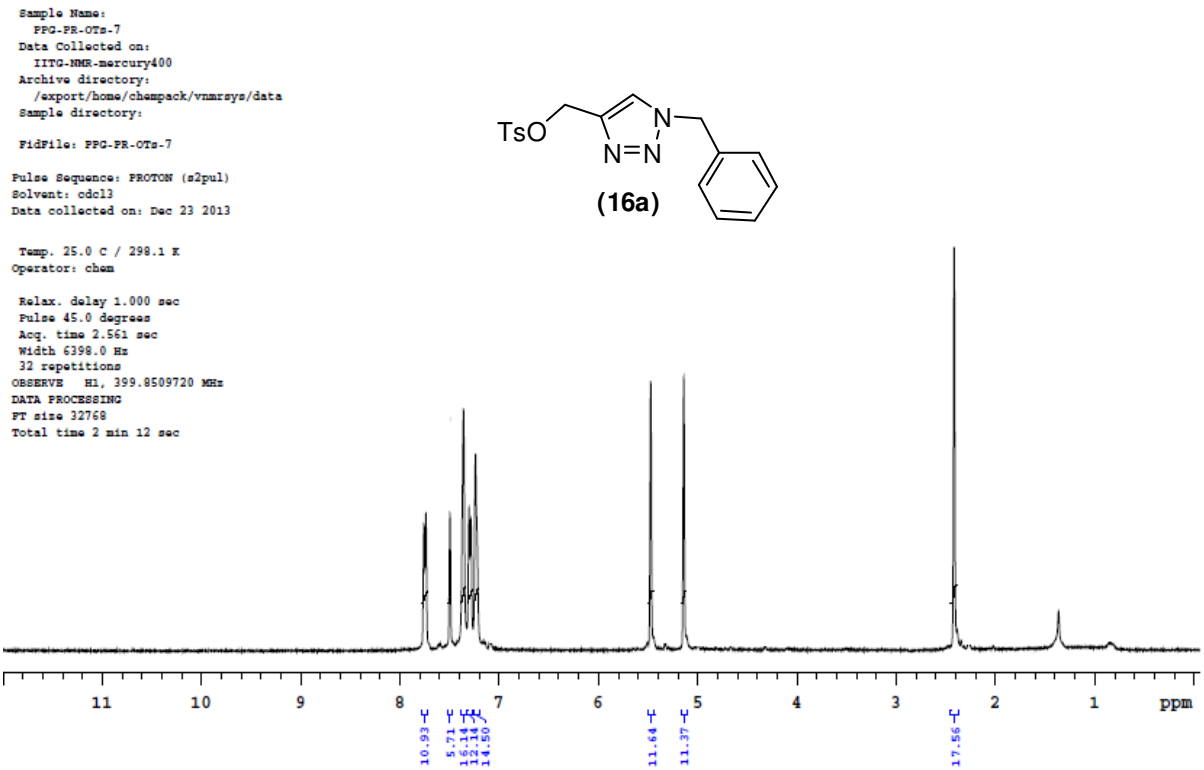
***^{1}H NMR (400 MHz, $CDCl_3$)**: (1-benzyl-1H-1,2,3-triazol-4-yl)methanol (**15a**)*



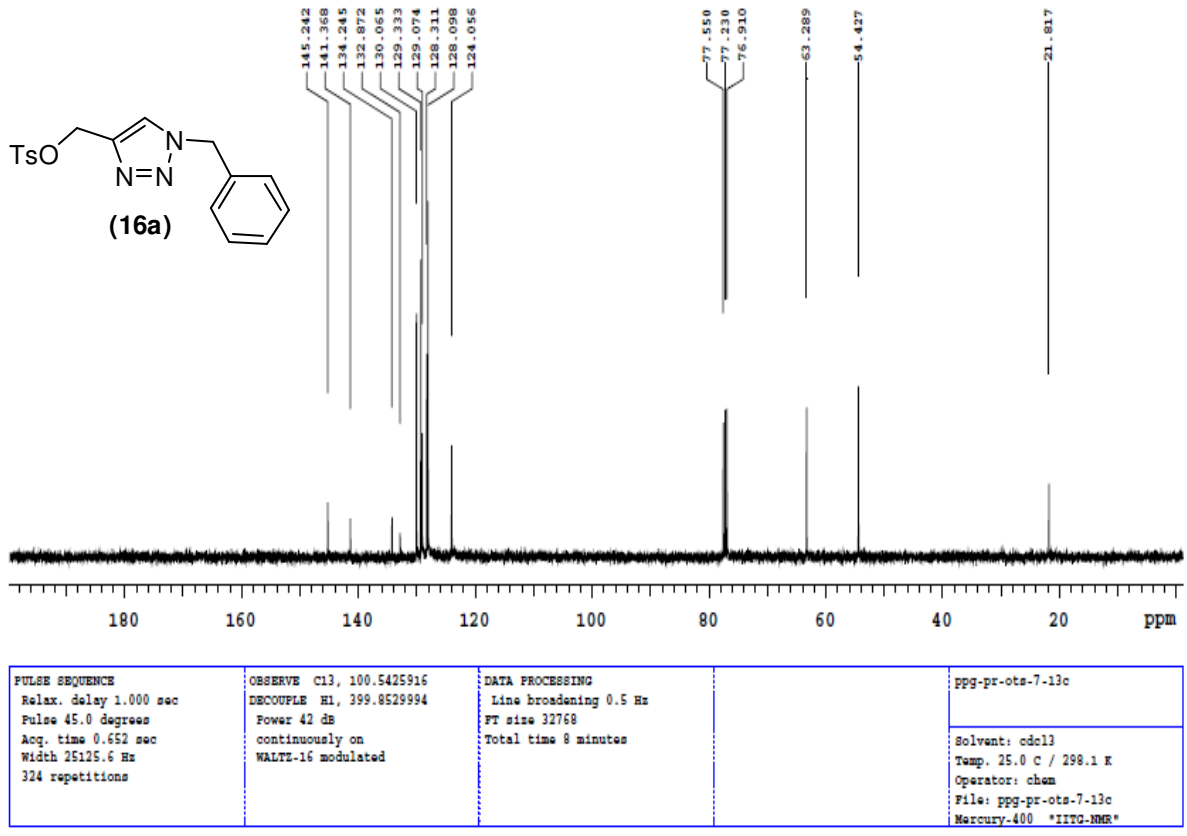
***^{13}C NMR (150 MHz, $CDCl_3$)**: (1-benzyl-1H-1,2,3-triazol-4-yl)methanol (**15a**)*



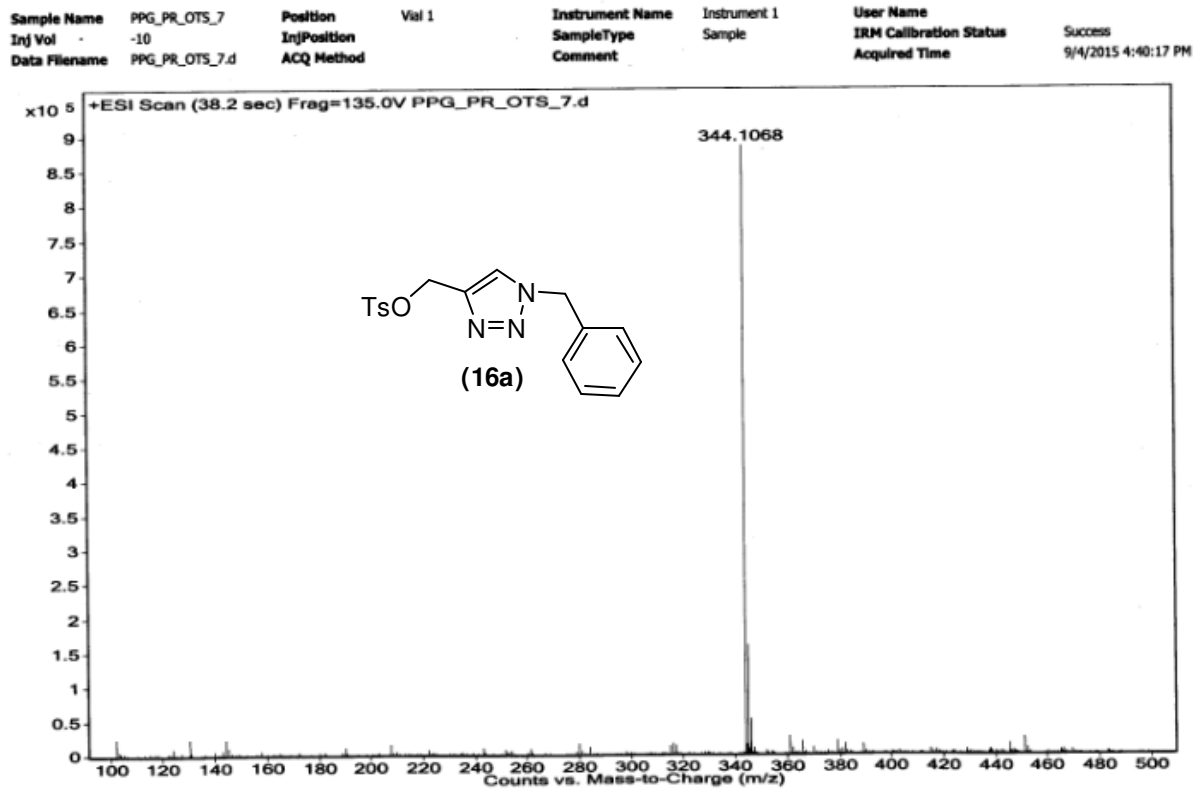
***^{1}H NMR (400 MHz, $CDCl_3$)**: (1-benzyl-1H-1,2,3-triazol-4-yl)methyl 4-methylbenzenesulfonate (**16a**)*



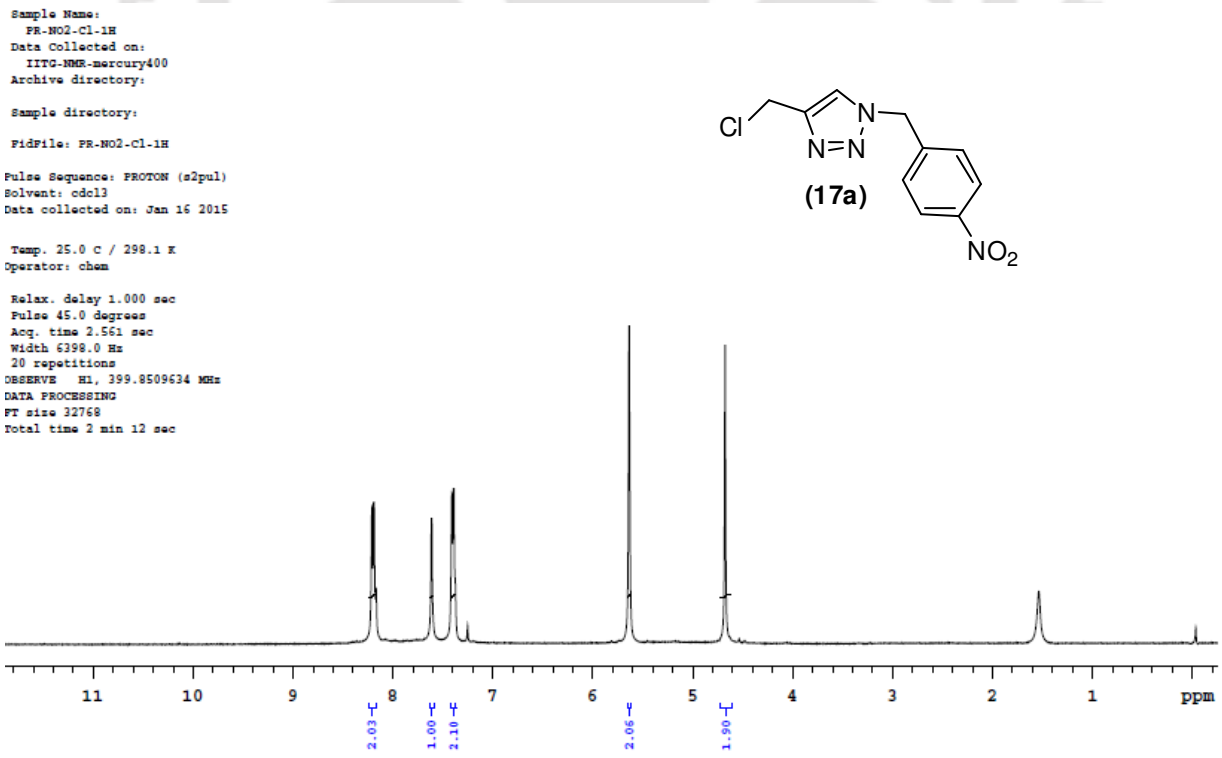
***^{13}C NMR (100 MHz, $CDCl_3$)**: (1-benzyl-1H-1,2,3-triazol-4-yl)methyl 4-methylbenzenesulfonate (**16a**)*



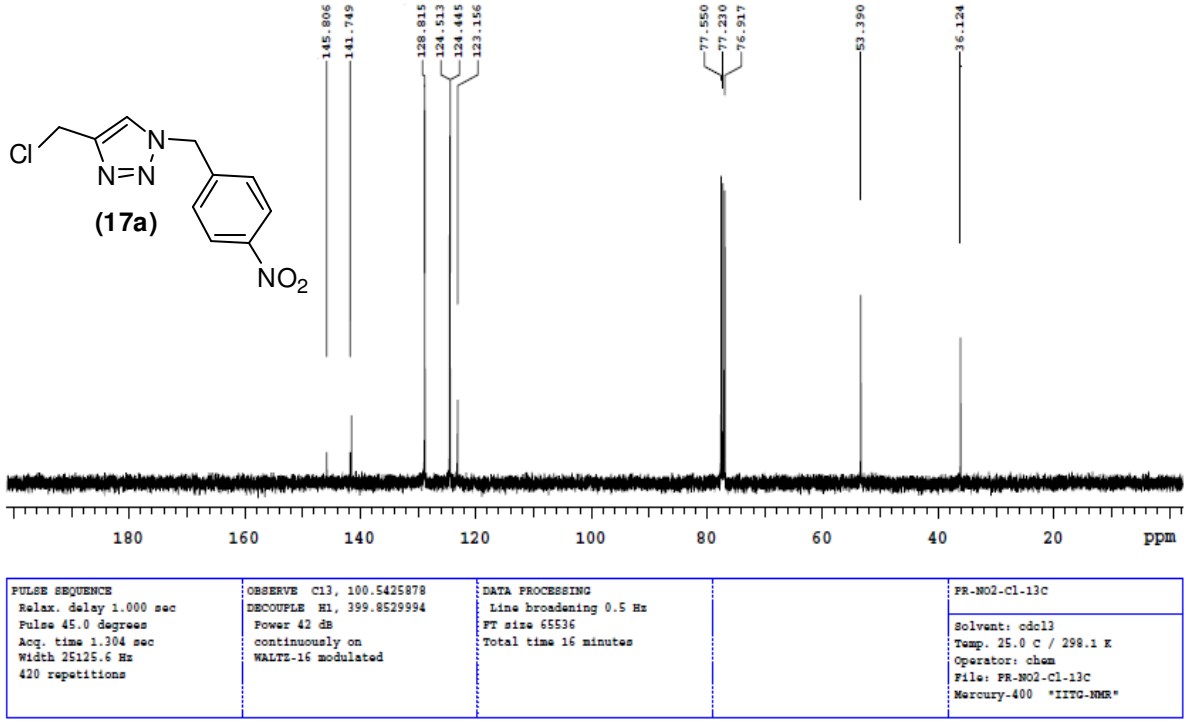
***HRMS** (ESI): 1-benzyl-1H-1,2,3-triazol-4-yl)methyl 4-methylbenzenesulfonate (**16a**)*



*^{1}H NMR (400 MHz, $CDCl_3$): 4-(chloromethyl)-1-(4-nitrobenzyl)-1H-1,2,3-triazole (**17a**)*

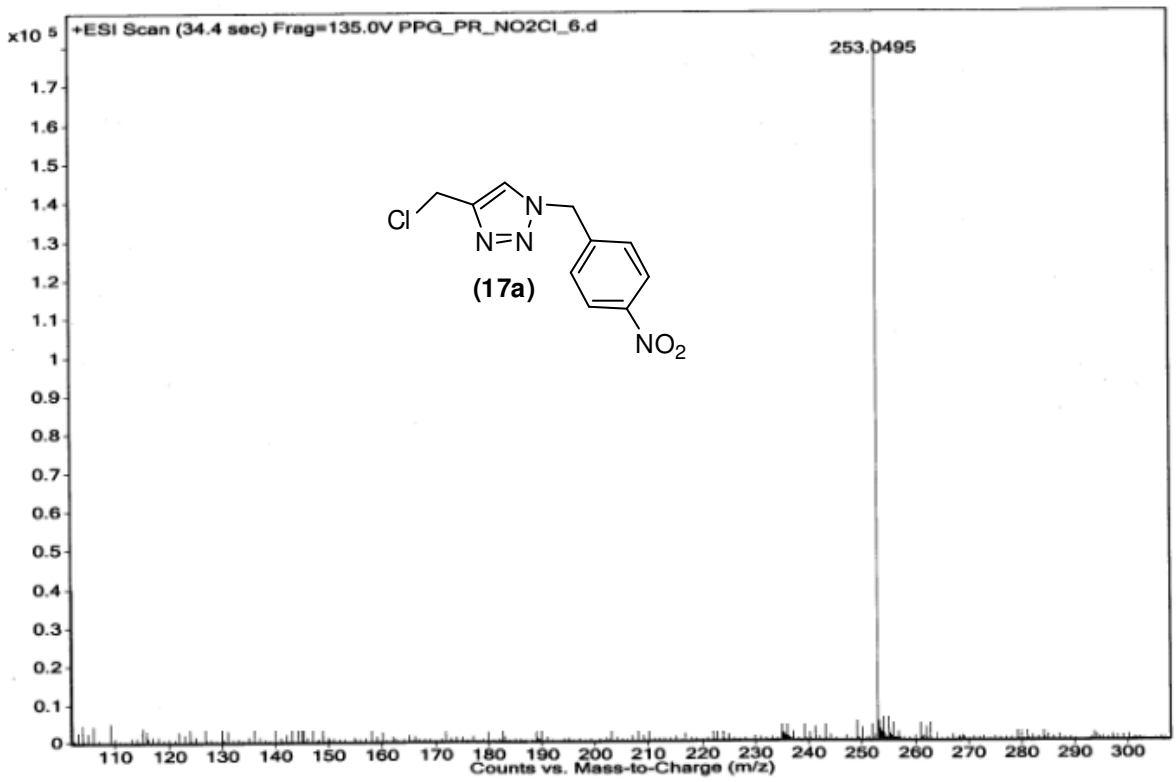


^{13}C NMR (100 MHz, $CDCl_3$): *4-(chloromethyl)-1-(4-nitrobenzyl)-1H-1,2,3-triazole (**17a**)*

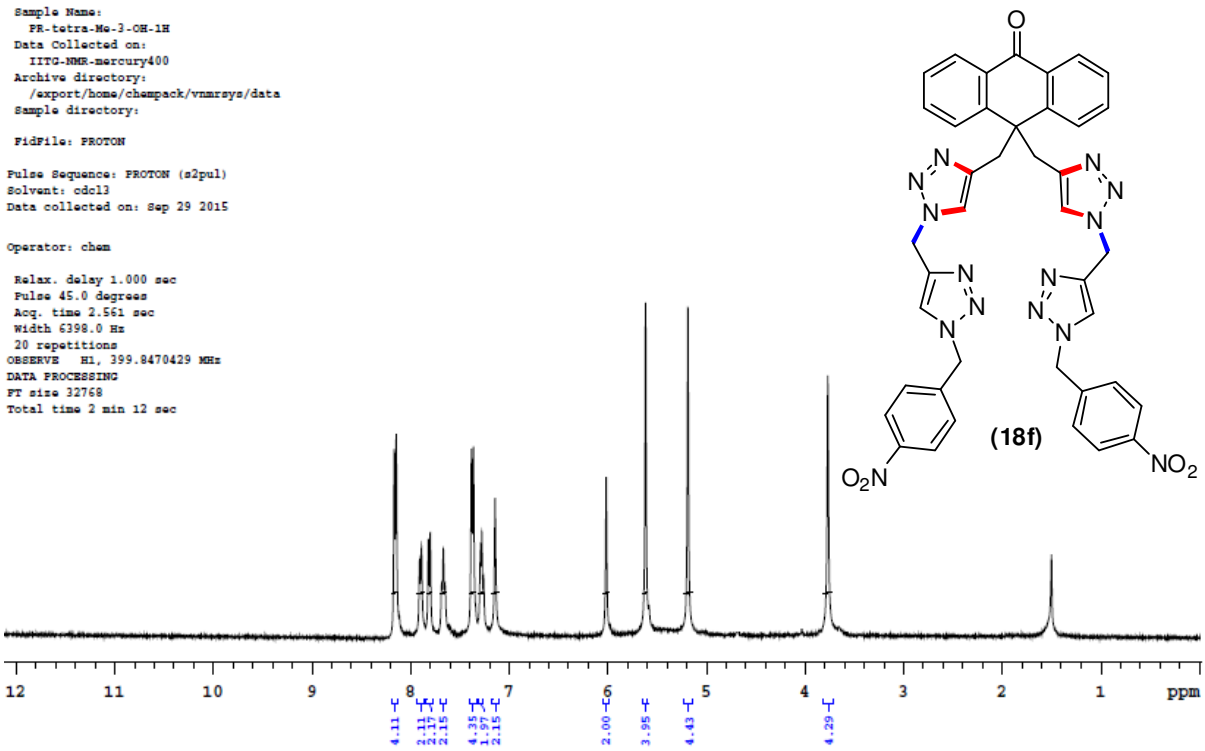


HRMS *(ESI): 4-(chloromethyl)-1-(4-nitrobenzyl)-1H-1,2,3-triazole (**17a**)*

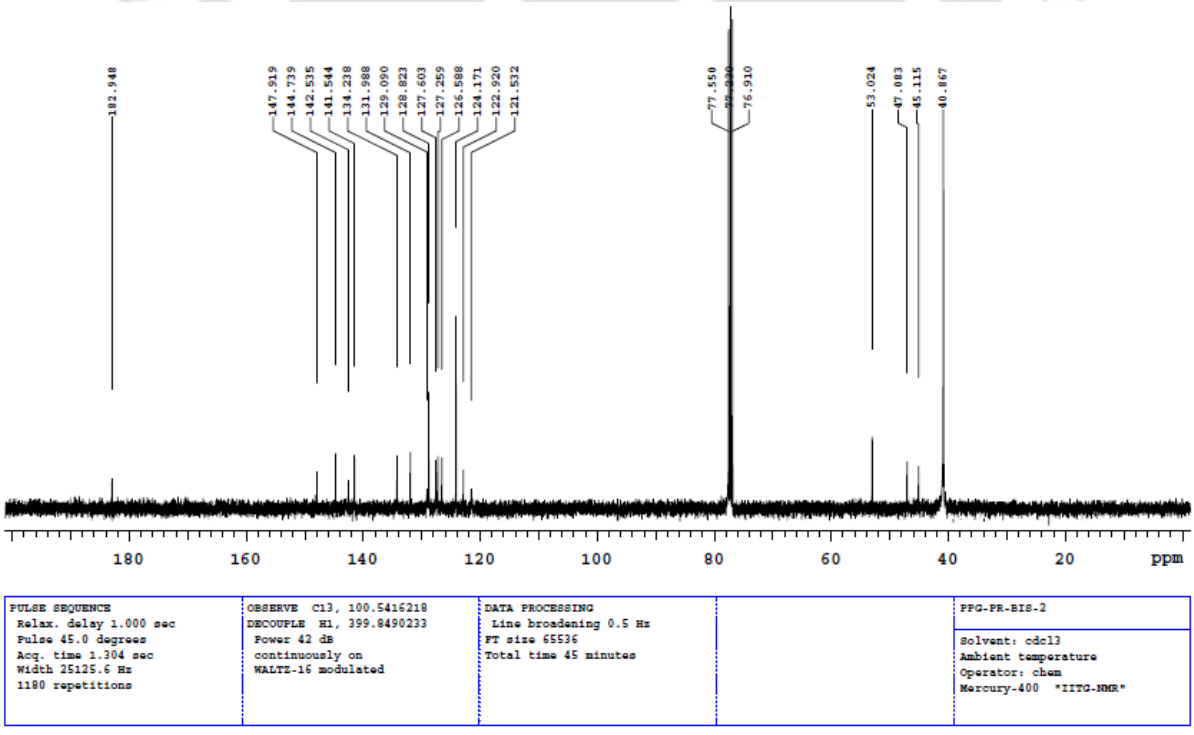
Sample Name	PPG_PR_NO2Cl_6	**Position**	Vial 1	**Instrument Name**	Instrument 1	**User Name**	
Inj Vol	-10	**InjPosition**		**SampleType**	Sample	**IRM Calibration Status**	Success
Data Filename	PPG_PR_NO2Cl_6.d	**ACQ Method**		**Comment**		**Acquired Time**	9/4/2015 4:43:16 PM



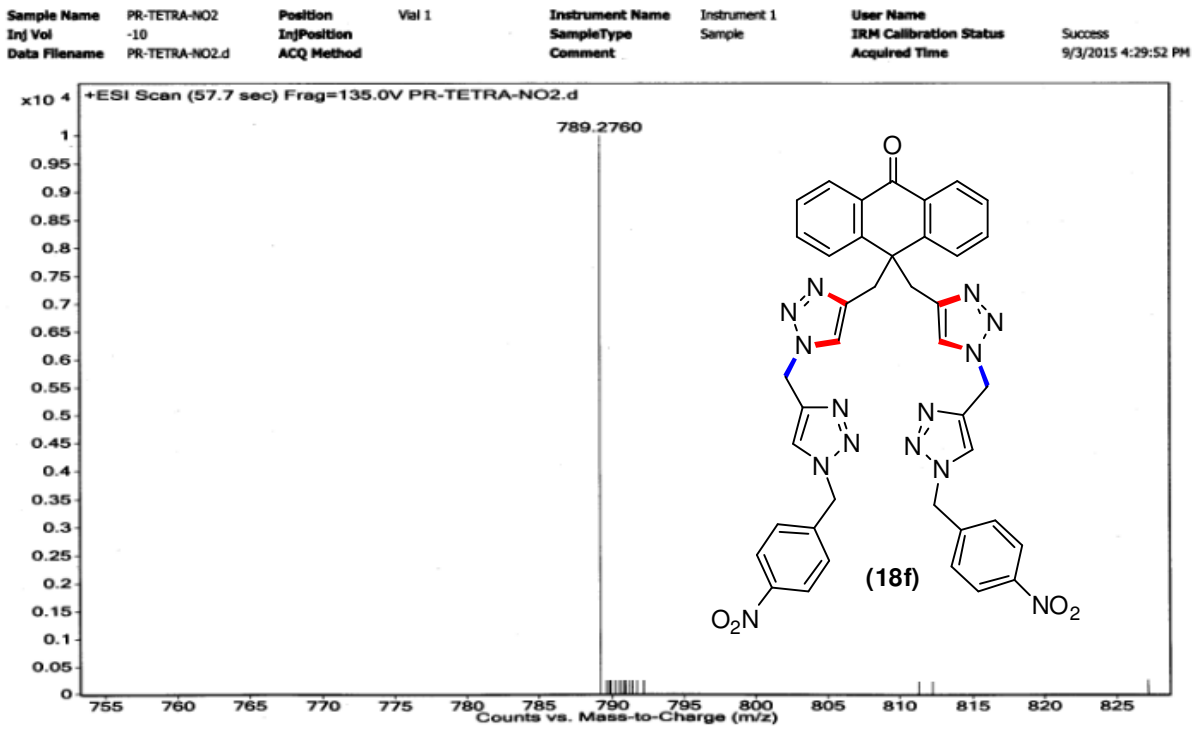
*^{1}H NMR (400 MHz, $CDCl_3$): 10,10-bis((1-((1-(4-nitrobenzyl)-1H-1,2,3-triazol-4-yl)methyl)-1H-1,2,3-triazol-4-yl)methyl) anthracen-9(10H)-one (**18f**)*



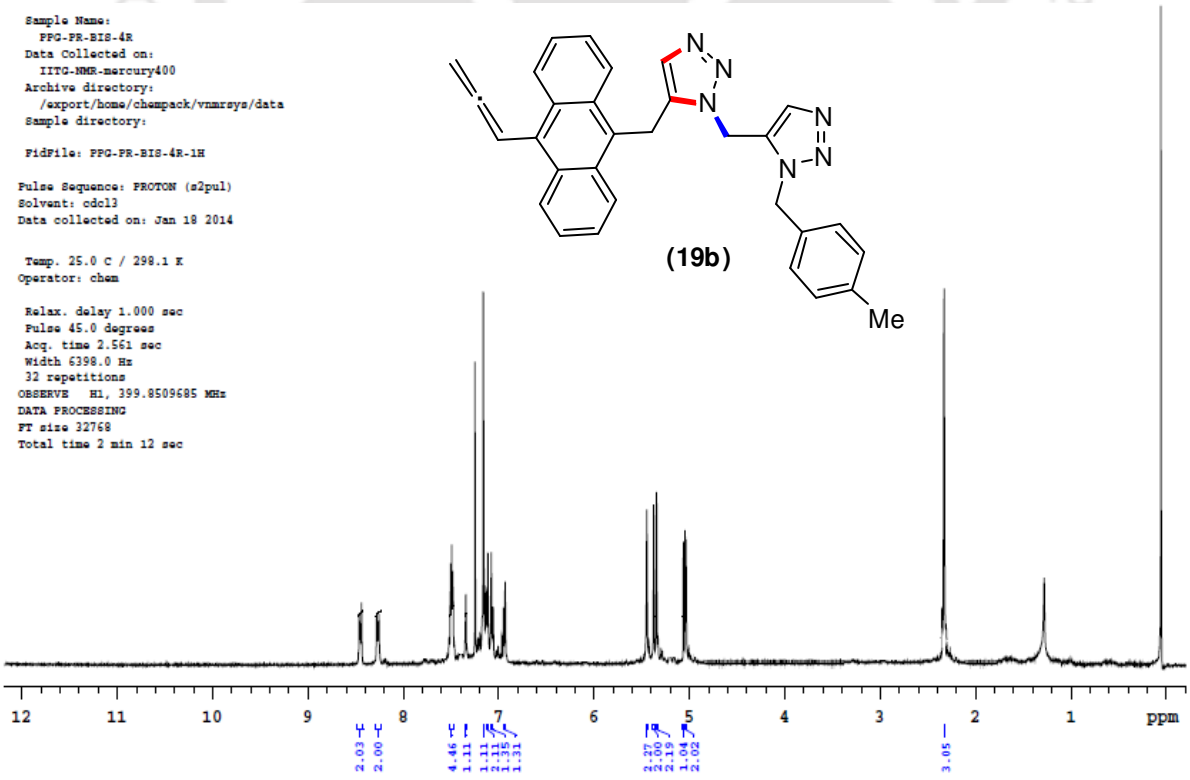
*^{13}C NMR (100 MHz, $CDCl_3$): 10,10-bis((1-((1-(4-nitrobenzyl)-1H-1,2,3-triazol-4-yl)methyl)-1H-1,2,3-triazol-4-yl)methyl) anthracen-9(10H)-one (**18f**)*



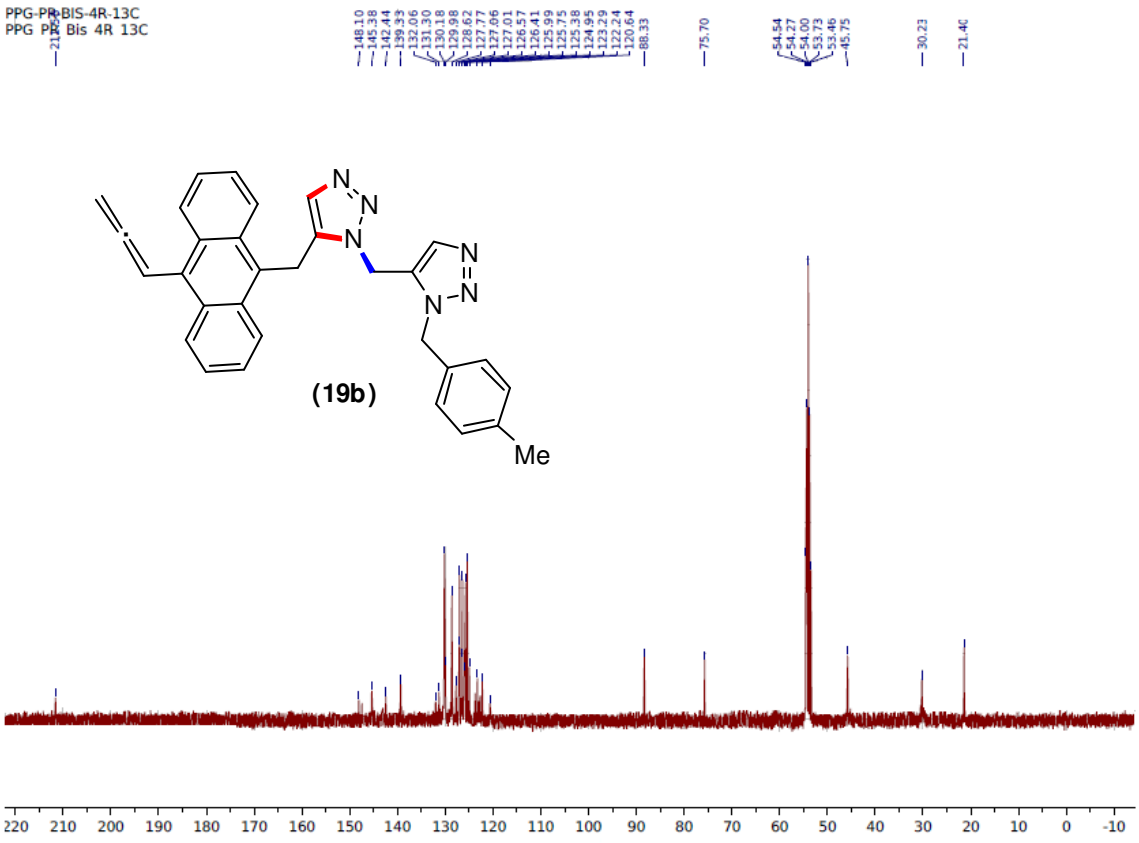
***HRMS** (ESI): 10,10-bis((1-((1-(4-nitrobenzyl)-1H-1,2,3-triazol-4-yl)methyl)-1H-1,2,3-triazol-4-yl)methyl) anthracen-9(10H)-one (**18f**)*



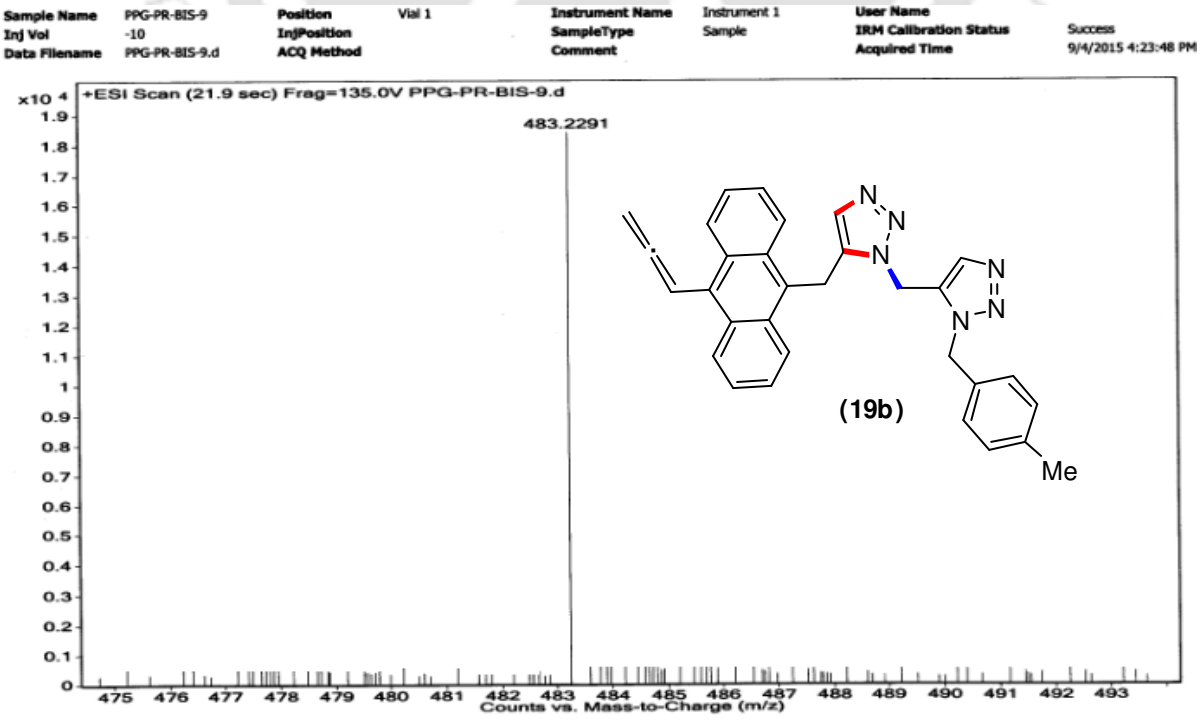
*^{1}H NMR (400 MHz, $CDCl_3$): 1-(4-methylbenzyl)-5-((5-((10-(propa-1,2-dien-1-yl)anthracen-9-yl)methyl)-1H-1,2,3-triazol-1-yl)methyl)-1H-1,2,3-triazole (**19b**)*



^{13}C NMR (100 MHz, $CDCl_3$): *1-(4-methylbenzyl)-5-((5-((10-(propa-1,2-dien-1-yl)anthracen-9-yl)methyl)-1H-1,2,3-triazol-1-yl)methyl)-1H-1,2,3-triazole (**19b**)*



***HRMS** (ESI): 1-(4-methylbenzyl)-5-((5-((10-(propa-1,2-dien-1-yl)anthracen-9-yl)methyl)-1H-1,2,3-triazol-1-yl)methyl)-1H-1,2,3-triazole (**19b**)*



Part A

Chapter III

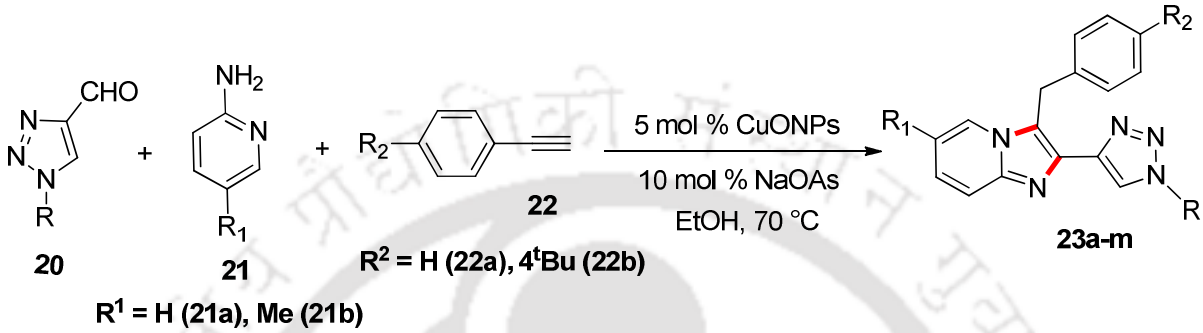
Synthesis of 2-triazolyl-imidazo[1,2-α]pyridine through a one-pot three-component reaction using a nano copper oxide assisted click-catalyst

Result & Discussion

Experimental Section

Results and Discussion

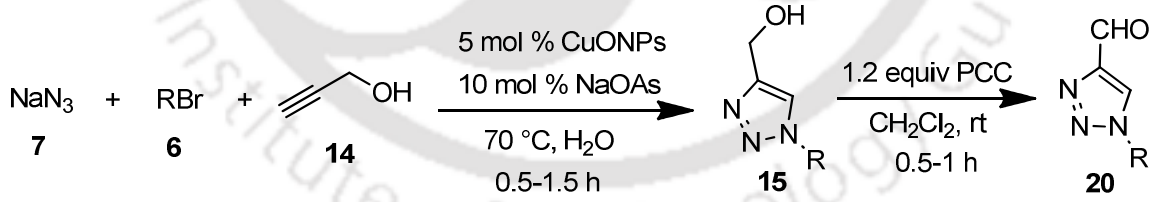
The synthetic strategies and the importance of imidazo[1,2-*a*]pyridine have already been described in Chapter 1. In this Chapter, we would like to report the synthesis of 2-triazolyl-imidazo[1,2-*a*]pyridine by employing one-pot three-component reaction of 2-triazolyl aldehyde, aromatic amidine and phenyl acetylene in the presence of copper oxide nanoparticle along with sodium ascorbate in ethanol at 70 ˚C as shown in Scheme 33.

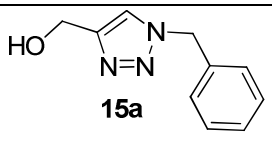
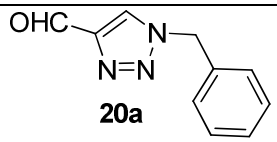


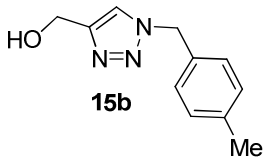
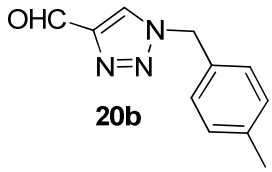
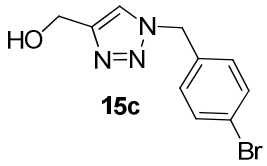
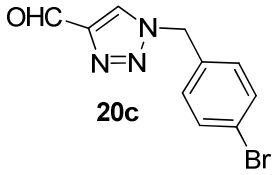
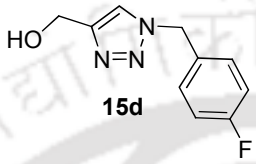
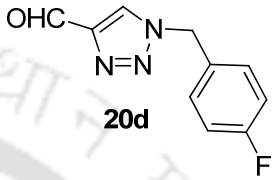
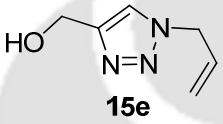
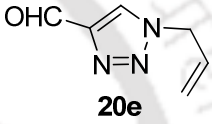
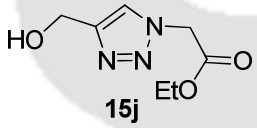
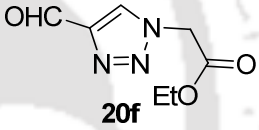
Scheme 33. *Synthesis of 2-triazolyl-imidazo[1,2-a]pyridine derivatives.*

The required triazole containing aldehydes (**20**) were prepared via two-step sequence which features the synthesis of key starting material, (1-alkyl-1H-1,2,3-triazol-4-yl)methanol (**15**), which was synthesized by following the earlier reported procedures in chapter II followed by the oxidation of the product **15** by pyridiniumchlorochromate (PCC) in dichloromethane at room temperature. The various synthesized triazole containing aldehydes (**20**) are shown in the Table 11.

Table 11. Synthesis of 1-alkyl-1,2,3-triazole-4-carbaldehyde[a]

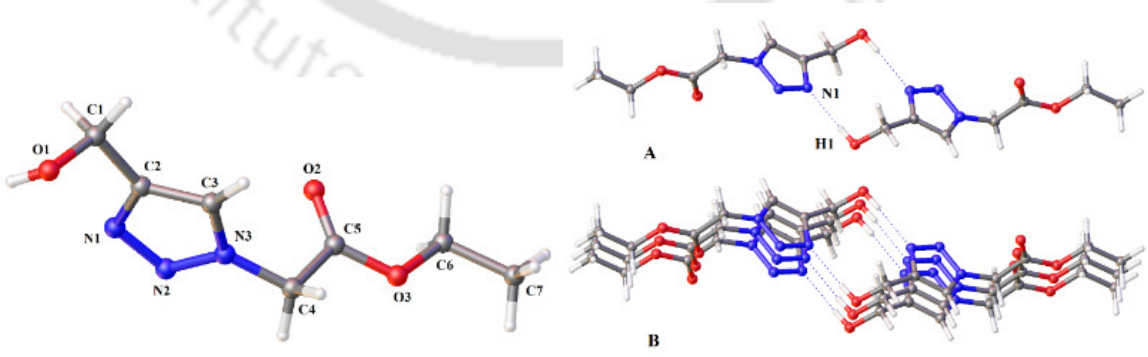


Entry	R(**6**)	Product (**15**)	Yield **15** (%)[b]	Product (**20**)	Yield 20 (%)[b]
1	$C_6H_5CH_2$ (**6a**)	 **15a**	92	 **20a**	82

2	4Me-$C_6H_5CH_2$ (**6b**)	 **15b**	90	 **20b**	78
3	4Br-$C_6H_5CH_2$ (**6c**)	 **15c**	86	 **20c**	76
4	4F-$C_6H_5CH_2$ (**6d**)	 **15d**	90	 **20d**	78
5	Allyl (**6e**)	 **15e**	80	 **20e**	72
6	Ethoxycarbonyl methyl (**6j**)	 **15j**	78	 **20f**	68

[a]*The reactions were performed in 10 mmol scale.* [b]*Isolated yield.*

All the products **15** and **20** were characterized by ^{1}H NMR, ^{13}C NMR spectra and HRMS. Moreover, the structure of alcoholic triazolyl precursor (**15j**) was confirmed through single X-ray analysis (Figure 14, I). The X-ray data shows an intermolecular hydrogen bonding along with layered structure as shown in Figure 14, II.

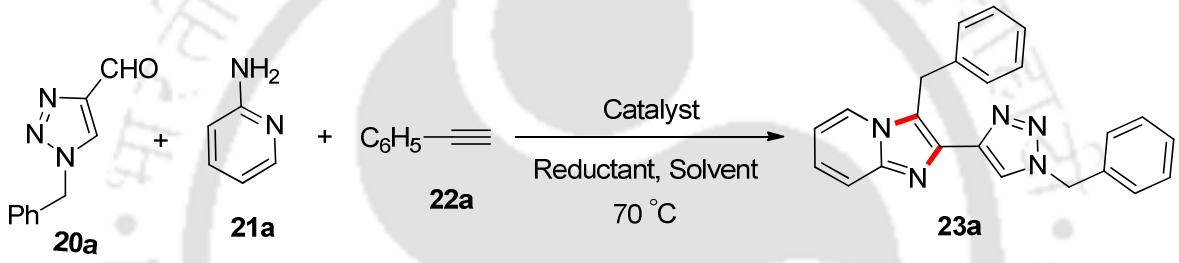


I **II**

Figure 14. **I**) X-ray structure of **15j**. **II**) A) Intermolecular H-Bonding. B) Layered-structure through intermolecular H-Bonding **15j**

After the synthesis of 1-alkyl-1,2,3-triazole-4-carbaldehyde (**20**), the trial reactions were carried out with 1-benzyl-1,2,3-triazole-4-carbaldehyde (**20a**), 2-aminopyridine (**21a**) and phenylacetylene (**22a**) to optimize the reaction conditions and the obtained results are represented in Table 12. To pursue our goal, a variety of Cu(II) source were examined with different reducing agent and the best result was obtained with 5 mol% of copper oxide nanoparticle along with 10 mol% sodium ascorbate in ethanol at 70 °C (Table 12). In addition Cu(I) source was also examined under the same reaction condition and it yielded to 51% (Table 12, entry 5). On screening with different polar protic (H_2O, EtOH), polar aprotic (CH_3CN) and nonpolar (toluene) solvents, ethanol was found to be the suitable choice for the synthesis of 2-triazolyl-imidazo[1,2-*a*]pyridine.

Table 12. Optimization of the reaction conditions[a]

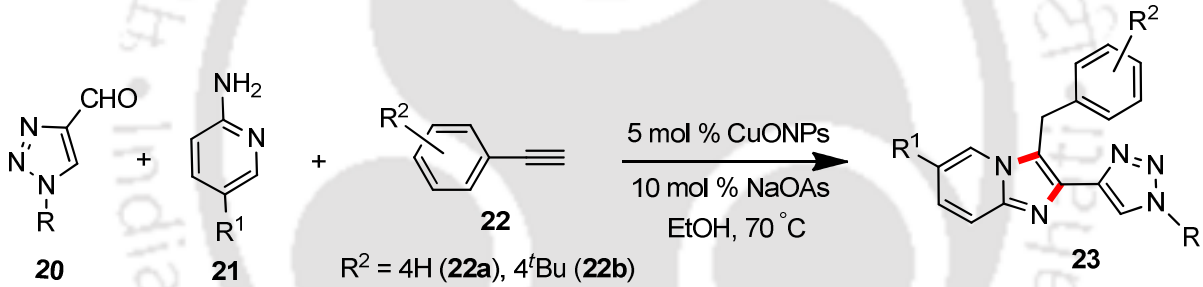


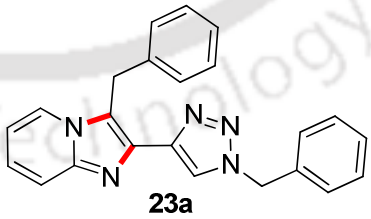
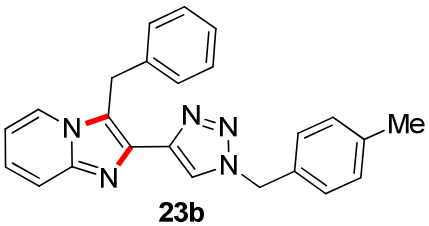
Entry	Catalyst	Mol %	Reductant (Mol%)	Solvent	Time (h)	Yield (%)[b]
1	$Cu(NO_3)_2{\cdot}3H_2O$	05	NaOAs (10)	EtOH	12	42
2	$CuCl_2$	05	NaOAs (10)	EtOH	12	45
3	$Cu(OAc)_2{\cdot}2H_2O$	05	NaOAs (10)	EtOH	12	44
4	$CuSO_4{\cdot}5H_2O$	05	NaOAs (10)	EtOH	12	47
5	CuI	05	-	EtOH	16	51
6	CuO Nanoparticle	05	-	EtOH	18	25
7	CuO Nanoparticle	05	D-Glucose (10)	EtOH	16	35
8	CuO Nanoparticle	05	D-Glucose (10)	H_2O	18	52
9	CuO Nanoparticle	05	NaOAs (10)	H_2O	16	58
10	$CuCl_2$	05	NaOAs (10)	H_2O	18	31
11	CuO Nanoparticle	02	NaOAs (5)	EtOH	11	75
12	**CuO Nanoparticle**	**05**	**NaOAs (10)**	**EtOH**	**10**	**84**
13	CuO Nanoparticle	10	NaOAs (20)	EtOH	11	78

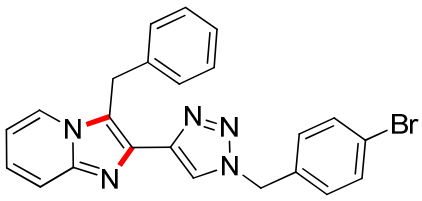
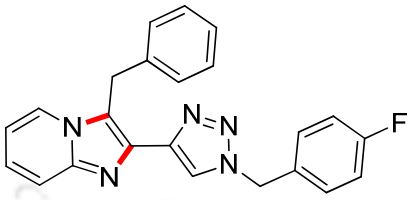
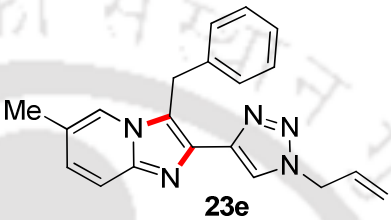
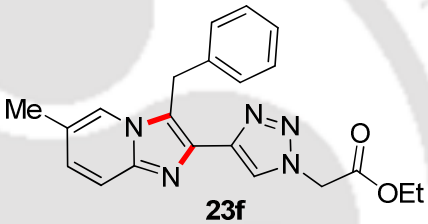
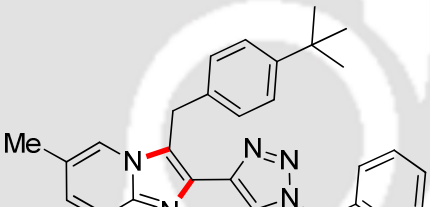
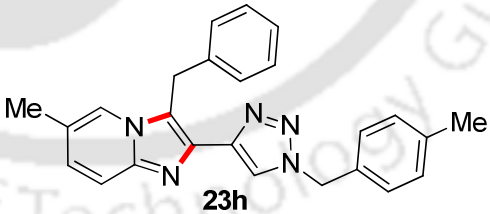
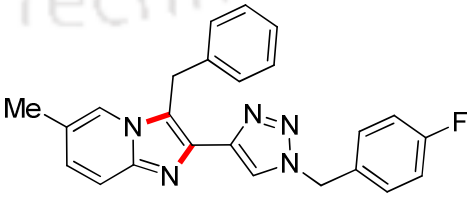
*[a]The reactions were carried out using each 1 mmol of 1-benzyl-1,2,3-triazole-4-carbaldehyde (**20a**), 2-aminopyridine (**21a**) and phenylacetylene(**22a**). [b]Isolated yield.*

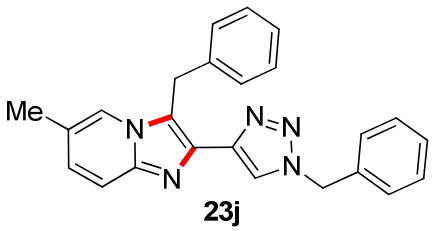
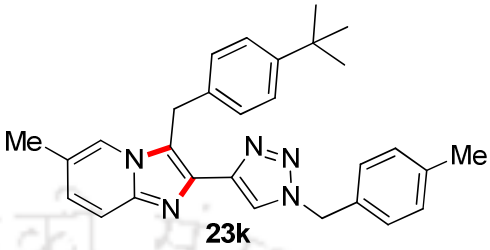
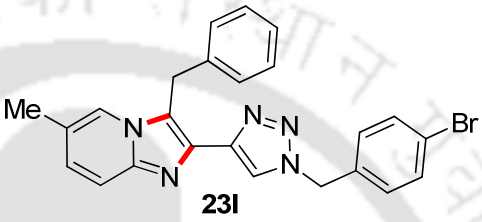
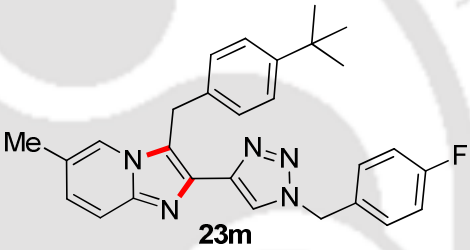
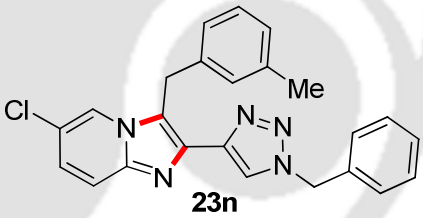
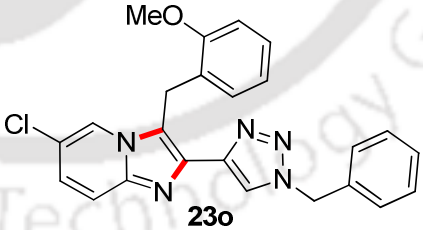
After optimization, we have conducted a reaction with 2-aminopyridine (**21a**), phenylacetylene (**22a**) and with a variety of substituent on triazole-4-carbaldehyde such as 4-methylbenzyl (**20b**), 4-bromobenzyl (**20c**) and 4-fluorobenzyl (**20d**) under similar reaction conditions to obtain the desired product **23b-d** with 80-82% yields (Table 13, entries 2-4). The reaction of 5-methyl-2-aminopyridine (**21b**) and phenylacetylene (**22a**) with Allyl (**20e**) and ethoxycarbonylmethyl (**20f**) substituted aliphatic triazole-4-carbaldehyde afford the required product **23e** and **23f** in 72% and 68% yield (Table 13, entries 5-6) respectively. Next, we prompt to investigate the present protocol with 5-methyl-2-aminopyridine (**21b**), 4-*tert* butylphenyl acetylene / phenyl acetylene and with a variety of substituted triazole-4-carbaldehyde such as benzyl (**20a**), 4-methylbenzyl (**20b**), 4-bromobenzyl (**20c**) and 4-fluorobenzyl (**20d**) derivatives under identical reaction conditions and the desired products **23g-m** were obtained in 80-85% yields (Table 13, entries 7-13).

Table 13. Synthesis of 3-alkyl-2-(1-alkyl-1,2,3-triazol-4-yl)-imidazo[1,2-*a*]pyridine[a]



Entry	Aldehyde (**20**)	R^1 (**21**)	R^2 (**22**)	Product (**23**)	Time (h)	Yield (%)[b]
01	**20a**	**21a**	**22a**	 **23a**	10	84
02	**20b**	**21a**	**22a**	 **23b**	11	80

03	**20c**	**21a**	**22a**	 **23c**	10	82
04	**20d**	**21a**	**22a**	 **23d**	09	82
05	**20e**	**21b**	**22a**	 **23e**	12	72
06	**20f**	**21b**	**22a**	 **23f**	12	68
07	**20a**	**21b**	**22b**	 **23g**	11	80
08	**20b**	**21b**	**22a**	 **23h**	10	82
09	**20d**	**21b**	**22a**	 **23i**	09	84

10	**20a**	**21b**	**22a**	 **23j**	10	85
11	**20b**	**21b**	**22b**	 **23k**	12	84
12	**20c**	**21b**	**22a**	 **23l**	10	82
13	**20d**	**21b**	**22b**	 **23m**	10	80
14	**20a**	**21c**	**22c**	 **23n**	11	75
15	**20a**	**21c**	**22d**	 **23o**	11	78

[a]*The reactions were performed in 0.5 mmol scale of 1-alkyl-1,2,3-triazole-4-carbaldehyde (**20**), aminopyridine (**21**) and terminal alkynes (**22**).* [b]*Isolated yield.*

Furthermore, the reaction was also performed with benzyl triazole-4-carbaldehyde (**20a**), 5-chloro-2-aminopyridine (**21c**) and with substituted phenylacetylene such as 3-methyl (**22c**) and 2-methoxy (**22d**) under similar reaction conditions afforded the desired products **23n** and **23o** in 75% and 78% yield (Table 13, entries 14-15) respectively.

The structure of the compound **23c** was confirmed through single-crystal X-ray analysis which is depicted in Figure 15, A. The molecule **23c** shows a dimer structure

with C-H…π interaction (H17b…C10) and its layered structure embrace a spectacular supramolecular assembly which is shown in Figure 15, B & C.

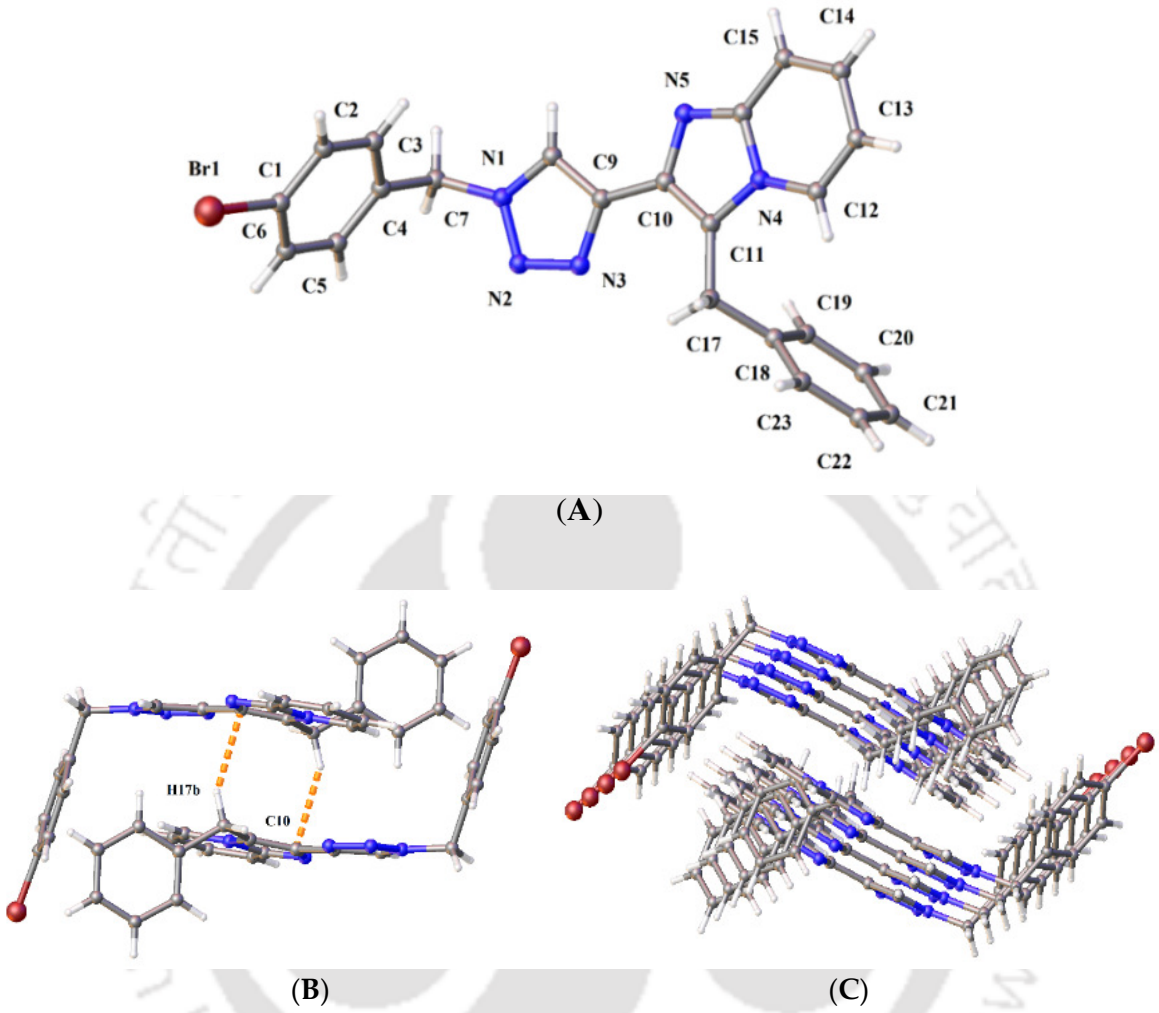


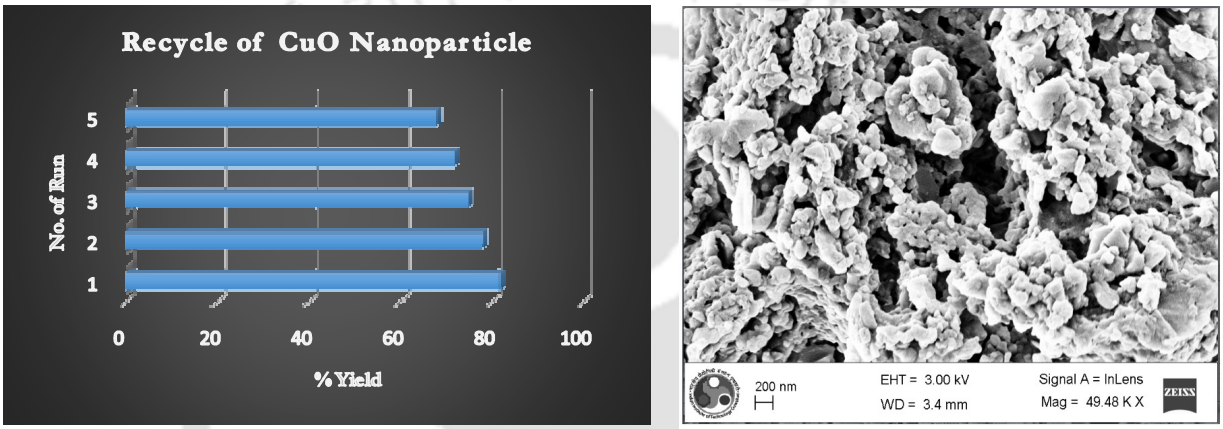
Figure 15. X-ray crystal structure (**A**), C-H…π interaction (**B**) and Layered structure (**C**) of **23c**

In addition, the recyclability of the catalyst was tested with **23c**. The obtained results are displayed in Table 14 and represented graphically in Figure 16A. In addition, the FESEM image of nano copper oxide catalyst after five cycles as shown in Figure 16B. Thus, it is concluded from the table 14 that even after five cycles our expected imidazole derivative could be achieved in moderate yield which shows the catalyst CuO nanoparticle is recyclable.

Table 14. Recycling of the CuO nanoparticle[a] in **23c**

Entry	No of cycle	mmol	Catalyst used	Catalyst Recovered	Time (h)	Yield (%)
01	01	07	28	25	10	81
02	02	05	20	18	11	77
03	03	04	16	13	12	72
04	04	03	12	09	14	68
05	05	02	08	5	18	58

[a]*CuO nanoparticle was filtered from the reaction mixture and washed with dichloromethane and dried before use for next cycle.*

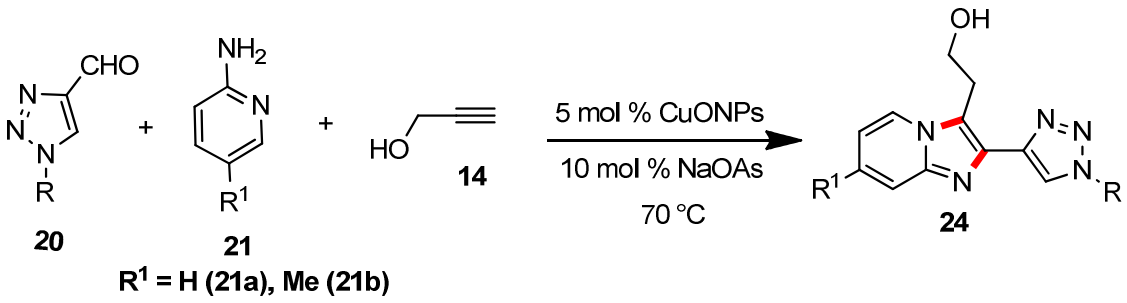


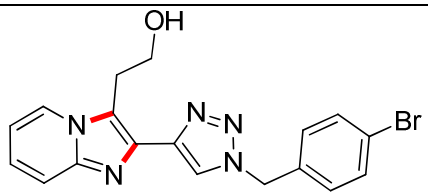
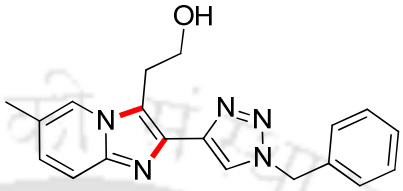
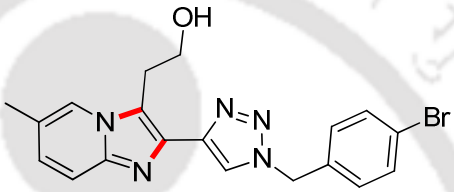
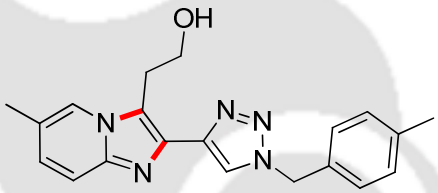
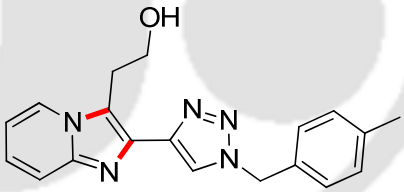
A **B**

Figure 16. (**A**) Recycle of the catalyst CuO nanoparticle and (**B**) FESEM image of CuO nanoparticle after five times recycling

The present protocol was further explored for the synthesis of 2-(2-(1-alkyl-1,2,3-triazol-4-yl)-imidazo[1,2-*a*]pyridin-3-yl)ethanol using propagyl alcohol (**14**), with different substituted triazole-4-carbaldehyde (**20**) and amidine (**21**) in the presence of catalytic amount of copper oxide nanoparticle along with sodium ascorbate under analogues reaction conditions and it offered the corresponding products **24a-e** with 72-78% yield which is depicted in Table 15.

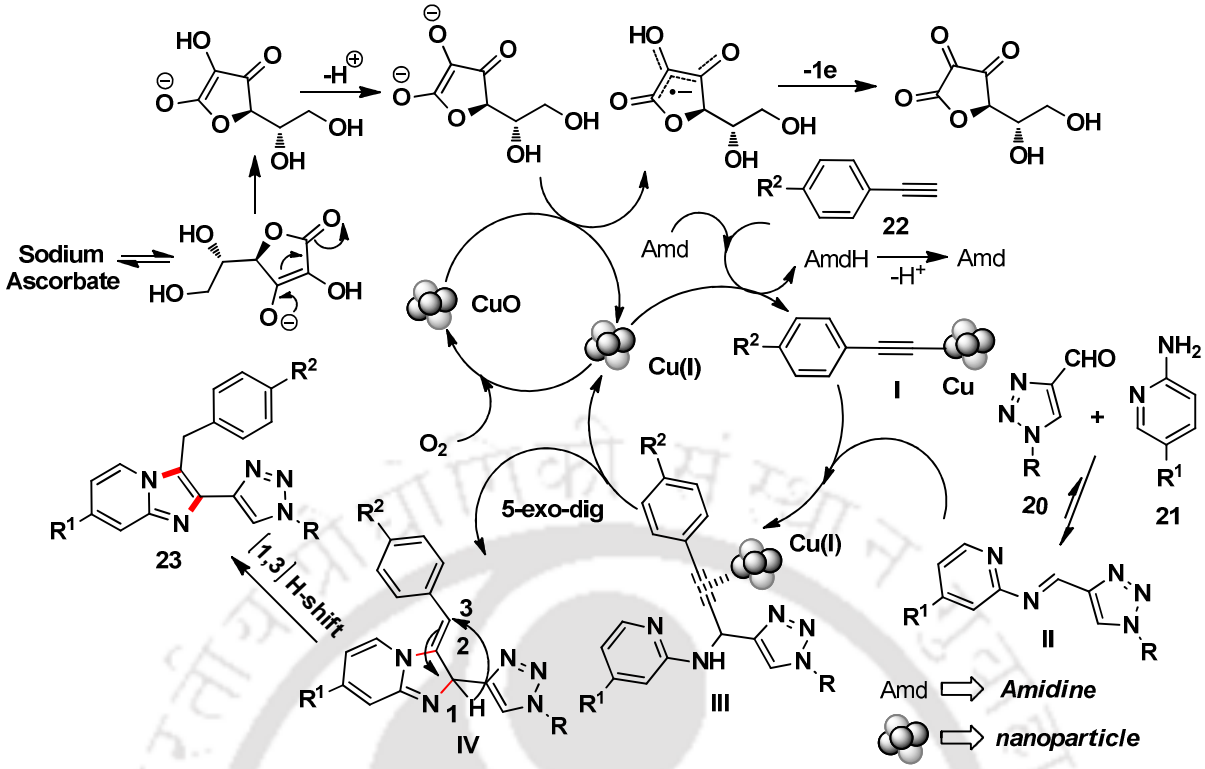
Table 15. Synthesis of 2-(2-(1-alkyl-1,2,3-triazol-4-yl)-imidazo[1,2-*a*]pyridin-3-yl)ethanol[a]



Entry	Aldehyde (**20**)	R^1(**21**)	Product (**24**)	Time (h)	Yield (%)[b]
01	**20c**	**21a**	 **24a**	12	72
02	**20a**	**21b**	 **24b**	11	74
03	**20c**	**21b**	 **24c**	11	76
04	**20b**	**21b**	 **24d**	10	78
05	**20b**	**21a**	 **24e**	11	76

[a]*The reactions were carried out in 0.5 mmol scale of 1-alkyl-1H-1,2,3-triazole-4-carbaldehyde (**20**), aminopyridine (**21**) and propargyl alcohol (**14**).* [b]*Isolated yield.*

The plausible mechanism for the formation of 2-triazolyl-imidazo[1,2-*a*]pyridine is outlined in Scheme 34. The copper(II) nanoparticle is reduced in the presence of sodium ascorbate to form copper(I) and then it forms a σ-adduct with the alkyne moiety to give the species **I**. The triazolyl aldehyde **20** reacts with amidine **21** to form imine **II**. Then the reaction of species **I** with imine **II** produces intermediate **III**. Subsequently, intermediate **III** undergoes favorable *5-exo-dig* cyclisation to form **IV** and it is followed by a 1,3-hydrogen shift to afford 2-triazolyl-imidazo[1,2-*a*]pyridine **23**.



Scheme 34. *Plausible mechanism for the formation of 2-triazolyl-imidazo[1,2-a]pyridine*

In conclusion, we have described here an one-pot three component reaction for the synthesis of 2-triazolyl-imidazo[1,2-*a*]pyridines via a nano copper oxide catalyzed A^3 coupling of triazolyl aldehyde, amidine and alkyne and followed by a *5-exo-dig* cyclisation. The decisive aspects of this present protocol are the use of an easy to handle, eco-friendly, recoverable and recyclable catalyst, high productivity and wide array of substrate compatibility. Moreover, this is the first reported method for the synthesis of 2-triazolyl-imidazo[1,2-*a*]pyridine by using nano click-catalyst. We have further explored the protocol for the synthesis of 2-(2-triazolyl-imidazo[1,2-*a*]pyridin-3-yl)ethanol, having the potential to act as a scaffold for the construction of predesigned molecules with promising bioactive applications. In addition, the dimeric and layer structure of **23c** displayed supramolecular architecture.

Experimental

Preparation of Pyridinium Chlorochromate (PCC)

Into 250 mL beaker CrO_3 (4.99 g, 50.0 mmol) was dissolved in 100 mL of 6 M HCl with constant stirring at room temperature. After 5 minutes, the homogeneous solution was cooled to 0 °C and pyridine (4.03 mL, 50.0 mmol) was carefully added over a period of 10 minutes. After 15 minutes, a yellow orange solid was precipitated out. The precipitate was filtered through a Büchner funnel and dried for 1 hr in vacuum pump to give pyridinium chlorochromate in 84% yield.

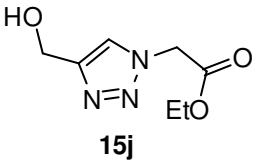
*General experimental procedure for the Synthesis of (1-alkyl-1,2,3-triazol-4-yl)methanol (**15**) and 1-alkyl-1,2,3-triazole-4-carbaldehyde (**20**)*

The starting materials, (1-alkyl-1H-1,2,3-triazol-4-yl)methanol (**15**), were synthesized by following earlier reported procedures in chapter II. Next, the product **15** was dissolved in 25 mL dichloromethane and it was added drop wise to the suspension of PCC in DCM and the reaction mixture was stirred at room temperature. After completion of the reaction, it was extracted with DCM (3 x 20 mL), washed with brine solution and the resulting organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Then, the crude residue was subjected to silica gel column chromatography to get the purified product **20**.

*General procedure for the Synthesis of 2-triazolyl-imidazo[1,2-a]pyridine (**23**) and 2-(2-(1-alkyl-1,2,3-triazol-4-yl)-imidazo[1,2-a]pyridin-3-yl)ethanol (**24**)*

To a 25 mL round bottomed flask was added 1-alkyl-1,2,3-triazole-4-carbaldehyde (**20**, 0.5 mmol), amidine (**21**, 0.5 mmol), CuO nanoparticle (1.99 mg), sodium ascorbate (9.9 mg) and ethanol (2 mL) at room temperature and allow it to stir for 10 min. Later on terminal alkyne (**22**, 0.5 mmol) was added and the resulting mixture was stirred at 70°C. After completion of reaction as checked by TLC, the reaction mixture was concentrated under reduced pressure. The obtained residue was extracted with DCM (2 x 10 mL) and washed twice with water followed by brine solution and dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Then the crude residue was purified over a silica gel column chromatography to obtain the pure products of 2-triazolyl-imidazo[1,2-*a*]pyridine **23**. The similar reaction procedure were followed for the synthesis of 2-(2-(1-alkyl-1,2,3-triazol-4-yl)-imidazo[1,2-*a*]pyridin-3-yl)ethanol **24**.

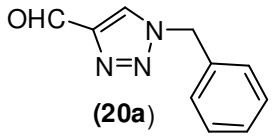
*Ethyl 2-(4-(hydroxymethyl)-1H-1,2,3-triazol-1-yl)acetate (**15j**)*



15j

White solid, M.p 68-69 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.65 (s, 1H), 5.09 (s, 2H), 4.64 (s, 2H), 4.17 (q, *J* = 7.2 Hz, 2H), 1.22 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 166.7, 148.3, 123.9, 62.4, 55.8, 50.9, 14.1; **IR** (KBr)ν_{max} 3260, 3133, 3088, 2993, 2936, 2865, 1744, 1556, 1455, 1421, 1400, 1379, 1345, 1237, 1145, 1063, 1021 cm^{-1}.

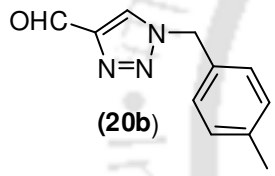
*1-benzyl-1H-1,2,3-triazole-4-carbaldehyde (**20a**)*



(20a)

White solid, M.p 90-91 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 10.12 (s, 1H), 7.98 (s, 1H), 7.41-7.39 (m, 3H), 7.31-7.29 (m, 2H), 5.58 (s, 2H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 185.2, 148.2, 133.5, 129.6, 129.5, 128.6, 125.3, 54.8; **IR** (KBr)ν_{max} 3127, 3049, 2995, 2925, 2854, 2775, 1694, 1586, 1534, 1495, 1456, 1358, 1237, 1166, 1048 cm^{-1}; **HRMS** (ESI) Calcd For $C_{10}H_{10}N_3O$ 188.0817 (M + H^+); Found 188.0819.

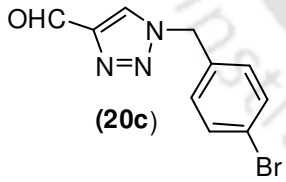
*1-(4-methylbenzyl)-1H-1,2,3-triazole-4-carbaldehyde (**20b**)*



(20b)

White solid, M.p 77-78 ˚C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 10.11 (s, 1H), 7.96 (s, 1H), 7.20 (s, 4H), 5.54 (s, 2H), 2.36 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 185.3, 148.1, 139.6, 130.5, 130.2, 128.6, 125.2, 54.6, 21.4; **IR** (KBr)ν_{max} 3132, 3041, 2988, 2924, 2854, 2768, 1699, 1610, 1532, 1517, 1463, 1437, 1355, 1243, 1160, 1044 cm^{-1}; **HRMS** (ESI) Calcd For $C_{11}H_{12}N_3O$ 202.0975 (M + H^+); Found 202.0975.

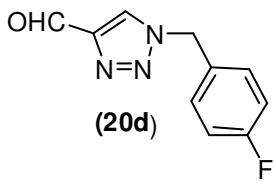
*1-(4-bromobenzyl)-1H-1,2,3-triazole-4-carbaldehyde (**20c**)*



(20c)

White solid, M.p 107-108 ˚C, **^{1}H NMR** (600 MHz, CD_2Cl_2): δ 10.8 (s, 1H), 8.06 (s, 1H), 7.55 (d, *J* = 8.4 Hz, 2H), 7.20 (d, *J* = 8.4 Hz, 2H), 5.55 (s, 2H); **^{13}C NMR** (150 MHz, CD_2Cl_2): δ 184.7, 148.1, 133.1, 133.0, 132.4, 130.1, 125.7, 125.6, 123.2, 53.2; **IR** (KBr)ν_{max} 3120, 3090, 3039, 2925, 2843, 2767, 1696, 1593, 1532, 1490, 1438, 1356, 1241, 1166, 1046 cm^{-1}; **HRMS** (ESI) Calcd For $C_{10}H_9BrN_3O$ 265.9924 (M + H^+); Found 265.9909.

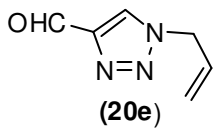
*1-(4-fluorobenzyl)-1H-1,2,3-triazole-4-carbaldehyde (**20d**)*



(20d)

White solid, M.p 73-74 ˚C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 10.08 (s, 1H), 7.97 (s, 1H), 7.27-7.29 (m, 2H), 7.03-7.08 (m, 2H), 5.53 (s, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 185.1, 164.4, 161.9, 148.1, 130.5, 130.4, 129.5, 129.4, 125.3, 116.6, 116.4, 53.9; **IR** (KBr)ν_{max} 3139, 3120, 3053, 2956, 2925, 2870, 1699, 1603, 1536, 1512, 1465, 1432, 1345, 1236, 1167, 1049 cm^{-1}; **HRMS** (ESI) Calcd For $C_{10}H_9FN_3O$ 206.0724 (M + H^+); Found 206.0722.

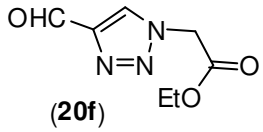
*1-allyl-1H-1,2,3-triazole-4-carbaldehyde (**20e**)*



(**20e**)

White solid, M.p 71-72 °C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 10.08 (s, 1H), 8.13 (s, 1H), 6.01 (s, 1H), 5.39-5.32 (m, 2H), 5.03 (s, 2H); **^{13}C** NMR (150 MHz, $CDCl_3$): δ 185.0, 147.9, 130.2, 125.4, 121.4, 53.1; **IR** (KBr)ν_{max} 3132, 3029, 2924, 2871, 1699, 1615, 1532, 1517, 1462, 1436, 1355, 1243, 1160, 1044 cm^{-1}; **MS** (ESI) Calcd For $C_6H_7N_3ONa$ 160.0481 ($M + Na^+$); Found 160.0816.

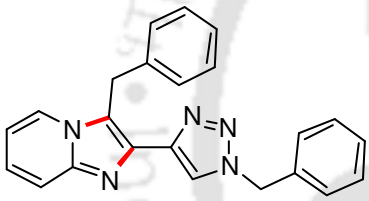
*Ethyl 2-(4-formyl-1H-1,2,3-triazol-1-yl)acetate (**20f**)*



(**20f**)

White solid, M.p 65-66 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.15 (s, 1H), 8.28 (s, 1H), 5.24 (s, 2H), 4.29 (br s, 2H), 1.31 (br s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 185.0, 165.6, 148.2, 127.0, 63.1, 51.2, 14.2; IR (KBr)ν_{max} 3132, 3062, 2997, 2959, 2849, 2781, 1745, 1703, 1540, 1478, 1416, 1397, 1379, 1249, 1170, 1049 cm^{-1}; HRMS (ESI) Calcd For $C_7H_{10}N_3O_3$ 184.0717 ($M + H^+$); Found 184.0715.

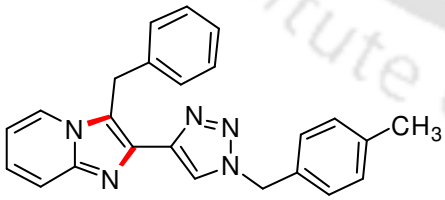
*3-benzyl-2-(1-benzyl-1H-1,2,3-triazol-4-yl)imidazo[1,2-a]pyridine (**23a**)*



(**23a**)

White solid, M.p 169-170 °C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.92 (s, 1H), 8.27 (s, 1H), 8.15 (d, *J* = 8.4 Hz, 1H), 7.76 (br s, 6H), 7.65-7.63 (m, 6H), 5.99 (s, 2H), 5.36 (s, 2H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 145.0, 144.6, 137.3, 134.6, 129.4, 128.9, 128.7, 128.4, 126.8, 125.0, 123.9, 122.1, 120.1, 117.1, 112.7, 54.5, 29.9; **IR** (KBr)ν_{max} 3139, 3061, 3028, 2923, 2853, 1602, 1536, 1504, 1494, 1454, 1359, 1297, 1225, 1077, 1047 cm^{-1}; **HRMS** (ESI) Calcd For $C_{23}H_{20}N_5$ 366.1713 ($M + H^+$); Found 366.1716.

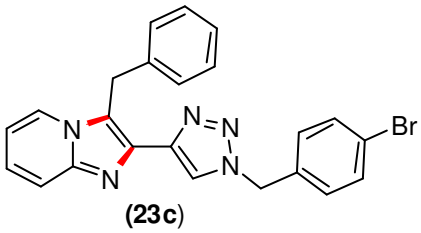
3-*benzyl-2-(1-(4-methylbenzyl)-1H-1,2,3-triazol-4-yl)imidazo[1,2-a]pyridine (**23b**)*



(**23b**)

White solid, M.p 146-147 °C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.03 (s, 1H), 7.78 (d, *J* = 7.2 Hz, 1H), 7.53 (d, *J* = 9.0 Hz, 1H), 7.26-7.22 (m, 6H), 7.19-7.16 (m, 3H), 7.14-7.12 (m, 1H), 6.68 (t, *J* = 6.8 Hz, 1H), 5.54 (s, 2H), 4.93 (s, 2H), 2.35 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 145.1, 144.8, 138.9, 137.4, 134.7, 131.5, 129.9, 128.8, 128.7, 128.3, 126.7, 124.6, 123.7, 121.7, 119.9, 117.2, 112.3, 54.2, 29.8, 21.3; **IR** (KBr)ν_{max} 3137, 3053, 3025, 2953, 2923, 2848, 1601, 1516, 1503, 1493, 1453, 1359, 1295, 1219, 1074, 1047 cm^{-1}; **HRMS** (ESI) Calcd For $C_{24}H_{22}N_5$ 380.1870 ($M + H^+$); Found 380.1870.

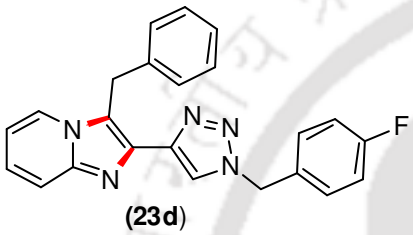
*3-benzyl-2-(1-(4-bromobenzyl)-1H-1,2,3-triazol-4-yl)imidazo[1,2-a]pyridine (**23c**)*



(23c)

White solid, M.p 177-178 °C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.58 (s, 1H), 7.89 (d, *J* = 7.2 Hz, 1H), 7.79 (d, *J* = 8.8 Hz, 1H), 7.51 (d, *J* = 8.4 Hz, 2H), 7.37 (t, *J* = 8.0 Hz, 1H), 7.28-7.21 (m, 7H), 6.89 (t, *J* = 7.2 Hz, 1H), 5.56 (s, 2H), 4.96 (s, 2H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 145.1, 144.9, 137.3, 134.4, 133.7, 132.4, 130.1, 128.9, 128.3, 126.8, 124.8, 123.8, 123.1, 121.9, 120.1, 117.2, 112.5, 53.7, 29.8; **IR** (KBr)ν_{max} 3142, 3052, 3020, 2948, 2923, 2853, 1601, 1503, 1490, 1453, 1358, 1296, 1225, 1071, 1047 cm^{-1}; **HRMS** (ESI) Calcd For $C_{23}H_{19}BrN_5$ 444.0819 ($M + H^+$); Found 444.0815.

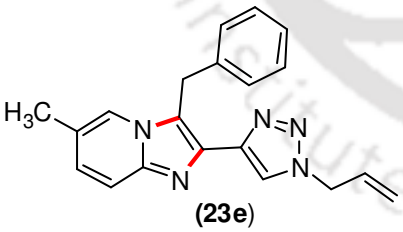
*3-benzyl-2-(1-(4-fluorobenzyl)-1H-1,2,3-triazol-4-yl)imidazo[1,2-a]pyridine (**23d**)*



(23d)

White solid, M.p 111-112 °C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.06 (s, 1H), 7.80 (d, *J* = 6.0 Hz, 1H), 7.55 (d, *J* = 8.8 Hz, 1H), 7.35 (br s, 2H), 7.27-7.23 (m, 5H), 7.18-7.14 (m, 1H), 7.08 (t, *J* = 8.4 Hz, 2H), 6.71 (br s, 1H), 5.57 (s, 2H), 4.93 (s, 2H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 163.9, 162.2, 145.0, 144.4, 137.2, 134.0, 130.6, 130.4, 130.3, 129.6, 128.9, 128.4, 128.3, 126.8, 125.1, 123.8, 122.2, 120.1, 117.0, 116.3, 116.2, 112.7, 53.6, 29.8; **IR** (KBr)ν_{max} 3138, 3064, 3028, 2956, 2924, 2853, 1603, 1511, 1494, 1454, 1359, 1296, 1224, 1073, 1048 cm^{-1}; **HRMS** (ESI) Calcd For $C_{23}H_{19}FN_5$ 384.1619 ($M + H^+$); Found 384.1618.

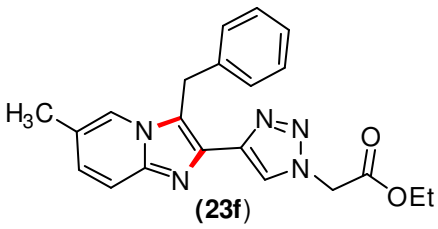
*2-(1-allyl-1H-1,2,3-triazol-4-yl)-3-benzyl-6-methylimidazo[1,2-a]pyridine (**23e**)*



(23e)

White solid, M.p 191-192 °C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.41 (s, 1H), 7.58 (s, 2H), 7.19-7.12 (m, 6H), 6.03-5.98 (m, 1H), 5.34 (s, 1H), 5.30 (d, *J* = 9.2 Hz, 1H), 4.99 (d, *J* = 4.0 Hz, 2H), 4.86 (s, 2H), 2.21 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 144.1, 143.7, 137.3, 133.6, 131.2, 128.8, 128.5, 128.3, 126.7, 122.6, 122.1, 121.5, 120.6, 119.8, 116.3, 52.9, 29.7, 18.5; **IR** (KBr)ν_{max} 3142, 3070, 2962, 2920, 2848, 1598, 1536, 1511, 1491, 1451, 1412, 1366, 1327, 1295, 1222, 1047 cm^{-1}; **HRMS** (ESI) Calcd For $C_{20}H_{20}N_5$ 330.1713 ($M + H^+$); Found 330.1724.

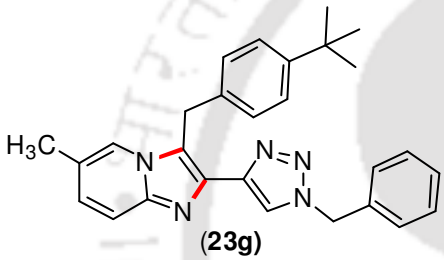
*Ethyl 2-(4-(3-benzyl-6-methylimidazo[1,2-a]pyridin-2-yl)-1H-1,2,3-triazol-1-yl)acetate (**23f**)*



(23f)

White solid, M.p 109-110 °C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.27 (s, 1H), 7.58 (s, 1H), 7.58 (d, *J* = 9.2 Hz, 1H), 7.25-7.23 (m, 4H), 7.20-7.18 (m, 1H), 7.03 (d, *J* = 9.2 Hz, 1H), 5.21 (s, 2H), 4.88 (s, 2H), 4.27 (q, *J* = 6.8 Hz, 2H), 2.24 (s, 3H), 1.29 (t, *J* = 6.8 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 166.3, 144.5, 142.8, 137.4, 133.7, 128.9, 128.4, 128.3, 126.8, 123.5, 122.5, 121.5, 119.9, 116.4, 62.6, 51.2, 29.9, 18.6, 14.3; **IR** (KBr)ν_{max} 3142, 2978, 2959, 2925, 2854, 1749, 1613, 1539, 1495, 1454, 1376, 1344, 1299, 1262, 1217, 1023 cm^{-1}; **HRMS** (ESI) Calcd For $C_{21}H_{22}N_5O_2$ 376.1768 (M + H^+); Found 376.1796.

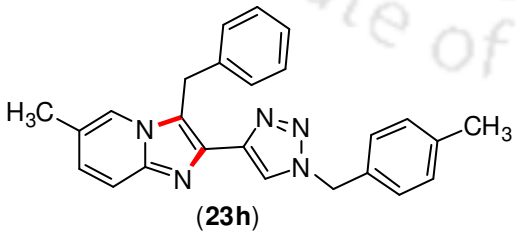
2-(1-benzyl-1H-1,2,3-triazol-4-yl)-3-(4-(tert-butyl)benzyl)-6-methylimidazo[1,2-a]pyridine ***(23g)***



(23g)

White solid, M.p 241-242 °C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.13 (s, 1H), 7.63 (s, 1H), 7.49 (d, *J* = 9.2 Hz, 1H), 7.38-7.36 (m, 5H), 7.27-7.23 (m, 2H), 7.15 (d, *J* = 8.0 Hz, 2H), 7.04 (d, *J* = 9.2 Hz, 1H), 5.58 (s, 2H), 4.85 (s, 2H), 2.26 (s, 3H), 1.27 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 149.4, 144.9, 144.0, 134.6, 134.4, 129.2, 128.9, 128.6, 127.9, 127.8, 125.7, 122.0, 121.7, 121.4, 119.9, 116.4, 54.4, 34.5, 31.5, 29.1, 18.5; **IR** (KBr)ν_{max} 3143, 3089, 3064, 2957, 2920, 2866, 1596, 1537, 1511, 1496, 1366, 1341, 1299, 1229, 1047 cm^{-1}; **HRMS** (ESI) Calcd For $C_{28}H_{30}N_5$ 436.2496 (M + H^+); Found 436.2496.

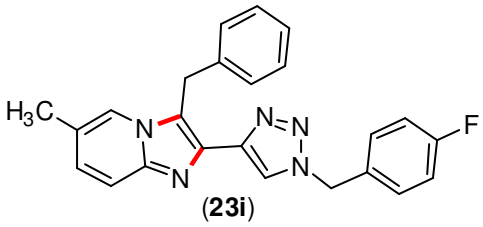
3-benzyl-6-methyl-2-(1-(4-methylbenzyl)-1H-1,2,3-triazol-4-yl)imidazo[1,2-a]pyridine ***(23h)***



(23h)

White solid, M.p 222-223 °C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.01 (s, 1H), 7.57 (s, 1H), 7.44 (d, *J* = 8.4 Hz, 1H), 7.26-7.19 (m, 9H), 6.99 (d, *J* = 8.0 Hz, 1H), 5.53 (s, 2H), 4.89 (s, 2H), 2.35 (s, 3H), 2.23 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 144.9, 138.8, 137.5, 134.5, 131.5, 129.9, 128.7, 128.6, 128.3, 127.7, 126.6, 121.9, 121.6, 121.3, 116.5, 54.2, 29.7, 21.3, 18.5; **IR** (KBr)ν_{max} 3133, 3065, 3022, 2921, 2853, 1602, 1536, 1514, 1494, 1452, 1344, 1298, 1230, 1047 cm^{-1}; **HRMS** (ESI) Calcd For $C_{25}H_{24}N_5$ 394.2026 (M + H^+); Found 394.2030.

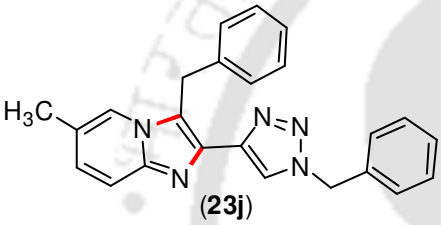
3-benzyl-2-(1-(4-fluorobenzyl)-1H-1,2,3-triazol-4-yl)-6-methylimidazo[1,2-a]pyridine ***(23i)***



(**23i**)

White solid, M.p 203-204 °C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.60 (s, 2H), 7.31-7.28 (m, 2H), 7.22-7.14 (m, 7H), 7.00 (t, *J* = 8.8 Hz, 2H), 5.51 (s, 2H), 4.87 (s, 2H), 2.22 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 163.9, 162.3, 144.1, 143.4, 137.1, 133.2, 130.5, 130.4, 128.9, 128.6, 128.3, 127.9, 126.8, 125.8, 122.9, 122.2, 121.6, 119.9, 116.3, 116.2, 116.1, 53.7, 29.8, 18.5; **IR** (KBr)ν_{max} 3131, 3062, 3025, 2951, 2919, 2845, 1602, 1537, 1511, 1494, 1453, 1343, 1296, 1227, 1065, 1046 cm^{-1}; **HRMS** (ESI) Calcd For $C_{24}H_{21}FN_5$ 398.1776 (M + H^+); Found 398.1776.

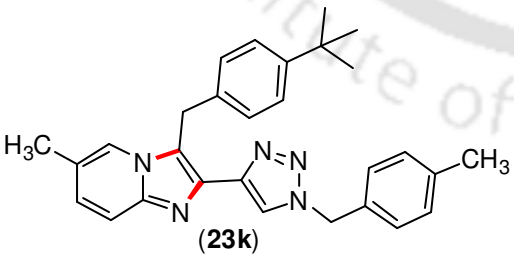
3-benzyl-2-(1-benzyl-1H-1,2,3-triazol-4-yl)-6-methylimidazo[1,2-a]pyridine ***(23j)***



(**23j**)

White solid, M.p 242-243 °C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.05 (s, 1H), 7.57 (s, 1H), 7.44 (d, *J* = 8.8 Hz, 1H), 7.37-7.36 (m, 5H), 7.25-7.23 (m, 4H), 7.19 (d, *J* = 7.2 Hz, 1H), 6.99 (s, *J* = 8.8 Hz, 1H), 5.58 (s, 2H), 4.89 (s, 2H), 2.23 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 145.0, 144.3, 137.6, 134.6, 129.3, 128.9, 128.8, 128.6, 128.4, 127.8, 126.6, 122.1, 121.7, 121.4, 119.7, 116.6, 54.5, 29.8, 18.6; **IR** (KBr)ν_{max} 3145, 3084, 3062, 3028, 2984, 2915, 2835, 1604, 1538, 1513, 1493, 1454, 1343, 1295, 1209, 1047 cm^{-1}; **HRMS** (ESI) Calcd For $C_{24}H_{22}N_5$ 380.1870 (M + H^+); Found 380.1871.

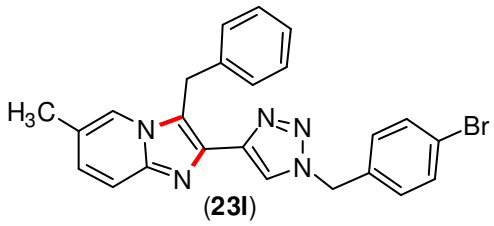
3-(4-(tert-butyl)benzyl)-6-methyl-2-(1-(4-methylbenzyl)-1H-1,2,3-triazol-4-yl)imidazo[1,2-a] pyridine ***(23k)***



(**23k**)

White solid, M.p 189-190 °C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.08 (s, 1H), 7.62 (s, 1H), 7.47 (d, *J* = 9.2 Hz, 1H), 7.27-7.23 (m, 4H), 7.18-7.14 (m, 4H), 7.01 (d, *J* = 9.2 Hz, 1H), 5.52 (s, 2H), 4.84 (s, 2H), 2.39 (s, 3H), 2.25 (s, 3H), 1.26 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 149.4, 144.7, 143.9, 138.8, 134.4, 131.6, 129.9, 128.7, 127.9, 125.7, 122.1, 121.8, 121.4, 119.9, 116.4, 54.2, 34.5, 31.5, 31.3, 29.1, 21.3, 18.6; **IR** (KBr)ν_{max} 3139, 3051, 3026, 2962, 2923, 2866, 1616, 1539, 1515, 1454, 1365, 1342, 1301, 1231, 1047 cm^{-1}; **HRMS** (ESI) Calcd For $C_{29}H_{32}N_5$ 450.2652 (M + H^+); Found 450.2652.

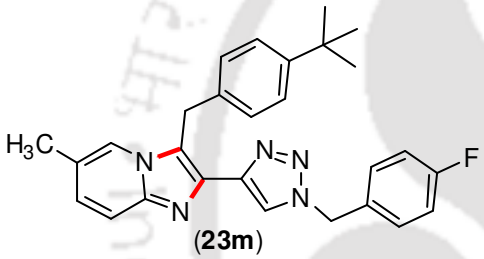
3-benzyl-2-(1-(4-bromobenzyl)-1H-1,2,3-triazol-4-yl)-6-methylimidazo[1,2-a]pyridine ***(23l)***



(23l)

White solid, M.p 179-180 °C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.19 (s, 1H), 7.54 (s, 1H), 7.48 (d, *J* = 9.6 Hz, 1H), 7.44 (d, *J* = 8.8 Hz, 2H), 7.21-7.13 (m, 7H), 7.03 (d, *J* = 8.8 Hz, 1H), 5.48 (s, 2H), 4.83 (s, 2H), 2.19 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 144.6, 143.9, 137.4, 133.7, 132.5, 130.2, 128.9, 128.4, 128.3, 126.7, 123.1, 122.5, 122.1, 121.4, 119.9, 116.4, 53.7, 29.9, 18.6; **IR** (KBr)ν_{max} 3142, 3059, 3025, 2951, 2924, 2853, 1602, 1540, 1512, 1489, 1453, 1342, 1298, 1230, 1046 cm^{-1}; **HRMS** (ESI) Calcd For $C_{24}H_{21}BrN_5$ 458.0975 ($M + H^+$); Found 458.0979.

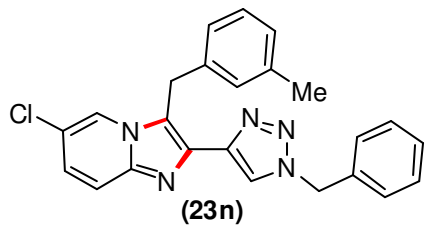
3-(4-(tert-butyl)benzyl)-2-(1-(4-fluorobenzyl)-1H-1,2,3-triazol-4-yl)-6-methylimidazo[1,2-a] pyridine ***(23m)***



(23m)

White solid, M.p 201-202 °C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.15 (s, 1H), 7.64 (s, 1H), 7.50 (d, *J* = 9.0 Hz, 1H), 7.35-7.33 (m, 2H), 7.27-7.25 (m, 2H), 7.14 (d, *J* = 7.8 Hz, 2H), 7.06 (t, *J* = 8.4 Hz, 3H), 5.55 (s, 2H), 4.85 (s, 2H), 2.26 (s, 3H), 1.26 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 164.3, 161.9, 149.6, 144.3, 143.6, 134.1, 133.3, 130.5, 130.4, 128.7, 127.9, 125.8, 122.7, 122.1, 121.6, 120.1, 116.4, 116.2, 53.7, 34.6, 31.5, 29.9, 18.6; **IR** (KBr)ν_{max} 3053, 2962, 2920, 2867, 1606, 1545, 1516, 1454, 1420, 1364, 1298, 1225, 1159, 1048 cm^{-1}; **HRMS** (ESI) Calcd For $C_{28}H_{29}FN_5$ 454.2402 ($M + H^+$); Found 454.2402.

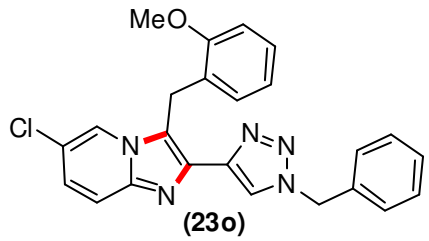
2-(1-benzyl-1H-1,2,3-triazol-4-yl)-6-chloro-3-(3-methylbenzyl)imidazo[1,2-a]pyridine ***(23n)***



(23n)

White solid, M.p 199-200 °C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.03 (s, 1H), 7.83 (s, 1H), 7.48 (d, *J* = 9.6 Hz, 1H), 7.39-7.35 (m, 5H), 7.15 (t, *J* = 7.2 Hz, 1H), 7.11 (d, *J* = 9.6 Hz, 1H), 7.02-6.99 (m, 3H), 5.59 (s, 2H), 4.86 (s, 2H), 2.26 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 144.6, 143.6, 138.7, 136.7, 135.8, 134.5, 129.4, 129.1, 128.9, 128.7, 127.8, 126.0, 125.4, 122.0, 121.7, 120.8, 120.7, 117.6, 54.6, 29.8, 21.6; **IR** (KBr)ν_{max} 3047, 2984, 2882, 2801, 1612, 1538, 1512, 1471, 1430, 1338, 1312, 1247, 1166, 1064 cm^{-1}; **HRMS** (ESI) Calcd For $C_{24}H_{21}ClN_5$ 414.1480 ($M + H^+$); Found 414.1486.

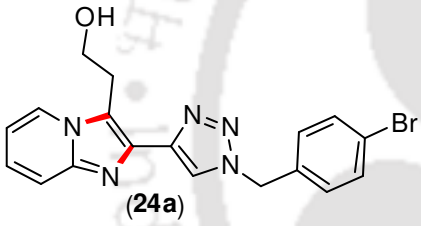
*2-(1-benzyl-1H-1,2,3-triazol-4-yl)-6-chloro-3-(2-methoxybenzyl)imidazo[1,2-a] pyridine (**23o**)*



(23o)

White solid, M.p 203-204 °C, **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.17 (s, 1H), 8.01 (s, 1H), 7.44 (d, *J* = 9.0 Hz, 1H), 7.40-7.35 (m, 5H), 7.18-7.16 (m, 2H), 7.09 (d, *J* = 9.6 Hz, 1H), 6.91 (d, *J* = 8.4 Hz, 1H), 6.77 (t, *J* = 7.2 Hz, 1H), 5.58 (s, 2H), 4.84 (s, 2H), 3.95 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 156.9, 144.7, 143.3, 135.5, 134.6, 130.2, 129.4, 129.0, 128.7, 128.1, 125.8, 125.4, 122.6, 121.9, 121.7, 121.2, 120.4, 117.4, 110.6, 55.5, 54.6, 29.9; **IR** (KBr)ν_{max} 3042, 2978, 2915, 2890, 2812, 1608, 1539, 1515, 1498, 1471, 1335, 1313, 1229, 1078, 1061 cm^{-1}; **HRMS** (ESI) Calcd For $C_{24}H_{21}ClN_5O$ 430.1429 ($M + H^+$); Found 430.1437.

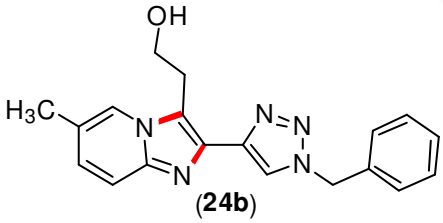
*2-(2-(1-(4-bromobenzyl)-1H-1,2,3-triazol-4-yl)imidazo[1,2-a]pyridin-3-yl)ethanol (**24a**)*



(24a)

Yellow solid, M.p 199-200 °C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.08 (d, *J* = 6.4 Hz, 1H), 8.01 (s, 1H), 7.52 (d, *J* = 8.0 Hz, 3H), 7.22 (d, *J* = 8.0 Hz, 2H), 7.17 (t, *J* = 8.8 Hz, 1H), 6.83 (t, *J* = 6.4 Hz, 1H), 5.53 (s, 2H), 4.09 (d, *J* = 5.6 Hz, 2H), 3.60 (d, *J* = 5.6 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 145.1, 144.8, 134.4, 133.5, 132.5, 130.2, 124.6, 123.6, 123.3, 121.8, 119.7, 117.4, 112.5, 61.5, 53.9, 27.1; **IR** (KBr)ν_{max}3126, 3051, 2923, 2850, 1591, 1503, 1489, 1432, 1407, 1359, 1298, 1226, 1070, 1045 cm^{-1}; **HRMS** (ESI) Calcd For $C_{18}H_{17}BrN_5O$ 398.0611 ($M + H^+$); Found 398.0611.

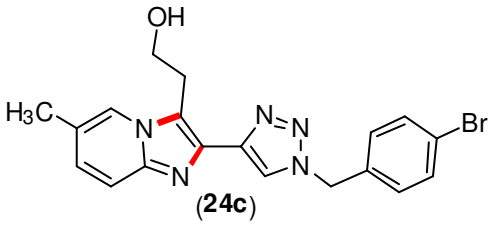
*2-(2-(1-benzyl-1H-1,2,3-triazol-4-yl)-6-methylimidazo[1,2-a]pyridin-3-yl)ethanol (**24b**)*



(24b)

Yellow solid, M.p 119-120 °C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.99 (s, 1H), 7.82 (s, 1H), 7.41-7.35 (m, 6H), 7.01 (d, *J* = 8.4 Hz, 1H), 5.56 (s, 2H), 4.06 (br s, 2H), 3.57 (br s, 2H), 2.34 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 144.6, 134.4, 129.4, 129.1, 128.6, 127.7, 122.2, 121.7, 121.1, 116.7, 61.4, 54.6, 27.1, 18.6; **IR** (KBr)ν_{max} 3145, 3062, 3028, 2923, 2855, 1587, 1540, 1512, 1497, 1455, 1366, 1345, 1303, 1230, 1124, 1046 cm^{-1}; **HRMS** (ESI) Calcd For $C_{19}H_{20}N_5O$ 334.1663 ($M + H^+$); Found 334.1664.

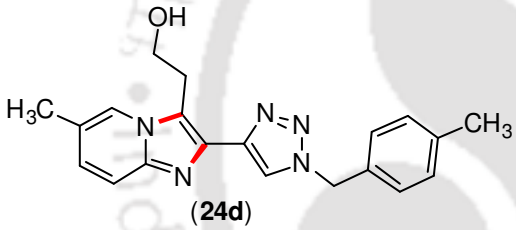
*2-(2-(1-(4-bromobenzyl)-1H-1,2,3-triazol-4-yl)-6-methylimidazo[1,2-a]pyridin-3-yl)ethanol (**24c**)*



(**24c**)

Yellow solid, M.p 207-208 °C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.99 (s, 1H), 7.83 (s, 1H), 7.51 (d, *J* = 8.4 Hz, 2H), 7.43 (d, *J* = 9.6 Hz, 1H), 7.21 (d, *J* = 8.4 Hz, 2H), 7.03 (d, *J* = 9.6 Hz, 1H), 5.23 (s, 2H), 4.06 (s, 2H), 3.57 (s, 2H), 2.35 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 144.9, 144.2, 134.2, 133.5, 132.5, 130.2, 127.8, 123.3, 122.3, 121.7, 121.2, 119.2, 116.7, 110.2, 61.4, 53.9, 27.1, 18.6; **IR** (KBr)ν_{max} 3144, 3056, 2959, 2923, 2850, 1589, 1488, 1451, 1407, 1341, 1304, 1229, 1069, 1046 cm^{-1}; **HRMS** (ESI) Calcd For $C_{19}H_{19}BrN_5O$ 412.0768 ($M + H^+$); Found 412.0766.

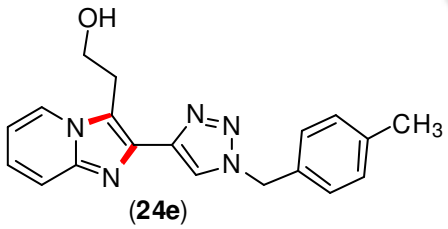
*2-(6-methyl-2-(1-(4-methylbenzyl)-1H-1,2,3-triazol-4-yl)imidazo[1,2-a]pyridin-3-yl)ethanol (**24d**)*



(**24d**)

Yellow solid, M.p 214-215 °C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.97 (s, 1H), 7.82 (s, 1H), 7.42 (d, *J* = 8.8 Hz, 1H), 7.26-7.22 (m, 2H), 7.19-7.17 (m, 2H), 7.02 (d, *J* = 8.8 Hz, 1H), 5.52 (s, 2H), 4.06 (br s, 2H), 3.57 (br s, 2H), 2.35 (br s 6H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 144.3, 138.5, 133.9, 131.3, 129.6, 128.3, 127.4, 121.7, 121.3, 116.2, 60.9, 53.9, 26.5, 21.1, 18.2; **IR** (KBr)ν_{max} 3141, 3051, 2953, 2922, 2845, 1601, 1553, 1539, 1500, 1456, 1363, 1297, 1215, 1121, 1048 cm^{-1}; **HRMS** (ESI) Calcd For $C_{20}H_{22}N_5O$ 348.1819 ($M + H^+$); Found 348.1827.

*2-(2-(1-(4-methylbenzyl)-1H-1,2,3-triazol-4-yl)imidazo[1,2-a]pyridin-3-yl)ethanol (**24e**)*



(**24e**)

Yellow solid, M.p 148-149 °C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.09-8.01 (m, 2H), 7.50 (br s, 1H), 7.27-7.17 (m, 5H), 6.81 (br s, 1H), 5.52 (s, 2H), 4.07 (s, 2H), 3.59 (s, 2H), 3.11 (br s, 1H), 2.35 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 141.1, 139.0, 138.9, 134.4, 131.4, 129.9, 128.7, 128.4, 124.7, 123.7, 122.1, 117.4, 112.6, 61.4, 54.4, 27.1, 21.3; **IR** (KBr)ν_{max} 3148, 3054, 2958, 2929, 2851, 1598, 1551, 1541, 1489, 1448, 1366, 1302, 1216, 1115, 1046 cm^{-1}; **HRMS** (ESI) Calcd For $C_{19}H_{20}N_5O$ 334.1663 ($M + H^+$); Found 334.1664.

XRD for Compounds **15f** and **23c**

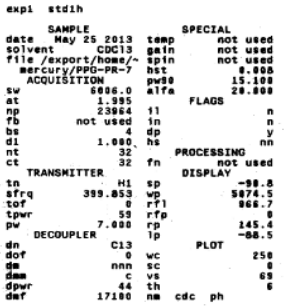
Complete crystallographic data of compounds **15f** and **23c** for the structural analyses have been deposited with the Cambridge Crystallographic Data Centre, CCDC No. are 979591 and 1019691 respectively. Copies of this information may be obtained free of charge from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44-1223-336033, e-mail: deposit@ccdc.cam.ac.uk or via: www.ccdc.cam.ac.uk).

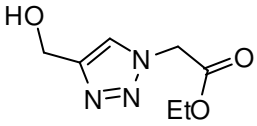
Table 16. Crystal Data and Structure Refinement for Compounds **15f** and **23c**

Entry	Identification code	Compound **15f**	Compound **23c**
01	Empirical formula	$C_7 H_{11} N_3 O_3$	$C_{23} H_{18} Br N_5$
02	Formula weight	185.19	444.32
03	Temperature	296(2) K	296(2) K
04	Wavelength	0.71073	0.71073
05	Radiation type	Mo K\a	Mo K\a
06	Radiation source	Fine-focus sealed tube	Fine-focus sealed tube
07	Crystal system	monoclinic	orthorhombic
08	Space group	P 21/n	P b c a
09	Cell length	a 7.9591(4) b 4.8417(3) c 23.7648(14)	a 10.5296(11) b 17.3251(18) c 22.405(2)
10	Cell Angle	α 90.0 β 94.296(5) δ 90.0	α 90.0 β 90.00 δ 90.0
11	Cell Volume	913.21(9)	4087.3(7)
12	Density	1.347	1.444
13	Completeness to theta	25.25° / 100%	26.61° / 98.4%
14	Absorption correction	multi-scan	multi-scan
15	Refinement method	Full-matrix least-squares on F2	Full-matrix least-squares on F2
16	Index ranges	-10<=h<=10, -6<=k<=3, -28<=l<=29	-11<=h<=13, -21<=k<=21, -26<=l<=27
17	Reflection number	1648	4219

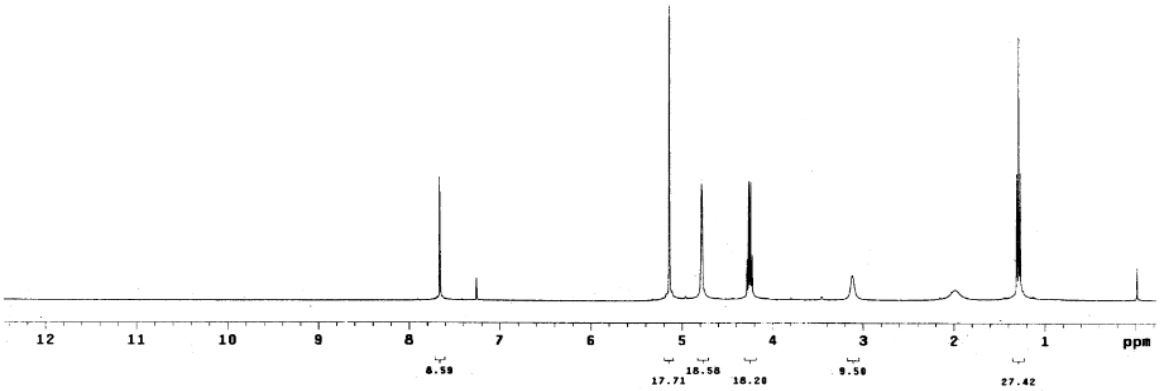
18	Theta range	3.44 - 25.25	1.82-26.61
19	Cell formula units Z	4	8
20	CCDC no	979591	1019691

***^{1}H NMR (400 MHz, $CDCl_3$)**: (Ethyl 2-(4-(hydroxymethyl)-1H-1,2,3-triazol-1-yl)acetate (**15j**)*

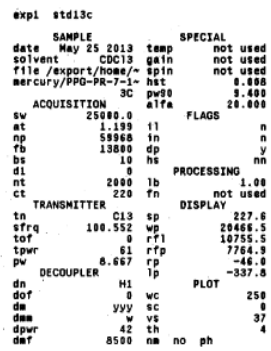


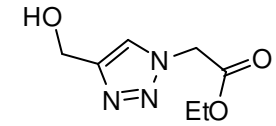


15j

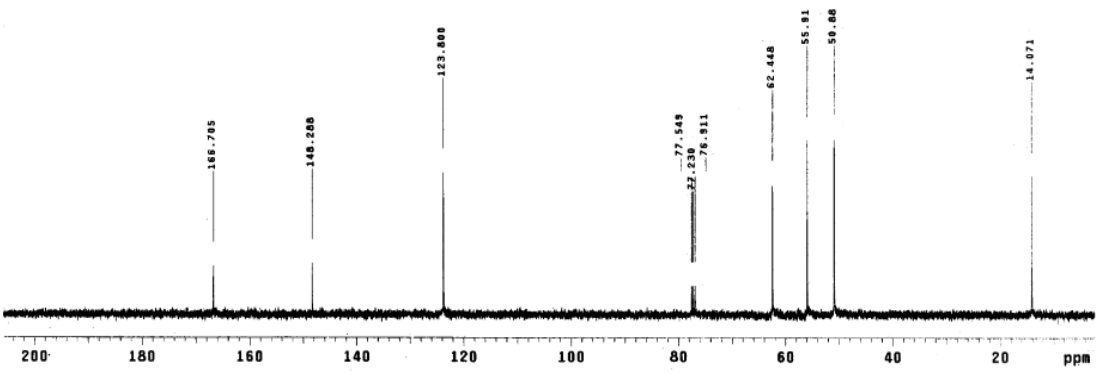


***^{13}C NMR (100 MHz, $CDCl_3$)**: Ethyl 2-(4-(hydroxymethyl)-1H-1,2,3-triazol-1-yl)acetate (**15j**)*

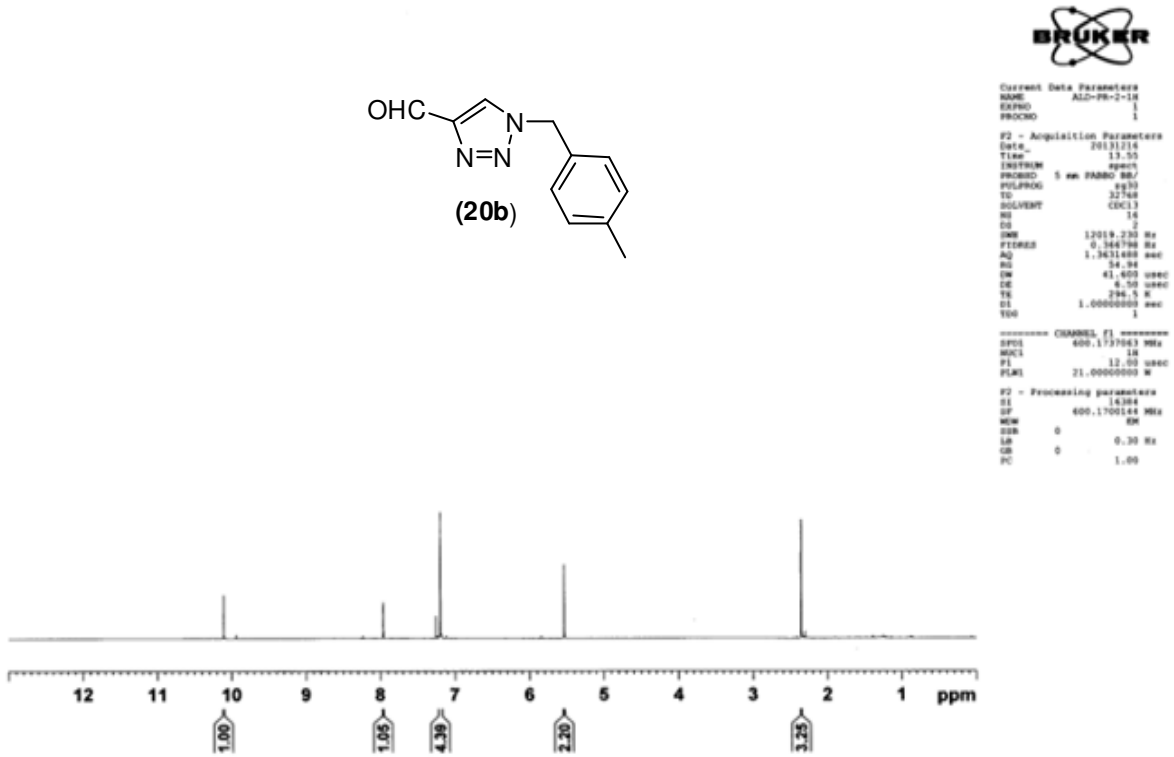




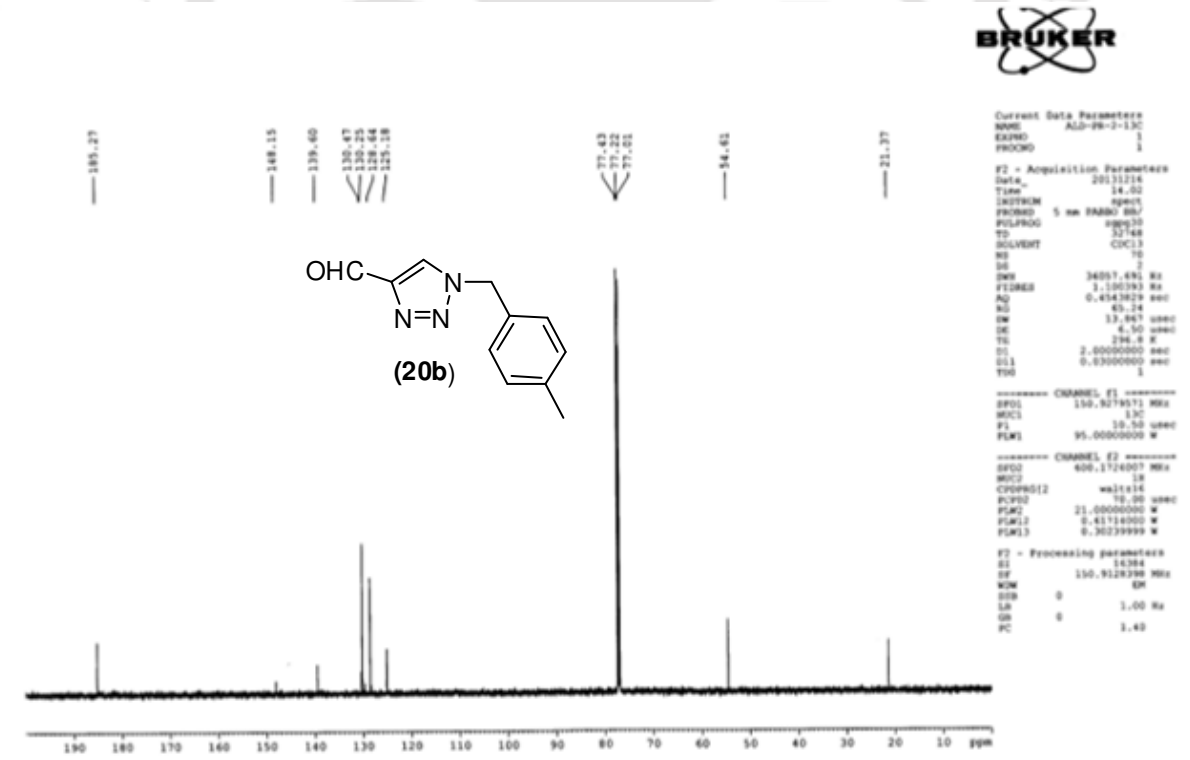
15j



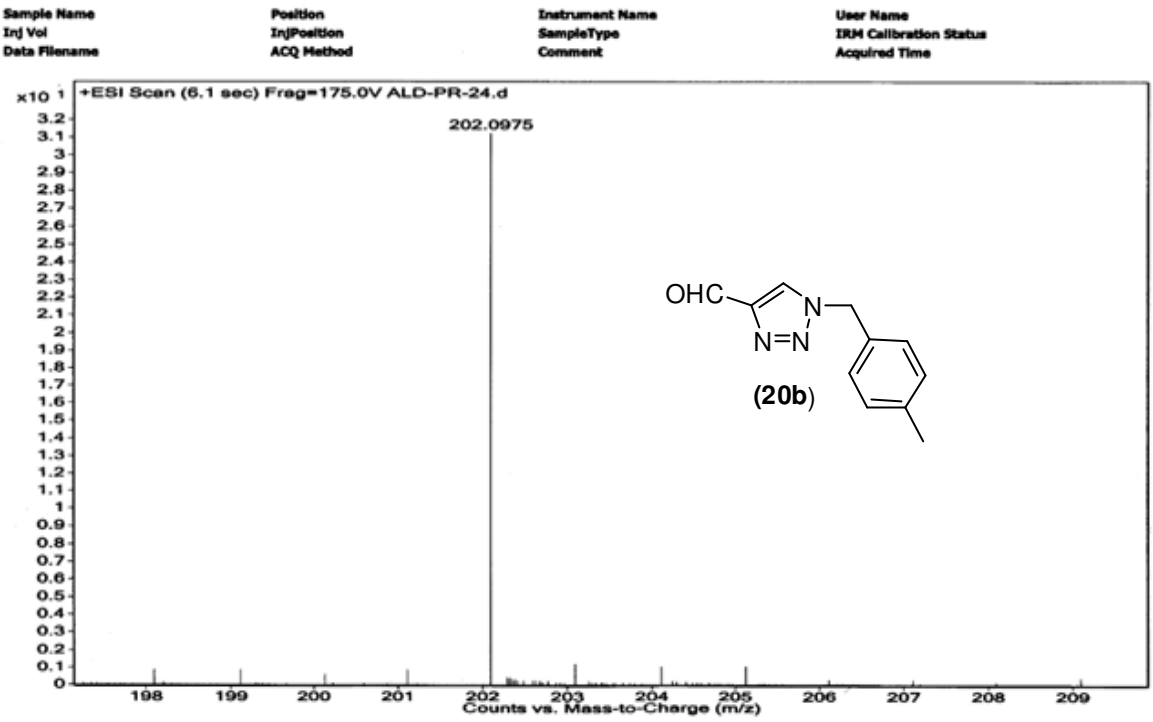
***^{1}H NMR (600 MHz, $CDCl_3$)**: 1-(4-methylbenzyl)-1H-1,2,3-triazole-4-carbaldehyde (**20b**)*



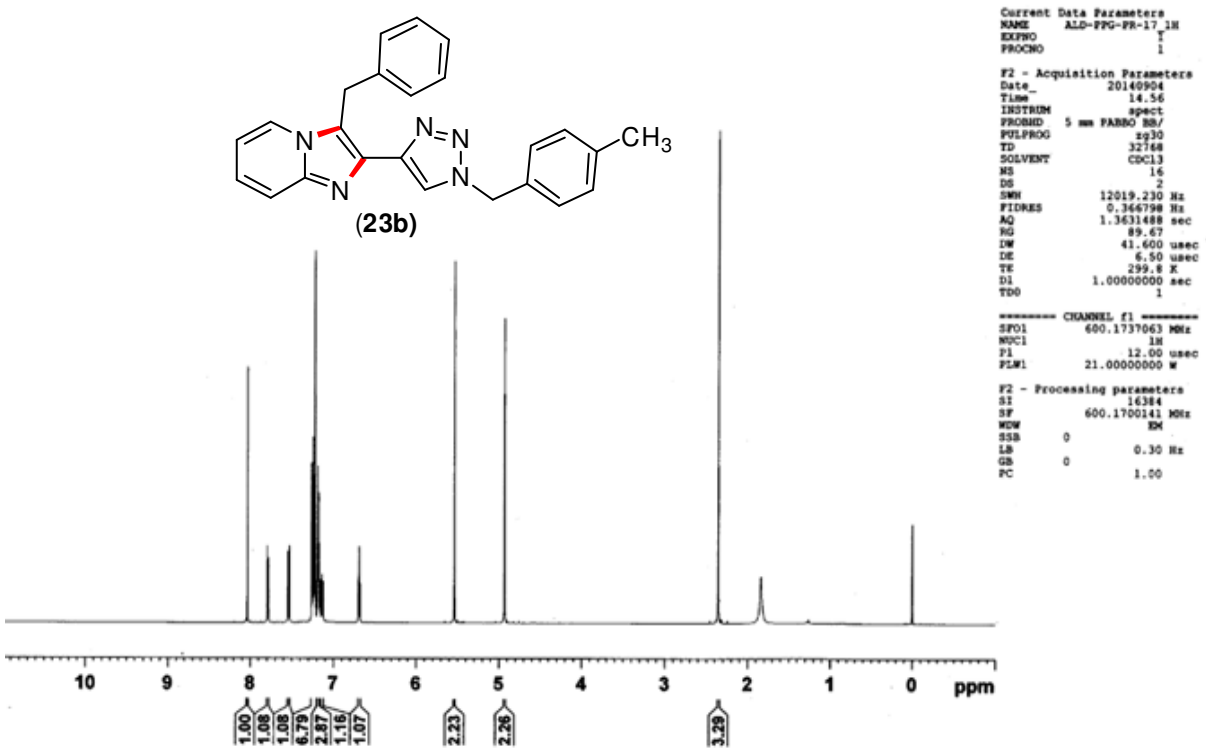
***^{13}C NMR (150 MHz, $CDCl_3$)**: 1-(4-methylbenzyl)-1H-1,2,3-triazole-4-carbaldehyde (**20b**)*



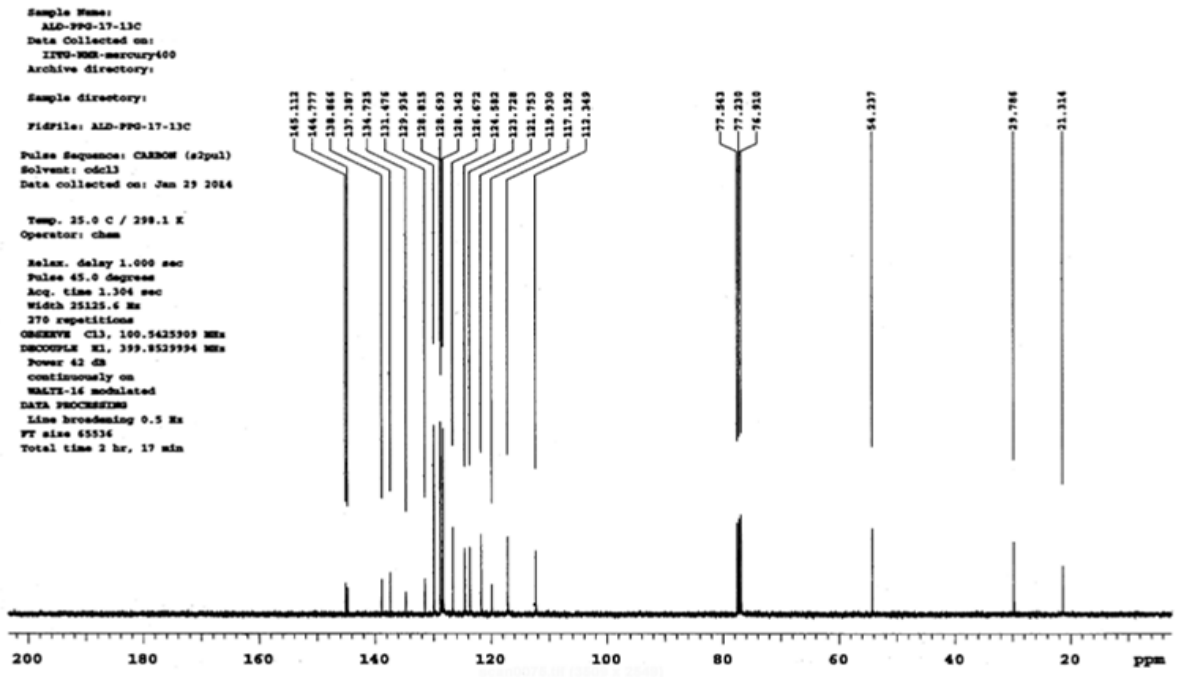
***HRMS** (ESI): 1-(4-methylbenzyl)-1H-1,2,3-triazole-4-carbaldehyde (**20b**)*



*^{1}H NMR (600 MHz, $CDCl_3$): 3-benzyl-2-(1-(4-methylbenzyl)-1H-1,2,3-triazol-4-yl)imidazo[1,2-a]pyridine (**23b**)*

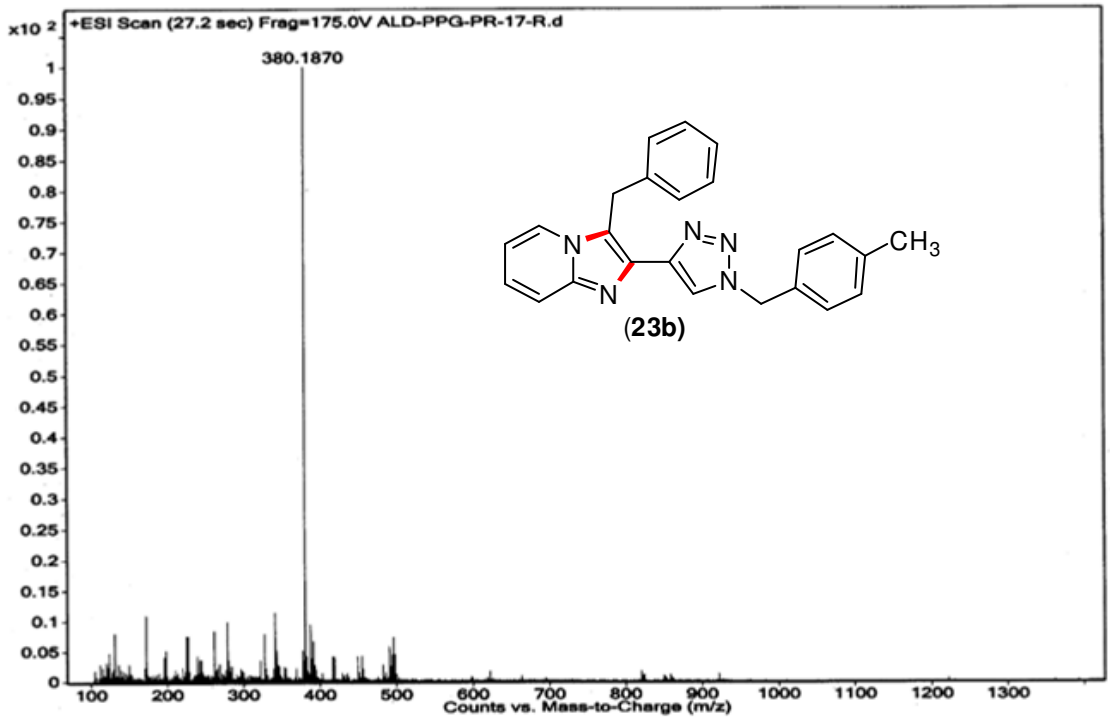


^{13}C NMR (100 MHz, $CDCl_3$): **3***-benzyl-2-(1-(4-methylbenzyl)-1H-1,2,3-triazol-4-yl)imidazo[1,2-a]pyridine (**23b**)*



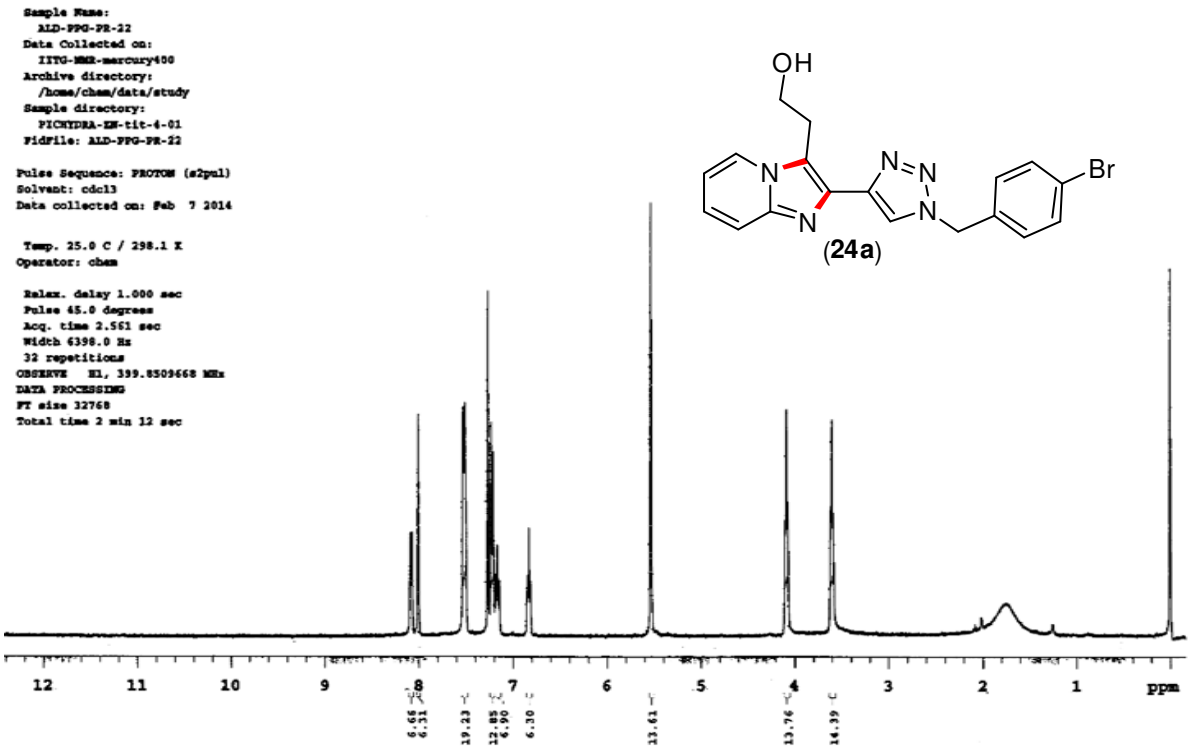
HRMS** (ESI):* **3-benzyl-2-(1-(4-methylbenzyl)-1H-1,2,3-triazol-4-yl)imidazo[1,2-a]pyridine (**23b**)*

Sample Name	ALD-PPG-PR-17-R	Position	-1	Instrument Name	Instrument 1	User Name	
Inj Vol	-10	InjPosition		SampleType	Sample	IRM Calibration Status	Success
Data Filename	ALD-PPG-PR-17-R.d	ACQ Method		Comment		Acquired Time	3/18/2014 2:35:40 PM

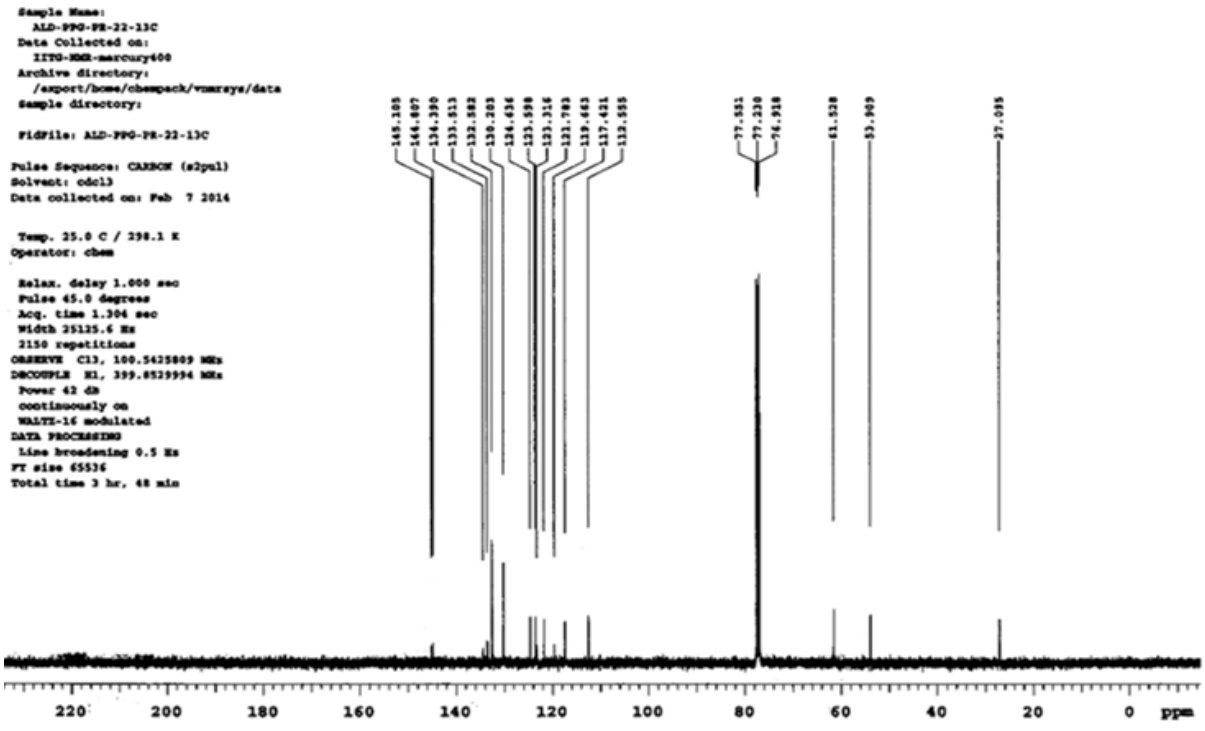


(23b)

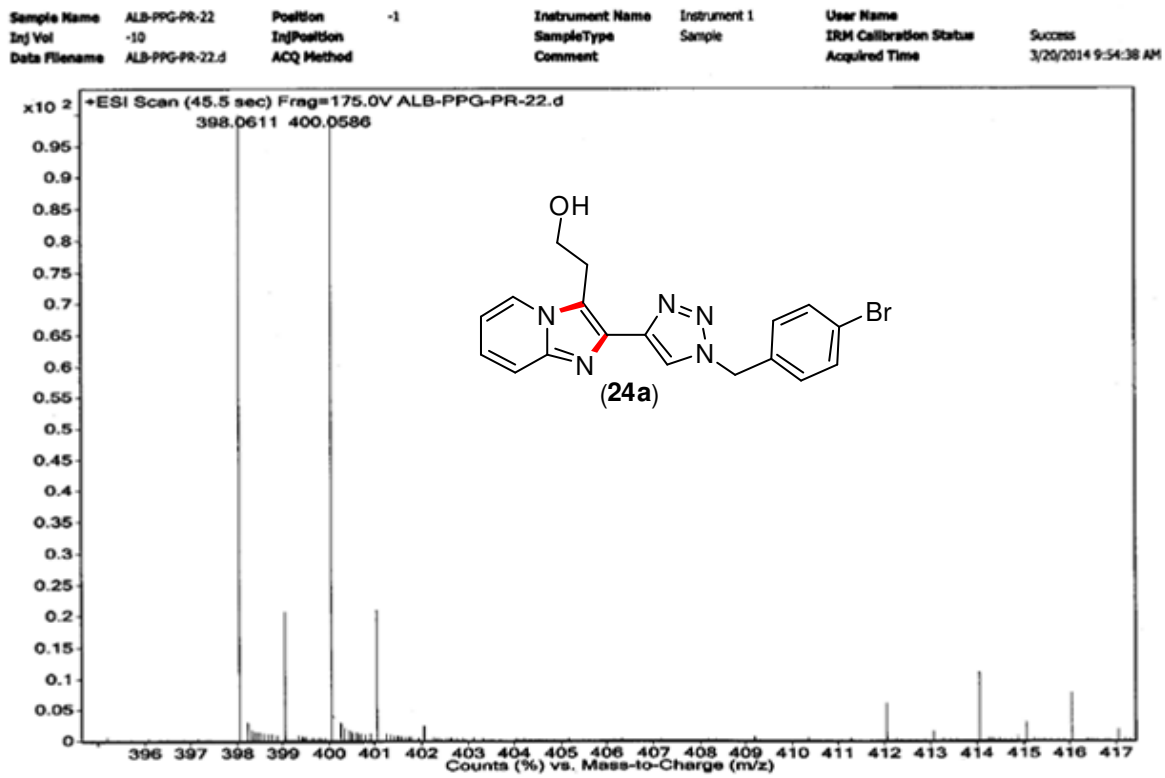
^{1}H NMR (400 MHz, $CDCl_3$): *2-(2-(1-(4-bromobenzyl)-1H-1,2,3-triazol-4-yl)imidazo[1,2-a]pyridin-3-yl)ethanol (**24a**)*



^{13}C NMR (100 MHz, $CDCl_3$): *2-(2-(1-(4-bromobenzyl)-1H-1,2,3-triazol-4-yl)imidazo[1,2-a]pyridin-3-yl)ethanol (**24a**)*



HRMS *(ESI): 2-(2-(1-(4-bromobenzyl)-1H-1,2,3-triazol-4-yl)imidazo[1,2-a]pyridin-3-yl)ethanol (**24a**)*



Part A

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Chapter I - Chapter III

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Part B

Chapter I

General Introduction to MCRs, Pyrroles and 1,4-Dihydropyridines

Review

1.1 Introduction

Multicomponent reactions (MCRs) are defined as the convergent process in which three or more starting materials react together through covalent bonds regardless of their mechanistic nature in a single chemical operation to form highly selective product where basically all or most of the atoms contribute to the newly formed product (Figure 1). They have significant advantages over conventional reactions in several aspects, such as (i) reduced cost and reaction time; (iii) readily available starting materials; (iv) operationally simple; (v) high bond forming efficiency (BFE); (vi) resource effective; (vii) superior atom economy and (viii) high substrates variability.[1]

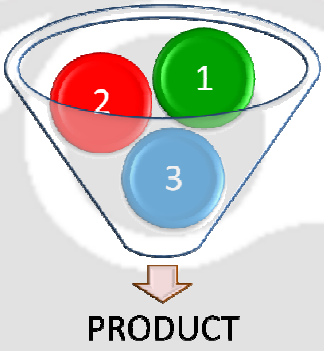


Figure 1

Multicomponent reactions (MCRs) admires an unusual attention owing to its direct access to structurally complex biomolecules in an easier synthetic pathway.[2] In addition, MCRs are well amenable for the construction of heterocyclic cores with high degree of complexity as well as diversity for a targeted set of scaffolds with a minimal number of synthetic operations.[3] Moreover, MCRs is an important development in the ties of drug discovery in the context of rapid identification and optimization of biologically active compounds.[4] Libraries of small organic molecule are perhaps the most desired class of potential drug candidates. With a small set of starting materials, very large libraries can be built up within short time, which may then be used in pharmaceuticals. As MCRs are conventionally one-pot reactions, they are easier to carry out as compared to multistep synthesis[5] which is shown below in Figure 2. Therefore, MCRs have become a rapidly evolving field in the context of drug discovery for the preparation of libraries of molecules in a time- and cost-effective manner, and they are now key tools in industrial and academic research.[6] It is apparent that development of novel multicomponent reactions is a great challenge in synthetic organic chemistry.

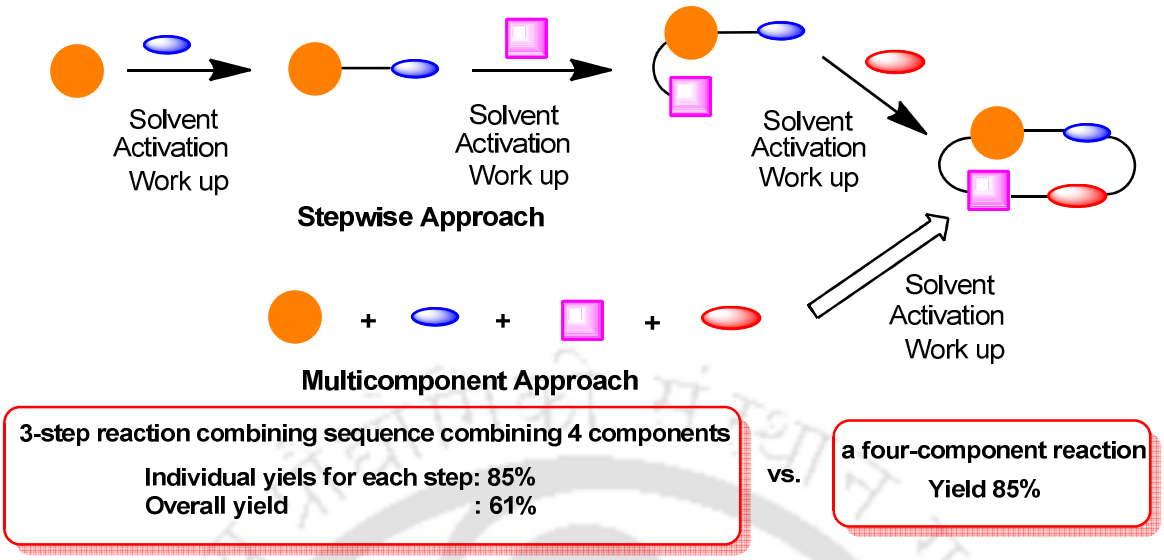
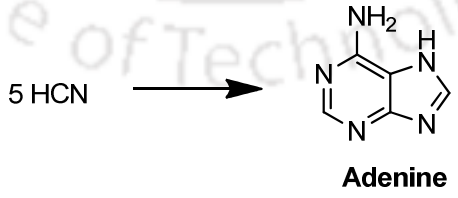


Figure 2 Stepwise vs Multicomponent Approach

1.2 History and Synthetic Application of MCRs

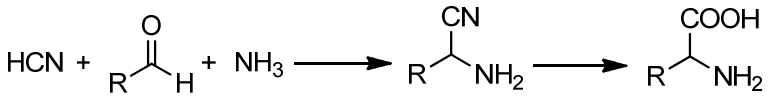
The history of MCRs could be traced out to the reactions done by Strecker[7] in 1850 and subsequently nourished over a period through Hantzsch,[8] Biginelli[9] and Ugi reaction.[10] The discovery of Ugi reaction turned the fate of Multicomponent reactions which lead to its emergence as a powerful synthetic strategy in recent years for the synthesis of natural products as well as for the discovery of biological probes and drugs.[11]

MCRs play an important role in mimicking nature, it plays a significant contribution towards the synthesis of adenine which is one of the major constituents of DNA and RNA. The synthesis of adenine was carried out by the condensation reaction of five molecules of HCN as shown in Scheme 1.[12]



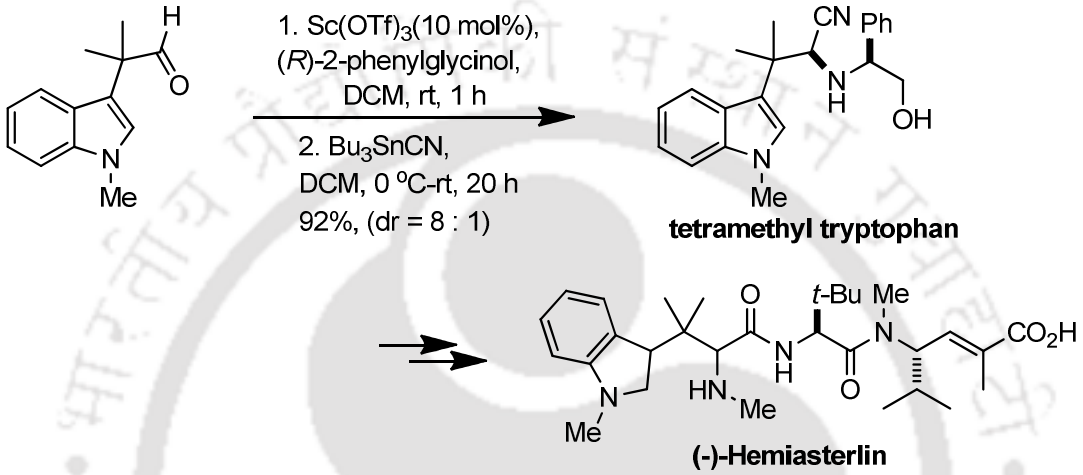
Scheme 1. *Synthesis of adenine*

In 1850, Strecker[7] *et al*. was established the synthesis of α-amino acids from aldehydes, HCN and NH_3 in a one-pot three component reaction manner and consequently, it was hydrolyzed to the corresponding α-amino acid as shown in Scheme 2.



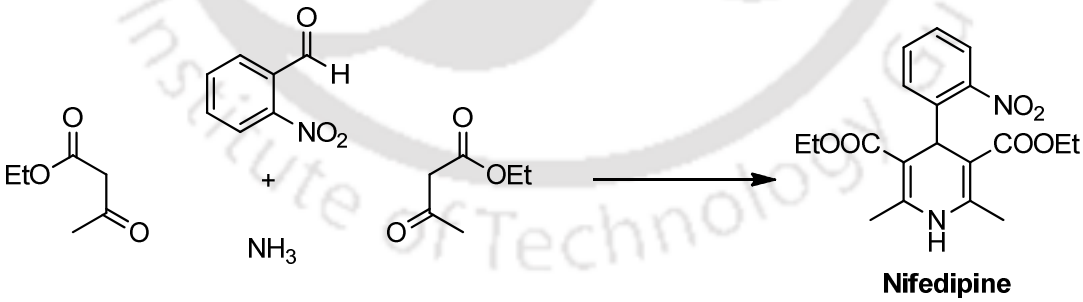
Scheme 2. *Strecker's synthesis of α-amino acids*

Vedejs and co-workers[13] explored the utility of asymmetric Strecker reaction in the construction of the key intermediate tetramethyl tryptophan for the enantioselective total synthesis of (-)-hemiasterlin, a marine tri-peptide having cytotoxic and antimitotic activity, as shown in Scheme 3.



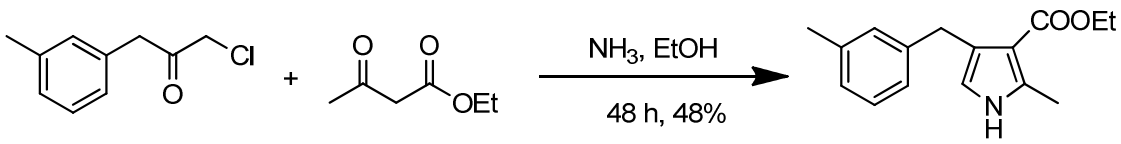
Scheme 3

In 1882 Hantzsch[8] developed a one-pot four-component condensation reaction of aldehydes along with two equivalents of β-keto ester and ammonia to synthesized symmetrically substituted dihydropyridines as shown in Scheme 4.



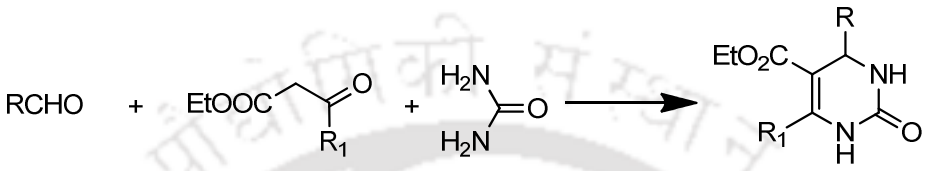
Scheme 4. *Hantzsch synthesis of 1,4-dihydropyridine derivatives*

In addition, Hantzsch also demonstrated a one pot three-component reaction for the synthesis of substituted pyrrole derivatives by using α-halogenated β-carbonyl compound, β-ketoesters, and ammonia (or primary amine) as in Scheme 5.[14]



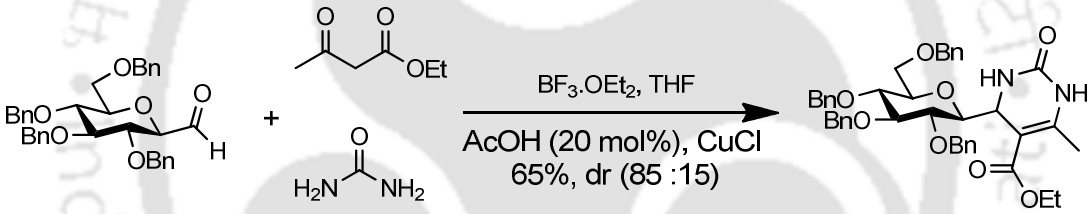
Scheme 5. *Hantzsch's synthesis of substituted pyrroles*

In 1891, Biginelli demonstrated[9] to the synthesis of functionalized 3,4-dihydropyrimidin-2(1*H*)-ones through a one-pot three-component reaction of aldehyde, ethyl acetoacetate and urea in the presence of catalysts as shown in Scheme 6.



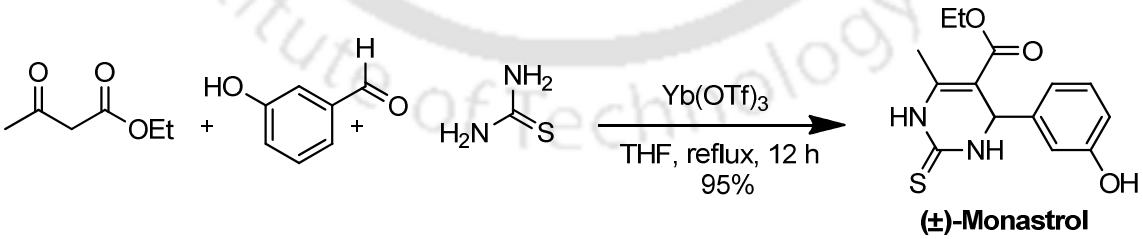
Scheme 6. *Biginelli synthesis of dihydropyrimidines*

Then, Aparicio *et al.*[15] modified Biginelli reaction for the synthesis of sugar containing dihydropyrimidine derivatives by using sugar aldehyde as depicted in Scheme 7.



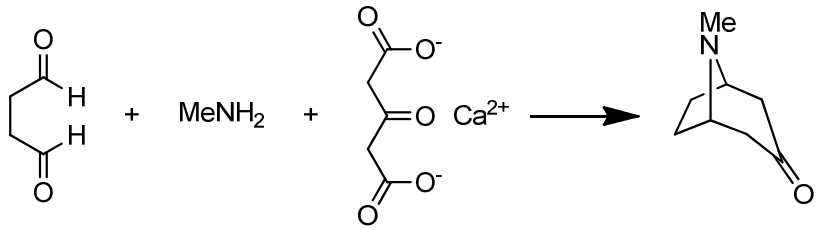
Scheme 7

Dondoni and his coworkers[16] reported the traditional intermolecular three-component version of the Biginelli reaction for the improved synthesis of racemic monastrol as shown in Scheme 8.



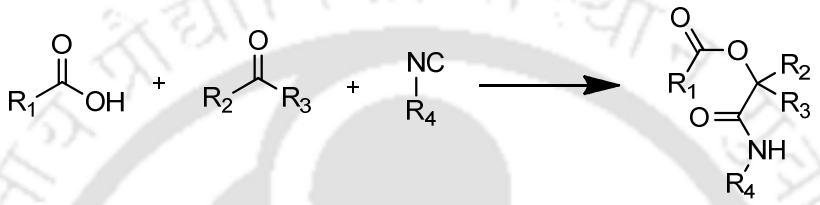
Scheme 8

In 1917, Robinson[17] first reported the important application of MCR in natural product for the synthesis of alkaloid tropinone from succinic dialdehyde, methylamine and calcium salt of acetonedicarboxylic acid as given in Scheme 9.



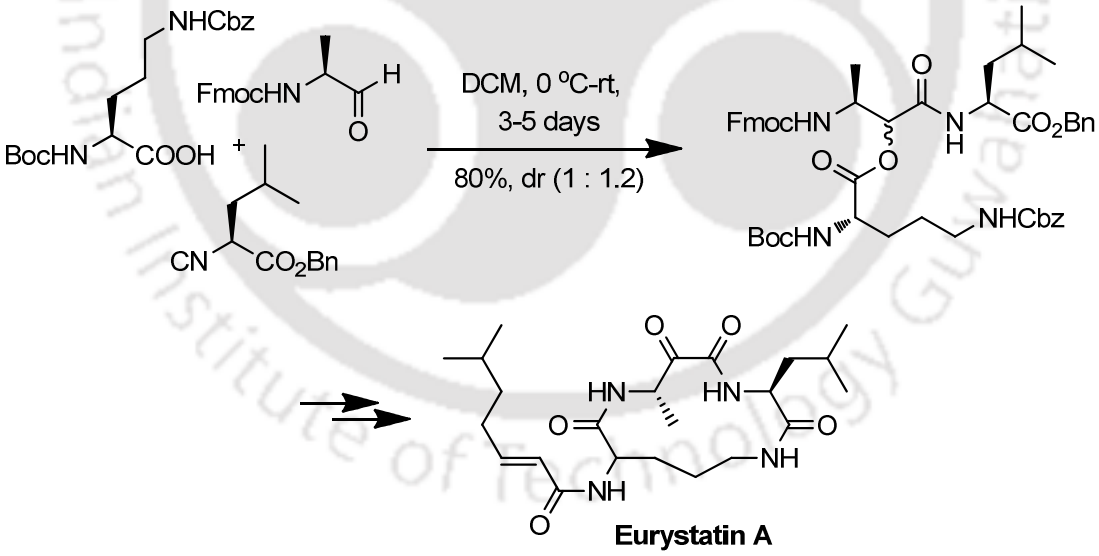
Scheme 9

In 1921, Mario Passerini demonstrated[18a] the isocyanide based MCR for the synthesis of α-acyloxy carboxamide by using carboxylic acid, carbonyl compound and isocyanide as shown in Scheme 10.



Scheme 10

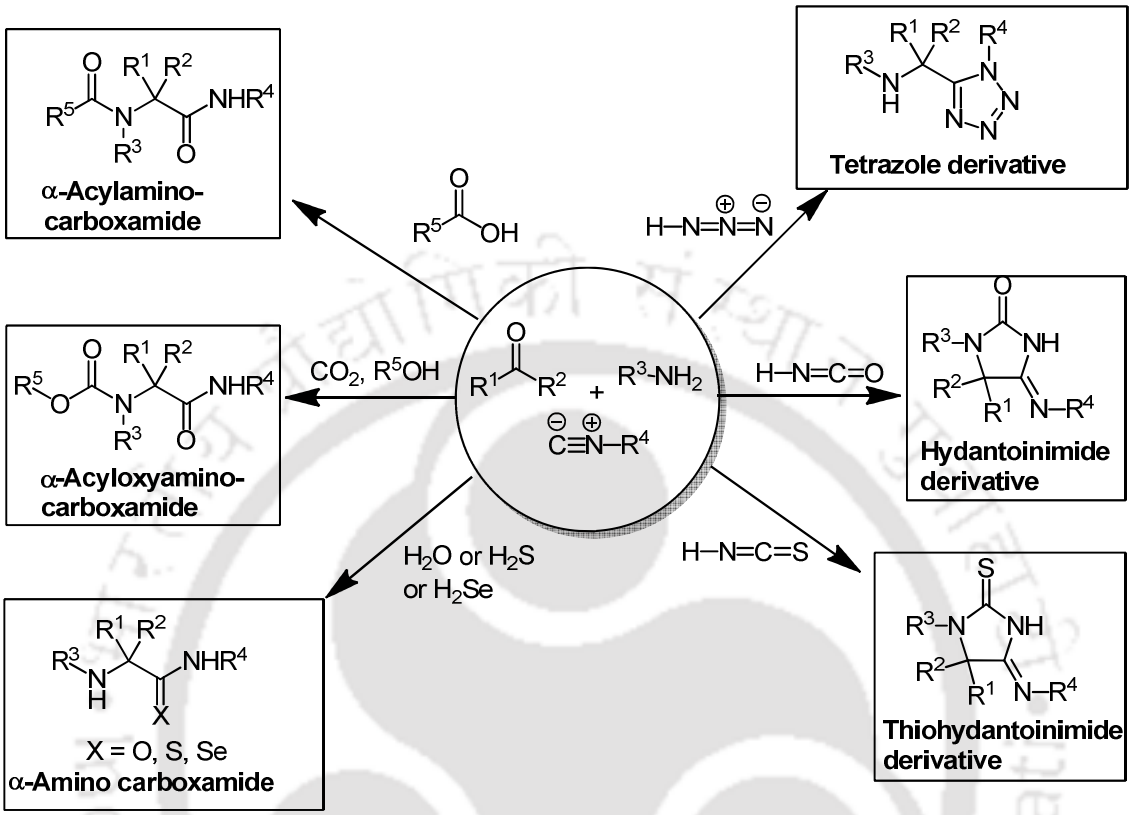
After that, Owens *et al.*[18b] utilized Passerini reaction for the synthesis of eurystatine A which is a 13-membered macrocyclic natural product as given in Scheme 11.



Scheme 11

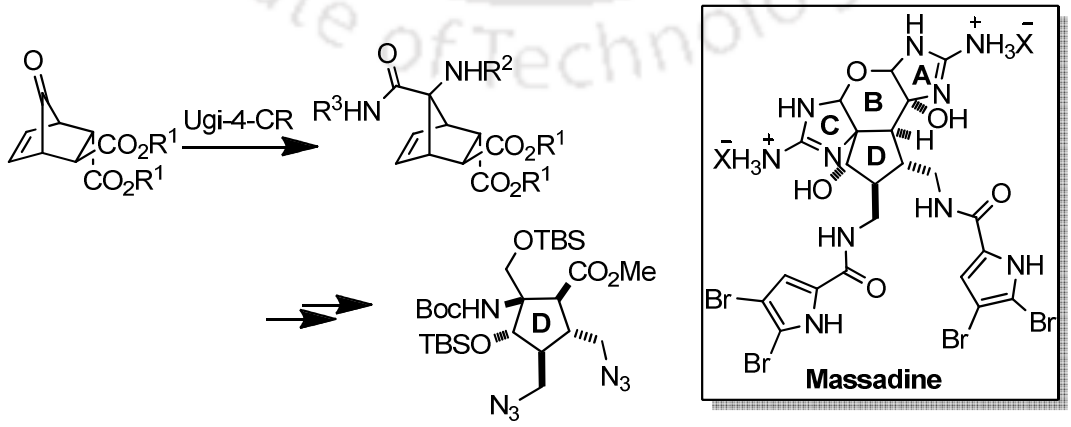
In 1959, Ugi and his co-workers had exposed the versatile isocyanides based multicomponent reactions which is one of the most important in literature. The isocyanides undergo a four-component reaction (4-CR) in the presence of an aldehyde or ketone, amine and a nucleophile to afford a single condensation product. The most commonly used nucleophiles are water, hydrogen sulfide, carboxylic acids, hydrazoic acid, cyanates, thiocyanates,

carbonic acid monoesters, and hydrogen selenide. Recently, this transformation is usually known as the Ugi's four-component reaction (Ugi-4CR).[10] Therefore, Ugi reaction found a widespread application in combinatorial chemistry as represented in Scheme 12.[19]



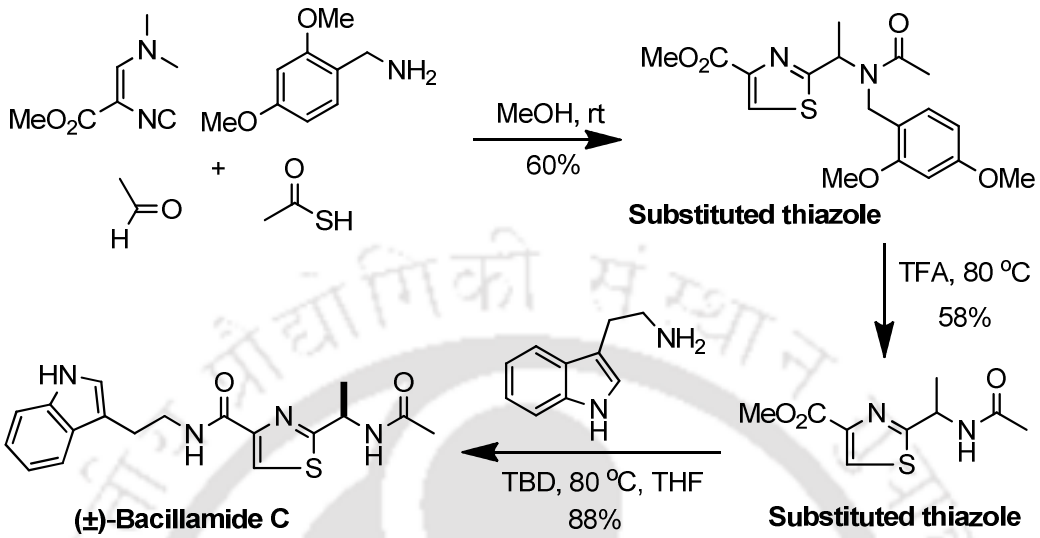
Scheme 12

After that, Ugi reaction was further utilized for the synthesis of various natural products and biologically active molecules. Recently, Chinigo *et al.*[20] utilized Ugi-4-CR as a key reaction for the synthesis of the D-ring sub-unit which rapidly gives functionalized core structure of massadine as shown in Scheme 13.



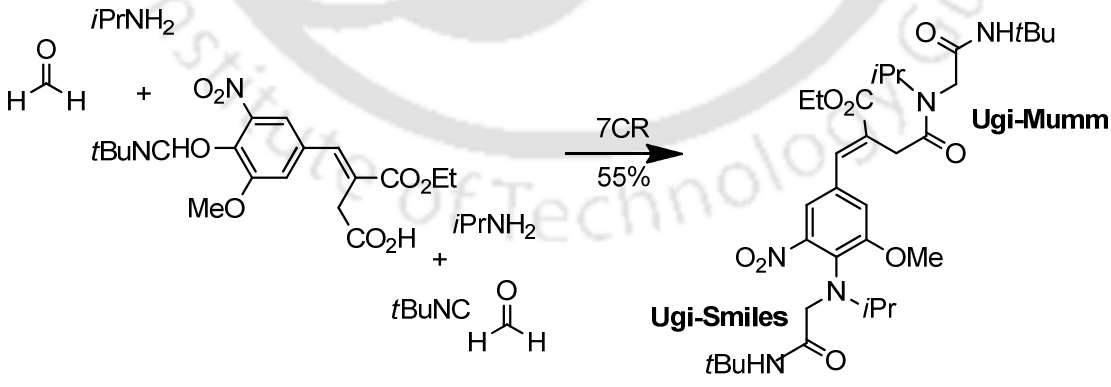
Scheme 13

Dömling and co-workers[21] described enantioselective synthesis of algicidal natural product such as bacillamide C which follows a convergent synthetic strategy where the key step is the alteration of the Ugi reaction leading to highly substituted thiazoles as shown in Scheme 14.



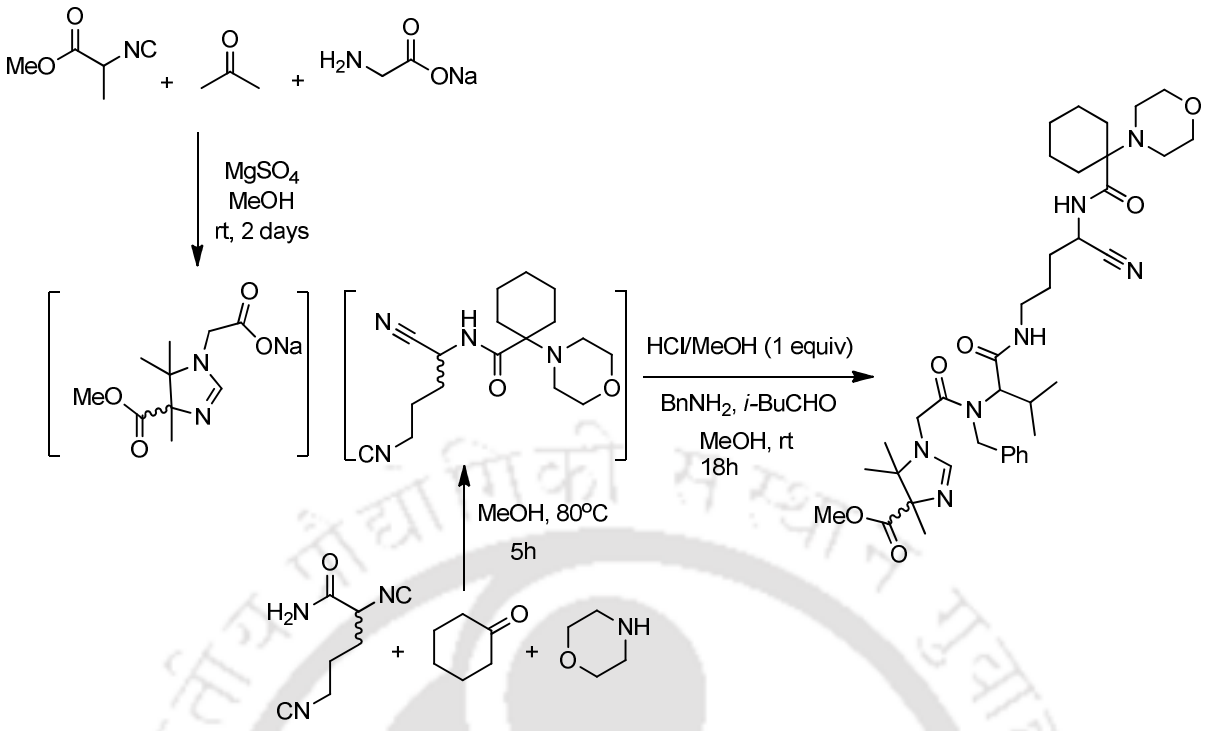
Scheme 14

Brauch *et al.* reported[22] a seven-component reaction by utilizing the different chemoselectivities of the Ugi–Smiles and the Ugi–Mumm reaction. The sequential multicomponent reaction has leads to highly diverse peptide and glycopeptide like structures from formaldehyde, isopropyl amine and *tert*-butyl isonitrile. The Ugi–Mumm/Ugi–Smiles product was formed in 55% yield and the yield for each bond forming step exceeds 90% as depicted in Scheme 15.



Scheme 15

In 2009, Orru and his co-worker[23] first reported of an eight component reaction. This 8CR unifies three different MCRs with nine new bonds formation, creating highly complex and structurally versatile drug-like compounds as shown in Scheme 16.



Scheme 16

In this context, it is apparent that the expansion of novel multicomponent reactions plays an important aspect in the field of synthetic organic chemistry. MCR captivates the research interest of chemists owing to its remarkable efficiency, diversity and a vast unexplored territory which ultimately encouraged us to work on this novel field of chemistry. This part of my research work is aimed at the synthesis of N-heterocycles such as substituted pyrrole and 1,4-dihydropyridine derivatives. I would like to concentrate on their importance as well as some recently developed synthetic methods as described below.

1.3 Pyrroles and its importance

Pyrrole and its derivatives are an important class of heterocyclic[24] compounds which are naturally occurring compounds and some of their synthetic strategies have been reviewed recently.[25] Many pyrrole derivatives have shown various biological activities such as antibacterial, antiviral, anticonvulsant, anticancer and antioxidant.[26] It has been found that highly functionalized pyrroles subunit are present in vitamin B complex, antibiotics, hemoglobin, chlorophylls, amino acids, ATP, dyes, drugs, the genetic materials and pyrrole alkaloids isolated from marine source[27] and also serves as valuable building blocks for synthesizing conducting polymers[28] and synthetic parmaceuticals.[29] The most common drugs containing pyrrole skeleton are Storniamide A, Lamellarin O, Lukianol A, Ningalin A, BM 212 and BM 212-analogue as shown in Figure 3.

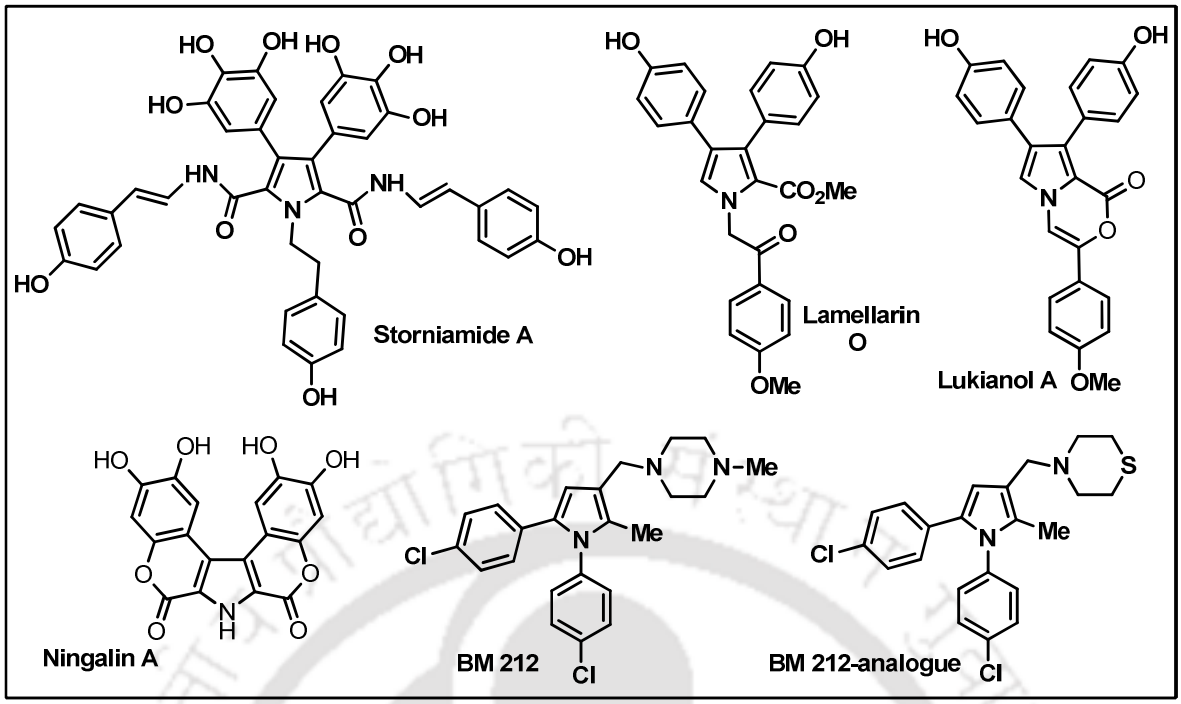
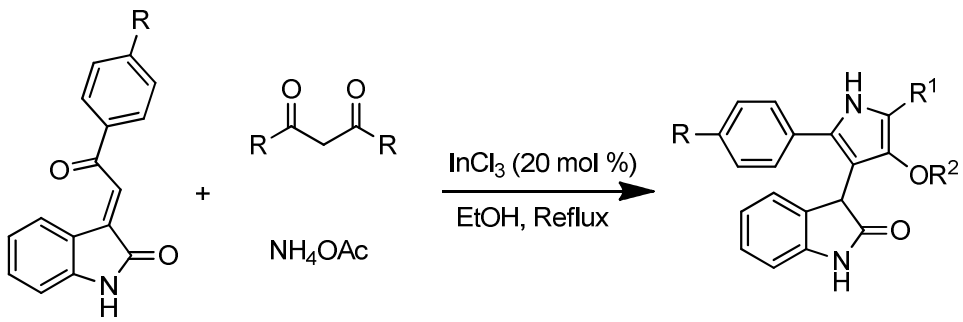


Figure 3

These derivatives also find its own way in the field of material science.[30] In addition, some of the pyrroles are promising lead molecule for cholesterol lowering agent.[31]

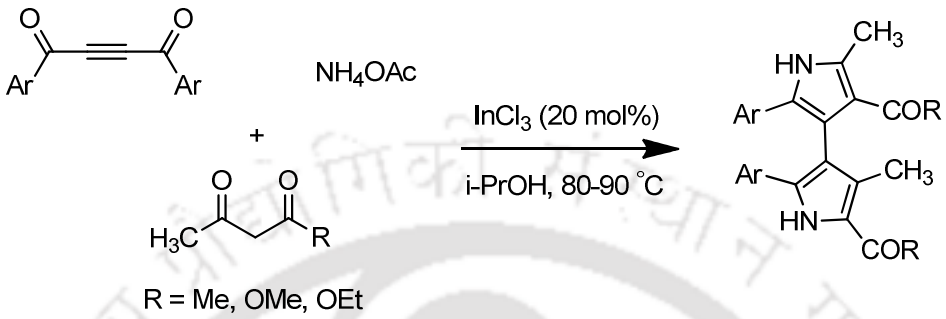
1.3a Synthetic utility of pyrrole derivatives

The improvement of new and simple methods for the synthesis of substituted pyrrole derivatives from readily available starting materials has left its door opened for the organic chemists. In this outlook, Perumal's and his coworker[32] had demonstrated an MCR for the synthesis of 2-pyrrolo-3′-yloxindoles from 3-phenacylideneoxindole, β-ketoesters and ammonium acetate in the presence of $InCl_3$-as a catalyst. The sequence involves Michael addition reaction of the enol form of the 1,3-dicarbonyl and 3-phenacylideneoxindole to afford 1,4-dicarbonyl intermediate, which then undergoes a Paal–Knorr condensation with ammonium acetate to form the pyrrole derivatives as shown in Scheme 17.



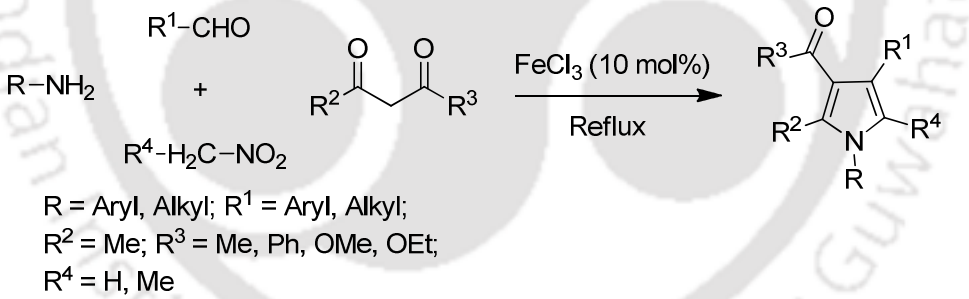
Scheme 17

Jaisankar *et al.*[33] demonstrated the synthesis of 3,3′- bis-pyrrole derivatives using three-component Michael addition reaction of diaroyl acetylenes, 1,3-dicarbonyls and ammonium acetate promoted by an Lewis acid-catalyst. Interestingly, these bis-pyrrole derivatives display conducting properties as well as a wide range of application in medicinal chemistry as shown in Scheme 18.



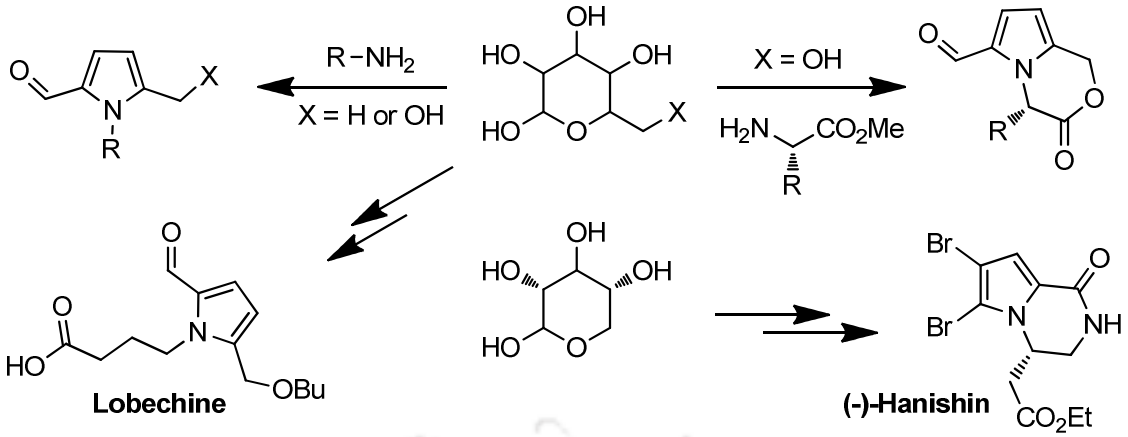
Scheme 18

Jana *et al.* had reported[34] a novel one pot multicomponent reaction for synthesis of fully substituted pyrroles from aldehydes, 1,3-dicarbonyl compounds, amines and nitroalkanes in the presence of $FeCl_3$ as a catalyst. In this context, nitroalkane acts such as solvent as well as reactant as given in Scheme 19.



Scheme 19

Very recently, Koo and had coworker have reported[35] a practical conversion method for the synthesis of N-substituted 5-(hydroxymethyl)pyrrole-2-carbaldehydes from the reaction of carbohydrates, primary amines and oxalic acid in DMSO at 90 °C. This protocol was further utilized for the synthesis of pyrrole fused poly-heterocyclic compounds as potential intermediates for drugs, food flavors, and functional materials as shown in Scheme 20.



Scheme 20

Over the years, various research groups has developed some other methods for the synthesis of substituted pyrrole using different catalysts such as palladium mediated suzuki coupling,[36a] $NiCl_2.6H_2O$,[36b] iodine,[37a] and ionic liquid [Hbim]BF_4.[37b] However, the above methods suffer from some of the drawbacks such as harsh reaction conditions, longer reaction time and need of expensive and excess amount of catalyst. Therefore, still there is an extent to upgrade a new methodology which might employment superior in terms of yield, reaction time, substrate scope compatibility and mild reaction condition.

1.4 Dihyropyridines and its importance

Nitrogen-containing heterocyclic motifs are ubiquitous in pharmaceuticals and biologically functional molecules. In particular molecules containing 1,4-Dihydropyridine (1,4-DHP) skeleton is present in many bioactive compounds and much attention has been paid on the synthesis of these compounds due to their high potential of pharmacological activities.[38] The 1,4-DHPs acts as both potent calcium channel antagonist such as Nifedipine, Nimodipine as well as other potent calcium channel agonist i.e. Bay K 8644, PN 202 791 respectively where as Felodipine and Amodipine are use for the treatment of high blood pressure and low blood pressure respectively as shown in Figure 4.[39] Many, 1,4-DHPs has been found to be associated with various biologically activities such as neuroprotectant,[40] HIV-I protease inhibition,[41] nitric oxide-like activities,[42] anticancer[43] antitubercular,[44] antimicrobial[45] antidiabetic, antiviral, antibacterial, membrane protecting, and heptaprotective agents.[46] Moreover, they can be used in the treatment of Alzheimer's disease owing to their antiischemic activity and as chemosensitizers in tumor therapy.[47] In addition, they also have irresistible utilization in the cardiovascular pharmacology as Ca^{2+} channel blockers (CCBs),[48] NMDA receptor antagonism (anticonvulsant)[49] and adenosine-A_3 receptor antagonism.[50]

Further, dihydropyridines have been reported to be potent R_{1a}-adrenoreceptor antagonists acting as inhibitors of human prostate contraction and hence are useful for treatment of benign prostate hyperplasia[51] and are also useful NADH models.[52]

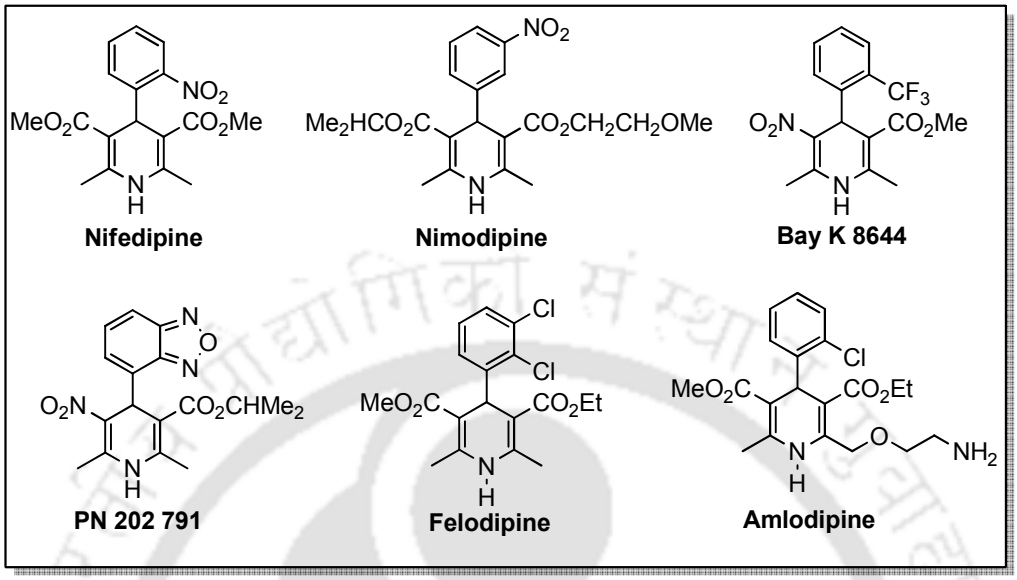
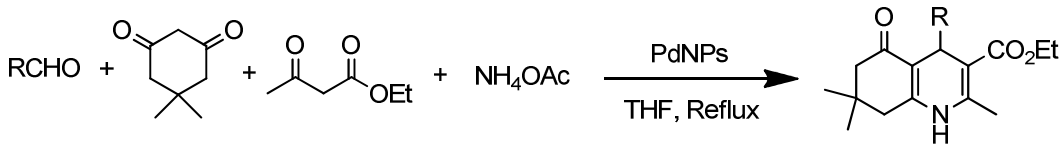


Figure 4

The unsymmetrical 1,4-DHPs display effective drug moiety or pharmacological activities.[53] Therefore, the synthesis of both symmetrical and unsymmetrical 1,4-DHPs are importance in terms of drug discovery.

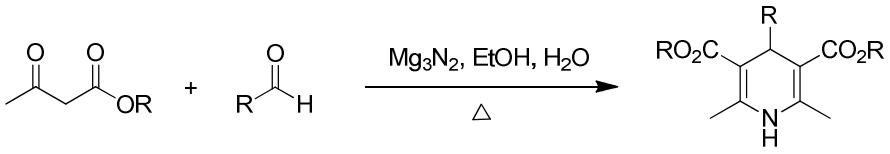
1.4a Synthetic utility of 1,4-dihydropyridine derivatives

In 1882, Hantzsch[8] demonstrated an important condensation multicomponent reaction for synthesis of 1,4-dihydropyridines known as Hantzsch 1,4-dihydropyridines (1,4-DHP). The traditional method for the synthesis of 1,4-dihydropyridines is the one-pot condensation reaction from aldehydes, ethyl acetoacetate and ammonia in the presence of acetic acid or alcohol under refluxing condition. Over the years numerous synthetic methods have been reported using microwave irradiation,[54a] ionic liquids,[54b] polymers,[54c] Lewis acid,[54d] Bakers' yeast,[54e] and metal triflates.[54f] Recently, Saha *et al.*[55] accomplished highly efficient palladium nanoparticle-catalyzed multicomponent reaction for the synthesis of 1,4-dihydropyridines under reflux condition in excellent yields as shown in Scheme 21.



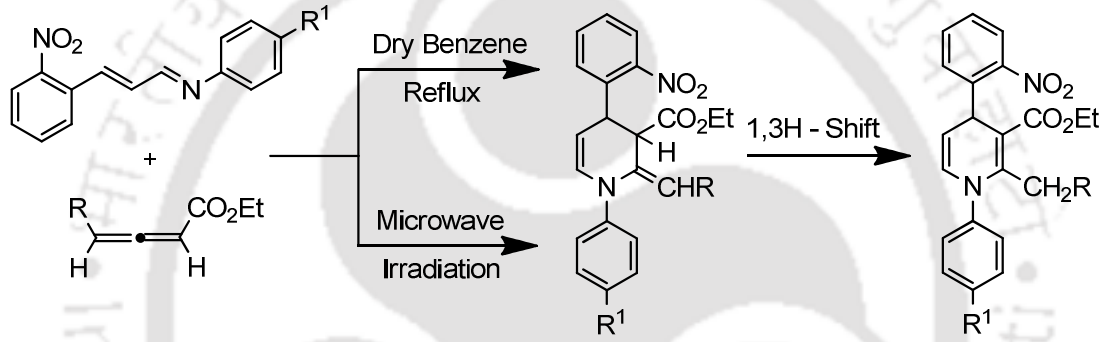
Scheme 21

Recently, Bridgwood *et al.*[56] established the synthesis of Hantzsch 1,4-dihydropyridines using magnesium nitride instated of ammonium acetate in the absence of any additional catalyst as shown in Scheme 22.



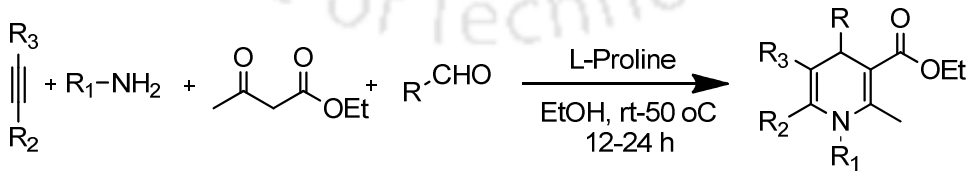
Scheme 22

Singh *et al.*[57] have reported the thermal and microwave promoted [4 + 2] cycloaddition reaction for the synthesis of unsymmetrically substituted 1,4-DHPs by using 1,4-diaryl-1-aza-1,3-butadiene and allenic ester as shown in Scheme 23.



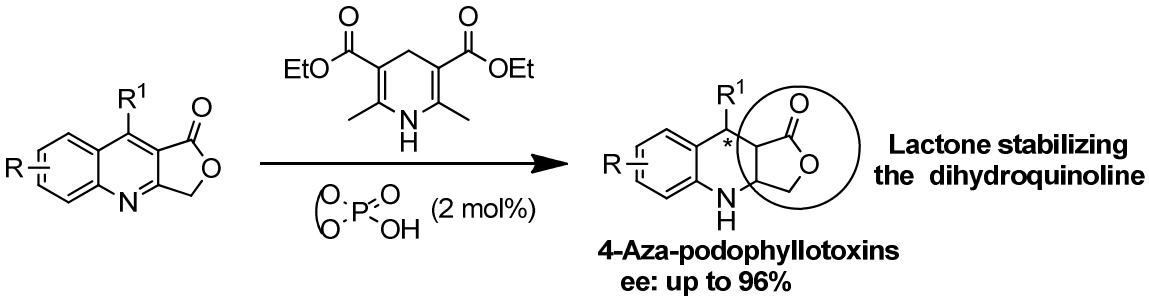
Scheme 23

Jiang *et al.*[58] reported the synthesis of fully substituted 1,4-dihydropyridines through a one-pot multicomponent reactions (MCRs) of alkynones or alkynoates, amines, β-dicarbonyl compounds and aldehyde in the presence of L-proline as a catalyst as represented in Scheme 24. In this context, 1,4-dihydropyridine derivatives was obtained involving Hydroamination, Knoevenagel condensation, Michael-type addition and intramolecular cyclization reaction as a key steps.



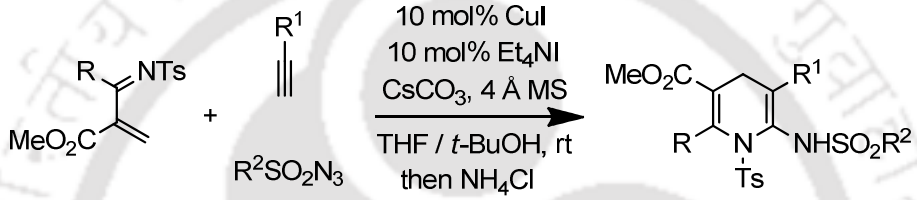
Scheme 24

Very recently, Bousquet and Pélinski *et al.*[59] have utilized of 1,4-dihydropyridine as a enantioselective organocatalyst for the hydrogenation reaction of lactone-fused quinolines as represented in Scheme 25.



Scheme 25

Very recently, Ma *et al.*[60] demonstrated the synthesis of functionalized 1,4-dihydropyridine derivatives via a formal inverse electron-demand [4 + 2] hetero-Diels–Alder reaction from sulfonyl azides, N-sulfonyl-1-aza-1,3-butadienes and terminal alkynes in the presence 10 mol% of CuI along with stoichiometric amounts of Cs_2CO_3 as shown in Scheme 26.



Scheme 26

From the literature it is evident that the substituted pyrrole and 1,4-dihydropyridine derivatives are present in natural products and exhibits wide range of biological activities. Therefore, the development of new methodologies related to synthesis of substituted pyrrole and 1,4-dihydropyridine are challenging task. Thus, the second part of my thesis work is to develop new synthetic methodologies for the synthesis of N-hetrocyclic compounds such as highly functionalized pyrrole and 1,4-dihydropyridine derivatives. In an endeavour to achieve our target, we have developed newer methodologies using BDMS and cobalt triflate catalysts. In the subsequent Chapters II and III of Part B, we have described multicomponent reactions leading to construction of substituted pyrrole and 1,4-dihydropyridine derivatives.

Part B

Chapter II

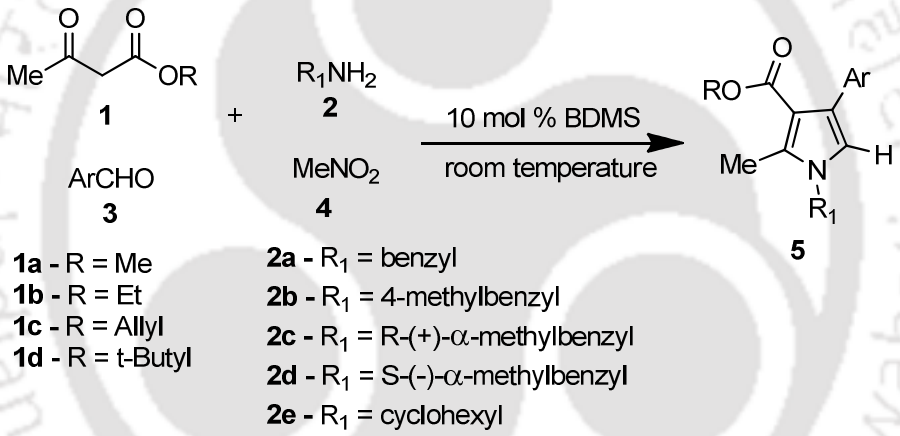
Bromodimethylsulfonium bromide (BDMS) catalyzed synthesis of substituted pyrroles through a one-pot four-component reaction

Result & Discussion

Experimental Section

Results and Discussion

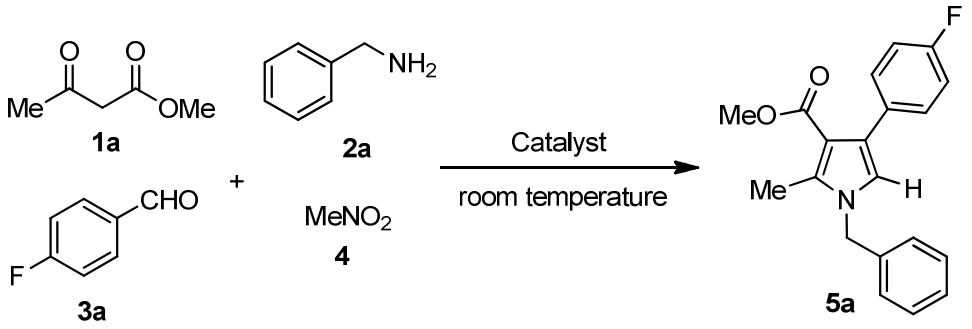
In continuation of our endeavour to explore the application of new reagents in organic synthesis, we wanted to investigation the organ catalyst BDMS for the development of novel methodology in multicomponent reactions leading to tetra-substituted pyrrole derivatives. The importance, synthetic utility and some recent strategies for the synthesis of tetra substituted pyrroles have been discussed in previous Chapter 1 Part B. We perceived that a new methodology is always agreeting for the synthesis of substituted pyrrole derivatives due to their medicinal and synthetic importance. In this chapter we will discuss our successful results for the synthesis of tetra substituted pyrrole derivatives involving one-pot four-component reaction by employing β-ketoesters, benzylamines, aromatic aldehydes and nitromethane in presence of 10 mol% bromodimethylsulfonium bromide (BDMS) as catalyst at room temperature, which is shown in Scheme 27.



Scheme 27. *Synthesis of tetra substituted pyrroles*

Bromodimethylsulfonium bromide (BDMS) can act as brominating reagent[61] as well as an efficient catalyst used for various organic transformations in the development of new methodologies in multicomponent reactions.[62] Our initial attempt began with from the preparation of the catalyst BDMS by known literature procedure. Next phase of our journey went on to optimize the reaction conditions by using methyl acetoacetate (**1a**), benzylamine (**2a**) and 4-fluorobenzaldehyde (**3a**) in nitromethane (**4**) at room temperature and the results are summarized in Table 1. It was observed that 10 mol% of BDMS was sufficient to provide the best result in terms of yield and reaction time.

Table 1: Optimization of reaction conditions for the synthesis of tetra-substituted pyrrole[a]



Entry	Catalyst	Catalytic amount (mol %)	Time (h)	% Yield[b]
1	No catalyst	-	24	NR
2	$HClO_4$	5	16	30
3	CSA	10	18	21
4	48% aq. HBr	10	14	41
5	TBATB	10	12	55
6	BDMS	5	9	65
7	**BDMS**	**10**	**7**	**78**
8	BDMS	15	8	75

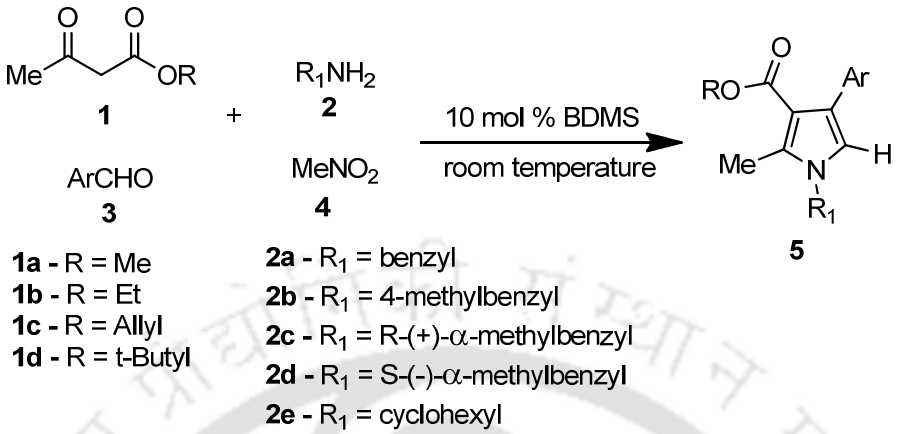
[a]*The reactions were carried out using 1 mmol of methyl acetoacetate (**1a**), 1 mmol of benzylamine(**2a**) and 1 mmol of 4-fluorobenzaldehyde (**3a**) in 1mL of nitromethane (**4**) at room temperature.* [b]*Isolated yield.*

The reactions were also scrutinized in different solvents such as CH_3CN, THF, DMF and MeOH which afforded not only lower yield as but also resulted in prolonged reaction time period. It is noteworthy to mention that here nitromethane act as reagent as well as solvent in the present protocol. The isolated product **5a** was characterized from ^1H NMR in which H-5 proton appears at δ 6.56 ppm as a singlet where as ^{13}C NMR shows C-5 carbon signal comes at δ 110.9 ppm, respectively.

After optimization, the reaction were examined with methyl acetoacetate (**1a**), benzylamine (**2a**) and with various aromatic aldehydes such as 4-chlorobenzaldehyde, benzaldehyde, 2-furfuryl aldehyde in nitromethane (**4**) in the presence of 10 mol% of BDMS at room temperature which eventually lead to the isolation of the desired products **5b-d** were isolated in 68-72% yields (Table 2, entries 2-4). Similarly, 4-methylbenzylamine (**2b**), methyl

acetoacetate (**1a**), and 4-chlorobenzaldehyde afforded the desired product **5e** in 75% yield (Table 2, entry 5) under identical reaction conditions.

Table 2: Synthesis of substituted pyrrole derivatives[a]



Entry	Aldehyde (**3**)	R(**1**)	R^1(**2**)	Product (**5**)	Time (h)	Yield (%)[b]
1	4-F-C_6H_4	**1a**	**2a**	**5a**	7	78
2	4-Cl-C_6H_4	**1a**	**2a**	**5b**	8	72
3	C_6H_5	**1a**	**2a**	**5c**	9	70
4	2-Furanyl	**1a**	**2a**	**5d**	8	68
5	4-Cl-C_6H_4	**1a**	**2b**	**5e**	7	75
6	C_6H_5	**1a**	**2c**	**5f**	5	76
7	4-Me-C_6H_4	**1a**	**2c**	**5g**	5	80
8	4-OMe-C_6H_4	**1a**	**2c**	**5h**	7	68
9	4-NO_2-C_6H_4	**1a**	**2c**	**5i**	8	70
10	4-Br-C_6H_4	**1a**	**2c**	**5j**	6	78
11	4-F-C_6H_4	**1a**	**2c**	**5k**	5	82
12	2-Napthyl	**1a**	**2c**	**5l**	8	62
13	4-F-C_6H_4	**1b**	**2c**	**5m**	5	75
14	3-OH-C_6H_4	**1b**	**2c**	**5n**	8	60
15	4-Br-C_6H_4	**1c**	**2c**	**5o**	6	67

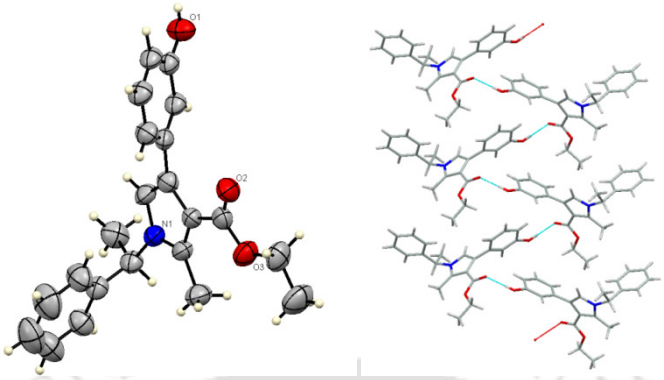
16	4-Br-C_6H_4	**1d**	**2c**	**5p**	7	65
17	4-Cl-C_6H_4	**1a**	**2d**	**5q**	5	78
18	4-Me-C_6H_4	**1b**	**2d**	**5r**	5	76
19	3-OH-C_6H_4	**1b**	**2d**	**5s**	8	60
20	2,4-Di-OMe-C_6H_3	**1b**	**2d**	**5t**	8	58
21	2-NO_2-C_6H_4	**1b**	**2d**	**5u**	8	67
22	2-F-C_6H_4	**1b**	**2d**	**5v**	5	68
23	3-F-C_6H_4	**1b**	**2d**	**5w**	6	62
24	4-Cl-C_6H_4	**1a**	**2e**	**5x**	9	62

[a]All the reactions were performed using β-ketoester(1mmol), benzylamine (1 mmol), aldehyde (1mmol) in nitromethane (1 mL) with BDMS (10 mol %) at room temperature. [b]Isolated yield.

The scope of the present protocol was further examined by carrying out reactions with methyl acetoacetate (**1a**) and *R*-(+)-α-methylbenzylamine (**2c**) with various aromatic aldehydes having substituents Me, OMe, NO_2, Br, and F in the aromatic ring under similar reaction conditions and the products **5f-k** were obtained in good yields (Table 2, entries 6-11). Likewise, a reaction with 2-naphthaldehyde, methyl acetoacetate (**1a**), *R*-(+)-α-methylbenzylamine (**2c**) and nitromethane under identical reaction conditions provided the desired product **5l** in 62% yield (Table 2, entry 12). In addition, a wide variety of β-ketoesters such as ethyl acetoacetate (**1b**), allyl acetoacetate (**1c**) and *t*-butyl acetoacetate (**1d**) and different aromatic aldehydes such as 4-fluorobenzaldehyde, 3-hydroxybenzaldehyde, 4-bromobenzaldehyde were treated with *R*-(+)-α-methylbenzylamine (**2c**) and nitromethane under similar reaction conditions, respectively and the desired products **5m-p** were obtained in good yields (Table 2, entries 13-16). Similarly, methyl acetoacetate (**1a**) or ethyl acetoacetate (**1b**), S-(−)-α-methylbenzylamine (**2d**), nitromethane reacted with different aromatic aldehydes having substituents such as Cl, Me, OH, OMe, NO_2 and F on the aromatic ring under similar reaction condition to afford the products **5q-w** were isolated in 58-78% yield (Table 2, entries 17-23).

Furthermore, tuning the reaction with cyclohexylamine (**2e**), methyl acetoacetate (**1a**) and 4-chlorobenzaldehyde in presence of 10 mol% BDMS at room temperature gave the product **5x** in 62% yield. All the products were characterized by IR, ^1H and ^{13}C NMR spectra as well as from their elemental analyses. The structure of the product **5n** was further

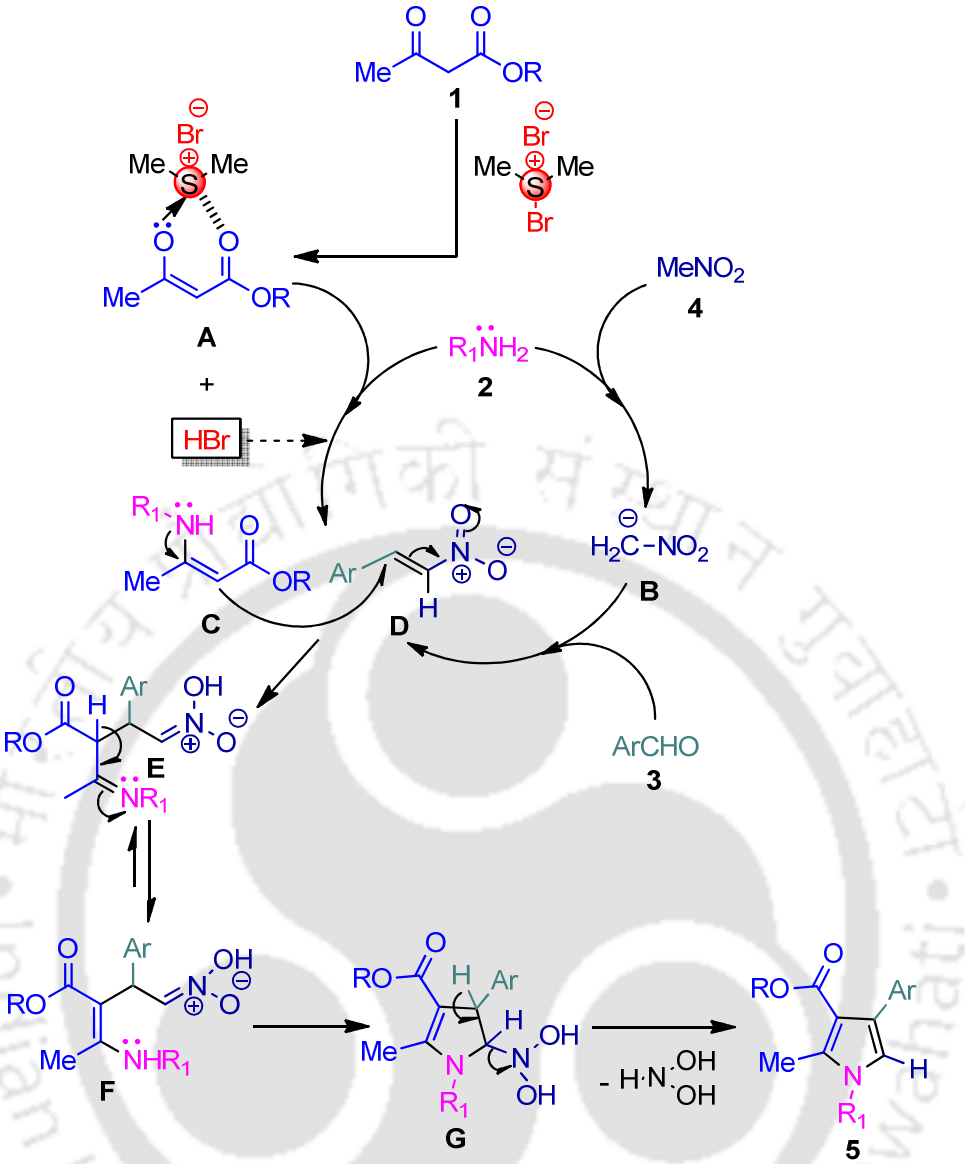
confirmed by single crystal XRD and the ORTEP diagram of **5n** and their intermolecular H-bonding interaction through O–H···O bonds (H···O = 0.821 Å, O···O = 2.823 Å, <O–H···O = 172.64°) as shown in Figure 5.



(a) **(b)**

Figure 5. (**a**) ORTEP diagram of **5n**. (**b**) Intermolecular H-bonding interactions (CCDC no. is 848584)

The formation of product **5** may be rationalized as follows: β-Ketoester on reaction with bromodimethylsulfonium bromide gives an intermediate **A** and HBr in the reaction medium. The liberated HBr catalyzes the formation of enamino ester **C** from β-ketoester and benzylamine. At the same time, carbanion **B** was generated from nitromethane **4** in the presence of benzylamine **2,** which reacts instantly with aromatic aldehyde **3** to form nitrostyrene **D**. Subsequently, the enamino ester **C** reacts with nitrostyrene **D** to form Michael adduct **E**, which undergoes tautomerization into **F**. Finally, it gives the intermediate **G** on cyclization, which is converted into the desired product **5** with the elimination of H_3NO_2 as shown in Scheme 28.



Scheme 28

In conclusion, we have devised a simple and efficient synthetic protocol for the synthesis of substituted pyrrole derivatives using β-ketoesters, benzylamines, aromatic aldehydes and nitromethane in the presence of 10 mol% BDMS at room temperature. The present protocol profits from the employment of metal-free catalyst, eco friendliness, mild reaction conditions, good yields and wide substrate compatibility. In addition, the molecule **5n** shows fascinating one-dimension zig-zag structure via inter-molecular hydrogen bonding interactions.

Experimental

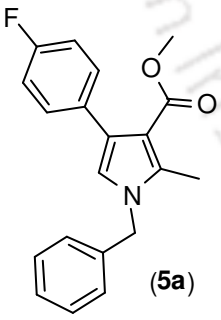
Preparation of bromodimethylsulfonium bromide (BDMS)

Into a 100 mL standard joint conical flask was taken a dimethyl sulfide (1.83 mL, 25 mmol) in 5 mL of dry dichloromethane under ice cold condition (0-5 ^{0}C). After that, 25 mmol bromine was dissolved in 5 mL dry DCM and it was added drop wise to the above dimethyl sulfide solution over a period of 5 minutes. The light orange crystals of bromodimethylsulfonium bromide begin to form in the additing time. After the complete addition of bromine, the crystals of bromodimethylsulfonium bromide were collected through Buchner funnel. The required solid was washed twice with dry hexane and dried under vacuum and the obtained yield was 77% (4.3g), m.p. 80 ^{o}C.

*General procedure for the synthesis of tetra substituted pyrroles (**5**)*

Bromodimethylsulfonium bromide (BDMS, 0.1 mmol) was added to a mixture of β-ketoester (1 mmol) and benzylamine (1 mmol) in 1 mL of nitromethane and the reaction mixture was stirred at room temperature for 10 minutes, until a yellow colour appeared. The aromatic aldehyde (1 mmol) was then added and stirring was continued until completion of the reaction. The mixture was concentrated to dryness under reduced pressure and the crude was purified on silica gel column (hexane / ethylacetate, 10:1) affording the pure products **5**.

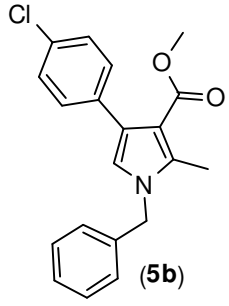
*Methyl-1-benzyl-4-(4-fluorophenyl)-2-methyl-1H-pyrrole-3-carboxylate (**5a**)*



(**5a**)

Yellow solid, M.p 75-77 °C; **IR** (KBr)ν_{max} 3027, 2946, 2846, 1698, 1523, 1438, 1284, 1215, 1204, 1187, 1143, 1061 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 2.48 (s, 3H), 3.68 (s, 3H), 5.06 (s, 2H), 6.56 (s, 1H), 7.02 (t, J = 8.8 Hz, 2H), 7.07 (d, J = 6.8 Hz, 2H), 7.28-7.35 (m, 5H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 11.8, 50.7, 110.9, 114.5, 114.7, 120.7, 125.5, 126.7, 128.4, 129.1, 130.8, 130.9, 132.0, 136.8, 166.3; **Anal. calcd** for $C_{20}H_{18}FNO_2$ C, 74.29; H, 5.61; N, 4.33; found C, 74.19; H, 5.55; N, 4.26.

*Methyl-1-benzyl-4-(4-chlorophenyl)-2-methyl-1H-pyrrole-3-carboxylate (**5b**)*

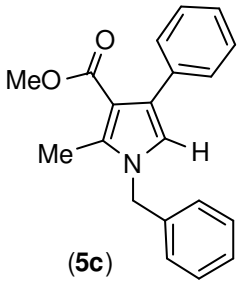


(**5b**)

Oily liquid, **IR** (KBr)ν_{max} 3030, 2948, 2845, 1696, 1520, 1435, 1282, 1212, 1203, 1185, 1142, 1060 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 2.47 (s, 3H), 3.68 (s, 3H), 5.07 (s, 2H), 6.57 (s, 1H), 7. 06 (d, J = 6.8 Hz, 2H), 7.29 (brs, 4H), 7.31-7.37 (m, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 11.7, 50.7, 110.9, 120.8, 125.2, 126.6, 127.9, 128.0, 129.1, 130.6, 132.3, 134.5,

136.7, 136.9, 166.1; **Anal. Calcd** for $C_{20}H_{18}ClNO_2$ C, 70.69; H, 5.34; N, 4.12; found C, 70.59; H, 5.28; N, 4.06.

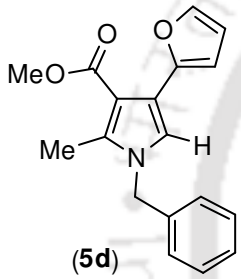
*Methyl-1-benzyl-2-methyl-4-phenyl-1H-pyrrole-3-carboxylate (**5c**)*



(**5c**)

Oily liquid, **IR** (KBr)ν_{max} 3030, 2926, 1698, 1604, 1525, 1496, 1451, 1435, 1410, 1284, 1204, 1185, 1144, 1124, 1066, 1028 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 2.47 (s, 3H), 3.67 (s, 3H), 5.07 (s, 2H), 6.59 (s, 1H), 7.07 (d, J = 7.6 Hz, 2H), 7.26-7.23 (m, 2H), 7.32 (t, J = 7.2 Hz, 4H), 7.38-7.36 (m 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 11.0, 50.7, 110.9, 120.8, 126.3, 126.7, 127.8, 127.9, 129.1, 129.3, 135.9, 136.7, 136.9, 166.5; **Anal. calcd** for $C_{20}H_{19}NO_2$ C, 78.66; H, 6.27; N, 4.59; found C, 78.59; H, 6.19; N, 4.48.

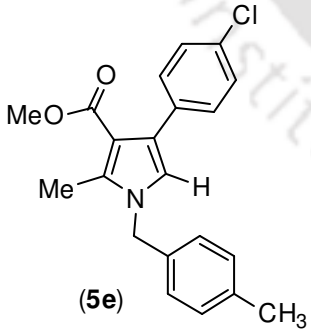
*Methyl-1-benzyl-4-(furan-2-yl)-2-methyl-1H-pyrrole-3-carboxylate (**5d**)*



(**5d**)

Oily liquid, **IR** (KBr)ν_{max} 2925, 2853, 1701, 1604, 1523, 1492, 1439, 1364, 1280, 1207, 1189, 1130, 1078 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 2.36 (s, 3H), 3.75 (s, 3H), 4.97 (s, 2H), 6.34 (dd, J = 3.2, 2.0 Hz, 1H), 6.66 (dd, J = 3.2, 0.8 Hz, 1H), 6.87 (s, 1H), 6.98 (d, J = 6.8 Hz, 2H), 7.17-7.31 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 11.9, 50.9, 107.2, 109.8, 111.3, 115.9, 120.7, 126.6, 127.8, 128.0, 129.1, 136.7, 136.9, 140.5, 149.7, 165.9; **Anal. calcd** for $C_{18}H_{17}NO_3$ C, 73.20; H, 5.80; N, 4.74; found C, 73.09; H, 5.71; N, 4.65.

*Methyl-1-(4-methylbenzyl)-4-(4-chlorophenyl)-2-methyl-1H-pyrrole-3-carboxylate (**5e**)*

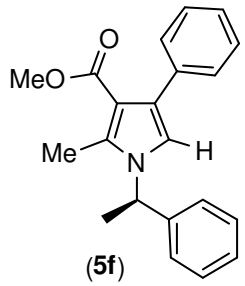


(**5e**)

Oily liquid, **IR** (KBr)ν_{max} 2925, 2851, 1703, 1518, 1486, 1437, 1415, 1282, 1198, 1188, 1143, 1089, 1014 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 2.67 (s, 3H), 2.80 (s, 3H), 4.01 (s, 3H), 5.34 (s, 2H), 6.88 (s, 1H), 7.29 (d, J = 7.2 Hz, 2H), 7.48 (d, J = 7.2 Hz, 2H), 7.62 (brs, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 11.7, 21.2, 22.9, 50.0, 110.7, 120.7, 125.2, 126.8, 127.9, 129.8, 130.6, 132.1, 133.7, 134.6, 136.9, 137.8, 166.3; **Anal. calcd** for $C_{21}H_{20}ClNO_2$ C, 71.28; H, 5.70; N, 3.96; found C, 71.21; H, 5.61; N, 3.88.

*(R)-Methyl-2-methyl-4-phenyl-1-(1-phenylethyl)-1H-pyrrole-3-carboxylate (**5f**)*

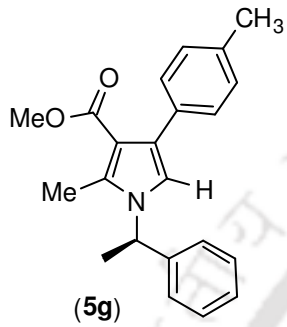
Oily liquid, $[\alpha]_D^{25}$ = -23.8° (c 0.5, $CHCl_3$); **IR** (KBr)ν_{max} 3029, 2925, 2854, 1698, 1603, 1524, 1494, 1234, 1208, 1276, 1212 ,1190, 1149, 1079, 1028 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.72 (d, J = 7.2 Hz, 3H), 2.35 (s, 3H), 3.56 (s, 3H), 5.26 (q, J = 6.8 Hz, 1H), 6.64 (s, 1H), 6.97 (d, J = 7.2 Hz, 2H), 7.12-7.18 (m, 2H), 7.19-7.26 (m, 4H), 7.29 (d, J = 7.2 Hz,



(**5f**)

2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 11.4, 22.1, 50.4, 55.1, 110.6, 116.9, 125.8, 125.9, 126.1, 127.6, 128.8, 129.1, 136.1, 136.5, 142.1, 166.4; **Anal. calcd** for $C_{21}H_{21}NO_2$ C, 78.97; H, 6.63; N, 4.39; found C, 78.89; H, 6.55; N, 4.28.

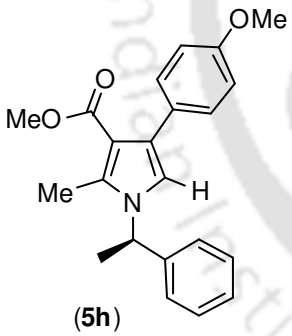
*(R)-Methyl-2-methyl-1-(1-phenylethyl)-4-(p-tolyl)-1H-pyrrole-3-carboxylate (**5g**)*



(**5g**)

Oily liquid, $[\alpha]_D^{25}$ = -31.6° (c 0.5, $CHCl_3$); **IR** (KBr)ν_{max} 2980, 2924, 2851, 1701, 1527, 1437, 1412, 1277, 1214, 1189, 1149, 1118, 1079, 1027 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.74 (d, *J* = 7.2 Hz, 3H), 2.28 (s, 3H), 2.36 (s, 3H), 3.58 (s, 3H), 5.28 (q, *J* = 6.8 Hz, 1H), 6.63 (s, 1H), 6.99 (d, *J* = 7.6 Hz, 2H), 7.06 (d, *J* = 8.0 Hz, 2H), 7.16-7.25 (m, 5H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 11.5, 21.2, 22.2, 50.5, 55.2, 110.7, 116.8, 125.8, 127.6, 128.5, 128.9, 129.0, 133.2, 135.6, 136.5, 144.2, 166.5; **Anal. calcd** for $C_{22}H_{23}NO_2$ C, 79.25; H, 6.95; N, 4.20; found C, 79.10; H, 6.85; N, 4.08.

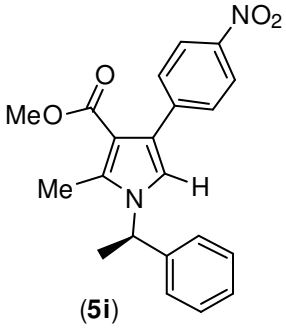
*(R)-Methyl-4-(4-methoxyphenyl)-2-methyl-1-(1-phenylethyl)-1H-pyrrole-3-carboxylate (**5h**)*



(**5h**)

Oily liquid, $[\alpha]_D^{25}$ = -117.7° (c 0.5, $CHCl_3$); **IR** (KBr)ν_{max} 2926, 2855, 1698, 1525, 1540, 1404, 1276, 1244, 1212, 1188, 1149, 1118, 1076, 1034 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.72 (d, *J* = 7.2 Hz, 3H), 2.34 (s, 3H), 3.57 (s, 3H), 3.72 (s, 3H), 5.26 (q, *J* = 7.2 Hz, 1H), 6.59 (s, 1H), 6.77-6.81 (m, 2H), 6.96-6.98 (m, 2H), 7.14-7.18 (m, 1H), 7.20-7.22 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 11.6, 22.2, 50.6, 55.2, 55.3, 110.7, 113.2, 116.7, 125.7, 125.9, 127.7, 128.7, 128.9, 130.2, 136.5, 142.3, 158.3, 166.6; **Anal. calcd** for $C_{22}H_{23}NO_3$ C, 75.62; H, 6.63; N, 4.01; found C, 75.55; H, 6.53; N, 3.92.

*(R)-Methyl-2-methyl-4-(4-nitrophenyl)-1-(1-phenylethyl)-1H-pyrrole-3-carboxylate (**5i**)*

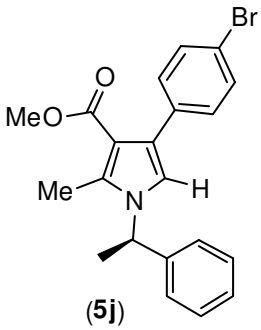


(**5i**)

Oily liquid, $[\alpha]_D^{25}$ = -51.4° (c 0.5, $CHCl_3$); **IR** (KBr)ν_{max} 2925, 2854, 1704, 1667, 1596, 1515, 1440, 1399, 1344, 1270, 1213, 1188, 1149, 1076 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.77 (d, *J* = 7.2 Hz, 3H), 2.38 (s, 3H), 3.60 (s, 3H), 5.34 (q, *J* = 7.2 Hz, 1H), 6.74 (s, 1H), 7.0 (d, *J* = 8.0 Hz, 2H), 7.18-7.22 (m, 1H), 7.24-7.28 (m, 2H), 7.44 (d, *J* = 8.8 Hz, 2H), 8.09 (d, *J* = 8.8 Hz, 2H); **^{13}C**

NMR (100 MHz, $CDCl_3$): δ 11.6, 22.1, 50.7, 55.5, 110.8, 118.2, 122.9, 124.0, 125.8, 127.9, 129.0, 129.5, 137.7, 141.6, 143.3, 146.1, 165.8; **Anal. calcd** for $C_{21}H_{20}N_2O_4$ C, 69.22; H, 5.53; N, 7.69; found C, 69.15; H, 5.42; N, 7.57.

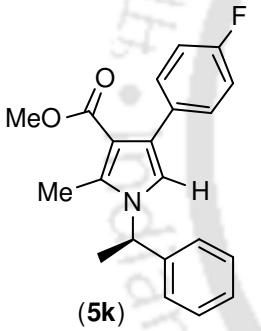
(R)-Methyl-4-(4-bromophenyl)-2-methyl-1-(1-phenylethyl)-1H-pyrrole-3-carboxylate ***(5j)***



(**5j**)

Oily liquid, $[\alpha]_D^{25}$ = -58.9° (c 0.5, $CHCl_3$); **IR** (KBr)ν_{max} 2925, 2851, 1698, 1524, 1437, 1412, 1277, 1211, 1188, 1149, 1118, 1071, 1009 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.73 (d, *J* = 6.8 Hz, 3H), 2.36 (s, 3H), 3.58 (s, 3H), 5.28 (q, *J* = 7.2 Hz, 1H), 6.62 (s, 1H), 6.98 (d, *J* = 7.2 Hz, 2H), 7.16-7.19 (m, 3H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 11.6, 22.3, 50.7, 55.3, 110.6, 117.1, 120.2, 124.9, 125.9, 127.8, 128.6, 129.0, 130.8, 130.9, 135.2, 136.9, 142.0, 166.3; **Anal. calcd** for $C_{21}H_{20}BrNO_2$ C, 63.33; H, 5.06; N, 3.52; found C, 63.24; H, 4.96; N, 3.46.

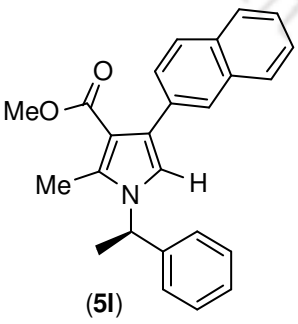
(R)-Methyl-4-(4-fluorophenyl)-2-methyl-1-(1-phenylethyl)-1H-pyrrole-3-carboxylate ***(5k)***



(**5k**)

Oily liquid, $[\alpha]_D^{25}$ = -55.4° (c 0.5, $CHCl_3$); **IR** (KBr)ν_{max} 2926, 2857, 1698, 1063, 1526, 1499, 1237, 1276, 1214, 1190, 1150, 1079 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.73 (d, *J* = 6.8 Hz, 3H), 2.35 (s, 3H), 3.56 (s, 3H), 5.28 (q, *J* = 6.8 Hz, 1H), 6.61 (s, 1H), 6.90-6.94 (m, 2H), 6.98 (d, *J* = 8.0 Hz, 2H), 7.15-7.18 (m, 1H), 7.22-7027 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 11.6, 22.2, 50.6, 55.2, 110.7, 114.3, 114.6, 116.9, 125.1, 125.8, 127.7, 128.9, 130.7, 130.8, 132.2, 136.7, 142.1, 166.4; **Anal. calcd** for $C_{21}H_{20}FNO_2$ C, 74.76; H, 5.97; N, 4.15; found C, 74.65; H, 5.88; N, 4.05.

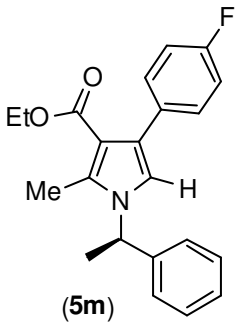
(R)-Methyl-2-methyl-4-(naphthalen-2-yl)-1-(1-phenylethyl)-1H-pyrrole-3-carboxylate ***(5l)***



(**5l**)

Yellow semi-solid, $[\alpha]_D^{25}$ = -106.7° (c 0.5, $CHCl_3$); **IR** (KBr)ν_{max} 3047, 2925, 2851, 1695, 1630, 1525, 1435, 1409, 1279, 1238, 1185, 1146, 1114, 1076, 1026 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.84 (d, *J* = 6.8 Hz, 3H), 2.47 (s, 3H), 3.63 (s, 3H), 5.39 (q, *J* = 6.8 Hz, 1H), 6.82 (s, 1H), 7.09 (d, *J* = 7.2 Hz, 2H), 7.27 (d, *J* = 7.2 Hz, 1H), 7.31 (t, *J* = 7.6 Hz, 2H), 7.41-7.44 (m, 2H), 7.52 (d, *J* = 10 Hz, 1H), 7.77 (s, 1H), 7.81 (t, *J* = 6.8 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 11.6, 22.3, 50.7, 55.3, 110.9, 117.4, 125.4, 125.9, 126.7, 126.9, 127.8, 127.9, 128.7, 129.1, 132.3, 133.6, 134.0, 136.9, 142.2, 166.6; **Anal. calcd** for $C_{25}H_{23}NO_2$ C, 81.27; H, 6.27; N, 3.79; found C, 81.16; H, 6.18; N, 3.70.

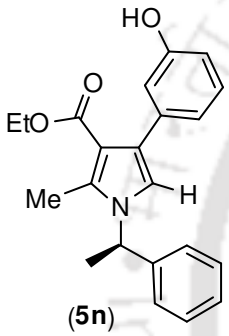
(R)-Ethyl-4-(4-fluorophenyl)-2-methyl-1-(1-phenylethyl)-1H-pyrrole-3-carboxylate ***(5m)***



(**5m**)

Oily liquid, $[\alpha]_D^{25}$ = -19.9° (c 0.5, $CHCl_3$); **IR** (KBr)ν_{max} 3049, 2926, 2855, 1694, 1525, 1499, 1422, 1276, 1214, 1186, 1155, 1116 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.02 (t, *J* = 7.2 Hz, 3H), 1.70 (d, *J* = 6.8 Hz, 3H), 2.35 (s, 3H), 4.04 (q, *J* = 7.2 Hz, 2H), 5.26 (q, *J* = 7.2 Hz, 1H), 6.59 (s, 1H), 6.87-6.91 (m, 2H), 6.97 (d, *J* = 7.6 Hz, 2H), 7.15 (d, *J* = 7.2 Hz, 2H), 7.19-7.25 (m, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 11.5, 14.2, 22.2, 55.2, 59.5, 111.0, 114.2, 114.4, 116.9, 125.1, 125.9, 127.7, 128.9, 130.8, 130.9, 136.6, 142.2, 165.9; **Anal. calcd** for $C_{22}H_{22}FNO_2$ C, 75.19; H, 6.31; N, 3.99; found C, 75.07; H, 6.22; N, 3.89.

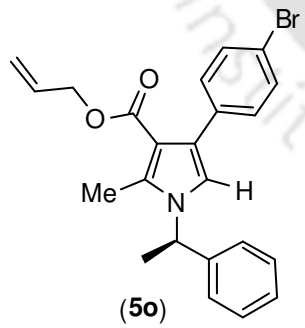
(R)-Ethyl-4-(3-hydroxyphenyl)-2-methyl-1-(1-phenylethyl)-1H-pyrrole-3-carboxylate ***(5n)***



(**5n**)

Yellow solid, M.p 78-80°C; $[\alpha]_D^{25}$ = -23.2° (c 0.5, $CHCl_3$); **IR** (KBr)ν_{max} 3025, 2918, 2851, 1667, 1605, 1448, 1412, 1289, 1236, 1144, 1018 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.13 (t, *J* =7.2 Hz, 3H), 1.79 (d, *J* = 6.8 Hz, 3H), 2.44 (s, 3H), 4.17 (q, *J* = 7.6 Hz, 2H), 5.33 (q, *J* = 7.6 Hz, 1H), 6.72 (s, 1H), 6.88 (brs, 1H), 6.92 (d, *J* = 7.6 Hz, 2H), 7.05 (d, *J* = 7.2 Hz, 2H), 7.15 (t, *J* = 8.0 Hz, 1H), 7.24-7.32 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 11.6, 14.1, 22.2, 55.2, 59.7, 110.9, 113.3, 116.5, 117.1, 121.4, 125.9, 127.7, 128.7, 128.9, 136.6, 137.5, 142.1, 155.2, 166.7; **Anal. calcd** for $C_{22}H_{23}NO_3$ C, 75.62; H, 6.63; N, 4.01; found C, 75.55; H, 6.53; N, 3.92.

(R)-Allyl-4-(4-bromophenyl)-2-methyl-1-(1-phenylethyl)-1H-pyrrole-3-carboxylate ***(5o)***

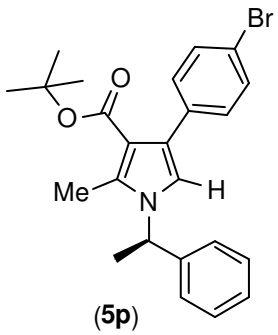


(**5o**)

Oily liquid, $[\alpha]_D^{25}$ = -63.3° (c 0.5, $CHCl_3$); **IR** (KBr)ν_{max} 2925, 2851, 1698, 1524, 1448, 1417, 1272, 1208, 1186, 1149, 1068 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.69 (d, *J* = 6.8 Hz, 3H), 2.34 (s, 3H), 4.49 (dd, *J* = 4.4, 1.2 Hz, 2H), 4.97-5.01 (m, 2H), 5.24 (q, *J* = 6.8 Hz, 1H), 5.66-5.75 (m, 1H), 6.60 (s, 1H), 6.95 (d, *J* = 6.8 Hz, 2H), 7.14-7.17 (m, 3H), 7.20 (t, *J* = 7.2 Hz, 2H), 7.31 (d, *J* = 8.8 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 11.6, 22.2, 55.2, 64.4, 110.5, 117.1, 117.7, 120.2, 124.9, 125.8, 127.8, 128.9, 130.7, 131.0, 132.6, 135.2, 137.0, 149.9, 165.4; **Anal. calcd** for $C_{23}H_{22}BrNO_2$ C, 65.10; H, 5.23; N, 3.30; found C, 64.96; H, 5.14; N, 3.20.

(R)-Tert-butyl-4-(4-bromophenyl)-2-methyl-1-(1-phenylethyl)-1H-pyrrole-3-carboxylate ***(5p)***

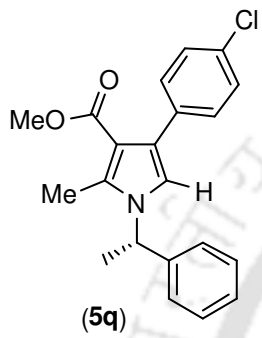
Oily liquid, $[\alpha]_D^{25}$ = -51.7° (c 0.5, $CHCl_3$); **IR** (KBr)ν_{max} 2921, 2848, 1701, 1523, 1445, 1415, 1275, 1205, 1188, 1145, 1065 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.28 (s, 9H), 1.72 (d, *J* =



(**5p**)

7.2 Hz, 3H), 2.35 (s, 3H), 5.27 (q, *J* = 7.2 Hz, 1H), 6.59 (s, 1H), 6.99 (d, *J* = 7.6 Hz, 2H), 7.15-7.19 (m, 3H), 7.23 (d, *J* = 7.6 Hz, 2H), 7.35 (d, *J* =8.4 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 11.5, 22.3, 28.3, 55.2, 79.9, 112.5, 116.7, 119.9, 124.7, 126.0, 127.8, 129.0, 130.7, 131.1, 135.7, 136.2, 142.1, 165.3; **Anal. calcd** for $C_{24}H_{26}BrNO_2$ C, 65.46; H, 5.95; N, 3.18; found C, 65.34; H, 5.84; N, 3.08.

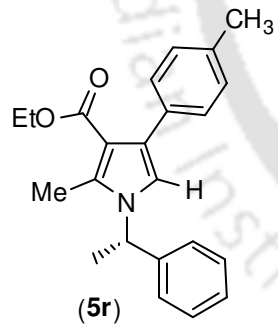
*(S)-Methyl-4-(4-chlorophenyl)-2-methyl-1-(1-phenylethyl)-1H-pyrrole-3-carboxylate (**5q**)*



(**5q**)

Oily liquid, $[\alpha]_D^{25}$ = +40.4° (c 0.5, $CHCl_3$); **IR** (KBr)ν_{max} 2925, 2854, 1698, 1526, 1487, 1436, 1416, 1277, 1212, 1190, 1149, 1121, 1090, 1015 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.73 (d, *J* = 7.2 Hz, 3H), 2.35 (s, 3H), 3.57 (s, 3H), 5.27 (q, *J* = 6.8 Hz, 1H), 6.62 (s, 1H), 6.97 (d, *J* = 8.4 Hz, 2H), 7.17 (d, *J* = 7.6 Hz, 2H), 7.19-7.21 (m, 3H), 7.22-7.27 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 11.6, 22.1, 50.6, 55.2, 110.6, 117.1, 124.8, 125.8, 127.7, 127.8, 128.9, 130.5, 131.9, 134.7, 136.9, 142.0, 166.3; **Anal. calcd** for $C_{21}H_{20}ClNO_2$ C, 71.28; H, 5.70; N, 3.96; found C, 71.15; H, 5.62; N, 3.87.

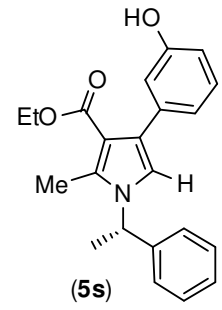
*(S)-Ethyl-2-methyl-1-(1-phenylethyl)-4-(p-tolyl)-1H-pyrrole-3-carboxylate (**5r**)*



(**5r**)

Yellow solid, M.p 67-69°C; $[\alpha]_D^{25}$ = +36.6° (c 0.5, $CHCl_3$); **IR** (KBr)ν_{max} 2978, 2924, 1675, 1526, 1451, 1400, 1272, 1216, 1191, 1150, 1071, 1041 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.13 (t, *J* = 7.2 Hz, 3H), 1.80 (d, *J* = 6.8 Hz, 3H), 2.35 (s, 3H), 2.43 (s, 3H), 4.16 (q, *J* = 7.2 Hz, 2H), 5.36 (q, *J* = 7.2 Hz, 1H), 6.70 (s, 1H), 7.06 (d, *J* = 7.6 Hz, 2H), 7.12 (d, *J* = 8.0 Hz, 2H), 7.23-7.32 (m, 5H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 11.5, 14.2, 21.2, 22.2, 55.1, 59.3, 110.9, 116.7, 125.8, 127.6 ,128.3, 128.8, 129.2, 133.2, 135.5, 136.2, 142.2, 166.1; **Anal. calcd** for $C_{23}H_{25}NO_2$ C, 79.51; H, 7.25; N, 4.03; found C, 79.43; H, 7.16; N, 3.95.

*(S)-ethyl-4-(3-hydroxyphenyl)-2-methyl-1-(1-phenylethyl)-1H-pyrrole-3-carboxylate (**5s**)*

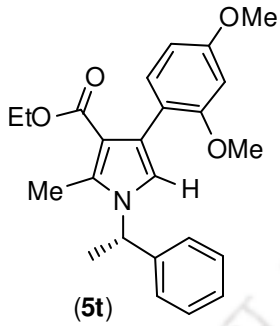


(**5s**)

Yellow solid, M.p 78-80°C; $[\alpha]_D^{25}$ = +12.8° (c 0.5, $CHCl_3$); **IR** (KBr)ν_{max} 3368, 2979, 2926, 1673, 1616, 1584, 1445, 1423, 1386, 1301, 1223, 1198, 1140, 1027 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.13 (t, *J* = 7.2 Hz, 3H), 1.79 (d, *J* = 7.2 Hz, 3H), 2.42 (s, 3H), 4.15 (q, *J* = 7.2 Hz, 2H), 5.34 (q, *J* = 7.2 Hz, 1H), 6.72 (s, 1H), 6.88 (brs, 1H), 6.93 (d, *J* = 8.0 Hz, 2H), 7.06

(d, *J* = 7.2 Hz, 2H), 7.15 (t, *J* = 8.0 Hz, 1H), 7.25 (s, 1H), 7.29-7.32 (m, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 11.6, 14.1, 22.3, 55.3, 59.9, 110.9, 113.4, 116.5, 117.1, 121.5, 125.8, 125.9, 127.7, 128.8, 129.0, 136.6, 137.6, 142.2, 155.5, 166.7; **Anal. calcd** for $C_{22}H_{23}NO_3$ C, 75.62; H, 6.63; N, 4.01; found C, 75.48; H, 6.55; N, 3.92.

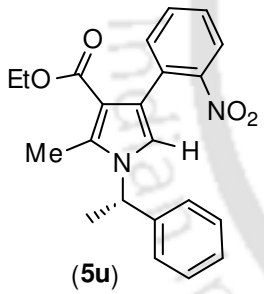
*(S)-Ethyl-4-(2,4-dimethoxyphenyl)-2-methyl-1-(1-phenylethyl)-1H-pyrrole-3-carboxylate (**5t**)*



(**5t**)

Oily liquid, $[\alpha]_D^{25}$ = +56.4° (c 0.5, $CHCl_3$); **IR** (KBr)ν_{max} 2979, 2937, 2836, 1695, 1613, 1582, 1532, 1495, 1274, 1208, 1158, 1037 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.05 (t, *J* = 7.6 Hz, 3H), 1.81 (d, *J* = 7.2 Hz, 3H), 2.39 (s, 3H), 3.74 (s, 3H), 3.83 (s, 3H), 4.07 (q, *J* = 7.6 Hz, 2H), 5.33 (q, *J* = 7.2 Hz, 1H), 6.45-6.49 (m, 2H), 6.70 (s, 1H), 7.07 (d, *J* = 7.2 Hz, 2H), 7.17-7.19 (m, 1H), 7.23-7.27 (m, 1H), 7.29-7.33 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 11.2, 14.1, 22.2, 55.1, 55.2, 55.3, 59.1, 98.3, 103.5, 112.6, 116.5, 118.5, 121.0, 125.8, 127.4, 128.8, 130.7, 135.1, 142.4, 158.1, 159.8, 166.3; **Anal. calcd** for $C_{24}H_{27}NO_4$ C, 73.26; H, 6.92; N, 3.56; found C, 73.12; H, 6.86; N, 3.47.

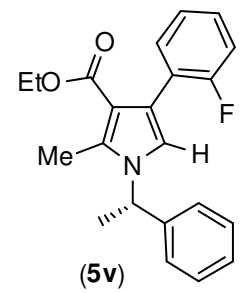
*(S)-Ethyl-2-methyl-4-(2-nitrophenyl)-1-(1-phenylethyl)-1H-pyrrole-3-carboxylate (**5u**)*



(**5u**)

Oily liquid, $[\alpha]_D^{25}$ = +4.8° (c 0.5, $CHCl_3$); **IR** (KBr)ν_{max} 2923, 2850, 1705, 1665, 1594,1514, 1435, 1395, 1265, 1212, 1177, 1145, 1076 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 0.99 (t, *J* = 7.6 Hz, 3H), 1.84 (d, *J* = 7.2 Hz, 3H), 2.44 (s, 3H), 4.00 (q, *J* = 7.2 Hz, 2H), 5.40 (q, *J* = 7.2 Hz, 1H), 6.76 (s, 1H), 7.05 (d, *J* = 7.6 Hz, 2H), 7.27 (d, *J* = 7.6 Hz, 1H), 7.34 (t, *J* = 7.6 Hz, 2H), 7.37 (t, *J* = 7.6 Hz, 2H), 7.53 (t, *J* = 7.6 Hz, 1H), 7.95 (d, *J* = 7.6 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 11.5, 13.8, 22.3, 55.3, 59.4, 111.0, 116.9, 121.6, 123.8, 125.7, 127.4, 127.7, 129.0, 132.0, 132.1, 133.0, 137.2, 142.3, 149.9, 165.2; **Anal. calcd** for $C_{22}H_{22}N_2O_4$ C, 69.83; H, 5.86; N, 7.40; found C, 69.76; H, 5.76; N, 7.28.

*(S)-Ethyl-4-(2-fluorophenyl)-2-methyl-1-(1-phenylethyl)-1H-pyrrole-3-carboxylate (**5v**)*

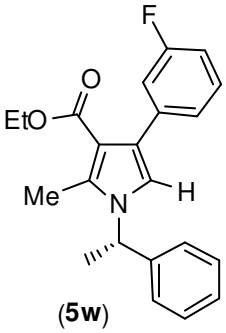


(**5v**)

Oily liquid, $[\alpha]_D^{25}$ = +71.7° (c 0.5, $CHCl_3$); **IR** (KBr)ν_{max} 2926, 2845, 1679, 1627, 155.2, 1493, 1339, 1275, 1207, 1104, 1036 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.05 (t, *J* = 7.2 Hz, 3H), 1.82 (d, *J* = 7.2 Hz, 3H), 2.45 (s, 3H), 4.11 (q, *J* = 7.2 Hz, 2H), 5.37 (q, *J* = 7.2 Hz, 1H), 6.76 (s, 1H), 7.02-7.05 (m, 1H), 7.06-7.08 (m, 1H), 7.09-7.12 (m, 1H), 7.19-7.21 (m, 1H), 7.22-7.23 (m, 1H), 7.25-7.27 (m, 2H), 7.30-7.34 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 11.3, 13.9, 22.2, 55.2, 59.4, 112.1, 114.9, 115.1, 117.3,

118.8, 123.4, 125.9, 127.7, 128.0, 128.1, 128.9, 131.4, 136.3, 142.2, 165.9; **Anal. calcd** for $C_{22}H_{22}FNO_2$ C, 75.19; H, 6.31; N, 3.99; found C, 75.06; H, 6.22; N, 3.90.

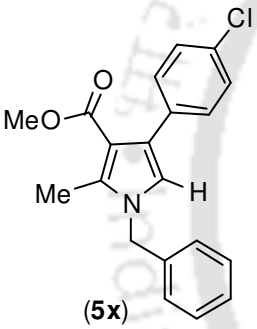
*(S)-Ethyl-4-(3-fluorophenyl)-2-methyl-1-(1-phenylethyl)-1H-pyrrole-3-carboxylate (**5w**)*



(**5w**)

Oily liquid, $[\alpha]_D^{25}$ = +69.8° (c 0.5, $CHCl_3$); **IR** (KBr)ν_{max} 2925, 2851, 1693, 1594, 1448, 1420, 1273, 1208, 1149, 1118, 1020 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.13 (t, *J* = 7.2 Hz, 3H), 1.82 (d, *J* = 7.2 Hz, 3H), 2.45 (s, 3H), 4.15 (q, *J* = 7.2 Hz, 2H), 5.36 (q, *J* = 7.2 Hz, 1H), 6.74 (s, 1H), 6.93 (t, *J* = 8.4 Hz, 1H), 7.07 (d, *J* = 7.2 Hz, 2H), 7.12-7.17 (m, 2H), 7.24-7.28 (m, 2H), 7.32 (t, *J* = 7.2 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 11.5, 14.1, 55.2, 59.5, 110.9, 112.7, 112.9, 116.2, 116.4, 117.2, 125.0, 125.9, 127.8, 128.8, 128.9, 136.8, 142.1, 165.9; **Anal. calcd** for $C_{22}H_{22}FNO_2$ C, 75.19; H, 6.31; N, 3.99; found C, 75.07; H, 6.22; N, 3.87.

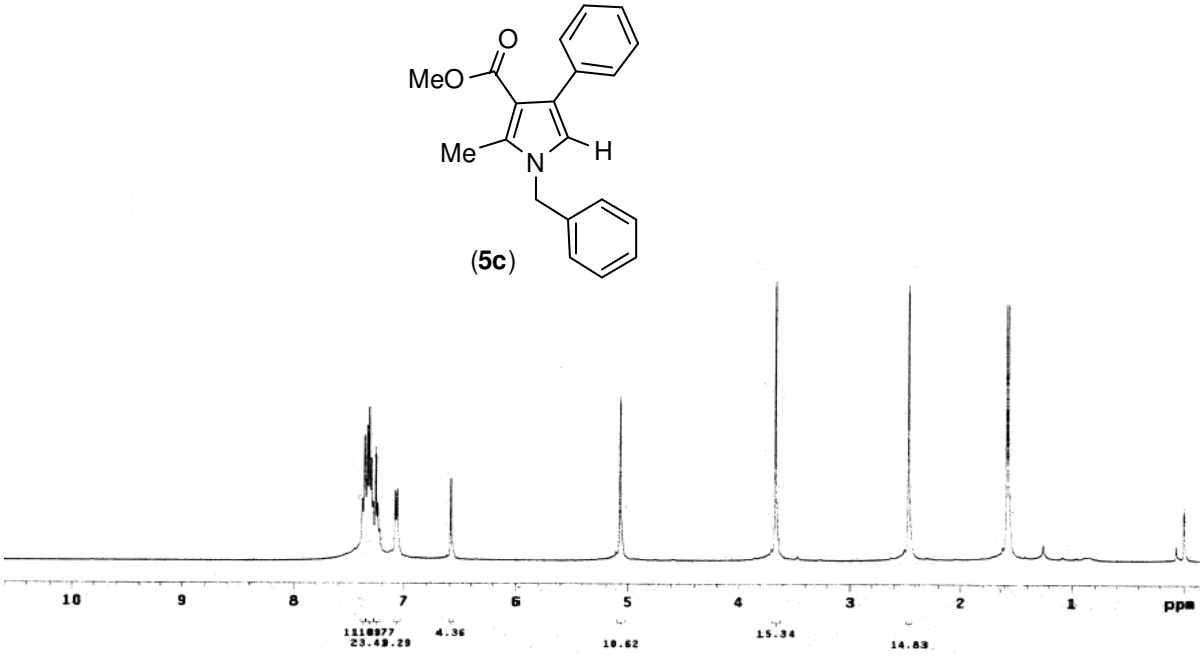
*Methyl-4-(4-chlorophenyl)-1-cyclohexyl-2-methyl-1H-pyrrole-3-carboxylate (**5x**)*



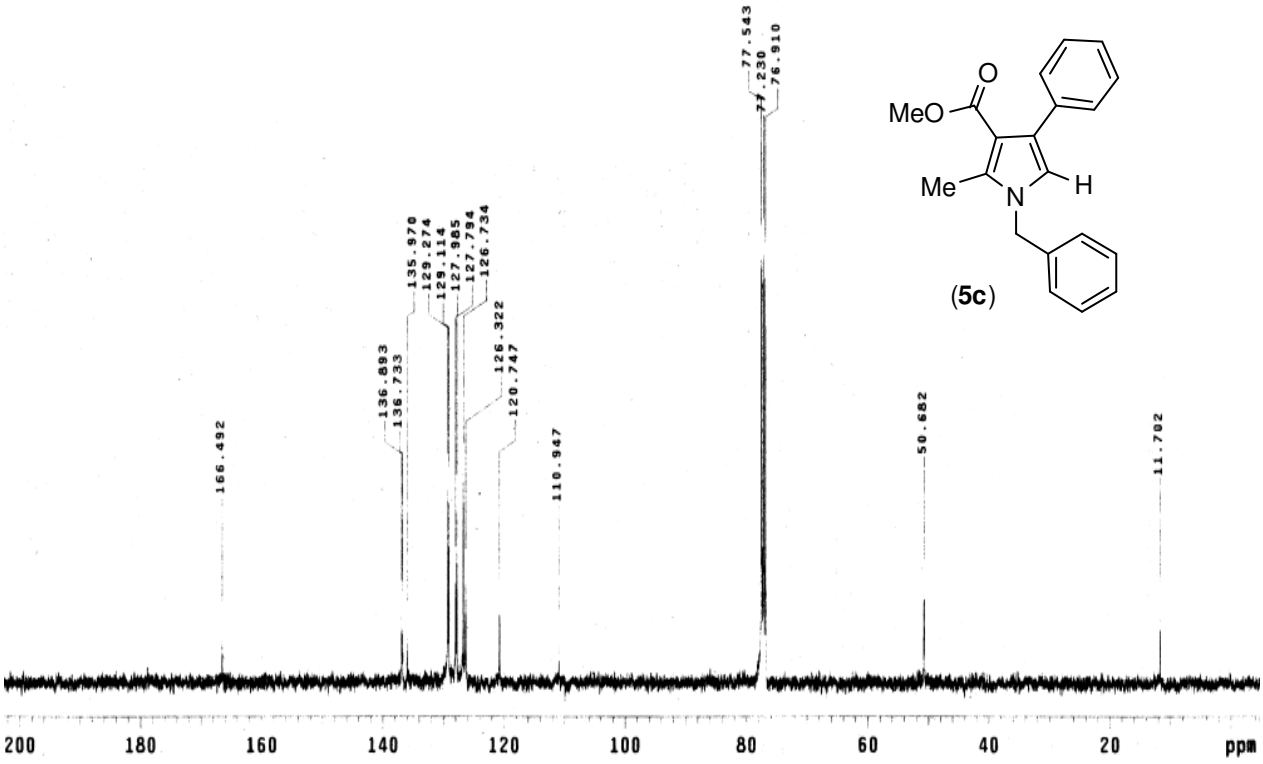
(**5x**)

Oily liquid, **IR** (KBr)ν_{max} 2930, 2855, 1698, 1522, 1436, 1412, 1277, 1200, 1155, 1133, 1083 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* 1.31-1.40 (m, 2H), 1.48-1.58 (m, 4H), 1.69 (d, *J* = 13.2 Hz, 2H), 1.77 (d, *J* = 13.6 Hz, 2H), 1.94 (d, *J* = 12 Hz, 1H), 2.47 (s, 3H), 3.58 (s, 3H), 6.54 (s, 1H), 7.20 (brs, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 11.4, 25.5, 26.0, 34.1, 50.6, 55.5, 109.9, 116.3, 124.9, 127.8, 130.5, 131.9, 135.0, 136.0, 166.5; **Anal. calcd** for $C_{19}H_{22}ClNO_2$ C, 68.77; H, 6.68; N, 4.22; found C, 68.65; H, 6.56; N, 4.12.

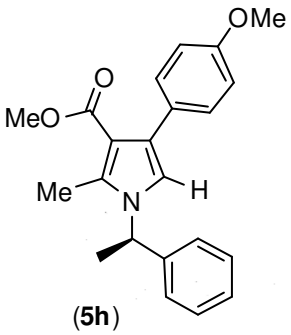
***^{1}H NMR (400 MHz, $CDCl_3$)**: Methyl-1-benzyl-2-methyl-4-phenyl-1H-pyrrole-3-carboxylate (**5c**)*



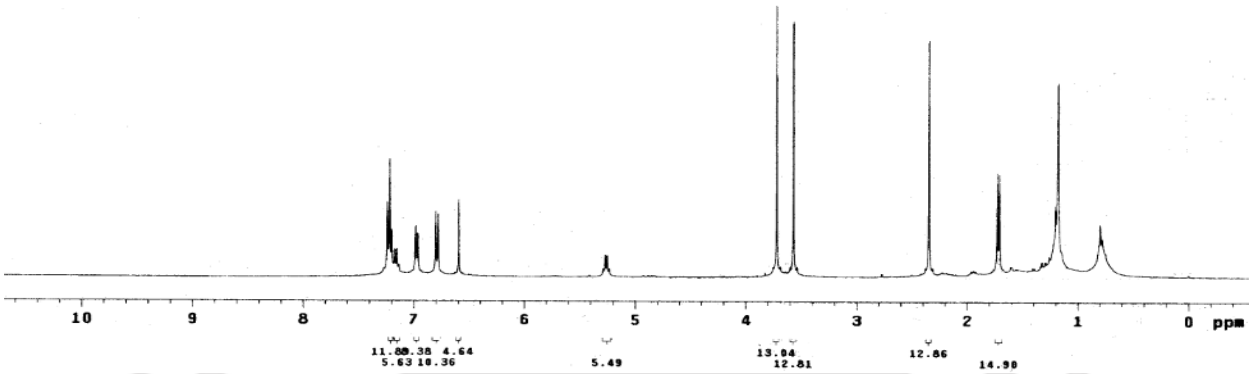
***^{13}C NMR (400 MHz, $CDCl_3$)**: Methyl-1-benzyl-2-methyl-4-phenyl-1H-pyrrole-3-carboxylate (**5c**)*



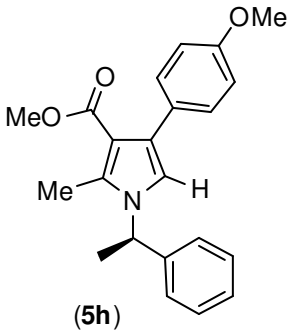
^{1}H NMR (400 MHz, $CDCl_3$): *(R)-Methyl-4-(4-methoxyphenyl)-2-methyl-1-(1-phenylethyl)-1H-pyrrole-3-carboxylate (**5h**)*



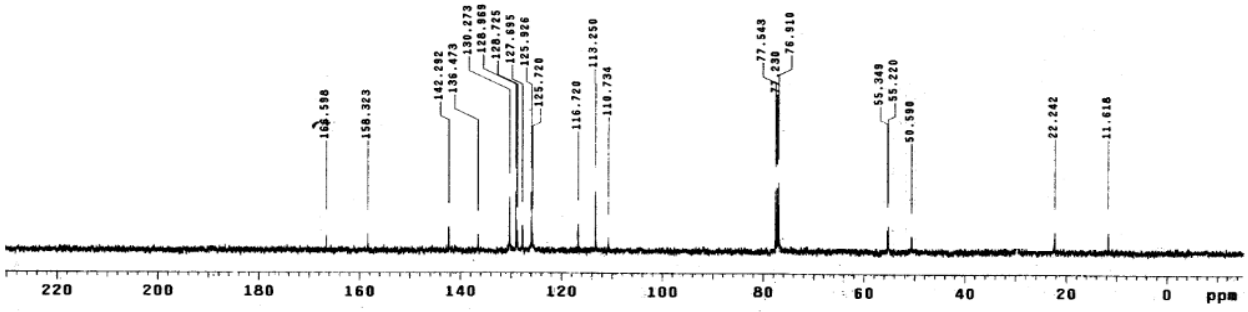
(**5h**)



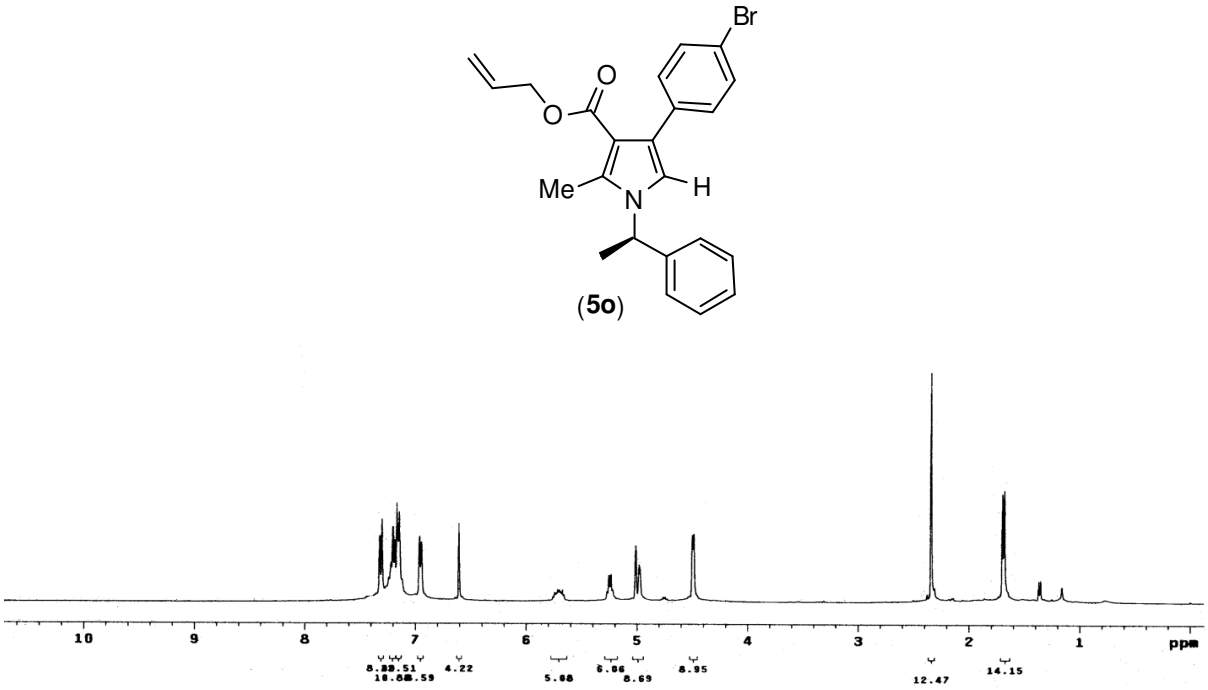
^{13}C NMR (400 MHz, $CDCl_3$): *(R)-Methyl-4-(4-methoxyphenyl)-2-methyl-1-(1-phenylethyl)-1H-pyrrole-3-carboxylate (**5h**)*



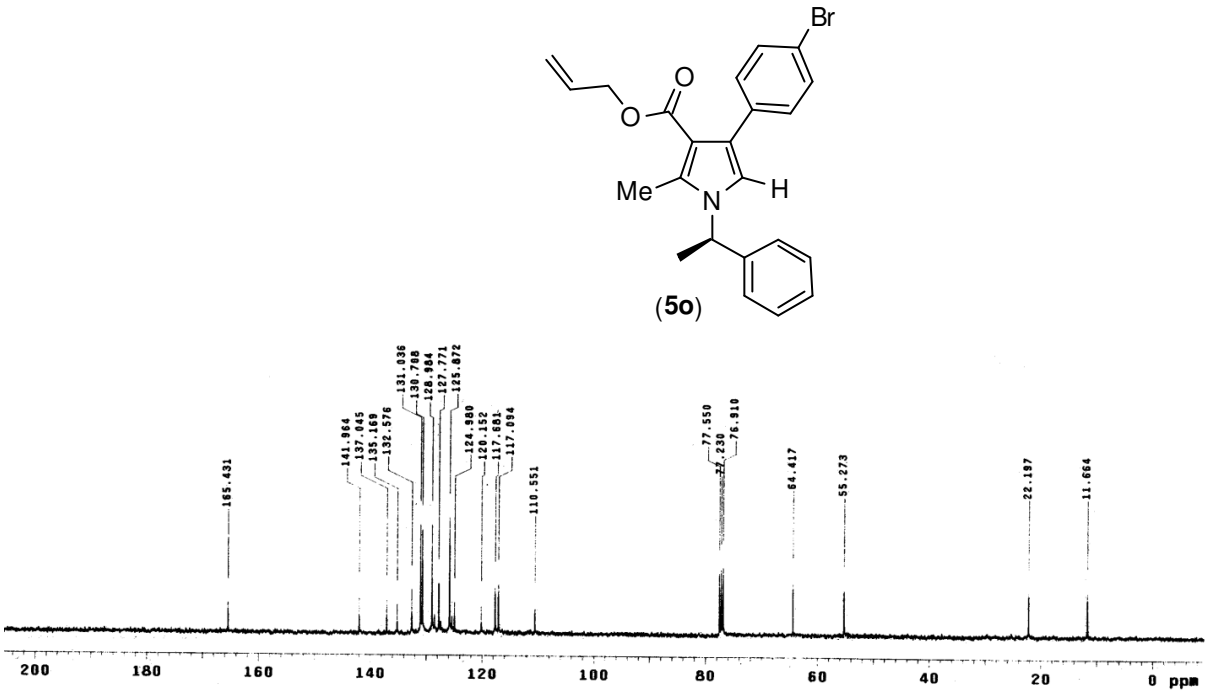
(**5h**)



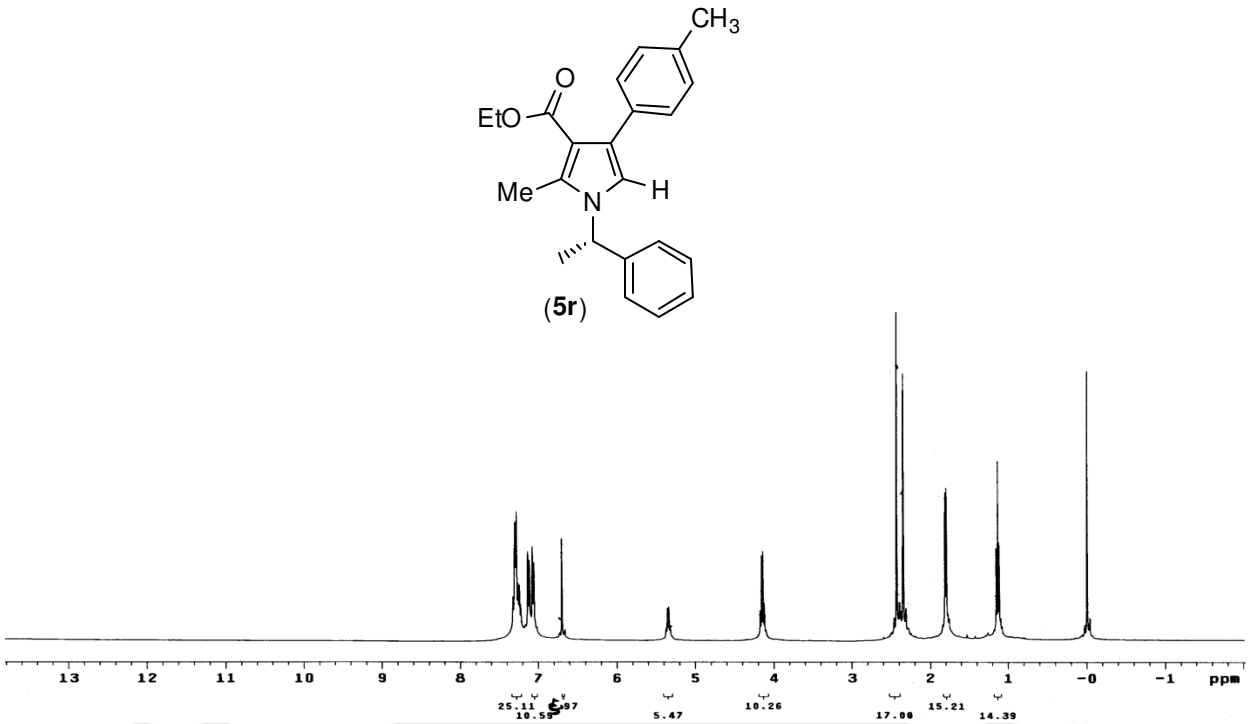
***^{1}H NMR (400 MHz, $CDCl_3$)**: (R)-Allyl-4-(4-bromophenyl)-2-methyl-1-(1-phenylethyl)-1H-pyrrole-3-carboxylate (**5o**)*



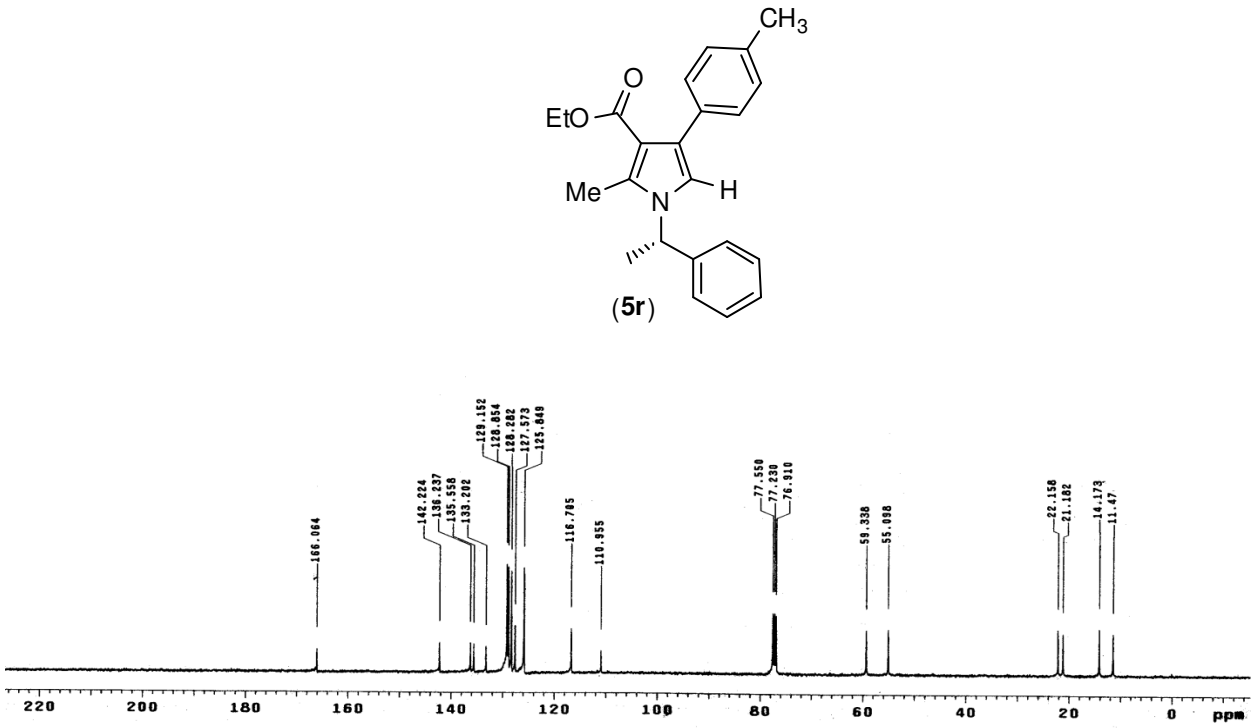
***^{1}H NMR (400 MHz, $CDCl_3$)**: (R)-Allyl-4-(4-bromophenyl)-2-methyl-1-(1-phenylethyl)-1H-pyrrole-3-carboxylate (**5o**)*



^{1}H NMR (400 MHz, $CDCl_3$): *(S)-Ethyl-2-methyl-1-(1-phenylethyl)-4-(p-tolyl)-1H-pyrrole-3-carboxylate (**5r**)*



^{13}C NMR (400 MHz, $CDCl_3$): *(S)-Ethyl-2-methyl-1-(1-phenylethyl)-4-(p-tolyl)-1H-pyrrole-3-carboxylate (**5r**)*



Part B

Chapter III

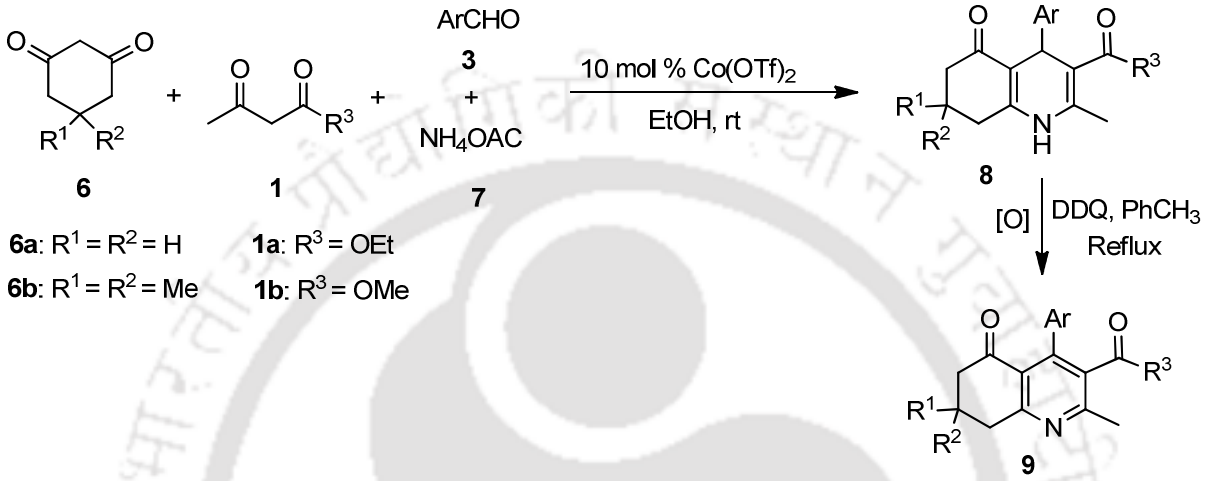
Cobalt triflate catalyzed one-pot synthesis of fluorophore 1,4-dihydropyridine derivatives via Hantzsch Reaction

Result & Discussion

Experimental Section

Results and Discussion

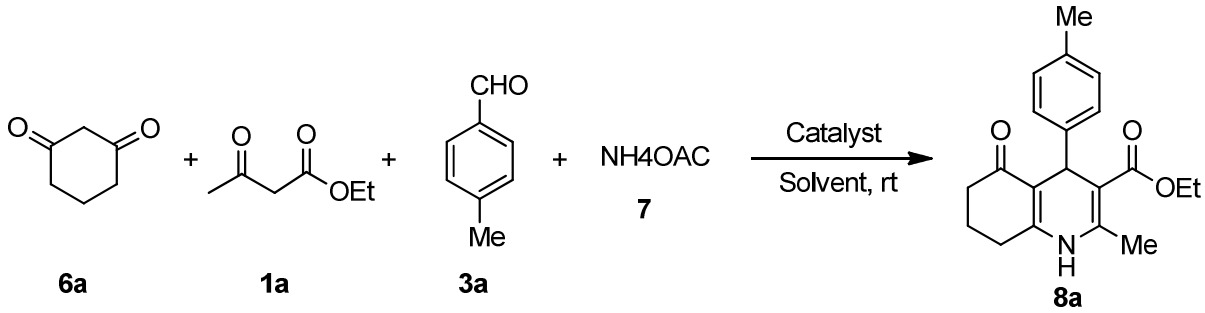
The synthetic strategies and importance of 1,4-dihydropyridines have already been described in Chapter 1 Part B. In this Chapter, we present a four-component Hantzsch reaction for the synthesis of substituted 1,4-dihydropyridines (DHPs) and its further utilization for the synthesis of tetrahydroquinolinederivatives through DDQ oxidation as illustrated in Scheme 29.



Scheme 29. *Synthesis of fused 1,4-dihydropyridines and tetrahydroquinoline derivatives*

For the present study, a mixture of 4-methylbenzaldehyde (1 mmol), ethyl acetoacetate (1 mmol), 1,3-cyclohexadione (1 mmol) and ammonium acetate (1 mmol) in 2 mL of ethanol was stirred in the presence of freshly prepared 5 mol % cobalt triflate (0.017 g) at room temperature. After 1 h of stirring, a solid product **8a** in 75% yield was precipitated out, this is characterized by recording ^{1}H NMR and ^{13}C NMR spectra as well as by elemental analysis. It was observed that some unreacted starting materials were present in the filtrate solution. For complete conversion, the similar reaction was performed in the presence of 10 mol % of cobalt triflate (0.035 g) at room temperature. Interestingly, the reaction was complete within 45 min and the isolated product was obtained in 96% yield (Table 3, entry 3). In order to find out the efficacy of cobalt triflate, the similar reactions were examined by using 5 and 10 mol % of $Mn(OTf)_2$ under identical reaction conditions as shown in Table 3 (entries 4 & 5).The role of solvent was also scrutinized by performing similar reaction in CH_3CN, DCM, MeOH, Et_2O and CH_3CN/DCM, respectively. Amongst them, EtOH proved superior in terms of yield and reaction time. Thus, 10 mol% cobalt triflate in EtOH at room temperature provided the best optimum condition for the reaction.

Table 3: Optimization of the reaction conditions[a]



6a **1a** **3a** **8a**

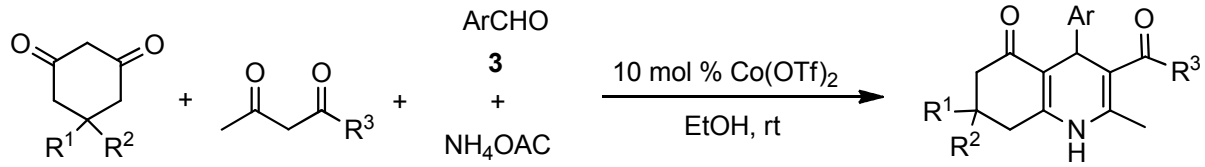
S.No	Catalyst used	Mol %	Solvent	Time (h)	Yield (%)[b]
1	$Co(OTf)_2$	5	EtOH	1.0	75
2	$Co(OTf)_2$	5	CH_3CN	2.0	55
3	$Co(OTf)_2$	10	EtOH	0.75	96
4	$Mn(OTf)_2$	5	CH_3CN	3.0	45
5	$Mn(OTf)_2$	10	EtOH	1.5	50
6	$Co(OTf)_2$	10	CH_3CN	2.5	65
7	$Co(OTf)_2$	10	DCM	3.0	40
8	$Co(OTf)_2$	10	MeOH	2.0	58
9	$Co(OTf)_2$	10	Et_2O	1.0	65
10	$Co(OTf)_2$	10	CH_3CN/DCM	3.0	60

[a]*The reactions were performed using (1 mmol) aldehyde, (1 mmol) cyclic-1,3-dione, (1 mmol), β-ketoester and (1 mmol) ammonium acetate.*[b]*Isolated yield.*

After optimization of the reaction conditions, the scope of the reaction was expanded with various aromatic aldehydes having different substituent in the ring. Stirring a mixture of 4-chlorobenzaldehyde, 1,3-cyclohexa-dione, ethylacetoacetate and ammonium acetate was stirred in the presence of 10 mol% $Co(OTf)_2$ in EtOH at room temperature gave the desired product **8b** was obtained in 92% yield (Table 4, entry 2). The reaction of various other aromatic aldehydes with 1,3-cyclohexadione, ethylacetoacetate and ammonium acetate under identical reaction conditions gave the products **8c-f** in good yields (Table 4, entries 3-6). Similarly, the reaction of 4-methylbenzaldehyde with dimedone, ethylacetoacetate and ammonium acetate was also carried out under identical reaction conditions and the products **8g** was obtained in excellent yield. Next the reaction of various aromatic aldehydes with dimedone, methylacetoacetae and ammonium acetate in a similar manner and afforded the desired products **8h-n** (Table 4, entries 8-14) in good yield. The reaction was also carried out

by the using 2-naphthaldehyde and 2-thiophenaldehyde, dimedone, methylacetoacetate and ammonium acetate with 10 mol% $Co(OTf)_2$ in EtOH at room temperature and the desired products **8o-p** (Table 4, entry 15 & 16) were obtained in good yield.

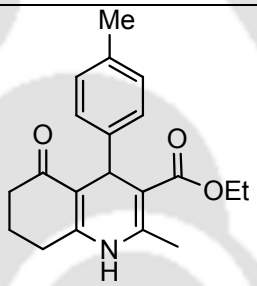
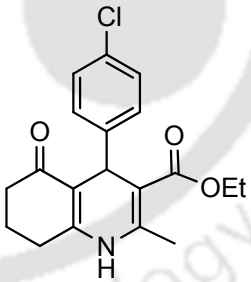
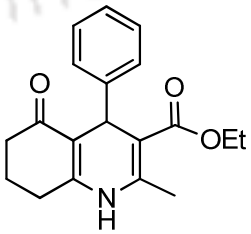
Table 4: $Co(OTf)_2$ catalyzed synthesis of 1,4-dihydropyridines

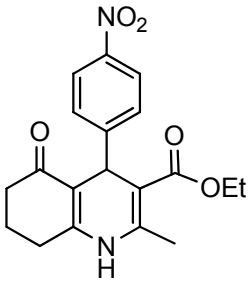
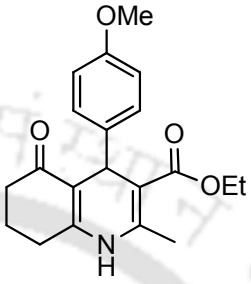
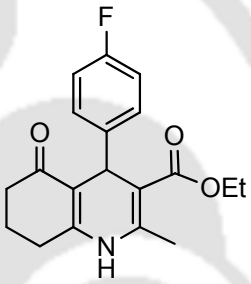
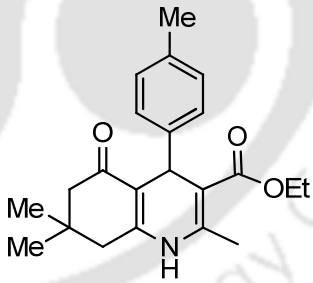
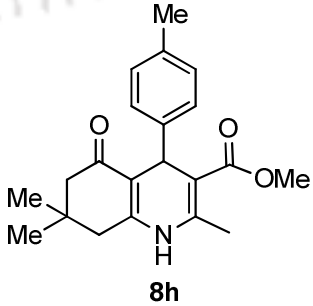


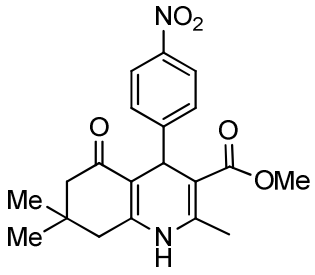
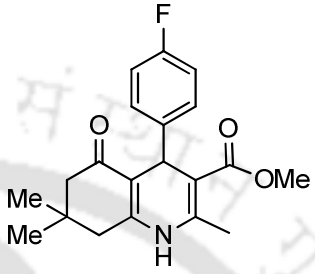
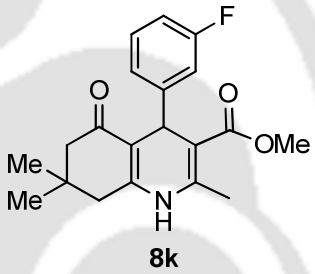
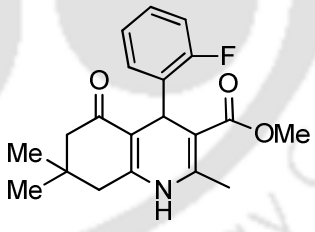
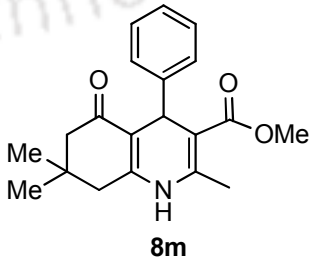
6 **1** **7** **8**

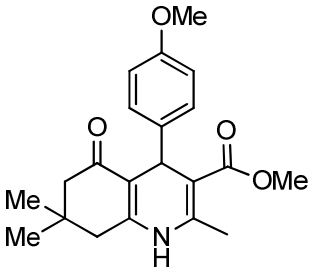
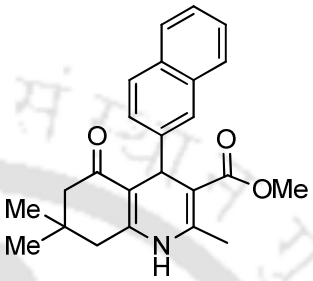
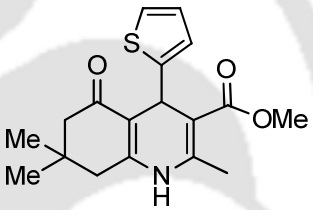
6a: $R^1 = R^2 = H$ **1a**: $R^3 = OEt$

6b: $R^1 = R^2 = Me$ **1b**: $R^3 = OMe$

S.No	**6**	β-ketoesters (**1**)	ArCHO (**3**)	Product (**8**)	Time (min)	Yield (%)[a]
1	**6a**	**1a**	4-Me-C_6H_4	 **8a**	45	96
2	**6a**	**1a**	4-Cl-C_6H_4	 **8b**	40	92
3	**6a**	**1a**	C_6H_5	 **8c**	50	96

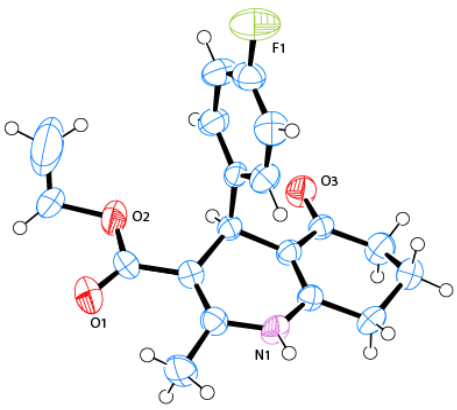
4	**6a**	**1a**	4-NO_2-C_6H_4	 **8d**	60	94
5	**6a**	**1a**	4-OMe-C_6H_4	 **8e**	65	96
6	**6a**	**1a**	4-F-C_6H_4	 **8f**	15	96
7	**6b**	**1a**	4-Me-C_6H_4	 **8g**	30	95
8	**6b**	**1b**	4-Me-C_6H_4	 **8h**	40	89

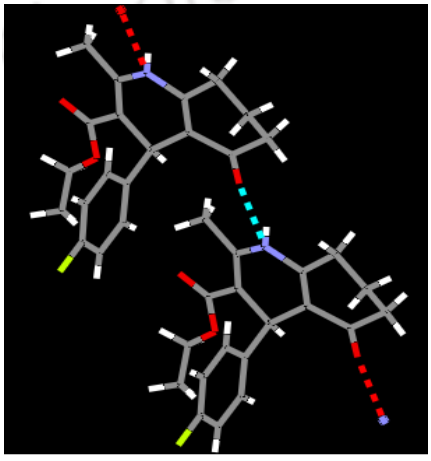
9	**6b**	**1b**	4-NO_2-C_6H_4	 **8i**	60	90
10	**6b**	**1b**	4-F-C_6H_4	 **8j**	15	90
11	**6b**	**1b**	3-F-C_6H_4	 **8k**	20	86
12	**6b**	**1b**	2-FC_6H_4	 **8l**	15	88
13	**6b**	**1b**	C_6H_5	 **8m**	30	93

14	**6b**	**1b**	4-OMe-C_6H_4	 **8n**	60	87
15	**6b**	**1b**	2-Napthyl	 **8o**	50	86
16	**6b**	**1b**	2-Thiophenyl	 **8p**	40	88

[a]All the reactions were carried out using (1 mmol) aldehyde, (1 mmol) cyclic-1,3-dione, (1 mmol) β-ketoester and (1 mmol) ammonium acetate. [b]Isolated yield.

The structure of the compound **8f** was determined by single-crystal X-ray crystallographic data (as shown in Figure 6a) and their intermolecular H-bonding interaction through N–H···O bonds (H···O = 2.13 Å, N···O = 2.92 Å, < N–H···O = 176°) as shown in Figure 6b.

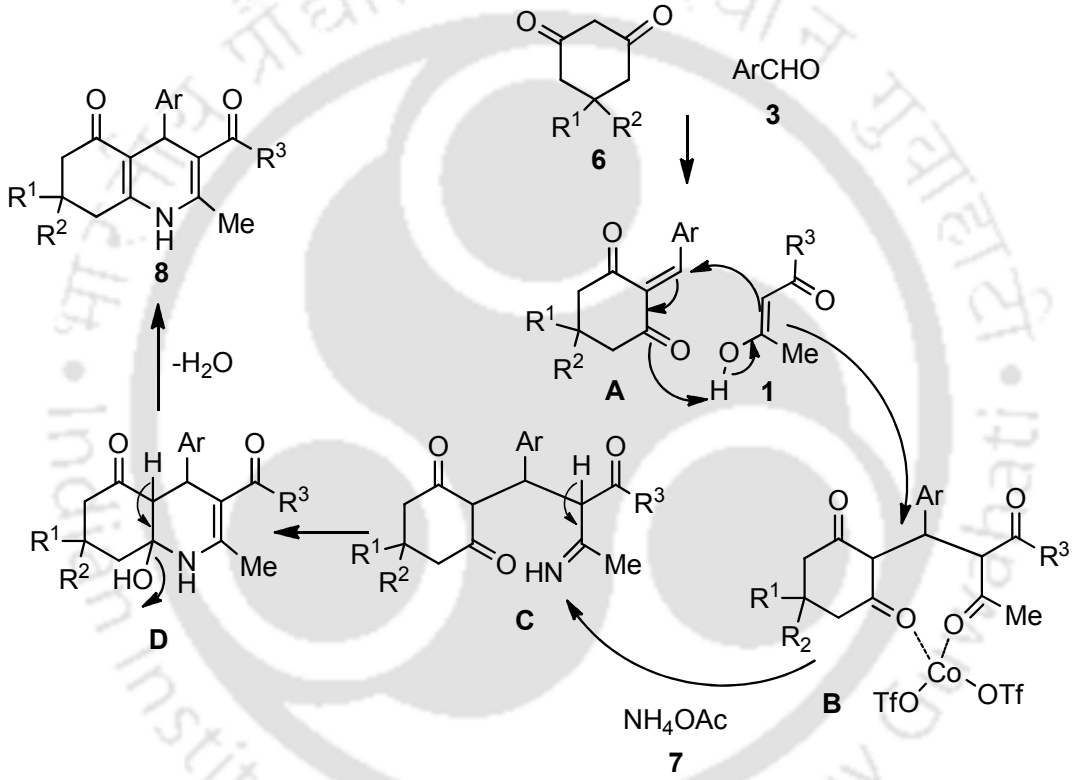




(a) **(b)**

Figure 6. (**a**) ORTEP diagram of compound **8f** (CCDC no. 886705) and **(b)** H-bonding interactions of **8f**

The formation of 1,4-dihydropyridine can be explained as follows: Initially 1,3-diketone (**6**) reacts with aldehyde **3** to give the knoevenagel product **A**. Then β-ketoester **1** reacts with the intermediate **A** to form Michael adduct **B**, which was stabilized through cobalt triflate. Subsequently, it converted into the intermediate **C** on reaction with NH_4OAc (**7**), which undergo concomitant cyclization to give intermediate **D.** Finally, it gives 1,4-dihydropyridine derivatives **8** with elimination of water molecule from **D** as shown in Scheme 30.



Scheme 30. *Plausible mechanism for the formation of 1,4-dihydropyridine 8*

The reusability test was accomplished as follows: The mixture of 4-chlorobenzaldehyde (10 mmol), 1,3-cyclohexadione (10 mmol), ethylacetoacetate (10 mmol) and ammonium acetate (10 mmol) was stirred in the presence of 0.350 g of $Co(OTf)_2$ under room temperature in ethanol. After completion of reaction, the solid product was precipitated out by filtration through a Büchner funnel. The precipitate was washed with ethanol and dried under reduced pressure and the desired product **8b** was obtained in 92% yield. The filtrate containing catalyst was reused for second cycle with the same combination of the substrates in a similar

manner. Likewise, we have performed another two cycles and the successful results are shown in Figure 7.

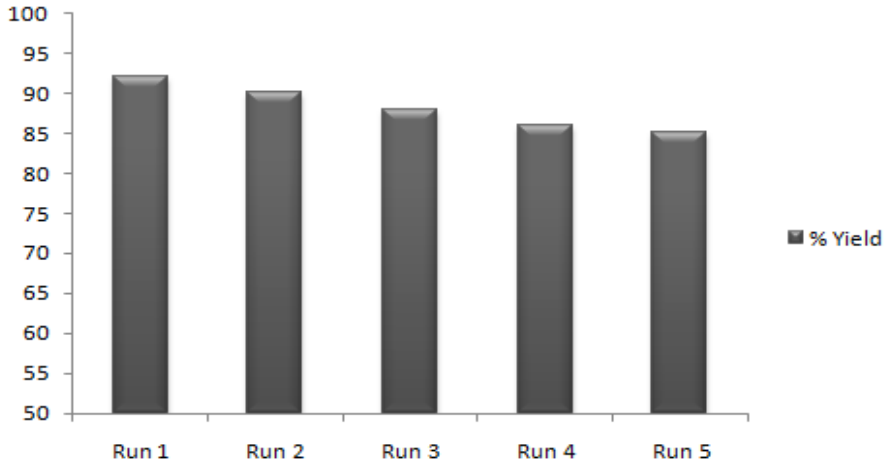
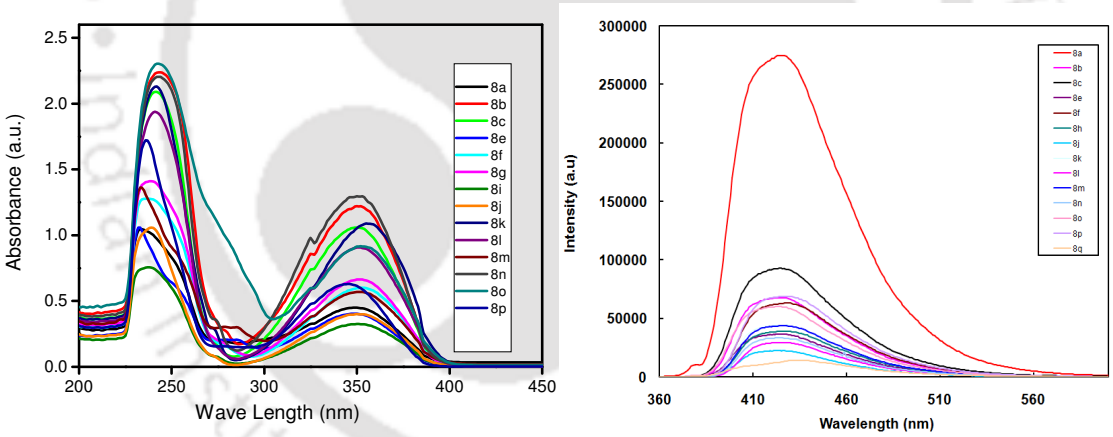


Figure 7. Reusability of the catalyst $Co(OTf)_2$ in ethanol

The photo physical properties of the 1,4-dihydropyridine results are summarized in Table 5, Figure 8. Furthermore, the UV-visible spectra of the 1,4-dihydropyridinecontain intense absorption maxima at 238 ± 5 and at 350 ± 5 nm.



(a) **(b)**

Figure 8. UV- Visible (**a**) and Fluorescence Spectra (**b**) of 1, 4-dihydropyridine (**8**)

Table 5. Photo physical data of 1,4-dihydropyridine derivatives (**8**) in CH_2Cl_2.

Entry	1,4-dihydropyridine (**8**)	Absorption[a] λ_{abs}[nm]ϵ [$M^{-1}cm^{1}$]		Fluorescence λ_{em}[b]
1.	**8a**	233 349	1046410 450330	424
2.	**8b**	243 350	2238570 1221330	424

3.	**8c**	242 350	2090640 1057290	425
4.	**8e**	232 349	1058470 404100	423
5.	**8f**	234 354	1272190 601550	429
6.	**8g**	239 351	1411190 663990	427
7.	**8i**	238 350	756390 326070	427
8.	**8j**	239 350	1059040 401530	428
9.	**8k**	241 351	1938390 908890	423
10.	**8l**	242 355	2129330 1088570	428
11.	**8m**	233 353	1362810 569170	424
12.	**8n**	243 353	2205050 1296530	423
13.	**8o**	242 352	2305360 916670	426
14.	**8p**	236 345	1721470 630860	435

[a]Measured at a concentration of 1.0 × 10^{-6}mol dm^{-3} at 25°C. [b]Emission maxima upon excitation at 351 nm.

Among the 1,4-dihydropyridine derivatives the substituent which bear a 2-fluorophenyl group at the C3 position **8l** which enhance the shift of the absorption maxima to longer wavelength 355 nm. In the case of the fluorescence spectra results clearly indicates that hetero-aromatic substituent at the C3 position of the 1,4-dihydropyridine **8p** which enhance

the fluorescence wavelength maxima 435 nm respectively. In addition to that the fluorescence of the 1,4-dihydropyridine derivatives **8** are shown in Figure 9.

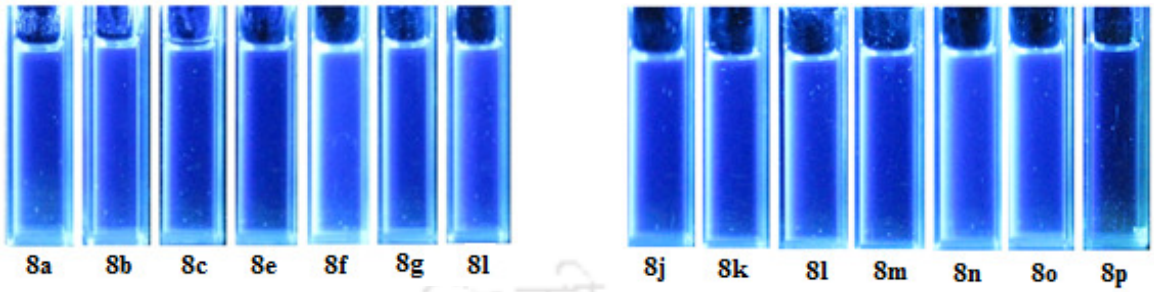
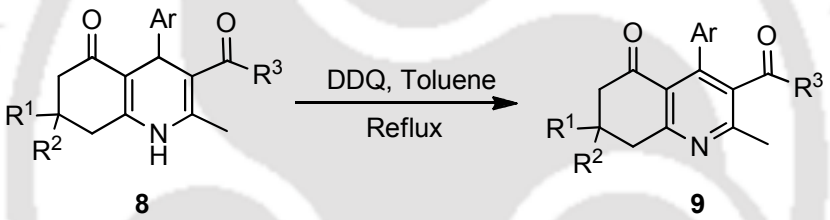


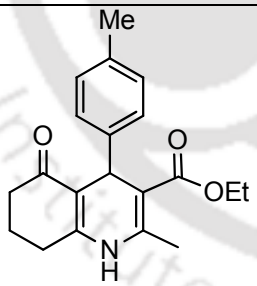
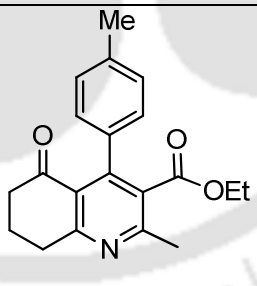
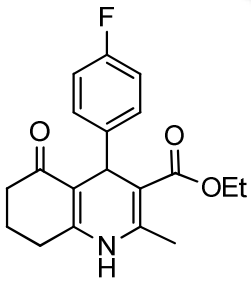
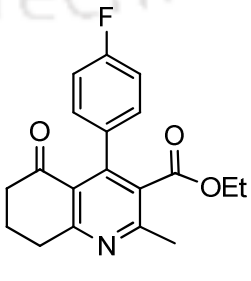
Figure 9. Fluorescence of **8** in CH_2Cl_2

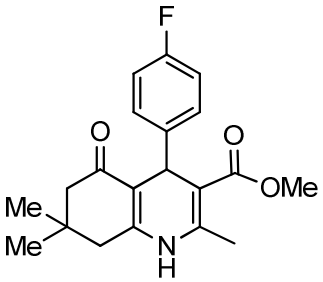
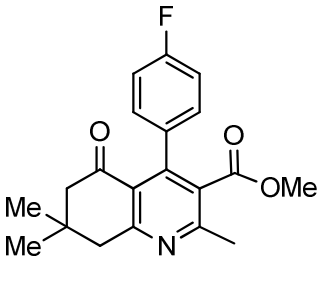
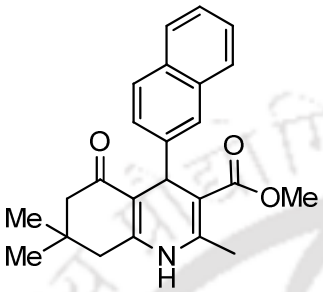
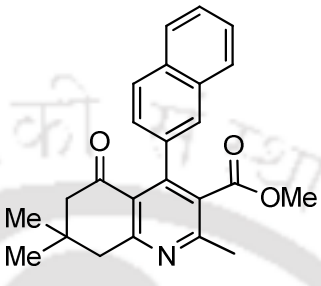
Next, partial aromatization of the 1,4-dihydropyridines was carried by refluxing with DDQ in toluene which provided 5,6,7,8-tetrahydro-quinoline-3-carboxylates (**9a-d**) in good to excellent yield and the reactions were complete within 1 hour as shown in Table 6.

Table 6: Aromatization of 1,4-dihydropyridines **9**[a]



8 **9**

Entry	Product(**8**)	Product (**9**)	Time (min)	Yield (%)[a]
1	 **8a**	 **9a**	50	95
2	 **8f**	 **9b**	50	95

3	 **8j**	 **9c**	45	95
4.	 **8o**	 **9d**	45	90

[a]*The reaction was performed using 1,4-dihydropyridine (**8**), DDQ (1.2 mmol) in toulene under reflux condition.* [b]*Isolated yield.*

Subsequently, the structure of the compound **9c** was also determined by using single-crystal X-ray data as shown in the Figure 10.

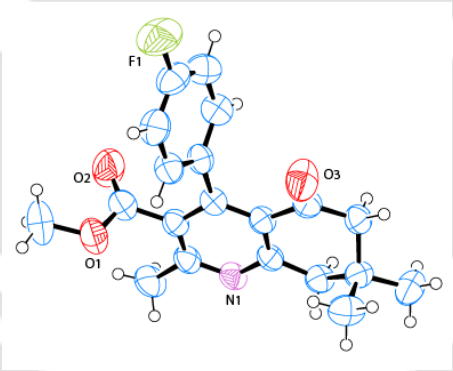


Figure 10. ORTEP diagram of compound **9c**

In short, we conceived the synthesis of 1,4-dihydropyridine derivatives using β-ketoester, aromatic aldehyde, 1,3-diketone and ammonium acetate in the presence of catalytic amount of $Co(OTf)_2$ in ethanol. The advantage of the present protocol was shorter reaction time, simplicity, mild reaction conditions, good yields, no need of chromatographic separation and catalyst recyclability. In addition, the synthesized 1,4-dihydropyridine derivatives can be converted easily into fused pyridine derivatives by refluxing with DDQ in toluene. Further studies on the synthesized fluorophore of 1,4-dihydropyridine derivatives in biomedical application are under investigation which will be reported in due course of time.

Experimental

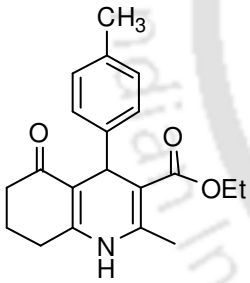
*General procedure for the synthesis of 1,4-Dihydropyridine derivatives (**8**)*

To a stirred mixture of aromatic aldehyde (1 mmol), β-ketoester (1 mmol), cyclic 1,3-dione (1 mmol) and ammonium acetate (1 mmol) in 2 mL ethanol was added the catalyst cobalt triflate (0.035g, 0.1 mmol) at room temperature and stirring was continued until the completion of the reaction as indicated by TLC. The solid product came out after stipulated time indicated in Table 4, which was filtered through a Büchner funnel and the precipitate was washed with ethanol, dried under vaccum and the pure product **8** was obtained.

*General experimental procedure for the synthesis of tetrahydroquinolines (**9**)*

Into a 25 mL round bottomed flask was taken a mixture of 1,4-Dihydropyridine derivatives (**8**, 1 mmol) and DDQ (1.2 mmol) in 3 mL of toluene. The above reaction mixture was kept for refluxing in hot oil bath. After completion (1 hrs) of the reaction, it was extracted with DCM (2 x 20 mL) and dried over anhydrous Na_2SO_4 and evaporated in vacuo, then the crude residue was purified through column chromatography and the pure products **9** was obtained.

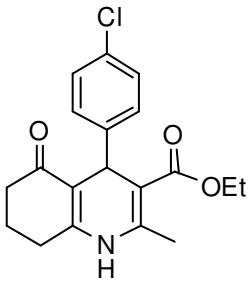
*Ethyl 2-methyl-5-oxo-4-(p-tolyl)-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (**8a**)*



(8a)

White solid, M.p 242-243 °C, **IR** (KBr)ν_{max} 3283, 3214, 3071, 2951, 2359, 2341, 1696, 1645, 1606, 1481, 1381, 1284, 1223, 1181, 1137, 1072 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.2 (t, *J* = *7.2* Hz, 3H), 1.92-1.98 (m, 2H), 2.26 (s, 3H), 2.29-2.35 (m, 2H), 2.37 (s, 3H), 2.39-2.44 (m, 2H), 4.07 (q, *J* = 7.2 Hz, 2H), 5.06 (s, 1H), 6.08 (br s, 1H), 7.01 (d, *J* = 7.6 Hz, 2H), 7.19 (d, *J* = 8.0 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 13.6, 18.1, 20.3, 20.5, 26.2, 35.1, 36.6, 58.7, 104.3, 111.7, 127.1, 127.8, 134.3, 144.0, 144.4, 150.8, 167.0, 195.1; **Anal. calcd** for $C_{20}H_{23}O_3N$: C, 73.82; H, 7.12; N, 4.30. found C, 73.78; H, 7.08; N, 4.25.

*Ethyl 4-(4-chlorophenyl)-2-methyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (**8b**)*

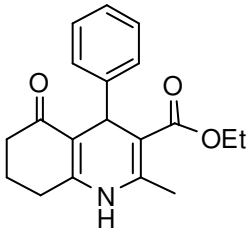


(8b)

White solid, M.p 235-236 °C, **IR** (KBr)ν_{max} 3284, 3218, 3076, 2977, 2955, 1721, 1625, 1607, 1481, 1381, 1285, 1224, 1182, 1137, 1073 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.18 (t, *J* = 7.2 Hz, 3H), 1.88-1.95 (m, 2H), 2.31-2.33 (m, 2H), 2.37 (s, 3H), 2.46 (s, 2H) 4.04 (q, *J* = 6.8 Hz, 2H), 5.03 (s, 1H), 7.14 (d, *J* = 8.0 Hz, 2H), 7.24 (d, *J* = 8.4 Hz, 2H), 8.14 (br s, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 14.1, 18.7, 20.9, 26.7, 35.9, 36.9, 59.5, 104.6, 112.0, 127.7, 129.3, 131.1, 144.7, 146.2, 151.5,

167.3, 195.9; **Anal. calcd** for $C_{19}H_{20}ClNO_3$: C, 65.99; H, 5.83; N, 4.05. found C, 65.94; H, 5.78; N, 3.55.

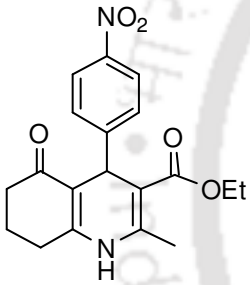
*Ethyl 2-methyl-5-oxo-4-phenyl-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (**8c**)*



(8c)

White solid, M.p 240-241 °C; **IR** (KBr)ν_{max} 3284, 3214, 3071, 2957, 1691, 1644, 1607, 1479, 1380, 1306, 1284, 1223, 1180, 1137, 1115, 1071 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.18 (t, *J* = 7.2 Hz, 3H), 1.88-1.98 (m, 2H), 2.28-2.35 (m, 2H), 2.37(s, 3H), 2.40-2.48 (m, 2H), 4.04 (q, *J* = 7.2 Hz, 2H), 5.06 (s, 1H), 7.08 (t, *J* = 7.2 Hz, 1H), 7.18 (t, *J* = 7.2 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 8.09 (br s, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 14.1, 18.7, 20.9, 26.8, 36.2, 36.9, 59.4, 105.1, 112.5, 125.7, 127.7, 127.9, 144.5, 147.6, 151.4, 167.6, 195.9; **Anal. calcd** for $C_{19}H_{21}NO_3$: C, 73.29; H, 6.80; N, 4.50. found C, 73.24; H, 6.75; N, 4.45.

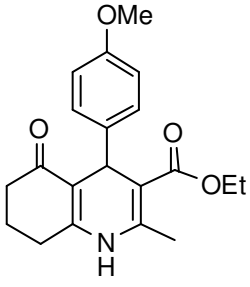
*Ethyl 2-methyl-4-(4-nitrophenyl)-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (**8d**)*



(8d)

Yellow solid, M.p 205-206 °C, **IR** (KBr)ν_{max} 3295, 3222, 3077, 2950, 1703, 1649, 1606, 1552, 1480, 1380, 1350, 1283, 1223, 1183, 1137, 1116, 1073 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.17 (t, *J* = 7.2 Hz, 3H), 1.92-2.02 (m, 2H), 2.32-2.39 (m, 2H), 2.42 (s, 3H), 2.44-2.54 (m, 2H), 4.08 (q, *J* = 7.2 Hz, 2H), 5.19 (s, 1H), 6.14 (br s, 1H), 7.48 (d, *J* = 8.8 Hz, 2H), 8.08 (d, *J* = 8.4 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 14.4, 19.4, 21.2, 27.3, 37.2, 37.4, 60.3, 104.8, 112.0, 123.5, 129.2, 145.2, 146.3, 151.9, 155.1, 167.3, 196.4; **Anal. calcd** for $C_{19}H_{20}N_2O_5$: C, 64.04; H, 5.66; N, 7.86. found C, 63.99; H, 5.61; N, 7.81.

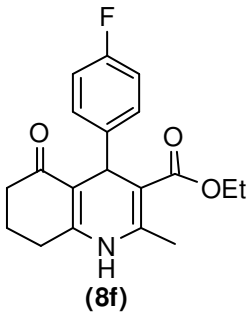
*Ethyl 4-(4-methoxyphenyl)-2-methyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (**8e**)*



(8e)

White solid, M.p 195-196 °C; **IR** (KBr)ν_{max} 3283, 3215, 3078, 2952, 2828, 2359, 2341, 1692, 1645, 1607, 1509, 1582, 1380, 1301, 1285, 1259, 1223, 1182, 1137, 1115, 1072, 1039 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.20 (t, *J* = 6.8 Hz, 3H), 1.88-1.98 (m, 2H), 2.29-2.38 (m, 7H), 3.73 (s, 3H), 4.06 (q, *J* = 6.8 Hz, 2H), 5.03 (s, 1H), 6.73 (d, *J* = 8.0 Hz, 2H), 6.84 (br s, 1H), 7.21 (d, *J* = 8.4 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 14.3, 19.1, 21.1, 26.9, 35.6, 37.2, 55.1, 59.8, 105.9, 113.3, 128.9, 140.1, 144.1, 151.8, 156.6, 157.9, 167.9, 196.6; **Anal. calcd** for $C_{20}H_{23}NO_4$: C, 70.36; H, 6.79; N, 4.10. found C, 70.31; H, 6.74; N, 4.05.

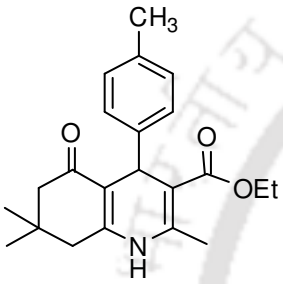
*Ethyl 4-(4-fluorophenyl)-2-methyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (**8f**)*



(8f)

White solid, M.p 245-246 °C; **IR** (KBr)ν_{max} 3293, 3217, 3077, 2963, 1697, 1646, 1609, 1505, 1481, 1379, 1286, 1222, 1180, 1136, 1073 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.17 (t, *J* = 7.2 Hz, 3H), 1.91-2.04 (m, 2H), 2.26-2.37 (m, 2H), 2.39 (s, 3H), 2.41-2.47 (m, 2H), 4.05 (q, *J* = 7.2 Hz, 2H), 5.07 (s, 1H), 5.80 (br s, 1H), 6.86-6.90 (m, 2H), 7.24-7.28 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 14.2, 18.8, 21.0, 26.9, 35.8, 37.1, 59.6, 105.1, 112.6, 114.3, 114.5, 129.4, 129.5, 143.6, 144.5, 151.1, 167.6, 196.0; **Anal. calcd** for $C_{19}H_{20}FNO_3$: C, 69.29; H, 6.12; N, 4.25. found C, 69.24; H, 6.07; N, 4.20.

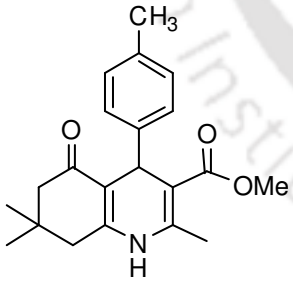
*Ethyl 2,7,7-trimethyl-5-oxo-4-(p-tolyl)-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (**8g**)*



(8g)

White solid, M.p 269-270 °C; **IR** (KBr)ν_{max} 3275, 3206, 3077, 2958, 2931, 1701, 1647, 1605, 1494, 1421, 1380, 1310, 1281, 1194, 1167, 1140, 1108, 1072, 1031 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 0.94 (s, 3H), 1.06 (s, 3H), 1.21 (t, *J* = 7.2 Hz, 3H), 2.16-2.21 (m, 4H), 2.25 (s, 3H), 2.34 (s, 3H), 4.06 (q, *J* = 6.8 Hz, 2H), 5.01 (s, 1H), 6.28 (br s, 1H), 6.99 (d, *J* = 8.4 Hz, 2H), 7.18 (d, *J* = 8.0 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 14.4, 19.3, 21.2, 27.3, 29.6, 32.8, 36.3, 40.8, 50.9, 59.9, 106.2, 111.9, 128.0, 128.7, 135.5, 143.9, 144.5, 149.5, 167.8, 196.1; **Anal. calcd** for $C_{22}H_{27}NO_3$: C, 74.76; H, 7.70; N, 3.96. found C, 74.71; H, 7.65; N, 3.91.

*Methyl 2,7,7-trimethyl-5-oxo-4-(p-tolyl)-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (**8h**)*

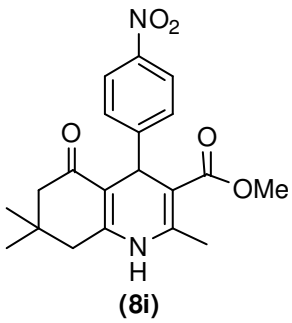


(8h)

White solid, M.p 275-276 °C; **IR** (KBr)ν_{max} 3282, 3190, 3071, 2957, 2929, 1698, 1643, 1603, 1490, 1452, 1435, 1382, 1333, 1227, 1139, 1114, 1073 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 0.94 (s, 3H), 1.07 (s, 3H), 2.18-2.22 (m, 4H), 2.25 (s, 3H), 2.37 (s, 3H), 3.61 (s, 3H), 5.03 (s, 1H), 5.99 (br s, 1H), 7.00 (d, *J* = 8.0 Hz, 2H), 7.18 (d, *J* = 8.0 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 18.4, 20.5, 26.6, 29.1, 32.0, 35.3, 50.3, 50.4, 104.2, 110.8, 127.2, 128.1, 134.5, 144.2, 144.6, 149.3, 167.7, 195.1; **Anal. calcd** for $C_{21}H_{25}NO_3$: C, 74.31; H, 7.42; N, 4.13. found C, 74.26, H, 7.37; N, 4.08.

*Methyl 2,7,7-trimethyl-4-(4-nitrophenyl)-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (**8i**)*

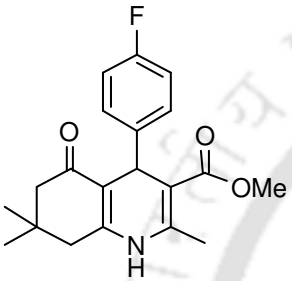
Yellow solid, M.p 271-272 °C; **IR** (KBr)ν_{max} 3247, 3189, 3072, 2969, 2945, 2875, 1709, 1649, 1607, 1517, 1493, 1431, 1388, 1377, 1345, 1280, 1187, 1167, 1108, 1074, 1014 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 0.91 (s, 3H), 1.09 (s, 3H), 2.13-2.27 (m, 4H), 2.42 (s, 3H),



(8i)

3.61 (s, 3H), 5.17 (s, 1H), 6.11 (br s, 1H), 7.48 (dd, *J* = 0.2, 6.8 Hz, 2H), 8.08 (dd, *J* = 0.2, 6.8 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 18.9, 26.9, 29.4, 32.5, 37.0, 40.5, 50.6, 51.0, 103.8, 110.5, 123.3, 128.8, 145.9, 146.1, 150.0, 154.7, 167.6, 195.6; **Anal. calcd** for $C_{20}H_{22}N_2O_5$: C, 64.85; H, 5.99; N, 7.56. found C, 64.80; H, 5.92; N, 7.50.

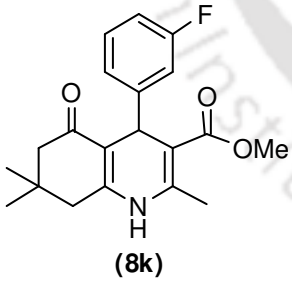
*Methyl 4-(4-fluorophenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxyl ate (**8j**)*



(8j)

White solid, M.p 245-246 °C; **IR** (KBr)ν_{max} 3282, 3194, 3072, 2960, 1679, 1643, 1609, 1501, 1436, 1383, 1334, 1227, 1151, 1139, 1115, 1075 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 0.72 (s, 3H), 0.88 (s, 3H), 1.88-2.01 (m, 2H), 2.05-2.15 (m, 2H), 2.18 (s, 3H), 3.41 (s, 3H), 4.82 (s, 1H), 6.65-6.69 (m, 2H), 7.05-7.08 (m, 2H), 8.01 (br s, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 18.0, 26.2, 28.8, 31.7, 34.9, 50.0, 103.6, 110.2, 113.5, 113.7, 128.5, 128.6, 142.9, 144.7, 149.1, 167.2, 194.7; **Anal. calcd** for $C_{20}H_{22}FNO_3$: C, 69.95; H, 6.46; N, 4.08. found C, 69.90; H, 6.41; N, 4.03.

Methyl 4-(3-fluorophenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxyl ate (**8k**)

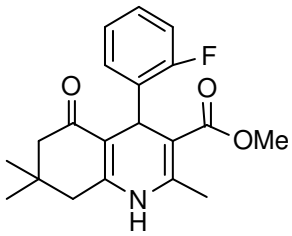


(8k)

White solid, M.p 248-250 °C; **IR** (KBr)ν_{max} 3278, 3202, 3078, 2963, 2932, 1713, 1647, 1610, 1486, 1380, 1280, 1213, 1170, 1146, 1124, 1109,1076 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 0.83 (s, 3H), 0.98 (s, 3H), 2.08-2.26 (m, 4H), 2.29 (s, 3H), 3.53 (s, 3H), 4.98 (s, 1H), 6.69 (t, *J* = 8.8 Hz, 1H), 6.88 (d, *J* = 8.8 Hz, 1H), 7.00-7.09 (m, 2H), 7.71 (br s, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 18.2, 26.4, 28.9, 31.9, 35.6, 50.2, 103.4, 110.1, 111.9, 112.1, 113.8, 113.9, 122.9, 128.6, 145.1, 149.5, 167.3, 194.9; **Anal. calcd** for $C_{20}H_{22}FNO_3$: C, 69.95; H, 6.46; N, 4.08. found C, 69.89; H, 6.40; N, 4.02.

*Methyl 4-(2-fluorophenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxyl ate (**8l**)*

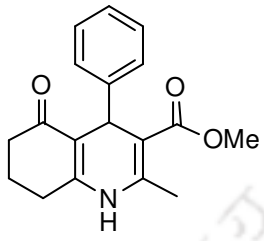
White solid, M.p 264-265 °C; **IR** (KBr)ν_{max} 3289, 3217, 3082, 2966, 2951, 2935, 1706, 1650, 1604, 1485, 1381, 1308, 1282, 1213, 1169, 1111, 1101, 1079 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 0.95 (s, 3H), 1.08 (s, 3H), 2.15-2.22 (m, 4H), 2.34 (s, 3H), 3.59 (s, 3H), 5.21 (s,



(8l)

1H), 5.92 (br s, 1H), 6.88-69.93 (m, 1H), 6.97-7.01 (m, 1H), 7.06-7.11 (m ,1H), 7.33-7.37 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 18.6, 26.7, 29.3, 31.8, 32.2, 50.4, 50.5, 103.3, 109.8, 114.7, 114.9, 123.3, 127.2, 127.3, 130.9, 133.8, 145.1, 149.6, 167.8, 194.9; **Anal. calcd** for $C_{20}H_{22}FNO_3$: C, 69.95; H, 6.46; N, 4.08. found C, 69.90; H, 6.38; N, 4.01.

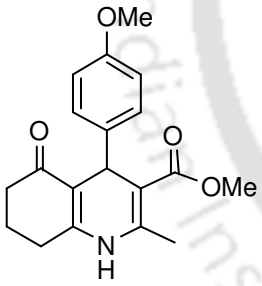
*Methyl 2,7,7-trimethyl-5-oxo-4-phenyl-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (**8m**)*



(8m)

White solid, M.p 265-266 °C; **IR** (KBr)ν_{max} 3278, 3203, 3078, 2964, 2951, 1708, 1647, 1606, 1488, 1380, 1309, 1280, 1250, 1214, 1168, 1108, 1072 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 0.92 (s, 3H), 1.06 (s, 3H), 2.13-2.31 (m, 4H), 2.37 (s, 3H), 3.61 (s, 3H), 5.06 (s, 1H), 6.14 (br s, 1H), 7.11 (t, *J* = 7.2 Hz, 1H), 7.21 (t, *J* = 7.6 Hz, 2H), 7.28 (d, *J* = 7.6 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 18.1, 26.4, 28.9, 31.8, 35.6, 50.1, 50.2, 103.8, 110.5, 125.1, 127.1, 127.2, 144.6, 146.9, 149.1, 167.4, 194.7; **Anal. calcd** for $C_{20}H_{23}NO_3$: C, 73.82; H, 7.12; N, 4.30. found C, 73.77, H, 7.07; N, 4.25.

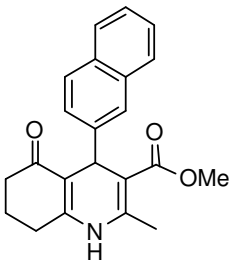
*Methyl 4-(4-methoxyphenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6, 7,8-hexahydroquinoline-3-carboxylate (**8n**)*



(8n)

White solid, M.p 255-256 °C; **IR** (KBr)ν_{max} 3272, 3185, 3068, 2953, 2927, 2939, 1704, 1649, 1605, 1497, 1379, 1280, 1214, 1192, 1167, 1070 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 0.88 (s, 3H), 1.02 (s, 3H), 1.98 (s, 2H), 2.12-2.19 (m, 2H), 2.33 (s, 3H), 3.57 (s, 3H), 3.69 (s, 3H), 4.95 (s, 1H), 6.68 (d, *J* = 8.4 Hz, 2H), 6.85 (br s, 1H), 7.16 (d, *J* = 8.8 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 18.0, 26.3, 28.8, 31.7, 34.5, 49.9, 50.1, 54.3, 103.8, 110.5, 112.4, 127.9, 139.4, 144.2, 148.7, 156.8, 167.3, 194.5; **Anal. calcd** for $C_{21}H_{25}NO_4$: C, 70.96; H, 7.09; N, 3.94. found C, 70.90; H, 7.02; N, 3.89.

*Methyl 2,7,7-trimethyl-4-(naphthalen-2-yl)-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (**8o**)*

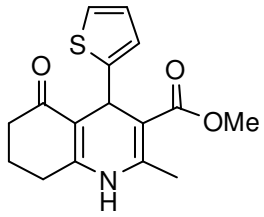


(8o)

White solid, M.p 296-298 °C; **IR** (KBr)ν_{max} 3286, 3196, 3074, 2950, 2932, 1683, 1643, 1605, 1488, 1381, 1330, 1226, 1140, 1111, 1072 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 0.89 (s, 3H), 1.05 (s, 3H), 2.15-2.29 (m, 4H), 2.44 (s, 3H), 3.59 (s, 3H), 5.25 (s, 1H), 6.02 (br s, 1H), 7.35-7.39 (m, 2H), 7.50 (d, *J* = 8.4 Hz, 1H), 7.64-7.71 (m, 2H), 7.74 (t, *J* = 7.2 Hz,

2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 18.3, 26.3, 28.9, 31.8, 35.9, 50.2, 103.8, 110.3, 124.9, 125.2, 126.5, 126.7, 126.8, 127.3, 131.5, 132.7, 144.5, 144.9, 149.3, 167.4, 194.9; **Anal. calcd** for $C_{24}H_{25}NO_3$: C, 76.77; H, 6.71; N, 3.73. found C, 76.70; H, 6.66; N, 3.68.

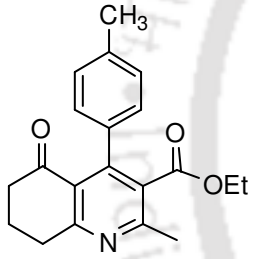
*Methyl 2,7,7-trimethyl-5-oxo-4-(thiophen-2-yl)-1,4,5,6,7,8-hexahydroquinoline-3-carboxyl ate (**8p**)*



(8p)

White solid, M.p 218-220 °C; **IR** (KBr)ν_{max} 3279, 3206, 3082, 2951, 1705, 1647, 1608, 1488, 1381, 1309, 1281, 1212, 1170, 1123, 1075 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.02 (s, 3H), 1.09 (s, 3H), 2.26 (s, 4H), 2.37 (s, 3H), 3.68 (s, 3H), 5.41 (s, 1H), 6.37 (br s, 1H), 6.80 (s, 2H), 7.02 (d, *J* = 3.2 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 18.0, 26.3, 28.8, 31.7, 34.5, 49.9, 50.1, 54.3, 103.9, 110.5, 112.4, 127.9, 139.4, 144.2, 148.6, 156.8, 167.3, 194.5; **Anal. calcd** for $C_{18}H_{21}NO_3S$: C, 65.23; H, 6.39; N, 4.23. found C, 65.18; H, 6.34; N, 4.18.

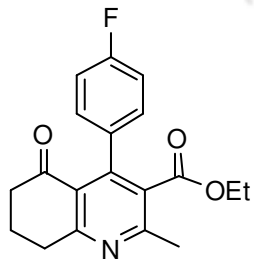
*Ethyl 2-methyl-5-oxo-4-(p-tolyl)-5,6,7,8-tetrahydroquinoline-3-carboxylate (**9a**)*



(9a)

White solid, M.p 138-140 °C; **IR** (KBr)ν_{max} 2965, 2934, 2877, 1731, 1687, 1549, 1514, 1383, 1324, 1272, 1220, 1175, 1135, 1086, 1076, 1021 cm^{-1}; **^{1}H NMR** (400 MHz, CDCl3): δ 0.89 (t, J = 7.2 Hz, 3H), 2.06-2.13 (m, 2H), 2.30 (s, 3H), 2.52 (s, 3H) 2.49-2.55 (m, 2H), 3.09-3.13 (m, 2H), 3.92 (q, J = 7.2 Hz, 2H), 6.94 (d, J = 8.0 Hz, 2H), 7.09 (d, J = 7.2 Hz, 2H); **^{13}C NMR** (100 MHz, CDCl3): δ 13.7, 21.4, 21.5, 23.3, 33.7, 40.2, 61.5, 124.3, 127.5, 128.6, 130.6, 134.6, 137.5, 149.2, 157.9, 164.5, 167.7, 197.3; **Anal. calcd** for $C_{20}H_{21}NO_3$: C, 74.28; H, 6.55; N, 4.33. found C, 74.23; H, 6.50; N, 4.26.

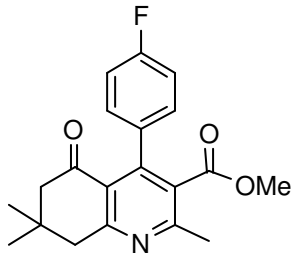
*Ethyl4-(4-fluorophenyl)-2-methyl-5-oxo-5,6,7,8-tetrahydroquinoline-3-carboxylate (**9b**)*



(9b)

White solid, M.p 105-106 °C; **IR** (KBr)ν_{max} 3056, 2950, 2865, 1731, 1682, 1547, 1431, 1401, 1285, 1231, 1210, 1083, 1036 cm^{-1}; **^{1}H NMR** (400 MHz, CDCl3): δ 0.98 (t, J = 7.2 Hz, 3H), 2.16-2.19 (m, 2H), 2.59 (s, 3H), 2.56-2.62 (m, 2H), 3.18-3.21 (m, 2H), 3.99 (q, J = 7.2 Hz, 2H), 7.04-7.12 (m, 4H); **^{13}C NMR** (100 MHz, CDCl3): δ 13.9, 21.5, 23.3, 33.7, 40.2, 61.7, 114.9, 115.1, 124.1, 128.6, 129.5, 129.6, 133.5, 148.1, 158.2, 164.7, 167.5, 197.3; **Anal. calcd** for $C_{19}H_{18}FNO_3$: C, 69.71; H, 5.54; N, 4.28. found C, 69.65; H, 5.45; N, 4.24.

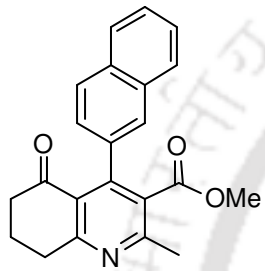
*Methyl 4-(4-fluorophenyl)-2,7,7-trimethyl-5-oxo-5,6,7,8-tetrahydroquinoline-3-carboxylate (**9c**)*



(9c)

White solid, M.p 142-143 °C; **IR** (KBr)ν_{max} 3030, 2947, 2871, 1732, 1694, 1574, 1511, 1433, 1283, 1231,1221, 1163, 1151, 1081, 1032 cm^{-1}; **^{1}H NMR** (400 MHz, CDCl3): δ 1.11 (s, 6H), 2.47 (s, 2H), 2.59 (s, 3H), 3.09 (s, 2H), 3.52 (s, 3H), 7.06-7.09 (m, 4H); **^{13}C NMR** (100 MHz, CDCl3): δ 23.4, 28.3, 32.5, 47.6, 52.4, 53.7, 114.9, 115.1, 123.0, 129.3, 129.4, 130.2, 133.3, 147.7, 158.5, 163.5, 168.1, 197.2; **Anal. calcd** for $C_{20}H_{20}FNO_3$: C, 70.37; H, 5.91; N, 4.10. found C, 70.32; H, 5.86; N, 4.04.

*Methyl 2,7,7-trimethyl-4-(naphthalen-2-yl)-5-oxo-5,6,7,8-tetrahydroquinoline-3-carboxyl ate (**9d**)*



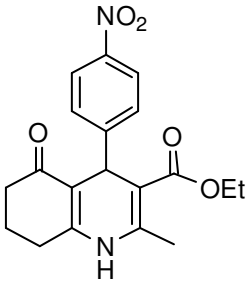
(9d)

White solid, M.p 134-135 °C; **IR** (KBr)ν_{max} 2978, 2956, 2930, 2869, 1727, 1685, 1549, 1509, 1459, 1266, 1218,1182, 1162,1085, 1065, 1016 cm^{-1}; **^{1}H NMR** (400 MHz, CDCl3): δ 1.12-1.14 (m, 6H), 2.47-2.49 (m, 2H), 2.62 (s, 3H), 3.12 (s, 2H), 3.37 (s, 3H), 7.25 (d, J = 8.4 Hz, 1H), 7.46-7.49 (m, 2H), 7.57 (s, 1H), 7.79 (d, J = 7.6 Hz, 1H), 7.84 (t, J = 8.4 Hz, 2H); **^{13}C NMR** (100 MHz, CDCl3): δ 23.4, 28.2, 28.3, 32.6, 47.6, 52.3, 53.7, 123.2, 125.8, 126.2, 126.3, 126.4, 127.2, 128.0, 128.2, 130.4, 132.8, 133.0, 135.3, 148.7, 158.6, 163.5, 168.2, 197.1; **Anal. calcd** for $C_{24}H_{23}NO_3$: C, 77.19; H, 6.21; N, 3.75. found C, 77.12; H, 6.15; N, 3.70.

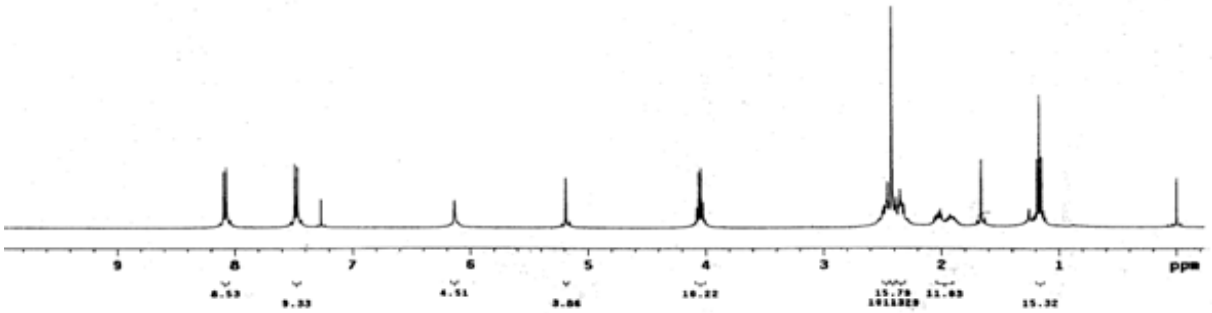
XRD for Compounds **8f** and **9c**

Complete crystallographic data of **8f** and **9c** for the structural analyses have been deposited with the Cambridge Crystallographic Data Centre, CCDC No. are 886705 and 886708 respectively. Copies of this information may be obtained free of charge from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44-1223-336033, e-mail: deposit@ccdc.cam.ac.uk or via: www.ccdc.cam.ac.uk).

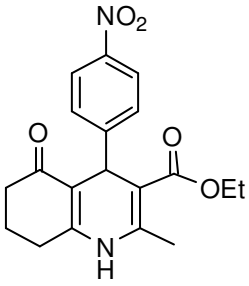
^{1}H NMR (400 MHz, $CDCl_3$): *Ethyl 2-methyl-4-(4-nitrophenyl)-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate* ***(8d)***



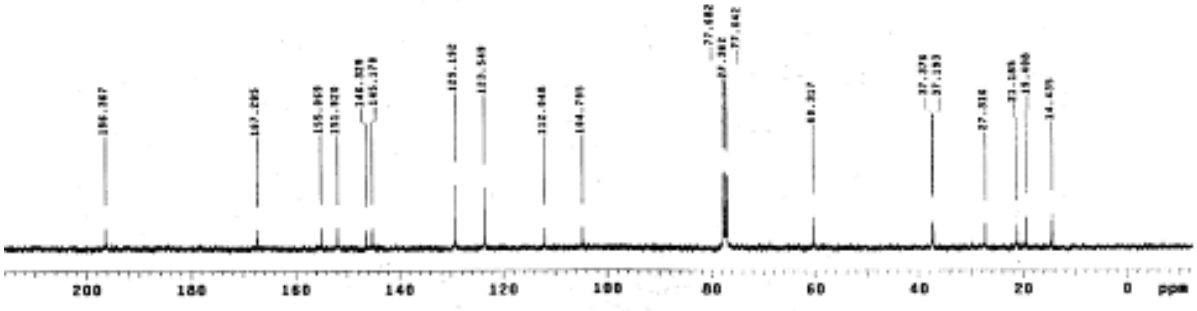
(8d)



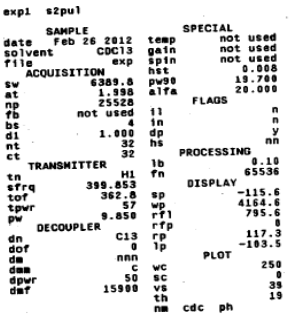
^{13}C NMR (100 MHz, $CDCl_3$): *Ethyl 2-methyl-4-(4-nitrophenyl)-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate* ***(8d)***

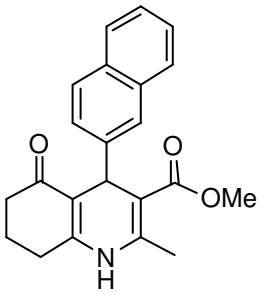


(8d)

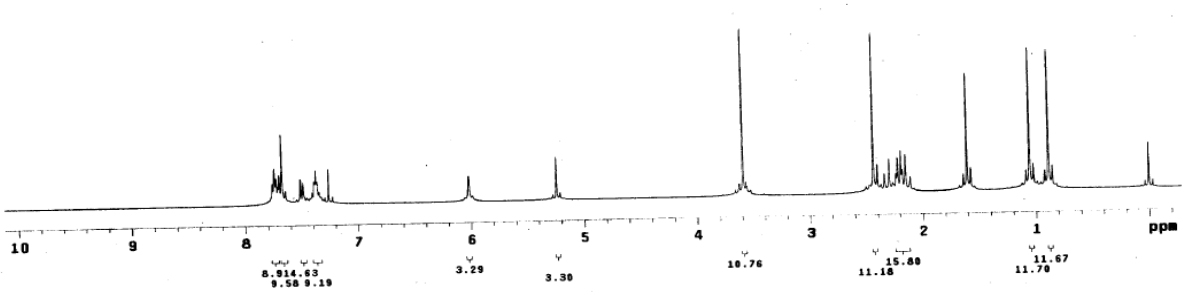


^{1}H NMR (400 MHz, $CDCl_3$)**: Methyl 2,7,7-trimethyl-4-(naphthalen-2-yl)-5-oxo-1,4,5,6,7,8-hexahydro quinoline-3-carboxylate **(8o)

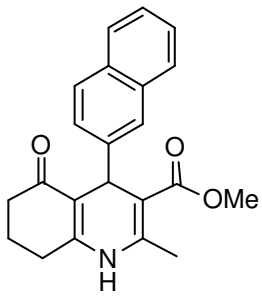




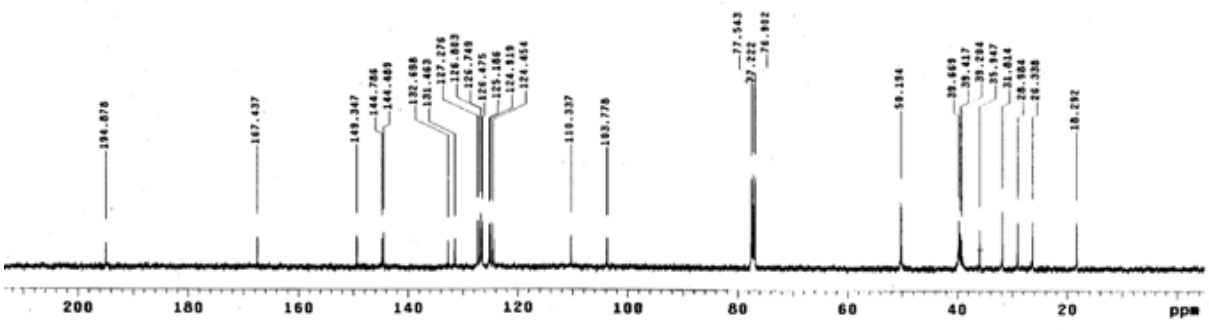
(8o)



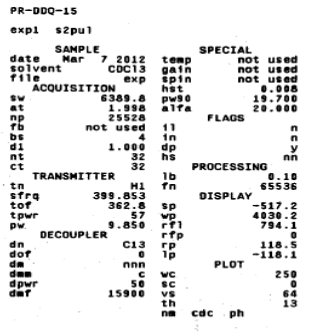
***^{13}C NMR (100 MHz, $CDCl_3$)**: Methyl 2,7,7-trimethyl-4-(naphthalen-2-yl)-5-oxo-1,4,5,6,7,8 -hexahydroquinoline-3-carboxylate (**8o**)*

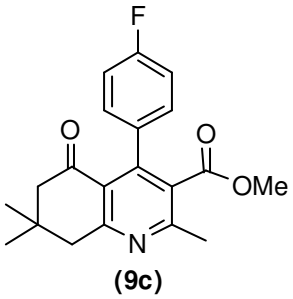


(8o)

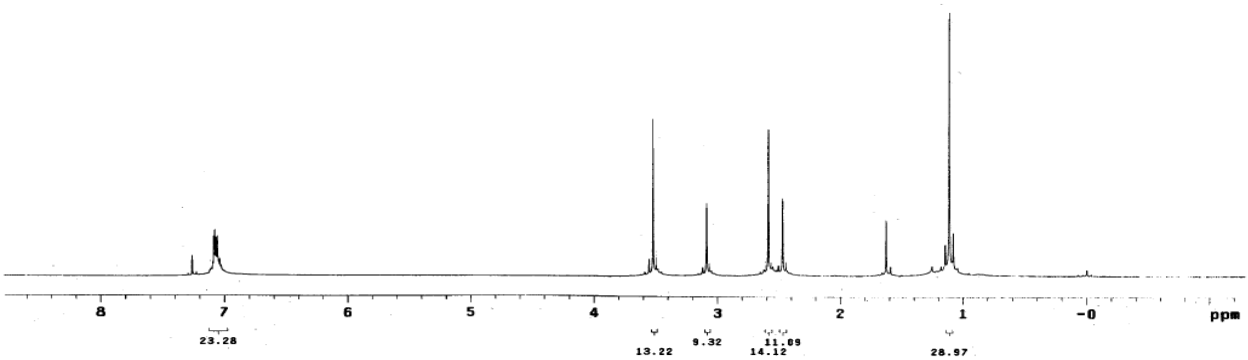


*^{1}H NMR (400 MHz, $CDCl_3$): Methyl 4-(4-fluorophenyl)-2,7,7-trimethyl-5-oxo-5,6,7,8-tetrahydroquinoline-3-carboxylate (**9c**)*

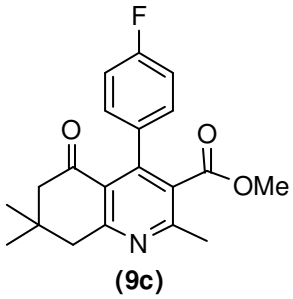




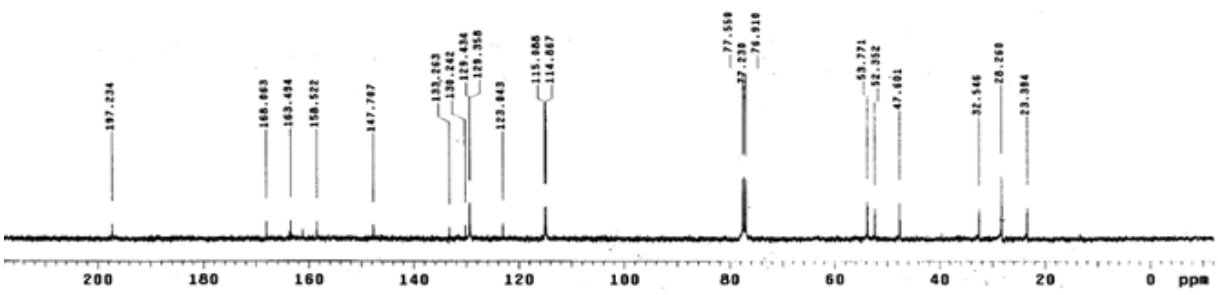
(9c)



*^{13}C NMR (100 MHz, $CDCl_3$): Methyl 4-(4-fluorophenyl)-2,7,7-trimethyl-5-oxo-5,6,7,8-tetrahydroquinoline-3-carboxylate (**9c**)*



(9c)



Part B

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Chapter I - Chapter III

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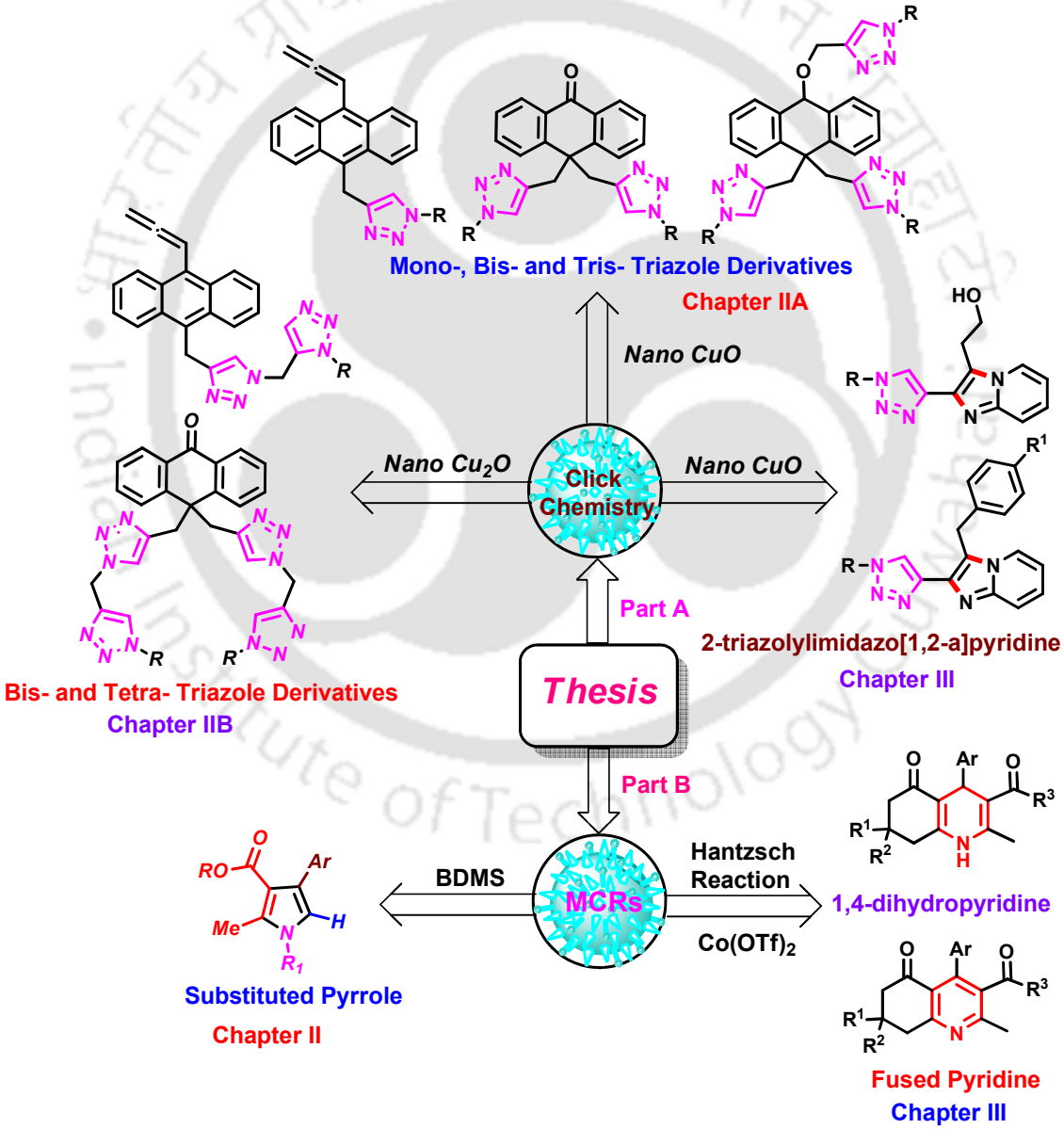
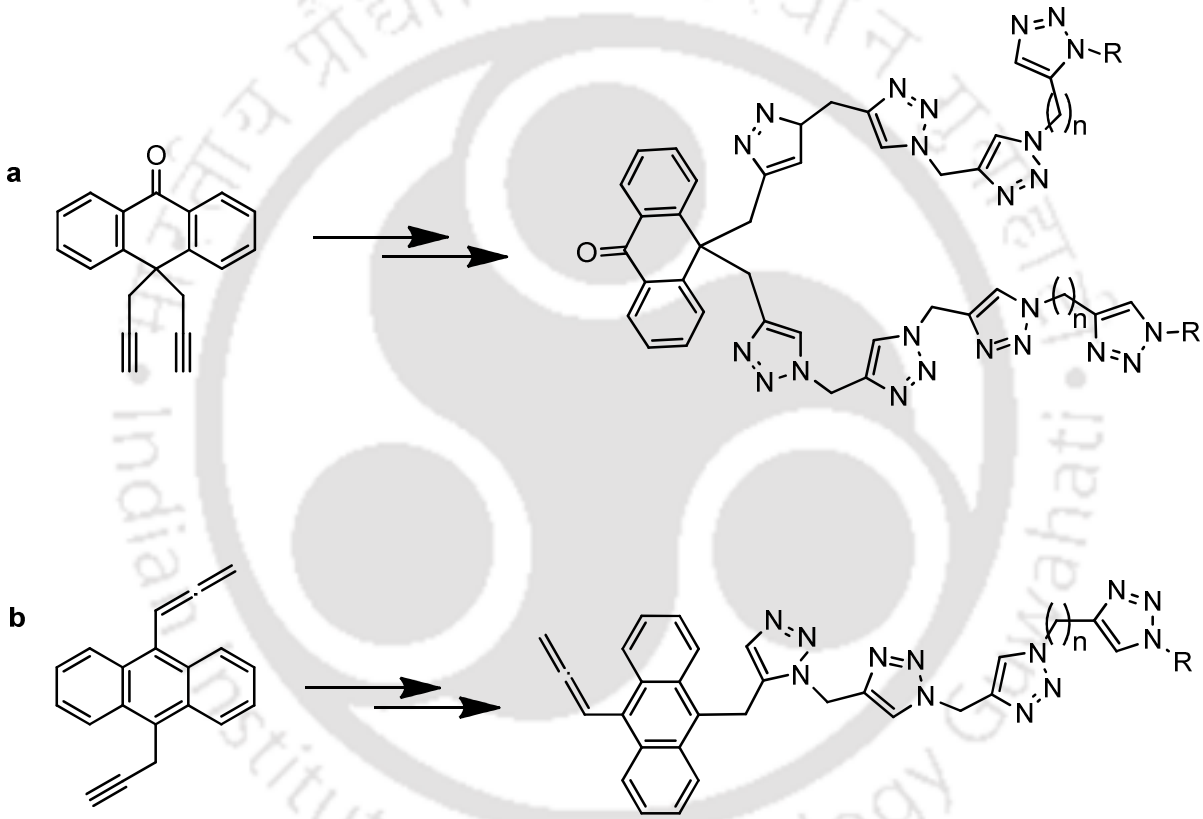
CONCLUSION AND FUTURE PERSPECTIVES

During the tenure of my PhD, I have focused my research work mainly on the utility of heterogeneous copper oxide nano catalyst for the synthesis of 1,4-triazole based new organic molecules such as mono-, bis-, tris- and tetra- triazolyl-anthrone, mono- and bis-triazolyl-allenyl-anthracene and 2-triazolyl-imidazo[1,2-*a*]pyridine derivatives as well as in the development of multicomponent reaction for the synthesis of substituted pyrroles using non-metallic catalyst from easily available starting material and environmentally benign condition and also for the regioselective synthesis of highly substituted 1,4-dihydropyridine and fused pyridine derivatives. The summarized results are shown below schematically.

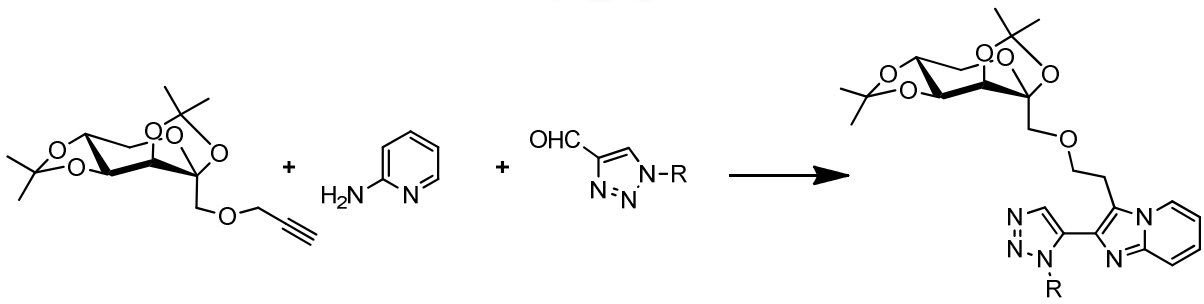


In future, we believe that these 1,4-triazole based new organic molecules could be utilized for target-oriented synthesis of natural products in modern organic synthesis. Moreover, we

believe that, the synthesized 1,4-triazole based new organic molecules as well as N-heterocyclic compounds prepared by these methods are useful classes of compounds which could be further studied for their potent biological activities in collaboration with other research groups. In future, we would try to achieve the synthesis of 1,4-triazole based polymer from 10,10-dipropargyl anthrone and 9-allenyl-10-propargyl anthracene their synthetic representation are shown in Scheme 1. In addition, we shall look forward towards the synthesis of 2-triazolyl new organic molecules using multicomponent reaction. In addition to that, we will try to achieve the sugar based multicomponent reaction as shown in Scheme 2.



Scheme 1



Scheme 2

LIST OF PUBLICATIONS AND COMMUNICATIONS

1. 'Copper oxide nanoparticle mediated 'click chemistry' for the synthesis of mono-, bis- and tris-triazole derivatives from 10,10-dipropargyl-9-anthrone as a key building block' **Prasanta Ray Bagdi**, Sidick Basha R, Pranjal Kumar Baruah, Abu T. Khan, *RSC Adv*. **2014**, *4*, 10652.
2. 'Bromodimethylsulfonium bromide (BDMS) catalyzed synthesis of substituted pyrroles through a one-pot four-component reaction' **Prasanta Ray Bagdi**, Sidick Basha R, Mohan Lal, Abu T. Khan, *Chem. Lett*, **2013**, *42*, 939.
3. 'Cobalttriflate Catalyzed One-pot Synthesis of Fluorophore 1,4-Dihydropyridine derivatives via Hantzsch Reaction' **Prasanta Ray Bagdi**, Sidick Basha R, Mohan Lal, Abu T. Khan, *J. Indian Chem. Soc*. **2013**, *90*, 1589. (Special Issue in honor of Prof. Sunil Kumar Talapatra).
4. 'Insights into the Inhibitory mechanism of Triazole-Based Small Molecules on Phosphatidylinositol-4,5-bisphosphate Binding Pleckstrin Homology Domain' Sukhamoy Gorai, **Prasanta Ray Bagdi**, Rituparna Borah, Abu T. Khan, Debasis Manna, *B. B. Report*, **2015**, *2*, 75.
5. 'Synthesis of 2-triazolyl-imidazo[1,2-a]pyridine through one-pot three-component reaction using nano copper oxide assisted Click-catalyst' **Prasanta Ray Bagdi**, Sidick Basha R, Abu T. Khan, *RSC Adv.* **2015**, *5*, 61337.
6. 'Click Precursor in 'Click chemistry' for the synthesis of bis-di-triazolyl-anthrone and di-triazolyl-allenyl-anthracene in One-pot Three Component Reaction catalyzed by Copper oxide Nanoparticle in Aqueous medium' **Prasanta Ray Bagdi**, Abu T. Khan (Communicated).
7. 'L-Proline catalysed unusual product formation from the reaction of 4-hydroxydithiocoumarin and aldehydes through a pseudo three-component reaction' Karuna Mahato, **Prasanta Ray Bagdi**, Abu T. Khan, *Synlett*, **2014**, *25*, 2438.
8. 'Synthesis of tetra-substituted pyrroles, a potential phosphodiesterase 4B inhibitor, through nickel(II) chloride hexahydrate catalyzed one-pot four-component reaction' Abu T. Khan, Mohan Lal, **Prasanta Ray Bagdi**, Sidick Basha R, Parameswaran Saravanan, Sanjukta Patra, *Tetrahedron Lett.,* **2012***, 53,* 4145. (Recognized as one of the Top 25 most downloaded article)

9. **‘**Ytterbium(III)trifluoromethanesulfonate catalyzed regioselective synthesis of unusual di- and tri- substituted 3,4-dihydrothiochromeno[3,2-e][1,3]thiazin-5(2H)-one through a pseudo four-component hetero-Diels-Alder reaction’ Karuna Mahato, **Prasanta Ray Bagdi**, Abu T. Khan, *RSC Adv*. **2015**, *5*, 48104.
10. ‘Synthesis and characterization of Symmetrical and Unsymmetrical Vanadium salen complexes’ R. Sidick Basha, **Prasanta Ray Bagdi**, Abu T. Khan (Manuscript under preparation).
11. ‘Camphorsulfonic acid catalysed synthesis of di subsituted 3-alkyl benzo[f]quinoline through a three-component hetero-Diels-Alder reaction’ Radhakrishna gattu, **Prasanta Ray Bagdi**, R. Sidick Basha, Abu T. Khan (Communicated).
12. ‘ABC and Pseudo AB type three component reaction for the synthesis of substituted 1,2 and 1,2,3-quinolone derivative catalysed by (±) Camphor sulfonic acid’ Radhakrishna gattu, **Prasanta Ray Bagdi**, R. Sidick Basha, Abu T. Khan (Communicated).
13. ‘Contractions of various benzoquinoline and quinoline derivatives through a one pot three-component aza-Diels-Alder Reaction using (±) Camphor sulfonic as a catalyst’ Radhakrishna gattu, **Prasanta Ray Bagdi**, Abu T. Khan (Manuscript under preparation).
14. ‘Base and acid mediated synthesis of thieno[2,3-b]thiochromen-4(3H)-one containing oxime and corresponding amine derivatives through a one-pot two-component Reaction’ Karuna Mahato, **Prasanta Ray Bagdi**, Abu T. Khan (Manuscript under preparation).