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# *Development of Direct Organocatalytic [3+2]-Annulation Reactions: Scope and Applications*

A

Thesis

Submitted for the Degree of

## Doctor of Philosophy

By


## GORACHAND BADARAITA





School of Chemistry

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Hyderabad-500046, India


August 2022

Dedicated to.....

*My Parents*

## DECLARATION

I hereby declare that the matter embodied in the thesis entitled **"Development of Direct Organocatalytic [3+2]-Annulation Reactions: Scope and Applications"** is the outcome of investigation carried out by me in the School of Chemistry, University of Hyderabad, Hyderabad, India, under the supervision of **Prof. Dhevalapally B. Ramachary**.

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# CERTIFICATE

Certified that the work contained in the thesis entitled "Development of Direct Organocatalytic [3+2]-Annulation Reactions: Scope and Applications" has been carried out by Mr. Gorachand Badarita under my supervision and the same has not been submitted elsewhere for a degree. This thesis is free from plagiarism and has not been submitted previously in part or in full to this or any other University or Institution for award of any degree or diploma.

**A. Parts of the thesis have been published in following publications:**

1. **B. Gorachand**, and Dhevalapally B. Ramachary. (*Manuscript under preparation*).
2. **B. Gorachand**, and Dhevalapally B. Ramachary (*Manuscript under preparation*).
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# *CONTENTS*

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***Gorachand Badaraita***

# *PREFACE*

*Annulation reaction is one of the powerful reaction method to generate multiple bonds in single step, among those 1,3-dipolar cycloadditions are considered as the "strongest pillar in the construction of complex molecular skeletons". More* importantly, *organocatalytic [3+2]-cycloadditions have become alternative to the metal mediated [3+2]-cycloadditions because of their simple operation technique, milder conditions, high efficiency, short reaction time, high regioselectivity, readily available precursors and potentially greener. The present thesis entitled* ***"Development of* Direct Organocatalytic [3+2]-Annulation Reactions: Scope and Applications"** *describes the reactions involving catalytic enolate and push-pull dienolate intermediates in the synthesis of highly functionalized 1,2,3-triazoles and pseudo terpenoids scaffolds and which have pharmaceutical and biological importance. In all these sections, a brief introduction is provided to keep the present work in proper perspective, the compounds are sequentially numbered (bold), and references are marked sequentially as superscript and listed at the end of the thesis. All the figures included in the thesis were obtained by DIRECT PHOTOCOPY OF THE ORIGINAL SPECTRA and in some of them uninformative areas have been cut to save the space.*

*In the first chapter, highly functionalized heterocyclic-1,2,3-triazoles have found wide applications in pharmaceutical, material and agrochemical fields. To synthesize these skeletons an efficient, green and sustainable protocol is required. Herein, we achieved those using simple starting materials such as diketoester, and aryl/alkyl/vinyl azides with a catalytic amount of tertiary amine. The organocatalytic enolate-mediated azide-carbonyl [3+2]-cycloaddition (OrgACC) reaction ensues in excellent yields with high chemo-, regioselectivity and it constitutes an alternative to the previous synthetic methods.*

*In the second chapter, In continuation to the development of catalytic OrgACC reaction through enolate-mediated synthesis of substituted benzothiazole containing 1,2,3-triazoles, we demonstrates the organocatalytic azide-ketone [3+2]-cycloaddition reaction to*

*accomplish fully decorated benzothiazole containing 1,2,3-triazoles in excellent yields with high regioselectivity. A variety of enolizable ketones and different azides are employed as starting materials under tertiary amine-catalysis. We developed an OrgACC strategy in metal-free synthesis of materially important benzothiazole containing 1,2,3-triazoles.*

*In the third chapter, we demonstrated metal-free, organocatalytic tandem coupling/ annulation reactions as green protocols for the synthesis of highly functionalized cedrane scaffolds with excellent yields, chemo- and distereoselectivities, and product ratios. Cedrane-type pseudo-terpenoids were synthesised using hydroxyl-p-quinone aldehydes and various phosphoranes or CH-acids under quinine catalysts in a series of Wittig reaction/intramolecular Michael/Michael, intramolecular Michael/aldol, and retro-intramolecular Michael/retro-intramolecular Michael/retro-intramolecular aldol reactions. It is an alternative to the previous methods for synthesizing complex bicyclo [3.2.1]-octane ring systems.*

# *LIST OF ABBREVIATIONS*

| | |
|---|---|
| Ac | acetyl |
| AcOH | acetic acid |
| $Ac_2O$ | acetic anhydride |
| Anal. | analysis |
| aq. | aqueous |
| Ar | aryl |
| Bn | benzyl |
| Bp | boiling point |
| br | broad |
| Bu | butyl |
| *t*Bu or $^t$Bu | *tertiar*y-butyl |
| *n*-BuLi | *n*-butyl lithium |
| calcd. | calculated |
| cat. | catalytic |
| cm | centimeter |
| CS/H | Claisen-Schmidt/Henry |
| CS/I | Claisen-Schmidt/isomerisation |
| CSP | chiral stationary phase |
| CuAAC | copper catalyzed azide-alkyne cycloaddition |
| DABCO | 1,4-Diazabicyclo[2.2.2]octane |
| dABq | doublet of AB quartet |
| DBU | 1,8-Diazabicyclo[5.4.0]undec-7-ene |
| DCE | 1,2-dichloroethane |
| DCM | dichloromethane |
| dd | doublet of doublet |
| ddd | doublet of doublet of doublet |
| DDQ | 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone |
| de | diastereomeric excess |
| DEPT | distortionless enhancement by polarization transfer |
| DFT | density functional theory |
| DIBAL-H | diisobutylaluminium hydride |
| DMAP | dimethylaminopyridine |
| DMF | *N*,*N*-dimethylformamide |
| DMSO | dimethyl sulfoxide |
| dr | diastereomeric ratio |
| dt | doublet of triplet |
| EDG | electron donating group |
| ee | enantiomeric excess |
| eq. | equation |
| equiv. | equivalent(s) |
| Et | ethyl |
| EtOH | ethyl alcohol |
| $Et_2O$ | diethylether |
| EWG | electron withdrawing group |
| Fg | functional group |
| Fig. | figure |
| gm | gram (s) |

| | |
|---|---|
| h | hour (s) |
| Hz | hertz |
| Hex | hexyl |
| HIV | human immunodeficiency virus |
| HOMO | highest occupied molecular orbital |
| HPLC | high-performance liquid chromatography |
| $^{i}$Pr | isopropyl |
| IR | infrared |
| $LiAlH_4$ | lithium aluminum hydride |
| lit. | literature |
| m | multiplet |
| *m*-CPBA | *m*-chloro perbenzoic acid |
| M | molarity |
| Mp. | melting point |
| Me | methyl |
| mg | milligram (s) |
| mGluR1 | metabotropic glutamate receptor 1 |
| mL | milliliter |
| mmol | millimole |
| MW | microwave |
| NMR | nuclear magnetic resonance |
| NMP | *N*-methylpyrrolidine |
| OrgAAC | organocatalytic azide-aldehyde cycloaddition |
| OrgAKC | organocatalytic azide-ketone cycloaddition |
| OrgRC | organocatalytic reductive coupling |
| PCC | pyridinium chlorochromate |
| PET | positron emission tomography |
| Ph | phenyl |
| ppm | parts per million |
| *p*-TSA | *p*-toluenesulfonic acid |
| py | pyridine |
| *pr* | product ratio |
| q | quartet |
| RT | room temperature |
| s | singlet |
| sec | secondary |
| t | triplet |
| TBHP | tertiary-butyl hydroperoxide |
| *t*BuOK | Potassium tertiarybutoxide |
| td | triplet of doublet |
| tert | tertiary |
| TFA | trifluoroacetic acid |
| THF | tetrahydrofuran |
| TLC | thin layer chromatography |
| TMS | trimethylsilyl |
| Ts | toluenesulphonyl |
| UV | ultraviolet |
| TMG | tetramethyl guanidine |

# Development of Direct Organocatalytic [3+2]-Annulation Reactions: Scope and Applications

## 1. Abstract

In the first chapter, we have discussed the synthesis of trisubstituted, mono-, bis-1,2,3-triazoles through an enolate-mediated organocatalytic aryl azide-carbonyl chemoselective [3+2]-cycloaddition (OrgACC) of various ketones with aryl/alkyl azides. It is an efficient intermolecular cycloaddition reaction with excellent outcomes concerning rate, yield, selectivity, operational simplicity, substrate scope, and vast applicability.

In the second chapter, the synthesis of benzothiazole containing triazoles through an enolate-mediated organocatalytic [3+2]-cycloaddition of a variety of benzothiazole ketones and aryl/alkyl azides was discussed. Mild and metal-free catalytic conditions are employed to synthesize a variety of benzothiazole containing 1,2,3-triazoles in high yields.

In the third chapter, structurally complex cedrane scaffolds were synthesized in a very good yields with high chemo- and diastereoselectivities in a sequential one-pot manner by using a combination of intermolecular olefination, intramolecular Michael and Michael reactions or intermolecular olefination, intramolecular Michael and aldol reactions as the key steps from the readily available hydroxy-*p*-quinone butanals and phosphoranes under the catalytic amounts of quinine at ambient temperature for few hours. This is one of the unique one-pot combination of coupling and annulation routes for the green synthesis of a library of tricyclic pseudo-terpenoids (cedrane scaffolds) with high selectivity and yields.

This thesis is divided into two sections. One section deals with the development of organocatalytic [3+2]-cycloaddition for the synthesis of functionally rich 1,2,3-triazoles. Another one deals with the synthesis and reactivity studies of 5-substituted 2-hydroxy-1,4-benzoquinones in the organocatalytic reductive coupling, Wittig reactions and followed by [3+2]-annulation reactions to furnish cedrane scaffolds. Herein, for the both sections, clear information with introduction is given.

# 2. Introduction

## Section-I: Organocatalytic Azide-Carbonyl [3+2]-Cycloadditions:

The enormous applications of triazoles in the realm of chemistry, ranging from drug discovery to material chemistry, has enthralled researchers to develop novel methodologies for its synthesis over the last three decades. Recent biological studies have established the bio-similarity of 1,2,3-triazole with amide linkage.[1] 1,2,3-Triazole is an amide bio-isostere which is highly inert to enzymatic degradation and hydrolysis. The characteristic similarity to amides in relative planarity, dipole moment and hydrogen bonding ability made it an interesting pharmacophore exhibiting extremely important pharmacological properties like anticancer, anti-tubercular, anti-microbial, anti-HIV, anti-convulsant, anti-tubulin and anti-inflammatory etc.[1] Some interesting physical and electronic properties of 1,2,3-triazole are discussed in Figure 1.

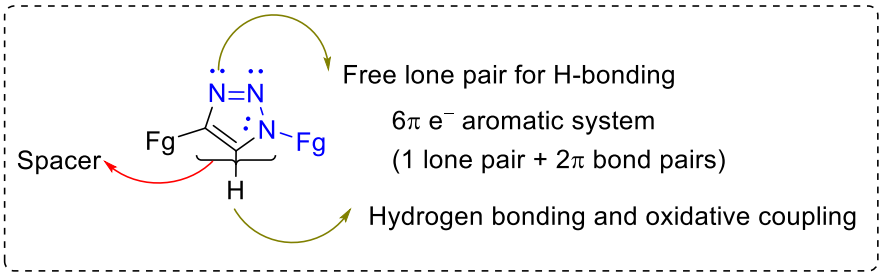



**Figure 1:** Properties of 1,2,3-Triazole.

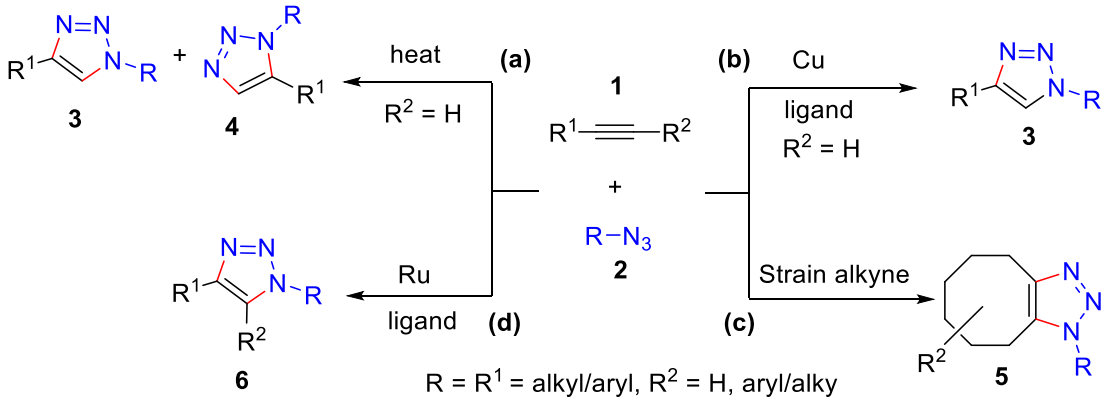
### 2.1 Previous Report on Metal Mediated Azide-Alkyne [3+2]-Cycloadditions:

Initially, Huisgen et al. in 1964 reported the direct synthesis of triazole via [3+2]-cycloaddition of alkyne **1** and azide **2** but the reaction proceeded only at the elevated temperature of 80-120 ºC with the reaction times of 12 to 24 h and also failed to achieve the regioselectivity (Scheme 1, path a).[2] In 2002, Sharpless et al. established the copper catalyzed azide-alkyne [3+2]-cycloaddition (CuAAC) click reactions which affords a highly regiospecific 1,4-disubstituted 1,2,3-triazoles **3** from the [3+2]-cycloaddition of alkyne **1** and azide **2** (Scheme 1, path b).[3] This novel discovery lead to the exponential growth of click chemistry.

Later, in 2004, Bertozzi et al. came up with an innovative catalyst free approach where a strained cyclooctyne **1** was chosen and reacted with azide **2** in [3+2]-cycloaddition fashion to afford

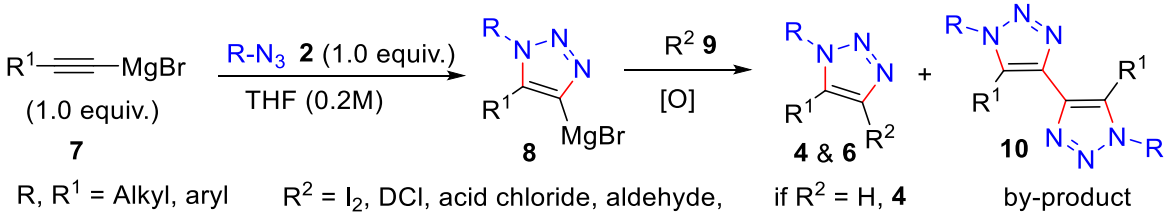
trazoles **5**. Since it is a strain-promoted click reaction, it produced two regeoisomeric triazoles **5** which were further used in the application of covalent labelling of biomolecules (Scheme 1, path c).[4] In 2005, Sharpless made an outstanding scientific breakthrough in click chemistry. They have introduced ruthenium as a catalyst in Huisgen azide-alkyne [3+2]-cycloaddition and achieved high selectivity in the product formation. The type of ligand employed in the Ru-click reaction and the type of alkyne (internal or terminal) determined the selectivity of the product **6** whether to be 1,4-disubstituted triazoles **3** or 1,5-disubstituted triazoles **4** or 1,4,5-trisubstituted triazoles **6** (Scheme 1, d).[5]

**Scheme 1:** Strategies for the Synthesis of Substituted 1,2,3-Triazoles



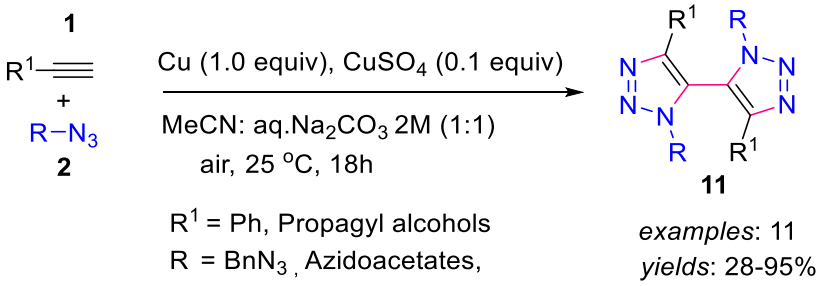

In 2004, Sharpless and his colleagues established the protocol for synthesizing 1,5-disubstituted triazoles **4** and 1,4,5-trisubstituted triazoles **6** *via* [3+2]-cycloaddition of bromomagnesium acetylids **7** and azides **2** (Scheme 2).[6] During the reaction, the intermediate **8** preferentially yielded 1,5-disubstituted triazoles **4** when they hydrolyzed the reaction, but when they added an electrophile **9**, reaction afforded 1,4,5-trisubstituted triazoles **6** in the presence of atmospheric oxygen which also led to the trace amount of bis-adduct **10** formation. This observation has triggered a new scope for the study of the synthesis of bis-triazoles.

**Scheme 2:** Synthesis of Triazoles using Mg-Induced Azide-Alkyne [3+2]-Cycloaddition



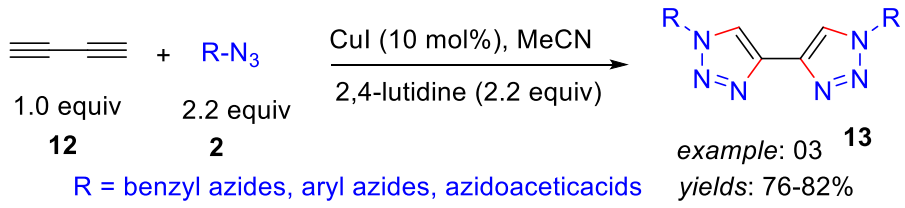
However, the formation of bis-products **10** was already reported by Sharpless and coworkers without characterization,[6] Burgess *et al*., in 2007 reported the synthesis of chiral 5,5-bistriazole scaffolds **11** through base-mediated CuAAC [Cupper catalyzed Azide Alkyne 3+2-Cycloaddition].[7] It was the first group to discover the perfect reaction conditions to synthesize chiral 5,5-bistriazole scaffolds **11** and also made clear that, the presence of Cu/$CuSO_4$ system in basic medium is very much important for the formation of chiral 5,5-bistriazole scaffolds **11** (Scheme 3). When the reaction was performed in the absence of basic medium, there was no formation of chiral 5,5-bistriazole scaffolds **11**. The disadvantage of this approach was the use of a stoichiometric quantity of Cu powder in the reaction.

**Scheme 3:** Synthesis of Chiral Bis-triazole by Base Mediated CuAAC Huisgen Cycloaddition



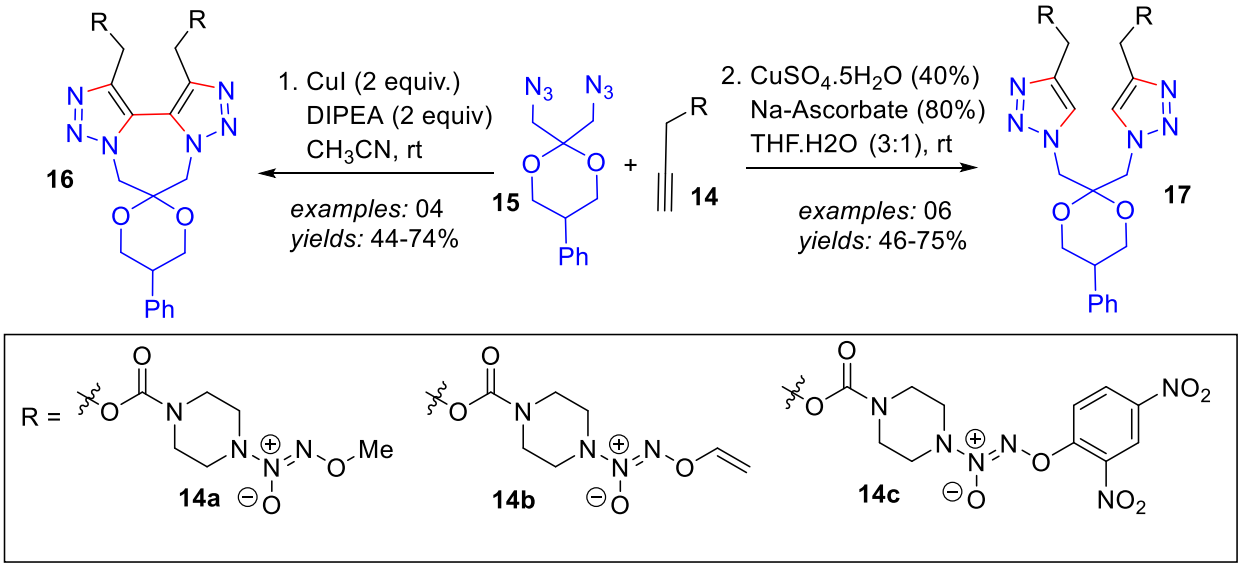

Later, In 2007, Monkowuis *et al*. came up with a novel methodology for synthesizing symmetric bis-triazole **13** in high yields using CuI-catalyzed [3+2]-cycloaddition of symmetric 1,3-butadiyne **12** and azide **2** (Scheme 4).[8] These symmetric bis-triazoles **13** had excellent ligand properties similar to 2,2-bipyridyls.

**Scheme 4:** Synthesis of Symmetric 1,2,3-Triazole by Azide-Alkyne [3+2]-Cycloaddition



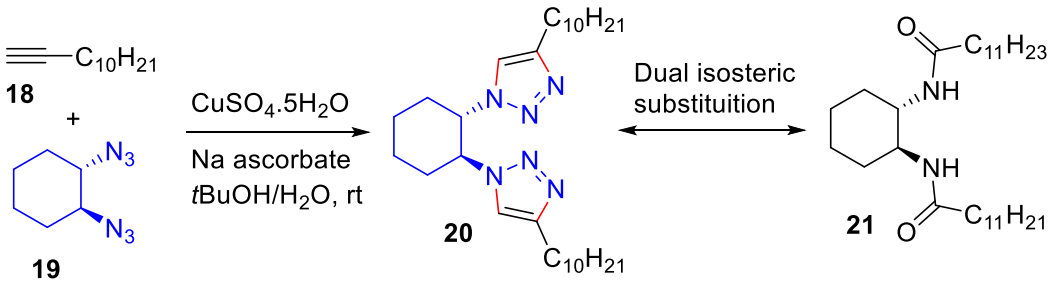
The next category of triazoles are unsymmetrical bis-triazoles. In 2010, Nundurdikar *et al*. developed a novel strategy for the synthesis of unsymmetrical bis-triazoles **17** and explored their pro-drug characteristics (Scheme 5).[9] In their reports, the reaction of substituted benzylidyne **14** and bis-azides **15** under $Cu^{I}$/diisopropylethylamine conditions yielded oxidative coupling products **16** with moderate to good yields i.e., 44-74%, whereas under Cu/Na-ascorbate conditions yielded bis-triazoles, **17** with up to 75% yields (Scheme 5).

**Scheme 5:** Synthesis of Nonsymmetric 1,2,3-Triazole by [3+2]-Cycloaddition




Next, In 2019, Davit *et al*. reported an article on the synthesis of (1*S*,2*S*)-1,2-bis(4-decyl-1*H*-1,2,3-triazol-1-yl) **20**.[10] Since the outcome of the reaction are interesting, Davit *et al*. compared their moieties with N,N'-((1*S*,2*S*)-cyclohexane-1,2-diyl)didodecanamide **21** and done substantial research on investigating its hydrogen bonding capabilities. Triazole **20** outperformed amide bonds in terms of antiparallel hydrogen bonding and van Dar Waals intermolecular interactions in their respective gels (Scheme 6).

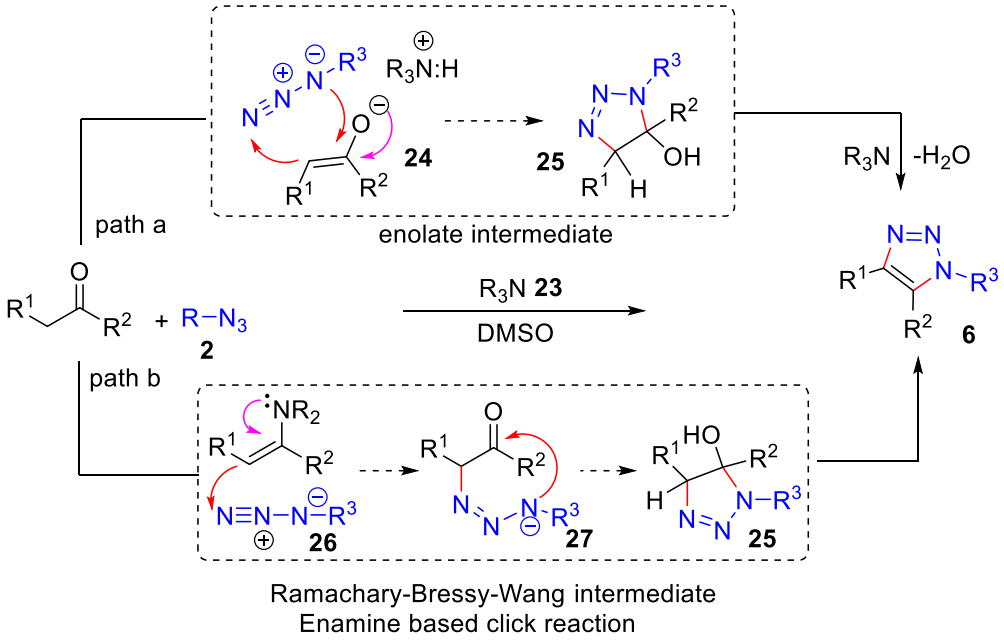
**Scheme 6:** Synthesis of Chiral 1,2,3-Triazoles for Drug Molecules




## 2.2 Previous Reports on Organocatalytic Enolate/Enamine Mediated [3+2]-Cycloadditions:

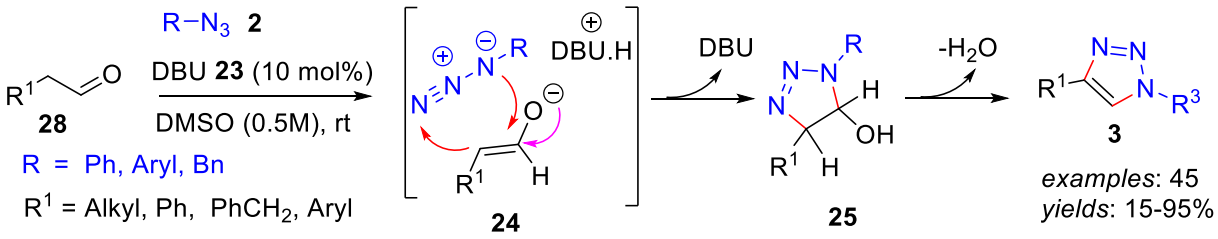
Although, the metal catalyzed reactions afforded the different varities of triazoles, it didn't escape from the drawbacks such as use of hazardous metals, costly ligands, multi-step processes etc. In order to overcome these difficulties, Ramachary,[11a] Brassy,[12] and Wang[13] independently reported in recent years on the synthesis of 1,4,5-trisubstituted and 1,4-disubstituted triazoles in high yields up to 99% via an enolate/enamine mediated [3+2]-cycloaddition click reaction using enolizable carbonyl compounds, azides, and a variety of amines as catalysts (Scheme 7).

**Scheme 7:** Synthesis of 1,4-Disubstituted and 1,4,5-Trisubstituted 1,2,3-Triazoles



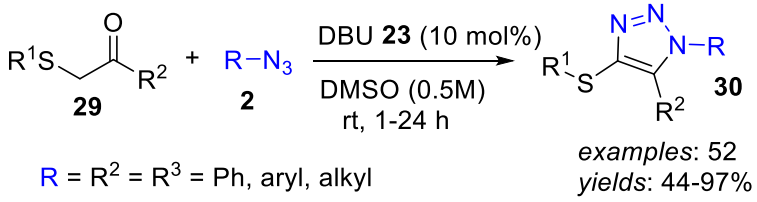
In 2014, Ramachary *et al*. developed a method for synthesising 1,4-disubtituted 1,2,3-triazoles **3** from readily accessible, enolizable aldehydes **28** and azides **2**.[11b] The enolate-intermediates **24** were generated by deprotonating active methylene proton of aldehydes with DBU **23** catalyst, followed by an organo-click [3+2]-cycloaddition reaction with azides. This well established reaction afforded the product with exceptional selectivity, yielding up to 95% of desired products (Scheme 8).

**Scheme 8:** Synthesis of 1,4-Disubstuted Triazoles from Enolizable Aldehydes




Then in 2015, Ramachary *et al*. reported a method that utilizes sulphur stabilized enolates in an organo-click reaction. They reacted sulphur stabilized enolates with a wide range of aryl azides **2** affording trisubstituted 1,2,3-triazoles **30** in up to 97% yields.[11c] The reactions were catalyzed using 10 mol% of DBU **23** as catalyst in DMSO solvent (Scheme 9).

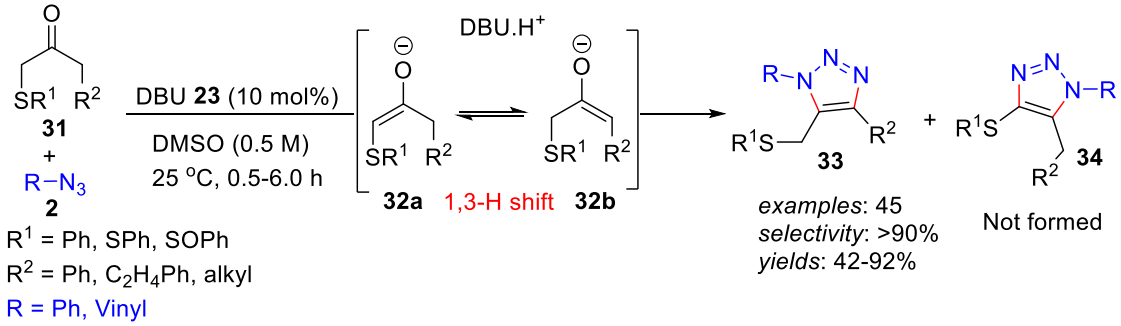
**Scheme 9:** Synthesis of 1,5-Diphenyl-4-(phenylthio)-1*H*-1,2,3-Triazoles




Later, In 2020, Ramachary *et al.* cameup with a novel methodology for the regiospecific synthesis of 1,4-diphenyl-5-((phenylthio)methyl)-1*H*-1,2,3-triazoles **33** with good to excellent yields of 42-92%.[11d] Since, the structure 1-phenyl-3-(phenylthio)propan-2-one **31** posseses two

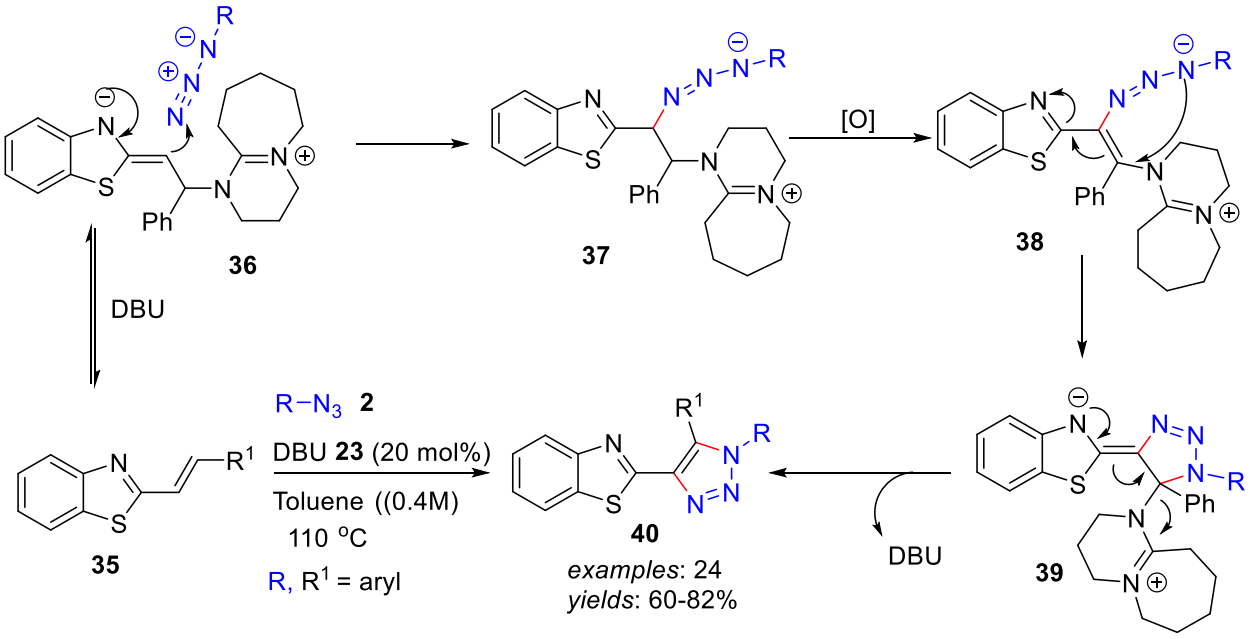
types of activated methylene groups, there were two possibilites where it may form a thermodynamic enolate **32a** and kinetic enolates **32b** via DBU **23** catalysis. Firstly, deprotonation occurred from sulfur methylene group of compound **31** resulting thermodynamic enolate intrmediate **32a**, which further undergo [1,3]-H shift to form kinetic enolate intermediate **32b**, proved by online NMR controlled experiments. This in situ generated kinetic enolate intermediate **32b** participated in [3+2]-cycloaddion with various aryl/alkyl/vinyl azides **2** to afford 1,2,3-triazoles **33** (Scheme 10).

**Scheme 10:** Regioselective Synthesis of Trisubstituted-1,2,3-Triazoles *via* [3+2]-Cycloaddition




In 2022, Shu *et al*. developed an organocatalytic 1,3-dipolar cycloaddition for the regiospecific synthesis of benzothiazole triazoles **40** from a variety of active olefins **35** and aryl azide **2** derivatives at 110 ºC with excellent yields of 60-82%.[14] Firstly, when DBU interacted with the activated olefin **35**, zwitter ion **36** was formed which then reacted with azidophile **2** affording intermediate **37**, which further underwent aerobic oxidation forming **38**. Then, intermediate **38** underwent cyclization followed by rearrangement furnishing benzothiazole triazoles **40** (Scheme 11).

**Scheme 11:** Synthesis of Benzothiazole Triazoles




## Section-II: Organocatalytic One-Pot Synthesis of Pseudo-Terpenoids

### 2.3 Previous Studies on Substituted 2-Hydroxy-1,4-Benzoquinones

Quinone scaffolds are structurally demanding because of their resemblance with the core structure of several natural products and pharmaceutical drugs. They serve as an excellent chromophore for natural and synthetic dyes, as well as potential anti-HIV drugs, anti-bacterial, anti-inflammatory agents, and efficient cytotoxic agents. This fundamental unit of 2-hydroxy-1,4-benzoquinone is used to create structurally complicated natural products. The versatile reactivity and structural form of 2-hydroxy 1,4-benzoquinone promotes it to become a fundamental source for synthesizing bicyclic[3.2.1] frames such as cedranes, methanoazulenes, and tricyclic quinone terpenoids. 2-Hydroxy 1,4-benzoquinone contains multi reactivity sites favoring different reactions such as intermolecular double Michael homodimerization, cross double Michael, Michael-Aldol cyclization, and intramolecular double Michael and Michael-Aldol annulation to occur in the molecule (Figure 2).

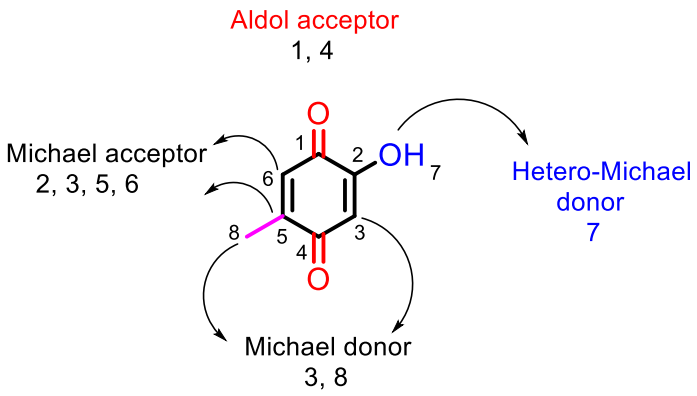
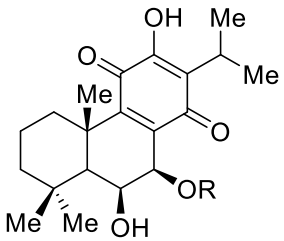



**Figure 2:** Nature of the reactivity of 2-hydroxy-1,4-benzoquinone.

In 1989, Vishwakarma *et al.* reported the extraction of abietane diterpenoids **41** from coleus zeylanicus plants, which were identified as 7*β*-acetoxy-6*β*-hydroxyroyleanone and 7*β*, 6*β*-dihydroxyleanone. The significance of these entities **41** were stated in ayurveda for the treatment of diarrhoea, glaucoma, congestive cardiomyopathy, and asthma, among others (Scheme 12).[15]

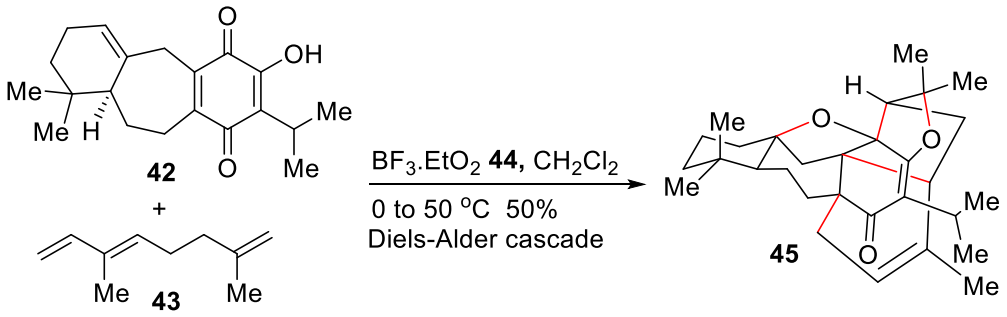
**Scheme 12:** The Extraction of Abietane Diterpenoids




**41** a. R = Ac
b. R = H

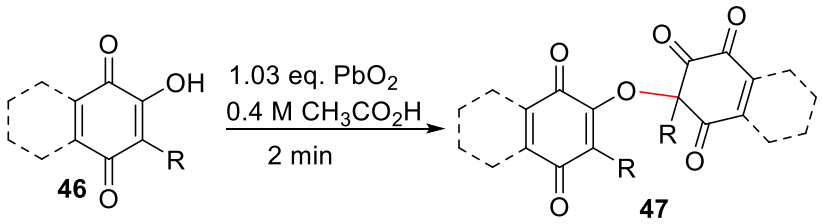
Later in 2011, Majetich *et al.* revealed the total synthesis of natural compounds (±)- and (+)-perovskone.[16] Here, quinone **42** behaved as a dienophile precursor which got cyclized with diene source *E*-α-ocimene **43** via the Diels-Alder cascade process yielded (+)-perovskone **45** in 50% yield at 0-50 ºC using $BF_3.Et_2O$ **44**. This intermolecular cyclization process generated three rings, five new bonds, and six stereo centers in a single operation (Scheme 13).

**Scheme 13:** Total Synthesis of (+)-Perovskone




In 2011, Silva *et al.* reported the synthesis of ether type quinonoid compounds **47** using non-benzenoids and benzenoids hydroxyl *p*-quinone **46** and investigated their pharmacological properties.[17] Here, benzenoids hydroxyl *p*-quinone **46** underwent self-intermolecular oxa-Michael reaction under acidic conditions to yield ether type quinonoid compounds **47** with good yields of up to 70% (Scheme 14).

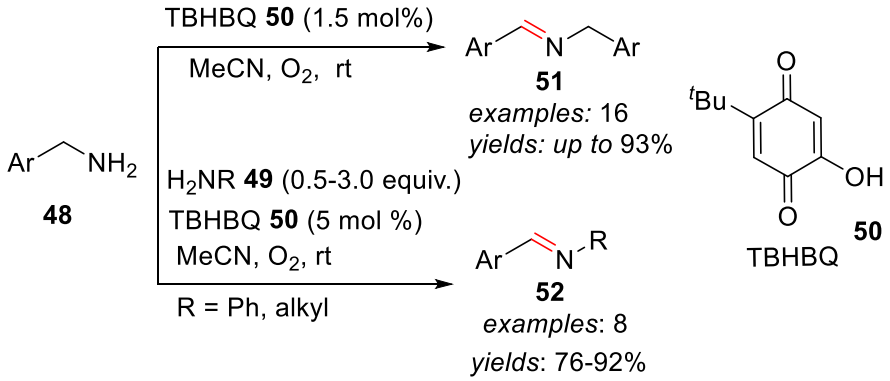
**Scheme 14:** Synthesis of Quinonoid Compounds




R = ispropyl, isobutyl, isopentane, isobutene

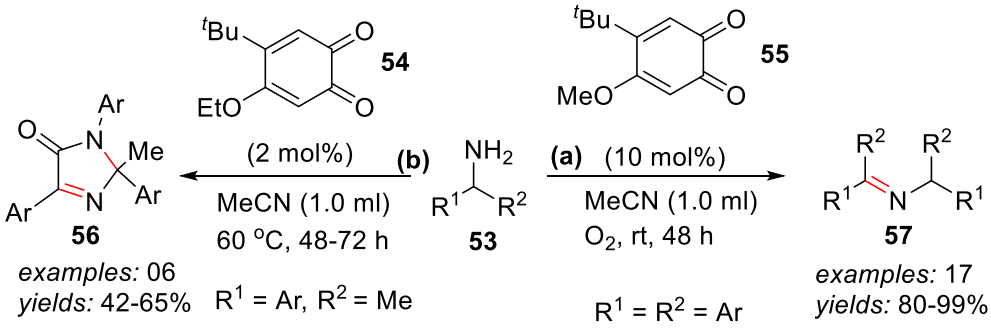
Interestingly, in 2012, Stahl *et al.* utilized *tert*-butyl 2-hydroxy benzoquinone **50** as a catalyst in biomimetic aerobic oxidation where primary amines **48** oxidized to secondary imines **51** in acetonitrile solvent under oxygen balloon at room temperature.[18] The catalytic amounts such as 1.5 mol% and 5 mol% of quinone **50** proceeded oxidative homo and hetero-coupling of benzylic amines **48** and amines **49** with excellent yield of up to 93% yields (Scheme 15).

**Scheme 15:** Biomimetic Aerobic Oxidation of Primary Amine




Later in 2015, Qin *et al*. discovered oxidative homo-coupling of primary amine **53** to secondary imine **57** with up to 99% yields in the presence of bioinspired catalysts ortho-quinone **55**, acetonitrile, and $O_2$ balloon (Scheme 16, a).[19] They further used the oxidative product imine **57** in trimerization process with primary amine either using elevated temperatures or using **54** as a catalyst with 2 mol% loading to produce imidazoline products with up to 65% yield in 48-72 hours (Scheme 16, b).

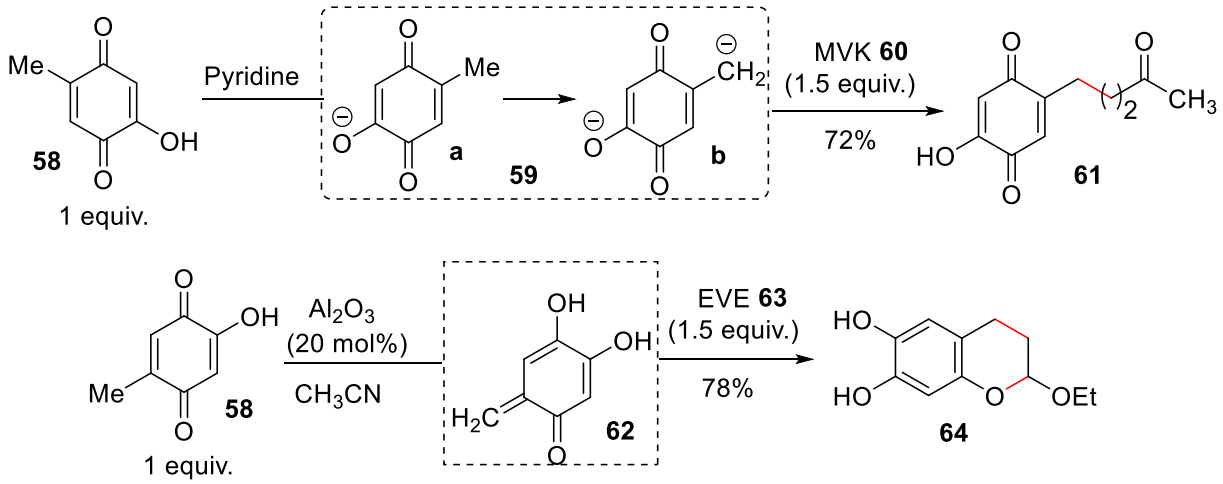
**Scheme 16:** Oxidative Homocoupling of Primary Amines




In 2017, Rosenau *et al*. studied the reactivity of the methyl substituted 2-hydroxy-1,4-benzoquinone **58** in acidic and basic media.[20] In alkaline medium, upon deprotonation of hydroxyl and methyl group, an anion **59a** and a dianion **59b** were generated, which were stabilized by resonance and then reacts inter-molecularly with Michael acceptor such as methyl

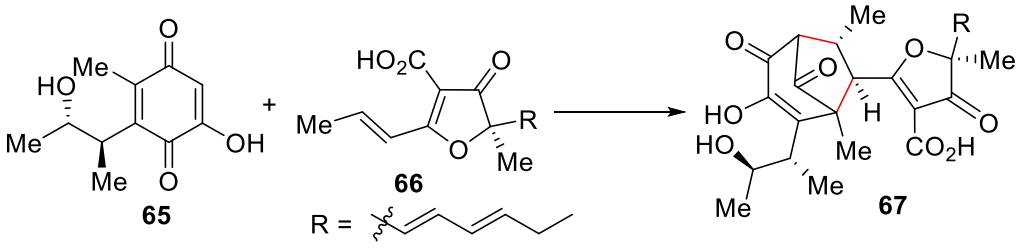
vinyl ketone **60** affording a Michael product **61** (Scheme 17). In acidic medium, quinone **58** formed a reactive isomeric intermediate **62**, which participated in the hetero-diels-alder reaction with ethyl vinyl ether **63**, yielding 78% of the desired 2-ethoxychromane-6,7-diol **64** (Scheme 17).

**Scheme 17:** Reactivity Investigation of 5-Methyl-2-hydroxy-1,4-benzoquinone in Acidic and Basic Medium



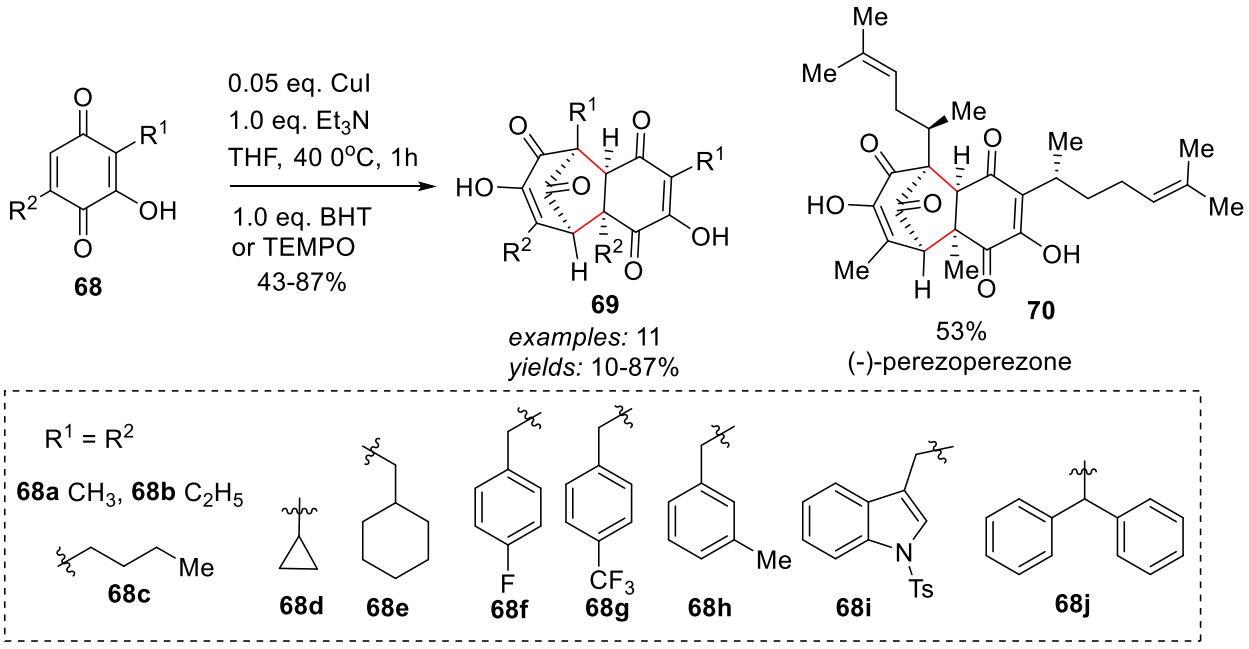

In 2018, Yang *et al.* isolated five natural products asperone A-E from the fungal metabolites of an *Aspergillus sp.* and also anticipated the synthetic route for obtaining dimeric polyketides **67** from two separate skeletons **65** and **66** by the crucial intermolecular double Michael [3+2] cycloadditions.[21] The isolated asperone A **67** is structurally complex and shows imperative cytotoxic activity (Scheme 18).

**Scheme 18:** Extraction of Natural Products Asperone A-E



In 2019, Deng *et al*. investigated intermolecular [3+2] double Michael homodimerization of 2-Hydroxyl-1,4-benzoquinone **68** for the total synthesis of (-)-perezopezone **70** and bicyclo[3.2.1]-octadienone scaffolds **69** with up to 87% yields and excellent distereoselectivities under basic condition with catalytic amount of CuI in THF solvent.[22] The quinone **68** motif possessed ambiguous nature of both Michael acceptor and donor. The reaction worked well with both linear and cyclic substituents on the quinone, whereas in case of electron-donating and withdrawing aryl, heteroaryl and sterically hindered substituents, the reaction and conversion rate was sluggish (Scheme 19).

**Scheme 19:** Synthesis of Natural Product Perezoperezone



# 3. Direct Organocatalytic Chemoselective Carbonyl-Azide [3+2]-Cycloaddition: Synthesis of Pharmaceutically Rich 1,2,3-Triazoles

## 3.1 Introduction

In recent years, chemists employed various strategies for the synthesis of functionalized 1,2,3-triazoles, because functionalized 1,2,3-triazoles found a wide range of applications for biological studies, therapeutic drug discovery, material chemistry, agrochemical industry.[23] The Huisgen azide-alkyne [3+2]-cycloaddition reaction was developed using copper(I)-catalyzed azide-alkyne [3+2]-cycloaddition reaction by Sharpless and Meldal, for the construction of highly regiospecific 1,4-disubstituted-1,2,3-triazoles with high yields.[3] Apart from Cu-catalysis, azide-alkyne [3+2]-cycloadditions were also done with ruthenium,[5] iridium,[24] nickel,[25] magnesium[6] and also using strain-promoted[4] manner. Besides transition metal-mediated azide-alkyne [3+2]-cycloaddition reaction, Ramachary,[11] Brassy[12] and Wang[13] developed green synthetic methods of azide-carbonyl [3+2]-cycloadditions independently employing variety of amines as oraganocatalyst.

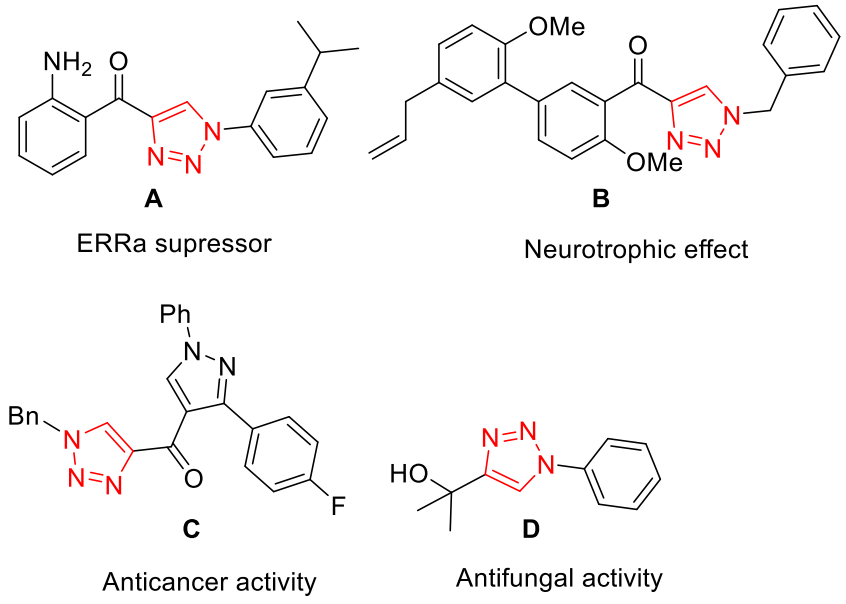
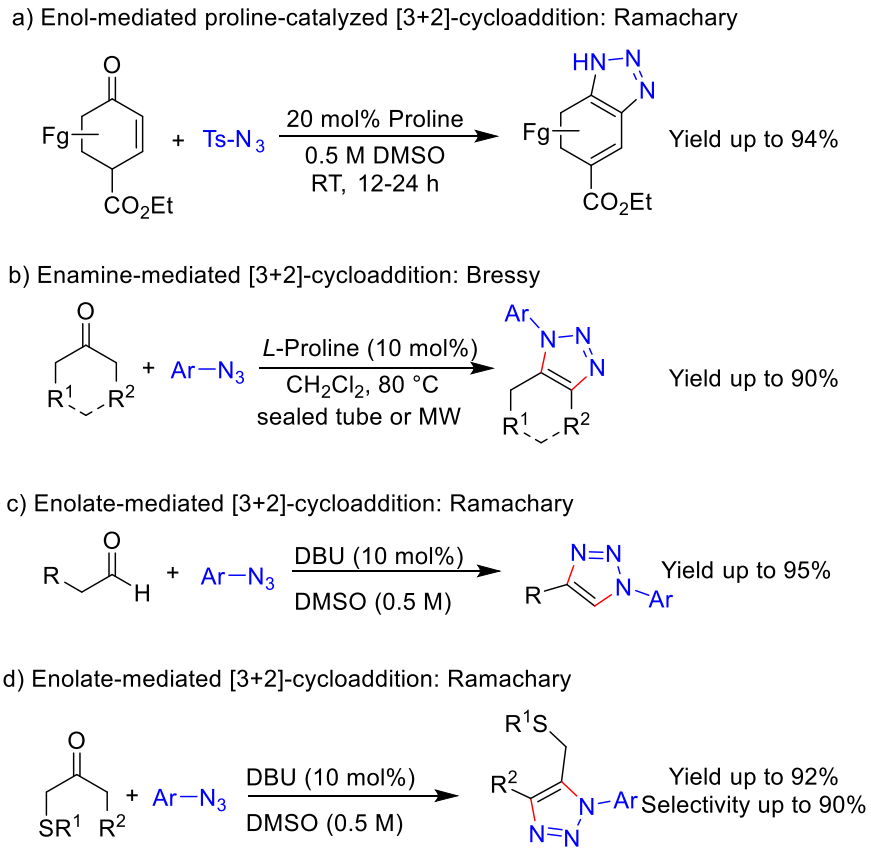



**Figure 3**. Biologically active 1,2,3-triazoles.

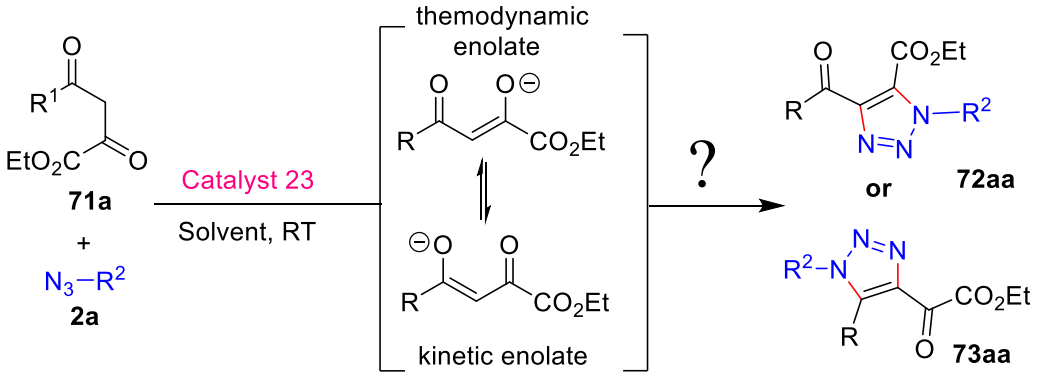
**Scheme 20**: Reaction Design for Organocatalytic Azide-Carbonyl [3+2]-Cycloaddition




In 2008, Ramachary and co-workers reported proline-catalyzed [3+2]-cycloaddition reaction between Hagemann's ester derivatives and tosyl azide, which was the initial footstep towards organocatalytic azide-carbonyl [3+2]-cycloaddition or organo-click reaction using push-pull dienamine strategy.[11] Later in 2011, Bressy *et al.* reported an enamine-mediated [3+2]-cycloaddition for the synthesis of 1,2,3-triazoles using a variety of unactivated cyclic and linear ketones with aryl azides (Scheme 20, a).[12] DBU-catalyzed organocatalytic [3+2]-cycloaddition of a variety of activated carbonyls and aryl azides for the synthesis of trisubstituted-1,2,3-triazoles was developed by Ramachary *et al.* (Scheme 20 b & c).[11] Previous studies showed that alkyl trisubstituted 1,2,3-triazole systems have least scope for the further functional groups modification because of the requirement of expensive reagents and harsh reaction conditions.[26] It is well know that modification of different positions on the 1,2,3-triazole system by incorporation or removal of different functional groups may work better for applications in material, medicinal and drug discoveries. It can be possible either by choosing functionalized starting materials or trisubstituted 1,2,3-triazoles can be further functionalized by various

reactions. Ester and carbonyl groups substituted 1,2,3-triazoles are the most fascinating scaffolds as the ester group and carbonyl can be converted very easily to another functional groups to produce biologically important molecules (Figure 3).[27] Despite of a huge demand, there are very less reports for the direct synthesis of acyl (ester and carbonyl) substituted 1,2,3-triazoles through organocatalytic [3+2]-cycloaddition, this may be due to an uncontrolled reactivity of active methylene compound containing 3 carbonyl groups, which acts as a potential synthon for 1,2,3-triazoles. To overcome the challenges and to understand the regioselectivity of unsymmetrical CH-acids towards [3+2]-cycloaddition, we have developed a suitable methodology to produce ester group containing trisubstituted 1,2,3-triazole through TMG-catalyzed [3+2]-cycloaddition between aryl/alkyl azides and 2,4-diketoesters at room temperature (Scheme 21).

**Scheme 21:** Reaction Design for the OrgAKC Reaction



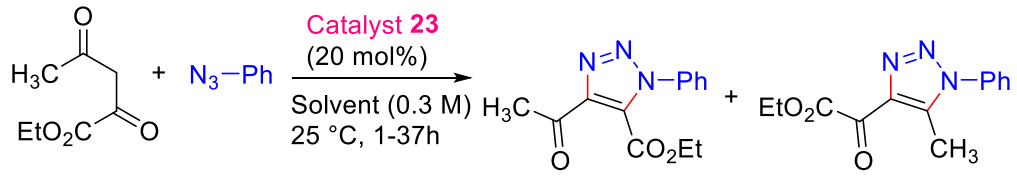

## 3.2 Results and Discussion

### 3.2.1 Reaction Optimization:

We started our optimization with the reaction between ethyl-2,4-dioxopentanoate **71a** (0.3 mmol) and 1.5 equiv. of aryl azide **2a** in presence of 20 mol% DBU **23a** as a base in DMSO solvent at room temperature, within 2 hours exclusively kinetic enolate derived 1,2,3-triazole product **72aa** were formed with a good yield of 80% (Table 1, entry 1). When the same reaction was carried out using a series of different catalysts like 20 mol% of TBD **23b**, TMG **23c**, DABCO **23d**, *L*-proline **23e**, pyrrolidine **23f**, $K_2CO_3$ **23g**, $Cs_2CO_3$ **3h**, and KO$^t$Bu **23i,** delightfully, we observed the best yield with TMG **23c** affording 84% of **72aa** within 1 h (Table

1, entry 2-9)**.** In case of secondary amine like *L*-proline **23e** and pyrrolidine **23f**, yields of the product **72aa** were unexpectedly low (5% and 30% respectively) with an unusual prolonged reaction time of 36 h and 144 h respectively (Table 1, entry 5-6).

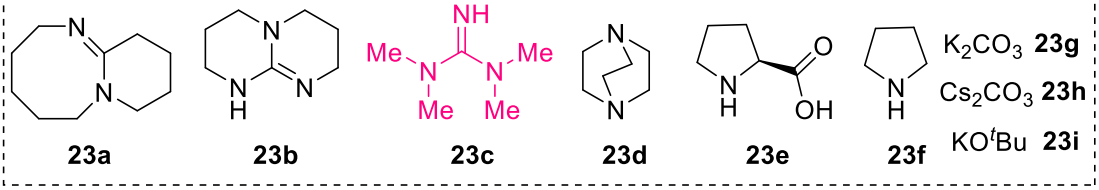
**Table 1:** Reaction optimization for chemoselective for OrgAKC [a]




**71a** **2a** **72aa** **73aa**

| Entry | Catalyst (20 mol%) | Solvent (0.3 M) | T (*h*) | Yield (%)[b] | Ratio[c] **72/73** |
|---|---|---|---|---|---|
| 1 | **23a** | DMSO | 3 | 80 | >20:1 |
| 2 | **23b** | DMSO | 5 | 63 | >20:1 |
| 3 | **23c** | DMSO | 1 | 84 | >20:1 |
| 4 | **23d** | DMSO | 6 | 64 | >20:1 |
| 5 | **23e** | DMSO | 36 | 05 | >20:1 |
| 6 | **23f** | DMSO | 144 | 30 | >20:1 |
| 7 | **23g** | DMSO | 1.7 | 79 | >20:1 |
| 8 | **23h** | DMSO | 2 | 70 | >20:1 |
| 9 | **23i** | DMSO | 2 | 75 | >20:1 |
| 10[d] | **23a** | DMF | 37 | 50 | >20:1 |
| 11[d] | **23a** | $CHCl_3$ | 22 | 15 | >20:1 |
| 12[d] | **23a** | $CH_3CN$ | 37 | 15 | >20:1 |
| 13[e] | **23c** | DMSO | 1 | 71 | >20:1 |
| 14[f] | **23c** | DMSO | 2 | 64 | >20:1 |

[a] Reaction carried out in solvent (0.3 M) with **71a** (0.3 mmol), **2a** ( 1.5 equiv.) and catalyst **23**, [b] Yield refers to column-purified product, [c] Ratio of isomers determined by $^1$H NMR analysis of the reaction mixture. [d] Starting material **71a** recovered with **23a** catalyst.[e,f] Catalyst **23c** is used 25 mol% and 10 mol% respectively.



This observation indicates that enolate chemistry was working faster than the enamine chemistry in our present protocol. After understanding the best catalyst, we further moved on screening different solvents like DMF, acetonitrile and chloroform, but none of them performed better than DMSO (Table 1, entry 10-12) and in all the cases, remaining starting material **71a** was recovered in a quantitative amount. Another two experiments were conducted for checking effectiveness of TMG **23c** via changing the catalytic loading from 20 mol% to 25 mol% and 10 mol%, but no improvement of yield was found (Table 1, entries 13 & 14). From the thorough investigation we have concluded that ethyl-2,4-dioxopentanoate **71a** (0.3 mmol) and 1.5 equiv. of aryl azide **2a** in presence of 20 mol% TMG **23c** as a base in DMSO solvent at room temperature is the most favorable condition for the present protocol (Table 1, entry 3).

The structure of the compound **72aa** was further confirmed by X-Ray crystallography (Figure 4).

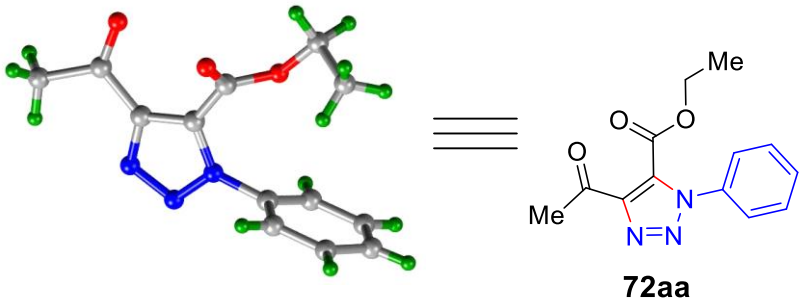



**Figure 4:** The crystal structure of ethyl 4-acetyl-1-phenyl-1*H*-1,2,3-triazole-5-carboxylate **72aa**.

$^{1}$H and $^{13}$C NMR spectra of **72aa** from optimization Table 1 depicted in Figure 5.

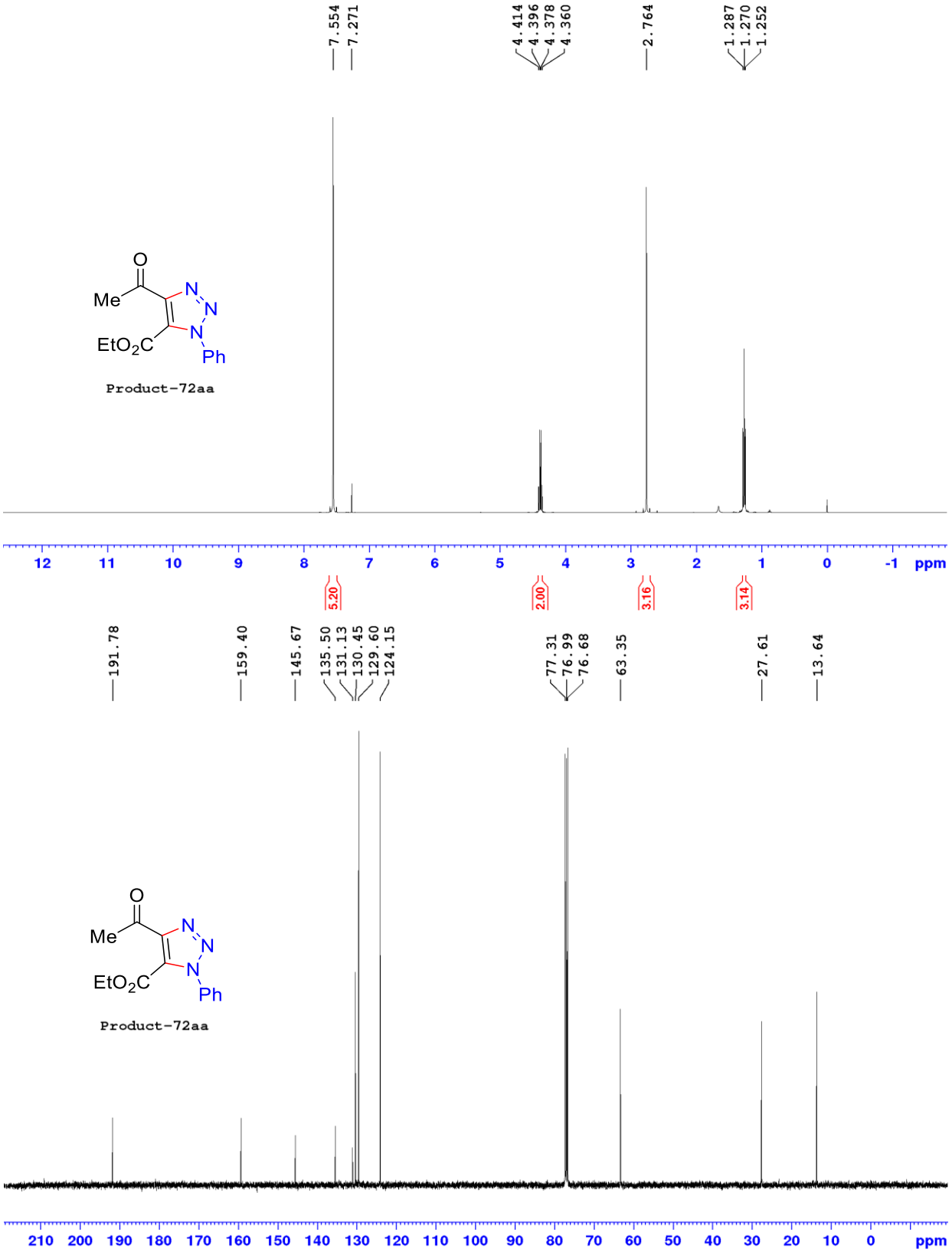
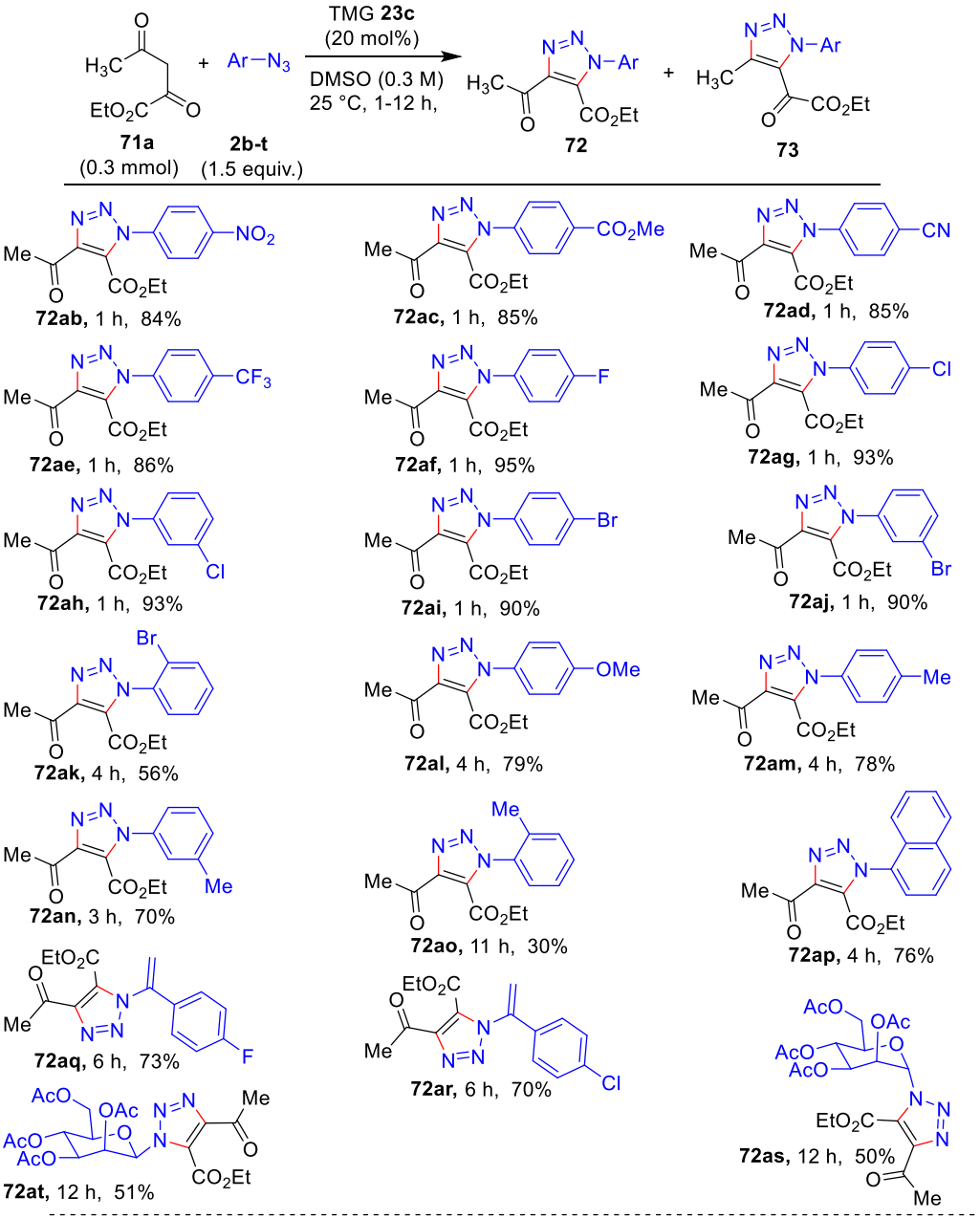



**Figure 5:** $^{1}$H NMR and $^{13}$C NMR spectra of product **72aa**.

### 3.2.2 Reaction Scope of Azides:

With the optimized condition in hand, the scope of aryl azides were investigated (Table 2). First, we decided to use aryl azides, vinyl azides and sugar azides **2b-2t** in the click reaction with **71a**.

**Table 2:** Reaction scope of azides for chemoselective OrgAKC.[a]




[a]Reactions were carried out in DMSO (0.3 M) with 1.5 equiv of **2** relative to **71a** (0.3 mmol) in the presence of 20 mol % **23c** at 25°C. Yield refers to the column-purified product.

All the electron-deficient aryl azides **2b**-**2e** reacted well with **1a** within a short time of 1 h forming product **71ab-71ae** with very good yield of 84-85% (Table 2). The halogens such as fluorine, chlorine and bromine substituted at *para-/meta*- position on the phenyl ring of azides **2f**-**2j** proceeded smoothly in this reaction to furnish **72af-72aj** with excellent yield of 90-95% within 1 h. When the bromine substituted at *ortho*- position of phenyl ring on azide **2k**, reaction furnished **72ak** with a low yield 56% in a longer reaction time of 4 h, indicating a clear effect of increased steric factor. Electron-rich *para*-methoxy substituted azide **2l** afforded **72al** with a yield of 79% in 4 h. When the substituent positions varied from *para*-, *meta*- to *ortho*-methyl substituted aryl azides **2m-o**, a clear effect of steric factor has observed with a gradual decrement of the yields with 78%, 70% and 30% within 3 h, 4 h and 11 h respectively. We explored the electron neutral 2-naphthyl azide **2p**, halogenated $\alpha$-azidostyrene **2q** and **2r**, reaction performed well producing **72ap**, **72aq** and **72ar** with 76%, 73% and 70% respectively. $\alpha$-sugar azide **2s** and $\beta$-sugar azide **2t** also produced impressive yield of **72as** and **72st** in 51% and 50% respectively within 12 h (Table 2).

$^{1}$H and $^{13}$C NMR spectra of few compounds from Table 2 have depicted in Figure 6-11.

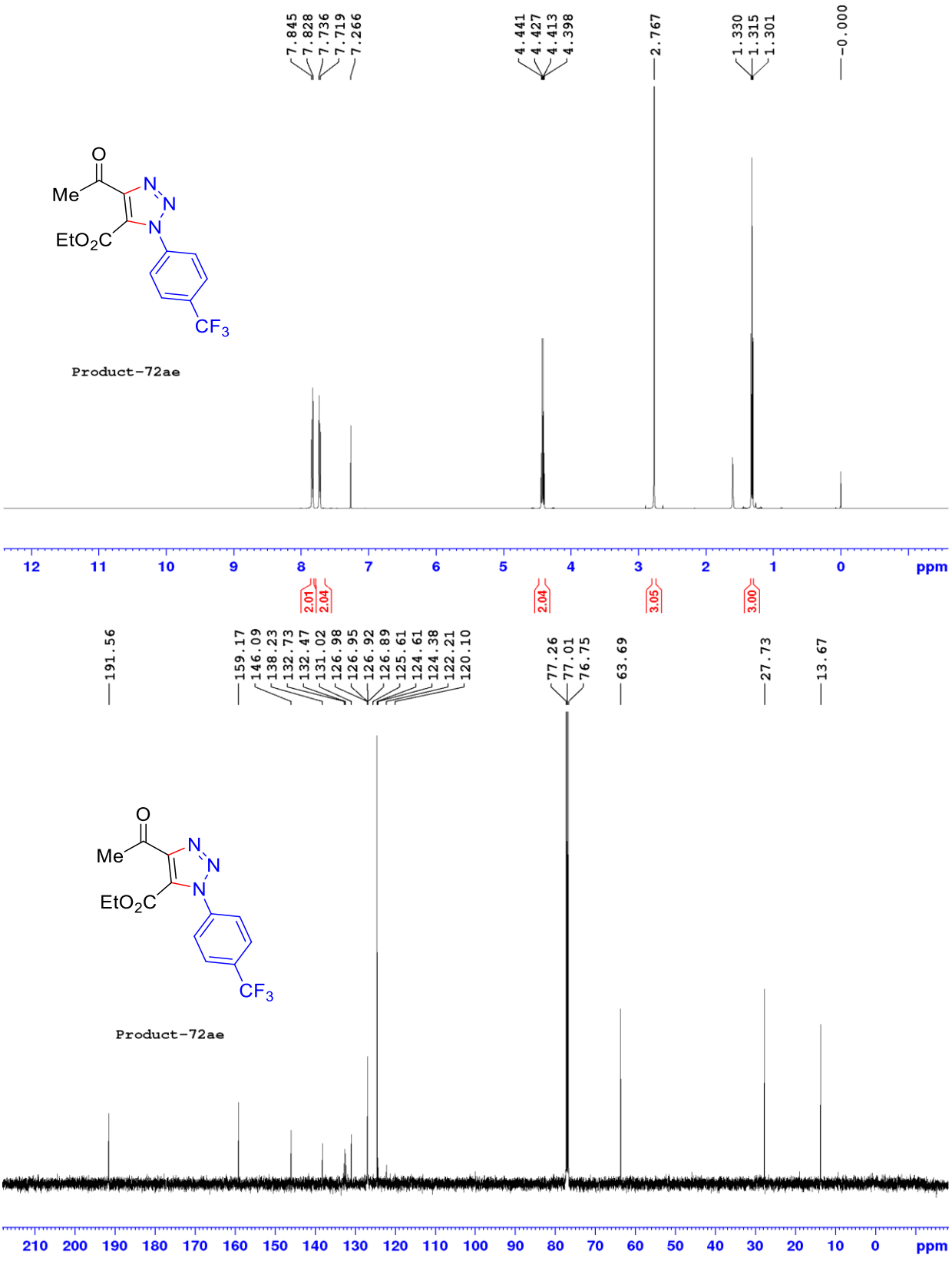



**Figure 6:** $^{1}$H NMR and $^{13}$C NMR spectra of product **72ae**.

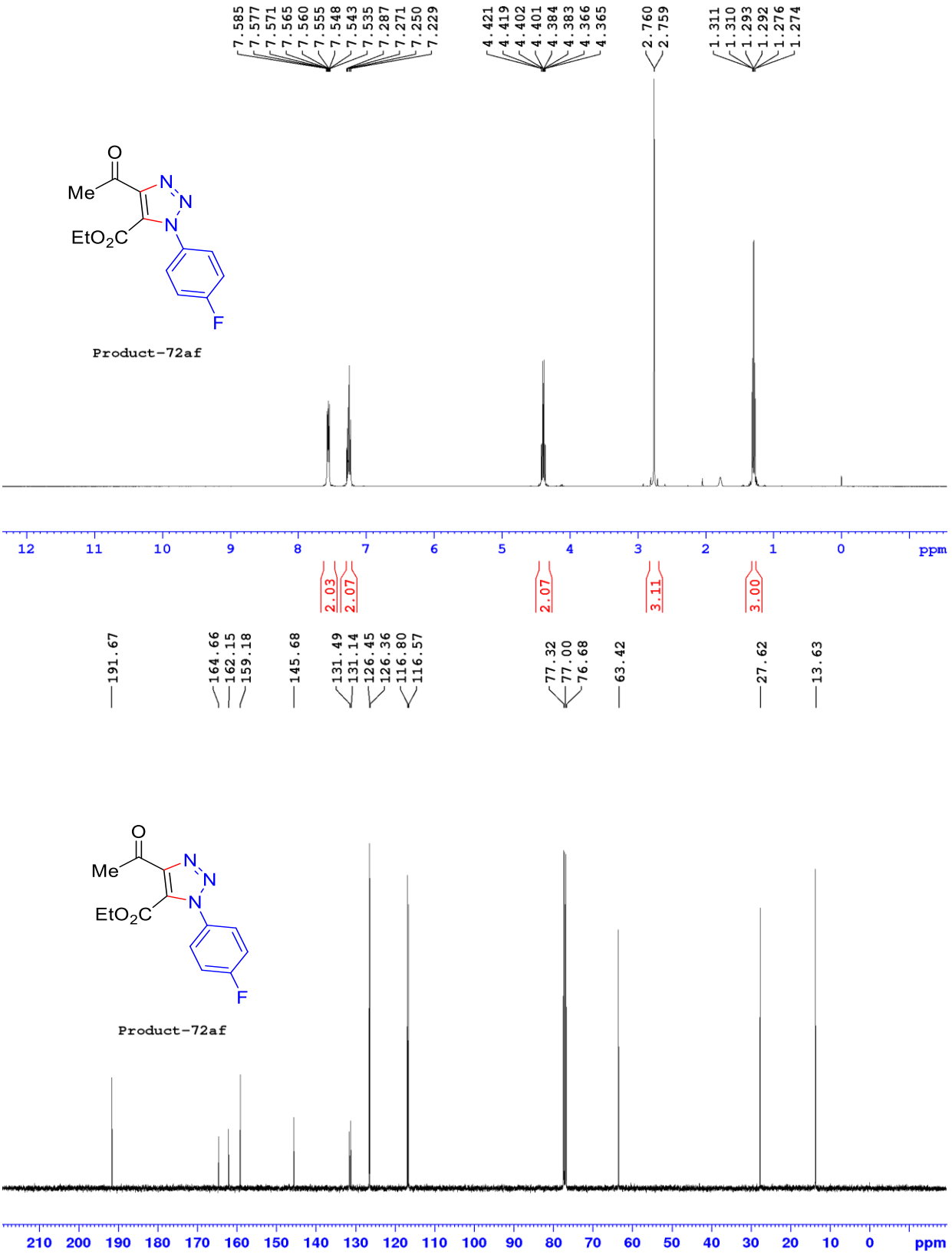



**Figure 7:** $^{1}$H NMR and $^{13}$C NMR spectra of product **72af**.

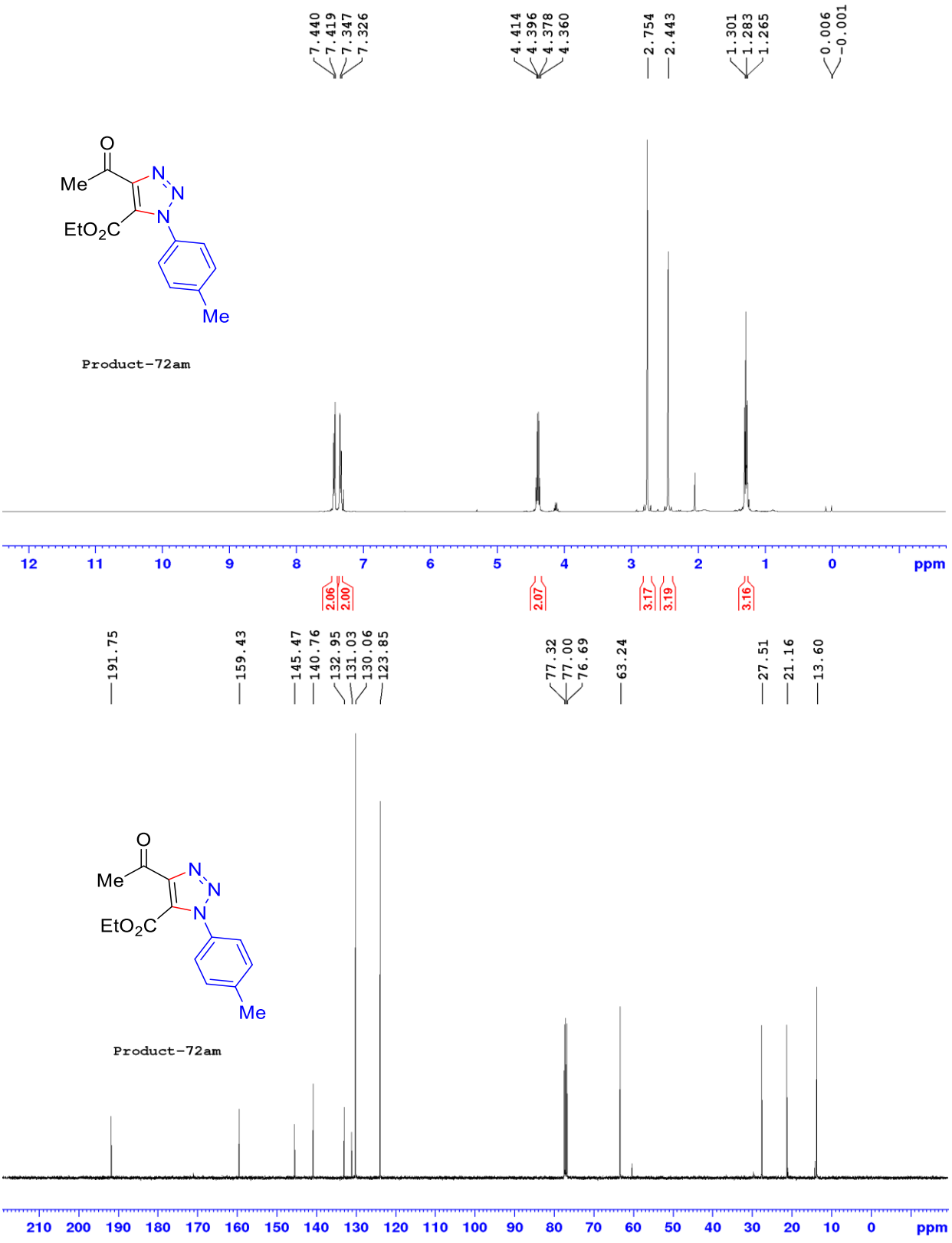



**Figure 8:** $^{1}$H NMR and $^{13}$C NMR spectra of product **72am**.

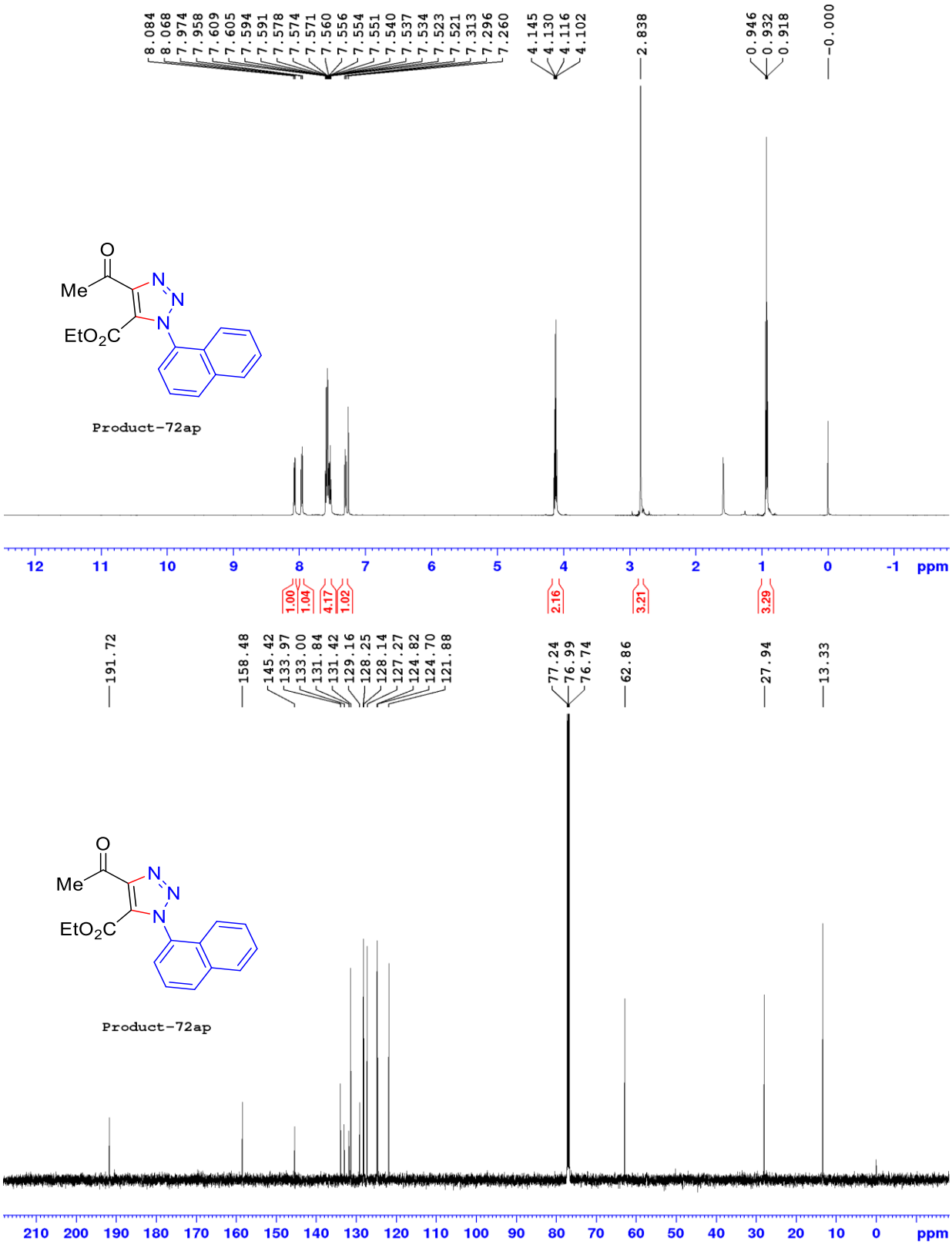



**Figure 9:** $^{1}$H NMR and $^{13}$C NMR spectra of product **72ap**.

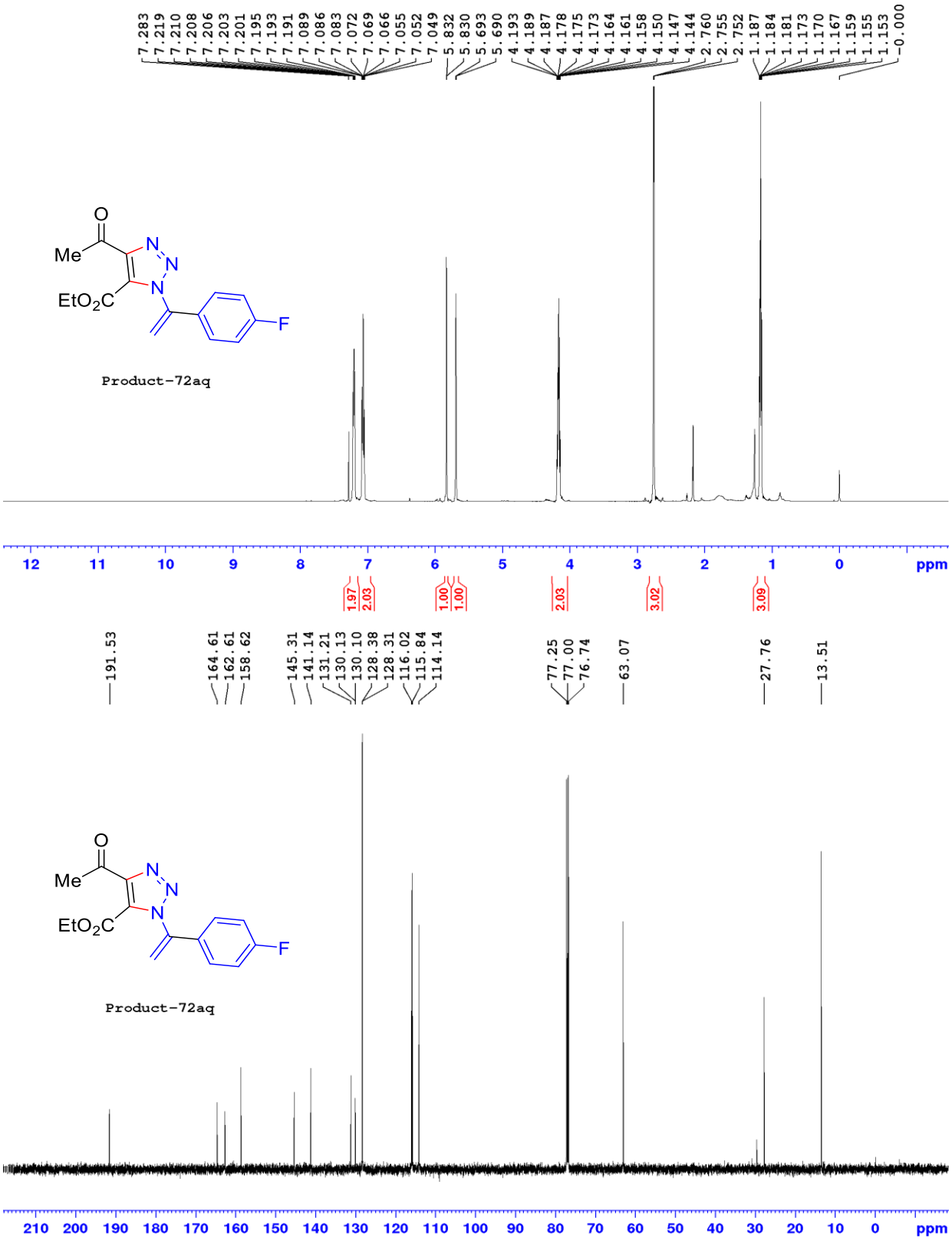



**Figure 10:** $^{1}$H NMR and $^{13}$C NMR spectra of product **72aq**.

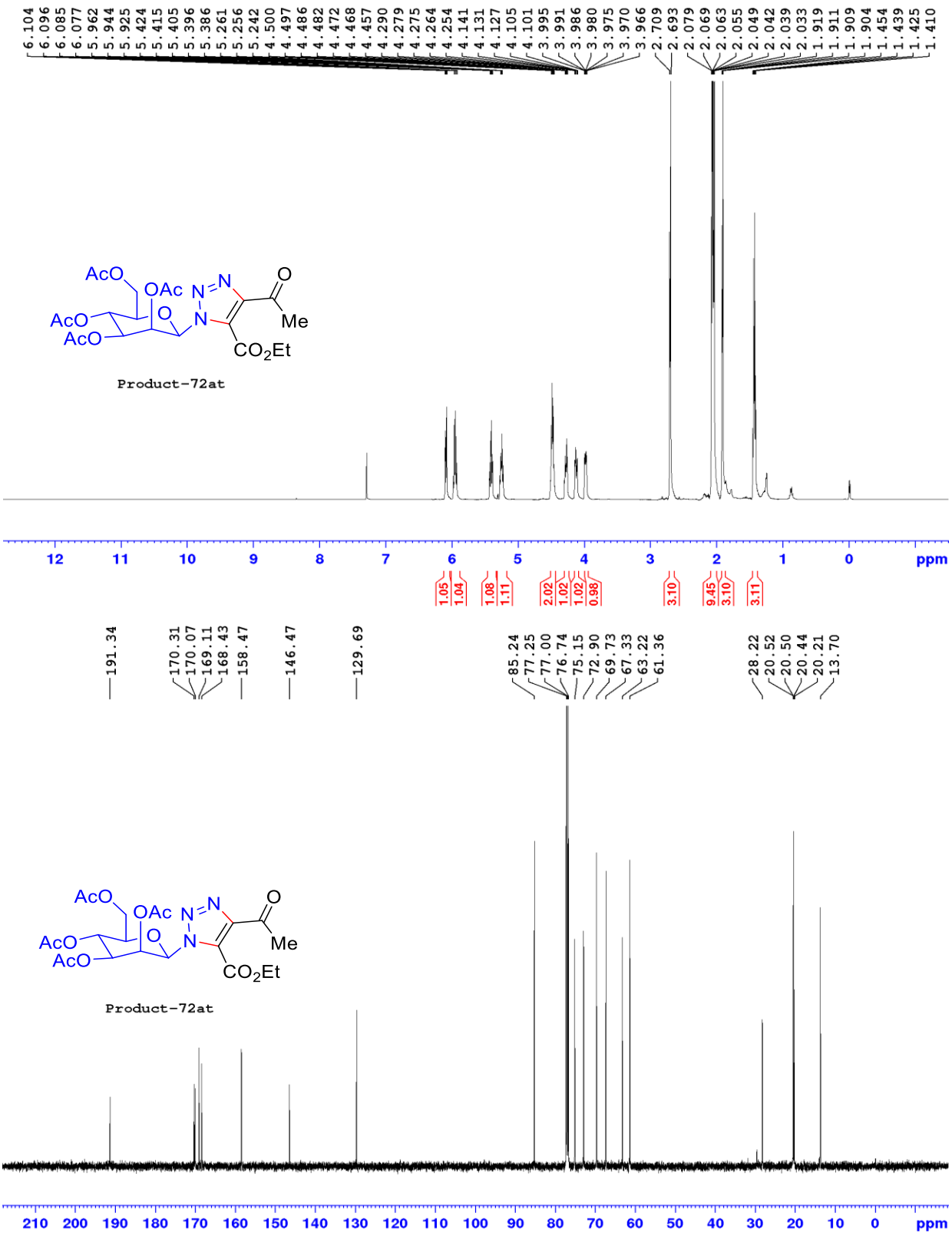
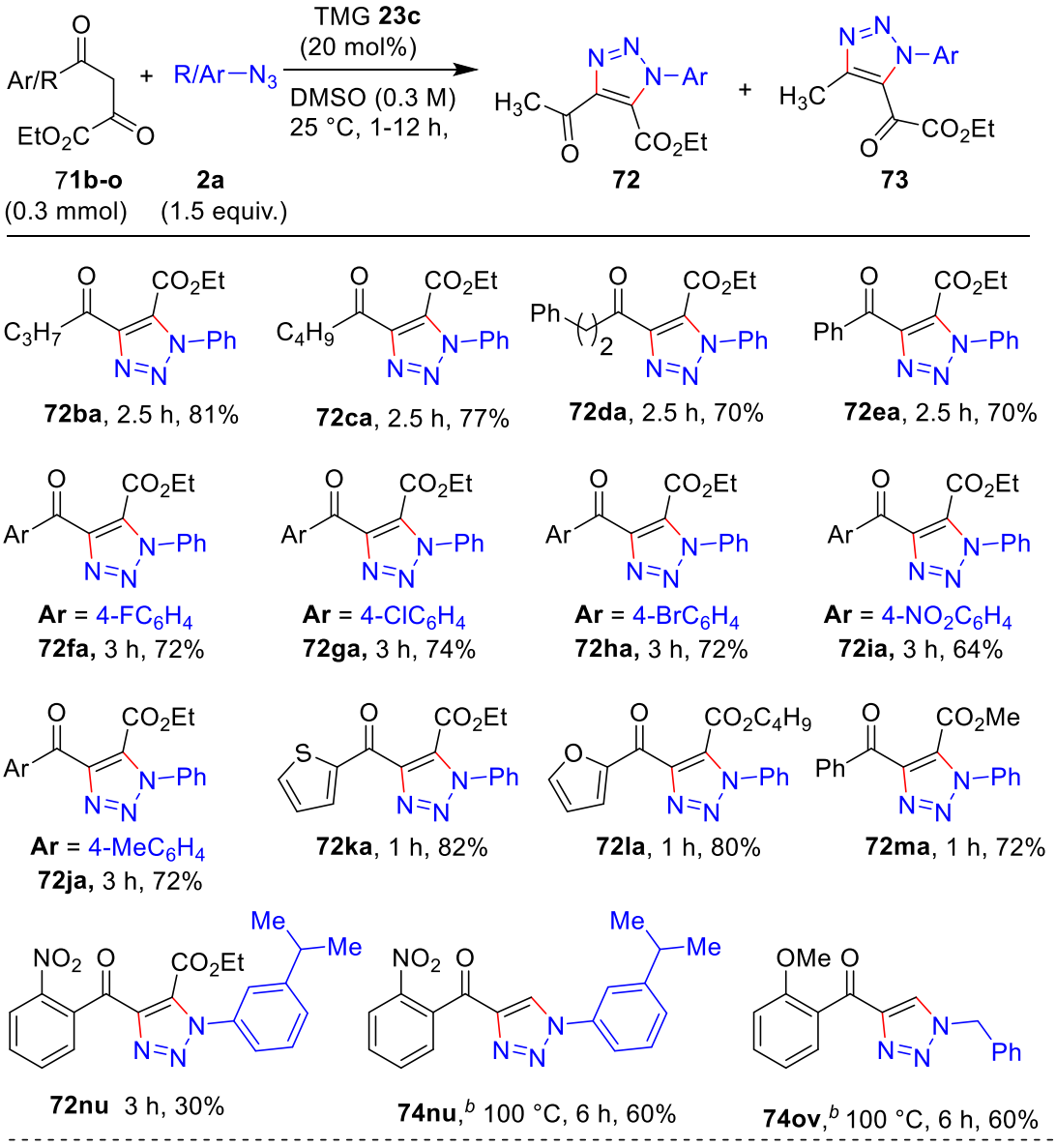



**Figure 11:** $^{1}$H NMR and $^{13}$C NMR spectra of product **72at**.

**3.2.3 Reaction Scope of different 2,4-diketoesters:** After having a thorough investigation of azide scopes, we further examined the scope of 2,4-diketosters **71b**–**71o** (Table 3). For the same, when alkyl-substituted 2,4-diketoester **71b-71d** reacted with aryl azides **2a** in the presence of 20 mol% of TMG **23c** at 25 ºC in DMSO solvent, reaction furnished **72ba**, **72ca** and **72da** in 81%, 77% and 70% yields within 2.5 h respectively (Table 3).

**Table 3:** Reaction scope with different diketoesters for chemoselective OrgAKC.[a]




[a] Reactions were carried out in DMSO (0.3 M) with 1.5 equiv of **2** relative to **71** (0.3 mmol) in the presence of 20 mol % **23c**. Yield refers to the column-purified product. [b] Reaction performed under $K_2CO_3$ at 100°C in DMSO (0.3 M) for **74nu** and dryDMF/EtOH (0.3 M) for **74ov**.

We extended our investigation towards different electronic factors by using electron neutral phenyl **72e**, halogen substituted phenyl ring containing 2,4-diketosters 7**1f-71i**, electron withdrawing group such as *p*-$NO_2$ substituted 2,4-diketosters **71i**, electron donating group such as *p*-Me substituted 2,4-diketosters **71j** and reacted with phenyl azide **2a** in presence of 20 mol% of TMG in DMSO solvent which furnished 1,2,3-triazoles **72ea-72ja** in 64-74% yield within 3 h (Table 3). With the same reaction conditions, heterocyclic aromatic ring containing 2,4-diketoester **71k**, **71l** and **71m** have utilized in our present protocol which afforded **72ka**, **72la** and **72ma** in good yields of 80%, 82% and 72% respectively within 1 h (Table 3). When *O*-Nitro substituted phenyl ring containing 2,4-dieketoester **71n** treated with electron-rich *meta*-$^{i}$Pr substituted aryl azide **2u**, the [3+2]-cycloaddition reaction afforded 1,4-disubstituted 1,2,3-triazole **72nu** with 30% yield in DMSO solvent within 3h (Table 3). Fascinatingly, the [3+2]-cycloaddition reactions using alkali base $K_2CO_3$ as catalyst for **71n** with **2u** in DMSO solvent and **71o** with **2v** in DMF or EtOH solvents (as in DMSO solvent reaction was not moving) at RT for 2 h followed by 100 ºC for 4 h, produced **74nu** and **74ov** with 60% yield in both the cases (Table 3).

The structure of compound **72ga** was further confirmed by X-Ray crystallography (Figure 12).

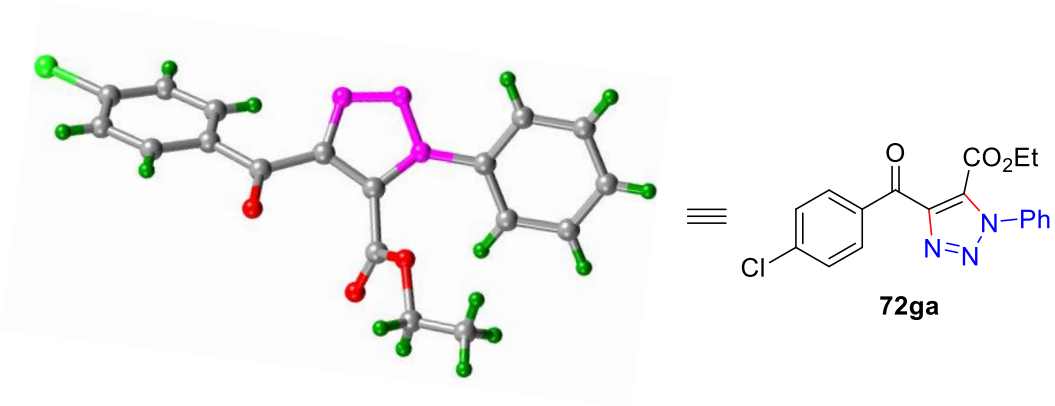



**Figure 12:** Crystal structure of Ethyl 4-(4-chlorobenzoyl)-1-phenyl-1*H*-1,2,3-triazole-5-carboxylate **72ga.**

$^{1}$H and $^{13}$C NMR spectra of few compounds from Table 3 have depicted in Figures 13-17.

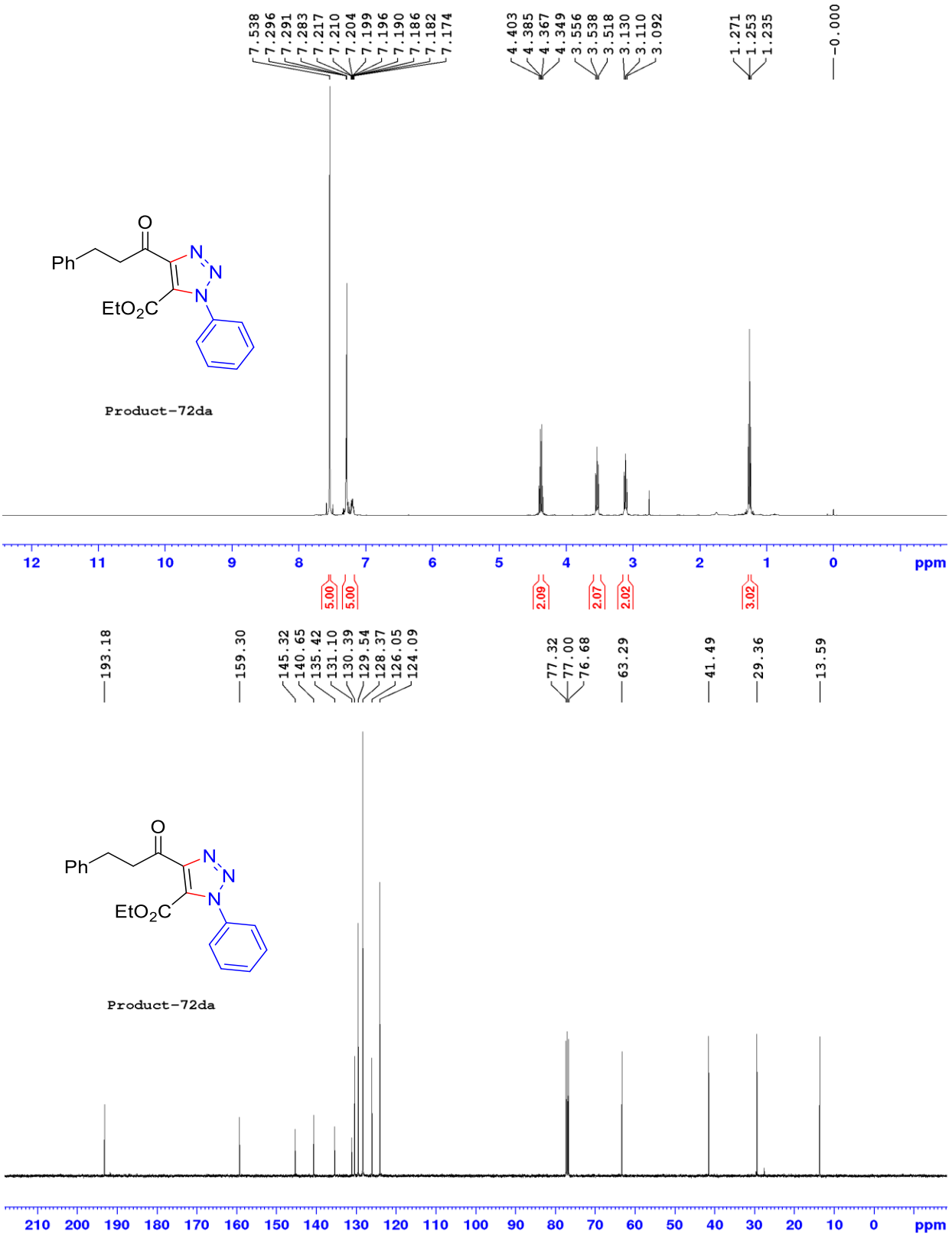



**Figure 13:** $^{1}$H NMR and $^{13}$C NMR spectra of product **72da.**

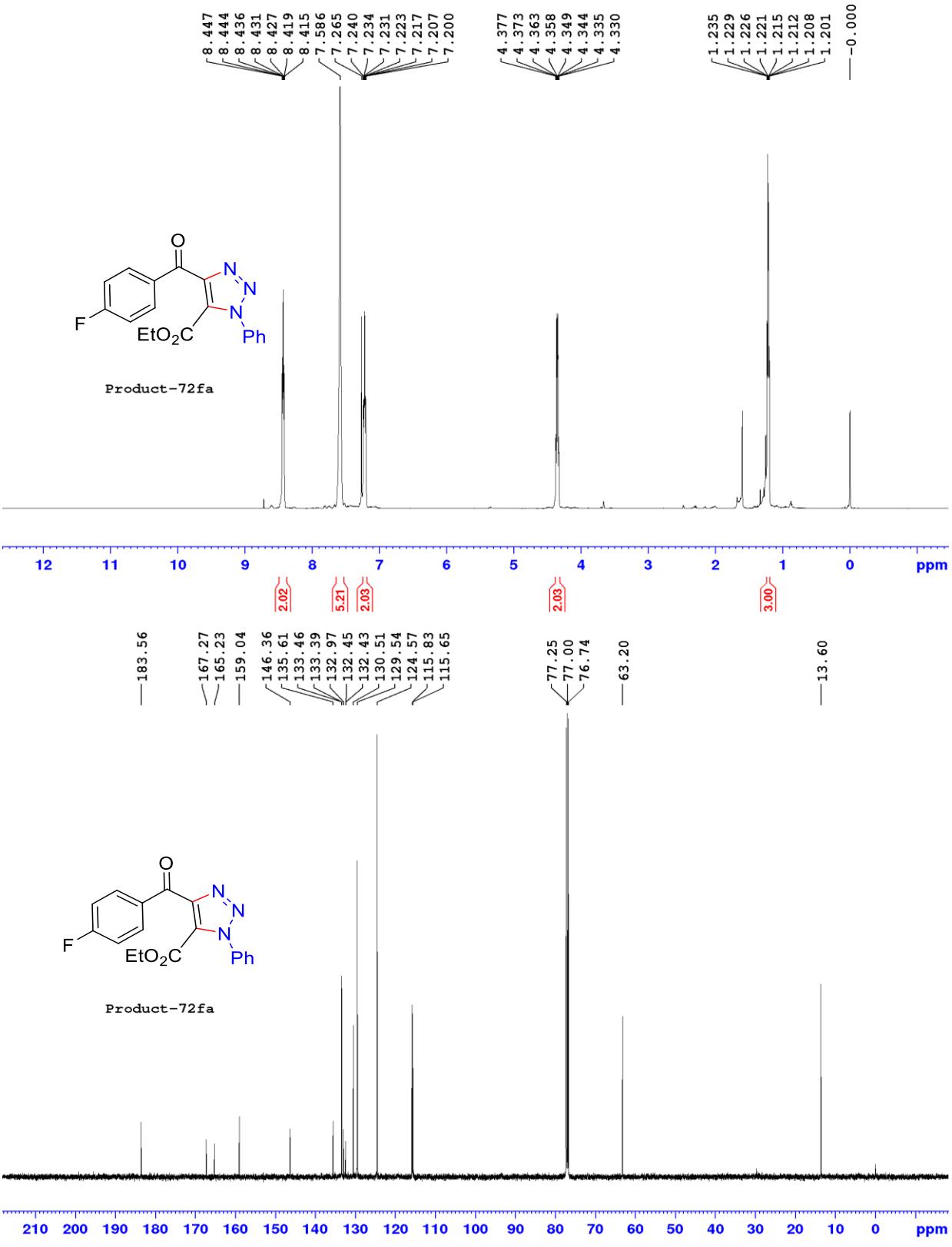



**Figure 14:** $^{1}$H NMR and $^{13}$C NMR spectra of product **72fa.**

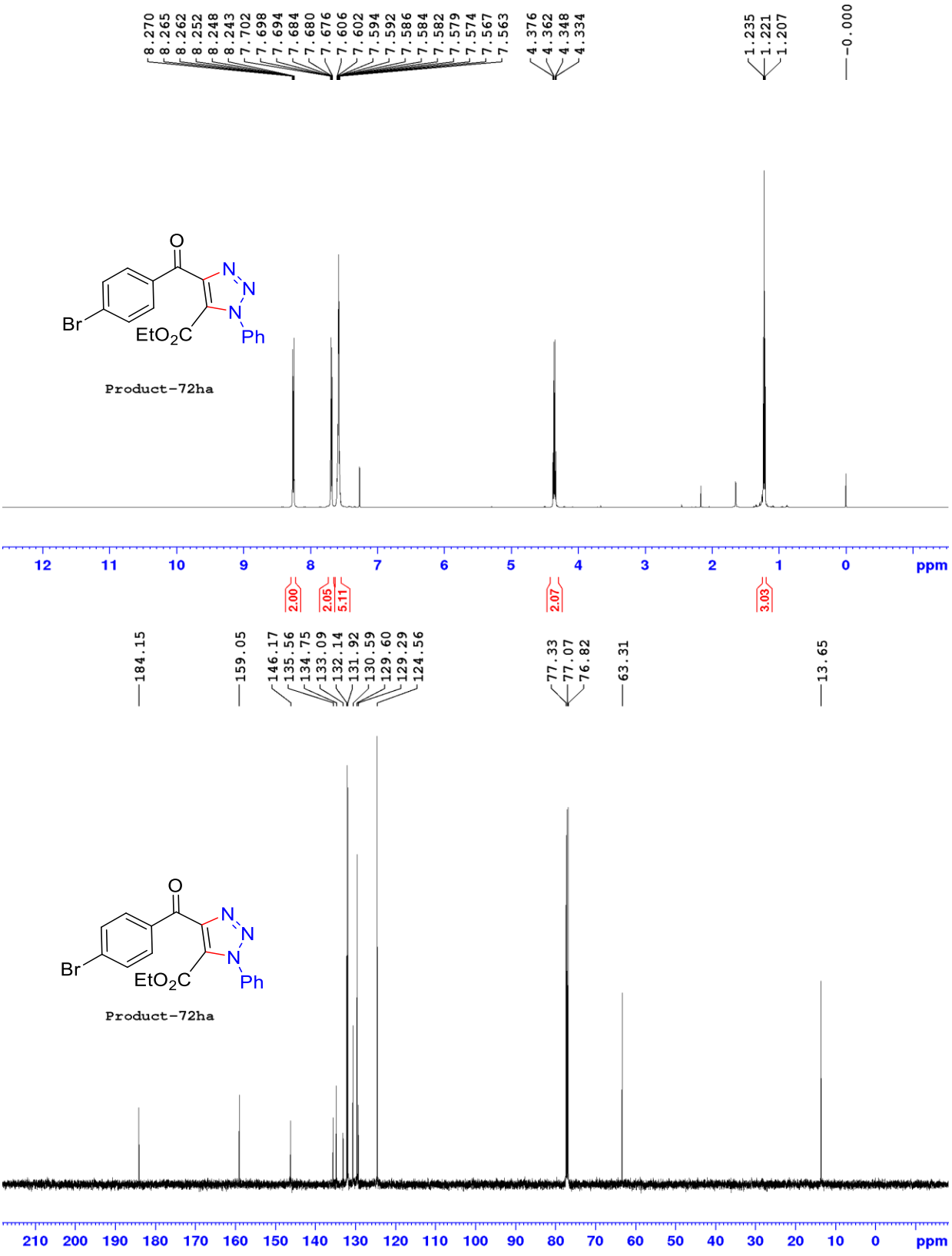



**Figure 15:** $^{1}$H NMR and $^{13}$C NMR spectra of product **72ha.**

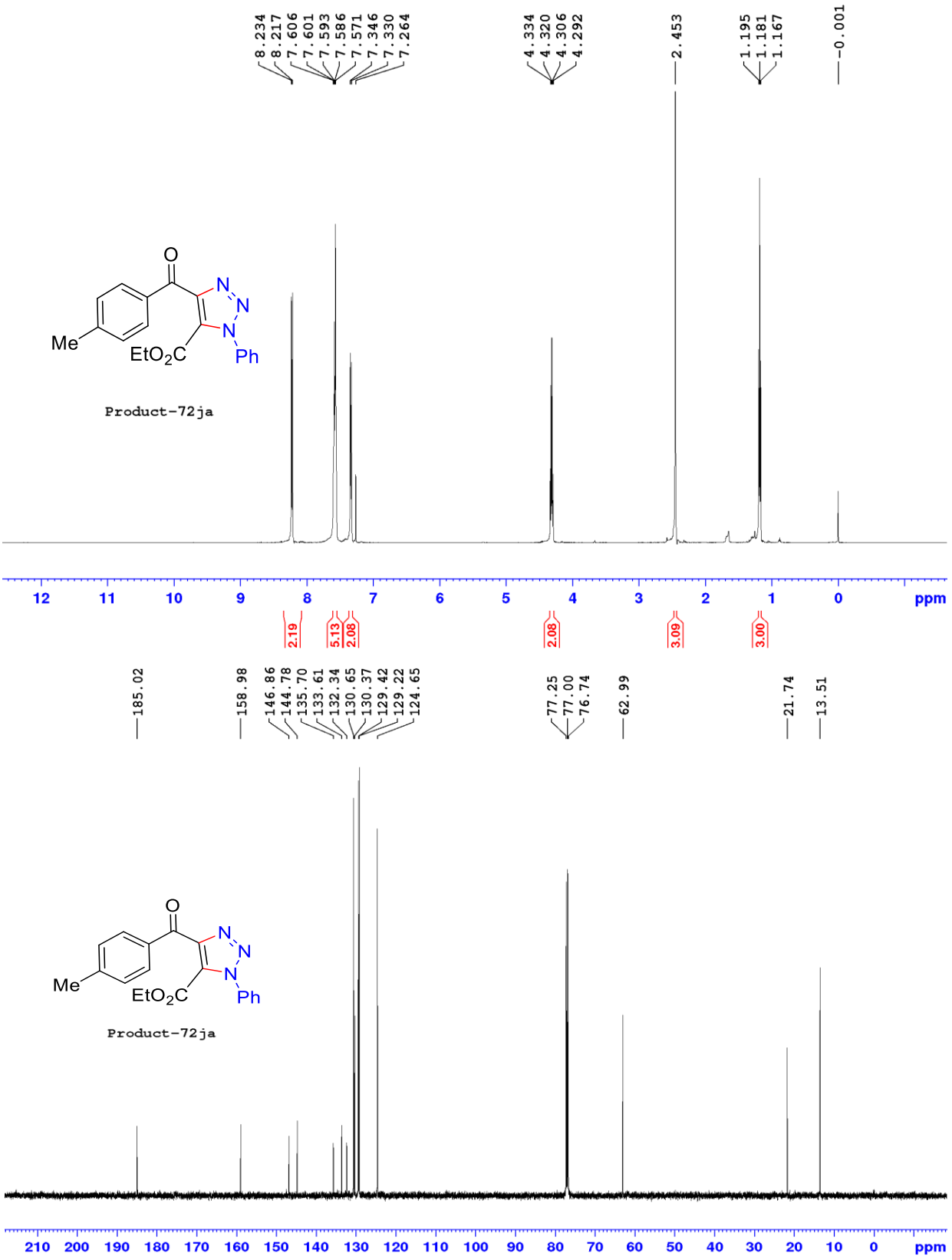



**Figure 16:** $^{1}$H NMR and $^{13}$C NMR spectra of product **72ja.**

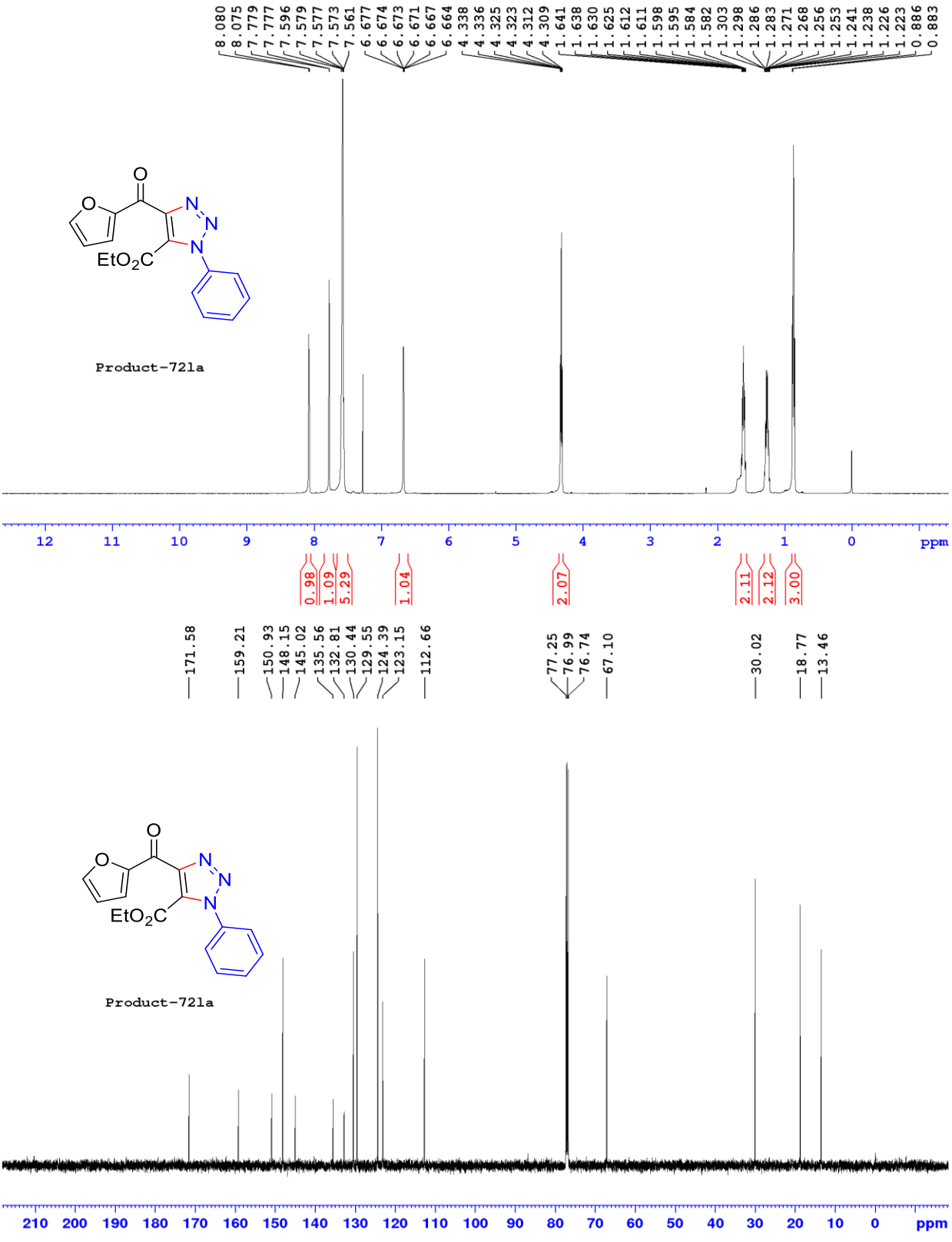
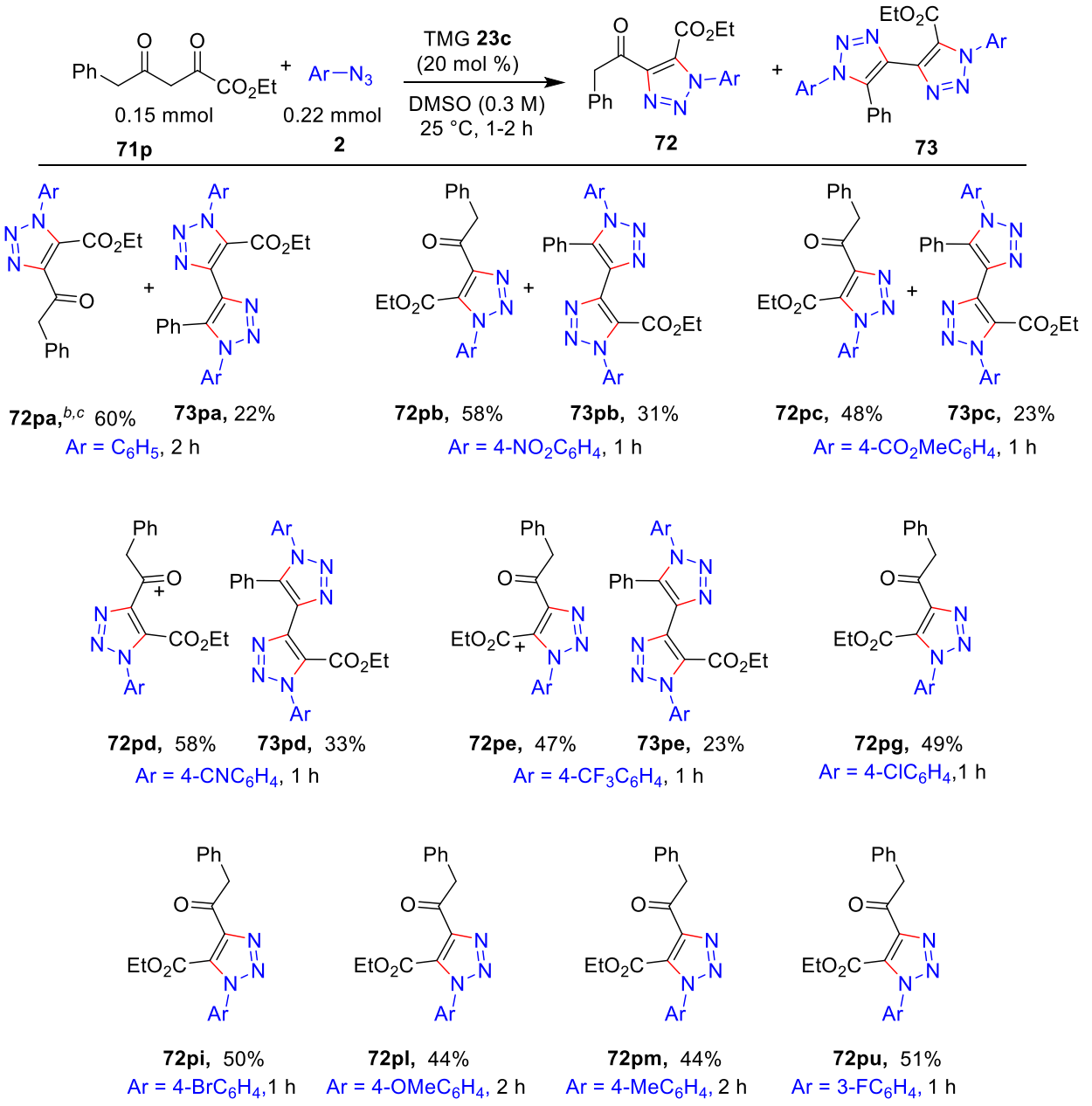



**Figure 17:** $^{1}$H NMR and $^{13}$C NMR spectra of product **72l**

**Table 4:** Reaction scope of azides.[a]




[a] Reactions were carried out in solvent (0.3 M) with 1.5 equiv of **2** relative to **71a** (0.15 mmol) in the presence of **23c.** Yields refers to the column-purified products. [b] 1.5 equiv. of **2a** with respect to 0.3 mmol of **71p.** [c] 2.0 equiv. of **2a** was used with **71p** (0.3 mmol) for 6 h.

There are few previous reports discussed about the synthesis of bis-triazoles through metal-mediated azide-alkyne [3+2]-cycloaddition reactions followed by oxidative dimerization of 1,2,3-triazoles using metal reagents.[6-10] Eagerly, we intended to employ our present protocol for the synthesis of bis-1,2,3-triazoles. For the same, we have performed the reaction of ethyl-2,4-

dioxo-5-phenylpentanoate **71p**, which has two activate methylene centres with phenyl azide **2a** (1.5 equiv.) under optimized reaction conditions, within 2 h, reaction afforded a mixture of mono-1,2,3-triazole **72pa** and bis-1,2,3-triazole **73pa** with 60% and 22% of yields respectively along with many unidentified by-products in trace amounts. When 2.0 equiv. of azide **2a** was used, there was no increment in the yield (Table 4). The reaction between **71p** (0.15 mmol) and electron-deficient aryl azides **2b-2e** (1.5 equiv.) in presence of 20 mol% of TMG **23c** in DMSO solvent, reaction produced **72pb** (58%) and **73pb** (31%), **72pc** (48%) and **73pc (**23%), **72pd** (58%) and **73pd (**33%), **72pe** (47 %) and **73pe** (23%) respectively within 1 h (Table 4). To understand the reactivity of compound **71p** towards different azides, we performed the reactions between **71p** and halogenated aryl azides **2g**, **2i** and **2u**, electron-rich azides **2l** and **2m**, to furnish **72pg**, **72pi**, **72pu**, **72pl** and **72pm** with 49%, 50%, 44%, 44% and 51% yields respectively within 1 h (Table 4). Bis-triazole products **73** were formed with <5% yield in all these (**2g**, **2i**, **2u**, **2l** and **2m**) cases confirmed through TLC analysis, but unable to isolate. we observed that after 1 h, **71p** was consumed totally but **2a** was still there in the reaction medium, with multiple unidentified spots along with the spots of compound **2a** and products **72** and **73** in the TLC analysis, which clearly indicates the decomposition of **71p** during the reaction, causing the less yield of **72** and **73** in case of **2g**, **2i**, **2u**, **2l** and **2m**.

The structure of compound **73pa** was further confirmed by X-Ray crystallography (Figure 18).

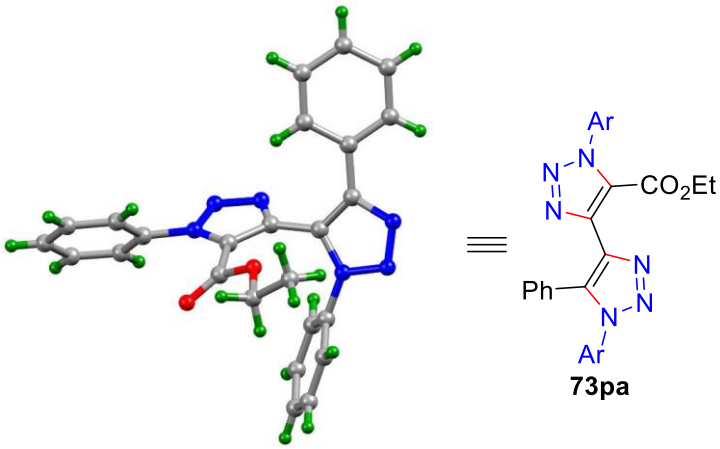



**Figure 18:** Crystal structure of ethyl 1,3',5'-triphenyl-1*H*,3'*H*-[4,4'-bi(1,2,3-triazole)]-5-carboxylate **73pa**.

$^{1}$H and $^{13}$C NMR spectra of few compounds from Table 4 have depicted in Figure 19-23.

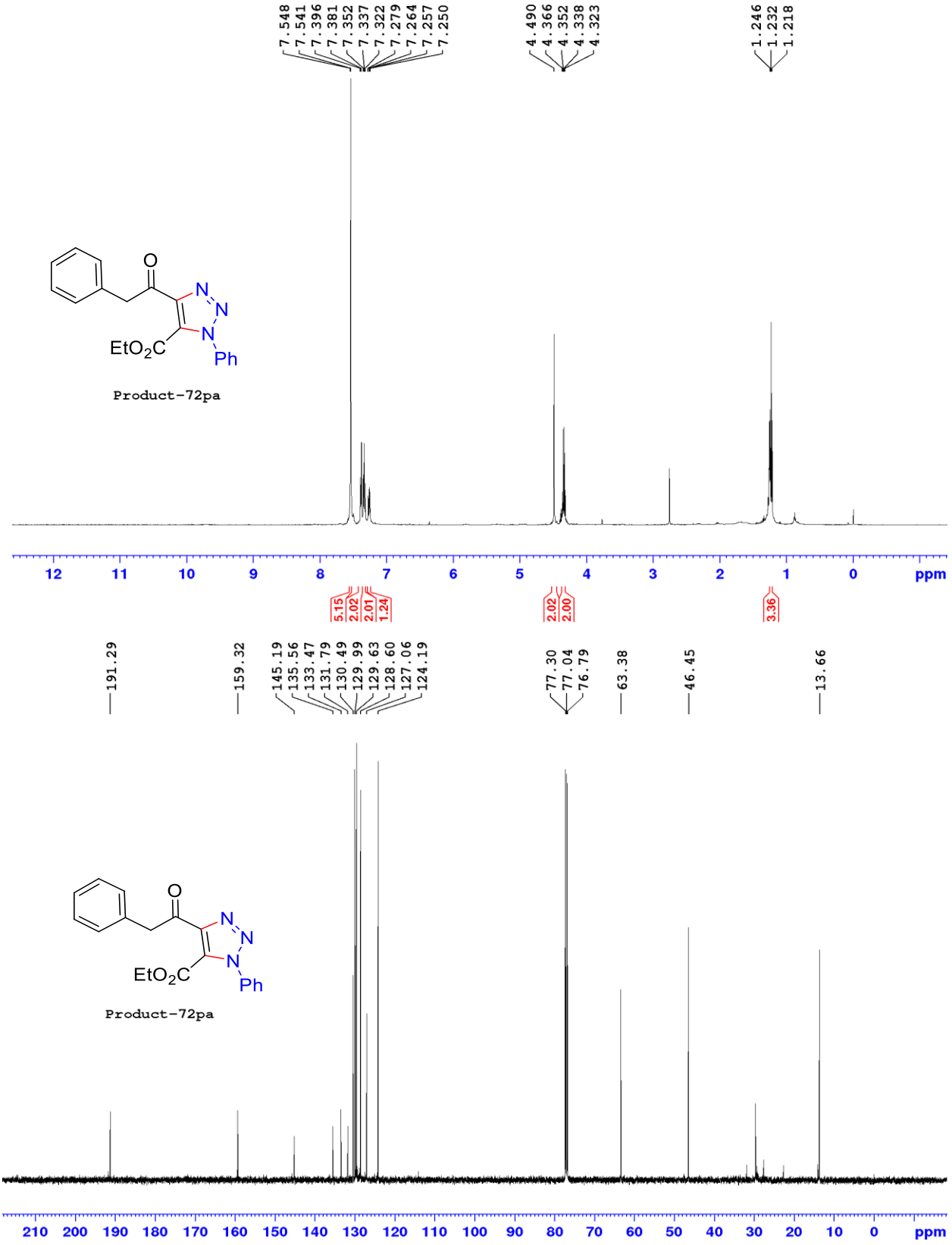



**Figure 19:** $^{1}H$ NMR and $^{13}C$ NMR spectra of product **72pa.**

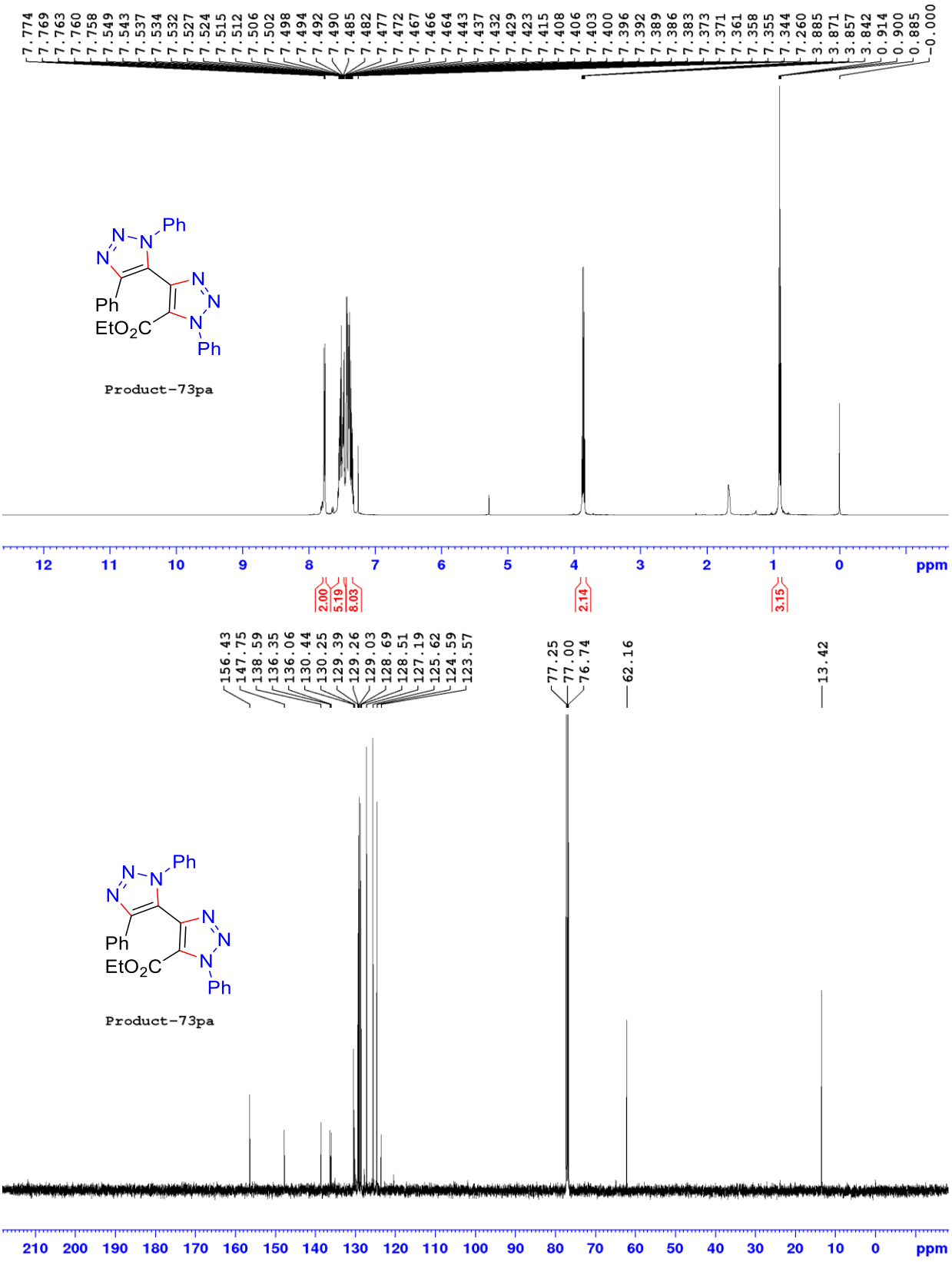



**Figure 20:** $^{1}$H NMR and $^{13}$C NMR spectra of product **73pa.**

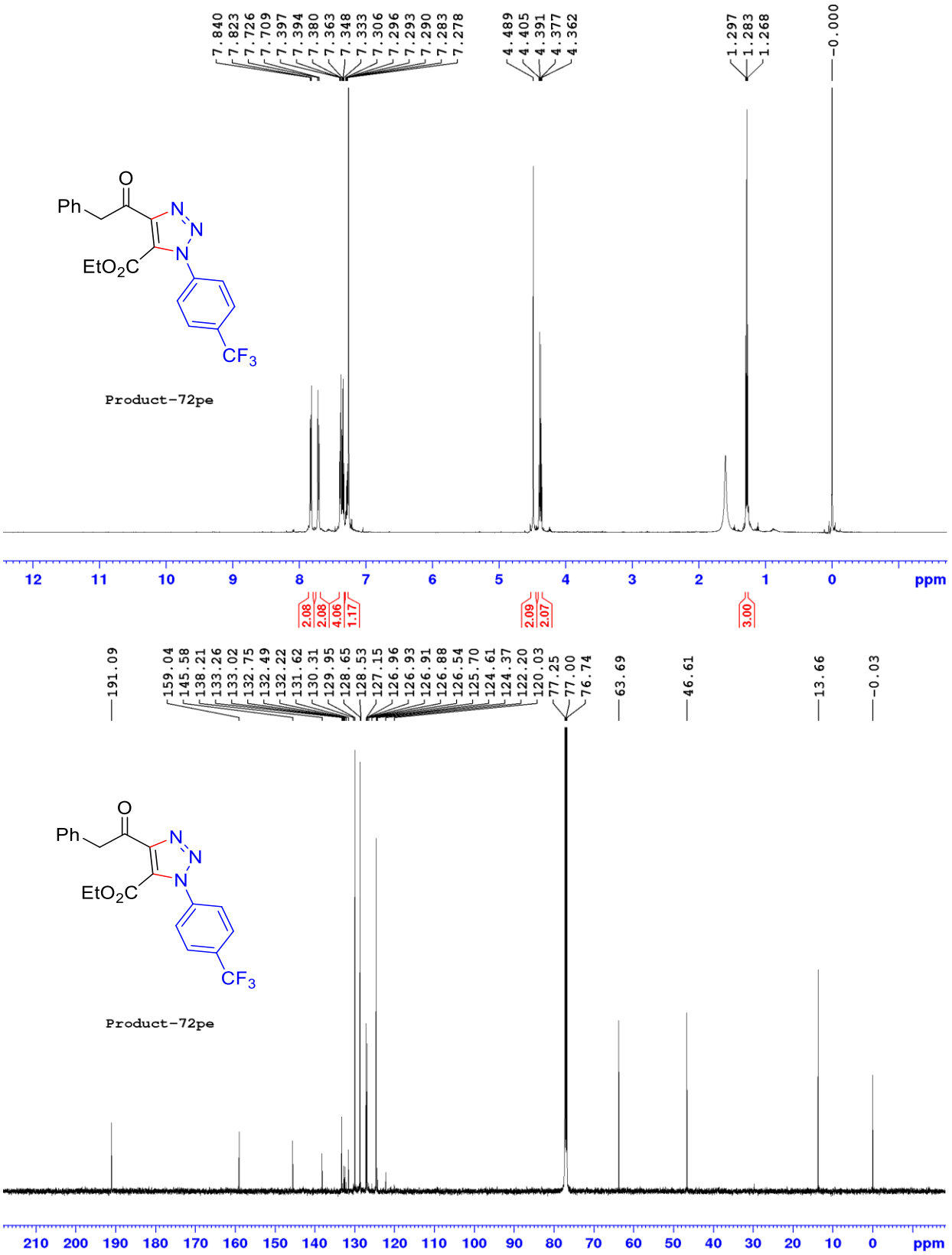



**Figure 21:** $^{1}$H NMR and $^{13}$C NMR spectra of product **72pe.**

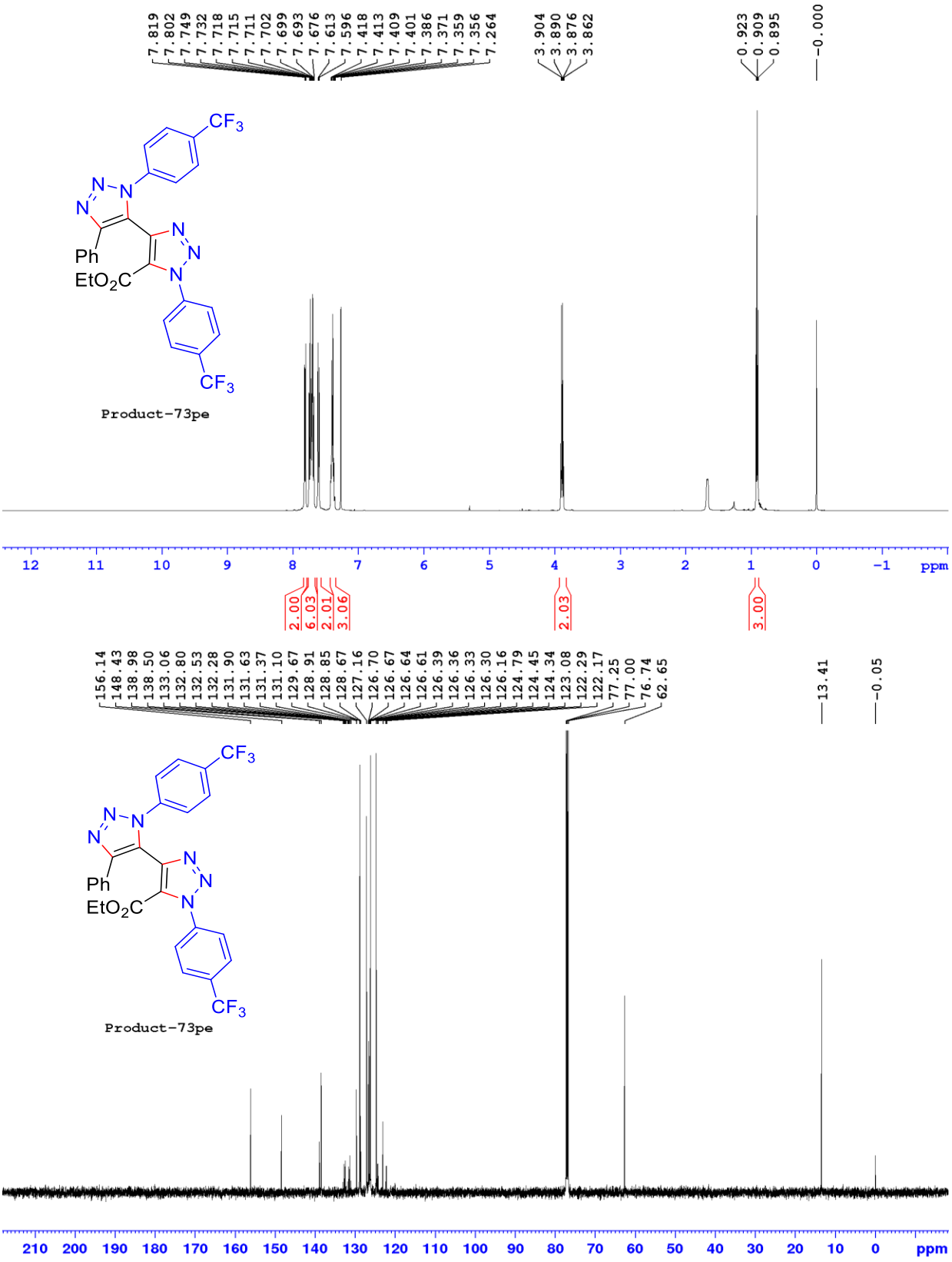



**Figure 22:** $^{1}$H NMR and $^{13}$C NMR spectra of product **73pe.**

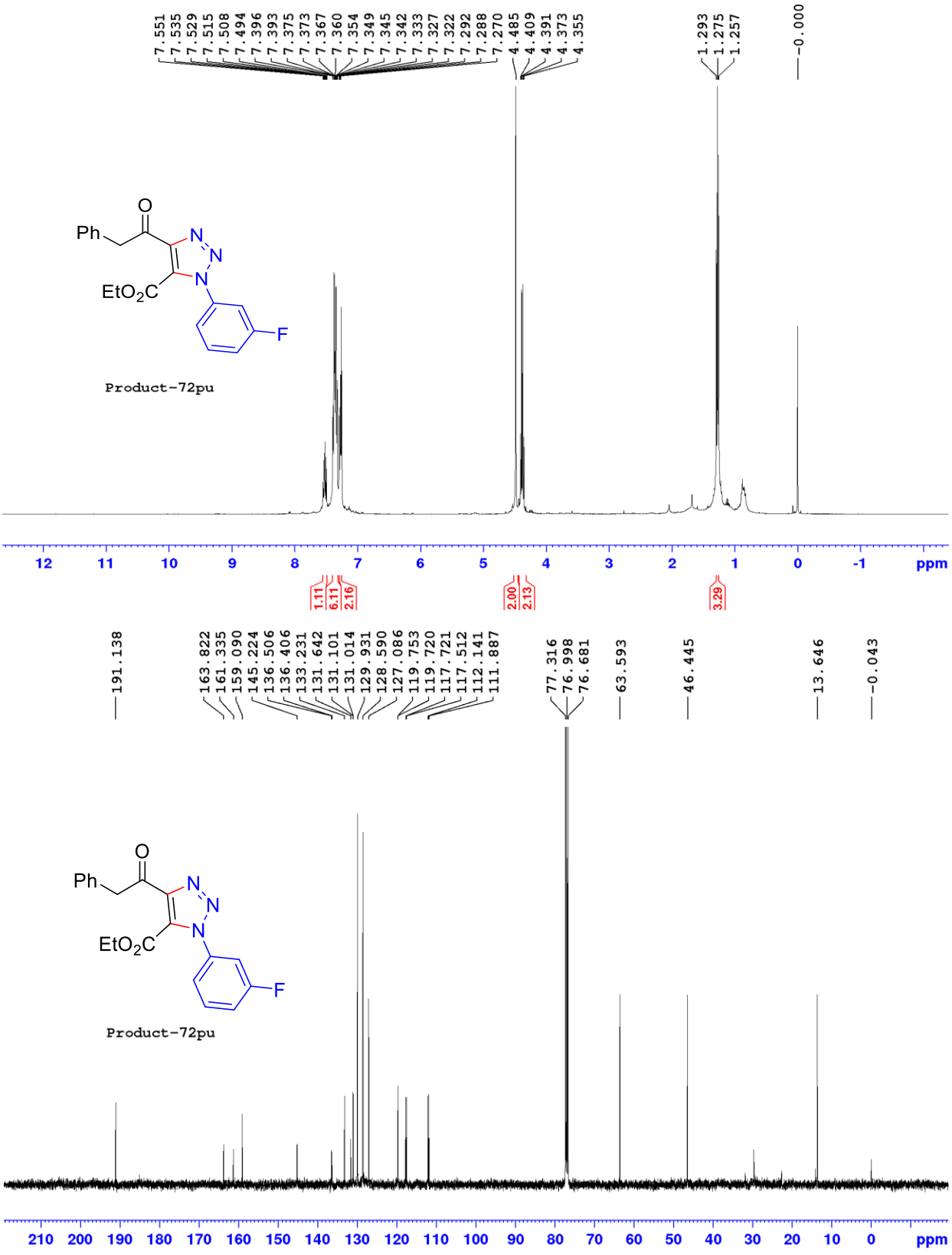
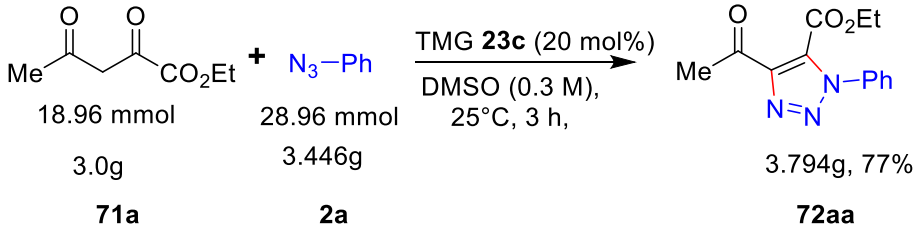



**Figure 23:** $^{1}$H NMR and $^{13}$C NMR spectra of product **72pu.**

### 3.2.4 Applications:

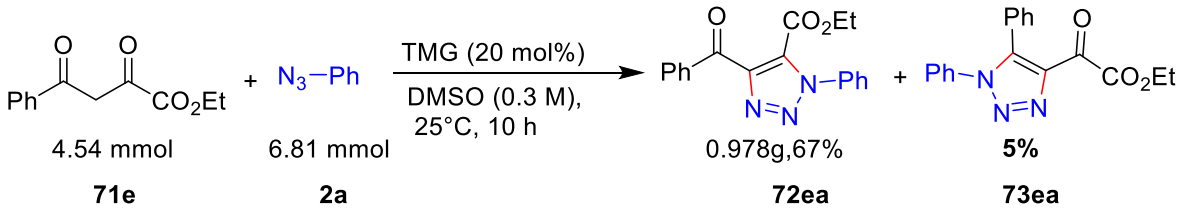
To investigate the bulk scale sustainability of the organocatalytic [3+2]-cycloaddition reaction, we planned a gram-scale reaction of ethyl 2,4-dioxopentanoate **71a** (3.0 g, 18.96 mmol) with phenyl azide **2a** (3.386 g, 28.96 mmol, 1.5 equiv.) in DMSO (63.23 mL, 0.3 M) with catalyst TMG **23c** 20 mol% (436.76mg) at 25 °C for 3 h, yielding 77% of **72aa** (3.794 g) in a chemoselective manner**.** This gram-scale reaction demonstrated the ease of use and importance of the enolate-mediated [3+2]-cycloaddition reaction in industrial applications (Scheme 22).

**Scheme 22**: Gram-scale Synthesis of OrgAKC Product **72aa**.




We performed another gram scale reaction for the investigation of reactivity, sustainability and selectivity of ethyl-2,4-dioxo-4-phenylbutanoate **71e** (1g, 4.54 mmol, 1 equiv.) with phenyl azide **2a** (0.811 g, 6.81 mmol, 1.5 equiv.) in DMSO (15 .13 mL, 0.3 M) in presence of catalyst TMG **23c** 20 mol% (104.58 mg) at 25 °C for 6 h which yielded 67% of thermodynamic enolate derived **4ea** and 5% of kinetic enolate derived **73ea** (Scheme 23).

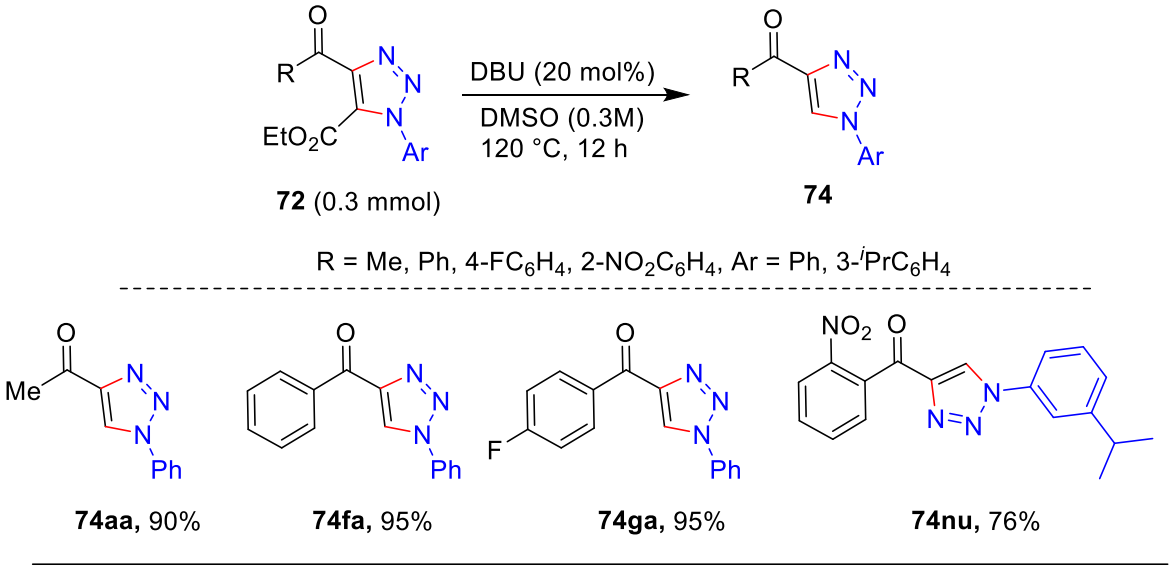
**Scheme 23:** Gram-scale synthesis of OrgAKC Product **72ea.**




The excellence of the [3+2]-cycloaddition reactions were demonstrated for the synthesis of similar core structure of highly medicinally rich acylated 1,4-disubstituted-1,2,3-tirazoles.[27] We performed the decarboxylation reactions with 1,4,5-trisubstituted-1,2,3-tirazoles **72** using 20

mol% of DBU **23a** in DMSO at 120 ºC to afford 1,4-disubstituted-1,2,3-tirazoles **74aa**, **74fa**, **74ga** and **74nu** in good to excellent yields (90%, 95%, 95% and 76% respectively) with in 12 h (Scheme 24).

**Scheme 24**: Synthesis of 1,4-Disubstituted-1,2,3-triazole from 1,4,5-Trisubstituted-1,2,3-triazole.




$^{1}$H and $^{13}$C NMR spectra of few compounds from Scheme 24 have depicted in Figures 24-26.

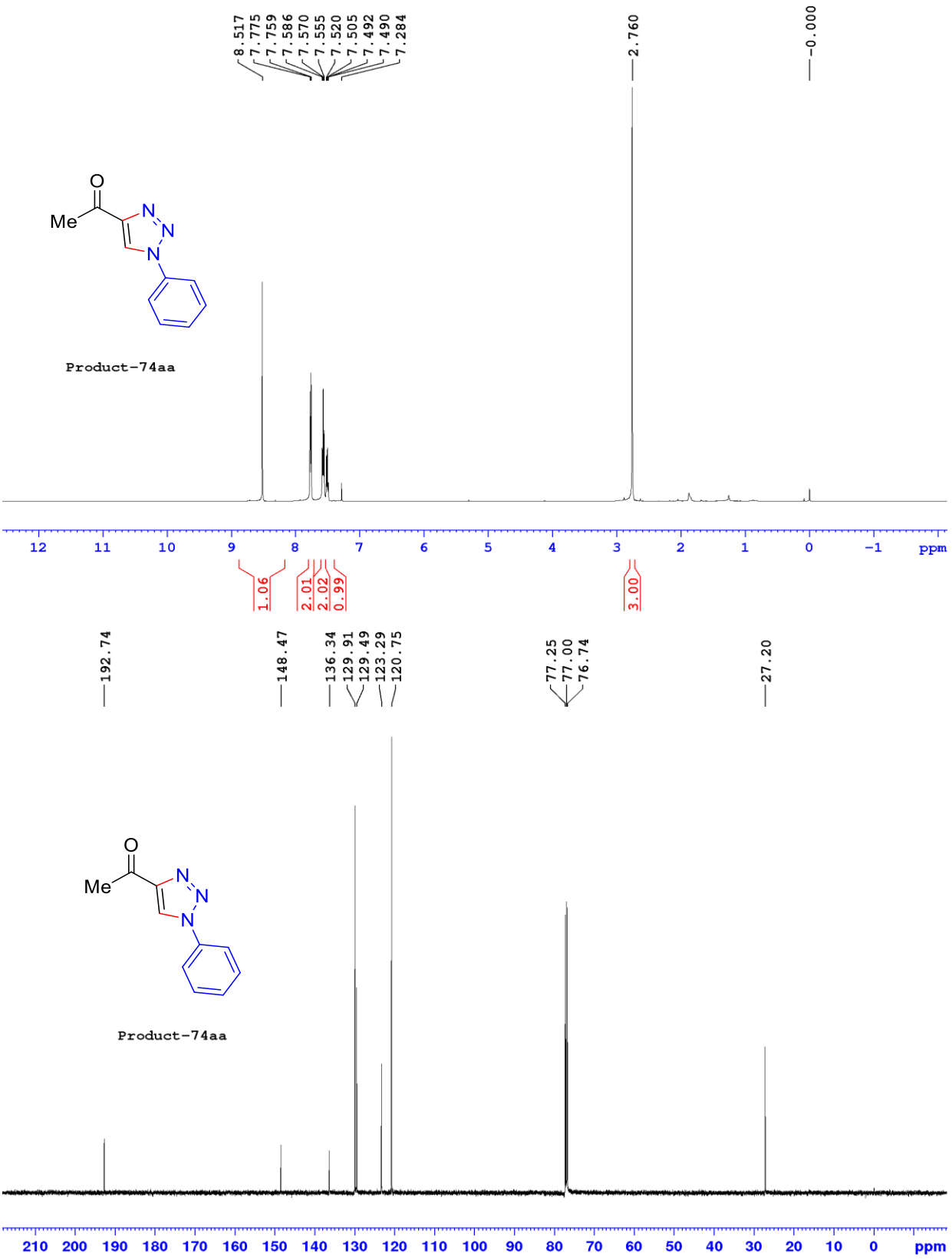



**Figure 24:** $^{1}$H NMR and $^{13}$C NMR spectra of product **74aa.**

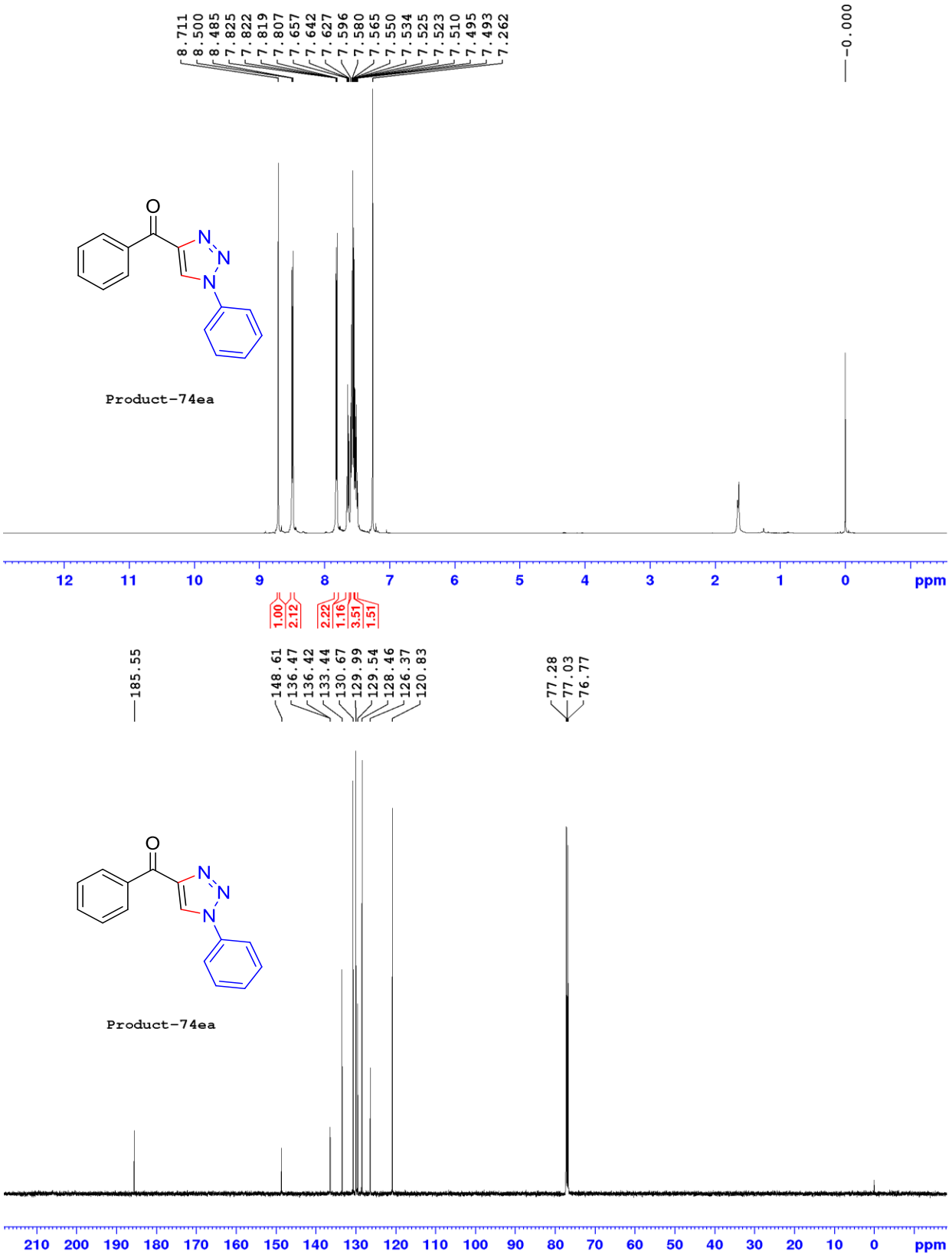



**Figure 25:** $^{1}$H NMR and $^{13}$C NMR spectra of product **74ea.**

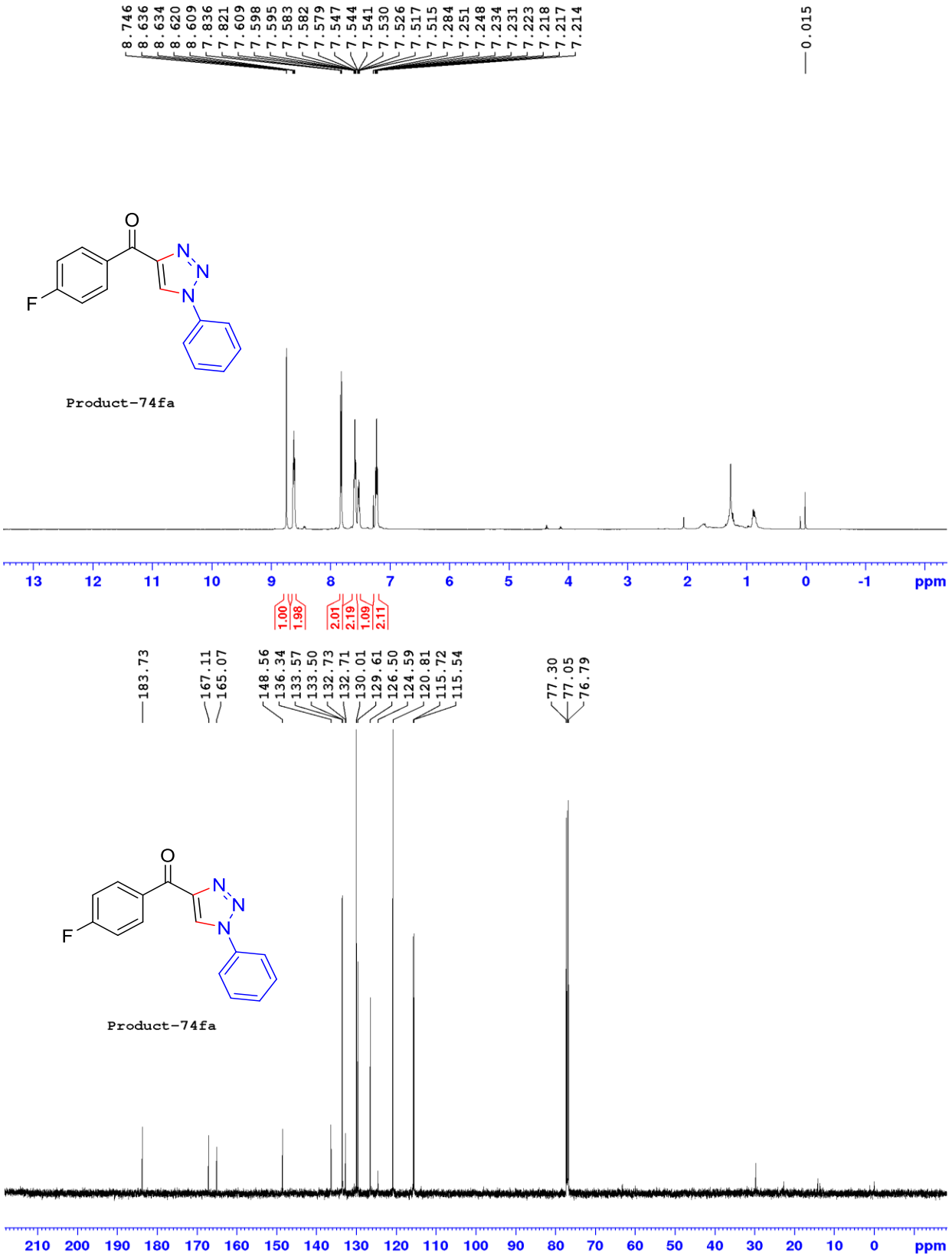
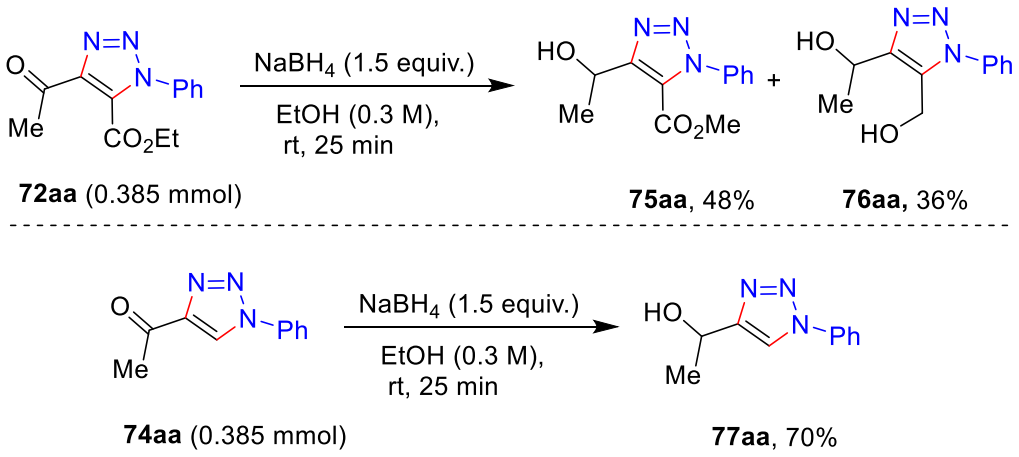



**Figure 26:** $^{1}$H NMR and $^{13}$C NMR spectra of product **74fa.**

When the acylated 1,2,3-triazole **72aa** was treated with sodium borohydride in ethanol solvent at room temperature, the corresponding secondary alcohol **75aa** was obtained with 48% of yield along with diol product **76aa** with 36% of yield within 0.4 h (Scheme 25). Similarly, **74aa** was reduced to **77aa** with 70% of yield within 0.4 h (Scheme 25).

**Scheme 25**: Reduction of Ketone and Ester of 1,2,3-Triazole




$^{1}$H and $^{13}$C NMR spectra of compound **75aa** from Scheme 25 have depicted in Figure 27.

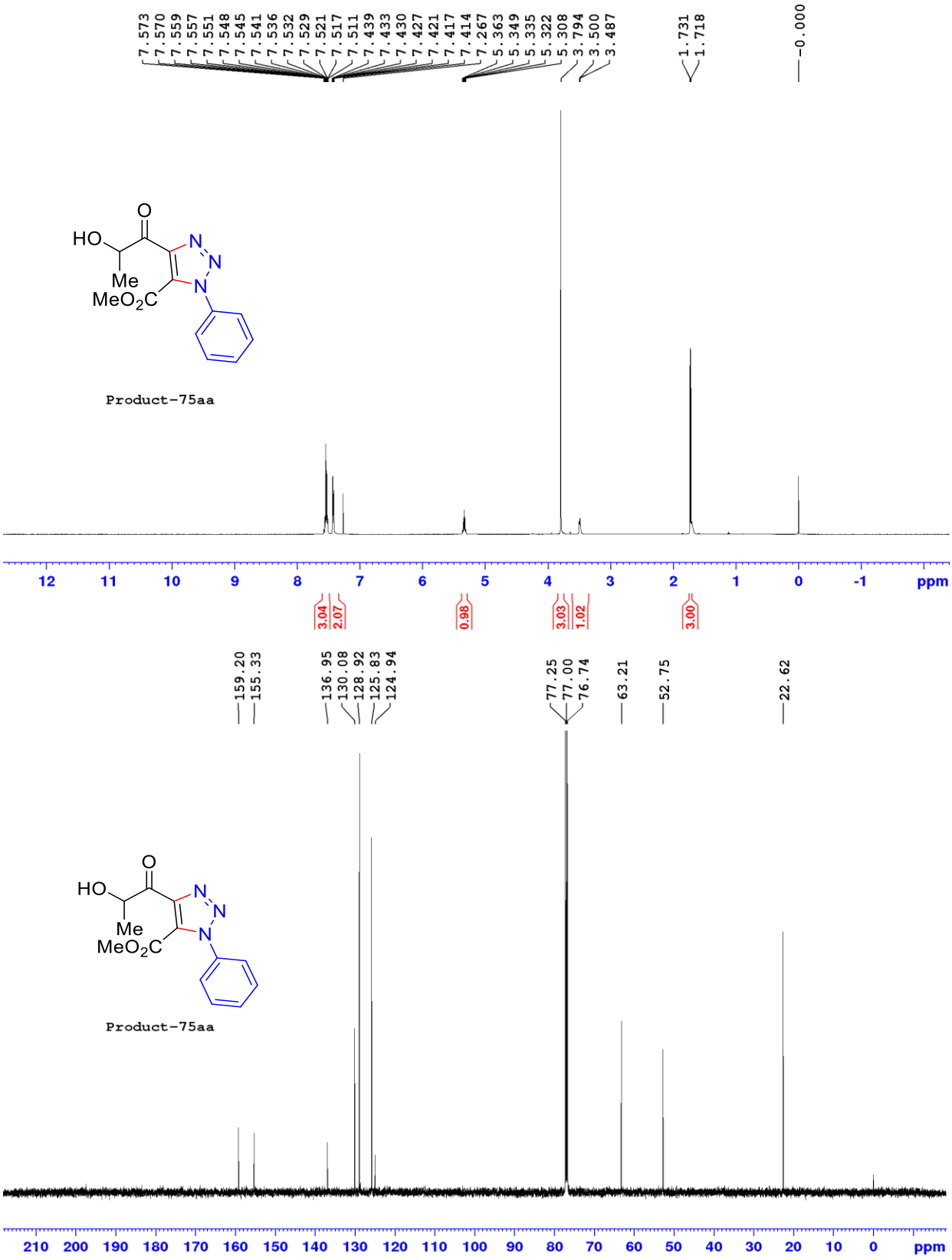
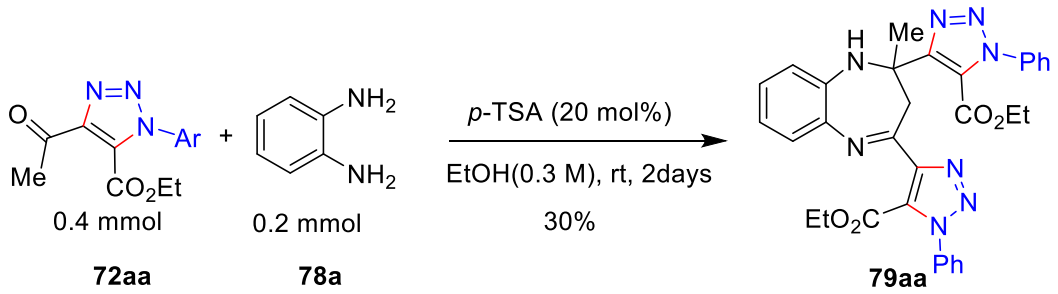



**Figure 27:** $^{1}$H NMR and $^{13}$C NMR spectra of product **74fa.**

As more nitrogen containing molecules are predominantly showing different biological activities, hence we try to utilize the two carbonyl groups of compound **72aa** to undergo condensation with diamine and furnished highly nitrogen-rich molecule. For the same, compound **72aa** was treated with ortho-phenylene diamine **78a** (0.5 equiv.) in the presence of 20 mol% of *p*-TSA in ethanol (0.3M) at room temperature, within 2 days, furnished an 7-membered heterocyclic product **79aa** with 30% yield (Scheme 26).

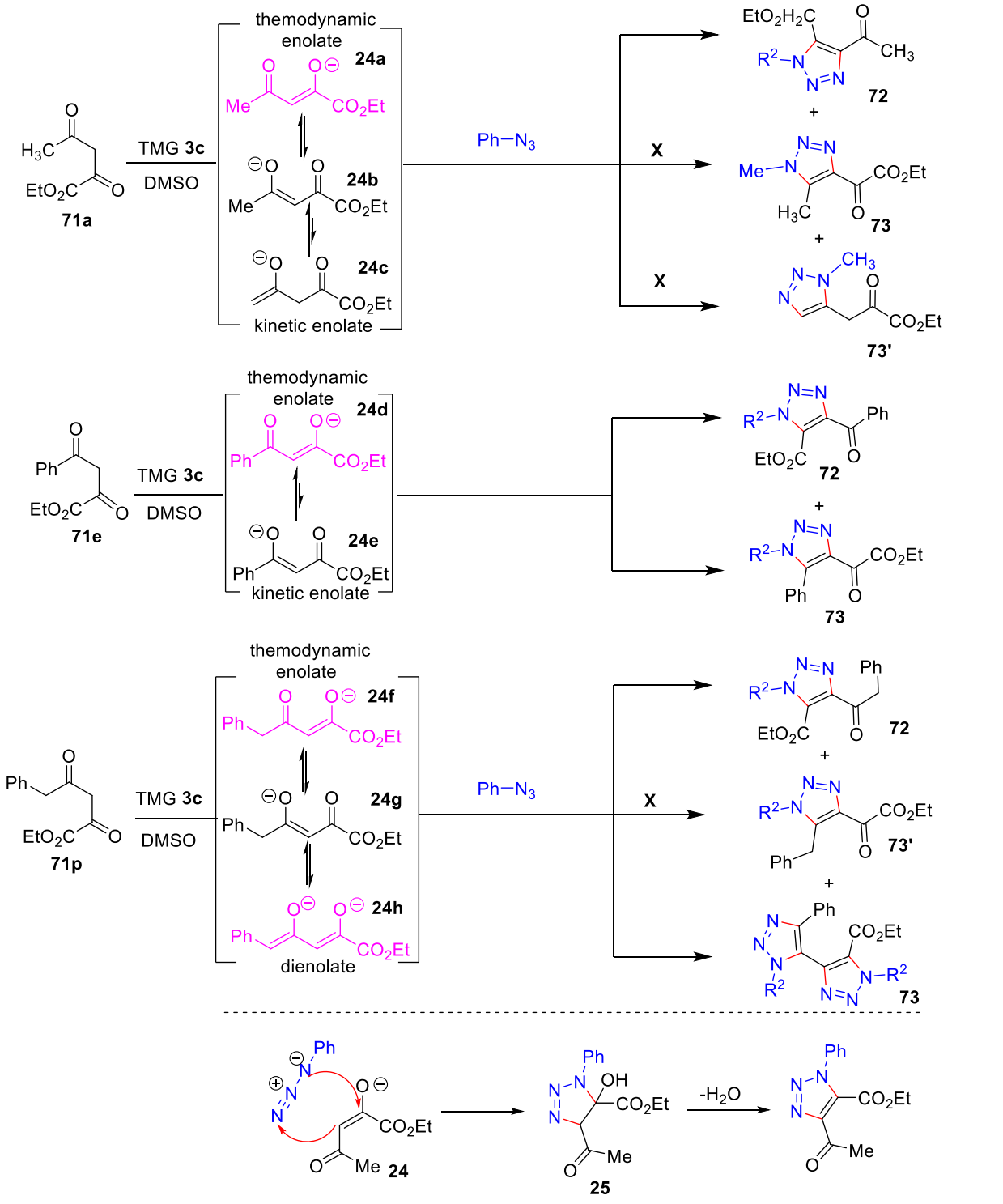
**Scheme 26**: Synthesis of Benzodiazipene Containing-1,2,3-Triazole




## 3.2.5 Reaction Mechanism:

A plausible mechanism is proposed for the present protocol depending on the formation of different products. When **71a** was treated with 20 mol% of TMG, three kind of enolates **24a**, **24b** and **24c** can be formed in the course of reaction, which are in equilibrium, among them selectively thermodynamic enolate **24a** was participated in the reaction to form the product **72aa.** In case of **71e**, two different enolates **24d** and **24e** can be formed when treated with the base, even then selectively thermodynamic enolate **24d** was participated in the reaction to from **72ea** chemoselectively. On the other hand, **71p** has two activated methylene centers, reaction went through both thermodynamic enolates **24f** and dienolate **24h** though major product **72pa** was obtained from thermodynamic enolate **24f**. The dienolate **24h** produced minor bis-triazole product **73pa** (Scheme 27).

**Scheme 27**: Reaction Mechanism



## 3.3 Conclusions

In summary, we have developed a simple metal-free organocatalytic enolate-mediated chemoselective synthesis of the medicinally important 1,4,5-triisubstituted-1,2,3-triazoles **72**, bis-1,2,3-triazoles **73** and acylated 1,4-disubstituted 1,2,3-triazoles **74** from the nonsymmetrical 2,4-diketoesters **71** and different azides **2** under ambient conditions through the organoctalytic [3 +2]-cycloaddition with very good yields and excellent chemo-/regio-selectivity. Few decarboxylation/reduction/condensation reactions were conducted on the resulting click products **72** to show their broad synthetic applications. We have performed some controlled and online NMR experiments to prove the possibility of the formation of kinetic and thermodynamic enolate and gave strong support to the proposed reaction mechanism. Further work is in progress to develop organocatalytic enolate-mediated synthesis of bis-triazoles as a single product with a good yield.

# 4. Direct Organocatalytic Carbonyl-Azide-[3+2]-Cycloaddition: Synthesis of Benzothiazole Containing 1,2,3-Triazoles

## 4.1 Introduction

Nitrogen-containing heterocyclic 1,2,3-triazoles are a central structure motif with a wide range of applications in drug discovery and industry. Although there is no natural abundance of 1,2,3-triazoles, synthetically functionalized 1,2,3-triazoles have numerous applications in organic chemistry, medicinal chemistry,[1,23] fluorescent imaging,[28] and material science (Figure 28). Organic chemists showed adequate interest to develop a direct and simple method to synthesize 1,2,3-traizoles. Among them, some of the popular approaches are metal catalyzed click chemistry[3-6] and organocatalyzed click carbonyl-azide cycloadditions.[11-14]

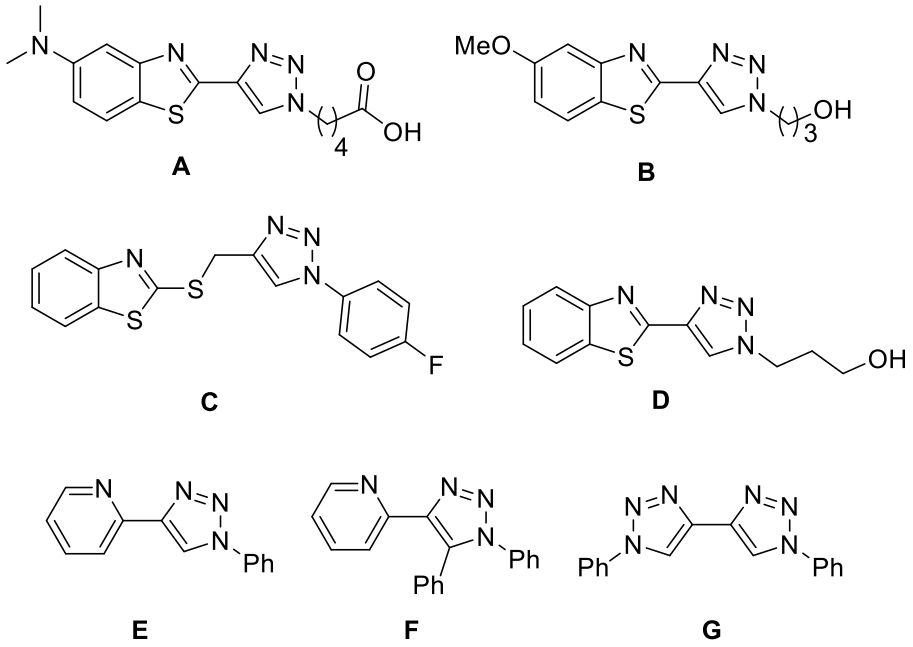
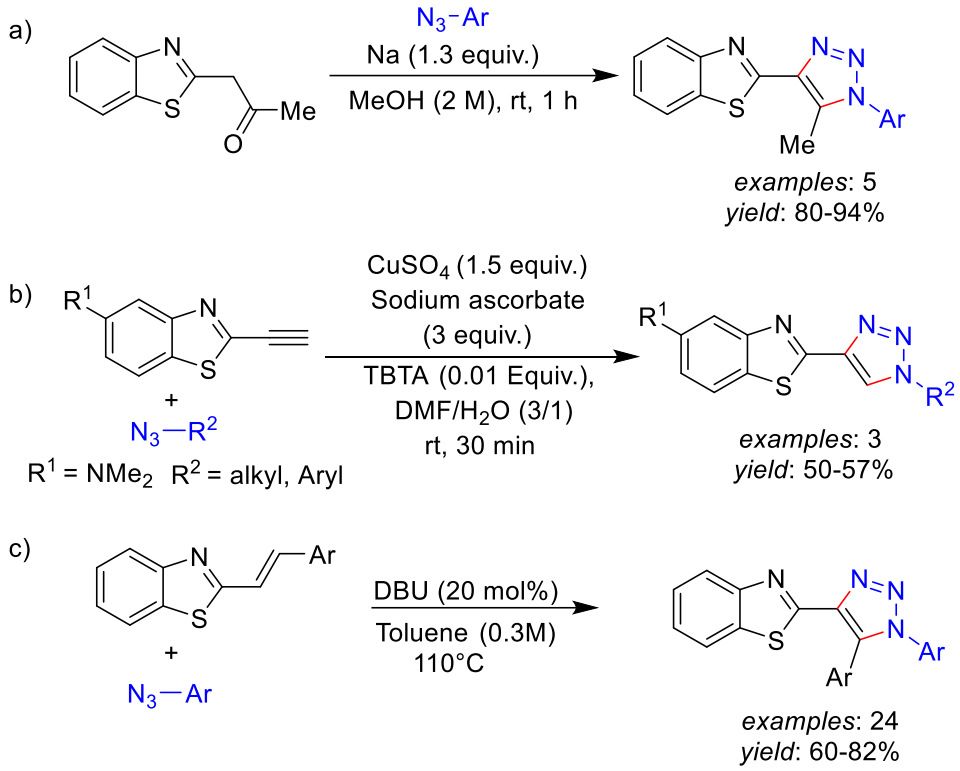



**Figure 28:** Biological active benzothiazole containing 1,2,3-triazoles.

Benzothiazoles are heterocyclic compounds with a wide range of pharmacological activities like antimicrobial, and antidiabetic, anticonvulsant, including antitumor and anti-inflammatory.[27] The enhancement in pharmacological action by combining two pharmacophores into a single molecule is well established. There are only a few reports on the synthesis and applications of benzothiazole triazole, formed by combining benzothiazole and 1,2,3-triazole. Obushak *et al.* synthesized the first benzothiazoletriazole in methanol using 2-benzothiazoleacetone and aryl

azides under basic conditions (Scheme 28, a).[29] Tung *et al*. reported the discovery of new fluorogenic dyes via copper catalyzed azide-alkyne [3+2]-cycloaddition using electron deficient alkyne and azide.[30]

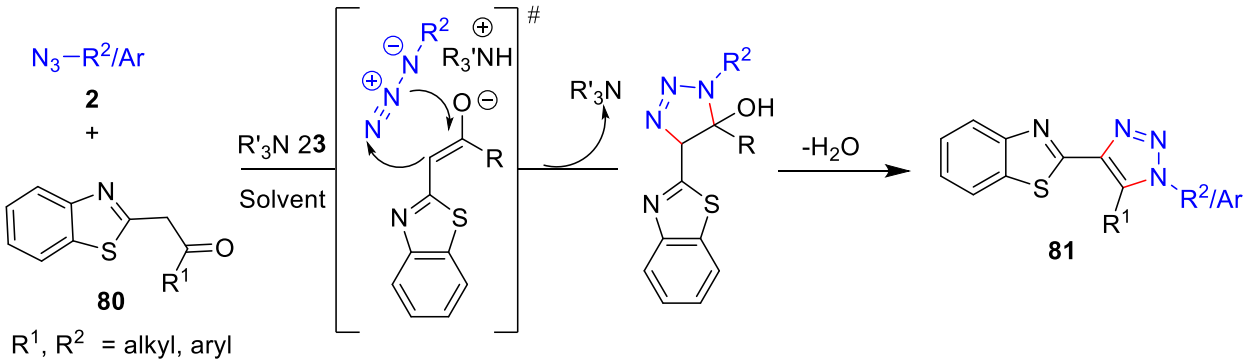
**Scheme 28**: Previous Method for the Synthesis of Benzothiazole-1,2,3-triazoles




They also performed a comparison study and found the best fluorophore showing biological application (Scheme 28, b).[30] Shu *et al.* recently reported the synthesis of trisubstituted triazoles in which activated olefin interacted with aryl azides at high temperatures via azide-olefin [3+2]-cycloaddition (Scheme 28, c).[14] Many of the above methods required toxic transition-metal catalysts, heavy ligands, and reagents and several sequence of steps for obtaining the desired product. Other procedures required higher temperatures, longer reaction times, and stoichiometric amounts of catalysts, thereby making these reaction conditions unendurable. These drawbacks motivated us to develop a general synthetic protocol for the high-yielding

regioselective synthesis of benzothiazole 1,2,3-triazoles using a well-known enolate-mediated organo-catalytic click reaction.[11] (Scheme 29).

**Scheme 29:** Reaction Design for Benzothiazole Containing-1,2,3-Triazoles



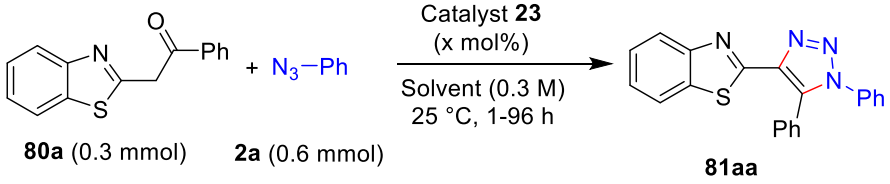

## 4.2 Results and Discussion

### 4.2.1 Reaction Optimization:

We optimized the designed enolate-mediated organo-click reaction under ambient conditions by screening simple series of organocatalysts **23a-23j** for the [3+2] cycloaddition of 2-(benzothiazol-2-yl)-1-phenylethan-1-one **80a** (0.3 mmol) with 2 equiv. of phenyl azide **2a**. Delightfully, the reaction between **80a** and **2a** in DMSO solvent in presence of 20 mol% of DBU **23a** as a catalyst resulted desired product **81aa** with 98% within 1 hour at 25 °C (Table 5, Entry 1). The same reaction when carried out with TBD **23b** as a catalyst, benzothiazole 1,2,3-triazole **81aa** was formed at a relatively slower rate for 2 h and lesser yield (96%) (Table 5, Entry 2). TMG **23c** has worked well as a catalyst and surprisingly the reaction was completed within one hour with almost quantitative yield of **81aa** (Table 5, Entry 3). We also examined DABCO **23d**, DBN **23e**, TEA **23f** and DMAP **23g** as catalysts, but none of them performed better than TMG **23c** (Table 5, Entry 4-7). In case of secondary amines like diethyl amine **23h,** pyrrolidine **23i** and *L*-proline **23j**, reactions were slower and yield also decreased (Table 5, Entry 8-10), which clearly reflect the fact that the enamine mediate reaction is slower compared to enolate mediated reaction. After screening several catalysts **23a-23j**, TMG **23c** proved to be the best. We further investigated the effectiveness of TMG **23c** by reducing the catalytic loading from 20 mol % to 10

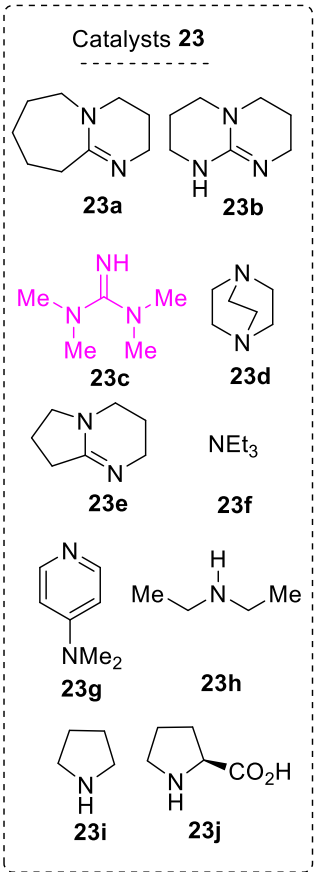
mol %, a sustainable yield (99%) with slightly prolonged reaction time (3 h) was observed (Table 5, Entry 11). When catalyst loading was further decreased to 5 mol% of **23c**, no better result was found (Table 5, Entry 12). A decrease in equivalent of **2a** from 2 to 1.5 did not produce a better result (Table 5, Entry 13). After getting the best catalyst **23c** in our hand, we have conducted a screening of different solvents like NMF, THF, DMF and acetonitrile, but none of them has performed better than the DMSO solvent (Table 5, Entry 14-17). Therefore, we concluded that the reaction between **80a** and **2a** (2 equiv.) in presence of 20 mol% of **23c** in DMSO solvent was the best suitable condition.

**Table 5:** Reaction optimization for OrgAKC[a]




| Entry | Catalyst | (x mol%) | Solvent | T *h* | Yields(%)[b] |
|---|---|---|---|---|---|
| 1 | **23a** | 20 | DMSO | 1 | 98 |
| 2 | **23b** | 20 | DMSO | 2 | 96 |
| 3 | **23c** | 20 | DMSO | 1 | 99 |
| 4 | **23d** | 20 | DMSO | 7 | 89 |
| 5 | **23e** | 20 | DMSO | 2 | 97 |
| 6 | **23f** | 20 | DMSO | 7 | 93 |
| 7 | **23g** | 20 | DMSO | 10 | 85 |
| 8 | **23h** | 20 | DMSO | 3 | 97 |
| 9 | **23i** | 20 | DMSO | 7 | 70 |
| 10 | **23j** | 20 | DMSO | 96 | 30 |
| 11 | **23c** | 10 | DMSO | 3 | 99 |
| 12 | **23c** | 05 | DMSO | 5 | 97 |
| 13[c] | **23c** | 10 | DMSO | 4 | 97 |
| 14 | **23c** | 10 | NMF | 12 | 64 |
| 15 | **23c** | 10 | THF | 48 | 60 |
| 16 | **23c** | 10 | DMF | 5 | 91 |
| 17 | **23c** | 10 | ACN | 48 | 65 |

[a] Reactions were carried in solvents (0.3 M) with 2 equiv. of **2a** relative to **81a** (0.3 mmol) in presence of catalysts **23** at 25-30 °C. [b ] Yield referes the column-purified products. [c] The reagent **2a** used in 1.5 equiv.




$^{1}$H and $^{13}$C NMR spectra of **81aa** compound from optimization Table 5 have depicted below Figure 29.

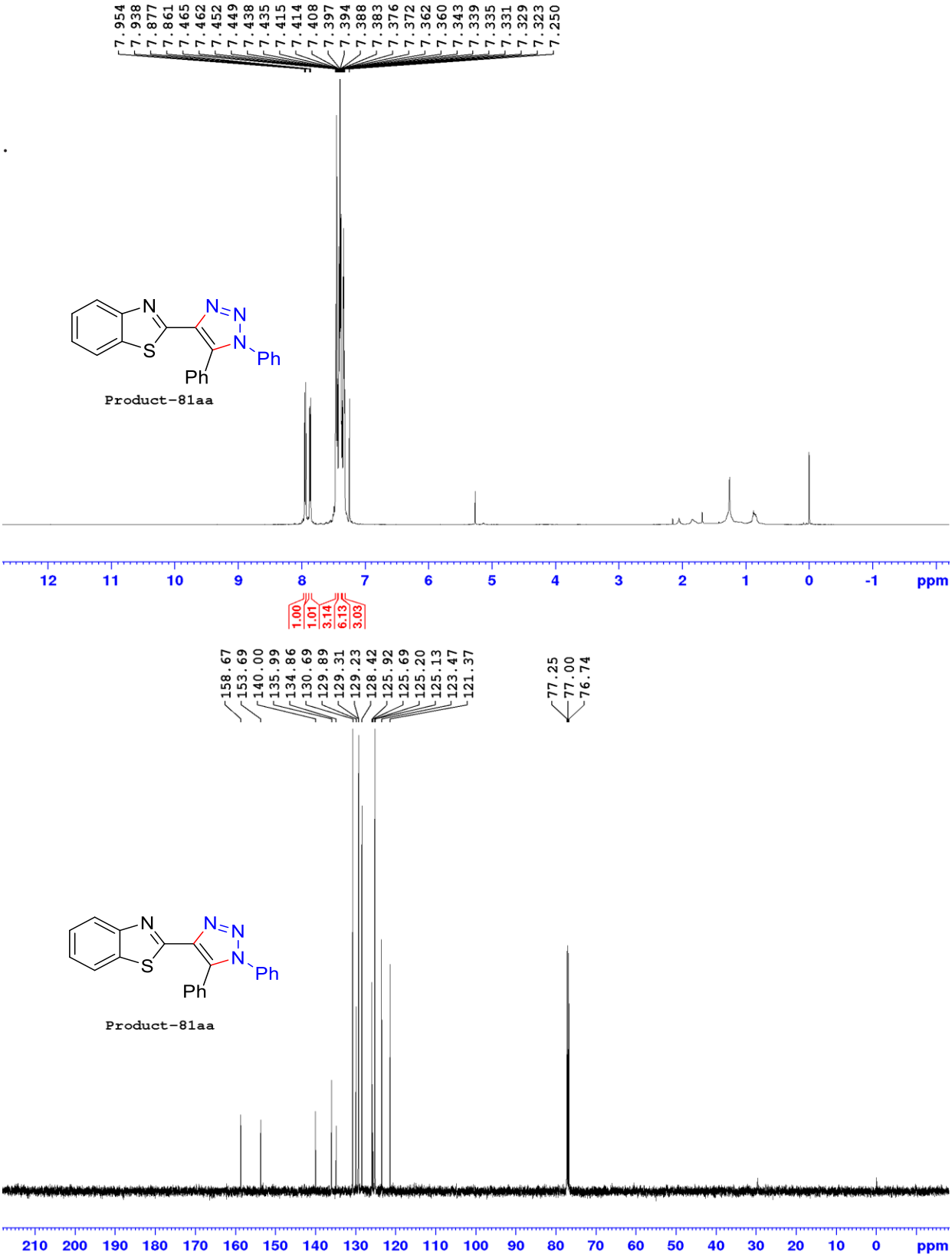
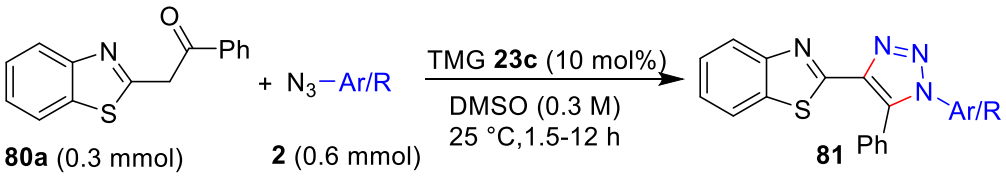



**Figure 29:** $^{1}$H NMR and $^{13}$C NMR spectra of product **81aa.**

## 4.2.2 Reaction Scope of Azides:

With optimization conditions in hand, OrgAKC reactions were kept using a variety of azides **2b-t** with **80a** in DMSO solvent for 1.2 to 12 hours at room temperature (Table 6). Interestingly, aryl azides **2b-e** with electron-deficient functional groups such as $NO_2$, $CO_2Et$, CN, and $CF_3$ at the para-position of the aromatic ring yielded **81ab-81ae** in high yields of 91-99% (Table 6, entry 1-4). Halogens *meta*-F **2f**, *para*-Cl **2g**, and *para*-Br **2g** at the meta and para positions of the aromatic ring of azides reaction proceeded smoothly with excellent yield of benzothiazole-1,2,3-triazoles, whereas *ortho*-substituted halogens **2i** and **2l** on the aromatic ring yielded very poor yields due to steric effect and they also required a higher temperature for faster consumption of starting materials compared to room temperature reactions. (Table 6, entry 5-11). Therefore, a correlation study was carried out to study the effect of temperature for the *ortho*-substituted halogen groups. Ortho-substituted azide **2i** treated with **80a** under 10 mol % of TMG **23c** in DMSO at room temperature provided 45% yield with longer reaction time, 9 h along with a side product (not mentioned in the table), whereas the same reaction when kept at 80 ºC, the reaction completed within 3 h with improved yield of 60% (Table 6, entry 8 & 11). Whereas, electron-rich substituents such as *para*- OMe **2m**, Me **2n** azides, planned in OrgAKC reaction with **80a** under 10 mol % of TMG at 25 º in DMSO furnished **81am**, **81an** with 70% yield each, for in 8 and 6 h respectively (Table 6, entry 12-13). After observing the above two reactions (Table 6, entry 12-13), we changed the reaction condition of OrgAKC for **2o** with **80a**, when treated under 20 mol% of TMG at 80 ºC in DMSO furnished **81ao** with an improved yield of 88% for 3 h (Table 6, entry 15). Fascinatingly, we investigated the OrgAKC reaction with a variety of other azides with **80a** under different catalysts and conditions in DMSO solvent. The azides such as 2-naphthyl **2p** and $\alpha$-azidostyrene **2q** when treated with **80a** under 10 mol % of TMG furnished **81ap** 93%, and **81aq** 61% for in 2 h and 10 h respectively. Another $\alpha$-azido-2-naphthyl **2r**, when performed OrgAKC reaction with **80a** under 20 mol % of TMG **23c** at 25 ºC afforded 80% of **81ar** in 2 h (Table 6, entry 17). Furthermore, alkyl azides like benzyl azide **2s,** $\alpha$-D-Mannopyranosyl azide **2t** when used for OrgAKC reaction by reacting with **80a** under 20 mol% of DBU at 80 ºC and 10 mol% TMG at 25 ºC in DMSO solvent afforded **81as** with 66% in 2 h and **81at** with 76 % in 12 h (Table 6, entry 18-19).

**Table 6:** Reaction scope of azides for OrgAKC[a]




**80a** (0.3 mmol) **2** (0.6 mmol) **81**

| Entry | **2** (R or Ar) | t [h] | Yield [%][b] |
|---|---|---|---|
| 1 | **2b:** Ar = 4-$NO_2C_6H_4$ | 1.3 | 99 **81ab** |
| 2 | **2c:** Ar = 4-$CO_2MeC_6H_4$ | 1.5 | 98 **81ac** |
| 3 | **2d:** Ar = 4-$CNC_6H_4$ | 1.5 | 99 **81ad** |
| 4 | **2e:** Ar = 4-$CF_3C_6H_4$ | 1.5 | 91 **81ae** |
| 5 | **2f:** Ar = 3-$FC_6H_4$ | 1.3 | 98 **81af** |
| 6 | **2g:** Ar = 4-$ClC_6H_4$ | 1.5 | 99 **81ag** |
| 7 | **2h:** Ar = 3-$ClC_6H_4$ | 2.0 | 93 **81ah** |
| 8[c] | **2i:** Ar = 2-$ClC_6H_4$ | 3.0 | 60 **81ai** |
| 9 | **2j:** Ar = 4-$BrC_6H_4$ | 1.5 | 93 **81aj** |
| 10 | **2k:** Ar = 3-$BrC_6H_4$ | 1.5 | 98 **81ak** |
| 11[c] | **2l:** Ar = 2-$BrC_6H_4$ | 3.0 | 60 **81al** |
| 12 | **2m:** Ar = 4-$OMeC_6H_4$ | 6.0 | 70 **81am** |
| 13 | **2n:** Ar = 4-$MeC_6H_4$ | 6.0 | 70 **81an** |
| 14[c,d] | **2o:** Ar = 3-$MeC_6H_4$ | 3.0 | 88 **81ao** |
| 15 | **2p:** Ar = Naphthyl | 2.0 | 93 **81ap** |
| 16 | **2q:** Ar = 1-vinylphenyl | 10 | 61 **81aq** |
| 17[d] | **2r:** Ar = 1-vinynapthyl | 2.0 | 80 **81ar** |
| 18[c,e] | **2s:** R = Bn | 2.0 | 66 **81as** |
| 19 | **2t:** chiral sugar azide | 12 | 76 **81at** |

[a] Reactions were carried out in DMSO (0.3 M) with **80a** (0.3 mmol) and **2b-s** (0.6 mmol) in the presence of TMG **23c** (10 mol%). [b] Yields refer to column-purified product. [c] Reaction kept at 80°C. [d] TMG was used 20 mol%. [e] Reaction kept with 20 mol% of DBU.

$^{1}H$ and $^{13}C$ NMR spectra of few compounds from Table 6 have depicted below Figure 30-32.

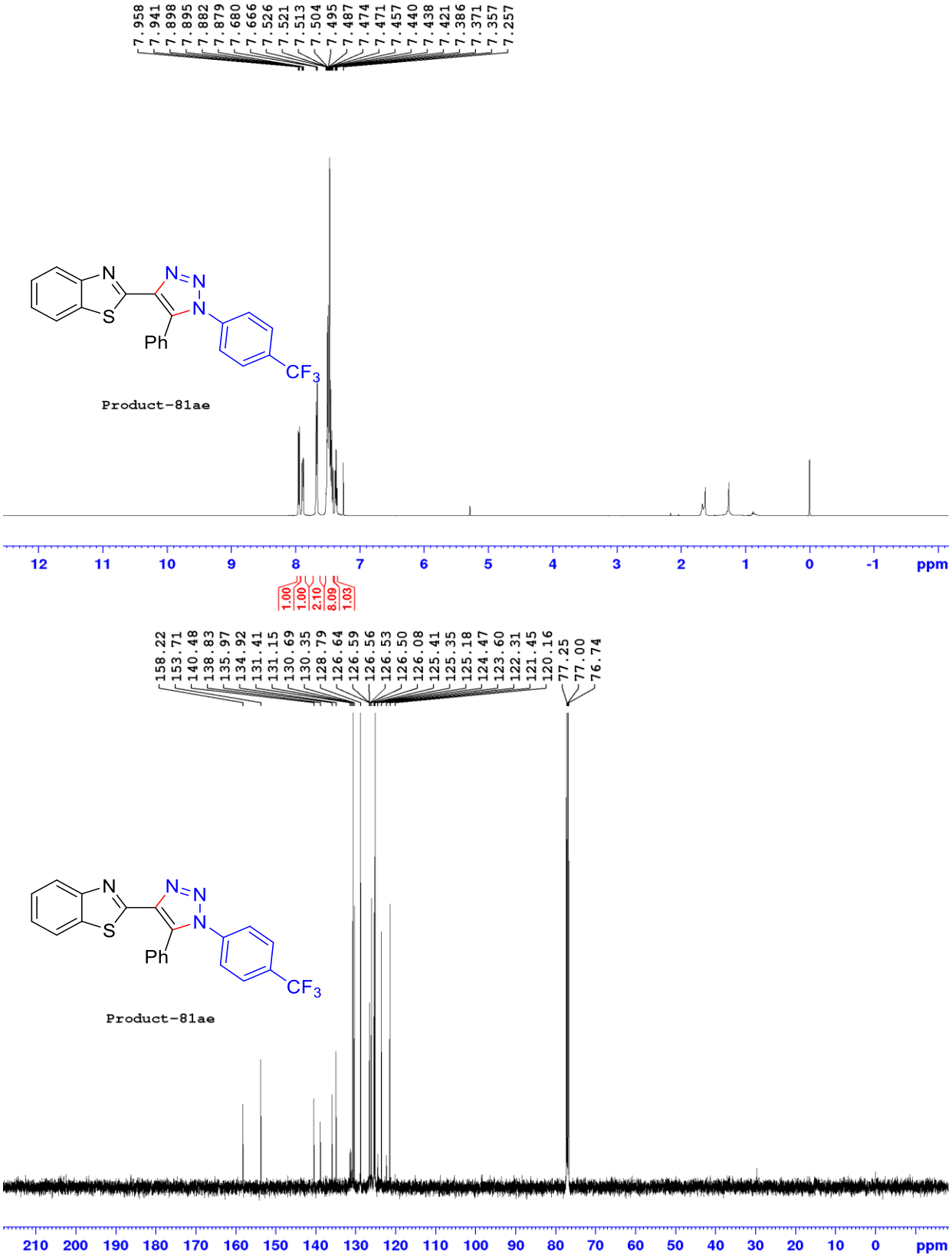



**Figure 30:** $^{1}$H NMR and $^{13}$C NMR spectra of product **81ae.**

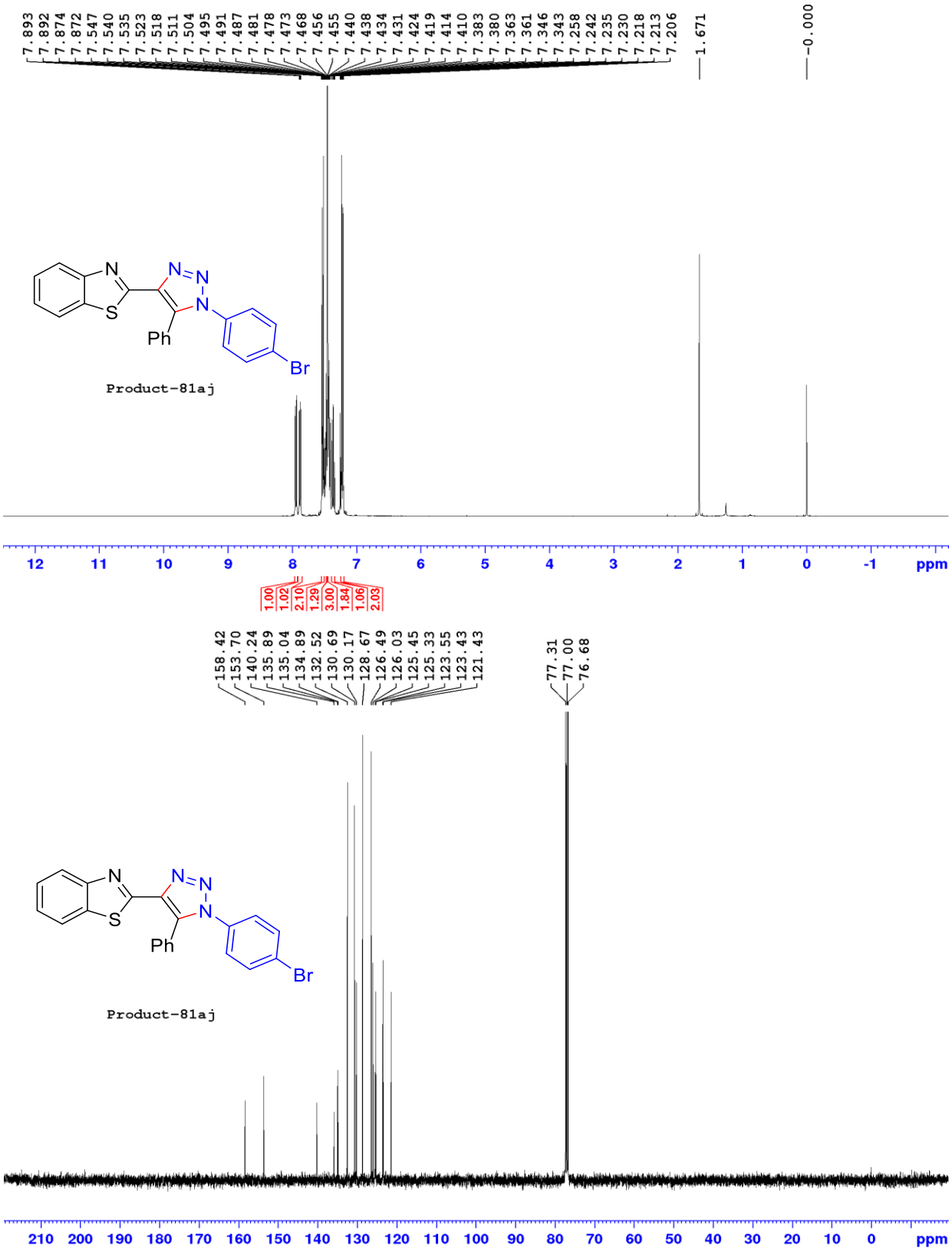



**Figure 31:** $^{1}$H NMR and $^{13}$C NMR spectra of product **81aj.**

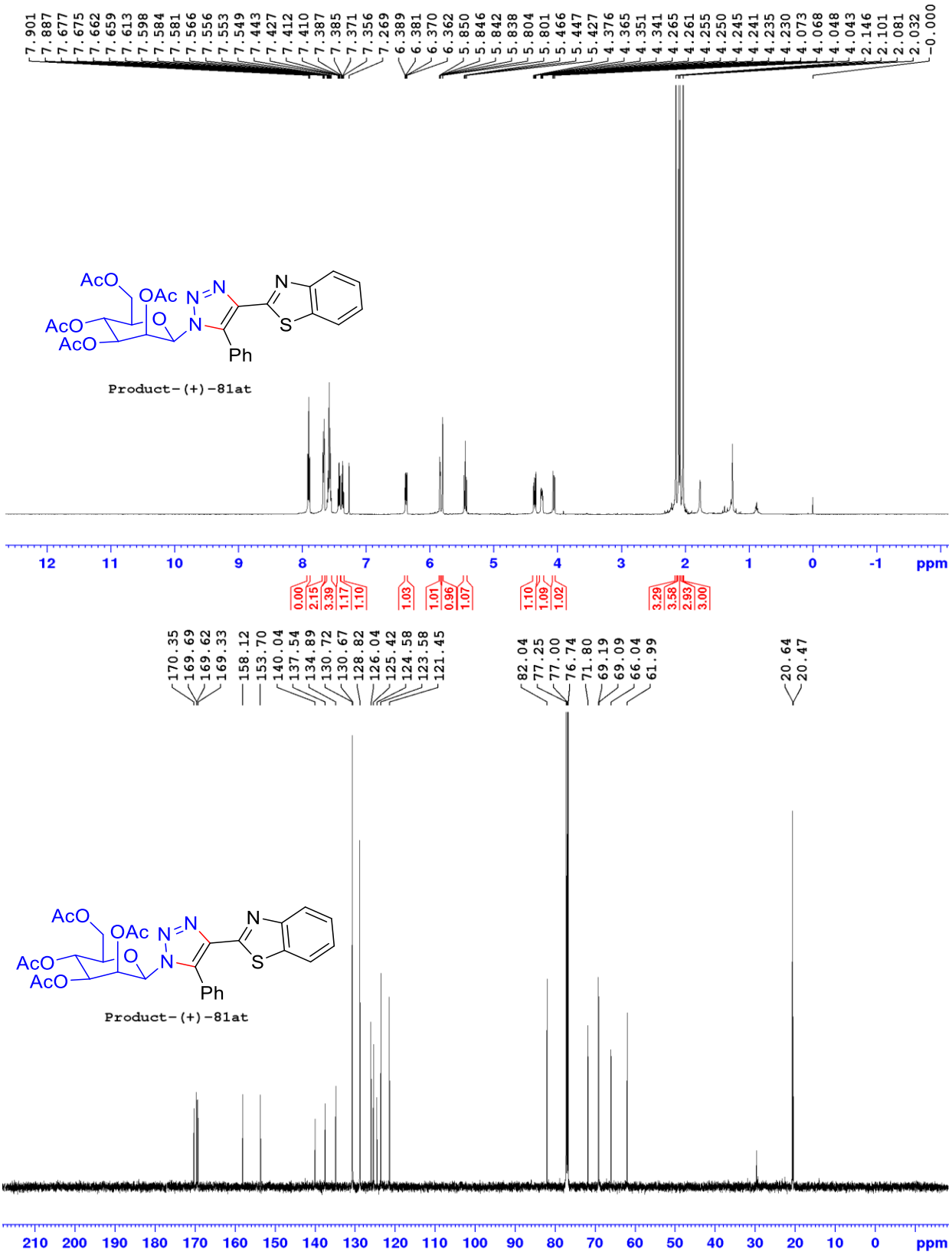


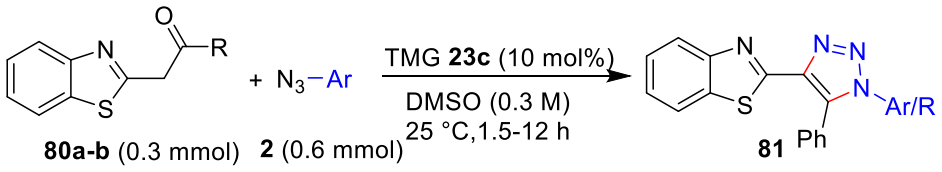

**Figure 32:** $^{1}$H NMR and $^{13}$C NMR spectra of product (+)-**81at.**

### 4.2.3 Reaction Scope of Benzothiazole Ketone:

After thoroughly understanding the optimization condition, reactivity, and nature of various azides **2** with **80a** in an OrgAKC-click reaction, we have investigated the nucleophilic nature of the enolate intermediates of various ketones **80**. A variety of ketones **80b**-**80f** bearing electron-withdrawing groups like 4-CN **80b**, 4-$CF_3$ **80c**, halogens 4-Cl **80d**, 3-Cl **80e**, and 4-Br **80f** on the aryl ring reacted in OrgAKC reaction with **2a** under 10 mol% of TMG at 25 ºC in DMSO to afford **81ba** with 96%, **81ca** with 82%, **81da** with 81%, **81ea** with 84%, and **81fa** with 90% in 2 h (Table 7, entry 1-5). Ortho-substitution with 2-F on aryl of compound **80g** revealed steric effect by resulting poor outcome in OrgAKC reaction with **2a** under 10 mol % of TMG at 25 ºC in DMSO to provide **81ga** in 45% yield with a longer reaction time of 8 h (not mentioned in the table). When the same reaction performed with a change in temperature from room temperature to 80 ºC, reaction afforded an improved yield of 60% within 2 h (Table 7, entry 6). Compounds with Bulky *ortho*-substituents like iodo- in **80h** and methyl in **80i** on aromatic rings, when treated with an activated azide **2b** in OrgAKC reaction under 10 mol % of TMG at RT, reaction furnished **81hb** with 58% and **81ib** with 61% yields in 7 h (Table 7, entry 7). When Compound **80i** treated with an unactivated azide **2a**, afforded 30% yield at room temperature under 10 mol% of TMG for 11 h (Not mentioned in the table) and 50% of yield at 80 ºC under 20 mol% TMG for 4 h (Table 7, entry 9). From these two reactions, *ortho*-substituent clearly indicated that steric effect influences the reaction rate even with changing reaction conditions. We also employed electron-donating groups such as 4-OMe **80j**, 4-$^t$Bu **80k** and two different hetero aromatic derivatives like 2-furyl **80l**, 2-pyridine **80m** with phenyl azide **2a** in the [3+2]-cycloaddition reaction under 10 mol % TMG **23c** at 25 ºC in DMSO, all furnished good to excellent yields of **81ja**-**4ma** i.e., 85-97% within 3 h (Table 7, entry 10-13). When trifluorobenzothiazole acetone **80n** and benzothiazole acetone **80o** were used as substrates in OrgAKC reaction, excellent yields of 96%, 97% of **81na** and **81oa** were obtained at 80ºC in DMSO within 2-3 h (Table 7, entry 14-15). We were curious to understand how the OrgAKC reaction would be if we introduce two activated methylene into a single substrate, i.e., one from benzylic $\alpha'$-methylene and the other from benzothiazole $\alpha$-methylene, as shown in the case of **80p**. Even though, there is a dual possibility of product formation, we have obtained only a single product regioselectively. When we performed the reaction with the ketone **80p** using a simple azide **2a**, activated azides **2d**, **2e**, and electron rich azide **2n,** we have furnished **81pa** with 78%, **81pd** with 93%, **81pe** with 92%,

and **81pn** with 89% in good to excellent yields with high regioselectivity within 2 h (Table 7, Entry 16-19). We did not observe any formation of isomer **81′** from this reaction (Table 7, 16-19). The electron-deficient benzothiazole group strongly influences $\alpha$-enolate formation and stabilization which is directing towards the exclusive formation of regiospecific 1,2,3-triazoles **81pa**, **81pd**, **81pe** and **81pn**.

**Table 7:** Reaction scope different carbonyl and azides for OrgAKC.[a]




**80a-b** (0.3 mmol) **2** (0.6 mmol) **81**

| Entry | **80** | $N_3-Ar$ | t [h] | Yield [%][b] | |
|---|---|---|---|---|---|
| 1 | **80b:** R = 4-$CNC_6H_4$ | **2a:** Ar = Ph | 2 | 96 | **81ba** |
| 2 | **80c:** R = 4-$CF_3C_6H_4$ | **2a:** Ar = Ph | 2 | 82 | **81ca** |
| 3 | **80d:** R = 4-$ClNC_6H_4$ | **2a:** Ar = Ph | 2 | 81 | **81da** |
| 4 | **80e:** R = 3-$ClC_6H_4$ | **2a:** Ar = Ph | 2 | 84 | **81ea** |
| 5 | **80f:** R = 4-$BrC_6H_4$ | **2a:** Ar = Ph | 2 | 90 | **81fa** |
| 6[c] | **80g:** R = 2-$FC_6H_4$ | **2a:** Ar = Ph | 2 | 60 | **81ga** |
| 7 | **80h:** R = 2-$IC_6H_4$ | **2b:** Ar = 4-$NO_2C_6H_4$ | 7 | 58 | **81hb** |
| 8 | **80i:** R = 2-$MeC_6H_4$ | **2b:** Ar = 4-$NO_2C_6H_4$ | 7 | 61 | **81ib** |
| 9[c] | **80i:** R = 2-$MeC_6H_4$ | **2a:** Ar = Ph | 4 | 50 | **81ia** |
| 10 | **80j:** R = 4-$OMerC_6H_4$ | **2a:** Ar = Ph | 2 | 94 | **81ja** |
| 11 | **80k:** R = 4-$^t$Bu$C_6H_4$ | **2a:** Ar = Ph | 1 | 87 | **81ka** |
| 12 | **80l:** R = 2-Furyl$C_6H_4$ | **2a:** Ar = Ph | 3 | 96 | **81la** |
| 13 | **80m:** R = 2-Pyridine | **2a:** Ar = Ph | 2 | 85 | **81ma** |
| 14[c] | **80n:** R = $CF_3$ | **2a:** Ar = Ph | 3 | 96 | **81na** |
| 15[c] | **80o:** R = $CH_3$ | **2a:** Ar = Ph | 2 | 99 | **81oa** |
| 16 | **80p:** R = Bn | **2a:** Ar = Ph | 1 | 78 | **81pa** |
| 17[c] | **80p:** R = Bn | **2d:** Ar = 4-$CNC_6H_4$ | 2 | 93 | **81pd** |
| 18 | **80p:** R = Bn | **2e:** Ar = 4-$CF_3C_6H_4$ | 1 | 92 | **81pe** |
| 19[c] | **80p:** R = Bn | **2n:** Ar = 4-$MeC_6H_4$ | 1 | 89 | **81pn** |

[a] Reactions were carried out in DMSO (0.3 M) with **80b-p** (0.3 mmol) and **2** (0.6 mmol) in the presence of TMG **23c** (10 mol%). [b] Yields refer to column-purified product. [c] Reaction kept at 80°C.

$^1$H and $^{13}$C NMR spectra of few compounds from Table 7 have depicted below Figure 33-37.

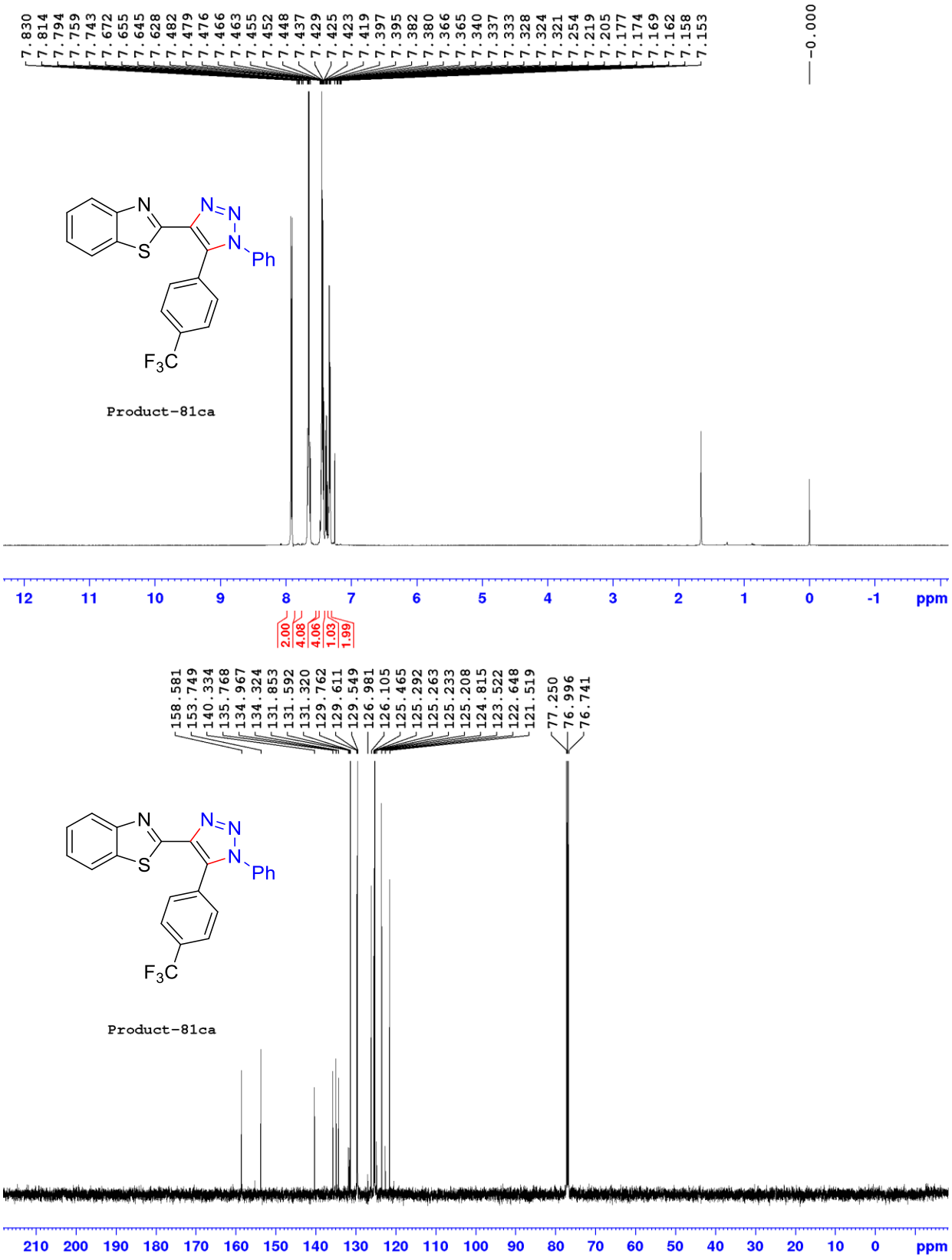



**Figure 33:** $^{1}$H NMR and $^{13}$C NMR spectra of product **81ca.**

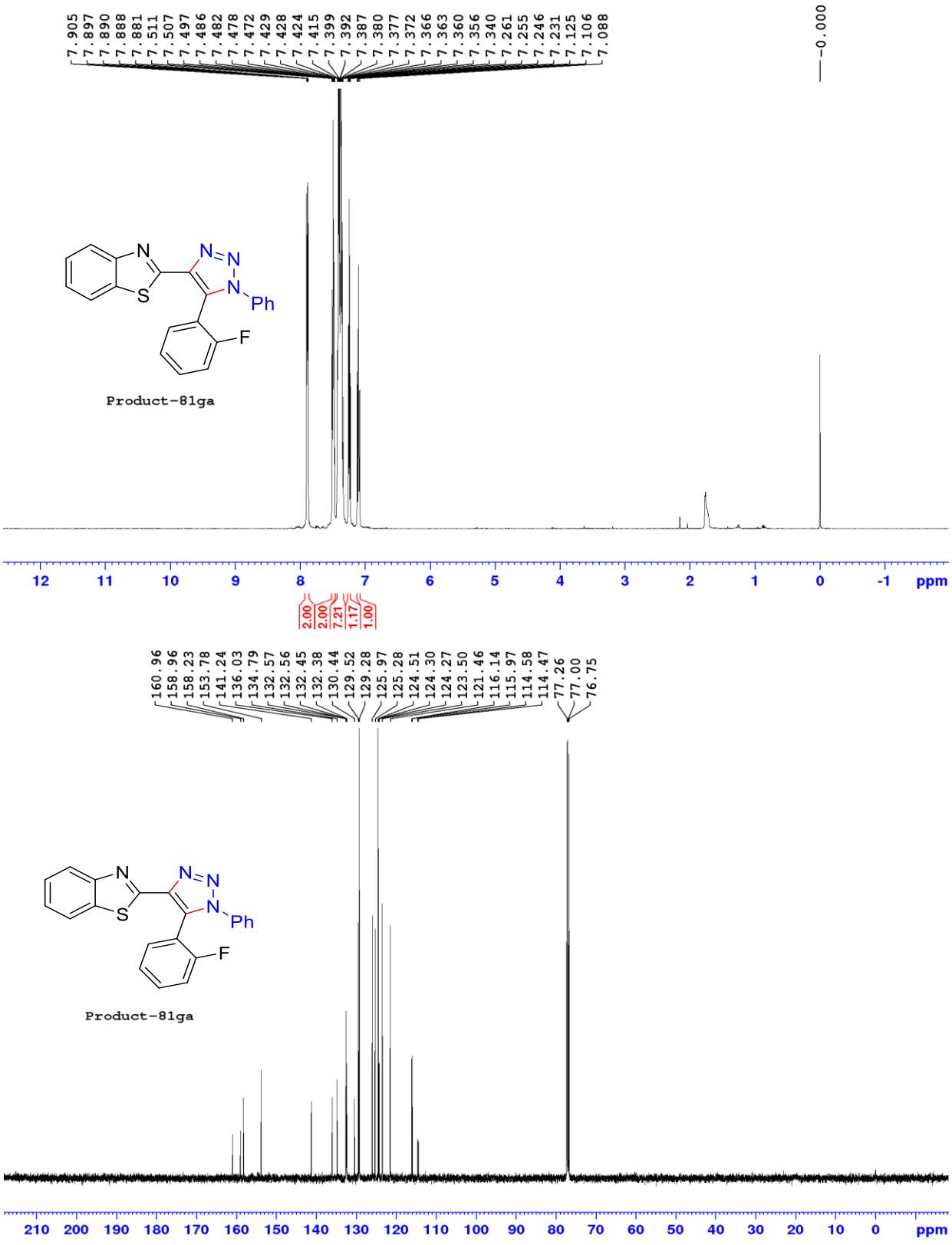



**Figure 34:** $^{1}$H NMR and $^{13}$C NMR spectra of product **81ga.**

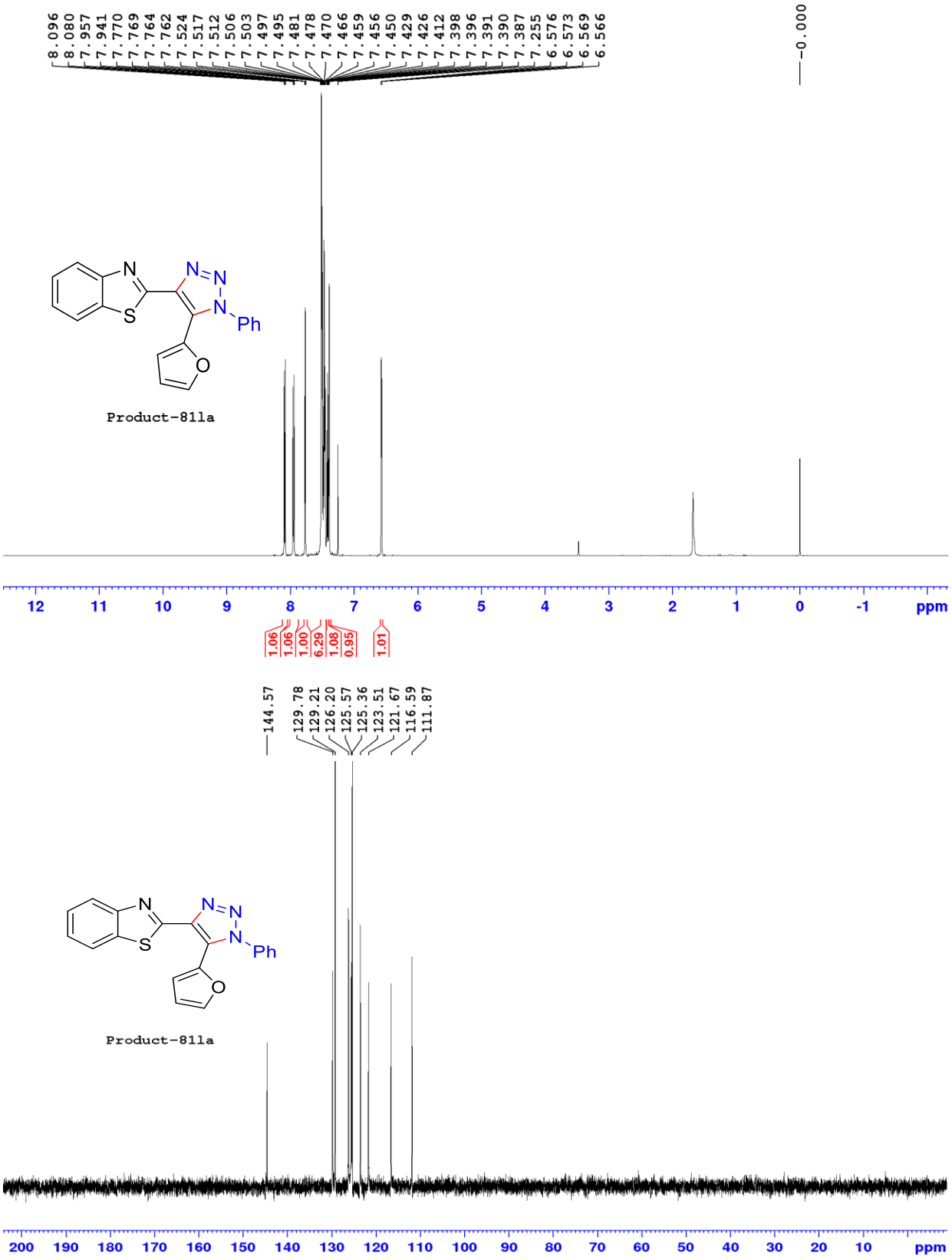



**Figure 35:** $^{1}$H NMR and $^{13}$C NMR spectra of product **81la.**

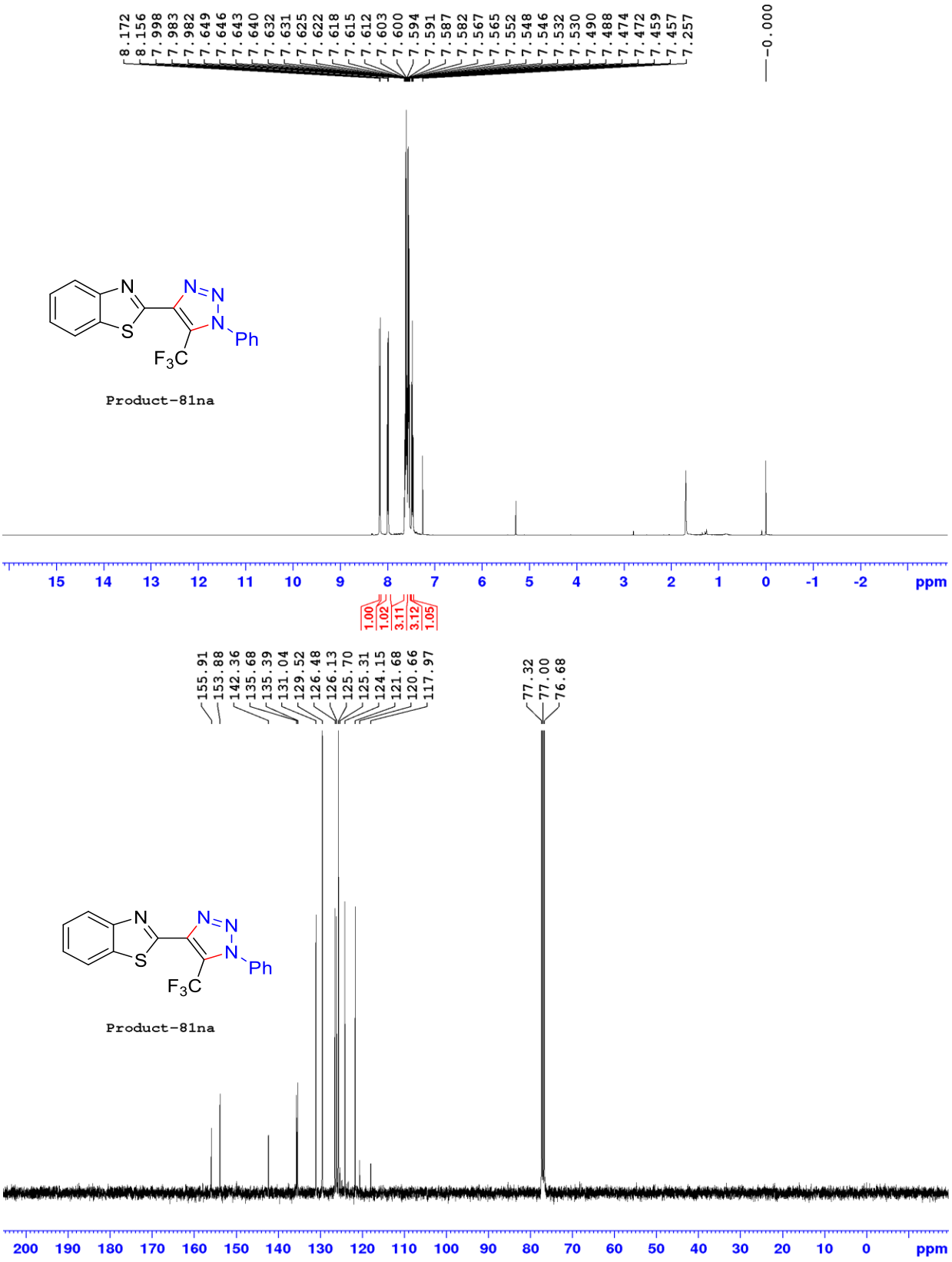



**Figure 36:** $^{1}$H NMR and $^{13}$C NMR spectra of product **81na.**

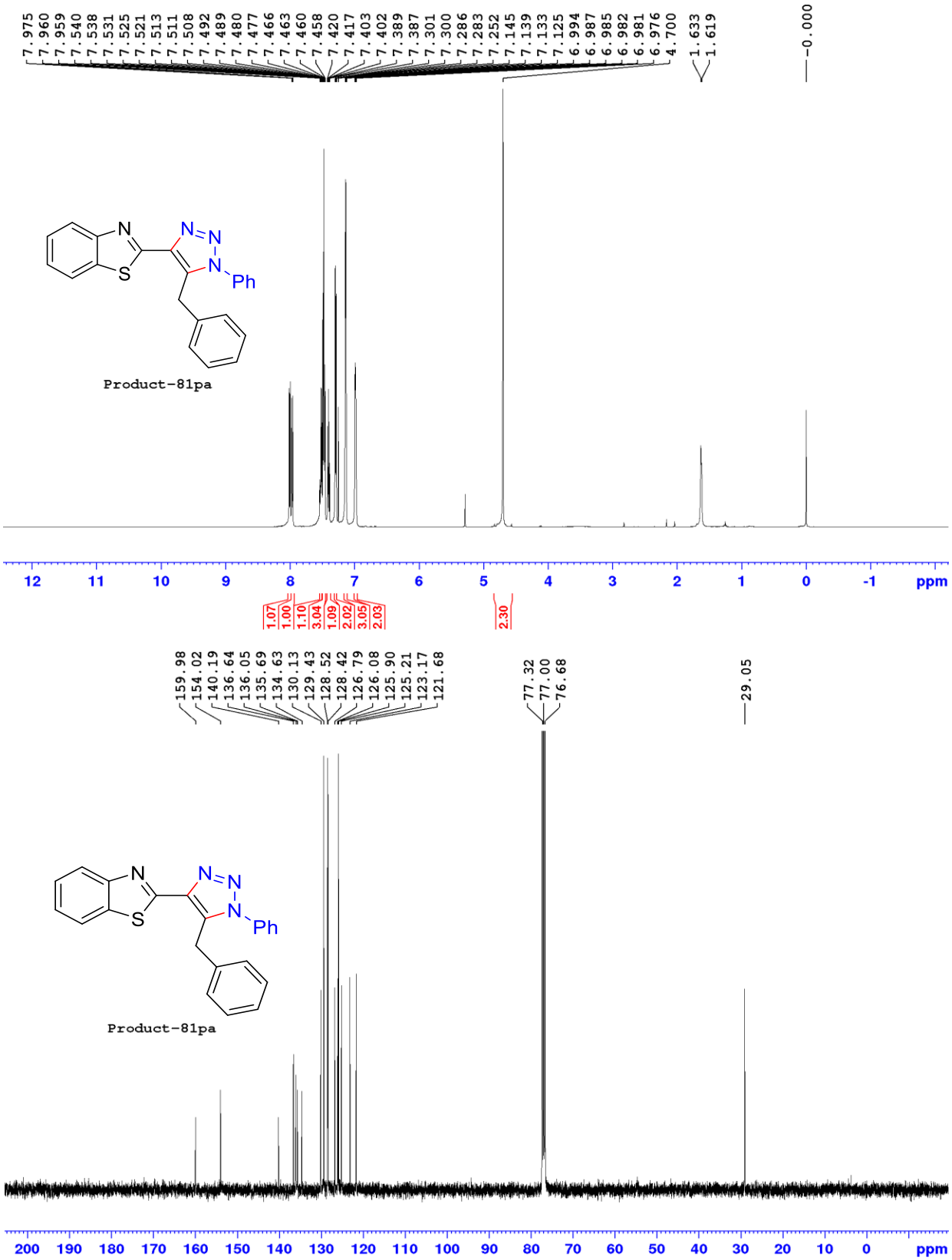
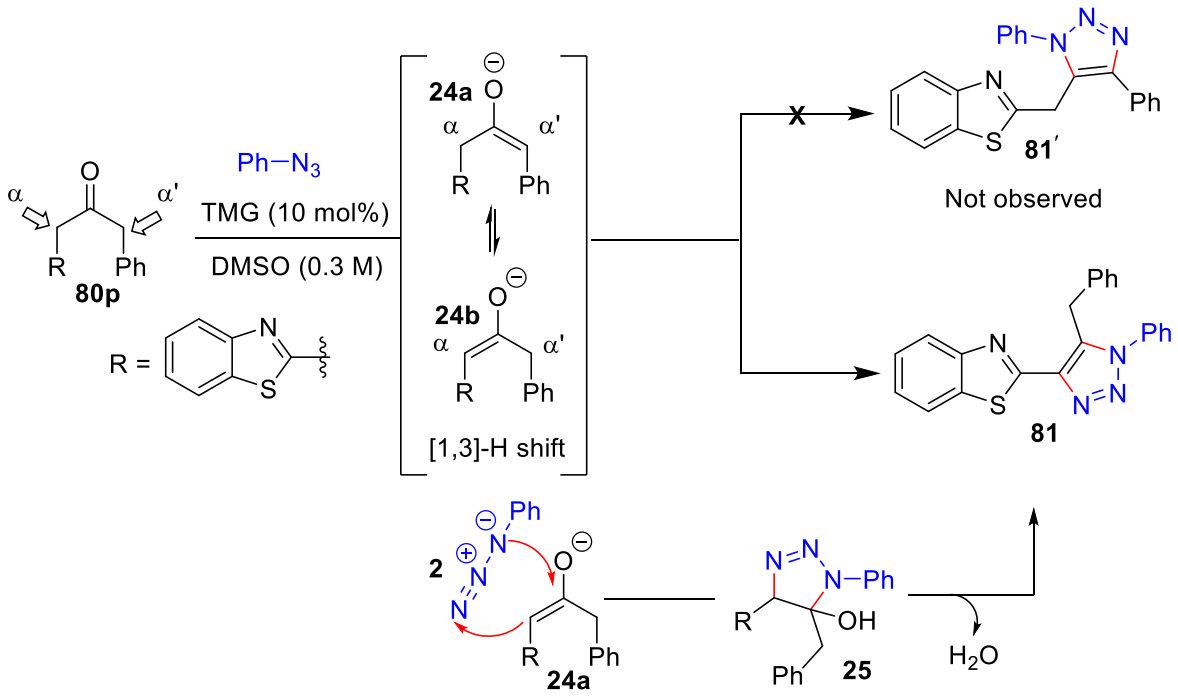



**Figure 37:** $^{1}$H NMR and $^{13}$C NMR spectra of product **81pa.**

## 4.2.4 Reaction Mechanism:

When a non-symmetrical ketone containing two active methylene groups i.e., *α* methylene *and α'* methylene as in case of **80p** is treated with catalyst TMG **23c** in an OrgAKC reaction, there is a possibility of formation of a kinetic enolate **24a** and a thermodynaic enolate **24b**. But in this case, the thermodynamic enolate intermediate is stabilized by the presence of an electron deficient benzothiazole group. Therefore, the thermodynamic product predominates when compared to the kinetic product. There is another possibility where kinetic enolate **24a** is formed initially which immediately undergoes a [1, 3]-hydride shift to form thermodynamic intermediate **24b,** which undergoes [3+2]-cycloaddition with azide followed by dehydration results in the exclusive formation of the desired regioselective isomer **81**.

**Scheme 30**: Reaction Mechanism of OrgAKC.



The structures **81pa** and **81pe** were confirmed by X-Ray analysis as shown below Figure 38 and 39.

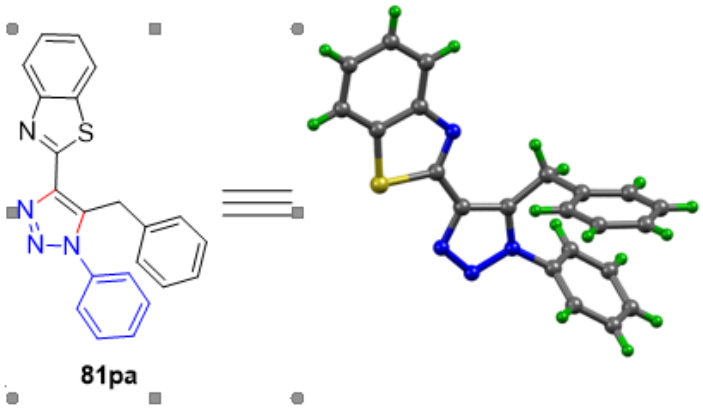



**Figure 38:** The crystal structure of 2-(5-benzyl-1-phenyl-1*H*-1,2,3-triazol-4-yl)benzo[*d*]thiazole **81pa**.

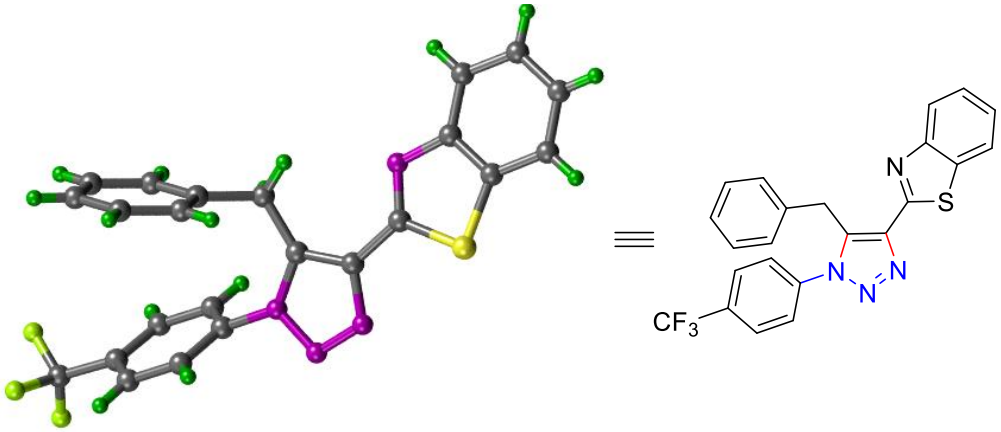



**Figure 39:** The crystal structure of 2-(5-benzyl-1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,3-triazol-4-yl)benzo[*d*]thiazole **81pe**.

## 4.3 Conclusions

To summarize, we have developed a general green protocol for the high-yielding synthesis of functionally rich benzothiazole containing 1,2,3-triazoles via an enolate-mediated organocatalytic formal [3 + 2]-cycloaddition of acyclic ketones and aryl/alkyl azides. This process is extremely useful in the synthesis of regioselective benzothiazole containing 1,2,3-triazoles **81**, which are useful intermediates in pharmaceutical chemistry and has many applications in materials chemistry.

# 5. Organocatalytic One-Pot Synthesis of Pseudo-Terpenoids

## 5.1 Introduction

**S**ynthesis of natural products, drugs, organic materials and their analogues through a sustainable one-pot mode by utilizing readily available starting materials/catalysts is a challenging task for synthetic chemists.[31-3] In the mode of linear, convergent or divergent synthesis of compounds, multiple steps involvement, each step column purification, heavy solvent consumption, harmful wastes, toxic metal catalysts and decrease in overall yields are some of the drawbacks. With these disadvantages in mind, from the last two decades more attention has been devoted towards the development of organocatalytic sequential multicatalysis cascade one-pot reactions.[34-46] Organocatalytic sequential multi-catalysis cascade one-pot reactions can address some of the problems associated with step-economy, columneconomy, and atom-economy to construct complex molecules.[34-46] Recently emerging organocatalytic one-pot reactions have been considered the green alternatives to the classical reactions.[34-46]

Among the organocatalytic reactions, few have made their way into the total synthesis of natural products and drugs. [47-59] Organocatalytic Michael,[60-62] aldol, [63,64] Diels-Alder,[65] aminoxylation,[66] and Friedel-Crafts,[67] reactions are used as key steps in the total synthesis of natural products, drugs and drug intermediates. Among the library of organocatalytic reactions, our three component organocatalytic reductive coupling (*OrgRC*) reaction has been utilized by many synthetic chemists in the total synthesis of natural products, drugs, intermediates and materials.[58-66] In our vision to develop more sustainable organocatalytic one-pot methods by including *OrgRC* as a key reaction and to apply those one-pot methods for the synthesis of natural products/drugs/analogues/materials, we considered biologically important structurally complex tricyclic cedrane (octahydro-methanoazulene as a basic skeleton) core as our synthetic target methods by including *OrgRC* as a key reaction and to apply those one-pot methods for the synthesis of natural products/drugs/analogues/materials, we considered biologically important structurally complex tricyclic cedrane (octahydro-methanoazulene as a basic skeleton) core as our synthetic target.

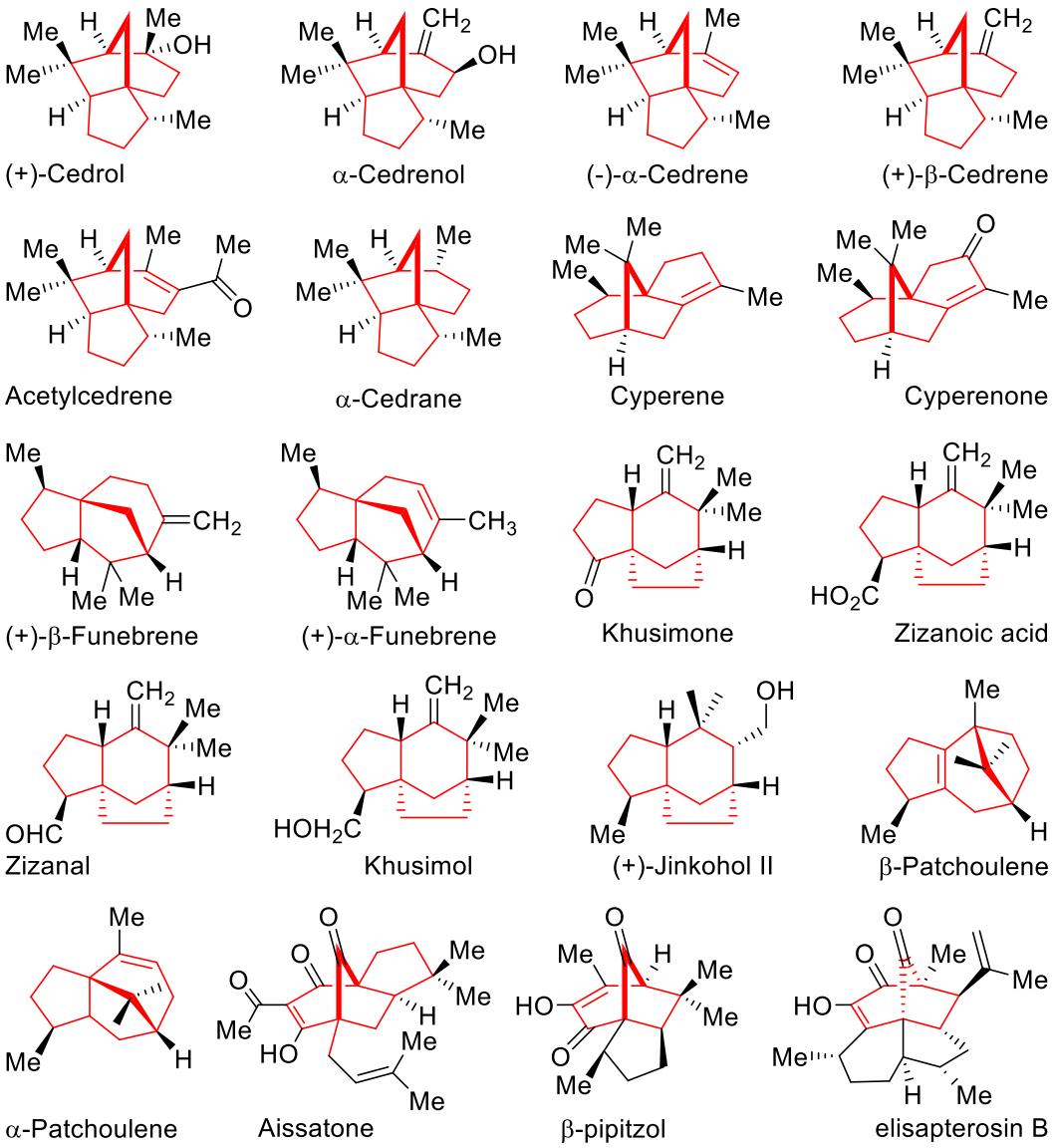
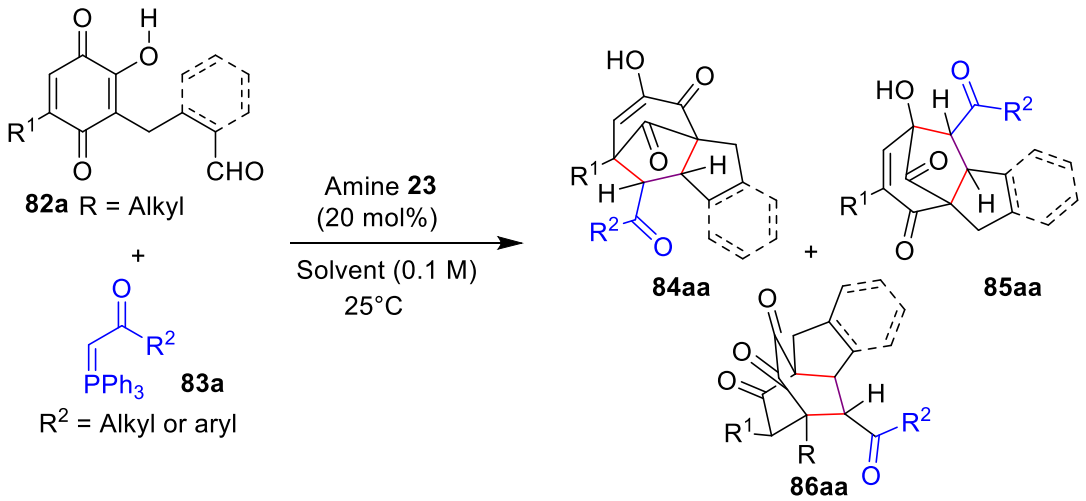



**Figure 40**: Natural products based on the octahydro-methanoazulene.

Octahydro-methanoazulene is found as a basic skeleton in more than 160 natural products, which are having many interesting biological activities including AVP Vla receptors, anti-inflammatory, anti-cancer, anti-tubercular, anti-bacterial, analgesic, anti-malarial, antibiotic, anti-proliferative, and microtubule depolymerization (Figure 40).[67-73] These compounds have been frequently challenged as synthetic targets, due to their demanding architecture and interesting biological activities. Many of these structurally diverse cedranes (Figure 40) have been synthesized by using combinations of various reactions like inter-/intramolecular [4+2]-

cycloaddition, oxidative dearomatization, [5+2]-cycloaddition, oxidation, ring expansion, acid-catalyzed cyclization, alkylation, reduction, intramoleculardiazoalkane-carbonyl ring expansion, intramolecular anionic cyclisation, and/or Wittig olefination as key steps in linear or convergent mode.[67-73] Herein, we plan of synthesizing a library of cedranes through organocatalysis in a one-pot manner with high rate of selectivity and yields. Reaction of the hydroxy-*p*-quinone butanals with alkyl carbonyl- or aryl carbonyl-methylene-triphenylphosphoranes under the catalytic amounts of amine at 25 ºC can generate Wittig olefination coupling intermediate, which immediately undergoes further intramolecular Michael reaction followed by another spontaneous Michael or aldol or Michael reaction leading to the tricyclic annulation compounds **84aa** or **85aa** or **86aa**, respectively based on the reaction conditions (Scheme 31). Previously,[60d] we have synthesized methanobenzo[*f*]azulenes from the lawsone-aldehydes and phosphoranes by using amine-catalyzed Wittig/Michael/aldol reactions. But, present reaction design is really challenging to study the outcome of the product **84aa**/**85aa**/**86aa** formation rate, distribution and selectivity from the coupling, first annulation and three different possible second annulation pathways under the mild reaction conditions (Scheme 31).

**Scheme 31:** Reaction Design for the One-pot Synthesis of Cedranes

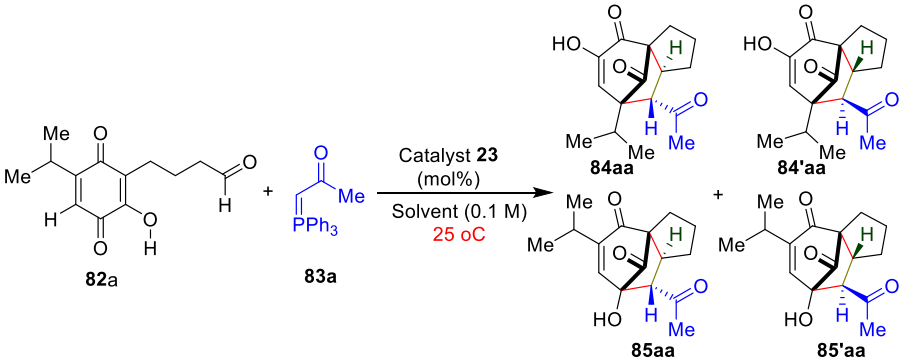


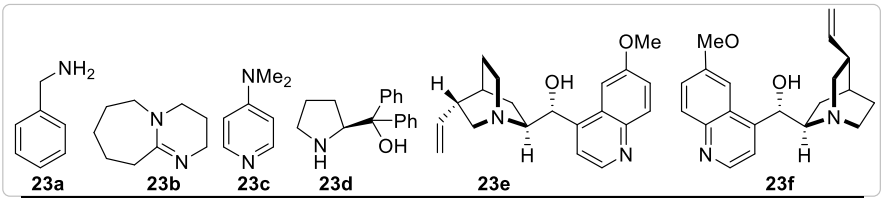
# 5.2 Results and Discussion

## 5.2.1 Reaction Optimization:

First we prepared the functionalized hydroxy-*p*-quinone butanal **82a** by using protection-free, one-pot (*S*)-proline-catalyzed reductive coupling of hydroxy-*p*-quinone with butanedial under the presence of Hantzsch ester in moderate yields.[60]

**Table 8:** Reaction optimization for new coupling/annulation.[a]




| Entry | Catalyst [mol%] | Solvent | t [h] | Yield [%][b] [84+85] | pr[c] [84:85] | dr[c] [84aa:84'aa] |
|---|---|---|---|---|---|---|
| 1 | - | DCM | 2.0 | 78 | 1:1 | 99:1 |
| 2 | **23a** (10 mol%) | DCM | 0.16 | 64 | 1.2:1 | 99:1 |
| 3 | **23b** (10 mol%) | DCM | 1.5 | 83 | 4:1 | 99:1 |
| 4 | **23c** (10 mol%) | DCM | 1.5 | 75 | 2.7:1 | 99:1 |
| 5 | **23d** (10 mol%) | DCM | 2.0 | 81 | 3.2:1 | 99:1 |
| 6 | **23e** (10 mol%) | DCM | 1.0 | 75 | 32:1 | 99:1 |
| 7 | **23f** (10 mol%) | DCM | 2.0 | 60 | 30:1 | 99:1 |
| 8 | **23e** (15 mol%) | DCM | 2.0 | 78 | 32:1 | 99:1 |
| 9 | **23e** (20 mol%) | DCM | 2.0 | 85 | 33:1 | 99:1 |
| 10 | **23e** (20 mol%) | toluene | 1.0 | 55 | 31:1 | 99:1 |
| 11 | **23e** (20 mol%) | benzene | 1.0 | 52 | 28:1 | 99:1 |
| 12 | **23e** (20 mol%) | $C_6F_6$ | 2.5 | 65 | 23:1 | 99:1 |
| 13 | **23e** (20 mol%) | $CH_3CN$ | 1.0 | 66 | 13:1 | 99:1 |
| 14 | **23e** (20 mol%) | $CHCl_3$ | 1.0 | 82 | 33:1 | 99:1 |
| 15 | **23e** (20 mol%) | DCE | 1.0 | 70 | 33:1 | 99:1 |
| 16[d] | **23e** (20 mol%) | DCM | 1.0 | 70 | 33:1 | 99:1 |
| 17[e] | **23e** (20 mol%) | DCM | 1.0 | 81 | 33:1 | 99:1 |
| 18[f] | **23e** (20 mol%) | DCM | 1.0 | 83 | 33:1 | 99:1 |

[a] Reactions were carried out in solvent (0.1 M) with1.3 equiv. of **83a** relative to the **82a** (0.2 mmol) in the presence of catalyst 3 at 25°C. [b] Yield refers to the overall yield of the column products. [c] Determined by $^1$H NMR analysis of crude products obtained through column filtration. [d] 1.0 equiv. of **83a** was used. [e] 1.2 equiv. of **83a** was used. [f] 1.5 equiv. of **83a** was used.

Surprisingly, the catalyst-free reaction of hydroxy-*p*-quinone butanal **82a** with 1.3 equiv. of Acetylmethylene-triphenylphosphorane **83a** in DCM (0.1 M) at 25 ºC for 2.0 h furnished only **84aa** and **85aa** type methanoazulene products without formation of **86aa** (Scheme 31 and Table 8). $^{1}$H NMR analysis of the filtered-crude products were able to show that tandem Wittig/intramolecular Michael/intramolecular Michael (W/IM/IM) product **84aa** and Wittig/intramolecular Michael/intramolecular aldol (W/IM/IA) product **85aa** were furnished in 78% yield with 1:1 product ratio (*pr*) and 99:1 *dr* for both of them through coupling/annulation mode (Table 8, entry 1).

Herein, the tandem W/IM/IM and W/IM/IA reactions are spontaneous reactions, where Wittig olefination initiated the tandem sequence. Even though methanoazulenes **84aa**/**85aa** are inspiring structures of cedrane-type terpenoids (Figure 40), it is a big challenge to control the product ratio (*pr*) of **84aa** versus **85aa** with single *dr* in this kind of reactions, where the catalyst-free reactions are able to give the products. First to achieve the high yield/*pr*/*dr* in the designed one-pot reaction, we investigated the treatment of **82a** with **83a** under different catalysts, equivalents and solvents at 25 ºC for 0.16 to 2.5 h (Table 8). Enlighteningly, the tandem reaction of **82a** with 1.3 equiv. of **83a** under the 10 mol% of benzylamine 2**3a**-catalysis in DCM at 25 ºC within 10 minutes furnished the methanoazulenes **84aa** and **85aa** in 64% yield with 1.2:1 *pr* and 99:1 *dr* out of the many possible structures (Table 8, entry 2). In a similar manner, the tandem reaction of **82a** with 1.3 equiv. of **83a** under the 10 mol% of DBU **23b**, DMAP **23c** or (*S*)-DPP **23d**-catalysis in DCM (0.1 M) at 25 ºC for 1.5 to 2.0 h furnished the methanoazulenes **4aa** and **5aa** in 83%, 75%, 81% yield with 4:1, 2.7:1, 3.2:1 *pr* and 99:1 *dr* respectively (Table 8, entries 3-5). Astonishingly, further optimization of the tandem reaction of **82a** with 1.3 equiv. of **83a** under the 10 to 20 mol% of quinine **23e**- or quinidine **23f**-catalysis in DCM at 25 ºC for 1-2 h furnished the methanoazulenes **84aa** and **85aa** in high yields and ratios (85% yield, 33:1 *pr* and 99:1 *dr*) as shown in Table 8, entries 6-9. After realizing the natural quinine **23e** as the best catalyst for tandem reaction, we performed the reaction of **82a** with 1.0 to 1.5 equiv. of **83a** under 20 mol% of quinine **23e** in a variety of solvents like toluene, benzene, hexafluorobenzene, acetonitrile, chloroform, 1,2-dichloroethane, and dichloromethane at 25 ºC for 1.0 to 2.5 h (Table 8, entries 10-18). Among these solvents and equivalents of **83a**, chloroform/DCM and 1.3 equiv. has shown promising result with respect to yield and *pr*/*dr* of **84aa** and **85aa**. Unfortunately, the observation of low *ee*'s (45% *ee* for **84aa** and 5% *ee* for **85aa**, see Figure 60) under the quinine

**23e**-catalysis forced us to drop/postpone the *ee* investigation in this work (Scheme S1, see SI). The final optimized condition for the tandem W/IM/IM reaction was established to be 20 mol% of quinine **23e**-catalysis in DCM (0.1 M) at 25 ºC for 2.0 h and generated **84aa** in 85% yield with 33:1 *pr* and 99:1 *dr* (Table 8, entry 9).

The relative stereochemistry of compound **84aa** was further confirmed by X-Ray analysis Figure 41.

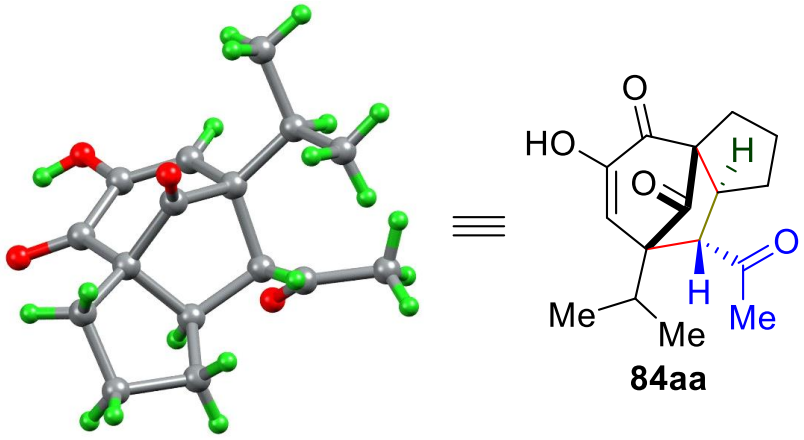



**Figure 41:** Crystal structure of (3a*R**,7*S**,8*S**,8a*S**)-8-acetyl-5-hydroxy-7-isopropyl-2,3,8,8a-tetrahydro-1*H*-3a,7-methanoazulene-4,9(7*H*)-dione **84aa**.

$^{1}$H and $^{13}$C NMR spectra of compound **84aa** are shown in Figure 42.

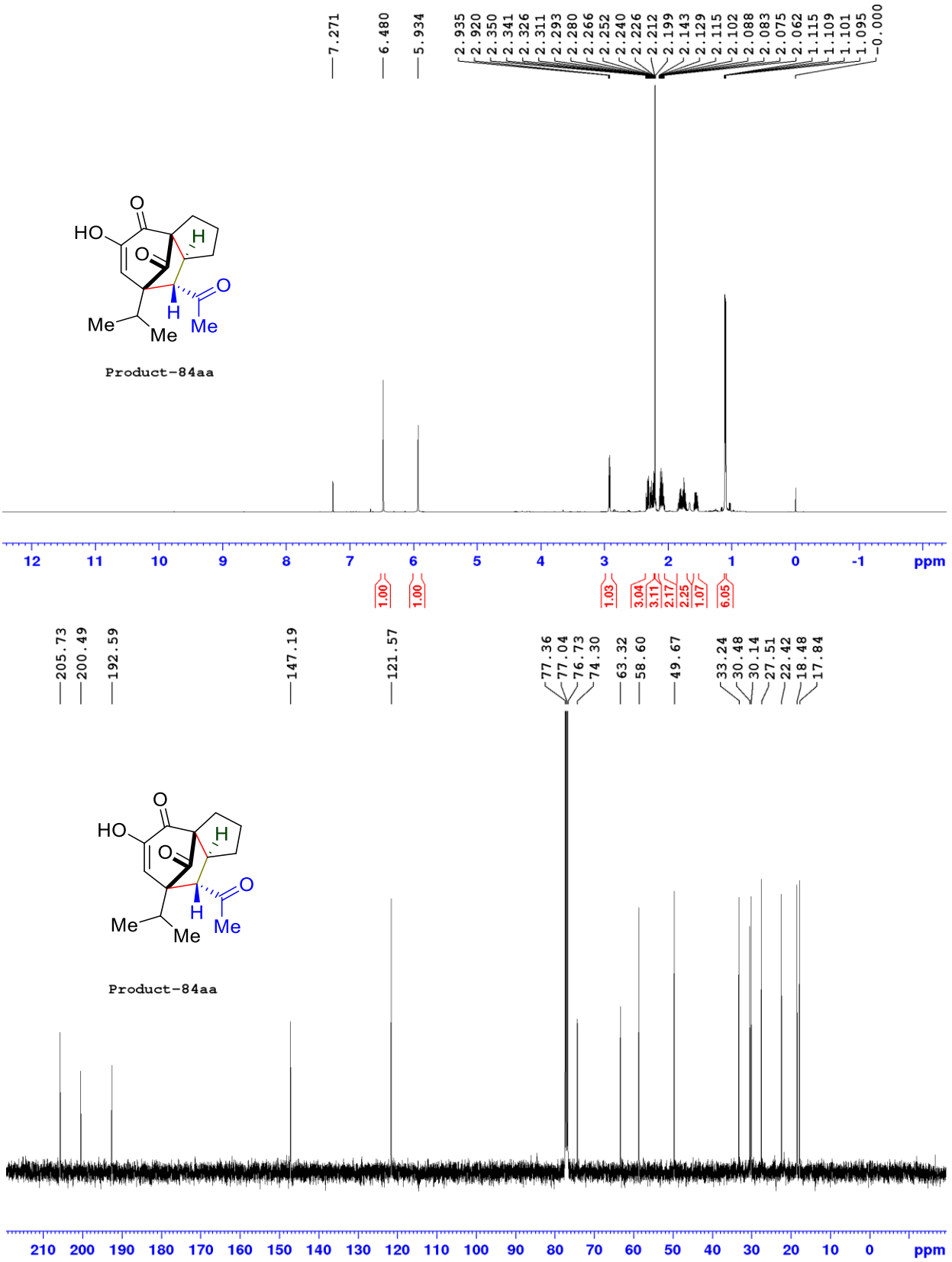
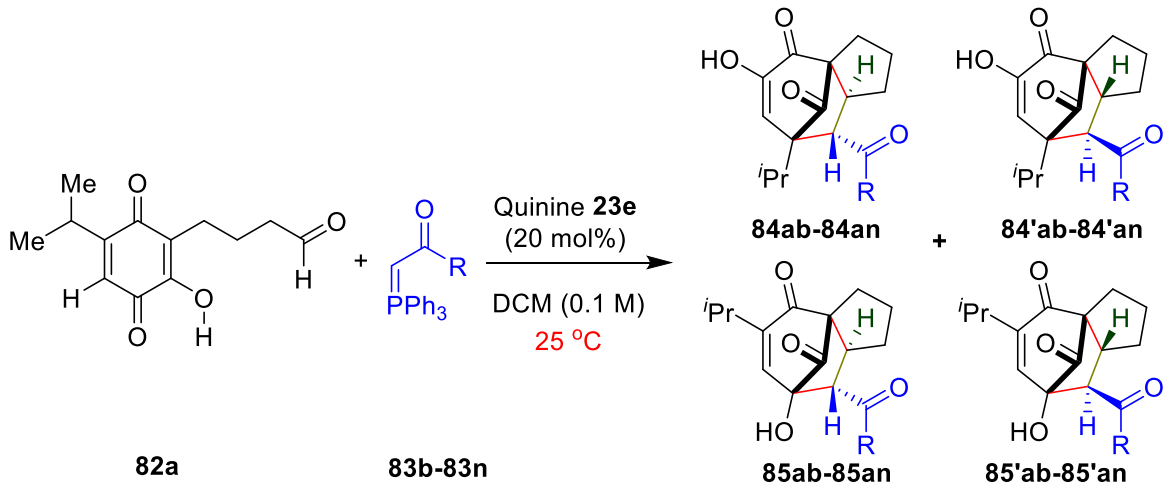



**Figure 42**: $^{1}H$ NMR and $^{13}C$ NMR spectra of product **84aa.**

### 5.2.2 Reaction Scope with Phosphoranes:

To study the various substituents effect on the tandem coupling/annulation reactions, first we studied a variety of methanoazulenes **84ab-84an/85ab-85an** synthesis by reacting **82a** with various substituted (alkyl/arylcarbonylmethylene)triphenylphosphoranes **83b-83n** under the quinine **23e** catalysis in DCM at 25 ºC for 1.5-20 h (Table 9). Notably, the tandem reactions of **82a** with Et and $^{n}$Pr substituted phosphoranes **83b-83c** performed smoothly at 25 ºC under **23e** catalysis for shorter reaction times (2.0 h) to furnish the methanoazulenes **84ab-84ac** and **85ab-85ac** in each 98% yield with very good (16:1, 17:1) *pr* and high (99:1) *dr* for the major products **84ab-84ac** (Table 9, entries 1-2). Surprisingly, the tandem reactions of **82a** with $C_6H_5$, 4-$MeC_6H_4$, 4-$MeOC_6H_4$, and 4-$PhC_6H_4$ substituted phosphoranes **83d-83g** under **23e**-catalysis at 25 ºC for 1.5 to 7.0 h furnished the methanoazulenes **84ad-84ag** and **85ad-85ag** in 87-96% yield with good to moderate (14:1 to 3.6:1) *pr* and high (99:1) *dr* for the major products **84ad-84ag** (Table 9, entries 3-6). In a similar manner, the tandem reactions of **82a** with 4-$FC_6H_4$, 4-$ClC_6H_4$, 4- $BrC_6H_4$, 4-$CF_3C_6H_4$, and 4-$NO_2C_6H_4$ substituted phosphoranes **83h-l** under **23e**-catalysis at 25 ºC for longer reaction times (7.0 to 20 h) furnished the methanoazulenes **84ah-84al** and **85ah-85al** in 86- 98% yield with good to poor (9.5:1 to 1:1.3) *pr* and high (99:1) *dr* for the major products **84ah-84al** (Table 9, entries 7-11). However, the tandem reactions of **82a** with furan-2-yl, and thiophen-2-yl substituted phosphoranes **83m**, **83n** in shorter reaction times (5.0, 3.0 h) furnished the methanoazulenes **84am**, **84an** and **85am**, **85an** in 97%, 98% yield with good (10:1, 6.8:1) *pr* and high (99:1) *dr* for the major products **84am**, **84an** (Table 9, entries 12, 13). The steric and electrostatic interactions between the quinone side-chain, *p*-quinone- alkyl/carbonyls, olefin configuration and quinine of **82a**, **83b-83n** and **23e** controlled the outcome of yield and selectivity of coupling/annulation products **84** and **85**.

**Table 9:** Reaction scope with different phosporanes.[a]




| Entry | 83 [R] | *t* [h] | Yield [%][b] [84+85] | Products | *pr*[c] [84:85] | *dr*[c] [84:84'] | *dr*[c] [85:85'] |
|---|---|---|---|---|---|---|---|
| 1 | **83b**: R = Et | 2.0 | 98 | **84ab**, **85ab** | 16:1 | 99:1 | 1.7:1 |
| 2 | **83c**: R = $^{n}$Pr | 2.0 | 98 | **84ac**, **85ac** | 17:1 | 99:1 | 2.9:1 |
| 3 | **83d**: R = Ph | 7.0 | 87 | **84ad**, **85ad** | 11:1 | 99:1 | 10:1 |
| 4 | **83e**: R = 4-Me$C_6H_4$ | 2.5 | 94 | **84ae**, **85ae** | 14:1 | 99:1 | 5.6:1 |
| 5 | **83f**: R = 4-MeO$C_6H_4$ | 1.5 | 92 | **84af**, **85af** | 7.6:1 | 99:1 | 5:1 |
| 6 | **83g**: R = 4-Ph$C_6H_4$ | 3.0 | 96 | **84ag**, **85ag** | 3.6:1 | 99:1 | 6:1 |
| 7 | **83h**: R = 4-F$C_6H_4$ | 7.0 | 95 | **84ah**, **85ah** | 9:1 | 99:1 | 1.5:1 |
| 8 | **83i**: R = 4-Cl$C_6H_4$ | 15.0 | 94 | **84ai**, **85ai** | 8:1 | 99:1 | 1.8:1 |
| 9 | **83j**: R = 4-Br$C_6H_4$ | 15.0 | 97 | **84aj**, **85aj** | 9.5:1 | 99:1 | 1.3:1 |
| 10 | **83k**: R = 4-$CF_3C_6H_4$ | 20.0 | 86 | **84ak**, **85ak** | 5:1 | 99:1 | 7.8:1 |
| 11[d] | **83l**: R = 4-$NO_2C_6H_4$ | 18.0 | 98 | **84al**, **85al** | 1:1.3 | 99:1 | 17:1 |
| 12 | **83m**: R = furan-2-yl | 5.0 | 97 | **84am**, **85am** | 10:1 | 99:1 | 1:1 |
| 13 | **83n**: R = thiophen-2-yl | 3.0 | 98 | **84an**, **85an** | 6.8:1 | 99:1 | 1.4:1 |

[a] Reactions were carried out in DCM (0.1 M) with 1.3 equiv. of **83b-n** relative to the **82a** (0.2 mmol) int the presence of 20 mol% of catalyst **23e** at 25 °C. [b] Yield refers to the overall yield of the column purified products. [c] Determined by $^{1}$H NMR analysis of crude products obtained through column filtration. [d] Reaction performed at 55°C.

$^{1}$H and $^{13}$C NMR spectra of few compounds from Table 9 have depicted below Figure 43-46.

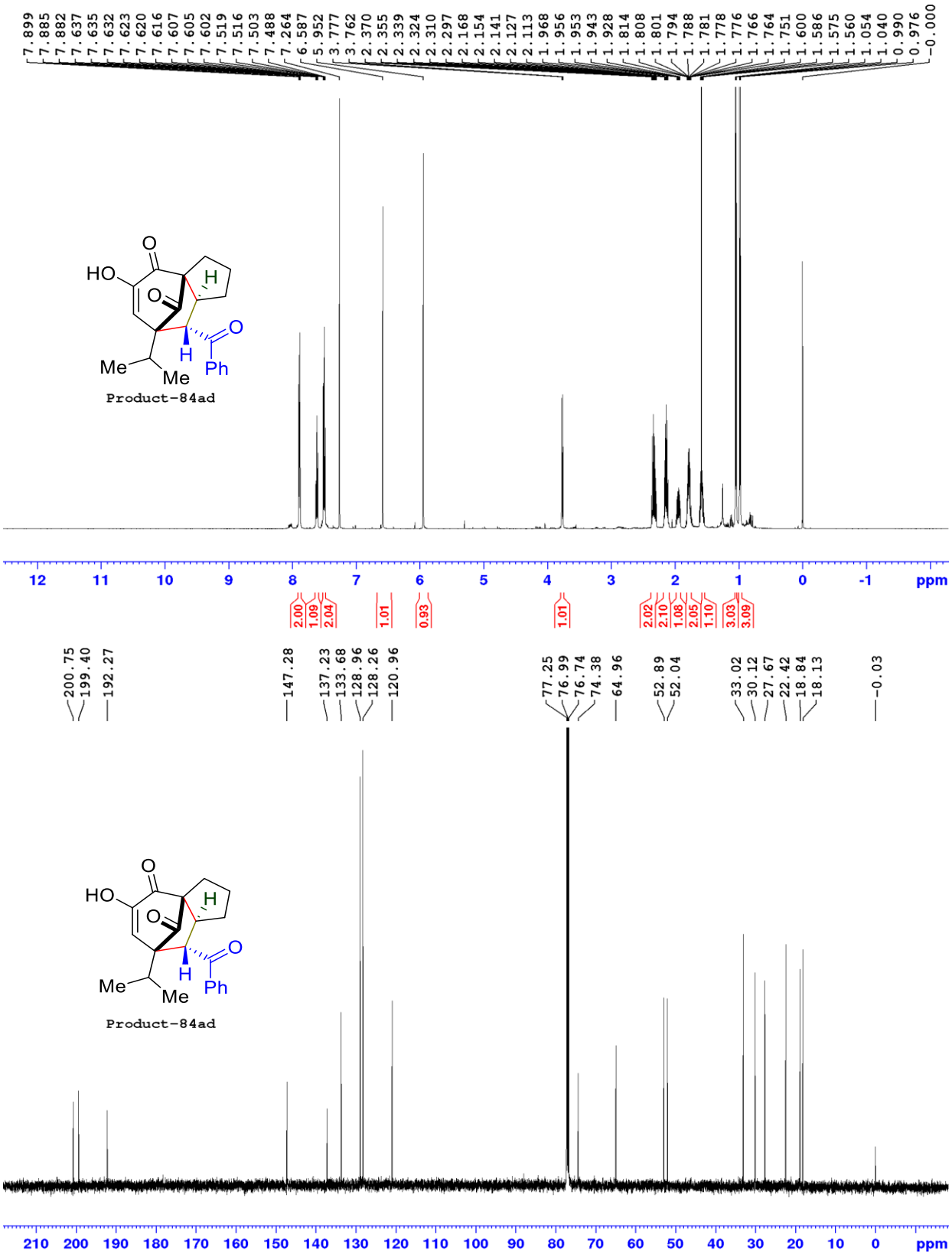



**Figure 43**: $^{1}H$ NMR and $^{13}C$ NMR spectra of product **84ad**.

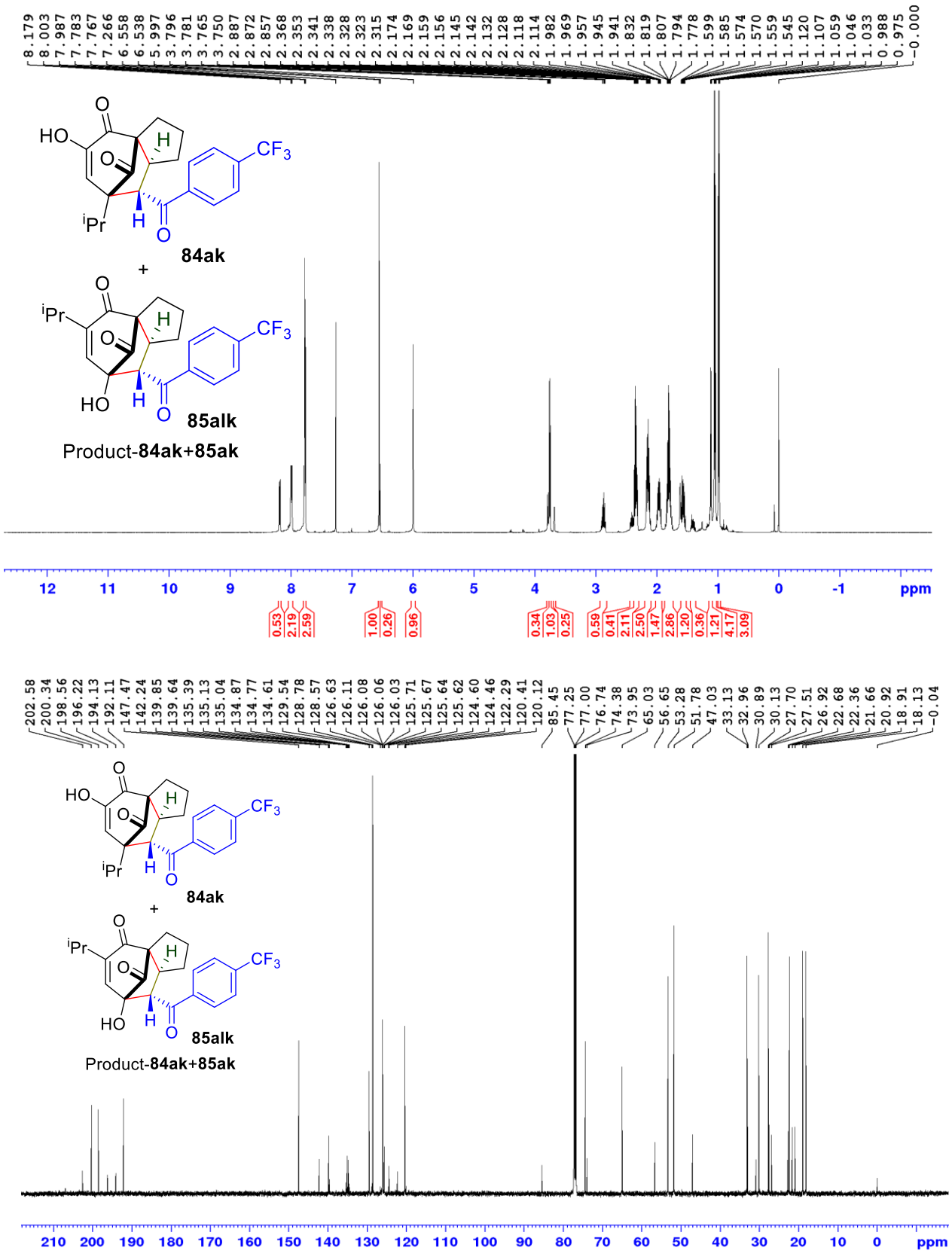



**Figure 44**: $^{1}$H NMR and $^{13}$C NMR spectra of product **84ak**+**85ak**.

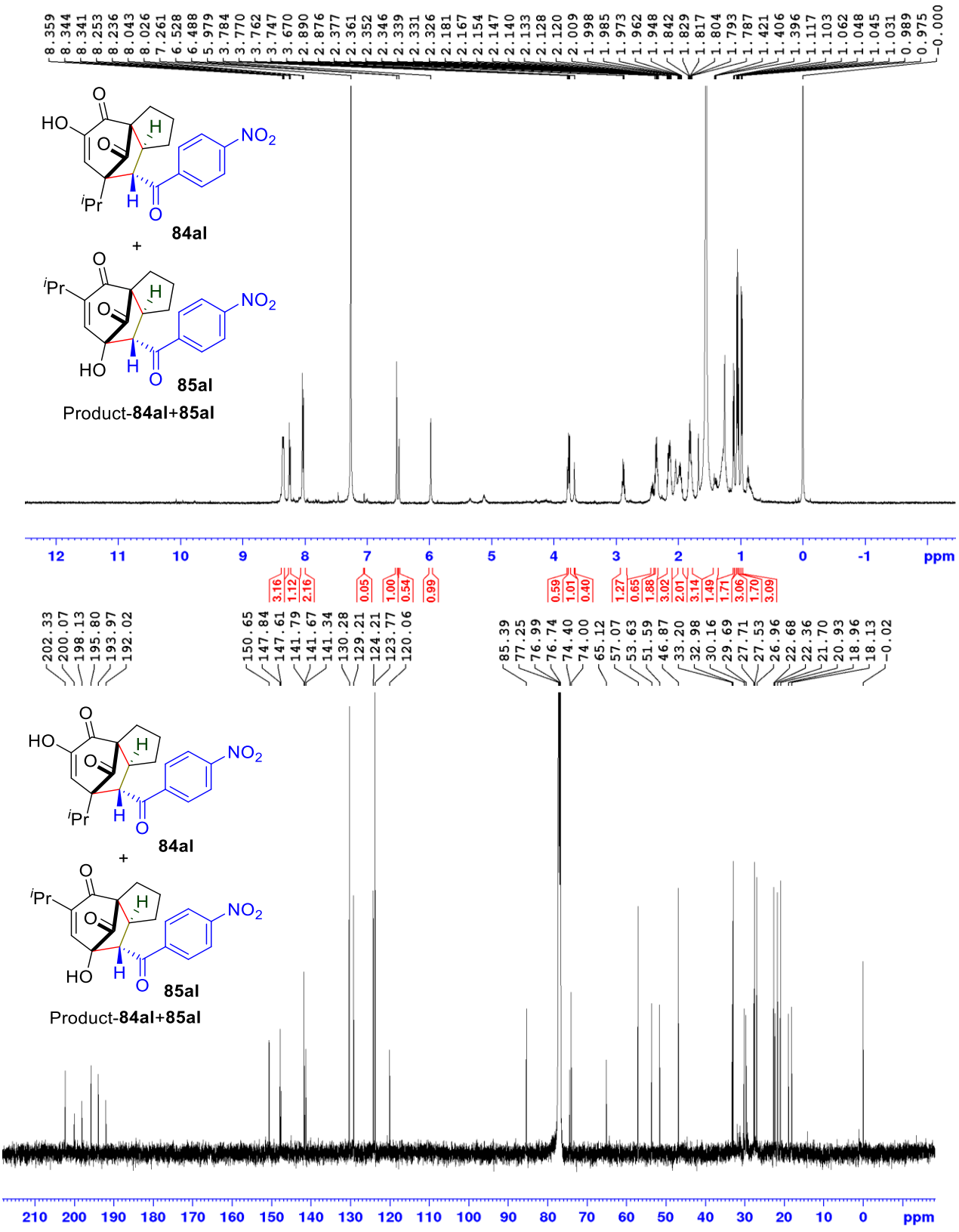



**Figure 45**: $^{1}H$ NMR and $^{13}C$ NMR spectra of product **84al**+**85al**.

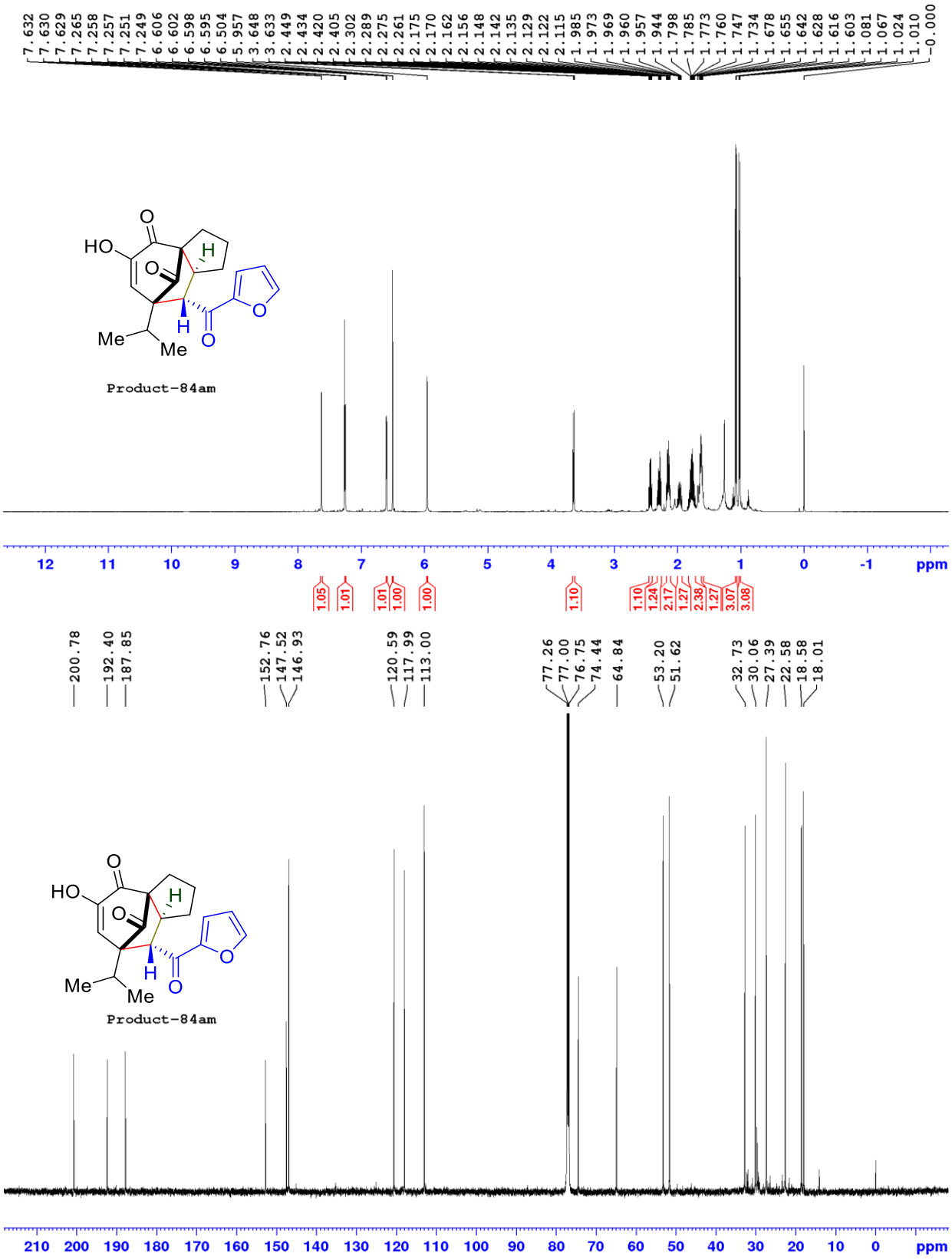



**Figure 46**: $^{1}H$ NMR and $^{13}C$ NMR spectra of product **84am.**

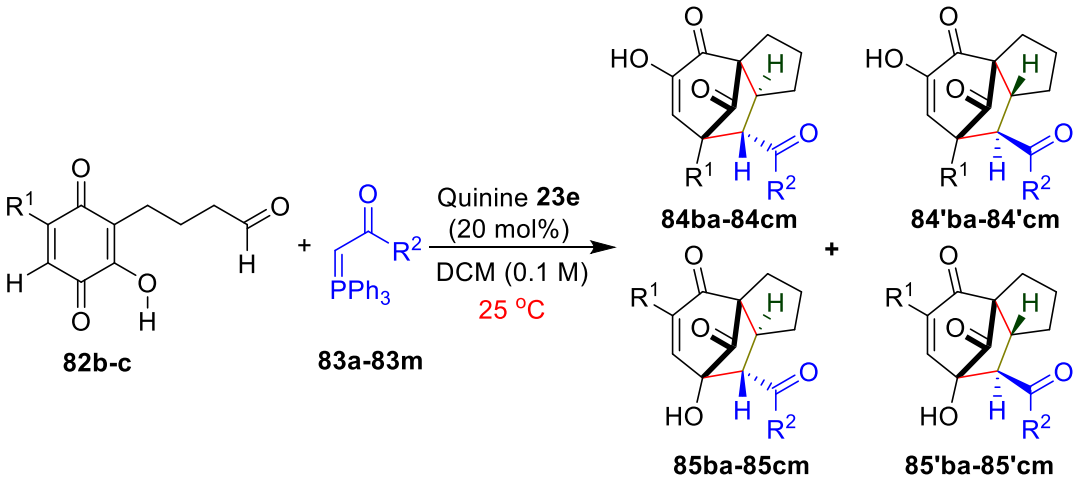
### 5.2.3 Reaction Scope with Hydroxy-*p*-Quinone Butanals:

We further attempted to synthesize the methanoazulenes **84ba-84cm**/**85ba-85cm** from the two different hydroxy-*p*-quinone butanals **82b** and **82c** with selected phosphoranes **83a-83m** under the **23e**-catalysis to investigate the steric and electronic factors on the outcome of yield/selectivity (Table 10). Herein, we explored the reaction of **82b** with **83a-83m** under the optimized condition for 1-48 h. Strikingly, all the tandem reactions occurred smoothly at 25 ºC for relatively longer reaction times and furnished only two column separated Products of methanoazulenes **84ba-84bm**/**85ba-85bm** in 80-98% yields with reduced (up to 10:1) *pr*, 99:1 *dr* for the major isomers and up to 17:1 *dr* for the minor isomers (Table 10, entries 1-7). In a similar manner, the reaction between **82c** and **83a-83m** took place in relatively less time (1-6 h), and the methanoazulenes **84ca-84cm**/**85ca-85cm** were furnished in 85-98% yield with up to 12:1 *pr* and 99:1 *dr* for the major isomers/10:1 *dr* for the minor isomers (Table 10, entries 8-14). Although, the tandem reaction of **82b**/**82c** with **83a-83m** furnished **84ba-84cm** in high yields with single isomer, **85ba-85cm** formed in various yields with good to moderate *dr*'s (Table 10). These results are showing not only how the functional groups on **82b**/**82c** and **83am** control the outcome of the tandem reaction yield/rate/*pr*/*dr*; but also how the side-chain controls it by interaction with the catalyst quinine **23e**.

### 5.2.4 Reaction Scope with Hydroxy-*p*-Quinone Benzaldehydes:

Next to investigate the side-chain electronics/conformations on the tandem reactions, we synthesized the methanoazulenes **84da-84fm**/**85da-85fm** from the three different hydroxy-*p*-quinone benzaldehydes **82d**, **82e** and **82f** with the selected phosphoranes **83a-83m** under the **23e**-catalysis (Table 11). Herein, treatment of **82d** with **83a-83m** for longer reaction times (2-72 h) gave the tandem products **84da-84dm**/**85da-85dm** smoothly in high (94-98%) yields with high (up to 37:1) *pr*, 99:1 *dr* for the major isomers and up to 4:1 *dr* for the minor isomers (Table 11, entries 1-7). In these reactions, aryl phosphoranes **83f-83m** took longer reaction times compared to alkyl phosphoranes **83a-83b**, which resulted in the formation of the tandem products **84df-84dm**/**85df-85dm** in reduced product ratio (*pr*) with less *dr*'s for the minor isomers **85df-85dm** (Table 11, entries 4-7).

**Table 10**: Reaction scope with different hydroxy-*p*-quinone butanal.[a]




| Entry | **82** [$R^1$] and **83** [$R^2$] | *t* [h] | Yield [%][b] [**84**+**85**] | Products | *pr*[c] [**84**:**85**] | *dr*[c] [**84**:**84'**] | *dr*[c] [**85**:**85'**] |
|---|---|---|---|---|---|---|---|
| 1 | **82b:** $R^1$ = $^t$Bu; **83a**: $R^2$ = Me | 1.0 | 88 | **84ba**, **85ba** | 7.5:1 | 99:1 | 3:1 |
| 2 | **82b:** $R^1$ = $^t$Bu; **83b**: $R^2$ = Et | 2.0 | 98 | **84bb**, **85bb** | 7.7:1 | 99:1 | 3:1 |
| 3 | **82b:** $R^1$ = $^t$Bu; **83d**: $R^2$ = Ph | 24.0 | 96 | **84bd**, **85bd** | 8.3:1 | 99:1 | 2.8:1 |
| 4 | **82b:** $R^1$ = $^t$Bu; **83f**: $R^2$ = 4-MeOC$_6$H$_4$ | 1.0 | 97 | **84bf**, **85bf** | 6.8:1 | 99:1 | 2.7:1 |
| 5 | **82b:** $R^1$ = $^t$Bu; **83j**: $R^2$ = 4-BrC$_6$H$_4$ | 2.0 | 85 | **84bj**, **85bj** | 10:1 | 99:1 | 1.5:1 |
| 6 | **82b:** $R^1$ = $^t$Bu; **83k**: $R^2$ = 4-CF$_3$C$_6$H$_4$ | 48.0 | 80 | **84bk**, **85bk** | 4.8:1 | 99:1 | 17:1 |
| 7 | **82b:** $R^1$ = $^t$Bu; **83m**: $R^2$ = furan-2-yl | 24.0 | 90 | **84bm**,**85bm** | 9.7:1 | 99:1 | 1.7:1 |
| 8 | **82c:** $R^1$ = $^s$Bu; **83a**: $R^2$ = Me | 2.0 | 88 | **84ca**, **85ca** | 12:1 | 99:1 | 5:1 |
| 9 | **82c:** $R^1$ = $^s$Bu; **83b**: $R^2$ = Et | 1.5 | 85 | **84cb**, **85cb** | 11:1 | 99:1 | 2.6:1 |
| 10 | **82c:** $R^1$ = $^s$Bu; **83d**: $R^2$ = Ph | 3.0 | 90 | **84cd**, **85cd** | 4.5:1 | 99:1 | 1:1 |
| 11 | **82c:** $R^1$ = $^s$Bu; **83f**: $R^2$ = 4-MeOC$_6$H$_4$ | 1.0 | 98 | **84cf**, **85cf** | 8.4:1 | 99:1 | 1.6:1 |
| 12 | **82c:** $R^1$ = $^s$Bu; **83j**: $R^2$ = 4-BrC$_6$H$_4$ | 6.0 | 98 | **84cj**, **85cj** | 1.4:1 | 99:1 | 10:1 |
| 13 | **82c:** $R^1$ = $^s$Bu; **83k**: $R^2$ = 4-CF$_3$C$_6$H$_4$ | 6.0 | 85 | **84ck**, **85ck** | 7.2:1 | 99:1 | 1.4:1 |
| 14 | **82c:** $R^1$ = $^s$Bu; **83m**: $R^2$ = furan-2-yl | 3.0 | 98 | **84cm**, **85cm** | 6:1 | 99:1 | 4:1 |

[a] Reaction were carried out in DCM (0.1 M) with 1.3 equiv. of **83a-m** relative to the **82b-c** (0.2 mmol) in the presence of 20 mol% of catalyst **23e** at 25°C.[ b] Yield refers to the overall yield of the column purified products. [c] Determined by $^1$H NMR analysis of crude products obtained through column filtration.

$^1$H and $^{13}$C NMR spectra of few compounds from Table 10 have depicted below Figure 47-50.

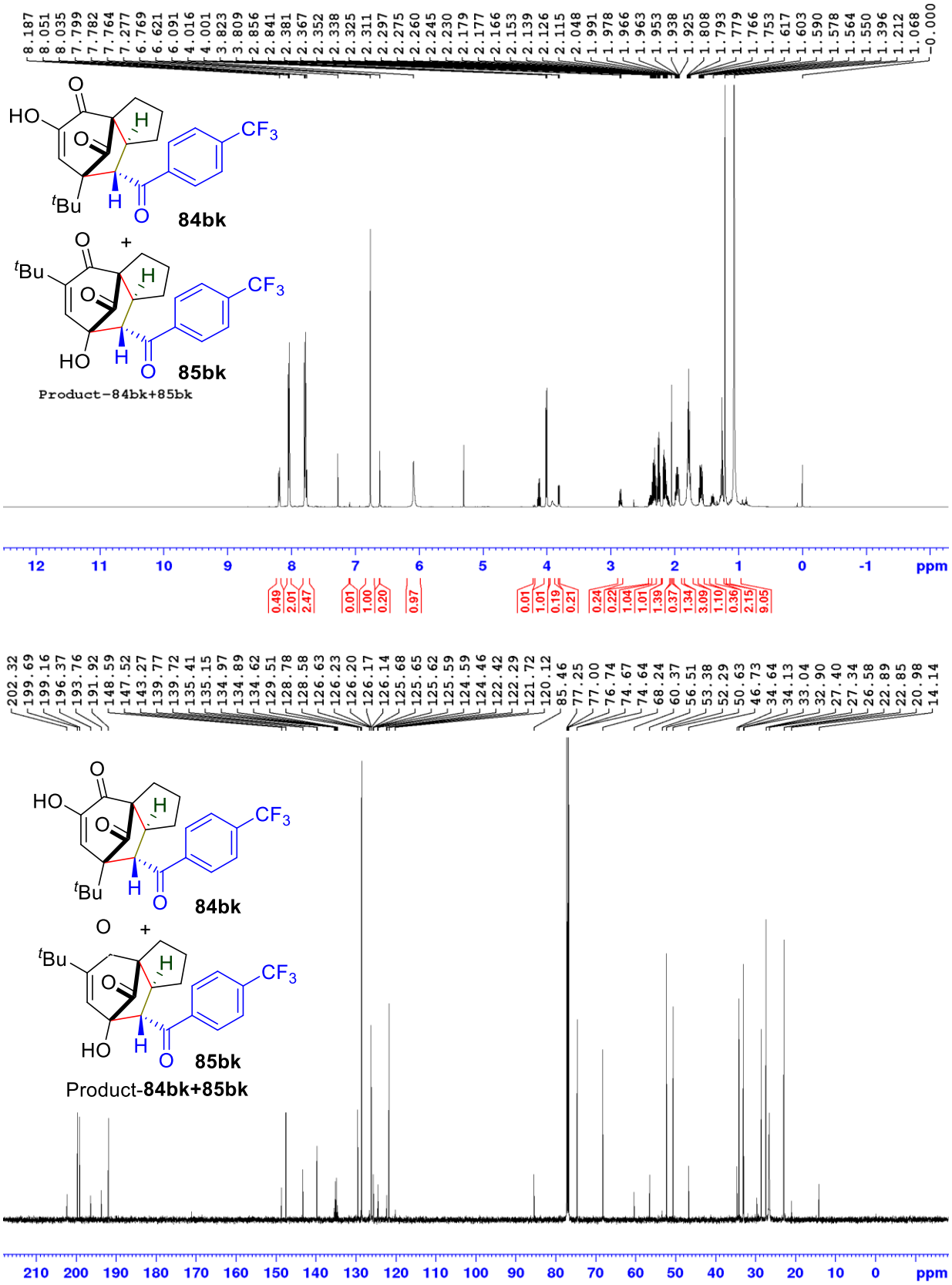



**Figure 47**: $^{1}$H NMR and $^{13}$C NMR spectra of products **84bk**+**85bk.**

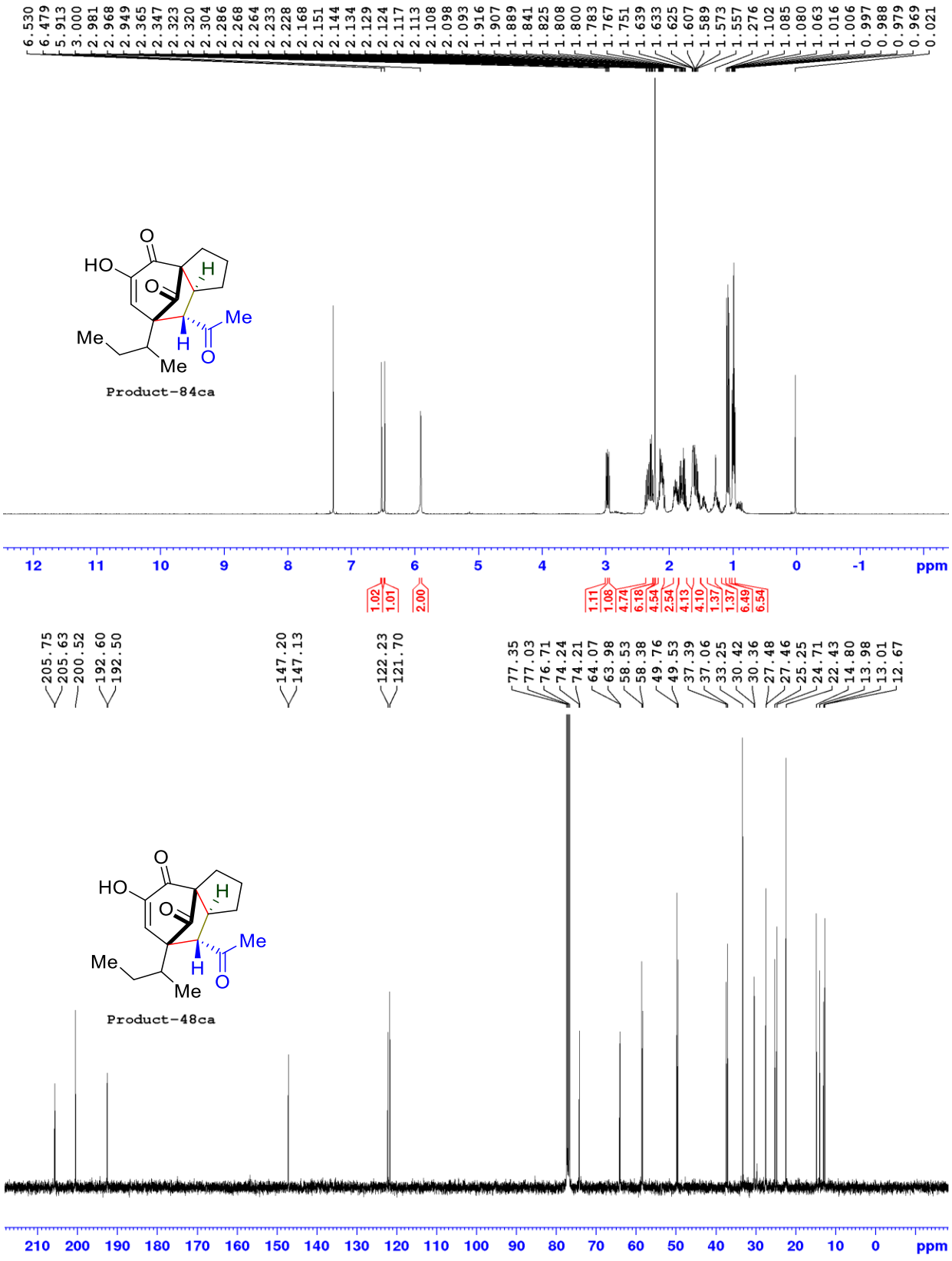



**Figure 48**: $^{1}H$ NMR and $^{13}C$ NMR spectra of product **84ca.**

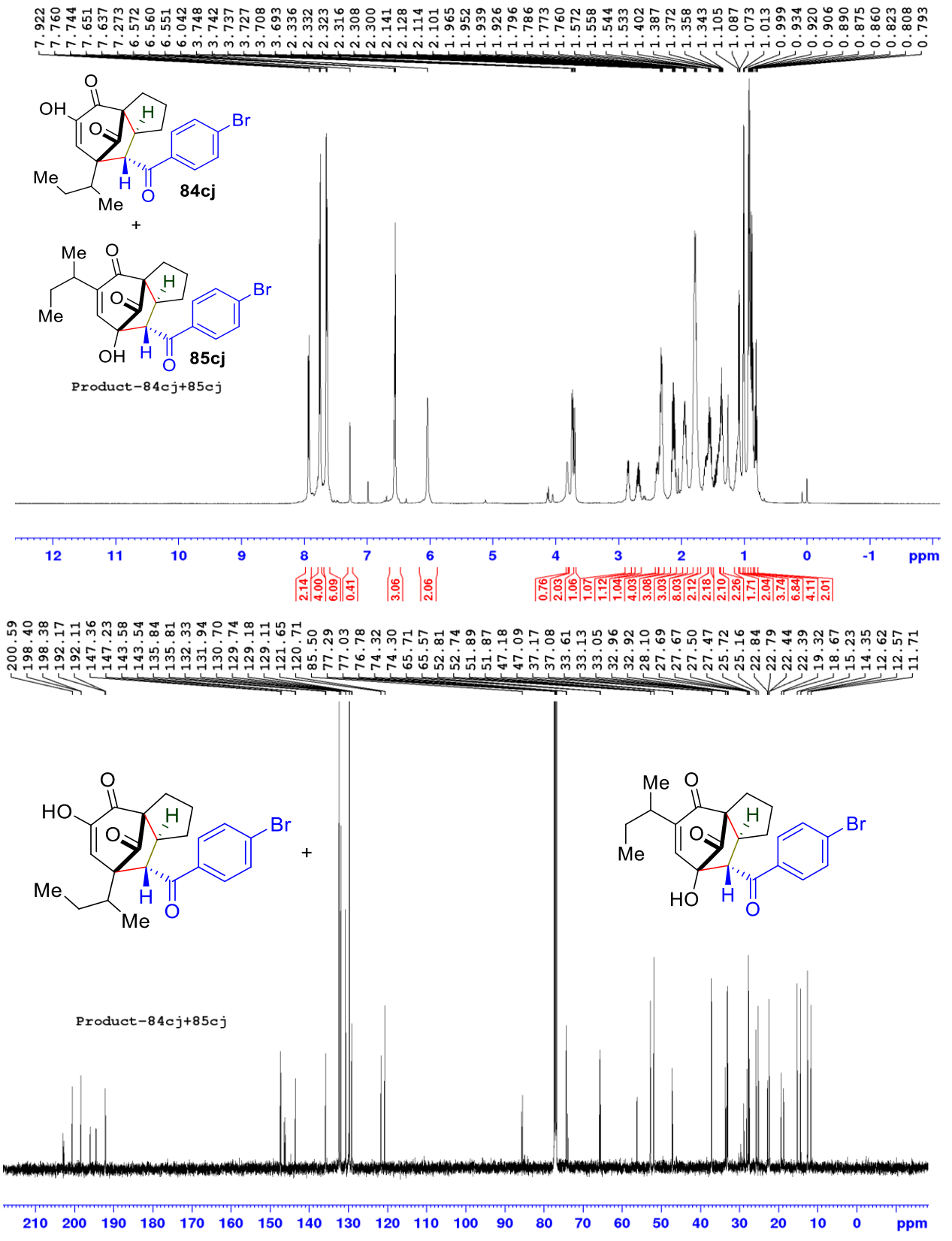



**Figure 49**: $^{1}$H NMR and $^{13}$C NMR spectra of products **84cj**+**85cj.**

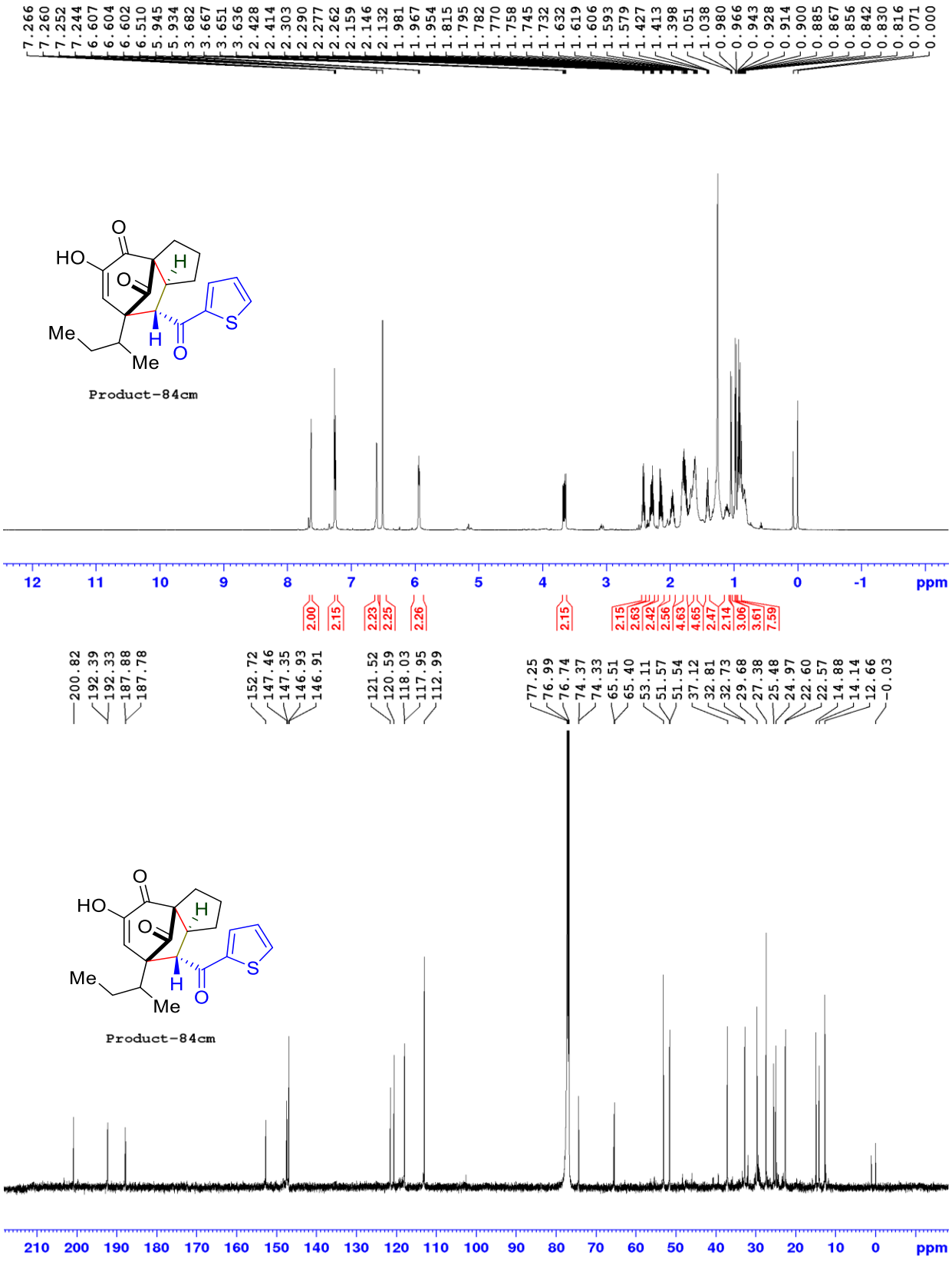



**Figure 50**: $^{1}$H NMR and $^{13}$C NMR spectra of product **84cm.**

In a similar manner, the reaction of **82e** with **83a-83m** in 2-48 h furnished the methanoazulenes **84ea-84em/85ea-85em** in 85-98% yield with up to 32:1 *pr* and 99:1 *dr* for the major isomers/8.2:1 *dr* for the minor isomers (Table 11, entries 8-14). Here also we observed similar trend compared to **82d**, except in the case of the **84ek/85ek** product ratio, where it is reversed (entry 13). Reaction of **82f** with **83a-m** under prolonged reaction time (6-96 h) furnished the methanoazulenes **84fa-84fm/85fa-85fm** in 80-95% yield with up to 18:1 *pr* and 99:1 *dr* for the major isomers/11:1 *dr* for the minor isomers (Table 11, entries 15-21). In this example also we observed similar trend compared to **82d-82e**, except in the case of **84fj-84fk/85fj-85fk** product ratio, where it is reversed (entries 19-20). These results are highlighting the importance of side-chain interactions with quinone-containing functional groups and with quinine to control the outcome of the tandem reaction yield/rate/*pr*/*dr*. We have analyzed the *ee*'s for some more tandem products **84**/**85**, and unfortunately observed low *ee*'s (11% *ee* for **84ac**, 47% *ee* for **84ba**, 26% *ee* for **85ba**, 46% *ee* for **84da** and 10% *ee* for **85da**) under the quinine **23e**-catalysis (Figure 61 for **84/85da**).

The relative stereochemistry of compound **84ed** was further confirmed by X-Ray analysis Figure 51.

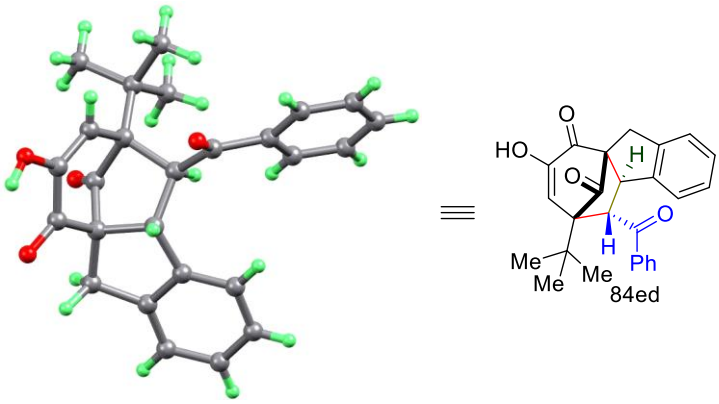
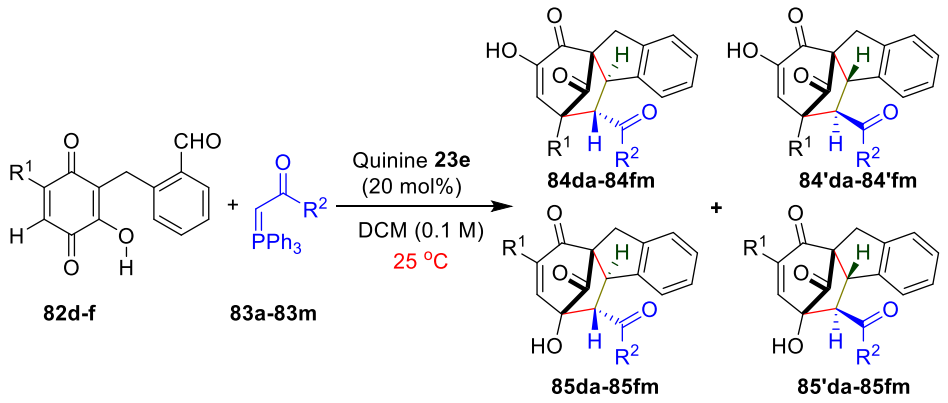



**Figure 51:** Crystal structure of (4b*R** 5*S**,6*S**,9a*R**)-5-benzoyl-6-(*tert*-butyl)-8-hydroxy-5,6-dihydro-4b*H*-6,9a-methanobenzo[*a*]azulene-9,11(10*H*)-dione [**84ed**].

**Table 11:** Reaction scope with different hydroxy-*p*-quinone benzaldehyde.[a]




| Entry | 82 [$R^1$] and 83 [$R^2$] | *t* [h] | Yield [%][b] [84+85] | Products | *pr*[c] [84:85] | *dr*[c] [84:84'] | *dr*[c] [85:85'] |
|---|---|---|---|---|---|---|---|
| 1 | **82d:** $R^1$ = $^i$Pr; **83a**: $R^2$ = Me | 2.0 | 98 | **84da**, **85da** | 20:1 | 99:1 | 4:1 |
| 2 | **82d:** $R^1$ = $^i$Pr; **83b**: $R^2$ = Et | 3.5 | 98 | **84db**, **85db** | 10:1 | 99:1 | 2:1 |
| 3 | **82d:** $R^1$ = $^i$Pr; **83d**: $R^2$ = Ph | 24.0 | 94 | **84dd**, **85dd** | 37:1 | 99:1 | 2:1 |
| 4 | **82d:** $R^1$ = $^i$Pr; **83f**: $R^2$ = 4-$MeOC_6H_4$ | 30.0 | 94 | **84df**, **85df** | 7:1 | 99:1 | 2.5:1 |
| 5 | **82d:** $R^1$ = $^i$Pr; **83j**: $R^2$ = 4-$BrC_6H_4$ | 48.0 | 98 | **84dj**, **85dj** | 6:1 | 99:1 | 2:1 |
| 6 | **82d:** $R^1$ = $^i$Pr; **83k**: $R^2$ = 4-$CF_3C_6H_4$ | 72.0 | 98 | **84dk**, **85dk** | 4:1 | 99:1 | 3.9:1 |
| 7 | **82d:** $R^1$ = $^i$Pr; **83m**: $R^2$ = furan-2-yl | 30.0 | 97 | **4dm**, **85dm** | 5:1 | 99:1 | 1.4:1 |
| 8 | **82e:** $R^1$ = $^t$Bu; **83a**: $R^2$ = Me | 2.0 | 94 | **84ea**, **85ea** | 20:1 | 99:1 | 5:1 |
| 9 | **82e:** $R^1$ = $^t$Bu; **83b**: $R^2$ = Et | 3.0 | 95 | **84eb**, **85eb** | 10:1 | 99:1 | 6.3:1 |
| 10 | **82e:** $R^1$ = $^t$Bu; **83d**: $R^2$ = Ph | 10.0 | 85 | **84ed**, **85ed** | 32:1 | 99:1 | 4.8:1 |
| 11 | **82e:** $R^1$ = $^t$Bu; **83f**: $R^2$ = 4-$MeOC_6H_4$ | 24.0 | 85 | **84ef**, **85ef** | 7:1 | 99:1 | 3.7:1 |
| 12 | **82e:** $R^1$ = $^t$Bu; **83j**: $R^2$ = 4-$BrC_6H_4$ | 24.0 | 97 | **84ej**, **85ej** | 11:1 | 99:1 | 1.3:1 |
| 13 | **82e:** $R^1$ = $^t$Bu; **83k**: $R^2$ = 4-$CF_3C_6H_4$ | 48.0 | 93 | **84ek**, **85ek** | 1:2 | 99:1 | 8.2:1 |
| 14 | **82e:** $R^1$ = $^t$Bu; **83m**: $R^2$ = furan-2-yl | 24.0 | 98 | **84em**, **85em** | 12:1 | 99:1 | 1.6:1 |
| 15 | **82f:** $R^1$ = $^s$Bu; **83a**: $R^2$ = Me | 6.0 | 80 | **84fa**, **85fa** | 10:1 | 99:1 | 1.6:1 |
| 16 | **82f:** $R^1$ = $^s$Bu; **83b**: $R^2$ = Et | 16.0 | 93 | **84fb**, **85fb** | 8:1 | 99:1 | 1.5:1 |
| 17 | **82f:** $R^1$ = $^s$Bu; **83d**: $R^2$ = Ph | 24.0 | 90 | **84fd**, **85fd** | 16:1 | 99:1 | 4:1 |
| 18 | **82f:** $R^1$ = $^s$Bu; **83f**: $R^2$ = 4-$MeOC_6H_4$ | 24.0 | 85 | **84ff**, **85ff** | 11:1 | 99:1 | 3:1 |
| 19 | **82f:** $R^1$ = $^s$Bu; **83j**: $R^2$ = 4-$BrC_6H_4$ | 50.0 | 95 | **84fj**, **85fj** | 1:4 | 99:1 | 5:1 |
| 20 | **82f:** $R^1$ = $^s$Bu; **83k**: $R^2$ = 4-$CF_3C_6H_4$ | 96.0 | 88 | **84fk**, **85fk** | 1:6 | 99:1 | 11:1 |
| 21 | **82f:** $R^1$ = $^s$Bu; **83m**: $R^2$ = furan-2-yl | 48.0 | 85 | **84fm**, **85fm** | 18:1 | 99:1 | 2.3:1 |

[a] Reactions were carried out in DCM (0.1 M) with 1.3 equiv. of **83a-m** relative to the **82d-f** (0.2 mmol) in the presence of catalyst **23e** at 25 °C. [b] Yield refers to the overall yield of the column purified products. [c] Determined by $^1$H NMR analysis of crude products obtained through column filtration.

$^1$H and $^{13}$C NMR spectra of few compounds from Table 11 have depicted below Figure 52-59.

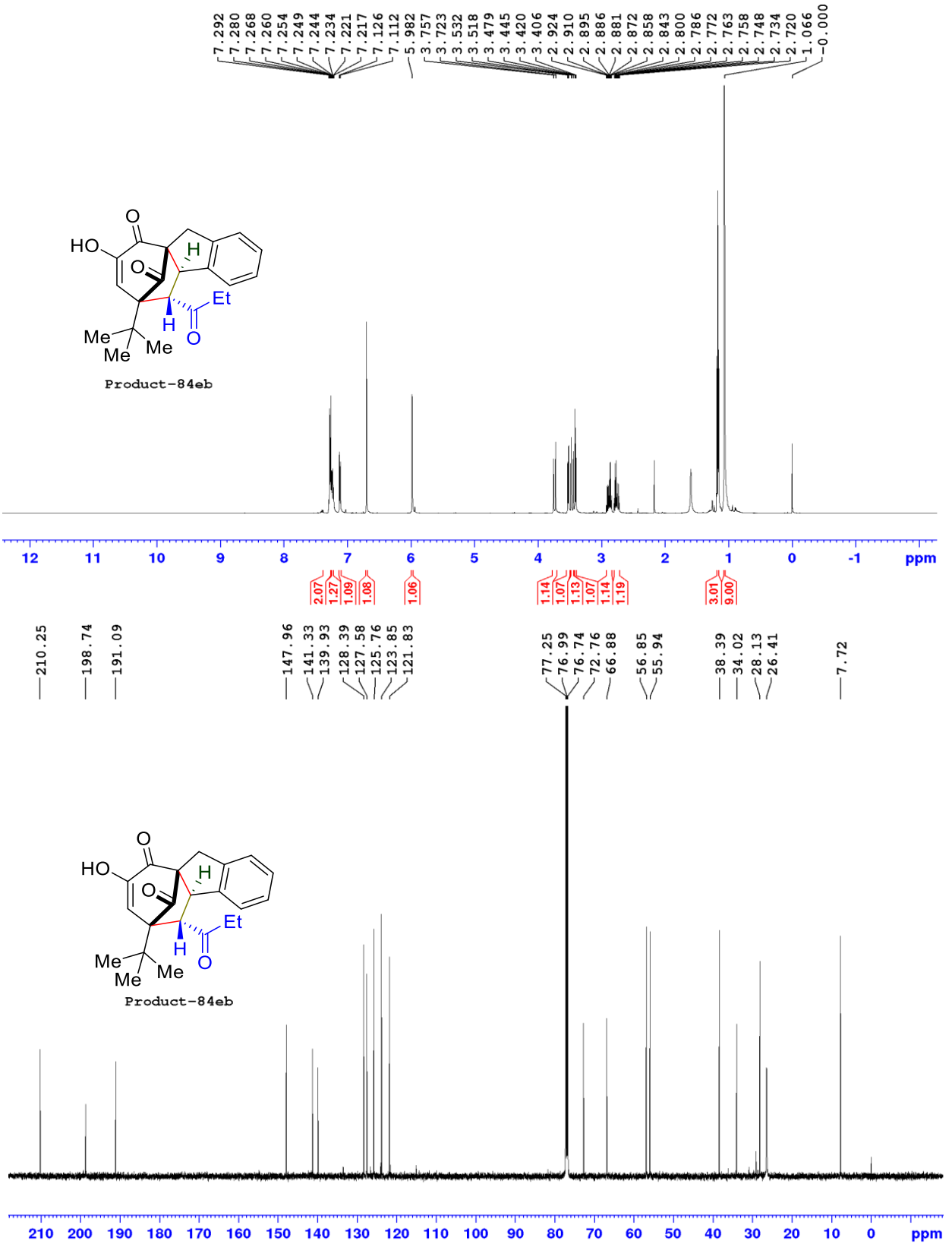



**Figure 52**: $^{1}H$ NMR and $^{13}C$ NMR spectra of product **84eb.**

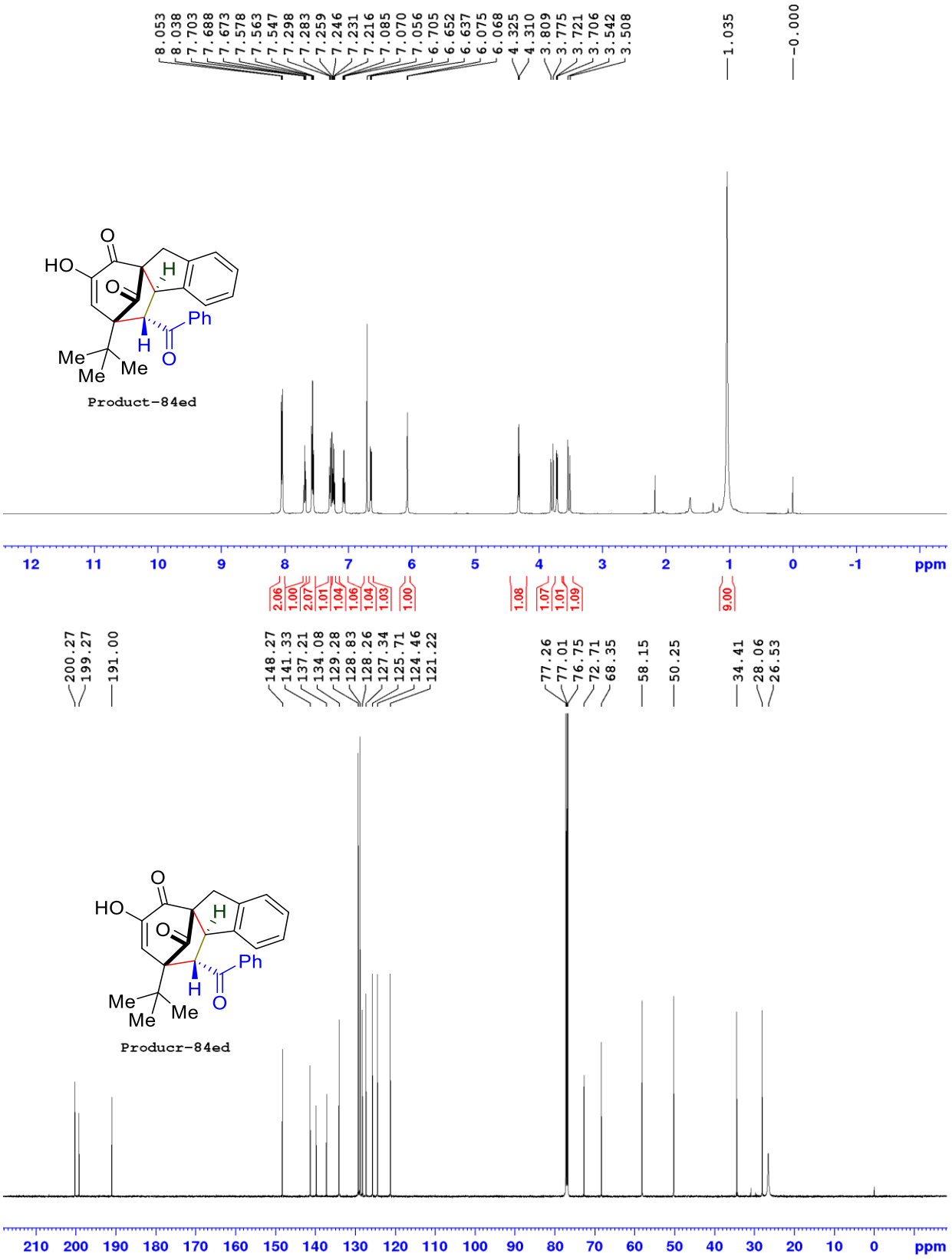



**Figure 53**: $^{1}H$ NMR and $^{13}C$ NMR spectra of product **84ed.**

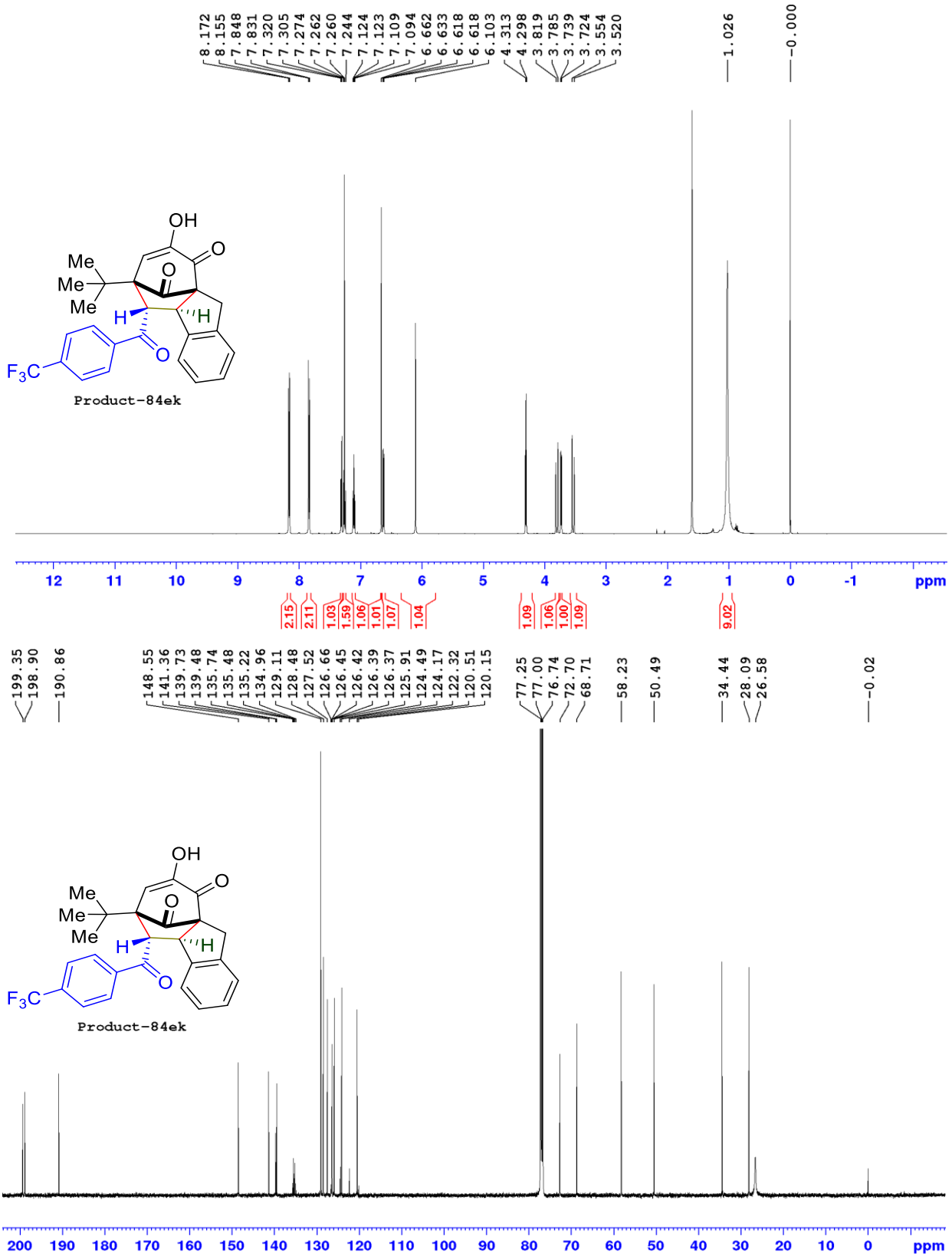



**Figure 54**: $^{1}H$ NMR and $^{13}C$ NMR spectra of product **84ek.**

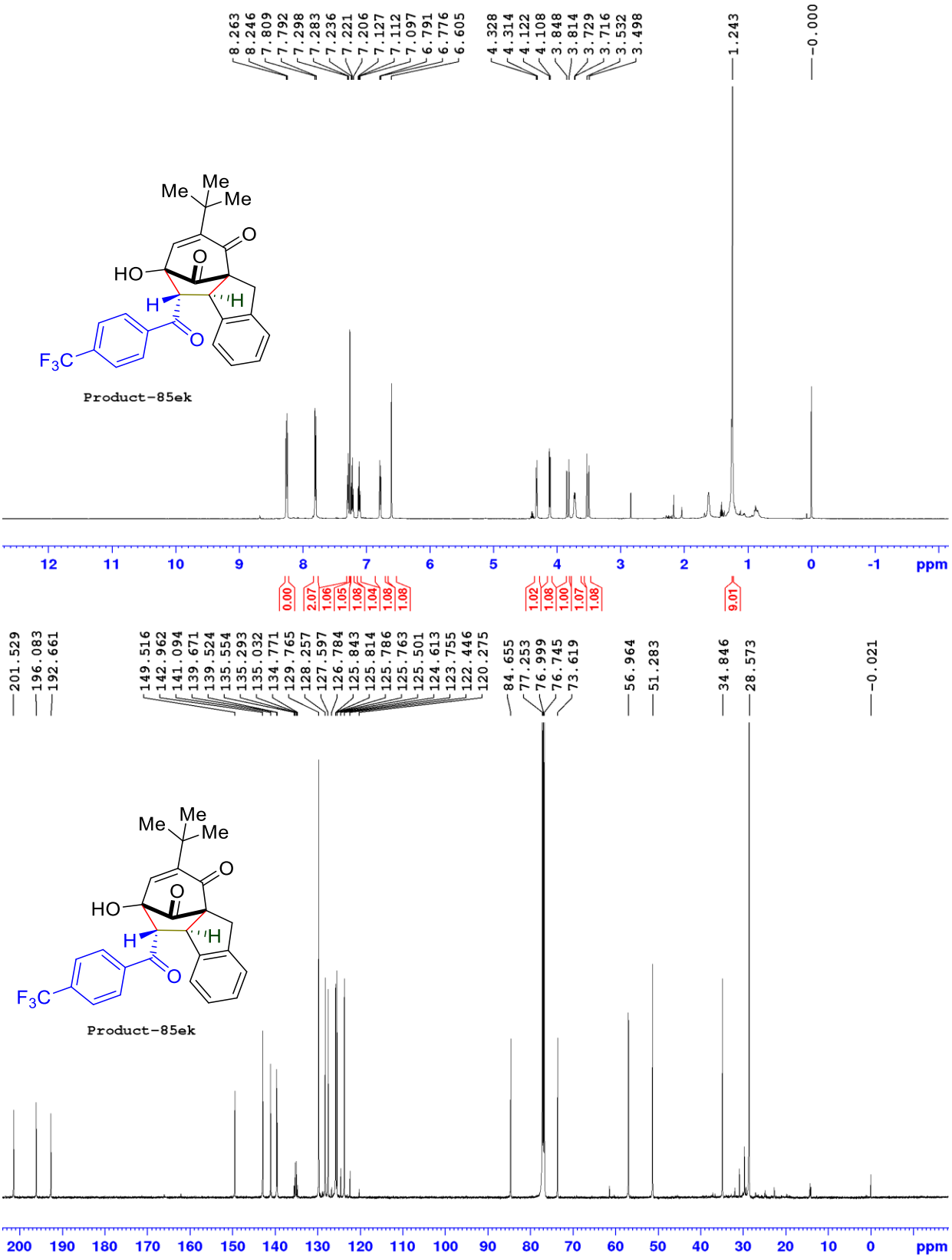



**Figure 55**: $^{1}H$ NMR and $^{13}C$ NMR spectra of product **85ek.**

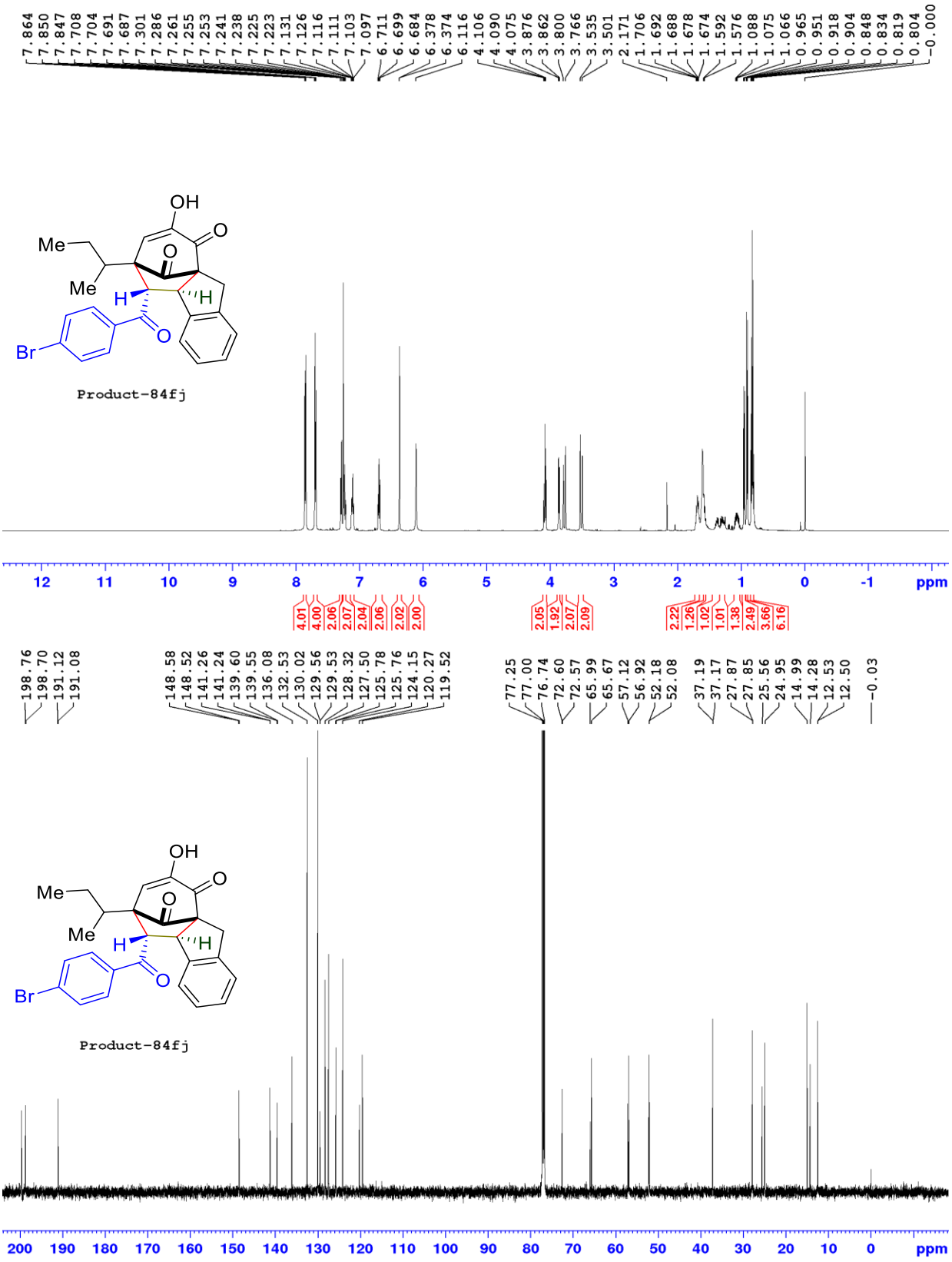



**Figure 56**: $^{1}H$ NMR and $^{13}C$ NMR spectra of product **84fj.**

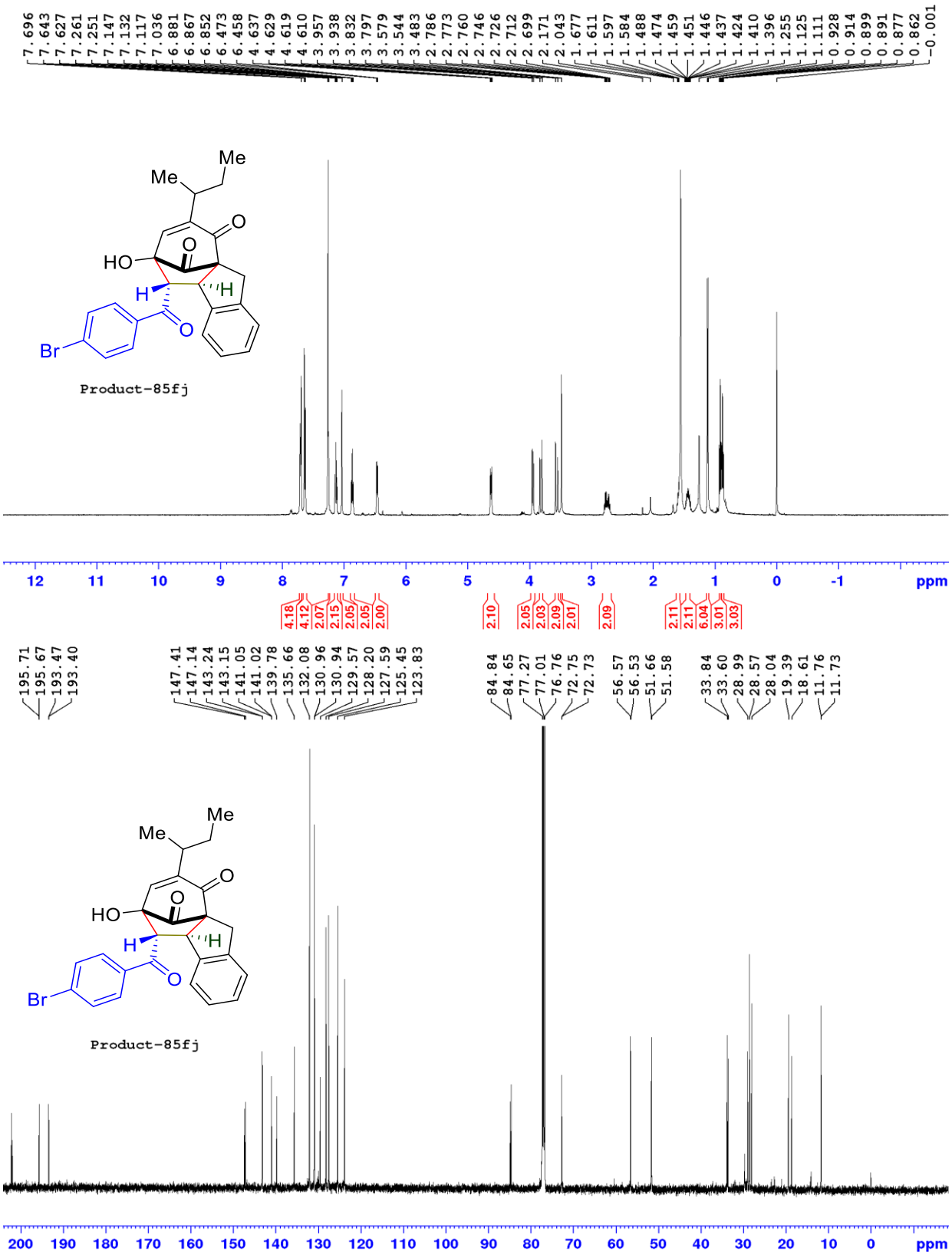



**Figure 57**: $^{1}H$ NMR and $^{13}C$ NMR spectra of product **85fj.**

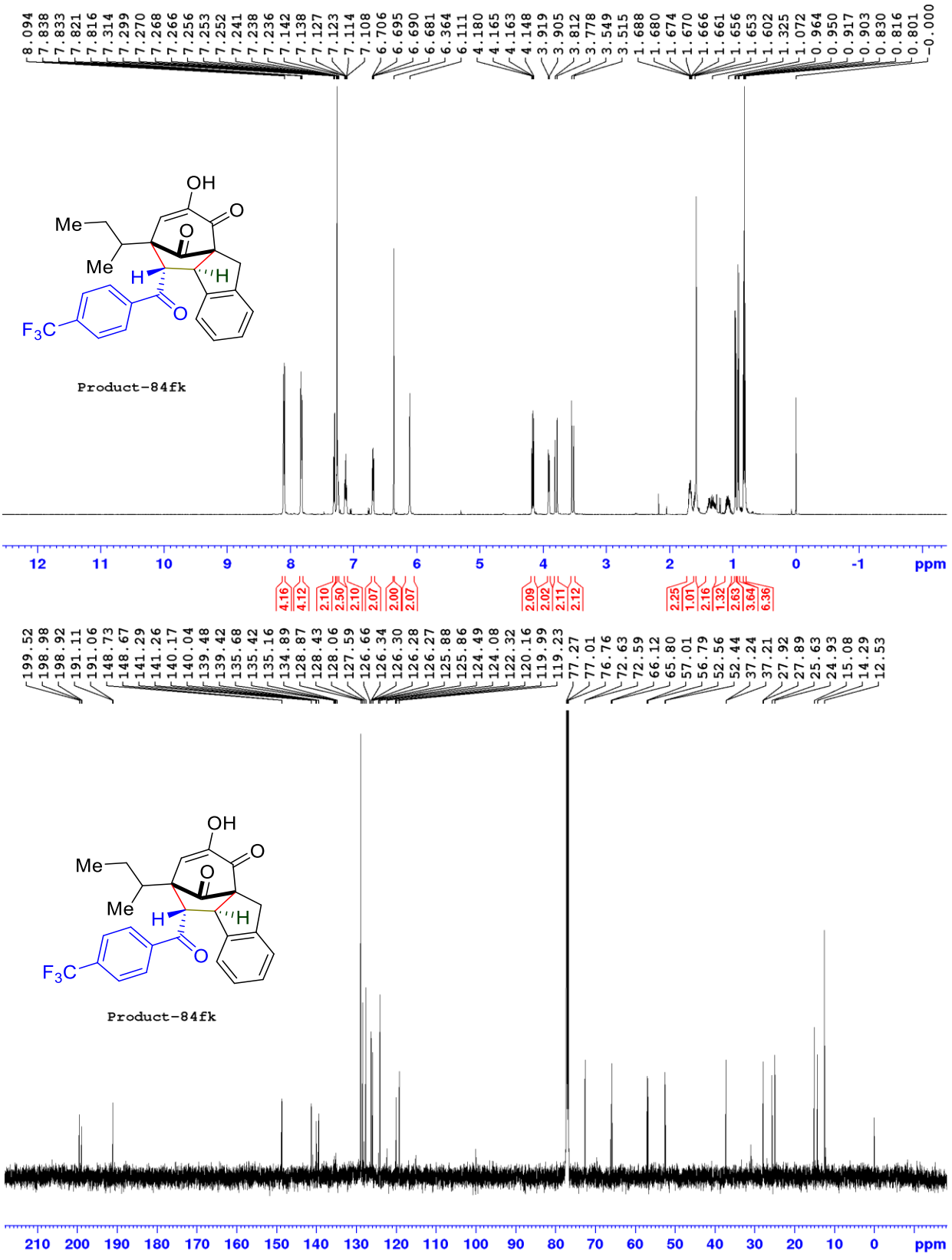



**Figure 58**: $^{1}H$ NMR and $^{13}C$ NMR spectra of product **84fk.**

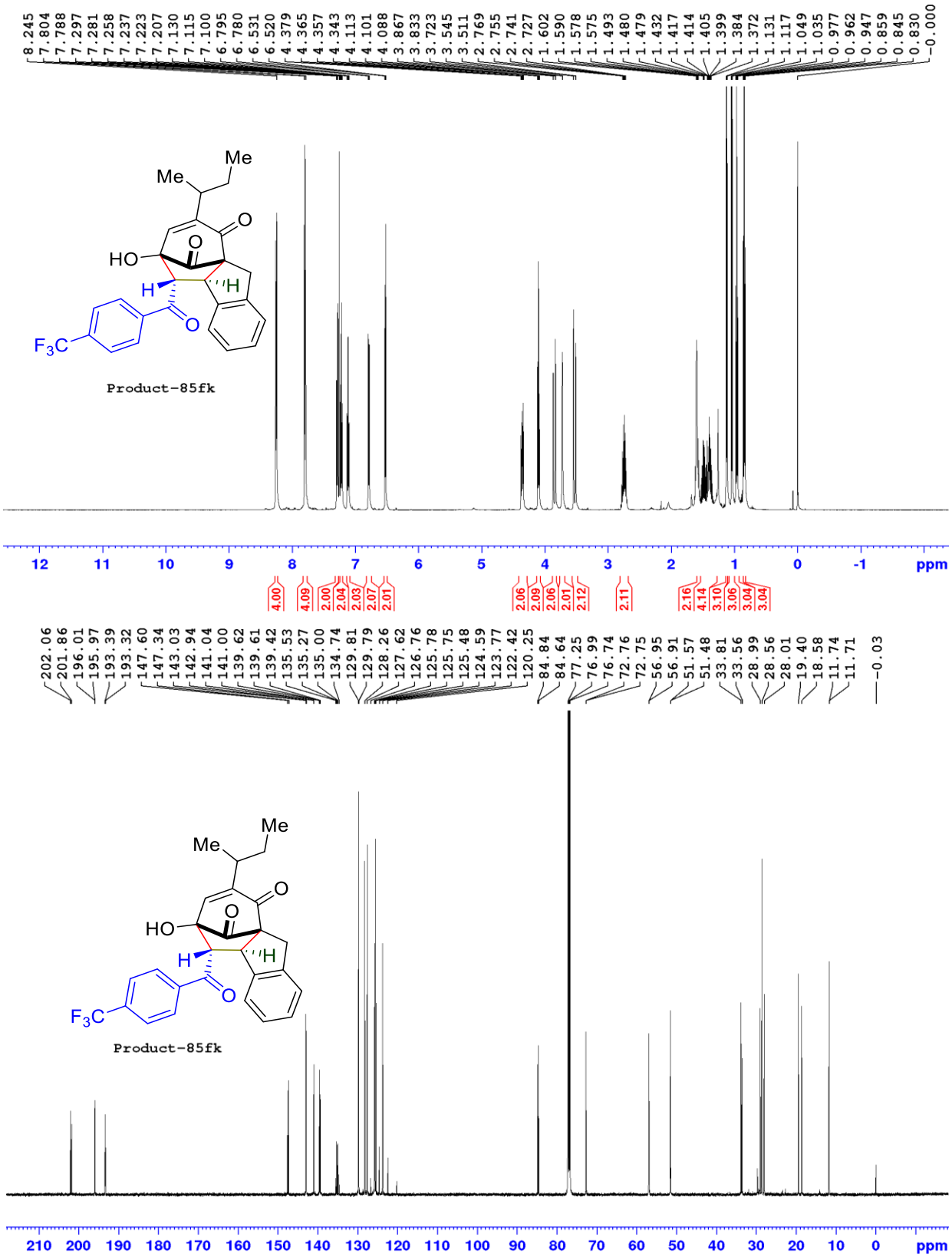
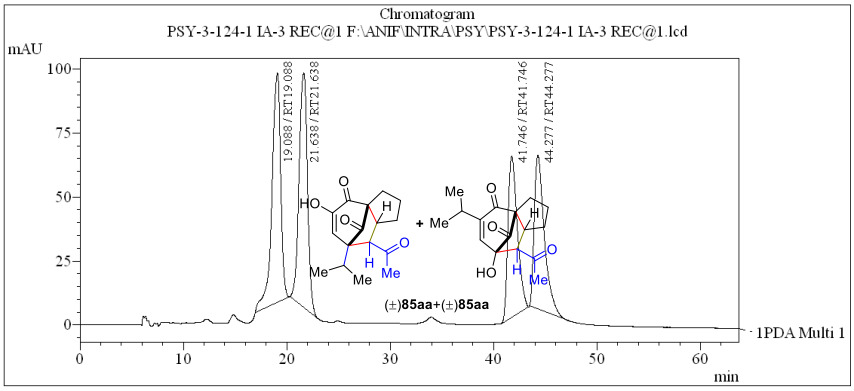



**Figure 59**: $^{1}H$ NMR and $^{13}C$ NMR spectra of products **85fk.**

Racemic **(±)-84aa** (Major) + **(±)-85aa** (Minor)**:**



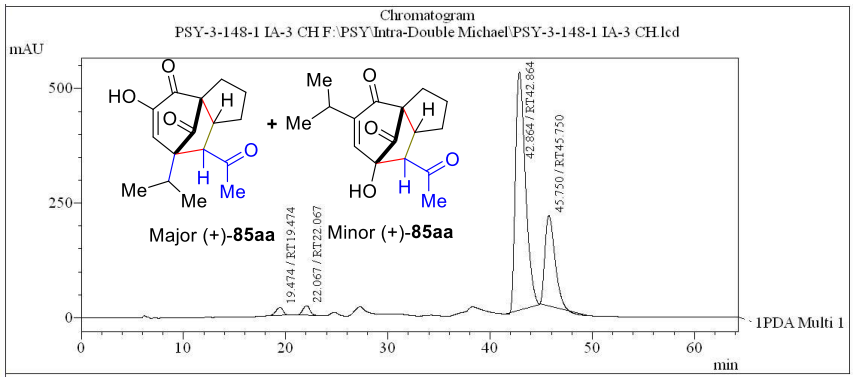

Chiralpak IA-3, Hexane/*i*-PrOH = 90:10, mL/Min, Flow Rate 1.0 mL/min, 254

PeakTable

PDA Ch1 254nm 4nm

| Peak# | Name | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|---|
| 1 | RT19.088 | 19.088 | 5271746 | 89610 | 28.471 | 29.464 |
| 2 | RT21.638 | 21.638 | 5182302 | 91640 | 27.988 | 30.131 |
| 3 | RT41.746 | 41.746 | 3970349 | 62924 | 21.443 | 20.689 |
| 4 | RT44.277 | 44.277 | 4091820 | 59965 | 22.099 | 19.716 |
| Total | | | 18516217 | 304139 | 100.000 | 100.000 |

Chiral **84aa** (Major) (45% *ee*) + **85aa** (Minor) (5% *ee*)**:**




Chiralpak IA-3, Hexane/*i*-PrOH = 95:5, mL/Min, Flow Rate 0.5 mL/min, 254

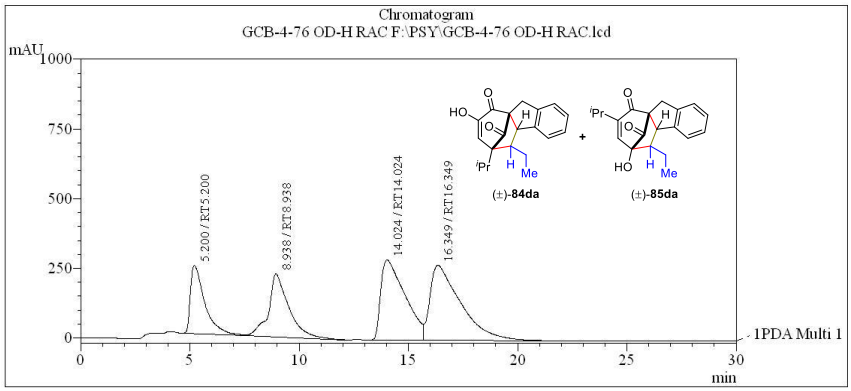
PeakTable

PDA Ch1 254nm 4nm

| Peak# | Name | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|---|
| 1 | RT19.474 | 19.474 | 859308 | 17388 | 1.697 | 2.305 |
| 2 | RT22.067 | 22.067 | 959358 | 20447 | 1.894 | 2.710 |
| 3 | RT42.864 | 42.864 | 35466332 | 519034 | 70.022 | 68.800 |
| 4 | RT45.750 | 45.750 | 13365356 | 197543 | 26.387 | 26.185 |
| Total | | | 50650354 | 754411 | 100.000 | 100.000 |

**Figure 60**: HPLC spectra of products **84aa**+**85aa.**

Racemic (±)-**84da** (Major) + (±)-**85da** (Minor)**:**



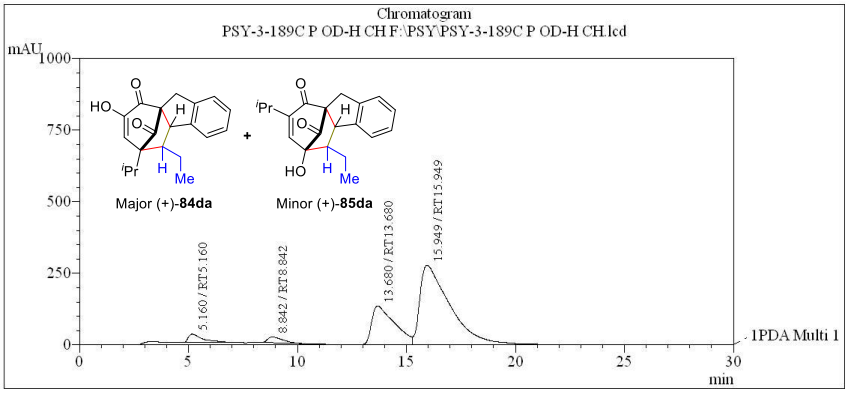

Chiralpak OD-H, Hexane/*i*-PrOH = 90:10, mL/Min, Flow Rate 1.0 mL/min,

PeakTable

PDA Ch1 254nm 4nm

| Peak# | Name | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|---|
| 1 | RT5.200 | 5.200 | 11104209 | 243514 | 14.983 | 23.728 |
| 2 | RT8.938 | 8.938 | 14581399 | 226275 | 19.674 | 22.048 |
| 3 | RT14.024 | 14.024 | 22139456 | 287732 | 29.872 | 28.036 |
| 4 | RT16.349 | 16.349 | 26289302 | 268758 | 35.471 | 26.188 |
| Total | | | 74114367 | 1026280 | 100.000 | 100.000 |

Chiral **84da** (Major) (46% *ee*) + **85da** (Minor) (10% *ee*)**:**




Chiralpak OD-H, Hexane/*i*-PrOH = 90:10, mL/Min, Flow Rate 1.0 mL/min,

PeakTable

PDA Ch1 254nm 4nm

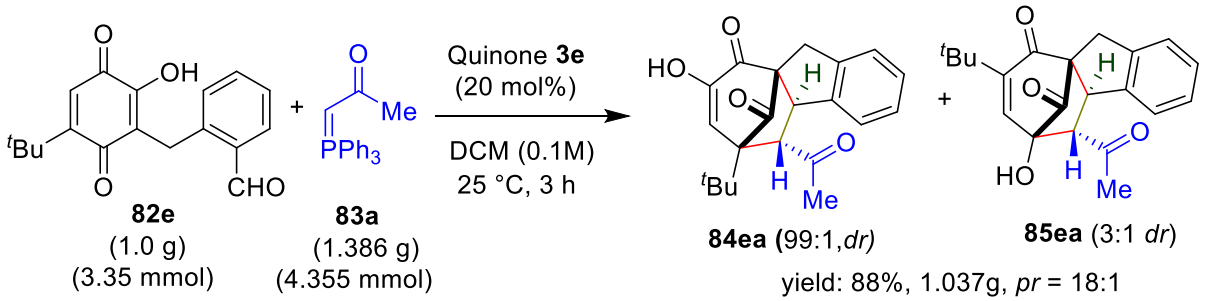
| Peak# | Name | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|---|
| 1 | RT5.160 | 5.160 | 1272076 | 28895 | 3.292 | 6.257 |
| 2 | RT8.842 | 8.842 | 1044778 | 21079 | 2.704 | 4.565 |
| 3 | RT13.680 | 13.680 | 9722773 | 134658 | 25.163 | 29.161 |
| 4 | RT15.949 | 15.949 | 26598773 | 277139 | 68.840 | 60.017 |
| Total | | | 38638399 | 461771 | 100.000 | 100.000 |

**Figure 61**: HPLC spectra of products **84da**+**85da.**

## 5.2.5 Development of Gram-Scale Tandem Reactions:

To prove the sustainable nature of these one-pot tandem coupling/annulation reactions to make the terpenoid skeletons, we planned to perform gram-scale reactions. Gram-scale reaction of **82e** (1.0 g) and **83a** (1.386 g) was studied and found to be sustained with respect to yield/*pr*/*dr*/rate as 1.037 g (88 % yield), 18:1 *pr*, 99:1 *dr* for the major isomer **84ea** and 3:1 *dr* for the minor isomer **85ea** were obtained within 3.0 h at 25 ºC (Scheme 32).

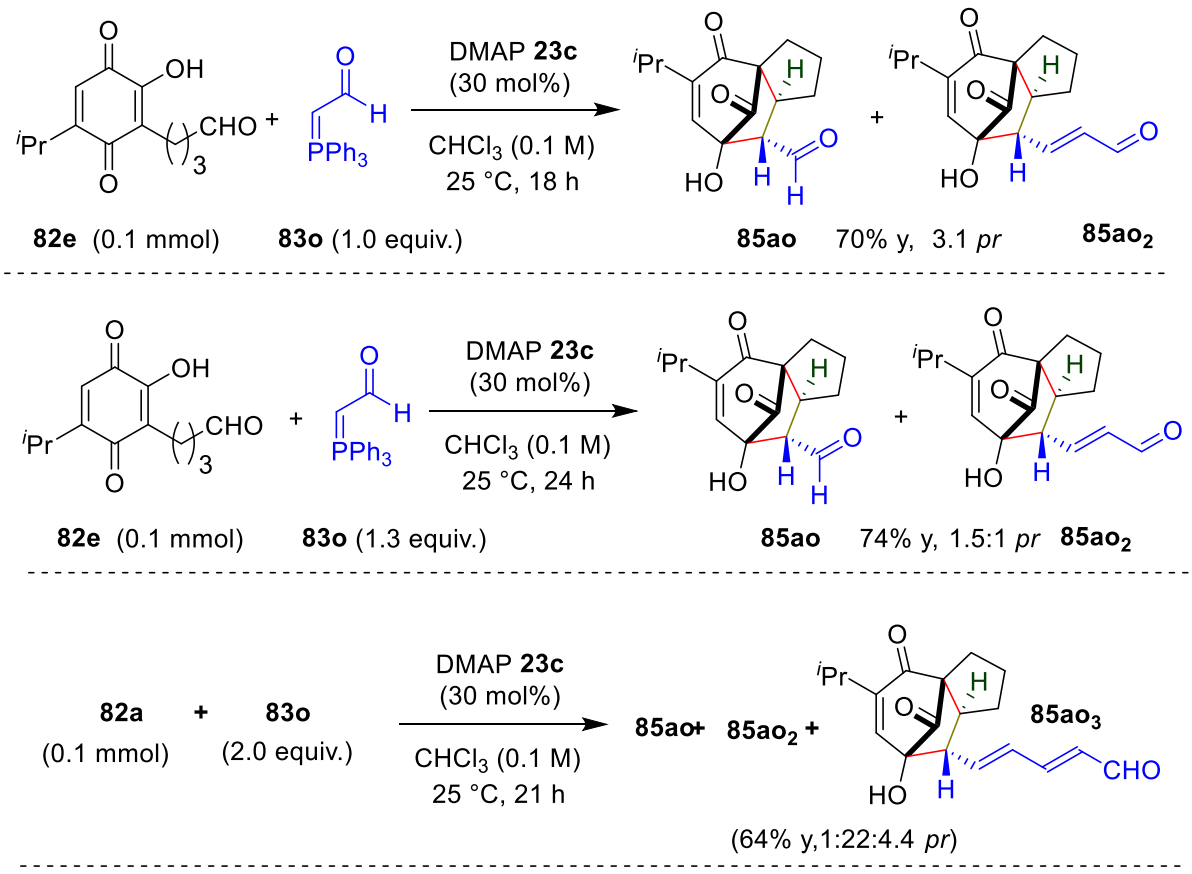
**Scheme 32:** Gram-scale Synthesis of Tandem Products.




## 5.2.6 Reaction Scope with Simple Phosphorane 83o:

For the *in situ* generation and investigation of the reactive formylmethylene Wittig intermediate to see in the outcome of tandem reaction sequence, we treated **82a** with 1.0 equiv. of (formylmethylene)triphenylphosphorane **83o** under the DMAP **23c**catalysis at 25 ºC for 18 h furnished only 3:1 mixture of products **85ao** and **85ao$_2$** in 70% yield with 99:1 *dr* through the sequence of W/IM/IA and W/IM/IA/W reactions, respectively (Scheme 33). Same reaction sequence with 1.3 equiv. of **83o** under **23c**-catalysis for 24 h furnished 1.5:1 mixture of **85ao** and **85ao$_2$** in 74% yield with 99:1 *dr*. Surprisingly, treatment of **82a** with 2.0 equiv. of **83o** under the **23c**-catalysis for 21 h furnished the 1:22:4.4 ratio of products **85ao**, **85ao$_2$** and **85ao$_3$** in 64% yield with 99:1 *dr*, respectively instead of forming single **85ao$_2$** product (Scheme 33). Similar reactions of **82a** with **83o** performed well under quinine **23e**-catalysis, but products **85ao**/**85ao$_2$** NMR purity is not clear compared to DMAP **23c**-catalysis (not shown in Scheme 3). In these tandem reactions, we are not observed formation of W/IM/IM **84ao** and able to see only formation of mono and double Wittig products on the W/IM/IA **85ao** may be due to the high reactivity nature of **83o** and subsequent olefin.

**Scheme 33:** Synthesis of Tandem Products **85ao** and **85ao$_3$**




$^{1}$H and $^{13}$C NMR spectra of compound **85ao**+**85ao$_2$** from Scheme **33** have depicted in Figure 62.

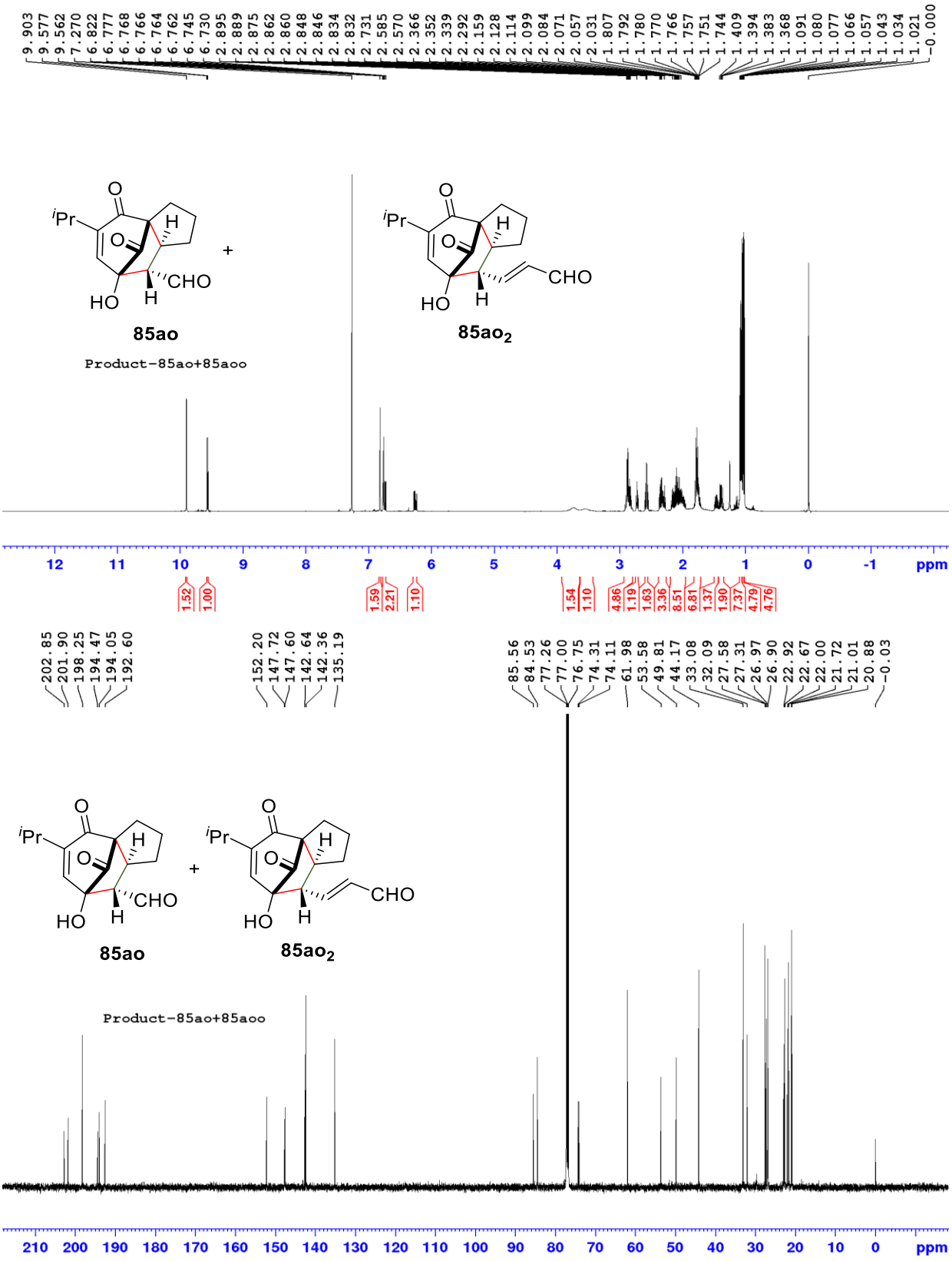
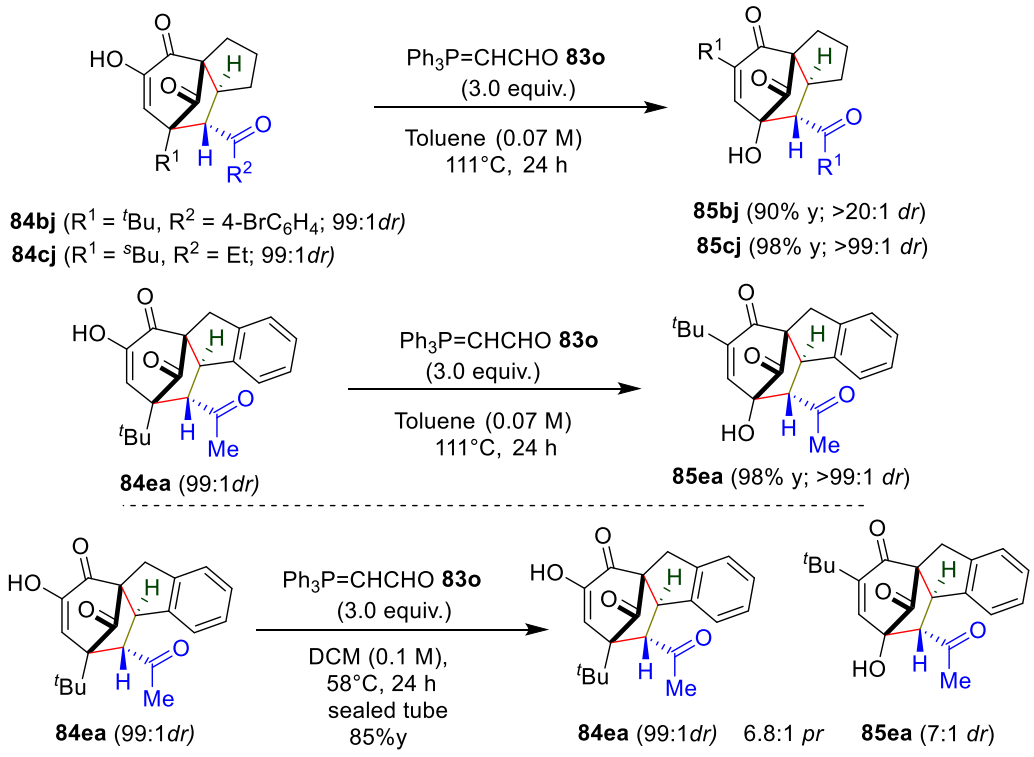



**Figure 62**: $^{1}H$ NMR and $^{13}C$ NMR spectra of products **84da**+**85da.**

### 5.2.7 Development of Ring Isomerism through *Retro*-cyclization and Cyclization Reactions:

The scope of the tandem reaction was demonstrated by converting the W/IM/IM **84** into the single isomer of W/IM/IA **85** by treatment with (formylmethylene)triphenylphosphorane **83o** (3.0 equiv.) in dry toluene at 111 ºC for 24 h through *retro*-IM, *retro*-IM, IM and IA reactions (Scheme 34). Surprisingly, treatment of **84bj** (99:1 *dr*) with phosphorane **83o** in dry toluene at 111 ºC for 24 h gave **85bj** in 90% yield with >20:1 *dr*, instead of simple olefination product. This interesting phosphorane-mediated *retro*-IM/*retro*-IM/IM/IA reactions on **84** was confirmed by two more examples to furnish the products **85cb** and **85ea** in each 98% yield with 99:1 *dr* (Scheme 34). Further we proved that phosphorane **83o**-catalysed *retro*-IM/*retro*-IM/IM/IA reactions on **84ea** were controlled by solvent and temperature to produce **85ea** as a major isomer (Scheme 34). In these reactions, phosphorane **83o** is acting as a phase transfer catalyst (PTC) to induce the *retro*-IM, *retro*-IM, IM and IA reactions on **84** to make single isomer of **85**.

**Scheme 34:** Transformation of Tandem Products W/IM/IM **84** into W/IM/IA **85** through Ring Isomerization




$^{1}H$ and $^{13}C$ NMR spectra of few compounds from Table 7 have depicted below Figure 63.

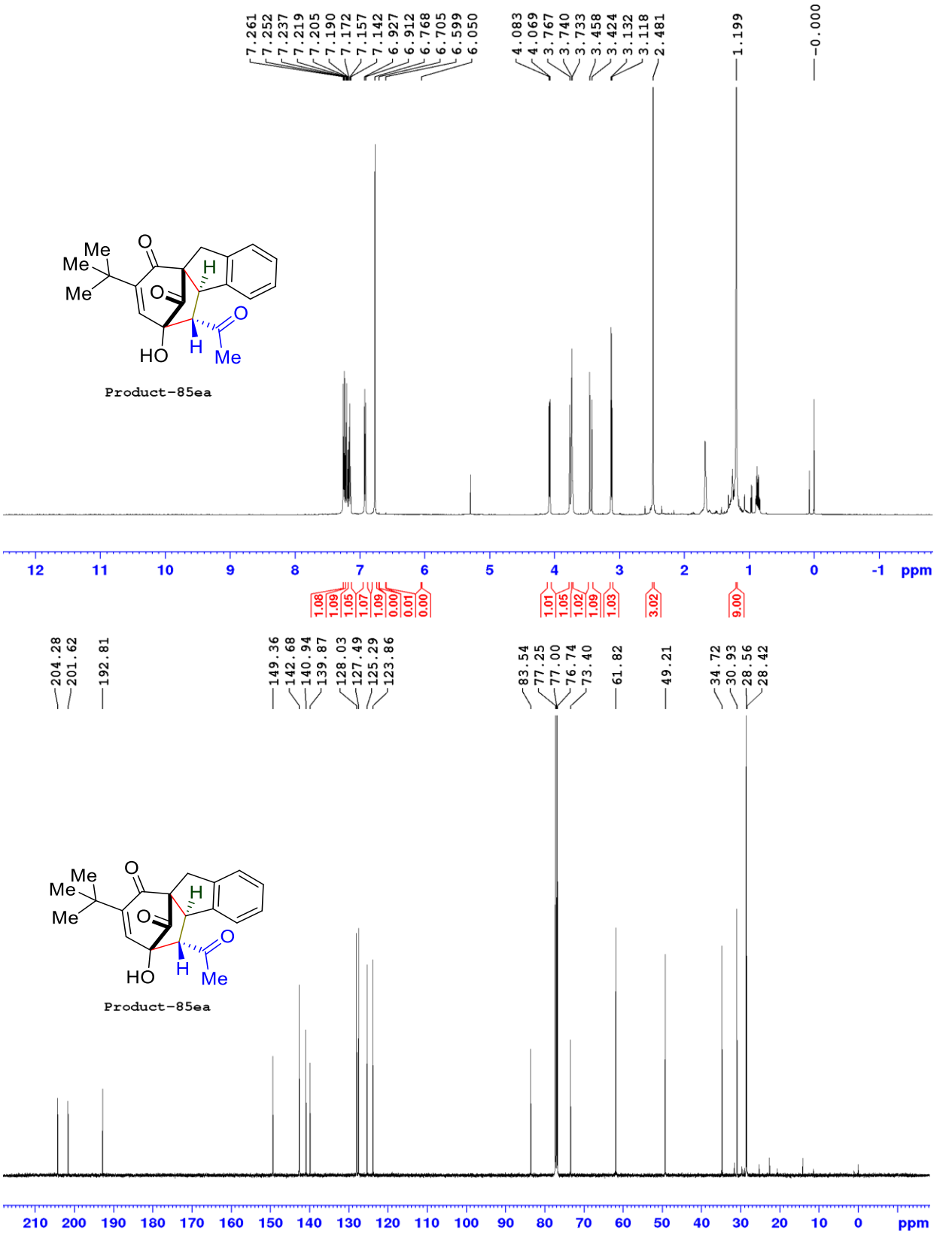
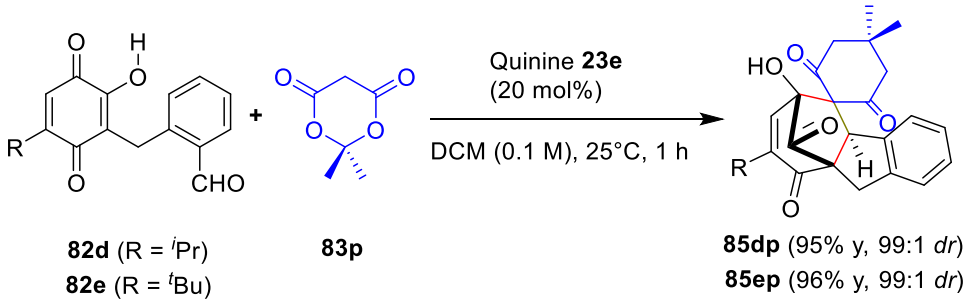



**Figure 63**: $^{1}H$ NMR and $^{13}C$ NMR spectra of product **85ea.**

## 5.2.8 Development of Tandem Reaction with Meldrum's Acid:

We thought of investigating *in situ* generation and reactivity pattern of more reactive and functionally rich olefin in the tandem coupling/annulation reactions to see outcome of the product formation rate and selectivity. For this investigation, we chose Meldrum's acid as the olefin source. Reaction of hydroxy-*p*quinone benzaldehyde **84d** with Meldrum's acid **83p** under the quinine **23e**-catalysis in DCM at 25 ºC for 1.0 h furnished the single thermodynamic product **85dp** in 95% yield with 99:1 *dr* through the sequence of tandem Knoevenagel condensation/intramolecular Michael/intramolecular aldol (KC/IM/IA) reactions (Scheme 35). Generality of this selective tandem KC/IM/IA reaction was confirmed by one more example as treatment of **82e** with **83p** under **23e**-catalysis furnished the single product **85ep** in 96% yield with 99:1 *dr* (Scheme 35). In this reaction, olefin-containing side-chain conformations and electronic nature of functional groups are controlled the outcome of the tandem products formation rate and selectivity.

**Scheme 35:** Synthesis of Tandem Products **85** through KC/IM/IA Reactions.




The relative stereochemistry of compound **85ep** was further confirmed by X-Ray analysis (Figure 64).

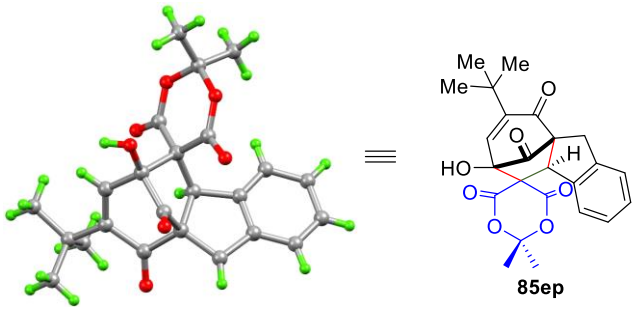



**Figure 64:** Crystal structure of (4b*R**,6*R**,9a*S**)-8-(*tert*-butyl)-6-hydroxy-2',2'-dimethylspiro[6,9a-methanobenzo[a]azulene-5,5'-[1,3]dioxane]-4',6',9,11(4b*H*,6*H*,10*H*)-tetraone [**85ep**].

$^{1}$H and $^{13}$C NMR spectra of product **85dp** from Scheme **35** have depicted below Figure 64.

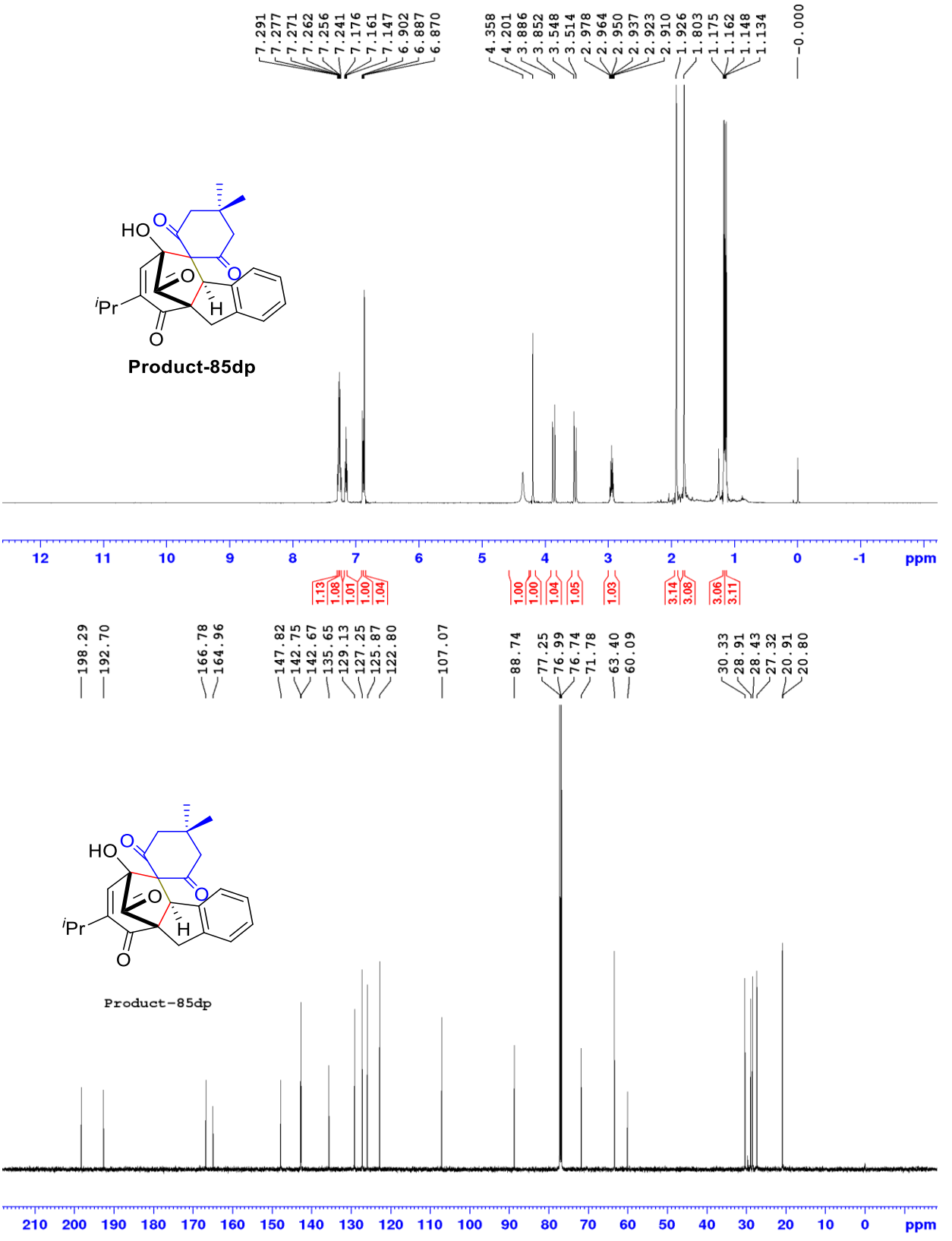
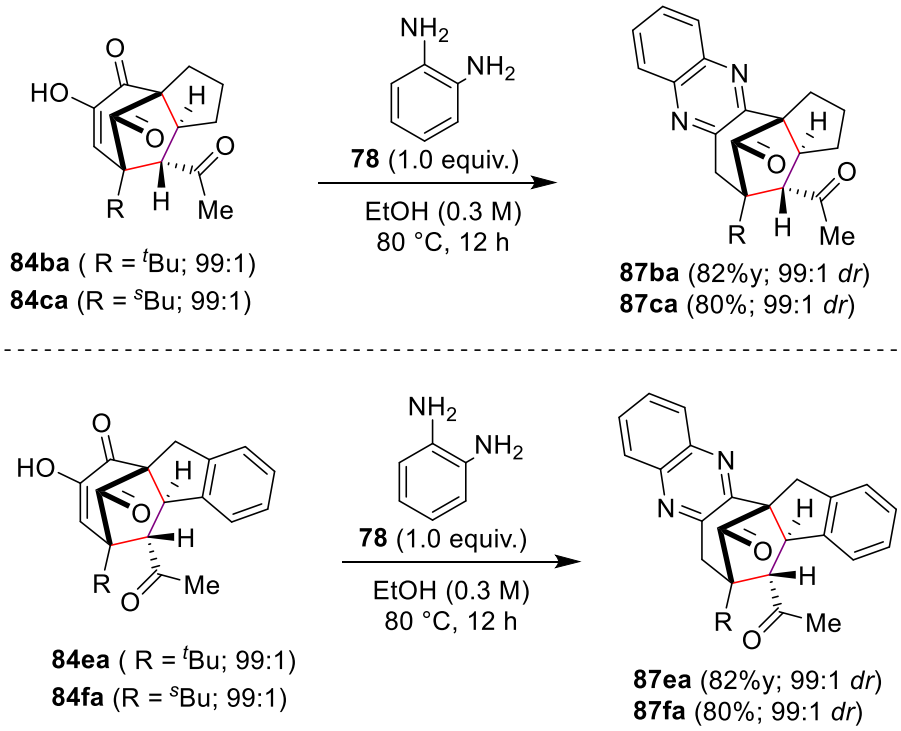



**Figure 64**: $^{1}H$ NMR and $^{13}C$ NMR spectra of product **85dp.**

## 5.2.9 Synthesis of Quinoxaline-methanoazulenes:

In a further application, the reaction of masked 1,2-dicarbonyls containing **84ba** with *o*-phenylenediamine in ethanol at 80 ºC for 12 h furnished the structurally important quinoxaline-methanoazulene **87ba** in 82% yield with 99:1 *dr* (Scheme 36). Sustainability of this quick cyclisation was further confirmed by three more examples in very good yields and selectivity (Scheme 36). These hybrid hetero pseudo-terpenoids will be inspirational to study the medicinal and material properties.[74] We established the structure of the tandem products **84/85/87** by IR/NMR/mass analysis and the relative stereochemistry was confirmed by X-ray structure analysis on **84aa**, **84ed**, and **85ep** (Figure 41, 51, and 64).[75]

**Scheme 36:** Synthesis of Selective Quinoxaline-methanoazulenes **87** from the Masked 1,2-Dicarbonyls **84.**




$^{1}$H and $^{13}$C NMR spectra of few compounds from Scheme **36** have depicted below Figure 66-67.

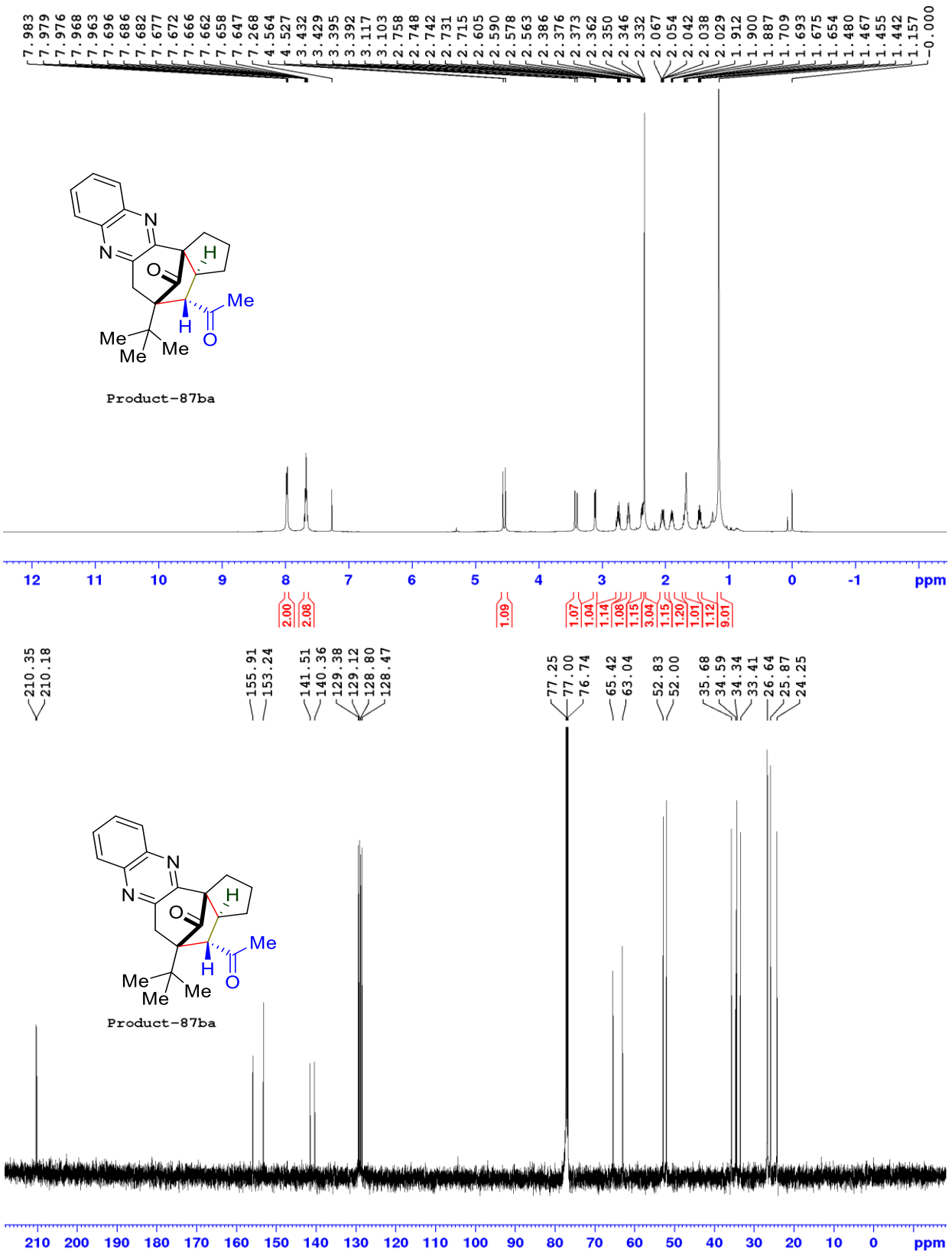



**Figure 66**: $^{1}H$ NMR and $^{13}C$ NMR spectra of product **87ba.**

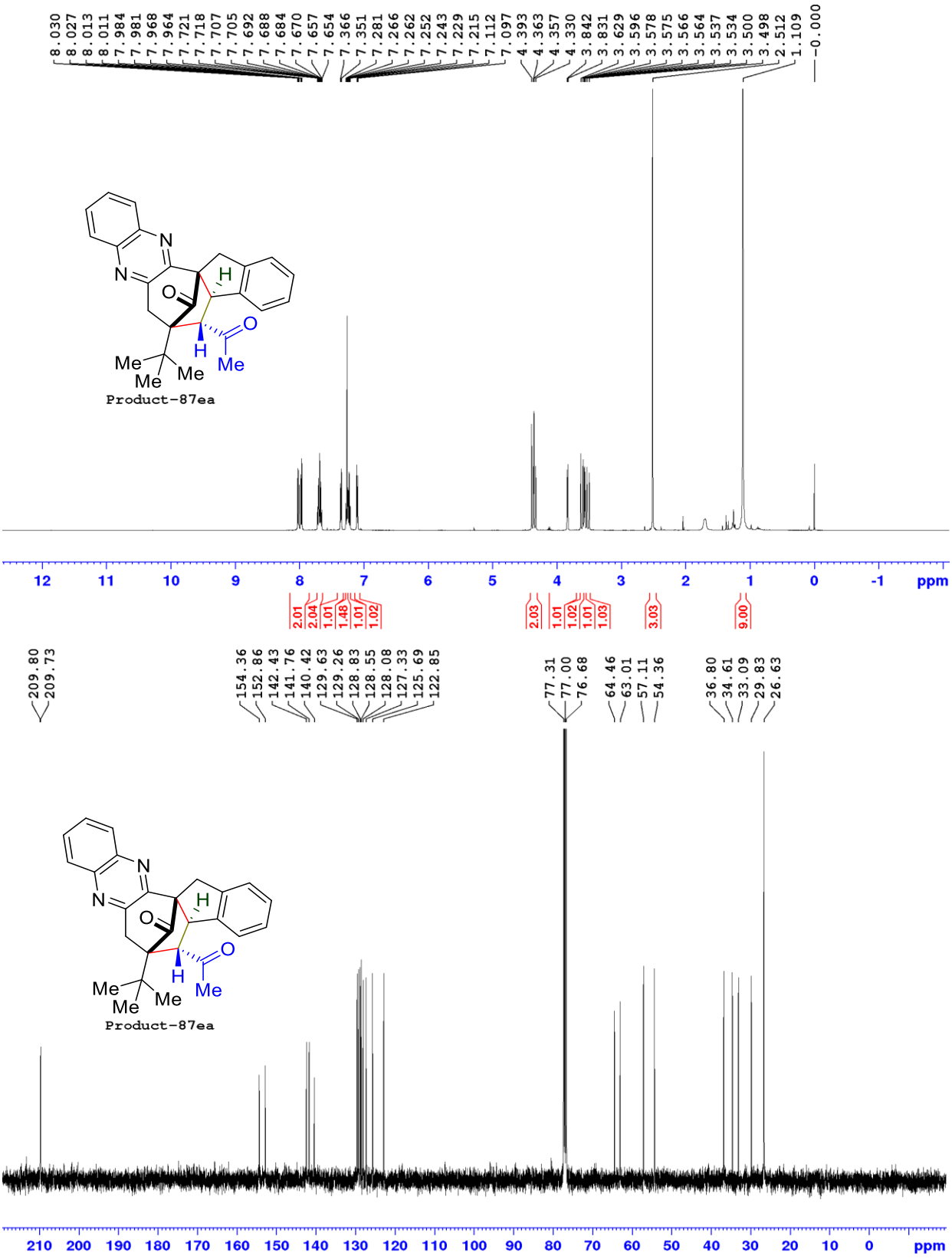
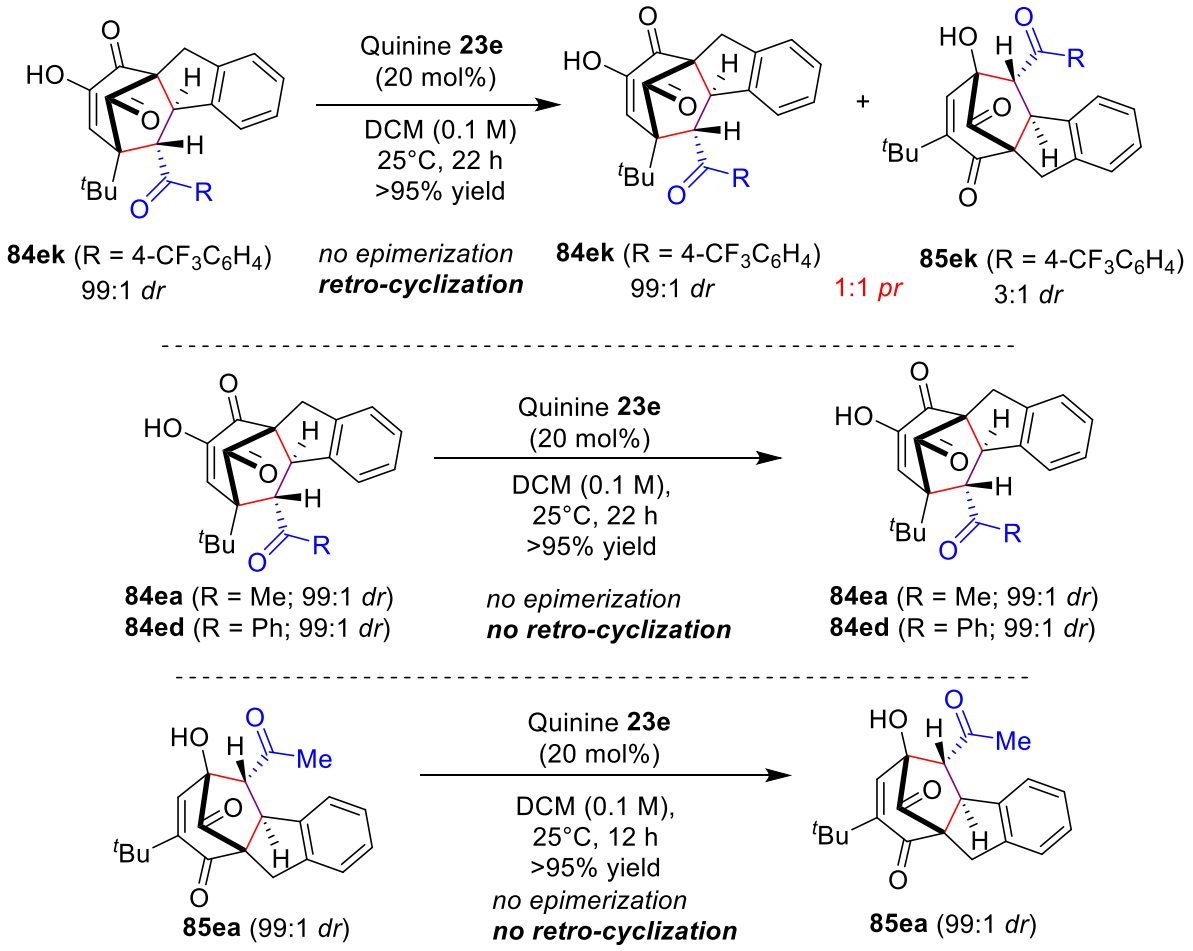



**Figure 67**: $^{1}H$ NMR and $^{13}C$ NMR spectra of product **87ea.**

## 5.2.10 Control Experiments to Understand the Ring Isomerization and Epimerization:

To explain suitable reasons for the poor *pr* and *dr* for some of the compounds obtained through the tandem reactions, we conducted a few controlled experiments (Scheme 37-39). Reaction of **84ek** (99:1 *dr*) with 20 mol% of **23e** in DCM at 25 ºC for longer times (22 h) furnished the 1:1 mixture of **84ek** (99:1 *dr*) and **85ek** (3:1 *dr*) in >95% yield through the *retro*-IM, *retro*-IM, IM and IA reactions (Scheme 37).

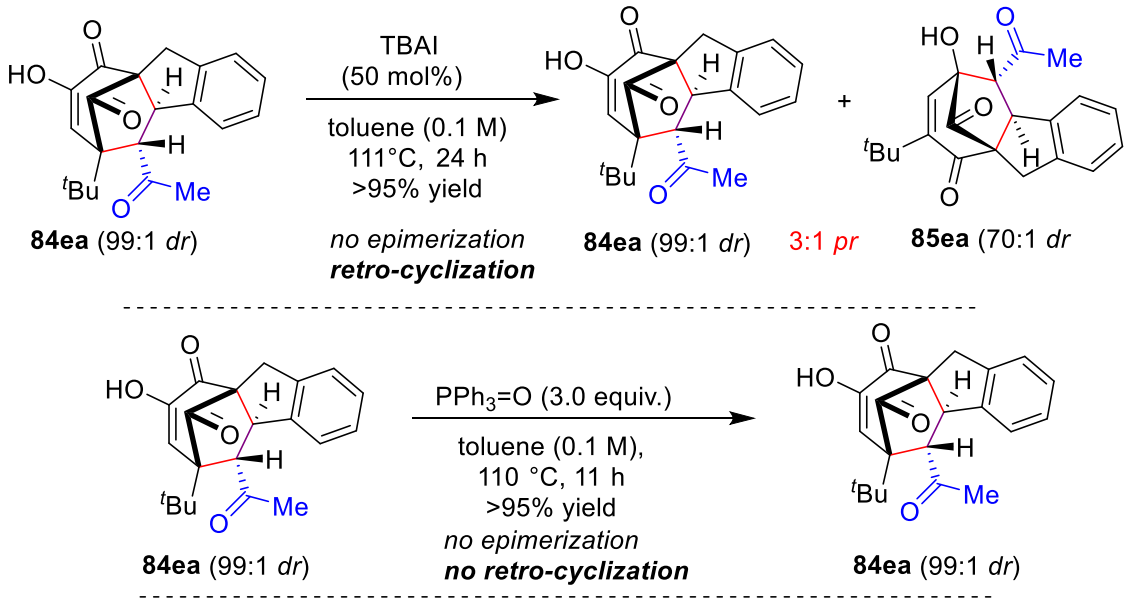
**Scheme 37:** Observation of Catalyst **23e** Effect on the Tandem Products **84** and **85**.



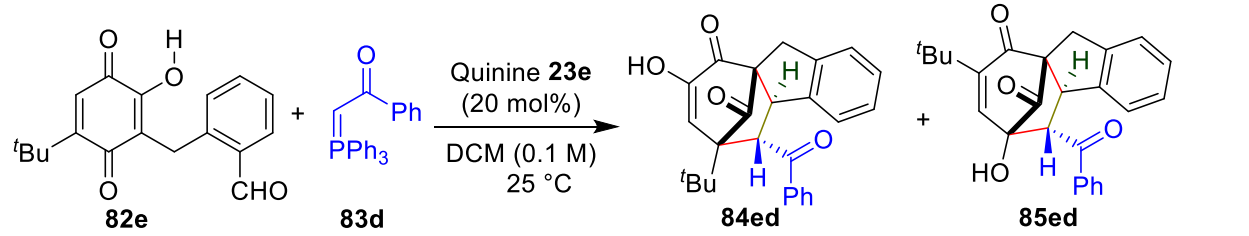

But similar treatment of **23e** (20 mol %) with **84ea**, **84ed** and **84ea** did not produce any change. Observation of no change in the *pr* and *dr* confirms that the electronic factors are controlled in epimerization or *retro*-cyclisation of **84** into **85** or vice versa under **23e**-catalysis (Scheme 37).

Refluxing **84ea** in dry toluene with or without DBU **23b** (1.1 equiv.) for 24 h didn't see epimerization or *retro*-cyclisation; but the same time treatment of **84ea** with KO$^t$Bu (1.1 equiv.) in dry toluene at 25 ºC or 70 ºC for 10 h compound **84ea** decomposed may be due to the more basic nature of KO$^t$Bu (results not shown in Scheme 37). Interestingly, the phase transfer catalyst tetra-*n*butylammonium iodide (TBAI) was able to catalyze **84ea** (99:1 *dr*) into a 3:1 mixture of **84ea** (99:1 *dr*) and **85ea** (70:1 *dr*) in 95% yield, but there is no change in the presence of Wittig reaction byproduct $Ph_3PO$ at 25 ºC to 110 ºC for 27 h (Scheme 38). To understand the dual role of Wittig reagents **83** as olefin source and as a phase transfer catalyst for the preparation and transformation of W/IM/IM into *retro*-IM/*retro*-IM/IM/IA in tandem reactions, we isolated and recorded products **84/85** NMR in two intervals for four different reactions (Scheme 39). In the starting of the coupling/annulation reaction sequence, W/IM/IM **84** formed as the major product in good to moderate yield with 99:1 *dr*, but prolonging the reaction time for higher yields purpose gave a mixture of the products **84** and **85** through combination of W/IM/IM, W/IM/IA and *retro*-IM/*retro*-IM/IM/IA reactions (Scheme 39).

**Scheme 38**: Observation of TBAI and $Ph_3PO$ Effect on the Tandem Products **84.**



**Scheme 39**: Observation of Dual Role of Wittig Reagents **83** in the Synthesis of Tandem Products **84** and **85**.




For 10 h; **85% y**, 32:1 *pr,* 99:1 *dr* (**4ed)**, 2.2:1 *dr* (**5ed**)

For 24 h; **85% y**, 3.6:1 *pr,* 99:1 *dr* (**4ed)**, 4.8:1 *dr* (**5ed**)

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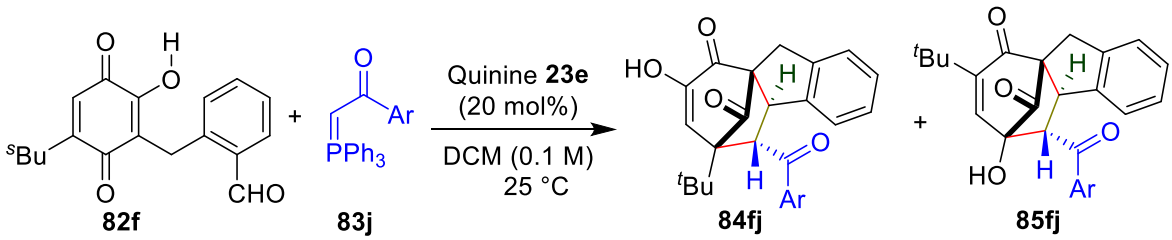


Ar = 4-$BrC_6H_4$

For 24 h; **45% y**, 99:1 *pr,* 99:1 *dr* (**4fj)**, 38% y (**1f**)

For 50 h; **85% y**, 1:4 *pr,* 99:1 *dr* (**4fj)**, 5:1 *dr* (**5fj**)

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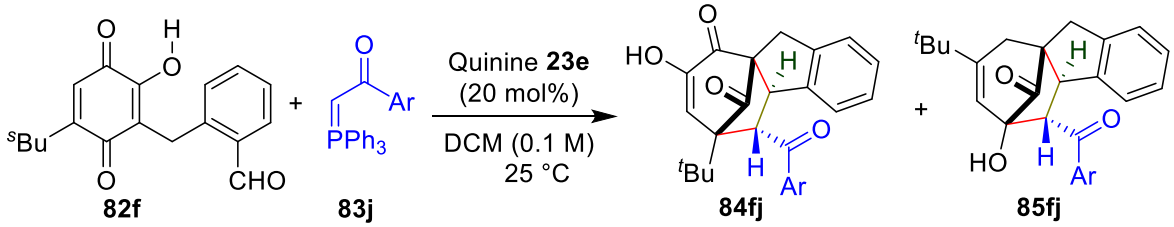


Ar = 4-$CF_3C_6H_4$

For 24 h; **40% y**, 99:1 *pr,* 99:1 *dr* (**4fk)**, 42% y (**1f**)

For 96 h; **86% y**, 1:6 *pr,* 99:1 *dr* (**4fk)**, 11:1 *dr* (**5fk**)

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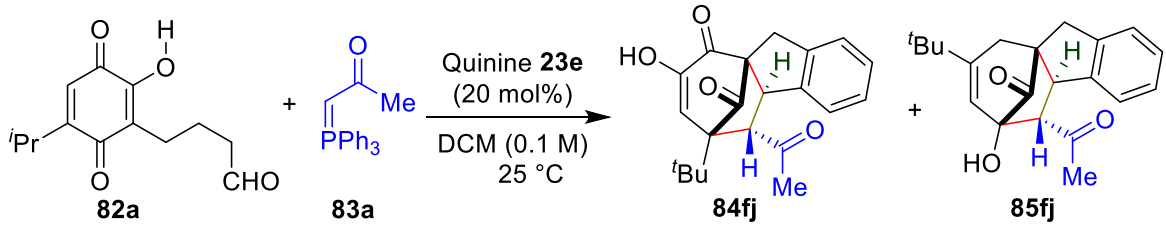


For 2 h; **85% y**, 33:1 *pr,* 99:1 *dr* (**4aa)**, 99:1 *dr* (**5aa**)

For 27 h; **75% y**, 12:1 *pr,* 99:1 *dr* (**4aa)**, 12:1 *dr* (**5aa**)

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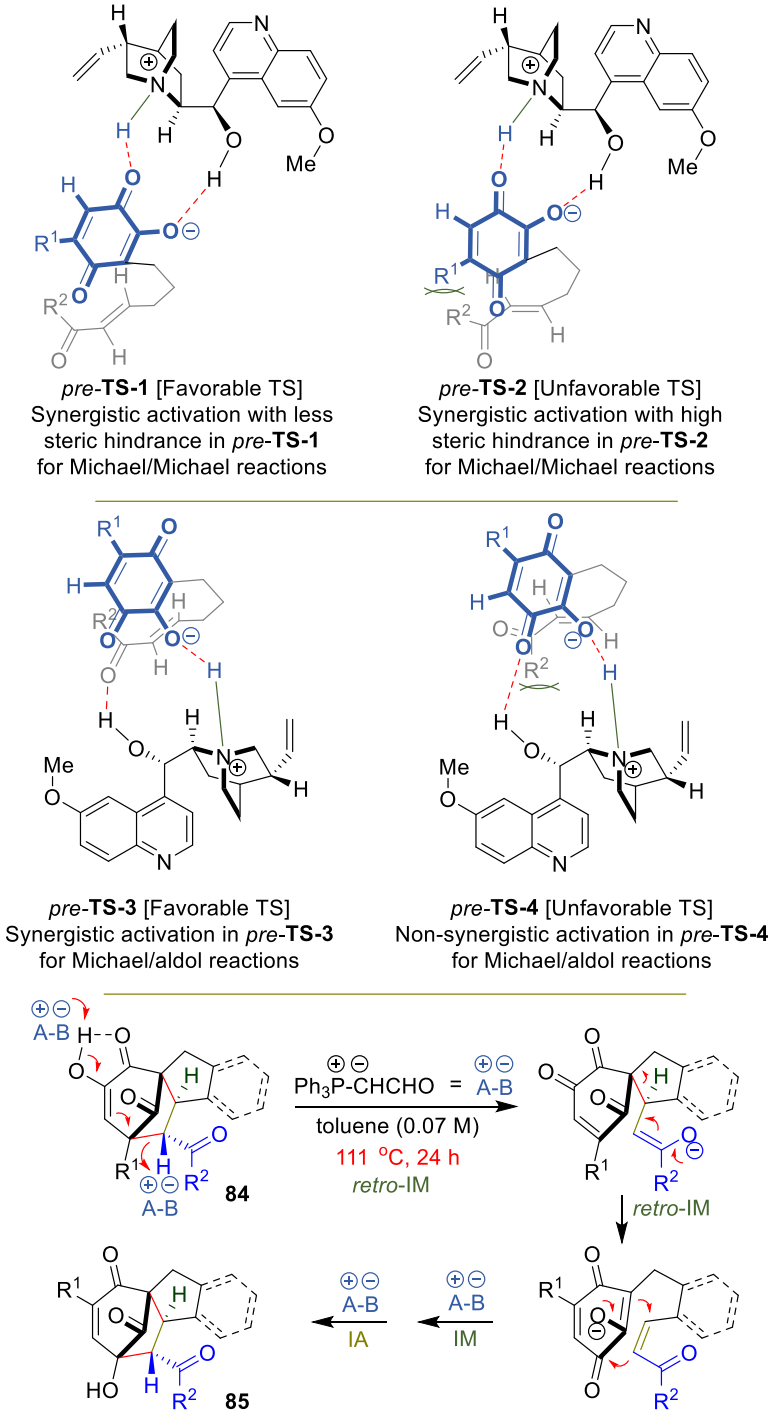
## 5.2.11 Reaction Mechanism:

The plausible mechanism for the tandem W/IM/IM, W/IM/IA and *retro*-IM/*retro*-IM/IM/IA reactions was discussed based on the controlled experiments and X-ray crystal structure data (Scheme 40).

**Scheme 40:** Reaction Mechanism for the Selective Formation of Cendrane Scaffolds **84** and **85**.



During the course of the coupling/annulation reaction, the protonated *tert*-amine of the quinine interacts with the carbonyl of hydroxy-*p*-quinone and enolate oxygen interacts with the quinine-O*H* through hydrogen bonding to make a stable assembly (*pre*-TS-1, Scheme 40). The major kinetic isomer of methanoazulenes **84** were furnished with high selectivity through the controlled two consecutive *5-(enolexo)-exo-trig* cyclizations (IM/IM reactions) by synergistic activation with less steric hindrance (*pre*-TS-1). The minor isomer of methanoazulenes **84'** were not furnished due to the possible high steric hindrance between side-chain conformer and hydroxy*p*-quinone alkyl groups (*pre*-TS-2), without much catalyst involvement. The major thermodynamic isomer of methanoazulenes **85** were furnished through the two consecutive *5-(enolexo)-exo-trig* cyclizations (IM/IA reactions) by synergistic activation with double hydrogen bonding (*pre*-TS-3). The minor isomer of methanoazulenes **85'** were furnished through the IM and IA reactions by non-synergistic activation with double hydrogen bonding with possible steric hindrance between side-chain and quinine (*pre*-TS-4). In the ring isomerization or *retro*-cyclisation of kinetic product **84** to thermodynamic **85**, PTC can initiate the *retro*- IM and *retro*-IM reactions on **84** by inducing the carbonyl groups polarization, *in situ* generated acyclic intermediate further undergoes conformational changes like ring flipping and followed by selective IM and IA reactions by inducing the polarization of carbonyl groups with PTC cations under the thermodynamic conditions (Scheme 40).

## 5.3 Conclusions

In summary, we have developed an organocatalytic tandem coupling/annulation reaction as a green protocol for the one-pot synthesis of cedrane scaffolds **84** and **85** in excellent yields with very good *pr*'s and *dr*'s. Hydroxy-*p*-quinone aldehydes **82** were treated with different phosphoranes or CH-acids **83** under the quinine **23e** catalysis at 25 ºC to generate a cedrane scaffolds **4-6** through the sequence of W/IM/IM, W/IM/IA, W/IM/IA/W, KC/IM/IA, and/or *retro*-IM/*retro*-IM/IM/IA reactions. As similar to cellular reactions, organocatalytic ring isomerization or structural rearrangement was highlighted through transforming kinetic isomer **84** into thermodynamic product **85**. The preliminary mechanistic aspects of sequential one-pot coupling and annulation reaction rate, *pr*'s and *dr*'s were explained with the help of controlled experiments. Furthermore, the feasibility of the asymmetric induction for this tandem coupling/annulation reactions was investigated, although moderate enantioselectivity was achieved at the current stage. Further work on the development of new chiral organocatalysts and their application in asymmetric tandem coupling/annulation transformations are underway in our laboratory, and the results will be reported in the due course.

# 6. Experimental Section

**General Methods:** The $^{1}H$ NMR and $^{13}C$ NMR spectra were recorded at 400 or 500 MHz and 100 or 125 MHz, respectively. The chemical shifts are reported in ppm downfield to TMS ($\delta = 0$) for $^{1}H$ NMR and relative to the central $CDCl_3$ resonance ($\delta = 77.0$) for $^{13}C$ NMR. In the $^{13}C$ NMR spectra, the nature of the carbons (C, CH, $CH_2$ or $CH_3$) was determined by recording the DEPT-135 experiment, and is given in parentheses. The coupling constants *J* are given in Hz. Column chromatography was performed using Acme's silica gel (particle size 0.063-0.200 mm). High-resolution mass spectra were recorded on micromass ESI-TOF MS. IR spectra were recorded on *J*ASCO FT/IR-5300 and Thermo Nicolet FT/IR-5700. The X-ray diffraction measurements were carried out at 298 K on an automated Enraf-Nonious MACH 3 diffractometer using graphite monochromated, Mo-Kα ($\lambda = 0.71073$ Å) radiation with CAD4 software or the X-ray intensity data were measured at 298 K on a Bruker SMART APEX CCD area detector system equipped with a graphite monochromator and a Mo-Kα fine-focus sealed tube ($\lambda = 0.71073$ Å). For thin-layer chromatography (TLC), silica gel plates Merck 60 F254 were used and compounds were visualized by irradiation with UV light and/or by treatment with a solution of *p*-anisaldehyde (23 mL), conc. $H_2SO_4$ (35 mL), acetic acid (10 mL), and ethanol (900 mL) followed by heating.

**Materials:** All solvents and commercially available chemicals were used as received without further purification unless otherwise stated.

## 1. General Experimental Procedure for Direct Organocatalytic Chemoselective Carbonyl-Azide [3+2]-Cycloaddition: Synthesis of Pharmaceutically Rich 1,2,3-Triazoles

**Procedure A:** **General procedure for the synthesis of 2,4-diketoester 71.**[75]

A mixture of diethyl oxalate (41.5 mmol) and aryl or alkyl ketone (41.5 mmol) was added dropwise to a stirred solution of NaOEt (1.15 g of sodium in 20mL of absolute ethanol) at 0 ºC. The resulting salt was stirred at room temperature for 24 h. The reaction was quenched with aqueous $H_2SO_4$ and extracted with ethyl acetate. The combined organic layers were washed with saturated $NaHCO_3$, dried over $MgSO_4$, and concentrated under vacum. Purification on silica gel (EtOAc/hexane, 2:8) provided the desired product **71**.

**Procedure B: General procedure for the synthesis of azides 2.**

To a solution of substituted aniline in $H_2O$ (7.84 mL) was added conc. hydrochloric acid (1.57 mL) at 0 °C. After that, a solution of $NaNO_2$ (4.70 mmol, 0.32 g) in water (4.89 mL) was added dropwise over a period of 10 min with constant stirring. After stirring the reaction mixture for 1 h at 0 °C, a solution of $NaN_3$ (4.70 mmol, 0.31 g) in water (4.89 mL) was added to this mixture and it was allowed to stir at room temperature for 2-3 h. After completion of the reaction, mixture was poured into water, extracted with ethyl acetate, dried over anhyd. Sodium sulphate, concentrated under vacuo to give azide which was used further without purification.

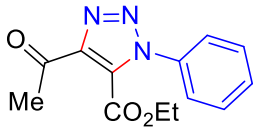
**Procedure C: General procedure for the synthesis of 72 and 73**: To an ordinary glass vial equipped with a magnetic stirring bar were added 0.3 mmol of **71**, 1.5 equiv of azides **2,** and 0.06 mmol of Tetramethyl guanidine (**23**) in 1mL of DMSO. The reaction mixture was allowed to stir until complete consumption of **71** (monitored by TLC) at room temperature. The corresponding products **72** and/or **73** were purified by column chromatography (silicagel: 100-200 mesh; eluent: EA/hexanes).

**Procedure D:** To an ordinary sealed tube equipped with a magnetic stirring bar were added 0.3 mmol of **72**, 20 mol % DBU and 1 ml of DMSO solvent. The reaction mixture was allowed to stir for 12 h at 120ºC. After complete consumption of compound **72** (monitored by TLC), work up was done by aqueous $NH_4Cl$ and DCM. The combined organic layer dried over anhydrous sodium sulphate, filtered and concentrated. Pure products **74** was obtained by column chromatography (silica gel, mixture of hexane and ethyl acetate).

**Procedure E:** To an ordinary glass vial equipped with a magnetic stirring bar were added 0.38 mmol of **72**, 1.5 equiv. of sodium borohydride in 1.2 ml of ethanol. The reaction mixture was allowed to stir until complete consumption of **72** (monitored by TLC) at room temperature. The corresponding product **75** and **76** were purified by column chromatography (silicagel: 100-200 mesh; eluent: EA/hexanes).

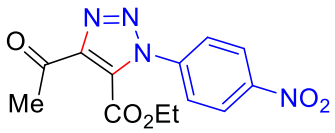
**Procedure F:** To an ordinary glass vial equipped with a magnetic stirring bar were added 0.4 mmol of **72**, 0.2 mmol of **78** and 20 mol % of p-toluenesulfunic acid in 1.3 ml of ethanol. The reaction mixture was allowed to stir until complete consumption of **72** (monitored by TLC) at room temperature. The corresponding product **79** were purified by column chromatography (silicagel: 100-200 mesh; eluent: EA/hexanes).

**Ethyl 4-acetyl-1-phenyl-1*H*-1,2,3-triazole-5-carboxylate (72aa):** The title compound was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a slightly brown solid compound. Yield: 84% (65.6 mg). Mp: 65-67 °C. IR (neat): $\nu_{max}$ 2918, 1739, 1693, 1501, 1438, 1373, 1280, 1188, 1068, 1005 and 763 cm$^{-1}$. $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.55 (5H, s), 4.39 (2H, q, $J$ = 7.2 Hz), 2.76 (3H, s), 1.27 (3H, t, $J$ = 7.2, 6.8 Hz). $^{13}$C NMR (100 MHz, $CDCl_3$, DEPT-135): $\delta$ 191.8 (C, *C*=O), 159.4 (C), 145.7 (C), 135.5 (C), 131.1 (C), 130.4 (CH), 129.6 (2 x CH), 124.1 (2 x CH), 63.3 ($CH_2$), 27.6 ($CH_3$), 13.6 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{13}H_{13}N_3O_3Na$ 282.0855; Found 282.0855.



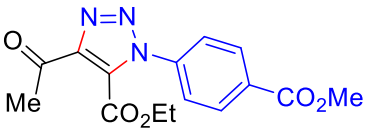
**72aa**

**Ethyl 4-acetyl-1-(4-nitrophenyl)-1*H*-1,2,3-triazole-5-carboxylate (72ab):** The title compounds was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a brown solid compound. Yield: 84% (77 mg). Mp: 116-119 °C. IR (neat): $\nu_{max}$ 2989, 1745, 1698, 1557, 1527, 1315, 1254, 1177, 1113, 1001, 853, 751 and 685 cm$^{-1}$. $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.44 (2H, dt, $J$ = 8.8, 2.8 Hz), 7.82 (2H, dt, $J$ = 9.2, 2.8 Hz), 4.45 (2H, q, $J$ = 7.2 Hz), 2.76 (3H, s), 1.35 (3H, t, $J$ = 7.2, 6.8 Hz). $^{13}$C NMR (100 MHz, $CDCl_3$, DEPT-135): $\delta$ 191.4 (C, *C*=O), 159.0 (C), 148.5 (C), 146.2 (C), 140.0 (C), 130.9 (C), 125.2 (2 x CH), 125.0 (2 x CH), 63.9 ($CH_2$), 27.8 ($CH_3$), 13.7 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{13}H_{12}N_4O_5Na$ 327.0705; Found 327.0705.



**72ab**

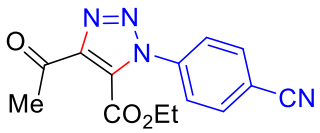
**Ethyl 4-acetyl-1-(4-(methoxycarbonyl)phenyl)-1*H*-1,2,3-triazole-5-carboxylate (72ac)**: The title compound was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a colourless semi solid compound. Yield: 85% (80.9 mg). IR (neat): $\nu_{max}$ 2953, 1742, 1712, 1689, 1438, 1203, 1109, 1066, 830, 769 and 690 cm$^{-1}$. $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 8.23 (2H, d, $J$ = 9.0 Hz), 7.66 (2H, d, $J$ = 8.5 Hz), 4.41 (2H, q, $J$ = 7.5 Hz), 3.97 (3H, S), 2.77 (3H, s), 1.30 (3H, t, $J$ = 7.0 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 191.6 (C, *C*=O), 165.5 (C), 159.2 (C), 145.9 (C), 138.8 (C), 131.9 (C), 130.0 (C), 131.0 (2 x CH), 123.9 (2 x CH), 63.6



**72ac**

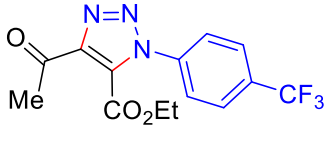
($CH_2$), 52.6 ($CH_3$), 27.6 ($CH_3$), 13.7 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{15}H_{15}N_3O_5Na$ 340.0909; Found 340.0909.

**Ethyl 4-acetyl-1-(4-cyanophenyl)-1*H*-1,2,3-triazole-5-carboxylate (72ad):** The title compound was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a colourless solid compound. Yield: 85% (73 mg). Mp: 80-82 °C. IR (neat): $\nu_{max}$ 1739, 1697, 1509, 1444, 1265, 1191, 1066, 732, 702 and 563 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.88 (2H, dt, *J* = 9.0, 2.0 Hz), 7.74 (2H, dt, *J* = 9.0, 2.0 Hz), 4.43 (2H, q, *J* = 7.0 Hz), 2.77 (3H, s), 1.33 (3H, t, *J* = 7.0 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 191.4 (C, *C*=O), 159.0 (C), 146.2 (C), 138.6 (C), 133.6 (2 x CH), 130.8 (C), 124.8 (2 x CH), 117.2 (C), 114.5 (C), 63.8 ($CH_2$), 27.7 ($CH_3$), 13.6 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{14}H_{12}N_4O_3Na$ 307.0807; Found 307.0809.



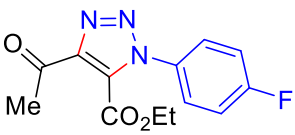
**72ad**

**Ethyl 4-acetyl-1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,3-triazole-5-carboxylate (72ae):** The title compound was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as solid compound. Yield: 86% (73 mg). Mp: 69-71 °C. IR (neat): $\nu_{max}$ 1740, 1705, 1361, 1220, 1173, 1131, 1063, 850 and 603 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.83 (2H, d, *J* = 8.5 Hz), 7.72 (2H, d, *J* = 8.5 Hz), 4.42 (2H, q, *J* = 7.0 Hz), 2.76 (3H, s), 1.31 (3H, t, *J* = 7.5 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 191.5 (C, *C*=O), 159.1 (C), 146.0 (C), 138.1 (C), 133.6 (2 x CH), 130.8 (C), 124.8 (2 x CH), 117.2 (C), 114.5 (C), 63.7 ($CH_2$), 27.7 ($CH_3$), 13.7 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{14}H_{12}F_3N_3O_3H$ 328.0908; Found 328.0908.



**72ae**

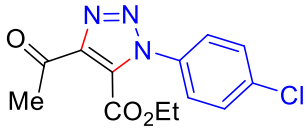
**Ethyl 4-acetyl-1-(4-fluorophenyl)-1H-1,2,3-triazole-5-carboxylate (72af):** The title compound was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as semi solid compound. Yield: 95% (79 mg). IR (neat): $\nu_{max}$ 2985, 1738, 1694, 1511, 1374, 1280, 1187, 1066, 1004 and 843 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.56-7.54 (2H, m), 7.29-7.23 (2H, m), 4.42 (2H, qd, *J* = 7.2, 0.4 Hz), 2.76 (3H, d, *J* = 0.8 Hz), 1.29 (3H, td, *J* = 6.8, 0.4 Hz). $^{13}C$ NMR



**72af**

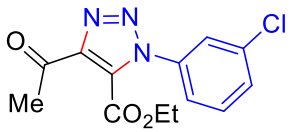
(100 MHz, $CDCl_3$, DEPT-135): $\delta$ 191.7 (C, *C*=O), 163.4 (C, d, *J* = 251.0 Hz), 159.2 (C), 145.7 (C), 131.52 (C, d, *J* = 3.0 Hz), 131.49 (C), 126.4 (2 x CH, d, *J* = 9.0 Hz), 116.7 (C, d, *J* = 23.0 Hz), 63.4 ($CH_2$), 27.6 ($CH_3$), 13.6 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{13}H_{12}FN_3O_3Na$ 300.0760; Found 300.0761.

**Ethyl 4-acetyl-1-(4-chlorophenyl)-1*H*-1,2,3-triazole-5-carboxylate (4ag):** The title compounds was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a semi solid compound. Yield: 93% (81.7 mg). IR (neat): $\nu_{max}$ 2984, 1739, 1695, 1498, 1373, 1253, 1189, 1094, 1066, 1001 and 835 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.55-7.50 (5H, m), 4.40 (2H, qd, *J* = 7.0, 1.0 Hz), 2.75 (3H, d, *J* = 1.0 Hz), 1.30 (3H, td, *J* = 7.0, 1.0 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 191.6 (C, *C*=O), 159.2 (C), 145.8 (C), 136.7 (C), 133.9 (C), 131.0 (C), 129.8 (2 x CH), 125.5 (2 x CH), 63.5 ($CH_2$), 27.6 ($CH_3$), 13.7 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{13}H_{12}ClN_3O_3H$ 294.0645; Found 294.0645.



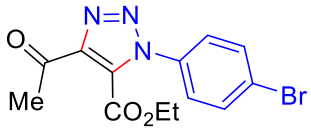
**72ag**

**Ethyl 4-acetyl-1-(3-chlorophenyl)-1*H*-1,2,3-triazole-5-carboxylate (72ah):** The title compounds was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a semi solid compound. Yield: 93% (81.7 mg). IR (neat): $\nu_{max}$ 2984, 1740, 1696, 1591, 1552, 1488, 1373, 1252, 1188, 1102, 1069 and 801 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.61-7.60 (1H, m), 7.55-7.53 (1H, m), 7.51-7.45 (2H, m), 4.42 (2H, q, *J* = 7.0 Hz), 2.76 (3H, s), 1.31 (3H, t, *J* = 7.0 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 191.6 (C, *C*=O), 159.1 (C), 145.8 (C), 136.3 (C), 135.4 (C), 131.0 (C), 130.65 (CH), 130.63 (CH), 124.5 (CH), 122.3 (CH), 63.6 ($CH_2$), 27.7 ($CH_3$), 13.7 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{13}H_{12}ClN_3O_3H$ 294.0645; Found 294.0649.



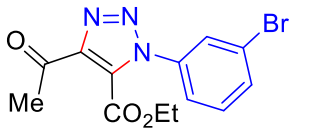
**72ah**

**Ethyl 4-acetyl-1-(4-bromophenyl)-1*H*-1,2,3-triazole-5-carboxylate (72ai):** The title compounds was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a solid compound. Yield: 90% (91.5 mg). Mp: 95-97 °C. IR (neat): $\nu_{max}$ 2923, 1741, 1696, 1495, 1444, 1291, 1254, 1191, 1066, 1000, 910, 830 and 440 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.69 (2H, d, $J$ = 9.0 Hz), 7.45 (2H, d, $J$ = 9.0 Hz), 4.40 (2H, q, $J$ = 7.0 Hz), 2.76 (3H, s), 1.31 (3H, t, $J$ = 7.5 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 191.6 (C, *C*=O), 159.2 (C), 145.8 (C), 134.4 (C), 132.8 (2 x CH), 130.9 (C), 125.7 (2 x CH), 124.7 (C), 63.5 ($CH_2$), 27.8 ($CH_3$), 13.7 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{13}H_{12}BrN_3O_3H$ 338.0140; Found 338.0140.



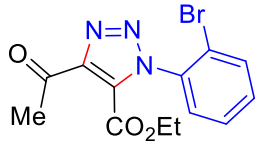
**72ai**

**Ethyl 4-acetyl-1-(3-bromophenyl)-1*H*-1,2,3-triazole-5-carboxylate (72aj):** The title compounds was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a semi solid compound. Yield: 90% (91.5 mg). IR (neat): $\nu_{max}$ 2929, 1740, 1695, 1586, 1551, 1485, 1372, 1294, 1252, 1187, 1067 and 790 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.75 (1H, t, $J$ = 2.0 Hz), 7.71-7.69 (1H, m), 7.52-7.50 (1H, m), 7.43 (1H, t, $J$ = 8.0 Hz), 4.42 (2H, q, $J$ = 7.5 Hz), 2.76 (3H, s), 1.31 (3H, t, $J$ = 7.0 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 191.6 (C, *C*=O), 159.1 (C), 145.8 (C), 136.4 (C), 133.6 (CH), 131.0 (C), 130.8 (CH), 127.3 (CH), 123.0 (CH), 122.8 (CH), 63.6 ($CH_2$), 27.7 ($CH_3$), 13.7 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{13}H_{12}BrN_3O_3H$ 338.0140; Found 338.0139.



**72aj**

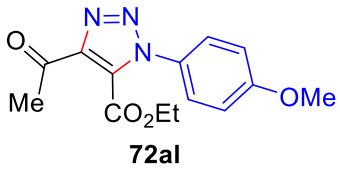
**Ethyl 4-acetyl-1-(2-bromophenyl)-1*H*-1,2,3-triazole-5-carboxylate (72ak):** The title compounds was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a semi solid compound. Yield: 56% (56.6 mg). IR (neat): $\nu_{max}$ 2975, 1740, 1691, 1488, 1371, 1285, 1184, 1079, 999, 755 and 656 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.77-7.75 (1H, m), 7.54-7.45 (3H, m), 4.28 (2H, q, $J$ = 7.0 Hz), 2.80 (3H, s), 1.17(3H, t, $J$ = 7.0 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 191.6 (C, *C*=O), 159.8 (C), 145.6 (C), 135.2 (C), 133.4 (CH), 132.2 (C), 131.4 (C), 128.7 (CH),



**72ak**

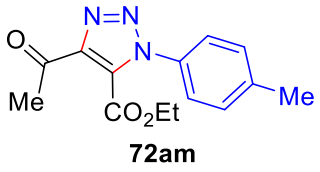
128.2 (CH), 120.7 (CH), 62.9 ($CH_2$), 28.3 ($CH_3$), 13.5 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{13}H_{12}BrN_3O_3H$ 338.0140; Found 338.0141.

**Ethyl 4-acetyl-1-(4-methoxyphenyl)-1*H*-1,2,3-triazole-5-carboxylate (72al):** The title compounds was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as solid compound. Yield: 79% (68.9 mg). Mp: 97-98 °C. IR (neat): $\nu_{max}$ 2987, 1737, 1691, 1513, 1421, 1280, 1250, 1186, 1066, 1016, 835 and 806 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.46 (2H, d, *J* = 9.0 Hz), 7.02 (2H, d, *J* = 9.0 Hz), 4.37 (2H, q, *J* = 7.0 Hz), 3.87 (3H, s), 2.74 (3H, s), 1.28 (3H, t, *J* = 7.5 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 191.7 (C, *C*=O), 160.0 (C), 159.4 (C), 145.5 (C), 131.2 (C), 128.4 (C), 125.7 (2 x CH), 114.7 (2 x CH), 63.5 ($CH_2$), 55.6 ($CH_3$), 27.5 ($CH_3$), 13.7 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{14}H_{15}N_3O_4H$ 290.1141; Found 290.1147.



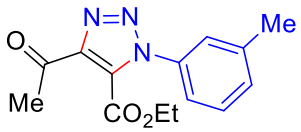
**72al**

**Ethyl 4-acetyl-1-(*p*-tolyl)-1*H*-1,2,3-triazole-5-carboxylate (72am):** The title compounds was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a colour less semi solid compound. Yield: 79% (68.9 mg). IR (neat): $\nu_{max}$ 2983, 1738, 1692, 1514, 1444, 1373, 1278, 1188, 1065, 1001, 954, 819 and 775 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.43 (2H, d, *J* = 8.4 Hz), 7.33 (2H, d, *J* = 8.4 Hz), 4.38 (2H, q, *J* = 7.2 Hz), 2.75 (3H, s), 2.44 (3H, s), 1.28 (3H, t, *J* = 7.2 Hz). $^{13}C$ NMR (100 MHz, $CDCl_3$, DEPT-135): $\delta$ 191.7 (C, *C*=O), 159.4 (C), 145.5 (C), 140.7 (C), 132.9 (C), 131.0 (C), 130.1 (2 x CH), 123.8 (2 x CH), 63.2 ($CH_2$), 27.5 ($CH_3$), 21.1 ($CH_3$), 13.7 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{14}H_{15}N_3O_3Na$ 296.1011; Found 296.1004.



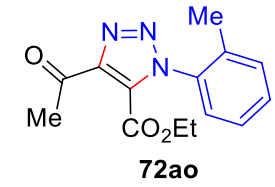
**72am**

**Ethyl 4-acetyl-1-(*m*-tolyl)-1*H*-1,2,3-triazole-5-carboxylate (72an):** The title compounds was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a colourless semi solid. Yield: 70% (57.9 mg). IR (neat): $\nu_{max}$ 2969, 1738, 1510, 1453, 1367, 1228, 1042, 995, 818 and 764 cm$^{-1}$. $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.44-7.31 (4H, m), 4.39 (2H, q, $J$ = 7.0 Hz), 2.76 (3H, s), 2.44 (3H, s), 1.28 (3H, t, $J$ = 7.2 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 191.7 (C, *C*=O), 159.4 (C), 145.5 (C), 139.9 (C), 135.3 (C), 131.13 (CH), 130.07 (C), 129.3 (CH), 124.6 (CH), 121.0 (CH), 63.2 ($CH_2$), 27.5 ($CH_3$), 21.2 ($CH_3$), 13.6 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{14}H_{15}N_3O_3Na$ 296.1011; Found 296.1004.



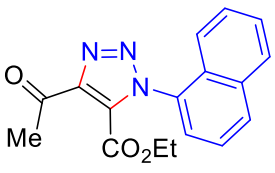
**72an**

**Ethyl 4-acetyl-1-(*o*-tolyl)-1*H*-1,2,3-triazole-5-carboxylate (72ao):** The title compounds was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a colourless semi solid compound. Yield: 30% (25 mg). IR (neat): $\nu_{max}$ 2964, 1731, 1511, 1454, 1366, 1227, 1040, 995, 817 and 764 cm$^{-1}$. $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.48 (1H, td, $J$ = 7.5, 1.0 Hz), 7.39 (1H, d, $J$ = 7.5 Hz), 7.34 (1H, t, $J$ = 8.0 Hz), 7.26 (1H, dt, $J$ = 8.0, 1.5 Hz), 4.26 (2H, q, $J$ = 7.0 Hz), 2.79 (3H, s), 2.11 (3H, s), 1.14 (3H, t, $J$ = 7.2 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 191.8 (C, *C*=O), 158.5 (C), 145.5 (C), 135.4 (C), 134.6 (C), 132.0 (C), 131.2 (CH), 131.0 (CH), 126.68 (CH), 126.67 (CH), 62.9 ($CH_2$), 27.8 ($CH_3$), 17.2 ($CH_3$), 13.5 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{14}H_{15}N_3O_3Na$ 296.1011; Found 296.1004.



**72ao**

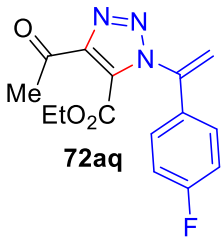
**Ethyl 4-acetyl-1-(naphthalen-1-yl)-1*H*-1,2,3-triazole-5-carboxylate (72ap):** The title compound was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a colourless semi solid compound. Yield: 84% (65.6 mg). IR (neat): $\nu_{max}$ 1738, 1701, 1439, 1362, 1281, 1224, 1193, 802 and 628 cm$^{-1}$. $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.07 (1H, d, $J$ = 8.0 Hz), 7.96 (1H, d, J = 8.0 Hz), 7.60-7.52 (4H, m), 7.30 (1H, d, $J$ = 8.5 Hz), 4.12 (2H, q, $J$ = 7.5 Hz), 2.83 (3H, s), 0.93 (3H, t, $J$ = 7.0 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 191.7 (C, *C*=O), 158.5 (C), 145.4 (C), 133.9 (C), 133.0 (C), 131.8 (C), 131.4 (CH), 129.1 (C), 128.2 (CH), 128.1 (CH),



**72ap**

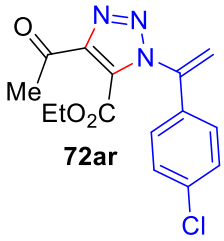
127.3 (CH), 124.8 (CH), 121.8 (CH), 62.8 ($CH_2$), 27.9 ($CH_3$), 13.3 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{17}H_{15}N_3O_3Na$ 332.1011; Found 332.1011.

**Ethyl 4-acetyl-1-(1-(4-fluorophenyl)vinyl)-1*H*-1,2,3-triazole-5-carboxylate (72aq):** The title compound was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a colourless solid compound. Yield: 72% (65.6 mg). Mp: 49-51 °C. IR (neat): $\nu_{max}$ 1738, 1701, 1439, 1362, 1281, 1224, 1193, 802 and 628 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.22-7.19 (2H, m), 7.09-7.05 (2H, m), 5.83 (1H, d, *J* = 1.0 Hz), 5.69 (1H, d, *J* = 1.5 Hz), 4.19-4.14 (2H, m), 2.75 (3H, t, *J* = 2.5 Hz), 1.19-1.17 (3H, m). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 191.5 (C, *C*=O), 163.6 (C, d, *J* = 250.0 Hz), 158.6 (C), 145.3 (C), 141.1 (C), 131.2 (C), 130.1 (C, d, *J* = 3.75 Hz), 128.35 (2 x CH, d, *J* = 8.75 Hz), 115.9 (2 x CH, d, *J* = 22.5), 114.1 ($CH_2$), 62.8 ($CH_2$), 27.9 ($CH_3$), 13.3 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{15}H_{14}FN_3O_3Na$ 326.0917; Found 326.0917.



**72aq**

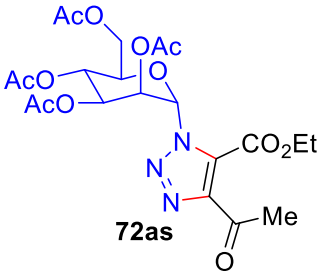
**Ethyl 4-acetyl-1-(1-(4-chlorophenyl)vinyl)-1*H*-1,2,3-triazole-5-carboxylate (72ar):** The title compound was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a colourless semi solid compound. Yield: 72% (65.6 mg). IR (neat): $\nu_{max}$ 2985, 1738, 1696, 1442, 1280, 1249, 1194, 1011, 833 and 732 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.35 (2H, dt, *J* = 8.5, 2.5 Hz), 7.14 (2H, dt, *J* = 8.5, 2.5 Hz), 5.87 (1H, d, *J* = 2.0 Hz), 5.71 (1H, d, *J* = 2.0 Hz), 4.17 (2H, q, *J* = 7.5 Hz), 2.75 (3H, s), 1.17 (3H, t, *J* = 7.5 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 191.4 (C, *C*=O), 158.5 (C), 145.3 (C), 141.1 (C), 136.1 (C), 132.3 (C), 131.1 (C), 129.0 (2 x CH), 127.5 (2 x CH), 114.7 ($CH_2$), 63.0 ($CH_2$), 27.7 ($CH_3$), 13.4 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{15}H_{14}ClN_3O_3H$ 320.0802; Found 320.0807.



**72ar**

**(2*R*,3*R*,4*S*,5*S*,6*S*)-2-(acetoxymethyl)-6-(4-acetyl-5-(ethoxycarbonyl)-1*H*-1,2,3-triazol-1-yl)tetrahydro-2*H*-pyran-3,4,5-triyl triacetate (72as):** The title compound was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (20:80 to 70:30) and isolated as a white solid compound. Yield: 50% (77.9 mg). $[\alpha]_D^{25}$ = +270.3° (c = 0.103, acetone). Mp: 109-111 °C. IR (neat): $\nu_{max}$ 2923, 1743, 1698, 1556,

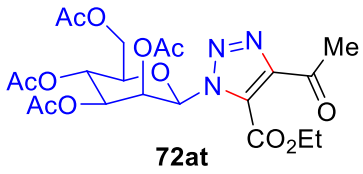
1435, 1370, 1210, 1135, 1087, 1049, 1013, 956, 792 and 735 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$):



**72as**

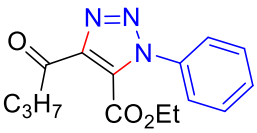
$\delta$ 6.36 (1H, d, $J$ = 1.0 Hz), 6.07 (1H, dd, $J$ = 4.0, 2.5 Hz), 5.91 (1H, dd, $J$ = 8.0, 4.0 Hz), 5.39 (1H, t, $J$ = 9.5 Hz), 4.48 (2H, q, $J$ = 7.5 Hz), 4.28 (1H, dd, $J$ = 12.5, 5.0 Hz), 4.02 (1H, dd, $J$ = 12.5, 5.0 Hz), 3.77-3.73 (1H, m), 2.74 (3H, s), 2.22 (3H, s), 2.08 (3H, s), 2.056 (3H, s), 2.051 (3H, s), 1.41 (3H, t, $J$ = 7.5 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 191.4 (C, *C*=O), 170.4 (C), 169.54 (C), 169.51 (C), 169.36 (C), 158.33 (C), 146.3 (C), 129.9 (C), 83.6 (CH), 72.1 (CH), 68.7 (CH), 67.7 (CH), 65.7 (CH), 63.5 ($CH_2$), 61.4 ($CH_2$), 28.2 ($CH_3$), 20.7 ($CH_3$), 20.6 ($2CH_3$), 20.5 ($CH_3$), 13.7 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{21}H_{27}N_3O_{12}Na$ 536.1492; Found 536.1498.

**(2*R*,3*R*,4*S*,5*S*,6*R*)-2-(acetoxymethyl)-6-(4-acetyl-5-(ethoxycarbonyl)-1*H*-1,2,3-triazol-1-yl)tetrahydro-2*H*-pyran-3,4,5-triyl triacetate (72at):** The title compound was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (20:80 to 70:30) and isolated as a white solid compound. Yield: 50% (77.9 mg). $[\alpha]_D^{25}$ = -9.0º (c = 0.100, methanol). Mp: 111-113 ºC. IR (neat): $\nu_{max}$ 1752, 1697, 1370, 1208, 1089, 1031, 956, 861, 634 and 598 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 6.06 (1H, dd, $J$ = 9.0, 4.5 Hz), 5.97-5.91 (1H, m), 5.40 (1H, td, $J$ = 9.5, 5.0 Hz), 5.26-5.21 (1H, m), 4.50-4.49 (2H, m), 4.29-4.24 (1H, m), 4.13-4.09 (1H, m), 3.98-3.95 (1H, m), 2.68 (3H, s), 2.07-2.02 (9H, m), 1.91-1.89 (3H, s), 1.41 (3H, t, $J$ = 7.5 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 191.3 (C, *C*=O), 170.3 (C), 170.1 (C), 169.1 (C), 168.4 (C), 158.5 (C), 146.5 (C), 129.7 (C), 85.2 (CH), 75.1 (CH), 72.9 (CH), 69.7 (CH), 67.3 (CH), 63.2 ($CH_2$), 61.3 ($CH_2$), 28.2 ($CH_3$), 20.5 ($CH_3$), 20.5 ($CH_3$), 20.4 ($CH_3$), 20.2 ($CH_3$), 13.7 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C2_1H_{27}N_3O_{12}Na$ 536.1492; Found 536.1498.



**72at**

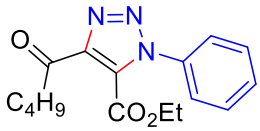
**Ethyl 4-butyryl-1-phenyl-1*H*-1,2,3-triazole-5-carboxylate (72ba):** The title compound was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a semi-solid compound. Yield: 81% (70 mg). IR (neat): $\nu_{max}$ 2964, 1738, 1690, 1499, 1462, 1375, 1298, 1191, 1013, 760 and 690 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.55 (5H, s), 4.38 (2H, q, $J$ = 7.0 Hz), 3.17 (2H, t, J = 7.5 Hz), 1.82



**72ba**

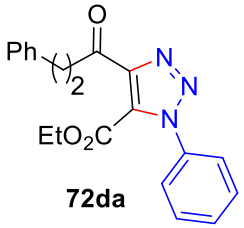
(2H, sxt, *J* = 7.5 Hz), 1.27 (3H, t, *J* = 7.5 Hz), 1.04 (3H, t, *J* = 7.5 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135): *δ* 194.4 (C, *C*=O), 159.5 (C), 145.7 (C), 135.6 (C), 131.1 (C), 130.4 (CH), 129.6 (2 x CH), 124.2 (2 x CH), 63.3 ($CH_2$), 41.9 ($CH_2$), 17.2 ($CH_2$), 13.7 ($CH_3$), 13.6 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{15}H_{17}N_3O_3Na$ 310.1168; Found 310.1165.

**Ethyl 4-pentanoyl-1-phenyl-1*H*-1,2,3-triazole-5-carboxylate (72ca):** The title compound was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a semi-solid. Yield: 77% (69.9 mg). IR (neat): $\nu_{max}$ 2932, 1739, 1690, 1499, 1374, 1250, 1017, 758 and 691 $cm^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$): *δ* 7.55 (5H, s), 4.38 (2H, q, *J* = 7.0 Hz), 3.19 (2H, t, *J* = 7.5 Hz), 1.80-1.74 (2H, m), 1.45 (2H, sext, *J* = 7.5 Hz), 1.27 (3H, t, *J* = 7.5 Hz), 0.97 (3H, t, *J* = 7.5 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135): *δ* 194.5 (C, *C*=O), 159.5 (C), 145.6 (C), 135.6 (C), 131.1 (C), 130.4 (CH), 129.6 (2 x CH), 124.2 (2 x CH), 63.3 ($CH_2$), 39.7 ($CH_2$), 25.7 ($CH_2$), 22.3 ($CH_2$), 13.8 ($CH_3$), 13.6 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{16}H_{19}N_3O_3Na$ 324.1324; Found 324.1326.



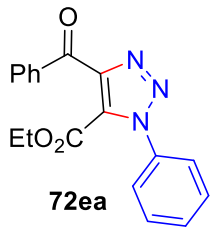
**72ca**

**Ethyl 1-phenyl-4-(3-phenylpropanoyl)-1*H*-1,2,3-triazole-5-carboxylate (72da):** The title compound was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a colourless semi solid compound. Yield: 70% (73.7 mg). IR (neat): $\nu_{max}$ 2929, 1738, 1691, 1549, 1498, 1438, 1280, 1251, 1190, 1147, 969, 784 and 691 $cm^{-1}$. $^1$H NMR (400 MHz, $CDCl_3$): *δ* 7.54 (5H, b s), 7.29-7.17 (5H, m), 4.37 (2H, q, *J* = 7.2 Hz), 3.54 (2H, t, *J* = 8.0 Hz), 3.11 (2H, t, *J* = 7.6 Hz), 1.25 (3H, t, *J* = 7.2 Hz). $^{13}$C NMR (100 MHz, $CDCl_3$, DEPT-135): *δ* 193.2 (C, *C*=O), 159.3 (C), 145.3 (C), 140. 6 (C), 135.4 (C), 131.1 (C), 130.4 (CH), 129.5 (2 x CH), 128.4 (2 x 2 x CH), 126.0 (CH), 124.1 (2 x CH), 63.3 ($CH_2$), 41.5 ($CH_2$), 29.4 ($CH_2$), 13.6 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{20}H_{19}N_3O_3H$ 350.1505; Found 350.1503.



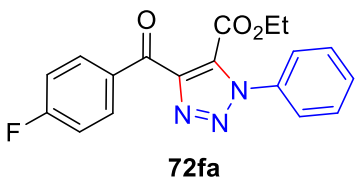
**72da**

**Ethyl 4-benzoyl-1-phenyl-1*H*-1,2,3-triazole-5-carboxylate (72ea):** The title compound was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a colourless semi solid compound. Yield: 66% (63.6 mg). IR (neat): $\nu_{max}$ 2993, 1736, 1652, 1498, 1275, 1188, 1108, 921 and 749 $cm^{-1}$. $^{1}H$ NMR (400 MHz, $CDCl_3$): $\delta$ 8.23-8.30 (2H, m), 7.64 (1H, tt, $J$ = 7.6, 2.0 Hz), 7.61-7.52 (7H, m), 4.31 (2H, q, $J$ = 7.2 Hz), 1.18 (3H, t, $J$ = 7.2 Hz). $^{13}C$ NMR (100 MHz, $CDCl_3$, DEPT-135): $\delta$ 185.4 (C, *C*=O), 158.9 (C), 146.5 (C), 136.0 (C), 135.6 (C), 133.8 (CH), 132.5 (C), 130.5 (2 x CH), 130.4 (CH), 129.4 (2 x CH), 128.5 (2 x CH), 124.6 (2 x CH), 63.1 ($CH_2$), 13.5 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{15}N_3O_3H$ 322.1192; Found 322.1194.



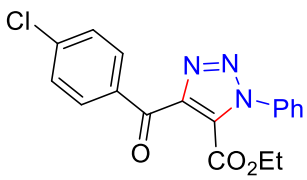
**72ea**

**Ethyl 4-(4-fluorobenzoyl)-1-phenyl-1*H*-1,2,3-triazole-5-carboxylate (72fa):** The title compound was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a colourless solid. Yield: 72% (73.4 mg). Mp: 63-65 $^{o}$C. IR (neat): $\nu_{max}$ 2986, 1737, 1646, 1592, 1498, 1249, 1191, 1107, 998, 922, 760 and 691 $cm^{-1}$. $^{1}H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.45-8.41 (2H, m), 7.58 (5H, b r s), 7.24-7.21 (2H, m), 4.38-4.33 (2H, m), 1.23-1.20 (3H, m). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 183.5 (C, *C*=O), 166.2 (C, d, $J$ = 255.0 Hz), 159.0 (C), 146.3 (C), 135.6 (C), 133.4 (2 x CH, d, $J$ = 8.75 Hz), 132.9 (C), 132.4 (C, d, $J$ = 2.5 Hz), 130.5 (CH), 129.5 (2 x CH), 124.6 (2 x CH), 115.7 (2 x CH, d, $J$ = 22.5 Hz), 63.2 ($CH_2$), 13.6 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{14}FN_3O_3H$ 340.1097; Found 340.1097.



**72fa**

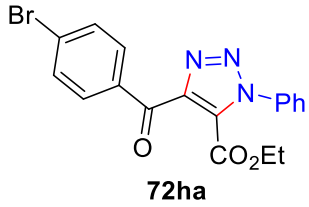
**Ethyl 4-(4-chlorobenzoyl)-1-phenyl-1*H*-1,2,3-triazole-5-carboxylate (72ga):** The title compound was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a colourless solid compound. Yield: 74% (79 mg). Mp: 94-97 $^{o}$C. IR (neat): $\nu_{max}$ 2969, 1740, 1648, 1586, 1498, 1373, 1273, 1108, 920 and 771 $cm^{-1}$. $^{1}H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.33 (2H, d, $J$ = 8.5 Hz), 7.59-7.57 (5H, m), 7.52 (2H, d, $J$ = 9.0 Hz), 4.35 (2H, q, $J$ = 7.0 Hz), 1.22 (3H, t, $J$ = 7.0 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 183.9 (C, *C*=O), 159.0 (C), 146.2 (C), 140.4 (C), 135.6 (C), 134.4 (C), 133.1 (C), 132.0 (2 x CH), 130.5 (CH), 129.5 (2 x CH), 128.9



**72ga**

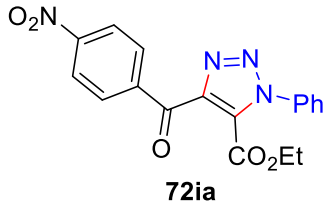
(2 x CH), 124.6 (2 x CH), 63.2 ($CH_2$), 13.6 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{14}ClN_3O_3H$ 356.0802; Found 356.0802.

**Ethyl 4-(4-bromobenzoyl)-1-phenyl-1*H*-1,2,3-triazole-5-carboxylate (72ha):** The title compound was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a colourless solid compound. Yield: 72% (86.9 mg). Mp: 95-97 °C. IR (neat): $\nu_{max}$ 2983, 1728, 1657, 1580, 1495, 1254, 1193, 1107, 918, 760 and 685 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.25 (2H, d, *J* = 8.5 Hz), 7.69 (2H, d, *J* = 8.5 Hz), 7.60-7.56 (5H, m), 4.35 (2H, q, *J* = 7.0 Hz), 1.22 (3H, t, *J* = 7.0 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 184.1 (C, *C*=O), 158.9 (C), 146.1 (C), 135.5 (C), 134.7 (C), 133.0 (C), 132.1 (2 x CH), 131.8 (2 x CH), 130.5 (CH), 129.5 (2 x CH), 129.2 (C), 124.5 (2 x CH), 63.2 ($CH_2$), 13.6 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{14}BrN_3O_3H$ 400.0297; Found 400.0297.



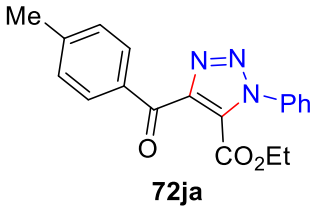
**72ha**

**Ethyl 4-(4-nitrobenzoyl)-1-phenyl-1*H*-1,2,3-triazole-5-carboxylate (72ia):** The title compound was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a brown solid. Yield: 64% (69.9 mg). Mp: 116-119 °C. IR (neat): $\nu_{max}$ 2983, 1737, 1658, 1522, 1498, 1279, 1253, 1190, 1109, 924, 868 and 692 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 8.57 (2H, d, *J* = 8.8 Hz), 8.38 (2H, d, *J* = 9.2 Hz), 7.56 (5H, s), 4.40 (2H, q, *J* = 7.2 Hz), 1.26 (3H, t, *J* = 7.2 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 183.3 (C, *C*=O), 158.9 (C), 150.5 (C), 145.4 (C), 140.5 (C), 135.4 (C), 133.7 (CH), 131.7 (2 x CH), 130.7 (CH), 129.6 (2 x CH), 124.4 (2 x CH), 123.6 (2 x CH), 63.5 ($CH_2$), 13.6 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{14}N_4O_5H$ 367.1042; Found 367.1042.



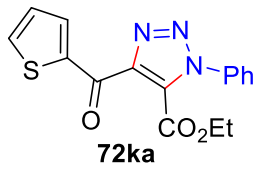
**72ia**

**Ethyl 4-(4-methylbenzoyl)-1-phenyl-1*H*-1,2,3-triazole-5-carboxylate (72ja):** The title compound was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a colourless solid. Yield: 72% (72.5 mg). Mp: 84-87 °C. IR (neat): $\nu_{max}$ 2925, 1732, 1652, 1600, 1372, 1248, 1107, 1007, 921, 758 and 689 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.22 (2H, d, $J$ = 8.5 Hz), 7.60-7.57 (5H, m), 7.33 (2H, d, $J$ = 8.5 Hz), 4.31 (2H, q, $J$ = 7.0 Hz), 2.45 (3H, s), 1.18 (3H, t, $J$ = 7.0 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 185.0 (C, *C*=O), 158.9 (C), 146.9 (C), 144.8 (C), 135.7 (C), 133.6 (C), 132.3 (C), 130.6 (2 x CH), 130.3 (CH), 129.4 (2 x CH), 129.2 (2 x CH), 124.6 (2 x CH), 62.9 ($CH_2$), 21.7 ($CH_3$), 13.5 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{19}H_{17}N_3O_3H$ 336.1348; Found 336.1349.



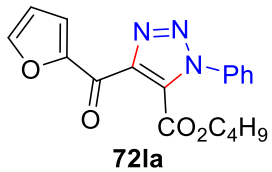
**72ja**

**Ethyl 1-phenyl-4-(thiophene-2-carbonyl)-1*H*-1,2,3-triazole-5-carboxylate (72ka):** The title compound was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a solid compound. Yield: 82% (80.5 mg). Mp: 77-80 °C. IR (neat): $\nu_{max}$ 2924, 1730, 1651, 1600, 1371, 1247, 1106, 1005, 920, 758 and 689 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.09-8.08 (1H, m), 7.78-7.77 (1H, m), 7.60-7.56 (5H, m), 6.68-6.67 (1H, m), 4.39 (2H, qt, $J$ = 7.0, 0.5 Hz), 1.28 (3H, tt, $J$ = 7.0, 1.0 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 171.5 (C, *C*=O), 159.1 (C), 150.8 (C), 148.2 (CH), 145.0 (C), 135.5 (C), 132.8 (C), 130.4 (CH), 129.5 (2 x CH), 124.3 (2 x CH), 123.2 (CH), 112.7 (CH), 63.3 ($CH_2$), 13.6 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{13}N_3O_3SH$ 328.0756; Found 328.0758.



**72ka**

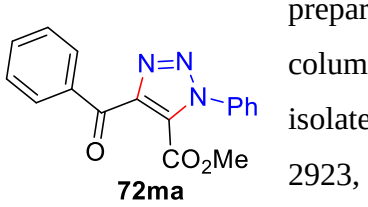
**Butyl 4-(furan-2-carbonyl)-1-phenyl-1*H*-1,2,3-triazole-5-carboxylate (72la):** The title compound was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a solid compound. Yield: 80% (81.3 mg). Mp: 77-80 °C. IR (neat): $\nu_{max}$ 2958, 1735, 1644, 1459, 1280, 1189, 1030, 872 and 762 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.07 (1H, d, $J$ = 2.5 Hz), 7.77 (1H, d, $J$ = 1.0 Hz), 7.59-7.56 (5H, m), 6.68-6.66 (1H, m), 4.34-4.31 (2H, m), 1.64-1.58 (2H, m), 1.30-1.22 (2H, m), 0.88-0.85 (3H, m). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 171.6 (C, *C*=O), 159.2 (C), 150.9 (C), 148.1 (CH), 145.0 (C), 135.5 (C), 132.8 (C), 130.4 (CH), 129.5 (2 x CH), 124.4 (2



**72la**

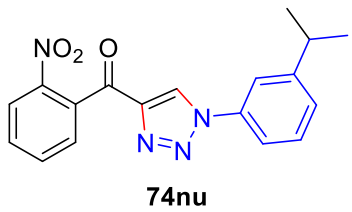
x CH), 123.1 (CH), 112.6 (CH), 67.1 ($CH_2$), 30.0 ($CH_2$), 18.8 ($CH_2$), 13.4 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{13}N_3O_3SH$ 340.1297; Found 340.1301.

**Methyl 4-benzoyl-1-phenyl-1*H*-1,2,3-triazole-5-carboxylate (72ma):** The title compound was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a semi-solid compound. Yield: 72% (66.3 mg). IR (neat): $\nu_{max}$ 2923, 1739, 1651, 1498, 1447, 1358, 1279, 1237, 1275, 914 and 761 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.33 (2H, d, $J$ = 7.5 Hz), 7.65 (1H, t, $J$ = 7.5 Hz), 7.58-7.53 (7H, m), 3.86 (3H, s). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 185.3 (C, *C*=O), 159.6 (C), 146.7 (C), 135.9 (C), 135.6 (C), 133.8 (CH), 132.3 (C), 130.6 (2 x CH), 130.4 (CH), 129.5 (2 x CH), 128.5 (2 x CH), 124.5 (2 x CH), 53.6 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{13}N_3O_3H$ 308.1035; Found 308.1035.



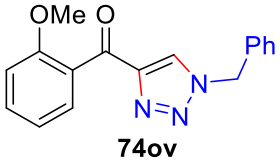
**72ma**

**(1-(3-isopropylphenyl)-1*H*-1,2,3-triazol-4-yl)(2-nitrophenyl)methanone (74nu):** The title compound was prepared following **Procedure C** with employing catalyst **23g**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a semi-solid. Yield: 60% (60.6 mg). IR (neat): $\nu_{max}$ 3080, 1730, 1637, 1605, 1515, 1343, 1258, 1118, 797, and 776 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.69 (1H, s), 8.23 (1H, d, $J$ = 8.0 Hz), 7.81 (1H, td, $J$ = 7.5, 1.0 Hz), 7.71 (1H, td, $J$ = 7.5, 1.5 Hz), 7.66 (1H, dd, $J$ = 7.5, 1.0 Hz), 7.62-7.61 (1H, m), 7.55-7.53 (1H, m), 7.47 (1H, t, $J$ = 7.0 Hz), 7.36 (1H, d, $J$ = 8.0 Hz), 3.02 (1H, quint, $J$ = 7.0 Hz). 1.30 (6H, d, $J$ = 7.0 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 186.2 (C, *C*=O), 151.4 (C), 147.6 (C), 147.4 (C), 136.3 (C), 135.0 (C), 134.2 (CH), 131.3 (CH), 129.9 (CH), 129.3 (CH), 128.0 (CH), 124.6 (CH), 124.3 (CH), 119.2 (CH), 118.4 (CH), 34.1 (CH), 23.8 ($2CH_3$). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{18}H_{16}N_4O_3Na$ 359..1120; Found 359.1126.



**74nu**

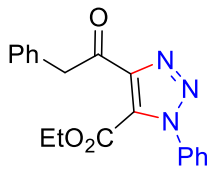
**(1-benzyl-1*H*-1,2,3-triazol-4-yl)(2-methoxyphenyl)methanone (74ov):** The title compound was prepared following **Procedure C** with employing catalyst **23g**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a colourless semi solid compound. Yield: 60% (52.8 mg). IR (neat): $\nu_{max}$ 3081, 1732, 1637, 1604, 1516, 1340, 1258, 1119, 797, and 776



**74ov**

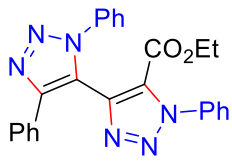
$cm^{-1}$. $^{1}H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.02 (1H, s), 7.58 (1H, dd, $J$ = 8.0, 2.0 Hz), 7.47 (1H, td, $J$ = 9.0, 2.0 Hz), 7.40-7.38 (3H, m), 7.30-7.29 (2H, m), 7.03 (1H, td, $J$ = 7.5, 0.5 Hz), 6.98 (1H, d, $J$ = 8.5 Hz), 5.57 (2H, s), 3.76 (3H, s). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 187.8 (C, *C*=O), 158.0 (C), 148.6 (C), 133.8 (C), 132.9 (CH), 130.4 (CH), 129.3 (2 x CH), 129.1 (CH), 128.3 (2 x CH), 127.9 (C), 127.1 (CH), 120.4 (CH), 111.8 (CH), 55.9 ($CH_3$), 54.4 ($CH_2$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{15}N_3O_2H$ 294.1243; Found 294.1244.

**Ethyl 1-phenyl-4-(2-phenylacetyl)-1*H*-1,2,3-triazole-5-carboxylate (72pa):** The title compound was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a colourless semi solid compound. Yield: 60% (60.4 mg). IR (neat): $\nu_{max}$ 3385, 2922, 1738, 1692, 1498, 1372, 1252, 1190, 996, 760 and 690 $cm^{-1}$. $^{1}H$ NMR (500 MHz, $CDCl_3$): For $\delta$ 7.53 (5H, m), 7.40-7.38 (2H, m), 7.35-7.32 (2H, m), 7.27-7.25 (1H, m), 4.49 (2H, s), 4.34 (2H, q, $J$ = 7.5 Hz), 1.23 (3H, t, $J$ = 7.5 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 191.2 (C, *C*=O), 159.2 (C), 145.0 (C), 135.4 (C), 133.3 (C), 131.7 (C), 130.4 (CH), 129.9 (2 x CH), 129.6 (2 x CH), 128.5 (2 x CH), 126.9 (CH), 124.1 (2 x CH), 63.3 ($CH_2$), 46.3 ($CH_2$), 13.6 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{19}H_{17}N_3O_3H$ 356.1348; Found 356.1348.



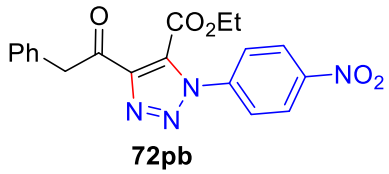
**72pa**

**Ethyl 1,3',5'-triphenyl-1*H*,3'*H*-[4,4'-bi(1,2,3-triazole)]-5-carboxylate (73pa):** The title compound was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a colourless semi solid compound. Yield: 22% (28.9 mg). IR (neat): $\nu_{max}$ 2987, 1732, 1594, 1498, 1461, 1447, 1282, 1268, 1184, 1067, 998, 762 and 689 $cm^{-1}$. $^{1}H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.78-7.76 (2H, m), 7.55-7.74 (5H, m), 7.44-7.34 (8H, m), 3.86 (2H, q, $J$ = 7.0 Hz), 0.90 (3H, t, $J$ = 7.5 Hz), $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 156.4 (C), 147.7 (C), 138.6 (C), 136.3 (C), 136.0 (C), 130.4 (CH), 130.2 (C), 129.4 (CH), 129.3 (2 x CH), 126.0 (2 x CH), 128.7 (2 x CH), 128.5 (CH), 127.2 (2 x CH), 125.6 (C, 2 x CH), 124.6 (2 x CH), 123.6 (C), 62.1 ($CH_2$), 13.4 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{25}H_{20}N_6O_2Na$ 459.1545; Found 459.1545.



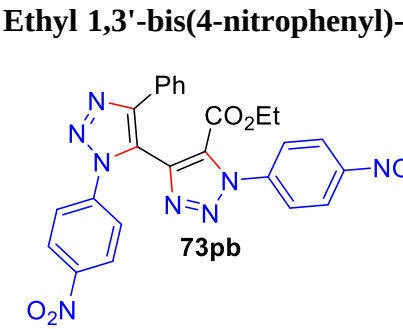
**73pa**

**Ethyl 1-(4-nitrophenyl)-4-(2-phenylacetyl)-1*H*-1,2,3-triazole-5-carboxylate (72pb):** The title compound was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a colourless semi solid compound. Yield: 58% (66.4 mg). IR (neat): $\nu_{max}$ 2921, 1740, 1703, 1595, 1374, 1343, 1312, 1076, 853, 750 and 686 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.42 (2H, d, $J$ = 9.0 Hz), 7.74 (2H, d, $J$ = 8.5 Hz), 7.39-7.33 (4H, m), 7.28 (1H, t, $J$ = 7.5 Hz), 4.49 (2H, s), 4.40 (2H, q, $J$ = 7.5 Hz), 1.31 (3H, t, $J$ = 7.5 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 190.9 (C, *C*=O), 158.9 (C), 148.5 (C), 145.7 (C), 139.9 (C), 133.0 (C), 131.5 (C), 129.9 (2 x CH), 128.6 (2 x CH), 127.2 (CH), 125.1 (2 x CH), 124.9 (2 x CH), 63.9 ($CH_2$), 46.6 ($CH_2$), 13.6 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{19}H_{16}N_4O_5H$ 381.1199; Found 381.1195.



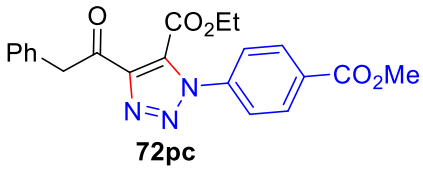
**72pb**

**Ethyl 1,3'-bis(4-nitrophenyl)-5'-phenyl-1*H*,3'*H*-[4,4'-bi(1,2,3-triazole)]-5-carboxylat (73pb):** The title compound was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a colourless semi solid compound. Yield: 31% (49.2 mg). IR (neat): $\nu_{max}$ 2923, 1733, 1596, 1526, 1500, 1345, 1282, 1175, 1110, 994, 855, 750 and 691 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.40 (2H, q, $J$ = 7.5 Hz), 8.33 (2H, d, $J$ = 9.0 Hz), 7.75 (2H, d, $J$ = 9.0 Hz), 7.70-7.68 (4H, m), 7.42-7.38 (3H, m), 3.95 (2H, d, $J$ = 7.0 Hz), 0.92 (3H, t, $J$ = 7.5 Hz), $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 155.9 (C), 148.8 (C), 148.6 (C), 147.8 (C), 140.9 (C), 140.2 (C), 138.5 (C), 129.3 (C), 129.1 (CH), 128.9 (2 x CH), 128.7 (C), 127.1 (2 x CH), 126.7 (2 x CH), 125.0 (2 x CH), 124.9 (2 x CH), 124.5 (2 x CH), 122.8 (C), 62.9 ($CH_2$), 13.5 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{25}H_{20}N_6O_2H$ 527.1428; Found 527.1429.



**73pb**

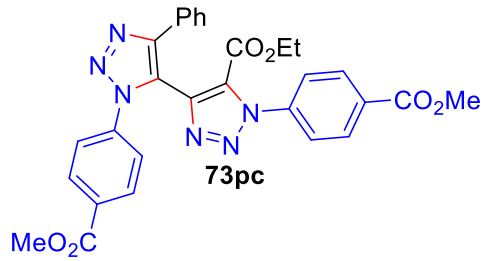
**Ethyl 1-(4-(methoxycarbonyl)phenyl)-4-(2-phenylacetyl)-1H-1,2,3-triazole-5-carboxylate (72pc):** The title compound was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a colourless semi solid compound. Yield: 48% (28.4 mg). IR (neat): $\nu_{max}$ 2922, 1725, 1699, 1443, 1279, 1253, 1191, 1111, 996, 975,



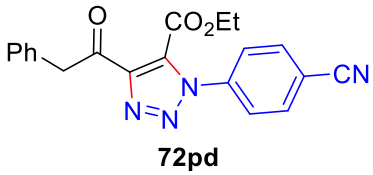
**72pc**

860, 769, 695 and 686 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.21 (2H, d, $J$ = 8.5 Hz), 7.64 (2H, d, $J$ = 8.5 Hz), 7.38 (1H, d, $J$ = 7.5 Hz), 7.35-7.32 (3H, m), 7.27 (1H, d, $J$ = 7.5 Hz), 4.48 (2H, s), 4.37 (2H, q, $J$ = 7.0 Hz), 3.97 (3H, s), 1.26 (3H, t, $J$ = 7.0 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): For $\delta$ 191.9 (C, *C*=O), 165.5 (C), 159.1 (C), 145.4 (C), 138.8 (C), 133.3 (C), 132.0 (C), 131.6 (C), 131.0 (2 x CH), 129.9 (2 x CH), 128.6 (2 x CH), 127.1 (CH), 123.9 (2 x CH), 63.6 ($CH_2$), 52.6 ($CH_3$), 46.5 ($CH_2$), 13.7 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{19}N_3O_5H$ 394.1403; Found 394.1404.

**Dimethyl 4,4'-(5-(ethoxycarbonyl)-5'-phenyl-1*H*,3'*H*-[4,4'-bi(1,2,3-triazole)]-1,3'-diyl)dibenzoate (73pc):** The title compound was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a colourless semi solid compound. Yield: 23% (19.1 mg). IR (neat): $\nu_{max}$ 3069, 1721, 1605, 1435, 1275, 1189, 1109, 994, 859, 770 and 696 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 8.19 (2H, dt, $J$ = 8.8, 2.0 Hz), 8.12 (2H, dt, $J$ = 8.4, 1.6 Hz), 7.75-7.72 (2H, m), 7.58 (2H, d, $J$ = 8.8 Hz), 7.52 (2H, d, $J$ = 8.4 Hz), 7.41-7.36 (3H, m), 3.96 (3H, s), 3.94 (3H, s), 3.89-3.84 (2H, m), 0.90 (3H, t, $J$ = 7.2 Hz), $^{13}C$ NMR (100 MHz, $CDCl_3$, DEPT-135): $\delta$ 165.7 (C), 165.6 (C), 156.1 (C), 148.3 (C), 139.6 (C), 139.2 (C), 138.6 (C), 132.1 (C), 130.9 (C), 130.7 (2 x CH), 130.4 (2 x CH), 129.8 (C), 128.8 (CH, 2 x CH), 128.7 (C), 127.2 (2 x CH), 125.6 (2 x CH), 124.2 (2 x CH), 123.1 (C), 62.5 ($CH_2$), 52.55 ($CH_3$), 52.47 ($CH_3$) 13.5 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{29}H_{24}N_6O_6H$ 553.1836; Found 553.1839.

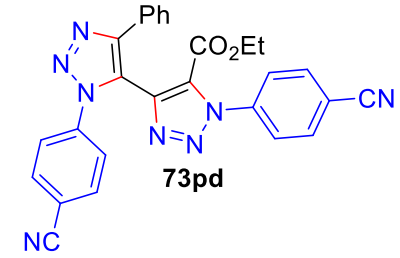



**Ethyl 1-(4-cyanophenyl)-4-(2-phenylacetyl)-1*H*-1,2,3-triazole-5-carboxylate (72pd):** The title compound was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a colourless semi solid compound. Yield: 58% (31.4 mg). IR (neat): $\nu_{max}$ 2922, 1728, 1694, 1508, 1444, 1373, 1294, 1252, 1252, 996, 976, 846, and 723 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.86 (2H, d, $J$ = 8.5 Hz), 7.72 (2H, d, $J$ = 8.5 Hz), 7.38-7.32 (4H, m), 7.28-7.26 (1H, m), 4.48 (2H, s), 4.38 (2H, q, $J$ = 7.0 Hz), 1.26 (3H, t, $J$ = 7.0 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 190.9 (C, *C*=O), 158.9 (C), 145.6 (C), 138.5 (C), 133.6 (2 x CH), 133.0 (C),



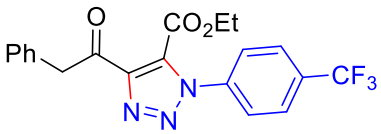
131.4 (C), 131.4 (2 x CH), 128.6 (2 x CH), 127.1 (CH), 124.7 (2 x CH), 117.2 (C), 114.5 (C), 63.8 ($CH_2$), 46.6 ($CH_2$), 13.6 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{20}H_{16}N_4O_3H$ 361.1301; Found 361.1302.

**Ethyl 1,3'-bis(4-cyanophenyl)-5'-phenyl-1*H*,3'*H*-[4,4'-bi(1,2,3-triazole)]-5-carboxylate (73pd):** The title compound was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a colourless semi solid compound. Yield: 33% (24.1 mg). IR (neat): $\nu_{max}$ 2923, 1733, 1605, 1509, 1448, 1377, 1271, 1229, 1176, 994, 908, 843, 729 and 696 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.85 (2H, dt, *J* = 9.0, 2.0 Hz), 7.77 (2H, dt, *J* = 8.5, 2.0 Hz), 7.69-7.66 (4H, m), 7.61 (2H, dt, *J* = 8.5, 2.0 Hz), 7.41-7.37 (3H, m), 3.88 (2H, q, *J* = 7.0 Hz), 0.91 (3H, t, *J* = 7.0 Hz), $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 156.0 (C), 148.7 (C), 139.5 (C), 138.9 (C), 138.5 (C), 133.4 (2 x CH), 133.0 (2 x CH), 129.4 (C), 129.1 (CH), 128.9 (2 x CH), 128.6 (C), 127.2 (2 x CH), 126.5 (2 x CH), 124.9 (2 x CH), 122.8 (C), 117.4 (C), 117.2 (C), 114.7 (C), 113.5 (C), 62.8 ($CH_2$), 13.4 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{27}H_{18}N_8O_2H$ 487.1631; Found 487.1636.



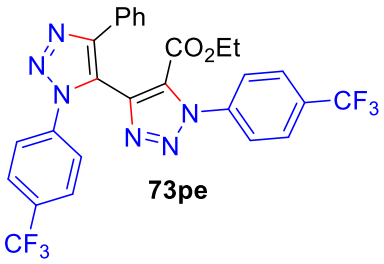
**73pd**

**Ethyl 4-(2-phenylacetyl)-1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,3-triazole-5-carboxylate (72pe):** The title compound was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a colourless semi solid compound. Yield: 47% (26.7 mg). IR (neat): $\nu_{max}$ 2987, 1739, 1697, 1519, 1496, 1446, 1321, 1170, 1128, 1076, 976, 847, and 698 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.83 (2H, d, *J* = 8.5 Hz), 7.72 (2H, d, *J* = 8.5 Hz), 7.39-7.33 (4H, m), 7.31-7.28 (1H, m), 4.49 (2H, s), 4.38 (2H, q, *J* = 7.0 Hz), 1.28 (3H, t, *J* = 7.0 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 190.1 (C, *C*=O), 159.0 (C), 145.6 (C), 138.2 (C), 133.3 (C), 132.6 (C, q, *J* = 33.75 Hz), 131.6 (C), 129.9 (2 x CH), 128.6 (2 x CH), 127.1 (CH), 126.9 (2 x CH, q, *J* = 3.75 Hz), 125.45 (C, q, *J* = 271.25 Hz), 124.6 (2 x CH), 63.7 ($CH_2$), 46.6 ($CH_2$), 13.7 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{20}H_{16}F_3N_3O_3H$ 404.1222; Found 404.1219.



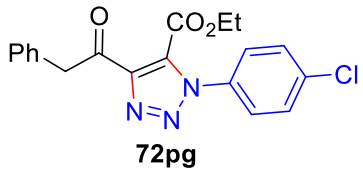
**72pe**

**Ethyl 5'-phenyl-1,3'-bis(4-(trifluoromethyl)phenyl)-1*H*,3'*H*-[4,4'-bi(1,2,3-triazole)]-5-carboxylate (73pe):** The title compound was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a colourless semi solid compound. Yield: 23% (19.75 mg). IR (neat): $\nu_{max}$ 2922, 1735, 1615, 1450, 1322, 1168, 1224, 1064, 994, 846, 777, 729, 696, 606 and 696 $cm^{-1}$. $^{1}H$ NMR (500 MHz, $CDCl_3$): For $\delta$ 7.80 (2H, d, $J$ = 8.5 Hz), 7.75-7.68 (6H, m), 7.60 (2H, d, $J$ = 8.5 Hz), 7.46-7.35 (3H, m), 3.88 (2H, q, $J$ = 7.0 Hz), 0.91 (3H, t, $J$ = 7.0 Hz), $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 156.4 (C), 148.4 (C), 138.9 (C), 138.5 (C), 138.6 (C, q, $J$ = 33.75 Hz), 131.2 (C, q, $J$ = 32.5 Hz), 129.7 (2C), 128.9 (CH), 128.8 (2 x CH), 128.7 (C), 127.1 (2 x CH), 126.75 (2 x CH, q, $J$ = 3.75 Hz), 126.33 (2 x CH, q, $J$ = 3.75 Hz), 126.9 (2 x CH), 124.8 (2 x CH), 124.4 (C, d, $J$ = 13.75 Hz), 123.1 (C), 122.23 (C, d, $J$ = 15.0 Hz), 62.6 ($CH_2$), 13.4 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{27}H_{18}F_6N_6O_2H$ 573.1474; Found 573.1475. $^{19}F$ NMR (470 MHz, $CDCl_3$): $\delta$ -62.71, -63.85 ($CF_3$).



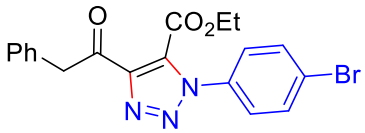
**73pe**

**Ethyl 1-(4-chlorophenyl)-4-(2-phenylacetyl)-1*H*-1,2,3-triazole-5-carboxylate (72pg):** The title compound was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a colourless semi solid compound. Yield: 49% (27.2 mg). IR (neat): $\nu_{max}$ 2922, 1738, 1694, 1496, 1444, 1372, 1254, 1191, 1093, 999, 834 and 701 $cm^{-1}$. $^{1}H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.53-7.49 (4H, m), 7.39-7.37 (2H, m), 7.35-7.32 (2H, m), 7.29-7.25 (1H, m), 4.48 (2H, s), 4.36 (2H, q, $J$ = 7.5 Hz), 1.27 (3H, t, $J$ = 7.0 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 191.2 (C, *C*=O), 159.1 (C), 145.3 (C), 136.7 (C), 133.9 (C), 133.3 (C), 131.6 (C), 129.9 (2 x CH), 128.8 (2 x CH), 128.6 (2 x CH), 127.1 (CH), 125.5 (2 x CH), 63.6 ($CH_2$), 46.5 ($CH_2$), 13.7 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{19}H_{16}ClN_3O_3H$ 370.0958; Found 370.0957.



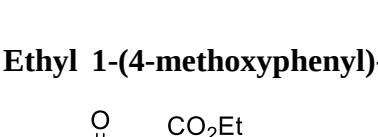
**72pg**

**Ethyl 1-(4-bromophenyl)-4-(2-phenylacetyl)-1*H*-1,2,3-triazole-5-carboxylate (72pi):** The title compound was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a colourless semi solid compound. Yield: 50% (31.1 mg). IR (neat): $\nu_{max}$ 2928, 1738, 1699, 1493, 1448, 1373, 1254, 1192, 1071, 999, 831 and 701 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.68 (2H, d, $J$ = 8.8 Hz), 7.44 (2H, d, $J$ = 8.8 Hz), 7.39-7.32 (4H, m), 7.30-7.25 (1H, m), 4.48 (2H, s), 4.36 (2H, q, $J$ = 7.2 Hz), 1.27 (3H, t, $J$ = 7.2 Hz). $^{13}C$ NMR (100 MHz, $CDCl_3$, DEPT-135): $\delta$ 191.1 (C, *C*=O), 159.1 (C), 145.3 (C), 134.4 (C), 133.3 (C), 132.8 (2 x CH), 131.6 (C), 129.9 (2 x CH), 128.6 (2 x CH), 127.1 (CH), 125.7 (2 x CH), 124.7 (C), 63.6 ($CH_2$), 46.5 ($CH_2$), 13.7 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+K]^+$ Calcd for $C_{19}H_{16}BrN_3O_3K$ 452.0012; Found 452.0012.



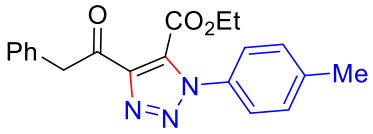
**72pi**

**Ethyl 1-(4-methoxyphenyl)-4-(2-phenylacetyl)-1*H*-1,2,3-triazole-5-carboxylate (72pl):** The title compound was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a colourless semi solid compound. Yield: 44% (23.7 mg). IR (neat): $\nu_{max}$ 2933, 1739, 1693, 1514, 1453, 1373, 1254, 1193, 1034, 977, 836 and 701 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.45 (2H, d, $J$ = 12.4 Hz), 7.40-7.27 (5H, m), 7.01 (2H, d, $J$ = 9.2 Hz), 4.48 (2H, s), 4.34 (2H, q, $J$ = 7.2 Hz), 3.87 (3H, s), 1.25 (3H, t, $J$ = 7.2 Hz). $^{13}C$ NMR (100 MHz, $CDCl_3$, DEPT-135): $\delta$ 191.3 (C, *C*=O), 161.0 (C), 159.4 (C), 144.9 (C), 133.5 (C), 131.8 (C), 129.9 (2 x CH), 128.5 (2 x CH), 128.3 (C), 127.0 (CH), 125.7 (2 x CH), 114.6 (2 x CH), 63.3 ($CH_2$), 55.6 ($CH_3$), 46.4 ($CH_2$), 13.7 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{20}H_{19}N_3O_4H$ 366.1454; Found 366.1454.



**72pl**

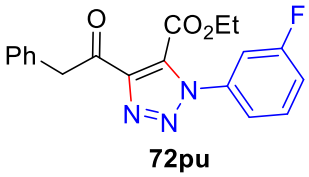
**Ethyl 4-(2-phenylacetyl)-1-(p-tolyl)-1*H*-1,2,3-triazole-5-carboxylate (72pm):** The title compound was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a colourless semi solid compound. Yield: 44% (23.1 mg). IR (neat): $\nu_{max}$ 2922, 1741, 1694, 1515, 1495, 1451, 1373, 1255, 1194, 999, 820 and 702 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.43-7.37 (4H, m), 7.35-7.31 (4H, m), 7.29-7.27 (1H, m), 4.48 (2H, s), 4.35 (2H, q, $J$ =



**72pm**

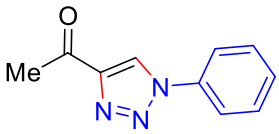
7.2 Hz), 2.44 (3H, s), 1.25 (3H, t, *J* = 7.2 Hz). $^{13}$C NMR (100 MHz, $CDCl_3$, DEPT-135): $\delta$ 191.3 (C, *C*=O), 159.4 (C), 145.0 (C), 140.8 (C), 133.4 (C), 133.0 (C), 131.7 (C), 130.1 (2 x CH), 129.9 (2 x CH), 128.5 (2 x CH), 127.0 (CH), 123.9 (2 x CH), 63.3 ($CH_2$), 46.4 ($CH_2$), 21.2 ($CH_3$), 13.7 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{20}H_{19}N_3O_3Na$ 372.1324; Found 372.1325.

**Ethyl 1-(3-fluorophenyl)-4-(2-phenylacetyl)-1*H*-1,2,3-triazole-5-carboxylate (72pu):** The title compound was prepared following **Procedure C** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a colourless semi solid compound. Yield: 51% (27.1 mg). IR (neat): $\nu_{max}$ 2923, 1738, 1604, 1495, 1373, 1252, 1177, 1150, 1005, 883, 786, 683 and 686 $cm^{-1}$. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.55-7.49 (1H, m), 7.39-7.32 (6H, m), 7.29-7.25 (2H, m), 4.48 (2H, s), 4.38 (2H, q, *J* = 7.2 Hz), 1.27 (3H, t, *J* = 7.2 Hz). $^{13}$C NMR (100 MHz, $CDCl_3$, DEPT-135): $\delta$ 191.1 (C, *C*=O), 162.6 (C, d, *J* = 249.0 Hz), 159.1 (C), 145.2 (C), 136.4 (C, d, *J* = 10.0 Hz), 133.2 (C), 131.6 (C), 131.05 (CH, d, *J* = 9.0 Hz), 129.9 (2 x CH), 128.6 (2 x CH), 127.1 (CH), 119.7 (CH, d, *J* = 3.0 Hz), 117.6 (CH, d, *J* = 21.0 Hz), 112.01 (CH, d, *J* = 25.0 Hz), 63.6 ($CH_2$), 46.4 ($CH_2$), 13.7 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{19}H_{16}FN_3O_3Na$ 376.1073; Found 376.1074.



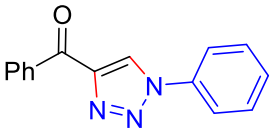
**72pu**

**1-(1-phenyl-1*H*-1,2,3-triazol-4-yl)ethan-1-one (74aa):** The title compound was prepared following **Procedure D** with employing catalyst **23a**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a colourless solid. Yield: 90% (50.54 mg). Mp: 115-117 °C. IR (neat): $\nu_{max}$ 3132, 2923, 1692, 1471, 1417, 1265, 1175, 759 and 666 $cm^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 8.52 (1H, s), 7.76 (2H, d, *J* = 8.0 Hz), 7.57 (2H, t, *J* = 8.0 Hz), 7.50 (1H, t, *J* = 7.5 Hz), 2.7 (3H, s). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 192.7 (C, *C*=O), 148.5 (C), 136.3 (C), 129.9 (2 x CH), 129.9 (CH), 123.3 (CH), 120.7 (2 x CH), 27 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{10}H_9N_3ONa$ 210.0643; Found 210.0643.



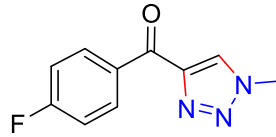
**74aa**

**Phenyl(1-phenyl-1*H*-1,2,3-triazol-4-yl)methanone (74fa):** The title compound was prepared following **Procedure D** with employing catalyst **23a**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a colourless semi solid compound. Yield: 95% (71.04 mg). IR (neat): $\nu_{max}$ 3140, 1719, 1641, 1600, 1524, 1264, 994, 904 and 719 $cm^{-1}$. $^{1}H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.71 (1H, s), 8.49 (2H, d, $J$ = 7.5 Hz), 7.81 (2H, dd, $J$ = 7.5, 1.5 Hz), 7.64 (1H, t, $J$ = 7.5 Hz), 7.58-7.49 (5H, s). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 185.55 (C, *C*=O), 148.6 (C), 136.5 (C), 136.4 (C), 133.4 (CH), 130.7 (2 x CH), 129.9 (2 x CH), 129.5 (CH), 128.4 (2 x CH), 126.4 (CH), 120.8 (2 x CH). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{15}H_{11}N_3ONa$ 272.0800; Found 272.0801.



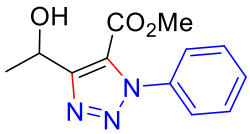
**74fa**

**(4-fluorophenyl)(1-phenyl-1*H*-1,2,3-triazol-4-yl)methanone (74fa):** The title compound was prepared following **Procedure D** with employing catalyst **23a**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as white semi solid. Yield: 95% (76.1 mg). IR (neat): $\nu_{max}$ 3148, 1709, 1641, 1595, 1524, 1502, 1266, 1232, 1155, 908 and 760 $cm^{-1}$. $^{1}H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.72 (1H, s), 8.61 (2H, dd, $J$ = 8.0, 6.0 Hz), 7.81 (2H, d, $J$ = 7.5 Hz), 7.58 (2H, t, $J$ = 8.0 Hz), 7.53-7.50 (1H, m), 7.22 (2H, t, $J$ = 8.5 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 183.7 (C, *C*=O), 166.1 (C, d, $J$ = 253.7 Hz), 148.5 (C), 136.3 (C), 133.5 (C), 133.4 (C), 130.0 (2 x CH), 129.6 (CH), 126.5 (CH), 120.8 (2 x CH), 115.6 (2 x CH, d, $J$ = 21.2 Hz). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{15}H_{10}FN_3OH$ 268.0886; Found 268.0888.



**74ga**

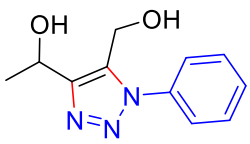
**Methyl 4-(1-hydroxyethyl)-1-phenyl-1*H*-1,2,3-triazole-5-carboxylate (75aa):** The title compound was prepared following **Procedure E** with employing reducing agent sodium borohydride, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 6.0:4.0) and isolated as a white semi solid compound. Yield: 48% (45.1 mg). IR (neat): $\nu_{max}$ 3409, 2955, 1731, 1498, 1446, 1276, 1202, 1104, 1071, 765 and 692 $cm^{-1}$. $^{1}H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.57-7.51 (3H, m), 7.44-7.41 (2H, m), 5.33 (1H, quint, $J$ = 7.0 Hz), 3.79 (3H, s), 1.72 (3H, d, $J$ = 6.5 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 159.2 (C), 155.3 (C), 136.9 (C), 130.1 (CH), 128.9 (2 x



**75aa**

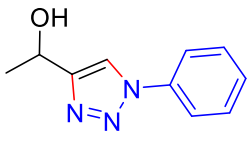
CH), 125.8 (2 x CH), 124.9 (C), 63.2 (CH), 52.7 ($CH_3$), 22.6 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{12}H_{13}N_3O_3Na$ 248.1035; Found 248.1036.

**1-(5-(hydroxymethyl)-1-phenyl-1H-1,2,3-triazol-4-yl)ethan-1-ol (76aa):** The title compound was prepared following **Procedure E** with employing reducing agent sodium borohydride, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 6.0:4.0) and isolated as a colourless semi solid compound. Yield: 36% (29.99 mg). IR (neat): $\nu_{max}$ 3367, 2977, 2498, 1498, 1249, 1088, 1038, 894, 792 and 766 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.67-7.65 (2H, m), 7.57-7.51 (3H, m), 5.20-5.16 (1H, m), 5.05 (1H, s), 4.67 (2H, s), 1.68 (3H, d, $J$ = 6.5 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 149.5 (C), 135.8 (C), 133.10 (C), 128.95 (2 x CH), 124.3 (2 x CH), 62.4 (CH), 51.6 ($CH_2$), 22.7 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{11}H_{13}N_3O_2H$ 220.1086; Found 220.1085.



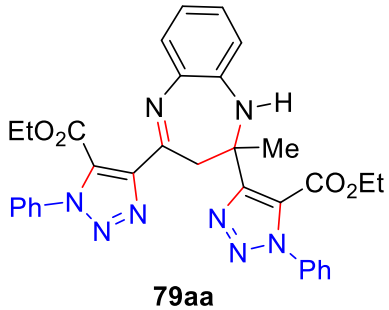
**76aa**

**1-(1-phenyl-1H-1,2,3-triazol-4-yl)ethan-1-ol (77aa):** The title compound was prepared following **Procedure E** with employing reducing agent sodium borohydride, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 6.0:4.0) and isolated as a colourless semi solid compound. Yield: 70% (39.7 mg). IR (neat): $\nu_{max}$ 3385, 1601, 1502, 1217, 1107, 1076, 1047, 907 and 758 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.97 (1H, s), 7.71-7.69 (2H, m), 7.51-7.47 (2H, m), 7.43-7.40 (1H, m), 5.17 (1H, q, $J$ = 6.5 Hz), 3.48 (1H, br s, O*H*), 1.65 (3H, dd, $J$ = 6.5, 2.0 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 153.1 (C), 136.9.8 (C), 129.6 (2 x CH), 128.6 (CH), 120.4 (2 x CH), 118.5 (CH), 62.9 (CH), 23.1 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{10}H_{11}N_3OH$ 190.0973; Found 190.0973.



**77aa**

**Diethyl 4,4'-(2-methyl-2,3-dihydro-1*H*-benzo[*b*][1,4]diazepine-2,4-diyl)bis(1-phenyl-1*H*-1,2,3-triazole-5-carboxylate) (79aa):** The title compound was prepared following **Procedure F** with employing catalyst *p*-toluene sulfonic acid, purified by column chromatography using ethyl acetate/hexanes (2.0:8.0 to 5.0:5.0) and isolated as a colourless semi solid compound. Yield: 30% (35.5 mg). IR (neat): $\nu_{max}$ 3341, 2923, 1731, 1499, 1467, 1282, 1264, 1188, 1061, 1002, 733 and 692 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.63-7.62 (2H, m), 7.56-7.52 (3H, m), 7.52-7.47 (3H, m), 7.40-7.38 (2H, m), 7.16 (1H, dd, $J$ = 7.5, 1.5 Hz), 7.01 (1H, td, $J$ = 8.0, 1.5 Hz), 7.94 (1H, td, $J$ = 8.0, 1.0 Hz), 6.88 (1H, dd, $J$ = 8.0, 1.5 Hz), 5.27 (1H, s), 4.36-4.31 (2H, m), 4.26-4.19 (2H, m), 3.92 (1H, d, $J$ = 8.5 Hz), 3.63 (1H, d, $J$ = 8.5 Hz), 1.89 (3H, s), 1.20 (3H, t, $J$ = 7.0 Hz), 1.07 (3H, t, $J$ = 7.0 Hz), $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 160.9 (C), 159.7 (C), 158.9 (C), 155.3 (C), 148.2 (C), 138.9 (C), 138.5 (C), 137.2 (C), 136.1 (C), 129.9 (CH), 129.8 (CH), 129.5 (2 x CH), 129.3 (CH), 129.0 (2 x CH), 128.8 (C), 126.9 (CH), 125.6 (C), 125.4 (2 x CH), 124.2 (2 x CH), 121.54 (CH), 121.49 (CH), 67.3 (C), 62.7 ($CH_2$), 62.6 ($CH_2$), 40.5 ($CH_2$), 30.4 ($CH_3$), 13.9 ($CH_3$), 13.5 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{32}H_{30}N_8O_4H$ 591.2468; Found 591.2463.




**79aa**

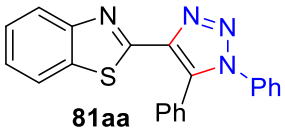
## 2. General Experimental Procedures of Direct Organocatalytic Carbonyl-Azide-[3+2]-Cycloaddition: Synthesis of Benzothiazole Containing 1,2,3-Triazoles

**Procedure A:** **General procedure for the synthesis of 80:**[76]

Sodium hydride (60w% in oil, 2.0 g, 50 mmol) was added to a THF (15 mL) solution of 2-methylbenzothiazole (2.5 g, 16.7 mmol) and methyl benzoate (2.96 g, 21.8 mmol) at room temperature. The solution was refluxed for 1 day. After cooling to room temperature, $NH_4Cl$ aq was added to the reaction mixture and extracted with diethyl ether. The extract was dried over $MgSO_4$ and concentrated in vacuo. Column chromatography of the residue on silica gel ($CH_2Cl_2$, $R_f$ = 0.3) gave **1** (3.18 g, 75%) as a yellow solid.

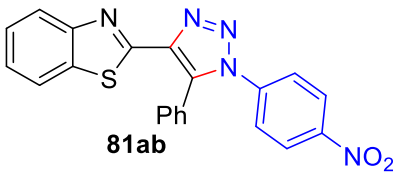
**Procedure B:** **General procedure for the synthesis of 81**: To an ordinary glass vial equipped with a magnetic stirring bar were added 0.3 mmol of **80**, 1.5 equiv of azides **2,** and 0.06 mmol of tetramethyl guanidine **23c**/DBU **23c** in 1mL of DMSO. The reaction mixture was allowed to stir until complete consumption of **80** (monitored by TLC) at 25 to 80 $^oC$. The corresponding products **81** were purified by column chromatography (silicagel: 100-200 mesh; eluent: EA/hexanes).

**2-(1,5-diphenyl-1*H*-1,2,3-triazol-4-yl)benzo[*d*]thiazole (81aa):** The title compound was prepared following **Procedure B** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a white semi solid compound. Yield: 99% (105.2 mg). IR (neat): $\nu_{max}$ 1590, 1492, 1454, 1308, 1150, 1077, 993, 760, 692 and 586 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.74 (1H, d, $J$ = 8.0 Hz), 7.86 (1H, d, $J$ = 8.0 Hz), 7.46-7.43 (3H, m), 7.41-7.37 (6H, m), 7.36-7.36 (3H, m). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 158.7 (C), 153.7 (C), 140.0 (C), 135.9 (2C), 134.8 (C), 130.7 (2 x CH), 129.9 (CH), 129.3 (CH), 129.2 (2 x CH), 128.4 (2 x CH), 125.9 (CH), 125.7 (C), 125.2 (CH), 125.1 (2 x CH), 123.5 (CH), 121.4 (CH). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{14}N_4SH$ 355.1017; Found 355.1017.



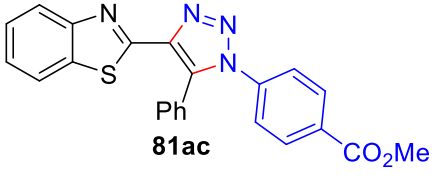
**81aa**

**2-(1-(4-nitrophenyl)-5-phenyl-1*H*-1,2,3-triazol-4-yl)benzo[*d*]thiazole (81ab):** The title compound was prepared following **Procedure B** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a solid compound. Yield: 99% (105.2 mg). Mp: 199-202 $^{o}$C. IR (neat): $\nu_{max}$ 1592, 1516, 1341, 1286, 993, 947, 852, 749, 726, 691 and 487 cm$^{-1}$. $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 8.24 (2H, d, $J$ = 9.0 Hz), 7.94 (1H, d, $J$ = 8.5 Hz), 7.88 (1H, d, $J$ = 8.0 Hz), 7.55-7.52 (3H, m), 7.49-7.47 (4H, m), 7.44 (1H, t, $J$ = 7.5 Hz), 7.37 (1H, d, $J$ = 8.0 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 157.9 (C), 153.7 (C), 147.5 (C), 140.75 (C), 140.70 (C), 135.9 (C), 134.9 (C), 130.4 (2 x CH), 130.5 (CH), 128.9 (2 x CH), 126.1 (CH), 125.5 (CH), 125.3 (2 x CH), 125.1 (C), 124.7 (2 x CH), 123.6 (CH), 121.4 (CH). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{14}N_5O_2SH$ 400.0688; Found 400.0701.



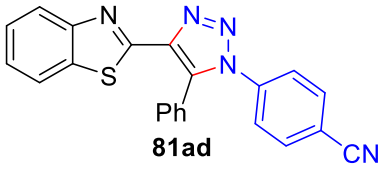
**81ab**

**Methyl 4-(4-(benzo[*d*]thiazol-2-yl)-5-phenyl-1*H*-1,2,3-triazol-1-yl)benzoate (81ac):** The title compound was prepared following **Procedure B** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a solid compound. Yield: 98% (105.2 mg). Mp: 161-163 $^{o}$C. IR (neat): $\nu_{max}$ 1715, 1602, 1477, 1276, 1100, 993, 9951, 770, 753, 694, and 534 cm$^{-1}$. $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 8.07-8.04 (2H, m), 7.94-7.92 (1H, m), 7.88-7.85 (1H, m), 7.49-7.46 (3H, m), 7.43-7.41 (5H, m), 7.37-7.32 (1H, m), 3.91 (3H, s). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135): For $\delta$ 165.7 (C), 158.3 (C), 153.7 (C), 140.3 (C), 139.4 (C), 135.9 (C), 134.9 (C), 130.7 (C), 130.7 (2 x CH), 130.6 (2 x CH), 130.1 (CH), 128.6 (2 x CH), 125.9 (CH), 125.4 (C), 125.3 (CH), 124.7 (2 x CH), 123.5 (CH), 121.4 (CH), 52.3 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{23}H_{16}N_4O_2SH$ 413.1072; Found 413.1075.



**81ac**

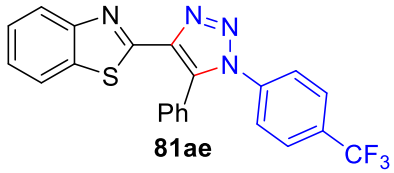
**4-(4-(benzo[*d*]thiazol-2-yl)-5-phenyl-1*H*-1,2,3-triazol-1-yl)benzonitrile (81ad):** The title compound was prepared following **Procedure B** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a solid compound. Yield: 99% (112.69 mg). Mp: 218 $^{o}$C. IR (neat): $\nu_{max}$ 2920, 1738, 1601, 1502, 1312, 1075, 991, 995, 945, 841, 765, 694, 563 and 534 cm$^{-1}$. $^{1}$H NMR



**81ad**

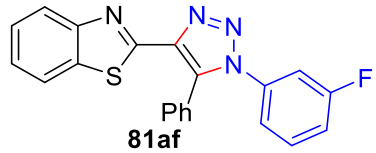
(500 MHz, $CDCl_3$): $\delta$ 7.94 (1H, d, $J$ = 8.0 Hz), 7.87 (1H, d, $J$ = 7.5 Hz), 7.68 (2H, d, $J$ = 9.0 Hz), 7.54-7.42 (8H, m), 7.39-7.35 (1H, m). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 157.9 (C), 153.6 (C), 140.6 (C), 139.3 (C), 135.9 (C), 134.9 (C), 133.2 (2 x CH), 130.6 (2 x CH), 130.5 (CH), 128.8 (2 x CH), 126.1 (CH), 125.4 (CH), 125.3 (2 x CH), 125.1 (C), 123.6 (CH), 121.4 (CH), 117.5 (C), 113.1 (C). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{22}H_{13}N_5SNa$ 402.0789; Found 402.0788.

**2-(5-phenyl-1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,3-triazol-4-yl)benzo[*d*]thiazole (4ae):** The title compound was prepared following **Procedure B** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a solid compound. Yield: 99% (115.3 mg). Mp: 158-161 $^o$C. IR (neat): $\nu_{max}$ 1612, 1518, 1422, 1319, 1167, 1117, 1063, 992, 946, 856, 753, 694, 692 and 606 $cm^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.94 (1H, d, $J$ = 8.5 Hz), 7.88 (1H, dd, $J$ = 8.0, 1.5 Hz), 7.67 (2H, d, $J$ = 7.0 Hz), 7.52-7.42 (8H, m), 7.37 (1H, t, $J$ = 7.5 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 158.2 (C), 153.7 (C), 140.5 (C), 138.8 (C), 135.9 (C), 134.9 (C), 131.3 (C, d, $J$ = 32.5 Hz), 130.7 (2 x CH), 130.3 (CH), 128.9 (2 x CH), 126.5 (2 x CH, q, $J$ = 3.75 Hz), 126.1 (CH), 125.4 (CH), 125.3 (C), 125.2 (2 x CH), 123.6 (CH), 123.4 (C, q, $J$ = 270.0 Hz), 121.4 (CH). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{13}F_3N_4SH$ 423.0891; Found 423.0888.



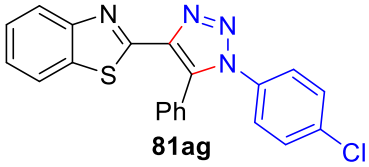
**81ae**

**2-(1-(3-fluorophenyl)-5-phenyl-1*H*-1,2,3-triazol-4-yl)benzo[*d*]thiazole (81af):** The title compound was prepared following **Procedure B** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a solid compound. Yield: 98% (109.5 mg). Mp: 131-133 $^o$C. IR (neat): $\nu_{max}$ 1599, 1522, 1492, 1451, 1217, 1138, 1074, 947, 863, 784, 760, 709, 690 and 674 $cm^{-1}$. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.94 (1H, dt, $J$ = 8.4, 0.4 Hz), 7.88 (1H, dt, $J$ = 8.0, 0.8 Hz), 7.51-7.40 (6H, m), 7.38-7.32 (2H, m), 7.15-7.10 (3H, m). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 162.4 (C, d, $J$ = 247.0 Hz), 158.3 (C), 153.7 (C), 140.2 (C), 137.2 (C, d, $J$ = 10.0 Hz), 135.9 (C), 134.9 (C), 130.6 (2 x CH), 130.5 (CH), 130.2 (CH), 128.6 (2 x CH), 126.0 (CH), 125.4 (C), 125.3 (CH), 123.5 (CH), 121.4 (CH), 120.7 (CH, d, $J$ = 3.0 Hz), 116.4 (CH, d, $J$ = 3.0 Hz), 112.7 (CH, d, $J$ = 5.0 Hz). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{21}H_{13}FN_4SNa$ 395.0743; Found 395.0743.



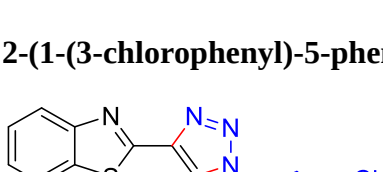
**81af**

**2-(1-(4-chlorophenyl)-5-phenyl-1*H*-1,2,3-triazol-4-yl)benzo[*d*]thiazole (81ag):** The title compound was prepared following **Procedure B** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a brown solid compound. Yield: 99% (100.6 mg). Mp: 150-153 °C. IR (neat): $\nu_{max}$ 1492, 1475, 1312, 1287, 1089, 945, 822, 757, 696 and 524 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.94 (1H, dd, *J* = 7.0, 0.1 Hz), 7.87 (1H, dd, *J* = 8.0, 0.5 Hz), 7.49-7.41 (6H, m), 7.38-7.34 (3H, m), 7.30-7.25 (2H, m). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 158.4 (C), 153.7 (C), 140.2 (C), 135.9 (C), 135.3 (C), 134.9 (C), 134.5 (C), 130.7 (2 x CH), 130.1 (CH), 129.5 (2 x CH), 128.6 (2 x CH), 126.2 (2 x CH), 126.0 (CH), 125.4 (C), 125.3 (CH), 123.5 (CH), 121.4 (CH). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{13}ClN_4SH$ 389.0628; Found 389.0625.



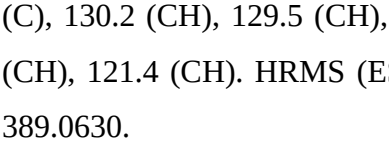
**81ag**

**2-(1-(3-chlorophenyl)-5-phenyl-1*H*-1,2,3-triazol-4-yl)benzo[*d*]thiazole (81ah):** The title compound was prepared following **Procedure B** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a pale solid compound. Yield: 92% (93.5 mg). Mp: 145-147 °C. IR (neat): $\nu_{max}$ 1688, 1629, 1514, 1453, 1382, 1347, 1191, 1120, 905, 724 and 647 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.95 (1H, d, *J* = 8.5 Hz), 7.88 (1H, d, *J* = 8.0 Hz), 7.51-7.41 (8H, m), 7.39-7.35 (1H, m), 7.30 (1H, t, *J* = 8.0 Hz), 7.16 (1H, d, *J* = 8.0 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 158.3 (C), 153.6 (C), 140.2 (C), 136.9 (C), 135.9 (C), 135.0 (C), 134.8 (C), 130.6 (3CH), 130.2 (C), 130.2 (CH), 129.5 (CH), 128.7 (2 x CH), 126.0 (CH), 125.3 (2 x CH), 123.5 (CH), 123.1 (CH), 121.4 (CH). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{13}ClN_4SH$ 389.0628; Found 389.0630.



**81ah**

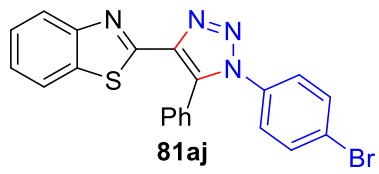
**2-(1-(2-chlorophenyl)-5-phenyl-1*H*-1,2,3-triazol-4-yl)benzo[*d*]thiazole (81ai):** The title compound was prepared following **Procedure B** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a pale brown solid compound. Yield: 60% (61 mg). Mp: 139-141 °C. IR (neat): $\nu_{max}$ 1479, 1439, 1366, 1281, 1217, 993, 849, 759, 727 and 692 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.95 (1H, d, *J* = 8.0 Hz), 7.89 (1H, d, *J* = 8.0 Hz), 7.48-7.33 (11H, m). $^{13}C$ NMR (125 MHz, $CDCl_3$,



**81ai**

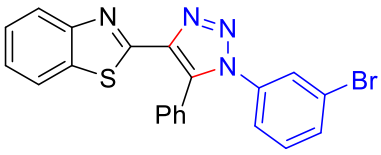
DEPT-135): $\delta$ 158.7 (C), 153.7 (C), 139.3 (C), 137.8 (C), 134.9 (C), 133.8 (C), 131.9 (C), 131.6 (CH), 130.5 (CH), 130.2 (2 x CH), 129.9 (CH), 129.5 (CH), 128.2 (2 x CH), 127.6 (CH), 125.9 (CH), 125.3 (CH), 125.1 (C), 123.5 (CH), 121.4 (CH). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{13}ClN_4SH$ 389.0628; Found 389.0627.

**2-(1-(4-bromophenyl)-5-phenyl-1*H*-1,2,3-triazol-4-yl)benzo[*d*]thiazole (81aj):** The title compound was prepared following **Procedure B** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a pale brown solid compound. Yield: 93% (120.9 mg). Mp: 158-160 $^oC$. IR (neat): $\nu_{max}$ 1484, 1367, 1217, 991, 946, 838, 819, 755, 726 and 519 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.94 (1H, d, $J$ = 9.0 Hz), 7.88 (1H, dd $J$ = 8.0, 0.8 Hz), 7.55-7.50 (2H, m), 7.49-7.47 (1H, m), 7.45-7.41 (5H, m), 7.36 (1H, td, $J$ = 7.6, 1.2 Hz), 7.24-7.20 (2H, m). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 158.4 (C), 153.7 (C), 140.2 (C), 135.9 (C), 135.0 (C), 134.9 (C), 132.5 (2 x CH), 130.7 (2 x CH), 130.2 (CH), 128.7 (2 x CH), 126.5 (2 x CH), 126.0 (CH), 125.4 (C), 125.3 (CH), 123.5 (CH), 123.4 (C), 121.4 (CH). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{13}BrN_4SH$ 433.0123; Found 433.0127.



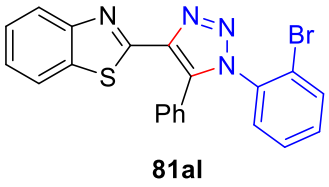
**81aj**

**2-(1-(3-bromophenyl)-5-phenyl-1*H*-1,2,3-triazol-4-yl)benzo[*d*]thiazole (81ak):** The title compound was prepared following **Procedure B** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a pale brown solid compound. Yield: 98% (127.4 mg). Mp: 144-147 $^oC$. IR (neat): $\nu_{max}$ 1582, 1479, 1429, 1298, 1248, 1072, 1039, 997, 947, 794, 764, 750 and 611 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.95 (1H, d, $J$ = 7.6 Hz), 7.89 (1H, dd, $J$ = 7.2, 0.8 Hz), 7.62 (1H, t, $J$ = 6.0 Hz), 7.57-7.54 (1H, m), 7.51-7.35 (7H, m), 7.27-7.18 (2H, m). $^{13}C$ NMR (100 MHz, $CDCl_3$, DEPT-135): $\delta$ 158.3 (C), 153.7 (C), 140.2 (C), 137.0 (C), 135.9 (C), 134.9 (C), 134.4 (CH), 130.7 (2 x CH), 130.4 (CH), 130.2 (CH), 128.7 (2 x CH), 128.2 (CH), 126.0 (CH), 125.3 (CH), 123.6 (2CH), 123.6 (C), 122.7 (C), 121.4 (CH). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{21}H_{13}BrN_4SNa$ 454.9942; Found 454. 9939.



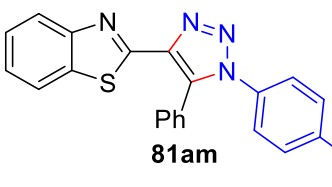
**81ak**

**2-(1-(2-bromophenyl)-5-phenyl-1*H*-1,2,3-triazol-4-yl)benzo[*d*]thiazole (81al):** The title compound was prepared following **Procedure B** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a pale brown solid compound. Yield: 9% (77.9 mg). Mp: 154-159 °C. IR (neat): $\nu_{max}$ 1624, 1573, 1509, 1354, 1233, 1218, 1124, 915, 799, 726, 714, 685 and 656 $cm^{-1}$. $^{1}H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.95 (1H, d, $J$ = 8.0 Hz), 7.89 (1H, d, $J$ = 8.0, Hz), 7.66 (1H, d, $J$ = 7.5 Hz), 7.48 (2H, d, $J$ = 7.5 Hz), 7.45-7.39 (4H, m), 7.38-7.33 (4H, m). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 158.7 (C), 153.7 (C), 139.3 (C), 137.6 (C), 135.5 (C), 134.9 (C), 133.7 (CH), 131.9 (CH), 130.4 (2 x CH), 129.9 (CH), 129.7 (2CH), 128.2 (2 x CH), 125.9 (CH), 125.3 (CH), 125.2 (C), 123.5 (CH), 121.8 (C), 121.4 (CH). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{13}BrN_4SH$ 433.0123; Found 433.0122.



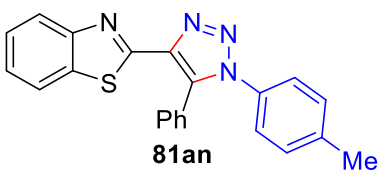
**81al**

**2-(1-(4-methoxyphenyl)-5-phenyl-1*H*-1,2,3-triazol-4-yl)benzo[*d*]thiaz**ole **(81am):** The title compound was prepared following **Procedure B** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a pale brown solid compound. Yield: 70% (80.73 mg). Mp: 190-193 °C. IR (neat): $\nu_{max}$ 1511, 1476, 1447, 1366, 1250, 1229, 1043, 946, 832, 766, 692 and 578 $cm^{-1}$. $^{1}H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.94 (1H, d, $J$ = 8.0 Hz), 7.87 (1H, d, $J$ = 8.0 Hz), 7.47-7.39 (6H, m), 7.37-7.33 (1H, m), 7.27-7.24 (2H, m), 6.88 (2H, dd, $J$ = 12.0, 3.0 Hz), 3.81 (3H, s). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 160.1 (C), 158.9 (C), 153.8 (C), 139.9 (C), 136.0 (C), 134.9 (C), 130.7 (2 x CH), 129.8 (2 x CH), 129.1 (C), 128.4 (2 x CH), 126.6 (2 x CH), 125.93 (CH), 125.91 (C), 125.2 (CH), 123.5 (CH), 121.4 (CH), 114.4 (2 x CH), 55.5 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{16}N_4OSH$ 385.1123; Found 385.1121.



**81am**

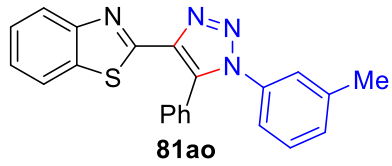
**2-(5-phenyl-1-(*p*-tolyl)-1*H*-1,2,3-triazol-4-yl)benzo[*d*]thiazole (81an):** The title compound was prepared following **Procedure B** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a pale brown solid compound. Yield: 70% (77.37 mg). Mp: 197-200 °C. IR (neat): $\nu_{max}$ 1738, 1510, 1367, 1228, 995, 946, 818, 764, 693, and 584 $cm^{-1}$. $^{1}H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.94



**81an**

(1H, d, *J* = 8.0 Hz), 7.86 (1H, d, *J* = 8.0 Hz), 7.46-7.38 (6H, m), 7.34 (1H, t, *J* = 7.5 Hz), 7.25-7.16 (4H, m), 2.36 (3H, s). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 158.8 (C), 153.7 (C), 139.9 (C), 139.5 (2C), 135.9 (C), 134.9 (C), 133.6 (C), 130.7 (2 x CH), 129.8 (2 x CH), 129.8 (CH), 128.4 (2 x CH), 125.9 (CH), 125.2 (CH), 124.9 (2 x CH), 123.5 (CH), 121.4 (CH), 21.1 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{22}H_{16}N_4SNa$ 391.0993; Found 391.0994.

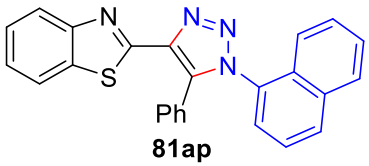
**2-(5-phenyl-1-(*m*-tolyl)-1*H*-1,2,3-triazol-4-yl)benzo[*d*]thiazole (81ao):** The title compound



**81ao**

was prepared following **Procedure B** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a pale brown solid. Yield: 70% (77.37 mg). Mp: 139-141 $^o$C. IR (neat): $\nu_{max}$ 1475, 1435, 1294, 1272, 1093, 1040, 946, 868, 783, 730 and 694 $cm^{-1}$. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.94 (1H, d, *J* = 8.0 Hz), 7.86 (1H, d, *J* = 8.0 Hz), 7.47-7.32 (7H, m), 7.24-7.19 (3H, m), 7.02 (1H, d, *J* = 7.2 Hz), 2.33 (3H, s). $^{13}$C NMR (100 MHz, $CDCl_3$, DEPT-135): $\delta$ 158.7 (C), 153.7 (C), 139.9 (C), 139.5 (C), 135.99 (C), 135.54 (C), 134.9 (C), 130.7 (2 x CH), 130.1 (CH), 129.8 (CH), 128.9 (CH), 128.4 (2 x CH), 125.9 (CH), 125.8 (C), 125.8 (CH), 125.2 (CH), 123.5 (CH), 122.1 (CH), 121.3 (CH), 21.2 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{16}N_4SH$ 369.1174; Found 369.1174.

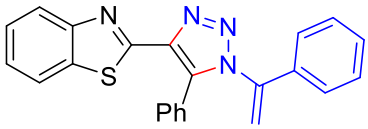
**2-(1-(naphthalen-1-yl)-5-phenyl-1*H*-1,2,3-triazol-4-yl)benzo[*d*]thiazole (81ap):** The title



**81ap**

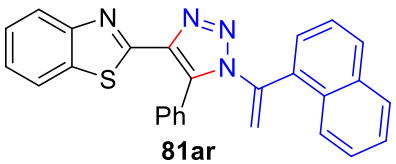
compound was prepared following **Procedure B** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a brown solid compound. Yield: 93% (112.8 mg). Mp: 203-205 $^o$C. IR (neat): $\nu_{max}$ 1595, 1510, 1471, 1418, 1313, 1272, 1126, 958, 944, 917, 798 and 758 $cm^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.96 (2H, d, *J* = 8.0 Hz), 7.92-7.90 (2H, m), 7.65-7.50 (4H, m), 7.47-7.42 (2H, m), 7.40-7.36 (4H, m), 7.29 (1H, t, *J* = 8.0 Hz), 7.21 (1H, t, *J* = 8.0 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 158.9 (C), 153.8 (C), 139.4 (C), 138.2 (C), 134.9 (C), 133.9 (C), 132.2 (C), 130.7 (CH), 130.1 (2 x CH), 129.8 (CH), 129.7 (C), 128.2 (CH), 128.2 (2 x CH), 127.9 (CH), 127.0 (CH), 126.0 (CH), 125.6 (CH), 125.4 (C), 125.3 (CH), 124.8 (CH), 123.5 (CH), 122.3 (CH), 121.4 (CH). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{25}H_{16}N_4SH$ 405.1174; Found 405.1175.

**2-(5-phenyl-1-(1-phenylvinyl)-1*H*-1,2,3-triazol-4-yl)benzo[*d*]thiazole (81aq):** The title compound was prepared following **Procedure B** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a solid. Yield: 61% (69.6 mg). Mp: 159-161 $^{o}$C. IR (neat): $\nu_{max}$ 1640, 1595, 1518, 1475, 1448, 1413, 1343, 1114, 1010, 947, 912, 773, 765 and 695 cm$^{-1}$. $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.93 (1H, d, $J$ = 8.0 Hz), 7.86 (1H, $J$ = 7.5 Hz), 7.45-7.40 (3H, m), 7.36-7.21 (4H, m), 7.29-7.21 (3H, m), 7.11 (2H, dd, $J$ = 8.0, 1.5 Hz), 5.87 (1H, s), 5.60 (1H, s). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 158.6 (C), 153.7 (C), 142.4 (C), 139.6 (C), 136.8 (C), 134.9 (C), 134.7 (C), 130.2 (2 x CH), 129.8 (CH), 129.4 (CH), 128.5 (2 x CH), 128.1 (2 x CH), 125.9 (CH), 125.8 (2 x CH), 125.6 (C), 125.2 (CH), 123.5 (CH), 121.4 (CH), 115.3 ($CH_2$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{23}H_{16}N_4SH$ 381.1174; Found 381.1173.



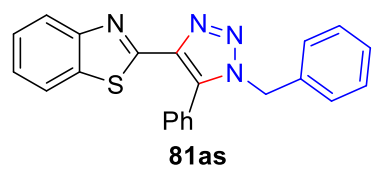
**81aq**

**2-(1-(naphthalen-1-yl)-5-phenyl-1*H*-1,2,3-triazol-4-yl)benzo[*d*]thiazole (81ar):** The title compound was prepared following **Procedure B** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a solid compound. Yield: 80% (103.3 mg). Mp: 177-180 $^{o}$C. IR (neat): $\nu_{max}$ 1688, 1628, 1543, 1478, 1434, 1282, 1227, 1015, 946, 898, 808, 753, 721 and 695 cm$^{-1}$. $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.97 (1H, d, $J$ = 8.0 Hz), 7.91 (1H, $J$ = 8.0 Hz), 7.80-7.74 (3H, m), 7.52-7.44 (6H, m), 7.40-7.35 (2H, m), 7.33-7.28 (3H, m), 6.05 (1H, s), 5.68 (1H, s). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 158.8 (C), 153.8 (C), 142.4 (C), 139.7 (C), 137.1 (C), 134.9 (C), 133.5 (C), 132.9 (C), 132.0 (C), 130.1 (2 x CH), 129.9 (CH), 128.6 (CH), 128.5 (CH), 128.2 (2 x CH), 127.6 (CH), 127.1 (CH), 126.7 (CH), 126.0 (CH), 125.7 (CH), 125.97 (C), 125.3 (CH), 123.6 (CH), 122.8 (CH), 121.4 (CH), 115.8 ($CH_2$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{27}H_{18}N_4SH$ 431.1330; Found 431.1332.



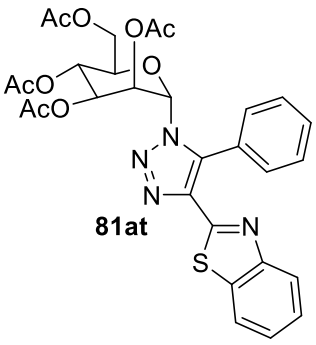
**81ar**

**2-(1-benzyl-5-phenyl-1*H*-1,2,3-triazol-4-yl)benzo[*d*]thiazole (81as):** The title compound was prepared following **Procedure B** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a brown semi solid compound. Yield: 66% (73.0 mg). IR (neat): $\nu_{max}$ 1594, 1521, 1449, 1433, 1311, 1229, 1119, 964, 937, 819, 765, 730 and 693 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.89 (1H, d, *J* = 3.0 Hz), 7.83 (1H, *J* = 2.5 Hz), 7.54 (1H, tt, *J* = 7.5, 1.0 Hz), 7.48 (2H, t, *J* = 7.5 Hz), 7.39 (1H, td, *J* = 8.0, 1.0 Hz), 7.35-7.31 (3H, m), 7.28-7.26 (3H, m), 7.07-7.05 (2H, m), 5.49 (2H, s). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 158.6 (C), 153.6 (C), 140.1 (C), 136.6 (C), 134.8 (C), 134.7 (C), 130.3 (2 x CH), 130.2 (CH), 128.8 (2 x 2 x CH), 128.3 (CH), 127.5 (2 x CH), 125.9 (CH), 125.8 (C), 125.1 (CH), 123.4 (CH), 121.4 (CH), 52.2 ($CH_2$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{16}N_4SH$ 369.1174; Found 369.1174.



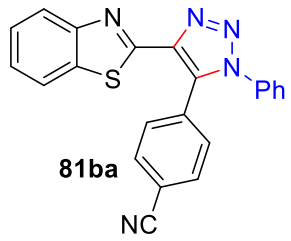
**81as**

**(2*R*,3*R*,5*S*,6*S*)-2-(acetoxymethyl)-6-(4-(benzo[*d*]thiazol-2-yl)-5-phenyl-1*H*-1,2,3-triazol-1 yl)tetrahydro-2*H*-pyran-3,4,5-triyl triacetate (81at):** The title compound was prepared following **Procedure B** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a white solid. Yield: 76% (138.7 mg). Mp: 201-204 °C. IR (neat): $\nu_{max}$ 1746, 1712, 1437, 1367, 1325, 1218, 1125, 1053, 950, 732 and 699 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.90 (2H, t, *J* = 7.5 Hz), 7.68-7.66 (2H, m), 7.61-7.55 (3H, m), 7.43 (1H, t, *J* = 8.0 Hz), 7.37 (1H, t, *J* = 8.5 Hz), 6.37 (1H, dd, *J* = 9.5, 4.0 Hz), 5.84 (1H, dd, *J* = 9.0, 2.0 Hz), 5.80 (1H, d, *J* = 1.5 Hz),.5.45 (1H, t, *J* = 10.0 Hz), 4.35 (1H, dd, *J* = 12.0, 5.5 Hz), 4.26-4.23 (1H, m), 4.05 (1H, dd, *J* = 12.5, 2.5 Hz), 2.14 ($CH_3$), 2.10 ($CH_3$), 2.08 ($CH_3$), 2.03 ($CH_3$). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 170.3 (C), 169.7 (C), 169.6 (C), 169.3 (C), 158.1 (C), 153.7 (C), 140.0 (C), 137.5 (C), 134.9 (C), 130.7 (2 x CH), 130.7 (CH), 128.8 (2 x CH), 126.0 (CH), 125.4 (CH), 124.6 (C), 123.6 (CH), 121.4 (CH), 82.0 (CH), 71.8 (CH), 69.2 (CH), 69.1 (CH), 66.0 (CH), 61.9 ($CH_2$), 20.6 ($3CH_3$), 20.5 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{29}H_{28}N_4O_9SH$ 608.1655; Found 608.1656.



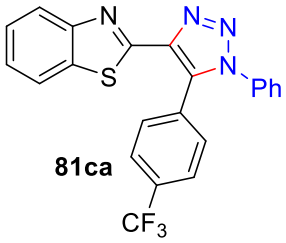
**81at**

**4-(4-(benzo[*d*]thiazol-2-yl)-1-phenyl-1*H*-1,2,3-triazol-5-yl)benzonitrile (81ba):** The title compound was prepared following **Procedure B** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a solid copound. Yield: 96% (109.2 mg). Mp: 159-162 $^{o}$C. IR (neat): $\nu_{max}$ 2234, 1738, 1591, 1454, 1435, 1313, 1272, 1161, 994, 948, 814, 841, 759, 730, 690 and 592 cm$^{-1}$. $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.92 (1H, d, $J$ = 7.5 Hz), 7.89 (1H, d, $J$ = 8.5 Hz), 7.69 (2H, d, $J$ = 8.5 Hz), 7.63 (2H, d, $J$ = 8.5 Hz), 7.50-7.44 (4H, m), 7.41-7.38 (1H, m), 7.33-7.31 (2H, m). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 158.4 (C), 153.7 (C), 140.4 (C), 135.6 (C), 134.9 (C), 133.8 (C), 131.9 (2 x CH), 131.6 (2 x CH), 130.6 (C), 129.9 (CH), 129.6 (2 x CH), 126.2 (CH), 125.6 (CH), 125.3 (2 x CH), 123.5 (CH), 121.6 (CH), 118.1 (C), 113.6 (C). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{13}N_5SH$ 380.0970; Found 380.0971.



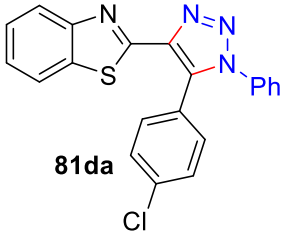
**81ba**

**2-(1-phenyl-5-(4-(trifluoromethyl)phenyl)-1*H*-1,2,3-triazol-4-yl)benzo[*d*]thiazole (81ca):** The title compound was prepared following **Procedure B** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a solid compound. Yield: 82% (103.9 mg). Mp: 178-180 $^{o}$C. IR (neat): $\nu_{max}$ 1623, 1594, 1553, 1493, 1434, 1322, 1156, 1130, 1067, 949, 843, 759, 730, 688 and 615 cm$^{-1}$. $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.92 (1H, d, $J$ = 8.0 Hz), 7.90 (1H, d, $J$ = 8.0 Hz), 7.67-7.63 (4H, m), 7.48-7.42 (4H, m), 7.38 (1H, td, $J$ = 7.5, 1.0 Hz), 7.34-7.32 (2H, m). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 158.6 (C), 153.7 (C), 140.3 (C), 135.7 (C), 134.9 (C), 134.3 (C), 131.7 (C, d, $J$ = 32.5 Hz), 131.3 (2 x CH), 129.7 (CH), 129.6 (C), 129.5 (2 x CH), 126.1 (CH), 125.5 (CH), 125.3 (2 x CH), 125.2 (2 x CH, q, $J$ = 3.75 Hz), 123.7 (C, q, $J$ = 270.1 Hz), 123.5 (CH), 121.5 (CH). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{13}F_3N_4SH$ 423.0891; Found 423.0891.



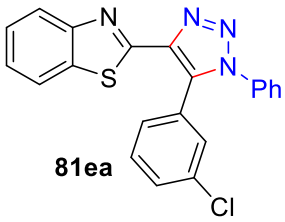
**81ca**

**2-(5-(4-chlorophenyl)-1-phenyl-1*H*-1,2,3-triazol-4-yl)benzo[*d*]thiazole (81da):** The title compound was prepared following **Procedure B** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a solid compound. Yield: 81% (94.5 mg). Mp: 86-88 $^{o}$C. IR (neat): $\nu_{max}$ 1594, 1495, 1476, 1455, 1267, 1091, 1074, 947, 848, 830, 756, 730, 688 and 612 cm$^{-1}$. $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.93 (1H, d, $J$ = 8.0 Hz), 7.89 (1H, d, $J$ = 8.0 Hz), 7.45-7.41 (6H, m), 7.39-7.36 (3H, m), 7.34-7.32 (2H, m). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 158.7 (C), 153.7 (C), 140.0 (C), 136.1 (C), 135.8 (C), 134.9 (C), 134.7 (C), 132.1 (2 x CH), 129.6 (CH), 129.5 (CH), 129.4 (2 x CH), 128.7 (2 x CH), 126.0 (CH), 125.3 (CH), 125.2 (2 x CH), 124.2 (C), 123.5 (CH), 121.5 (CH). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{13}ClN_4SH$ 389.0629; Found 389.0627.



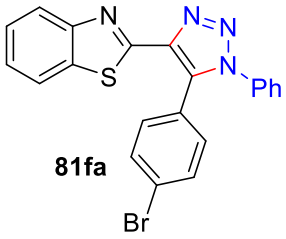
**81da**

**2-(5-(3-chlorophenyl)-1-phenyl-1*H*-1,2,3-triazol-4-yl)benzo[*d*]thiazole (81ea):** The title compound was prepared following **Procedure B** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a solid compound. Yield: 84% (98 mg). Mp: 157-160 $^{o}$C. IR (neat): $\nu_{max}$ 1591, 1562, 1493, 1436, 1283, 1155, 1073, 951, 882, 788, 760, 628 and 697 cm$^{-1}$. $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.94 (1H, d, $J$ = 8.0 Hz), 7.90 (1H, d, $J$ = 8.0 Hz), 7.63 (1H, t, $J$ = 1.5 Hz), 7.45-7.41 (5H, m), 7.39-7.35 (3H, m), 7.31 (1H, t, $J$ = 7.5 Hz), 7.28-7.27 (1H, m). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 158.5 (C), 153.7 (C), 140.2 (C), 135.8 (C), 134.9 (C), 134.4 (C), 134.3 (C), 130.9 (CH), 130.0 (CH), 129.6 (CH), 129.6 (CH), 129.4 (2 x CH), 128.8 (CH), 127.5 (C), 126.1 (CH), 125.4 (CH), 125.2 (2 x CH), 123.6 (CH), 121.5 (CH). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{13}ClN_4SH$ 389.0629; Found 389.0629.



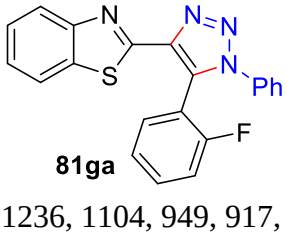
**81ea**

**2-(5-(4-bromophenyl)-1-phenyl-1*H*-1,2,3-triazol-4-yl)benzo[*d*]thiazole (81fa):** The title compound was prepared following **Procedure B** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a solid compound. Yield: 90% (117 mg). Mp: 208-210 °C. IR (neat): $\nu_{max}$ 1591, 1493, 1476, 1452, 1434, 1272, 1157, 1067, 1037, 946, 831, 758, 731 and 690 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.93 (1H, dt, $J$ = 8.0, 1.0 Hz), 7.91 (1H, dt, $J$ = 8.0, 1.0 Hz), 7.53 (2H, td, J = 7.5, 2.5 Hz), 7.45-7.43 (4H, m), 7.39-7.35 (3H, m), 7.34-7.25 (2H, m). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 158.7 (C), 153.7 (C), 140.0 (C), 135.8 (C), 134.9 (C), 134.7 (C), 134.7 (C), 132.3 (2 x CH), 131.7 (2 x CH), 129.6 (CH), 129.5 (2 x CH), 126.0 (CH), 125.4 (CH), 125.2 (2 x CH), 124.7 (C), 124.5 (C), 123.5 (CH), 121.5 (CH). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{13}BrN_4SH$ 433.0123; Found 433.0123.



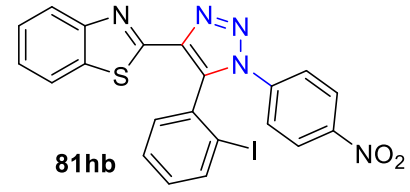
**81fa**

**2-(5-(2-fluorophenyl)-1-phenyl-1*H*-1,2,3-triazol-4-yl)benzo[*d*]thiazole (81ga):** The title compound was prepared following **Procedure B** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a pale yellow solid. Mp: 162-164 °C. Yield: 60% (67 mg). IR (neat): $\nu_{max}$ 1675, 1626, 1593, 1477, 1452, 1432, 1236, 1104, 949, 917, 816, 761, 725 and 689 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.90-7.88 (2H, m), 7.51-7.47 (2H, m), 7.43-7.34 (7H, m), 7.2 (1H, t, $J$ = 7.5 Hz), 7.10 (1H, t, $J$ = 9.5 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 159.9 (C, d, $J$ = 250.0 Hz), 158.2 (C), 153.8 (C), 141.2 (C), 136.0 (C), 134.8 (C), 132.5 (CH, d, $J$ = 1.25 Hz), 132.4 (CH, d, $J$ = 8.75 Hz), 130.4 (C), 129.5 (CH), 129.3 (2 x CH), 125.9 (CH), 125.3 (CH), 124.5 (2 x CH), 124.2 (CH, d, $J$ = 3.75 Hz), 123.5 (CH), 121.4 (CH), 116.0 (CH, d, $J$ = 21.2 Hz), 114.5 (C, d, $J$ = 13.75 Hz). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{13}FN_4SH$ 373.0923; Found 373.0926.



**81ga**

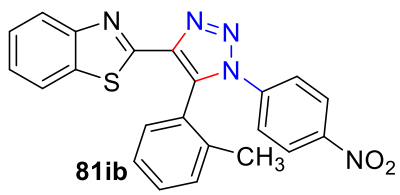
**2-(5-(2-fluorophenyl)-1-(4-nitrophenyl)-1*H*-1,2,3-triazol-4-yl)benzo[*d*]thiazole (81hb)**: The title compound was prepared following **Procedure B** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a solid compound. Yield: 58% (91.4 mg). Mp: 122-125 °C. IR (neat): $\nu_{max}$ 1638, 1578, 1503, 1472, 1428, 1347, 1274, 1239, 1039, 1015, 911, 782, 743 and 635



**81hb**

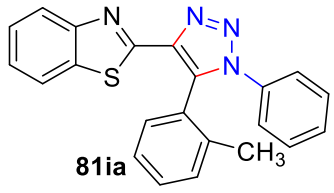
cm$^{-1}$. $^{1}$H NMR (400 MHz, $CDCl_3$ +$MeOD_4$): $\delta$ 8.31-8.27 (2H, m), 8.02-7.92 (2H, m), 7.89-7.84 (1H, m), 7.67-7.61 (2H, m), 7.59-7.52 (1H, m), 7.50-7.44 (2H, m), 7.42-7.40 (1H, m), 7.38-7.32 (1H, m). $^{13}$C NMR (125 MHz, $CDCl_3$+$MeOD_4$,DEPT-135): $\delta$ 156.8 (C), 153.3 (C), 147.6 (C), 141.2 (C), 140.5 (C), 139.9 (CH), 137.8 (C), 134.6 (C), 132.2 (CH), 132.0 (CH), 131.1 (C), 128.8 (CH), 126.2 (CH), 125.5 (CH), 124.7 (2 x 2 x CH, 4CH), 123.4 (CH), 121.4 (CH), 99.7 (C). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{12}IN_5SH$ 525.9835; Found 525.9834.

**2-(1-(4-nitrophenyl)-5-(o-tolyl)-1*H*-1,2,3-triazol-4-yl)benzo[*d*]thiazole (81ib):** The title compound was prepared following **Procedure B** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a solid compound. Yield: 61% (75.6 mg). Mp: 159-162 $^{o}$C. IR (neat): $\nu_{max}$ 1738, 1593, 1525, 1496, 1474, 1434, 1344, 1275, 1160, 1113, 991, 946, 849, 762 and 683 cm$^{-1}$. $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.24-8.22 (2H, m), 8.95 (1H, d, $J$ = 8.0 Hz), 7.84 (1H, d, $J$ = 7.5 Hz), 7.56 (2H, d, $J$ = 8.0 Hz), 7.50 (1H, t, $J$ = 8.0 Hz), 7.45-7.43 (1H, m), 7.38-7.30 (4H, m), 2.01 (3H, s). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 176.3 (C), 153.6 (C), 147.5 (C), 141.6 (C), 140.9 (C), 138.2 (C), 135.6 (C), 134.8 (C), 131.1 (CH), 131.0 (CH), 130.7 (CH), 126.7 (CH), 126.2 (CH), 125.5 (CH), 125.3 (C), 124.8 (2 x CH), 124.1 (2 x CH), 123.7 (CH), 121.4 (CH), 19.7 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{15}N_5O_2SH$ 414.1025;Found 414.1026.



81ib

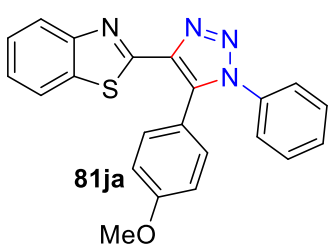
**2-(1-phenyl-5-(o-tolyl)-1*H*-1,2,3-triazol-4-yl)benzo[*d*]thiazole (81ia):** The title compound was prepared following **Procedure B** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a solid compound. Yield: 30% (33.1 mg). Mp: 185-189 $^{o}$C. IR (neat): $\nu_{max}$ 1738, 1593, 1494, 1436, 1364, 1434, 1225, 994, 945, 759, 732 and 689 cm$^{-1}$. $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.96 (1H, d, $J$ = 8.0 Hz), 7.83 (1H, d, $J$ = 7.5, 1.0 Hz), 7.45-7.40 (2H, m), 7.38-7.32 (6H, m), 7.32-7.30 (1H, m), 7.30-7.26 (2H, m), 2.05 (3H, s). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 158.1 (C), 153.7 (C), 140.9 (C), 138.3 (C), 136.2 (C), 135.7 (C), 134.7 (C), 130.9 (CH), 130.7 (CH), 130.4 (CH), 129.6 (2 x CH), 129.2 (CH), 126.3 (CH), 126.0 (CH), 125.9 (C), 125.2 (CH), 124.1 (2 x CH), 123.6 (CH),



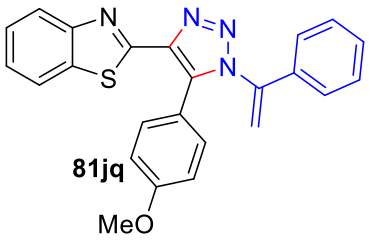
81ia

121.4 (CH), 19.8 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{16}N_4SH$ 369.1174; Found 369.1173.

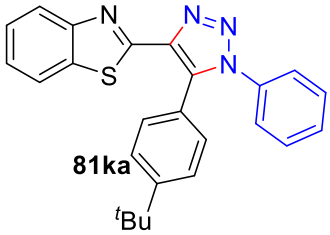
**2-(5-(4-methoxyphenyl)-1-phenyl-1*H*-1,2,3-triazol-4-yl)benzo[*d*]thiazole (81ja):** The title compound was prepared following **Procedure B** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a solid. Yield: 94% (108.4 mg). Mp: 199-201 °C. IR (neat): $\nu_{max}$ 1613, 1598, 1492, 1464, 1449, 1295, 1254, 1175, 1016, 945, 834, 755, 685, and 588 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.98 (1H, d, $J$ = 8.0 Hz), 7.88 (1H, t, $J$ = 7.0 Hz), 7.44-7.26 (9H, m), 7.30-7.26 (2H, dd, $J$ = 8.5, 3.0 Hz), 3.84 (3H, d, $J$ = 7.0 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 160.7 (C), 158.9 (C), 153.7 (C), 139.8 (C), 136.2 (C), 136.0 (C), 134.9 (C), 132.2 (2 x CH), 129.3 (2 x CH, CH), 125.9 (CH), 125.22 (2 x CH), 125.18 (CH), 123.5 (CH), 121.4 (CH), 117.5 (C), 113.9 (2 x CH), 55.3 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{16}N_4SH$ 385.1123; Found 385.1125.



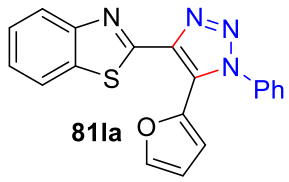

**2-(5-(4-methoxyphenyl)-1-(1-phenylvinyl)-1*H*-1,2,3-triazol-4-yl)benzo[*d*]thiazole (81jq):** The title compound was prepared following **Procedure B** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a solid compound. Yield: 80% (98.5 mg). Mp: 86-88 °C. IR (neat): $\nu_{max}$ 1613, 1598, 1492, 1464, 1449, 1295, 1254, 1175, 1016, 945, 834, 755, 685, and 588 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.96 (1H, d, $J$ = 8.0 Hz), 7.87 (1H, d, $J$ = 8.0 Hz), 7.44-7.38 (3H, m), 7.37-7.33 (1H, m), 7.27-7.23 (3H, m), 7.13 (2H, dd, $J$ = 8.0, 1.5 Hz), 6.83 (2H, d, $J$ = 8.5 Hz), 5.89 (1H, d, $J$ = 0.5 Hz), 5.58 (1H, d, $J$ = 1.0 Hz), 3.79 (3H, s). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 160.7 (C), 158.9 (C), 153.8 (C), 142.6 (C), 139.4 (C), 136.9 (C), 134.9 (C), 134.8 (C), 131.7 (2 x CH), 129.5 (CH), 128.6 (2 x CH), 126.0 (CH), 125.8 (2 x CH), 125.2 (CH), 123.5 (CH), 121.4 (CH), 117.5 (C), 115.4 ($CH_2$), 113.8 (2 x CH), 55.3 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{24}H_{18}N_4OSH$ 411.1280; Found 411.1281.



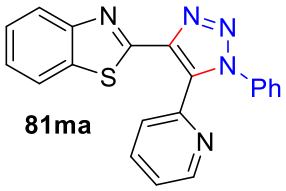
**2-(5-(4-(tert-butyl)phenyl)-1-phenyl-1*H*-1,2,3-triazol-4-yl)benzo[*d*]thiazole (81ka):** The title compound was prepared following **Procedure B** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a brown solid compound. Yield: 87% (107.1 mg). Mp: 169-171 °C. IR (neat): $\nu_{max}$ 1610, 1597, 1490, 1463, 1449, 1295, 1254, 1175, 1016, 942, 834, 750, 685, and 588 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.98 (1H, d, $J$ = 8.0 Hz), 7.88 (1H, dd, $J$ = 8.0, 0.5 Hz), 7.45-7.43 (1H, m), 7.42-7.39 (7H, m), 3.36-7.34 (3H, m), 1.34 (9H, s). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 158.9 (C), 153.7 (C), 153.2 (C), 139.9 (C), 136.2 (C), 136.1 (C), 134.9 (C), 130.4 (2 x CH), 129.3 (CH), 129.2 (2 x CH), 125.9 (CH), 125.4 (2 x CH), 125.2 (2 x CH), 125.2 (CH), 123.5 (CH), 122.4 (C), 121.4 (CH), 34.8 (C), 31.1 (3 x $CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{25}H_{22}N_4SH$ 411.1643; Found 411.1643.




**2-(5-(furan-2-yl)-1-phenyl-1*H*-1,2,3-triazol-4-yl)benzo[*d*]thiazole (81la):** The title compound was prepared following **Procedure B** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a solid compound. Yield: 96% (99 mg). Mp: 198-200 °C. IR (neat): $\nu_{max}$ 1739, 1511, 1476, 1453, 1311, 1227, 1076, 1042, 996, 818, 763, 736, 711 and 711 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.08 (1H, d, $J$ = 8.0 Hz), 7.94 (1H, d, $J$ = 8.0 Hz), 7.76 (1H, dd, $J$ = 8.0, 0.5 Hz), 6.57 (1H, d, $J$ = 8.5, 1.5 Hz), 7.52-7.45 (6H, m), 7.43-7.39 (1H, m), 7.39-7.38 (1H, m). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 158.8 (C), 153.8 (C), 144.4 (CH), 139.5 (C), 139.2 (C), 137.0 (C), 134.9 (C), 129.7 (CH), 129.0 (2 x CH), 126.9 (C), 126.1 (CH), 125.4 (CH), 125.2 (2 x CH), 123.4 (CH), 121.5 (CH), 116.5 (CH), 111.7 (CH). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{19}H_{12}N_4OSH$ 345.0810; Found 345.0808.

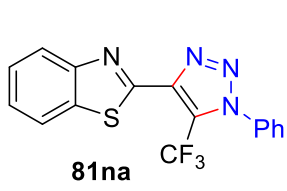


**2-(1-phenyl-5-(pyridin-2-yl)-1*H*-1,2,3-triazol-4-yl)benzo[*d*]thiazole (81ma):** The title compound was prepared following **Procedure B** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as pale yellow solid.. Yield: 85% (90.6 mg). Mp: 145-149 ºC. IR (neat): $\nu_{max}$ 1737, 1511, 1475, 1452, 1310, 1228, 1077, 1043, 997, 819, 762, 733 and 711 $cm^{-1}$. $^{1}H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.60 (1H, d, $J$ = 4.5 Hz), 7.93-7.90 (3H, m), 7.83 (1H, td, $J$ = 8.0, 1.5 Hz), 7.45-7.34 (8H, m). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 158.6 (C), 153.7 (C), 149.7 (CH), 134.1 (C), 140.4 (C), 136.4 (C), 136.2 (CH), 134.9 (C), 134.8 (C), 129.2 (CH), 129.0 (2 x CH), 127.1 (CH), 125.9 (CH), 125.3 (CH), 125.0 (2 x CH), 124.1 (CH), 123.4 (CH), 121.4 (CH). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{20}H_{13}N_5SH$ 356.0970; Found 356.0970.



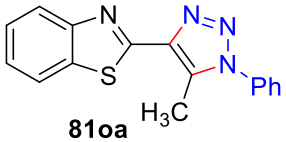
**81ma**

**2-(1-phenyl-5-(pyridin-2-yl)-1*H*-1,2,3-triazol-4-yl)benzo[*d*]thiazole (81na):** The title compound was prepared following **Procedure B** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a solid compound. Mp: 120-123 ºC. Yield: 96% (99.7 mg). IR (neat): $\nu_{max}$ 1593, 1496, 1428, 1345, 1253, 1144, 1129, 954, 757, 728 and 683 $cm^{-1}$. $^{1}H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.16 (1H, d, $J$ = 8.0 Hz), 7.99 (1H, d, $J$ = 8.0 Hz), 7.65-7.58 (3H, m), 7.57-7.53 (3H, m). 7.49-7.46 (1H, m). $^{13}C$ NMR (100 MHz, $CDCl_3$, DEPT-135): $\delta$ 155.9 (C), 153.8 (C), 142.3 (C), 135.7 (C), 135.4 (C), 131.0 (CH), 129.5 (2 x CH), 126.5 (CH), 126.1 (CH), 125.7 (2 x CH), 125.3 (C), 124.1 (CH), 121.7 (CH), 119.3 (C, q, $J$ = 269.0 Hz). $^{19}F$ NMR (376 MHz, $CDCl_3$): $\delta$ -55.4. HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_9F_3N_4SH$ 347.0578;Found 347.0577.



**81na**

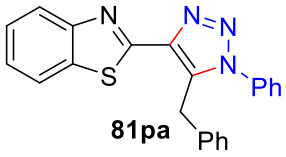
**2-(5-methyl-1-phenyl-1*H*-1,2,3-triazol-4-yl)benzo[*d*]thiazole (81oa):** The title compound was prepared following **Procedure B** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a solid compound. Yield: Mp: 135-137 ºC. 99% (86.8 mg). IR (neat): $\nu_{max}$ 1596, 1579, 1501, 1454, 1431, 1342, 1312, 1264, 1101, 1070, 957, 754, 716 and 692 $cm^{-1}$. $^{1}H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.04 (1H, d, $J$ = 8.0 Hz), 7.94 (1H, d, $J$ = 8.0 Hz), 7.61-7.53 (5H, m), 7.48 (1H, t, $J$ = 7.5 Hz). 7.39 (1H, t, $J$ = 8.0 Hz), 2.81 (3H, s). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 160.3 (C), 153.9 (C), 139.9 (C), 135.6



**81oa**

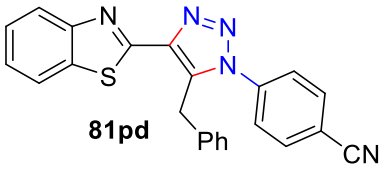
(C), 134.4 (C), 133.3 (C), 129.8 (CH), 129.6 (2 x CH), 126.0 (CH), 125.13 (2 x CH), 125.08 (CH), 122.9 (CH), 121.6 (CH), 10.3 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{12}N_4SH$ 293.0861; Found 293.0862.

**2-(5-benzyl-1-phenyl-1*H*-1,2,3-triazol-4-yl)benzo[*d*]thiazole (81pa):** The title compound was prepared following **Procedure B** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a white solid. Mp: 174-176 ºC. Yield: 78% (86.2 mg). IR (neat): $\nu_{max}$ 1594, 1505, 1452, 1431, 1344, 1259, 1141, 1071, 964, 783, 764, 717 and 695 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.00 (1H, d, $J$ = 8.5 Hz), 7.96 (1H, d, $J$ = 8.0 Hz), 7.54-7.51 (1H, m), 7.49-7.7.46 (3H, m), 7.42-7.39 (1H, m), 7.30-7.28 (2H, m), 7.14-7.12 (3H, m), 6.99-6.97 (2H, m), 4.7 (2H, s). $^{13}C$ NMR (100 MHz, $CDCl_3$, DEPT-135): $\delta$ 159.9 (C), 154.0 (C), 140.2 (C), 136.6 (C), 136.0 (C), 135.7 (C), 134.6 (C), 130.1 (CH), 129.4 (2 x CH), 128.5 (2 x CH), 128.4 (2 x CH), 126.8 (CH), 126.1 (CH), 125.9 (2 x CH), 125.2 (CH), 123.2 (CH), 121.7 (CH), 29.0 ($CH_2$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{16}N_4SH$ 369.1174; Found 369.1175.



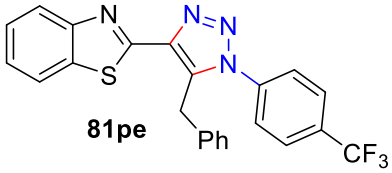
**81pa**

**4-(4-(benzo[*d*]thiazol-2-yl)-5-benzyl-1*H*-1,2,3-triazol-1-yl)benzonitrile (81pd):** The title compound was prepared following **Procedure B** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a white solid. Mp: 159-162 ºC. Yield: 93% (109.77 mg). IR (neat): $\nu_{max}$ 2230, 1600, 1508, 1453, 1439, 1414, 1268, 1069, 957, 841, 753, 724 and 693 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.99 (1H, d, $J$ = 8.0 Hz), 7.96 (1H, d, $J$ = 8.5 Hz), 7.75 (2H, d, $J$ = 8.5 Hz), 7.49-7.45 (3H, m), 7.43-7.39 (1H, m), 7.18-7.16 (3H, m), 6.99-6.98 (2H, m), 4.76 (2H, s). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 159.2 (C), 153.9 (C), 140.9 (C), 139.1 (C), 136.0 (C), 135.8 (C), 134.5 (C), 133.4 (2 x CH), 128.8 (2 x CH), 128.2 (2 x CH), 127.1 (CH), 126.2 (2 x CH, CH), 125.4 (CH), 123.2 (CH), 121.7 (CH), 117.4 (C), 113.9 (C), 29.1 ($CH_2$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{23}H_{15}N_5SH$ 394.1126; Found 394.1127.



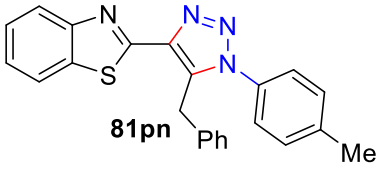
**81pd**

**2-(5-benzyl-1-(4-(trifluoromethyl)phenyl)-1*H*-1,2,3-triazol-4-yl)benzo[*d*]thiazole (81pe):** The title compound was prepared following **Procedure B** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a semi solid compound. Mp: 162-165 $^{o}$C. Yield: 92% (120.4 mg). IR (neat): $\nu_{max}$ 1614, 1599, 1573, 1521, 1454, 1319, 1263, 1166, 1128, 1107, 1054, 960, 845 and 766 cm$^{-1}$. $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.99 (1H, d, $J$ = 8.0 Hz), 7.96 (1H, d, $J$ = 8.0 Hz), 7.74 (2H, d, $J$ = 8.0 Hz), 7.49-7.40 (4H, m), 7.18-7.16 (3H, m), 7.01-6.99 (2H, m), 4.74 (2H, s). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 159.5 (C), 153.9 (C), 140.7 (C), 138.5 (C), 136.3 (C), 135.9 (C), 134.6 (C), 132.1 (C, q, $J$ = 6.75 Hz), 128.7 (2 x CH), 128.3 (2 x CH), 127.0 (CH), 126.6 (2 x CH, q, $J$ = 3.75 Hz), 126.2 (CH), 126.1 (2 x CH), 125.4 (CH), 123.4 (C, q, $J$ = 271.2), 123.3 (CH), 121.7 (CH), 29.1 ($CH_2$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{23}H_{15}F_3N_4SH$ 437.1048; Found 437.1051.



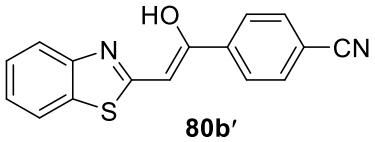
81pe

**2-(5-benzyl-1-(p-tolyl)-1*H*-1,2,3-triazol-4-yl)benzo[*d*]thiazole (81pn):** The title compound was prepared following **Procedure B** with employing catalyst **23c**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a semi solid compound. Yield: 89% (102.12 mg). IR (neat): $\nu_{max}$ 1601, 1515, 1493, 1452, 1311, 1272, 1074, 957, 819, 753, 726 and 692 cm$^{-1}$. $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 8.00 (1H, d, $J$ = 8.0 Hz), 7.96 (1H, d, $J$ = 7.5 Hz), 7.47 (1H, td, $J$ = 8.0, 1.0 Hz), 7.40 (1H, td, $J$ = 8.0, 1.0 Hz), 7.28-7.25 (2H, m), 7.18-7.16 (5H, m), 7.02-7.00 (2H, m), 4.67 (2H, s), 2.44 (3H, s). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 160.1 (C), 154.0 (C), 140.4 (C), 140.1 (C), 136.8 (C), 136.0 (C), 134.6 (C), 133.1 (C), 129.9 (2 x CH), 128.5 (2 x CH), 128.4 (2 x CH), 126.7 (CH), 126.0 (CH), 125.7 (2 x CH), 125.1 (CH), 123.1 (CH), 121.6 (CH), 29.0 ($CH_2$), 21.3 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{23}H_{18}N_4SH$ 383.1330; Found 383.1327.



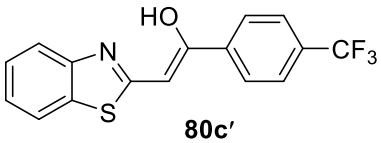
81pn

**(Z)-4-(2-(benzo[*d*]thiazol-2-yl)-1-hydroxyvinyl)benzonitrile** (**80b′**)**:** The title compound was prepared following **Procedure A** with using sodium hydride, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a yellow solid compound. Yield: 90% (419.6 mg). Mp: 182-184 $^{o}$C. IR (neat): $\nu_{max}$ 2966, 2879, 1769, 1611, 1471, 1245, 1112, 1052, 838, 757, 728 and 614 cm$^{-1}$. $^{1}$H NMR (500 MHz, $CDCl_3$, keto : enol ratio **80b** : **80b'** = 1:8, major isomer): $\delta$ 13.81 (1H, s), 7.95 (2H, d, $J$ = 8.0 Hz), 7.85 (1H, d, $J$ = 8.0 Hz), 7.81 (1H, d, $J$ = 8.0 Hz), 7.71 (2H, d, $J$ = 8.5 Hz), 7.48 (1H, t, $J$ = 7.5 Hz), 7.34 (1H, t, $J$ = 7.5 Hz), 6.42 (1H, s). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135, keto : enol ratio **80b** : **80b'** = 1:8, major isomer): $\delta$ 167.4 (C), 163.0 (C), 150.0 (C), 139.0 (C), 132.6 (2 x CH), 131.5 (C), 126.8 (CH), 126.3 (2 x CH), 124.7 (CH), 121.5 (CH), 120.3 (CH), 118.5 (C), 113.3 (C). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{10}N_2OSH$ 279.0592; Found 279.0592.



**80b′**

**(Z)-4-(2-(benzo[*d*]thiazol-2-yl)-1-hydroxyvinyl)benzonitrile** (**80c′**)**:** The title compound was prepared following **Procedure A** with using sodium hydride, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a yellow solid compound. Yield: 90% (419.6 mg). Mp: 160-162 $^{o}$C. IR (neat): $\nu_{max}$ 2967, 2878, 1767, 1610, 1470, 1243, 1112, 1052, 838, 757, 728 and 614 cm$^{-1}$. $^{1}$H NMR (500 MHz, $CDCl_3$, keto : enol ratio **80c** : **80c'** = 1:7, major isomer): $\delta$ 13.95 (1H, br s), 7.96 (2H, d, $J$ = 8.0 Hz), 7.83 (1H, d, $J$ = 8.0 Hz), 7.79 (1H, d, $J$ = 8.0 Hz), 7.75 (2H, d, $J$ = 8.5 Hz), 7.46 (1H, td, $J$ = 7.5, 1.0 Hz), 7.34 (1H, t, $J$ = 7.5, 1.0 Hz), 6.41 (1H, s). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135, keto : enol ratio **80c** : **80c'** = 1:7, major isomer): $\delta$ 167.7 (C), 163.8 (C), 150.2 (C), 138.2 (C), 131.8 (C, d, $J$ = 32.1 Hz), 131.5 (C), 126.7 (CH), 126.2 (2 x CH), 125.5 (2 x CH, q, $J$ = 3.75 Hz), 124.5 (CH), 123.9 (C, q, $J$ = 270.75 Hz), 121.5 (CH), 120.2 (CH), 92.0 (CH). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{10}F_3NOSH$ 322.0513; Found 322.0528.



**80c′**

**2-(benzo[*d*]thiazol-2-yl)-1-(4-chlorophenyl)ethan-1-one (80d) and (Z)-2-(benzo[*d*]thiazol-2-yl)-1-(4-chlorophenyl)ethen-1-ol (80d′):** The title compound was prepared following **Procedure A** with using sodium hydride, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a yellow solid compound. Yield: 80% (384.44 mg). Mp: 139-141 °C. IR (neat): $\nu_{max}$ 2965, 2937, 1769, 1613, 1468, 1266, 1248, 1087, 1053, 850, 759, 724 and 688 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$, keto : enol ratio **80d** : **80d'** = 1:3, major isomer): $\delta$ 8.03-7.99 (2H, m), 7.87-7.86 (1H, m), 7.69 (1H, td, $J$ = 9.0 Hz), 7.81-7.77 (2H, m), 7.48-7.42 (1H, m), 7.41-7.36 (1H, m), 4.78 (2H, s). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135, keto : enol ratio **80d** : **80d'** = 1:3, major isomer): $\delta$ 192.9 (C), 163.0 (C), 152.7 (C), 140.4 (C), 135.8 (C), 134.1 (C), 130.2 (2 x CH), 129.2 (2 x CH), 126.1 (CH), 125.2 (CH), 122.7 (CH), 121.6 (CH), 43.9 ($CH_2$). $^1H$ NMR (500 MHz, $CDCl_3$, keto : enol ratio **80d** : **80d'** = 1:3, minor isomer): $\delta$ 13.52 (1H, br s), 7.81-7.77 (3H, m), 7.48-7.42 (2H, m), 7.41-7.36 (1H, m), 7.32-7.28 (2H, m), 6.32 (1H, s). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135, keto : enol ratio **80d** : **80d'** = 1:3, minor isomer): $\delta$ 167.8 (C), 164.7 (C), 150.1 (C), 133.8 (C), 131.7 (2 x CH), 131.3 (C), 127.3 (2 x CH), 126.6 (CH), 124.7 (C), 124.3 (CH), 121.5 (CH), 119.9 (CH), 90.9 (CH). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{15}H_{10}ClNOSNa$ 310.0069; Found 310.0069.

**2-(benzo[*d*]thiazol-2-yl)-1-(4-bromophenyl)ethan-1-one (80f) and (Z)-2-(benzo[*d*]thiazol-2-yl)-1-(4-bromophenyl)ethen-1-ol (80f′):** The title compound was prepared following **Procedure A** with using sodium hydride, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a yellow solid compound. Yield: 70% (384.44 mg). Mp: 138-142 °C. IR (neat): $\nu_{max}$ 2965, 2924, 1769, 1677, 1608, 1584, 1468, 1270, 1247, 1067, 1052, 882, 757, and 724 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$, keto : enol ratio **80f** : **80f'**= 1:2, major isomer): $\delta$ 8.00 (1H, d, $J$ = 8.0 Hz), 7.93 (2H, d, $J$ = 8.0 Hz ), 7.86 (1H, d, $J$ = 8.0 Hz ), 7.62 (2H, d, $J$ = 8.5 Hz), 7.46 (1H, td, $J$ = 7.5 1.0 Hz), 7.33 (1H, td, $J$ = 8.0 1.0 Hz), 4.76 (2H, s). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135, keto : enol ratio **80f** : **80f'**= 1:2, major isomer): $\delta$ 192.9 (C), 163.0 (C), 152.7 (C), 140.4 (C), 135.8 (C), 134.1 (C), 132.2 (2 x CH), 130.2 (2 x CH), 129.2 (CH),

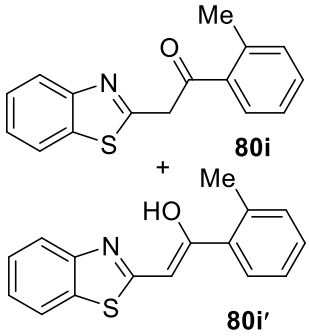
126.1 (CH), 125.2 (CH), 122.7 (CH), 121.6 (CH), 43.9 ($CH_2$). $^1$H NMR (500 MHz, $CDCl_3$, keto : enol ratio **80f** : **80f'**= 1:2, minor isomer): $\delta$ 13.76 (1H, br s), 7.80 (1H, d, $J$ = 8.0 Hz), 7.77 (1H, d, $J$ = 8.0 Hz), 7.72 (2H, d, $J$ = 8.0 Hz), 7.55 (2H, d, $J$ = 8.0 Hz), 7.45 (1H, td, $J$ = 8.0, 1.0 Hz), 7.30 (1H, td, $J$ = 8.0, 1.0 Hz ), 6.33 (1H, s). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135): For **80f'**: $\delta$ 167.8 (C), 164.7 (C), 150.0 (C), 136.3 (C), 133.3 (C), 131.2 (C), 128.8 (2 x CH), 127.3 (2 x CH), 126.6 (CH), 124.3 (CH), 121.5 (CH), 119.9 (CH), 90.9 (CH).HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{15}H_{10}BrNOSH$ 331.9745; Found 331.9740.

**2-(benzo[*d*]thiazol-2-yl)-1-(2-fluorophenyl)ethan-1-one (80g) and (Z)-2-(benzo[*d*]thiazol-2-yl)-1-(2-fluorophenyl)ethen-1-ol (80g′):** The title compound was prepared following **Procedure A** with using sodium hydride, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a white solid semi compound. Yield: 65% (294.5 mg). IR (neat): $\nu_{max}$ 3064, 1698, 1667, 1596, 1481, 1462, 1320, 1303, 1263, 1239, 1205, 1013, 881, 755 and 727 cm$^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$, keto : enol ratio **80g** : **80g'** = 10:1, major isomer): $\delta$ 8.14(1H, d, $J$ = 6.5 Hz), 8.12 (1H, d, $J$ = 6.0 Hz ), 8.03-8.01 (1H, m), 7.61 (1H, td, $J$ = 8.0, 1.5 Hz), 7.548 (1H, d, $J$ = 6.0 Hz), 7.546 (1H, d, $J$ = 6.0 Hz), 7.15 (1H, t, $J$ = 7.5 Hz), 6.42 (1H, d, $J$ = 7.0 Hz), 3.58 (2H, s). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135, keto : enol ratio **80g** : **80g'** = 10:1, major isomer): $\delta$ 191.6 (C), 186.45 (C), 162.0 (C, d, $J$ = 345 Hz), 153.7 (C), 137.0 (CH), 136.4 (C), 130.5 (CH), 125.9 (CH), 122.9 (C), 122.4 (CH), 121.8 (CH), 112.5 (CH), 55.9 ($CH_2$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{15}H_{10}FNOSH$ 372.0545; Found 372.0545.

**2-(benzo[*d*]thiazol-2-yl)-1-(2-iodophenyl)ethan-1-one (80h) and (Z)-2-(benzo[*d*]thiazol-2-yl)-1-(2-iodophenyl)ethen-1-ol (80h′):** The title compound was prepared following **Procedure A** with using sodium hydride, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a yellow solid compound. Yield: 50% (316.6 mg). Mp: 150-152 $^o$C. IR (neat): $\nu_{max}$ 2966, 2937, 1774, 1570, 1471, 1431, 1344, 1234, 1203, 1012, 896, 866, 729 and 674 cm$^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$, keto : enol ratio **80h** : **80h'** = 1:5, major isomer): $\delta$ 13.40 (1H, br s), $\delta$ 7.96 (1H, dd, $J$ = 8.0, 1.0 Hz), 7.79 (2H, t, $J$ = 7.0 Hz ), 7.52 (1H, dd, $J$ = 8.0, 1.5 Hz ), 7.49-7.46

(1H, m), 7.42 (1H, td, *J* = 7.5, 1.0 Hz), 7.33 (1H, td, *J* = 8.0, 1.0 Hz), 7.11 (1H, td, *J* = 7.5, 1.5 Hz), 6.02 (1H, s). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135, keto : enol ratio **80h** : **80h'** = 1:5, major isomer): $\delta$ 171.7 (C), 167.1 (C), 148.6 (C), 141.8 (C), 140.2 (CH), 130.6 (CH), 130.4 (C), 129.5 (CH), 126.7 (C), 128.0 (CH), 126.7 (CH), 124.2 (CH), 121.5 (CH), 119.0 (CH), 94.5 (CH). HRMS (ESI-TOF) *m/z*: $[M+NH]^+$ Calcd for $C_{16}H_{10}INOSH$ 379.9606; Found 379.9603.

**2-(benzo[*d*]thiazol-2-yl)-1-(o-tolyl)ethan-1-one (80i) and (Z)-2-(benzo[*d*]thiazol-2-yl)-1-(4-bromophenyl)ethen-1-ol (80i′):** The title compound was prepared following **Procedure A** with using sodium hydride, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a yellow semi solid compound. Yield: 85% (379.48 mg). IR (neat): $\nu_{max}$ 1614, 1553, 1468, 1266, 1249, 1087, 1052, 849, 828, 758 and 725 cm$^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$, keto : enol ratio **80i** : **80i'** = 1:5, major isomer): $\delta$ 8.00 (1H, d, *J* = 8.0 Hz), 7.86 (1H, d, *J* = 7.0 Hz ), 7.85 (1H, d, *J* = 8.5 Hz ), 7.47-7.35 (3H, m), 7.32-7.28 (1H, m), 7.26-7.21 (1H, m), 4.76 (2H, s), 2.56 (3H, s). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135, keto : enol ratio **80i** : **80i'** = 1:5, major isomer): $\delta$ 197.1 (C), 163.7 (C), 152.7 (C), 136.0 (C), 135.9 (C), 132.3 (CH), 132.3 (CH), 131.2 (C), 129.3 (CH), 125.97 (CH), 125.90 (CH), 125.0 (CH), 122.9 (CH), 121.5 (CH), 46.2 ($CH_2$), 21.6 ($CH_3$). $^1$H NMR (500 MHz, $CDCl_3$, keto : enol ratio **80i** : **80i'** = 1:5, minor isomer): $\delta$ 13.76 (1H, br s), $\delta$ 7.81 (1H, d, *J* = 8.5 Hz), 7.77 (1H, d, *J* = 8.0 Hz ), 7.50 (1H, d, *J* = 8.0 Hz ), 7.47-7.35 (1H, m), 7.32-7.28 (2H, m), 7.26-7.21 (2H, m), 5.95 (1H, s), 2.54 (3H, s). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135, keto : enol ratio **80i** : **80i'** = 1:5, minor isomer): $\delta$ 169.2 (C), 167.9 (C), 150.2 (C), 139.5 (C), 136.6 (C), 135.9 (C), 130.9 (CH), 129.4 (CH), 128.3 (CH), 126.4 (CH), 125.7 (CH), 124.1 (CH), 121.4 (CH), 119.9 (CH), 94.6 (CH), 20.6 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{16}H_{13}NOSH$ 268.0796; Found 268.0795.



**2-(benzo[d]thiazol-2-yl)-1-(4-methoxyphenyl)ethan-1-one (80j) and (Z)-2-(benzo[d]thiazol-2-yl)-1-(4-methoxyphenyl)ethen-1-ol (80j′):** The title compound was prepared following **Procedure A** with using sodium hydride, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a yellow solid compound. Yield: 70% (347.62 mg). Mp: 120-123 $^{o}$C. IR (neat): $\nu_{max}$ 2966, 2940, 1769, 1646, 1603, 1470, 1452, 1246, 1135, 1015, 828, 763 and 720 cm$^{-1}$. $^{1}$H NMR (500 MHz, $CDCl_3$, keto : enol ratio **80j** : **80j'** = 4:1, major isomer): $\delta$ 8.05 (2H, d, $J$ = 8.5 Hz), 7.99 (1H, d, $J$ = 8.0 Hz ), 7.85 (1H, d, $J$ = 7.5 Hz), 7.75 (1H, t, $J$ = 8.5 Hz), 7.45 (1H, t, $J$ = 8.0 Hz), 6.94 (2H, d, $J$ = 9.0 Hz), 4.75 (2H, s). 3.85 (3H, s). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135, keto : enol ratio **80j** : **80j'** = 4:1, major isomer): $\delta$ 192.5 (C), 164.1 (C), 163.9 (C), 152.7 (C), 135.9 (C), 131.1 (2 x CH), 128.9 (C), 125.4 (CH), 124.9 (CH), 122.8 (CH), 121.5 (CH), 114.0 (2 x CH), 55.5 ($CH_3$), 43.6 ($CH_2$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{13}NO_2SH$ 284.0745; Found 284.0749.

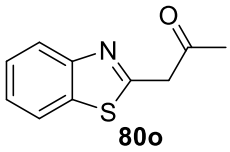
**2-(benzo[*d*]thiazol-2-yl)-1-(furan-2-yl)ethan-1-one (80l) and (Z)-2-(benzo[*d*]thiazol-2-yl)-1-(furan-2-yl)ethen-1-ol (80l′):** The title compound was prepared following **Procedure A** with using sodium hydride, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a yellow solid compound. Yield: 85% (692.7 mg). Mp: 86-88 $^{o}$C. IR (neat): $\nu_{max}$ 2922, 1612, 1553, 1508, 1469, 1357, 1266, 1122, 1054, 854, 815, 722 and 753 cm$^{-1}$. $^{1}$H NMR (500 MHz, $CDCl_3$, keto : enol ratio **80l** : **80l'** = 1.2:1, major isomer): $\delta$ 8.00 (1H, d, $J$ = 8.0 Hz), 7.65 (1H, d, $J$ = 8.0 Hz), 7.71 (1H, t, $J$ = 8.0 Hz), 7.47-7.44 (1H, m), 7.42-7.35 (1H, m), 7.27-7.24 (1H, m), 6.67-6.56 (1H, m), 4.67 (2H, s). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135, keto : enol ratio **80l** : **80l'** = 1.2:1, major isomer): $\delta$ 182.6 (C), 167.2 (C), 162.8 (C), 150.1 (C), 147.3 (CH), 135.9 (C), 126.5 (CH), 125.9 (CH), 122.9 (CH), 121.5 (CH), 118.8 (CH), 112.7 (CH), 43.5 ($CH_2$). $^{1}$H NMR (500 MHz, $CDCl_3$, keto : enol ratio **80l** : **80l'** = 1.2:1, minor isomer): $\delta$ 7.71 (1H, t, $J$ = 8.0 Hz), 7.64-7.63 (1H, m), 7.50 (1H, s), 7.42-7.35 (1H, m), 7.27-7.24 (1H, m), 6.96 (1H, d, $J$ = 8.5 Hz), 6.52-6.51 (1H, m), 6.52 (1H, s). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135, keto : enol ratio **80l** : **80l'** = 1.2:1, minor isomer): $\delta$ 159.1 (C), 152.7 (C), 151.6 (C), 148.8 (C), 144.1 (CH), 130.3 (C), 125.1 (CH), 123.9 (CH), 121.4 (CH),

118.9 (CH), 112.1 (CH), 111.6 (CH), 89.5 ($CH_2$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{13}H_9NO_2SH$ 244.0432; Found 244.0430.

**2-(benzo[d]thiazol-2-yl)-1-(pyridin-2-yl)ethan-1-one (80m) and (Z)-2-(benzo[*d*]thiazol-2-yl)-1-(pyridin-2-yl)ethen-1-ol (80m′):** The title compound was prepared following **Procedure A** with using sodium hydride, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a yellow solid compound. Yield: 80% (347.62 mg). Mp: 112-125 °C. IR (neat): $\nu_{max}$ 2965, 2940, 1768, 1646, 1603, 1472, 1452, 1246, 1135, 1015, 828, 763 and 721 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$, keto : enol ratio **80m** : **80m'** = 1.5:4, major isomer): $\delta$ 13.49 (1H, br s), $\delta$ 8.63 (1H, m), 8.00 (1H, d, *J* = 8.0 Hz), 7.86-7.82 (1H, m), 7.81 (1H, m), 7.49-7.42 (1H, m), 7.67-7.28 (2H, m), 7.10 (1H, s), 5.09 (1H, s). $^{13}C$ NMR (100 MHz, $CDCl_3$, DEPT-135, keto : enol ratio **80m** : **80m'** = 1.5:4, major isomer): $\delta$ 167.9 (C), 162.7 (C), 152.1 (C), 150.4 (C), 149.1 (CH), 136.9 (CH), 131.9 (C), 126.4 (CH), 124.4 (CH), 124.3 (CH), 121.4 (CH), 120.8 (CH), 120.2 (CH), 92.4 (CH). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{14}H_{10}N_2OSH$ 255.0592; Found 255.0592.

**(Z)-1-(benzo[d]thiazol-2-yl)-3,3,3-trifluoroprop-1-en-2-ol (80n′):** The title compound was prepared following **Procedure A** with using sodium hydride, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a yellow solid compound. Yield: 70% (287.6 mg). Mp: 240-245 °C. IR (neat): $\nu_{max}$ 3066, 2724, 1607, 1583, 1494, 1337, 1259, 1172, 984, 957, 712 and 666 $cm^{-1}$. $^1H$ NMR (500 MHz, DMSO-$D_6$, keto : enol ratio **80n** : **80n'** = 1:9, major isomer): $\delta$ 13.54 (1H, br s), 7.97 (1H, d, *J* = 8.0 Hz), 7.53 (1H, d, *J* = 7.5 Hz), 7.50 (1H, td, *J* = 8.0, 1.0 Hz), 7.34 (1H, t, *J* = 8.0 Hz), $^{13}C$ NMR (100 MHz, $CDCl_3$, DEPT-135, keto : enol ratio **80n** : **80n'** = 1.5:4, major isomer): $\delta$ 166.7. (C), 138.8 (C), 128.0 (CH), 126.9 (C), 124.3 (CH), 123.5 (CH), 118.6 (C, q, *J* = 288.0 Hz), 113.6 (CH), 84.3 (CH). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{10}H_6F_3NOSH$ 246.0200; Found 246.0200.

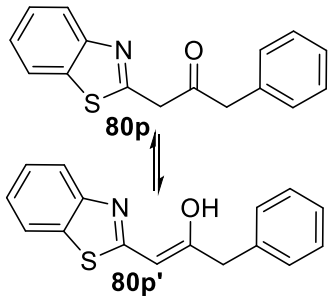
**1-(benzo[d]thiazol-2-yl)propan-2-one (80o):** The title compound was prepared following



**80o**

**Procedure A** with using sodium hydride, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a brown solid. Yield: 70% (223.55 mg). Mp: 118-121°C. IR (neat): $\nu_{max}$ 2725, 1606, 1583, 1493, 1441, 1404, 1337, 1259, 1171, 957, 813, 745 and 661 $cm^{-1}$. $^{1}H$ NMR (500 MHz, $CDCl_3$, keto : enol ratio **80o** : **80o'** = 1:4, major isomer): $\delta$ 8.00 (1H, d, $J$ = 8.0 Hz), 7.86 (1H, d, $J$ = 8.0 Hz), 7.47 (1H, t, $J$ = 8.0 Hz), 7.41-7.37 (1H, m), 4.24 (2H, s), 2.32 (3H, s). $^{13}C$ NMR (100 MHz, $CDCl_3$, DEPT-135, keto : enol ratio **80o** : **80o'** = 1:4, major isomer): $\delta$ 202.3 (C), 162.8 (C), 152.9 (C), 135.8 (C), 1126.2 (CH), 125.2 (C), 122.9 (CH), 121.6 (CH), 48.3 ($CH_2$), 29.97 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{10}H_9NOSH$ 192.0483; Found 192.0478.

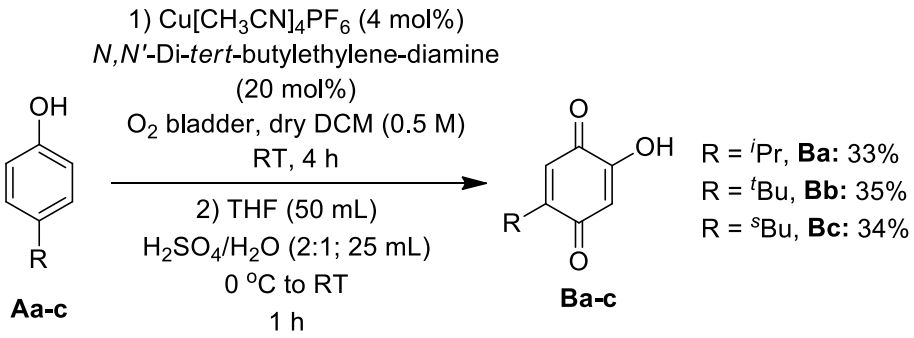
**1-(benzo[d]thiazol-2-yl)-3-phenylpropan-2-one (80p) and (Z)-1-(benzo[d]thiazol-2-yl)-3-phenylprop-1-en-2-ol (80p'):** The title compound was prepared following **Procedure A** with using sodium hydride, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a semi solid compound. Yield: 80% (537.35 mg). IR (neat): $\nu_{max}$ 1722, 1623, 1515, 1493, 1478, 1311, 1272, 1074, 903, 819, 753, 726 and 692 $cm^{-1}$. $^{1}H$ NMR (500 MHz, $CDCl_3$, keto : enol ratio **80p** : **80p'** = 2.3:1, major isomer): $\delta$ 8.00 (1H, d, $J$ = 8.0 Hz), 7.75 (1H, d, $J$ = 8.0 Hz), 7.69 (1H, td, $J$ = 9.0 Hz), 7.40-7.38 (1H, m), 7.35-7.32 (3H, m), 7.29-7.26 (1H, m), 7.25-7.22 (2H, m), 4.24 (2H, s), 3.89 (2H, s). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135, keto : enol ratio **80p** : **80p'** = 2.3:1, major isomer): $\delta$ 202.1 (C), 172.3 (C), 162.8 (C), 152.8 (C), 133.2 (C), 129.6 (2 x CH), 128.9 (2 x CH), 127.4 (CH), 126.1 (CH), 125.2 (CH), 122.9 (CH), 121.6 (CH), 49.9 ($CH_2$), 46.6 ($CH_2$). $^{1}H$ NMR (500 MHz, $CDCl_3$, keto : enol ratio **80p** : **80p'** = 2.3:1, minor isomer): $\delta$ 13.52 (1H, br s), 7.46 (2H, td, $J$ = 7.5, 2.0 Hz), 7.40-7.38 (1H, m), 7.35-7.32 (3H, m), 7.29-7.26 (2H, m), 7.25-7.22 (2H, m), 5.56 (1H, s), 3.65 (2H, s). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): For **80p'**: $\delta$ 176.7 (C), 149.6 (C), 136.6 (C), 135.8 (C), 130.7 (C), 129.4 (2 x CH), 128.6 (2 x CH), 126.9 (CH), 126.4 (CH), 124.0 (CH), 121.4 (CH), 119.3 (CH), 92.7 (CH), 42.7 ($CH_2$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{13}NOSH$ 268.0796; Found 268.0796.



## 3. General Experimental Procedure for Organocatalytic One-Pot Synthesis of Pseudo-Terpenoids

**Procedure A: Synthesis of 2-Hydroxy-5-alkylcyclohexa-2,5-diene-1,4-diones (Ba-c) and Succinaldehyde (Ca):**

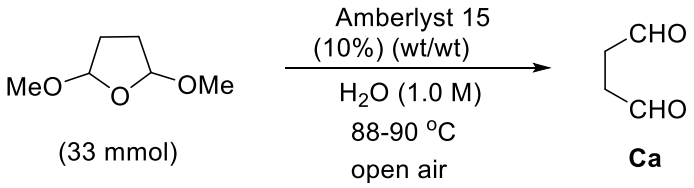
**Step-1: Synthesis of 2-Hydroxy-5-alkylcyclohexa-2,5-diene-1,4-diones (Ba-c):**[77]




An oven dried 50 mL of round bottom flask equipped with a magnetic stirring bar was charged with 0.8 mmol (298.17 mg; 4 mol%) of tetrakis(acetonitrile)copper(I) hexafluorophosphate catalyst and 20 mL of anhydrous DCM at room temperature under $N_2$ atmosphere. To this solution, after stirring for some time, 4 mmol (0.86 mL; 20 mol%) of ligand *N,N'*-di-*tert*-butylethylenediamine was added in one-portion and the stirring was continued at RT until clear solution obtained. This clear pink color solution was added to the corresponding 4-alkylphenol **Aa-c** (20 mmol; 1 equiv.) dissolved in 20 mL of anhydrous DCM in a separate 250 mL of round bottom flask equipped with a magnetic stirring bar under $N_2$ atmosphere. Next, the resulting solution was purged with oxygen to remove $N_2$ atmosphere and then stirring was continued under oxygen atmosphere at RT for 4 h. After completion of the reaction (monitored by TLC), oxygen bladder was removed and the reaction mass was diluted with 50 mL of THF. The resulting solution was cooled to 0 °C and was added 25 mL of $H_2SO_4/H_2O$ (2:1) dropwise for 20-30 min. Next, the reaction temperature was raised to RT and stirring was continued for 1 h. Next, the reaction was further diluted with 50 mL of water and the product mixture was extracted with DCM. The total volume of combined organic layers were reduced to 25-30 mL on rotary evaporator (water bath temperature <30 °C and vacuum pressure >350 Mbar) and the desired **Ba-c** compounds were isolated from mixture by treating this combined organic layers with 30 mL of saturated $NaHCO_3$ solution (5 to 7 times or until disappearance of **B** in organic layer by TLC). The combined aqueous

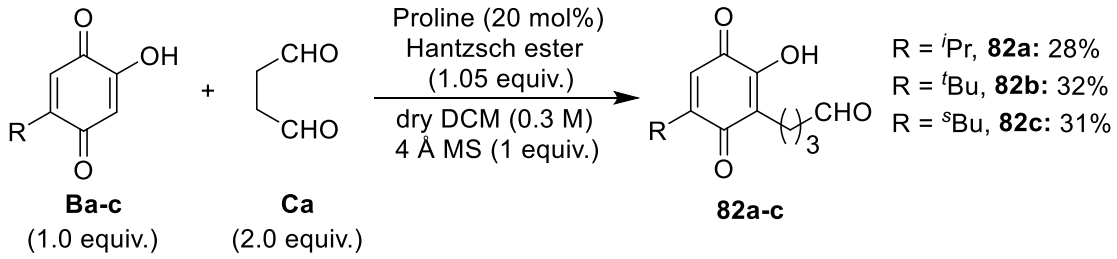
layers contain corresponding **Ba-c** in the form of their sodium salt. These combined aqueous layers were cautiously acidified with 3N HCl and the desired **Ba-c** were extracted with DCM, dried over anhydrous $Na_2SO_4$, concentrated on rotary evaporator (water bath temperature <30 °C and vacuum pressure >350 Mbar) to give 33-35% of **Ba-c** and this compounds were directly used for next reaction without further purification.

**Step-2: Synthesis of Succinaldehyde (Ca):**




To a 100 mL round flask equipped with a magnetic stirring bar were added 4.36 g (33 mmol) of 2,5-dimethoxytetrahydrofuran (*cis* and *trans* mixture), 33 mL of water and 0.436 g of amberlyst 15. The resulting mixture was stirred at 88-90 °C in an open-air atmosphere for 3-4 h. Next, the reaction temperature was cooled to RT and was added 20 mL of brine solution and stirred for 30 min. The succinaldehyde present in this aqueous solution was extracted with DCM (7 x 50 mL), dried over anhydrous $Na_2SO_4$, concentrated on rotary evaporator (water bath temperature <40 °C and vacuum pressure >200 Mbar) and then directly used for next step without further purification.

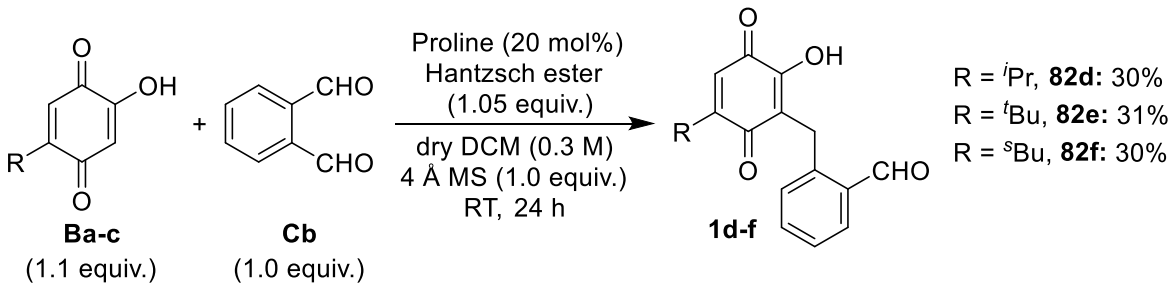
**Procedure B: Part 1: Synthesis of 4-(2-Hydroxy-5-alkyl-3,6-dioxocyclohexa-1,4-dien-1-yl)butanals (82a-c):**




An oven dried 100 mL round bottom flask equipped with a magnetic stirring bar was charged with 4 Å MS (1.1-1.2 g), succinaldehyde (obtained through step-2 of Procedure A), 149.4 mg of L-proline, 1.75 g of Hanztsch ester and 10 mL of dry DCM at room temperature (RT). To this well stirred solution, the corresponding **B** (obtained through step-1 of Procedure A) dissolved in 10 mL of dry DCM was added in one-portion at RT and stirring was continued for 24 h at the same

temperature. Next, the reaction mixture was passed through dry silica (230-400 mesh) packed column using DCM as an eluent. Next, the total volume of DCM solution of product mixture was concentrated to 20-30 mL and was treated with 15 mL of saturated $NaHCO_3$ solution (5 to 7 times or until product disappearance in organic layer by TLC). The combined aqueous layers were acidified with 3N HCl and the corresponding product **82** was extracted with DCM, dried over anhydrous $Na_2SO_4$ and concentrated. At this stage, the product contains some impurities. The product **82** was further purified by column chromatography (silica gel; eluent: EA/hexanes or $CHCl_3$/hexanes).

**Procedure B: Part 2: Synthesis of 2-((2-Hydroxy-5-alkyl-3,6-dioxocyclohexa-1,4-dien-1-yl)methyl)benzaldehydes (1d-f):**




An oven dried 100 mL round bottom flask equipped with a magnetic stirring bar was charged with 4 Å MS 1.1 g, phthalaldehyde **Cb** (6.0 mmol; 1 equiv.), 135.8 mg of L-proline, 1.59 g of Hanztsch ester and 10 mL of dry DCM at room temperature (RT). To this well stirred solution, the corresponding **B** (obtained through step-1 of Procedure A) dissolved in 10 mL of dry DCM was added in one-portion at RT and stirring was continued for 24 h at the same temperature. Next, the reaction mixture was passed through dry silica (230-400 mesh) packed column using DCM as an eluent. Next, the total volume of DCM solution of product mixture was concentrated to 20-30 mL and was treated with 15 mL of saturated $NaHCO_3$ solution (5 to 7 times or until product disappearance in organic layer by TLC). The combined aqueous layers were acidified with 3N HCl and the corresponding product **82** was extracted with DCM, dried over anhydrous $Na_2SO_4$ and concentrated. At this stage, the product contains some impurities. The product **82** was further purified by column chromatography (silica gel; eluent: EA/hexanes or $CHCl_3$/hexanes).

**Procedure C: General procedure for the synthesis of 84 and 85**: To an ordinary glass vial equipped with a magnetic stirring bar were added 0.2 mmol of **82**, 0.04 mmol of quinine (**23e**) and 2 mL of DCM. To this well stirred solution, 1.3 equiv. of corresponding Wittig reagent **83** was added at RT and the resulting mixture was allowed to stir until complete consumption of **82** (monitored by TLC). The corresponding products **84** and/or **85** were purified by column chromatography (silica gel: 100-200 mesh; eluent: EA/hexanes).

**Procedure D: General procedure for the synthesis of 85dp and 85ep**: To an ordinary glass vial equipped with a magnetic stirring bar were added 0.21 mmol (1.05 equiv.) of **82d** or **82e**, 0.04 mmol of quinine (**23e**) and 2 mL of DCM. To this well stirred solution, 0.2 mmol (1.0 equiv.) of Meldrum's acid **83p** was added at RT and the resulting mixture was allowed to stir until complete consumption of **83p** (monitored by TLC). The corresponding products **85dp** or **85ep** were purified by column chromatography (silica gel: 100-200 mesh; eluent: EA/hexanes).

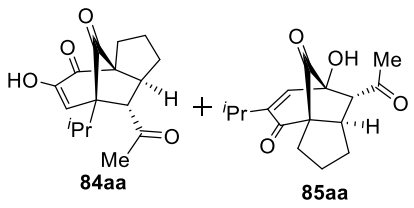
**Procedure E: General procedure for transformation of 84 to 85:** To an oven dried 5 mL round bottom flask equipped with a magnetic stirring bar and refluxing condenser were added 0.2 mmol of **84**, 3.0 equiv. of triphenylphosporanylidene acetaldehyde and 1.0 mL of toluene. The reaction mixture was allowed to stir under reflux conditions until complete transformation of **84** to **85** (monitored by TLC). The corresponding products of **85** were purified by column chromatography (silica gel: 100-200 mesh; eluent: EA/hexanes).

**Procedure F: General procedure for the synthesis of 87:** To an oven dried 5 mL round bottom flask equipped with a magnetic stirring bar and refluxing condenser were added 0.1 mmol of **84**, 0.1 mmol of *o*-phenylenediamine **78** and 0.33 mL of ethanol. The resulting mixture was allowed to stir under reflux conditions for overnight. The corresponding products **87** were purified by column chromatography (silica gel: 100-200 mesh; eluent: EA/hexanes).

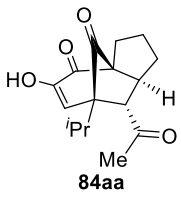
**Procedure G: General procedure for the 23e-catalysed *retro*-cyclisation:** To an ordinary glass vial equipped with a magnetic stirring bar were added 0.2 mmol of **84** or **85**, 0.04 mmol of quinine (**23e**) and 2 mL of DCM. The resulting reaction mixtures were allowed to stir for 15 to 24 h for

checking isomerization of **84** to **85** or vice versa (monitored by TLC). The corresponding products **84** or **85** were purified by column chromatography (silica gel: 100-200 mesh; eluent: EA/hexanes).

**(3a*R**,7*S**,8*S**,8a*S**)-8-Acetyl-5-hydroxy-7-isopropyl-1,2,3,7,8,8a-hexahydro-4*H*-3a,7-methanoazulene-4,9-dione (84aa) and (3a*R**,7*S**,8*R**,8a*R**)-8-Acetyl-7-hydroxy-5-isopropyl-1,2,3,7,8,8a-hexahydro-4*H*-3a,7-methanoazulene-4,9-dione (85aa):** The mixture of compounds prepared following **Procedure C** without employing catalyst **23e**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a colourless liquid. Yield: 78% (43 mg). IR (neat): $\nu_{max}$ 3420, 2963, 2871, 1764, 1709, 1673, 1386, 1365, 1299, 1264, 1182, 1040, 941, 733, 702 and 437 $cm^{-1}$. $^{1}H$ NMR (500 MHz, $CDCl_3$): For **84aa**: $\delta$ 6.48 (1H, s, *vinylic*-C*H*), 5.98 (1H, s, *enolic*-O*H*), 2.93 (1H, d, *J* = 7.5 Hz), 2.35-2.30 (2H, m), 2.29-2.24 (1H, m), 2.22 (3H, s), 2.14-2.04 (2H, m), 1.86-1.79 (1H, m), 1.78-1.71 (1H, m), 1.57 (1H, qd, *J* = 13.0, 7.0 Hz), 1.11 (3H, d, *J* = 7.0 Hz), 1.10 (3H, d, *J* = 7.0 Hz). For **85aa**: $\delta$ 6.69 (1H, s, *vinylic*-C*H*), 3.77 (1H, s, *t*-O*H*), 2.87 (1H, d, *J* = 7.0 Hz), 2.83 (1H, sextet, *J* = 7.0 Hz), 2.62 (1H, q, *J* = 7.5 Hz), 2.35 (3H, s), 2.25-2.20 (1H, m), 2.10-2.05 (1H, m), 2.03-1.97 (1H, m), 1.79-1.71 (2H, m), 1.35 (1H, qd, *J* = 12.75, 7.5 Hz), 1.035 (3H, d, *J* = 6.5 Hz), 1.031 (3H, d, *J* = 7.0 Hz). $^{13}C$ NMR (100 MHz, $CDCl_3$, DEPT-135): For **84aa**: $\delta$ 205.7 (C, *C*=O), 200.4 (C, *C*=O), 192.6 (C, *C*=O), 147.1 (C, C=*C*-OH), 121.5 (CH, *vinylic*-*C*H), 74.3 (C), 63.3 (C), 58.6 (CH), 49.6 (CH), 33.2 ($CH_2$), 30.4 (CH), 30.1 ($CH_3$), 27.5 ($CH_2$), 22.4 ($CH_2$), 18.4 ($CH_3$), 17.8 ($CH_3$). For **85aa**: $\delta$ 204.3 (C, *C*=O), 202.6 (C, *C*=O), 194.3 (C, *C*=O), 147.2 (C), 142.1 (CH, *vinylic*-*C*H), 84.6 (C, *C*-OH), 73.9 (C), 61.4 (CH), 45.4 (CH), 33.0 ($CH_2$), 30.6 (CH), 27.5 ($CH_2$), 26.8 ($CH_3$), 22.6 ($CH_2$), 21.7 ($CH_3$), 20.9 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{16}H_{20}O_4Na$ 299.1259; Found 299.1256.

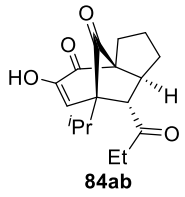


**(3a*R**,7*S**,8*S**,8a*S**)-8-Acetyl-5-hydroxy-7-isopropyl-1,2,3,7,8,8a-hexahydro-4*H*-3a,7-methanoazulene-4,9-dione (84aa):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0.0:1.0 to 1.5:8.5) and isolated as a colourless solid. Yield: 85% (47 mg). Mp: 86-88 °C. IR (neat): $\nu_{max}$ 3400, 2969, 2873, 1761, 1733, 1708, 1676, 1460, 1238, 1166, 750, 540 and 418 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 6.48 (1H, s, *vinylic*-C*H*), 5.93 (1H, s, *enolic*-O*H*), 2.93 (1H, d, *J* = 7.5 Hz), 2.35-2.27 (2H, m), 2.27-2.20 (1H, m), 2.21 (3H, s), 2.14-2.06 (2H, m), 1.86-1.79 (1H, m), 1.78-1.71 (1H, m), 1.57 (1H, qd, *J* = 13.0, 7.5 Hz), 1.11 (3H, d, *J* = 7.0 Hz), 1.10 (3H, d, *J* = 7.0 Hz). $^{13}C$ NMR (100 MHz, $CDCl_3$, DEPT-135): $\delta$ 205.7 (C, *C*=O), 200.4 (C, *C*=O), 192.5 (C, *C*=O), 147.1 (C, C=*C*-OH), 121.5 (CH, *vinylic*-*C*H), 74.2 (C), 63.3 (C), 58.5 (CH), 49.6 (CH), 33.2 ($CH_2$), 30.4 (CH), 30.1 ($CH_3$), 27.5 ($CH_2$), 22.4 ($CH_2$), 18.4 ($CH_3$), 17.8 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{16}H_{20}O_4Na$ 299.1259; Found 299.1256.



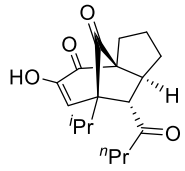
**84aa**

**(3a*R**,7*S**,8*S**,8a*S**)-5-Hydroxy-7-isopropyl-8-propionyl-1,2,3,7,8,8a-hexahydro-4*H*-3a,7-methanoazulene-4,9-dione (84ab):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a white solid. Yield: 98% (57 mg). Mp: 88-90 °C. IR (neat): $\nu_{max}$ 3410, 2963, 1750, 1714, 1671, 1382, 1238, 1207, 1111, 1060, 1033, 841 and 575 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 6.47 (1H, s, *vinylic*-C*H*), 5.94 (1H, s, *enolic*-O*H*), 2.91 (1H, d, *J* = 7.5 Hz), 2.55-2.45 (1H, m), 2.50 (1H, sept, *J* = 7.5 Hz), 2.31-2.24 (2H, m), 2.22-2.17 (1H, m), 2.13-2.03 (2H, m), 1.85-1.77 (1H, m), 1.76-1.69 (1H, m), 1.59-1.53 (1H, m), 1.09 (3H, d, *J* = 7.5 Hz), 1.07 (3H, d, *J* = 7.5 Hz), 1.06 (3H, t, *J* = 7.5 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 208.6 (C, *C*=O), 200.5 (C, *C*=O), 192.5 (C, *C*=O), 147.1 (C, C=*C*-OH), 121.5 (CH, *vinylic*-*C*H), 74.2 (C), 63.5 (C), 57.7 (CH), 50.2 (CH), 36.6 ($CH_2$), 33.1 ($CH_2$), 30.1 (CH), 27.4 ($CH_2$), 22.4 ($CH_2$), 18.4 ($CH_3$), 17.8 ($CH_3$), 7.5 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{17}H_{22}O_4Na$ 313.1416; Found 313.1414.



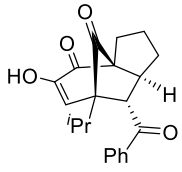
**84ab**

**(3a*R**,7*S**,8*S**,8a*S**)-8-Butyryl-5-hydroxy-7-isopropyl-1,2,3,7,8,8a-hexahydro-4*H*-3a,7-methanoazulene-4,9-dione (84ac):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a colourless liquid. Yield: 98% (59.6 mg). IR (neat): $\nu_{max}$ 3406, 2962, 2875, 1764, 1707, 1371, 1238, 1204, 1156, 1119, 1049, 988, 735 and 456 $cm^{-1}$. $^{1}H$ NMR (500 MHz, $CDCl_3$): $\delta$ 6.49 (1H, s, *vinylic*-C*H*), 5.88 (1H, s, *enolic*-O*H*), 2.89 (1H, d, $J$ = 7.5 Hz), 2.50-2.39 (2H, m), 2.30-2.24 (2H, m), 2.19 (1H, sept, $J$ = 7.0 Hz), 2.14-2.04 (2H, m), 1.85-1.78 (1H, m), 1.77-1.70 (1H, m), 1.64-1.59 (2H, m), 1.56-1.53 (1H, m), 1.09 (3H, d, $J$ = 7.5 Hz), 1.08 (3H, d, $J$ = 7.0 Hz), 0.91 (3H, t, $J$ = 7.5 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 208.1 (C, *C*=O), 200.5 (C, *C*=O), 192.5 (C, *C*=O), 147.0 (C, C=*C*-OH), 121.6 (CH, *vinylic*-*C*H), 74.2 (C), 63.5 (C), 57.9 (CH), 50.1 (CH), 45.3 ($CH_2$), 33.2 ($CH_2$), 30.1 (CH), 27.5 ($CH_2$), 22.4 ($CH_2$), 18.5 ($CH_3$), 17.9 ($CH_3$), 16.8 ($CH_2$), 13.6 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{18}H_{24}O_4Na$ 327.1572; Found 327.1576.



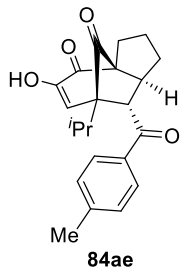
**84ac**

**(3a*R**,7*S**,8*S**,8a*S**)-8-Benzoyl-5-hydroxy-7-isopropyl-1,2,3,7,8,8a-hexahydro-4*H*-3a,7-methanoazulene-4,9-dione (84ad):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a colourless liquid. Yield: 87% (59 mg). IR (neat): $\nu_{max}$ 3407, 2960, 2872, 1758, 1668, 1447, 1388, 1369, 1215, 1179, 1054, 1000, 734, 701 and 437 $cm^{-1}$. $^{1}H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.89 (2H, dd, $J$ = 6.5, 1.5 Hz), 7.62 (1H, tt, $J$ = 7.5, 1.5 Hz), 7.50 (2H, tt, $J$ = 7.5, 1.5 Hz), 6.59 (1H, s, *vinylic*-C*H*), 5.95 (1H, s, *enolic*-O*H*), 3.77 (1H, d, $J$ = 7.5 Hz), 2.37-2.30 (2H, m), 2.14 (2H, quint, $J$ = 7.0 Hz), 1.98-1.91 (1H, m), 1.84-1.73 (2H, m), 1.58 (1H, sept, $J$ = 7.0 Hz), 1.05 (3H, d, $J$ = 7.0 Hz), 0.98 (3H, d, $J$ = 7.0 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 200.7 (C, *C*=O), 199.4 (C, *C*=O), 192.3 (C, *C*=O), 147.3 (C, C=*C*-OH), 137.2 (C), 133.7 (CH), 129.0 (2 x CH), 128.3 (2 x CH), 121.0 (CH, *vinylic*-*C*H), 74.4 (C), 65.0 (C), 52.9 (CH), 52.0 (CH), 33.0 ($CH_2$), 30.1 (CH), 27.7 ($CH_2$), 22.4 ($CH_2$), 18.8 ($CH_3$), 18.1 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{21}H_{22}O_4Na$ 361.1416; Found 361.1414.



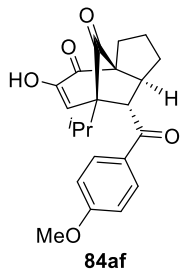
**84ad**

**(3a*R**,7*S**,8*S**,8a*S**)-5-Hydroxy-7-isopropyl-8-(4-methylbenzoyl)-1,2,3,7,8,8a-hexahydro-4*H*-3a,7-methanoazulene-4,9-dione (84ae):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a colourless liquid. Yield: 94% (66 mg). IR (neat): $\nu_{max}$ 3426, 2960, 2871, 1760, 1669, 1605, 1386, 1224, 1181, 1156, 1053, 1012, 974 and 734 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.80 (2H, d, $J$ = 8.5 Hz), 7.29 (2H, d, $J$ = 8.0 Hz), 6.58 (1H, s, *vinylic*-C*H*), 5.94 (1H, s, *enolic*-O*H*), 3.74 (1H, d, $J$ = 7.5 Hz), 2.43 (3H, s), 2.36-2.29 (2H, m), 2.14 (2H, quint, $J$ = 7.0 Hz), 1.97-1.90 (1H, m), 1.82-1.73 (2H, m), 1.60-1.54 (1H, m), 1.04 (3H, d, $J$ = 7.0 Hz), 0.98 (3H, d, $J$ = 7.0 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 200.9 (C, *C*=O), 198.9 (C, *C*=O), 192.3 (C, *C*=O), 147.2 (C, C=*C*-OH), 144.8 (C), 134.7 (C), 129.7 (2 x CH), 128.4 (2 x CH), 121.0 (CH, *vinylic*-*C*H), 74.3 (C), 64.9 (C), 52.7 (CH), 52.2 (CH), 33.0 ($CH_2$), 30.1 (CH), 27.7 ($CH_2$), 22.4 ($CH_2$), 21.6 ($CH_3$), 18.8 ($CH_3$), 18.2 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{22}H_{24}O_4Na$ 375.1572; Found 375.1574.



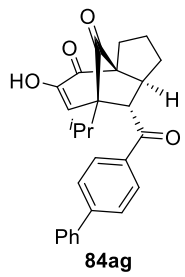
**84ae**

**(3a*R**,7*S**,8*S**,8a*S**)-5-Hydroxy-7-isopropyl-8-(4-methoxybenzoyl)-1,2,3,7,8,8a-hexahydro-4*H*-3a,7-methanoazulene-4,9-dione (84af):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexane (0:10 to 1.5:8.5) and isolated as a colourless liquid. Yield: 92% (68 mg). IR (neat): $\nu_{max}$ 3470, 3020, 2965, 1762, 1672, 1599, 1405, 1263, 1216, 1172, 754, 668 and 422 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.89 (2H, d, $J$ = 9.0 Hz), 6.97 (2H, d, $J$ = 9.0 Hz), 6.59 (1H, s, *vinylic*-C*H*), 5.95 (1H, br s, *enolic*-O*H*), 3.88 (3H, s), 3.70 (1H, d, $J$ = 7.5 Hz), 2.36-2.28 (2H, m), 2.17-2.11 (2H, m), 1.97-1.91 (1H, m), 1.78 (2H, quint, $J$ = 7.0 Hz), 1.61-1.54 (1H, m), 1.04 (3H, d, $J$ = 7.0 Hz), 0.98 (3H, d, $J$ = 7.0 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 200.9 (C, *C*=O), 197.7 (C, *C*=O), 192.3 (C, *C*=O), 164.1 (C), 147.1 (C, C=*C*-OH), 130.7 (2 x CH), 130.1 (C), 121.1 (CH, *vinylic*-*C*H), 114.1 (2 x CH), 74.3 (C), 64.9 (C), 55.6 ($CH_3$, O*C*$H_3$), 52.5 (CH), 52.4 (CH), 32.9 ($CH_2$), 30.1 (CH), 27.7 ($CH_2$), 22.4 ($CH_2$), 18.8 ($CH_3$), 18.2 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{22}H_{24}O_5Na$ 391.1521; Found 391.1523.



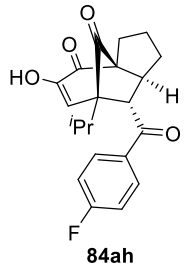
**84af**

**(3a*R**,7*S**,8*S**,8a*S**)-8-([1,1'-Biphenyl]-4-carbonyl)-5-hydroxy-7-isopropyl-1,2,3,7,8,8a-hexahydro-4*H*-3a,7-methanoazulene-4,9-dione (84ag):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a colourless solid. Yield: 96% (79.6 mg). Mp: 170-172 °C. IR (neat): $\nu_{max}$ 3407, 2956, 1760, 1659, 1628, 1599, 1369, 1257, 1218, 1187, 1167, 1035, 988, 754, 738, 703 and 616 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.97 (2H, d, $J$ = 8.0 Hz), 7.72 (2H, d, $J$ = 8.0 Hz), 7.63 (2H, d, $J$ = 8.0 Hz), 7.48 (2H, dt, $J$ = 7.5, 1.0 Hz), 7.42 (1H, dt, $J$ = 7.5, 1.0 Hz), 6.61 (1H, s, *vinylic*-C*H*), 5.98 (1H, s, *enolic*-O*H*), 3.80 (1H, d, $J$ = 7.5 Hz), 2.38 (1H, q, $J$ = 7.5 Hz), 2.36-2.31 (1H, m), 2.20 -2.13 (2H, m), 2.02-1.95 (1H, m), 1.84-1.76 (2H, m), 1.65-1.58 (1H, m), 1.07 (3H, d, $J$ = 6.5 Hz), 1.01 (3H, d, $J$ = 6.5 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 200.8 (C, *C*=O), 198.9 (C, *C*=O), 192.3 (C, *C*=O), 147.3 (C, C=*C*-OH), 146.5 (C), 139.5 (C), 135.8 (C), 129.0 (2 x CH), 128.9 (2 x CH), 128.5 (CH), 127.6 (2 x CH), 127.2 (2 x CH), 121.0 (CH, *vinylic*-*C*H), 74.4 (C), 65.1 (C), 52.9 (CH), 52.2 (CH), 33.1 ($CH_2$), 30.2 (CH), 27.7 ($CH_2$), 22.4 ($CH_2$), 18.9 ($CH_3$), 18.2 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{27}H_{26}O_4Na$ 437.1729; Found 437.1732.



84ag

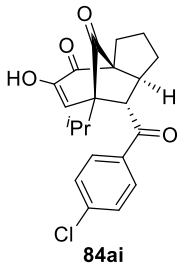
**(3a*R**,7*S**,8*S**,8a*S**)-8-(4-Fluorobenzoyl)-5-hydroxy-7-isopropyl-1,2,3,7,8,8a-hexahydro-4*H*-3a,7-methanoazulene-4,9-dione (84ah):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a colourless solid. Yield: 95% (67.7 mg). Mp: 150-152 °C. IR (neat): $\nu_{max}$ 3463, 2965, 2874, 1763, 1675, 1597, 1507, 1467, 1448, 1405, 1368, 1301, 1222, 1157, 910, 732 and 649 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.95-7.91 (2H, m), 7.20-7.15 (2H, m), 6.57 (1H, s, *vinylic*-C*H*), 5.96 (1H, s, *enolic*-O*H*), 3.71 (1H, d, $J$ = 7.5 Hz), 2.33 (1H, q, $J$ = 7.0 Hz), 2.34-2.30 (1H, m), 2.14 (2H, sept, $J$ = 7.0 Hz), 1.98-1.92 (1H, m), 1.83-1.73 (2H, m), 1.58-1.53 (1H, m), 1.04 (3H, d, $J$ = 7.0 Hz), 0.97 (3H, d, $J$ = 7.0 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 200.6 (C, *C*=O), 197.7 (C, *C*=O), 192.2 (C, *C*=O), 166.1 (C, d, $J_{C\text{-}F}$ = 255.0 Hz), 147.3 (C, C=*C*-OH), 133.6 (C, d, $J_{C\text{-}F}$ = 2.5 Hz), 130.9 (2 x CH, d, $J_{C\text{-}F}$ = 8.75 Hz), 120.7 (CH, *vinylic*-*C*H), 116.2 (2 x CH, d, $J_{C\text{-}F}$ = 22.5 Hz), 74.4 (C), 65.0 (C), 52.9 (CH), 52.1 (CH), 33.0 ($CH_2$), 30.1 (CH), 27.7



84ah

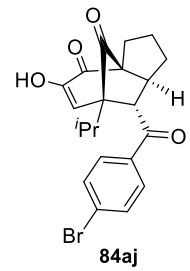
($CH_2$), 22.4 ($CH_2$), 18.8 ($CH_3$), 18.1 ($CH_3$). $^{19}F$ NMR (376.42 MHz, $CDCl_3$): $\delta$ -103.7. HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{22}FO_4$ 357.1502; Found 357.1505.

**(3a*R**,7*S**,8*S**,8a*S**)-8-(4-Chlorobenzoyl)-5-hydroxy-7-isopropyl-1,2,3,7,8,8a-hexahydro-4*H*-3a,7-methanoazulene-4,9-dione (84ai):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a colourless sticky solid. Yield: 94% (70 mg). IR (neat): $\nu_{max}$ 3418, 2961, 2872, 1760, 1670, 1587, 1467, 1399, 1259, 1213, 1177, 1092, 1054, 1010, 734, 702 and 535 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.85 (2H, td, *J* = 8.5, 2.5 Hz), 7.49 (2H, td, *J* = 8.5, 2.5 Hz), 6.57 (1H, s, *vinylic*-C*H*), 6.01 (1H, s, *enolic*-O*H*), 3.71 (1H, d, *J* = 8.0 Hz), 2.37-2.31 (2H, m), 2.19-2.10 (2H, m), 2.00-1.93 (1H, m), 1.84-1.74 (2H, m), 1.60-1.53 (1H, m), 1.06 (3H, d, *J* = 7.0 Hz), 0.99 (3H, d, *J* = 7.0 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 200.5 (C, *C*=O), 198.2 (C, *C*=O), 192.2 (C, *C*=O), 147.4 (C, C=*C*-OH), 140.4 (C), 135.5 (C), 129.6 (2 x CH), 129.3 (2 x CH), 120.6 (CH, *vinylic*-*C*H), 74.4 (C), 65.0 (C), 52.9 (CH), 52.0 (CH), 33.0 ($CH_2$), 30.1 (CH), 27.7 ($CH_2$), 22.4 ($CH_2$), 18.9 ($CH_3$), 18.1 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{21}H_{21}ClO_4Na$ 395.1026; Found 395.1025.



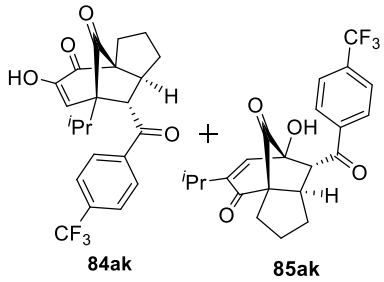
84ai

**(3a*R**,7*S**,8*S**,8a*S**)-8-(4-Bromobenzoyl)-5-hydroxy-7-isopropyl-1,2,3,7,8,8a-hexahydro-4*H*-3a,7-methanoazulene-4,9-dione (84aj):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a colourless liquid. Yield: 97% (81 mg). IR (neat): $\nu_{max}$ 3463, 2965, 2873, 1764, 1676, 1610, 1584, 1398, 1256, 1215, 1178, 1110, 1072, 1008, 909, 731, 649 and 472 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.75 (2H, td, *J* = 9.0, 2.0 Hz), 7.64 (2H, td, *J* = 9.0, 2.0 Hz), 6.55 (1H, s, *vinylic*-C*H*), 5.95 (1H, s, *enolic*-O*H*), 3.69 (1H, d, *J* = 7.5 Hz), 2.35-2.30 (2H, m), 2.17-2.09 (2H, m), 1.98-1.91 (1H, m), 1.84-1.73 (2H, m), 1.58-1.51 (1H, m), 1.04 (3H, d, *J* = 7.0 Hz), 0.97 (3H, d, *J* = 7.0 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 200.5 (C, *C*=O), 198.4 (C, *C*=O), 192.1 (C, *C*=O), 147.3 (C, C=*C*-OH), 135.8 (C), 132.3 (2 x CH), 129.7 (2 x CH), 129.1 (C), 120.6 (CH, *vinylic*-*C*H), 74.3 (C), 65.0 (C), 52.9 (CH), 52.0 (CH), 33.0 ($CH_2$), 30.1 (CH), 27.7 ($CH_2$), 22.4 ($CH_2$), 18.9 ($CH_3$), 18.1 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[(M+Na]^+$ Calcd for $C_{21}H_{21}BrO_4Na$ 441.0500; Found 441.0504.



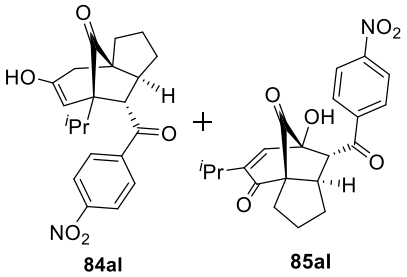
84aj

**(3a*R**,7*S**,8*S**,8a*S**)-5-Hydroxy-7-isopropyl-8-(4-(trifluoromethyl)benzoyl)-1,2,3,7,8,8a-hexahydro-4*H*-3a,7-methanoazulene-4,9-dione (84ak) and (3a*R**,7*S**,8*R**,8a*R**)-7-Hydroxy-5-isopropyl-8-(4-(trifluoromethyl)benzoyl)-1,2,3,7,8,8a-hexahydro-4*H*-3a,7-methanoazulene-4,9-dione (85ak):** The mixture of compounds were prepared following



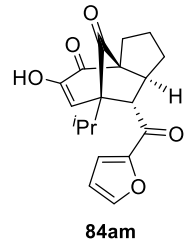

**Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a colourless liquid. Yield: 86% (70 mg). IR (neat): $\nu_{max}$ 3431, 2964, 2875, 1763, 1674, 1408, 1321, 1215, 1168, 1128, 1065, 1013, 770, 736, 702, 484 and 442 $cm^{-1}$. $^{1}H$ NMR (500 MHz, $CDCl_3$): for **84ak**: $\delta$ 7.99 (2H, d, $J$ = 8.0 Hz), 7.77 (2H, d, $J$ = 8.0 Hz), 6.56 (1H, s, *vinylic*-C*H*), 6.00 (1H, s, *enolic*-O*H*), 3.76 (1H, d, $J$ = 7.5 Hz), 2.34 (1H, q, $J$ = 7.5 Hz), 2.35-2.31 (1H, m), 2.18-2.10 (2H, m), 1.99-1.93 (1H, m), 1.86-1.74 (2H, m), 1.60-1.53 (1H, m), 1.05 (3H, d, $J$ = 7.0 Hz), 0.98 (3H, d, $J$ = 7.0 Hz). For **85ak** (major diastereomer): $\delta$ 8.19 (2H, d, $J$ = 8.0 Hz), 7.77 (2H, d, $J$ = 8.0 Hz), 6.54 (1H, s, *vinylic*-C*H*), 3.79 (1H, d, $J$ = 7.0 Hz), 3.68 (1H, br s, *t*-O*H*), 2.93-2.84 (2H, m), 2.44-2.38 (1H, m), 2.18-2.10 (1H, m), 2.01-1.93 (1H, m), 1.86-1.74 (2H, m), 1.44-1.37 (1H, m), 1.11 (3H, d, $J$ = 7.0 Hz), 1.04 (3H, d, $J$ = 7.0 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): For **84ak**: $\delta$ 200.3 (C, *C*=O), 198.6 (C, *C*=O), 192.1 (C, *C*=O), 147.5 (C, C=*C*-OH), 139.8 (C), 135.0 (C, q, $J_{C\text{-}F}$ = 32.5 Hz), 128.6 (2 x CH), 126.1 (2 x CH, q, $J_{C\text{-}F}$ = 3.75 Hz), 123.4 (C, q, $J_{C\text{-}F}$ = 271.25 Hz, *C*$F_3$), 120.4 (*vinylic*-*C*H), 74.4 (C), 65.0 (C), 53.3 (CH), 51.8 (CH), 33.1 ($CH_2$), 30.1 (CH), 27.7 ($CH_2$), 22.4 ($CH_2$), 18.9 ($CH_3$), 18.1 ($CH_3$). For **85ak** (major diastereomer): $\delta$ 202.6 (C, *C*=O), 196.2 (C, *C*=O), 194.1 (C, *C*=O), 147.5 (C), 142.2 (CH, *vinylic*-*C*H), 139.6 (C), 134.9 (C, q, $J_{C\text{-}F}$ = 33.75 Hz), 129.5 (2 x CH), 125.6 (2 x CH, q, $J_{C\text{-}F}$ = 3.75 Hz), 123.5 (C, q, $J_{C\text{-}F}$ = 268.75 Hz, *C*$F_3$), 85.4 (C, *C*-OH), 73.9 (C), 56.6 (CH), 47.0 (CH), 33.0 ($CH_2$), 27.5 ($CH_2$), 26.9 (CH), 22.7 ($CH_2$), 21.7 ($CH_3$), 20.9 ($CH_3$). $^{19}F$ NMR (376.42 MHz, $CDCl_3$): $\delta$ -63.70, -63.21 (*C*$F_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{22}F_3O_4$ 407.1470; Found 407.1471.

**(3a*R**,7*S**,8*S**,8a*S**)-5-Hydroxy-7-isopropyl-8-(4-nitrobenzoyl)-1,2,3,7,8,8a-hexahydro-4*H*-3a,7-methanoazulene-4,9-dione (84al) and (3a*R**,7*S**,8*R**,8a*R**)-7-Hydroxy-5-isopropyl-8-(4-nitrobenzoyl)-1,2,3,7,8,8a-hexahydro-4*H*-3a,7-methanoazulene-4,9-dione (85al):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a white solid. Yield: 98% (75 mg). Mp: 138-140



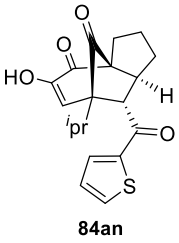

°C. IR (neat): $\nu_{max}$ 3409, 2961, 2871, 1766, 1678, 1525, 1345, 1319, 1214, 1024, 983, 910, 825 and 732 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): For **84al**: $\delta$ 8.353 (2H, d, $J$ = 9.0 Hz), 8.03 (2H, d, $J$ = 8.5 Hz), 6.53 (1H, s, *vinylic*-C*H*), 5.98 (1H, s, *enolic*-O*H*), 3.75 (1H, d, $J$ = 7.5 Hz), 2.90-2.86 (1H, m), 2.36-2.34 (1H, m), 2.18-2.11 (2H, m), 2.01-1.93 (1H, m), 1.85-1.79 (2H, m), 1.42-1.36 (1H, m), 1.05 (3H, d, $J$ = 7.0 Hz), 0.98 (3H, d, $J$ = 7.0 Hz). For **85al** (major diastereomer): $\delta$ 8.350 (2H, d, $J$ = 9.0 Hz), 8.24 (2H, d, $J$ = 8.5 Hz), 6.49 (1H, s, *vinylic*-C*H*), 3.78 (1H, d, $J$ = 7.0 Hz), 3.67 (1H, br s, *t*-O*H*), 2.90-2.86 (1H, m), 2.42 (1H, quint, $J$ = 6.5 Hz), 2.18-2.11 (2H, m), 2.01-1.93 (1H, m), 1.85-1.79 (2H, m), 1.42-1.36 (1H, m), 1.11 (3H, d, $J$ = 7.0 Hz), 1.04 (3H, d, $J$ = 7.0 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): for **84al:** $\delta$ 200.1 (C, *C*=O), 198.1 (C, *C*=O), 192.0 (C, *C*=O), 150.6 (C), 147.6 (C, C=*C*-OH), 141.7 (C), 129.2 (2 x CH), 124.2 (2 x CH), 120.1 (CH, *vinylic*-*C*H), 74.4 (C), 65.1 (C), 53.6 (CH), 51.6 (CH), 33.2 ($CH_2$), 30.2 (CH), 27.7 ($CH_2$), 22.4 ($CH_2$), 18.9 ($CH_3$), 18.1 ($CH_3$). for **85al** (major diastereomer)**:** $\delta$ 202.3 (C, *C*=O), 195.8 (C, *C*=O), 193.9 (C, *C*=O), 150.6 (C), 147.8 (C), 141.8 (C), 141.3 (CH, *vinylic*-*C*H), 130.3 (2 x CH), 123.8 (2 x CH), 85.4 (C, *C*-OH), 74.0 (C), 57.1 (CH), 46.9 (CH), 32.9 ($CH_2$), 27.5 ($CH_2$), 26.9 (CH), 22.7 ($CH_2$), 21.7 ($CH_3$), 20.9 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{21}H_{21}NO_6Na$ 406.1267; Found 406.1265.

**(3a*R**,7*S**,8*S**,8a*S**)-8-(Furan-2-carbonyl)-5-hydroxy-7-isopropyl-1,2,3,7,8,8a-hexahydro-4*H*-3a,7-methanoazulene-4,9-dione (84am):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a pale yellow solid. Yield: 97% (63.7 mg). Mp: 106-108 °C. IR (neat): $\nu_{max}$ 3411, 2960, 1759, 1667, 1564, 1463, 1387, 1247, 1046, 1015, 768 and 593 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.63 (1H, dd, $J$ = 1.5, 0.5 Hz), 7.25 (1H, dd, $J$ = 3.5, 0.5 Hz), 6.60 (1H, dd, $J$ = 3.5, 2.0 Hz), 6.50 (1H, s, *vinylic*-C*H*), 5.98 (1H, s, *enolic*-O*H*), 3.64 (1H, d, $J$ = 7.5 Hz), 2.43 (1H, q, $J$ = 7.5 Hz), 2.32-2.26 (1H, m), 2.18-2.10 (2H, m), 2.00-1.93 (1H, m), 1.82-1.71 (2H, m), 1.65-1.59 (1H, m), 1.07 (3H, d, $J$ = 7.0 Hz), 1.02 (3H, d, $J$ = 7.0 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 200.8 (C, *C*=O), 192.4 (C, *C*=O), 187.8 (C, *C*=O), 152.8 (C), 147.5 (C, C=*C*-OH), 146.9 (CH), 120.6 (CH, *vinylic*-*C*H), 118.0 (CH), 113.0 (CH), 74.4 (C), 64.8 (C), 53.2 (CH), 51.6 (CH), 32.7 ($CH_2$), 30.1 (CH), 27.4 ($CH_2$), 22.6 ($CH_2$), 18.6 ($CH_3$), 18.0 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{19}H_{21}O_5$ 329.1389; Found 329.1388.



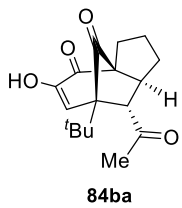
84am

**(3a*R**,7*S**,8*S**,8a*S**)-5-Hydroxy-7-isopropyl-8-(thiophene-2-carbonyl)-1,2,3,7,8,8a-hexahydro-4*H*-3a,7-methanoazulene-4,9-dione (84an):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a white solid. Yield: 98% (67.5 mg). Mp: 170-172 °C. IR (neat): $\nu_{max}$ 3358, 1763, 1643, 1403, 1384, 1316, 1243, 1214, 1064, 825, 719, 655, 544 and 450 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.73 (2H, d, $J$ = 4.5 Hz), 7.18 (1H, t, $J$ = 4.5 Hz), 6.56 (1H, s, *vinylic*-C*H*), 6.04 (1H, s, *enolic*-O*H*), 3.52 (1H, d, $J$ = 7.5 Hz), 2.41 (1H, q, $J$ = 7.5 Hz), 2.33-2.28 (1H, m), 2.22-2.12 (2H, m), 2.01-1.95 (1H, m), 1.84-1.72 (2H, m), 1.64-1.58 (1H, m), 1.06 (3H, d, $J$ = 6.5 Hz), 1.02 (3H, d, $J$ = 7.0 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 200.6 (C, *C*=O), 192.2 (C, *C*=O), 191.7 (C, *C*=O), 147.4 (C, C=*C*-OH), 144.6 (C), 135.2 (CH), 132.1 (CH), 128.5 (CH), 120.5 (CH, *vinylic*-*C*H), 74.4 (C), 65.1 (C), 54.6 (CH), 52.4 (CH), 32.9 ($CH_2$), 30.1 (CH), 27.5 ($CH_2$), 22.6 ($CH_2$), 18.6 ($CH_3$), 18.1 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{19}H_{20}O_4SNa$ 367.0980; Found 367.0984.



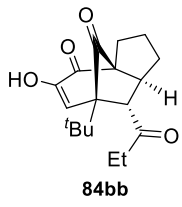
84an

**(3a*R**,7*S**,8*S**,8a*S**)-8-Acetyl-7-(*tert*-butyl)-5-hydroxy-1,2,3,7,8,8a-hexahydro-4*H*-3a,7-methanoazulene-4,9-dione (84ba):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a colourless sticky liquid. Yield: 88% (51 mg). IR (neat): $\nu_{max}$ 3411, 2957, 2922, 1692, 1670, 1648, 1598, 1401, 1364, 1330, 1259, 1183, 1152, 1115, 1077, 966, 893, 805, 736, 702, 593, 479, 459 and 422 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 6.72 (1H, *s*, *vinylic*-C*H*), 5.92 (1H, s, *enolic*-O*H*), 3.10 (1H, d, *J* = 7.0 Hz), 2.30-2.25 (1H, m), 2.24 (3H, s), 2.13 (2H, q, *J* = 7.0 Hz), 2.10-2.04 (1H, m), 1.81 (1H, sept, *J* = 6.5 Hz), 1.73 (1H, sept, *J* = 6.5 Hz), 1.58 (1H, sept, *J* = 6.0 Hz), 1.09 (9H, s, 3 x $CH_3$). $^{13}C$ NMR (100 MHz, $CDCl_3$, DEPT-135): $\delta$ 207.1 (C, *C*=O), 199.7 (C, *C*=O), 192.2 (C, *C*=O), 147.1 (C, C=*C*-OH), 122.0 (CH, *vinylic*-*C*H), 74.4 (C), 66.7 (C), 57.1 (CH), 50.6 (CH), 33.8 (C), 32.9 ($CH_2$), 31.1 ($CH_3$), 27.2 ($CH_2$), 26.5 (3 x $CH_3$), 22.9 ($CH_2$). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{17}H_{22}O_4Na$ 313.1416 Found. 313.1417.



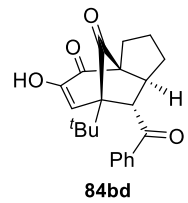
84ba

**(3a*R**,7*S**,8*S**,8a*S**)-7-(*tert*-Butyl)-5-hydroxy-8-propionyl-1,2,3,7,8,8a-hexahydro-4*H*-3a,7-methanoazulene-4,9-dione (84bb):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a colourless sticky liquid. Yield: 98% (59.6 mg). IR (Neat): $\nu_{max}$ 3410, 2957, 2873, 1755, 1715, 1669, 1633, 1467, 1391, 1368, 1307, 1252, 1211, 1128, 1104, 1064, 989, 949, 910, 731, 485, 468, 460, 451 and 428 $cm^{-1}$. $^1$HNMR (500 MHz, $CDCl_3$): $\delta$ 6.73 (1H, s), 5.94 (1H, s, *enolic*-O*H*), 3.09 (1H, d, *J* = 7.5 Hz), 2.63 (1H, qd, *J* = 18.5, 7.0 Hz), 2.49 (1H, qd, *J* = 18.2, 7.0 Hz), 2.30-2.24 (1H, m), 2.15-2.10 (2H, m), 2.08-2.01 (1H, m), 1.81 (1H, sept, *J* = 6.5 Hz), 1.70 (1H, sept, *J* = 6.5 Hz), 1.58 (1H, sextet, *J* = 6.5 Hz), 1.08 (9H, s, 3 x $CH_3$), 1.07 (3H, t, *J* = 7.5 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 209.9 (C, *C*=O), 199.8 (C, *C*=O), 192.2 (C, *C*=O), 147.2 (C), 122.1 (CH, *vinylic*-*C*H), 74.4 (C), 66.9 (C), 56.0 (CH), 51.1 (CH), 37.7 ($CH_2$), 33.8 (C), 33.1 ($CH_2$), 27.2 ($CH_2$), 26.5 (3 x $CH_3$), 22.9 ($CH_2$), 7.6 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{25}O_4$ 305.1753; Found: 305.1758.



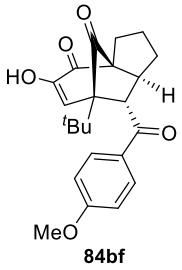
84bb

**(3a*R**,7*S**,8*S**,8a*S**)-8-Benzoyl-7-(*tert*-butyl)-5-hydroxy-1,2,3,7,8,8a-hexahydro-4*H*-3a,7-methanoazulene-4,9-dione (84bd):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a yellow solid. Mp: 133-135 °C. Yield: 96% (67.6 mg). IR (Neat): $\nu_{max}$ 3416, 2959, 2870, 1756, 1672, 1594, 1447, 1392, 1368, 1209, 1111, 1048, 1000, 848, 752, 701, 472, 432 and 425 $cm^{-1}$. $^{1}$HNMR (500 MHz, $CDCl_3$): $\delta$ 7.93 (2H, d, *J* = 7.5 Hz), 7.63 (1H, t, *J* = 7.5 Hz), 7.52 (2H, t, *J* = 8.0 Hz), 6.79 (1H, *s*, *vinylic*-C*H*), 5.97 (1H, s, *enolic*-O*H*), 4.01 (1H, d, *J* = 7.5 Hz), 2.28 (2H, m), 2.15 (1H, m), 1.93 (1H, sextet, *J* = 6.5 Hz), 1.81-1.72 (2H, m), 1.59 (1H, sextet, *J* = 6.5 Hz), 1.07 (9H, s, 3 x $CH_3$). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 200.1 (C, *C*=O), 200.0 (C, *C*=O), 122.1 (C, *C*=O), 147.3 (C), 137.2 (C), 133.8 (CH), 129.1 (2 x CH), 128.3 (2 x CH), 122.2 (CH, *vinylic*-*C*H), 74.6 (C), 68.1(C), 52.5 (CH), 50.2 (CH), 34.2 (C), 32.9 ($CH_2$), 27.4 ($CH_2$), 26.6 (3 x $CH_3$), 22.9 ($CH_2$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{25}O_4$ 353.1753; Found: 353.1752.

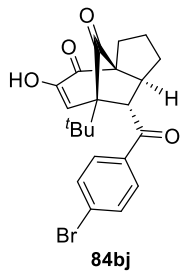


**84bd**

**(3a*R**,7*S**,8*S**,8a*S**)-7-(*tert*-Butyl)-5-hydroxy-8-(4-methoxybenzoyl)-1,2,3,7,8,8a-hexahydro-4*H*-3a,7-methanoazulene-4,9-dione (84bf):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a white solid. Yield: 97% (74 mg). Mp: 163-165 °C. IR (neat): $\nu_{max}$ 3410, 2958, 1755, 1666, 1596, 1573, 1391, 1239, 1210, 1169, 1022, 911, 850, 731, 609, 587, 509, 488, 462 and 438 $cm^{-1}$. $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.92 (2H, d, *J* = 9.0 Hz), 6.98 (2H, d, *J* = 9.0 Hz), 6.78 (1H, *s*, *vinylic*-C*H*), 5.98 (1H, s, *enolic*-O*H*), 3.94 (1H, d, *J* = 7.5 Hz), 3.89 (3H, s), 2.30 (1H, q, *J* = 6.5 Hz), 2.28-2.23 (1H, m), 2.17-2.11 (1H, m), 1.95-1.89 (1H, m), 1.80-1.70 (2H, m), 1.61-1.55 (1H, m), 1.06 (9H, s, 3 x $CH_3$). $^{13}$C NMR (100 MHz, $CDCl_3$, DEPT-135): $\delta$ 200.3 (C, *C*=O), 198.5 (C, *C*=O), 192.1 (C, *C*=O), 164.1 (C), 147.2 (C, C=*C*-OH), 130.7 (2 x CH), 130.2 (C), 122.4 (CH, *vinylic*-*C*H), 114.3 (2 x CH), 74.6 (C), 68.0 (C), 55.6 ($CH_3$, $OCH_3$), 52.6 (CH), 49.9 (CH), 34.2 (C), 32.8 ($CH_2$), 27.4 ($CH_2$), 26.6 (3 x $CH_3$), 23.0 ($CH_2$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{23}H_{27}O_5$ 383.1858; Found 383.1858.



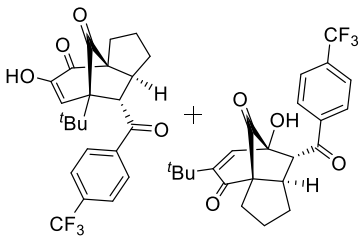
**84bf**

**(3a*R**,7*S**,8*S**,8a*S**)-8-(4-Bromobenzoyl)-7-(*tert*-butyl)-5-hydroxy-1,2,3,7,8,8a-hexahydro-4*H*-3a,7-methanoazulene-4,9-dione (84bj):** 

84bj

The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a white solid. Yield: 85% (73 mg). Mp: 163-165 °C. IR (neat): $\nu_{max}$ 3415, 2958, 2871, 1754, 1668, 1635, 1582, 1565, 1466, 1446, 1393, 1369, 1238, 1205, 1178, 1113, 1070, 1006, 973, 949, 908, 882, 848, 767, 727, 685, 647, 510, 486, 438 and 430 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.79 (2H, d, $J$ = 8.5 Hz), 7.65 (2H, d, $J$ = 8.0 Hz), 6.75 (1H, *s*, *vinylic*-C*H*), 5.98 (1H, br s, *enolic*-O*H*), 3.93 (1H, d, $J$ = 7.5 Hz), 2.33-2.27 (1H, m), 2.23 (1H, q, $J$ = 7.5 Hz), 2.14 (1H, quint, $J$ = 7.0 Hz), 1.93 (1H, sextet, $J$ = 6.5 Hz), 1.82-1.71 (2H, m), 1.56 (1H, sextet, $J$ = 7.0 Hz), 1.05 (9H, s, 3 x $CH_3$). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 199.8 (C, *C*=O), 199.0 (C, *C*=O), 191.9 (C, *C*=O), 147.4 (C), 135.8 (C), 132.5 (2 x CH), 129.7 (2 x CH), 129.2 (C), 121.8 (CH, *vinylic*-*C*H), 74.6 (C), 68.1 (C), 52.4 (CH), 50.2 (CH), 34.1 (C), 32.9 ($CH_2$), 27.4 ($CH_2$), 26.6 (3 x $CH_3$), 22.9 ($CH_2$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{24}BrO_4$ 431.0858; Found 431.0854.

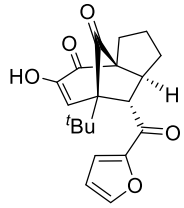
**(3a*R**,7*S**,8*S**,8a*S**)-7-(*tert*-Butyl)-5-hydroxy-8-(4-(trifluoromethyl)benzoyl)-1,2,3,7,8,8a-hexahydro-4*H*-3a,7-methanoazulene-4,9-dione (84bk) and (4b*S**,5*R**,6*S**,9a*R**)-8-(*tert*-Butyl)-6-hydroxy-5-(4-(trifluoromethyl)benzoyl)-4b,5,6,10-tetrahydro-9*H*-6,9a-methanobenzo[*a*]azulene-9,11-dione (85bk):** The compounds were prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a colourless solid. Yield: 80% (67 mg). Mp: 140-143 °C. IR (neat): $\nu_{max}$ 3468, 2964, 2873, 1758, 1674, 1513, 1408, 1393, 1321, 1208, 1171, 1132, 1065, 1013, 906, 8s50, 728, 648, 592 and 511 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): For **84bk**: $\delta$ 8.04 (2H, d, $J$ = 8.0 Hz), 7.79 (2H, d, $J$ = 8.5 Hz), 6.77 (1H, *s*, *vinylic*-C*H*), 6.09 (1H, br s, *enolic*-O*H*), 4.00 (1H, d, $J$ = 7.5 Hz), 2.32 (1H, quint, $J$ = 7.0 Hz), 2.25 (1H, q, $J$ = 7.5 Hz), 2.18-2.13 (1H, m), 2.00-1.92 (1H, m), 1.78 (2H, quint, $J$ = 6.5 Hz), 1.58 (1H, sextet, $J$ = 7.0 Hz), 1.06 (9H, s, 3 x $CH_3$). For **85bk** (major diastereomer): $\delta$ 8.19 (2H, d, $J$ = 8.0 Hz), 7.77 (2H, d, $J$ = 9.0 Hz), 6.62 (1H, *s*, *vinylic*-C*H*), 3.92 (1H, br s, *t*-O*H*), 3.81 (1H, d, $J$ = 7.0 Hz), 2.41-2.35 (1H, m), 2.25 (1H, q, $J$ = 7.5 Hz), 2.18-2.10 (1H, m), 2.00-1.92 (1H, m), 1.78 (2H, quint, $J$ = 6.5



84bk 85bk

Hz), 1.44-1.37 (1H, m), 1.21 (9H, s, 3 x $CH_3$). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): For **84bk**: $\delta$ 199.7 (C, *C*=O), 199.2 (C, *C*=O), 192.9 (C, *C*=O), 147.5 (C, C=*C*-OH), 139.8 (C), 135.0 (C, q, $J_{C\text{-}F}$ = 32.5 Hz), 128.6 (2 x CH), 126.2 (2 x CH, q, $J_{C\text{-}F}$ = 3.7 Hz), 123.4 (C, q, $J_{C\text{-}F}$ = 271.2 Hz, $CF_3$), 121.7 (CH, *vinylic*-*C*H), 74.6 (C), 68.2 (C), 52.3 (CH), 50.6 (CH), 34.1 (C), 33.0 ($CH_2$), 27.4 ($CH_2$), 26.6 (3 x $CH_3$), 22.9 ($CH_2$). For **85bk** (major diastereomer): $\delta$ 202.3 (C, *C*=O), 196.4 (C, *C*=O), 193.8 (C, *C*=O), 148.6 (C), 143.3 (CH, *vinylic*-*C*H), 139.7 (C), 134.9 (C, q, $J_{C\text{-}F}$ = 32.5 Hz), 129.5 (2 x CH), 125.6 (2 x CH, q, $J_{C\text{-}F}$ = 3.75 Hz), 123.4 (C, q, $J_{C\text{-}F}$ = 271.2 Hz), 85.5 (C, *C*-OH), 74.7 (C), 56.5 (CH), 46.7 (CH), 34.6 (C), 32.9 ($CH_2$), 27.3 ($CH_2$), 26.6 (3 x $CH_3$), 22.8 ($CH_2$). $^{19}F$ NMR (470.59 MHz, $CDCl_3$): $\delta$ -63.21 (*C*$F_3$), -63.24 (*C*$F_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{23}H_{24}F_3O_4$ 421.1627; Found 421.1627.

**(3a*R**,7*S**,8*S**,8a*S**)-7-(*tert*-Butyl)-8-(furan-2-carbonyl)-5-hydroxy-1,2,3,7,8,8a-hexahydro-4*H*-3a,7-methanoazulene-4,9-dione (84bm):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a colourless semisolid. Yield: 90% (61.5 mg). Mp: 172-174 °C. IR (neat): $\nu_{max}$ 3400, 3129, 2954, 1762, 1659, 1632, 1459, 1404, 1391, 1367, 1251, 1212, 1162, 1059, 1042, 918, 882, 832, 790, 767, 622, 592, 468, 457 and 411 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.65 (1H, s), 7.26 (1H, t, *J* = 3.5 Hz), 6.71 (1H, *s*, *vinylic*-C*H*), 6.61-6.01 (1H, m), 5.99 (1H, s, *enolic*-O*H*), 3.85 (1H, d, *J* = 7.5 Hz), 2.32 (H, q, *J* = 8.0 Hz), 2.29-2.23 (1H, m), 2.16 (1H, quint, *J* = 6.5 Hz), 1.93 (1H, sextet, *J* = 7.0 Hz), 1.83-1.75 (1H, m), 1.74-1.67 (1H, m), 1.07 (9H, s, 3 x $CH_3$). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 200.1 (C, *C*=O), 192.2 (C, *C*=O), 188.8 (C, *C*=O), 152.8 (C), 147.6 (C, C=*C*-OH), 147.0 (CH), 121.4 (CH, *vinylic*-*C*H), 117.9 (CH), 113.0 (CH), 74.6 (C), 67.9 (C), 52.1 (CH), 50.9 (CH), 34.1 (C), 32.6 ($CH_2$), 27.1 ($CH_2$), 26.4 (3 x $CH_3$), 23.1 ($CH_2$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{20}H_{23}O_5$ 343.1545; Found 343.1544.



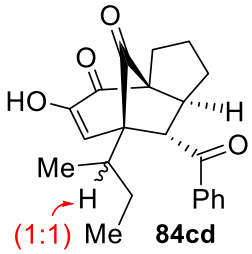
84bm

**(3a*R**,7*S**,8*S**,8a*S**)-8-Acetyl-7-(*sec*-butyl)-5-hydroxy-1,2,3,7,8,8a-hexahydro-4*H*-3a,7-methanoazulene-4,9-dione (84ca):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a colorless sticky liquid. Yield: 88% (51 mg). IR (neat): $\nu_{max}$ 3409, 2962, 2873, 1760, 1708, 1671, 1393, 1361, 1251, 1180, 1058, 702 and 495 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$, 1:1 *dr*): $\delta$ 6.53 (1H, *s*, *vinylic*-C*H*), 6.48 (1H, *s*, *vinylic*-C*H*), 5.91 (2H, s, *enolic*-O*H*), 2.99 (1H, d, *J* = 7.6 Hz), 2.96 (1H, d, *J* = 7.6 Hz), 2.38-2.26 (4H, m), 2.23 (3H, s), 2.228 (3H, s), 2.17-2.08 (4H, m), 1.94-1.87 (2H, m), 1.86-1.81 (2H, m), 1.80-1.72 (2H, m), 1.64-1.53 (4H, m), 1.48-1.40 (1H, m), 1.26-1.20 (1H, m), 1.09 (3H, d**,** *J* = 6.8 Hz), 1.07 (3H, d, *J* = 6.8 Hz), 1.00 (3H, t, *J* = 7.6 Hz), 0.99 (3H, t, *J* = 7.6 Hz). $^{13}C$ NMR (100 MHz, $CDCl_3$, DEPT-135, 1:1 *dr*): $\delta$ 205.7 (C, *C*=O), 205.6 (C, *C*=O), 200.5 (2 x C, *C*=O), 192.6 (C, *C*=O), 192.5 (C, *C*=O), 147.2 (C, C=*C*-OH), 147.1 (C, C=*C*-OH), 122.2 (CH, *vinylic*-*C*H), 121.7 (CH, *vinylic*-*C*H), 74.24 (C), 74.21 (C), 64.1 (C), 64.0 (C), 58. 5 (CH), 58.4 (CH), 49.8 (CH), 49.5 (CH), 37.4 (CH), 37.1 (CH), 33.2 ($2CH_2$), 30.4 ($CH_3$), 30.36 ($CH_3$), 27.48 ($CH_2$), 27.46 ($CH_2$), 25.2 ($CH_2$) 24.7 ($CH_2$), 22.4 ($2CH_2$), 14.8 ($CH_3$), 14.0 ($CH_3$), 13.0 ($CH_3$), 12.7 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{23}O_4$ 291.1596; Found 291.1592.

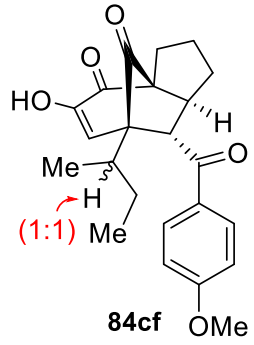
**(3a*R**,7*S**,8*S**,8a*S**)-7-(*sec*-Butyl)-5-hydroxy-8-propionyl-1,2,3,7,8,8a-hexahydro-4*H*-3a,7-methanoazulene-4,9-dione (84cb):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a colorless sticky liquid. Yield: 85% (52 mg). IR (neat): $\nu_{max}$ 2968, 2926, 1720, 1672, 1596, 1446, 1372, 1282, 1256, 1231, 1105, 1043, 767, 750 and 422 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$, 1:1 *dr*): $\delta$ 6.51 (1H, *s*, *vinylic*-C*H*), 6.46 (1H, *s*, *vinylic*-C*H*), 5.95 (2H, s, *enolic*-O*H*), 2.95 (1H, d, *J* = 8.0 Hz), 2.91 (1H, d, *J* = 7.5 Hz), 2.56-2.43 (4H, m), 2.33-2.24 (4H, m), 2.13-2.03 (4H, m), 1.89-1.83 (2H, m), 1.80 (2H, q, *J* = 7.0 Hz), 1.73 (2H, quint, *J* = 6.5 Hz), 1.65-1.47 (4H, m), 1.45-1.37 (1H, m), 1.23-1.14 (1H, m), 1.064 (6H, t, *J* = 7.0 Hz), 1.060 (3H, t, *J* = 7.0 Hz), 1.02 (3H, d, *J* = 6.5 Hz), 0.97 (3H, t, *J* = 7.5 Hz), 0.96 (3H, t, *J* = 7.5 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135, 1:1 *dr*): $\delta$ 208.7 (C, *C*=O), 208.5 (C, *C*=O), 200.6 (2C, *C*=O), 192.5 (C, *C*=O), 192.4 (C, *C*=O), 147.1 (C, C=*C*-OH), 147.0 (C, C=*C*-OH), 122.3 (CH, *vinylic*-*C*H), 121.7 (CH, *vinylic*-

*C*H), 74.2 (C), 74.1 (C), 64.3 (C), 64.2 (C), 57.6 (CH), 57.4 (CH), 50.3 (CH), 49.9 (CH), 37.3 (CH), 37.0 (CH), 36.6 ($CH_2$), 36.5 ($CH_2$), 33.2 ($2CH_2$), 27.45 ($CH_2$ ), 27.42 ($CH_2$ ), 25.2 ($CH_2$), 24.7 ($CH_2$), 22.4 ($2CH_2$), 14.8 ($CH_3$), 13.9 ($CH_3$), 12.9 ($CH_3$), 12.6 ($CH_3$), 7.55 ($CH_3$), 7.51 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{25}O_4$ 305.1753; Found 305.1750.

**(3a*R**,7*S**,8*S**,8a*S**)-8-Benzoyl-7-(*sec*-butyl)-5-hydroxy-1,2,3,7,8,8a-hexahydro-4*H*-3a,7-methanoazulene-4,9-dione (84cd):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a colorless sticky liquid. Yield: 90% (63 mg). IR (neat): $\nu_{max}$ 3416, 2962, 2932, 2873, 1758, 1670, 1595, 1447, 1347, 1396, 1309, 1215, 1055, 1001, 912, 845, 754 and 689 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$, 1:1 *dr*): $\delta$ 7.88 (4H, d, *J* = 8.0 Hz), 7.62 (2H, t, *J* = 7.5 Hz), 7.5 (4H, t, *J* = 7.5 Hz), 6.59 (1H, *s*, *vinylic*-C*H*), 6.58 (1H, *s*, *vinylic*-C*H*), 5.96 (1H, s, *enolic*-O*H*), 5.95 (1H, s, *enolic*-O*H*), 3.80 (1H, d, *J* = 8.0 Hz), 3.77 (1H, d, *J* = 7.5 Hz), 2.33 (4H, sextet, *J* = 7.5 Hz), 2.13 (2H, quint, *J* = 6.5 Hz), 1.94 (2H, sextet, *J* = 6.5 Hz), 1.84-1.73 (6H, m), 1.65-1.53 (4H, m), 1.38 (1H, sept, *J* = 7.0 Hz), 1.16-1.06 (1H, m), 1.01 (3H, d**,** *J* = 7.0 Hz), 0.94 (3H, d, *J* = 7.0 Hz), 0.89 (3H, t, *J* = 7.5 Hz), 0.87 (3H, t, *J* = 7.5 Hz). $^{13}C$ NMR (100 MHz, $CDCl_3$, DEPT-135, 1:1 *dr*): $\delta$ 200.8 (2C, 2*C*=O), 199.4 (2C, 2*C*=O), 192.3 (C, *C*=O), 192.2 (C, *C*=O), 147.2 (C, C=*C*-OH), 147.1 (C, C=*C*-OH), 137.2 (C), 137.1 (C), 133.7 (2CH), 128.9 (2 x 2CH), 128.3 (2 x 2CH), 121.9 (CH, *vinylic*-*C*H), 120.9 (CH, *vinylic*-*C*H), 74.3 (2C), 65.6 (C), 65.5 (C), 52.8 (CH), 52.7 (CH), 51.95 (CH), 51.91 (CH), 37.16 (CH), 37.09 (CH), 33.1 ($CH_2$), 33.0 ($CH_2$), 27.6 ($2CH_2$), 25.7 ($CH_2$), 25.1 ($CH_2$), 24.44 ($CH_2$), 22.39 ($CH_2$), 15.2 ($CH_3$), 14.3 ($CH_3$), 12.6 ($2CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{25}O_4$ 353.1753; Found 353.1751.

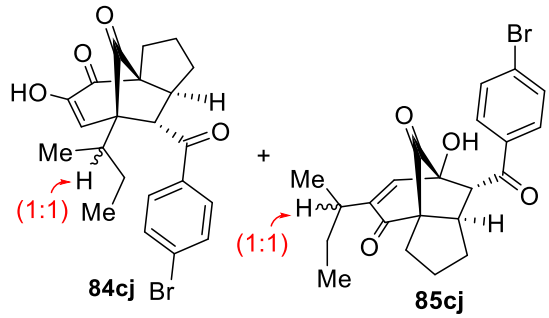


**(3a*R**,7*S**,8*S**,8a*S**)-7-(*sec*-Butyl)-5-hydroxy-8-(4-methoxybenzoyl)-1,2,3,7,8,8a-hexahydro-4*H*-3a,7-methanoazulene-4,9-dione (84cf):** The compound was prepared following




**Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a colorless semi solid. Yield: 98% (74.7 mg). IR (neat): $\nu_{max}$ 3401, 2961, 1758, 1667, 1600, 1573, 1396, 1260, 1220, 1170, 1026, 837 and 511 $cm^{-1}$. $^{1}H$ NMR (500 MHz, $CDCl_3$, 1:1 *dr*): $\delta$ 7.88 (4H, d, *J* = 8.5 Hz), 6.97 (2H, d, *J* = 9.0 Hz), 6.96 (2H, d, *J* = 9.0 Hz), 6.60 (1H, *s*, *vinylic*-C*H*), 6.59 (1H, *s*, *vinylic*-C*H*), 5.95 (1H, s, *enolic*-O*H*), 5.94 (1H, s, *enolic*-O*H*), 3.889 (3H, s, OC$H_3$), 3.887 (3H, s, OC$H_3$), 3.74 (1H, d, *J* = 7.5 Hz), 3.70 (1H, d, *J* = 7.5 Hz), 2.37-2.26 (4H, m), 2.17-2.09 (2H, m), 1.98-1.90 (2H, m), 1.84-1.73 (6H, m), 1.68-1.52 (4H, m), 1.41-1.34 (1H, m), 1.13-1.07 (1H, m), 1.01 (3H, d**,** *J* = 6.5 Hz), 0.93 (3H, d, *J* = 7.0 Hz), 0.91 (3H, t, *J* = 7.5 Hz), 0.87 (3H, t, *J* = 7.5 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135, 1:1 *dr*): $\delta$ 201.0 (C, *C*=O), 200.9 (C, *C*=O), 197.7 (C, *C*=O), 197.6 (C, *C*=O), 192.3 (C, *C*=O), 192.2 (C, *C*=O), 164.4 (C), 164.0 (C), 147.1 (C, C=*C*-OH), 146.9 (C, C=*C*-OH), 130.7 (2 x 2CH), 122.2 ( CH, *vinylic*-*C*H), 121.1 (CH, *vinylic*-*C*H), 114.1 (2 x 2CH), 74.3 (C), 74.2 (C), 65.6 (C), 65.5 (C), 55.5 ($2CH_3$), 52.5 (CH), 52.3 (2CH), 52.2 (CH), 37.2 (CH), 37.1 (CH), 32.99 ($CH_2$), 32.92 ($CH_2$), 27.7 ($CH_2$), 27.6 ($CH_2$), 25.6 ($CH_2$), 25.2 ($CH_2$), 22.5 ($CH_2$), 22.4 ($CH_2$), 15.1 ($CH_3$), 14.3 ($CH_3$), 12.62 ($CH_3$), 12.56 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{23}H_{27}O_5$ 383.1858; Found 383.1858.

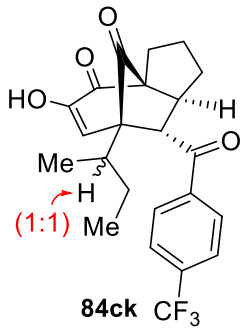
**(3a*R**,7*S**,8*S**,8a*S**)-8-(4-Bromobenzoyl)-7-(*sec*-butyl)-5-hydroxy-1,2,3,7,8,8a-hexahydro-4*H*-3a,7-methanoazulene-4,9-dione (84cj) and (3a*R**,7*S**,8*R**,8a*R**)-8-(4-Bromobenzoyl)-5-(*sec*-butyl)-7-hydroxy-1,2,3,7,8,8a-hexahydro-4*H*-3a,7-methanoazulene-4,9-dione (85cj):**



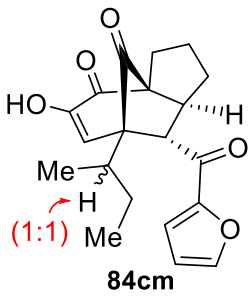

The mixture of compounds was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and the mixture isolated as a colorless sticky liquid. Yield: 98% (84.5 mg). IR (neat): $\nu_{max}$ 3423, 2961, 1760, 1669, 1583, 1461, 1396, 1213, 1070, 1007, 910, 765, 730 and 440 $cm^{-1}$. $^{1}H$ NMR (500 MHz, $CDCl_3$, 1:1 *dr*): For **84cj** $\delta$ 7.76 (4H, d, *J* = 8.0 Hz), 7.64 (4H, d, *J* = 7.0 Hz), 6.56 (1H, *s*, *vinylic*-C*H*), 6.55

(1H, *s*, *vinylic*-C*H*), 6.04 (1H, s, *enolic*-O*H*), 6.03 (1H, s, *enolic*-O*H*), 3.73 (1H, d, *J* = 7.5 Hz), 3.71 (1H, d, *J* = 7.5 Hz), 2.87-2.82 (1H, m), 2.73-2.56 (1H, m), 2.35-2.30 (2H, m), 2.12 (2H, sextet, *J* = 7.0 Hz), 1.94 (2H, sextet, *J* = 6.5 Hz), 1.79-1.73 (4H, m), 1.64-1.50 (4H, m), 1.48-1.33 (4H, m), 1.01 (3H, d, *J* = 7.0 Hz), 0.93 (3H, d**,** *J* = 7.0 Hz), 0.92 (3H, t, *J* = 7.0 Hz), 0.87 (3H, t, *J* = 7.5 Hz). For **85cj** (major diastereomer): *δ* 7.93 (4H, d, *J* = 8.5 Hz), 7.64 (4H, d, *J* = 7.0 Hz), 6.57 (2H, *s*, *vinylic*-C*H*), 3.81 (2H, br s, *t*-O*H*), 3.73 (2H, d, *J* = 7.5 Hz), 2.41-2.37 (2H, m), 2.35-2.30 (2H, m), 2.12 (2H, sextet, *J* = 7.0 Hz), 1.94 (2H, sextet, *J* = 6.5 Hz), 1.79-1.76 (4H, m), 1.64-1.50 (4H, m), 1.48-1.33 (4H, m), 1.08 (3H, d, *J* = 7.0 Hz), 1.01 (3H, d, *J* = 7.0 Hz), 0.87 (3H, t**,** *J* = 7.5 Hz), 0.81 (3H, t**,** *J* = 7.5 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135, 1:1 *dr*): For **84cj**: *δ* 200.59 (C, *C*=O), 200.56 (C, *C*=O), 198.40 (C, *C*=O), 198.38 (C, *C*=O), 192.2 (C, *C*=O), 192.1 (C, *C*=O), 147.4 (C, C=*C*-OH), 147.2 (C, C=*C*-OH), 135.84 (C), 135.81 (C), 132.3 (2 x 2CH), 129.7 (2 x 2CH), 129.2 (C), 129.1 (C), 121.6 (CH, *vinylic*-*C*H), 120.7 (CH, *vinylic*-*C*H), 74.32 (C), 74.30 (C), 65.7 (C), 65.6 (C), 52.8 (CH), 52.7 (CH), 51.89 (CH), 51.87 (CH), 37.2 (CH), 37.1 (CH), 33.1 ($CH_2$ ), 33.0 ($CH_2$), 27.69 ($CH_2$), 27.67 ($CH_2$), 25.7 ($CH_2$), 25.2 ($CH_2$), 22.44 ($CH_2$), 22.39 ($CH_2$), 15.2 ($CH_3$), 14.3 ($CH_3$), 12.62 ($CH_3$), 12.57 ($CH_3$). For **85cj** (major diastereomer): *δ* 202.9 (C, *C*=O), 202.8 (C, *C*=O), 196.03 (C, *C*=O), 195.98 (C, *C*=O), 194.54 (C, *C*=O), 194.48 (C, *C*=O), 146.40 (C), 146.2 (C), 143.6 (CH, *vinylic*-*C*H), 143.5 (CH, *vinylic*-*C*H), 132.3 (2C), 131.9 (2 x 2CH), 130.7 (2 x 2CH), 129.9 (2C), 85.66 (C, *C*-OH), 85.50 (C, *C*-OH), 73.94 (C), 73.89 (C), 56.19 (CH), 56.16 (CH), 47.2 (CH), 47.1 (CH), 33.6 (CH), 33.4 (CH), 32.96 ($CH_2$), 32.92 ($CH_2$), 28.8 ($CH_2$), 28.1 ($CH_2$), 27.50 ($CH_2$), 27.47 ($CH_2$), 22.84 ($CH_2$), 22.79 ($CH_2$), 19.3 ($CH_3$), 18.67 ($CH_3$), 11.7 ($2CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{24}BrO_4$ 431.0858; Found 431.0859.

**(3a*R**,7*S**,8*S**,8a*S**)-7-(*sec*-Butyl)-5-hydroxy-8-(4-(trifluoromethyl)benzoyl)-1,2,3,7,8,8a-hexahydro-4*H*-3a,7-methanoazulene-4,9-dione (84ck):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a colorless liquid. Yield: 85% (71.5 mg). IR (neat): $\nu_{max}$ 3459, 2966, 2931, 2874, 1759, 1674, 1510, 1461, 1407, 1322, 1215, 1170, 1131, 1066, 1013, 905, 849, 728, 648, 541 and 509 $cm^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$, 1:1 *dr*): *δ* 7.99 (4H, d, *J* = 8.5 Hz), 7.76 (4H, d, *J* = 7.0 Hz), 6.57 (1H, s, *vinylic*-C*H*), 6.56 (1H, s, *vinylic*-C*H*), 6.10 (2H,



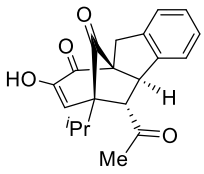
br s, *enolic*-O*H*), 3.80 (1H, d, *J* = 8.0 Hz), 3.76 (1H, d, *J* = 7.5 Hz), 2.34 (4H, quint, *J* = 7.5 Hz), 2.17-2.10 (2H, m), 1.95 (2H, sextet, *J* = 6.0 Hz), 1.84-1.74 (6H, m), 1.59-1.52 (4H, m), 1.39-1.06 (2H, m), 1.01 (3H, d**,** *J* = 7.0 Hz), 0.93 (3H, d, *J* = 7.0 Hz), 0.91 (3H, t, *J* = 7.5 Hz), 0.88 (3H, t, *J* = 7.5 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135, 1:1 *dr*): *δ* 200.39 (C, *C*=O), 200.36 (C, *C*=O), 198.6 (C, *C*=O), 198.5 (C, *C*=O), 192.12 (C, *C*=O), 192.06 (C, *C*=O), 147.46 (C, C=*C*-OH), 147.33 (C, C=*C*-OH), 139.8 (2C), 134.9 (2C, q, $J_{C\text{-}F}$ = 32.5 Hz), 128.6 (2 x 2CH), 126.0 (2 x 2CH, q, $J_{C\text{-}F}$ = 3.75 Hz), 123.4 (2C, q, $J_{C\text{-}F}$ = 271.2 Hz, 2*C*$F_3$), 121.4 (CH, *vinylic*-*C*H), 120.5 (CH, *vinylic*-*C*H), 74.32 (C), 74.30 (C), 65.7 (C), 65.6 (C), 53.2 (CH), 53.1 (CH), 51.7 (2CH), 37.2 (CH), 37.1 (CH), 33.2 ($CH_2$), 33.1 ($CH_2$), 27.68 ($CH_2$), 27.66 ($CH_2$), 25.8 ($CH_2$), 25.1 ($CH_2$), 22.4 ($CH_2$), 22.3 ($CH_2$), 15.3 ($CH_3$), 14.3 ($CH_3$), 12.6 ($CH_3$), 12.5 ($CH_3$). $^{19}$F NMR (470.59 MHz, $CDCl_3$): *δ* -63.11, -63.22, -63.23 (*C*$F_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{23}H_{24}F_3O_4$ 421.1627; Found 421.1625.

**(3a*R**,7*S**,8*S**,8a*S**)-7-(*sec*-Butyl)-8-(furan-2-carbonyl)-5-hydroxy-1,2,3,7,8,8a-hexahydro-4*H*-3a,7-methanoazulene-4,9-dione (84cm):** 

**84cm**

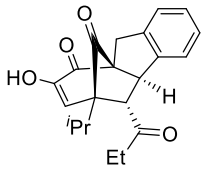
The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a colorless liquid. Yield: 98% (67 mg). IR (neat): $\nu_{max}$ 2962, 2929, 1760, 1670, 1565, 1463, 1395, 1275, 1251, 1165, 1087, 1047, 882, 765, 538, 512, 454, 430 and 421 $cm^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$, 1:1 *dr*): *δ* 7.63 (2H, s), 7.25 (2H, t, *J* = 6.0 Hz), 6.61-6.60 (2H, m), 6.51 (2H, s, *vinylic*-C*H*), 5.94 (1H, s, *enolic*-O*H*), 5.93 (1H, s, *enolic*-O*H*), 3.67 (1H, d, *J* = 7.5 Hz), 3.64 (1H, d, *J* = 7.5 Hz), 2.42 (2H, q, *J* = 7.5 Hz), 2.29 (2H, quint, *J* = 7.5 Hz), 2.15 (2H, quint, *J* = 7.0 Hz), 1.96 (2H, sept, *J* = 6.5 Hz), 1.83-1.73 (4H, m), 1.63-1.58 (4H, m), 1.41 (2H, quint, *J* = 7.5 Hz), 1.16-1.08 (2H, m), 1.04 (3H, d**,** *J* = 6.5 Hz, ), 0.97 (3H, d, *J* = 7.0 Hz), 0.93 (3H, t, *J* = 7.5 Hz), 0.91 (3H, t, *J* = 7.5 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135, 1:1 *dr*): *δ* 200.8 (2C, 2*C*=O), 192.4 (C, *C*=O), 192.3 (C, *C*=O), 187.9 (C, *C*=O), 187.8 (C, *C*=O), 152.7 (2C), 147.5 (C, C=*C*-OH), 147.3 (C, C=*C*-OH), 146.93 (CH), 146.91 (CH), 121.5 (CH, *vinylic*-*C*H), 120.6 (CH, *vinylic*-*C*H), 118.0 (CH), 117.9 (CH), 112.9 (2CH), 74.4 (C), 74.3 (C), 65.5 (C), 65.4 (C), 53.1 (2CH), 51.6 (CH), 51.5 (CH), 37.1 (2CH), 32.8 ($CH_2$), 32.7 ($CH_2$), 27.4 (2$CH_2$), 25.5 ($CH_2$), 24.9 ($CH_2$), 22.60 ($CH_2$), 22.57 ($CH_2$), 14.9 ($CH_3$), 14.1 ($CH_3$), 12.7 (2$CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{20}H_{23}O_5$ 343.1545; Found 343.1547.

**(4b*R**,5*S**,6*S**,9a*R**)-5-Acetyl-8-hydroxy-6-isopropyl-4b,5,6,10-tetrahydro-9*H*-6,9a-methanobenzo[*a*]azulene-9,11-dione (84da):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a colourless liquid. Yield: 98% (65 mg). IR (neat): $\nu_{max}$ 3411, 2967, 1761, 1706, 1672, 1388, 1239, 1165, 1079, 1042, 946, 913, 734, 701 and 460 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.27, (1H, d, $J$ = 7.5 Hz), 7.26 (1H, t, $J$ = 8.0 Hz), 7.22 (1H, t, $J$ = 8.0 Hz), 7.07 (1H, d, $J$ = 7.5 Hz), 6.35 (1H, s, *vinylic*-C*H*), 6.03 (1H, br s, *enolic*-O*H*), 3.86 (1H, d, $J$ = 6.5 Hz), 3.74 (1H, d, $J$ = 17.0 Hz), 3.46 (1H, d, $J$ = 17.0 Hz), 3.32 (1H, d, $J$ = 6.5 Hz), 2.43 (3H, s), 2.22 (1H, sept, $J$ = 7.0 Hz), 1.15 (3H, d, $J$ = 7.0 Hz), 1.13 (3H, d, $J$ = 7.0 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 205.7 (C, *C*=O), 199.3 (C, *C*=O), 191.5 (C, *C*=O), 148.4 (C, C=*C*-OH), 141.2 (C), 139.9 (C), 128.3 (CH), 127.6 (CH), 125.6 (CH), 123.9 (CH), 120.8 (CH, *vinylic*-*C*H), 72.8 (C), 62.9 (C), 58.8 (CH), 53.6 (CH), 31.6 (CH), 30.5 ($CH_3$), 27.9 ($CH_2$), 18.2 ($CH_3$), 17.6 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{20}H_{21}O_4$ 325.1440; Found 325.1445.



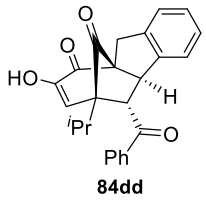
**84da**

**(4b*R**,5*S**,6*S**,9a*R**)-8-Hydroxy-6-isopropyl-5-propionyl-4b,5,6,10-tetrahydro-9*H*-6,9a-methanobenzo[*a*]azulene-9,11-dione (84db):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a colourless liquid. Yield: 98% (66 mg). IR (neat): $\nu_{max}$ 3406, 2969, 1760, 1710, 1671, 1458, 1388, 1237, 1111, 1057, 1021, 946, 909, 728, 648 and 458 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.28 (1H, d, $J$ = 7.5 Hz), 7.25 (1H, t, $J$ = 7.5 Hz), 7.22 (1H, t, $J$ = 7.5 Hz), 7.05 (1H, d, $J$ = 7.5 Hz), 6.33 (1H, *s*, *vinylic*-C*H*), 6.03 (1H, s, *enolic*-O*H*), 3.84 (1H, d, $J$ = 6.5 Hz), 3.74 (1H, d, $J$ = 17.0 Hz), 3.46 (1H, d, $J$ = 17.0 Hz), 3.30 (1H, d, $J$ = 6.5 Hz), 2.79-2.66 (2H, m), 2.17 (1H, sept, $J$ = 7.0 Hz), 1.18 (3H, t, $J$ = 7.0 Hz), 1.13 (3H, d, $J$ = 7.0 Hz), 1.12 (3H, d, $J$ = 7.0 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 208.7 (C, *C*=O), 199.4 (C, *C*=O), 191.5 (C, *C*=O), 148.3 (C, C=*C*-OH), 141.2 (C), 140.0 (C), 128.2 (CH), 127.6 (CH), 125.6 (CH), 123.9 (CH), 121.0 (CH, *vinylic*-*C*H), 72.7 (C), 63.1 (C), 57.9 (CH), 54.0 (CH), 37.9 ($CH_2$), 30.5 (CH), 27.9 ($CH_2$), 18.2 ($CH_3$), 17.7 ($CH_3$), 7.8 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{23}O_4$ 339.1596; Found 339.1593.



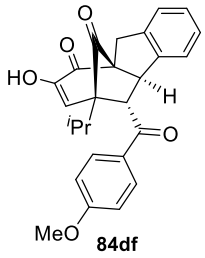
**84db**

**(4b*R**,5*S**,6*S**,9a*R**)-5-Benzoyl-8-hydroxy-6-isopropyl-4b,5,6,10-tetrahydro-9*H*-6,9a-methanobenzo[*a*]azulene-9,11-dione (84dd):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a white solid. Yield: 94% (72.6 mg). Mp: 216-218 °C. IR (neat): $\nu_{max}$ 3348, 2923, 1757, 1681, 1662, 1594, 1398, 1371, 1219, 1188, 1154, 1074, 1024, 973, 955, 791, 755, 720, 701, 678, 628, 607 and 554 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.00 (2H, d, $J$ = 7.5 Hz), 7.68 (1H, t, $J$ = 7.5 Hz), 7.55 (2H, t, $J$ = 7.5 Hz), 7.29 (1H, d, $J$ = 7.5 Hz), 7.23 (1H, t, $J$ = 7.5 Hz), 7.10 (1H, t, $J$ = 7.5 Hz), 6.72 (1H, d, $J$ = 7.5 Hz), 6.41 (1H, s, *vinylic*-C*H*), 6.13 (1H, s, *enolic*-O*H*), 4.14 (1H, d, $J$ = 7.5 Hz), 3.89 (1H, d, $J$ = 7.5 Hz), 3.79 (1H, d, $J$ = 17.0 Hz), 3.53 (1H, d, $J$ = 17.0 Hz), 2.04 (1H, sept, $J$ = 7.0 Hz), 1.00 (3H, d, $J$ = 7.0 Hz), 0.96 (3H, d, $J$ = 7.0 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 199.8 (C, *C*=O), 199.7 (C, *C*=O), 191.2 (C, *C*=O), 148.5 (C, C=*C*-OH), 141.3 (C), 139.7 (C), 137.5 (C), 134.0 (CH) 129.1 (2 x CH), 128.6 (2 x CH), 128.2 (CH), 127.4 (CH), 125.7 (CH), 124.3 (CH), 119.9 (CH, *vinylic*-*C*H), 72.7 (C), 65.1 (C), 57.0 (CH), 52.3 (CH), 30.1 (CH), 27.8 ($CH_2$), 18.6 ($CH_3$), 18.0 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{25}H_{22}O_4Na$ 409.1416; Found 409.1419.



**84dd**

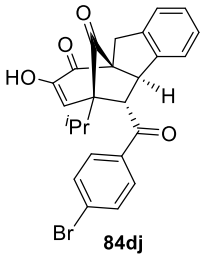
**(4b*R**,5*S**,6*S**,9a*R**)-8-Hydroxy-6-isopropyl-5-(4-methoxybenzoyl)-4b,5,6,10-tetrahydro-9*H*-6,9a-methanobenzo[*a*]azulene-9,11-dione (84df):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a white solid. Yield: 94% (78.3 mg). Mp: 187-189 °C. IR (neat): $\nu_{max}$ 3345, 1758, 1674, 1660, 1595, 1398, 1385, 1372, 1271, 1221, 1170, 749, 732 and 593 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.00, (2H, d, $J$ = 9.0 Hz), 7.29 (1H, d, $J$ = 8.0 Hz), 7.23 (1H, t, $J$ = 7.5 Hz), 7.09 (1H, t, $J$ = 7.5 Hz), 7.01 (2H, d, $J$ = 9.0 Hz), 6.73 (1H, d, $J$ = 7.5 Hz), 6.44 (1H, *s*, *vinylic*-C*H*), 6.17 (1H, br s, *enolic*-O*H*), 4.06 (1H, d, $J$ = 7.5 Hz), 3.92 (3H, s), 3.85 (1H, d, $J$ = 7.0 Hz), 3.78 (1H, d, $J$ = 17.0 Hz), 3.52 (1H, d, $J$ = 17.0 Hz), 2.07 (1H, sept, $J$ = 7.0 Hz), 1.10 (3H, d, $J$ = 7.0 Hz), 0.96 (3H, d, $J$ = 7.0 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 200.0 (C, *C*=O), 197.9 (C, *C*=O), 191.2 (C, *C*=O), 164.3 (C), 148.3 (C, C=*C*-OH), 141.2 (C), 139.9 (C), 131.1 (2 x CH) 130.3 (C), 128.1 (CH), 127.3 (CH), 125.6 (CH), 124.3 (CH), 120.2 (CH, *vinylic*-*C*H), 114.3 (2 x CH), 72.6 (C),



**84df**

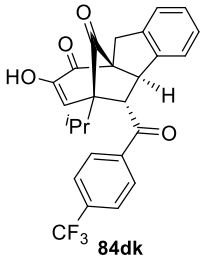
65.0 (C), 57.3 (CH), 55.6 ($CH_3$), 51.9 (CH), 30.1 (CH), 27.7 ($CH_2$), 18.5 ($CH_3$), 18.0 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{26}H_{25}O_5$ 417.1702; Found 417.1700.

**(4b*R**,5*S**,6*S**,9a*R**)-5-(4-Bromobenzoyl)-8-hydroxy-6-isopropyl-4b,5,6,10-tetrahydro-9*H*-6,9a-methanobenzo[*a*]azulene-9,11-dione (84dj):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as colourless liquid: 98% (92 mg). Mp: 175-178 °C. IR (neat): $\nu_{max}$ 3420, 1760, 1664, 1581, 1398, 1247, 1216, 1071, 1005, 977, 910 and 752 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.87 (2H, td, *J* = 9.0, 2.0 Hz), 7.70 (2H, td, *J* = 9.0, 2.0 Hz), 7.30 (1H, d, *J* = 7.5 Hz), 7.25 (1H, t, *J* = 7.5 Hz), 7.12 (1H, t, *J* = 7.5 Hz), 6.70 (1H, d, *J* = 7.5 Hz), 6.39 (1H, s, *vinylic*-C*H*), 6.11 (1H, s, *enolic*-O*H*), 4.06 (1H, d, *J* = 7.5 Hz), 3.87 (1H, d, *J* = 7.5 H), 3.79 (1H, *J* = 17.0 Hz), 3.52 (1H, d, *J* = 17.0 Hz), 2.04 (1H, sept, *J* = 7.0 Hz), 0.99 (3H, d, *J* = 6.5 Hz), 0.95 (3H, d, *J* = 7.0 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 199.6 (C, *C*=O), 198.7 (C, *C*=O), 191.1 (C, *C*=O), 148.6 (C, C=*C*-OH), 141.3 (C), 139.6 (C), 136.1 (C), 132.6 (2 x CH), 130.0 (2 x CH), 129.6 (C), 128.3 (CH), 127.5 (CH), 125.8 (CH), 124.2 (CH), 119.5 (CH, *vinylic*-*C*H), 72.6 (C), 65.2 (C), 57.2 (CH), 52.3 (CH), 30.1 (CH), 27.8 ($CH_2$), 18.6 ($CH_3$), 18.0 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{25}H_{22}BrO_4$ 465.0701; Found 465.0700.



84dj

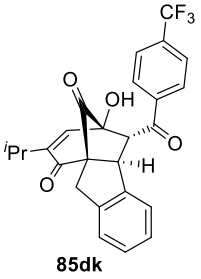
**(4b*R**,5*S**,6*S**,9a*R**)-8-Hydroxy-6-isopropyl-5-(4-(trifluoromethyl)benzoyl)-4b,5,6,10-tetrahydro-9*H*-6,9a-methanobenzo[*a*]azulene-9,11-dione (84dk):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a white solid. Yield: 78% (71 mg). Mp: 154-156 °C. IR (neat) $\nu_{max}$ 3429, 1762, 1675, 1388, 1320, 1216, 1169, 1130, 1112, 1013, 908, 855, 832, 750, 730 and 424 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.11 (2H, d, *J* = 8.0 Hz), 7.82 (2H, d, *J* = 8.0 Hz), 7.31 (1H, d, *J* = 7.5 Hz), 7.26 (1H, t, *J* = 7.5 Hz), 7.13 (1H, t, *J* = 7.5 Hz), 6.70 (1H, d, *J* = 7.5 Hz), 6.37 (1H, *s*, *vinylic*-C*H*), 6.13 (1H, s, *enolic*-O*H*), 4.13 (1H, d, *J* = 7.0 Hz), 3.91 (1H, d, *J* = 7.0 H), 3.80 (1H, d, *J* = 17.0 Hz), 3.54 (1H, d, *J* = 17.0 Hz), 2.03 (1H, sept, *J* = 7.0 Hz), 1.00 (3H, d, *J* = 7.0 Hz), 0.95 (3H, d, *J* = 7.0 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 199.4 (C, *C*=O), 198.9 (C, *C*=O), 191.1 (C, *C*=O), 148.8 (C, C=*C*-OH), 141.3 (C), 140.1 (C), 139.4 (C), 135.3 (C, q, $J_{C\text{-}F}$ = 32.5 Hz), 128.9 (2 x CH), 128.4 (CH), 127.6 (CH), 126.3 (2 x CH, q, $J_{C\text{-}F}$



84dk

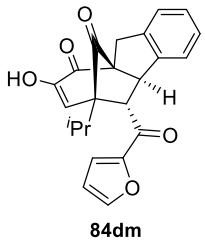
= 3.75 Hz), 125.9 (CH), 124.1 (CH), 123.4 (C, q, $J_{C\text{-}F}$ = 271.25 Hz, *C*$F_3$), 119.2 (CH, *vinylic*-*C*H), 72.6 (C), 65.3 (C), 57.0 (CH), 52.6 (CH), 30.2 (CH), 27.8 ($CH_2$), 18.7 ($CH_3$), 18.0 ($CH_3$). $^{19}$F NMR (376.42 MHz, $CDCl_3$): $\delta$ -63.15 (*C*$F_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{26}H_{22}F_3O_4$ 455.1470; Found 455.1470.

**(4b*S**,5*R**,6*S**,9a*R**)-6-Hydroxy-8-isopropyl-5-(4-(trifluoromethyl)benzoyl)-4b,5,6,10-tetrahydro-9*H*-6,9a-methanobenzo[*a*]azulene-9,11-dione (84dk):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a white solid. Yield: 20% (18 mg). Mp: 224-226 °C. IR (neat): $\nu_{max}$ 3492, 1771, 1675, 1322, 1288, 1222, 1168, 1138, 1064, 1012, 909, 747 and 424 $cm^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.94 (2H, d, *J* = 8.0 Hz), 7.76 (2H, d, *J* = 8.0 Hz), 7.28 (1H, d, *J* = 8.0 Hz), 7.15 (1H, t, *J* = 7.5 Hz), 7.06 (1H, d, *J* = 1.0 Hz), 6.88 (1H, t, *J* = 7.5 Hz), 6.47 (1H, d, *J* = 8.0 Hz), 4.70 (1H, d, *J* = 9.0 Hz), 3.97 (1H, d, *J* = 9.5 Hz), 3.83 (1H, d, *J* = 17.0 Hz), 3.58 (1H, d, *J* = 17.0 Hz), 3.58 (1H, s, *t*-O*H*), 2.97-2.89 (1H, m), 1.15 (3H, d, *J* = 7.0 Hz), 1.14 (3H, d, *J* = 7.0 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 201.5 (C, *C*=O), 198.8 (C, *C*=O), 194.1 (C, *C*=O), 146.8 (C), 144.3 (CH, *vinylic*-*C*H), 142.5 (C), 140.8 (C), 137.0 (C), 135.0 (C, q, $J_{C\text{-}F}$ = 32.0 Hz), 128.7 (2 x CH), 128.2 (CH), 126.6 (CH), 126.0 (2 x CH, q, $J_{C\text{-}F}$ = 4.0 Hz), 125.8 (CH), 123.6 (CH), 122.4 (C, q, $J_{C\text{-}F}$ = 270.0 Hz, *C*$F_3$), 86.1 (C, *C*-OH), 71.8 (C), 53.7 (CH), 49.9 (CH), 28.6 ($CH_2$), 27.1 (CH), 21.7 ($CH_3$), 20.9 ($CH_3$). $^{19}$F NMR (376.42 MHz, $CDCl_3$): $\delta$ -63.18 (*C*$F_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{26}H_{22}F_3O_4$ 455.1470; Found 455.1470.



85dk

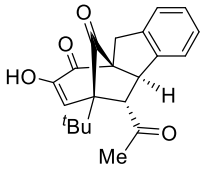
**(4b*R**,5*S**,6*S**,9a*R**)-5-(Furan-2-carbonyl)-8-hydroxy-6-isopropyl-4b,5,6,10-tetrahydro-9*H*-6,9a-methanobenzo[*a*]azulene-9,11-dione (84dm):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a white solid. Yield: 97% (73 mg). Mp: 207-208 °C. IR (neat): $\nu_{max}$ 3321, 1756, 1684, 1655, 1458, 1398, 1382, 1234, 1215, 1052, 1025, 925, 762, 745 and 522 $cm^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.70 (1H, dd, *J* = 2.0 0.5 Hz), 7.35 (1H, dd, *J* = 3.5, 0.5 Hz), 7.28 (1H, d, *J* = 7.5 Hz), 7.24 (1H, t, *J* = 7.5 Hz), 7.13 (1H, t, *J* = 7.5 Hz), 6.80 (1H, d, *J* = 7.5 Hz), 6.67 (1H, dd, *J* = 3.5, 2.0 Hz), 6.39 (1H, *s*, *vinylic*-C*H*), 6.13 (1H, s, *enolic*-O*H*), 4.02 (1H, d, *J* = 7.0 Hz), 3.88 (1H, d, *J* = 7.0 Hz), 3.78 (1H, d, *J* = 17.0 Hz), 3.50 (1H, d, *J* = 17.0 Hz), 2.10 (1H, sept, *J* = 7.0 Hz), 1.05 (3H,



84dm

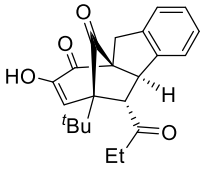
d, *J* = 7.0 Hz), 1.00 (3H, d, *J* = 7.0 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$+$CD_3OD$ (1:1), DEPT-135): *δ* 199.9 (C, *C*=O), 190.6 (C, *C*=O), 187.9 (C, *C*=O), 152.3 (C), 149.4 (C, C=*C*-OH), 147.7 (CH), 140.5 (C), 139.4 (C), 127.5 (CH), 126.8 (CH), 124.8 (CH), 123.6 (CH), 119.8 (CH, *vinylic*-*C*H), 118.9 (CH), 112.8 (CH), 72.9 (C), 64.3 (C), 55.5 (CH), 52.8 (CH), 29.5 (CH), 27 .3 ($CH_2$), 17.3 ($CH_3$), 16.9 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{23}H_{21}O_5$ 377.1389; Found 377.1387.

**(4b*R**,5*S**,6*S**,9a*R**)-5-Acetyl-6-(*tert*-butyl)-8-hydroxy-4b,5,6,10-tetrahydro-9*H*-6,9a-methanobenzo[*a*]azulene-9,11-dione (84ea):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a white solid. Yield: 94% (63.6 mg). Mp: 148-150 °C. IR (neat): $\nu_{max}$ 3411, 2959, 1759, 1673, 1391, 1367, 1240, 1210, 1161, 1112, 1062, 1041, 949, 906, 748 and 541 $cm^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$): *δ* 7.29-7.27 (2H, m), 7.24-7.23 (1H, m), 7.15 (1H, d, *J* = 7.5 Hz), 6.72 (1H, s, *vinylic*-C*H*), 6.01 (1H, d, *J* = 0.5 Hz, *enolic*-O*H*), 3.75 (1H, d, *J* = 17.0 Hz), 3.54 (1H, d, *J* = 7.0 Hz), 3.47 (1H, d, *J* = 17.0 Hz), 3.44 (1H, d, *J* = 7.0 Hz), 2.48 (3H, s), 1.08 (9H, s, 3 x $3CH_3$). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135): *δ* 207.6 (C, *C*=O), 198.6 (C, *C*=O), 191.1 (C, *C*=O), 148.0 (C, C=*C*-OH), 141.2 (C), 139.8 (C), 128.4 (CH), 127.7 (CH), 125.7 (CH), 123.9 (CH), 121.7 (CH, *vinylic*-*C*H), 72.8 (C), 66.7 (C), 57.8 (CH), 55.5 (CH), 34.1 (C), 31.9 ($CH_3$), 28.2 ($CH_2$), 26.4 (3 x $CH_3$). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{21}H_{22}O_4Na$ 361.1416; Found 361.1415.



**84ea**

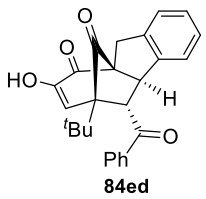
**(4b*R**,5*S**,6*S**,9a*R**)-6-(*tert*-Butyl)-8-hydroxy-5-propionyl-4b,5,6,10-tetrahydro-9*H*-6,9a-methanobenzo[*a*]azulene-9,11-dione (84eb):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a white solid. Yield: 95% (67 mg). Mp: 151-153 °C. IR (neat): $\nu_{max}$ 3413, 2963, 1758, 1714, 1671, 1459, 1392, 1369, 1245, 1212, 1109, 1058, 951, 734, 702 and 602 $cm^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$): *δ* 7.29-7.25 (2H, m), 7.25-7.20 (1H, m), 7.12 (1H, d, *J* = 7.0 Hz), 6.70 (1H, s, *vinylic*-C*H*), 5.98 (1H, s, *enolic*-O*H*), 3.74 (1H, d, *J* = 17.0 Hz), 3.52 (1H, d, *J* = 7.0 Hz), 3.46 (1H, d, *J* = 17.0 Hz), 3.41 (1H, d, *J* = 7.0 Hz), 2.88 (1H, qd, *J* = 18.5, 7.0 Hz), 2.76 (1H, qd, *J* = 19.0, 7.0 Hz), 1.17 (3H, t, *J* = 7.0 Hz), 1.07 (9H, s, 3 x $3CH_3$). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135): *δ* 210.2 (C, *C*=O), 198.7 (C, *C*=O), 191.1 (C, *C*=O), 148.0 (C, C=*C*-OH), 141.3 (C), 139.9 (C), 128.4 (CH), 127.6 (CH), 125.8



**84eb**

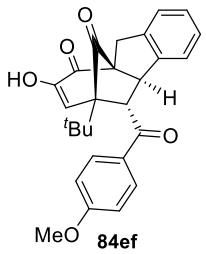
(CH), 123.8 (CH), 121.8 (*vinylic*-*C*H), 72.8 (C), 66.9 (C), 56.8 (CH), 55.9 (CH), 38.4 ($CH_2$), 34.0 (C), 28.1 ($CH_2$), 26.4 (3 x $CH_3$), 7.7 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{22}H_{24}O_4Na$ 375.1572; Found 375.1575.

**(4b*R**,5*S**,6*S**,9a*R**)-5-Benzoyl-6-(*tert*-butyl)-8-hydroxy-4b,5,6,10-tetrahydro-9*H*-6,9a-methanobenzo[*a*]azulene-9,11-dione (84ed):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a white solid. Yield: 85% (68 mg). Mp: 188-190 °C. IR (neat): $\nu_{max}$ 3364, 2962, 1756, 1672, 1391, 1368, 1298, 1238, 1212, 1183, 1110, 1061, 1026, 1004, 907, 840, 732, 700, 683, 646 and 570 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.04 (2H, d, *J* = 7.5 Hz), 7.69 (1H, t, *J* = 7.5 Hz), 7.56 (2H, t, *J* = 7.5 Hz), 7.29 (1H, d, *J* = 7.5 Hz), 7.23 (1H, t, *J* = 7.5 Hz), 7.07 (1H, t, *J* = 7.5 Hz), 6.71 (1H, s, *vinylic*-C*H*), 6.64 (1H, d, *J* = 7.5 Hz), 6.07 (1H, s, *enolic*-O*H*), 4.32 (1H, d, *J* = 7.5 Hz), 3.79 (1H, d, *J* = 17.0 Hz), 3.71 (1H, d, *J* = 7.5 Hz), 3.52 (1H, d, *J* = 17.0 Hz), 1.04 (9H, s, 3 x $3CH_3$). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 200.3 (C, *C*=O), 199.3 (C, *C*=O), 191.0 (C, *C*=O), 148.3 (C, C=*C*-OH), 141.3 (C), 139.8 (C), 137.2 (C), 134.1 (CH), 129.3 (2 x CH), 128.8 (2 x CH), 128.2 (CH), 127.3 (CH), 125.7 (CH), 124.4 (CH), 121.2 (CH, *vinylic*-*C*H), 72.7 (C), 68.3 (C), 58.1 (CH), 50.2 (CH), 34.4 (C), 28.1 ($CH_2$), 26.5 (3 x $CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{26}H_{25}O_4$ 401.1753; Found 401.1757.



**84ed**

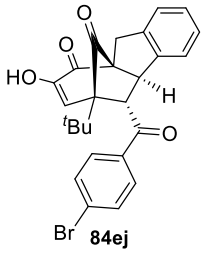
**(4b*R**,5*S**,6*S**,9a*R**)-6-(*tert*-Butyl)-8-hydroxy-5-(4-methoxybenzoyl)-4b,5,6,10-tetrahydro-9*H*-6,9a-methanobenzo[*a*]azulene-9,11-dione (84ef):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a white solid. Yield: 85% (73.2 mg). Mp: 169-171 °C. IR (neat): $\nu_{max}$ 3415, 2963, 2923, 1757, 1668, 1595, 1460, 1392, 1236, 1212, 1169, 1110, 1024, 907, 839, 729, 595, and 515 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.03 (2H, d, *J* = 9.0 Hz), 7.29 (1H, d, *J* = 7.5 Hz), 7.23 (1H, t, *J* = 7.5 Hz), 7.08 (1H, t, *J* = 7.5 Hz), 7.02 (2H, d, *J* = 9.0 Hz), 6.71 (1H, s, *vinylic*-C*H*), 6.68 (1H, d, *J* = 7.5 Hz), 6.08 (1H, s, *enolic*-O*H*), 4.24 (1H, d, *J* = 7.5 Hz), 3.93 (3H, s, O$CH_3$), 3.79 (1H, d, *J* = 17.0 Hz), 3.70 (1H, d, *J* = 7.5 Hz), 3.52 (1H, d, *J* = 17.0 Hz), 1.03 (9H, s, 3 x $3CH_3$). $^{13}C$ NMR (100 MHz, $CDCl_3$, DEPT-135): $\delta$ 199.4 (C, *C*=O), 198.5 (C, *C*=O), 191.0 (C, *C*=O), 164.3 (C), 148.1 (C, C=*C*-OH), 141.3 (C), 139.9 (C), 131.2 (2 x CH), 130.1 (C), 128.1 (CH), 127.3 (CH),



**84ef**

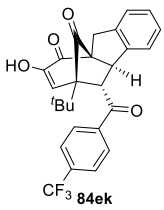
125.6 (CH), 124.4 (CH), 121.5 (CH, *vinylic*-*C*H), 114.4 (2 x CH), 72.6 (C), 68.1 (C), 58.1 (CH), 55.6 (CH), 49.9 ($CH_3$, O$CH_3$), 34.4 (C), 28.0 ($CH_2$), 26.4 (3 x $CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{27}H_{27}O_5$ 431.1858; Found 431.1862.

**(4b*R**,5*S**,6*S**,9a*R**)-5-(4-Bromobenzoyl)-6-(*tert*-butyl)-8-hydroxy-4b,5,6,10-tetrahydro-9*H*-6,9a-methanobenzo[*a*]azulene-9,11-dione (84ej):** The compound was prepared following




**Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a white solid. Yield: 97% (93 mg). Mp: 208-210 °C. IR (neat): $\nu_{max}$ 3365, 2966, 2920, 1755, 1676, 1636, 1580, 1437, 1391, 1367, 1238, 1210, 1071, 1028, 1004, 953, 906, 836, 756, 730, 644 and 514 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.91 (2H, d, *J* = 8.5 Hz), 7.71 (2H, d, *J* = 8.5 Hz), 7.30 (1H, d, *J* = 7.5 Hz), 7.24 (1H, d, *J* = 7.5 Hz), 7.10 (1H, t, *J* = 7.5 Hz), 6.66 (1H, s, *vinylic*-C*H*), 6.64 (1H, d, *J* = 7.5 Hz), 6.09 (1H, s, *enolic*-O*H*), 4.23 (1H, d, *J* = 7.0 Hz), 3.79 (1H, d, *J* = 17.0 Hz), 3.70 (1H, d, *J* = 7.5 Hz), 3.52 (1H, d, *J* = 17.0 Hz), 1.02 (9H, s, 3 x 3CH). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 199.2 (C, *C*=O), 199.0 (C, *C*=O), 190.9 (C, *C*=O), 148.4 (C, C=*C*-OH), 141.3 (C), 139.6 (C), 135.8 (C), 132.7 (2 x CH), 130.2 (2 x CH), 129.7 (C), 128.4 (CH), 127.4 (CH), 125.8 (CH), 124.2 (CH), 120.8 (CH, *vinylic*-*C*H), 72.6 (C), 68.5 (C), 58.2 (CH), 50.1 (CH), 34.4 (C), 28.0 ($CH_2$), 26.5 (3 x $CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{26}H_{24}BrO_4$ 479.0858; Found 479.0863.

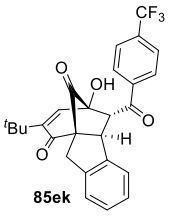
**(4b*R**,5*S**,6*S**,9a*R**)-6-(*tert*-Butyl)-8-hydroxy-5-(4-(trifluoromethyl)benzoyl)-4b,5,6,10-tetrahydro-9*H*-6,9a-methanobenzo[*a*]azulene-9,11-dione (84ek):** The mixture of compounds




were prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a white solid. Yield: 33% (31 mg). Mp: 175-178 °C. IR (neat): $\nu_{max}$ 3454, 2968, 2923, 2853, 1738, 1680, 1409, 1367, 1321, 1229, 1215, 1169, 1131, 1066, 1014, 908, 749 and 516 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): For **84ek**: $\delta$ 8.15 (2H, d, *J* = 8.5 Hz), 7.84 (2H, d, *J* = 8.5 Hz), 7.31 (1H, d, *J* = 7.5 Hz), 7.26 (1H, t, *J* = 7.0 Hz), 7.11 (1H, t, *J* = 7.5 Hz), 6.66 (1H, s, *vinylic*-C*H*), 6.62 (1H, d, *J* = 7.5 Hz), 6.10 (1H, s, *enolic*-O*H*), 4.30 (1H, d, *J* = 7.5 Hz), 3.80 (1H, d, *J* = 17.0 Hz), 3.73 (1H, d, *J* = 7.5 Hz), 3.54 (1H, d, *J* = 17.0 Hz), 1.03 (9H, s, 3 x 3$CH_3$). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): For **84ek**: $\delta$ 199.3 (C, *C*=O), 198.9 (C, *C*=O), 190.9 (C, *C*=O), 148.5 (C, C=*C*-OH), 141.4 (C), 139.7 (C), 139.5 (C), 135.3 (C, q, $J_{C\text{-}F}$ = 32.5 Hz), 129.1 (2 x CH), 128.5 (CH),

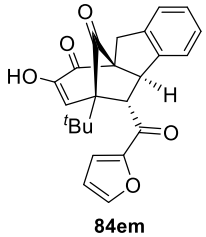
127.5 (CH), 126.4 (2 x CH, q, $J_{C\text{-}F}$ = 3.75 Hz), 125.9 (CH), 124.2 (CH), 123.4 (C, q, $J_{C\text{-}F}$ = 271.2 Hz, *C*$F_3$), 120.5 (CH, *vinylic*-*C*H), 72.7 (C), 68.7 (C), 58.2 (CH), 50.5 (CH), 34.4 (C), 28.1 ($CH_2$), 26.6 (3 x $CH_3$). $^{19}$F NMR (470.59 MHz, $CDCl_3$): $\delta$ -63.18 (*C*$F_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{27}H_{24}F_3O_4$ 469.1627; Found 469.1627.

**(4b*S**,5*R**,6*S**,9a*R**)-8-(*tert*-Butyl)-6-hydroxy-5-(4-(trifluoromethyl)benzoyl)-4b,5,6,10-tetrahydro-9*H*-6,9a-methanobenzo[*a*]azulene-9,11-dione (85ek):** The mixture of compounds were prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a white solid. Yield: 60% (56 mg). Mp: 175-178 °C. IR (neat): $\nu_{max}$ 3408, 2923, 1754, 1728, 1696, 1674, 1461, 1324, 1259, 1171, 1133, 1067, 1029, 803, 648, 525 and 507 cm$^{-1}$. For **85ek**: $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 8.25 (2H, d, *J* = 8.0 Hz), 7.80 (2H, d, *J* = 8.0 Hz), 7.29 (1H, d, *J* = 7.5 Hz), 7.22 (1H, t, *J* = 7.5 Hz), 7.11 (1H, t, *J* = 7.5 Hz), 6.78 (1H, d, *J* = 8.0 Hz), 6.60 (1H, s, *vinylic*-C*H*), 4.32 (1H, d, *J* = 6.5 Hz), 4.11 (1H, d, *J* = 7.0 Hz), 3.83 (1H, d, *J* = 17.0 Hz), 3.72 (1H, d, *J* = 6.0 Hz, *t*-O*H*), 3.51 (1H, d, *J* = 17.0 Hz), 1.24 (9H, s, 3 x 3$CH_3$). For **85ek**: $\delta$ 201.5 (C, *C*=O), 196.1 (C, *C*=O), 192.7 (C, *C*=O), 149.5 (C, *C*=C-OH), 143.0 (CH, *vinylic*-CH), 141.1 (C), 139.7 (C), 139.5 (C), 135.2 (C, q, $J_{C\text{-}F}$ = 32.5 Hz), 129.7 (2 x CH), 128.3 (CH), 127.6 (CH), 125.8 (2 x CH, q, $J_{C\text{-}F}$ = 2.5 Hz), 125.5 (CH), 123.7 (CH), 123.5 (C, q, $J_{C\text{-}F}$ = 270.0 Hz, *C*$F_3$), 84.6 (C, *C*-OH), 73.6 (C), 57.0 (CH), 51.3 (CH), 34.8 (C), 28.63 ($CH_2$), 28.57 (3 x $CH_3$). $^{19}$F NMR (470.59 MHz, $CDCl_3$): $\delta$ -63.21 (*C*$F_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{27}H_{24}F_3O_4$ 469.1627; Found 469.1627.



85ek

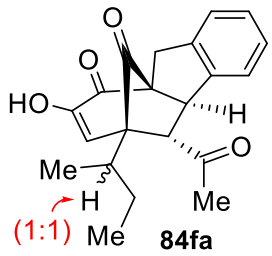
**(4b*R**,5*S**,6*S**,9a*R**)-6-(*tert*-Butyl)-5-(furan-2-carbonyl)-8-hydroxy-4b,5,6,10-tetrahydro-9*H*-6,9a-methanobenzo[*a*]azulene-9,11-dione (84em):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a white solid. Yield: 98% (76.5 mg). Mp: 188-190 °C. IR (neat): $\nu_{max}$ 3409, 2967, 1748, 1669, 1460, 1392, 1242, 1203, 1087, 1061, 1020, 949, 911, 832, 780, 747, 585 and 521 cm$^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.71 (1H, s), 7.35 (1H, d, *J* = 3.5 Hz), 7.28 (1H, d, *J* = 7.5 Hz), 7.23 (1H, t, *J* = 7.5 Hz), 7.12 (1H, t, *J* = 7.5 Hz), 6.74 (1H, d, *J* = 8.0 Hz), 6.68 (1H, dd, *J* = 3.0, 1.5 Hz), 6.65 (1H, s, *vinylic*-C*H*), 6.06 (1H, s, *enolic*-O*H*), 4.19 (1H, d, *J* = 7.5 Hz), 3.78 (1H, d, *J* = 17.0 Hz), 3.72 (1H, d, *J* = 7.0 Hz), 3.50 (1H, d, *J* = 17.0 Hz), 1.05 (9H, 3 x 3$CH_3$). $^{13}$C NMR (125 MHz,



84em

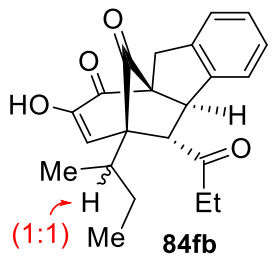
$CDCl_3$, DEPT-135): $\delta$ 199.2 (C, *C*=O), 191.1 (C, *C*=O), 188.8 (C, *C*=O), 153.0 (C), 148.4 (C, C=*C*-OH), 147.5 (CH), 141.2 (C), 139.9 (C), 128.2 (CH), 127.4 (CH), 125.6 (CH), 124.2 (CH), 120.8 (CH, *vinylic*-C*H*), 118.7 (CH), 113.3 (CH), 72.8 (C), 68.0 (C), 57.3 (CH), 51.4 (CH), 34.3 (C), 28.1 ($CH_2$), 26.3 (3 x $CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{24}H_{23}O_5$ 391.1545; Found 391.1445.

**(4b*R**,5*S**,6*S**,9a*R**)-5-Acetyl-6-(*sec*-butyl)-8-hydroxy-4b,5,6,10-tetrahydro-9*H*-6,9a-methanobenzo[*a*]azulene-9,11-dione (84fa):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a white semi solid. Yield: 80% (54 mg). IR (neat): $\nu_{max}$ 3415, 2965, 1761, 1673, 1459, 1394, 1358, 1237, 1164, 1080, 1074, 945, 917, 749, 668 and 422 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$, 1:1 *dr*): $\delta$ 7.28-7.20 (6H, m), 7.07 (2H, t, *J* = 9.5 Hz), 6.40 (1H, s, *vinylic*-C*H*), 6.31 (1H, s, *vinylic*-C*H*), 6.05 (2H, br s, *enolic*-O*H*), 3.89 (1H, d, *J* = 6.5 Hz), 3.84 (1H, d, *J* = 7.0 Hz), 3.73 (2H, d, *J* = 17.0 Hz), 3.45 (2H, d, *J* = 17.0 Hz), 3.35 (1H, d, *J* = 6.5 Hz), 3.34 (1H, d, *J* = 6.5 Hz), 2.42 (6H, s), 1.91-1.84 (2H, m), 1.68-1.57 (3H, m), 1.52-1.45 (1H, m), 1.10 (3H, d, *J* = 7.0 Hz), 1.09 (3H, d, *J* = 7.0 Hz), 0.97 (6H, t, *J* = 7.5 Hz). $^{13}C$ NMR (100 MHz, $CDCl_3$, DEPT-135, 1:1 *dr*): $\delta$ 205.9 (C, *C*=O), 205.7 (C, *C*=O), 199.41 (C, *C*=O), 199.37 (C, *C*=O), 191.5 (C, *C*=O), 191.4 (C, *C*=O), 148.3 (C, C=*C*-OH), 148.2 (C, C=*C*-OH), 141.1 (2C), 139.91 (C), 139.86 (C), 128.2 (2CH), 127.6 (2CH), 125.6 (2CH), 123.9 (2CH), 121.3 (CH, *vinylic*-C*H*), 121.1 (CH, *vinylic*-C*H*), 72.7 (2C), 63.6 (C), 63.4 (C), 58.6 (CH), 58.5 (CH), 53.5 (CH), 53.3 (CH), 37.9 (CH), 37.3 (CH), 31.64 (CH), 31.59 (CH), 27.9 ($2CH_2$), 25.1 ($CH_2$) 24.4 ($CH_2$), 14.6 ($CH_3$), 13.9 ($CH_3$), 13.1 ($CH_3$), 12.6 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{23}O_4$ 339.1596; Found 339.1597.



**84fa**

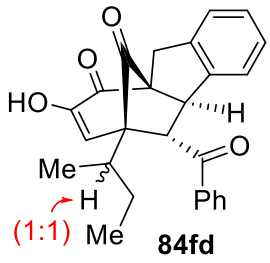
**(4b*R**,5*S**,6*S**,9a*R**)-6-(*sec*-Butyl)-8-hydroxy-5-propionyl-4b,5,6,10-tetrahydro-9*H*-6,9a-methanobenzo[*a*]azulene-9,11-dione (84fb):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a brown solid. Mp: 140-142 °C. Yield: 93% (65.6 mg). IR (neat): $\nu_{max}$ 3398, 2970, 2929, 1762, 1711, 1675, 1459, 1397, 1237, 1112, 1061, 947, 851, 750 and 422 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$, 1:1 *dr*): $\delta$ 7.30-7.26 (2H, m), 7.25-7.20 (4H, m), 7.10-7.05 (2H,



**84fb**

m), 6.37 (1H, s, *vinylic*-C*H*), 6.29 (1H, s, *vinylic*-C*H*), 6.01 (2H, br s, *enolic*-O*H*), 3.84 (1H, d, *J* = 7.0 Hz), 3.83 (1H, d, *J* = 6.5 Hz), 3.71 (2H, d, *J* = 17.0 Hz), 3.45 (2H, d, *J* = 17.0 Hz), 3.34 (1H, d, *J* = 6.5 Hz), 3.34 (1H, d, *J* = 6.5 Hz), 2.73-2.70 (4H, m), 1.87-1.77 (2H, m), 1.68-1.52 (4H, m), 1.18 (3H, t, *J* = 7.5 Hz), 1.17 (3H, t, *J* = 7.5 Hz), 1.08 (3H, d, *J* = 6.5 Hz), 1.07 (3H, d, *J* = 7.0 Hz), 0.96 (6H, t, *J* = 7.5 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135, 1:1 *dr*): *δ* 208.7 (C, *C*=O), 208.5 (C, *C*=O), 199.53 (C, *C*=O), 199.48 (C, *C*=O), 191.5 (C, *C*=O), 191.4 (C, *C*=O), 148.3 (C, C=*C*-OH), 148.1 (C, C=*C*-OH), 141.2 (2C), 140.0 (C), 139.9 (C), 128.25 (CH), 128.21 (CH), 127.5 (2CH), 125.6 (2CH), 123.9 (2CH), 121.5 (CH, *vinylic*-*C*H), 121.2 (CH, *vinylic*-*C*H), 72.66 (C), 72.63 (C), 63.8 (C), 63.7 (C), 57.8 (CH), 57.7 (CH), 54.0 (CH), 53.8 (CH), 37.8 ($2CH_2$), 37.8 (CH), 37.3 (CH), 27.9 ($2CH_2$), 25.1 ($CH_2$), 24.4 ($CH_2$), 14.6 ($CH_3$), 13.9 ($CH_3$), 13.1 ($CH_3$), 12.7 ($CH_3$), 7.80 ($CH_3$), 7.77 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{25}O_4$ 353.1753; Found 353.1753.

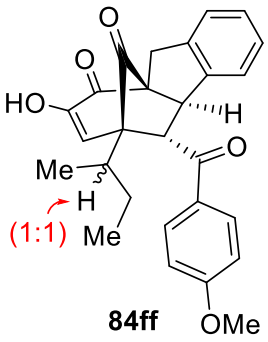
**(4b*R**,5*S**,6*S**,9a*R**)-5-Benzoyl-6-(*sec*-butyl)-8-hydroxy-4b,5,6,10-tetrahydro-9*H*-6,9a-methanobenzo[*a*]azulene-9,11-dione (84fd):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a pale yellow solid. Mp: 157-159 °C. Yield: 90% (72 mg). IR (neat): $\nu_{max}$ 3412, 2970, 2926, 2856, 1763, 1676, 1448, 1397, 1218, 1074, 1024, 748, 689, 668 and 517 $cm^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$, 1:1 *dr*): *δ* 7.99-7.97 (4H, m), 7.68 (2H, t, *J* = 7.5 Hz), 7.56-7.53 (4H, m), 7.29 (2H, d, *J* = 7.5 Hz), 7.23 (2H, t, *J* = 7.5 Hz), 7.09 (2H, t, *J* = 7.5 Hz), 6.71 (2H, d, *J* = 7.5 Hz), 6.398 (1H, s, *vinylic*-C*H*), 6.394 (1H, s, *vinylic*-C*H*), 6.08 (2H, s, *enolic*-O*H*), 4.17 (1H, d, *J* = 7.5 Hz), 4.17 (1H, d, *J* = 7.0 Hz), 3.91-3.90 (2H, m), 3.78 (2H, d, *J* = 17.0 Hz), 3.52 (2H, d, *J* = 17.0 Hz), 1.70-1.62 (2H, m), 1.44-1.38 (2H, m), 1.35-1.26 (1H, m), 1.14-1.05 (1H, m), 0.96 (3H, d, *J* = 6.5 Hz), 0.92 (3H, d, *J* = 6.5 Hz), 0.80 (6H, t, *J* = 7.5 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135, 1:1 *dr*): *δ* 199.93 (C, *C*=O), 199.89 (C, *C*=O), 199.8 (C, *C*=O), 199.7 (C, *C*=O), 191.3 (C, *C*=O), 191.2 (C, *C*=O), 148.5 (C, C=*C*-OH), 148.4 (C, C=*C*-OH), 141.3 (C), 141.2 (C), 139.79 (C), 139.76 (C), 137.6 (C), 137.5 (C), 133.98 (CH), 133.95 (CH), 129.1 (2 x 2CH), 128.6 (2 x CH), 128.5 (2 x CH), 128.2 (2CH), 127.4 (2CH), 125.69 (CH), 125.67 (CH), 124.34 (CH), 124.32 (CH), 120.6 (CH, *vinylic*-*C*H), 119.9 (CH, *vinylic*-*C*H), 72.64 (C), 72.62 (C), 65.8 (C), 65.5 (C), 56.9 (CH), 56.7 (CH), 52.3 (CH), 52.2 (CH), 37.22 (CH), 37.18



**84fd**

(CH), 27.89 ($CH_2$), 27.86 ($CH_2$), 25.5 ($CH_2$), 24.9 ($CH_2$), 14.9 ($CH_3$), 14.2 ($CH_3$), 12.51 ($CH_3$) 12.5 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{26}H_{25}O_4$ 401.1753; Found 401.1753.

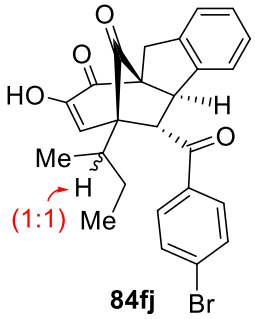
**(4b*R**,5*S**,6*S**,9a*R**)-6-(*sec*-Butyl)-8-hydroxy-5-(4-methoxybenzoyl)-4b,5,6,10-tetrahydro-9*H*-6,9a-methanobenzo[*a*]azulene-9,11-dione (84ff):** The compound was prepared following



**84ff**

**Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a pale yellow solid. Mp: 152-154 °C. Yield: 85% (73 mg). IR (neat): $\nu_{max}$ 3409, 2924, 1762, 1671, 1597, 1510, 1459, 1397, 1261, 1222, 1171, 1024, 839 and 750 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$, 1:1 *dr*): $\delta$ 7.99 (2H, d, *J* = 9.0 Hz), 7.98 (2H, d, *J* = 9.0 Hz), 7.28 (2H, d, *J* = 7.5 Hz), 7.22 (2H, t, *J* = 7.5 Hz), 7.11-7.07 (2H, m), 7.012 (2H, d, *J* = 8.5 Hz), 7.009 (2H, d, *J* = 9.0 Hz), 6.73-6.71 (2H, m), 6.43 (2H, s, *vinylic*-C*H*), 6.09 (2H, s, *enolic*-O*H*), 4.10 (1H, d, *J* = 7.5 Hz), 4.08 (1H, d, *J* = 7.0 Hz), 3.92 (6H, s), 3.86-3.84 (2H, m), 3.78 (2H, d, *J* = 17.0 Hz), 3.51 (2H, d, *J* = 17.0 Hz), 1.75-1.69 (2H, m), 1.64-1.39 (2H, m), 1.35-1.29 (1H, m), 1.12-1.05 (1H, m), 0.97 (3H, d, *J* = 6.5 Hz), 0.92 (3H, d, *J* = 7.0 Hz), 0.84 (3H, t, *J* = 7.5 Hz), 0.81 (3H, t, *J* = 7.5 Hz). $^{13}C$ NMR (100 MHz, $CDCl_3$, DEPT-135, 1:1 *dr*): $\delta$ 200.1 (2C, 2*C*=O), 197.95 (C, *C*=O), 197.92 (C, *C*=O), 191.22 (C, *C*=O), 191.18 (C, *C*=O), 164.3 (2C), 148.3 (C, C=*C*-OH), 148.2 (C, C=*C*-OH), 141.2 (2C), 139.91 (C), 139.87 (C), 131.1 (2 x 2CH), 130.3 (2C), 128.1 (2CH), 127.3 (2CH), 125.6 (2CH), 124.3 (2CH), 121.0 (CH, *vinylic*-*C*H), 120.2 (CH, *vinylic*-*C*H), 114.3 (2 x 2CH), 72.5 (2C), 65.7 (C), 65.4 (C), 57.3 (CH), 57.1 (CH), 55.6 ($2CH_3$), 51.8 (CH), 51.7 (CH), 37.1 (2CH), 27.8 ($2CH_2$), 25.4 ($CH_2$), 24.9 ($CH_2$), 14.8 ($CH_3$), 14.2 ($CH_3$), 12.6 ($CH_3$), 12.5 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{27}H_{27}O_5$ 431.1858; Found 431.1856.

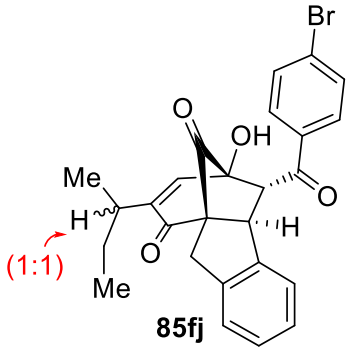
**(4b*R**,5*S**,6S*,9a*R**)-5-(4-Bromobenzoyl)-6-(*sec*-butyl)-8-hydroxy-4b,5,6,10-tetrahydro-9*H*-6,9a-methanobenzo[*a*]azulene-9,11-dione (84fj):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a pale yellow pale yellow semi solid**.** Yield: 67% (64 mg). IR (neat): $\nu_{max}$ 3415, 2965, 2932, 1762, 1674, 1582, 1482, 1397, 1215, 1072, 1007 and 752 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$, 1:1 *dr*): $\delta$ 7.86 (2H, d, *J* = 8.5 Hz), 7.85 (2H, d, *J* = 8.5 Hz), 7.699 (2H, d, *J* = 8.5 Hz), 7.695 (2H, d, *J* = 8.5 Hz), 7.29 (2H, d, *J* = 7.5 Hz), 7.24



**84fj**

(1H, t, *J* = 7.0 Hz), 7.23 (1H, t, *J* = 7.5 Hz), 7.117 (1H, t, *J* = 7.5 Hz), 7.111 (1H, t, *J* = 7.5 Hz), 6.70 (1H, d, *J* = 6.0 Hz), 6.69 (1H, d, *J* = 7.5 Hz), 6.38 (1H, s, *vinylic*-C*H*), 6.37 (1H, s, *vinylic*-C*H*), 6.12 (2H, s, *enolic*-O*H*), 4.09 (1H, d, *J* = 8.0 Hz), 4.08 (1H, d, *J* = 7.5 Hz), 3.87 (2H, d, *J* = 7.0 Hz), 3.78 (2H, d, *J* = 17.0 Hz), 3.52 (2H, d, *J* = 17.0 Hz), 1.72-1.66 (2H, m), 1.59-1.53 (1H, m), 1.42-1.34 (1H, m), 1.31-1.27 (1H, m), 1.12-1.03 (1H, m), 0.96 (3H, d, *J* = 7.0 Hz), 0.91 (3H, d, *J* = 7.0 Hz), 0.83 (3H, t, *J* = 7.5 Hz), 0.82 (3H, t, *J* = 7.5 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135, 1:1 *dr*): *δ* 199.71 (C, *C*=O), 199.67 (C, *C*=O), 198.76 (C, *C*=O), 198.70 (C, *C*=O), 191.12 (C, *C*=O), 191.08 (C, *C*=O), 148.6 (C, C=*C*-OH), 148.5 (C, C=*C*-OH), 141.3 (C), 141.2 (C), 139.6 (C), 139.5 (C), 136.1 (2C), 132.5 (2 x 2CH), 130.0 (2 x 2CH), 129.6 (C), 129.5 (C), 128.3 (2CH), 127.5 (2CH), 125.78 (CH), 125.76 (CH), 124.1 (2CH), 120.3 (CH, *vinylic*-*C*H), 119.5 (CH, *vinylic*-*C*H), 72.6 (C), 72.57 (C), 65.9 (C), 65.7 (C), 57.1 (CH), 56.9 (CH), 52.2 (CH), 52.1 (CH), 37.19 (CH), 37.17 (CH), 27.9 ($CH_2$), 27.8 ($CH_2$), 25.6 ($CH_2$), 24.9 ($CH_2$), 14.9 ($CH_3$), 14.3 ($CH_3$), 12.53 ($CH_3$), 12.50 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{26}H_{24}BrO_4$ 479.0858; Found 479.0859.

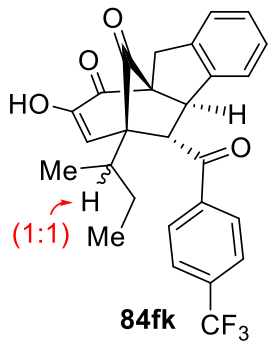
**(4b*S**,5*R**,6*S**,9a*R**)-5-(4-Bromobenzoyl)-8-(*sec*-butyl)-6-hydroxy-4b,5,6,10-tetrahydro-9*H*-6,9a-methanobenzo[*a*]azulene-9,11-dione (85fj):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a pale yellow semi solid. Yield: 28% (26.7 mg). IR (neat): $\nu_{max}$ 3433, 2962, 2926, 1674, 1583, 1483, 1458, 1397, 1215, 1178, 1007, 983, 852, 749 and 464 $cm^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$, 1:1 *dr*): *δ* 7.70 (4H, d, *J* = 8.5 Hz), 7.63 (4H, d, *J* = 8.0 Hz), 7.25 (2H, m), 7.13 (2H, t, *J* = 7.5 Hz), 7.03 (2H, s, *vinylic*-*C*H), 6.87 (2H, t, *J* = 7.5 Hz), 6.46 (2H, d, *J* = 7.5 Hz), 4.63 (1H, d, *J* = 9.0 Hz), 4.62 (1H, d, *J* = 9.5 Hz), 3.95 (2H, d, *J* = 9.5 Hz), 3.81 (2H, d, *J* = 17.5 Hz), 3.56 (2H, d, *J* = 17.5 Hz), 3.48 (2H, s, *t*-O*H*), 2.80-2.68 (2H, m), 1.68-1.49 (2H, m), 1.47-1.38 (2H, m), 1.11 (6H, d, *J* = 7.0 Hz), 0.91 (3H, t, *J* = 7.5 Hz), 0.88 (3H, t, *J* = 7.5 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135, 1:1 *dr*): *δ* 202.2 (C, *C*=O), 202.0 (C, *C*=O), 195.71 (C, *C*=O), 195.67 (C, *C*=O), 193.5 (C, *C*=O), 193.4 (C, *C*=O), 147.4 (C, C=*C*-OH), 147.1 (C, C=*C*-OH), 143.2 (CH, *vinylic*-*C*H), 143.1 (CH, *vinylic*-*C*H), 141.05 (C), 141.02 (C), 139.8 (2C), 135.7 (2C), 132.1 (2 x 2CH), 130.96 (2 x CH), 130.94 (2 x CH), 129.6 (2C), 128.2 (2CH), 127.6 (2CH), 125.4



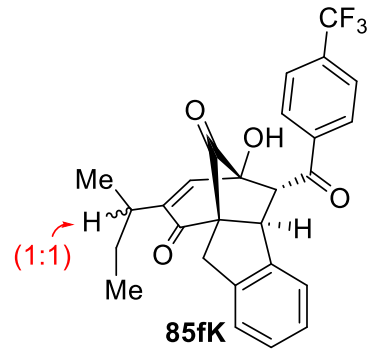
**85fj**

(2CH), 123.8 (2CH), 84.84 (C, *C*-OH), 84.6 (C, *C*-OH), 72.75 (C), 72.73 (C), 56.6 (CH), 56.5 (CH), 51.66 (CH), 51.58 (CH), 33.8 (CH), 33.6 (CH), 28.9 ($CH_2$), 28.6 ($2CH_2$), 28.0 ($CH_2$), 19.4 ($CH_3$), 18.6 ($CH_3$), 11.76 ($CH_3$), 11.73 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{26}H_{24}BrO_4$ 479.0858; Found 479.0859.

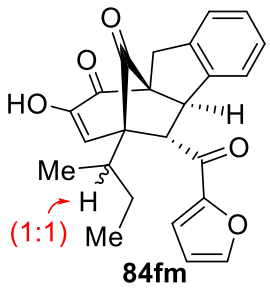
**(4b*R**,5*S**,6*S**,9a*R**)-6-(*sec*-Butyl)-8-hydroxy-5-(4-(trifluoromethyl)benzoyl)-4b,5,6,10-tetrahydro-9*H*-6,9a-methanobenzo[*a*]azulene-9,11-dione (84fk)**: The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a pale yellow semi solid. Yield: 22% (20.6 mg). IR (neat): $\nu_{max.}$ 3422, 2967, 2939, 2878, 1763, 1678, 1407, 1322, 1216, 1169, 1132, 1067, 1014, 910, 750, 733 and 527 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$, 1:1 *dr*): $\delta$ 8.10 (4H, d, *J* = 8.0 Hz), 7.83 (4H, d, *J* = 8.5 Hz), 7.82 (2H, d, *J* = 8.5 Hz), 7.31 (2H, d, *J* = 7.5 Hz), 7.27-7.24 (2H, m), 7.13 (1H, t, *J* = 7.5 Hz), 7.12 (1H, t, *J* = 7.5 Hz), 6.70 (1H, d, *J* = 8.0 Hz), 6.69 (1H, d, *J* = 7.0 Hz), 6.36 (2H, s, *vinylic*-C*H*), 6.11 (2H, s, *enolic*-O*H*), 4.17 (1H, d, *J* = 8.5 Hz), 4.16 (1H, d, *J* = 8.5 Hz), 3.91 (1H, d, *J* = 7.0 Hz), 3.90 (1H, d, *J* = 7.0 Hz), 3.79 (2H, d, *J* = 17.0 Hz), 3.53 (2H, d, *J* = 17.0 Hz), 1.71-1.63 (2H, m), 1.62-1.53 (1H, m), 1.42-1.27 (2H, m), 1.12-1.03 (1H, m), 0.96 (3H, d, *J* = 7.0 Hz), 0.91 (3H, d, *J* = 7.0 Hz), 0.82 (6H, t, *J* = 7.5 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135, 1:1 *dr*): $\delta$ 199.54 (C, *C*=O), 199.49 (C, *C*=O), 198.95 (C, *C*=O), 198.89 (C, *C*=O), 191.1 (C, *C*=O), 191.0 (C, *C*=O), 148.74 (C, C=*C*-OH), 148.68 (C, C=*C*-OH), 141.28 (C), 141.26 (C), 140.1 (2C), 139.5 (C), 139.4 (C), 135.3 (2C, q, $J_{C-F}$ = 32.5 Hz), 128.8 (2 x 2CH), 128.8 (2CH), 128.4 (2CH), 127.6 (2CH), 126.3 (2 x CH, q, $J_{C-F}$ = 3.75 Hz), 125.8 (2 x CH, q, $J_{C-F}$ = 2.5, 1.25 Hz), 124.1 (2CH), 123.4 (2C, q, $J_{C-F}$ = 247.25 Hz, *C*$F_3$), 119.9 (CH, *vinylic*-*C*H), 119.2 (CH, *vinylic*-*C*H), 72.63 (C), 72.59 (C), 66.1 (C), 65.8 (C), 56.9 (CH), 56.8 (CH), 52.6 (CH), 52.5 (CH), 37.24 (CH), 37.21 (CH), 27.91 ($CH_2$), 27.88 ($CH_2$), 25.6 ($CH_2$), 24.9 ($CH_2$), 15.1 ($CH_3$), 14.3 ($CH_3$), 12.5 ($2CH_3$). $^{19}F$ NMR (470.59 MHz, $CDCl_3$): $\delta$ -63.16 (*C*$F_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{27}H_{24}F_3O_4$ 469.1627; Found 469.1628.



**(4b*S**,5*R**,6*S**,9a*R**)-8-(*sec*-Butyl)-6-hydroxy-5-(4-(trifluoromethyl)benzoyl)-4b,5,6,10-tetrahydro-9*H*-6,9a-methanobenzo[*a*]azulene-9,11-dione (85fk):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a pale yellow semi solid. Yield: 66% (61.8 mg). IR (neat): $\nu_{max.}$ 3424, 2963, 2926, 1770, 1680, 1321, 1216, 1168, 1129, 1066, 984, 750 and 480 $cm^{-1}$. $^{1}H$ NMR (500 MHz, $CDCl_3$, 1:1 *dr*): $\delta$ 8.25 (4H, d, *J* = 8.0 Hz), 7.79 (4H, d, *J* = 8.0 Hz), 7.30 (2H, d, *J* = 8.0 Hz), 7.22 (2H, t, *J* = 8.0 Hz), 7.11 (2H, t, *J* = 7.5 Hz), 6.79 (2H, d, *J* = 7.5 Hz), 6.53 (1H, s, *vinylic*-C*H*), 6.52 (1H, s, *vinylic*-C*H*), 4.37 (1H, d, *J* = 7.0 Hz), 4.35 (1H, d, *J* = 7.0 Hz), 4.11 (1H, d, *J* = 6.5 Hz), 4.09 (1H, d, *J* = 7.0 Hz), 3.85 (2H, d, *J* = 17.0 Hz), 3.72 (2H, s, *t*-O*H*), 3.52 (2H, d, *J* = 17.0 Hz), 2.79-2.70 (2H, m), 1.54-1.33 (4H, m), 1.12 (3H, d, *J* = 7.0 Hz), 1.04 (3H, d, *J* = 7.0 Hz), 0.96 (3H, t, *J* = 7.5 Hz), 0.84 (3H, t, *J* = 7.5 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135, 1:1 *dr*): $\delta$ 202.1 (C, *C*=O), 201.9 (C, *C*=O), 196.0 (C, *C*=O), 195.9 (C, *C*=O), 193.4 (C, *C*=O), 193.3 (C, *C*=O), 147.6 (C, *C*=C-OH), 147.3 (C, *C*=C-OH), 143.0 (CH, *vinylic*-*C*H), 142.9 (CH, *vinylic*-*C*H), 141.04 (C), 141.00 (C), 139.6 (C), 139.4 (C), 135.1 (2C, q, $J_{C\text{-}F}$ = 26.0 Hz), 129.8 (2 x 2CH), 128.3 (2CH), 127.6 (2CH), 125.7 (2 x CH, d, $J_{C\text{-}F}$ = 3.75 Hz), 125.5 (2CH), 123.8 (2CH), 123.5 (2C, q, $J_{C\text{-}F}$ = 271.2 Hz, *C*$F_3$), 84.8 (C, *C*-OH), 84.6 (C, *C*-OH), 72.76 (C), 72.75 (C), 56.95 (CH), 56.91 (CH), 51.6 (CH), 51.5 (CH), 33.8 (CH), 33.5 (CH), 28.9 ($CH_2$), 28.6 ($2CH_2$), 28.0 ($CH_2$), 19.4 ($CH_3$), 18.6 ($CH_3$), 11.74 ($CH_3$), 11.71 ($CH_3$). $^{19}F$ NMR (470.59 MHz, $CDCl_3$): $\delta$ -63.24 (*C*$F_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{27}H_{24}F_3O_4$ 469.1627; Found 469.1628.

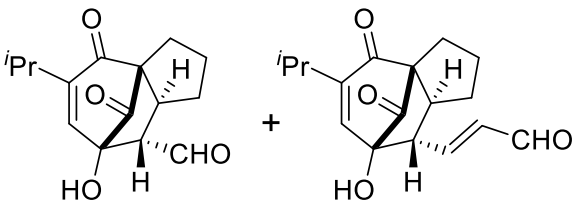



**(4b*R**,5*S**,6*S**,9a*R**)-6-(*sec*-Butyl)-5-(furan-2-carbonyl)-8-hydroxy-4b,5,6,10-tetrahydro-9*H*-6,9a-methanobenzo[*a*]azulene-9,11-dione (84fm):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a pale brown semi solid. Yield: 85% (66.4 mg). IR (neat): $\nu_{max}$ 3416, 2964, 2927, 1763, 1669, 1563, 1461, 1395, 1248, 1155, 1080, 1022, 918, 883, 752, 668, 593 and 415 $cm^{-1}$. $^{1}H$ NMR (500 MHz, $CDCl_3$, 1:1 *dr*): $\delta$ 7.69 (2H, d, *J* = 4.5 Hz), 7.34 (2H, t, *J* = 4.0 Hz), 7.28 (2H, d, *J* = 7.5 Hz), 7.23 (2H, t, *J* = 7.5 Hz),



7.13 (2H, t, *J* = 7.5 Hz), 6.80 (2H, d, *J* = 7.5 Hz), 6.67 (2H, d, *J* = 3.0 Hz), 6.39 (1H, s, *vinylic*-C*H*), 6.38 (1H, s, *vinylic*-C*H*), 6.10 (2H, s, *t*-OH), 4.05 (1H, d, *J* = 7.5 Hz), 4.04 (1H, d, *J* = 7.5 Hz), 3.88 (2H, d, *J* = 7.0 Hz), 3.79 (2H, d, *J* = 16.5 Hz), 3.50 (2H, d, *J* = 17.0 Hz), 1.76-1.65 (4H, m), 1.43-1.36 (1H, m), 1.12-1.06 (1H, m), 1.03 (3H, d, *J* = 7.0 Hz), 0.96 (3H, d, *J* = 7.0 Hz), 0.88 (3H, t, *J* = 7.5 Hz), 0.86 (3H, t, *J* = 7.5 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135, 1:1 *dr*): *δ* 199.9 (C, *C*=O), 199.8 (C, *C*=O), 191.35 (C, *C*=O), 191.30 (C, *C*=O), 187.9 (C, *C*=O), 187.8 (C, *C*=O), 152.9 (2C), 148.53 (C, C=*C*-OH), 148.46 (C, C=*C*-OH), 147.5 (CH), 147.4 (CH), 141.2 (C), 141.1 (C), 139.9 (C), 139.8 (C), 128.2 (2CH), 127.4 (2CH), 125.6 (2CH), 124.2 (2CH), 120.7 (CH, *vinylic*-*C*H), 119.9 (CH, *vinylic*-*C*H), 118.8 (CH), 118.6 (CH), 113.3 (CH), 113.2 (CH), 72.75 (C), 72.71 (C), 65.6 (C), 65.4 (C), 56.2 (CH), 56.1 (CH), 53.0 (CH), 52.9 (CH), 37.23 (CH), 37.20 (CH), 28.0 ($CH_2$), 27.9 ($CH_2$), 25.3 ($CH_2$), 24.7 ($CH_2$), 14.6 ($CH_3$), 14.0 ($CH_3$), 12.66 ($CH_3$), 12.64 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{24}H_{23}O_5$ 391.1545; Found 391.1545.

**(3a*S**,7*R**,8*S**,8a*S**)-7-Hydroxy-5-isopropyl-4,9-dioxo-2,3,4,7,8,8a-hexahydro-1*H*-3a,7-methanoazulene-8-carbaldehyde (85ao) and (*E*)-3-((3a*S**,7*S**,8*S**,8a*S**)-7-Hydroxy-5-isopropyl-4,9-dioxo-2,3,4,7,8,8a-hexahydro-1*H*-3a,7-methanoazulen-8-yl)acrylaldehyde**

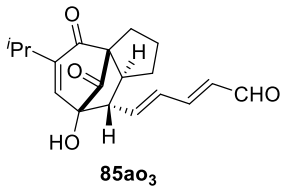



**85ao** **85ao$_2$**

**(85ao$_2$):** The compound was prepared following **Procedure C**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a pale yellow sticky liquid. Yield: 74% (20 mg). IR (neat): $\nu_{max}$ 3417, 2963, 2872, 1768, 1677, 1369, 1297, 1265, 1127, 1023, 733 and 702 $cm^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$, 1.5:1 *pr*): For **85ao:** *δ* 9.90 (1H, d, *J* = 1.0 Hz), 6.82 (1H, s, *vinylic*-C*H*), 3.74 (1H, br s, *t*-*OH*), 2.93-2.81 (1H, m), 2.57 (1H, q, *J* = 7.5 Hz), 2.35 (1H, q, *J* = 7.0, 6.5 Hz), 2.19-1.96 (2H, m), 1.82-1.72 (3H, m), 1.42-1.35 (1H, m), 1.24 (3H, d, *J* = 7.0 Hz), 1.02 (3H, d, *J* = 6.5 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135, 1.5:1 *pr*): *δ* 201.9 (C, *C*=O), 198.2 (C, *C*HO), 194.0 (C, *C*=O), 147.6 (C), 142.3 (CH, *vinylic*-*C*H), 84.5 (C, *C*-OH), 74.3 (C), 61.9 (CH), 44.2 (CH), 33.1 ($CH_2$), 27.6 ($CH_2$), 26.9 (CH), 22.7 ($CH_2$), 21.7 ($CH_3$), 20.9 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{15}H_{18}O_4Na$ 285.1103; Found 285.1095. For **85ao$_2$:** $^1$H NMR (500 MHz, $CDCl_3$, 1.5:1 *pr*): *δ* 9.57 (1H, d, *J* = 7.5 Hz), 6.76 (1H, s, *vinylic*-C*H*), 6.75 (1H, d, *J* = 16.0, 7.5 Hz), 6.26 (1H, ddd, *J* = 15.75, 7.5, 1.5 Hz), 3.55 (1H, br s, *t*-O*H*), 2.93-2.81 (2H, m), 2.73 (1H, t, *J* = 7.5 Hz),

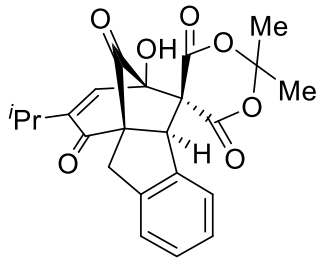
2.34-2.28 (1H, m), 2.19-1.96 (2H, m), 1.82-1.72 (2H, m), 1.49-1.43 (1H, m), 1.08 (3H, d, *J* = 7.0 Hz), 1.07 (3H, d, *J* = 7.0 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135, 1.5:1 *pr*): *δ* 202.8 (C, *C*=O), 194.4 (C, *C*=O), 192.6 (C, *C*HO), 152.2 (CH, *vinylic*-*C*H), 147.7 (C), 142.6 (CH, *vinylic*-*C*H), 135.2 (CH, *vinylic*-*C*H), 85.5 (C, *C*-OH), 74.1 (C), 53.6 (CH), 49.8 (CH), 32.1 ($CH_2$), 27.3 ($CH_2$), 26.9 (CH), 22.9 ($CH_2$), 21.9 ($CH_3$), 21.0 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{17}H_{20}O_4Na$ 311.1259; Found 311.1256.

**(2*E*,4*E*)-5-((3a*S**,7*S**,8*S**,8a*S**)-7-Hydroxy-5-isopropyl-4,9-dioxo-2,3,4,7,8,8a-hexahydro-1*H*-3a,7-methanoazulen-8-yl)penta-2,4-dienal (85ao$_3$)**: $^1$H NMR (500 MHz, $CDCl_3$): *δ* 9.65 (1H, d, *J* = 8.0 Hz), 7.45 (1H, dd, *J* = 15.0, 7.5 Hz), 6.76 (1H, s, *vinylic*-C*H*), 6.53 (1H, dd, *J* = 13.0, 10.5 Hz), 6.25 (1H, dd, *J* = 15.5, 8.0 Hz), 5.72 (1H, t, *J* = 10.5 Hz), 3.57 (1H, s, *t*-O*H*), 3.01 (1H, dd, *J* = 10.0, 7.5 Hz), 2.92-2.87 (1H, m), 2.31 (1H, quint, *J* = 7.0 Hz), 2.19-2.06 (2H, m), 1.99 (1H, sextet, *J* = 6.5 Hz), 1.82-1.73 (2H, m), 1.50-1.45 (1H, m). 1.09-1.06 (6H, m). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{19}H_{22}O_4Na$ 337.1418; Found 337.1416.



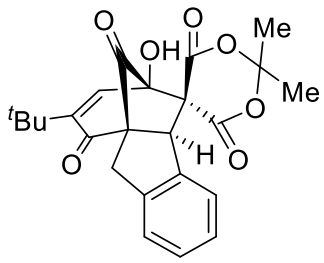
85ao$_3$

**(4bS*,6S*,9aR*)-6-Hydroxy-8-isopropyl-2',2'-dimethylspiro[6,9a-methanobenzo[a]azulene-5,5'-[1,3]dioxane]-4',6',9,11(4b*H*,6*H*,10*H*)-tetraone (85dp)**: The compound was prepared following **Procedure D**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a white solid. Mp: 126-128 °C. Yield: 95% (78 mg). IR (neat): $\nu_{max}$ 3572, 3314, 2962, 1771, 1731, 1682, 1461, 1383, 1323, 1282, 1201, 1174, 1115, 1060, 1021, 960, 920 and 752 cm$^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$): *δ* 7.28 (1H, d, *J* = 7.0 Hz), 7.26 (1H, t, *J* = 7.5 Hz), 7.16 (1H, t, *J* = 7.5 Hz), 6.89 (1H, d, *J* = 7.5 Hz), 6.87 (1H, s, *vinylic*-C*H*), 4.36 (1H, br s, *t*-O*H*), 4.20 (1H, s), 3.87 (1H, d, *J* = 17.0 Hz), 3.53 (1H, d, *J* = 17.0 Hz), 2.95 (1H, sept, *J* = 7.0 Hz), 1.93 (3H, s), 1.80 (3H, s), 1.17 (3H, d, *J* = 6.5 Hz), 1.14 (3H, d, *J* = 7.0 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135): *δ* 198.3 (C, *C*=O), 192.7 (C, *C*=O), 166.8 (C, *C*=O), 165.0 (C, *C*=O), 147.8 (C), 142.75 (CH, *vinylic*-*C*H), 142.67 (C), 135.6 (C), 129.1 (CH), 127.2 (CH), 125.9 (CH), 122.8 (CH), 107.1 (C), 88.7 (C, *C*-OH), 71.8 (C), 63.4 (CH), 60.1 (C), 30.3 (CH), 28.9 ($CH_2$), 28.4 ($CH_3$), 27.3 ($CH_3$), 20.9 ($CH_3$), 20.8 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+NH_4]^+$ Calcd for $C_{23}H_{26}O_7N$ 428.1709; Found 428.1714.



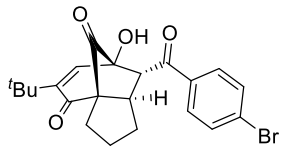
85dp

**(4bS*,6S*,9aR*)-8-(*tert*-Butyl)-6-hydroxy-2',2'-dimethylspiro[6,9a-methanobenzo[a] azulene-5,5'-[1,3]dioxane]-4',6',9,11(4b*H*,6*H*,10*H*)-tetraone (85ep)**: The compound was prepared following **Procedure D**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a white solid. Mp: 248-250 °C (decomposition). Yield: 96% (81.5 mg). IR (neat): $\nu_{max}$ 3512, 2964, 1782, 1754, 1712, 1687, 1459, 1383, 1343, 1304, 1200, 1082, 1044, 925, 903, 808, 749 and 725 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.31 (1H, d, $J$ = 7.0 Hz), 7.28 (1H, t, $J$ = 7.0 Hz), 7.19 (1H, t, $J$ = 7.5 Hz), 6.98 (1H, s, *vinylic*-C*H*), 6.92 (1H, d, $J$ = 7.5 Hz), 4.24 (1H, *t*-O*H*), 4.21 (1H, s), 3.88 (1H, d, $J$ = 17.5 Hz), 3.54 (1H, d, $J$ = 17.5 Hz), 1.95 (3H, s), 1.83 (3H, s), 1.29 (9H, s, 3 x $3CH_3$). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 197.9 (C, *C*=O), 192.1 (C, *C*=O), 166.8 (C, *C*=O), 165.1 (C, *C*=O), 149.1 (C), 143.6 (CH, *vinylic*-*C*H), 142.7 (C), 135.7 (C), 129.2 (CH), 127.3 (CH), 125.9 (CH), 122.8 (CH), 107.1 (C), 88.6 (C, *C*-OH), 72.6 (C), 63.2 (CH), 60.1 (C), 35.0 (C), 30.4 ($CH_3$), 29.1 ($CH_2$), 28.44 ($CH_3$), 28.36 (3 x $CH_3$). HRMS (ESI-TOF) *m/z*: $[M+NH_4]^+$ Calcd for $C_{24}H_{28}O_7N$ 442.1866; Found 442.1866.



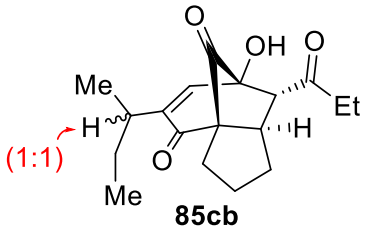
**85ep**

**(3a*R**,7*S**,8*R**,8a*R**)-8-(4-Bromobenzoyl)-5-(*tert*-butyl)-7-hydroxy-1,2,3,7,8,8a-hexahydro-4*H*-3a,7-methanoazulene-4,9-dione (85bj):** The compound was prepared following **Procedure E**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a colourless semi solid. Yield: 94% (81 mg). IR (neat): $\nu_{max}$ 2963, 2927, 1766, 1677, 1584, 1484, 1462, 1398, 1363, 1321, 1231, 1136, 1055, 1027, 904, 725 and 648 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.93 (2H, d, $J$ = 8.5 Hz), 7.64 (2H, d, $J$ = 8.5 Hz), 6.61 (1H, s, *vinylic*-C*H*), 3.72 (1H, d, $J$ = 7.5 Hz), 3.68 (1H, br s, *t*-OH), 2.82 (1H, d, $J$ = 7.5 Hz), 2.39-2.33 (1H, m), 2.10 (1H, quint, $J$ = 7.0 Hz), 1.98-1.92 (1H, m), 1.80-1.73 (2H, m), 1.42-1.36 (1H, m), 1.20 (9H, s, 3 x $3CH_3$). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 202.5 (C, *C*=O), 196.0 (C, *C*=O), 193.8 (C, *C*=O), 148.5 (C), 143.4 (CH, *vinylic*-*C*H), 135.9 (C), 131.9 (2 x CH), 130.7 (2 x CH), 129.2 (C), 85.4 (C, *C*-OH), 74.7 (C), 56.2 (CH), 46.8 (CH), 34.6 (C), 32.9 ($CH_2$), 28.6 (3 x $CH_3$), 27.4 ($CH_2$), 22.9 ($CH_2$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{24}BrO_4$ 431.0858; Found 431.0860.



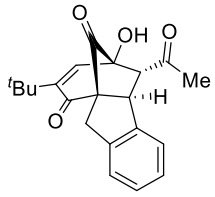
**85bj**

**(3a*R**,7*S**,8*R**,8a*R**)-5-((*S**)-*sec*-Butyl)-7-hydroxy-8-propionyl-1,2,3,7,8,8a-hexahydro-4*H*-3a,7-methanoazulene-4,9-dione (85cb)** The compound was prepared following **Procedure E**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a colourless sticky liquid. Yield: 98% (59.7 mg). IR (Neat): $\nu_{max}$ 3437, 2962, 2937, 1767, 1711, 1677, 1457, 1373, 1288, 1223, 1132, 1223, 1132, 1026, 976, 905, 728, 648 and 518 $cm^{-1}$. $^{1}H$ NMR (500 MHz, $CDCl_3$, 1:1 *dr*): $\delta$ 6.66 (1H, s, *vinylic*-C*H*), 6.64 (1H, s, *vinylic*-C*H*), 2.85 (1H, d, *J* = 7.0 Hz), 2.84 (1H, d, *J* = 7.5 Hz), 2.79 (1H, q, *J* = 7.0 Hz), 2.75 (1H, q, *J* = 7.0 Hz), 2.70-2.60 (4H, m), 2.59-2.52 (2H, m), 2.32 (2H, quint, *J* = 7.0 Hz), 2.07 (2H, quint, *J* = 7.0 Hz), 1.98 (2H, sextet, *J* = 7.0 Hz), 1.80-1.73 (4H, m), 1.52-1.43 (2H, m), 1.40-1.30 (4H, m), 1.09 (3H, t, *J* = 7.0 Hz), 1.08 (3H, t, *J* = 7.0 Hz), 1.02 (3H, t, *J* = 7.0 Hz), 1.01 (3H, t, *J* = 7.0 Hz), 0.85 (3H, t, *J* = 7.5 Hz), 0.80 (3H, t, *J* = 7.5 Hz). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135, 1:1 *dr*): $\delta$ 207.21 (C, *C*=O), 207.17 (C, *C*=O), 202.8 (C, *C*=O), 202.6 (C, *C*=O), 194.62 (C, *C*=O), 194.55 (C, *C*=O), 146.0 (C), 145.9 (C), 143.51 (CH, *vinylic*-*C*H), 143.45 (CH, *vinylic*-*C*H), 84.9 (C, *C*-OH), 84.8 (C, *C*-OH), 73.9 (C), 73.8 (C), 60.5 (2CH), 45.9 (CH), 45.8 (CH), 36.9 ($CH_2$), 36.8 ($CH_2$), 33.6 (CH), 33.2 (CH), 32.9 ($2CH_2$), 28.7 ($CH_2$), 28.1 ($CH_2$), 27.51 ($CH_2$), 27.47 ($CH_2$), 22.78 ($CH_2$), 22.74 ($CH_2$), 19.3 ($CH_3$), 18.6 ($CH_3$), 11.7 ($CH_3$), 11.5 ($CH_3$), 7.5 ($2CH_3$). HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{18}H_{24}O_4Na$ 327.1572; Found: 327.1570.



**85cb**

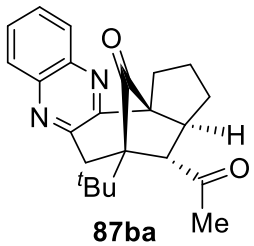
**(4b*S**,5*R**,6*S**,9a*R**)-5-Acetyl-8-(*tert*-butyl)-6-hydroxy-4b,5,6,10-tetrahydro-9*H*-6,9a-methanobenzo[*a*]azulene-9,11-dione (85ea):** The compound was prepared following **Procedure E**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 1.5:8.5) and isolated as a colourless semi solid. Yield: 98% (63 mg). IR (neat): $\nu_{max}$ 3449, 2966, 1759, 1712, 1674, 1392, 1369, 1264, 1160, 1111, 1062, 1040, 906, 732, 701, 559 and 509 $cm^{-1}$. $^{1}H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.24 (1H, d, *J* = 7.5 Hz), 7.20 (1H, t, *J* = 7.5 Hz), 7.16 (1H, t, *J* = 7.5 Hz), 6.91 (1H, d, *J* = 7.5 HZ), 6.77 (1H, s, *vinylic*-C*H*), 4.07 (1H, d, *J* = 7.0 Hz), 3.75 (1H, d, *J* = 17.0 Hz), 3.74 (1H, s, *t*-OH), 3.43 (1H, d, *J* = 17.0 Hz), 3.12 (1H, d, *J* = 7.0 Hz), 2.48 (3H, s), 1.20 (9H, s, 3 x $3CH_3$). $^{13}C$ NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 204.3 (C, *C*=O), 201.6 (C, *C*=O), 192.8 (C, *C*=O), 149.4 (C), 142.7 (CH, *vinylic*-*C*H), 140.9 (C), 139.9 (C), 128.0 (CH), 127.5 (CH), 125.3



**85ea**

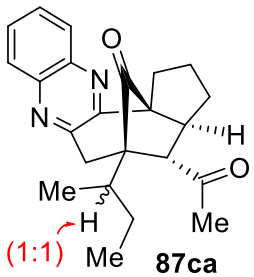
(CH), 123.8 (CH), 83.5 (C, *C*-OH), 73.4 (C), 61.8 (CH), 49.2 (CH), 34.7 (C), 30.9 ($CH_3$), 28.6 (3 x $CH_3$), 28.4 ($CH_2$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{23}O_4$ 339.1596; Found 339.1597.

**(3a*S**,4*S**,5*S**,12b*S**)-4-Acetyl-5-(*tert*-butyl)-2,3,3a,4,5,6-hexahydro-1*H*-5,12b-methanoazuleno[4,5-*b*]quinoxalin-13-one (87ba):** The compound was prepared following **Procedure F**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 2.0:8.0) and isolated as a pale yellow solid. Yield: 82% (29.7 mg). Mp: 170-173 °C. IR (Neat): $\nu_{max}$ 2955, 2873, 1748, 1364, 1167, 763, 517, 492, 456, 435 and 406 $cm^{-1}$. $^1$HNMR (500 MHz, $CDCl_3$): $\delta$ 7.98-7.96 (2H, m), 7.70-7.64 (2H, m), 4.54 (1H, d, *J* = 18.5 Hz), 3.41 (1H, d, *J* =18.5 Hz), 3.11 (1H, d, *J* = 7.0 Hz), 2.75 (1H, dt, *J* = 13.5, 8.0 Hz), 2.60-2.56 (1H, m), 2.38-2.35 (1H, m), 2.33 (3H, s), 2.08-2.01 (1H, m), 1.94-1.86 (1H, m), 1.51-1.44 (1H, m), 1.16 (9H, s, 3 x $3CH_3$). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 210.3 (C, *C*=O), 210.2 (C, *C*=O), 155.9 (C), 153.2 (C), 141.5 (C), 140.4 (C), 129.4 (CH), 129.1 (CH), 128.8 (CH), 128.5 (CH), 65.4 (C), 63.0 (C), 52.8 (CH), 52.0 (CH), 35.7 ($CH_2$), 34.6 (C), 34.3 ($CH_2$), 33.4 ($CH_3$), 26.6 (3 x $CH_3$), 25.9 ($CH_2$), 24.2 ($CH_2$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{23}H_{27}N_2O_2$ 363.2073; Found: 363.2072.



**87ba**

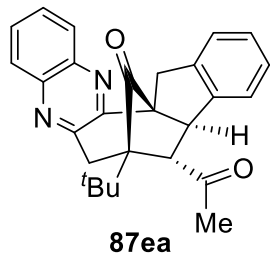
**(3a*S**,4*S**,5*R**,12b*S**)-4-Acetyl-5-(*sec*-butyl)-2,3,3a,4,5,6-hexahydro-1*H*-5,12b-methanoazuleno[4,5-*b*]quinoxalin-13-one (87ca):** The compound was prepared following **Procedure F**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 2.0:8.0) and isolated as a pale yellow solid. Mp: 128-130 °C. Yield: 80% (29 mg). IR (Neat): $\nu_{max}$ 2960, 2926, 1748, 1705, 1461, 1259, 1120, 1171, 1089, 1023, 801, 762, 735, 701, 438 and 416 $cm^{-1}$. $^1$HNMR (500 MHz, $CDCl_3$, 1:1 *dr*): $\delta$ 7.99-7.95 (4H, m), 7.69-7.65 (4H, m), 4.31 (1H, d, *J* = 18.5 Hz), 4.24 (1H, d, *J* = 18.5 Hz), 3.07-3.00 (4H, m), 2.82 (1H, t, *J* = 8.0 Hz), 2.79 (1H, t, *J* = 8.0 Hz), 2.68 (2H, q, *J* = 6.5 Hz), 2.38-2.33 (2H, m), 2.30 (3H, s), 2.29 (3H, s), 2.11-2.04 (2H, m), 2.02-1.96 (2H, m), 1.95-1.87 (2H, m), 1.76-1.68 (4H, m), 1.56-1.50 (1H, m), 1.46-1.39 (2H, m), 1.25-1.16 (1H, m), 1.065 (3H, t, *J* = 7.5 Hz), 1.064 (3H, d, *J* = 6.5 Hz), 1.02 (3H, d, *J* = 7.0 Hz), 1.01 (3H, t, *J* = 7.0 Hz). $^{13}$C NMR (125MHz, $CDCl_3$, DEPT-135, 1:1 *dr*): $\delta$ 212.6 (C, *C*=O), 212.5 (C, *C*=O), 209.7 (C, *C*=O), 209.6 (C, *C*=O), 156.20 (C),



**87ca**

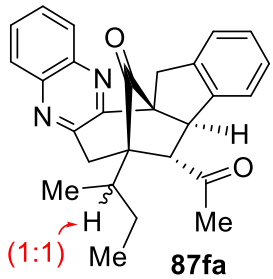
156.16 (C), 152.3 (2C), 141.4 (2C), 140.4 (2C), 129.4 (2CH), 129.2 (2CH), 128.8 (2CH), 128.5 (2CH), 65.3 (2C), 61.7 (C), 61.2 (C), 53.5 (CH), 53.1 (CH), 52.3 (CH), 52.2 (CH), 40.7 ($CH_2$), 40.3 ($CH_2$), 38.5 (CH), 38.4 (CH), 34.9 ($CH_2$), 34.8 ($CH_2$), 32.9 ($2CH_3$), 26.7 ($CH_2$), 26.3 ($CH_2$), 26.2 ($CH_2$), 24.7 ($CH_2$), 24.4 ($CH_2$), 24.3 ($CH_2$), 15.3 ($CH_3$), 14.1 ($CH_3$), 12.8 ($CH_3$), 12.7 ($CH_3$). HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{23}H_{27}N_2O_2$ 363.2072; Found: 363.2073.

**(7*S**,8*S**,8a*R**,13a*S**)-8-Acetyl-7-(*tert*-butyl)-7,8,8a,13-tetrahydro-6*H*-7,13a-methanobenzo [1,2]azuleno[4,5-*b*]quinoxalin-15-one (87ea):** The compound was prepared following **Procedure F**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 2.0:8.0) and isolated as a pale yellow solid. Mp: 170-173 °C. Yield: 98% (40 mg). IR (Neat): $\nu_{max}$, 2958, 2166, 2017, 1748, 1706, 1482, 1419, 1397, 1358, 1293, 1192, 1161, 1122, 1015, 897, 752 and 621 $cm^{-1}$. $^1$HNMR (500 MHz, $CDCl_3$): $\delta$ 8.02 (1H, dd, *J* = 8.25, 1.5 Hz), 7.97 (1H, dd, *J* = 8.25, 1.5Hz), 7.72-7.65 (2H, m), 7.35 (1H, d, *J* = 7.5 Hz), 7.26 (1H, t, *J* = 7.5 Hz), 7.23 (1H, t, *J* =7.0 Hz), 7.10 (1H, d, *J* = 7.5 Hz), 4.37 (1H, d, *J* = 18.0 Hz), 4.34 (1H, d, *J* = 16.5 Hz), 3.83 (1H, d, *J* = 5.5 Hz), 3.61 (1H, d, *J* = 16.5 Hz), 3.57 (1H, dd, *J* = 5.75, 1.5 Hz), 3.52 (1H, dd, *J* = 18.0, 1.5 Hz), 2.51 (3H, s), 1.11 (9H, s, 3 x $3CH_3$). $^{13}$C NMR (100 MHz, $CDCl_3$, DEPT-135): $\delta$ 209.8 (C, *C*=O), 209.7 (C, *C*=O), 154.3 (C), 152.8 (C), 142.4 (C), 141.7 (2C), 140.4 (C), 129.6 (CH), 129.3 (CH), 128.8 (CH), 128.5 (CH), 128.1 (CH), 127.3 (CH), 125.7 (CH), 122.8 (CH), 64.4 (C), 63.0 (C), 57.1 (CH), 54.4 (CH), 36.8 ($CH_2$), 34.6 (C), 33.1 ($CH_3$), 29.8 ($CH_2$), 26.6 (3 x $CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{27}H_{27}N_2O_2$ 411.2072; Found: 411.2079.



**87ea**

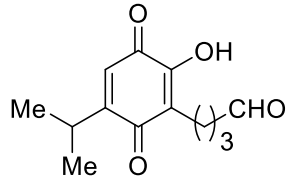
**(7*R**,8*S**,8a*R**,13a*S**)-8-Acetyl-7-(*sec*-butyl)-7,8,8a,13-tetrahydro-6*H*-7,13a-methanobenzo[1,2]azuleno[4,5-*b*]quinoxalin-15-one (87fa):** The compound was prepared following **Procedure F**, purified by column chromatography using ethyl acetate/hexanes (0:10 to 2.0:8.0) and isolated as a pale yellow semi solid. Yield: 90% (37 mg). IR (Neat): $\nu_{max}$ 2963, 2926, 1752, 1707, 1676, 1483, 1459, 1356, 1200, 1164, 1108, 754 and 433 $cm^{-1}$. $^1$HNMR (500 MHz, $CDCl_3$, 1:1 *dr*): $\delta$ 7.99 (4H, t, *J* = 8.0 Hz), 7.72-7.66 (4H, m), 7.34 (2H, d, *J* = 7.5 Hz), 7.26-7.20 (4H, m), 7.04 (2H, t, *J* = 7.5 Hz), 4.36 (1H, d, *J* =16.5 Hz), 4.35 (1H, d, *J* =17.0 Hz), 4.08 (1H, d, *J* = 18.0 Hz), 4.04 (1H, d, *J* = 18.0 Hz), 3.99-



**87fa**

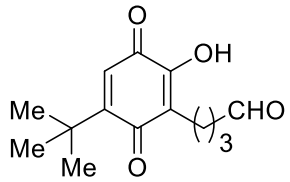
3.98 (2H, m), 3.624 (1H, d, *J* = 16.5 Hz), 3.619 (1H, d, *J* = 17.0 Hz), 3.48 (2H, d, *J* = 4.5 Hz), 3.14 (1H, d, *J* = 18.5 Hz), 3.10 (1H, d, *J* = 18.0 Hz), 2.48 (3H, s), 2.47 (3H, s), 2.04-2.00 (2H, m), 1.75-1.71 (2H, m), 1.27-1.07 (2H, m), 1.03 (3H, d, *J* = 7.0 Hz), 1.00-0.98 (3H, m), 0.95 (3H, t, *J* =7.5 Hz), 0.92 (3H, d, *J* = 6.5 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135, 1:1 *dr*): $\delta$ 212.0 (C, *C*=O), 211.89 (C, *C*=O), 209.6 (C, *C*=O), 209.4 (C, *C*=O), 154.6 (C), 154.5 (C), 151.8 (2C), 142.3 (C), 142.2 (C), 141.1 (C), 142.0 (C), 141.5 (2C), 140.4 (2C), 129.7 (2CH), 129.4 (2CH), 128.8 (2CH), 128.6 (2CH), 127.9 (2CH), 127.37 (CH), 127.36 (CH), 125.5 (2CH), 122.9 (2CH), 64.2 (2C), 61.4 (C), 60.9 (C), 57.2 (CH), 57.0 (CH), 54.7 (CH), 54.4 (CH), 41.9 (CH), 41.5 (CH), 38.3 (CH), 38.2 (CH), 32.9 ($2CH_3$), 30.02 ($CH_2$), 30.00 ($CH_2$), 26.7 ($CH_2$), 24.6 ($CH_2$), 15.3 ($CH_3$), 14.2 ($CH_3$), 12.8 ($CH_3$), 12.6 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{27}H_{27}N_2O_2$ 411.2072; Found: 411.2073.

**4-(2-Hydroxy-5-isopropyl-3,6-dioxocyclohexa-1,4-dien-1-yl)butanal (82a)**: The compound was prepared following **Procedure B**, purified by the process mentioned in general **Procedure B** and isolated as a yellow solid. Mp: 50-52 °C; Yield: 28% (436 mg). IR (Neat): $\nu_{max}$ 3357, 2963, 2930, 1718, 1637, 1609, 1459, 1385, 1363, 1256, 1208, 1185, 888, 836, 810 and 743 $cm^{-1}$. $^1$HNMR (500 MHz, $CDCl_3$): $\delta$ 9.77 (1H, t, *J* = 1.0 Hz, C*H*O), 7.13 (1H, br s, *enolic*-O*H*), 6.51 (1H, s, *vinylic*-C*H*), 3.12 (1H, sept, *J* = 7.0 Hz), 2.53-2.47 (4H, m), 1.84 (2H, quint, *J* =7.5 Hz), 1.13 (6H, d, *J* = 7.0 Hz, 2 x $CH_3$). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 202.2 (CH, *C*HO), 186.8 (C, *C*=O), 183.5 (C, *C*=O), 158.3 (C), 151.0 (C), 125.6 (CH, *vinylic*-*C*H), 120.4 (C), 43.4 ($CH_2$), 27.2 (CH), 22.2 ($CH_2$), 21.6 (2 x $CH_3$), 20.6 ($CH_2$). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{13}H_{16}O_4Na$ 259.0946; Found: 259.0940.



**82a**

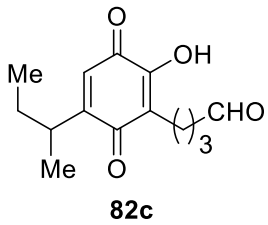
**4-(5-*(tert*-Butyl)-2-hydroxy-3,6-dioxocyclohexa-1,4-dien-1-yl)butanal (82b)**: The compound was prepared following **Procedure B**, purified by the process mentioned in general **Procedure B** and isolated as a reddish yellow sticky liquid. Yield: 32% (560 mg). IR (Neat): $\nu_{max}$ 2968, 1738, 1642, 1599, 1438, 1377, 1216, 1105, 904, 727 and 649 $cm^{-1}$. $^1$HNMR (500 MHz, $CDCl_3$): $\delta$ 9.77 (1H, s, C*H*O), 6.90 (1H, br s, *enolic*-O*H*), 6.57 (1H, s, *vinylic*-C*H*), 2.51-2.46 (4H, m), 1.82 (2H, quint, *J* =7.5 Hz), 1.29 (9H, s, 3 x $CH_3$). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 202.2 (CH, *C*HO), 187.1 (C, *C*=O), 183.7 (C, *C*=O), 159.3 (C), 150.4 (C),



**82b**

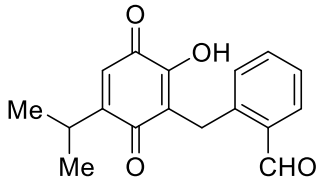
126.9 (CH, *vinylic-C*H), 121.6 (C), 43.4 ($CH_2$), 35.9 (C), 29.6 (3 x $CH_3$), 22.3 ($CH_2$), 20.7 ($CH_2$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{14}H_{19}O_4$ 251.1283; Found: 251.1284.

**4-(5-(*sec*-Butyl)-2-hydroxy-3,6-dioxocyclohexa-1,4-dien-1-yl)butanal (82c)**: The compound was prepared following **Procedure B**, purified by the process mentioned in general **Procedure B** and isolated as a reddish yellow sticky liquid. Yield: 31% (543 mg). IR (Neat): $\nu_{max}$ 3388, 2960, 2928, 1708, 1640, 1608, 1500, 1441, 1366, 1283, 1214, 1170, 876, 831 and 548 $cm^{-1}$. $^1$HNMR (400 MHz, $CDCl_3$): $\delta$ 9.77 (1H, s, C*H*O), 7.00 (1H, br s, *enolic*-O*H*), 6.47 (1H, d, *J* = 0.8 Hz, *vinylic*-C*H*), 2.94 (1H, sextet, *J* = 7.2 Hz), 2.53-2.45 (4H, m), 1.83 (2H, quint, *J* =7.6 Hz), 1.61-1.50 (1H, m), 1.47-1.36 (1H, m), 1.11 (3H, d, *J* = 7.2 Hz), 0.89 (3H, t, *J* = 7.2 Hz). $^{13}$C NMR (100 MHz, $CDCl_3$, DEPT-135): $\delta$ 202.1 (CH, *C*HO), 186.9 (C, *C*=O), 183.4 (C, *C*=O), 157.5 (C), 150.9 (C), 126.3 (CH, *vinylic-C*H), 120.4 (C), 43.4 ($CH_2$), 33.6 (CH), 28.9 ($CH_2$), 22.3 ($CH_2$), 20.6 ($CH_2$), 19.0 ($CH_3$), 11.7 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{14}H_{19}O_4$ 251.1283; Found: 251.1282.



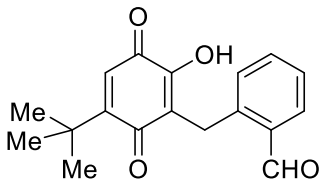
**82c**

**2-((2-Hydroxy-5-isopropyl-3,6-dioxocyclohexa-1,4-dien-1-yl)methyl)benzaldehyde (82d)**: The compound was prepared following **Procedure B**, purified by the process mentioned in general **Procedure B** and isolated as a yellow solid. Mp: 110-112 °C. Yield: 30% (563 mg). IR (Neat): $\nu_{max}$ 2979, 1670, 1634, 1595, 1377, 1352, 1324, 1202, 1181, 967, 760, 634 and 530 $cm^{-1}$. $^1$HNMR (500 MHz, $CDCl_3$): $\delta$ 10.51 (1H, s, C*H*O), 7.84 (1H, dd, *J* = 7.5, 1.0 Hz), 7.47 (1H, dt, *J* = 7.5, 1.0 Hz), 7.36 (1H, t, *J* = 7.5 Hz), 7.35 (1H, d, *J* = 7.5 Hz), 7.24 (1H, br s, *enolic*-O*H*), 6.52 (1H, s, *vinylic*-C*H*), 4.25 (2H, s), 3.10 (1H, sept, *J* = 7.0 Hz), 1.11 (6H, d, *J* = 7.0 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 192.9 (CH, *CH*O), 186.5 (C, *C*=O), 183.4 (C, *C*=O), 158.4 (C), 151.3 (C), 141.0 (C), 133.9 (C), 133.8 (CH), 130.8 (CH), 130.7 (CH), 126.8 (CH), 125.8 (CH), 119.2 (C), 27.2 (CH), 24.8 ($CH_2$), 21.6 (2 x $CH_3$). HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{17}H_{16}O_4Na$ 307.0946; Found: 307.0947.



**82d**

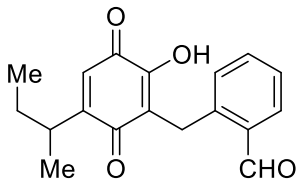
**2-((5-(*tert*-Butyl)-2-hydroxy-3,6-dioxocyclohexa-1,4-dien-1-yl)methyl)benzaldehyde (82e)**:




**82e**

The compound was prepared following **Procedure B**, purified by the process mentioned in general **Procedure B** and isolated as a yellow sticky liquid. Yield: 31% (647 mg). IR (Neat): $\nu_{max}$ 2960, 2923, 1690, 1643, 1456, 1363, 1264, 1218, 734 and 703 $cm^{-1}$. HNMR (400 MHz, $CDCl_3$): $\delta$ 10.50 (1H, s, C*H*O), 7.84 (1H, dd, *J* = 7.5, 1.5 Hz), 7.47 (1H, dt, *J* = 7.5, 1.5 Hz), 7.35 (1H, t, *J* = 7.5 Hz), 7.32 (1H, d, *J* = 7.5 Hz), 7.19 (1H, br s, *enolic*-O*H*), 6.59 (1H, s, *vinylic*-C*H*), 4.24 (2H, s), 1.27 (9H, s, 3 x $CH_3$). $^{13}$C NMR (100 MHz, $CDCl_3$, DEPT-135): $\delta$ 193.0 (C, *C*HO), 186.8 (C, *C*=O), 183.7 (C, *C*=O), 159.3 (C), 150.7 (C), 141.1 (C), 133.8 (C), 133.8 (CH), 131.0 (CH), 130.6 (CH), 127.1 (CH), 126.8 (CH), 120.3 (C), 36.0 (C), 29.5 (3 x $CH_3$), 24.8 ($CH_2$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{19}O_4$ 299.1283; Found: 299.1285.

**2-((5-(*sec*-Butyl)-2-hydroxy-3,6-dioxocyclohexa-1,4-dien-1-yl)methyl)benzaldehyde (82f)**:




**82f**

The compound was prepared following **Procedure B**, purified by the process mentioned in general **Procedure B** and isolated as a yellow sticky liquid. Yield: 30% (626 mg). IR (Neat): $\nu_{max}$ 3339, 2964, 1690, 1641, 1609, 1453, 1362, 1217, 978 and 758 $cm^{-1}$. $^1$HNMR (500 MHz, $CDCl_3$): $\delta$ 10.50 (1H, s, C*H*O), 7.84 (1H, dd, *J* = 7.5, 1.0 Hz), 7.47 (1H, dt, *J* = 7.5, 1.0 Hz), 7.36 (1H, t, *J* = 7.5 Hz), 7.34 (1H, d, *J* = 7.5 Hz), 7.29 (1H, br s, *enolic*-O*H*), 6.49 (1H, d, *J* = 1.0 Hz, *vinylic*-C*H*), 4.26 (2H, s), 2.93 (1H, sextet, *J* = 7.0 Hz), 1.58-1.49 (1H, m), 1.44-1.35 (1H, m), 1.09 (3H, *d*, *J* = 7.0 Hz), 0.87 (3H, t, *J* = 7.5 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$, DEPT-135): $\delta$ 192.9 (CH, *C*HO), 186.6 (C, *C*=O), 183.3 (C, *C*=O), 157.6 (C), 151.2 (C), 141.0 (C), 133.9 (C), 133.7 (CH), 130.9 (CH), 130.7 (CH), 126.8 (CH), 126.5 (CH), 119.2 (C), 33.6 (CH), 28.9 ($CH_2$), 24.8 ($CH_2$), 18.9 ($CH_3$), 11.6 ($CH_3$). HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{19}O_4$ 299.1283; Found: 299.1286.

# 7. References


1. a) Tornøe, C. W.; Christensen, C.; Meldal, M. Peptidotriazoles on Solid Phase: [1,2,3]-Triazoles by Regiospecific Copper(I)-Catalyzed 1,3-Dipolar Cycloadditions of TerminalAlkynes to Azides, *J. Org. Chem.* **2002,** *67*, 3057-3064. b) Brik, A.; Alexandratos, j.; Chuan Lin, Y.; Elder, J. H.; Olson, A. J.; Wlodawer, A.; Goodsell, D. S.; Wong. C. H. 1,2,3-Triazole as a Peptide Surrogate in the Rapid Synthesis of HIV-1 Protease Inhibitors. *ChemBioChem*. **2005**, *6*, 1167 –1169. c) Moses J. E.; Moorhouse. A. D. The growing applications of click chemistry. *Chem. Soc. Rev*. **2007**, *36*, 1249–1262. d) Angell. Y. L.; Burgess, K. Peptidomimetics via copper-catalyzed azide–alkyne cycloadditions. *Chem. Soc. Rev*. **2007**, *36*, 1674–1689. e) Mamidyala, S. K.; Finn, M. G. In situ click chemistry: probing the binding landscapes of biological molecules. *Chem. Soc. Rev*. **2010**, *39*, 1252–1261. f) Mascarin, A.; Valverde, I. E.; Vomstein, S.; Mindt, T. L. 1,2,3-Triazole Stabilized Neurotensin-Based Radiopeptidomimetics for Improved Tumor Targeting. *Bioconjugate Chem.* **2015**, *26*, 2143-2152. g) Valverde, I. E.; Vomstein, S.; Fischer, C. A.; Mascarin, A.; Mindt. T. L. Probing the Backbone Function of Tumor Targeting Peptides by an Amide-to-Triazole Substitution Strategy. *J. Med. Chem.* **2015**, *58*, 7475–7484.
2. R. Huisgen in 1,3-Dipolar Cycloaddition Chemistry (Ed.: A. Padwa), Wiley, New York, **1984**, pp. 1-176; b) A. Padwa in Comprehensive Organic Synthesis, Vol. 4 (Ed.: B. M. Trost), Pergamon, Oxford, **1991**, pp. 1069- 1109;
3. Rostovtsev, V. V.; Green, L. G.; Fokin, V. V.; Sharpless, K. B. A Stepwise Huisgen Cycloaddition Process:Copper(I)-Catalyzed Regioselective "Ligation" of Azides and Terminal Alkynes. *Angew. Chem. Int. Ed*. **2002**, *41*, 2596-2599.
4. a) Agard, N. J.; Prescher, J. A.; Bertozzi, C. R. A Strain-Promoted [3+2] Azide-Alkyne Cycloaddition for Covalent Modification of Biomolecules in Living Systems. *J. Am. Chem. Soc.* **2004**, *126*, 15046-15047. b) Laughlin, S. T.; Baskin, J, M.; Amacher, S. L.; Bertozzi, C. R. In Vivo Imaging of Membrane-Associated Glycans in Developing Zebrafish. *Science.* **2008**, *320*, 664–667. c) Gartner, Z. J.; Bertozzi, C. R. Programmed assembly of 3-dimensional microtissues with defined cellular connectivity. *Proc. Natl. Acad. Sci. U. S. A.* **2009**, *106*, 4606–4610. d) Debets, M. F.; Doelen, C. W. J. F.; Rutjes,

P. J. T.; Delft, F. L. Azide: A Unique Dipole for Metal-Free Bioorthogonal Ligations. *ChemBioChem* **2010**, *11*, 1168 – 1184. e) Shelbourne, M.; Chen, X.; Brownz, T.; Sagheerz, A. H. E. Fast copper-free click DNA ligation by the ring-strain promoted alkyne-azide cycloaddition reaction. *Chem. Commun.* **2011**, *47*, 6257–6259

5. Zhang, L.; Chen, X.; Xue, P.; Sun, H. H. Y.; Williams, I. D.; Sharpless, K. B.; Fokin, V. V.; Jia, G. Ruthenium-Catalyzed Cycloaddition of Alkynes and Organic Azides. *J. Am. Chem. Soc.* **2005**, *127*, 15998-15999.
6. Krasin´ ski, A.; Fokin, V.V.; Sharpless, K. B. Direct Synthesis of 1,5-Disubstituted-4-magnesio-1,2,3-triazoles, Revisited. *Org. Lett.* **2004**, *6*, 1237-1240.
7. Angell, Y.; Burgess, K. Base Dependence in Copper-Catalyzed Huisgen Reactions:Efficient Formation of Bistriazoles. *Angew. Chem. Int. Ed*. **2007**, *46*, 3649 – 3651.
8. Monkowius, U.; Ritter, S.; König, B.; Zabel, M.; Yersin, H. Synthesis, Characterisation and Ligand Properties of Novel Bi-1,2,3-triazole Ligands. *Eur. J. Inorg. Chem.* **2007**, 4597–4606.
9. Oladeinde, O. A.; Hong, S. Y.; Holland, R. J.; Maciag, A. E.; Keefer, L. K.; Saavedra, J. E.; Nandurdikar, R. S. "Click" Reaction in Conjunction with Diazeniumdiolate Chemistry: Developing High-Load Nitric Oxide Donors. *Org. Lett.* **2010**, *12*, 4256–4259.
10. Tautz, M.; Saldıas, C.; Gorrin, A. D. L.; Diaz, D. D. Use of a bis-1,2,3-triazole gelator for the preparation of supramolecular metallogels and tabilization of gold nanoparticles. *New J. Chem.*, **2019**, *43*, 13850—13856.
11. a) Ramachary, D. B.; Ramakumar, K.; Narayana. V. V. Amino Acid-Catalyzed Cascade [3+2]-Cycloaddition/Hydrolysis Reactions Based on the Push–Pull Dienamine Platform: Synthesis of Highly Functionalized *N*H-1,2,3-Triazoles. *Chem. Eur. J.* **2008**, *14*, 9143 – 9147. b) Ramachary, D. B.; Shashank, A. B.; Karthik, S. An Organocatalytic Azide–Aldehyde [3+2]-Cycloaddition: High-Yielding Regioselective Synthesis of 1,4-Disubstituted 1,2,3-Triazoles. *Angew. Chem. Int. Ed.* **2014**, *53*, 10420 –10424. c) Ramachary, D. B.; Krishna, P. M.; Gujral, J.; Reddy. G. S. *Chem. Eur. J.* **2015**, *21*, 16775 – 16780. d) Reddy, G. S.; Reddy, L. M.; Kumar, A. S.; Ramachary. D. B Organocatalytic Selective [3 + 2]-Cycloadditions: Synthesis of Functionalized 5-Arylthiomethyl-1,2,3-triazoles and 4-Arylthio-1,2,3-triazoles. *J. Org. Chem.* **2020**, *85*, 15488-15501.

12. Belkheira, M.; Abed, D. E.; Jean-Marc Pons, J. M.; Bressy, C. Organocatalytic Synthesis of 1,2,3-Triazoles from Unactivated Ketones and Arylazides. *Chem. Eur. J.* **2011**, *17*, 12917 – 12921.
13. a) Danence, L. J. T.; Gao, Y.; Li, M.; Huang, Y.; Wang, J. Organocatalytic Enamide–Azide Cycloaddition Reactions: Regiospecific Synthesis of 1,4,5-Trisubstituted-1,2,3-Triazoles. *Chem. Eur. J.* **2011**, *17*, 3584 – 3587. b) Wang, L.; Peng, S.; Danence, L. J. T,; Gao, Y.; Wang, J. Amine-Catalyzed [3+2] Huisgen Cycloaddition Strategy for the Efficient Assembly of Highly Substituted 1,2,3-Triazoles. *Chem. Eur. J.* **2012**, *18*, 6088 – 6093. c) Jia, Q.; Yang, G.; Chen, L.; Du, Z.; Wei, J.; Zhong, Y.; Wang. J.; A Facile One-Pot Metal-Free Synthesis of 1,4-Disubstituted 1,2,3-Triazoles. *Eur. J. Org. Chem.* **2015**, 3435–3440.
14. Shu, M.; Ran, L.; Liu, K.; Yang, W.; Wang, Q. An efficient and regiospecific synthesis of 1,5-diaryl-4-benzothiazolyl-1,2,3-triazoles by organocatalytic 1,3-dipolar cycloaddition reactions. *Synth. Commun.* **2020**, *50*, 1863–1870.
15. Mehrotra, R.; Vishwakarma, R. A.; Thakur, R. S. ABIETANE DITERPENOIDS FROM *COLE US ZE YLANICUS. Phytochemistry*, **1989**, *28*, 3135-3137.
16. Majetich, G.; Zhang, Y.; Tian, X.; Britton, J. E.; Li Y.; Phillips. R. Synthesis of (±)-and (+)-perovskone. *Tetrahedron.* **2011**, 67, 10129-10146.
17. Silva Jr. E. N. D.; Cavalcanti b, B. C.; Guimarães, T. T.; Pinto, M. C. F. R.; Cabral, I. O.; Pessoa, C.; Costa-Lotufo, L. V.; Moraes, M, O.; Andrade, C. K. Z.; Santos, M. R.; Goulart, C. A. S. M.; Pinto, A. V. Synthesis and evaluation of quinonoid compounds against tumor cell lines. *Eur. J. Med. Chem.* **2011**, *46*, 399-410.
18. Wendlandt A. E.; Stahl. S. S. Chemoselective Organocatalytic Aerobic Oxidation of Primary Amines to Secondary Imines. *Org. Lett.* **2012**, *14*, 2850–2853.
19. Qin, Y.; Zhang, L.; Lv, J.; Luo, S.; Cheng. J. P. Bioinspired Organocatalytic Aerobic C−H Oxidation of Amines with an ortho-Quinone Catalyst. *Org. Lett.* **2015,** *17*, 1469−1472.
20. Rosenau, T.; Zwirchmayr, N. S.; Hosoya, T.; Horvath, A. H.; Bacher, M.; Potthast. A. Janus-faced 5-methyl group in 2-hydroxy-5-methyl-[1,4]-Benzoquinone. *Tetrahedron.* **2017**, *73*, 6421-6427.
21. Yin, G. P.; Wu, Y. R.; Han, C.; Wang, X. B.; Gao, H. L.; Yin, Y.; Kong, L. Y.; Yang, M. H. Asperones A–E, five dimeric polyketides with new carbon skeletons from the fungus Aspergillus sp. AWG 1–15. *Org. Chem. Front.* **2018**, *5*, 2432–2436.

22. Long, Y.; Ding, Y.; Wu, H.; Qu, C.; Liang, H.; Zhang, M.; Zhao, X.; Long, X.; Wang, S.; Puno, P. T.; Deng. J. Total Synthesis of (-)-Perezoperezone through an Intermolecular [5+2] Homodimerization of Hydroxy p-Quinone. *Angew. Chem. Int. Ed.* **2019**, *58*, 17552 –17557.
23. A) Hitotsuyanagi, Y.; Motegi, S.; Fukaya, H.; Takeya, K. A *cis* Amide Bond Surrogate Incorporating 1,2,4-Triazole. *J. Org. Chem.* **2002**, *67*, 3266-3271. b) Horne, W. S.; Yadav, M. K.; Stout, C. D.; Ghadiri, M. R. Heterocyclic Peptide Backbone Modifications in an r-Helical Coiled Coil. *J. Am. Chem. SOC*. **2004**, *126*, 15366-15367. c) Hua. Y.; Flood. A. H. Click chemistry generates privileged CH hydrogen-bonding triazoles: the latest addition to anion supramolecular chemistry. *Chem. Soc. Rev*. **2010**, *39*, 1262–1271. d) Qin, A.; Lam, J. W. Y.; Tang. B. Z.; Click polymerization. *Chem. Soc. Rev.* **2010**, *39*, 2522–2544. e) Hanni, K. D.; Leigh, D. A. The application of CuAAC 'click' chemistry to catenane and rotaxane synthesis. *Chem. Soc. Rev.* **2010**, *39*, 1240–1251. f) Kantheti, S.; Narayan, R.; Raju, K. V. S. N. The impact of 1,2,3-triazoles in the design of functional coatings. *RSC Adv.* **2015**, *5*, 3687–3708. g) Li, S.; Wang, L.; Yu, F.; Zhu, Z.; Shobaki, D.; Chen, H.; Wang, M.; Wang, J.; Qin, G.; Erasquin, U. J.; Ren, L.; Wang, Y.; Cai, C. Copper-catalyzed click reaction on/in live cells. *Chem. Sci.* **2017**, *8*, 2107–2114. h) Huo, J.; Hu, H.; Zhang, M.; Hu, X.; Chen, M.; Chen, D.; Liu, J.; Xiao, G.; Wanga, Y.; Wen, Z. A mini review of the synthesis of poly-1,2,3-triazole-based functional materials. *RSC Adv*. **2017**, *7*, 2281–2287.
24. a) Luo, Q.; Jia, G.; Sun, J.; Lin, Z. Theoretical Studies on the Regioselectivity of Iridium-Catalyzed 1,3-Dipolar Azide−Alkyne Cycloaddition Reactions. *J. Org. Chem.* **2014**, *79*, *24*, 11970–11980. b) Ding, S.; Jia, G.; Sun, J. Iridium-Catalyzed Intermolecular Azide–Alkyne Cycloaddition of Internal Thioalkynes under Mild Conditions. *Angew. Chem. Int. Ed*. **2014**, *53*, 1877 –1880.
25. a) Kim, W. G.:, Kang, M. E.; Bin Lee, J. L.; Jeon, M. H.; Lee, S.; Lee, J.; Choi, B.; Cal, P, M. S. D.; Kang, S. Kee, J. M.; Bernardes, G. J. L.; Rohde, J. U.; Choe, W.; Hong. S. Y. Nickel-Catalyzed Azide−Alkyne Cycloaddition To Access 1,5-Disubstituted 1,2,3-Triazoles in Air and Water. *J. Am. Chem. Soc.* **2017**, *139*, 12121−12124. b) Kim, W.; G.; Baek, S. Y.; Jeong, S. Y.; Nam, D.; Jeon, J. H.; Choe, W. Baik, M. H.; Hong, S. Y. Chemo- and regioselective click reactions through nickel-catalyzed azide–alkyne cycloaddition.

*Org. Biomol. Chem.* **2020**, *18*, 3374–3381. c) Liu, E. C.; Topczewski, J. J. Enantioselective Nickel-Catalyzed Alkyne−Azide Cycloaddition by Dynamic Kinetic Resolution. *J. Am. Chem. Soc.* **2021**, *143*, 5308−5313.

26. a) Szuroczki, P.; Molnar, L.; Dornyei, A.; Kollar, L.; Facile, High-Yielding Synthesis of 4-Functionalised 1,2,3-Triazoles via Amino- and Aryloxycarbonylation. *ChemistrySelect* **2020**, *5*, 448–451. b) Albuquerque, D. Y.; Moraes, J. R.; Schwab, R. S. Palladium-Catalyzed Aminocarbonylation Reaction to Access 1,2,3-Triazole-5-carboxamides Using Dimethyl Carbonate as Sustainable Solvent. *Eur. J. Org. Chem.* **2019**, 6673–6681. c) Xu, S.; Mao, L.; Ding, P.; Zhuang, X.; Zhou, Y.; Yu. L.; Liu, Y.; Nie, Tao.; Xu T.; Xu, Y.; Liu, J.; Smaill. J.; Ren, X.; Donghai Wu. D.; Ding. K. 1-Benzyl-4-phenyl-1*H*-1,2,3-triazoles improve the transcriptional functions of estrogen-related receptor c and promote the browning of white adipose. *Bioorg. Med. Chem.* **2015**, *23*, 3751–3760.
27. a) Calderone, V.; Fiamingo, F. L.; Amato, G.; Giorgi, I.; Livi, O.; Martelli, A.; Martinotti, E. 1,2,3-Triazol-carboxanilides and 1,2,3-triazol-(N-benzyl)-carboxamides as BK-potassium channel activators. XII. *Eur. J. Med. Chem.* **2008**, *43*, 2618-2626. b) Xu, S.; Zhuang, X.; Pan, X.; Zhang, Z.; Duan, L.; Liu, Y.; Zhang, L.; Ren, X.; Ding, K. 1-Phenyl-4-benzoyl-1*H*-1,2,3-triazoles as Orally Bioavailable Transcriptional Function Suppressors of Estrogen-Related Receptor α. *J. Med. Chem.* **2013**, *56*, 11, 4631-4640. c) Gao, Z.; Du, Y.; Sheng, X.; Shen, J. Molecular Dynamics Simulations Based on 1-Phenyl-4-Benzoyl-1-Hydro-Triazole ERR Inverse Agonists. *Int. J. Mol. Sci.* **2021**, *22*, 3724. d) Ahmed, D. M.; Chen, J. M.; Sanders, D. A. R. Pyrazole and Triazole Derivatives as Mycobacterium tuberculosis UDP-Galactopyranose Inhibitors. *Pharmaceuticals* **2022**, *15*, 197.
28. a) Droumaguet, C. L.; Wangab, C.; Wang, Q. Fluorogenic click reaction. *Chem. Soc. Rev*.**2010**, *39*, 1233–1239. b) Qi, J.; Tung, C. H. Development of benzothiazole 'click-on' fluorogenic dyes. *Bioorg. Med. Chem. Lett.* **2011**, *21*, 320–323. c) Han, J.; Engler, A.; Qi, J.; Tung, C. H. Ultra pseudo-Stokes shift near infrared dyes based on energy transfer. *Tetrahedron Letters.* **2013**, *54*, 502–505. d) Zhang, G.; Gruskos, J. J.; Afzal, M. S.; Buccella, D. Visualizing changes in mitochondrial $Mg^{2+}$ duringapoptosis with organelle-targeted triazole-based ratiometric fluorescent sensors. Chem. Sci., **2015**, *6*, 6841–6846. e) Reddy, G. S.; Ramachary, D. B. Reaction engineering and photophysical studies of fully enriched C-vinyl-1,2,3-triazoles. *Org. Chem. Front*. **2019**, *6*, 3620–3628.

29. Pokhodylo, N. T.; Matiychuk, V. S.; Obushak, N. B. SYNTHESIS OF 1H-1,2,3-TRIAZOLE DERIVATIVES BY THE CYCLIZATION OF ARYL AZIDES WITH 2-BENZOTHIAZOLYLACETONONE, 1,3-BENZO-THIAZOL-2-YLACETONITRILE, AND (4-ARYL- 1,3-THIAZOL-2-YL)ACETONITRILES. *Chemistry of Heterocyclic Compounds.* **2009**, *45*, 483-488.
30. Qi, J.; Han, M. S.; Chang, Y. C.; Tung, C. H. Developing Visible Fluorogenic 'Click-On' Dyes for Cellular Imaging. *Bioconjugate Chem.* **2011**, *22*, 1758–1762.
31. Walji, A.; MacMillan, D. W. C. Strategies to Bypass the Taxol Problem. Enantioselective Cascade Catalysis, a New Approach for the Efficient Construction of Molecular Complexity. *Synlett.* 2007, 1477-1489.
32. Jones, S. B.; Simmons, B.; Mastracchio, A.; MacMillan, D. W. C. Collective synthesis of natural products by means of organocascade catalysis. *Nature* 2011, *475*, 183-188.
33. Ramachary, D. B.; Jain, S. Sequential one-pot combination of multi-component and multi-catalysis cascade reactions: an emerging technology in organic synthesis. *Org. Biomol. Chem.* 2011, *9*, 1277-1300.
34. Tietze, L. F. Domino Reactions in Organic Synthesis. *Chem. Rev.* **1996**, *96*, 115-136.
35. Nicolaou, K. C.; Montagnon, T.; Snyder, S. A. Tandem reactions, cascade sequences, and biomimetic strategies in total synthesis. *Chem. Commun.* 2003, 551-564.
36. a) Ramon, D. J.; Yus, M. Asymmetric Multicomponent Reactions (AMCRs): The New Frontier. *Angew. Chem. Int. Ed.* **2005**, *44*, 1602-1634, b) Asymmetrische SynthesenNeue Entwicklungen in der asymmetrischenMehrkomponenten-Reaktion. *Angew. Chem.* **2005**, *117*, 1628-1661.
37. Erkkila, A.; Majander, I.; Pihko, P. M. Iminium Catalysis. *Chem. Rev.* 2007, *107*, 5416-5470.
38. Grondal, C.; Jeanty, M.; Enders, D. Organocatalytic cascade reactions as a new tool in total synthesis. *Nat. Chem.* **2010**, *2*, 167-178.
39. Ramachary, D. B.; Reddy, Y. V. Dienamine catalysis: an emerging technology in organic synthesis. *Eur. J. Org. Chem.* **2012**, 865-887.
40. Ramachary, D. B.; Chowdari, N. S.; Barbas III, C. F. Organocatalytic Asymmetric Domino Knoevenagel/Diels–Alder Reactions: A Bioorganic Approach to the Diastereospecific and Enantioselective Construction of Highly Substituted Spiro[5,5]undecane-1,5,9-triones.

*Angew. Chem. Int. Ed.* **2003**, *42*, 4233-4237. Organocatalytic Asymmetric Domino Knoevenagel/Diels–Alder Reactions: A Bioorganic Approach to the Diastereospecific and Enantioselective Construction of Highly. *Angew. Chem.* **2003**, *115*, 4365-4369.

41. Yang, J. W.; Fonseca, M. T. H.; List, B. Catalytic asymmetric reductive Michael cyclization. *J. Am. Chem. Soc.* **2005**, *127*, 15036-15037.
42. Jiang, X.; Tan, B.; Barbas, C. F. III. Core-Structure-Motivated Design of Iminium–Enolate Organocascade Reactions: Enantioselective Syntheses of 5, 6-Dihydroindolizines. *Angew. Chem. Int. Ed.* **2013**, *52*, 9261-9265, *Angew. Chem.* **2013**, *125*, 9431-9435.
43. Enders, D.; Huttl, M. R. M.; Grondal, C.; Raabe, G. Control of four stereocentres in a triple cascade organocatalytic reaction. *Nature* **2006**, *441*, 861-863.
44. Carlone, A.; Cabrera, S.; Marigo, M.; Jørgensen, K. A. A new approach for an organocatalytic multicomponent domino asymmetric reaction. *Angew. Chem. Int. Ed.* **2007**, *46*, 1101-1104, *Angew. Chem.* **2007**, *119*, 1119-1122.
45. Jiang, K.; Jia, Z.–J.; Yin, X.; Wu, L.; Chen, Y.–C. Asymmetric quadruple aminocatalytic domino reactions to fused carbocycles incorporating a spirooxindole motif. *Org. Lett.* **2010**, *12*, 2766-2769.
46. Rueping, M.; Haack, K.–L.; Ieawsuwan, W.; Sunden, H.; Blanco, M.; Schoepke, F. R.; Nature-inspired cascade catalysis: reaction control through substrate concentration—double vs. quadruple domino reactions. *Chem. Commun.* **2011**, *47*, 3828-3830.
47. Ishikawa, H.; Suzuki, T.; Hayashi, Y. High-yielding synthesis of the anti-influenza neuramidase inhibitor (−)-oseltamivir by three "one-pot" operations. *Angew. Chem. Int. Ed.* **2009**, *48*, 1304-1307, *Angew. Chem.* **2009**, *121*, 1330-1333.
48. Ramachary, D. B.; Venkaiah, Ch.; Krishna, P. M. Discovery of 2-aminobuta-1, 3-enynes in asymmetric organocascade catalysis: construction of drug-like spirocyclic cyclohexanes having five to six contiguous. *Chem. Commun.* **2012**, *48*, 2252-2254.
49. a) Ramachary, D. B.; Reddy, Y. V.; Banerjee, A.; Banerjee, S. Design, synthesis and biological evaluation of optically pure functionalized spiro [5, 5] undecane-1, 5, 9-triones as HIV-1 inhibitors. *Org. Biomol. Chem.* **2011**, *9*, 7282-7286; b) D. B. Ramachary, M. Kishor, G. B. Reddy. Development of drug intermediates by using direct organocatalytic multi-component reactions. *Org. Biomol. Chem.* **2006**, *4*, 1641-1646.

50. Mangion, I. K.; MacMillan, D. W. C. Total synthesis of brasoside and littoralisone. *J. Am. Chem. Soc.* **2005**, *127*, 3696-3697.
51. Nicolaou, K. C.; Wu, T. R.; Sarlah, D.; Shaw, D. M.; Rowcliffe, E.; Burton, D. R. Total synthesis, revised structure, and biological evaluation of biyouyanagin A and analogues thereof. *J. Am. Chem. Soc.* **2008**, *130*, 11114-11121.
52. Jensen, K. L.; Weise, C. F.; Dickmeiss, G.; Morana, F.; Davis, R. L.; Jørgensen, K. A. Selective Access to Both Diastereoisomers in an Enantioselective Intramolecular Michael Reaction by Using a Single Chiral Organocatalyst and Application in the Formal Total Synthesis of (−)-Epibatidine. *Chem. Eur. J.* **2012**, *18*, 11913-11918.
53. Northrup, N. A. B.; MacMillan, D. W. C. Two-step synthesis of carbohydrates by selective aldol reactions. *Science* **2004**, *305*, 1752-1755.
54. Chandler, C. L.; List, B. Catalytic, asymmetric transannular aldolizations: Total synthesis of (+)-hirsutene. *J. Am. Chem. Soc.* **2008**, *130*, 6737-6739.
55. Horning, B. D.; MacMillan, D. W. C. Nine-step enantioselective total synthesis of (−)-vincorine. *J. Am. Chem. Soc*. **2013**, *135*, 6442-6445.
56. Kumar, P.; Dwivedi, N. Proline Catalyzed α-Aminoxylation Reaction in the Synthesis of Biologically Active Compounds. *Acc. Chem. Res.* **2013**, *46*, 289-299.
57. Nicolaou, K. C.; Reingruber, R.; Sarlah, D.; Brase, S. Enantioselective intramolecular Friedel− Crafts-type α-arylation of aldehydes. *J. Am. Chem. Soc*. **2009**, *131*, 2086-2087.
58. a) Ramachary, D. B.; Kishor, M.; Reddy,. Y. V. Development of Pharmaceutical Drugs, Drug Intermediates and Ingredients by Using Direct Organo-Click Reactions. *Eur. J. Org. Chem.* **2008**, 975-993; b) Ramachary, D. B.; Sakthidevi, R. Combining multi-catalysis and multi-component systems for the development of one-pot asymmetric reactions: stereoselective synthesis of highly functionalized bicyclo[4.4.0]decane-1,6-diones. *Org. Biomol. Chem.* **2008**, *6*, 2488-2492.
59. a) Ramachary, D. B.; Kishor, M. Organocatalytic Sequential One-Pot Double Cascade Asymmetric Synthesis of Wieland−Miescher Ketone Analogues from a Knoevenagel/Hydrogenation/Robinson Annulation Sequence: Scope and Applications of Organocatalytic Biomimetic Reductions. *J. Org. Chem.* **2007**, *72*, 5056-5068; b) Ramachary, D. B.; Kishor, M. Direct amino acid-catalyzed cascade biomimetic reductive alkylations: application to the asymmetric synthesis of Hajos–Parrish ketone analogues.

*Org. Biomol. Chem.* **2008**, *6*, 4176-4187; c) Ramachary, D. B.; Reddy, Y. V.; Kishor, M. Multi-catalysis reactions: direct organocatalytic sequential one-pot synthesis of highly functionalized cyclopenta[*b*]chromen-1-ones. *Org. Biomol. Chem.* **2008**, *6*, 4188-4197.

60. a) Ramachary, D. B.; Reddy, Y. V. A General Approach to Chiral Building Blocks via Direct Amino Acid-Catalyzed Cascade Three-Component Reductive Alkylations: Formal Total Synthesis of HIV-1 Protease Inhibitors, Antibiotic Agglomerins, Brefeldin A, and (R)-γ-Hexanolide. *J. Org. Chem.* **2010**, *75*, 74-85; b) Ramachary, D. B.; Pasha, M. A.; Thirupathi, G. Organocatalytic Asymmetric Formal [3+2] Cycloaddition as a Versatile Platform to Access Methanobenzo[7]annulenes. *Angew. Chem. Int. Ed.* **2017**, *56*, 12930-12934, *Angew. Chem.* **2017**, *129*, 13110-13114; c) Kumar, A. S.; Thirupathi, G.; Reddy, G. S.; Ramachary, D. B. Stereoselective Insertion of Benzynes into Lawsones: Synthesis of Biologically Important Benzannulated Bicyclo [3.3.0] octanes. *Chem. Eur. J.* **2019**, *25*, 1177-1183; d) Swamy, P.; Pasha, M. A.; Thirupathi, G.; Ramachary, D. B. Organocatalytic Formal Intramolecular [3+2]-Cycloaddition to Acquire Biologically Important Methanodibenzo[a,f]azulenes and Methanobenzo[*f*]azulenes. *Chem. Eur. J.* **2019**, *25*, 14036-14041; e) Pasha, M. A.; Swamy, P.; Ramachary, D. B. Catalytic Asymmetric Synthesis of Benzobicyclo[3.2.1]octanes. *Chem. Eur. J.* **2021**, *27*, 10563-10568; f) Thirupathi, G.; Ashok, E.; Kumar, A. S.; Ramachary, D. B. Parts-per-Million-Level, Catalytic [3+2]-Annulations for the Asymmetric Synthesis of Methanobenzo[7]annulenes. *Chem. Eur. J.* **2021**, *27*, 18033-18038; g) Pasha, M. A.; Anebouselvy, K.; Ramachary, D. B. Lawsone as synthon in the catalytic asymmetric reactions. *Tetrahedron* **2022**, *117-118*, 132793 [doi.org/10.1016/j.tet.2022.132793].
61. Ide, N. D.; Ragan, J. A.; Bellavance, G.; Brenek, S. J.; Cordi, E. M.; Jensen, G. O.; Jones, K. N.; LaFrance, D.; Leeman, K. R.; Letendre, L. J.; Place, D.; Stanchina, C. L.; Sluggett, G. W.; Strohmeyer, H.; Blunt, J.; Meldrum, K.; Taylor, S.; Byrne, C.; Lynch, D.; Mullane, S.; O'Sullivan, M. M.; Whelan, M. Synthesis of Filibuvir. Part III. Development of a Process for the Reductive Coupling of an Aldehyde and a β-Keto-lactone. *Org. Process. Res. Dev*. **2014**, *18*, 45-56.
62. Tummatorn, J.; Dudley, G. B. Generation of Medium-Ring Cycloalkynes by Ring Expansion of Vinylogous Acyl Triflates. *Org. Lett.* **2011**, *13*, 1572-1575.

63. Wong, Y.–C.; Tseng, C.–T.; Kao, T.–T.; Yeh, Y.–C.; Shia, K.–S. Tandem Cyclization of α-Cyano α-Alkynyl Aryl Ketones Induced by tert-Butyl Hydroperoxide and Tetrabutylammonium Iodide. *Org. Lett.* **2012**, *14*, 6024-6027.
64. Miao, L.; Shu, H.; Noble, A. R.; Fournet, S. P.; Stevens, E. D.; Trudell, M. L. An enantioselective formal synthesis of (+)-gephyrotoxin 287C. *Arkivoc* **2010**, *4*, 6-14.
65. Hiroya, K.; Suwa, Y.; Ichihashi, Y.; Inamoto, K.; Doi, T. Total Synthesis of Optically Active Lycopladine A by Utilizing Diastereoselective Protection of Carbonyl Group in a 1,3-Cyclohexanedione Derivative. *J. Org. Chem.* **2011**, *76*, 4522-4532.
66. Elamparuthi, E.; Fellay, C.; Neuburger, M.; Gademann, K. Total Synthesis of Cyrneine A. *Angew. Chem. Int. Ed.* **2012**, *51*, 4071-4073, *Angew. Chem.* **2012**, *124*, 4147-4149.
67. Rao, R. C.; Gal, S.-L. C.; Granger, I.; Gleye, J.; Augereau, J.–M.; Bessibes, C. Khusimol, a Non-Peptide Ligand for Vasopressin V1a Receptors. *J. Nat. Prod.* **1994**, *57*, 1329-1335.
68. Presset, M.; Coquerel, Y.; Rodriguez, J. Syntheses and Applications of Functionalized Bicyclo [3.2.1] octanes: Thirteen Years of Progress. *Chem. Rev.* **2013**, *113*, 525-595.
69. Tajabadi, F. M.; Pouwer, R. H.; Liu, M.; Dashti, Y.; Campitelli, M. R.; Murtaza, M.; Mellick, G. D.; Wood, S. A.; Jenkins, I. D.; Quinn, R. J. Design and Synthesis of Natural Product Inspired Libraries Based on the Three-Dimensional (3D) Cedrane Scaffold: Toward the Exploration of 3D Biological Space. *J. Med. Chem.* **2018**, *61*, 6609-6628.
70. Long, Y.; Ding, Y.; Wu, H.; Qu, C.; Liang, H.; Zhang, M.; Zhao, X.; Long, X.; Wang, S.; Puno, P.-T.; Deng, J. Total Synthesis of (−)-Perezoperezone through an Intermolecular [5+2] Homodimerization of Hydroxy p-Quinone. *Angew. Chem. Int. Ed.* **2019**, *58*, 17552-17557. *Angew. Chem.* **2019**, *131*, 17716-17721.
71. Rauscher, N.; Næsborg, L.; Jandl, C.; Bach, T. Concise Total Synthesis of Agarozizanol B via a Strained Photocascade Intermediate. *Angew. Chem. Int. Ed.* **2021**, *60*, 24039-24042, *Angew. Chem.* **2021**, *133*, 24241-24244.
72. Franov, L. J.; Hart, J. D.; Pullella, G. A.; Sumby, C. J.; George, J. H. BioinspiredTotalSynthesisof ErectonesA and B, and the RevisedStructureof Hyperelodione D, *Angew. Chem. Int. Ed.* **2022**, *61*, e202200420. *Angew. Chem.* **2022**, *134*, e202200420.

73. Yin, G.–P.; Wu, Y.–R.; Han, C.; Wang, X.–B.; Gao, H.–L.; Yin, Y.; Kong, L.–Y.; Yang, M.–H. Asperones A–E, five dimeric polyketides with new carbon skeletons from the fungus Aspergillus sp. AWG 1–15. *Org. Chem. Front.* **2018**, *5*, 2432-2436.
74. For excellent review on pseudo natural products, see: G. Karageorgis, D. J. Foley, L. Laraia, S. Brakmann, H. Waldmann, Pseudo Natural Products-Chemical Evolution of Natural Product Structure. *Angew. Chem. Int. Ed.* **2021**, *60*, 15705-15723, *Angew. Chem.* **2021**, *133*, 15837-15855.

# ABOUT THE AUTHOR

The author, **Mr. Gorachand Badaraita** was born on 19th April 1992 in Mandal Sahi, Gajapati, and Odisha. He obtained his B.Sc. (H) Chemistry degree in 2014 from Govt. Samanta Chandra Sekhar (A) Collage, Puri, affiliated to Utkal University, Bhubaneswar. Thereafter, he obtained his M.Sc. degree with a general in organic chemistry in 2016 from Ravenshaw University, Cuttack. He continued as a research scholar at the School of Chemistry, University of Hyderabad for the Ph.D. course from August 2016 onwards.

# LIST OF PUBLICATIONS

*1*. An Organocatalytic Chemoselective Carbonyl-Azide[3+2]-Cycloaddition: Synthesis of Pharmaceutically Rich 1,2,3-Triazoles, **B. Gorachand**, and D. B. Ramachary (*Manuscript under preparation*).

*2*. An Oganocatalytic Carbonyl-Azide [3+2]-Cycloaddition: Synthesis of Benzothiazole Containing 1,2,3-Triazoles. **B. Gorachand** and D. B. Ramachary (*Manuscript under preparation*).

*3*. Organocatalytic One-pot Synthesis of Pseudo-Terpenoids. Swamy Peraka, Badaraita Gorachand, Akram Hussain, Revoju Sravanthi, and Dhevalapally B. Ramachary. *Eur. J. Org. Chem.* **2022**, DOI: 10.1002/ejoc.202200674.

**Other publications as a co-author during the Ph.d**

*4*. An Aldehyde-Azomethine Imine [3+2]-Cycloaddition: High-Yielding Regioselective Synthesis of Substituted *N,N*-Bicyclic Pyrazolidinones. Jagjeet Gujral, T. Prabhakar Reddy, **B. Gorachand** and D. B. Ramachary, *ChemistrySelect.* **2018**, *3*, 7900 – 7905.

*5.* Organocatalytic Asymmetric Formal [3+3]-Cycloaddition to Access 2,3-Diazaspiro[4.5]deca-3,6-dien-1-ones. A.Vamshi Krishna, G. Surendra Reddy, **B. Gorachand** and D. B. Ramachary, *Eur. J. Org. Chem.* **2020**, *42*, 6623–6628.

# *Oral Presentations and Conferences*

1. ChemFest 2021 (oral presentation), Title of the talk: *An Organocatalytic Chemoselective Carbonyl-Azide [3+2]-Cycloaddition: Synthesis of Pharmaceutical Rich 1,2,3-Triazoles*. Organized by School of Chemistry, University of Hyderabad.
2. Junior National Organic Symposium (XVII, J-NOST) 2022, (oral presentation and volunteer) Organized by Royal Society of Chemistry. Title of the talk: *An Organocatalytic Chemoselective Carbonyl-Azide [3+2]-Cycloaddition: Synthesis of Pharmaceutical Rich 1,2,3-Triazoles*. Le Meridien, Hyderabad.
3. ChemFest conference attended 2017, 2018, 2019. Organized by School of Chemistry, University of Hyderabad.
4. Participated in Prof. *A. Srikrishna memorial lecture series 2017 organized by Prof. ASK trust* at school of chemistry, university of Hyderabad
5. Participated in Prof. *A. Srikrishna memorial lecture series 2019 organized by Prof. ASK trust* at school of chemistry, university of Hyderabad
6. Participated in Prof. *A. Srikrishna memorial lecture series 2021 organized by Prof. ASK trust* at school of chemistry, university of Hyderabad.

# Development of Direct Organocatalytic [3+2]-Annulation Reactions: Scope and Applications

*by* Gorachand Badaraita

# Development of Direct Organocatalytic [3+2]-Annulation Reactions: Scope and Applications

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---

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---

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---

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