ISOQUINOLINIUM SALTS, GENERATED *IN SITU*, AS ELECTROPHILES IN BAYLIS–HILLMAN REACTION AND APPLICATIONS

A THESIS SUBMITTED FOR THE DEGREE OF

DOCTOR OF PHILOSOPHY

BY

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OCTOBER 2019

To
My Family
&
Friends

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DECLARATION

I **THAMIZHARASI PERUMAL** hereby declare that this thesis entitled "**ISOQUINOLINIUM SALTS, GENERATED *IN SITU,* AS ELECTROPHILES IN BAYLIS–HILLMAN REACTION AND APPLICATIONS**" submitted by me under the guidance and supervision of **Professor D. BASAVAIAH** is a bonafide research work which is also free from plagiarism. I also declare that it has not been submitted previously in part or in full to this University or any other University or Institution for the award of any degree or diploma. I hereby agree that my thesis can deposit in Shodganga/INFLIBNET.

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CERTIFICATE

This is to certify that the thesis entitled “**ISOQUINOLINIUM SALTS, GENERATED *IN SITU*, AS ELECTROPHILES IN BAYLIS–HILLMAN REACTION AND APPLICATIONS**” submitted by **THAMIZHARASI PERUMAL** bearing registration number **10CHPH14** in partial fulfillment of the requirements for award of Doctor of Philosophy in the School of Chemistry is a bonafide work carried out by her under my supervision and guidance.

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1. Basavaiah, D., Thamizharasi, P. *Eur. J. Org. Chem.* **2017**, 5135.

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1. Poster cum Oral presentation at *ChemFest*-2018.
2. Poster presentation at *ICCCS-8*. 2017.

Further the student has passed the following courses towards fulfillment of coursework requirement for Ph.D.:

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1.	CY-801	Research Proposal	3	Pass
2.	CY-805	Instrumental Methods A	3	Pass
3.	CY-882	Organometallic Chemistry	2	Pass
4.	CY-886	Supramolecular Chemistry	2	Pass
5.	CY-892	Stereoselective Organic Synthesis	2	Pass

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P. Thamizharasi

CONTENTS

ABBREVIATIONS

Ac	acetyl
AcOH	acetic acid
Ar	aryl
aq.	aqueous
BH	Baylis-Hillman
BINOL	1, 1'-bi-2-naphthol
Bn	benzyl
Boc	*tert*-butoxycarbonyl
^{n}Bu	*n*-butyl
^{t}Bu	*tert*-butyl
^{o}C	degree Celsius / centigrade (temperature)
cat.	catalyst
Conc.	Concentrated
^{13}C NMR	carbon-13 nuclear magnetic resonance
d	day(s)
DABCO	1,4-diazabicyclo[2.2.2]octane
dba	dibenzylideneacetone
DBU	1,8-diazabicyclo(5.4.0)undec-7-ene

DCM	dichloromethane
DDQ	2,3-Dichloro-5,6-dicyano-1,4-benzoquinone
de	diastereomeric excesse
DEMS	diethoxymethylsilane
DEPT	Distortionless Enhancement of Polarization Transfer
DIPEA	N, N-diisopropylethylamine
DMA	*N,N*-dimethylacetamide
DMAP	dimethylaminopyridine
DMC	dimethyl carboanate
DME	dimethoxyethane
DMF	*N,N*-dimethylformamide
DMSO	dimethyl sulfoxide
dppb	1,4-Bis[diphenylphosphino]butane
dr	diastereomeric ratio
ee	enantiomeric excess
Eq.	equation
equiv	equivalent(s)
Et	ethyl
EWG	electron withdrawing group
Me	methyl

Mp	melting point
MVK	methyl vinyl ketone
NBS	N-bromosuccinamide
NHC	*N*-heterocyclic carbene
NMP	*N*-methyl 2-pyrrolidinone
MOM	methoxymethylacetal
Nu	nucleophile
ORTEP	Oak Ridge Thermal Ellipsoid Plot
PG	protecting group
Ph	phenyl
^{i}Pr	*iso*-propyl
^{n}Pr	^{n}propyl
PMP	*para* methoxyphenyl
PTA	1,3,5-triaza-7-phosphaadamantane
PTSA	*p*-toluenesulfonic acid
rt or RT	room temperature
S-Phos	2-dicyclohexylphosphino-2’, 6’-dimethoxybiphenyl
TBDMS	*tert* butyldimethylsilylchloride
TBHP	*tert* butylhydroperoxide
TDMPP	tris(2, 6-dimethoxyphenyl)phosphine

Tf	trifluoromethanesulfonyl
TFA	trifluoroacetic acid
TFAA	trifluoroacetic anhydride
TFE	trifluoro ethanol
THF	tetrahydrofuran
TIPBS	2,4,6-triisopropylbenzenesulfonyl
TMEDA	tetramethylethylenediamine
Tol	*p*-tolyl
Ts	*p*-toluenesulfonyl

ABSTRACT

Bond construction and bond cleavage reactions are fundamental and essential reactions in organic chemistry in general and in organic synthesis in particular. Among these reactions, construction of carbon–carbon bond is considered to be the most fundamental reaction in organic chemistry. Carbon–carbon bond formation in principle can be performed in inter-molecular as well as in intramolecular fashion. Due to its fundamental importance, a number of diverse carbon–carbon bond forming reactions have been discovered and developed during the past several decades. The Baylis–Hillman (BH) [also known as the Morita– Baylis–Hillman (MBH)] reaction is one such C–C bond forming reaction developed systematically and meticulously in recent years. The Baylis–Hillman reaction is essentially C–H functionalization process providing interesting classes of molecules, containing a minimum of three proximal functional groups, *via* the coupling between an electrophile and the α-position of an activated alkene under the influence of a catalyst. Usually the catalysts are organic molecules such as tertiary amines and trialkyl/aryl phosphines and therefore this reaction represents one of the best examples for organo-catalytic reactions.

This thesis deals with the utilization of less explored *in situ* generated isoquinolinium salts as electrophiles for Baylis–Hillman reaction and applications of the resulting BH adducts as substrates for 3-aza-Cope rearrangement and is divided into three chapters 1) Introduction 2) Objectives, Results & Discussion and 3) Experimental. The first chapter, *i.e.* Introduction presents a brief account of literature on the development of the Baylis–Hillman reaction and

also the applications of Baylis–Hillman adducts in organic synthesis. The second chapter describes the objectives, work plan and discussion of the experimental results. The thesis has the following objectives.

1) To utilize less explored *in situ* generated isoquinolinium salts (**A**) as electrophiles for Baylis–Hillman coupling with representative activated alkenes with an objective of understanding the potential of these salts as electrophiles and also with a view to develop a simple strategy for synthesis of substituted dihydroisoquinoline derivatives.

   We plan to use different acrylates of varying steric requirements such as (1) methyl acrylate (2) ethyl acrylate (3) *tert.*butyl acrylate (4) phenyl acrylate and also (5) acrylonitrile for coupling with *in situ* generated isoquinolinium salts (**A**) as electrophiles.

2) To examine the applications of Baylis–Hillman adducts, obtained *via* the reaction between *in situ* generated isoquinolinium salts and alkyl acrylates or acrylonitrile, as substrates for 3-aza-Cope rearrangement with a view to develop a facile synthetic protocol for obtaining substituted phenanthridine derivatives containing dihydronaphthalene moiety.

Baylis–Hillman reaction*: In situ* generated isoquinolinium salts as excellent electrophiles for coupling with alkyl acrylates and acrylonitrile

Discovering/uncovering new components for BH reaction has been considered to be a challenging endeavor in the area of Baylis–Hillman chemistry because such efforts would enormously increase the utility of this reaction in synthetic chemistry. Even though *in situ* prepared isoquinolinium salts are well employed as electrophiles for reaction with a number of nucleophiles for the past several years; their applications as electrophiles in Baylis–Hillman reaction for coupling with various activated alkenes are not well explored. We have therefore focused our efforts in this direction. Thus we have developed a facile protocol for synthesis of substituted methyl 2-[2,3-disubstituted-1,2-dihydroisoquinolin-1-yl]acrylates **(103a-l**) in 55-79% yields *via* the reaction of *in situ* generated isoquinolinium salts [from 2-(arylethynyl)benzaldehyde (**82a-d**), arylamine (**83a-i**) in the presence of AgOTf] with methyl acrylate (as activated alkene) using DABCO as a catalyst in acetonitrile as a solvent following the reaction sequences as shown in Eq. 12, Eq. 13, Eq. 14 and Table 2. In order to understand the generality of this protocol we have successfully used three more acrylates, ethyl acrylate, sterically more hindered *tert*-butyl acrylate and phenyl acrylate, as activated alkenes for coupling with *in situ* generated isoquinolinium salts according to reaction sequences described in Eq. 17-20 and Table 3. Resulting Baylis–Hillman adducts (**104**, **105a-c**, **106**) were obtained in 54-67% yields (Eq. 17-20 and Table 3).

We have also extended this reaction strategy to acrylonitrile as activated alkene for coupling with isoquinolinium salts [generated from 2-(phenylethynyl)benzaldehyde (**82a**) and anilines [aniline **83a**, 3-chloroaniline (**83d**) and 3,4-dimethoxyaniline (**83h**)] (Table 4) to provide desired BH adducts (**107a-c**) in 72-80% yields (Table 4).

Application of Baylis–Hillman adducts obtained from isoquinolinium salts

It is interesting to note that BH adducts (**103-107**) contain allyl-enamine framework. Therefore it occurred to us that these compounds could serve as interesting substrates for 3-

aza-Cope rearrangement to provide dihydronaphthalene derivatives. Accordingly we have subjected 2-(2,3-diphenyl-1,2-dihydroisoquinolin-1-yl)acrylonitrile (**107a**) for Cope rearrangement (Scheme 48). Unfortunately our attempts did not result in the formation of the expected dihydronaphthalene derivative (**108**) and noticed that the starting material remained intact.

Failure of this experiment gave us an indication that the BH adduct (**107a**) is not the appropriate substrate for 3-aza-Cope rearrangement. Then we felt that if we tie the two aromatic rings as described in the red color in Scheme 49, the resulting *in situ* generated phenanthridine substrate(s) (**128a**) might undergo 3-aza-Cope rearrangement to provide the desired dihydronaphthalene derivative (**129a**) containing phenanthridine framework. This means that we need to generate the phenanthridine ring (**128a**) *in situ* from the BH adduct (derived from appropriate isoquinolinium salts), by a coupling strategy. We felt that *in situ* phenanthridine substrates (**128a**) can be generated from BH adducts 2-[3-(2-bromophenyl)-2-aryl-1,2-dihydroisoquinolin-1-yl]acrylonitriles (**127**).

Thus we have prepared the required 2-[3-(2-bromophenyl)-2-aryl-1,2-dihydroisoquinolin-1-yl]acrylonitriles (**127a-c**) *via* the reaction between 2-(2-bromophenylethynyl)benzaldehyde (**82c**), arylamines [**83**, R = H, 4-Me, 3,5-$(Me)_2$] and acrylonitrile following the reaction sequence as described in Table 6 in 58-80% yield. Subsequently these BH adducts (**127a-c**) were subjected to simultaneous coupling and 3-aza-Cope rearrangement with $Pd(OAc)_2$ (Cat.)/ PPh_3 to provide the resulting dihydronaphthalene derivatives (**129a-c**) in 51-67% isolated yields (Table 7).

We have next prepared representative BH adducts from 2-(2-bromophenylethynyl)-benzaldehyde (**82c**) and selected arylamine derivatives (**83**, R = H, 4-MeO, 4-Me, 3,5-(Me)$_2$, 4-CN, 4-Cl) and methyl acrylate to provide the resulting BH adducts (**103j**, **131a-e**) in good yields (Scheme 52 and Table 8). These adducts were subjected to the treatment with Pd(OAc)$_2$(cat.)/ PPh$_3$ following a similar procedure as in the case of (**127**) which provided the required phenanthridine containing dihydronaphthalene derivatives (**130**, **132a-e**) in 40-70% isolated yields (Scheme 52 and Table 9).

With a view to further understanding the scope of this strategy we have used ethyl and *tert*-butyl acrylates as the activated alkenes for coupling with in situ generated isoquinolinium salts [produced from 2-(2-bromophenylethynyl)benzaldehyde (**82c**) and aniline derivatives (**83**, R = H, 4-Me, 3,5-(Me)$_2$)] following the reaction sequence shown in Scheme 54 (Table 10). Required BH adducts (**135**) and (**137a-c**) were obtained in 30-58% yields. We then subjected these BH adducts (**135** and **137a-c**) to 3-aza-Cope rearrangement which gave the expected product phenanthridine containing dihydronaphthalene derivatives (**136**, **138a-c**) in 47-71% yields (Scheme 54 and Table 11).

Next with a view to understand the influence of bicyclic aromatic amine on the formation of BH adduct and subsequent 3-aza-Cope rearrangement we have employed 4-aminoindane (**83l**) for reaction with 2-(2-bromophenylethynyl)benzaldehyde (**82c**) and activated alkenes (acrylonitrile and methyl acrylate). It is gratifying to see the formation of resulting BH adduct **127e** (EWG = CN) and **133** (EWG = COOMe) in 66 and 48% isolated yields respectively (Scheme 51 and Scheme 53). Subsequent 3-aza-Cope rearrangement of these

BH adducts, **127e** and **133** with $Pd(OAc)_2$ /PPh_3 provided the desired phenanthridine derivatives **129e** and **134** in 68 and 53% yields respectively (Scheme 51 and Scheme 53).

In conclusion, the Baylis-Hillman adducts, obtained *via* the reaction between *in situ* generated isoquinolinium salts (**A**) as electrophiles and activated alkenes (acrylates and acrylonitrile) serve as excellent substrates for 3-aza-Cope rearrangement to provide an interesting class of phenanthridine derivatives containing dihydronaphthalene units.

Third chapter presents detailed experimental procedures including melting points, IR, ^1H & ^{13}C NMR, and HRMS spectral data as well as single crystal X-ray data.

INTRODUCTION

Carbon–Carbon bond forming reactions

Bond construction and bond cleavage reactions are the fundamental and essential reactions in organic chemistry in general and in organic synthesis in particular. Among these reactions, construction of carbon─carbon bond is considered to be the most fundamental reaction in organic chemistry.[1-4] Carbon─carbon bond formation in principle can be performed in inter-molecular as well as in intramolecular fashion (Fig.1).[5-7] Due to its fundamental importance, a number of diverse carbon─carbon bond forming reactions have been discovered and developed during the past several decades. A few such examples are: Friedel–Crafts reaction,[1-4, 8] Diels─Alder reaction,[1-4, 9] aldol reaction,[1-4, 10] Michael reaction,[1-4, 11] Grignard reaction,[1-4, 12] Wittig reaction,[1-4, 13] olefin metathesis,[1-4, 14] cross coupling reaction (Heck, Suzuki, Negishi and Sonogashira etc.)[1-4, 15] which are well documented and also systematically described in organic chemistry text books.

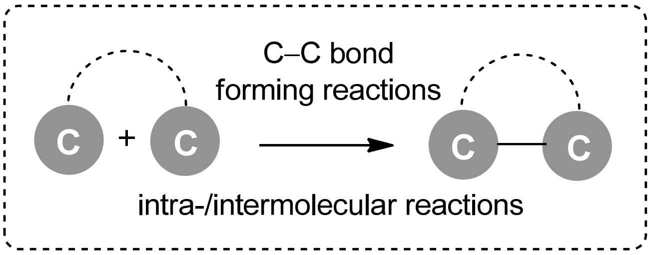


Figure 1. Carbon─carbon bond forming reactions

Baylis–Hillman reaction

Over the decades organic chemistry has undergone multi-directional changes and the current status demands discovery of new C─C bond forming reactions embodied with the concepts like i) atom-economy and organocatalysis ii) C─H functionalization iii) potential to offer the provisions such as asymmetric version and intramolecular version and iv) potential to provide multi-functional groups for further applications to build the desired organic structural frameworks (Fig 2).

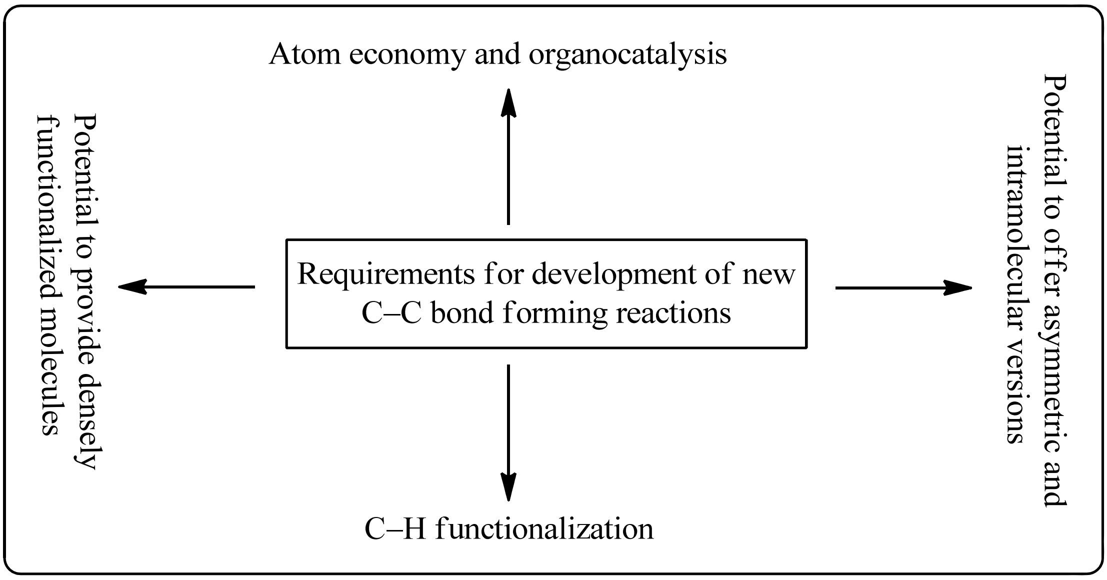
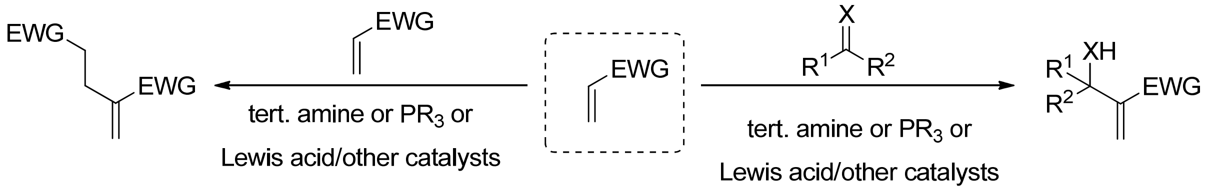


Figure 2. The present day C–C bond forming reaction requirements

The Baylis–Hillman (BH) [also known as the Morita–Baylis–Hillman (MBH)] reaction is one such C–C bond forming reaction systematically and meticulously developed in recent years.[16-26] This reaction is well equipped with the above-mentioned requirements (Fig. 2) and provides molecules containing densely functionalized groups in proximity [usually referred to as the Baylis–Hillman (BH) / Morita–Baylis–Hillman (MBH) adducts]. This reaction originates from the works of Baylis–Hillman (1972-patent),[27] Morita (1968 two publications),[28] and Rauhut and Courrier (1967 Patent)[29].

The Baylis–Hillman reaction is essentially C–H functionalization process providing an interesting classes of molecules, containing proximal functional groups, *via* the coupling reaction between an electrophile and the α-position of an activated alkene under the influence of a catalyst. Usually the catalysts are organic molecules such as tertiary amines and trialkyl/aryl phosphines and therefore this reaction represents one of the best examples for organo-catalytic reactions.[20] It is also well known that this reaction can also be promoted/catalyzed by metal salts.[16, 17, 20] The general Baylis–Hillman reaction is presented in Scheme 1. This reaction has three important reactions partners/components i) activated alkene ii) electrophile iii) catalyst. During the past four decades this fascinating reaction has grown in all directions with respect to i) all the three reaction components (activated alkene, electrophile and catalysts), ii) asymmetric version, iii) intramolecular version and iv) the applications of the Baylis–Hillman adducts. Now the reaction has attained the status of a popular and well documented name reaction [Baylis–Hillman (BH)/Morita–Baylis–Hillman (MBH) reaction] and also become a powerful synthetic tool in organic chemistry.[20]

Scheme 1

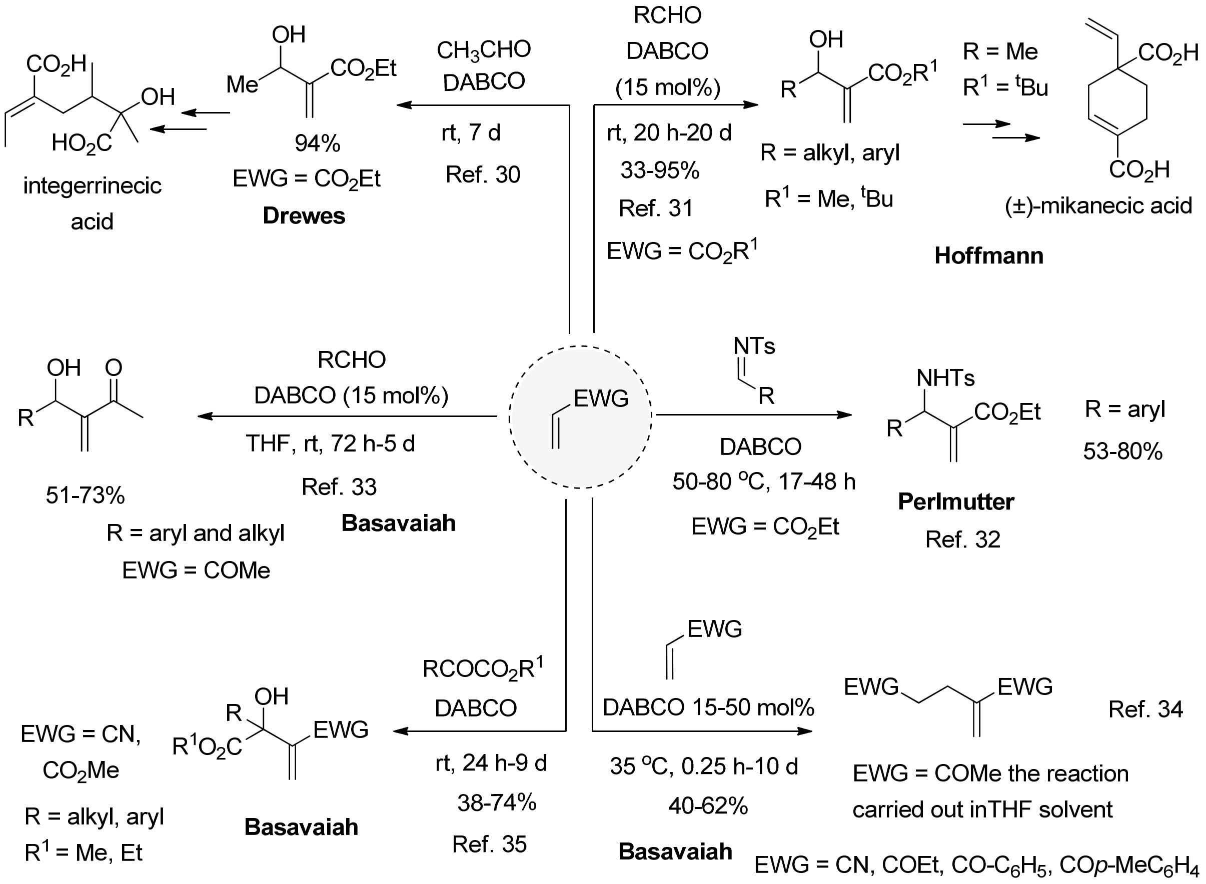


known as Rauhut and Currier reaction

R^1 = alkyl, aryl, heteroaryl etc.
R^2 = H, COOR, alkyl, etc.
X = O, NCO_2R, NTs, NSO_2Ph etc.
EWG = COR, CHO, CN, COOR, $PO(OEt)_2$,
SOPh, SO_2Ph, SO_3Ph etc.

During the past several years a number of activated alkenes (representative examples: alkyl vinyl ketones, alkyl/aryl acrylates, acrylonitrile, nitroalkenes, vinyl sulfoxides etc.) electrophiles (selected examples: aldehydes, α-keto esters, aldimines, allyl halides etc.) and catalysts (some important examples: DABCO, DBU, DMAP, trialkyl/aryl phosphines etc.) have been extensively employed in this fascinating reaction.[20, 30-35] Some of the initial reports on this fascinating reaction are presented in Scheme 2. This section also describes some such examples giving more emphasis on recent developments.

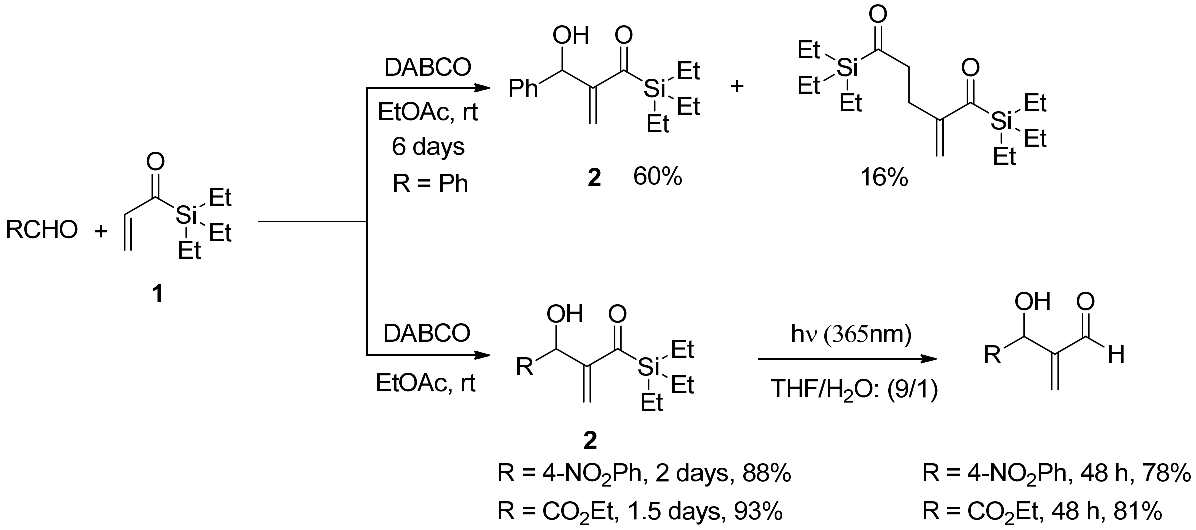
Scheme 2



Recent Developments

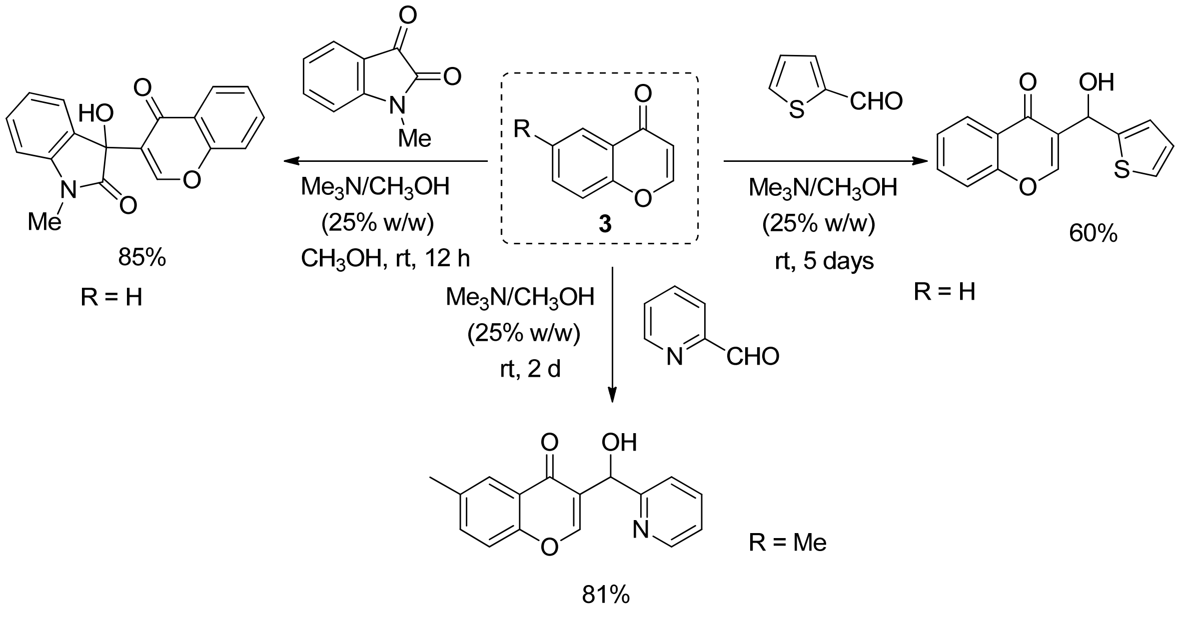
α-β-Unsaturated acyl silanes (**1**) have been elegantly employed as activated alkenes for the BH-reaction with aryl and alky aldehyde in the presence of DABCO as catalyst by Marri and co-workers[36] to provide the resulting BH adducts (**2**) in high yields along with minor amounts of dimerized products. Resulting acylsilane-MBH adducts adducts were converted into corresponding aldehydes under photo catalytic condition according to Scheme 3 (selected examples were presented).

Scheme 3



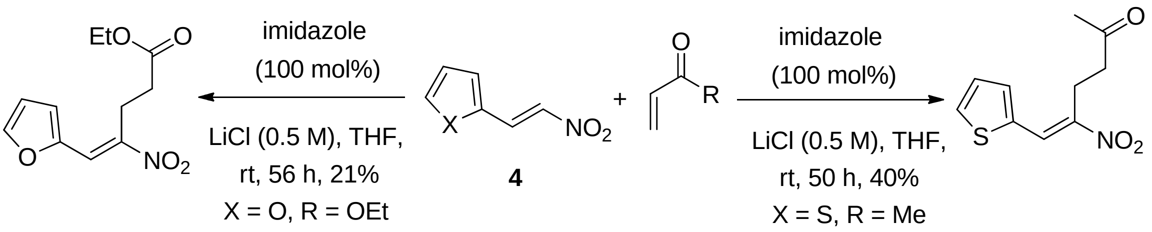
Our research group[37] has successfully demonstrated 1-benzopyran-4(4*H*)-one derivatives (**3**) as excellent activated alkenes in Baylis–Hilman reaction for coupling with reactive aromatic, hetero-aromatic aldehydes and isatin derivatives as electrophiles to provide the resulting allylic alcohols (three examples are given in Scheme.4).

Scheme 4



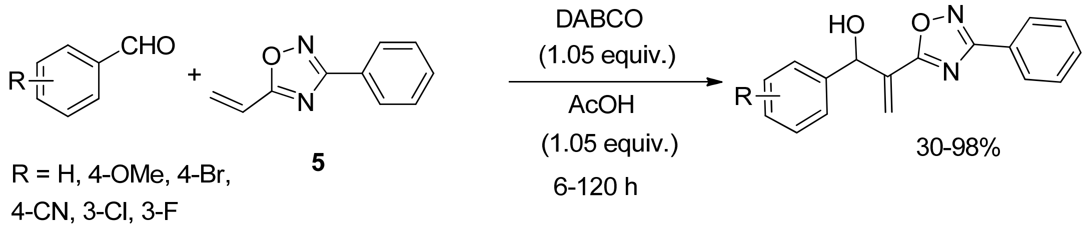
Namboothiri and co-workers[38] have meticulously utilized nitroalkenes (**4**) as activated alkenes for coupling with methyl vinyl ketone/ethyl acrylate as electrophiles. Representative examples are given in Scheme 5.

Scheme 5



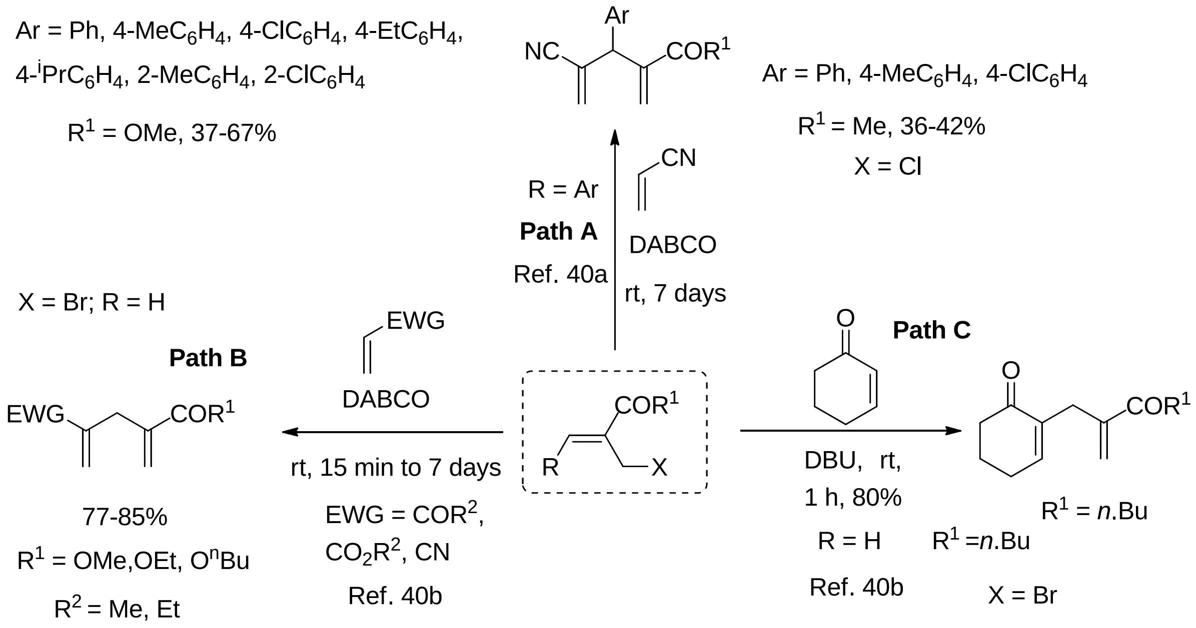
Coelho and co-workers[39] have demonstrated the elegant applications of vinyl-oxadiazole (**5**) as excellent activated alkene for coupling with aldehydes in the presence of DABCO catalyst to provide the resulting adducts in 30-98% yields. Representative examples given in Scheme 6.

Scheme 6



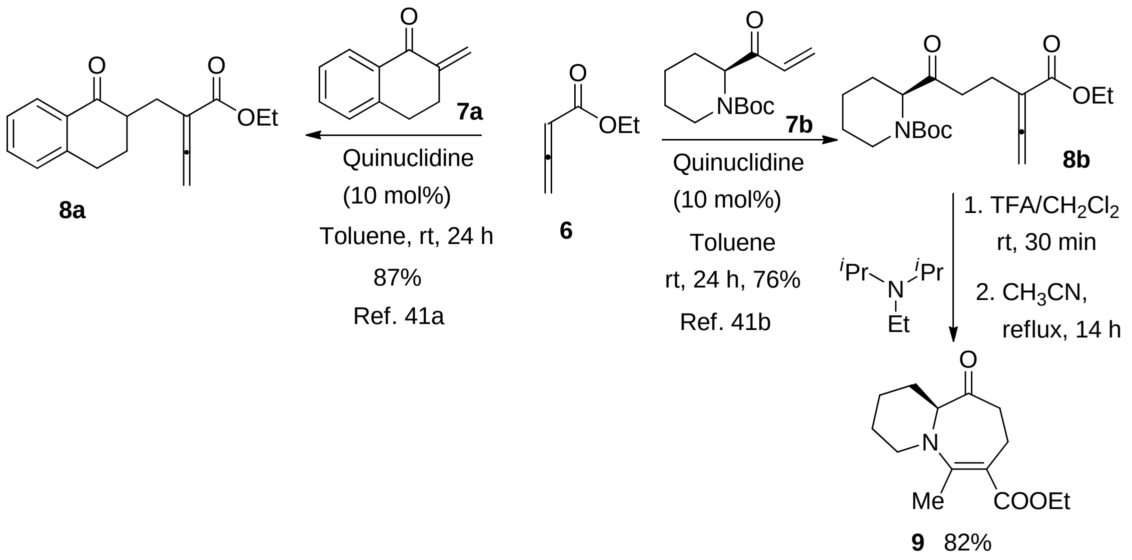
Our research group has effectively utilized halides of the Baylis–Hillman alcohols (derived from aldehydes and acrylates/MVK) as electrophiles in coupling reaction with acrylonitrile as activated alkene in the presence of DABCO to produce the resulting products 1,4-penatadiene derivatives in good yields as in Path A in Scheme 7.[40a] Subsequently our research group extended the same protocol for bromides of the BH alcohols, obtained from HCHO and acrylates, as electrophiles for coupling with different activated alkenes (representative examples are shown in Paths B and Scheme 7).[40b]

Scheme 7

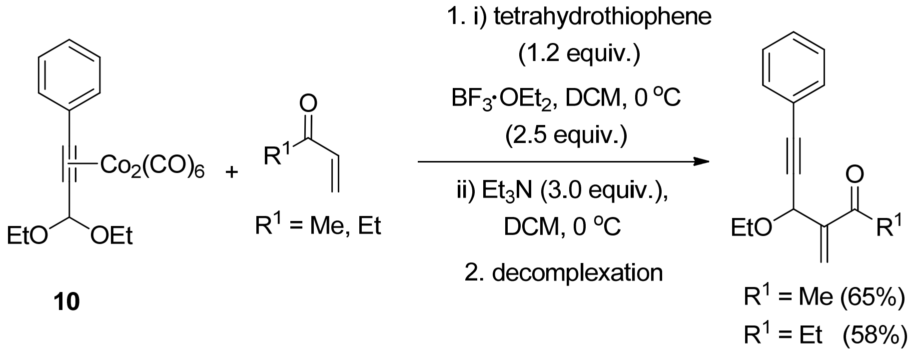


An interesting quinuclidine catalyzed Baylis–Hillman reaction between allenic ester (**6**) and *α,β*-unsaturated ketones (**7a** and **7b**) has been reported by Miller and co-workers.[41a,b] Resulting BH adducts *α*-alkylated allenic esters (**8a** and **8b**) were obtained in good to excellent yield. Two examples are given in Scheme 8. The BH adduct (**8b**) was converted into bicyclic compounds (**9**) as shown in Scheme 8.

Scheme 8



Krafft and co-workers[42] reported an interesting BF_3·OEt_2 and tetrahydrothiophene mediated Baylis–Hillman reaction between dicobalthexacarbonylacetylenicacetal complex (**10**) and alkyl vinyl ketones to provide enynones in moderate to good yields after decomplexation following the reaction sequence as shown in Eq. 1 (two selected examples were presented).

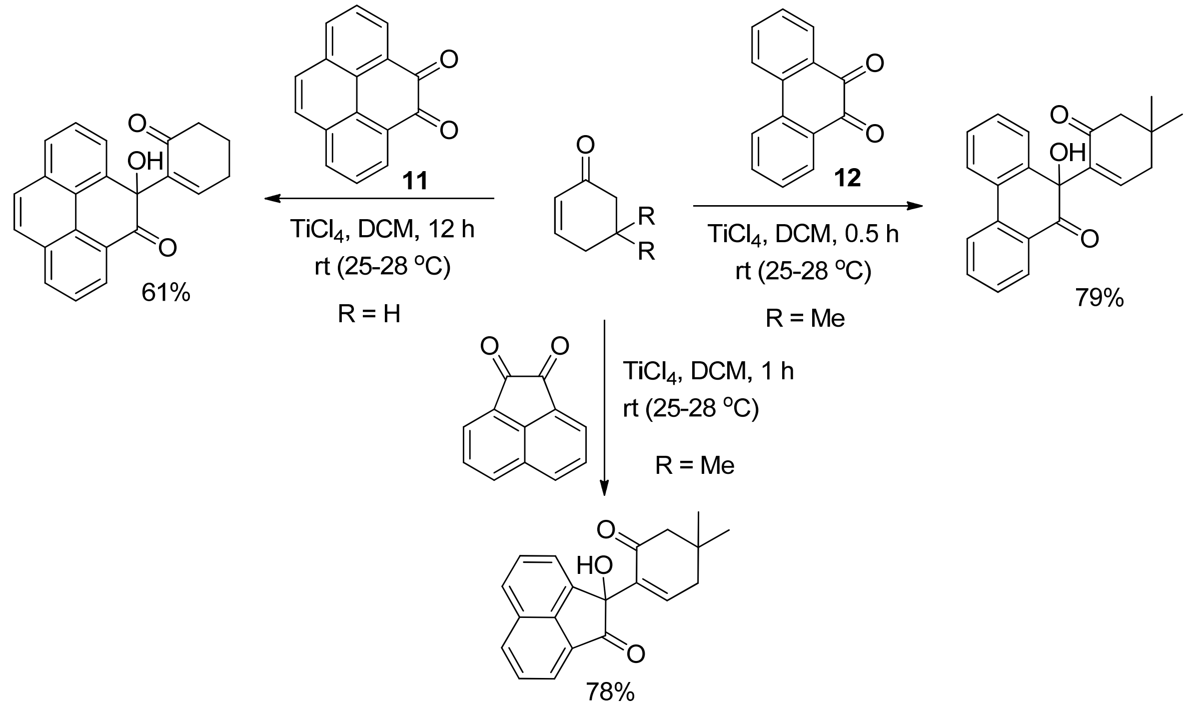


Eq. 1

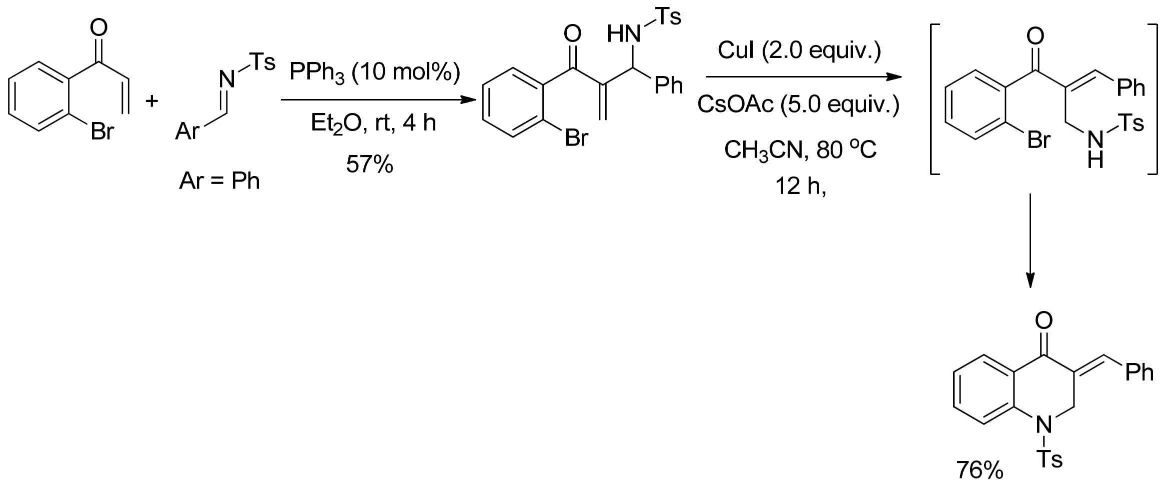
Our research group reported[43] a facile $TiCl_4$ mediated Baylis-Hillman coupling between cyclic 1,2-diones as electrophiles (such as 9,10-phenanthrenedione **11**, pyrene-4,5-dione **12** and 1,2-acenaphthenequinone) with cyclohex-2-enone and 5,5-dimethylcyclohe-x-2none as activated alkenes to produce the resulting adducts in high yields. Representative examples are presented in Scheme 9.

Pozo and co-workers[44] reported a simple and facile synthesis of 3-alkyliden-2,3-dihydro-4-quinolones derivatives using the BH adducts derived [from tosylimines (as electrophile) and vinyl 2-bromoaryl ketones (as activated alkenes) in the presence of triphenyl phosphine (catalyst)] using CuI/CsOAc following the reaction strategy as presented in Scheme 10. This reaction is believed to proceed through BH reaction, 1,3-arylmigration and intramolecular amination reaction is highly remarkable.

Scheme 9



Scheme 10

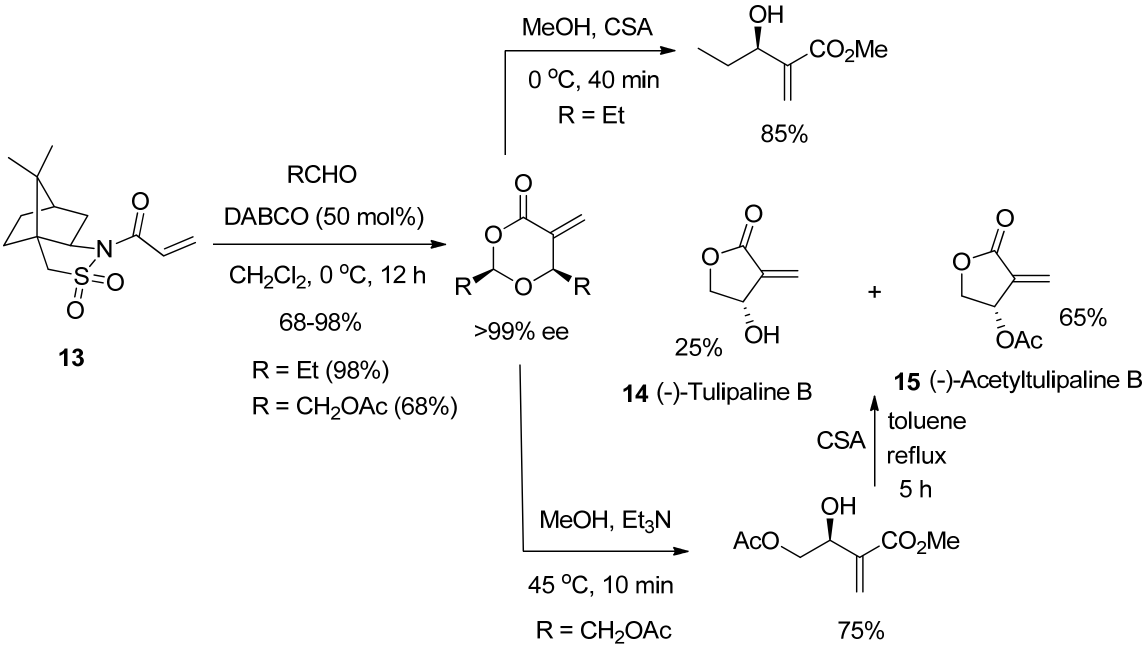


Asymmetric Baylis–Hillman reaction

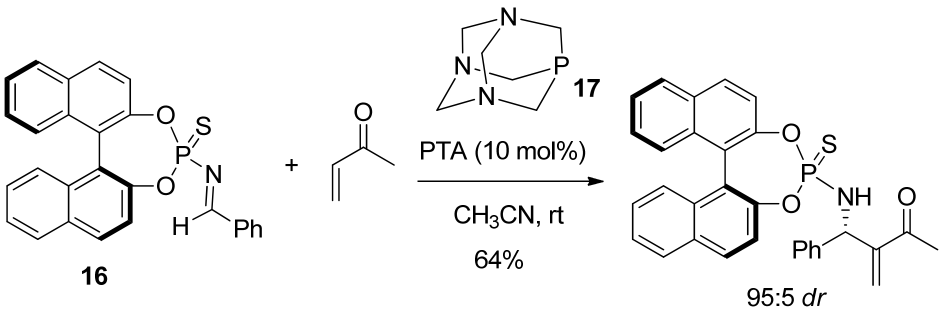
As mentioned in the beginning of this chapter Baylis–Hillman reaction offers opportunities/ challenges for developing its asymmetric version in the case of prochiral electophiles.[20] Literature survey clearly demonstrates that asymmetric BH reaction has been and continues to attract many leading research groups because of the large scope in expanding this area with respective to i) chiral activated alkenes, ii) chiral electrophiles iii) chiral catalysts and additives.[20] It is gratifying to note that during the past four decades significant developments have been made in asymmetric version of BH reaction.

One of the interesting applications of asymmetric BH reaction using chiral activated alkene (**13**) is reported by Leahy employing Oppolzer's sultam as a chiral auxiliary. Coupling of chiral acrylate (**13**) with aldehydes under the influence of DABCO as catalyst produced the desired BH adducts in high enantioselectivties after the removal of the chiral auxiliary following the reaction sequence as shown in Scheme 11 (two examples are given). One such BH alcohol obtained, has been meticulously employed for synthesis of biologically active tulipalin B (**14**) and acetyltulipalin B (**15**) as shown in Scheme 11.[45]

Scheme 11

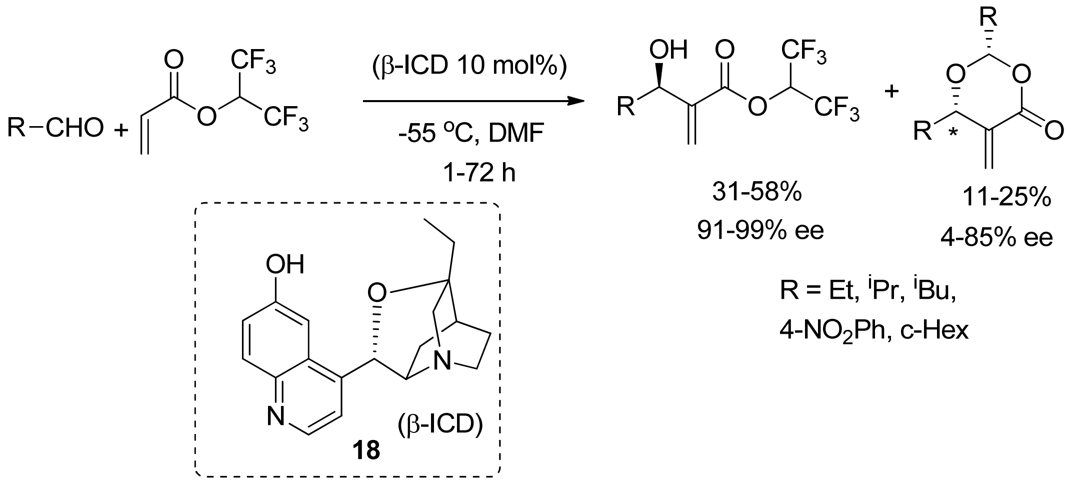


Chiral imine (**16**) has been very efficiently used as chiral electrophile by Zhou and Co-workers[46a,b] for coupling with activated alkenes in the presence air-stable nucleophilic trialkyl-phosphine organocatalyst PTA (**17**). One such example is described in Eq. 2 using methyl vinyl ketone as activated alkene providing the resulting BH adduct in 95:5 diastereoselectivity.



Eq. 2

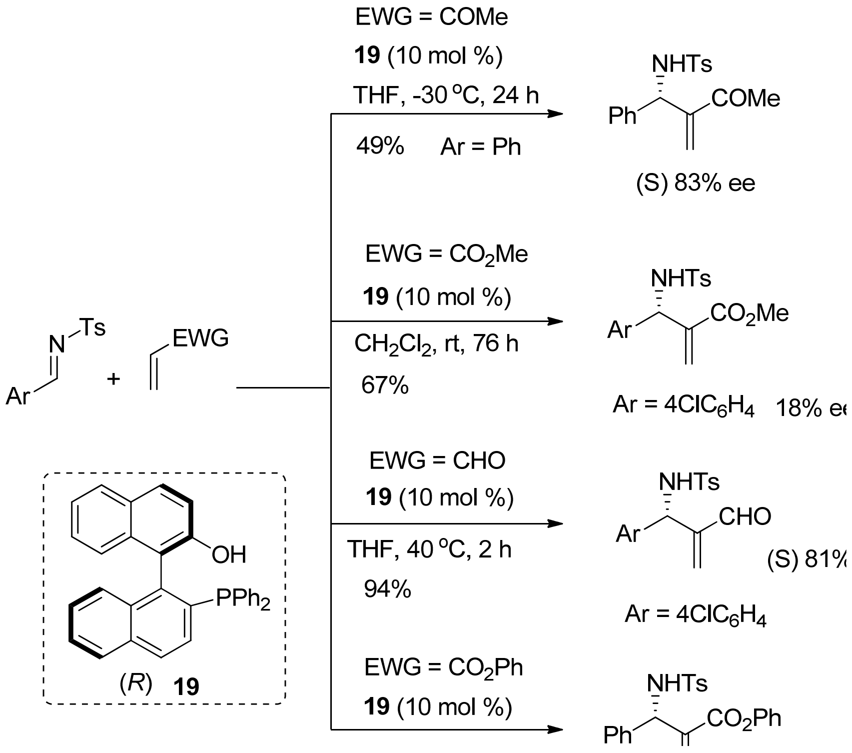
Hatakeyama and coworkers[47] have used (β-ICD) (derived from quinidine) (**18)** as an effective chiral catalyst for enantioselective Baylis–Hillman reaction between various aldehyde derivatives and 1,1,1,3,3,3-hexafluoroisopropyl acrylate (HFIPA) to yield the resulting BH alcohols with high enantioselectivity as shown in Eq. 3.



Eq. 3

Shi and coworkers[48] have used chiral phosphine as a catalyst (**19**) for coupling between activated alkenes, such as acrylates, acrolein and alkyl vinyl ketones with aldimine derivatives to provide the corresponding BH-adducts in moderate enantioselectivities (Scheme 12).

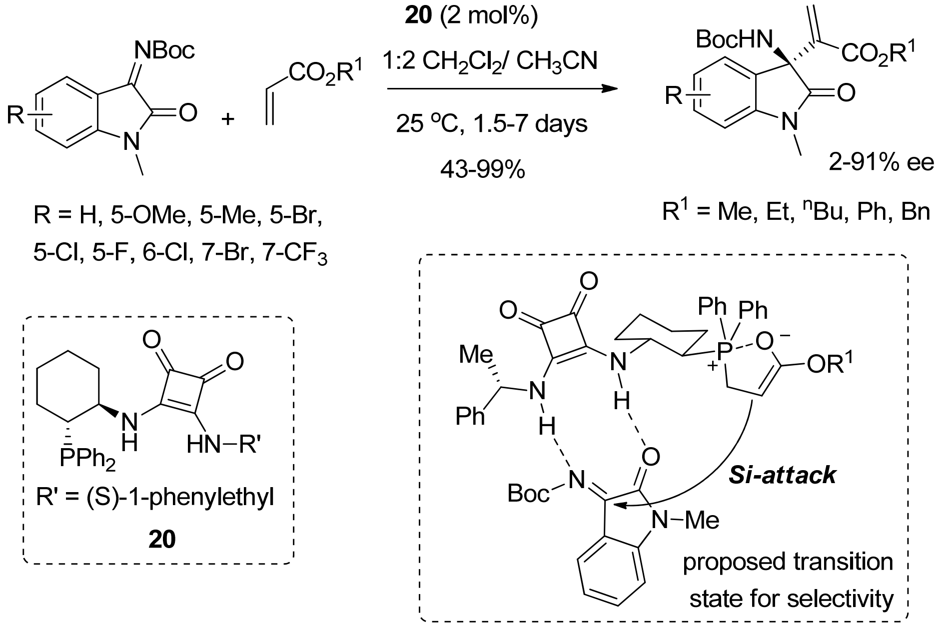
Scheme 12



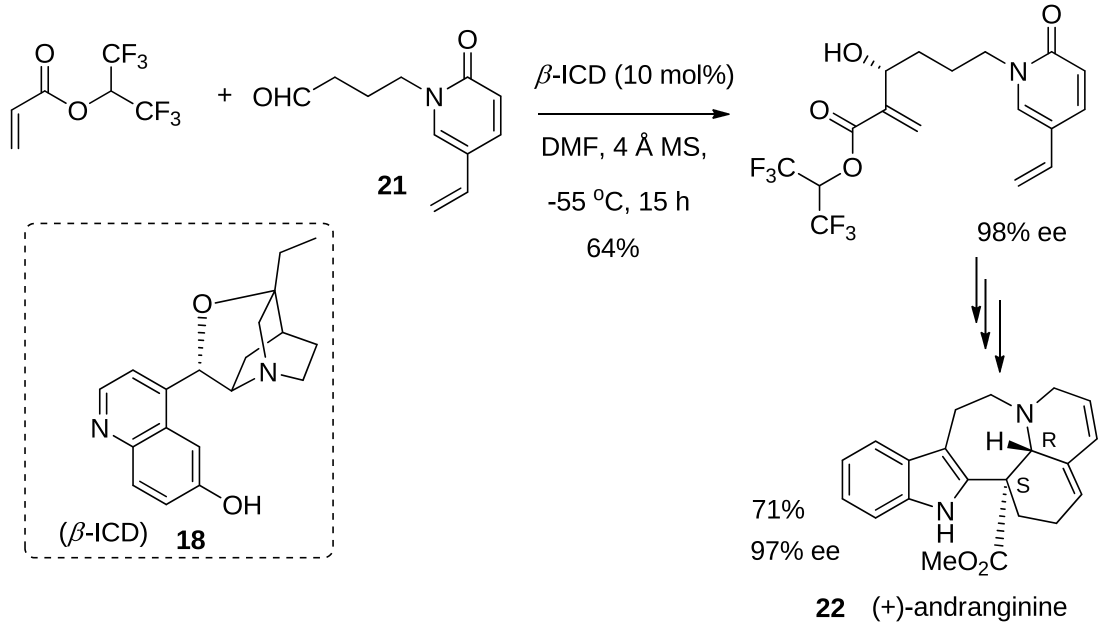
Wu and co-workers[49] have meticulously used bifunctional phosphine-squaramide (**20**) as a catalyst for enantioselective BH reaction of acrylates with isatin-derived ketamine to produce 3-substituted-3-amino-2-oxindoles derivatives. Resulting BH adducts were obtained upto 91% enantioselectivity as described in Scheme 13.

Catalytic asymmetric Baylis–Hillman reaction has been employed as the key step in the total synthesis of (+)-andranginine by the research group of Takayama. Reaction of the aldehyde (**21**) with 1,1,1,3,3,3-hexafluoroisopropyl acrylate (HFIPA) with *β*-isocupreidine (*β*-ICD) (**18**) as catalyst provided the corresponding BH-adduct in high enantiomeric excess which was subsequently transformed into of (+)-andranginine (**22**) natural product following the reaction sequence as described in Scheme 14.[50]

Scheme 13



Scheme 14

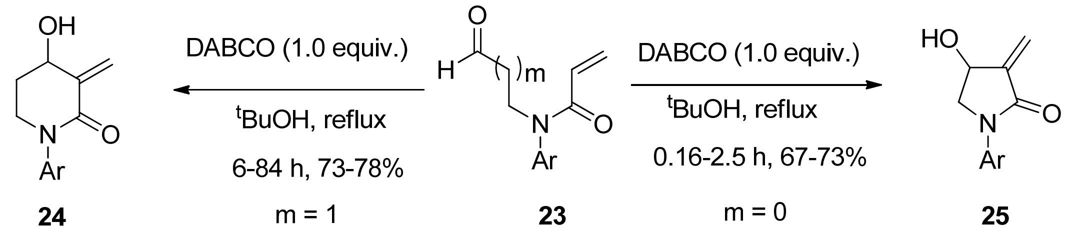


Intramolecular Baylis–Hillman (IBH) reaction

If the substrate contains activated alkene component along-with electrophile species in appropriate position there is a possibility of performing intramolecular Baylis–Hillrman reaction using appropriate catalyst or reagent. Thus BH reaction offers challenges and opportunities to design substrate for intra-molecular version and in fact significant developments have been reported during the past several years. This section presents some such relevant and recent examples.

Recently our research group[51] demonstrated intramolecular Baylis–Hillman (IBH) reaction of substrates (**23**) containing less reactive acrylamide as activated alkene and aldehyde as electrophile components to provide the cyclic BH adducts (**24** and **25**) following the reaction strategy shown in Scheme 15.

Scheme 15



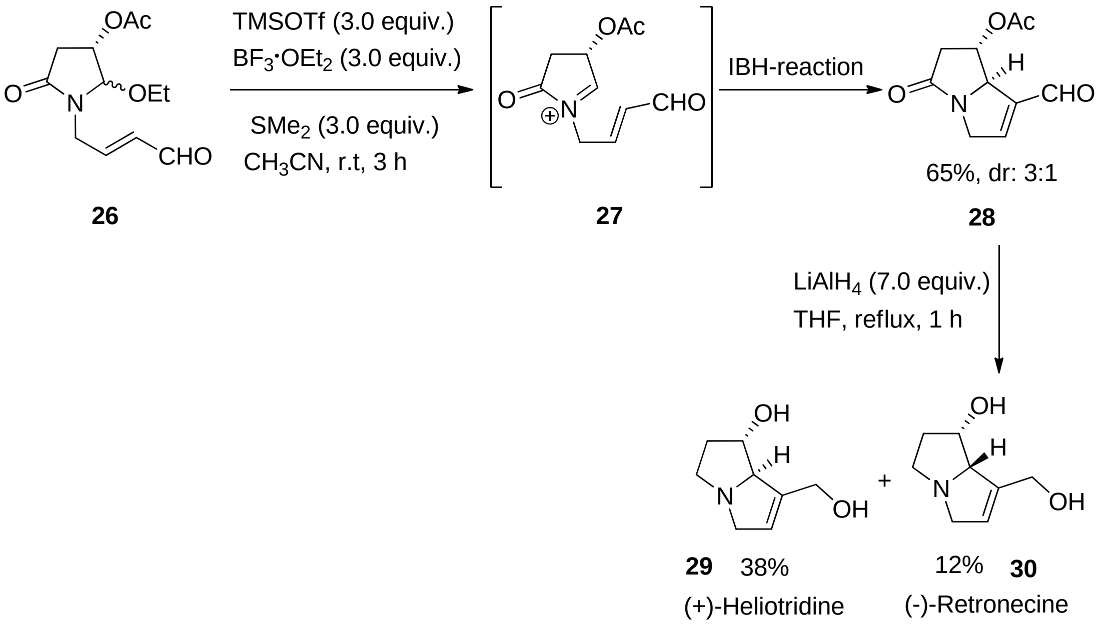
Ar = Ph, 4-ClC$_6$H$_4$, 4-BrC$_6$H$_4$,
3,5(Me)$_2$C$_6$H$_3$, 2-MeOC$_6$H$_4$

Ar = Ph, 4-ClC$_6$H$_4$, 4-BrC$_6$H$_4$,
3,5(Me)$_2$C$_6$H$_3$, 2-MeOC$_6$H$_4$,
1-naphthyl

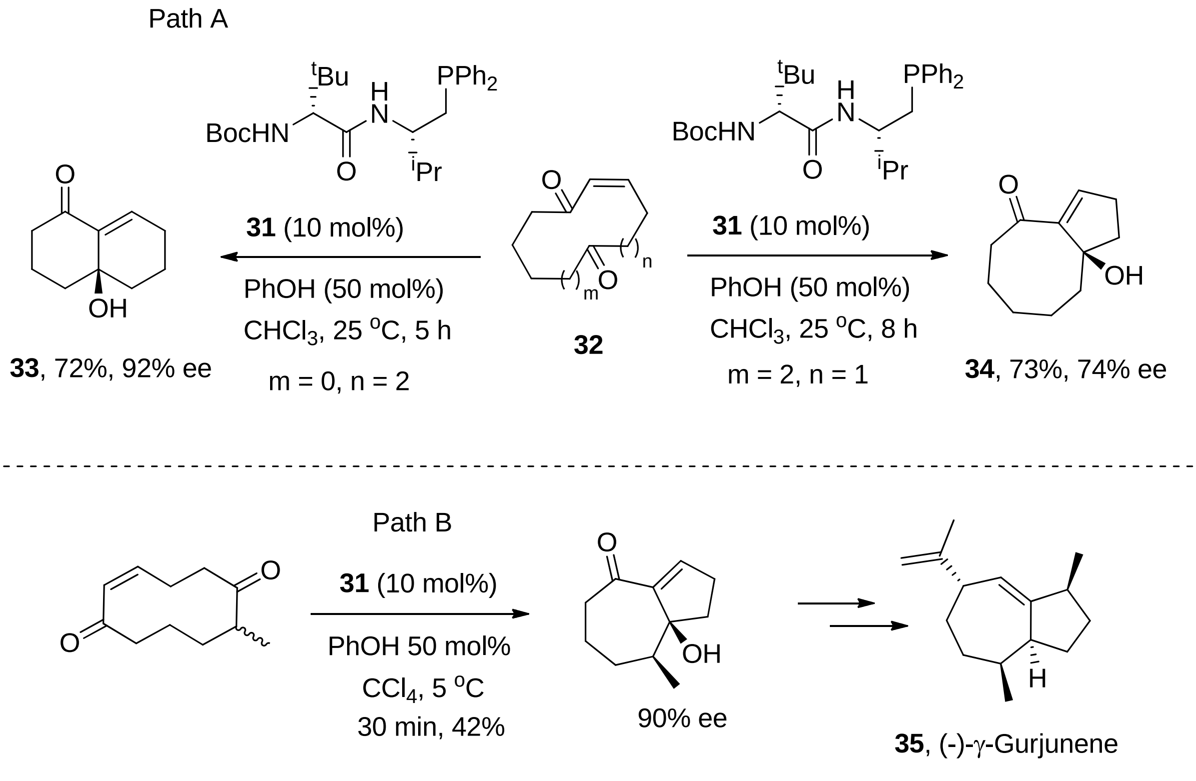
Aggarwal and co-workers[52] have elegantly reported an intramolecular Baylis–Hillman (IBH) reaction of the intermediate (**27**) generated *in situ* from (**26**) to provide the resulting BH (**28**) adduct in excellent yield (Scheme 16). Resulting BH adduct (**28**) was transformed into natural product (+)-heliotridine (**29**) and its unnatural isomer (-)-retronecine (**30**) as shown in Scheme 16.

The chiral enantiopure bifunctional phosphine (**31**) catalyzed efficient intramolecular Morita−Baylis−Hillman reaction of enone-ketones (**32**) has been reported by Vicario and co-workers[53] to provide the bicyclic frameworks (**33** and **34**) in high enantioselectivties as shown in path A in Scheme 17. They have successfully employed this strategy as the key step for the first enantioselective total synthesis of (-)-γ-gurjunene (**35**), a sesquiterpene natural product (Path B, Scheme 17).

Scheme 16

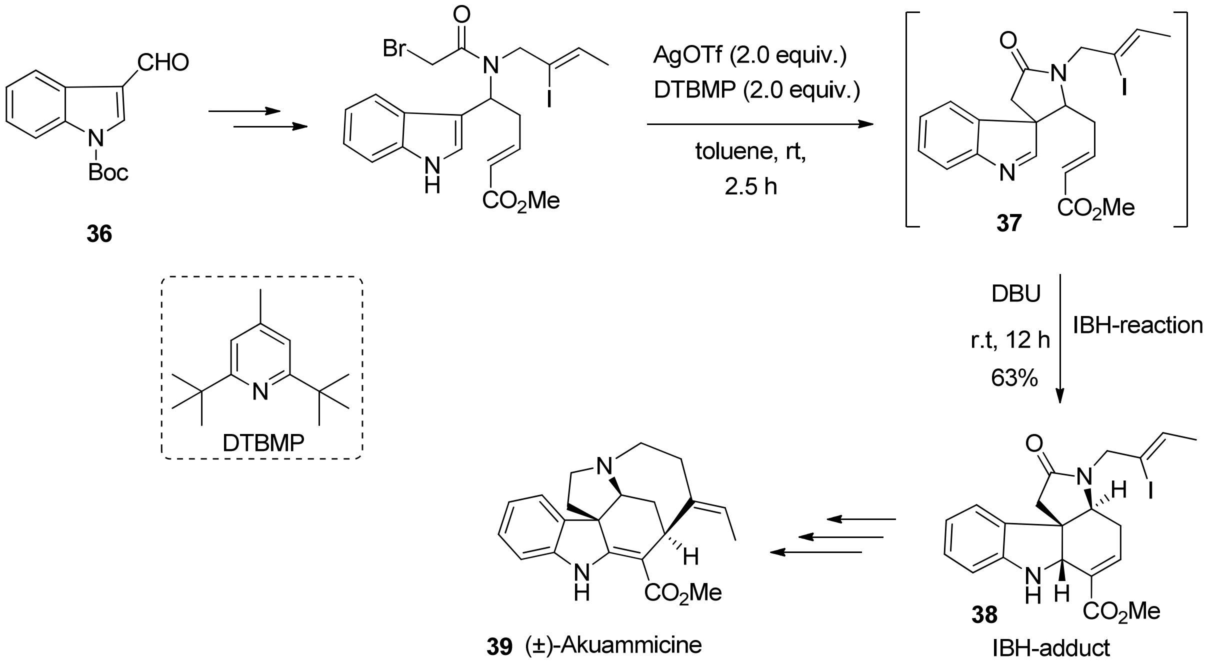


Scheme 17



Andrade and co-workers[54] reported an efficient synthesis of important biologically active complex natural product (**39**) using intramolecular Baylis–Hillman reaction as the key step. Thus the in situ generated imine (**37**) from the indole derivative (**36**) underwent IBH reaction in the presence of DBU to provide the tetracyclic compound (**38**) which was further transformed into natural products (±)-akauammicine (**39**) as shown in Scheme 18.

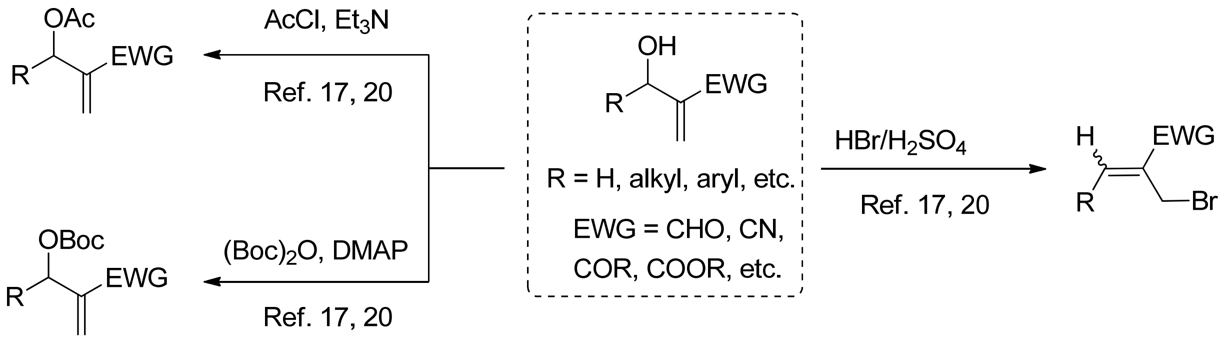
Scheme 18



Application of Baylis–Hillman adducts

The Baylis–Hillman alcohols contain three proximal functional groups and were easily converted into the corresponding acetates, bromides, carbonates and other derivatives shown in Scheme 19.[20] Because of the presence of (a minimum of three) proximal functional groups; Baylis–Hillman adducts and derivatives offer opportunities for discovering novel organic transformation methodologies and due to this fact, these adducts have become powerful synthons and substrates for a number of synthetic transformations/reactions.[17, 20] Literature survey clearly demonstrates that the BH adducts have been extensively used for a variety of synthetic transformation methodologies and also in synthesis of several natural products and bioactive compounds. This section presents briefly some important and recent such applications of the BH adducts.

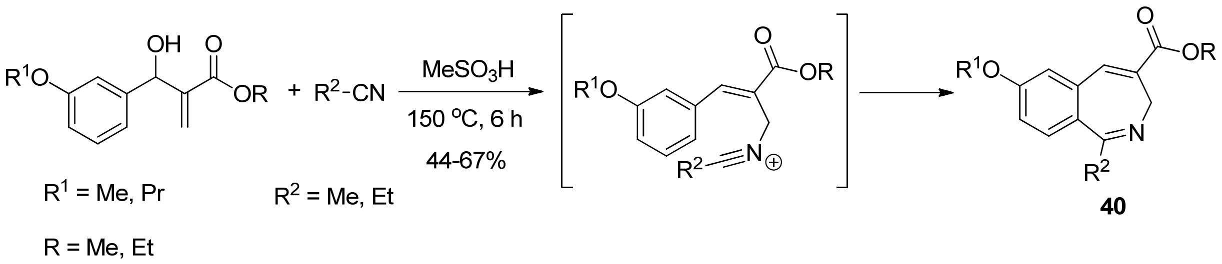
Scheme 19



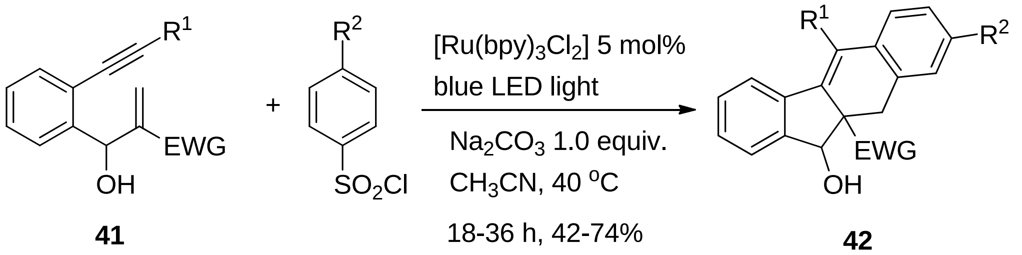
Applications of the BH alcohols

Our research group[55] reported a facile strategy for the synthesis of 2-benzazepine derivatives (**40**) using Baylis–Hillman alcohols (derived from electron rich aryl aldehydes and acrylates) *via* the treatment with alkylnitriles in the presence of methanesulfonic acid. The first step involves Ritter (C–N bond formation) reaction while the second step proceeds through the C–C bond formation (Houben–Hoesch reaction) as described in Scheme 20.

Scheme 20



Li et al. have reported a facile methodology for transformation of BH-alcohol (**41**), derived from alkynylaldehydes, into functionalized polyfused cyclic molecules (**42**) *via* the reaction with arylsulfonyl chlorides under the photoredox catalysis (Eq. 4)[56]. This strategy also demonstrates the importance of arylsulfonyl chlorides in organic synthesis.



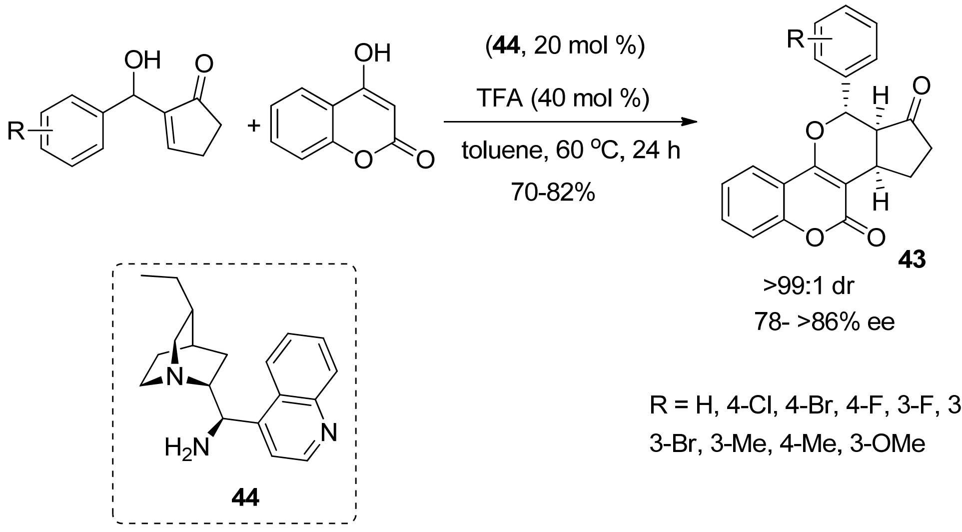
Eq. 4

R^1 = C_6H_5, 4-$MeOC_6H_4$, 4-MeC_6H_4, 4-CNC_6H_4, 2-ClC_6H_4, 4-$COMeC_6H_4$

EWG = CO_2Me, CN, $CO_2{}^nBu$

R^2 = CN, OMe, Cl, NO_2

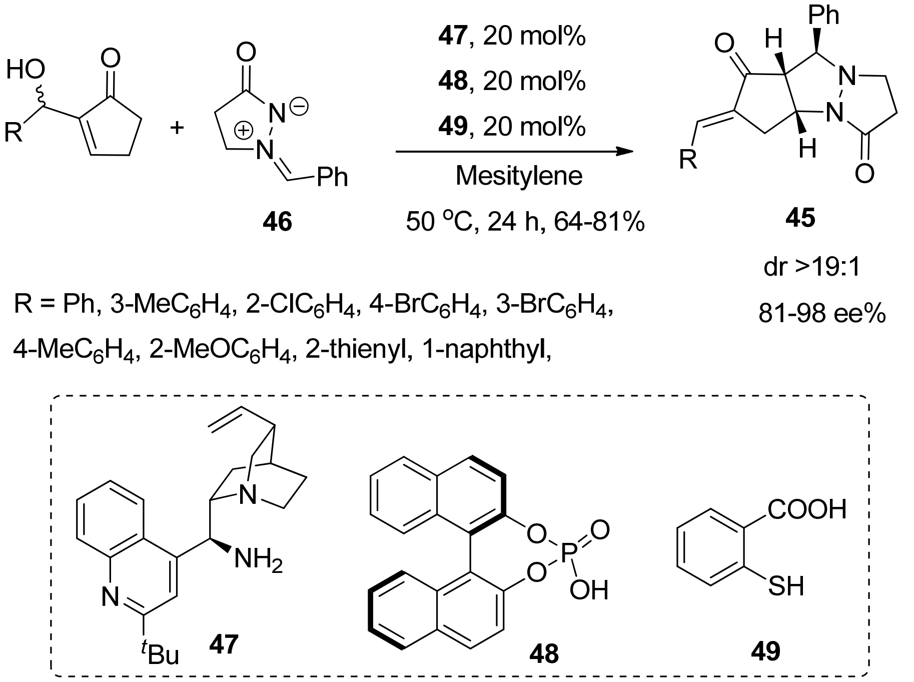
Liu et al.[57] have reported a facile synthetic strategy for obtaining tetracyclic frameworks (**43**) from BH-alcohol, derived from cyclopentenone and aldehydes, *via* reaction with 4-hydroxycoumarins in the presence of cinchonine (**44**) and BrØnsted acid. The reaction is believed to proceed through tandem allylic alkylation followed by intramolecular oxa-Michael addition reaction to give pyranocoumarin products in high regio-, diastereo- and enantioselectivities shown in Eq. 5.



Eq. 5

R = H, 4-Cl, 4-Br, 4-F, 3-F, 3-Cl, 3-Br, 3-Me, 4-Me, 3-OMe

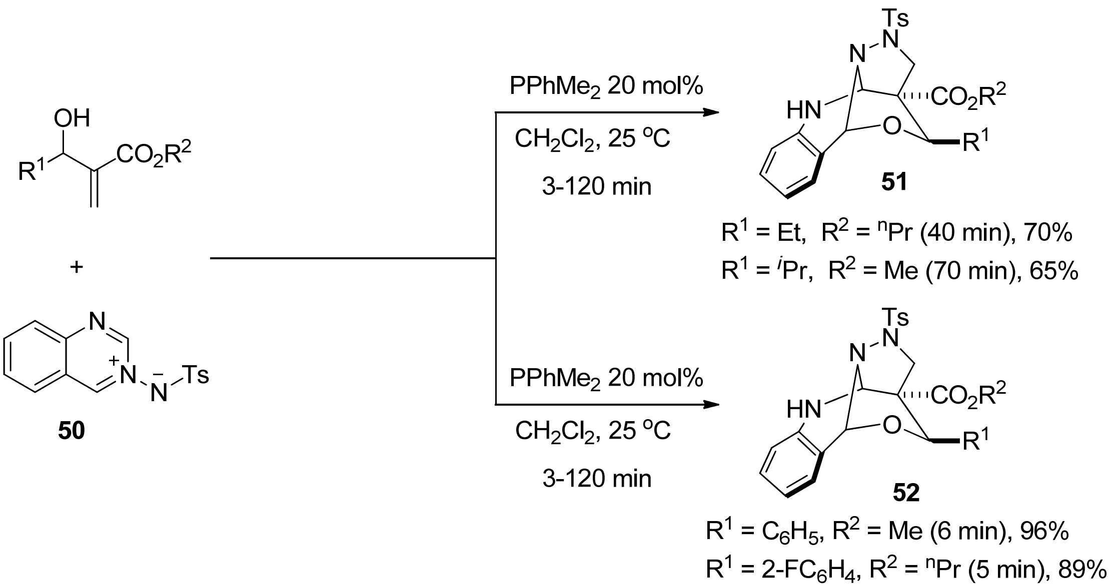
Subsequently Chen research group[58] has successfully utilized the BH adducts derived from 2-cyclopentenone and aldehydes for synthesis of tricylic molecules (**45**) in high yields with good stereoselectivity (up to 98% ee, >19:1 dr) *via* the treatment with cyclic azomethine imines (**46**) under the catalytic influence of cinchona alkaloid (**47**), phosphoric acid (**48**), and 2-mercaptobenzoic acid (**49**) (Eq. 6).



Eq. 6

Baylis–Hillman alcohols were transformed into (epoxymethano)-pyrazolo[5,1-b]-quinazoline derivatives (**51** and **52**) in high diastereo-selectivity by Zhang et al.[59] *via* phosphine mediated annulation with azomethine imines (**50**) in a tandem process. Representative examples are described in Scheme 21.

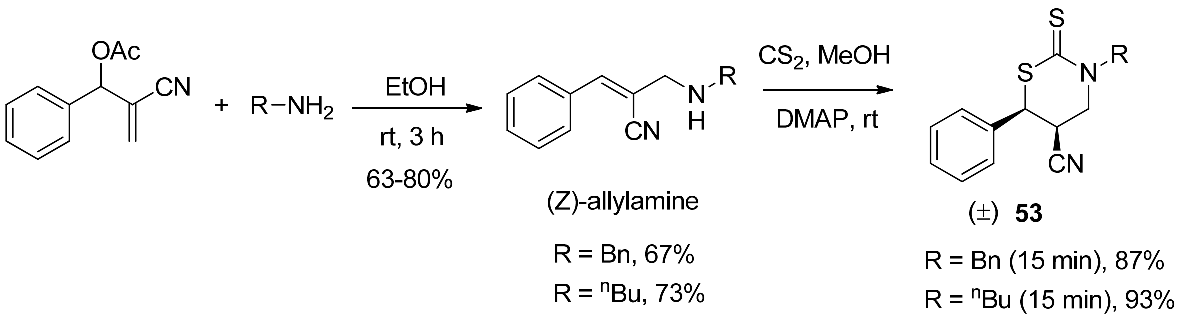
Scheme 21



Applications of the BH acetates, bromides and carbonates

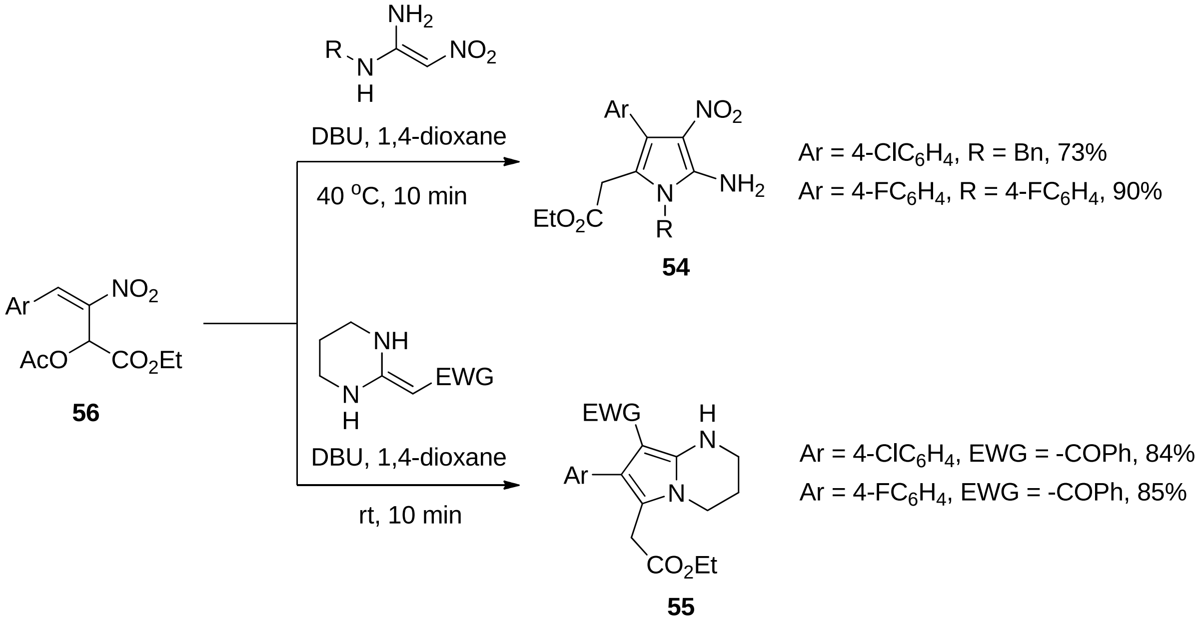
Our research group[60] has developed a convenient method for the synthesis of *cis*-5,6-disubstituted-1,3-thiazinane-2-thione derivatives (**53**) starting from the BH acetates following the reaction sequence as described in Scheme 22 (two examples are given). In this strategy first step involves the treatment of BH acetates with a primary amine followed by the reaction the resulting allyl amine with CS_2 in the presence of DMAP (Scheme 22).

Scheme 22



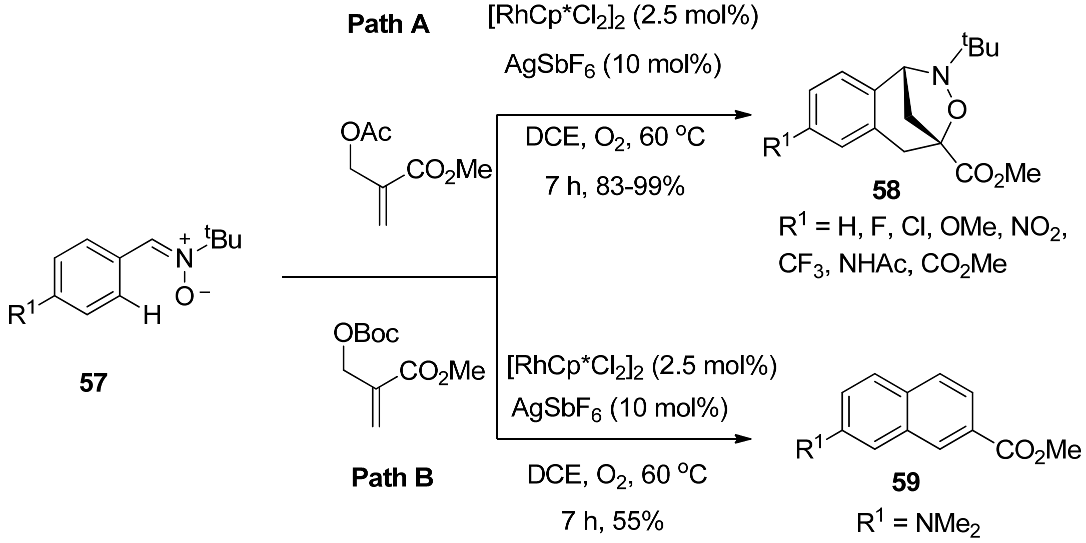
Yan and co-workers[61] recently reported an efficient and novel procedure for the synthesis of fully substituted pyrrole (**54**) and 1,2,3,4-tetrahydrobicyclic pyrroles (**55**) using BH acetates (**56**) as the starting materials following the reaction strategy as shown in Scheme 23.

Scheme 23



Kim research group[62] has reported interesting reactions of BH acetates and BH carbonates with aryl nitrones (**57**). Rhodium(III)-catalyzed reaction of BH acetate with aryl nitrones provided bridged benzoxazepine derivative (**58**) (Path A in Scheme 24) while a similar reaction of BH carbonate with aryl nitrones gave naphthalene derivatives (**59**) (Path B in Scheme 24).

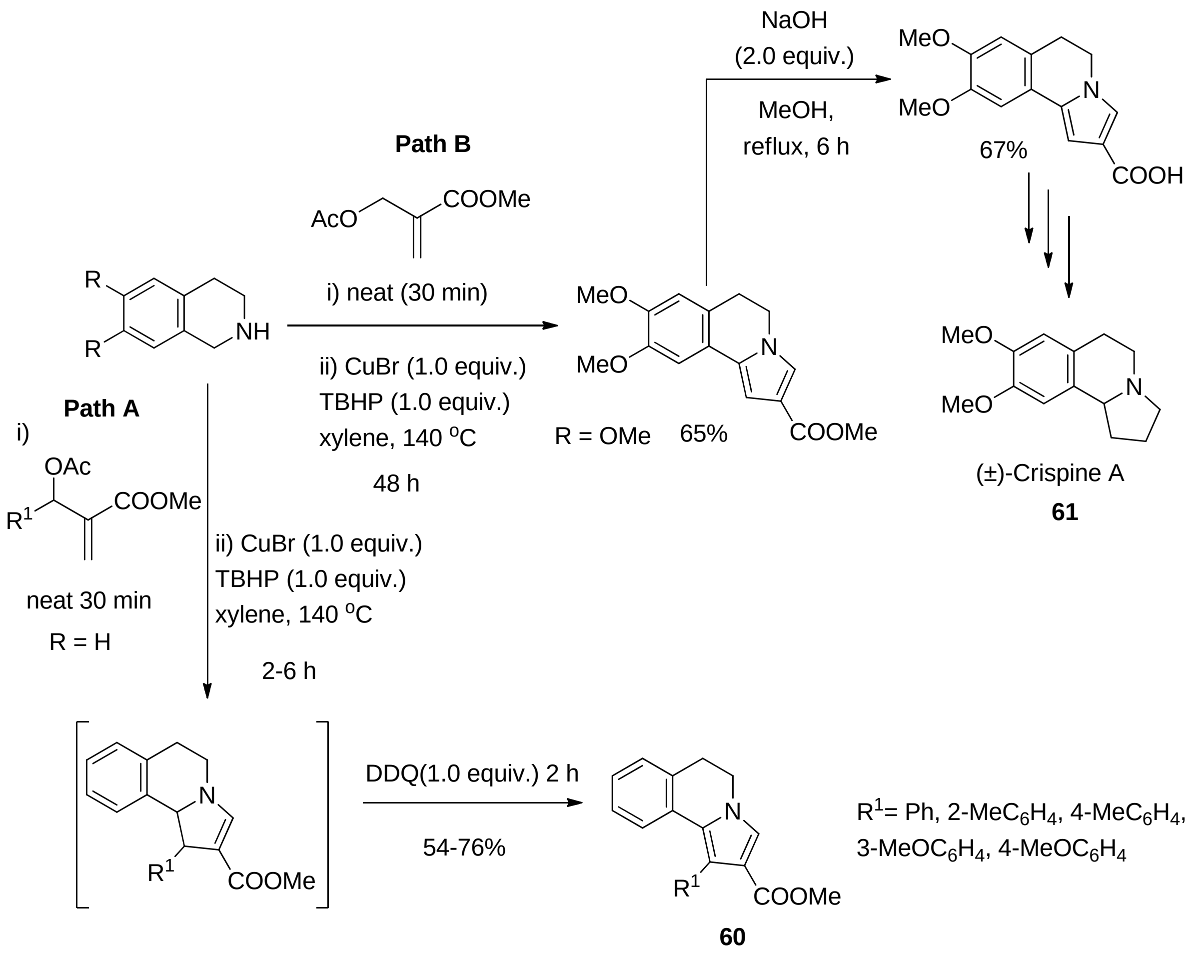
Scheme 24

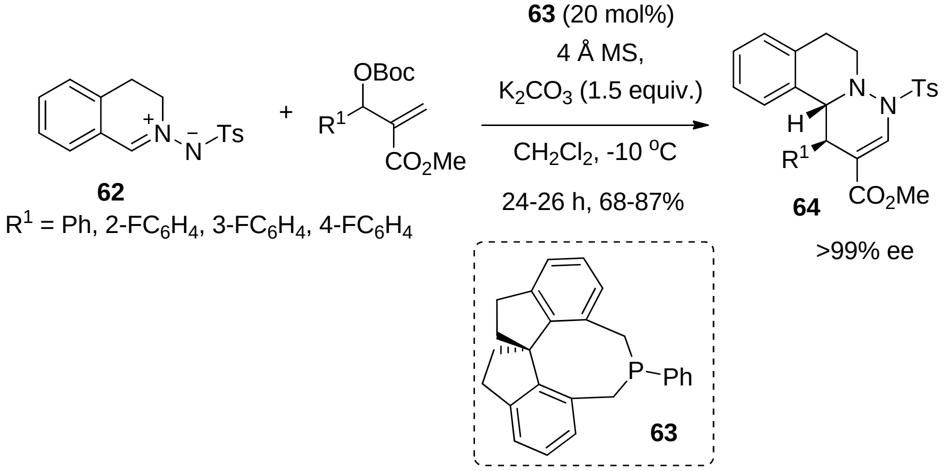


Our research group[63] reported a convenient route for the synthesis of pyrrolo[2,1-*a*]isoquinolines (**60**) from the acetates of Baylis–Hillman alcohols (prepared from methyl acrylate and aldehydes) following the reaction strategy as shown in Scheme 25 (Path A) . First step involves the alkylation of tetrahydroisoqunilines with BH acetates followed by oxidation, intramolecular 1,5-cyclization, and aromatization in the presence of CuBr/tert-butylhydroperoxide. The applicability of this protocol was elegantly demonstrated by synthesis of biologically active (±)-crispine A (**61**) (Path B in Scheme 25).

Highly enantio-diastereoselective synthesis of 4,6,7,11b-tetrahydro-1H-pyridazino[6, 1-a]iso-quinoline derivatives (**64**) from BH carbonates *via* siprocyclic phosphine (**63**) catalyzed [3+3] cycloaddition reaction with cyclic azomethine imines (**62**) was reported by Guo et al following the reaction sequence as described in Eq. 7 (Representative examples are given).[64]

Scheme 25

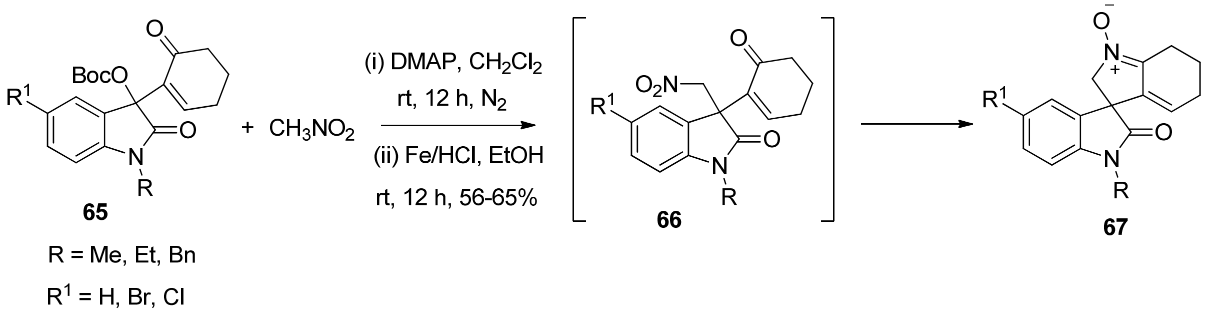




Eq. 7

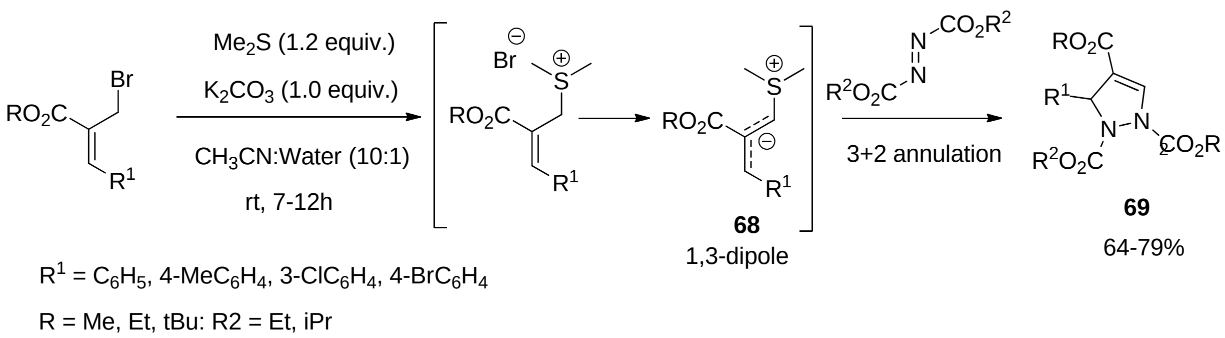
Synthesis of nitrone-spiro-oxindole frameworks (**67**) from the carbonates of BH (**65**) alcohols (derived from isatins and cyclohexenone) *via* the reaction with nitromethane in the presence of DMAP followed by reductive cyclization of the resulting in situ generated intermediate (**66**)] with Fe/HCl in one-pot procedure as described in the synthetic sequence in Scheme 26 was reported by our research group.[65]

Scheme 26



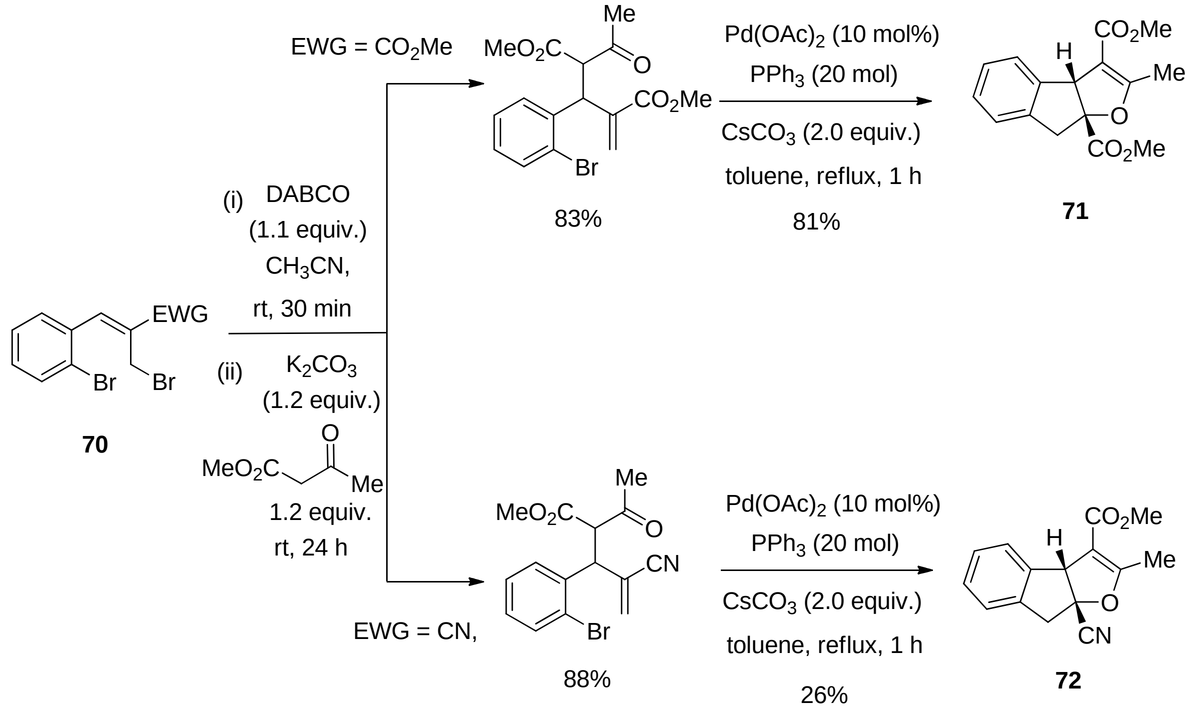
Our research group[66] has meticulously shown the BH-bromides as excellent 1,3 dipolar species (**68**) for the [3+2] annulation reaction with dialkyl azodicarboxylates to provide functionalized dihydropyrazole derivatives (**69**) in good to excellent yields in the presence of dimethyl sulphide and K_2CO_3 base (Scheme 27).

Scheme 27

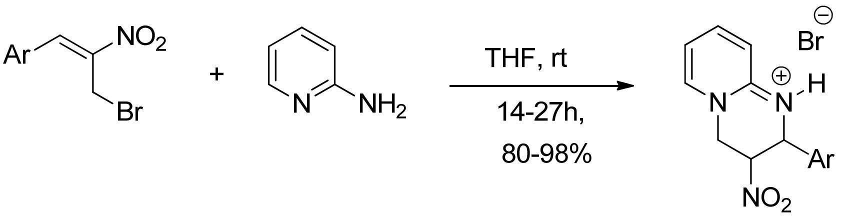


Kim and co-workers[67] reported the novel palladium-catalyzed construction of structurally interesting dihydroindenofuran derivative (**71** and **72**) *via* the reaction of appropriate BH-bromides (**70**) with acetylacetone following the reaction sequence described in Scheme 28. The key step in this reaction is believed to be Pd-catalyzed 5-*endo*-trig-carbopalladation followed by enolate O-alkylation cascade (Scheme 28).

Scheme 28



Namboothiri and co-workers[68] have used bromides of BH alcohols, derived from nitroalkenes and HCHO, for obtaining 3,4-dihydro-2Hpyrido[1,2-a]pyrimidines (**73**) *via* the reaction with 2-aminopyridines in the absence of any reagent under mild condition Eq. 8.



Eq. 8

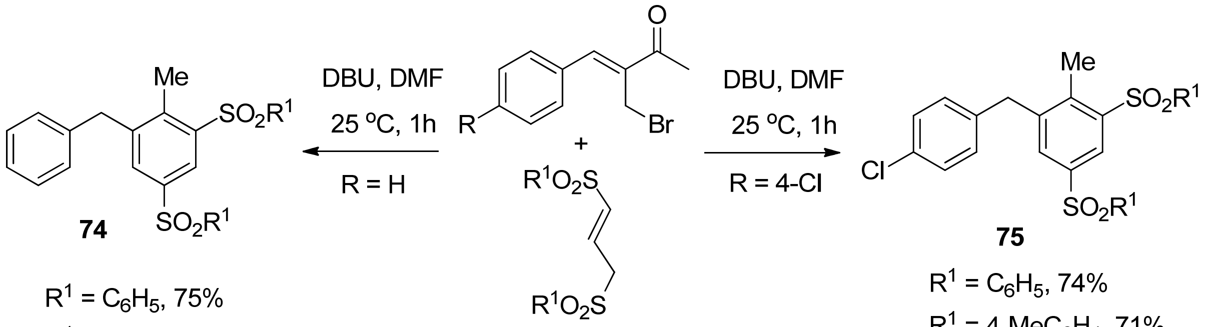
Ar = 4-MeOC$_6$H$_4$, 3,4-(MeO)$_2$C$_6$H$_3$, 4-MeC$_6$H$_4$,
1-Naphthyl, 4-ClC$_6$H$_4$, 3-BrC$_6$H$_4$,
3,4-(OCH$_2$O)$_2$C$_6$H$_3$

73

dr = 64:36-95:05

A facile approach for the synthesis of biarylmethanes (**74**, **75**) from BH bromides *via* regionselective [3 + 3] benzannulation reaction with 1,3-bis-sulfonylpropenes derivatives in the presence of DBU in DMF was reported by Menon et al. (Scheme 29).[69]

Scheme 29



74

R^1 = C$_6$H$_5$, 75%
R^1 = 4-MeC$_6$H$_4$, 74%

75

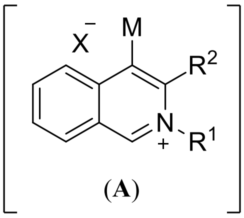
R^1 = C$_6$H$_5$, 74%
R^1 = 4-MeC$_6$H$_4$, 71%

Objectives, Results and Discussion

The previous chapter clearly demonstrates that the Baylis–Hillman reaction is well *known name reaction* whic has become a powerful synthetic tool in organic chemistry providing a diverse classes of molecules containg a minimum of three functional groups in proximity.[20] During the past 35-36 years our research group has been actively working in this fascinating research program and contributed significantly for growth of this reaction. As a part of our continuous ongoing research program on Baylis–Hillman reaction this thesis deals with the following two main objectives:

Objectives

1) To utilize less explored *in situ* generated isoquinolinium salts (**A**) as electrophiles for Baylis–Hillman coupling with representative activated alkenes with an objective of understanding the potential of these salts as electrophiles and also with a view to develop a simple strategy for synthesis of substituted dihydroisoquinoline derivatives.



(A)

Isoquinolinium salts

to understand the potential of these salts as electrophiles in BH reaction

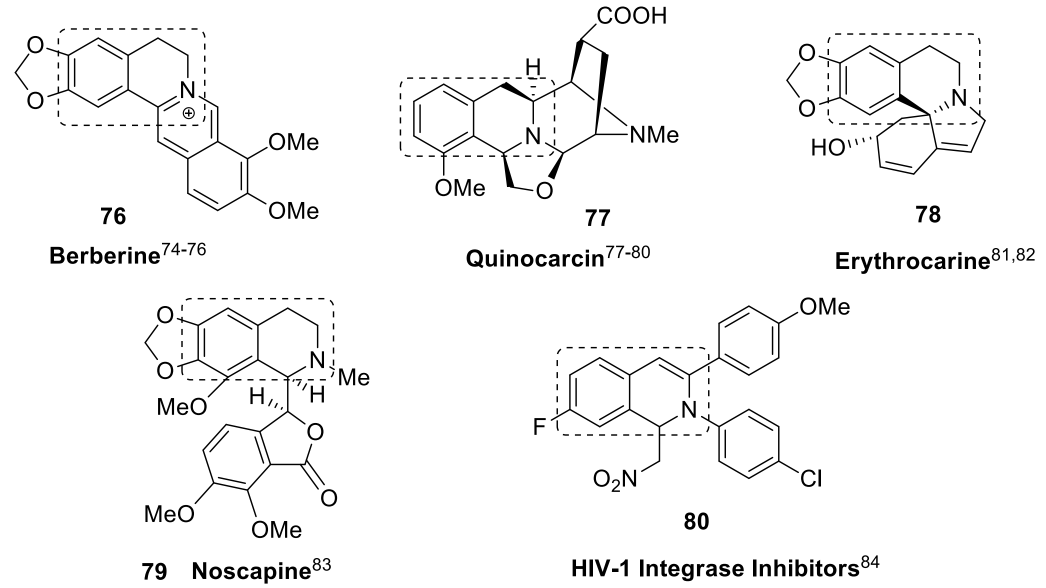
We plan to use different acrylates of varying steric requirements such as (1) methyl acrylate (2) ethyl acrylate (3) *tert.*butyl acrylate (4) phenyl acrylate and also (5) acrylonitrile for coupling with *in situ* generated isoquinolinium salts (**A**) as electrophiles.

2) To examine the applications of Baylis–Hillman adducts, obtained *via* the reaction between *in situ* generated isoquinolinium salts and alkyl acrylates or acrylonitrile, as substrates for 3-aza-Cope rearrangement with a view to develop a facile synthetic protocol for obtaining substituted phenanthridine derivatives containing dihydronaphthalene moiety.

Results and Discussion

Baylis–Hillman reaction*: In situ* generated isoquinolinium salts as excellent electrophiles for coupling with alkyl acrylates and acrylonitrile

Discovering/uncovering new components for BH reaction has been considered to be a challenging endeavor in the area of Baylis–Hillman chemistry because such efforts would enormously increase the utility of this reaction in synthetic chemistry. Since this section deals with the applications of *in situ* prepared isoquinolinium salts as electrophiles in Baylis–Hillman reaction it is appropriate to present here the importance of isoquinoline framework[70-84] as well as the applications of isoquinolinium salts in synthetic chemistry. In recent years synthesis of *in situ* generated isoquinolinum salts gained much importance due to the presence of isoquinoline frameworks in a number of natural products and bioactive compounds and selected examples **76-80** are presented in Fig 3.[74-84] Eventhough *in situ* prepared isoquinolinium salts are well known electrophiles in the literature for the past several years; their applications as electrophiles in Baylis–Hillman reaction for coupling with various activated alkenes is not well explored.[85-98]



76 **Berberine**[74-76]

77 **Quinocarcin**[77-80]

78 **Erythrocarine**[81,82]

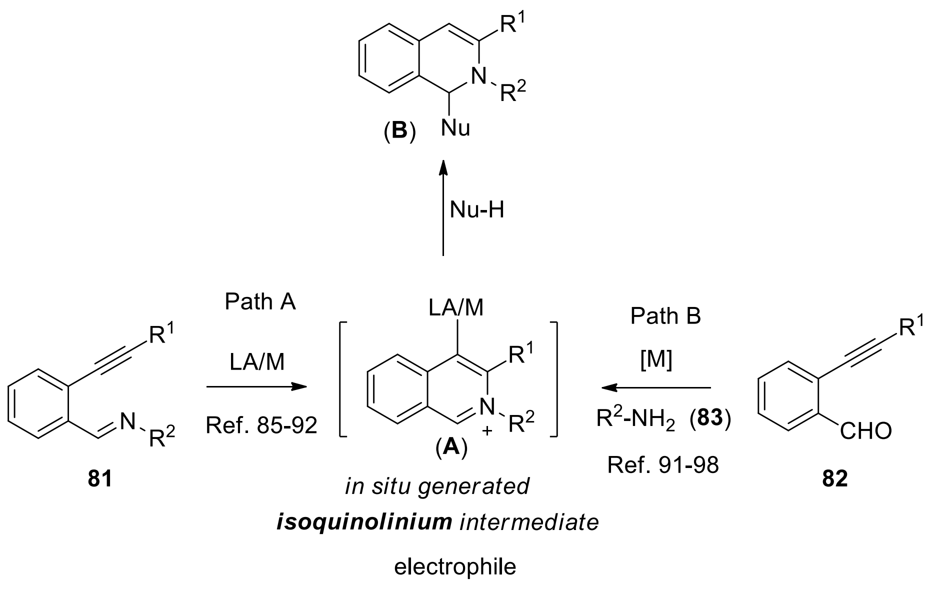
79 **Noscapine**[83]

80 **HIV-1 Integrase Inhibitors**[84]

Figure 3: Natural products and bioactive molecules with isoquinoline frameworks

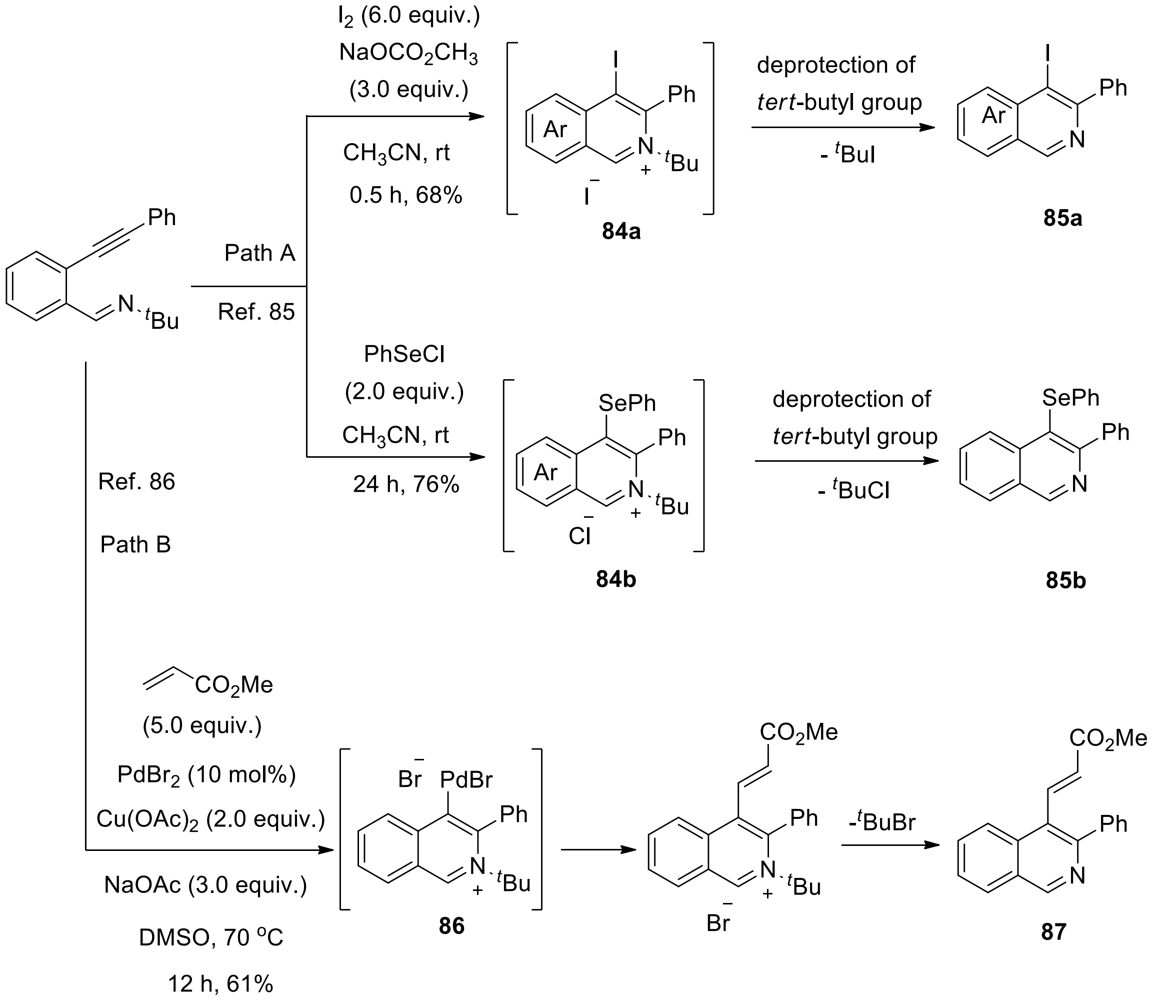
Isoquinolinium metal salts (**A**) are usually prepared *in situ*, either from 2-(1-alkynyl)aryl-aldimines (**81**) (Path A, Scheme 1)[85-92] or from 2-(1-alkynyl)arylaldehydes (**82**) (Path B)[91-98] in the presence of arylamines (**83**), *via* the treatment with metal salts. In fact, these salts have attracted the attention of synthetic and medicinal chemists because of their high potential as electrophiles to react with various nucleophiles for obtaining densely substituted 1,2-dihydroisoquinoline/ isoquinoline derivatives (**B**) (Scheme 30).

Scheme 30



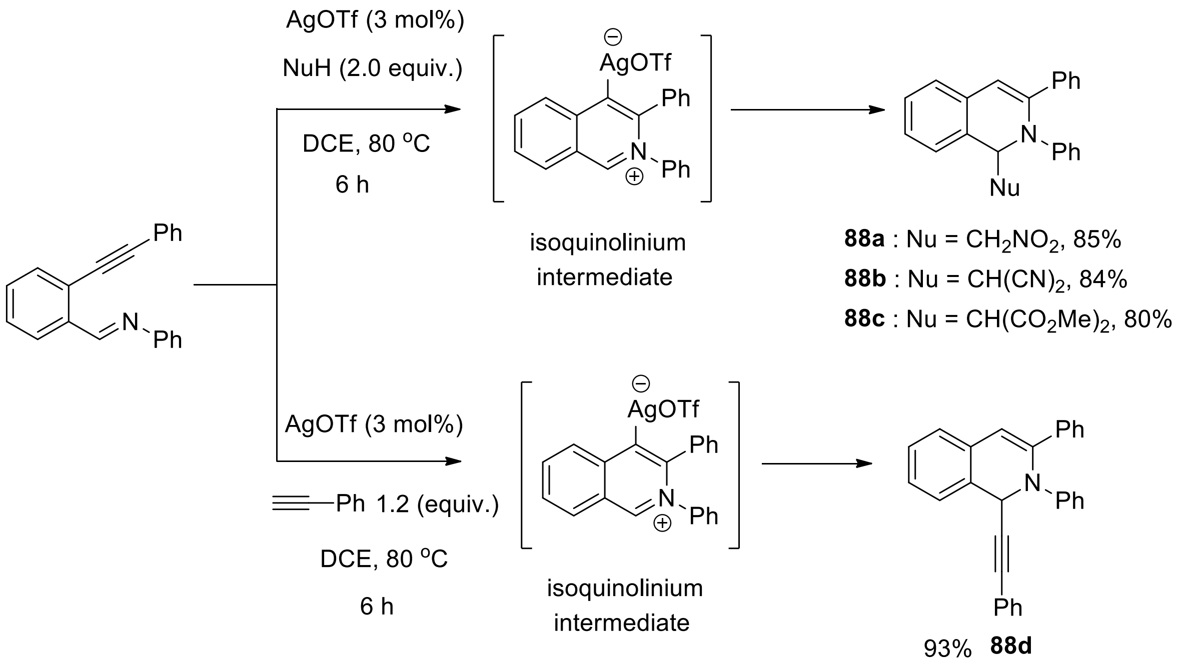
In 2001, Larock and coworkers[85,86] reported a simple preparation of isoquinolines derivatives from iminoalkyne in the presence of various electrophiles (two electrophiles I_2, and PhSeCl). This reaction is believed to proceed through *in situ* generated N-*tert*-butylisoquinolinium intermediate (**84a**, **84b**) which would lose *tert*-butyl chloride to give desired isoquinoline derivatives (**85a**, **85b**) respectively**.** (Path A in Scheme 31)[85]. Later Larock and coworkers[86] have also reported Pd(II) catalyzed cyclization of iminoalkyne in the prersence of activated alkene to provide 4-substituted isoquinoline derivative (**87**). In this case also reaction proceeds through *in situ* generated N-*tert*-butylisoquinolinium intermediate (**86**) as shown in Path B in Scheme 31.

Scheme 31



Asao and coworkers reported a facile silver catalyzed synthesis of dihydroisoquinoline derivatives (**88a-d**) from o-alkynylaryl-aldimine with carbon nucleophiles such as CH_3NO_2, $CH_2(CO_2Me)_2$, $CH_2(CN)_2$ and phenylacetylene. The key step is the formation of isoqunolinium intermediate as shown in Scheme 32.[88]

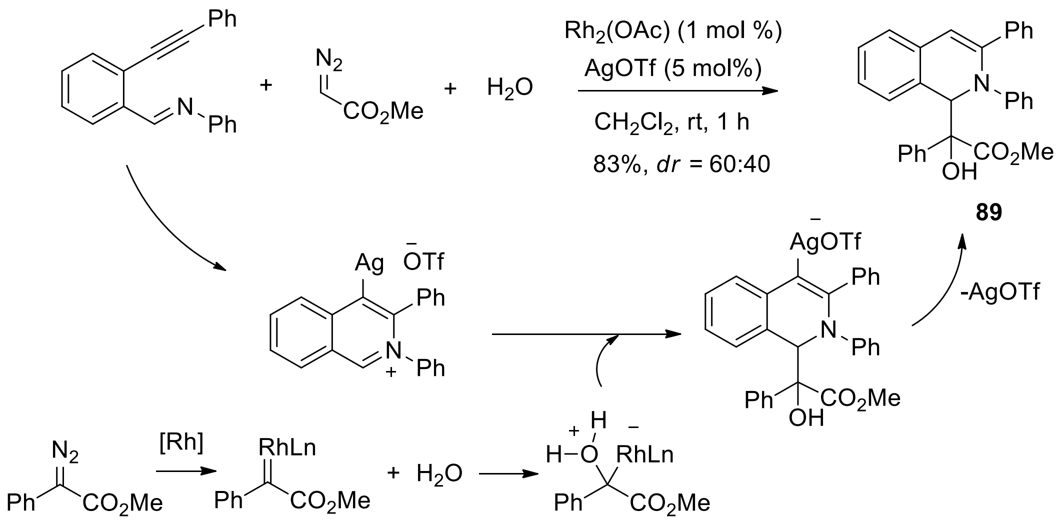
Scheme 32



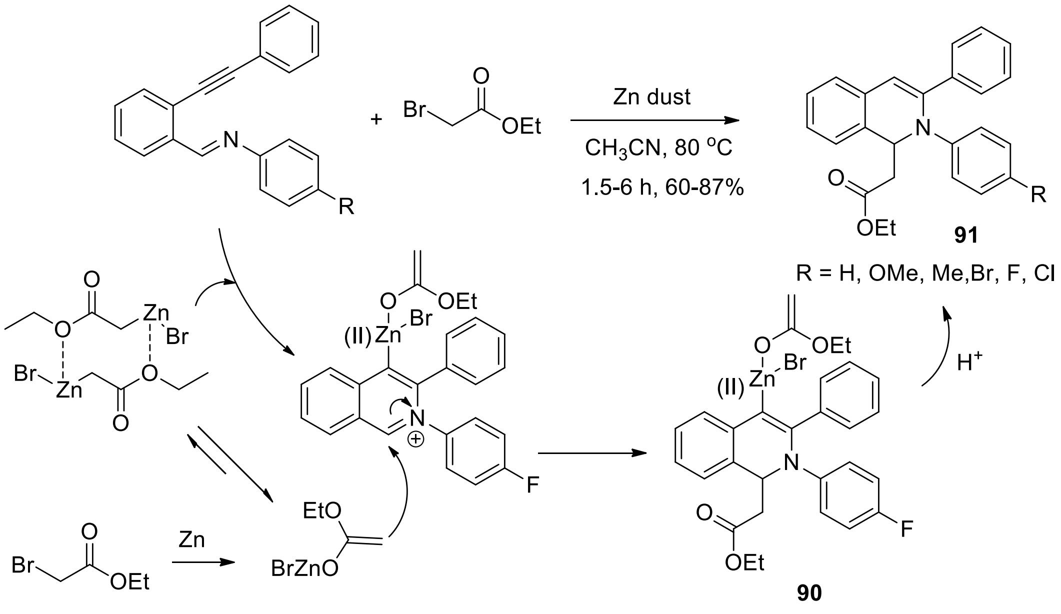
The efficient rhodium and silver cooperative catalyzed reaction between 2-alkynylarylaldimines and diazo compound for synthesis of 1,2-dihydroisoquinolines (**89**) containing α-hydroxyl-β-amino carboxylate moiety was reported by Hu and coworkers[89] following the reaction strategy described in Scheme 33.

Recently Tandon et al. reported novel synthetic approach for the synthesis of highly functionalized 1,2-dihydroisoquinoline derivatives (**91**) from *o*-alkynylarylaldimines *via* treatment with α-bromo acetate in the presence of Zn-dust (Scheme 34). The reaction proceeds through isoquinolinium intermediate (**90**) demonstrating the dual role of Reformatsky reagent i) for activation of alkyne ii) as nucleophilic reagent for adding to *in situ* generated isoqunolinium cationic intermediate (Representative examples are presented in Scheme 34).[90]

Scheme 33

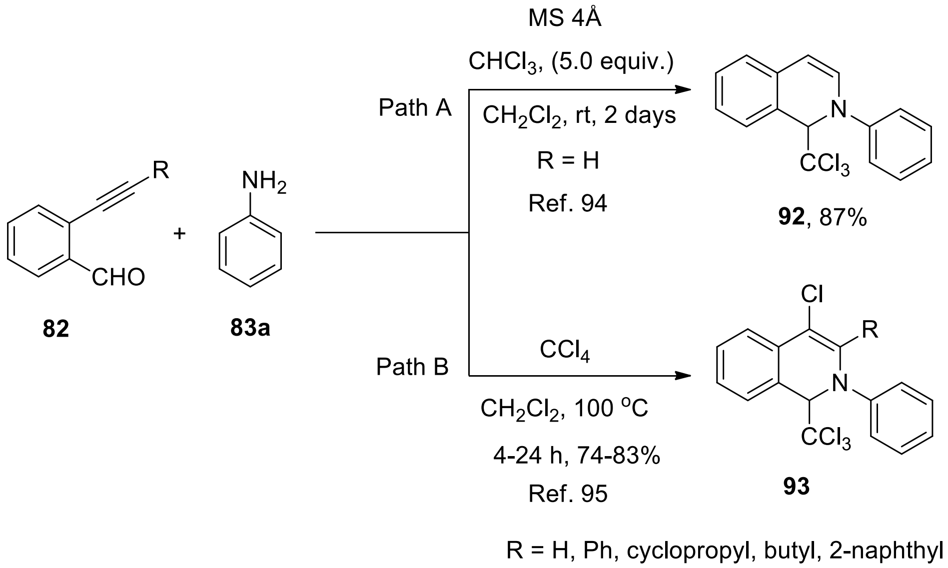


Scheme 34



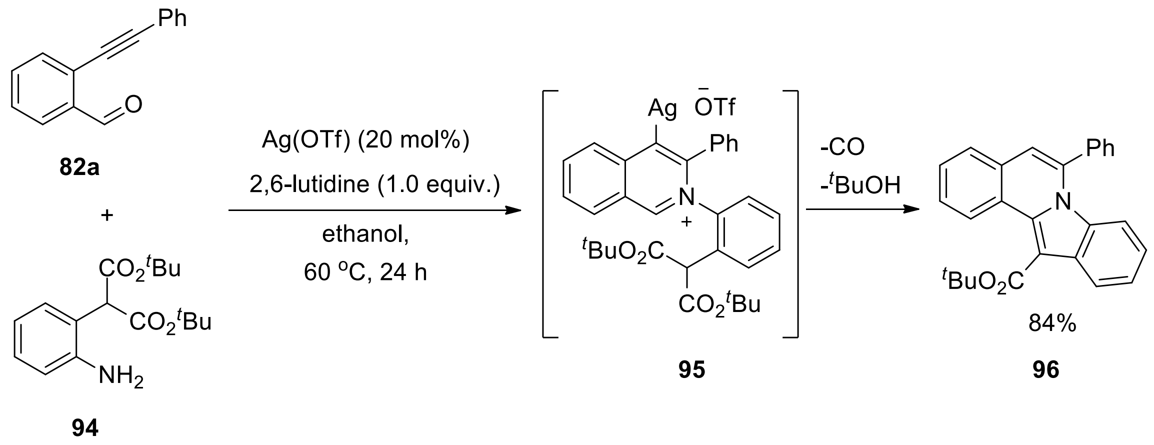
Subsequently Asao and coworkers repoprted an efficient and catalyst free synthetic strategy for the synthesis of 1,2-dihydroisoquinoline derivatives (**92**) *via* a three component reaction, i.e reaction between o-alkynylbenzaldehyde (**82**), aniline (**83a**) and chloroform (as pronucleophile). In this reaction chloroform acts as an electrophile by giving its acidic proton as well as nucleophile (Cl_3C^-) by adding onto *in situ* formed cationic isoquinolinium intermediate (**A**) following the reaction sequence as shown Path A in Scheme 35 (one example is given).[94] Wang and Tian have reported the application of CCl_4 as an electrophile as well as nucleophile for synthesis of isoquinoline derivatives (**93**) as shown in Path B in Scheme 35.[95] This strategy is similar to that of Asao.

Scheme 35

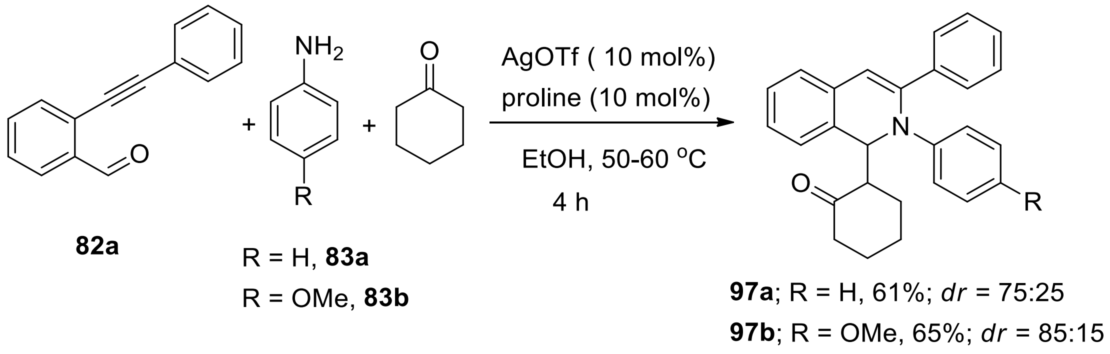


An interesting silver catalyzed intramolecular nucleophilic addition reaction onto isoquinolinium ion for obtaining polycyclic alkaloid-scaffods **96** was meticuously reported by Waldmann's research group[96] following the reaction as described in Scheme 36. This strategy invovles the reaction between 2-alkynylbenzaldehyde (**82a**) and aniline dereivative (**94**) having active methylene group (malonate nucleophile), in the presence of silver catalyst to generate isoquinolinium intermediate followed by subsequent intramolecular nucleophilic addition of active malonate group onto isoquinolinium intermediate (**95**) thus providing the desired polycyclic alkaloid-scaffods.

Scheme 36



Wu and co-workers[97] reported a convenient strategy for the synthesis of 1,2-dihydroisoquinoline derivatives (**97a, 97b**) in 61, 65% yield respectively *via* Lewis-acid-oganocatalyst-cooperative catalyzed reaction between 2-alkynylbenzaldehydes, aniline derivatives (**83**) and cyclohexanone following the reaction strategy as described in Eq. 9.



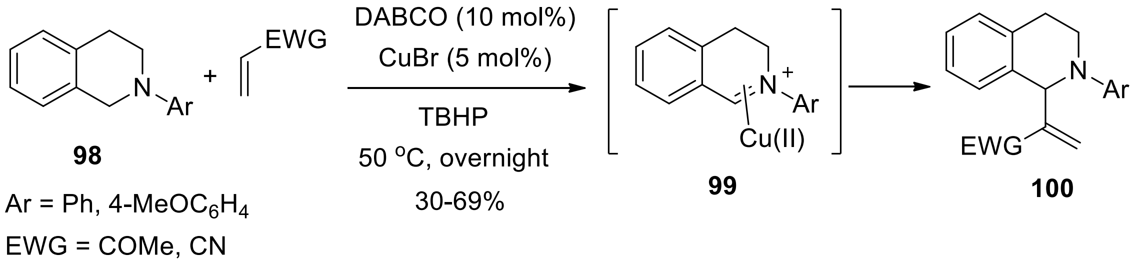
Eq. 9

Fascinated by the remarkable applications of *in situ* generated isoquinolinium salts in synthetic organic chemistry for a variety of heterocyclic compounds we felt that isoquinolinium salts can serve as beautiful electrophiles in Baylis–Hillman reaction.

Although a large number of activated alkenes, electrophiles and catalysts have been extensively and successfully employed in various BH reactions providing different classes of BH adducts, potential of isoquinolinium metal salts **(A)** as electrophiles in BH reaction was not well explored.

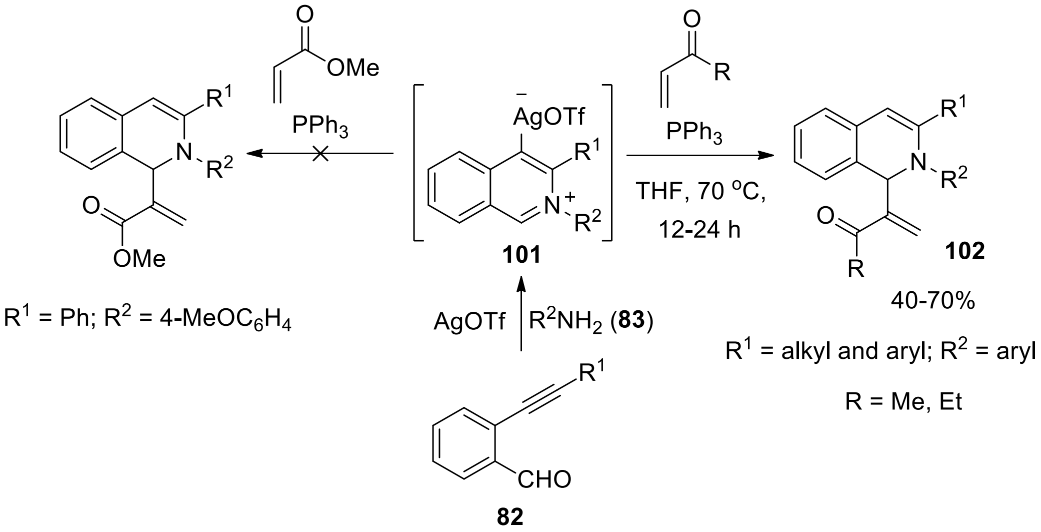
There is an interesting report by Li et al. on the Baylis–Hillman reaction using iminium ions as electrophiles.[99] This report describes an application of tetrahydroisoqunilinium compounds (**99**), generated *in situ* from tetrahydroisoquinoline (**98**) in the presence of copper catalyst, for coupling with activated alklenes (methyl vinyl ketone/acrylonitrile) under the catalytic influence of DABCO to provide a 1,2-disubstituted tetrahydroisoquinoline derivatives (**100**) according to Scheme 37.

Scheme 37



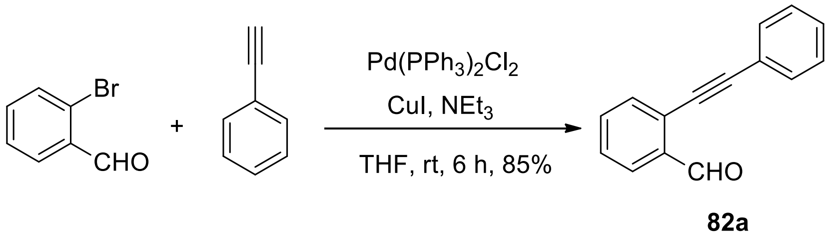
To the best of our knowledge there is one report in the literature by Ye and Wu[100] who described the application of isoquinolinium-silver triflate salts (**101**) (generated *in situ* from alkynylarylaldehydes (**82**), aryl amine (**83**) in the presence of AgOTf) as electrophiles for coupling with alkyl vinyl ketones in the presence of PPh_3 for obtaining dihydroisoquinoline frameworks (**102**) (Scheme 38). This is, in fact, very useful and an excellent methodology for synthesis of dihydroisoquinoline derivatives. Unfortunately this methodology fails if methyl acrylate [a less reactive activated alkene than methyl vinyl ketone (MVK)] is used in the place of alkyl vinyl ketones.

Scheme 38



Therefore we envisaged that development of any BH protocol utilizing alkyl acrylates and acrylonitrile as activated alkenes for coupling with, *in situ*, generated isoquinolinium-silver triflate salts would not only provide differently substituted dihydroisoquinoline frameworks, but also expand the scope of isoquinolinium-silver triflate salts as useful electrophiles in BH reactions. Accordingly we have concentrated our efforts in this direction.We have selected 2-phenylethynylbenzaldehyde (**82a**), aniline (**83a**) for generating *in situ* isoquinolinium salt in the presence of appropriate metal salts and methyl acrylate as activated alkene for performing the Baylis–Hillman reaction.

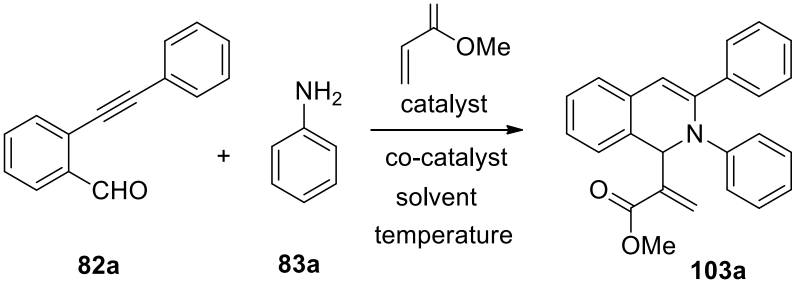
Accordingly we have synthesized desired product 2-(phenylethynyl)benzaldehyde (**82a**) *via* Sonogashira reaction of 2-bromobenzaldehyde with phenylacetylene in the presence of Pd catalyst, CuI, and triethylamine at room temperature in 85% yield following known procedure with slight modification (Eq. 10).[101]



Eq. 10

We have then carried out the reaction between 2-phenylethynylbenzaldehyde (**82a**), aniline (**83a**), and methyl acrylate using AgOTf as a catalyst (10 mol%) and acetonitrile as solvent. We were pleased to note that the reaction went smoothly at room temperature providing the desired Baylis–Hillman product [methyl 2-(2,3-diphenyl-1,2-dihydroisoquinolin-1-yl)acrylate] (**103a**) in 66% yield in 84 h (Table 1, entry 1). The structure of the product (**103a**) was confirmed by IR, ^{1}H NMR, ^{13}C NMR, and HRMS spectral data analysis. This result is indeed very encouraging. Therefore with a view to have better yields and improve the rate of reaction we have performed the same reaction under various conditions as described in Table 1. From the Table 1 it was very clear that the best result was obtained using AgOTf as a catalyst (for formation of isoquinolinium salt) and DABCO as a catalyst (for performing BH reaction) in acetonitrile as a solvent to provide the desired product in 72% yield in 2 h time (Table 1, Entry 8). The BH product thus obtained was identical with that obtained in entry 1 in Table 1.

Table 1. Optimization of the reaction conditions[a]



Entry	Solvent	Metal salt (10 mol%)	Amine (mol%)	Temp (°C)	Time (h)	Yield **103a**^{b}(%)
1	CH_3CN	AgOTf	DABCO (50)	rt	84	66
2	THF	AgOTf	DABCO (50)	reflux	12	53
3	DMF	AgOTf	DABCO (50)	70	1.5	65
4	DMF	AgOTf	DABCO (50)	100	0.75	55
5	CH_3CN	AgOTf	DABCO (10)	70	8	61
6	CH_3CN	AgOTf	DABCO (25)	70	4	68
7	CH_3CN	AgOTf	DABCO (50)	reflux	1	50
8	**CH_3CN**	**AgOTf**	**DABCO (50)**	**70**	**2**	**72**
9	CH_3CN	AgOTf	DABCO (100)	70	2	70
10^c	CH_3CN	AgOTf	DABCO (50)	70	2	68
11	CH_3CN	AgOTf	DMAP (50)	70	24	29
12	CH_3CN	AgOTf	DBU (50)	70	12	NR
13	CH_3CN	$Cu(OTf)_2$	DABCO (50)	70	6	64
14	CH_3CN	CuI	DABCO (50)	70	12	51
15	CH_3CN	$Cu(OAc)_2$	DABCO (50)	70	24	14
16	CH_3CN	$AgNO_3$	DABCO (50)	70	5	70
17	CH_3CN	Ag_2CO_3	DABCO (50)	70	14	51
18	CH_3CN	AgOAc	DABCO (50)	70	11	69

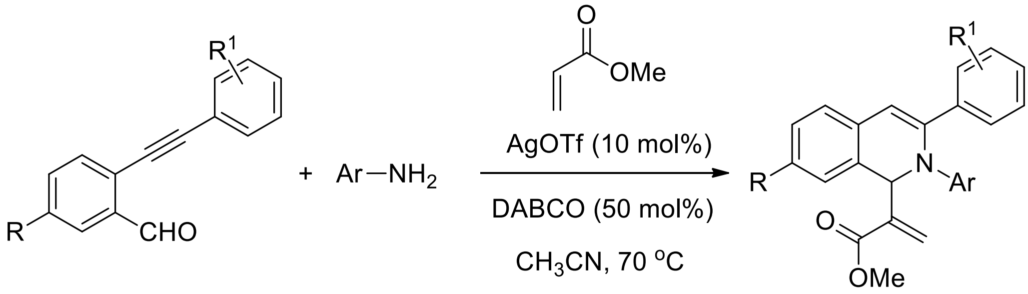
a) In all the reactions, a mixture of **82a** (1.0 mmol) and aniline **83a** (1.2 equiv.) was heated with stirring at appropriate temperature for 5-10 minutes and then treated with methyl acrylate (3.0 equiv.), DABCO, in the presence of metal salt in different solvents (1.0 mL).

b) Isolated yields based on **82a**.

c) 20 mol% AgOTf was used

Encouraged by this fascinating result we planned to extend this strategy for different aniline derivatives. Thus the anilines (**83a-i**) having various substitution pattern have been successfully utilized for obtaining the *in situ* generated isoquuinolinium salts in reaction with 2-(arylethynyl)benzaldehyde (**82a-d**) in presence of AgOTf. Resulting *in situ* generated salts on BH reaction with methyl acrylate in the presence of DABCO provided the expected BH adducts (**103a-l**) in high yields (Tasble 2). Structures of all the products were confirmed by IR, ^{1}H NMR, ^{13}C NMR, and HRMS spectral data analysis. We have also confirmed the structure by single crystal X-ray data analysis in the case of compounds **103d** and **103k** (for ORTEP diagram see in Figure 4 and 5).

Table. 2. Synthesis of 1,2-dihydroisoquinoline drivatives using methyl acrylate[a,b]



82 **83** **103a-l**

82a: R = H, R^1 = H
82b: R = OMe, R^1 = H
82c: R = H, R^1 = 2-Br
82d: R = H, R^1 = 4-Me

83a: Ar = C_6H_5; **83b**: Ar = 4-MeOC_6H_4
83c: Ar = 4-MeC_6H_4; **83d**: Ar = 3-ClC_6H_4
83e: Ar = 2-IC_6H_4; **83f**: Ar = 4-IC_6H_4
83g: Ar = 3-$O_2NC_6H_4$; **83h**: Ar = 3,4-$(MeO)_2C_6H_3$
83i: Ar = 1-Naphthyl

Entry	R	R^1	Amine Ar	Time (h)	BH-adduct[#]	Yield[c] (%)
1	H	H	C_6H_5	2	**103a**	72
2	H	H	4-MeOC_6H_4	3	**103b**	70
3	H	H	4-MeC_6H_4	3	**103c**	74
4	H	H	3-ClC_6H_4	4	**103d**[d]	77
5	H	H	2-IC_6H_4	3	**103e**	58

6	H	H	4-IC_6H_4	2.5	**103f**	67
7	H	H	3-$NO_2C_6H_4$	6	**103g**	61
8	H	H	3,4-$(MeO)_2C_6H_3$	2.5	**103h**	77
9	OMe	H	C_6H_5	6	**103i**	65
10	H	2-Br	C_6H_5	4	**103j**	55
11	H	4-Me	C_6H_5	3.5	**103k**[d]	79
12	H	H	1-Naphthyl	3	**103l**	61

a) In all reactions; a mixture of aldehyde (**82**) (1.0 mmol) and aryl amine (**83**) (1.2 equiv.) was heated for 5-10 minutes at 70 °C and then treated with methyl acrylate (3.0 equiv.) in the presence of DABCO (50 mol%), AgOTf (10 mol%) in acetonitrile (1.0 mL) at 70 °C.

b) All compounds were fully characterized.

c) The isolated yields are based on aldehyde (**82**).

d) The structure of this molecule was also confirmed by single crystal X-ray data analysis.

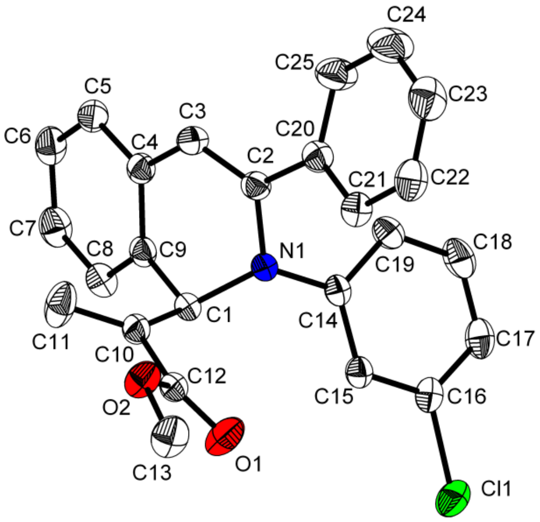


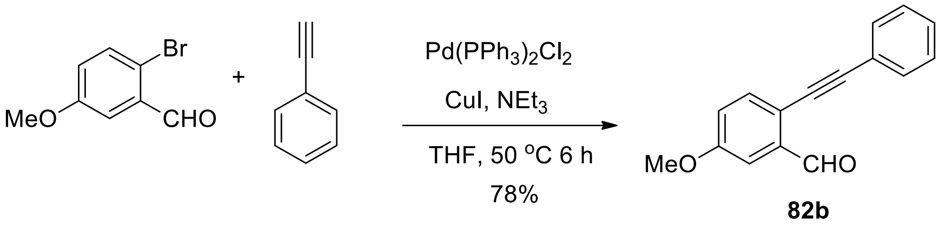
Figure 4: ORTEP of compound **103d**

[#] In order to have continuity and easy understanding we have given numbering **103a-l** for BH adducts.

Table I. Crystal data and structure refinement for compound **103d**

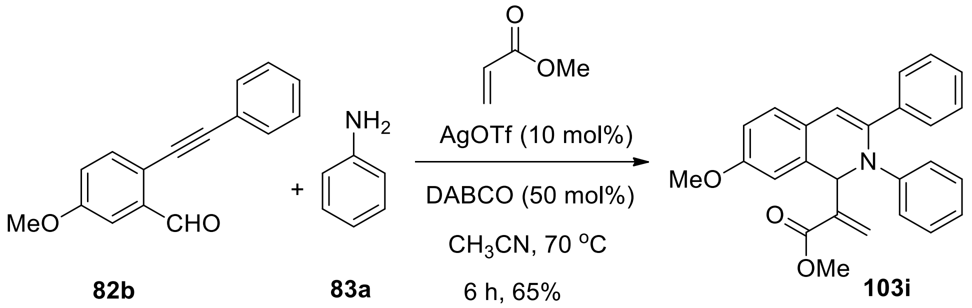
Identification code	**103d**	
Empirical formula	$C_{25} H_{20} Cl N O_2$	
Formula weight	401.87	
Temperature	298(2) K	
Wavelength	1.54184 Å	
Crystal system	Monoclinic	
Space group	P 21/c	
Unit cell dimensions	a = 10.3318(2) Å	α= 90°.
	b = 11.2160(2) Å	β= 102.745(2)°.
	c = 18.0161(3) Å	γ = 90°.
Volume	2036.29(7) Å^3	
Z	4	
Density (calculated)	1.311 Mg/m^3	
Absorption coefficient	1.823 mm^{-1}	
F(000)	840	
Crystal size	0.41 x 0.22 x 0.21 mm^3	
Theta range for data collection	4.387 to 71.856°.	
Index ranges	-12<=h<=12, -10<=k<=13, -22<=l<=17	
Reflections collected	7847	
Independent reflections	3898 [R(int) = 0.0181]	
Completeness to theta = 67.684°	99.6 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7007 and 0.5219	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3898 / 0 / 264	
Goodness-of-fit on F^2	1.048	
Final R indices [I>2sigma(I)]	R1 = 0.0443, wR2 = 0.1250	
R indices (all data)	R1 = 0.0491, wR2 = 0.1298	
Extinction coefficient	0.0017(2)	
Largest diff. peak and hole	0.436 and -0.536 e.Å^{-3}	

With a view to understand substituent effects, next we have selected 5-methoxy-2-(phenylethynyl)benzaldehyde (**82b**) (substituted alkynaldehydes) for reaction with aniline. The required aldehyde was prepared *via* reaction of 2-bromo-5-methoxybenzaldehyde with phenylacetylene in the presence of Pd catalyst, CuI, and triethylamine at 50 °C in 78% yield from the following known procedure with slight modification (Eq. 11).[102]



Eq. 11

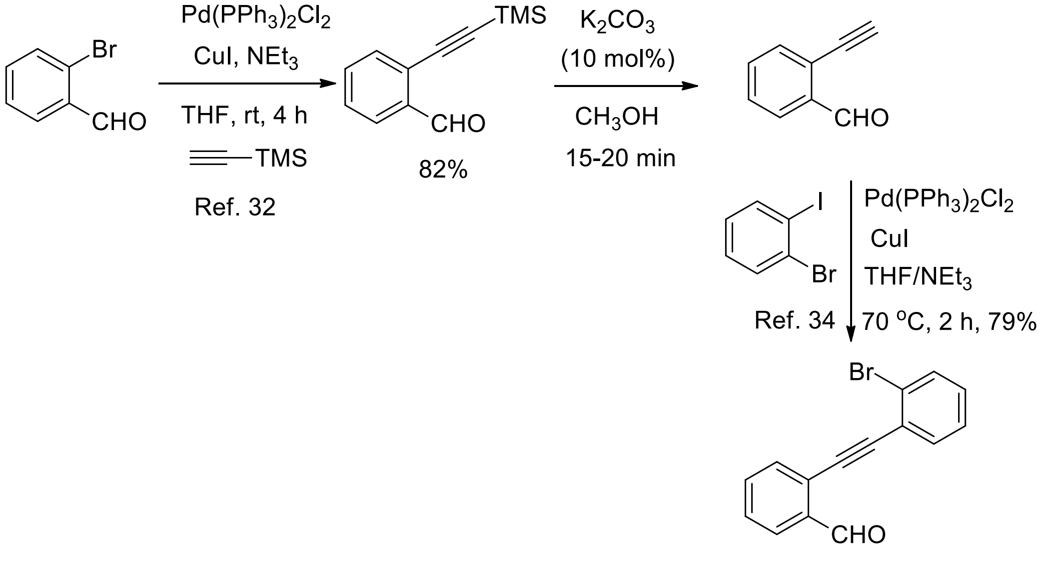
We have then performed the reaction between the aldehyde (**82b**), aniline (**83a**) in the presence of AgOTf and then treated the *in situ* genated isoquinolinium salt with methyl acrylate in the presence of DABCO (Eq. 12). Resulting BH adduct methyl 2-(7-methoxy-2,3-diphenyl-1,2-dihydroisoquinolin-1-yl)acrylate (**103i**) was obtained in 65% yield. Structure of this molecule (**103i**) was confirmed by IR, ^{1}H NMR, ^{13}C NMR, and HRMS spectral data analysis.



Eq. 12

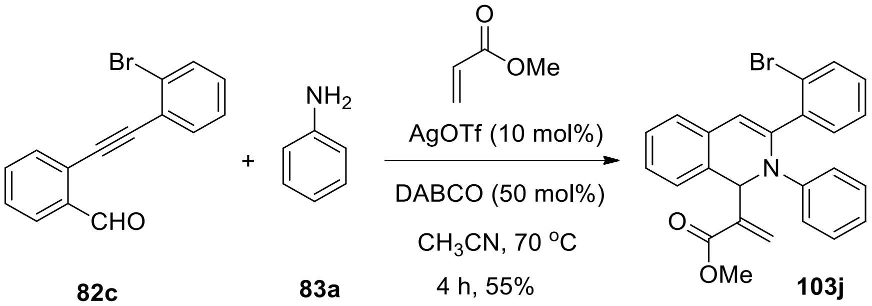
Next, we have selected 2-[(2-bromophenyl)ethynyl]benzaldehyde (**82c**) (*ortho*-bromo substituted alkynyl aldehydes) for obtaining *in situ* generated isoquinolinium salts for coupling with methyl acrylate. Required aldehyde (**82c**) was prepared by treating 2-bromobenzaldehyde with trimethylsilylacetylene (under Sonogashira couping conditions) followed by desilylation with K_2CO_3. Reaction of the resuting 2-ethynylbenzaldehyde with 1-bromo-2-iodobenzene in the presence of Pd catalyst, CuI, and triethylamine at 70 °C gave the desired aldehyde (**82c**) in 79% yield following the literature procedure with slight modification (Scheme 39).[101, 103]

Scheme 39



82c

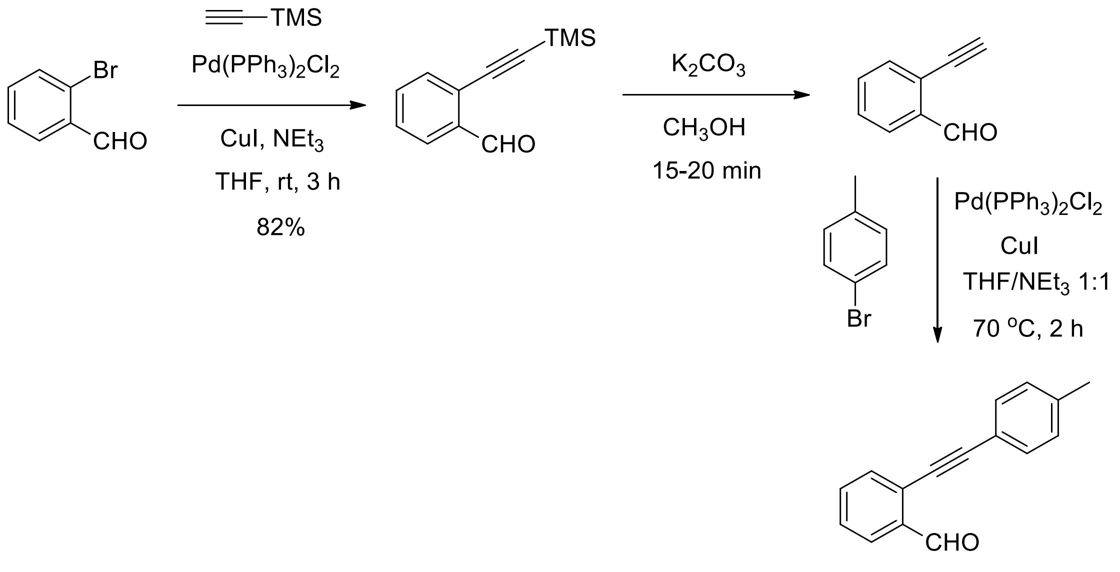
Reaction of 2-[(2-bromophenyl)ethynyl]benzaldehyde (**82c**) with aniline (**83a**) followed by the treatment with methyl acrylate following the procedure as indicated in Table 1 gave the desired product methyl 2-[3-(2-bromophenyl)-2-phenyl-1,2-dihydroisoquinolin-1-yl]acrylate (**103j**) in 55% isolated in 4 h time (Eq. 13). IR, ^1H NMR, ^{13}C NMR, and HRMS spectral data analysis confirm the structure of this molecule (**103j**).



Eq. 13

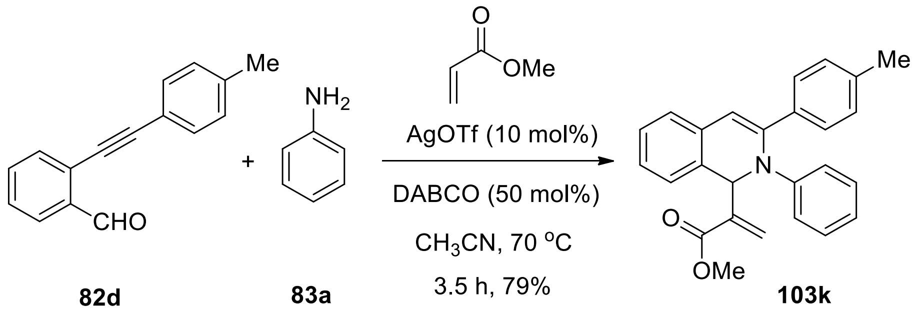
Next we have selected 2-(*p*-tolylethynyl)benzaldehyde (**82d**) for preparing the isoquinolinium salt (**A**) for utilizing as electrophile in BH reaction. Required aldehyde (**82d**) was conveniently prepared following the reaction strategy as described in Scheme 40 with slight modification.[101, 103]

Scheme 40



82d, 75%

Reaction of 2-(*p*-tolylethynyl)benzaldehyde (**82d**) with aniline (**83a**) followed by the reaction of the *in situ* generated isoquinolinium salt treatment with methyl acrylate following the optimized reaction conditions afforded the required product methyl 2-[2-phenyl-3-(*p*-tolyl]-1,2-dihydroisoquinolin-1-yl)acrylate (**103k**) in 79% isolated in 3.5 h time (Eq. 14). We have confirmed the structure of this molecule by spectral data analysis (IR, ^{1}H NMR, ^{13}C NMR, and HRMS) and further confirmed by single crystal X-ray data analysis (Figure 5).



Eq. 14

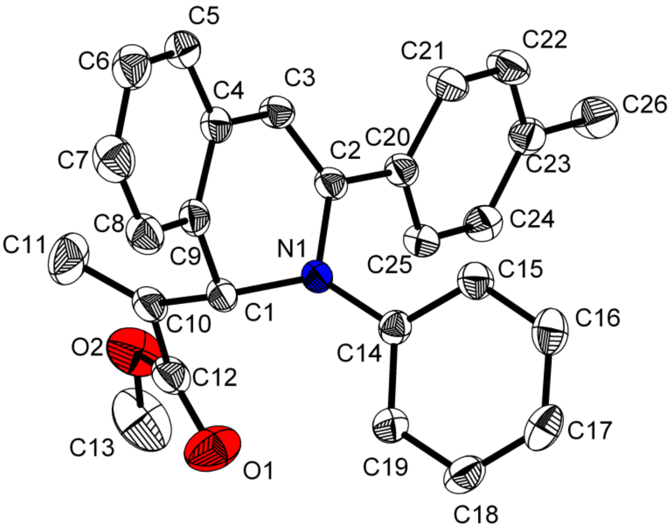


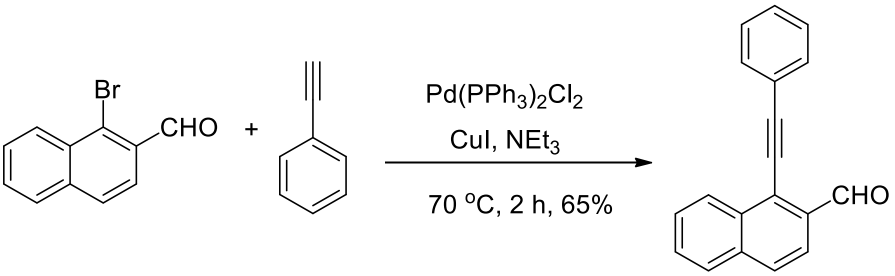
Figure 5: ORTEP of compound **103k**

Table II. Crystal data and structure refinement for compound **103k**

Identification code	**103k**	
Empirical formula	$C_{26} H_{23} N O_2$	
Formula weight	381.45	
Temperature	298(2) K	
Wavelength	1.54184 Å	
Crystal system	Monoclinic	
Space group	P 21/n	
Unit cell dimensions	a = 13.4168(4) Å	α= 90°.
	b = 10.8421(3) Å	β= 100.638(3)°.
	c = 14.3882(5) Å	γ = 90°.
Volume	2057.03(11) $Å^3$	
Z	4	
Density (calculated)	1.232 Mg/m^3	
Absorption coefficient	0.609 mm^{-1}	
F(000)	808	
Crystal size	0.39 x 0.22 x 0.20 mm^3	
Theta range for data collection	5.141 to 71.828°.	
Index ranges	-16<=h<=15, -13<=k<=7, -17<=l<=16	

Reflections collected	7992
Independent reflections	3911 [R(int) = 0.0203]
Completeness to theta = 67.684°	99.2 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.8878 and 0.7970
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3911 / 0 / 264
Goodness-of-fit on F^2	1.045
Final R indices [I>2sigma(I)]	R1 = 0.0520, wR2 = 0.1442
R indices (all data)	R1 = 0.0607, wR2 = 0.1554
Extinction coefficient	n/a
Largest diff. peak and hole	0.300 and -0.215 e.Å^{-3}

With a view to understand the application of 1-(2-phenylethynyl)-2-naphthaldehyde (**82e**) in this reaction strategy we have prepared this aldehyde *via* reaction of 1-bromo-2-naphthaldehyde with phenylacetylene in the presence of Pd catalyst, CuI, and triethylamine at 70 °C in 65% yield the following known procedure with slight modification (Eq. 15)[104]

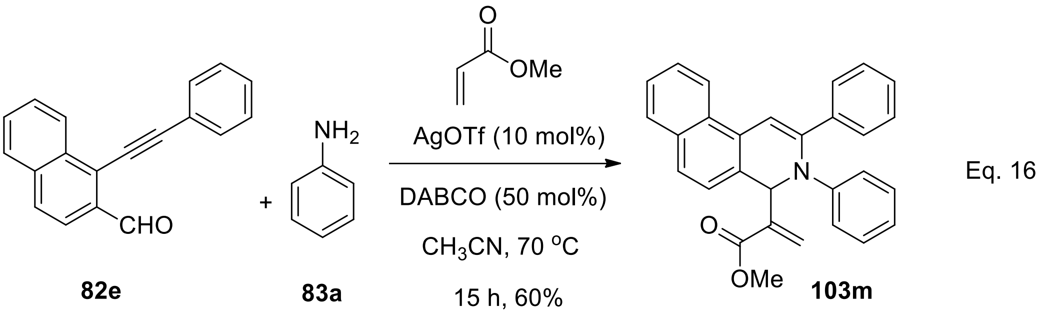


82e

Eq. 15

Subsequent reaction of this molecule (**82e**) with aniline (**83a**) and then with methyl acrylate following the strategy as desribed in the case of BH adduct (**103m**) provided the expected BH adduct, methyl 2-(2,3-diphenyl-3,4-dihydrobenzo[*f*]isoquinolin-4-yl)acrylate in 15 h in 60% isolated yield (Eq. 16). We have established the structure on the basis of spectral data (IR, ^{1}H

NMR, ^{13}C NMR, and HRMS) analysis. Also further confirmed by single crystal X-ray data analysis (Figure 6).



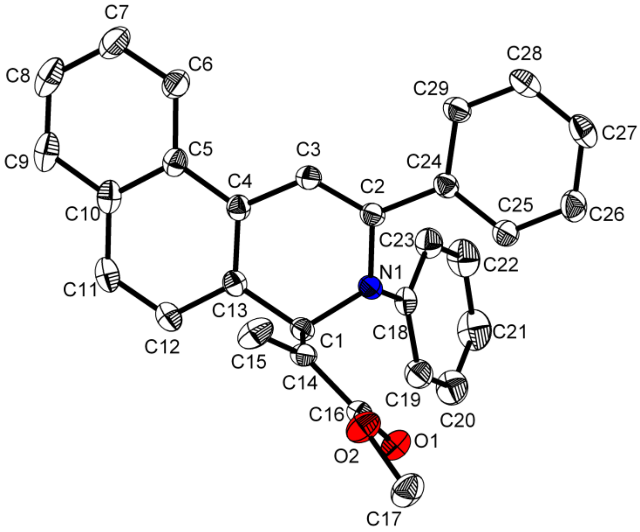


Figure 6: ORTEP of compound **103m**

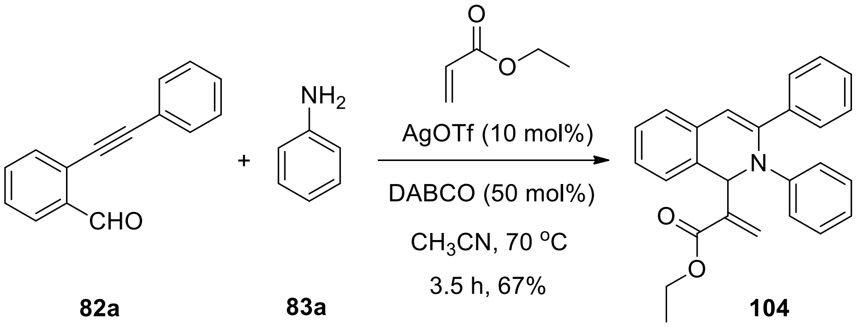
Table III. Crystal data and structure refinement for compound **103m**

Identification code	**103m**
Empirical formula	$C_{29} H_{23} N O_2$
Formula weight	417.48
Temperature	298(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P -1

Unit cell dimensions	a = 7.9242(8) Å	α= 94.588(3)°.
	b = 10.9826(10) Å	β= 103.101(3)°.
	c = 13.0474(13) Å	γ = 95.395(3)°.
Volume	1095.01(19) Å^3	
Z	2	
Density (calculated)	1.266 Mg/m^3	
Absorption coefficient	0.079 mm^{-1}	
F(000)	440	
Crystal size	0.22 x 0.17 x 0.12 mm^3	
Theta range for data collection	4.232 to 28.359°.	
Index ranges	-10<=h<=10, -14<=k<=14, -17<=l<=17	
Reflections collected	21620	
Independent reflections	5315 [R(int) = 0.0200]	
Completeness to theta = 25.242°	95.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9906 and 0.9828	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5315 / 0 / 290	
Goodness-of-fit on F^2	1.042	
Final R indices [I>2sigma(I)]	R1 = 0.0514, wR2 = 0.1360	
R indices (all data)	R1 = 0.0573, wR2 = 0.1412	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.266 and -0.193 e.Å^{-3}	

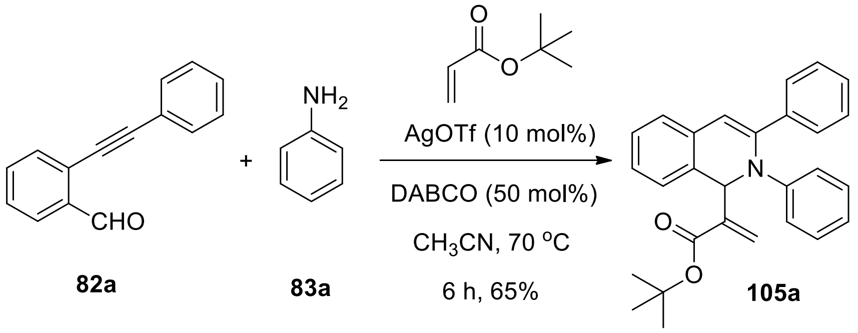
In order to understand the generality of this protocol we have examined the application of ethyl acrylate as activated alkene in this strategy. Thus the reaction between 2-phenylethynylbenzaldehyde (**82a**), aniline (**83a**), ethyl acrylate was performed following the optimized procedure. We were pleased to see that the expected BH adduct ethyl-2-(2,3-diphenyl-1,2-dihydroisoquinolin-1-yl)acrylate (**104**) was obtained in 67% yield (Eq. 17).

Structure of (**104**) was confirmed by spectral data (IR, ^{1}H NMR, ^{13}C NMR, and HRMS) analysis.



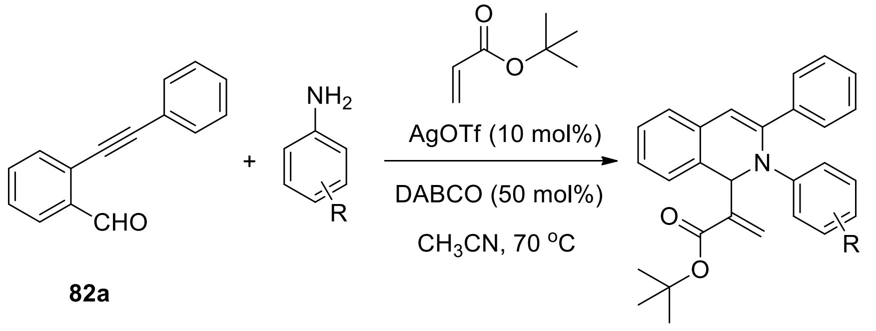
Eq. 17

Then we have employed *tert.*butyl acrylate as activated alkene for coupling with the *in situ* generated isoquinolinium salt [prepared from 2-(phenylethynyl)benzaldehyde (**82a**) and aniline (**83a**)]. This reaction worked well providing the required product, *tert*-butyl-2-(2,3-diphenyl-1,2-dihydroisoquinolin-1-yl)acrylate (**105a**), in 65% yield as presented in Eq. 18.



Eq. 18

Next we have extended this strategy to two more anilines, i.e. 3-chloroaniline (**83d**) and 3,4-dimethoxy aniline (**83h**) for reaction with 2-(phenylethynyl)benzaldehyde (**82a**) to give the isoquinolnium salts and then with *tert.*butyl acrylate which provided the desired BH adducts (**105b** and **105c**) in 54 and 66% yields respectively (Eq. 19)$^{\#}$. We have confirmed structures of these three compounds by analyzing their spectral data (IR, ^{1}H NMR, ^{13}C NMR, and HRMS).

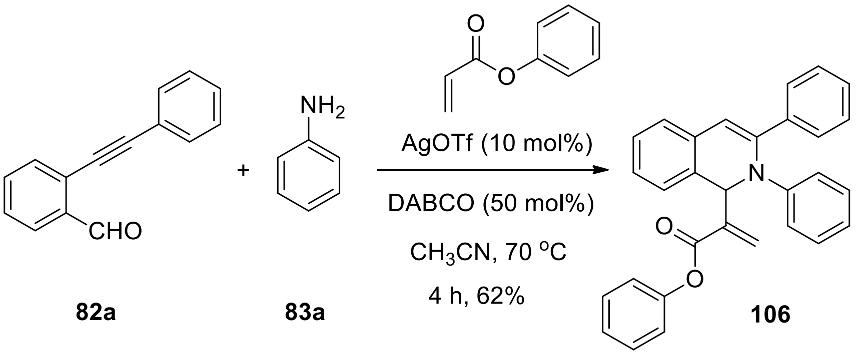


Eq. 19

83d: R = 3-Cl **105b**: R = 3-Cl, 10 h, 54%

83h: R = 3,4-$(OMe)_2$ **105c**: R = 3,4-$(OMe)_2$, 4 h, 66%

After achieving encouraging results using alky acrylates as activated alkenes for coupling with *in situ* prepared isoquinolinium salts we have turned our attention towards application of phenyl acrylate as activated alkene in this protocol. We were happy to note this reaction worked well and provided the expected Baylis–Hillman aduuct, phenyl 2-(2,3-diphenyl-1,2-dihydroisoquinolin-1-yl)acrylate (**106**), in 62% yield when we treated phenyl acrylate with 2-(phenylethynyl)benzaldehyde (**82a**), aniline (**83a**) for 4 h as described in the Eq. 20. Structure of this adduct was fully characterized by the spectral data analysis and also further confirmed by single crystal X-ray data analysis (Figure 7).



Eq. 20

[#]In order to have continuity and easy understanding we have given numbering **105b, 105c** for BH adducts.

[@] Exact mass calcd .values for Ar = Ar^1 = Ph : **IA** [M+H] m/z : 282.1283, **IIA** $[M\text{-}OH^-]$ m/z : 282.1277, **IIIA** $[M\text{-}OH^-]$ m/z : 480.2646, **103a** [M-H] m/z : 366.1489. Ar = Phenyl, Ar^1 = 1-naphthyl: **IB** [M+H] m/z : 332.1439, **IIB** $[M\text{-}OH^-]$ m/z : 332.1434, **IIB** $[M\text{-}OH^-]$ m/z : 530.2802, **103l** [M-H] m/z : 416.1645.

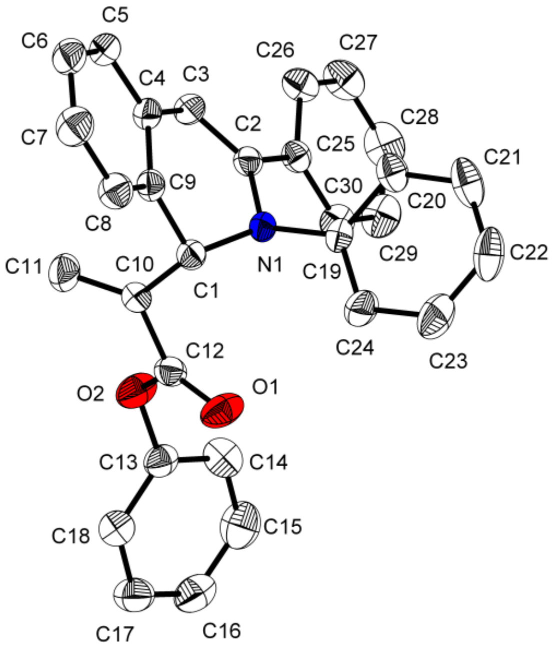


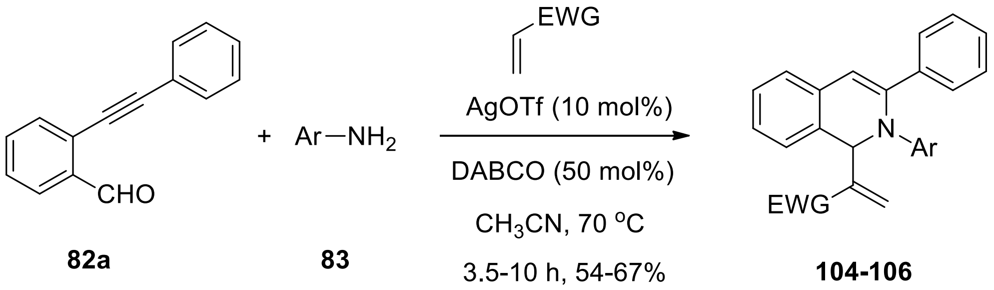
Figure 7: ORTEP of compound **106**

Table IV. Crystal data and structure refinement for compound **106**

Identification code	**106**	
Empirical formula	$C_{30} H_{23} N O_2$	
Formula weight	429.49	
Temperature	298(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P -1	
Unit cell dimensions	a = 10.7728(8) Å	α= 97.782(4)°.
	b = 10.9986(9) Å	β= 118.156(3)°.
	c = 11.2740(9) Å	γ = 95.158(4)°.
Volume	1148.66(16) $Å^3$	
Z	2	
Density (calculated)	1.242 Mg/m^3	
Absorption coefficient	0.077 mm^{-1}	
F(000)	452	
Crystal size	0.32 x 0.25 x 0.19 mm^3	
Theta range for data collection	2.52 to 27.63°.	

Index ranges	-14<=h<=14, -14<=k<=14, -14<=l<=14
Reflections collected	56454
Independent reflections	5322 [R(int) = 0.0635]
Completeness to theta = 27.63°	99.5 %
Absorption correction	None
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5322 / 0 / 301
Goodness-of-fit on F^2	0.603
Final R indices [I>2sigma(I)]	R1 = 0.0583, wR2 = 0.1624
R indices (all data)	R1 = 0.1018, wR2 = 0.2197
Largest diff. peak and hole	0.213 and -0.306 e.Å^{-3}

Table. 3. Synthesis of 1,2-dihydroisoquinoline drivatives using alkyl/aryl acrylate[a,b]



83a: Ar = C_6H_5
83d: Ar = 3-ClC_6H_4
83h: Ar = 3,4-$(MeO)_2C_6H_3$

EWG = CO_2Et, $CO_2{}^tBu$, CO_2Ph

104: Ar = C_6H_5, EWG = CO_2Et
105a: Ar = C_6H_5, EWG = $CO_2{}^tBu$
105b: Ar = 3-ClC_6H_4, EWG = $CO_2{}^tBu$
105c: Ar = 3,4-$(MeO)_2C_6H_3$, EWG = $CO_2{}^tBu$
106: Ar = C_6H_5, EWG = CO_2Ph

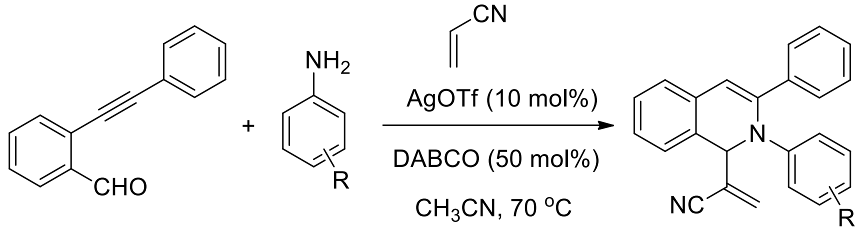
Entry	Aldehyde	Ar	EWG	Time (h)	BH-adduct	Yield[c] (%)
1	**82a**	C_6H_5 (**83a**)	CO_2Et	3.5	**104**	67
2	**82a**	C_6H_5 (**83a**)	$CO_2{}^tBu$	6	**105a**	65
3	**82a**	3-ClC_6H_4 (**83d**)	$CO_2{}^tBu$	10	**105b**	54
4	**82a**	3,4-$(MeO)_2C_6H_3$ (**83h**)	$CO_2{}^tBu$	4	**105c**	66
5	**82a**	C_6H_5 (**83a**)	CO_2Ph	4	**106**[d]	62

a) All reactions were carried out with **82a** (1.0 mmol), arylamine **83** (1.2 equiv), alkyl/aryl acrylate (3.0 equiv.), in CH_3CN (1.0 mL) following the optimized reaction conditions

b) All compounds were fully characterized.
c) The isolated yields are based on aldehyde **82a**.
d) The structure of this molecule was also confirmed by single crystal X-ray data analysis

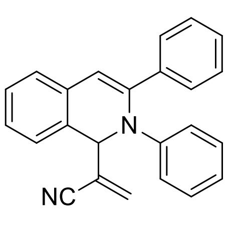
Finally we have focused our attention towards utilization of acrylonitrile as activated alkene for coupling with isoquinolinium salts generated *via* the reaction of 2-(phenylethynyl)benzaldehyde (**82a**) and anilines (aniline **83a**, 3-chloroaniline (**83d**) and 3,4-dimethoxy aniline (**83h**). All these reactions worked smoothly and gave the desired adducts 2-(2,3-diphenyl-1,2-dihydroisoquinolin-1-yl)acrylonitrile (**107a**), 2-[2-(3-chlorophenyl)-3-phenyl-1,2-dihydroisoquinolin-1-yl]acrylonitrile (**107b**), 2-(2-(3,4-dimethoxyphenyl)-3-phenyl-1,2-dihydroisoquinolin-1-yl)acrylonitrile (**107c**) in 72, 75 and 80% yields respectively (Table. 4). All the three BH adducts were fully characterized. We have also confirmed the structure by single crystal X-ray data analysis in this case of compound (**107a**) (Figure 8).

Table. 4. Synthesis of 1,2-dihydroisoquinoline drivatives using acrylonitrile[a,b,c,#]

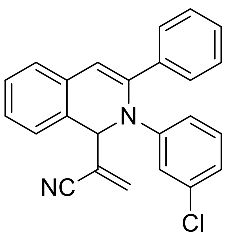


82a **83a,d,h** **107a-c**

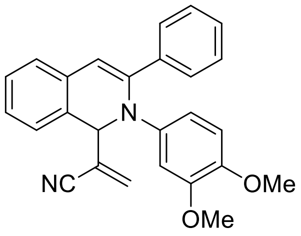
83a: R = C_6H_5; **83d**: R = 3-ClC_6H_4
83h: R = 3,4-$(MeO)_2C_6H_3$



107a, 1.5 h, 72%[d]



107b, 4 h, 75%



107c, 2 h, 80%

[#] In order to have continuity and easy understanding we have given numbering **107a-c** for BH adducts.

a) All reactions were carried out with **82a** (2.0 mmol), arylamine **83** (1.2 equiv.), acrylonitrile (3.0 equiv.), in CH_3CN (1.0 mL).

b) All compounds were fully characterized.

c) Isolated yields are based on **82a**.

d) The structure of this molecule was also confirmed by single crystal X-ray data analysis

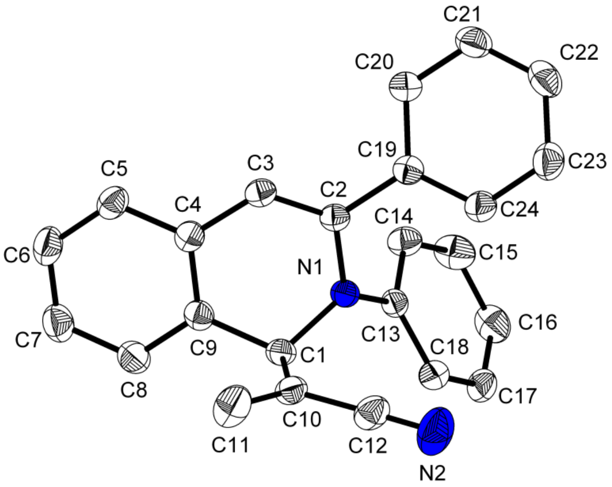


Figure 8: ORTEP of compound **107a**

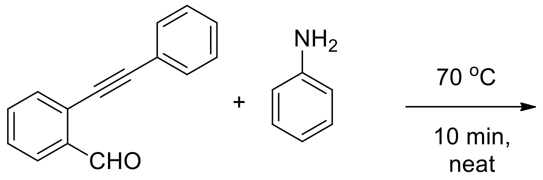
Table V. Crystal data and structure refinement for compound **107a**

Identification code	**107a**	
Empirical formula	$C_{24} H_{18} N_2$	
Formula weight	334.40	
Temperature	298(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 8.0221(11) Å	α= 90°.
	b = 10.0179(13) Å	β= 90°.
	c = 22.589(3) Å	γ = 90°.
Volume	1815.4(4) $Å^3$	
Z	4	
Density (calculated)	1.224 Mg/m^3	
Absorption coefficient	0.072 mm^{-1}	

F(000)	704
Crystal size	0.40 x 0.21 x 0.20 mm^3
Theta range for data collection	1.803 to 26.026°.
Index ranges	-9<=h<=9, -12<=k<=12, -27<=l<=24
Reflections collected	15303
Independent reflections	3568 [R(int) = 0.0271]
Completeness to theta = 25.242°	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9858 and 0.9718
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3568 / 0 / 235
Goodness-of-fit on F^2	1.103
Final R indices [I>2sigma(I)]	R1 = 0.0382, wR2 = 0.0873
R indices (all data)	R1 = 0.0410, wR2 = 0.0888
Absolute structure parameter	-0.2(10)
Extinction coefficient	n/a
Largest diff. peak and hole	0.147 and -0.243 e.$Å^{-3}$

From this study it is clear that *in situ* generated isoquinolinium-species are emerging as novel electrophiles in BH reaction and we even predict these electrophiles will play a dominating role in future BH reactions. A plausible mechanistic[17,20] pathway (Path A and Path B) (based on that of Ye and Wu)[100] for the formation of dihydroisoquinoline framework in the DABCO/ AgOTf promoted Baylis–Hillman coupling between 2-alkynylaryl aldehydes, aryl amines and alkyl acrylates (or acrylonitrile) is presented in Scheme 41.

HRMS studies for monitoring the reaction have been elegantly employed to understand the mechanism of the BH reaction.[105-110] Coelho and coworkers systematically studied the reaction between methyl acrylate and representative aldehydes (or tosylimines) under the influence of DABCO as catalyst using HRMS.[105-109] Their studies clearly demonstrate the formation of methyl acrylate-DABCO adduct and methyl acrylate-DABCO-aldehyde (or tosylamine) adduct, thus provides a clear insight into the reaction mechanism.[105-109] To have a quick look at the mechanism of our reaction we felt that it is appropriate to monitor the reaction by HRMS and look for the activated alkene-catalyst-electrophile adduct ion peak.[@] (We did not mention here about DABCO-methyl acrylate adduct ion peak becauae it was already elegantly demonstrated by Coelho). Accordingly we have treated aldehyde (**82a**) (Ar^1 = phenyl) with aniline (**83a**) at 70 °C under neat conditions for ≈ 10 minutes. ESI-MS (HRMS) of this crude showed major ion peak at m/z 282.1286 (M+H) indicating the formation of imine **IA** (Ar = Ar^1 = phenyl). Then acetonitrile (as solvent) AgOTf, methyl acrylate, and DABCO, were added to this mixture at 70 °C and HRMS was recorded after 30 minutes showed major ion peak at m/z 480.2726 (ESI-MS) indicating the presence of [**IIIA**-OH^-] [methyl acrylate-DABCO-isoquinolinium-addduct, Ar = Ar^1 = phenyl)], at m/z 282.1308 (ESI-MS) [imine **IA**+H] or [isoquinolinium ion **IIA**-OH^-, Ar = Ar^1 = pheny], at m/z 366.1504 [**103a** (BH adduct)-H] and at m/z 199.1499 (DABCO-methyl acrylate adduct + H). After 2 h HRMS showed major ion peak at m/z 480.2667 (**IIIA**-OH^-); at m/z 282.1256 (low intensity, **IA**+H or **IIA**-OH^-) and at m/z 366.1451 [**103a** (BH adduct)-H] (very low intensity).[@] The major ion peak at m/z 480.2667 demonstrates the presence of methyl acrylate-DABCO-isoquinolinium-addduct Ar = Ar^1 = phenyl) (**IIIA**- OH^-) (See HRMS spectrum). We have also monitored the reaction between **82a** and 1-naphthylamine (**83i**) by HRMS[@] (for details see Scheme 41-Mechanism). In this case also, the major peak at m/z 530.2825 (ESI-MS) (See HRMS spectrum) indicates the formation of methyl acrylate-DABCO-isoquinolinium-addduct [**IIIB**-OH^-**]** Ar^1 = phenyl, Ar = naphthyl.[@] Although this HRMS study is not adequate enough to draw a concrete conclusion on mechanism, this present study certainly provides some additional insight towards understanding the mechanism.



82a **83a**

UOH -SCHOOL OF CHEMISTRY -HRMS

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Sample Name	PT-ANILI-1 10 MIN	Instrument	maXis 10138
Comment			

Acquisition Parameter

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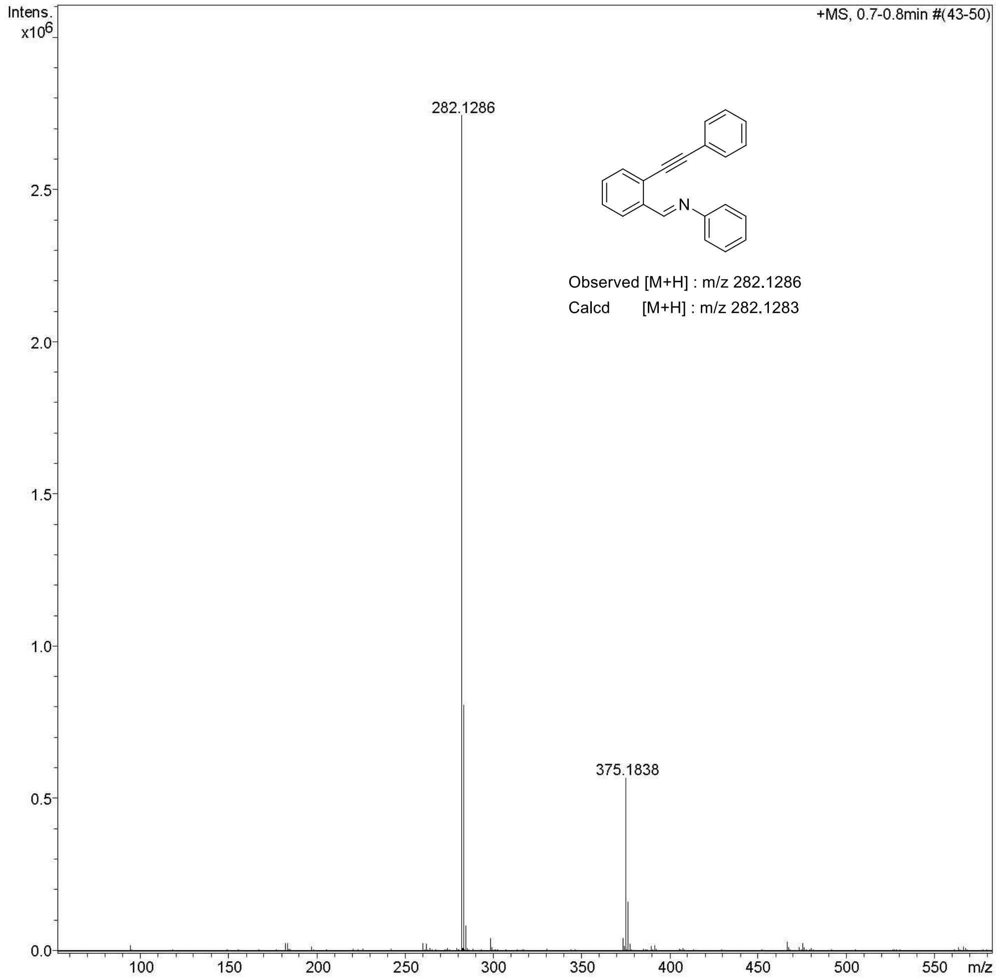

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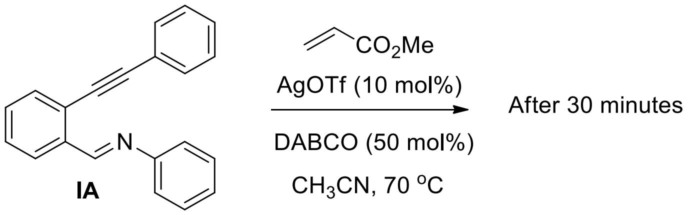
Calcd [M+H] : m/z 282.1283

Bruker Compass DataAnalysis 4.0 printed: 5/8/2017 5:33:32 PM Page 1 of 1



UOH -SCHOOL OF CHEMISTRY -HRMS

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Sample Name	PT-ANILI-3 30 MIN	Instrument	maXis 10138
Comment			

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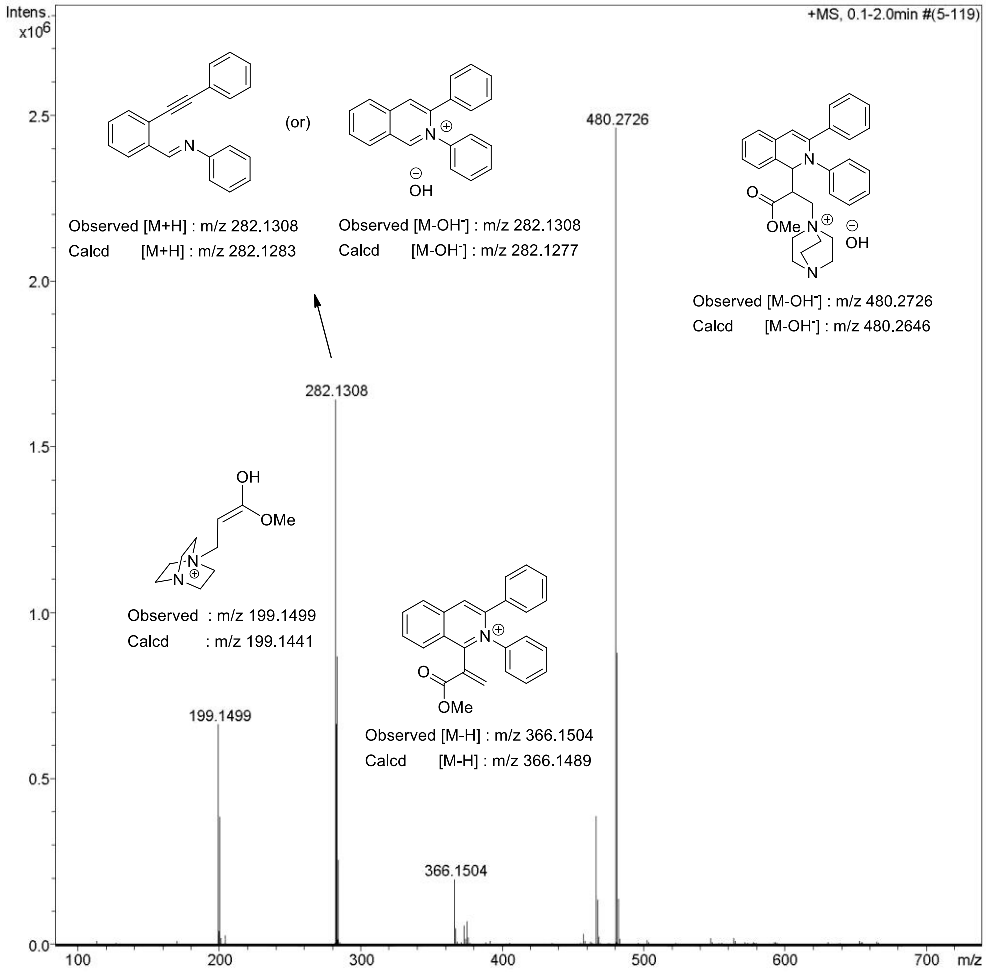

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Calcd [M+H] : m/z 282.1283

Observed [M-OH⁻] : m/z 282.1308
Calcd [M-OH⁻] : m/z 282.1277

Observed [M-OH⁻] : m/z 480.2726
Calcd [M-OH⁻] : m/z 480.2646

Observed : m/z 199.1499
Calcd : m/z 199.1441

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Calcd [M-H] : m/z 366.1489

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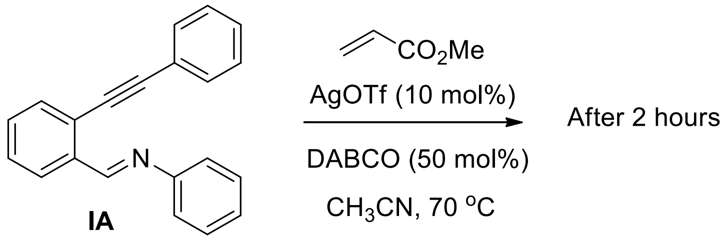
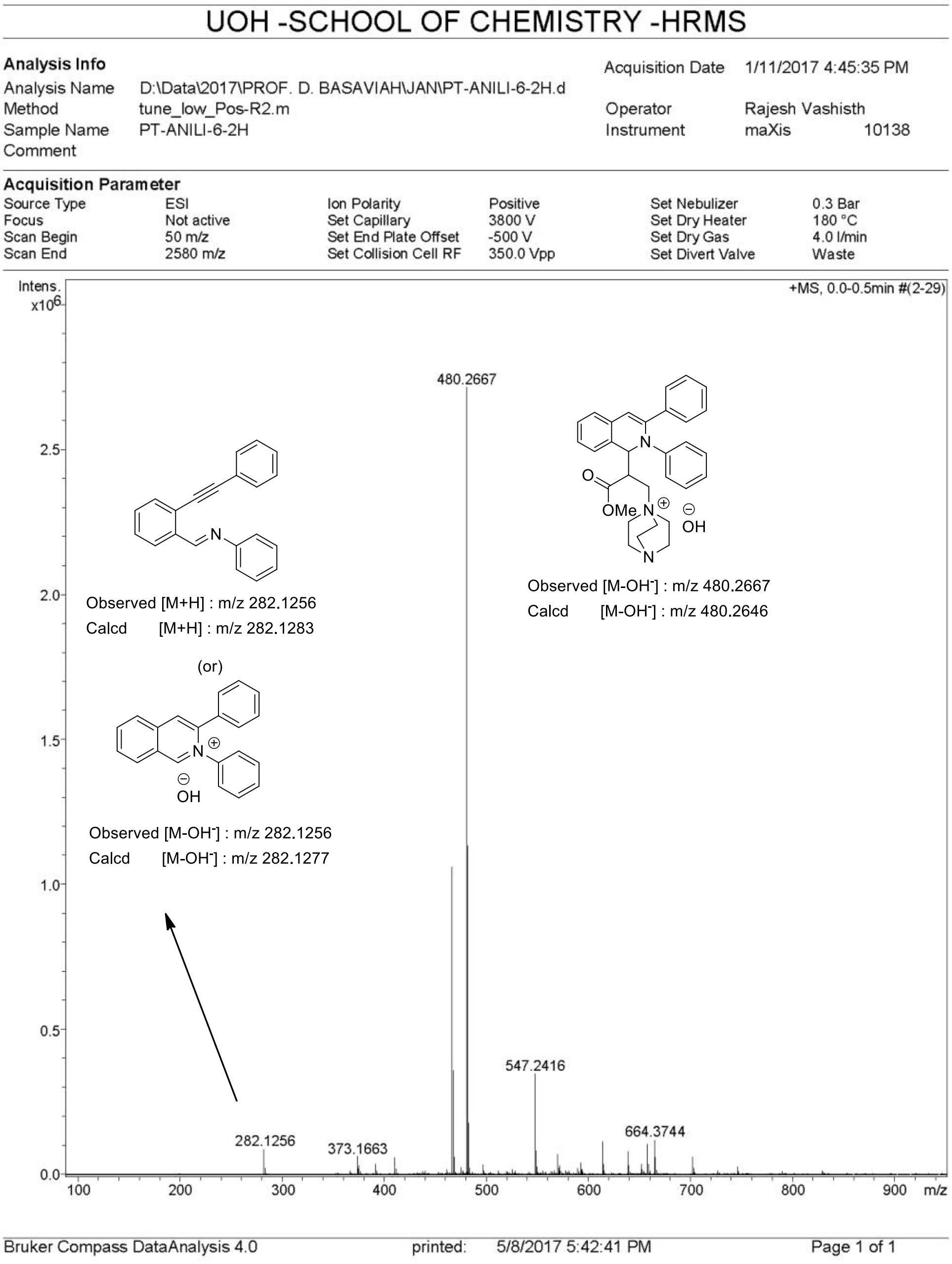


IA



UOH -SCHOOL OF CHEMISTRY -HRMS

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Sample Name PT-ANILI-6-2H
Comment

Acquisition Date 1/11/2017 4:45:35 PM
Operator Rajesh Vashisth
Instrument maXis 10138

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Observed [M+H] : m/z 282.1256
Calcd [M+H] : m/z 282.1283

(or)

Observed [M-OH$^-$] : m/z 282.1256
Calcd [M-OH$^-$] : m/z 282.1277

Observed [M-OH$^-$] : m/z 480.2667
Calcd [M-OH$^-$] : m/z 480.2646

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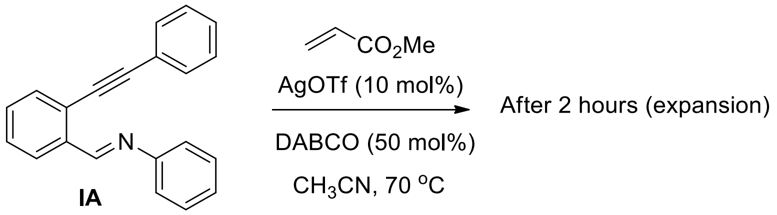

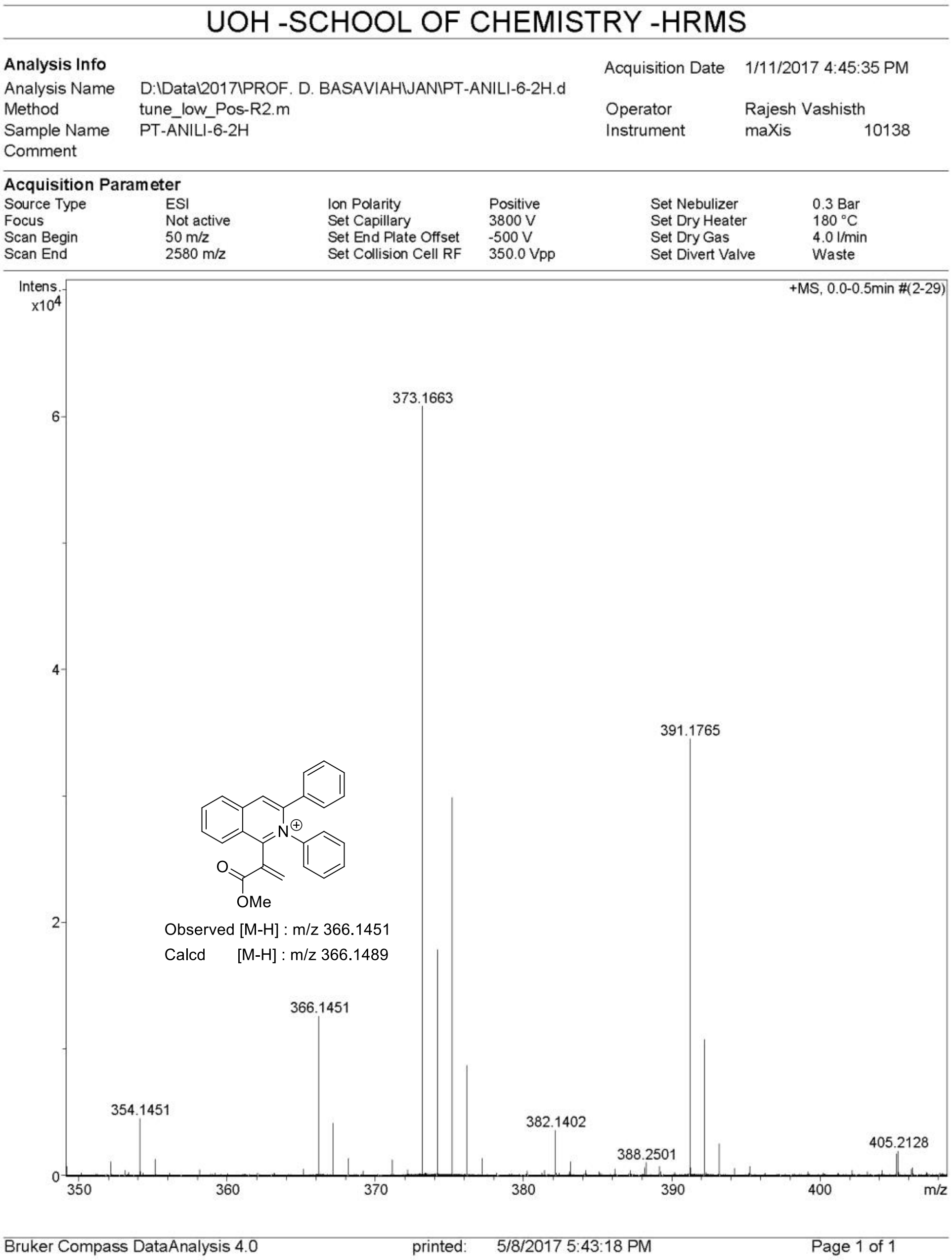

UOH -SCHOOL OF CHEMISTRY -HRMS

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Sample Name	PT-ANILI-6-2H	Instrument	maXis 10138
Comment			

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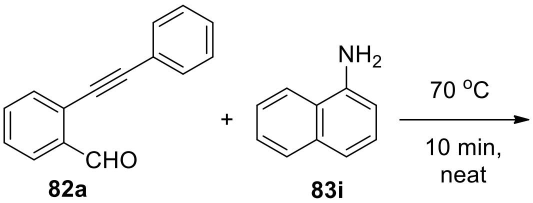
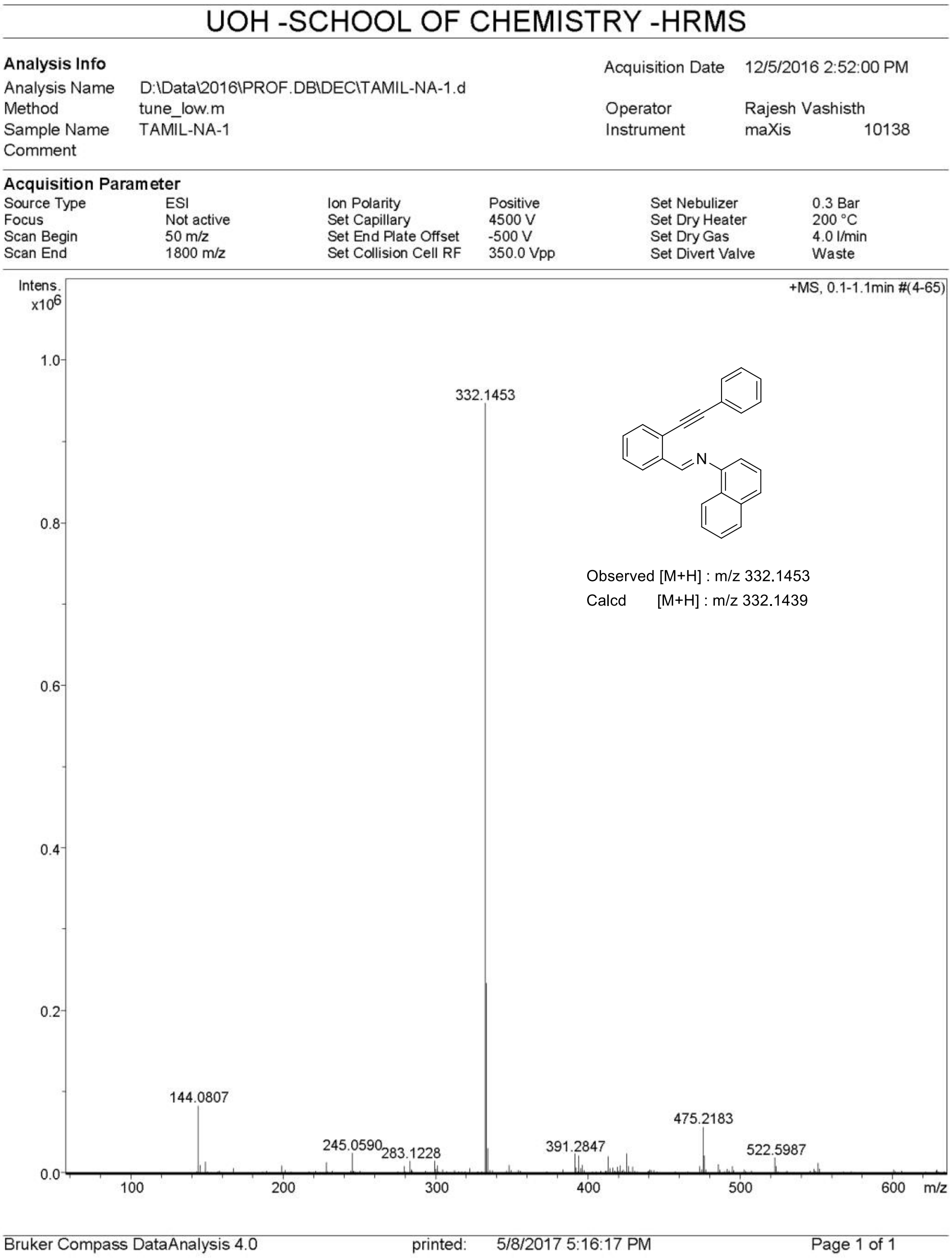
Bruker Compass DataAnalysis 4.0 printed: 5/8/2017 5:43:18 PM Page 1 of 1



82a **83i**



UOH -SCHOOL OF CHEMISTRY -HRMS

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Sample Name TAMIL-NA-1
Comment

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Operator Rajesh Vashisth
Instrument maXis 10138

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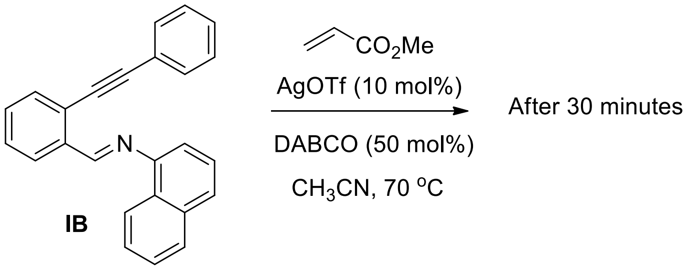

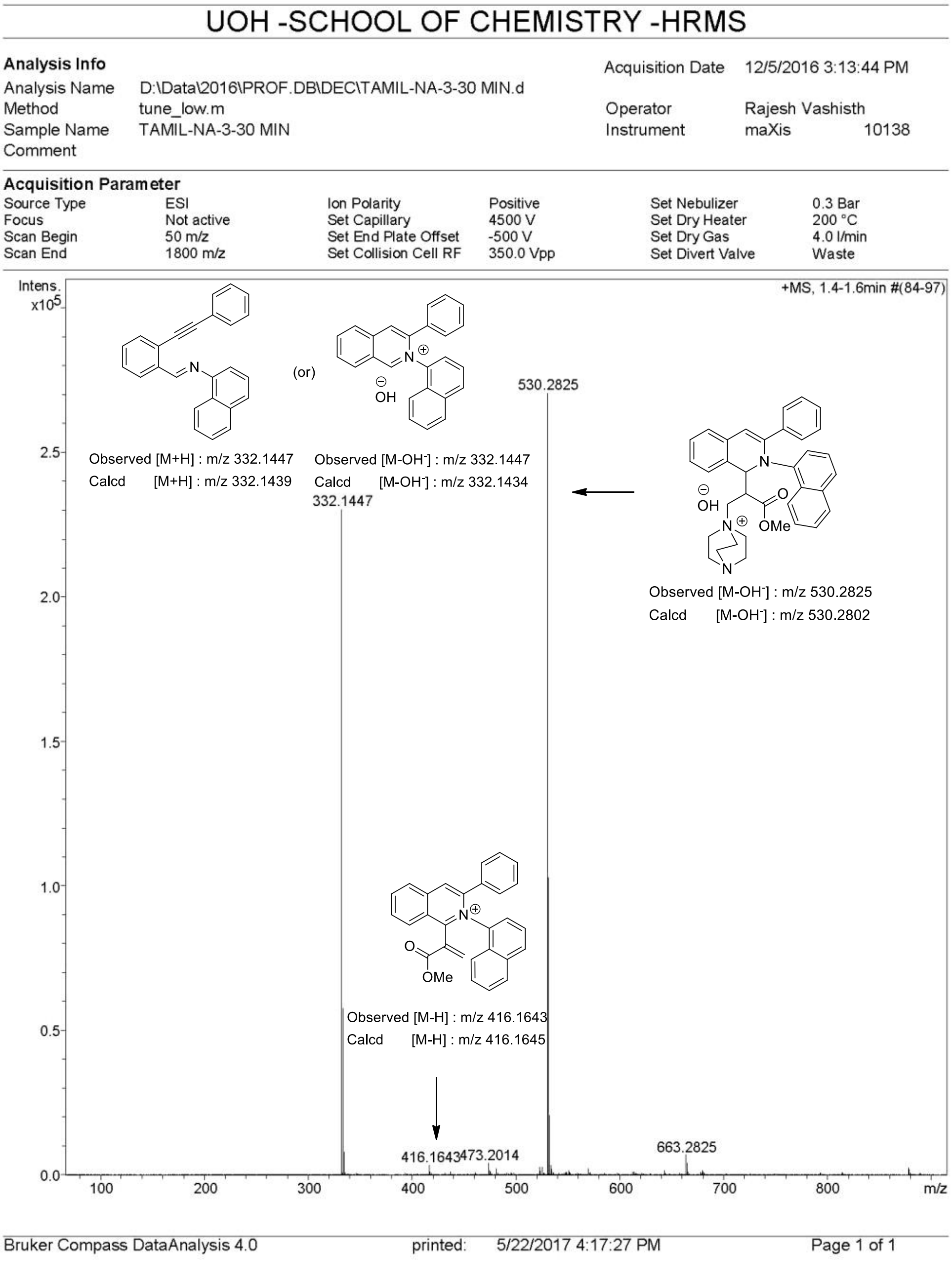

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Sample Name	TAMIL-NA-3-30 MIN	Instrument	maXis 10138
Comment			

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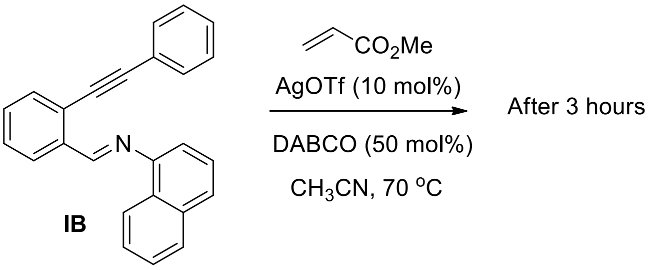
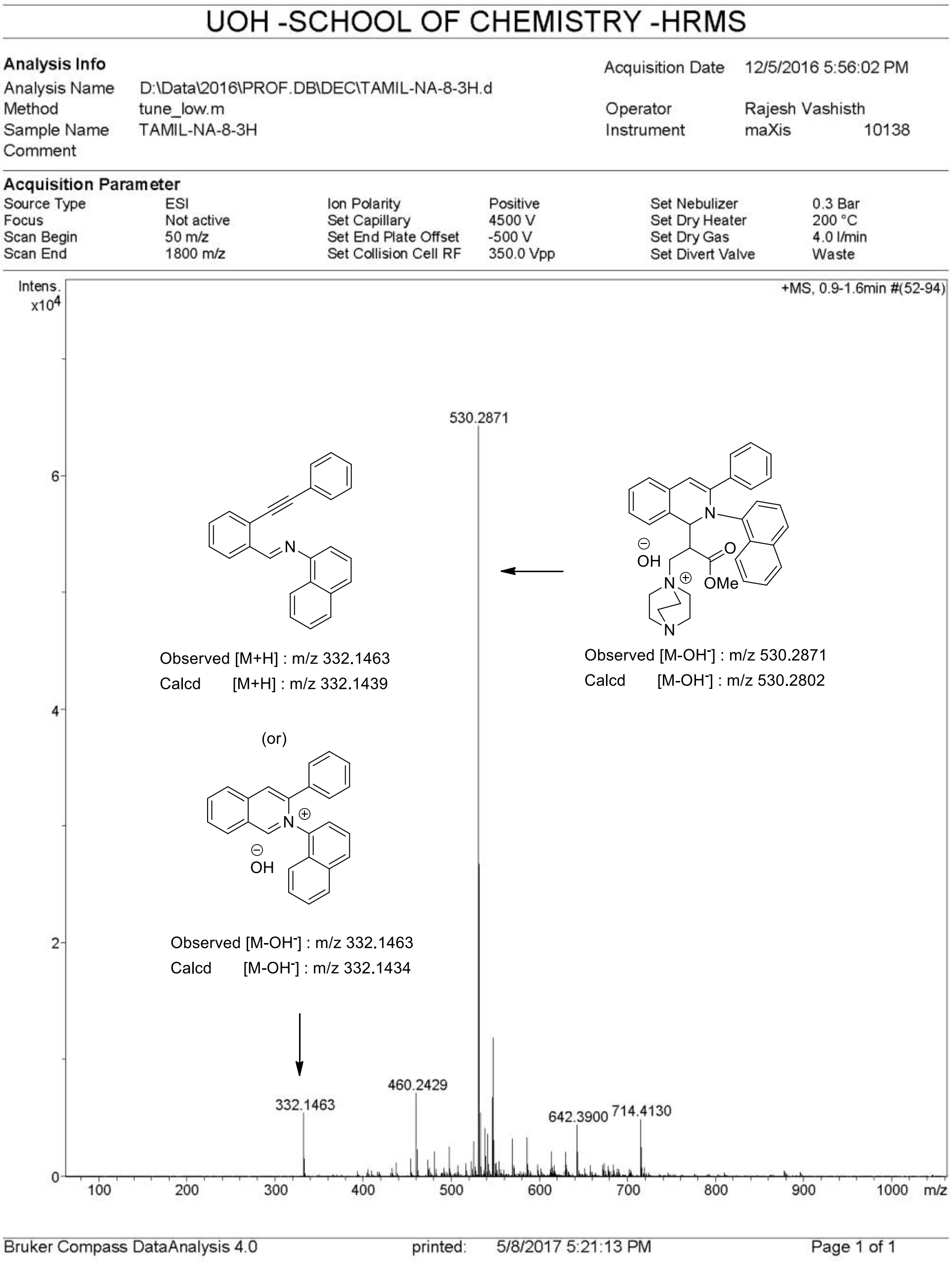
Focus	Not active	Set Capillary	4500 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	1800 m/z	Set Collision Cell RF	350.0 Vpp	Set Divert Valve	Waste

Bruker Compass DataAnalysis 4.0 printed: 5/22/2017 4:17:27 PM Page 1 of 1



IB



UOH -SCHOOL OF CHEMISTRY -HRMS

Analysis Info

Analysis Name D:\Data\2016\PROF.DB\DEC\TAMIL-NA-8-3H.d
Method tune_low.m
Sample Name TAMIL-NA-8-3H
Comment
Acquisition Date 12/5/2016 5:56:02 PM
Operator Rajesh Vashisth
Instrument maXis 10138

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Not active	Set Capillary	4500 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	1800 m/z	Set Collision Cell RF	350.0 Vpp	Set Divert Valve	Waste

Observed [M+H] : m/z 332.1463
Calcd [M+H] : m/z 332.1439

(or)

Observed [M-OH$^-$] : m/z 332.1463
Calcd [M-OH$^-$] : m/z 332.1434

Observed [M-OH$^-$] : m/z 530.2871
Calcd [M-OH$^-$] : m/z 530.2802

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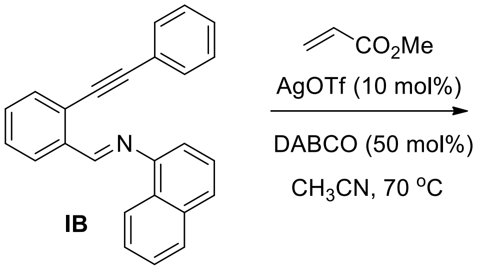
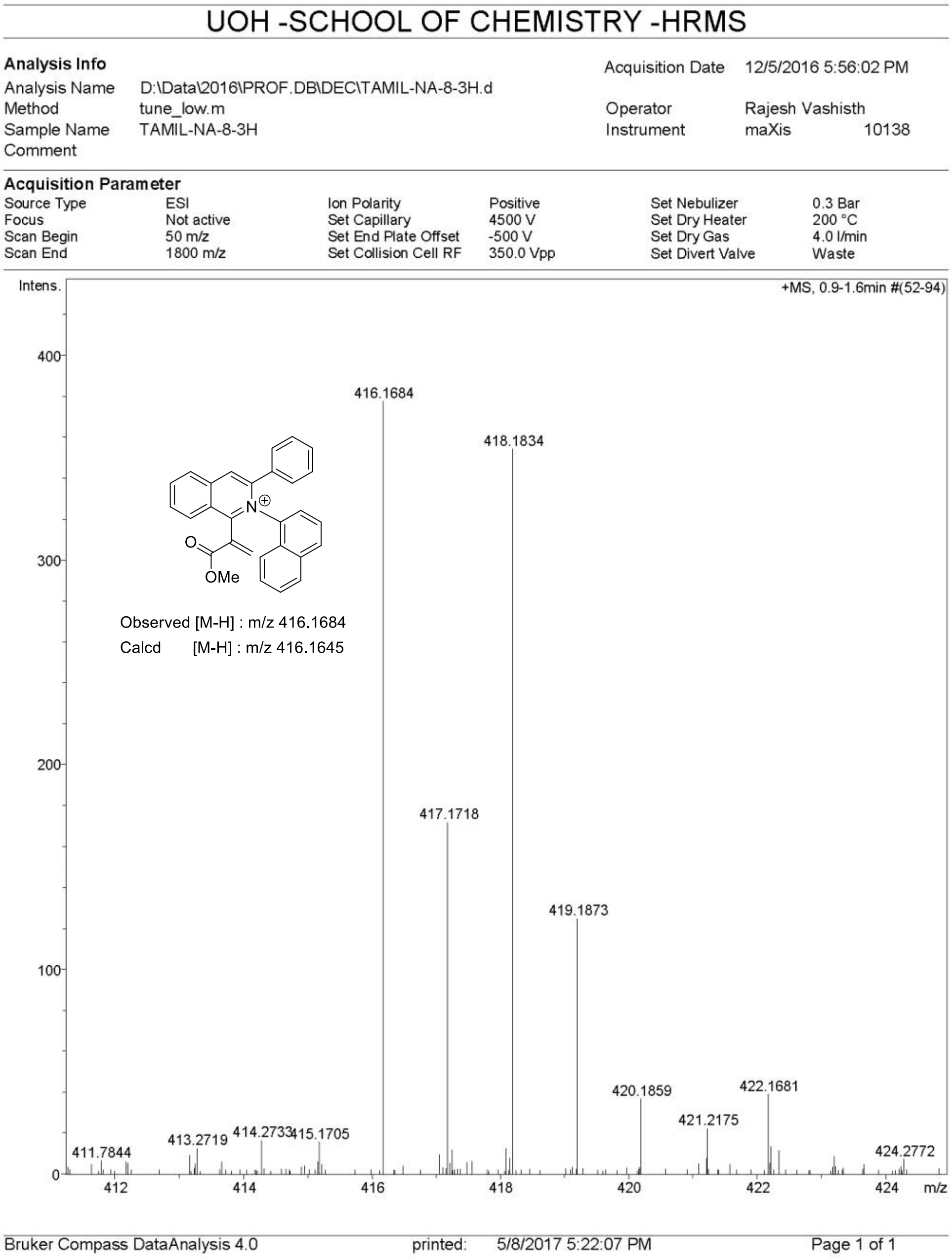


IB

After 3 hours (expansion)



UOH -SCHOOL OF CHEMISTRY -HRMS

Analysis Info
Analysis Name D:\Data\2016\PROF.DB\DEC\TAMIL-NA-8-3H.d
Method tune_low.m
Sample Name TAMIL-NA-8-3H
Comment
Acquisition Date 12/5/2016 5:56:02 PM
Operator Rajesh Vashisth
Instrument maXis 10138

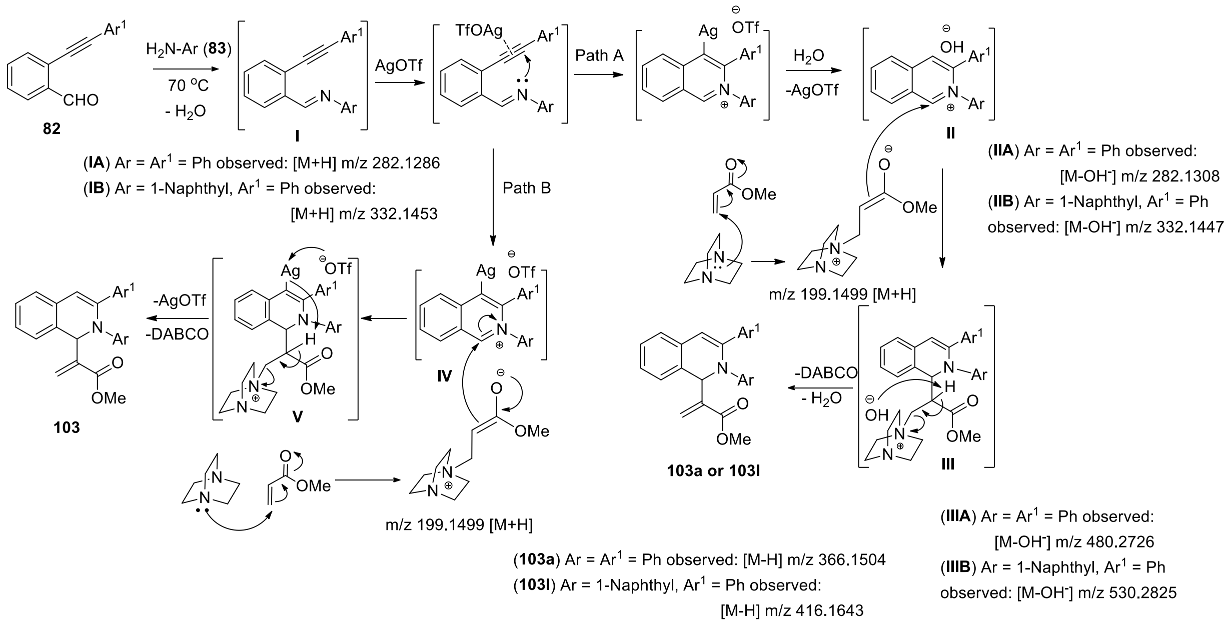
Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Not active	Set Capillary	4500 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	1800 m/z	Set Collision Cell RF	350.0 Vpp	Set Divert Valve	Waste

Observed [M-H] : m/z 416.1684
Calcd [M-H] : m/z 416.1645

Bruker Compass DataAnalysis 4.0 printed: 5/8/2017 5:22:07 PM Page 1 of 1

Scheme 41. Plausible mechanism



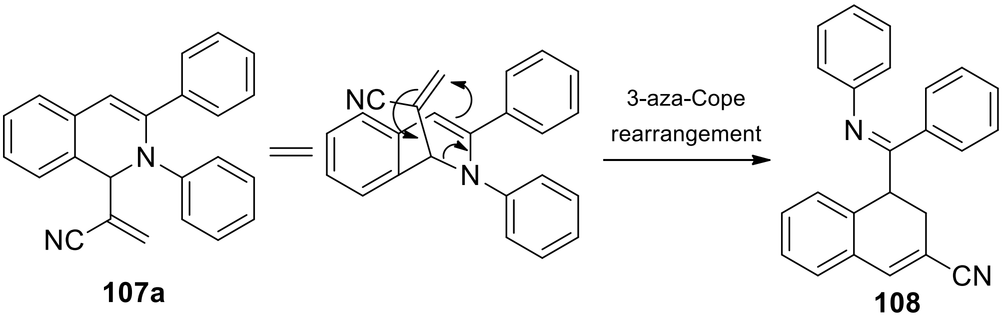
HRMS (ESI-MS) ion peaks belong to reactions (in both cases) monitored after 30 minutes

Conclusion

Isoquinolinium silver triflate salts, generated *in situ*, (from 2-alkynylbenzaldehydes, aryl amines and AgOTf) have been successfully employed as excellent electrophiles for Baylis–Hillman coupling with activated alkenes such as alkyl acrylates, phenyl acrylate, acrylonitrile, under the influence of DABCO to provide 1,2,3-trisubstituted dihydroisoquinoline derivatives in high yields. Thus our study not only demonstrates the potential of *in situ* generated isoquinolinium-species as excellent electrophiles in BH reactions, but also provides a simple and convenient protocol for obtaining 1,2,3-trisubstituted dihydro-isoquinoline derivatives with different substitution pattern.

Application of Baylis–Hillman adducts obtained from isoquinolinium salts

From the previous section it is quite clear that *in situ* generated isoquinolinium salts act as excellent electrophiles for Baylis–Hillman coupling with alkyl acrylates and acrylonitrile to produce an interesting class of 1,2-dihydroisoquinoline compounds of synthetic importance. Since these BH adducts have allyl-enamine framework it occurred to us that these compounds could serve as interesting substrates for 3-aza-Cope rearrangement and such rearrangement would expected to provide 2,4-disubstituted-3,4-dihydronaphthalene derivatives (**108**) shown in Eq. 21.

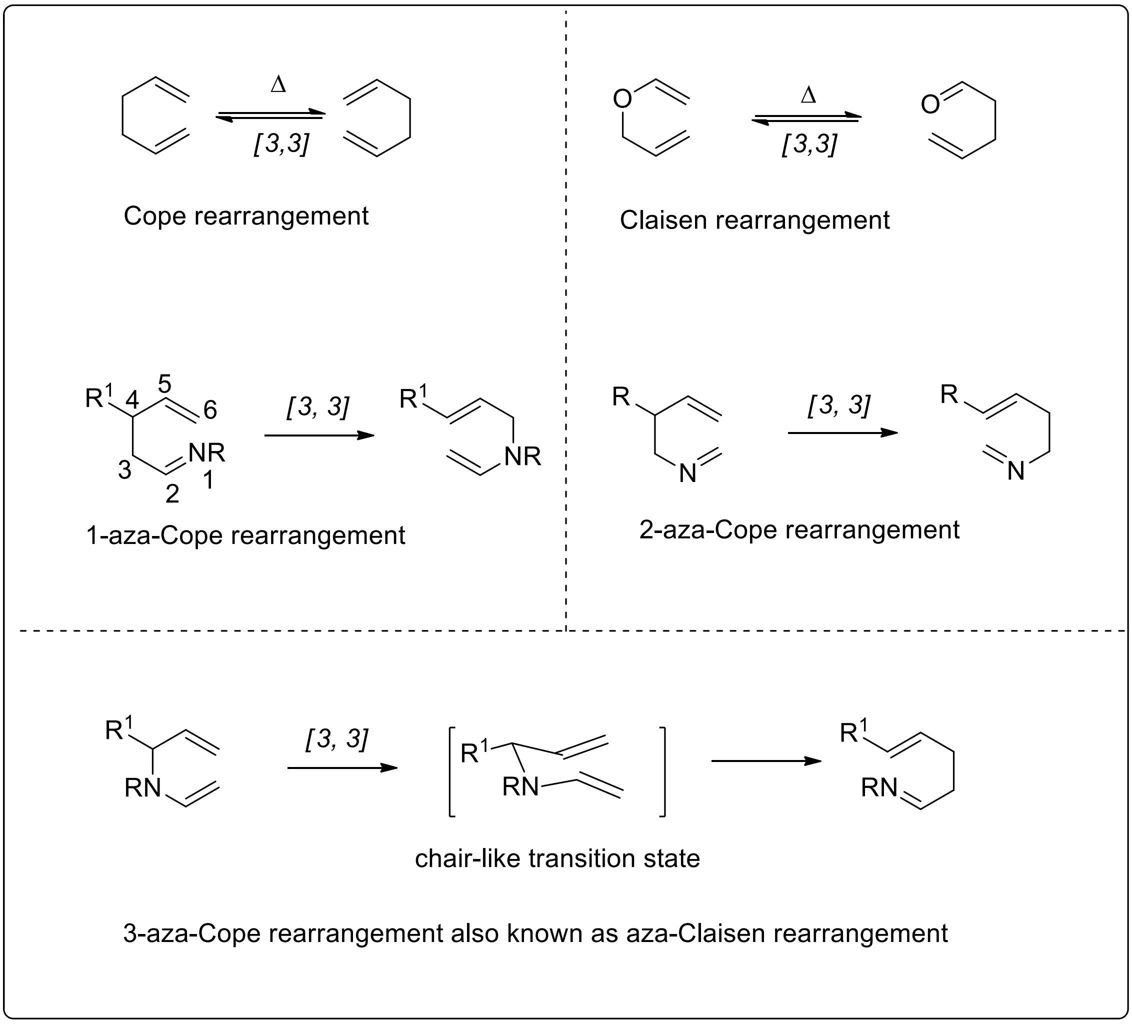


Eq. 21

Cope rearrangement

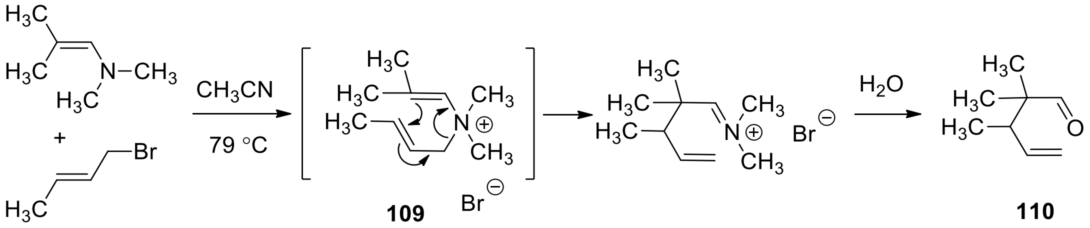
Since this section deals with 3-aza-Cope rearrangement of BH adducts (such as **107a**) it would be appropriate to present here succinct introduction about Cope and aza-Cope rearrangements and its applications in organic synthesis.[3, 4, 111-113] The Cope rearrangement is one of the highly important and widely used transformations in organic chemistry which involves thermal reorganization of a 1,5-diene leading to a regioisomeric 1,5-diene *via* [3,3]-sigmatropic rearrangement. Replacing one of the carbons of the 1,5-diene by nitrogen, would result in aza version of Cope rearrangement which, in fact, would provide three possible ways of aza-Cope rearrngements. Based on the position of nitrogen atom present in the 1,5-diene, these rearrangements are generally classified as 1-aza-Cope rearrangement, 2-aza-Cope rearrangement and 3-aza-Cope rearrangement as described in Scheme 13.[3,4] The 3-aza-Cope rearrangement is also known as the aza-Claisen rearrangement (Scheme 42). Since our work deals with 3-aza-Cope rearrangement of BH adducts, some important and relevant literature reports regarding this kind of rearrangements are presented in this section.

Scheme 42



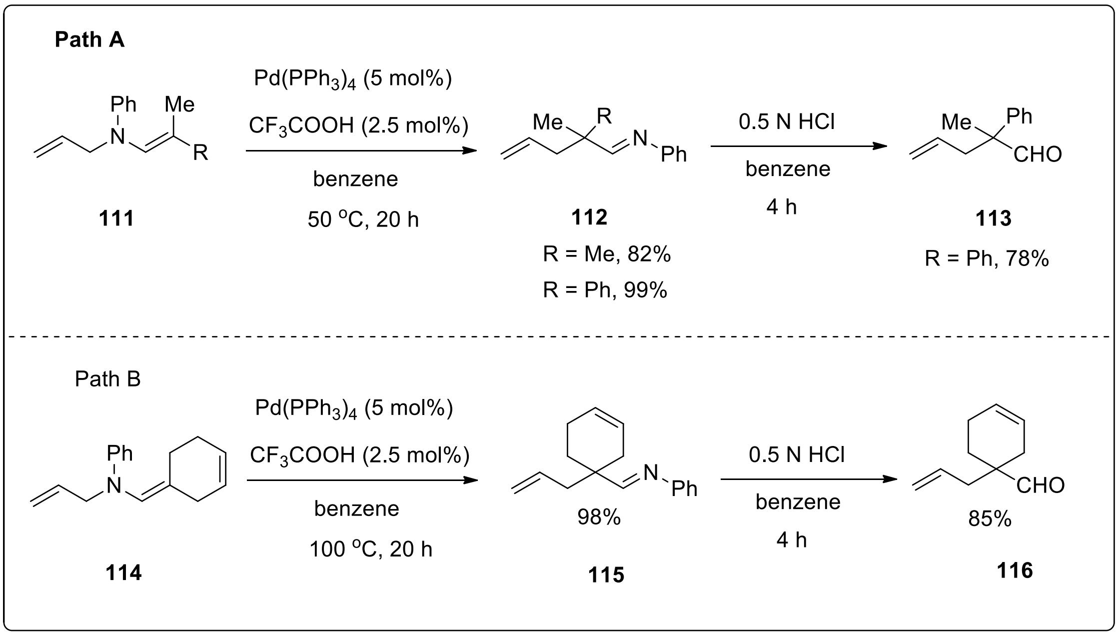
Burpitt *et al*. reported an interesting aza-Claisen rearrangement of allyl vinyl-amine-quaternary salt (**109**), otained by treatment of crotyl bromide with N,N-dimethylisobutenylamines, to provide substituted pentenal (**110**) after hydrolysis as described in Scheme 43.[114]

Scheme 43



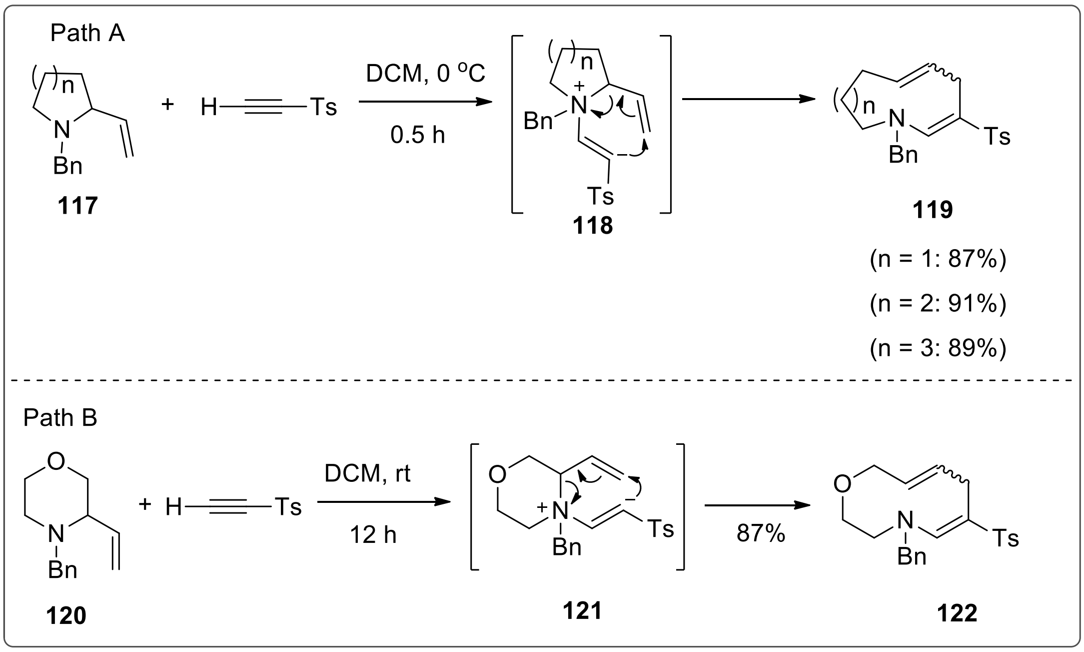
A facile Pd(0) catalysed 3-aza-Cope rearrangement of N-allylenamines (**111**, **114**) in the presence of trifluoroacetic acid was reported by Murahashi et al. The resulting imines (**112**, **115**) were obtained in high yields; subsequent hydrolysis gave the desired aldehyde (**113**, **116**) according to Paths A and B respectively in Scheme 44.[115]

Scheme 44



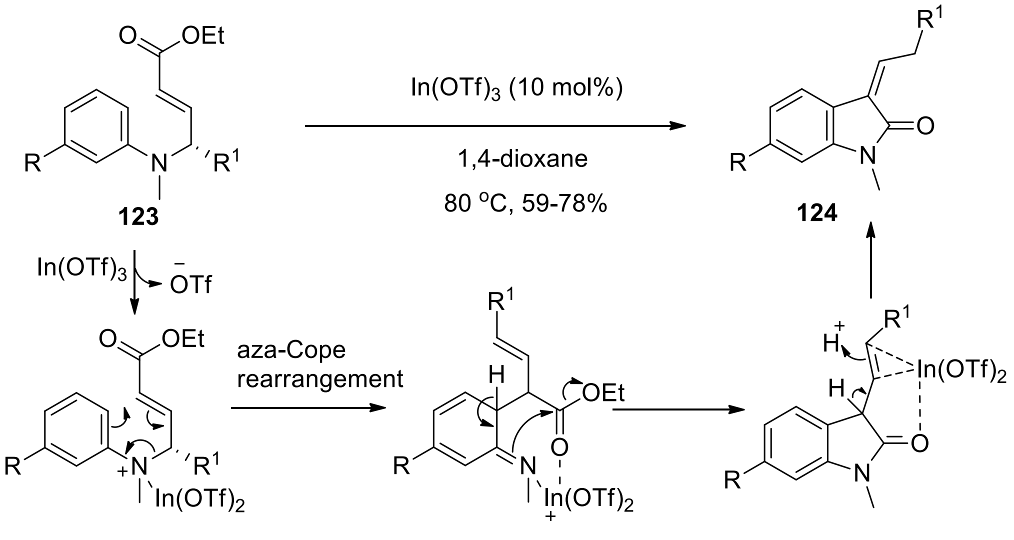
Back et al. described the metal free synthesis of medium and larger cyclic amine derivatives *via* 3-aza-Cope rearrangement following the reaction sequence shown in Scheme 45. Allyl – enamines (**118**, **121**) generated *in situ* from 2-vinyl nitrogen heterocyclic compounds (**117**, **120**) on reaction with tosylacetylene gave medium/large nitrogen heterocyclic compounds (**119**, **122**) respectively as described in Paths A and B in Scheme 45.[116]

Scheme 45



Panda *et al.* reported an elegant application of 3-aza-Cope rearrangement for synthesis of Z-alkylideneoxindole derivatives (**124**) from N-allylanilines (**123**) using In(OTf)$_3$ as a catalyst (Scheme 46). This reaction proceeds first through 3-aza-Cope rearrangement followed by cyclization as presented in Scheme 46.[117] (Selected examples are presented).

Scheme 46

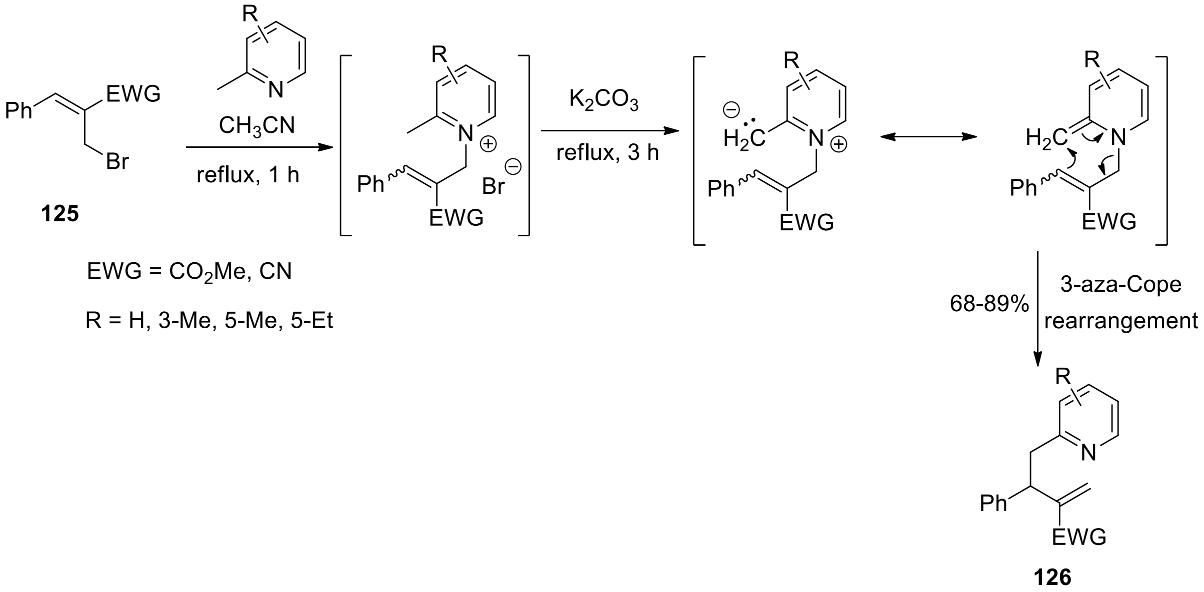


R = H, OMe

R^1 = ^{i}Pr, Bn, ^{i}butyl, but-2-yl, 4-OMeC$_6$H$_4$CH$_2$

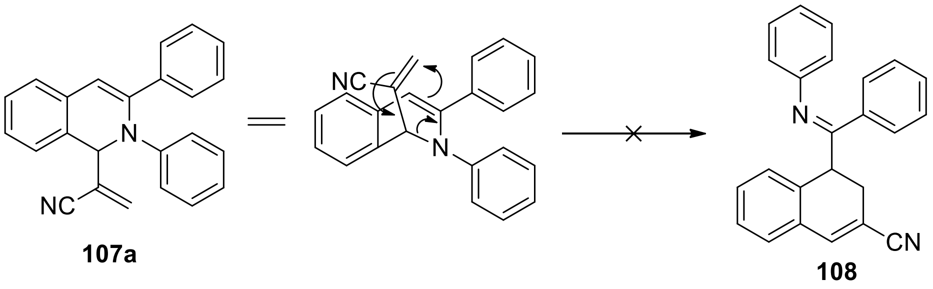
Kim and co-workers[118] have developed a simple strategy for alkylation of 2-methylpyridines (**126**) (at methyl group) *via* the reaction with Baylis–Hillman bromide (**125**). The key step in this transformation is 3-aza-Cope rearrangement as described in the Scheme 47.

Scheme 47



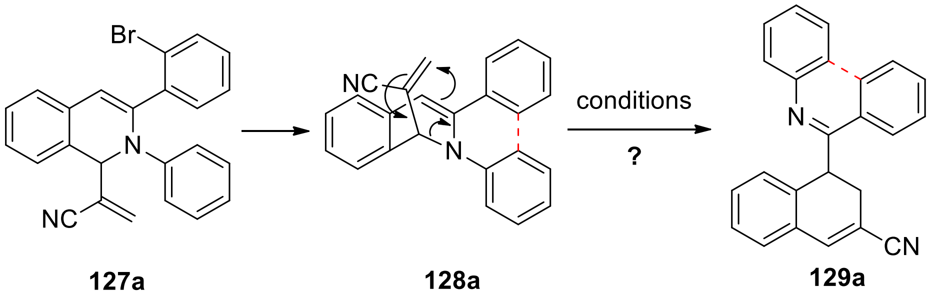
Fascinated by many important applications of 3-aza-Cope rearrangement known in the literature, we have directed our efforts towards 3-aza-Cope rearrangement of Baylis–Hillman adduct (**107a**) as these adducts contain ally-enamine framework. Accordingly we have subjected 2-(2,3-diphenyl-1,2-dihydroisoquinolin-1-yl)acrylonitrile (**107a**) [for preparation see page 27 Table 4] for Cope rearrangement in the presence of $Pd(OAc)_2$ (10 mol%) / PPh_3 (30 mol%) K_3PO_4. Unfortunately our attempts did not result in the formation of (**108**) even at 130 ^{o}C (*m*-xylene) for 18 h and noticed that the starting material remained intact (Scheme 48).

Scheme 48

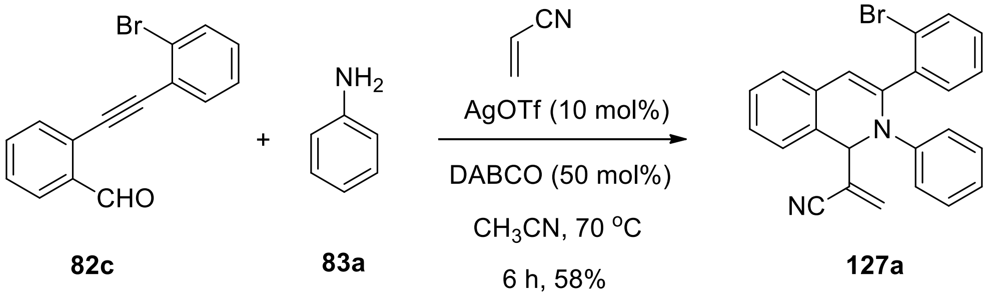


Failure of this experiment gave us an indication that the BH adduct (**107a**) is not the appropriate substrate for 3-aza-Cope rearrangement. If we tie the two aromatic rings as described in the red color as in Scheme 49, the resulting *in situ* generated phenanthridine substrate(s) (**128a**) might undergo 3-aza-Cope rearrangement to provide the desired dihydronaphthalene derivative (**129a**) containing phenanthridine framework. This means that we need to generate the phenanthridine ring (**128a**) *in situ* from the BH adduct (derived from appropriate isoquinolinium salts), by a coupling strategy. We felt that *in situ* phenanthridine substrates (**128a**) can be generated from BH adducts 2-[3-(2-bromophenyl)-2-phenyl-1,2-dihydroisoquinolin-1-yl]acrylonitrile (**127a**).

Scheme 49



Accordingly we have selected the BH adduct (**127a**) for obtaining *in situ* generated phenanthridine derivative (**129a**) for 3-aza-Cope rearrangement. We predicted that *ortho*-bromo substituent on 2-arylethynyl group would couple with *ortho* position of phenyl ring attached to nitrogen through an appropriate coupling reaction. Thus we have prepared the required 2-[3-(2-bromophenyl)-2-phenyl-1,2-dihydroisoquinolin-1-yl]acrylonitrile (**127a**) *via* the reaction between 2-(2-bromophenylethynyl)benzaldehyde (**82c**), aniline (**83a**) and acrylonitrile following the optimized conditions (see Table 1) in 58% yield (Eq. 22). Structure of this molecule was fully characterized by the spectral data analysis. We have also further confirmed structure by single crystal analysis (ORTEP diagram Figure 9).



Eq. 22

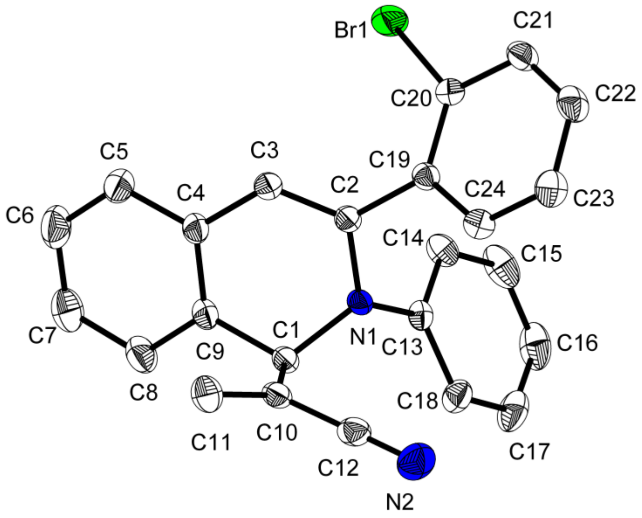


Figure 9: ORTEP of compound **127a**

Table VI. Crystal data and structure refinement for compound **127a**

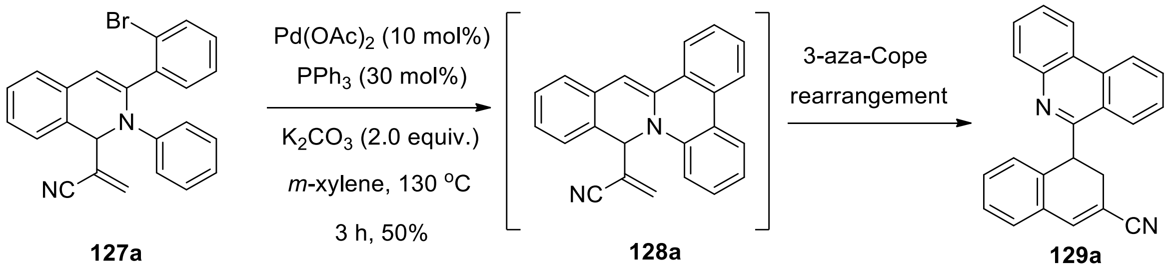
Identification code	**127a**
Empirical formula	$C_{24} H_{17} Br N_2$
Formula weight	413.31
Temperature	300(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	C 2/c

Unit cell dimensions	a = 31.963(3) Å	α= 90°.
	b = 8.8147(8) Å	β= 113.448(3)°.
	c = 14.9945(13) Å	γ = 90°.
Volume	3875.8(6) Å^3	
Z	8	
Density (calculated)	1.417 Mg/m^3	
Absorption coefficient	2.131 mm^{-1}	
F(000)	1680	
Crystal size	0.39 x 0.28 x 0.17 mm^3	
Theta range for data collection	2.68 to 27.54°.	
Index ranges	-41<=h<=41, -11<=k<=11, -18<=l<=19	
Reflections collected	48008	
Independent reflections	4439 [R(int) = 0.0392]	
Completeness to theta = 27.54°	99.2 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.696 and 0.494	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4439 / 0 / 247	
Goodness-of-fit on F^2	0.822	
Final R indices [I>2sigma(I)]	R1 = 0.0426, wR2 = 0.1669	
R indices (all data)	R1 = 0.0544, wR2 = 0.1901	
Largest diff. peak and hole	1.170 and -0.972 e.Å^{-3}	

Next our attention was focused towards generating *in situ* phenanthridine ring (**128a**) from (**127a**) and subsequent 3-aza-Cope rearrangement so as to obtain the 4-(phenanthridin-6-yl)-3,4-dihydronaphthalene-2-carbonitrile (**129a**) containing dihydronaphthalene and phenanthridine frameworks. In this direction we have treated (**127a**) (0.4 mmol) with Pd(OAc)$_2$ (10 mol%)/PPh$_3$ (30 mol%) in *m*-xylene in the presence of K$_2$CO$_3$. We were pleased to note that the expected compound (**129a**) was obtained in 50% isolated yield in 3 h Scheme 50. Structure of this compound was thoroughly established by IR, ^{1}H NMR, ^{13}C

NMR, and HRMS spectral data analysis. We have also further confirmed this structure by single crystal X-ray data analysis (Figure 10).

Scheme 50



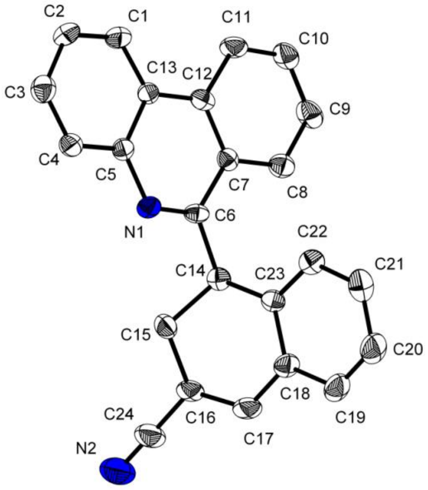


Figure 10: ORTEP of compound **129a**

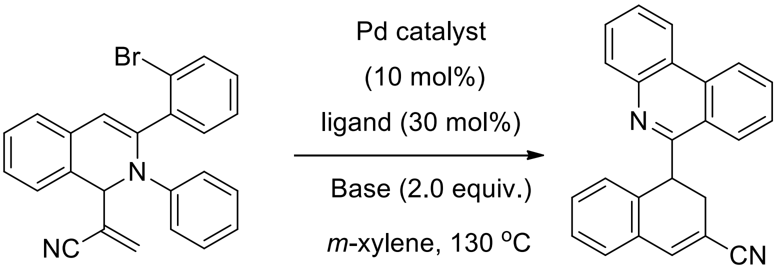
Table VII. Crystal data and structure refinement for compound **129a**

Identification code	**129a**	
Empirical formula	$C_{24} H_{16} N_2$	
Formula weight	332.39	
Temperature	300(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P -1	
Unit cell dimensions	a = 4.6658(15) Å	α= 72.31(2)°.
	b = 15.400(6) Å	β= 84.87(3)°.
	c = 25.126(11) Å	γ = 81.374(17)°.

Volume	1698.8(11) Å^3
Z	4
Density (calculated)	1.300 Mg/m^3
Absorption coefficient	0.077 mm^{-1}
F(000)	696
Crystal size	0.35 x 0.28 x 0.20 mm^3
Theta range for data collection	2.50 to 27.63°.
Index ranges	-6<=h<=5, -20<=k<=20, -32<=l<=32
Reflections collected	59833
Independent reflections	7717 [R(int) = 0.10]
Completeness to theta = 27.63°	98.2 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.985 and 0.974
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	7717 / 0 / 475
Goodness-of-fit on F^2	0.911
Final R indices [I>2sigma(I)]	R1 = 0.1392, wR2 = 0.3084
R indices (all data)	R1 = 0.3343, wR2 = 0.21
Largest diff. peak and hole	0.302 and -0.390 e.Å^{-3}

This result is very encouraging even though the final yield is only 50%. This reaction clearly indicates that coupling reaction, generating *in situ* the required phenanthridine ring, and 3-aza-Cope rearrangement occur simultaneously. With a view to improve the yield we have carried out the reaction under various conditions as described in Table 5. From this Table it is clear that the best yield (67%) of the required compound was obtained in *m*-xylene using $Pd(OAc)_2$ (10 mol%) / PPh_3 (30 mol%) K_3PO_4 (2.0 equiv.) at 130 °C for 3.5 h (entry 7 Table 5).

Table. 5. Optimization of the reaction conditions[a]



127a **129a**

Entry	cat (10 mol%)	ligand (30 mol%)	Base	Temp (°C)	Time (h)	Yield **129a**[b](%)
1	Pd(OAc)$_2$	PPh$_3$	K_2CO_3	130	3	50
2	Pd(OAc)$_2$	PPh$_3$	Cs_2CO_3	130	6	57
3	Pd(OAc)$_2$	PPh$_3$	Na_2CO_3	130	3.5	45
4	Pd(OAc)$_2$	P(*o*-tol)$_3$	K_3PO_4	130	6	54
5	Pd(TFA)$_2$	PPh$_3$	K_3PO_4	130	3.5	25
6	Pd(OAc)$_2$	PPh$_3$	K_3PO_4	120	6	40
7	**Pd(OAc)$_2$**	**PPh$_3$**	**K_3PO_4**	**130**	**3.5**	**67**
8[c]	Pd(OAc)$_2$	PPh$_3$	K_3PO_4	130	7	38
9	Pd(OAc)$_2$	PPh$_3$	-	130	12	trace
10	-	-	K_3PO_4	130	12	nd
11[d]	Pd(OAc)$_2$	PPh$_3$	K_3PO_4	130	3.5	53
12	Pd(PPh$_3$)$_2$	-	K_3PO_4	130	5	complex mixture

a) All the reactions were carried out in 0.4 mmol scale of **127a** using Pd (10 mol%), ligand (30 mol%), base (2.0 equiv.) in *m*-xylene (6.0 mL) at 130 °C

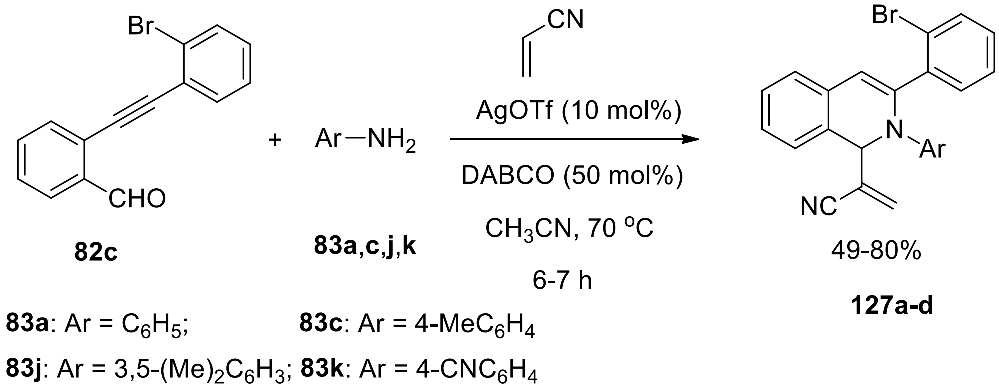
b) Isolated yields based on **127a**.

c) 1.2 equiv. of base was used in this case

d) 4.0 mL solvent was used

Encouraged by this result we have prepared representaive appropriate BH adducts from 2-(2-bromophenylethynyl)benzaldehyde (**82c**) and different aniline (**83**) derivatives as shown in Table 6. Structures of all these adducts (**127b-127d**) were thoroughly established by all spectral data (IR, ^{1}H NMR, ^{13}C NMR and HRMS).

Table. 6. Synthesis of *o*-bromo substituted 1,2-dihydroisoquinoline drivatives using acrylonitrile[a, b, #]



Entry	aldehyde	Ar	Time (h)	BH-adduct[b]	Yield[c] (%)
1	**82c**	C_6H_5 (**83a**)	6	**127a**[d]	58
2	**82c**	4-MeC_6H_4 (**83c**)	6	**127b**	80
3	**82c**	3,5-$(Me)_2C_6H_3$ (**83j**)	6	**127c**	66
4	**82c**	4-CNC_6H_4 (**83k**)	7	**127d**	49

a) All reactions were carried out with (**82c**) (2.0 mmol), arylamine (**83**)(1.2 equiv.), acrylonitrile (3.0 equiv.), in CH_3CN (2.0 mL) following a similar procedure described for **103**

b) All compounds were fully characterized.

c) Isolated yields are based on (**82c**)

d) The structure of this molecule was also confirmed by single crystal X-ray data analysis

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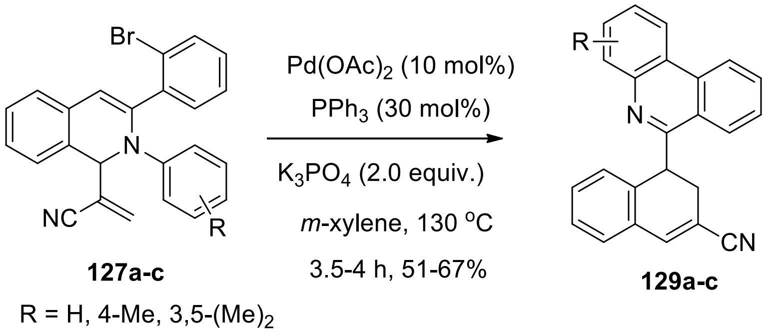
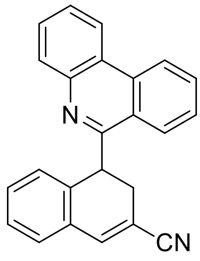
[#] In order to have continuity and easy understanding we have given numbering **127a-d** for *o*-bromo substituted 1,2-dihydroisoquinoline drivatives.

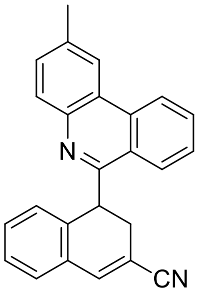
Subsequently these adducts were subjected to simultaneous coupling and 3-aza-Cope rearrangement reactions. Resulting products (**129a-c**) were obtained in 51-67% isolated yields. All these products were fully characterized. Unfortunately the compound (**127d**) prepared from 4-cyanoaniline (**83k**) did not provide the required phenanthradine derivative (**129d**). Reason for this failure is not clear to us. It looks that presence of electron withdrawing group in *para* position to amino group in the anilines might not favour this coupling reaction. It needs more study to understand and draw any conclusion on failure of the 3-aza-Cope rearrangement on this substrate.

Table. 7. Synthesis of Phenanthradine drivatives using acrylonitrile containing BH adducts[a,b,c]

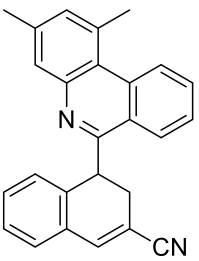




129a, 3.5 h, 67%[d]



129b, 4 h, 57%

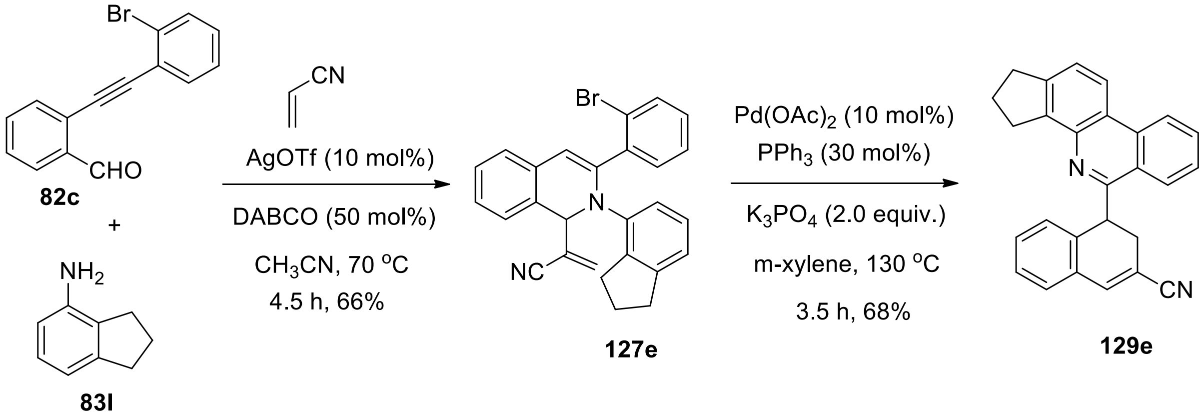


129c, 4 h, 51%

a) All the reactions were carried out in 0.4 mmol scale of (**127**) using $Pd(OAc)_2$ (10 mol%), PPh_3 (30 mol%), K_3PO_4 (2.0 equiv.) in *m*-xylene (6.0 mL) at 130 °C
b) All compounds were fully characterized.
c) Isolated yields based on BH adducts (**127**).
d) The structure of this molecule was also confirmed by single crystal X-ray data analysis.

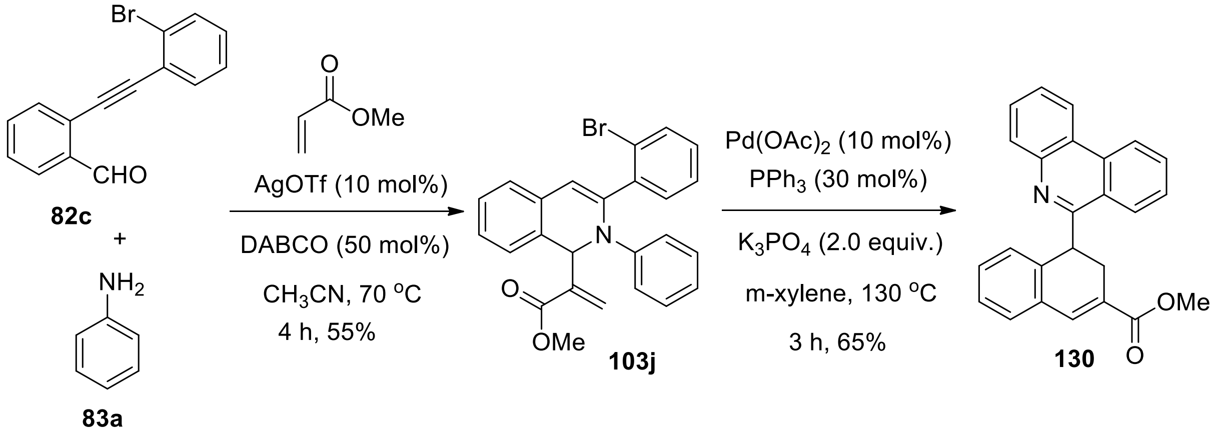
With a view to understand the structural effect on the formation of BH adduct as well as in subsequent step to obtain dihydronaphthalene-phenanthridine compound (**129e**), we have used 4-aminoindan (**83l**) for reaction with 2-(2-bromophenylethynyl)benzaldehyde (**82c**). It is gratifying to note that the required BH adduct (**127e**) was obtained in 66% yield Scheme 51. Subsequent treatment with $Pd(OAc)_2/PPh_3$ as per optimized contions provided the desired phenanthridine compound having 3,4-dihydronaphthalene moiety (Scheme 51). These two compounds were thoroughly characterized.

Scheme 51



Thus we have demonstrated the potential of BH adducts, derived from *in situ* generated iosoquinolinium salts and acrylonitrile, as useful substrates for 3-aza-Cope rearramngement to provide phenanthridine dcerivatives having dihydronaphthalene moiety. Next we focussed our attention towards utilizing of BH adducts prepared from *in situ* generated iosoquinolinium salts and methyl acrylate. We have therefore first selected the BH adduct (**103j**) Eq. 13 for this study. Treatment of (**103j**) with $Pd(OAc)_2$ /PPh_3 under the optimized conditions gave the expected phenanthridine derivative (**130**) (Scheme 52) as confirmed by the spectral data analysis and also single crystal X-ray data analysis (Figure 11).

Scheme 52



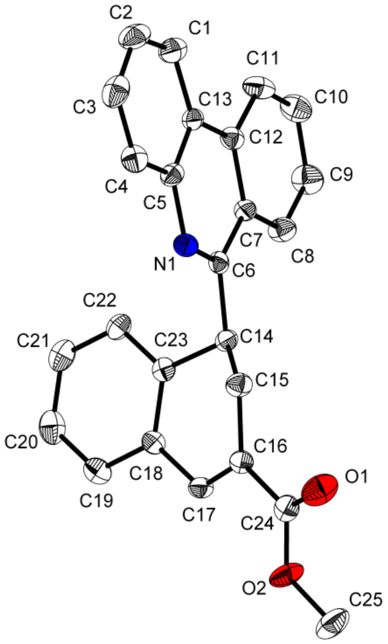


Figure 11: ORTEP of compound **130**

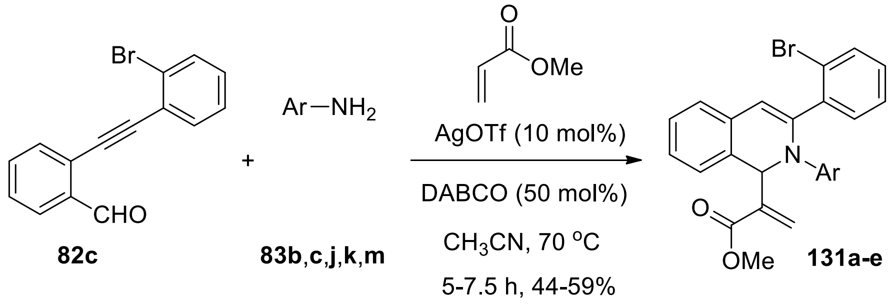
Table VIII. Crystal data and structure refinement for compound **130**

Identification code	**130**	
Empirical formula	$C_{25} H_{19} N O_2$	
Formula weight	365.41	
Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 5.0921(5) Å	α= 90°.
	b = 16.4447(17) Å	β= 90°.
	c = 22.142(2) Å	γ = 90°.
Volume	1854.1(3) $Å^3$	
Z	4	
Density (calculated)	1.309 Mg/m^3	
Absorption coefficient	0.083 mm^{-1}	
F(000)	768	
Crystal size	0.18 x 0.15 x 0.13 mm^3	
Theta range for data collection	2.48 to 28.29°.	
Index ranges	-5<=h<=6, -20<=k<=21, -29<=l<=28	
Reflections collected	17358	
Independent reflections	4561 [R(int) = 0.10]	
Completeness to theta = 28.29°	99.6 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9893 and 0.9852	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4561 / 0 / 258	
Goodness-of-fit on F^2	1.007	
Final R indices [I>2sigma(I)]	R1 = 0.0826, wR2 = 0.1213	
R indices (all data)	R1 = 0.2306, wR2 = 0.1536	
Absolute structure parameter	2(3)	
Extinction coefficient	0.0120(17)	

Largest diff. peak and hole	0.193 and -0.176 e.Å^{-3}

We have next prepared representative BH adducts from 2-(2-bromophenylethynyl)benzaldehyde (**82c**) and selected arylamine derivatives (**83**) and methyl acrylate to provide the resulting adducts (**131a-e**) in good yields (Table 8). These adducts were subjected to the treatment with Pd(OAc)$_2$, PPh$_3$ following the procedure described for (**103j**). We were pleased to see the required products (**132a-e**) were obtained in average to good yields. We have analyzed these compounds thoroughly by the spectral data analysis Table 9.

Table. 8. Synthesis of *o*-bromo substituted 1,2-dihydroisoquinoline drivatives using methylacrylate[a, b]



83b: Ar = 4-MeOC$_6$H$_4$; **83c**: Ar = 4-MeC$_6$H$_4$
83j: Ar = 3,5-(Me)$_2$C$_6$H$_3$; **83k**: Ar = 4-CNC$_6$H$_4$
83m: Ar = 4-ClC$_6$H$_4$

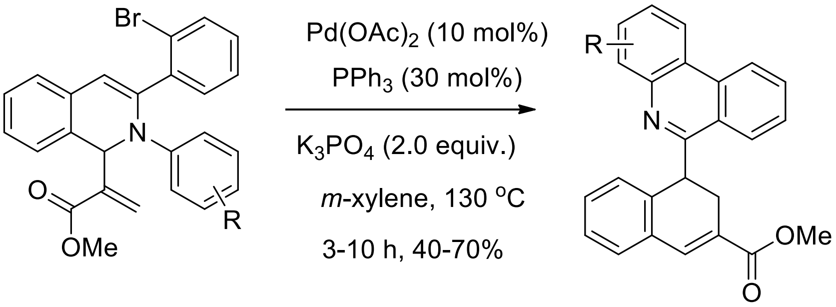
Entry	aldehyde	Ar	Time (h)	BH-adduct	Yield[c] (%)
1	**82c**	4-MeOC$_6$H$_4$ (**83b**)	5	**131a**	55
2	**82c**	4-MeC$_6$H$_4$ (**83c**)	6	**131b**	59
3	**82c**	3,5-(Me)$_2$C$_6$H$_3$ (**83j**)	6	**131c**	55
4	**82c**	4-CNC$_6$H$_4$ (**83k**)	7.5	**131d**	47
5	**82c**	4-ClC$_6$H$_4$ (**83m**)	7	**131e**	44

a) In all reactions a mixture of aldehyde (**82c**) (2.0 mmol) and aryl amine (**83**) (1.2 equiv.) was heated for 5-10 minutes at 70 °C and then treated with methyl acrylate (3.0 equiv.) in the presence of DABCO (50 mol%), AgOTf (10 mol%) in acetonitrile (2.0 mL) at 70 °C.

b) All compounds were fully characterized.

c) The isolated yields are based on aldehydes (**82c**).

Table. 9. Synthesis of Phenanthradine drivatives using methyl acrylate containg BH adducts[a,b]



131a-e **132a-e**

R = 4-MeO, 4-Me, 3,5-(Me)$_2$, 4-CN, 4-Cl

Entry	BH-adduct	R	Time (h)	Product	Yield[c] (%)
1	**131a**	4-MeO	3.5	**132a**	70
2	**131b**	4-Me	3	**132b**	62
3	**131c**	3,5-(Me)$_2$	4	**132c**	53
4	**131d**	4-CN	10	**132d**	40
5	**131e**	4-Cl	3.5	**132e**	48

a) All the reactions were carried out in 0.4 mmol scale of (**131**) using Pd(OAc)$_2$ (10 mol%), PPh$_3$ (30 mol%), K$_3$PO$_4$ (2.0 equiv.) in *m*-xylene (6.0 mL) at 130 °C

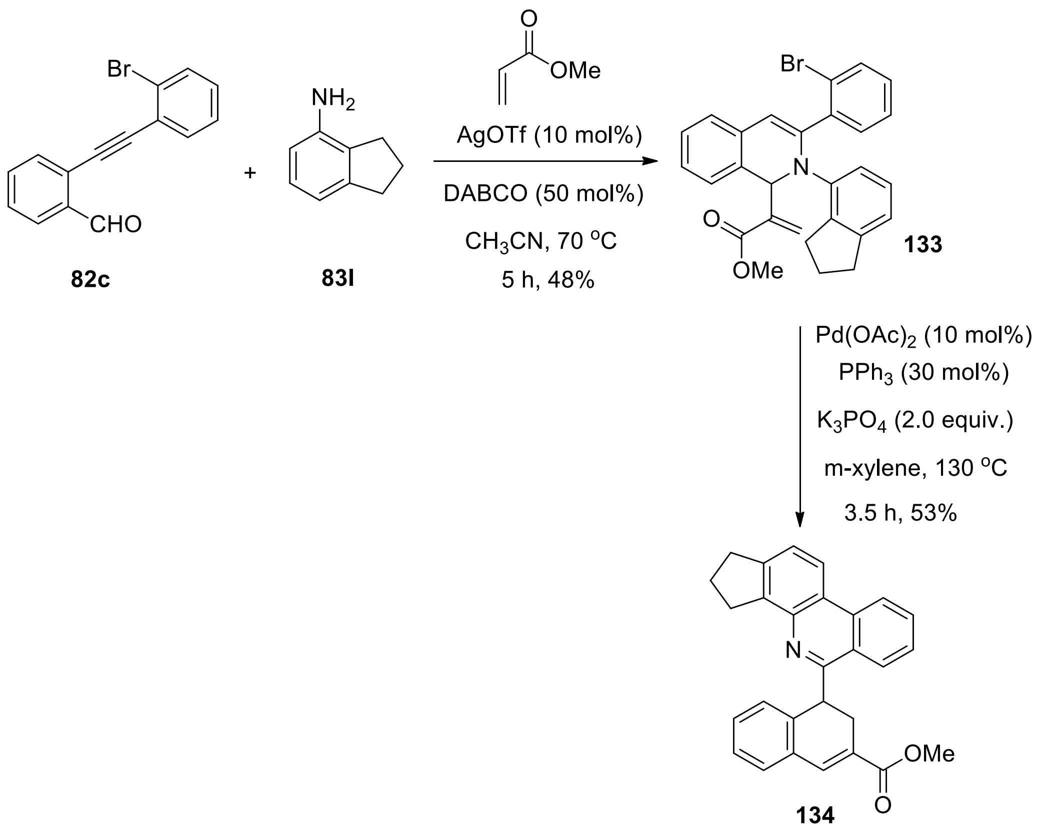
b) All compounds were fully characterized.

c) Isolated yields based on **131**).

Next with a view to understand the influence of bicyclic aromatic amine on the formation of BH adduct and subsequent 3-aza-Cope rearrangement we have employed 4-aminoindan (**83l**) for reaction 2-(2-bromophenylethynyl)benzaldehyde (**82c**) and methyl acrylate. It is gratifying to see the formation of resulting BH adduct methyl 2-(3-(2-bromophenyl)-2-(2,3-

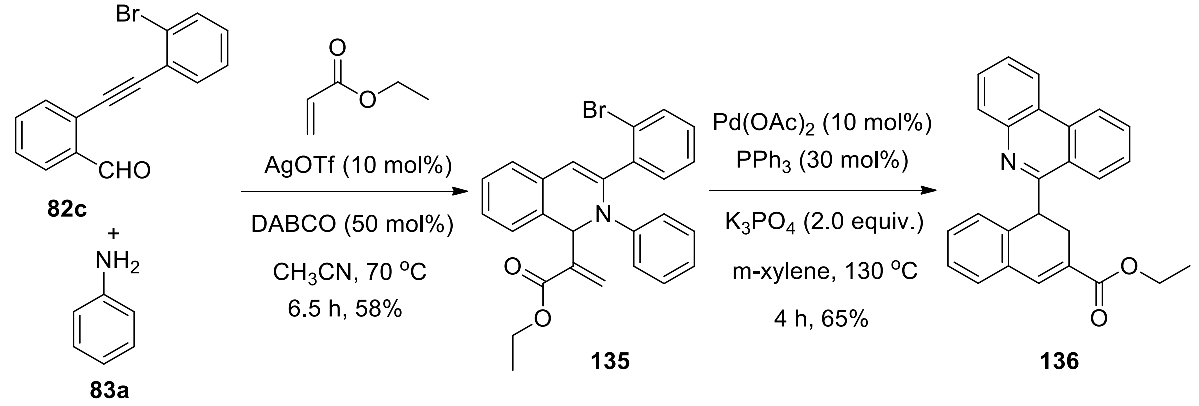
dihydro-1*H*-inden-4-yl)-1,2-dihydroisoquinolin-1-yl)acrylate (**133**) in 48% isolated yield. Subsequent treatment of this adduct with Pd(OAc)$_2$ /PPh$_3$ as per optimized contions provided the desired compound methyl 4-[2,3-dihydro-1*H*-cyclopenta[*c*]phenanthridin-5-yl]-3,4-dihydronaphtha-lene-2-carboxylate (Scheme 53) in (**134**) 53% yield. Structures of both these molecules were confirmed by IR, ^{1}H NMR, ^{13}C NMR and HRMS spectral data analysis.

Scheme 53



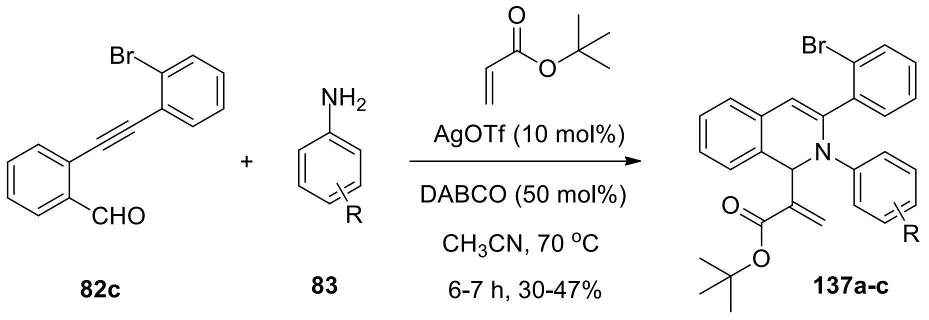
With a view to further understanding the scope of this strategy we have used ethyl acrylate as the activated alkenes for coupling with *in situ* generated isoquinolinium salts [produced from 2-(2-bromophenylethynyl)benzaldehyde (**82c**) and aniline (**83a**)] following the reaction sequence shown in Scheme 54. Required BH adduct (**135**) Ethyl 2-[3-(2-bromophenyl)-2-phenyl-1,2-dihydroisoquinolin-1-yl]acrylate in 58% yield. We then subjected this compound to the reaction with Pd(OAc)$_2$, PPh$_3$ following the optimized procedure as described for (**103j**) which gave the expected product ethyl 4-(phenanthridin-6-yl)-3,4-dihydronaphthalene-2-carboxylate (**136**) in 65% yield. Both these compounds (**135**) and (**136**) were fully characterized.

Scheme 54



Then we have extended this strategy to *tert.*butyl acrylate as activated alkene for coupling with *in situ* generated isoquinolinium salts (obtaned from 2-(2-bromophenylethynyl)-benzaldehyde (**82c**) and aniline derivatives (**83**). The resulting BH adducts (**137a-c**) were obtained in 30-47% yield (Table 10). Next we have subjected these adducts to the reactuion with $Pd(OAc)_2$ /PPh_3 to produce required phenanthridine derivatives (**138a-c**) in 47-71% yields (Table 11). All these compounds (**137a-c**) and (**138a-c**) were thoroughly characterized by spectral data analysis. We have also confirmed the structure by single crystal X-ray data analysis in this case of compound (**138a**) in Figure 12 .

Table. 10. Synthesis if *o*-bromo substituted 1,2-dihydroisoquinoline drivatives using *tert*-butyl acrylate[a, b]



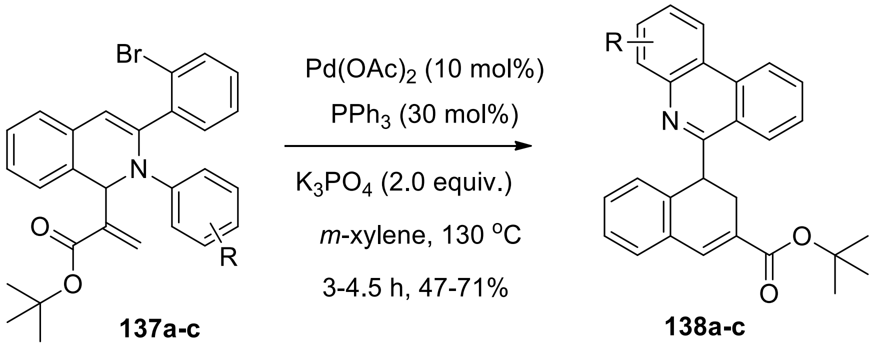
82c **83** **137a-c**

83a; R = H
83c; R = 4-Me
83j; R = $3,5-(Me)_2$

Entry	aldehyde	R	Time (h)	BH-adduct	Yield[c] (%)
1	**82c**	H (**83a**)	7	**137a**	47
2	**82c**	4-Me (**83c**)	6	**137b**	45
3	**82c**	$3,5-(Me)_2$ (**83j**)	7	**137c**	30

a) All reactions were carried out with (**82c**) (2.0 mmol), arylamine (**83**) (1.2 equiv), *tert*-butyl acrylate (3.0 equiv.), in CH_3CN (2.0 mL).
b) All compounds were fully characterized.
c) The isolated yields are based on aldehyde (**82c**).

Table. 11. Synthesis of Phenanthradine drivatives using *tert*-butyl acrylate containg BH adducts[a, b]



137a-c **138a-c**

R = H, 4-Me, $3,5-(Me)_2$

Entry	B-H adduct	R	Time (h)	Product	Yield[c] (%)
2	**137a**	H	3	**138a**[d]	71
3	**137b**	4-Me	4.5	**138b**	68
4	**137c**	3,5-(Me)$_2$	4	**138c**	47

a) All the reactions were carried out in 0.4 mmol scale of (**137**) using Pd(OAc)$_2$ (10 mol%), PPh$_3$ (30 mol%), K$_3$PO$_4$ (2.0 equiv.) in *m*-xylene (6.0 mL) at 130 °C

b) All compounds were fully characterized.

c) Isolated yields based on (**137**).

d) The structure of this molecule was also confirmed by single crystal X-ray data analysis.

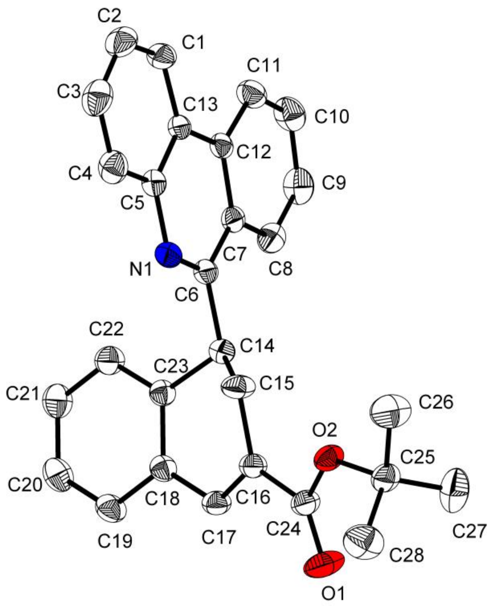


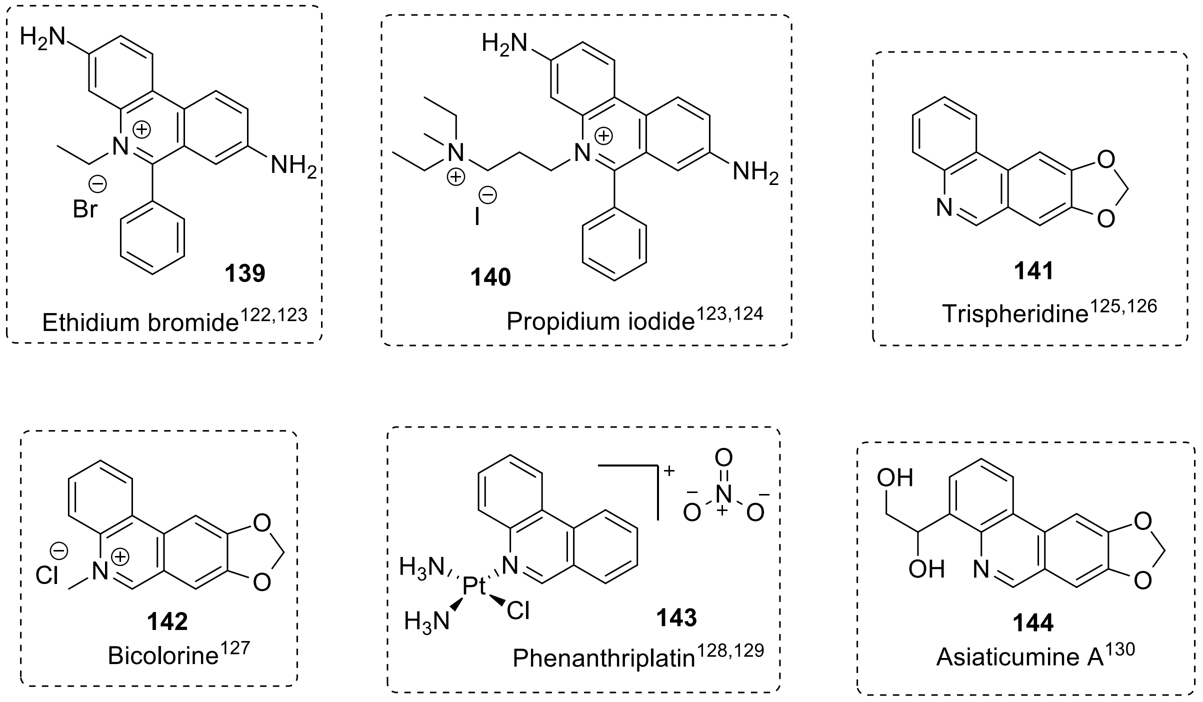
Figure 12: ORTEP of compound **138a**

Table IX. Crystal data and structure refinement for compound **138a**

Identification code	**138a**
Empirical formula	$C_{28} H_{25} N O_2$
Formula weight	407.49
Temperature	299(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P-1

Unit cell dimensions	a = 8.3659(8) Å	α= 66.038(4)°.
	b = 11.2167(12) Å	β= 76.553(4)°.
	c = 13.2350(14) Å	γ = 81.913(4)°.
Volume	1102.3(2) Å^3	
Z	2	
Density (calculated)	1.228 Mg/m^3	
Absorption coefficient	0.077 mm^{-1}	
F(000)	432	
Crystal size	0.37 x 0.25 x 0.18 mm^3	
Theta range for data collection	2.75 to 27.50°.	
Index ranges	-10<=h<=10, -14<=k<=14, -17<=l<=17	
Reflections collected	52332	
Independent reflections	5036 [R(int) = 0.0440]	
Completeness to theta = 27.50°	99.3 %	
Absorption correction	None	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5036 / 0 / 286	
Goodness-of-fit on F^2	1.056	
Final R indices [I>2sigma(I)]	R1 = 0.0514, wR2 = 0.1355	
R indices (all data)	R1 = 0.0751, wR2 = 0.1497	
Largest diff. peak and hole	0.294 and -0.186 e.Å^{-3}	

Thus we have developed a simple synthesis of phenanthridine derivatives (**129**, **130**, **132**, **134**, **136**, **138**) using the BH adducts (**103j**, **127**, **131**, **133**, **135**, **137**). At this point we feel appropriate to highlight the importance of phenanthridine framework in organic and medicinal chemistry. Phenanthridine derivatives[119-121] are well known and well studied compounds for DNA/RNA binding proficiency.[122-124] Several medicinally relevant natural products and alkaloids contain phenanthridine frameworks as the key structural motifs. Some of the selective natural products and drug molecules (**139-144**) having phenanthridine core are depicted in figure 13.[125-130]



139 Ethidium bromide[122,123]

140 Propidium iodide[123,124]

141 Trispheridine[125,126]

142 Bicolorine[127]

143 Phenanthriplatin[128,129]

144 Asiaticumine A[130]

Figure 13. Phenanthridine core containing natural products and drug molecules

In conclusion we have successfully employed the the Baylis–Hillman adducts, prepared from *in situ* generated isoquinolinium salts and representative activated alkenes for synthesis of phenanthridine derivatives having dihydronaphthalene units at 4-position. The key step in this synthesis is the 3-aza-Cope rearrangement of the *in situ* formed phenanthridine derivatives *via* coupling between bromoaryl group and N-aryl group.

CONCLUSION

The thesis work is focused on two main objectives described briefly at the beginning of this chapter. Considerable progress has been made in achieving the these two objectives. We have preapeard representative *in situ* isoquinolinium salts from alkynylarylaldehydes, arlyamines in the presence of AgOTf and successfully employed them as electrophiles for coupling with methyl, ethyl, tert.butyl and phenyl acrylates and also with acrylonitrile. Resulting Baylis–Hillman adducts were obtained in mederate to high yields. Our studies clearly not only demonstrate the potential of *in situ* generated isoquinolinium salts as excellent electrophiles for BH coupling with acrylates and acrylonitrile but also provides a simple and facile strategy for obtaining substituted isoquinoline derivatives.

All these resulting BH adducts possess vinylic-allylamine structure (3-aza-1,5-pentadiene) thus containing the required moiety for 3-aza-Cope rearrangement. From our studies it is clear that these BH adducts, containing appropriate substitution pattern, undergo simultaneous coupling and 3-aza-Cope rearrangement to provide phenanthridine derivatives containing dihydronaphthalene moiety at 4-position. Thus our studies demonstrate that BH adducts prepared, from *in situ* substituted isoquinolium salts containing aprropriate substitution pattern, and activated alkenes serve as excellent substrates for aryl-aryl copuling and 3-aza-Cope rearrangement thus providing an excellent synthetic protocol for obtaining an important class of compounds, i.e phenanthridine frame work possessing dihydronaphthalene units.

EXPERIMENTAL

General: All the required solvents were dried and distilled prior to use under suitable drying agents. Moisture sensitive reactions were carried out under N_2 (nitrogen) atmosphere using standard syringe-septum techniques.

Chromatography: All reactions were monitored using TLC (Thin Layer Chromatography). Analytical TLC (Thin Layer Chromatography) was performed on glass plates (7×2 cm) coated with FINAR's silica gel GF 254 (254 mμ) containing 13% calcium sulfate as a binder. The spots were visualized/recognized by short exposure to UV (ultraviolet) light or iodine vapour. Column chromatography was carried out using FINAR's silica gel (60-120 mesh or 100-200 mesh or 230-400 mesh).

Infrared Spectra: Infrared spectra were recorded on a NICOLET 5700 FT-IR, Thermo scientific Nicolet iS5 (iD7) spectrophotometer. All the spectra were calibrated against polystyrene absorption at 1601 cm^{-1}. Liquid samples as thin film between NaCl plates and solid samples were recorded as KBr wafers, peaks are reported in cm^{-1}.

Melting Points: Melting points were determined on MR-Vis^{+} visual melting point range apparatus of LABINDIA instruments private limited and were uncorrected.

Nuclear Magnetic Resonance Spectra: Proton magnetic resonance (^{1}H NMR) spectra, carbon-13 magnetic resonance (^{13}C NMR) spectra were recorded on BRUKER-AVANCE-400 or 500 spectrometers. ^{1}H NMR (400 or 500 MHz) spectra for all the compounds were measured in chloroform-*d* ($CDCl_3$) with TMS ($\delta = 0$ ppm) as an internal standard. ^{13}C NMR (100 or 125 MHz) spectra for all the samples were measured in chloroform-*d* ($CDCl_3$) with its middle peak of the triplet ($\delta = 77.10$ ppm) as an internal standard. The spectral assignments are as follows: (1) chemical shifts on the δ scale, (2) standard abbreviation for peaks multiplicity, that is, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublet, ddd = doublet of doublet of doublet, bs = broad singlet, dABq = doublet of AB quartet, (3) coupling constant *J* in Hertz, (4) number of hydrogens integrated for the signal.

Single Crystal X-ray Diffraction Study: Single crystal X-ray diffraction data for compounds **107a** were collected on a Bruker SMART APEX CCD area detector system [λ(Mo-Kα) = 0.71073 Å] at 298K, graphite monochromator with a ω scan width of 0.3°, crystal-detector distance 60 mm, collimator 0.5 mm. The SMART software (Version 5.630) was used for the intensity data acquisition and for the data extraction SAINTPLUS Software (Version 6.45) was used. In each case, absorption correction was performed by using SADABS program, an empirical absorption correction with equivalent reflections was carried out using the program. Single crystal X-ray diffraction data for compounds **103m, 106, 127a, 129a, 130, 138a** were collected on a Bruker D8 Quest CCD diffractometer using Mo-Kα radiation with the wavelength of λ = 0.71073 Å at 298 K. Single crystal X-ray data for compounds **103d** and **103k** were collected on Oxford Diffraction Xcalibur Eos Gemini diffractometer with graphite-monochromated Cu-Kα radiation with the wavelength of 1.54184 Å at 298K. Data were analyzed by using the ‘‘CrysAlis PRO’’ software and the collected data were also reduced with ‘‘CrysAlis PRO’’ program. An empirical absorption correction using spherical harmonics was implemented in ‘‘SCALE3 ABSPACK’’ scaling algorithm. The structures were solved by using SHELXS-97, and full-matrix least-squares refinement against F^2 was carried out using SHELXL-97. All non-hydrogen atoms were refined anisotropically. The software used to prepare the material is *WinGx* v1.70.01 (L. Farrugia, 2005). The DIAMOND (Version 2.1e) software was used for molecular graphics.

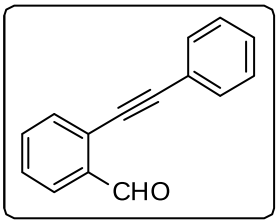
HRMS Analysis: HRMS spectra were recorded on Bruker maXis ESI-TOF mass spectrometer.

2-(Phenylethynyl)benzaldehyde (82a)

This was prepared according to the literature procedure with slight modification.[101]

To a mixture of 2-bromobenzaldehyde (20 mmol, 3.7g) with Pd(PPh$_3$)$_2$Cl$_2$ (0.8 mmol, 560 mg,) and CuI (0.8 mmol, 305 mg) in THF (30 mL) was added phenylacetylene (24 mmol, 2.6 mL), and triethylamine (60 mmol, 8.4 mL) sequentially. The mixture was stirred for 6 h at room temperature under N$_2$ atmosphere. After filtration through a celite pad and evaporation, the residue obtains, was purified by column chromatography (silica gel 1% EtOAc in hexanes) to provide the 2-(phenylethynyl)benzaldehyde (**82a**) as a brownish red liquid in 85% (3.5 g) yield.

IR (neat) : ν 2214, 1693 cm^{-1}



^{1}H NMR (400 MHz) : δ 7.36–7.41 (m, 3H), 7.45 (t, J = 7.2 Hz, 1H), 7.54–7.61 (m, 3H), 7.64 (d, J = 7.6 Hz, 1H), 7.95 (d, J = 8.0 Hz, 1H), 10.65 (s, 1H).

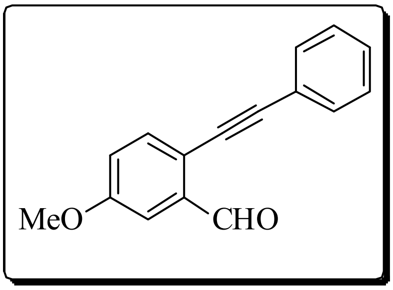
^{13}C NMR (100 MHz) : δ 84.96, 96.40, 122.41, 126.94, 127.33, 128.59, 128.68, 129.14, 131.75, 133.29, 133.84, 135.92, 191.74.

5-Methoxy-2-(phenylethynyl)benzaldehyde (82b)

This was prepared according to the literature procedure with slight modification.[102]

To a mixture of 2-bromo-5-methoxybenzaldehyde (4.5 mmol, 0.9677g) with Pd(PPh$_3$)$_2$Cl$_2$ (0.09 mmol, 63 mg,) and CuI (0.45 mmol, 86 mg) in 18 mL of triethylamine (1mmol/ 4mL) was added and phenylacetylene (5.4 mmol, 0.59 mL) sequentially. After stirring for 6 h at 50 °C under N$_2$ atmosphere, the reaction mixture was filtered through a celite pad and solvent evaporated. The crude, obtained was purified by column chromatography (silica gel 3%

EtOAc in hexanes) to provide the 5-methoxy-2-(phenylethynyl)benzaldehyde (**82b**) as a yellow solid in 78% (0.82 g) yield.



IR (neat) : *v* 1909, 1682 cm^{-1}

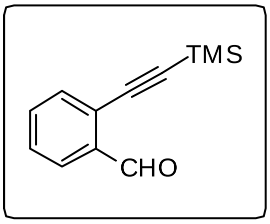
^{1}H NMR (400 MHz) : δ 3.89 (s, 3H), 7.15 (dd, J = 8.4, 2.8 Hz, 1H), 7.35−7.40 (m, 3H), 7.44 (d, J = 2.4 Hz, 1H), 7.53−7.59 (m, 3H), 10.62 (s, 1H).

^{13}C NMR (100 MHz) : δ 53.39, 83.84, 96.65, 114.24, 127.24, 127.39, 128.27, 133.08, 133.28, 133.81, 135.68, 160.29, 191.91.

2-[(Trimethylsilyl)ethynyl]benzaldehyde

This was prepared according to the literature procedure with slight modification.[101]

To a mixture of 2-bromobenzaldehyde (50 mmol, 9.25g) with Pd(PPh$_3$)$_2$Cl$_2$ (1.0 mmol, 701 mg,) and CuI (2.0 mmol, 381 mg) in THF (75 mL) was added trimethylsilyl acetylene (60 mmol, 8.3 mL), and triethylamine (150 mmol, 21 mL) sequentially. Reaction mixture was stirred for 4 h at room temperature under N$_2$ atmosphere. After filtration through a celite pad and evaporation of the solvent, the residue thus obtained was purified by column chromatography (silica gel 1% EtOAc in hexanes) to provide the 2-[(trimethylsilyl)ethynyl]benzaldehyde as a brown liquid in 82% (8.3 g) yield.



IR (neat) : *v* 2150, 1693 cm^{-1}

^{1}H NMR (400 MHz) : δ 0.28 (s, 9H), 7.40–7.45 (m, 1H), 7.51–7.59 (m, 2H), 7.88–7.94 (m, 1H), 7.64 (d, *J* = 0.4 Hz, 1H).

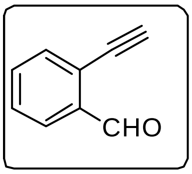
^{13}C NMR (100 MHz) : δ -0.16, 100.14, 102.50, 126.87, 126.95, 128.90, 133.57, 133.74, 136.25, 191.92.

2-Ethynylbenzaldehyde

This was prepared according to the literature procedure with slight modification.[103]

A mixture of 2-[(trimethylsilyl)ethynyl]benzaldehyde (37 mmol, 7.48g) and K_2CO_3 (3.7 mmol, 511 mg,) in MeOH (37 mL) was stirred for 15 minutes at room temperature. Solvent was removed under the reduced pressure. The residue was extracted with dichloromethane and the extract was washed with brine solution and dried over Na_2SO_4. The filtrate was concentrated under reduced pressure to give a yellow crystalline solid which was without further purification directly used for next step.

IR (neat) : ν 2216, 1694 cm^{-1}



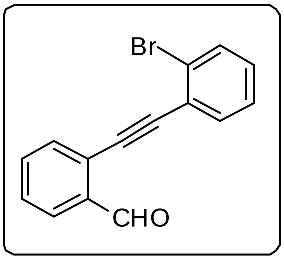
^{1}H NMR (400 MHz) : δ 3.48 (s, 1H), 7.50 (t, *J* = 7.6 Hz, 1H), 7.53–7.64 (m, 2H), 7.90–7.96 (m, 1H), 10.54 (s, 1H).

^{13}C NMR (100 MHz) : δ 79.21, 84.36, 125.50, 127.24, 129.24, 133.76, 13393, 136.52, 191.43.

2-[(2-Bromophenyl)ethynyl]benzaldehyde (82c)

This was prepared according to the literature procedure with slight modification.[103]

A mixture of 2-ethynylbenzaldehyde (24 mmol, 3.12 g), 1-bromo-2-iodobenzene (20 mmol, 5.66 g), CuI (2.0 mmol, 381 mg), $Pd(PPh_3)_2Cl_2$ (0.4 mmol, 281 mg) and triethylamine (40 mL) in THF (40 mL) was stirred at 70 °C for 2 h under N_2 atmosphere, and filtrated through a celite pad. After evaporation of the solvent and the residue was purified by column chromatography (silica gel 1% EtOAc in hexanes) to provide the 2-[(2-bromophenyl)ethynyl]benzaldehyde (**82c**) as a white solid in 79% (4.5 g) yield.



IR (neat) : ν 2150, 1687 cm^{-1}

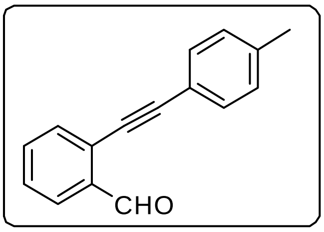
^{1}H NMR (400 MHz) : δ 7.23 (td, J = 8.0, 2.0 Hz, 1H), 7.33 (td, J = 7.6, 1.2 Hz, 1H), 7.45–7.51 (m, 1H), 7.57–7.66 (m, 3H), 7.67–7.72 (m, 1H), 7.97 (dd, J = 8.0, 1.2 Hz, 1H), 10.76 (d, J = 0.4 Hz, 1H).

^{13}C NMR (100 MHz) : δ 89.39, 94.71, 124.69, 125.86, 126.52, 127.23, 127.26, 129.07, 130.22, 132.69, 133.44, 133.56, 133.83, 136.19, 191.97.

2-(*p*-Tolylethynyl)benzaldehyde (82d)

This was prepared according to the literature procedure with slight modification.[103]

A mixture of 2-ethynylbenzaldehyde (12 mmol, 1.56 g), 4-iodotoluene (10 mmol, 2.18 g), CuI (1.0 mmol, 190 mg), $PdCl_2(PPh_3)_2$ (0.2 mmol, 140 mg) and triethylamine (20 mL) in THF (20 mL) was stirred at 70 °C for 2 h under N_2 atmosphere, and filtrated through a celite pad. Solvent and excess triethyl amine was evaporated. Residue was purified by column chromatography (silica gel 3% EtOAc in hexanes) to provide the 2-(*p*-tolylethynyl)benzaldehyde (**82d**) as a yellow solid in 75% (1.6 g) yield.



IR (neat) : ν 2212, 1685 cm^{-1}

^{1}H NMR (500 MHz) : δ 2.39 (s, 3H), 7.19 (d, *J* = 8.0 Hz, 2H), 7.42–7.48 (m, 3H), 7.56 (td, *J* = 7.5, 1.5 Hz, 1H), 7.61–7.65 (m, 1H), 7.94 (dd, *J* = 8.0, 1.0 Hz, 1H), 10.65 (d, *J* = 1.0 Hz, 1H).

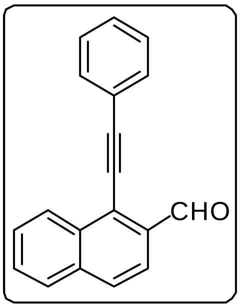
^{13}C NMR (125 MHz) : δ 21.64, 84.36, 96.71, 119.29, 127.94, 127.22, 128.46, 129.35, 131.63, 133.18, 133.82, 135.78, 139.43, 191.88.

1-(Phenylethynyl)-2-naphthaldehyde (82e)

To a mixture of 1-bromo-2-naphthaldehyde (10 mmol, 2.35 g), copper(I) iodide (0.2 mmol, 38 mg) and $PdCl_2(PPh_3)_2$ (0.1 mmol, 70 mg), was added phenylacetylene (12 mmol, 1.32 mL), and triethylamine (20 mL, 2 mL per mmol) sequentially. The mixture was stirred for 2 h at 70 °C under N_2 atmosphere. When the reaction was completed as monitored by TLC, the dark suspension was allowed to cool to ambient temperature and filtrated through a celite pad. Filtered was concentrated and, the residue was purified by column chromatography (silica gel 4% EtOAc in hexanes) to provide the 1-(phenylethynyl)-2-naphthaldehyde (**82e**) as a brown color solid in 65% (1.66 g) yield.

IR (neat) : ν 2201, 1672 cm^{-1}

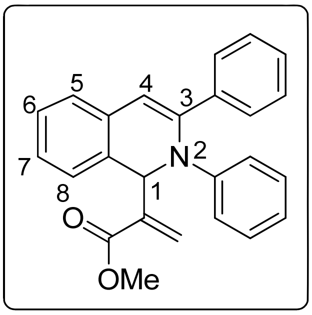
^{1}H NMR (500 MHz)	: δ 7.40–7.44 (m, 3H), 7.62–7.69 (m, 4H), 7.81–7.88 (m, 2H), 7.95 (d, J = 8.5 Hz, 1H), 8.57 (dd, J = 8.5 , 3.5 Hz, 1H), 10.85 (s, 1H).



^{13}C NMR (125 MHz)	: δ 82.99, 102.39, 122.08, 122.39, 127.26, 127.48, 127.73, 128.51, 128.70, 128.92, 129.40, 131.82, 133.13, 134.23, 135.81, 192.11.

Methyl 2-(2,3-diphenyl-1,2-dihydroisoquinolin-1-yl)acrylate (103a)

A mixture of 2-phenylethynylbenzaldehyde (**82a)** (1.0 mmol, 0.2062 g) and aniline (**83a)** (1.2 mmol, 0.1118 g, 0.11 mL) was heated at 70 °C with stirring for 5-10 minutes. Reaction mixture was then diluted with acetonitrile (1 mL) followed by sequential addition of AgOTf (10 mol%, 0.026 g), methyl acrylate (3.0 mmol, 0.2583 g, 0.27 mL) and DABCO (50 mol%, 0.056 g) at 70 °C. After stirring for 2 h at the same temperature (monitored by TLC), solvent and excess methyl acrylate were removed under reduced pressure. The residue, thus obtained, was purified by column chromatography (silica gel, 2% EtOAc in hexanes) to provide the title compound (0.2650 g) in 72% yield as yellow solid.



Mp	: 144–146 °C
IR (KBr)	: ν 1715, 1620 cm^{-1}
^{1}H NMR (400 MHz)	: δ 3.85 (s, 3H), 5.18 (s, 1H), 6.07 (s, 1H), 6.13 (s, 1H), 6.71 (s, 1H), 6.79–6.85 (m, 1H), 7.05–7.30 (m, 11H)*, 7.49 (d, J = 5.6 Hz, 2H).

[*] It also contains $CHCl_3$ peak.

^{13}C NMR (100 MHz) : δ 52.03, 63.74, 112.83, 122.21, 122.43, 124.69, 126.24, 126.81, 126.83, 127.17, 127.89, 128.10, 128.48, 128.67, 129.62, 132.64, 137.39, 139.89, 140.70, 147.26, 167.80.

HRMS (ESI) exact mass calc′d for $C_{25}H_{21}NO_2$+H $(M+H)^+$: 368.1651;

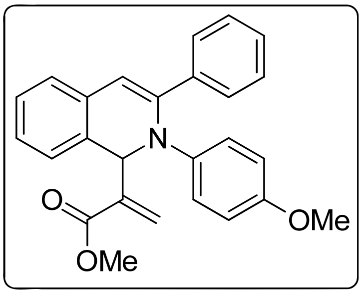
Found : 368.1656.

Methyl 2-[2-(4-methoxyphenyl)-3-phenyl-1,2-dihydroisoquinolin-1-yl]acrylate (103b)

Reaction time : 3 h

Yield : 70% as a yellow solid.

Mp : 92–94 °C



IR (KBr) : ν 1721, 1605 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.64 (s, 3H), 3.86 (s, 3H), 5.14 (s, 1H), 5.94 (s, 1H), 6.11 (s, 1H), 6.60–6.68 (m, 3H), 7.05–7.11 (m, 3H), 7.13–7.30 (m, 6H)*, 7.45–7.54 (m, 2H).

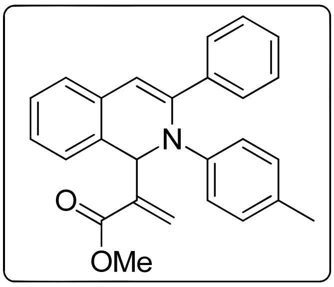
* It also contains $CHCl_3$ peak.

^{13}C NMR (100 MHz) : δ 52.04, 55.35, 64.33, 111.81, 113.98, 124.10, 124.49, 126.10, 126.67, 126.89, 127.32, 127.81, 128.04, 128.40, 128.91, 132.77, 137.44, 139.93, 140.88, 141.12, 155.25, 167.91.

HRMS (ESI) exact mass calc′d for $C_{26}H_{23}NO_3$+H $(M+H)^+$: 398.1756;

Found : 398.1756.

Methyl 2-[3-phenyl-2-(*p*-tolyl)-1,2-dihydroisoquinolin-1-yl]acrylate (103c)



Reaction time : 3 h

Yield : 74% as a yellow solid.

Mp : 88–90 °C

IR (KBr) : *v* 1715, 1605 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.15 (s, 3H), 3.85 (s, 3H), 5.16 (s, 1H), 6.01 (s, 1H), 6.11 (s, 1H), 6.68 (s, 1H), 6.89 (d, J = 8.4 Hz, 2H), 7.04 (d, J = 8.4 Hz, 2H), 7.07–7.30 (m, 7H)*, 7.50 (d, J = 7.2 Hz, 2H).

* It also contains $CHCl_3$ peak.

^{13}C NMR (100 MHz) : δ 20.69, 52.05, 63.92, 112.36, 122.44, 124.56, 126.13, 126.70, 126.85, 127.19, 127.81, 128.04, 128.45, 129.30, 131.70, 132.66, 137.46, 139.88, 140.84, 144.87, 167.86.

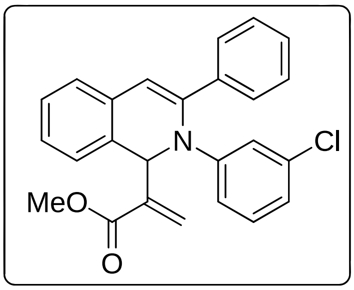
HRMS (ESI) exact mass calc′d for $C_{26}H_{23}NO_2$+H $(M+H)^+$: 382.1807;

Found : 382.1803.

Methyl 2-[2-(3-chlorophenyl)-3-phenyl-1,2-dihydroisoquinolin-1-yl]acrylate (103d)

Reaction time : 4 h

Yield : 77% as a yellow solid.



Mp : 190–191 ^{o}C

IR (KBr) : *v* 1715, 1610 cm^{-1}

^{1}H NMR (400 MHz) : *δ* 3.87 (s, 3H), 5.07 (s, 1H), 6.02 (s, 1H), 6.15 (s, 1H), 6.77 (s, 1H), 6.79 (dt, *J* = 7.2, 2.0 Hz, 1H), 6.94–7.03 (m, 2H), 7.11 (d, *J* = 7.2 Hz, 1H), 7.16–7.33 (m, 7H)*, 7.44–7.49 (m, 2H).

* It also contains CHCl$_3$ peak.

^{13}C NMR (100 MHz) : *δ* 52.14, 63.57, 113.91, 120.51, 122.16, 122.18, 124.95, 126.75, 126.97, 127.17, 128.10, 128.35, 128.65, 129.56, 129.70, 132.48, 134.30, 136.86, 139.19, 139.89, 148.46, 167.64.

HRMS (ESI) exact mass calc′d for C$_{25}$H$_{20}$ClNO$_2$+H (M+H)$^+$: 402.1261;

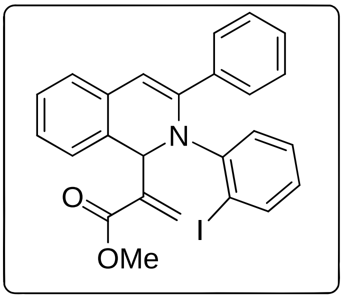
Found : 402.1258.

Methyl 2-[2-(2-iodophenyl)-3-phenyl-1,2-dihydroisoquinolin-1-yl]acrylate (103e)

Reaction time : 3 h

Yield : 58% as a yellow solid.

Mp : 122–124 °C



IR (KBr) : ν 1715, 1611 cm^{-1}

^1H NMR (400 MHz) : δ 3.73 (s, 3H), 5.60 (s, 1H), 6.04 (s, 1H), 6.18 (s, 1H), 6.60 (d, J = 7.6 Hz, 1H), 6.66 (t, , J = 7.2 Hz, 1H), 6.80–6.94 (m, 2H), 7.11–7.34 (m, 7H)*, 7.73 (d, J = 7.6 Hz, 2H), 7.82 (d, J = 7.6 Hz, 1H).

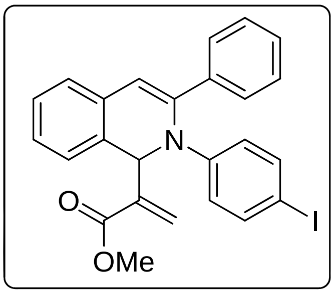
[*] It also contains $CHCl_3$ peak.

^{13}C NMR (100 MHz) : δ 51.87, 63.41, 96.64, 113.06, 123.59, 124.75, 126.74, 127.05, 127.28, 127.65, 127.79, 127.95, 128.60, 128.65, 131.77, 136.66, 139.99, 140.37, 143.34, 148.88, 166.81.

HRMS (ESI) exact mass calc′d for $C_{25}H_{20}INO_2$+H $(M+H)^+$: 494.0617;

Found : 494.0614.

Methyl 2-[2-(4-iodophenyl)-3-phenyl-1,2-dihydroisoquinolin-1-yl]acrylate (103f)



Reaction time : 2.5 h

Yield : 67% as a yellow solid.

Mp : 103–105 °C

IR (KBr) : ν 1715, 1616 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.86 (s, 3H), 5.07 (s, 1H), 5.99 (s, 1H), 6.14 (s, 1H), 6.75 (s, 1H), 6.91–6.98 (m, 2H), 7.09 (d, J = 7.6 Hz, 1H), 7.15–7.31 (m, 6H)*, 7.34–7.39 (m, 2H), 7.42–7.48 (m, 2H).

* It also contains $CHCl_3$ peak.

^{13}C NMR (100 MHz) : δ 52.16, 63.46, 85.39, 113.69, 124.26, 124.87, 126.71, 126.97, 127.11, 128.07, 128.32, 128.64, 129.56, 132.45, 136.86, 137.55, 139.17, 139.84, 146.92, 167.72.

HRMS (ESI) exact mass calc′d for $C_{25}H_{20}INO_2$+H $(M+H)^+$: 494.0617;

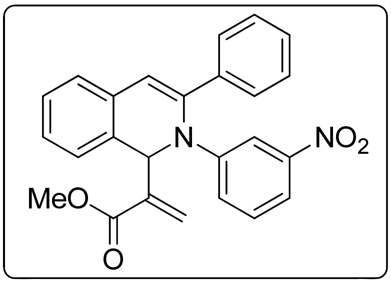
Found : 494.0613

Methyl 2-[2-(3-nitrophenyl)-3-phenyl-1,2-dihydroisoquinolin-1-yl]acrylate (103g)

Reaction time : 6 h

Yield : 61% as a yellow solid.

Mp : 199–200 °C



IR (KBr) : ν 1732, 1610 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.91 (s, 3H), 5.02 (s, 1H), 6.09 (s, 1H), 6.23 (s, 1H), 6.86 (s, 1H), 7.11 (d, J = 6.0 Hz, 1H), 7.18–7.28 (m, 5H)*, 7.30–7.37 (m, 2H), 7.43–7.51 (m, 3H), 7.66 (dd, J = 6.4, 1.6 Hz,1H), 8.16 (t, J = 1.6 Hz, 1H).

* It also contains $CHCl_3$ peak.

^{13}C NMR (100 MHz) : *δ* 52.31, 63.31, 115.04, 116.39, 116.52, 125.25, 126.64, 126.90, 127.51, 127.72, 128.37, 128.61, 128.83, 129.30, 129.74, 132.38, 136.32, 138.50, 139.17, 148.13, 148.79, 167.55.

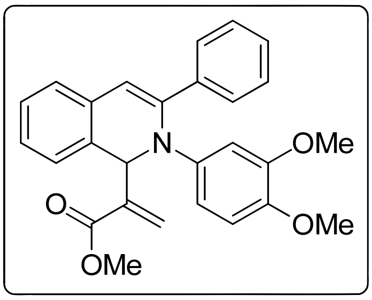
HRMS (ESI) exact mass calc′d for $C_{25}H_{20}N_2O_4$+H $(M+H)^+$: 413.1501;

Found : 413.1493.

Methyl 2-[2-(3,4-dimethoxyphenyl)-3-phenyl-1,2-dihydroisoquinolin-1-yl]acrylate (103h)

Reaction time : 2.5 h

Yield : 77% as a yellow solid.



Mp : 165−166 °C

IR (KBr) : *ν* 1710, 1620 cm^{-1}

^{1}H NMR (400 MHz) : *δ* 3.71 (s, 3H), 3.72 (s, 3H), 3.86 (s, 3H), 5.14 (s, 1H), 6.00 (s, 1H), 6.12 (s, 1H), 6.57 (d, *J* = 8.8 Hz, 1H), 6.60–6.68 (m, 2H), 6.85 (d, *J* = 2.4 Hz, 1H), 7.10 (d, *J* = 7.6 Hz, 1H), 7.14−7.31 (m, 6H)*, 7.45−7.51 (m, 2H).

* It also contains $CHCl_3$ peak.

^{13}C NMR (100 MHz) : *δ* 52.06, 55.75, 55.98, 64.10, 107.52, 111.19, 111.90, 114.44, 124.53, 126.20, 126.72, 126.83, 127.18, 127.83, 128.05, 128.42, 129.05, 132.69, 137.63, 139.87, 140.94, 141.14, 144.70, 148.85, 167.92.

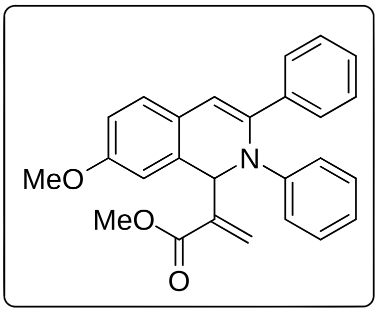
HRMS (ESI) exact mass calc′d for $C_{27}H_{25}NO_4$+H $(M+H)^+$: 428.1862;

Found : 428.1864.

HRMS (ESI) exact mass calc′d for $C_{27}H_{25}NO_4$+Na $(M+Na)^+$: 450.1682;

Found : 450.1683.

Methyl 2-(7-methoxy-2,3-diphenyl-1,2-dihydroisoquinolin-1-yl)acrylate (103i)



Reaction time : 6 h

Yield : 65% as a yellow solid.

Mp : 131−132 °C

IR (KBr) : *v* 1715, 1610 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.75 (s, 3H), 3.87 (s, 3H), 5.15 (s, 1H), 6.02 (s, 1H), 6.14 (s, 1H), 6.68 (d, J = 2.4 Hz, 1H), 6.73 (s, 1H), 6.79−6.86 (m, 2H), 7.06−7.12 (m, 2H), 7.13−7.28 (m, 6H)*, 7.44−7.50 (m, 2H).

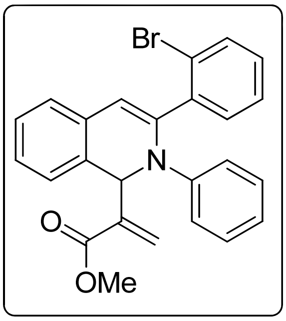
* It also contains $CHCl_3$ peak.

^{13}C NMR (100 MHz) : δ 52.10, 55.40, 63.68, 111.92, 112.92, 113.98, 121.93, 122.05, 125.87, 125.99, 126.59, 126.77, 127.76, 128.46, 128.69, 131.35, 137.46, 138.41, 139.48, 147.38, 158.98, 167.87.

HRMS (ESI) exact mass calc′d for $C_{26}H_{23}NO_3$+H $(M+H)^+$: 398.1756;

Found : 398.1752.

Methyl 2-[3-(2-bromophenyl)-2-phenyl-1,2-dihydroisoquinolin-1-yl]acrylate (103j)



Reaction time : 4 h

Yield : 55% as a yellow solid.

Mp : 118–120 °C

IR (KBr) : ν 1709, 1621 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.90 (s, 3H), 5.21 (s, 1H), 6.08 (s, 1H), 6.26 (s, 1H), 6.65 (s, 1H), 6.85 (t, J = 7.2 Hz, 1H), 6.99 (td, J = 7.6, 1.6 Hz, 1H), 7.04–7.13 (m, 4H), 7.19 (td, J = 7.2, 1.6 Hz, 1H), 7.21–7.33 (m, 5H)*, 7.53 (dd, J = 8.0, 1.2 Hz, 1H).

* It also contains $CHCl_3$ peak.

^{13}C NMR (100 MHz) : δ 52.24, 63.20, 116.75, 122.73, 122.80, 123.13, 124.67, 126.47, 127.24, 127.28, 127.83, 127.93, 128.68, 129.06, 129.09, 131.36, 132.08, 134.12, 137.50, 138.23, 139.58, 146.96, 167.89.

HRMS (ESI) exact mass calc′d for $C_{25}H_{20}BrNO_2$+Na (M+Na)$^+$: 468.0575;

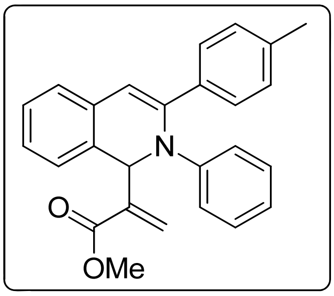
Found : 468.0568.

Methyl 2-[2-phenyl-3-(*p*-tolyl)-1,2-dihydroisoquinolin-1-yl]acrylate (103k):

Reaction time : 3.5 h

Yield : 79% as a yellow solid.

Mp : 175–176 °C



IR (KBr) : *ν* 1715, 1627 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.27 (s, 3H), 3.85 (s, 3H), 5.18 (s, 1H), 6.05 (s, 1H), 6.12 (s, 1H), 6.68 (s, 1H), 6.79–6.86 (m, 1H), 7.00–7.18 (m, 8H), 7.22–7.28 (m, 2H)*, 7.38 (d, *J* = 8.0 Hz, 2H).

* It also contains $CHCl_3$ peak.

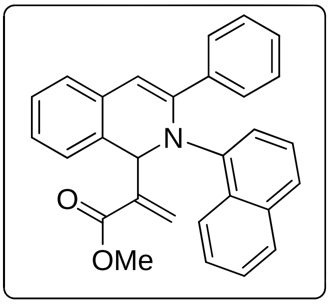
^{13}C NMR (100 MHz) : δ 21.25, 52.06, 63.65, 112.14, 122.06, 122.34, 124.56, 126.24, 126.61, 126.79, 127.02, 127.84, 128.64, 129.24, 129.53, 132.71, 134.46, 138.02, 139.70, 140.57, 147.30, 167.83.

HRMS (ESI) exact mass calc′d for $C_{26}H_{23}NO_2$+H (M+H)$^+$: 382.1807;

Found : 382.1803.

Methyl 2-[2-(naphthalen-1-yl)-3-phenyl-1,2-dihydroisoquinolin-1-yl]acrylate (103l)

Reaction time : 3 h



Yield : 61% as a red solid.

Mp : 190–191 °C

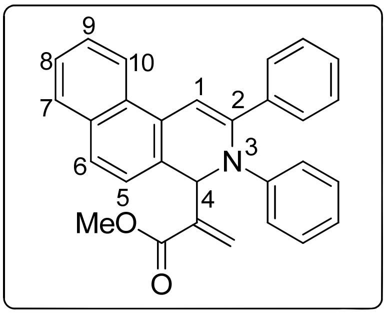
IR (KBr) : *ν* 1710, 1606 cm^{-1}

^{1}H NMR (400 MHz)	: δ 3.71 (s, 3H), 5.80 (s, 1H), 6.23 (s, 1H), 6.32 (s, 1H), 6.71(d, J = 7.2 Hz, 1H), 6.87 (s, 1H), 6.99 (t, J = 8.0 Hz, 1H), 7.07–7.30 (m, 7H)*, 7.46 (d, J = 8.0 Hz, 1H), 7.51 (t, J = 7.2 Hz, 1H), 7.60 (t, J = 7.2 Hz,1H), 7.67–7.73 (m, 2H), 7.81 (d, J = 8.4 Hz, 1H), 8.35 (d, J = 8.0 Hz, 1H). * It also contains $CHCl_3$ peak.
^{13}C NMR (100 MHz)	: δ 51.89, 63.71, 112.23, 123.44, 123.51, 123.54, 124.77, 125.33, 125.44, 126.00, 126.56, 126.69, 126.77, 127.67, 127.85, 128.40, 128.56, 128.67, 128.78, 130.02, 131.79, 134.99, 137.15, 140.32, 143.45, 143.66, 166.90.

HRMS (ESI) exact mass calc′d for $C_{29}H_{23}NO_2$+H $(M+H)^+$: 418.1807;

Found : 418.1801.

Methyl 2-(2,3-diphenyl-3,4-dihydrobenzo[*f*]isoquinolin-4-yl)acrylate (103m)



Reaction time	: 15 h
Yield	: 60% as a yellow solid.
Mp	: 176–178 °C
IR (KBr)	: ν 1710, 1620 cm^{-1}
^{1}H NMR (400 MHz)	: δ 3.87 (s, 3H), 5.19 (s, 1H), 6.15 (s, 1H), 6.21 (s, 1H), 6.79–6.88 (m, 1H), 7.05–7.13 (m, 2H), 7.17–7.32 (m, 6H)*, 7.41 (s, 1H), 7.46–7.53 (m, 1H), 7.56–7.63 (m, 3H), 7.66 (d, J

= 8.4 Hz, 1H), 7.82 (d, , *J* = 8.0 Hz, 1H), 8.36 (d, *J* = 8.4 Hz, 1H).

[*] It also contains $CHCl_3$ peak.

^{13}C NMR (100 MHz)	: δ 52.13, 64.24, 108.97, 122.36, 122.46, 123.13, 125.46, 125.78, 126.20, 126.26, 126.90, 127.44, 128.31, 128.41, 128.58, 128.60, 128.68, 128.71, 133.38, 137.57, 139.13, 141.18, 146.97, 167.89.

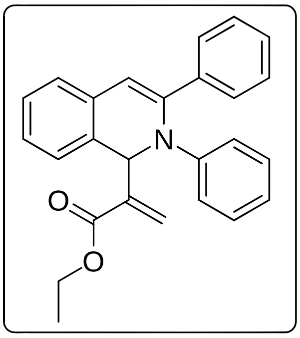
HRMS (ESI) exact mass calc′d for $C_{29}H_{23}NO_2$+H $(M+H)^+$: 418.1807;

Found : 418.1806.

Ethyl 2-(2,3-diphenyl-1,2-dihydroisoquinolin-1-yl)acrylate (104)

A mixture of 2-phenylethynylbenzaldehyde **(82a)** (1.0 mmol, 0.2062 g) and aniline **(83a)** (1.2 mmol, 0.1118 g, 0.11 mL) was heated at 70 °C for 5-10 minutes with stirring. Then acetonitrile (1.0 mL) was added to the reaction mixture. Subsequently AgOTf (10 mol%, 0.026 g), ethyl acrylate (3.0 mmol, 0.33 mL) and DABCO (50 mol%, 0.056 g) were added successively to the reaction mixture at the same temperature. Stirring was continued at the same temperature for further 3.5 h (reaction was monitored by TLC). Acetonitrile and the excess ethyl acrylate were removed under reduced pressure. The crude product, thus obtained, was directly subjected to column chromatography (silica gel, 3% EtOAc in hexanes) to provide 0.2558 g (67%) of the title compound as a yellow solid.

Mp : 91–93 °C



IR (KBr) : ν 1710, 1620 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.35 (t, J = 7.2 Hz, 3H), 4.26– 4.42 (m, 2H), 5.13 (s, 1H), 6.08 (s, 1H), 6.12 (s, 1H), 6.72 (s, 1H), 6.79–6.86 (m, 1H), 7.05–7.13 (m, 3H), 7.13–7.31 (m, 8H)*, 7.47–7.53 (m, 2H).

* It also contains $CHCl_3$ peak.

^{13}C NMR (100 MHz) : δ 14.38, 61.08, 63.60, 112.97, 122.09, 122.33, 124.67, 126.10, 126.81, 127.15, 127.86, 128.09, 128.47, 128.64, 129.68, 132.64, 137.39, 140.03, 140.60, 147.21, 167.42.

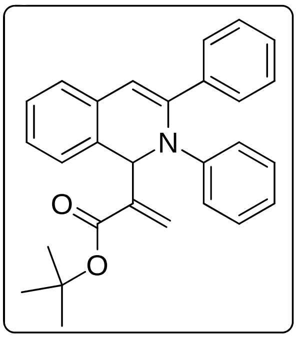
HRMS (ESI) exact mass calc′d for $C_{26}H_{23}NO_2$+H (M+H)$^+$: 382.1807;

Found : 382.1805.

***tert*-Butyl 2-(2,3-diphenyl-1,2-dihydroisoquinolin-1-yl)acrylate (105a)**

A stirring mixture of 2-phenylethynylbenzaldehyde (**82a)** (1.0 mmol, 0.2062 g) and aniline (**83a)** (1.2 mmol, 0.1118 g, 0.11 mL) was heated at 70 °C for 5-10 minutes. Reaction mixture was then diluted with acetonitrile (1.0 mL) followed by the successive addition of AgOTf (10 mol%, 0.026 g), *tert*-butyl acrylate (3.0 mmol, 0.44 mL) and DABCO (50 mol%, 0.056 g) at 70 °C. After stirring for 6 h at the same temperature (monitored by TLC), acetonitrile and the remaining *tert*-butyl acrylate were removed under reduced pressure. The residue, thus obtained, was directly subjected for purification by column chromatography (silica gel, 1% EtOAc in hexanes) to yield the title compound (0.2653 g, 65%) as a yellow solid.

Mp : 162–163 °C



IR (KBr) : *v* 1704, 1627 cm^{-1}

^{1}H NMR (400 MHz) : *δ* 1.57 (s, 9H), 5.01 (s, 1H), 6.00 (s, 1H), 6.05 (s, 1H), 6.71 (s, 1H), 6.81 (t, *J* = 7.2 Hz, 1H), 7.04–7.11 (m, 3H), 7.12–7.30 (m, 8H)*, 7.48–7.57 (m, 2H).

* It also contains $CHCl_3$ peak.

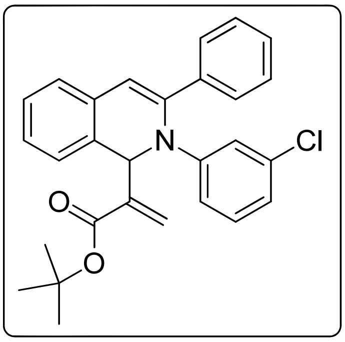
^{13}C NMR (100 MHz) : *δ* 28.26, 63.54, 81.26, 113.07, 122.00, 122.38, 124.64, 125.03, 126.76, 126.78, 127.26, 127.78, 128.05, 128.42, 128.62, 129.99, 132.75, 137.60, 140.70, 141.37, 147.37, 166.74.

HRMS (ESI) exact mass calc′d for $C_{28}H_{27}NO_2$+H (M+H)$^+$: 410.2120;

Found : 410.2126.

***tert*-Butyl 2-[2-(3-chlorophenyl)-3-phenyl-1,2-dihydroisoquinolin-1-yl]acrylate (105b)**

Reaction time : 10 h



Yield : 54% as a yellow solid.

Mp : 177–178 °C

IR (KBr) : *v* 1700, 1622 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.58 (s, 9H), 4.91 (s, 1H), 6.00 (s, 1H), 6.02 (s, 1H), 6.74–6.82 (m, 2H), 6.98 (t, J = 7.6 Hz, 1H), 7.03–7.12 (m, 2H), 7.15–7.32 (m, 7H)*, 7.48–7.54 (m, 2H).

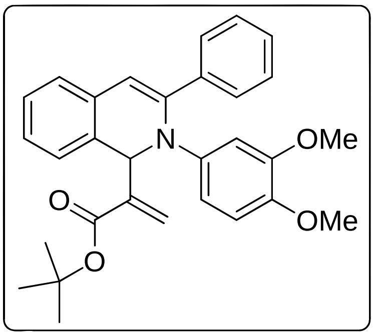
* It also contains $CHCl_3$ peak.

^{13}C NMR (100 MHz) : δ 28.25, 63.37 , 81.47, 114.14, 120.42, 121.97, 122.06, 124.91, 125.98, 126.69, 127.07, 127.12, 127.99, 128.30, 128.58, 129.52, 130.11, 132.58, 134.23, 137.08, 139.92, 140.76, 148.56, 166.53.

HRMS (ESI) exact mass calc′d for $C_{28}H_{26}ClNO_2$+H (M+H)$^+$: 444.1730;

Found : 444.1736.

***tert*-Butyl 2-[2-(3,4-dimethoxyphenyl)-3-phenyl-1,2-dihydroisoquinolin-1-yl]acrylate (105c)**



Reaction time : 4 h

Yield : 66% as a yellow solid.

Mp : 177–178 °C

IR (KBr) : ν 1701, 1610 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.57 (s, 9H), 3.71 (s, 3H), 3.72 (s, 3H), 4.98 (s, 1H), 5.98 (s, 1H), 6.00 (s, 1H), 6.56 (d, J = 7.2 Hz, 1H), 6.62–6.66 (m, 2H), 6.94 (d, J = 2.0 Hz, 1H), 7.09 (d, J = 6.0 Hz, 1H), 7.14–7.30 (m, 6H)*, 7.49–7.54 (m, 2H).

[*] It also contains $CHCl_3$ peak.

^{13}C NMR (100 MHz) : δ 28.24, 55.78, 56.00, 63.87, 81.18, 107.64, 111.19, 112.01, 114.54, 124.47, 124.73, 126.67, 126.77, 127.30, 127.72, 127.98, 128.35, 129.40, 132.82, 137.90, 140.98, 141.32, 141.42, 144.61, 148.88, 166.95.

HRMS (ESI) exact mass calc′d for $C_{30}H_{31}NO_4$+H $(M+H)^+$: 470.2331;

Found : 470.2334.

HRMS (ESI) exact mass calc′d for $C_{30}H_{31}NO_4$+Na $(M+Na)^+$: 492.2151

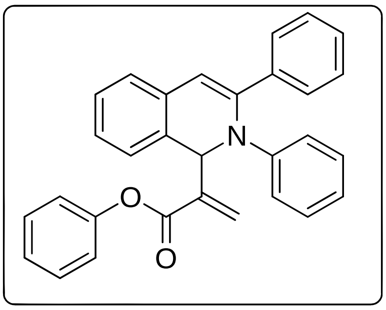
Found : 492.2152.

Phenyl 2-(2,3-diphenyl-1,2-dihydroisoquinolin-1-yl)acrylate (106)

A stirring mixture of 2-phenylethynylbenzaldehyde (**82a)** (1.0 mmol, 0.2062 g) and aniline (**83a)** (1.2 mmol, 0.1118 g, 0.11 mL) was heated at 70 °C for 5-10 minutes. Then acetonitrile (1 mL) was added to the reaction mixturte. Subsequently AgOTf (10 mol%, 0.026 g), phenyl acrylate (3.0 mmol, 0.41 mL) and DABCO (50 mol%, 0.056 g) were added in that order to the reaction mixture at 70 °C. Stirring was continued for further 3 h at the same temperature (reaction was continuously monitored by TLC). Then solvent and the remaining phenyl acrylate (excess) were removed under reduced pressure. Residue, thus obtained, was directly purified by column chromatography (silica gel, 2% EtOAc in hexanes) to afford the title compound (0.2646 g) in 62% yield as yellow solid.

Mp : 188–189 °C

IR (KBr) : ν 1726, 1610 cm^{-1}



^{1}H NMR (400 MHz) : δ 5.29 (d, J = 1.2 Hz, 1H), 6.13 (s, 1H), 6.42 (s, 1H), 6.80 (s, 1H), 6.81–6.85 (m, 1H), 7.04–7.10 (m, 2H), 7.13–7.35 (m, 12H)*, 7.40–7.46 (m, 2H), 7.55–7.61 (m, 2H).

* It also contains $CHCl_3$ peak.

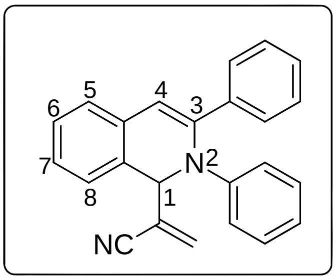
^{13}C NMR (100 MHz) : δ 63.73, 113.15, 121.80, 122.27, 122.47, 124.78, 126.09, 126.89, 126.98, 127.18, 128.06, 128.23, 128.32, 128.56, 128.71, 129.36, 129.65, 132.75, 137.32, 139.17, 140.61, 147.09, 150.88, 165.92.

HRMS (ESI) exact mass calc′d for $C_{30}H_{23}NO_2$+H (M+H)$^+$: 430.1807;

Found : 430.1805.

2-(2,3-Diphenyl-1,2-dihydroisoquinolin-1-yl)acrylonitrile (107a)

A mixture of 2-phenylethynylbenzaldehyde (**82a)** (1.0 mmol, 0.2062 g) and aniline (**83a)** (1.2 mmol, 0.1118 g, 0.11 mL) was stirred at 70 °C for 5-10 minutes. Reaction mixture was then diluted with acetonitrile (1 mL) followed by addition of AgOTf (10 mol%, 0.026 g), acrylonitrile (3.0 mmol, 0.2 mL) and DABCO (50 mol%, 0.056 g) successively at 70 °C. After stirring for further 1.5 h at the same temperature (monitored by TLC), acetonitrile and excess acrylonitrile were removed from the reaction mixture under reduced pressure. The crude compound thus obtained, was directly subjected for purification by column chromatography (silica gel, 5% EtOAc in hexanes) to provide the title compound (0.2386 g) in 72% yield as a yellow solid.



Mp : 186–188 °C

IR (KBr) : *ν* 2219, 1620 cm^{-1}

^{1}H NMR (400 MHz) : *δ* 5.23 (d, *J* = 2.0 Hz, 1H), 5.65 (s, 1H), 5.99 (d, *J* = 1.6 Hz, 1H), 6.65 (s, 1H), 6.86–6.94 (m, 1H) 7.03–7.15 (m, 5H), 7.17–7.37 (m, 6H)*, 7.60–7.70 (m, 2H).

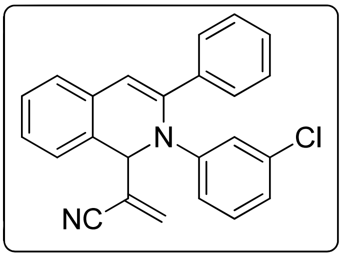
* It also contains $CHCl_3$ peak.

^{13}C NMR (100 MHz) : *δ* 66.44, 111.76, 118.79, 123.17, 123.34, 124.14, 124.83, 126.20, 126.74, 127.12, 127.73, 128.42, 128.57, 128.79, 128.95, 131.81, 132.56, 136.62, 140.52, 146.74.

HRMS (ESI) exact mass calc′d for $C_{24}H_{18}N_2$+H (M+H)$^+$: 335.1548;

Found : 335.1549.

2-[2-(3-Chlorophenyl)-3-phenyl-1,2-dihydroisoquinolin-1-yl]acrylonitrile (107b)



Reaction time : 4 h

Yield : 75% as a yellow solid.

Mp : 120–121 °C

IR (KBr) : *ν* 2219, 1610 cm^{-1}

^{1}H NMR (400 MHz) : δ 5.22 (d, J = 2.0 Hz, 1H), 5.62 (t, J = 1.6 Hz, 1H), 6.00 (d, J = 1.6 Hz, 1H), 6.69 (s, 1H), 6.86–6.91 (m, 1H), 6.93–6.98 (m, 1H), 7.00–7.07 (m, 2H), 7.10 (dd, J = 7.6, 0.4 Hz, 1H), 7.20–7.40 (m, 6H)*, 7.62–7.67 (m, 2H).

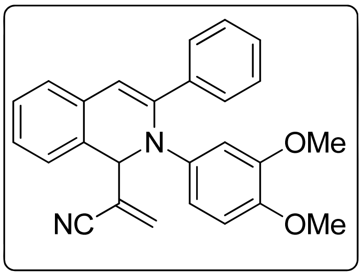
* It also contains CHCl$_3$ peak.

^{13}C NMR (100 MHz) : δ 66.29, 112.69, 118.61, 121.21, 123.04, 123.47, 123.75, 125.10, 126.26, 127.07, 127.10, 127.60, 128.69, 128.75, 129.00, 129.90, 132.14, 132.29, 134.53, 136.12, 139.86, 147.95.

HRMS (ESI) exact mass calc′d for C$_{24}$H$_{17}$ClN$_2$+Na (M+Na)$^+$: 391.0978;

Found : 391.0976.

2-[2-(3,4-Dimethoxyphenyl)-3-phenyl-1,2-dihydroisoquinolin-1-yl]acrylonitrile (107c)



Reaction time : 2 h

Yield : 80% as a yellow solid.

Mp : 159–161 °C

IR (KBr) : ν 2224, 1610 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.68 (s, 3H), 3.74 (s, 3H), 5.20 (d, J = 2.0 Hz,1H), 5.59 (t, J = 1.6 Hz, 1H), 5.99 (d, J = 1.6 Hz. 1H), 6.57 (s, 1H), 6.59–6.68 (m, 3H), 7.07 (d, J = 7.2 Hz, 1H), 7.18–7.38 (m, 6H)*, 7.61–7.67 (m, 2H).

[*] It also contains $CHCl_3$ peak.

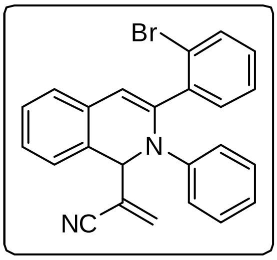
^{13}C NMR (100 MHz) : δ 55.82 , 55.98, 66.84, 108.11, 110.72, 111.26, 115.28, 119.03, 124.17, 124.70, 125.67, 126.63, 127.15, 127.76, 128.37, 128.51, 128.74, 131.77, 132.64, 136.92, 140.44, 140.89, 145.56, 148.98.

HRMS (ESI) exact mass calc′d for $C_{26}H_{22}N_2O_2$+H $(M+H)^+$: 395.1759;

Found : 395.1758.

Representative procedure: 2-[3-(2-Bromophenyl)-2-phenyl-1,2-dihydroisoquinolin-1-yl]acrylonitrile (127a)

A mixture of 2-[(2-bromophenyl)ethynyl]benzaldehyde (**82c)** (2.0 mmol) and aniline (**83a)** **(**2.4 mmol), was heated at 70 °C with stirring for 5-10 minutes. Reaction mixture was then diluted with acetonitrile (2.0 mL) followed by sequential addition of AgOTf (10 mol%), methyl acrylate (6.0 mmol) and DABCO (50 mol%) at 70 °C. After stirring at the same temperature for 4 h (monitored by TLC), solvent and excess methyl acrylate were removed under reduced pressure. The residue, thus obtained, was purified by column chromatography (silica gel, 2% EtOAc in hexanes) to provide the title compound (0.4821 g) in 58% yield as yellow solid.



Mp : 185−187 °C

IR (neat) : ν 2215, 1613 cm^{-1}

^{1}H NMR (400 MHz) : δ 5.15 (d, J = 1.6 Hz, 1H), 5.66 (s, 1H), 6.06 (d, J = 0.8 Hz, 1H), 6.56 (s, 1H), 6.92 (t, J = 7.2 Hz, 1H), 6.99−7.06 (m, 2H), 7.10–7.27 (m, 6H)*, 7.32–7.38 (m, 2H), 7.55 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.61 (dd, *J* = 7.6, 1.6 Hz, 1H).

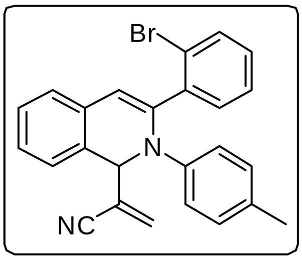
* It also contains CHCl$_3$ peak.

^{13}C NMR (100 MHz) : δ 66.35, 115.61, 119.28, 123.41, 123.45, 123.78, 123.84, 124.76, 125.23, 126.96, 127.09, 127.57, 128.89, 128.99, 129.41, 132.06, 132.10, 133.08, 133.96, 136.83, 137.91, 146.28.

HRMS (ESI) exact mass calc′d for C$_{24}$H$_{17}$BrN$_2$+H (M+H)$^+$: 413.0653;

Found : 413.0654.

2-[3-(2-Bromophenyl)-2-(*p*-tolyl)-1,2-dihydroisoquinolin-1-yl]acrylonitrile (127b)



Reaction time : 6 h

Yield : 80% as a yellow solid.

Mp : 131–133 °C

IR (neat) : *v* 2219, 1607 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.17 (s, 3H), 5.13 (d, *J* = 1.6 Hz, 1H), 5.60 (t, *J* = 1.2 Hz, 1H), 6.04 (d, *J* = 1.2 Hz, 1H), 6.51 (s, 1H), 6.91–6.95 (m, 2H), 6.99–7.05 (m, 2H), 7.08–7.12 (m, 2H), 7.15–7.25 (m, 2H)*, 7.32–7.37 (m, 2H), 7.54 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.62 (dd, *J* = 8.0, 2.0 Hz, 1H).

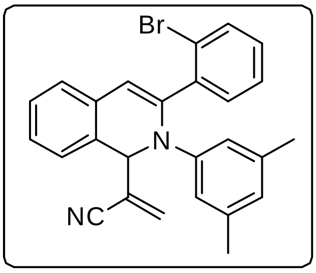
[*] It also contains $CHCl_3$ peak.

^{13}C NMR (100 MHz) : δ 20.76, 66.63, 114.94, 119.32, 123.42, 123.62, 123.97, 124.65, 125.03, 126.95, 126.98, 127.52, 128.82, 129.35, 129.59, 132.18, 132.21, 132.85, 133.63, 133.90, 137.01, 138.29, 143.95.

HRMS (ESI) exact mass calc′d for $C_{25}H_{19}BrN_2$+Na $(M+Na)^+$: 449.0629;

Found : 449.0629.

2-[3-(2-Bromophenyl)-2-(3,5-dimethylphenyl)-1,2-dihydroisoquinolin-1-yl]acrylonitrile (127c)



Reaction time : 6 h

Yield : 66% as a yellow solid.

Mp : 161−163 °C

IR (neat) : ν 2218, 1596 cm^{-1}

^1H NMR (500 MHz) : δ 2.15 (s, 6H), 5.12 (d, J = 2.0 Hz, 1H), 5.63 (s, 1H), 6.05 (d, J = 1.0 Hz, 1H), 6.52 (s, 1H), 6.56 (s, 1H), 6.84 (s, 2H), 6.99−7.05 (m, 2H), 7.16−7.27 (m, 2H)*, 7.32−7.37 (m, 2H), 7.55 (dd, J = 8.0, 0.5 Hz, 1H), 7.62 (dd, J = 7.5, 1.5 Hz, 1H).

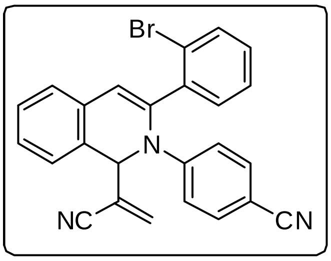
[*] It also contains $CHCl_3$ peak.

^{13}C NMR (125 MHz) : δ 21.26, 66.34, 115.52, 119.29, 121.26, 123.41, 124.00, 124.71, 125.23, 125.81, 126.96, 127.03, 127.56, 128.80, 129.31, 132.02, 132.15, 132.91, 133.84, 137.15, 138.18, 138.52, 146.29.

HRMS (ESI) exact mass calc′d for $C_{26}H_{21}BrN_2$+Na $(M+Na)^+$: 463.0786;

Found : 463.0787.

4-[3-(2-Bromophenyl)-2-(4-cyanophenyl)isoquinolin-1-yl]acrylonitrile (127d)



Reaction time : 7 h

Yield : 49% as a yellow solid.

Mp : 161−163 °C

IR (neat) : ν 2221, 1610 cm^{-1}

^{1}H NMR (500 MHz) : δ 5.17 (d, J = 1.5 Hz, 1H), 5.74 (s, 1H), 6.13 (d, J = 1.0 Hz, 1H), 6.70 (s, 1H), 7.07−7.12 (m, 2H), 7.18−7.24 (m, 3H), 7.28−7.32 (m, 1H), 7.36−7.44 (m, 4H), 7.53 (dd, J = 7.5, 1.5 Hz, 1H), 7.61 (dd, J = 8.0, 1.0 Hz, 1H).

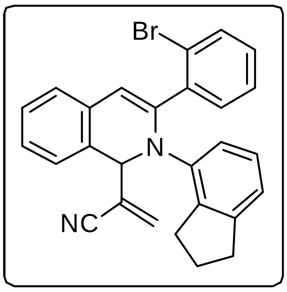
* It also contains $CHCl_3$ peak.

^{13}C NMR (125 MHz) : δ 65.21, 105.87, 118.43, 118.96, 122.26, 122.46, 123.21, 125.37, 125.73, 126.85, 127.84, 127.93, 129.34, 129.88, 131.42, 131.45, 133.15, 134.22, 134.27, 135.91, 135.93, 149.53.

HRMS (ESI) exact mass calc′d for $C_{25}H_{16}BrN_3$+Na $(M+Na)^+$: 460.0425;

Found : 460.0427.

2-[3-(2-Bromophenyl)-2-(2,3-dihydro-1*H*-inden-4-yl)-1,2-dihydroisoquinolin-1-yl]acrylonitrile (127e)



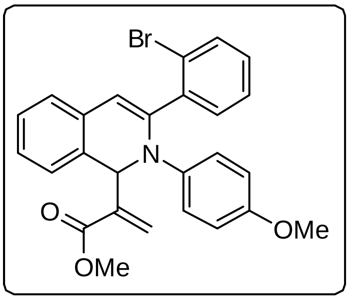
Reaction time	: 4.5 h
Yield	: 66% as a yellow solid.
Mp	: 171–173 °C
IR (neat)	: ν 2218, 1610 cm^{-1}
^{1}H NMR (500 MHz)	: δ 1.90–2.09 (m, 2H), 2.71–2.94 (m, 3H), 2.95–3.11 (m, 1H), 5.33 (s, 1H), 5.37 (s, 1H), 6.00 (d, J = 1.0 Hz, 1H), 6.52 (s, 1H), 6.85–7.08 (m, 5H), 7.17–7.27 (m, 2H)*, 7.29–7.38 (m, 2H), 7.50 (dd, J = 8.0, 1.0 Hz, 1H), 7.74 (d, J = 7.5 Hz, 1H). * It also contains $CHCl_3$ peak.
^{13}C NMR (125 MHz)	: δ 25.35, 31.54$^\#$, 33.06, 65.04$^\#$, 119.08, 122.17, 123.41, 124.53, 124.68, 125.74, 126.84, 126.87, 127.26, 128.72, 129.44, 132.17, 132.24, 132.36, 133.94, 136.72, 139.96, 142.52, 146.27.

Peak hights of δ 31.54, 65.04 are small because they are broad (DEPT experiment showed that the peak at δ 31.54 is due to CH_2 carbon and peak at δ 65.04 is due to CH carbon).

HRMS (ESI) exact mass calc′d for $C_{27}H_{21}BrN_2$-H $(M-H)^+$: 451.0810;

Found : 451.0810.

Methyl 2-[3-(2-bromophenyl)-2-(4-methoxyphenyl)-1,2-dihydroisoquinolin-1-yl]acrylate (131a)



Reaction time : 5 h

Yield : 55% as a yellow solid.

Mp : 129−131 °C

IR (neat) : *ν* 1718, 1609 cm^{-1}

^{1}H NMR (400 MHz) : *δ* 3.65 (s, 3H), 3.90 (s, 3H), 5.17 (s, 1H), 5.95 (s, 1H), 6.24 (s, 1H), 6.52 (s, 1H), 6.61−6.66 (m, 2H), 6.96−7.06 (m, 2H), 7.08−7.31 (m, 7H)*, 7.50 (dd, *J* = 8.0, 0.8 Hz, 1H).

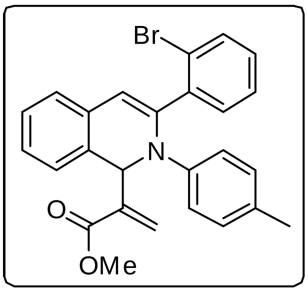
* It also contains $CHCl_3$ peak.

^{13}C NMR (100 MHz) : *δ* 52.17, 55.34, 63.88, 113.91, 115.00, 123.24, 124.42, 125.00, 126.57, 127.03, 127.17, 127.57, 127.87, 128.29, 129.09, 131.75, 132.37, 133.96, 137.73, 139.21, 139.78, 140.59, 155.82, 167.98.

HRMS (ESI) exact mass calc′d for $C_{26}H_{22}BrNO_3$-H $(M-H)^+$: 474.0705;

Found : 474.0706.

Methyl 2-[3-(2-bromophenyl)-2-(*p*-tolyl)-1,2-dihydroisoquinolin-1-yl]acrylate (131b)



Reaction time : 6 h

Yield : 59%

Mp : 137–139 °C

IR (neat) : ν 1717, 1630 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.15 (s, 3H), 3.89 (s, 3H), 5.18 (s, 1H), 6.02 (s, 1H), 6.24 (s, 1H), 6.59 (s, 1H), 6.90 (d, J = 8.4 Hz, 2H), 7.00 (td, J = 8.0, 1.6 Hz, 1H), 7.05 (d, J = 7.2 Hz, 1H), 7.08–7.14 (m, 3H), 7.17 (td, J = 7.6, 2.0 Hz, 1H), 7.24–7.32 (m, 3H)*, 7.52 (dd, J = 7.6, 1.6 Hz, 1H).

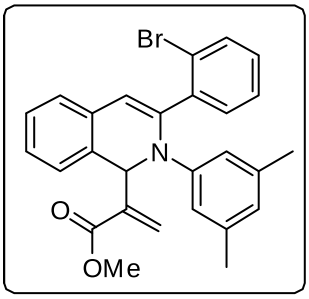
* It also contains $CHCl_3$ peak.

^{13}C NMR (100 MHz) : δ 20.73, 52.20, 63.46, 116.05, 122.98, 123.14, 124.53, 126.51, 127.09, 127.24, 127.64, 127.86, 128.73, 129.04, 129.29, 131.48, 132.18, 132.37, 134.05, 137.64, 138.58, 139.67, 144.62, 167.94.

HRMS (ESI) exact mass calc′d for $C_{26}H_{22}BrNO_2$-H (M-H)$^+$: 458.0756;

Found : 458.0757.

Methyl 2-[3-(2-bromophenyl)-2-(3,5-dimethylphenyl)-1,2-dihydroisoquinolin-1-yl]acrylate (131c)



Reaction time : 6 h

Yield : 55% as a yellow solid.

Mp : 144–146 °C

IR (neat) : ν 1709, 1619 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.14 (s, 6H), 3.91 (s, 3H), 5.17 (s, 1H), 6.05 (s, 1H), 6.23 (s, 1H), 6.49 (s, 1H), 6.60 (s, 1H), 6.88 (s, 2H), 6.95–7.01 (m, 1H), 7.04–7.12 (m, 2H), 7.17 (td, J = 7.2, 1.6 Hz, 1H), 7.21–7.32 (m, 3H)*, 7.53 (dd, J = 8.0, 0.8 Hz, 1H).

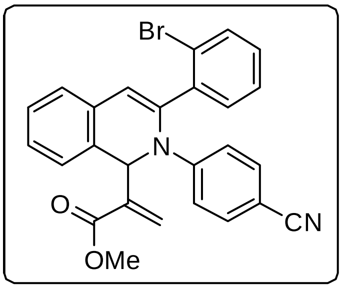
[*] It also contains $CHCl_3$ peak.

^{13}C NMR (100 MHz) : δ 21.37, 52.15, 63.23, 116.74, 120.57, 123.17, 124.61, 124.69, 125.56, 127.11, 127.26, 127.49, 127.84, 128.96, 129.03, 131.25, 132.10, 133.98, 137.82, 138.06, 138.38, 139.79, 146.95, 167.89.

HRMS (ESI) exact mass calc′d for $C_{27}H_{24}BrNO_2$+Na (M+Na)$^+$: 496.0888;

Found : 496.0888.

Methyl 2-[3-(2-bromophenyl)-2-(4-cyanophenyl)-1,2-dihydroisoquinolin-1-yl]acrylate (131d)



Reaction time : 7.5 h

Yield : 47% as a yellow solid.

Mp : 99−101 °C

IR (neat) : ν 2218, 1710 cm^{-1}

^{1}H NMR (500 MHz) : δ 3.92 (s, 3H), 5.12 (s, 1H), 6.14 (s, 1H), 6.34 (s, 1H), 6.85 (s, 1H), 7.04–7.16 (m, 4H), 7.23–7.27 (m, 1H)*, 7.31–7.41 (m, 6H), 7.59 (dd, J = 8.0, 1.0 Hz, 1H).

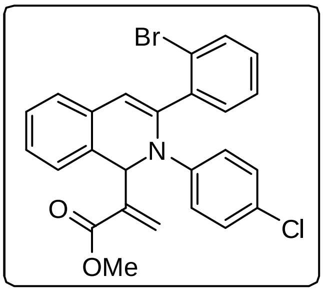
* It also contains $CHCl_3$ peak.

^{13}C NMR (125 MHz) : δ 52.43, 62.16, 104.46, 119.44, 120.05, 121.55, 122.80, 125.37, 126.30, 127.63, 128.06, 128.41, 129.54, 129.66, 129.87, 130.77, 131.59, 132.92, 134.46, 136.16, 136.58, 138.15, 150.27, 167.67.

HRMS (ESI) exact mass calc′d for $C_{26}H_{19}BrN_2O_2$-H (M-H)$^+$: 469.0552;

Found : 469.0553.

Methyl 2-[3-(2-bromophenyl)-2-(4-chlorophenyl)-1,2-dihydroisoquinolin-1-yl]acrylate (131e)



Reaction time : 7 h

Yield : 44% as a yellow solid.

Mp : 96–98 °C

IR (neat) : ν 1708, 1610 cm^{-1}

^{1}H NMR (500 MHz) : δ 3.91 (s, 3H), 5.12 (s, 1H), 6.00 (s, 1H), 6.27 (s, 1H), 6.69 (s, 1H), 7.01–7.08 (m, 4H), 7.10–7.16 (m, 1H), 7.18–7.35 (m, 6H)*, 7.54 (d, J = 8.0 Hz, 1H).

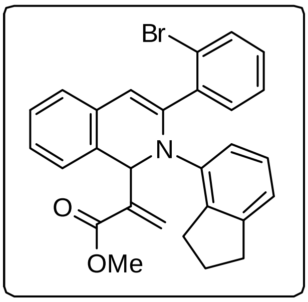
* It also contains $CHCl_3$ peak.

^{13}C NMR (125 MHz) : δ 52.32, 63.26, 117.52, 123.04, 123.98, 124.82, 126.45, 127.40, 127.51, 127.92, 128.10, 128.51, 128.72, 128.84, 129.31, 131.34, 131.99, 134.20, 137.09, 137.70, 138.99, 145.55, 167.87.

HRMS (ESI) exact mass calc′d for $C_{25}H_{19}BrClNO_2$-H (M-H)$^+$: 478.0209;

Found : 478.0206.

Methyl 2-[3-(2-bromophenyl)-2-(2,3-dihydro-1*H*-inden-4-yl)-1,2-dihydroisoquinolin-1-yl]acrylate (133)



Reaction time : 5 h

Yield : 48% as a yellow solid.

Mp : 157–159 ^{o}C

IR (neat) : *v* 1708, 1621 cm^{-1}

^{1}H NMR (500 MHz) : *δ* 1.88–2.07 (m, 2H), 2.65–2.74 (m, 1H), 2.75–2.94 (m, 3H), 3.77 (s, 3H), 5.78 (s, 1H), 5.87 (s, 1H), 6.26 (s, 1H), 6.34 (s, 1H), 6.71 (d, *J* = 7.5 Hz, 1H), 6.80 (t, *J* = 8.0 Hz, 1H), 6.86 (d, *J* = 8.0 Hz, 1H), 6.98–7.03 (m, 1H), 7.11 (td, *J* = 7.5, 1.5 Hz, 1H), 7.13–7.17 (m, 2H), 7.20–7.26 (m, 2H)*, 7.40 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.51 (dd, *J* = 8.0, 1.0 Hz, 1H).

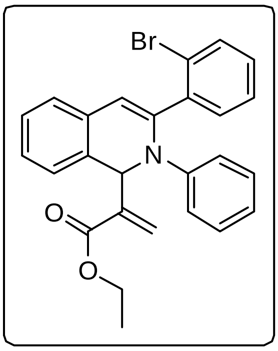
* It also contains $CHCl_3$ peak.

^{13}C NMR (125 MHz) : *δ* 25.50, 31.51, 33.16, 51.99, 62.21, 111.77, 121.41, 123.65, 124.35, 124.55, 125.21, 126.38, 126.49, 126.61, 126.96, 127.63, 128.46, 129.10, 131.06, 131.92, 133.94, 137.76, 140.43, 140.79, 141.10, 143.61, 145.92, 167.36.

HRMS (ESI) exact mass calc′d for $C_{28}H_{24}BrNO_2$-H (M-H)$^{+}$: 484.0912;

Found : 484.0914.

Ethyl 2-[3-(2-bromophenyl)-2-phenyl-1,2-dihydroisoquinolin-1-yl]acrylate (135)



Reaction time : 6.5 h

Yield : 58% as a yellow solid.

Mp : 135−137 °C

IR (neat) : ν 1733, 1618 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.39 (t, J = 7.2 Hz, 3H), 4.30–4.46 (m, 2H), 5.15 (t, J = 0.8 Hz, 1H), 6.09 (s, 1H), 6.25 (s, 1H), 6.67 (s, 1H), 6.81−6.87 (m, 1H), 6.97−7.03 (m, 1H), 7.05−7.13 (m, 4H), 7.16−7.33 (m, 6H)*, 7.54 (dd, J = 7.6, 1.2 Hz, 1H).

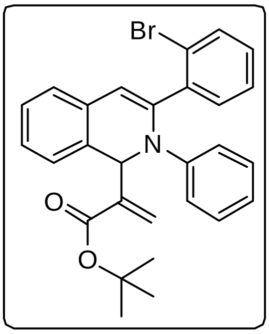
[*] It also contains $CHCl_3$ peak.

^{13}C NMR (100 MHz) : δ 14.43, 61.22, 63.12, 116.95, 122.62, 122.69, 123.10, 124.67, 126.47, 127.23, 127.57, 127.90, 128.65, 129.07, 129.14, 131.40, 132.10, 134.10, 137.52, 138.12, 139.80, 146.97, 167.51.

HRMS (ESI) exact mass calc′d for $C_{26}H_{22}BrNO_2$-H (M-H)$^+$: 458.0756;

Found : 458.0753.

***tert*-Butyl 2-[3-(2-bromophenyl)-2-phenyl-1,2-dihydroisoquinolin-1-yl]acrylate (137a)**



Reaction time : 7 h

Yield : 47% as a yellow solid.

Mp : 165–167 °C

IR (neat) : ν 1704, 1614 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.60 (s, 9H), 5.01 (t, J = 1.2 Hz, 1H), 6.06 (s, 1H), 6.11 (s, 1H), 6.68 (s, 1H), 6.81–6.86 (m, 1H), 6.97–7.03 (m, 1H), 7.04–7.13 (m, 4H), 7.18 (td, J = 7.2, 1.6 Hz, 1H), 7.24–7.35 (m, 5H)*, 7.54 (dd, J = 8.0, 1.2 Hz, 1H).

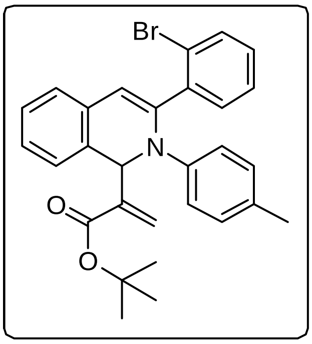
* It also contains $CHCl_3$ peak.

^{13}C NMR (100 MHz) : δ 28.26, 63.02, 81.39, 117.17, 122.47, 122.62, 123.08, 124.66, 126.45, 126.52, 127.13, 127.21, 127.83, 128.63, 129.02, 129.43, 131.56, 132.17, 134.06, 137.64, 138.02, 141.05, 147.03, 166.87.

HRMS (ESI) exact mass calc′d for $C_{28}H_{26}BrNO_2$-H (M-H)$^+$: 486.1069;

Found : 486.1068.

***tert*-Butyl 2-[3-(2-bromophenyl)-2-(*p*-tolyl)-1,2-dihydroisoquinolin-1-yl]acrylate (137b)**



Reaction time : 6 h

Yield : 45% as a yellow solid.

Mp : 169–171 °C

IR (neat) : *ν* 1697, 1609 cm^{-1}

^{1}H NMR (500 MHz) : δ 1.60 (s, 9H), 2.15 (s, 3H), 4.99 (s, 1H), 6.00 (s, 1H), 6.10 (s, 1H), 6.63 (s, 1H), 6.90 (d, *J* = 8.0 Hz, 2H), 7.00 (td, *J* = 8.0, 2.0 Hz, 1H), 7.04 (d, *J* = 7.5 Hz, 1H), 7.09 (td, *J* = 7.5, 1.5 Hz, 1H), 7.15–7.19 (m, 3H), 7.23–7.31 (m, 2H)*, 7.33 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.53 (dd, *J* = 8.0, 1.5 Hz, 1H).

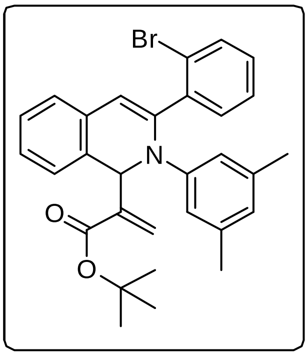
* It also contains $CHCl_3$ peak.

^{13}C NMR (125 MHz) : δ 20.72, 28.29, 63.33, 81.31, 116.44, 122.87, 123.14, 124.54, 126.24, 126.51, 127.09, 127.76, 128.96, 129.18, 129.26, 131.73, 132.11, 132.31, 134.00, 137.87, 138.46, 141.29, 144.75, 166.92.

HRMS (ESI) exact mass calc′d for $C_{29}H_{28}BrNO_2$+Na (M+Na)$^+$: 524.1201;

Found : 524.1204.

tert-Butyl 2-[3-(2-bromophenyl)-2-(3,5-dimethylphenyl)-1,2-dihydroisoquinolin-1-yl] acrylate (137c)



Reaction time : 7 h

Yield : 30% as a yellow solid.

Mp : 144–146 °C

IR (neat) : ν 1701, 1610 cm^{-1}

^{1}H NMR (500 MHz) : δ 1.61 (s, 9H), 2.15 (s, 6H), 5.00 (s, 1H), 6.03 (s, 1H), 6.07 (s, 1H), 6.48 (s, 1H), 6.61 (s, 1H), 6.90 (s, 2H), 7.00 (td, J = 8.0, 2.0 Hz, 1H), 7.06 (d, J = 7.5 Hz, 1H), 7.10 (td, J = 7.5, 1.5 Hz, 1H), 7.17 (td, J = 7.5, 1.5 Hz, 1H), 7.24–7.34 (m, 3H)*, 7.55 (dd, J = 8.0, 1.0 Hz, 1H).

[*] It also contains $CHCl_3$ peak.

^{13}C NMR (125 MHz) : δ 21.36, 28.30, 62.97, 81.35, 116.93, 120.38, 123.14, 124.46, 124.63, 125.91, 126.51, 127.08, 127.12, 127.74, 128.91, 129.53, 131.47, 132.16, 133.92, 138.02, 138.29, 141.54, 147.00, 166.98.

HRMS (ESI) exact mass calc′d for $C_{30}H_{30}BrNO_2$-H (M-H)$^+$: 514.1382;

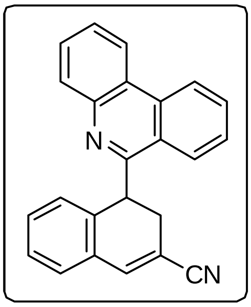
Found : 514.1382.

Representative procedure: 4-(phenanthridin-6-yl)-3,4-dihydronaphthalene-2-carbonitrile (129a)

A mixture of 2-[3-(2-bromophenyl)-2-phenyl-1,2-dihydroisoquinolin-1-yl]acrylonitrile (**127a)** (0.4 mmol, 0.165 g), $Pd(OAc)_2$ (10 mol%, 0.04 mmol, 9mg), PPh_3 (30 mol%, 0.3 mmol, 31mg), and K_3PO_4 (2 equiv, 0.8 mmol, 170mg) in *m*-xylene (6.0 mL) was stirred for 3.5 h at 130 °C. Reaction mixture was then diluted with hexane (30 mL) the mixture was filtered through a celite pad followed by EtOAc (20 mL). Filtrate was concentrated. The residue, thus obtained, was purified by column chromatography (silica gel, 5% EtOAc in hexanes) to provide the title compound (0.0882 g) in 67% yield as yellow solid.

Mp : 224–126 °C

IR (neat) : *ν* 2205, 1612 cm^{-1}



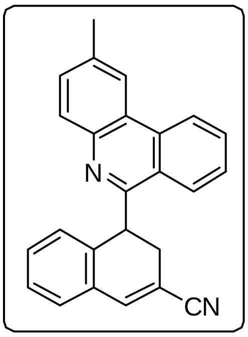
^{1}H NMR (400 MHz) : *δ* 2.82 (dd, *J* = 17.2, 6.8 Hz, 1H), 3.61–3.72 (m, 1H), 5.36 (dd, *J* = 14.4, 6.8 Hz, 1H), 6.59 (d, *J* = 7.6 Hz, 1H), 7.08 (td, *J* = 7.6, 1.6 Hz, 1H), 7.20–7.30 (m, 2H)*, 7.35 (d, *J* = 2.8 Hz, 1H), 7.64–7.77 (m, 3H), 7.86–7.92 (m, 1H), 8.09–8.13 (m, 1H), 8.17 (d, *J* = 8.0 Hz, 1H), 8.62 (dd, *J* = 8.0, 1.2 Hz, 1H), 8.75 (d, *J* = 8.0 Hz, 1H).

[*] It also contains $CHCl_3$ peak.

^{13}C NMR (100 MHz) : δ 30.32, 41.72, 110.25, 119.58, 122.02, 122.96, 123.72, 125.50, 126.03, 127.22, 127.33, 127.63, 127.70, 128.24, 128.87, 130.21, 130.55, 130.72, 131.61, 133.37, 137.30, 141.46, 143.70, 160.12.

HRMS (ESI) exact mass calc′d for $C_{24}H_{16}N_2$+H (M+H)$^+$: 333.1392;
Found : 333.1393.

4-(2-Methylphenanthridin-6-yl)-3,4-dihydronaphthalene-2-carbonitrile (129b)



Reaction time : 4 h

Yield : 57% as a yellow solid.

Mp : 227–229 ^{o}C

IR (neat) : ν 2203, 1614 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.63 (s, 3H), 2.79 (dd, J = 17.2, 6.8 Hz, 1H), 3.57–3.72 (m, 1H), 5.33 (dd, J = 14.4, 6.8 Hz, 1H), 6.57 (d, J = 7.6 Hz, 1H), 7.01–7.09 (m, 1H), 7.15–7.28 (m, 2H)*, 7.32 (d, J = 2.4 Hz, 1H), 7.55 (d, J = 8.4 Hz, 1H), 7.62 (t, J = 7.6 Hz, 1H), 7.84 (t, J = 7.6 Hz, 1H), 8.00 (d, J = 8.4 Hz, 1H), 8.12 (d, J = 8.4 Hz, 1H), 8.38 (s, 1H), 8.71 (d, J = 8.4 Hz, 1H).

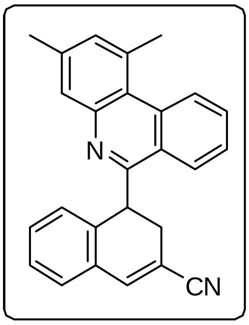
* It also contains CHCl$_3$ peak.

^{13}C NMR (100 MHz) : δ 22.07, 30.30, 41.67, 110.25, 119.57, 121.61, 122.90, 123.55, 125.51, 126.00, 127.27, 127.45, 127.69, 128.21, 129.83, 130.53, 130.60, 131.56, 133.12, 137.16, 137.37, 141.43, 159.03.

HRMS (ESI) exact mass calc′d for $C_{25}H_{18}N_2$+H $(M+H)^+$: 347.1548;

Found : 347.1547.

4-(1,3-Dimethylphenanthridin-6-yl)-3,4-dihydronaphthalene-2-carbonitrile (129c)



Reaction time : 4 h

Yield : 51% as a yellow solid.

Mp : 249–251 °C

IR (neat) : ν 2202, 1609 cm^{-1}

^{1}H NMR (500 MHz) : δ 2.52 (s, 3H), 2.78 (dd, J = 17.5, 7.0 Hz, 1H), 3.10 (s, 3H), 3.61–3.72 (m, 1H), 5.33 (dd, J = 14.0, 7.0 Hz, 1H), 6.58 (d, J = 8.0 Hz, 1H), 7.05 (t, J = 7.5 Hz, 1H), 7.20 (t, J = 7.5 Hz, 1H), 7.24 (d, J = 6.5 Hz, 1H)*, 7.32 (d, J = 2.5 Hz, 1H), 7.36 (s, 1H), 7.62 (t, J = 7.5 Hz, 1H), 7.78–7.87 (m, 2H), 8.18 (d, J = 8.0 Hz, 1H), 8.93 (d, J = 9.0 Hz, 1H).

[*] It also contains $CHCl_3$ peak.

^{13}C NMR (125 MHz) : *δ* 21.11, 26.71, 30.29, 41.52, 110.36, 119.61, 121.04, 125.90, 126.16, 126.36, 127.06, 127.25, 127.74, 128.16, 128.74, 129.80, 130.50, 131.66, 133.23, 134.66, 134.69, 137.40, 137.99, 141.41, 145.36, 159.48.

HRMS (ESI) exact mass calc′d for $C_{26}H_{20}N_2$+H (M+H)$^+$: 361.1705;

Found : 361.1706

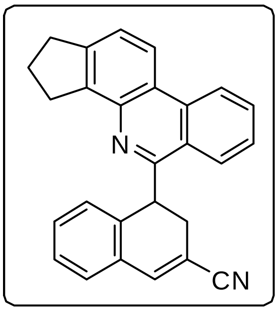
HRMS (ESI) exact mass calc′d for $C_{26}H_{20}N_2$+Na (M+Na)$^+$: 383.1524;

Found : 383.1508.

HRMS (ESI) exact mass calc′d for $C_{26}H_{20}N_2$+K (M+K)$^+$: 399.1264;

Found : 399.1247.

4-(2,3-dihydro-1*H*-cyclopenta[*c*]phenanthridin-5-yl)-3,4-dihydronaphthalene-2-carbonitrile (129e)



Reaction time : 3.5 h

Yield : 68% as a yellow solid.

Mp : 187−189 °C

IR (neat) : *ν* 2207, 1610 cm^{-1}

^{1}H NMR (500 MHz) : δ 2.17–2.28 (m, 2H), 2.86 (dd, J = 17.0, 7.0 Hz, 1H), 3.10–3.21 (m, 2H), 3.26–3.35 (m, 1H), 3.35–3.43 (m, 1H), 3.58–3.67 (m, 1H), 5.31 (dd, J = 12.5, 7.0 Hz, 1H), 6.67 (d, J = 7.5 Hz, 1H), 7.08 (t, J = 7.5 Hz, 1H), 7.22 (t, J = 7.5 Hz, 1H), 7.24–7.29 (m, 1H)*, 7.34 (d, J = 1.0 Hz, 1H), 7.56 (d, J = 8.0 Hz, 1H), 7.62 (t, J = 7.5 Hz, 1H), 7.84 (t, J = 7.5 Hz, 1H), 8.16 (d, J = 8.0 Hz, 1H), 8.42 (d, J = 8.5 Hz, 1H), 8.70 (d, J = 8.5 Hz, 1H).

* It also contains $CHCl_3$ peak.

^{13}C NMR (125 MHz) : δ 25.02, 30.36, 31.00, 33.93, 41.30, 110.32, 119.79, 120.35, 121.85, 123.06, 123.83, 124.76, 125.87, 126.87, 127.20, 127.89, 128.08, 130.35, 130.37, 131.88, 133.91, 137.56, 140.51, 141.37, 143.25, 145.05, 158.97.

HRMS (ESI) exact mass calc′d for $C_{27}H_{20}N_2$+H (M+H)$^+$: 373.1705;

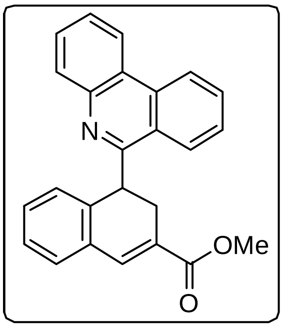
Found : 373.1708.

Methyl 4-(phenanthridin-6-yl)-3,4-dihydronaphthalene-2-carboxylate (130)

Reaction time : 3 h

Yield : 65% as a yellow solid.

Mp : 183−185 °C



IR (neat) : *ν* 1702, 1630 cm^{-1}

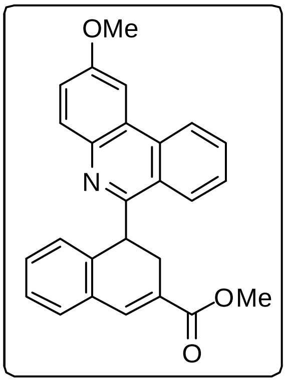
^{1}H NMR (400 MHz) : *δ* 3.12 (dd, *J* = 17.2, 7.2 Hz, 1H), 3.45–3.56 (m, 1H), 3.81 (s, 3H), 5.31 (dd, *J* = 14.8, 7.2 Hz, 1H), 6.60 (d, *J* = 7.6, 1H), 7.00–7.07 (m, 1H), 7.19 (t, *J* = 7.6 Hz, 1H), 7.33 (d, *J* = 7.2 Hz, 1H), 7.60 (t, *J* = 7.6 Hz, 1H), 7.64–7.75 (m, 3H), 7.79–7.87 (m, 1H), 8.13 (d, *J* = 7.6 Hz, 1H), 8.18 (d, *J* = 8.4 Hz, 1H), 8.60 (d, *J* = 8.0 Hz, 1H), 8.71 (d, *J* = 8.4 Hz, 1H).

^{13}C NMR (100 MHz) : *δ* 28.48, 43.38, 51.94, 121.96, 122.82, 123.71, 125.52, 126.56, 126.95, 127.01, 127.35, 127.47, 128.73, 128.79, 129.28, 129.82, 130.18, 130.48, 132.74, 133.39, 136.47, 138.43, 143.79, 161.65, 167.78.

HRMS (ESI) exact mass calc′d for $C_{25}H_{19}NO_2$+H (M+H)$^+$: 366.1494;

Found : 366.1495.

Methyl 4-(2-methoxyphenanthridin-6-yl)-3,4-dihydronaphthalene-2-carboxylate (132a)



Reaction time : 3.5 h

Yield : 70% as a yellow solid.

Mp : 160−162 °C

IR (neat) : *ν* 1709, 1631 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.11 (dd, J = 17.6, 7.2 Hz, 1H), 3.42–3.55 (m, 1H), 3.81 (s, 3H), 4.02 (s, 3H), 5.27 (dd, J = 15.2, 7.2 Hz, 1H), 6.60 (d, J = 7.6 Hz, 1H), 7.03 (td, J = 7.6, 1.2 Hz, 1H), 7.16–7.22 (m, 1H), 7.30–7.38 (m, 2H), 7.55–7.62 (m, 1H), 7.69 (d, J = 2.4 Hz, 1H), 7.77–7.84 (m, 1H), 7.93 (d, J = 2.4 Hz, 1H), 8.05 (d, J = 8.8 Hz, 1H), 8.15 (d, J = 8.0 Hz, 1H), 8.63 (d, J = 8.4 Hz, 1H).

^{13}C NMR (100 MHz) : δ 28.48, 43.24, 51.93, 55.74, 102.90, 118.54, 122.82, 124.74, 125.64, 126.57, 126.96, 127.38, 127.46, 128.77, 129.36, 129.81, 130.02, 131.60, 132.74, 132.91, 136.47, 138.62, 139.17, 158.46, 158.88, 167.82.

HRMS (ESI) exact mass calc′d for $C_{26}H_{21}NO_3$+H $(M+H)^+$: 396.1600;

Found : 396.1600.

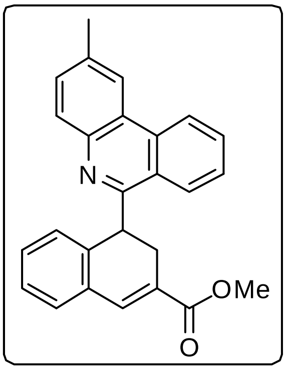
Methyl 4-(2-methylphenanthridin-6-yl)-3,4-dihydronaphthalene-2-carboxylate (132b)

Reaction time : 3 h

Yield : 62% as a yellow solid.

Mp : 166–168 °C

IR (neat) : ν 1703, 1609 cm^{-1}



^{1}H NMR (400 MHz) : δ 2.63 (s, 3H), 3.12 (dd, J = 17.6, 7.2 Hz, 1H), 3.43–3.56 (m, 1H), 3.81 (s, 3H), 5.30 (dd, J = 14.8, 7.2 Hz, 1H), 6.59 (d, J = 8.0 Hz, 1H), 7.03 (td, J = 7.6, 1.2 Hz, 1H), 7.16–7.22 (m, 1H), 7.30–7.35 (m, 1H), 7.52–7.61 (m, 2H), 7.69 (d, J = 2.8 Hz, 1H), 7.78–7.84 (m, 1H), 8.02 (d, J = 8.4 Hz, 1H), 8.15 (d, J = 8.4 Hz, 1H), 8.38 (s, 1H), 8.70 (d, J = 8.0 Hz, 1H).

^{13}C NMR (100 MHz) : δ 22.07, 28.49, 43.39, 51.94, 121.58, 122.79, 123.56, 125.58, 126.56, 126.98, 127.18, 127.48, 128.78, 129.34, 129.82, 129.88, 130.27, 130.46, 132.73, 133.18, 136.47, 136.84, 138.55, 142.10, 160.59, 167.81.

HRMS (ESI) exact mass calc′d for $C_{26}H_{21}NO_2$+H $(M+H)^+$: 380.1651;

Found : 380.1652.

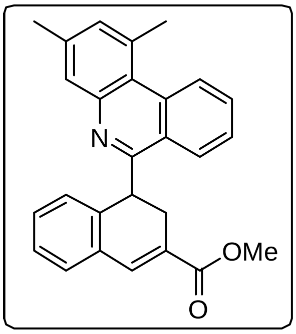
Methyl 4-(1,3-dimethylphenanthridin-6-yl)-3,4-dihydronaphthalene-2-carboxylate (132c)

Reaction time : 4 h

Yield : 53% as a yellow solid.

Mp : 189–191 °C

IR (neat) : ν 1711, 1631 cm^{-1}



^{1}H NMR (500 MHz) : δ 2.51 (s, 3H), 3.07–3.14 (m, 4H)$^{\#}$, 3.46–3.56 (m, 1H), 3.81 (s, 3H), 5.29 (dd, *J* = 14.5, 7.0 Hz, 1H), 6.60 (d, *J* = 7.5 Hz, 1H), 7.03 (td, *J* = 8.0, 1.0 Hz, 1H), 7.16–7.21 (m, 1H), 7.29–7.36 (m, 2H), 7.54–7.60 (m, 1H), 7.69 (d, *J* = 2.5 Hz, 1H), 7.76–7.87 (m, 2H), 8.22 (d, *J* = 8.0 Hz, 1H), 8.91 (d, *J* = 8.5 Hz, 1H).

$^{\#}$ It contains a singlet at 3.09 for 3H and a dd for 1H.

^{13}C NMR (125 MHz) : δ 21.11, 26.73, 28.42, 43.20, 51.91, 121.04, 126.11, 126.22, 126.44, 126.93, 126.96, 127.50, 128.72, 128.77, 129.44, 129.57, 129.79, 132.81, 132.98, 134.59, 134.73, 136.46, 137.80, 138.58, 145.50, 161.01, 167.82.

HRMS (ESI) exact mass calc′d for $C_{27}H_{23}NO_2$+H (M+H)$^+$: 394.1807;

Found : 394.1809.

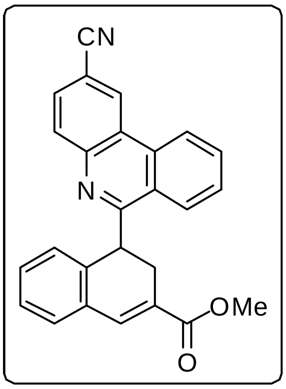
Methyl 4-(2-cyanophenanthridin-6-yl)-3,4-dihydronaphthalene-2-carboxylate (132d)

Reaction time : 10 h

Yield : 40% as a yellow solid.

Mp : 267–269 °C

IR (neat) : ν 2221, 1713, 1632 cm^{-1}



^{1}H NMR (500 MHz) : δ 3.12 (dd, J = 17.5, 7.0 Hz, 1H), 3.42–3.53 (m, 1H), 3.82 (s, 3H), 5.33 (dd, J = 14.0, 7.0 Hz, 1H), 6.58 (d, J = 7.5 Hz, 1H), 7.07 (t, J = 7.5 Hz, 1H), 7.20–7.28 (m, 1H)*, 7.36 (d, J = 7.0 Hz, 1H), 7.69–7.77 (m, 2H), 7.89 (dd, J = 8.5, 1.0 Hz, 1H), 7.95 (t, J = 7.5 Hz, 1H), 8.16 (d, J = 8.5 Hz, 1H), 8.27 (d, J = 8.5 Hz, 1H), 8.68 (d, J = 8.5 Hz, 1H), 8.94 (s, 1H).

* It also contains $CHCl_3$ peak.

^{13}C NMR (125 MHz) : δ 28.45, 43.26, 52.02, 110.27, 119.24, 122.79, 123.91, 125.91, 126.79, 127.31, 127.35, 127.85, 128.79, 128.94, 128.98, 129.89, 130.31, 131.44, 131.61, 132.25, 132.87, 136.49, 137.80, 145.45, 165.39, 167.66.

HRMS (ESI) exact mass calc′d for $C_{26}H_{18}N_2O_2$+H $(M+H)^+$: 391.1447;

Found : 391.1448.

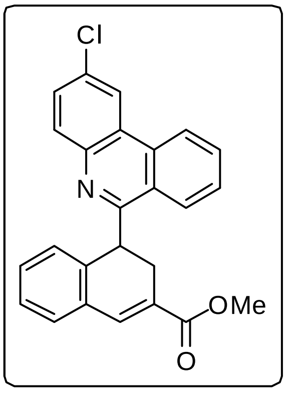
Methyl 4-(2-chlorophenanthridin-6-yl)-3,4-dihydronaphthalene-2-carboxylate (132e)

Reaction time : 3.5 h

Yield : 48% as a yellow solid.

Mp : 202–204 °C

IR (neat) : ν 1700, 1632 cm^{-1}



^{1}H NMR (400 MHz) : δ 3.10 (dd, J = 17.2, 7.2 Hz, 1H), 3.41–3.54 (m, 1H), 3.82 (s, 3H), 5.28 (dd, J = 14.4, 7.2 Hz, 1H), 6.57 (d, J = 7.6 Hz, 1H), 7.05 (td, J = 7.6, 1.2 Hz, 1H), 7.18–7.23 (m, 1H), 7.34 (dd, J = 7.2, 1.2 Hz, 1H), 7.61–7.67 (m, 2H), 7.70 (d, J = 2.8 Hz, 1H), 7.82–7.88 (m, 1H), 8.03 (d, J = 8.8 Hz, 1H), 8.19 (d, J = 8.0 Hz, 1H), 8.54 (d, J = 2.0 Hz, 1H), 8.61 (d, J = 8.0 Hz, 1H).

^{13}C NMR (100 MHz) : δ 28.43, 43.21, 51.97, 121.64, 122.86, 124.78, 125.69, 126.57, 127.11, 127.39, 128.06, 128.83, 129.22, 129.84, 130.77, 131.70, 132.36, 132.81, 136.46, 138.22, 142.22, 161.98, 167.73.

HRMS (ESI) exact mass calc′d for $C_{25}H_{18}ClNO_2$+H $(M+H)^+$: 400.1104;

Found : 400.1105.

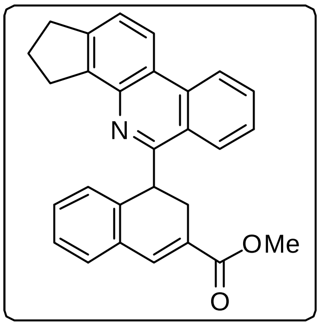
Methyl 4-(2,3-dihydro-1*H*-cyclopenta[*c*]phenanthridin-5-yl)-3,4-dihydronaphthalene-2-carboxylate (134)

Reaction time : 3.5 h

Yield : 53% as a yellow solid.

Mp : 239–241 °C

IR (neat) : ν 1702, 1630 cm^{-1}



^{1}H NMR (500 MHz) : δ 2.17–2.26 (m, 2H), 3.06–3.17 (m, 3H), 3.26–3.43 (m, 2H), 3.48–3.57 (m, 1H), 3.81 (s, 3H), 5.28 (dd, J = 13.0, 7.0 Hz, 1H), 6.67 (d, J = 7.5 Hz, 1H), 7.03–7.09 (m, 1H), 7.21 (t, J = 7.5 Hz, 1H), 7.34 (d, J = 7.5 Hz, 1H), 7.54 (d, J = 8.5 Hz, 1H), 7.56–7.61 (m, 1H), 7.69 (d, J = 2.0 Hz, 1H), 7.78–7.83 (m, 1H), 8.19 (d, J = 8.5 Hz, 1H), 8.41 (d, J = 8.0 Hz, 1H), 8.68 (d, J = 8.5 Hz, 1H).

^{13}C NMR (125MHz) : δ 25.05, 28.39, 31.03, 33.95, 42.97, 51.88, 120.31, 121.83, 122.94, 123.54, 124.89, 126.39, 126.63, 126.88, 127.69, 128.61, 129.38, 129.64, 130.13, 133.11, 133.92, 136.48, 138.86, 140.66, 143.26, 144.84, 160.42, 167.92.

HRMS (ESI) exact mass calc′d for $C_{28}H_{23}NO_2$+H $(M+H)^+$: 406.1807;

Found : 406.1806.

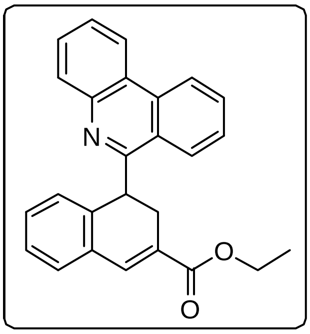
Ethyl 4-(phenanthridin-6-yl)-3,4-dihydronaphthalene-2-carboxylate (136)

Reaction time : 4 h

Yield : 65% as a yellow solid.

Mp : 139–141 °C

IR (neat) : ν 1738, 1627 cm^{-1}



^{1}H NMR (400 MHz) : δ 1.33 (t, J = 7.2 Hz, 3H), 3.13 (dd, J = 17.6, 7.2 Hz, 1H), 3.44–3.56 (m, 1H), 4.23–4.31 (m, 2H), 5.31 (dd, J = 15.2, 7.2 Hz, 1H), 6.59 (d, J = 7.6, 1H), 7.02 (td, J = 7.6, 1.2 Hz, 1H), 7.15–7.21 (m, 1H), 7.33 (dd, J = 7.6, 1.2 Hz, 1H), 7.55–7.60 (m, 1H), 7.62–7.67 (m, 1H), 7.68–7.74 (m, 2H), 7.78–7.84 (m, 1H), 8.11–8.20 (m, 2H), 8.58 (dd, J = 8.4, 1.2 Hz, 1H), 8.70 (d, J = 8.4 Hz, 1H).

^{13}C NMR (100 MHz) : δ 14.38, 28.47, 43.55, 60.75, 121.95, 122.78, 123.70, 125.47, 126.63, 126.94, 126.97, 127.30, 127.41, 128.72, 128.74, 129.61, 129.72, 130.10, 130.47, 132.73, 133.38, 136.17, 138.41, 143.73, 161.75, 167.30.

HRMS (ESI) exact mass calc′d for $C_{26}H_{21}NO_2$+H (M+H)$^+$: 380.1651;

Found : 380.1652.

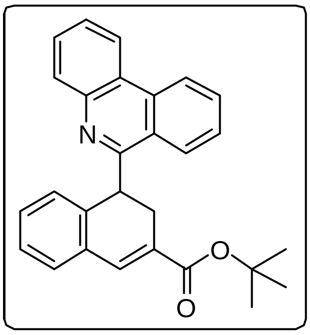
tert-Butyl 4-(phenanthridin-6-yl)-3,4-dihydronaphthalene-2-carboxylate (138a)

Reaction time : 3 h

Yield : 71% as a yellow solid.

Mp : 210–212 ^{o}C

IR (neat) : ν 1701, 1626 cm^{-1}



^{1}H NMR (400 MHz) : δ 1.54 (s, 9H), 3.08 (dd, J = 17.6, 7.2 Hz, 1H), 3.37–3.50 (m, 1H), 5.29 (dd, J = 15.2, 7.2 Hz, 1H), 6.58 (d, J = 7.6 Hz, 1H), 7.01 (td, J = 7.6, 1.2 Hz, 1H), 7.15–7.21 (m, 1H), 7.30–7.35 (m, 1H), 7.55–7.63 (m, 2H), 7.64–7.69 (m, 1H), 7.70–7.75 (m, 1H), 7.79–7.85 (m, 1H), 8.12–8.20 (m, 2H), 8.60 (dd, J = 8.0, 1.2 Hz, 1H), 8.71 (d, J = 8.4 Hz, 1H).

^{13}C NMR (100 MHz) : δ 28.26, 28.62, 44.09, 80.70, 121.98, 122.80, 123.76, 125.48, 126.88, 126.93, 127.24, 127.38, 128.64, 128.73, 129.50, 130.17, 130.44, 131.24, 132.88, 133.45, 135.35, 138.40, 143.85, 162.02, 166.59.

HRMS (ESI) exact mass calc′d for $C_{28}H_{25}NO_2$+H $(M+H)^+$: 408.1964;

Found : 408.1965.

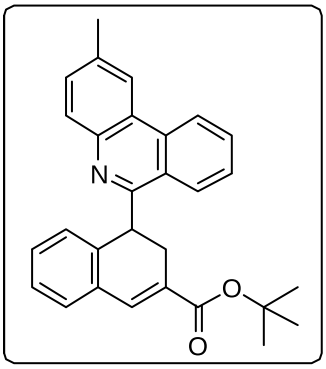
***tert*-Butyl 4-(2-methylphenanthridin-6-yl)-3,4-dihydronaphthalene-2-carboxylate (138b)**

Reaction time : 4.5 h

Yield : 68% as a yellow solid.

Mp : 244–246 °C

IR (neat) : ν 1700, 1626 cm^{-1}



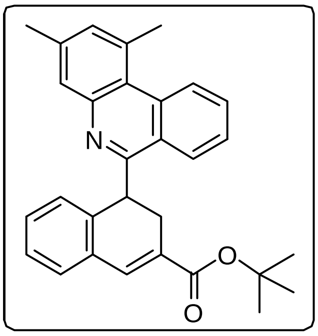
^{1}H NMR (500 MHz) : δ 1.53 (s, 9H), 2.63 (s, 3H), 3.07 (dd, J = 17.5, 7.5 Hz, 1H), 3.36–3.47 (m, 1H), 5.26 (dd, J = 15.5, 7.5 Hz, 1H), 6.57 (d, J = 7.5 Hz, 1H), 7.00 (td, J = 7.5, 1.0 Hz, 1H), 7.17 (t, J = 7.5 Hz, 1H), 7.31 (d, J = 7.0 Hz, 1H), 7.53–7.58 (m, 2H), 7.60 (d, J = 2.5 Hz, 1H), 7.77–7.83 (m, 1H), 8.03 (d, J = 8.5 Hz, 1H), 8.15 (d, J = 8.0 Hz, 1H), 8.38 (s, 1H), 8.69 (d, J = 8.5 Hz, 1H).

^{13}C NMR (125 MHz) : δ 22.06, 28.26, 28.61, 44.10, 80.66, 121.58, 122.76, 123.58, 125.54, 126.85, 126.88, 127.06, 127.38, 128.61, 129.48, 129.90, 130.18, 130.43, 131.30, 132.87, 133.21, 135.34, 136.77, 138.53, 142.21, 160.92, 166.61.

HRMS (ESI) exact mass calc′d for $C_{29}H_{27}NO_2$+H $(M+H)^+$: 422.2120;

Found : 422.2123.

***tert*-Butyl 4-(1,3-dimethylphenanthridin-6-yl)-3,4-dihydronaphthalene-2-carboxylate (138c)**



Reaction time : 4 h

Yield : 47% as a yellow solid.

Mp : 177–179 °C

IR (neat) : ν 1696, 1624 cm^{-1}

^{1}H NMR (500 MHz) : δ 1.53 (s, 9H), 2.52 (s, 3H), 3.01–3.14 (m, 4H)$^{\#}$, 3.44 (t, J = 15.5 Hz, 1H), 5.27 (dd, J = 15.0, 7.0 Hz, 1H), 6.58 (d, J = 7.0 Hz, 1H), 7.00 (t, J = 7.0 Hz, 1H), 7.18 (t, J = 7.0 Hz, 1H), 7.28–7.38 (m, 2H)$^{\$}$, 7.52–7.64 (m, 2H)$^{@}$, 7.79 (t, J = 7.5 Hz, 1H), 7.85 (s, 1H), 8.22 (d, J = 8.5 Hz, 1H), 8.92 (d, J = 8.5 Hz, 1H).

$^{\#}$ It contains a singlet at 3.11 for 3H and a dd for 1H

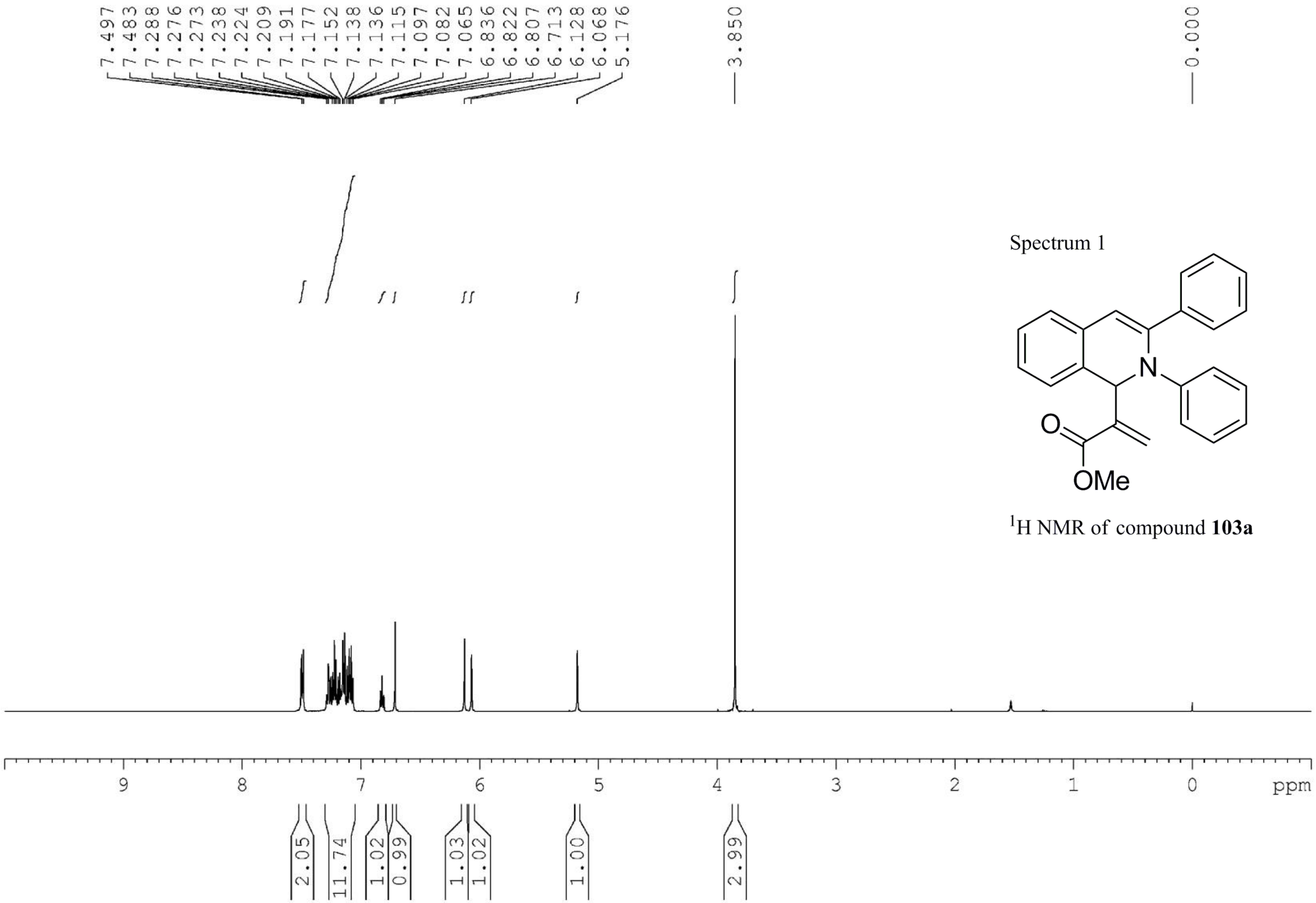
$^{\$}$ It contains a doublet at 7.32 for 1H and a singlet at 7.35 for 1H

$^{@}$ It contains a triplet at 7.56 for 1H and a singlet at 7.60 for 1H

^{13}C NMR (125 MHz) : δ 21.12, 26.72, 28.29, 28.59, 43.92, 80.64, 121.09, 126.01, 126.20, 126.76, 126.85, 126.96, 127.43, 128.58, 128.79, 129.47, 129.51, 131.42, 132.96, 134.61, 134.81, 135.33, 137.80, 138.57, 145.59, 161.41, 166.63.

HRMS (ESI) exact mass calc′d for $C_{30}H_{29}NO_2$+H (M+H)$^+$: 436.2277;

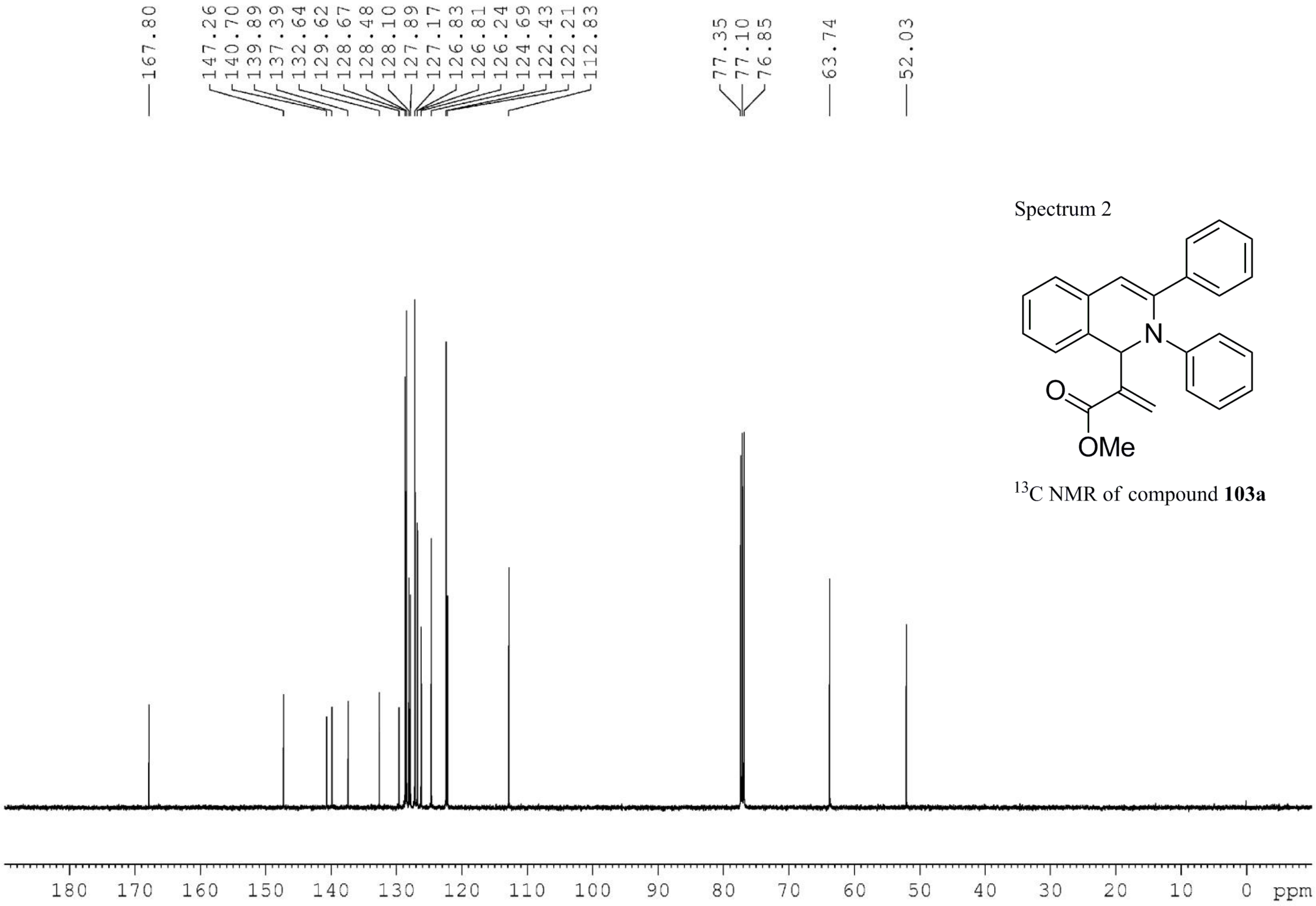
Found : 436.2277.



Spectrum 1

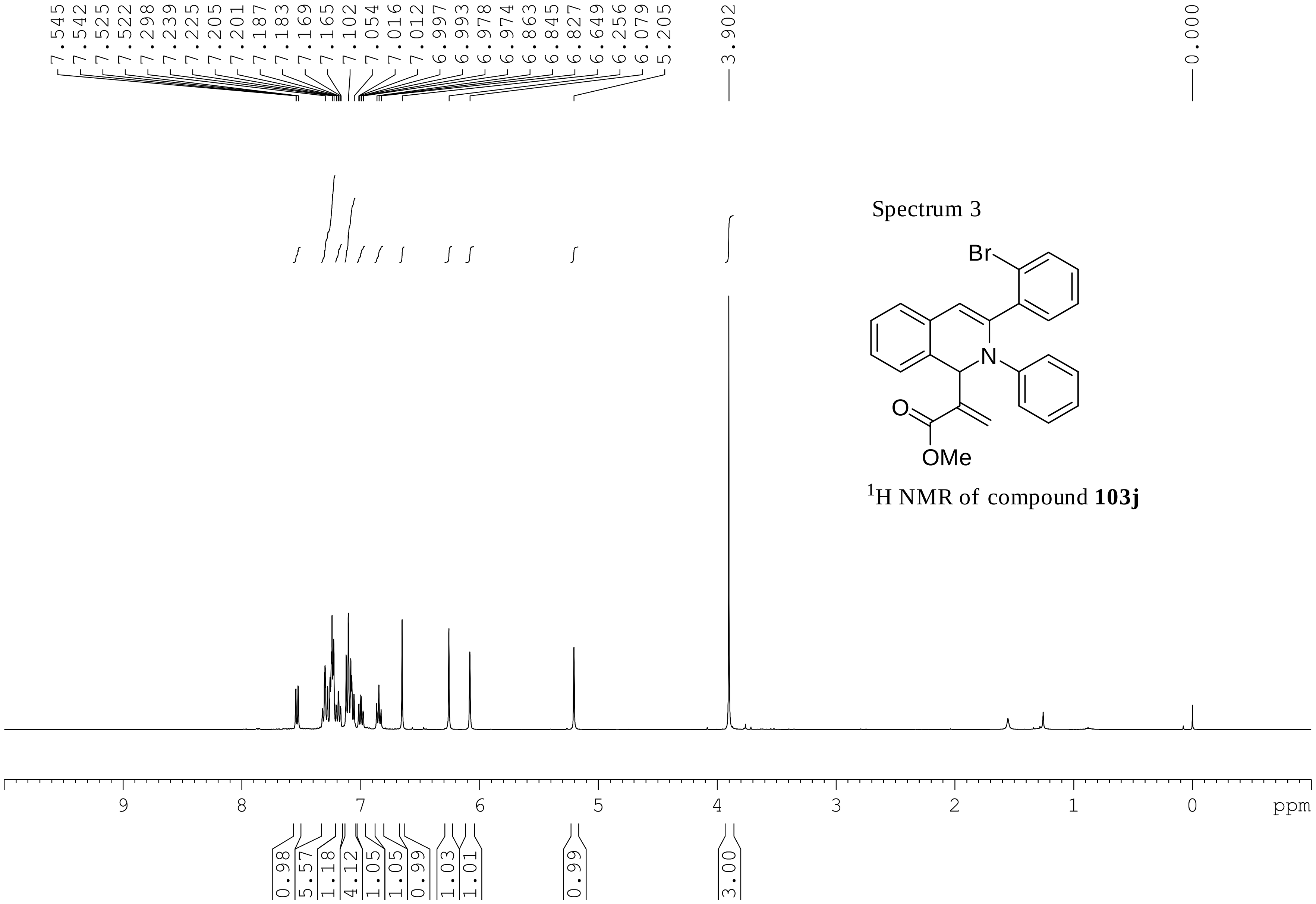
^{1}H NMR of compound **103a**

Spectrum 2



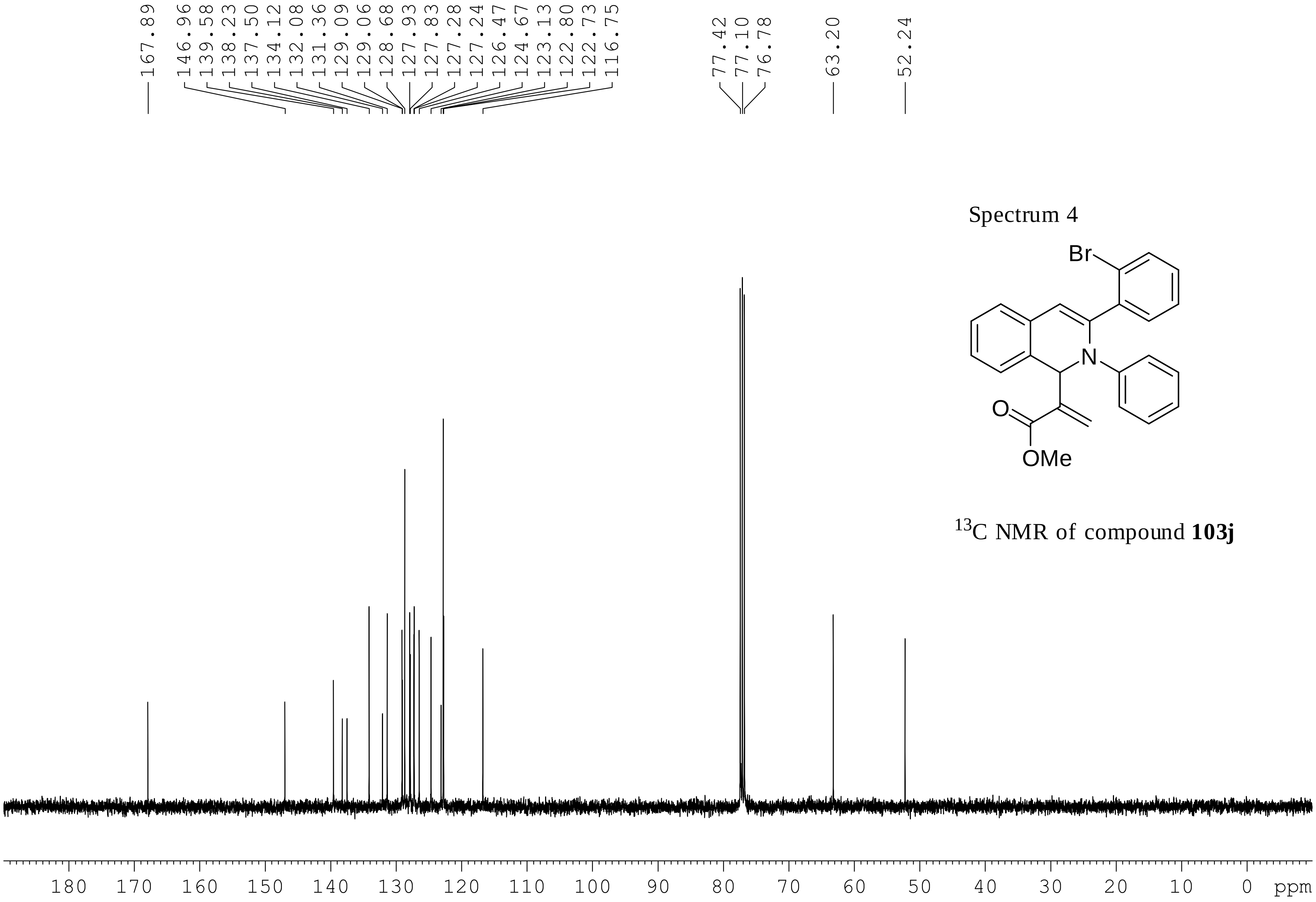
^{13}C NMR of compound **103a**

Spectrum 3



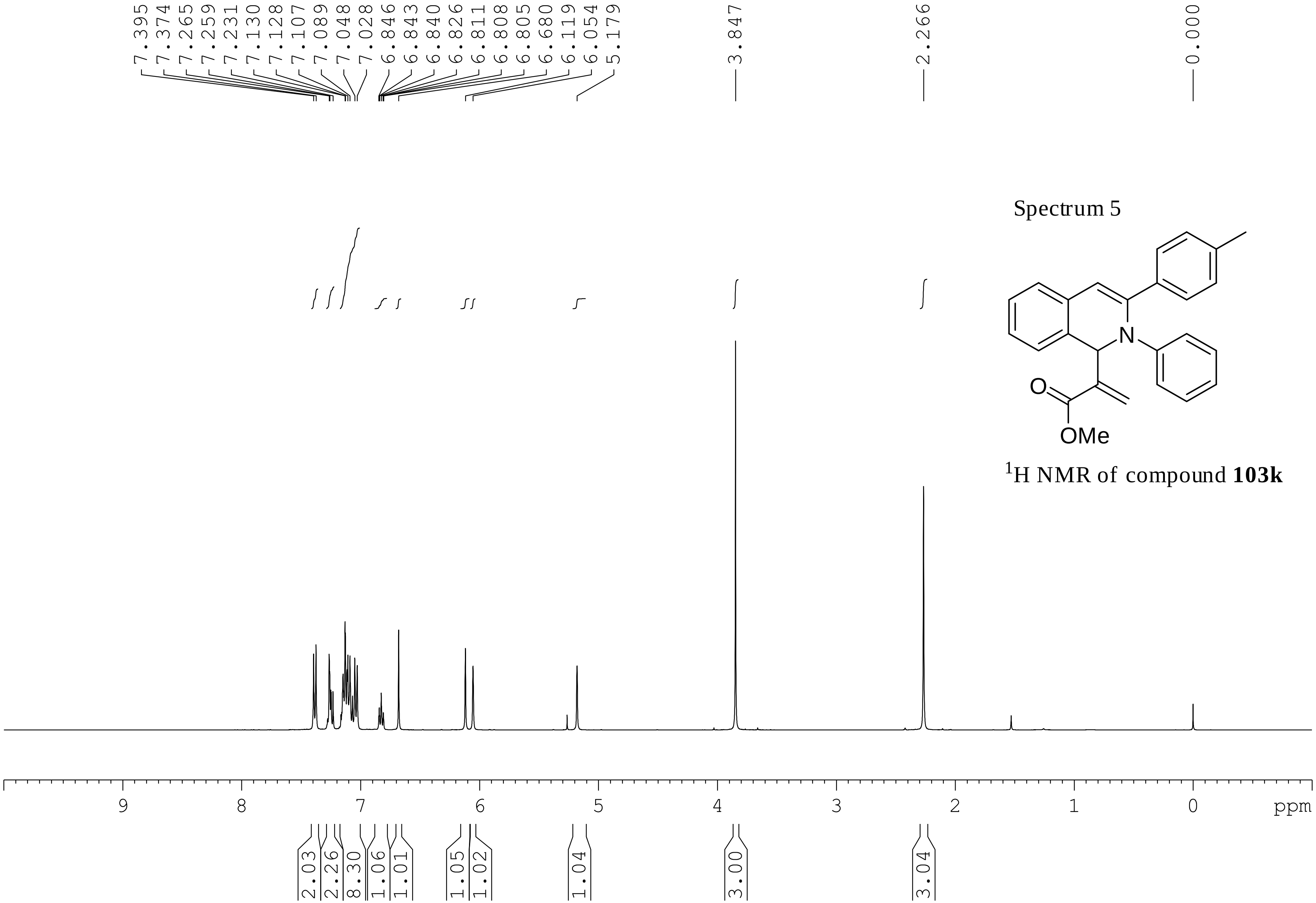
^{1}H NMR of compound **103j**

Spectrum 4



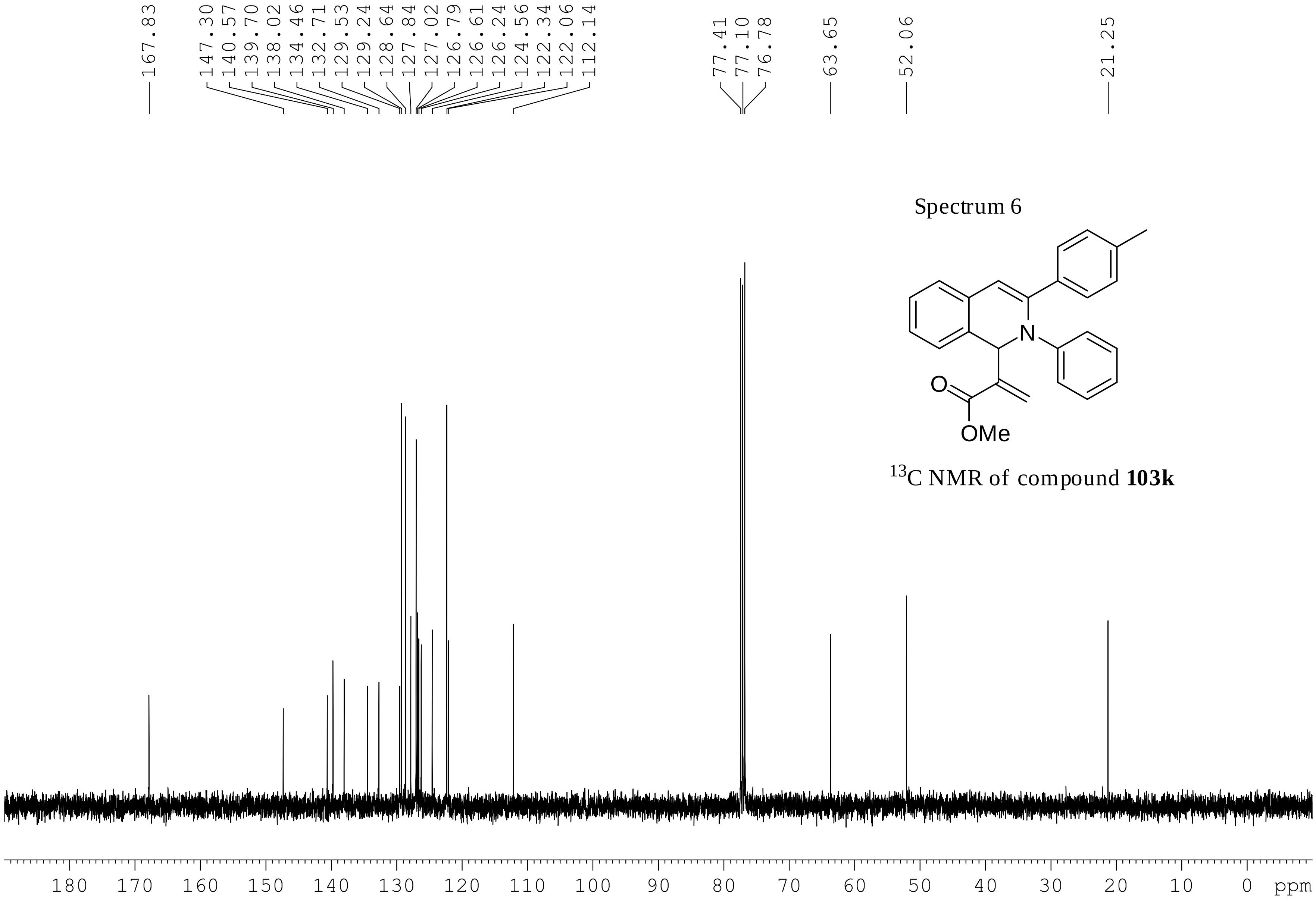
^{13}C NMR of compound **103j**

Spectrum 5



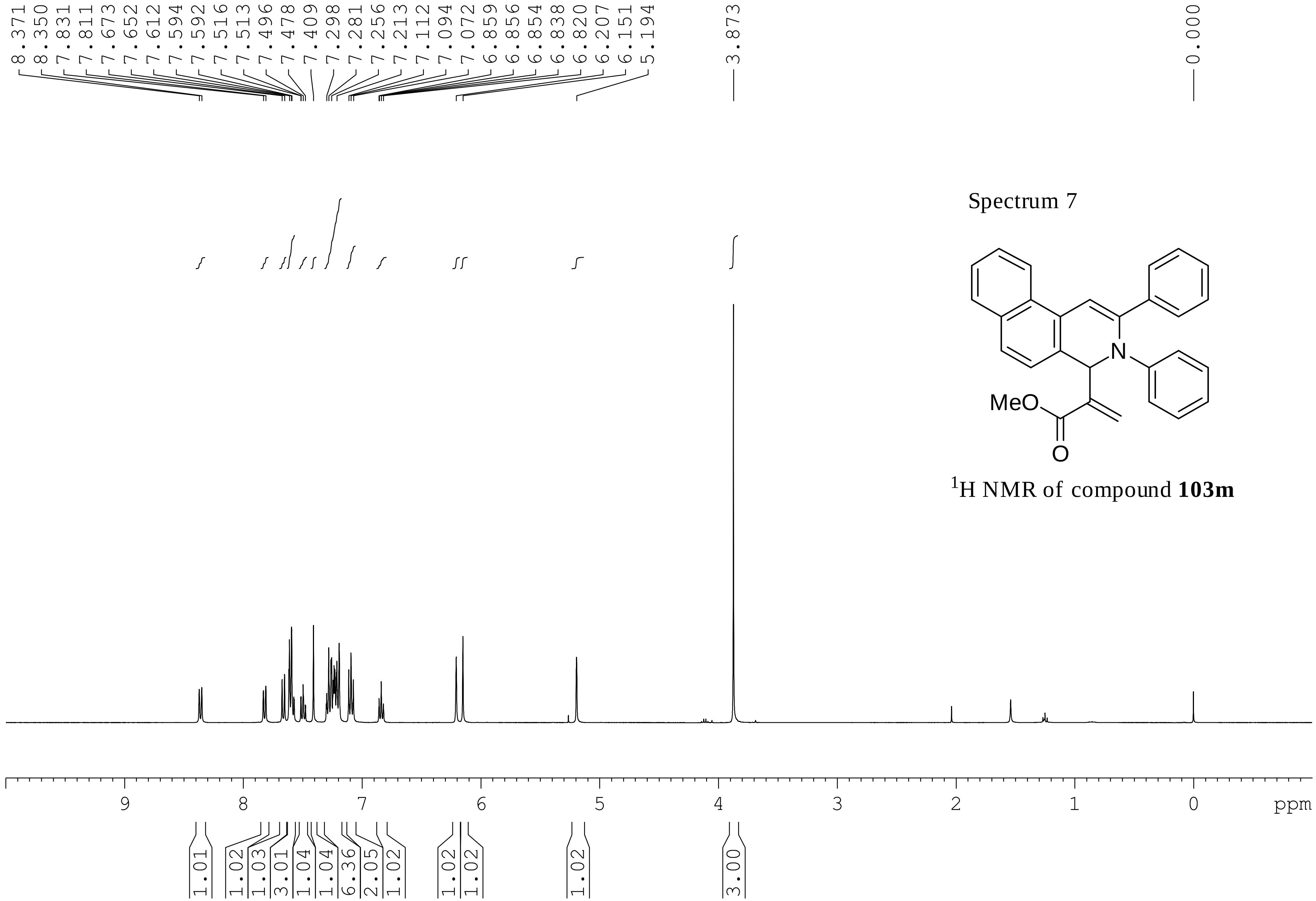
^{1}H NMR of compound **103k**

Spectrum 6



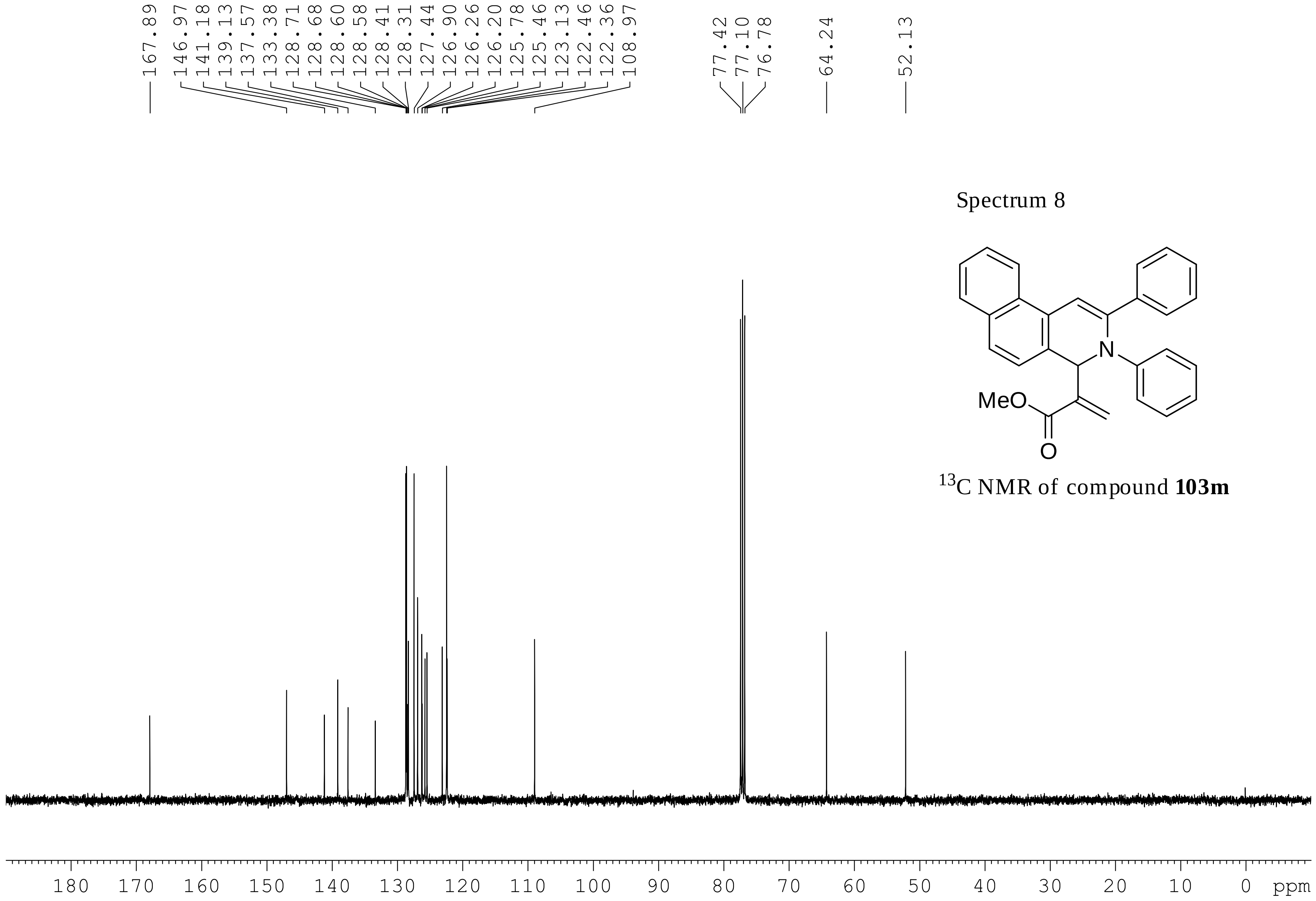
^{13}C NMR of compound **103k**

Spectrum 7



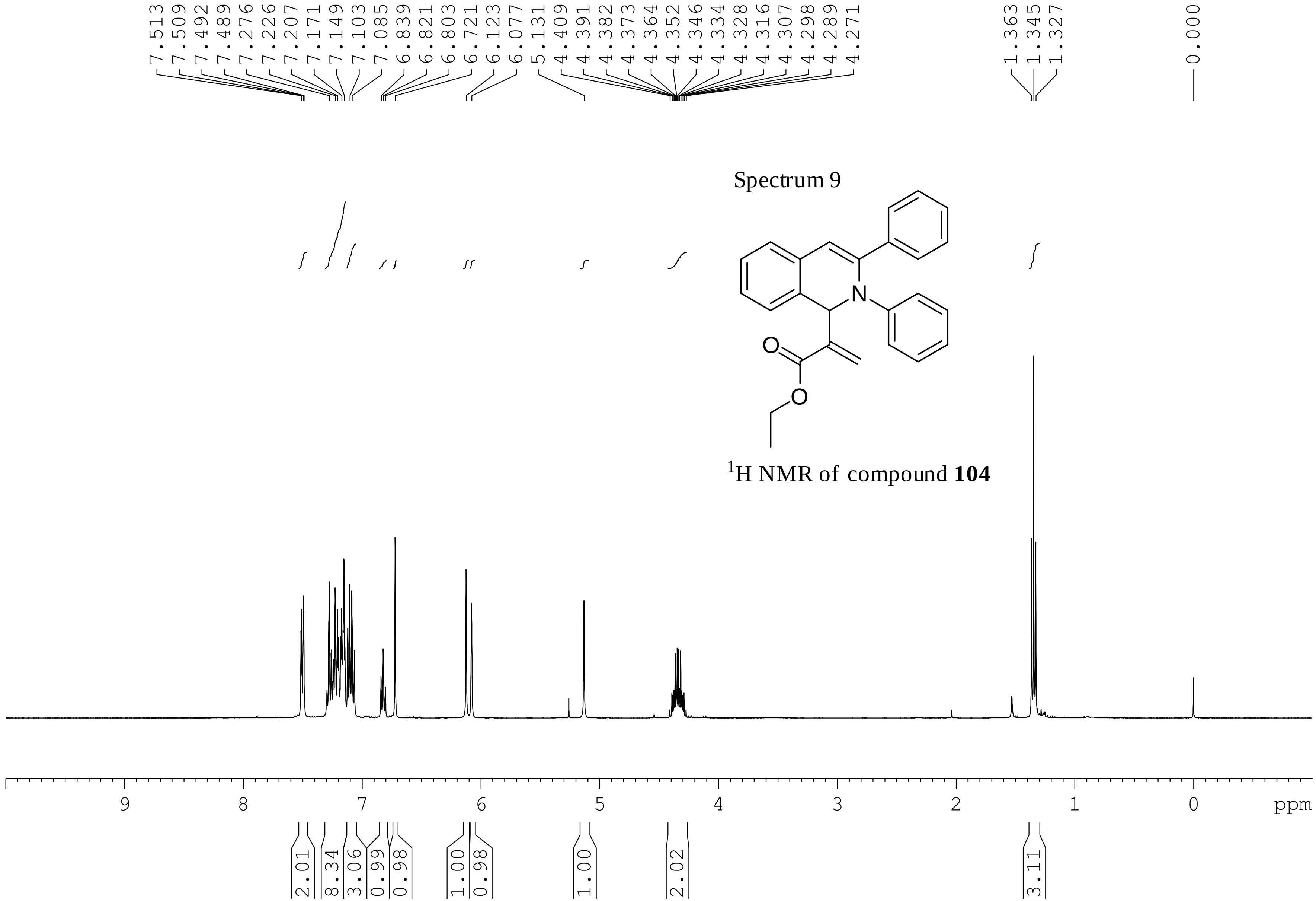
^{1}H NMR of compound **103m**

Spectrum 8

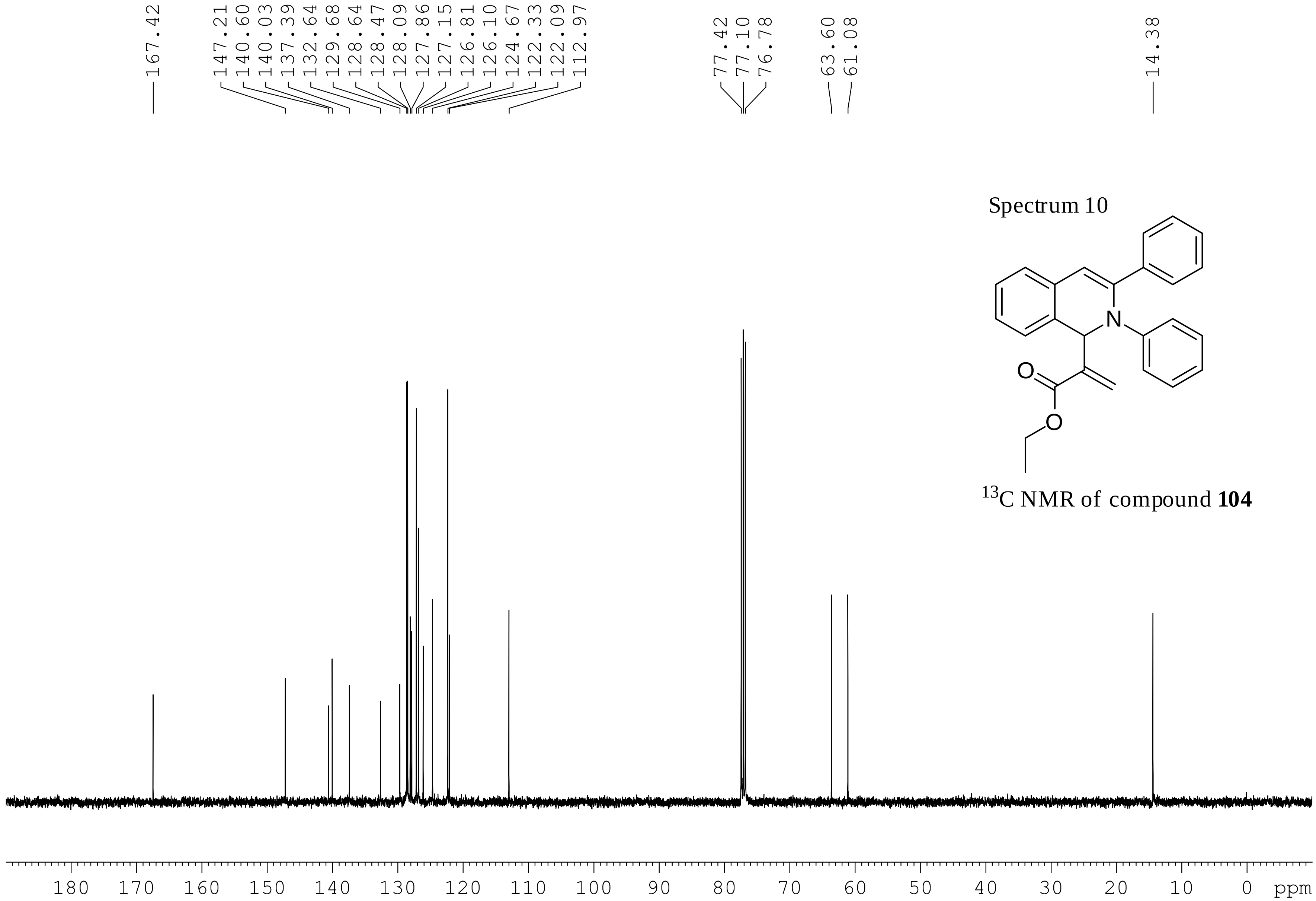


^{13}C NMR of compound **103m**

Spectrum 9



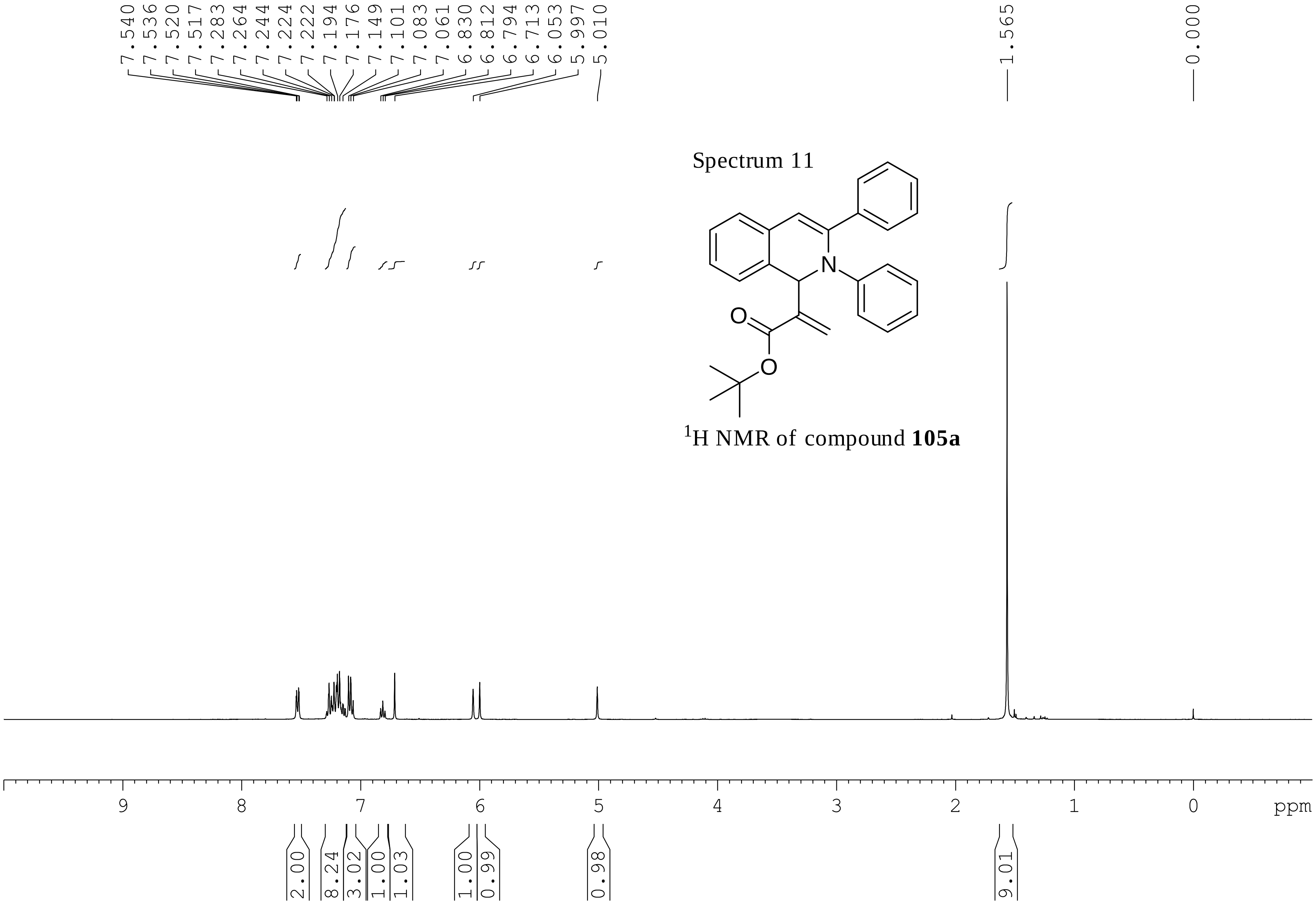
^{1}H NMR of compound **104**



Spectrum 10

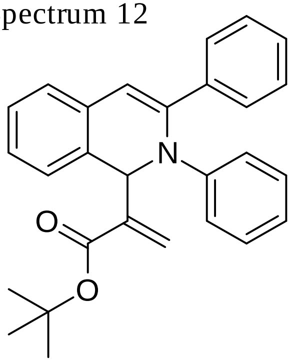
^{13}C NMR of compound **104**

Spectrum 11

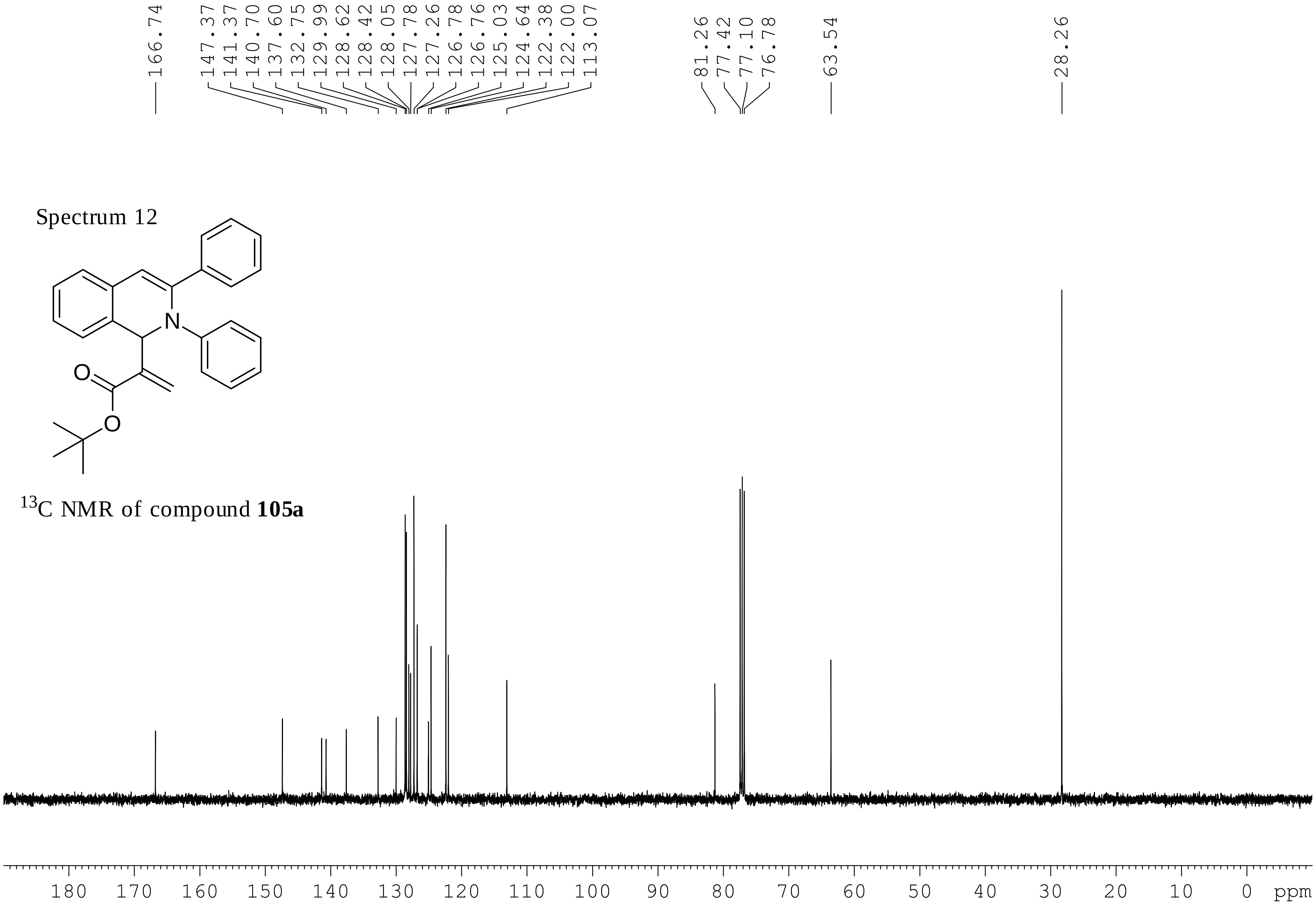


^{1}H NMR of compound **105a**

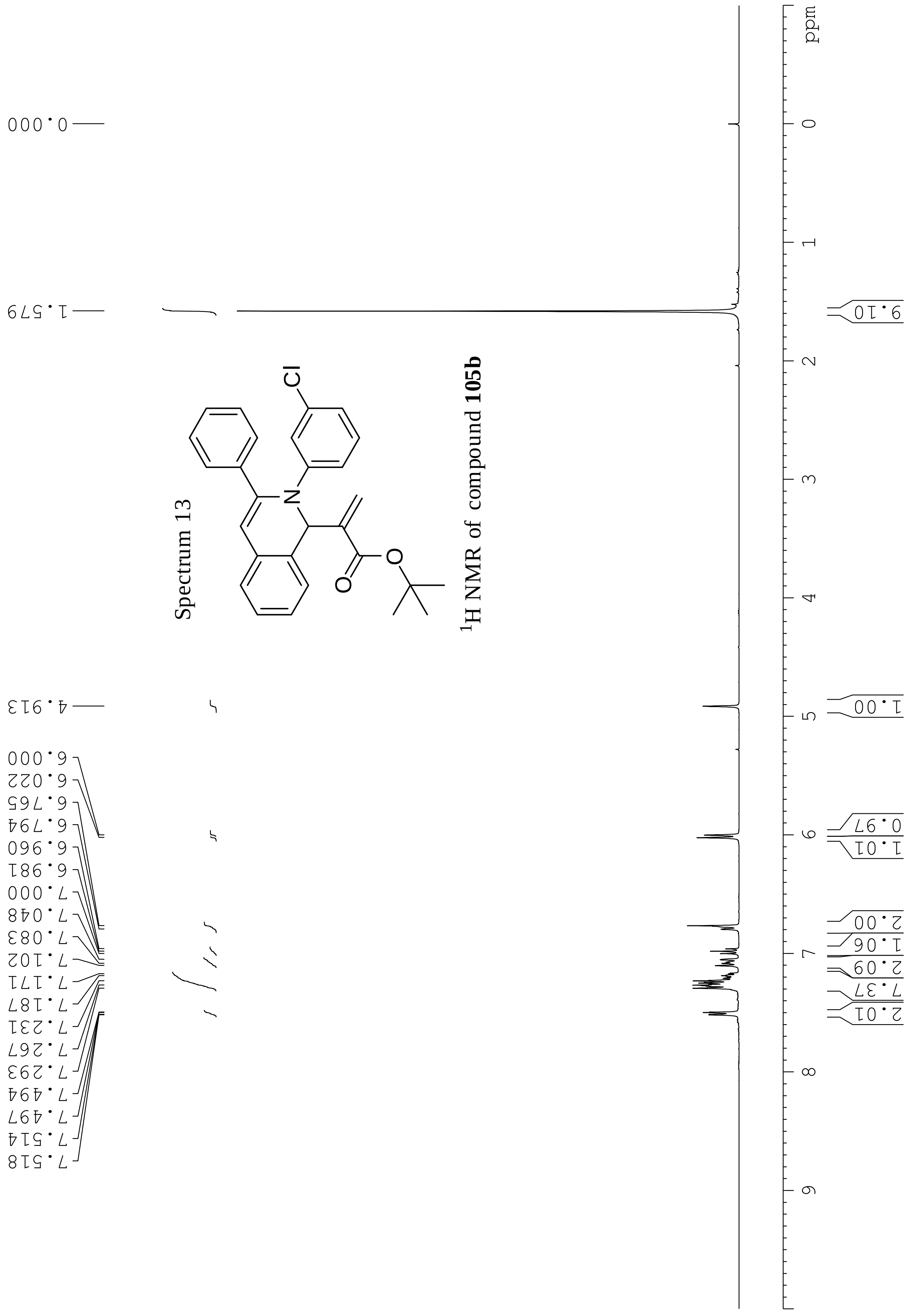
Spectrum 12



^{13}C NMR of compound **105a**

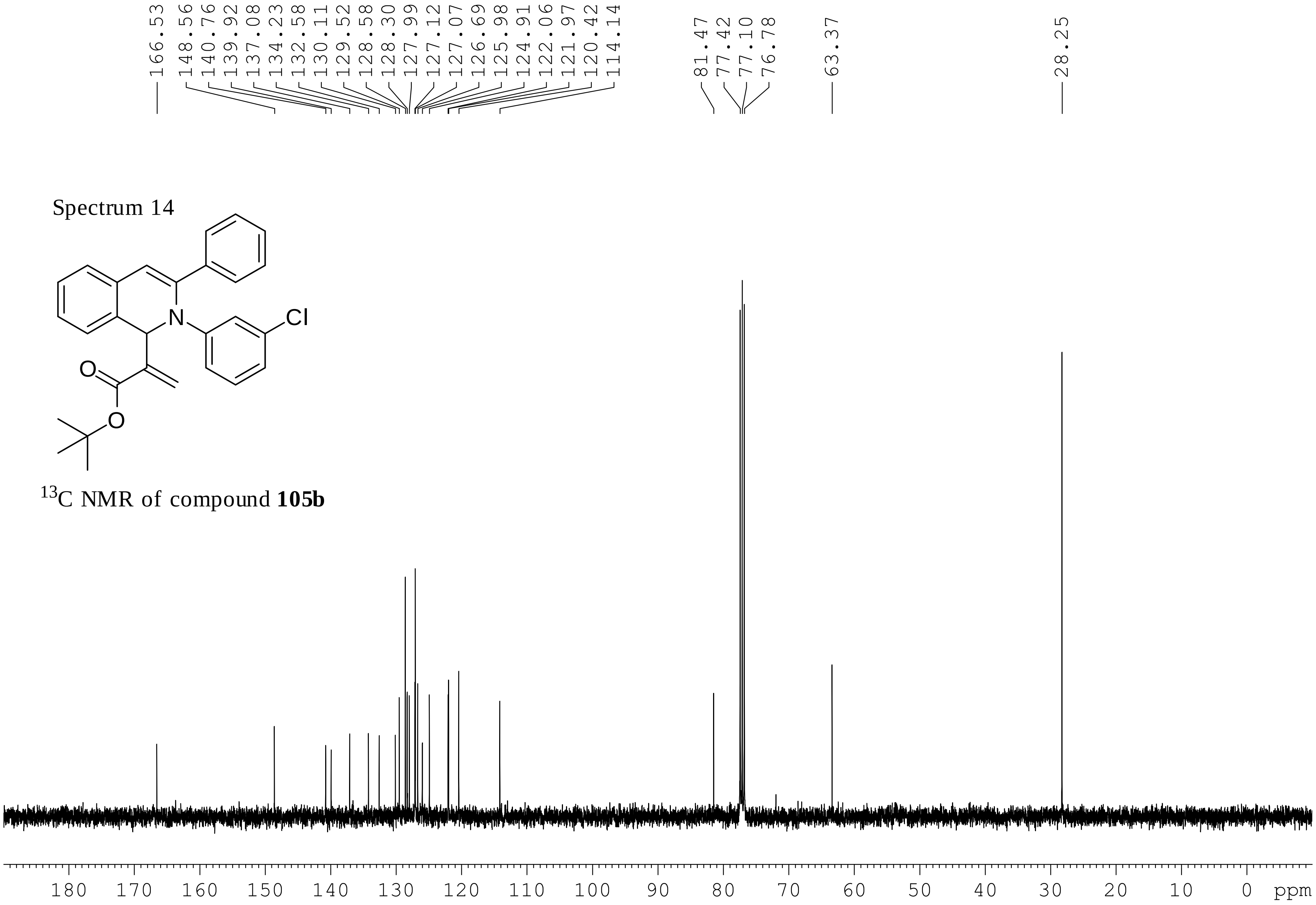


Spectrum 13



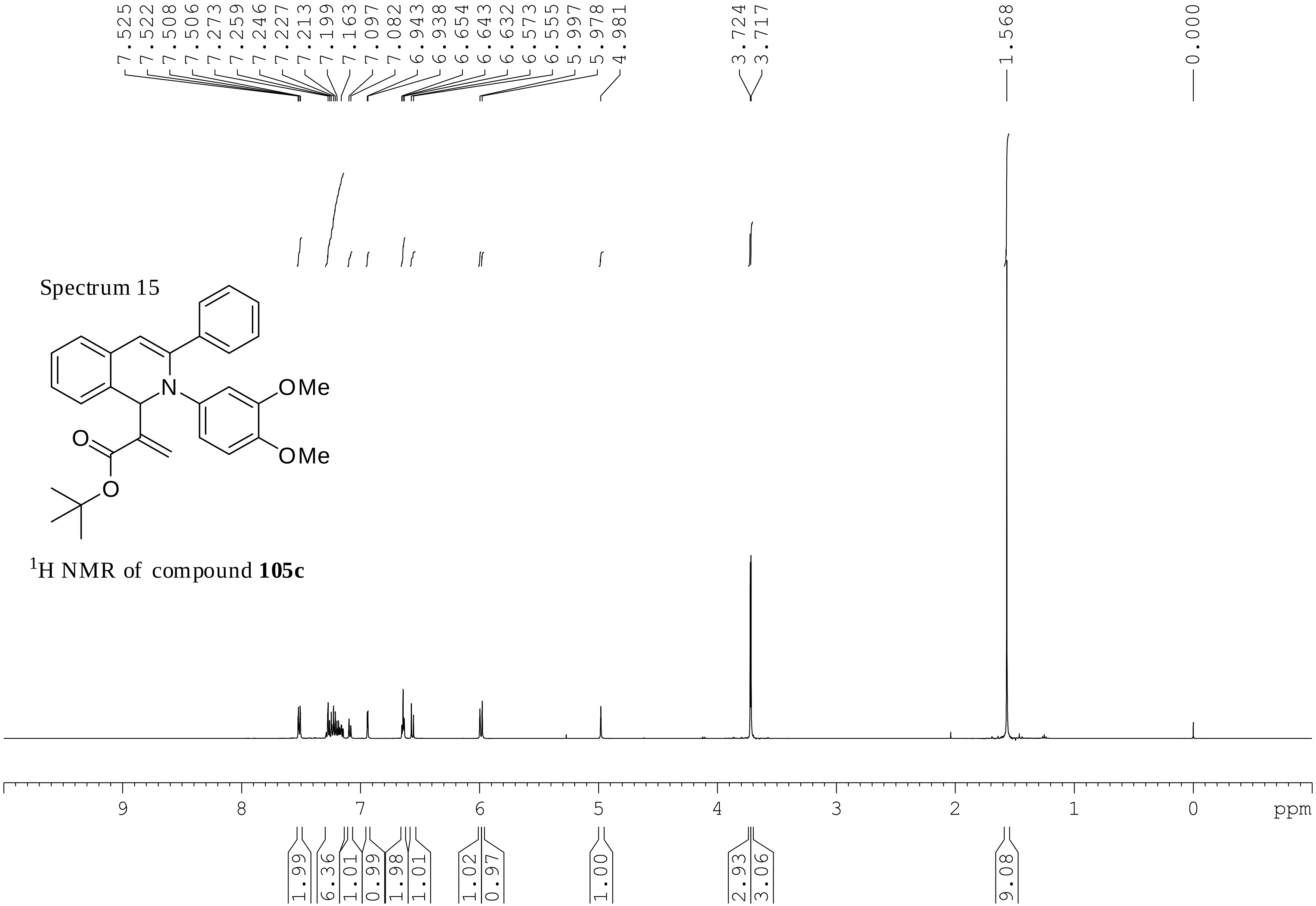
^{1}H NMR of compound **105b**

Spectrum 14

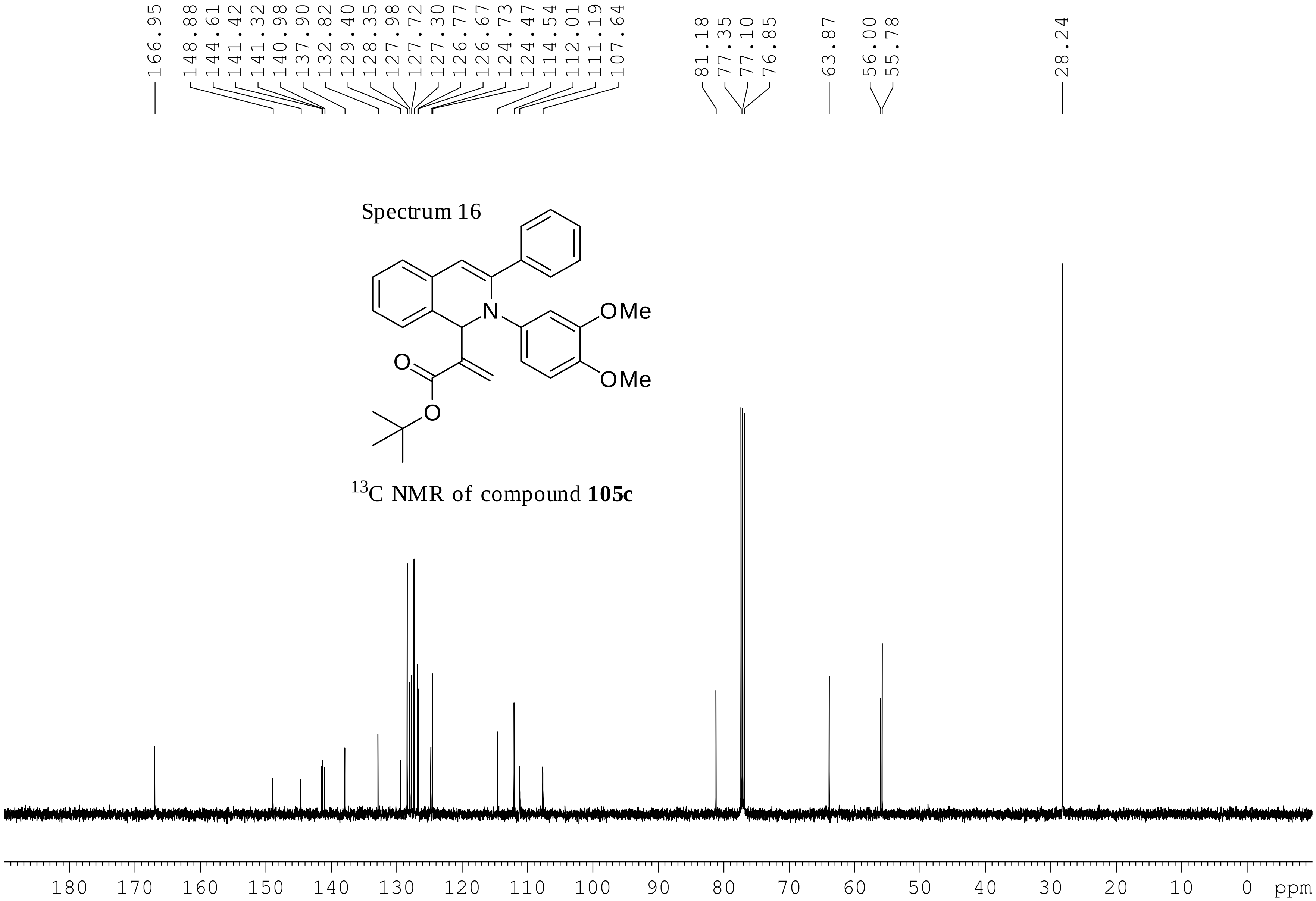


^{13}C NMR of compound **105b**

Spectrum 15



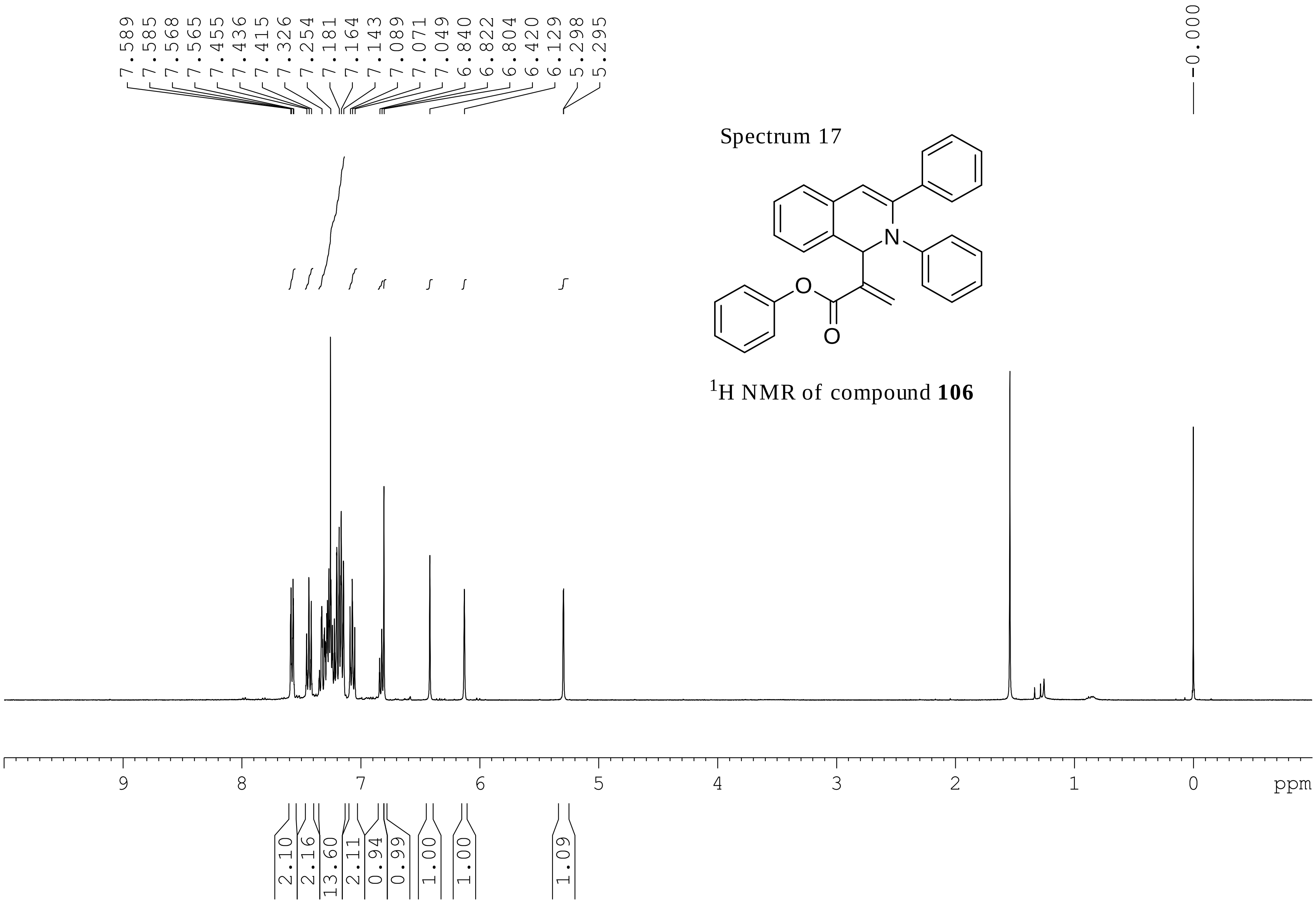
^{1}H NMR of compound **105c**



Spectrum 16

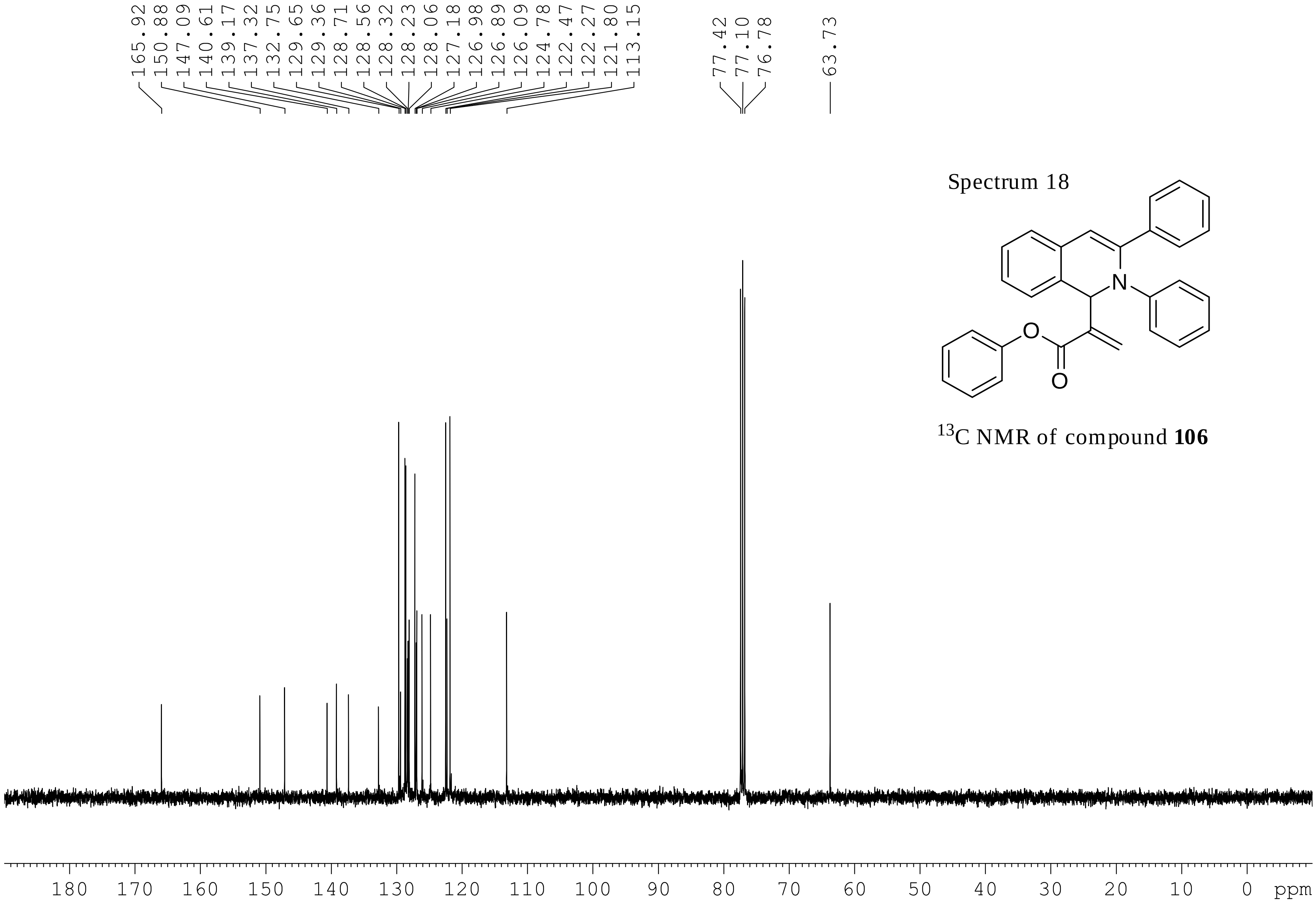
^{13}C NMR of compound **105c**

Spectrum 17



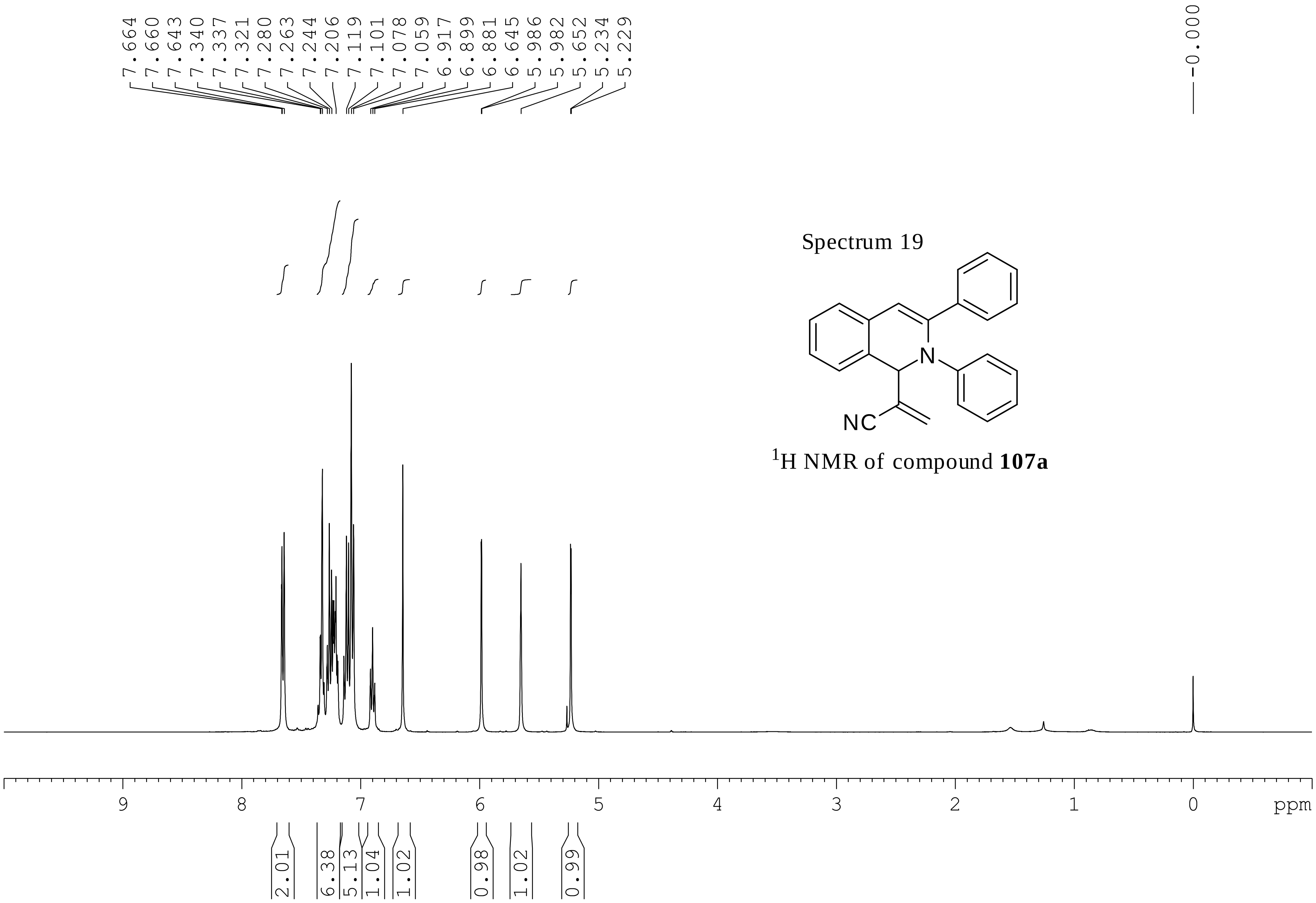
^{1}H NMR of compound **106**

Spectrum 18



^{13}C NMR of compound **106**

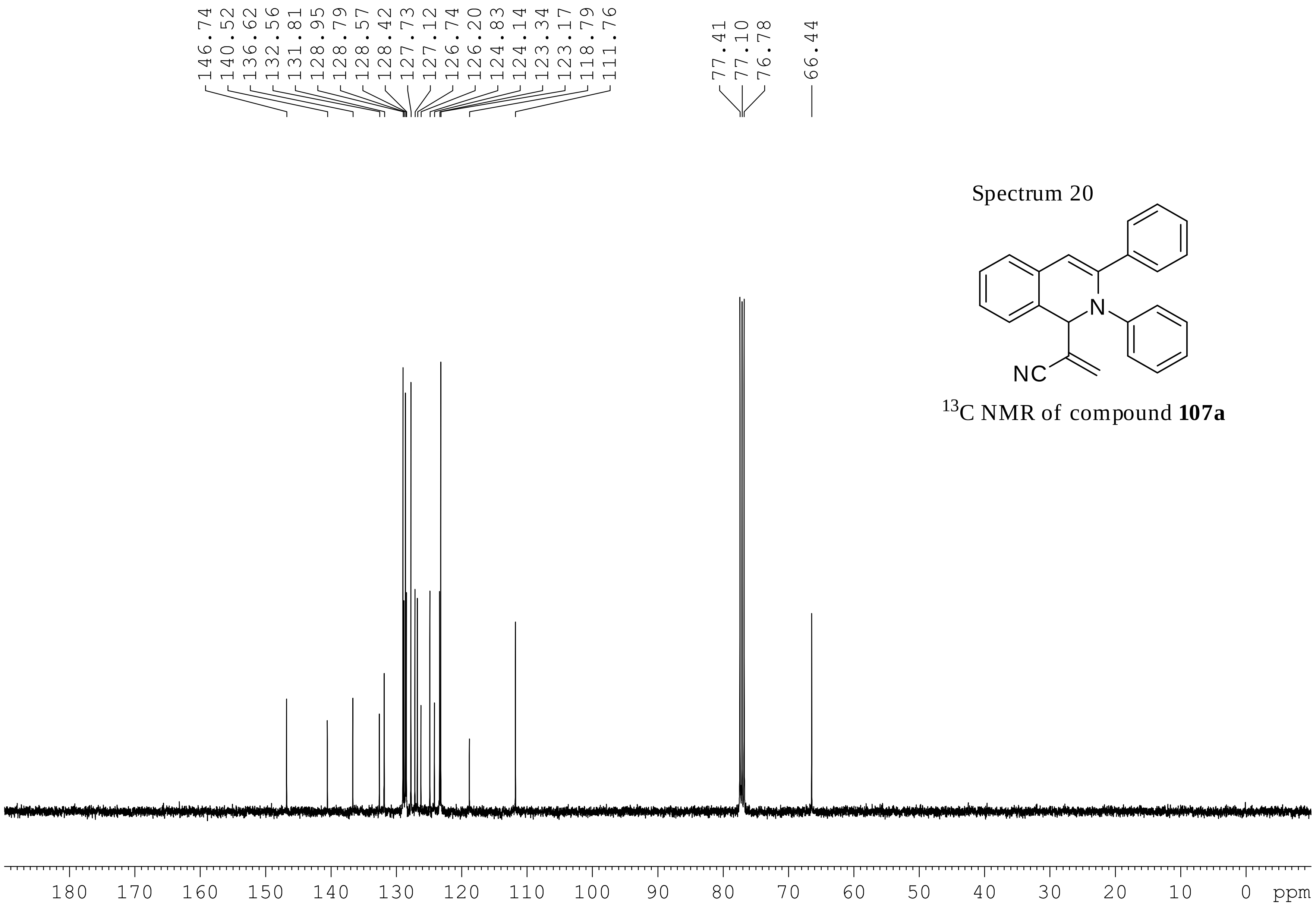
Spectrum 19



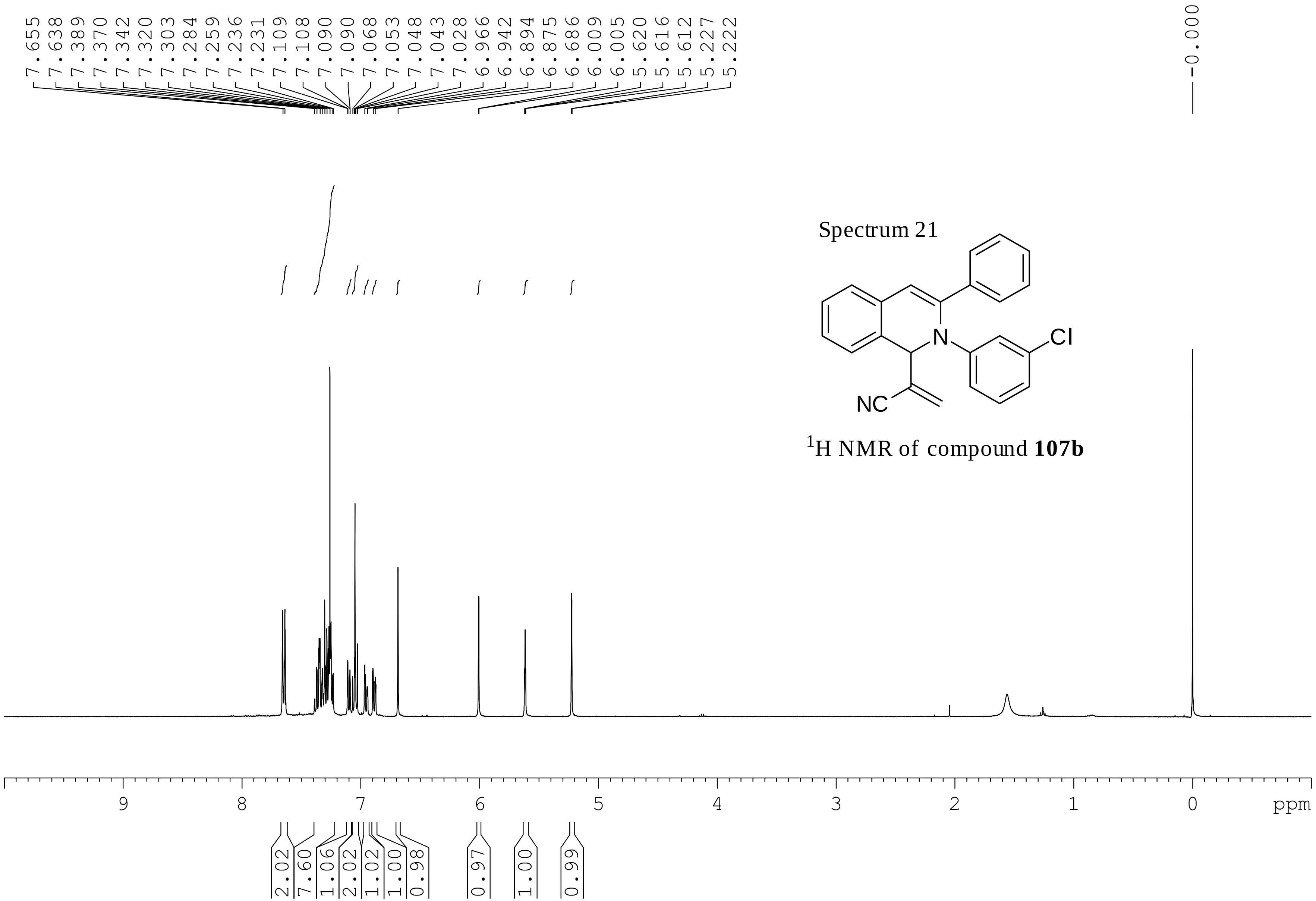
^{1}H NMR of compound **107a**

Spectrum 20

^{13}C NMR of compound **107a**

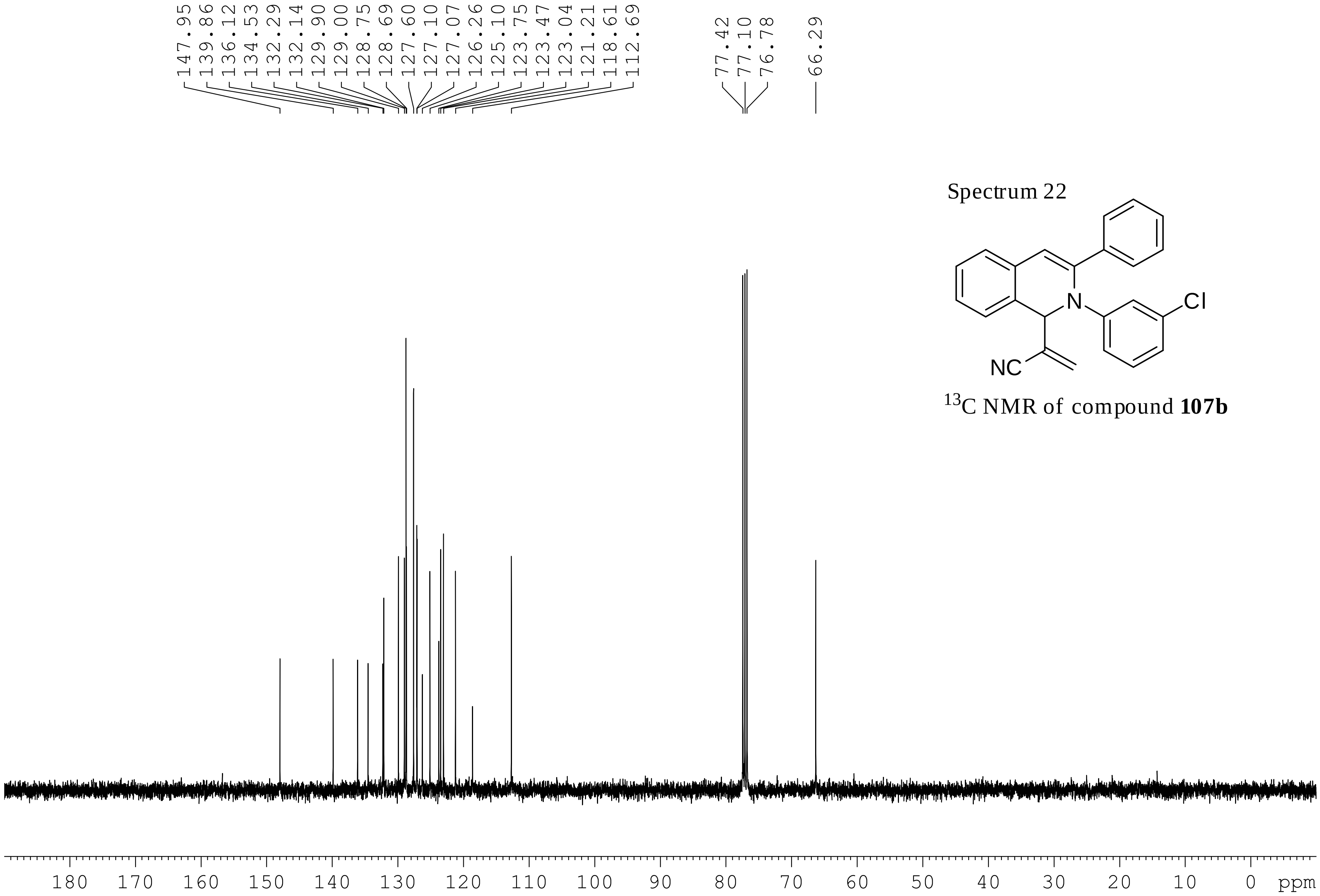


Spectrum 21

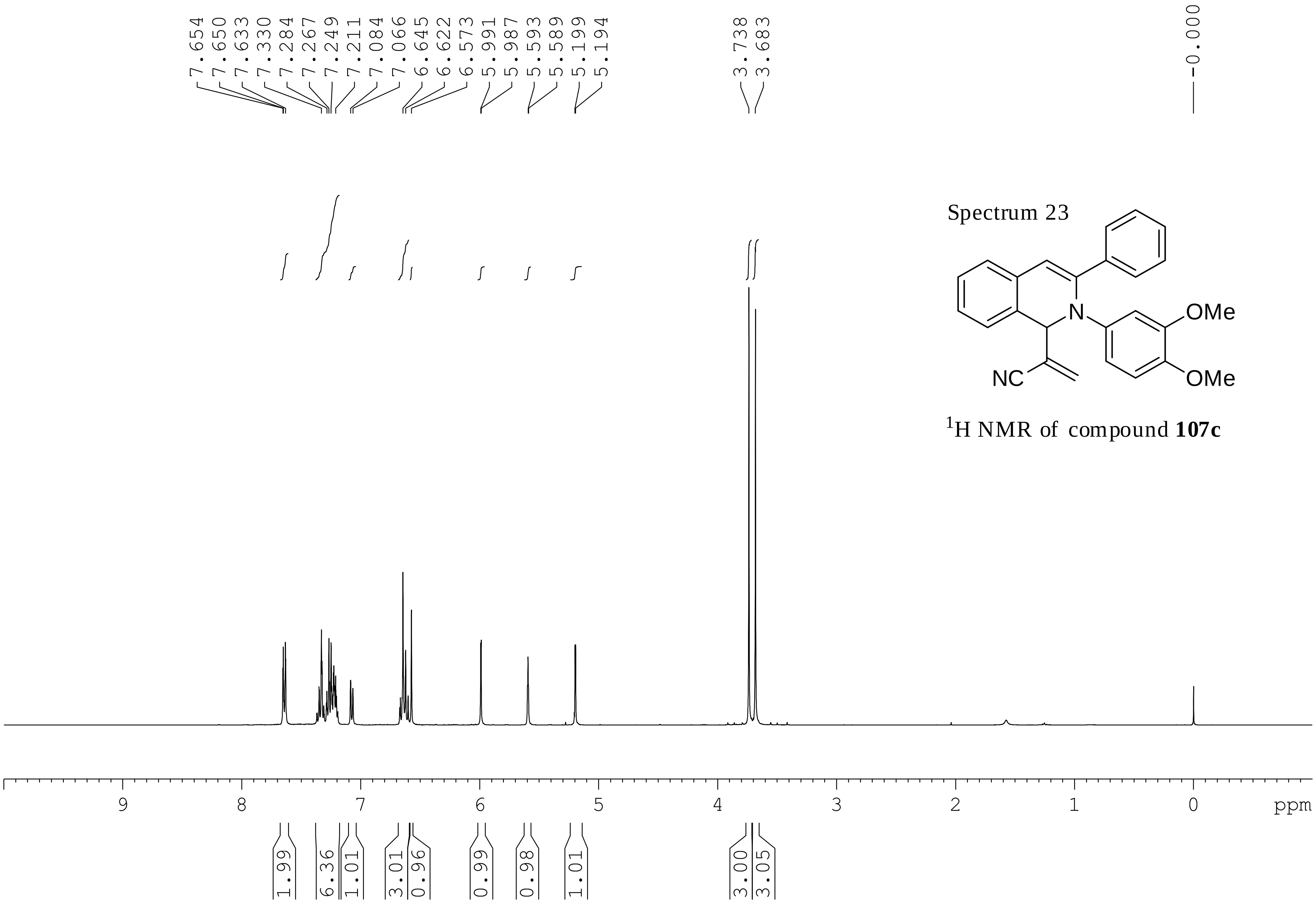


^{1}H NMR of compound **107b**

Spectrum 22



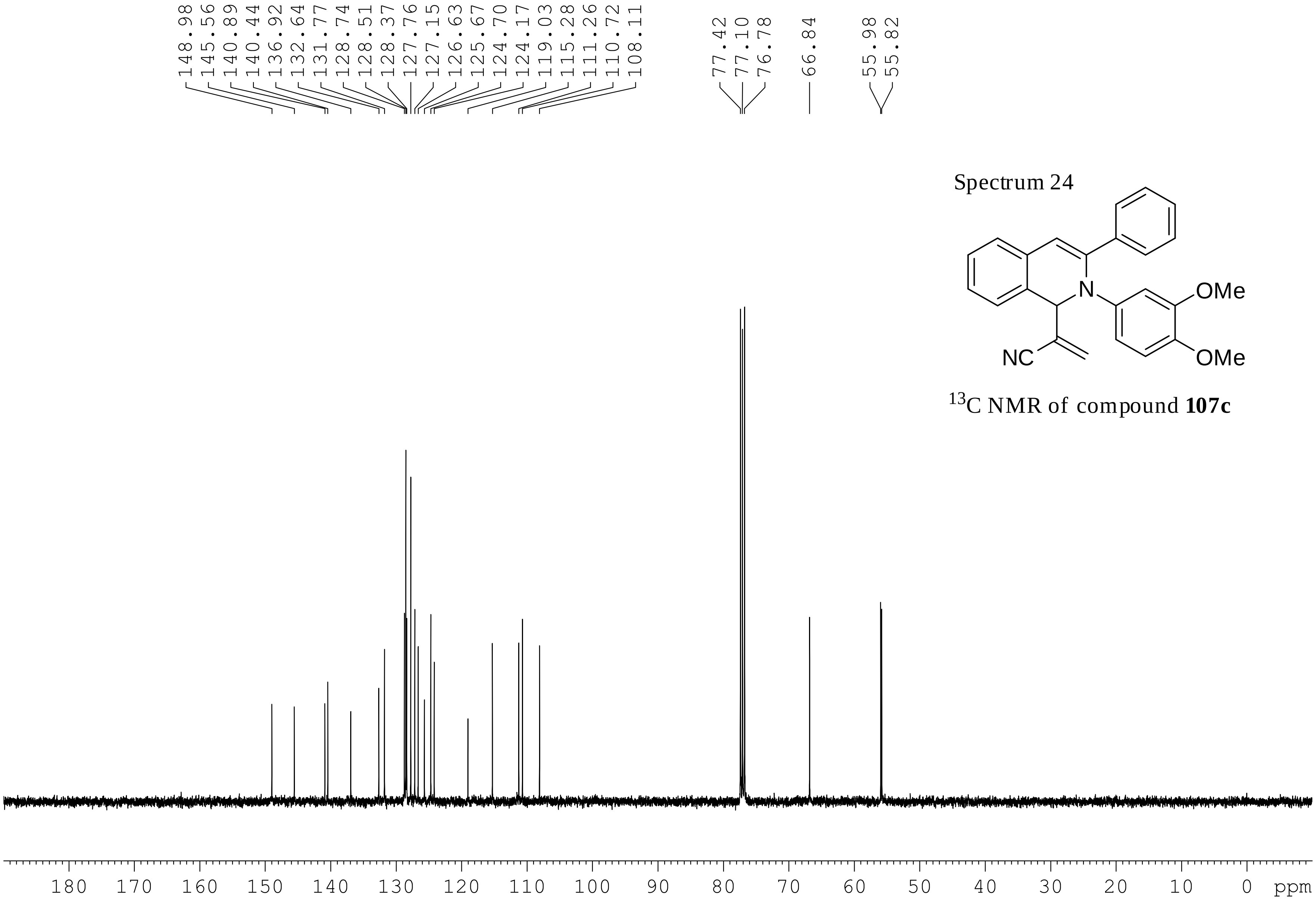
^{13}C NMR of compound **107b**



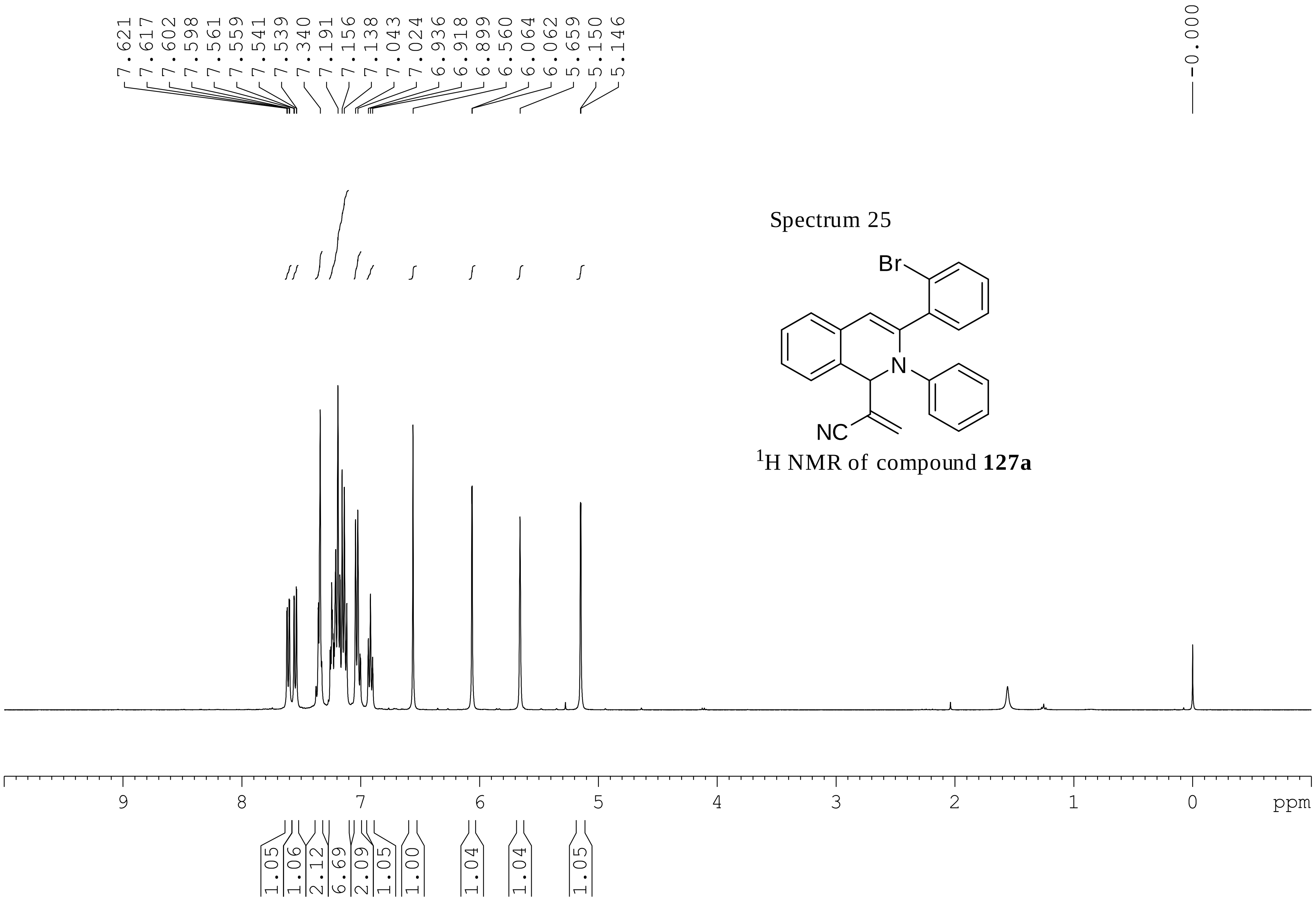
Spectrum 23

^{1}H NMR of compound **107c**

Spectrum 24



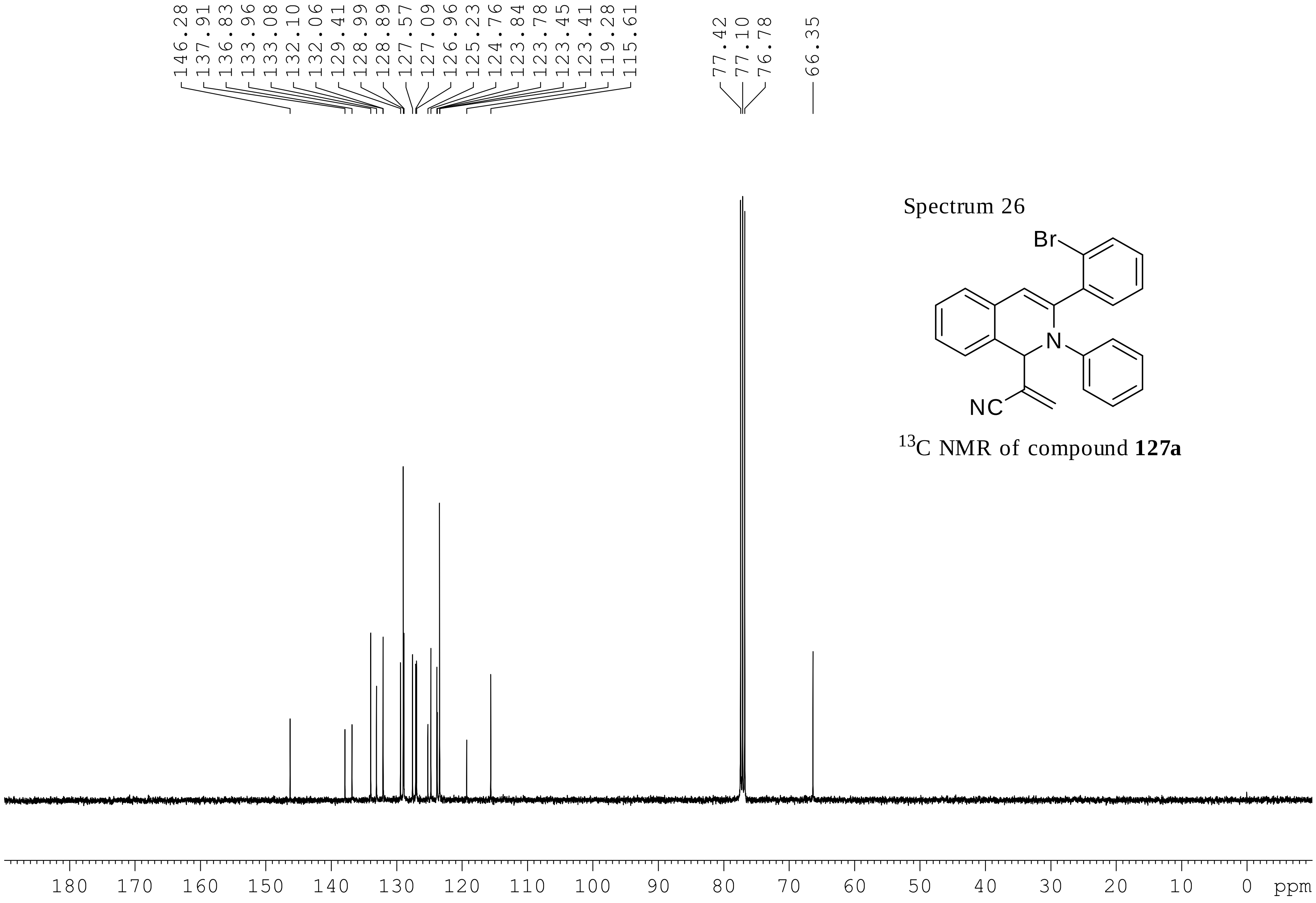
^{13}C NMR of compound **107c**



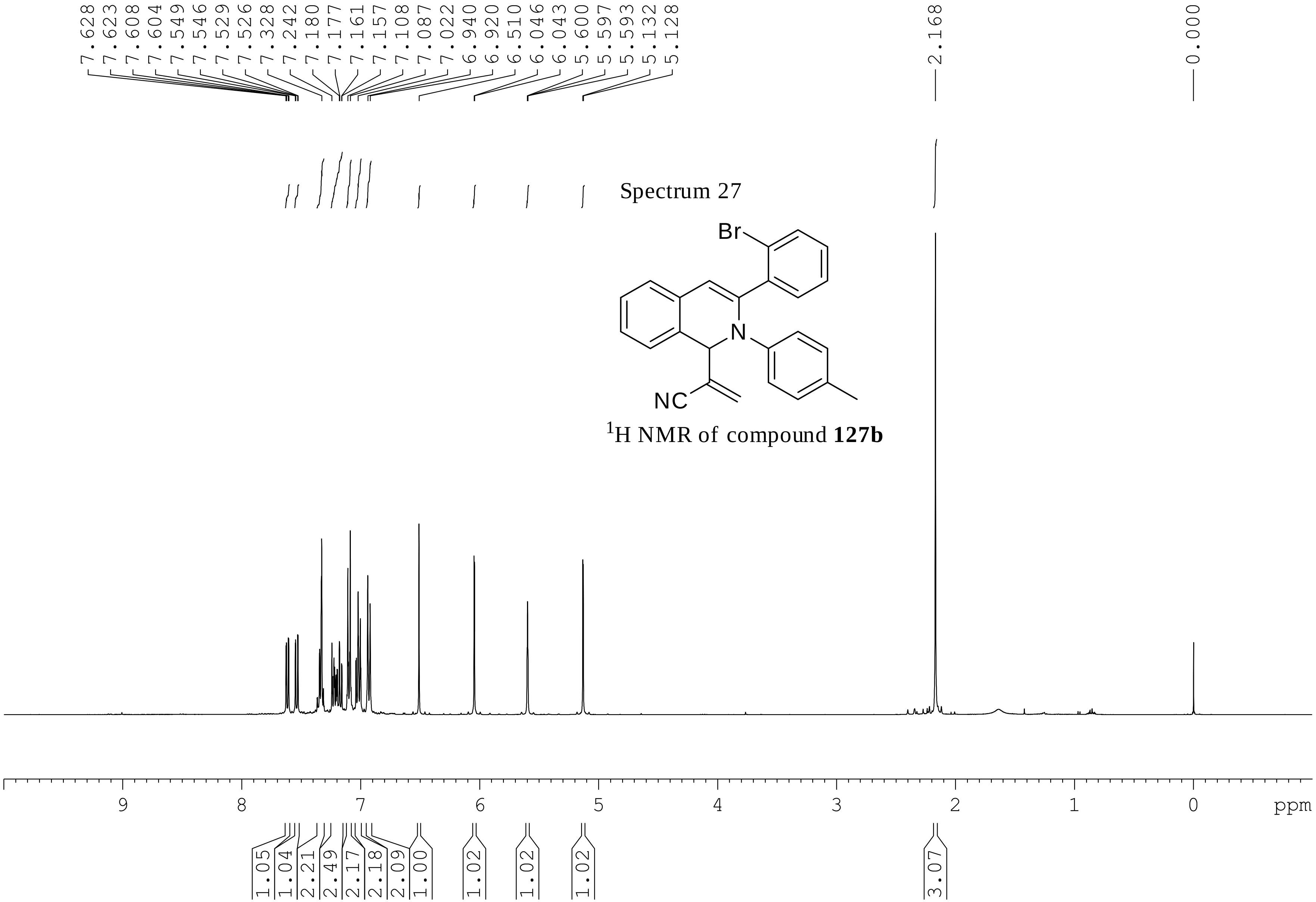
Spectrum 25

^{1}H NMR of compound **127a**

Spectrum 26



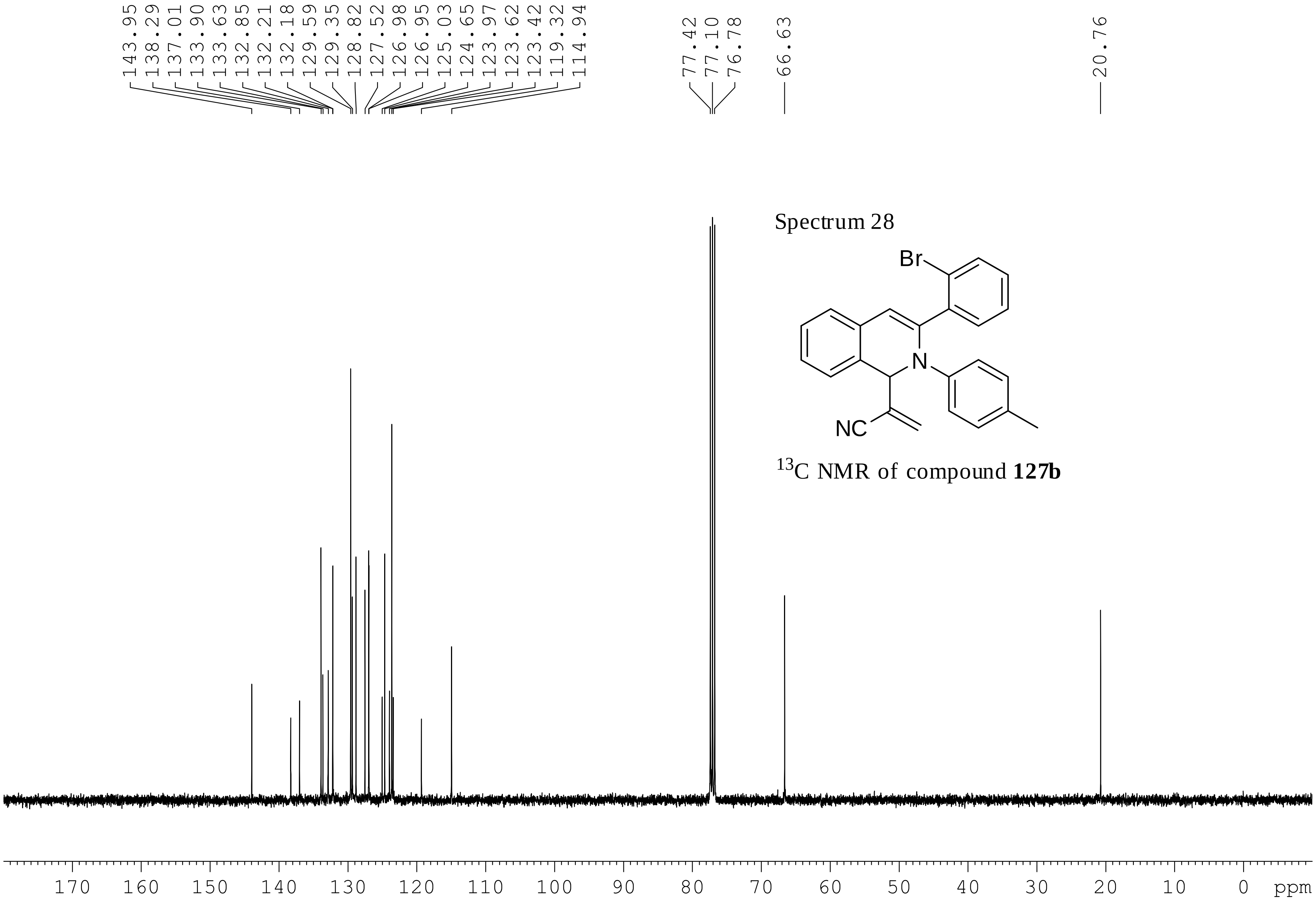
^{13}C NMR of compound **127a**



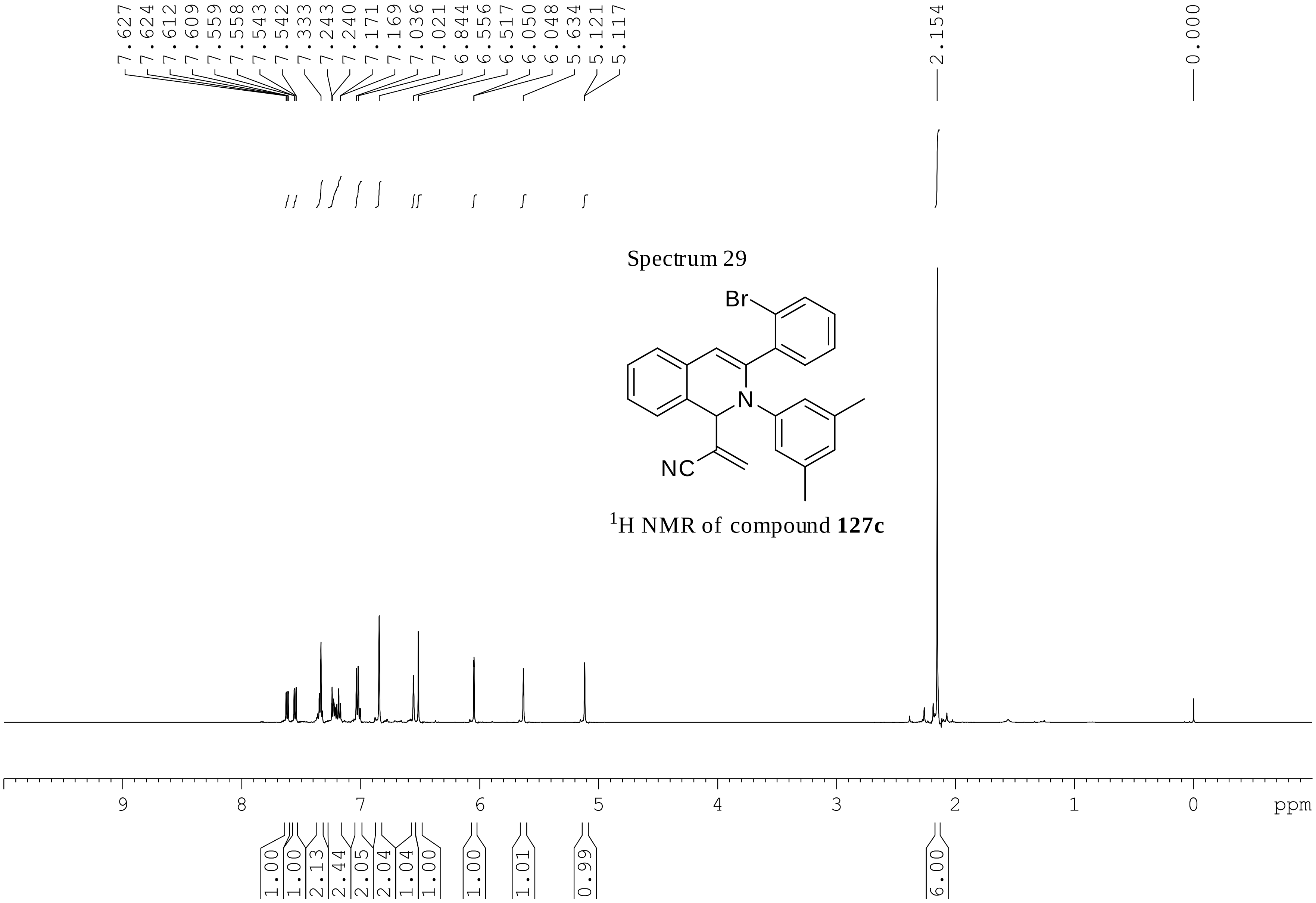
Spectrum 27

^{1}H NMR of compound **127b**

Spectrum 28

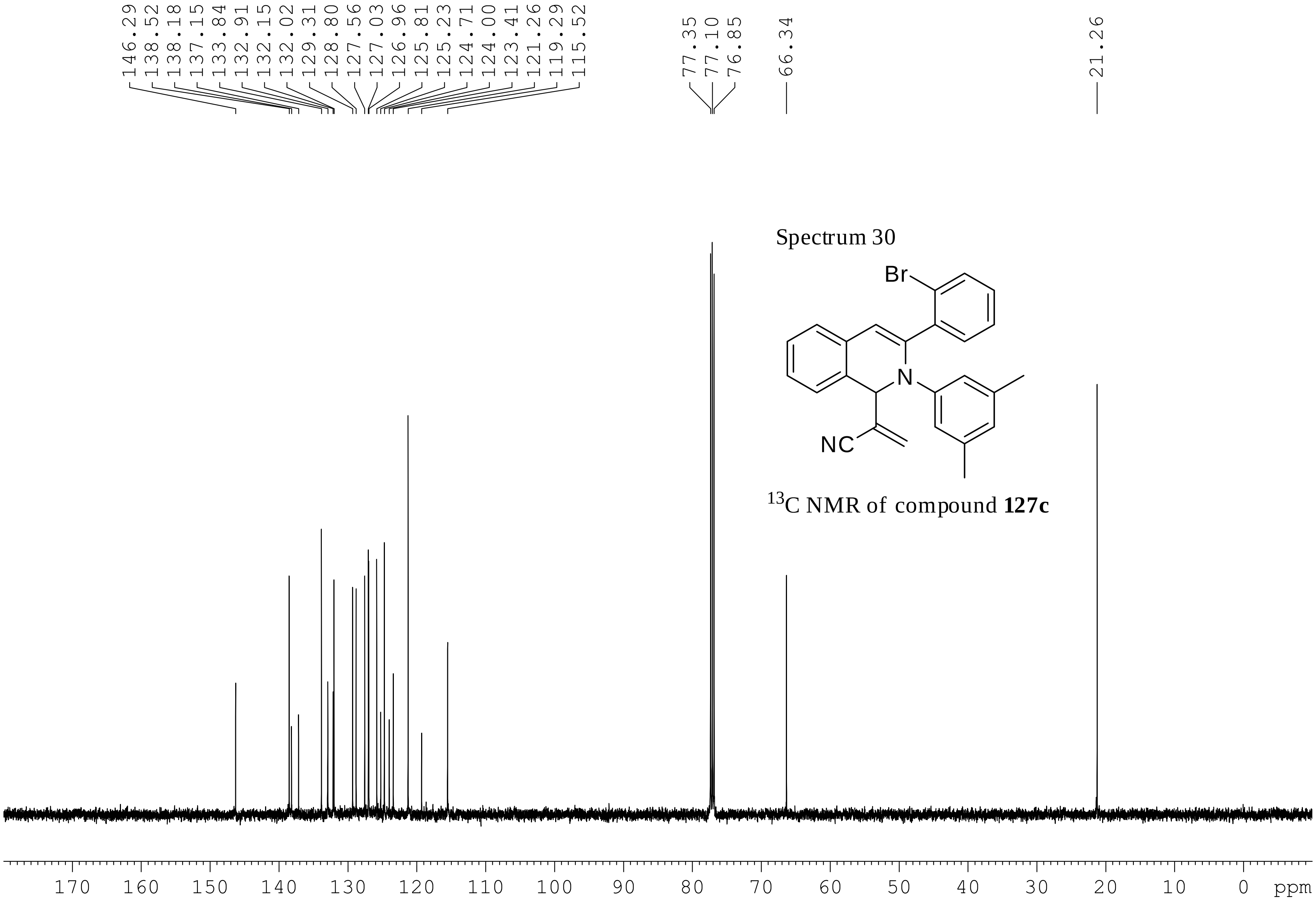


^{13}C NMR of compound **127b**

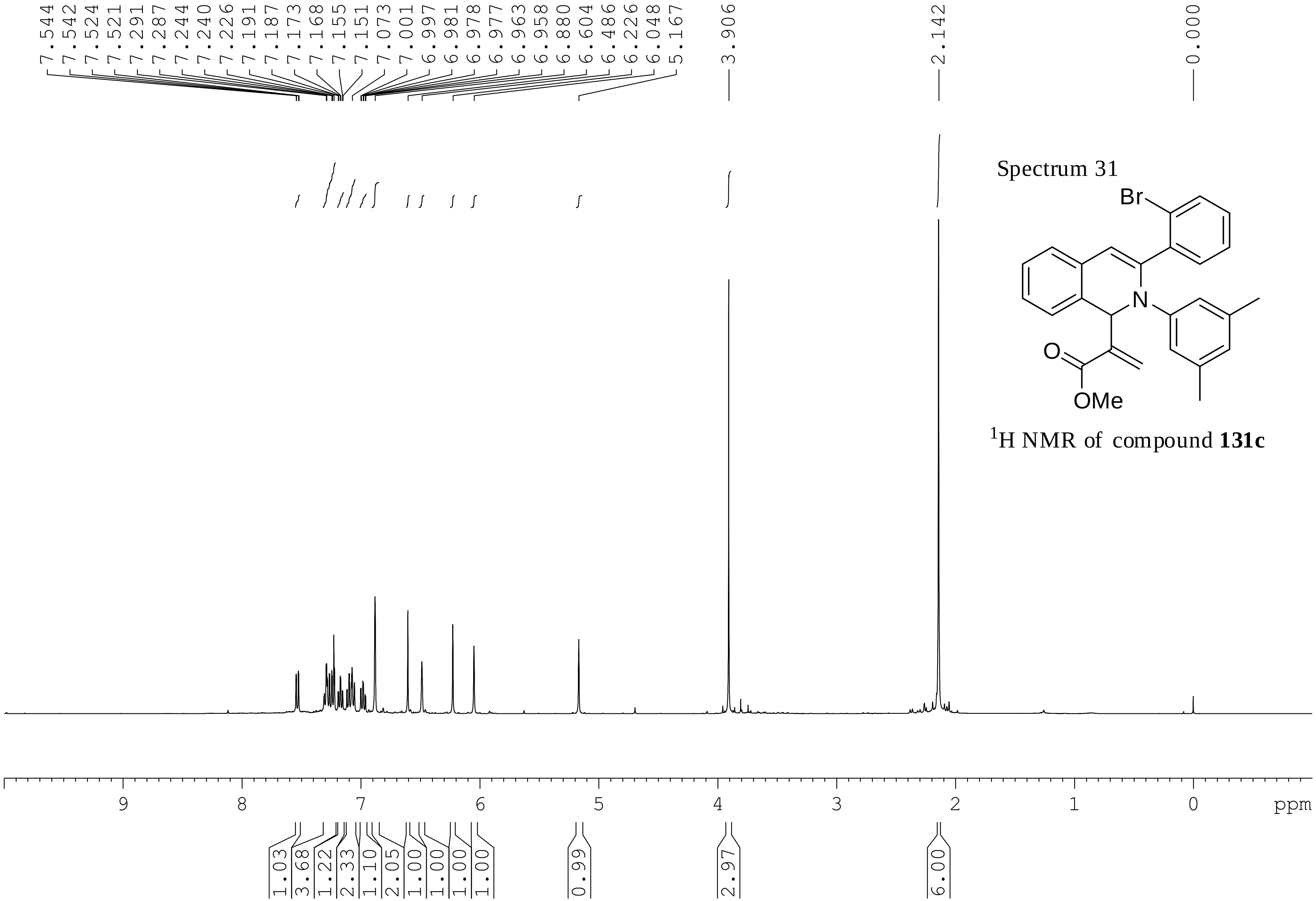


Spectrum 29

^{1}H NMR of compound **127c**

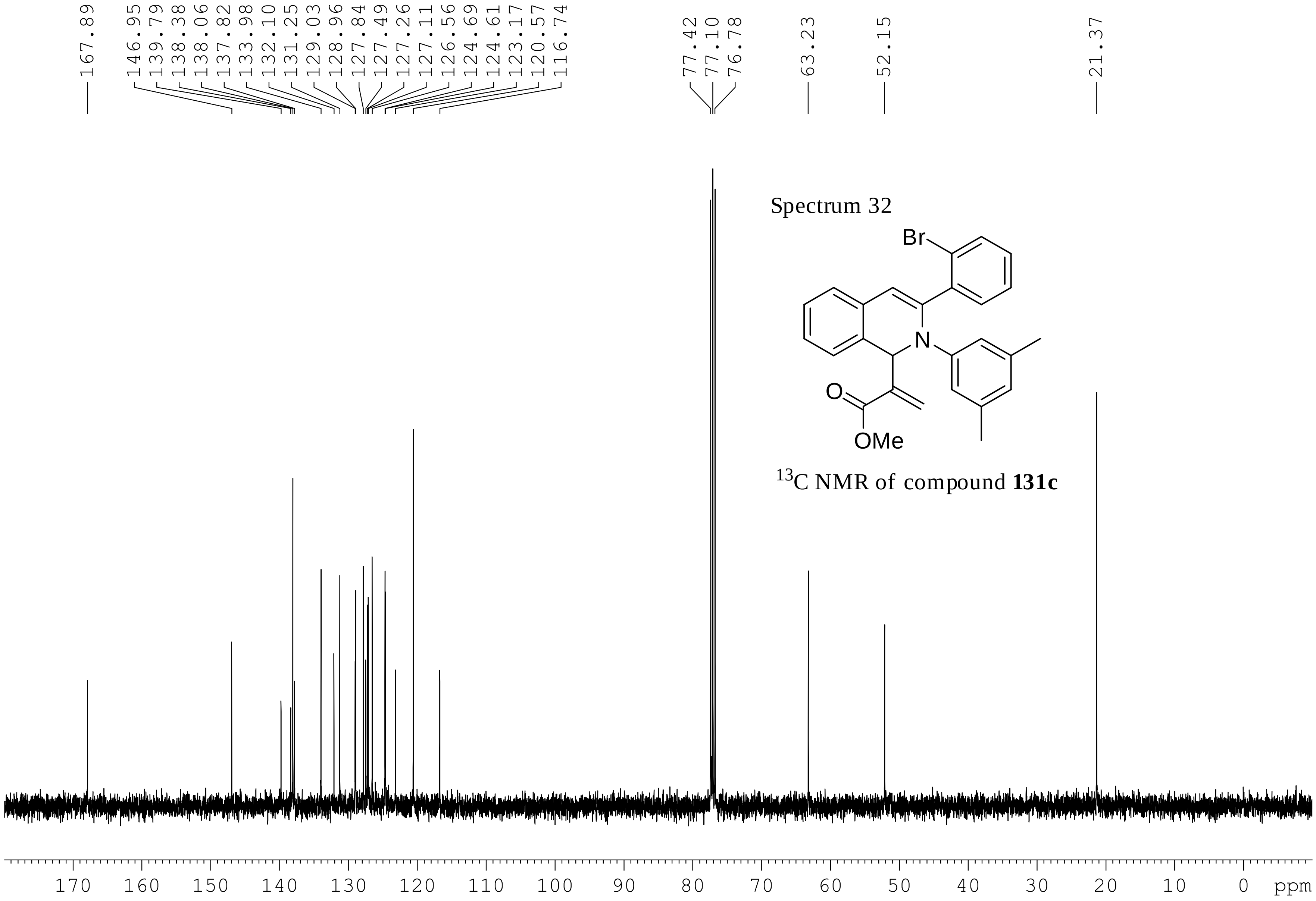

Spectrum 30

^{13}C NMR of compound **127c**


Spectrum 31

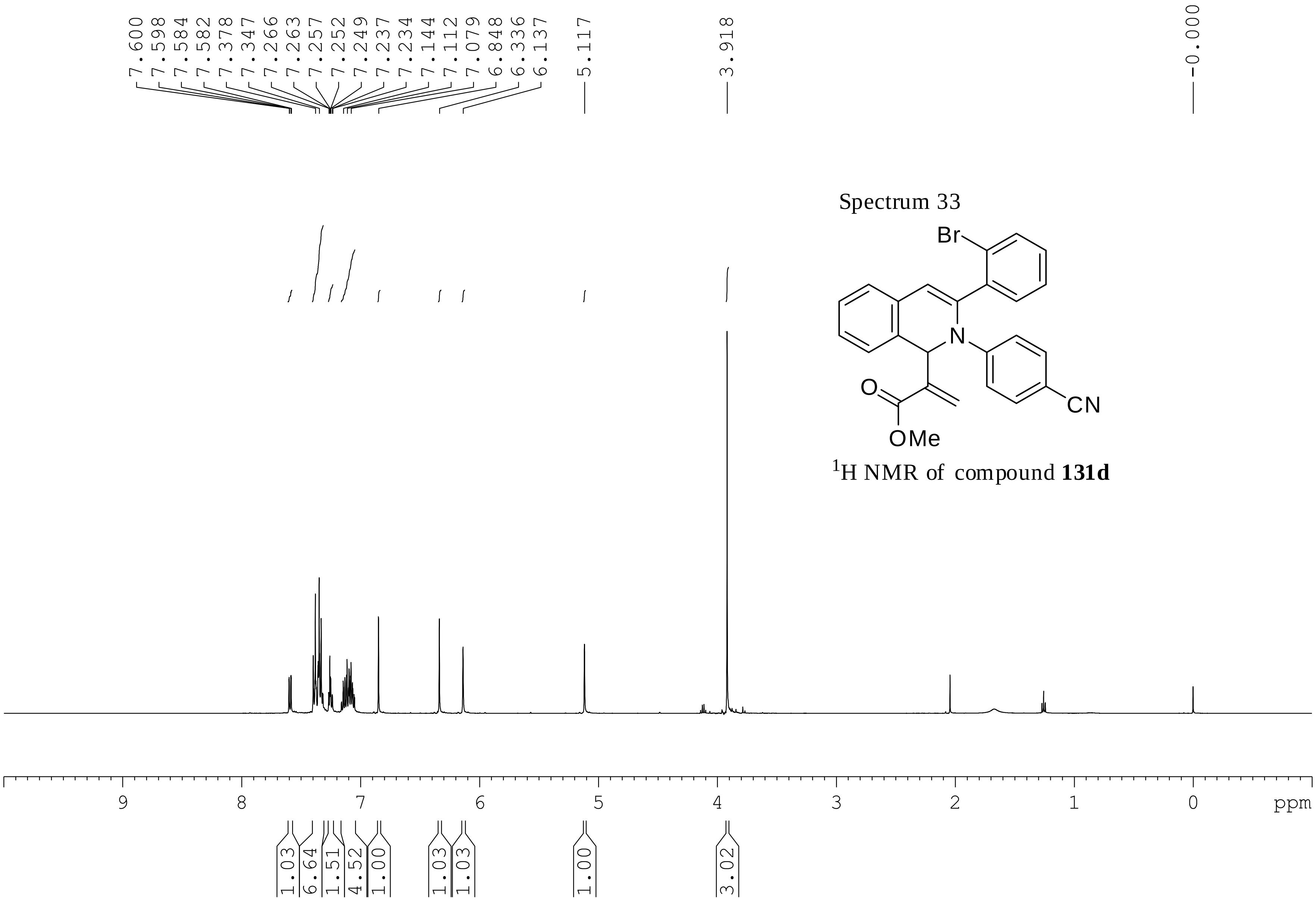
^{1}H NMR of compound **131c**

Spectrum 32



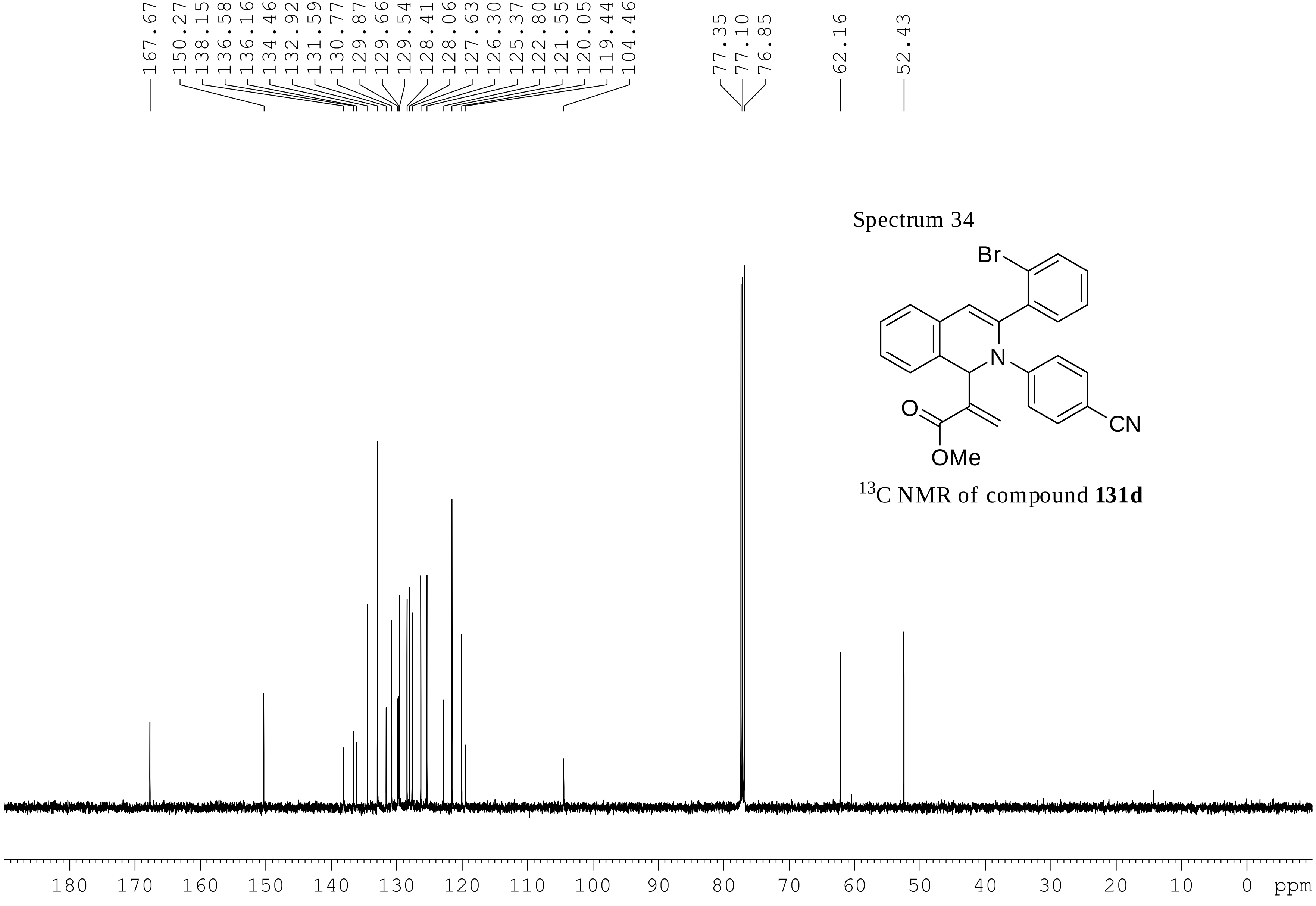
^{13}C NMR of compound **131c**

Spectrum 33



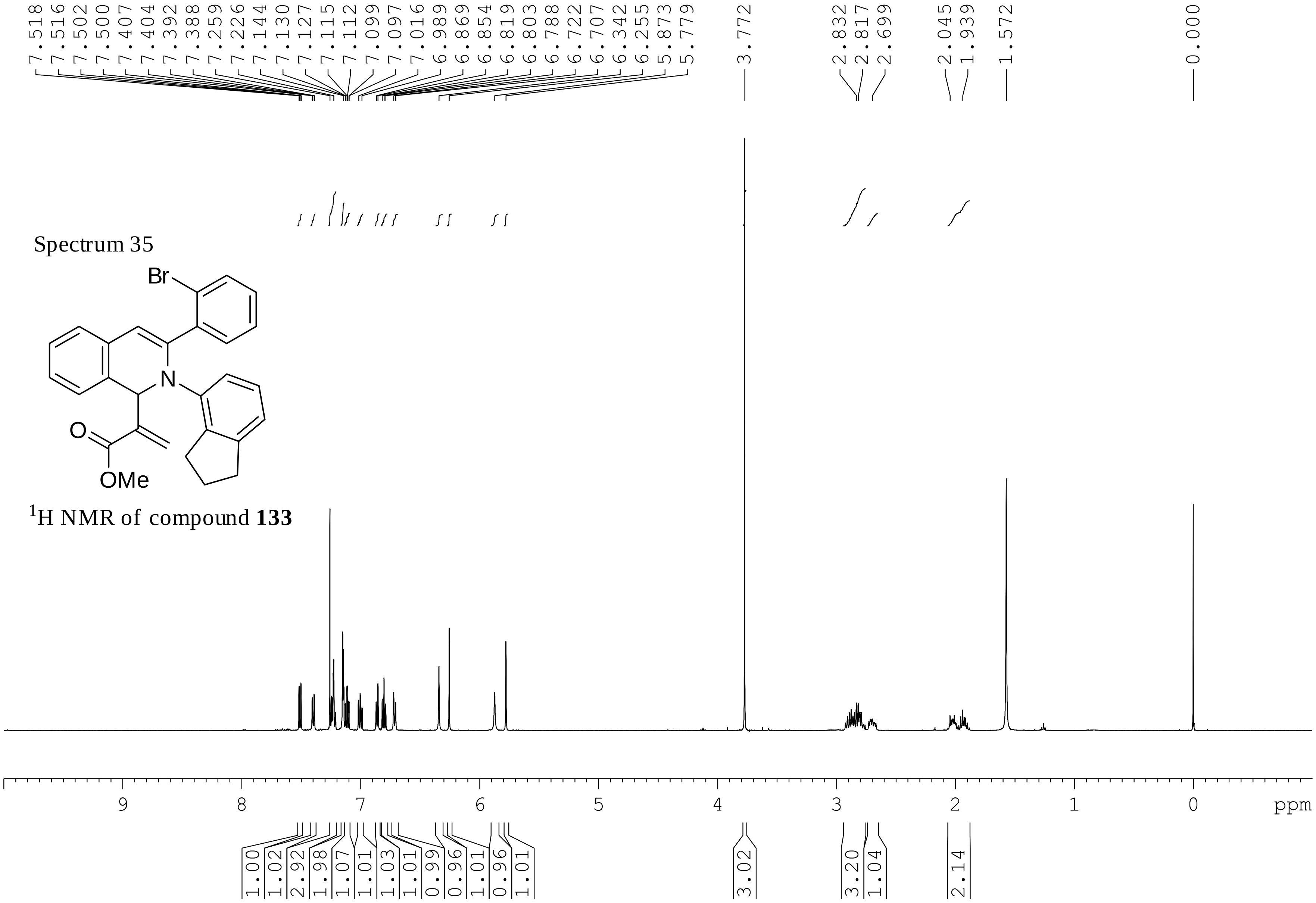
^{1}H NMR of compound **131d**

Spectrum 34



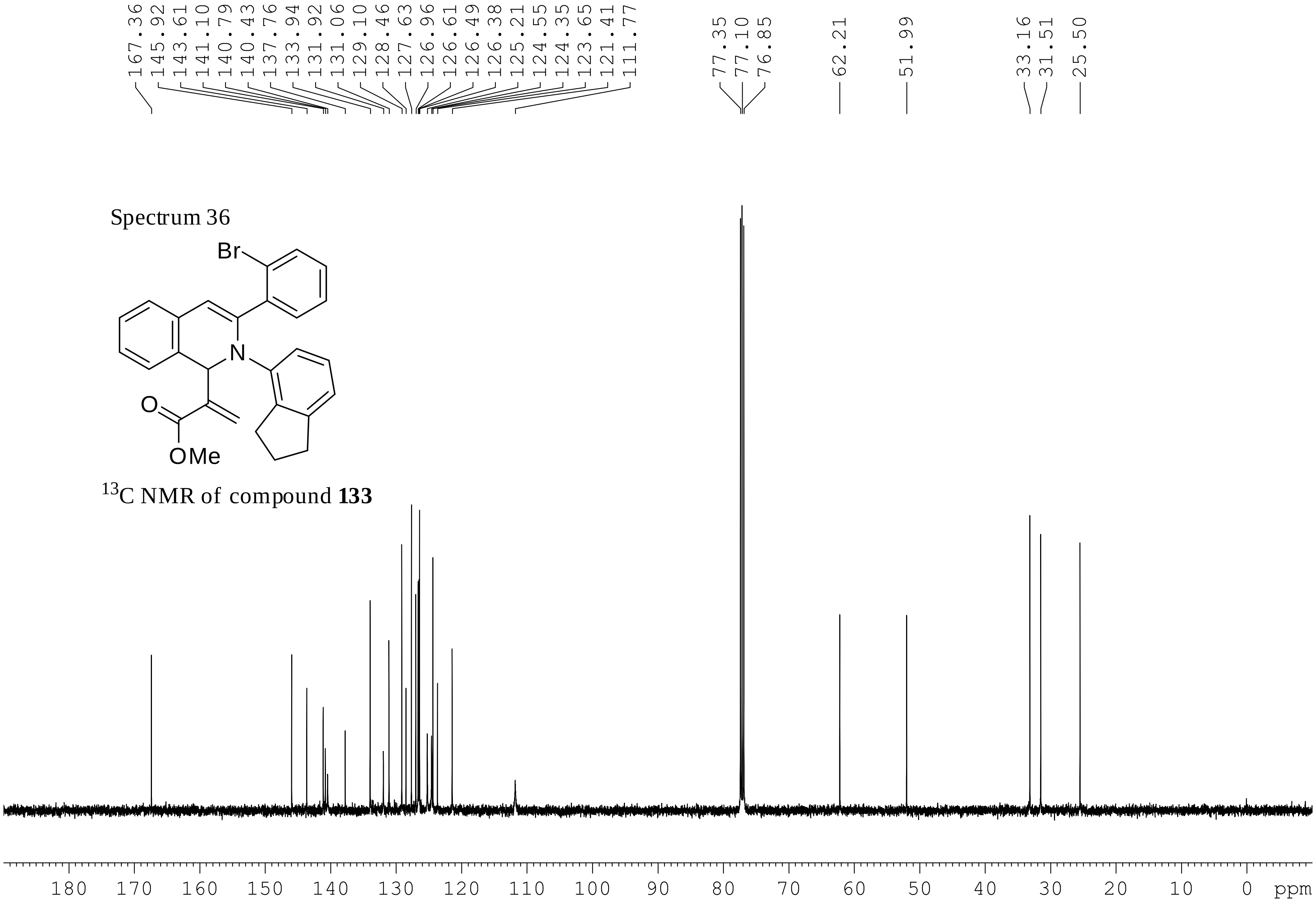
^{13}C NMR of compound **131d**

Spectrum 35



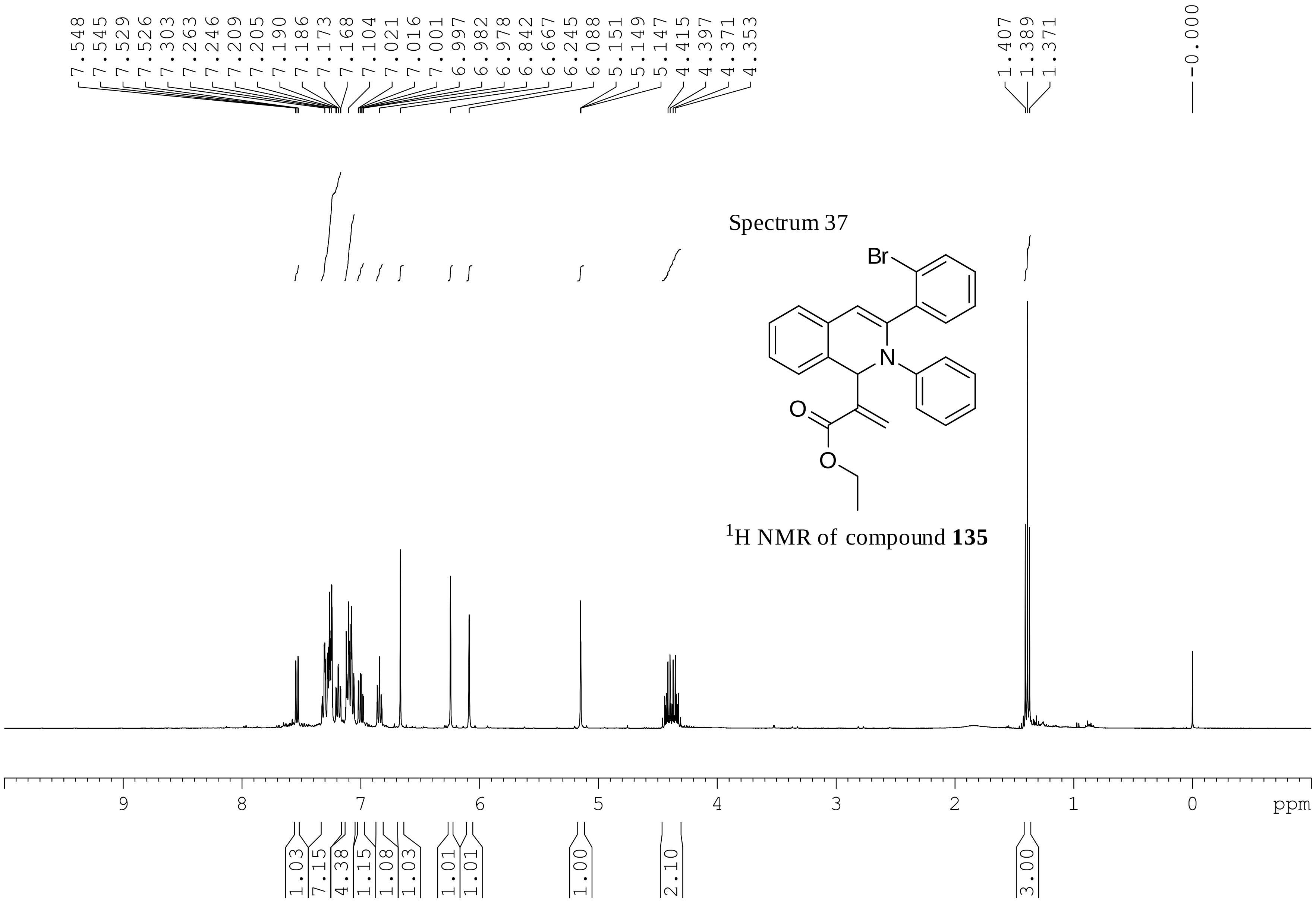
^{1}H NMR of compound **133**

Spectrum 36



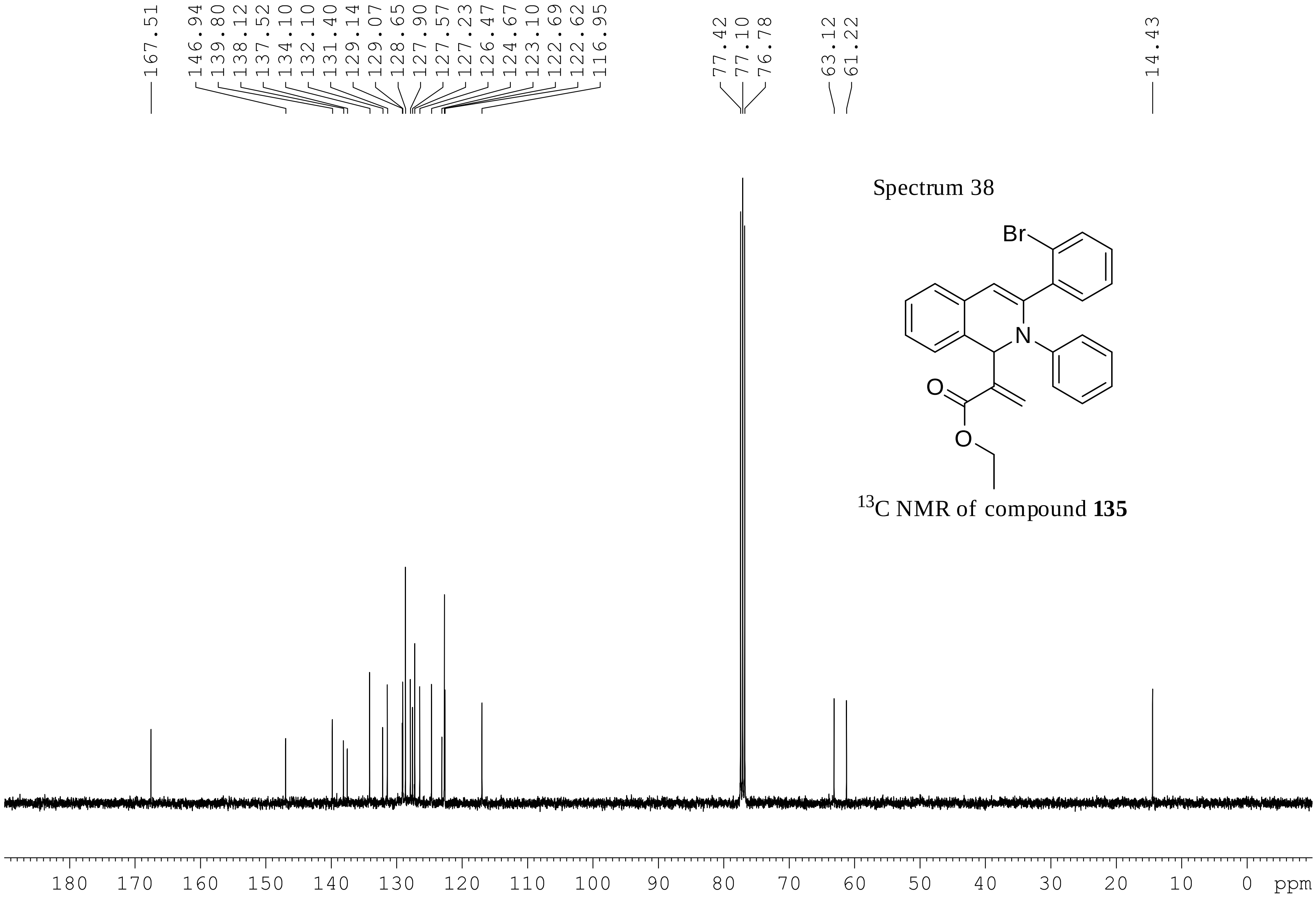
^{13}C NMR of compound **133**

Spectrum 37

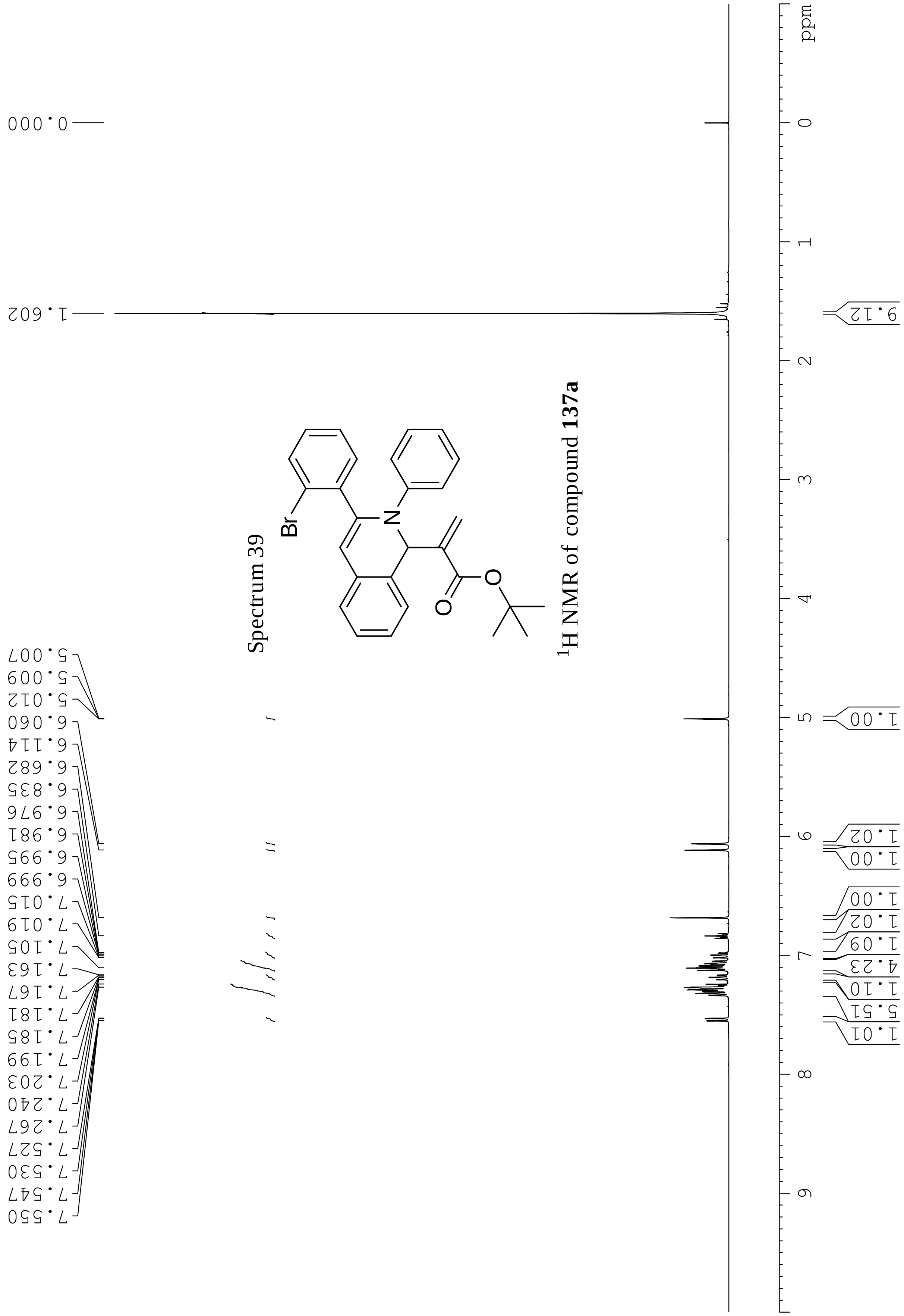


^{1}H NMR of compound **135**

Spectrum 38



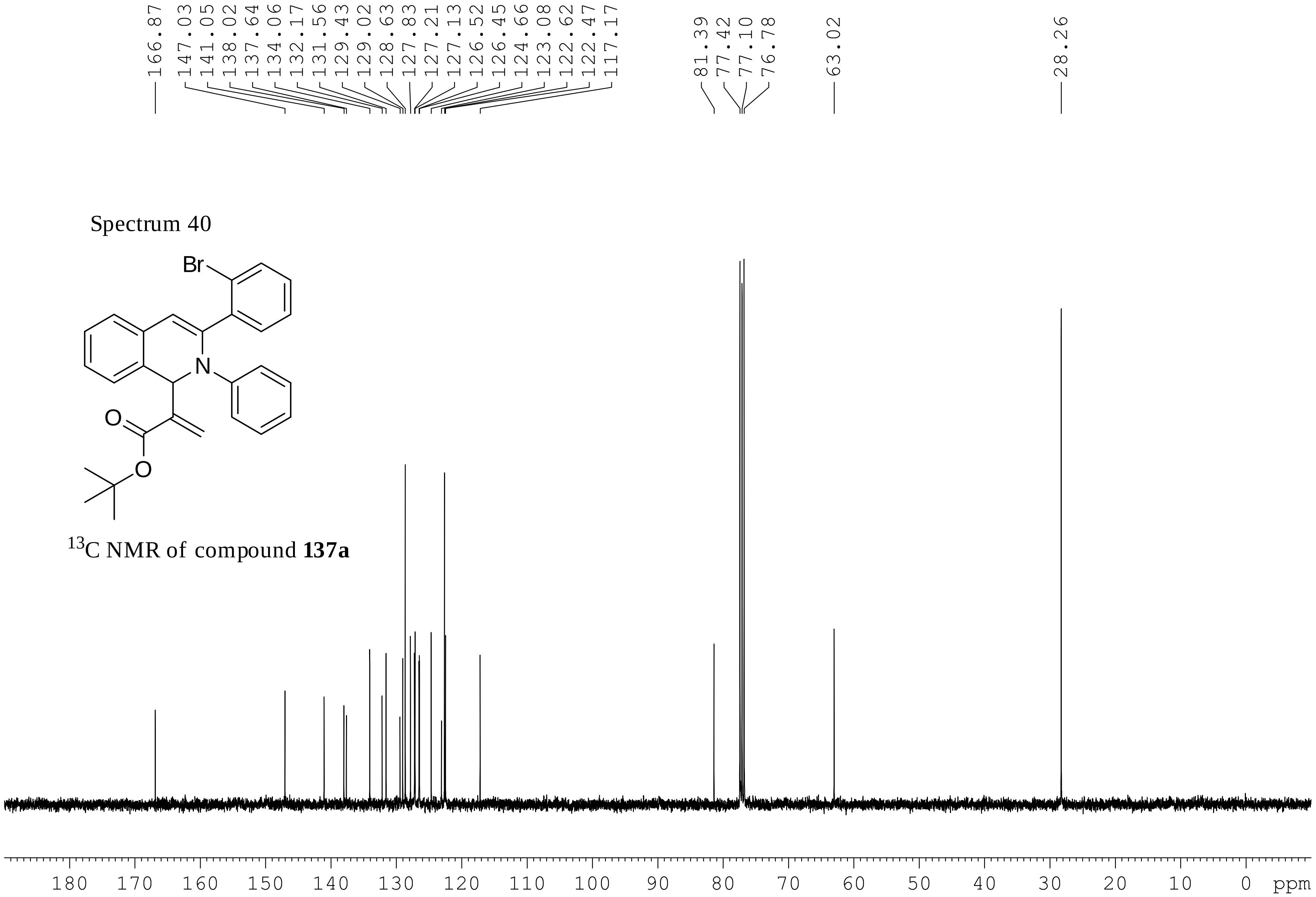
^{13}C NMR of compound **135**



Spectrum 39

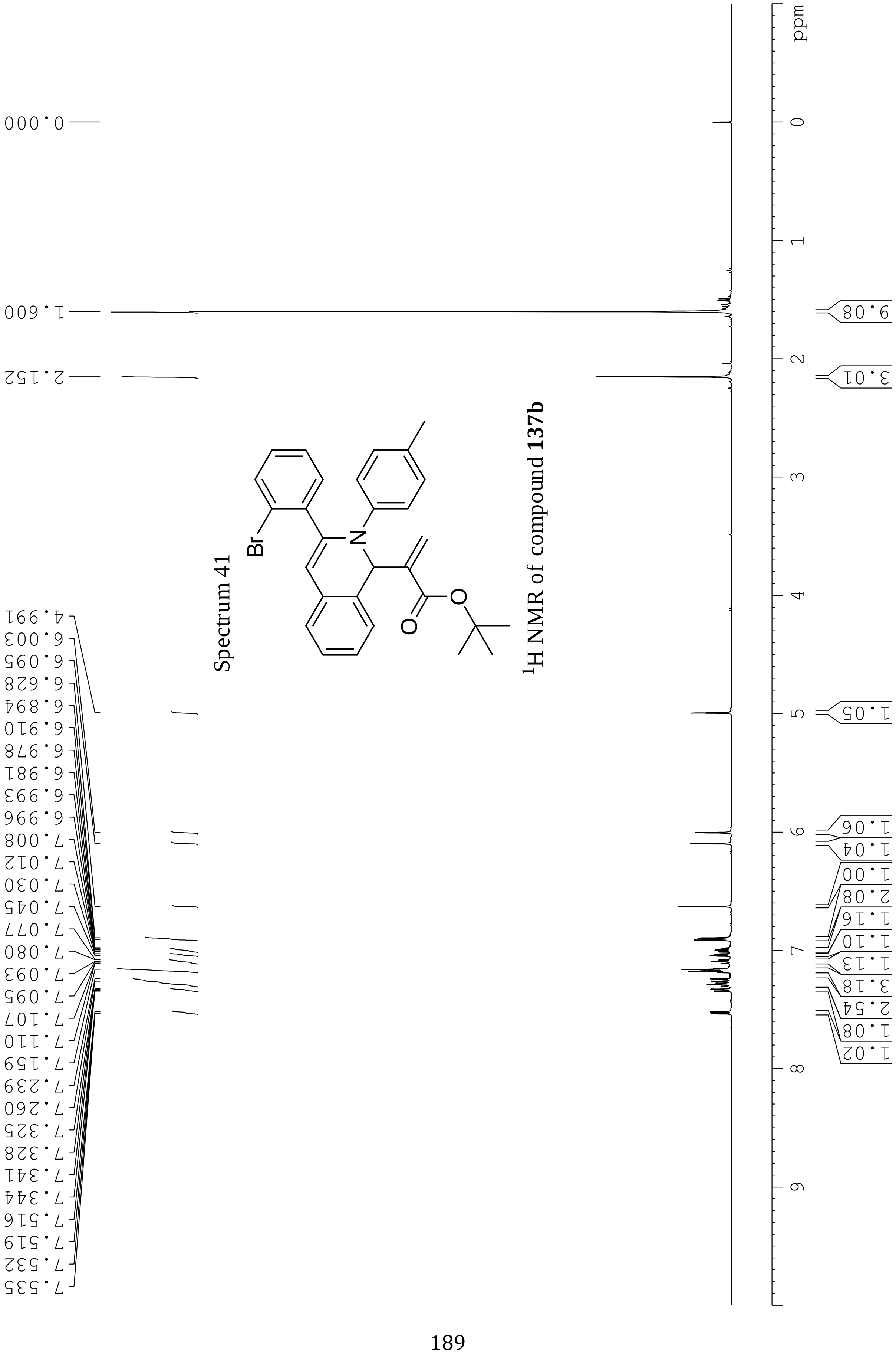
^{1}H NMR of compound **137a**

Spectrum 40



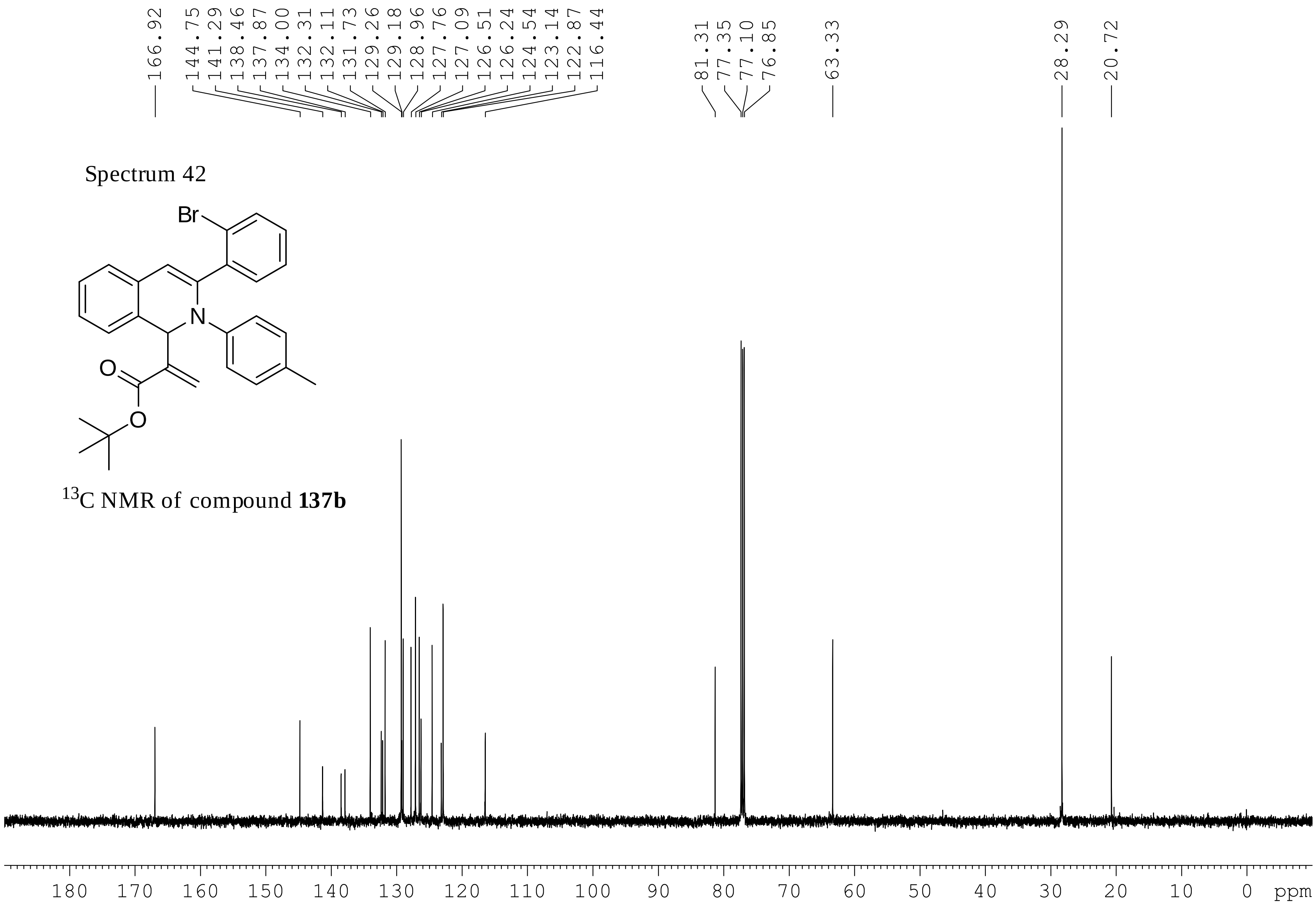
^{13}C NMR of compound **137a**

Spectrum 41

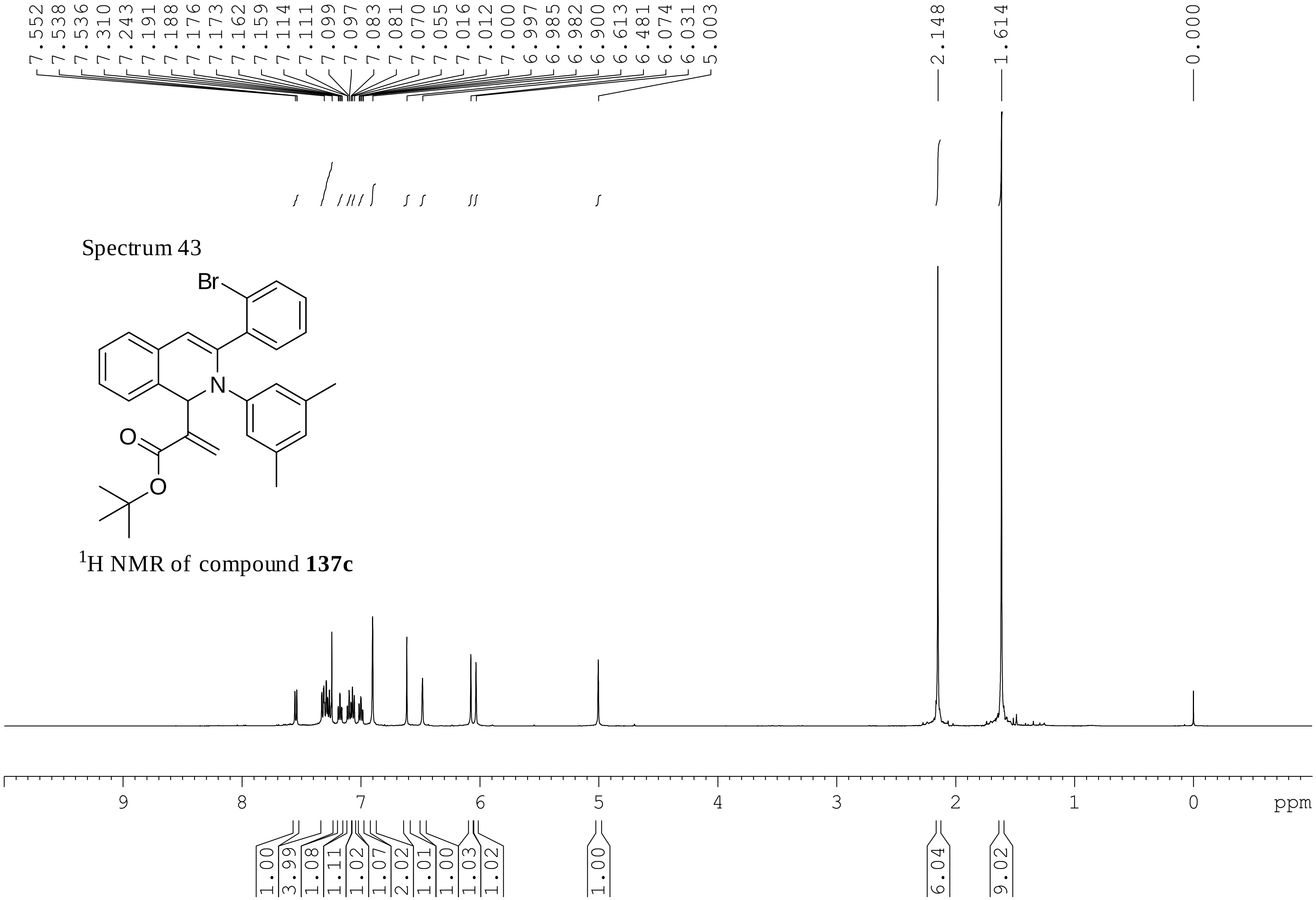


^{1}H NMR of compound **137b**

Spectrum 42



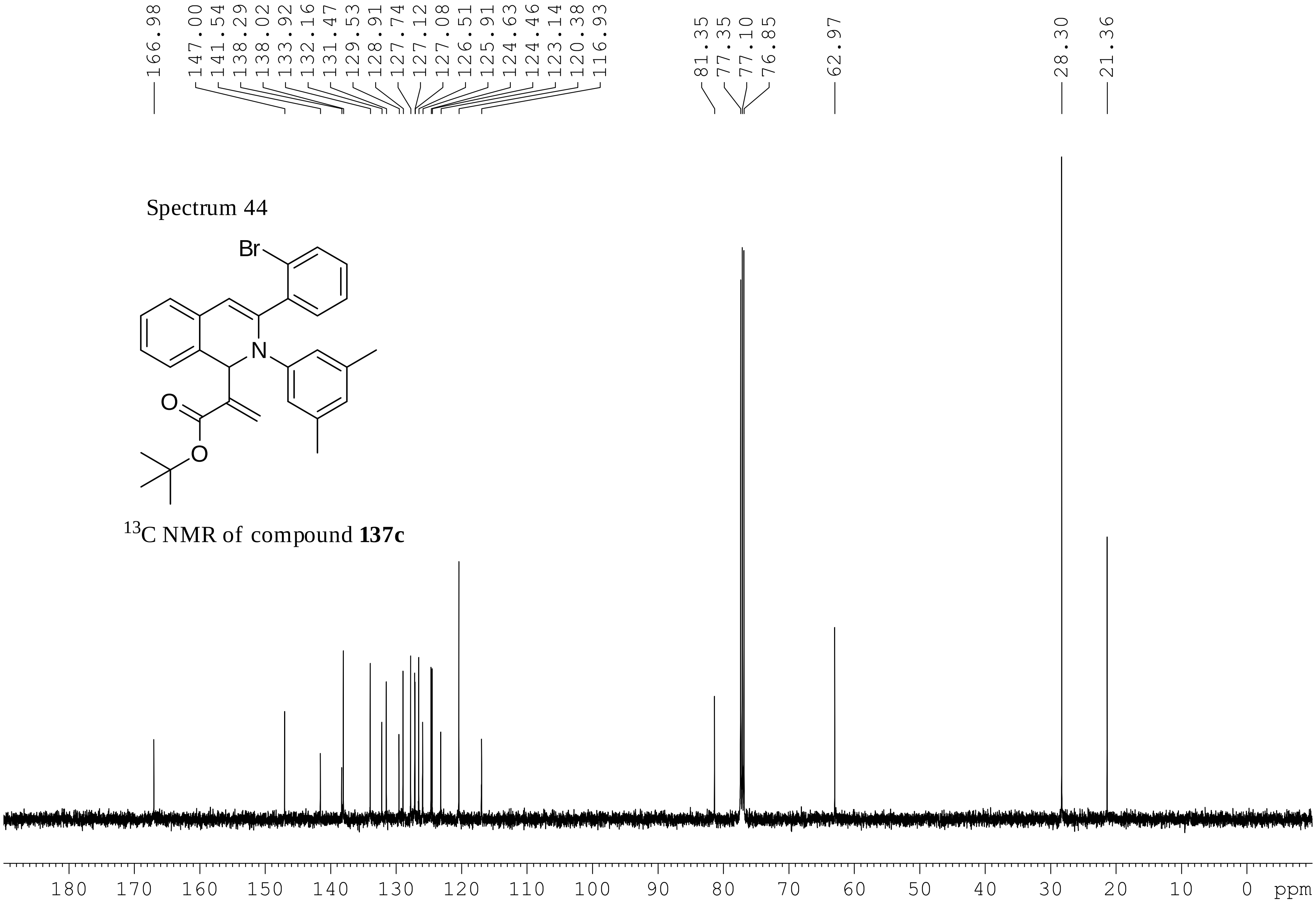
^{13}C NMR of compound **137b**



Spectrum 43

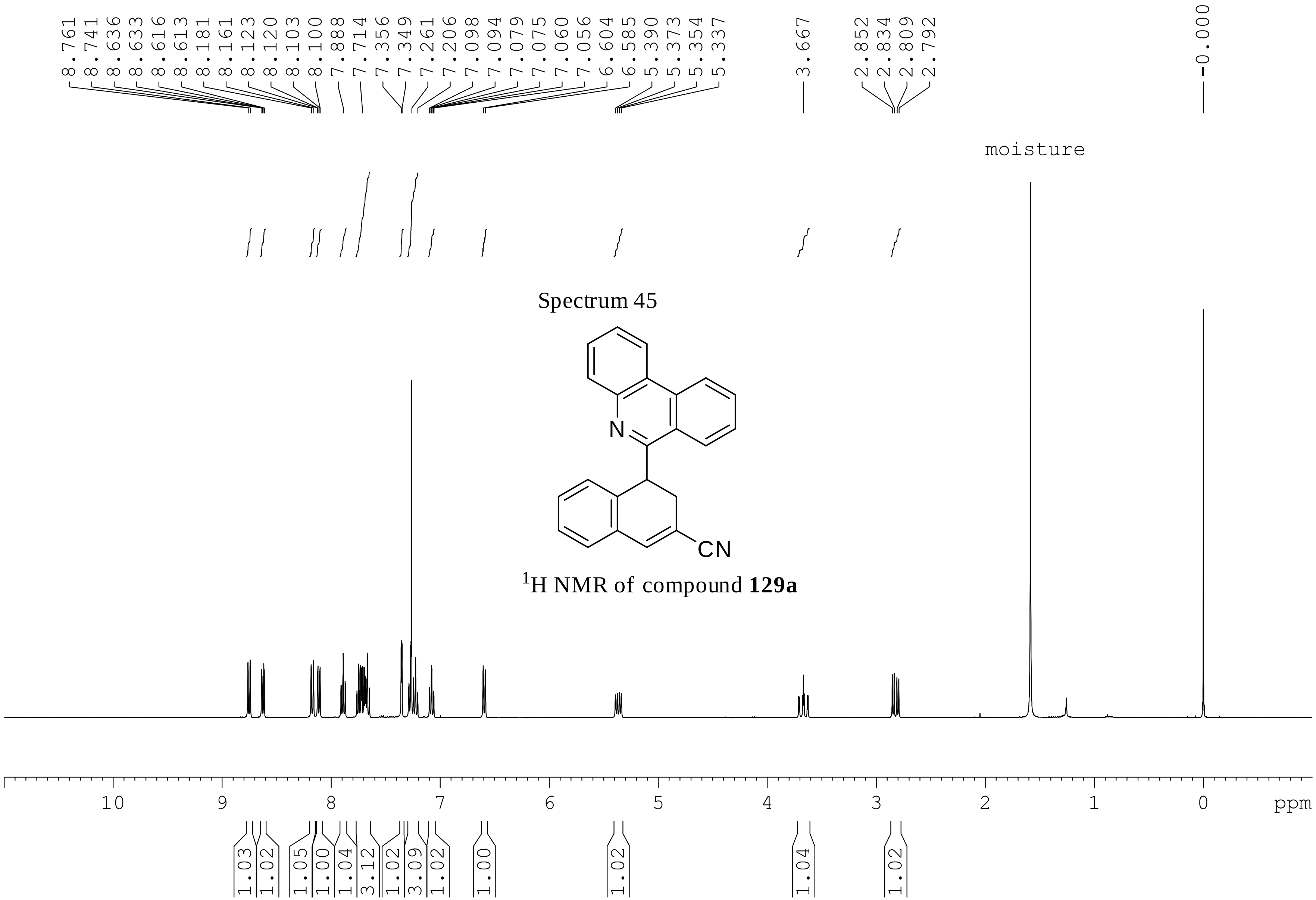
^{1}H NMR of compound **137c**

Spectrum 44



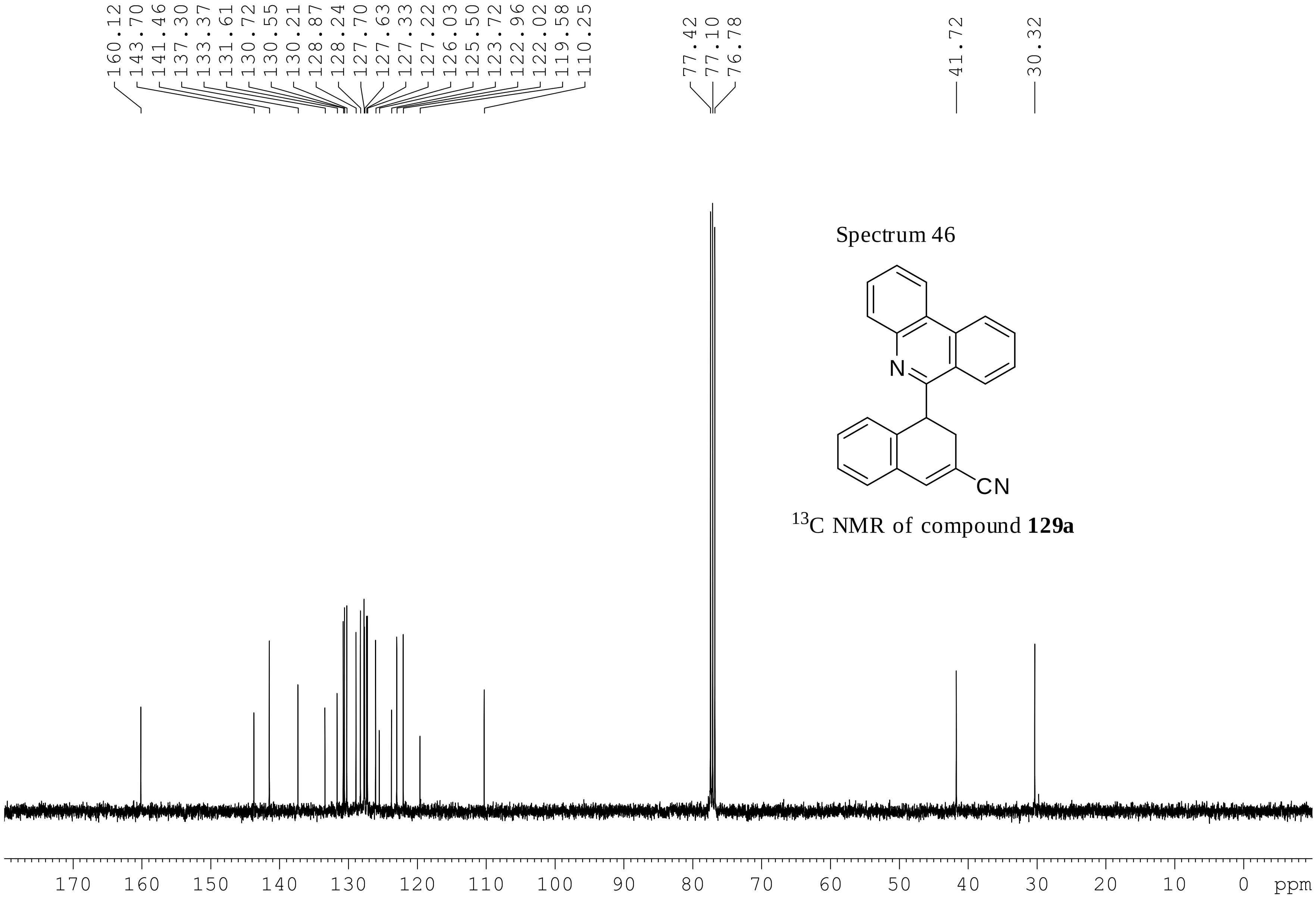
^{13}C NMR of compound **137c**

Spectrum 45



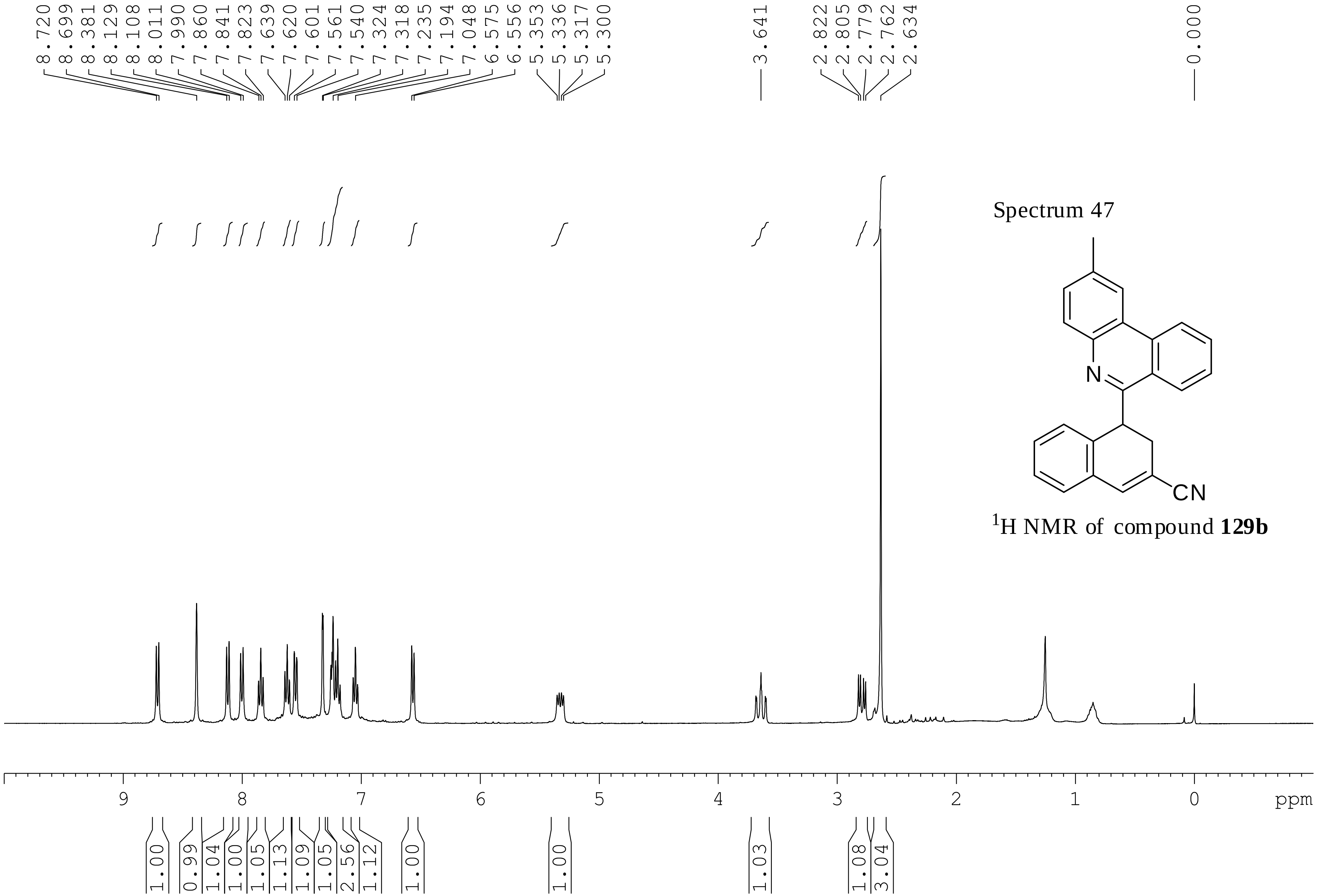
^{1}H NMR of compound **129a**

Spectrum 46

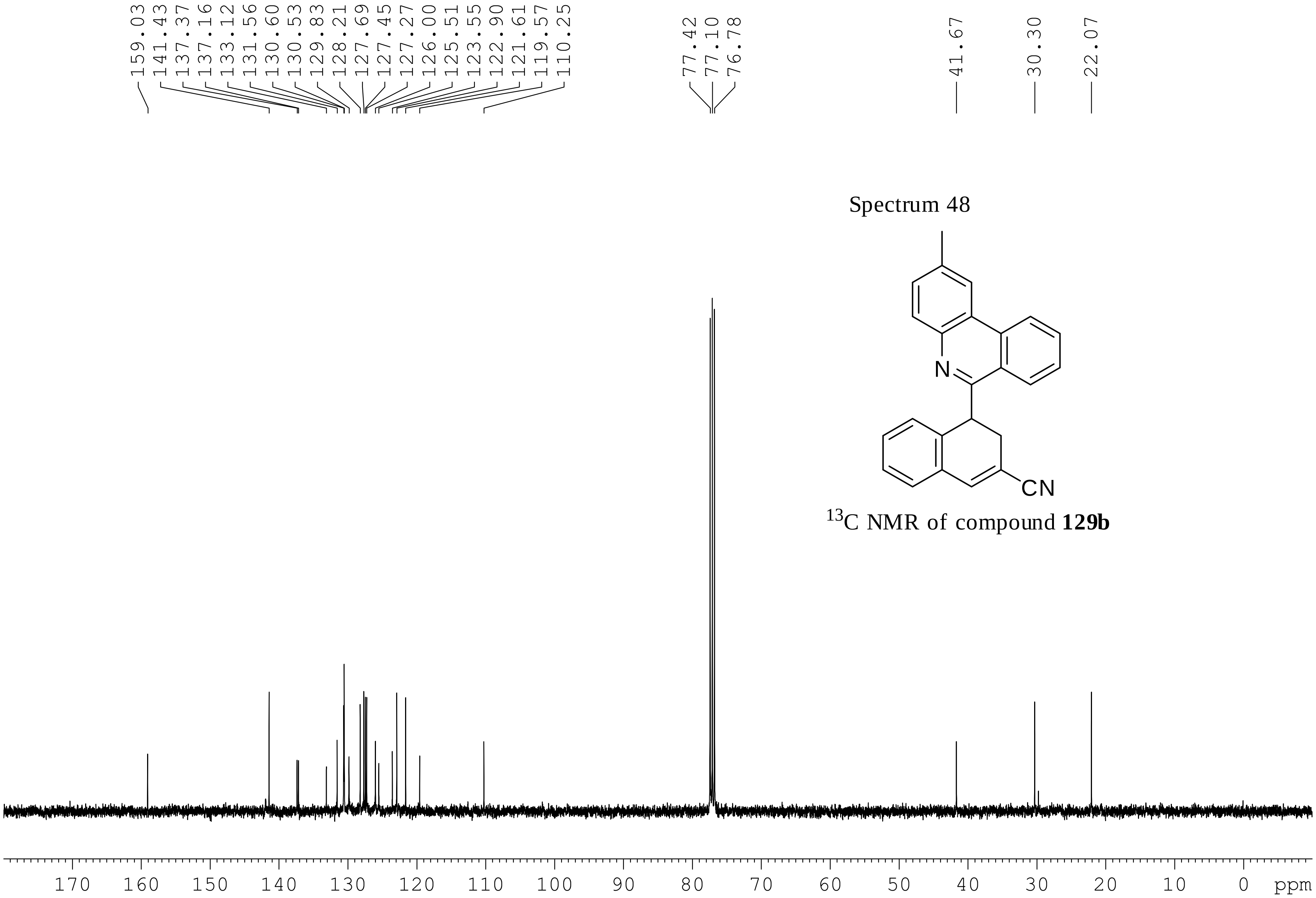


^{13}C NMR of compound **129a**

Spectrum 47

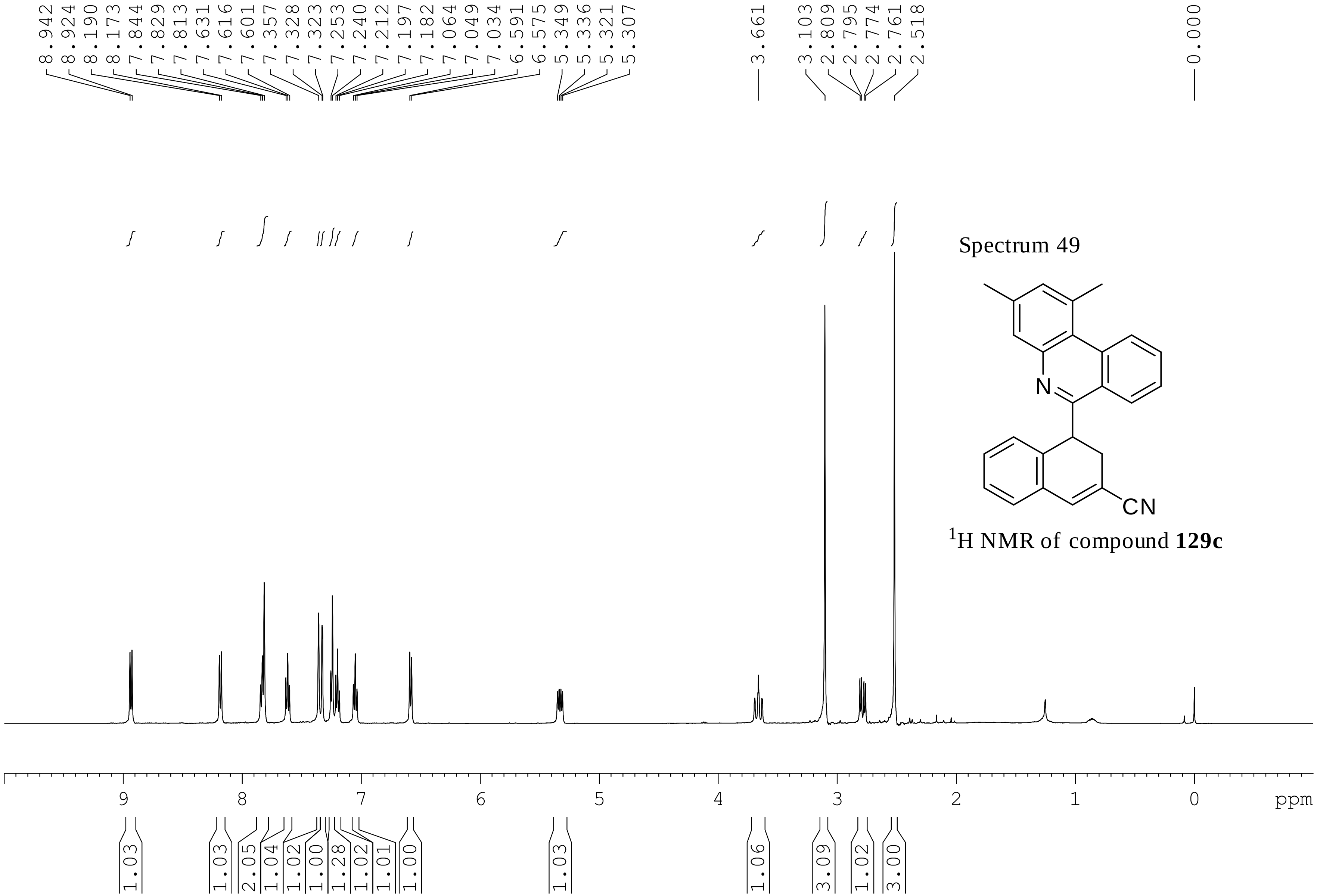


^{1}H NMR of compound **129b**



Spectrum 48

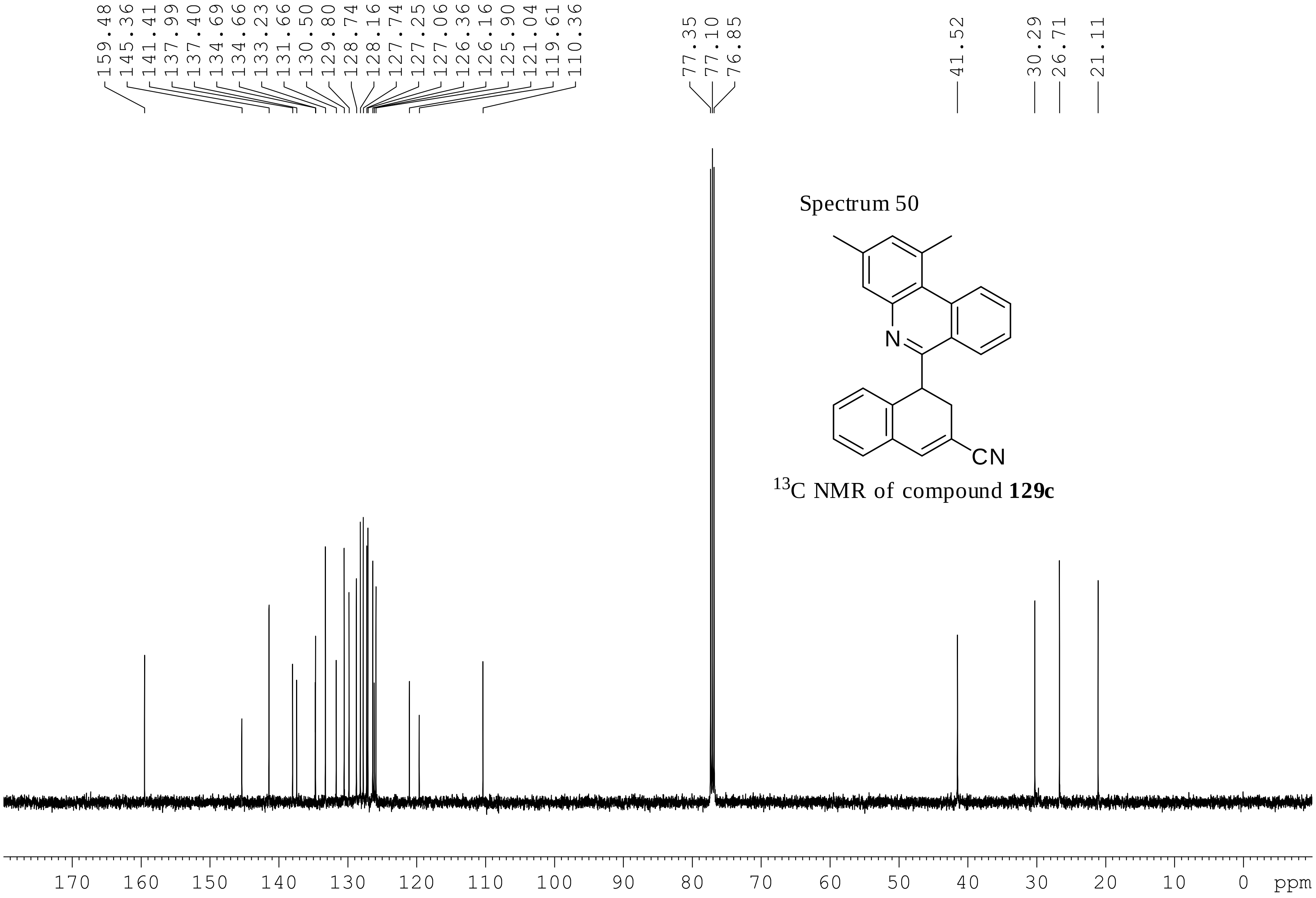
^{13}C NMR of compound **129b**



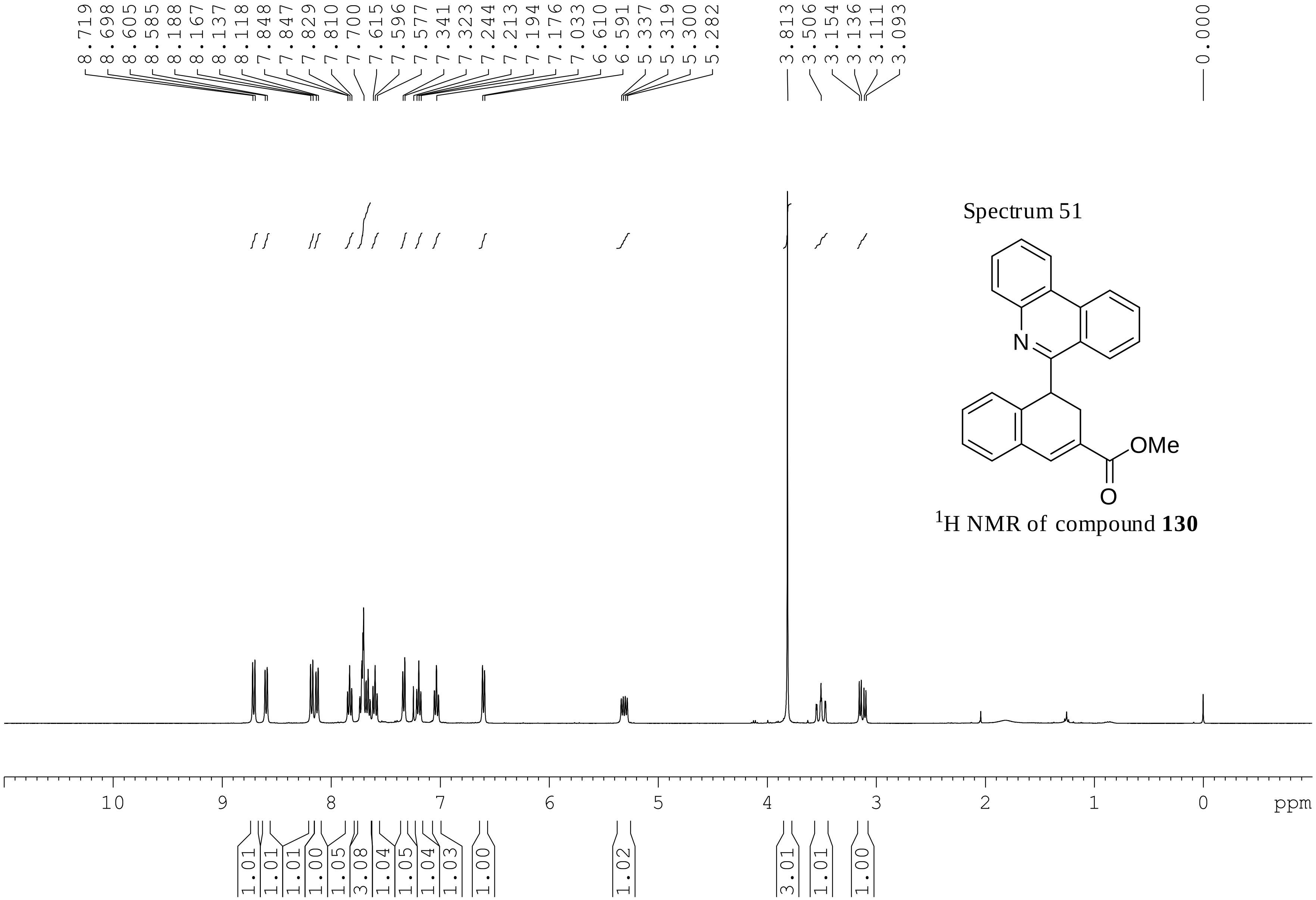
Spectrum 49

^{1}H NMR of compound **129c**

Spectrum 50

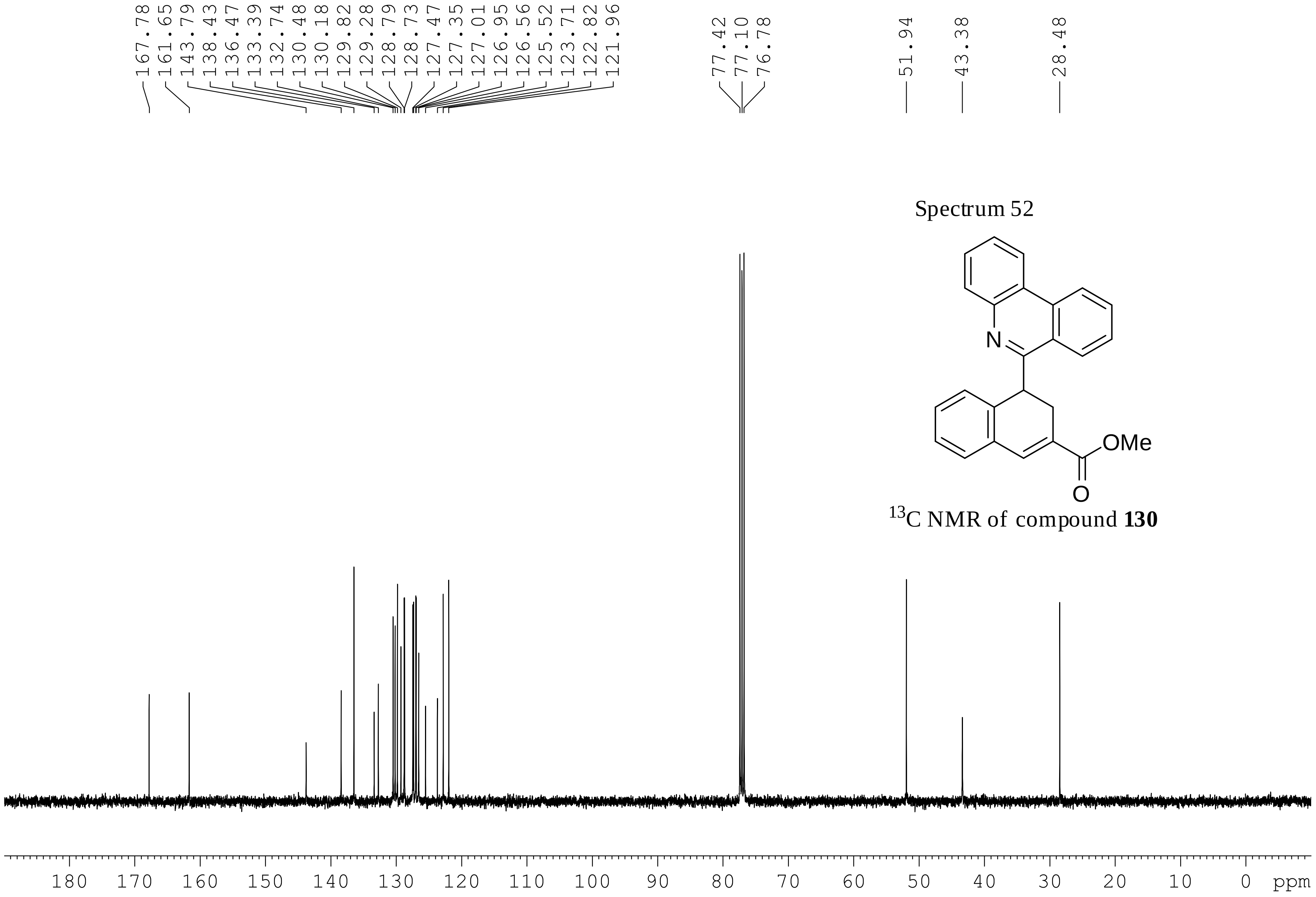


^{13}C NMR of compound **129c**



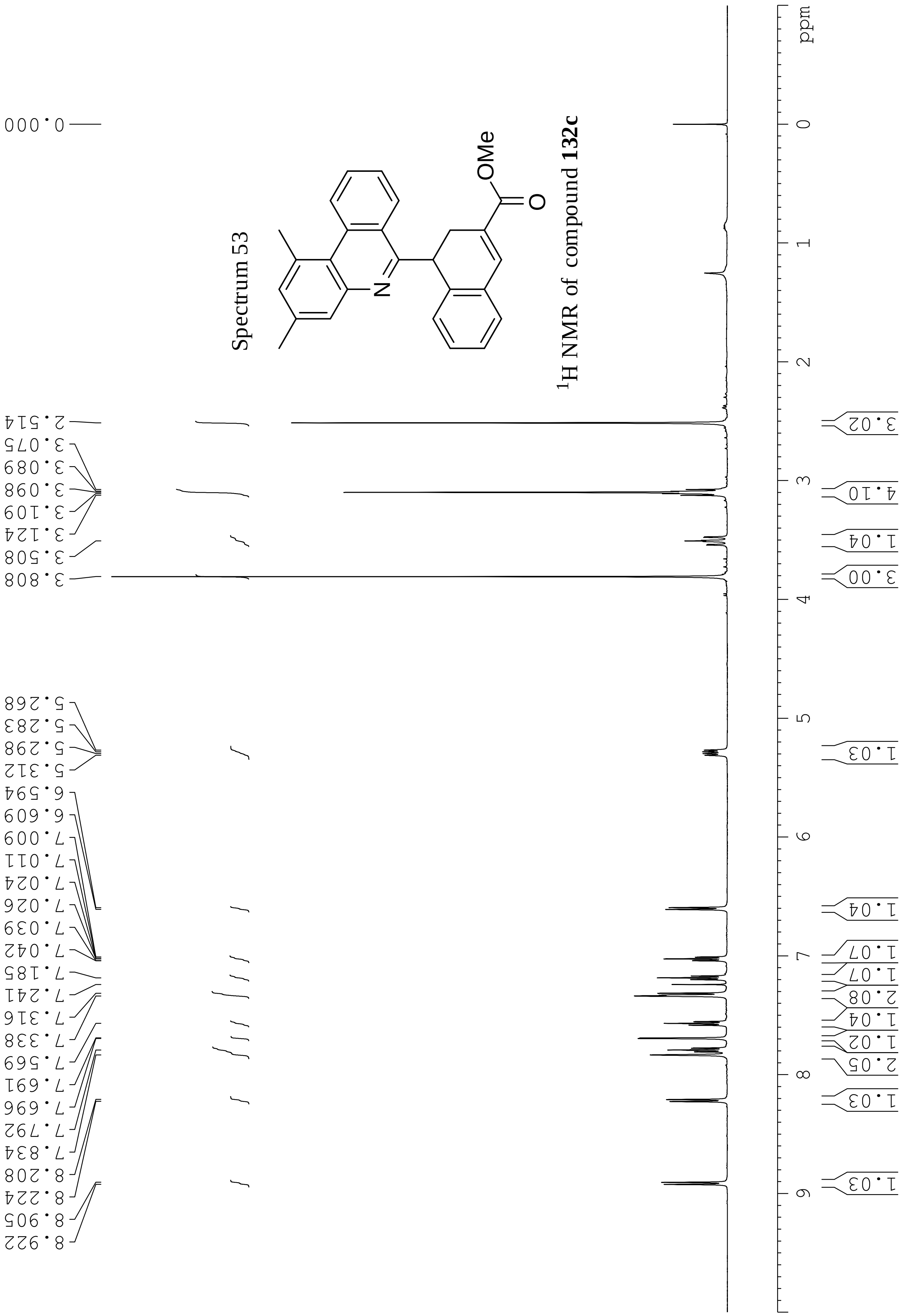
Spectrum 51

^{1}H NMR of compound **130**



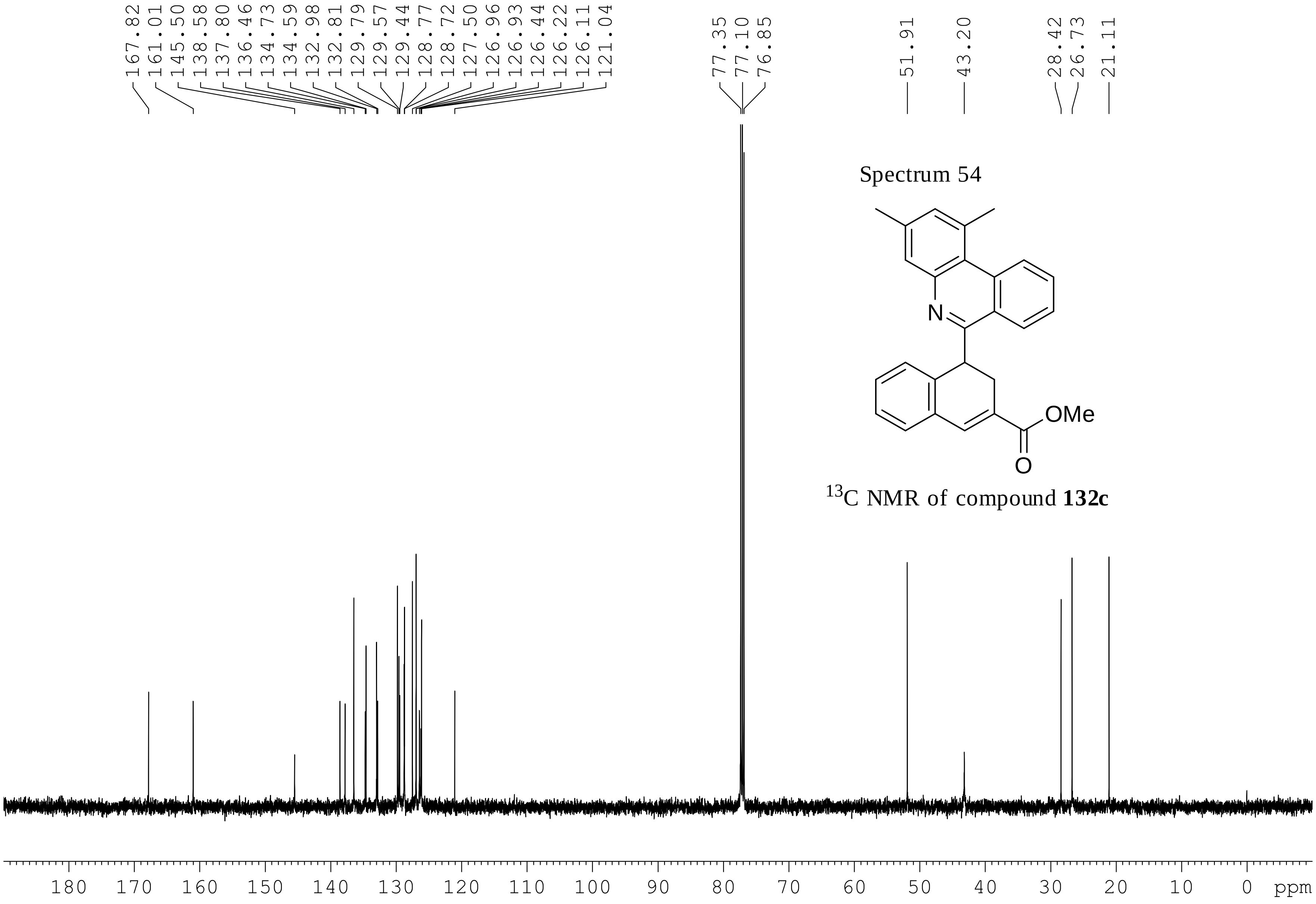
Spectrum 52

^{13}C NMR of compound **130**



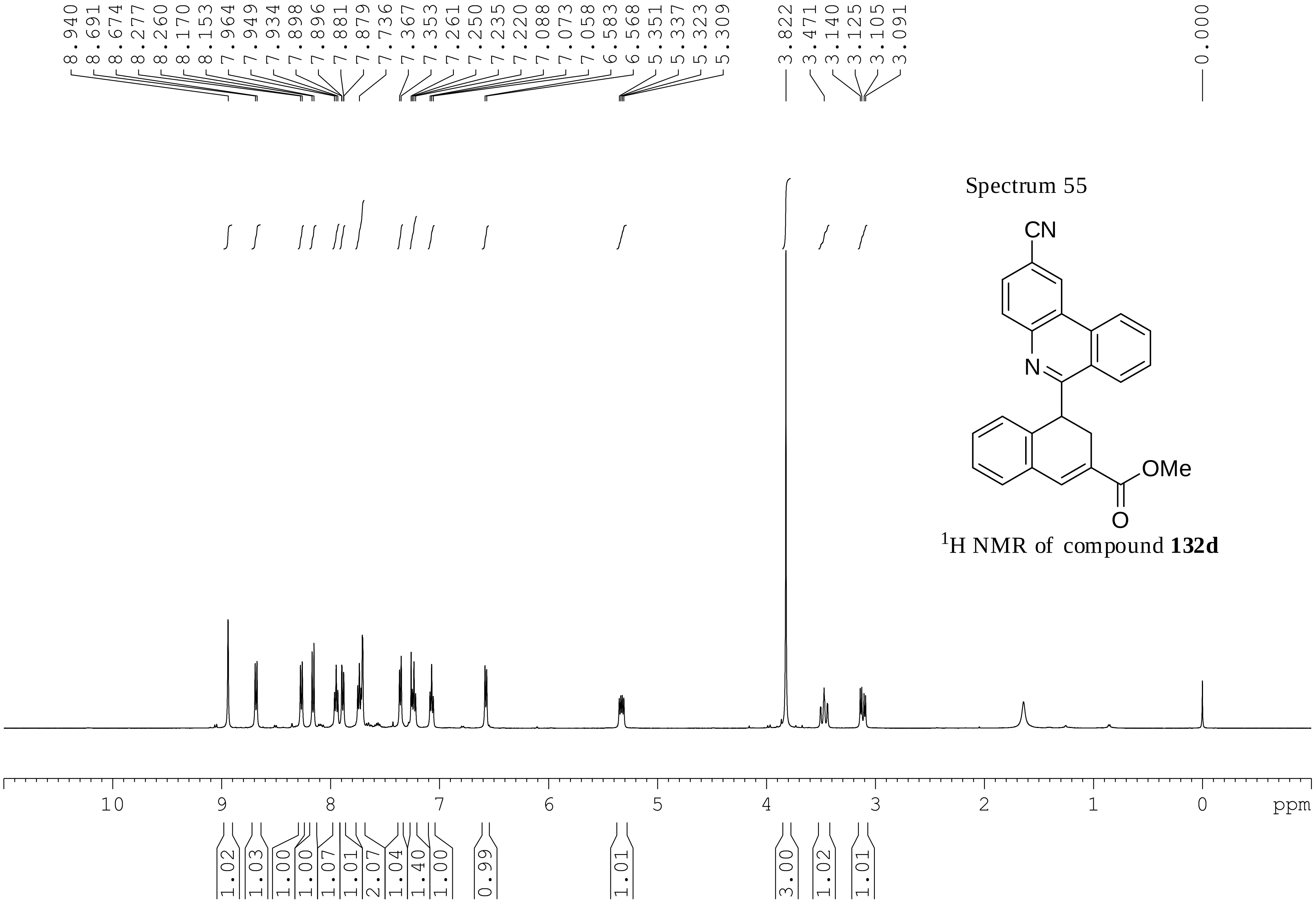
Spectrum 53

^{1}H NMR of compound **132c**



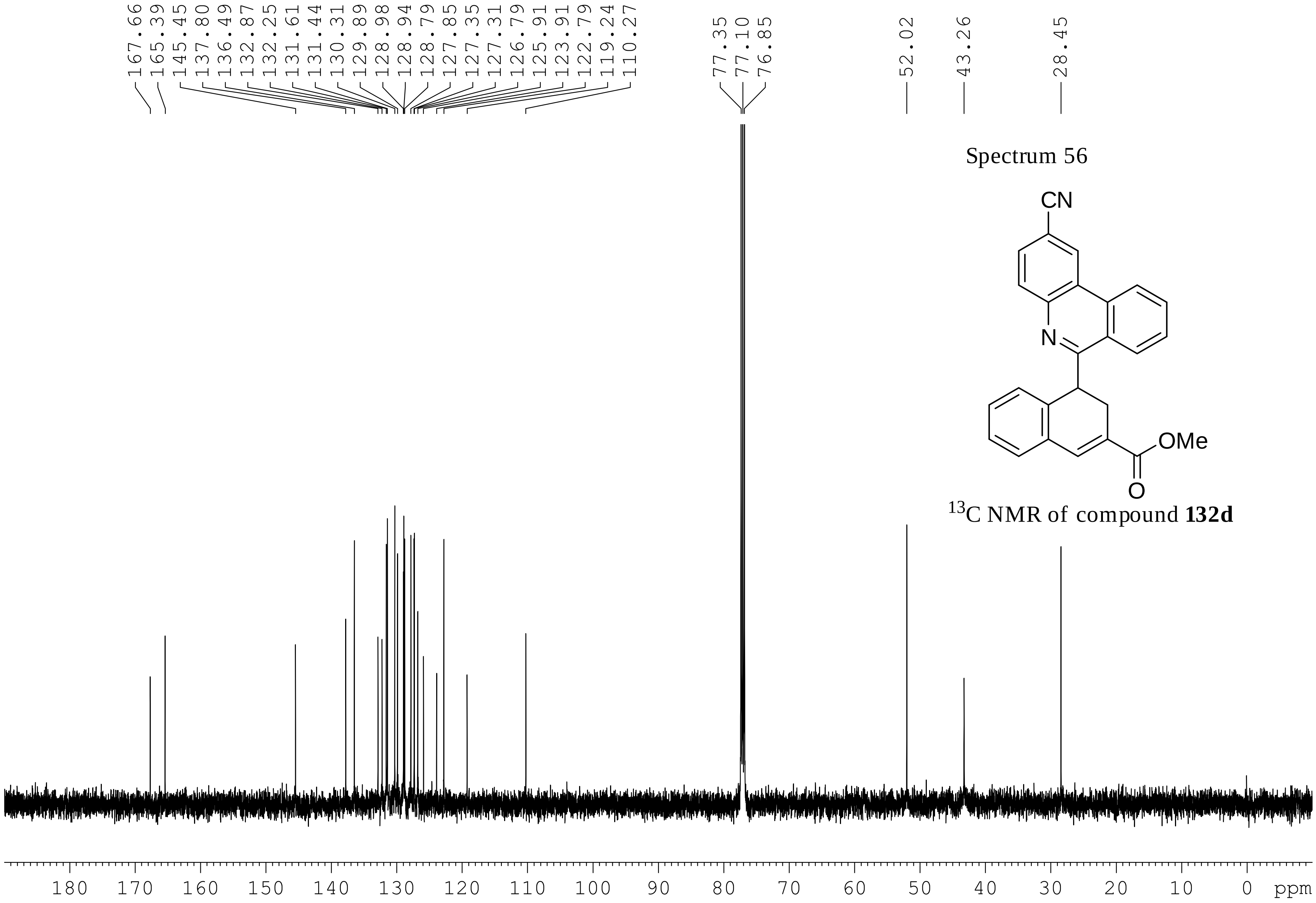
Spectrum 54

^{13}C NMR of compound **132c**



Spectrum 55

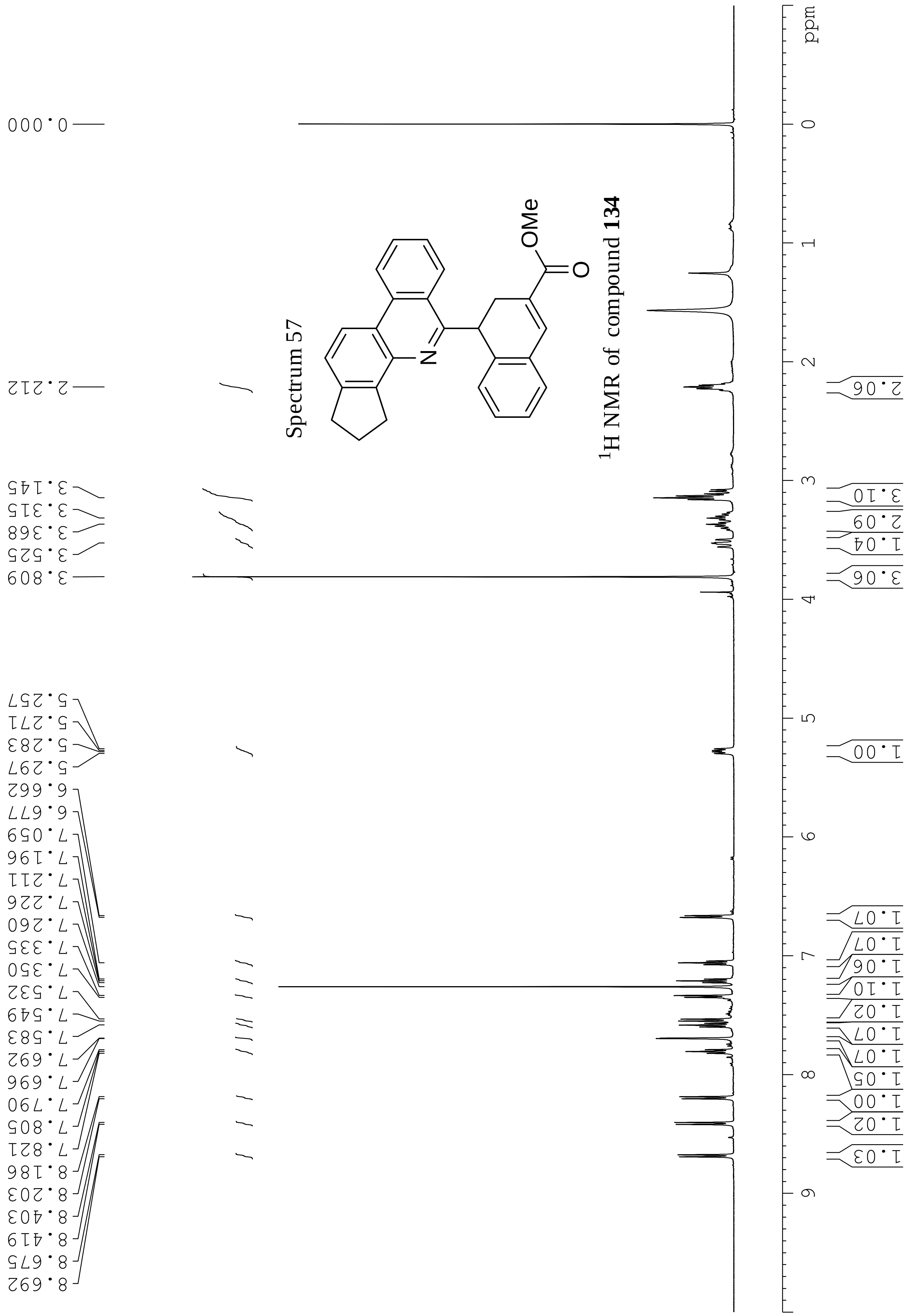
^{1}H NMR of compound **132d**



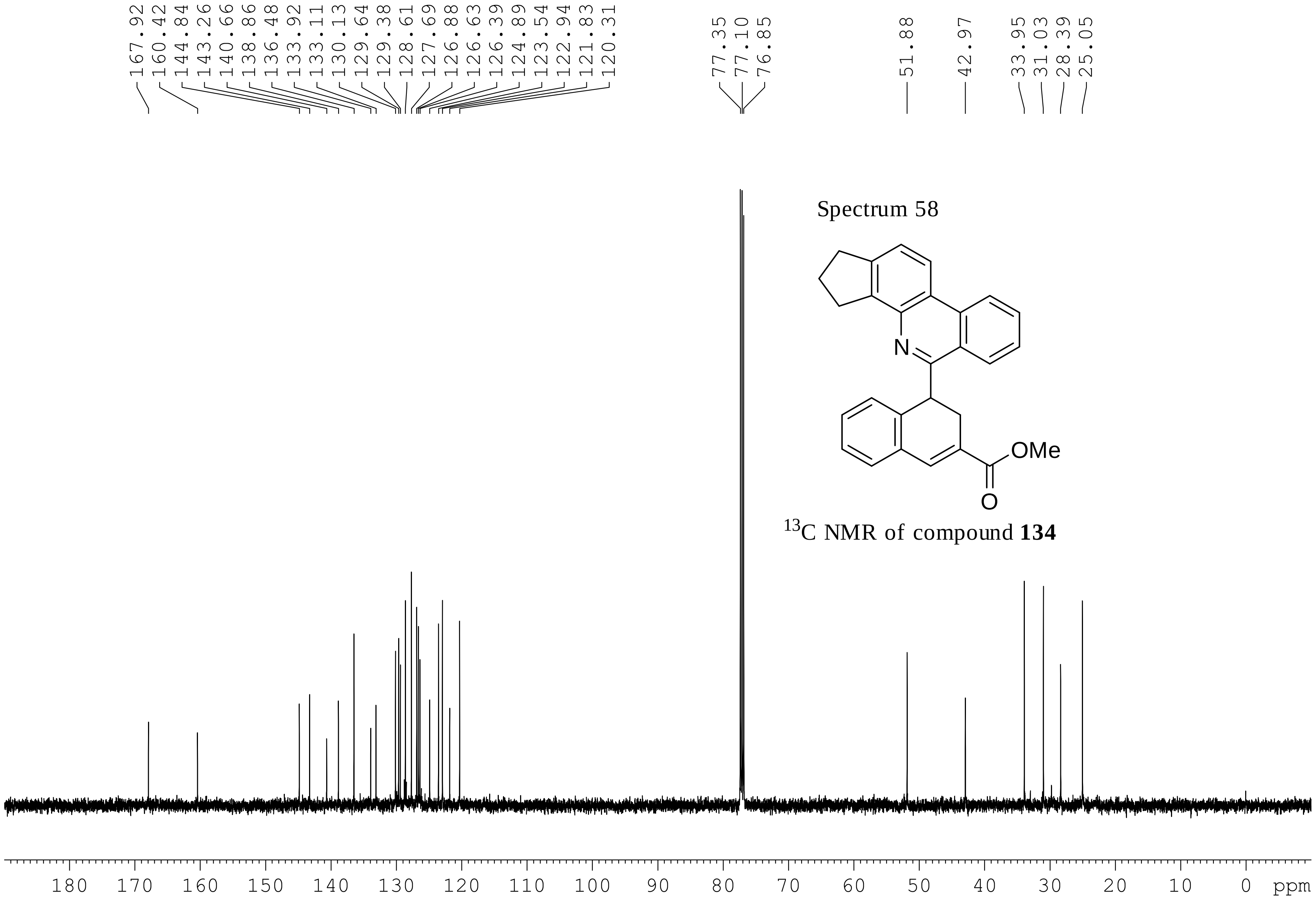
Spectrum 56

^{13}C NMR of compound **132d**

Spectrum 57



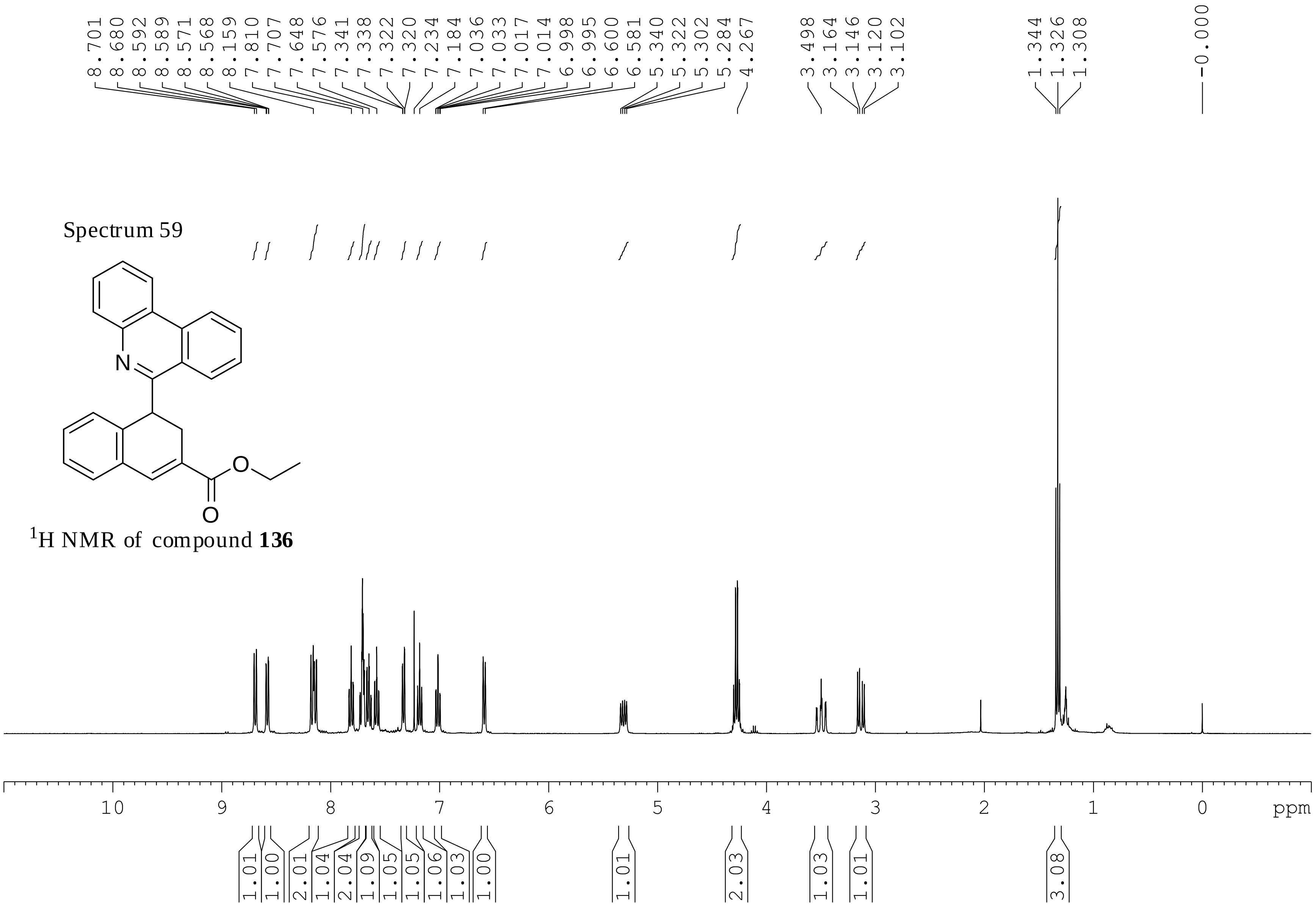
^{1}H NMR of compound **134**



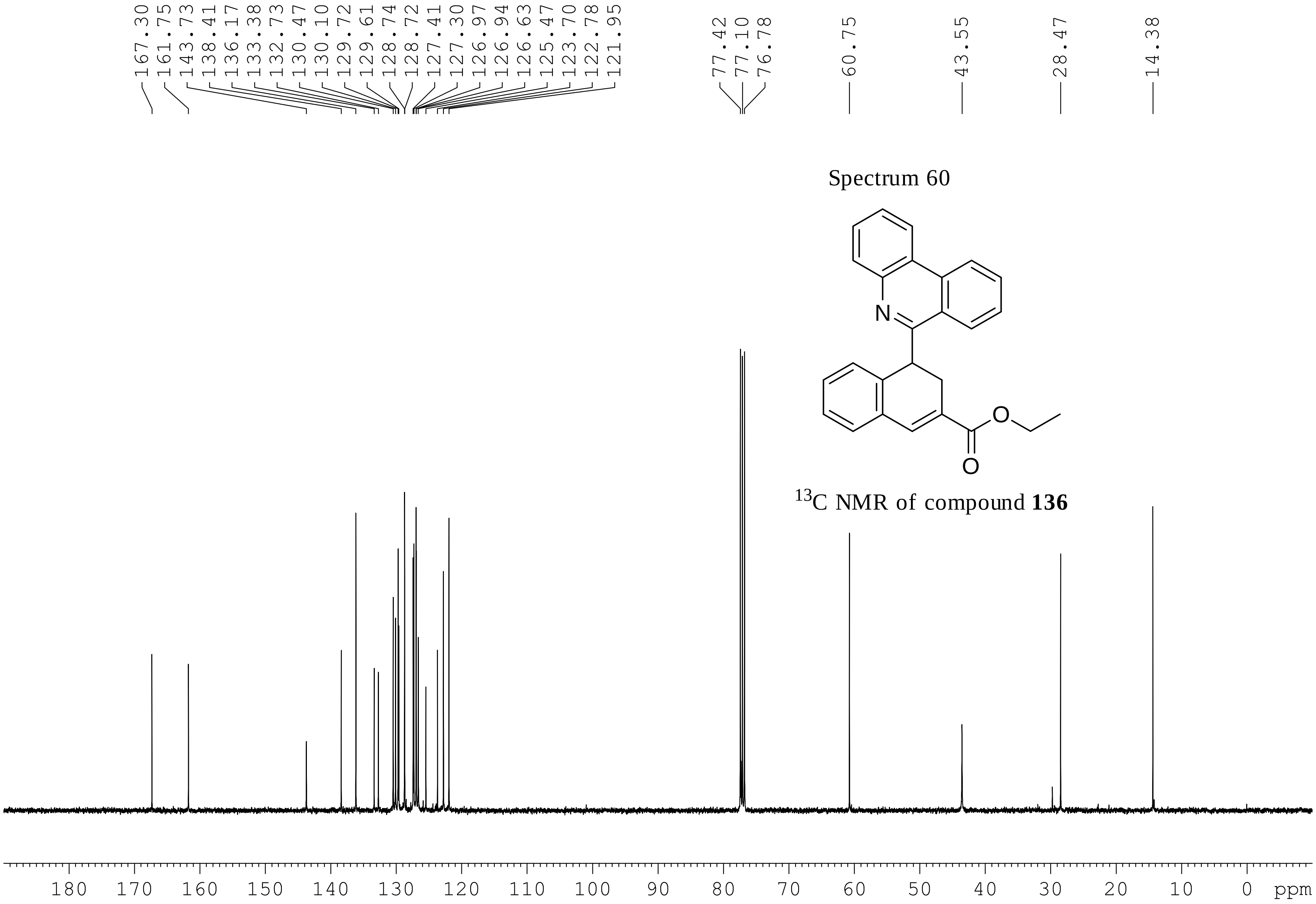
Spectrum 58

^{13}C NMR of compound **134**

Spectrum 59

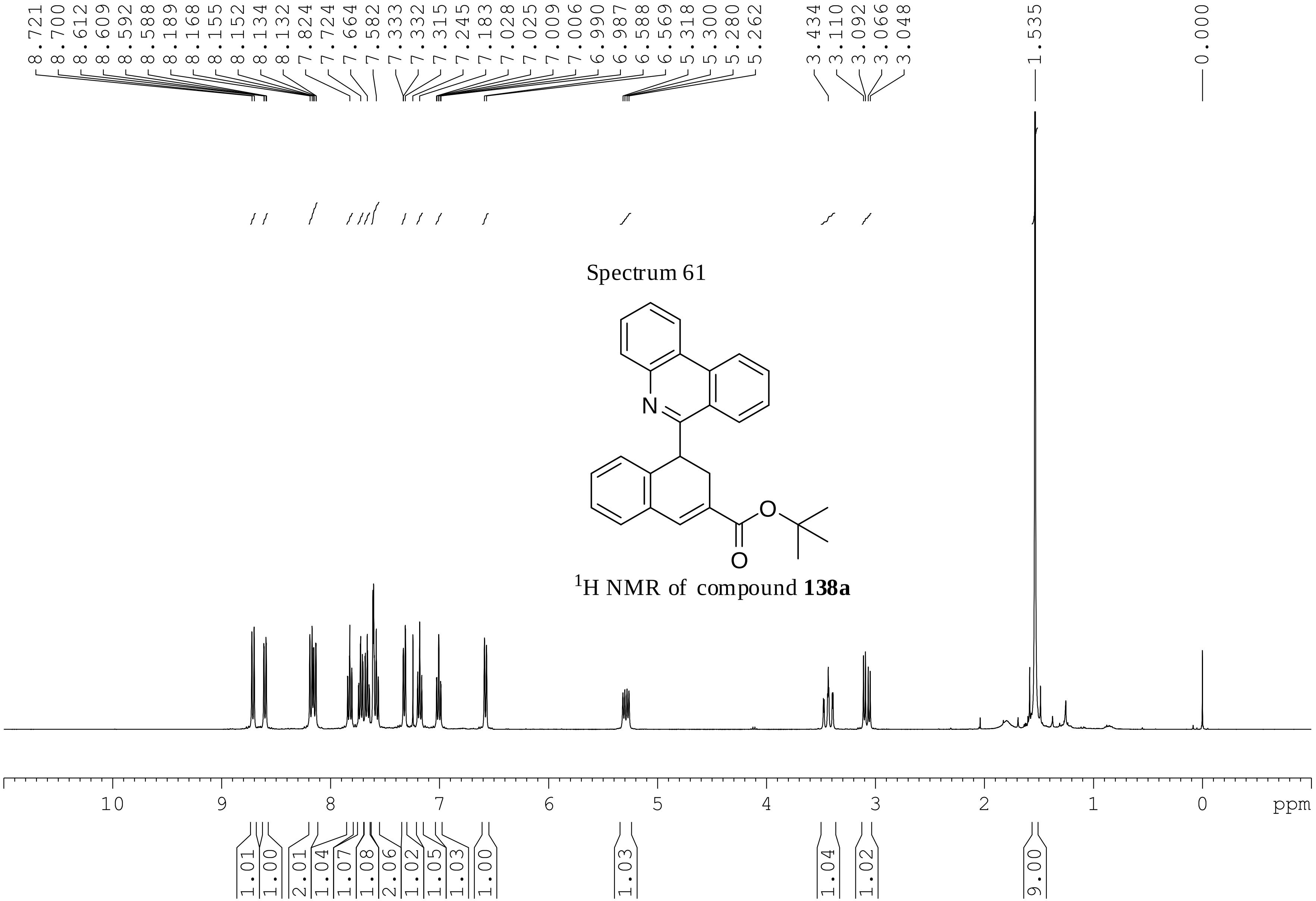


^{1}H NMR of compound **136**



Spectrum 60

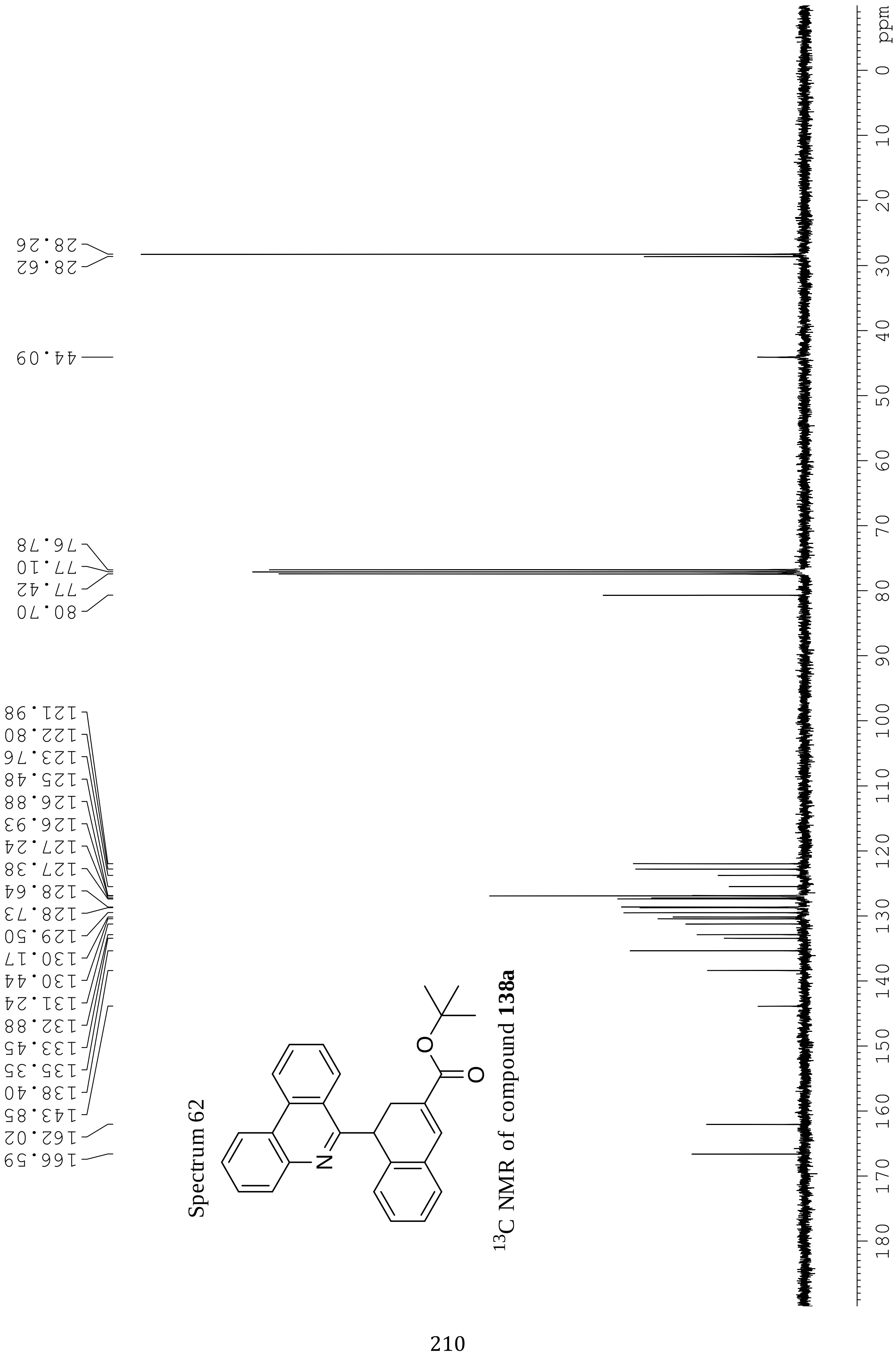
^{13}C NMR of compound **136**



Spectrum 61

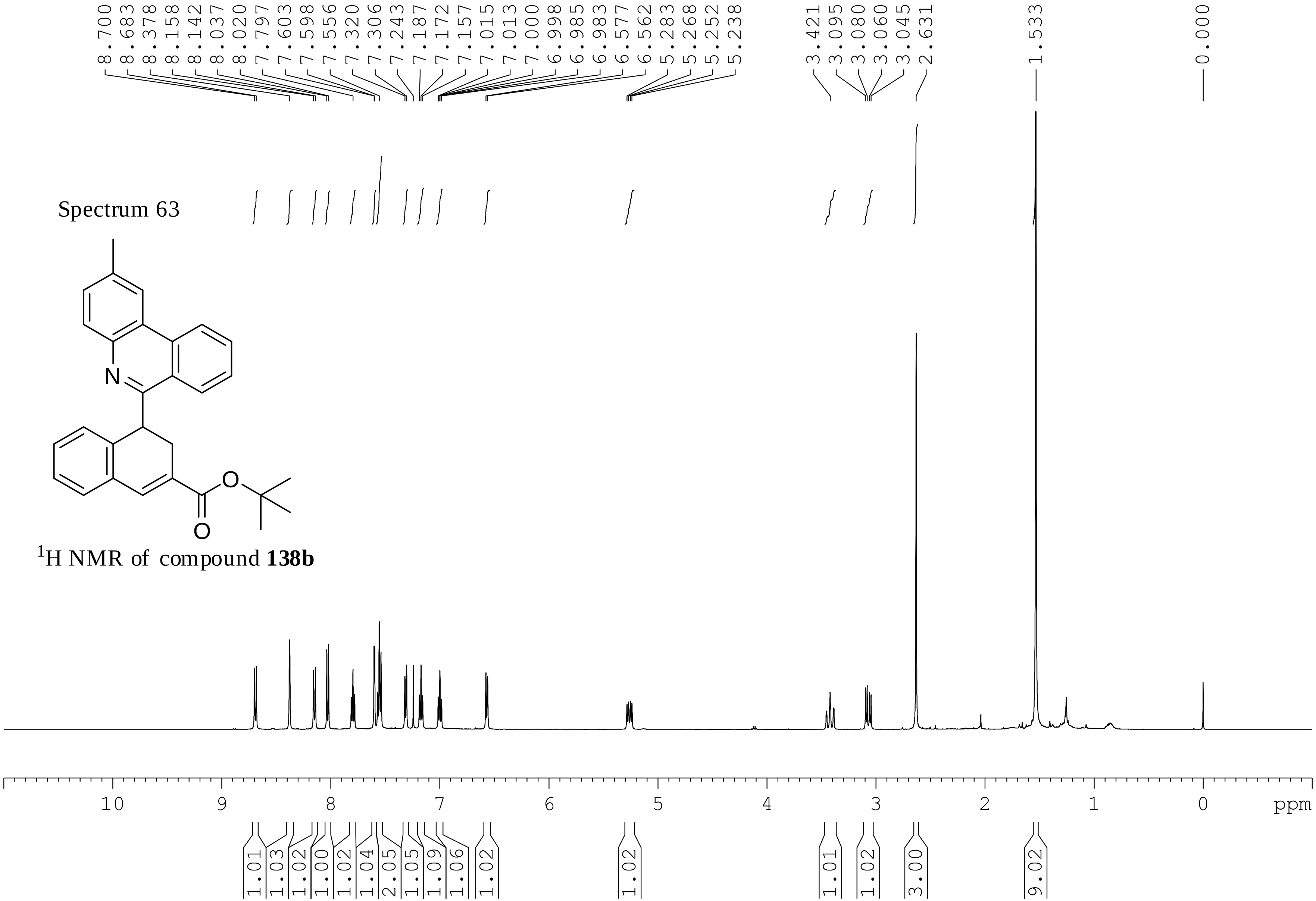
^{1}H NMR of compound **138a**

Spectrum 62

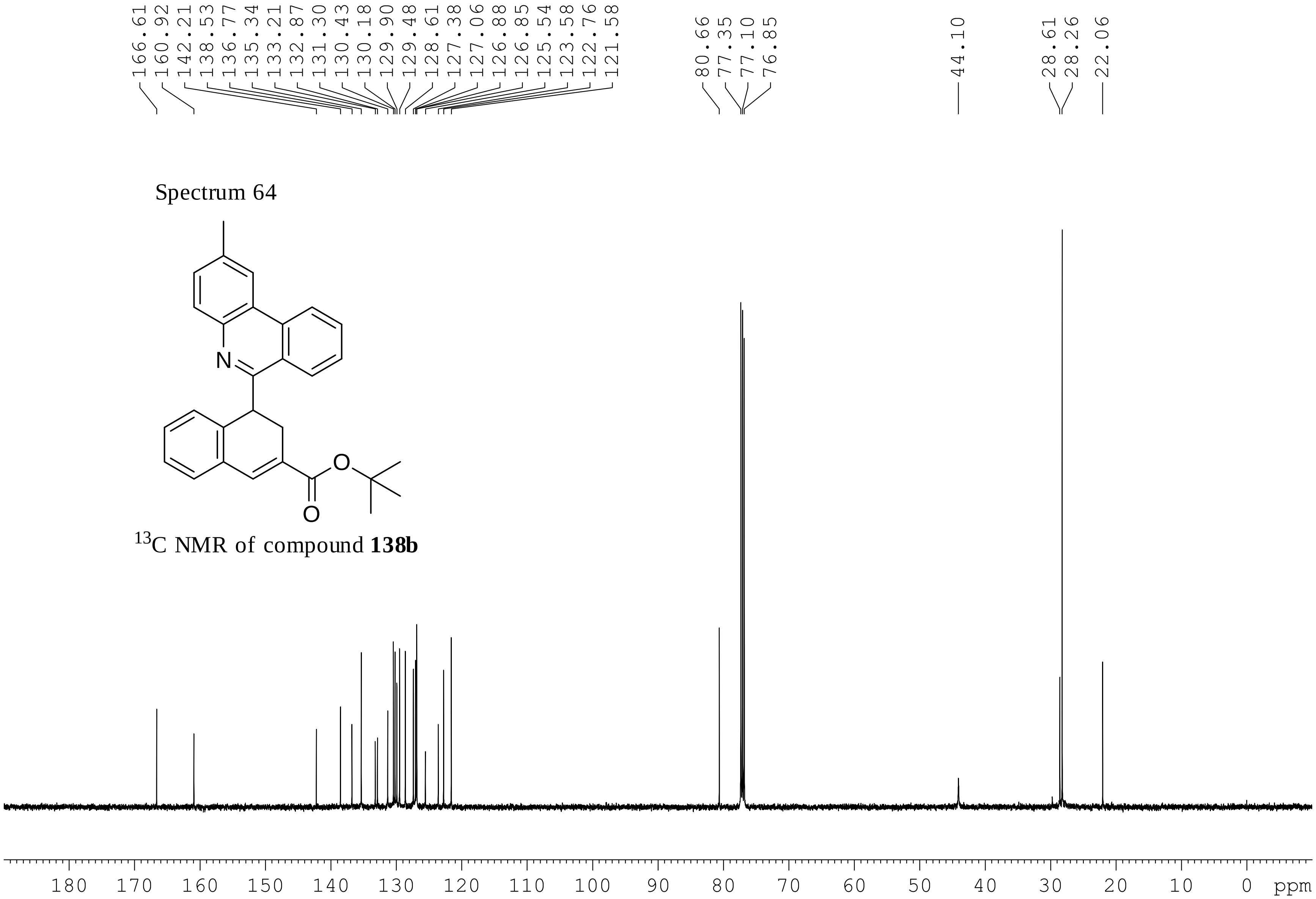


^{13}C NMR of compound **138a**

Spectrum 63



^{1}H NMR of compound **138b**



Spectrum 64

^{13}C NMR of compound **138b**

APPENDIX

(X-RAY CRYSTALLOGRAPHIC DATA)

Table I. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for **103d**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	x	y	z	U(eq)
C(1)	5298(2)	6085(2)	2325(1)	38(1)
C(2)	5710(2)	7705(2)	1501(1)	41(1)
C(3)	4447(2)	8061(2)	1435(1)	45(1)
C(4)	3433(2)	7231(2)	1553(1)	43(1)
C(5)	2076(2)	7408(2)	1260(1)	51(1)
C(6)	1174(2)	6531(2)	1336(1)	58(1)
C(7)	1596(2)	5477(2)	1701(1)	59(1)
C(8)	2937(2)	5295(2)	2008(1)	50(1)
C(9)	3845(2)	6169(2)	1946(1)	40(1)
C(10)	5621(2)	6732(2)	3087(1)	43(1)
C(11)	4739(2)	7282(3)	3390(1)	76(1)
C(12)	7020(2)	6635(2)	3524(1)	43(1)
C(13)	8662(2)	7507(3)	4497(1)	69(1)
C(14)	6677(2)	5751(2)	1380(1)	38(1)
C(15)	7457(2)	4823(2)	1745(1)	41(1)
C(16)	7974(2)	4003(2)	1319(1)	45(1)
C(17)	7766(2)	4090(2)	539(1)	57(1)
C(18)	7016(3)	5015(2)	186(1)	63(1)
C(19)	6461(2)	5849(2)	593(1)	50(1)
C(20)	6754(2)	8453(2)	1289(1)	45(1)
C(21)	8074(2)	8352(2)	1661(1)	50(1)
C(22)	9024(2)	9104(2)	1479(1)	61(1)
C(23)	8677(3)	9952(2)	929(2)	74(1)
C(24)	7376(3)	10054(3)	547(2)	88(1)
C(25)	6424(2)	9306(2)	721(2)	70(1)

Cl(1)	8900(1)	2817(1)	1786(1)	64(1)
N(1)	6115(1)	6577(1)	1816(1)	38(1)
O(1)	7747(2)	5823(2)	3468(1)	71(1)
O(2)	7360(1)	7542(1)	4001(1)	58(1)

Table II. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for **103k**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	x	y	z	U(eq)
C(1)	7060(1)	6000(2)	2505(1)	42(1)
C(2)	5913(1)	7616(1)	1768(1)	40(1)
C(3)	6677(1)	8066(2)	1375(1)	43(1)
C(4)	7513(1)	7286(2)	1230(1)	42(1)
C(5)	8139(1)	7569(2)	585(1)	52(1)
C(6)	8868(2)	6735(2)	421(2)	63(1)
C(7)	8984(2)	5621(2)	894(2)	67(1)
C(8)	8385(2)	5345(2)	1551(2)	57(1)
C(9)	7664(1)	6177(2)	1734(1)	43(1)
C(10)	7542(1)	6679(2)	3407(1)	51(1)
C(11)	8433(2)	7221(3)	3526(2)	91(1)
C(12)	6996(2)	6624(2)	4203(1)	56(1)
C(13)	6757(3)	7599(3)	5601(2)	109(1)
C(14)	5242(1)	5536(1)	1897(1)	39(1)
C(15)	4589(1)	5636(2)	1033(1)	48(1)
C(16)	3864(2)	4730(2)	749(2)	60(1)
C(17)	3805(2)	3718(2)	1301(2)	61(1)
C(18)	4442(2)	3615(2)	2161(2)	58(1)
C(19)	5152(1)	4525(2)	2469(1)	48(1)
C(20)	4995(1)	8343(2)	1828(1)	41(1)
C(21)	4636(2)	9217(2)	1140(1)	54(1)
C(22)	3827(2)	9970(2)	1218(2)	58(1)

C(23)	3327(1)	9872(2)	1972(1)	50(1)
C(24)	3666(1)	8978(2)	2646(1)	51(1)
C(25)	4482(1)	8221(2)	2578(1)	47(1)
C(26)	2434(2)	10687(2)	2039(2)	69(1)
N(1)	6004(1)	6440(1)	2194(1)	40(1)
O(1)	6499(2)	5744(2)	4363(1)	90(1)
O(2)	7155(2)	7607(2)	4750(1)	86(1)

Table III. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for **103m**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	x	y	z	U(eq)
C(1)	760(2)	2081(1)	1156(1)	33(1)
C(2)	-108(2)	3125(1)	2633(1)	34(1)
C(3)	895(2)	4148(1)	2532(1)	37(1)
C(4)	2346(2)	4079(1)	2024(1)	35(1)
C(5)	3789(2)	5022(1)	2212(1)	38(1)
C(6)	3953(2)	6082(1)	2934(1)	49(1)
C(7)	5378(2)	6944(2)	3109(1)	63(1)
C(8)	6697(2)	6796(2)	2571(2)	69(1)
C(9)	6581(2)	5796(2)	1872(1)	60(1)
C(10)	5137(2)	4873(1)	1672(1)	45(1)
C(11)	5025(2)	3809(1)	966(1)	50(1)
C(12)	3662(2)	2908(1)	814(1)	44(1)
C(13)	2317(2)	3040(1)	1345(1)	35(1)
C(14)	-710(2)	2328(1)	252(1)	36(1)
C(15)	-708(2)	3333(1)	-237(1)	56(1)
C(16)	-2139(2)	1304(1)	-131(1)	37(1)
C(17)	-4782(2)	635(2)	-1378(1)	63(1)
C(18)	678(2)	1041(1)	2775(1)	36(1)
C(19)	573(2)	-163(1)	2315(1)	46(1)

C(20)	1126(2)	-1081(1)	2931(1)	60(1)
C(21)	1754(3)	-835(2)	4010(2)	68(1)
C(22)	1820(2)	346(2)	4473(1)	63(1)
C(23)	1305(2)	1285(1)	3867(1)	46(1)
C(24)	-1533(2)	3119(1)	3195(1)	35(1)
C(25)	-2869(2)	2151(1)	2987(1)	43(1)
C(26)	-4240(2)	2175(2)	3483(1)	51(1)
C(27)	-4303(2)	3160(2)	4188(1)	53(1)
C(28)	-2988(2)	4121(2)	4408(1)	52(1)
C(29)	-1611(2)	4101(1)	3922(1)	44(1)
N(1)	138(1)	1986(1)	2136(1)	35(1)
O(1)	-2073(1)	283(1)	139(1)	51(1)
O(2)	-3473(1)	1620(1)	-841(1)	56(1)

Table IV. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for **106**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	x	y	z	U(eq)
C(1)	7024(2)	3826(2)	5703(2)	45(1)
C(2)	8138(2)	2349(2)	4904(2)	44(1)
C(3)	9195(2)	2481(2)	6206(2)	50(1)
C(4)	8974(2)	2913(2)	7353(2)	48(1)
C(5)	9838(3)	2712(2)	8672(3)	59(1)
C(6)	9533(3)	3097(3)	9700(3)	68(1)
C(7)	8388(3)	3680(3)	9448(3)	72(1)
C(8)	7529(3)	3899(3)	8158(3)	60(1)
C(9)	7837(2)	3536(2)	7115(2)	47(1)
C(10)	7760(2)	4985(2)	5540(2)	49(1)
C(11)	9042(3)	5608(3)	6456(3)	77(1)
C(12)	6917(2)	5387(2)	4230(3)	49(1)
C(13)	7091(3)	6559(2)	2690(3)	55(1)
C(14)	6858(4)	5877(3)	1486(4)	78(1)

C(15)	6370(4)	6422(4)	344(4)	87(1)
C(16)	6142(3)	7632(3)	448(3)	77(1)
C(17)	6367(3)	8285(3)	1662(3)	75(1)
C(18)	6839(3)	7749(3)	2800(3)	65(1)
C(19)	5541(2)	1906(2)	3939(2)	45(1)
C(20)	5525(3)	641(2)	3792(3)	59(1)
C(21)	4236(4)	-183(3)	3070(4)	80(1)
C(22)	2970(3)	242(4)	2529(3)	85(1)
C(23)	2976(3)	1497(4)	2686(4)	85(1)
C(24)	4250(3)	2338(3)	3378(3)	67(1)
C(25)	8275(2)	1838(2)	3696(2)	46(1)
C(26)	9327(3)	1126(2)	3835(3)	58(1)
C(27)	9485(4)	666(3)	2726(4)	72(1)
C(28)	8596(4)	893(3)	1459(4)	78(1)
C(29)	7557(4)	1590(3)	1299(3)	74(1)
C(30)	7395(3)	2069(2)	2407(3)	57(1)
N(1)	6852(2)	2768(2)	4647(2)	44(1)
O(1)	5650(2)	5137(2)	3532(2)	75(1)
O(2)	7745(2)	6081(2)	3894(2)	72(1)

Table V. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^2x 10^3) for **107a**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	x	y	z	U(eq)
C(1)	9739(2)	5564(2)	7720(1)	41(1)
C(2)	8234(2)	7200(2)	8319(1)	38(1)
C(3)	7600(2)	7722(2)	7818(1)	42(1)
C(5)	6469(3)	7281(2)	6804(1)	50(1)
C(6)	6376(3)	6466(3)	6313(1)	61(1)
C(7)	7315(3)	5316(3)	6281(1)	63(1)
C(8)	8367(3)	4985(2)	6742(1)	54(1)
C(9)	8497(2)	5805(2)	7232(1)	42(1)

C(4)	7519(2)	6959(2)	7275(1)	43(1)
C(10)	11395(3)	6274(2)	7599(1)	47(1)
C(11)	11849(3)	6774(3)	7086(1)	76(1)
C(12)	12535(3)	6329(3)	8089(1)	59(1)
C(13)	8736(2)	4965(2)	8727(1)	38(1)
C(14)	7187(3)	4870(2)	8992(1)	48(1)
C(15)	6903(3)	3893(2)	9415(1)	63(1)
C(16)	8122(3)	2995(2)	9564(1)	62(1)
C(17)	9651(3)	3077(2)	9297(1)	55(1)
C(18)	9970(3)	4067(2)	8885(1)	47(1)
C(19)	8159(2)	7885(2)	8899(1)	41(1)
C(20)	6800(3)	8691(2)	9040(1)	50(1)
C(21)	6742(3)	9349(2)	9577(1)	59(1)
C(22)	8005(3)	9215(2)	9978(1)	62(1)
C(23)	9354(3)	8419(2)	9845(1)	62(1)
C(24)	9429(3)	7759(2)	9309(1)	51(1)
N(1)	9074(2)	5969(2)	8298(1)	40(1)
N(2)	13434(3)	6352(3)	8476(1)	93(1)

Table VI. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **127a**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	x	y	z	U(eq)
Br(1)	5243(1)	6328(1)	1177(1)	66(1)
C(1)	6536(1)	2698(2)	3936(2)	34(1)
C(2)	6110(1)	4893(2)	3027(2)	32(1)
C(3)	5773(1)	4567(2)	3321(2)	36(1)
C(4)	5721(1)	3052(3)	3639(2)	38(1)
C(5)	5312(1)	2524(4)	3654(2)	51(1)
C(6)	5268(1)	1021(4)	3856(3)	66(1)
C(7)	5625(1)	31(4)	4052(3)	65(1)

C(8)	6040(1)	538(3)	4076(2)	52(1)
C(9)	6089(1)	2049(3)	3878(2)	36(1)
C(10)	6808(1)	3422(3)	4918(2)	38(1)
C(11)	6701(1)	3424(3)	5690(2)	51(1)
C(12)	7216(1)	4200(3)	4990(2)	43(1)
C(13)	6570(1)	3404(2)	2366(2)	32(1)
C(14)	6252(1)	3499(3)	1421(2)	41(1)
C(15)	6372(1)	3047(3)	659(2)	58(1)
C(16)	6794(1)	2471(3)	835(2)	62(1)
C(17)	7110(1)	2375(4)	1780(2)	58(1)
C(18)	7006(1)	2864(3)	2549(2)	44(1)
C(19)	6167(1)	6392(2)	2635(2)	32(1)
C(20)	5828(1)	7181(3)	1892(2)	37(1)
C(21)	5904(1)	8602(3)	1591(2)	45(1)
C(22)	6324(1)	9274(3)	2030(2)	49(1)
C(23)	6672(1)	8523(3)	2769(2)	47(1)
C(24)	6594(1)	7104(3)	3061(2)	37(1)
N(1)	6460(1)	3828(2)	3167(1)	31(1)
N(2)	7541(1)	4790(3)	5030(2)	63(1)

Table VII. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for **129a**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	x	y	z	U(eq)
C(1)	14369(16)	820(5)	9139(3)	52(2)
C(2)	16471(18)	608(5)	8770(4)	60(2)
C(3)	17045(16)	1279(6)	8267(3)	55(2)
C(4)	15394(15)	2118(5)	8145(3)	46(2)
C(5)	13251(14)	2344(4)	8513(3)	39(2)
C(6)	9547(14)	3431(4)	8690(3)	38(2)
C(7)	8853(14)	2814(4)	9244(3)	37(2)

C(8)	6667(15)	3077(5)	9611(3)	49(2)
C(9)	6073(17)	2480(6)	10126(3)	57(2)
C(10)	7638(17)	1628(5)	10289(3)	55(2)
C(11)	9784(17)	1338(5)	9949(3)	52(2)
C(12)	10463(15)	1935(4)	9405(3)	41(2)
C(13)	12706(14)	1670(4)	9035(3)	37(2)
C(14)	7738(15)	4357(5)	8479(3)	40(2)
C(15)	7563(17)	4660(5)	7845(3)	51(2)
C(16)	5802(16)	5591(5)	7654(3)	49(2)
C(17)	5838(18)	6222(5)	7918(3)	60(2)
C(18)	7623(16)	6029(5)	8392(3)	49(2)
C(19)	8378(19)	6742(5)	8565(4)	64(2)
C(20)	10070(20)	6572(6)	9001(4)	72(3)
C(21)	11103(17)	5683(6)	9281(4)	62(2)
C(22)	10346(15)	4958(5)	9123(3)	48(2)
C(23)	8684(14)	5110(4)	8675(3)	42(2)
C(24)	4250(20)	5829(6)	7154(4)	69(3)
C(25)	9328(17)	4187(5)	5859(3)	54(2)
C(26)	10834(17)	4379(5)	6242(3)	58(2)
C(27)	11591(16)	3730(5)	6735(4)	56(2)
C(28)	10718(15)	2873(5)	6859(3)	48(2)
C(29)	9101(13)	2662(4)	6478(3)	37(2)
C(30)	6647(13)	1572(4)	6302(3)	36(2)
C(31)	5939(13)	2181(4)	5761(3)	36(2)
C(32)	4374(15)	1927(5)	5393(3)	47(2)
C(33)	3677(16)	2512(6)	4878(3)	58(2)
C(34)	4568(17)	3382(5)	4710(3)	58(2)
C(35)	6084(16)	3649(5)	5057(3)	53(2)
C(36)	6789(14)	3072(4)	5589(3)	40(2)
C(37)	8421(13)	3315(4)	5969(3)	38(2)
C(38)	5599(16)	633(5)	6519(3)	44(2)
C(39)	5091(16)	346(5)	7149(3)	51(2)
C(40)	4070(15)	-587(5)	7351(3)	46(2)
C(41)	4994(18)	-1211(5)	7087(3)	61(2)

C(42)	7072(16)	-1029(5)	6609(3)	48(2)
C(43)	8661(19)	-1735(6)	6434(4)	63(2)
C(44)	10640(20)	-1564(6)	6003(4)	70(3)
C(45)	11070(17)	-673(6)	5714(4)	63(2)
C(46)	9452(15)	48(5)	5871(3)	49(2)
C(47)	7456(15)	-112(4)	6324(3)	41(2)
C(48)	2220(20)	-822(5)	7844(4)	66(2)
N(1)	11612(12)	3201(4)	8366(2)	42(2)
N(2)	2990(20)	6007(6)	6757(4)	96(3)
N(3)	8195(12)	1781(3)	6643(2)	41(1)
N(4)	750(20)	-1012(5)	8248(4)	95(3)

Table VIII. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for **130**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	x	y	z	U(eq)
C(1)	-381(8)	3422(2)	1715(2)	48(1)
C(2)	-2156(9)	3988(3)	1517(2)	56(1)
C(3)	-2323(9)	4751(3)	1795(2)	55(1)
C(4)	-736(8)	4924(2)	2270(2)	43(1)
C(5)	1042(7)	4359(2)	2491(2)	36(1)
C(6)	4126(7)	4051(2)	3228(1)	30(1)
C(7)	4615(8)	3257(2)	2961(2)	32(1)
C(8)	6438(8)	2709(2)	3207(2)	44(1)
C(9)	6898(9)	1971(2)	2939(2)	56(1)
C(10)	5516(10)	1747(2)	2424(2)	55(1)
C(11)	3695(9)	2260(2)	2181(2)	50(1)
C(12)	3180(8)	3030(2)	2445(2)	33(1)
C(13)	1289(7)	3589(2)	2205(2)	35(1)
C(14)	5449(8)	4293(2)	3814(2)	32(1)
C(15)	6151(8)	5201(2)	3845(2)	39(1)
C(16)	7295(8)	5413(2)	4444(2)	32(1)

C(17)	6452(7)	5036(2)	4942(2)	37(1)
C(18)	4422(8)	4413(2)	4918(2)	32(1)
C(19)	3009(8)	4196(2)	5432(2)	46(1)
C(20)	1043(9)	3620(2)	5397(2)	51(1)
C(21)	482(8)	3258(2)	4857(2)	47(1)
C(22)	1916(7)	3464(2)	4344(2)	37(1)
C(23)	3846(7)	4043(2)	4365(2)	29(1)
C(24)	9261(8)	6073(2)	4473(2)	40(1)
C(25)	12263(9)	6785(2)	5096(2)	70(1)
N(1)	2484(7)	4573(2)	2998(1)	36(1)
O(1)	9935(7)	6484(2)	4054(1)	66(1)
O(2)	10217(6)	6182(2)	5030(1)	58(1)

Table IX. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for **138a**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	x	y	z	U(eq)
C(1)	4482(2)	7006(2)	5627(1)	51(1)
C(2)	3093(3)	6871(2)	6443(2)	64(1)
C(3)	1647(3)	6510(2)	6323(2)	67(1)
C(4)	1600(2)	6298(2)	5390(2)	59(1)
C(5)	3006(2)	6434(2)	4540(1)	42(1)
C(6)	4150(2)	6317(2)	2807(1)	40(1)
C(7)	5724(2)	6705(1)	2812(1)	39(1)
C(8)	7090(2)	6886(2)	1912(2)	50(1)
C(9)	8565(2)	7202(2)	1983(2)	61(1)
C(10)	8763(2)	7345(2)	2934(2)	62(1)
C(11)	7461(2)	7208(2)	3805(2)	53(1)
C(12)	5901(2)	6903(1)	3766(1)	37(1)
C(13)	4483(2)	6779(1)	4655(1)	37(1)
C(14)	3924(2)	5982(2)	1845(1)	44(1)

C(15)	2880(3)	4807(2)	2288(2)	55(1)
C(16)	2623(2)	4478(2)	1346(1)	43(1)
C(17)	2445(2)	5439(2)	369(1)	45(1)
C(18)	2520(2)	6805(2)	188(1)	42(1)
C(19)	1876(2)	7813(2)	-676(1)	53(1)
C(20)	1865(3)	9093(2)	-796(2)	62(1)
C(21)	2514(3)	9387(2)	-67(2)	61(1)
C(22)	3181(2)	8401(2)	787(2)	52(1)
C(23)	3186(2)	7108(2)	932(1)	40(1)
C(24)	2491(2)	3100(2)	1517(1)	47(1)
C(25)	2507(2)	876(2)	2998(2)	52(1)
C(26)	2443(4)	457(2)	4244(2)	84(1)
C(27)	4098(3)	404(2)	2431(3)	90(1)
C(28)	1013(3)	455(2)	2800(2)	81(1)
N(1)	2876(2)	6194(1)	3614(1)	46(1)
O(1)	2397(2)	2745(1)	791(1)	77(1)
O(2)	2487(2)	2311(1)	2594(1)	50(1)

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LIST OF PUBLICATIONS

1. Baylis-Hillman reaction: *In Situ* generated isoquinolinium species as excellent electrophiles for coupling with alkyl acrylates and acrylonitrile.

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Poster and Oral Presentations

1. *In Situ* generated isoquinolinium species as valuable electrophiles for Baylis–Hillman reaction.

   Poster cum Oral presentation at *ChemFest* 2018.

2. *In Situ* generated isoquinolinium species as valuable electrophiles for Baylis–Hillman reaction.
   Poster presentation at *International Collaborative & Cooperative Chemistry (ICCCS-8.* 2017.

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by Thamizharasi Perumal

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