METAL MEDIATED SYNTHESIS OF 2, 3-DIHYDRO BENZOFURAN DERIVATIVES

M.Sc. THESIS

A

DISSERTATION SUBMITTED IN PARTIAL

FULFILLMENT OF THE REQUIREMENT FOR THE

DEGREE OF

MASTER OF SCIENCE (M.Sc.)

IN

CHEMISTRY

SUBMITTED BY

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SESSION: APRIL-2017
NOVEMBER, 2019

ORGANIC CHEMISTRY LABORATORY
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DHAKA-1000

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The thesis titled **"METAL MEDIATED SYNTHESIS OF 2, 3-DIHYDRO BENZOFURAN DERIVATIVES"** submitted by ASHUTOSH NATH, Roll No.: 0417032602F, Registration No.: 0417032602F, Session: April-2017 has been accepted as satisfactory in partial fulfilment of the requirement for the degree of Master of Science (M.Sc.) in Chemistry on **November 30, 2019**.

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STUDENT'S DECLARATION

I hereby certify that this material, which I now submit for assessment on the programme of study leading to the award of M.Sc is entirely my own work, and I also declare this thesis or any part of it has not been submitted elsewhere for the award of any degree or diploma.

Signature of the Student

Date:……..

……...……

ASHUTOSH NATH (Candidate)

St. ID: 0417032602F

Dedicated

to

My Beloved Family

&

Honorable supervisor

Acknowledgement

At the beginning, I humbly acknowledge my deepest gratitude to the almighty, the most gracious, benevolent and merciful creator for his infinite mercy bestowed on me in carrying out the research work presented in the dissertation.

It is a great pleasure for me to acknowledge my deepest sense of gratitude, sincere, appreciation, heartfelt indebtedness and solemn regards to my reverend teacher and supervisor Dr. Md. Wahab Khan, Professor, Department of Chemistry, Bangladesh University of Engineering and Technology (BUET), for his kind supervision, indispensable guidance, valuable and constructive suggestions, liberal help and continuous encouragement during the whole period. It is obvious that his attributive contribution and efforts have greatly shaped me into what I am today. In fact, I am quite lucky to be a part of his ambitious research team.

It is my great honor to convey my sincere gratitude to my respected teacher Professor Dr. Md. Abdur Rashid, honorable Head of the Department of Chemistry, BUET for giving me his wonderful support to move through the academic processes during this M.Sc. program.

I would like to convey my deepest gratitude to Assistant Professor Dr. Md. Wahab Khan for giving me an opportunity to use all instrument, apparatus from his laboratory.

I am thankful to all other respected teachers of the Department of Chemistry, BUET, for their continuous support. I would also like to thank all of my undergraduate teachers Md. Jahangir Alam, Sayad Mohammad Monzurul Karim, Dr. Md. Edris Ali, Sadia Alam Chowdhury & Chandan Kanti Dey.

I am highly thankful to M.A.AShofi Sarkar, scientific Officer, BCSIR, Dhaka; Md. Moniruzzaman, Department of Chemistry, BUET, Dhaka for his cooperation in taking FT-IR spectrums; Md. Emdad Hossain, Scientist, WMSRC, Jahangirnagar University for helping me during characterizations of my samples.

I am highly grateful to all members of the board of examiners for their valuable suggestions and appreciated comments.

I am thankful to my dear consociate and all the members of MW Khan Research Group Walid Bin Kader, AjoyKumer, Tanvir Sultana, Laila Afrin, Saidul Islam, Md. Jahir Khan and Khadiza for their friendly behavior and fruitful suggestions.

My special thanks to Md. Johir Khan, Khadizafor their continuous help during the research.

In particular, I am grateful to Md. Johir Khan (for any organic synthesis problem sessions).

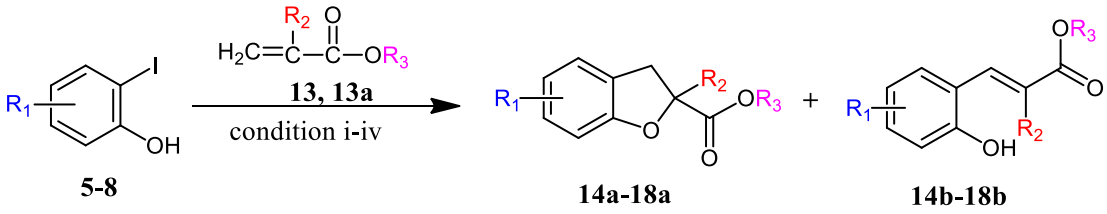
Lastly, I am very grateful to my family and Mrs. Masuda Khanam, Md. Nasir Uddin, Subrata Mallik, Rohit Das, Gandhi Devi, Titu Roy Chowdhury, Md. Abdul Kadir Chowdhury, Rony Saha, Monzur Ahmed, SoniyaAkter and ParitoshBarai for giving me inspiration, advice and my brother Paritosh Nath supporting me spiritually throughout my life.

Finally, I would like to express my heartfelt indebtedness and profound gratitude to my beloved father, mother, brother and sisters for their continuous inspiration and immeasurable sacrifices throughout the period of my study.

Author
(ASHUTOSH NATH)

Abstract

Dihydrobenzofuran (DHB) is the key structure moiety of many highly bilogically active materials, constructing pharmaceuticals (furadm), lignans and other biologically natural compounds (pterocarpans). Pterocarpans have a 2,3-Dihydrobenzofuran skeleton which could be response to fungi infections and biological activities against such as HIV, central nervous system(CNS) injury and malaria. An efficient one pot synthesis of 2,3-dihydrobenzofurans (**14a-18a**) derivatives by bis-triphenyl phosphine palladium(II) chloride, bis-triphenyl phosphine cobalt(II) chloride, bis-triphenyl phosphine nickel(II) bromide and Pd/Cu bimetallic nano particles catalyzed reactions of 2-iodophenol derivatives with terminal alkenes is reported. The reactions of 2-iodophenol derivatives (**5-8**) with acrylic esters (**13,13a**) were performed in presence of different catalyst [$Pd(Ph_3P)_2Cl_2$, $Co(Ph_3P)_2Cl_2$, $Ni(Ph_3P)_2Br_2$, Pd/Cu Bimetallic nano particles], triethylamine (Et_3N) and DMF under nitrogen atmosphere for 20-24 hrs at 80-120 ^oC to obtain alkyl 2, 3-dihydrobenzofuran-2-ylcarboxylates (**14a-18a)** in good yield %(50-70) as shown in the **scheme**



5-8 **14a-18a** **14b-18b**

5, 14 R^1 = *p*-Cl;
6, 15 R^1 = *m*-CH_3;
7, 16 R^1 = *o*-CH_3;
8, 17 R^1 = C_6H_6

R^2 = **13, 14-17** CH_3
R^2 = **13a, 18** H

R^3 = **13, 14-17** CH_3
R^3 = **13a, 18** C_4H_9

Condition	
i	$Pd(Ph_3P)_2Cl_2$, DMF, Et_3N, N_2, 80-100 ^oC, 20-24 hrs
ii	$Co(Ph_3P)_2Cl_2$, DMF, Et_3N, N_2, 80-100 ^oC, 20-24 hrs
iii	$Ni(Ph_3P)_2Br_2$, DMF, Et_3N, N_2, 80-100 ^oC, 20-24 hrs
iv	Pd/Cu Bimetallic nano particles, DMF, Et_3N, N_2, 80-100 ^oC, 20-24 hrs

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List of abbreviations of technical symbols and terms

Elaborations	Abbreviations
Succinic Acid	SA
n-octylamine	NOA
Broad singlet	br s
Mega Hertz	MHz
Hertz	Hz
Singlet	s
Doublet	d
Triplet	t
Quartet	q
Multiplet	m
Melting point	m.p.
Ultra Violet-Visible	UV-Vis
Infrared Spectroscopy	IR
Nuclear Magnetic Resonance	NMR
Mass Spectrometry	MS
Round bottomed flask	RB
Thin Layer Chromatography	TLC
Gas Chromatography-Mass Spectrometry	GC-MS
Proton NMR	^{1}H-NMR
Carbon-13 NMR	^{13}C-NMR

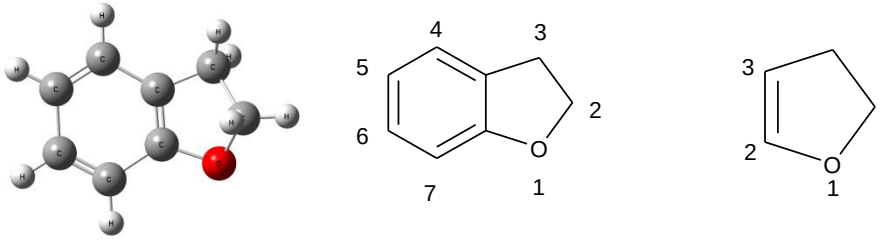
CHAPTER 1

Introduction

1. Background of the Present Work

1.1 Introduction :

The 2,3-dihydrobenzofuran (DHB) skeleton **1** comprises a saturated 5-membered oxygen heterocycle fused to a benzene ring with the oxygen atom adjacent to the aromatic system (**Fig. 1**). This ring system confers a rigid shape to a molecule, with a well-defined spatial arrangement of substituents in a similar manner to strained small rings such as cyclopropanes and cyclobutanes. However, the ring-strain in the DHB system is moderate, and somewhat smaller than in the corresponding dihydrofuran system **2** without the fused benzene ring [1]. The older name "coumarone" is nearly obsolete. The corresponding formal hydrogenation of the furan ring gives the 2,3-dihydrobenzofuran (1) nucleus (older name coumarane).



1 **2**

Fig. 1 : The structures of 2,3-dihydrobenzofuran (DHB) and 2,3-dihydrofuran

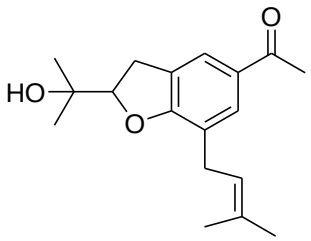
The dihydrobenzofuran moiety has been known for a long time, and a first report on its synthesis dates back to 1892 [2]. Successively, various methods have been applied for the preparation of 2,3-dihydrobenzofurans. Clearly, many of the methods for the preparation of substituted 2,3-dihydrobenzofurans developed in the early days of the last century do not appear to be satisfactory from the standpoint of yield, selectivity and generality [3].

1.2 Biological importance of DHBs:

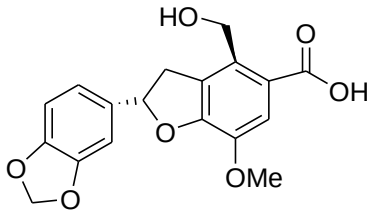
Many bioactive molecules containing the DHB structural motif have been reported including a vast array of natural products (selected examples shown in **Fig. 2**, **3–8**) [4-10] and numerous synthetic compounds with useful biological activity (selected examples shown in (**Fig. 3**, **9–14**). DHB containing natural products have been reported with activity against cancer (**4–5**) [4, 5, 10-12]. tuberculosis, [13] malaria [14] and cataracts [15] as well as activity at specific targets such as HIF-1 (**8**), [8]^{6} αglucosidase, [16] aldose reductase, [8] 5-LOX (7), [9] COX-2 (7), [10] NF-κβ [6] and the muscarinic M_3 receptor [15-18]. Other DHB natural products show antioxidant and/or cytoprotective properties [19] and insecticidal activity [20] **Figure 1** shows only a fraction of the many known DHB natural products — more than 500 DHB-containing natural products were reported in 2009–2010 alone. [A Reaxys® search of DHB containing natural products reported during this time period produced 562 substance hits. Note that this includes previously known structures (re-isolations, etc) as well as structurally novel natural products.]

It should also be noted that a DHB system forms part of the skeleton of the morphine alkaloids, although the synthesis of these more complex polycyclic systems will not be considered here.

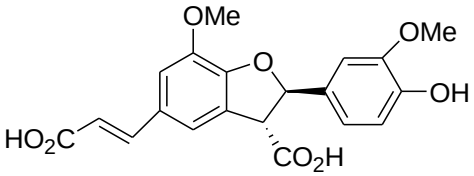
Synthetic DHB derivatives include recently reported molecules such as the GPR4 Agonist **9** [21] imidazolium compound **10** (cytotoxic) [22], triazole **11** (antitubercular) [23], diester **12** (active against leishmaniasis) [24], and the drugs Prucalopride **13** [25] (treatment of constipation) and Efaroxan**14** (α_2-adrenoceptor antagonist) [26].



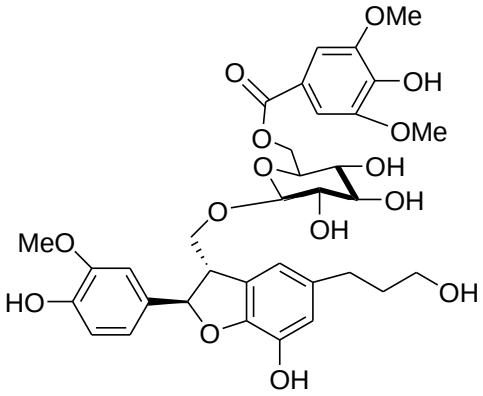
Senecio vulgaris DHB **3**



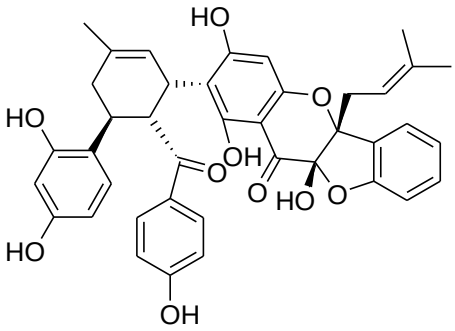
Cedralin A **4** (weakly cytotoxic)



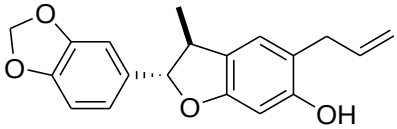
Benfur **5** (anti-mitotic)



Lophanthoside B **6**

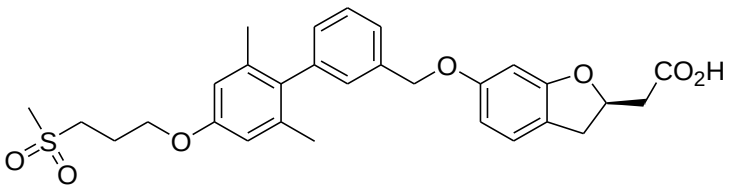


Sanggenon C **8** (HIF-1Inhibitor)

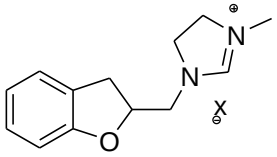


Liliflol A **7** (COX-2 and 5-LOX inhibitior)

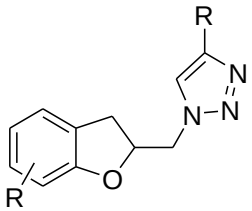
Fig. 2 : Selected DHB natural products



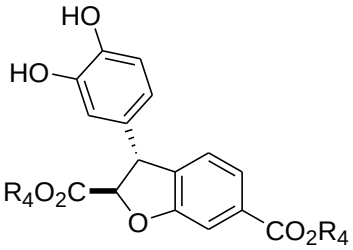
GPR4 Agonist **9**



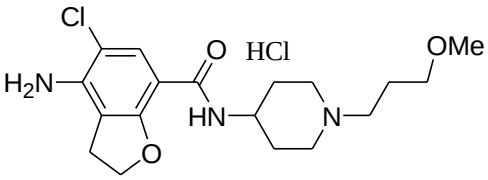
Cytotoxin **10**



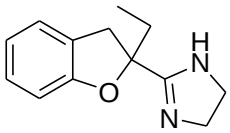
Antitubercular **11**



Antileishmanial **12**



Prucalopride **13**

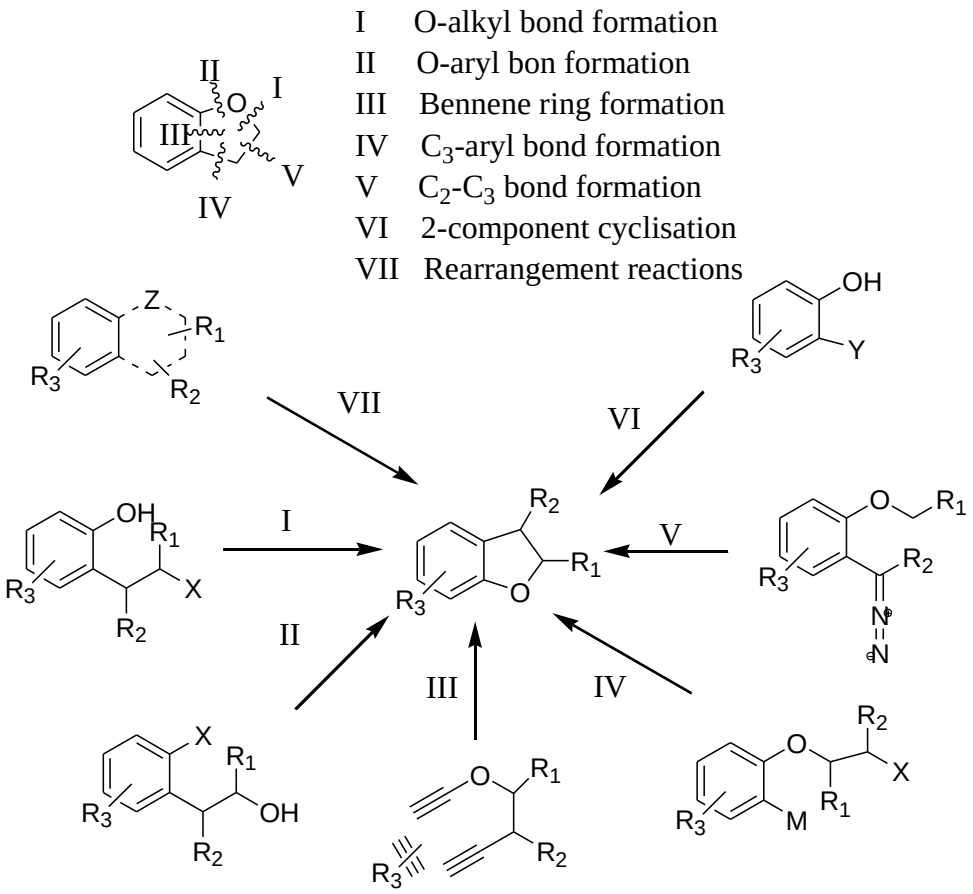


Efaroxan **14**

Fig. 3 : Some synthetic DHBs with useful biological activity

1.3 General Methods for the Synthesis of Benzofurans:

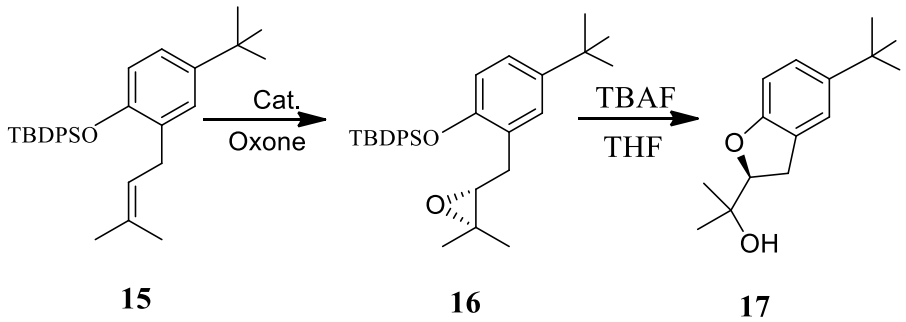
It is considered as one of the important heterocyclic rings because of its diverse biological profile [27]. Medicinal chemists are actively involved in the synthesis of benzofuran ring containing molecules due to its clinical importance [28]. Many of the clinically approved drugs are synthetic and naturally occurring substituted benzofuran derivatives containing mono and fused benzofuran ring in conjunction with other heterocycles. As a consequence of the diverse biological activities displayed by these compounds, synthetic chemists have developed many effective methods for accessing the DHB skeleton. The DHBs moiety has been known for a long time, and first report on its synthesis dates back to 1892 [29]. The synthetic approaches are classified according to the method by which the saturated oxygen ring is constructed. Plausible synthetic approaches to the DHB skeleton are shown in **Scheme 1**. The most obvious strategy involves a classical phenol alkylation approach (**I**, O-alkyl bond formation). Alternatively, the O-aryl bond can be constructed via a transition-metal catalysed cross coupling (**II**). The direct construction of the aromatic ring itself (**III**) is an approach that has rarely been applied in DHB synthesis. In contrast, the construction of the C-aryl bond (**IV**) is a well explored approach (e.g. via lithation of an aryl halide). The formation of the alkyl C–C bond (**V**) is commonly achieved via transition-metal mediated carbene C–H insertion processes using diazo compounds. Finally, more complex strategies involving either the formation of two or more bonds in a single reaction (**VI**), or the rearrangement of an existing ring system (**VII**) can be employed.


I O-alkyl bond formation
II O-aryl bon formation
III Bennene ring formation
IV C_3-aryl bond formation
V C_2-C_3 bond formation
VI 2-component cyclisation
VII Rearrangement reactions
I
II
III
IV
V
VI
VII

Scheme 1

1.3.1 Formation of the *o*-alkyl bond

The intramolecular alkylation of a phenol is perhaps the most common method for the construction of DHBs. Given that many natural products contain a hydroxyalkyl group joined to the ring system at C_2, the ring opening of an epoxide is a particularly useful approach and has been explored extensively in recent years. For example, the chiral ketone **15** was used to access enantioenriched epoxides **16** which gave the corresponding DHB derivatives **17** in good yield and high (**Scheme 2**), after deprotection of the phenol with fluoride [30].

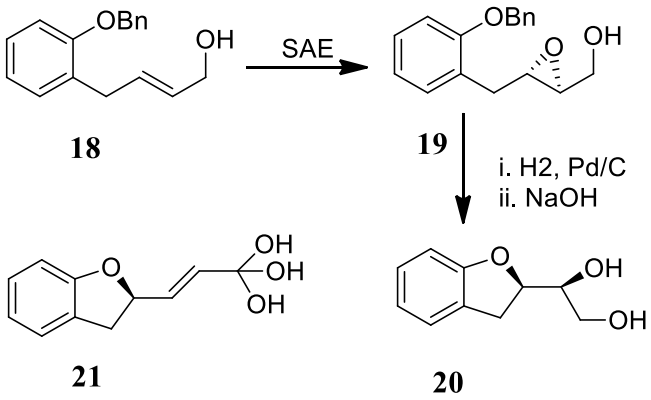


15 **16** **17**

Scheme 2

This approach was used in the synthesis of the DHB containing natural product (+)-marmesin [31]. In a similar fashion, Sharpless asymmetric epoxidation of allylic alcohols such as **18** gave enantioenriched epoxides **19** (**Scheme 3**). Deprotection of the phenol and cyclisation with base enabled chiral diol **20** to be synthesised in good

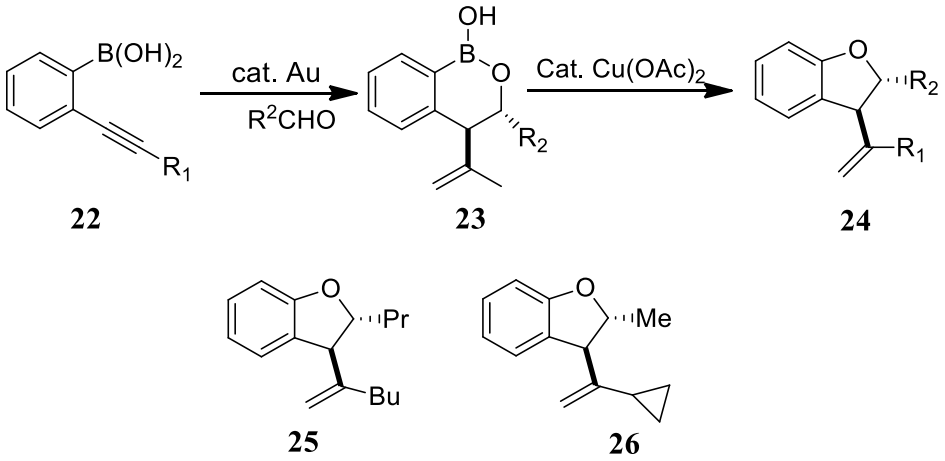
yield [32]. This approach was used to access the core structure (**21**) of heliannuols G and H [33].



Scheme 3

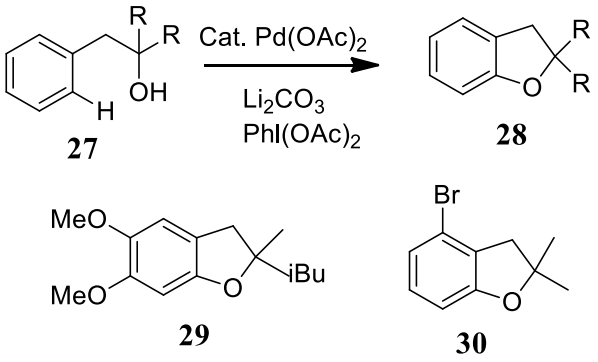
1.3.2 Synthesis of DHBs by formation of the O-aryl bond

The intramolecular copper or palladium-catalysed coupling of an aliphatic alcohol with an aryl halide is an effective strategy to access DHB derivatives which was developed several years ago [34-37]. Surprisingly there have been few recent developments in this area, despite the high level of interest in the development of novel catalytic methods for aryl-heteroatom bond formation. An unusual approach to DHBs via a catalytic intramolecular Chan–Lam coupling reaction has recently been reported (**Scheme 4**) [38]. o-Alkynlbenzeneboronic acids **22** undergo Au-catalysed enolate formation and aldol reaction to give cyclic borates **23**. These compounds can be cyclised to the corresponding 2,3-disubstituted DHBs**24** containing a pendant ketone group at C_3 with very good yields over this three step reaction process. It is notable that this crosscoupling reaction involves the arylation of an aliphatic alcohol and also only requires catalytic quantities of copper; both of these factors being somewhat unusual in Chan-Lam coupling reactions [39]. This approach is potentially quite versatile as variation of the groups at R_1 and R_2 can easily be achieved (e.g. **25–26**).



Scheme 4

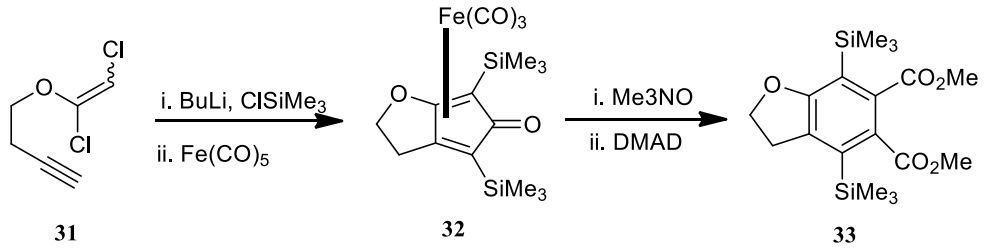
Yu and co-workers recently reported a Pd-mediated C-H activation protocol for the direct cyclisation of homo-benzylic alcohols **27**, which proceeds in high yield to give 2,2-disubstituted DHBs**28** (**Scheme 5**) [39]. These reactions were much more efficient for the formation of 2,2-disubstituted DHBs (e.g. **29**–**30**), with the corresponding reactions of secondary alcohols proceeding in lower yield. Nevertheless, this methodology is potentially very powerful as it does not require pre-functionalisation of the aromatic ring. It is also compatible with the presence of aryl bromides, enabling the construction of halogenated DHBs (**30**) which can then be further elaborated via traditional transition-metal catalysed coupling reactions.



Scheme 5

1.3.3 Synthesis of DHBs by formation of the aromatic ring

The direct formation of the benzene ring has rarely been used in the construction of DHBs, despite the fact that Rh-catalysed [2+2+2] cycloadditions for the formation of closely related fused benzofurans have been reported [40]. An iron-mediated approach proceeding via the Fe-complexed cyclopentadienone **31** was reported in 2001 (**Scheme 10**) [41]. An alkynyl homopropargyl ether, generated from the dichlorovinyl ether **32**, underwent cyclisation in the presence of iron pentacarbonyl to give **33** in moderate yield over the two steps. After oxidative decomplexation, the free cyclopentadienone system readily undergoes cycloaddition with dimethyl acetylenedicarboxylate (DMAD) followed by extrusion of CO, to give the polysubstitutedDHB**32** in moderate yield over two steps. This example serves to illustrate how this type of approach can be used to construct DHBs containing a highly substituted aromatic ring.



31 32 33

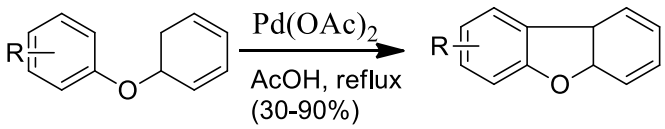
Scheme 6

1.3.4 Synthesis of DHBs by Palladium-Catalyzed

Due to the versatility, availability and utility of organopalladium complexes, palladium is one of the most extensively used transition metal for synthetic purpose [42-43].The recent trend is to develop palladium catalyzed heteroannulation procedure for the synthesis and functionalization of various heterocyclic moieties.

The initial reports of palladium catalyzed synthesis of benzofurans involved use of stoichiometric amount of costly palladium complexes. However, over the years, a number of very efficient catalytic systems has been developed, making the procedure competitive with the available methods of synthesis.

A stoichiometric palladium acetate catalyzed cyclization of diphenyl ethers **34** and related compounds in acetic acid was reported in 1975 [44] **35** (**Scheme 7**).



34 35

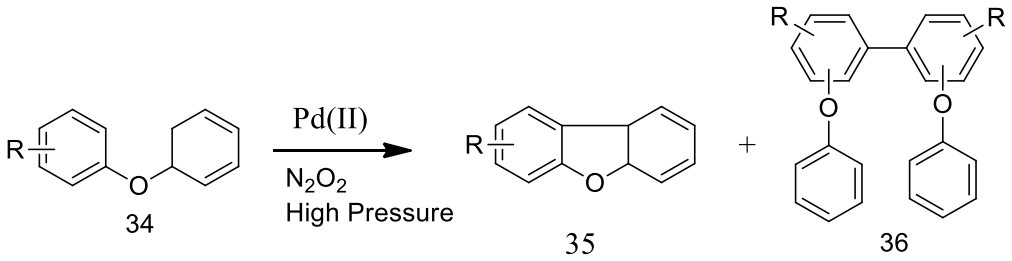
94 : R = H

Scheme 7

The rate of cyclization and required amount of palladium acetate were found to depend upon electron supply in the aromatic ring. In the presence of electron releasing groups cyclization was rapid (0.5-1h) and required one equivalent of the catalyst. Presence of electron withdrawing groups on the aromatic rings

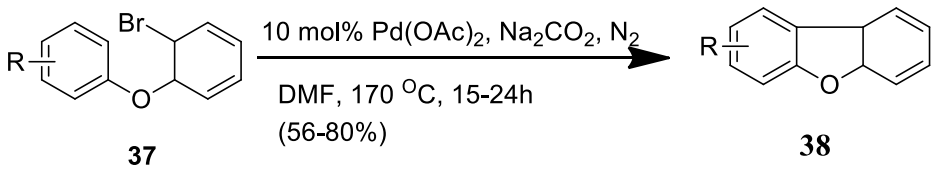
necessiateduse of two equivalents of palladium acetate and the reaction took longer time (≅ 2 hours) to get completed. The reaction was found to be catalyzed by acids.

The palladium acetate catalyzed cyclization of diphenyl ethers **34** under acidic condition reported by Akermark*et a1*[44]in 1975 required stoichiometric amounts of palladium acetate. It could be made catalytic by carrying out the reaction at high pressure in 1:1 mixture of nitrogen and oxygen [45]. However lack of selectivity led to intermolecular hydrogenative coupling to give **36** as a side product **(Scheme 8).**



Scheme 8

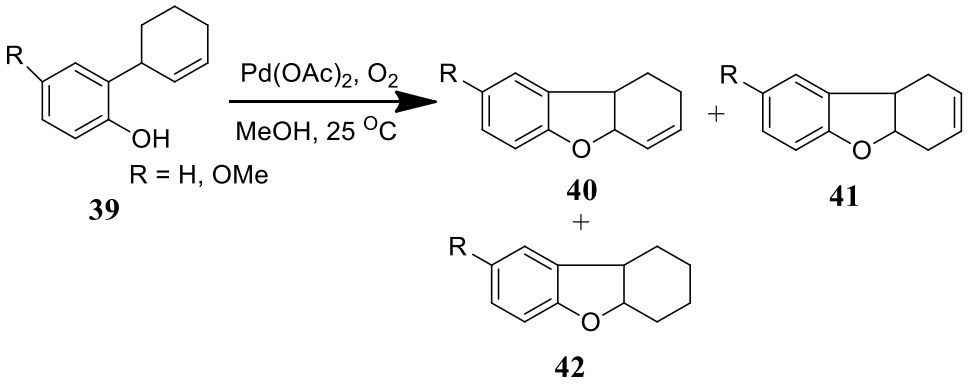
A general procedure was reported [46] for cyclization of substituted 2-bromophenyl ethers **37** to obtain substituted dibenzofurans **38** under basic condition. The process required only 10 mol% of palladium acetate and could tolerate electron withdrawing as well as electron releasing groups (**Scheme 9**).



R= H, 2-NO_2, 3-NO_2, 4-NO_2, 4-OH-CH_2, 3-OH-CH_2, 4-COOH.

Scheme 9

2-Allylphenols **39** having a cyelohexenyl moiety could be cyclized by an equimolecular amount of palladium acetate in methanol at room temperature and in the presence of air togive a mixture of cis-1, 2,4a, 9b-tetrahydrobenzofuran**40** and cis-1,4,4a,9b-tetrahydrobenzofuran**41** in 1:1 ratio, along with small amount of 2,3-butanobenzofuran**42** (**Scheme 10**) [47].

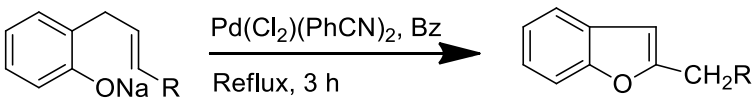


Scheme 10

The reaction could be carried out catalytically with respect to palladium catalyst in presence of oxygen (one atm.). For the production of one mole of cyclized product **(40** + **41 + 42**), 0.5 molar equivalent of oxygen was consumed under these condition; co-oxidants e.g. copper (II) were not required. The distribution of the products **(40, 41** and **42**) were found to depend upon substrate concentrations; e.g. in presence of excess substrate, the major product was **40**. Furthermore, addition of nine equivalents of cyclohexene was found to increase the proportion of **40** at the expense of **41** and **42.**

The observed change in product distribution was explained in terms of alternation of reaction palladium(II) species and interaction of palladium(II) complexes with olefins.

In 1973, Hosakawa*et a1*[48]synthesized benzofurans **43**, **44** by refluxing sodium salt of 2-allylphenols **102** prepared from 2-allylphenol and sodium methoxide with a stoichiometric amount of dichloro bis(benzonitrile) palladium **(Scheme 11).**

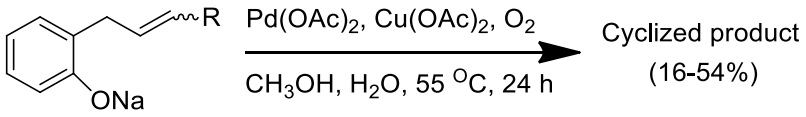


43 **44**

Scheme 11

2-Propenylphenol could not be cyclized, indicating that cyclization proceeded not via first isomerization of starting olefin, but through coupling of oxygen and α-carbon of alkyl group.

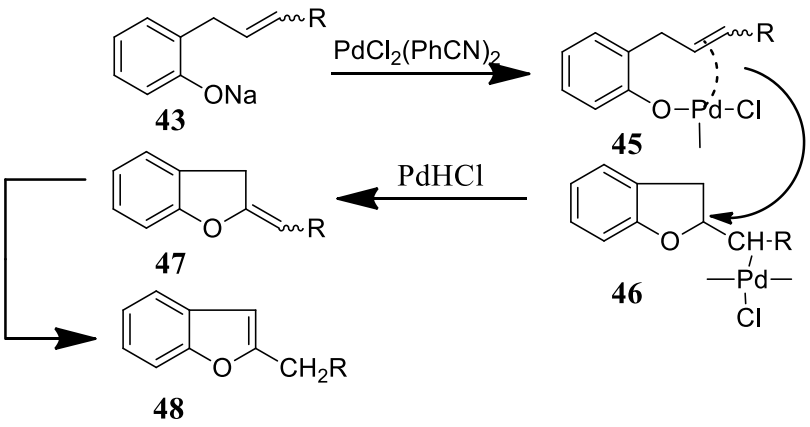
Later on, the cyclization was made catalytic by using palladium acetate, cupric acetate and oxygen [49] **(Scheme 12).** 2-Allylnaphth-l-ol did not undergo cyclization, but gave polymeric material, due to oxidation with oxygen.



43

Scheme 12

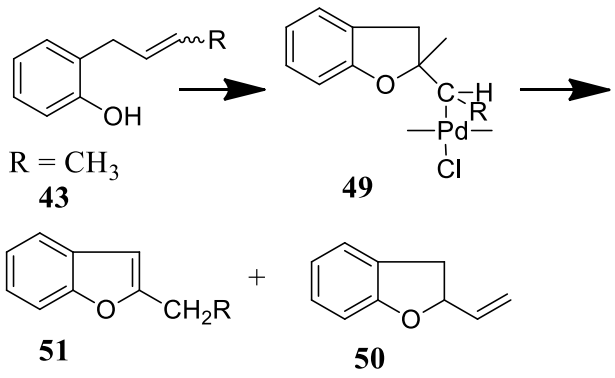
The formation of cyclized products was explained by intramolecular oxypalladation followedby β-elimination of 'PdHCl' species (**Scheme 13**).



R= H, Ph

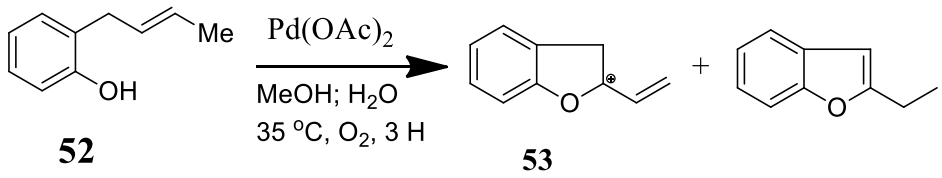
Scheme 13

When R = H or Ph, the intermediate **49** showed that C-2 hydrogen was the only β-hydrogen that could be eliminated as 'PdHCI'. However when R = CH_3, two β-hydrogens were available. Predominance of unsaturated product **50** was in sharp contrast to stoichiometric cyclization, where 2-ethylbenzofurans**51** was the main product **(Scheme 14).**



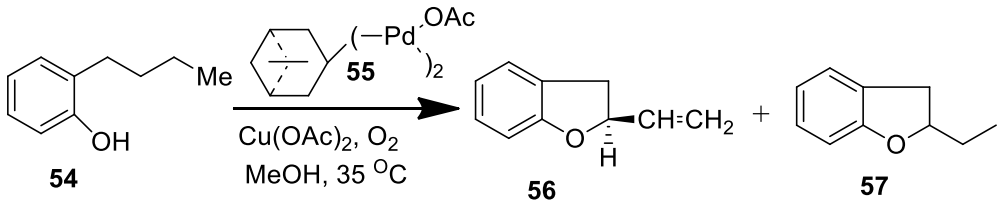
Scheme 14

Hosokawa *et a1*[50]reported a palladium(II) catalyzed asymmetric synthesis of 2,3-dihydrobenzofurans from 2-allylphenols **52** by using a catalytic amount β-pinene as the source of chirality. The catalytic system consisted of 10 mol% palladium acetate, 10 mol% (-) β-pinene and one equivalent of cupric acetate. 19:1 (v/v) Methanol in water was used as solvent and the reaction was carried out at 35°C under oxygen **(Scheme 15).** When an excess of β-pinene was used, no cyclization occurred with **53** assubstrate; whereas (±)-2-(cyclopent-2-enyl)phenol reacted with palladium acetate even in the presence of excess β-pinene.



Scheme 15

To gain an insight into the mechanism, the intramolecular cyclization of trans-2-(2-butenyl)phenal**54** was studied with 10 mol% (+)-(2,3,10-η-pinene)palladium(II) acetate **55** and 10 mol% cupric acetate in the presence of oxygen as effective catalytic system [51].An overall yield of 77-81 % was obtained as shown below in **(Scheme 16)**.



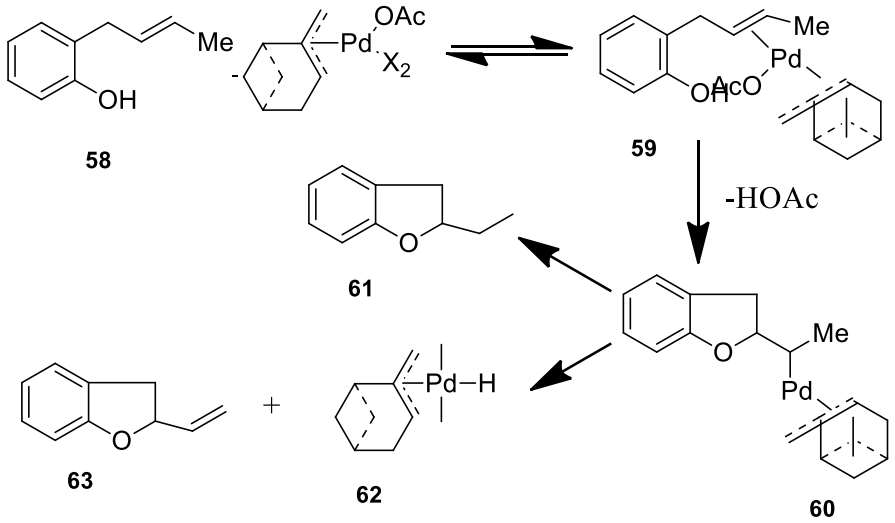
Scheme 16

No cyclization occurred in coordinating solvents e.g. DMF or pyridine, while the reaction proceeded sluggishly in benzene, THF and acetic acid.

The reaction was thought to proceed via reversible coordination of the substrate **58** to the dimeric palladium complexto form the monomeric palladium(II) acetate **59.** Intramolecular nucleophelic attack by the phenoxy group and simultaneous removal of acetate ligand as acetic acid led to the oxypalladation species **60.** A look at this species showed the presence of two β-hydrogens making the following two pathways possible:

(i) Elimination of a β-hydrogen from the methyl group of **61** gave the product **62** and Pd-H species **63.**

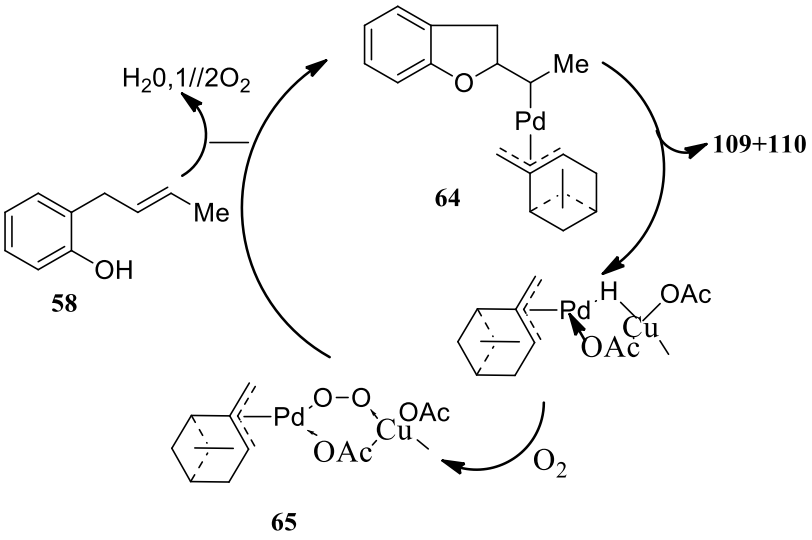
(ii) Elimination of β-hydrogen from C-2, followed by rearrangement gave **63** (**Scheme 17**).



Scheme 17

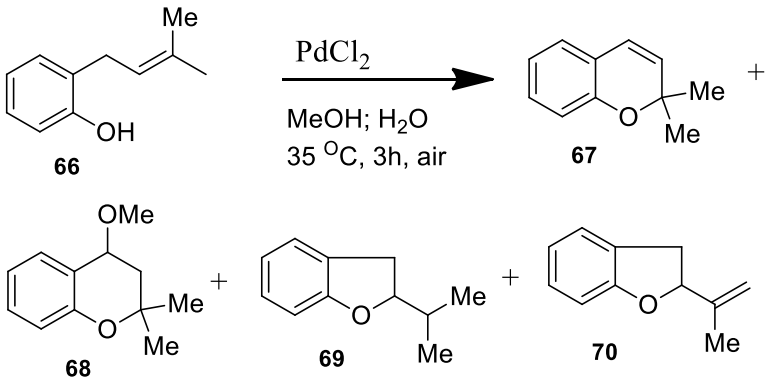
The role played by cuprous acetate was not clear. The acetate ion may interact with palladium(II) due to its ready availability to form bridging legands.

The generation of catalytically active species involved oxygenation of Pd-H bond in **64.** Thus formed palladium(II) hydroperoxide was supposed to be a Pd-Cu bimetallic complex, since regeneration of active catalyst required cupric acetate as well as oxygen. The presence of acetate bridge in **65** was supported by the experimental observation that reactivity and enantioselectivity were influenced by steric and electronic factors of the carboxylate ligands associated with copper (II) **(Scheme 18).**



Scheme 18

2-(3-Methyl-2-butenyl)phenol**66** underwent palladium chloride catalyzed to give 2,2-dimethylchromone**67** and 2,2-dimethyl-4-methoxychroman**68** as the predominant products along with < 2% 2-isopropylbenzofuran**69** and 2-isopropenyl-2,3-dihydrobenzofuran**70** (**Scheme 19**) [52].

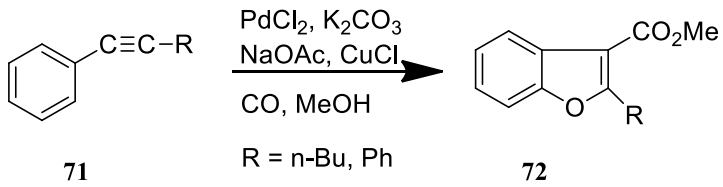


Scheme 19

Formation of these products could be explained by nucleophilic attack by phenoxy group at 2 or 3 position of the allylic side chain. Use of nitrogen or argon instead of air led to poorer yields although the relative ratios among the cyclized products did not change. While the presence of sodium salt of carboxylic acids bearing electron-withdrawing substituents resulted in predominant formation of six-membered products; addition of sodium salts of carboxylic acids bearing electron donars led to formation of benzofurans **69**, **70** and six membered products **67**, **68** in equal amounts.

Addition of sodium acetate or use of palladium acetate resulted in non-formation of **67.** Increase in the amount of sodium acetate added led to higher overall yield accompanied by an increase in the presence of **70**. These result were ascribed to change in palladium(II) species through coordination of sodium carboxylate to palladium. The resulting change in electron density of palladium seemed to affect the regioselectivity.

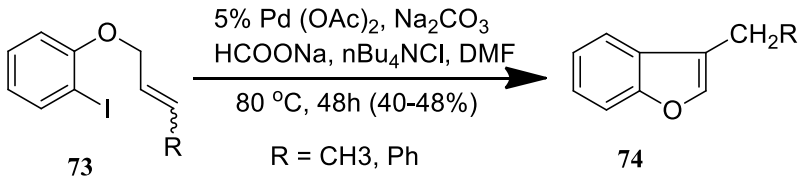
Carbonylation of 2-acetylenic phenols **71** with carbonmonoxide in methanol containing sodium acetate, cuprous chloride and palladium chloride led to intermolecular cycloaddition to give benzofurans **72 (Scheme 20)** [53]**.**



71 72

Scheme 20

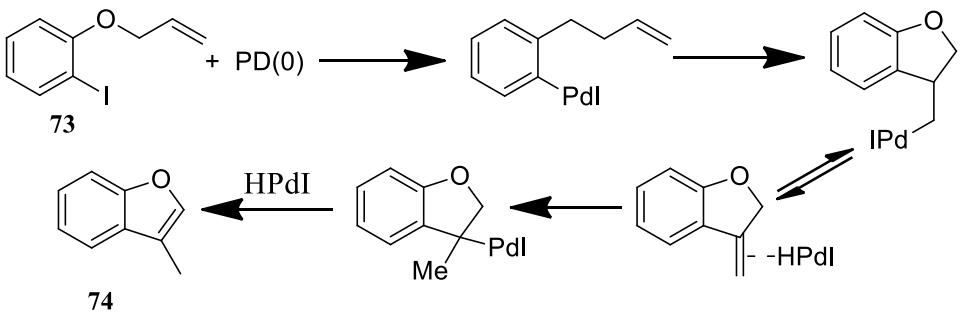
In 1988, Larock and Stinn [54] found that 2-iodoaryl allyl ethers **73** could be cyclized into 3-substituted benzofurans **74(a)** in the presence of 5% palladium acetate under phase transfer condition **(Scheme 21**).



73 74

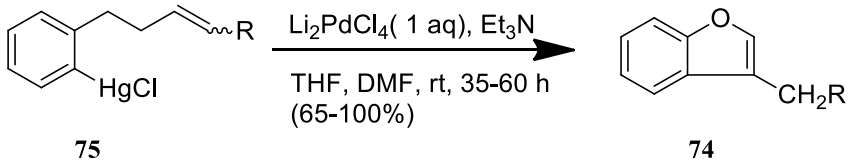
Scheme 21

It was found that the yields of benzofurans **74** decreased with less hindered double bond and with better aryl leaving groups. The observation was consistent with the idea that insertion into the C–O bond was the major side reaction. The formation was thought to reduce a π-allylpalladium intermediate formed by C–O insertion and thus keeping the palladium(0) catalyst active. A mechanism was forwarded **(Scheme 22)**.



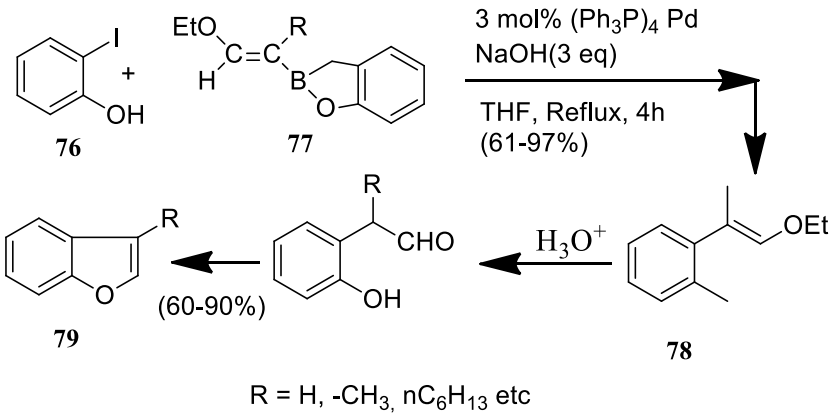
Scheme 22

The palladium(II) catalyzed cyclization of analogusarylmercurials**75** were examined with an idea to improve the yield. Although, the yields were better (65-100%), the procedure required stoichiometric amounts of lithium tetrachloropalladate **(Scheme 23).**



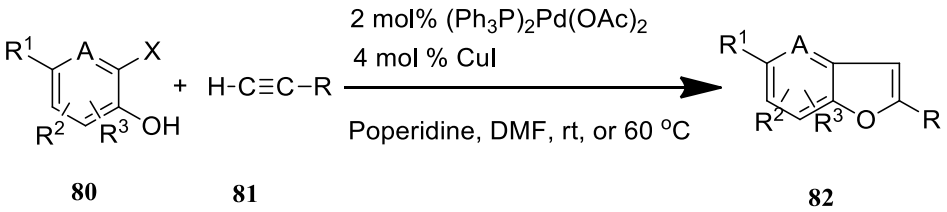
Scheme 23

Palladium catalyzed cross coupling between (1-ethoxy-l-alken-2-yl)boranes**77** and 2-iodophenol**76** gave ortho-functionalized styryl ethers **78** in high yields. The latter could be converted into 3-substituted benzofurans **79** by cyclodehydration under acidic condition [55] **(Scheme 24).** The reaction could be utilized for the synthesis of indoles as well.



Scheme 24

Arcadi*et a1*[56]found that when 2-hydroxyaryl or 2-hydroxyheteroaryl halides **80** were treated with terminal alkynes **81** in the presence of a base, $(Ph_3P)_2Pd(OAc)_2$ and cuprous iodide at room temperature or at 60°C, 2-substituted benzoburans**82** were obtained in good yields. The reaction could accommodate a variety of functional groups, both in the phenol and in the alkyne moiety. Piperidine was found to give the best results. Other bases like sodium acetate gave moderate yields, while use of n-tributyl amine led toMichael adduct in poor yields (**Scheme 25**).



A= CH, N

X= I, Br

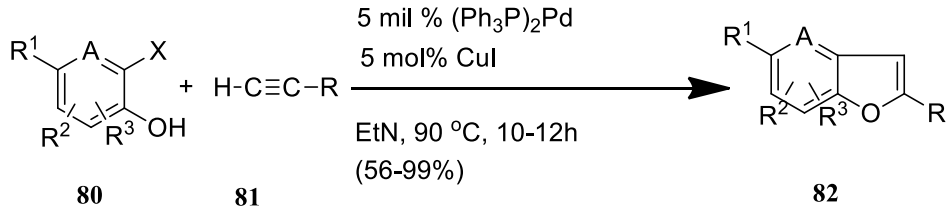
R^1= H; R^2 = H, 2-Me, 1-CHO

R^3= H, 3-OMe

R = $–C_4H_{9(n)}$, C_6H_5, $–CH_2OH$, $–CH(OH)C_6H_5$ etc.

Scheme 25

Latter, Torri *et a1*[57]treated 2-hydroxylaryl on 2-hydroxyheteroaryl iodides **80** with terminal alkynes **81** in the presence of bis (triphenylphosphine) palladium (II) chloride (5 mol %) and cuprous iodide in triethylamine at 90°C for 10-12 hours, to obtain 2-substituted benzofurans **82** in 56 - 99% yields **(Scheme 26).**



80 **81** **82**

A = CH, N

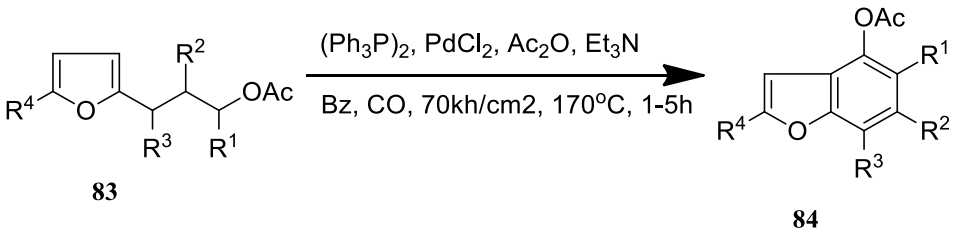
X = I

R^1= H, Me, CI

R^2 = R^3 H; R = = $–CH_2OTHP$, $–CMe_2OH$, $–C_6H_{13}$, Ph etc.

Scheme 26

Cyclocarbonylation of 3-furylallyl acetates **83** in the presence of acetic anhydride, trietylamine and a catalytic amount of bis (triphenylphosphine) palladium(II) chloride at 130 – 170 °C udder 50 -70 atmospheric pressure of carbon monoxide was found to give acetoxybenzofurans**84 (Scheme 27).** 3-(3-Furyl)allylacetate was found to cyclize selectively at the 2-position of the heterocyclic nucleus to give 7-acetoxybenzofuran. Reaction temperature >130°C was necessary to obtain high yield. At lower temperature, side reactions gave unidentifiable high boiling by products. Triethylamine and acetic anhydride were used to esterify *in situ* the phenols produced.

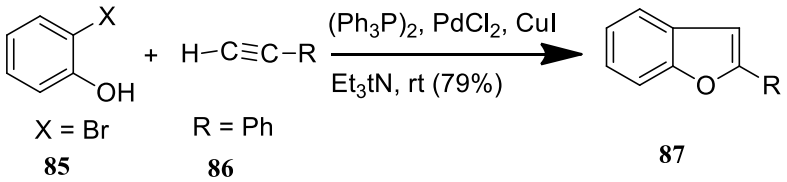


83 **84**

Scheme 27

Secondary allyl acetate **83** (R^1 = CH3, R^2 = R^3 = R^4 = H) did not undergo cyclocarbonylation due to elimination of acetic acid and polymerization of the resulting diene. Furtheremoreγ-substituted allyl acetate **84** (R^1 = R^2 = R^4 = H, R^3 = CH_3) gave poor yield due to diene formation and subsequent polymerization.

It was found that 2-bromophenol **85** (X = Br) reacted with terminal acetylenes like phenylacetylene **86** (R = Ph) at room temperature, in the presence of a base, bis(triphenylphosphine)palladium(II) chloride and cuprous iodide [59]**(Scheme 28)** to give 2-substituted benzofruans**87**.

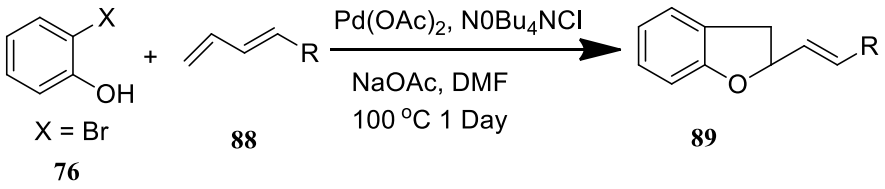


85 **86** **87**

Scheme 28

Heteroatom-containing aryl iodides have been found to react with 1,3-dienes **88** in the presence of a palladium catalyst and appropriate base to afford a variety of oxygen and nitrogen heterocycles **89**. The catalytic system developed by Larok*et al*

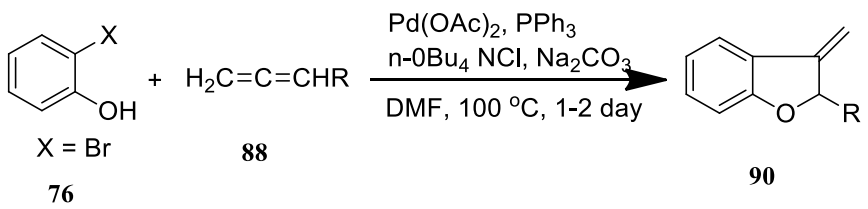
[59]to effect this reaction consisted of 5% $Pd(OAc)_2$ or $Pd(dba)_2$, one equivalent n-Bu_4NC1, 3.5 equivalent of appropriate base, with or without triphenyl phosphine **(Scheme 29).**



Scheme 29

Recently, aryl halides possessing a heteroatom or potential carbanion containing a functionality in the 2-position were found to undergo regioselective reaction with 1,2-dienes, in the presence of a palladium catalyst and a carbonate base, to give five and six membered cyclic compounds in heigh yields [60].Regioselectivity of this annulation procedure was very high; most unsymmetrically substituted 1,2-dienes gave only one regioisomer. The formation of five membered ring involved exclusive annulation across the more highly substituted carbon-carbon double bond.

For the heteroannulation process 5% each of palladium acetate and triphenylphosphine, l equivalent of n-tetrabutyl ammonium chloride and 3 equivalent of carbonate base with DMF as solvent was found to give the best results of bezofuranose**90** (**Scheme 30**).



Scheme 30

Y. Nan *et all* [62]reported an efficient new synthetic technology for the synthesis of 2,3-disubstituted benzo[b]furans. A highly effective cocatalysis system (PdI_2-thiourea and corbon tetrabromide) was developed for carbonylative cyclization of both electron rich and electron deficient o-hydroxylarylacetylenes to the corresponding methyl benzo[b]furan-3--carboxylates.

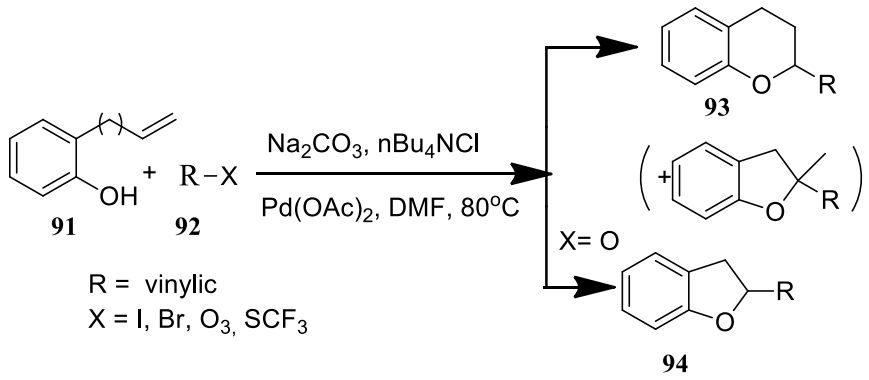
The Pd-catalyzed reaction of 2-alkynylphenols with tertiary propargyl carbonates yielded 2-substituted-3-allenylbenzo[b]furans in moderate to good yields [62]. That heteroanulation promoted by a σ-allenylpalladium complex proceeded under neutral conditions.

The Pd-catalyzed cross-coupling of *o*-allylic and *o*-vinylic phenols with vinylic halides and triflates produced substituted dihydrobenzopyrans and dihydrobenzofurans respectively in good to high yields [63].The proposed mechanism involves vinylpalladium addition to the olefin, rearrangement to a π-allylpaladium intermediate and subsequent intermolecular nuclephilic displacement of palladium.

Substituted 2-methylbenzofurans were obtained from 2-allylphenols via Pd^{2+} catalyzed oxidative cyclization using $Cu(OAc)_2$- LiCl as a reoxidant and wet DMF as a solvent [64].

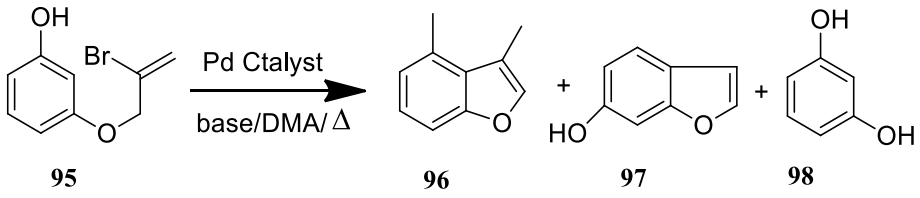
The Pd-catalyzed annulation of silyl-protected alkynols with $2\text{-}IC_6H_4OH$ gives silyl protected (3-hydroxyalkyl) benzofurans [65]. The use of silyl-protected propynols bearing a free OH or an OFt_3Si protective group resulted in the formation of 1-oxa-2-silyclopent-3-cues as a major products. Removal of the silyl protective groups affords 3-(hydroxyalkyl)benzo[b]furans in good yields.

The palladium catalyzed cross coupling of o-allylic and o-vinylic phenols **91** with vinylic halide **92** and triflates produces substituted dihydrobenzopyrans and dihydrobenzofurans respectively in good to high yields. R. C. Larock*et all* [66]reported a conceptually related palladium-catalyzed coupling on vinylic halides and triflates with *o*-allylic and vinylic phenols, which provides a convenient, general route to dihydrobenzopyrans**93** and dihydrobenzofurans**94** respectively (**Scheme 31).**



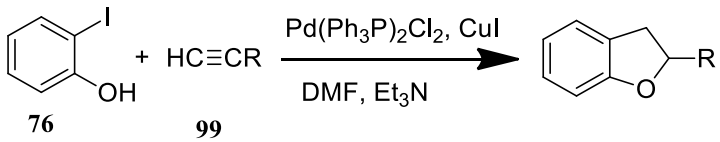
Scheme 31

The general strategy was illustrated through the cyclization of vinyl bromide 177 **(Scheme 32).** Heating a mixture of bromide **95** and Cs2C03 in dimethylacetamide (DMA) in the presence of catalytic amount of Herrmann's palladacyclic catalyst (HC) [67]promoted cyclization to the ortho and para benzofurens**96** and 97 which were formed in a 1:1 ratio along with a small amount of resorcinol **98.**

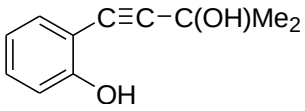


Scheme 32

A mixture of *o*-iodophenyl **76** and an alkyne **99,** with a terminal acetylenic function, when heated in the presence of a palladium catalyst, copper(1) iodide and a base in dimethylformamide, gave the 2-substituted benzofurans in good yields [68].



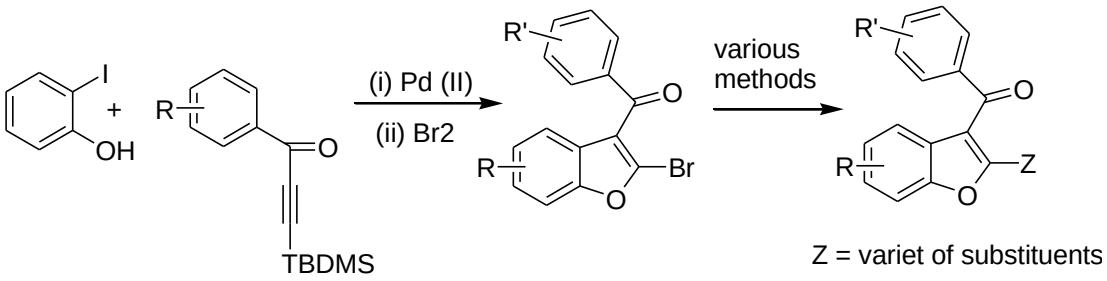
76 **99**



Scheme 33

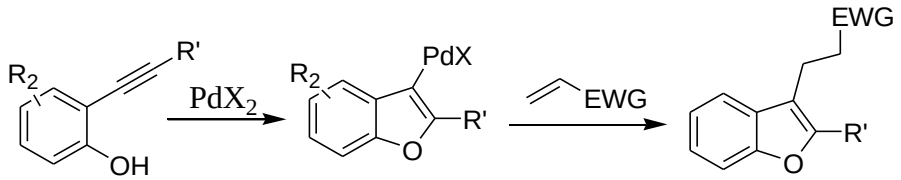
The reactions were usually carried out for 16h at 60°C, lower temperature leading to poor yields. The reaction when carried out in DMF at room temperature in the presence of tetrabutylammonium chloride (PTC), gave a mixture of the cyclic product and the corresponding acyclic product. The overall yield and the proportion of the cyclic product increasing the time. At the higher temperature (50°C) for 6h the cyclic productwas formed exclusively. This indicated the acyclic product was an intermediate in the formation of the benzofuran. However, with several aryl acetylenic carbinols a slightly higher temperature (80°C) and longer reaction period were required to derive the optimum yields. The reaction could not be carried out with methoxycarbonyland acetylene gas**.**

A convenient method for the synthesis of 2-bromo-3-aroyl-benzo[b]furans from readily accessible precursors has been developed [69]. The 2-bromo group has been employed as a versatile synthetic handle in both palladium-mediated coupling and direct nucleophilic substitutions to give access to a wide range of 2-substituted -3-aroyl-benzo [b] furans **(Scheme 34)**.



Scheme 34

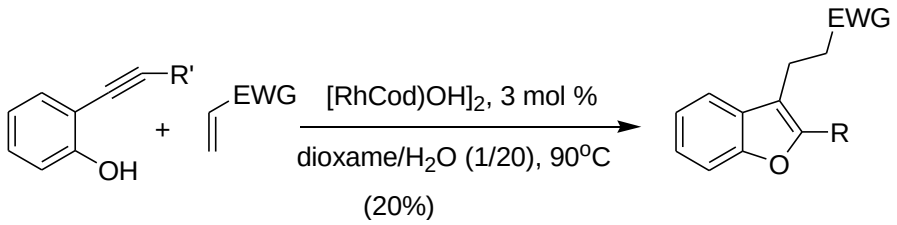
A new Pd-catalyzed tandem intramolecular oxypalladation / Heck-type coupling between 2-alkynyl phenols and alkenes is reported [70], leading to 3-(1-alkenyl)benzofurans**(Scheme 36)**.



Scheme 36

Mark Lautens and NaohiroIsono reported [71] a rhodium-catalyzed cyclization of *o*-alkynyl-phenols followed by intramolecular conjugate addition that succeeded with

alkyl and aryl alkynes. In this reaction, 2-3-disubstituted benzofurans were obtained in good to excellent yields **(Scheme 37).**



(Scheme 37)

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CHAPTER 2

Experimental

2.1 Materials and instruments

2.1.1 Chemicals and reagents

The chemicals and reagents used in this research were analytical grade and commercial grade. *n*-hexane, chloroform, phenol derivatives Acrylic acid butyl ester and 2-Methyl-acrylic acid methyl ester chemicals were analytical grade used without further purification. The chemicals and reagents which were used in this research are given below:

1. 4-chlorophenol (C_6H_5ClO)
2. *m*-cresol (C_7H_8O)
3. *o*-cresol (C_7H_8O)
4. 2-Naphthol ($C_{10}H_8O$)
5. Acrylic acid butyl ester
6. 2-Methyl-acrylic acid methyl ester
7. Chloroform ($CHCl_3$)
8. *n*-hexane (C_6H_{14})
9. Methanol (CH_3OH)
10. Triethylamine ($C_6H_{15}N$) Et_3N
11. Dimethylformamide (C_3H_7NO)
12. Acetonitrile(C_2H_3N)
13. 1,4-Dioxane($C_4H_8O_2$)
14. Silica gel 60-120 Mesh (For Column Chromatography)
15. bis (triphenyl phosphine) Palladium (II) chloride [$Pd(Ph_3P)_2Cl_2$]
16. bis (triphenyl phosphine) Cobalt (II) chloride [$Co(Ph_3P)_2Cl_2$]
17. bis (triphenyl phosphine) Nickel (II) bromide [$Ni(Ph_3P)_2Br_2$]
18. TLC plate(Silica gel precoated)
19. Bimetalic nano catalyst

2.1.2 Instruments

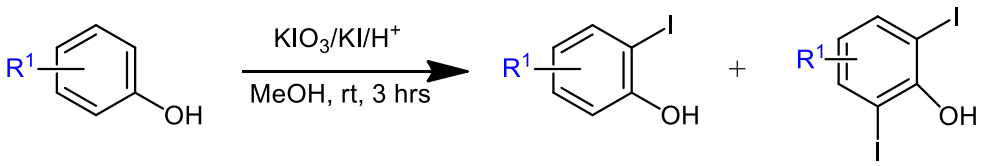
The synthesized diamides and catalyst were analysed using the following instruments:

- UV-visible Spectrophotometer (Shimadzu-1800)
- Fourier Transform Infrared Spectrophotometer (Shimadzu FT-IR-8400)
- Nuclear Magnetic Resonance Spectrometer (Bruker BPX- 400)
- Gas Chromatography Mass Spectrometer (Shimadzu GC-MS)
- Digital Balance (Precision electrical balance)
- Rotatory evaporator
- Melting point apparatus
- Oven
- UV-light

2.2 Synthesis of 2-iodophenol 5-8 :

Aromatic iodo compounds are an important class of compounds in synthetic organic chemistry. They are useful for the preparation of organ metallic reagents and some are potential intermediates for the synthesis of pharmaceutical and bioactive materials. They are useful in metal catalyzed coupling reaction which are widely applied in the preparation of complex molecules.

A mixture of potassiam iodide and potassium iodate is used in the presence of an acid for in situ iodination of aromatic compounds.



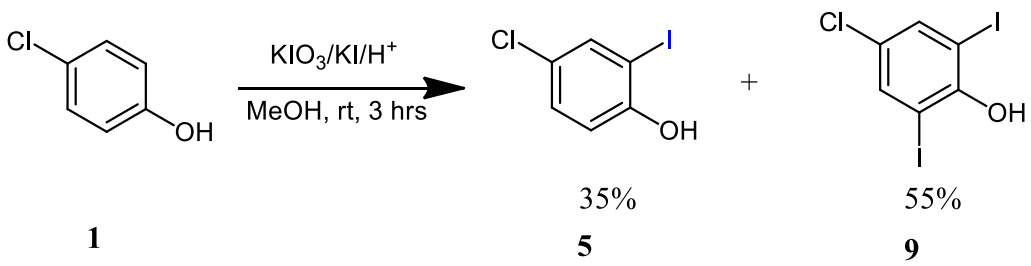
1-4 **5-8** **9-12**

1, 5, 9 R^1 = *p*-Cl;
2, 6, 10 R^1 = *m*-CH_3;
3, 7, 11 R^1 = *o*-CH_3;
4, 8, 12 R^1 = C_6H_6

Scheme 1

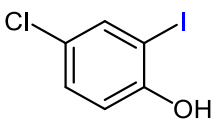
2.2.1 Synthesis of 5-methyl-2-iodophenol 5:

A solution of *p*-chlorophenol (5 g, 38.89 mmol), potassium iodide (4.326 g, 26.05 mmol), potassium iodate (2.75 g,12.834 mmol) was prepared in methanol (25 mL) and water (40 mL). This mixture was treated at room temperature with dilute HCl (9.5 mmol) and stirred for 2-4 hrs. The reaction mixture was diluted with water (50 mL) and neutralized by using saturated solution of $NaHCO_3$ extracted with chloroform (25 mL×3). The organic extract was washed with dilute $Na_2S_2O_3$ (5%) and water, dried over anhydrous sodium sulfate and concentrated under reduced pressure to give crude oil. The latter was purified by chromatography on a column of silica gel (60-120 mesh) with *n*-hexane/ chloroform and 1:1 and two compounds (**5** and **9**) were isolated.



Scheme 2

4-chloro-2-iodophenol**5:**



4-chloro-2-iodophenol

5

MF :$C_6H_4OClI_2$

MW : 256.473

Physical analysis:

White crystal solid, mp. 70-72 ^{o}C, odorless, 35% yield.

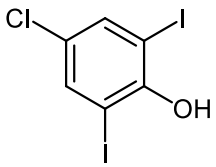
Analytical analysis:

UV(EtOH) : λ_{max} 322.40 nm.

IR(KBr) :ν_{max} 3452.3, 3286.5, 3100.0, 1571.9, 1407.9, 810.0 and 690.5 cm^{-1}.

^{1}H NMR(400 MHz, $CDCl_3$) : δ_H 5.69 (br. s, 1H, Ar–OH), 6.90(s, 1H, Ar–H), 7.19 (d, 1H, J=2.8 Hz, Ar–H), 7.62 (d, 1H, J=2.4 Hz, Ar–CH).

4-chloro-2,6-diiodophenol **9**:



4-chloro-2,6-diiodophenol

9

MF :$C_6H_3OClI_2$

MW : 383.373

Physical analysis:

Yellow amorphous, mp. 70-77 ^{o}C, odorless, 55 % yield.

Analytical analysis:

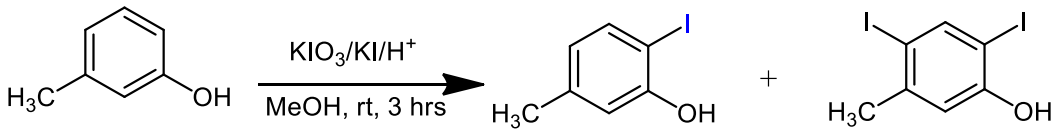
UV(EtOH) :λ_{max}302.80 nm.

IR(KBr) : ν_{max} 3460.1, 3068.5, 1531.4, 1427.2, 1143.7, 850.5 and 705.9 cm^{-1}.

^{1}H NMR(400 MHz, $CDCl_3$) : δ_H 5.55 (br.s, 1H, Ar–OH), 7.65(s, 2H, Ar–H).

2.2.2 Synthesis of 4-chloro-2-iodophenol 6:

According to the above iodination reaction **(2.2.1)** compounds (**6** and **10**) were isolated from m-cresol **2**, 6 gm (0.0462 mmol), potassium iodide (4.326g, 26.05 mmol), potassium iodate (2.75 g,12.834 mmol), methanol (25 mL).

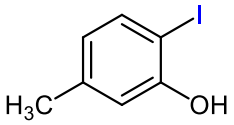


50% 50%

2 **6** **10**

Scheme 3

2-iodo-5-methylphenol**6:**



2-iodo-5-methylphenol

6

MF :C_7H_7OI

MW : 233.97

Physical analysis:

Yellow crystalline solid, mp. 32-36 ^oC, odorless and 60% yield

Analytical analysis:

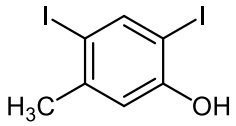
UV(EtOH) :λ_{max} 283.60 nm.

IR(KBr) :ν_{max} 3421.5, 1649.0, 1456.2 and 800 cm^{-1}.

^{1}H NMR(400 MHz, $CDCl_3$) :δ_H 2.19 (s, 3H, Ar–CH_3), 5.28(br.s, 1H,Ar–OH), 6.42(s, 1H, Ar–H), 6.74(d, 1H, J=7.6 Hz, Ar–H), 7.43(d, 1H, J=8 Hz, Ar–H).

^{13}C NMR (100 MHz, $CDCl_3$): δ_C 20.97(Ar–CH_3), 111.97(Ar–C), 115.84 (Ar–CH), 123.37(Ar–CH), 137.80(Ar–CH), 140.46(Ar–CH), 154.64(Ar–C).

2,4-diiodo-5-methylphenol**10**:



2,4-diiodo-5-methylphenol

10

MF :$C_7H_6OI_2$

MW : 359.93

Physical analysis :

White crystal, low melting (30-32 ^{o}C), odorless and 30% yield.

Analytical analysis:

UV(EtOH) :λ_{max} 287.60 nm.

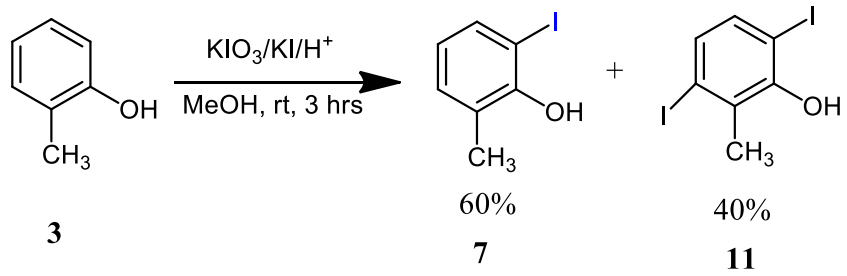
IR(KBr) : ν_{max} 3460.1, 1300, 1449.9 and 800 cm^{-1}.

^{1}HNMR(400 MHz, $CDCl_3$) : δ_H 1.61 (s, 3H, Ar–CH_3), 5.62(s, 1H, Ar–OH), 6.59(s, 1H, Ar–H), 7.28(s, 1H, Ar–H).

^{13}CNMR (100 MHz, $CDCl_3$): δ_C 28.45(Ar–CH_3), 77.84(Ar–C), 90.22 (Ar–C), 123.48(Ar–CH), 137.98 (Ar–CH), 143.55 (Ar–C), 153.21(Ar–C).

2.2.3 Synthesis of 2-Iodo-6-methyl-phenol 7:

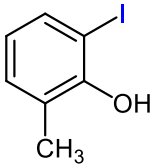
According to the above iodination reaction **(2.2.1)** compounds (**7** and **11**) were isolated from *o*-cresol **3** 6 gm (0.0462 mmol), potassium iodide (4.326g, 26.05 mmol), potassium iodate (2.75 g,12.834 mmol), methanol (25 mL).



3 **7** **11**

Scheme 4

2-iodo-6-methylphenol**7:**



2-iodo-6-methylphenol

7

MF **:**C_7H_7OI

MW **:** 233.97

Physical analysis:

Yellow crystalline solid, mp. 40-45 ^oC, odorless and 60% yield

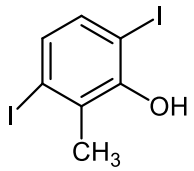
Analytical analysis:

UV(EtOH) :λ_{max} 283.60 nm.

IR(KBr) :ν_{max} 3421.5, 1649.0, 1456.2 and 800 cm^{-1}.

^{1}H NMR(400 MHz, $CDCl_3$) : δ 2.18 (3H, s), 6.96 (1H, dd, *J* = 8.1, 1.3 Hz), 7.06 (1H, dd, *J* = 8.1, 7.7 Hz), 7.29 (1H, dd, *J* = 7.7, 1.3 Hz).

3,6-diiodo-2-methylphenol**11**:



3,6-diiodo-2-methylphenol

11

MF :$C_7H_6OI_2$

MW : 359.93

Physical analysis :

White crystal, low melting (30-32 ^oC), odorless and 30% yield.

Analytical analysis:

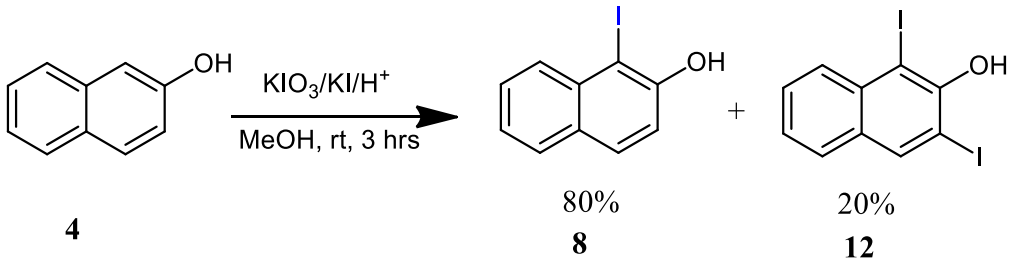
UV(EtOH) :λ_{max} 287.60 nm.

IR(KBr) : ν_{max} 3460.1, 1300, 1449.9 and 800 cm^{-1}.

^{1}HNMR(400 MHz, $CDCl_3$): δ 2.30 (3H, s), 7.26 (1H, d, *J* = 7.6 Hz), 7.31 (1H, d, *J* = 7.6 Hz).

2.2.4 Synthesis of 1-iodo-naphthalen-2-ol 8:

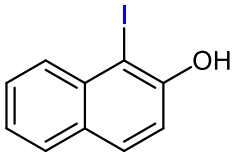
According to the above iodination reaction **(2.2.1)** compounds(**8** and **12**) were isolated from naphthalen-2-ol **4**, 6 gm (0.0462 mmol), potassium iodide (4.326g, 26.05 mmol), potassium iodate (2.75 g,12.834 mmol), methanol (25 mL).



4 **8** **12**

Scheme 5

1-iodonaphthalen-2-ol**8:**



1-iodonaphthalen-2-ol

8

MF **:** $C_{10}H_7IO$

MW **:** 269.95

Physical analysis:

Yellow crystalline solid, mp. 60-36 ºC, odorless and 60% yield

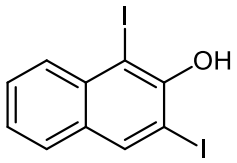
Analytical analysis:

UV(EtOH) :λ_{max}283.60 nm.

IR(KBr) : ν_{max} 3421.5, 1649.0, 1456.2 and 800 cm^{-1}.

^{1}H NMR(400 MHz, $CDCl_3$) : δ 7.08 (1H, dd, *J* = 8.8, 0.5 Hz), 7.46-7.66 (3H, 7.51 (dddd, *J* = 7.9, 7.5, 1.7, 0.5 Hz), 7.61 (ddd, *J* = 8.6, 7.5, 1.5 Hz), 7.49 (dddd, *J* = 8.8, 1.9, 0.5, 0.5 Hz)), 7.73 (1H, dddt, *J* = 7.9, 1.9, 1.5, 0.5 Hz), 7.89 (1H, ddt, *J* = 8.6, 1.7, 0.5 Hz).

1,3-diiodonaphthalen-2-ol**12**:



1,3-diiodonaphthalen-2-ol

12

MF :$C_{10}H_6I_2O$

MW : 395.85

Physical analysis :

White crystal, low melting (45-50 ºC), odorless and 30% yield.

Analytical analysis:

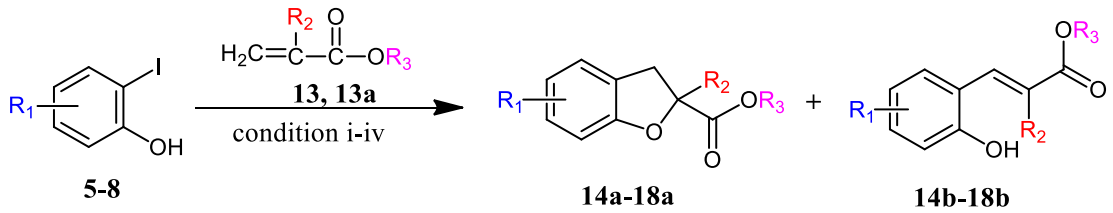
UV(EtOH) :λ_{max} 287.60 nm.

IR(KBr) **:** ν_{max} 3460.1, 1300, 1449.9 and 800 cm^{-1}.

^{1}HNMR(400 MHz, $CDCl_3$) δ 7.47-7.62 (3H, 7.51 (dddd, *J* = 7.9, 7.5, 1.6, 0.5 Hz), 7.57 (ddd, *J* = 8.6, 7.5, 1.6 Hz), 7.57 (dddd, *J* = 7.9, 2.0, 1.6, 0.4 Hz)), 8.00 (1H, dddd, *J* = 8.6, 1.6, 0.5, 0.4 Hz), 8.23 (1H, dt, *J* = 2.0, 0.5 Hz).

2.3 Synthesis of substituted 2,3-dihydrobenzofuran14a-17a:

2-iodophenol**5-8** were converted to the substituted 2,3-dihydrobenzofuran**14a-22a**on the treatment with terminal alkenes **13** in the condition of (i-iv) as shown in the **Scheme 6**.



5, 14 R^1 = *p*-Cl;
6, 15 R^1 = *m*-CH_3;
7, 16 R^1 = *o*-CH_3;
8, 17 R^1 = C_6H_6

R^2 = **13, 14-17** CH_3
R^2 = **13a, 18** H

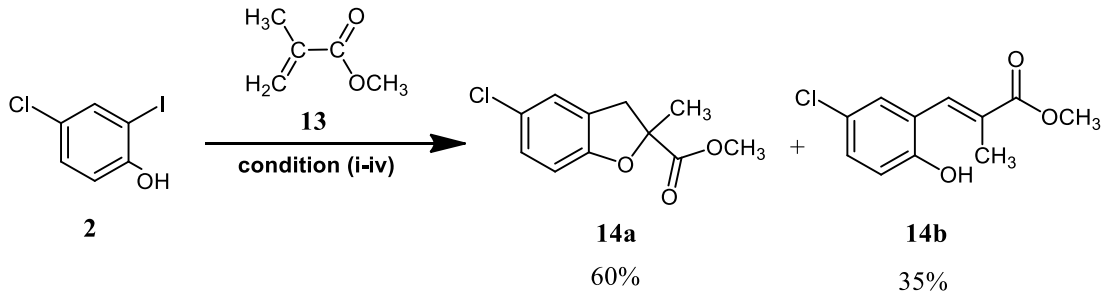
R^3 = **13, 14-17** CH_3
R^3 = **13a, 18** C_4H_9

S.L	Condition
i	$Pd(Ph_3P)_2Cl_2$, DMF, Et_3N, N_2, 80-100 °C, 20-24 hrs
ii	$Co(Ph_3P)_2Cl_2$, DMF, Et_3N, N_2, 80-100 °C, 20-24 hrs
iii	$Ni(Ph_3P)_2Br_2$, DMF, Et_3N, N_2, 80-100 °C, 20-24 hrs
iv	Bimetallic nano catalyst, DMF, Et_3N, N_2, 80-100 °C, 20-24 hrs

Scheme 6

2.3.1 Synthesis of methyl 5-chloro-2-methyl-2, 3-dihydrobenzofuran-2-carboxylate 14a

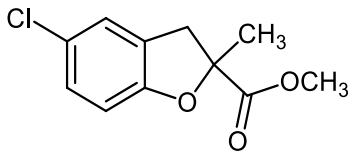
A mixture of 4-chloro-2-iodophenol**2**0.5g, (2.283 mmol) in condition (i-iv) catalyst (0.056 g, 3.5 mol%) and triethylamine (Et_3N) (0.924 g, 4 equiv) was stirred in DMF (10 mL) under nitrogen atmosphere for 1h. Then, 2-methyl-acrylic acid methyl ester **13** 0.236 g, (3 equiv) was added to the reaction mixture. The solution was heated at 80-120 ^oC for 20-24 hrs. The progress of the reaction was monitored by TLC (*n*-hexane/chloroform 1:1). After completion of the reaction, the mixture was evaporated to dryness under reduced pressure and the residue was extracted with chloroform (3×50 mL). The combined chloroform extract was washed with distilled water (50 mL) dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to obtain reddish gum. The latter was purified by chromatography on a column of silica gel (60-120 mesh) with *n*-hexane / chloroform 3:1 and chloroform. 5-chloro-2-methyl-2,3-dihydrobenzofuran-2-carboxylate**14a**and methyl 3-(5-chloro-2-hydroxyphenyl)-2-methylpropanoate**14b** and small amount of deiodinated product were obtained (**Scheme 7**)



Condition	
i	$Pd(Ph_3P)_2Cl_2$, DMF, Et_3N, N_2, 80-100 ^oC, 20-24 hrs
ii	$Co(Ph_3P)_2Cl_2$, DMF, Et_3N, N_2, 80-100 ^oC, 20-24 hrs
iii	$Ni(Ph_3P)_2Br_2$, DMF, Et_3N, N_2, 80-100 ^oC, 20-24 hrs
iv	Bimetallic nano catalyst, DMF, Et_3N, N_2, 80-100 ^oC, 20-24 hrs

Scheme 7

methyl-5-chloro-2-methyl-2,3-dihydrobenzofuran-2-carboxylate 14a



14a

MF: $C_{11}H_{11}ClO_3$

MW: 226.04

Physical Analysis :

White crystalline solid; mp. 64-69 ^oC;

IR: ν_{max} (KBr) 3066.92, 2953.12, 2854.74, 1706.09, 1592.29, 1457.27, 1264.38, 1230.63, 1127.43, 1065.71 cm^{-1}.

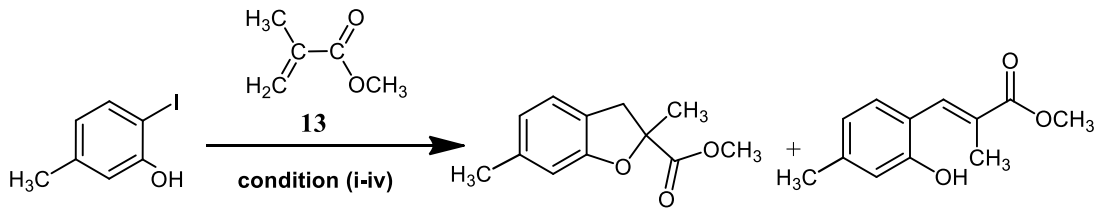
^{1}H NMR (400 MHz, $CDCl_3$): δ2.25 (s, 3H, CH_3), 3.25 (d, 1H, *J* = 15.2), 3.32 (d, 1H, *J* = 15.2 Hz), 3.85 (s, 3H, OCH_3), 7.39(d, 1H, *J* = 7.6), 7.41(d, 1H, *J* = 7.6), 7.84 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$):δ23.28 (-CH_3), 42.72 (CH_2), 52.32 (-OCH_3), 87.21 (C), 120.74 (Ar–CH), 125.96 (Ar–CH), 126.13 (Ar–C), 130.52 (Ar–CH), 130.96 (Ar–CH), 160.96 (Ar–C), 168.08 (–C=O).

Anal. Calc. for $C_{11}H_{11}ClO_3$: C, 58.29; H, 4.89; Cl, 15.64; Found: C, 58.22; H, 4.77.

2.3.2 Synthesis of methyl 2,6-dimethyl-2, 3-dihydrobenzofuran-2-carboxylate 15a

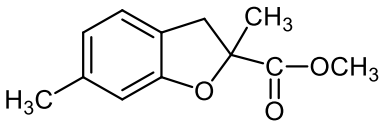
A mixture of **5** and **13** in the above procedure for **2.3.1** was followed for the preparation of methyl 2,6-dimethyl-2,3-dihydrobenzofuran-2-carboxylate **15a**and methyl 3-(2-hydroxy-4-methylphenyl)-2-methylpropanoate**15b** and small amount of deiodinated product were obtained (**Scheme 8**)



Condition	
i	$Pd(Ph_3P)_2Cl_2$, DMF, Et_3N, N_2, 80-100 ^oC, 20-24 hrs
ii	$Co(Ph_3P)_2Cl_2$, DMF, Et_3N, N_2, 80-100 ^oC, 20-24 hrs
iii	$Ni(Ph_3P)_2Br_2$, DMF, Et_3N, N_2, 80-100 ^oC, 20-24 hrs
iv	Bimetallic nano catalyst, DMF, Et_3N, N_2, 80-100 ^oC, 20-24 hrs

Scheme 8

methyl 2, 6-dimethyl-2, 3-dihydrobenzofuran-2-carboxylate 15a



15a

Molecular Formula: $C_{12}H_{14}O_3$

Molecular Weight: 206.24

Physical Analysis :

Deep Light crystalline solid; mp 70-75 ^oC;

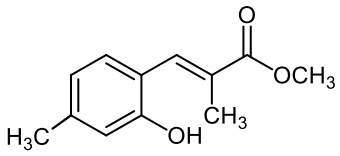
IR: ν_{max} (KBr) 3183.91, 2949.26, 1683.91, 1573.00, 1436.05, 1284.63, 1126.47, 1020.38 cm^{-1};

^{1}H NMR (400 MHz, $CDCl_3$): δ2.01 (s, 3H, CH_3), 2.26 (s, 3H, Ar–CH_3), 2.81 (d, 1H, *J* = 15.2 Hz), 3.05 (d, 1H, *J* = 15.2 Hz), 3.84 (s, 3H, OCH_3), 6.70-6.79 (m, 2H, Ar–H), 7.13(dd, 1H, Ar–H),

^{13}C NMR (100 MHz, $CDCl_3$): δ21.32 (CH_3), 23.09 (Ar–CH_3), 43.51 (-CH_2), 52.21 (OCH_3), 87.03 (C–1), 117.01 (Ar–CH), 129.0 (Ar–CH), 121.27 (Ar–CH), 129.14 (Ar–CH), 138.17 (Ar–C), 155.84 (Ar–C), 169.12 (C=O).

Anal. Calc. for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84; Found: C, 69.73; H, 6.88.

methyl 3-(2-hydroxy-4-methylphenyl)-2-methylacrylate15b



15b

Molecular Formula: $C_{12}H_{14}O_3$

Molecular Weight: 206.24

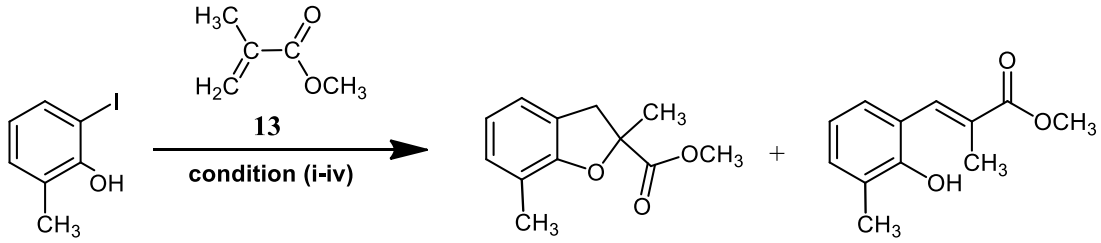
Physical Analysis :

IR: ν_{max} (KBr) 3379.40, 2949.26, 1683.91, 1611.58, 1573.00, 1436.05, 1284.63, 1126.47. 2020.38 cm^{-1};

^{1}H NMR (400 MHz, $CDCl_3$): δ2.01 (s, 3H, CH_3), 2.20 (s, 3H, Ar–CH_3), 3.84 (s, 3H, -OCH3), 5.7(br. s 1H OH), 6.73 (d, 1H, *J* = 8.8 Hz), 6.74 (s, 1H, Ar-H), 7.14(d, 1H, J=8.4, Ar-H), 7.74(s, 1H, vinylic–H),

2.3.3 Synthesis of methyl 2,7-dimethyl-2,3-dihydrobenzofuran-2-carboxylate 16a

A mixture of **8** and **13** in the above procedure for **2.3.1** was followed for the preparation of methyl 2,7-dimethyl-2,3-dihydrobenzofuran-2-carboxylate **16a**and butyl 3-(2-hydroxy-3-methylphenyl) propanoate **16b** and small amount of deiodinated product were obtained (**Scheme 9**)

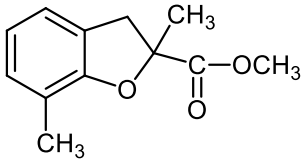


8 **16a** 70% **16b** 27%

Condition	
i	$Pd(Ph_3P)_2Cl_2$, DMF, Et_3N, N_2, 80-100 ^oC, 20-24 hrs
ii	$Co(Ph_3P)_2Cl_2$, DMF, Et_3N, N_2, 80-100 ^oC, 20-24 hrs
iii	$Ni(Ph_3P)_2Br_2$, DMF, Et_3N, N_2, 80-100 ^oC, 20-24 hrs
iv	Bimetallic nano catalyst, DMF, Et_3N, N_2, 80-100 ^oC, 20-24 hrs

Scheme 9

methyl- 2,7-dimethyl-2,3-dihydrobenzofuran-2-carboxylate16a



16a

Molecular Formula: $C_{12}H_{14}O_3$

Molecular Weight: 206.24

Physical Analysis :

crystalline solid; mp. 32-37 ^oC;

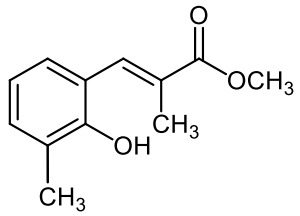
IR: ν_{max} (KBr) 3104.55, 2956.97, 2360.95, 2070.65, 1894.16, 1659.80, 1599.04, 1504.53, 1430.26, 1363.72, 1262.56, 1112.0 cm^{-1};

^{1}H NMR (400 MHz, $CDCl_3$): δ2.15 (s, 3H, CH_3), 2.28 (s, 3H, Ar–CH_3), 2.71 (d, 1H, *J* = 15.2 Hz, CH_2), 3.10 (d, 1H, *J* = 15.2 Hz, CH_2), 3.82 (s, 3H, OCH_3), 6.82 (t, 1H, *J* = 5.2 Hz, Ar–H), 7.19 (dd, 2H, *J* = 8.4 Hz Ar–H).

^{13}C NMR (100 MHz, $CDCl_3$): δ15.94 (Ar-CH_3), 23.14 (–CH_3), 42.18 (-CH_2), 52.01 (OCH_3), 87.14 (C–1), 123.96 (Ar–CH), 124.34 (Ar–CH), 127.40(Ar–CH), 128.03(Ar–CH), 131.23(Ar–CH), 154.44 (Ar–C), 169.59 (C=O).

Anal. Calc. for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84; Found: C, 69.90; H, 6.78.

methyl -3-(2-hydroxy-3-methylphenyl)-2-methylacrylate16b



16b

Molecular Formula: $C_{12}H_{14}O_3$

Molecular Weight: 206.24

Physical Analysis :

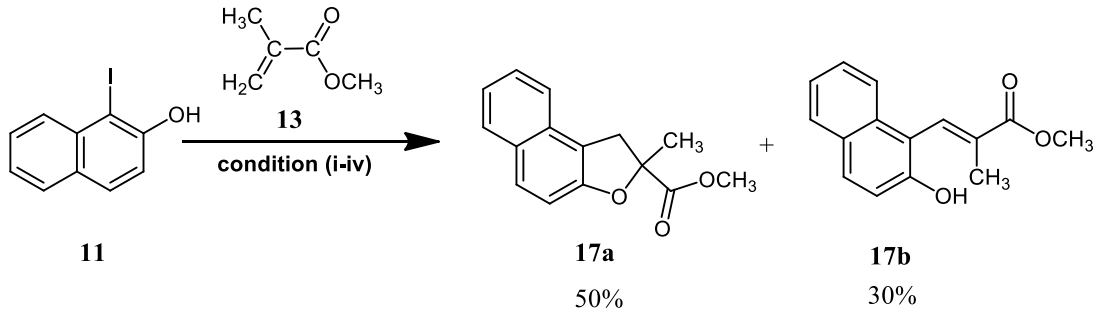
crystalline solid; mp. 35-39 ^oC;

IR: ν_{max} (KBr) 3350.40, 2949.26, 1683.91, 1611.58, 1573.00, 1436.05, 1284.63, 1126.47. 2020.38 cm^{-1};

^{1}H NMR (400 MHz, $CDCl_3$): δ2.12 (s, 3H, CH_3), 2.28 (s, 3H, Ar–CH_3), 3.82 (s, 3H, -OCH3), 5.61(s, 1H OH), 6.84 (d, 1H, *J* = 8.4 Hz), 7.20(d, 1H, J=8.4, Ar-H), 7.22 (s, 1H, Ar-H), 7.63(s, 1H, vinylic–H),

2.3.4 Synthesis of methyl 2-methyl-1, 2-dihydronaphtho [2, 1-b] furan-2-carboxylate 17a

A mixture of **11** and **13** in the above procedure for **2.3.1** was followed for the preparation of methyl 2-methyl-1,2-dihydronaphtho[2,1-b]furan-2-carboxylate **17a**and methyl 3-(2-hydroxynaphthalen-1-yl)propanoate **17b** and small amount of diiodinated product were obtained (**Scheme 10**)

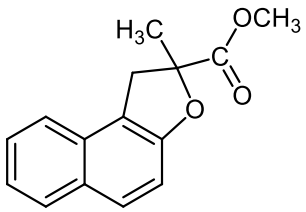


11 **17a** 50% **17b** 30%

Condition	
i	$Pd(Ph_3P)_2Cl_2$, DMF, Et_3N, N_2, 80-100 ^oC, 20-24 hrs
ii	$Co(Ph_3P)_2Cl_2$, DMF, Et_3N, N_2, 80-100 ^oC, 20-24 hrs
iii	$Ni(Ph_3P)_2Br_2$, DMF, Et_3N, N_2, 80-100 ^oC, 20-24 hrs
iv	Bimetallic nano catalyst, DMF, Et_3N, N_2, 80-100 ^oC, 20-24 hrs

Scheme 10

methyl 2-methyl-1,2-dihydronaphtho[2,1-b]furan-2-carboxylate17a



17a

Molecular Formula: $C_{15}H_{14}O_3$
Molecular Weight: 242.27

Physical Analysis :

Deep Red solid; mp. 60-65 ^oC;

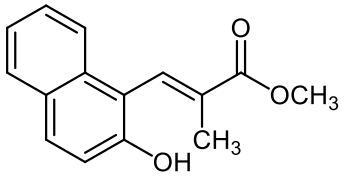
IR: ν_{max} (KBr) 3060.17, 2925.15, 28.54.74, 1621.22, 1510.31, 1462.09, 1384.94, 1244.13, 1120.68 cm^{-1};

^{1}H NMR (400 MHz, $CDCl_3$): δ1.33 (s, 3H, CH_3), 3.61 (d, 1H, *J* = 15.2 Hz, CH_2), 3.70 (s, 3H, OCH_3), 3.81 (d, 1H, *J* = 15.2 Hz, CH_2), 7.20 (d, 1H *J* = 9.2 Hz, Ar–H), 7.62-7.86 (m, 3H, Ar–H), 8.41 (d, 1H *J* = 8.8 Hz, Ar–H), 8.54 (d, 1H *J* = 8.8 Hz, Ar–H).

^{13}C NMR (100 MHz, $CDCl_3$): δ179.59(C=O), 155.44(Ar–CH), 131.25(Ar–CH),129.46(Ar–CH), 128.78(Ar–CH), 128.72(Ar–CH), 128.42(Ar–CH),124.26(Ar–CH),123.63(Ar–CH), 118.01(Ar–CH), 109.48(Ar–CH), 87.14(C–1), 52.01(OCH_3), 42.18(-CH_2), 28.14(–CH_3).

Anal. Calc. for $C_{15}H_{14}O_3$: C, 74.36; H, 5.82; Found: C, 74.48; H, 5.79.

methyl 3-(2-hydroxynaphthalen-1-yl)acrylate17b



17b

Molecular Formula: $C_{15}H_{14}O_3$

Molecular Weight: 242.27

Physical Analysis :

Deep Red solid; mp. 60-65 ^oC;

IR: ν_{max} (KBr) 3370.17, 2925.15, 28.54.74, 1621.22, 1510.31, 1462.09, 1384.94, 1244.13, 1120.68 cm^{-1};

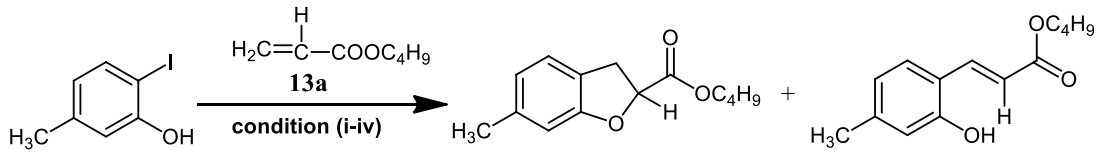
^{1}H NMR (400 MHz, $CDCl_3$): δ1.43 (s, 3H, CH_3), 3.71 (s, 3H, OCH_3), 5.22(s, 1H OH), 7.20 (d, 1H *J* = 9.2 Hz, Ar–H), 7.62-7.86 (m, 3H, Ar–H), 8.41 (d, 1H *J* = 8.8 Hz, Ar–H), 8.54 (d, 1H *J* = 8.8 Hz, Ar–H).

The data of UV, IR, ^{1}H NMR and ^{13}C NMR spectra were found to be consistent with the structure of this compound as shown below:

Anal. Calc. for $C_{15}H_{14}O_3$: C, 74.36; H, 5.82; O, 19.81

2.3.5 Synthesis of butyl 6-methyl-2,3-dihydrobenzofuran-2-carboxylate18a

A mixture of **5** and **13a** in the above procedure for **2.3.1** was followed for the preparation of butyl 6-methyl-2,3-dihydrobenzofuran-2-carboxylate**18a**and butyl 3-(2-hydroxy-4-methylphenyl)acrylate**18b** and small amount of diiodinated product were obtained (**Scheme 11**)

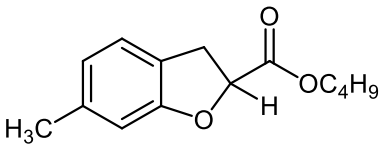


6 **18a** 69% **18b** 20%

Condition	
i	$Pd(Ph_3P)_2Cl_2$, DMF, Et_3N, N_2, 80-100 ^oC, 20-24 hrs
ii	$Co(Ph_3P)_2Cl_2$, DMF, Et_3N, N_2, 80-100 ^oC, 20-24 hrs
iii	$Ni(Ph_3P)_2Br_2$, DMF, Et_3N, N_2, 80-100 ^oC, 20-24 hrs
iv	Bimetallic nano catalyst, DMF, Et_3N, N_2, 80-100 ^oC, 20-24 hrs

Scheme 11

butyl 6-methyl-2,3-dihydrobenzofuran-2-carboxylate18a



18a

Light pink crystalline solid; mp. 98-100 ^oC;

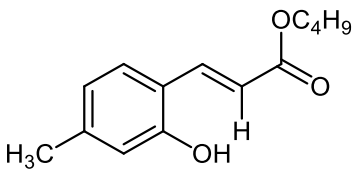
IR: ν_{max} (KBr) 3141.8, 3022.2, 2956.7, 1670.2, 16.4.7, 1575.7, 1423.4, 1305.7, 1209.3, 1166.9, 1041.5, 1004.8 cm^{-1};

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.96 (t, 3H, *J* = 7.4 Hz, CH_3), 1.46 (m, 2H, CH_2),1.67 (m, 2H, CH_2), 2.29 (s, 3H, Ar–CH_3), 4.22 (t, 2H, *J* = 6.8 Hz, OCH_2), 6.59 (d, 1H, *J* = 16.4 Hz, H-3), 6.66 (s, 1H, H-3), 6.71(d, 1H, *J* = 8 Hz, Ar–H), 6.75 (s, 1H, Ar–H), 7.33 (d, 1H, *J* = 7.8 Hz, Ar–H), 7.98 (d, 1H, *J* = 16 Hz, H-2).

^{13}C NMR (100 MHz, $CDCl_3$): δ13.70 (CH_3), 19.14 (CH_2), 28.20 (CH_2), 30.69 (Ar–CH_3), 67.42 (OCH_2), 116.46 (C–3), 117.92 (C–2), 120.92 (Ar–C), 121.60 (Ar–CH), 129.18 (Ar–CH), 131.44 (Ar–CH), 141.18 (Ar–C), 155.86 (Ar–C), 169.59 (C=O).

Anal. Calc. for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74; Found: C, 71.64; H, 7.80.

butyl 3-(2-hydroxy-4-methylphenyl)acrylate18b



18b

Molecular Formula: $C_{14}H_{18}O_3$

Molecular Weight: 234.13

Physical Analysis :

Ash solid; mp. 59-67^{o}C;

^{1}H NMR (400 MHz, $CDCl_3$): δ0.80 (t, 3H, *J* = 7.6 Hz, CH_3), 1.49 (m, 2H, CH_2),1.67 (m, 2H, CH_2), 2.17 (m, 2H, CH_2), 2.30 (s, 3H, Ar–CH_3), 3.65 (t, 2H, *J* = 6.8 Hz, OCH_2), 5.51(br. s 1H OH), 6.55 (d, 1H, *J* = 5.6 Hz, 1H), 6.84 (d, 1H, *J* = 8.4, Ar-H), 6.04 (s, 1H, Ar–H), 7.29(d, 1H, *J* = 7.2 Hz, Ar–H), 7.64 (d, 1H, *J* = 5.6 Hz, 1H).

2.4 Characterization of synthesized product

2.4.1. UV-Visible spectrophotometer

The UV-Visible spectral analysis was performed with a double beam UV-Visible spectrophotometer. The analyses were involved within 200-800 nm range. For, UV-Vis spectral analyses, purified and dried 2,3-dihydrobenzofurans were dissolved in chloroform solvent. The dissolved sample was placed in the sample cuvette while the reference cuvette was filled with the corresponding solvents. All the analysis was performed at room temperature 30°C (±2°C).

2.4.2. Fourier Transform Infrared (FTIR) analysis

The infrared spectra of the synthesized 2,3-dihydrobenzofurans were recorded on an FTIR spectrometer in the region of 4000 – 500 cm^{-1}. All the 2,3-dihydrobenzofurans samples had dried. A small portion of samples were taken and mixed with KBr. The powder mixtures were then compressed in a metal holder under pressure to make pellets. The pellets were then placed in the path of IR beam for measurements.

2.4.3. Nuclear Magnetic Resonance (NMR) analysis

^{1}H and ^{13}C-NMR spectra were recorded by Bruker BPX- 400 spectrophotometer operating at 400.23 MHz and 100.63 MHz respectively and $CDCl_3$ used as solvent, tetramethylsilane (TMS) as an internal standard. All chemical shifts (δ) were

reported in ppm and coupling constants (*J*) in Hz. Chemical shifts were performed relative to tetramethylsilane (TMS) and *d*-solvent peaks (7.28 ppm in ^{1}H and 77.00 ppm in ^{13}C, chloroform), respectively. Abbreviations used in the NMR experiments: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet.

2.4.4. Gas Chromatography Mass Spectrum (GC-MS) analysis

Retention time and mass spectrum for *N*, *N*-dioctyl-butanediamide was recorded in chloroform using column: Rxi-5ms, 30m, 0.25mm ID, 0.25µ df by Shimadzu GC-MS.

2.4.5. Melting Point

Melting points for 2,3-dihydrobenzofurans were determined in open capillary tubes in melting point apparatus.

2.4.6. Solubility

All the 2,3-dihydrobenzofurans were soluble in chloroform solvent.

CHAPTER 3

Results& Discussion

3. PRESENT WORK: METAL MEDIATED SYNTHESIS OF 2, 3-DIHYDRO BENZOFURAN DERIVATIVES

3.1 Rationale

Benzofurans are an important class of heterocyclic compounds[1] with unique biological activities. [2] Notable instances include derivatives of benzofurans acting as antitumor agents, [3] angiotensin II inhibitors, [4] and 5-lipoxygenase inhibitors etc.[5]. Because of their occurrence as natural products and their biological activities, various classical methods have been developed over the years for elaborating the benzofuran structure [1a,2a]. A rhodium-catalyzed cyclization of 2-alkynyl phenols followed by intermolecular conjugate addition has been reported[5]. A new Pd-catalyzed tandem intramolecular Oxypalladation/Heck-type coupling between 2-alkynylphenols and alkenes was reported,[6] leading to 3- (1-alkenyl) benzofurans. A method for the synthesis of 2-bromo-3-aroyl-benzo[b]furans from readily accessible precursors has been developed[7].

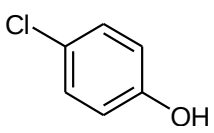
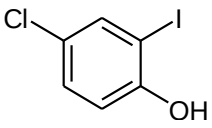
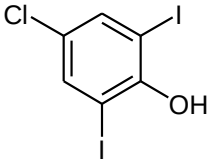
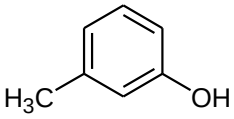
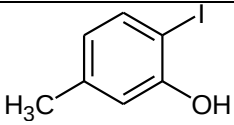
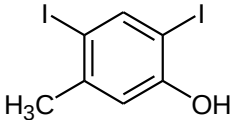
N.G. Kundu *et al* reported a study of the heteroannulation of 2-iodophenol with acetylenic substrate through palladium-copper catalysis leading to the synthesis of the 2- substituted benzofurans. M.W. Khan *et* al[8] reported the synthesis of 2-acyl/aroyl benzofurans through combined palladium-catalyzed and Friedel-Crafts reactions of 2-iodophenol. The acylated benzofuran compounds demonstrated mild to significant growth inhibition against antibiotic-susceptible standard and clinically isolated strains of Gram-positive and Gram-negative bacteria as well as human fungal pathogens.

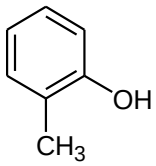
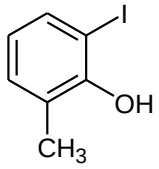
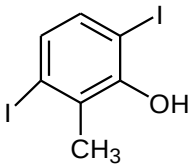
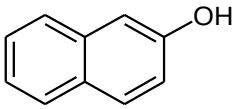
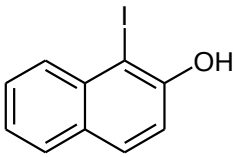
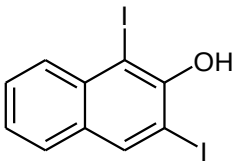
For the last few decades palladium-catalyzed reactions have been of great significance in carbon-carbon[131] and carbon-heteroatom bonds formations[9]. Recently, our research group has developed methods for the synthesis of various benzofused heterocyclic compound e.g. benzofurans[10], isoindolinones and isoquinolinones[11] through combined palladium-catalyzed and Friedel-Crafts reactions with terminal alkynes and acid chloride. Although a number of synthetic methods for the preparation of benzofurans have been reported, simple and efficient approaches still remain scarce for the synthesis of substituted dihydrobenzofurans.

In view of the extensive natural occurrence and biological importance of dihydrobenzofurans, it was planned to develop a convenient method for the synthesis of substituted 2, 3-dihydrobenzofuran derivatives from the reaction of substituted 2-iodophenol and terminal alkenes (acrylic ester) by palladium-catalyzed reactions.

3.2 Preparation and Characterization of 2-iodophenol 2, 6, 8, 11

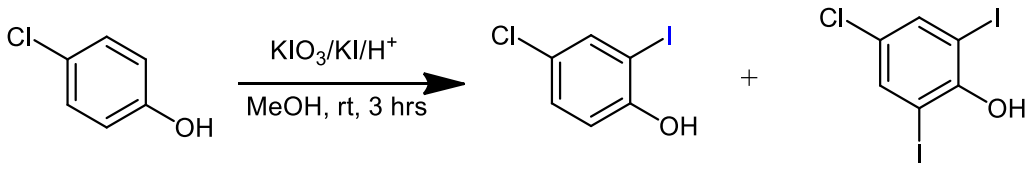
Table-1: Synthesis of 2-iodophenol 2, 5, 8, 11:

Entry	Substrate	Reagent and condition	Product	Yield%
I	 **1**	KIO_3, KI, H^+, solvent MeOH, rt, 3h	 **5** +  **9**	70 30
II	 **2**		 **6** +  **10**	60 15

III	 **3**		 **7** +  **11**	35 55
IV	 **4**	KIO_3, KI, H^+, solvent MeOH, rt, 3h	 **8** +  **12**	80 10

3.2.1 Preparation of 4-chloro-2-iodophenol 2

The compound *p*-chlorophenol **1** underwent a smooth reaction with potassium iodide, potassium iodate in methanol and aqueous solution of HCl to produce desired products 4-chloro-2-iodophenol**5** and 4-choro-2,6-diiodophenol**9** in good yields, as shown in the



35% 55%

1 **5** **9**

3.2.1a. Characterization of 4-chloro-2-iodophenol 5

A white color crystal was obtained with 35% yield, mp. 70-72 ^{o}C, which was moisture sensitive. The structure of the compound was predicted by various spectral data.

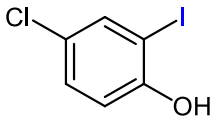
UV(EtOH) : λ_{max} = 322.40 nm

IR : The IR spectrum showed the following absorption bands at υ_{max} 3286.5. 1571.9, 1300, 810 and 690.5 cm^{-1} indicating the stretching of –OH, –C=C, –C–H, –C–I and –C–Cl groups in the compound respectively.

^{1}H NMR : The ^{1}H NMR spectra of the compound **7** revealed one proton singlet at δ 5.65 (br. s, 1H, Ar–OH) of Ar–OH group. The chemical shift position at δ 6.91 (s, 1H, Ar–H) indicated one aromatic hydrogen, doublet at δ 7.19 (d, 1H, J=2.8 Hz, Ar–H) for one aromatic hydrogen, the chemical shift position at δ 7.62 (d, 1H, J=2,4 Hz, Ar–H) indicated one aromatic hydrogen.

A white color crystal was obtained with yield of 66%, mp.70-75 ^{o}C, the compound was moisture sensitive. The structure of the compound was assigned by different spectral data.

All spectral data were found to be consistent with the following structure.



2

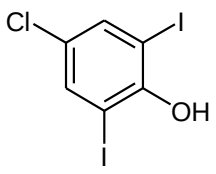
3.2.1b. Characterization of 4-chloro-2,6-diiodophenol9

A white colour crystal was obtained with 55% yield, mp 70-77 ^{o}C, which was moisture sensitive. The structure of the compound was predicted by various spectral data. In UV (EtOH) spectrum, the λ_{max} value was found at 302.80 nm.

The IR spectrum showed the following absorption bands at υ_{max} 3460.1, 3068.5, 1531.4, 850.5 and 705.9 cm^{-1} indicating the stretching of –OH, aromatic C–H, –C=C, –C–I disubstitued and –C–I groups in the compound **8** respectively.

The ^{1}H NMR spectra of compound **8** indicated δ 5.55 (br. s, 1H, Ar–OH) for one hydrogen of –OH group, the chemical shift position at δ 7.65 (s, 2H, Ar–H) indicated two aromatic hydrogen.

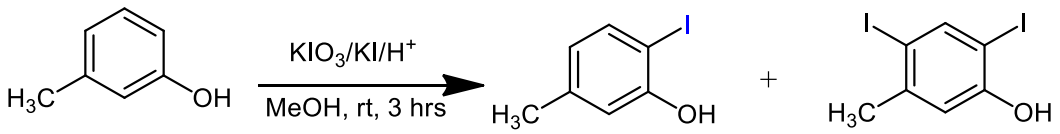
The above data of UV, IR and ^{1}H NMR spectra were found to be consistent with the structure of this compound as shown below:



9

3.2.2 Preparation of 5-methyl-2-iodophenol 6

According to the above iodination reaction(**3.2.1**) from **2** synthesized of 2-Iodo-5-methyl-phenol **6** and small amount of diiodinated product 2,4-Diiodo-5-methyl-phenol **10** .



50% 50%

2 **6** **10**

3.2.2a. Characterization of 5-methyl-2-iodophenol5

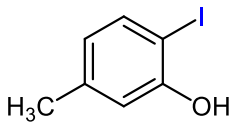
A yellowish solid was obtained with 60% yield, mp 32-36 ^{o}C, which was moisture sensitive. The structure of the compound was established by various spectral data. In UV λ_{max} was found 283.60 nm for the compound.

The IR (KBr) spectrum of this compound exhibited absorption bands at υ_{max} 3421.5,1649.0, 1456.2 & 800 cm^{-1} for the stretching of –OH, –C=C, H_3C–C and –C–I groups in the compound **5** respectively.

The ^{1}H NMR spectra showed presence of seven (7) hydrogens in the compound. Chemical shift position at δ 2.19 (s, 3H, Ar–CH_3) showed for three hydrogen in methyl group, δ 5.28 (br.s, 1H, OH) for –OH proton, δ 6.42 (s, 1H, Ar–H) for one aromatic hydrogen, doublet at δ 6.74(d, 1H, J=7.6 Hz, Ar–H) and 7.43(d, 1H, J=8 Hz, Ar–H) also for two aromatic hydrogen.

The ^{13}C NMR spectral data showed presence of seven (7) carbon atoms in the compound. Chemical shift 20.97 was due to the presence of one carbon in methyl group (Ar–CH_3), chemical shift of δ 111.97 and 115.84 for the (Ar–C) and (Ar–CH), δ 123.37, 137.80 for (Ar–CH), δ 140.46 and 154.64 for (Ar–C) were obtained.

On the basis of UV, IR, ^1H NMR and ^{13}C NMR spectra and elementary data, the structure of this compound was predicted as the following structure:



5

3.2.2b. Characterization of 5-methyl-2,6-diiodophenol 6

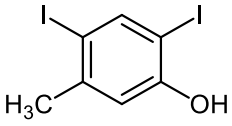
A white crystal with 30% yield was obtained, mp 30-32 ^oC, this compound was moisture sensitive. The structure of the compound was established by different spectral data. The UV (EtOH) spectrum was showed λ_{max} 287.60 nm for the compound.

The IR (KBr) spectrum of this compound showed absorption bands at υ_{max}3460.1cm^{-1} for the stretching of –OH group. Stretching bands υ_{max} 1449.9, 1300 and 800 cm^{-1} indicated the presence of –C–H, –C–O, and –C–I groups in the compound **6** respectively.

The ^1H NMR spectra of compound **6** revealed three protons singlet at δ 1.61 (s, 3H, Ar–CH_3) of methyl group, chemical shift δ 5.62(s, 1H, OH) was for one aldehyde hydrogen, singlet at δ 6.59 & 7.28 (s, 1H, Ar–H) for two hydrogens of aromatic ring.

The structure of the compound was further confirmed by its ^{13}C NMR data. Chemical shift position at δ 28.45 indicated presence of one carbon of methyl group (Ar–CH_3), δ 77.84 and 90.22 obtained for the two tertiary carbons of aromatic ring (Ar–C), chemical shift at δ 123.48 and 137.98 presented two carbons in aromatic ring (Ar–CH), δ 143.55 and 153.21 for the two tertiary carbons of benzene ring (Ar–C).

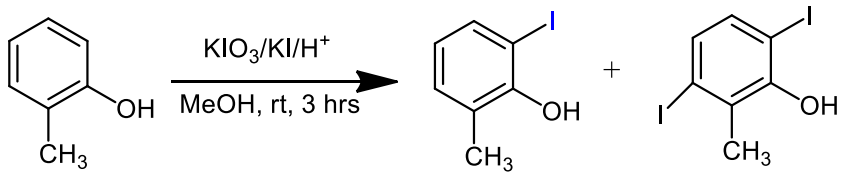
The data of UV, IR, ^{1}H NMR and ^{13}C NMR spectra were found to be consistent with compound as follows:



6

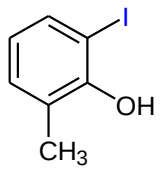
3.2.3 Preparation of 2-iodo-6-methyl-phenol 8

According to the above iodination reaction(**3.2.1**) from **3** synthesized of 2-Iodo-6-methyl-phenol **7** and small amount of 3,6-Diiodo-2-methyl-phenol **11** .



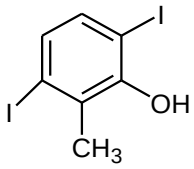
3 60% **7** 40% **11**

3.2.3a. Characterization of 2-iodo-6-methyl-phenol 8



7

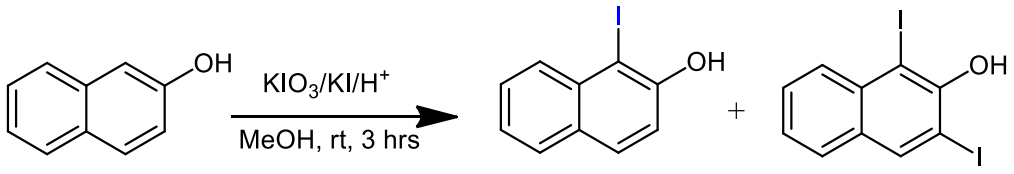
3.2.3b. Characterization of 3,6-diiodo-2-methylphenol 9



11

3.2.4 Preparation of 1-iodo-naphthalen-2-ol 11:

According to the above iodination reaction(**3.2.1**) from **4** synthesized of 1-Iodo-naphthalen-2-ol**8** and small amount of diiodinated product 1,3-diiodo-naphthalen-2-ol**12**.



4

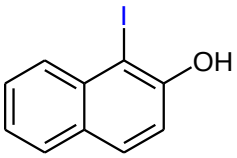
80%

8

20%

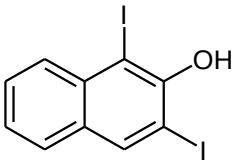
12

3.2.4a. Characterization of 1-iodonaphthalen-2-ol11



11

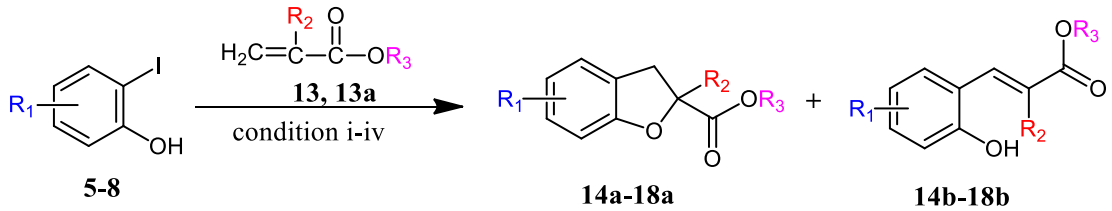
3.2.4b. Characterization of 1,3-diiodonaphthalen-2-ol 12



12

3.3 Preparation and characterization of substituted 2, 3-dihydrobenzofuran14a-17a

2-iodophenol**5-8** were converted to the substituted 2,3-dihydrobenzofuran**14a-17a**on the treatment with terminal alkenes in the condition of **(i-iv)** as shown in the **Scheme 5**.



5, 14 R^1 = *p*-Cl;
6, 15 R^1 = *m*-CH_3;
7, 16 R^1 = *o*-CH_3;
8, 17 R^1 = C_6H_6

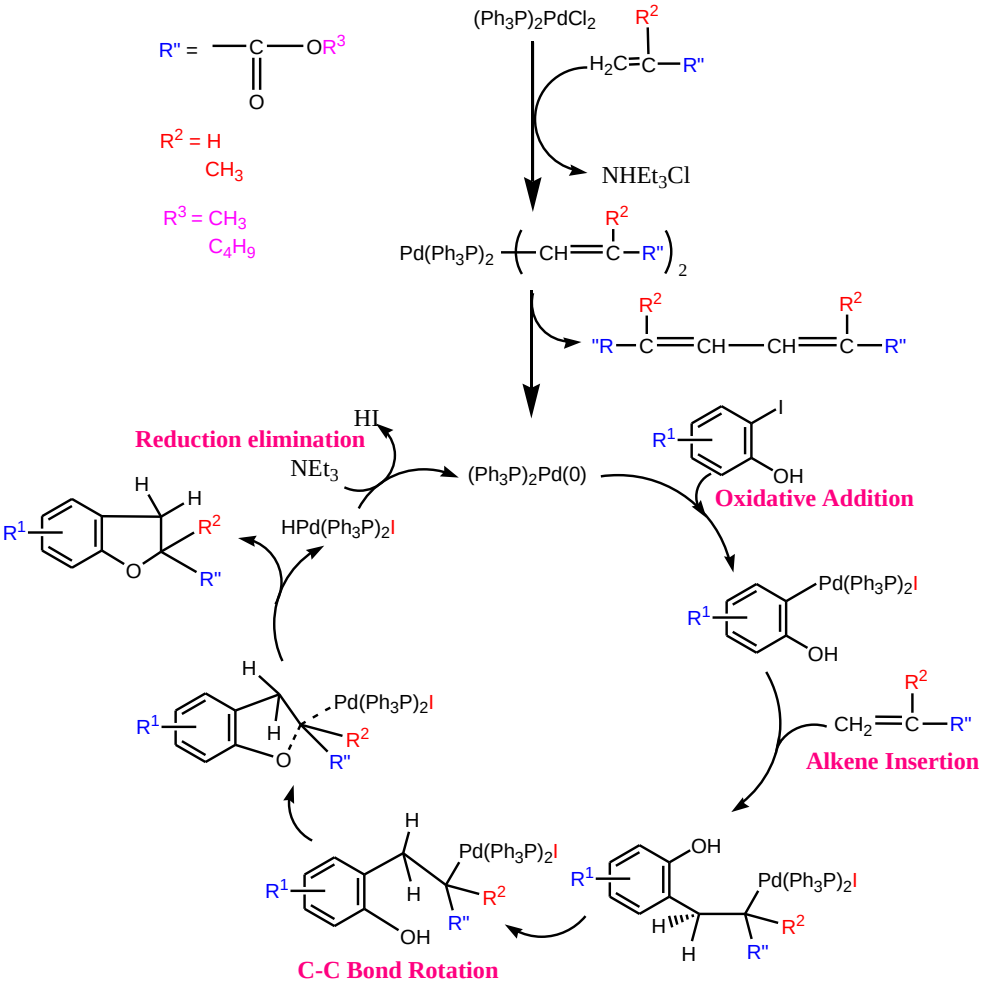
R^2 = **13, 14-17** CH_3
R^2 = **13a, 18** H

R^3 = **13, 14-17** CH_3
R^3 = **13a, 18** C_4H_9

Condition	
i	$Pd(Ph_3P)_2Cl_2$, DMF, Et_3N, N_2, 80-100 °C, 20-24 hrs
ii	$Co(Ph_3P)_2Cl_2$, DMF, Et_3N, N_2, 80-100 °C, 20-24 hrs
iii	$Ni(Ph_3P)_2Br_2$, DMF, Et_3N, N_2, 80-100 °C, 20-24 hrs
iv	Bimetallic nano catalyst, DMF, Et_3N, N_2, 80-100 °C, 20-24 hrs

Scheme 5

3.3.1 Mechanism :

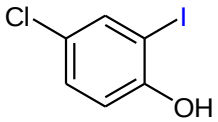
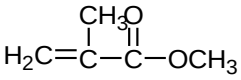
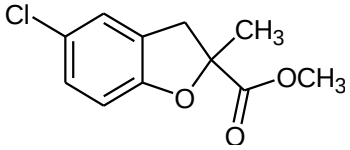
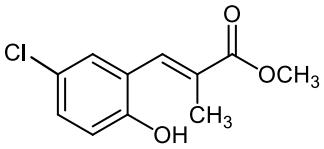
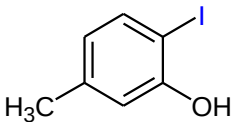
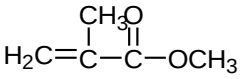
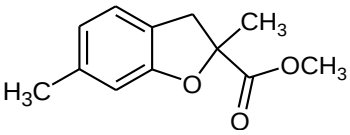
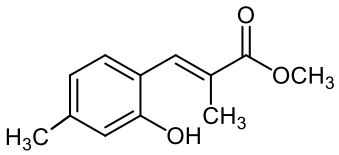
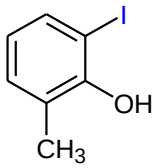
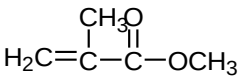
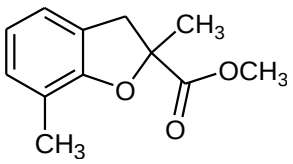


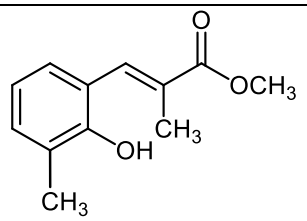
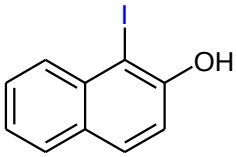
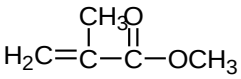
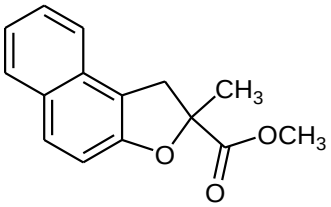
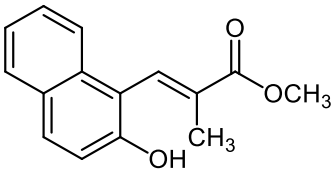
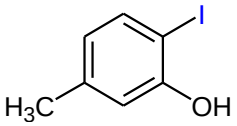
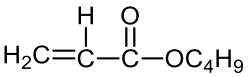
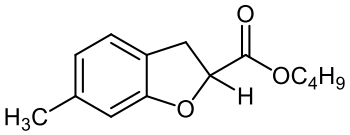
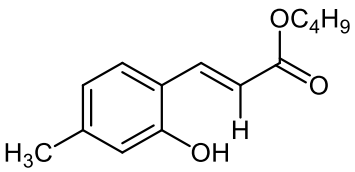
Scheme-6

A plausible mechanism for the formation of substituted **2,3**-dihydro benzofuran **14a-17a** through palladium catalyzed reaction of iodophenol**5-8** with terminal alkenes (acrylic ester) (**13**) is illustrated in **Scheme 6.**

Once formed the highly coordinative unsaturated 14-electron palladium (0) complex participates in an oxidative addition reaction with the *o*-iodophenol**4** to give a *o*-aryl palladium (II) complex which then trans-metallats with terminal alkenes (**13**) to generate the arylalkynyl palladium (II) species. The intermediate arylalkynyl palladium (II) involves a simple bond rotation. This event is essential because it establishes the necessary syn relationship between a β-hydrogen and the palladium atom in a common plane, the β-hydride elimination can take place to give the coupling product substituted 2,3-dihydrobenzofurans (**14a-17a**) and the hydridopalladium complex. Finally, a base triethyl amine assisted reductive elimination of HI from the latter regenerates the palladium (0) catalyst, thus permitting a subsequent turn through the cycle.

Table 2: Synthesis of 2-alkyl-2,3-dihydrobenzofuran acetate 14a-17a:

Entry	Substrate	Alkenes	Products	[a]Yield %
1.	 **5**	 **13**	 **14a**	60
			 **14b**	35
2.	 **6**	 **13**	 **15a**	50
			 **15b**	40
3.	 **7**	 **13**	 **16a**	70

			 **16b**	27
4.	 **8**	 **13**	 **17a**	50
			 **17b**	30
	 **6**	 **13a**	 **18a**	69
			 **18b**	20

[a] yield % was calculated on the basis of 2-iodophenol.

3.4 Characterization of 2,3-dihydrobenzofuran14a-17a

3.4.1 Characterization of methyl 5-chloro-2-methyl-2,3-dihydrobenzofuran-2-carboxylate 14a

A white color crystal was obtained will yield of 60%, mp. 64-69 ^{o}C, the compound was moisture sensitive. The structure of the compound was assigned by different spectral data.

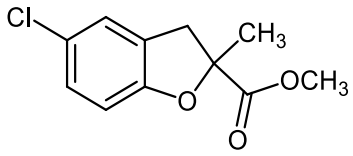
The **IR**spectrum [**Fig. 8**] of **14a**compound presented absorption bands at ν_{max} 3066.92 and 2953.12 cm^{-1} for stretching of aromatic C-H, aliphatic C-H groups respectively and1706.09, 1592.29, 1457.27, 1264.38 and 1127.43 cm^{-1} indicated stretching bands ofand -C=O, -C=C, COO^{-}, -C-O and -C-O-C groups in the compound respectively.

The**^{1}H NMR** spectrum [**Fig. 9a,b,c**] of the compound **14a** indicated the chemical shiftδ2.25 (s, 3H, -CH_3) for three hydrogens in methyl group at C_2 position. The chemical shift δ3.25 (d, 1H, *J* = 15.2*Hz*, C3H_a) and 3.32 (d, 1H, *J* = 15.2 *Hz*, C3H_b) for two doublet for two hydrogen in -CH_2 at C3 position, the chemical shift δ3.85 (s, 3H, -OCH_3) for methoxy group, δ 7.39(d, 1H, *J* = 7.6*Hz*, Ar-H), 7.41(d, 1H, *J* = 7.6 *Hz*, Ar-H), 7.84 (s, 1H, Ar-H) for three hydrozens in benzene ring. Total eleven(11) hydrogen atoms were indicate in the compound by ^{1}H NMRspectrum.

The structure of the compound**14a** was further confirmed by**^{13}C NMR**spectural data [**Fig. 10**]. Chemical shitf atδ23.28 (-CH_3) and 42.72 (C_3 positon CH_2) for C2 postion methyl and C_3 position CH_2 carbons. The Chemical shitf atδ52.32 (-OCH_3), 87.21 (for C2position C), and 120.74 (Ar–CH), 125.96 (Ar–CH), 126.13 (Ar–C), 130.52 (Ar–CH), 130.96 (Ar–CH), 160.96 (Ar–C) indicated the carbons of benzene ring, The chemical shift at δ168.08 indicated the presence of carbonyl carbon (–C=O) in ester group.Total carbons presence in the compound were eleven (11).

Anal. Calc. for $C_{11}H_{11}ClO_3$: C, 58.29; H, 4.89; Cl, 15.64; Found: C, 58.22; H, 4.77.

The above data of **IR**, **^{1}H NMR** and **^{13}C NMR** spectra were found to be consistent with the structure of this compound as shown below:



14a

3.4.2 Characterization of methyl 2, 6-dimethyl-2, 3-dihydrobenzofuran-2-carboxylate 15a

A deep Light crystalline solid was obtained with yield 50%, mp 70-75 ^oC, which was very moisture sensitive. The structure of the compound was established by different spectral data.

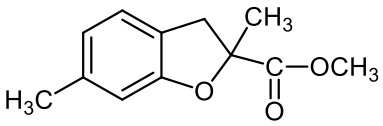
The **IR**: ν_{max} (KBr) spectrum [**Fig. 11**] of the compound **15a** exhibited bands3183.91 2949.26, 1683.91cm^{-1} for stretching of aromatic C-H, aliphatic C-H and C=O groups respectively. Stretching bands 1573.00, 1284.63cm^{-1}indicated -C=C, and -C-O groups in the compound respectively.

Inthe**^{1}H NMR** spectrum [**Fig. 12a,b,c**] of the compound **15a** chemical shiftδ2.01 (s, 3H, CH_3), 2.26 (s, 3H, Ar–CH_3) indicated for hydrozens in C_2 position methyl and aromatic methyl groups.Chemical shift δ2.81 (d, 1H, *J* = 15.2 *Hz*, C3Ha), 3.05 (d, 1H, *J* = 15.2 *Hz*, C3Hb) was two doublet for two hydrozen at C3 position CH_2, chemial shift δ 3.84 (s, 3H, OCH_3) for methoxy methyl group and chemical shiftδ6.70-6.79 (m, 2H, Ar–H), 7.13(dd, 1H, Ar–H) for two hydrozen in benzene ring. Total carbons presence in the compoud **15a** were fourteen (14).

Thestructure of the compound **15a**was furtherconfirmed by**^{13}C NMR** spectral data [**Fig. 13**]. Chemical shift at δ21.32 for C2 position methyl groups (-CH_3), 23.09 for benzine ring methyl groups(Ar–CH_3). The chemical shift δ43.51 (-CH_2) indicated for C3 position Carbon in CH_2 and 52.21 (OCH_3) for methoxy methyl group. The chemical shift δ 87.03 (C-2) for C2 postion carbons, and 117.01 (Ar–CH), 119.75 (Ar–CH), 129.0 (Ar–CH), 121.27 (Ar–CH), 129.14 (Ar–CH), 138.17 (Ar–C), 155.84 (Ar–C) were benzen ring carbons. Chemical shift δ169.12 indicated the presence of carbonyl carbon (C=O) in ester group. Total carbons presence in the compound were twelve (12).

Anal. Calc. for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84; Found: C, 69.73; H, 6.88.

The above data of IR, ^{1}H NMR and ^{13}C NMR spectra were found to be consistent with the structure of this compound as shown below:



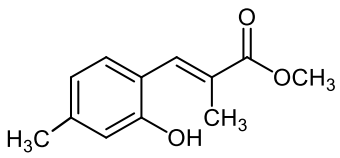
15a

3.4.3 Characterization of methyl 3-(2-hydroxy-4-methylphenyl)-2-methylacrylate15b

A light red crystalline solid was obtained with yield 40%, mp75-78^{o}C, which was very moisture sensitive. The structure of the compound was established by different spectral data.

Inthe**^{1}H NMR** spectrum [**Fig. 14a,b,c**] of the compound **15b** chemical shiftδ2.01 (s, 3H, CH_3) for C2 position methyl, δ2.20 (s, 3H, Ar–CH_3) for benzene methyl, 3.84 (s, 3H, -OCH3) for methoxy methyl. The chemical shift δ 5.7(br. s 1H OH) showed for -OH group and δ 6.73 (d, 1H, *J* = 8.8 Hz), 6.74 (s, 1H, Ar-H), 7.14(d, 1H, J=8.4, Ar-H) indicated benzen protons. The chemical shift δ7.74(s, 1H, vinylic–H) indicated C3-position position. Total hydrogen presence in the compoud **15b** were fourteen (14).

The above data of^{1}H NMRspectra were found to be consistent with the structure of this compound as shown below:



15b

3.4.4 Characterization of methyl 2,7-dimethyl-2,3-dihydrobenzofuran-2-carboxylate16a

A crystalline solid was obtained with yield 70%,mp32-37^{o}C, which was very moisture sensitive. The structure of the compound was established by different spectral data.

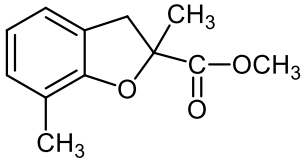
The **IR**spectrum [**Fig. 15**]ν_{max}3104.55, 2956.97, 1894.16, 1659.80 cm^{-1}stretching ofaromatic C-H, aliphatic C-H and C=O groups respectively in the compound **16a**. ν_{max}1599.04 and 1262.56cm^{-1} indicated -C=C, and -C-O groups in the compound respectively.

The**^{1}H NMR** spectra [**Fig. 16a, b, c**] showedat chemical shiftδ2.15 (s, 3H, CH_3) singlet pic for C2 position methyl group, δ2.28 (s, 3H, Ar–CH_3) showed for benzene methyl group. At chemical shift3.71 (d, 1H, *J* = 15.2 Hz, CH_2), 3.10 (d, 1H, *J* = 15.2 Hz, CH_2) indicated two doublet for C-3 position two hydrozen. Chemical shift δ3.82 (s, 3H, OCH_3) showed for methoxy methyl group and δ6.82 (t, 1H, *J* = 5.2 Hz, Ar–H), 7.19 (dd, 2H, *J* = 8.4 Hz Ar–H) indicated for three hydrogen in aromatic ring. Total carbons presence in the compoud **16a** were fourteen (14).

In the**^{13}C NMR**spectral[**Fig. 17**] data of compound **16a**chemical shift δ15.94 (Ar-CH_3) indicated the presence of one carbon in benzene methyl group, chemical shiftδ23.14 (–CH_3) showed for one C2 position methyl group. Chemical shiftδ42.18 (-CH_2) for C3 position carbon andδ52.01 (OCH_3) showed for methoxy methyl carbon. The chemical shift 87.14 (C–2) showed for C-2 position carbon and 123.96 (Ar–CH), 124.34 (Ar–CH), 127.40(Ar–CH), 128.03(Ar–CH), 131.23(Ar–CH), 154.44 (Ar–C) indicated the presence of aromatic ring carbon. The chemical shift δ169.59 (C=O) showed for acytyl group carbon. Total carbons presence in the compound were twelve (12) .

Anal. Calc. for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84; Found: C, 69.90; H, 6.78.

The above data of IR, ^{1}H NMR and ^{13}C NMR spectra were found to be consistent with the structure of this compound as shown below:



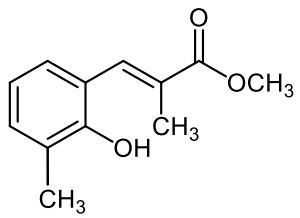
16a

3.4.5 Characterization of methyl 3-(2-hydroxy-3-methylphenyl)-2-methylacrylate16b

A light red crystalline solid was obtained with yield 27%,mp35-39 ^{o}C, which was very moisture sensitive. The structure of the compound was established by different spectral data.

Inthe**^{1}H NMR** spectrum [**Fig. 18a,b,c**] of the compound **16b** chemical shift showedδ2.12 (s, 3H, CH_3) for C2 positioin methyl group, 2.28 (s, 3H, Ar–CH_3) for benzene methyl group, 3.82 (s, 3H, -OCH3) for methoxy methyl group, 5.61(s, 1H OH) for -OH group. 6.84 (d, 1H, *J* = 8.4 Hz), 7.20(d, 1H, J=8.4, Ar-H), 7.22 (s, 1H, Ar-H) indicted of benzene proton. Chemical shift 7.63(s, 1H, vinylic–H) indicated C3-position position hydrogen.Total hydrogen presence in the compoud **16b** were fourteen (14).

The data of ^{1}H NMRspectra were found to be consistent with the structure of this compound as shown below:



16b

3.4.6 Characterization of methyl 2-methyl-1,2-dihydronaphtho[2,1-b]furan-2-carboxylate17a

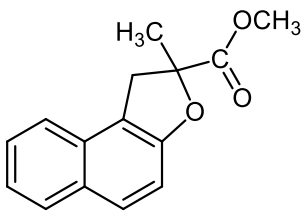
Deep Red solid was obtained with yield 50%, mp60-65^{o}C, which was very moisture sensitive. The structure of the compound was established by different spectral data.

The**IR** spectrum [**Fig. 19**] showed ν_{max} 3060.17, 2925.151621.22 cm^{-1} stretching bands represented =C-H, -C-H aliphatic and C=O groups in the compound **17a**. ν_{max}1510.31, 1462.09, 1244.13cm^{-1} indicated stretching bands of aromatics C-C, and ether-C-O.

The**^{1}H NMR** spectra **[Fig. 20a, b, c]** showedsingletδ1.33 (s, 3H, CH_3) for three hydorgen in C2 position methyl group and doublet at δ3.61 (d, 1H, *J* = 15.2 Hz, CH_2) for C3 position two one hydrogen H_a and 3.81 (d, 1H, *J* = 15.2 Hz, CH_2) showed C3 position two one hydrogen H_b. The chemical shift at 3.70 (s, 3H, OCH_3) showed for for methoxy group. Chemical shift at 7.20 (d, 1H *J* = 9.2 Hz, Ar–H), 7.62-7.86 (m, 3H, Ar–H), 8.41 (d, 1H *J* = 8.8 Hz, Ar–H), 8.54 (d, 1H *J* = 8.8 Hz, Ar–H) indicated the presence of napthol hydrogen. Total hydrogen presence in the compoud **17a** were fourteen (14).

Anal. Calc. for $C_{15}H_{14}O_3$: C, 74.36; H, 5.82; Found: C, 74.48; H, 5.79.

The data of IR, ^{1}H and NMRspectra were found to be consistent with the structure of this compound as shown below:



17a

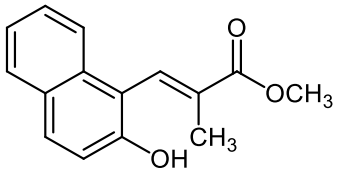
3.4.7 Characterization of methyl 3-(2-hydroxynaphthalen-1-yl)acrylate17b

Deep Red solid; mp. 60-65 ^{o}C;

Inthe**^{1}H NMR** spectrum [**Fig. 21a,b**] of the compound **17b** chemical shift showed δ1.43 (s, 3H, CH_3) for C2 positioin methyl group and chemical shift 3.71 (s, 3H, OCH_3) for methoxy methyl group. The chemical shift showed atδ5.22(s, 1H OH), for -OH group and the chemical shift 7.20 (d, 1H *J* = 9.2 Hz, Ar–H), 7.62-7.86 (m, 3H, Ar–H), 8.41 (d, 1H *J* = 8.8 Hz, Ar–H), 8.54 (d, 1H *J* = 8.8 Hz, Ar–H) indicted of napthol proton. Chemical shift 7.36(s, 1H, vinylic–H) indicated C3-position position hydrogen.Total hydrogen presence in the compoud **17b** were fourteen (14).

The data of^{1}H NMRspectra were found to be consistent with the structure of this compound as shown below:

Anal. Calc. for $C_{15}H_{14}O_3$: C, 74.36; H, 5.82; O, 19.81



17b

3.4.8 Characterization of butyl 6-methyl-2,3-dihydrobenzofuran-2-carboxylate18a

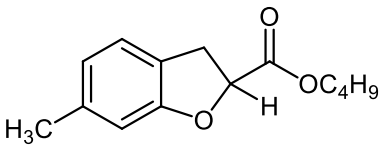
Light pink crystalline solid; mp. 98-100 ^{o}C;

IR: ν_{max} (KBr) 3141.8, 3022.2, 2956.7, 1670.2, 16.4.7, 1575.7, 1423.4, 1305.7, 1209.3, 1166.9, 1041.5, 1004.8 cm^{-1};

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.96 (t, 3H, *J* = 7.4 Hz, CH_3), 1.46 (m, 2H, CH_2),1.67 (m, 2H, CH_2), 2.29 (s, 3H, Ar–CH_3), 4.22 (t, 2H, *J* = 6.8 Hz, OCH_2), 6.59 (d, 1H, *J* = 16.4 Hz, H-3), 6.66 (s, 1H, H-3), 6.71(d, 1H, *J* = 8 Hz, Ar–H), 6.75 (s, 1H, Ar–H), 7.33 (d, 1H, *J* = 7.8 Hz, Ar–H), 7.98 (d, 1H, *J* = 16 Hz, H-2).

^{13}C NMR (100 MHz, $CDCl_3$): δ13.70 (CH_3), 19.14 (CH_2), 28.20 (CH_2), 30.69 (Ar–CH_3), 67.42 (OCH_2), 116.46 (C–3), 117.92 (C–2), 120.92 (Ar–C), 121.60 (Ar–CH), 129.18 (Ar–CH), 131.44 (Ar–CH), 141.18 (Ar–C), 155.86 (Ar–C), 169.59 (C=O).

The above data of IR, ^{1}H NMR and ^{13}C NMR spectra were found to be consistent with the structure of this compound as shown below:



18a

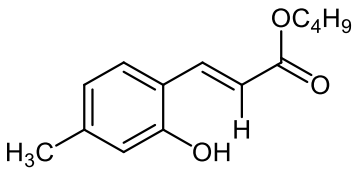
3.4.9 Characterization of butyl 3-(2-hydroxy-4-methylphenyl)acrylate18b

Yellowish Red solid; mp. 55-60^{o}C;

The**^{1}H NMR** spectra [**Fig. 22**] showed triplet at δ0.80 (t, 3H, *J* = 7.6 Hz, CH_3) for three proton, chemicial shift at 1.49 (m, 2H, CH_2) multilate for apliphatic CH_2, at 1.67 (m, 2H, CH_2) for another alophatic CH2, and chemical shift at 2.17 (m, 2H, CH_2) for aliphatic CH_2. The chemical shift at 2.30 (s, 3H, Ar–CH_3) for aromatic CH_3 tree proton, and chemical shift at 3.65 (t, 2H, *J* = 6.8 Hz, OCH_2) for OCH_2, In spectra chemical shift at 5.51(br. s 1H OH) singlet broght pick showed for phenolic OH, and chemical shift at 6.55 (d, 1H, *J* = 5.6 Hz, 1H), 6.84 (d, 1H, *J* = 8.4, Ar-H), 6.04 (s, 1H, Ar–H), 7.29(d, 1H, *J* = 7.2 Hz, Ar–H) showed for aromatic hydrogen. 7.64 (d, 1H, *J* = 5.6 Hz, 1H). Total hydrogen presence in the compound **18b** were eighteen.

The data of^{1}H NMRspectra were found to be consistent with the structure of this compound as shown below:

The data of^{1}H NMRspectra were found to be consistent with the structure of this compound as shown below:



18b

3.5Catalyst screening for synthesis 2,3-dihydrobenzofuran14a-17a

3.5.1 Catalyst screening of methyl 5-chloro-2-methyl-2, 3-dihydrobenzofuran-2-carboxylate 14a

Model Reaction

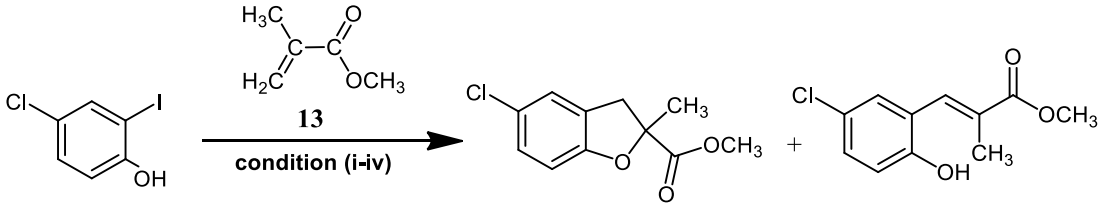


Table-3: Catalyst screening for model reaction

	Condition	Yeild %
i	$Pd(Ph_3P)_2Cl_2$, DMF, Et_3N, N_2, 80-100 ^oC, 20-24 hrs	60
ii	$Co(Ph_3P)_2Cl_2$, DMF, Et_3N, N_2, 80-100 ^oC, 20-24 hrs	50
iii	$Ni(Ph_3P)_2Br_2$, DMF, Et_3N, N_2, 80-100 ^oC, 20-24 hrs	47
iv	Bimetallic nano catalyst, DMF, Et_3N, N_2, 80-100 ^oC, 20-24 hrs	58

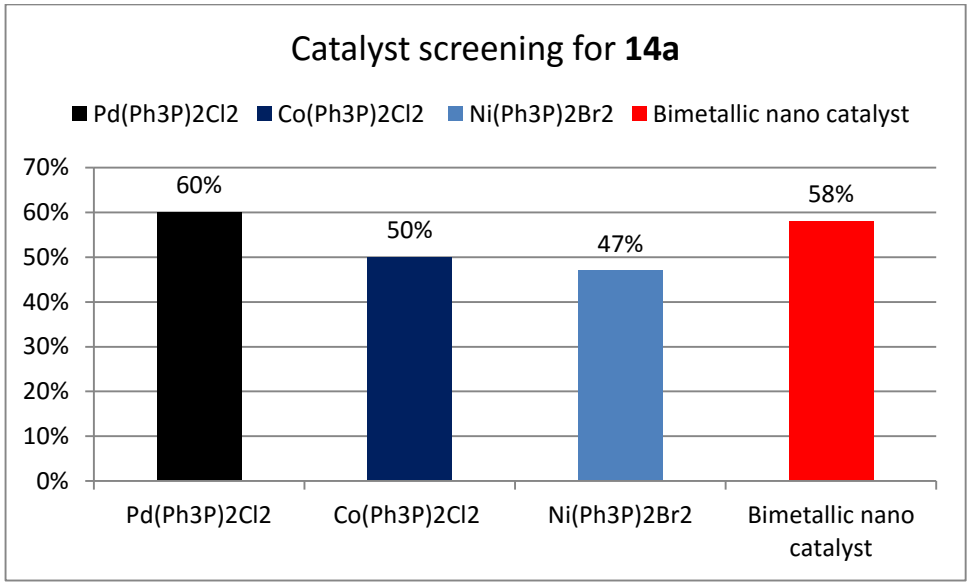
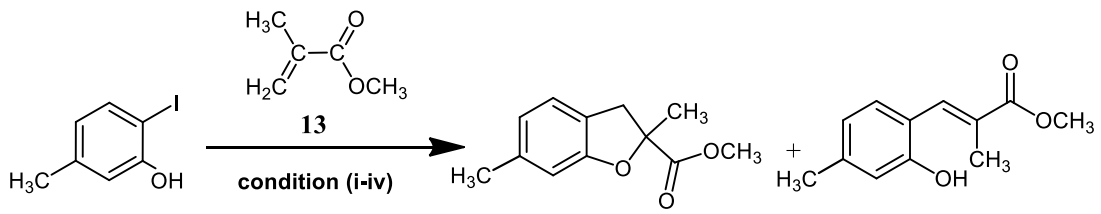


Fig. 4 Catalyst screening for synthesis **14a**

3.5.2 Catalyst screening of methyl 2,6-dimethyl-2, 3-dihydrobenzofuran-2-carboxylate 15a

Model Reaction



5 **15a** 50% **5b** 40%

Table-4: Catalyst screening for model reaction

	Condition	Yeild %
i	$Pd(Ph_3P)_2Cl_2$, DMF, Et_3N, N_2, 80-100 ^oC, 20-24 hrs	50
ii	$Co(Ph_3P)_2Cl_2$, DMF, Et_3N, N_2, 80-100 ^oC, 20-24 hrs	30
iii	$Ni(Ph_3P)_2Br_2$, DMF, Et_3N, N_2, 80-100 ^oC, 20-24 hrs	35
iv	Bimetallic nano catalyst, DMF, Et_3N, N_2, 80-100 ^oC, 20-24 hrs	45

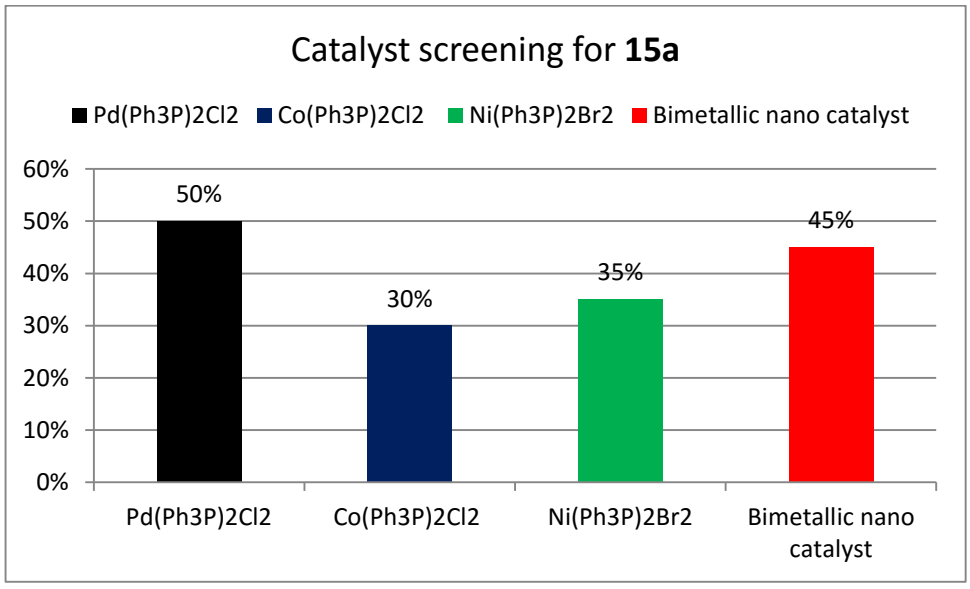
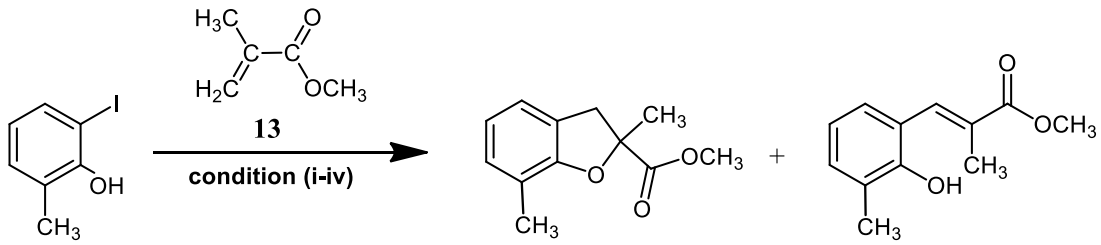


Fig. 5 Catalyst screening for synthesis **15a**

3.5.3 Catalyst screeningof methyl 2,7-dimethyl-2,3-dihydrobenzofuran-2-carboxylate 16a

Model Reaction



8 **16a** 70% **16b** 27%

Table-5: Catalyst screening for model reaction

	Condition	Yeild %
i	$Pd(Ph_3P)_2Cl_2$, DMF, Et_3N, N_2, 80-100 ^oC, 20-24 hrs	70
ii	$Co(Ph_3P)_2Cl_2$, DMF, Et_3N, N_2, 80-100 ^oC, 20-24 hrs	40
iii	$Ni(Ph_3P)_2Br_2$, DMF, Et_3N, N_2, 80-100 ^oC, 20-24 hrs	45
iv	Bimetallic nano catalyst, DMF, Et_3N, N_2, 80-100 ^oC, 20-24 hrs	60

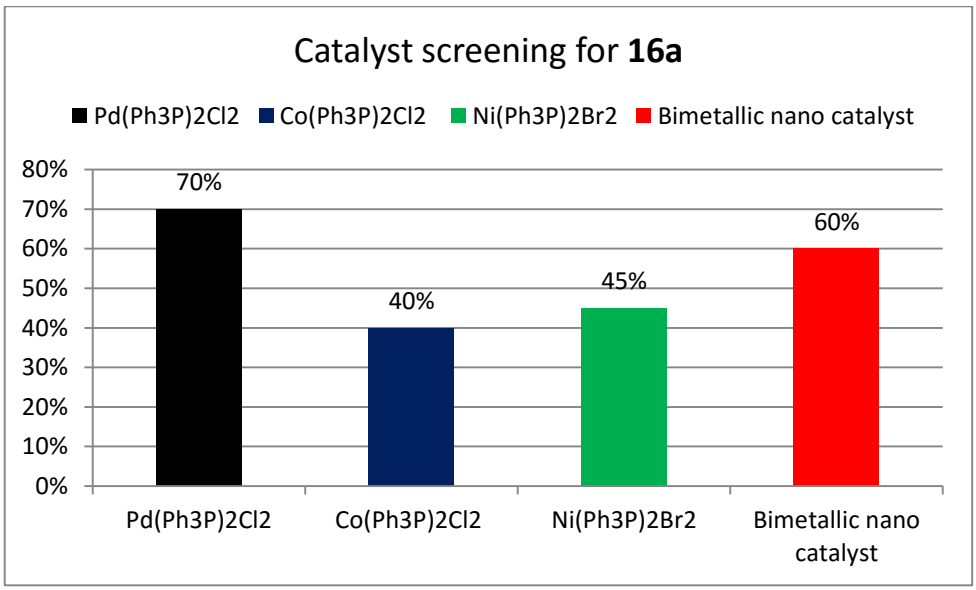
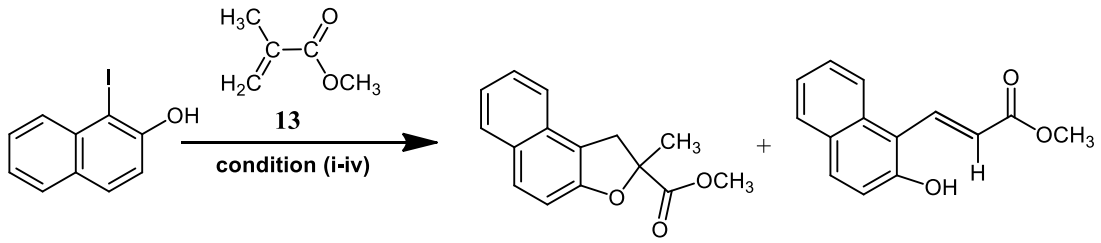


Fig. 6 Catalyst screening for synthesis **16a**

3.5.4 Catalyst screening of methyl 2-methyl-1, 2-dihydronaphtho [2, 1-b] furan-2-carboxylate 17a

Model Reaction



11 **17a** 50% **17b** 30%

Table-6: Catalyst screening for model reaction

	Condition	Yeild %
i	$Pd(Ph_3P)_2Cl_2$, DMF, Et_3N, N_2, 80-100 °C, 20-24 hrs	50
ii	$Co(Ph_3P)_2Cl_2$, DMF, Et_3N, N_2, 80-100 °C, 20-24 hrs	38
iii	$Ni(Ph_3P)_2Br_2$, DMF, Et_3N, N_2, 80-100 °C, 20-24 hrs	42
iv	Bimetallic nano catalyst, DMF, Et_3N, N_2, 80-100 °C, 20-24 hrs	43

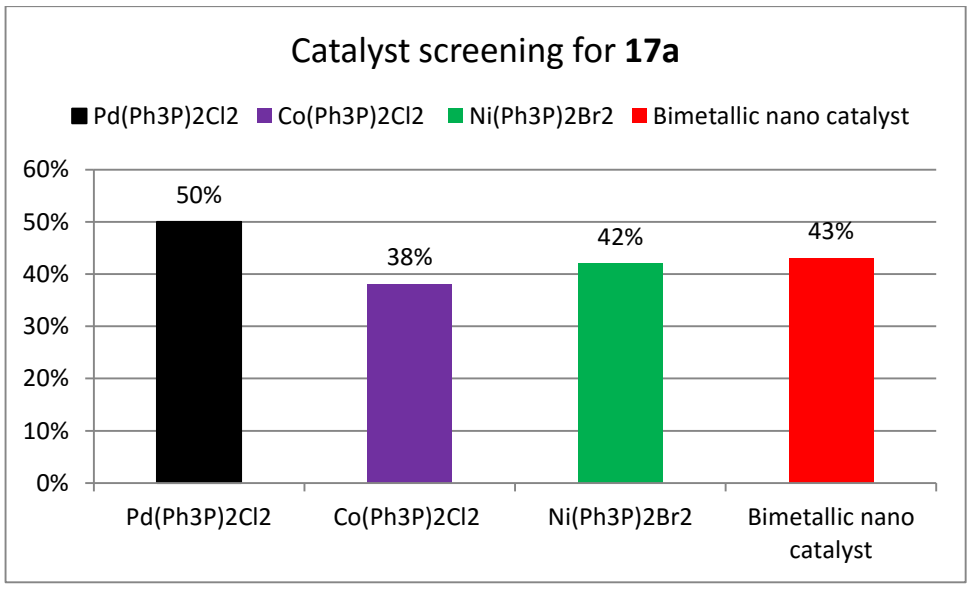


Fig. 7 Catalyst screening for synthesis **17a**

3.6Spectra14a-17a

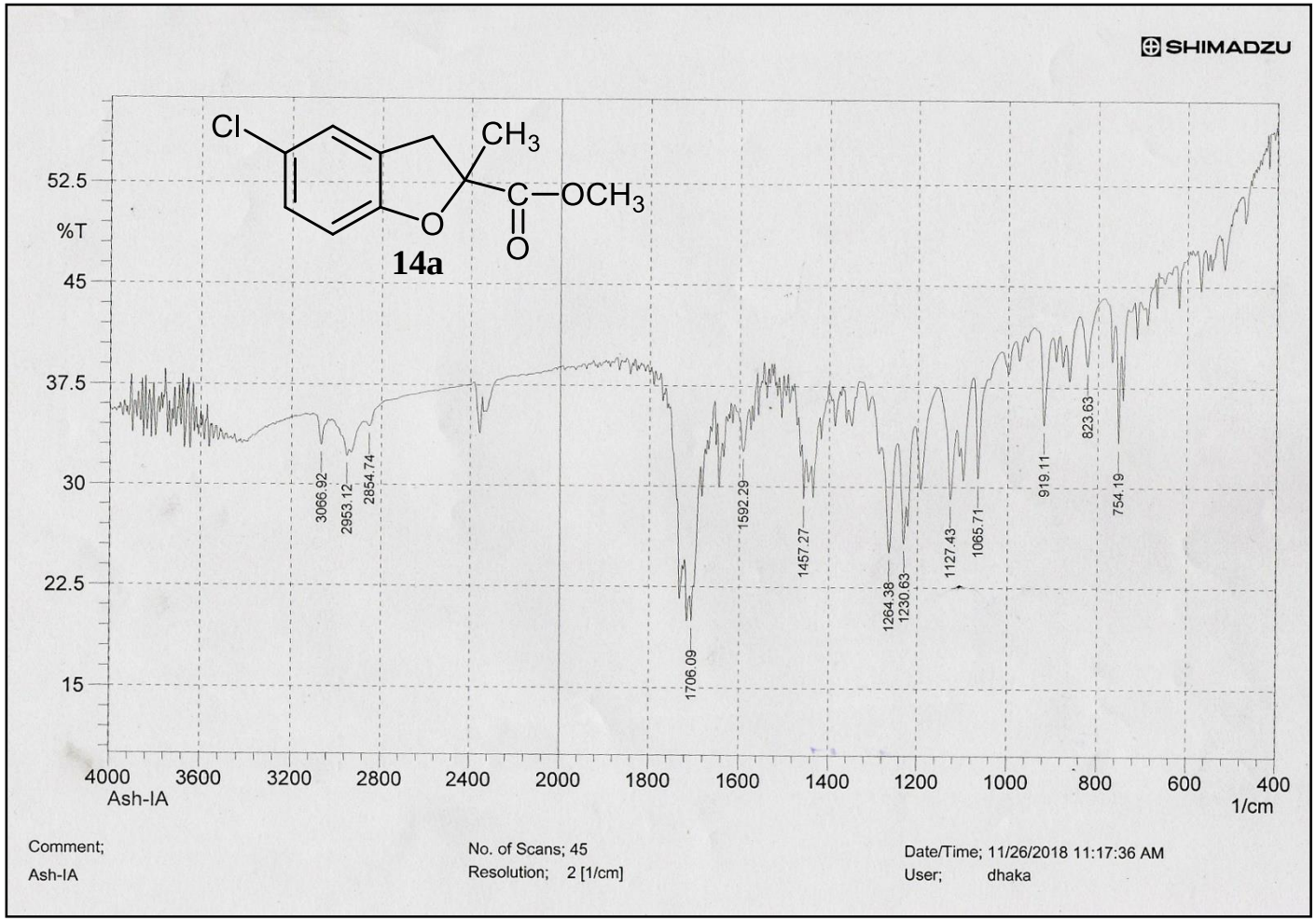


Fig. 8IR of Compound 14a

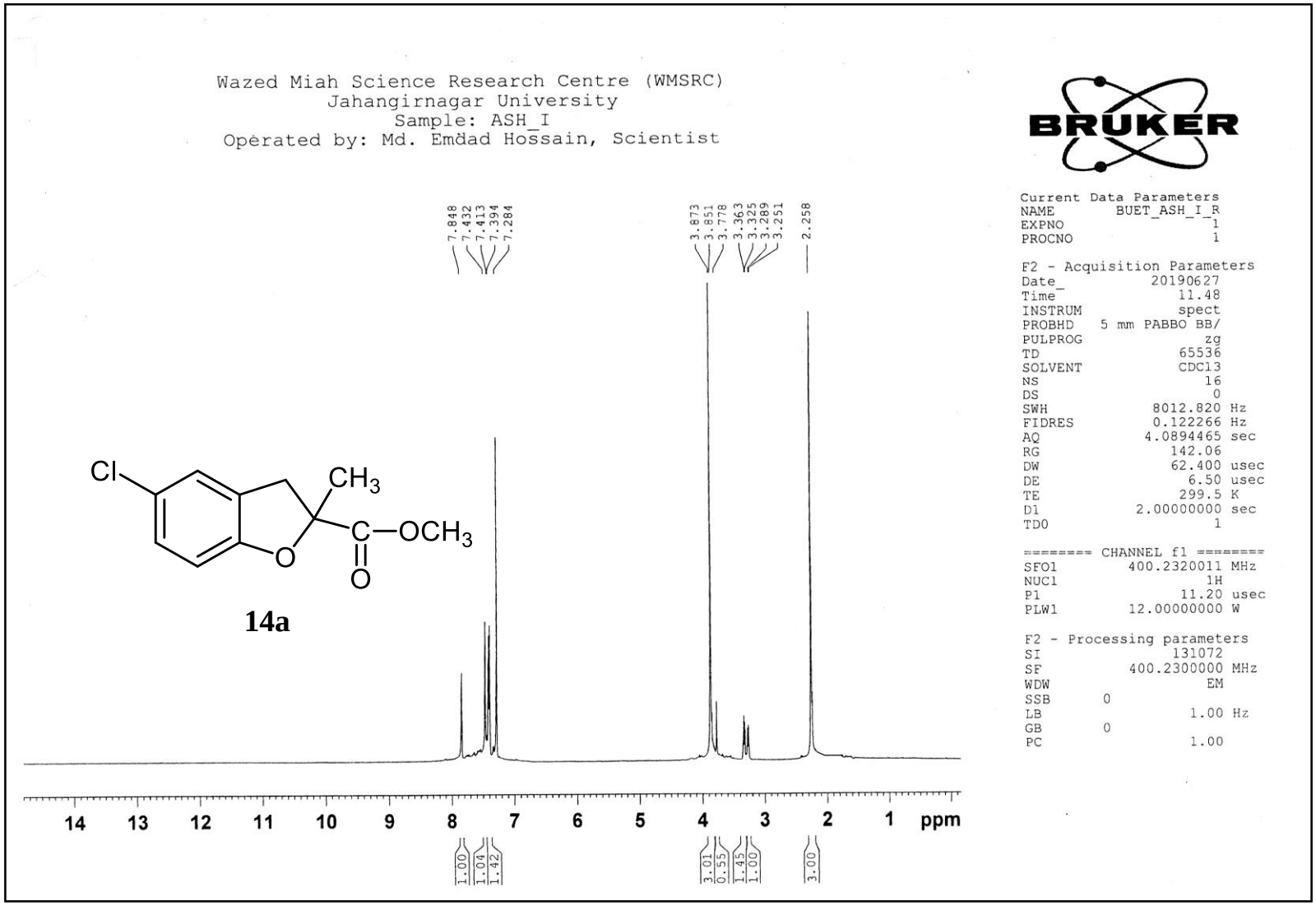


Fig. 9.a ^{1}H NMR of Compound 14a

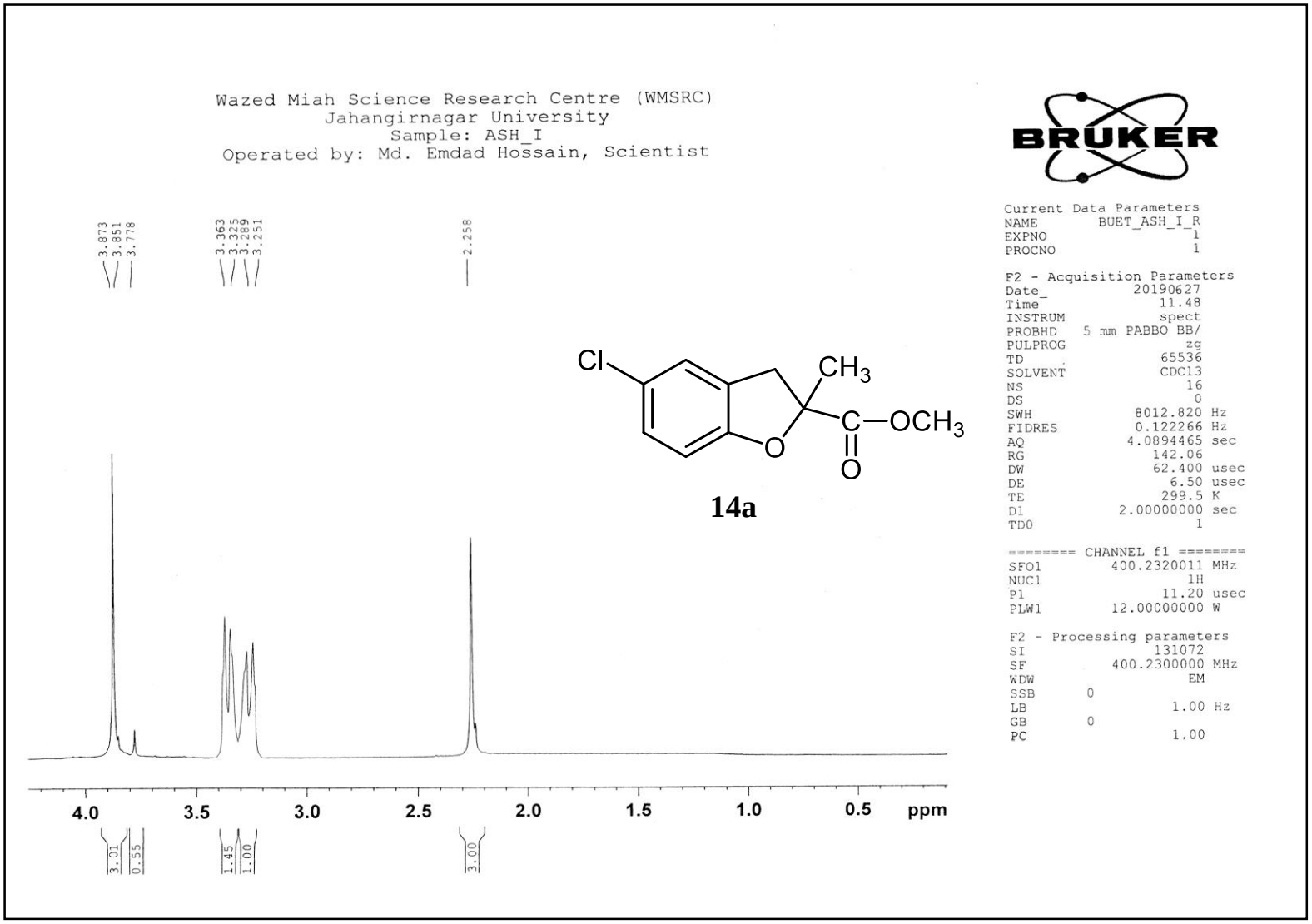


Fig. 9.b ^{1}H NMR of Compound 14a

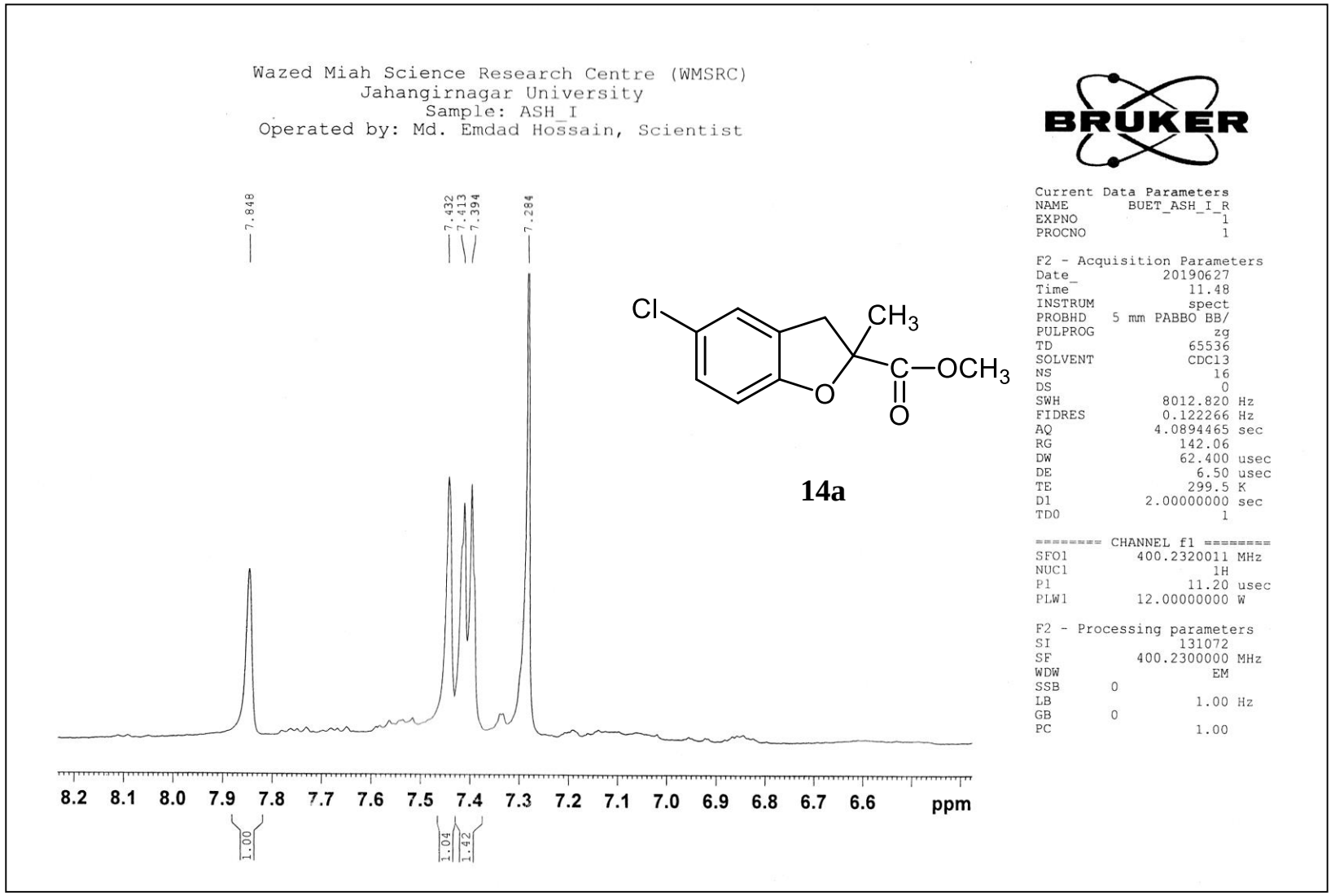


Fig. 9.c^{1}H NMR of Compound 14a

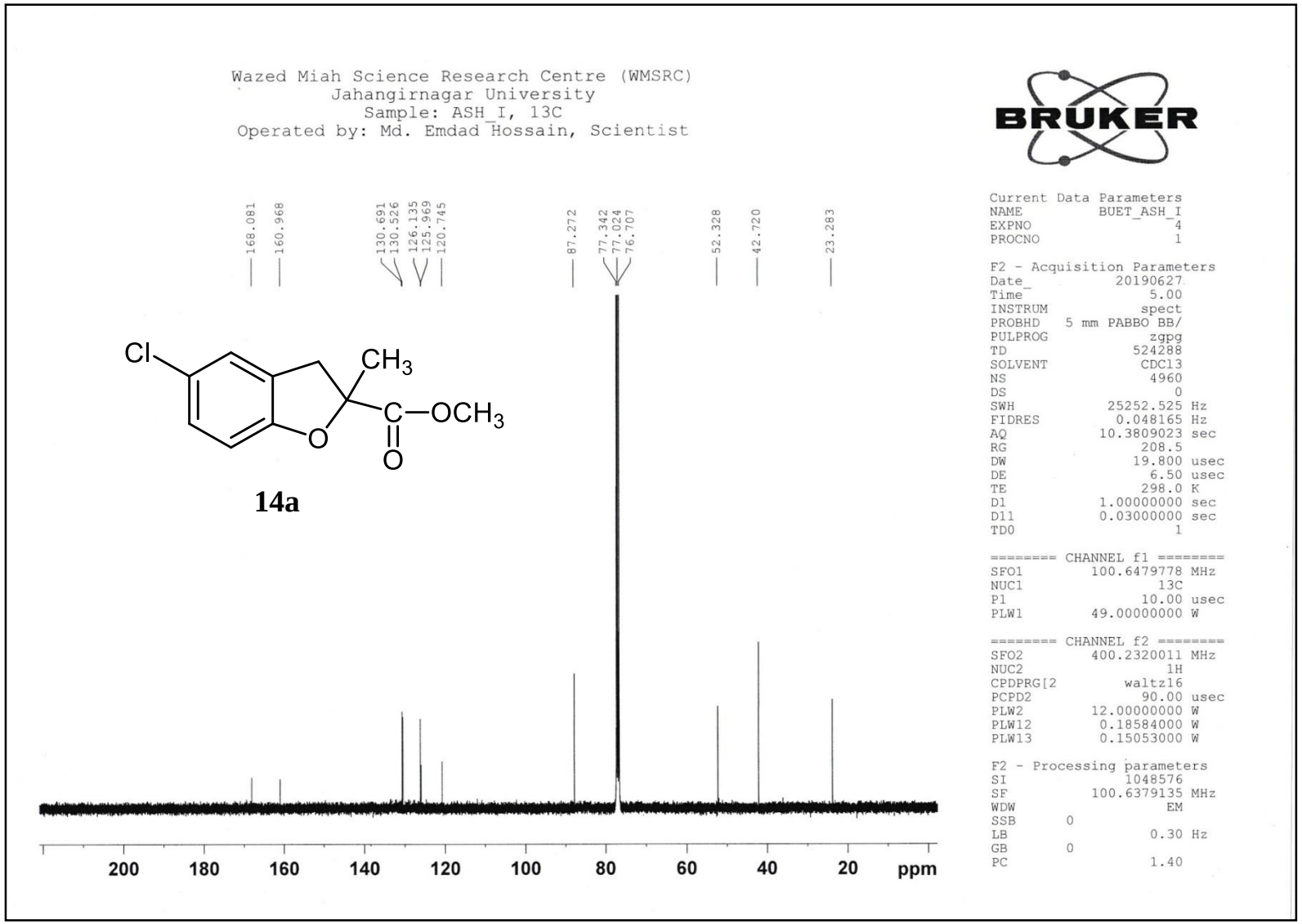


Fig. 10[13]C NMR of Compound 14a

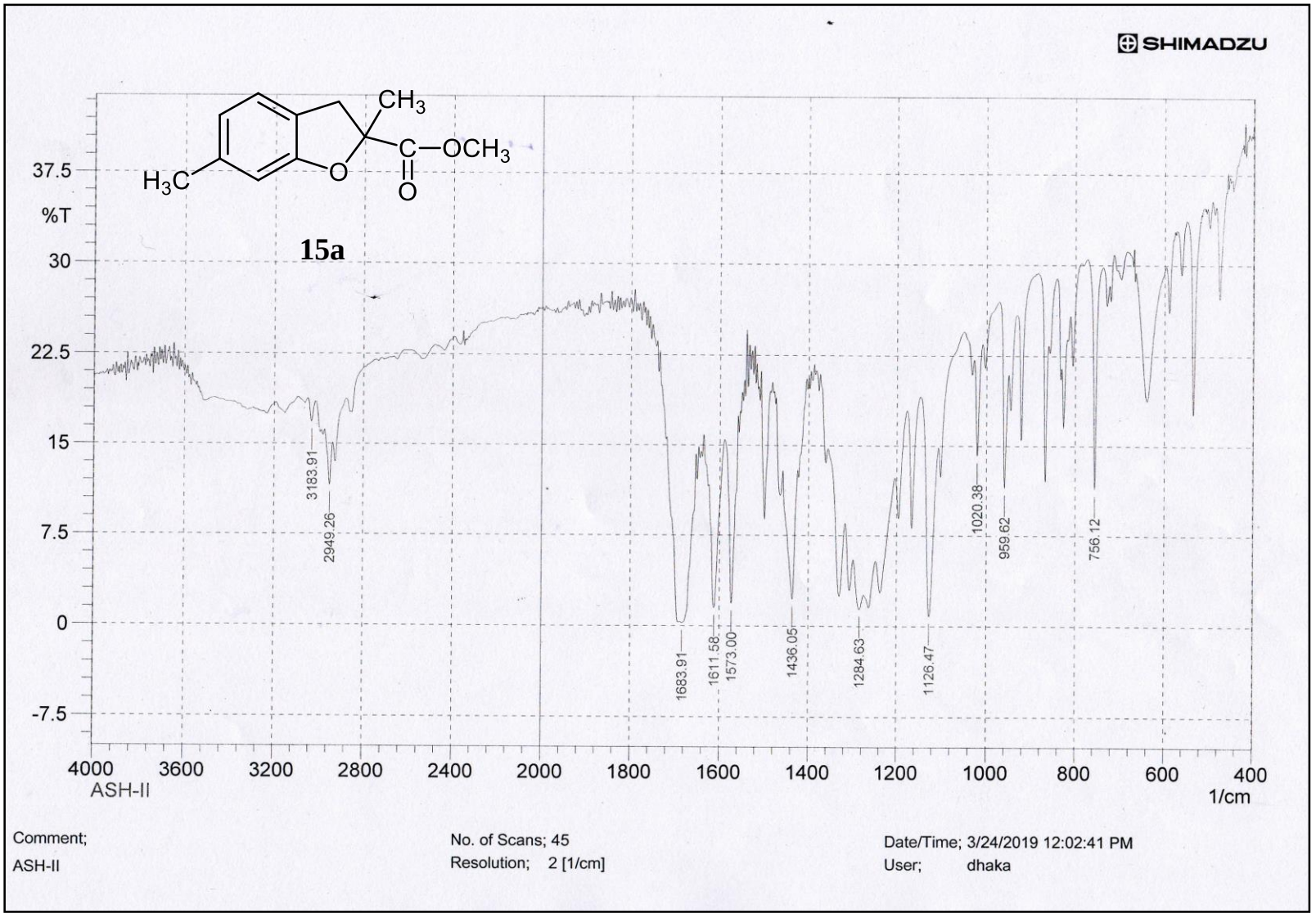
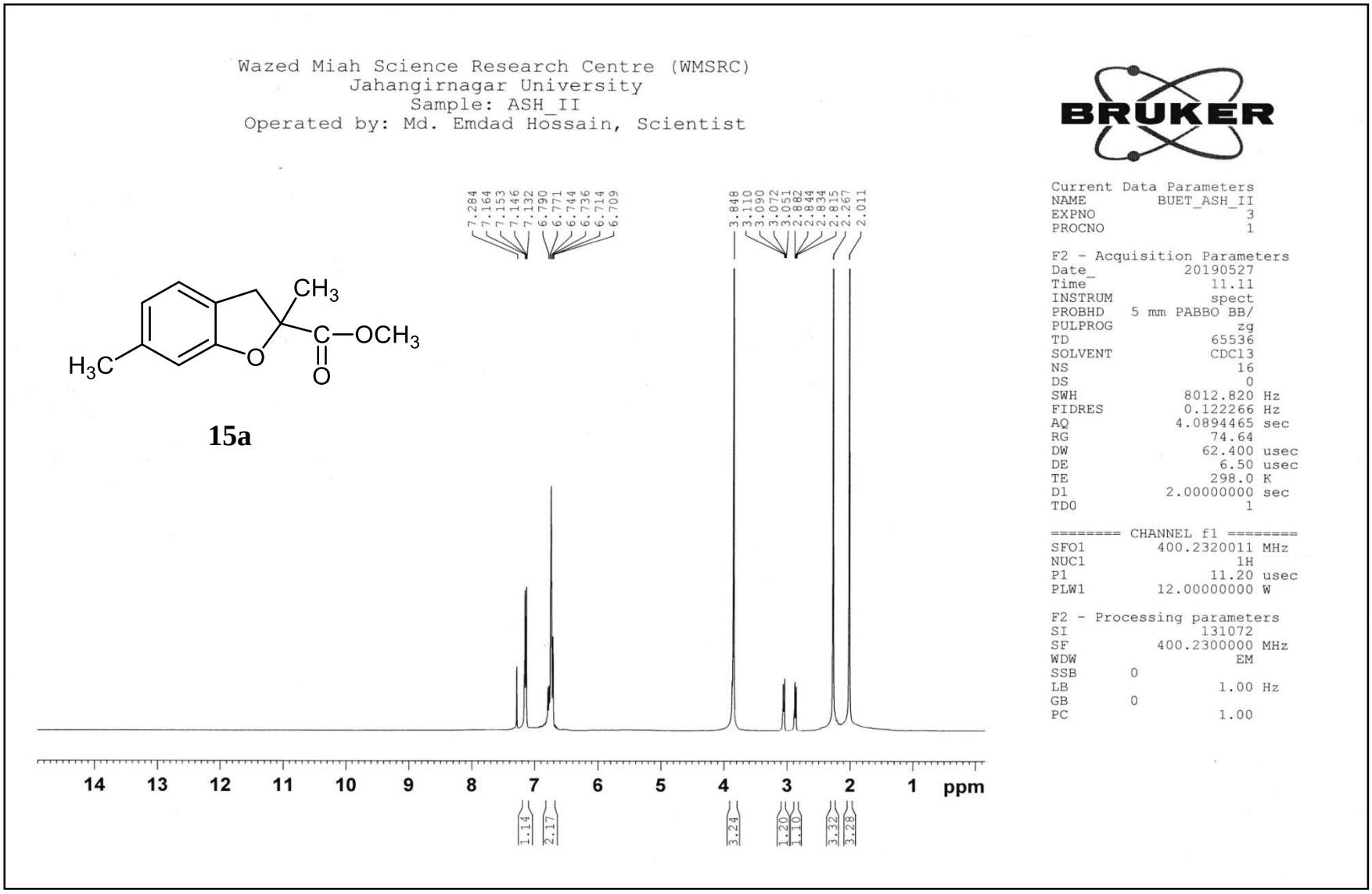


Fig. 11IR of Compound 15a



15a

Fig. 12.a ^{1}H NMR of Compound 15a

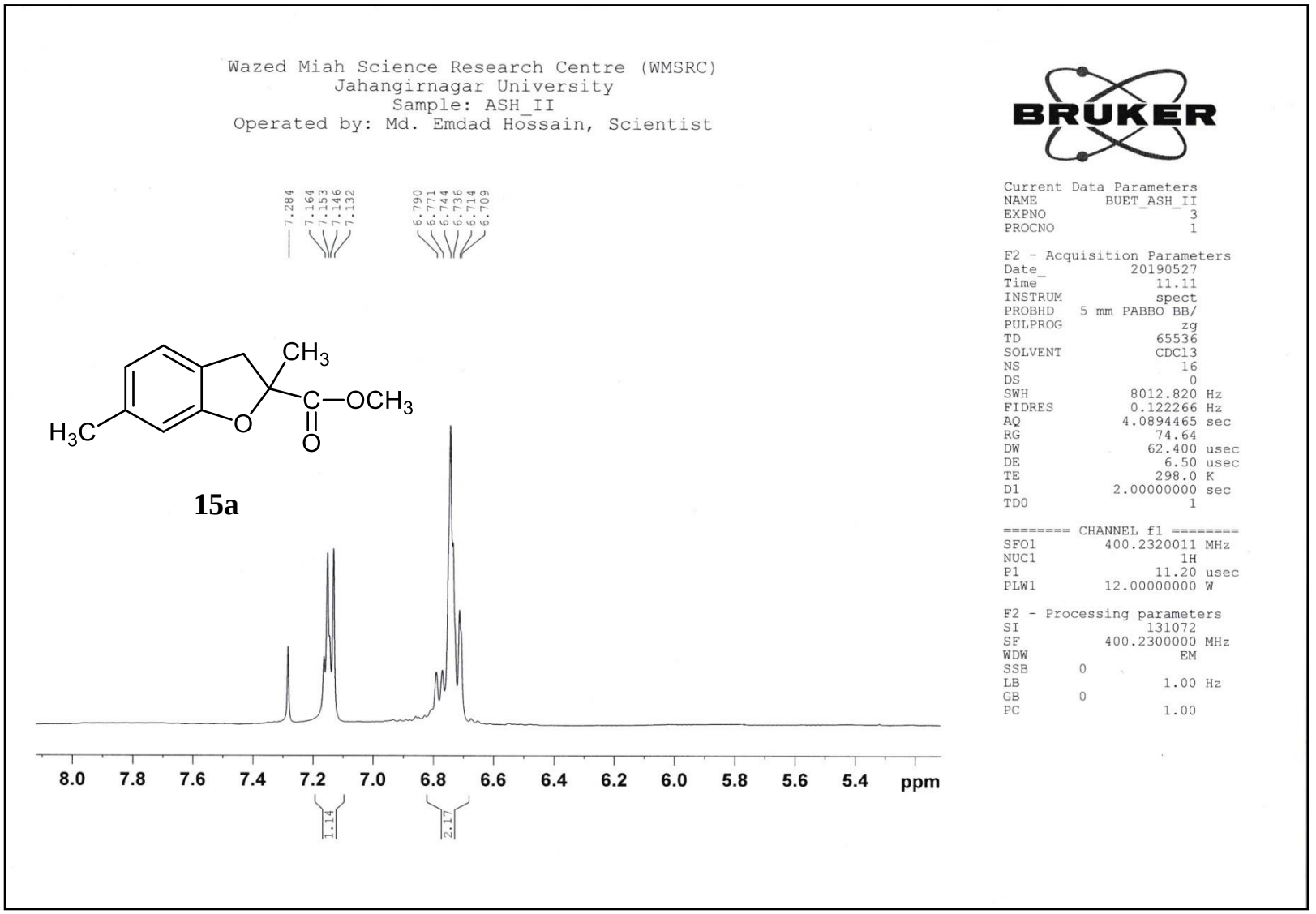


Fig. 12.b ^{1}H NMR of Compound 15a

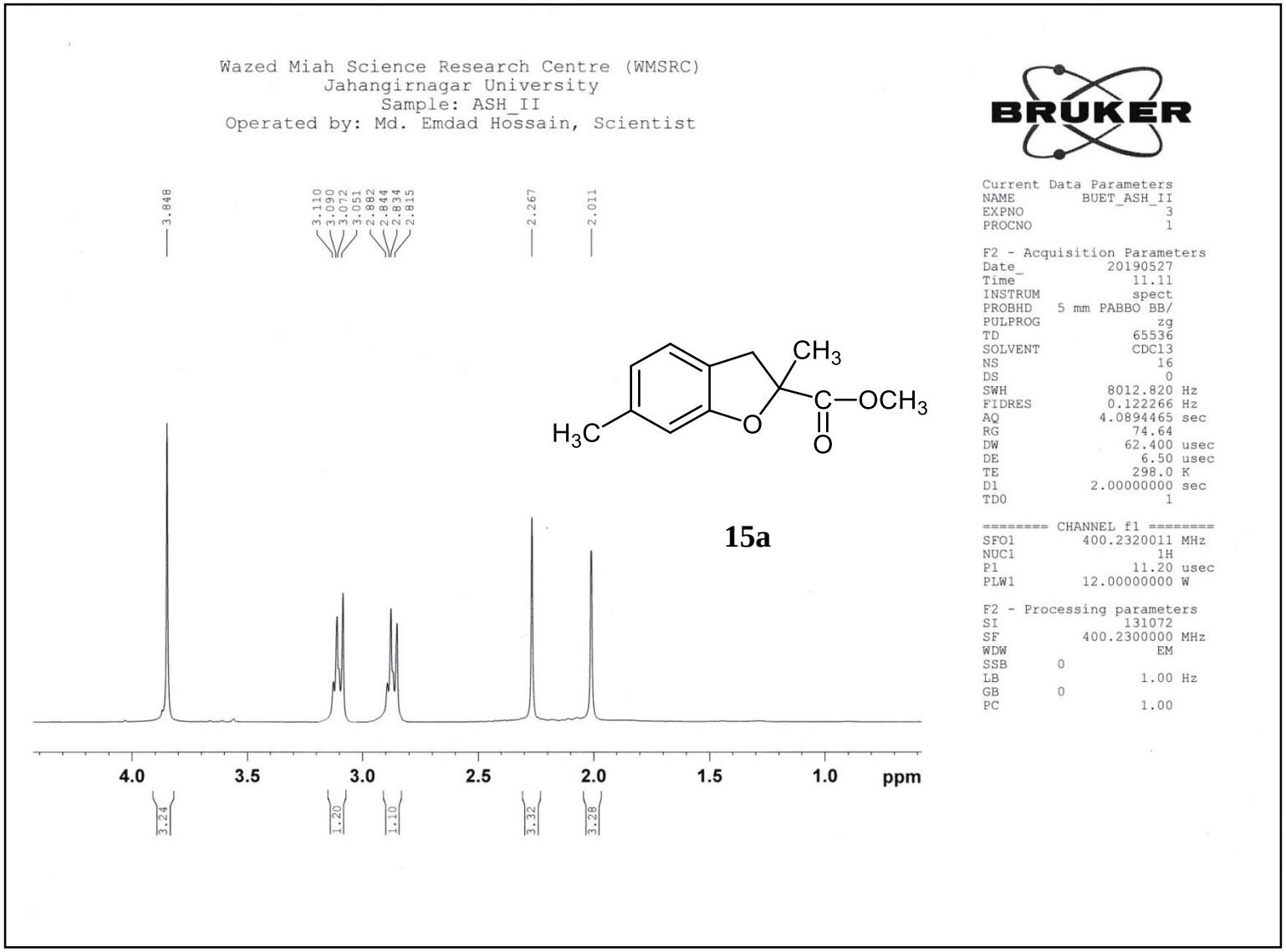


Fig. 12.c^{1}H NMR of Compound 15a

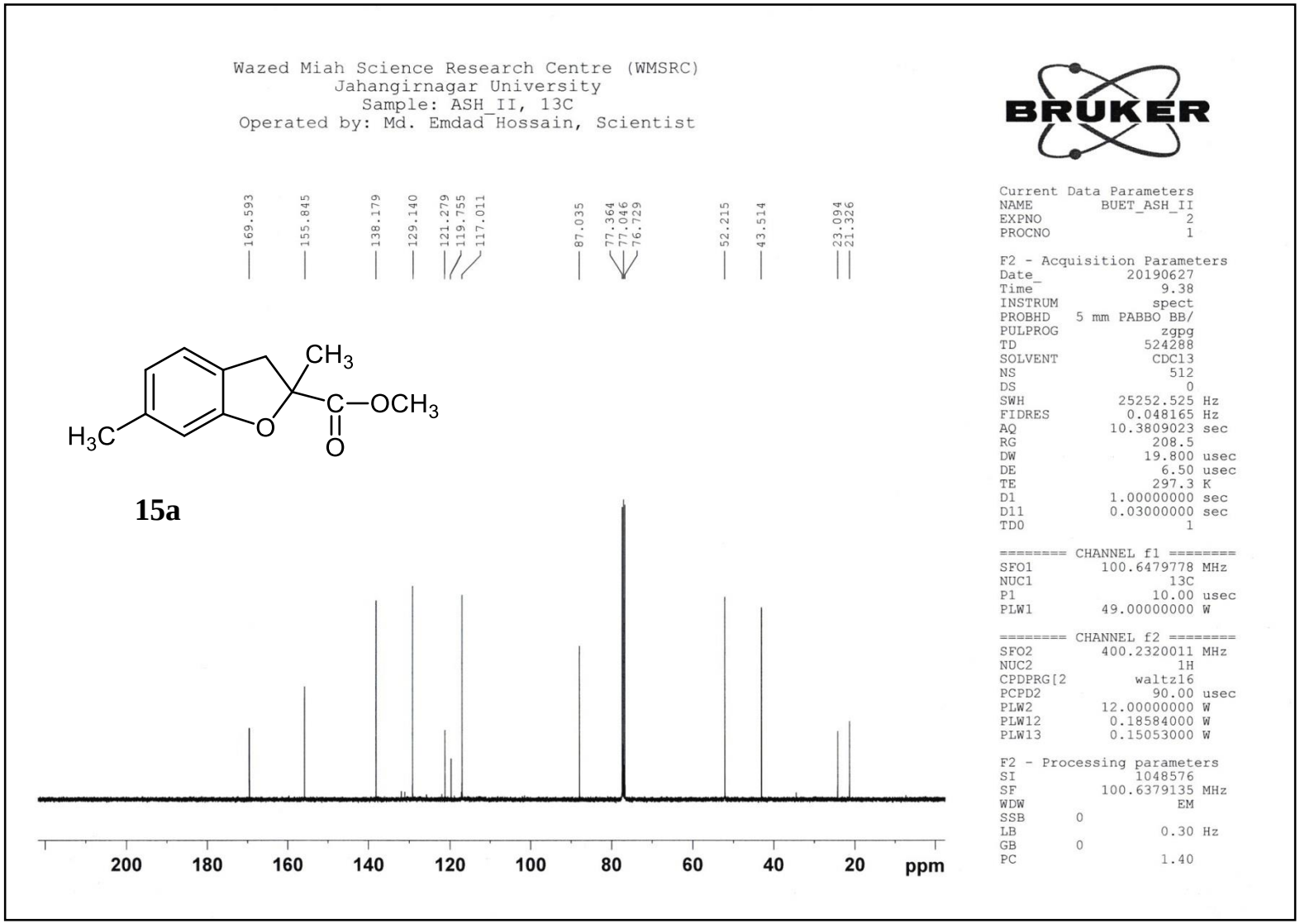


Fig. 13^{13}C NMR of Compound 15a

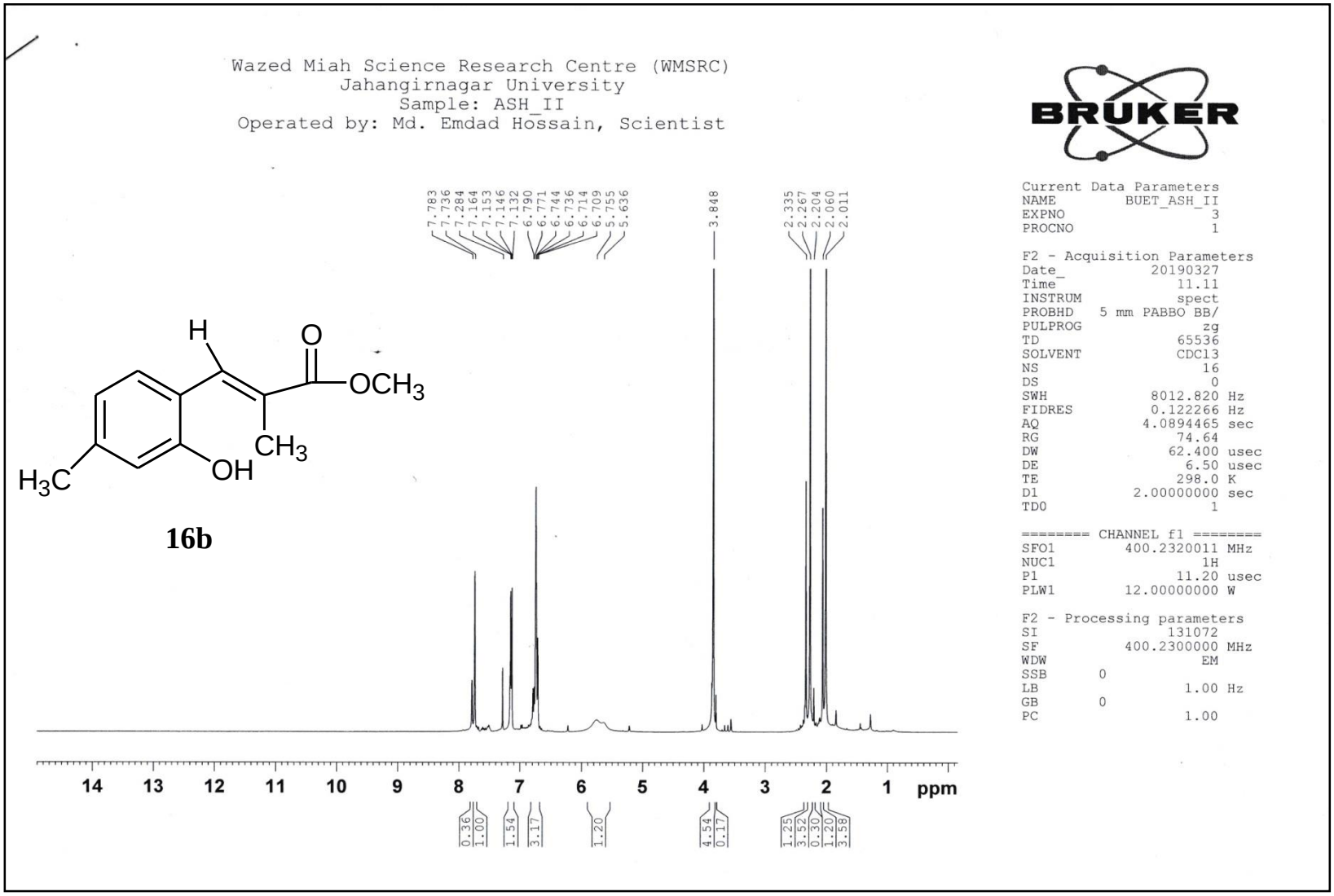


Fig. 14.a ^{1}H NMR of Compound 15b

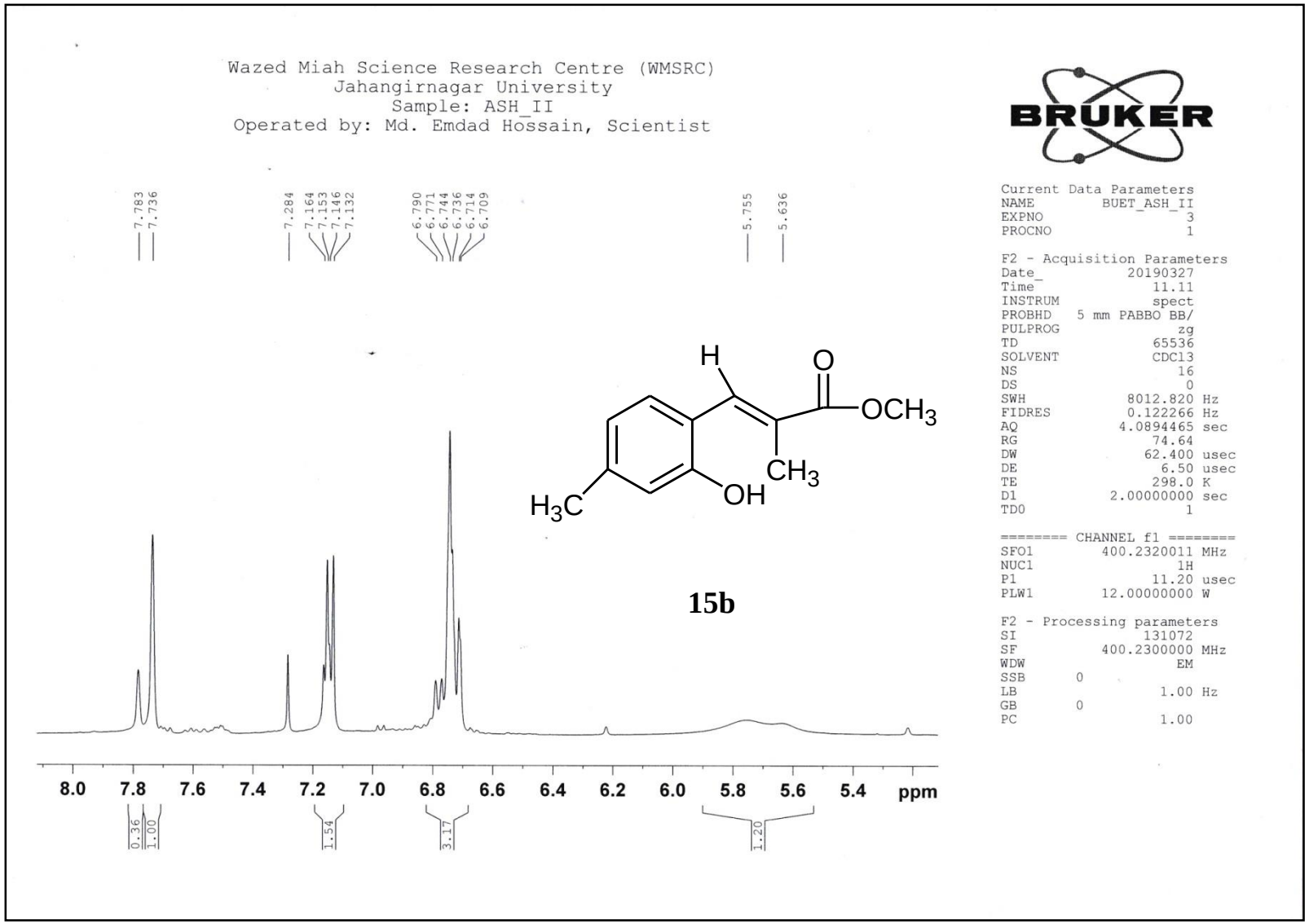


Fig. 14.b ^{1}H NMR of Compound 15b

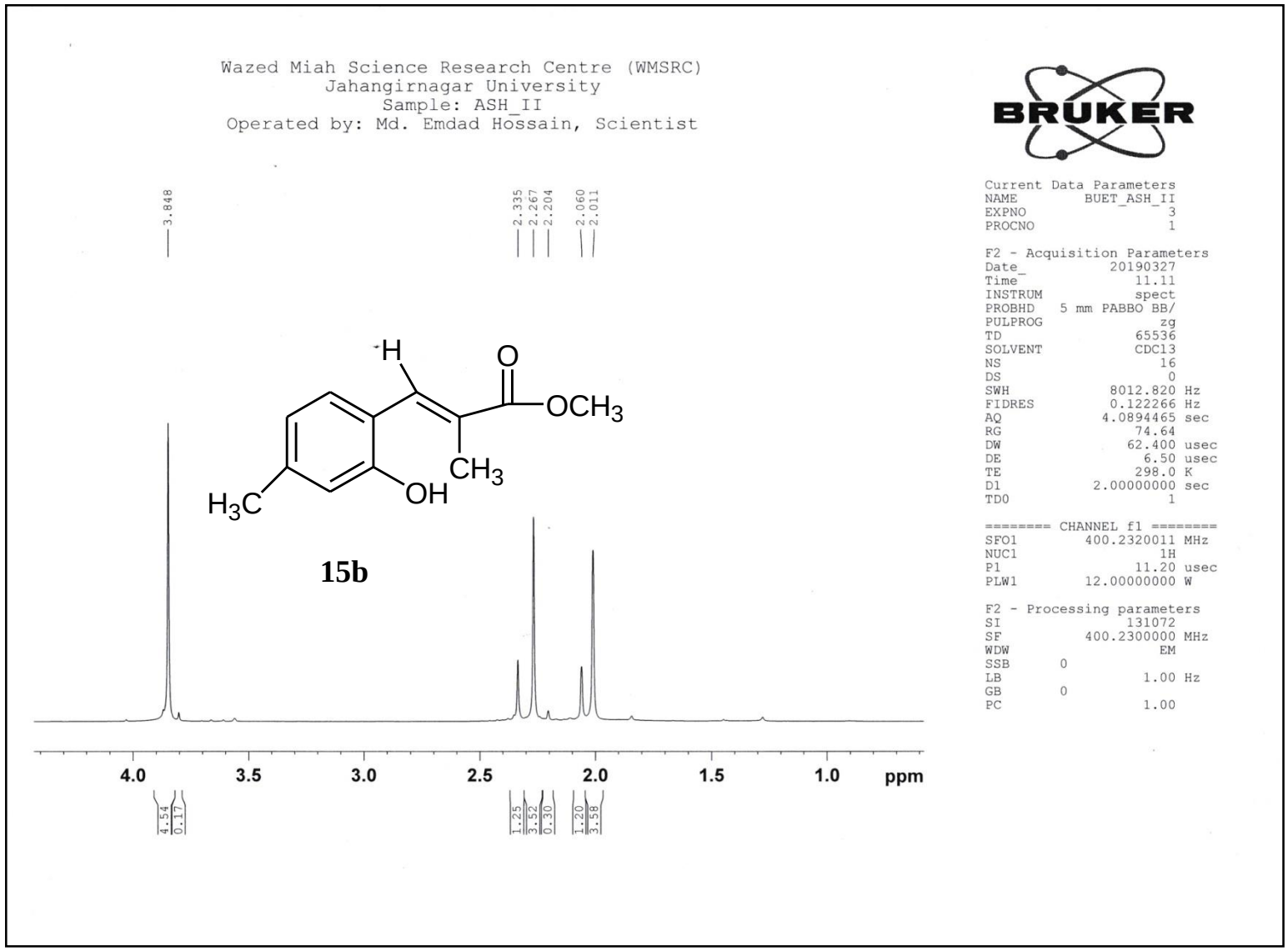


Fig. 14.c^{1}H NMR of Compound 15b

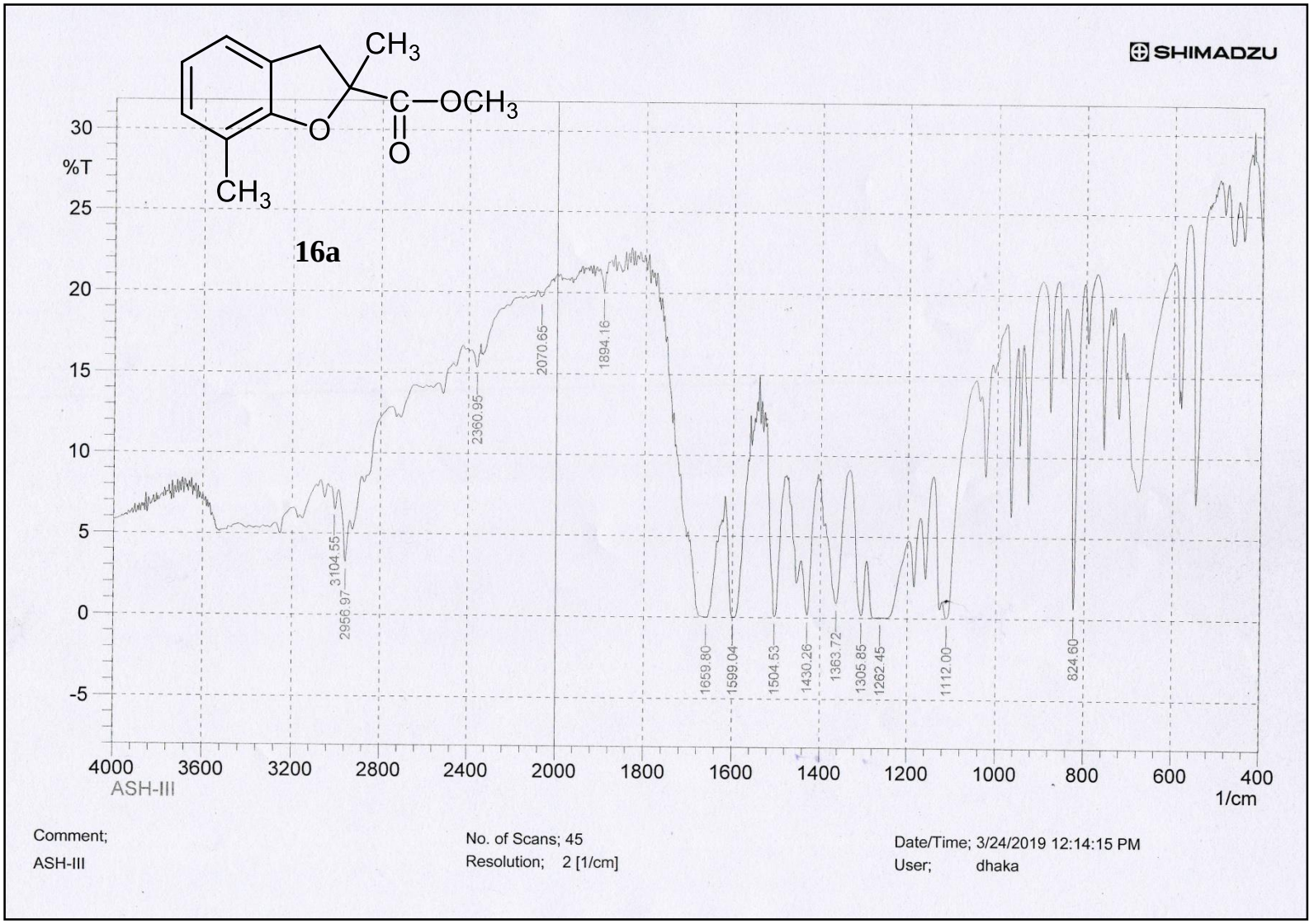


Fig. 15IR of Compound 16a

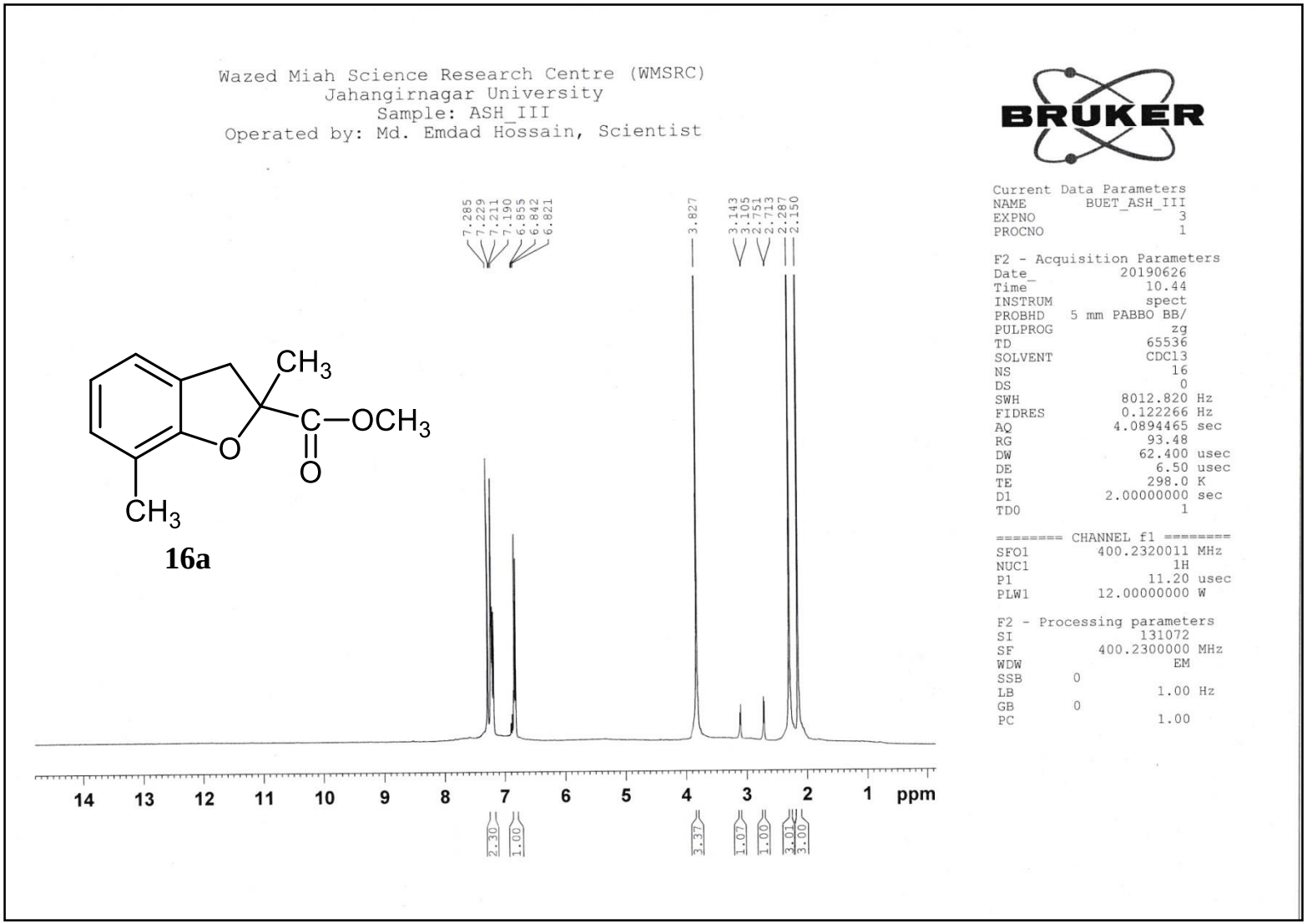


Fig. 16.a ^{1}H NMR of Compound 16a

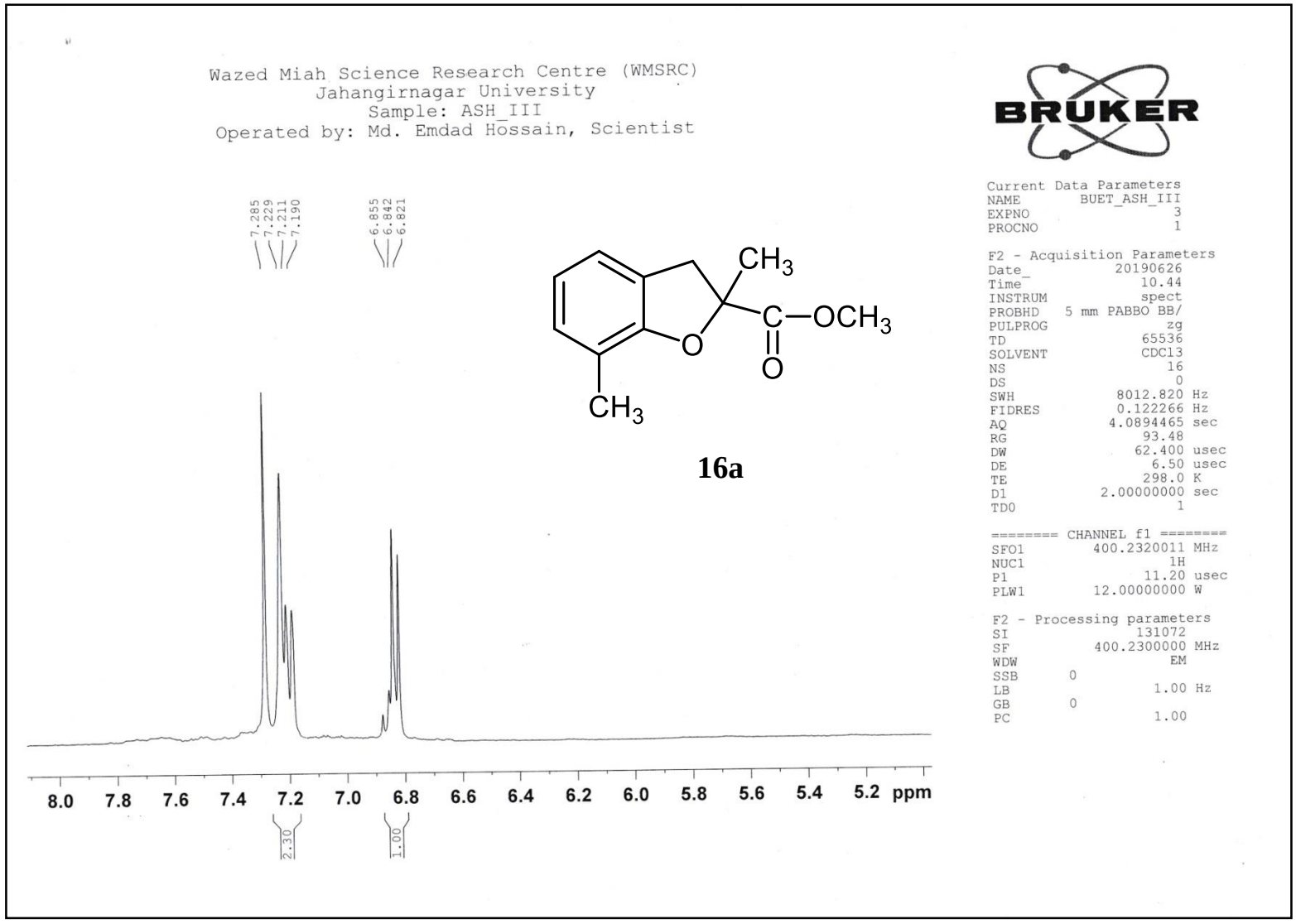


Fig. 16.b ^{1}H NMR of Compound 16a

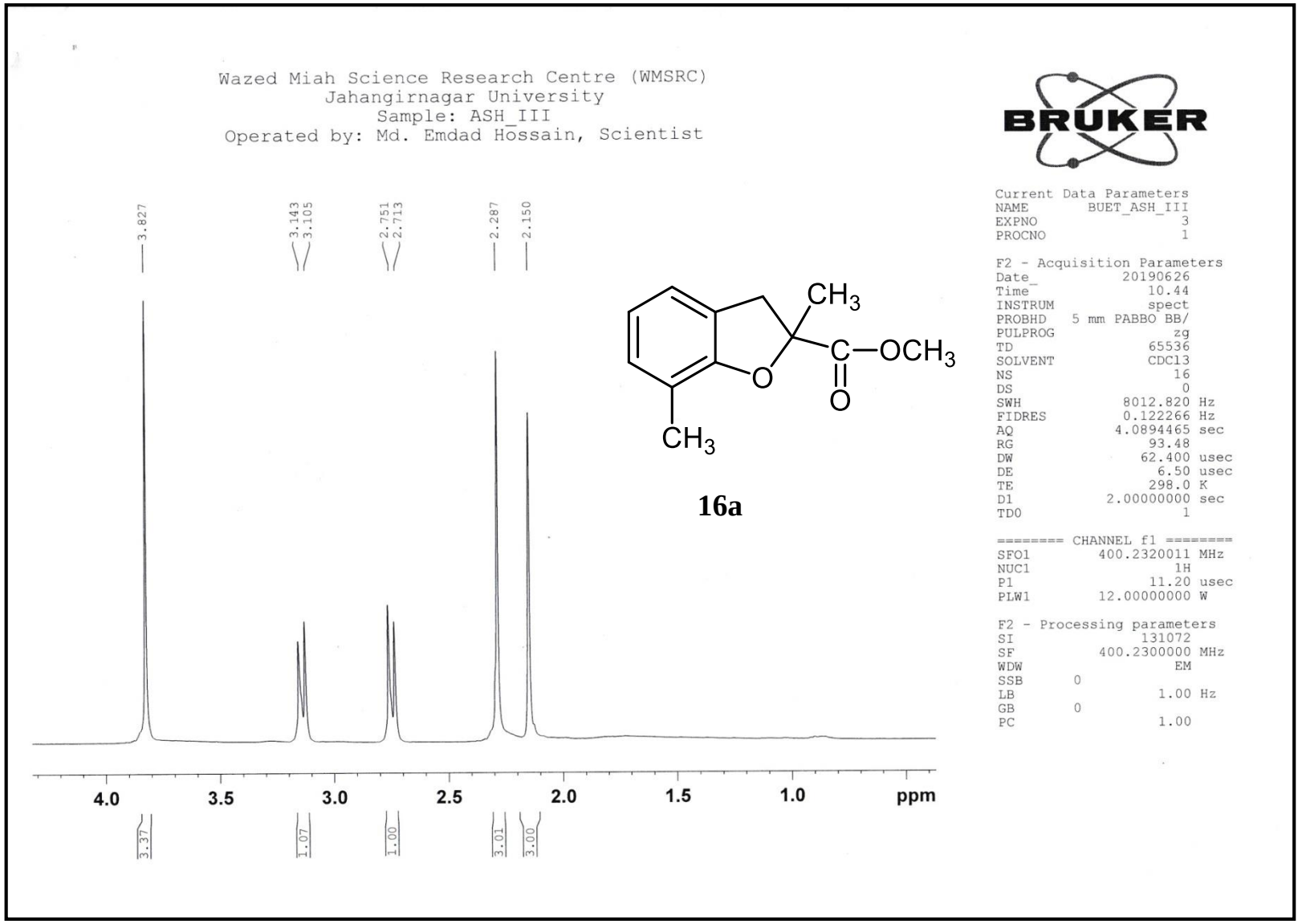


Fig. 16.c^{1}H NMR of Compound 16a

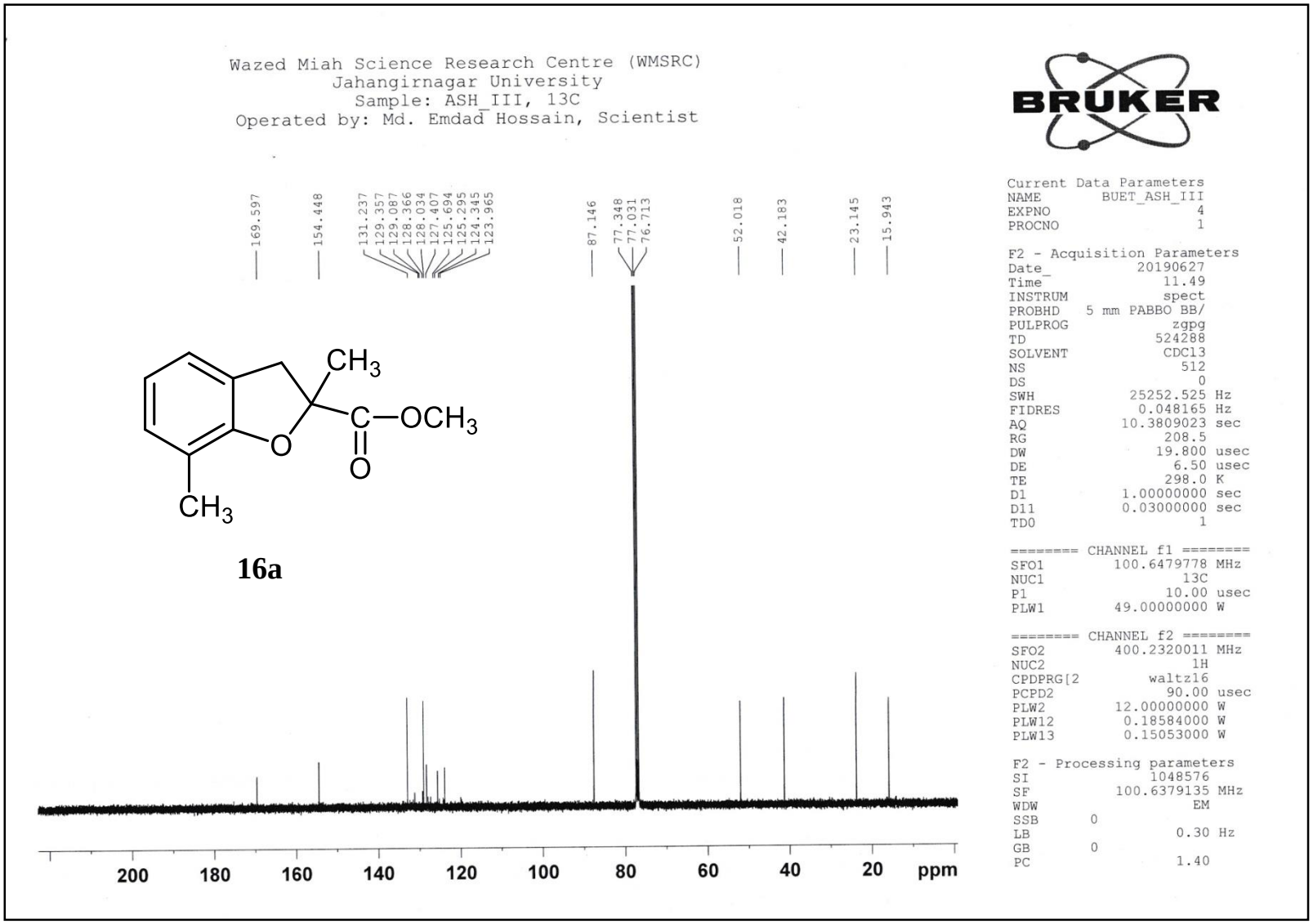


Fig. 17 ^{13}C NMR of Compound 16a

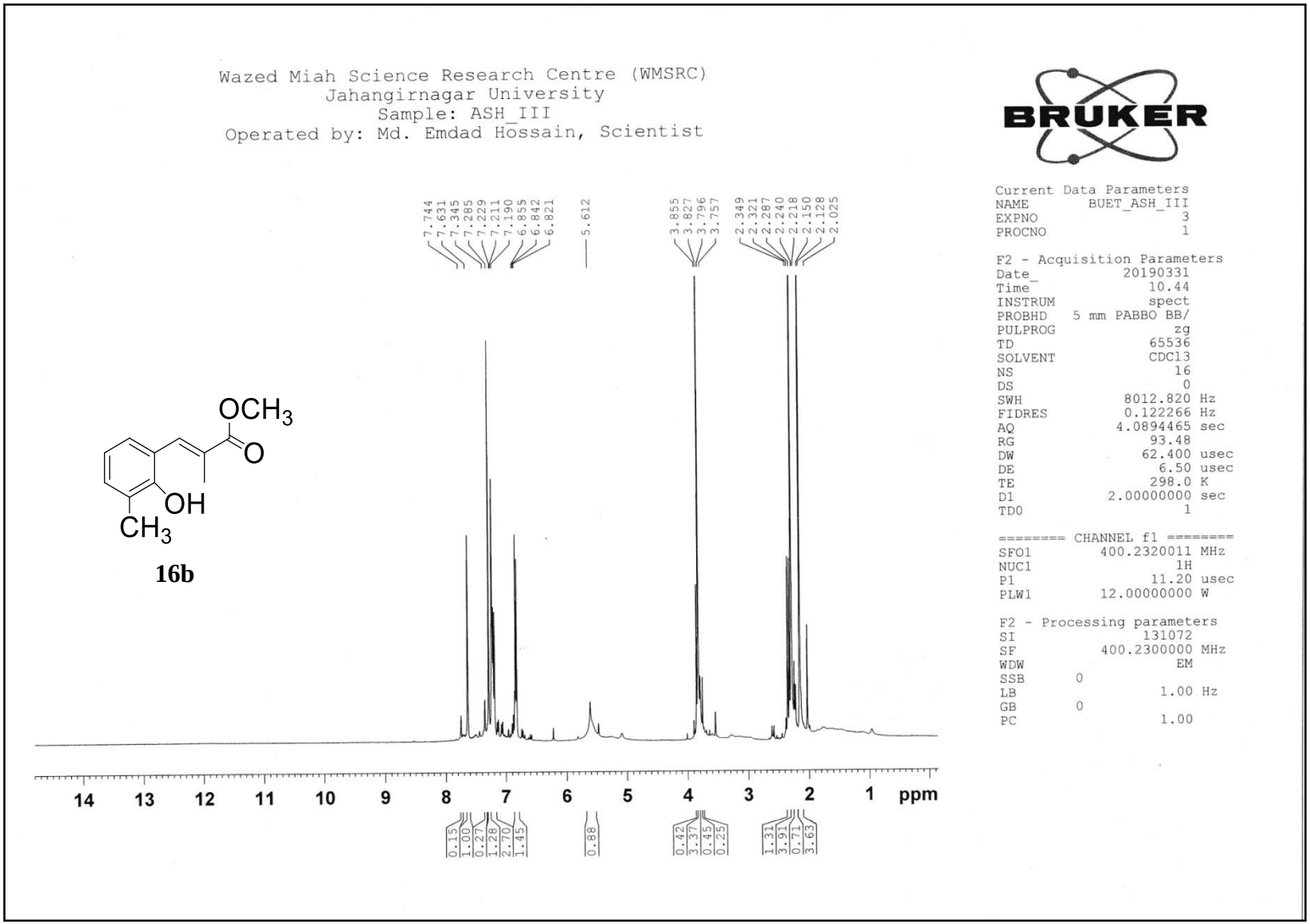


Fig. 18.a ^{1}H NMR of Compound 16b

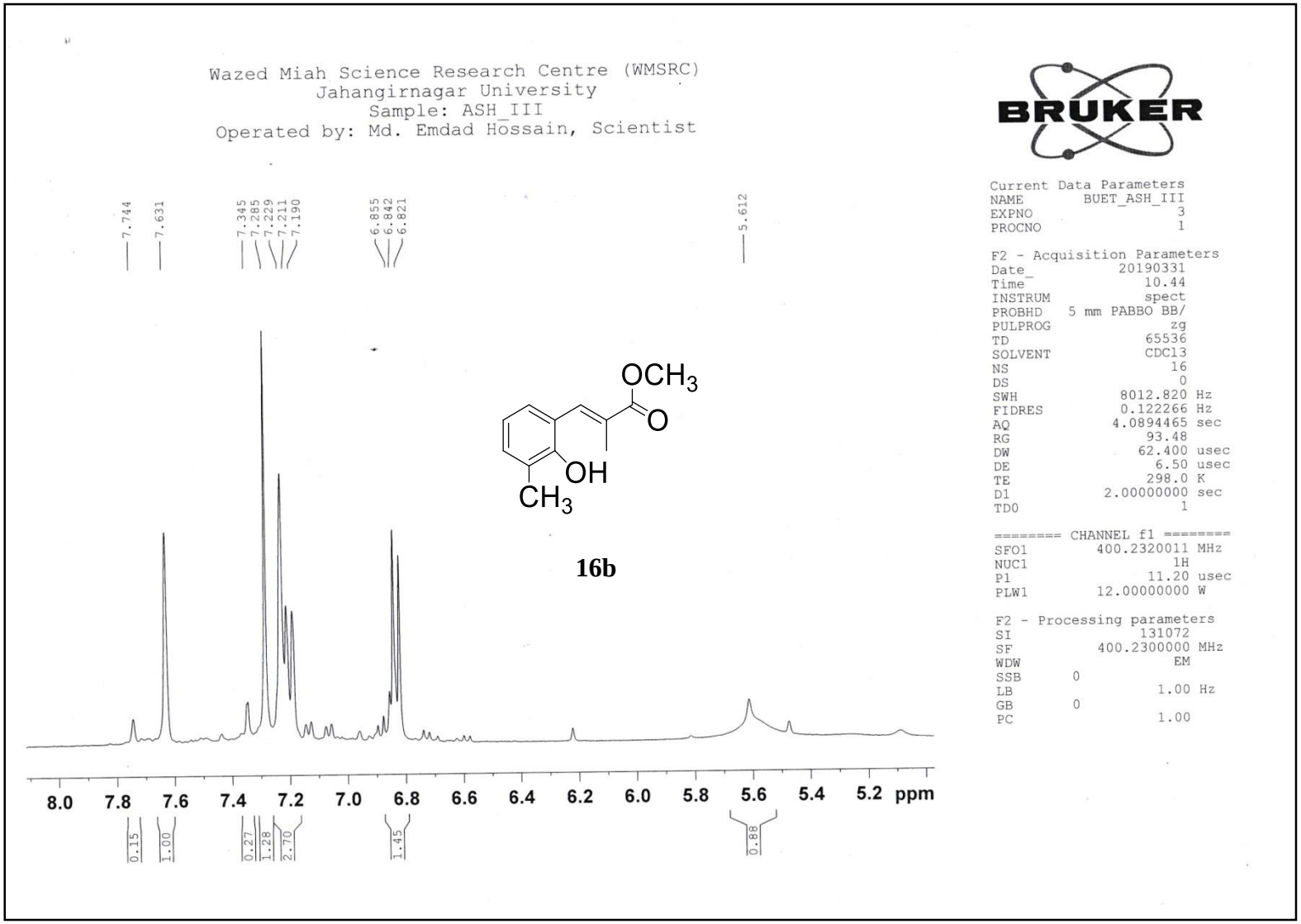


Fig. 18.b ^{1}H NMR of Compound 16b

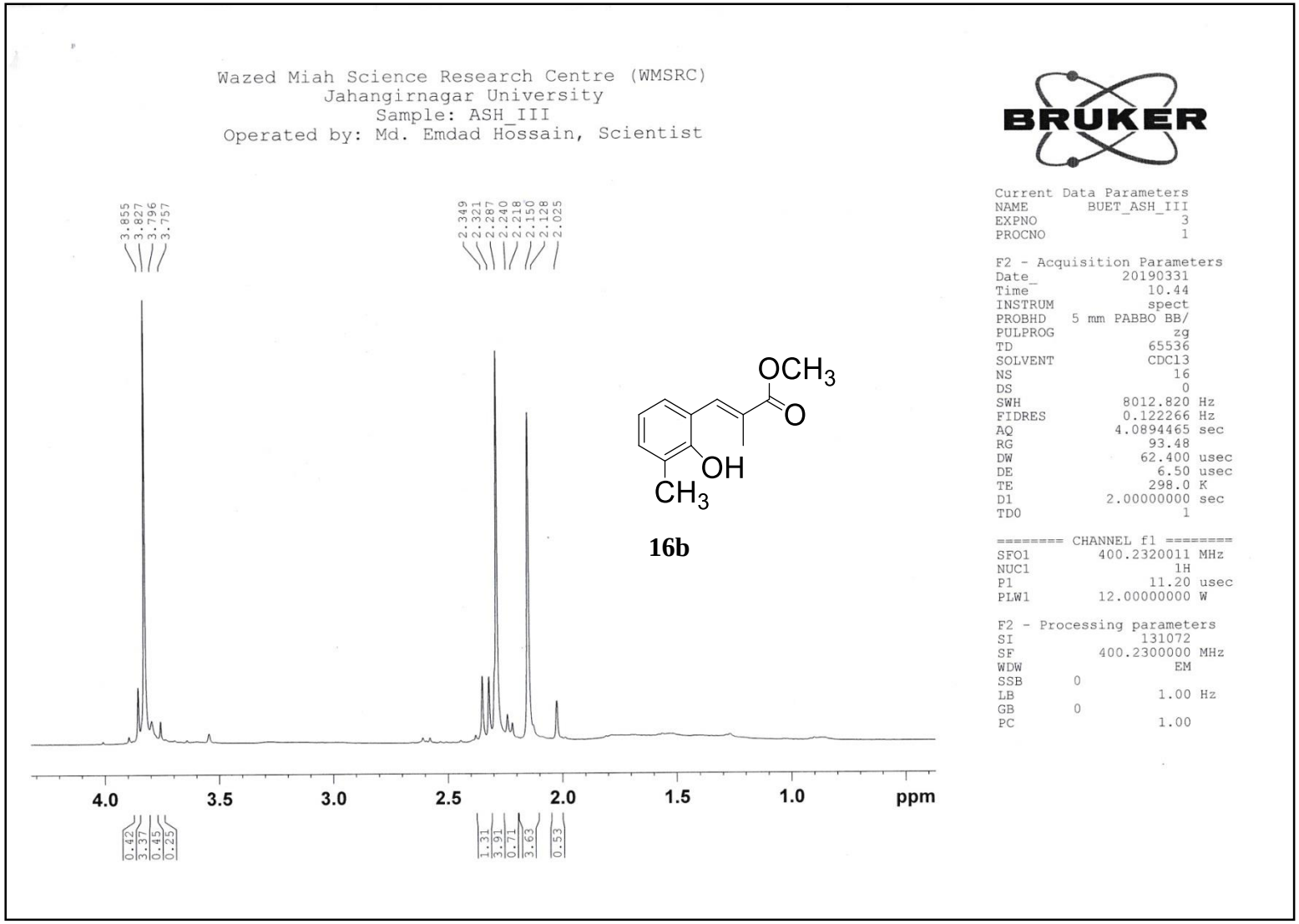


Fig. 18.c^{1}H NMR of Compound 16b

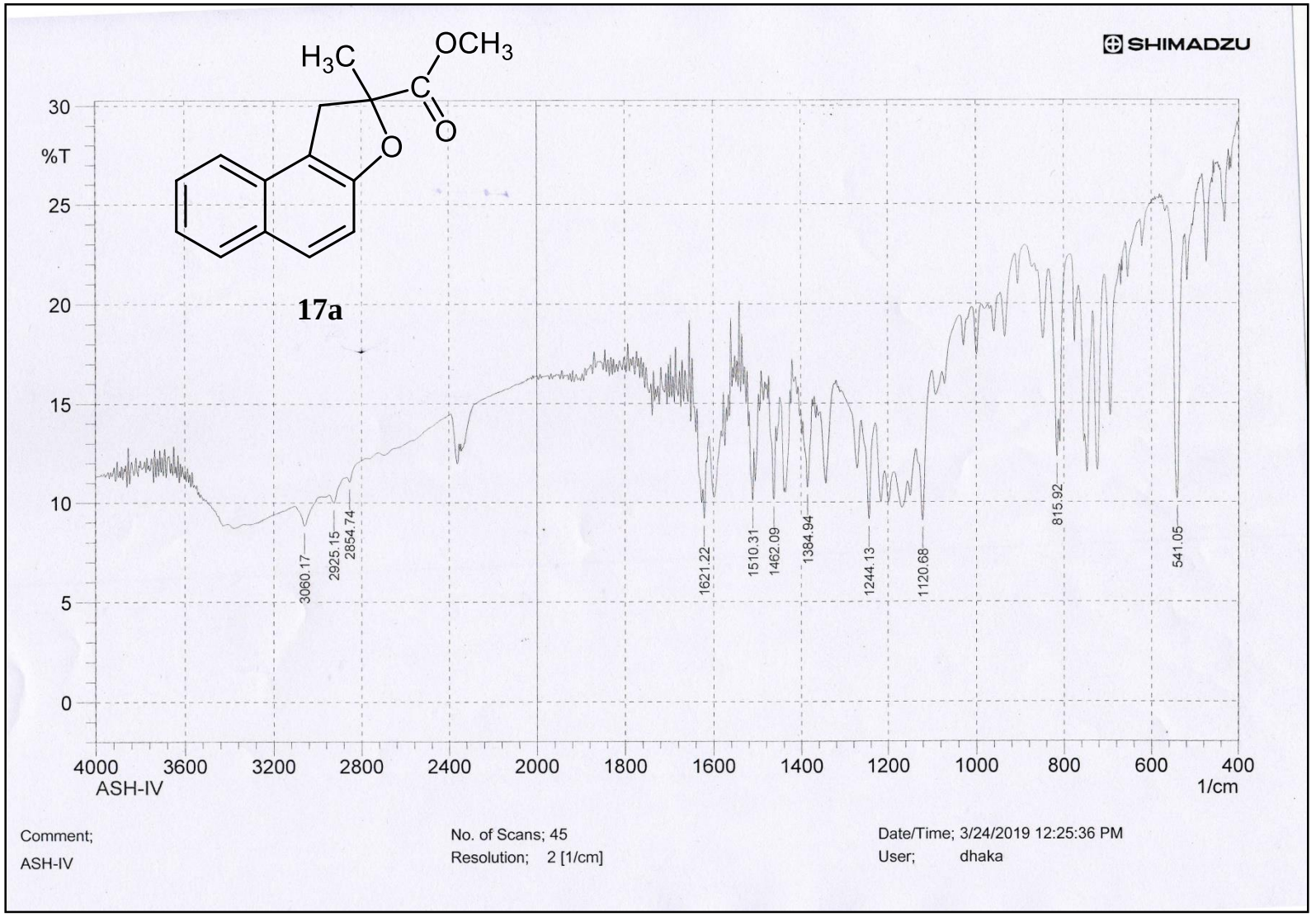


Fig. 19IR of Compound 17a

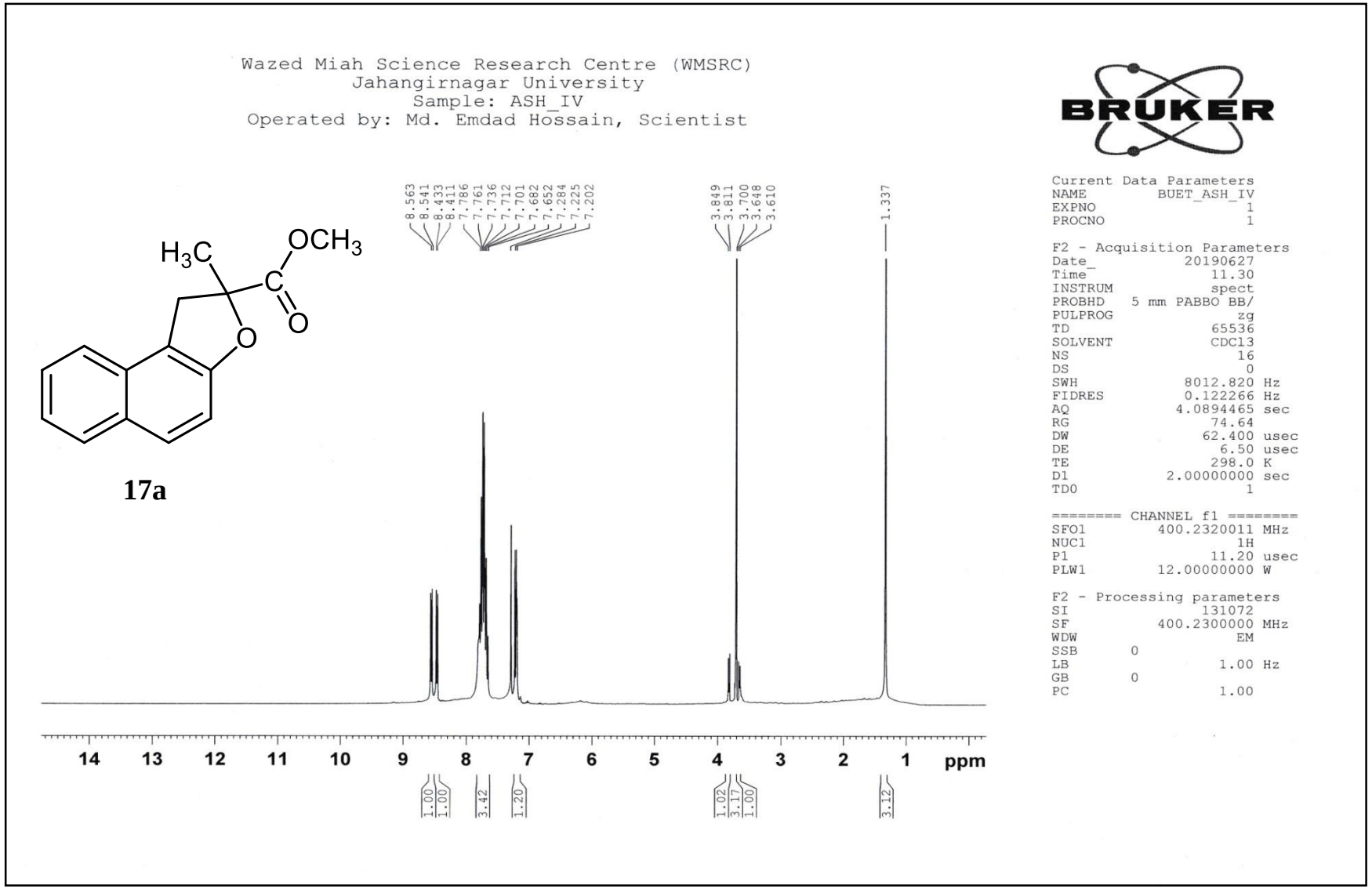


Fig. 20.a ^{1}H NMR of Compound 17a

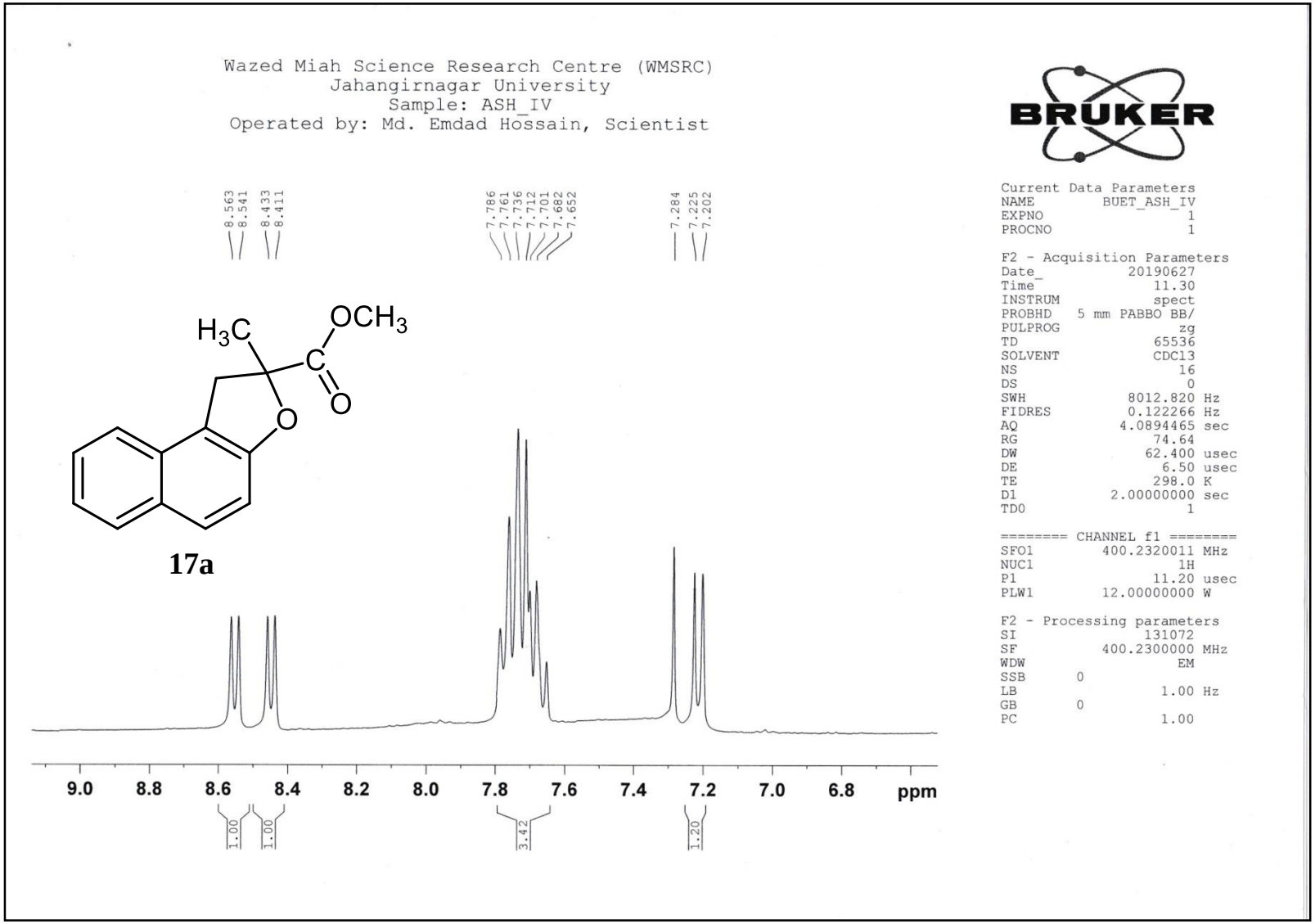


Fig. 20.b ^{1}H NMR of Compound 17a

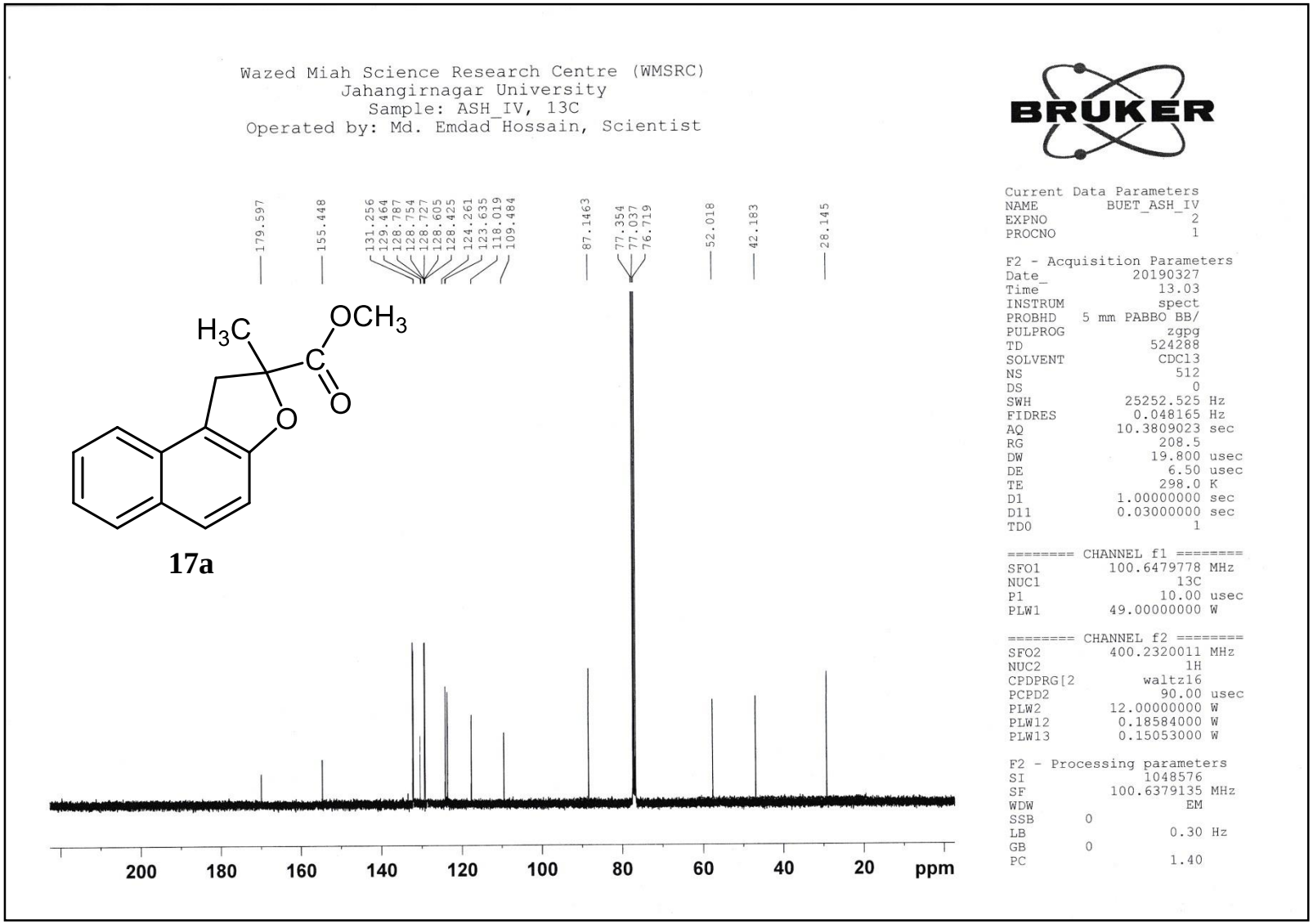


Fig. 20.c^{13}C NMR of Compound 17a

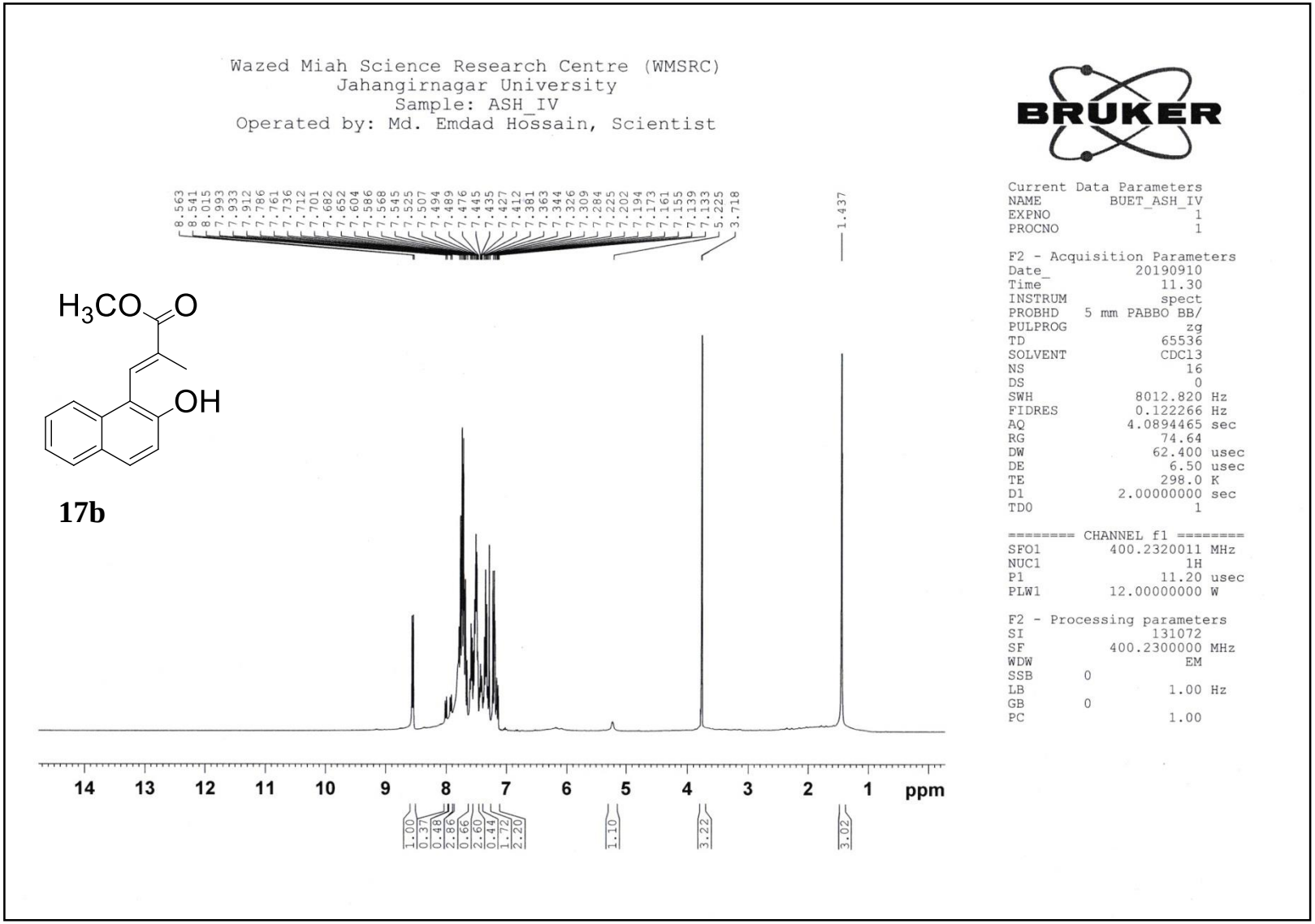


Fig. 21.a ^{1}H NMR of Compound 17b

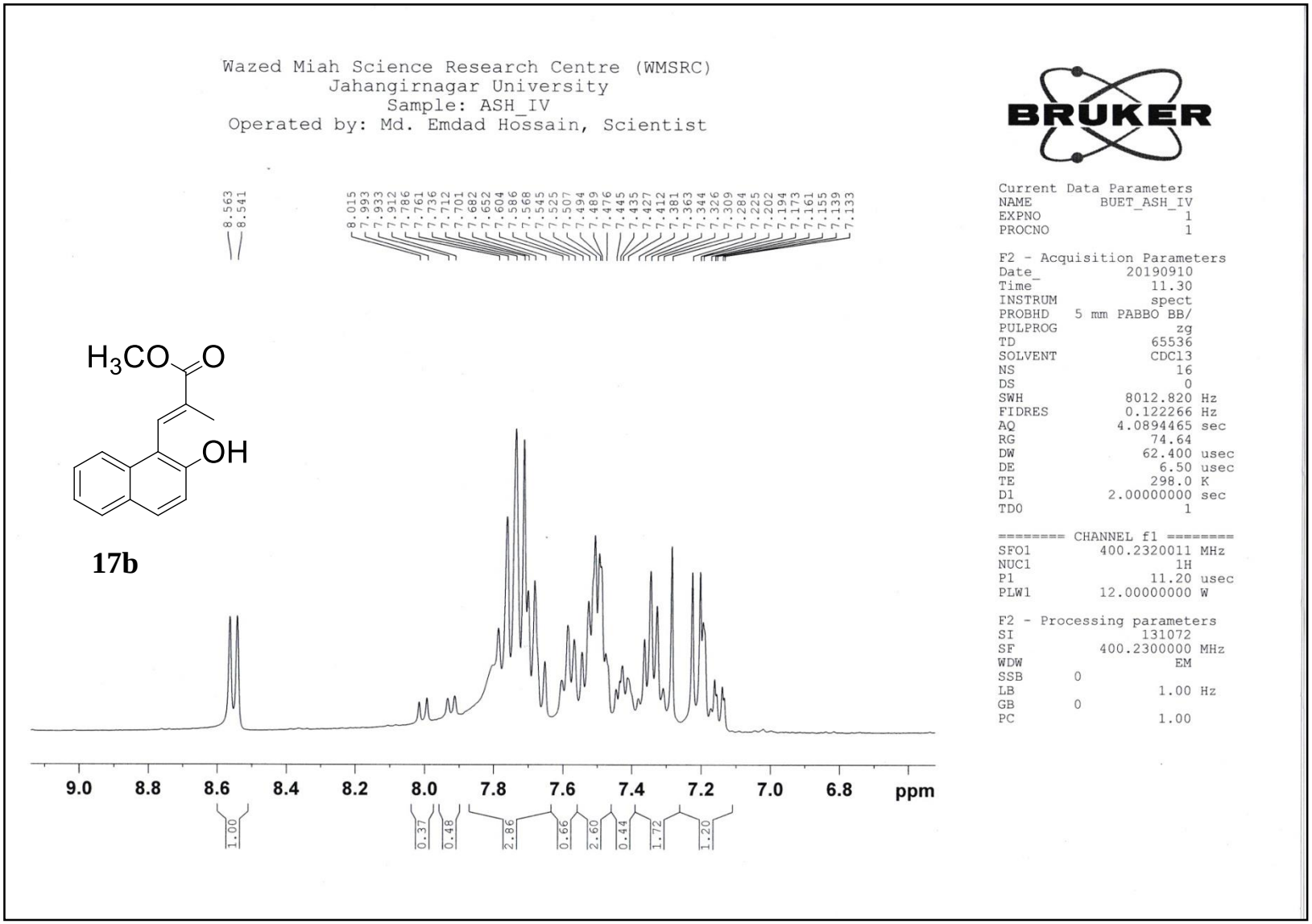


Fig. 21.b ^{1}H NMR of Compound 17b

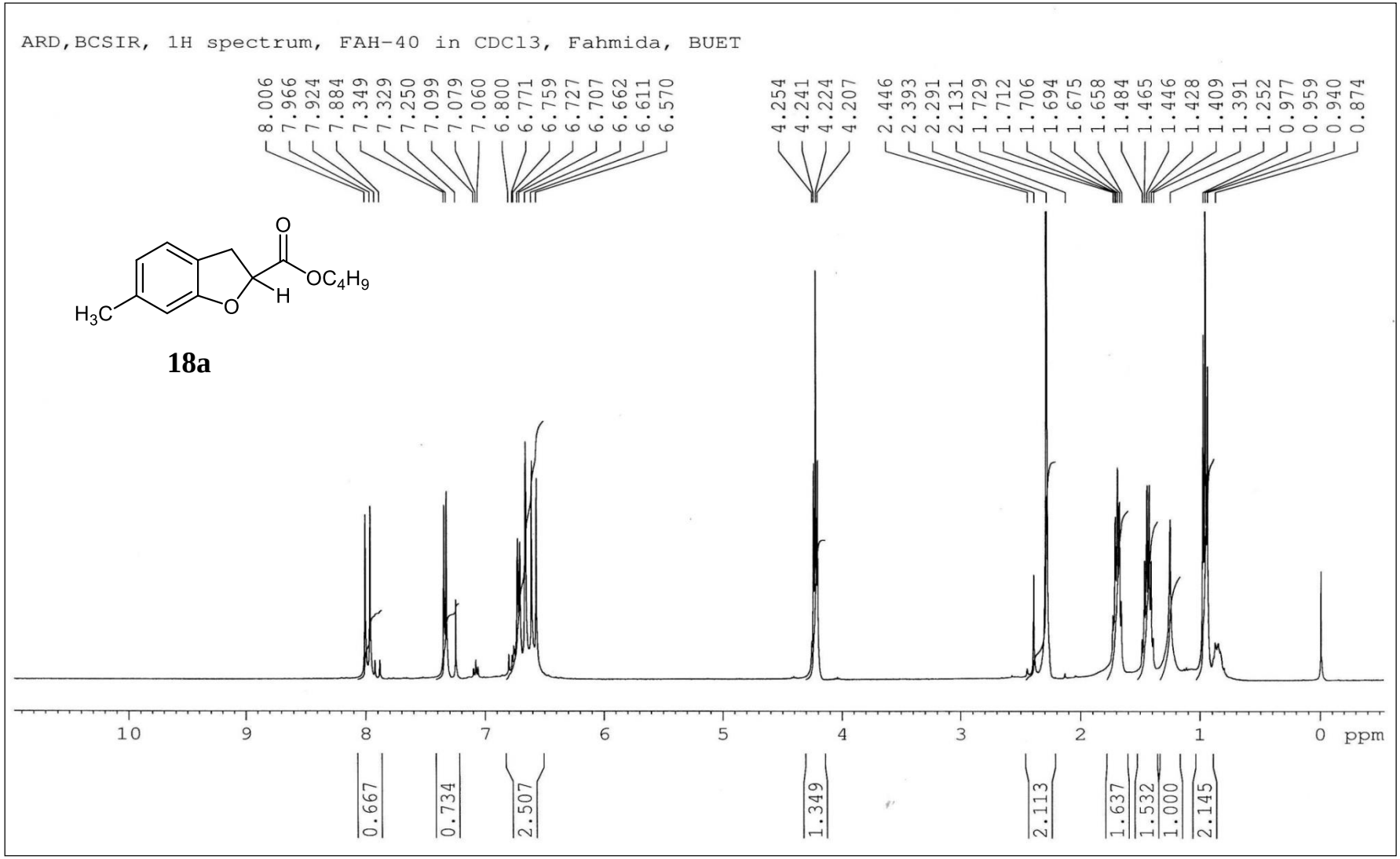


Fig. 22.a ^{1}H NMR of Compound 18a

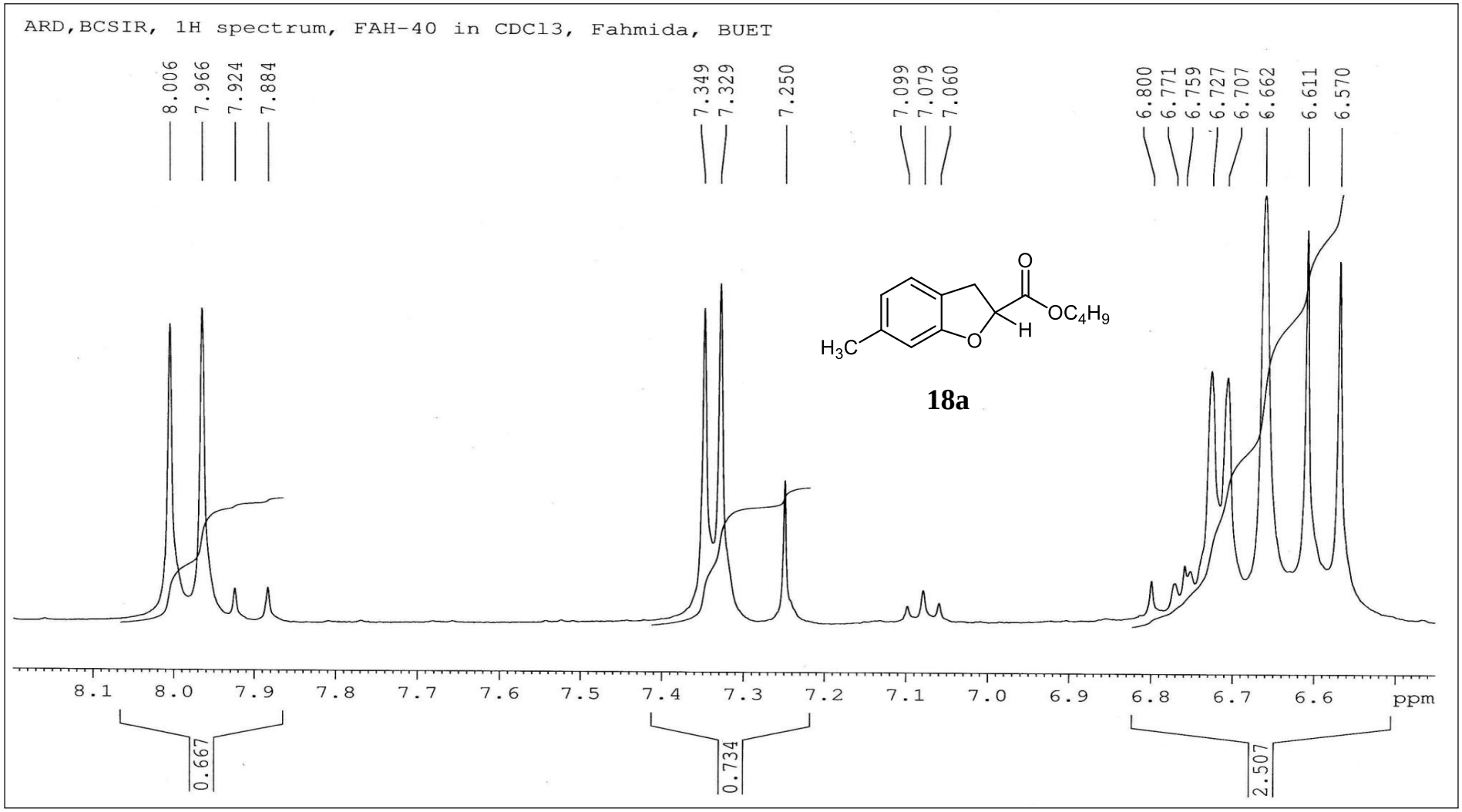


Fig. 22.b ^{1}H NMR of Compound 18b

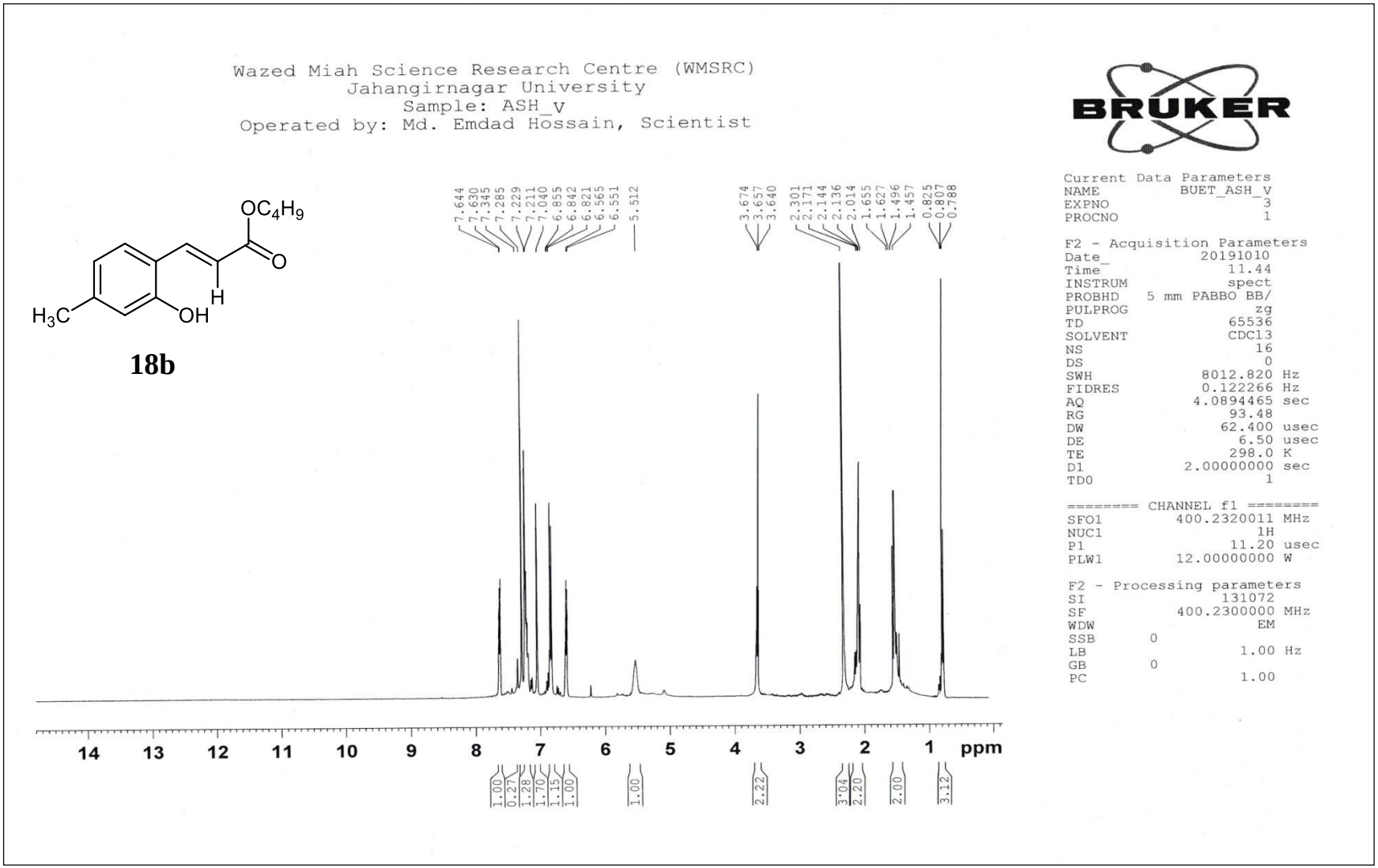


Fig. 23.a ^{1}H NMR of Compound 18b

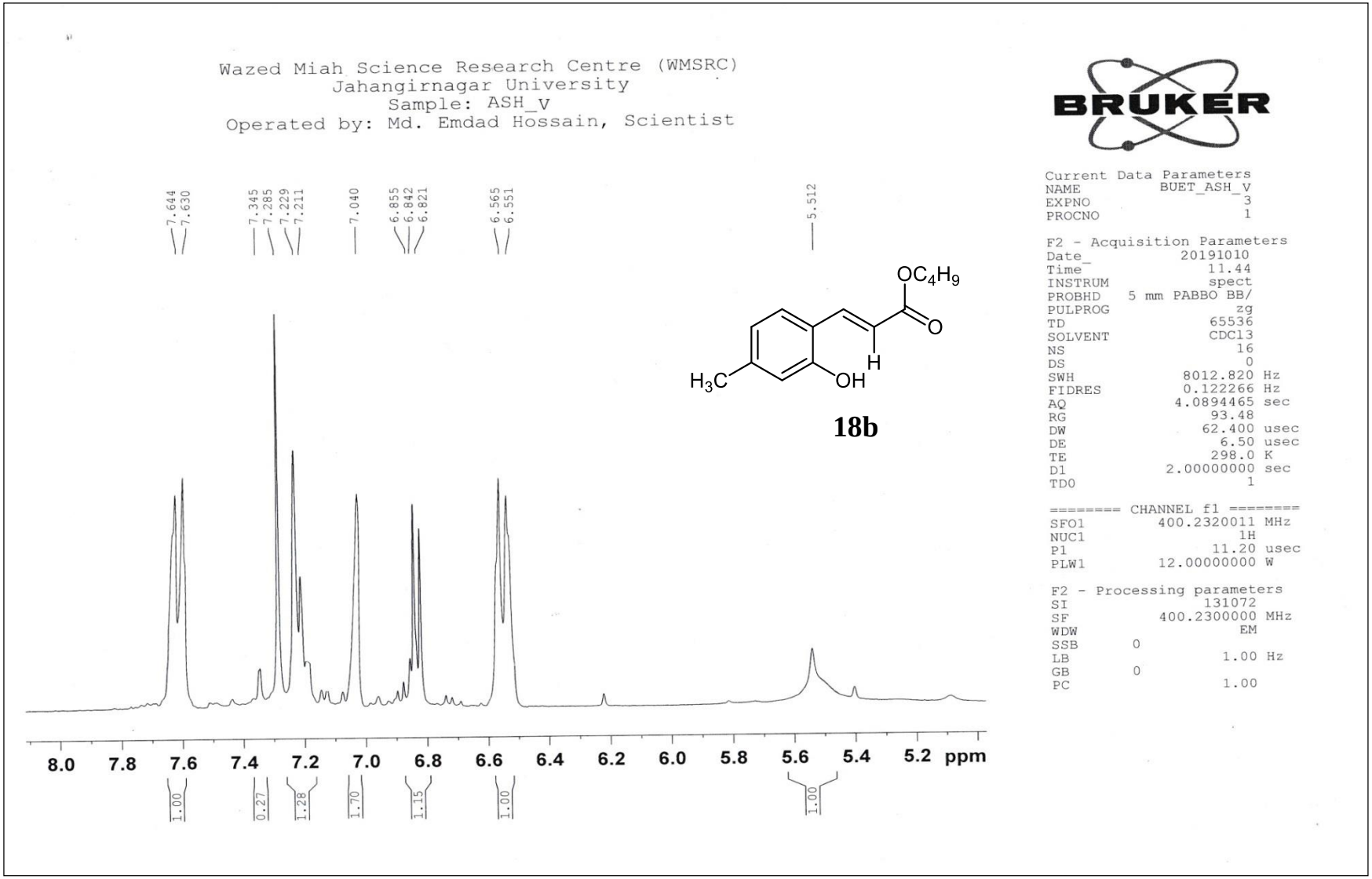


Fig. 23.b ^{1}H NMR of Compound 18b

3.7Computational Studies for14a-17a

3.7.1 Computational details

The Gaussian 16W software package was used for geometrical optimizations and computational spectroscopic characterization of **14a-17a** using DFTcalculations. The B3LYP, APFD exchange-correlation functional has been used with 3-21G basis set. The Gauss View 6.0.16 software was used for visualization.

The time-dependent DFT (TD-DFT) calculations using321G basis set with Gaussian 16W software package have been also used to study the properties such as HOMO-LUMO energies, MEP, global chemical reactivity descriptors, absorption wavelengths, oscillator strengths and electronic excitation energies of **14a-17a**.

3.7.2 Vibrational assignments

The vibrational spectroscopy is broadly employed in organic chemistry to recognize the various functional groups of organic compounds. The **14a-17a**molecule made up of 25-32 atoms, thus has minimum 69 and maximum 90 modes of vibrations according to the vibrational degree of freedom (3N-6) for the non-linear molecule and this molecule belongs to the C_1 point group. The theoretical calculations were performed using B3LYP/3-21G basis set. The optimized molecular geometry of **14a-17a** was obtained by optimization with DFT method is displayed in **Fig. 24**.

The computed vibration vibrational (unscaled and scaled) frequencies and experimental (FT-IR) measurements are summarized in **Table 7**.The experimental and simulated FT-IR spectra of **14a-17a** are presented in **Fig.25(a, b, c)**. The computed frequencies are normally greater than the related experimental wavenumbers due to the correlation effects of electron and basis set inadequacy. As a result of scaling the theorical frequencies are matching in accordance with experimental values.

3.7.2.1 C-H Vibrations

The title molecules have four C-H stretching modes, three from the benzene ring and one form furan ring. Normally in the benzene ring, C-H stretching assignments are present in the array of 3100-3000 cm^{-1} whereas in furan, C-H stretches are seen at 3180-3090 cm^{-1}. In **14a-17a**C-H vibrations of the benzene ring are showed at 3060-3183 cm^{-1} in FT-IR in experiment spectra. The computed valuse of benzene and furan rings are found to be 3248, 3207, 3216 and 3217 cm^{-1} respectively by DFT method. These results comply that both experimental and simulated data are in good agreement.

3.7.2.2 CH_3 Vibrations

In benzene ring, the CH_3 asymmetric stretching modes are predicted to be in the span of 3000-2925 cm^{-1} and symmetric stretching modes are largely fallen in the extent of 2940-2905 cm^{-1}. In **14a-17a**, the CH_3 asymmetric stretching vibrations are theoretically calculated at 3072-3075 cm^{-1} and experimental FT-IR peaks are observed at 2925-2956 cm^{-1}.

3.7.2.3 C-C Stretching Vibrations

In benzene ring, C-C stretching vibration modes falls in the range of 1625-1430 cm^{-1}. It is quoted that, the peaks are with changeable intensities at 1380-1280, 1465-1430, 1540-1470, 1590-1575 and 1625-1590 cm^{-1}. In **14a-17a** the C-C stretching modes are assigned 1615-1644 cm^{-1} and experimentally found at 1510-1599 cm^{-1}.

3.7.2.4 C=O Stretching Vibrations

In **14a-17a**, C=O stretching vibrations are showed at 1706, 1683.91, 1659.80, 1621.22, cm^{-1}respectively in FT-IR and computed at 1791, 1758.73, 1789.28, 1758.90cm^{-1}respectively.

3.7.2.5 Other vibration modes

In furan ring for **14a-17a**, C-O stretching vibrations are appeared at 1264, 1284.63, 1262.56, 1244.13 cm^{-1} respectively in FT-IR and computed at 1247, 1274.31, 1237.63, 1282.46 cm^{-1}respectively.

3.7.3Frontier molecular orbital studies

The reaction rate is comparative with the energy gap between the highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO). The LUMO is considered as an electrophilic, as it attracts electrons and HOMO can be a nucleophile that donates electrons to an electrophile. The energy gap of HOMO and LUMO determines the chemical stability of the molecule. A sample with large energy gap will have a good stability with high chemical hardness whereas with a small energy gap the molecule is considered to be soft and has good chemical reactivity. The hard molecule is less polarizable than soft one. From the HOMO and LUMO energies of the 14a-17a molecules, we can find out the global reactivity descriptors viz. electron affinity (EA), ionization potential (IP), chemical potential (V), electronegativity (χ), softness (S), global hardness (η) and electrophilicity index () the computed values of E_{HOMO}, E_{LUMO} and corresponding energy gap (ΔE = LUMO-HOMO) of the 14a-17a molecules are presented in **Table 8** and HOMO-LUMO energy diagram is presented in **Fig. 26(a, b, c, d)**.

According to the Koopmans' theorem ionization potential (IP) and electron affinity (EA) are the negative energies of HOMO and LUMO respectively.

IP = -EHOMO

EA = - ELUMO

Electronegativity (χ) is defined by

$$\chi = (IP + EA)/2$$

and chemical potential (V) is a negative of electrongaativity

V = -(IP+EA)/2

both are estimated rom the values of IP and EA. The chemical hardness (χ) is defined by

$$\chi = (IP - EA)/2$$

and chemical softness (S) is inverse of chemical hardness

$$S = \frac{1}{\chi}.$$

The extreme stream of electrons between donor (HOMO) and the acceptor (LUMO) result is lowering of energy considered to be electrophilicity index. The electrophilicity index of the title compound is found to be

$$\omega = \frac{\mu^2}{2\eta}, \quad \text{here } \mu = -\chi$$

From above calculations, I can conclude that **14a-17a** molecules has good chemical reactivityand soft.

3.7.4NMR spectra and calculations.

The NMR is a high-ranking instrument used for the determination of structure of molecules the combined experimental and simulated studies. of NMR give more confirmation about the structure of the molecules. Theoretical ^{1}H NMR and ^{13}C NMR chemical shifts were computed through GIAO method by using APFD/6-311G+ (d, p)basis set. The experimental and theoretical ^{13}C and ^{1}H NMR spectra are presented in **Figs 27(a, b, c, d)** and **Table 9** and **10.**

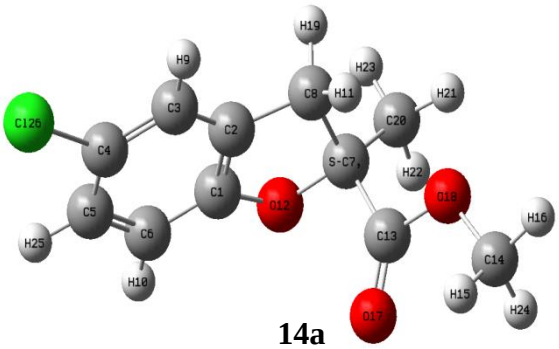
All experimental ^{13}C-NMR and ^{1}H-NMR chemical shifts correspond with the calculated data.

3.7.5Molecular Electrostatic potential.

The MEP gives the essential information regarding molecular shape, size and nature such as neutral negative and positive electrostatic potential areas which are represented in the form of color coding. It also delivers the most concerning idea regarding the nucleophilic and electrophilic reactivity of molecules. Being a real physical property V(r) can be determined experimentally by diffraction or computational methods. To examine the chemical reactivity of the molecule, on the optimized geometry of the **14a-17a,** MEP map was framed and presented in **Fig. 28(a, b, c, d).**Over the surface on the MEP red color indicates the electrophilic attack *i.e.,* maximum negative region and blue color indicates the nucleophilic *i.e*., maximum positive region. The potential reduces in the order of blue>green>yellow>orange>red. The color code of MEP diagram lies in between -0.02546 a.u (dark red) and 0.02546 a.u (dark blue) for **14a-17a.**

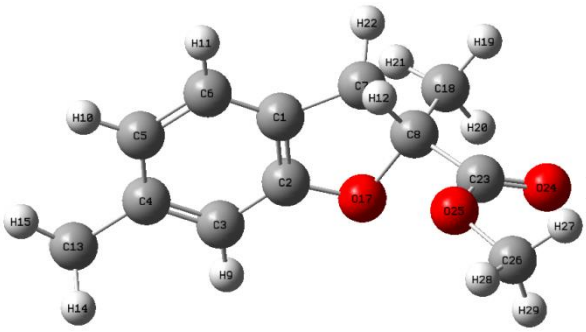
In the present maps, the most negative electrostatic potential area are localized in the region of the O and H atoms. The positive electrostatic potential are localized on the O17, O12, Cl26 atoms in **14a**; O24, O17 atoms in **15a**; O17, O12 atoms in **16a**; and O32, O26 atoms in **17a**.The H24, 19, 16, 15, 9 atoms in **14a**; H29, 28, 22, 11 atoms in **15a**; H16, 15, 14 atoms in **16a**; and H30, 29, 19, 11 atoms in **17a** have most positive region to nucleophilic attack.

From this discussion, it is clear that C=O, C-O-C and C-H are the most favoured region for an electrophilic and a nucleophilic attack.



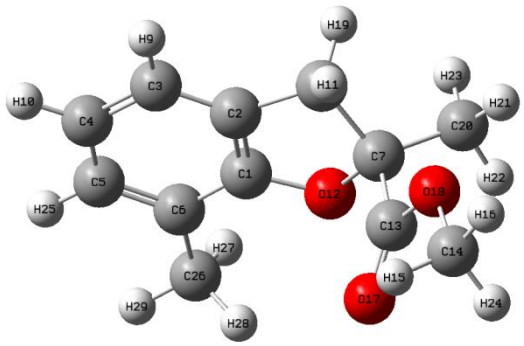
Electronic Energy=-1105.88Hartree
Dipole Moment =4.21Debye
Polarizability (α)= 119.94 a.u.

14a



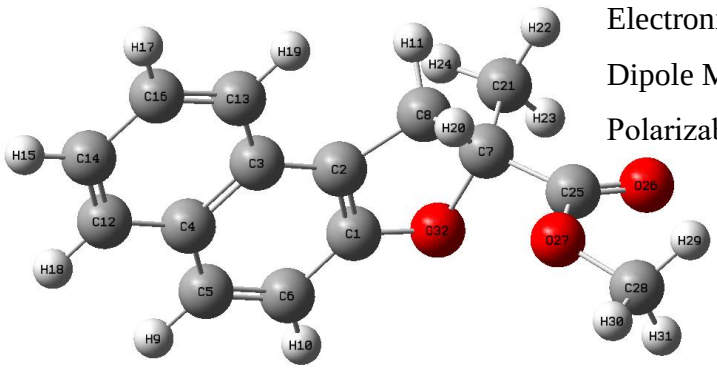
Electronic Energy=-687.59Hartree
Dipole Moment = 1.99Debye
Polarizability (α)= 122.33 a.u.

15a



Electronic Energy=-687.60Hartree
Dipole Moment = 2.694332Debye
Polarizability (α)= 119.73 a.u.

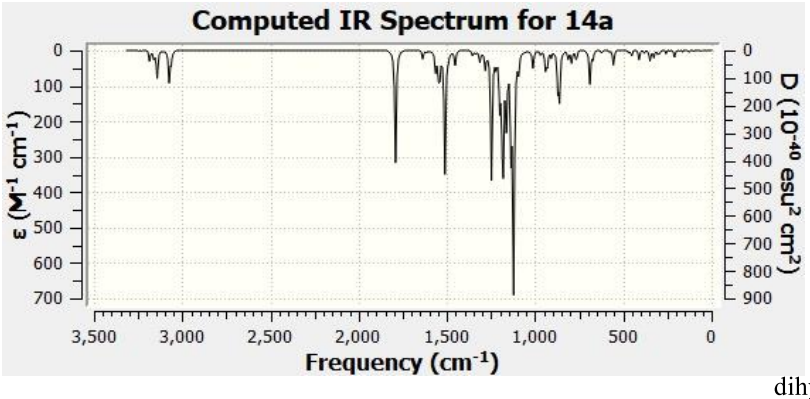
16a

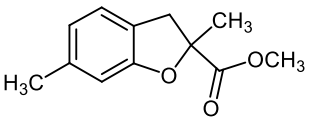


Electronic Energy=-801.29Hartree
Dipole Moment =1.86Debye
Polarizability (α)= 153.96 a.u.

17a

Fig. 24: Optimized geometric structure with atoms numbering of 14a-17a





methyl 2,6-dimethyl-2,3-dihydrobenzofuran-2-carboxylate

15a

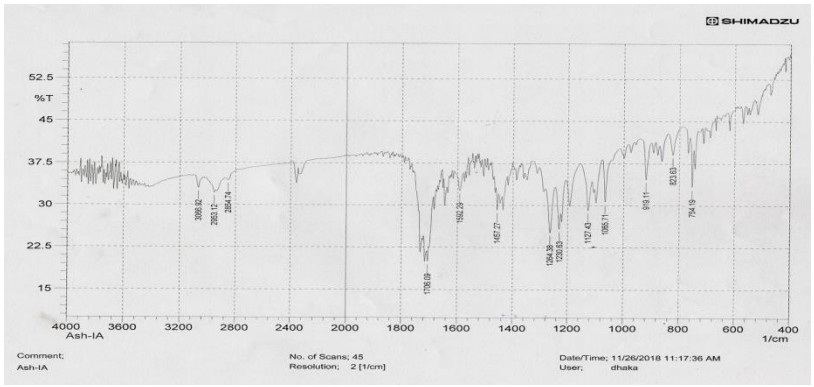
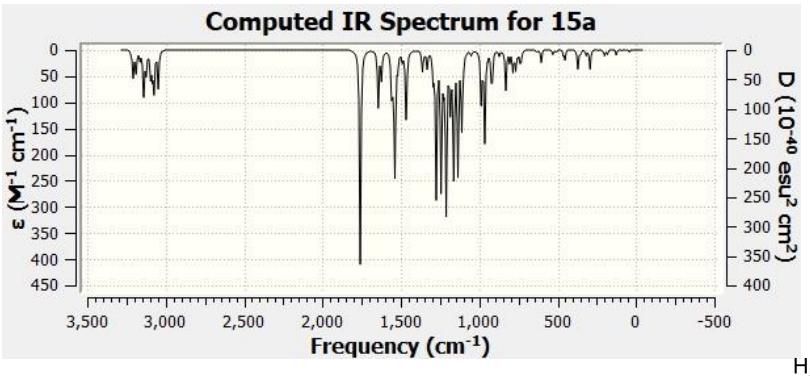
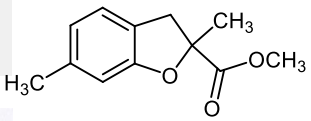


Fig. 25(a) Theoretical and Experimental IR spectra for 14a





methyl 2,6-dimethyl-2,3-dihydrobenzofuran-2-carboxylate

15a

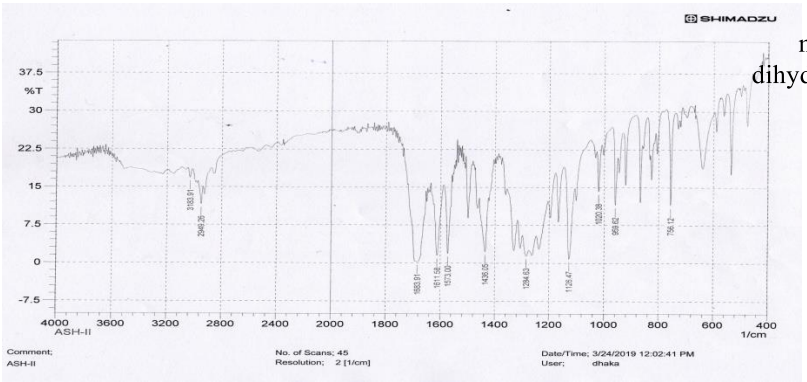
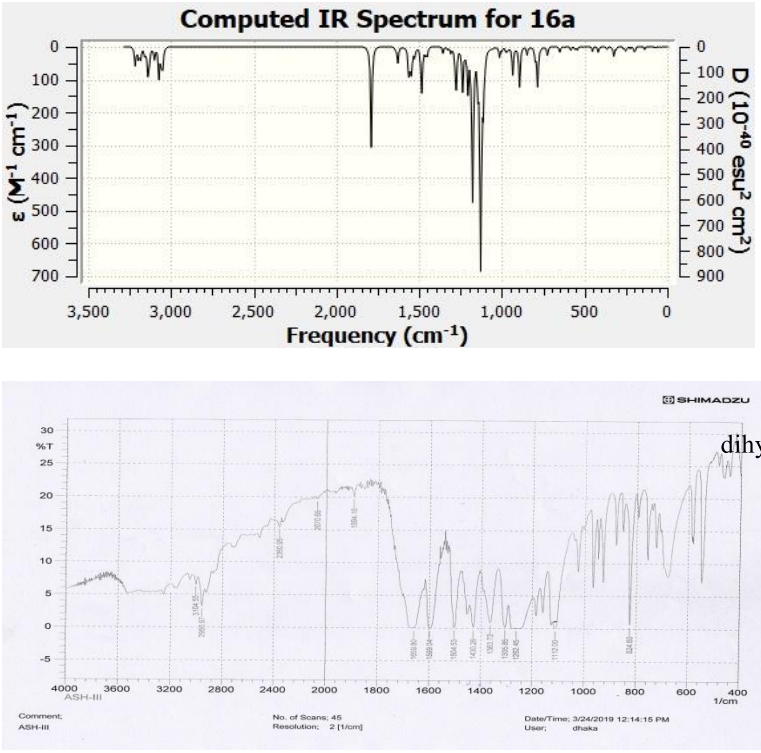
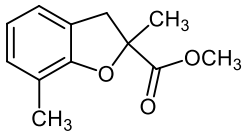


Fig. 25(b) Theoretical and Experimental IR spectra for 15a

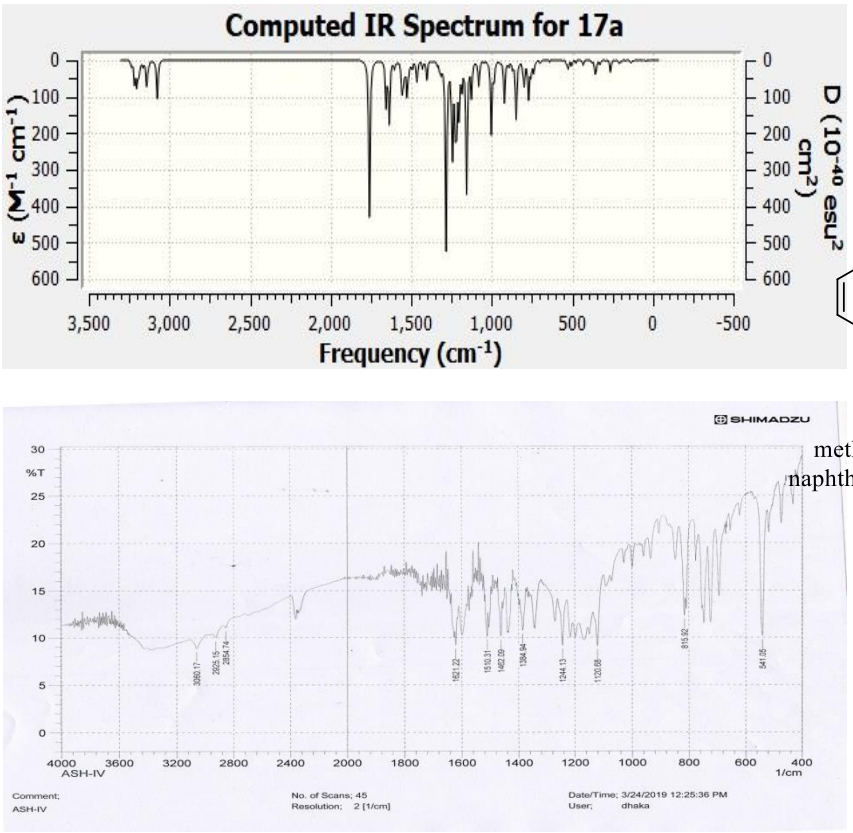


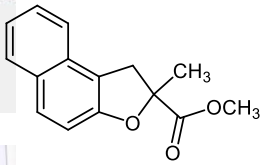


methyl 2,7-dimethyl-2,3-dihydrobenzofuran-2-carboxylate

16a

Fig. 25(c) Theoretical and Experimental IR spectra for 16a





methyl 2-methyl-1,2-dihydro-naphtho[2,1-*b*]furan-2-carboxylate

17a

Fig. 25(d) Theoretical and Experimental IR spectra for 17a

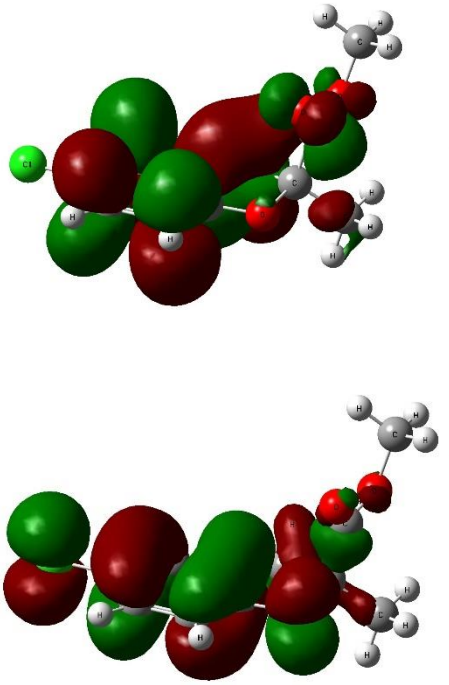


Fig. 26(a): HOMO-LUMO gap of 14a

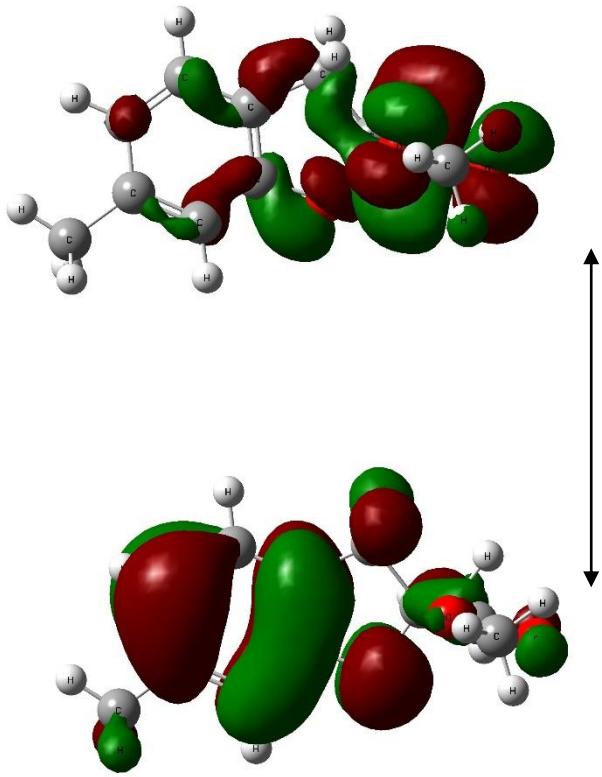


Fig. 26(b): HOMO-LUMO gap of 15a

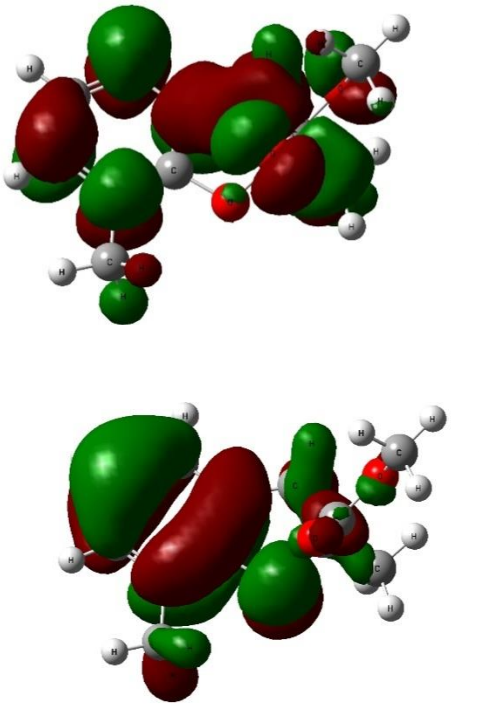


Fig. 26(c): HOMO-LUMO gap of 16a

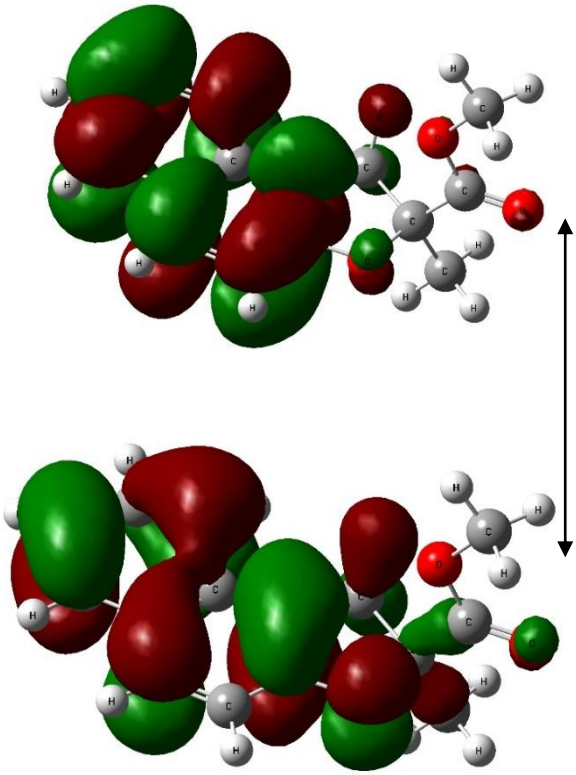


Fig. 26(d): HOMO-LUMO gap of 17a

Table 7. Some important assignments of experimental and theoretical IR spectral bandsof14a-17a

Functional Group	Litterateur IR (cm^{-1})	14a		15a		16a		17a	
		Computed B3LYP/ 3-21G (cm^{-1})	Expt. (cm^{-1})	Computed B3LYP/ 3-21G (cm^{-1})	Expt. (cm^{-1})	Computed B3LYP/ 3-21G (cm^{-1})	Expt. (cm^{-1})	Computed B3LYP/ 3-21G (cm^{-1})	Expt. (cm^{-1})
Aromatic υ**(C-H)**str.	3000-3100	3248.14	3066.92	3207.26	3183.91	3216.19	3104.55	3217.29	3060.17
Aliphatic υ **(C-H)**str.	3000-2850	3074.15	2953	3074.32	2949.26	3072.60	2956.97	3075.71	2925.15
υ**(C=O)** str.	1750-1735	1791	1706	1758.73	1683.91	1789.28	1659.80	1758.90	1621.22
Aromatic υ**(C-C)** str. in ring	1600-1400	1615	1592.29	1644.08	1573.00	1643.17	1599.04	1635.57	1510.31
υ**(C-O)**str.	1320-1000	1247	1264	1274.31	1284.63	1237.63	1262.56	1282.46	1244.13
Aromatic υ**(C-Cl)**str.	800-600	689.19	754.19	-	-	-	-	-	-

Table 8. Calculated energy values of 14a-17a by B3LYP/321G method

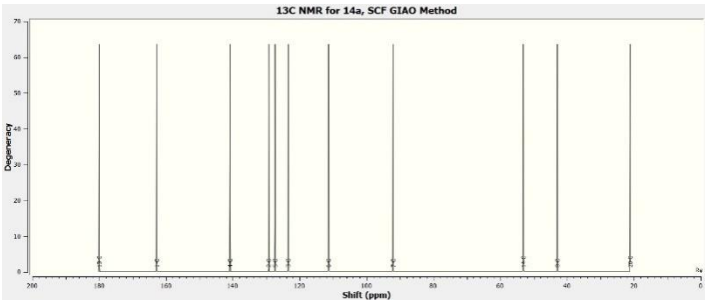
Different parameters	DFT, B3LYP/321G method			
	14a	**15a**	**16a**	**17a**
E_{HOMO} (*eV*)	- 0.26751	- 0.20877	- 0.20878	- 0.20048
E_{LUMO} (*eV*)	- 0.03301	- 0.00773	- 0.00167	- 0.03515
Energy gap**ΔE** (*eV*)	0.23450	0.20104	0.20711	0.16533
Ionization potential **IP**(*eV*)	0.26751	0.20877	0.20878	0.20048
Electron affinity**EA** (*eV*)	0.03301	0.00773	0.00167	0.03515
Electronegativity χ(*eV*)	0.15026	0.10825	0.10522	0.11781
Chemical potential **V**	- 0.15026	- 0.10825	- 0.10522	- 0.11781
Chemical hardness η (*eV*)	0.11725	0.10052	0.10355	0.08266
Softness S $(eV)^{-1}$	8.52878	9.94826	9.65640	12.09702
electrophilicity index (**ω**) **eV**	0.09628	0.05828	0.05345	0.08395

Table 9. Theoretical and Experimental of ^{13}C isotropic chemical shift (with respect to TMS, all values in ppm) for14a-17a by APFD/6311G++(d, p) method

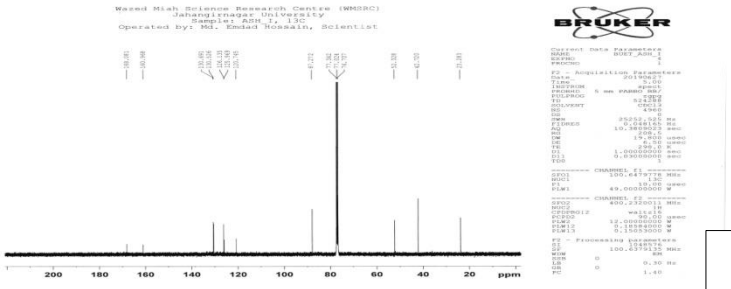
^{13}C NMR chemical shift, DFT, APFD/6311G+(d, p)method											
14a			15a			16a			17a		
Atom	Theoretical	Experimental	Atom	Theoretical	Experimental	Atom	Theoretical	Experimental	Atom	Theoretical	Experimental
13-C	179.99	168.08	23-C	187.37	169.12	13-C	181.68	169.59	25-C	180.18	179.59
1-C	162.80	160.96	2-C	167.82	155.84	1-C	162.50	154.44	1-C	160.36	155.44
4-C	140.85	130.96	4-C	146.53	138.17	5-C	129.37	131.23	3-C	131.86	131.25
2-C	129.22	130.52	1-C	130.78	129.14	2-C	126.59	128.03	4-C	130.97	129.46
5-C	127.37	126.13	6-C	129.19	129.0	6-C	123.15	127.40	5-C	129.79	128.78
3-C	123.41	125.96	5-C	126.62	121.27	3-C	121.51	124.34	12-C	129.58	128.72
6-C	111.37	120.74	3-C	114.07	117.01	4-C	121.37	123.96	16-C	127.09	128.42
7-C	92.09	87.21	8-C	96.824	87.03	7-C	91.70	87.14	14-C	122.79	124.26
14-C	53.11	52.32	26-C	59.15	52.21	14-C	53.32	52.01	13-C	122.33	123.63
8-C	42.91	42.72	7-C	44.80	43.51	8-C	43.75	42.18	2-C	119.89	118.01
20-C	21.14	23.28	18-C	23.56	23. 09	20-C	21.26	23.14	6-C	111.59	109.48
			13-C	22.78	21.32	26-C	13.88	15.94	7-C	91.993	87.14
									28-C	54.393	52.01
									8-C	39.575	42.18
									21-C	19.703	28.14

Table 10. Theoretical and Experimental of ^{1}H isotropic chemical shift (with respect to TMS, all values in ppm) for14a-17a by APFD/6311G++(d, p) method

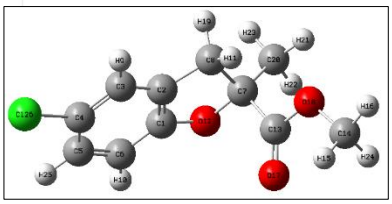
DFT, APFD/6311G+(d, p)method – Chemical shift											
14a			**15a**			**16a**			**17a**		
Atom	**Theoretical**	**Experimental**	**Atom**	**Theoretical**	**Experimental**	**Atom**	**Theoretical**	**Experimental**	**Atom**	**Theoretical**	**Experimental**
			11-H	7.24	7.13	25-H	7.39	7.19	18-H	8.33	8.54
			10-H	6.91	6.79	9-H	7.28	7.19	9-H	8.22	8.54
25-H	7.37	7.84	9-H	6.78	6.70	10-H	7.19	6.82	19-H	8.02	8.54
9-H	7.25	7.41	12-H	4.09	3.84	24-H	3.93	3.82	17-H	7.96	8.41
10-H	7.00	7.39	27-H	3.99	3.84	15-H	3.92	3.82	15-H	7.78	7.62
15-H	3.92	3.85	29-H	3.89	3.84	11-H	3.80	3.82	10-H	7.45	7.70
24-H	3.88	3.85	28-H	3.78	3.05	16-H	3.67	3.10	20-H	4.57	7.86
16-H	3.71	3.85	22-H	3.04	2.81	19-H	3.53	2.71	29-H	4.13	7.20
11-H	3.70	3.32	16-H	2.54	2.26	28-H	2.90	2.28	31-H	4.02	3.81
19-H	3.36	3.25	14-H	2.54	2.26	27-H	2.46	2.28	30-H	3.68	3.70
21-H	2.13	2.25	15-H	2.04	2.26	21-H	2.15	2.28	11-H	3.57	3.70
22-H	2.00	2.25	20-H	2.01	2.01	29-H	2.05	2.15	23-H	2.43	3.70
23-H	1.76	2.25	21-H	1.39	2.01	22-H	2.02	2.15	24-H	1.60	3.61
			19-H	1.27	2.01	23-H	1.79	2.15	22-H	1.50	1.33

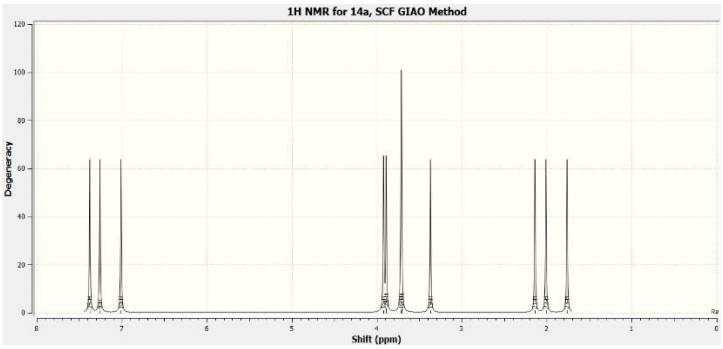


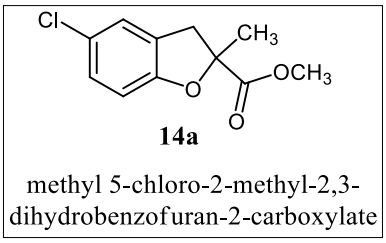
Theoretical[1]C spectrafor **14a**



Experimental[1]C spectra for **14a**

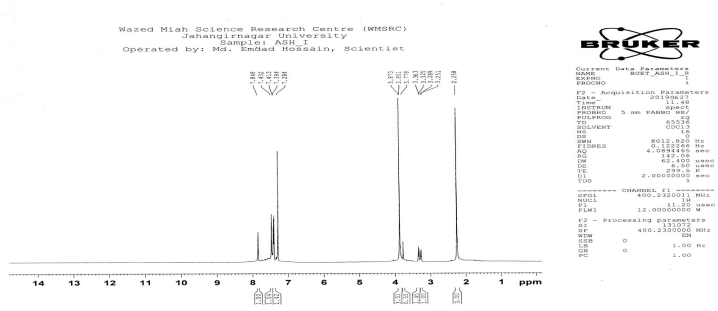






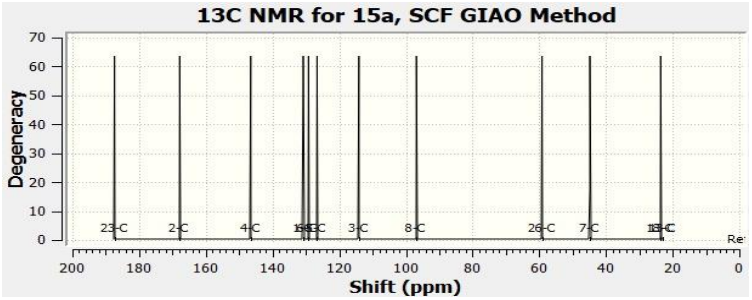
methyl 5-chloro-2-methyl-2,3-dihydrobenzofuran-2-carboxylate

Theoretical [1]H spectra for **14a**

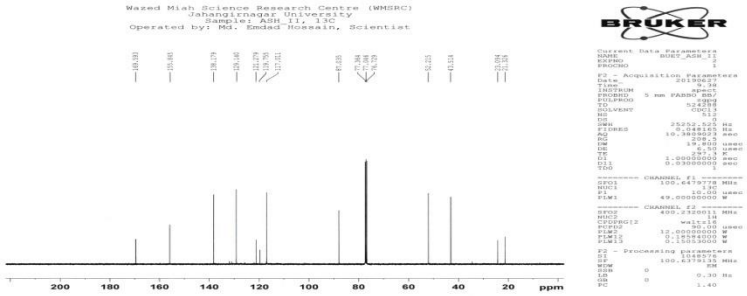


Experimental [1]H spectra for **14a**

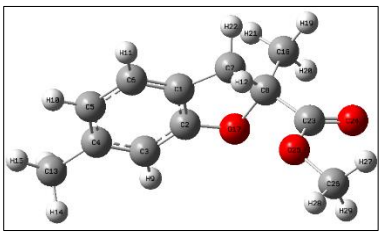
Fig. 27(a) Theoretical and Experimental[13]C&[1]H spectra for 14a

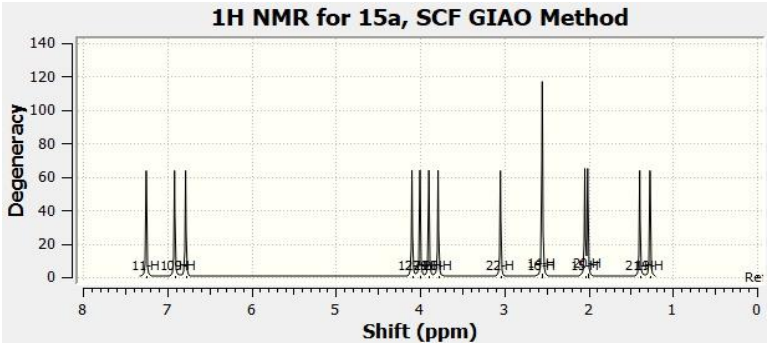


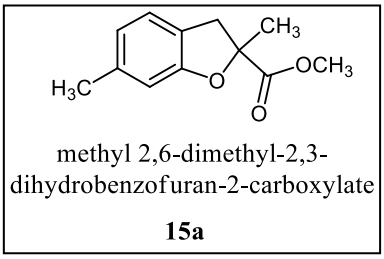
Theoretical ^{1}C spectra for **15a**



Experimental ^{1}C spectra for **15a**



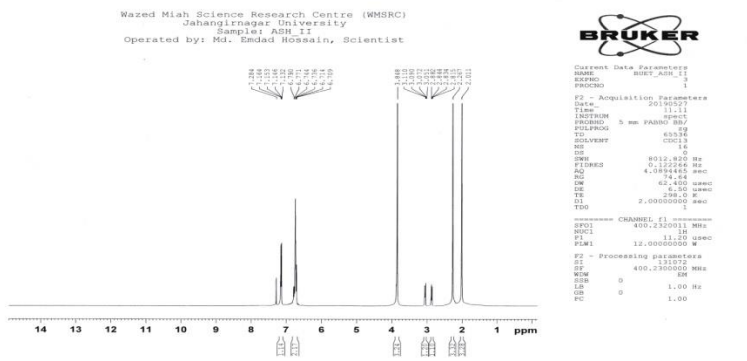




methyl 2,6-dimethyl-2,3-dihydrobenzofuran-2-carboxylate

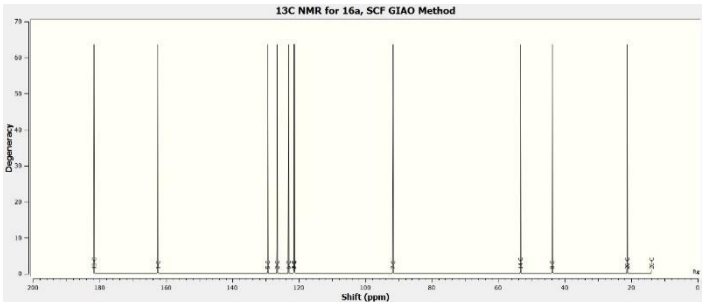
15a

Theoretical ^{1}H spectra for **15a**

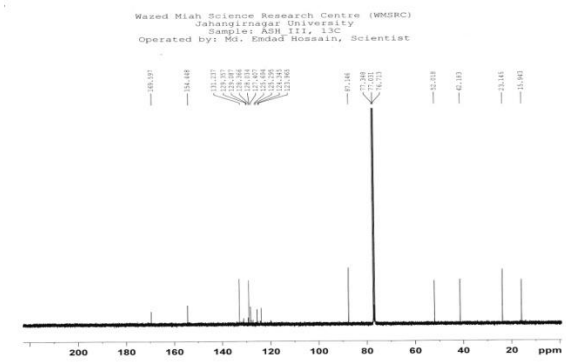


Experimental ^{1}H spectra for **15a**

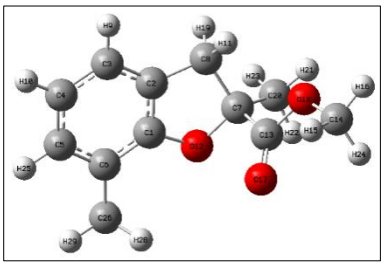
Fig. 27(b) Theoretical and Experimental^{13}C&^{1}H spectra for 15a

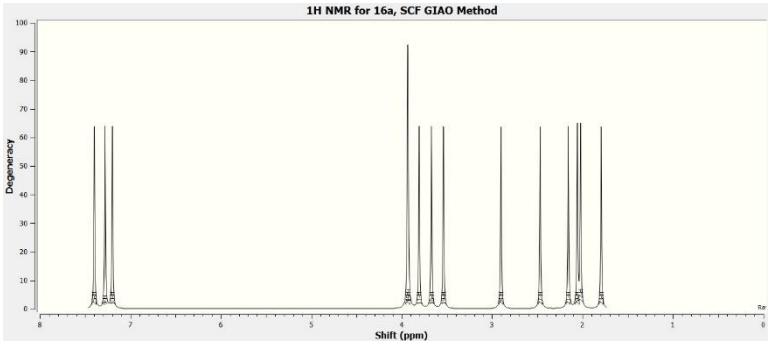


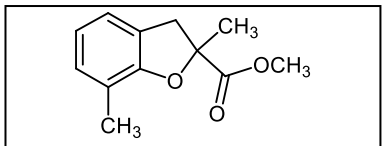
Theoretical [1]C spectra for **16a**



Experimental [1]C spectra for **16a**



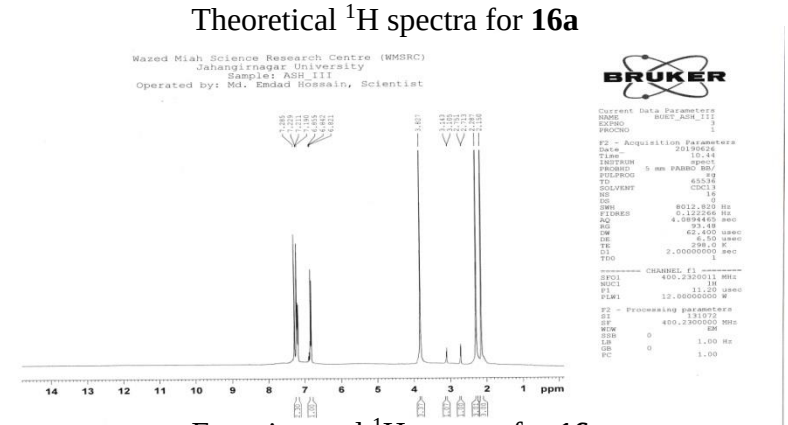




methyl 2,7-dimethyl-2,3-dihydrobenzofuran-2-carboxylate

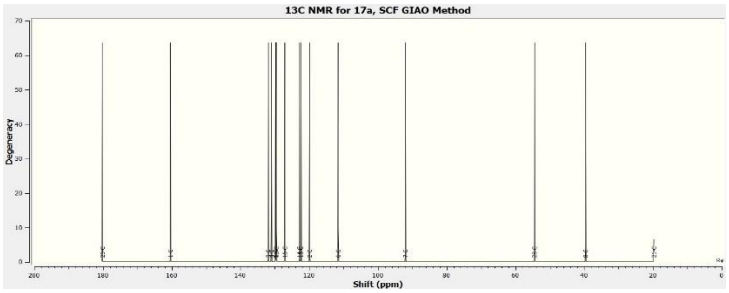
16a

Theoretical [1]H spectra for **16a**

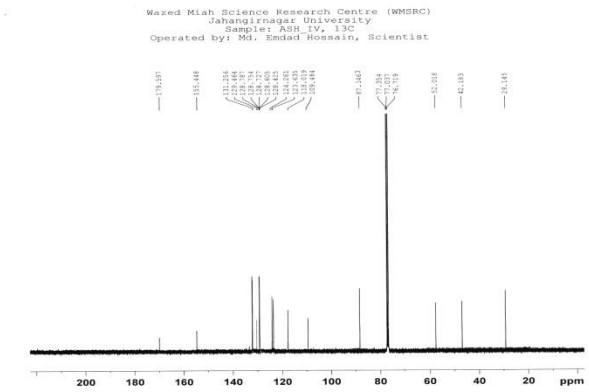


Experimental [1]H spectra for **16a**

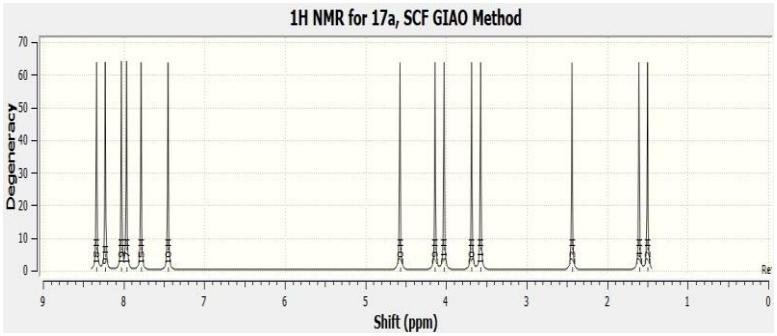
Fig. 27(c) Theoretical and Experimental[13]C&[1]H spectra for 16a

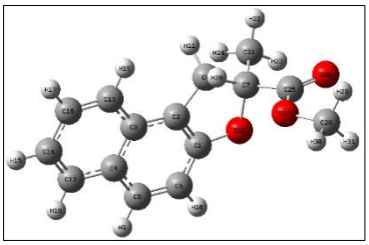


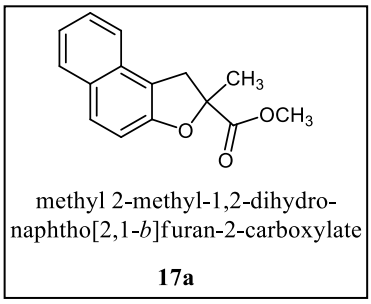
Theoretical ^{1}C spectra (**17a**)



Experimental ^{1}C spectra (**17a**)



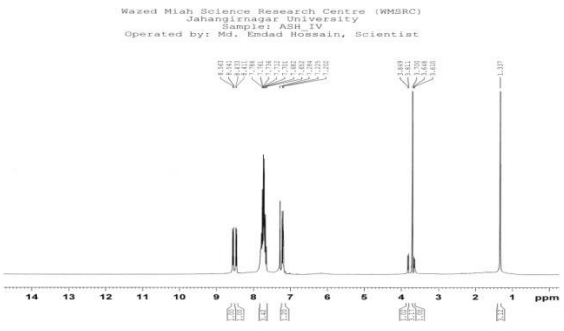




methyl 2-methyl-1,2-dihydro-naphtho[2,1-*b*]furan-2-carboxylate

17a

Theoretical ^{1}H spectra (**17a)**



Experimental ^{1}H spectra (**17a**)

Fig. 27(d) Theoretical and Experimental^{13}C&^{1}H spectra for 17a

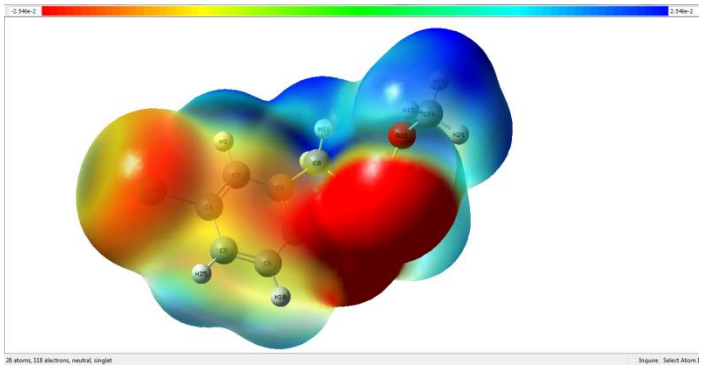


Fig. 28(a)Computed molecular electrostatic potential surface for 14a

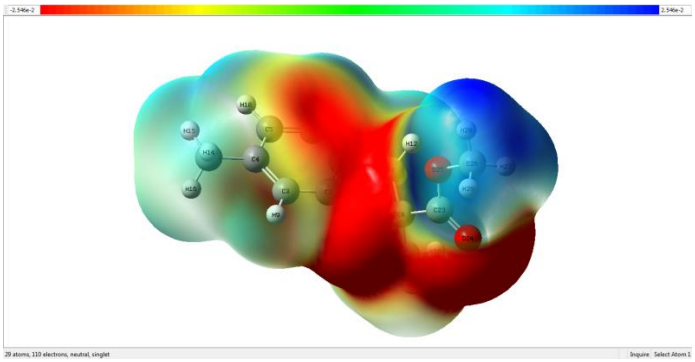


Fig. 28(b)Computed molecular electrostatic potential surface for 15a

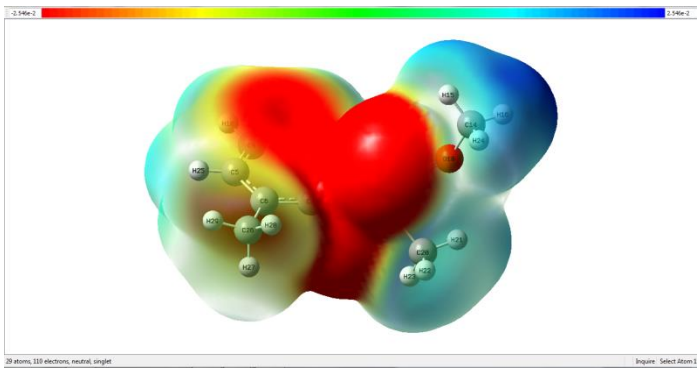


Fig. 28(c)Computed molecular electrostatic potential surface for 16a

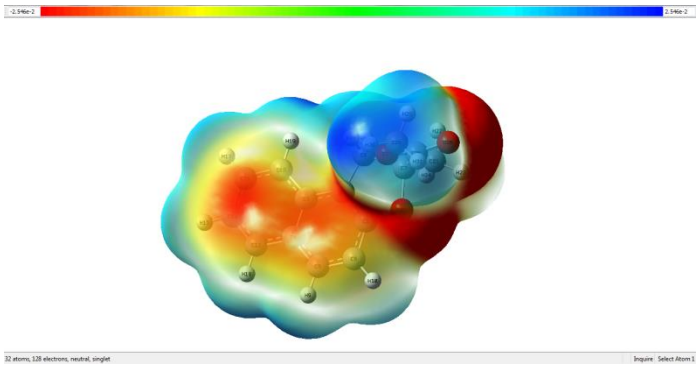
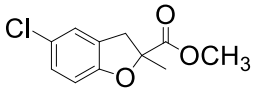
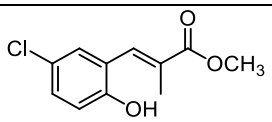
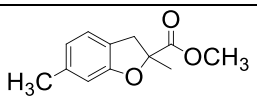
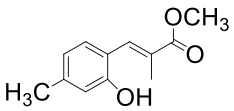
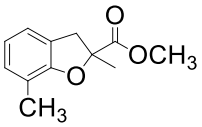
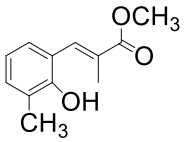
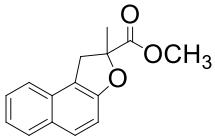
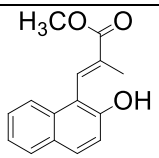
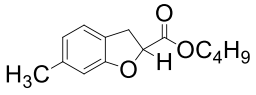
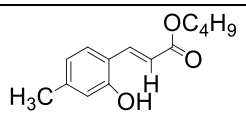


Fig. 28(d)Computed molecular electrostatic potential surface for 17a

3.8Comparative Spectra Data Study between Cyclic(14a-17a) and acyclic (14b-17b)

Structure	IR	^{1}NMR	melting point
 **14a**	Showed -C-O-C- stretching	δ3.25 (d, 1H, *J* = 15.2*Hz*) δ3.32 (d, 1H, *J* = 15.2*Hz*)	64-69 °C
 **14b**	Showed -OH stretching	δ5.3 (br. s 1H OH),	56-61 °C
 **15a**	Showed -C-O-C- stretching	δ2.81 (d, 1H, *J* = 15.2 *Hz*) δ3.05 (d, 1H, *J* = 15.2 *Hz*)	70-75°C
 **15b**	Showed -OH stretching	δ5.7(br. s 1H OH), δ7.74(s, 1H, vinylic–H)	50-55 °C
 **16a**	Showed -C-O-C- stretching	δ2.71 (d, 1H, *J* = 15.2 *Hz*) δ3.10 (d, 1H, *J* = 15.2*Hz*)	32-37°C
 **16b**	Showed -OH stretching	δ5.61(br. s, 1H OH) δ7.63(s, 1H, vinylic–H)	40-45°C
 **17a**	Showed -C-O-C- stretching	δ3.61 (d, 1H, *J* = 15.2 *Hz*) δ3.81 (d, 1H, *J* = 15.2 *Hz*)	60-65 °C
 **17b**	Showed -OH stretching	δ5.22(br. s, 1H OH)	53-58 °C
 **18a**	Showed -C-O-C- stretching	δ6.59 (d,1H, *J* = 16.4 Hz, H3) δ6.66 (s, 1H, H-3) δ7.98 (d, 1H, *J* = 16 Hz, H-2)	98-100°C
 **18b**	Showed -OH stretching	δ5.51(br. s 1H OH)	65-69°C

CHAPTER 4

Conclusion

4.0 Conclusion

In conclusion, we have successfully developed a convenient general and facile method for the synthesis of alkyl 2,3-dihydrobenzofuran-2-ylcarboxylatesthrough $(Ph_3P)_2Cl_2$, $Co(Ph_3P)_2Cl_2$, $Ni(Ph_3P)_2Br_2$, Bimetallic nano catalyzed reaction of 2-iodophenol with terminal alkenes (acrylic ester) in one pot reaction separately and characterized by different spectroscopic methods such as FT-IR, NMR spectral analysis. The experimentally observed FT-IR, spectra were well agreed with the computed vibrational frequencies using DFT calculations. The HOMO-LUMO energy gap found to be around 0.23450, 0.20104, 0.20711, 0.16533*eV*, which shows that the **14a-18a**moleculehas good chemical reactivity and softness. The MEP indicates the C=O is the most favoured region for an electrophilic.

The most important features of the synthesis were that:

- Readily available inexpensive starting materials were used under relatively mild conditions and relatively good yields.
- No toxic and hazardous compounds are produced by this synthesis.
- A variety of functional groups can be introduced at the C-5 and C-6 position of the benzofuran ring by this procedure.
- Therefore, this methodology could be utilized to synthesize the biologically important benzofuran derivatives. This method will be attractive to both organic and medicinal chemists.