Domino Transformations: Synthesis of 7-Methyl-5*H*-dibenzo[*a*,*c*][7]annulen-5-ones, Bi-aryls, 1,3-Dihydroisobenzofurans, Bi-aryl acetylenes via [Pd]-Catalysis

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A Dissertation Submitted to
Indian Institute of Technology Hyderabad
In Partial Fulfillment of the Requirements for
The Degree of Doctor of Philosophy

Department of Chemistry

January, 2015

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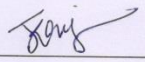
I declare that this written submission represents my ideas in my own words, and where others' ideas or words have been included, I have adequately cited and referenced the original sources. I also declare that I have adhered to all principles of academic honesty and integrity and have not misrepresented or fabricated or falsified any idea/data/fact/source in my submission. I understand that any violation of the above will be a cause for disciplinary action by the Institute and can also evoke penal action from the sources that have thus not been properly cited, or from whom proper permission has not been taken when needed.



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Acknowledgements

It gives me immense pleasure to express my profound gratitude to my research supervisor **Dr. G. Satyanarayana**, for giving me an opportunity to work with him in his research group. I am eternally thankful him all the time for his valuable guidance, encouragement and constant motivation during my research in the lab. I will always remain grateful to him and consider myself privileged to be associated with him.

I sincerely thank:

- Head of the Department (Prof. F. A. Khan) and other faculties of the Department of chemistry IIT Hyderabad.
- Late Prof. A. Srikrishna (IISc Bangalore).
- Prof. K. R. Prasad (IISc Bangalore), Prof. Martin E Maier (Universität Tübingen-Germany), Dr. Dattatraya H. Dethe (IIT-Kanpur), Dr. Santosh J Gharpure (IIT-Bombay) and Dr. P. C. Ravi Kumar (IIT Mandi) towards their valuable suggestions.
- Faculties during my master degree Dr. Y. Jayaprakash Rao, Prof. M. Adinarayana, Prof. P. Venkateswar Rao, Prof. K. Nageswar Rao, Prof. P. Jaya Prasada Rao.
- My B. Sc. teachers Mr. Jagadeeshwar Reddy and Mr. Venkateshwar Reddy.
- My previous organization colleagues (Dr. Reddy's Laboratories Pvt. Ltd) Dr. P. Pratap Reddy, Dr. P. V. R Acharyulu, Dr. Cherukupalli Praveen, Dr. G. Madhusudhan Reddy, Dr. Y. V. Madhavi, Dr. N. Srinivas, Dr. R Vijaya Anand, Dr. Arnab Roy, Dr. Dinesh Bhalerao, Dr. Rakeshwar Bandichhor, Dr. Pranab Haldar, Dr. P Seetha Rama Sarma, Dr. K. Srihari Babu, Mr. P. Srinivas, Mr. V. Krishna, Mr. P. Narasimha Rao, Mr. I. Babu and Mrs. P. Shailaja.
- Dr. K. Srinivas (Scientist-IICT-Hyderabad) and Dr. Y. V. Madhavi (Asst. prof. NIPER-Hyderabad) for their valuable support towards the upgradation from JRF to SRF.
- Dr. A. Gopi Krishna Reddy and Mr. Md. Samiuddin for recording NMR spectra.
- Mr. L. Mahendar and Mr. Md. Samiuddin for recording the HR-MS spectra.

- Dr. K. Ravi Kumar and Mr. Kishor Sudhir Naktode for X-Ray difractometer measurements and analysis of single crystal samples.
- Mr. L. Mahendar for recording IR samples.
- Technical and non-teaching staff of IIT Hyderabad, in particular Mr. M. Kumar Das, Mr. Sadique, Mr. Mosim, Mr. Srinivas, Mr. Shiva, Mr. Rajesh, Mr. Sastry, Mr. Lingamaiah, Mr. Vijay, Mr.Rama Krishna and Mr. Praveen for their support.
- My lab collegues Dr. A. Gopi Krishna Reddy, Ms. Niharika, Mr. Ravi Kumar, Mr. Suchand Basuli, Mr. L. Mahendar, Mr. B. Venkat Ramulu, Mr. Mritunjoy, Ms. Madhurima, Mr. Debyendu Das, Mr. Akash, Ms. Amrita, Ms. Jyoti, Mr. K. Ramesh and Mr. Kailash for their support, co-operation and providing a congenial lab environment.
- Mr. Ravi Kumar, Mr. Suchand basuli, Ms. Madhurima Hazra, Dr. A. Gopi Krishna Reddy and Ms. Niharika for their help during thesis preparation.
- All other departmental friends Mr. Laxmaiah, Dr. Manoj Reddy, K. Krishna Murthy, S. Rambabu, Mr. Naresh, Dr. Karuppiah, Dr. Linga Reddy, Dr. Dayamani, Dr. Unnisa, Dr. B. Narasimha Reddy, Dr. Remya, Mrs. Sranvanthi, Mr. Raveendra Babu, Mr. Narendar, Mr. K.S.V. Srinivas, Dr. H. Surendar, Mr. B.M. Basavraj, Dr. P. Suresh, Dr. A. Satyanarayana, Mr. Ch. Nagababu, Mr. K. Srinivas, Dr. K. Ravikumar, Mr. K. Ramesh, Mr. Kishor, Mr. A. Srinivas, Mr. Shinde vidya charan, Mr. Anand H. Shinde, Mr. Sagar Arepally, Ms. Srilaxmi and Mr. Harinath for their help and company.
- Indian Institute of Technology Hyderabad for providing the required facilities and the Council of Scientific and Industrial Research (CSIR) for their financial support.
- My spiritual masters Rama Krishna Paramahamsa, Sri Sharadha Devi and Swami Vivekananda.
- My dearest parents (Lalitha and Prem Kumar), my sisters (Lavanaya and Kiran mai) for their love and affection. Without their support, I would be nowhere near where I am today.

Dedicated to

My Parents

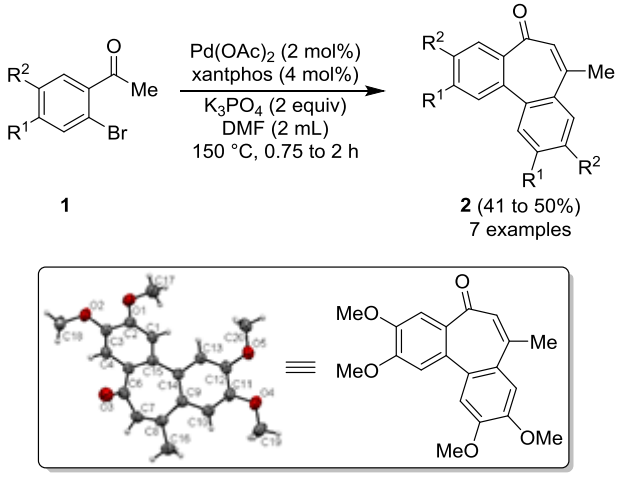
Abstract

Constituting a carbon-carbon bond is one of the most fundamental operations in organic synthesis. In general, the synthesis of organic molecules involves a step-wise operation for the construction of individual bonds. These synthetic transformations become more efficient and viable when several bonds are formed in a one-pot fashion and/or in a sequential one-pot manner without isolating the reaction intermediates/intermediate products, such reactions can be called as domino or sequential domino one-pot reactions, respectively. The latter one would be feasible by altering the reaction conditions or by the addition of reagents to promote the subsequent reaction(s) once after the initial step(s) is/are completed. Particularly, the domino processes promoted by [Pd]-catalysis possesses a great potential for elaboration and the development of new synthetic methods that eventually represent a new frontier to conquer in organic chemistry. These domino strategies elaborate the scope of the traditional cross-coupling chemistry due to more efficient and fast construction of molecular complexity from comparatively uncomplicated building blocks. Such transformations are also called as tandem, sequential, cascade, consecutive, iterative, zipper or one-pot (one-flask) reactions and these link several transformations together in a single synthetic operation. Domino reactions have gained wide acceptance due to increase in efficiency of a reaction by decreasing the number of synthetic transformations, the quantity of reagents and solvents used for workup procedures, column chromatography and minimization of waste and energy. Therefore these reactions have their own significance with respect to ecological and economical aspects.

Synthesis 7-Methyl-5H-dibenzo[a,c][7]annulen-5-ones via domino [Pd]-catalysis:

Therefore, we became interested in the development of novel [Pd]-catalyzed domino transformations in a one-pot or sequential one-pot manner. As a result, in the first chapter, we have presented a domino [Pd]-catalyzed transformation, for the synthesis of

novel 7-methyl-5*H*-dibenzo[*a*,*c*][7]annulen-5-ones **2** starting from simple 2-bromoacetophenones **1**. The reaction might proceed through an unprecedented path that benefits the entire process by constructing a C-C σ-bond (i.e., intermolecular homo bi-aryl coupling) and a C=C π-bond (i.e., intramolecular Aldol type condensation), as depicted in Scheme 1. Although, the product 7-methyl-5*H*-dibenzo[*a*,*c*][7]annulen-5-ones **2** was obtained in moderate yields, for a one-pot domino process of two individual steps (i.e., biphenyl coupling and Aldol condensation) it accounted for approximately 70% yield of each individual step. Therefore, the method is still considered to be an efficient one. Furthermore, the present method was found to be significant when compared to earlier reports which involved not less than four steps with an overall 15% yield to accomplish such structurally relevant compounds.



Scheme 1

Significantly, 7-methyl-5*H*-dibenzo[*a*,*c*][7]annulen-5-ones **2** represents the entire carbon core structure of biologically active dibenzocycloheptanoid (**3-5**) and colchicinoid (**6-8**) based natural products (Figure 1).

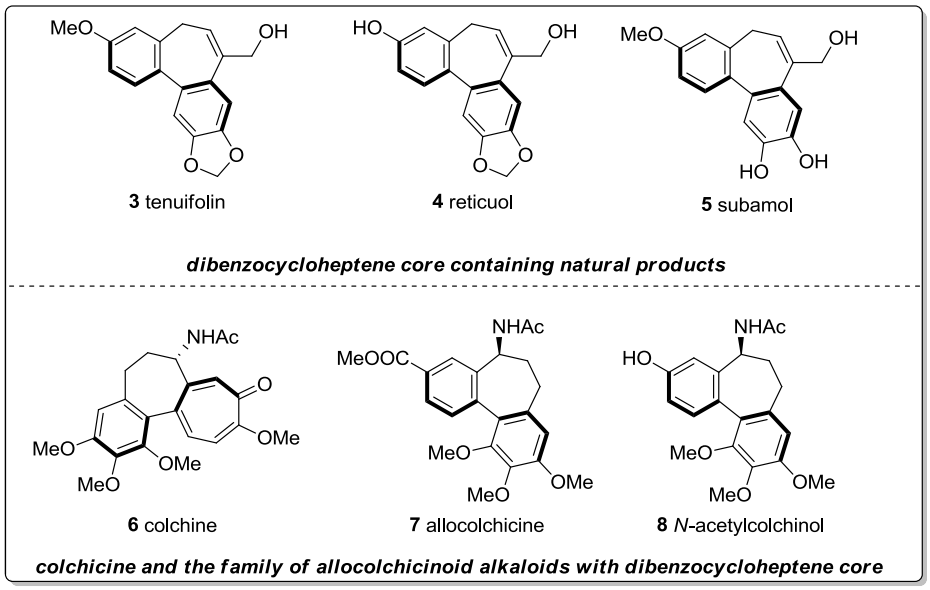
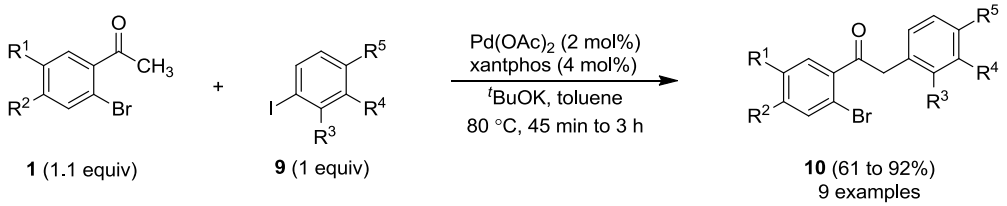


Figure 1

Synthesis of α-aryl ketones via [Pd]-catalysis:

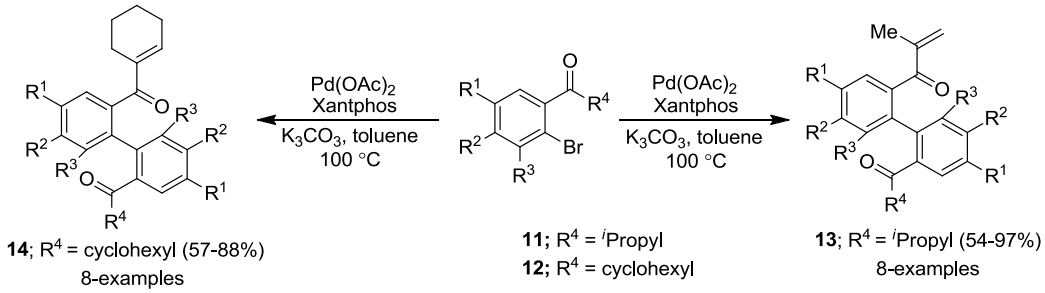
After the accomplishment of 7-methyl-5*H*-dibenzo[*a*,*c*][7]annulen-5-ones **2**, we were interested to know the outcome in the presence of external haloarenes. Therefore, 2-bromoacetophenones **1** were treated with external iodoarenes **9** in the presence of a [Pd]-catalyst. To our surprise, the expected bi-aryl product was not observed, rather impeded at α-arylation and furnished **10** without affecting the bromo-substituent of **1**. The reaction was successful under slightly different conditions to that mentioned in Scheme 2. The reaction was amenable with different iodoarenes **9** having electron withdrawing and electron donating substituents on the aromatic ring. The reaction was completed in a shorter reaction time (i.e., typically 45 min to 3 h) and furnished the α-arylation products **10** in very good yields as shown in Scheme 2.



Scheme 2

Synthesis of bi-aryls via domino [Pd]-catalysis:

After the successful accomplishment of 7-methyl-5*H*-dibenzo[*a*,*c*][7]annulen-5-ones **2** and the synthesis of α-arylation products **10** through [Pd]-catalysis, we were fascinated about the outcome when 2-bromoarylisopropyl ketones **11** or 2-bromoarylcyclohexylketones **12** were subjected to palladium catalysis. Hence, 2-bromoarylisopropyl ketones **11** or 2-bromoarylcyclohexylketones **12** were reacted in the presence of the [Pd]-catalyst. Quite surprisingly, slight modification of the reaction conditions (i.e., with base K_2CO_3 and solvent toluene), showed a dramatic effect and was furnished only the bi-aryl products **13**/**14** in a controlled fashion (Scheme 3).



Scheme 3

In addition to the NMR and other spectroscopic studies for structural elucidation, the structure of bi-aryl **13** was further unambiguously confirmed by single crystal X-ray diffraction analysis (Figure 2).

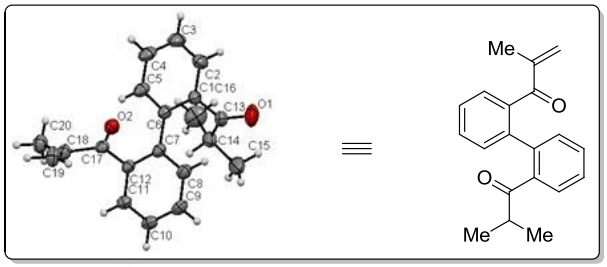


Figure 2

Significantly, the biaryl core constitutes a privileged structural motif that is found in approximately 4.3% of all biologically active natural products. Some of the notable examples are (+)-isoschizandrin **15**, valoneaic acid **16** and valsartan **17** (Figure 3).

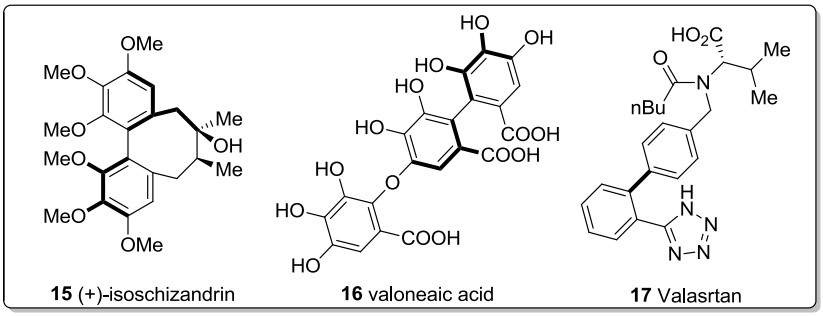
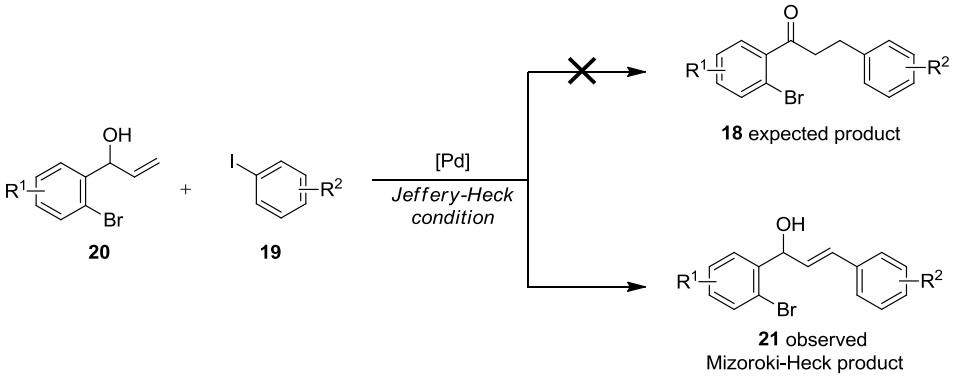


Figure 3

Synthesis of β-aryl allylic alcohols via [Pd]-catalysis:

In continuation with our research interest on [Pd]-catalysis in the second chapter, it was envisioned that the targeted dihydrochalcones **18** could be achieved by employing [Pd]-catalyzed cross-coupling of aryl halides **19** with allylic alcohols **20** under traditional Jeffery-Heck conditions (Scheme 4**)**.

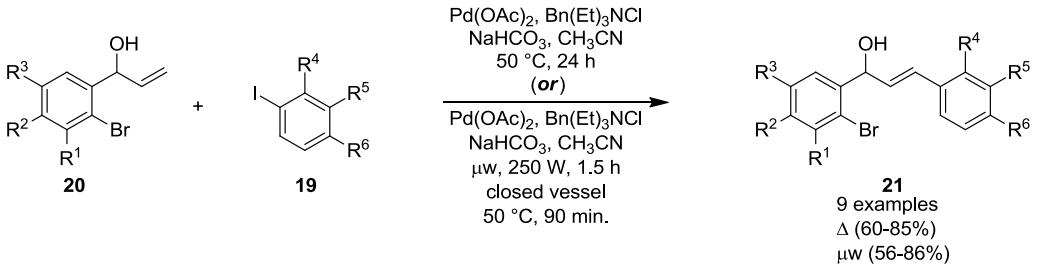


Scheme 4

Therefore, the palladium catalyzed coupling was carried out between the aryl iodide **19** and the allylic alcohol **20**, under typical Jeffery-Heck conditions. To our

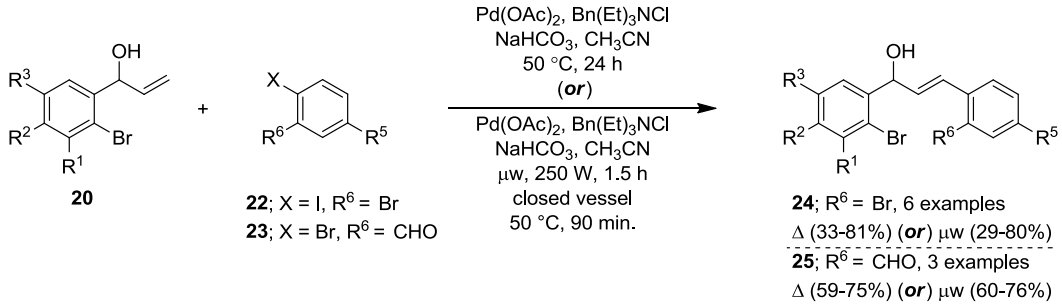
surprise, exclusively β-aryl allylic alcohol **21** was isolated rather than the expected β-aryl carbonyls **18**. Based on the careful study of the literature, we realized that the usual Heck followed by double bond isomerization to give the carbonyl compounds was observed only for those substrates having no *ortho*-substituents on the aromatic ring of the allylic alcohols. As a result, from the present study, it was thought that the bromo-substituent at the *ortho*-position on the aromatic moiety of the allylic alcohol plays a major role to confine the rotation around C-C bond of the PdCH−CH(OH)Ar intermediate. The reason for the restricted rotation of the Pd-intermediate around the C-C bond may be due to the more bulky nature of *ortho*-bromoaryl moiety of the allylic alcohol and thus suppresses the formation of enol via the double isomerization. As a result, the reaction impeded after Mizoroki-Heck coupling and furnished β-aryl allylic alcohol **21**.

Thus, the optimized conditions were applied to different aryl iodides **19** in conjunction with allylic alcohols **20**. Interestingly, the method was quite successful on a variety of aryl iodides **19** in combination with allylic alcohols **20**, and furnished the corresponding products **21** in fair to very good yields using conventional conditions (60 to 84%, Scheme 5). Also, it was found that the reaction was amenable under microwave irradiation condtions and delivered products **21** in comparable yields to that of conventional ones (56 to 86%, Scheme 5).



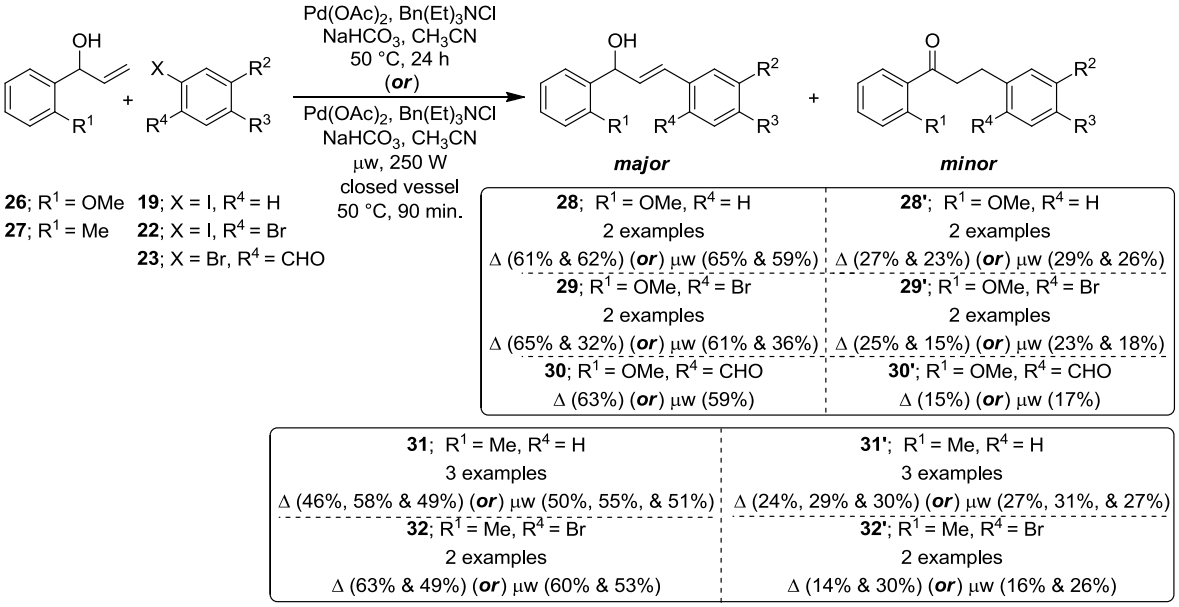
Scheme 5

Interestingly, the method was also successful with 1-bromo-2-iodobenzenes **22** as well as 2-bromobenzaldehydes **23** as coupling partners to the allylic alcohols **20** and furnished β-aryl allylic alcohols **24**/**25** (Scheme 6).



Scheme 6

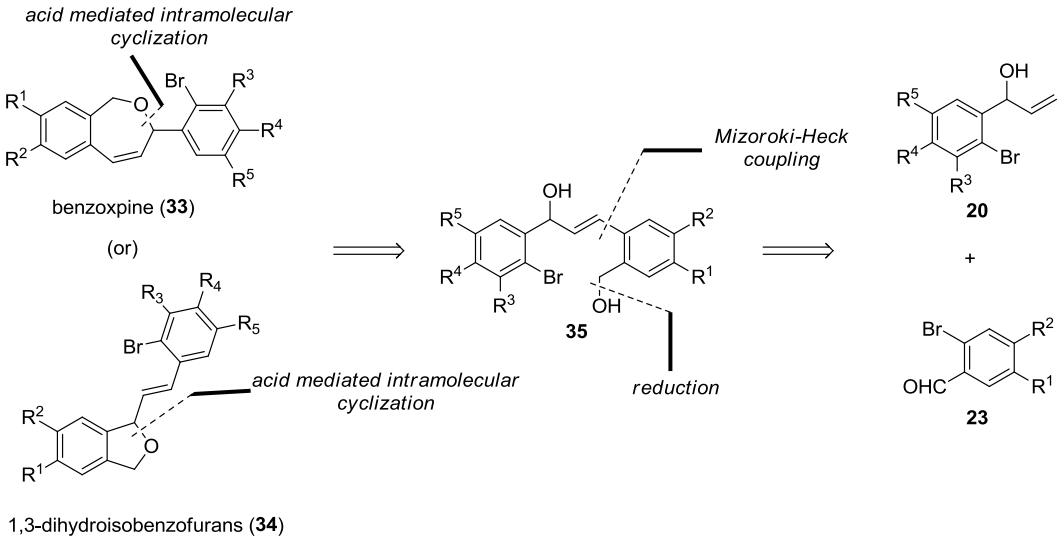
Assuming that the steric hindrance of the substituents at the *ortho* position accounted for the resulting β-aryl allylic alcohols and to probe this hypothesis of *ortho* effect, bromine at *ortho* position was replaced with methoxy or methyl group. Finally, to better understand the nature of steric and electroinc factors that influence the selective formation of β-aryl allylic alcohols **21**/**24**/**25**, we performed the reaction by choosing 2-methoxy/methyl aryl allylic alcohol **26**/**27** as coupling partners. As expected, the reaction favored the formation of β-aryl allylic alcohols **28-32** as a major product in a highly regio- and stereoselective manner along with the β-aryl carbonyls **28'-32'** as minor products (Scheme 7).



Scheme 7

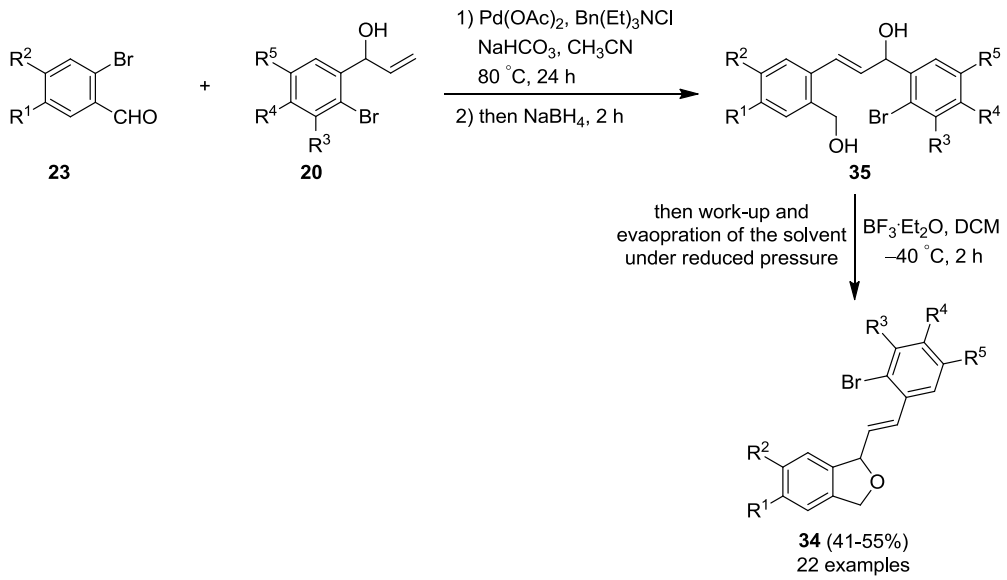
Sequential one-pot approach for the synthesis of 1, 3-dihydroisobenzofurans via [Pd]-catalysis:

Significantly, the above method enabled us with interesting β-aryl allylic alcohols with dense functionality on either of the aromatic rings. Amongst the β-aryl allylic alcohols **21**, **24**, **25**, **28**, **29**, **30**, **31** & **32** those with aldehyde functionality on the aromatic ring (i.e., **25**) appeared to be the potential synthetic precursor for the synthesis of oxygen containing heterocyclic compounds. In this regard, we envisioned a short and efficient synthesis of interesting cyclic ethers such as benzoxepines **33** or 1,3-dihydroisobenzofurans **34** that could be possible by employing reduction and acid mediated intramolecular cyclization protocol on β-aryl allylic alcohols **20**. According to our retrosynthetic analysis, the possible benzoxepine **33** or 1,3-dihydroisobenzofurans **34** can be obtained by acid mediated cyclization of diol, which in turn can be synthesized easily from reduction of readily synthesized **25** (Scheme 8).



Scheme 8

Thus, the [Pd]-catalyzed coupling of 2-bromobenzaldehydes **23** with the allylic alcohols **20** followed by $NaBH_4$ induced in-situ reduction of the coupled aldehyde products **25** gave the desired diols **35**. In order to make the method more efficient, the crude diols **25** without the column purification was subjected to the Lewis acid ($BF_3{\cdot}Et_2O$) mediated cyclization at **–**40 ^oC. Gratifyingly, the reaction was found to be smooth on the crude diols **35** (i.e., on the crude diol **25** which was obtained after the work-up followed by concentration under reduced pressure) and exclusively furnished the product **34** in moderate over all yields (Scheme 9). This may be due to the reason that the formation of five membered cyclic ether **34** would be feasible over the seven membered one **33**. It is worth mentioning that, although, the yields of the cyclic ether products **34** are moderate, they actually represent the overall yield of three individual reactions. Therefore, each step contributes for at least 75% yield and hence the method still stands efficient.



Scheme 9

Oxygen containing heterocyclic compounds are widely assayed for their substantial therapeutic applications such as tetrahydroisobezofurans motifs. They are pervasive structural elements in biologically relevant small molecules (Figure 4). 3-Deoxyisochracinic acid **36** was isolated from cladosporium species shows antibacterial activity by inhibiting the growth of B.subtilis. The cyclic ether pestacin **37** was obtained from microorganism pestalotipsis microspore and shows antifungal, antimycotic and antioxidant activity. FR 198248 **38** was isolated from aspergillus flavipes F543 whereas FR 202306 **39** was obtained from aspergillus terreus 13830. Both of them show antibacterial activity and inhibitory activity against staphylococcus aureus peptide deeformylase and also exhibit anti-influenza activity (Figure 4).

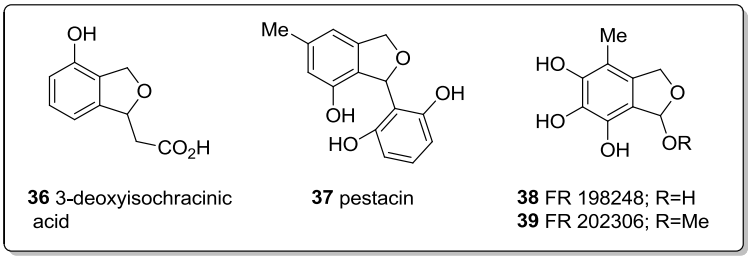
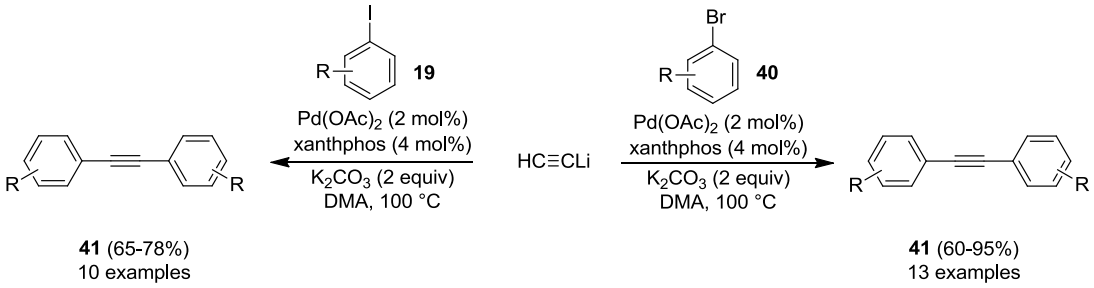


Figure 4

Domino [Pd]-catalysis: synthesis of bi-aryl acetylenes:

In the third chapter, we have described a domino [Pd]-catalysis by the direct cross coupling of commercially available simple and cheap lithium acetylide (i.e., as the source of acetylene) with aryl halides, in a domino one-pot manner. At first this method was successfully implemented on bromoarenes **40** as coupling partners for the synthesis of symmetrical bi-aryl aceteylenes. Significantly, the reaction showed a wide range of functional group tolerance. For example, halo arenes with alkyl, aryl, alkyloxy, chloro, trifluoromethyl and nitro groups were successful in delivering the bi-aryl aceteylenes **41**. Interestingly, the reaction was successful with hetero aryl bromides as well. To further check the scope of the method, we next explored the reaction with iodoarenes **19** as coupling partners. Quite interestingly, the reaction showed a very good functional group tolerance, particularly, when there was a bromo-substituent along with iodo one on the aromatic ring, the bromo-substituent did not involve in the reaction and remained intact in the products (Scheme 10).



Scheme 10

LIST OF ABBREVIATIONS

Ac	:	acetyl
Anal	:	analysis
Anhy	:	anhydrous
APCI	:	atmospheric pressure chemical ionization
Ar	:	aryl
aq	:	aqueous
Bn	:	benzyl
br. s	:	broad singlet
calcd	:	calculated
cm	:	centi meter
cy	:	cyclohexyl
CPD	:	carbon proton decoupling
DCE	:	dichloro ethane
DCM	:	dichloro methane
dd	:	doublet of a doublet
ddd	:	doublet of a doublet of doublet
dt	:	doublet of a triplet
DIPA	:	N,N-diisopropyl amine
DMA	:	N,N-Dimethyl acetamide
DMF	:	N,N-dimethyl formamide
DMSO	:	dimethyl sulfoxide
equiv	:	equivalents
Et	:	ethyl
ESI	:	electron spray ionization
Fig.	:	figure
g	:	gram(s)

h	:	hour(s)
HR-MS	:	high resolution mass spectrum
Hz	:	Hertz
^{i}pr	:	iso propyl
IR	:	infrared
Liq	:	liquid
Lit.	:	literature
m	:	multiplet
Me	:	methyl
mg	:	milli gram(s)
MHz	:	mega hertz
min	:	minute(s)
mL	:	milliliter(s)
mmol	:	milli mole(s)
M.P	:	melting point
MS	:	molecular sieves
NMR	:	Nuclear Magnetic Resonance
ph	:	phenyl
q	:	quartet
R_f	:	Retention factor
rt	:	room temperature
sept	:	septet
t	:	triplet
TEBAC	:	triethylbenzylammonium chloride
tert	:	tertiary
THF	:	tetrahydrofuran
TLC	:	thin layer chromatography
UV	:	ultra violet

Contents

CHAPTER I

DOMINO [Pd]-CATALYSIS: SYNTHESIS OF 7-METHYL-5H-DIBENZO[a,c][7]ANNULEN -5-ONES AND BI-ARYLS

I.1 INTRODUCTION:

Constituting a carbon-carbon bond is one of the most fundamental operations in organic synthesis. In general, the synthesis of organic molecules involves a step-wise operation for the construction of individual bonds. These synthetic transformations become more efficient and viable when several bonds are formed in a one-pot fashion and/or in a sequential one-pot manner without isolating the reaction intermediates/intermediate products, such reactions can be called as domino or sequential domino one-pot reactions, respectively. The latter one would be feasible by altering the reaction conditions or by the addition of reagents to promote the subsequent reaction(s) once after the initial step(s) is/are completed. Particularly, the domino processes promoted by [Pd]-catalysis possesses a great potential for elaboration and the

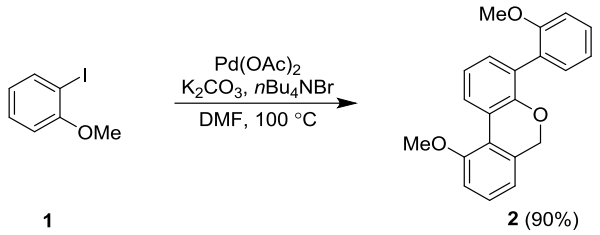
development of new synthetic methods that eventually represent a new frontier to conquer in organic chemistry. These domino strategies elaborate the scope of the traditional cross-coupling chemistry due to more efficient and fast construction of molecular complexity from comparatively uncomplicated building blocks. Such transformations are also called as tandem, sequential, cascade, consecutive, iterative, zipper or one-pot (one-flask) reactions and these link several transformations together in a single synthetic operation. Domino reactions have gained wide acceptance due to increase in efficiency of a reaction by decreasing the number of synthetic transformations, the quantities of reagents and solvents used for workup procedures, column chromatography and minimization of waste and energy. Therefore, these reactions have their own significance with respect to ecological and economical aspects.[1]

One of the leading proponents, Prof. L. F. Tietze, Georg-August University in Gottingen, Germany, the term "domino reaction" is defined as follows: domino reaction is a process which involves two or more bond-forming transformations (usually C-C bonds) that take place under the same reaction conditions without adding additional reagents and catalysts and in which the subsequent reactions result as a consequence of the functionality formed in the previous step.[2]

I.2 BACKGROUND:

Domino organic transformations have been successfully applied in many kinds of organic reactions. Significantly, in the recent past many research groups have explored one-pot domino transition-metal-catalysis. In this regard, [Pd]-metal was found to be one amongst the transition metals employed in domino transformation. Some of the interesting examples of domino transformations mediated by [Pd]-catalyst are described as follows:

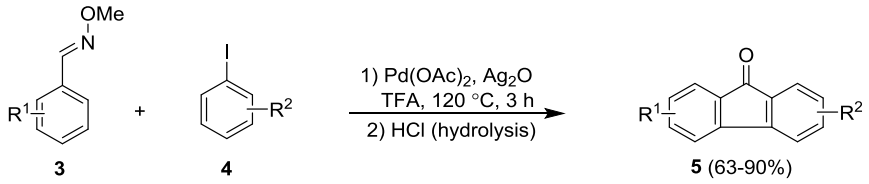
In 1994 the research group of Gerald Dyker discovered an efficient method for the synthesis of annulated pyran derivative **2** from 2-iodoanisole **1**. The reaction proceeded through an unprecedented domino [Pd]-catalysis by the C-H activation of methoxy group (Scheme I.1).[3]



1 **2** (90%)

Scheme I.1

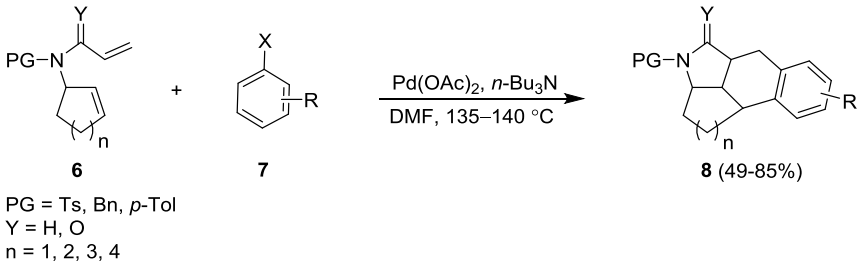
Cheng and co-workers reported the synthesis of fluorenones **5** from aromatic aldoxime ethers **3** and aryl halides **4** by [Pd]-catalyzed dual C-H activation. This strategy is based on the directing-group-assisted activation of *ortho* aromatic C-H bonds and subsequent C-C bond formation (Scheme I.2). [4]



3 **4** **5** (63-90%)

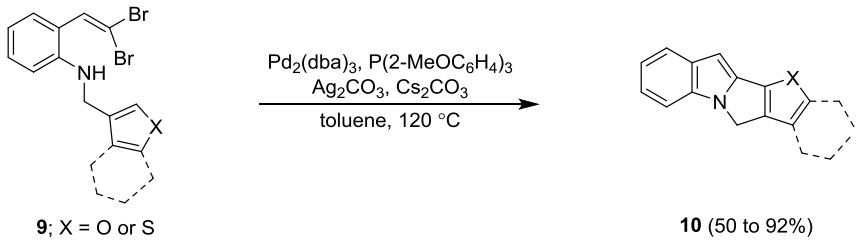
Scheme I.2

Hu et al. discovered a novel domino Heck cyclization method involving carbopalladation and the subsequent regioselective functionalization of an unactivated C-H bond for the preparation of benzocyclo[penta- to octa-]isoindole core **8** (Scheme I.3).[5]



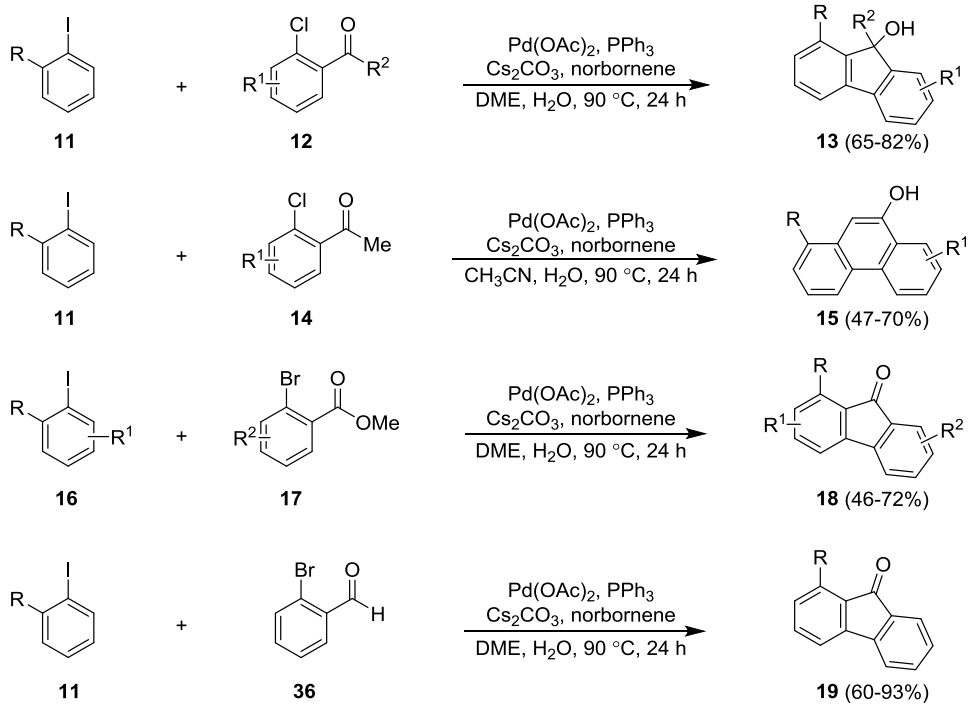
Scheme I.3

Mark Lautens and co-workers reported an efficient strategy for the synthesis of polycyclic heteroaromatics **10** from [Pd]-catalyzed domino Buchwald-Hartwig amination/direct arylation reaction from readily available gem-dibromovinyl substrates **9** (Scheme I.4).[6]



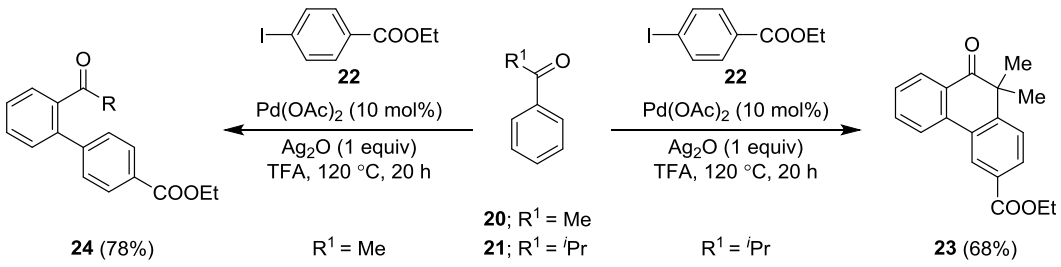
Scheme I.4

The same research group developed sequential domino *ortho*-arylation and a subsequent addition to the carbonyl group for the synthesis of fluorene derivatives **13**, **18** and **19** and various phenanthrenes **15**. The reaction was performed on 2-chloroaryl ketones **12** and **14**, 2-bromobenzoates **17** and **2-**bromobenzaldehydes **35** with aryl iodides **11** and **16** as coupling partners (Scheme I.5).[7]



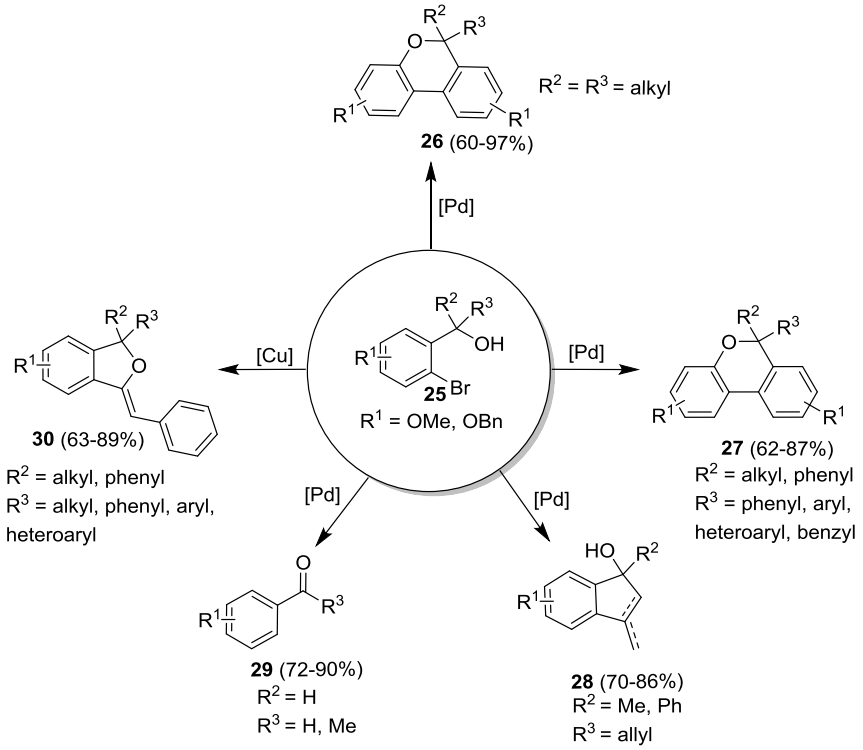
Scheme I.5

Since $Pd(OAc)_2/Ag_2O$ is known to be an effective catalyst system for *ortho* C-H functionalization, the research group of Cheng used [Pd]-catalysis for the reaction of acetophenone **20** as well as on aryl isopropyl ketone **21** with aryl iodides **22**. The reaction gave a simple *ortho*-arylated product **24** with acetophenone **20** whereas phenanthrone derivative **23** was obtained as the product with aryl isopropyl ketone **21** through *ortho* arylation followed by intramolecular C-H activation. (Scheme I.6).[8]



Scheme I.6

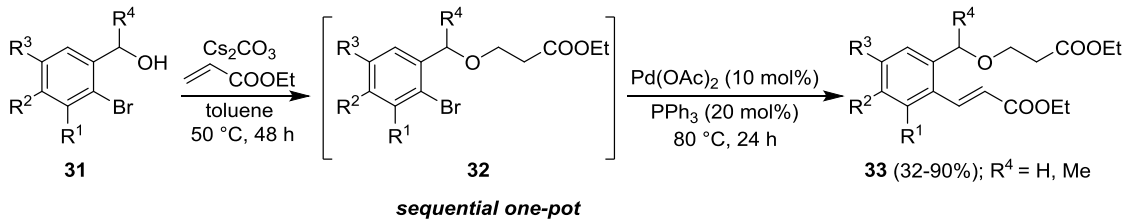
As a part of our research interest on domino transition-metal catalysis,[9] we have disclosed an efficient and unprecedented [Pd]-catalyzed domino transformation of *ortho*-bromobenzyl tertiary alcohols **25** to chromenes **26** and **27**, indenols **28** (Scheme I.7).[9k, l] Whereas, in the case of primary/secondary benzylic alcohols furnished the simple carbonyl products **29** as shown in Scheme I.7. Also, we have accomplished the synthesis of isobenzofurans **30** using domino [Cu]-catalyzed Sonogashira coupling of *ortho*-bromobenzyl tertiary alcohols **25** with terminal aryl-acetylenes and intramolecular anti-5-exo-dig cyclization.[9m] These structures are present in many biologically active natural products.



Scheme I.7

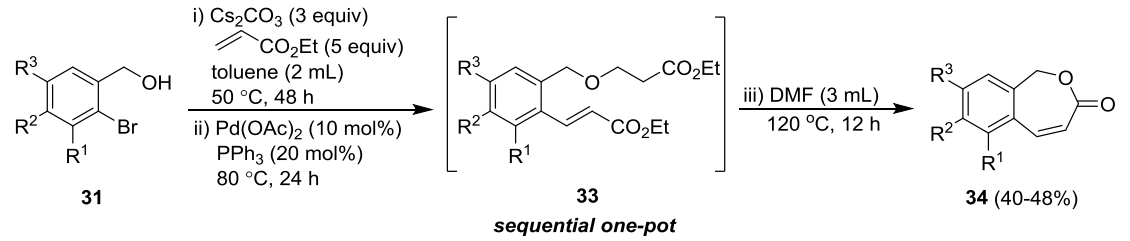
Also, we successfully carried out the synthesis of functionalized diester **33** in a novel domino sequential one-pot process starting from readily available 2-bromobenzyl

alcohols **31**. The reaction proceeds through an intermolecular oxy-Michael addition and intermolecular Heck coupling for the formation of the diester **33** (Scheme I.8).[9d]



Scheme I.8

Further, the method was successfully applied to the synthesis of interesting 2-benzoxepin-3(1*H*)-ones **34** in a sequential one-pot manner (Scheme I.9). Significantly, these 2-benzoxepin-3(1*H*)-ones **34** constitutes the major core of biologically active natural products. Notably, the base promoted condensation involves an interesting reaction path as follows: (i) intramolecular degradation (retro-oxy-Michael addition), (ii) intramolecular Michael addition, (iii) cyclo revision through double isomerization and (iv) finally, intramolecular condensation (Scheme I.9).[9f]

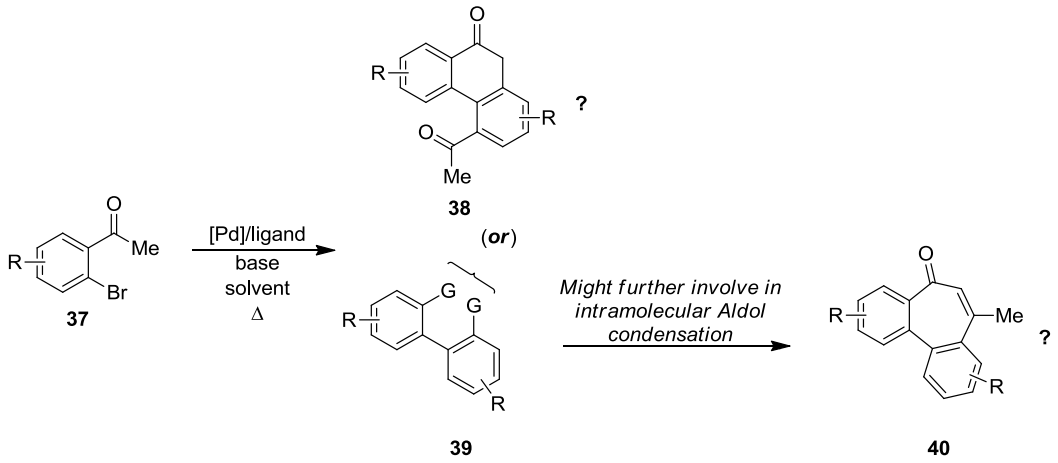


Scheme I.9

I.3. RESULTS AND DISCUSSION:

I.3.1 Synthesis 7-Methyl-5H-dibenzo[a,c][7]annulen-5-ones via domino [Pd]-catalysis:

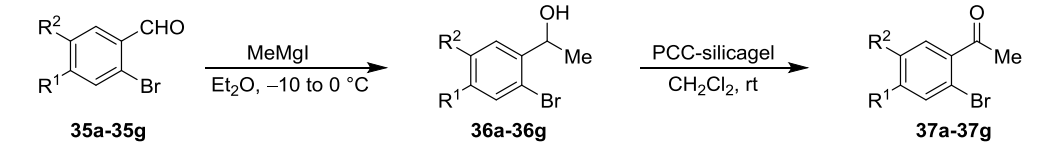
With this background and based on our research interest on transition-metal catalyzed domino/sequential one-pot processes to develop new synthetic methods, we became interested to explore the [Pd]-catalysis on 2-bromoacetophenones **37**. The inspiration behind this study is based on the efficient synthesis of chromenes **26** and **27** from *ortho*-bromobenzyl tertiary alcohols **25**,[9k] which involves a domino homo coupling of two molecules that establish the bi-aryl bond in the presence of the [Pd]-catalyst (Scheme I.7). Therefore, we envisioned that the [Pd]-catalyzed reaction of 2-bromoacetophenones **37** might lead to the formation of homo bi-aryl ketones **38**. On the other hand, the reaction might not simply stop at the homo bi-aryl ketones **38**, rather could proceed further to give either phenanthroline derivative or 7-methyl-5*H*-dibenzo[*a*,*c*][7]annulen-5-ones **40** via intramolecular Buchwald-Hartwig coupling or Aldol condensation, as depicted in Scheme I.10.[9e]



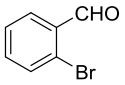
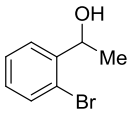
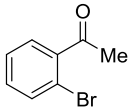
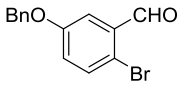
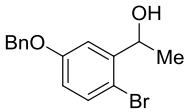
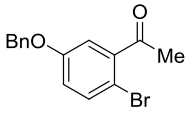
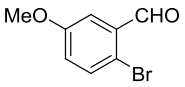
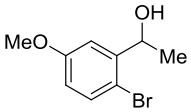
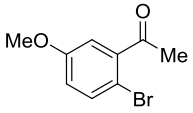
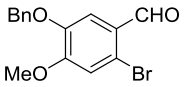
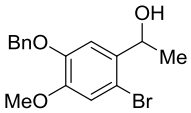
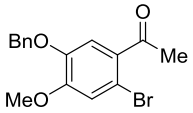
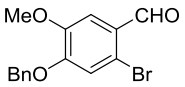
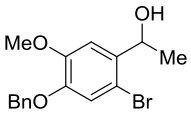
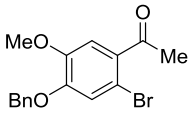
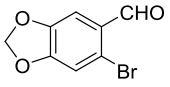
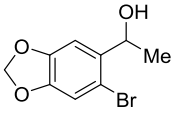
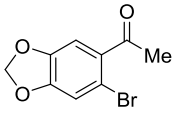
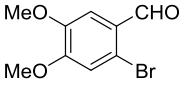
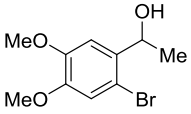
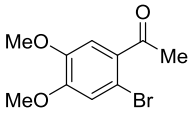
Scheme I.10

The required 2- bromoacetophenone **37** were accomplished by the addition of methyl Grignard reagent to 2-bromobenzaldehydes **35** furnished secondary alcohols **36** in very good to excellent yields (82-95%, Table I.1). Oxidation of the secondary alcohols **36** with PCC-silica gel, gave 2-bromoacetophenone **37** in good to excellent yields (73-97%, Table I.1).[10]

Table I.1: Synthesis of 2-bromoacetophenones **37a-37g** from corresponding 2-bromobenzaldehydes **35a-35g**.[a]



35a-35g **36a-36g** **37a-37g**

 **35a**	 **36a** (90%)	 **37a** (94%)
 **35b**	 **36b** (95%)	 **37b** (99%)
 **35c**	 **36c** (95%)	 **37c** (97%)
 **35d**	 **36d** (95%)	 **37d** (97%)
 **35e**	 **36e** (82%)	 **37e** (92%)
 **35f**	 **36f** (90%)	 **37f** (73%)
 **35g**	 **36g** (86%)	 **37g** (94%)

Reaction conditions: [a]Yields in the parentheses are isolated yields of chromatographically pure products.

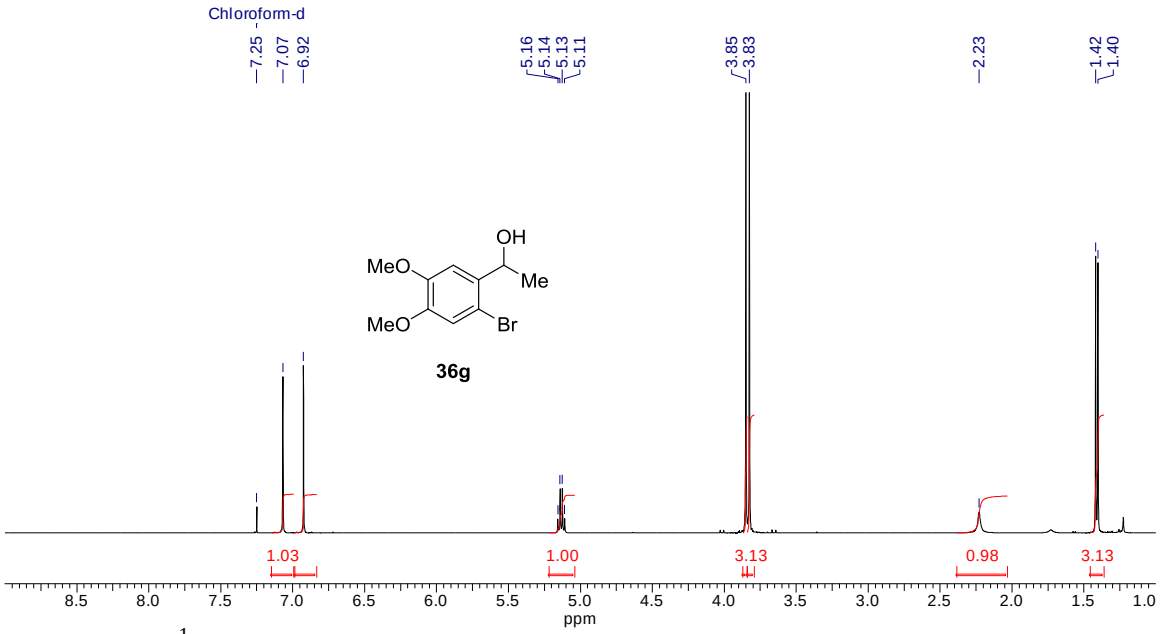


Figure I.1.1: ^{1}H-NMR (400 MHz) spectrum of **36g** in $CDCl_3$

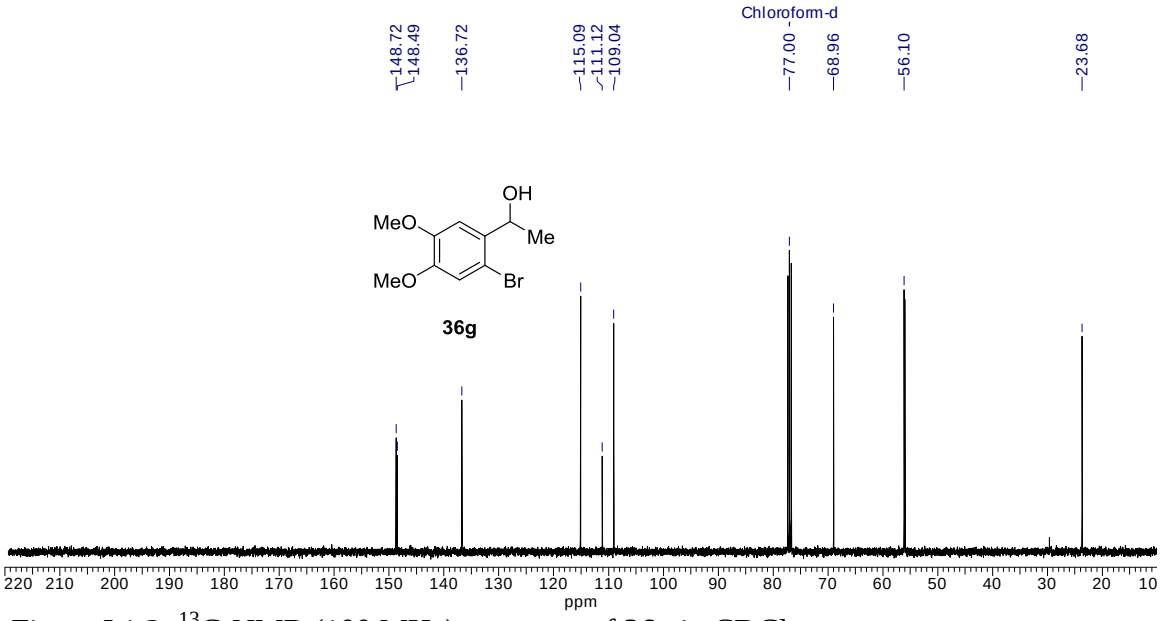


Figure I.1.2: ^{13}C-NMR (100 MHz) spectrum of **36g** in $CDCl_3$

The structure of secondary alcohol **36g** was confirmed from the spectral data analysis. IR spectra shows the absence of the absorption band due to carbonyl stretching

of aldehyde group and the presence of broad absorption band due to OH stretching at 3416 cm^{-1}. In the ^{1}H-NMR spectrum (Figure I.1.1), the presence of two singlets at δ 7.07 and 6.92 due to two aromatic protons, presence of quartet at δ 5.14 having *J*=6.4 Hz due to benzylic methine group proton, two singlets at δ 3.85 and 3.83 due to six protons of two methoxy groups, presence of broad singlet at δ 2.23 due to hydroxyl proton and presence of doublet at δ 1.41 ppm having *J*=6.4 Hz due to three protons of methyl group, elucidated the structure of secondary alcohol **36g**. In addition, the 10 signals in ^{13}C-NMR spectrum (Figure I.1.2) in which four quaternary carbon resonates at δ 148.7, 148.5, 136.7 and 111.1 were due to four aromatic carbons, the presence of two aromatic methine carbons at δ 115.1 and 109.0, benzylic methine carbon resonates at δ 69.0, two quartets at δ 56.1 and 55.9 were due to two methoxy groups and quartet at δ 23.7 ppm was due to methyl group. The presence of $[(M+H)-H_2O]^+$ peak at m/z $[C_{10}H_{12}{}^{91}BrO_2]^+$= 244.9979 in the mass spectrum further established the structure of secondary alcohol **36g**.

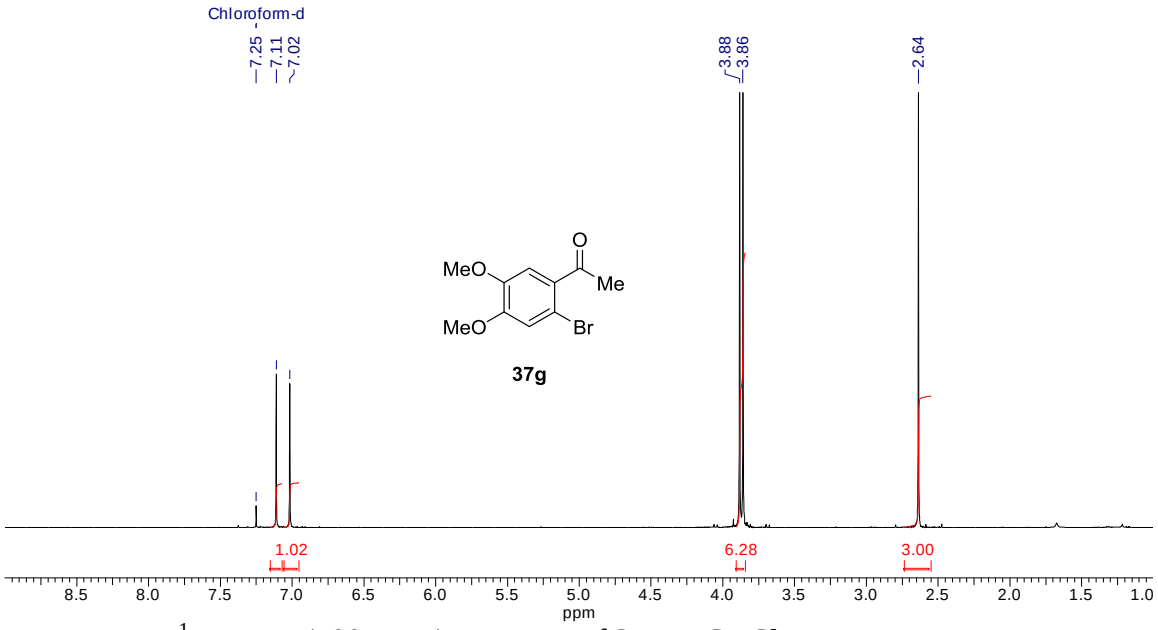


Figure I.2.1: ^{1}H-NMR (400 MHz) spectrum of **37g** in $CDCl_3$

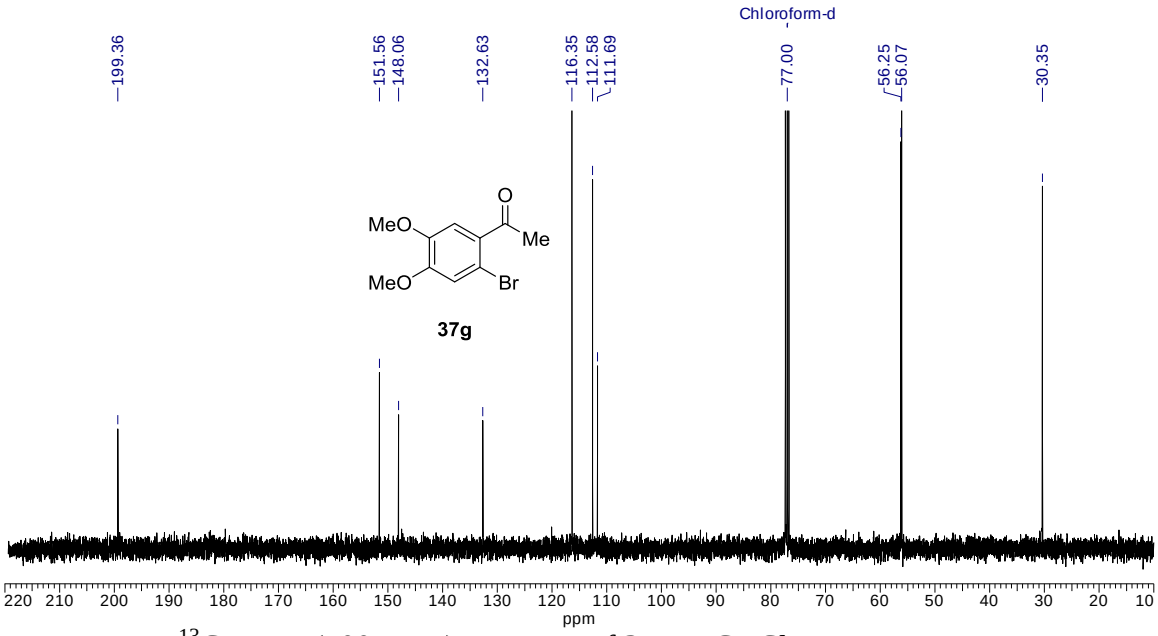
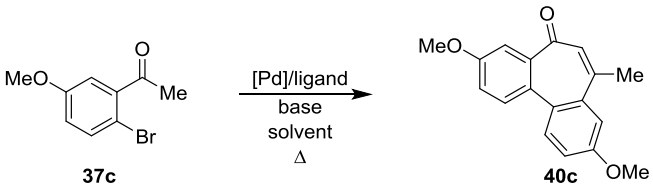


Figure I.2.2: ^{13}C-NMR (100 MHz) spectrum of **37g** in $CDCl_3$

The structure of 2-bromoacetophenone **37g** was confirmed from the spectral data analysis. IR spectra shows the absence of broad absorption band due to OH group stretching and the presence of absorption band due to carbonyl group stretching at 1687 cm^{-1}. In the ^{1}H-NMR spectrum (Figure I.2.1), the presence of two individual singlets at δ 7.11 and 7.02 due to two aromatic protons, two singlets at δ 3.88 and 3.86 due to six protons of two methoxy groups, the presence of singlet at δ 2.64 ppm due to three protons of methyl group, elucidated the structure of 2-bromoacetophenone **37g**. In addition to it, 10 signals appeared in ^{13}C-NMR spectrum (Figure I.2.2) in which one quaternary carbon resonates at δ 199.4 was due to carbonyl carbon, four quaternary carbon resonates at δ 151.6, 148.1, 132.6 and 111.7 were due to four aromatic carbons, the presence of two aromatic methine carbons at δ 116.4 and 112.6, two quartets at δ 56.2 and 56.1 were due to two methoxy groups and a quartet at δ 30.3 ppm was due to methyl group. Presence of the $[M+H]^+$ peak at m/z $[C_{10}H_{12}BrO_3]^+$=258.9950 and $[C_{10}H_{12}{}^{81}BrO_3]^+$=260.9943 in the mass spectrum further established the structure of 2-bromoacetophenone **37g**.

Now the requisite 2-bromoacetophenone **37c** in hand, the 2-bromoacetophenone **37c** was chosen as the model compound for the [Pd]-catalysis as depicted in Table I.2. Initially, the reaction was performed with $Pd(OAc)_2$ (5 mol%), PPh_3 (10 mol%) and Cs_2CO_3 in toluene at 110 °C for 26 h. Interestingly, the reaction furnished 7-methyl-5*H*-dibenzo[*a*,*c*][7]annulen-5-one **40c** as an exclusive product albeit in very poor yield (13%, Table I.2, entry 1). In order to find out the best optimized reaction conditions for the synthesis of 7-methyl-5*H*-dibenzo[*a*,*c*][7]annulen-5-ones **40c**, the reaction was explored under different set of reaction conditions and the results are summarized in the Table I.2. Thus, using DMF and dioxane as solvents slightly improved the yield of the product **40c** (Table I.2, entry 2 and 3). On one hand, the reaction under different ligands (PPh_3, dppf, **L1**, **L2**, **L3** and **L4**) in conjuction with the base K_3PO_4 was unsuccessful to improve the yield (Table I.2, entries 5-11) while the combination of $Pd(OAc)_2$ and $P(Cy)_3$ furnished the product **40c** with slight increment of the yield (32%, Table I.2, entry 12). On the other hand, the use of different catalysts in combination with either Cs_2CO_3 or K_3PO_4 led to a less progressive yield (Table I.2, entries 13-16). There was a further drop in the yield, when the reaction was conducted with bi-aryl ligand **L5** (16%, Table I.2, entry 17). The yield of the product still remains poor in the presence of the ligand **L5** with the bases K_3PO_4/Cs_2CO_3 (Table I.2, entries 18-21). Interestingly, the ligand **L5**, furnished the product in moderate yield (50% Table I.2, entry 22). To improve the yield further, the reaction was explored with various additives, however, there was no considerable impact on the yield of the product **40c** (Table I.2, entries 23 to 32). Moreover, an extensive survey of bases, solvents, time and temperature by keeping the ligand **L5** as constant failed to improve the yield of product **40c** (Table I.2, entries 33 to 48) and also the reaction with $Pd(OAc)_2$ without the ligand while keeping all the other parameters constant (yield 30%, Table I.2, entry 49) was also not fruitful.

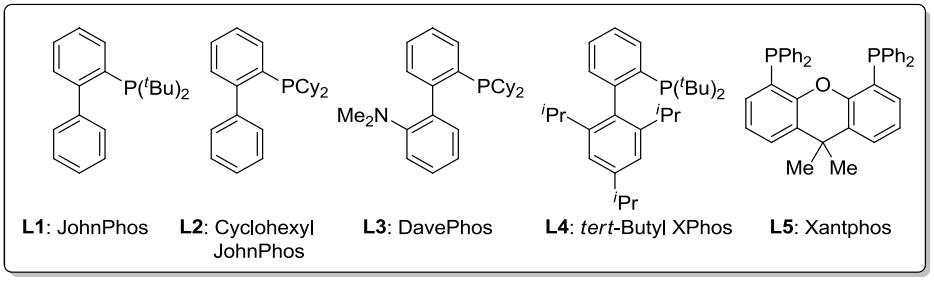
Table **I.2**: Optimization table for the synthesis of 3,9-dimethoxy-7-methyl-5*H*-dibenzo [*a*,*c*] [7]annulen-5-one **40c**.



Entry[a]	Catalyst (mol%)	Ligand (mol%)	Additive (equiv)	Solvent (mL)	Base (equiv)	Temp (°C)	Time (h)	Yield (%)[b]
1	$Pd(OAc)_2$ (5)	PPh_3 (10)	-	toluene (3)	Cs_2CO_3 (2)	110	26	13
2	$Pd(OAc)_2$ (10)	PPh_3 (20)	-	DMF (1.5)	Cs_2CO_3 (2)	120	24	22
3	$Pd(OAc)_2$ (5)	PPh_3 (10)	-	THF (2)	Cs_2CO_3 (2)	50	60	0[c]
4	$Pd(OAc)_2$ (5)	PPh_3(10)	-	dioxane (2)	Cs_2CO_3 (2)	110	60	22
5	$Pd(OAc)_2$ (5)	PPh_3 (10)	-	DMF (2)	K_3PO_4 (2)	120	5	29
6	$Pd(OAc)_2$ (5)	dppf (10)	-	DMF (2)	K_3PO_4 (4)	100	10	26
7	$Pd(OAc)_2$ (5)	dppf (10)	-	DMF (2)	K_3PO_4 (4)	140	1.5	27
8	$Pd(OAc)_2$ (2)	**L1**(4)	-	DMF (2)	K_3PO_4 (4)	150	3	8
9	$Pd(OAc)_2$ (2)	**L2** (4)	-	DMF (2)	K_3PO_4 (4)	150	3	25
10	$Pd(OAc)_2$ (2)	**L3** (4)	-	DMF (2)	K_3PO_4 (4)	150	3	15
11	$Pd(OAc)_2$ (2)	**L4** (4)	-	DMF (2)	K_3PO_4 (4)	150	3	16
12	$Pd(OAc)_2$ (5)	$P(Cy)_3$ (10)	-	DMF (2)	K_3PO_4 (4)	150	3	32
13	Pd (dppf)Cl_2	-	-	DMF (2)	Cs_2CO_3 (2)	100	18	32
14	$Pd(PPh_3)_4$ (2)	-	-	DMF (2)	Cs_2CO_3 (4)	120	34	11
15	$Pd(PPh_3)_4$ (5)	-	-	DMF (2)	K_3PO_4 (4)	150	3	21
16	$Pd(PPh_3)_2Cl_2$ (5)	-	-	DMF (2)	K_3PO_4 (4)	150	3	30
17	$Pd(OAc)_2$ (2)	**L5** (4)	-	toluene (2)	K_3PO_4 (2)	120	26	16
18	$Pd(OAc)_2$ (2)	**L5** (4)	-	DMF (2)	K_3PO_4 (2)	120	3	27
19	$Pd(OAc)_2$ (4)	**L5** (4)	-	DMF (2)	K_3PO_4 (2)	150	2	32

20	$Pd(OAc)_2$ (2)	**L5** (4)	-	DMF (2)	K_3PO_4 (2)	120	12	29
21	$Pd(OAc)_2$ (2)	**L5** (4)	-	DMF (2)	Cs_2CO_3 (2)	120	3	33
22	**$Pd(OAc)_2$ (2)**	**L5 (4)**	-	**DMF (2)**	**K_3PO_4 (2)**	**150**	**2**	**50**
23	$Pd(OAc)_2$ (2)	**L5** (4)	4Å MS (100mg)	DMF (2)	K_3PO_4 (2)	150	2	45
24	$Pd(OAc)_2$ (2)	**L5** (4)	H_2O (40)	DMF (2)	K_3PO_4 (2)	150	12	23
25	$Pd(OAc)_2$ (2)	**L5** (4)	H_2O (8)	DMF (2)	K_3PO_4 (2)	80	12	22
26	$Pd(OAc)_2$ (2)	**L5** (4)	$ZnCl_2$ (0.2)	DMF (2)	K_3PO_4 (2)	150	2	36
27	$Pd(OAc)_2$ (2)	**L5** (4)	$^nBu_4NBr$ (0.2)	DMF (2)	K_3PO_4 (2)	150	3	25
28	$Pd(OAc)_2$ (2)	**L5** (4)	$^nBu_4NI$ (0.2)	DMF (2)	K_3PO_4 (2)	150	3	24
29	$Pd(OAc)_2$ (2)	**L5** (4)	H_2O (40)	toluene (2)	$CsCO_3$ (2)	80	24	8
30	$Pd(OAc)_2$ (2)	**L5** (4)	H_2O (48)	DMF (3)	K_3PO_4 (2)	150	2	24
31	$Pd(OAc)_2$ (2)	**L5** (4)	Ag_2O	DMF (2)	K_3PO_4 (2)	150	2	0[c]
32	$Pd(OAc)_2$ (2)	**L5** (4)	AgCl	DMF (2)	K_3PO_4 (2)	150	2	0[c]
33	$Pd(OAc)_2$ (2)	**L5** (4)	-	DMSO (2)	K_3PO_4 (2)	150	1	24
34	$Pd(OAc)_2$ (4)	**L5** (4)	-	DMF (2)	^tBuOK(3)	120	12	5
35	$Pd(OAc)_2$ (2)	**L5** (4)	-	DMA (2)	K_3PO_4 (2)	150	2	23
36	$Pd(OAc)_2$ (4)	**L5** (4)	-	DMF (2)	K_3PO_4 (2) and ^tBuOK(2)	120	2	11
37	$Pd(OAc)_2$ (2)	**L5** (4)	-	xylene (2)	K_3PO_4 (2)	150	2	0[c]
38	$Pd(dba)_2$ (2)	–	-	DMF (2)	K_3PO_4 (2)	150	2	20
39	$Pd(dba)_2$ (2)	**L5** (4)	-	DMF (2)	K_3PO_4 (2)	150	2	14
40	$Pd(OAc)_2$ (2)	**L5** (4)	-	DMF (2)	K_2CO_3 (2)	120	24	13
41	$Pd(OAc)_2$ (2)	**L5** (4)	-	DMF (2)	DBU (2)	150	3	0[c]
42	$Pd(OAc)_2$ (2)	**L5** (4)	-	DMF (2)	TEA (4)	150	2	0[c]
43	$Pd(OAc)_2$ (2)	**L5** (4)	-	DMF (2)	DIPEA (5)	120	24	0[c]
44	$Pd(OAc)_2$ (2)	**L5** (4)	-	DMF (2)	2,4,6-colldidine (2)	150	20	0[c]
45	$Pd(OAc)_2$ (2)	**L5** (4)	-	DMF (2)	DABCO (2)	150	3	0[c]
46	$Pd(OAc)_2$ (2)	**L5** (4)	-	DMF (2)	NaOH (3)	120	12	0[c]
47	$Pd(OAc)_2$ (2)	**L5** (4)	-	DMF (2)	KOH (3)	120	12	0[c]
48	$Pd(OAc)_2$ (2)	**L5** (4)	-	DMF (2)	NaH (3)	80	2	0[c]
49	$Pd(OAc)_2$ (2)	–	-	DMF (2)	K_3PO_4 (2)	150	2	30

[a]All reactions were performed on 100 mg (0.44 mmol) scale of **37c**, in 0.22 M concentration, in DMF (2 mL). [b]Isolated yields of chromatographically pure products. [c]No product was formed.

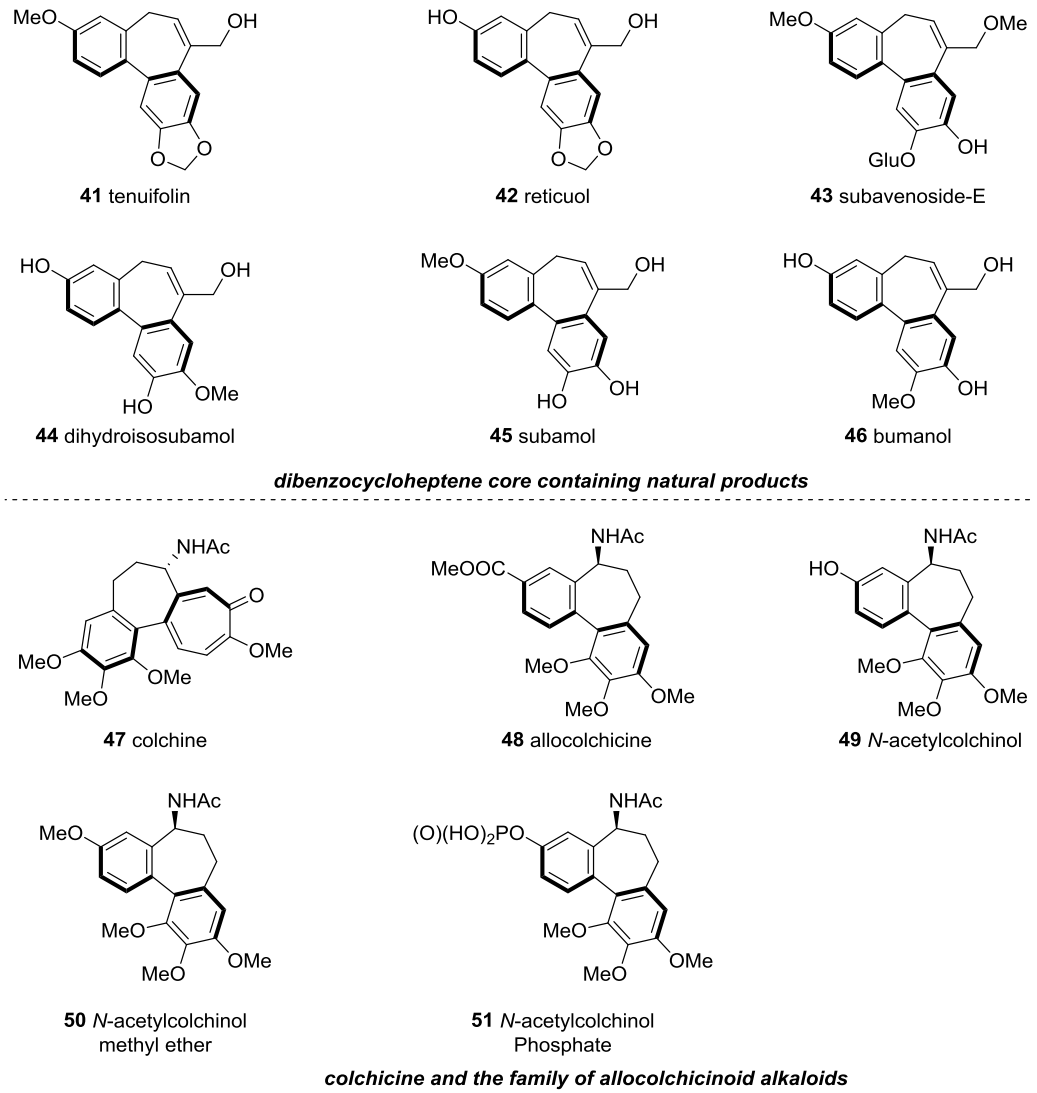


(Figure I.3)

Quite interestingly, from the literature search, it was found that the entire carbon core structure 7-methyl-5*H*-dibenzo[*a*,*c*][7]annulen-5-one **40c** demonstrated biologically active natural products such as dibenzocycloheptanoids and colchicinoids (Figure I.3).[11] For example, tenuifolin **41**,[11a,b] shows antiproliferative activity against tumor cell line DU145. The natural reticuol **42**,[11c,d] acts as the inhibitor of cytochrom P450 (CYP3 A4). Subavenoside-E **43**,[11e] exhibits inhibitory activity against α-glucosidase type IV from Bacillus stearothermophilus. Similarly dihydroisosubamol **44**,[11e] subamol **45**.[11f,g] and bumanol **46**,[11h] also reported to show biological activities. The colchicine **47** and its biphenyl structural analogues are known as allocolchicinoids. The natural cochicinoids namely allocholchicine **48**, N-acetylcholchinol **49**, its methylether **50** and its phosphate **51** are having greater therapeutic activities[11o-q] such as anti-tumour activity, in particular, the main mode of action by binding to cytoskeletal protein tubulin and disruption of the tubulin-microtubule equilibrium (in microtubulin polymerisation) in the cell, thereby causing suppression of the mitosis and cell division. methylether **51** has higher tubulin affinity and better stability than colchicine **47**.[11j-q]

From literature, few reports are available for the synthesis of bi-aryl tricyclic core, which were accomplished using intermolecular Suzuki-Miyaura coupling followed by Aldol condensation protocol,[12] or by intramolecular Heck reaction,[13] or using bi-aryl oxidative coupling[14] or Lewis acid mediated Nicholas cyclization[15]

reaction. It is worth mentioning that all of the above methods were based on step-wise approaches. Significantly, the present method describes about the accomplishment of such tricyclic systems in a domino one pot fashion.

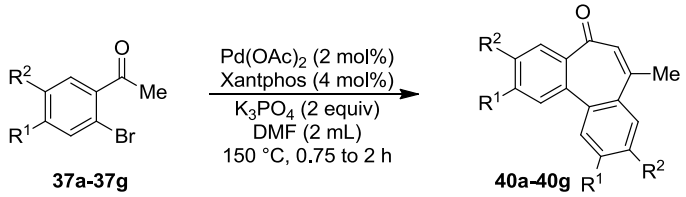


(Figure I.4)

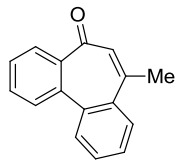
Among all the above screened reaction conditions, the conditions mentioned in Table 2, entry 23 was found to be the best [i.e., 2 mol% of $Pd(OAc)_2$, Xantphos **L5** (4 mol%) and 2.0 equiv of K_3PO_4 in DMF at 150 ^oC]. Although, the product 7-methyl-5*H*-dibenzo[*a*,*c*][7]annulen-5-ones **40c** was obtained in moderate yield 50%, but for a one-

pot domino process of two individual steps (i.e., biphenyl coupling and Aldol condensation) that accounts for approximately 70% yield of each individual step. Therefore, the method is still considered to be an efficient one. Furthermore, the present method was found to be significant when compared with earlier reports which involved more than four steps with overall yield (15%) to accomplish such structurally relevant compounds.[16] Therefore, these optimized conditions (Table 2, entry 23) were applied to other 2-bromoacetophenones **37a-37g** as well. Gratifyingly, the method was amenable and afforded bi-aryl cyclic products **40a-40g** in moderate yields (41-50%), as shown in Table I.3.

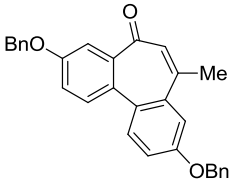
Table I.3: Domino [Pd]-catalyzed synthesis of 7-methyl-5*H*-dibenzo[*a*,*c*][7]annulen-5-ones **40a**-**40g** from 2-bromoacetophenones **37a**-**37g**.[a,b]



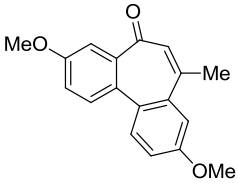
37a-37g **40a-40g**



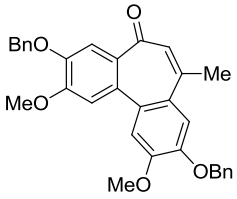
40a (45%)



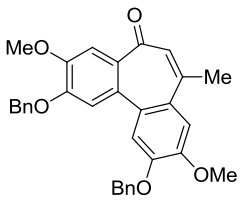
40b (41%)



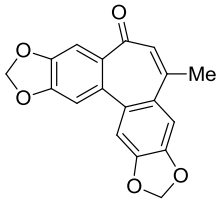
40c (50%)



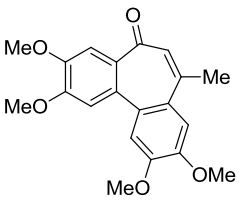
40d (43%)



40e (41%)



40f (41%)



40g (44%)

[a]Reaction conditions: All the reactions were carried out with 2-bromoacetophenones **37a**-**37g** (100-150 mg, 0.30 to 0.58 mmol), in DMF. [b]Yields in the parentheses are isolated yields of chromatographically pure products.

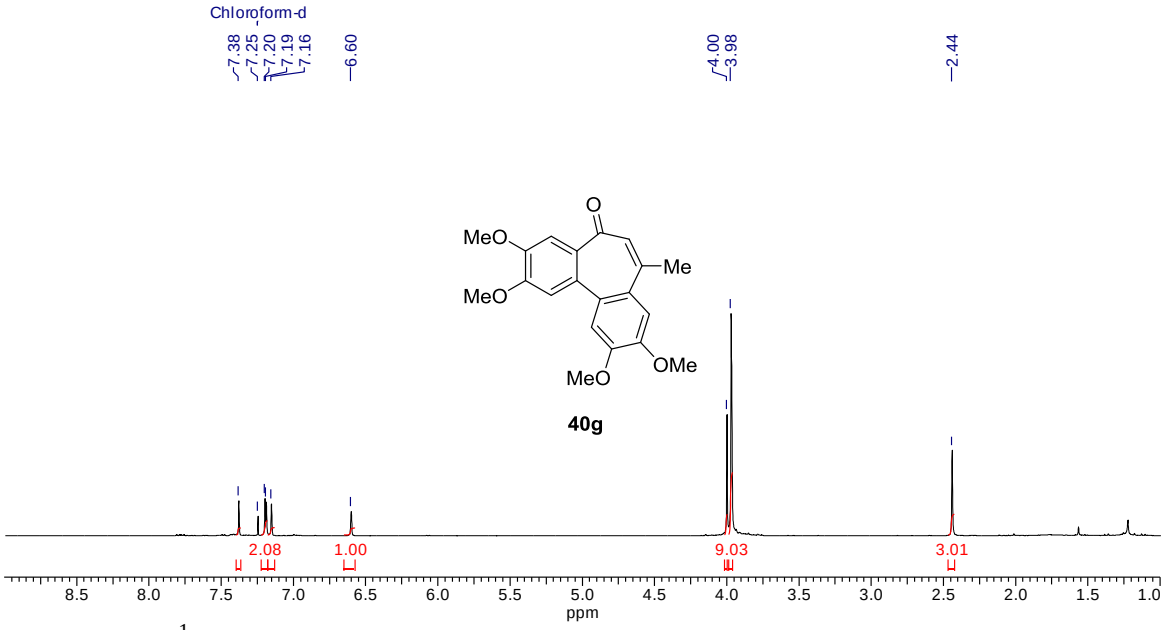


Figure I.5.1: ^{1}H-NMR (400 MHz) spectrum of **40g** in $CDCl_3$

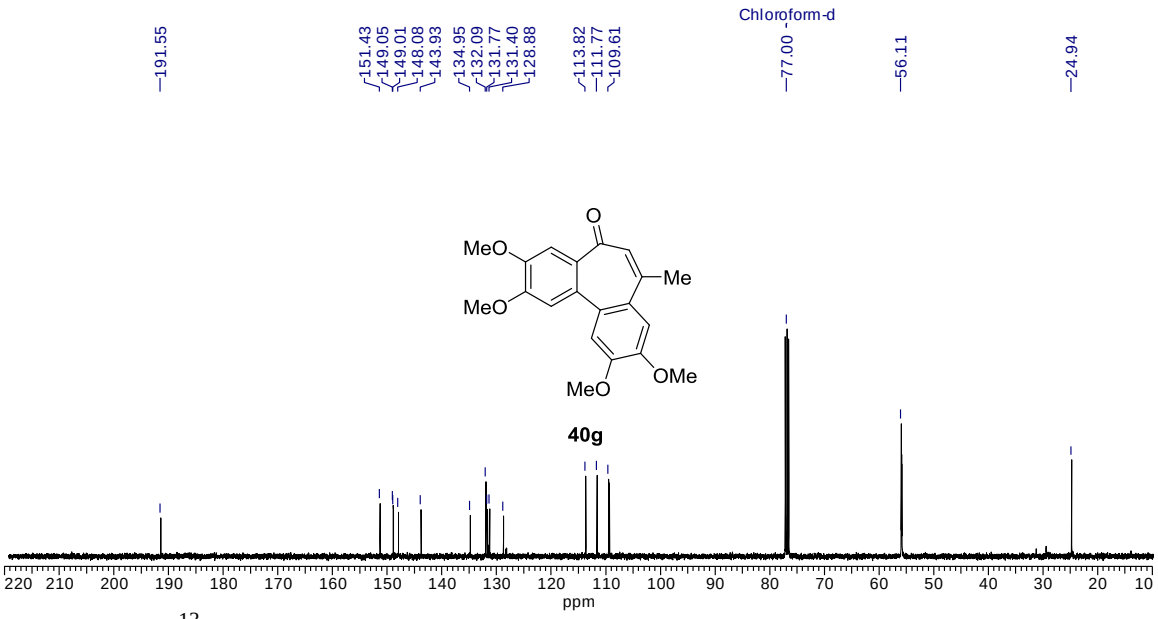


Figure I.5.2: ^{13}C-NMR (100 MHz) spectrum of **40g** in $CDCl_3$

The structure of 7-methyl-5*H*-dibenzo[*a*,*c*][7]annulen-5-one **40g** was confirmed by IR and NMR data analysis. IR spectra shows the presence of the absorption band at

1629 cm^{-1} due to enone carbonyl group stretching. In the ^{1}H-NMR spectrum (Figure I.5.1), the presence of five individual singlets at δ 7.38, 7.20, 7.19, 7.16 and 6.60 were due to five aromatic protons, the presence of singlet at δ 4.00 was due to three protons of methoxy group, whereas the singlet at δ 3.98 was due to nine protons of three methoxy groups and the presence of singlet at δ 2.44 ppm was due to three protons of methyl group that elucidated the structure of 7-methyl-5*H*-dibenzo[*a*,*c*][7]annulen-5-one **40g**. In addition to it, 19 signals appeared in ^{13}C-NMR spectrum (Figure I.5.2) in which one quaternary carbon resonates at δ 191.5 due to carbonyl carbon, nine quaternary carbon resonates at δ 151.4, 149.0, 149.0, 148.1, 143.9, 134.9, 131.8, 131.4 and 128.9 were due to nine aromatic carbons, the presence of five aromatic methine resonates carbons at δ 132.1, 113.8, 111.8, 109.6 and 109.5, four quartets at δ 56.1 (2C), 56.0 and 55.9 were due to four methoxy groups and methyl group carbon resonates at δ 24.9 ppm. The presence of the $[M+Na]^{+}$ peak at m/z $[C_{20}H_{20}NaO_5]^{+}$=363.1201 in the mass spectrum further established the structure of 7-methyl-5*H*-dibenzo[*a*,*c*][7]annulen-5-one **40g**.

Further to the spectroscopic evidence in confirming the structure of the 7-methyl-5*H*-dibenzo[*a*,*c*][7]annulen-5-ones **40a-40g,** the complete structure was unambiguously confirmed by the single crystal X-ray diffraction analysis of **40g** (Figure I.6).

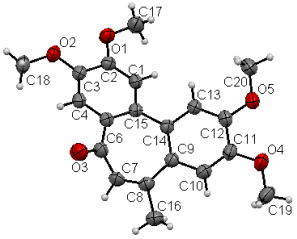
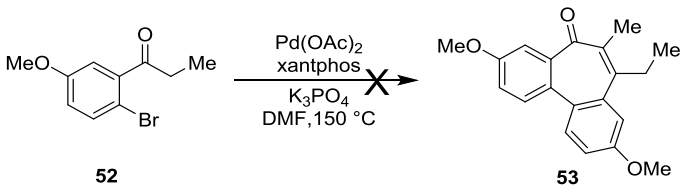


Figure I.6 (40g)

After the successful synthesis of 7-methyl-5*H*-dibenzo[*a*,*c*][7]annulen-5-ones **40** starting from 2-bromoacetophenones **37**, this method was implemented on another

system such as 1-(2-bromophenyl)propan-1-one **52**. However, the reaction was unsuccessful to deliver the desired product **53**, as no clear spot was seen on TLC (Scheme I.11). This might have been due to the availability of β-hydrogen to the feasible five membered palladacycle intermediate, which may collapse through intramolecular *syn*-β elimination, instead of intermolecular bi-aryl coupling.

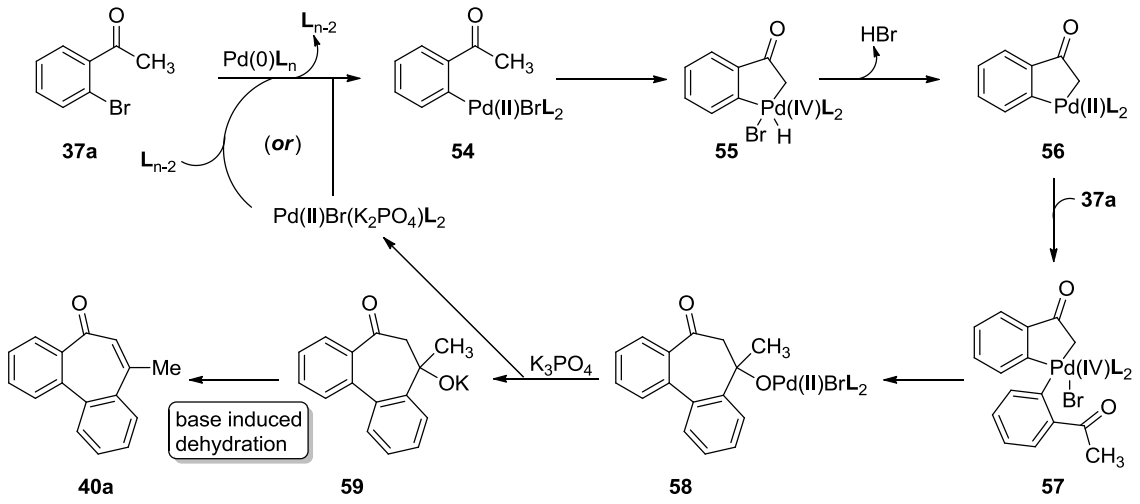


52 **53**

Scheme I.11

The plausible mechanism for the formation of 7-methyl-5*H*-dibenzo[*a*,*c*][7]annulen-5-one **40** can be explained as depicted in Scheme I.12. The first step is an oxidative insertion of Pd (0)-catalyst into the Ar-Br bond of **37a** resulting in the formation of Pd(II)-intermediate **54**. It would then be inserted into sp^3 C-H bond of the ketone and result in a five membered Pd(IV)-intermediate **55**. The intermediate **55** undergoes reductive elimination and would result in the formation of Pd(II)-intermediate **56**. Now the key five membered palladacycle **56** combines with a second molecule **37a** and generates Pd(IV)-complex **57**.[17] Bi-aryl bond formation would lead to acyclic bi-aryl Pd(II)-intermediate that may undergo intramolecular nucleophilic addition by Pd(II)-species to keto group of second aromatic ring and result in Pd(II)-species **58**. Expulsion of [Pd]-complex **58**[18] by base may produce tertiaryalkoxide **59** and Pd(II)-species. Finally, the catalytic cycle completes the transformation of tertiaryalkoxide **59** into product **40a** by base induced dehydration. The so formed Pd(II)-catalyst during the course of a catalytic cycle may regenerate Pd(0) or the Pd(II)-catalyst itself might further be able to catalyze the reaction. Since Ar-Br bond of electron deficient 1-(2-bromophenyl)ethanones **37c** is relatively more reactive than the simple Ar-Br one. This has been proved by performing the reaction only with $Pd(OAc)_2$

without using the ligand while keeping all the other parameters constant (30%, Table I.2, entry 49).

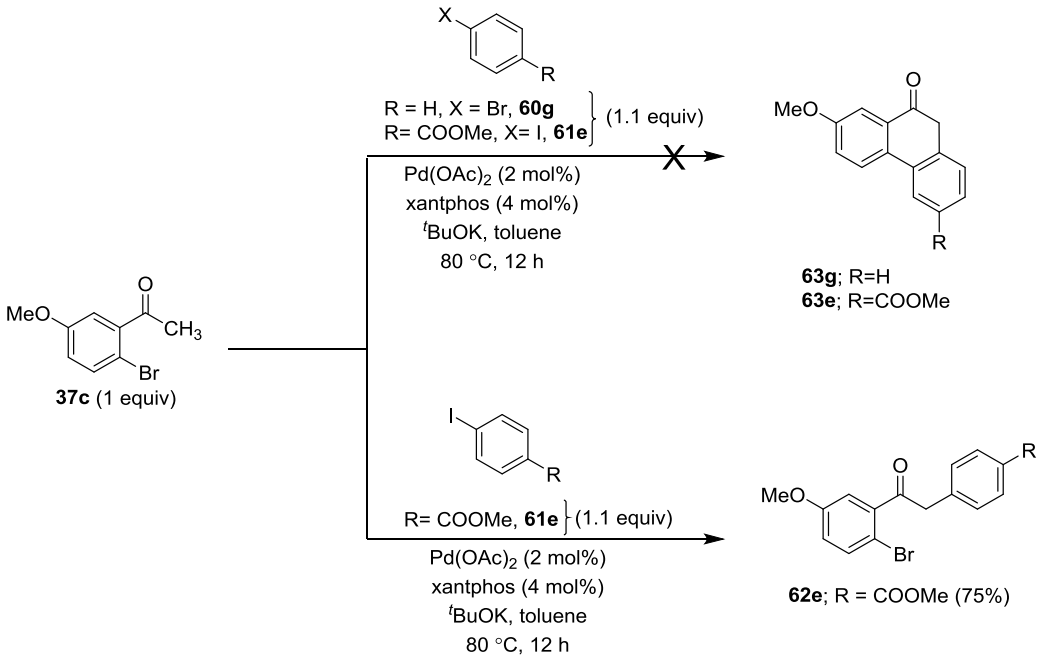


Scheme I.12

I.3.2 Synthesis of α-aryl ketones via [Pd]-catalysis:

With this background of an unprecedented one-pot domino [Pd]-catalysis for the synthesis of 7-methyl-5*H*-dibenzo[*a*,*c*][7]annulen-5-ones **40**,[9e] we have anticipated the formation of tricyclic ketones **63** corresponding aromatic motifs by performing [Pd]-catalysis in the presence of external haloarene **60g/61e**. The formation of tricyclic products **63** was expected to be feasible via heterobiaryl formation followed by intramolecular Buchwald-Hartwig cyclization sequence. Though, initially, the reaction was performed using above optimized reaction conditions (Table I.2, entry 23) in the presence of phenyl bromide **60g** as well as the more reactive iodoarene **61e** as external haloarenes. The reaction however was not clean and did not furnish the expected products **63g**/**63e** [i.e., neither the starting material **37c** nor the product was isolated]. Nevertheless, after screening the reaction under different set of conditions, it was observed that the combination of $Pd(OAc)_2$ (2 mol%)/Xantphos (5 mol%) and the base ^{t}BuOK in toluene at 80 °C for 12 h was successful, but, the reaction was impeded after α-C-H activation of the ketone and gave exclusively the simple α-arylated product **62e**

instead of the expected product **63e**. It is worth mentioning that the above set of reaction conditions was successful in delivering the products **62e** only with the more reactive iodarene **61e** but not with the bromo one **60g** (Scheme I.13). [9j]

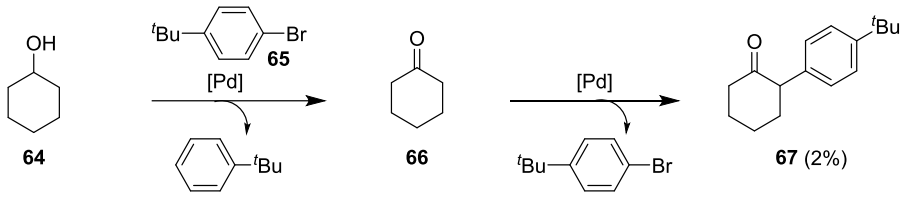


Scheme I.13

The transition-metal mediated α-arylation for the synthesis of corresponding α-arylated products identified as an important transformation, as applied in a variety of applications is a key step for synthesis of various intermediates present in many natural and unnatural products.[19] Many traditional methods are available for the synthesis of α-aryl ketones. Those are arduous due to different arylating reagents that were developed for the synthesis of α-aryl ketones and these reagents are used as stochiometric ratio using main group enol ethers[20] or bismuth/lead reagents.[21] Due to these drawbacks, transition-metal catalyzed direct arylation methods have gained more importance for the synthesis of α-aryl products.

It was an unprecedented discovery of α-arylation by Buchwald and Hartwig in 1997. Buchwald carried out $Pd_2(dba)_3$/Tol-BINAP catalyzed coupling of sodium

alkoxides (generated in-situ by the reaction of alcohol **64** with NaH with electron-deficient aryl bromides **65** to give arylethers. Interestingly, unexpected α-arylated product **67** was observed with 2% yield. This was the foundation for the discovery of α–arylation of ketones by Buchwald (Scheme I.14).[22]



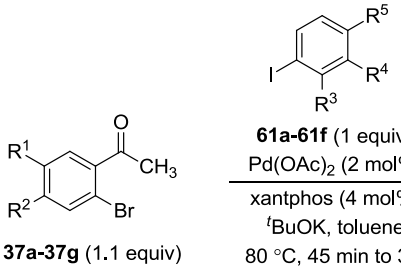
Scheme I.14

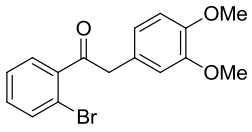
The basis of the development of α-arylation of carbonyl compounds was laid when Hartwig conducted the amination reaction in acetone, and interestingly it led to the formation of α-arylated product as a by-product.[23]

Subsequently, the research groups of Buchwald and Hartwig developed various methods for the α-arylation of ketones.[24] Recently, α-arylation had also been reported using 1-bromo-2-iodobenzenes as coupling partners by Willis et al.[25] The present work describes α-arylation, the bromo-substituent is part of a relatively more reactive 2-bromoacetophenones **37** (Scheme I.13). Notably, after several screenings, we realized that our above reported conditions[9e] for longer reaction time were not that much applicable for other systems. In general, in many instances bi-α-arylation products along with a small amount of other by-products were also formed. This may be due to the fact that the slightly excess amount (1.1 equiv) of iodoarenes with respect to 2-bromoacetophenones **37** would tend to involve in second α-arylation. Thus, various set of conditions were explored to identify optimized reaction conditions. To our delight, the reaction conditions reported by Buchwald et al.[24a] were found to be suitable for our systems (i.e., with 1 equiv of iodo-arene **61e** and 1.1 equiv of 2-bromoacetophenone **37**). Further, these optimized conditions were found to be general and amenable to

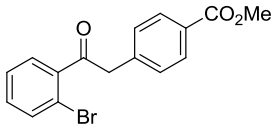
various iodoarenes containing electron withdrawing and electron donating substituents on the aromatic ring. The reaction was completed in shorter reaction time (i.e., typically 45 min to 3 h) and furnished the α-arylation products **62ag-62gf** in very good yields as shown in Table I.4.[9j]

Table I.4: [Pd]-Catalyzed synthesis of 1-(2-bromophenyl)-2-phenylethanone **63ag-63gf** from 2-bromoacetophenones **37a-37g** with iodoarene **61a-61f**.[a,b,c]

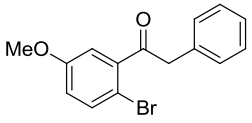




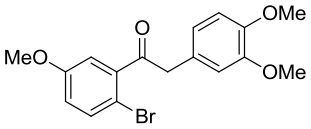
62ac (45 min, 92%)



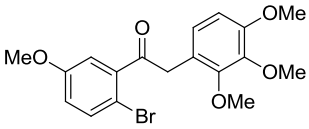
62ae (45 min, 80%)



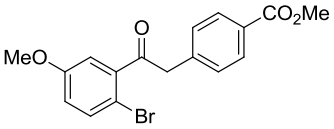
62ca (2 h, 80%)



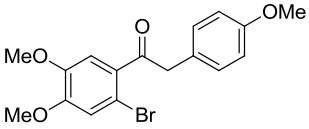
62cc (2 h, 75%)



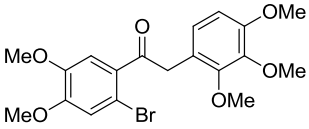
62cd (2 h, 84%)



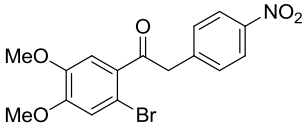
62ce (2 h, 76%)



62gb (3 h, 79%)



62gd (3 h, 81%)



62gf (3 h, 61%)

[a]All reactions were carried out on 0.5 mmol scale of iodoarenes of **61a-61f** in 4 mL of toluene (0.12 M). [b]Isolated yields of chromatographically pure products. [c]For compounds **62ag-62gf** the first alphabet letter refers to the 2-bromoacetophenes **37a-37g** whereas the second letter indicates the aromatic ring coming from iodoarenes **61a-61f**.

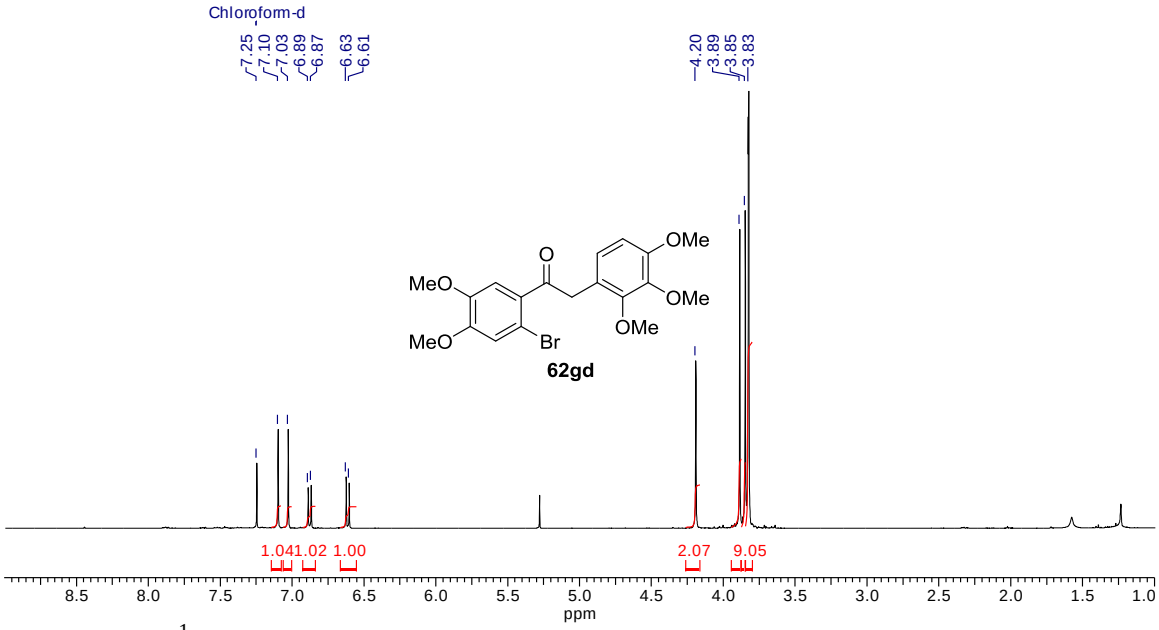


Figure I.7.1: ^{1}H-NMR (400 MHz) spectrum of **62gd** in $CDCl_3$

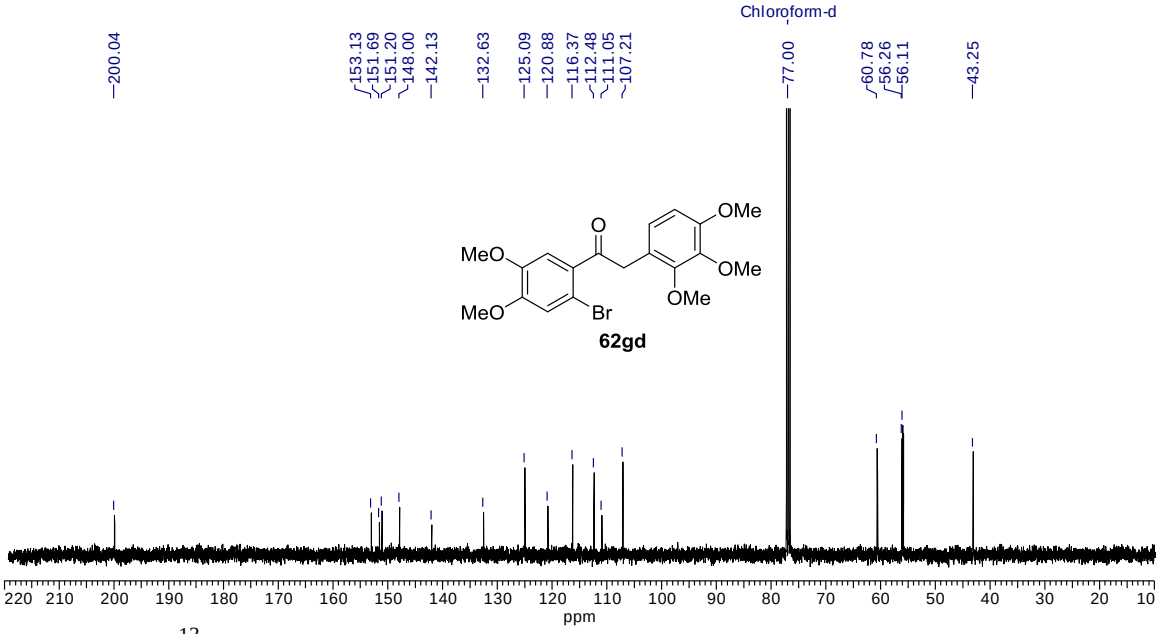


Figure I.7.2: ^{13}C-NMR (100 MHz) spectrum of **62gd** in $CDCl_3$

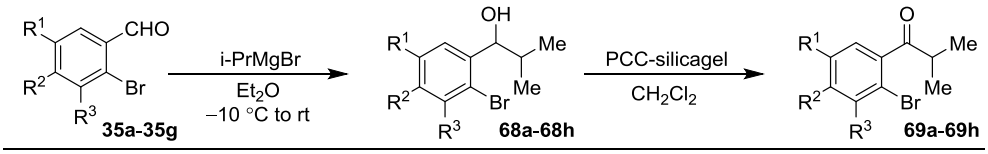
The structure of 1-(2-bromophenyl)-2-phenylethanone **62gd** was confirmed by IR and NMR data analysis. IR spectra show the presence of the absorption band due to carbonyl stretching at 1694 cm^{-1}. In the ^{1}H-NMR spectrum (Figure I.7.1), the presence

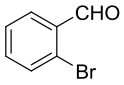
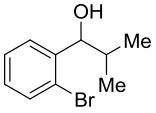
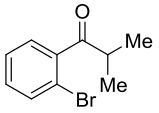
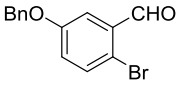
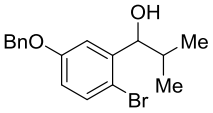
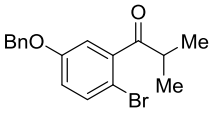
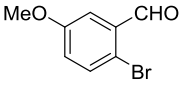
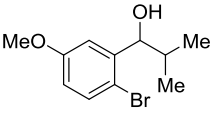
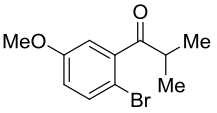
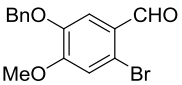
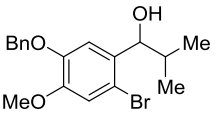
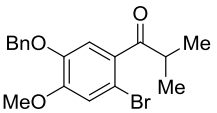
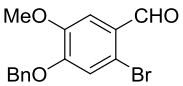
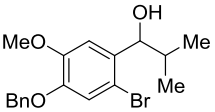
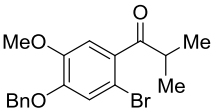
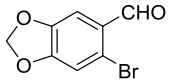
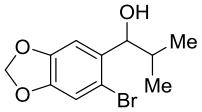
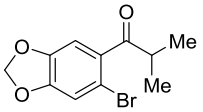
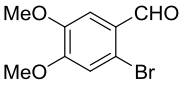
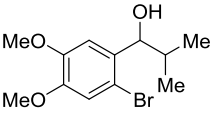
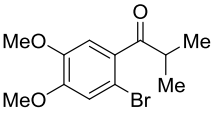
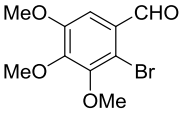
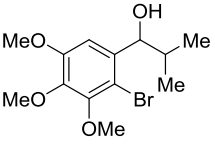
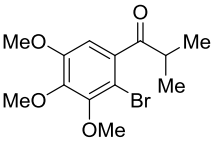
of two singlets at δ 7.10 and δ 7.03 due to two aromatic protons, two doublets at δ 6.88 having *J*=8.8 Hz and δ 6.62 having *J*=8.8 Hz due to two aromatic protons, the presence of singlet at δ 4.20 due to methylene group and the presence of three singlets at δ 3.89(3H), 3.85(3H) and 3.83(9H) ppm due to fifteen protons of five methoxy groups, elucidated the structure of 1-(2-bromophenyl)-2-phenylethanone **62gd**. In addition to it, 19 signals appeared in ^{13}C-NMR spectrum (Figure I. 7.2) in which carbonyl carbon resonates at δ 200.1, eight aromatic quaternary carbons resonates at δ 153.2, 151.7, 151.2, 148.0, 142.2, 132.6, 120.9, and 111.1, the presence of four aromatic methine carbons at δ 125.1, 116.4, 112.5, and 107.2, five quartets at δ 60.8, 60.7, 56.3, 56.1 and 56.0 were due to methoxy groups, methylene group carbon resonates at δ 43.3 ppm. The presence of $[M+H]^+$ peak at m/z $[C_{19}H_{22}BrO_6]^+$= 425.0605 in the mass spectrum further established the structure of 1-(2-bromophenyl)-2-phenylethanone **62gd**.

I.3.3 Synthesis of bi-aryls via domino [Pd]-catalysis:

After the successful accomplishment of 7-methyl-5*H*-dibenzo[*a*,*c*][7]annulen-5-ones **41,**[9e] and the synthesis of α-arylation products **62,**[9j] through [Pd]-catalysis, we further became interested to check the outcome of 2-bromoarylisopropyl ketones **69** in the presence of [Pd]-catalyst. The requisite 1-(2-bromophenyl)-2-methylpropan-1-one **69** derivatives were readily obtained in two reaction steps starting from 2-bromobenzaldehydes **35**. Thus, the addition of isopropyl Grignard reagent to the corresponding 2-bromobenzaldehydes **35a-35h** gave secondary alcohols **68a-68h** in good to very good yields (70-86%, Table 5). Oxidation of the secondary alcohols **69** with PCC furnished 1-(2-bromophenyl)-2-methylpropan-1-one **69a-69h** in excellent yields (93-99%, Table 5), as summarized in Table I.5.[9i]

Table I.5: Synthesis of 1-(2-bromophenyl)-2-methylpropan-1-one **69a-69h** from corresponding 2-bromobenzaldehydes **35a-35h**.[a]



 **35a**	 **68a** (73%)	 **69a** (99%)
 **35b**	 **68b** (75%)	 **69b** (95%)
 **35c**	 **68c** (86%)	 **69c** (96%)
 **35d**	 **68d** (84%)	 **69d** (98%)
 **35e**	 **68e** (76%)	 **69e** (96%)
 **35f**	 **68f** (70%)	 **69f** (95%)
 **35g**	 **68g** (71%)	 **69g** (93%)
 **35h**	 **68h** (73%)	 **69h** (95%)

[a]Reaction conditions: Yields in the parentheses are isolated yields of chromatographically pure products.

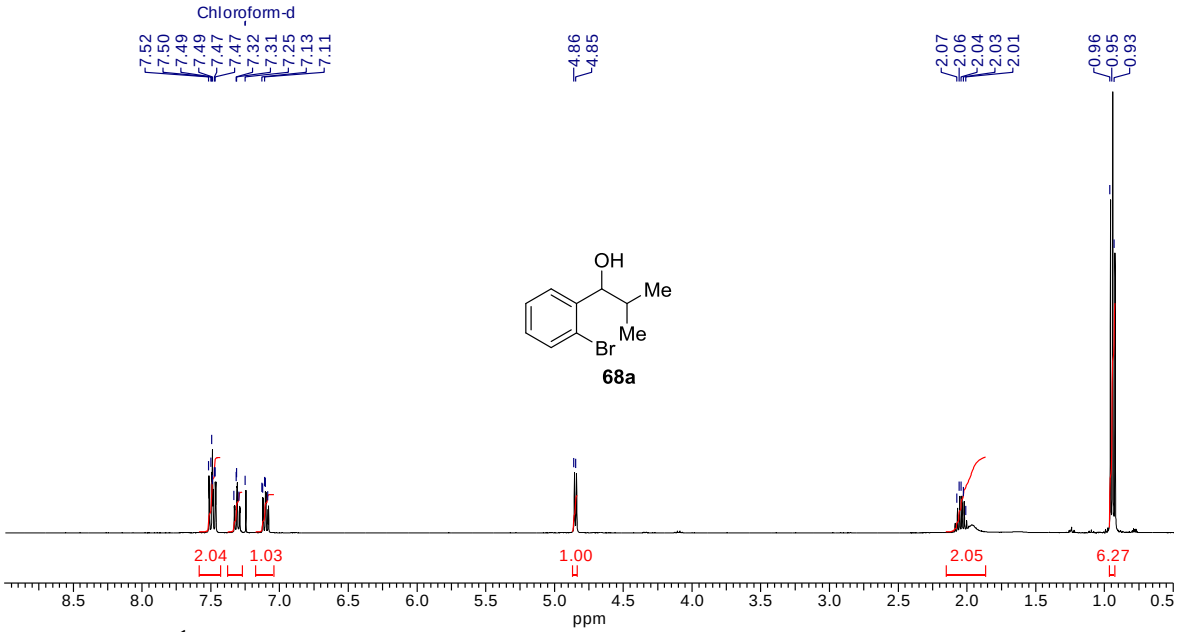


Figure I.8.1: ^{1}H-NMR (400 MHz) spectrum of **68a** in $CDCl_3$

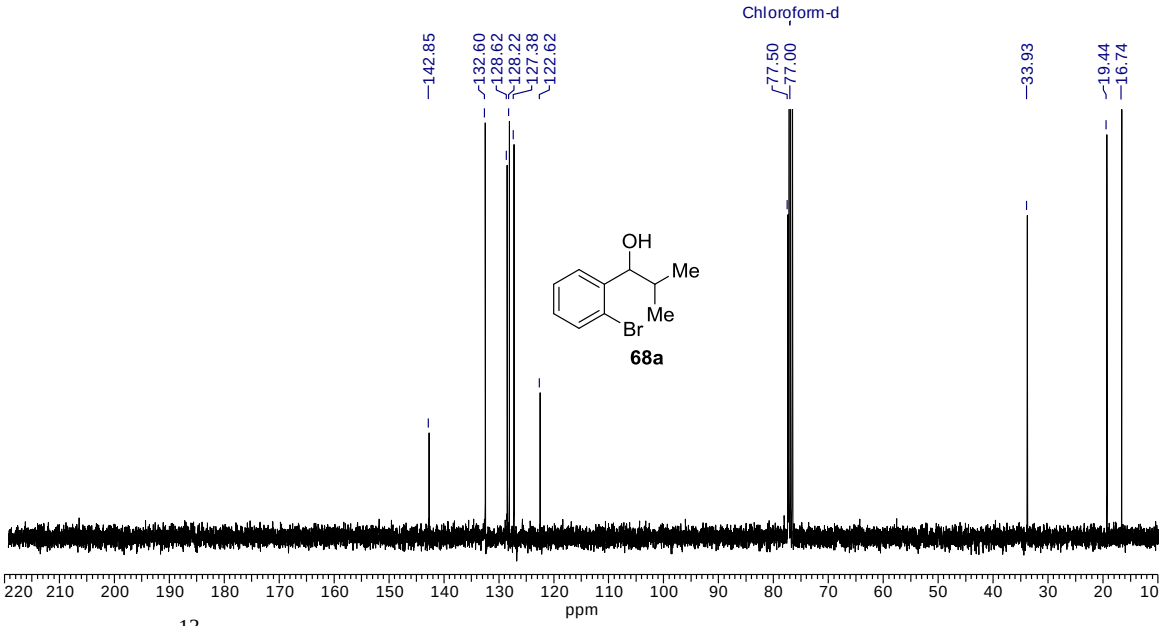


Figure I.8.2: ^{13}C-NMR (100 MHz) spectrum of **68a** in $CDCl_3$

The structure of secondary alcohol **68a** was confirmed by IR and NMR data analysis. IR spectra shows the absence of the absorption band due to carbonyl stretching of aldehyde group and the presence of broad absorption band due to OH stretching at 3397 cm^{-1}. In the ^{1}H-NMR spectrum (Figure I.8.1), the presence of doublet of a doublet

at δ 7.51 having *J*=7.8 and 1.0 Hz due to one aromatic proton, doublet of a doublet at δ 7.48 having *J*=7.8 and 2.0 Hz due to one aromatic proton, doublet of a doublet of doublet at δ 7.31 having *J*=8.8, 7.3 and 1.0 Hz due to one aromatic proton, doublet of a doublet of doublets at δ 7.11 having *J*=8.8, 7.3 and 2.0 Hz due to one aromatic proton, presence of doublet at δ 4.86 having *J*=5.9 Hz due to benzylic proton, septet of doublet at δ 2.05 having *J*= 5.9 and 1.0 Hz due to one proton, br. s, at δ 1.97 ppm due to hydroxy proton, the presence of two doublets at δ 0.95 and 0.94 ppm having *J*= 6.4 and 6.4 Hz due to two methyl groups, elucidated the structure of secondary alcohols **68a**. In addition to it, 10 signals appeared in ^{13}C-NMR spectrum (Figure I.8.2) in which two quaternary carbon resonates at δ 142.8 and 122.6 were due to two aromatic carbons, the presence of four aromatic methine carbons at δ 132.6, 128.6, 128.2 and 127.4, benzylic carbon resonates at δ 77.5, the presence of δ 33.9 was due to *C*H$(CH_3)_2$ group and two methyl carbons resonates at δ 19.4 and 16.7 ppm. The presence of $[(M+H)–H_2O]^+$ peak at m/z $[C_{10}H_{12}Br]^+$=211.0117 in the mass spectrum further established the structure of secondary alcohols **68a**.

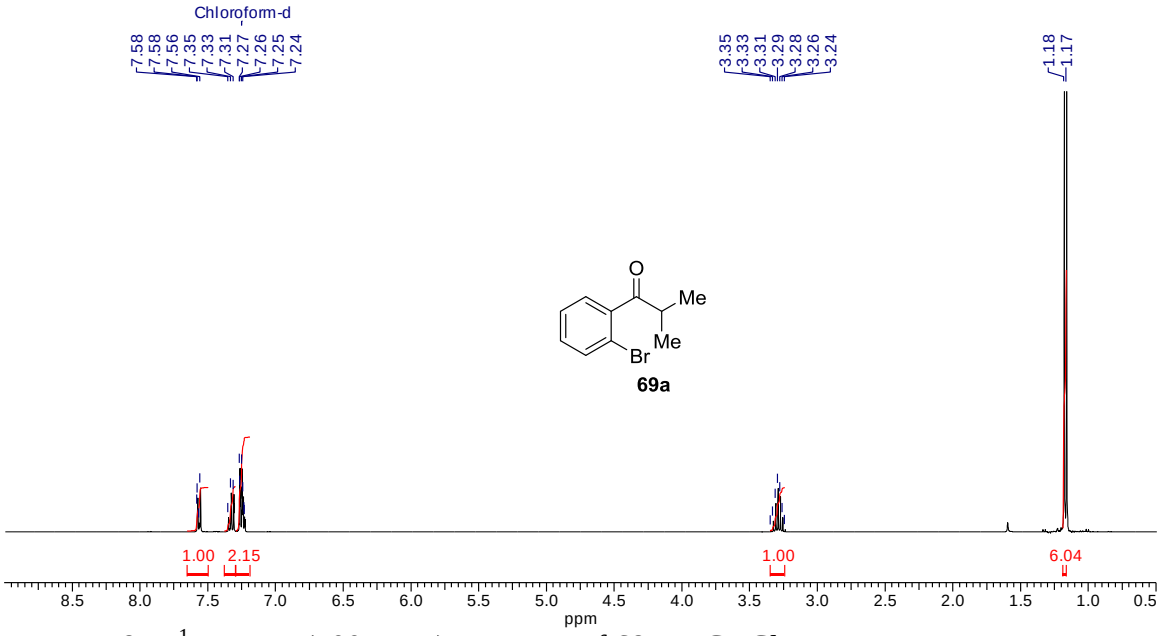


Figure I.9.1: ^{1}H-NMR (400 MHz) spectrum of **69a** in $CDCl_3$

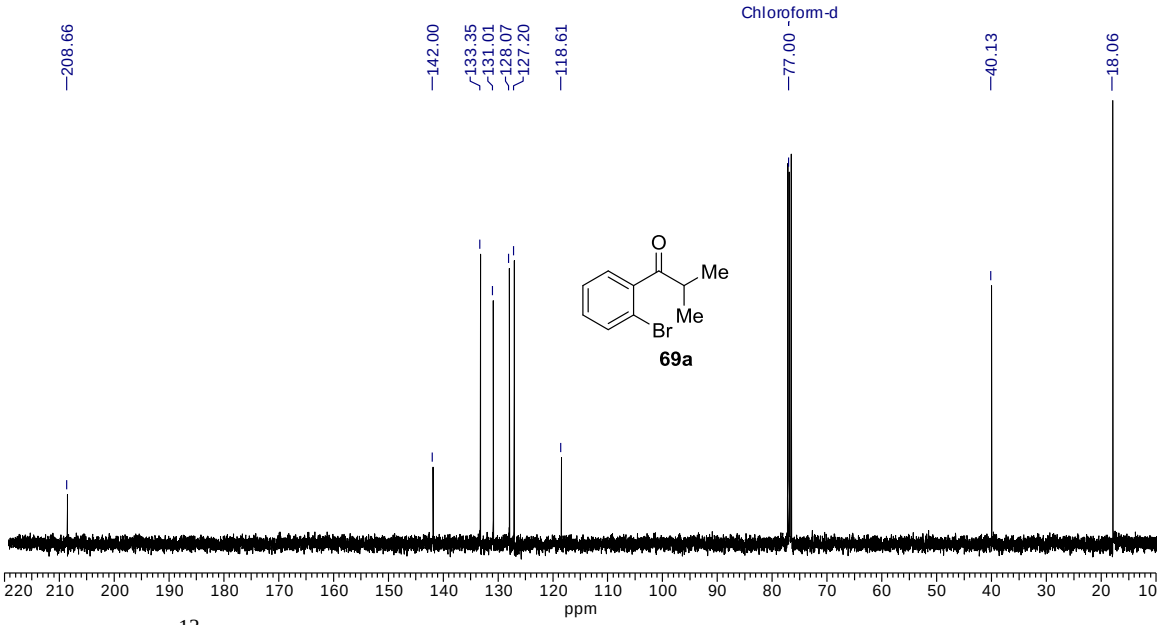


Figure I.9.2: ^{13}C-NMR (100 MHz) spectrum of **69**a in $CDCl_3$

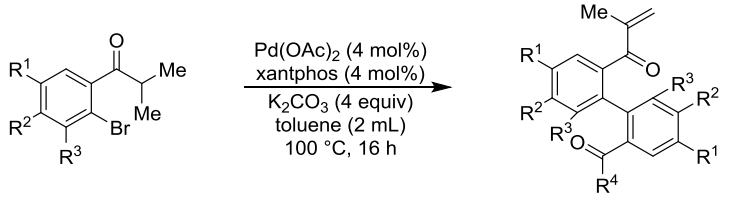
The structure of 1-(2-bromophenyl)-2-methylpropan-1-one **69a** was confirmed by IR and NMR data analysis. IR spectra shows the absence of the absorption band due to stretching of OH group and the presence of absorption band due to carbonyl stretching at 1700 cm^{-1}. In the ^{1}H-NMR spectrum (Figure I.9.1), doublet of a doublet at δ 7.59 having *J*=7.8 and 1.5 Hz due to one aromatic proton, doublet of a doublet of doublet at δ 7.36 having *J*=9.3, 7.8 and 1.5 Hz due to one aromatic proton, doublet of a doublet at δ 7.29 having *J*=7.8 and 1.5 Hz due to one aromatic proton, doublet of a doublet of doublet at δ 7.27 having *J*=9.3, 7.8 and 1.5 Hz due to one aromatic proton, presence of septet at δ 3.32 having *J*= 6.8 Hz due to C*H*$(CH_3)_2$ group, and doublet at δ 1.20 ppm having *J*= 6.8 Hz due to six protons of two methyl groups, elucidated the structure of 1-(2-bromophenyl)-2-methylpropan-1-one **69a**. In addition to it, 10 signals appeared in ^{13}C-NMR spectrum (Figure I.9.2) in which quaternary carbon resonates at δ 208.7 were due to carbonyl carbon, two quaternary carbon resonates at δ 142.0 and 118.6 were due to two aromatic carbons, the presence of four aromatic methine carbons at δ 133.3, 131.0, 128.1 and 127.2, the presence of δ 40.1 was due to *C*H$(CH_3)_2$, two

methyl groups carbon resonates δ 18.1 (2C) ppm. The presence of $[M+H]^+$ peak at m/z $[C_{10}H_{12}BrO]^+$=227.0065 in the mass spectrum further established the structure of 1-(2-bromophenyl)-2-methylpropan-1-one **69a**.

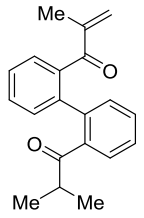
Now the requisite 1-(2-bromophenyl)-2-methylpropan-1-ones **69** in hand, post which the [Pd]-catalysis was explored. However, the reaction was unsuccessful under the above optimized conditions (Table I.2, entry 23) that were applied on 2-bromoacetophenone **37**.[9e] Quite surprisingly, slight modification of the reaction conditions (i.e., with base K_2CO_3 and solvent toluene), showed a dramatic effect and furnished only the bi-aryl product **70** in a controlled fashion, in excellent yield (97%, Table I.6). The formation of bi-aryl product **70** can be justified on the basis of mild base K_2CO_3 which would not be strong enough to deprotonate the acidic α-hydrogen of isopropyl ketone **69**, hence, it was assumed that a simple sp^3 C-H activation would be feasible to yield the five-membered palladacycle by the initially formed aryl Pd(II)-species. It may be true that the five-membered palladacycle would proceed through a tight transition state and might have sufficient longer life time so as to combine with the second molecule to establish the bi-aryl bond. This five membered palladacycle would in turn couple with the second molecule **69** to form the bi-aryl bond and finally may undergo rapid reductive *syn*-β-elimination (due to the availability of β-hdrogens) than the intramolecular Aldol reaction (for details, see; Scheme I.15). Notably, there were clear cut distinctions between the reaction conditions of 2-bromoacetophenones **37** and 2-bromoisopropylphenones **69**. The former one possessing relatively more acidic hydrogens than that of the isopropyl ketones **70** and the strong base K_3PO_4 was suitable for deprotonation of 2-bromoacetophenones **37**, to facilitate the formation of five membered palladacycle followed by bi-aryl coupling and then intramolecular aldol condensation (due to non-availability of β-hydrogens) to furnish the 7-Methyl-5*H* dibenzo[*a*,*c*][7]annulen-5-ones **41**.[9e] Whereas in the case of 2-bromoisopropylphenones **69**, definitely, the formation of enolate would not be feasible, however, the requisite five-membered palladacycle would be resulted only by direct sp^3 C-H activation after

the initial formation of aryl-Pd-species. With these conditions in hand, for the formation of bi-aryl product **70**, to check the scope and limitations of the method, the [Pd]-catalysis was explored on other systems of 1-(2-Bromophenyl)-2-methylpropan-1-ones **69**. Agreeably, it was observed that the optimized conditions are amenable to other 1-(2-bromophenyl)-2-methylpropan-1-ones **69** and furnished bi-aryl products **70** in very good to excellent yields (Table I.6). However, in case of **69h**, the product **70h** was formed in moderate yield (Table I.6). This can be justified due to steric hindrance of the di-*ortho*-substituents on the aromatic rings of the bi-aryl product **70h**.[9i]

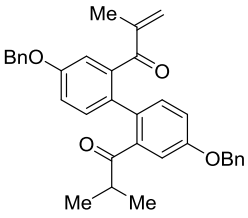
Table I.6: Synthesis of bi-aryls **70a**-**70h** from 1-(2-bromophenyl)-2-methylpropan-1-ones **69a**-**69h.**



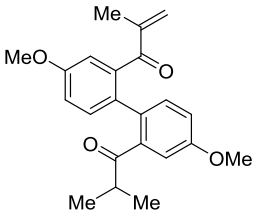
69a-69h **70a-70h**



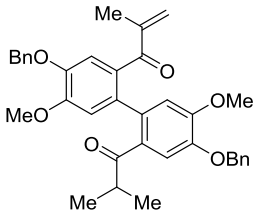
70a (97%)



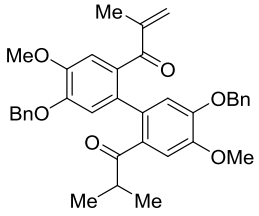
70b (85%)



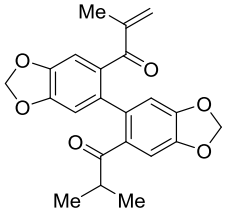
70c (91%)



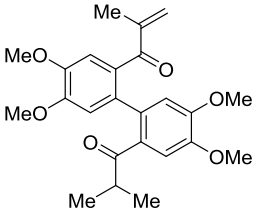
70d (84%)



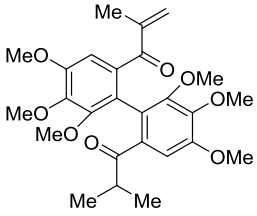
70e (95%)



70f (95%)



70g (85%)



70h (54%)[c]

[a]Reaction conditions: All the reactions carried out with **69a**-**69h** (100 mg, 0.27 to 0.44 mmol), in toluene. [b]Isolated yields are chromatographically pure products. [c]Isolated yield of chromatographically pure product based on the starting material recovery.

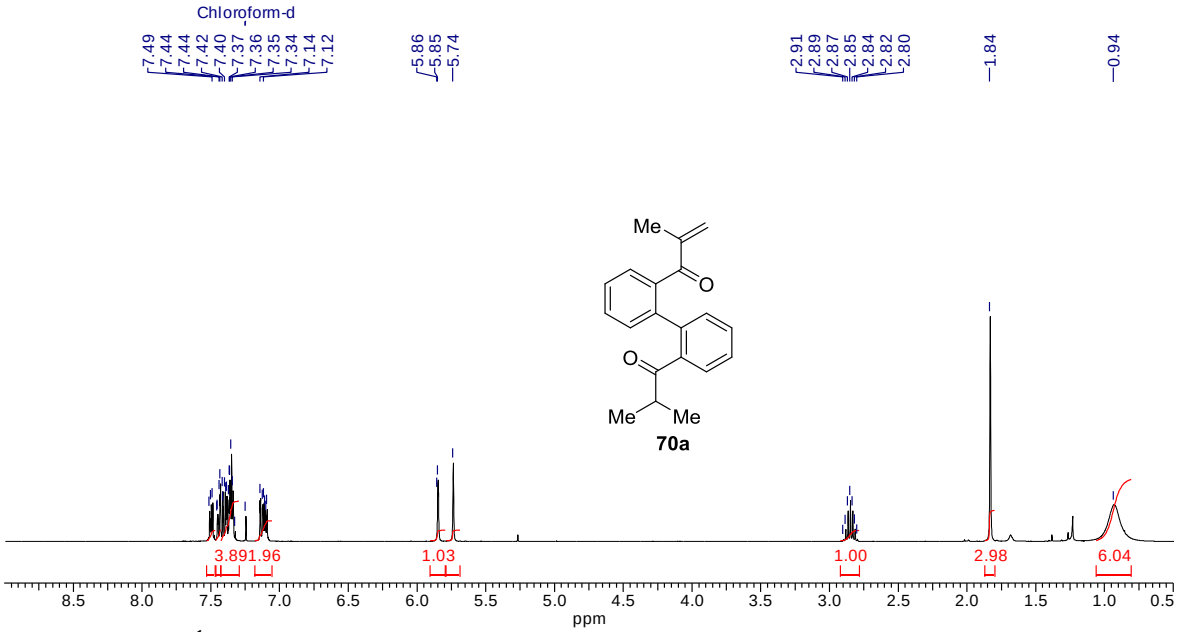


Figure I.10.1: ^{1}H-NMR (400 MHz) spectrum of **70a** in $CDCl_3$

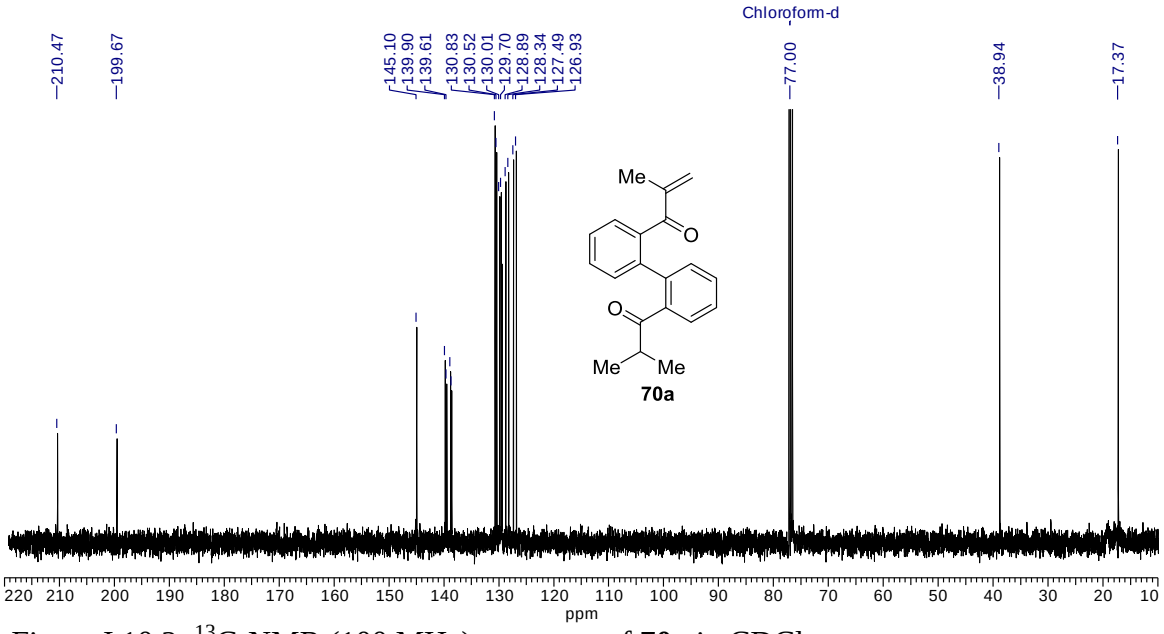
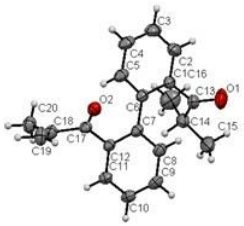


Figure I.10.2: ^{13}C-NMR (100 MHz) spectrum of **70a** in $CDCl_3$

The structure of bi-aryl **70a** was confirmed by IR and NMR data analysis. IR spectra shows the presence of absorption band due to carbonyl stretching at 1687 cm^{-1}. In the ^{1}H-NMR spectrum (Figure I.10.1) a multiplet in the region of δ 7.55–7.47 due to one aromatic proton, doublet of a doublet at δ 7.44 having *J*=7.3 and 1.5 Hz due to one aromatic proton, doublet of a doublet at δ 7.40 having *J*=7.3 and 2.0 Hz due to one aromatic proton, doublet of a doublet at δ 7.39 having *J*=5.4 and 2.0 Hz due to one aromatic proton, a multiplet in the region of δ 7.38–7.30 due to two aromatic protons, doublet of a doublet at δ 7.14 having *J*=7.3 and 2.0 Hz due to one aromatic proton, a multiplet in the region of δ 7.12–7.06 due to one aromatic proton, presence of two individual singlets at δ 5.85 and 5.74 due to olefinic methylene protons, septet at δ 2.85 having *J*= 6.8 Hz due to C*H*$(CH_3)_2$, singlet at δ 1.84 due to three protons of methyl group and br. s, at δ 0.94 ppm which accounts for six protons of two methyl groups, elucidated the structure of bi-aryl **70a**. In addition to it, 18 signals appeared in ^{13}C-NMR spectrum (Figure I.10.2) in which two quaternary carbon resonates at δ 210.5 and 199.7 due to two carbonyl carbons, five quaternary carbon resonates at δ 145.1, 140.0, 139.6, 138.9 and 138.7 were due to four aromatic carbons and one for olefinic carbon, presence of eight aromatic methine carbons resonates at δ 130.8, 130.5, 130.0, 129.7, 129.7, 128.3, 127.5 and 126.9, olefinic methylene carbon resonates at δ 129.6, the presence of δ 38.9 due to *C*H$(CH_3)_2$ group and three methyl group resonates at δ 17.4 ppm. The presence of $[M+Na]^+$ peak at m/z $[C_{20}H_{20}NaO_2]^+$=315.1361 in the mass spectrum further established the structure of bi-aryl **70a**.

In addition to the NMR and other spectroscopic studies for structural elucidation, the structure of bi-aryl **70a-70h** was further unambiguously confirmed by the single crystal X-ray diffraction analysis of **70a** (Figure I.11).



(Figure I.11) (70a)

Interestingly, the bi-aryl core constitutes a privileged structural motif that is found in approximately 4.3% of all biologically active natural products (Figure I.12).[26-38] For example, (+)-isoschizandrin **71**,[26] a lignin from schizandra chinesis, has been used in the chinese traditional medicines as an antitussive, steganone **72**,[27] was found to inhibit tubulin polymerization both *in-vitro* and *in-vivo*. The derivatives of valoneaic acid **73**,[28] are widely distributed in many kinds of higher plants possessing interesting biological activities such as antioxidant and anti-tumor properties. The bi-aryl natural product mastigophorene (A) **74** exhibits nerve-growth stimulating activity.[29] The natural korupensamine A **75** shows good antimalarial activity *in-vitro* and *in-vivo*,[30] whereas the binaphthalene gossypol **76**, [31] possesses antispermatogenic, [32] antitumor, [33] and antimalarial [34] activities and agrochemical specialties and also the valsartan **77**, [35] lotarsan **78**, [36] buflavine **79**, [37] exhibits interesting biological activity. Due to their physical properties polyaromatics are widely used as organic conductors or semiconductors. Some of the bi-aryls which contain di- or tri-aromatic rings are often used as selective ligands for asymmetric catalysis, when atropisomerism is possible.[38]

The transition-metal catalyzed cross-coupling reactions are powerful synthetic tools for preparation of these bi-aryl scaffolds. Numerous traditional methods exist for the synthesis of bi-aryls like Kumada coupling (using arylmagnesium halides), Stille (using organotin reagents), Suzuki (using organoboron derivatives), Suzuki-Miyaura (using organoboron derivatives), Negishi (using organozinc reagent) and Hiyama (using organosilanes).[39] Despite their remarkable effectiveness, these methods suffer from several key drawbacks such as the requirement of large amount of expensive and toxic

organometallic reagent in stoichiometric amount in addition to the transition-metal catalyst. Therefore, these methods are not considered as efficient ones with respect to economic and environmental point of view. Therefore, direct arylation methods are gaining more importance for the synthesis of bi-aryls. In this regard, a good number of methods have been developed for the synthesis of bi-aryl scaffolds using simple [Pd]-catalyst.[40]

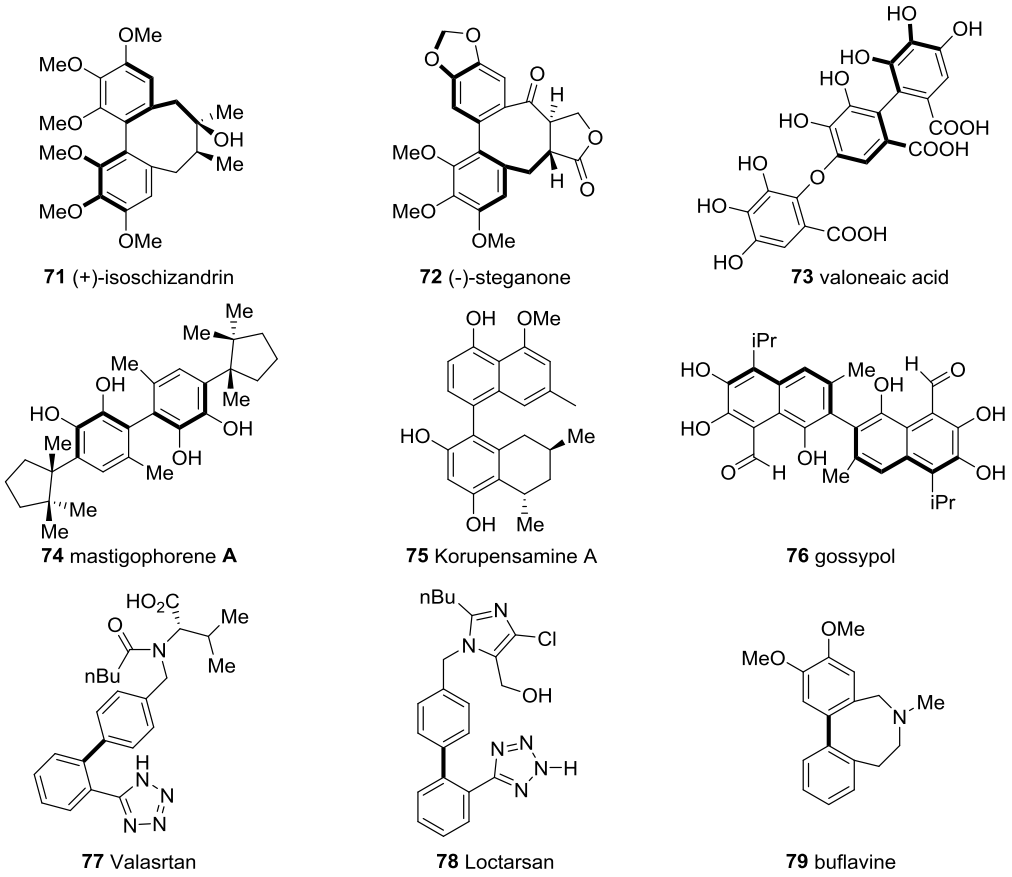
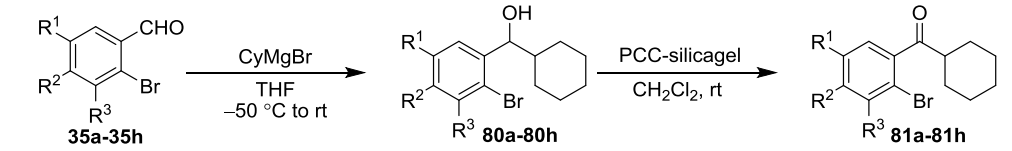
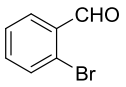
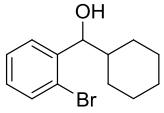
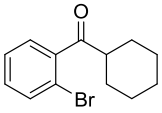
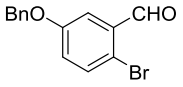
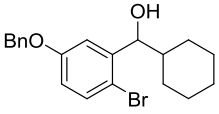
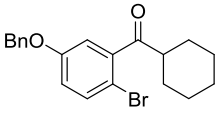
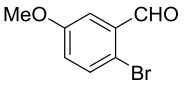
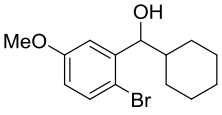
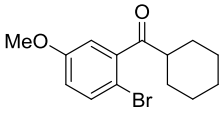
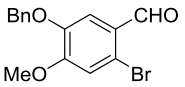
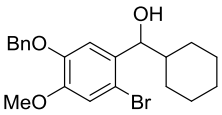
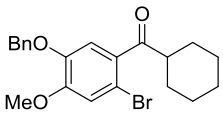
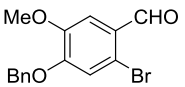
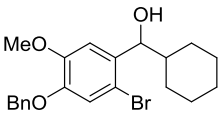
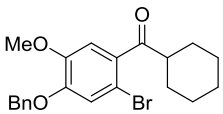
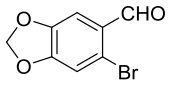
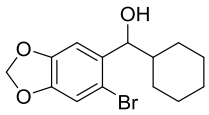
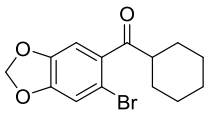
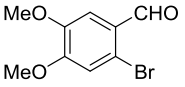
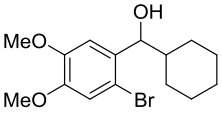
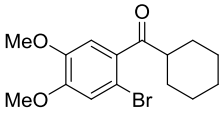
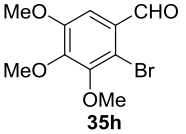
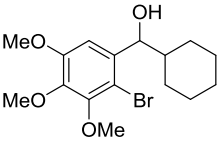
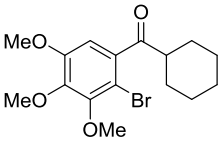


Figure I.12

After successful synthesis of bi-aryls **70**, we turned our attention towards the scope and generality of the method. Hence, the requisite (2-Bromophenyl) (cyclohexyl) methanones **81** were synthesized using the standard procedure [i.e., cyclohexyl Grignard reagent addition and PCC oxidation protocol] and the yields are as summarized in Table I.**7**.[9i]

Table I.7: Synthesis of (2-bromophenyl)(cyclohexyl)methanone **81a-81h** from 2-bromobenzaldehydes **35a-35h**.[a]



 **35a**	 **80a** (52%)	 **81a** (91%)
 **35b**	 **80b** (52%)	 **81b** (95%)
 **35c**	 **80c** (48%)	 **81c** (93%)
 **35d**	 **80d** (60%)	 **81d** (91%)
 **35e**	 **80e** (72%)	 **81e** (96%)
 **35f**	 **80f** (40%)	 **81f** (95%)
 **35g**	 **80g** (70%)	 **81g** (99%)
 **35h**	 **80h** (55%)	 **81h** (92%)

[a]Reaction conditions:Yields in the parentheses are isolated yields of chromatographically pure products.

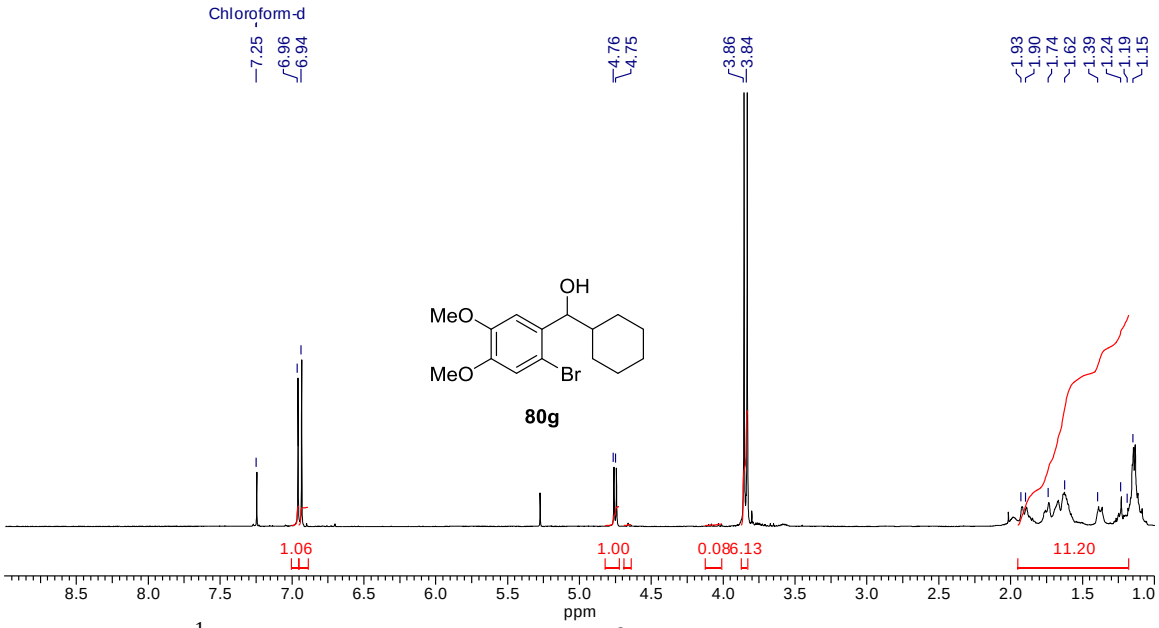


Figure I.13.1: ^{1}H-NMR (400 MHz) spectrum of **80g** in $CDCl_3$

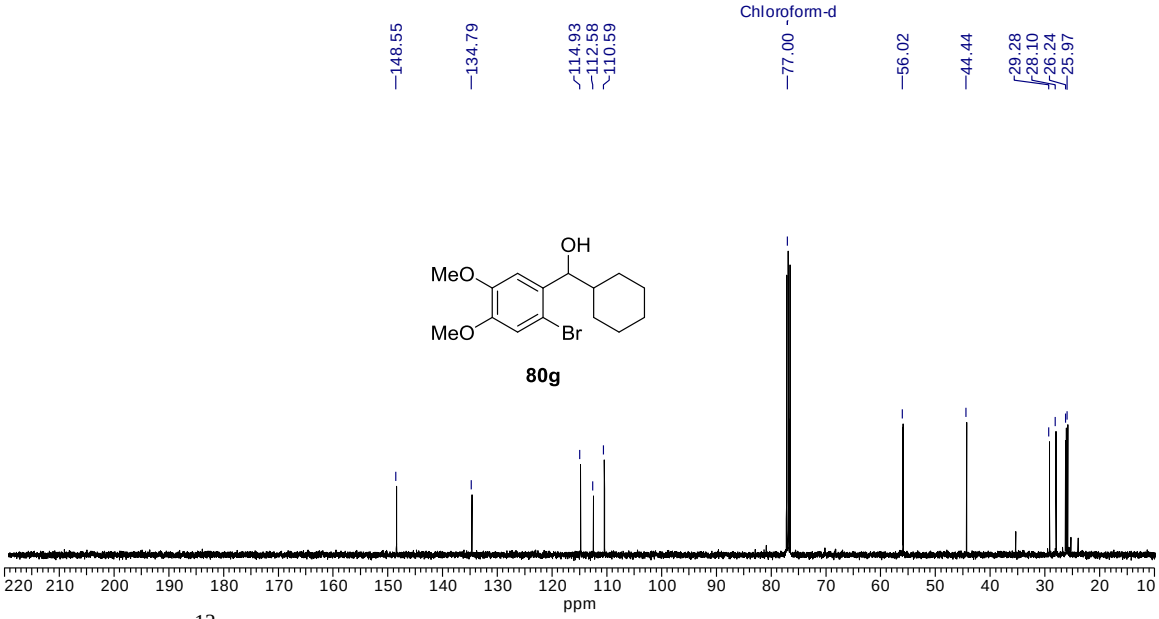


Figure I.13.2: ^{13}C-NMR (100 MHz) spectrum of **80g** in $CDCl_3$

The structure of (2-bromophenyl)(cyclohexyl)methanol **80g** was confirmed by IR and NMR data analysis. IR spectra shows the absence of the absorption band due to carbonyl stretching of aldehyde group and the presence of broad absorption band due to

OH stretching at 3400 cm^{-1}. In the ^{1}H-NMR spectrum (Figure I.13.1), the presence of two singlets at δ 6.96 and 6.94 due to two aromatic protons, the presence of doublet at δ 4.75 having *J*=6.8 Hz due to benzylic proton, two singlets at δ 3.86 and 3.44 due to six protons of two methoxy groups and a multiplet at δ 2.30–0.60 ppm due to cyclohexyl and hydroxy group twelve protons, elucidated the structure of (2-bromophenyl)(cyclohexyl)methanol **80g**. In addition to it, 14 signals appeared in ^{13}C-NMR spectrum (Figure I.13.2) in which four quaternary carbon resonates at δ 148.5(2C), 134.8 and 112.6 were due to four aromatic carbons, the presence of two aromatic methine carbons at δ 114.9 and 110.6, benzylic carbon resonates at δ 76.9, two methoxy group carbons resonates at δ 56.1 and 56.0, the presence of δ 44.4 was due to *C*H$(CH_3)_2$ group and cyclohexyl five carbon resonates at δ 29.3, 28.1, 26.4, 26.2 and 26.0 ppm. The presence of $[(M+H)–H_2O]^+$ peak at m/z $[C_{15}H_{20}{}^{79}BrO_2]^+$= 311.0640 in the mass spectrum further established the structure of (2-bromophenyl)(cyclohexyl)methanol **80g**.

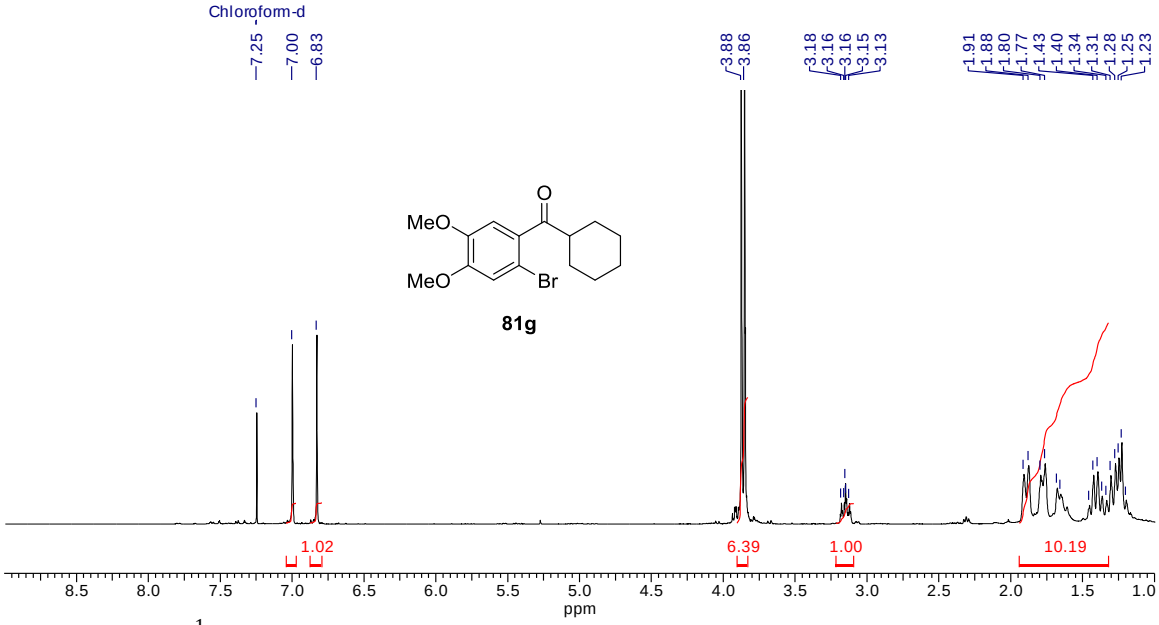


Figure I.14.1: ^{1}H-NMR (400 MHz) spectrum of **81g** in $CDCl_3$

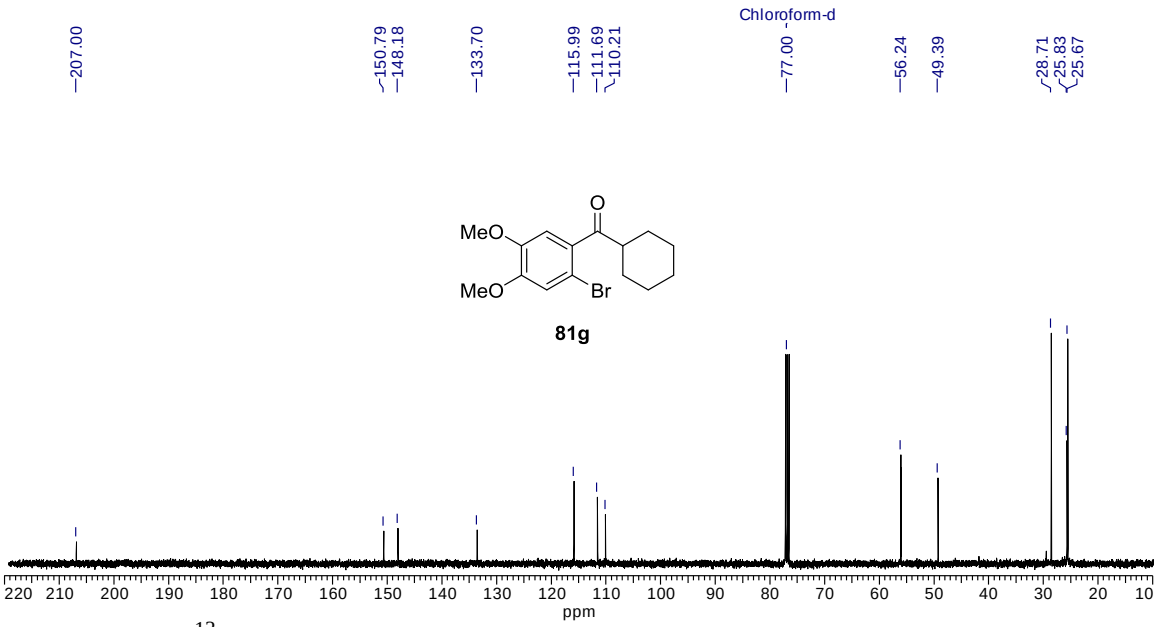


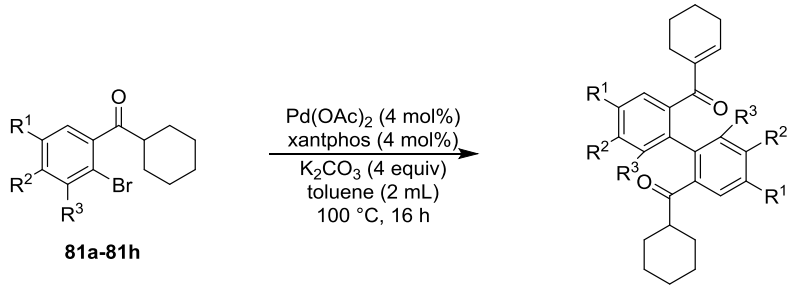
Figure I.14.2: ^{13}C-NMR (100 MHz) spectrum of **81g** in $CDCl_3$

The structure of (2-bromophenyl) (cyclohexyl) methanone **81g** was confirmed by IR and NMR data analysis. IR spectra shows the absence of the broad absorption band, due to stretching of OH group and the presence of absorption band due to carbonyl stretching at 1688 cm^{-1}. In the ^{1}H-NMR spectrum (Figure I.14.1), the presence of two singlets at δ 7.00 and 6.83 were due to two aromatic protons, two singlets at δ 3.88 and 3.86 were due to six protons of two methoxy groups, the presence of triplet of triplets at δ 3.01 having *J*=11.2 Hz was due to one proton and a multiplet at δ 2.10–1.10 ppm was due to cyclohexyl ten protons, elucidated the structure of (2-bromophenyl)(cyclohexyl) methanone **81g**. In addition to it, 13 signals appeared in ^{13}C-NMR spectrum (Figure I.14.2) in which one quaternary carbon resonates at δ 207.0 was due to carbonyl carbon, the presence of four quaternary carbon resonates at δ 150.8, 148.2, 133.7 and 110.2 were due to four aromatic carbons, the presence of two aromatic methine carbons at δ 116.0 and 110.2, two methoxy group carbons resonates at δ 56.2 and 56.1, the presence of δ 49.4 was due to Cy-CH group and cyclohexyl five carbon resonates at signals at δ 28.7(2C), 25.8, 25.7(2C) ppm. The presence of $[M+H]^+$ peak at

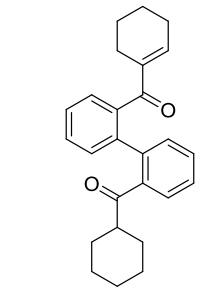
m/z $[C_{15}H_{20}{}^{79}BrO_3]^+$=327.0592 in the mass spectrum further established the structure of (2-bromophenyl) (cyclohexyl) methanone **81g**.

Finally, [Pd]-catalysis was applied on (2-bromophenyl)(cyclohexyl)methanones **81g**. Interestingly, the method was also quite successful on **81a-81h** and furnished **82a-82h** in very good yields as shown in Table I.8. Once again, the steric effect due to *ortho*-substituents was observed for **81h** which lowered the yield of the product **81h** when compared with the other substrates.[9i]

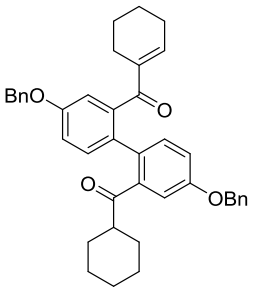
Table I.8 Synthesis of bi-aryls **82a-82h** from (2-bromophenyl)(cyclohexyl)methanones **81a-81h**.



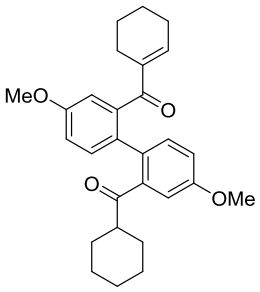
81a-81h **82a-82h**



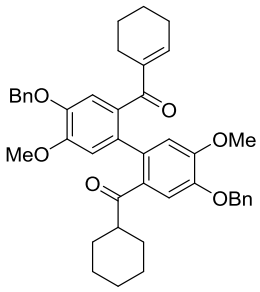
82a (87%)



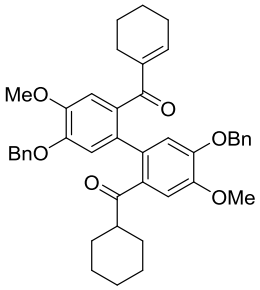
82b (78%)



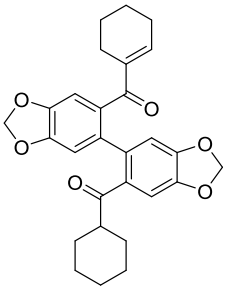
82c (83%)



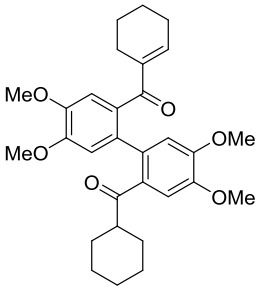
82d (85%)



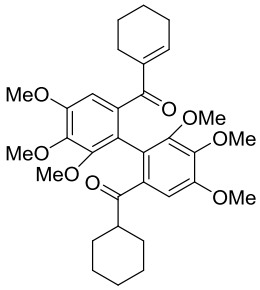
82e (88%)



82f (88%)



82g (80%)



82h (57%)[c]

[a]Reaction conditions: All the reactions were carried out with **81a-81h** (100 mg, 0.25 to 0.37 mmol) in toluene. [b]Isolated yields are chromatographically pure products. [c]Isolated yield of chromatographically pure product based on the starting material recovery.

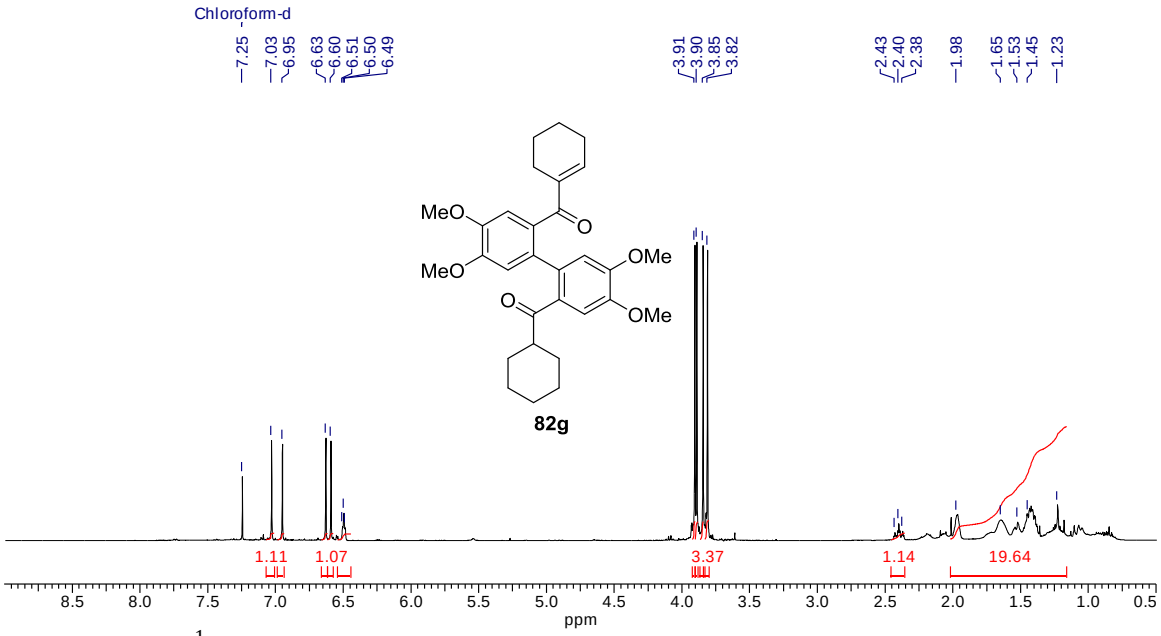


Figure I.15.1: ^{1}H-NMR (400 MHz) spectrum of **82g** in $CDCl_3$

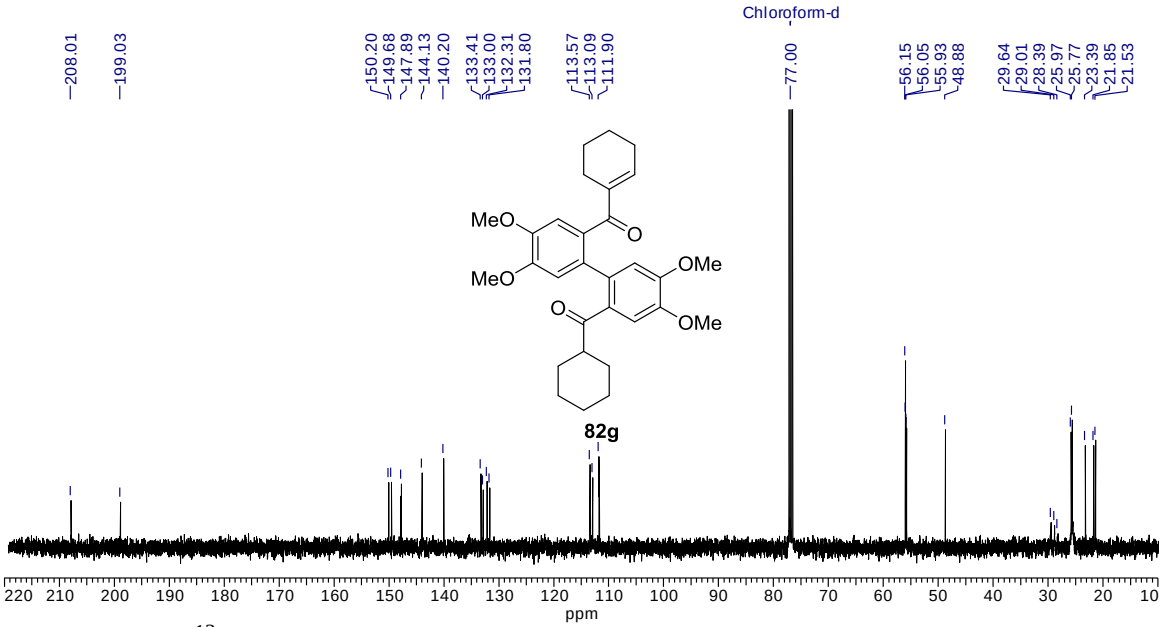
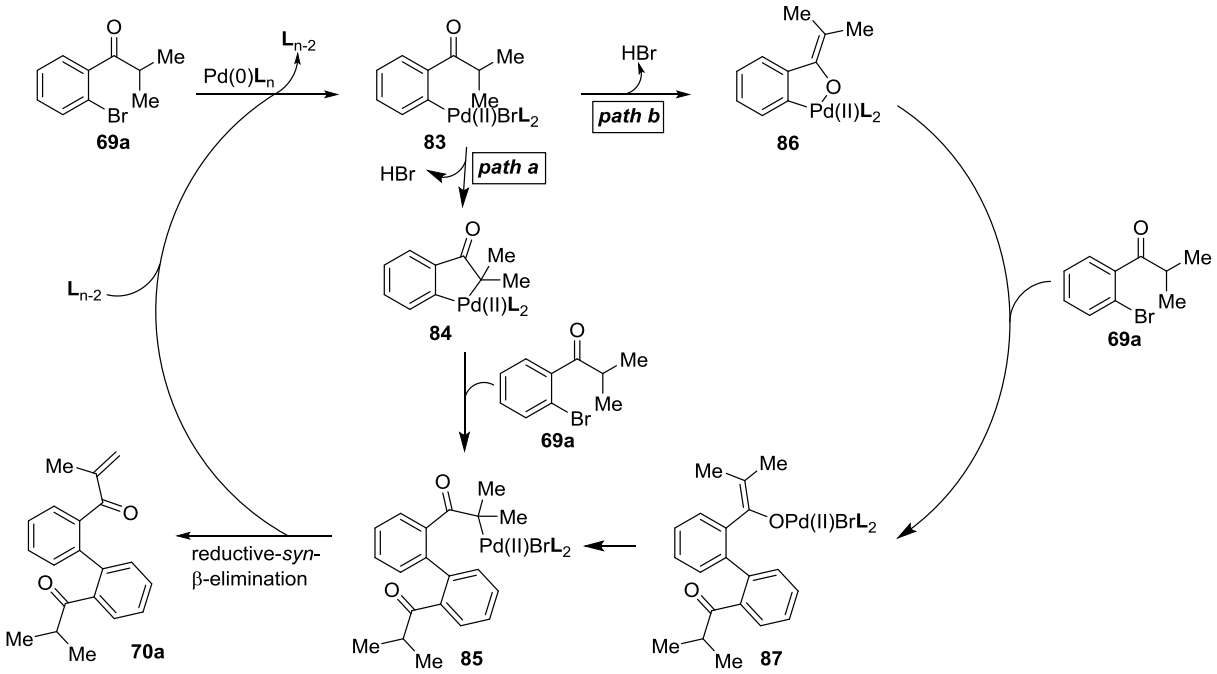


Figure I.15.2: ^{13}C-NMR (100 MHz) spectrum of **82g** in $CDCl_3$

The structure of bi-aryl **82g** was confirmed by IR and NMR data analysis. IR spectra show the presence of the absorption band at 1673 cm^{-1}. In the ^{1}H-NMR spectrum (Figure I.15.1), the presence of four individual singlets at δ 7.03, 6.95, 6.63 and 6.60 were due to four aromatic protons, a multiplet in the region at δ 6.55–6.45 was due to one olefinic proton, four singlets at δ 3.91, 3.90, 3.85 and 3.82 were due to twelve protons of four methoxy groups, presence of triplet of triplets at δ 2.4 having *J*=11.2 and 3.4 Hz due Cy-CH group and a multiplet in the region at δ 2.30–0.50 was due to eighteen cyclohexyl protons, elucidated the structure of bi-aryl **82g**. In addition to it, 29 signals appeared in ^{13}C-NMR spectrum (Figure I.15.2) in which two quaternary carbon resonates at δ 208.0 and 199.0 were due to two carbonyl carbons, nine quaternary carbon resonates at δ 150.2, 149.7 ,148.0 , 147.9 , 140.2, 133.4, 133.0, 132.3 and 131.8, whereas eight accounts for aromatic carbons and one accounts for olefinic carbon, the presence of five methine carbons at δ 144.1, 113.6, 113.1, 111.9 and 111.9 were due to four aromatic methine carbons and one for olefinic methine carbon, four methoxy group carbons resonates at δ 56.1 for 2C, 56.0 and 55.9, the presence of δ 48.9 due to CyCH group, and two cylohexyl group nine carbon resonates at δ 29.7, 29.1, 26.0, 25.8, 25.7, 25.6, 23.4, 21.8 and 21.5 ppm. The presence of $[M+H]^{+}$ peak at m/z $[C_{30}H_{37}O_6]^{+}$=493.2587 in the mass spectrum further established the structure of bi-aryl **82g**.

The plausible mechanistic pathways (***path a*** and ***path b***) for the formation of **70a** were described in Scheme I.15. Initially, oxidative insertion of Pd(0)-catalyst (i.e., via ***path a***) would lead to aryl-palladium(II) species **83**,[14] and then intramolecular sp^3 C-H activation bond furnishes the five-membered palladacycle **84** [as discussed earlier, in the present case, the mild base K_2CO_3 would not be strong enough to deprotonate α-hydrogen of isopropyl ketone, therefore, it is assumed that direct sp^3 C-H activation would be triggered by Pd(II) species of intermediate **84** of the ketone and concomitant elimination of HBr might lead to the formation of a five-membered palladacycle **84**. Then the key palladacycle **84** combines with a second molecule of **69a** and an

instantaneous bi-aryl bond formation would yield Pd(II) [41] complex **85**. Finally, expulsion of Pd-species through reductive *syn*-β-elimination generates the bi-aryl product **70a**. On the other hand, generation of five membered palladacycle **86** could also be feasible through chelation of aryl Pd(II)-species with the oxygen of ketone moiety (i.e., via ***path b***). The second molecule of **69a** could couple with the palladacycle **86**, thus furnishing the bi-aryl intermediate **87**, which could be converted to intermediate **85** upon isomerization that has been formed via ***path a***.

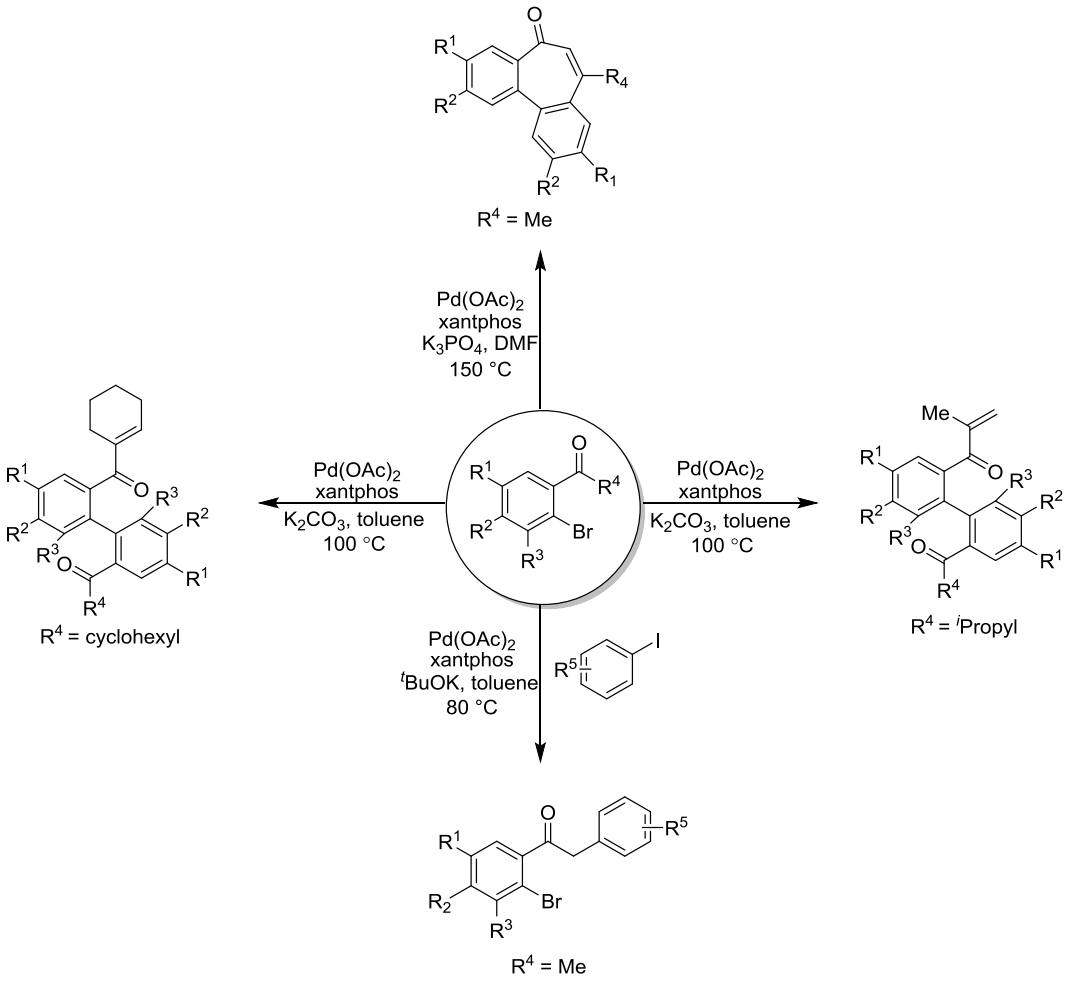


Scheme I.15

I.4. CONCLUSIONS:

In conclusion, we have developed an unprecedented and novel domino [Pd]-catalysis for the synthesis of 7-methyl-5*H*-dibenzo[*a*,*c*][7]annulen-5-ones. Significantly, these tricyclic systems constitute the major core of biologically active natural products. Also, we have demonstrated a [Pd]-catalyzed selective α-arylation of 2-

bromoacetophenones, for the synthesis of 1-(2-bromophenyl)-2-phenylethanones. External iodoarenes were identified as suitable coupling partners than bromoarenes. In addition, quite surprisingly, [Pd]-catalysis of 1-(2-bromophenyl)isopropyl ketones gave bi-aryls through homo-coupling. Delightfully, these bi-aryls scaffolds are present in many biologically active bi-aryl based natural products. This method is competent and proficient to deliver the bi-aryls with dense functionalities on the aromatic moieties. Overall, it was realized that the change in the alkyl group and slight modification in the reaction conditions altered the fate of the reaction.



Scheme I.16

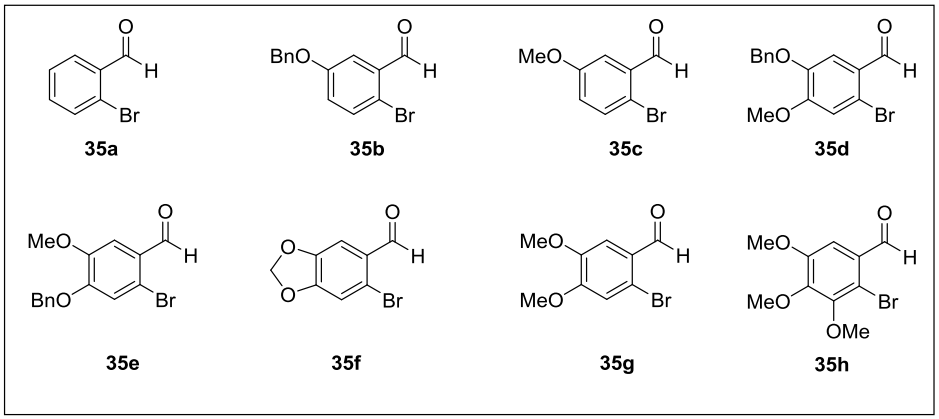
I.5 EXPERIMENTAL SECTION:

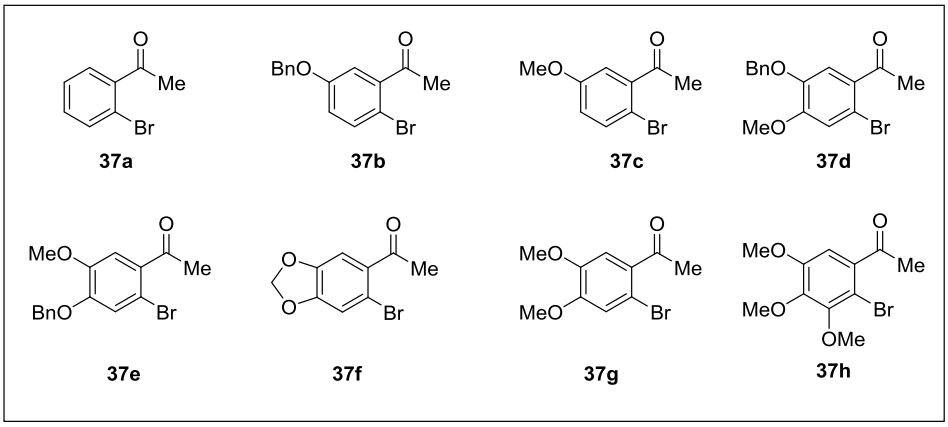
General:

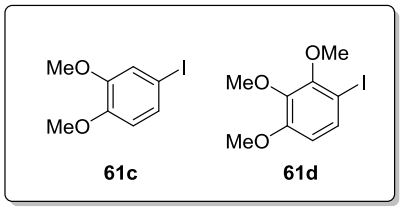
IR spectra were recorded on a Bruker Tensor 37 (FT-IR) spectrophotometer. ^{1}H-NMR spectra were recorded on Bruker Avance 400 (400 MHz) spectrometer at 295 K in $CDCl_3$; chemical shifts (δ in ppm) and coupling constants (J in Hz) are reported in standard fashion with reference to either internal standard tetramethylsilane (TMS) (δ_H = 0.00 ppm) or $CHCl_3$ (δ_H = 7.25 ppm). ^{13}C-NMR spectra were recorded on Bruker Avance 400 (100 MHz) spectrometer at RT in $CDCl_3$; chemical shifts (δ in ppm) are reported relative to $CHCl_3$ [δ_C = 77.00 ppm (central line of triplet)]. In the ^{13}C-NMR, the nature of carbons (C, CH, CH_2 and CH_3) was determined by recording the DEPT-135 spectra, and is given in parentheses and noted as s = singlet (for C), d = doublet (for CH), t = triplet (for CH_2) and q = quartet (for CH_3). In the ^{1}H-NMR, the following abbreviations were used throughout: s = singlet, d = doublet, t = triplet, q = quartet, qui = quintet, m = multiplet and br. s = broad singlet, septd = septet of doublets. The assignment of signals was confirmed by ^{1}H, ^{13}C CPD and DEPT spectra. High-resolution mass spectra (HR-MS) were recorded on an Agilent 6538 UHD Q-TOF using multimode source. X-ray crystal structure data was measured using the Oxford Super Nova instrument. All small scale dry reactions were carried out using the standard syringe-septum technique. Reactions were monitored by TLC on silica gel using a mixture of petroleum ether and ethyl acetate as eluents. Reactions were generally run under an argon or nitrogen atmosphere. All solvents were distilled to prior use; petroleum ether with a boiling range of 60 to 80 °C, diethyl ether, dichloromethane (DCM), ethyl acetate, toluene (with purity 99%), DMF (with purity 99%), DMA (with purity 99%), THF (with purity 99%), acetonitrile (with purity 99.9%), purchased from locally available commercial sources were used. All aromatic aldehydes (with purity 98%), bromine (with purity 99%), iodine (with purity 99%), methyl iodide (with purity 99%), ethyl bromide (with purity 99%), isopropyl bromide (with purity 99%), magnesium metal, 4 Å molecular sieves, sodium metal, silica gel (60–120 mesh) and ^{t}BuOK (with purity 98%) purchased from locally available commercial sources were

used. Palladium(II) acetate (with purity 98%), 4,5-Bis(diphenylphosphino)-9,9-dimethylxanthene (Xantphos) (with purity 97%), 2-dicyclohexylphosphino-2′-(*N*,*N*-dimethylamino)biphenyl (DavePhos) (with purity 99%), (2-biphenyl)dicyclohexylphosphine (cyclohexyl JohnPhos) (with purity 97%)**,** (2-biphenyl)di-*tert*-butylphosphine (JohnPhos) (with purity 97%), 1,1'-bis(diphenylphosphino)ferrocene (dppf) (with purity 97%), 2-di-*tert*-butylphosphino-2′,4′,6′-triisopropylbiphenyl (*tert*-Butyl XPhos) (with purity 97%), triphenylphosphine (PPh_3) (with purity 99%), Pd(dppf)Cl_2 (with purity 97%), Pd(PPh_3)$_4$ (with purity 99%), Pd(dba)$_2$ (with purity 98%), Pd(PPh_3)$_2Cl_2$ (with purity 98%), P(Cy)$_3$ (with purity 99%), N,N-diisopropylethylamine (DIPEA) (with purity 99%), 1,8-diazabicycloundec-7-ene (DBU) (with purity 98%), 1,4-diazabicyclo[2.2.2]octane (DABCO) (with purity 98%), *n*-tetrabutylammoniumiodide (*n*-Bu_4NI) (with purity 98%), *n*-tetrabutylammoniumbromide (*n*-Bu_4NBr) (with purity 98%), zinc chloride ($ZnCl_2$) (with purity 98%), dimethyl sulphoxide (DMSO) (with purity 99.7%) and potassium carbonate (with purity 99%), K_3PO_4 (with purity 98%), Cs_2CO_3 (with purity 99%), purchased from Sigma-Aldrich were used without further purification. The bases K_2CO_3, K_3PO_4 and Cs_2CO_3 dried at 150–170 $^{\circ}$C over oil bath and ^{t}BuOK dried with hot air gun. Diethyl ether and toluene were dried over sodium/ benzophenone. DCM, DCE, DMF and DMA dried over calcium hydride. Acetonitrile dried over P_2O_5. Acme's silica gel (60–120 mesh) was used for column chromatography (approximately 20 g per one gram of crude material).

The following 2-bromobenzaldehydes **35a-35h** [42] were synthesized using literature reported bromination of corresponding benzaldehydes and 2-bromoacetophenones **37a-37h**[9k] were synthesized using literature reported bromination of corresponding 2-bromobenzaldehydes. aryl iodides such as 4-iodo-1,2-dimethoxybenzene **61c** and 1-iodo-2,3,4-trimethoxybenzene **61d** were synthesized using literature reported bromination of corresponding 1,2-dimethoxybenzene, 1,2,3-trimethoxybenzene.[43]





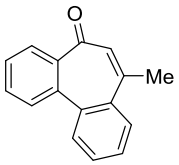


I.5.1 Synthesis of 3,9-dimethoxy-7-methyl-5H dibenzo[a,c][7]annulen-5-one:

General Procedure-1 for [Pd]-Mediated Cyclization (GP-1):

In an oven dried Schlenk tube, under nitrogen atmosphere were added 2-bromoacetophenones **37** (100–150 mg, 0.30 to 0.58 mmol), $Pd(OAc)_2$ (2 mol%), Xantphos (4 mol%) and K_3PO_4 (0.60 to 1.16 mmol) followed by addition of dry DMF (2 mL). The resulted reaction mixture was stirred at 150 °C for 45 min to 2 h. The

progress of the reaction was monitored by TLC till the reaction was completed. The reaction mixture was then quenched with saturated aqueous NH_4Cl solution and the aqueous layer was extracted with ethyl acetate (3 × 20 mL). The organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate) furnished the product **40** (41-50%).



40a

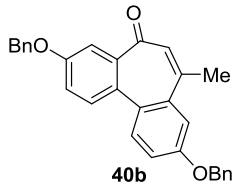
7-Methyl-5*H*-dibenzo[*a*,*c*][7]annulen-5-one (40a): **GP-1** was carried out with 2-bromoacetophenone **37a** (100 mg, 0.50 mmol), $Pd(OAc)_2$ (2.3 mg, 2 mol%), Xantphos (11.6 mg, 4 mol%), K_3PO_4 (213 mg, 1.00 mmol) and dry DMF (2 mL). The resulted reaction mixture was stirred at preheated oil bath 150 °C for 45 min. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 96:04 to 92:08) furnished the product **40a** (25 mg, 45%), as viscous liquid. [TLC control R_f(**37a**)=0.55, R_f(**40a**)=0.50 (petroleum ether/ethyl acetate 90:10, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3062, 2957, 2853, 1652, 1593, 1439, 1377, 1356, 1307, 1250, 1121, 1003, 850, 771, 735, 621cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.79 (dd, 2H, *J*=7.6 and 5.3 Hz, Ar-H), 7.74–7.69 (m, 2H, Ar-H), 7.63 (ddd, 1H, *J*=7.7, 7.6 and 1.3 Hz, Ar-H), 7.53 (dd, 1H, *J*=7.7 and 7.6 Hz, Ar-H), 7.49 (d, 1H, *J*=3.3 Hz, Ar-H), 7.47 (d, 1H, *J*=3.3 Hz, Ar-H), 6.62 (s, 1H, Ar-H), 2.44 (s, 3H, CH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=194.0 (s, Ar-C=O), 144.8 (s, Ar-C), 142.0 (s, Ar-C), 137.5 (s, Ar-C), 137.3 (s, Ar-C), 135.7 (s, Ar-C), 133.2 (d, Ar-CH), 131.9 (d, Ar-H), 131.2 (d, Ar-CH), 130.0 (d, Ar-CH), 128.6 (d, Ar-CH), 128.1 (d, Ar-CH), 127.8 (d, Ar-CH), 127.3 (d, Ar-CH), 127.1 (d, Ar-CH), 24.4 (q, CH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{32}H_{25}O_2]^+$=[2(M+H)]$^+$: 441.1849; found 441.1836.



40b

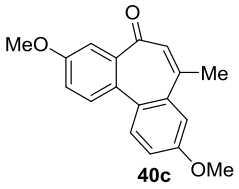
3,9-Bis(benzyloxy)-7-methyl-5*H*-dibenzo[*a*,*c*][7]annulen-5-one (40b): **GP-1** was carried out with 2-bromoacetophenone **37b** (120 mg, 0.39 mmol), $Pd(OAc)_2$ (1.8 mg, 2 mol%), Xantphos (9.1 mg, 4 mol%), K_3PO_4 (167 mg, 0.79 mmol) and dry DMF (2 mL). The resulted reaction mixture was stirred at preheated oil bath 150 °C for 1.5 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 92:08 to 85:15) furnished the product **40b** (35 mg, 41%), as viscous liquid. [TLC control R_f(**37b**)=0.50, R_f(**40b**)=0.40 (petroleum ether/ethyl acetate 80:20, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3064, 3034, 2923, 2855, 1644, 1602, 1570, 1483, 1410, 1337, 1279, 1236, 1182, 1026, 813, 735, 696 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.68 (d, 1H, *J*=8.9 Hz, Ar-H), 7.65 (d, 1H, *J*=8.9 Hz, Ar-H), 7.54–7.29 (m, 11H, Ar-H), 7.27 (d, 1H, *J*=2.6 Hz, Ar-H), 7.24 (dd, 1H, *J*=8.8 and 2.9 Hz, Ar-H), 7.09 (dd, 1H, *J*=8.8 and 2.6 Hz, Ar-H), 6.60 (s, 1H, Ar-H), 5.15 (s, 2H, Ph-CH_2O), 5.14 (s, 2H, Ph-CH_2O), 2.39 (s, 3H, CH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=193.4 (s, Ar-C=O), 158.2 (s, Ar-C), 157.5 (s, Ar-C), 144.8 (s, Ar-C), 142.2 (s, Ar-C), 136.5 (s, Ar-C), 136.4 (s, Ar-C), 136.3 (s, Ar-C), 132.9 (d, Ar-CH), 132.8 (d, Ar-H), 131.3 (d, Ar-CH), 130.7 (s, Ar-C), 130.6 (s, Ar-C), 128.7 (d, 2C, Ar-CH), 128.6 (d, 2C, Ar-CH), 128.2 (d, Ar-CH), 128.1 (d, Ar-CH), 127.6 (d, 2C, Ar-CH), 127.5 (d, 2C, Ar-CH), 119.9 (d, Ar-CH), 115.3 (d, Ar-CH), 113.3 (d, Ar-CH), 110.9 (d, Ar-CH), 70.3 (t, Ph-CH_2O), 70.2 (t, Ph-CH_2O), 24.6 (q, CH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{30}H_{24}NaO_3]^+$=$[M+Na]^+$: 455.1618; found 455.1611.



40c

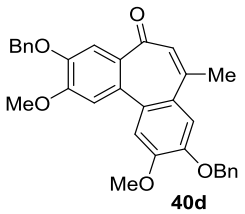
3,9-Dimethoxy-7-methyl-5*H*-dibenzo[*a*,*c*][7]annulen-5-one (40c): GP-1 was carried out with 2-bromoacetophenone **37c** (100 mg, 0.44 mmol), $Pd(OAc)_2$ (2.0 mg, 2 mol%), Xantphos (10.1 mg, 4 mol%), K_3PO_4 (185 mg, 0.87 mmol) and dry DMF (2 mL). The resulted reaction mixture was stirred at preheated oil bath 150 °C for 1.5 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 85:15 to 80:20) furnished the product **40c** (31 mg, 50%), as white solid (recrystallized from a mixture of petroleum ether/dichloromethane). m. p.: 125–127 °C. [TLC control R_f(**37c**)=0.50, R_f(**40c**)=0.40 (petroleum ether/ethyl acetate 80:20, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3001, 2934, 2837, 1643, 1603, 1571, 1484, 1408, 1337, 1281, 1240, 1174, 1039, 814, 753, 722, 614 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.69 (d, 1H, *J*=8.9 Hz, Ar-H), 7.66 (d, 1H, *J*=8.9 Hz, Ar-H), 7.28 (d, 1H, *J*=2.9 Hz, Ar-H), 7.20 (d, 1H, *J*=2.8 Hz, Ar-H), 7.18 (dd, 1H, *J*=8.9 and 2.9 Hz, Ar-H), 7.04 (dd, 1H, *J*=8.9 and 2.8 Hz, Ar-H), 6.61 (d, 1H, *J*=0.9 Hz, Ar-H), 3.89 (s, 3H, Ar-OCH_3), 3.88 (s, 3H, Ar-OCH_3), 2.43 (s, 3H, CH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=193.6 (s, Ar-C=O), 159.0 (s, Ar-C), 158.4 (s, Ar-C), 144.8 (s, Ar-C), 142.3 (s, Ar-C), 136.3 (s, Ar-C), 132.9 (d, Ar-CH), 132.8 (d, Ar-CH), 131.3 (d, Ar-CH), 130.5 (s, Ar-C), 130.4 (s, Ar-C), 119.4 (d, Ar-CH), 114.5 (d, Ar-CH), 112.2 (d, Ar-CH), 109.7 (d, Ar-CH), 55.6 (q, Ar-OCH_3), 55.4 (q, Ar-OCH_3), 24.6 (q, CH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{18}H_{17}O_3]^+$=$[M+H]^+$: 281.1172; found 281.1161.



40d

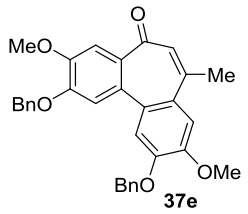
3,9-Bis(benzyloxy)-2,10-dimethoxy-7-methyl-5*H*-dibenzo[*a*,*c*][7]annulen-5-one (40d): **GP-1** was carried out with 2-bromoacetophenone **37d** (100 mg, 0.30 mmol), $Pd(OAc)_2$ (1.3 mg, 2 mol%), Xantphos (6.9 mg, 4 mol%), K_3PO_4 (127 mg, 0.60 mmol) and dry DMF (2 mL). The resulted reaction mixture was stirred at preheated oil bath 150 °C for 2 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 80:20 to 70:30) furnished the product **40d** (32 mg, 43%), as brownish yellow semi-solid. [TLC control R_f(**37d**)=0.60, R_f(**40d**)=0.40 (petroleum ether/ethyl acetate 60:40, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2932, 1630, 1589, 1509, 1455, 1383, 1257, 1218, 1162, 1070, 1020, 858, 734, 698 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.41 (d, 2H, *J*=7.1 Hz, Ar-H), δ=7.41 (s, 2H, Ar-H), 7.32 (dd, 2H, *J*=7.1 and 7.1 Hz, Ar-H), 7.31 (dd, 2H, *J*=7.1 and 7.1 Hz, Ar-H), 7.28–7.20 (m, 2H, Ar-H), 7.18 (s, 1H, Ar-H), 7.16 (s, 2H, Ar-H), 7.11 (s, 1H, Ar-H), 6.48 (s, 1H, Ar-H), 5.19 (s, 2H, $PhCH_2O$), 5.17 (s, 2H, $PhCH_2O$), 3.94 (s, 3H, Ar-OCH_3), 3.93 (s, 3H, Ar-OCH_3), 2.23 (s, 3H, CH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=191.4 (s, Ar-C=O), 152.0 (s, Ar-C), 149.7 (s, Ar-C), 148.4 (s, Ar-C), 147.2 (s, Ar-C), 143.8 (s, Ar-C), 136.7 (s, Ar-C), 136.4 (s, Ar-C), 135.0 (s, Ar-C), 132.1 (d, Ar-CH), 132.0 (s, Ar-C), 131.9 (s, Ar-C), 128.9 (s, Ar-C), 128.7 (d, 2C, Ar-CH), 128.6 (d, 2C, Ar-CH), 128.1 (d, Ar-CH), 128.0 (d, Ar-CH), 127.6 (d, 2C, Ar-CH), 127.4 (d, 2C, Ar-CH), 114.5 (d, Ar-CH), 113.0 (d, Ar-CH), 112.4 (d, Ar-CH), 111.5 (d, Ar-CH), 71.4 (t, $PhCH_2O$), 70.9 (t, $PhCH_2O$), 56.3 (q, Ar-OCH_3), 56.2 (q, Ar-OCH_3), 24.8 (q, CH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{32}H_{28}NaO_5]^+$=$[M+Na]^+$: 515.1829; found 515.1834.



37e

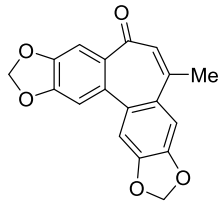
2,10-Bis(benzyloxy)-3,9-dimethoxy-7-methyl-5*H*-dibenzo[*a*,*c*][7]annulen-5-one (40e): **GP-1** was carried out with 2-bromoacetophenone **37e** (150 mg, 0.45 mmol), $Pd(OAc)_2$ (2.0 mg, 2 mol%), Xantphos (10.4 mg, 4 mol%), K_3PO_4 (190 mg, 0.89 mmol) and dry DMF (3 mL). The resulted reaction mixture was stirred at preheated oil bath 150 °C for 2 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 80:20 to 75:25) furnished the product **40e** (45 mg, 41%), as white solid (recrystallized from a mixture of petroleum ether/dichloromethane). m.p.: 160–162 °C. [TLC control R_f(**37e**)=0.60, R_f(**40e**)=0.30 (petroleum ether/ethyl acetate 60:40, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2923, 2852, 1630, 1591, 1508, 1461, 1391, 1255, 1163, 1068, 1035, 1012, 859, 737, 697 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.43 (d, 2H, *J*=7.8 Hz, Ar-H), 7.40 (d, 2H, *J*=7.5 Hz, Ar-H), 7.38 (dd, 2H, *J*=7.8 and 7.8 Hz, Ar-H), 7.37 (dd, 2H, *J*=7.5 and 7.5 Hz, Ar-H), 7.29 (t, 1H, *J*=7.8 Hz, Ar-H), 7.29 (t, 1H, *J*=7.5 Hz, Ar-H), 7.16 (s, 1H, Ar-H), 6.94 (s, 1H, Ar-H), 6.93 (s, 1H, Ar-H), 6.60 (s, 1H, Ar-H), 5.10 (s, 2H, $PhCH_2O$), 5.05 (s, 2H, $PhCH_2O$), 3.98 (s, 3H, Ar-OCH_3), 3.97 (s, 3H, Ar-OCH_3), 2.44 (s, 3H, CH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=191.5 (s, Ar-C=O), 150.4 (s, Ar-C), 149.4 (s, Ar-C), 148.4 (s, Ar-C), 148.0 (s, Ar-C), 143.9 (s, Ar-C), 136.6 (s, Ar-C), 136.4 (s, Ar-C), 135.0 (s, Ar-C), 132.1 (d, Ar-CH), 131.5 (s, Ar-C), 131.2 (s, Ar-C), 129.0 (s, Ar-C), 128.8 (d, 2C, Ar-CH), 128.7 (d, 2C, Ar-CH), 128.1 (d, Ar-CH), 128.0 (d, Ar-CH), 127.2 (d, 2C, Ar-CH), 127.1 (d, 2C, Ar-CH), 116.0 (d, Ar-CH), 113.9 (d, Ar-CH), 110.1 (d, Ar-CH), 109.7 (d, Ar-CH), 70.8 (t, 2C, 2 × $PhCH_2O$), 56.1 (q, 2C, 2 × Ar-OCH_3), 24.9 (q, CH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{32}H_{28}NaO_5]^+$=$[M+Na]^+$: 515.1829; found 515.1837.



40f

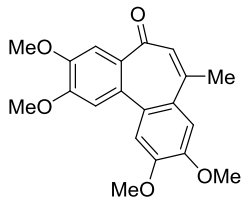
2,3,9,10-Bis(di-1,3-benzodioxol)-7-methyl-5*H*-dibenzo[*a*,*c*][7]annulen-5-one (40f): **GP-1** was carried out with 2-bromoacetophenone **37f** (100 mg, 0.41 mmol), $Pd(OAc)_2$ (1.8 mg, 2 mol%), Xantphos (9.5 mg, 4 mol%), K_3PO_4 (175 mg, 0.0.82 mmol) and dry DMF (2 mL). The resulted reaction mixture was stirred at preheated oil bath 150 °C for 2 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 85:15 to 80:20) furnished the product **40f** (26 mg, 41%), as yellow semi-solid. [TLC control R_f(**37f**)=0.65, R_f(**40f**)=0.40 (petroleum ether/ethyl acetate 75:25, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2921, 1641, 1608, 1503, 1485, 1415, 1397, 1243, 1034, 926, 863 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.27 (s, 1H, Ar-H), 7.16 (s, 1H, Ar-H), 7.15 (s, 2H, Ar-H), 6.55 (d, 1H, J=0.9 Hz, Ar-H), 6.08 (s, 2H, O-CH_2-O), 6.06 (s, 2H, O-CH_2-O), 2.39 (s, 3H, CH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=191.8 (s, Ar-C=O), 150.5 (s, Ar-C), 148.0 (s, Ar-C), 147.9 (s, Ar-C), 147.2 (s, Ar-C), 143.6 (s, Ar-C), 137.1 (s, Ar-C), 133.8 (s, Ar-C), 132.8 (s, Ar-C), 131.7 (d, Ar-CH), 130.4 (s, Ar-C), 111.0 (d, Ar-CH), 109.2 (d, Ar-CH), 106.8 (d, Ar-CH), 106.4 (d, Ar-CH), 102.0 (t, O-CH_2-O), 101.8 (t, O-CH_2-O), 24.9 (q, CH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{18}H_{12}NaO_5]^+$=$[M+Na]^+$: 331.0577; found 331.0576.



40g

2,3,9,10-Tetramethoxy-7-methyl-5*H*-dibenzo[*a*,*c*][7]annulen-5-one (40g): GP-1 was carried out with 2-bromoacetophenone **37g** (150 mg, 0.58 mmol), $Pd(OAc)_2$ (2.6 mg, 2 mol%), Xantphos (13.4 mg, 4 mol%), K_3PO_4 (246 mg, 1.16 mmol) and dry DMF (3 mL). The resulted reaction mixture was stirred at preheated oil bath 150 °C for 2 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 55:45 to 40:60) furnished the product **40g** (43 mg, 44%), as yellow solid (recrystallized from a mixture of petroleum ether/dichloromethane). m.p.: 180–183 °C. [TLC control R_f(**37g**)=0.60, R_f(**40g**)=0.30 (petroleum ether/ethyl acetate 6:4, UV detection)]

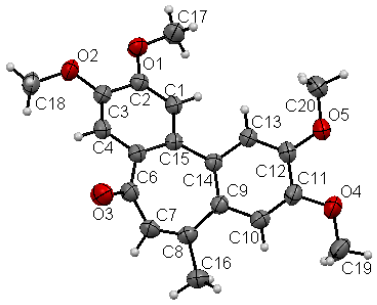
IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2927, 2852, 1629, 1593, 1511, 1464, 1390, 1258, 1204, 1163, 1071, 1034, 861, 788, 732 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.38 (s, 1H, Ar-H), 7.20 (s, 1H, Ar-H), 7.19 (s, 1H, Ar-H), 7.16 (s, 1H, Ar-H), 6.60 (s, 1H, Ar-H), 4.00 (s, 3H, Ar-OCH_3), 3.98 (s, 9H, 3 × Ar-OCH_3), 2.44 (s, 3H, CH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=191.5 (s, Ar-C=O), 151.4 (s, Ar-C), 149.0 (s, Ar-C), 149.0 (s, Ar-C), 148.1 (s, Ar-C), 143.9 (s, Ar-C), 134.9 (s, Ar-C), 132.1 (d, Ar-CH), 131.8 (s, Ar-C), 131.4 (s, Ar-C), 128.9 (s, Ar-C), 113.8 (d, Ar-CH), 111.8 (d, Ar-CH), 109.6 (d, Ar-CH), 109.5 (d, Ar-CH), 56.1 (q, 2C, Ar-OCH_3), 56.0 (q, Ar-OCH_3), 55.9 (q, Ar-OCH_3), 24.9 (q, CH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{20}H_{20}NaO_5]^+$=$[M+Na]^+$: 363.1203; found 363.1201.

X-ray crystal structure data for the 2, 3, 9, 10-tetramethoxy-7-methyl-5*H*-dibenzo[*a*,*c*][7]annulen-5-one (40g): CCDC 910650

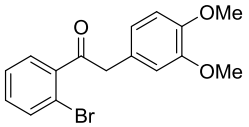


Operator	**K. Ravikumar**
Instrument	**Oxford SuperNova**
Temperature/K	150.00(10)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	7.7665(6)
b/Å	18.0904(8)
c/Å	12.1119(6)
α/°	90.00
β/°	103.846(6)
γ/°	90.00
Volume/$Å^3$	1652.27(16)
Z	4
$\rho_{calc}mg/mm^3$	1.368
m/mm^{-1}	0.806
F(000)	720.0
Crystal size/mm^3	0.15 × 0.13 × 0.12
2Θ range for data collection	8.96 to 141.36°
Index ranges	$-7 \le h \le 9$, $-22 \le k \le 16$, $-14 \le l \le 11$
Reflections collected	6556
Independent reflections	3116[R(int) = 0.0242]
Data/restraints/parameters	3116/0/231
Goodness-of-fit on F^2	0.978
Final R indexes [I>=2σ (I)]	R_1 = 0.0448, wR_2 = 0.1306
Final R indexes [all data]	R_1 = 0.0585, wR_2 = 0.1487
Largest diff. peak/hole / e $Å^{-3}$	0.14/-0.18

I.5.2 Synthesis of α-aryl ketones:

General procedure-2 for α-arylation of ketones (GP-2):

In an oven dried Schlenk tube under nitrogen atmosphere, were added aryliodides 61**a-61f** (0.50 mmol), 2-bromoacetophenone **37a-37c** (0.55 mmol), $Pd(OAc)_2$ (2 mol%), Xantphos (4 mol%) and ^{t}BuOK (0.65 mmol) followed by addition of dry toluene (4 mL). The resulted reaction mixture was stirred at 80 °C for 45 min to 3 h. The progress of the reaction was monitored by TLC till the reaction was completed. The reaction mixture was then quenched with saturated aqueous NH_4Cl and the aqueous layer was extracted with ethyl acetate (3 × 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under in vacuo. The crude product was purified on a silica gel column chromatography using petroleum ether/ethyl acetate which furnished the product **62ag-62gf** (61–92%).



62ac

1-(2-Bromophenyl)-2-(3,4-dimethoxyphenyl)ethanone (62ac): **GP-2** was carried out with aryliodide **61c** (132.0 mg, 0.50 mmol**)**, 2-bromoacetophenone **37a** (109.4 mg, 0.55 mmol**)**, $Pd(OAc)_2$ (2.2 mg, 2 mol%), Xantphos (11.6 mg, 4 mol%), ^{t}BuOK (72.9 mg, 0.65 mmol) and dry toluene (4 mL) at 80 °C for 45 min. Purification of the residue on a Silica gel column chromatography (petroleum ether/ethyl acetate, 85:15 to 80:20) furnished the product **62ac** (155 mg, 92%) as yellow solid, recrystallized the solid with dichloromethane/hexane, m. p. 74–76 °C. [TLC control (petroleum ether/ethyl acetate 90:10), R_f(**37a**)=0.55, R_f(**61c**)=0.45 and R_f(**62ac**)=0.20, UV detection].

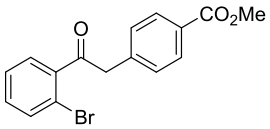
IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2956, 2923, 2852, 1697, 1587, 1512, 1463, 1422, 1259, 1154, 1140, 1025, 791, 757, 678 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.57 (d, 1H, J=7.8 Hz, Ar-H), 7.35–7.15 (m, 3H, Ar-H), 6.78 (d, 1H, J=8.7 Hz, Ar-H), 6.76 (dd, 1H, J=8.7 and 1.9 Hz, Ar-H), 6.74

(d, 1H. *J*=1.9 Hz, Ar-H), 4.15 (s, 2H, CH_2), 3.83 (s, 3H, Ar-OCH_3), 3.82 (s, 3H, Ar-OCH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=201.8 (s, Ar-C=O), 148.9 (s, Ar-C), 148.1 (s, Ar-C), 141.4 (s, Ar-C), 133.5 (d, Ar-CH), 131.4 (d, Ar-CH), 128.6 (d, Ar-CH), 127.2 (d, Ar-CH), 125.8 (s, Ar-C), 121.9 (d, Ar-CH), 118.6 (s, Ar-C), 112.7 (d, Ar-CH), 111.2 (d, Ar-CH), 55.8 (q, 2C, 2 × Ar-OCH_3), 49.0 (t, CH_2) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{16}H_{16}{}^{79}BrO_3]^+$=$[M+H]^+$: 335.0277; found 335.0294, $[C_{16}H_{16}{}^{81}BrO_3]^+$=$[M+H]^+$: 337.0259; found 337.0274.



62ae

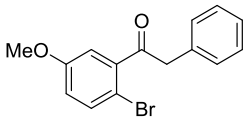
Methyl-4-[2-(2-bromophenyl)-2-oxoethyl]benzoate (62ae): GP-2 was carried out with aryliodide **61e** (131.0 mg, 0.50 mmol**)**, 2-bromoacetophenone **37a** (109.4 mg, 0.55 mmol**)**, $Pd(OAc)_2$ (2.2 mg, 2 mol%), Xantphos (11.6 mg, 4 mol%), ^{t}BuOK (72.9 mg, 0.65 mmol) and dry toluene (4 mL) at 80 °C for 45 min. Purification of the residue on a Silica gel column chromatography (petroleum ether/ethyl acetate, 92:8 to 85:15) furnished the product **62ae** (139.8 mg, 80%) as yellow semi-solid. [TLC control (petroleum ether/ethyl acetate 95:10), R_f(**37a**)=0.55, R_f(**61e**)=0.75 and R_f(**62ae**)=0.30, UV detection].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2919, 2850, 1717, 1587, 1463, 1434, 1280, 1198, 1181, 1107, 1022, 988, 757 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.98 (d, 2H, *J*=8.3 Hz, Ar-H), 7.59 (d, 1H, *J*=7.8 Hz, Ar-H), 7.40–7.20 (m, 5H, Ar-H), 4.28 (s, 2H, CH_2), 3.89 (s, 3H, CH_3) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ=200.7 (s, Ar-C=O), 166.8 (s, COOMe), 141.2 (s, Ar-C), 138.7 (s, Ar-C), 133.6 (d, Ar-CH), 131.7 (d, Ar-CH), 129.9 (d, 2C, Ar-CH), 129.8 (d, 2C, Ar-CH), 129.0 (s, Ar-C), 128.6 (d, Ar-CH), 127.4 (d, Ar-CH), 118.6 (s, Ar-C), 52.1 (q, CH_3), 49.3 (t, CH_2) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{16}H_{13}BrNaO_3]^+$=$[M+Na]^+$: 354.9940; found 354.9944.



62ca

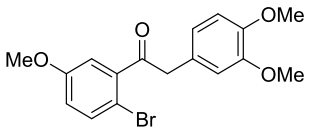
1-(2-Bromo-5-methoxyphenyl)-2-phenylethanone (62ca): GP-2 was carried out with aryliodide **61a** (102 mg, 0.50 mmol**)**, 2-bromoacetophenone **37c** (125.9 mg, 0.55 mmol**)**, $Pd(OAc)_2$ (2.2 mg, 2 mol%), Xantphos (11.6 mg, 4 mol%), ^{t}BuOK (72.9 mg, 0.65 mmol) and dry toluene (4 mL) at 80 °C for 2 h. Purification of the residue on a Silica gel column chromatography (petroleum ether/ethyl acetate, 90:10 to 85:15) furnished the product **62ca** (121.6 mg, 80%) as brown viscous liquid. [TLC control R_f(**37c**)=0.50, R_f(**61a**)=0.50 and R_f(**62ca**)=0.85 (petroleum ether/ethyl acetate 90:10, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2924, 1701, 1592, 1569, 1467, 1403, 1314, 1289, 1240, 1171, 1026, 815, 727, 698 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.35 (d, 1H, Ar-H), 7.29–7.16 (m, 3H, Ar-H), 7.15 (d, 2H, *J*=7.8 Hz, Ar-H), 6.70 (dd, 1H, *J*=8.3 and 3.4 Hz, Ar-H), 6.69 (s, 1H, Ar-H), 4.13 (s, 2H, CH_2), 3.63 (s, 3H, Ar-OCH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=201.5 (s, C=O), 158.6 (s, Ar-C), 142.1 (s, Ar-C), 134.2 (d, Ar-CH), 133.4 (s, Ar-C), 129.7 (d, 2C, Ar-CH), 128.5 (d, 2C, Ar-CH), 127.1 (d, Ar-CH), 117.5 (d, Ar-CH), 113.9 (d, Ar-CH), 108.7 (s, Ar-C), 55.5 (q, Ar-OCH_3), 49.3 (t, CH_2) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{15}H_{14}{}^{79}BrO_2]^+$=$[M+H]^+$: 305.0172; found 305.0163, $[C_{15}H_{14}{}^{81}BrO_2]^+$=$[M+H]^+$: 307.0151; found 307.0144.



62cc

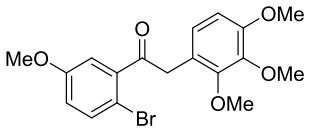
1-(2-Bromo-5-methoxyphenyl)-2-(3,4-dimethoxyphenyl)ethanone (**62cc**): **GP-2** was carried out with aryliodide **61c** (132.0 mg, 0.50 mmol**)**, 2-bromoacetophenone **37c** (126.0 mg, 0.55 mmol**)**, $Pd(OAc)_2$ (2.2 mg, 2 mol%), Xantphos (11.6 mg, 4 mol%), ^tBuOK (72.9 mg, 0.65 mmol) and dry toluene (4 mL) at 80 °C for 2 h. Purification of the residue on a Silica gel column chromatography (petroleum ether/ethyl acetate, 85:15 to 80:20) furnished the product **62cc** (137 mg, 75%) as brown viscous liquid. [TLC control (petroleum ether/ethyl acetate 80:20), R_f(**37c**)=0.50, R_f(**61c**)=0.40 and R_f(**62cc**)=0.20, UV detection].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2936, 1699, 1592, 1569, 1514, 1464, 1261, 1235, 1026, 905, 724 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.43 (d, 1H, J=8.3 Hz, Ar-H), 7.00–6.60 (m, 5H, Ar-H), 4.14 (s, 2H, CH_2), 3.83 (s, 3H, Ar-OCH_3), 3.82 (s, 3H, Ar-OCH_3), 3.72 (s, 3H, Ar-OCH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=201.7 (s, Ar-C=O), 158.6 (s, Ar-C), 148.9 (s, Ar-C), 148.1 (s, Ar-C), 142.1 (s, Ar-C), 134.2 (d, Ar-CH), 125.8 (s, Ar-C), 121.9 (d, Ar-CH), 117.3 (d, Ar-CH), 114.1 (d, Ar-CH), 112.7 (d, Ar-CH), 111.2 (d, Ar-CH), 108.7 (s, Ar-C), 55.8 (q, 2C, 2 × Ar-OCH_3), 55.5 (q, Ar-OCH_3), 48.8 (t, CH_2) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{17}H_{18}BrO_4]^+$=$[M+H]^+$: 365.0383; found 365.0380.



62cd

1-(2-Bromo-5-methoxyphenyl)-2-(2,3,4-trimethoxyphenyl)ethanone (62cd): **GP-2** was carried out with aryliodide **61d** (147 mg, 0.50 mmol**)**, 2-bromoacetophenone **37c**

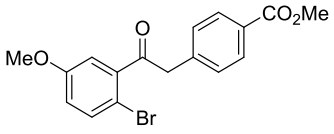
(126 mg, 0.55 mmol**)**, $Pd(OAc)_2$ (2.2 mg, 2 mol%), Xantphos (11.6 mg, 4 mol%), ^{t}BuOK (72.9 mg, 0.65 mmol) and dry toluene (4 mL) at 80 °C for 2 h. Purification of the residue on a Silica gel column chromatography (petroleum ether/ethyl acetate, 85:15 to 80:20) furnished the product **62cd** (167 mg, 84%) as pale yellow viscous liquid. [TLC control (petroleum ether/ethyl acetate 80:20), R_f(**37c**)=0.50, R_f(**61d**)=0.50 and R_f(**62cd**)=0.25, UV detection].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2922, 2850, 1702, 1592, 1569, 1494, 1465, 1418, 1274, 1238, 1095, 1017, 794, 733 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.44 (d, 1H, *J*=8.8 Hz, Ar-H), 6.93 (d, 1H, *J*=3.4 Hz, Ar-H), 6.88 (d, 1H, *J*=8.8 Hz, Ar-H), 6.80 (dd, 1H, *J*=8.8 and 3.4 Hz, Ar-H), 6.62 (d, 1H, *J*=8.8 Hz, Ar-H), 4.15 (s, 2H, CH_2), 3.85 (s, 3H, Ar-OCH_3), 3.84 (s, 3H, Ar-OCH_3), 3.83 (s, 3H, Ar-OCH_3), 3.77 (s, 3H, Ar-OCH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=201.6 (s, Ar-C=O), 158.6 (s, Ar-C), 153.2 (s, Ar-C), 151.8 (s, Ar-C), 142.4 (s, Ar-C), 142.0 (s, Ar-C), 134.2 (d, Ar-CH), 125.2 (d, Ar-CH), 120.1 (s, Ar-C), 117.3 (d, Ar-CH), 114.0 (d, Ar-CH), 108.7 (s, Ar-C), 107.1 (d, Ar-CH), 60.7 (q, Ar-OCH_3), 60.6 (q, Ar-OCH_3), 55.9 (q, Ar-OCH_3), 55.5 (q, Ar-OCH_3), 43.6 (t, CH_2) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{18}H_{19}{}^{79}BrNaO_5]^+$=$[M+Na]^+$: 417.0308; found 417.0308, $[C_{18}H_{19}{}^{81}BrNaO_5]^+$=$[M+Na]^+$: 419.0290; found 419.0301, $[C_{18}H_{20}BrO_5]^+$=$[M+H]^+$: 395.0489; found 395.0480 and $[C_{18}H_{20}{}^{81}BrO_5]^+$=$[M+H]^+$: 397.0470; found 397.0488.



62ce

Methyl-4-[2-(2-bromo-5-methoxyphenyl)-2-oxoethyl]benzoate (62ce): GP-2 was carried out with aryliodide **61e** (131.0 mg, 0.50 mmol**)**, 2-bromoacetophenone **37c** (125.9 mg, 0.55 mmol**)**, $Pd(OAc)_2$ (2.2 mg, 2 mol%), Xantphos (11.6 mg, 4 mol%), ^{t}BuOK (72.9 mg, 0.65 mmol) and dry toluene (4 mL) at 80 °C for 2 h. Purification of

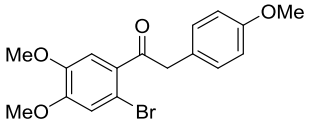
the residue on a Silica gel column chromatography (petroleum ether/ethyl acetate, 85:15 to 80:20) furnished the product **62ce** (137.5 mg, 76%) as pale yellow viscous liquid. [TLC control R_f(**37c**)=0.65, R_f(**61e**)=0.45 and R_f(**62ce**)=0.45 (petroleum ether/ethyl acetate 80:20, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2925, 2852, 1718, 1610, 1591, 1467, 1435, 1278, 1241, 1109, 966, 742 cm^{-1}.

^{1}H-NMR (CDCl$_3$, 400 MHz): δ=7.98 (d, 2H, *J*=8.3 Hz, Ar-H), 7.46 (d, 1H, *J*=8.3 Hz, Ar-H), 7.32 (d, 2H, *J*= 7.8 Hz, Ar-H), 6.87–6.78 (m, 2H, Ar-H), 4.28 (s, 2H, CH_2), 3.89 (s, 3H, $COOCH_3$), 0.74 (s, 3H, Ar-OCH_3) ppm.

^{13}C-NMR (CDCl$_3$, 100 MHz): δ=200.7 (s, ArCO), 166.8 (s, COOMe), 158.8 (s, Ar-C), 141.9 (s, Ar-C), 138.7 (s, Ar-C), 134.4 (d, Ar-CH), 129.7 (d, 2C, Ar-CH), 129.8 (d, 2C, Ar-CH), 129.0 (s, Ar-C), 117.7 (d, Ar-CH), 114.0 (d, Ar-CH), 108.7 (s, Ar-C), 55.6 (q, Ar-OCH_3), 52.1 (q, COO*C*H_3), 49.1 (t, CH_2) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{17}H_{16}{}^{79}BrO_4]^+$=$[M+H]^+$: 363.0226; found 363.0218, $[C_{17}H_{16}{}^{81}BrO_4]^+$=$[M+H]^+$: 365.0206; found 365.0201.



62gb

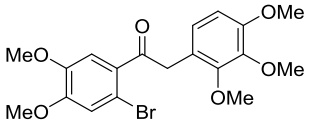
1-(2-Bromo-4,5-dimethoxyphenyl)-2-(4-methoxyphenyl)ethanone (62gb): GP-2 was carried out with aryliodide **61b** (117 mg, 0.50 mmol**)**, 2-bromoacetophenone **37g** (142.5 mg, 0.55 mmol**)**, $Pd(OAc)_2$ (2.2 mg, 2 mol%), Xantphos (11.6 mg, 4 mol%), ^{t}BuOK (72.9 mg, 0.65 mmol) and dry toluene (4 mL) at 80 °C for 3 h. Purification of the residue on a Silica gel column chromatography (petroleum ether/ethyl acetate, 85:15 to 80:20) furnished the product **62gb** (144.2 mg, 79%) as pale yellow viscous liquid. [TLC control (petroleum ether/ethyl acetate 70:30), R_f(**37g**)=0.50, R_f(**61b**)=0.90 and R_f(**62gb**)=0.40, UV detection].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2924, 1689, 1593, 1506, 1461, 1371, 1247, 1209, 1161, 1024, 852, 794 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.14 (d, 2H, *J*=8.8 Hz, Ar-H), 7.02 (s, 1H, Ar-H), 6.91 (s, 1H, Ar-H), 6.83 (d, 2H, *J*=8.8 Hz, Ar-H), 4.21 (s, 2H, CH_2), 3.88 (s, 3H, Ar-OCH_3), 3.80 (s, 3H, Ar-OCH_3), 3.77 (s, 3H, Ar-OCH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=200.5 (s, Ar-C=O), 158.6 (s, Ar-C), 151.2 (s, Ar-C), 148.0 (s, Ar-C), 132.7 (s, Ar-C), 130.6 (d, 2C, Ar-CH), 126.1 (s, Ar-C), 116.2 (d, Ar-CH), 114.0 (d, 2C, Ar-CH), 112.3 (d, Ar-CH), 110.8 (s, Ar-C), 56.2 (q, Ar-OCH_3), 56.1 (q, Ar-OCH_3), 55.2 (q, Ar-OCH_3), 48.2 (t, CH_2) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{17}H_{18}BrO_4]^+$=$[M+H]^+$: 365.0383; found 365.0397.



62gd

1-(2-Bromo-4,5-dimethoxyphenyl)-2-(2,3,4-trimethoxyphenyl)ethanone (62gd): GP-2 was carried out with aryliodide **61d** (147 mg, 0.50 mmol**)**, 2-bromoacetophenone **37g** (142.5 mg, 0.55 mmol**)**, $Pd(OAc)_2$ (2.2 mg, 2 mol%), Xantphos (11.6 mg, 4 mol%), ^{t}BuOK (72.9 mg, 0.65 mmol) and dry toluene (4 mL) at 80 °C for 3 h. Purification of the residue on a Silica gel column chromatography (petroleum ether/ethyl acetate, 80:20 to 75:25) furnished the product **62gd** (171.7 mg, 81%) as Color less viscous liquid. [TLC control (petroleum ether/ethyl acetate 70:30), R_f(**37g**)=0.50, R_f(**61d**)=0.80 and R_f(**62gd**)=0.35, UV detection].

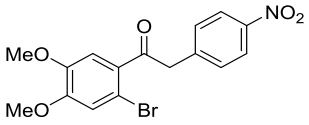
IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2936, 1694, 1594, 1495, 1466, 1371, 1257, 1210, 1165, 1096, 1018, 793 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.10 (s, 1H, Ar-H), 7.03 (s, 1H, Ar-H), 6.88 (d, 1H, *J*=8.8 Hz, Ar-H), 6.62 (d, 1H, *J*=8.8 Hz, Ar-H), 4.20 (s, 2H, CH_2), 3.89 (s, 3H, Ar-OCH_3), 3.85 (s, 3H, Ar-OCH_3), 3.83 (s, 9H, 3 × Ar-OCH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=200.1 (s, Ar-C=O), 153.2 (s, Ar-C), 151.7 (s, Ar-C), 151.2 (s, Ar-C), 148.0 (s, Ar-C), 142.2 (s, Ar-C), 132.6 (s, Ar-C), 125.1 (d, Ar-CH), 120.9 (s, Ar-C), 116.4 (d, Ar-CH), 112.5 (d, Ar-CH), 111.1 (s, Ar-C), 107.2 (d,

Ar-CH), 60.8 (q, Ar-OCH_3), 60.7 (q, Ar-OCH_3), 56.3 (q, Ar-OCH_3), 56.1 (q, Ar-OCH_3), 56.0 (q, Ar-OCH_3), 43.3 (t, CH_2) ppm.

HR-MS (ESI^+) m/z calculated for $[C_{19}H_{22}BrO_6]^+=[M+H]^+$: 425.0594; found 425.0605.



62gf

1-(2-Bromo-4,5-dimethoxyphenyl)-2-(4-nitrophenyl)ethanone (62gf): GP-2 was carried out with aryliodide **61f** (124.5 mg, 0.50 mmol**)**, 2-bromoacetophenone **37g** (142.5 mg, 0.55 mmol**)**, $Pd(OAc)_2$ (2.2 mg, 2 mol%), Xantphos (11.6 mg, 4 mol%), ^{t}BuOK (72.9 mg, 0.65 mmol) and dry toluene (4 mL) at 80 °C for 3 h. Purification of the residue on a Silica gel column chromatography (petroleum ether/ethyl acetate, 80:20 to 75:25) furnished the product **62gf** (115.9 mg, 61%) as brownish yellow semi-solid. [TLC control (petroleum ether/ethyl acetate 95:05), R_f(**37g**)=0.50, R_f(**61f**)=0.70 and R_f(**62gf**)=0.25, UV detection].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2923, 1691, 1592, 1505, 1462, 1372, 1343, 1257, 1209, 1164, 1109, 1054, 1017, 909, 855, 727 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=8.17 (d, 2H, *J*=8.8 Hz, Ar-H), 7.42 (d, 2H, *J*=8.8 Hz, Ar-H), 7.05 (s, 1H, Ar-H), 7.01 (s, 1H, Ar-H), 4.43 (s, 2H, CH_2), 3.91 (s, 3H, Ar-OCH_3), 3.85 (s, 3H, Ar-OCH_3) ppm.

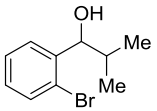
^{13}C-NMR ($CDCl_3$, 100 MHz): δ=198.2 (s, Ar-C=O), 151.9 (s, Ar-C), 148.3 (s, Ar-C), 147.1 (s, Ar-C), 141.7 (s, Ar-C), 132.1 (s, Ar-C), 130.6 (d, 2C, Ar-CH), 123.6 (d, 2C, Ar-CH), 116.4 (d, Ar-CH), 112.5 (d, Ar-CH), 111.4 (s, Ar-C), 56.3 (q, Ar-OCH_3), 56.2 (q, Ar-OCH_3), 48.4 (t, CH_2) ppm.

HR-MS (ESI^+): m/z calculated for $[C_{16}H_{15}BrNO_5]^+=[M+H]^+$: 380.0128; found 380.0140.

I.5.3 Synthesis of bi-aryls:

General Procedure-3 for synthesis isopropyl secondary alcohol (GP-3):

To a cold (–10 °C), magnetically stirred 2-bromobenzaldehyde **35** (1 mmol), was added isopropylmagnesium bromide (8 mmol) [prepared from magnesium (8 mmol) and isopropyl bromide (16 mmol) and a catalytic amount of iodine in 10 mL of dry ether]. The reaction mixture was stirred at –10 °C to RT for 4 h. It was then poured into a cold saturated aqueous NH_4Cl solution and the aqueous layer was extracted with ethyl acetate (3 × 30 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. Purification of the residue on a Silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **68** (70-86%).



68a

1-(2-Bromophenyl)-2-methylpropan-1-ol (68a): GP-3 was carried out with 2-bromobenzaldehyde **35a** (1.5 g, 8.11 mmol), isopropylmagnesium bromide (64.88 mmol) [prepared from magnesium (1.5 g, 64.88 mmol), isopropyl bromide (12.2 mL, 129.76 mmol) and catalytic amount of iodine in 80 mL of dry ether]. The reaction stirred at –10 °C to RT for 4 h Purification of the residue on a Silica gel column chromatography (petroleum ether/ethyl acetate 97:03 to 95:05) furnished the product **68a** (1.3 g, 73%) as colorless oil. [TLC control (petroleum ether/ethyl acetate 95:05, R_f(**35a**)=0.70, R_f(**68a**)=0.60, UV detection)].

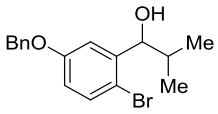
IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3397, 2960, 2922, 2851, 1466, 1439, 1282, 1366, 1197, 1006, 749, 682 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.51 (dd, 1H, *J*=7.8 and 1.0 Hz, Ar-H), 7.48 (dd, 1H, *J*=7.8 and 2.0 Hz, Ar-H), 7.31 (ddd, 1H, *J*=8.8, 7.3 and 1.0 Hz, Ar-H), 7.11 (ddd, 1H, *J*=8.8, 7.3 and 2.0 Hz, Ar-H), 4.86 (d, 1H, *J*=5.9 Hz, Ar-C*H*OH), 2.05 [septd,

1H, *J*=5.9 and 1.0 Hz, C*H*$(CH_3)_2$], 1.97 (br. s, 1H, OH), 0.95 [d, 3H, *J*=6.4 Hz, CH(C*H*$_3)_a(CH_3)_b$], 0.94 [d, 3H, *J*=6.4 Hz, CH$(CH_3)_a$(C*H*$_3)_b$] ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=142.8 (s, Ar-C), 132.6 (d, Ar-CH), 128.6 (d, Ar-CH), 128.2 (d, Ar-CH), 127.4 (d, Ar-CH), 122.6 (s, Ar-C), 77.5 (d, Ar-CHOH), 34.0 [d, *C*H$(CH_3)_2$], 19.4 [q, CH(*C*H$_3)_a(CH_3)_b$], 16.7 [q, CH$(CH_3)_a$(*C*H$_3)_b$] ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{10}H_{12}Br]^+$=$[(M+H)–H_2O]^+$: 211.0117; found 211.0117.



68b

1-[5-(Benzyloxy)-2-bromophenyl]-2-methylpropan-1-ol (68b): GP-3 was carried out with 2-bromobenzaldehyde **35b** (1.0 g, 3.44 mmol), isopropylmagnesium bromide (27.52 mmol) [prepared from magnesium (660 mg, 27.49 mmol), isopropyl bromide (5.1 ml, 55.04 mmol) and catalytic amount of iodine in 35 mL of dry ether]. The reaction stirred at –10 °C to RT for 4 h Purification of the residue on a Silica gel column chromatography (petroleum ether/ethyl acetate 90:05 to 92:08) furnished the product **68b** (869 mg, 75%) as colorless oil. [TLC control (petroleum ether/ethyl acetate 90:10, R_f(**35b**)=0.60, R_f(**68b**)=0.45, UV detection)].

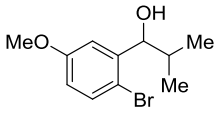
IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3405, 2962, 2927, 2873, 1593, 1570, 1463, 1381, 1291, 1233, 1166, 1008, 735, 697, 642 1cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.48–7.26 (m, 6H, Ar-H), 7.14 (d, 1H, *J*=2.9 Hz, Ar-H), 6.76 (dd, 1H, *J*=8.8 and 2.9 Hz, Ar-H), 5.06 (d, 1H, *J*=11.7 Hz, PhC*H*$_a$H$_b$O), 5.04 (d, 1H, *J*=11.7 Hz, Ph-CH$_a$*H*$_b$O), 4.80 (d, 1H, *J*=5.4 Hz, Ar-C*H*OH), 2.03 [septd, 1H, *J*=6.8 and 5.4 Hz, C*H*$(CH_3)_2$], 1.91 (br. s, 1H, OH), 0.95 [d, 3H, *J*=6.8 Hz, CH(C*H*$_3)_a(CH_3)_b$], 0.93 [d, 3H, *J*=6.8 Hz, CH$(CH_3)_a$(C*H*$_3)_b$] ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=158.1 (s, Ar-C), 144.0 (s, Ar-C), 136.6 (s, Ar-C), 133.2 (d, Ar-CH), 128.6 (d, 2C, Ar-CH), 128.0 (d, Ar-CH), 127.5 (d, 2C, Ar-CH),

115.7 (d, Ar-CH), 114.5 (d, Ar-CH), 113.2 (s, Ar-C), 77.5 (d, Ar-CHOH), 70.2 (t, Ph-CH_2O), 33.8 [d, *C*H$(CH_3)_2$], 19.5 [q, CH(*C*H$_3)_a(CH_3)_b$], 16.6 [q, CH$(CH_3)_a$(*C*H$_3)_b$] ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{17}H_{19}{}^{79}BrNaO_2]^+$=[M+Na]$^+$: 357.0461; found 357.0469, $[C_{17}H_{19}{}^{81}BrNaO_2]^+$=[M+Na]$^+$: 359.0446; found 359.0463.



68c

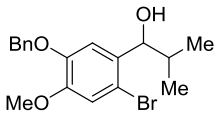
1-(2-Bromo-5-methoxyphenyl)-2-methylpropan-1-ol (68c): **GP-3** was carried out with 2-bromobenzaldehyde **35c** (500 mg, 2.32 mmol), isopropylmagnesium bromide (18.56 mmol) [prepared from magnesium (445.4 mg, 18.56 mmol), isopropyl bromide (3.5 mL, 37.12 mmol) and catalytic amount of iodine in 25 mL of dry ether]. The reaction stirred at −10 °C to RT for 4 h. Purification of the residue on a Silica gel column chromatography (petroleum ether/ethyl acetate 95:05 to 90:10) furnished the product **68c** (523 mg, 86%) as pale yellow oil. [TLC control (petroleum ether/ethyl acetate 90:10, R_f(**35c**)=0.50, R_f(**68c**)=0.40, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3394, 2960, 2929, 2872, 1594, 1572, 1465, 1416, 1284, 1231, 1162, 1007, 749, 811, 595 cm^{-1}.

^{1}H-NMR (CDCl$_3$, 400 MHz): δ=7.36 (d, 1H, *J*=8.8 Hz, Ar-H), 7.03 (d, 1H, *J*=2.9 Hz, Ar-H), 6.66 (dd, 1H, *J*=8.8 and 2.9 Hz, Ar-H), 4.78 (d, 1H, *J*=5.4 Hz, Ar-C*H*OH), 3.77 (s, 3H, Ar-OCH_3), 2.19 (br. s, 1H, OH), 2.13–1.92 (m, 1H, C*H*$(CH_3)_2$), 0.94 [d, 3H, *J*=6.8 Hz, CH(C*H*$_3)_a(CH_3)_b$], 0.93 [d, 3H, *J*=6.8 Hz, CH$(CH_3)_a$(C*H*$_3)_b$] ppm.

^{13}C-NMR (CDCl$_3$, 100 MHz): δ=158.9 (s, Ar-C), 143.9 (s, Ar-C), 133.1 (d, Ar-CH), 114.7 (d, Ar-CH), 113.4 (d, Ar-CH), 112.9 (s, Ar-C), 77.4 (d, Ar-CHOH), 55.4 (q, Ar-OCH_3), 33.9 [d, *C*H$(CH_3)_2$], 19.4 [q, CH(*C*H$_3)_a(CH_3)_b$], 16.7 [q, CH$(CH_3)_a$(*C*H$_3)_b$] ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{11}H_{14}{}^{79}BrO]^+$=[(M+H)–$H_2O$]$^+$: 241.0223; found 241.0229, $[C_{11}H_{14}{}^{81}BrO]^+$=[(M+H)–$H_2O$]$^+$: 243.0202; found 243.0208.



68d

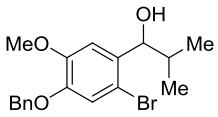
1-[5-(Benzyloxy)-2-bromo-4-methoxyphenyl]-2-methylpropan-1-ol (68d): **GP-3** was carried out with 2-bromobenzaldehyde **35d** (2.0 g, 6.23 mmol), isopropylmagnesium bromide (49.84 mmol) [prepared from magnesium (1.2 g, 49.84 mmol), isopropyl bromide (9.4 mL, 99.68 mmol) and catalytic amount of iodine in 60 mL of dry ether]. The reaction stirred at −10 °C to RT for 4 h. Purification of the residue on a Silica gel column chromatography (petroleum ether/ethyl acetate (85:15 to 80:20) furnished the product **68d** (1.9 g, 84%) as brown viscous liquid. [TLC control (petroleum ether/ethyl acetate 70:30, R_f(**35d**)=0.64, R_f(**68d**)=0.40, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3491, 2960, 1602, 1500, 1456, 1439, 1379, 1255, 1206, 1157, 1029, 803, 739, 697 cm^{-1}.

^{1}H-NMR (CDCl$_3$, 400 MHz): δ=7.41 (d, 2H, *J*=7.3 Hz, Ar-H), 7.34 (dd, 2H, *J*=7.3 and 6.8 Hz, Ar-H), 7.27 (t, 1H, *J*=6.8 Hz, Ar-H), 7.01 (s, 1H, Ar-H), 6.97 (s, 1H, Ar-H), 5.14 (d, 1H, *J*=12.2 Hz, PhCH_aH$_b$O), 5.12 (d, 1H, *J*=12.2 Hz, PhCH$_a$$H_b$O), 4.70 (d, 1H, *J*=5.4 Hz, Ar-C*H*OH), 3.85 (s, 3H, Ar-OCH$_3$), 1.95–1.80 [m, 2H, C*H*(CH$_3$)$_2$ and OH], 0.88 [d, 3H, *J*=6.8 Hz, CH(CH_3)$_a$(CH$_3$)$_b$], 0.82 [d, 3H, *J*=6.8 Hz, CH(CH$_3$)$_a$(CH_3)$_b$] ppm.

^{13}C-NMR (CDCl$_3$, 100 MHz): δ=149.2 (s, Ar-C), 147.3 (s, Ar-C), 136.6 (s, Ar-C), 134.8 (s, Ar-C), 128.5 (d, 2C, Ar-CH), 127.9 (d, Ar-CH), 127.5 (d, 2C, Ar-CH), 115.5 (d, Ar-CH), 113.5 (d, Ar-CH), 113.0 (s, Ar-C), 77.3 (d, Ar-CHOH), 71.0 (t, Ph-CH$_2$O), 56.1 (q, Ar-OCH$_3$), 34.2 [d, *C*H(CH$_3$)$_2$], 19.2 [q, CH(*C*H$_3$)$_a$(CH$_3$)$_b$], 17.0 [q, CH(CH$_3$)$_a$(*C*H$_3$)$_b$] ppm.

HR-MS (ESI$^+$): m/z calculated for [C$_{18}$H$_{20}$^{79}BrO$_2$]$^+$=[(M+H)–H$_2$O]$^+$: 347.0641; found 347.0641, [C$_{18}$H$_{20}$^{81}BrO$_2$]$^+$=[(M+H)–H$_2$O]$^+$: 349.0621; found 349.0634.



68e

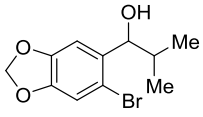
1-[4-(Benzyloxy)-2-bromo-5-methoxyphenyl]-2-methylpropan-1-ol (68e): **GP-3** was carried out with 2-bromobenzaldehyde **35e** (3.0 g, 9.34 mmol), isopropylmagnesium bromide (74.72 mmol) [prepared from magnesium (1.80 g, 74.72 mmol) and isopropyl bromide (14.0 mL, 149.44 mmol) and catalytic amount of iodine in 90 mL of dry ether]. The reaction stirred at −10 °C to RT for 4 h. Purification of the residue on a Silica gel column chromatography (petroleum ether/ethyl acetate 85: 15 to 80:20) furnished the product **68e** (2.60 g, 76%) as colorless oil. [TLC control (petroleum ether/ethyl acetate 90:10, R_f(**35e**)=0.35, R_f(**68e**)=0.25, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3395, 2956, 2929, 2872, 1602, 1497, 1497, 1455, 1439, 1377, 1246, 1203, 1027, 911, 870, 842, 801, 734, 696, 637 cm^{-1}.

^{1}H-NMR (CDCl$_3$, 400 MHz): δ=7.43 (d, 2H, *J*=7.3 Hz, Ar-H), 7.37 (dd, 2H, *J*=7.3 and 7.3 Hz, Ar-H), 7.31 (t, 1H, *J*=7.3 and 7.3 Hz, Ar-H), 7.01 (s, 2H, Ar-H), 5.08 (s, 2H, Ph-CH_2O), 4.74 (d, 1H, *J*=5.9 Hz, Ar-C*H*OH), 3.86 (s, 3H, Ar-OCH_3), 2.05–1.90 [m, 2H, C*H*$(CH_3)_2$ and OH], 0.99 [d, 3H, *J*=6.8 Hz, CH(C*H*$_3)_a(CH_3)_b$], 0.89 [d, 3H, *J*=6.8 Hz, CH$(CH_3)_a$(C*H*$_3)_b$] ppm.

^{13}C-NMR (CDCl$_3$, 100 MHz): δ=149.1 (s, Ar-C), 147.7 (s, Ar-C), 136.4 (s, Ar-C), 135.5 (s, Ar-C), 128.6 (d, 2C, Ar-CH), 128.0 (d, Ar-CH), 127.4 (d, 2C, Ar-CH), 117.4 (d, Ar-CH), 112.3 (s, Ar-C), 111.0 (d, Ar-CH), 77.4 (d, Ar-CHOH), 71.2 (t, Ph-CH_2O), 56.1 (q, Ar-OCH_3), 34.4 [d, *C*H$(CH_3)_2$], 19.2 [q, CH(*C*H$_3)_a(CH_3)_b$], 17.3 [q, CH$(CH_3)_a$(*C*H$_3)_b$] ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{18}H_{21}BrO_3]^+$=$[M]^+$: 364.0669; found 364.0678.



68f

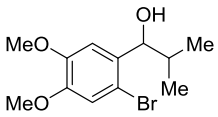
1-(6-Bromo-1,3-benzodioxol-5-yl)-2-methylpropan-1-ol (68f): **GP-3** was carried out with 2-bromobenzaldehyde **35f** (500 mg, 2.18 mmol), isopropylmagnesium bromide (17.44 mmol) [prepared from magnesium (418.6 mg, 17.44 mmol) and isopropyl bromide (3.2 mL, 34.88 mmol) and catalytic amount of iodine in 25 mL of dry ether]. The reaction stirred at −10 °C to RT for 4 h. Purification of the residue on a Silica gel column chromatography (petroleum ether/ethyl acetate 92: 08 to 88:12) furnished the product **68f** (417 mg, 70%) as pale yellow viscous liquid. [TLC control (petroleum ether/ethyl acetate 90:10, R_f(**35f**)=0.55, R_f(**68f**)=0.45, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3397, 2960, 2922, 2853, 1502, 1472, 1406, 1387, 1228, 1124, 1102, 1037, 936, 874, 838, 787, 678cm^{-1}.

^{1}H-NMR (CDCl$_3$, 400 MHz): δ=6.95 (s, 1H, Ar-H), 6.93 (s, 1H, Ar-H), 5.95 (d, 1H, J=2.9 Hz, O-CH_aH$_b$-O), 5.94 (d, 1H, J=2.9 Hz, O-CH$_a$$H_b$-O), 4.74 (d, 1H, J=6.4 Hz, Ar-CHOH), 2.03 (br. s, 1H, OH), 1.94 [sept, 1H, J=6.8 Hz, CH(CH$_3$)$_2$], 0.96 [d, 3H, J=6.8 Hz, CH(CH_3)$_a$(CH$_3$)$_b$], 0.88 [d, 3H, J=6.8 Hz, CH(CH$_3$)$_a$(CH_3)$_b$] ppm.

^{13}C-NMR (CDCl$_3$, 100 MHz): 147.4 (s, Ar-C), 147.3 (s, Ar-C), 136.3 (s, Ar-C), 112.8 (s, Ar-C), 112.2 (d, Ar-CH), 107.8 (d, Ar-CH), 101.6 (t, O-CH$_2$-O), 77.4 (d, Ar-CHOH), 34.3 [d, CH(CH$_3$)$_2$], 19.2 [q, CH(CH$_3$)$_a$(CH$_3$)$_b$], 17.2 [q, CH(CH$_3$)$_a$(CH$_3$)$_b$] ppm.

HR-MS (ESI$^+$): m/z calculated for [C$_{11}$H$_{12}$^{79}BrO$_2$]$^+$=[(M+H)–H$_2$O]$^+$: 255.0015; found 255.0016, [C$_{11}$H$_{12}$^{81}BrO$_2$]$^+$=[(M+H)–H$_2$O]$^+$: 256.9995; found 257.0003.



68g

1-(2-Bromo-4, 5-dimethoxyphenyl)-2-methylpropan-1-ol (68g): **GP-3** was carried out with 2-bromobenzaldehyde **35g** (2.0 g, 8.16 mmol), isopropylmagnesium bromide (65.30 mmol) [prepared from magnesium (1.57 mg, 65.30 mmol) and isopropyl bromide(3.5 mL, 130.6 mmol) and catalytic amount of iodine in 80 mL of dry ether]. The reaction stirred at −10 °C to RT for 4 h. Purification of the residue on a Silica gel

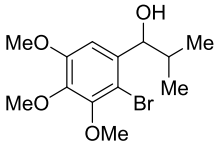
column chromatography (petroleum ether/ethyl acetate 90:10 to 85:15) furnished the product **68g** (1.67 mg, 71%) as colorless oil. [TLC control (petroleum ether/ethyl acetate 90:10, R_f(**35g**)=0.50, R_f(**68g**)=0.40, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3496, 2959, 1603, 1500, 1463, 1439, 1380, 1255, 1207, 1156, 1031, 804, 750 cm^{-1}.

^{1}H-NMR (CDCl$_3$, 400 MHz): δ=6.99 (s, 1H, Ar-H), 6.95 (s, 1H, Ar-H), 4.75 (d, 1H, *J*=6.4 Hz, Ar-C*H*OH), 3.86 (s, 3H, Ar-OCH$_3$), 3.85 (s, 3H, Ar-OCH$_3$), 2.18 (br. s, 1H, OH), 1.98 [sept, 1H, *J*=6.8 Hz, C*H*(CH$_3$)$_2$], 0.99 [d, 3H, *J*=6.8 Hz, CH(C*H*$_3$)$_a$(CH$_3$)$_b$], 0.89 [d, 3H, *J*=6.8 Hz, CH(CH$_3$)$_a$(C*H*$_3$)$_b$] ppm.

^{13}C-NMR (CDCl$_3$, 100 MHz): 148.4 (s, 2C, Ar-C), 134.9 (s, Ar-C), 114.8 (d, Ar-CH), 112.3 (s, Ar-C), 110.3 (d, Ar-CH), 77.4 (d, Ar-CHOH), 56.0 (q, Ar-OCH$_3$), 55.9 (q, ArO-CH$_3$), 34.4 [d, *C*H(CH$_3$)$_2$], 19.2 [q, CH(*C*H$_3$)$_a$(CH$_3$)$_b$], 17.3 [q, CH(CH$_3$)$_a$(*C*H$_3$)$_b$] ppm.

HR-MS (ESI$^+$): m/z calculated for [C$_{12}$H$_{16}$^{79}BrO$_2$]$^+$=[(M+H)-H$_2$O]$^+$: 271.0328; found 271.0325, [C$_{12}$H$_{16}$^{81}BrO$_2$]$^+$=[(M+H)–H$_2$O]$^+$: 273.0308; found 273.0302.



68h

1-(2-Bromo-3,4,5-trimethoxyphenyl)-2-methylpropan-1-ol (68h): **GP-3**was carried out with 2-bromobenzaldehyde **35h** (2.0 g, 7.27 mmol), isopropylmagnesium bromide (58.18 mmol) [prepared from magnesium (2.8 g, 58.18 mmol) and isopropyl bromide (10.9 mL, 116.36 mmol) and catalytic amount of iodine in 80 mL of dry ether]. The reaction stirred at −10 °C to RT for 4 h. Purification of the residue on a Silica gel column chromatography (petroleum ether/ethyl acetate 90:10 to 80:20) furnished the product **68h** (1.70 mg, 73%) as yellow viscous liquid. [TLC control (petroleum ether/ethyl acetate 80:20, R_f(**35h**)=0.65, R_f(**68h**)=0.55, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3494, 2960, 2936, 1590, 1568, 1480, 1463, 1393, 1324, 1235, 1195, 1103, 1008, 912, 820 cm^{-1}.

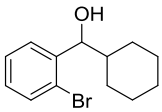
^{1}H-NMR ($CDCl_3$, 400 MHz): δ=6.83 (s, 1H, Ar-H), 4.79 (d, 1H, *J*=5.4 Hz, Ar-C*H*OH), 3.81 (s, 6H, 2 × Ar-OCH_3), 3.80 (s, 3H, Ar-OCH_3), 2.40 (br. s, 1H, OH), 1.94 [sept, 1H, *J*=6.4 Hz, C*H*$(CH_3)_2$], 0.89 [dd, 6H, *J*=6.4 Hz, CH(C*H*$_3)_a$(C*H*$_3)_b$] ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=152.4 (s, Ar-C), 149.9 (s, Ar-C), 141.7 (s, Ar-C), 138.6 (s, Ar-C), 108.6 (s, Ar-C), 106.5 (d, Ar-CH), 76.5 [d, Ar-CHOH], 60.7 (q, 2C, Ar-OCH_3), 55.8 (q, Ar-OCH_3), 33.8 [d, *C*H$(CH_3)_2$], 19.2 [d, *C*H(*C*H$_3)_a$(CH$_3)_b$], 16.6 [d, *C*H$(CH_3)_a$(*C*H$_3)_b$] ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{13}H_{18}{}^{79}BrO_3]^+$=$[(M+H)-H_2O]^+$: 301.0434; found 301.0431, $[C_{13}H_{18}{}^{81}BrO_3]^+$=$[(M+H)–H_2O]^+$: 303.0413; found 303.0414.

General Procedure-4 for synthesis of cyclohexyl secondary alcohol (GP-4):

To a cold (–50 °C), magnetically stirred 2-bromobenzaldehyde **35** (1 mmol) in THF (2 mL), was added cyclohexylmagnesium bromide (4 mmol) in Dry THF 2 mL [prepared from magnesium (4 mmol) and cyclohexyl bromide (4 mmol) and a catalytic amount of iodine in 5 mL of dry THF]. The reaction mixture was stirred at –50 °C to RT for 2 h. It was then poured into a cold saturated aqueous NH_4Cl solution and the aqueous layer was extracted with ethyl acetate (3 × 30 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue on a Silica gel column chromatography (petroleum ether/ethyl acetate) furnished the product **80** (40-72%).



80a

(2-Bromophenyl)(cyclohexyl)methanol (80a): GP-4 was carried out with 2-bromobenzaldehyde **35a** (2.0 mg, 10.81 mmol) in 15 mL THF, cyclohexylmagnesium bromide (43.24 mmol) [prepared from magnesium (1.04 g, 43.24 mmol), cyclohexyl

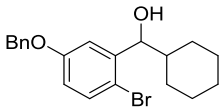
bromide (5.0 mL, 43.24 mmol) and catalytic amount of iodine in 25 mL of dry THF]. The reaction stirred at −50 °C to RT for 2 h. Purification of the residue on a Silica gel column chromatography (petroleum ether/ethyl acetate 97:3 to 95:5) furnished the product **80a** (1.51 g, 52%) colorless viscous liquid. [TLC control (petroleum ether/ethyl acetate 90:10, R_f(**35a**)=0.70, R_f(**80a**)=0.55, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3392, 2924, 2851, 1567, 1467, 1448, 1346, 1263, 1082, 1016, 754, 729 cm^{-1}.

^{1}H-NMR (CDCl$_3$, 400 MHz): δ=7.49 (dd, 1H, *J*=7.8 and 1.5 Hz, Ar-H), 7.46 (dd, 1H, *J*=7.8 and 1.5 Hz, Ar-H), 7.30 (ddd, 1H, *J*=7.8, 7.8 and 1.5 Hz, Ar-H), 7.10 (ddd, 1H, *J*=7.8, 7.8 and 1.5 Hz, Ar-H), 4.85 (d, 1H, *J*=5.9 Hz, Ar-C*H*OH), 2.10 (br. s, 1H, OH), 1.95–1.00 (m, 11H, Cy-H) ppm.

^{13}C-NMR (CDCl$_3$, 100 MHz): δ=142.7 (s, Ar-C), 132.5 (d, Ar-CH), 128.5 (d, Ar-CH), 128.4 (d, Ar-CH), 127.3 (d, Ar-CH), 122.7 (s, Ar-C), 77.0 (d, Ar-CHOH), 43.9 (d, Cy-CH), 29.5 (t, Cy-CH_2), 27.5 (t, Cy-CH_2), 26.3 (t, Cy-CH_2), 26.2 (t, Cy-CH_2), 26.0 (t, Cy-CH_2) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{13}H_{16}Br]^+$=$[M+H]^+$: 251.0430; found 251.0356.



80b

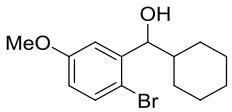
[5-(Benzyloxy)-2-bromophenyl](cyclohexyl)methanol (80b): GP-4 was carried out with 2-bromobenzaldehyde **35b** (1.5 g, 5.15 mmol) in 15 mL THF, cyclohexylmagnesium bromide (20.61 mmol) [prepared from magnesium (495 mg, 20.61 mmol), cyclohexyl bromide (2.5 mL, 20 mmol) and catalytic amount of iodine in 25 mL of dry THF]. The reaction stirred at −50 °C to RT for 2 h. Purification of the residue on a Silica gel column chromatography (petroleum ether/ethyl acetate 95:5 to 90:10) furnished the product **80b** (1.0 g, 52%) as colorless viscous liquid. [TLC control (petroleum ether/ethyl acetate 90:10, R_f(**35b**)=0.60, R_f(**80b**)=0.50, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3353, 2924, 2850, 1593, 1572, 1451, 1293, 1232, 1163, 1010, 734, 696 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.50–7.35 (m, 5H, Ar-H), 7.31 (t, 1H, *J*=7.3 Hz, Ar-H), 7.10 (d, 1H, *J*=3.4 Hz, Ar-H), 6.75 (dd, 1H, *J*=8.8 and 3.4 Hz, Ar-H), 5.05 (s, 2H, Ph-CH_2O), 4.80 (d, 1H, *J*=5.4 Hz, Ar-C*H*OH), 2.00 (br. s, 1H, OH), 1.90–0.70 (m, 11H, Cy-H) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=158.0 (s, Ar-C), 143.7 (s, Ar-C), 136.6 (s, Ar-C), 133.1 (d, Ar-CH), 128.6 (d, 2C, Ar-CH), 128.0 (d, Ar-CH), 127.5 (d, 2C, Ar-CH), 115.7 (d, Ar-CH), 114.6 (d, Ar-CH), 113.3 (s, Ar-C), 77.0 (d, Ar-CHOH), 70.1 (t, PhCH_2), 43.8 (d, Cy-CH), 29.5 (t, Cy-CH_2), 27.3 (t, Cy-CH_2), 26.4 (t, Cy-CH_2), 26.3 (t, Cy-CH_2), 26.0 (t, Cy-CH_2) ppm.

HR-MS (ESI^{+}): m/z calculated for $[C_{20}H_{22}{}^{79}BrO]^{+}$=$[(M+H)–H_2O]^{+}$: 357.0849; found 357.0849, $[C_{20}H_{22}{}^{81}BrO]^{+}$=$[(M+H)–H_2O]^{+}$: 359.0828; found 359.0834.



80c

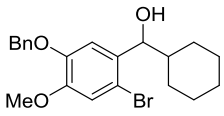
(2-Bromo-5-methoxyphenyl)(cyclohexyl)methanol (80c): GP-4 was carried out with 2-bromobenzaldehyde **35c** (2.0 g, 9.30 mmol) in 15 mL THF, cyclohexylmagnesium bromide (37.21 mmol) [prepared from magnesium (893 mg, 37.21 mmol), cyclohexyl bromide (4.4 mL, 37.21 mmol) and catalytic amount of iodine in 25 mL of dry THF]. The reaction stirred at –50 °C to RT for 2 h. Purification of the residue on a Silica gel column chromatography (petroleum ether/ethyl acetate 95:5 to 90:10) furnished the product **80c** (1.0 g, 52%) as colorless viscous liquid. [TLC control (petroleum ether/ethyl acetate 90:10, R_f(**35c**)=0.55, R_f(**80c**)=0.40, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3385, 2923, 2850, 1594, 1572, 1468, 1449, 1284, 1233, 1161, 1049, 1012, 811 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.37 (d, 1H, *J*=8.3 Hz, Ar-H), 7.01 (d, 1H, *J*=2.9 Hz, Ar-H), 6.66 (dd, 1H, *J*=8.3 and 2.9 Hz, Ar-H), 4.79 (d, 1H, *J*=6.4 Hz, Ar-C*H*OH), 3.78 (s, 3H, Ar-OCH_3), 2.13 (br. s, 1H, OH), 1.90–1.00 (m, 11H, Cy-H) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=159.0 (s, Ar-C), 143.8 (s, Ar-C), 133.0 (d, Ar-CH), 114.7 (d, Ar-CH), 113.6 (d, Ar-CH), 113.0 (s, Ar-C), 77.0 (d, Ar-CHOH), 55.4 (q, Ar-OCH3), 43.9 (d, Cy-CH), 29.5 (t, Cy-CH_2), 27.4 (t, Cy-CH_2), 26.3 (t, Cy-CH_2), 26.2 (t, Cy-CH_2), 26.0 (t, Cy-CH_2) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{14}H_{18}{}^{79}BrO]^+$=$[(M+H)–H_2O]^+$: 281.0536; found 281.0549, $[C_{14}H_{18}{}^{81}BrO]^+$=$[(M+H)–H_2O]^+$: 283.0515; found 283.0530.



80d

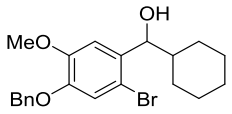
[5-(Benzyloxy)-2-bromo-4-methoxyphenyl](cyclohexyl)methanol (80d): GP-4 was carried out with 2-bromobenzaldehyde **35d** (2.0 g, 6.23 mmol) in 20 mL THF, cyclohexylmagnesium bromide (20 mmol) [prepared from magnesium (598 mg, 24.92 mmol), cyclohexyl bromide (3.0 mL, 24.92 mmol) and catalytic amount of iodine in 25 mL of dry THF]. The reaction stirred at –50 °C to RT for 2 h. Purification of the residue on a Silica gel column chromatography (petroleum ether/ethyl acetate 90:10 to 80:20) furnished the product **80d** (1.5 g, 60%) as brownish yellow viscous liquid. [TLC control (petroleum ether/ethyl acetate 80:20, R_f(**35d**)=0.50, R_f(**80d**)=0.45, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3382, 2923, 2850, 1602, 1499, 1451, 1439, 1379, 1251, 1204, 1154, 1027, 803, 734, 696 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.40 (d, 2H, *J*=7.3 Hz, Ar-H), 7.33 (dd, 2H, *J*=7.3 and 6.8 Hz, Ar-H), 7.27 (t, 1H, *J*=6.8 Hz, Ar-H), 6.97 (s, 1H, Ar-H), 6.96 (s, 1H, Ar-H), 5.17 (d, 1H, *J*=12.2 Hz, PhC$H_a$$H_b$O), 5.11 (d, 1H, *J*=12.2 Hz, PhC$H_a$$H_b$O), 4.70 (d, 1H, *J*=6.4 Hz, Ar-C*H*OH), 3.84 (s, 3H, Ar-OCH_3), 2.50–0.5 (m, 12H, Cy-H and OH) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=149.3 (s, Ar-C), 147.3 (s, Ar-C), 136.7 (s, Ar-C), 134.6 (s, Ar-C), 128.5 (d, 2C, Ar-CH), 127.9 (d, Ar-CH), 127.5 (d, 2C, Ar-CH), 115.5 (d, Ar-CH), 113.7 (d, Ar-CH), 113.1 (s, Ar-C), 76.7 (d, Ar-CHOH), 70.9 (t, Ph-CH_2O), 56.2 (q, Ar-OCH_3), 44.2 (d, Cy-CH), 29.3 (t, Cy-CH_2), 27.8 (t, Cy-CH_2), 26.4 (t, Cy-CH_2), 26.2 (t, Cy-CH_2), 26.0 (t, Cy-CH_2) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{21}H_{24}BrO_2]^+$=$[(M+H)–H_2O]^+$: 387.0954; found 387.0962, $[C_{21}H_{24}{}^{81}BrO_2]^+$=$[(M+H)–H_2O]^+$: 389.0934; found 389.0952.



80e

[4-(Benzyloxy)-2-bromo-5-methoxyphenyl](cyclohexyl)methanol (80e): GP-4 was carried out with 2-bromobenzaldehyde **35e** (2.0 g, 6.32 mmol) in 20 mL THF, cyclohexylmagnesium bromide (24.92 mmol) [prepared from magnesium (598 mg, 24.92 mmol), cyclohexyl bromide (3.0 mL, 24.92 mmol) and catalytic amount of iodine in 25 mL of dry THF]. The reaction stirred at –50 °C to RT for 2 h. Purification of the residue on a Silica gel column chromatography (petroleum ether/ethyl acetate 90:10 to 80:10) furnished the product **80e** (1.8 g, 72%) as colorless viscous liquid. [TLC control (petroleum ether/ethyl acetate 80:20, R_f(**35e**)=0.55, R_f(**80e**)=0.40, UV detection)]

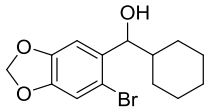
IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3390, 2923, 2851, 1601, 1500, 1453, 1383, 1256, 1201, 1157, 1022, 861, 741, 697 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.42 (d, 2H, *J*=7.3 Hz, Ar-H), 7.36 (dd, 2H, *J*=7.3 and 7.3 Hz, Ar-H), 7.30 (t, 1H, *J*=7.3 Hz, Ar-H), 7.00 (s, 1H, Ar-H), 6.99 (s, 1H, Ar-H), 5.08 (s, 2H, Ph-CH_2O), 4.74 (d, 1H, *J*=6.8 Hz, Ar-C*H*OH), 3.86 (s, 3H, Ar-OCH_3), 2.50–0.50 (m, 12H, Cy-H and OH) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=149.2 (s, Ar-C), 147.8 (s, Ar-C), 136.5 (s, Ar-C), 135.4 (s, Ar-C), 128.6 (d, 2C, Ar-CH), 128.1 (d, Ar-CH), 127.4 (d, 2C, Ar-CH), 117.4 (d, Ar-CH), 112.5 (s, Ar-C), 111.2 (d, Ar-CH), 76.9 (d, Ar-CHOH), 71.3 (t, Ph-

CH_2O), 56.1 (q, Ar-OCH_3), 44.4 (d, Cy-CH), 29.3 (t, Cy-CH_2), 28.1 (t, Cy-CH_2), 26.4 (t, Cy-CH_2), 26.3 (t, Cy-CH_2), 26.0 (t, Cy-CH_2) ppm.

HR-MS (ESI^+): m/z calculated for $[C_{21}H_{24}{}^{79}BrO_2]^+$=$[(M+H)–H_2O]^+$: 387.0954; found 387.0967, $[C_{21}H_{24}{}^{81}BrO_2]^+$= $[(M+H)–H_2O]^+$: 389.0934; found 389.0966.



80f

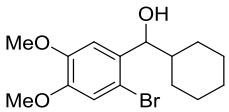
(6-Bromo-1,3-benzodioxol-5-yl)(cyclohexyl)methanol (80f): GP-4 was carried out with 2-bromobenzaldehyde **35f** (2.0 g, 8.73 mmol) in 20 mL THF, cyclohexylmagnesium bromide (20 mmol) [prepared from magnesium (838 mg, 34.93 mmol), cyclohexyl bromide (4.3 mL, 34.93 mmol) and catalytic amount of iodine in 25 mL of dry THF]. The reaction stirred at –50 °C to RT for 2 h. Purification of the residue on a Silica gel column chromatography (petroleum ether/ethyl acetate 92:08 to 85:15) furnished the product **80f** (1.1 g, 40%) as brown viscous liquid. [TLC control (petroleum ether/ethyl acetate 90:10, R_f(**35f**)=0.55, R_f(**80f**)=0.50, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3386, 2925, 2851, 1503, 1478, 1410, 1239, 1124, 1105, 1040, 934 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=6.94 (s, 1H, Ar-H), 6.93 (s, 1H, Ar-H), 5.95 (s, 2H, O-CH_2-O), 4.76 (d, 1H, *J*=6.8 Hz, Ar-C*H*OH), 2.30 (m, 12H, Cy-H and OH) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ=147.5 (s, Ar-C), 147.3 (s, Ar-C), 136.1 (s, Ar-C), 113.0 (s, Ar-C), 112.2 (d, Ar-CH), 108.0 (d, Ar-CH), 101.6 (t, O-CH_2-O), 76.9 (d, Ar-CHOH), 44.2 (d, Cy-CH), 29.3 (t, Cy-CH_2), 27.9 (t, Cy-CH_2), 26.3 (t, Cy-CH_2), 26.2 (t, Cy-CH_2), 26.0 (t, Cy-CH_2) ppm.

HR-MS (ESI^+): m/z calculated for $[C_{14}H_{16}{}^{79}BrO_2]^+$=$[(M+H)–H_2O]^+$: 295.0328; found 295.0328, $[C_{14}H_{18}{}^{81}BrO]^+$=$[(M+H)–H_2O]^+$: 297.0308; found 297.0353.



80g

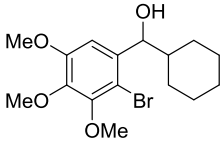
(2-Bromo-4,5-dimethoxyphenyl)(cyclohexyl)methanol (80g): GP-4 was carried out with 2-bromobenzaldehyde **35g** (2.0 g, 8.16 mmol) in 20 mL THF, cyclohexylmagnesium bromide (20 mmol) [prepared from magnesium (784 g, 32.65 mmol), cyclohexyl bromide (4.0 mL, 32.65 mmol) and catalytic amount of iodine in 25 mL of dry THF]. The reaction stirred at –50 °C to RT for 2 h. Purification of the residue on a Silica gel column chromatography (petroleum ether/ethyl acetate 90:10 to 80:20) furnished the product **80g** (1.90 g, 70%) as pale yellow viscous liquid. [TLC control (petroleum ether/ethyl acetate 90:10, R_f(**35g**)=0.50, R_f(**80g**)=0.40, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3400, 2924, 2850, 1603, 1503, 1462, 1447, 1381, 1257, 1209, 1156, 1033, 802 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=6.96 (s, 1H, Ar-H), 6.94 (s, 1H, Ar-H), 4.75 (d, 1H, *J*=6.8 Hz, Ar-C*H*OH), 3.86 (s, 3H, Ar-OCH_3), 3.84 (s, 3H, Ar-OCH_3), 2.30–0.6 (m, 12H, Cy-H and OH) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=148.5 (s, 2C, Ar-C), 134.8 (s, Ar-C), 114.9 (d, Ar-CH), 112.6 (s, Ar-C), 110.6 (d, Ar-CH), 76.9 (d, Ar-CHOH), 56.1 (q, Ar-OCH_3), 56.0 (q, ArO-CH_3), 44.4 [d, Cy-CH] 29.3 (t, Cy-CH_2), 28.1 (t, Cy-CH_2), 26.4 (t, Cy-CH_2), 26.2 (t, Cy-CH_2), 26.0 (t, Cy-CH_2) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{15}H_{20}{}^{79}BrO_2]^+$=$[(M+H)–H_2O]^+$: 311.0641; found 311.0640, $[C_{15}H_{20}{}^{81}BrO_2]^+$=$[(M+H)–H_2O]^+$: 313.0621; found 313.0625.



80h

(2-Bromo-3,4,5-trimethoxyphenyl)(cyclohexyl)methanol (80h): GP-4 was carried out with 2-bromobenzaldehyde **35h** (2.0 g, 7.27 mmol) in 15 mL dry THF,

cyclohexylmagnesium bromide (29.09 mmol) [prepared from magnesium (698 mg, 29.09 mmol), cyclohexyl bromide (3.4 mL, 29.09 mmol) and catalytic amount of iodine in 25 mL of dry THF]. The reaction stirred at −50 °C to RT for 2 h. Purification of the residue on a Silica gel column chromatography (petroleum ether/ethyl acetate 95:5 to 85:15) furnished the product **80h** (1.43 g, 55%) as colorless viscous liquid. [TLC control (petroleum ether/ethyl acetate 85:15, R_f(**35h**)=0.55, R_f(**80h**)=0.40, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3462, 2925, 2850, 1568, 1480, 1447, 1392, 1322, 1238, 1195, 1161, 1102, 1009, 813, 730 cm^{-1}.

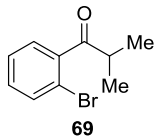
^{1}H-NMR (CDCl$_3$, 400 MHz): δ=6.81 (s, 1H, Ar-H), 4.81 (d, 1H, *J*=6.4 Hz, Ar-C*H*OH), 3.83 (s, 3H, Ar-OCH$_3$), 3.82 (s, 3H, Ar-OCH$_3$), 3.81 (s, 3H, Ar-OCH$_3$), 2.39 (br. s, 1H, OH), 1.90–1.00 (m, 11H, Cy-H) ppm.

^{13}C-NMR (CDCl$_3$, 100 MHz): δ=152.6 (s, Ar-C), 150.0 (s, Ar-C), 141.9 (s, Ar-C), 138.5 (s, Ar-C), 108.9 (s, Ar-C), 106.7 (d, Ar-CH), 76.7 (d, Ar-CHOH), 60.9 (q, Ar-OCH$_3$), 60.8 (q, Ar-OCH$_3$), 56.0 (q, Ar-OCH$_3$), 44.0 (d, Cy-CH), 29.4 (t, Cy-CH$_2$), 27.4 (t, Cy-CH$_2$), 26.3 (t, Cy-CH$_2$), 26.2 (t, Cy-CH$_2$), 25.9 (t, Cy-CH$_2$) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{16}H_{23}{}^{79}BrNaO_4]^+$=$[M+Na]^+$: 381.0672; found 381.0670, $[C_{16}H_{23}{}^{81}BrNaO_4]^+$=$[M+Na]^+$: 383.0651; found 383.0648.

General procedure-5 for ketones (GP-5):

To a magnetically stirred solution of the secondary alcohol **68/80** (1 mmol) in dry CH_2Cl_2 (2 mL) was added a homogeneous mixture of PCC (3 mmol) and silica gel stirred at RT for 2 h. Filtration of the reaction mixture through a short silica gel column chromatography with excess CH_2Cl_2 furnished the pure product **69/81** (93-99%)/(91-96%).



69

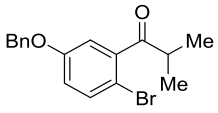
1-(2-Bromophenyl)-2-methylpropan-1-one (69a): **GP-5** was carried out with the secondary alcohol **68a** (1.10 g, 4.80 mmol), dry CH_2Cl_2 (10 mL), and a homogeneous mixture of PCC (3.0 g, 14.40 mmol) and silica gel (3.0 g). The reaction mixture was stirred at RT for 2 h. Filtration through short silica gel column chromatography with CH_2Cl_2 furnished the product **69a** (1.0 g, 99%) as pale yellow oil. [TLC control (petroleum ether/ethyl acetate 95:05, R_f(**68a**)=0.55, R_f(**69a**)=0.60, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2970, 2928, 2872, 1700, 1587, 1462, 1428, 1382, 1344, 1266, 1216, 1052, 1028, 976, 769, 737, 667, 633cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.59 (dd, 1H, *J*=7.8 and 1.5 Hz, Ar-H), 7.36 (ddd, 1H, *J*=9.3, 7.8 and 1.5 Hz, Ar-H), 7.29 (dd, 1H, *J*=7.8 and 1.5 Hz, Ar-H), 7.27 (ddd, 1H, *J*=9.3, 7.8 and 1.5 Hz, Ar-H), 3.32 [sept, 1H, *J*=6.8 Hz, C*H*(CH_3)$_2$], 1.20 [d, 6H, *J*=6.8 Hz, CH(C*H*$_3$)$_2$] ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=208.7 (s, Ar-C=O), 142.0 (s, Ar-C), 133.3 (d, Ar-CH), 131.0 (d, Ar-CH), 128.1 (d, Ar-CH), 127.2 (d, Ar-CH), 118.6 (s, Ar-C), 40.1 [d, *C*H(CH_3)$_2$], 18.1 [q, 2C, CH(*C*H$_3$)$_2$] ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{10}H_{12}BrO]^+$=$[(M+H)]^+$: 227.0066; found 227.0065.



69b

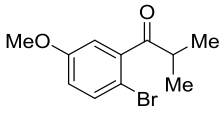
1-[5-(Benzyloxy)-2-bromophenyl]-2-methylpropan-1-one (69b): **GP-5** was carried out with the secondary alcohol **68b** (800 mg, 2.39 mmol), dry CH_2Cl_2 (5 mL), and a homogeneous mixture of PCC (1.5 g, 7.17 mmol) and silica gel (1.5 g) stirred at RT for 2 h. Filtration through short silica gel column chromatography with CH_2Cl_2 furnished the product **69b** (755 mg, 95%) as pale yellow oil. [TLC control (petroleum ether/ethyl acetate 90:10, R_f(**68b**)=0.45, R_f(**69b**)=0.50, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2970, 2926, 2872, 2852, 1702, 1590, 1567, 1460, 1383, 1287, 1236, 1191, 1016, 988, 818, 737, 697 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.44 (dd, 1H, *J*=7.8 and 2.9 Hz, Ar-H), 7.45–7.28 (m, 5H, Ar-H), 6.89 (dd, 1H, *J*=7.8 and 2.9 Hz, Ar-H), 6.87 (s, 1H, Ar-H), 5.04 (s, 2H, Ph-CH_2O), 3.39 [sept, 1H, *J*=7.3 Hz, C*H*(CH_3)$_2$], 1.17 [d, 6H, *J*=7.3 Hz, CH(C*H*$_3$)$_2$] ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): 208.4 (s, Ar-C=O), 157.8 (s, Ar-C), 142.7 (s, Ar-C), 136.0 (s, Ar-C), 134.1 (d, Ar-CH), 128.7 (d, 2C, Ar-CH), 128.2 (d, Ar-CH), 127.5 (d, 2C, Ar-CH), 117.7 (d, Ar-CH), 114.8 (d, Ar-CH), 109.1 (s, Ar-C), 70.4 (t, Ph-CH_2O), 40.1 [d, *C*H(CH_3)$_2$], 18.1 [q, 2C, CH(*C*H$_3$)$_2$] ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{17}H_{18}BrO_2]^+$=$[M+H]^+$: 333.0485; found 333.0481.



69c

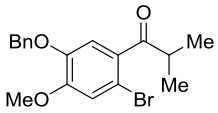
1-(2-Bromo-5-methoxyphenyl)-2-methylpropan-1-one (69c): GP-5 was carried out with the secondary alcohol **68c** (1.8 g, 6.95 mmol), dry CH_2Cl_2 (12 mL), and a homogeneous mixture of PCC (4.48 g, 20.85 mmol) and silica gel (4.48 g) stirred at RT for 2 h. Filtration through short silica gel column chromatography with CH_2Cl_2 furnished the product **69c** (1.7 g, 96%) as pale yellow oil. [TLC control (petroleum ether/ethyl acetate 90:10, R_f(**68c**)=0.4, R_f(**69c**)=0.55, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2969, 2929, 2872, 2851, 1701, 1591, 1569, 1464, 1392, 1289, 1201, 1161, 1022, 988, 825 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.43 (d, 1H, *J*=8.8 Hz, Ar-H), 6.80 (dd, 1H, *J*=8.8 and 2.9 Hz, Ar-H), 6.78 (d, 1H, *J*=2.9 Hz, Ar-H), 3.78 (s, 3H, Ar-OCH_3), 3.30 [sept, 1H, *J*=6.8 Hz, C*H*(CH_3)$_2$], 1.18 [d, 6H, *J*=6.8 Hz, CH(C*H*$_3$)$_2$] ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): 208.5 (s, Ar-C=O), 158.7 (s, Ar-C), 142.7 (s, Ar-C), 134.1 (d, Ar-CH), 116.8 (d, Ar-CH), 113.7 (d, Ar-CH), 108.8 (s, Ar-C), 55.6 (q, Ar-OCH_3), 40.0 [d, *C*H(CH_3)$_2$], 18.1 [q, 2C, CH(*C*H$_3$)$_2$] ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{11}H_{14}BrO_2]^+=[M+H]^+$: 257.0172; found 257.0183.



69d

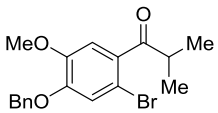
1-[5-(Benzyloxy)-2-bromo-4-methoxyphenyl]-2-methylpropan-1-one (69d): GP-5 was carried out with the secondary alcohol **68d** (1.32 g, 3.63 mmol) in dry CH_2Cl_2 (8 mL) was added a homogeneous mixture of PCC (2.33 g, 10.89 mmol) and silica gel (2.33 g) stirred at RT for 2 h. Filtration through short silica gel column chromatography with CH_2Cl_2 furnished the product **69d** (1.30 g, 98%), as white solid (recrystallized from a mixture of petroleum ether/dichloromethane), m.p.: 56–58 °C. [TLC control (petroleum ether/ethyl acetate 70:30, R_f(**68d**)=0.40, R_f(**69d**)=0.65, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2969, 1693, 1592, 1504, 1456, 1439, 1373, 1330, 1252, 1215, 1195, 1175, 1044, 1025, 999, 907, 846, 732, 696 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.39 (d, 2H, *J*=7.3 Hz, Ar-H), 7.35 (dd, 2H, *J*=7.3 and 7.3 Hz, Ar-H), 7.29 (dd, 1H, *J*=7.3 and 7.3 Hz, Ar-H), 7.04 (s, 1H, Ar-H), 6.90 (s, 1H, Ar-H), 5.11 (s, 2H, $PhCH_2$), 3.87 (s, 3H, Ar-OCH_3), 3.31 [sept, 1H, *J*=6.8 Hz, C*H*$(CH_3)_2$], 1.09 [d, 6H, *J*=6.8 Hz, CH(C*H*$_3)_2$] ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): 207.3 (s, Ar-C=O), 151.5 (s, Ar-C), 146.9 (s, Ar-C), 136.1 (s, Ar-C), 132.9 (s, Ar-C), 128.6 (d, 2C, Ar-CH), 128.1 (d, Ar-CH), 127.4 (d, 2C, Ar-CH), 116.5 (d, Ar-CH), 114.5 (d, Ar-CH), 110.9 (s, Ar-C), 71.2 (t, Ph-CH_2O), 56.2 (q, Ar-OCH_3), 39.3 [d, *C*H$(CH_3)_2$], 18.3 [q, 2C, CH(*C*H$_3)_2$] ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{18}H_{20}{}^{79}BrO_3]^+=[M+H]^+$: 363.0590; found 363.0591, $[C_{18}H_{20}{}^{81}BrO_3]^+=[M+H]^+$: 365.057; found 365.0569.



69e

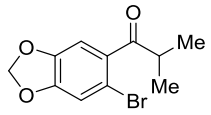
1-[4-(Benzyloxy)-2-bromo-5-methoxyphenyl]-2-methylpropan-1-one (69e): GP-5 was carried out with the secondary alcohol **68e** (800 mg, 2.19 mmol), dry CH_2Cl_2 (4 mL), and a homogeneous mixture of PCC (1.41 g, 6.57 mmol) and silica gel (1.41 g) stirred at RT for 2 h. Filtration through short silica gel column chromatography with CH_2Cl_2 furnished the product **69e** (765 mg, 96%) as pale yellow viscous liquid. [TLC control (petroleum ether/ethyl acetate 90:10, R_f(**68e**)=0.25, R_f(**69e**)=0.45, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2968, 2927, 2871, 2850, 1694, 1592, 1504, 1456, 1439, 1374, 1254, 1216, 1196, 1176, 1156, 1027, 847, 698 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.45–7.30 (m, 5H, Ar-H), 7.07 (s, 1H, Ar-H), 6.88 (s, 1H, Ar-H), 5.13 (s, 2H, $PhCH_2$), 3.86 (s, 3H, Ar-OCH_3), 3.44 [sept, 1H, J=6.8 Hz, C*H*$(CH_3)_2$], 1.17 [d, 6H, J=6.8 Hz, CH(C*H*$_3)_2$] ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): 207.8 (s, Ar-C=O), 150.1 (s, Ar-C), 148.8 (s, Ar-C), 135.8 (s, Ar-C), 133.9 (s, Ar-C), 128.7 (d, 2C, Ar-CH), 128.3 (d, Ar-CH), 127.4 (d, 2C, Ar-CH), 118.2 (d, Ar-CH), 112.1 (d, Ar-CH), 110.0 (s, Ar-C), 71.2 (t, Ar-OCH_2), 56.3 (q, Ar-OCH_3), 39.5 [d, *C*H$(CH_3)_2$], 18.5 [q, 2C, CH(*C*H$_3)_2$] ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{18}H_{19}{}^{79}BrNaO_3]^+$=$[M+Na]^+$: 385.0410; found 385.0416. $[C_{18}H_{19}{}^{81}BrNaO_3]^+$=$[M+Na]^+$: 387.0389; found 387.0402.



69f

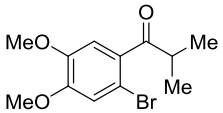
1-(6-Bromo-1,3-benzodioxol-5-yl)-2-methylpropan-1-one (69f): **GP-5** was carried out with the secondary alcohol **68f** (1.50 g, 5.49 mmol), dry CH_2Cl_2 (10 mL), and a homogeneous mixture of PCC (3.50 g, 16.47 mmol) and silica gel (3.50 g) stirred at RT for 2 h. Filtration through short silica gel column chromatography with CH_2Cl_2 furnished the product **69f** (1.40 g, 95%) as pale yellow viscous oil. [TLC control (petroleum ether/ethyl acetate 90:10, R_f(**68f**)=0.45, R_f(**69f**)=0.60, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2971, 2930, 2873, 1696, 1614, 1503, 1474, 1406, 1385, 1236, 1117, 932, 868, 852, 721, 605 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=6.99 (s, 1H, Ar-H), 6.78 (s, 1H, Ar-H), 6.00 (s, 2H, O-CH_2-O), 3.30 [sept, 1H, J=6.8 Hz, C*H*(CH_3)$_2$], 1.14 [d, 6H, J=6.8 Hz, CH(C*H*$_3$)$_2$] ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=207.5 (s, Ar-C=O), 149.6 (s, Ar-C), 147.2 (s, Ar-C), 134.9 (s, Ar-C), 113.5 (d, Ar-CH), 110.6 (s, Ar-C), 108.4 (d, Ar-CH), 102.2 (t, O-CH_2-O), 39.8 [d, *C*H(CH_3)$_2$], 18.3 [q, 2C, CH(*C*H$_3$)$_2$] ppm.

HR-MS (ESI$^+$): m/z calculated for [$C_{11}H_{12}{}^{79}BrO_3$]$^+$=[M+H]$^+$: 270.9964; found 270.9972, [$C_{11}H_{12}{}^{81}BrO_3$]$^+$=[M+H]$^+$: 272.9944; found 272.9954.



69g

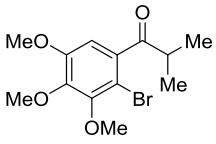
1-(2-Bromo-4,5-dimethoxyphenyl)-2-methylpropan-1-one (69g): GP-5 was carried out with the secondary alcohol **68g** (1.50 g, 5.19 mmol), dry CH_2Cl_2 (10 mL), and a homogeneous mixture of PCC (3.35 g, 15.57 mmol) and silica gel (3.35 g) stirred at RT for 2 h. Filtration through short silica gel column chromatography with CH_2Cl_2 furnished the product **69g** (1.39 g, 93%) as pale brown viscous liquid. [TLC control (petroleum ether/ethyl acetate 70:30, R_f(**68g**)=0.45, R_f(**69g**)=0.60, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2969, 1694, 1593, 1504, 1461, 1439, 1372, 1333, 1254, 1201, 1175, 1156, 1050, 1025, 848, 789 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.04 (s, 1H, Ar-H), 6.88 (s, 1H, Ar-H), 3.90 (s, 3H, Ar-OCH_3), 3.88 (s, 3H, Ar-OCH_3), 3.47 [sept, 1H, J=6.9 Hz, C*H*(CH_3)$_2$], 1.19 [d, 6H, J=6.9 Hz, CH(C*H*$_3$)$_2$] ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): 207.6 (s, Ar-C=O), 150.9 (s, Ar-C), 148.2 (s, Ar-C), 133.5 (s, Ar-C), 116.1 (d, Ar-CH), 111.8 (d, Ar-CH), 110.3 (s, Ar-C), 56.2 (q, Ar-OCH_3), 56.1 (q, Ar-OCH_3), 39.5 [d, *C*H(CH_3)$_2$], 18.4 [q, 2C, CH(*C*H$_3$)$_2$] ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{12}H_{16}{}^{79}BrO_3]^+=[M+H]^+$: 287.0277; found 287.0282, $[C_{12}H_{16}{}^{81}BrO_3]^+=[M+H]^+$: 289.0257; found 289.0266.



69h

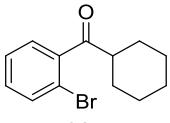
1-(2-Bromo-3,4,5-trimethoxyphenyl)-2-methylpropan-1-one (69h): GP-5 was carried out with the secondary alcohol **68h** (700 mg, 2.19 mmol), dry CH_2Cl_2 (3 mL), and a homogeneous mixture of PCC (1.41 g, 6.58 mmol) and silica gel (1.41 g) stirred at RT for 2 h. Filtration through short silica gel column chromatography with CH_2Cl_2 furnished the product **69h** (660 mg, 95%) as brown viscous liquid. [TLC control (petroleum ether/ethyl acetate 90:10, R_f(**68h**)=0.30, R_f(**69h**)=0.55, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2968, 2930, 2851, 1696, 1593, 1562, 1482, 1463, 1384, 1327, 1243, 1201, 1164, 1126, 1107, 1005, 948, 838, 751 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=6.59 (s, 1H, Ar-H), 3.89 (s, 3H, Ar-OCH_3), 3.88 (s, 3H, Ar-OCH_3), 3.84 (s, 3H, Ar-OCH_3), 3.34 [sept, 1H, J=6.8 Hz, C*H*$(CH_3)_2$], 1.17 [d, 6H, J=6.8 Hz, CH(C*H*$_3)_2$] ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=208.5 (s, Ar-C=O), 152.9 (s, Ar-C), 151.0 (s, Ar-C), 144.4 (s, Ar-C), 137.6 (s, Ar-C), 107.1 (d, Ar-CH), 105.5 (s, Ar-C), 61.1 (q, Ar-OCH_3), 61.0 (q, Ar-OCH_3), 56.2 (q, Ar-OCH_3), 40.1 [d, *C*H$(CH_3)_2$], 18.2 [q, 2C, CH(*C*H$_3)_2$] ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{13}H_{18}{}^{79}BrO_4]^+=[M+H]^+$: 317.0383; found 317.0389, $[C_{13}H_{18}{}^{81}BrO_4]^+=[M+H]^+$: 319.0363; found 319.0371.



81a

(2-Bromophenyl)(cyclohexyl)methanone (81a): GP-5 was carried out with the secondary alcohol **80a** (500 mg, 1.86 mmol), dry CH_2Cl_2 (2 mL), and a homogeneous

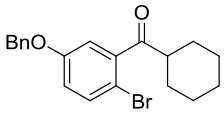
mixture of PCC (1.20 g, 5.59 mmol) and silica gel (1.20 g) stirred at RT for 2 h. Filtration through short silica gel column chromatography with CH_2Cl_2 furnished the product **81a** (452 mg, 91%) as colorless viscous liquid. [TLC control (petroleum ether/ethyl acetate 90:10, R_f(**80a**)=0.55, R_f(**81**)=0.68, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2929, 2853, 1698, 1587, 1448, 1428, 1243, 1205, 1026, 973, 762, 736 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.56 (d, 1H, *J*=7.8 Hz, Ar-H), 7.33 (dd, 1H, *J*=7.8 and 7.3 Hz, Ar-H), 7.29–7.20 (m, 2H, Ar-H), 3.01 (tt, 1H, *J*=11.2 and 3.4 Hz, ArCOCH), 2.05–1.00 (m, 10H, Cy-H) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): 207.9 (s, Ar-C=O), 142.1 (s, Ar-C), 133.3 (d, Ar-CH), 130.9 (d, Ar-CH), 128.0 (d, Ar-CH), 127.1 (d, Ar-CH), 118.6 (s, Ar-C), 49.8 (d, Cy-CH), 28.3 (t, 2C, Cy-CH_2), 25.8 (t, Cy-CH_2), 25.6 (t, 2C, Cy-CH_2) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{13}H_{16}{}^{79}BrO]^+$=$[M+H]^+$: 267.0379; found 267.0381, $[C_{13}H_{16}{}^{81}BrO]^+$=$[M+H]^+$: 269.0359; found 269.0372.



81b

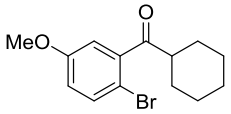
[5-(Benzyloxy)-2-bromophenyl](cyclohexyl)methanone (81b): GP-5 was carried out with the secondary alcohol **80b** (900 mg, 2.40 mmol), dry CH_2Cl_2 (3 mL), and a homogeneous mixture of PCC (1.55 g, 7.20 mmol) and silica gel (1.55 g) stirred at RT for 2 h. Filtration through short silica gel column chromatography with CH_2Cl_2 furnished the product **81b** (850 mg, 95%) as yellow viscous liquid. [TLC control (petroleum ether/ethyl acetate 90:10, R_f(**80b**)=0.50, R_f(**81b**)=0.75, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2926, 2852, 1700, 1591, 1567, 1499, 1453, 1379, 1288, 1231, 1170, 1014, 981, 816, 737, 697 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.44 (d, 1H, *J*=8.8 Hz, Ar-H), 7.43–7.20 (m, 4H, Ar-H), 6.95–6.80 (m, 2H, Ar-H), 5.04 (s, 2H, Ph-CH_2O), 2.99 (tt, 1H, *J*=11.2 and 3.4 Hz, ArCOCH), 2.30–1.00 (m, 10H, Cy-H) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=207.6 (s, Ar-C=O), 157.7 (s, Ar-C), 142.8 (s, Ar-C), 136.1 (s, Ar-C), 134.1 (d, Ar-CH), 128.7 (d, 2C, Ar-CH), 128.2 (d, Ar-CH), 127.5 (d, 2C, Ar-CH), 117.6 (d, Ar-CH), 114.8 (d, Ar-CH), 109.1 (s, Ar-C), 70.4 (t, Ph-CH_2O), 49.8 [d, Cy-CH], 28.3 (t, 2C, Cy-CH_2), 25.8 (t, Cy-CH_2), 25.6 (t, 2C, Cy-CH_2) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{20}H_{22}{}^{79}BrO_2]^+$=$[M+H]^+$: 373.0798; found 373.0800, $[C_{20}H_{22}{}^{81}BrO_2]^+$: 375.0777; found 375.0782.



81c

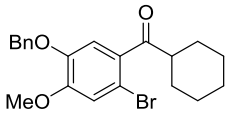
(2-Bromo-5-methoxyphenyl)(cyclohexyl)methanone (81c): GP-5 was carried out with the secondary alcohol **80c** (500 mg, 1.67 mmol), dry CH_2Cl_2 (3 mL), and a homogeneous mixture of PCC (1.0 g, 5.03 mmol) and silica gel (1.0 g) stirred at RT for 2 h. Filtration through short silica gel column chromatography with CH_2Cl_2 furnished the product **81c** (462 mg, 93%) as colorless viscous liquid. [TLC control (petroleum ether/ethyl acetate 90:10, R_f(**80c**)=0.40, R_f(**81c**)=0.50, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2925, 2852, 1700, 1590, 1570, 1464, 1450, 1393, 1289, 1234, 1169, 1017, 982, 816, 772 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.43 (d, 1H, J=8.8 Hz, Ar-H), 6.79 (dd, 1H, J=8.8 and 2.9 Hz, Ar-H), 6.75 (d, 1H, J=2.9 Hz, Ar-H), 3.78 (s, 3H, Ar-OCH_3), 3.01 (tt, 1H, J=11.2 and 3.4 Hz, ArCOCH), 2.00–1.10 (m, 10H, Cy-H) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=207.8 (s, Ar-C=O), 158.7 (s, Ar-C), 142.9 (s, Ar-C), 134.0 (d, Ar-CH), 116.7 (d, Ar-CH), 113.7 (d, Ar-CH), 108.7 (s, Ar-C), 55.6 (q, Ar-OCH_3), 49.8 (d, Cy-CH), 28.3 (t, 2C, Cy-CH_2), 25.8 (t, Cy-CH_2), 25.6 (t, 2C, Cy-CH_2) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{14}H_{18}BrO_2]^+$=$[M+H]^+$: 297.0485; found 297.0484.



81d

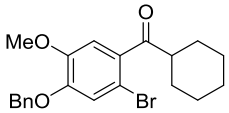
[5-(Benzyloxy)-2-bromo-4-methoxyphenyl](cyclohexyl)methanone (81d): GP-5 was carried out with the secondary alcohol **80d** (1.1 g, 2.71 mmol), dry CH_2Cl_2 (5 mL), and a homogeneous mixture of PCC (1.75 g, 8.15 mmol) and silica gel (1.75 g) stirred at RT for 2 h. Filtration through short silica gel column chromatography with CH_2Cl_2 furnished the product **81d** (1.0 g, 92%) as red viscous liquid. [TLC control (petroleum ether/ethyl acetate 80:20, R_f(**80d**)=0.45, R_f(**81d**)=0.60, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2926, 2851, 1689, 1592, 1502, 1456, 1440, 1376, 1331, 1254, 1214, 1195, 1163, 1026, 847, 737, 697 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.39 (d, 2H, J=7.3 Hz, Ar-H), 7.35 (dd, 2H, J=7.8 and 7.3 Hz, Ar-H), 7.29 (t, 1H, J=7.8 Hz, Ar-H), 7.03 (s, 1H, Ar-H), 6.87 (s, 1H, Ar-H), 5.12 (s, 2H, $PhCH_2$), 3.88 (s, 3H, Ar-OCH_3), 2.99 (tt, 1H, J=11.2 and 3.4 Hz, ArCOCH), 2.00–1.50 (m, 5H, Cy-H), 1.45–1.00 (m, 5H, Cy-H) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=206.4 (s, Ar-C=O), 151.5 (s, Ar-C), 146.9 (s, Ar-C), 136.2 (s, Ar-C), 133.1 (s, Ar-C), 128.6 (d, 2C, Ar-CH), 128.1 (d, Ar-CH), 127.4 (d, 2C, Ar-CH), 116.5 (d, Ar-CH), 114.6 (d, Ar-CH), 110.9 (s, Ar-C), 71.3 (t, Ph-CH_2O), 56.2 (q, Ar-OCH_3), 49.2 (d, Cy-CH), 28.6 (t, 2C, Cy-CH_2), 25.8 (t, Cy-CH_2), 25.6 (t, 2C, Cy-CH_2) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{21}H_{24}{}^{79}BrO_3]^+$=$[M+H]^+$:403.0903; found 403.0902, $[C_{21}H_{24}{}^{81}BrO_3]^+$: 405.0883; found 405.0889.



81e

[4-(Benzyloxy)-2-bromo-5-methoxyphenyl](cyclohexyl)methanone (81e): GP-5 was carried out with the secondary alcohol **80e** (1.1 g, 2.71 mmol), dry CH_2Cl_2 (5 mL), and a homogeneous mixture of PCC (1.75 g, 8.15 mmol) and silica gel (1.75 g) stirred at RT

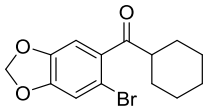
for 2 h. Filtration through short silica gel column chromatography with CH_2Cl_2 furnished the product **81e** (1.0 g, 96%) as red viscous liquid. [TLC control (petroleum ether/ethyl acetate 80:20, R_f(**80e**)=0.40, R_f(**81e**)=0.55, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2927, 2851, 1689, 1591, 1499, 1451, 1381, 1331, 1255, 1213, 1165, 1024, 997, 860 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.41(d, 2H, *J*=7.3 Hz, Ar-H), 7.37 (dd, 2H, *J*=7.8 and 7.3 Hz, Ar-H), 7.32 (t, 1H, *J*=7.8 Hz, Ar-H), 7.06 (s, 1H, Ar-H), 6.86 (s, 1H, Ar-H), 5.12 (s, 2H, $PhCH_2$), 3.86 (s, 3H, Ar-OCH_3), 3.15 (tt, 1H, *J*=11.2 and 3.4 Hz, ArCOCH), 1.90 (d, 2H, *J*=15.2 Hz, Cy-CH_2), 1.80–1.60 (m, 3H, Cy-CH_2), 1.50–1.00 (m, 5H, Cy-CH_2) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): 207.0 (s, Ar-C=O), 150.0 (s, Ar-C), 148.7 (s, Ar-C), 135.8 (s, Ar-C), 134.1 (s, Ar-C), 128.6 (d, 2C, Ar-CH), 128.2 (d, Ar-CH), 127.4 (d, 2C, Ar-CH), 118.1 (d, Ar-CH), 112.1 (d, Ar-CH), 110.0 (s, Ar-C), 71.1 (t, $PhCH_2$), 56.2 (q, Ar-OCH_3), 49.4 [d, ArCO*C*H], 28.7 (t, 2C, Cy-CH_2), 25.8 (t, Cy-CH_2), 25.6 (t, 2C, Cy-CH_2) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{21}H_{24}{}^{79}BrO_3]^+$=$[M+H]^+$:403.0903; found 403.0909, $[C_{21}H_{24}{}^{81}BrO_3]^+$: 405.0883; found 405.0894.



81f

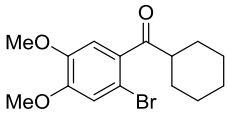
(6-Bromo-1,3-benzodioxol-5-yl)(cyclohexyl)methanone (81f): GP-5 was carried out with the secondary alcohol **80f** (750 mg, 2.40 mmol), dry CH_2Cl_2 (4 mL), and a homogeneous mixture of PCC (1.54 g, 7.19 mmol) and silica gel (1.54 g) stirred at RT for 2 h. Filtration through short silica gel column chromatography with CH_2Cl_2 furnished the product **81f** (707 mg, 95%) as yellow viscous liquid. [TLC control (petroleum ether/ethyl acetate 90:10, R_f(**80f**)=0.4, R_f(**81f**)=0.65, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2927, 2852, 1695, 1503, 1477, 1406, 1340, 1239, 1113, 1036, 996, 936 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=6.99 (s, 1H, Ar-H), 6.76 (s, 1H, Ar-H), 6.00 (s, 2H, O-CH_2-O), 3.01 (tt, 1H, *J*=11.2 and 3.4 Hz, ArCOCH), 2.10–1.00 (m, 10H, Cy-CH_2) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=206.8 (s, Ar-C=O), 149.5 (s, Ar-C), 147.2 (s, Ar-C), 135.1 (s, Ar-C), 124.2 (s, Ar-C), 113.4 (d, Ar-CH), 108.4 (d, Ar-CH), 102.2 (t, O-CH_2-O), 49.7 [d, ArCO*C*H], 28.5 (t, 2C, Cy-CH_2), 25.8 (t, Cy-CH_2), 25.6 (t, 2C, Cy-CH_2) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{14}H_{16}BrO_3]^+$=$[M+H]^+$: 311.0283; found 311.0289, $[C_{21}H_{24}{}^{81}BrO_3]^+$: 313.0262; found 313.0270.



81g

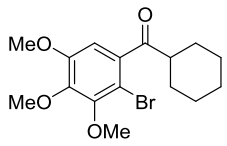
(2-Bromo-4,5-dimethoxyphenyl)(cyclohexyl)methanone (81g): GP-5 was carried out with the secondary alcohol **80g** (2.2 g, 6.68 mmol), dry CH_2Cl_2 (10 mL), and a homogeneous mixture of PCC (4.31 g, 20.04 mmol) and silica gel (4.31 g) stirred at RT for 2 h. Filtration through short silica gel column chromatography with CH_2Cl_2 furnished the product **81g** (2.1 g, 99%) as red viscous liquid. [TLC control (petroleum ether/ethyl acetate 90:10, R_f(**80g**)=0.4, R_f(**81g**)=0.55, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2925, 2851, 1688, 1593, 1503, 1461, 1441, 1375, 1331, 1255, 1213, 1164, 1027, 768 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.00 (s, 1H, Ar-H), 6.83 (s, 1H, Ar-H), 3.88 (s, 3H, Ar-OCH_3), 3.86 (s, 3H, Ar-OCH_3), 3.01 (tt, 1H, *J*=11.2 and 3.4 Hz, ArCOCH), 2.10–1.10 (m, 10H, Cy-CH_2) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=207.0 (s, Ar-C=O), 150.8 (s, Ar-C), 148.2 (s, Ar-C), 133.7 (s, Ar-C), 116.0 (d, Ar-CH), 110.2 (d, Ar-CH), 110.2 (s, Ar-C), 56.2 (q, Ar-OCH_3), 56.1 (q, Ar-OCH_3), 49.4 (d, CyCH), 28.7 (t, 2C, Cy-CH_2), 25.8 (t, Cy-CH_2), 25.7 (t, 2C, Cy-CH_2) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{15}H_{20}{}^{79}BrO_3]^+$=$[M+H]^+$:327.0590; found 327.0592.



81h

(2-Bromo-3,4,5-trimethoxyphenyl)(cyclohexyl)methanone (81h): GP-5 was carried out with the secondary alcohol **80h** (500 mg, 1.39 mmol), dry CH_2Cl_2 (3 mL), and a homogeneous mixture of PCC (901 mg, 4.89 mmol) and silica gel (901 mg) stirred at RT for 2 h. Filtration through short silica gel column chromatography with CH_2Cl_2 furnished the product **81h** (457 mg, 92%) as pale yellow viscous liquid. [TLC control (petroleum ether/ethyl acetate 85:15, R_f(**80h**)=0.40, R_f(**81h**)=0.50, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2927, 2852, 1696, 1562, 1479, 1448, 1383, 1335, 1198, 1165, 1107, 1007, 932, 749 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=6.61 (s, 1H, Ar-H), 3.91 (s, 6H, 2 × Ar-OCH_3), 3.87 (s, 3H, Ar-OCH_3), 3.07 (tt, 1H, J=11.2 and 3.4 Hz, ArCOCH), 2.10–1.10 (m, 10H, Cy-H) ppm.

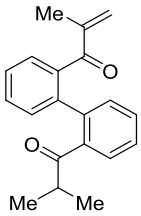
^{13}C NMR ($CDCl_3$, 100 MHz): δ=207.5 (s, Ar-C=O), 152.8 (s, 2C, Ar-C), 150.8 (s, Ar-C), 144.1 (s, Ar-C), 137.6 (s, Ar-C), 107.0 (d, Ar-CH), 105.3 (s, Ar-C), 61.0 (q, Ar-OCH_3), 60.9 (q, Ar-OCH_3), 56.1 (q, Ar-OCH_3), 49.8 (d, Cy-CH), 28.4 (t, 2C, Cy-CH_2), 25.7 (t, Cy-CH_2), 25.5 (t, 2C, Cy-CH_2) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{16}H_{22}BrO_4]^+$=$[M+H]^+$: 357.0696; found 357.0694.

General procedure for the synthesis of bi-aryls (GP-6):

In an oven dried Schlenk tube under nitrogen atmosphere, were added *ortho*-bromoisopropylketone/*ortho*-bromocyclohexylketone **69/81** (100 mg, 0.27 to 0.44 mmol), $Pd(OAc)_2$ (4 mol%), Xantphos (4 mol%) and K_2CO_3 (1.08 to 1.76 mmol) followed by addition of dry toluene (2 mL). The resulted reaction mixture was stirred at

100°C for 16 h. The progress of the reaction was monitored by TLC till the reaction was completed. The reaction mixture was quenched by an addition of aqueous NH_4Cl and the aqueous layer was extracted with ethyl acetate (3 × 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate) furnished the product **70/82** (54-97%)/(57-88%).



70a

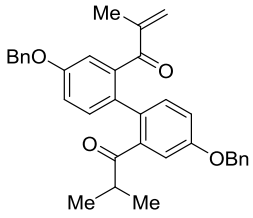
1-(2'-Isobutyryl-1,1'-biphenyl-2-yl)-2-methylprop-2-en-1-one (70a): GP-6 was carried out with *ortho*-bromoisopropylketone **69a** (100 mg, 0.44 mmol), $Pd(OAc)_2$ (4.0 mg, 0.018 mmol), Xantphos (10.2 mg, 0.018 mmol), K_2CO_3 (243 mg, 1.76 mmol), dry toluene (2 mL) at 100 °C for 16 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 92:08 to 85:15) furnished the product **70a** (62 mg, 97%), as white solid (recrystallized from a mixture of petroleum ether/dichloromethane), m.p.: 60–62 °C. [TLC control R_f(**69a**)=0.60, R_f(**70a**)=0.45 (petroleum ether/ethyl acetate 90:10, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2965, 2924, 2852, 1687, 1658, 1594, 1466, 1435, 1379, 1328, 1214, 1196, 1015, 977, 948, 906, 750 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.55–7.47 (m, 1H, Ar-H), 7.44 (dd, 1H, *J*=7.3 and 1.5 Hz, Ar-H), 7.40 (dd, 1H, *J*=7.3 and 2.0 Hz, Ar-H), 7.39 (dd, 1H, *J*=5.4 and 2.0 Hz, Ar-H), 7.38–7.30 (m, 2H, Ar-H), 7.14 (dd, 1H, *J*=7.3 and 2.0 Hz, Ar-H), 7.12–7.06 (m, 1H, Ar-H), 5.85 [s, 1H, (CO)C=CH_aH$_b$], 5.74 [s, 1H, (CO)C=CH$_a$$H_b$], 2.85 [sept, 1H, *J*=6.8 Hz, CH(CH_3)$_2$], 1.84 [s, 3H, H_3C(CO)C=CH$_2$], 0.94 [br. s, 6H, CH(CH_3)$_2$] ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=210.5 (s, Ar-CO), 199.7 (s, Ar-CO), 145.1 [s, $H_3C(CO)\mathit{C}=CH_2$], 140.0 (s, Ar-C), 139.6 (s, Ar-C), 138.9 (s, Ar-C), 138.7 (s, Ar-C), 130.8 (d, Ar-C), 130.5 (d, Ar-CH), 130.0 (d, Ar-CH), 129.7 (d, Ar-CH), 129.6[t, $H_3C(CO)C=\mathit{C}H_2$], 129.0 (d, Ar-CH), 128.3 (d, Ar-CH), 127.5 (d, Ar-CH), 126.9 (d, Ar-CH), 38.9 [d, $\mathit{C}H(CH_3)_2$], 17.4 [3 × q, 3C, $CH(\mathit{C}H_3)_a(CH_3)_b$, $CH(CH_3)_a(\mathit{C}H_3)_b$ and $H_3\mathit{C}(CO)C=CH_2$] ppm.

HR-MS (ESI+): m/z calculated for $[C_{20}H_{20}NaO_2]^+$=$[M+Na]^+$: 315.1356; found 315.1361.



70b

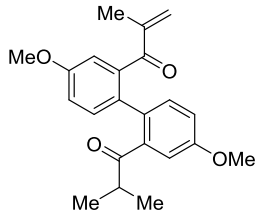
1-[4,4'-Bis(benzyloxy)-2'-isobutyryl-1,1'-biphenyl-2-yl]-2-methylprop-2-en-1-one (70b): GP-6 was carried out with *ortho*-bromoisopropylketone **69b** (100 mg, 0.39 mmol), $Pd(OAc)_2$ (3.5 mg, 0.016 mmol), Xantphos (9.0 mg, 0.016 mmol), K_2CO_3 (166 mg, 1.56 mmol) and dry toluene (2 mL) at 100 °C for 16 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 90:10 to 85:15) furnished the product **70b** (65 mg, 85%), as viscous liquid. [TLC control R_f(**69b**)=0.5, R_f(**70b**)=0.3 (petroleum ether/ethyl acetate 90:10, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2961, 2923, 2852, 1688, 1659, 1601, 1564, 1497, 1464, 1380, 1287, 1225, 1171, 1020, 996, 818, 736, 697 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.43 (d, 4H, *J*=7.3 Hz, Ar-H), 7.39 (dd, 4H, *J*=7.8 and 7.3 Hz, Ar-H), 7.33 (t, 2H, *J*=7.8 Hz, Ar-H), 7.06 (d, 1H, *J*=2.4 Hz, Ar-H), 7.05–6.97 (m, 4H, Ar-H), 6.96 (dd, 1H, *J*=8.3 and 2.4 Hz, Ar-H), 5.83 [s, 1H, $(CO)C=C\mathit{H}_aH_b$], 5.70 [s, 1H, $(CO)C=CH_a\mathit{H}_b$], 5.09 (s, 2H, Ph-CH_2O), 5.06 (s, 2H, Ph-CH_2O), 2.78 [sept, 1H, *J*=6.8 Hz, $C\mathit{H}(CH_3)_2$], 1.84 [s, 3H, $\mathit{H}_3C(CO)C=CH_2$], 0.92 [br. s, 6H, $CH(C\mathit{H}_3)_2$] ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): 210.8 (s, Ar-CO), 199.5 (s, Ar-CO), 157.8 (s, Ar-C), 157.3 (s, Ar-C), 144.9 [s, $H_3C(CO)\mathit{C}=CH_2$], 141.0 (s, Ar-C), 139.9 (s, Ar-C), 136.4 (s, Ar-C), 136.3 (s, Ar-C), 132.2 (d, Ar-CH), 131.9 (d, Ar-CH), 131.8 (s, Ar-C), 130.9 (s, Ar-C), 129.6 [t, $H_3C(CO)C=\mathit{C}H_2$], 128.7 (d, 2C, Ar-CH), 128.6 (d, 2C, Ar-CH), 128.2 (d, Ar-CH), 128.1 (d, Ar-CH), 127.6 (d, 2C, Ar-CH), 127.5 (d, 2C, Ar-CH), 116.5 (d, Ar-CH), 116.2 (d, Ar-CH), 115.3 (d, Ar-CH), 114.4 (d, Ar-CH), 70.2 (t, Ph-CH_2O), 70.1 (t, Ph-CH_2O), 39.1 [d, $\mathit{C}H(CH_3)_2$], 17.4 [3×q, 3C, $CH(\mathit{C}H_3)_a(CH_3)_b$, $CH(CH_3)_a(\mathit{C}H_3)_b$ and $H_3\mathit{C}(CO)C=CH_2$] ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{34}H_{32}NaO_4]^+=[M+Na]^+$: 527.2193; found 527.2194.



70c

1-(2'-Isobutyryl-4,4'-dimethoxybiphenyl-2-yl)-2-methylprop-2-en-1-one (70c): GP-6 was carried out with *ortho*-bromoisopropylketone **69c** (100 mg, 0.44 mmol), $Pd(OAc)_2$ (4.0 mg, 0.018 mmol), Xantphos (9.0 mg, 0.018 mmol), K_2CO_3 (215 mg, 1.76 mmol) and dry toluene (2 mL) at 100 °C for 16 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 80:20 to 75:25) furnished the product **70c** (62 mg, 91%), as viscous liquid. [TLC control R_f(**69c**)=0.55, R_f(**70c**)=0.35 (petroleum ether/ethyl acetate 90:10, UV detection)]

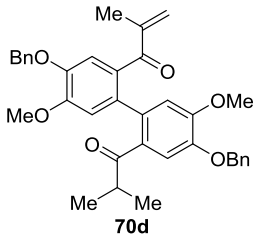
IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2966, 2932, 2872, 2838, 1687, 1658, 1602, 1474, 1288, 1224, 1163, 1053, 1021, 818, 750, 666 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.05–6.90 (m, 5H, Ar-H), 6.87 (dd, 1H, J=8.3 and 2.9 Hz, Ar-H), 5.83 [s, 1H, (CO)C=CH_aH$_b$], 5.71 [s, 1H, (CO)C=CH$_a\mathit{H}_b$], 3.82 (s, 3H, Ar-OCH_3), 3.80 (s, 3H, Ar-OCH_3), 2.77 [sept, 1H, J=6.8 Hz, C$\mathit{H}(CH_3)_2$], 1.83 [s,

3H, $H_3C(CO)C=CH_2$], 0.93 [br. s, 3H, $CH(CH_3)_a(CH_3)_b$], 0.92 [br. s, 3H, $CH(CH_3)_a(CH_3)_b$] ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=210.9 (s, Ar-CO), 199.6 (s, Ar-CO), 158.5 (s, Ar-C), 158.2 (s, Ar-C), 145.0 [s, $H_3C(CO)C=CH_2$], 141.0 (s, Ar-C), 140.0 (s, Ar-C), 132.1 (d, Ar-CH), 131.9 (d, Ar-CH), 131.4 (s, Ar-C), 130.6 (s, Ar-C), 129.4 [t, $H_3C(CO)C=CH_2$], 115.7 (d, Ar-CH), 115.2 (d, Ar-CH), 114.2 (d, Ar-CH), 113.3 (d, Ar-CH), 55.4 (s, Ar-OCH_3), 55.3 (s, Ar-OCH_3), 39.1 [d, $CH(CH_3)_2$], 17.3 [3 × q, 3C, $CH(CH_3)_a(CH_3)_b$, $CH(CH_3)_a(CH_3)_b$ and $H_3C(CO)C=CH_2$] ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{22}H_{24}NaO_4]^+$=$[M+Na]^+$: 375.1567; found 375.1586.



70d

1-[4,4'-Bis(benzyloxy)-2'-isobutyryl-5,5'-dimethoxy-1,1'-biphenyl-2-yl]-2-methylprop-2-en-1-one (70d): GP-6 was carried out with *ortho*-bromoisopropylketone **69d** (100 mg, 0.27 mmol), $Pd(OAc)_2$ (2.5 mg, 0.011 mmol), Xantphos (6.4 mg, 0.011 mmol), K_2CO_3 (152 mg, 1.08 mmol) and dry toluene (2 mL) at 100 °C for 16 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 75:25 to 65:35) furnished the product **70d** (65 mg, 84%), as pale brown solid (recrystallized from a mixture of petroleum ether/dichloromethane), m.p.: 126–130 °C. [TLC control R_f(**69d**)=0.55, R_f(**70d**)=0.35 (petroleum ether/ethyl acetate 90:10, UV detection)]

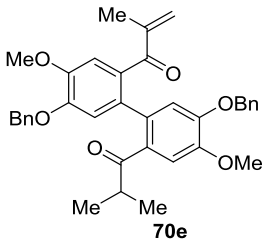
IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2966, 1678, 1653, 1596, 1501, 1455, 1441, 1368, 1329, 1253, 1208, 1154, 1128, 1025, 908, 725, 695 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.42 (d, 4H, J=7.3 Hz, Ar-H), 7.36 (dd, 4H, J=7.8 and 7.3 Hz, Ar-H), 7.29 (t, 2H, J=7.8 Hz, Ar-H), 7.10 (s, 1H, Ar-H), 7.02 (s, 1H,

Ar-H), 6.63 (s, 1H, Ar-H), 6.58 (s, 1H, Ar-H), 5.63 (s, 1H, C=CH_aH$_b$), 5.50 (s, 1H, C=CH$_a$$H_b$), 5.15 (s, 4H, Ph-CH$_2$O), 3.84 (s, 3H, Ar-OCH$_3$), 3.79 (s, 3H, Ar-OCH$_3$), 2.74 [sept, 1H, *J*=6.8 Hz, C*H*(CH$_3$)$_2$], 1.79 [s, 3H, H_3C(CO)C=CH$_2$], 0.92 [br. s, 3H, CH(CH_3)$_a$(CH$_3$)$_b$], 0.89 [br. s, 3H, CH(CH$_3$)$_a$(CH_3)$_b$] ppm.

^{13}C-NMR (CDCl$_3$, 100 MHz): δ=209.0 (s, Ar-C=O), 199.0 (s, Ar-C=O), 150.7 (s, Ar-C), 150.5 (s, Ar-C), 146.8 (s, Ar-C), 146.4 (s, Ar-C), 144.9 [s, H$_3$C(CO)*C*=CH$_2$], 136.4 (s, Ar-C), 136.3 (s, Ar-C), 133.9 (s, Ar-C), 133.4 (s, Ar-C), 131.4 (s, Ar-C), 130.8 (s, Ar-C), 128.5 (d, 2C, Ar-CH), 128.4 (d, 2C, Ar-CH), 128.0 [t, H$_3$C(CO)C=*C*H$_2$], 127.9 (d, 2C, Ar-CH), 127.4 (d, 2C, Ar-CH), 127.3 (d, 2C, Ar-CH), 114.8 (d, Ar-CH), 114.3 (d, Ar-CH), 113.9 (d, Ar-CH), 113.7 (d, Ar-CH), 71.0 (t, 2C, Ph-CH$_2$O), 55.9 (q, Ar-OCH$_3$), 55.8 (q, Ar-OCH$_3$), 38.5 [d, *C*H(CH$_3$)$_2$], 19.5 [q, CH(*C*H$_3$)$_a$(CH$_3$)$_b$], 18.1 [q, CH(CH$_3$)$_a$(*C*H$_3$)$_b$], 17.5 [q, H$_3$*C*(CO)C=CH$_2$] ppm.

HR-MS (ESI$^+$): m/z calculated for [C$_{36}$H$_{36}$NaO$_6$]$^+$=[M+Na]$^+$: 587.2404; found 587.2411.



70e

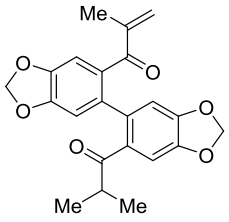
1-[5,5'-Bis(benzyloxy)-2'-isobutyryl-4,4'-dimethoxy-1,1'-biphenyl-2-yl]-2-methylprop-2-en-1-one (70e): GP-6 was carried out with 2-bromoisopropylketone **69e** (100 mg, 0.27 mmol), Pd(OAc)$_2$ (2.5 mg, 0.011 mmol), Xantphos (6.4 mg, 0.011 mmol), K$_2$CO$_3$ (150 mg, 1.08 mmol) and dry toluene (2 mL) at 100 °C for 16 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 70:30) furnished the product **70e** (73 mg, 95%), as white crystalline solid (recrystallized from a mixture of petroleum ether/dichloromethane), m. p.: 122–125 °C. [TLC control R_f(**69e**)=0.45, R_f(**70e**)=0.30 (petroleum ether/ethyl acetate 90:10, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2957, 2922, 2852, 1680, 1655, 1596, 1559, 1502, 1454, 1441, 1367, 1329, 1254, 1209, 1155, 1129, 1025, 870, 748, 697cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.43 (d, 4H, *J*=7.8 Hz, Ar-H), 7.36 (dd, 4H, *J*=7.8 and 7.3 Hz, Ar-H), 7.30 (t, 2H, *J*=7.3 Hz, Ar-H), 7.09 (s, 1H, Ar-H), 7.01 (s, 1H, Ar-H), 6.62 (s, 1H, Ar-H), 6.57 (s, 1H, Ar-H), 5.63 [s, 1H, (CO)C=CH_aH_b], 5.50 [s, 1H, (CO)C=CH_aH_b], 5.16 (s, 4H, Ph-CH_2O), 3.84 (s, 3H, Ar-OCH_3), 3.80 (s, 3H, Ar-OCH_3), 2.73 [sept, 1H, *J*=6.8 Hz, C$H(CH_3)_2$], 1.79 [s, 3H, H_3C(CO)C=CH_2], 0.92 [br. s, 3H, CH(CH_3)$_a$(CH_3)$_b$], 0.89 [br. s, 3H, CH(CH_3)$_a$(CH_3)$_b$] ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=209.1 (s, Ar-C=O), 199.1 (s, Ar-C=O), 150.8 (s, Ar-C), 150.6 (s, Ar-C), 146.9 (s, Ar-C), 146.5 (s, Ar-C), 145.0 [s, H_3C(CO)*C*=CH_2], 136.5 (s, Ar-C), 136.4 (s, Ar-C), 134.8 (s, Ar-C), 133.5 (s, Ar-C), 131.4 (s, Ar-C), 130.9 (s, Ar-C), 128.6 (d, 4C, Ar-CH), 128.1 [t, H_3C(CO)C=*C*H_2], 128.0 (d, 2C, Ar-CH), 127.5 (d, 2C, Ar-CH), 127.4 (d, 2C, Ar-CH), 114.9 (d, Ar-CH), 114.4 (d, Ar-CH), 114.0 (d, Ar-CH), 113.8 (d, Ar-CH), 71.1 (t, Ph-CH_2O), 71.0 (t, Ph-CH_2O), 56.0 (q, Ar-OCH_3), 55.9 (q, Ar-OCH_3), 38.6 [d, *C*H(CH_3)$_2$], 19.6 [q, CH(*C*H_3)$_a$(CH_3)$_b$], 18.2 [q, CH(CH_3)$_a$(*C*H_3)$_b$], 17.6 [q, H_3*C*(CO)C=CH_2] ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{36}H_{36}NaO_6]^+$=$[M+Na]^+$: 587.2404; found 587.2413.



70f

1-(6'-Isobutyryl-5,5'-bi-1, 3-benzodioxol-6-yl)-2-methylprop-2-en-1-one (70f): **GP-6** was carried out with *ortho*-bromoisopropylketone **69f** (100 mg, 0.37 mmol), $Pd(OAc)_2$ (3.2 mg, 0.015 mmol), Xantphos (8.5 mg, 0.015 mmol), K_2CO_3 (204 mg, 1.48 mmol) and dry toluene (2 mL) at 100 °C for 16 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 80:20 to 70:30) furnished the

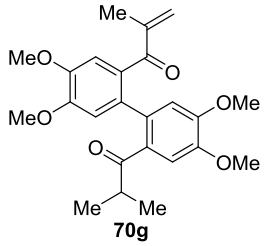
product **70f** (67 mg, 95%), as viscous liquid. [TLC control R_f(**69f**)=0.60, R_f(**70f**)=0.30 (petroleum ether/ethyl acetate 90:10, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2961, 2921, 2852, 1681, 1656, 1612, 1504, 1475, 1382, 1347, 1237, 1116, 1075, 1036, 1016, 932, 873, 733 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.00 (s, 1H, Ar-H), 6.92 (s, 1H, Ar-H), 6.58 (s, 1H, Ar-H), 6.52 (s, 1H, Ar-H), 6.03 (s, 2H, O-CH_2-O), 6.00 (s, 2H, O-CH_2-O), 5.75 [s, 1H, (CO)C=CH_aH$_b$], 5.63 [s, 1H, (CO)C=CH$_a$$H_b$], 2.83 [sept, 1H, J=6.8 Hz, CH(CH_3)$_2$], 1.82 [s, 3H, H_3C(CO)C=CH_2], 1.00 [d, 3H, J=6.8 Hz, CH(CH_3)$_a$(CH_3)$_b$], 0.90 [d, 3H, J=6.8 Hz, CH(CH_3)$_a$(CH_3)$_b$] ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=208.1 (s, Ar-C=O), 198.4 (s, Ar-C=O), 149.1 (s, Ar-C), 148.9 (s, Ar-C), 147.0 (s, Ar-C), 146.5 (s, Ar-C), 144.9 [s, H_3C(CO)C=CH_2], 135.4 (s, Ar-C), 134.9 (s, Ar-C), 133.1 (s, Ar-C), 132.4 (s, Ar-C), 128.3 [t, H_3C(CO)C=CH$_2$], 110.8 (d, Ar-CH), 110.7 (d, Ar-CH), 109.6 (d, Ar-CH), 108.8 (d, Ar-CH), 101.8 (t, O-CH_2-O), 101.7 (t, O-CH_2-O), 38.6 [d, CH(CH_3)$_2$], 19.4 [q, CH(CH$_3$)$_a$(CH_3)$_b$], 18.3 [q, CH(CH_3)$_a$(CH$_3$)$_b$], 17.6 [q, H_3C(CO)C=CH_2] ppm.

HR-MS (ESI$^+$): m/z calculated for [$C_{22}H_{20}NaO_6$]$^+$=[M+Na]$^+$: 403.1152; found 403.1158.



70g

1-(2'-Isobutyryl-4,4',5,5'-tetramethoxy-1,1'-biphenyl-2-yl)-2-methylprop-2-en-1-one (70g): GP-6 was carried out with *ortho*-bromoisopropylketone **69g** (100 mg, 0.35 mmol), $Pd(OAc)_2$ (3.1 mg, 0.014 mmol), Xantphos (8.0 mg, 0.014 mmol), K_2CO_3 (193 mg, 1.40 mmol) and dry toluene (2 mL) at 100 °C for 16 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 60:40 to 50:50) furnished the product **70g** (61 mg, 85%), as pale yellow solid (recrystallized from a

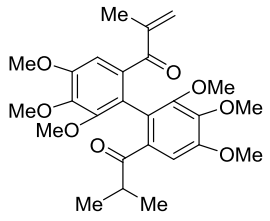
mixture of petroleum ether/dichloromethane), m.p.: 160–162 °C. [TLC control R_f(**69g**)=0.55, R_f(**70g**)=0.35 (petroleum ether/ethyl acetate 70:30, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2964, 1677, 1653, 1597, 1560, 1503, 1462, 1440, 1371, 1330, 1252, 1201, 1155, 1127, 1052, 1024, 916, 871, 729 cm^{-1}.

^{1}H-NMR (CDCl$_3$, 400 MHz): δ=7.02 (s, 1H, Ar-H), 6.97 (s, 1H, Ar-H), 6.60 (s, 1H, Ar-H), 6.56 (s, 1H, Ar-H), 5.72 (s, 1H, C=CH_aH$_b$), 5.64 (s, 1H, C=CH$_a$$H_b$), 3.90 (s, 3H, Ar-OCH$_3$), 3.89 (s, 3H, Ar-OCH$_3$), 3.83 (s, 3H, Ar-OCH$_3$), 3.79 (s, 3H, Ar-OCH$_3$), 2.76 [sept, 1H, J=6.8 Hz, CH(CH$_3$)$_2$], 1.82 [s, 3H, H_3C(CO)C=CH$_2$], 0.97 [br. s, 3H, CH(CH_3)$_a$(CH$_3$)$_b$], 0.90 [br. s, 3H, CH(CH$_3$)$_a$(CH_3)$_b$] ppm.

^{13}C-NMR (CDCl$_3$, 100 MHz): δ=209.5 (s, Ar-C=O), 199.4 (s, Ar-C=O), 150.1 (s, Ar-C), 149.8 (s, Ar-C), 147.9 (s, Ar-C), 147.6 (s, Ar-C), 145.3 [s, H$_3$C(CO)C=CH$_2$], 133.2 (s, Ar-C), 132.8 (s, Ar-C), 131.8 (s, Ar-C), 131.3 (s, Ar-C), 128.0 [t, H$_3$C(CO)C=CH$_2$], 113.6 (d, Ar-CH), 113.4 (d, Ar-CH), 112.0 (d, Ar-CH), 111.6 (d, Ar-CH), 56.0 (q, Ar-OCH$_3$), 55.9 (q, 2C, Ar-OCH$_3$), 55.8 (q, Ar-OCH$_3$), 38.8 [d, CH(CH$_3$)$_2$], 19.7 [q, CH(CH$_3$)$_a$(CH$_3$)$_b$], 18.2 [q, CH(CH$_3$)$_a$(CH$_3$)$_b$], 17.6 [q, H$_3$$C$(CO)C=CH$_2$] ppm.

HR-MS (ESI$^+$): m/z calculated for [C$_{24}$H$_{28}$NaO$_6$]$^+$=[M+Na]$^+$: 435.1778; found 435.1784.



70h

1-(6'-Isobutyryl-2',3',4,4',5,6-hexamethoxy-1,1'-biphenyl-2-yl)-2-methylprop-2-en-1-one (70h): GP-6 was carried out with *ortho*-bromoisopropylketone **69h** (100 mg, 0.32 mmol), Pd(OAc)$_2$ (2.8 mg, 0.013 mmol), Xantphos (7.3 mg, 0.013 mmol), K$_2$CO$_3$ (174.9 mg, 1.26 mmol) and dry toluene (2 mL) at 100 °C for 48 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 80:20 to

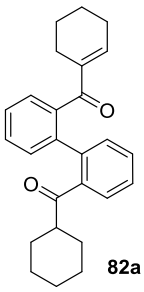
70:30) furnished the product **70h** (20 mg, 54%) yield calculated based on 50% of the staring material recovery, as pale yellow viscous liquid. [TLC control R_f(**69h**)=0.50, R_f(**70h**)=0.30 (petroleum ether/ethyl acetate 70:30, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2954, 2922, 2851, 1684, 1657, 1589, 1482, 1462, 1381, 1343, 1317, 1196, 1161, 1132, 1104, 1005 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=6.93 (s, 1H, Ar-H), 6.82 (s, 1H, Ar-H), 5.71 (s, 1H, C=CH_aH$_b$), 5.64 (s, 1H, C=CH$_a$$H_b$), 3.90 (s, 3H, Ar-OCH$_3$), 3.89 (s, 3H, Ar-OCH$_3$), 3.88 (s, 3H, Ar-OCH$_3$), 3.87 (s, 3H, Ar-OCH$_3$), 3.62 (s, 6H, 2 × Ar-OCH$_3$), 2.91 [sept, 1H, J=6.8 Hz, CH(CH$_3$)$_2$], 1.79 [s, 3H, H_3C(CO)C=CH$_2$], 0.98 [d, 3H, J=6.8 Hz, CH(CH_3)$_a$(CH$_3$)$_b$], 0.90 [d, 3H, J=6.8 Hz, CH(CH$_3$)$_a$(CH_3)$_b$] ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ =207.3 (s, ArCO), 197.8 (s, ArCO), 151.5 (s, Ar-C), 151.4 (s, Ar-C), 144.3 [s, H$_3$C(CO)C=CH$_2$], 144.0 (s, Ar-C), 143.9 (s, Ar-C), 134.7 (s, Ar-C), 134.3 (s, Ar-C), 128.6 (s, Ar-C), 127.9 [t, H$_3$C(CO)C=CH$_2$], 127.4 (s, Ar-C), 123.4 (s, Ar-C), 122.6 (s, Ar-C), 108.6 (d, Ar-CH), 107.5 (d, Ar-CH), 60.8 (q, Ar-OCH$_3$), 60.7 (q, Ar-OCH$_3$), 60.4 (q, Ar-OCH$_3$), 60.2 (q, Ar-OCH$_3$), 56.1 (q, Ar-OCH$_3$), 56.0 (q, Ar-OCH$_3$), 37.9 [d, CH(CH$_3$)$_2$], 19.2 [q, CH(CH$_3$)$_a$(CH$_3$)$_b$], 19.0 [q, CH(CH$_3$)$_a$(CH$_3$)$_b$], 17.9 [q, H$_3$$C$(CO)C=CH$_2$] ppm.

HR-MS (ESI$^+$): m/z calculated for [$C_{26}H_{33}O_8$]$^+$=[M+H]$^+$: 473.2170; found 473.2171.



82a

Cyclohex-1-en-1-yl(2'-(cyclohexanecarbonyl)-[1,1'-biphenyl]-2-yl)methanone (82a): GP-6 was carried out with *ortho*-bromocyclohexylketone **81a** (100 mg, 0.37 mmol), Pd(OAc)$_2$ (3.4 mg, 0.015 mmol), Xantphos (8.7 mg, 0.015 mmol), K_2CO_3 (207 mg, 1.48 mmol) and dry toluene (2 mL) at 100 °C for 16 h. Purification of the residue

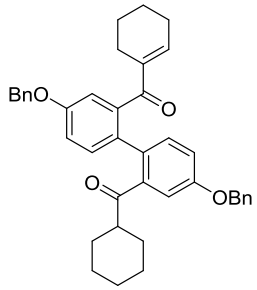
on a silica gel column chromatography (petroleum ether/ethyl acetate 95:5 to 85:15) furnished the product **81a** (60 mg, 87%), as colorless viscous liquid. [TLC control (petroleum ether/ethyl acetate 90:10, R_f(**81a**)=0.55, R_f(**82a**)=0.35, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2926, 2853, 1685, 1649, 1448, 1378, 1283, 1244, 1204, 1135, 973, 773, 750 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.50 (dd, 1H, *J*=7.3 and 2.0 Hz, Ar-H), 7.46–7.30 (m, 5H, Ar-H), 7.12 (ddd, 2H, *J*=7.3, 7.3 and 2.0 Hz, Ar-H), 6.65–6.40 [m, 1H, $H_2C(CO)C$=CH], 2.55 (tt, 1H, *J*=11.2 and 3.4 Hz, ArCOCH), 2.21–0.58 (m, 18H, Cy-H) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=209.0 (s, Ar-CO), 199.3 (s, Ar-CO), 145.5 [d, $H_2C(CO)C$=*C*H], 140.0 [s, $H_2C(CO)C$=CH], 139.8 (s, Ar-C), 139.5 (s, Ar-C), 139.4 (s, Ar-C), 139.3 (s, Ar-C), 130.6 (d, Ar-CH), 130.4 (d, Ar-CH), 130.0 (d, Ar-CH), 129.3 (d, Ar-CH), 128.8 (d, Ar-CH), 128.4 (d, Ar-CH), 127.3 (d, Ar-CH), 127.0 (d, Ar-CH), 48.9 (d, Cy-CH), 29.6 (t, Cy-CH_2), 29.5 (t, Cy-CH_2), 26.0 (t, Cy-CH_2), 25.8 (t, Cy-CH_2), 25.7 (t, Cy-CH_2), 25.6 (t, Cy-CH_2), 23.1 (t, Cy-CH_2), 21.8 (t, Cy-CH_2), 21.4 (t, Cy-CH_2) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{26}H_{29}O_2]^+$=$[M+H]^+$: 373.2162; found 373.2166.



82b

(4,4'-Bis(benzyloxy)-2'-(cyclohex-1-enecarbonyl)-[1,1'-biphenyl]-2-yl)(cyclohexyl) methanone (82b): GP-6 was carried out with *ortho*-bromocyclohexylketone **81b** (100 mg, 0.27 mmol), $Pd(OAc)_2$ (2.4 mg, 0.011 mmol), Xantphos (6.2 mg, 0.011 mmol), K_2CO_3 (150 mg, 1.08 mmol) and dry toluene (2 mL) at 100 °C for 16 h. Purification of

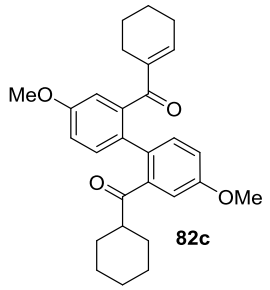
the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 95:05 to 90:10) furnished the product **82b** (61 mg, 78%), as pale yellow viscous liquid. [TLC control R_f(**81b**)=0.75, R_f(**82b**)=0.45 (petroleum ether/ethyl acetate 90:10, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2924, 2852, 1697, 1650, 1600, 1567, 1497, 1453, 1380, 1287, 1229, 1171, 1016, 981, 800, 737, 696 cm^{-1}.

^{1}H-NMR (CDCl$_3$, 400 MHz): δ=7.55–7.28 (m, 10H, Ar-H), 7.07 (d, 1H, Ar-H), 7.05–6.97 (m, 4H, Ar-H), 6.95 (dd, 1H, *J*=8.3 and 2.4 Hz, Ar-H), 6.65–6.45 (m, 1H, Cy=CH), 5.10 (s, 2H, Ph-CH$_2$O), 5.07 (s, 2H, Ph-CH$_2$O), 2.49 [tt, 1H, *J*=11.2 and 3.4 Hz, cyH], 2.14 [br. s, 2H, cyH], 2.03 [m, 2H, cyH], 1.80–0.6 (m, 14H, CyH) ppm.

^{13}C-NMR (CDCl$_3$, 100 MHz): δ=209.3 (s, Ar-CO), 199.0 (s, Ar-CO), 157.6 (s, 2C, Ar-C), 157.4 (s, Ar-C), 145.6 (d, Cy=*C*H), 140.7 (s, 2C, Cy*C*=CH and Ar-C), 139.8 (s, Ar-C), 136.5 (s, 2C, Ar-C), 132.0 (d, Ar-CH), 131.9 (d, Ar-CH), 131.8 (d, Ar-CH), 131.4 (s, Ar-CH), 128.6 (d, 4C, Ar-CH), 128.1 (d, Ar-CH), 127.5 (d, 2C, Ar-CH), 127.4 (d, 2C, Ar-CH), 116.4 (d, Ar-CH), 115.9 (d, Ar-CH), 115.0 (d, Ar-CH), 114.5 (d, Ar-CH), 70.1 (t, 2C, 2 × PhCH$_2$), 49.0 (d, CyCH), 29.7 (t, Cy-CH$_2$), 29.3 (t, Cy-CH$_2$), 26.0 (t, Cy-CH$_2$), 25.8 (t, Cy-CH$_2$), 25.7 (t, Cy-CH$_2$), 25.6 (t, Cy-CH$_2$), 23.1 (t, Cy-CH$_2$), 21.8 (t, Cy-CH$_2$), 21.5 (t, Cy-CH$_2$) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{40}H_{41}O_4]^+$=$[M+H]^+$: 585.2999; found 585.3007.



82c

Cyclohex-1-en-1-yl(2'-(cyclohexanecarbonyl)-4,4'-dimethoxy-[1,1'-biphenyl]-2-yl)methanone (82c): GP-6 was carried out with *ortho*-bromocyclohexylketone **81c** (100 mg, 0.33 mmol), Pd(OAc)$_2$ (3.0 mg, 0.013 mmol), Xantphos (7.8 mg, 0.013

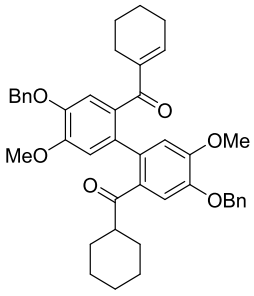
mmol), K_2CO_3 (182.9 mg, 1.32 mmol) and dry toluene (2 mL) at 100 °C for 16 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 95:5 to 80:20) furnished the product **82c** (60.3 mg, 83%), as colorless viscous liquid. [TLC control (petroleum ether/ethyl acetate 85:15, R_f(**81c**)=0.60, R_f(**82c**)=0.40, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2927, 2852, 1684, 1650, 1602, 1475, 1449, 1406, 1312, 1286, 1222, 1168, 1042, 981, 819, 733 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.02 (d, 1H, *J*=7.8 Hz, Ar-H), 7.00 (d, 1H, *J*=8.3 Hz, Ar-H), 6.97 (d, 1H, *J*=2.9 Hz, Ar-H), 6.92 (dd, 1H, *J*=7.8 and 2.9 Hz, Ar-H), 6.91 (d, 1H, *J*=2.9 Hz, Ar-H), 6.87 (dd, 1H, *J*=8.3 and 2.9 Hz, Ar-H), 6.63–6.48 [m, 1H, Cy=CH], 3.83 (s, 3H, Ar-OCH_3), 3.81 (s, 3H, Ar-OCH_3), 2.48 (tt, 1H, *J*=11.2 and 3.4 Hz, ArCOCH), 2.30–0.75 (m, 18H, Cy-H) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=209.5 (s, Ar-CO), 199.1 (s, Ar-CO), 158.5 (s, Ar-C), 158.3 (s, Ar-C), 145.5 [d, $H_2C(CO)C=CH$], 140.8 [s, $H_2C(CO)C=CH$], 140.7 (s, Ar-C), 139.9 (s, Ar-C), 131.9 (d, Ar-CH), 131.8 (d, Ar-CH), 131.5 (s, Ar-C), 131.2 (s, Ar-C), 115.7 (d, Ar-CH), 115.0 (d, Ar-CH), 114.0 (d, Ar-CH), 113.4 (d, Ar-CH), 55.5 (q, Ar-OCH_3), 55.4 (q, Ar-OCH_3), 49.0 (d, Cy-CH), 29.7 (t, Cy-CH_2), 29.6 (t, Cy-CH_2), 26.1 (t, Cy-CH_2), 25.8 (t, Cy-CH_2), 25.7 (t, Cy-CH_2), 25.6 (t, Cy-CH_2), 23.1 (t, Cy-CH_2), 21.8 (t, Cy-CH_2), 21.5 (t, Cy-CH_2) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{28}H_{33}O_4]^+=[M+H]^+$: 433.2373; found 433.2370.



82d

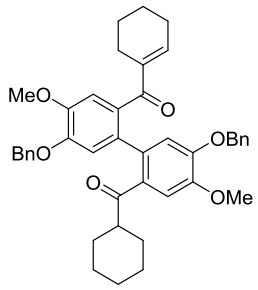
(4,4'-Bis(benzyloxy)-2'-(cyclohex-1-enecarbonyl)-5,5'-dimethoxy-[1,1'-biphenyl]-2-yl)(cyclohexyl)methanone (82d): GP-6 was carried out with *ortho*-bromocyclohexylketone **81d** (100 mg, 0.25 mmol), $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), Xantphos (5.7 mg, 0.01 mmol), K_2CO_3 (138.6 mg, 1.0 mmol) and dry toluene (2 mL) at 100 °C for 16 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 90:10 to 80:20) furnished the product **82d** (68 mg, 85%), as yellow viscous liquid. [TLC control R_f(**81d**)=0.60, R_f(**82d**)=0.30 (petroleum ether/ethyl acetate 80:20, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2926, 2853, 1675, 1632, 1595, 1500, 1452, 1377, 1325, 1252, 1198, 1174, 1153, 1024, 867, 778, 736, 697 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.43 (d, 4H, *J*=7.3 Hz, Ar-H), 7.36 (dd, 4H, *J*=7.8 and 7.3 Hz, Ar-H), 7.30 (t, 2H, *J*=7.8 Hz, Ar-H), 7.08 (s, 1H, Ar-H), 6.98 (s, 1H, Ar-H), 6.62 (s, 1H, Ar-H), 6.59 (s, 1H, Ar-H), 6.45–6.35 (m, 1H, Cy=CH), 5.17 (s, 4H, 2 × Ph-CH_2O), 3.84 (s, 3H, Ar-OCH_3), 3.81 (s, 3H, Ar-OCH_3), 2.40 [tt, 1H, *J*=11.2 and 3.4 Hz, ArCOCH], 2.30–0.50 (m, 18H, CyH) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=207.4 (s, ArCO), 198.8 (s, ArCO), 150.8 (s, ArC), 150.3 (s, ArC), 146.8 (s, ArC), 146.7 (s, ArC), 144.3 (d, Cy=*C*H), 139.9 (s, Cy*C*=CH), 136.7 (s, ArC), 136.6 (s, ArC), 134.1 (s, ArC), 133.7 (s, ArC), 131.9 (s, ArC), 131.1 (s, ArC), 128.6 (d, 2C, Ar-CH), 128.5 (d, 2C, Ar-CH), 128.0 (d, Ar-CH), 127.9 (d, Ar-CH), 127.5 (d, 2C, Ar-CH), 127.4 (d, 2C, Ar-CH), 114.7 (d, Ar-CH), 114.6 (d, Ar-CH), 114.1 (d, Ar-CH), 113.6 (d, Ar-CH), 71.2 (t, Ph-CH_2O), 71.1 (t, Ph-CH_2O), 56.1 (q, Ar-OCH_3), 56.0 (q, Ar-OCH_3), 48.7 (d, ArCO*C*H), 29.6 (t, Cy-CH_2), 29.5 (t, Cy-CH_2), 25.9 (t, Cy-CH_2), 25.8 (t, Cy-CH_2), 25.7 (t, Cy-CH_2), 25.6 (t, Cy-CH_2), 23.4 (t, Cy-CH_2), 21.9 (t, Cy-CH_2), 21.5 (t, Cy-CH_2) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{42}H_{45}O_6]^+$=$[M+H]^+$: 645.3211; found 645.3217.



82e

(5,5'-Bis(benzyloxy)-2'-(cyclohex-1-enecarbonyl)-4,4'-dimethoxy-[1,1'-biphenyl]-2-yl)(cyclohexyl)methanone (82e): GP-6 was carried out with *ortho*-bromocyclohexylketone **81e** (100 mg, 0.25 mmol), $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), Xantphos (5.7 mg, 0.01 mmol), K_2CO_3 (138.6 mg, 1.0 mmol) and dry toluene (2 mL) at 100 °C for 16 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 90:10 to 80:20) furnished the product **82e** (70.3 mg, 88%), as yellow viscous liquid. [TLC control R_f(**81e**)=0.55, R_f(**82e**)=0.35 (petroleum ether/ethyl acetate 80:20, UV detection)]

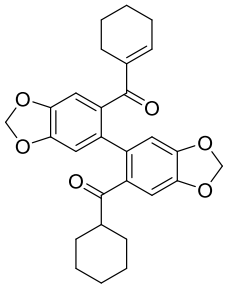
IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2923, 2851, 1673, 1634, 1595, 1499, 1454, 1441, 1384, 1326, 1253, 1153, 1102, 1138, 868, 776, 735, 697 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.41 (d, 2H, *J*=7.3 Hz, Ar-H), 7.40 (d, 2H, *J*=7.3 Hz, Ar-H), 7.36 (dd, 4H, *J*=7.8 and 7.3 Hz, Ar-H), 7.29 (t, 2H, *J*=7.8 Hz, Ar-H), 7.05 (s, 1H, Ar-H), 6.98 (s, 1H, Ar-H), 6.66 (s, 1H, Ar-H), 6.60 (s, 1H, Ar-H), 6.45–6.33 (m, 1H, Cy=CH), 5.10 (s, 2H, Ph-CH_2O), 5.04 (s, 2H, Ph-CH_2O), 3.91 (s, 3H, Ar-OCH_3), 3.89 (s, 3H, Ar-OCH_3), 2.34 (tt, 1H, *J*=11.2 and 3.4 Hz, ArCOCH), 2.20–0.50 (m, 18H, CyH) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=207.7 (s, ArCO), 198.8 (s, ArCO), 149.6 (s, ArC), 149.0 (s, ArC), 148.5 (s, ArC), 148.3 (s, Ar-C), 143.9 (d, CyC=*C*H), 139.9 (s, Cy*C*=CH), 136.4 (s, ArC), 136.3 (s, ArC), 133.4 (s, ArC), 133.0 (s, ArC), 132.7 (s, ArC), 132.1 (s, ArC), 128.6 (d, 4C, Ar-CH), 128.0 (d, Ar-CH), 127.9 (d, Ar-CH), 127.3 (d, 2C, Ar-CH), 127.2 (d, 2C, Ar-CH), 115.5 (d, Ar-CH), 115.0 (d, Ar-CH), 112.4 (d, Ar-CH), 112.3 (d, Ar-CH), 70.9 (t, Ph-CH_2O), 70.8 (t, Ph-CH_2O), 56.2 (q, 2C, 2 × Ar-OCH_3), 48.7 (d, ArCOCH), 29.6 (t, Cy-CH_2), 29.3 (t, Cy-CH_2), 29.1 (t, Cy-CH_2), 25.8

(t, Cy-CH_2), 25.7 (t, 2C, 2 × Cy-CH_2), 23.3 (t, Cy-CH_2), 21.8 (t, Cy-CH_2), 21.5 (t, Cy-CH_2) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{42}H_{45}O_6]^+$=$[M+H]^+$: 645.3211; found 645.3210.



82f

Cyclohex-1-en-1-yl(6'-(cyclohexanecarbonyl)-[5,5'-bibenzo[d][1,3]dioxol]-6-yl)methanone (82f): GP-6was carried out with *ortho*-bromocyclohexylketone **81f** (100 mg, 0.32 mmol), $Pd(OAc)_2$ (2.9 mg, 0.013 mmol), Xantphos (7.4 mg, 0.013 mmol), K_2CO_3 (178.2 mg, 1.28 mmol) and dry toluene (2 mL) at 100 °C for 16 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 85:15 to 80:20) furnished the product **82f** (**65** mg, 89%), as colorless viscous liquid. [TLC control R_f(**81f**)=0.80, R_f(**82f**)=0.45 (petroleum ether/ethyl acetate 85:15, UV detection)]

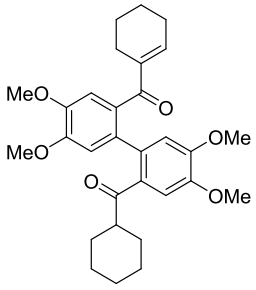
IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2918, 2850, 1712, 1680, 1645, 1613, 1504, 1476, 1382, 1338, 1239, 1135, 1037, 1016, 933, 870 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.01 (s, 1H, Ar-H), 6.89 (s, 1H, Ar-H), 6.56 (s, 1H, Ar-H), 6.52 (s, 1H, Ar-H), 6.52–6.42 (m, 1H, Cy=CH), 6.00 (s, 2H, O-CH_2-O), 5.98 (s, 2H, O-CH_2-O), 2.52 (tt, 1H, *J*=11.2 and 3.4 Hz, ArCOCH), 2.30–0.50 (m, 18H, CyH) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=206.6 (s, ArCO), 198.0 (s, ArCO), 149.0 (s, Ar-C), 148.5 (s, Ar-C), 146.9 (s, Ar-C), 146.6 (s, Ar-C), 144.2 (d, Cy=*C*H), 139.8 (s, Cy*C*=CH), 135.5 (s, Ar-C), 135.1 (s, Ar-C), 133.3 (s, Ar-C), 132.8 (s, Ar-C), 110.9 (d, ArCH), 110.4 (d, ArCH), 109.3 (d, ArCH), 108.8 (d, ArCH), 101.7 (t, OCH_2O), 101.6

(t, OCH_2O), 48.6 (d, ArCOCH), 29.6 (t, Cy-CH_2), 29.5 (t, Cy-CH_2), 28.8 (t, Cy-CH_2), 25.9 (t, Cy-CH_2), 25.8 (t, Cy-CH_2), 25.7 (t, Cy-CH_2), 23.3 (t, Cy-CH_2), 21.8 (t, Cy-CH_2), 21.5 (t, Cy-CH_2) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{28}H_{28}NaO_6]^+$=$[M+Na]^+$: 483.1778; found 483.1783.



82g

Cyclohex-1-en-1-yl(2'-(cyclohexanecarbonyl)-4,4',5,5'-tetramethoxy-[1,1'-biphenyl]-2-yl)methanone (82g): GP-6 was carried out with *ortho*-bromocyclohexylketone **81g** (100 mg, 0.30 mmol), $Pd(OAc)_2$ (2.7 mg, 0.012 mmol), Xantphos (7.0 mg, 0.012 mmol), K_2CO_3 (166.3 mg, 1.2 mmol) and dry toluene (2 mL) at 100 °C for 16 h]. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 70:30 to 60:40) furnished the product **82g** (60 mg, 80%), as colorless viscous liquid. [TLC control R_f(**81g**)=0.85, R_f(**82g**)=0.50 (petroleum ether/ethyl acetate 70:30, UV detection)

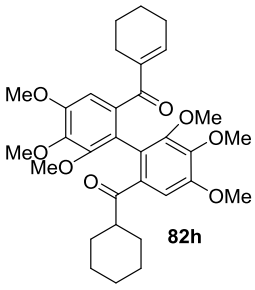
IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2928, 2852, 1673, 1633, 1597, 1561, 1502, 1462, 1449, 1384, 1326, 1253, 1204, 1152, 1027, 868, 771, 731 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.03 (s, 1H, Ar-H), 6.95 (s, 1H, Ar-H), 6.63 (s, 1H, Ar-H), 6.60 (s, 1H, Ar-H), 6.55–6.45 (m, 1H, Cy=CH), 3.91 (s, 3H, Ar-OCH_3), 3.90 (s, 3H, Ar-OCH_3), 3.85 (s, 3H, Ar-OCH_3), 3.82 (s, 3H, Ar-OCH_3), 2.40 (tt, 1H, *J*=11.2 and 3.4 Hz, ArCOCH), 2.30–0.50 (m, 18H, CyH) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): 208.0 (s, ArCO), 199.0 (s, ArCO), 150.2 (s, ArC), 149.7 (s, ArC), δ=148.0 (s, ArC), 147.9 (s, ArC), 144.1 (d, Cy=*C*H), 140.2 (s, Cy*C*=CH), 133.4 (s, ArC), 133.0 (s, ArC), 132.3 (s, ArC), 131.8 (s, ArC), 113.6 (d, Ar-

CH), 113.1 (d, Ar-CH), 111.9 (d, Ar-CH), 111.9 (d, Ar-CH), 56.1 (2q, 2C, 2 × Ar-OCH_3), 56.0 (q, Ar-OCH_3), 55.9 (q, Ar-OCH_3), 48.9 (d, ArCOCH), 29.7 (t, Cy-CH2), 29.1 (t, Cy-CH_2), 26.0 (t, Cy-CH_2), 25.8 (t, Cy-CH_2), 25.7 (t, Cy-CH_2), 25.6 (t, Cy-CH_2), 23.4 (t, Cy-CH_2), 21.8 (t, Cy-CH_2), 21.5 (t, Cy-CH_2) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{30}H_{37}O_6]^+$=$[M+H]^+$: 493.2585; found 493.2587.



82h

Cyclohex-1-en-1-yl(6'-(cyclohexanecarbonyl)-2',3',4,4',5,6-hexamethoxy-[1,1'-biphenyl]-2-yl)methanone (82h): GP-6 was carried out with *ortho*-bromocyclohexylketone **81h** (100 mg, 0.28 mmol), $Pd(OAc)_2$ (2.5 mg, 0.011 mmol), Xantphos (6.4 mg, 0.011 mmol), K_2CO_3 (155.2 mg, 1.12 mmol) and dry toluene (2 mL) at 100 °C for 16 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 90:10 to 70:30) furnished the product **82h** (26.6 mg, 57%) yield calculated based on 41% of the staring material recovery, as pale brown viscous liquid. [TLC control (petroleum ether/ethyl acetate 70:30, R_f(**81h**)=0.60, R_f(**82h**)=0.35, UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2927, 2852, 1679, 1648, 1587, 1481, 1459, 1406, 1385, 1326, 1123, 1102, 997, 731 cm^{-1}.

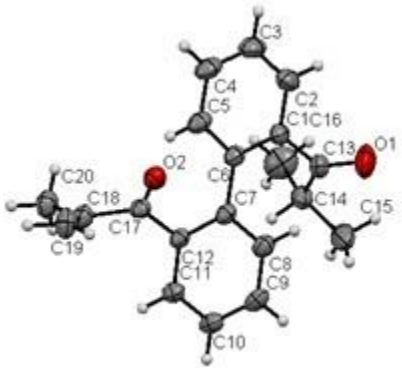
^{1}H-NMR ($CDCl_3$, 400 MHz): δ=6.89 (s, 1H, Ar-H), 6.75 (s, 1H, Ar-H), 6.55–6.42 [m, 1H, Cy=CH], 3.91 (s, 3H, Ar-OCH_3), 3.89 (s, 3H, Ar-OCH_3), 3.88 (s, 6H, 2 × Ar-OCH_3), 3.67 (s, 3H, Ar-OCH_3), 3.66 (s, 3H, Ar-OCH_3), 2.55 (tt, 1H, J=11.2 and 3.4 Hz, ArCOCH), 2.15–1.00 (m, 18H, Cy-H) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=206.3 (s, Ar-CO), 197.6 (s, Ar-CO), 152.4 (s, Ar-C), 152.3 (s, Ar-C), 151.4 (s, Ar-C), 151.3 (s, Ar-C), 144.1 (s, Ar-C), 144.0 [d,

(CO)C=*C*H], 143.3 (s, Ar-C), 139.0 [s, (CO)*C*=CH], 135.3 (s, Ar-C), 134.6 (s, Ar-C), 123.1 (s, Ar-C), 122.8 (s, Ar-C), 108.1 (d, Ar-CH), 107.6 (d, Ar-CH), 60.8 (q, Ar-OCH_3), 60.6 (q, Ar-OCH_3), 60.4 (q, Ar-OCH_3), 60.3 (q, Ar-OCH_3), 56.1 (q, Ar-OCH_3), 56.0 (q, Ar-OCH_3), 48.3 (d, Cy-CH), 29.7 (t, Cy-CH_2), 29.6 (t, Cy-CH_2), 26.1 (t, Cy-CH_2), 26.0 (t, Cy-CH_2), 25.9 (t, Cy-CH_2), 25.8 (t, Cy-CH_2), 23.4 (t, Cy-CH_2), 21.9 (t, Cy-CH_2), 21.6 (t, Cy-CH_2) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{32}H_{41}O_8]^+$=$[M+H]^+$: 553.2796; found 553.2798.

X-ray crystal structure data for the 1-(2'-isobutyryl-1,1'-biphenyl-2-yl)-2-methylprop-2-en-1-one (70a): CCDC 910647



Operator	**K. Ravikumar**
Instrument	**Oxford SuperNova**
Temperature/K	150.00 (10)
Crystal system	triclinic
Space group	P_{-1}
a/Å	9.2383 (18)
b/Å	9.6936 (19)
c/Å	10.2422 (19)
α/°	67.423 (18)
β/°	88.231 (16)

γ/°	89.557 (16)
Volume/Å^3	846.5 (3)
Z	2
ρ_{calc}mg/mm^3	1.147
m/mm^{-1}	0.572
F(000)	312.0
Crystal size/mm^3	0.24 × 0.21 × 0.19
2Θ range for data collection	9.36 to 140.98°
Index ranges	$-11 \leq h \leq 10$, $-9 \leq k \leq 11$, $-12 \leq l \leq 12$
Reflections collected	5601
Independent reflections	3162 [$R_{(int)}$ = 0.0210]
Data/restraints/parameters	3162/0/211
Goodness-of-fit on F^2	1.088
Final R indexes [I>=2σ (I)]	R_1 = 0.0585, wR_2 = 0.1797
Final R indexes [all data]	R_1 = 0.0820, wR_2 = 0.2017
Largest diff. peak/hole / e Å^{-3}	0.15/-0.14

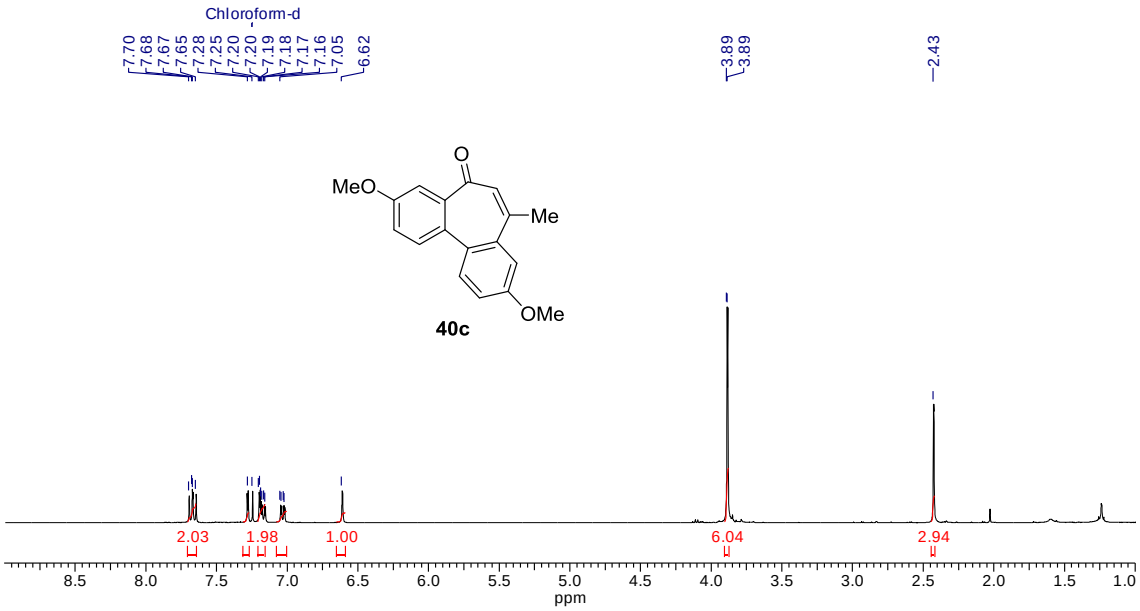


Figure I.16.1: ^{1}H-NMR (400 MHz) spectrum of **40c** in $CDCl_3$

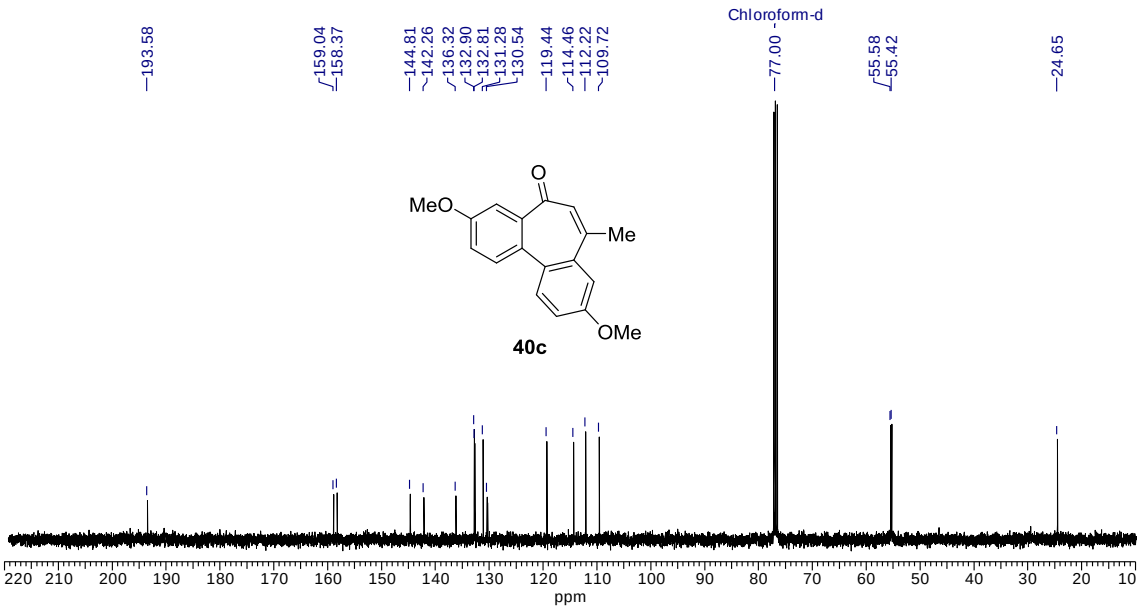


Figure I.16.2: ^{13}C-NMR (100 MHz) spectrum of **40c** in $CDCl_3$

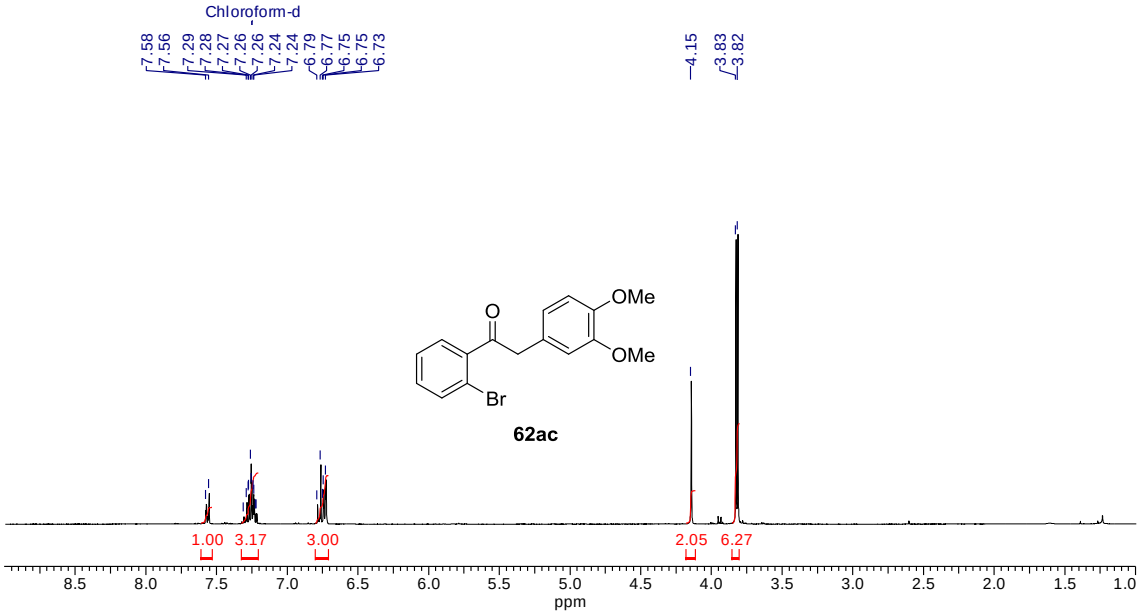


Figure I.16.1: ^{1}H-NMR (400 MHz) spectrum of **62ac** in $CDCl_3$

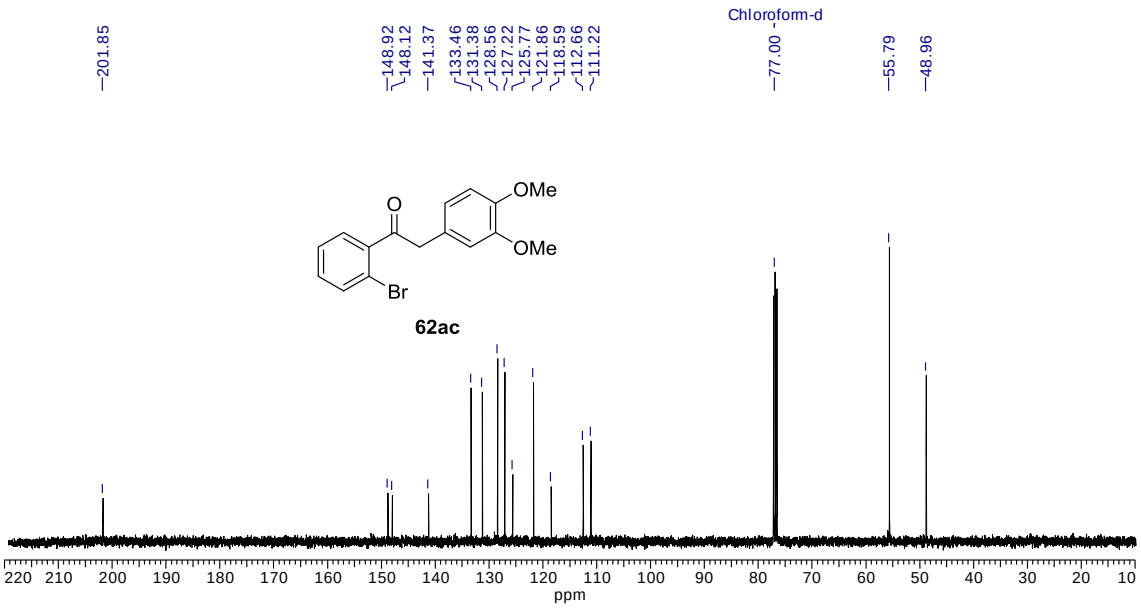


Figure I.16.2: ^{13}C-NMR (100 MHz) spectrum of **62ac** in $CDCl_3$

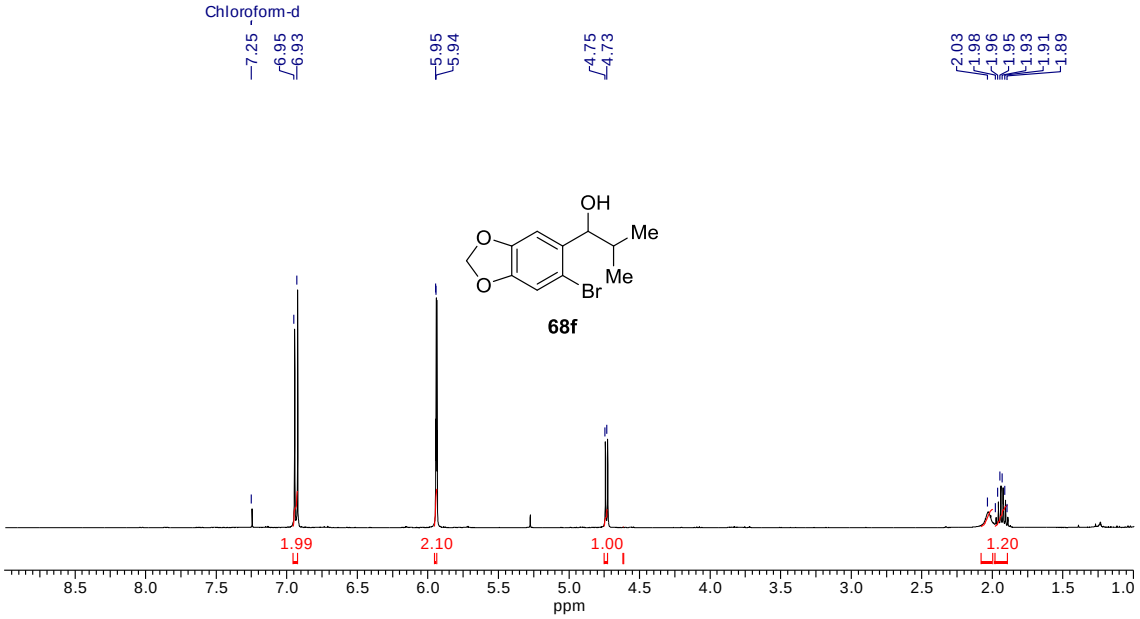


Figure I.16.1: ^{1}H-NMR (400 MHz) spectrum of **68f** in $CDCl_3$

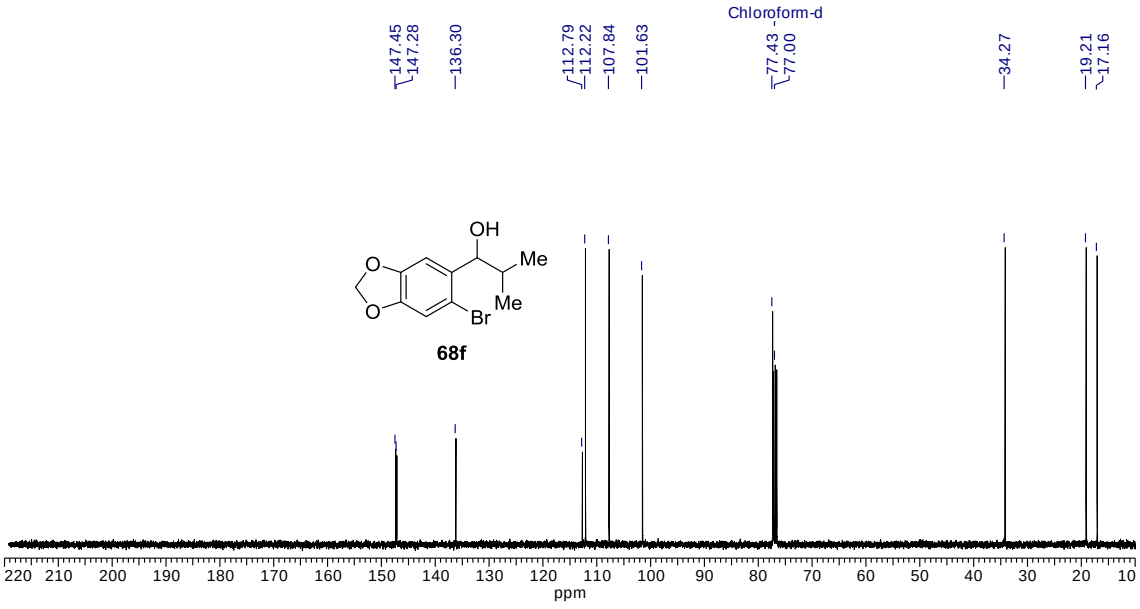


Figure I.16.2: ^{13}C-NMR (100 MHz) spectrum of **68f** in $CDCl_3$

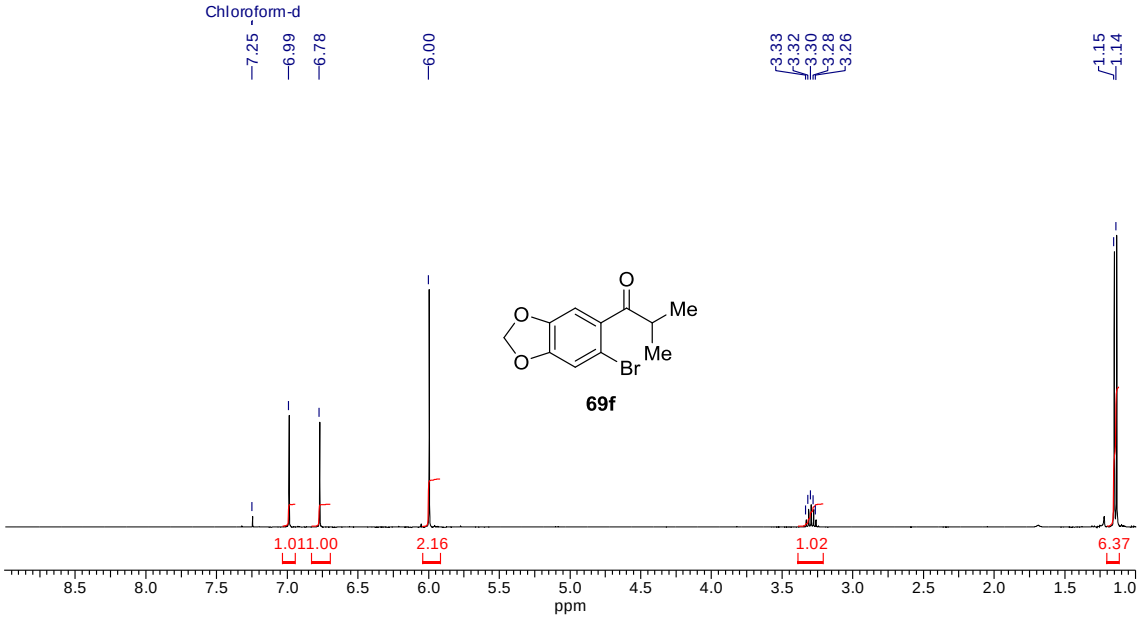


Figure I.16.1: ^{1}H-NMR (400 MHz) spectrum of **69f** in $CDCl_3$

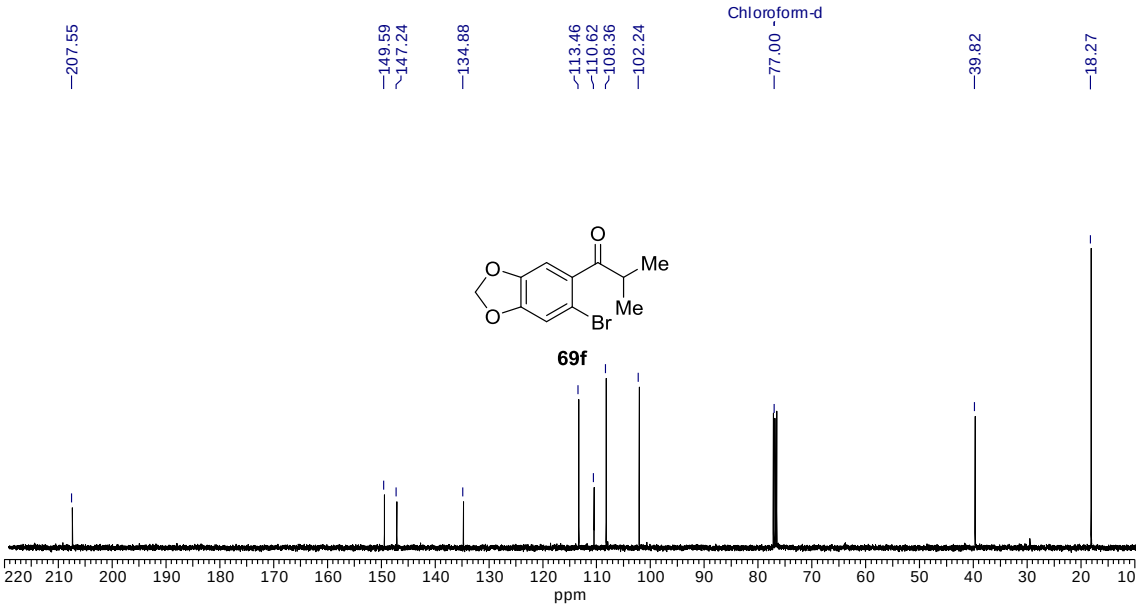


Figure I.16.2: ^{13}C-NMR (100 MHz) spectrum of **69f** in $CDCl_3$

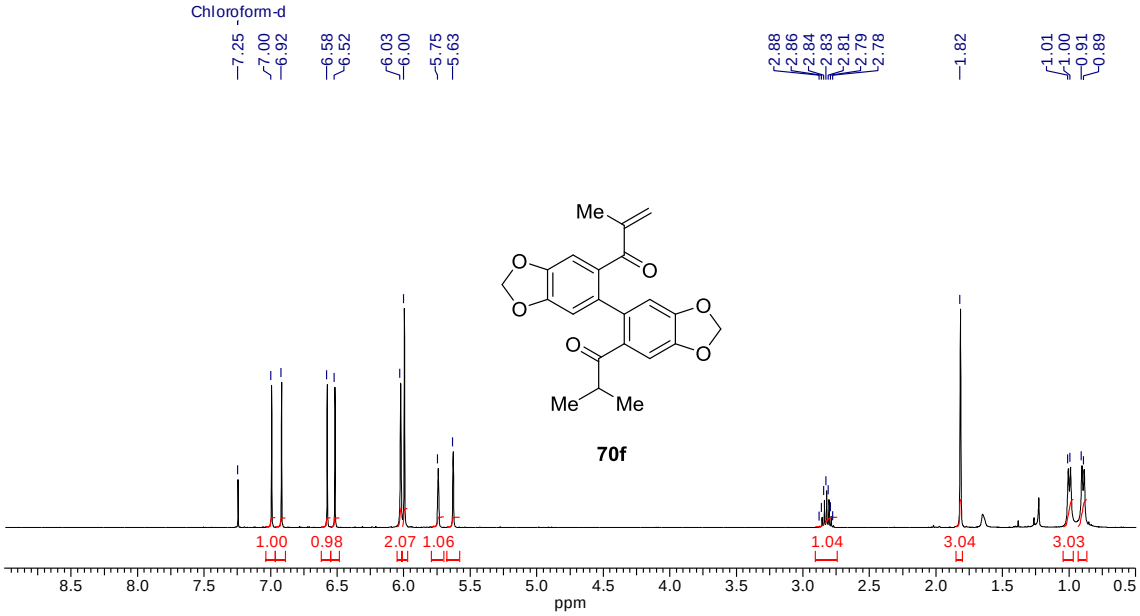


Figure I.16.1: ^{1}H-NMR (400 MHz) spectrum of **70f** in $CDCl_3$

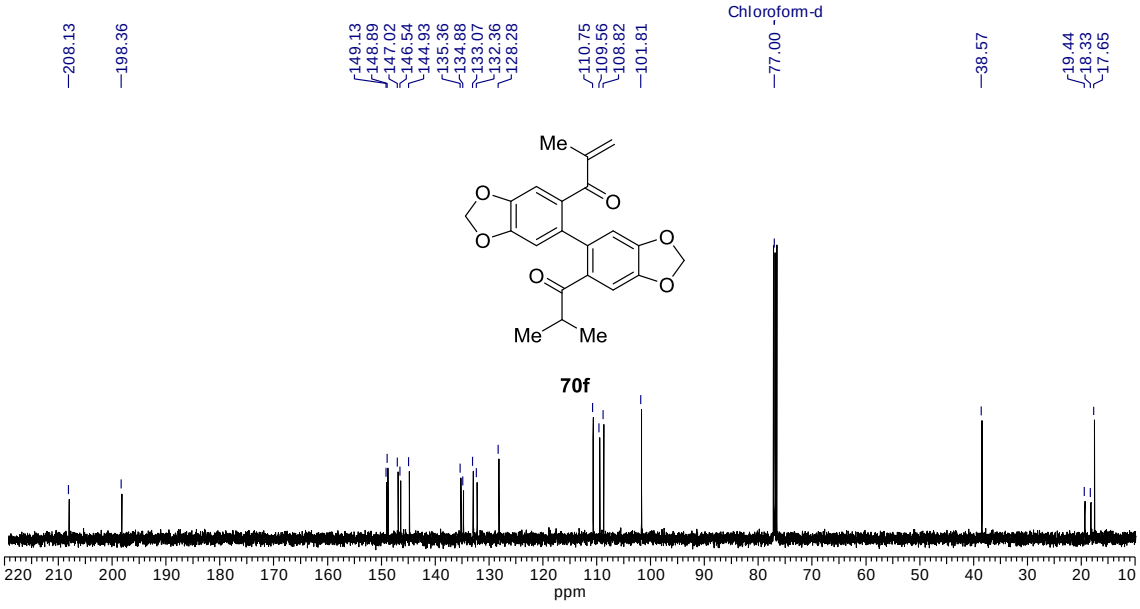


Figure I.16.2: ^{13}C-NMR (100 MHz) spectrum of **70f** in $CDCl_3$

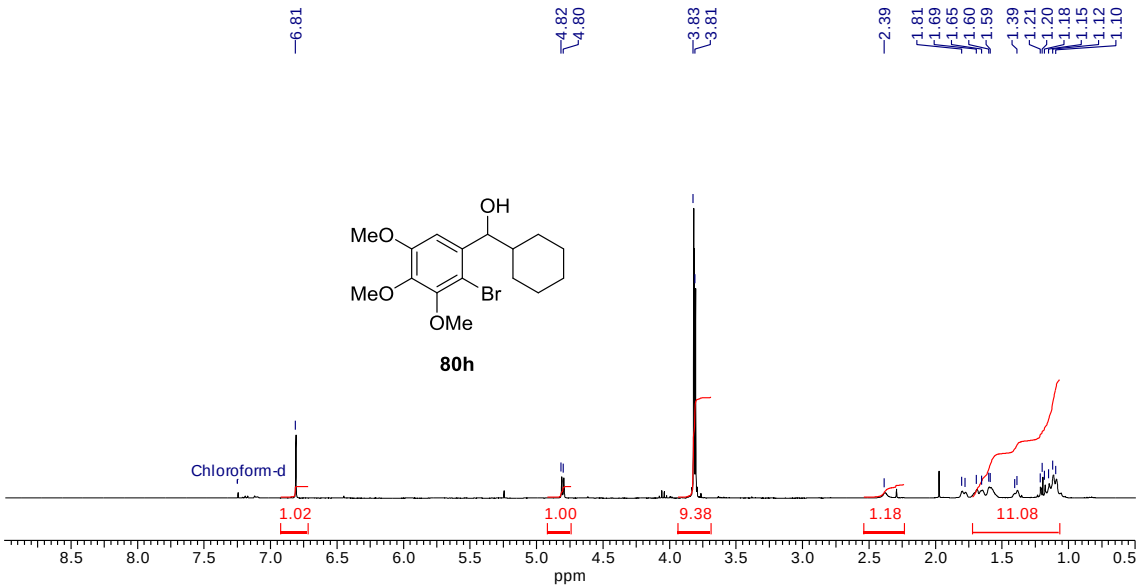


Figure I.16.1: ^{1}H-NMR (400 MHz) spectrum of **80h** in $CDCl_3$

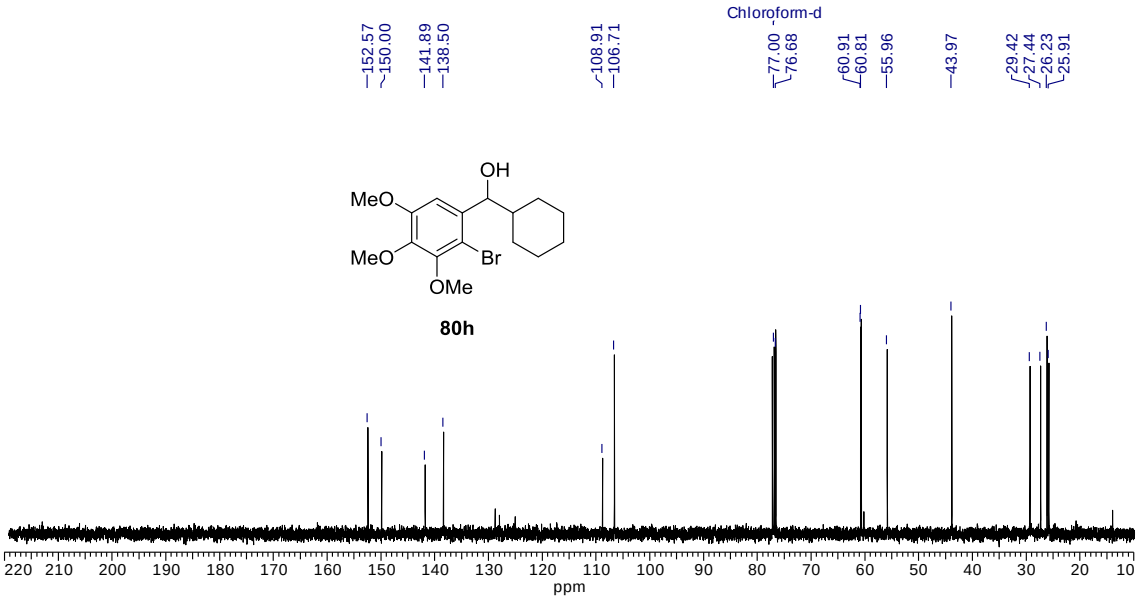


Figure I.16.2: ^{13}C-NMR (100 MHz) spectrum of **80h** in $CDCl_3$

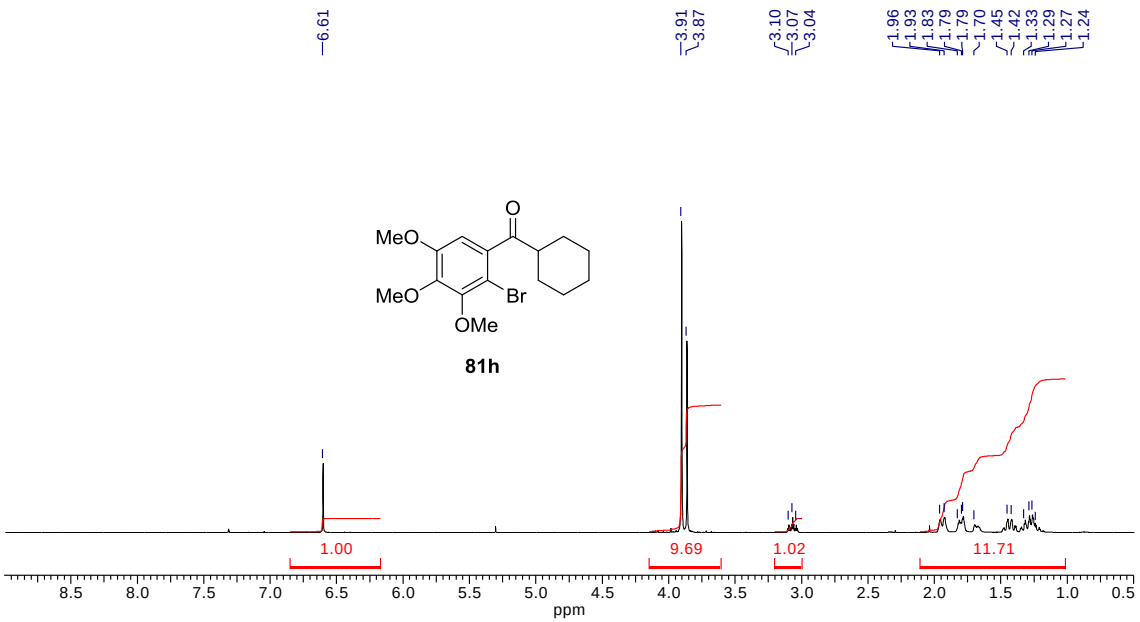


Figure I.16.1: ^{1}H-NMR (400 MHz) spectrum of **81h** in $CDCl_3$

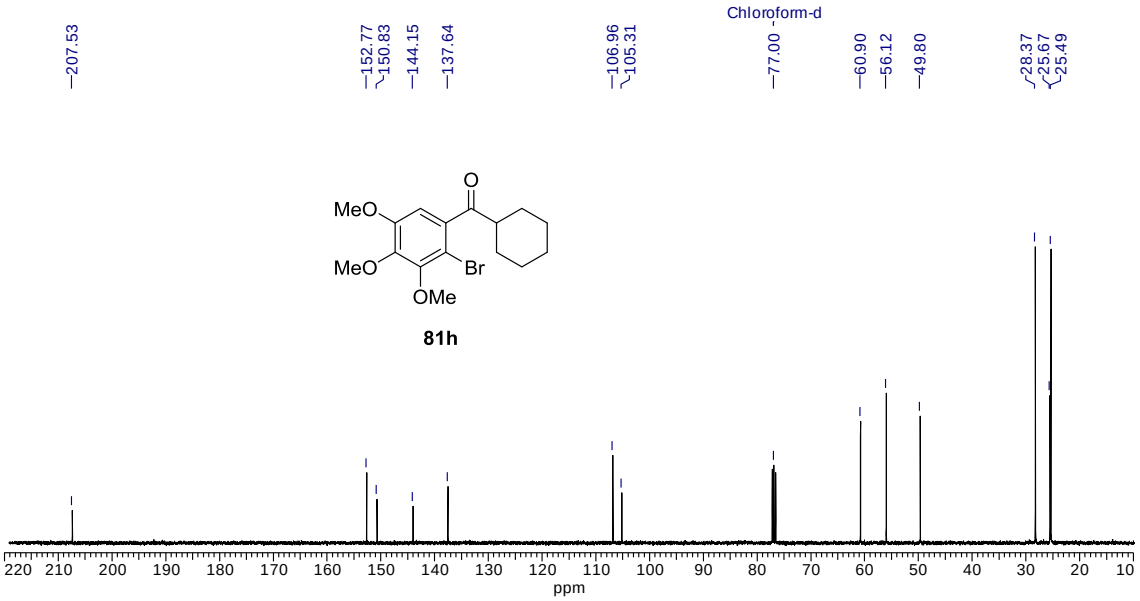


Figure I.16.2: ^{13}C-NMR (100 MHz) spectrum of **81h** in $CDCl_3$

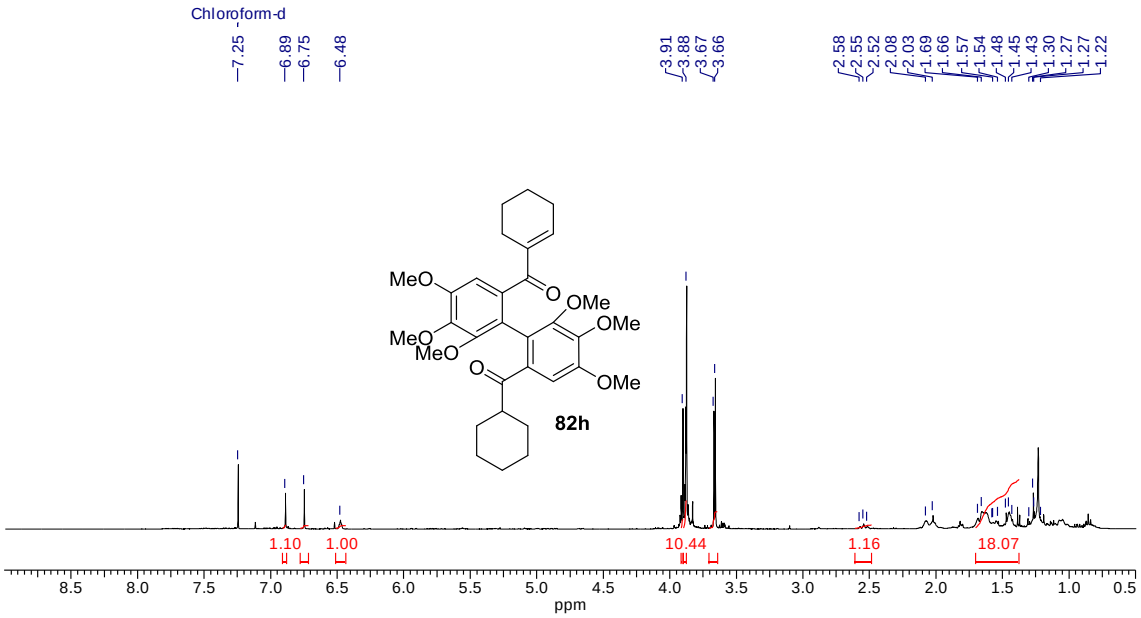


Figure I.16.1: ^{1}H-NMR (400 MHz) spectrum of **82h** in $CDCl_3$

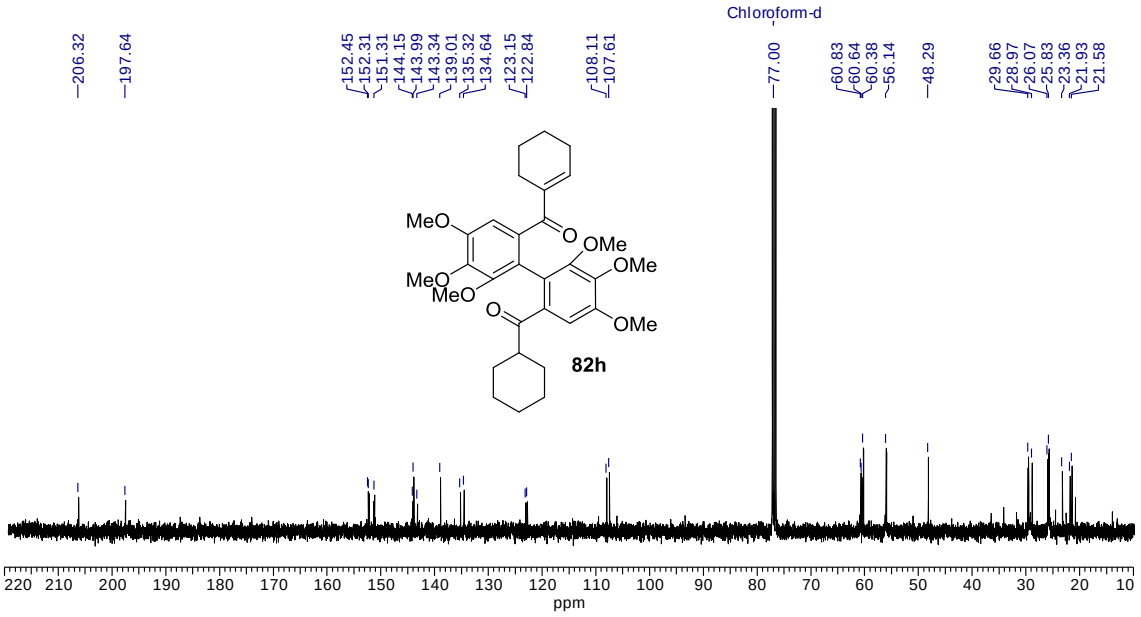


Figure I.16.2: ^{13}C-NMR (100 MHz) spectrum of **82h** in $CDCl_3$

CHAPTER II

SYNTHESIS OF β-ARYL ALLYLIC ALCOHOLS AND SEQUENTIAL DOMINO PROCESS TO 1,3–DIHYDRO ISOBENZOFURANS THROUGH [Pd]-CATALYSIS

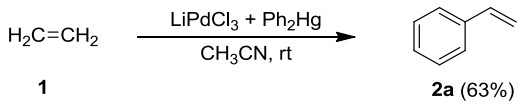
II.1 INTRODUCTION:

Transition-metal mediated reactions are potent synthetic tools for the construction of natural products of biological significance or for building different analogues containing the fundamental core of natural products. These transition metals help in complexness with the reactants to bring organic molecules proximally closer and in turn help in the formation of C-C, C-O and C-N bonds through cross-coupling

reactions, which otherwise which are very difficult to be constructed by various classical methods. Amongst the various transition metals available, Pd-catalyzed transformations play a key role in affording various functionally advanced materials, fluorescent compounds, pharmaceutical lead molecules and other high-value commercial products.[44] In particular, [Pd]-catalyzed approaches are highly valued for their utility in the construction of C-C and C-heteroatom bonds in the field of synthetic organic chemistry. Palladium is known to catalyze numerous cross-coupling reactions, in this context, notable [Pd]-catalyzed cross coupling reactions are Heck,[45] Stille,[46] Suzuki,[47] Sonogashira,[48] Buckwald-Hartwig,[49] Mizoroki-Heck[50] and Jeffery-Heck.[51] Efficiency in delivering the desired products, reducing the formation of non-toxic by-products and the wide functional group tolerance makes transition-metals extremely useful in synthetic organic chemistry.

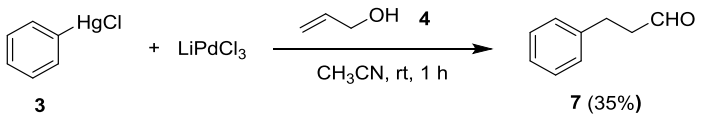
II.2 BACKGROUND:

[Pd]-mediated oxidative coupling reactions have been known since 1960's. In 1968, Heck reported cross coupling reactions of olefins with diphenyl-mercury. In the catalytic cycle, initially, the aryl-palladium-halide species were generated in-situ by the reaction of the catalyst $LiPdCl_3$ with diphenyl-mercury, which upon reacting with ethylene gas **1** gave the styrene product **2a** (Scheme II.1).[52]



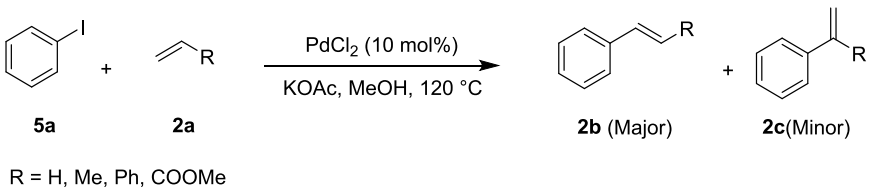
Scheme II.1

Subsequently, in the same year (1968), coupling of phenyl-mercury salt **3** with allylic alcohol **4** in the presence of [Pd]-catalyst was reported by Heck. Interestingly, in this case, unlike the reaction with isolated olefins, it produced the β-phenyl propanaldehyde **7** as the end product, albeit in poor yield (Scheme II.2).[53]



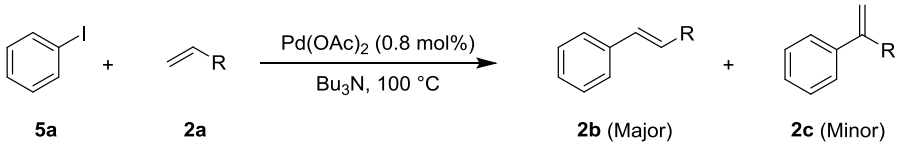
Scheme II.2

Interestingly, as a subsequent development to the Heck coupling, in the year 1971 Mizoroki first reported [Pd]-catalyzed cross coupling of iodobenzene **5a** with olefins **2a** for the formation of styrenes **2b** and **2c** using catalytic amount of palladium chloride and in the presence of base KOAc in methanol (Scheme II.3).[54]



Scheme II.3

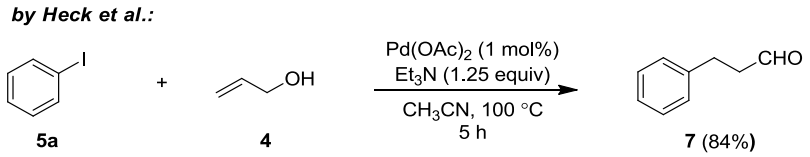
One year later, in 1972, Heck reported an optimized and improved condition to the coupling reaction developed by Mizoroki, for the coupling of iodobenzene **5a** with olefins **2a** by employing $Pd(OAc)_2$ and Bu_3N (Scheme II.4).[55]



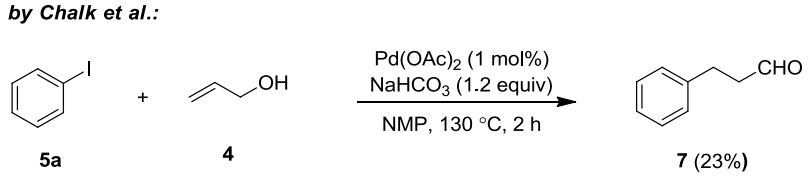
Scheme II.4

Later, in the year 1976, Heck[56] (Schemes II.5) and Chalk[57] (Scheme II.6) independently and at the same time demonstrated that aryl palladium halide can be obtained by using aryl halide **5a** and catalytic amount of a palladium catalyst, instead of using stoichiometric amounts of mercury salts. Interestingly, the coupling using aryl

halide **5a** furnished the carbonyl compounds **7** with improved yield, under the conditions developed by Heck.

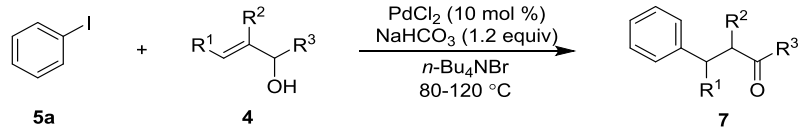


Scheme II.5



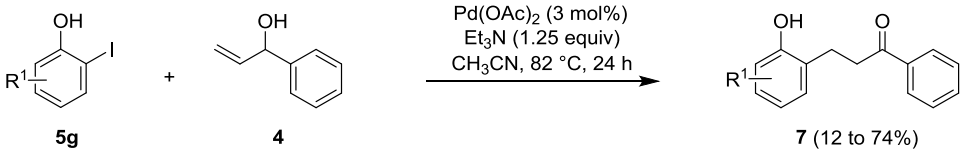
Scheme II.6

Muzart and co-workers had also demonstrated an approach for the synthesis of β-aryl ketones **7** from allylic alcohols **4** (Scheme II.7). In this reaction, the Heck arylation of allylic alcohols **4** was carried out in molten salts without using any solvents and ligands.[58]



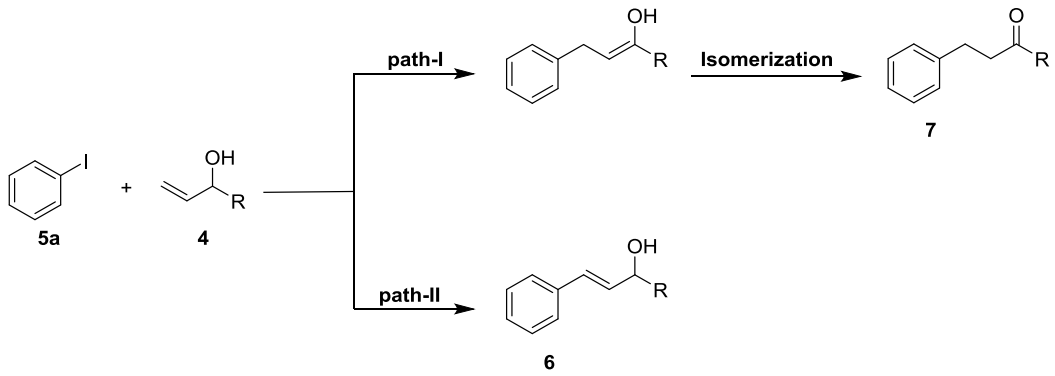
Scheme II.7

The research groups of Wagner and Mioskowski developed a [Pd]-mediated synthesis of dihydrochalcones **7** using allylic alcohols **4** and aryl iodide **5g** as coupling partners (Scheme II.8).[59]



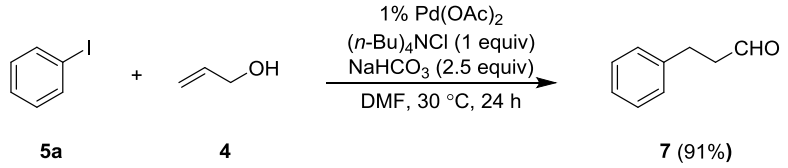
Scheme II.8

Normally, the Heck reaction is carried out at elevated temperatures. Therefore, Jeffery developed a mild catalytic method for the arylation of allylic alcohols **4** which led to the formation of either β-aryl carbonyls **7** or β-aryl allylic alcohols **6** based on the conditions employed at low temperature range (Scheme II.9).[51]

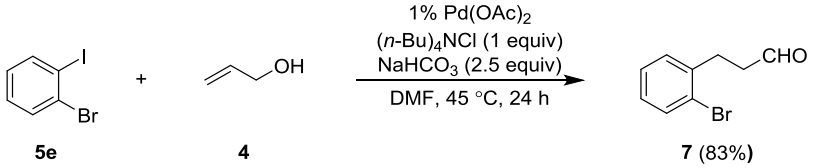


Scheme II.9

Jeffery used stoichiometric amount of phase transfer reagent *n*-Bu_4NCl as an additive. These reagents allow the reaction to proceed near to the room temperature and direct the formation of selective β-aryl carbonyl compounds **7** (Scheme II.10).[60] Therefore, this reaction was named as Jeffery-Heck reaction. In the case of 1-bromo-2-iodobenzene **5e**, under traditional Jeffery's conditions, relatively more reactive iodo substituent reacted selectively with allylic alcohol **4** than the bromo one (Scheme II.11).[61]

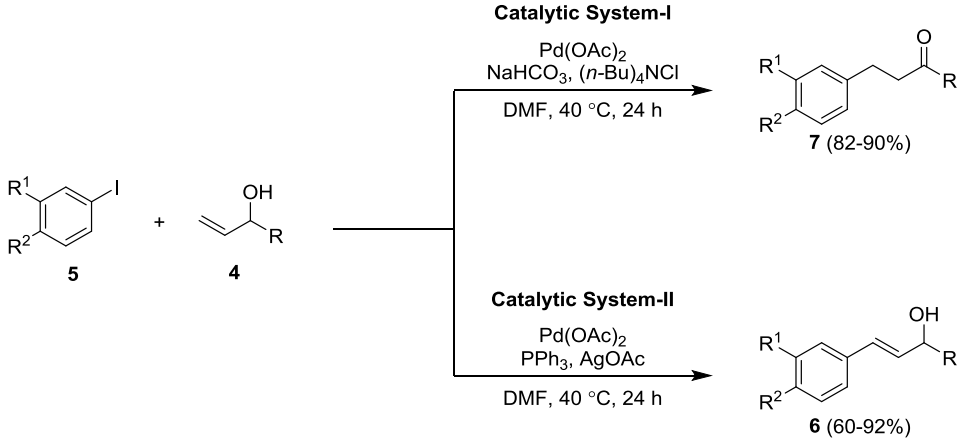


Scheme II.10



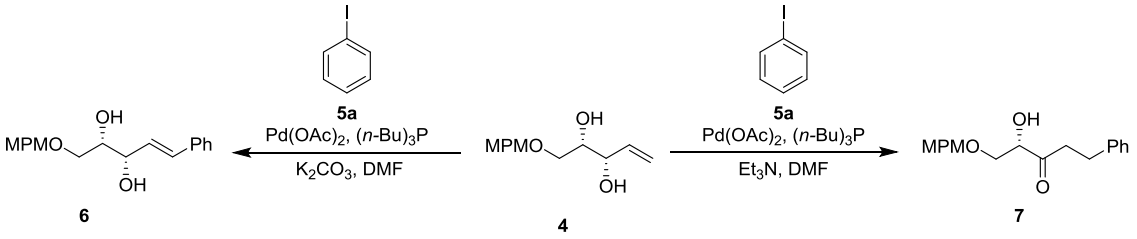
Scheme II.11

In our quest for the synthesis of β-aryl allylic alcohol **6**, the research group of Jeffery extensively investigated on the Heck reaction. As a result, in 1991, Jeffery discovered a new catalytic system for the coupling of aryl iodide **5** with allylic alcohols **4** using silver salts (AgOAc or Ag_2CO_3) as additives to the traditional Jeffery conditions, which selectively furnished the β-aryl allylic alcohols **6** by preventing the subsequent C-C double bond isomerization (Scheme II.12).[62]

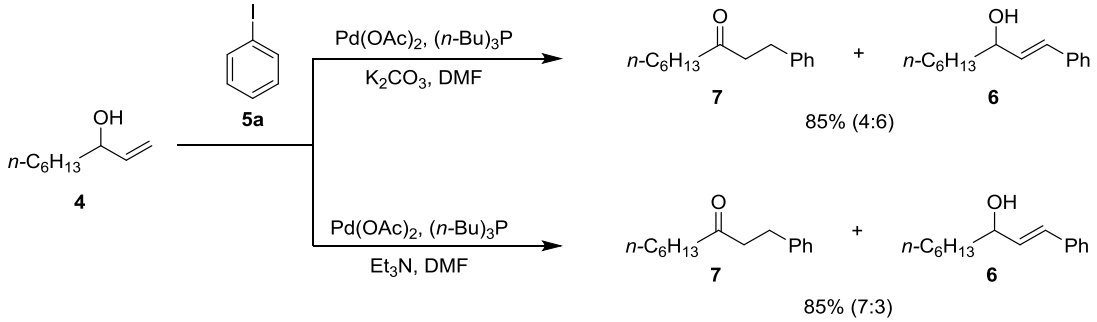


Scheme II.12

S-K Kang et al. reported the cross coupling between iodobenzene **5a** and allylic diols **4** using $Pd(OAc)_2$/*n*-Bu_3P as the catalytic system. When Et_3N was used as a base, furnished phenyl-substituted hydroxy ketone **7**, whereas, the reaction with K_2CO_3, gave phenyl substituted allylic diol **7** (Scheme II.13). This selectivity is attributed to the chelation of β-hydroxy group with palladium metal. The necessity and the role of hydroxyl group at β-position are proved by performing the reaction on the substrate without β-hydroxyl group, which furnished two isomeric products (Scheme II.14).[63]



Scheme II.13



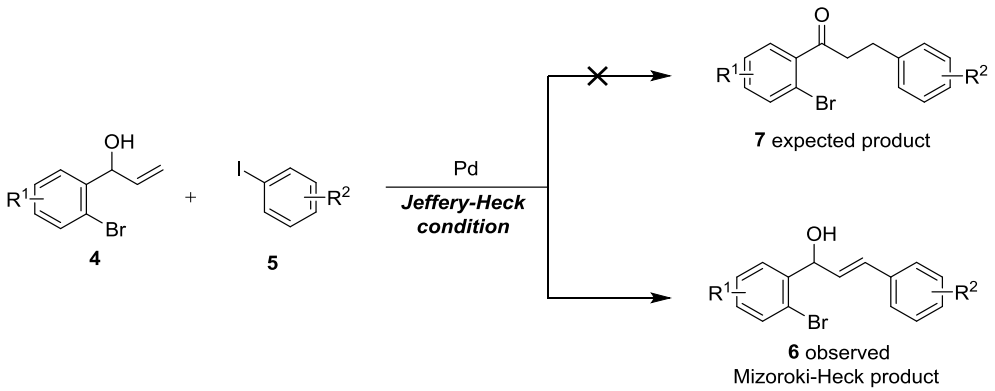
Scheme II.14

II.*3. RESULTS AND DISCUSSION*:

II.3.1.Synthesis of β-aryl allylic alcohols via [Pd]-catalysis:

In continuation of our research interest on [Pd]-catalysis, it was envisioned that the targeted dihydrochalcones **7** could be achieved by employing [Pd]-catalyzed cross-

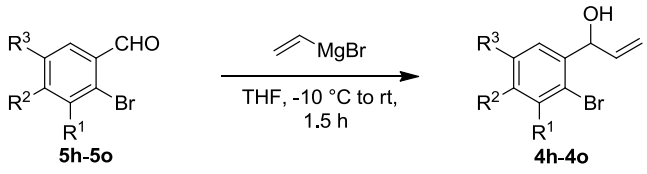
coupling of aryl halides **5** with allylic alcohols **4** under traditional Jeffery-Heck conditions (Scheme II.15**)**.[60]

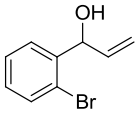
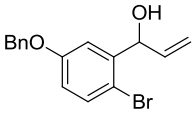
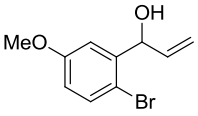
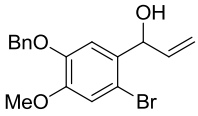
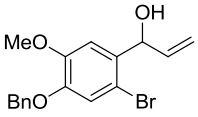
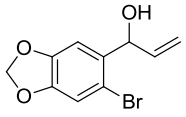
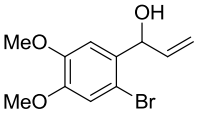
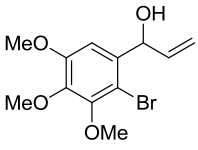


Scheme II.15

Thus, the synthetic study was initiated with the bromination of benzaldehydes under reported conditions.[42] The required allylic alcohols **4h-4o** were synthesized by using the standard vinylmagnesium bromide addition to 2-bromobenzaldehydes **5h-5o**. The corresponding secondary allylic alcohols **4h-4o** were obtained in very good to excellent yields (80–94%), as described in Table II.1.[64]

Table II.1: Synthesis of *ortho*-bromo aryl allylic alcohols **4h-4o** from 2-bromo benzaldehydes **5h-5o.**



 **4h** (80%)	 **4i** (88%)	 **4j** (92%)	 **4k** (85%)
 **4l** (80%)	 **4m** (80%)	 **4n** (94%)	 **4o** (90%)

Reaction conditions: [a]All the reactions carried out with 2-bromobenzaldehydes **5h-5o** 10 mmol, 0.5 M in THF. [b]Isolated yields of chromatographically pure products.

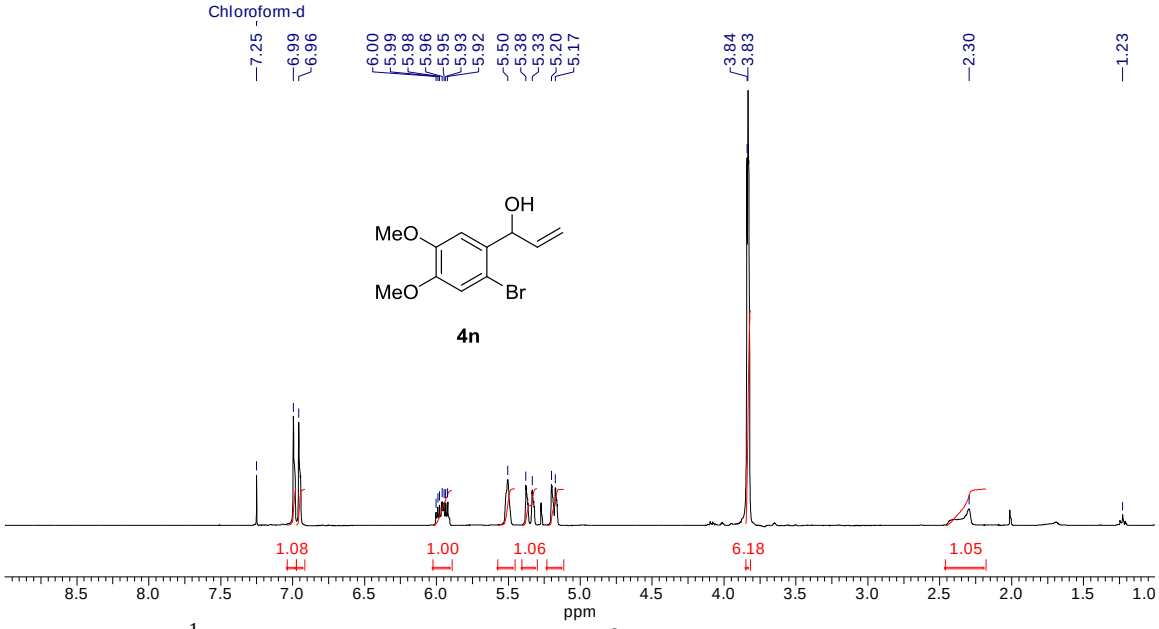


Figure II.1.1: ^{1}H-NMR (400 MHz) spectrum of **4n** in $CDCl_3$

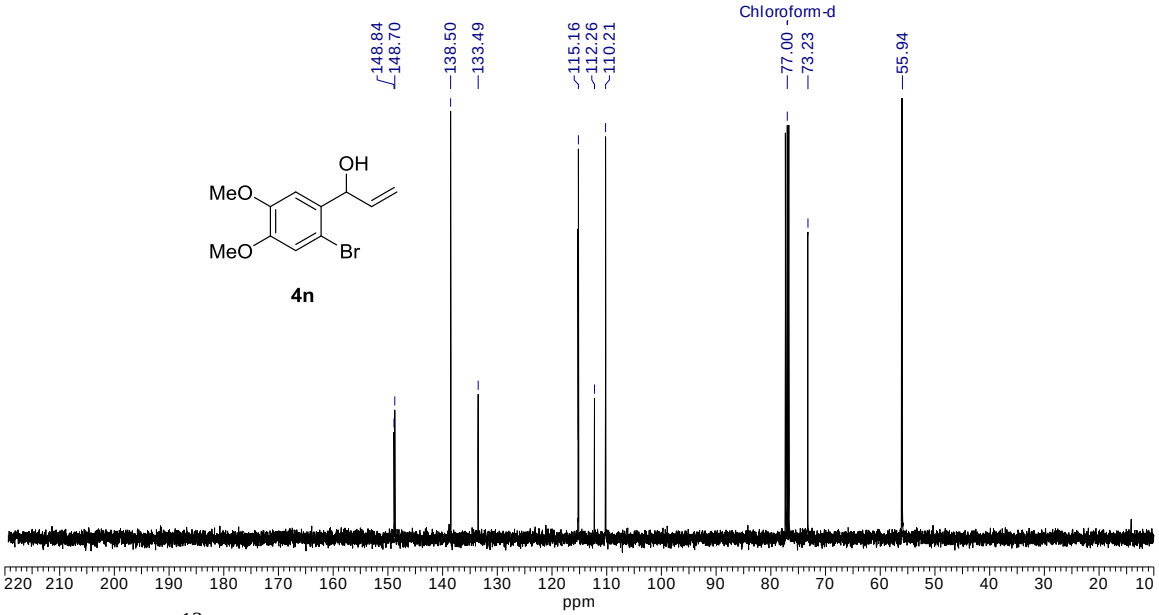


Figure II.1.2: ^{13}C-NMR (100 MHz) spectrum of **4n** in $CDCl_3$

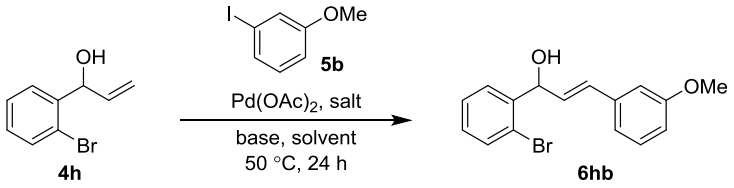
The structure of *ortho*-bromo aryl allylic alcohols **4n** was confirmed from the spectral data analysis. IR spectra shows the absence of the absorption band due to carbonyl stretching of CHO group and the presence of broad absorption band due to OH stretching at 3451 cm^{-1}. In the ^{1}H-NMR spectrum (Figure II.1.1), the presence of two individual singlets at δ 6.99 and 6.96 was due to two aromatic protons, the presence of doublet of a doublet of doublets at δ 5.96 having *J*=15.6, 10.3 and 5.4 Hz was due to olefinic methine group proton, the presence of doublet at δ 5.50 having *J*=5.4 Hz was due to C*H*OH group proton, the presence of doublet at δ 5.35 having coupling constant J_{trans}=15.6 Hz and one more doublet at δ 5.18 having coupling constant J_{cis}=10.8 Hz were due to olefinic methylene group two protons, δ 3.84 due to methoxy group three protons, δ 3.83 due to methoxy group three protons and the presence of broad singlet at δ 2.30 ppm was due OH group proton, elucidated the structure of *ortho*-bromo aryl allylic alcohols **4n**. In addition, the 11 signals appeared in ^{13}C-NMR spectrum (Figure II.1.2) in which four quaternary carbon resonates at δ 148.8, 148.7, 133.5 and 112.3 due to four aromatic carbons, three methine carbons at δ 138.5, 115.1 and 110.2 due to two aromatic methine carbons and one olefinic methine carbon, the presence of olefinic methylene carbon resonates at δ 115.2, the presence of δ 73.3 ppm was due to CHOH group carbon, the presence of δ 56.1 and 55.9 ppm were due to two methoxy group carbons, confirmed the structure of *ortho*-bromo aryl allylic alcohols **4n**. The presence of the $[M+Na]^+$ peak at m/z $[C_{11}H_{13}BrNaO_3]^+$=294.9941 in the mass spectrum further established the structure **4n**.

Now with the allylic alcohols **4h** in hand, the [Pd]-catalysis was carried out between 3-iodoanisole **5b** and the allylic alcohol **4h**. The reaction was performed under typical Jeffery-Heck conditions. To our surprise, exclusively β-aryl allylic alcohol **6hb** was isolated rather than the expected β-aryl carbonyl compound **7hb**.[9b] After careful study of the literature, we realized that the usual Heck followed by double bond isomerization to give the carbonyl compounds was observed for those substrates having no *ortho*-substituents on the aromatic ring of the allylic alcohols.[17] Therefore, from the

present study, it was thought that the bromo substituent at the *ortho*-position on the aromatic moiety of the allylic alcohol plays a major role to confine the rotation around C-C bond of the PdCH−CH(OH)Ar intermediate. The reason for the restricted rotation of the Pd-intermediate around the C-C bond may be due to the more bulky nature of *ortho*-bromoaryl moiety of the allylic alcohol and thus suppresses the formation of enol via the double isomerization. As a result, the reaction impeded after Mizoroki-Heck coupling and furnished β-aryl allylic alcohol **6hb**.

To further optimize the reaction, it was investigated under different conditions and the results are as summarized in Table II.2. Initially, the reaction explored the allylic alcohol **4h** and 3-iodoanisole **5b**. Thus, reaction in the presence of $Pd(OAc)_2$ catalyst, base $NaHCO_3$ and $Bn(Et)_3NCl$ as phase transfer reagent as an additive, in DMF as solvent at 50 °C, gave the β-aryl allylic alcohol **6hb** in fair yield (67%, Table II.2, entry 1). Replacing $Bn(Et)_3NCl$ with TBAI, the desired product **6hb** was obtained in poor yield (33%, Table II.2, entry 2). While changing the base to K_2CO_3 in the présence of TBAI and keeping other reaction parameters constant, furnished the product **6hb** in moderate yield (51%, Table II.2, entry 3). Switching the solvents to toluene/acetonitrile, in the presence of bases K_2CO_3/$NaHCO_3$ and with the quaternary ammonium salts TBAI/TBAB produced the product **6hb** in poor to moderate yields (Table II.2, entries 4 to 8,). Interestingly, switching the bases to Cs_2CO_3/K_2CO_3 in the presence of $Bn(Et)_3NCl$ in CH_3CN, gave the product **6hb** in good yields (Table II.2, entries 9 and 10). On the other hand, the reaction in the presence of strong base Cs_2CO_3 with TBAI in CH_3CN furnished the product **6hb** in moderate yields (51%, Table II.2, entry 11). Gratifyingly, the product **6hb** yield was improved with the base $NaHCO_3$ in the presence of $Bn(Et)_3NCl$ in solvent CH_3CN (80%, Table II.2, entry 12).

Table II.2: Optimization table for the synthesis of β-aryl allylic alcohol **6hb**.



Entry[a]	Base (2 equiv)	Salt (1 equiv)	Solvent (2 mL)	Yield of 6hb (%)[b]
1.	$NaHCO_3$	$Bn(Et)_3NCl$	DMF	67
2.	$NaHCO_3$	TBAI	DMF	33
3.	K_2CO_3	TBAI	DMF	51
4.	$NaHCO_3$	TBAI	toluene	33
5.	K_2CO_3	TBABr	toluene	50
6.	$NaHCO_3$	$Bn(Et)_3NCl$	toluene	55
7.	$NaHCO_3$	TBAI	acetonitrile	39
8.	$NaHCO_3$	TBABr	acetonitrile	30
9.	Cs_2CO_3	$Bn(Et)_3NCl$	acetonitrile	70
10.	K_2CO_3	$Bn(Et)_3NCl$	acetonitrile	67
11.	Cs_2CO_3	TBAI	acetonitrile	51
12.	**$NaHCO_3$**	**$Bn(Et)_3NCl$**	**acetonitrile**	**80**

[a]All reactions were carried out with $Pd(OAc)_2$ (5 mol%), $NaHCO_3$ (2 equiv), $Bn(Et)_3NCl$ (1 equiv) under nitrogen atmosphere. [b]Isolated yields of chromatographically pure products; for compounds **6hb**, the first alphabet letter refers to the allylic alcohol part (**4h**) whereas the second letter indicates the aromatic ring coming from the aryl iodide **5b**.

Microwave reactors have helped to decrease the reaction time required for many organic transformations. Also, it was proved in some cases that the yield of the products improved.[65] Therefore, in addition to the conventional conditions, we became interested to apply microwave assisted conditions to the above developed reaction. Gratifyingly, the palladium catalysed reaction amenable under microwave irradiation as well (closed vessel, power: 250 W, temperature: 50 °C). The reactions were completed in much shorter reaction times (1.5 h) at 50 °C and afforded the desired β-aryl allylic alcohol

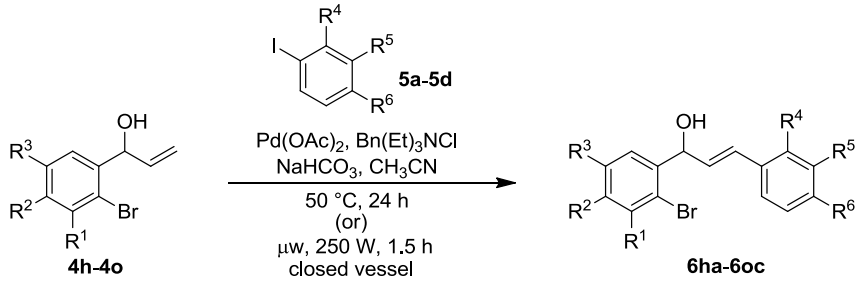
6hb with comparable yields to that of the conventional one (i.e., for 24 h at 50 °C in an oil bath).

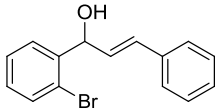
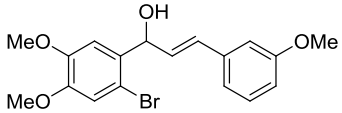
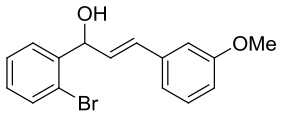
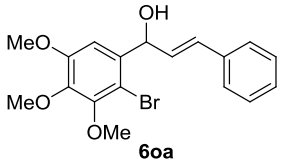
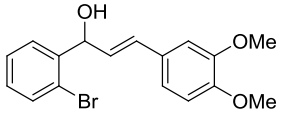
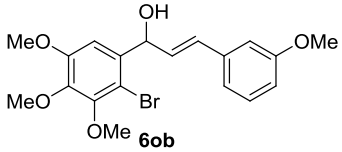
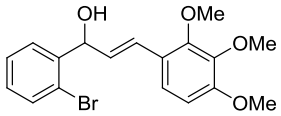
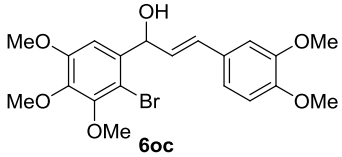
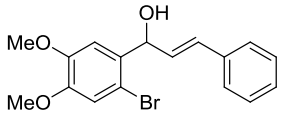
Now with the optimized conditions for the synthesis of β-aryl allylic alcohols **6hb** in hand, we next aimed to check the scope and limitations of the method by performing the reaction on other systems as well. Thus, the optimized conditions were applied to different aryl iodides **5a**-**5d** in conjunction with allylic alcohols **4h**-**4o**. Interestingly, the method was quite successful on a variety of aryl iodides **5a**-**5d** in combination with allylic alcohols **4h**-**4o**, and furnished the corresponding products **6ha**-**6oc** in fair to very good yields using conventional conditions (60 to 84%, Table II.3). Also, it was found that the reaction was amenable under microwave irradiation conditions and delivered the products **6ha**-**6oc** in comparable yields to that of the conventional one (56 to 86%, Table II.3).

The structure of β-aryl allylic alcohol **6hb** was further confirmed by IR and NMR data analysis. The presence of broad absorption band at 3475 cm^{-1} because of OH stretching in the IR spectrum indicated the formation of the β-aryl allylic alcohol **6hb**. In the ^{1}H-NMR spectrum (Figure II.2.1), the presence of doublet of a doublet at δ 7.60 having *J*=7.8 and 1.5 Hz was due to one aromatic proton, doublet of a doublet at δ 7.55 having *J*=7.8 and 1.5 Hz was due to one aromatic proton, doublet of doublet of doublets at δ 7.34 having *J*=7.8, 7.3 and 1.0 Hz was due to one aromatic proton, doublet of a doublet at δ 7.22 having *J*=7.8 and 7.8 Hz was due to one aromatic proton, doublet of a doublet of doublet at δ 7.15 having *J*=7.8, 7.3 and 2.0 Hz was due to one aromatic proton, doublet at δ 6.98 having *J*=7.8 Hz was due to one aromatic proton, doublet of a doublet at δ 6.92 having *J*=2.0 and 2.0 Hz was due to one aromatic proton, doublet of a doublet at δ 6.80 having *J*=7.8 and 2.0 Hz was due to one aromatic proton, the presence of doublet at δ 6.71 having coupling constant J_{trans}=16.1 Hz was due to olefinic methine group, the presence of doublet of a doublet at δ 6.32 having J_{trans}=16.1 Hz and *J*=5.8 Hz was due to olefinic methine group proton, doublet at δ 5.76 having coupling constant *J*=5.8 Hz due to C*H*OH group proton, singlet at δ 3.79 due to Ar-OCH_3 group three

protons and broad singlet at δ 2.56 ppm was due to due to hydroxyl proton, elucidated the structure of allylic alcohol **6hb**.

Table II.3: [Pd]-catalyzed reaction of allylic alcohol **4h-4o** with aryl iodides **5a-5d** to give β-aryl allylic alcohol **6ha-6oc**.



Entry[a]	β-aryl allylic alcohol-6	Yield (%)[b]	Entry[a]	β-aryl allylic alcohol-6	Yield (%)[b]
1.	 **6ha**	Δ (82) *μw* (86)	6.	 **6nb**	Δ (73) *μw* (68)
2.	 **6hb**	Δ (80) *μw* (81)	7.	 **6oa**	Δ (84) *μw* (77)
3.	 **6hc**	Δ (72) *μw* (68)	8.	 **6ob**	Δ (77) *μw* (82)
4.	 **6hd**	Δ (60) *μw* (56)	9.	 **6oc**	Δ (61) *μw* (65)
5.	 **6na**	Δ (85) *μw* (79)			

[a]Reaction conditions: All the reactions carried out with allylic alcohol **4h-4o** (60-100 mg, 0.20 to 0.47 mmol), in CH_3CN. [b]Yields in the parentheses are isolated yields of chromatographically pure products.

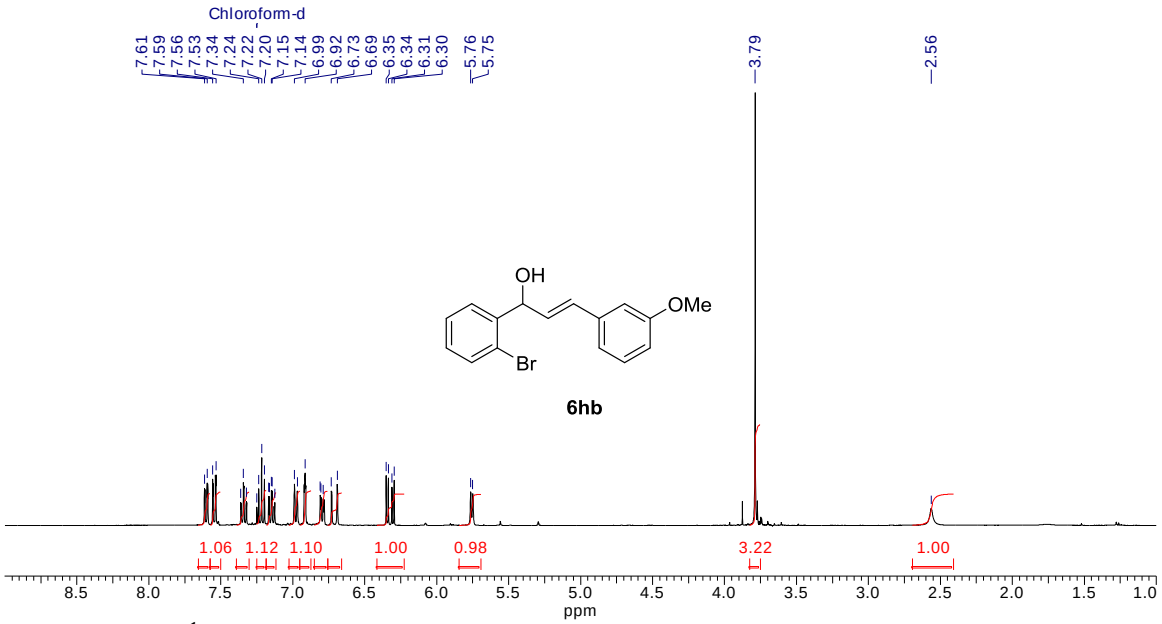


Figure II.2.1: ^{1}H-NMR (400 MHz) spectrum of **6hb** in $CDCl_3$

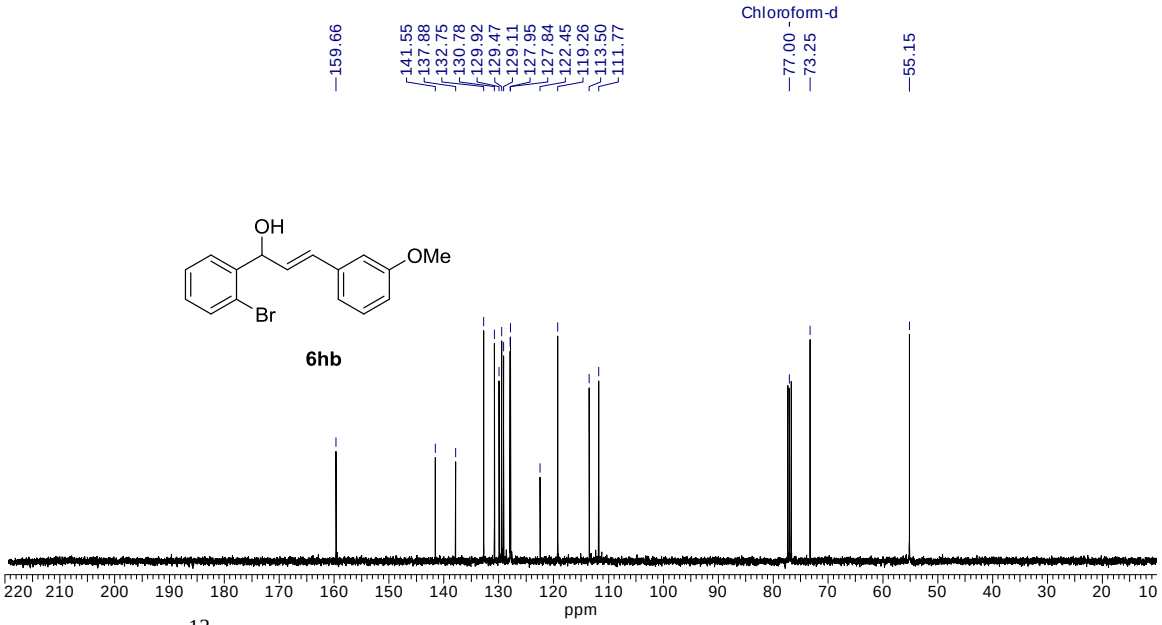


Figure II.2.2: ^{13}C-NMR (100 MHz) spectrum of **6hb** in $CDCl_3$

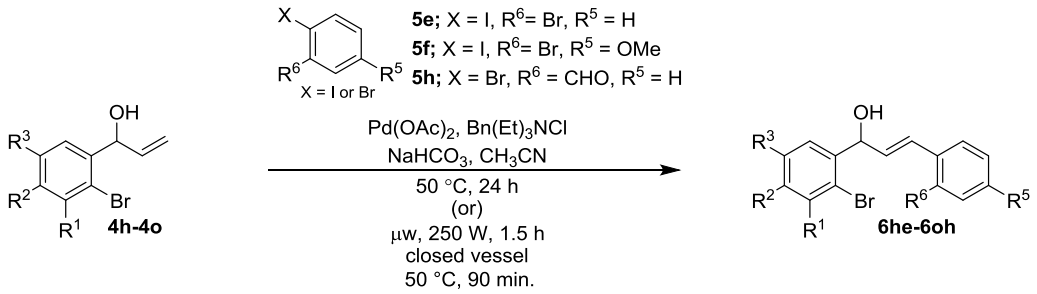
In addition to it, 16 signals appeared in ^{13}C-NMR spectrum (Figure II.2.2), in which four quaternary carbons resonates at δ 159.7, 141.5, 137.9 and 122.4 were due to four aromatic carbons, the presence of 10 methine carbons at δ 132.7, 130.8, 129.9, 129.5, 129.1, 127.9, 127.8, 119.3, 113.5 and 111.8 were due to eight aromatic methine carbons and two olefinic methine carbons, δ 73.2 was due to CH(OH) group carbon and δ 55.1 ppm was due to Ar-OCH_3 group carbon, confirmed the structure of allylic alcohol **6hb**. The presence of the $[M+Na]^+$ peak at m/z $[C_{16}H_{15}BrNaO_2]^+$=341.0153. In the mass spectral data further confirmed the structure of β-aryl allylic alcohol **6hb**.

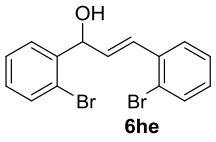
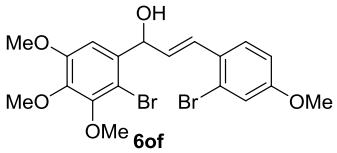
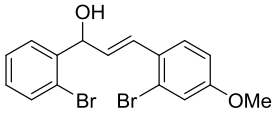
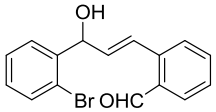
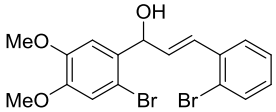
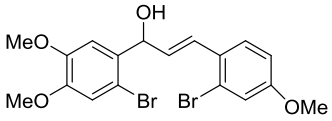
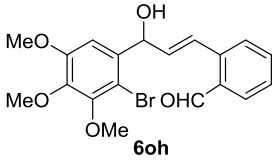
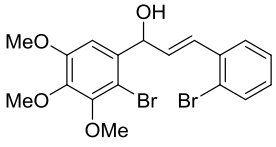
After successful accomplishment of β-aryl allylic alcohols **6ha**-**6oc**, to show the generality and applicability of the method, we further explored the reaction with 1-bromo-2-iodobenzenes **5e**-**5f** as coupling partners to the allylic alcohols **4h**-**4o**. The optimized reaction conditions were implemented on 1-bromo-2-iodobenzenes **5e**-**5f** as coupling partners to the allylic alcohols **4** to obtain β-aryl allylic alcohols **6**. Quite interestingly, the reaction was successful and furnished the desired β-aryl allylic alcohols **6he**-**6of** (Table II.4). Notably, in the present case the reaction was undertaken in a highly selective manner by making use of more reactive iodo substituent without effecting the bromo one (Table II.4).

To make the method more interesting, we were fascinated to employ the reaction on 2-bromobenzaldehyde **5h** as a coupling partner to that of allylic alcohols **4**, in which we envisioned the preferential reactivity of bromo substituent of 2-bromobenzaldehyde **5h** over the other bromo substituent of the allylic alcohol partner **4**. Because, the bromo substituent on the electron deficient aromatic ring would be more reactive than that connected to a relatively more electron rich aromatic ring. Gratifyingly, the reaction under standard conditions was amenable and products **6hh**-**6oh** were obtained in good yields as summarized in Table II.4. As anticipated, the bromo substituent of 2-bromobenzaldehyde **5h** was more reactive towards the

palladium catalyst and certainly gave the corresponding coupled products **6hh**-**6oh** (Table II.4).

Table II.4: [Pd]-catalyzed reaction of allylic alcohols **4h-4o** with bromo-iodobenzenes **5e**-**5f**, and 2-bromobenzaldehyde **5h** to furnish **6he-6oh**.[a,b]



Entry[a]	β-arylallylic alcohol	Yield (%)[b]	Entry[a]	β-arylallylic alcohol	Yield (%)[b]
1.	 **6he**	Δ (80) *μw* (75)	6.	 **6of**	Δ (58) *μw* (52)
2.	 **6hf**	Δ (40) *μw* (36)	7.	 **6hh**	Δ (59) *μw* (63)
3	 **6ne**	Δ (81) *μw* (80)	8.	 **6nh**	Δ (64) *μw* (60)
4.	 **6nf**	Δ (33) *μw* (29)	9.	 **6oh**	Δ (75) *μw* (76)
5.	 **6oe**	Δ (75) *μw* (77)			

[a]Reaction conditions: All the reactions were carried out with allylic alcohols **4h-4o** (100 mg, 0.33 to 0.56 mmol), in CH_3CN. [b]Yields in the parentheses are isolated yields of chromatographically pure products.

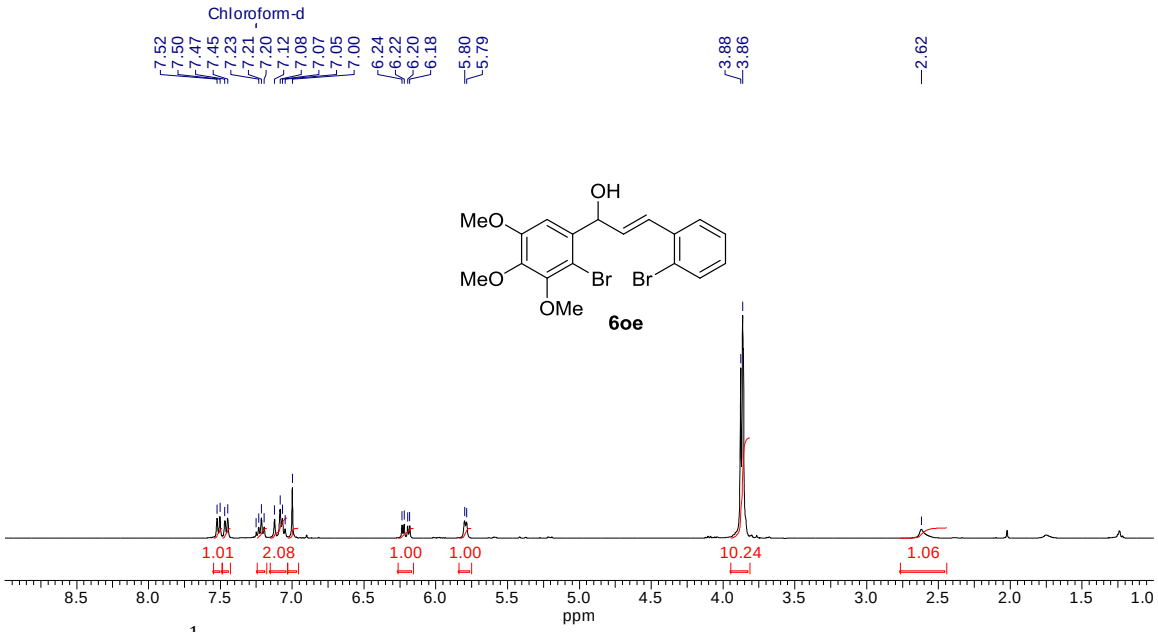


Figure II.3.1: ^{1}H-NMR (400 MHz) spectrum of **6oe** in $CDCl_3$

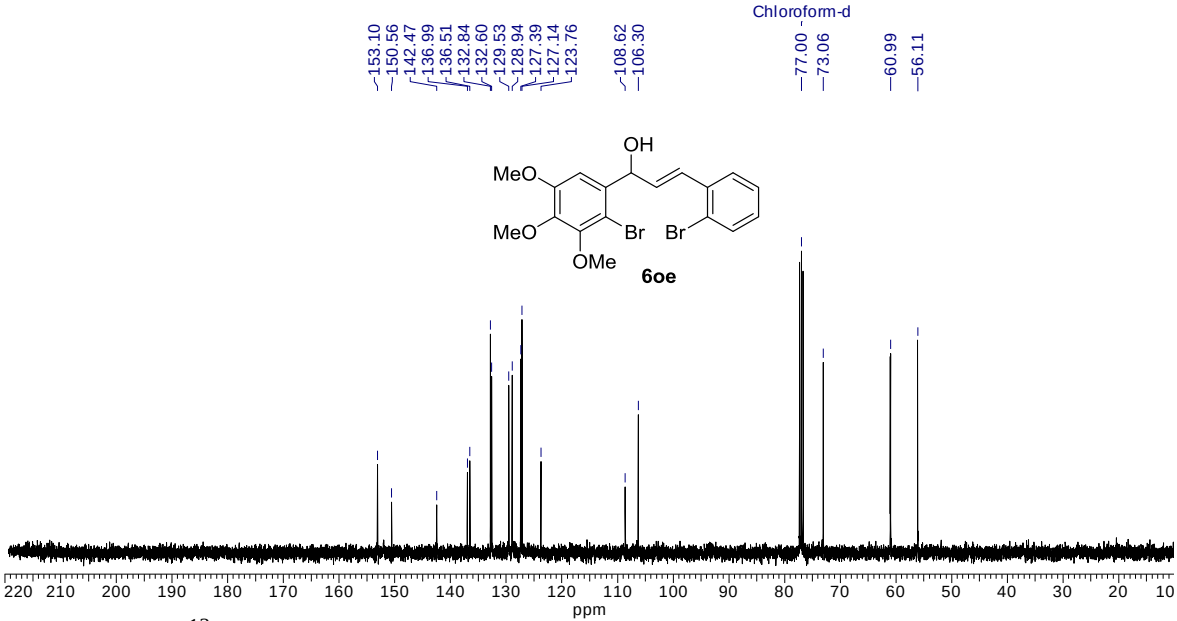


Figure II.3.2: ^{13}C-NMR (100 MHz) spectrum of **6oe** in $CDCl_3$

The structure of β-aryl allylic alcohol **6oe** was further confirmed by IR and NMR data analysis. The presence of broad absorption band at 3448 cm^{-1} because of OH stretching in the IR spectrum indicated the formation of the β-aryl allylic alcohol **6oe**. In the ^{1}H-NMR spectrum (Figure II.3.1), the presence of doublet at δ 7.51 having *J*=7.8 Hz was due to one aromatic proton, doublet at δ 7.46 having *J*=7.8 Hz was due to one aromatic proton, doublet of a doublet at δ 7.21 having *J*=7.5 and 7.5 Hz was due to one aromatic proton, the presence of doublet at δ 7.10 having coupling constant J_{trans}=15.8 Hz was due to olefinic methine group proton, doublet of a doublet at δ 7.07 having *J*=7.5 and 7.5 Hz was due to one aromatic proton, singlet at δ 7.00 due to one aromatic proton, doublet of a doublet at δ 6.21 having J_{trans}=15.8 and 5.5 Hz was due to olefinic methine group proton, doublet at δ 5.80 having *J*=5.5 Hz was due to benzylic methine proton, singlet at δ 3.88 was due to three methoxy protons, singlet at δ 3.86 was due to six protons of two methoxy groups and broad singlet at δ 2.62 ppm was due to OH group proton, elucidated the structure of allylic alcohol **6oe**. In addition to it, 18 signals appeared in ^{13}C-NMR spectrum (Figure II.3.2) in which seven quaternary carbon resonates at δ 153.1, 150.6, 143.5, 137.0, 136.5, 123.8 and 108.6 due to seven aromatic carbons, the presence of seven methine carbons resonates at δ 132.8, 132.6, 129.5, 128.9, 127.4, 127.1 and 106.3 were due to five aromatic methine carbons and two olefinic methine carbons, δ 73.1 was due to CH(OH) group carbon, δ 61.0 was due to $ArOCH_3$ group carbon, δ 60.9 was due to $ArOCH_3$ group carbon and δ 56.1 ppm was due to $ArOCH_3$ group carbon, elucidated the structure of allylic alcohol **6oe**. The presence of the $[M+Na]^+$ peak at m/z $[C_{18}H_{18}Br_2NaO_4]^+$= 478.9464 in the mass spectrum further established the structure of β-aryl allylic alcohol **6oe**.

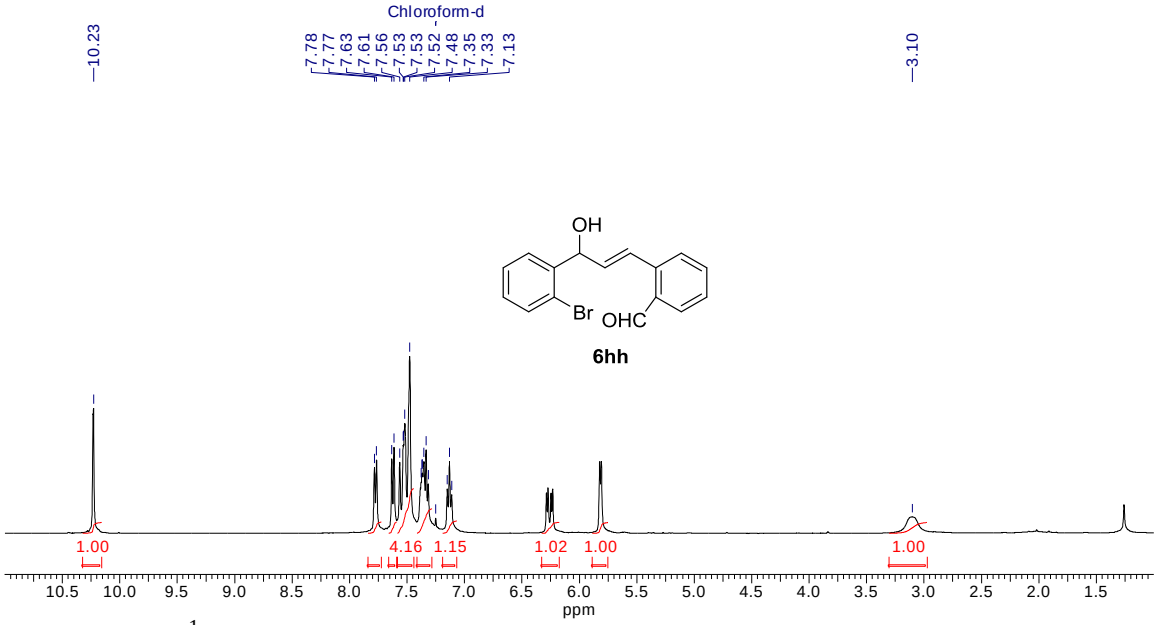


Figure II.4.1: ^{1}H-NMR (400 MHz) spectrum of **6hh** in $CDCl_3$

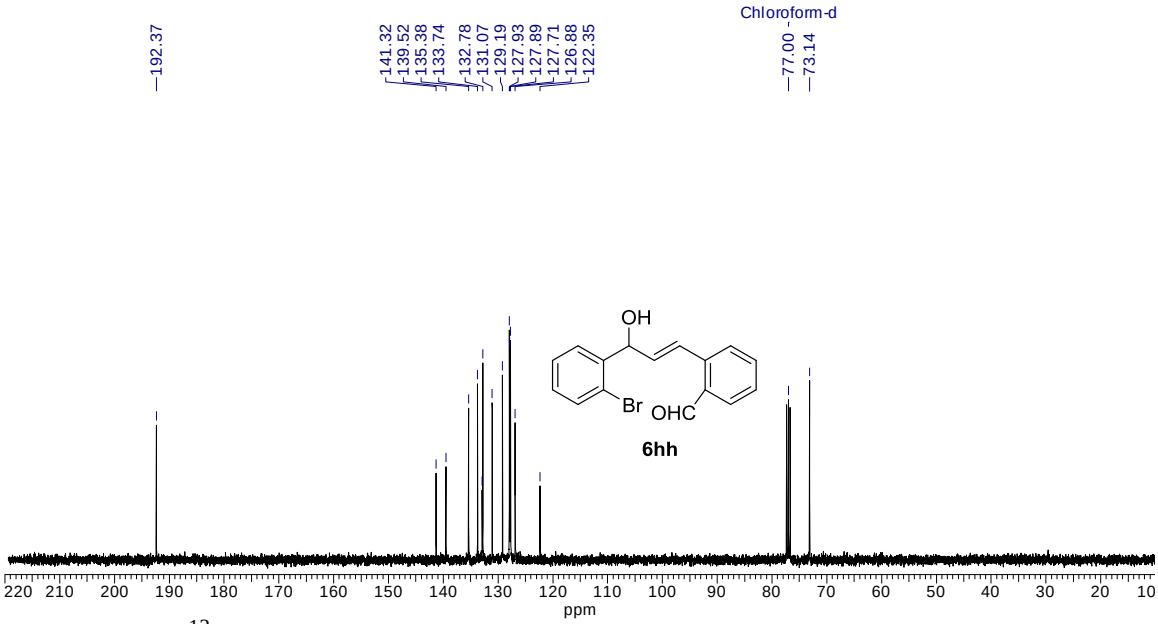


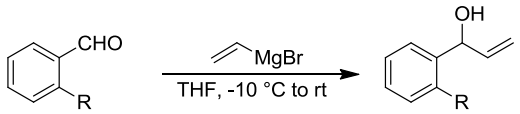
Figure II.4.2: ^{13}C-NMR (100 MHz) spectrum of **6hh** in $CDCl_3$

The structure of β-aryl allylic alcohol **6hh** was further confirmed by IR and NMR data analysis. The presence of strong absorption band in IR spectrum at 1688 cm^{-1} due of the C=O stretch of the aldehyde group and broad absorption band at 3409 cm^{-1} because of OH stretching indicated the formation of the β-aryl allylic alcohol **6hh**. In the ^{1}H-NMR spectrum (Figure II.4.1), the presence of singlet at δ 10.23 was due to CHO group proton, δ 7.77 having *J*=7.5 Hz was due to one aromatic proton, δ 7.62 having *J*=7.8 Hz was due to one aromatic proton, a multiplet in the region δ 7.57–7.27 accounts for the five aromatic protons and one olefinic proton, doublet of a doublet δ 7.13 having *J*=15.0 and 7.5 Hz was due to one aromatic proton, the presence of doublet of a doublet at δ 6.26 having J_{trans}=15.0 and *J*=5.5 Hz was due to olefinic methine group proton, doublet at δ 5.82 having *J*=5.5 Hz was due to benzylic methine proton and broad singlet at δ 3.10 ppm was due to OH group proton, elucidated the structure of β-aryl allylic alcohol **6hh**. In addition to it, 16 signals appeared in ^{13}C-NMR spectrum (Figure II.4.2), at δ 192.4 indicate the presence of C=O group carbon, in which four aromatic quaternary carbon resonates at δ 141.3, 139.5, 132.9 and 122.4, the presence of 10 methine carbons at δ 135.4, 133.7, 132.8, 131.1, 129.2, 127.9, 127.8, 127.7, 127.6 and 126.9 were due to eight aromatic methine carbons and two olefinic methine carbons, and δ 73.1 ppm was due to CH(OH) group carbon, elucidated the structure of β-aryl allylic alcohol **6hh**. The presence of the $[M+Na]^{+}$ peak at m/z $[C_{16}H_{13}BrNaO_2]^{+}$=338.9988 in the mass spectrum further established the structure of β-aryl allylic alcohol **6hh**.

Assuming that the steric hindrance of the substituents at the *ortho* position accounted for the formation of β-aryl allylic alcohols **7** and to probe this hypothesis of *ortho* effect, bromine at *ortho* position was replaced with a methoxy or methyl group. The requisite *ortho*-methoxy/methyl phenyl allylic alcohols **4p/4q** was synthesized by the nucleophilic addition of 1.0 M vinylmagnesium bromide to its corresponding *ortho*-methoxy/methyl benzaldehydes **5p/5q.**[66,67] Addition of vinylmagensium bromide was

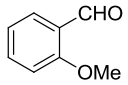
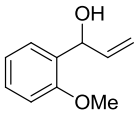
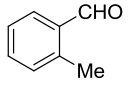
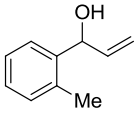
carried out at 0 °C and then slowly allowed to reach rt and stirred for 1.5 h. The secondary allylic alcohols **4p**/**4q** were obtained in excellent yields (90-95%, Table II.5).

Table II.5: Synthesis of 2-methoxy/methyl phenyl allylic alcohols **4p**/**4q** from the corresponding 2-methoxy/methyl benzaldehydes **5p**/**5q**.



5p; R = OMe
5q; R = Me

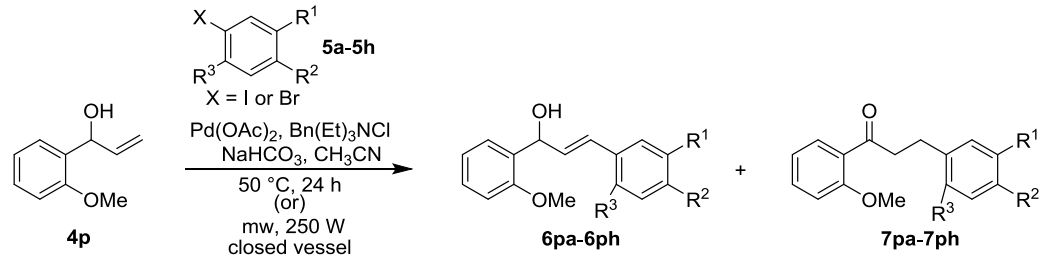
4p; R = OMe
4q; R = Me

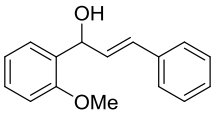
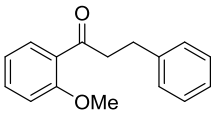
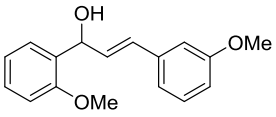
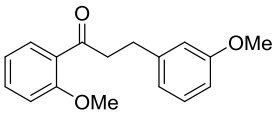
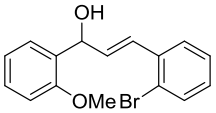
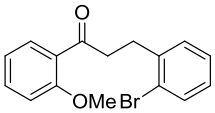
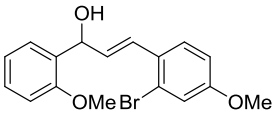
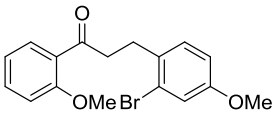
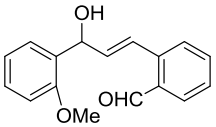
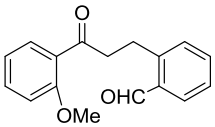
Entry[a]	aldehyde (5)	aryl allyllic alcohol (4)	Yield[b]
1.	 **5p**	 **4p**	90%
2.	 **5q**	 **4q**	95%

[a]Reaction conditions: All the reactions were carried out with 2-methoxy/methyl benzaldehyde **5p**/**5q** 10 mmol, 0.5 M in THF. [b] Isolated yields of chromatographically pure products.

Finally, to better understand the nature of steric and electronic factors that influence the selective formation of β-aryl allylic alcohols **6**, we further performed the reaction by choosing 2-methoxy/methyl benzaldehydes **5p**/**5q** as coupling partners. As expected, the reaction favors the regio- and stereoselective formation of β-aryl allylic alcohols **6** as major products along with the β-aryl carbonyls **7** as minor products (Tables II.6 and II.7). This can be justified based on the relatively smaller size of 2-methoxy/methyl substituents when compared to that of bromo one, that might slightly favors the formation of Jeffery-Heck product.

Table II.6: [Pd]-catalyzed reaction of 1-(2-methoxyphenyl)prop-2-en-1-ol **4p** with iodobenzenes **5a**-**5f**, and 2-bromobenzaldehyde **5h** to furnish β-aryl allylic alcohol **6pa**-**6ph** and β-aryl carbonyls **7pa**-**7ph**.



Entry[a]	β-arylallylic alcohol	Yield (%)[b]	β-arylcarbonyl compound	Yield (%)[b]
1.	 **6pa**	Δ (61) *μw* (65)	 **7pa**	Δ (27) *μw* (29)
2.	 **6pb**	Δ (62) *μw* (59)	 **7pb**	Δ (23) *μw* (26)
3.	 **6pe**	Δ (65) *μw* (61)	 **7pe**	Δ (25) *μw* (23)
4.	 **6pf**	Δ (32) *μw* (36)	 **7pf**	Δ (15) *μw* (18)
5.	 **6ph**	Δ (63) *μw* (59)	 **7ph**	Δ (15) *μw* (17)

[a]Reaction conditions: All the reactions carried out with 1-(2-methoxyphenyl)prop-2-en-1-ol **4p** (100 mg, 0.60 mmol), 0.30 M CH_3CN. [b]Yields in the parentheses are isolated yields of chromatographically pure products.

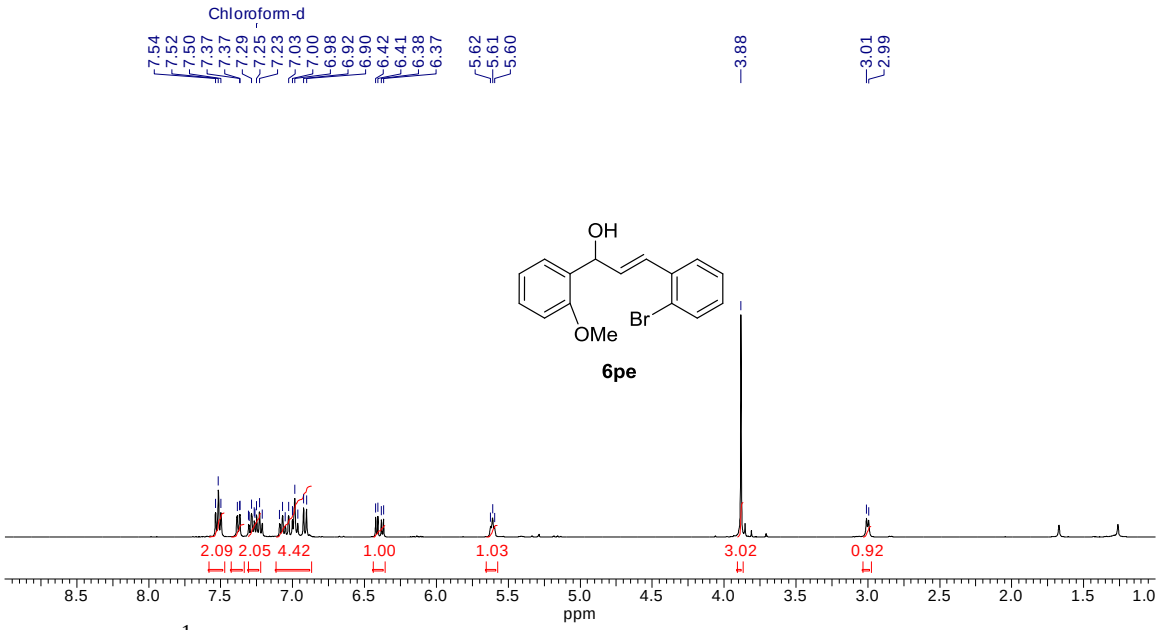


Figure II.5.1: ^{1}H-NMR (400 MHz) spectrum of **6pe** in $CDCl_3$

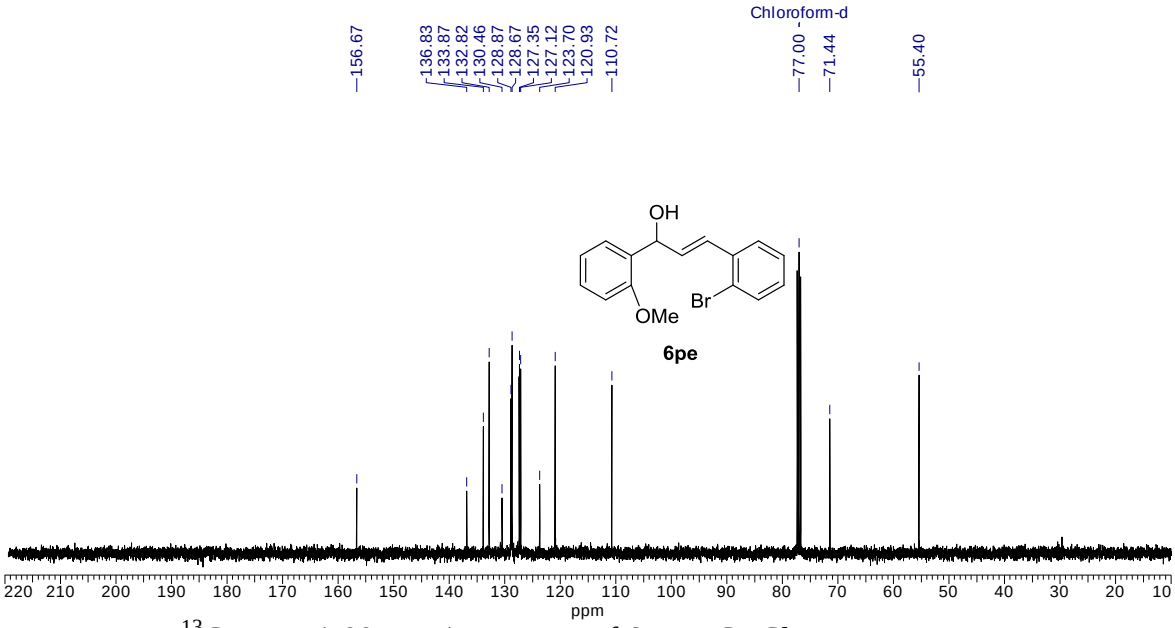


Figure II.5.2: ^{13}C-NMR (100 MHz) spectrum of **6pe** in $CDCl_3$

The structure of β-aryl allylic alcohol **6pe** was further confirmed by IR and NMR data analysis. Broad absorption band at 3381 cm^{-1} because of the OH stretching in the IR spectrum indicated the formation of the β-aryl allylic alcohol **6pe**. In the ^{1}H-NMR spectrum (Figure I.5.1), the presence of doublet of a doublet at δ 7.52 having

J=8.0 and 7.2 Hz was due to two aromatic protons, doublet of a doublet at δ 7.37 having *J*=7.5 and 1.5 Hz was due to one aromatic protons, a multiplet in the region δ 7.33-7.17 was due to two aromatic protons, a multiplet in the region δ 7.12-6.85 was due to three aromatic and one olefinic protons, the presence of doublet of a doublet at δ 6.39 having J_{trans}=15.8 and 5.5 Hz was due to olefinic methine group proton, doublet of a doublet at δ 5.61 having *J*=5.5 and 5.5 Hz was due to benzylic methine proton, singlet at δ 3.88 was due to three protons of methoxy group, doublet at δ 3.00 ppm having *J*=5.5 Hz was due to hydroxyl proton, elucidated the structure of β-aryl allylic alcohol **6pe**. In addition to it, 16 signals ^{13}C-NMR spectrum (Figure I.5.2) in which four quaternary carbon resonates at δ 156.7, 136.8, 130.5 and 123.7 were due to four aromatic carbons, presence of 10 methine carbons at δ 133.9, 132.8, 128.9, 128.7, 128.6, 127.4, 127.3, 127.1, 120.9 and 110.7 were due eight aromatic methine carbons two olefinic methine carbons, δ 71.4 was due to benzylic methine carbon and δ 55.4 ppm was due to methoxy group carbon, elucidated the structure of β-aryl allylic alcohol **6pe**. Presence of the $[M+Na]^+$ peak at m/z $[C_{16}H_{15}BrNaO_2]^+$=341.0148 in the mass spectrum further established the structure of β-aryl allylic alcohol **6pe**.

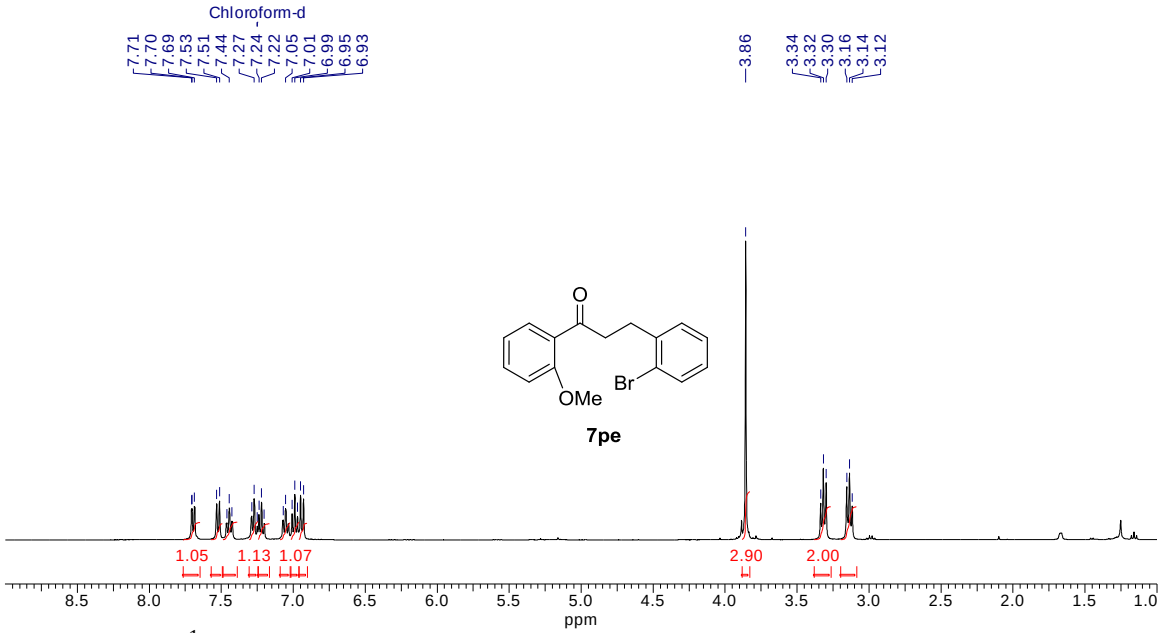


Figure II.6.1: ^{1}H-NMR (400 MHz) spectrum of **7pe** in $CDCl_3$

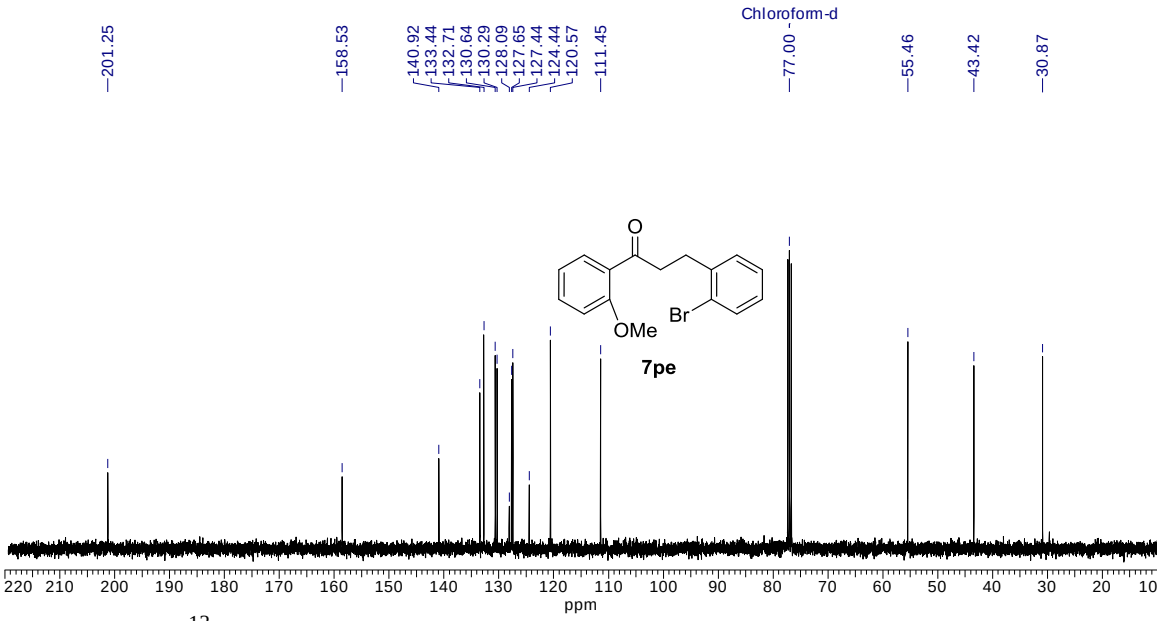


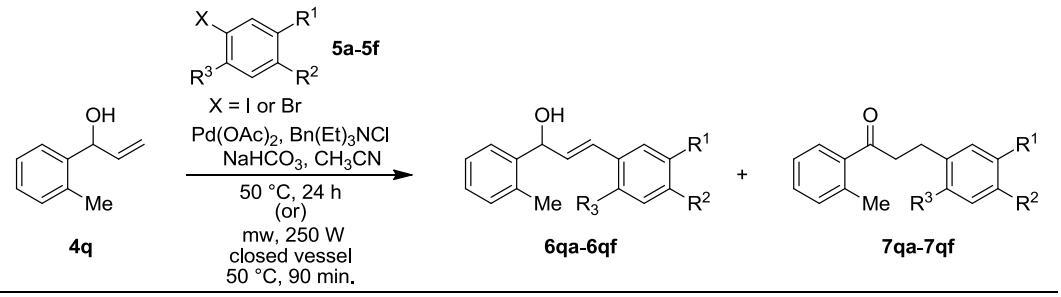
Figure II.6.2: ^{13}C-NMR (100 MHz) spectrum of **7pe** in $CDCl_3$

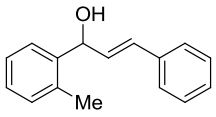
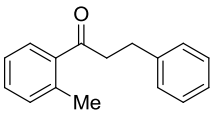
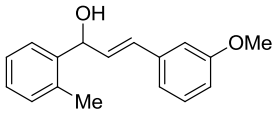
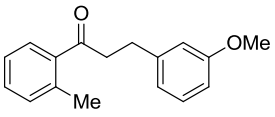
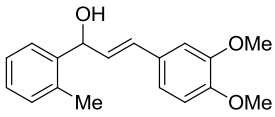
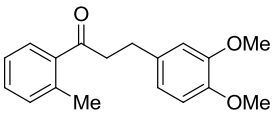
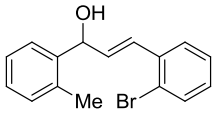
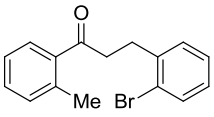
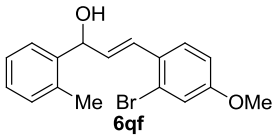
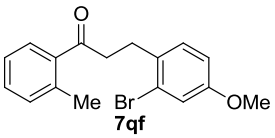
The structure of β-aryl carbonyl **7pe** was confirmed by IR and NMR data analysis. The presence of the strong absorption band in IR spectrum at 1676 cm^{-1} because of the C=O stretch indicated the formation of the β-aryl carbonyl **7pe**. In the ^{1}H-NMR spectrum (Figure II.6.1), doublet of a doublet at δ 7.69 having *J*=7.7 and 1.5 Hz was due to one aromatic proton, doublet at δ 7.52 having *J*=7.7 Hz was due to one aromatic proton, doublet of a doublet doublets at δ 7.44 having *J*=8.5, 7.7 and 1.5 Hz was due to one aromatic proton, doublet of a doublet at δ 7.27 having *J*=7.7 and 7.5 Hz was due to one aromatic proton, doublet of a doublet at δ 7.22 having *J*=7.5 and 7.2 Hz was due to one aromatic proton, doublet of a doublet at δ 7.05 having *J*=8.0 and 7.5 Hz was due to one aromatic proton, doublet of a doublet at δ 6.99 having *J*=7.5 and 7.5 Hz was due to one aromatic proton, doublet at δ 6.94 having *J*=8.0 Hz was due to one aromatic proton, singlet at δ 3.86 was due to three protons of methoxy group and the presence of two individual triplets at δ 3.32 and 3.14 ppm having *J*=7.5 Hz and *J*=7.5 Hz were due to methylene group protons, elucidated the structure of β-aryl carbonyl **7pe**. In addition to it, 17 signals appeared in ^{13}C-NMR spectrum (Figure II.6.2) in which δ 201.2 indicates the C=O group carbon, four aromatic quaternary carbon resonates at δ

158.5, 140.9, 128.1 and 124.4, the presences eight aromatic methine carbons resonates at δ 133.4, 132.7, 130.6, 130.3, 127.6, 127.4, 120.6 and 111.4, the presence of δ 55.5 was due to methoxy group carbon and the presence of δ 43.4 and 30.9 ppm were due to two methylene group carbons, elucidated the structure of β-aryl carbonyl **7pe**. The presence of the $[M+Na]^+$ peak at m/z $[C_{16}H_{14}BrNaO_2]^+$= 340.0148 in the mass spectrum further established the structure of β-aryl carbonyl **7pe**.

The structure of β-aryl allylic alcohol **6qe** was confirmed by IR and NMR data analysis. Broad absorption band at 3325 cm^{-1} because of the OH stretching in the IR spectrum indicated the formation of the β-aryl allylic alcohol **6qe**. In the ^{1}H-NMR spectrum (Figure II.7.1), the presence of doublet at δ 7.51 having coupling constant *J*=8.3 Hz was due to two aromatic protons, doublet at δ 7.45 having coupling constant *J*=8.3 Hz was due to one aromatic proton, a multiplet in the region of δ 7.30-7.10 was due to four aromatic protons, doublet of a doublet at δ 7.06 having *J*=8.0 Hz was due to one aromatic proton, the presence of doublet at δ 7.00 having coupling constant J_{trans}=15.8 Hz was due to olefinic methine group proton, doublet of a doublet at δ 6.24 having J_{trans}=15.8 Hz and *J*=6.3 Hz was due to olefinic methine group proton, doublet at δ 5.58 having *J*=6.3 Hz was due to benzylic methine proton, singlet at δ 2.38 ppm was due to three protons of methyl and br. s at δ 2.22 was due to hydroxyl proton illustrated the structure of the structure of β-aryl allylic alcohol **6qe**. In addition to it, 16 signals appeared in ^{13}C-NMR spectrum (Figure II.7.2) in which four aromatic quaternary carbon resonates at δ 140.3, 136.5, 135.3 and 123.7, the presence of 10 methine carbons at δ 133.7, 132.8, 130.6, 129.3, 128.9, 127.7, 127.4, 127.2, 126.4 and 125.8 were due to eight aromatic methine carbons and two olefinic methine carbons, presence of δ 71.7 was due to benzylic methine carbon and δ 19.2 ppm was due to methyl group carbon, illustrated the structure of the structure of β-aryl allylic alcohol **6qe**. The presence of the $[M+Na]^+$ peak at m/z $[C_{16}H_{15}BrNaO]^+$= 325.0198 in the mass spectrum further established the structure of β-aryl allylic alcohol **6qe**.

Table II.7: [Pd]-catalyzed reaction of 1-(2-methylphenyl)prop-2-en-1-ol **4q** with iodobenzenes **5a-5f** to furnish β-aryl allylic alcohols **6qa-6qf** and β-aryl carbonyls **7qa-7qf**.



Entry[a]	β-aryl allylic alcohol	Yield (%)[b]	β-aryl carbonyl compound	Yield (%)[b]
1.	 **6qa**	Δ (46) *μw* (50)	 **7qa**	Δ (24) *μw* (27)
2.	 **6qb**	Δ (58) *μw* (55)	 **7qb**	Δ (29) *μw* (31)
3.	 **6qc**	Δ (49) *μw* (51)	 **7qc**	Δ (30) *μw* (27)
4.	 **6qe**	Δ (63) *μw* (60)	 **7qe**	Δ (14) *μw* (16)
5.	 **6qf**	Δ (49) *μw* (53)	 **7qf**	Δ (30) *μw* (26)

[a]Reaction conditions: All the reactions were carried out with 1-(2-methylphenyl)prop-2-en-1-ol **4q** (100 mg, 0.67 mmol), 0.33 M CH_3CN. [b]Yields in the parentheses are isolated yields of chromatographically pure products.

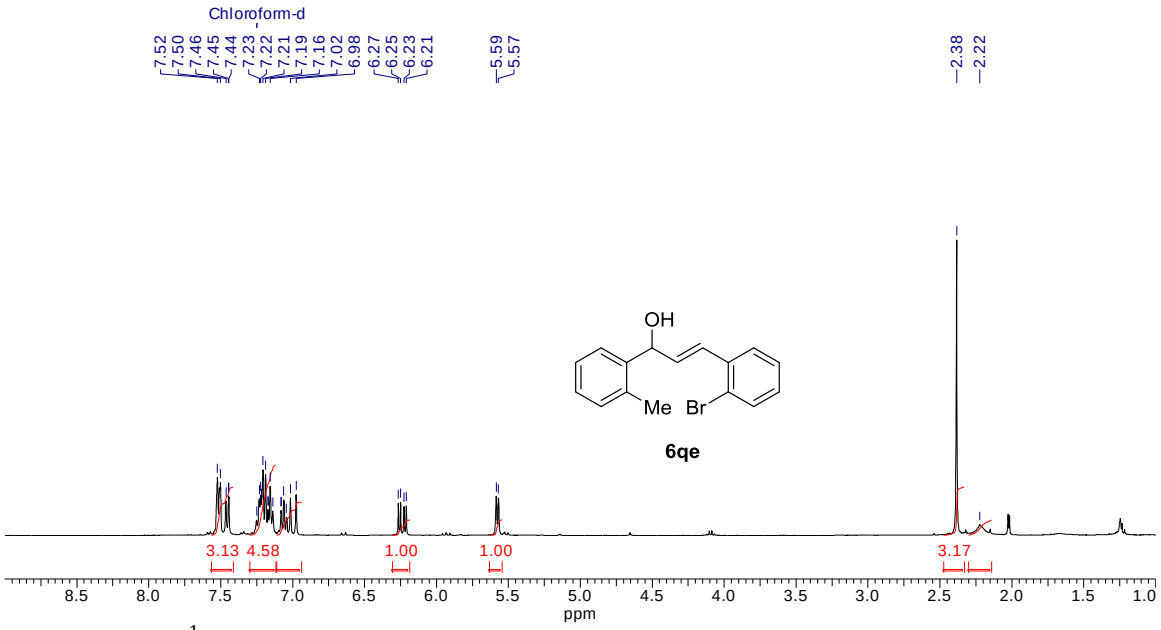


Figure II.7.1: ^{1}H-NMR (400 MHz) spectrum of **6qe** in $CDCl_3$

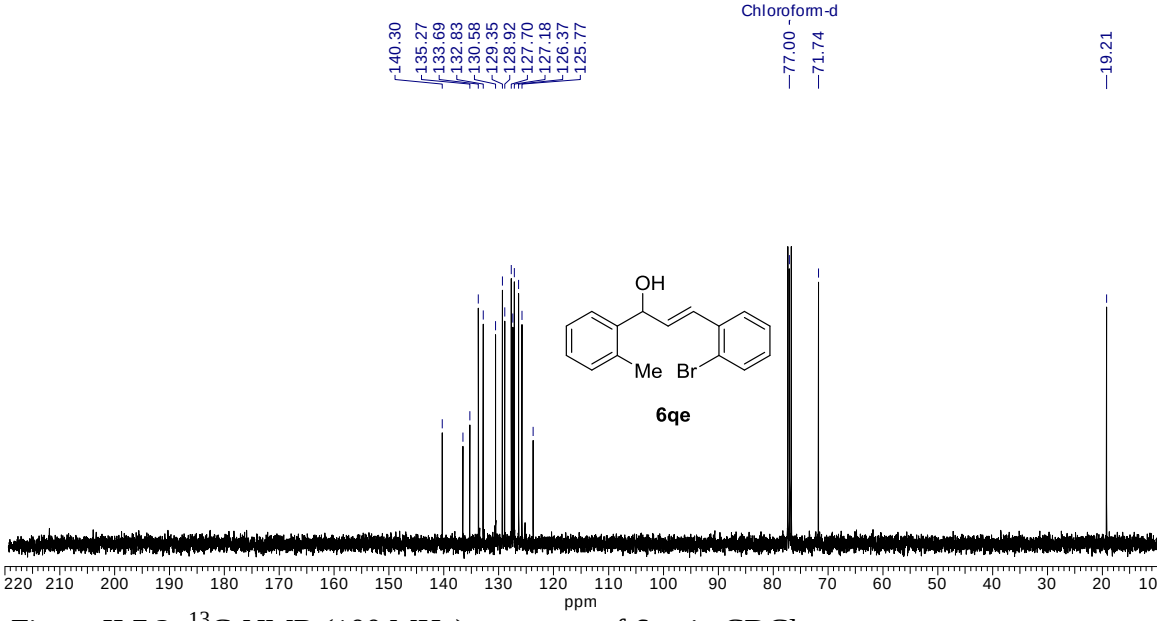


Figure II.7.2: ^{13}C-NMR (100 MHz) spectrum of **6qe** in $CDCl_3$

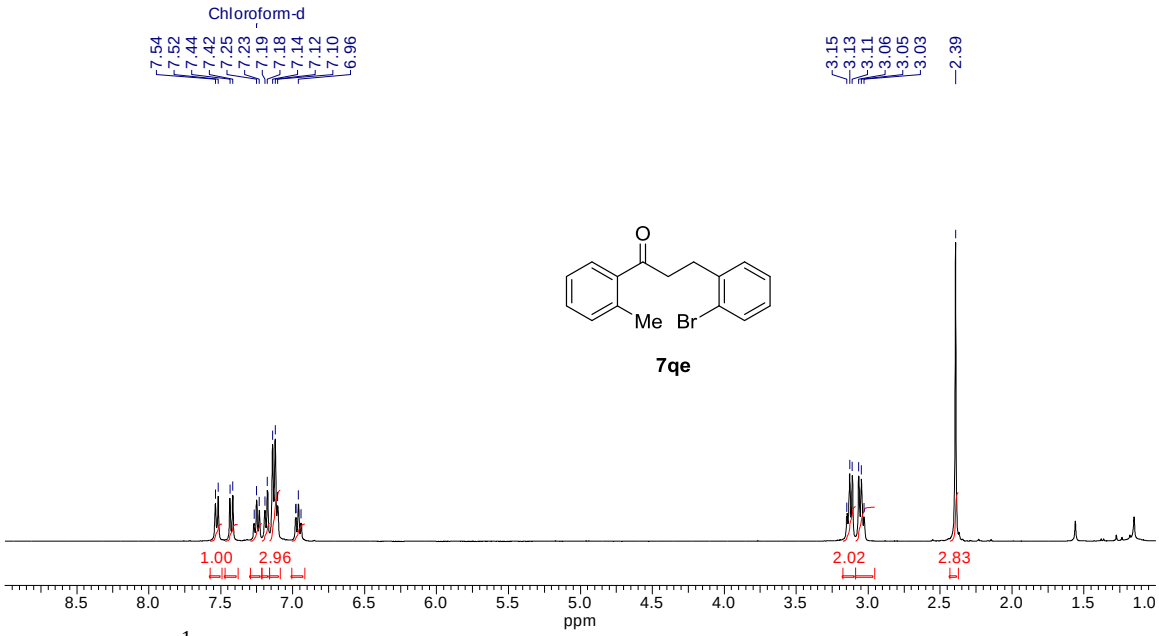


Figure II.8.1: ^{1}H-NMR (400 MHz) spectrum of **7qe** in $CDCl_3$

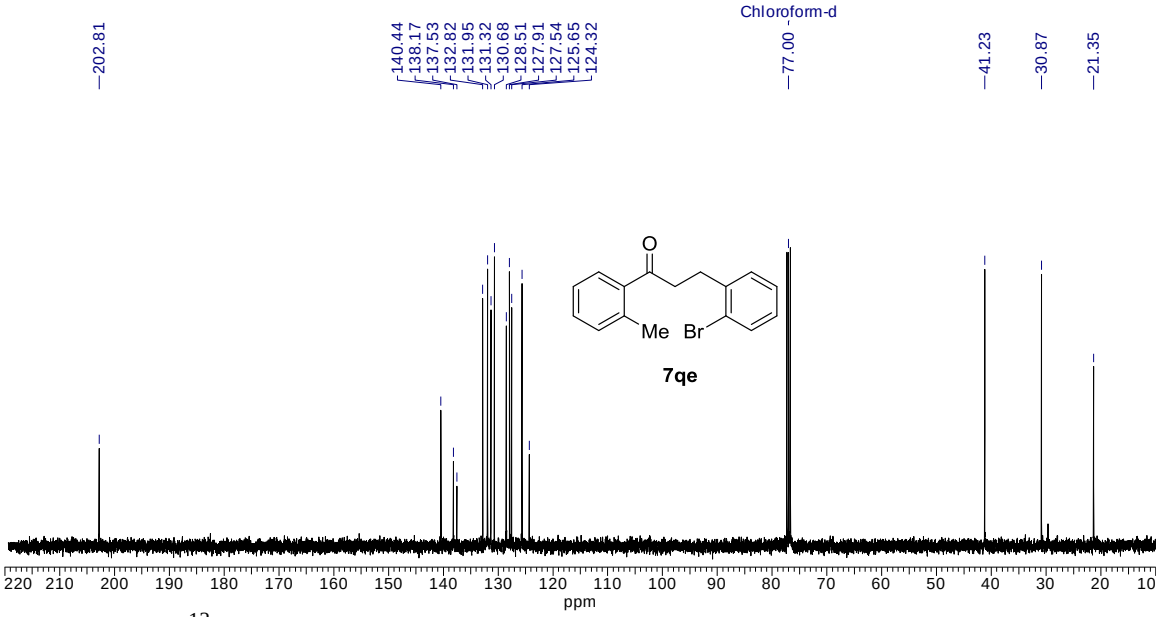


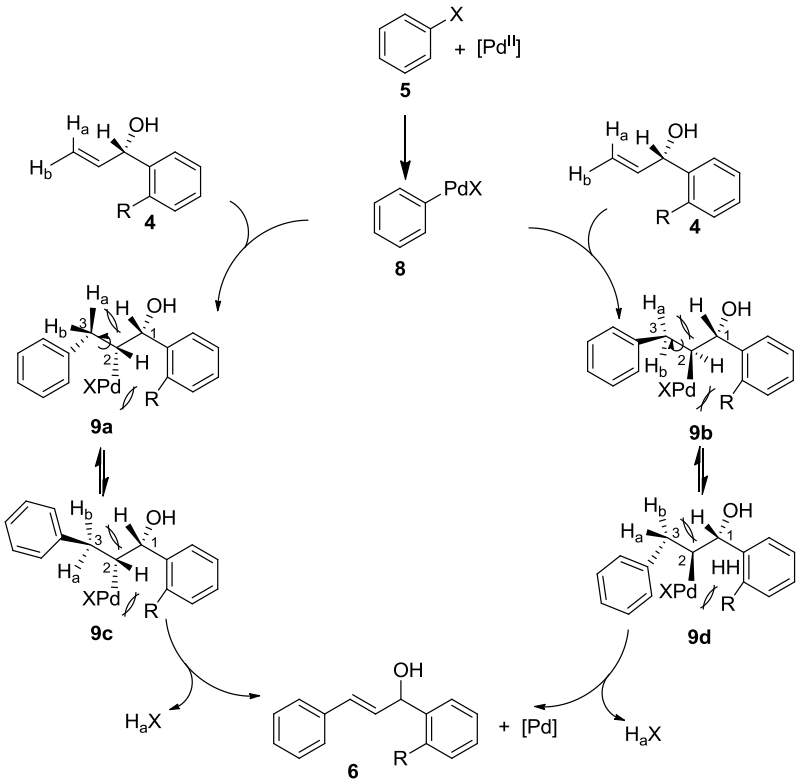
Figure II.8.2: ^{13}C-NMR (100 MHz) spectrum of **7qe** in $CDCl_3$

The structure of β-aryl carbonyl **7qe** was further confirmed by IR and NMR data analysis. Presence of strong absorption band at 1684 cm^{-1} due to C=O stretch of the group IR spectrum indicated the formation of the β-aryl carbonyl **7qe**. In the ^{1}H-NMR

spectrum (Figure II.8.1), the presence of doublet at δ 7.53 having *J*=7.5 Hz was due to one aromatic proton, doublet at δ 7.43 having *J*=7.8 Hz was due to one aromatic proton, doublet of a doublet at δ 7.25 having *J*=7.2 and 7.0 Hz was due to one aromatic proton, the presence of doublet of a doublet at δ 7.18 having *J*=7.5 and 1.3 Hz was due to one aromatic proton, doublet at δ 7.13 having *J*=7.3 Hz was due to one aromatic proton, the presence of doublet of a doublet at δ 7.12 having *J*=7.3 and 7.3 Hz was due to two aromatic protons, doublet of a doublet at δ 6.96 having *J*=7.8 and 7.3 Hz was due to one aromatic proton, the presence of two individual triplets at δ 3.13 having *J*=7.8 Hz and at δ 3.05 ppm having *J*=7.8 Hz were due to methylene protons, elucidated the structure of β-aryl carbonyl **7qe**. In addition to it, in 17 signals appeared in ^{13}C-NMR spectrum (Figure II.8.2) in which the presence of δ 202.8 indicates the C=O group carbon, four quaternary carbon resonates at δ 140.4, 138.2, 137.5 and 124.3 were due to four aromatic carbons, the presence of eight aromatic methine carbons resonates at δ 132.8, 131.9, 131.3, 130.7, 128.5, 127.9, 127.5 and 125.6, the presence of δ 41.2 and 30.9 were due to two methylene group carbons and δ 21.3 ppm was due to methyl group carbon, elucidated the structure of β-aryl carbonyl **7qe**. The presence of the $[M+Na]^+$ peak at m/z $[C_{16}H_{15}BrNaO]^+$=325.0198 in the mass spectrum further established the structure of β-aryl carbonyl **7qe**.

The reason for high selectivity for the formation of β-aryl allylic alcohols **6** in case of *ortho*-bromo substituent can be explained based on the following factors of bond lengths and polarization effects: (i) the C-Br bond length (1.94 Å) is longer than C-C (1.54 Å) and C-O (1.43 Å) bond lengths, therefore bromine is far away from its parent aromatic ring and becomes close to [Pd]-species at C-2, which might exert some steric strain and thus restrict the rotation about C_1-C_2 bond. (ii) The other reason might be due to the chelating capacity bromo substituent to form complex with Pd-species at C-2 carbon due to its ligation ability and high polarizability which could restrict the rotation, thus furnishing the desired β-aryl allylic alcohols **6** as a predominant product (Scheme II.16).

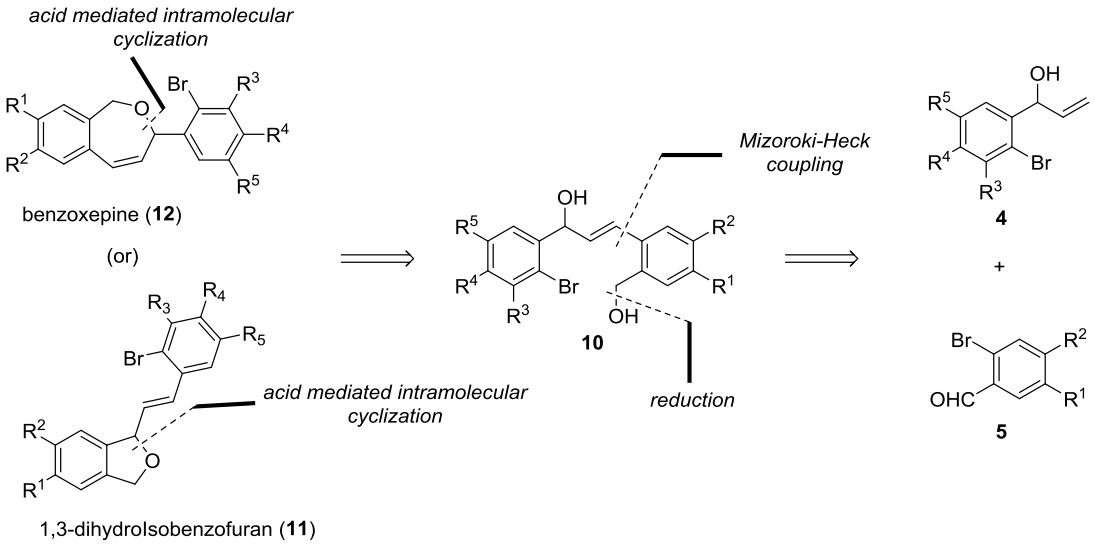
A plausible mechanistic route for the formation of β-aryl allylic alcohols **6** is predicted as shown in Scheme I.16. The first is the oxidative addition in which Pd(II)-catalyst inserts into Ar-X bond resulting in the formation of the intermediate **8**. Now, the addition of aryl palladium intermediate **8** to both faces of double bond of the allylic alcohol **4** would furnish *syn*-(**9a**) and *anti*-(**9b**) intermediates with respect to the hydroxyl group. At this stage, two pathways for the β-hydride-PdX elimination might be possible. Despite the fact that *syn*-β-hydride-PdX elimination seems feasible in case of intermediate **9b,** it might be confined due to the bulky nature of the benzylic alcohol part. Therefore, the rotation around C_1-C_2 bond could be confined in both intermediates **9a** and **9b**, respectively. However, to the direction of minimal eclipsed interaction, the rotation of 120^o around C_2-C_3 bond of **9a** and **9b**, which led to the formation of intermediates **9c** and **9d** respectively. Ultimately, the catalytic cycle completed by *syn*-β-hydride-PdX elimination from both **9c** and **9d** furnishes the same β-aryl allylic alcohol as product **6** (Scheme II.16).



Scheme II.16

II.3.2. Sequential one-pot approach for the synthesis of 1,3-dihydroisobenzofurans via [Pd]-catalysis

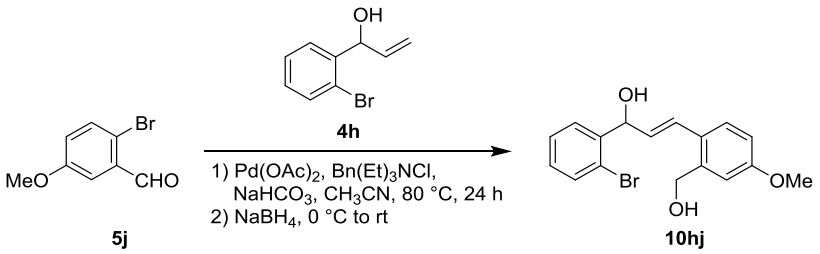
Significantly, the above method enabled us with interesting β-aryl allylic alcohols **6** with dense functionality on either of the aromatic rings.[9b] Amongst the β-aryl allylic alcohols **6**, those with aldehyde functionality on the aromatic ring appears to be the potential synthetic precursor for the synthesis of oxygen containing heterocyclic compounds. In this regard, we envisioned a short and efficient synthesis of interesting cyclic ethers such as benzoxepines **12** or 1,3-dihydroisobenzofurans **11** which could be achieved by employing reduction and acid mediated intramolecular cyclization protocol on β-aryl allylic alcohols **6**. According to our retrosynthetic analysis, the possible benzoxepine **12** or 1,3-dihydroisobenzofurans **11** can be obtained by acid mediated cyclization of diol **10**, which in turn can be synthesized easily from reduction of the coupled products **6** (Scheme II.17).



Scheme II.17

We thought that the process can be made more efficient by developing a sequential one-pot method for the direct synthesis of diol **10** starting from aryl allylic alcohols **4** and 2-bromobenzaldehydes **5h-5o**. This can be achieved by the [Pd]-

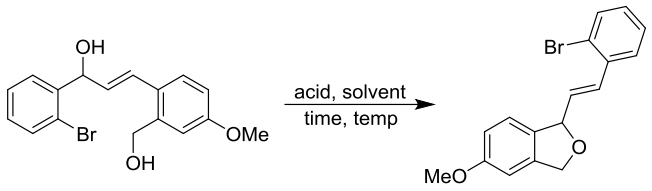
catalysed coupling for the formation of β-aryl allylic alcohols **6** and in-situ reduction of the aldehyde functionality. Thus, the [Pd]-catalyzed coupling of 2-bromobenzaldehyde **5j** with the aryl allylic alcohol **4h** followed by $NaBH_4$ induced in-situ reduction of the coupled product aldehyde **6hj** gave the desired diol **10hj** in very good yield (Scheme II.18). The idea behind this hypothesis is to minimize the number of steps, to minimize waste and to improve the overall yield of the reaction over the step-wise approach. However, the diol **10** could not be characterized due to its insolubility in $CDCl_3$ and hence, proceeded to the next reaction.



Scheme II.18

With the required diol **10hj** in hand, next the acid promoted cyclization was explored under different set of conditions and the results are summarized in the Table II.8. Thus, the reaction when carried out with the Lewis acid ($BF_3{\cdot}Et_2O$) at 0 ^oC and as well as at –10 ^oC led to the decomposition of the product (Table II.8, entries 1 and 2). Therefore, further decreasing the temperature to –20 ^oC the product **11hj** was furnished in poor yield (30%, Table II.8, entry 3). Interestingly, further decrease of temperature (–40 ^oC), gave the product **11hj** in excellent yield (95%, Table II.8, entry 4). On the other hand, exploring the reaction with different acids such as protic acid (*p*-TSA) or Lewis acid ($AlCl_3$) resulted the product **11hj** in moderate to very good yield (Table II.8, entries 5-7), whereas the reaction with H_2SO_4, gave the product in poor yield (20%, Table II.8, entries 8).

Table II.8: Optimization table for the synthesis of 1,3-dihydroisobezofuran **11hj** from the diol **10hj**.



10hj **11hj**

Entry[a]	Acid (equiv)	Solvent (5 mL)	Temp (^{o}C)	Time Min.	Yield of 11hj (%)[b]
1.	$BF_3.Et_2O$ (2.0)	DCM	0	15	-
2.	$BF_3.Et_2O$ (4.0)	DCM	–10	15	-
3.	$BF_3.Et_2O$ (5.0)	DCM	–20	15	30
4.	$BF_3.Et_2O$ (5.0)	DCM	–40	120	95
5.	*p*-TSA (3.0)	DCM	–40	60	50
6.	$AlCl_3$ (1.2)	DCM	–40	10	70
7.	$AlCl_3$ (1.2)	DCE	–40	10	80
8.	H_2SO_4 (3.0)	DCM	–40	30	20

[a]Reaction conditions: All the reactions were carried out with diol **10hj** (0.10 mmol) in DCM. [b]Isolated yields of chromatographically pure products.

Oxygen containing heterocyclic compounds are widely assayed for their substantial therapeutic applications.[68] They are pervasive structural elements in biologically relevant small molecules (Figure II I.9). 3-Deoxyisochracinic acid **13** was isolated from cladosporium species shows antibacterial activity by inhibiting the growth of *Bacillus subtilis*.[68a] The cyclic ether pestacin **14** was obtained from microorganism pestalotipsis microspore and shows antifungal, antimycotic and antioxidant activity.[68b] FR 198248 **15** was isolated from aspergillus flavipes F543 where as FR 202306 **16** was obtained from aspergillus terreus 13830. Both of them show antibacterial activity and inhibitory activity against staphylococcus aureus peptide deeformylase and also exhibit anti-influenza activity.[68c-f] The 1,4-dimethoxy-3-(3*R*-hydroxy-3*R*-methyl-1-tetralone)-1(3*H*)-isobenzofuran **17** was isolated from broth of marine streptomyces species M268 and was identified as cytotoxic against human cancer cell, HL-60, A549 and BEL-

7402.[68g] 7-Bromo-1-(2,3-dibromo-4,5-dihydroxyphenyl)-5,6-dihydroxy-1,3-dihydroisobenzo- furan **18** was isolated from brown *alga leathesia nana* and showed potential usefulness for malignant tumors and cardiovascular disease.[68h] While flavimycins A (**19**) and B (**20**) were isolated from aspergillus flavipes and inhibited staphylococcus aureus peptide deformylase; flavimycins A (**19**) had stronger antibacterial activity than B (**20**).[68i] 1,3-dihydrobenzo[c]furan glycone **21** showed stronger antibacterial activity, antidepressant drug,[68j] and escitalopram was used for the treatment of major depressive and general anxiety disorders in adults. The (*S*)-(+)-enantiomer **22** was known as escitalopram seemed to be more potent than the other (*S*)-(−)-enantiomer.[68k-n]

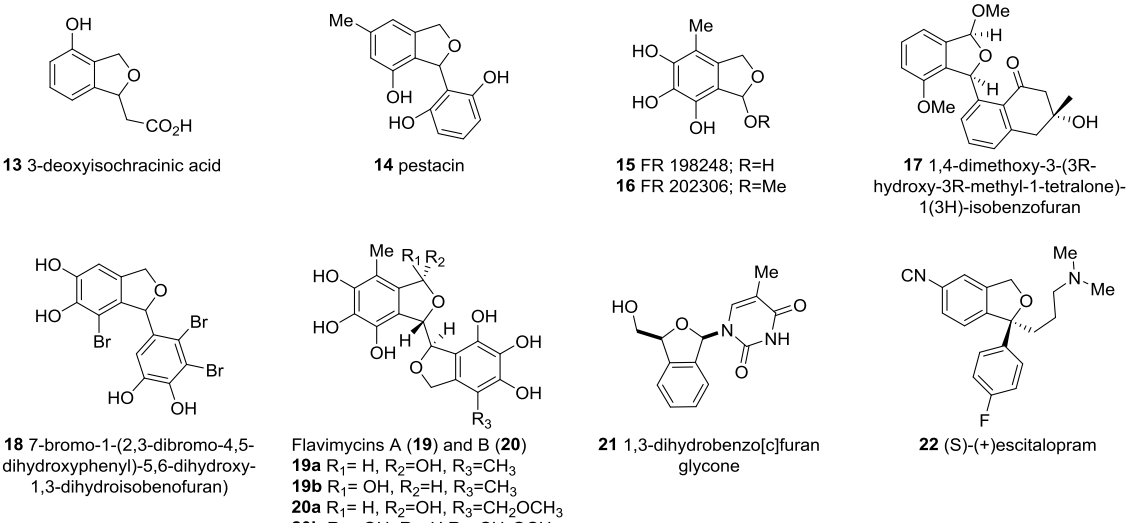
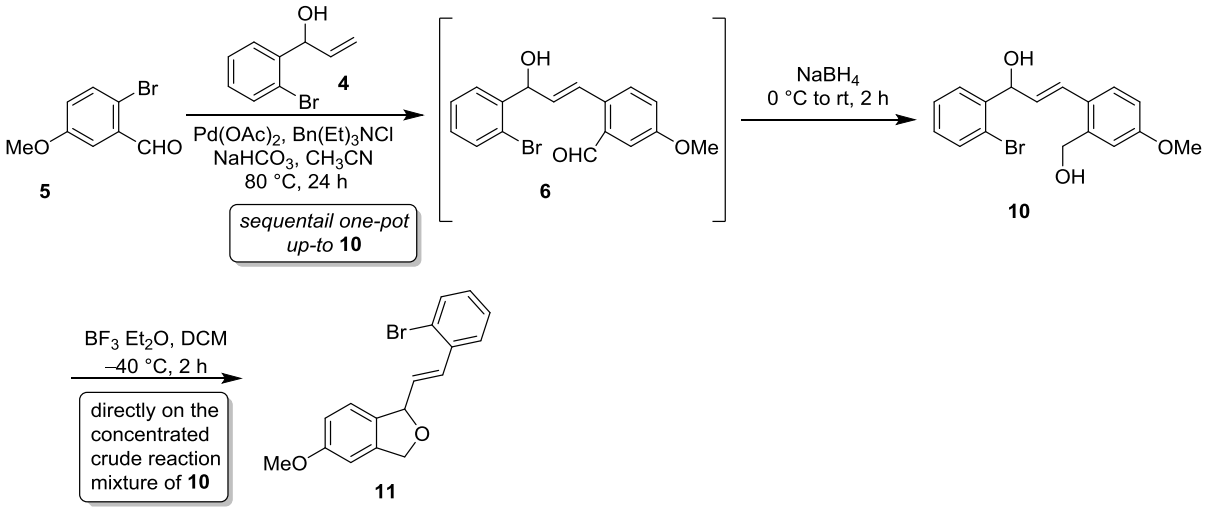


Figure II.9

Having established the reaction conditions for the synthesis of 1,3-dihydroisobenzofuran **11**, we thought that the method can still be made more efficient by performing cyclization directly on crude diol **10** without the column purification. Interestingly, the reaction was found to be smooth on the crude diol **10** (i.e., on the crude diol which was obtained the after the work-up followed by concentration under reduced pressure) and final product was obtained in 48% overall yield (Scheme II.19). The structure of the cyclic ether **11hj** was confirmed from the spectroscopic data. ^{1}H-NMR data unambiguously confirmed

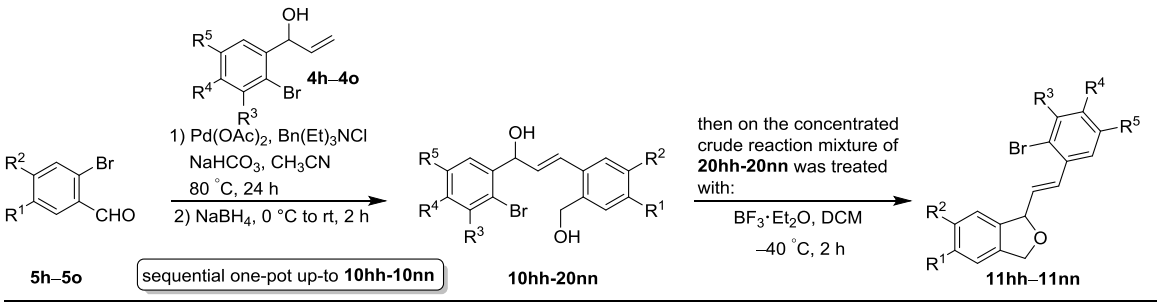
the geometry of the double bond as *trans* one by calculating the coupling constant (J = 15.5 to 15.6 Hz, see; experimental section). Therefore, the other possibility for the formation of seven membered cyclic ether **12hj** was ruled out, because it must contain *cis* double bond. In addition, the formation of five membered cyclic ether **11hj** is geometrically favoured over the seven membered one.

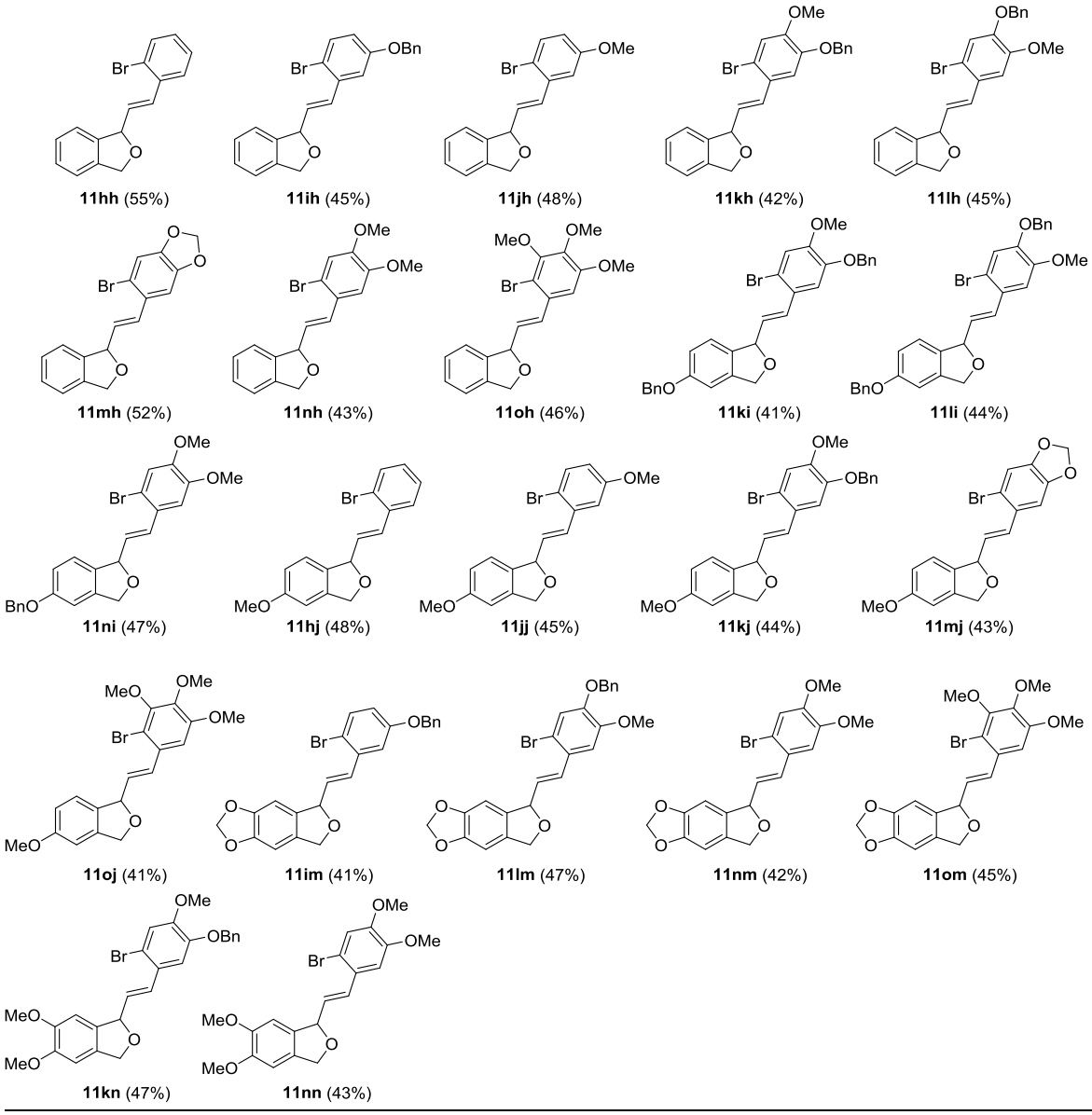


Scheme II.19

Now with the optimized reaction conditions in hand, to check the scope and limitations of the method, we have investigated this sequential one-pot method on various 2-bromobezaldehydes **5h-5o** in conjuction with aryl allylic alcohols **4h-4o**. Quite interestingly, the method was amenable on various systems possessing dense functionalities and furnished the products in moderate yields (41-55%) as summarized in Table II.9. It is worth mentioning that although the yields of the cyclic ether products **11** are moderate, it actually represents the overall yield of three individual reactions. Therefore, each step contributes to at least 75% yield and hence the method still stands efficient.

Table II.9: Synthesis of 1,3-dihydroisobenzofurans **11hh-11nn** from 2-bromobenzaldehyde **5h-5o** and aryl allylic alcohol **4h-4o**.





[a]Reaction conditions: All the reactions were carried out with 2-bromobenzadehydes **5** (0.50 mmol). [b]Isolated yields of chromatographically pure products. for compounds **11hh-11nn** the first alphabet letter

refers to the allylic alcohol part **4h-4o**, whereas the second letter indicates the aromatic ring coming from the bromo aldehyde **5h-5o**.

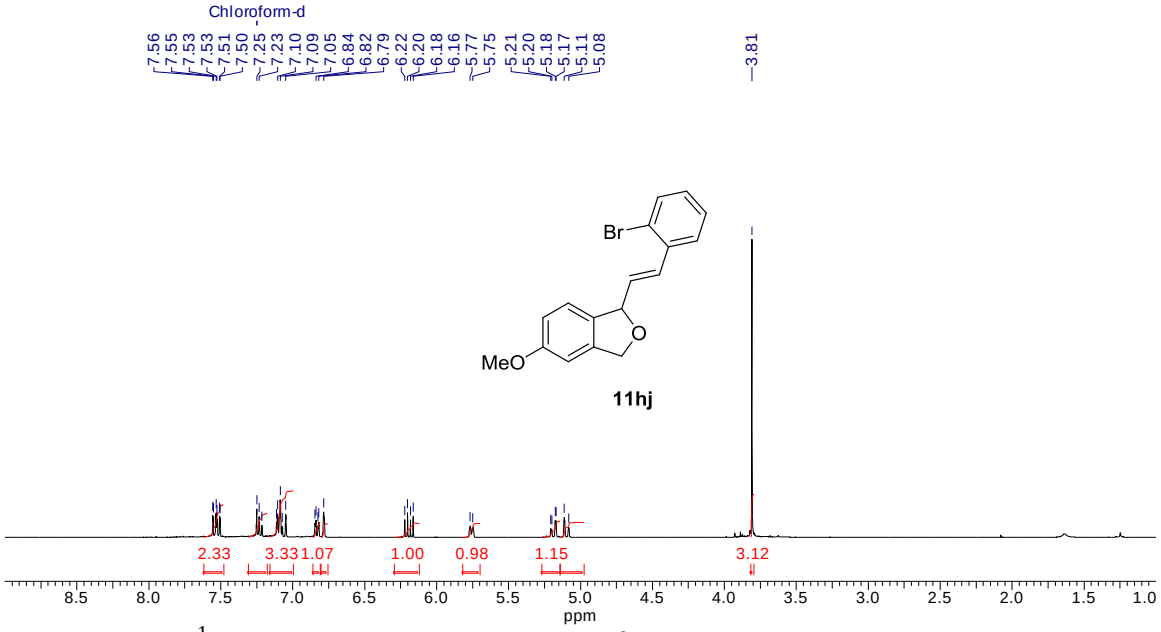


Figure II.10.1: ^{1}H-NMR (400 MHz) spectrum of **11hj** in $CDCl_3$

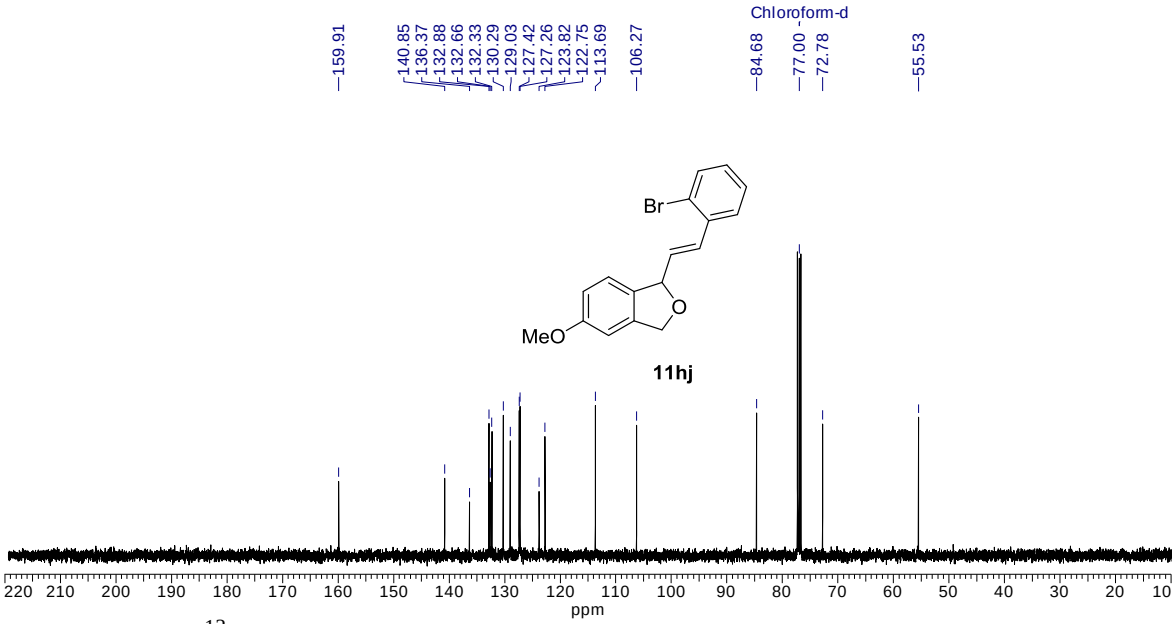


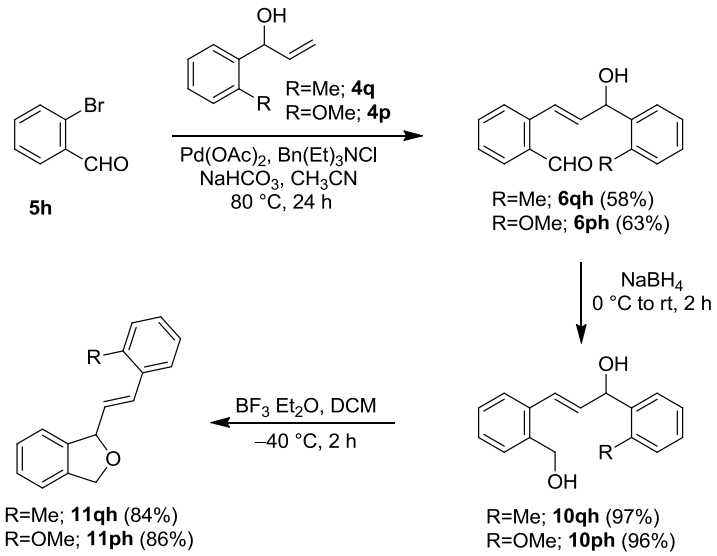
Figure II.10.2: ^{13}C-NMR (100 MHz) spectrum of **11hj** in $CDCl_3$

The structure of 1,3-dihydroisobenzofuran **11hj** was confirmed by IR and NMR data analysis. The absence of broad absorption band was due to OH stretching and the

presence of strong absorption band at 1611 cm^{-1} was due to the C=C stretch indicated the formation of 1,3-dihydroisobenzofuran **11hj**. In the ^{1}H-NMR spectrum (Figure II.10.1), the presence of doublet of a doublet at δ 7.54 having *J*=7.8 and 1.5 Hz was due to one aromatic proton, doublet of a doublet at δ 7.51 having *J*=7.8 and 1.5 Hz was due to one aromatic proton, doublet of a doublet at δ 7.22 having *J*=7.8 and 1.0 Hz was due to one aromatic proton, a multiplet in the region of δ 7.15–7.00 was due to two aromatic protons and one olefinic proton, doublet of a doublet at δ 6.83 having *J*=8.3 and 2.4 Hz was due to one aromatic proton, doublet at δ 6.78 having *J*=8.3 Hz was due to one aromatic proton, doublet of a doublet at δ 6.19 having *J*=16.1 and 7.8 Hz was due to olefinic methine group proton, doublet at δ 5.76 having *J*=7.8 Hz was due to benzylic methine group proton, doublet of a doublet at δ 5.19 having *J*=12.0 and 2.0 Hz was due to benzylic methylene group proton, doublet at δ 5.11 having *J*=12.0 Hz was due to benzylic methylene group proton, the presence of singlet δ 3.81was due to methoxy group three protons elucidated the structure of 1,3-dihydroisobenzofuran **11hj**. In addition to it, 16 signals appeared in ^{13}C-NMR spectrum (Figure II.9.2) in which five quaternary carbon resonates at δ 159.9, 140.8, 136.4 132.7 and 123.8 were due to five aromatic carbons, the presence of nine methine carbon resonates at δ at δ 132.9, 132.3, 130.3, 129.0, 127.4, 127.3, 122.7, 113.7 and 106.3 were due to seven aromatic methane group carbons and two olefin methane group protons, δ 84.7 was due to benzylic methine group carbon, δ 72.8 was due to benzylic methylene group carbon and δ 55.5 ppm was due to methoxy group carbon elucidated the structure of 1,3-dihydroisobenzofuran **11hj**. The presence of the $[M+Na]^{+}$ peak at m/z $[C_{17}H_{15}BrNaO_2]^{+}$= 353.0164 in the mass spectrum further established the structure of 1,3-dihydroisobenzofuran **11hj**.

After the successful synthesis of 1, 3-dihydroisobenzofurans **11**, we planned to increase the scope of this protocol by employing the allylic alcohols possessing a methyl/methoxy group **4q**/**4p** in the *ortho* position. During the sequential one-pot approach, we observed the formation of the regular Jeffery-Heck product along with the

Mizoroki-Heck product.[9b] This (Jeffery-Heck product) interfered in the further steps and hindered the isolation of clean products. Thus, we proceeded in a step-wise approach and achieved the targeted 1, 3-dihydroisobenzofurans **11qh** and **11ph** in a moderate overall yield (47% and 52%). It is worth mentioning that in these cases, we were also able to characterize the diol **10** (Scheme II.20).

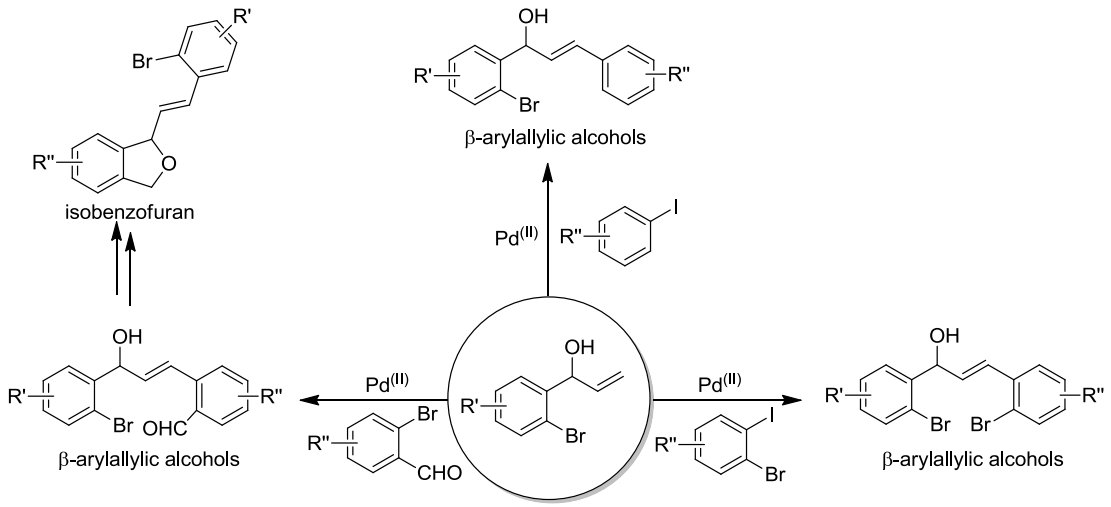


Scheme II.20

II.*4. CONCLUSIONS*:

We have developed an efficient method for synthesis of β-aryl allylic alcohols in highly regio- and stereoselective manner under [Pd]-catalysis using aryl iodides or 1-bromo-2-iodobenzenes or 2-bromobenzaldehydes as coupling partners to various allylic alcohols. As a consequence, wide ranges of β-aryl allylic alcohols were accomplished. This observation was unanticipated under traditional Jeffery-Heck conditions without the help of silver salt. This method is expeditious and amenable functioned consistently on different systems of simple to electron rich aromatic moieties and furnished the products with dense functionality on the aromatic rings. Significantly, based on this method, an efficient sequential one-pot process was developed for the synthesis of *iso*-

benzofurans, an important core structure present in many biologically active natural products (Scheme II.21).



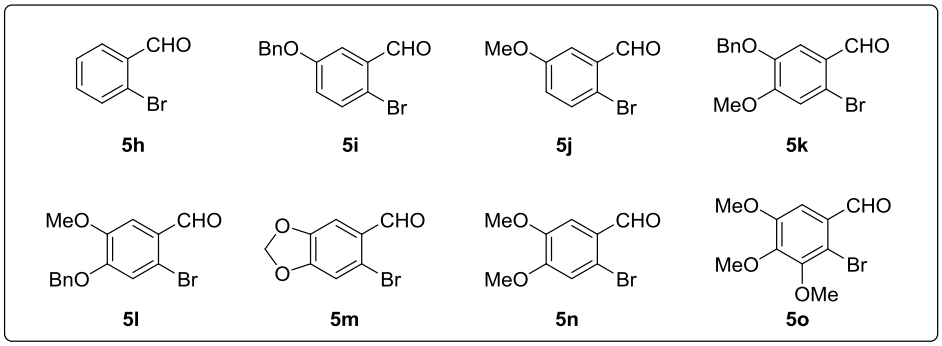
Scheme II.21

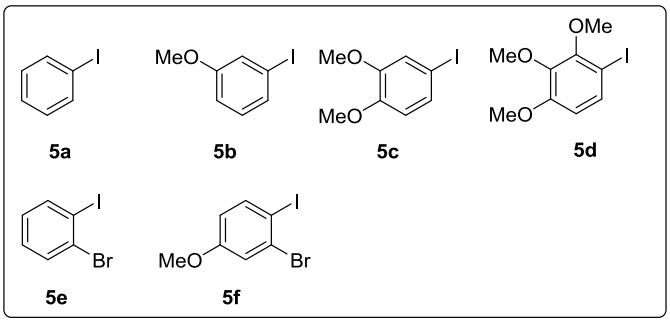
II.*5. EXPERIMENTAL SECTION*:

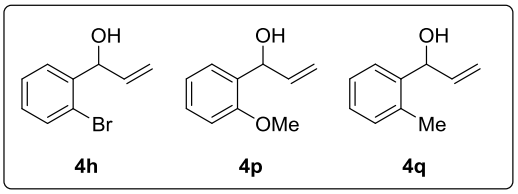
IR spectra were recorded on a Bruker Tensor 37 (FT-IR) spectrophotometer. ^{1}H-NMR spectra were recorded on Bruker Avance 400 (400 MHz) spectrometer at 295 K in $CDCl_3$; chemical shifts (δ in ppm) and coupling constants (J in Hz) are reported in standard fashion with reference to either internal standard tetramethylsilane (TMS) (δ_H = 0.00 ppm) or $CHCl_3$ (δ_H = 7.25 ppm). ^{13}C-NMR spectra were recorded on Bruker Avance 400 (100 MHz) spectrometer at RT in $CDCl_3$; chemical shifts (δ in ppm) are reported relative to $CHCl_3$ [δ_C = 77.00 ppm (central line of triplet)]. In the ^{13}C-NMR, the nature of carbons (C, CH, CH_2 and CH_3) was determined by recording the DEPT-135 spectra, and is given in parentheses and noted as s = singlet (for C), d = doublet (for CH), t = triplet (for CH_2) and q = quartet (for CH_3). In the ^{1}H-NMR, the following abbreviations were used throughout: s = singlet, d = doublet, t = triplet, q = quartet, qui = quintet, m = multiplet and br. s = broad singlet, septd = septet of doublets. The assignment of signals was confirmed by ^{1}H, ^{13}C CPD and DEPT spectra. High-

resolution mass spectra (HR-MS) were recorded on an Agilent 6538 UHD Q-TOF using multimode source. The X-ray crystal structure data was measured using Oxford Super Nova instrument. All small scale dry reactions were carried out using the standard syringe-septum technique. Reactions were monitored by TLC on the silica gel using a mixture of petroleum ether and ethyl acetate as eluents. Reactions were generally run under an argon or nitrogen atmosphere. All solvents were distilled to prior use; petroleum ether with a boiling range of 60 to 80 °C, diethyl ether, dichloromethane (DCM), ethyl acetate, toluene (with purity 99%), THF (with purity 99%), acetonitrile (with purity 99.9%), purchased from locally available commercial sources were used. All aromatic aldehydes (with purity 98%), bromine (with purity 99%), iodine (with purity 99%), $Bn(Et)_3NCl$ (with purity 99%), $Pd(OAc)_2$ (with purity 98%), 3-iodoanisole (with purity 99%), 2-bromoiodobenzene (with purity 99%), $NaBH_4$ (with purity 99%), K_2CO_3 (with purity 99%), and $NaHCO_3$ (with purity 99.5%) were purchased from Sigma-Aldrich, whereas vinylmagnesium bromide (with purity 99%), $BF_3{\cdot}Et_2O$ (with purity XX%), iodobenzene (with purity 99%) and Cs_2CO_3 (with purity 99%) were purchased from other commercial sources and used as received. The bases K_2CO_3, $NaHCO_3$ and Cs_2CO_3 were dried at 150–170 $^{\circ}$C over oil bath. Diethyl ether and toluene were dried over sodium/ benzophenone. DCM, DCE, DMF and DMA dried over calcium hydride. Acetonitrile dried over P_2O_5. Acme's silica gel (60–120 mesh) was used for column chromatography (approximately 20 g per one gram of crude material).

The following 2-bromobenzaldehydes **5h-5o** (except 2-bromobenzaldehyde) were synthesized using literature reported bromination of corresponding benzaldehydes.[42] 1-(2-bromophenyl)prop-2-en-1-ol **4h**,[69] 1-(2-methoxyphenyl)prop-2-en-1-ol (**4p**),[66] and 1-(2-methylphenyl)prop-2-en-1-ol (**4q**),[67] and were synthesized using literature reported procedure from corresponding 2-bromobenzaldehyde **5h**, 2-methoxybenzaldehyde **5p** and 2-methylbenzaldehyde **5q**. 4-iodo-1,2-dimethoxybenzene **5c**, 1-iodo-2,3,4-trimethoxybenzene **5d** and 2-bromo-1-iodo-4-methoxybenzene **5f** were synthesized using literature reported procedure from corresponding starting material.[43]





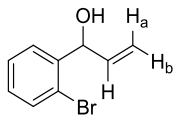


II.5.1 Synthesis of β-aryl allylic alcohols:

General procedure for the synthesis of 2-bromo aryl allylic alcohol 4h-4o, 2-methoxy phenyl allylic alcohol 4p and 2-methyl phenyl allylic alcohol 4q (GP-1):

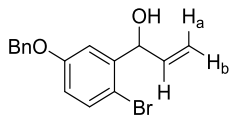
To a magnetically stirred solution of 2-bromobenzaldehyde **5** or 2-methoxybenzaldehyde **5p** or 2-methylbenzaldehyde **5q** (10 mmol) in a THF (20 mL) in a round bottom flask at 0 °C under nitrogen atmosphere was added 1.0 M vinylmagnesium bromide solution (20 mL, 20 mmol, 1.0 M in THF) and the resultant reaction mixture was slowly allowed to reach room temperature and stirred for 1.5 h. The reaction mixture was quenched with saturated aqueous NH_4Cl solution and extracted with ethyl acetate (3 × 20 mL). The organic layer was washed with saturated

NaCl solution, dried over anhydrous Na_2SO_4 and filtered. Evaporation of the filtrate under reduced pressure and purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate) furnished the product 2-bromo aryl allylic alcohol **4h-4o** (80–95%) or 2-methoxy phenyl allylic alcohol **4p** (90%) or 2-methyl phenyl allylic alcohol **4q** (95%).



4h

1-(2-Bromophenyl)prop-2-en-1-ol (**4h**): **GP-1** carried out with 2-bromobenzaldehyde **5h** (1.85 g, 10 mmol), in THF (20 mL), was added 1.0 M vinylmagnesium bromide (20 mL, 20 mmol, 1.0 M in THF). Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 97:3 to 90:10) furnished the product **4h** (1.7 g, 80%) as pale yellow viscous liquid. [TLC control R_f(**5h**)=0.75, R_f(**4h**)=0.70 (petroleum ether/ethyl acetate 95:05 , UV detection)].



4i

1-[5-(Benzyloxy)-2-bromophenyl]prop-2-en-1-ol (4i): GP-1 carried out with 2-bromobenzaldehyde **5i** (2.91 g, 10 mmol), in THF (20 mL), was added 1.0 M vinylmagnesium bromide (20 mL, 20 mmol, 1.0M in THF). Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 90:10 to 80:20) furnished the product **4i** (2.80 g, 88%) as pale yellow viscous liquid. [TLC control R_f(**5i**)=0.60, R_f(**4i**)=0.40 (petroleum ether/ethyl acetate 90:10 , UV detection)].

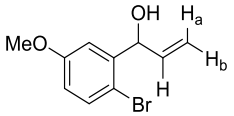
IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3371, 3032, 2920, 1592, 1571, 1462, 1291, 1380, 1291, 1233, 1163, 1010, 927, 736, 697 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.50–7.28 (m, 6H, Ar-H), 7.19 (d, 1H, *J*=2.9 Hz, Ar-H), 6.78 (dd, 1H, *J*=8.8 and 2.9 Hz, Ar-H), 5.99 (ddd, 1H, *J*=15.8, 10.3 and 5.4

Hz, C*H*=CH_2), 5.54 (d, 1H, *J*=5.4 Hz, ArC*H*-OH), 5.40 (td, 1H, *J*=15.8 and 1.5 Hz, C=C$H_a$$H_b$), 5.22 (td, 1H, *J*=10.3 and 1.5 Hz, C=$CH_a$$H_b$), 5.04 (s, 2H, Ph$CH_2$O), 2.25 (d, 1H, *J*=3.9 Hz, OH) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=158.4 (s, Ar-C), 142.5 (s, Ar-C), 138.1 (d, *C*H=CH_2), 136.4 (s, Ar-C), 133.3 (d, Ar-CH), 128.6 (d, 2C, Ar-CH), 128.1 (d, Ar-CH), 127.5 (d, 2C, Ar-CH), 115.9 (d, Ar-CH), 115.7 (t, CH=*C*H_2), 114.2 (d, Ar-CH), 112.9 (s, Ar-C), 73.4 (d, Ar-*C*HOH), 70.2 (t, PhCH_2) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{16}H_{14}BrO]^+$=$[(M+H)–H_2O]^+$: 301.0223; found 301.0213.



4j

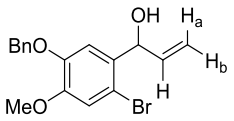
1-(2-Bromo-5-methoxyphenyl)prop-2-en-1-ol (4j): GP-1 carried out with 2-bromobenzaldehyde **5j** (2.15 g, 10 mmol), in THF (20 mL), was added 1.0 M vinylmagnesium bromide (20 mL, 20 mmol, 1.0M in THF). Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 90:10 to 80:20) furnished the product **4j** (2.20 mg, 92%) as pale yellow viscous liquid. [TLC control R_f(**5j**)=0.80, R_f(**4j**)=0.50 (petroleum ether/ethyl acetate 80:20, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3380, 2922, 2851, 1593, 1572, 1468, 1416, 1290, 1233, 1161, 1047, 1013, 928, 807, 771 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.39 (d, 1H, *J*=8.8 Hz, Ar-H), 7.07 (d, 1H, *J*=3.4 Hz, Ar-H), 6.69 (dd, 1H, *J*=8.8 and 3.4 Hz, Ar-H), 5.99 (ddd, 1H, *J*=17.1, 10.3 and 5.4 Hz, C*H*=CH_2), 5.53 (d, 1H, *J*=5.4 Hz, ArC*H*-OH), 5.38 (td, 1H, *J*=17.1 and 1.5 Hz, C=C$H_a$$H_b$), 5.21 (td, 1H, *J*=10.3 and 1.5 Hz, C=$CH_a$$H_b$), 3.78 (s, 3H, Ar-$OCH_3$), 2.34 (br. s, 1H, OH) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=159.3 (s, Ar-C), 142.4 (s, Ar-C), 138.1 (d, *C*H=CH_2), 133.3 (d, Ar-CH), 115.7 (t, CH=*C*H_2), 115.2 (d, Ar-CH), 113.0 (d, Ar-CH), 112.7 (s, Ar-C), 73.4 (d, Ar-*C*HOH), 55.4 (q, Ar-OCH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{10}H_{10}BrO]^+$=$[(M+H)–H_2O]^+$: 224.9910; found 224.9903.



4k

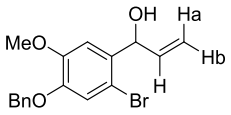
1-[5-(Benzyloxy)-2-bromo-4-methoxyphenyl]prop-2-en-1-ol (4k): GP-1 carried out with 2-bromobenzaldehyde **5k** (3.21 g, 10 mmol), in THF (20 mL), was added 1.0 M vinylmagnesium bromide (20 mL, 20 mmol, 1.0M in THF). Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 90:10 to 80:20) furnished the product **4k** (2.96 g, 85%) as yellow viscous liquid. [TLC control R_f(**5k**)=0.60, R_f(**4k**)=0.30 (petroleum ether/ethyl acetate 90:10, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}= IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3392, 2933, 2847, 1599, 1497, 1454, 1381, 1251, 1120, 1155, 1120, 1039, 1023, 861, 834, 696, 665 cm^{-1}.

^{1}H-NMR (CDCl$_3$, 400 MHz): δ=7.42 (dd, 2H, *J*=7.3 and 6.8 Hz, Ar-H), 7.37 (t, 2H, *J*=7.3 Hz, Ar-H), 7.31 (ddd, 1H, *J*=7.3 and 6.8 Hz, Ar-H), 7.03 (s, 1H, Ar-H), 7.02 (s, 1H, Ar-H), 5.98 (ddd, 1H, *J*=15.6, 10.3 and 4.9 Hz, C*H*=CH$_2$), 5.51 (d, 1H, *J*=5.4 Hz, ArC*H*-OH), 5.38 (td, 1H, *J*=15.6 and 1.5 Hz, C=C*H*$_a$H$_b$), 5.20 (td, 1H, *J*=10.3 and 1.5 Hz, C=CH$_a$*H*$_b$), 5.09 (s, 2H, PhCH$_2$O), 3.38 (s, 3H, Ar-OCH$_3$), 2.29 (d, 1H, *J*=2.9 Hz, OH) ppm.

^{13}C-NMR (CDCl$_3$, 100 MHz): δ=149.4 (s, Ar-C), 148.1 (s, Ar-C), 138.5 (d, *C*H=CH$_2$), 136.3 (s, Ar-C), 134.0 (s, Ar-C), 128.6 (d, 2C, Ar-CH), 128.0 (d, Ar-CH), 127.3 (d, 2C, Ar-CH), 117.6 (d, Ar-CH), 115.3 (t, CH=*C*H$_2$), 112.1 (s, Ar-C), 110.7 (d, Ar-CH), 73.3 (d, Ar-*C*HOH), 71.2 (t, PhCH$_2$), 56.0 (q, Ar-OCH$_3$) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{17}H_{16}BrO_2]^+$=$[(M+H)-H_2O]^+$: 331.0328; found 331.0332.



4l

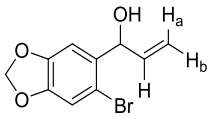
1-[4-(Benzyloxy)-2-bromo-5-methoxyphenyl]prop-2-en-1-ol (4l): GP-1 carried out with 2-bromobenzaldehyde **5l** (3.21 g, 10 mmol), in THF (20 mL), was added 1.0 M vinylmagnesium bromide (20 mL, 20 mmol, 1.0M in THF). Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 90:10 to 80:20) furnished the product **4l** (2.79 g, 80%) as yellow viscous liquid. [TLC control R_f(**5l**)=0.60, R_f(**4l**)=0.30 (petroleum ether/ethyl acetate 90:10, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3404, 3032, 3008, 2932, 1600, 1502, 1502, 1439, 1379, 1257, 1156, 1120, 1029, 925, 863, 777 cm^{-1}.

^{1}H-NMR (CDCl$_3$, 400 MHz): δ=7.42 (d, 2H, J=7.3 Hz, Ar-H), 7.35 (dd, 2H, J=7.3 and 6.8 Hz, Ar-H), 7.29 (t, 1H, J=7.3 Hz, Ar-H), 7.06 (s, 1H, Ar-H), 7.00 (s, 1H, Ar-H), 5.90 (ddd, 1H, J=15.6, 10.3 and 4.9 Hz, C*H*=CH$_2$), 5.49 (d, 1H, J=5.4 Hz, ArC*H*-OH), 5.35 (td, 1H, J=15.6 and 1.5 Hz, C=C*H*$_a$H$_b$), 5.31 (td, 1H, J=10.3 and 1.5 Hz, C=CH$_a$*H*$_b$), 5.11 (d, 1H, J=12.2 Hz, PhC*H*$_a$H$_b$O), 5.10 (d, 1H, J=12.2 Hz, PhCH$_a$*H*$_b$O), 3.85 (s, 3H, Ar-OCH$_3$), 2.10 (d, 1H, J=2.4 Hz, OH) ppm.

^{13}C-NMR (CDCl$_3$, 100 MHz): δ=149.6 (s, Ar-C), 147.8 (s, Ar-C), 138.4 (d, *C*H=CH$_2$), 136.5 (s, Ar-C), 133.4 (s, Ar-C), 128.5 (d, 2C, Ar-CH), 128.0 (d, Ar-CH), 127.6 (d, 2C, Ar-CH), 115.7 (d, Ar-CH), 115.3 (t, CH=*C*H$_2$), 113.1 (s, Ar-C), 112.9 (d, Ar-CH), 73.2 (d, Ar-*C*HOH), 71.1 (t, PhCH$_2$), 56.2 (q, Ar-OCH$_3$) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{17}H_{16}BrO_2]^+$=$[(M+H)-H_2O]^+$: 331.0328; found 331.0334.



4m

1-(6-Bromo-1,3-benzodioxol-5-yl)prop-2-en-1-ol (4m): GP-1 carried out with 2-bromobenzaldehyde **5m** (2.29 g, 10 mmol), in THF (20 mL), was added 1.0 M

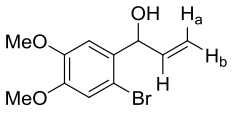
vinylmagnesiumbromide (20 mL, 20 mmol, 1.0 M in THF Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 90:10 to 80:20) furnished the product **4m** (2.0 g, 80%) as yellow viscous liquid. [TLC control R_f(**5m**)=0.60, R_f(**4m**)=0.50 (petroleum ether/ethyl acetate 80:20, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3346, 2897, 1501, 1471, 1407, 1230, 1107, 1035, 930, 840, 798 cm^{-1}.

^{1}H-NMR (CDCl$_3$, 400 MHz): δ=6.98 (s, 1H, Ar-H), 6.96 (s, 1H, Ar-H), 5.95 (d, 1H, J=5.4 Hz, OCH_aH$_b$O), 5.94 (d, 1H, J=5.4 Hz, OCH$_a$$H_b$O), 5.93 (ddd, 1H, J=15.6, 10.3 and 5.4 Hz, CH=CH$_2$), 5.51 (d, 1H, J=5.4 Hz, ArCH-OH), 5.37 (td, 1H, J=15.6 and 1.5 Hz, C=CH_aH$_b$), 5.20 (td, 1H, J=10.3 and 1.5 Hz, C=CH$_a$$H_b$), 2.26 (d, 1H, J=2.9 Hz, OH) ppm.

^{13}C-NMR (CDCl$_3$, 100 MHz): δ=147.8 (s, Ar-C), 147.7 (s, Ar-C), 138.4 (d, CH=CH$_2$), 134.8 (s, Ar-C), 115.3 (t, CH=CH$_2$), 112.8 (s, Ar-C), 112.5 (d, Ar-CH), 107.7 (d, Ar-CH), 101.7 (t, OCH$_2$O), 73.3 (d, Ar-CHOH) ppm.

HR-MS (ESI$^+$): m/z calculated for [C$_{10}$H$_9$BrNaO$_3$]$^+$=[M+Na]$^+$: 278.9627; found 278.9639.



4n

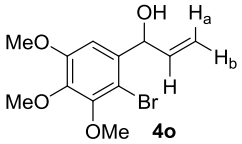
1-(2-Bromo-4,5-dimethoxyphenyl)prop-2-en-1-ol (4n): **GP-1** carried out with 2-bromobenzaldehyde **5n** (2.45 g, 10 mmol), in THF (20 mL), was added 1.0 M vinylmagnesiumbromide (20 mL, 20 mmol, 1.0M in THF). Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 80:20 to 70:30) furnished the product **4n** (2.50 g, 94%) as pale yellow viscous liquid. [TLC control R_f(**5n**)=0.55, R_f(**4n**)=0.45 (petroleum ether/ethyl acetate 70:30 , UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3451, 2960, 1601, 1500, 1441, 1254, 1205, 1032, 923, 865, 810, 758 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=6.99 (s, 1H, Ar-H), 6.96 (s, 1H, Ar-H), 5.95 (ddd, 1H, *J*=15.8, 10.4 and 5.3 Hz, C*H*=CH_2), 5.50 (d, 1H, *J*=5.3 Hz, ArC*H*-OH), 5.36 (d, 1H, *J*=15.8 Hz, C=CH_{2a}), 5.18 (d, 1H, *J*=10.4 Hz, C=CH_{2b}), 3.84 (s, 3H, Ar-OCH_3), 3.83 (s, 3H, Ar-OCH_3), 2.30 (br. s, 1H, OH) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=148.8 (s, Ar-C), 148.7 (s, Ar-C), 138.5 (d, *C*H=CH_2), 133.5 (s, Ar-C), 115.2 (t, CH=*C*H_2), 115.2 (d, Ar-CH), 112.3 (s, Ar-C), 110.2 (d, Ar-CH), 73.2 (d, Ar-*C*HOH), 56.1 (q, Ar-OCH_3), 55.9 (q, Ar-OCH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{11}H_{13}BrNaO_3]^+$=$[M+Na]^+$: 294.9940; found 294.9941.



4o

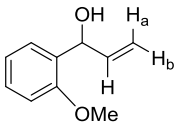
1-(2-Bromo-3,4,5-trimethoxyphenyl)prop-2-en-1-ol (4o): GP-1 carried out with 2-bromobenzaldehyde **5o** (2.75 g, 10 mmol), in THF (20 mL), was added 1.0 M vinylmagnesiumbromide (20 mL, 20 mmol, 1.0 M in THF). Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 70:30 to 50:50) furnished the product **4o** (2.70 g, 90%) as pale yellow viscous liquid. [TLC control R_f(**5o**)=0.40, R_f(**4o**)=0.30 (petroleum ether/ethyl acetate 70:30 , UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3463, 2937, 1570, 1475, 1397, 1108, 930 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=6.90 (s, 1H, Ar-H), 5.98 (ddd, 1H, *J*=16.7, 11.4 and 6.3 Hz, C*H*=CH_2), 5.59 (d, 1H, *J*=4.8 Hz, ArC*H*-OH), 5.39 (d, 1H, *J*=17.2 Hz, C=CH_{2a}), 5.20 (d, 1H, *J*=10.4 Hz, C=CH_{2b}), 3.87 (s, 3H, Ar-OCH_3), 3.85 (s, 3H, Ar-OCH_3), 3.84 (s, 3H, Ar-OCH_3), 2.34 (br. s, 1H, OH) ppm.

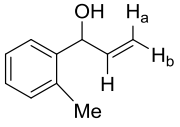
^{13}C-NMR ($CDCl_3$, 100 MHz): δ=153.1 (s, Ar-C), 150.6 (s, Ar-C), 142.5 (s, Ar-C), 138.3 (d, Ar-CH), 137.1 (s, Ar-C), 115.5 (d, *C*H=CH), 108.8 (s, Ar-C), 106.3 (d, CH=*C*H_2), 73.4 (d, Ar-*C*HOH), 61.1 (q, Ar-OCH_3), 60.99 (q, Ar-OCH_3), 56.1 (q, Ar-OCH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{12}H_{14}BrNaO_4]^+$=$[M+Na]^+$: 325.0046; found 325.0051.



4p

1-(2-Methoxyphenyl)prop-2-en-1-ol (**4p**): **GP-1** carried out with 2-Methoxybenzaldehyde **5p** (1.36 g, 10 mmol), in THF (20 mL), was added 1.0 M vinylmagnesiumbromide (20 mL, 20 mmol, 1.0 M in THF). Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 95:5 to 90:10) furnished the product **4p** (1.4 g, 90%) as pale yellow viscous liquid. [TLC control R_f(**5p**)=0.70, R_f(**4p**)=0.50 (petroleum ether/ethyl acetate 70:30 , UV detection)].



4q

1-(2-Methylphenyl)prop-2-en-1-ol (**4q**): **GP-1** carried out with 2-Methylbenzaldehyde **5q** (1.2 g, 10 mmol), in THF (20 mL), was added 1.0 M vinylmagnesiumbromide (20 mL, 20 mmol, 1.0 M in THF). Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 95:5 to 90:10) furnished the product **4q** (1.4 g, 95%) as pale yellow viscous liquid. [TLC control R_f(**5q**)=0.50, R_f(**4q**)=0.30 (petroleum ether/ethyl acetate 80:20 , UV detection)].

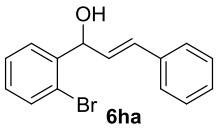
General procedure for β-arylation for the synthesis of product 6 (under conventional conditions) (GP-2):

In an oven dried round bottom flask under nitrogen atmosphere, were added $Pd(OAc)_2$ (5 mol%), $Bn(Et)_3NCl$ (0.20–0.67 mmol), $NaHCO_3$ (0.40–1.34 mmol), aryl allyl alcohol **4** (0.20–0.67 mmol) and aryl halide **5** (0.24–0.80 mmol) followed by

acetonitrile (2 mL). The resulted reaction mixture was stirred for 24 h at 50 °C, then reaction mixture was quenched by addition of aq. NH_4Cl and extracted with ethyl acetate (3 × 10 mL). The organic layer was dried over Na_2SO_4 and filtered. Evaporation of the filtrate under reduced pressure and purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate) furnished the β-arylated coupled products **6** (33-81%).

General procedure for β-arylation for the synthesis of product 6 (under microwave irradiation conditions) (GP-3):

In an oven dried microwave 10 ml vial under nitrogen atmosphere, were added $Pd(OAc)_2$ (5 mol%), $Bn(Et)_3NCl$ (0.20–0.67 mmol), $NaHCO_3$ (0.40–1.34 mmol), aryl allylic alcohol **4** (0.20–0.67 mmol) and aryl halide **5** (0.24–0.80 mmol) followed by acetonitrile (2 mL) and sealed the vial. The resulted reaction mixture was irradiated under the microwave (250 W, 50 °C) for 90 min. Then, the reaction mixture was quenched by an addition of aq. NH_4Cl and extracted with ethyl acetate (3 × 10 mL). The organic layer was dried over Na_2SO_4 and filtered. Evaporation of the filtrate under reduced pressure and the purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate) furnished the β-arylated coupled products **6** (29-86%).



6ha

(E)-1-(2-Bromophenyl)-3-phenylprop-2-en-1-ol (6ha): GP-2 was carried out on bromoaryl allyl alcohol **4h** (100 mg, 0.47 mmol) with $Pd(OAc)_2$ (5.2 mg, 5 mol%), $Bn(Et)_3NCl$ (106 mg, 0.47 mmol), $NaHCO_3$ (78 mg, 0.94 mmol), iodobenzene **5a** (114 mg, 0.56 mmol) in dry acetonitrile (2 mL), and the reaction mixture was heated at 50 °C for 24 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 95:5 to 80:20) furnished the product **6ha** (110 mg, 82%), (followed **GP-3** under microwave irradiation conditions, 115 mg, 86%) as brown viscous liquid.

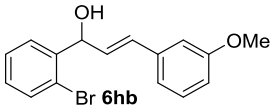
[TLC control R_f(**4h**)=0.30, R_f(**6ha**)=0.20 (petroleum ether/ethyl acetate 90:10, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3333, 3036, 2915, 1578, 1442, 1014, 964, 746 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.6 (d, 1H, *J*=7.7 Hz, Ar-H), 7.54 (d, 1H, *J*=7.9 Hz, Ar-H), 7.45–7.15 (m, 6H, Ar-H), 7.11 (dd, 1H, *J*=7.7 and 7.5 Hz, Ar-H), 6.73 (d, 1H, *J*=15.9 Hz, CH=C*H*-Ar), 6.32 (dd, 1H, *J*=15.9 and 6.1 Hz, C*H*=CH-Ar), 5.75 [d, 1H, *J*=6.1 Hz, Ar-C*H*(OH)-CH=CH], 2.65 (br. s, 1H, OH) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=141.7 (s, Ar-C), 136.5 (s, Ar-C), 132.8 (d, CH=*C*H-Ar), 131.0 (d, Ar-CH), 129.7 (d, *C*H=CH-Ar), 129.2 (d, Ar- CH), 128.6 (d, 2C, Ar-CH), 128.1 (d, Ar- CH), 128.0 (d, Ar- CH), 127.9 (d, Ar- CH), 126.7 (d, 2C, Ar-CH), 122.6 (s, Ar-C), 73.4 (d, Ar-*C*HOH) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{15}H_{13}BrNaO]^+$=$[M+Na]^+$: 311.0042; found 311.0047.



6hb

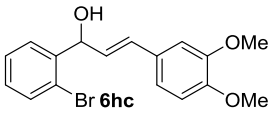
(E)-1-(2-Bromophenyl)-3-(3-methoxyphenyl)prop-2-en-1-ol (6hb): GP-2 was carried out on bromoaryl allylic alcohol **4h** (60 mg, 0.28 mmol) with $Pd(OAc)_2$ (3.1 mg, 5 mol%), $Bn(Et)_3NCl$ (64 mg, 0.28 mmol), $NaHCO_3$ (47 mg, 0.56 mmol), iodoanisole **5b** (79 mg, 0.33 mmol) in dry acetonitrile (2 mL), and the reaction mixture was heated at 50 °C for 24 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 95:5 to 80:20) furnished the product **6hb** (72 mg, 80%), (followed **GP-3** under microwave irradiation conditions, 73 mg, 81%) as brown viscous liquid. [TLC control R_f(**4h**)=0.30, R_f(**6hb**)=0.20 (petroleum ether/ethyl acetate 80:20, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3404, 2935, 1587, 1443, 1260, 1159, 1031, 757, 684 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.60 (dd, 1H, *J*=7.8 and 1.5 Hz, Ar-H), 7.55 (dd, 1H, *J*=7.8 and 1.5 Hz, Ar-H), 7.34 (dd, 1H, *J*=7.8 and 7.3 Hz, Ar-H), 7.22 (dd, 1H, *J*=7.8 and 7.8 Hz, Ar-H), 7.15 (ddd, 1H, *J*=7.8, 7.3 and 2.0 Hz, Ar-H), 6.98 (d, 1H, *J*=7.8 Hz, Ar-H), 6.92 (dd, 1H, *J*=2.0 and 2.0 Hz, Ar-H), 6.80 (dd, 1H, *J*=7.8 and 2.0 Hz, Ar-H), 6.71 (d, 1H, *J*=16.1 Hz, CH=C*H*-Ar), 6.32 (dd, 1H, *J*=16.1 and 5.8 Hz, C*H*=CH-Ar), 5.76 [d, 1H, *J*=5.8 Hz, Ar-C*H*(OH)-CH=CH], 3.79 (s, 3H, Ar-OCH_3), 2.56 (br. s, 1H, OH) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=159.7 (s, Ar-C), 141.5 (s, Ar-C), 137.9 (s, Ar-C), 132.7 (d, Ar-CH), 130.8 (d, CH=*C*H-Ar), 129.9 (d, Ar-CH), 129.5 (d, Ar-CH), 129.1 (d, *C*H=CH-Ar), 127.9 (d, Ar-CH), 127.8 (d, Ar-CH), 122.4 (s, Ar-C), 119.3 (d, Ar-CH), 113.5 (d, Ar-CH), 111.8 (d, Ar-CH), 73.2 (d, Ar-*C*HOH), 55.1 (q, Ar-OCH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{16}H_{15}BrNaO_2]^+$=$[M+Na]^+$: 341.0148; found 341.0153.



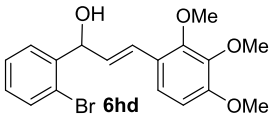
(E)-1-(2-Bromophenyl)-3-(3,4-dimethoxyphenyl)prop-2-en-1-ol (6hc): GP-2 was carried out on bromo aryl allyl alcohol **4h** (60 mg, 0.28 mmol) with $Pd(OAc)_2$ (3.1 mg, 5 mol%), $Bn(Et)_3NCl$ (64 mg, 0.28 mmol), $NaHCO_3$ (47 mg, 0.56 mmol), iodovaratrole **5c** (89 mg, 0.33 mmol) in dry acetonitrile (2 mL), and the reaction mixture was heated at 50 °C for 24 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 90:10 to 70:30) furnished the product **6hc** (71 mg, 72%), (followed **GP-3** under microwave irradiation conditions, 67 mg, 68%) as brown viscous liquid. [TLC control R_f(**4h**)=0.60, R_f(**6hc**)=0.30 (petroleum ether/ethyl acetate 70:30, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3503, 2942, 2839, 1592, 1458, 1257, 1141, 1024, 910, 730, 649 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.60 (d, 1H, *J*=7.6 Hz, Ar-H), 7.51 (d, 1H, *J*=7.8 Hz, Ar-H), 7.32 (dd, 1H, *J*=7.4 and 7.3 Hz, Ar-H), 7.12 (dd, 1H, *J*=7.4 and 7.4 Hz, Ar-H), 6.89 (s, 2H, Ar-H), 6.76 (d, 1H, *J*=8.2 Hz, Ar-H), 6.63 (d, 1H, *J*=15.8 Hz, CH=C*H*-Ar), 6.16 (dd, 1H, *J*=15.7 and 5.9 Hz, C*H*=CH-Ar), 5.71 [d, 1H, *J*=5.9 Hz, Ar-C*H*(OH)-CH=CH], 3.83 (s, 6H, 2 Ar-OCH_3), 2.58 (br. s, 1H, OH) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=148.9 (s, 2C, Ar-C), 141.9 (s, Ar-C), 132.8 (d, Ar-CH), 130.9 (d, Ar-CH), 129.5 (s, Ar-C), 129.0 (d, CH=*C*H-Ar), 128.0 (d, Ar-CH), 127.9 (d, *C*H=CH-Ar), 127.8 (d, Ar-CH), 122.5 (s, Ar-C), 120.0 (d, Ar-CH), 111.0 (d, Ar-CH), 108.9 (d, Ar-CH), 73.5 (d, Ar-*C*HOH), 55.9 (q, Ar-OCH_3), 55.8 (q, Ar-OCH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{17}H_{17}BrNaO_3]^+$=$[M+Na]^+$: 371.0253; found 371.0259.



(E)-1-(2-Bromophenyl)-3-(2,3,4-trimethoxyphenyl)prop-2-en-1-ol (6hd): GP-2 was carried out on bromo aryl allylic alcohol 4h (100 mg, 0.47 mmol) with $Pd(OAc)_2$ (5.2 mg, 5 mol%), $Bn(Et)_3NCl$ (106 mg, 0.47 mmol), $NaHCO_3$ (78 mg, 0.94 mmol), trimethoxyiodobenzene 5d (165 mg, 0.56 mmol) in dry acetonitrile (2 mL), and the reaction mixture was heated at 50 °C for 24 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 85:15 to 70:30) furnished the product **6hd** (107 mg, 60%), (followed **GP-3** under microwave irradiation conditions, 100 mg, 56%) as yellow viscous liquid. [TLC control R_f(4h)=0.30, R_f(**6hd**)=0.20 (petroleum ether/ethyl acetate 70:30 UV detection)].

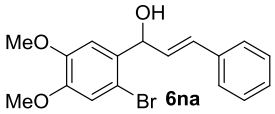
IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3409, 2933, 1595, 1493, 1461, 1291, 1092, 902, 755, 681 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.61 (d, 1H, *J*=7.6 Hz, Ar-H), 7.52 (d, 1H, *J*=7.9 Hz, Ar-H), 7.32 (dd, 1H, *J*=7.5 and 7.4 Hz, Ar-H), 7.12 (dd, 2H, *J*=8.4 and 6.0 Hz, Ar-H), 6.92 (d, 1H, *J*=15.9 Hz, CH=C*H*-Ar), 6.60 (d, 1H, *J*=8.7 Hz, Ar-H),

6.21(dd, 1H, *J*=16.0 and 6.5 Hz, C*H*=CH-Ar), 5.73 [d, 1H, *J*=6.5 Hz, Ar-C*H*(OH)-CH=CH], 3.84 (s, 3H, Ar-OCH_3), 3.82 (s, 6H, 2 Ar-OCH_3), 2.58 (br. s, 1H, OH) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=153.3 (s, Ar-C), 151.6 (s, Ar-C), 142.3 (s, Ar-C), 142.0 (s, Ar-C), 132.8 (d, Ar-CH), 129.2 (d, CH=*C*H-Ar), 129.0 (d, Ar-CH), 127.9 (d, Ar-CH), 127.8 (d, Ar-CH), 125.6 (d, *C*H=CH-Ar), 123.6 (s, Ar-C), 122.4 (s, Ar-C), 121.2 (d, Ar-CH), 107.7 (d, Ar-CH), 73.9 (d, Ar-*C*HOH), 61.3 (q, Ar-OCH_3), 60.9 (q, Ar-OCH_3), 56.0 (q, Ar-OCH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{18}H_{19}BrNaO_4]^+$=$[M+Na]^+$: 401.0359; found 401.0364.



6na

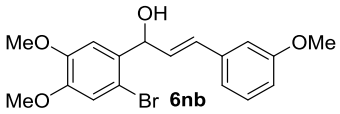
(E)-1-(2-Bromo-4,5-dimethoxyphenyl)-3-phenylprop-2-en-1-ol (6na): GP-2 was carried out on bromo aryl allylic alcohol 4n (100 mg, 0.37 mmol) with $Pd(OAc)_2$ (4.1 mg, 5 mol%), $Bn(Et)_3NCl$ (83.2 mg, 0.4 mmol), $NaHCO_3$ (62 mg, 0.73 mmol), iodobenzene 5a (89.7 mg, 0.44 mmol) in dry acetonitrile (2 mL), and the reaction mixture was heated at 50 °C for 24 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 90:10 to 80:20) furnished the product **6na** (109 mg, 85%), (followed **GP-3** under microwave irradiation conditions, 101 mg, 79%) as yellow viscous liquid. [TLC control R_f(4n)=0.50, R_f(**6na**)=0.49 (petroleum ether/ethyl acetate 70:30, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3470, 2945, 1599, 1499, 1447, 1255, 1205, 1153, 1031, 965, 732 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.30 (d, 2H, *J*=7.4 Hz, Ar-H), 7.22 (dd, 2H, *J*=7.7 and 7.2 Hz, Ar-H), 7.17 (dd, 1H, *J*=7.2 and 4.4 Hz, Ar-H), 7.02 (s, 1H, Ar-H), 6.92 (s, 1H, Ar-H), 6.63 (d, 1H, *J*=15.8 Hz, CH=C*H*-Ar), 6.22 (dd, 1H, *J*=15.8 and 5.9 Hz, C*H*=CH-Ar), 5.62 [d, 1H, *J*=5.9 Hz, Ar-C*H*(OH)-CH=CH], 3.79 (s, 3H, Ar-OCH_3), 3.78 (s, 3H, Ar-OCH_3), 2.29 (br. s, 1H, OH) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=149.0 (s, Ar-C), 148.9 (s, Ar-C), 136.5 (s, Ar-C), 133.7 (s, Ar-C), 130.7 (d, Ar-CH), 129.9 (d, Ar-CH), 128.6 (d, 2C, Ar-CH), 127.8 (d, Ar-CH), 126.6 (d, 2C, Ar-CH), 115.3 (d, CH=*C*H-Ar), 112.3 (s, Ar-C), 110.3 (d, *C*H=CH-Ar), 73.3 (d, Ar-*C*HOH), 56.2 (q, Ar-OCH_3), 56.1 (q, Ar-OCH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{17}H_{17}BrNaO_3]^+$=$[M+Na]^+$: 371.0253; found 371.0251.



6nb

(E)-1-(2-Bromo-4,5-dimethoxyphenyl)-3-(3-methoxyphenyl)prop-2-en-1-ol (6nb): **GP-2** was carried out on bromo aryl allylic alcohol **4n** (100 mg, 0.37 mmol) with $Pd(OAc)_2$ (4.1 mg, 5 mol%), $Bn(Et)_3NCl$ (83.2 mg, 0.4 mmol), $NaHCO_3$ (62 mg, 0.73 mmol), iodoanisole **5b** (103 mg, 0.44 mmol) in dry acetonitrile (2 mL), and the reaction mixture was heated at 50 °C for 24 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 90:10 to 80:20) furnished the product **6nb** (101 mg, 73%), (followed **GP-3** under microwave irradiation conditions, 94 mg, 68%) as yellow viscous liquid. [TLC control R_f(**4n**)=0.50, R_f(**6nb**)=0.45 (petroleum ether/ethyl acetate 7:3, UV detection)].

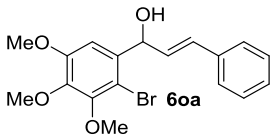
IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3475, 2949, 1593, 1498, 1256, 1154, 1036, 910, 781 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.14 (dd, 1H, *J*=8.0 and 7.9 Hz, Ar-H), 7.02 (s, 1H, Ar-H), 6.92 (s, 1H, Ar-H), 6.90 (d, 1H, *J*=8.0 Hz, Ar-H), 6.83 (s, 1H, Ar-H), 6.71 (dd, 1H, *J*=7.9 and 1.9 Hz, Ar-H), 6.60 (d, 1H, *J*=15.8 Hz, CH=C*H*-Ar), 6.21 (dd, 1H, *J*=15.8 and 5.9 Hz, C*H*=CH-Ar), 5.62 [d, 1H, *J*=5.9 Hz, Ar-C*H*(OH)-CH=CH], 3.80 (s, 3H, Ar-OCH_3), 3.78 (s, 3H, Ar-OCH_3), 3.72 (s, 3H, Ar-OCH_3), 2.33 (br. s, 1H, OH) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=159.8 (s, Ar-C), 149.0 (s, Ar-C), 148.9 (s, Ar-C), 138.0 (s, Ar-C), 133.7 (s, Ar-C), 130.5 (d, Ar-CH), 130.2 (d, Ar-CH), 129.5 (d, Ar-CH), 119.3 (d, Ar-CH), 115.3 (d, CH=*C*H-Ar), 113.5 (d, Ar-CH), 112.3 (s, Ar-C), 111.9

(d, Ar-CH), 110.3 (d, *C*H=CH-Ar), 73.2 (d, Ar-*C*HOH), 56.2 (q, Ar-OCH_3), 56.1 (q, Ar-OCH_3), 55.2 (q, Ar-OCH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{18}H_{19}BrNaO_4]^+$=$[M+Na]^+$: 401.0359; found 401.0360.



6oa

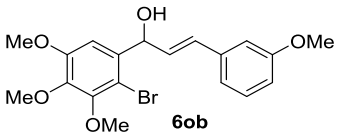
(E)-1-(2-Bromo-3,4,5-trimethoxyphenyl)-3-phenylprop-2-en-1-ol (6oa): GP-2 was carried out on bromo aryl allylic alcohol **4o** (100 mg, 0.33 mmol) with $Pd(OAc)_2$ (3.7 mg, 5 mol%), $Bn(Et)_3NCl$ (74 mg, 0.33 mmol), $NaHCO_3$ (55 mg, 0.66 mmol), iodobenzene **5a** (80.7 mg, 0.39 mmol) in dry acetonitrile (2 mL), and the reaction mixture was heated at 50 °C for 24 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 88:12 to 70:30) furnished the product **6oa** (105 mg, 84%), (followed **GP-3** under microwave irradiation conditions, 96 mg, 77%) as yellow viscous liquid. [TLC control R_f(**4o**)=0.40, R_f(**6oa**)=0.30 (petroleum ether/ethyl acetate 70:30, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3461, 2949, 2888, 2835, 1573, 1474, 1392, 1240, 1102, 1008, 745 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.37 (d, 2H, *J*=7.7 Hz, Ar-H), 7.28 (dd, 2H, *J*=7.5 and 7.4 Hz, Ar-H), 7.22 (dd, 1H, *J*=7.0 and 6.1 Hz, Ar-H), 7.00 (s, 1H, Ar-H), 6.73 (d, 1H, *J*=15.8 Hz, CH=C*H*-Ar), 6.28 (d, 1H, *J*=15.8 and 6.0 Hz, C*H*=CH-Ar), 5.75 [d, 1H, *J*=6.0 Hz, Ar-C*H*(OH)-CH=CH], 3.87 (s, 3H, Ar-OCH_3), 3.85 (s, 3H, Ar-OCH_3), 3.78 (s, 3H, Ar-OCH_3), 2.83 (br. s, 1H, OH) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=153.1 (s, Ar-C), 150.6 (s, Ar-C), 142.4 (s, Ar-C), 137.4 (s, Ar-C), 136.5 (s, Ar-C), 130.7 (d, Ar-CH), 129.6 (d, CH=*C*H-Ar), 128.6 (d, 2C, Ar-CH), 127.8 (d, *C*H=CH-Ar), 126.6 (d, 2C, Ar-CH), 108.7 (s, Ar-C), 106.3 (d, Ar-CH), 73.3 (d, Ar-*C*HOH), 61.1 (q, Ar-OCH_3), 61.0 (q, Ar-OCH_3), 56.1 (q, Ar-OCH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{18}H_{19}BrKO_4]^+=[M+K]^+$: 417.0098; found 417.0097.



6ob

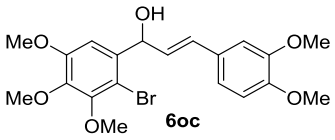
(E)-1-(2-Bromo-3,4,5-trimethoxyphenyl)-3-(3-methoxyphenyl)prop-2-en-1-ol (6ob): GP-2 was carried out on bromo aryl allylic alcohol **4o** (100 mg, 0.33 mmol) with $Pd(OAc)_2$ (3.7 mg, 5 mol%), $Bn(Et)_3NCl$ (74 mg, 0.33 mmol), $NaHCO_3$ (55 mg, 0.66 mmol), iodoanisole **5b** (93 mg, 0.39 mmol) in dry acetonitrile (2 mL), and the reaction mixture was heated at 50 °C for 24 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 88:12 to 70:30) furnished the product **6ob** (103 mg, 77%), (followed **GP-3** under microwave irradiation conditions, 109 mg, 82%) as yellow viscous liquid. [TLC control R_f(**4o**)=0.40, R_f(**6ob**)=0.25 (petroleum ether/ethyl acetate 70:30, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3420, 2933, 2842, 1580, 1474, 1390, 1249, 1101, 1006, 776 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.19 (dd, 1H, *J*=7.8 and 7.7 Hz, Ar-H), 6.97 (d, 2H, *J*=5.7 Hz, Ar-H), 6.89 (s, 2H, Ar-H), 6.76 (d, 1H, *J*=8.4 Hz, Ar-H), 6.69 (d, 1H, *J*=15.8 Hz, CH=C*H*-Ar), 6.26 (dd, 1H, *J*=15.9 and 5.9 Hz, C*H*=CH-Ar), 5.74 [d, 1H, *J*=5.9 Hz, Ar-C*H*(OH)-CH=CH], 3.87 (s, 3H, Ar-OCH_3), 3.86 (s, 3H, Ar-OCH_3), 3.84 (s, 3H, Ar-OCH_3), 3.81 (s, 3H, Ar-OCH_3), 2.83 (br. s, 1H, OH) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=159.7 (s, Ar-C), 153.1 (s, Ar-C), 150.6 (s, Ar-C), 142.4 (s, Ar-C), 138.0 (s, Ar-C), 137.4 (s, Ar-C), 130.6 (d, Ar-CH), 130.0 (d, Ar-CH), 129.5 (d, Ar-CH), 119.3 (d, Ar-CH), 113.4 (d, CH=*C*H-Ar), 111.9 (d, CH=*C*H-Ar), 108.7 (s, Ar-C), 106.3 (d, Ar-CH), 73.2 (d, Ar-*C*HOH), 61.1 (q, Ar-OCH_3), 61.1 (q, Ar-OCH_3), 56.1 (q, Ar-OCH_3), 55.2 (q, Ar-OCH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{19}H_{21}BrNaO_5]^+=[M+Na]^+$: 431.0465; found 431.0470.



6oc

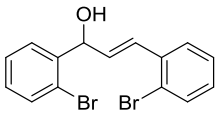
(E)-1-(2-Bromo-3,4,5-trimethoxyphenyl)-3-(3,4-dimethoxyphenyl)prop-2-en-1-ol (6oc): GP-2 was carried out on bromo aryl allylic alcohol **4o** (60 mg, 0.20 mmol) with $Pd(OAc)_2$ (2.2 mg, 5 mol%), $Bn(Et)_3NCl$ (45 mg, 0.20 mmol), $NaHCO_3$ (33.3 mg, 0.40 mmol), iodovaratrole **5c** (62.3 mg, 0.24 mmol) in dry acetonitrile (2 mL), and the reaction mixture was heated at 50 °C for 24 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 88:12 to 70:30) furnished the product **6oc** (52 mg, 61%) as yellow viscous liquid, (followed **GP-3** under microwave irradiation conditions, 55 mg, 65%). [TLC control R_f(**4o**)=0.60, R_f(**6oc**)=0.**30** (petroleum ether/ethyl acetate 70:30, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3497, 2935, 2839, 1573, 1512, 1469, 1387, 1247, 1150, 1012, 807, 768 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.00 (s, 1H, Ar-H), 6.90 (s, 2H, Ar-H), 6.78 (d, 1H, *J*=4.2 Hz, Ar-H), 6.65 (d, 1H, *J*=15.8 Hz, CH=C*H*-Ar), 6.15 (dd, 1H, *J*=15.8 and 6.2 Hz, C*H*=CH-Ar), 5.73 [d, 1H, *J*=6.2 Hz, Ar-C*H*(OH)-CH=CH], 3.91 (s, 3H, Ar-OCH_3), 3.87 (s, 3H, Ar-OCH_3), 3.86 (s, 6H, 2 Ar-OCH_3), 3.84 (s, 3H, Ar-OCH_3), 2.83 (br. s, 1H, OH) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=153.1 (s, Ar-C), 150.6 (s, Ar-C), 149.0 (s, 2C, Ar-C), 142.4 (s, Ar-C), 137.5 (s, Ar-C), 130.8 (d, CH=*C*H-Ar), 129.5 (s, Ar-C), 127.6 (d, *C*H=CH-Ar), 119.9 (d, Ar-CH), 111.0 (d, Ar-CH), 108.9 (d, Ar-CH), 108.7 (s, Ar-C), 106.3 (d, Ar-CH), 73.4 (d, Ar-*C*HOH), 61.0 (q, Ar-OCH_3), 61.0 (q, Ar-OCH_3), 56.1 (q, Ar-OCH_3), 55.9 (q, Ar-OCH_3), 55.8 (q, Ar-OCH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{20}H_{23}BrNaO_6]^+$=$[M+Na]^+$: 461.0570; found 461.0576.



6he

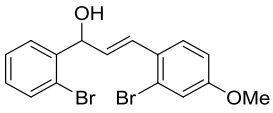
(E)-1,3-Bis(2-bromophenyl)prop-2-en-1-ol (6he): GP-2 was carried out on bromo aryl allylic alcohol **4h** (100 mg, 0.47 mmol) with $Pd(OAc)_2$ (5.2 mg, 5 mol%), $Bn(Et)_3NCl$ (106 mg, 0.47 mmol), $NaHCO_3$ (78 mg, 0.94 mmol), bromoiodobenzene **5e** (159 mg, 0.56 mmol) in dry acetonitrile (2 mL), and the reaction mixture was heated at 50 °C for 24 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 95:5 to 80:10) furnished the product **6he** (137 mg, 80%) as yellow viscous liquid, (followed **GP-3** under microwave irradiation conditions, 128 mg, 75%). [TLC control R_f(**4h**)=0.30, R_f(**6he**)=0.25 (petroleum ether/ethyl acetate 90:10, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3340, 3060, 2922, 1571, 1464, 1431, 1266, 1121, 1016, 746, 673 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.62 (d, 1H, *J*=7.7 Hz, Ar-H), 7.55 (dd, 2H, *J*=7.7 and 7.6 Hz, Ar-H), 7.48 (d, 1H, *J*=7.8 Hz, Ar-H), 7.36 (dd, 1H, *J*=7.3 and 7.3 Hz, Ar-H), 7.23 (dd, 1H, *J*=7.6 and 7.6 Hz, Ar-H), 7.20–7.00 (m, 3H, Ar-H and CH=C*H*-Ar), 6.26 (dd, 1H, *J*=15.8 and 5.9 Hz, C*H*=CH-Ar), 5.81 [d, 1H, *J*=5.9 Hz, Ar-C*H*(OH)-CH=CH], 2.51 (br. s, 1H, OH) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=141.3 (s, Ar-C), 136.5 (s, Ar-C), 132.9 (d, Ar-CH), 132.9 (d, CH=*C*H-Ar), 132.6 (d, Ar-CH), 129.8 (d, Ar-CH), 129.3 (d, *C*H=CH-Ar), 129.1 (d, Ar-CH), 128.0 (d, 2C, Ar-CH), 127.5 (d, Ar-CH), 127.2 (d, Ar-CH), 123.9 (s, Ar-C), 122.5 (s, Ar-C), 73.3 (d, Ar-*C*HOH) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{15}H_{12}Br_2NaO]^+$=$[M+Na]^+$: 388.9147; found 388.9150.



6hf

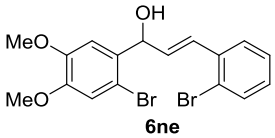
(E)-1-(2-Bromo-4,5-dimethoxyphenyl)-3-(2-bromophenyl)prop-2-en-1-ol (6hf): **GP-2** was carried out on bromo aryl allylic alcohol **4h** (100 mg, 0.47 mmol) with $Pd(OAc)_2$ (5.2 mg, 5 mol%), $Bn(Et)_3NCl$ (106 mg, 0.47 mmol), $NaHCO_3$ (78 mg, 0.94 mmol), 3-iodo-4-bromoanisole **5f** (175 mg, 0.56 mmol) in dry acetonitrile (2 mL), and the reaction mixture was heated at 50 °C for 24 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 95:5 to 85:15) furnished the product **6hf** (74 mg, 40%) as yellow viscous liquid (followed **GP-3** under microwave irradiation conditions, 66 mg, 36%). [TLC control R_f(**4h**)=0.50, R_f(**6hf**)=0.35 (petroleum ether/ethyl acetate 80:20, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3401, 3062, 2949, 2838, 1645, 1600, 1487, 1393, 1287, 1245, 1029, 734 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.54 (dd, 1H, *J*=7.8 and 1.5 Hz, Ar-H), 7.47 (dd, 1H, *J*=8.0 and 0.8 Hz, Ar-H), 7.32 (d, 1H, *J*=8.7 Hz, Ar-H), 7.27 (dd, 1H, *J*=7.64 and 7.38 Hz, Ar-H), 7.07 (dd, 1H, *J*=7.64 and 7.64 Hz, Ar-H), 7.00–6.90 (m, 2H, Ar-H and C*H*=C*H*-Ar), 6.72 (dd, 1H, *J*=8.7 and 2.5 Hz, Ar-H), 6.06 (dd, 1H, *J*=15.7 and 5.9 Hz, C*H*=CH-Ar), 5.69 [d, 1H, *J*=5.9 Hz, Ar-C*H*(OH)-CH=CH], 3.70 (s, 3H, Ar-OCH_3), 2.27 (br. s, 1H, OH) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=159.6 (s, Ar-C), 141.6 (s, Ar-C), 132.9 (d, Ar-CH), 130.5 (d, Ar-CH), 129.5 (d, Ar-CH), 129.2 (d, Ar-CH), 129.0 (s, Ar-C), 127.9 (d, 2C, Ar-CH), 127.7 (d, Ar-CH), 124.3 (s, Ar-C), 122.5 (s, Ar-C), 117.6 (d, CH=*C*H-Ar), 114.1 (d, *C*H=CH-Ar), 73.5 (d, Ar-*C*HOH), 55.6 (q, Ar-OCH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{16}H_{14}Br_2NaO_2]^+$=$[M+Na]^+$: 418.9253; found 418.9257.



6ne

(E)-1-(2-Bromo-4,5-dimethoxyphenyl)-3-(2-bromophenyl)prop-2-en-1-ol (6ne): **GP-2** was carried out on bromo aryl allylic alcohol **4n** (100 mg, 0.37 mmol) with $Pd(OAc)_2$ (4.1 mg, 5 mol%), $Bn(Et)_3NCl$ (83.2 mg, 0.4 mmol), $NaHCO_3$ (62 mg, 0.73

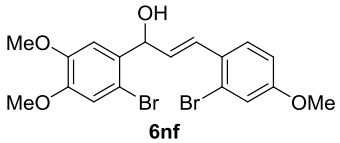
mmol), 2-bromoiodobenzene **5e** (124 mg, 0.44 mmol) in dry acetonitrile (2 mL), and the reaction mixture was heated at 50 °C for 24 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 90:10 to 80:20) furnished the product **6ne** (127 mg, 81%) as brown viscous liquid, (followed **GP-3** under microwave irradiation conditions, 125 mg, 80%). [TLC control R_f(**4n**)=0.50, R_f(**6ne**)=0.51 (petroleum ether/ethyl acetate 70:30, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3491, 3061, 2935, 2842, 1597, 1500, 1255, 1205, 1153, 1027, 965, 744 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.45 (dd, 1H, *J*=8.0 and 0.8 Hz, Ar-H), 7.39 (dd, 1H, *J*=7.8 and 1.3 Hz, Ar-H), 7.15 (dd, 1H, *J*=7.5 Hz and 7.5 Hz, Ar-H), 7.04 (s, 1H, Ar-H), 7.03 (d, 1H, *J*=15.8 Hz, CH=C*H*-Ar), 7.00 (ddd, 1H, *J*=7.5, 7.5 and 1.5 Hz, Ar-H), 6.92 (s, 1H, Ar-H), 6.14 (dd, 1H, *J*=15.8 and 5.8 Hz, C*H*=CH-Ar), 5.67 [dd, 1H, *J*=5.8 and 1.0 Hz, Ar-C*H*(OH)-CH=CH], 3.81 (s, 3H, Ar-OCH_3), 3.79 (s, 3H, Ar-OCH_3), 2.39 (br. s, 1H, OH) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=149.0 (s, Ar-C), 148.9 (s, Ar-C), 136.6 (s, Ar-C), 133.4 (s, Ar-C), 132.9 (d, 2C, Ar-CH), 129.5 (d, Ar-CH), 129.0 (d, Ar-CH), 127.5 (d, Ar-CH), 127.2 (d, Ar-CH), 123.8 (s, Ar-C), 115.3 (d, CH=*C*H-Ar), 112.3 (s, Ar-C), 110.2 (d, *C*H=CH-Ar), 73.2 (d, Ar-*C*HOH), 56.2 (q, Ar-OCH_3), 56.1 (q, Ar-OCH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{17}H_{16}Br_2NaO_3]^+$=$[M+Na]^+$: 448.9358; found 448.9356.



6nf

(E)-1-(2-Bromo-4,5-dimethoxyphenyl)-3-(2-bromo-4-methoxyphenyl)prop-2-en-1-ol (6nf): GP-2 was carried out on bromo aryl allylic alcohol **4n** (100 mg, 0.37 mmol) with $Pd(OAc)_2$ (4.1 mg, 5 mol%), $Bn(Et)_3NCl$ (83.2 mg, 0.4 mmol), $NaHCO_3$ (62 mg, 0.73 mmol), 3-bromo-4-iodoanisole **5f** (138 mg, 0.44 mmol) in dry acetonitrile (2 mL),

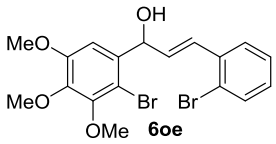
and the reaction mixture was heated at 50 °C for 24 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 88:12 to 75:25) furnished the product **6nf** (55.2 mg, 33%) as yellow viscous liquid, (followed **GP-3** under microwave irradiation conditions, 48 mg, 29%). [TLC control R_f(**4n**)=0.50, R_f(**6nf**)=0.40 (petroleum ether/ethyl acetate 70:30, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3494, 2934, 2847, 1601, 1498, 1254, 1033, 905, 726 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.33 (d, 1H, *J*=8.7 Hz, Ar-H), 7.06 (s, 1H, Ar-H), 7.01 (d, 1H, *J*=2.6 Hz, Ar-H), 6.95 (d, 1H, *J*=15.8 Hz, CH=C*H*-Ar), 6.93 (s, 1H, Ar-H), 6.73 (dd, 1H, *J*=8.7 and 2.5 Hz, Ar-H), 6.04 (dd, 1H, *J*=15.8 and 6.0 Hz, C*H*=CH-Ar), 5.65 [d, 1H, *J*=6.0 Hz, Ar-C*H*(OH)-CH=CH], 3.82 (s, 3H, Ar-OCH_3), 3.79 (s, 3H, Ar-OCH_3), 3.71 (s, 3H, Ar-OCH_3), 2.19 (br. s, 1H, OH) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=159.6 (s, Ar-*C*), 149.0 (s, Ar-*C*), 148.9 (s, Ar-*C*), 133.6 (s, Ar-C), 130.8 (d, Ar-CH), 129.1 (d, Ar-CH), 129.1 (s, Ar-C), 127.7 (d, Ar-CH), 124.2 (s, Ar-C), 117.6 (d, Ar-CH), 115.3 (d, CH=*C*H-Ar), 114.1 (d, Ar-CH), 112.3 (s, Ar-C), 110.2 (d, *C*H=CH-Ar), 73.3 (d, Ar-*C*HOH), 56.2 (q, Ar-OCH_3), 56.1 (q, Ar-OCH_3), 55.6 (q, Ar-OCH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{18}H_{18}Br_2NaO_4]^+$=$[M+Na]^+$: 478.9464; found 478.9468.



6oe

(E)-1-(2-Bromo-3,4,5-trimethoxyphenyl)-3-(2-bromophenyl)prop-2-en-1-ol (6oe): **GP-2** was carried out on bromo aryl allylic alcohol **4o** (100 mg, 0.33 mmol) with $Pd(OAc)_2$ (3.7 mg, 5 mol%), $Bn(Et)_3NCl$ (74 mg, 0.33 mmol), $NaHCO_3$ (55 mg, 0.66 mmol), bromoiodobenzene **5e** (112 mg, 0.39 mmol) in dry acetonitrile (2 mL), and the reaction mixture was heated at 50 °C for 24 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 90:10 to 80:20) furnished the

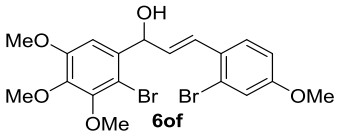
product **6oe** (113 mg, 75%) as yellow viscous liquid, (followed **GP-3** under microwave irradiation conditions, 116 mg, 77%). [TLC control R_f(**4o**)=0.40, R_f(**6oe**)=0.35 (petroleum ether/ethyl acetate 70:30, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3447, 2935, 1572, 1471, 1434, 1389, 1159, 1008, 750 cm^{-1}.

^{1}H-NMR (CDCl$_3$, 400 MHz): δ=7.51 (d, 1H, *J*=7.8 Hz, Ar-H), 7.46 (d, 1H, *J*=7.8 Hz, Ar-H), 7.21 (dd, 1H, *J*=7.5 and 7.5 Hz, Ar-H), 7.10 (d, 1H, *J*=15.8 Hz, CH=C*H*-Ar), 7.07 (dd, 1H, *J*=7.5 and 7.5 Hz, Ar-H), 7.00 (s, 1H, Ar-H), 6.21 (dd, 1H, *J*=15.8 and 5.8 Hz, CH=C*H*-Ar), 5.80 [d, 1H, *J*=5.8 Hz, Ar-C*H*(OH)-CH=CH], 3.88 (s, 3H, Ar-OCH$_3$), 3.86 (s, 6H, 2 × Ar-OCH$_3$), 2.62 (br. s, 1H, OH) ppm.

^{13}C-NMR (CDCl$_3$, 100 MHz): δ=153.1 (s, Ar-C), 150.6 (s, Ar-C), 142.5 (s, Ar-C), 137.0 (s, Ar-C), 136.5 (s, Ar-C), 132.8 (d, Ar-CH), 132.6 (d, CH=*C*H-Ar), 129.5 (d, Ar-CH), 128.9 (d, *C*H=CH-Ar), 127.4 (d, Ar-CH), 127.1 (d, Ar-CH), 123.8 (s, Ar-C), 108.6 (s, Ar-C), 106.3 (d, Ar-CH) 73.1 (d, Ar-*C*HOH), 61.1 (q, Ar-OCH$_3$), 61.0 (q, Ar-OCH$_3$), 56.1 (q, Ar-OCH$_3$) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{18}H_{18}Br_2NaO_4]^+$=$[M+Na]^+$: 478.9464; found 478.9464.



6of

(E)-1-(2-Bromo-3,4,5-trimethoxyphenyl)-3-(2-bromo-4-methoxyphenyl)prop-2-en-1-ol (6of): GP-2 was carried out on bromo aryl allylic alcohol **4o** (100 mg, 0.33 mmol) with Pd(OAc)$_2$ (3.7 mg, 5 mol%), Bn(Et)$_3$NCl (74 mg, 0.33 mmol), NaHCO$_3$ (55 mg, 0.66 mmol), bromoiodoanisole **5f** (123 mg, 0.39 mmol) in dry acetonitrile (2 mL), and the reaction mixture was heated at 50 °C for 24 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 80:20 to 65:35) furnished the product **6of** (93 mg, 58%) as yellow viscous liquid, (followed **GP-3** under microwave

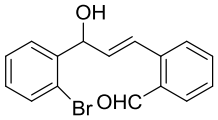
irradiation conditions, 83 mg, 52%). [TLC control R_f(**4o**)=0.60, R_f(**6of**)=0.58 (petroleum ether/ethyl acetate 50:50, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3471, 2933, 2841, 1595, 1569, 1478, 1390, 1240, 1101, 1012, 807 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.37 (d, 1H, *J*=7.9 Hz, Ar-H), 7.1–6.90 (m, 3H, Ar-H and CH=C*H*-Ar), 6.81 (s, 1H, Ar-H), 6.08 (dd, 1H, *J*=15.2 and 4.7 Hz, C*H*=CH-Ar), 5.79 [s, 1H, Ar-C*H*(OH)-CH=CH], 3.91 (s, 3H, Ar-OCH_3), 3.85 (s, 3H, Ar-OCH_3), 3.80 (s, 3H, Ar-OCH_3), 3.75 (s, 3H, Ar-OCH_3), 2.83 (br. s, 1H, OH) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=159.5 (s, Ar-C), 153.1 (s, Ar-C), 150.6 (s, Ar-C), 142.4 (s, Ar-C), 137.3 (s, Ar-C), 130.6 (d, Ar-CH), 129.2 (d, Ar-CH), 129.0 (s, Ar-C), 127.6 (d, CH=*C*H-Ar), 124.2 (s, Ar-C), 117.6 (d, CH=*C*H-Ar), 114.1 (d, Ar-CH), 108.6 (s, Ar-C), 106.3 (d, Ar-CH), 73.3 (d, Ar-*C*HOH), 61.1 (q, Ar-OCH_3), 61.0 (q, Ar-OCH_3), 56.1 (q, Ar-OCH_3), 55.5 (q, Ar-OCH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{19}H_{20}Br_2NaO_5]^+$=$[M+Na]^+$: 508.9570; found 508.9575.



6hh

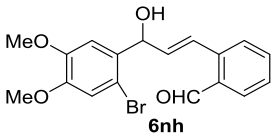
2-((E)-3-(2-Bromophenyl)-3-hydroxyprop-1-enyl)benzaldehyde (6hh): GP-2 was carried out on bromo aryl allylic alcohol **4h** (120 mg, 0.56mmol) with $Pd(OAc)_2$ (6.3 mg, 5 mol%), $Bn(Et)_3NCl$ (127 mg, 0.56 mmol), $NaHCO_3$ (94 mg, 1.12 mmol), bromobenzaldehyde **5h** (125 mg, 0.67 mmol) in dry acetonitrile (2 mL), and the reaction mixture was heated at 50 °C for 24 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 90:10 to 80:20) furnished the product **6hh** (105 mg, 59%) as brown viscous liquid, (followed **GP-3** under microwave irradiation conditions, 112 mg, 63%). [TLC control R_f(**4h**)=0.40, R_f(**6hh**)=0.20 (petroleum ether/ethyl acetate 80:20, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3409, 3061, 2923, 2856, 1688, 1592, 1462, 1197, 1018, 746 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ= 10.23 (s, 1H, Ar-C*H*O), 7.77 (d, 1H, *J*=7.5 Hz, Ar-H), 7.62 (d, 1H, *J*=7.8 Hz, Ar-H), 7.57–7.27 (m, 6H, Ar-H and CH=C*H*-Ar), 7.13 (dd, 1H, *J*=7.5 and 7.5 Hz, Ar-H), 6.26 (dd, 1H, *J*=15.0 and 5.5 Hz, C*H*=CH-Ar), 5.82 [d, 1H, *J*=5.5 Hz, Ar-C*H*(OH)-CH=CH], 3.10 (br. s, 1H, OH) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=192.4 (s, Ar-CHO), 141.3 (s, Ar-C), 139.5 (s, Ar-C), 135.4 (d, CH=*C*H-Ar), 133.7 (d, Ar-CH), 132.9 (s, Ar-C), 132.8 (d, *C*H=CH-Ar), 131.1 (d, Ar-CH), 129.2 (d, Ar-CH), 128.0 (d, Ar-CH), 127.9 (d, Ar-CH), 127.8 (d, Ar-CH), 127.7 (d, Ar-CH), 126.9 (d, Ar-CH), 122.3 (s, Ar-C), 73.1 (d, Ar-*C*HOH) ppm.

HR-MS (ESI^{+}): m/z calculated for $[C_{16}H_{13}BrNaO_2]^{+}$=$[M+Na]^{+}$: 338.9991; found 338.9989.



6nh

2-((E)-3-(2-Bromo-4,5-dimethoxyphenyl)-3-hydroxyprop-1-enyl)benzaldehyde (6nh): GP-2 was carried out on bromo aryl allylic alcohol **4n** (100 mg, 0.37 mmol) with $Pd(OAc)_2$ (4.1 mg, 5 mol%), $Bn(Et)_3NCl$ (83.2 mg, 0.4 mmol), $NaHCO_3$ (62 mg, 0.73 mmol), 2-bromobenzaldehyde **5h** (81.3 mg, 0.44 mmol) in dry acetonitrile (2 mL), and the reaction mixture was heated at 50 °C for 24 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 88:12 to 80:20) furnished the product **6nh** (83 mg, 64%) as yellow viscous liquid, (followed **GP-3** under microwave irradiation conditions, 77 mg, 60%). [TLC control R_f(**4n**)=0.50, R_f(**6nh**)=0.49 (petroleum ether/ethyl acetate 70:30, UV detection)].

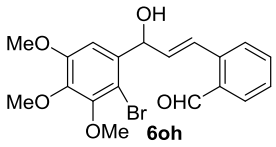
IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3468, 2926, 1690, 1500, 1255, 1203, 1032, 967, 759 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=10.18 (s, 1H, Ar-CHO), 7.72 (d, 1H, *J*=7.6 Hz, Ar-H), 7.48 (dd, 1H, *J*=15.8 and 1.0 Hz, CH=C*H*-Ar), 7.44 (d, 1H, *J*=5.2 Hz, Ar-H),

7.43 (d, 1H, *J*=2.5 Hz, Ar-H), 7.32 (ddd, 1H, *J*=8.0, 5.6 and 2.7 Hz, Ar-H), 7.07 (s, 1H, Ar-H), 6.92 (s, 1H, Ar-H), 6.16 (dd, 1H, *J*=15.8 and 5.8 Hz, C*H*=CH-Ar), 5.69 [dd, 1H, *J*=5.8 and 1.1 Hz, Ar-C*H*(OH)-CH=CH], 3.81 (s, 3H, Ar-OCH_3), 3.78 (s, 3H, Ar-OCH_3), 2.79 (br. s, 1H, OH) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=192.5 (d, Ar-*C*=O), 149.0 (s, Ar-*C*), 148.9 (s, Ar-*C*), 139.6 (s, Ar-C), 135.5 (d, Ar-CH), 133.8 (d, Ar-CH), 133.3 (s, Ar-C), 132.9 (s, Ar-C), 131.4 (d, Ar-CH), 127.8 (d, Ar-CH), 127.8 (d, Ar-CH), 126.7 (d, Ar-CH), 115.3 (d, CH=*C*H-Ar), 112.2 (s, Ar-C), 110.2 (d, *C*H=CH-Ar), 73.1 (d, Ar-*C*HOH), 56.2 (q, Ar-OCH_3), 56.1 (q, Ar-OCH_3) ppm.

HR-MS (ESI+): m/z calculated for $[C_{18}H_{17}BrNaO_4]^+$=$[M+Na]^+$: 399.0202; found 399.0206.



6oh

2-((E)-3-(2-Bromo-3,4,5-trimethoxyphenyl)-3-hydroxyprop-1-enyl)benzaldehyde (6oh): GP-2 was carried out on bromo aryl allylic alcohol **4o** (100 mg, 0.33 mmol) with $Pd(OAc)_2$ (3.7 mg, 5 mol%), $Bn(Et)_3NCl$ (74 mg, 0.33 mmol), $NaHCO_3$ (55 mg, 0.66 mmol), bromobenzaldehyde **5h** (73 mg, 0.39 mmol) in dry acetonitrile (2 mL), and the reaction mixture was heated at 50 °C for 24 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 80:20 to 70:30) furnished the product **6oh** (100 mg, 75%) as yellow viscous liquid, (followed **GP-3** under microwave irradiation conditions, 101 mg, 76%). [TLC control R_f(**4o**)=0.60, R_f(**6oh**)=0.40 (petroleum ether/ethyl acetate 50:50, UV detection)].

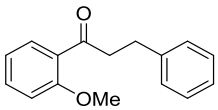
IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3452, 2933, 2851, 1691, 1567, 1473, 1389, 1101, 758 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=10.19 (s, 1H, Ar-CHO), 7.73 (d, 1H, *J*=7.6 Hz, Ar-H), 7.52 (d, 1H, *J*=15.7 Hz, CH=C*H*-Ar), 7.44 (d, 2H, *J*=3.5 Hz, Ar-H), 7.40–7.25 (m, 1H, Ar-H), 6.96 (s, 1H, Ar-H), 6.17 (dd, 1H, *J*=15.8 and 5.8 Hz, C*H*=CH-Ar), 5.76

[d, 1H, *J*=5.4 Hz, Ar-C*H*(OH)-CH=CH], 3.82 (s, 3H, Ar-OCH_3), 3.80 (s, 6H, 2 × Ar-OCH_3), 2.74 (br. s, 1H, -OH) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=192.5 (s, Ar-CHO), 153.3 (s, Ar-C), 150.7 (s, Ar-C), 142.6 (s, Ar-C), 139.5 (s, Ar-C), 137.0 (s, Ar-C), 135.2 (d, CH=*C*H-Ar), 133.8 (s, Ar-C), 133.0 (d, Ar-CH), 131.5 (d, Ar-CH), 127.9 (d, Ar-CH), 127.8 (d, Ar-CH), 126.9 (d, *C*H=CH-Ar), 108.6 (s, Ar-C), 106.3 (d, Ar-CH), 73.2 (d, Ar-*C*HOH), 61.1 (q, Ar-OCH_3), 61.1 (q, Ar-OCH_3), 56.2 (q, Ar-OCH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{19}H_{19}BrNNaO_5]^+$=$[M+Na]^+$: 429.0314; found 429.0314.



7pa

1-(2-Methoxyphenyl)-3-phenylpropan-1-one (7pa) and (E)-1-(2-Methoxyphenyl)-3-phenylprop-2-en-1-ol (6pa): GP-2 was carried out on methoxy phenyl allylic alcohol **4p** (100 mg, 0.60 mmol) with $Pd(OAc)_2$ (6.8 mg, 5mol%), $Bn(Et)_3NCl$ (138 mg, 0.60 mmol), $NaHCO_3$ (102 mg, 1.20 mmol), iodobenzene **5a** (149 mg, 0.72 mmol) in dry acetonitrile (2 mL), and the reaction mixture was heated at 50 °C for 24 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 95:5) furnished the product **7pa** (40 mg, 27%) as yellow liquid, (followed **GP-3** under microwave irradiation conditions, 43 mg, 29%).

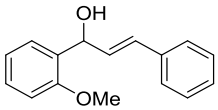
For compound **7pa:**

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3021, 2932, 2845, 1672, 1593, 1470, 1450, 1242, 1022, 981, 751 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.70 (dd, 1H, *J*=7.7 and 1.7 Hz, Ar-H), 7.46 (ddd, 1H, *J*=7.7 and 1.7 Hz, Ar- H), 7.35-7.10 (m, 5H, Ar-H), 7.00 (t, 1H, *J*=7.5 Hz, Ar-H), 6.96 (d, 1H, *J*=8.2 Hz, Ar-H), 3.88 (s, 3H, Ar-OCH_3), 3.31 (t, 2H, *J*=7.3 Hz, ArCOCH_2), 3.03 [t, 2H, *J*=7.3 Hz, Ar(CO)CH_2CH_2] ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=201.7 (s, Ar-CO), 158.5 (s, Ar-C), 141.7 (s, Ar-C), 133.4 (d, Ar-CH), 130.3 (d, Ar-CH), 128.4 (d, 2C, Ar-CH), 128.3 (d, 2C, Ar-CH), 128.2 (s, Ar-C), 125.8 (d, Ar-CH), 120.6 (d, Ar-CH), 111.4 (d, Ar-CH), 55.4 (q, Ar-OCH_3), 45.4 (t, $ArCOCH_2$), 30.4 (t, $PhCH_2$) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{16}H_{16}NaO_2]^+$=$[M+Na]^+$: 263.1043; found 263.1042.



6pa

Further elution of column (petroleum ether/ethyl acetate 93:7 to 80:20) furnished the product **6pa** (89 mg, 61%) as brown viscous liquid, (followed **GP-3** under microwave irradiation conditions, 94 mg, 65%). [TLC control R_f(**4p**)=0.30, R_f(**7pa**)=0.50 and R_f(**6pa**)=0.20 (petroleum ether/ethyl acetate 8:2, UV detection)].

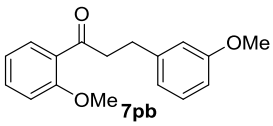
For compound **6pa**

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3385, 3026, 2928, 1593, 1489, 1453, 1238, 1022, 967, 745 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.40-7.15 (m, 7H, Ar-H), 6.95 (dd, 1H, *J*=7.5 and 7.2 Hz, Ar-H), 6.88 (d, 1H, *J*=8.3 Hz, Ar-H), 6.63 (d, 1H, *J*=16.0 Hz, CH=C*H*-Ph), 6.45 (dd, 1H, *J*=16.0 and 6.0 Hz, C*H*=C*H*-Ph), 5.55 [br. s, 1H, Ar-C*H*(OH)], 3.84 (s, 3H, Ar-OCH_3), 2.95 (br. s, 1H, -OH) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ= 156.7 (s, Ar-C), 137.0 (s, Ar-C), 130.9 (d, Ar-CH), 130.8 (s, Ar-C), 130.0 (d, *C*H=CH-Ph), 128.9 (d, CH=*C*H-Ph), 128.5 (d, 2C, Ar-CH), 127.6 (d, Ar-CH), 127.5 (d, Ar-CH), 126.6 (d, 2C, Ar-CH), 121.0 (d, Ar-CH), 110.8 (d, Ar-CH), 71.6 (d, ArCHOH), 55.5 (q, Ar-OCH_3)ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{16}H_{16}NaO_2]^+$=$[M+Na]^+$: 263.1042; found 263.1042.



7pb

1-(2-Methoxyphenyl)-3-(3-methoxyphenyl)propan-1-one (7pb) and (E)-1-(2-Methoxyphenyl)-3-(3-methoxyphenyl)prop-2-en-1-ol (6pb): GP-2 was carried out on methoxy phenyl allylic alcohol **4p** (100 mg, 0.60 mmol) with $Pd(OAc)_2$ (6.8 mg 5 mol%), $Bn(Et)_3NCl$ (138 mg, 0.60 mmol), $NaHCO_3$ (102 mg, 1.20 mmol), iodoanisole **5b** (171 mg, 0.72 mmol) in dry acetonitrile (2 mL), and the reaction mixture was heated at 50 °C for 24 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 95:5) furnished the product **7pb** (37 mg, 23%) as yellow liquid, (followed **GP-3** under microwave irradiation conditions, 41 mg, 26%).

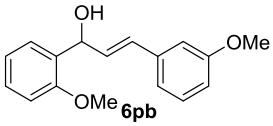
For compound **7pb:**

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2941, 2839, 1672, 1592, 1477, 1449, 1247, 1032, 983, 758 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.69 (dd, 1H, *J*=7.7 and 1.5 Hz, Ar-H), 7.45 (ddd, 1H, *J*=7.7 and 1.5 Hz, Ar- H), 7.20 (dd, 1H, *J*=8.0 and 7.8 Hz, Ar-H), 6.99 (dd, 1H, *J*=7.5 and 7.5 Hz, Ar-H), 6.95 (d, 1H, *J*=7.5 Hz, Ar-H), 6.85-6.70 (m, 3H, Ar-H), 3.87 (s, 3H, Ar-OCH_3), 3.79 (s, 3H, Ar-OCH_3), 3.30 (t, 2H, *J*=7.3 Hz, ArCOCH_2), 3.00 [t, 2H, *J*=7.3 Hz, Ar(CO)CH_2CH_2] ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=201.7 (s, Ar-CO), 159.6 (s, Ar-C), 158.5 (s, Ar-C), 143.3 (s, Ar-C), 133.4 (d, Ar-CH), 130.3 (d, Ar-CH), 129.3 (d, Ar-CH), 128.2 (s, Ar-C), 120.8 (d, Ar-CH), 120.6 (d, Ar-CH), 114.2 (d, Ar-CH), 111.4 (d, Ar-CH), 111.1 (d, Ar-CH), 55.4 (q, Ar-OCH_3), 55.1 (q, Ar-OCH_3), 45.3 (t, $ArCOCH_2$), 30.5 (t, $PhCH_2$) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{17}H_{18}NaO_3]^+$=$[M+Na]^+$: 293.1148; found 293.1145.



6pb

Further elution of column (petroleum ether/ethyl acetate 93:7 to 80:20) furnished the product **6pb** (102 mg, 62%) as brown viscous liquid, (followed **GP-3** under microwave irradiation conditions, 97 mg, 59%). [TLC control R_f(**4p**)=0.30, R_f(**7pb**)=0.50 and R_f(**6pb**)=0.20 (petroleum ether/ethyl acetate 80:20, UV detection)].

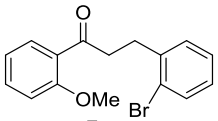
For compound **6pe:**

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3431, 3003, 2931, 2839, 1590, 1481, 1455 1239, 1035, 966, 752 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.26 (d, 1H, *J*=7.5 Hz, Ar-H), 7.16 (dd, 1H, *J*=7.5 and 7.4 Hz, Ar- H), 7.10 (dd, 1H, *J*=7.9 and 7.9 Hz, Ar-H), 6.87 (d, 2H, *J*=7.4 Hz, Ar-H), 6.81 (d, 1H, *J*=7.4 Hz, Ar-H), 6.78 (s, 1H, Ar-H), 6.67 (d, 1H, *J*=8.1 Hz, Ar-H), 6.52 (d, 1H, *J*=15.9 Hz, CH=C*H*-Ar), 6.36 (dd, 1H, *J*=15.9 and 5.9 Hz, C*H*=CH-Ar), 5.48 [d, 1H, *J*=5.9, Ar-C*H*(OH)-CH=CH], 3.74 (s, 3H, Ar-OCH_3), 3.67 (s, 3H, Ar-OCH_3), 2.98 (br. s, 1H, OH) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=159.8 (s, Ar-C), 156.7 (s, Ar-C), 138.5 (s, Ar-C), 131.3 (d, Ar-CH), 130.9 (s, Ar-C), 129.8 (d, CH=*C*H-Ar), 129.5 (d, Ar-CH), 128.9 (d, *C*H=CH-Ar), 127.5 (d, Ar-CH), 121.0 (d, Ar-CH), 119.3 (d, Ar-CH), 113.2 (d, Ar-CH), 111.9 (d, Ar-CH), 110.8 (d, Ar-CH), 71.2 (d, Ar-*C*HOH), 55.5 (q, Ar-OCH_3), 55.2 (q, Ar-OCH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{17}H_{18}NaO_3]^+$=$[M+Na]^+$: 293.1148; found 293.1147.



7pe

3-(2-Bromophenyl)-1-(2-methoxyphenyl)propan-1-one (7pe) and (E)-3-(2-Bromophenyl)-1-(2-methoxyphenyl)prop-2-en-1-ol (6pe): GP-2 was carried out on methoxy phenyl allylic alcohol **4p** (100 mg, 0.60 mmol) with $Pd(OAc)_2$ (6.8 mg, 5 mol%), $Bn(Et)_3NCl$ (138 mg, 0.60 mmol), $NaHCO_3$ (102 mg, 1.20 mmol), bromoiodobenzene **5e** (206 mg, 0.72 mmol) in dry acetonitrile (2 mL), and the reaction

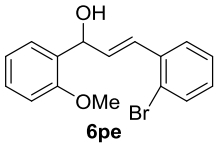
mixture was heated at 50 °C for 24 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 97:3) furnished the product **7pe** (48 mg, 25%) as color less solid, (followed GP-2 under microwave irradiation conditions, 44 mg, 23%), which was recrystallized from a mixture of dichloromethane and hexane, M.P. 78–83 °C.

For compound **7pe:** IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3065, 2941, 2845, 1676, 1596, 1472, 1293, 1027, 756 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.69 (dd, 1H, *J*=7.7 and 1.5 Hz, Ar-H), 7.52 (d, 1H, *J*=7.7 Hz, Ar-H), 7.44 (ddd, 1H, *J*=8.5, 7.7 and 1.5 Hz, Ar-H), 7.27 (td, 1H, *J*=7.7 and 7.5 Hz, Ar-H), 7.22 (dd, 1H, *J*=7.5 and 7.2 Hz, Ar-H), 7.05 (dd, 1H, *J*=8.0 and 7.5 Hz, Ar-H), 6.99 (dd, 1H, *J*=7.5 and 7.5 Hz, Ar-H), 6.94 (d, 1H, *J*= 8.0 Hz, Ar-H), 3.86 (s, 3H, Ar-OCH_3), 3.32 [t, 2H, *J*=7.5 Hz, Ar(CO)CH_2], 3.14 [t, 2H, *J*=7.5 Hz, Ar(CO)CH_2CH_2] ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=201.2 (s, Ar-CO), 158.5 (s, Ar-C), 140.9 (s, Ar-C), 133.4 (d, Ar-CH), 132.7 (d, Ar-CH), 130.6 (d, Ar-CH), 130.3 (d, Ar-CH), 128.1 (s, Ar-C), 127.6 (d, Ar-CH), 127.4 (d, Ar-CH), 124.4 (s, Ar-C), 120.6 (d, Ar-CH), 111.4 (d, Ar-CH), 55.5 (q, Ar-OCH_3), 43.4 (t, Ar-CO-CH_2), 30.9 (t, Ar-CO-CH_2-CH_2) ppm.

HR-MS (ESI+): m/z calculated for $[C_{16}H_{15}BrNaO_2]^+$=$[M+Na]^+$: 341.0148; found 341.01451.



6pe

Further elution of column (petroleum ether/ethyl acetate 93:7 to 80:20) furnished the product **6pe** (126 mg, 65%) as brown viscous liquid, (followed **GP-3** under microwave irradiation conditions, 118 mg, 61%). [TLC control R_f(**4p**)=0.30, R_f(**7pe**)=0.6 and R_f(**6pe**)=0.20 (petroleum ether/ethyl acetate 80:20, UV detection)].

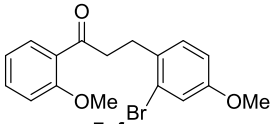
For compound **6pe:**

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3381, 2927, 2844, 1593, 1460, 1238, 1022, 746 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.52 (dd, 2H, *J*=8.0 and 7.2 Hz, Ar-H), 7.37 (dd, 1H, *J*=7.5 and 1.5 Hz, Ar-H), 7.33–7.17 (m, 2H, Ar-H), 7.12–6.85 (m, 4H, Ar-H and CH=C*H*-Ar), 6.39 (dd, 1H, *J*=15.8 and 5.5 Hz, C*H*=CH-Ar), 5.61 [dd, 1H, *J*=5.5 and 5.5 Hz, Ar-C*H*(OH)-CH=CH], 3.88 (s, 3H, Ar-OCH_3), 3.00 (d, 1H, *J*=5.5 Hz, OH) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=156.7 (s, Ar-C), 136.8 (s, Ar-C), 133.9 (d, Ar-CH), 132.8 (d, CH=*C*H-Ar), 130.5 (s, Ar-C), 128.9 (d, *C*H=CH-Ar), 128.8 (d, Ar-CH), 128.7 (d, Ar-CH), 127.4 (d, Ar-CH), 127.3 (d, Ar-CH), 127.1 (d, Ar-CH), 123.7 (s, Ar-C), 120.9 (d, Ar-CH), 110.7 (d, Ar-CH), 71.4 (d, Ar-*C*HOH), 55.4 (q, Ar-OCH_3) ppm.

HR-MS (ESI^{+}): m/z calculated for $[C_{16}H_{15}BrNaO_2]^{+}$=$[M+Na]^{+}$: 341.0147; found 341.0147.



7pf

3-(2-Bromo-4-methoxyphenyl)-1-(2-methoxyphenyl)propan-1-one (7pf) and (E)-3-(2-Bromo-4-methoxyphenyl)-1-(2-methoxyphenyl)prop-2-en-1-ol (6pf): GP-2 was carried out on methoxy phenyl allylic alcohol **4p** (100 mg, 0.60 mmol) with $Pd(OAc)_2$ (6.8 mg, 5 mol%), $Bn(Et)_3NCl$ (138 mg, 0.60 mmol), $NaHCO_3$ (102 mg, 1.20 mmol), bromoiodoanisole **5f** (228 mg, 0.72 mmol) in dry acetonitrile (2 mL), and the reaction mixture was heated at 50 °C for 24 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 95:5) furnished the product **7pf** (31 mg, 15%) as colorless liquid, (followed **GP-3** under microwave irradiation conditions, 37 mg, 18%).

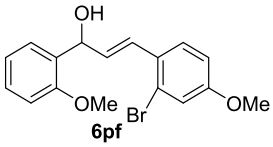
For compound **7pf:**

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3068, 2923, 2851, 1672, 1597, 1484, 1242, 1030, 756 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.59 (d, 1H, *J*=6.2 Hz, Ar-H), 7.36 (d, 1H, *J*=6.8 Hz, Ar-H), 7.1 (d, 1H, *J*=8.0 Hz, Ar-H), 7.00 (s, 1H, Ar-H), 6.95–6.80 (m, 2H, Ar-H), 6.70 (d, 1H, *J*=8.0 Hz, Ar-H), 3.77 (s, 3H, Ar-OCH_3), 3.67 (s, 3H, Ar-OCH_3), 3.18 [t, 2H, *J*=6.6 Hz Ar(CO)-C*H*$_2$-], 2.99 [t, 2H, *J*=6.6 Hz, Ar(CO)-CH_2-C*H*$_2$] ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=201.7 (s, Ar-CO), 158.6 (s, Ar-C), 158.4 (s, Ar-C), 133.4 (d, Ar-CH), 132.9 (s, Ar-C), 131.0 (d, Ar-CH), 130.3 (d, Ar-CH), 128.3 (s, Ar-C), 124.5 (s, Ar-C), 120.6 (d, Ar-CH), 117.9 (d, Ar-CH), 113.6 (d, Ar-CH), 111.5 (d, Ar-CH), 55.5 (q, Ar-OCH_3), 43.8 (q, Ar-OCH_3), 30.0 (t, Ar-CH_2), 25.0 (t, Ar-CH_2-*C*H_2) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{17}H_{17}BrNaO_3]^+$=$[M+Na]^+$: 371.0253; found 371.0259.



6pf

Further elution of column (petroleum ether/ethyl acetate 92:8 to 80:20) furnished the product **6pf** (67 mg, 32%), (followed **GP-3** under microwave irradiation conditions, 75 mg, 36%) as yellow liquid. [TLC control R_f(**4p**)=0.30, R_f(**7pf**)=0.40 and R_f(**6pf**)=0.15 (petroleum ether/ethyl acetate 80:20, UV detection)].

For compound **6pf:**

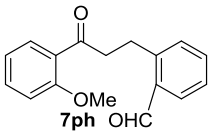
IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3407, 2930, 2843, 1594, 1481, 1237, 1025, 750 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.33 (d, 1H, *J*=8.7 Hz, Ar-H), 7.28 (d, 1H, *J*=7.4 Hz, Ar-H), 7.18 (dd, 1H, *J*=8.4 and 7.3 Hz, Ar-H), 6.98 (d, 1H, *J*=2.6 Hz, Ar-H), 7.0–6.75 (m, 3H, 2 × Ar-H and CH=C*H*-Ar), 6.70 (dd, 1H, *J*=8.7 and 2.5 Hz, Ar-H), 6.19 (dd, 1H, *J*=15.8 and 6.0 Hz, C*H*=CH-Ar), 5.49 [d, 1H, *J*=6.0 Hz, Ar-C*H*(OH)-CH=CH], 3.78 (s, 3H, Ar-OCH_3), 3.67 (s, 3H, Ar-OCH_3), 2.93 (br. s, 1H, OH) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=159.6 (s, Ar-C), 156.7 (s, Ar-C), 131.9 (d, CH=*C*H-Ar), 130.8 (s, Ar-C), 130.0 (s, Ar-C), 128.8 (d, *C*H=CH-Ar), 128.3 (d, Ar-CH),

127.6 (d, Ar-CH), 127.4 (d, Ar-CH), 124.1 (s, Ar-C), 121.0 (d, Ar-CH), 117.6 (d, Ar-CH), 114.1 (d, Ar-CH), 110.8 (d, Ar-CH), 71.5 (d, Ar-*C*HOH), 55.6 (q, Ar-OCH_3), 55.5 (q, Ar-OCH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{17}H_{18}BrO_3]^+$=$[M+H]^+$: 349.0434; found 349.0258 and $[C_{17}H_{16}BrO_3]^+$=$[M-H]^+$: 347.0277; found 347.0279.



2-(3-(2-Methoxyphenyl)-3-oxopropyl)benzaldehyde (7ph) and 2-((E)-3-Hydroxy-3-(2-methoxyphenyl)proenyl)benzaldehyde (6ph): GP-2 was carried out on methoxy phenyl allylic alcohol **4p** (100 mg, 0.60 mmol) with $Pd(OAc)_2$ (6.8 mg, 5 mol%), $Bn(Et)_3NCl$ (138 mg, 0.60 mmol), $NaHCO_3$ (102 mg, 1.20 mmol), 2-bromobenzaladehyde **5h** (135 mg, 0.72 mmol) in dry acetonitrile (2 mL), and the reaction mixture was heated at 50 °C for 24 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 95:6 to 90:10) furnished the product **7ph** (24 mg, 15%), (followed **GP-3** under microwave irradiation conditions, 27 mg, 17%) as yellow viscous liquid.

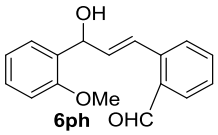
For compound **7ph:**

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3068, 2926, 2845, 2741, 1687, 1593, 1479, 1243, 1025, 759 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=10.22 (s, 1H, Ar-CHO), 7.75 (d, 1H, *J*=7.6 Hz, Ar-H), 7.60 (dd, 1H, *J*=1.7 and 1.7 Hz, Ar-H), 7.43 (dd, 1H, *J*=7.5 and 7.5 Hz, Ar-H), 7.36 (dd, 1H, *J*=8.0 and 7.6 Hz, Ar-H), 7.32 (s, 1H, Ar-H), 7.28 (dd, 1H, *J*=7.6 and 4.1 Hz, Ar-H), 6.90 (dd, 1H, *J*=7.4 and 7.4 Hz, Ar-H), 6.86 (d, 1H, *J*=8.3 Hz, Ar-H), 3.76 (s, 3H, Ar-OCH_3), 3.35 [t, 2H, *J*=7.3 Hz Ar(CO)CH_2], 3.24 [t, 2H, *J*=7.3 Hz, Ar(CO)$CH_2C\mathit{H}_2$] ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=201.1 (s, Ar-CHO), 192.5 (s, Ar-CO), 158.6 (s, Ar-C), 144.4 (s, Ar-C), 133.9 (d, Ar-CH), 133.9 (s, Ar-C), 133.5 (d, Ar-CH), 132.1 (d, Ar-CH), 131.4 (d, Ar-CH), 130.4 (d, Ar-CH), 128.1 (s, Ar-C), 126.7 (d, Ar-CH), 120.7 (d, Ar-CH), 111.5 (s, Ar-C), 55.5 (q, Ar-OCH_3), 45.3 [t, *J*=7.3 and 6.7 Hz, Ar(CO)*C*H_2], 27.2 [t, *J*=7.3 and 6.8 Hz, Ar(CO)-CH_2*C*H_2] ppm.

HR-MS (ESI+): m/z calculated for $[C_{17}H_{16}NaO_3]^+$=$[M+Na]^+$: 291.0991; found 291.0992.



6ph

Further elution of column (petroleum ether/ethyl acetate 85:15 to 70:30) furnished the product **3dg** (102 mg, 63%), (followed **GP-3** under microwave irradiation conditions, 95 mg, 59%) as yellow liquid. [TLC control R_f(**4p**)=0.50, R_f(**7ph**)=0.35 and R_f(**6ph**)=0.10 (petroleum ether/ethyl acetate 70:30, UV detection)].

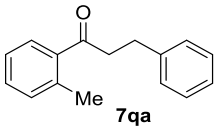
For compound **6ph:**

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3421, 2927, 2847, 2745, 1686, 1592, 1475, 1238, 1026, 748cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=10.18 (s, 1H, Ar-C*H*O), 7.71 (d, 1H, *J*=7.6 Hz, Ar-H), 7.41 (d, 3H, *J*=6.8 Hz, Ar-H), 7.37 (d, 1H, *J*=15.8 Hz, CH=C*H*-Ar), 7.29 (dd, 1H, *J*=6.1 and 5.2 Hz, Ar-H), 7.19 (dd, 1H, *J*=8.2 and 7.5 Hz, Ar-H), 6.89 (dd, 1H, *J*=7.4 and 7.3 Hz, Ar-H), 6.82 (d, 1H, *J*=8.2 Hz, Ar-H), 6.31 (dd, 1H, *J*=15.8 and 5.7 Hz, C*H*=CH-Ar), 5.56 [d, 1H, *J*=5.7 Hz, Ar-C*H*(OH)-CH=CH], 3.8 (s, 3H, Ar-OCH_3), 3.08 (br. s, 1H, OH) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=192.3 (s, Ar-CHO), 156.7 (s, Ar-C), 140.1 (s, Ar-C), 137.0 (d, Ar-CH), 133.8 (d, Ar-CH), 132.9 (s, Ar-C), 130.7 (d, CH=*C*H-Ar), 130.5 (s, Ar-C), 129.0 (d, *C*H=CH-Ar), 127.8 (d, Ar-CH), 127.6 (d, Ar-CH), 127.4 (d, Ar-CH), 125.6 (d, Ar-CH), 121.0 (d, Ar-CH), 110.8 (d, Ar-CH), 71.2 (d, Ar-*C*HOH), 55.5 (q, Ar-OCH_3) ppm.

HR-MS (ESI+): m/z calculated for $[C_{17}H_{16}NaO_3]^+$=$[M+Na]^+$: 291.0991; found 291.0992.



7qa

3-Phenyl-1-o-tolyl-propan-1-one (7qa) and 3-Phenyl-1-o-tolyl-prop-2-en-1-ol (6qa): **GP-2** was carried out on methyl phenyl allylic alcohol **4q** (100 mg, 0.67 mmol) with $Pd(OAc)_2$ (7.5 mg, 5 mol%), Bn $(Et)_3NCl$ (153 mg, 0.67 mmol), $NaHCO_3$ (113 mg, 1.34 mmol), iodobenzene **5a** (165 mg, 0.80 mmol) in dry acetonitrile (2 mL), and reaction mixture was heated at 50 °C for 24 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 96:4 to 94:6) furnished the product **7qa** (36 mg, 24%), (followed **GP-3** under microwave irradiation conditions, 40 mg, 27%) as colorless liquid.

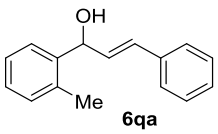
For compound **7qa:**

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2926, 1684, 1492, 1450, 1205, 746, 700 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.50 (d, 1H, J=7.9 Hz, Ar-H), 7.35–7.00 (m, 8H, Ar-H), 3.12 (t, 2H, J=7.3 Hz, ArCOCH_2), 2.95 [t, 2H, J=7.4 Hz, Ar(CO)CH_2CH_2], 2.38 (s, 3H, Ar-CH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=203.4 (s, Ar-CO), 141.2 (s, Ar-C), 138.1 (s, Ar-C), 137.9 (s, Ar-C), 132.0 (d, Ar-CH), 131.3 (d, Ar-CH), 128.5 (d, 2C, 2 × Ar-CH), 128.4 (d, 2C, 2 × Ar-CH), 128.4 (d, Ar-CH), 126.2 (d, Ar-CH), 125.7 (d, Ar-CH), 43.2 [t, Ar(CO)-CH_2], 30.4 (t, Ar(CO)-CH_2-CH_2), 21.3 (s, Ar-CH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{16}H_{17}O]^+$=$[M+H]^+$: 225.1274; found 225.1274.



6qa

Further elution of column (petroleum ether/ethyl acetate 90:10 to 80:20) furnished the product **6qa** (69 mg, 46%), (followed **GP-3** under microwave irradiation conditions, 75 mg, 50%) as yellow viscous liquid. [TLC control R_f(**4q**)=0.30, R_f(**7qa**)=0.60,R_f(**6qa**)=0.20 (petroleum ether/ethyl acetate 95:5, UV detection)].

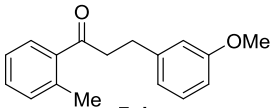
For compound **6qa:**

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3337, 3026, 2923, 1598, 1486, 1450, 966, 742 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.57 (d, 1H, *J*=7.3 Hz, Ar-H), 7.41 (d, 2H, *J*=7.3 Hz, Ar-H), 7.33 (dd, 2H, *J*=7.6 and 7.3 Hz, Ar-H), 7.26 (dd, 2H, *J*=7.6 and 8.3 Hz, Ar-H), 7.21 (dd, 2H, *J*=7.0 and 6.8 Hz, Ar-H), 6.68 (d, 1H, *J*=15.8 Hz, CH=C*H*-Ar), 6.39 (dd, 1H, *J*=15.8 and 6.3 Hz, C*H*=CH-Ar), 5.61 [d, 1H, *J*=6.3 Hz, Ar-C*H*(OH)], 2.42 (s, 3H, Ar-CH_3), 2.06 (br. s, 1H, -OH) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=140.7 (s, Ar-C), 136.6 (s, Ar-C), 135.3 (s, Ar-C), 130.7 (d, Ar-CH), 130.6 (d, Ar-CH), 130.6 (d, Ar-CH), 128.6 (d, 2C, Ar-H and CH=*C*H-Ar), 127.8 (d, Ar-CH), 127.7 (d, Ar-CH), 126.6 (d, 2C, 2 × Ar-CH), 126.4 (s, Ar-C), 125.8 (d, *C*H=CH-Ar), 71.89 (d, Ar-*C*HOH), 19.3 (q, Ar-CH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{16}H_{16}NaO]^+$=$[M+Na]^+$: 247.1093; found 247.1093.



7qb

3-(3-Methoxy-phenyl)-1-o-tolyl-propan-1-one (R_f(7qb)=0.60,) and 3-(3-Methoxy-phenyl)-1-o-tolyl-prop-2-en-1-ol (6qb): GP-2 was carried out on methyl phenyl allylic alcohol **4q** (100 mg, 0.67 mmol) with $Pd(OAc)_2$ (7.5 mg, 5 mol%), $Bn(Et)_3NCl$ (153 mg, 0.67 mmol), $NaHCO_3$ (113 mg, 1.34 mmol), iodoanisole **5b** (190 mg, 0.80 mmol) in dry acetonitrile (2 mL), and reaction mixture was heated at 50 °C for 24 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 93:7 to 91:9) furnished the product **7qb** (50 mg, 29%), (followed

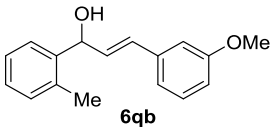
GP-3 under microwave irradiation conditions, 53 mg, 31%) as colorless liquid. For compound **7qb:**

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2941, 2837, 1683, 1593, 1448, 1255, 1155, 1043, 971, 756, 697 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.51 (d, 1H, *J*=8.0 Hz, Ar-H), 7.26 (dd, 1H, *J*=7.1 and 7.8 Hz, Ar-H), 7.13 (dd, 2H, *J*=7.5 and 8.0 Hz, Ar-H), 7.09 (s, 1H, Ar-H), 6.73 (d, 1H, *J*=7.6 Hz, Ar-H), 6.69 (s, 1H, Ar-H), 6.65 (dd, 1H, *J*=2.2 and 2.2 Hz, Ar-H), 3.69 (s, 3H,Ar-OCH_3), 3.13 (t, 2H, *J*=7.3 Hz, ArCOCH_2), 2.93 [t, 2H, *J*=7.4 Hz, Ar(CO)CH_2CH_2], 2.39 (s, 3H, Ar-CH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=203.3 (s, Ar-*C*O), 159.7 (s, Ar-C), 142.8 (s, Ar-C), 138.1 (s, Ar-C), 137.8 (s, Ar-C), 132.0 (d, Ar-CH), 131.3 (d, Ar-CH), 129.5 (d, Ar-CH), 128.4 (d, Ar-CH), 125.7 (d, Ar-CH), 120.8 (d, Ar-CH), 114.2 (d, Ar-CH), 111.5 (d, Ar-CH), 55.2 (q, Ar-O*C*H$_3$), 43.1 (t, Ar-CO-*C*H$_2$), 30.4 (t, Ar-CO-CH_2-*C*H$_2$-), 21.3 (q, Ar-*C*H$_3$) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{17}H_{18}NaO_2]^+$=$[M+Na]^+$: 277.1199; found 277.1197.



6qb

Further elution of column (petroleum ether/ethyl acetate 88:12 to 80:20) furnished the product **6qb** (99 mg, 58%), (followed **GP-3** under microwave irradiation conditions, 93 mg, 55%) as yellow viscous liquid. [TLC control R_f(**4q**)=0.50, R_f(**7qb**)=0.60, and R_f(**6qb**)=0.30 (petroleum ether/ethyl acetate 80:20, UV detection)].

For compound **6qb:**

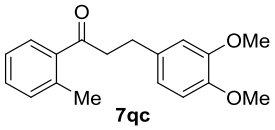
IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3376, 2933, 1591, 1479, 1265, 1160, 1041, 970, 765, 689 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.44 (d, 1H, *J*=7.3 Hz, Ar-H), 7.25–7.00 (m, 4H, Ar-H), 6.88 (d, 1H, *J*=7.6 Hz, Ar-H), 6.82 (s, 1H, Ar-H), 6.70 (dd, 1H, *J*=2.3 and

2.2 Hz, Ar-H), 6.53 (d, 1H, *J*=15.8 Hz, CH=C*H*-Ar), 6.26 (dd, 1H, *J*=15.8 and 6.2 Hz, C*H*=CH-Ar), 5.48 [d, 1H, *J*=6.2 Hz, Ar-C*H*(OH)-CH=CH], 3.71 (s, 3H, Ar-OCH_3), 2.30 (s, 3H, Ar-CH_3), 1.97 (br. s, 1H, -OH) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=159.8 (s, Ar-C), 140.6 (s, Ar-C), 138.0 (s, Ar-C), 135.3 (s, Ar-C), 131.1 (d, Ar-CH), 130.6 (d, Ar-CH), 130.5 (d, Ar-CH), 129.6 (d, Ar-CH), 127.7 (d, CH=*C*H-Ar), 126.4 (d, *C*H=CH-Ar), 125.9 (d, Ar-CH), 119.3 (d, Ar-CH), 113.6 (d, Ar-CH), 111.7 (d, Ar-CH), 71.8 (d, Ar-*C*HOH), 55.3 (q, Ar-OCH_3), 19.26 (q, Ar-CH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{17}H_{18}NaO_2]^+$=$[M+Na]^+$: 277.1199; found 277.1200.



7qc

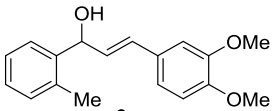
3-(3,4-Dimethoxy-phenyl)-1-o-tolyl-propan-1-one (7qc) and 3-(3,4-Dimethoxy-phenyl)-1-o-tolyl-prop-2-en-1-ol (6qc): GP-2 was carried out on methyl phenyl allylic alcohol **4q** (100 mg, 0.67 mmol) with $Pd(OAc)_2$ (7.5 mg, 5 mol%), $Bn(Et)_3NCl$ (153 mg, 0.67 mmol), $NaHCO_3$ (113 mg, 1.34 mmol), dimethoxyiodobenzene **5c** (215 mg, 0.80 mmol) in dry acetonitrile (2 mL), and reaction mixture was heated at 50 °C for 24 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 92:8 to 90:10) furnished the product **7qc** (60 mg, 30%), (followed **GP-3** under microwave irradiation conditions, 54 mg, 27%) as colorless liquid. For compound **7qc:**

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2937, 2836, 1683, 1513, 1453, 1250, 1145, 1028, 756 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.50 (d, 1H, *J*=7.9 Hz, Ar-H), 7.26 (dd, 1H, *J*=7.4 and 7.0 Hz, Ar-H), 7.20–7.00 (m, 2H, Ar-H), 6.76–6.61 (m, 3H, Ar-H), 3.76 (s, 3H, Ar-OCH_3), 3.75 (s, 3H, Ar-OCH_3), 3.11 (t, 2H, *J*=7.4 Hz, Ar-CO-CH_2-), 2.90 [t, 2H, *J*=7.4 Hz, Ar(CO)CH_2CH_2], 2.37 (s, 3H, Ar-CH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=203.6 (s, Ar-*C*O), 148.9 (s, Ar-C), 147.4 (s, Ar-C), 138.0 (s, Ar-C), 138.0 (s, Ar-C), 133.8 (s, Ar-C), 131.9 (d, Ar-CH), 131.3 (d, Ar-CH), 128.4 (d, Ar-CH), 125.7 (d, Ar-CH), 120.2 (d, Ar-CH), 111.8 (d, Ar-CH), 111.3 (d, Ar-CH), 55.9 (q, Ar-O*C*H_3), 55.8 (q, Ar-O*C*H_3), 43.5 (t, Ar-CO-*C*H_2), 29.9 [t, Ar(CO)CH_2*C*H_2], 21.3 (t, Ar-CH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{18}H_{20}NaO_3]^+$=$[M+Na]^+$: 307.1305; found 307.1306.



6qc

Further elution of column (petroleum ether/ethyl acetate 85:15 to 80:20) furnished the product **6qc** (93 mg, 49%), (followed **GP-3** under microwave irradiation conditions, 97 mg, 51%) as yellow viscous liquid. [TLC control R_f(**4q**)=0.60, R_f(**7qc**)=0.70 and R_f(**6qc**)=0.40 (petroleum ether/ethyl acetate 70:30, UV detection)].

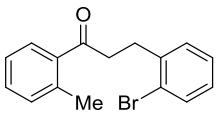
For compound **6qc:**

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3501, 2932, 2841, 1593, 1510, 1456, 1254, 1141, 1021, 965, 739 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.58 (d, 1H, *J*=7.4 Hz, Ar-H), 7.35–7.10 (m, 3H, Ar-H), 6.95 (s, 1H, Ar-H), 6.92 (d, 1H, *J*=1.8 Hz, Ar-H), 6.82 (d, 1H, *J*=8.0 Hz, Ar-H), 6.59 (d, 1H, *J*=15.8 Hz, CH=C*H*-Ar), 6.24 (dd, 1H, *J*=15.8 and 6.5 Hz, C*H*=CH-Ar), 5.58 [d, 1H, *J*=6.5 Hz, Ar-C*H*(OH)-CH=CH], 3.89 (s, 6H, 2 × Ar-OCH_3), 2.40 (s, 3H, Ar-CH_3), 2.05 (br. s, 1H, -OH) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=149.0 (s, Ar-C), 148.9 (s, Ar-C), 140.9 (s, Ar-C), 135.2 (s, Ar-C), 130.6 (d, Ar-CH), 130.5 (d, Ar-CH), 129.6 (s, Ar-C), 128.7 (d, Ar-CH), 127.6 (d, CH=*C*H-Ar), 126.4 (d, Ar-CH), 125.8 (d, *C*H=CH-Ar), 119.9 (d, Ar-CH), 111.0 (d, Ar-CH), 108.8 (d, Ar-CH),71.9 (d, Ar-*C*HOH), 55.9 (q, Ar-OCH_3), 55.8(q, Ar-OCH_3), 19.3 (q, Ar-*C*H_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{18}H_{20}KO_3]^+$=$[M+K]^+$: 323.1044; found 323.1047.



7qe

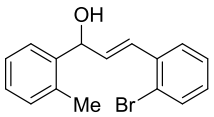
3-(2-Bromo-phenyl)-1-o-tolyl-propan-1-one (7qe) and 3-(2-Bromo-phenyl)-1-o-tolyl-prop-2-en-1-ol (6qe): GP-2 was carried out on methyl phenyl allylic alcohol **4q** (100 mg, 0.67 mmol) with $Pd(OAc)_2$ (7.5 mg, 5 mol%), $Bn(Et)_3NCl$ (153 mg, 0.67 mmol), $NaHCO_3$ (113 mg, 1.34 mmol), bromoiodobenzene **5e** (229 mg, 0.80 mmol) in dry acetonitrile (2 mL), and reaction mixture was heated at 50°C for 24 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 94:6 to 92:8) furnished the product **7qe** (30 mg, 14%), (followed **GP-3** under microwave irradiation conditions, 34 mg, 16%) as colorless liquid. For compound **7qe:**

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3061, 2967, 1684, 1448, 1291, 1025, 970, 746 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.53 (d, 1H, *J*=7.5 Hz, Ar-H), 7.43 (d, 1H, *J*=7.8 Hz, Ar-H), 7.25 (dd, 1H, *J*=7.2 and 7.0 Hz, Ar-H), 7.18 (dd, 1H, *J*=7.5 and 1.3 Hz, Ar-H), 7.13 (d, 3H, *J*=7.3 Hz, Ar-H), 7.12 (dd, 1H, *J*=7.3 and 7.3 Hz, Ar-H), 6.96 (dd, 1H, *J*=7.8 and 7.3 Hz, Ar-H), 3.13 (t, 2H, *J*=7.8 Hz, Ar-CO-CH_2-), 3.05 [t, 2H, *J*=7.8 Hz, Ar(CO)CH_2CH_2], 2.41 (s, 3H, Ar-CH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=202.8 (s, Ar-CO), 140.4 (s, Ar-C), 138.2 (s, Ar-C), 137.5 (s, Ar-C), 132.8 (d, Ar-CH), 131.9(d, Ar-CH), 131.3 (d, Ar-CH), 130.7 (d, Ar-CH), 128.5 (d, Ar-CH), 127.9 (d, Ar-CH), 127.5 (d, Ar-CH), 125.6 (d, Ar-CH), 124.3 (s, Ar-CH), 41.2 [t, Ar(CO)CH_2], 30.9 [t, Ar(CO)CH_2CH_2], 21.3 (q, Ar-CH_3) ppm.

HR-MS (ESI^+): m/z calculated for $[C_{16}H_{15}BrNaO]^+$=$[M+Na]^+$: 325.0198; found 325.0199.



6qe

Further elution of column (petroleum ether/ethyl acetate 91:9 to 80:20) furnished the product **6qe** (130 mg, 63%), (followed **GP-3** under microwave irradiation conditions, 124 mg, 60%) as yellow viscous liquid. [TLC control R_f(**4e**)=0.40, R_f(**7qe**)=0.60 and R_f(**6qe**)=0.20 (petroleum ether/ethyl acetate 80:20, UV detection)].

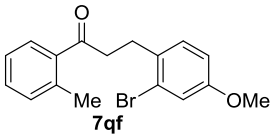
For compound **6qe:**

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3325, 3057, 2925, 1589, 1458, 1257, 1018, 964, 745 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.51 (d, 2H, *J*=8.3 Hz, Ar-H), 7.45 (d, 1H, *J*=8.3 Hz, Ar-H), 7.30–7.10 (m, 4H, Ar-H), 7.06 (dd, 1H, *J*=8.0 and 1.5 Hz, Ar-H), 7.00 (d, 1H, *J*=15.8 Hz, CH=C*H*-Ar), 6.24 (dd, 1H, *J*=15.8 and 6.3 Hz, C*H*=CH-Ar), 5.58 [d, 1H, *J*=6.3 Hz, Ar-C*H*(OH)-CH=CH], 2.38 (s, 3H, Ar-CH_3), 2.22 (br. s, 1H, OH) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=140.3 (s, Ar-C), 136.5 (s, Ar-C), 135.3 (s, Ar-C), 133.87 (d, Ar-CH), 132.8 (d, Ar-CH), 130.6 (d, Ar-CH), 129.3 (d, Ar-CH), 128.9 (d, Ar-CH), 127.7 (d, CH=*C*H-Ar), 127.4 (d, Ar-CH), 127.2 (d, Ar-CH), 126.4 (d, Ar-CH), 125.8 (d, *C*H=CH-Ar), 123.7 (s, Ar-C), 71.7 (s, Ar-*C*HOH), 19.2 (q, Ar-CH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{16}H_{15}BrNaO]^+$=$[M+Na]^+$: 325.0199; found 325.0199.



7qf

3-(2-Bromo-4-methoxy-phenyl)-1-o-tolyl-propan-1-one (7qf) and 3-(2-Bromo-4-methoxy-phenyl)-1-o-tolyl-prop-2-en-1-ol (6qf): GP-2 was carried out on methyl phenyl allylic alcohol **4q** (100 mg, 0.67 mmol) with $Pd(OAc)_2$ (7.5 mg, 5 mol%), $Bn(Et)_3Cl$ (153 mg, 0.67 mmol), $NaHCO_3$ (113 mg, 1.34 mmol), bromoiodoanisole **5f** (253 mg, 0.80 mmol) in dry acetonitrile (2 mL), and reaction mixture was heated at 50

°C for 24 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 96:4 to 94:6) furnished the product **7qf** (67 mg, 30%), (followed **GP-3** under microwave irradiation conditions, 58 mg, 26%) as colorless liquid.

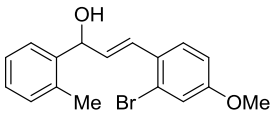
For compound **7qf:**

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3065, 2930, 2846, 1685, 1594, 1484, 1287, 1236, 1034, 845, 749 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.55 (d, 1H, *J*=7.9 Hz, Ar-H), 7.28 (dd, 1H, *J*=7.9 and 6.6 Hz, Ar-H), 7.20–7.08 (m, 3H, Ar-H), 7.02 (d, 1H, *J*=2.6 Hz, Ar-H), 6.71 (dd, 1H, *J*=8.5 and 2.6 Hz, Ar-H), 3.71 (s, 3H, Ar-OCH_3), 3.12 [t, 2H, *J*=7.6 Hz, Ar(CO)CH_2], 3.01 [t, 2H, *J*=7.6 Hz, Ar(CO)CH_2CH_2], 2.41 (s, 3H, Ar-CH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=203.2 (s, Ar-CO), 158.6 (s, Ar-C), 138.1 (s, Ar-C), 137.7 (s, Ar-C), 132.4 (s, Ar-C), 132.0 (d, Ar-CH), 131.3 (d, Ar-CH), 131.1 (d, Ar-CH), 128.5 (d, Ar-CH), 125.7 (d, Ar-CH), 124.4 (s, Ar-C), 118.0 (d, Ar-CH), 113.7 (d, Ar-CH), 55.5 (q, Ar-OCH_3), 41.7 (t, Ar(CO)-CH_2-), 30.0 (t, Ar(CO)-CH_2-CH_2), 21.32 (q, Ar-CH_3) ppm.

HR-MS (ESI^{+}): m/z calculated for $[C_{17}H_{17}BrNaO_2]^+$=$[M+Na]^+$: 355.0304; found 355.0311.



6qf

Further elution of column (petroleum ether/ethyl acetate 91:9 to 85:15) furnished the product **6qf** (109 mg, 49%), (followed **GP-3** under microwave irradiation conditions, 118 mg, 53%) as yellow viscous liquid. [TLC control R_f(**4q**)=0.50, R_f(**7qf**)=0.70 and R_f(**6qf**)=0.50 and (petroleum ether/ethyl acetate 70:30, UV detection)].

For compound **6qf:**

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3373, 3018, 2926, 2847, 1599, 1485, 1242, 1027, 966, 850, 750 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.44 (d, 1H, *J*=7.1 Hz, Ar-H), 7.30 (d, 1H, *J*=8.7 Hz, Ar-H), 7.20–7.00 (m, 3H, Ar-H), 6.97 (d, 1H, *J*=2.6 Hz, Ar-H), 6.84 (d, 1H, *J*=15.8 Hz, CH=C*H*-Ar), 6.69 (dd, 1H, *J*=8.7 and 2.5 Hz, Ar-H), 6.04 (dd, 1H, *J*=15.8 and 6.7 Hz, C*H*=CH-Ar), 5.47 [d, 1H, *J*=6.7 Hz, Ar-C*H*(OH)-CH=CH], 3.67 (s, 3H, Ar-OCH_3), 2.29 (s, 3H, Ar-CH_3), 2.20 (br. s, 1H, OH) ppm.

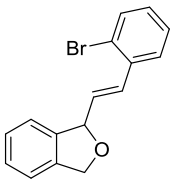
^{13}C-NMR ($CDCl_3$, 100 MHz): δ=159.5 (s, Ar-C), 140.6 (s, 2C, Ar-C), 135.3 (s, Ar-C), 131.7 (s, Ar-C), 130.6 (d, Ar-CH), 129.0 (d, Ar-CH), 127.7 (d, Ar-CH), 127.7 (d, Ar-CH), 126.4 (d, CH=*C*H-Ar), 125.7 (d, *C*H=CH-Ar), 124.2 (d, Ar-CH), 117.6 (d, Ar-CH), 114.1 (d, Ar-CH), 71.9 (d, Ar-*C*HOH), 55.6 (s, Ar-O*C*H_3), 19.3 (s, Ar-*C*H_3) ppm.

HR-MS (ESI^+): m/z calculated for $[C_{17}H_{17}BrNaO_2]^+$=$[M+Na]^+$: 355.0310; found 355.0308.

II.*5.2 Synthesis of 1,3-dihydroisobenzofurans:*

General procedure-4 for the synthesis of 1,3-dihydroisobenzofurans (11hh–11nn):
In an oven dried Schlenk under nitrogen atmosphere, were added $Pd(OAc)_2$ (5 mol%), $Bn(Et)_3NCl$ (0.50 mmol), $NaHCO_3$ (1 mmol), 2-bromobenzaldehyde **5h**–**5o** (0.50 mmol) and bromo aryl allylic alcohol **4h**–**4o** (0.60 mmol) followed by dry acetonitrile (4 mL). The resulted reaction mixture was stirred for 24 h at 80 °C. The reaction was allowed the reaction to 0 °C where added $NaBH_4$ (1.50 mmol), stirred for two hours at rt. The reaction mixture was quenched with saturated aq. NH_4Cl solution and extracted with ethyl acetate (3 × 20 mL). The organic layer was washed with saturated NaCl solution, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Traces of solvents were removed under high vacuum. To the above crude, dry DCM 20 mL was added. The reaction was cooled to –40 °C, $BF_3.Et_2O$ (2.5 mmol) was added. The reaction was then stirred for 2 h at the same temperature. The reaction mixture was then quenched with saturated aqueous $NaHCO_3$ solution and the aqueous layer was extracted with DCM (3 × 20 mL). The organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue on a silica gel

column chromatography (petroleum ether/ethyl acetate) furnished the product **11hh**–**11nn** (40%-55%).



11hh

1-[(E)-2-(2-Bromophenyl)vinyl]-1,3-dihydro-2-benzofuran (11hh): Reaction was carried out according to the **GP-4** by adding $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), $Bn(Et)_3NCl$ (114.0 mg, 0.50 mmol), $NaHCO_3$ (84.0 mg, 1.00 mmol), 2-bromobenzaldehyde **5h** (93 mg, 0.50 mmol) and bromo aryl allylic alcohol **4h** (128.0 mg, 0.60 mmol) followed by acetonitrile (4 mL). The resultant reaction mixture was stirred for 24 h at 80 °C. $NaBH_4$ (57.0 mg, 1.50 mmol) was added at 0 °C and stirred for 2 h at rt. Worked up the reaction, followed by dry DCM (20 mL) addition and cooled the reaction to –40 °C. $BF_3.Et_2O$ (0.74 mL, 2.5 mmol) was added and stirred for 2 h. Purification of the residue on a silica gel column chromatography (petroleum ether) furnished the product **11hh** (83 mg, 55%) as yellow viscous liquid. [TLC control R_f(**5h**)=0.80, R_f(**4h**)=0.70 and R_f(**11hh**)=0.85 (petroleum ether/ethyl acetate 95:5, UV detection)]

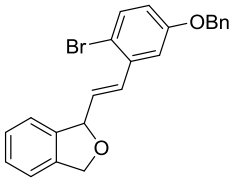
IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2922, 2852, 1588, 1465, 1437, 1357, 1284, 1246, 1158, 1122, 1107, 1021, 963, 747, 698, 665 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.53 (dd, 1H, *J*=7.8 and 1.5 Hz, Ar-H), 7.50 (dd, 1H, *J*=7.8 and 1.5 Hz, Ar-H), 7.35–7.15 (m, 5H, Ar-H), 7.10 (d, 1H, *J*=15.6 Hz, ArC*H*=CH), 7.08 (ddd, 1H, *J*=9.3, 7.8 and 1.5 Hz, Ar-H), 6.21 (dd, 1H, *J*=15.6 and 7.8 Hz, ArCH=C*H*), 5.80 [d, 1H, *J*=7.8 Hz, PhC*H*(O)CH=CH], 5.22 (d, 1H, *J*=11.7 Hz, PhCH_aH$_b$OCHCH=CH), 5.14 (d, 1H, *J*=11.7 Hz, PhCH$_a$$H_b$OCHCH=CH) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=140.6 (s, Ar-C), 139.1 (s, Ar-C), 136.4 (s, Ar-C), 132.9 (d, Ar-CH), 132.0 (d, Ar-CH), 130.5 (d, Ar-CH-CH=*C*H-Ar), 129.1 (d, Ar-CH-*C*H=CH-Ar), 127.8 (d, Ar-CH), 127.5 (d, Ar-CH), 127.4 (d, Ar-CH), 127.3 (d, Ar-

CH), 123.8 (s, Ar-C), 122.0 (d, Ar-CH), 121.1 (d, Ar-CH), 85.0 (d, Ph-*C*HCH=CH), 72.9 (t, Ph-*C*H_2OCHCH=CH) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{16}H_{13}BrNaO]^+$=$[M+Na]^+$: 323.0042; found 323.0041.



11ih

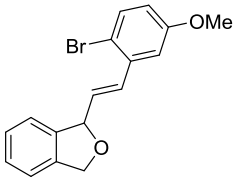
1-{(E)-2-[5-(Benzyloxy)-2-bromophenyl]vinyl}-1,3-dihydro-2-benzofuran (11ih): Reaction was carried out according to the **GP-4** by adding $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), $Bn(Et)_3NCl$ (114.0 mg, 0.50 mmol), $NaHCO_3$ (84.0 mg, 1.00 mmol), 2-bromobenzaldehyde **5h** (93.0 mg, 0.50 mmol) and bromo aryl allylic alcohol **4i** (192.0 mg, 0.60 mmol) followed by acetonitrile (4 mL). The resultant reaction mixture was stirred for 24 h at 80 °C. $NaBH_4$ (57.0 mg, 1.50 mmol) was added at 0 °C and stirred for 2 h at rt. Worked up the reaction, followed by dry DCM (20 mL) addition and cooled the reaction to –40 °C. $BF_3.Et_2O$ (0.74 mL, 2.5 mmol) was added and stirred for 2 h. Purification of the residue on a silica gel column chromatography (petroleum ether) furnished the product **11ih** (92 mg, 45%) as pale yellow viscous liquid. [TLC control (petroleum ether/ethyl acetate 95:5, R_f(**5h**)=0.80, R_f(**4i**)=0.50 and R_f(**11ih**)=0.65 UV detection)]

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}= 2922, 2852, 1590, 1563, 1459, 1286, 1238, 1173, 1028, 1013, 963, 739, 697 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.41 (d, 1H, *J*=8.3 Hz, Ar-H), 7.39–7.20 (m, 8H, Ar-H), 7.19 (dd, 1H, *J*=8.3 and 2.4 Hz, Ar-H), 7.14 (d, 1H, *J*=2.9 Hz, Ar-H), 7.05 (d, 1H, *J*=15.6 Hz, ArC*H*=CH), 6.73 (dd, 1H, *J*=8.8 and 2.9 Hz, Ar-H), 6.19 (dd, 1H, *J*=15.6 and 7.3 Hz, ArCH=C*H*), 5.80 [d, 1H, *J*=7.3 Hz, PhC*H*(O)CH=CH], 5.22 (dd, 1H, *J*=12.2 and 2.4 Hz, PhC$H_a$$H_b$OCHCH=CH), 5.13 (dd, 1H, *J*=12.2 and 1.0 Hz, PhC$H_a$$H_b$OCHCH=CH), 4.98 (s, 2H, PhCH_2O) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=158.0 (s, Ar-C), 140.5 (s, Ar-C), 139.1 (s, Ar-C), 137.1 (s, Ar-C), 136.4 (s, Ar-C), 133.4 (d, Ar-CH), 132.1 (d, Ar-CH), 130.5 (d, Ar-CH), 128.5 (d, 2C, Ar-CH), 128.0 (d, Ar-CH-CH=*C*H-Ar), 127.8 (d, Ar-CH-*C*H=CH-Ar), 127.5 (d, Ar-CH), 127.4 (d, 2C, Ar-CH), 122.0 (d, Ar-CH), 121.1 (d, Ar-CH), 116.2 (d, Ar-CH), 114.8 (s, Ar-C), 113.3 (d, Ar-CH), 84.8 (d, Ph-*C*HCH=CH), 72.8 (t, Ph-*C*H_2OCHCH=CH) 70.1 (t, PhCH_2O) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{23}H_{18}{}^{79}BrO]^+$=$[(M+H)–H_2O]^+$: 389.0536; found 389.0545 and $[C_{23}H_{18}{}^{81}BrO]^+$=$[(M+H)–H_2O]^+$: 391.0515; found 391.0529.



11jh

1-[(E)-2-(2-Bromo-5-methoxyphenyl)vinyl]-1,3-dihydro-2-benzofuran (11jh): Reaction was carried out according to the **GP-4** by adding $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), $Bn(Et)_3NCl$ (114.0 mg, 0.50 mmol), $NaHCO_3$ (84.0 mg, 1.00 mmol), 2-bromobenzaldehyde **5h** (93 mg, 0.50 mmol) and bromo aryl allylic alcohol **4j** (146.0 mg, 0.60 mmol) followed by acetonitrile (4 mL). The resultant reaction mixture was stirred for 24 h at 80 °C. $NaBH_4$ (57.0 mg, 1.50 mmol) was added at 0 °C and stirred for 2 h at rt. Worked up the reaction, followed by dry DCM (20 mL) addition and cooled the reaction to –40 °C. $BF_3.Et_2O$ (0.74 mL, 2.5 mmol) was added and stirred for 2 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 97:3 to 95:5), furnished the product **11jh** (80 mg, 48%) as pale brown viscous liquid. [TLC control (petroleum ether/ethyl acetate 95:5, R_f(**5h**)=0.75, R_f(**4j**)=0.35 and R_f(**11jh**)=0.50 UV detection)].

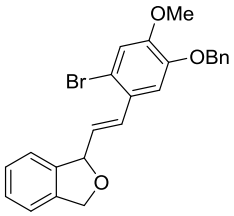
IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2959, 2929, 1592, 1571, 1464, 1287, 1236, 1161, 1014, 802, 754, 733, 599 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.35 (d, 1H, *J*=8.8 Hz, Ar-H), 7.30–7.05 (m, 4H, Ar-H), 7.01 (d, 1H, *J*=15.5 Hz, ArC*H*=CH), 6.97 (d, 1H, *J*=2.2 Hz, Ar-H), 6.62 (dd,

1H, *J*=8.7 and 3.0 Hz, Ar-H), 6.13 (dd, 1H, *J*=15.5 and 7.5 Hz, ArCH=C*H*), 5.74 [d, 1H, *J*=7.5 Hz, PhC*H*(O)CH=CH], 5.16 (dd, 1H, *J*=12.3 and 2.2 Hz, PhC$H_a$$H_b$OCHCH=CH), 5.08 (d, 1H, *J*=12.3 Hz, PhC$H_a$$H_b$OCHCH=CH), 3.68 (s, 3H, Ar-OCH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=158.9 (s, Ar-C), 140.5 (s, Ar-C), 139.1 (s, Ar-C), 140.0 (s, Ar-C), 133.4 (d, Ar-CH), 132.0 (d, Ar-CH), 130.7 (d, Ar-CH), 127.8 (d, Ar-CH-CH=*C*H-Ar), 127.5 (d, Ar-CH-*C*H=CH-Ar), 122.0 (d, Ar-CH), 121.1 (d, Ar-CH), 115.7 (d, Ar-CH), 114.5 (s, Ar-C), 112.0 (d, Ar-CH), 84.9 (d, Ph-*C*HCH=CH), 72.9 (t, Ph-*C*H_2OCHCH=CH), 55.4 (q, Ar-OCH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{17}H_{14}BrO]^+$=$[(M+H)–H_2O]^+$: 313.0223; found 313.0212, $[C_{17}H_{14}{}^{81}BrO]^+$=$[(M+H)–H_2O]^+$: 315.0202; found 315.0189 and $[C_{17}H_{19}BrNO_2]^+$=$[M+NH_4]^+$: 348.0594; found 348.0587.



11kh

1-{(E)-2-[5-(Benzyloxy)-2-bromo-4-methoxyphenyl]vinyl}-1,3-dihydro-2-benzofuran (11kh): Reaction was carried out according to the **GP-4** by adding $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), $Bn(Et)_3NCl$ (114.0 mg, 0.50 mmol), $NaHCO_3$ (84.0 mg, 1.00 mmol), 2-bromobenzaldehyde **5h** (93 mg, 0.50 mmol) and bromo aryl allylic alcohol **4k** (209 mg, 0.60 mmol) followed by acetonitrile (4 mL). The resultant reaction mixture was stirred for 24 h at 80 °C. $NaBH_4$ (57.0 mg, 1.50 mmol) was added at 0 °C and stirred for 2 h at rt. Worked up the reaction, followed by dry DCM (20 mL) addition and cooled the reaction to –40 °C. $BF_3.Et_2O$ (0.74 mL, 2.5 mmol) was added and stirred for 2 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 95:5 to 90:10), furnished the product **11kh** (92 mg, 42%)

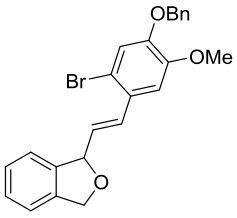
as brown viscous liquid. [TLC control (petroleum ether/ethyl acetate 90:10, R_f(**5h**)=0.80, R_f(**4k**)=0.20 and R_f(**11kh**)=0.30 UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}= 2918, 2850, 1595, 1502, 1461, 1385, 1260, 1200, 1166, 1024, 861, 750, 697 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.43 (d, 2H, *J*=7.3 Hz, Ar-H), 7.38 (dd, 2H, *J*=7.3 and 6.8 Hz, Ar-H), 7.35–7.25 (m, 4H, Ar-H), 7.22 (dd, 1H, *J*=7.8 and 2.0 Hz, Ar-H), 7.06 (s, 1H, Ar-H), 7.04 (s, 1H, Ar-H), 7.03 (d, 1H, *J*=15.6 Hz, ArC*H*=CH), 6.13 (dd, 1H, *J*=15.6 and 7.8 Hz, ArCH=C*H*), 5.81 [d, 1H, *J*=7.8 Hz, PhC*H*(O)CH=CH], 5.25 (dd, 1H, *J*=12.2 and 2.4 Hz, PhCH_aH$_b$OCHCH=CH), 5.14 (d, 1H, *J*=12.2 Hz, PhCH$_a$$H_b$OCHCH=CH), 5.10 (s, 2H, PhCH_2O) 3.83 (s, 3H, Ar-OCH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=149.1 (s, Ar-C), 148.6 (s, Ar-C), 140.7 (s, Ar-C), 139.2 (s, Ar-C), 136.2 (s, Ar-C), 130.7 (d, Ar-CH-CH=*C*H-Ar), 130.0 (d, Ar-CH-*C*H=CH-Ar), 128.8 (s, Ar-C), 128.6 (d, 2C, Ar-CH), 128.1 (d, Ar-CH), 127.8 (d, Ar-CH), 127.5 (d, Ar-CH), 127.4 (d, 2C, Ar-CH), 122.1 (d, Ar-CH), 121.1 (d, Ar-CH), 117.6 (d, Ar-CH), 114.4 (s, Ar-C), 109.6 (d, Ar-CH), 85.2 (d, Ph-*C*HCH=CH), 72.8 (t, Ph-*C*H_2OCHCH=CH), 71.1 (t, PhCH_2O), 56.1 (q, Ar-OCH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{24}H_{21}BrNaO_3]^+$=$[M+Na]^+$: 459.0566; found 459.0583 and $[C_{24}H_{21}BrNaO_3]^+$=$[M+Na]^+$: 461.0546; found 461.0561.



11lh

1-{(E)-2-[4-(Benzyloxy)-2-bromo-5-methoxyphenyl]vinyl}-1,3-dihydro-2-benzofuran (11lh): Reaction was carried out according to the **GP-4** by adding $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), $Bn(Et)_3NCl$ (114.0 mg, 0.50 mmol), $NaHCO_3$ (84.0 mg, 1.00 mmol), 2-bromobenzaldehyde **5h** (93 mg, 0.50 mmol) and bromo aryl allylic alcohol **4l** (209 mg, 0.60 mmol) followed by acetonitrile (4 mL). The resultant reaction

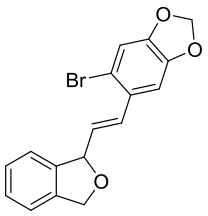
mixture was stirred for 24 h at 80 °C. $NaBH_4$ (57.0 mg, 1.50 mmol) was added at 0 °C and stirred for 2 h at rt. Worked up the reaction, followed by dry DCM (20 mL) addition and cooled the reaction to –40 °C. $BF_3.Et_2O$ (0.74 mL, 2.5 mmol) was added and stirred for 2 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 95:5 to 90:10), furnished the product **11lh** (100 mg, 45%) as brown viscous liquid. [TLC control (petroleum ether/ethyl acetate 90:10, R_f(**5h**)=0.80, R_f(**4l**)=0.20 and R_f(**11lh**)=0.35 UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2957, 2920, 2851, 1503, 1462, 1441, 1379, 1261, 1206, 1163, 1026, 743 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.40 (d, 2H, *J*=6.8 Hz, Ar-H), 7.34 (dd, 2H, *J*=7.3 and 6.8 Hz, Ar-H), 7.31–7.24 (m, 4H, Ar-H), 7.20 (dd, 1H, *J*=8.3 and 2.4 Hz, Ar-H), 7.08 (s, 1H, *J*=9.3 Hz, Ar-H), 7.03 (s, 1H, *J*=9.3 Hz, Ar-H), 7.00 (d, 1H, *J*=15.6 Hz, ArC*H*=CH), 6.02 (dd, 1H, *J*=15.6 and 7.8 Hz, ArCH=C*H*), 5.78 [d, 1H, *J*=7.8 Hz, PhC*H*(O)CH=CH], 5.23 (dd, 1H, *J*=12.2 and 2.4 Hz, PhCH_aH_bOCHCH=CH), 5.13 (d, 1H, *J*=12.2 Hz, PhCH_aH_bOCHCH=CH), 5.06 (s, 2H, $PhCH_2O$) 3.86 (s, 3H, Ar-OCH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=150.2 (s, Ar-C), 147.7 (s, Ar-C), 140.8 (s, Ar-C), 139.2 (s, Ar-C), 136.5 (s, Ar-C), 130.6 (d, Ar-CH-CH=*C*H-Ar), 129.9 (d, Ar-CH-*C*H=CH-Ar), 128.6 (d, 2C, Ar-CH), 128.4 (s, Ar-C), 128.1 (d, Ar-CH), 127.8 (d, Ar-CH), 127.6 (d, 2C, Ar-CH), 127.5 (d, Ar-CH), 122.1 (d, Ar-CH), 121.1 (d, Ar-CH), 115.8 (d, Ar-CH), 115.2 (s, Ar-C), 112.1 (d, Ar-CH), 85.2 (d, Ph-*C*HCH=CH), 72.9 (t, Ph-*C*H_2OCHCH=CH), 71.3 (t, $PhCH_2O$), 56.2 (q, Ar-OCH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{24}H_{22}BrO_3]^+$=$[M+H]^+$: 437.0747; found 437.0735 and $[C_{24}H_{22}{}^{81}BrO_3]^+$=$[M+H]^+$: 439.0726; found 439.0732.



11mh

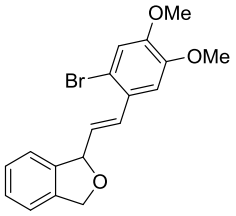
5-Bromo-6-[(E)-2-(1, 3-dihydro-2-benzofuran-1-yl)vinyl]-1,3-benzodioxole (11mh): Reaction was carried out according to the **GP-4** by adding $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), $Bn(Et)_3NCl$ (114.0 mg, 0.50 mmol), $NaHCO_3$ (84.0 mg, 1.00 mmol), 2-bromobenzaldehyde **5h** (93 mg, 0.50 mmol) and bromo aryl allylic alcohol **4m** (154 mg, 0.60 mmol) followed by acetonitrile (4 mL). The resultant reaction mixture was stirred for 24 h at 80 °C. $NaBH_4$ (57.0 mg, 1.50 mmol) was added at 0 °C and stirred for 2 h at rt. Worked up the reaction, followed by dry DCM (20 mL) addition and cooled the reaction to –40 °C. $BF_3.Et_2O$ (0.74 mL, 2.5 mmol) was added and stirred for 2 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 95:5 to 90:10), furnished the product **11mh** (90 mg, 52%) as pale yellow viscous liquid. [TLC control (petroleum ether/ethyl acetate 90:10, R_f(**5h**)=0.80, R_f(**4m**)=0.30 and R_f(**11mh**)=0.65 UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2901, 2852, 1502, 1474, 1412, 1247, 1229, 1116, 1034, 978, 961, 933, 863, 838, 750 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.35–7.23 (m, 3H, Ar-H), 7.19 (dd, 1H, *J*=8.3 and 2.4 Hz, Ar-H), 7.03 (d, 1H, *J*=15.6 Hz, ArC*H*=CH), 6.99 (d, 2H, *J*=2.4 Hz, Ar-H), 6.07 (dd, 1H, *J*=15.5 and 7.8 Hz, ArCH=C*H*), 5.94 (s, 2H, OCH_2O), 5.78 [d, 1H, *J*=7.8 Hz, PhC*H*(O)CH=CH], 5.22 (dd, 1H, *J*=12.2 and 2.4 Hz, PhCH_aH_bOCHCH=CH), 5.13 (d, 1H, *J*=12.2 Hz, PhCH_aH_bOCHCH=CH) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=148.1 (s, Ar-C), 147.6 (s, Ar-C), 140.7 (s, Ar-C), 139.1 (s, Ar-C), 130.5 (d, Ar-CH-CH=*C*H-Ar), 130.3 (d, Ar-CH-*C*H=CH-Ar), 129.6 (s, Ar-C), 127.8 (d, Ar-CH), 127.4 (d, Ar-CH), 122.0 (d, Ar-CH), 121.1 (d, Ar-CH), 115.0 (s, Ar-C), 112.6 (d, Ar-CH), 106.4 (d, Ar-CH), 101.7 (d, Ar-CH), 85.0 (d, Ph-*C*HCH=CH), 72.8 (t, Ph-*C*H_2OCHCH=CH) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{17}H_{13}BrNaO_3]^+$=$[M+Na]^+$: 366.9940; found 366.9938 and $[C_{17}H_{13}{}^{81}BrNaO_3]^+$=$[M+Na]^+$: 368.9920; found 368.9918.



11nh

1-[(E)-2-(2-Bromo-4,5-dimethoxyphenyl)vinyl]-1,3-dihydro-2-benzofuran (11nh): Reaction was carried out according to the **GP-4** by adding $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), $Bn(Et)_3NCl$ (114.0 mg, 0.50 mmol), $NaHCO_3$ (84.0 mg, 1.00 mmol), 2-bromobenzaldehyde **5h** (93 mg, 0.50 mmol) and bromo aryl allylic alcohol **4n** (164 mg, 0.60 mmol) followed by acetonitrile (4 mL). The resultant reaction mixture was stirred for 24 h at 80 °C. $NaBH_4$ (57.0 mg, 1.50 mmol) was added at 0 °C and stirred for 2 h at rt. Worked up the reaction, followed by dry DCM (20 mL) addition and cooled the reaction to –40 °C. $BF_3.Et_2O$ (0.74 mL, 2.5 mmol) was added and stirred for 2 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 90:10 to 85:15), furnished the product **11nh** (78 mg, 43%) as yellow viscous liquid. [TLC control (petroleum ether/ethyl acetate 90:10, R_f(**5h**)=0.80, R_f(**4n**)=0.15 and R_f(**11nh**)=0.30 UV detection)].

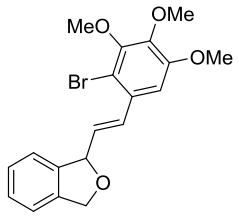
IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2928, 2847, 1502, 1462, 1439, 1380, 1256, 1160, 1024, 751 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.30–7.15 (m, 4H, Ar-H), 7.00 (d, 1H, *J*=15.6 Hz, ArC*H*=CH), 6.99 (s, 1H, Ar-H), 6.98 (s, 1H, Ar-H), 6.10 (dd, 1H, *J*=15.6 and 7.8 Hz, ArCH=C*H*), 5.78 [d, 1H, *J*=7.8 Hz, PhC*H*(O)CH=CH], 5.21 (dd, 1H, *J*=12.2 and 2.4 Hz, PhCH_aH_bOCHCH=CH), 5.13 (d, 1H, *J*=12.2 Hz, PhCH_aH_bOCHCH=CH), 3.83 (s, 3H, Ar-OCH_3), 3.81 (s, 3H, Ar-OCH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=149.4 (s, Ar-C), 148.4 (s, Ar-C), 140.6 (s, Ar-C), 139.1 (s, Ar-C), 130.6 (d, Ar-CH-CH=*C*H-Ar), 129.8 (d, Ar-CH-*C*H=CH-Ar), 128.2

(s, Ar-C), 127.7 (d, Ar-CH), 127.4 (d, Ar-CH), 122.0 (d, Ar-CH), 121.0 (d, Ar-CH), 115.2 (d, Ar-CH), 114.5 (s, Ar-C), 109.0 (d, Ar-CH), 85.2 (d, Ph-*C*HCH=CH), 72.8 (t, Ph-*C*H_2OCHCH=CH), 56.0 (q, Ar-OCH_3), 56.9 (q, Ar-OCH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{18}H_{17}BrNaO_3]^+$=$[M+Na]^+$: 383.0253; found 383.0254.



11oh

1-[(E)-2-(2-Bromo-3,4,5-trimethoxyphenyl)vinyl]-1,3-dihydro-2-benzofuran (11oh): Reaction was carried out according to the **GP-4** by adding $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), $Bn(Et)_3NCl$ (114.0 mg, 0.50 mmol), $NaHCO_3$ (84.0 mg, 1.00 mmol), 2-bromobenzaldehyde **5h** (93 mg, 0.50 mmol) and bromo aryl allylic alcohol **4o** (182 mg, 0.60 mmol) followed by acetonitrile (4 mL). The resultant reaction mixture was stirred for 24 h at 80 °C. $NaBH_4$ (57.0 mg, 1.50 mmol) was added at 0 °C and stirred for 2 h at rt. Worked up the reaction, followed by dry DCM (20 mL) addition and cooled the reaction to –40 °C. $BF_3.Et_2O$ (0.74 mL, 2.5 mmol) was added and stirred for 2 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 80:20 to 75:25), furnished the product **11oh** (90 mg, 46%) as yellow viscous liquid. [TLC control (petroleum ether/ethyl acetate 90:10, R_f(**5h**)=0.80, R_f(**4o**)=0.10 and R_f(**11oh**)=0.25 UV detection)].

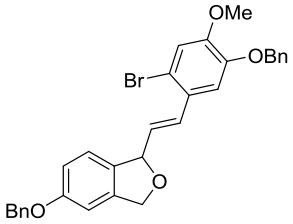
IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2923, 2851, 1559, 1480, 1426, 1391, 1325, 1201, 1166, 1106, 1009, 926, 753 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.45–7.15 (m, 4H, Ar-H), 7.10 (d, 1H, *J*=15.6 Hz, ArC*H*=CH), 6.87 (s, 1H, Ar-H), 6.13 (dd, 1H, *J*=15.6 and 7.8 Hz, ArCH=C*H*), 5.81 [d, 1H, *J*=7.8 Hz, PhC*H*(O)CH=CH], 5.23 (dd, 1H, *J*=12.2 and 2.4 Hz,

PhC$H_a$$H_b$OCHCH=CH), 5.14 (d, 1H, J=12.2 Hz, PhC$H_a$$H_b$OCHCH=CH), 3.88 (s, 3H, Ar-OCH_3), 3.87 (s, 3H, Ar-OCH_3), 3.82 (s, 3H, Ar-OCH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=152.7 (s, Ar-C), 150.8 (s, Ar-C), 143.0 (s, Ar-C), 140.6 (s, Ar-C), 139.1 (s, Ar-C), 131.9 (s, Ar-C), 131.2 (d, Ar-CH-CH=*C*H-Ar), 130.9 (d, Ar-CH-*C*H=CH-Ar), 127.8 (d, Ar-CH), 127.5 (d, Ar-CH), 122.1 (d, Ar-CH), 121.1 (d, Ar-CH), 110.8 (s, Ar-C), 105.6 (d, Ar-CH), 85.1 (d, Ph-*C*HCH=CH), 72.9 (t, Ph-*C*H_2OCHCH=CH), 61.1 (q, Ar-OCH_3), 61.0 (q, Ar-OCH_3), 56.1 (q, Ar-OCH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{19}H_{18}BrO_3]^+$=$[(M+H)–H_2O]^+$: 373.0434; found 373.0416 and $[C_{19}H_{18}{}^{81}BrO_3]^+$=$[(M+H)–H_2O]^+$: 375.0413; found 375.0401.



11ki

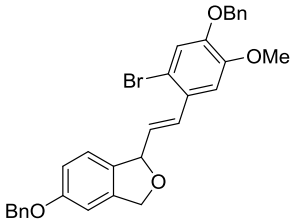
5-(Benzyloxy)-1-{(E)-2-[5-(benzyloxy)-2-bromo-4-methoxyphenyl]vinyl}-1,3-dihydro-2-benzofuran (11ki): Reaction was carried out according to the **GP-4** by adding $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), $Bn(Et)_3NCl$ (114.0 mg, 0.50 mmol), $NaHCO_3$ (84.0 mg, 1.00 mmol), 2-bromobenzaldehyde **5i** (146 mg, 0.50 mmol) and bromo aryl allylic alcohol **4k** (210 mg, 0.60 mmol) followed by acetonitrile (4 mL). The resultant reaction mixture was stirred for 24 h at 80 $^\circ$C. $NaBH_4$ (57.0 mg, 1.50 mmol) was added at 0 $^\circ$C and stirred for 2 h at rt. Worked up the reaction, followed by dry DCM (20 mL) addition and cooled the reaction to –40 $^\circ$C. $BF_3.Et_2O$ (0.74 mL, 2.5 mmol) was added and stirred for 2 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 95:5 to 90:10), furnished the product **11ki** (111 mg, 41%) as yellow viscous liquid. [TLC control (petroleum ether/ethyl acetate 90:10, R_f(**5i**)=0.70, R_f(**4k**)=0.30 and R_f(**11ki**)=0.50 UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2956, 2922, 2852, 1600, 1500, 1455, 1383, 1260, 1166, 1025, 737, 697 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.50–7.25 (m, 10H, Ar-H), 7.11 (d, 1H, *J*=7.8 Hz, Ar-H), 7.06 (s, 1H, Ar-H), 7.05 (d, 1H, *J*=8.3 Hz, Ar-H), 7.00 (d, 1H, *J*=15.6 Hz, ArC*H*=CH), 6.92 (d, 1H, *J*=7.8 Hz, Ar-H), 6.87 (s, 1H, Ar-H), 6.10 (dd, 1H, *J*=15.6 and 7.8 Hz, ArCH=C*H*), 5.75 [d, 1H, *J*=7.8 Hz, ArC*H*(O)CH=CH], 5.18 (dd, 1H, *J*=12.7 and 2.0 Hz, ArC$H_a$$H_b$OCHCH=CH), 5.12 (d, 1H, *J*=12.7 Hz, ArC$H_a$$H_b$OCHCH=CH), 5.10 (s, 2H, PhCH_2O), 5.08 (s, 2H, PhCH_2O), 3.83 (s, 3H, Ar-OCH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=159.1 (s, Ar-C), 149.1 (s, Ar-C), 148.6 (s, Ar-C), 140.9 (s, Ar-C), 136.8 (s, Ar-C), 136.2 (s, Ar-C), 133.0 (s, Ar-C), 130.4 (d, Ar-CH-CH=*C*H-Ar), 130.3 (d, Ar-CH-*C*H=CH-Ar), 128.8 (s, Ar-C), 128.6 (d, 3C, Ar-CH), 128.1 (d, Ar-CH), 128.0 (d, Ar-CH), 127.4 (d, 5C, Ar-CH), 122.9 (d, Ar-CH), 117.6 (d, Ar-CH), 114.6 (d, Ar-CH), 114.3 (s, Ar-C), 109.6 (d, Ar-CH), 107.3 (d, Ar-CH), 84.9 (d, Ar-*C*HCH=CH), 72.7 (t, Ar-*C*H_2OCHCH=CH), 71.1 (t, PhCH_2O), 70.3 (t, PhCH_2O), 56.0 (q, Ar-OCH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{31}H_{28}BrO_4]^+$=$[M+H]^+$: 543.1165; found 543.1140 and $[C_{31}H_{28}{}^{81}BrO_4]^+$=$[M+H]^+$: 545.1145; found 545.1130, $[C_{31}H_{27}BrNaO_4]^+$=$[M+Na]^+$: 565.0985; found 565.0959 and $[C_{31}H_{27}{}^{81}BrNaO_4]^+$=$[M+Na]^+$: 567.0964; found 567.0977.



11li

5-(Benzyloxy)-1-{(E)-2-[4-(benzyloxy)-2-bromo-5-methoxyphenyl]vinyl}-1,3-dihydro-2-benzofuran (11li): Reaction was carried out according to the **GP-4** by adding $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), $Bn(Et)_3NCl$ (114.0 mg, 0.50 mmol), $NaHCO_3$ (84.0 mg, 1.00 mmol), 2-bromobenzaldehyde **5i** (146 mg, 0.50 mmol) and bromo aryl allylic alcohol **4l** (210 mg, 0.60 mmol) followed by acetonitrile (4 mL). The resultant reaction mixture was stirred for 24 h at 80 $^{\circ}$C. $NaBH_4$ (57.0 mg, 1.50 mmol) was added

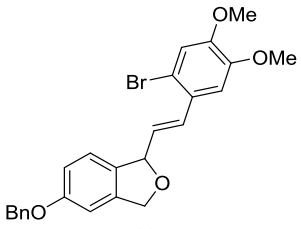
at 0 °C and stirred for 2 h at rt. Worked up the reaction, followed by dry DCM (20 mL) addition and cooled the reaction to –40 °C. $BF_3.Et_2O$ (0.74 mL, 2.5 mmol) was added and stirred for 2 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 95:5 to 90:10), furnished the product **11li** (119 mg, 44%) as brown viscous liquid. [TLC control (petroleum ether/ethyl acetate 90:10, R_f(**5i**)=0.70, R_f(**4l**)=0.30 and R_f(**11li**)=0.55 UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2923, 2852, 1600, 1502, 1455, 1439, 1380, 1259, 1163, 1026, 737, 697 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.50–7.20 (m, 10H, Ar-H), 7.09 (s, 1H, Ar-H), 7.05 (d, 1H, *J*=7.8 Hz, Ar-H), 7.03 (s, 1H, Ar-H), 6.98 (d, 1H, *J*=15.6 Hz, ArC*H*=CH), 6.91 (dd, 1H, *J*=8.3 and 2.0 Hz, Ar-H), 6.86 (d, 1H, *J*=2.0 Hz, Ar-H), 6.09 (dd, 1H, *J*=15.6 and 7.8 Hz, ArCH=C*H*), 5.74 [d, 1H, *J*=7.8 Hz, ArC*H*(O)CH=CH], 5.17 (dd, 1H, *J*=12.2 and 2.0 Hz, ArCH_aH_bOCHCH=CH), 5.10 (d, 1H, *J*=12.2 Hz, ArCH_aH_bOCHCH=CH), 5.07 (s, 2H, PhCH_2O), 5.07 (s, 2H, PhCH_2O), 3.83 (s, 3H, Ar-OCH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=159.1 (s, Ar-C), 150.2 (s, Ar-C), 148.6 (s, Ar-C), 140.9 (s, Ar-C), 136.8 (s, Ar-C), 136.2 (s, Ar-C), 133.1 (s, Ar-C), 130.5 (d, Ar-CH-*C*H=CH-Ar), 130.2 (d, Ar-CH-CH=*C*H-Ar), 128.7 (d, 2C, Ar-CH), 128.6 (d, 2C, Ar-CH), 128.1 (s, Ar-C), 128.0 (d, 2C, Ar-CH), 127.4 (d, 2C, Ar-CH), 127.4 (d, 2C, Ar-CH), 122.9 (d, Ar-CH), 117.5 (d, Ar-CH), 114.6 (s, Ar-C), 114.4 (d, Ar-CH), 109.5 (d, Ar-CH), 107.3 (d, Ar-CH), 84.8 (d, Ar-*C*HCH=CH), 72.7 (t, Ar-*C*H_2OCHCH=CH), 71.1 (t, PhCH_2O), 70.3 (t, PhCH_2O), 56.1 (s, 3H, Ar-OCH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{31}H_{28}BrO_4]^+$=$[M+H]^+$: 543.1165; found 543.1142 and $[C_{31}H_{28}{}^{81}BrO_4]^+$=$[M+H]^+$: 545.1145; found 545.1126, $[C_{31}H_{27}BrNaO_4]^+$=$[M+Na]^+$: 565.0985; found 565.0962 and $[C_{31}H_{27}{}^{81}BrNaO_4]^+$=$[M+Na]^+$: 567.0964; found 567.0987.



11ni

5-(Benzyloxy)-1-[(E)-2-(2-bromo-4,5-dimethoxyphenyl)vinyl]-1,3-dihydro-2-benzofuran (11ni): Reaction was carried out according to the **GP-4** by adding $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), $Bn(Et)_3NCl$ (114.0 mg, 0.50 mmol), $NaHCO_3$ (84.0 mg, 1.00 mmol), 2-bromobenzaldehyde **5i** (146 mg, 0.50 mmol) and bromo aryl allylic alcohol **4n** (164 mg, 0.60 mmol) followed by acetonitrile (4 mL). The resultant reaction mixture was stirred for 24 h at 80 °C. $NaBH_4$ (57.0 mg, 1.50 mmol) was added at 0 °C and stirred for 2 h at rt. Worked up the reaction, followed by dry DCM (20 mL) addition and cooled the reaction to –40 °C. $BF_3.Et_2O$ (0.74 mL, 2.5 mmol) was added and stirred for 2 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 90:10 to 85:15), furnished the product **11ni** (108 mg, 47%) as brown viscous liquid. [TLC control (petroleum ether/ethyl acetate 90:10, R_f(**5i**)=0.70, R_f(**4n**)=0.15 and R_f(**11ni**)=0.40 UV detection)].

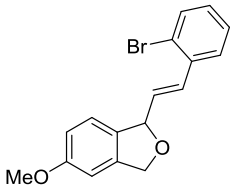
IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2922, 2851, 1600, 1503, 1462, 1439, 1259, 1162, 1027, 801, 737, 697 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.42 (dd, 2H, *J*=8.3 and 1.5 Hz, Ar-H), 7.38 (ddd, 2H, *J*=8.3, 5.8 and 1.5 Hz, Ar-H), 7.33 (ddd, 1H, *J*=8.3, 5.8 and 1.5 Hz, Ar-H), 7.11 (d, 1H, *J*=8.3 Hz, Ar-H), 7.02 (d, 1H, *J*=15.6 Hz, ArC*H*=CH), 7.01 (s, 1H, Ar-H), 7.00 (s, 1H, Ar-H), 5.91 (dd, 1H, *J*=8.3 and 2.4 Hz, Ar-H), 6.86 (d, 1H, *J*=2.0 Hz, Ar-H), 6.09 (dd, 1H, *J*=15.6 and 7.8 Hz, ArCH=C*H*), 5.75 [d, 1H, *J*=7.8 Hz, ArC*H*(O)CH=CH], 5.18 (dd, 1H, *J*=12.2 and 2.4 Hz, ArCH_aH_bOCHCH=CH), 5.09 (d, 1H, *J*=12.2 Hz, ArCH$_a$*H*$_b$OCHCH=CH), 5.07 (s, 2H, $PhCH_2O$), 3.86 (s, 3H, Ar-OCH_3), 3.83 (s, 3H, Ar-OCH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=159.1 (s, Ar-C), 149.4 (s, Ar-C), 148.5 (s, Ar-C), 140.9 (s, Ar-C), 136.8 (s, Ar-C), 133.1 (s, Ar-C), 130.4 (d, Ar-CH-CH=*C*H-Ar),

130.1 (d, Ar-CH-*C*H=CH-Ar), 128.5 (d, 2C, Ar-CH), 128.3 (s, Ar-C), 128.0 (d, Ar-CH), 127.4 (d, 2C, Ar-CH), 122.9 (d, Ar-CH), 115.2 (d, Ar-CH), 114.6 (d, Ar-CH), 114.5 (s, Ar-C), 109.1 (d, Ar-CH), 107.3 (d, Ar-CH), 84.9 (d, Ar-*C*HCH=CH), 72.7 (t, Ar-*C*H_2OCHCH=CH), 70.3 (t, PhCH_2O), 56.1 (q, Ar-OCH_3), 55.9 (q, Ar-OCH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{25}H_{24}BrO_4]^+$=$[M+H]^+$: 467.0852; found 467.0824 and $[C_{25}H_{24}{}^{81}BrO_4]^+$=$[M+H]^+$: 469.0832; found 469.0817, $[C_{25}H_{23}BrNaO_4]^+$=$[M+Na]^+$: 489.0672; found 489.0646 and $[C_{25}H_{23}{}^{81}BrNaO_4]^+$=$[M+Na]^+$: 491.0651; found 491.0649.



11hj

1-[(E)-2-(2-Bromophenyl)vinyl]-5-methoxy-1,3-dihydro-2-benzofuran (11hj): Reaction was carried out according to the **GP-4** by adding $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), $Bn(Et)_3NCl$ (114.0 mg, 0.50 mmol), $NaHCO_3$ (84.0 mg, 1.00 mmol), 2-bromobenzaldehyde **5j** (108 mg, 0.50 mmol) and bromo aryl allylic alcohol **4h** (128 mg, 0.60 mmol) followed by acetonitrile (4 mL). The resultant reaction mixture was stirred for 24 h at 80 °C. $NaBH_4$ (57.0 mg, 1.50 mmol) was added at 0 °C and stirred for 2 h at rt. Worked up the reaction, followed by dry DCM (20 mL) addition and cooled the reaction to –40 °C. $BF_3.Et_2O$ (0.74 mL, 2.5 mmol) was added and stirred for 2 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 90:10 to 80:20), furnished the product **11hj** (79 mg, 48%) as yellow vicous liquid. [TLC control (petroleum ether/ethyl acetate 90:10, R_f(**5j**)=0.70, R_f(**4h**)=0.40 and R_f(**11hj**)=0.50 UV detection)].

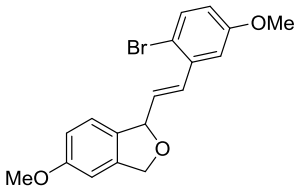
IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2956, 2924, 2854, 1610, 1493, 1466, 1275, 1117, 1025, 821, 748, 665 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.54 (d, 1H, *J*=7.8 and 1.5 Hz, Ar-H), 7.51 (d, 1H, *J*=7.8 and 1.5 Hz, Ar-H), 7.22 (dd, 1H, *J*=7.8 and 1.5 Hz, Ar-H), 7.15–7.00 (m, 3H,

Ar-H and ArC*H*=CH), 6.83 (dd, 1H, *J*=8.3 and 2.4 Hz, Ar-H), 6.79 (d, 1H, *J*=2.4 Hz, Ar-H), 6.19 (dd, 1H, *J*=15.6 and 7.8 Hz, ArCH=C*H*), 5.75 [d, 1H, *J*=7.8 Hz, ArC*H*(O)CH=CH], 5.18 (dd, 1H, *J*=12.2 and 2.4 Hz, ArCH_aH_bOCHCH=CH), 5.09 (d, 1H, *J*=12.2 Hz, ArCH_aH_bOCHCH=CH), 3.81 (s, 3H, Ar-OCH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=160.0 (s, Ar-C), 140.9 (s, Ar-C), 136.4 (s, Ar-C), 132.9 (d, Ar-CH), 132.7 (s, Ar-C), 132.4 (d, Ar-CH), 130.3 (d, Ar-CH-CH=*C*H-Ar), 129.0 (d, Ar-CH-*C*H=CH-Ar), 127.4 (d, Ar-CH), 127.3 (d, Ar-CH), 123.8 (s, Ar-C), 122.8 (d, Ar-CH), 113.7 (d, Ar-CH), 106.3 (d, Ar-CH), 84.7 (d, Ar-*C*HCH=CH), 72.8 (t, Ar-*C*H_2OCHCH=CH), 55.6 (q, Ar-OCH_3) ppm.

HR-MS (ESI^+) m/z calculated for $[C_{17}H_{15}BrNaO_2]^+$=[M+Na]: 353.0148; found 353.0164.



11jj

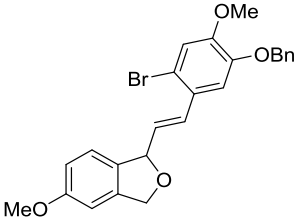
1-[(E)-2-(2-Bromo-5-methoxyphenyl)vinyl]-5-methoxy-1,3-dihydro-2-benzofuran (11jj): Reaction was carried out according to the **GP-4** by adding $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), $Bn(Et)_3NCl$ (114.0 mg, 0.50 mmol), $NaHCO_3$ (84.0 mg, 1.00 mmol), 2-bromobenzaldehyde **5j** (108 mg, 0.50 mmol) and bromo aryl allylic alcohol **4j** (146.0 mg, 0.60 mmol) followed by acetonitrile (4 mL). The resultant reaction mixture was stirred for 24 h at 80 °C. $NaBH_4$ (57.0 mg, 1.50 mmol) was added at 0 °C and stirred for 2 h at rt. Worked up the reaction, followed by dry DCM (20 mL) addition and cooled the reaction to –40 °C. $BF_3.Et_2O$ (0.74 mL, 2.5 mmol) was added and stirred for 2 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 90:10 to 8:20), furnished the product **11jj** (71 mg, 45%) as brown viscous liquid. [TLC control (petroleum ether/ethyl acetate 90:10, R_f(**5j**)=0.70, R_f(**4j**)=0.50 and R_f(**11jj**)=0.60 UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2957, 2922, 2852, 1594, 1465, 1284, 1241, 1016, 804 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.42 (d, 1H, *J*=8.8 Hz, Ar-H), δ=7.10 (d, 1H, *J*=8.3 Hz, Ar-H), δ=7.04 (d, 1H, *J*=3.3 Hz, Ar-H), 7.02 (d, 1H, *J*=15.6 Hz, ArC*H*=CH), 6.83 (dd, 1H, *J*=8.3 and 1.9 Hz, Ar-H), 6.79 (d, 1H, *J*=1.9 Hz, Ar-H), 6.69 (dd, 1H, *J*=8.8 and 2.9 Hz, Ar-H), 6.18 (dd, 1H, *J*=15.6 and 7.8 Hz, ArCH=C*H*), 5.75 [d, 1H, *J*=7.8 Hz, ArC*H*(O)CH=CH], 5.19 (dd, 1H, *J*=12.2 and 2.4 Hz, ArCH_aH$_b$OCHCH=CH), 5.10 (d, 1H, *J*=12.2 Hz, ArCH$_a$$H_b$OCHCH=CH), 3.81 (s, 3H, Ar-OCH_3), 3.76 (s, 3H, Ar-OCH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=160.0 (s, Ar-C), 158.9 (s, Ar-C), 140.9 (s, Ar-C), 137.1 (s, Ar-C), 133.5 (d, Ar-CH), 132.6 (s, Ar-C), 132.4 (d, Ar-CH-CH=*C*H-Ar), 130.5 (d, Ar-CH-*C*H=CH-Ar), 122.8 (d, Ar-CH), 115.7 (d, Ar-CH), 114.6 (s, Ar-C), 113.7 (d, Ar-CH), 112.0 (d, Ar-CH), 106.3 (d, Ar-CH), 84.7 (d, Ar-*C*HCH=CH), 72.8 (t, Ar-*C*H_2OCHCH=CH), 55.6 (s, Ar-OCH_3), 55.5 (s, Ar-OCH_3) ppm.

HR-MS (ESI^+) m/z calculated for $[C_{18}H_{16}BrO_2]^+$=[M+Na]: 343.0328; found 343.0314.



11kj

1-{(E)-2-[5-(Benzyloxy)-2-bromo-4-methoxyphenyl]vinyl}-5-methoxy-1,3-dihydro-2-benzofuran (11kj): Reaction was carried out according to the **GP-4** by adding $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), $Bn(Et)_3NCl$ (114.0 mg, 0.50 mmol), $NaHCO_3$ (84.0 mg, 1.00 mmol), 2-bromobenzaldehyde **5j** (108 mg, 0.50 mmol) and bromo aryl allylic alcohol **4k** (210 mg, 0.60 mmol) followed by acetonitrile (4 mL). The resultant reaction mixture was stirred for 24 h at 80 °C. $NaBH_4$ (57.0 mg, 1.50 mmol) was added at 0 °C and stirred for 2 h at rt. Worked up the reaction, followed by dry DCM (20 mL) addition and cooled the reaction to –40 °C. $BF_3.Et_2O$ (0.74 mL, 2.5 mmol) was added

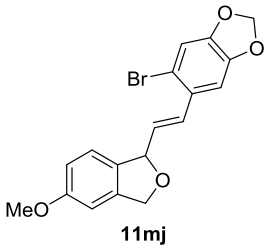
and stirred for 2 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 90:10 to 8:20), furnished the product **11kj** (103 mg, 44%) as brown viscous liquid. [TLC control (petroleum ether/ethyl acetate 90:10, R_f(**5j**)=0.70, R_f(**4k**)=0.30 and R_f(**11kj**)=0.40 UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2924, 2853, 1597, 1497, 1465, 1261, 1201, 1166, 1117, 1029, 813, 743, 698 cm^{-1}.

^{1}H-NMR (CDCl$_3$, 400 MHz): δ=7.42 (d, 2H, *J*=7.3 Hz, Ar-H), 7.37 (dd, 2H, *J*=7.8 and 7.3 Hz, Ar-H), 7.31 (t, 1H, *J*=7.3 Hz, Ar-H), 7.10 (d, 1H, *J*=8.3 Hz, Ar-H), 7.06 (s, 1H, Ar-H), 7.04 (s, 1H, Ar-H), 6.99 (d, 1H, *J*=15.6 Hz, ArC*H*=CH), 6.84 (dd, 1H, *J*=8.3 and 2.0 Hz, Ar-H), 6.79 (d, 1H, *J*=2.0 Hz, Ar-H), 6.10 (dd, 1H, *J*=15.6 and 7.8 Hz, ArCH=C*H*), 5.75 [d, 1H, *J*=7.8 Hz, ArC*H*(O)CH=CH], 5.19 (dd, 1H, *J*=12.2 and 2.4 Hz, ArCH_aH$_b$OCHCH=CH), 5.10 (s, 2H, PhCH$_2$O), 5.09 (d, 1H, *J*=12.2 Hz, ArCH$_a$$H_b$OCHCH=CH), 3.83 (s, 3H, Ar-OCH$_3$), 3.81 (s, 3H, Ar-OCH$_3$) ppm.

^{13}C-NMR (CDCl$_3$, 100 MHz): δ=159.9 (s, Ar-C), 149.1 (s, Ar-C), 148.6 (s, Ar-C), 140.9 (s, Ar-C), 136.2 (s, Ar-C), 132.7 (s, Ar-C), 130.4 (d, Ar-CH-CH=*C*H-Ar), 130.3 (d, Ar-CH-*C*H=CH-Ar), 128.8 (s, Ar-C), 128.6 (d, 2C, Ar-CH), 128.1 (d, Ar-CH), 127.4 (d, 2C, Ar-CH), 122.9 (d, Ar-CH), 117.5 (d, Ar-CH), 114.3 (s, Ar-C), 113.7 (d, Ar-CH), 109.5 (d, Ar-CH), 106.2 (d, Ar-CH), 84.9 (d, Ar-*C*HCH=CH), 72.7 (t, Ar-*C*H$_2$OCHCH=CH), 71.1 (t, PhCH$_2$O), 56.1 (q, Ar-OCH$_3$), 55.5 (q, Ar-OCH$_3$) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{25}H_{24}BrO_4]^+$=$[M+H]^+$: 467.0852; found 467.0826 and $[C_{25}H_{24}{}^{81}BrO_4]^+$=$[M+H]^+$: 469.0832; found 469.0812.



11mj

5-Bromo-6-[(E)-2-(5-methoxy-1,3-dihydro-2-benzofuran-1-yl)vinyl]-1,3-benzodioxole (11mj): Reaction was carried out according to the **GP-4** by adding

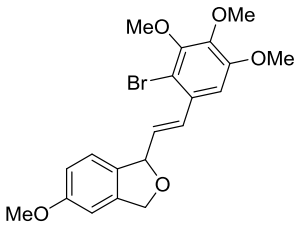
$Pd(OAc)_2$ (5.6 mg, 0.025 mmol), $Bn(Et)_3NCl$ (114.0 mg, 0.50 mmol), $NaHCO_3$ (84.0 mg, 1.00 mmol), 2-bromobenzaldehyde **5j** (108 mg, 0.50 mmol) and bromo aryl allylic alcohol **4m** (155 mg, 0.60 mmol) followed by acetonitrile (4 mL). The resultant reaction mixture was stirred for 24 h at 80 °C. $NaBH_4$ (57.0 mg, 1.50 mmol) was added at 0 °C and stirred for 2 h at rt. Worked up the reaction, followed by dry DCM (20 mL) addition and cooled the reaction to –40 °C. $BF_3.Et_2O$ (0.74 mL, 2.5 mmol) was added and stirred for 2 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 90:10 to 80:20), furnished the product **11mj** (80 mg, 43%) as pale yellow liquid. [TLC control (petroleum ether/ethyl acetate 90:10, R_f(**5j**)=0.70, R_f(**4m**)=0.50 and R_f(**11mj**)=0.55 UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2921, 2852, 1605, 1500, 1474, 1235, 1106, 1036, 932, 870, 822 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.07 (d, 1H, *J*=8.3 Hz, Ar-H), 6.99 (s, 2H, Ar-H), 6.98 (d, 1H, *J*=15.6 Hz, ArC*H*=CH), 6.82 (dd, 1H, *J*=8.3 and 2.4 Hz, Ar-H), 6.77 (d, 1H, *J*=2.4 Hz, Ar-H), 6.04 (dd, 1H, *J*=15.6 and 7.8 Hz, ArCH=C*H*), 5.94 (s, 2H, OCH_2O), 5.72 [d, 1H, *J*=7.8 Hz, ArC*H*(O)CH=CH], 5.17 (dd, 1H, *J*=12.2 and 2.4 Hz, ArCH_aH_bOCHCH=CH), 5.08 (d, 1H, *J*=12.2 Hz, ArCH_aH_bOCHCH=CH), 3.81 (s, 3H, Ar-OCH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=160.0 (s, Ar-C), 148.1 (s, Ar-C), 147.6 (s, Ar-C), 140.8 (s, Ar-C), 132.7 (s, Ar-C), 130.6 (d, Ar-CH-CH=*C*H-Ar), 130.2 (d, Ar-CH-*C*H=CH-Ar), 129.7 (s, Ar-C), 122.7 (d, Ar-CH), 115.0 (s, Ar-C), 113.7 (d, Ar-CH), 112.6 (d, Ar-CH), 106.4 (d, Ar-CH), 106.2 (d, Ar-CH), 101.7 (t, OCH_2O), 84.7 (d, Ar-*C*HCH=CH), 72.7 (t, Ar-*C*H_2OCHCH=CH), 55.5 (q, Ar-OCH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{18}H_{16}BrO_4]^+$=$[M+H]^+$: 375.0226; found 375.0212 and $[C_{18}H_{16}{}^{81}BrO_4]^+$=$[M+H]^+$: 377.0206; found 377.0189.



11oj

1-[(E)-2-(2-Bromo-3,4,5-trimethoxyphenyl)vinyl]-5-methoxy-1,3-dihydro-2-benzofuran (11oj): Reaction was carried out according to the **GP-4** by adding $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), $Bn(Et)_3NCl$ (114.0 mg, 0.50 mmol), $NaHCO_3$ (84.0 mg, 1.00 mmol), 2-bromobenzaldehyde **5j** (108 mg, 0.50 mmol) and bromo aryl allylic alcohol **4o** (182 mg, 0.60 mmol) followed by acetonitrile (4 mL). The resultant reaction mixture was stirred for 24 h at 80 °C. $NaBH_4$ (57.0 mg, 1.50 mmol) was added at 0 °C and stirred for 2 h at rt. Worked up the reaction, followed by dry DCM (20 mL) addition and cooled the reaction to –40 °C. $BF_3.Et_2O$ (0.74 mL, 2.5 mmol) was added and stirred for 2 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 85:15 to 80:20), furnished the product **11oj** (86 mg, 41%) as pale yellow viscous liquid. [TLC control (petroleum ether/ethyl acetate 80:20, R_f(**5j**)=0.95, R_f(**4o**)=0.25 and R_f(**11oj**)=0.45 UV detection)].

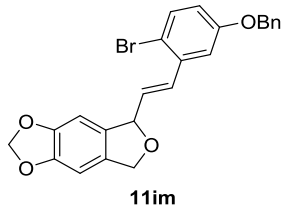
IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2923, 2852, 1563, 1481, 1463, 1427, 1392, 1326, 1274, 1200, 1165, 1107, 1031, 1011, 926, 813 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.08 (d, 1H, *J*=8.8 Hz, Ar-H), 7.06 (d, 1H, *J*=15.6 Hz, ArC*H*=CH), 6.86 (s, 1H, Ar-H), 6.83 (dd, 1H, *J*=8.3 and 2.4 Hz, Ar-H), 6.78 (d, 1H, *J*=2.4 Hz, Ar-H), 6.10 (dd, 1H, *J*=15.6 and 7.8 Hz, ArCH=C*H*), 5.75 (d, 1H, *J*=7.8 Hz, ArC*H*(O)CH=CH), 5.18 (dd, 1H, *J*=12.2 and 2.4 Hz, ArCH_aH$_b$OCHCH=CH), 5.09 (d, 1H, *J*=12.2 Hz, ArCH$_a$$H_b$OCHCH=CH), 3.88 (s, 3H, Ar-OCH_3), 3.87 (s, 3H, Ar-OCH_3), 3.82 (s, 3H, Ar-OCH_3), 3.80 (s, 3H, Ar-OCH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=160.0 (s, Ar-C), 152.6 (s, Ar-C), 150.8 (s, Ar-C), 143.0 (s, Ar-C), 140.8 (s, Ar-C), 132.6 (s, Ar-C), 131.9 (s, Ar-C), 131.5 (d, Ar-CH-CH=*C*H-Ar), 130.6 (d, Ar-CH-*C*H=CH-Ar), 122.8 (d, Ar-CH), 113.7 (d, Ar-CH), 110.8 (s, Ar-C), 106.2 (d, Ar-CH), 105.6 (d, Ar-CH), 84.7 (d, Ar-*C*HCH=CH), 72.7 (t, Ar-

CH_2OCHCH=CH), 61.1 (q, Ar-O*C*H_3), 60.9 (q, Ar-O*C*H_3), 56.1 (q, Ar-O*C*H_3), 55.5 (q, Ar-O*C*H_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{20}H_{21}BrNaO_5]^+$=$[M+Na]^+$: 443.0465; found 443.0448.



11im

5-{(E)-2-[5-(Benzyloxy)-2-bromophenyl]vinyl}-5,7-dihydrofuro[3,4-f][1,3]benzodioxole (11im): Reaction was carried out according to the **GP-4** by adding $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), $Bn(Et)_3NCl$ (114.0 mg, 0.50 mmol), $NaHCO_3$ (84.0 mg, 1.00 mmol), 2-bromobenzaldehyde **5m** (115 mg, 0.50 mmol) and bromo aryl allylic alcohol **4i** (191 mg, 0.60 mmol) followed by acetonitrile (4 mL). The resultant reaction mixture was stirred for 24 h at 80 °C. $NaBH_4$ (57.0 mg, 1.50 mmol) was added at 0 °C and stirred for 2 h at rt. Worked up the reaction, followed by dry DCM (20 mL) addition and cooled the reaction to –40 °C. $BF_3.Et_2O$ (0.74 mL, 2.5 mmol) was added and stirred for 2 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 95:5 to 90:10), furnished the product **11im** (92 mg, 41%) as pale yellow viscous liquid. [TLC control (petroleum ether/ethyl acetate 90:10, R_f(**5m**)=0.30, R_f(**4i**)=0.45 and R_f(**11im**)=0.40 UV detection)].

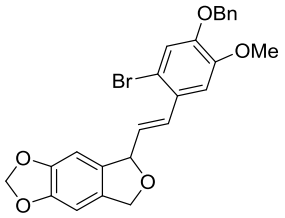
IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2920, 2851, 1591, 1501, 1464, 1378, 1278, 1239, 1173, 1122, 1039, 939, 851, 737, 698 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.50–7.27 (m, 6H, Ar-H), 7.14 (d, 1H, *J*=2.9 Hz, Ar-H), 7.01 (d, 1H, *J*=15.6 Hz, ArC*H*=CH), 6.76 (dd, 1H, *J*=8.8 and 2.9 Hz, Ar-H), 6.68 (s, 1H, Ar-H), 6.62 (s, 1H, Ar-H), 6.14 (dd, 1H, *J*=15.6 and 7.8 Hz, ArCH=C*H*), 5.97 (d, 1H, *J*=2.9 Hz, OC$H_a$$H_b$O), 5.97 (d, 1H, *J*=2.9 Hz, OCH$_a$$H_b$O), 5.70 (d, 1H, *J*=7.8 Hz, ArC*H*(O)CH=CH), 5.12 (dd, 1H, *J*=11.7 and 2.9 Hz,

ArC*H*$_a$H$_b$OCHCH=CH), 5.04 (d, 1H, *J*=11.7 Hz, ArCH$_a$*H*$_b$OCHCH=CH), 5.01 (s, 2H, PhCH$_2$O) ppm.

^{13}C-NMR (CDCl$_3$, 100 MHz): δ=158.1 (s, Ar-C), 148.0 (s, Ar-C), 147.7 (s, Ar-C), 137.1 (s, Ar-C), 136.4 (s, Ar-C), 133.5 (d, Ar-CH-CH=*C*H-Ar), 133.4 (s, Ar-C), 132.3 (d, Ar-CH-*C*H=CH-Ar), 131.9 (s, Ar-C), 130.5 (d, Ar-CH), 128.6 (d, 2C, Ar-CH), 128.1 (d, Ar-CH), 127.4 (d, 2C, Ar-CH), 116.3 (d, Ar-CH), 114.8 (s, Ar-C), 113.3 (d, Ar-CH), 102.6 (d, Ar-CH), 101.6 (d, Ar-CH), 101.5 (t, OCH$_2$O), 84.9 (d, Ar-*C*HCH=CH), 72.9 (t, Ar-*C*H$_2$OCHCH=CH), 70.2 (t, PhCH$_2$O) ppm.

HR-MS (ESI$^+$): m/z calculated for [C$_{24}$H$_{19}$BrNaO$_4$]$^+$=[M+Na]$^+$: 473.0359; found 473.0330 and [C$_{24}$H$_{19}$^{81}BrNaO$_4$]$^+$=[M+Na]$^+$: 475.0338; found 475.0317.



11lm

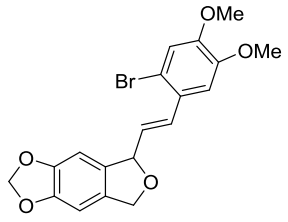
5-{(E)-2-[4-(Benzyloxy)-2-bromo-5-methoxyphenyl]vinyl}-5,7-dihydrofuro[3,4-f][1,3] benzodioxole (11lm): Reaction was carried out according to the **GP-4** by adding Pd(OAc)$_2$ (5.6 mg, 0.025 mmol), Bn(Et)$_3$NCl (114.0 mg, 0.50 mmol), NaHCO$_3$ (84.0 mg, 1.00 mmol), 2-bromobenzaldehyde **5m** (115 mg, 0.50 mmol) and bromo aryl allylic alcohol **4l** (210 mg, 0.60 mmol) followed by acetonitrile (4 mL). The resultant reaction mixture was stirred for 24 h at 80 °C. NaBH$_4$ (57.0 mg, 1.50 mmol) was added at 0 °C and stirred for 2 h at rt. Worked up the reaction, followed by dry DCM (20 mL) addition and cooled the reaction to –40 °C. BF$_3$.Et$_2$O (0.74 mL, 2.5 mmol) was added and stirred for 2 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 90:10 to 80:20), furnished the product **11lm** (113 mg, 47%) as brown viscous liquid. [TLC control (petroleum ether/ethyl acetate 80:20, R_f(**5m**)=0.70, R_f(**4l**)=0.30 and R_f(**11lm**)=0.50 UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2956, 2924, 2853, 1598, 1502, 1439, 1259, 1162, 1033, 852, 803, 735, 698 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.41 (d, 2H, *J*=7.3 Hz, Ar-H), 7.34 (dd, 2H, *J*=7.8 and 7.3 Hz, Ar-H), 7.30 (t, 1H, *J*=7.3 Hz, Ar-H), 7.07 (s, 1H, Ar-H), 7.02 (s, 1H, Ar-H), 6.95 (d, 1H, *J*=15.6 Hz, ArC*H*=CH), 6.68 (s, 1H, Ar-H), 6.60 (s, 1H, Ar-H), 6.96 (dd, 1H, *J*=15.6 and 7.8 Hz, ArCH=C*H*), 5.97 (s, 2H, OCH_2O), 5.67 (d, 1H, *J*=7.8 Hz, ArC*H*(O)CH=CH), 5.11 (dd, 1H, *J*=11.7 and 2.9 Hz, ArCH_aH_bOCHCH=CH), 5.07 (s, 2H, $PhCH_2O$), 5.02 (dd, 1H, *J*=11.7 and 2.9 Hz, ArCH_aH_bOCHCH=CH), 3.85 (s, 3H, Ar-OCH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=150.2 (s, Ar-C), 148.0 (s, Ar-C), 147.6 (s, 2C, Ar-C), 136.5 (s, Ar-C), 133.6 (s, Ar-C), 131.9 (s, Ar-C), 130.5 (d, Ar-CH-CH=*C*H-Ar), 130.0 (d, Ar-CH-*C*H=CH-Ar), 128.5 (d, 2C, Ar-CH), 128.3 (s, Ar-C), 128.0 (d, Ar-CH), 127.5 (d, 2C, Ar-CH), 115.7 (d, Ar-CH), 115.1 (s, Ar-C), 112.1 (d, Ar-CH), 102.6 (d, Ar-CH), 101.6 (d, Ar-CH), 101.5 (t, OCH_2O), 85.1 (d, Ar-*C*HCH=CH), 72.8 (t, Ar-*C*H_2OCHCH=CH), 71.2 (t, $PhCH_2O$), 56.2 (q, Ar-OCH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{25}H_{22}BrO_5]^+$=$[M+H]^+$: 481.0645; found 481.0615 and $[C_{25}H_{22}{}^{81}BrO_5]^+$=$[M+H]^+$: 483.0625; found 483.0602, $[C_{25}H_{21}BrNaO_5]^+$=$[M+Na]^+$: 503.0465; found 503.0438 and $[C_{25}H_{21}Br^{81}NaO_5]^+$=$[M+Na]^+$: 505.0444; found 505.0422.



11nm

5-[(E)-2-(2-Bromo-4,5-dimethoxyphenyl)vinyl]-5,7-dihydrofuro[3,4-f][1,3]benzodioxole (11nm): Reaction was carried out according to the **GP-4** by adding $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), $Bn(Et)_3NCl$ (114.0 mg, 0.50 mmol), $NaHCO_3$ (84.0 mg, 1.00 mmol), 2-bromobenzaldehyde **5m** (115 mg, 0.50 mmol) and bromo aryl allylic

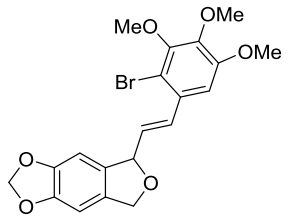
alcohol **4n** (164 mg, 0.60 mmol) followed by acetonitrile (4 mL). The resultant reaction mixture was stirred for 24 h at 80 °C. $NaBH_4$ (57.0 mg, 1.50 mmol) was added at 0 °C and stirred for 2 h at rt. Worked up the reaction, followed by dry DCM (20 mL) addition and cooled the reaction to –40 °C. $BF_3.Et_2O$ (0.74 mL, 2.5 mmol) was added and stirred for 2 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 85:15 to 80:20), furnished the product **11nm** (85 mg, 42%) as pale yellow viscous liquid. [TLC control (petroleum ether/ethyl acetate 80:20, R_f(**5m**)=0.70, R_f(**4n**)=0.30 and R_f(**11nm**)=0.55 UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2924, 2852, 1600, 1503, 1473, 1380, 1261, 1208, 1163, 1035, 937, 860, 736, 698, 665 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.00 (s, 2H, Ar-H), 6.98 (d, 1H, *J*=15.6 Hz, ArC*H*=CH), 6.67 (s, 1H, Ar-H), 6.63 (s, 1H, Ar-H), 6.06 (dd, 1H, *J*=15.6 and 7.8 Hz, ArCH=C*H*), 5.97 (d, 1H, *J*=2.9 Hz, OC*H*$_a$H$_b$O), 5.96 (d, 1H, *J*=2.9 Hz, OCH$_a$*H*$_b$O), 5.69 (d, 1H, *J*=7.8 Hz, ArC*H*(O)CH=CH), 5.11 (dd, 1H, *J*=11.7 and 2.0 Hz, ArC*H*$_a$H$_b$OCHCH=CH), 5.02 (dd, 1H, *J*=11.7 and 2.0 Hz, ArCH$_a$*H*$_b$OCHCH=CH), 3.86 (s, 3H, Ar-OCH_3), 3.83 (s, 3H, Ar-OCH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=149.5 (s, Ar-C), 148.5 (s, Ar-C), 148.0 (s, Ar-C), 147.7 (s, Ar-C), 133.6 (s, Ar-C), 131.9 (s, Ar-C), 130.7 (d, Ar-CH-CH=*C*H-Ar), 130.0 (d, Ar-CH-*C*H=CH-Ar), 128.2 (s, Ar-C), 115.3 (d, Ar-CH), 114.6 (s, Ar-C), 109.1 (d, Ar-CH), 102.7 (d, Ar-CH), 101.6 (d, Ar-CH), 101.5 (t, OCH_2O), 85.2 (d, Ar-*C*HCH=CH), 72.8 (t, Ar-*C*H_2OCHCH=CH), 56.1 (q, Ar-OCH_3), 56.0 (q, Ar-OCH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{19}H_{17}BrNaO_5]^+$=$[M+Na]^+$: 427.0152; found 427.0127 and $[C_{19}H_{17}{}^{81}BrNaO_5]^+$=$[M+Na]^+$: 429.0137; found 429.0121, HR-MS (ESI$^+$) m/z calculated for $[C_{19}H_{18}BrO_5]^+$=$[M+H]^+$: 405.0332; found 405.0304 and $[C_{19}H_{18}{}^{81}BrO_5]^+$=$[M+H]^+$: 407.0312; found 407.0294.



11om

5-[(E)-2-(2-Bromo-3,4,5-trimethoxyphenyl)vinyl]-5,7-dihydrofuro[3,4-f][1,3]benzodioxole (11om): Reaction was carried out according to the **GP-4** by adding $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), $Bn(Et)_3NCl$ (114.0 mg, 0.50 mmol), $NaHCO_3$ (84.0 mg, 1.00 mmol), 2-bromobenzaldehyde **5m** (115 mg, 0.50 mmol) and bromo aryl allylic alcohol **4o** (182 mg, 0.60 mmol) followed by acetonitrile (4 mL). The resultant reaction mixture was stirred for 24 h at 80 °C. $NaBH_4$ (57.0 mg, 1.50 mmol) was added at 0 °C and stirred for 2 h at rt. Worked up the reaction, followed by dry DCM (20 mL) addition and cooled the reaction to –40 °C. $BF_3.Et_2O$ (0.74 mL, 2.5 mmol) was added and stirred for 2 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 80:20 to 75:25), furnished the product **11om** (98 mg, 45%) as pale brown viscous liquid. [TLC control (petroleum ether/ethyl acetate 80:20, R_f(**5m**)=0.70, R_f(**4o**)=0.20 and R_f(**11om**)=0.40 UV detection)].

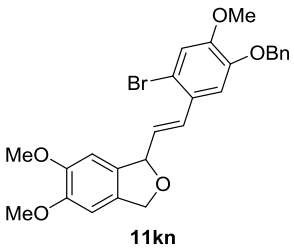
IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2928, 2854, 1566, 1503, 1482, 1394, 1329, 1264, 1198, 1164, 1107, 1037, 1010, 934, 814, 739 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.05 (d, 1H, J=15.6 Hz, ArC*H*=CH), 6.86 (s, 1H, Ar-H), 6.68 (s, 1H, Ar-H), 6.64 (s, 1H, Ar-H), 6.07 (dd, 1H, J=15.6 and 7.8 Hz, ArCH=C*H*), 5.96 (d, 1H, J=2.9 Hz, OCH_aH_bO), 5.95 (d, 1H, J=2.9 Hz, OCH_aH_bO), 5.69 (d, 1H, J=7.8 Hz, ArC*H*(O)CH=CH), 5.11 (dd, 1H, J=11.7 and 2.9 Hz, ArCH_aH_bOCHCH=CH), 5.03 (dd, 1H, J=11.7 and 2.9 Hz, ArCH_aH_bOCHCH=CH), 3.88 (s, 3H, Ar-OCH_3), 3.87 (s, 3H, Ar-OCH_3), 3.83 (s, 3H, Ar-OCH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=152.6 (s, Ar-C), 150.8 (s, Ar-C), 148.0 (s, Ar-C), 147.7 (s, Ar-C), 143.0 (s, Ar-C), 133.4 (s, Ar-C), 131.9 (s, Ar-C), 131.8 (s, Ar-C), 131.3 (d, Ar-CH-CH=*C*H-Ar), 130.8 (d, Ar-CH-*C*H=CH-Ar), 110.8 (s, Ar-C), 105.6 (d, Ar-CH), 102.6 (d, Ar-CH), 101.6 (d, Ar-CH), 101.5 (t, OCH_2O), 85.0 (d, Ar-

*C*HCH=CH), 72.9 (t, Ar-*C*H_2OCHCH=CH), 61.1 (q, Ar-OCH_3), 60.9 (q, Ar-OCH_3), 56.1 (q, Ar-OCH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{20}H_{19}BrNaO_6]^+$=$[M+Na]^+$: 457.0257; found 457.0257 and $[C_{20}H_{19}{}^{81}BrNaO_6]^+$=$[M+Na]^+$: 459.0237; found 459.0236.



11kn

1-{(E)-2-[5-(Benzyloxy)-2-bromo-4-methoxyphenyl]vinyl}-5,6-dimethoxy-1,3-dihydro-2-benzofuran (11kn): Reaction was carried out according to the general procedure-4 by adding $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), $Bn(Et)_3NCl$ (114.0 mg, 0.50 mmol), $NaHCO_3$ (84.0 mg, 1.00 mmol), 2-bromobenzaldehyde **5n** (122 mg, 0.50 mmol) and bromo aryl allylic alcohol **4k** (209 mg, 0.60 mmol) followed by acetonitrile (4 mL). The resultant reaction mixture was stirred for 24 h at 80 °C. $NaBH_4$ (57.0 mg, 1.50 mmol) was added at 0 °C and stirred for 2 h at rt. Worked up the reaction, followed by dry DCM (20 mL) addition and cooled the reaction to –40 °C. $BF_3.Et_2O$ (0.74 mL, 2.5 mmol) was added and stirred for 2 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 75:25 to 70:30), furnished the product **11kn** (116 mg, 47%) as brown viscous liquid. [TLC control (petroleum ether/ethyl acetate 70:30, R_f(**5n**)=0.65, R_f(**4k**)=0.55 and R_f(**11kn**)=0.40 UV detection)].

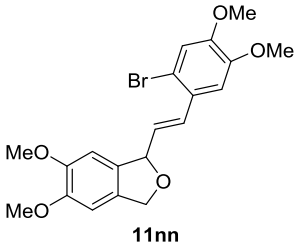
IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2926, 2853, 1598, 1503, 1463, 1384, 1261, 1203, 1166, 1032, 859, 737, 698 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.41 (d, 2H, *J*=7.3 Hz, Ar-H), 7.36 (dd, 2H, *J*=7.8 and 7.3 Hz, Ar-H), 7.31 (t, 1H, *J*=7.3 Hz, Ar-H), 7.05 (s, 2H, Ar-H), 7.00 (d, 1H, *J*=15.6 Hz, ArC*H*=CH), 6.77 (s, 1H, Ar-H), 6.69 (s, 1H, Ar-H), 6.10 (dd, 1H, *J*=15.6 and 8.3 Hz, ArCH=C*H*), 5.75 (d, 1H, *J*=8.3 Hz, ArC*H*(O)CH=CH), 5.18 (dd, 1H, *J*=11.7 and 2.0 Hz, ArCH_aH_bOCHCH=CH), 5.10 (s, 2H, $PhCH_2O$), 5.07 (dd, 1H,

J=11.2 and 2.9 Hz, $ArCH_aH_bOCHCH=CH$), 3.88 (s, 3H, Ar-OCH_3), 3.86 (s, 3H, Ar-OCH_3), 3.83 (s, 3H, Ar-OCH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=149.3 (s, Ar-C), 149.1 (s, Ar-C), 149.0 (s, Ar-C), 148.6 (s, Ar-C), 136.2 (s, Ar-C), 132.1 (s, Ar-C), 130.6 (s, Ar-C), 130.6 (d, Ar-CH-CH=CH-Ar), 130.2 (d, Ar-CH-CH=CH-Ar), 128.7 (s, Ar-C), 128.6 (d, 2C, Ar-CH), 128.1 (d, Ar-CH), 127.3 (d, 2C, Ar-CH), 117.5 (d, Ar-CH), 114.4 (s, Ar-C), 109.5 (d, Ar-CH), 104.9 (d, Ar-CH), 103.9 (d, Ar-CH), 85.6 (d, Ar-*C*HCH=CH), 73.0 (t, Ar-*C*H_2OCHCH=CH), 71.1 (t, $PhCH_2O$), 56.2 (q, Ar-OCH_3), 56.1 (q, Ar-OCH_3), 56.0 (q, Ar-OCH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{26}H_{25}BrNaO_5]^+$=$[M+Na]^+$: 519.0778; found 519.0753 and $[C_{26}H_{25}{}^{81}BrNaO_5]^+$=$[M+Na]^+$: 521.0757; found 521.0735.



11nn

1-[(E)-2-(2-Bromo-4,5-dimethoxyphenyl)vinyl]-5,6-dimethoxy-1,3-dihydro-2-benzofuran (11nn): Reaction was carried out according to the **GP-4** by adding $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), $Bn(Et)_3NCl$ (114.0 mg, 0.50 mmol), $NaHCO_3$ (84.0 mg, 1.00 mmol), 2-bromobenzaldehyde **5n** (122 mg, 0.50 mmol) and bromo aryl allylic alcohol **4n** (164 mg, 0.60 mmol) followed by acetonitrile (4 mL). The resultant reaction mixture was stirred for 24 h at 80 °C. $NaBH_4$ (57.0 mg, 1.50 mmol) was added at 0 °C and stirred for 2 h at rt. Worked up the reaction, followed by dry DCM (20 mL) addition and cooled the reaction to –40 °C. $BF_3.Et_2O$ (0.74 mL, 2.5 mmol) was added and stirred for 2 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 70:30 to 60:40), furnished the product **11nn** (90 mg, 43%) as brown viscous liquid. [TLC control (petroleum ether/ethyl acetate 70:30, R_f(**5n**)=0.65, R_f(**4n**)=0.45 and R_f(**11nn**)=0.35 UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2924, 2852, 1600, 1504, 1462, 1264, 1210, 1163, 1121, 1029, 863 cm^{-1}.

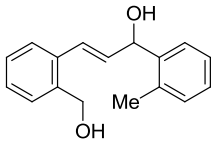
^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.02 (s, 1H, Ar-H), 7.01 (d, 1H, *J*=15.6 Hz, ArC*H*=CH), 7.00 (s, 1H, Ar-H), 6.77 (s, 1H, Ar-H), 6.69 (s, 1H, Ar-H), 6.09 (dd, 1H, *J*=15.6 and 7.8 Hz, ArCH=C*H*), 5.74 (d, 1H, *J*=7.8 Hz, ArC*H*(O)CH=CH), 5.17 (dd, 1H, *J*=11.2 and 2.9 Hz, ArCH_aH_bOCHCH=CH), 5.07 (dd, 1H, *J*=11.2 and 2.9 Hz, ArCH_aH_bOCHCH=CH), 3.88 (s, 3H, Ar-OCH_3), 3.86 (s, 6H, Ar-OCH_3), 3.83 (s, 3H, Ar-OCH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=149.5 (s, Ar-C), 149.4 (s, Ar-C), 149.1 (s, Ar-C), 148.5 (s, Ar-C), 132.2 (s, Ar-C), 130.7 (s, Ar-C), 130.6 (d, Ar-CH-CH=*C*H-Ar), 130.1 (d, Ar-CH-*C*H=CH-Ar), 128.3 (s, Ar-C), 115.3 (d, Ar-CH), 114.6 (s, Ar-C), 109.1 (d, Ar-CH), 105.0 (d, Ar-CH), 104.0 (d, Ar-CH), 85.6 (d, Ar-*C*HCH=CH), 73.0 (t, Ar-*C*H_2OCHCH=CH), 56.2 (q, Ar-OCH_3), 56.1 (q, Ar-OCH_3), 56.0 (q, Ar-OCH_3), 55.9 (q, Ar-OCH_3) ppm.

HR-MS (ESI^{+}): m/z calculated for $[C_{20}H_{21}BrNaO_5]^+$=$[M+Na]^+$: 443.0465; found 443.0468.

General procedure-5 for the synthesis of 1,3-dihydroisobenzofurans (11qh & 11ph): In an oven dried Schlenk under nitrogen atmosphere, were added $Pd(OAc)_2$ (5 mol%), $Bn(Et)_3NCl$ (0.50 mmol), $NaHCO_3$ (1 mmol), 2-bromobenzaldehydes **5h** (0.50 mmol) and *ortho*-Methyl/Methoxy aryl allylic alcohol **4q**/**4p** (0.60 mmol) followed by dry acetonitrile (4 mL). The resulted reaction mixture was stirred for 24 h at 80 °C. The reaction mixture was quenched using saturated aq. NH_4Cl solution and compound was extracted in ethyl acetate, concentrated under reduced pressure. The aldehyde **6qh/6ph** was isolated by silica gel column chromatography (petroleum ether/ethyl acetate). The aldehyde **6qh/6ph** was subjected to 0 °C and added $NaBH_4$ (1.50 mmol), stirred for two hours at rt. The reaction mixture was quenched with saturated aq. NH_4Cl solution and extracted with ethyl acetate (3 × 20 mL). The organic layer was washed with saturated NaCl solution, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Traces of solvents removed under high vacuum, to the above crude dry DCM 20 mL

was added cooled the reaction to –40 °C, $BF_3.Et_2O$ (2.5 mmol) added, stir the reaction for 2 h at the same temperature. The reaction mixture was then quenched with saturated aqueous $NaHCO_3$ solution and the aqueous layer was extracted with DCM (3 × 20 mL). The organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **(11qh & 11ph)** (47-52%).



10**qh**

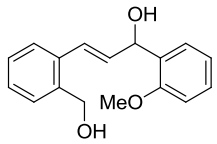
(2*E*)-3-[2-(hydroxymethyl)phenyl]-1-(2-methylphenyl)prop-2-en-1-ol (10qh): GP-5 was carried out and the product **10qh** (65 mg, 97%) was furnished as yellow colored viscous liquid. [TLC control (petroleum ether/ethyl acetate 70:30, R_f(**6qh**)=0.70, R_f(**10qh**)=0.30 UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3330, 1485, 1459, 1006, 967, 753, 564 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.52–7.46 (m, 1H, Ar-H), 7.44 (d, 1H, *J*=7.8 Hz, Ar-H), 7.32–7.10 (m, 6H, Ar-H), 6.98 (d, 1H, *J*=15.6 Hz, ArC*H*=CH), 6.21 (dd, 1H, *J*=15.6 and 5.9 Hz, ArCH=C*H*), 5.47 [d, 1H, *J*=5.9 Hz, PhC*H*(OH)CH=CH], 4.63 (d, 1H, *J*=12.2 Hz, PhC$H_a$$H_b$OH), 4.62 (d, 1H, *J*=12.2 Hz, PhC$H_a$$H_b$OH), 3.76 (br.s, 1H, OH), 3.29 (br.s, 1H, OH), 2.35 (s, 3H, Ar-CH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=140.4 (s, Ar-C), 137.5 (s, Ar-C), 135.8 (s, Ar-C), 135.2 (s, Ar-C), 133.2 (d, Ar-CH-CH=*C*H-Ar), 130.4 (d, Ar-CH), 128.7 (d, Ar-CH-*C*H=CH-Ar), 128.1 (d, Ar-CH), 127.6 (d, Ar-CH), 127.5 (d, Ar-CH), 126.9 (d, Ar-CH), 126.2 (2 × d, 2C, Ar-CH), 125.9 (d, Ar-CH), 71.4 (d, Ph-*C*HCH=CH), 63.1 (t, Ph-*C*H_2OH), 19.1 (q, Ar-CH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{17}H_{18}NaO_2]^+$=$[M+Na]^+$: 277.1199; foun d277.1197.



10ph

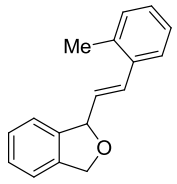
(2*E*)-3-[2-(hydroxymethyl)phenyl]-1-(2-methoxyphenyl)prop-2-en-1-ol (10ph): GP-5 was carried out and the product **10ph** (67 mg, 96%) was furnished as colorless viscous liquid. [TLC control (petroleum ether/ethyl acetate 70:30, R_f(**6ph**)=0.80, R_f(**10ph**)=0.30 UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3320, 1597, 1489, 1461, 1244, 1023, 753 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.39 (ddd, 2H, *J*=8.8, 7.8 and 1.5 Hz, Ar-H), 7.32–7.10 (m, 4H, Ar-H), 6.99 (d, 1H, *J*=16.1 Hz, ArC*H*=CH), 6.87 (dd, 1H, *J*=7.8 and 7.3 Hz, Ar-H), 6.82 (d, 1H, *J*=8.3 Hz, Ar-H), 6.43 (dd, 1H, *J*=16.1 and 5.9 Hz, ArCH=C*H*), 5.52 [d, 1H, *J*=5.9 Hz, PhC*H*(OH)CH=CH], 4.66 (s, 2H, ArCH_2OH), 3.77 (s, 3H, Ar-OCH_3), 3.64 (br.s, 2H, 2 × OH) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=156.7 (s, Ar-C), 141.1 (s, Ar-C), 138.5 (s, Ar-C), 131.0 (d, Ar-CH-CH=*C*H-Ar), 130.0 (d, Ar-CH), 128.8 (d, Ar-CH-*C*H=CH-Ar), 128.3 (d, Ar-CH), 128.1 (d, Ar-CH), 127.8 (d, Ar-CH), 127.0 (d, Ar-CH), 125.5 (s, Ar-C), 125.4 (d, Ar-CH), 120.6 (d, Ar-CH), 110.8 (d, Ar-CH), 73.2 (d, Ph-*C*HCH=CH), 63.5 (t, Ph-*C*H_2OH), 55.4 (q, Ar-OCH_3) ppm.

HR-MS (ESI+): m/z calculated for $[C_{17}H_{19}O_3]^+$=$[M+H]^+$: 271.1329; found 271.1320.



11qh

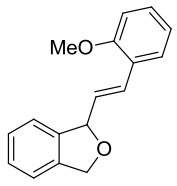
1-[(*E*)-2-(2-methylphenyl)vinyl]-1,3-dihydro-2-benzofuran (11qh): GP-5 was carried out and the product **11qh** (50 mg, 84%) was furnished as colorless viscous liquid. [TLC control (petroleum ether/ethyl acetate 95:5, R_f(**10ph**)=0.15, R_f(**11qh**)=0.80 UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2924, 2853, 1731, 1460, 1029, 965, 747, 697 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.45 (d, 1H, *J*=8.3 Hz, Ar-H), 7.36–7.25 (m, 3H, Ar-H), 7.24–7.10 (m, 4H, Ar-H), 6.97 (d, 1H, *J*=15.6 Hz, ArC*H*=CH), 6.16 (dd, 1H, *J*=15.6 and 7.8 Hz, ArCH=C*H*), 5.79 [d, 1H, *J*=7.8 Hz, PhC*H*(O)CH=CH], 5.23 (dd, 1H, *J*=12.2 and 2.4 Hz, PhCH_aH_bOCHCH=CH), 5.14 (d, 1H, *J*=12.2 Hz, PhCH_aH_bOCHCH=CH), 2.39 (s, 3H, Ar-CH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=141.0 (s, Ar-C), 139.2 (s, Ar-C), 135.7 (s, Ar-C), 135.5 (s, Ar-C), 130.3 (2 × d, 2C, Ar-CH-CH=*C*H-Ar and Ar-CH), 129.9 (d, Ar-CH), 127.7 (2 × d, 2C, Ar-CH-*C*H=CH-Ar and Ar-CH), 127.4 (d, Ar-CH), 126.0 (d, Ar-CH), 125.9 (d, Ar-CH), 122.0 (d, Ar-CH), 121.1 (d, Ar-CH), 85.5 (d, Ph-*C*HCH=CH), 72.8 (t, Ph-*C*H_2OCHCH=CH), 19.9 (q, Ar-CH_3) ppm.

HR-MS (ESI+): m/z calculated for $[C_{17}H_{16}NaO]^+$=$[M+Na]^+$: 259.1093; found 259.1099.



11ph

1-[(*E*)-2-(2-methoxyphenyl)vinyl]-1,3-dihydro-2-benzofuran (11ph): GP-5 was carried out and the product **11ph** (53 mg, 86%) was furnished as colorless viscous liquid. [TLC control (petroleum ether/ethyl acetate 95:5, R_f(**10ph**)=0.10, R_f(**11ph**)=0.70 UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2904, 2838, 1489, 1461, 1244, 1028, 749, 697 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.45 (dd, 1H, *J*=7.8 and 1.5 Hz, Ar-H), 7.36–7.15 (m, 5H, Ar-H), 7.09 (d, 1H, *J*=15.6 Hz, ArC*H*=CH), 6.91 (d, 1H, *J*=7.3 Hz, Ar-H), 6.87 (d, 1H, *J*=7.3 Hz, Ar-H), 6.30 (dd, 1H, *J*=15.6 and 7.8 Hz, ArCH=C*H*), 5.78 [d, 1H, *J*=7.8 Hz, PhC*H*(O)CH=CH], 5.23 (dd, 1H, *J*=12.2 and 2.4 Hz, PhC$H_a$$H_b$OCHCH=CH), 5.13 (d, 1H, *J*=12.2 Hz, PhC$H_a$$H_b$OCHCH=CH), 3.86 (s, 3H, Ar-OCH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=156.9 (s, Ar-C), 141.2 (s, Ar-C), 139.2 (s, Ar-C), 129.4 (d, Ar-CH-CH=*C*H-Ar), 128.9 (d, Ar-CH), 127.6 (d, Ar-CH-*C*H=CH-Ar), 127.4 (d, Ar-CH), 127.1 (d, Ar-CH), 127.0 (d, Ar-CH), 125.4 (s, Ar-C), 122.1 (d, Ar-CH), 121.0 (d, Ar-CH), 120.5 (d, Ar-CH), 110.8 (d, Ar-CH), 85.9 (d, Ph-*C*HCH=CH), 72.7 (t, Ph-*C*H_2OCHCH=CH), 55.4 (q, Ar-OCH_3) ppm.

HR-MS (ESI+): m/z calculated for $[C_{17}H_{17}O_2]^+$=$[M+H]^+$:253.1223; found 253.1219.

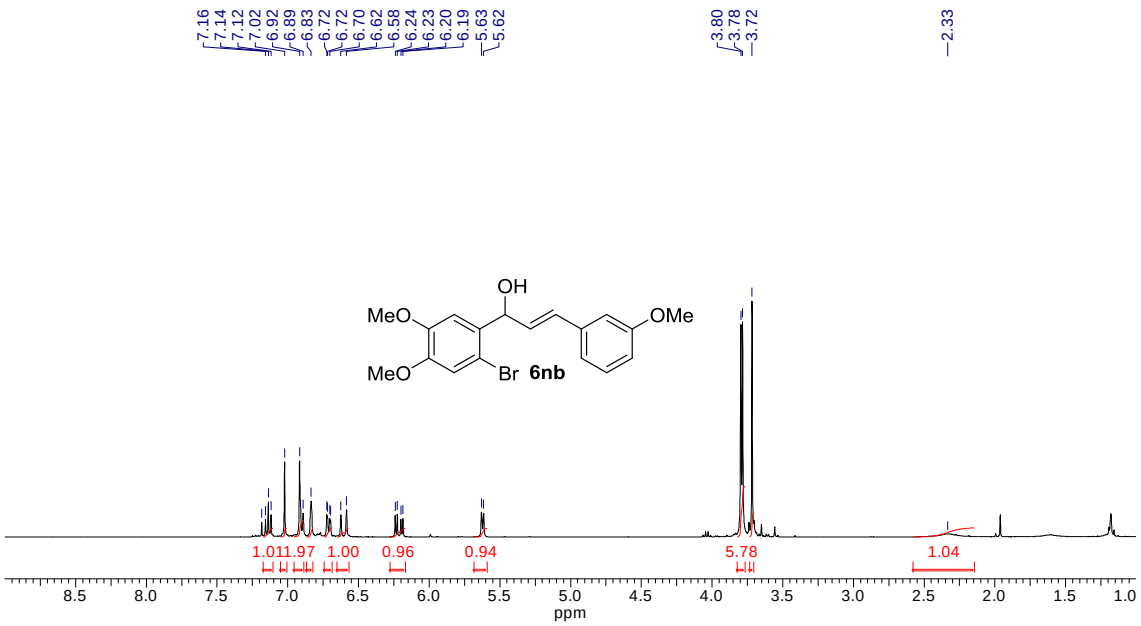


Figure II.11.1: ^{1}H-NMR (400 MHz) spectrum of **6nb** in $CDCl_3$

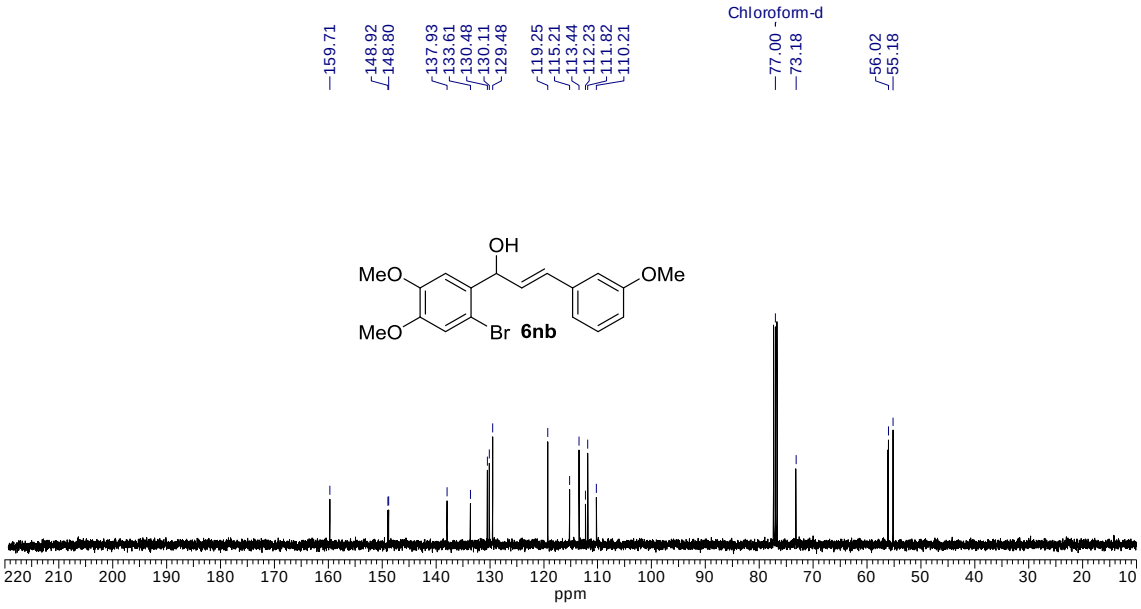


Figure II.11.2: ^{13}C-NMR (100 MHz) spectrum of **6nb** in $CDCl_3$

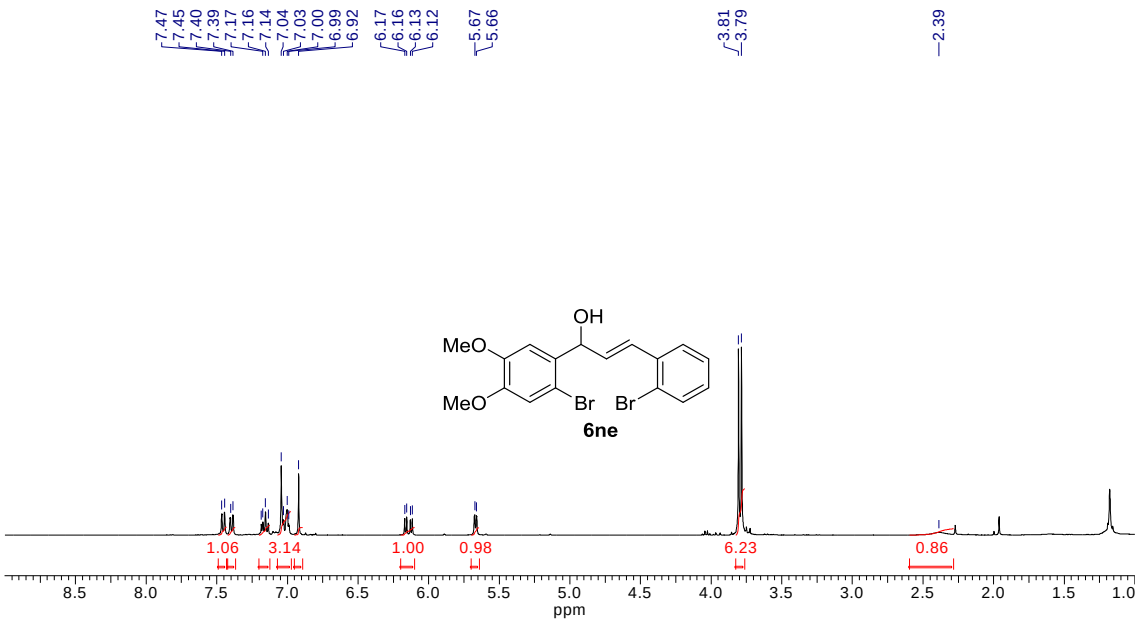


Figure II.12.1: ^{1}H-NMR (400 MHz) spectrum of **6ne** in $CDCl_3$

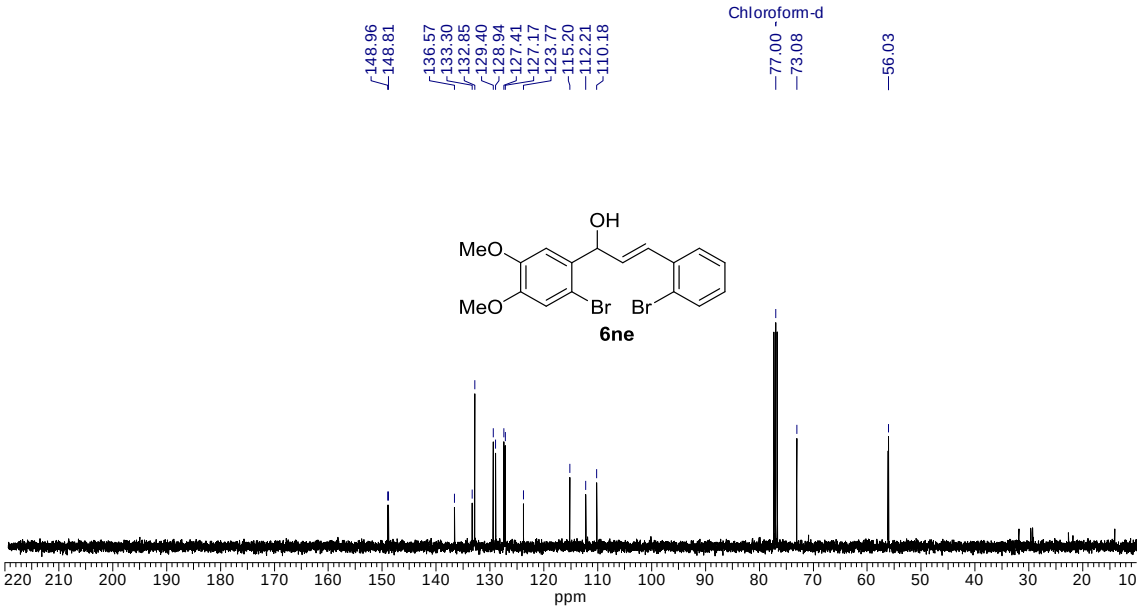


Figure II.12.2: ^{13}C-NMR (100 MHz) spectrum of **6ne** in $CDCl_3$

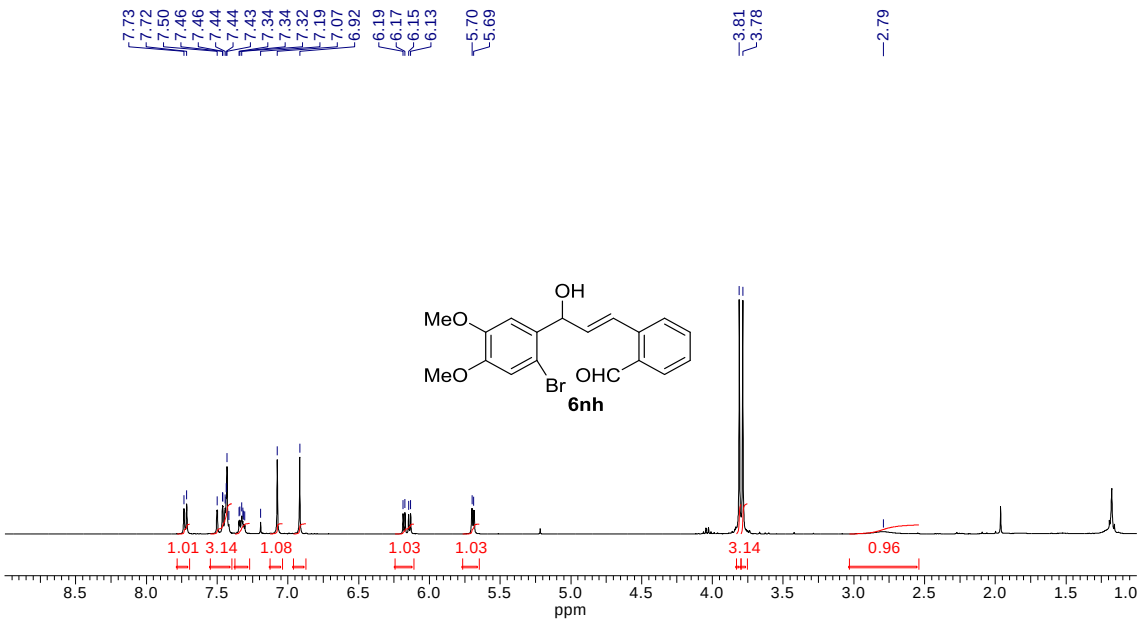


Figure II.13.1: ^{1}H-NMR (400 MHz) spectrum of **6nh** in $CDCl_3$

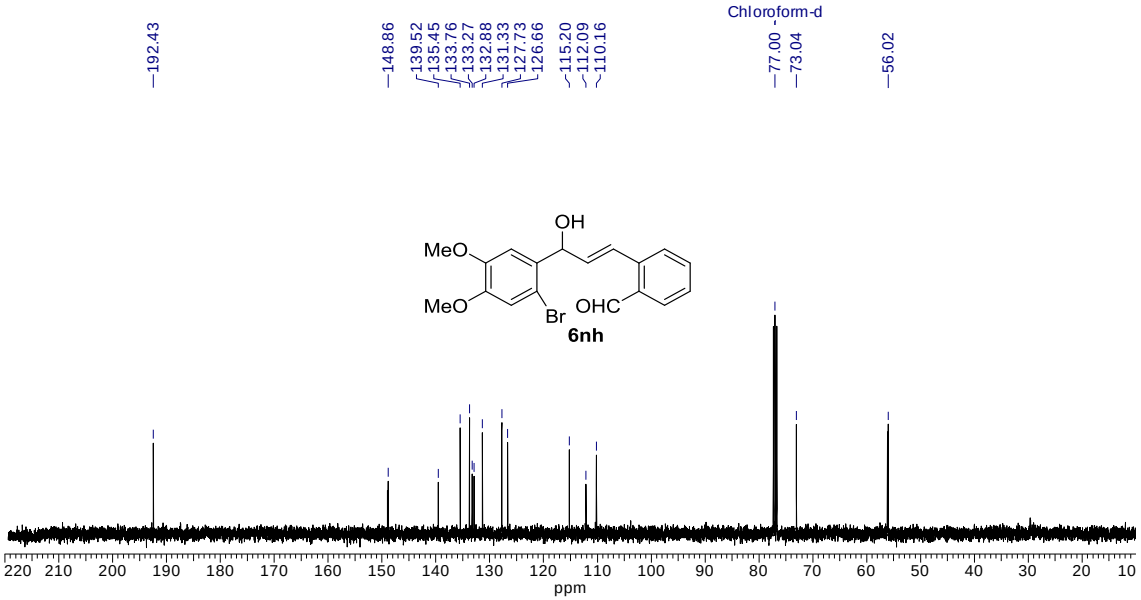


Figure II.13.2: ^{13}C-NMR (100 MHz) spectrum of **6nh** in $CDCl_3$

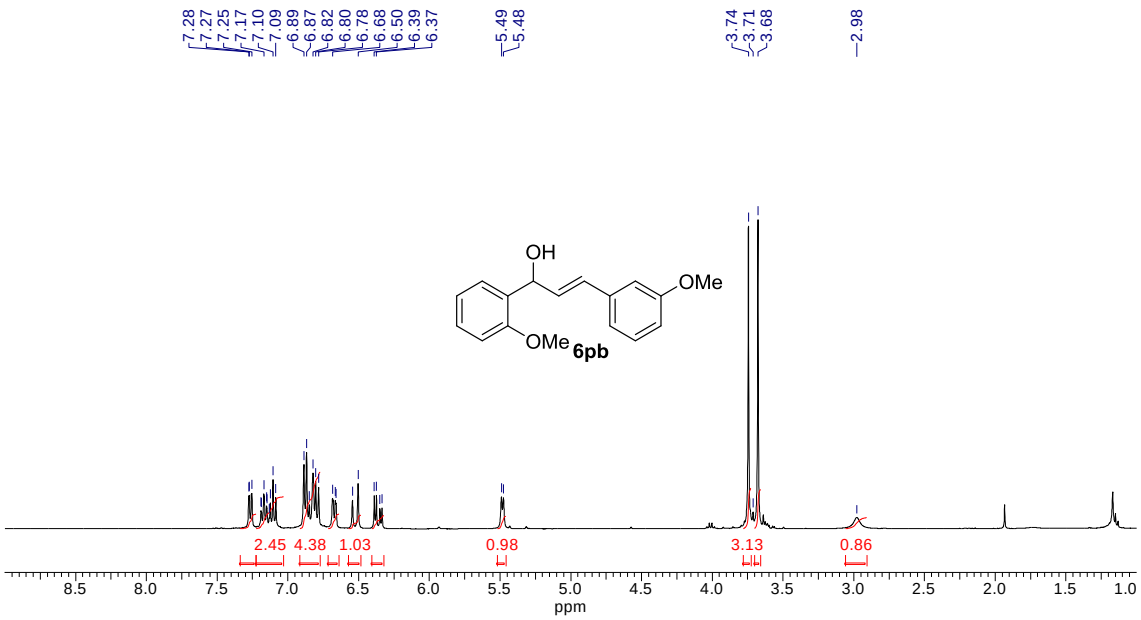


Figure II.14.1: ^{1}H-NMR (400 MHz) spectrum of **6pb** in $CDCl_3$

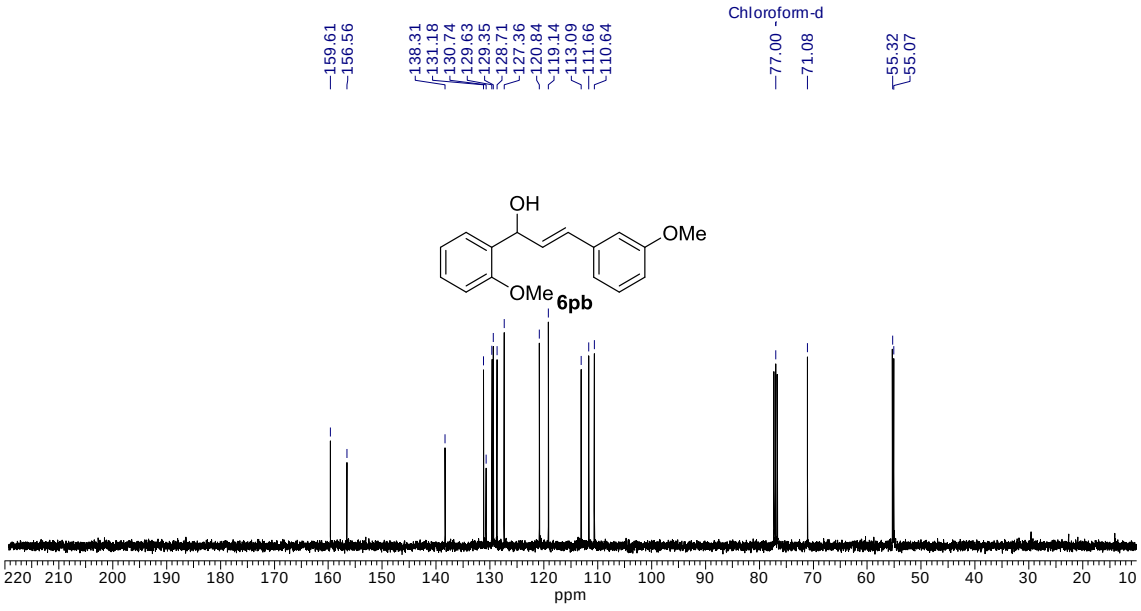


Figure II.14.2: ^{13}C-NMR (100 MHz) spectrum of **6pb** in $CDCl_3$

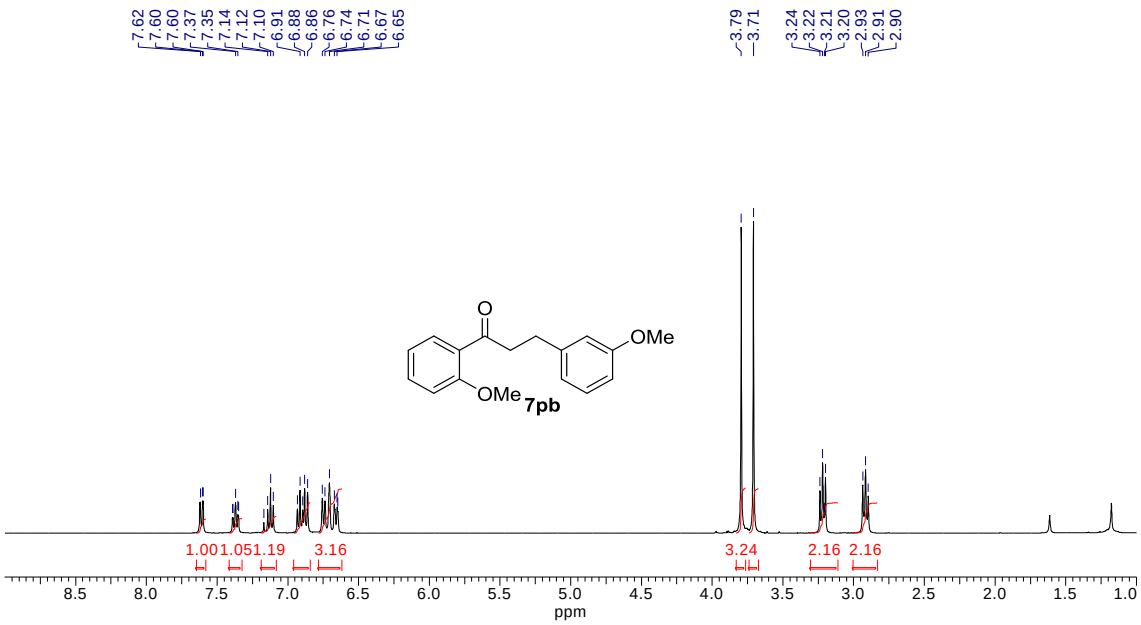


Figure II.15.1: ^{1}H-NMR (400 MHz) spectrum of **7pb** in $CDCl_3$

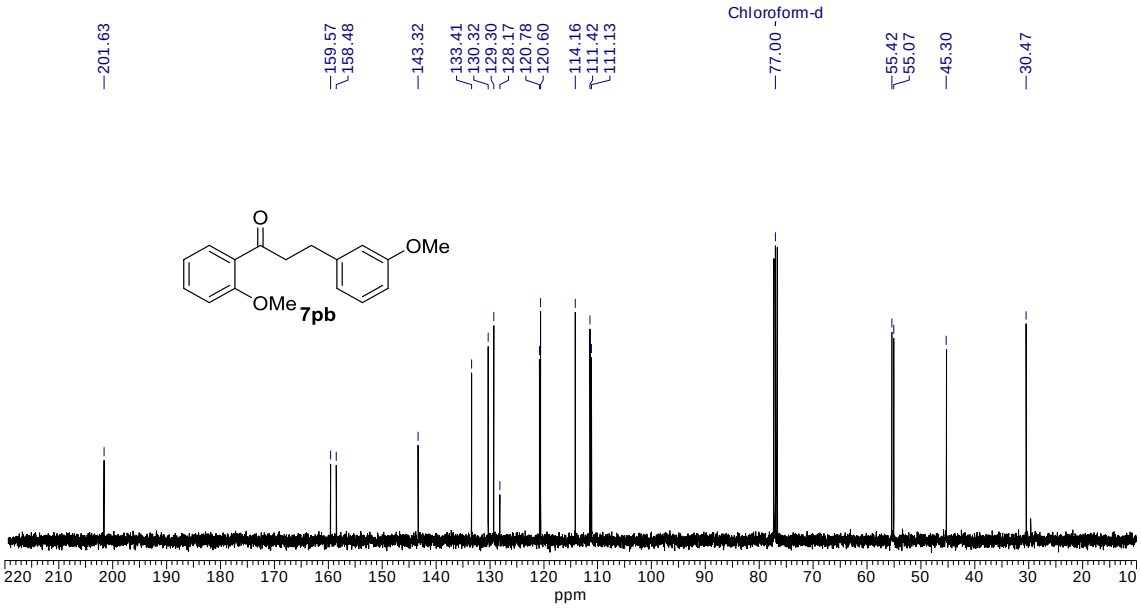


Figure II.15.2: ^{13}C-NMR (100 MHz) spectrum of **7pb** in $CDCl_3$

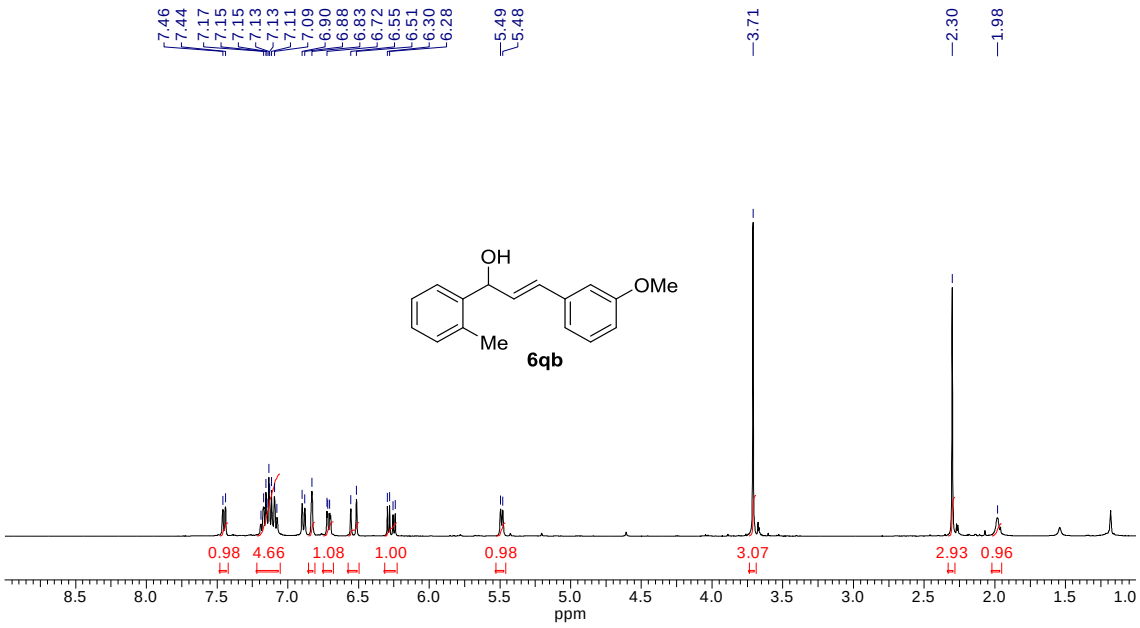


Figure II.16.1: ^{1}H-NMR (400 MHz) spectrum of **6qb** in $CDCl_3$

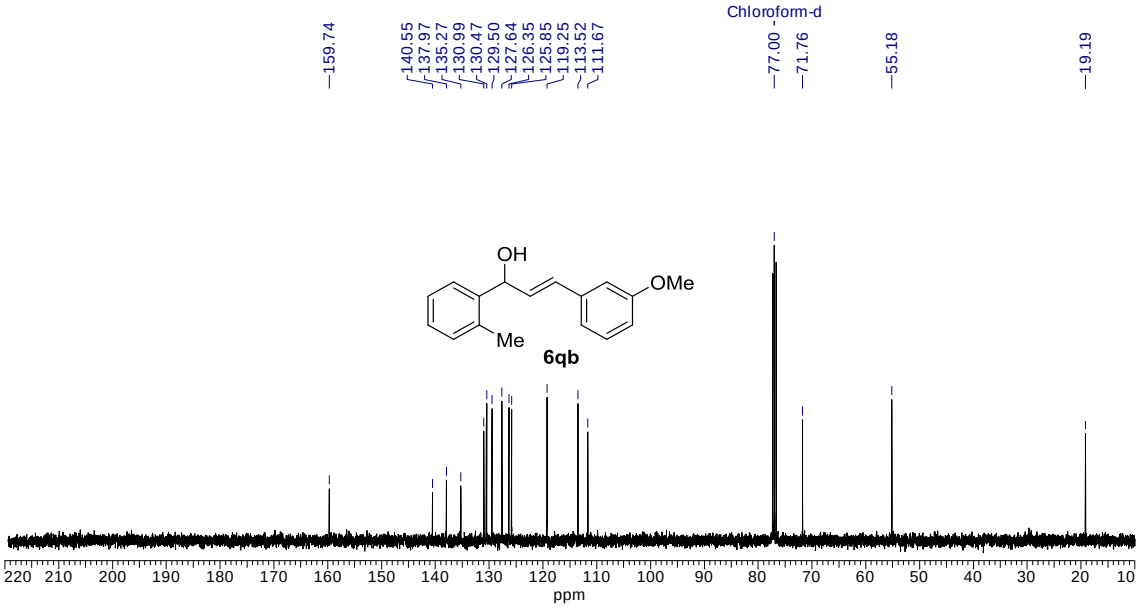


Figure II.16.2: ^{13}C-NMR (100 MHz) spectrum of **6qb** in $CDCl_3$

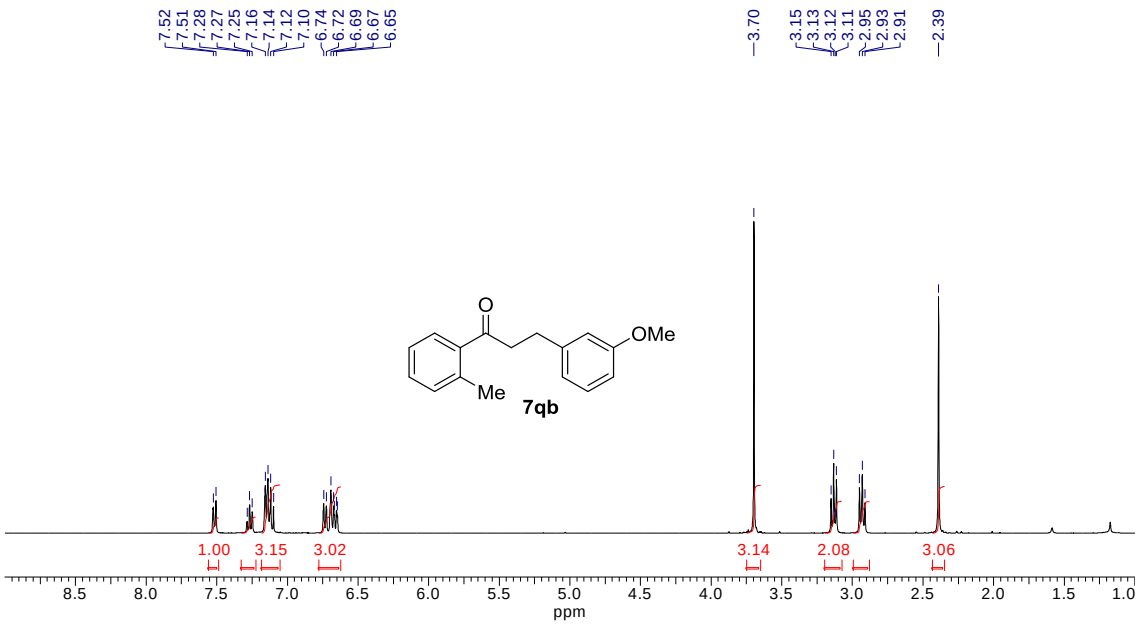


Figure II.17.1: ^{1}H-NMR (400 MHz) spectrum of **7qb** in $CDCl_3$

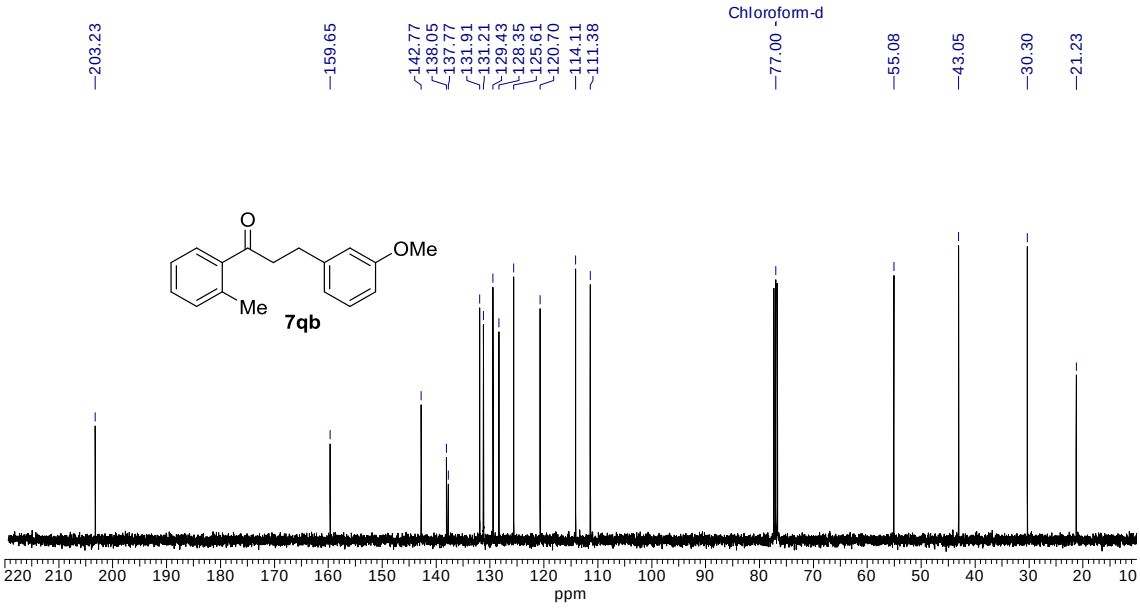


Figure II.17.2: ^{13}C-NMR (100 MHz) spectrum of **7qb** in $CDCl_3$

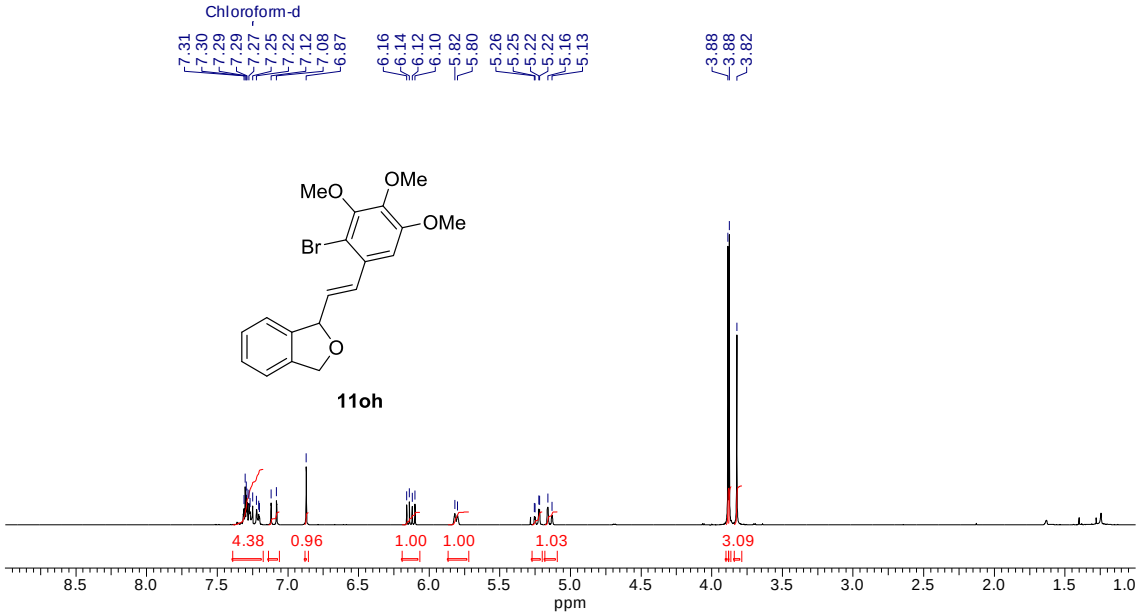


Figure II.18.1: ^{1}H-NMR (400 MHz) spectrum of **11oh** in $CDCl_3$

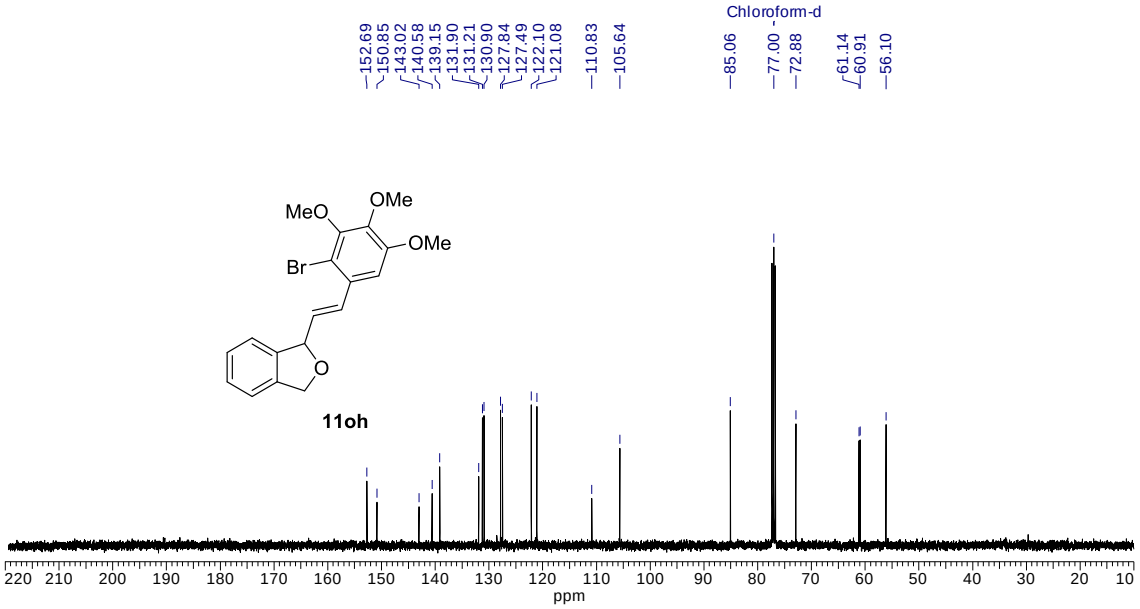


Figure II.18.2: ^{13}C-NMR (100 MHz) spectrum of **11oh** in $CDCl_3$

CHAPTER III

DOMINO [Pd]-CATALYSIS: SYNTHESIS OF BI-ARYL ACETYLENES

III.1 INTRODUCTION:

Transition-metal catalyzed C-C bond forming reactions are considered to be an important tool in the arena of organic synthesis. Amongst Sonogashira reaction that involves palladium-copper catalyzed Csp^2-Csp bond formation between terminal alkyne and aryl halide for the synthesis of di-substituted acetylenes. The Sonogashira reaction has been evidence as an efficient method for the synthesis of various alkynes. It has gained much significance in construction of complex molecules because of its electronic properties and linear geometry.[70] In literature, molecules containing (*Z*)-enediynes or related unsaturated framework are found to have potent antitumor,

antibiotic activity or contraceptive pill. Chiral molecules having propargylic stereo center are found to be much useful building blocks in the synthesis of natural products and pharmaceuticals and functional materials.[71,72,73]

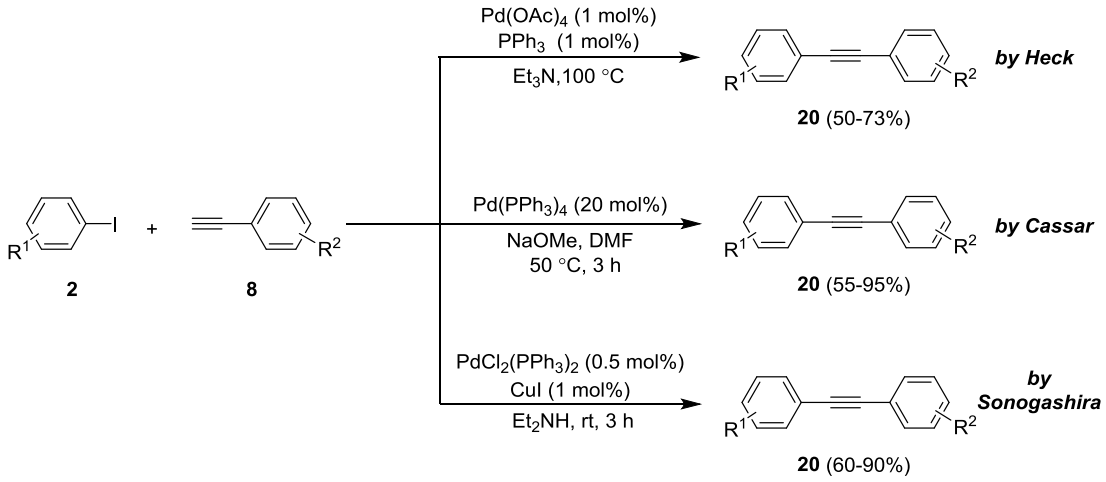
Usually, this reaction was performed by using either $Pd(PPh_3)_2Cl_2$ or $Pd(PPh_3)_4$ as a catalyst and copper(I)-iodide as the co-catalyst. The most commonly used bases for this purpose are triethylamine, diethylamide and di-isopropylethylamine (Hünig's base). The solvents that are commonly employed in this reaction are benzene, toluene, THF, DMF, and dioxane and in some cases amine itself acts as a solvent when taken in excess amount.[74]

It is observed that sonogashira reaction requires copper salts as a co-catalyst and it involves in-situ generation of copper acetylide. These copper salts involves generally generate the Glaser coupling product as the byproduct upon exposure to oxidative agents or air,[75] thus effecting the reaction course and yields of the bi-aryl acetylenes. Since these byproducts are usually difficult to separate, this side reaction is a major concern. Due to these reasons, preparation of terminal alkynes is very difficult or it is costly. On the other hand, copper acetylide is a potential explosive reagent; hence, the reaction is not environmental friendly. In literature, many alterations have been developed to improve the Sonogashira reaction such as the use of phase-transfer reaction conditions,[76] performing the reaction in aqueous medium,[77] solvent-free reaction conditions etc.,[78] but it still requires copper as a co-catalyst. Therefore, the reaction without the assistance of copper salt as co-catalyst would be the most significant method for the preparation of bi-aryl acetylenes.

III.2 BACKGROUND:

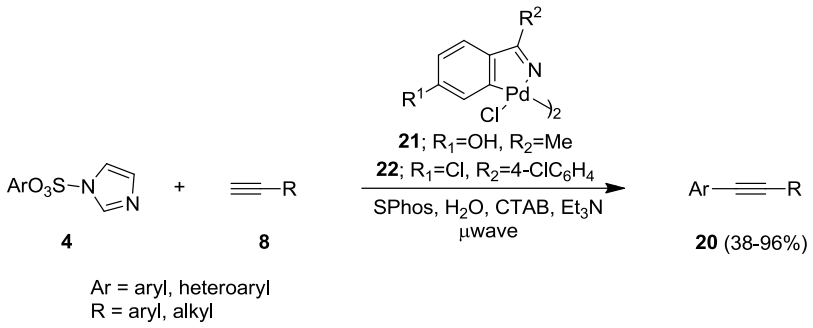
In the year 1975, three research groups independently developed a method for the synthesis of bi-aryl acetylenes **20** by Heck,[79] Cassar[80] Sonogashira and Hagihara[81]

(Scheme III.1). Heck's strategy was based on the known Mizoroki-Heck reaction and by using $Pd(OAc)_2$ and Ph_3P as a catalytic system and triethylamine as a base as well as a solvent, whereas Cassar's process involved the use of $Pd(PPh_3)_4$ as a catalyst, sodium methoxide as a base and DMF as a solvent. Both methods generally required high temperature. At the same time, Sonogashira and Hagihara disclosed a method for the synthesis of bi-aryl acetylenes **20** by adding CuI as co-catalyst at room temperature involving short reaction time. Afterwards this method became popular and was known as Sonogashira coupling.



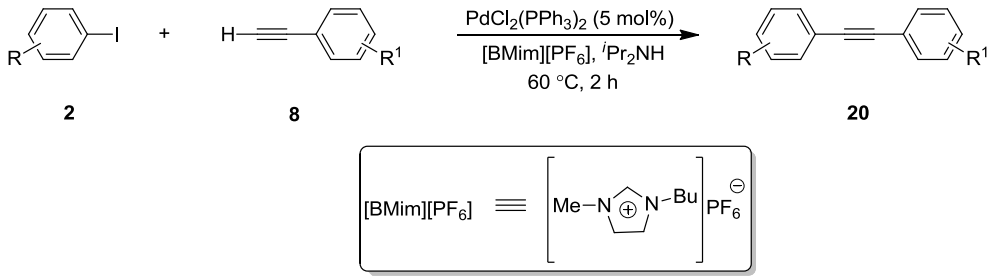
Scheme III.1

Carmen Najera reported a microwave assisted strategy for the synthesis of di-substituted alkynes from aryl imidazol-1-ylsulfonates **4** and aryl-, alkyl- acetylenes **8** in aqueous medium without the assistance of copper co-catalyst. This method was successfully carried out in the presence of 0.5 mol% of an oxime palladacycle as pre-catalyst **21** and **22**, SPhos and hexadecyltrimethylammonium bromide (CTAB). Various di-substituted alkynes **20** have been prepared in poor to excellent yields in 30 mins short span of time (Scheme III.2).[82]



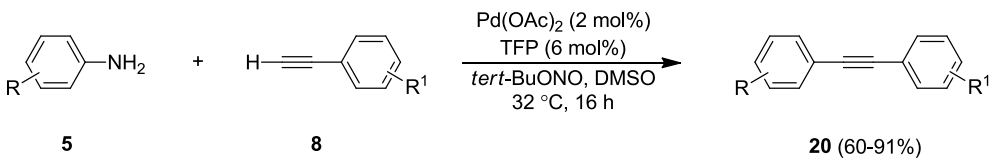
Scheme III.2

Ryu et al. disclosed a novel copper-free Sonogashira coupling reaction for the synthesis of bi-aryl substituted acetylenes **20** by using ionic liquid ([BMIm][PF_6]) and the products were obtained in very good to excellent yields (Scheme III.3).[83]



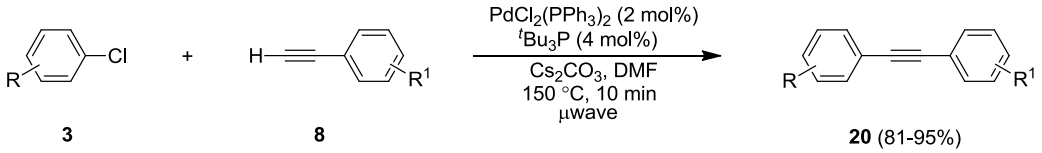
Scheme III.3

Matthias Beller and co-workers presented a very convenient and novel strategy for the synthesis of bi-aryl acetylenes **20** directly from aromatic anisignals **5** and terminal aryl acetylene **8** by in-situ generated arenediazonium salts (Scheme III.4).[84]



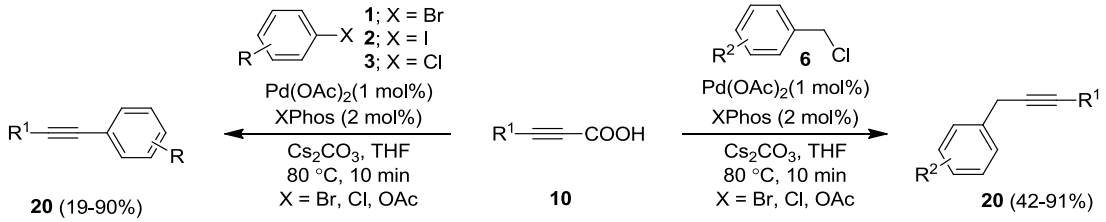
Scheme III.4

Liu et al. developed a rapid and quick access to bi-aryl acetylene **20** by copper-free [Pd]-catalyzed Sonogahira cross coupling of aryl chloride **3** and terminal aryl alkyne **8**. The generality of this method was checked on various aryl chlorides **8**, which include electron-rich, electron-neutral, electron deficient and sterically hindered aryl chloride **8** (Scheme III.5).[85]



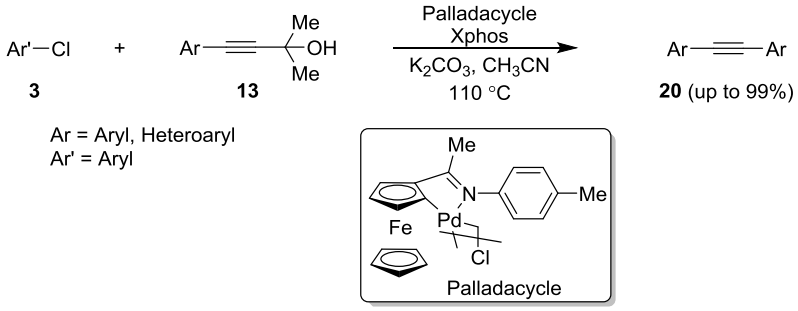
Scheme III.5

Li and co-workers have also contributed to the copper and amine free mediated synthesis of di-substituted alkynes **20**. It is [Pd]-catalyzed decarboxylative coupling reactions between alkynyl carboxylic acids **10** and benzyl halides **6** or aryl halides **1**, **2** and **3** which lead to the formation of di-substituted alkynes **20** (Scheme III.6).[86]



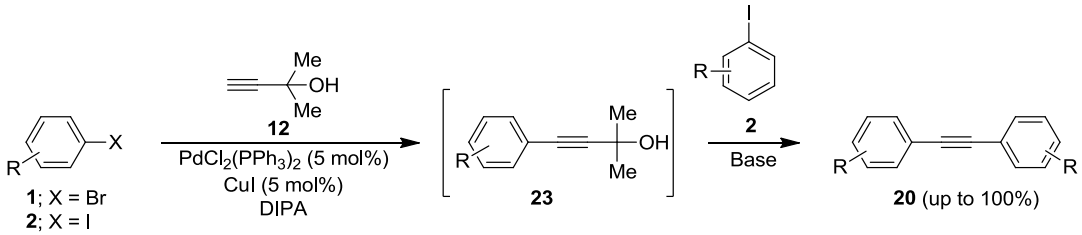
Scheme III.6

Yang and Wu developed an interesting methodology for executing di-substituted symmetrical as well as unsymmetrical acetylenes **20**. It is a palladacycle mediated deacetonative Sonogashira coupling of aryl propargyl alcohols **13** with aryl chlorides **3**, which furnished the di substituted bi-aryl acetylene products **20** in excellent yields (Scheme III.7).[87]



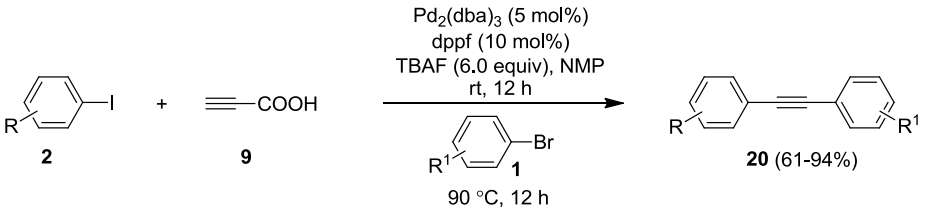
Scheme III.7

Kotschy disclosed an interesting tandem Sonogashira coupling for the synthesis of bi-aryl acetylenes **20**. The reaction is based on [Pd]- and [Cu]-catalyzed coupling between 2-methyl-3-butyn-2-ols **12** and aryl halides **1** and **2**. The reaction proceeds through a sequential one-pot process, i.e., initial Sonogashira coupling of aryl halide to give **23** followed by deprotection of acetylene under the influence of a strong base and then second Sonogashira coupling with aryl halide **2** to furnish the bi-aryl acetylenes **20** (Scheme III.8).[88]



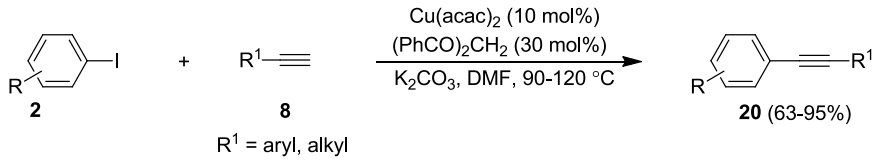
Scheme III.8

Lee demonstrated a novel approach for the synthesis of bi-aryl alkynes **20** using the tandem approach based on a [Pd]-catalyzed Sonogashira coupling and a subsequent decarboxylative Sonogashira reaction in one-pot. This method was successful in delivering the symmetrical as well as unsymmetrical bi-aryl or aryl hetero-aryl acetylenes **20** (Scheme III.9).[89]



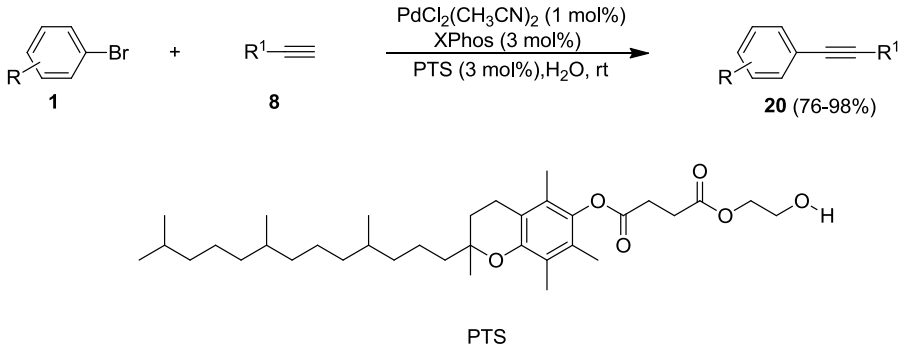
Scheme III.9

Monnier and Taillefer developed cost effective catalytic system for the synthesis of di-substituted alkynes **8** in good to excellent yields. This method describes the utility of copper/ligand combination under palladium-free conditions (Scheme III.10).[90]



Scheme III.10

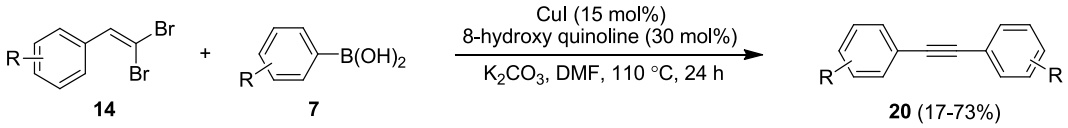
Lipshutz reported an interesting copper-free [Pd]-catalyzed Sonogashira cross-coupling of aryl bromides **1** at ambient temperature in water by the addition of a small amount of nonionic amphiphile PTS (Scheme III.11).[91]



Scheme III.11

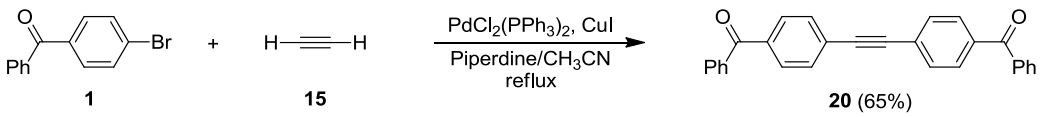
Mao and co-workers developed a practical and cost effective catalytic system for the synthesis of bi-aryl acetylenes **20** by a domino cross coupling of 1,1-dihalo-1-

alkenes **14** with aryl boronic acids **7** in the presence of cheap 8-hydroxylquinoline as the ligand (Scheme III.12).[92]



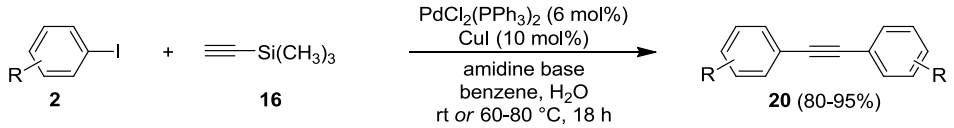
Scheme III.12

Rathore carried out the synthesis of bi-aryl acetylene **20** using [Pd]-catalyzed coupling of commercially available aryl halide **1** with gaseous acetylene **15** (Scheme III.13).[93]



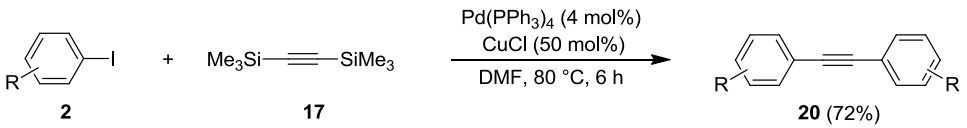
Scheme III.13

Mio and co-workers implemented a modified Sonogashira cross-coupling for the synthesis of symmetrical as well as unsymmetrical bi-aryl acetylenes **20** in one pot via in-situ deprotection of trimethylsilylethynylene **16** intermediates using amidine base and a sub stoichiometric amount of water (Scheme III.14).[94]



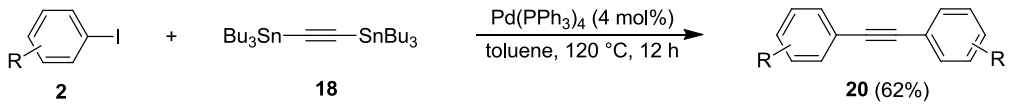
Scheme III.14

Nishihara described a strategy for the synthesis of bi-aryl acetylenes **20** using [Pd]/[Cu]-catalyzed sila-Sonogashira coupling of aryl-iodides **2** with an alkyne source bis(trimethylsilyl)acetylene **17** (Scheme III.15).[95]



Scheme III.15

The research groups of Fand and Shi individually carried out [Pd]-catalyzed cross coupling between aryl iodide **2** and bis(tributylstannyl) acetylene **18** for the synthesis of symmetrical bi-aryl alkynes **20** (Scheme III.16).[96]

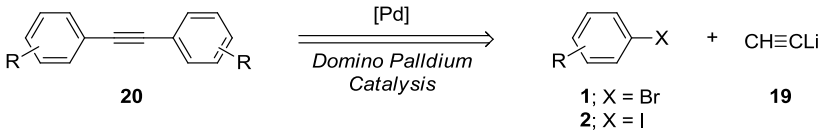


Scheme III.16

III.3 RESULTS AND DISCUSSION:

In the wake of a new, efficient and practical methodology for the synthesis of bi-aryl acetylene, in our quest, we came across numerous methods that appeared in the literature for the synthesis of bi-aryl acetylenes **20**.[79-96] In this regard, as described above, many research groups used different alkyne sources such as terminal aryl alkyne,[79-81] 2-methylbut-3-yn-2-ol **12**,[88] propiolic acid **9** or 2-ccetylenedicarboxylic acid **11**,[89] gaseous acetylene **15**,[93] trimethylsilyl acetylene **16**,[94] bis(trimethylsilyl)acetylene **17**,[95] bis(tributylstannyl)acetylene **18**.[96] Nevertheless, the synthesis of bi-aryl acetylenes still remains challenging and there is a need to develop efficient methods. The above methods still suffer from some sort of disadvantages such as high cost of acetylene based reagents, difficulty in handling the gaseous form of acetylene, production of an equivalent of metal or organic waste, use of copper as a co-catalyst and the formation of toxic organometallic waste. On the other hand, some of the approaches made use of expensive palladacycle based catalysts[82,87] and ionic liquids.[83] As a part of our ongoing research interest on transition-metal mediated organic transformations in one-pot

fashion,[9] we envisioned that the synthesis of bi-aryl acetylenes could be achieved under [Pd]-catalysis by the direct cross coupling of commercially available simple lithium acetylide (i.e., as the source of acetylene) with aryl halides, in domino one-pot manner (Scheme III.17).

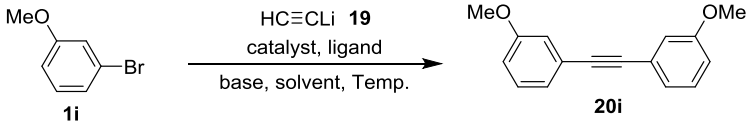


Scheme III.17

Thus, the domino Sonogashira cross-coupling of lithium acetylide **19** with aryl halide **1/2** in the presence of [Pd]-catalyst was screened under different conditions and the results are as summarized in Table III.1. Initially, the reaction with the $Pd(OAc)_2$ (2 mol%) and PPh_3 (4 mol%), in DMA and using K_2CO_3 as the base at 100 °C furnished product **20i** in moderate yield (42%, Table III.1, entry 1). There was a further drop in the yield, when the reaction was conducted with the 2-P(2-furyl)$_3$ (15%, Table III.1, entry 2). Interestingly, the yield was improved to 66% with the $Pd(PPh_3)_2Cl_2$ (Table III.1, entry 3). Similarly, with other ligands such as Diphos, Mephos and dpephos, furnished the product **20i** in moderate to good yields, respectively (Table III.1, entries 4 to 6). On the other hand, the yield was moderate by changing the ligand to xanthphos (4 mol%), in CH_3CN at 80 °C (50%, Table III.1, entry 7). Interestingly, by switching the solvent to DMF, it delivered the product **20i** in very good yield (80%, Table III.1, entry 8). Also, the ligand dppf proved to be good in DMA solvent (79%, Table III.1, entry 9). Interestingly, using Xantphos in DMA furnished the product **20i** in excellent yield (95%, Table III.1, entry 10). The other variation with different bases furnished the product **20i** in poor to moderate yields (Table III.1, entries 11 to 13). However, the reaction with excess of aryl bromide **1i** gave the produt **20i** in poor yield along with the usual homo bi-aryl product (Table 1, entry 14). While the reaction with 1:1 ratio of both

Lithium acetylide ethylenediamine complex and the aryl bromide **1i** was furnished the product **20i** in moderate yield (Table 1, entry 15).

Table III.1: Optimization table for the synthesis of bi-aryl acetylene **20i**.



Entry[a]	Catalyst (mol%)	Ligand (mol%)	Base (2 equiv)	Solvent (2 mL)	Temp (^oC)	Time (h)	Yield of 20i (%)[b]
1.	$Pd(OAc)_2$ (5)	PPh_3 (10)	K_2CO_3	DMA	100	3	42
2.	$Pd(OAc)_2$ (2)	P(2-furyl)$_3$ (4)	K_2CO_3	DMA	100	2	15
3.	Pd $(PPh_3)_2Cl_2$ (2)	-	K_2CO_3	DMA	100	3	66
4.	$Pd(OAc)_2$ (2)	DiPhos (4)	K_2CO_3	DMA	100	3	50
5.	$Pd(OAc)_2$ (2)	MePhos (4)	K_2CO_3	DMA	100	2	58
6.	$Pd(OAc)_2$ (2)	DPEPhos (4)	K_2CO_3	DMA	100	2	68
7.	$Pd(OAc)_2$ (2)	Xantphos (4)	K_2CO_3	CH_3CN	80	12	50
8.	$Pd(OAc)_2$ (2)	Xantphos (4)	K_2CO_3	DMF	100	3	80
9.	$Pd(OAc)_2$ (2)	dppf (4)	K_2CO_3	DMA	100	3	79
10.	**$Pd(OAc)_2$ (2)**	**Xantphos (4)**	**K_2CO_3**	**DMA**	**100**	**3**	**95**
11.	$Pd(OAc)_2$ (2)	Xantphos (4)	TEA	DMA	100	2	52
12.	$Pd(OAc)_2$ (2)	Xantphos (4)	DIPEA	DMA	100	2	30
13	$Pd(OAc)_2$ (2)	Xantphos (4)	Cy_2NMe	DMA	100	2	41
14	$Pd(OAc)_2$ (2)	Xantphos (4)	K_2CO_3	DMA	100	3	30[c]
15	$Pd(OAc)_2$ (2)	Xantphos (4)	K_2CO_3	DMA	100	3	55[d]

[a]All reactions were performed on (0.50 mmol) scale of **1i**, in 0.25 M concentration.[b]Isolated yields of chromatographically pure products. [c]Reaction conducted with Lithium acetylide ethylenediamine complex (0.5 mmol) and aryl bromide **1i** (2.0 mmol). [d]Reaction conducted with Lithium acetylide ethylenediamine complex (0.5 mmol) and aryl bromide **1i** (1.0 mmol).

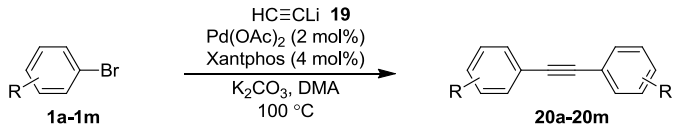
Among all the above screened reaction conditions, the conditions mentioned in Table III.1, entry 10 was the best [i.e., 2 mol% of $Pd(OAc)_2$, 4 mol% of and 2.0 equiv of K_2CO_3, in DMA as a solvent at 100 ^oC]. Therefore, this condition was applied on

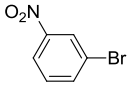
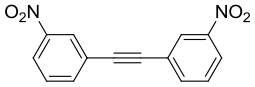
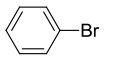
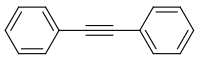
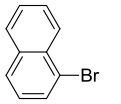
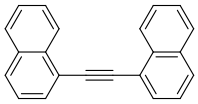
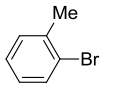
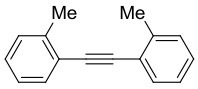
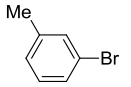
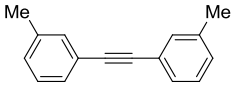
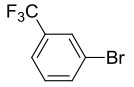
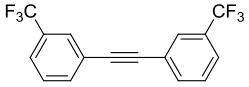
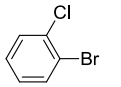
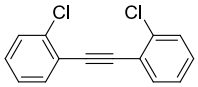
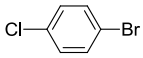
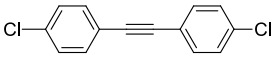
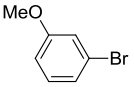
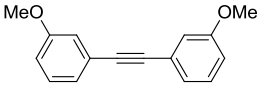
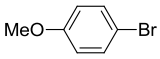
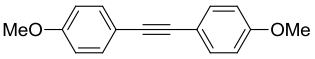
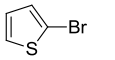
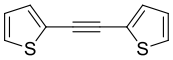
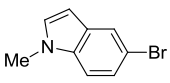
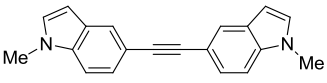
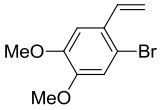
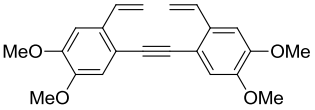
other aryl bromides **1a-1m**. Delightfully, the method was found amenable to a variety of electron-poor, neutral and electron-rich aryl bromides and furnished the symmetrical bi-aryl acetylenes **20a-20m** in very good to excellent yields (60-95%, Table III.2). Significantly, the reaction showed a wide range of functional group tolerance. For example, halo arenes with alkyl, aryl, alkyloxy, chloro, trifluoromethyl and nitro groups were successful in delivering the products **20a-20m**. Interestingly, the reaction was successful with hetero aryl bromides as well.

Even though many methods have been reported on Sonogashira coupling, for the synthesis of bi-aryl acetylenes **20**, some of these methodologies found to be efficient. However, they usually require pre-functionalization of substrates, which impact their atom economy. In this perspective, the present method seems to be very efficient as it makes use of the commercially available cheap lithium acetylide as the acetylene equivalent.

The structure of bi-aryl acetylene **20a** was confirmed by IR and NMR data analysis. IR spectra did not show the characteristic absorption band for acetylenic group. In the ^{1}H-NMR spectrum (Figure III.1.1), the presence of doublet of a doublet at δ 8.39 having *J*=1.5 and 1.5 Hz accounts for two aromatic protons, doublet of a doublet at δ 8.22 having *J*=8.3 and 1.5 Hz accounts for two aromatic protons, doublet at δ 7.85 having *J*=7.8 Hz accounts for two aromatic protons, doublet of a doublet at δ 7.57 having *J*=7.8 and 7.8 Hz accounts for another set off two aromatic protons, which elucidated the structure of bi-aryl acetylene **20a**. In addition to it, 7 signals appeared in ^{13}C-NMR spectrum (Figure III.1.2) in which four quaternary carbon resonates at δ 148.2 (2C), 124.0 (2C) were due to four aromatic carbon, the presence of eight aromatic methine carbons resonates at δ 137.4 (2C), 129.6 (2C), 126.6 (2C) and 123.6 (2C) and presence δ 89.1 ppm was due to acetylenic carbons. The presence of the $[M+Na]^{+}$ peak at m/z $[C_{14}H_8N_2NaO_4]^{+}$=291.0375 in the mass spectrum further established the structure of bi-aryl acetylene **20a**.

Table III.2: Domino [Pd]-catalyzed synthesis of bi-aryl acetylenes **20a-20m** from aryl bromides **1a-1m**.



Entry[a]	Substrates (1a-1m)		Products (20a-20m)		Time (h)	Yield (%)[b]
1.		**1a**		**20a**	0.25	75
2.		**1b**		**20b**	1.0	88
3.		**1c**		**20c**	1.0	83
4.		**1d**		**20d**	1.0	76
5.		**1e**		**20e**	1.0	70
6.		**1f**		**20f**	0.5	72
7.		**1g**		**20g**	0.25	74
8.		**1h**		**20h**	0.25	69
9.		**1i**		**20i**	3.0	95
10.		**1j**		**20j**	0.5	70
11.		**1k**		**20k**	0.25	60
[c]12.		**1l**		**20l**	12.0	73
13.		**1m**		**20m**	1.0	80

[a]All reactions were carried out on 0.5 mmol scale of **1** in 2 mL of DMA (0.25 M).[b] Isolated yields of chromatographically pure products. [c]Reaction carried out at 150 °C.

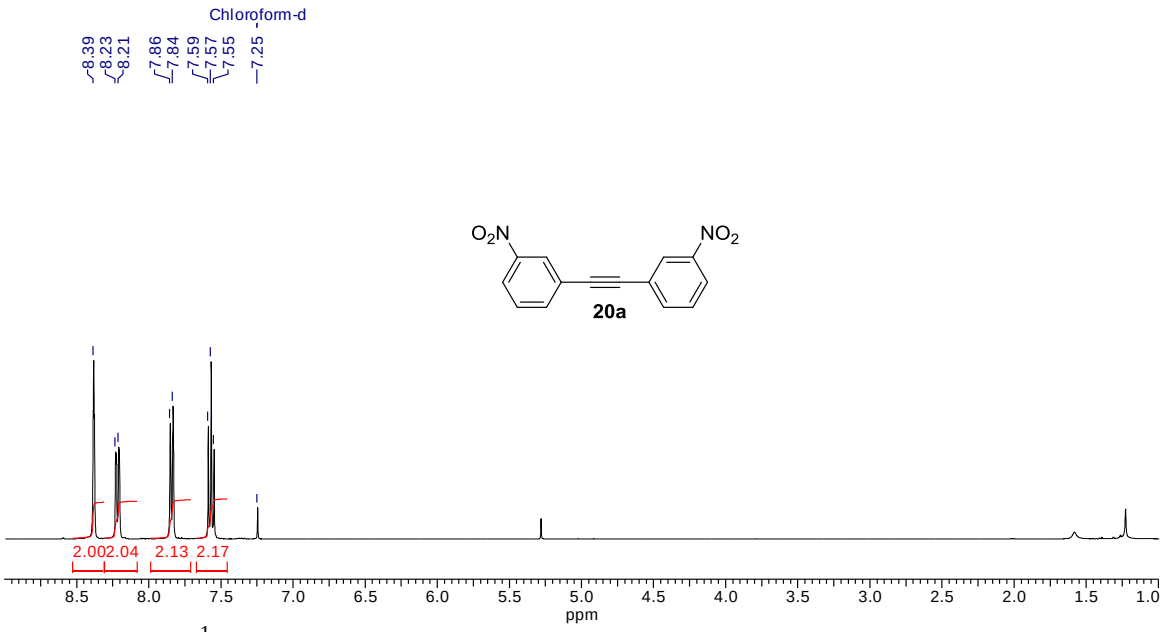


Figure III.1.1: ^{1}H-NMR (400 MHz) spectrum of **20a** in $CDCl_3$

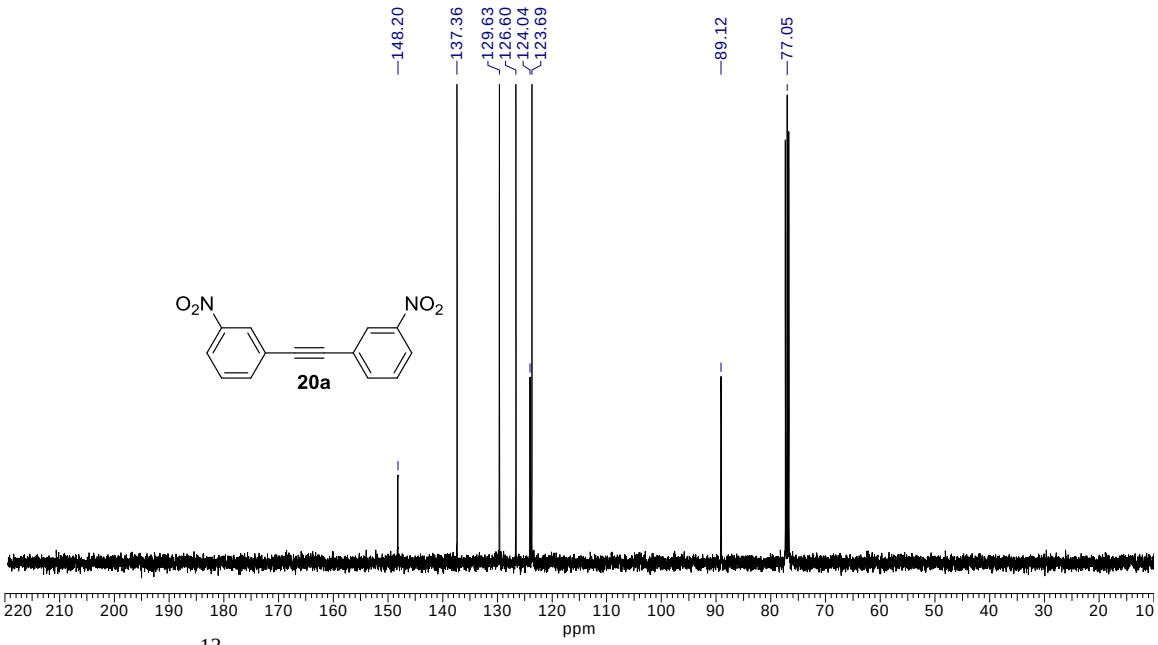
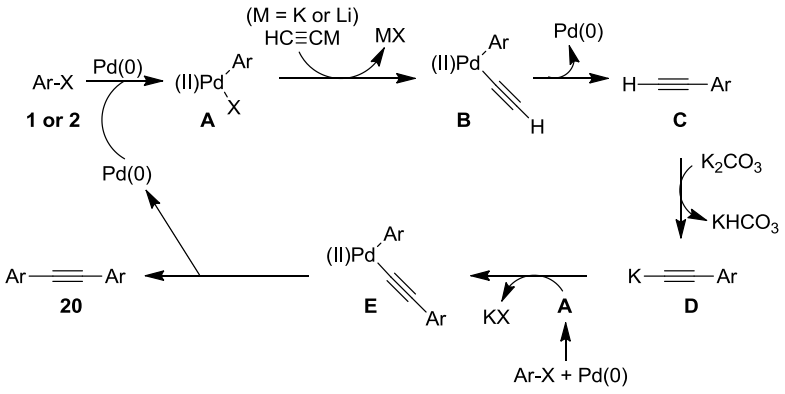


Figure III.1.2: ^{13}C-NMR (100 MHz) spectrum of **20a** in $CDCl_3$

After the successful accomplishment of symmetrical bi-aryl aceteylenes **20a-20m** using bromoarenes **1a-1m** as coupling partners, to further check the scope of the method, we next explored the reaction with iodoarenes **2a-2j** as coupling partners. Delightfully, the reaction proved to be efficient with iodoarene coupling partners **2a-2j** as well and gave the products **20a-20r** in good to very good yield (65-78%, Table III.3). Quite interestingly, the reaction showed a very good functional group tolerance, particularly, when there is a bromo substituent along with iodo one on the aromatic ring, the bromo substituent does not involve in the reaction and remains intact in the products **20n** and **20o** (Table III.3).

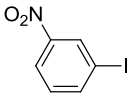
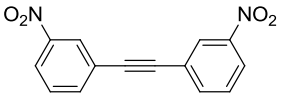
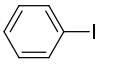
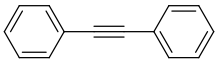
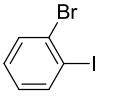
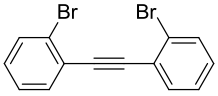
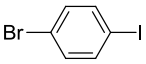
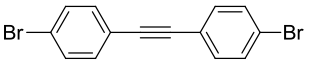
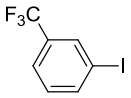
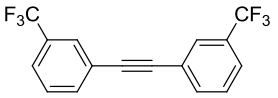
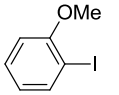
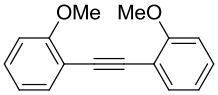
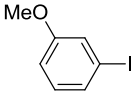
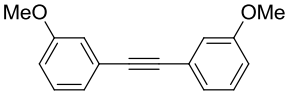
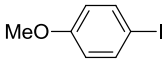
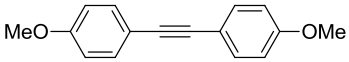
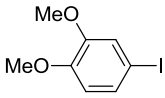
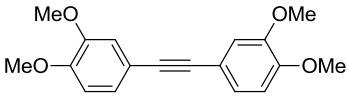
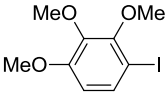
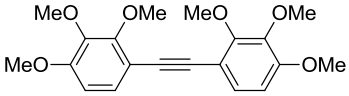
A plausible mechanistic path for the formation of di-aryl alkynes **20** is as shown in Scheme III.18. The first step is an oxidative addition in which Pd(0)-catalyst inserts into Ar-X (**1** or **2**) bond to give the aryl Pd(II)-intermediate **A**. Now, the subsequent reaction with acetylide, would furnish alkynylpalladium(II) species **B**. Reductive elimination of **B** generates the terminal acetylene **C**. The base mediated de-protonation of the terminal alkyne **C** might lead to the acetalyde **D**, which upon coupling with the Pd(II)-species **A** yields the intermediated **E**. Finally, the reductive elimination of the intermediate **E** furnishes the di-aryl alkyne **20** and Pd(0) to fulfil the catalytic cycle.



Scheme III.18

Table III.3: Domino [Pd]-catalyzed synthesis of bi-aryl acetylenes **20a-20r** from iodoarenes **2a-2j**.

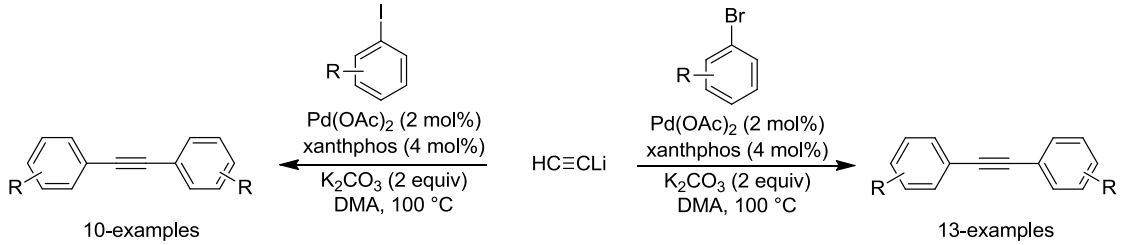
2a-2j **20a-20r**

Entry[a]	Substrates (2a-2j)		Products (20a-20r)		Time (h)	Yield (%)[b]
1.		**2a**		**20a**	0.25	69
2.		**2b**		**20b**	0.25	70
3.		**2c**		**20n**	0.25	73
4.		**2d**		**20o**	0.25	65
5.		**2e**		**20f**	0.25	65
6.		**2f**		**20p**	0.5	75
7.		**2g**		**20i**	0.5	78
8.		**2h**		**20j**	0.25	68
9.		**2i**		**20q**	1.0	75
10.		**2j**		**20r**	1.0	78

[a]All reactions were carried out on 0.5 mmol scale of iodoarenes **2**, in 2 mL of DMA (0.25 M). [b]Isolated yields of chromatographically pure products.

III.4. CONCLUSIONS

A novel and tandem process has been developed for expeditious synthesis of homo bi-aryl acetylenes. Notably, the process was successful in the presence of [Pd]-catalyst without the need of [Cu]-catalyst as a co-catalyst. Significantly, the method enabled the use of commercially available cheap lithium acetylide as the equivalent of acetyelene under domino [Pd]-catalysis. This method is applicable to a wide range of bromo or iodoarenes bearing electron withdrawing, neutral, electron rich substituents.



Scheme III.19

I.5 EXPERIMENTAL SECTION:

General:

IR spectra were recorded on a Bruker Tensor 37 (FT-IR) spectrophotometer. ^{1}H-NMR spectra were recorded on Bruker Avance 400 (400 MHz) spectrometer at 295 K in $CDCl_3$; chemical shifts (δ in ppm) and coupling constants (J in Hz) are reported in standard fashion with reference to either internal standard tetramethylsilane (TMS) (δ_H=0.00 ppm) or $CHCl_3$ (δ_H=7.25 ppm). ^{13}C-NMR spectra were recorded on Bruker Avance 400 (100 MHz) spectrometer at RT in $CDCl_3$; chemical shifts (δ in ppm) are reported relative to $CHCl_3$ [δ_C=77.00 ppm (central line of triplet)]. In the ^{13}C-NMR, the nature of carbons (C, CH, CH_2 and CH_3) was determined by recording the DEPT-135 spectra, and is given in parentheses and noted as s=singlet (for C), d=doublet (for CH), t=triplet (for CH_2) and q=quartet (for CH_3). In the ^{1}H-NMR, the following abbreviations were used throughout: s = singlet, d = doublet, t = triplet, q = quartet, qui = quintet, m = multiplet and br. s=broad singlet, septd=septet of doublets. The assignment of signals

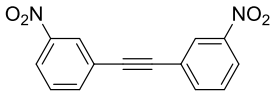
was confirmed by ^{1}H, ^{13}C CPD and DEPT spectra. High-resolution mass spectra (HR-MS) were recorded on an Agilent 6538 UHD Q-TOF using multimode source. All small scale dry reactions were carried out using the standard syringe-septum technique. Reactions were monitored by TLC on a silica gel using a mixture of petroleum ether and ethyl acetate as eluents. Reactions were generally run under an argon or nitrogen atmosphere. All solvents were distilled prior to use; petroleum ether with a boiling range of 60 to 80 °C, ethyl acetate, DMF (with purity 99%), DMA (with purity 99%), Acetonitrile (with purity 99.9%), Triethylamine (with purity 98%) and silica gel (60-120 mesh) purchased from locally available commercial sources were used. Palladium(II)acetate (with purity 98%), 4,5-Bis(diphenylphosphino)-9,9-dimethylxanthene (Xantphos) (with purity 97%), 1,1'-bis(diphenylphosphino)ferrocene (dppf) (with purity 97%), triphenylphosphine **(**PPh_3) (with purity 99%), Tri(2-furyl)phosphine (with purity 99%), Ethylenebis(diphenylphosphine)(Diphos) (with purity 99%), $Pd(PPh_3)_2Cl_2$ (with purity 98%), 2-Dicyclohexylphosphino-2′-methylbiphenyl,2-Methyl-2′-dicyclohexylphosphinobiphenyl (MePhos) (with purity 97%), (Oxydi-2,1-phenylene)bis(diphenylphosphine) (DPEPhos) (with purity 98%), N,N-diisopropylethylamine (DIPEA) (with purity 99%), N,N-Dicyclohexylmethylamine (with purity 97%), lithium acetylide ethylenediamine complex (with assay 90%) and K_2CO_3(with purity 99%) purchased from Sigma-Aldrich were used without further purification. The base K_2CO_3 was dried at 150-170 $^{\circ}C$ over an oil bath. DMF and DMA dried over calcium hydride. Acetonitrile dried over P_2O_5. Triethylamine dried over KOH. Acme's silica gel (60-120 mesh) was used for column chromatography (approximately 20 g per one gram of crude material).

The compounds **20n** and **20o**,[97] know in the literature.

General Procedure-1 for Pd-Mediated bi-aryl acetylene synthesis (GP-1):

In an oven dried Schlenk tube under nitrogen atmosphere, were added aryl halide **1** (0.50 mmol), $Pd(OAc)_2$ (2 mol%), Xantphos (4 mol%), K_2CO_3 (1.0 mmol) and lithium acetylide ethylenediamine complex **19** (1.0 mmol) followed by addition of dry DMA (2

mL). The resulted reaction mixture was stirred at 100 °C for 15 min to 12 h. The progress of the reaction was monitored by TLC till the reaction was completed. The reaction mixture was then quenched with saturated aqueous NH_4Cl solution and the aqueous layer was extracted with ethyl acetate (3 × 20 mL). The organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate) furnished the product **20** (60-95%).



20a

1-Nitro-3-[(3-nitrophenyl)ethynyl]benzene (20a): GP-1 was carried out with aryl bromide **1a** (101 mg, 0.50 mmol), $Pd(OAc)_2$ (2.2 mg, 2 mol%), Xantphos (11.6 mg, 4 mol%), K_2CO_3 (138 mg, 1.00 mmol), lithium acetylide ethylenediamine complex **19** (102 mg, 1.0 mmol) and dry DMA (2 mL). The resulted reaction mixture was stirred at preheated oil bath 100 °C for 0.25 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 90:10 to 85:15) furnished the product **20a** (50 mg, 75%). [TLC control R_f(**1a**)=0.60, R_f(**20a**)=0.45 (petroleum ether/ethyl acetate 80:20, UV detection)].

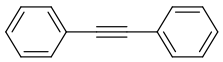
Reaction with aryl iodide: GP-1 was carried out with aryl iodide **2a** (124 mg, 0.50 mmol) for 0.25 h furnished the product (46 mg, 69%) [TLC control R_f(**2a**)=0.70, R_f(**20a**)=0.45 (petroleum ether/ethyl acetate 80:20, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3082, 2958, 2922, 2853, 1529, 1402, 1352, 1236, 904, 823, 805, 734, 670 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=8.39 (dd, 2H, J=1.5 and 1.5 Hz, 2 × Ar-H), 8.22 (dd, 2H, J=8.3 and 1.5 Hz, 2 × Ar-H), 7.85 (d, 2H, J=7.8 Hz, 2 × Ar-H), 7.57 (dd, 2H, J=7.8 and 7.8 Hz, 2 × Ar-H) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=148.1 (s, 2C, 2 × Ar-C), 137.3 (d, 2C, 2 × Ar-C), 129.6 (d, 2C, 2 × Ar-C), 126.5 (d, 2C, 2 × Ar-C), 124.0 (d, 2C, 2 × Ar-C), 123.6 (d, 2C, 2 × Ar-C), 89.1 (s, 2C, 2 × Ar-C≡) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{14}H_8N_2NaO_4]^+$=$[M+Na]^+$: 291.0376; found 291.0368.



20b

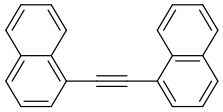
(Phenylethynyl)benzene (20b): GP-1 was carried out with aryl bromide **1b** (78.5 mg, 0.50 mmol), $Pd(OAc)_2$ (2.2 mg, 2 mol%), Xantphos (11.6 mg, 4 mol%), K_2CO_3 (138 mg, 1.00 mmol), lithium acetylide ethylenediamine complex **19** (102 mg, 1.0 mmol) and dry DMA (2 mL). The resulted reaction mixture was stirred at preheated oil bath 100 °C for 1 h. Purification of the residue on a silica gel column chromatography (petroleum ether) furnished the product **20b** (50 mg, 88%) as white solid. [TLC control R_f(**1b**)=0.80, R_f(**20b**)=0.80 (petroleum ether/ethyl acetate 95:5, UV detection)].

Reaction with aryl iodide: GP-1 was carried out with aryl iodide **2b** (102 mg, 0.50 mmol) for 0.25 h furnished the product **20b** (31 mg, 70%) [TLC control R_f(**2b**)=0.85, R_f(**20b**)=0.80 (petroleum ether, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2957, 2922, 2852, 1602, 1498, 1442, 1260, 1069, 1025, 799, 753, 688 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.57 (m, 4H, Ar-H), 7.36 (m, 6H, Ar-H) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=131.6 (d, 4C, 4 × Ar-CH), 128.3 (d, 4C, 4 × Ar-CH), 128.2 (d, 2C, 2 × Ar-CH), 123.2 (s, 2C, 2 × Ar-C), 89.4 (s, 2C, 2 × Ar-C≡) ppm.



20c

1-(1-Naphthylethynyl)naphthalene (20c): GP-1 was carried out with aryl bromide **1c** (103.5 mg, 0.50 mmol), $Pd(OAc)_2$ (2.2 mg, 2 mol%), Xantphos (11.6 mg, 4 mol%), K_2CO_3 (138 mg, 1.00 mmol), lithium acetylide ethylenediamine complex **19** (102 mg, 1.0 mmol) and dry DMA (2 mL). The resulted reaction mixture was stirred at preheated oil bath 100 °C for 1 h. Purification of the residue on a silica gel column

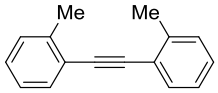
chromatography (petroleum ether/ethyl acetate 98:2 to 97:3) furnished the product **20c** (57 mg, 83%). [TLC control R_f(**1c**)=0.80, R_f(**20c**)=0.70 (petroleum ether/ethyl acetate 95:5, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3053, 2955, 2923, 2852, 1700, 1585, 1504, 1404, 1213, 1017, 862, 796, 770 cm^{-1}.

^{1}H-NMR (CDCl$_3$, 400 MHz): δ=8.58 (d, 2H, *J*=8.3 Hz, Ar-H), 7.97–7.80 (m, 6H, Ar-H) 7.66 (dd, 1H, *J*=6.8 and 1.0 Hz, Ar-H), 7.63 (dd, 1H, *J*=6.8 and 1.0 Hz, Ar-H), 7.58 (dd, 1H, *J*=6.8 and 1.0 Hz, Ar-H), 7.56 (dd, 1H, *J*=6.8 and 1.0 Hz, Ar-H), 7.53 (d, 1H, *J*=8.3 Hz, Ar-H), 7.52 (d, 1H, *J*=8.3 Hz, Ar-H) ppm.

^{13}C-NMR (CDCl$_3$, 100 MHz): δ=133.3 (s, 4C, 4 × Ar-C), 130.6 (d, 2C, 2 × Ar-CH), 128.9 (d, 2C, 2 × Ar-CH), 128.4 (d, 2C, 2 × Ar-CH), 126.9 (d, 2C, 2 × Ar-CH), 126.5 (d, 2C, 2 × Ar-CH), 126.3 (d, 2C, 2 × Ar-CH), 125.3 (d, 2C, 2 × Ar-CH), 121.1 (s, 2C, 2 × Ar-C), 92.4 (s, 2C, 2 × Ar-C≡) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{22}H_{15}]^+$=$[M+H]^+$: 279.1168; found 279.1172.



20d

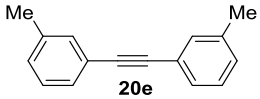
1-Methyl-2-[(2-methylphenyl)ethynyl]benzene (20d): GP-1 was carried out with aryl bromide **1d** (85.5 mg, 0.50 mmol), $Pd(OAc)_2$ (2.2 mg, 2 mol%), Xantphos (11.6 mg, 4 mol%), K_2CO_3 (138 mg, 1.00 mmol), lithium acetylide ethylenediamine complex **19** (102 mg, 1.0 mmol) and dry DMA (2 mL). The resulted reaction mixture was stirred at preheated oil bath 100 °C for 1 h. Purification of the residue on a silica gel column chromatography (petroleum ether) furnished the product **20d** (39 mg, 76%). [TLC control R_f(**1d**)=0.85, R_f(**20d**)=0.80 (petroleum ether UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3059, 3021, 2923, 2853, 1601, 1491, 1457, 1404, 1238, 1116, 755, 716 cm^{-1}.

^{1}H-NMR (CDCl$_3$, 400 MHz): δ=7.52 (d, 2H, *J*=8.3 Hz, 2 × Ar-H), 7.30–7.10 (m, 6H, 2 × Ar-H) 2.54 (s, 6H, 2 × Ar-CH$_3$) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=139.9 (s, 2C, 2 × Ar-C), 131.8 (d, 2C, 2 × Ar-CH), 129.5 (d, 2C, 2 × Ar-CH), 128.2 (d, 2C, 2 × Ar-CH), 125.6 (d, 2C, 2 × Ar-CH), 123.3 (s, 2C, 2 × Ar-C), 92.3 (s, 2C, 2 × Ar-C≡), 20.9 (q, 2C, 2 × Ar-CH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{16}H_{15}]^+$=$[M+H]^+$: 207.1168; found 207.1164.



20e

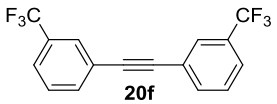
1-Methyl-3-[(3-methylphenyl)ethynyl]benzene (20e): GP-1 was carried out with aryl bromide **1e** (85.5 mg, 0.50 mmol), $Pd(OAc)_2$ (2.2 mg, 2 mol%), Xantphos (11.6 mg, 4 mol%), K_2CO_3 (138 mg, 1.00 mmol), lithium acetylide ethylenediamine complex **19** (102 mg, 1.0 mmol) and dry DMA (2 mL). The resulted reaction mixture was stirred at preheated oil bath 100 °C for 1 h. Purification of the residue on a silica gel column chromatography (petroleum ether) furnished the product **20e** (36 mg, 70%). [TLC control R_f(**1e**)=0.85, R_f(**20e**)=0.80 (petroleum ether)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3037, 2956, 2923, 2853, 1603, 1489, 1458, 1404, 1240, 1120, 999, 783, 691 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.37–7.27 (m, 4H, 4 × Ar-H), 7.22 (dd, 2H, *J*=7.8 ad 7.3 Hz, 2 × Ar-H), 7.13 (d, 2H, *J*=7.3 Hz, 2 × Ar-H), 2.34 (s, 6H, 2 × Ar-CH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=138.0 (s, 2C, 2 × Ar-C), 131.1 (d, 2C, 2 × Ar-CH), 129.1 (d, 2C, 2 × Ar-CH), 128.6 (d, 2C, 2 × Ar-CH), 128.2 (d, 2C, 2 × Ar-CH), 123.1 (s, 2C, 2 × Ar-C), 89.2 (s, 2C, 2 × Ar-C≡), 21.2 (q, 2C, 2 × Ar-CH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{16}H_{15}]^+$=$[M+H]^+$: 207.1168; found 207.1171.



20f

1-(Trifluoromethyl)-3-{[3-(trifluoromethyl)phenyl]ethynyl}benzene (20f): GP-1 was carried out with aryl bromide **1f** (112 mg, 0.50 mmol), $Pd(OAc)_2$ (2.2 mg, 2

mol%), Xantphos (11.6 mg, 4 mol%), K_2CO_3 (138 mg, 1.00 mmol), lithium acetylide ethylenediamine complex **19** (102 mg, 1.0 mmol) and dry DMA (2 mL). The resulted reaction mixture was stirred at preheated oil bath 100 °C for 0.5 h. Purification of the residue on a silica gel column chromatography (petroleum ether) furnished the product **20f** (56 mg, 72%). [TLC control R_f(**1f**)=0.90, R_f(**20f**)=0.80 (petroleum ether, UV detection)].

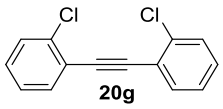
Reaction with aryl iodide: GP-1 was carried out with aryl iodide **2e** (136 mg, 0.50 mmol) for 0.25 h furnished the product **20f** (51 mg, 65%) [TLC control R_f(**2e**)=0.90, R_f(**20f**)=0.80 (petroleum ether , UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2931, 1622, 1450, 1396, 1264, 1188, 1013 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.81 (s, 2H, Ar-H), 7.70 (d, 2H, *J*=7.8 Hz, Ar-H), 7.61 (d, 2H, *J*=7.8 Hz, Ar-H), 7.49 (dd, 2H, *J*=7.8 and 7.8 Hz, Ar-H) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=134.7 (s, 1C, Ar-C), 131.2 (q, 2C), 131.2 (q, 2C), 129.0 (s, 1C, Ar-CH), 128.5 (q, 2C), 125.3 (q, 2C), 123.6 (q, 2C), 123.5 (s, 2C), 89.2 (s, 2C, 2 × Ar-C≡) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{16}H_9F_6]^+$=$[M+H]^+$: 315.0603; found 315.0581.



20g

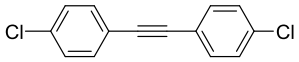
1-Chloro-2-[(2-chlorophenyl)ethynyl]benzene (20g): GP-1 was carried out with aryl bromide **1g** (123.5 mg, 0.50 mmol), $Pd(OAc)_2$ (2.2 mg, 2 mol%), Xantphos (11.6 mg, 4 mol%), K_2CO_3 (138 mg, 1.00 mmol), lithium acetylide ethylenediamine complex **19** (102 mg, 1.0 mmol) and dry DMA (2 mL). The resulted reaction mixture was stirred at preheated oil bath 100 °C for 0.25 h. Purification of the residue on a silica gel column chromatography (petroleum ether) furnished the product **20g** (45 mg, 74%). [TLC control R_f(**1g**)=0.90, R_f(**20g**)=0.80 (petroleum ether, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2931, 1622, 1450, 1396, 1264, 1188, 1013 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.61 (dd, 1H, *J*=2.0 and 1.0 Hz, Ar-H), 7.60 (d, 1H, *J*=2.4 Hz, Ar-H), 7.45 (d, 1H, *J*=1.5 Hz, Ar-H), 7.43 (dd, 1H, *J*=2.0 and 1.0 Hz, Ar-H), 7.35–7.2 (m, 4H, Ar-H) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=136.0 (s, 2C, 2 × Ar-C), 133.5 (d, 2C, 2 × Ar-CH), 129.6 (d, 2C, 2 × Ar-CH), 129.3 (d, 2C, 2 × Ar-CH), 126.4 (d, 2C, 2 × Ar-CH), 122.9 (s, 2C, 2 × Ar-C), 91.1 (s, 2C, 2 × Ar-C≡) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{14}H_9Cl_2]^+$=$[M+H]^+$: 247.0076; found 247.0076.



20h

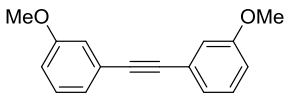
1-Chloro-4-[(4-chlorophenyl)ethynyl]benzene (20h): GP-1 was carried out with aryl bromide **1h** (123.5 mg, 0.50 mmol), $Pd(OAc)_2$ (2.2 mg, 2 mol%), Xantphos (11.6 mg, 4 mol%), K_2CO_3 (138 mg, 1.00 mmol), lithium acetylide ethylenediamine complex **19** (102 mg, 1.0 mmol) and dry DMA (2 mL). The resulted reaction mixture was stirred at preheated oil bath 100 °C for 0.25 h. Purification of the residue on a silica gel column chromatography (petroleum ether) furnished the product **20h** (42 mg, 69%). [TLC control R_f(**1h**)=0.90, R_f(**20h**)=0.80 (petroleum ether, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3058, 2923, 2853, 1598, 1493, 1402, 1234 1089, 829, 749, 695 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.50–7.40 (m, 4H, Ar-H), 7.37–7.27 (m, 4H, Ar-H) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=134.5 (s, 2C, 2 × Ar-C), 132.8 (d, 4C, 2 × Ar-CH), 128.7 (d, 4C, 2 × Ar-CH), 121.4 (s, 2C, 2 × Ar-C), 89.1 (s, 2C, 2 × Ar-C≡) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{14}H_9Cl_2]^+$=$[M+H]^+$: 247.0076; found 247.0076.



20i

1-Methoxy-3-[(3-methoxyphenyl)ethynyl]benzene (20i): GP-1 was carried out with aryl bromide **1i** (93.5 mg, 0.50 mmol), $Pd(OAc)_2$ (2.2 mg, 2 mol%), Xantphos (11.6 mg, 4 mol%), K_2CO_3 (138 mg, 1.00 mmol), lithium acetylide ethylenediamine complex **19** (102 mg, 1.0 mmol) and dry DMA (2 mL). The resulted reaction mixture was stirred at preheated oil bath 100 °C for 3 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 97:3 to 95:5) furnished the product **20i** (56 mg, 95%). [TLC control R_f(**1i**)=0.65, R_f(**20i**)=0.45 (petroleum ether/ethyl acetate 95:5, UV detection)].

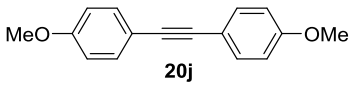
Reaction with aryl iodide: GP-1 was carried out with aryl iodide **2g** (117 mg, 0.50 mmol) for 0.5 h furnished the product **20i** (46 mg, 78%) [TLC control R_f(**2g**)=0.70, R_f(**20i**)=0.45 (petroleum ether/ethyl acetate 95:5, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2957, 2922, 2852, 1563, 1462, 1403, 1237 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.25 (dd, 2H, *J*=7.8 and 7.8 Hz, 2 × Ar-H), 7.13 (ddd, 2H, *J*=7.8, 2.4 and 1.5 Hz, 2 × Ar-H), 7.07–7.02 (m, 2H, *J*=Hz, 2 × Ar-H), 6.89 (dd, 2H, *J*=2.4 and 1.0 Hz, 2 × Ar-H) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=159.3 (s, 2C, 2 × Ar-C), 129.4 (d, 2C, 2 × Ar-CH), 124.2 (d, 2C, 2 × Ar-CH), 124.1 (s, 2C, 2 × Ar-C), 116.3 (d, 2C, 2 × Ar-CH), 115.0 (s, 2C, 2 × Ar-CH), 89.1 (s, 2C, 2 × Ar-C≡), 55.3 (q, 2C, 2 × Ar-OCH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{16}H_{15}O_2]^+$=$[M+H]^+$: 239.1067; found 239.1068.



20j

1-Methoxy-4-[(4-methoxyphenyl)ethynyl]benzene (20j): GP-1 was carried out with aryl bromide **1j** (93.5 mg, 0.50 mmol), $Pd(OAc)_2$ (2.2 mg, 2 mol%), Xantphos (11.6 mg, 4 mol%), K_2CO_3 (138 mg, 1.00 mmol), lithium acetylide ethylenediamine complex **19** (102 mg, 1.0 mmol) and dry DMA (2 mL). The resulted reaction mixture was stirred at preheated oil bath 100 °C for 0.5 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 97:3 to 95:5) furnished the product **20j**

(41 mg, 70%). [TLC control R_f(**1j**)=0.70, R_f(**20j**)=0.50 (petroleum ether/ethyl acetate 95:5, UV detection)].

Reaction with aryl iodide: GP-1 was carried out with aryl iodide **2h** (117 mg, 0.50 mmol) for 0.25 h furnished the product **20j** (40 mg, 68%) [TLC control R_f(**2h**)=0.75, R_f(**20j**)=0.50 (petroleum ether/ethyl acetate 95:5, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2957, 2921, 2851, 1607, 1511, 1462, 1403, 1248, 1172, 1026, 834, 750 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.46 (d, 4H, J=8.8 Hz, 4 × Ar-H), 6.87 (d, 4H, J=8.8 Hz, 4 × Ar-H), 3.81 (s, 6H, 2 × Ar-OCH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=159.3 (s, 2C, 2 × Ar-C), 132.8 (d, 4C, 4 × Ar-CH), 115.6 (s, 2C, 2 × Ar-C), 113.9 (d, 4C, 4 × Ar-CH), 87.9 (s, 2C, 2 × Ar-C≡), 55.2 (q, 2C, 2 × Ar-OCH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{16}H_{15}O_2]^+$=$[M+H]^+$: 239.1067; found 239.1068.

20k

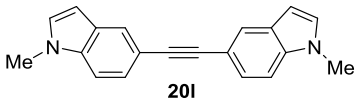
2-(Thien-2-ylethynyl)thiophene (20k): GP-1 was carried out with aryl bromide **1k** (81.5 mg, 0.50 mmol), $Pd(OAc)_2$ (2.2 mg, 2 mol%), Xantphos (11.6 mg, 4 mol%), K_2CO_3 (138 mg, 1.00 mmol), lithium acetylide ethylenediamine complex **19** (102 mg, 1.0 mmol) and dry DMA (2 mL). The resulted reaction mixture was stirred at preheated oil bath 100 °C for 15 min. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 99:1 to 97:3) furnished the product **20k** (28 mg, 60%). [TLC control R_f(**1k**)=0.60, R_f(**20k**)=0.60 (petroleum ether/ethyl acetate 97:3, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2957, 2923, 2853, 1536, 1433, 1408, 1199, 1041, 851, 826, 700 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.30 (dd, 2H, J=5.4 and 1.5 Hz, 2 × Ar-H), 7.27 (dd, 2H, J=3.9 and 1.5 Hz, 2 × Ar-H), 7.00 (dd, 2H, J=5.4 and 3.9 Hz, Ar-H) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=132.1 (d, 2C, 2× Ar-CH), 127.6 (d, 2C, 2 × Ar-CH), 127.1 (d, 2C, 2 × Ar-CH), 122.9 (s, 2C, 2 × Ar-C), 86.2 (s, 2C, 2 × Ar-C≡) ppm.

HR-MS (ESI^+): m/z calculated for $[C_{10}H_7S_2]^+=[M+H]^+$: 190.9984; found 190.9980.



20l

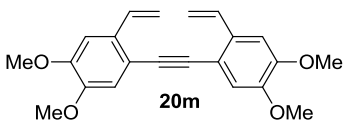
1-Methyl-5-[(1-methyl-1H-indol-5-yl)ethynyl]-1H-indole(20l): GP-1 was carried out with aryl bromide **1l** (105 mg, 0.50 mmol), $Pd(OAc)_2$ (2.2 mg, 2 mol%), Xantphos (11.6 mg, 4 mol%), K_2CO_3 (138 mg, 1.00 mmol), lithium acetylide ethylenediamine complex **19** (102 mg, 1.0 mmol) and dry DMA (2 mL). The resulted reaction mixture was stirred at preheated oil bath 150 °C for 12 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 90:10 to 80:20) furnished the product **20l** (51 mg, 73%). [TLC control R_f(**1l**)=0.70, R_f(**20l**)=0.40 (petroleum ether/ethyl acetate 70:30, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2922, 2852, 1510, 1493, 1466, 1368, 1340, 1243, 1102, 1081, 882, 761, 722 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.86 (s, 2H, 2 × Ar-H), 7.43 (d, 2H, J=7.3 Hz, 2 × Ar-H), 7.28 (d, 2H, J=7.3 Hz, 2 × Ar-H), 7.07 (d, 2H, J=2.9 Hz, 2 × Ar-H), 6.49 (d, 2H, J=2.9 Hz, 2 × Ar-H), 3.78 (s, 6H, 2 × Ar-CH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ= 136.1(s, 2C, 2 × Ar-C), 129.6 (d, 2C, 2 × Ar-CH), 128.3 (s, 2C, 2 × Ar-C), 125.1 (d, 2C, 2 × Ar-CH), 124.4 (d, 2C, 2 × Ar-CH), 114.5 (s, 2C, 2 × Ar-C), 109.2 (d, 2C, 2 × Ar-CH), 101.1 (d, 2C, 2 × Ar-CH), 88.5 (s, 2C, 2 × Ar-C≡), 32.9 (q, 2C, 2 × ArCH_3) ppm.

HR-MS (ESI^+): m/z calculated for $[C_{20}H_{17}N_2]^+=[M+H]^+$: 285.1386; found 285.1389.



20m

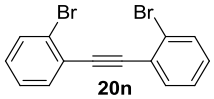
1-[(4,5-dimethoxy-2-vinylphenyl)ethynyl]-4,5-dimethoxy-2-vinylbenzene (20m): GP-1 was carried out with aryl bromide **1m** (121.5 mg, 0.50 mmol), $Pd(OAc)_2$ (2.2 mg, 2 mol%), Xantphos (11.6 mg, 4 mol%), K_2CO_3 (138 mg, 1.00 mmol), lithium acetylide ethylenediamine complex **19** (102 mg, 1.0 mmol) and dry DMA (2 mL). The resulted reaction mixture was stirred at preheated oil bath 150 °C for 12 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 90:10 to 80:20) furnished the product **20m** (70 mg, 80%).[TLC control R_f(**1m**) = 0.70, R_f(**20m**) = 0.30 (petroleum ether/ethyl acetate 80:20, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max} = 3001, 2922, 2852, 1600, 1510, 1462, 1352, 1232, 1125, 1031, 860, 748 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.25 (dd, 2H, J = 16.6 and 10.8 Hz), 7.06 (s, 2H), 6.97 (s, 2H), 5.70 (d, 2H, J = 16.6 Hz), 5.28 (d, 2H, J = 10.8 Hz), 3.92 (s, 6H), 3.89 (s, 6H) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=149.4 (2 × C_q), 148.5 (2 × C_q), 134.7 (2 × CH), 132.5 (2 × C_q), 114.6 (2 × C_q), 114.0 (2 × CH), 113.5 (2 × CH_2), 106.8 (2 × CH), 91.0 (2 × C_q), 55.9 (2 × CH_3), 55.8 (2 × CH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{22}H_{22}NaO_4]^+$=$[M+Na]^+$: 373.1410; found 373.1413.



20n

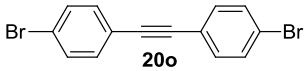
1-bromo-2-[(2-bromophenyl)ethynyl]benzene (20n): GP-1 was carried out with aryl iodide **2c** (141.5 mg, 0.50 mmol), $Pd(OAc)_2$ (2.2 mg, 2 mol%), Xantphos (11.6 mg, 4 mol%), K_2CO_3 (138 mg, 1.00 mmol), lithium acetylide ethylenediamine complex **19** (102 mg, 1.0 mmol) and dry DMA (2 mL). The resulted reaction mixture was stirred at preheated oil bath 100 °C for 15 min. Purification of the residue on a silica gel column chromatography (petroleum ether) furnished the product **20n** (60 mg, 73%). [TLC control R_f(**2c**)=0.80, R_f(**20n**)=0.75 (petroleum ether, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2922, 2852, 1556, 1479, 1434, 1400, 1237, 1048, 750 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.62 (dd, 2H, *J*=2.9 and 1.5 Hz, 2 × Ar-H), 7.61 (dd, 2H, *J*=2.9 and 1.0 Hz, 2 × Ar-H), 7.30 (ddd, 2H, *J*=7.8, 7.3 and 1.5 Hz, Ar-H), 7.19 (ddd, 2H, *J*=7.8, 7.3 and 1.5 Hz, Ar-H) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=133.6 (d, 2C, 2 × Ar-CH), 132.5 (d, 2C, 2 × Ar-CH), 129.7 (d, 2C, 2 × Ar-CH), 127.0 (d, 2C, 2 × Ar-CH), 125.5 (s, 2C, 2 × Ar-C), 125.1 (s, 2C, 2 × Ar-C), 92.2 (s, 2C, 2 × Ar-C≡) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{14}H_8Br_2]^+$=$[M]^+$: 333.8987; found 333.8986.



20o

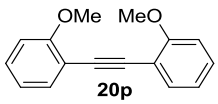
1-Bromo-4-[(4-bromophenyl)ethynyl]benzene (20o): GP-1 was carried out with aryl iodide **2d** (141.5 mg, 0.50 mmol), $Pd(OAc)_2$ (2.2 mg, 2 mol%), Xantphos (11.6 mg, 4 mol%), K_2CO_3 (138 mg, 1.00 mmol), lithium acetylide ethylenediamine complex **19** (102 mg, 1.0 mmol) and dry DMA (2 mL). The resulted reaction mixture was stirred at preheated oil bath 100 °C for 15 min. Purification of the residue on a silica gel column chromatography (petroleum ether) furnished the product **20o** (54 mg, 65%). [TLC control R_f(**2d**)=0.85, R_f(**20o**)=0.80 (petroleum ether, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2922, 2852, 1589, 1493, 1463, 1391, 1074, 1009, 824 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.48 (d, 4H, *J*=8.8 Hz, 4 × Ar-H), 7.37 (d, 4H, *J*=8.8 Hz, 4 × Ar-H) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=133.0 (d, 4C, 4 × Ar-CH), 131.7 (d, 4C, 4 × Ar-CH), 122.8 (s, 2C, 2 × Ar-C), 121.9 (s, 2C, 2 × Ar-C), 89.4 (s, 2C, 2 × Ar-C≡) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{14}H_9Br_2]^+$ = $[M+H]^+$: 334.9066; found 334.9057.



20p

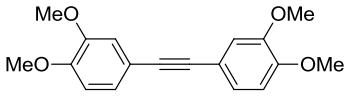
1-methoxy-2-[(2-methoxyphenyl)ethynyl]benzene (20p): GP-1 was carried out with aryl iodide **2f** (117 mg, 0.50 mmol), $Pd(OAc)_2$ (2.2 mg, 2 mol%), Xantphos (11.6 mg, 4 mol%), K_2CO_3 (138 mg, 1.00 mmol), lithium acetylide ethylenediamine complex **19** (102 mg, 1.0 mmol) and dry DMA (2 mL). The resulted reaction mixture was stirred at preheated oil bath 100 °C for 30 min. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 97:3 to 95:5) furnished the product **20p** (45 mg, 75%). [TLC control R_f(**2f**)=0.60, R_f(**20p**)=0.30 (petroleum ether/ethyl acetate 95:5, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2958, 2923, 2852, 1596, 1462, 1435, 1275, 1245, 1024, 751cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.53 (dd, 2H, *J*=7.8 and 2.0 Hz, 2 × Ar-H), 7.28 (dd, 1H, *J*=7.3 and 2.0 Hz, 2 × Ar-H), 7.26 (dd, 1H, *J*=7.3 and 2.0 Hz, 2 × Ar-H), 6.92 (ddd, 2H, *J*=8.3, 7.3 and 1.0 Hz, 2 × Ar-H), 6.87 (d, 2H, *J*=8.3 Hz, 2 × Ar-H) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=159.8 (s, 2C, 2 × Ar-C), 133.4 (d, 2C, 2 × Ar-CH), 129.5 (d, 2C, 2 × Ar-CH), 120.3 (d, 2C, 2 × Ar-CH), 112.7 (s, 2C, 2 × Ar-C), 110.6 (d, 2C, 2 × Ar-CH), 89.7 (s, 2C, 2 × Ar-C≡), 55.8 (q, 2C, 2 × Ar-OCH_3) ppm.

HR-MS (ESI$^+$): m/z calculated for $[C_{16}H_{15}O_2]^+$=$[M+H]^+$: 239.1067; found 239.1063.



20q

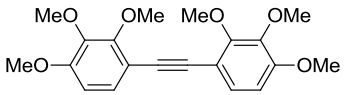
4-[(3,4-dimethoxyphenyl)ethynyl]-1,2-dimethoxybenzene (20q): GP-1 was carried out with aryl iodide **2i** (132 mg, 0.50 mmol), $Pd(OAc)_2$ (2.2 mg, 2 mol%), Xantphos (11.6 mg, 4 mol%), K_2CO_3 (138 mg, 1.00 mmol), lithium acetylide ethylenediamine complex **19** (102 mg, 1.0 mmol) and dry DMA (2 mL). The resulted reaction mixture was stirred at preheated oil bath 100 °C for 2 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 90:10 to 80:20) furnished the product **20q** (56 mg, 75%). [TLC control R_f(**2i**)=0.50, R_f(**20q**)=0.80 (petroleum ether/ethyl acetate 70:30, UV detection)].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2956, 2921, 2851, 1597, 1514, 1464, 1246, 1138, 1025, 765 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.11 (dd, 2H, *J*=8.3 and 2.0 Hz, 2 × Ar-H), 7.02 (d, 2H, *J*=2.0 Hz, 2 × Ar-H), 6.82 (d, 2H, *J*=8.3 Hz, 2 × Ar-H), 3.89 (s, 12H, 3 × 4 Ar-OCH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=149.3 (s, 2C, 2 × Ar-C), 148.6 (s, 2C, 2 × Ar-C), 124.7 (d, 2C, 2 × Ar-CH), 115.6 (s, 2C, 2 × Ar-C), 114.2 (d, 2C, 2 × Ar-CH), 111.0 (d, 2C, 2 × Ar-CH), 88.0 (s, 2C, 2 × Ar-C≡), 55.9 (q, 4C, 4 × Ar-OCH_3) ppm.

HR-MS (ESI^{+}): m/z calculated for $[C_{18}H_{19}O_4]^+$=$[M+H]^+$: 299.1278; found 299.1282.



20r

1,2,3-trimethoxy-4-[(2,3,4-trimethoxyphenyl)ethynyl]benzene (20r): GP-1 was carried out with aryl iodide **2j** (132 mg, 0.50 mmol), $Pd(OAc)_2$ (2.2 mg, 2 mol%), Xantphos (11.6 mg, 4 mol%), K_2CO_3 (138 mg, 1.00 mmol), lithium acetylide ethylenediamine complex **19** (102 mg, 1.0 mmol) and dry DMA (2 mL). The resulted reaction mixture was stirred at preheated oil bath 100 °C for 2 h. Purification of the residue on a silica gel column chromatography (petroleum ether/ethyl acetate 90:10 to 80:20) furnished the product **20r** (70 mg, 78%). [TLC control R_f(**2j**) = 0.**70**, R_f(**20r**) = 0.**40** (petroleum ether/ethyl acetate 70:30, UV detection)].

^{1}H-NMR ($CDCl_3$, 400 MHz): δ=7.19 (d, 2H, *J* = 8.3 Hz, Ar-H), 6.62 (d, 2H, *J* = 8.3 Hz, Ar-H), 4.02 (s, 6H, 2 × Ar-OCH_3), 3.86 (s, 6H, 2 × Ar-OCH_3), 3.85 (s, 6H, 2 × Ar-OCH_3) ppm.

^{13}C-NMR ($CDCl_3$, 100 MHz): δ=154.6 (2 × C_q), 154.0 (2 × C_q), 142.1 (2 × C_q), 127.8 (2 × CH), 110.7 (2 × C_q), 107.2 (2 × CH), 88.1 (2 × C_q), 61.2 (2 × Ar-OCH_3), 61.0 (2 × Ar-OCH_3), 56.0 (2 × Ar-OCH_3) ppm.

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2936, 2839, 1596, 1499, 1463, 1410, 1289, 1234, 1097, 1060, 1011, 801, 695 cm^{-1}.

HR-MS (ESI$^+$): m/z calculated for $[C_{20}H_{22}NaO_6]^+$=$[M+Na]^+$: 381.1309; found 381.1310.

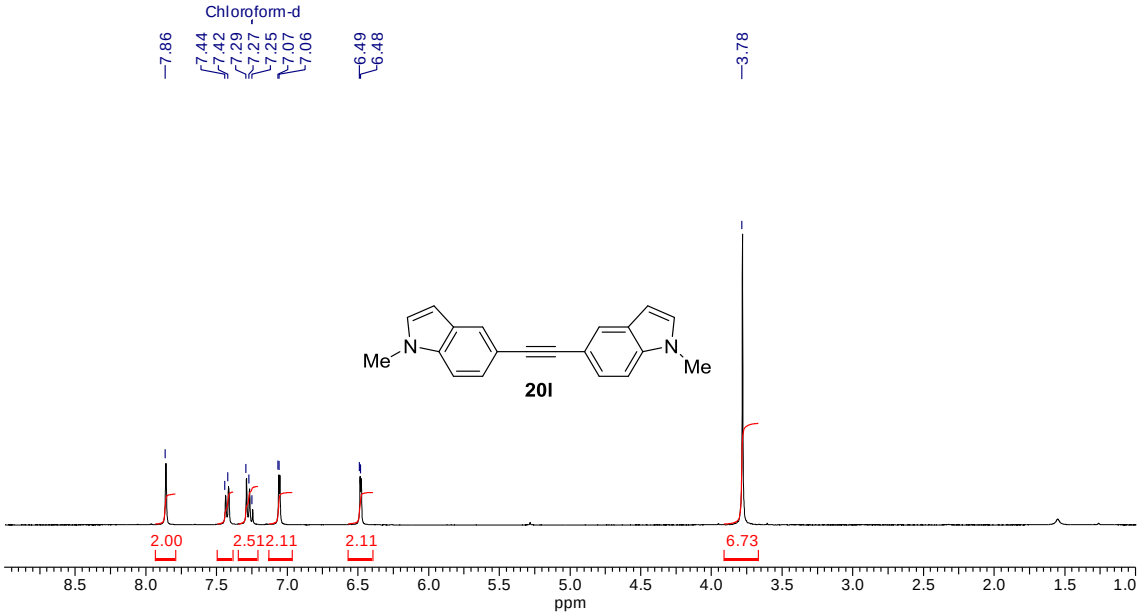


Figure III.2.1: ^{1}H-NMR (400 MHz) spectrum of **20l** in $CDCl_3$

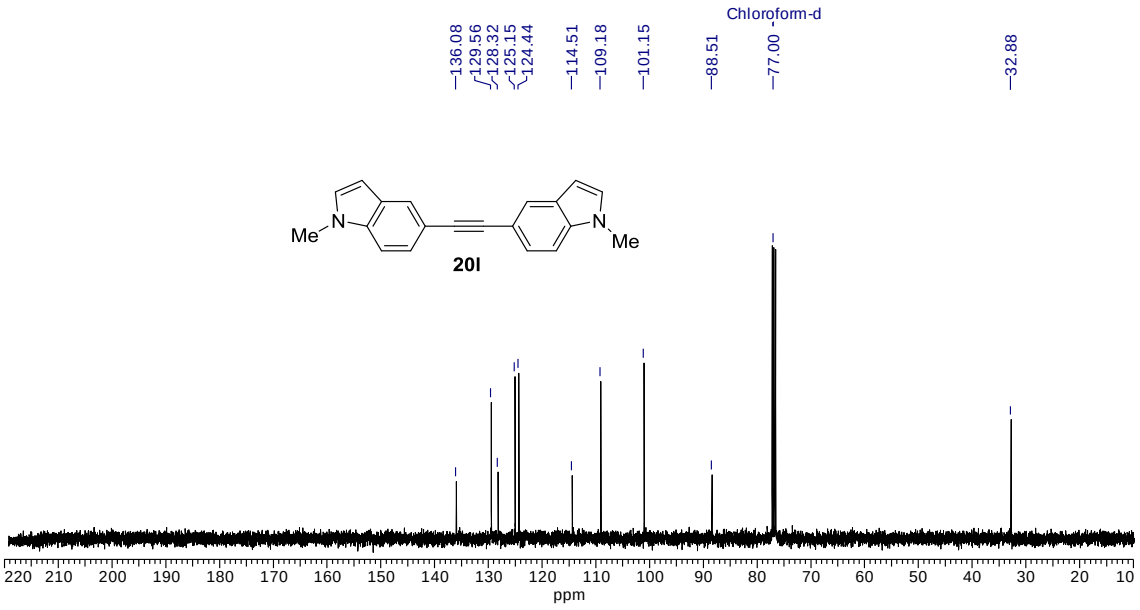


Figure III.2.1: ^{13}c-NMR (100 MHz) spectrum of **20l** in $CDCl_3$

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