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

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The Degree of Doctor of Philosophy

Department of Chemistry

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Declaration

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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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-5H-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 biaryl coupling) and a C=C π-bond (i.e., intramolecular Aldol type condensation), as depicted in Scheme 1. Although, the product 7-methyl-5H-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-5H-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).
Synthesis of α-aryl ketones via [Pd]-catalysis:

After the accomplishment of 7-methyl-5H-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.
**Synthesis of bi-aryls via domino [Pd]-catalysis:**

After the successful accomplishment of 7-methyl-5H-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-bromoarylcylohexylketones 12 were subjected to palladium catalysis. Hence, 2-bromoarylisopropyl ketones 11 or 2-bromoarylcylohexylketones 12 were reacted in the presence of the [Pd]-catalyst. Quite surprisingly, slight modification of the reaction conditions (i.e., with base K₂CO₃ 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](image)

**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](image)
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, valoneic 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](image)

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 conditions 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).

\[ \text{Scheme 6} \]

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).
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).
Thus, the [Pd]-catalyzed coupling of 2-bromobenzaldehydes 23 with the allylic alcohols 20 followed by NaBH₄ 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 (BF₃•Et₂O) mediated cyclization at −40 °C. 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 8
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-Deoxyisorhacmic 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 deeryamylase 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 acetylenes. Significantly, the reaction showed a wide range of functional group tolerance. For example, halo arenes with alkyl, aryl, alkylxoy, chloro, trifluoromethyl and nitro groups were successful in delivering the bi-aryl acetylenes 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](image-url)
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<td>Ac</td>
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<td>APCI</td>
<td>atmospheric pressure chemical ionization</td>
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<td>DIPA</td>
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CHAPTER I

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

1.1 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).  

![Scheme I.1](image)

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).  

![Scheme I.2](image)

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).
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).  

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).
Since Pd(OAc)$_2$/Ag$_2$O 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).
As a part of our research interest on domino transition-metal catalysis, 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). 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. 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).  

Further, the method was successfully applied to the synthesis of interesting 2-benzoxepin-3(1H)-ones 34 in a sequential one-pot manner (Scheme I.9). Significantly, these 2-benzoxepin-3(1H)-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).  

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 $25$, 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.

![Scheme I.10](image)

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

<table>
<thead>
<tr>
<th>Reaction conditions:</th>
<th>35a-35g</th>
<th>MeMgl</th>
<th>Et_2O, -10 to 0 °C</th>
<th>36a-36g</th>
<th>PCC-silicagel</th>
<th>CH_2Cl_2, rt</th>
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</tbody>
</table>

Reaction conditions: *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$_3$

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 \(\delta\) 7.07 and 6.92 due to two aromatic protons, presence of quartet at \(\delta\) 5.14 having \(J=6.4\) Hz due to benzylic methine group proton, two singlets at \(\delta\) 3.85 and 3.83 due to six protons of two methoxy groups, presence of broad singlet at \(\delta\) 2.23 due to hydroxyl proton and presence of doublet at \(\delta\) 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 \(\delta\) 148.7, 148.5, 136.7 and 111.1 were due to four aromatic carbons, the presence of two aromatic methine carbons at \(\delta\) 115.1 and 109.0, benzylic methine carbon resonates at \(\delta\) 69.0, two quartets at \(\delta\) 56.1 and 55.9 were due to two methoxy groups and quartet at \(\delta\) 23.7 ppm was due to methyl group. The presence of \([\text{M}+\text{H}-\text{H}_2\text{O}]^+\) peak at m/z \([\text{C}_{10}\text{H}_{12}^9\text{BrO}_2]^+\) = 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\(_3\)](image-url)
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 $\delta$ 7.11 and 7.02 due to two aromatic protons, two singlets at $\delta$ 3.88 and 3.86 due to six protons of two methoxy groups, the presence of singlet at $\delta$ 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 $\delta$ 199.4 was due to carbonyl carbon, four quaternary carbon resonates at $\delta$ 151.6, 148.1, 132.6 and 111.7 were due to four aromatic carbons, the presence of two aromatic methine carbons at $\delta$ 116.4 and 112.6, two quartets at $\delta$ 56.2 and 56.1 were due to two methoxy groups and a quartet at $\delta$ 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$_{12}$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 \(\text{Pd(OAc)}_2\) (5 mol%), PPh\(_3\) (10 mol%) and Cs\(_2\)CO\(_3\) 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 conjunction with the base K\(_3\)PO\(_4\) was unsuccessful to improve the yield (Table I.2, entries 5-11) while the combination of \(\text{Pd(OAc)}_2\) 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\(_2\)CO\(_3\) or K\(_3\)PO\(_4\) 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\(_3\)PO\(_4\)/Cs\(_2\)CO\(_3\) (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 \(\text{Pd(OAc)}_2\) 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-5H-dibenzo[a,c] [7]annulen-5-one 40c.

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<th>Entry</th>
<th>Catalyst (mol%)</th>
<th>Ligand (mol%)</th>
<th>Additive (equiv)</th>
<th>Solvent (mL)</th>
<th>Base (equiv)</th>
<th>Temp (°C)</th>
<th>Time (h)</th>
<th>Yield (%)^b</th>
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<td>-</td>
<td>toluene (3)</td>
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<td>13</td>
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<td>-</td>
<td>DMF (1.5)</td>
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<td>22</td>
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<td>-</td>
<td>THF (2)</td>
<td>Cs(_2)CO(_3) (2)</td>
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<td>dioxane (2)</td>
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<td>-</td>
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<td>11</td>
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<td>Pd(dba)$_2$ (2)</td>
<td>-</td>
<td>-</td>
<td>DMF (2)</td>
<td>K$_3$PO$_4$ (2)</td>
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<td>-</td>
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<td>DIPEA (5)</td>
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<td>24</td>
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<tr>
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<td>L$_5$ (4)</td>
<td>-</td>
<td>DMF (2)</td>
<td>2,4,6-collidine (2)</td>
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<td>-</td>
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<td>L$_5$ (4)</td>
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<tr>
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<td>L$_5$ (4)</td>
<td>-</td>
<td>DMF (2)</td>
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<td>DMF (2)</td>
<td>K$_3$PO$_4$ (2)</td>
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<td>30</td>
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All reactions were performed on 100 mg (0.44 mmol) scale of 37c, in 0.22 M concentration, in DMF (2 mL). Isolated yields of chromatographically pure products. No product was formed.

Quite interestingly, from the literature search, it was found that the entire carbon core structure 7-methyl-5H-dibenzo[a,c][7]annulen-5-one 40c demonstrated biologically active natural products such as dibenzocycloheptanoids and colchicinoids (Figure I.3). For example, tenuifolin 4111ab shows antiproliferative activity against tumor cell line DU145. The natural reticul 4211cd acts as the inhibitor of cytochrom P450 (CYP3 A4). Subavenoside-E 4311e exhibits inhibitory activity against α-glucosidase type IV from Bacillus stearothermophilus. Similarly dihydroisosubamol 4411e subamol 4511fg and bumanol 4611h 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 activities11o-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 4711j-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 coupling14 or Lewis acid mediated Nicholas cyclization15.
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.

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$_3$PO$_4$ in DMF at 150 °C]. 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.\textsuperscript{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-5H-dibenzo[a,c][7]annulen-5-ones 40a-40g from 2-bromoacetophenones 37a-37g.\textsuperscript{a,b}

\[
\begin{align*}
\text{Reaction conditions:} & \quad \text{All the reactions were carried out with 2-bromoacetophenones 37a-37g (100-150 mg, 0.30 to 0.58 mmol), in DMF.} \\
& \quad \text{Yields in the parentheses are isolated yields of chromatographically pure products.}
\end{align*}
\]
Figure I.5.1: $^1$H-NMR (400 MHz) spectrum of 40g in CDCl$_3$

The structure of 7-methyl-5H-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 \(\delta\) 7.38, 7.20, 7.19, 7.16 and 6.60 were due to five aromatic protons, the presence of singlet at \(\delta\) 4.00 was due to three protons of methoxy group, whereas the singlet at \(\delta\) 3.98 was due to nine protons of three methoxy groups and the presence of singlet at \(\delta\) 2.44 ppm was due to three protons of methyl group that elucidated the structure of 7-methyl-5H-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 \(\delta\) 191.5 due to carbonyl carbon, nine quaternary carbon resonates at \(\delta\) 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 \(\delta\) 132.1, 113.8, 111.8, 109.6 and 109.5, four quartets at \(\delta\) 56.1 (2C), 56.0 and 55.9 were due to four methoxy groups and methyl group carbon resonates at \(\delta\) 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-5H-dibenzo[a,c][7]annulen-5-one 40g.

Further to the spectroscopic evidence in confirming the structure of the 7-methyl-5H-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)](image)

After the successful synthesis of 7-methyl-5H-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.

![Scheme I.11](image)

The plausible mechanism for the formation of 7-methyl-5H-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 sp³ 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. 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 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-5H-dibenzo[\textit{a,c}][\textit{7}]annulen-5-ones 40,\textsuperscript{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)\textsubscript{2} (2 mol\%)/Xantphos (5 mol\%) and the base '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).

Scheme I.13

The transition-metal mediated $\alpha$-arylation for the synthesis of corresponding $\alpha$-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. Many traditional methods are available for the synthesis of $\alpha$-aryl ketones. Those are arduous due to different arylating reagents that were developed for the synthesis of $\alpha$-aryl ketones and these reagents are used as stochiometric ratio using main group enol ethers or bismuth/lead reagents. Due to these drawbacks, transition-metal catalyzed direct arylation methods have gained more importance for the synthesis of $\alpha$-aryl products.

It was an unprecedented discovery of $\alpha$-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).  

![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.  

Subsequently, the research groups of Buchwald and Hartwig developed various methods for the α-arylation of ketones. Recently, α-arylation had also been reported using 1-bromo-2-iodobenzenes as coupling partners by Willis et al. 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 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. 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.\(^a\)

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

\[^a\] 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-bromoacetophenones 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-arylels via domino [Pd]-catalysis:

After the successful accomplishment of 7-methyl-5H-dibenzo[a,c][7]annulen-5-ones 41,9e and the synthesis of α-arylation products 62,9i 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.
Reaction conditions: Yields in the parentheses are isolated yields of chromatographically pure products.
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 CH(CH$_3$)$_2$ group and two methyl carbons resonates at δ 19.4 and 16.7 ppm. The presence of [(M+H)–H$_2$O]$^+$ 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$_3$
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 \(\delta\ 7.59\) having \(J=7.8\) and 1.5 Hz due to one aromatic proton, doublet of a doublet of doublet at \(\delta\ 7.36\) having \(J=9.3,\ 7.8\) and 1.5 Hz due to one aromatic proton, doublet of a doublet at \(\delta\ 7.29\) having \(J=7.8\) and 1.5 Hz due to one aromatic proton, doublet of a doublet of doublet at \(\delta\ 7.27\) having \(J=9.3,\ 7.8\) and 1.5 Hz due to one aromatic proton, presence of septet at \(\delta\ 3.32\) having \(J= 6.8\) Hz due to \(CH(CH_3)_2\) group, and doublet at \(\delta\ 1.20\) 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 \(\delta\ 208.7\) were due to carbonyl carbon, two quaternary carbon resonates at \(\delta\ 142.0\) and 118.6 were due to two aromatic carbons, the presence of four aromatic methine carbons at \(\delta\ 133.3,\ 131.0,\ 128.1\) and 127.2, the presence of \(\delta\ 40.1\) was due to \(CH(CH_3)_2\), 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$_2$CO$_3$ 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$_2$CO$_3$ 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-hydrogens) 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$_3$PO$_4$ 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-5H 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.

<table>
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<th>R&lt;sup&gt;1&lt;/sup&gt;, R&lt;sup&gt;2&lt;/sup&gt;, R&lt;sup&gt;3&lt;/sup&gt;</th>
<th>Reaction conditions: All the reactions carried out with 69a-69h (100 mg, 0.27 to 0.44 mmol), in toluene.</th>
<th>Isolated yields are chromatographically pure products.</th>
<th>Isolated yield of chromatographically pure product based on the starting material recovery.</th>
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<tr>
<td>Me&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Pd(OAc)&lt;sub&gt;2&lt;/sub&gt; (4 mol%) xanthos (4 mol%) K&lt;sub&gt;2&lt;/sub&gt;CO&lt;sub&gt;3&lt;/sub&gt; (4 equiv)</td>
<td>toluene (2 mL) 100 °C, 16 h</td>
<td></td>
</tr>
<tr>
<td>Me&lt;sup&gt;3&lt;/sup&gt;</td>
<td>69a-69h</td>
<td>70a-70h</td>
<td></td>
</tr>
</tbody>
</table>

70a (97%)  
70b (85%)  
70c (91%)  
70d (84%)  
70e (95%)  
70f (95%)  
70g (85%)  
70h (54%)  

<sup>a</sup> Reaction conditions: All the reactions carried out with 69a-69h (100 mg, 0.27 to 0.44 mmol), in toluene.  
<sup>b</sup> Isolated yields are chromatographically pure products.  
<sup>c</sup> 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 \(\delta 7.55–7.47\) due to one aromatic proton, doublet of a doublet at \(\delta 7.44\) having \(J=7.3\) and 1.5 Hz due to one aromatic proton, doublet of a doublet at \(\delta 7.40\) having \(J=7.3\) and 2.0 Hz due to one aromatic proton, doublet of a doublet at \(\delta 7.39\) having \(J=5.4\) and 2.0 Hz due to one aromatic proton, a multiplet in the region of \(\delta 7.38–7.30\) due to two aromatic protons, doublet of a doublet at \(\delta 7.14\) having \(J=7.3\) and 2.0 Hz due to one aromatic proton, a multiplet in the region of \(\delta 7.12–7.06\) due to one aromatic proton, presence of two individual singlets at \(\delta 5.85\) and 5.74 due to olefinic methylene protons, septet at \(\delta 2.85\) having \(J=6.8\) Hz due to CH(CH\(_3\))\(_2\), singlet at \(\delta 1.84\) due to three protons of methyl group and br. s, at \(\delta 0.94\) 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 \(\delta 210.5\) and 199.7 due to two carbonyl carbons, five quaternary carbon resonates at \(\delta 145.1, 140.0, 139.6, 138.9\) and 138.7 were due to four aromatic carbons and one for olefinic carbon, presence of eight aromatic methine carbons resonates at \(\delta 130.8, 130.5, 130.0, 129.7, 129.7, 128.3, 127.5\) and 126.9, olefinic methylene carbon resonates at \(\delta 129.6\), the presence of \(\delta 38.9\) due to CH(CH\(_3\))\(_2\) group and three methyl group resonates at \(\delta 17.4\) 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).
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). For example, (+)-isoschizandrin 71, a lignin from schizandra chinesis, has been used in the Chinese traditional medicines as an antitussive, steganone 72 was found to inhibit tubulin polymerization both in-vitro and in-vivo. The derivatives of valoneic acid 73 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. The natural korupensamine A 75 shows good antimalarial activity in-vitro and in-vivo, whereas the binaphthalene gossypol 76 possesses antispermatogenic, antitumor, and antimalarial activities and agrochemical specialties and also the valsartan 77, lotarsan 78, buflavine 79 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.

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). 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.\(^\text{40}\)

![Chemical structures](image)

**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.\(^\text{9i}\)
Table I.7: Synthesis of (2-bromophenyl)(cyclohexyl)methanone 81a-81h from 2-bromobenzaldehydes 35a-35h.\(^a\)

\[
\begin{array}{c}
\begin{align*}
35\text{a-35h} & \quad \xrightarrow{\text{CyMgBr, THF, } -50 \degree \text{C to rt}} \quad 80\text{a-80h} & \quad \xrightarrow{\text{PCC-silicagel, CH}_{2}\text{Cl}_{2}, \text{rt}} \quad 81\text{a-81h}
\end{align*}
\end{array}
\]

\[
\begin{array}{c}
\begin{align*}
35\text{a} & \quad \text{CHO} & \quad 80\text{a} (52\%) & \quad 81\text{a} (91\%)
\end{align*}
\end{array}
\]

\[
\begin{array}{c}
\begin{align*}
35\text{b} & \quad \text{BnO-CHO} & \quad 80\text{b} (52\%) & \quad 81\text{b} (95\%)
\end{align*}
\end{array}
\]

\[
\begin{array}{c}
\begin{align*}
35\text{c} & \quad \text{MeO-CHO} & \quad 80\text{c} (48\%) & \quad 81\text{c} (93\%)
\end{align*}
\end{array}
\]

\[
\begin{array}{c}
\begin{align*}
35\text{d} & \quad \text{BnO-CHO} & \quad 80\text{d} (60\%) & \quad 81\text{d} (91\%)
\end{align*}
\end{array}
\]

\[
\begin{array}{c}
\begin{align*}
35\text{e} & \quad \text{MeO-CHO} & \quad 80\text{e} (72\%) & \quad 81\text{e} (96\%)
\end{align*}
\end{array}
\]

\[
\begin{array}{c}
\begin{align*}
35\text{f} & \quad \text{O-CHO} & \quad 80\text{f} (40\%) & \quad 81\text{f} (95\%)
\end{align*}
\end{array}
\]

\[
\begin{array}{c}
\begin{align*}
35\text{g} & \quad \text{MeO-CHO} & \quad 80\text{g} (70\%) & \quad 81\text{g} (99\%)
\end{align*}
\end{array}
\]

\[
\begin{array}{c}
\begin{align*}
35\text{h} & \quad \text{OMe-CHO} & \quad 80\text{h} (55\%) & \quad 81\text{h} (92\%)
\end{align*}
\end{array}
\]

\(^a\)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 $\delta$ 6.96 and 6.94 due to two aromatic protons, the presence of doublet at $\delta$ 4.75 having $J$=6.8 Hz due to benzylic proton, two singlets at $\delta$ 3.86 and 3.44 due to six protons of two methoxy groups and a multiplet at $\delta$ 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 $\delta$ 148.5(2C), 134.8 and 112.6 were due to four aromatic carbons, the presence of two aromatic methine carbons at $\delta$ 114.9 and 110.6, benzylic carbon resonates at $\delta$ 76.9, two methoxy group carbons resonates at $\delta$ 56.1 and 56.0, the presence of $\delta$ 44.4 was due to CH(CH$_3$)$_2$ group and cyclohexyl five carbon resonates at $\delta$ 29.3, 28.1, 26.4, 26.2 and 26.0 ppm. The presence of [(M+H)--H$_2$O]$^+$ 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$_3$
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 \(\delta 7.00\) and 6.83 were due to two aromatic protons, two singlets at \(\delta 3.88\) and 3.86 were due to six protons of two methoxy groups, the presence of triplet of triplets at \(\delta 3.01\) having \(J=11.2\) Hz was due to one proton and a multiplet at \(\delta 2.10\)–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 \(\delta 207.0\) was due to carbonyl carbon, the presence of four quaternary carbon resonates at \(\delta 150.8, 148.2, 133.7\) and 110.2 were due to four aromatic carbons, the presence of two aromatic methine carbons at \(\delta 116.0\) and 110.2, two methoxy group carbons resonates at \(\delta 56.2\) and 56.1, the presence of \(\delta 49.4\) was due to Cy-CH group and cyclohexyl five carbon resonates at signals at \(\delta 28.7(2C), 25.8, 25.7(2C)\) 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.
Reaction conditions: All the reactions were carried out with \textbf{81a-81h} (100 mg, 0.25 to 0.37 mmol) in toluene. Isolated yields are chromatographically pure products. Isolated yield of chromatographically pure product based on the starting material recovery.

Figure I.1.1: $^1$H-NMR (400 MHz) spectrum of $82g$ in CDCl$_3$

Figure I.1.2: $^{13}$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 \(\delta\) 7.03, 6.95, 6.63 and 6.60 were due to four aromatic protons, a multiplet in the region at \(\delta\) 6.55–6.45 was due to one olefinic proton, four singlets at \(\delta\) 3.91, 3.90, 3.85 and 3.82 were due to twelve protons of four methoxy groups, presence of triplet of triplets at \(\delta\) 2.4 having \(J\)=11.2 and 3.4 Hz due Cy-CH group and a multiplet in the region at \(\delta\) 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 \(\delta\) 208.0 and 199.0 were due to two carbonyl carbons, nine quaternary carbon resonates at \(\delta\) 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 \(\delta\) 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 \(\delta\) 56.1 for 2C, 56.0 and 55.9, the presence of \(\delta\) 48.9 due to CyCH group, and two cylohexyl group nine carbon resonates at \(\delta\) 29.7, 29.1, 26.0, 25.8, 25.7, 25.6, 23.4, 21.8 and 21.5 ppm. The presence of \([\text{M+H}]^+\) peak at m/z \([\text{C}_{30}\text{H}_{37}\text{O}_{6}]^+\)=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\(_2\)CO\(_3\) would not be strong enough to deprotonate \(\alpha\)-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) 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](image)

**I.4. CONCLUSIONS:**

In conclusion, we have developed an unprecedented and novel domino [Pd]-catalysis for the synthesis of 7-methyl-5H-dibenzo[α,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 (dpf) (with purity 97%), 2-di-tert-butylphosphino-2',4',6'-triisopropylbiphenyl (tert-Butyl XPhos) (with purity 97%), triphenylphosphine (PPh3) (with purity 99%), Pd(dpff)Cl2 (with purity 97%), Pd(PPh3)4 (with purity 99%), Pd(dba)2 (with purity 98%), Pd(PPh3)2Cl2 (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-Bu4NI) (with purity 98%), n-tetrabutylammoniumbromide (n-Bu4NBr) (with purity 98%), zinc chloride (ZnCl2) (with purity 98%), dimethyl sulphoxide (DMSO) (with purity 99.7%) and potassium carbonate (with purity 99%), K3PO4 (with purity 98%), Cs2CO3 (with purity 99%), purchased from Sigma-Aldrich were used without further purification. The bases K2CO3, K3PO4 and Cs2CO3 dried at 150–170 °C over oil bath and 4BuOK 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 P2O5. 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-35h42 were synthesized using literature reported bromination of corresponding benzaldehydes and 2-bromoacetophenones 37a-37h9k 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$_3$PO$_4$ (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 NH₄Cl solution and the aqueous layer was extracted with ethyl acetate (3 × 20 mL). The organic layers were dried over anhydrous Na₂SO₄, 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%).

![Image of chemical structure](image)

**7-Methyl-5H-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%), K₃PO₄ (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):** \( \nu_{max}=3062, 2957, 2853, 1652, 1593, 1439, 1377, 1356, 1307, 1250, 1121, 1003, 850, 771, 735, 621 cm⁻¹. \)

**¹H-NMR (CDCl₃, 400 MHz):** \( \delta=7.79 \) (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, CH₃) ppm.

**¹³C-NMR (CDCl₃, 100 MHz):** \( \delta=194.0 \) (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, CH₃) ppm.
HR-MS (ESI\(^+\)): m/z calculated for [C\(_{32}\)H\(_{25}\)O\(_2\)]\(^+\)=[2(M+H)]\(^+\): 441.1849; found 441.1836.

3,9-Bis(benzyloxy)-7-methyl-5H-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\(_3\)PO\(_4\) (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\(^{-1}\)): \(v_{\text{max}}\)=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): \(\delta=7.68\) (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\(_2\)O), 5.14 (s, 2H, Ph-CH\(_2\)O), 2.39 (s, 3H, CH\(_3\)) ppm.

\(^{13}\)C-NMR (CDCl\(_3\), 100 MHz): \(\delta=193.4\) (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\(_2\)O), 70.2 (t, Ph-CH\(_2\)O), 24.6 (q, CH\(_3\)) ppm.
HR-MS (ESI^+): m/z calculated for \([\text{C}_{30}\text{H}_{24}\text{NaO}_3]^+=[\text{M}+\text{Na}]^+\): 455.1618; found 455.1611.

\[ \text{3,9-Dimethoxy-7-methyl-5H-dibeno[}a,e][7]\text{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 \text{ mol\%}), \text{Xantphos (10.1 mg, 4 \text{ mol\%}), K}_3\text{PO}_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}): \( \nu_{\text{max}}=3001, 2934, 2837, 1643, 1603, 1571, 1484, 1408, 1337, 1281, 1240, 1174, 1039, 814, 753, 722, 614 \text{ cm}^{-1}. \)

\(^1\text{H}-\text{NMR (CDCl}_3, 400 \text{ MHz}): \delta=7.69 (d, 1H, J=8.9 \text{ Hz}, \text{Ar-H}), 7.66 (d, 1H, J=8.9 \text{ Hz}, \text{Ar-H}), 7.28 (d, 1H, J=2.9 \text{ Hz}, \text{Ar-H}), 7.20 (d, 1H, J=2.8 \text{ Hz}, \text{Ar-H}), 7.18 (dd, 1H, J=8.9 and 2.9 Hz, Ar-H), 7.04 (dd, 1H, J=8.9 and 2.8 Hz, Ar-H), 6.61 (d, 1H, J=0.9 Hz, Ar-H), 3.89 (s, 3H, Ar-OCH}_3, 3.88 (s, 3H, Ar-OCH}_3, 2.43 (s, 3H, CH}_3) \text{ ppm.} \)

\(^{13}\text{C}-\text{NMR (CDCl}_3, 100 \text{ MHz}): \delta=193.6 (s, \text{Ar-C}=\text{O}), 159.0 (s, \text{Ar-C}), 158.4 (s, \text{Ar-C}), 144.8 (s, \text{Ar-C}), 142.3 (s, \text{Ar-C}), 136.3 (s, \text{Ar-C}), 132.9 (d, \text{Ar-CH}), 132.8 (d, \text{Ar-CH}), 131.3 (d, \text{Ar-CH}), 130.5 (s, \text{Ar-C}), 130.4 (s, \text{Ar-C}), 119.4 (d, \text{Ar-CH}), 114.5 (d, \text{Ar-CH}), 112.2 (d, \text{Ar-CH}), 109.7 (d, \text{Ar-CH}), 55.6 (q, \text{Ar-OCH}_3), 55.4 (q, \text{Ar-OCH}_3), 24.6 (q, \text{CH}_3) \text{ ppm.} \)

HR-MS (ESI^+): m/z calculated for \([\text{C}_{18}\text{H}_{17}\text{O}_3]^+=[\text{M}+\text{H}]^+\): 281.1172; found 281.1161.
3,9-Bis(benzyloxy)-2,10-dimethoxy-7-methyl-5H-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$_3$PO$_4$ (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$^{-1}$):** $\nu_{max}$=2932, 1630, 1589, 1509, 1455, 1383, 1257, 1218, 1162, 1070, 1020, 858, 734, 698 cm$^{-1}$.

$^1$H-NMR (CDCl$_3$, 400 MHz): $\delta$=7.41 (d, 2H, $J$=7.1 Hz, Ar-H), $\delta$=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$_2$O), 5.17 (s, 2H, PhCH$_2$O), 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): $\delta$=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$_2$O), 70.9 (t, PhCH$_2$O), 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.
2,10-Bis(benzylxy)-3,9-dimethoxy-7-methyl-5H-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$_3$PO$_4$ (190 mg, 0.89 mmol) and dry DMF (3 mL). The resulted reaction mixture was stirred at preheated oil bath 150 ºC 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 ºC. [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$^{-1}$):** $\nu_{max}$=2923, 2852, 1630, 1591, 1508, 1461, 1391, 1255, 1163, 1068, 1035, 1012, 859, 737, 697 cm$^{-1}$.

$^1$H-NMR (CDCl$_3$, 400 MHz): $\delta$=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$_2$O), 5.05 (s, 2H, PhCH$_2$O), 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): $\delta$=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), 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$_2$O), 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.

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\(_{2}\)PO\(_{4}\) (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\(^{-1}\)): \(\nu_{max}\)=2921, 1641, 1608, 1503, 1485, 1415, 1397, 1243, 1034, 926, 863 cm\(^{-1}\).

\(^1\)H-NMR (CDCl\(_3\), 400 MHz): \(\delta\)=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): \(\delta\)=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.
2,3,9,10-Tetramethoxy-7-methyl-5H-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$_3$PO$_4$ (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$^{-1}$):** $\nu_{\text{max}}$=2927, 2852, 1629, 1593, 1511, 1464, 1390, 1258, 1204, 1163, 1071, 1034, 861, 788, 732 cm$^{-1}$.

**$^1$H-NMR (CDCl$_3$, 400 MHz):** $\delta$=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 $\times$ Ar-OCH$_3$), 2.44 (s, 3H, CH$_3$) ppm.

**$^{13}$C-NMR (CDCl$_3$, 100 MHz):** $\delta$=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-5H-dibenzo[a,c][7]annulen-5-one (40g): CCDC 910650

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I.5.2 Synthesis of \( \alpha \)-aryl ketones:

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

In an oven dried Schlenk tube under nitrogen atmosphere, were added aryl iodides 61a-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\(_4\)Cl and the aqueous layer was extracted with ethyl acetate (3 \( \times \) 20 mL). The combined organic layers were dried over anhydrous Na\(_2\)SO\(_4\), 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%).

![Chemical structure](image)

1-(2-Bromophenyl)-2-(3,4-dimethoxyphenyl)ethanone (62ac): GP-2 was carried out with aryl iodide 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\(^{-1}\))**: \( \nu_{max}=2956, 2923, 2852, 1697, 1587, 1512, 1463, 1422, 1259, 1154, 1140, 1025, 791, 757, 678 \) cm\(^{-1}\).

**\(^1\)H-NMR (CDCl\(_3\), 400 MHz)**: \( \delta=7.57 \) (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, CH₂), 3.83 (s, 3H, Ar-OCH₃), 3.82 (s, 3H, Ar-OCH₃) ppm.

$^{13}$C-NMR (CDCl₃, 100 MHz): $\delta$=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-OCH₃), 49.0 (t, CH₂) ppm.

HR-MS (ESI⁺): m/z calculated for [C$_{16}$H$_{16}$BrO$_3$]$^+$=[M+H]$^+$: 335.0277; found 335.0294, [C$_{16}$H$_{16}$BrO$_3$]$^+$=[M+H]$^+$: 337.0259; found 337.0274.

Methyl-4-[2-(2-bromophenyl)-2-oxoethyl]benzoate (62ae): GP-2 was carried out with aryl iodide 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%), tBuOK (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$^{-1}$): $\nu_{max}$=2919, 2850, 1717, 1587, 1463, 1434, 1280, 1198, 1181, 1107, 1022, 988, 757 cm$^{-1}$.

$^1$H-NMR (CDCl₃, 400 MHz): $\delta$=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, CH₂), 3.89 (s, 3H, CH₃) ppm.

$^{13}$C NMR (CDCl₃, 100 MHz): $\delta$=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, CH₃), 49.3 (t, CH₂) ppm.
HR-MS (ESI\(^+\)): m/z calculated for [C\(_{16}\)H\(_{13}\)BrNaO\(_3\)]\(^+\)=[M+Na]\(^+\): 354.9940; found 354.9944.

1-(2-Bromo-5-methoxyphenyl)-2-phenylethanone (62ca): GP-2 was carried out with aryl iodide 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%), '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\(^{-1}\)): \(\nu_{max}=2924, 1701, 1592, 1569, 1467, 1403, 1314, 1289, 1240, 1171, 1026, 815, 727, 698\) cm\(^{-1}\).

\(^1\)H-NMR (CDCl\(_3\), 400 MHz): \(\delta=7.35\) (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): \(\delta=201.5\) (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.
1-(2-Bromo-5-methoxyphenyl)-2-(3,4-dimethoxyphenyl)ethanone (62cc): GP-2 was carried out with aryl iodide 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$^{-1}$):** $\nu_{\text{max}}=2936, 1699, 1592, 1569, 1514, 1464, 1261, 1235, 1026, 905, 724$ cm$^{-1}$.

**$^1$H-NMR (CDCl$_3$, 400 MHz):** $\delta=7.43$ (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):** $\delta=201.7$ (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.

1-(2-Bromo-5-methoxyphenyl)-2-(2,3,4-trimethoxyphenyl)ethanone (62cd): GP-2 was carried out with aryl iodide 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%), 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 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$^{-1}$): $\nu_{max}$=2922, 2850, 1702, 1592, 1569, 1494, 1465, 1418, 1274, 1238, 1095, 1017, 794, 733 cm$^{-1}$.

$^1$H-NMR (CDCl$_3$, 400 MHz): $\delta$=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): $\delta$=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$_{19}$BrNaO$_5$]$^+$=[M+Na]$^+$: 417.0308; found 417.0308, [C$_{18}$H$_{19}$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$_{20}$BrO$_5$]$^+$=[M+H]$^+$: 397.0470; found 397.0488.

Methyl-4-[2-(2-bromo-5-methoxyphenyl)-2-oxoethyl]benzoate (62ce): GP-2 was carried out with aryl iodide 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%), 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 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\(^{-1}\)):** \( \nu_{max}=2925, 2852, 1718, 1610, 1591, 1467, 1435, 1278, 1241, 1109, 966, 742 \) cm\(^{-1}\).

**\(^1\)H-NMR (CDCl\(_3\), 400 MHz):** \( \delta=7.98 \) (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\(_3\)), \( 3.89 \) (s, 3H, Ar-OCH\(_3\)) ppm.

**\(^{13}\)C-NMR (CDCl\(_3\), 100 MHz):** \( \delta=200.7 \) (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\(_3\)) ppm.

**HR-MS (ESI\(^+\)):** \( m/z \) calculated for \([C_{17}H_{16}^{79}\text{BrO}_4]^+=[M+H]^+\): 363.0226; found 363.0218, \([C_{17}H_{16}^{81}\text{BrO}_4]^+=[M+H]^+\): 365.0206; found 365.0201.

**1-(2-Bromo-4,5-dimethoxyphenyl)-2-(4-methoxyphenyl)ethanone (62gb):** GP-2 was carried out with aryl iodide 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\(^\text{BuOK} \) (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\(^{-1}\)):** \( \nu_{max}=2924, 1689, 1593, 1506, 1461, 1371, 1247, 1209, 1161, 1024, 852, 794 \) cm\(^{-1}\).

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1H-NMR (CDCl₃, 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, CH₂), 3.88 (s, 3H, Ar-OCH₃), 3.80 (s, 3H, Ar-OCH₃), 3.77 (s, 3H, Ar-OCH₃) ppm.

13C-NMR (CDCl₃, 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-OCH₃), 56.1 (q, Ar-OCH₃), 55.2 (q, Ar-OCH₃), 48.2 (t, CH₂) ppm.

HR-MS (ESI⁺): m/z calculated for [C₁₇H₁₈BrO₄]⁺=[M+H]⁺: 365.0383; found 365.0397.

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%), iBuOK (72.9 mg, 0.65 mmol) and dry toluene (4 mL) at 80 ºC 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), R₂(37g)=0.50, R₂(61d)=0.80 and R₂(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.

1H-NMR (CDCl₃, 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, CH₂), 3.89 (s, 3H, Ar-OCH₃), 3.85 (s, 3H, Ar-OCH₃), 3.83 (s, 9H, 3 × Ar-OCH₃) ppm.

13C-NMR (CDCl₃, 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-OCH₃), 60.7 (q, Ar-OCH₃), 56.3 (q, Ar-OCH₃), 56.1 (q, Ar-OCH₃), 56.0 (q, Ar-OCH₃), 43.3 (t, CH₂) ppm.

HR-MS (ESI⁺) m/z calculated for [C₁₉H₂₂BrO₆]⁺=[M+H]⁺: 425.0594; found 425.0605.

1-(2-Bromo-4,5-dimethoxyphenyl)-2-(4-nitrophenyl)ethanone (62gf): GP-2 was carried out with aryl iodide 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%), tBuOK (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), Rf(37g)=0.50, Rf(61f)=0.70 and Rf(62gf)=0.25, UV detection].

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

¹H-NMR (CDCl₃, 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, CH₂), 3.91 (s, 3H, Ar-OCH₃), 3.85 (s, 3H, Ar-OCH₃) ppm.

¹³C-NMR (CDCl₃, 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-OCH₃), 56.2 (q, Ar-OCH₃), 48.4 (t, CH₂) ppm.

HR-MS (ESI⁺): m/z calculated for [C₁₆H₁₃BrNO₅]⁺=[M+H]⁺: 380.0128; found 380.0140.
1.5.3 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 NH₄Cl solution and the aqueous layer was extracted with ethyl acetate (3 × 30 mL). The combined organic layers were dried over anhydrous Na₂SO₄, 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%).

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): \( \nu_{max}=3397, 2960, 2922, 2851, 1466, 1439, 1282, 1366, 1197, 1006, 749, 682 \) cm⁻¹.

\(^1\)H-NMR (CDCl₃, 400 MHz): \( \delta=7.51 \) (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-CHOH), 2.05 [septd,
1H, J=5.9 and 1.0 Hz, CH(CH₃)₂, 1.97 (br. s, 1H, OH), 0.95 [d, 3H, J=6.4 Hz, CH(CH₃)₃(CH₃)b], 0.94 [d, 3H, J=6.4 Hz, CH(CH₃)₃(CH₃)b] ppm.

¹³C-NMR (CDCl₃, 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, CH(CH₃)₂], 19.4 [q, CH(C₃H₃)ₑ(CH₃)₃b], 16.7 [q, CH(CH₃)₃(CH₃)b] ppm.

HR-MS (ESI⁺): m/z calculated for [C₁₀H₁₂Br]⁺=(M+H–H₂O)⁺: 211.0117; found 211.0117.

1-[5-(Benzylxoy)-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, Rf(35b)=0.60, Rf(68b)=0.45, UV detection)].

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

¹H-NMR (CDCl₃, 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, PhCH₃H₃bO), 5.04 (d, 1H, J=11.7 Hz, PhCH₃H₃bO), 4.80 (d, 1H, J=5.4 Hz, Ar-CHOH), 2.03 [septd, 1H, J=6.8 and 5.4 Hz, CH(CH₃)₂], 1.91 (br. s, 1H, OH), 0.95 [d, 3H, J=6.8 Hz, CH(CH₃)₃(CH₃)b], 0.93 [d, 3H, J=6.8 Hz, CH(CH₃)₃(CH₃)b] ppm.

¹³C-NMR (CDCl₃, 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-CH₂O), 33.8 [d, CH(CH₃)₂], 19.5 [q, CH(CH₃)a(CH₃)b], 16.6 [q, CH(CH₃)a(CH₃)b] ppm.

**HR-MS (ESI⁺)**: m/z calculated for [C₁₇H₁₉⁷⁹BrNaO₂]⁺=[M+Na]⁺: 357.0461; found 357.0469, [C₁₇H₁₉⁸¹BrNaO₂]⁺=[M+Na]⁺: 359.0446; found 359.0463.

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, Rf(35c)=0.50, Rf(68c)=0.40, UV detection)]

**IR (MIR-ATR, 4000–600 cm⁻¹):** νmax=3394, 2960, 2929, 2872, 1594, 1572, 1465, 1416, 1284, 1231, 1162, 1007, 749, 811, 595 cm⁻¹.

**¹H-NMR (CDCl₃, 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-CHOH), 3.77 (s, 3H, Ar-OCH₃), 2.19 (br. s, 1H, OH), 2.13–1.92 (m, 1H, CH(CH₃)₂), 0.94 [d, 3H, J=6.8 Hz, CH(CH₃)a(CH₃)b], 0.93 [d, 3H, J=6.8 Hz, CH(CH₃)a(CH₃)b] ppm.

**¹³C-NMR (CDCl₃, 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-OCH₃), 33.9 [d, CH(CH₃)₂], 19.4 [q, CH(CH₃)a(CH₃)b], 16.7 [q, CH(CH₃)a(CH₃)b] ppm.

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\(^{-1}\))**: \( \nu_{max}=3491, 2960, 1602, 1500, 1456, 1439, 1379, 1255, 1206, 1157, 1029, 803, 739, 697 \text{ cm}\(^{-1}\).**

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

**\( ^{13}\text{C-NMR (CDCl\(_3\), 100 MHz)}\)**: \( \delta=149.2 \) (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, CH(CH\(_3\))\(_2\)], 19.2 [q, CH(CH\(_3\))\(_3\text{a(CH}_3\text{)}_3\text{b} \)], 17.0 [q, CH(CH\(_3\))\(_3\text{a(CH}_3\text{)}_3\text{b} \)] ppm.

**HR-MS (ESI\(^+\))**: m/z calculated for \([C_{18}H_{20}^{79}\text{BrO}_2]^+=[(M+H–H}_2\text{O}]^+\): 347.0641; found 347.0641, \([C_{18}H_{20}^{81}\text{BrO}_2]^+=[(M+H–H}_2\text{O}]^+\): 349.0621; found 349.0634.
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\(^{-1}\))**: \(v_{\text{max}}\)=3395, 2956, 2929, 2872, 1602, 1497, 1497, 1455, 1439, 1377, 1246, 1203, 1027, 911, 870, 842, 801, 734, 696, 637 cm\(^{-1}\).

**\(\text{\(^1\)H-NMR (CDCl}_3, 400 \text{ MHz})\)**: \(\delta=7.43\) (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-\(\text{CH}_2\)O), 4.74 (d, 1H, \(J=5.9\) Hz, Ar-\(\text{CHOH}\)), 3.86 (s, 3H, Ar-\(\text{OCH}_3\)), 2.05–1.90 [m, 2H, CH(\(\text{CH}_3\))\(_2\) and OH], 0.99 [d, 3H, \(J=6.8\) Hz, CH(\(\text{CH}_3\)_a(\(\text{CH}_3\)_b)], 0.89 [d, 3H, \(J=6.8\) Hz, CH(\(\text{CH}_3\)_a(\(\text{CH}_3\)_b)] ppm.

**\(\text{\(^{13}\)C-NMR (CDCl}_3, 100 \text{ MHz})\)**: \(\delta=149.1\) (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-\(\text{CHOH}\)), 71.2 (t, Ph-\(\text{CH}_2\)O), 56.1 (q, Ar-\(\text{OCH}_3\)), 34.4 [d, CH(\(\text{CH}_3\)_2)], 19.2 [q, CH(\(\text{CH}_3\)_a(\(\text{CH}_3\)_b)], 17.3 [q, CH(\(\text{CH}_3\)_a(\(\text{CH}_3\)_b)] ppm.

**HR-MS (ESI\(^+\))**: m/z calculated for [\(\text{C}_{18}\text{H}_{21}\text{BrO}_3\)]\(^+\)=[M]\(^+\): 364.0669; found 364.0678.
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\(^{-1}\))**: \( \nu_{max} = 3397, 2960, 2922, 2853, 1502, 1472, 1406, 1387, 1228, 1124, 1102, 1037, 936, 874, 838, 787, 678 \text{cm}^{-1} \).

**\(^1H\)-NMR (CDCl\(_3\), 400 MHz)**: \( \delta = 6.95 \text{ (s, 1H, Ar-H)}, 6.93 \text{ (s, 1H, Ar-H)}, 5.95 \text{ (d, 1H, J=2.9 Hz, O-CH\(_2\)H\(_3\)-O)}, 5.94 \text{ (d, 1H, J=2.9 Hz, O-CH\(_2\)H\(_3\)-O)}, 4.74 \text{ (d, 1H, J=6.4 Hz, Ar-CH\(_2\)OH)}, 2.03 \text{ (br. s, 1H, OH)}, 1.94 \text{ [sept, 1H, J=6.8 Hz, CH(CH\(_3\))\(_2\)]}, 0.96 \text{ [d, 3H, J=6.8 Hz, CH(CH\(_3\))\(_2\)(CH\(_3\))\(_b\)]} \text{ ppm.}

**\(^13C\)-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-CH\(_2\)OH), 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 \([\text{C}_{11}\text{H}_{12}^{79}\text{BrO}_2]^+=[(\text{M+H})–\text{H}_2\text{O}])^+ = 255.0015;\) found 255.0016, \([\text{C}_{11}\text{H}_{12}^{81}\text{BrO}_2]^+=[(\text{M+H})–\text{H}_2\text{O}])^+ = 256.9995;\) found 257.0003.

![Diagram](https://via.placeholder.com/150)

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\(^{-1}\))**: \(\nu_{max}=3496, 2959, 1603, 1463, 1439, 1380, 1255, 1207, 1156, 1031, 804, 750 \text{ cm}^{-1}\).

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

**\(^{13}\)C-NMR (CDCl\(_3\), 100 MHz)**: 148.4 (s, 2\text{C, 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, CH(CH\(_3\))\(_2\)], 19.2 [q, CH(CH\(_3\))\(_a(CH}_3)_b], 17.3 [q, CH(CH\(_3\))\(_a(CH}_3)_b] \text{ ppm.}

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

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 \(-10^\circ\text{C}\) 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):** \( \nu_{max}\) = 3494, 2960, 2936, 1590, 1568, 1480, 1463, 1393, 1324, 1235, 1195, 1103, 1008, 912, 820 cm⁻¹.

**¹H-NMR (CDCl₃, 400 MHz):** \( \delta\) = 6.83 (s, 1H, Ar-H), 4.79 (d, 1H, \( J = 5.4 \) Hz, Ar-CHOH), 3.81 (s, 6H, 2 \times Ar-OCH₃), 3.80 (s, 3H, Ar-OCH₃), 2.40 (br. s, 1H, OH), 1.94 [sept, 1H, \( J = 6.4 \) Hz, CH(CH₃)₂], 0.89 [dd, 6H, \( J = 6.4 \) Hz, CH(CH₃)ₐ(CH₃)ₐ] ppm.

**¹³C-NMR (CDCl₃, 100 MHz):** \( \delta\) = 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-OCH₃), 55.8 (q, Ar-OCH₃), 33.8 [d, CH(CH₃)₂], 19.2 [d, CH(CH₃)ₐ(CH₃)ₐ], 16.6 [d, CH(CH₃)ₐ(CH₃)ₐ] ppm.

**HR-MS (ESI⁺):** m/z calculated for \([C_{13}H_{18}^{79}BrO₃]^+ = [(M+H)-H₂O]^+\): 301.0434; found 301.0431, \([C_{13}H_{18}^{81}BrO₃]^+ = [(M+H)-H₂O]^+\): 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 NH₄Cl solution and the aqueous layer was extracted with ethyl acetate (3 × 30 mL). The combined organic layers were dried over anhydrous Na₂SO₄, 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%).

![Diagram](image)

**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\(^{-1}\)):** \( v_{\text{max}}=3392, 2924, 2851, 1567, 1467, 1448, 1346, 1263, 1082, 1016, 754, 729 \) cm\(^{-1}\).

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

\[ ^{13}C\text{-NMR (CDCl}_3, 100 MHz): \delta=142.7 \text{ (s, Ar-C)}, 132.5 \text{ (d, Ar-CH)}, 128.5 \text{ (d, Ar-CH)}, 128.4 \text{ (d, Ar-CH)}, 127.3 \text{ (d, Ar-CH)}, 122.7 \text{ (s, Ar-C)}, 77.0 \text{ (d, Ar-CHOH)}, 43.9 \text{ (d, Cy-CH)}, 29.5 \text{ (t, Cy-CH}_2\text{)}, 27.5 \text{ (t, Cy-CH}_2\text{)}, 26.3 \text{ (t, Cy-CH}_2\text{)}, 26.2 \text{ (t, Cy-CH}_2\text{)}, 26.0 \text{ (t, Cy-CH}_2\text{)} \text{ ppm.} \]

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

![diagram](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\(^{-1}\)): \(v_{\text{max}}=3353, 2924, 2850, 1593, 1572, 1451, 1293, 1232, 1163, 1010, 734, 696 \text{ cm}^{-1}\).

\(^1\)H-NMR (CDCl\(_3\), 400 MHz): \(\delta=7.50–7.35\) (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\(_2\)O), 4.80 (d, 1H, \(J=5.4\) Hz, Ar-CHOH), 2.00 (br. s, 1H, OH), 1.90–0.70 (m, 11H, Cy-H) ppm.

\(^{13}\)C-NMR (CDCl\(_3\), 100 MHz): \(\delta=158.0\) (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\(_2\)O]^+: 357.0849; found 357.0849, [C\(_{20}\)H\(_{22}\)\(^{81}\)BrO]^+: [(M+H)--H\(_2\)O]^+: 359.0834.

(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\(^{-1}\)): \(v_{\text{max}}=3385, 2923, 2850, 1594, 1572, 1468, 1449, 1284, 1233, 1161, 1049, 1012, 811 \text{ cm}^{-1}\).
\[ ^1\text{H-NMR (CDCl}_3, \text{ 400 MHz):} \delta = 7.37 \text{ (d, 1H, J=8.3 Hz, Ar-H), 7.01 \text{ (d, 1H, J=2.9 Hz, Ar-H), 6.66 \text{ (dd, 1H, J=8.3 and 2.9 Hz, Ar-H), 4.79 \text{ (d, 1H, J=6.4 Hz, Ar-CHOH), 3.78 \text{ (s, 3H, Ar-OCH}_3 \text{), 2.13 \text{ (br. s, 1H, OH), 1.90–1.00 \text{ (m, 11H, Cy-H ppm.}}}}
\]

\[ ^{13}\text{C-NMR (CDCl}_3, \text{ 100 MHz):} \delta = 159.0 \text{ (s, Ar-C), 143.8 \text{ (s, Ar-C), 133.0 \text{ (d, Ar-CH), 114.7 \text{ (d, Ar-CH), 113.6 \text{ (d, Ar-CH), 113.0 \text{ (s, Ar-C), 77.0 \text{ (d, Ar-CHOH), 55.4 \text{ (q, Ar-OCH}_3 \text{), 43.9 \text{ (d, Cy-CH), 29.5 \text{ (t, Cy-CH}_2 \text{), 27.4 \text{ (t, Cy-CH}_2 \text{), 26.3 \text{ (t, Cy-CH}_2 \text{), 26.2 \text{ (t, Cy-CH}_2 \text{), 26.0 \text{ (t, Cy-CH}_2 \text{ ppm.}}}}}
\]

**HR-MS (ESI\(^+\))**: m/z calculated for [C\(_{14}\)H\(_{18}\)\(^{79}\)BrO\(^+\)=[(M+H)–H\(_2\)O]\(^+\): 281.0536; found 281.0549, [C\(_{14}\)H\(_{18}\)\(^{81}\)BrO\(^+\)=[(M+H)–H\(_2\)O]\(^+\): 283.0515; found 283.0530.

[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 \(-50^\circ\text{C}\) 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\(^{-1}\))**: \(\nu_{\text{max}}=3382, 2923, 2850, 1602, 1499, 1451, 1439, 1379, 1251, 1204, 1154, 1027, 803, 734, 696 \text{ cm}^{-1}\).

\[ ^1\text{H-NMR (CDCl}_3, \text{ 400 MHz):} \delta = 7.40 \text{ (d, 2H, J=7.3 Hz, Ar-H), 7.33 \text{ (dd, 2H, J=7.3 and 6.8 Hz, Ar-H), 7.27 \text{ (t, 1H, J=6.8 Hz, Ar-H), 6.97 \text{ (s, 1H, Ar-H), 6.96 \text{ (s, 1H, Ar-H), 5.17 \text{ (d, 1H, J=12.2 Hz, PhCH}_3\text{H}_2\text{O}, 5.11 \text{ (d, 1H, J=12.2 Hz, PhCH}_3\text{H}_2\text{O}, 4.70 \text{ (d, 1H, J=6.4 Hz, Ar-CHOH), 3.84 \text{ (s, 3H, Ar-OCH}_3 \text{), 2.50–0.5 \text{ (m, 12H, Cy-H and OH ppm.}}}}}
\]
\textsuperscript{13}C-NMR (CDCl\textsubscript{3}, 100 MHz): \(\delta=149.3\) (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-CH\textsubscript{O}), 70.9 (t, Ph-CH\textsubscript{2}O), 56.2 (q, Ar-OCH\textsubscript{3}), 44.2 (d, Cy-CH), 29.3 (t, Cy-CH\textsubscript{2}), 27.8 (t, Cy-CH\textsubscript{2}), 26.4 (t, Cy-CH\textsubscript{2}), 26.2 (t, Cy-CH\textsubscript{2}), 26.0 (t, Cy-CH\textsubscript{2}) ppm.

HR-MS (ESI\textsuperscript{+}): m/z calculated for [C\textsubscript{21}H\textsubscript{24}BrO\textsubscript{2}]\textsuperscript{+}=[(M+H)–H\textsubscript{2}O]\textsuperscript{+}: 387.0954; found 387.0962, [C\textsubscript{21}H\textsubscript{24}\textsuperscript{81}BrO\textsubscript{2}]\textsuperscript{+}=[(M+H)–H\textsubscript{2}O]\textsuperscript{+}: 389.0934; found 389.0952.

[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\textsuperscript{-1}): \(\nu_{max}=3390, 2923, 2851, 1601, 1500, 1453, 1383, 1256, 1201, 1157, 741, 697\) cm\textsuperscript{-1}.

\textsuperscript{1}H-NMR (CDCl\textsubscript{3}, 400 MHz): \(\delta=7.42\) (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\textsubscript{2}O), 4.74 (d, 1H, \(J=6.8\) Hz, Ar-CHO\textsubscript{H}), 3.86 (s, 3H, Ar-OCH\textsubscript{3}), 2.50–0.50 (m, 12H, Cy-H and OH) ppm.

\textsuperscript{13}C-NMR (CDCl\textsubscript{3}, 100 MHz): \(\delta=149.2\) (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-CHO\textsubscript{H}), 71.3 (t, Ph-
(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\(^{-1}\)) \( \nu_{max}=3386, 2925, 2851, 1503, 1478, 1410, 1239, 1124, 1105, 1040, 934 \) cm\(^{-1}\).

\(^1\)H-NMR (CDCl\(_3\), 400 MHz): \( \delta=6.94 \) (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-CHOH), 2.30 (m, 12H, Cy-H and OH) ppm.

\(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \( \delta=147.5 \) (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.
(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\(^{-1}\)): \( \nu_{max}=3400, 2924, 2850, 1603, 1503, 1462, 1447, 1381, 1257, 1209, 1156, 1033, 802 \text{ cm}^{-1} \).

\(^1\text{H-NMR (CDCl}_3, 400 \text{ MHz})\): \( \delta=6.96 \text{ (s, 1H, Ar-H)}, 6.94 \text{ (s, 1H, Ar-H)}, 4.75 \text{ (d, 1H, J=6.8 Hz, Ar-CHOH)}, 3.86 \text{ (s, 3H, Ar-OCH}_3\text{)}, 3.84 \text{ (s, 3H, Ar-OCH}_3\text{)}, 2.30–0.6 \text{ (m, 12H, Cy-H and OH) ppm.}

\(^{13}\text{C-NMR (CDCl}_3, 100 \text{ MHz})\): \( \delta=148.5 \text{ (s, 2C, Ar-C)}, 134.8 \text{ (s, Ar-C)}, 114.9 \text{ (d, Ar-CH)}, 112.6 \text{ (s, Ar-C)}, 110.6 \text{ (d, Ar-CH)}, 76.9 \text{ (d, Ar-CHOH)}, 56.1 \text{ (q, Ar-OCH}_3\text{)}, 56.0 \text{ (q, ArO-CH}_3\text{)}, 44.4 \text{ [d, Cy-CH] 29.3 \text{ (t, Cy-CH}_2\text{)}, 28.1 \text{ (t, Cy-CH}_2\text{)}, 26.4 \text{ (t, Cy-CH}_2\text{)}, 26.2 \text{ (t, Cy-CH}_2\text{)}, 26.0 \text{ (t, Cy-CH}_2\text{) ppm.}

HR-MS (ESI\(^+\)): m/z calculated for \([C_{15}H_{20}^{79}\text{BrO}_2]^+=[(M+H)–\text{H}_2\text{O}]^+\): 311.0641; found 311.0640, \([C_{15}H_{20}^{81}\text{BrO}_2]^+=[(M+H)–\text{H}_2\text{O}]^+\): 313.0621; found 313.0625.

(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\(^{-1}\))**: \( \nu_{max} = 3462, 2925, 2850, 1568, 1480, 1447, 1392, 1322, 1238, 1195, 1161, 1102, 1009, 813, 730 \text{ cm}^{-1} \).

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

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

**HR-MS (ESI\(^+\))**: \( m/z \) calculated for \([C_{16}H_{23}^{79}\text{BrNaO}_4]^{+}[M+Na]^+: 381.0672; \) found 381.0670, \([C_{16}H_{23}^{81}\text{BrNaO}_4]^+[M+Na]^+: 383.0651; \) 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\(_2\)Cl\(_2\) (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\(_2\)Cl\(_2\) furnished the pure product 69/81 (93-99%)/(91-96%).
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$_2$Cl$_2$ (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$_2$Cl$_2$ 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$^{-1}$): $\nu_{max}$=2970, 2928, 2872, 1700, 1587, 1462, 1428, 1382, 1344, 1266, 1216, 1052, 976, 769, 737, 667, 633 cm$^{-1}$.

$^1$H-NMR (CDCl$_3$, 400 MHz): $\delta$=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, CH(CH$_3$)$_2$], 1.20 [d, 6H, $J$=6.8 Hz, CH(CH$_3$)$_2$] ppm.

$^{13}$C-NMR (CDCl$_3$, 100 MHz): $\delta$=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, CH(CH$_3$)$_2$], 18.1 [q, 2C, CH(CH$_3$)$_2$] ppm.

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

1-[5-(Benzylxy)-2-bromophenyl]-2-methylpropan-1-one (69b): GP-5 was carried out with the secondary alcohol 68b (800 mg, 2.39 mmol), dry CH$_2$Cl$_2$ (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$_2$Cl$_2$ 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$^{-1}$): $\nu_{max}$=2970, 2926, 2872, 2852, 1702, 1590, 1567, 1460, 1383, 1287, 1236, 1191, 1016, 988, 818, 737, 697 cm$^{-1}$. 

![Image of chemical structure]
**1H-NMR (CDCl₃, 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-CH₂O), 3.39 [sept, 1H, J=7.3 Hz, CH(CH₃)₂], 1.17 [d, 6H, J=7.3 Hz, CH(CH₃)₂] ppm.

**13C-NMR (CDCl₃, 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-CH₂O), 40.1 [d, CH(CH₃)₂], 18.1 [q, 2C, CH(CH₃)₂] ppm.

**HR-MS (ESI⁺):** m/z calculated for [C₁₇H₁₈BrO₂]⁺=[M+H]⁺: 333.0485; found 333.0481.

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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 CH₂Cl₂ (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 CH₂Cl₂ 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):** \( \nu_{max}=2969, 2929, 2872, 2851, 1701, 1591, 1569, 1464, 1392, 1289, 1201, 1161, 1022, 988, 825 \) cm⁻¹.

**1H-NMR (CDCl₃, 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-OCH₃), 3.30 [sept, 1H, J=6.8 Hz, CH(CH₃)₂], 1.18 [d, 6H, J=6.8 Hz, CH(CH₃)₂] ppm.

**13C-NMR (CDCl₃, 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-OCH₃), 40.0 [d, CH(CH₃)₂], 18.1 [q, 2C, CH(CH₃)₂] ppm.
HR-MS (ESI⁺): m/z calculated for [C₁₁H₁₄BrO₂]⁺=[M+H]⁺: 257.0172; found 257.0183.

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 CH₂Cl₂ (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 CH₂Cl₂ 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, Rₛ(68d)=0.40, Rₛ(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.

¹H-NMR (CDCl₃, 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, PhCH₂), 3.87 (s, 3H, Ar-OCH₃), 3.31 [sept, 1H, J=6.8 Hz, CH(CH₃)₂], 1.09 [d, 6H, J=6.8 Hz, CH(CH₃)₂] ppm.

¹³C-NMR (CDCl₃, 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-CH₂O), 56.2 (q, Ar-OCH₃), 39.3 [d, CH(CH₃)₂], 18.3 [q, 2C, CH(CH₃)₂] ppm.

HR-MS (ESI⁺): m/z calculated for [C₁₈H₂₀⁷⁹BrO₃]⁺=[M+H]⁺: 363.0590; found 363.0591, [C₁₈H₂₀⁸¹BrO₃]⁺=[M+H]⁺: 365.057; found 365.0569.
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 CH₂Cl₂ (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 CH₂Cl₂ furnished the product 69e (765 mg, 96%) as pale yellow viscous liquid. [TLC control (petroleum ether/ethyl acetate 90:10, Rₛ(68e)=0.25, Rₛ(69e)=0.45, UV detection)]

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

¹H-NMR (CDCl₃, 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, PhCH₂), 3.86 (s, 3H, Ar-OCH₃), 3.44 [sept, 1H, J=6.8 Hz, CH(CH₃)₂], 1.17 [d, 6H, J=6.8 Hz, CH(CH₃)₂] ppm.

¹³C-NMR (CDCl₃, 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-OCH₂), 56.3 (q, Ar-OCH₃), 39.5 [d, CH(CH₃)₂], 18.5 [q, 2C, CH(CH₃)₂] ppm.

HR-MS (ESI⁺): m/z calculated for [C₁₈H₁₉⁷⁹BrNaO₃]⁺=[M+Na]⁺: 385.0410; found 385.0416. [C₁₈H₁₉⁸¹BrNaO₃]⁺=[M+Na]⁺: 387.0389; found 387.0402.

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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 CH₂Cl₂ (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 CH₂Cl₂ furnished the product 69f (1.40 g, 95%) as pale yellow viscous oil. [TLC control (petroleum ether/ethyl acetate 90:10, Rₛ(68f)=0.45, Rₛ(69f)=0.60, UV detection)]

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

\(^1\)H-NMR (CDCl\(_3, 400\) MHz): \(\delta=6.99\) (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, CH(CH\(_3\))\(_2\)], 1.14 [d, 6H, \(J=6.8\) Hz, CH(CH\(_3\))\(_2\)] ppm.

\(^{13}\)C-NMR (CDCl\(_3, 100\) MHz): \(\delta=207.5\) (s, Ar-C=O), 149.6 (s, Ar-C), 147.2 (s, Ar-C), 134.9 (s, Ar-C), 113.5 (d, Ar-CH), 108.4 (d, Ar-CH), 102.2 (t, O-CH\(_2\)-O), 39.8 [d, CH(CH\(_3\))\(_2\)], 18.3 [q, 2C, CH(CH\(_3\))\(_2\)] 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.

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\(_2\)Cl\(_2\) (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\(_2\)Cl\(_2\) 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\(^{-1}\)): \(\nu_{\text{max}}=2969, 1694, 1593, 1504, 1461, 1439, 1372, 1333, 1254, 1201, 1175, 1156, 1050, 1025, 848, 789\) cm\(^{-1}\).

\(^1\)H-NMR (CDCl\(_3, 400\) MHz): \(\delta=7.04\) (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, CH(CH\(_3\))\(_2\)], 1.19 [d, 6H, \(J=6.9\) Hz, CH(CH\(_3\))\(_2\)] 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, CH(CH\(_3\))\(_2\)], 18.4 [q, 2C, CH(CH\(_3\))\(_2\)] ppm.
HR-MS (ESI⁺): m/z calculated for [C₁₂H₁₆⁷⁹BrO₃]⁺=[M+H]⁺: 287.0277; found 287.0282, [C₁₂H₁₆⁸¹BrO₃]⁺=[M+H]⁺: 289.0257; found 289.0266.

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 CH₂Cl₂ (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 CH₂Cl₂ furnished the product 69h (660 mg, 95%) as brown viscous liquid. [TLC control (petroleum ether/ethyl acetate 90:10, Rₜ(68h)=0.30, Rₜ(69h)=0.55, UV detection)]

IR (MIR-ATR, 4000–6000 cm⁻¹): vₘₐₓ=2968, 2930, 2851, 1696, 1593, 1562, 1482, 1463, 1384, 1327, 1243, 1201, 1164, 1126, 1107, 948, 838, 751 cm⁻¹.

¹H-NMR (CDCl₃, 400 MHz): δ=6.59 (s, 1H, Ar-H), 3.89 (s, 3H, Ar-OCH₃), 3.88 (s, 3H, Ar-OCH₃), 3.84 (s, 3H, Ar-OCH₃), 3.34 [sept, 1H, J=6.8 Hz, CH(CH₃)₂], 1.17 [d, 6H, J=6.8 Hz, CH(CH₃)₂] ppm.

¹³C-NMR (CDCl₃, 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-OCH₃), 61.0 (q, Ar-OCH₃), 56.2 (q, Ar-OCH₃), 40.1 [d, CH(CH₃)₂], 18.2 [q, 2C, CH(CH₃)₂] ppm.

HR-MS (ESI⁺): m/z calculated for [C₁₃H₁₈⁷⁹BrO₄]⁺=[M+H]⁺: 317.0383; found 317.0389, [C₁₃H₁₈⁸¹BrO₄]⁺=[M+H]⁺: 319.0363; found 319.0371.

(2-Bromophenyl)(cyclohexyl)methanone (81a): GP-5 was carried out with the secondary alcohol 80a (500 mg, 1.86 mmol), dry CH₂Cl₂ (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$_2$Cl$_2$ 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$^{-1}$): $v_{max}$=2929, 2853, 1698, 1587, 1448, 1428, 1243, 1205, 1026, 973, 762, 736 cm$^{-1}$.

$^1$H-NMR (CDCl$_3$, 400 MHz): $\delta$=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$_{16}$BrO]$^+$=[M+H]$^+$: 267.0379; found 267.0381, [C$_{13}$H$_{16}$BrO]$^+$=[M+H]$^+$: 269.0359; found 269.0372.

[5-(Benzyloxy)-2-bromophenyl](cyclohexyl)methanone (81b): GP-5 was carried out with the secondary alcohol 80b (900 mg, 2.40 mmol), dry CH$_2$Cl$_2$ (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$_2$Cl$_2$ 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$^{-1}$): $v_{max}$=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): $\delta$=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$_2$O), 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): \(\delta=207.6\) (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\(_2\)O), 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 \([C_{20}H_{22}^{79}\text{BrO}_{2}]^+=[\text{M+H}]^+\): 373.0798; found 373.0800, \([C_{20}H_{22}^{81}\text{BrO}_{2}]^+=[\text{M+H}]^+\): 375.0777; found 375.0782.

(2-Bromo-5-methoxyphenyl)(cyclohexyl)methanone (81c): GP-5 was carried out with the secondary alcohol 80c (500 mg, 1.67 mmol), dry CH\(_2\)Cl\(_2\) (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\(_2\)Cl\(_2\) 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\(^{-1}\)): \(\nu_{max}=2925, 2852, 1700, 1590, 1570, 1464, 1450, 1393, 1289, 1234, 1169, 1017, 982, 816, 772 \text{ cm}^{-1}\).

\(^1\)H-NMR (CDCl\(_3\), 400 MHz): \(\delta=7.43\) (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): \(\delta=207.8\) (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 \([C_{14}H_{18}\text{BrO}_{2}]^+=[\text{M+H}]^+\): 297.0485; found 297.0484.
[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$_2$Cl$_2$ (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$_2$Cl$_2$ 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$^{-1}$): $\nu_{max}=2926$, 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): $\delta=7.39$ (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): $\delta=206.4$ (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$_2$O), 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$_{24}$BrO$_3$]$^+=[M+H]$^+:403.0903; found 403.0902, [C$_{21}$H$_{24}$BrO$_3$]$^+_{81}$: 405.0883; found 405.0889.

[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$_2$Cl$_2$ (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 CH₂Cl₂ furnished the product **81e** (1.0 g, 96%) as red viscous liquid. [TLC control (petroleum ether/ethyl acetate 80:20, *R*<sub>f</sub>(80e)=0.40, *R*<sub>f</sub>(81e)=0.55, UV detection)]

**IR (MIR-ATR, 4000–600 cm<sup>-1</sup>):** *ν*<sub>max</sub>=2927, 2851, 1689, 1591, 1499, 1451, 1381, 1331, 1255, 1213, 1165, 1024, 997, 860 cm<sup>-1</sup>.

**<sup>1</sup>H-NMR (CDCl<sub>3</sub>, 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, PhCH₂), 3.86 (s, 3H, Ar-OCH₃), 3.15 (tt, 1H, *J*=11.2 and 3.4 Hz, ArCOCH), 1.90 (d, 2H, *J*=15.2 Hz, Cy-CH₂), 1.80–1.60 (m, 3H, Cy-CH₂), 1.50–1.00 (m, 5H, Cy-CH₂) ppm.

**<sup>1</sup>C-NMR (CDCl<sub>3</sub>, 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, PhCH₂), 56.2 (q, Ar-OCH₃), 49.6 (d, ArCOCH), 28.7 (t, 2C, Cy-CH₂), 25.8 (t, Cy-CH₂), 25.6 (t, 2C, Cy-CH₂) ppm.

**HR-MS (ESI<sup>+</sup>):** m/z calculated for [C<sub>21</sub>H<sub>24</sub>BrO₃]<sup>+</sup>[M+H]<sup>+</sup>:403.0903; found 403.0909, [C<sub>21</sub>H<sub>24</sub>BrO₃]<sup>+</sup>: 405.0883; found 405.0894.

(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 CH₂Cl₂ (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 CH₂Cl₂ furnished the product **81f** (707 mg, 95%) as yellow viscous liquid. [TLC control (petroleum ether/ethyl acetate 90:10, *R*<sub>f</sub>(80f)=0.4, *R*<sub>f</sub>(81f)=0.65, UV detection)]

**IR (MIR-ATR, 4000–600 cm<sup>-1</sup>):** *ν*<sub>max</sub>=2927, 2852, 1695, 1503, 1477, 1406, 1340, 1239, 1113, 1036, 996, 936 cm<sup>-1</sup>.
**1H-NMR (CDCl$_3$, 400 MHz):** $\delta=6.99$ (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.

**13C-NMR (CDCl$_3$, 100 MHz):** $\delta=206.8$ (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, ArCOCH], 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}$BrO$_3$]$^+$: 313.0262; found 313.0270.

(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$_2$Cl$_2$ (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$_2$Cl$_2$ 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$^{-1}$):** $\nu_{max}=2925, 2851, 1688, 1593, 1503, 1461, 1441, 1375, 1331, 1255, 1213, 1164, 1027, 768$ cm$^{-1}$.

**1H-NMR (CDCl$_3$, 400 MHz):** $\delta=7.00$ (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.

**13C-NMR (CDCl$_3$, 100 MHz):** $\delta=207.0$ (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 [C₁₅H₂₀⁷⁹BrO₃]⁺=[M+H]⁺:327.0590; found 327.0592.

(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 CH₂Cl₂ (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 CH₂Cl₂ furnished the product 81h (457 mg, 92%) as pale yellow viscous liquid. [TLC control (petroleum ether/ethyl acetate 85:15, Rᶠ(80h)=0.40, Rᶠ(81h)=0.50, UV detection)]

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

¹H-NMR (CDCl₃, 400 MHz): δ=6.61 (s, 1H, Ar-H), 3.91 (s, 6H, 2 × Ar-OCH₃), 3.87 (s, 3H, Ar-OCH₃), 3.07 (tt, 1H, J=11.2 and 3.4 Hz, ArCOCH), 2.10–1.10 (m, 10H, Cy-H) ppm.

¹³C NMR (CDCl₃, 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-OCH₃), 60.9 (q, Ar-OCH₃), 56.1 (q, Ar-OCH₃), 49.8 (d, Cy-CH), 28.4 (t, 2C, Cy-CH₂), 25.7 (t, Cy-CH₂), 25.5 (t, 2C, Cy-CH₂) ppm.

HR-MS (ESI⁺): m/z calculated for [C₁₆H₂₂BrO₄]⁺=[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-bromoaisopropylketone/ortho-bromocyclohexylketone 69/81 (100 mg, 0.27 to 0.44 mmol), Pd(OAc)₂ (4 mol%), Xantphos (4 mol%) and K₂CO₃ (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 NH₄Cl and the aqueous layer was extracted with ethyl acetate (3 × 20 mL). The combined organic layers were dried over anhydrous Na₂SO₄, 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%).

1-(2'-Isobutryl-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), K₂CO₃ (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 Rₓ(69a)=0.60, Rₓ(70a)=0.45 (petroleum ether/ethyl acetate 90:10, UV detection)]

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

¹H-NMR (CDCl₃, 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=CH₃H₆], 5.74 [s, 1H, (CO)C=CH₃H₆], 2.85 [sept, 1H, J=6.8 Hz, CH(CH₃)₂], 1.84 [s, 3H, H₃C(CO)C=CH₂], 0.94 [br. s, 6H, CH(CH₃)₂] ppm.
$^1$C-NMR (CDCl$_3$, 100 MHz): $\delta$=210.5 (s, Ar-CO), 199.7 (s, Ar-CO), 145.1 [s, H$_3$(CO)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$_3$(CO)C=CH$_2$], 129.0 (d, Ar-CH), 128.3 (d, Ar-CH), 127.5 (d, Ar-CH), 126.9 (d, Ar-CH), 38.9 [d, C$_3$(CH$_3$)$_2$], 17.4 [3 $\times$ q, 3C, CH(CH$_3$)$_a$(CH$_3$)$_b$, CH(CH$_3$)$_a$(CH$_3$)$_b$ and H$_3$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.

IR (MIR-ATR, 4000–600 cm$^{-1}$): $\nu_{max}$=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): $\delta$=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=CH$_a$(H$_b$)], 5.70 [s, 1H, (CO)C=CH$_a$(H$_b$)], 5.09 (s, 2H, Ph-CH$_2$O), 5.06 (s, 2H, Ph-CH$_2$O), 2.78 [sept, 1H, $J$=6.8 Hz, CH(CH$_3$)$_2$], 1.84 [s, 3H, H$_3$C(CO)C=CH$_2$], 0.92 [br. s, 6H, CH(CH$_3$)$_2$] ppm.

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$_2$CO$_3$ (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)]
\(^{13}\)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\(_3\)C(CO)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\(_3\)C(CO)C=CH\(_2\)], 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), 70.1 (t, Ph-CH\(_2\)O), 70.0 (t, Ph-CH\(_2\)O), 39.1 [d, CH(CH\(_3\))\(_2\)], 17.4 [3\(\times\)q, 3C, CH(CH\(_3\))\(_3\)a(CH\(_3\))\(_b\), CH(CH\(_3\))\(_a\)(CH\(_3\))\(_b\) and H\(_3\)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.

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\(_2\)CO\(_3\) (215 mg, 1.76 mmol) and dry toluene (2 mL) at 100 \(^\circ\)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\(^{-1}\)):** \(\nu_{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): \(\delta=7.05–6.90\) (m, 5H, Ar-H), 6.87 (dd, 1H, \(J=8.3\) and 2.9 Hz, Ar-H), 5.83 [s, 1H, (CO)C=CH\(_4\)H\(_8\)], 5.71 [s, 1H, (CO)C=CH\(_4\)H\(_8\)], 3.82 (s, 3H, Ar-OCH\(_3\)), 3.80 (s, 3H, Ar-OCH\(_3\)), 2.77 [sept, 1H, \(J=6.8\) Hz, CH(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): $\delta=210.9$ (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.

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$_2$CO$_3$ (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$^{-1}$): $\nu_{max}=2966, 1678, 1653, 1596, 1501, 1455, 1441, 1368, 1329, 1253, 1208, 1154, 1128, 1025, 908, 725, 695 cm$^{-1}.$

$^1H$-NMR (CDCl$_3$, 400 MHz): $\delta=7.42$ (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$_a$H$_b$), 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, CH(CH$_3$)$_2$], 1.79 [s, 3H, H$_3$C(CO)C=CH$_2$], 0.92 [br. s, 3H, CH(CH$_3$)$_3$(CH$_3$)$_b$], 0.89 [br. s, 3H, CH(CH$_3$)$_3$(CH$_3$)$_b$] ppm.

$^{13}$C-NMR (CDCl$_3$, 100 MHz): $\delta$=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=CH$_2$], 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, CH(CH$_3$)$_2$], 19.5 [q, CH(CH$_3$)$_3$(CH$_3$)$_b$], 18.1 [q, CH(CH$_3$)$_3$(CH$_3$)$_b$], 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.

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\(^{-1}\)): \(\nu_{\text{max}}\)=2957, 2922, 2852, 1680, 1655, 1596, 1559, 1502, 1454, 1441, 1367, 1329, 1254, 1209, 1155, 1129, 1025, 870, 748, 697 cm\(^{-1}\).

\(^1\)H-NMR (CDCl\(_3\), 400 MHz): \(\delta=7.43\) (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\(_a\)H\(_b\)], 5.50 [s, 1H, (CO)C=CH\(_a\)H\(_b\)], 5.16 (s, 4H, Ph-CH\(_2\)O), 3.84 (s, 3H, Ar-OCH\(_3\)), 3.80 (s, 3H, Ar-OCH\(_3\)), 2.73 [sept, 1H, \(J=6.8\) Hz, CH(CH\(_3\))\(_2\)], 1.79 [s, 3H, H\(_3\)C(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): \(\delta=209.1\) (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\(_3\)C(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\(_3\)C(CO)C=CH\(_2\)], 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\(_2\)O), 71.0 (t, Ph-CH\(_2\)O), 56.0 (q, Ar-OCH\(_3\)), 55.9 (q, Ar-OCH\(_3\)), 38.6 [d, CH(CH\(_3\))\(_2\)], 19.6 [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\(_{36}\)H\(_{36}\)NaO\(_6\)]\(^+\)=[M+Na]\(^+\): 587.2404; found 587.2413.

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\(_2\)CO\(_3\) (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\(^{-1}\))**: \(\nu_{max}=2961, 2921, 2852, 1681, 1656, 1612, 1504, 1475, 1382, 1347, 1237, 1116, 1075, 1036, 1016, 932, 873, 733\) cm\(^{-1}\).

\(^1\)H-NMR (CDCl\(_3\), 400 MHz): \(\delta=7.00\) (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\(_2\), 5.63 (s, 1H, (CO)C=CH\(_2\)), 2.83 (sept, 1H, \(J=6.8\) Hz, CH(CH\(_3\))\(_2\)), 1.82 (s, 3H, H\(_3\)C(CO)C=CH\(_2\)), 1.00 (d, 3H, \(J=6.8\) Hz, CH(CH\(_3\))\(_2\)), 0.90 (d, 3H, \(J=6.8\) Hz, CH(CH\(_3\))\(_2\)) ppm.

\(^{13}\)C-NMR (CDCl\(_3\), 100 MHz): \(\delta=208.1\) (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\(_3\)C(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\(_3\)C(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\(_3\))\(_2\)), 18.3 (q, CH(CH\(_3\))\(_2\)), 17.6 (q, H\(_3\)C(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.

<Chemistry image>

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\(_2\)CO\(_3\) (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\(^{-1}\))**: \(\nu_{\text{max}}=2964, 1677, 1597, 1560, 1503, 1462, 1440, 1371, 1330, 1252, 1201, 1155, 1127, 1052, 1024, 916, 871, 729 \text{ cm}^{-1}\).

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

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

**HR-MS (ESI\(^+\))**: m/z calculated for \([\text{C}_{24}\text{H}_{28}\text{NaO}_{6}]^{+}=\text{[M+Na]}^{+}\): 435.1778; found 435.1784.

![Chemical Structure](image.png)

1-(6'-Isobutylryl-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 starting 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\(^{-1}\))**: \( v_{\text{max}}=2954, 2922, 2851, 1684, 1589, 1482, 1462, 1381, 1343, 1317, 1161, 1132, 1104, 1005 \text{ cm}^{-1} \).

\(^1\text{H-NMR (CDCl}_3, 400 \text{ MHz)}\): \( \delta=6.93 \text{ (s, 1H, Ar-H), 6.82 \text{ (s, 1H, Ar-H), 5.71 \text{ (s, 1H, C=CH}_a\text{H}_b), 5.64 \text{ (s, 1H, C=CH}_a\text{H}_b), 3.90 \text{ (s, 3H, Ar-OCH}_3\text{), 3.89 \text{ (s, 3H, Ar-OCH}_3\text{), 3.88 \text{ (s, 3H, Ar-OCH}_3\text{), 3.87 \text{ (s, 3H, Ar-OCH}_3\text{), 3.62 \text{ (s, 6H, 2 x Ar-OCH}_3\text{), 2.91 [sept, 1H, J=6.8 Hz, CH(CH}_3\text{)\textsubscript{2}]), 1.79 [s, 3H, H}_3\text{C(CO)C=CH}_2\text{], 0.98 [d, 3H, J=6.8 Hz, CH(CH}_3\text{)\textsubscript{a}(CH}_3\text{)\textsubscript{b}], 0.90 [d, 3H, J=6.8 Hz, CH(CH}_3\text{)\textsubscript{a}(CH}_3\text{)\textsubscript{b}], ppm.}}

\(^{13}\text{C-NMR (CDCl}_3, 100 \text{ MHz)}\): \( \delta=207.3 \text{ (s, ArCO), 197.8 \text{ (s, ArCO), 151.5 \text{ (s, Ar-C), 151.4 \text{ (s, Ar-C), 144.3 \text{ [s, H}_3\text{C(CO)C=CH}_2\text{], 144.0 \text{ (s, Ar-C), 143.9 \text{ (s, Ar-C), 134.7 \text{ (s, Ar-C), 134.3 \text{ (s, Ar-C), 128.6 \text{ (s, Ar-C), 127.9 [t, H}_3\text{C(CO)C=CH}_2\text{], 127.4 (s, Ar-C), 123.4 \text{ (s, Ar-C), 122.6 (s, Ar-C), 108.6 (d, Ar-CH), 107.5 (d, Ar-CH), 60.8 (q, Ar-OCH}_3\text{), 60.7 (q, Ar-OCH}_3\text{), 60.4 (q, Ar-OCH}_3\text{), 60.2 (q, Ar-OCH}_3\text{), 56.1 (q, Ar-OCH}_3\text{), 56.0 (q, Ar-OCH}_3\text{), 37.9 [d, CH(CH}_3\text{)\textsubscript{2}]), 19.2 [q, CH(CH}_3\text{)\textsubscript{a}(CH}_3\text{)\textsubscript{b}], 19.0 [q, CH(CH}_3\text{)\textsubscript{a}(CH}_3\text{)\textsubscript{b}], 17.9 [q, H}_3\text{C(CO)C=CH}_2\text{] ppm.}}

**HR-MS (ESI\(^+\))**: m/z calculated for [C\(_{26}\)H\(_{33}\)O\(_8\)]\(^+\)=[M+H]\(^+\)\,: 473.2170; found 473.2171.

\[ \text{Cyclohex-1-en-1-yl(2'-}(\text{cyclohexanecarbonyl})-[1,1'-\text{biphenyl}]\text{-2-yl)methanone (82a): GP-6 was carried out with ortho-bromocyclohexylketone 81a (100 mg, 0.37 mmol), Pd(OAc)}_2 \text{ (3.4 mg, 0.015 mmol), Xantphos (8.7 mg, 0.015 mmol), K}_2\text{CO}_3 \text{ (207 mg, 1.48 mmol) and dry toluene (2 mL) at 100 °C for 16 h. Purification of the residue} \]
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$^{-1}$):** $\nu_{max}=2926, 2853, 1685, 1448, 1378, 1283, 1244, 1204, 1135, 973, 773, 750$ cm$^{-1}$.

$^1$H-NMR (CDCl$_3$, 400 MHz): $\delta=7.50$ (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$_2$C(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): $\delta=209.0$ (s, Ar-CO), 199.3 (s, Ar-CO), 145.5 [d, H$_2$C(CO)C=CH], 140.0 [s, H$_2$C(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.

(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$_2$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 95:05 to 90:10) furnished the product 82b (61 mg, 78%), as pale yellow viscous liquid. [TLC control $R_f(\text{81b})=0.75$, $R_f(\text{82b})=0.45$ (petroleum ether/ethyl acetate 90:10, UV detection)]

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

$^{1}$$H$-NMR (CDCl$_3$, 400 MHz): $\delta=7.55–7.28$ (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), 5.10 (s, 2H, Ph-CH$_2$O), 2.49 [tt, 1H, $J=11.2$ and 3.4 Hz, cy-H], 2.14 [br. s, 2H, cy-H], 2.03 [m, 2H, cy-H], 1.80–0.6 (m, 14H, Cy-H) ppm.

$^{13}$$C$-NMR (CDCl$_3$, 100 MHz): $\delta=209.3$ (s, Ar-CO), 199.0 (s, Ar-CO), 157.6 (s, 2C, Ar-C), 157.4 (s, Ar-C), 145.6 (d, Cy=CH), 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 $\times$ PhCH$_2$), 49.0 (d, Cy-CH$_3$), 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.

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$_2$CO$_3$ (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$^{-1}$):** $\nu_{max}=2927, 2852, 1684, 1650, 1602, 1475, 1449, 1406, 1312, 1286, 1222, 1168, 1042, 981, 819, 733$ cm$^{-1}$.

**$^1$H-NMR (CDCl$_3$, 400 MHz):** $\delta=7.02$ (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):** $\delta=209.5$ (s, Ar-CO), 199.1 (s, Ar-CO), 158.5 (s, Ar-C), 158.3 (s, Ar-C), 145.5 [d, H$_2$(CO)C=CH], 140.8 [s, H$_2$(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.

![Structure of 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$_2$CO$_3$ (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$^{-1}$):** $\nu_{max}$=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):** $\delta$=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$_2$O), 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):** $\delta$=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=CH), 139.9 (s, CyC=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$_2$O), 71.1 (t, Ph-CH$_2$O), 56.1 (q, Ar-OCH$_3$), 56.0 (q, Ar-OCH$_3$), 48.7 (d, ArCOCH), 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.
(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$_2$CO$_3$ (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$^{-1}$): $v_{max}$=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): $\delta$=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$_2$O), 5.04 (s, 2H, Ph-CH$_2$O), 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): $\delta$=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=CH), 139.9 (s, CyC=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$_2$O), 70.8 (t, Ph-CH$_2$O), 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-CH₂), 25.7 (t, 2C, 2 × Cy-CH₂), 23.3 (t, Cy-CH₂), 21.8 (t, Cy-CH₂), 21.5 (t, Cy-CH₂) ppm.

HR-MS (ESI⁺): m/z calculated for [C₄₂H₄₅O₆]⁺=[M+H]⁺: 645.3211; found 645.3210.

Cyclohex-1-en-1-yl(6’-(cyclohexanecarbonyl)-[5,5’-bibenzo[d][1,3]dioxol]-6-yl)methanone (82f): GP-6 was 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), K₂CO₃ (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 Rf(81f)=0.80, Rf(82f)=0.45 (petroleum ether/ethyl acetate 85:15, UV detection)]

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

¹H-NMR (CDCl₃, 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-CH₂-O), 5.98 (s, 2H, O-CH₂-O), 2.52 (tt, 1H, J=11.2 and 3.4 Hz, ArCOCH), 2.30–0.50 (m, 18H, CyH) ppm.

¹³C-NMR (CDCl₃, 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=CH), 139.8 (s, CyC=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, OCH₂O), 101.6
(t, OCH2O), 48.6 (d, ArCOCH), 29.6 (t, Cy-CH2), 29.5 (t, Cy-CH2), 28.8 (t, Cy-CH2), 25.9 (t, Cy-CH2), 25.8 (t, Cy-CH2), 25.7 (t, Cy-CH2), 23.3 (t, Cy-CH2), 21.8 (t, Cy-CH2), 21.5 (t, Cy-CH2) ppm.

HR-MS (ESI⁺): m/z calculated for [C28H28NaO6]⁺=[M+Na]⁺: 483.1778; found 483.1783.

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), K₂CO₃ (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 Rf(81g)=0.85, Rf(82g)=0.50 (petroleum ether/ethyl acetate 70:30, UV detection)

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

¹H-NMR (CDCl₃, 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-OCH₃), 3.90 (s, 3H, Ar-OCH₃), 3.85 (s, 3H, Ar-OCH₃), 3.82 (s, 3H, Ar-OCH₃), 2.40 (tt, 1H, J=11.2 and 3.4 Hz, ArCOCH), 2.30–0.50 (m, 18H, CyH) ppm.

¹³C-NMR (CDCl₃, 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=CH), 140.2 (s, CyC=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-OCH₃), 56.0 (q, Ar-OCH₃), 55.9 (q, Ar-OCH₃), 48.9 (d, ArCOCH), 29.7 (t, Cy-CH₂), 29.1 (t, Cy-CH₂), 26.0 (t, Cy-CH₂), 25.8 (t, Cy-CH₂), 25.7 (t, Cy-CH₂), 25.6 (t, Cy-CH₂), 23.4 (t, Cy-CH₂), 21.8 (t, Cy-CH₂), 21.5 (t, Cy-CH₂) ppm.

**HR-MS (ESI⁺):** m/z calculated for [C₃₀H₃₇O₆]⁺=[M+H]⁺: 493.2585; found 493.2587.

![Chemical Structure](image)

**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), K₂CO₃ (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, Rf(81h)=0.60, Rf(82h)=0.35, UV detection)]

**IR (MIR-ATR, 4000–600 cm⁻¹):** νmax=2927, 2852, 1679, 1648, 1587, 1481, 1459, 1406, 1385, 1326, 1123, 1102, 997, 731 cm⁻¹.

**¹H-NMR (CDCl₃, 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-OCH₃), 3.89 (s, 3H, Ar-OCH₃), 3.88 (s, 6H, 2 × Ar-OCH₃), 3.67 (s, 3H, Ar-OCH₃), 3.66 (s, 3H, Ar-OCH₃), 2.55 (tt, 1H, J=11.2 and 3.4 Hz, ArCOCH), 2.15–1.00 (m, 18H, Cy-H) ppm.

**¹³C-NMR (CDCl₃, 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=CH], 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-OCH₃), 60.6 (q, Ar-OCH₃), 60.4 (q, Ar-OCH₃), 60.3 (q, Ar-OCH₃), 56.1 (q, Ar-OCH₃), 56.0 (q, Ar-OCH₃), 48.3 (d, Cy-CH), 29.7 (t, Cy-CH₂), 29.6 (t, Cy-CH₂), 26.1 (t, Cy-CH₂), 26.0 (t, Cy-CH₂), 25.9 (t, Cy-CH₂), 25.8 (t, Cy-CH₂), 23.4 (t, Cy-CH₂), 21.9 (t, Cy-CH₂), 21.6 (t, Cy-CH₂) ppm.

**HR-MS (ESI⁺):** m/z calculated for [C₃₂H₄₁O₈]⁺=[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

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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.\textsuperscript{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,\textsuperscript{45} Stille,\textsuperscript{46} Suzuki,\textsuperscript{47} Sonogashira,\textsuperscript{48} Buckwald-Hartwig,\textsuperscript{49} Mizoroki-Heck\textsuperscript{50} and Jeffery-Heck.\textsuperscript{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.

\textbf{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\textsubscript{3} with diphenyl-mercury, which upon reacting with ethylene gas \textbf{1} gave the styrene product \textbf{2a} (Scheme II.1).\textsuperscript{52}

\begin{equation}
\text{H}_2\text{C} = \text{CH}_2 \xrightarrow{\text{LiPdCl}_3 + \text{Ph}_2\text{Hg}} \text{CH}_3\text{CN, rt}} \textbf{2a} (63\%)
\end{equation}

\textbf{Scheme II.1}

Subsequently, in the same year (1968), coupling of phenyl-mercury salt \textbf{3} with allylic alcohol \textbf{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 \textbf{7} as the end product, albeit in poor yield (Scheme II.2).\textsuperscript{53}
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).

$$\text{Scheme II.3}$$

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$_3$N (Scheme II.4).

$$\text{Scheme II.4}$$

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.

**by Heck et al.**

\[ \text{5a} + \text{4} \rightarrow \text{7} \text{ (84\%)} \]

**Scheme II.5**

**by Chalk et al.**

\[ \text{5a} + \text{4} \rightarrow \text{7} \text{ (23\%)} \]

**Scheme II.6**

Muzart and co-workers had also demonstrated an approach for the synthesis of \( \beta \)-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.\(^{58}\)

\[ \text{5a} + \text{4} \rightarrow \text{7} \text{ (80-120 \degree C)} \]

**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).\(^{59}\)
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).\(^{51}\)

Jeffery used stoichiometric amount of phase transfer reagent \(n\)-Bu\(_4\)NCl 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).\(^{61}\)
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 Ag₂CO₃) 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
S-K Kang et al. reported the cross coupling between iodobenzene 5a and allylic diols 4 using Pd(OAc)$_2$/n-Bu$_3$P as the catalytic system. When Et$_3$N was used as a base, furnished phenyl-substituted hydroxy ketone 7, whereas, the reaction with K$_2$CO$_3$, 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).

![Scheme II.13](image)

![Scheme II.14](image)

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).  

Scheme II.15

Thus, the synthetic study was initiated with the bromination of benzaldehydes under reported conditions. 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.

Table II.1: Synthesis of ortho-bromo aryl allylic alcohols 4h-4o from 2-bromo benzaldehydes 5h-5o.
Reaction conditions: \textsuperscript{a}All the reactions carried out with 2-bromobenzaldehydes 5h-5o 10 mmol, 0.5 M in THF. \textsuperscript{b}Isolated yields of chromatographically pure products.

Figure II.1.1: \textsuperscript{1}H-NMR (400 MHz) spectrum of 4n in CDCl\textsubscript{3}

Figure II.1.2: \textsuperscript{13}C-NMR (100 MHz) spectrum of 4n in CDCl\textsubscript{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 \(\delta\) 6.99 and 6.96 was due to two aromatic protons, the presence of doublet of a doublet of doublets at \(\delta\) 5.96 having \(J=15.6\), 10.3 and 5.4 Hz was due to olefinic methine group proton, the presence of doublet at \(\delta\) 5.50 having \(J=5.4\) Hz was due to CHOH group proton, the presence of doublet at \(\delta\) 5.35 having coupling constant \(J_{\text{trans}}=15.6\) Hz and one more doublet at \(\delta\) 5.18 having coupling constant \(J_{\text{cis}}=10.8\) Hz were due to olefinic methylene group two protons, \(\delta\) 3.84 due to methoxy group three protons, \(\delta\) 3.83 due to methoxy group three protons and the presence of broad singlet at \(\delta\) 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 \(\delta\) 148.8, 148.7, 133.5 and 112.3 due to four aromatic carbons, three methine carbons at \(\delta\) 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 \(\delta\) 115.2, the presence of \(\delta\) 73.3 ppm was due to CHOH group carbon, the presence of \(\delta\) 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 \([\text{C}_{11}\text{H}_{13}\text{BrNaO}_3]\)^+=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 \textit{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 \textit{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 \(\beta\)-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)\(_3\)NCl as phase transfer reagent as an additive, in DMF as solvent at 50 °C, gave the \(\beta\)-aryl allylic alcohol 6hb in fair yield (67%, Table II.2, entry 1). Replacing Bn(Et)\(_3\)NCl with TBAI, the desired product 6hb was obtained in poor yield (33%, Table II.2, entry 2). While changing the base to K\(_2\)CO\(_3\) 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\(_2\)CO\(_3\)/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\(_2\)CO\(_3\)/K\(_2\)CO\(_3\) in the presence of Bn(Et)\(_3\)NCl in CH\(_3\)CN, 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\(_2\)CO\(_3\) with TBAI in CH\(_3\)CN 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)\(_3\)NCl in solvent CH\(_3\)CN (80%, Table II.2, entry 12).
**Table II.2:** Optimization table for the synthesis of β-aryl allylic alcohol 6hb.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Base</th>
<th>Salt</th>
<th>Solvent</th>
<th>Yield of 6hb (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>NaHCO₃</td>
<td>Bn(Et)₃NCl</td>
<td>DMF</td>
<td>67</td>
</tr>
<tr>
<td>2.</td>
<td>NaHCO₃</td>
<td>TBAI</td>
<td>DMF</td>
<td>33</td>
</tr>
<tr>
<td>3.</td>
<td>K₂CO₃</td>
<td>TBAI</td>
<td>DMF</td>
<td>51</td>
</tr>
<tr>
<td>4.</td>
<td>NaHCO₃</td>
<td>TBAI</td>
<td>toluene</td>
<td>33</td>
</tr>
<tr>
<td>5.</td>
<td>K₂CO₃</td>
<td>TBABr</td>
<td>toluene</td>
<td>50</td>
</tr>
<tr>
<td>6.</td>
<td>NaHCO₃</td>
<td>Bn(Et)₃NCl</td>
<td>toluene</td>
<td>55</td>
</tr>
<tr>
<td>7.</td>
<td>NaHCO₃</td>
<td>TBAI</td>
<td>acetonitrile</td>
<td>39</td>
</tr>
<tr>
<td>8.</td>
<td>NaHCO₃</td>
<td>TBABr</td>
<td>acetonitrile</td>
<td>30</td>
</tr>
<tr>
<td>9.</td>
<td>Cs₂CO₃</td>
<td>Bn(Et)₃NCl</td>
<td>acetonitrile</td>
<td>70</td>
</tr>
<tr>
<td>10.</td>
<td>K₂CO₃</td>
<td>Bn(Et)₃NCl</td>
<td>acetonitrile</td>
<td>67</td>
</tr>
<tr>
<td>11.</td>
<td>Cs₂CO₃</td>
<td>TBAI</td>
<td>acetonitrile</td>
<td>51</td>
</tr>
<tr>
<td>12.</td>
<td>NaHCO₃</td>
<td>Bn(Et)₃NCl</td>
<td>acetonitrile</td>
<td>80</td>
</tr>
</tbody>
</table>

*All reactions were carried out with Pd(OAc)₂ (5 mol%), NaHCO₃ (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. 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
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 \(J_{\text{trans}}=16.1\) Hz was due to olefinic methine group, the presence of doublet of a doublet at δ 6.32 having \(J_{\text{trans}}=16.1\) 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 CHO\(_2\) 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.

![Reaction Scheme]

<table>
<thead>
<tr>
<th>Entry</th>
<th>β-aryl allylic alcohol-6</th>
<th>Yield (%)</th>
<th>Entry</th>
<th>β-aryl allylic alcohol-6</th>
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*Reaction conditions: All the reactions carried out with allylic alcohol 4h-4o (60-100 mg, 0.20 to 0.47 mmol), in CH₃CN. *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 resonate 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.$^{a,b}$

![Chemical structure](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>β-arylallylic alcohol</th>
<th>Yield (%)$^b$</th>
<th>Entry</th>
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<td>μw (77)</td>
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$^a$Reaction conditions: All the reactions were carried out with allylic alcohols 4h-4o (100 mg, 0.33 to 0.56 mmol), in CH$_3$CN. $^b$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 \(J_{\text{trans}}=15.8\) 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 \(J_{\text{trans}}=15.8\) 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 \([\text{C}_{18}\text{H}_{18}\text{Br}_2\text{NaO}_4]\)^+ = 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 \(J_{\text{trans}}=15.0\) 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 vinylmagnesium 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.

![Chemical structure](image)

<table>
<thead>
<tr>
<th>Entry(^a)</th>
<th>aldehyde (5)</th>
<th>aryl allylic alcohol (4)</th>
<th>Yield(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td><img src="image" alt="Chemical structure" /></td>
<td><img src="image" alt="Chemical structure" /></td>
<td>90%</td>
</tr>
<tr>
<td>2.</td>
<td><img src="image" alt="Chemical structure" /></td>
<td><img src="image" alt="Chemical structure" /></td>
<td>95%</td>
</tr>
</tbody>
</table>

\(^a\)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.

![Diagram of reaction](image)

<table>
<thead>
<tr>
<th>Entry(^a)</th>
<th>β-aryl allylic alcohol</th>
<th>Yield (%)(^b)</th>
<th>β-aryl carbonyl compound</th>
<th>Yield (%)(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td><img src="image" alt="Image of 6pa" /></td>
<td>Δ (61) (\mu)w (65)</td>
<td><img src="image" alt="Image of 7pa" /></td>
<td>Δ (27) (\mu)w (29)</td>
</tr>
<tr>
<td>2.</td>
<td><img src="image" alt="Image of 6pb" /></td>
<td>Δ (62) (\mu)w (59)</td>
<td><img src="image" alt="Image of 7pb" /></td>
<td>Δ (23) (\mu)w (26)</td>
</tr>
<tr>
<td>3.</td>
<td><img src="image" alt="Image of 6pe" /></td>
<td>Δ (65) (\mu)w (61)</td>
<td><img src="image" alt="Image of 7pe" /></td>
<td>Δ (25) (\mu)w (23)</td>
</tr>
<tr>
<td>4.</td>
<td><img src="image" alt="Image of 6pf" /></td>
<td>Δ (32) (\mu)w (36)</td>
<td><img src="image" alt="Image of 7pf" /></td>
<td>Δ (15) (\mu)w (18)</td>
</tr>
<tr>
<td>5.</td>
<td><img src="image" alt="Image of 6ph" /></td>
<td>Δ (63) (\mu)w (59)</td>
<td><img src="image" alt="Image of 7ph" /></td>
<td>Δ (15) (\mu)w (17)</td>
</tr>
</tbody>
</table>

\(^a\)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\(_3\)CN. \(^b\)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$_3$

![1H-NMR spectrum of 6pe in CDCl$_3$](image)

Figure II.5.2: $^{13}$C-NMR (100 MHz) spectrum of 6pe in CDCl$_3$

![13C-NMR spectrum of 6pe in CDCl$_3$](image)

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 [C₁₆H₁₄BrNaO₂]⁺ = 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 ¹H-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 Jₜₐₓₚₖₜₜ=15.8 Hz was due to olefinic methine group proton, doublet of a doublet at δ 6.24 having Jₜₐₓₚₖₜₜ=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 ¹³C-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 [C₁₆H₁₅BrNaO]⁺ = 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.

![Chemical structure](image)

<table>
<thead>
<tr>
<th>Entry&lt;sup&gt;a&lt;/sup&gt;</th>
<th>β-aryl allylic alcohol</th>
<th>Yield (%)&lt;sup&gt;b&lt;/sup&gt;</th>
<th>β-aryl carbonyl compound</th>
<th>Yield (%)&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>6qa</td>
<td>Δ (46) µw (50)</td>
<td>7qa</td>
<td>Δ (24) µw (27)</td>
</tr>
<tr>
<td>2.</td>
<td>6qb</td>
<td>Δ (58) µw (55)</td>
<td>7qb</td>
<td>Δ (29) µw (31)</td>
</tr>
<tr>
<td>3.</td>
<td>6qc</td>
<td>Δ (49) µw (51)</td>
<td>7qc</td>
<td>Δ (30) µw (27)</td>
</tr>
<tr>
<td>4.</td>
<td>6qe</td>
<td>Δ (63) µw (60)</td>
<td>7qe</td>
<td>Δ (14) µw (16)</td>
</tr>
<tr>
<td>5.</td>
<td>6qf</td>
<td>Δ (49) µw (53)</td>
<td>7qf</td>
<td>Δ (30) µw (26)</td>
</tr>
</tbody>
</table>

<sup>a</sup>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 CH₃CN.  
<sup>b</sup>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 13C-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 [C16H15BrNaO]+=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 C1-C2 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 C₁-C₂ bond could be confined in both intermediates 9a and 9b, respectively. However, to the direction of minimal eclipsed interaction, the rotation of 120° around C₂-C₃ 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).
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 benzoepines 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 benzoepine 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](image)

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 NaBH₄ 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 CDCl₃ 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 (BF₃·Et₂O) at 0 °C and as well as at −10 °C led to the decomposition of the product (Table II.8, entries 1 and 2). Therefore, further decreasing the temperature to −20 °C the product 11hj was furnished in poor yield (30%, Table II.8, entry 3). Interestingly, further decrease of temperature (−40 °C), 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 (AlCl₃) resulted the product 11hj in moderate to very good yield (Table II.8, entries 5-7), whereas the reaction with H₂SO₄, 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.
<table>
<thead>
<tr>
<th>Entry&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Acid (equiv)</th>
<th>Solvent (5 mL)</th>
<th>Temp (°C)</th>
<th>Time Min.</th>
<th>Yield of 11hj (%)&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>BF&lt;sub&gt;3&lt;/sub&gt;.Et&lt;sub&gt;2&lt;/sub&gt;O (2.0)</td>
<td>DCM</td>
<td>0</td>
<td>15</td>
<td>-</td>
</tr>
<tr>
<td>2.</td>
<td>BF&lt;sub&gt;3&lt;/sub&gt;.Et&lt;sub&gt;2&lt;/sub&gt;O (4.0)</td>
<td>DCM</td>
<td>−10</td>
<td>15</td>
<td>-</td>
</tr>
<tr>
<td>3.</td>
<td>BF&lt;sub&gt;3&lt;/sub&gt;.Et&lt;sub&gt;2&lt;/sub&gt;O (5.0)</td>
<td>DCM</td>
<td>−20</td>
<td>15</td>
<td>30</td>
</tr>
<tr>
<td>4.</td>
<td>BF&lt;sub&gt;3&lt;/sub&gt;.Et&lt;sub&gt;2&lt;/sub&gt;O (5.0)</td>
<td>DCM</td>
<td>−40</td>
<td>120</td>
<td>95</td>
</tr>
<tr>
<td>5.</td>
<td>p-TSA (3.0)</td>
<td>DCM</td>
<td>−40</td>
<td>60</td>
<td>50</td>
</tr>
<tr>
<td>6.</td>
<td>AlCl&lt;sub&gt;3&lt;/sub&gt; (1.2)</td>
<td>DCM</td>
<td>−40</td>
<td>10</td>
<td>70</td>
</tr>
<tr>
<td>7.</td>
<td>AlCl&lt;sub&gt;3&lt;/sub&gt; (1.2)</td>
<td>DCE</td>
<td>−40</td>
<td>10</td>
<td>80</td>
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<tr>
<td>8.</td>
<td>H&lt;sub&gt;2&lt;/sub&gt;SO&lt;sub&gt;4&lt;/sub&gt; (3.0)</td>
<td>DCM</td>
<td>−40</td>
<td>30</td>
<td>20</td>
</tr>
</tbody>
</table>

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

Oxygen containing heterocyclic compounds are widely assayed for their substantial therapeutic applications. They are pervasive structural elements in biologically relevant small molecules (Figure II 1.9). 3-Deoxyisochracinic acid 13 was isolated from cladosporium species shows antibacterial activity by inhibiting the growth of Bacillus subtilis. The cyclic ether pestacin 14 was obtained from microorganism pestalotipsis microspore and shows antifungal, antimycotic and antioxidant activity. 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 deformylase and also exhibit anti-influenza activity. The 1,4-dimethoxy-3-(3R-hydroxy-3R-methyl-1-tetralone)-1(3H)-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-
7-Bromo-1-(2,3-dibromo-4,5-dihydroxyphenyl)-5,6-dihydroxy-1,3-
-dihydroisobenzofuran 18 was isolated from brown alga leathesia nana and showed
potential usefulness for malignant tumors and cardiovascular disease. 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). 1,3-dihydrobenzo[c]furan glycone 21 showed
stronger antibacterial activity, antidepressant drug, 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.

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 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. ¹H-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 conjunction 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.
Reaction conditions: All the reactions were carried out with 2-bromobenzadehydes 5 (0.50 mmol).

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 \(\delta \) 7.54 having \(J=7.8\) and 1.5 Hz was due to one aromatic proton, doublet of a doublet at \(\delta \) 7.51 having \(J=7.8\) and 1.5 Hz was due to one aromatic proton, doublet of a doublet at \(\delta \) 7.22 having \(J=7.8\) and 1.0 Hz was due to one aromatic proton, a multiplet in the region of \(\delta \) 7.15–7.00 was due to two aromatic protons and one olefinic proton, doublet of a doublet at \(\delta \) 6.83 having \(J=8.3\) and 2.4 Hz was due to one aromatic proton, doublet at \(\delta \) 6.78 having \(J=8.3\) Hz was due to one aromatic proton, doublet of a doublet at \(\delta \) 6.19 having \(J=16.1\) and 7.8 Hz was due to olefinic methine group proton, doublet at \(\delta \) 5.76 having \(J=7.8\) Hz was due to benzylic methine group proton, doublet of a doublet at \(\delta \) 5.19 having \(J=12.0\) and 2.0 Hz was due to benzylic methylene group proton, doublet at \(\delta \) 5.11 having \(J=12.0\) Hz was due to benzylic methylene group proton, the presence of singlet \(\delta \) 3.81 was 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 \(\delta \) 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 \(\delta \) at \(\delta \) 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, \(\delta \) 84.7 was due to benzylic methine group carbon, \(\delta \) 72.8 was due to benzylic methylene group carbon and \(\delta \) 55.5 ppm was due to methoxy group carbon elucidated the structure of 1,3-dihydroisobenzofuran 11hj. The presence of the \([\text{M+Na}]^+\) peak at m/z \([\text{C}_{17}\text{H}_{15}\text{BrNaO}_2]^+\) = 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.\textsuperscript{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 \textit{11qh} and \textit{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 \textit{10} (Scheme II.20).

\textbf{Scheme II.20}

\textbf{II.4. CONCLUSIONS:}

We have developed an efficient method for synthesis of $\beta$-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 $\beta$-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 \textit{iso}-
benzofurans, an important core structure present in many biologically active natural products (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 ($\delta$ in ppm) and coupling constants ($J$ in Hz) are reported in standard fashion with reference to either internal standard tetramethylsilane (TMS) ($\delta_H = 0.00$ ppm) or CHCl$_3$ ($\delta_H = 7.25$ ppm). $^{13}$C-NMR spectra were recorded on Bruker Avance 400 (100 MHz) spectrometer at RT in CDCl$_3$; chemical shifts ($\delta$ in ppm) are reported relative to CHCl$_3$ [$\delta_C = 77.00$ 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-bromooiodobenzene (with purity 99%), NaBH4 (with purity 99%), K2CO3 (with purity 99%), and NaHCO3 (with purity 99.5%) were purchased from Sigma-Aldrich, whereas vinlylmagnesium bromide (with purity 99%), BF3·Et2O (with purity XX%), iodobenzene (with purity 99%) and Cs2CO3 (with purity 99%) were purchased from other commercial sources and used as received. The bases K2CO3, NaHCO3 and Cs2CO3 were dried at 150–170 °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 P2O5. 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 NH₄Cl solution and extracted with ethyl acetate (3 × 20 mL). The organic layer was washed with saturated
NaCl solution, dried over anhydrous Na$_2$SO$_4$ 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%).

**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 \( R_f(4h)=0.70 \) (petroleum ether/ethyl acetate 95:05 , UV detection)].

**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$^{-1}$):** \( \nu_{max}=3371, 3032, 2920, 1592, 1571, 1462, 1291, 1380, 1291, 1233, 1163, 1010, 927, 736, 697 \) cm$^{-1}$.

**$^1$H-NMR (CDCl$_3$, 400 MHz):** \( \delta=7.50–7.28 \) (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, Ar-H).
Hz, CH=CH₂), 5.54 (d, 1H, J=5.4 Hz, ArCH-OH), 5.40 (td, 1H, J=15.8 and 1.5 Hz, C=CH₃H₆), 5.22 (td, 1H, J=10.3 and 1.5 Hz, C=CH₃H₆), 5.04 (s, 2H, PhCH₂O), 2.25 (d, 1H, J=3.9 Hz, OH) ppm.

**^13^C-NMR (CDCl₃, 100 MHz):** δ=158.4 (s, Ar-C), 142.5 (s, Ar-C), 138.1 (d, CH=CH₂), 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=CH₂), 114.2 (d, Ar-CH), 112.9 (s, Ar-C), 73.4 (d, Ar-CHOH), 70.2 (t, PhCH₂) ppm.

**HR-MS (ESI⁺):** m/z calculated for [C₁₆H₁₄BrO]⁺=[(M+H)–H₂O]⁺: 301.0223; found 301.0213.

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 Rₗ(5j)=0.80, Rₗ(4j)=0.50 (petroleum ether/ethyl acetate 80:20, UV detection)].

**IR (MIR-ATR, 4000–600 cm⁻¹):** νmax=3380, 2922, 2851, 1593, 1572, 1468, 1416, 1290, 1233, 1161, 1047, 1013, 928, 807, 771 cm⁻¹.

**^1H-NMR (CDCl₃, 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, CH=CH₂), 5.53 (d, 1H, J=5.4 Hz, ArCH-OH), 5.38 (td, 1H, J=17.1 and 1.5 Hz, C=CH₃H₆), 5.21 (td, 1H, J=10.3 and 1.5 Hz, C=CH₃H₆), 3.78 (s, 3H, Ar-OCH₃), 2.34 (br. s, 1H, OH) ppm.

**^13^C-NMR (CDCl₃, 100 MHz):** δ=159.3 (s, Ar-C), 142.4 (s, Ar-C), 138.1 (d, CH=CH₂), 133.3 (d, Ar-CH), 115.7 (t, CH=CH₂), 115.2 (d, Ar-CH), 113.0 (d, Ar-CH), 112.7 (s, Ar-C), 73.4 (d, Ar-CHOH), 55.4 (q, Ar-OCH₃) ppm.
HR-MS (ESI^+): m/z calculated for [C\textsubscript{10}H\textsubscript{10}BrO]^+=[(M+H)–H\textsubscript{2}O]^+: 224.9910; found 224.9903.

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

\(^1\text{H}-\text{NMR (CDCl}_3, 400 \text{ MHz)}: \delta = 7.42 (\text{dd, 2H, } J=7.3 \text{ and } 6.8 \text{ Hz, Ar-H}), 7.37 (t, 2H, \text{J=7.3 Hz, Ar-H}), 7.31 (\text{ddd, 1H, } J=7.3 \text{ and } 6.8 \text{ Hz, Ar-H}), 7.03 (\text{s, 1H, Ar-H}), 7.02 (\text{s, 1H, Ar-H}), 5.98 (\text{ddd, 1H, } J=15.6, 10.3 \text{ and } 4.9 \text{ Hz, } CH=CH_2), 5.51 (\text{d, 1H, } J=5.4 \text{ Hz, ArCH-OH}), 5.38 (\text{td, 1H, } J=15.6 \text{ and } 1.5 \text{ Hz, } C=CH_2H_b), 5.20 (\text{td, 1H, } J=10.3 \text{ and } 1.5 \text{ Hz, } C=CH_2H_b), 5.09 (\text{s, 2H, PhCH}_2O), 3.38 (\text{s, 3H, Ar-OCH}_3), 2.29 (\text{d, 1H, } J=2.9 \text{ Hz, OH}) \text{ ppm.}

\(^1\text{C}-\text{NMR (CDCl}_3, 100 \text{ MHz)}: \delta = 149.4 (\text{s, Ar-C}), 148.1 (\text{s, Ar-C}), 138.5 (\text{d, CH=CH}_2), 136.3 (\text{s, Ar-C}), 134.0 (\text{s, Ar-C}), 128.6 (\text{d, 2C, Ar-CH}), 128.0 (\text{d, Ar-CH}), 127.3 (\text{d, 2C, Ar-CH}), 117.6 (\text{d, Ar-CH}), 115.3 (\text{t, CH=CH}_2), 112.1 (\text{s, Ar-C}), 110.7 (\text{d, Ar-CH}), 73.3 (\text{d, Ar-CHOH}), 71.2 (\text{t, PhCH}_2), 56.0 (\text{q, Ar-OCH}_3) \text{ ppm.}

HR-MS (ESI^+): m/z calculated for [C\textsubscript{17}H\textsubscript{16}BrO\textsubscript{2}]^+=[(M+H)-H\textsubscript{2}O]^+: 331.0328; found 331.0332.
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\(^{-1}\))**: \( \nu_{\text{max}} = 3404, 3032, 3008, 2932, 1600, 1502, 1502, 1439, 1379, 1257, 1156, 1120, 1029, 925, 863, 777 \) cm\(^{-1}\).

**\(^1\)H-NMR (CDCl\(_3\), 400 MHz)**: \( \delta = 7.42 \) (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, \( CH=CH_2 \)), 5.49 (d, 1H, \( J = 5.4 \) Hz, ArCH-OH), 5.35 (td, 1H, \( J = 15.6 \) and 1.5 Hz, \( C=CH_2H_b \)), 5.31 (td, 1H, \( J = 10.3 \) and 1.5 Hz, \( C=CH_2H_b \)), 5.11 (d, 1H, \( J = 12.2 \) Hz, PhCH\(_3\)H\(_3\)O), 5.10 (d, 1H, \( J = 12.2 \) Hz, PhCH\(_3\)H\(_3\)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)**: \( \delta = 149.6 \) (s, Ar-C), 147.8 (s, Ar-C), 138.4 (d, \( CH=CH_2 \)), 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, \( CH=CH_2 \)), 113.1 (s, Ar-C), 112.9 (d, Ar-CH), 73.2 (d, Ar-CHOH), 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\(_2\)O]\(^+\): 331.0328; found 331.0334.

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$^{-1}$):** $v_{max}=3346, 2897, 1501, 1471, 1407, 1230, 1107, 1035, 930, 840, 798$ cm$^{-1}$.

$^1$H-NMR (CDCl$_3$, 400 MHz): $\delta=6.98$ (s, 1H, Ar-H), 6.96 (s, 1H, Ar-H), 5.95 (d, 1H, $J=5.4$ Hz, OCH$_2$H$_2$O), 5.94 (d, 1H, $J=5.4$ Hz, OCH$_3$H$_2$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$_2$H$_2$), 5.20 (td, 1H, $J=10.3$ and 1.5 Hz, C=CH$_2$H$_2$), 2.26 (d, 1H, $J=2.9$ Hz, OH) ppm.

$^{13}$C-NMR (CDCl$_3$, 100 MHz): $\delta=147.8$ (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 $[C_{10}H_9BrNaO_3]^+=[M+Na]^+$: 278.9627; found 278.9639.

![Chemical Structure](image_url)

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$^{-1}$):** $v_{max}=3451, 2960, 1601, 1500, 1441, 1254, 1205, 1032, 923, 865, 810, 758$ cm$^{-1}$.
$^1$H-NMR (CDCl$_3$, 400 MHz): $\delta$=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, CH=CH$_2$), 5.50 (d, 1H, $J$=5.3 Hz, ArCH-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$_3$), 3.84 (s, 3H, Ar-OCH$_3$), 2.30 (br. s, 1H, OH) ppm.

$^{13}$C-NMR (CDCl$_3$, 100 MHz): $\delta$=148.8 (s, Ar-C), 148.7 (s, Ar-C), 138.5 (d, CH=CH$_2$), 133.5 (s, Ar-C), 115.2 (t, CH=CH$_2$), 115.2 (d, Ar-CH), 112.3 (s, Ar-C), 110.2 (d, Ar-CH), 73.2 (d, Ar-CH$_3$), 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.

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$^{-1}$): $\nu_{max}$=3463, 2937, 1570, 1475, 1397, 1108, 930 cm$^{-1}$.

$^1$H-NMR (CDCl$_3$, 400 MHz): $\delta$=6.90 (s, 1H, Ar-H), 5.98 (ddd, 1H, $J$=16.7, 11.4 and 6.3 Hz, CH=CH$_2$), 5.59 (d, 1H, $J$=4.8 Hz, ArCH-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): $\delta$=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, CH=CH), 108.8 (s, Ar-C), 106.3 (d, CH=CH$_2$), 73.4 (d, Ar-CH$_3$), 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 \([\text{C}_{12}\text{H}_{14}\text{BrNaO}_4]^+=[\text{M+Na}]^+\): 325.0046; found 325.0051.

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 \(R_f(4p)=0.50\) (petroleum ether/ethyl acetate 70:30 , UV detection)].

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 \(R_f(4q)=0.30\) (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. NH₄Cl and extracted with ethyl acetate (3 × 10 mL). The organic layer was dried over Na₂SO₄ 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), NaHCO₃ (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. NH₄Cl and extracted with ethyl acetate (3 × 10 mL). The organic layer was dried over Na₂SO₄ 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%).

(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), NaHCO₃ (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$^{-1}$):** $\nu_{max}$=3333, 3036, 2915, 1578, 1442, 1014, 964, 746 cm$^{-1}$.

$^1$H-NMR (CDCl$_3$, 400 MHz): $\delta$=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=CH-Ar), 6.32 (dd, 1H, $J$=15.9 and 6.1 Hz, CH=CH-Ar), 5.75 [d, 1H, $J$=6.1 Hz, Ar-CH(OH)-CH=CH], 2.65 (br. s, 1H, OH) ppm.

$^{13}$C-NMR (CDCl$_3$, 100 MHz): $\delta$=141.7 (s, Ar-C), 136.5 (s, Ar-C), 132.8 (d, CH=CH-Ar), 131.0 (d, Ar-CH), 129.7 (d, CH=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-CHOH) ppm.

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

(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)$_3$NCl (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 $^\circ$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$^{-1}$):** $\nu_{max}$=3404, 2935, 1587, 1443, 1260, 1159, 1031, 757, 684 cm$^{-1}$.
$^{1}$H-NMR (CDCl$_3$, 400 MHz): $\delta$=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 (dddd, 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=CH-Ar), 6.32 (dd, 1H, $J$=16.1 and 5.8 Hz, CH=CH-Ar), 5.76 [d, 1H, $J$=5.8 Hz, Ar-CH(OH)-CH=CH], 3.79 (s, 3H, Ar-OCH$_3$), 2.56 (br. s, 1H, OH) ppm.

$^{13}$C-NMR (CDCl$_3$, 100 MHz): $\delta$=159.7 (s, Ar-C), 141.5 (s, Ar-C), 137.9 (s, Ar-C), 132.7 (d, Ar-CH), 130.8 (d, CH=CH-Ar), 129.9 (d, Ar-CH), 129.5 (d, Ar-CH), 129.1 (d, CH=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-CHOH), 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)$_3$NCl (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$^{-1}$): $\nu_{max}$=3503, 2942, 2839, 1592, 1458, 1257, 1141, 1024, 910, 730, 649 cm$^{-1}$. 

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**$^1$H-NMR (CDCl$_3$, 400 MHz):** $\delta$=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=CH-Ar), 6.16 (dd, 1H, $J$=15.7 and 5.9 Hz, CH=CH-Ar), 5.71 [d, 1H, $J$=5.9 Hz, Ar-CH(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):** $\delta$=148.9 (s, 2C, Ar-C), 141.9 (s, Ar-C), 132.8 (d, Ar-C), 130.9 (d, Ar-CH), 129.5 (s, Ar-C), 129.0 (d, CH=CH-Ar), 128.0 (d, Ar-CH), 127.9 (d, CH=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-CHOH), 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)$_3$NCl (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$^{-1}$):** $\nu_{max}$=3409, 2933, 1595, 1493, 1461, 1291, 1092, 902, 755, 681 cm$^{-1}$.

**$^1$H-NMR (CDCl$_3$, 400 MHz):** $\delta$=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=CH-Ar), 6.60 (d, 1H, $J$=8.7 Hz, Ar-H),
6.21 (dd, 1H, J=16.0 and 6.5 Hz, CH=CH-Ar), 5.73 [d, 1H, J=6.5 Hz, Ar-CH(OH)-CH=CH], 3.84 (s, 3H, Ar-OCH₃), 3.82 (s, 6H, 2 Ar-OCH₃), 2.58 (br. s, 1H, OH) ppm.

¹³C-NMR (CDCl₃, 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=CH-Ar), 129.0 (d, Ar-CH), 127.9 (d, Ar-CH), 127.8 (d, Ar-CH), 125.6 (d, CH=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-CHOH), 61.3 (q, Ar-OCH₃), 60.9 (q, Ar-OCH₃), 56.0 (q, Ar-OCH₃) ppm.

HR-MS (ESI⁺): m/z calculated for [C₁₈H₁₉BrNaO₄]⁺=[M+Na]⁺: 401.0359; found 401.0364.

(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)₃Cl (83.2 mg, 0.4 mmol), NaHCO₃ (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 Rₜ(4n)=0.50, Rₜ(6na)=0.49 (petroleum ether/ethyl acetate 70:30, UV detection)].

IR (MIR-ATR, 4000–600 cm⁻¹): νₘₐₓ=3470, 2945, 1599, 1499, 1447, 1255, 1205, 1153, 1031, 965, 732 cm⁻¹.

¹H-NMR (CDCl₃, 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=CH-Ar), 6.22 (dd, 1H, J=15.8 and 5.9 Hz, CH=CH-Ar), 5.62 [d, 1H, J=5.9 Hz, Ar-CH(OH)-CH=CH], 3.79 (s, 3H, Ar-OCH₃), 3.78 (s, 3H, Ar-OCH₃), 2.29 (br. s, 1H, OH) ppm.
**13C-NMR (CDCl₃, 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=CH-Ar), 112.3 (s, Ar-C), 110.3 (d, CH=CH-Ar), 73.3 (d, Ar-CHOH), 56.2 (q, Ar-OCH₃), 56.1 (q, Ar-OCH₃) ppm.

**HR-MS (ESI⁺):** m/z calculated for [C₁₇H₁₇BrNaO₃]⁺=[M+Na]⁺: 371.0253; found 371.0251.

**IR (MIR-ATR, 4000–600 cm⁻¹):** νₓₓₓ=3475, 2949, 1593, 1498, 1256, 1154, 1036, 910, 781 cm⁻¹.

**1H-NMR (CDCl₃, 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=CH-Ar), 6.21 (dd, 1H, J=15.8 and 5.9 Hz, CH=CH-Ar), 5.62 [d, 1H, J=5.9 Hz, Ar-CH(OH)-CH=CH], 3.80 (s, 3H, Ar-OCH₃), 3.78 (s, 3H, Ar-OCH₃), 3.72 (s, 3H, Ar-OCH₃), 2.33 (br. s, 1H, OH) ppm.

**13C-NMR (CDCl₃, 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=CH-Ar), 113.5 (d, Ar-CH), 112.3 (s, Ar-C), 111.9

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(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), NaHCO₃ (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 Rₓ(4n)=0.50, Rₓ(6nb)=0.45 (petroleum ether/ethyl acetate 7:3, UV detection)].
(d, Ar-CH), 110.3 (d, CH=CH-Ar), 73.2 (d, Ar-CHOH), 56.2 (q, Ar-OCH₃), 56.1 (q, Ar-OCH₃), 55.2 (q, Ar-OCH₃) ppm.

**HR-MS (ESI⁺):** m/z calculated for [C₁₈H₁₉BrNaO₄]⁺=[M+Na]⁺: 401.0359; found 401.0360.

(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), NaHCO₃ (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 Rₜ(4o)=0.40, Rₜ(6oa)=0.30 (petroleum ether/ethyl acetate 70:30, UV detection)].

**IR (MIR-ATR, 4000–600 cm⁻¹):** νmax=3461, 2949, 2888, 2835, 1573, 1474, 1392, 1240, 1102, 1008, 745 cm⁻¹.

**¹H-NMR (CDCl₃, 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=CH-Ar), 6.28 (d, 1H, J=15.8 and 6.0 Hz, CH=CH-Ar), 5.75 [d, 1H, J=6.0 Hz, Ar-CH(OH)-CH=CH], 3.87 (s, 3H, Ar-OCH₃), 3.85 (s, 3H, Ar-OCH₃), 3.78 (s, 3H, Ar-OCH₃), 2.83 (br. s, 1H, OH) ppm.

**¹³C-NMR (CDCl₃, 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=CH-Ar), 128.6 (d, 2C, Ar-CH), 127.8 (d, CH=CH-Ar), 126.6 (d, 2C, Ar-CH), 108.7 (s, Ar-C), 106.3 (d, Ar-CH), 73.3 (d, Ar-CHOH), 61.1 (q, Ar-OCH₃), 61.0 (q, Ar-OCH₃), 56.1 (q, Ar-OCH₃) ppm.
HR-MS (ESI⁺): m/z calculated for [C₁₈H₁₉BrKO₄]⁺=[M+K]⁺: 417.0098; found 417.0097.

(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), NaHCO₃ (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 Rf(4o)=0.40, Rf(6ob)=0.25 (petroleum ether/ethyl acetate 70:30, UV detection)].

IR (MIR-ATR, 4000–600 cm⁻¹): νmax=3420, 2933, 2842, 1580, 1474, 1390, 1249, 1101, 1006, 776 cm⁻¹.

¹H-NMR (CDCl₃, 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=CH-Ar), 6.26 (dd, 1H, J=15.9 and 5.9 Hz, CH=CH-Ar), 5.74 [d, 1H, J=5.9 Hz, Ar-CH(OH)-CH=CH] , 3.87 (s, 3H, Ar-OCH₃), 3.86 (s, 3H, Ar-OCH₃), 3.84 (s, 3H, Ar-OCH₃), 3.81 (s, 3H, Ar-OCH₃), 2.83 (br. s, 1H, OH) ppm.

¹³C-NMR (CDCl₃, 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=CH-Ar), 111.9 (d, CH=CH-Ar), 108.7 (s, Ar-C), 106.3 (d, Ar-CH), 73.2 (d, Ar-CHOH), 61.1 (q, Ar-OCH₃), 61.1 (q, Ar-OCH₃), 56.1 (q, Ar-OCH₃), 55.2 (q, Ar-OCH₃) ppm.

HR-MS (ESI⁺): m/z calculated for [C₁₀H₂₁BrNaO₅]⁺=[M+Na]⁺: 431.0465; found 431.0470.
(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)$_3$NCl (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$^{-1}$):** $\nu_{max}$=3497, 2935, 2839, 1573, 1512, 1469, 1387, 1247, 1150, 1012, 807, 768 cm$^{-1}$.

**$^1$H-NMR (CDCl$_3$, 400 MHz):** $\delta$=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=CH-Ar), 6.15 (dd, 1H, $J$=15.8 and 6.2 Hz, CH=CH-Ar), 5.73 [d, 1H, $J$=6.2 Hz, Ar-CH(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):** $\delta$=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=CH-Ar), 129.5 (s, Ar-C), 127.6 (d, CH=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-CH(OH)), 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.
(E)-1,3-Bis(2-bromophenyl)prop-2-en-1-ol (6he): GP-2 was carried out on bromoaryl allylic alcohol 4h (100 mg, 0.47 mmol) with Pd(OAc)$_2$ (5.2 mg, 5 mol%), Bn(Et)$_3$NCl (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$^{-1}$):** $\nu_{max}=$3340, 3060, 2922, 1571, 1464, 1431, 1266, 1121, 1016, 746, 673 cm$^{-1}$.

**$^1$H-NMR (CDCl$_3$, 400 MHz):** $\delta=$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=CHAr), 6.26 (dd, 1H, $J=15.8$ and 5.9 Hz, CH=CH-Ar), 5.81 [d, 1H, $J=5.9$ Hz, Ar-CH(OH)-CH=CH], 2.51 (br. s, 1H, OH) ppm.

**$^{13}$C-NMR (CDCl$_3$, 100 MHz):** $\delta=$141.3 (s, Ar-C), 136.5 (s, Ar-C), 132.9 (d, Ar-CH), 132.9 (d, CH=CHAr), 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-CHOH) ppm.

**HR-MS (ESI$^+$):** m/z calculated for [C$_{15}$H$_{12}$Br$_2$NaO]$^+=[M+Na]$^+$: 388.9147; found 388.9150.
(E)-1-(2-Bromo-4,5-dimethoxyphenyl)-3-(2-bromophenyl)prop-2-en-1-ol (6hf): GP-2 was carried out on bromo aryl allylic alcohol 4h (100 mg, 0.47 mmol) with Pd(OAc)$_2$ (5.2 mg, 5 mol%), Bn(Et)$_3$NCl (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 $R_f$(6hf)=0.35 (petroleum ether/ethyl acetate 80:20, UV detection)].

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

$^1$H-NMR (CDCl$_3$, 400 MHz): $\delta$=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 CH=CH-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, CH=CH-Ar), 5.69 [d, 1H, $J=5.9$ Hz, Ar-CH(OH)-CH=CH], 3.70 (s, 3H, Ar-OCH$_3$), 2.27 (br. s, 1H, OH) ppm.

$^{13}$C-NMR (CDCl$_3$, 100 MHz): $\delta$=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=CH-Ar), 114.1 (d, CH=CH-Ar), 73.5 (d, Ar-CH$_2$OH), 55.6 (q, Ar-OCH$_3$) ppm.

**HR-MS (ESI$^+$):** m/z calculated for [C$_{16}$H$_{14}$Br$_2$NaO$_2$]$^+=[M+Na]$^+$: 418.9253; found 418.9257.

(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)$_3$NCl (83.2 mg, 0.4 mmol), NaHCO$_3$ (62 mg, 0.73...
mmol), 2-bromiodobenzene 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\(^{-1}\)):** \( \nu_{max}=3491, 3061, 2842, 1597, 1500, 1255, 1205, 1153, 1027, 965, 744 \text{ cm}^{-1}. \)

**\(^1H\)-NMR (CDCl\(_3\), 400 MHz):** \( \delta=7.45 \text{ (dd, 1H, } J=8.0 \text{ and 0.8 Hz, Ar-H)}, \ 7.39 \text{ (dd, 1H, } J=7.8 \text{ and 1.3 Hz, Ar-H)}, \ 7.15 \text{ (dd, 1H, } J=7.5 \text{ Hz and 7.5 Hz, Ar-H)}, \ 7.04 \text{ (s, 1H, Ar-H)}, \ 7.03 \text{ (d, 1H, } J=15.8 \text{ Hz, CH=CH-Ar)}, \ 7.00 \text{ (ddd, 1H, } J=7.5, 7.5 \text{ and 1.5 Hz, Ar-H)}, \ 6.92 \text{ (s, 1H, Ar-H)}, \ 6.14 \text{ (dd, 1H, } J=15.8 \text{ and 5.8 Hz, CH=CH-Ar)}, \ 5.67 \text{ [dd, 1H, } J=5.8 \text{ and 1.0 Hz, Ar-CH(OH)-CH=CH}], \ 3.81 \text{ (s, 3H, Ar-OCH\(_3\))}, \ 3.79 \text{ (s, 3H, Ar-OCH\(_3\))}, \ 2.39 \text{ (br. s, 1H, OH)} \text{ ppm}. \)

**\(^13C\)-NMR (CDCl\(_3\), 100 MHz):** \( \delta=149.0 \text{ (s, Ar-C)}, \ 148.9 \text{ (s, Ar-C)}, \ 136.6 \text{ (s, Ar-C)}, \ 133.4 \text{ (s, Ar-C)}, \ 132.9 \text{ (d, 2C, Ar-CH)}, \ 129.5 \text{ (d, Ar-CH)}, \ 129.0 \text{ (d, Ar-CH)}, \ 127.5 \text{ (d, Ar-CH)}, \ 127.2 \text{ (d, Ar-CH)}, \ 123.8 \text{ (s, Ar-C)}, \ 115.3 \text{ (d, CH=CH-Ar)}, \ 112.3 \text{ (s, Ar-C)}, \ 110.2 \text{ (d, CH=CH-Ar)}, \ 73.2 \text{ (d, Ar-CHOH)}, \ 56.2 \text{ (q, Ar-OCH\(_3\))}, \ 56.1 \text{ (q, Ar-OCH\(_3\))} \text{ ppm}. \)

**HR-MS (ESI\(^+\)):** m/z calculated for [C\(_{17}\)H\(_{16}\)Br\(_2\)NaO\(_3\)]\(^+\)=[M+Na\(^+\)]: 448.9358; found 448.9356.

![Diagram](image)

**(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)\(_3\)NCl (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$^{-1}$):** $\nu_{max}=3494, 2934, 2847, 1601, 1498, 1254, 1033, 905, 726$ cm$^{-1}$.

**$^1$H-NMR (CDCl$_3$, 400 MHz):** $\delta=7.33$ (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=CH-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, CH=CH-Ar), 5.65 [d, 1H, $J=6.0$ Hz, Ar-CH(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):** $\delta=159.6$ (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=CH-Ar), 114.1 (d, Ar-CH), 112.3 (s, Ar-C), 110.2 (d, CH=CH-Ar), 73.3 (d, Ar-CHOH), 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$_2$NaO$_4$]$^+=[M+Na]$^+: 478.9464; found 478.9468.

(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)$_3$NCl (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 60e (113 mg, 75%) as yellow viscous liquid, (followed GP-3 under microwave irradiation conditions, 116 mg, 77%). [TLC control \( R_f(4o) = 0.40 \), \( R_f(60e) = 0.35 \) (petroleum ether/ethyl acetate 70:30, UV detection)].

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

\(^1\)H-NMR (CDCl\(_3\), 400 MHz): \( \delta = 7.51 \) (d, 1H, \( J = 7.8 \text{ Hz} \), Ar-H), 7.46 (d, 1H, \( J = 7.8 \text{ Hz} \), Ar-H), 7.21 (dd, 1H, \( J = 7.5 \text{ and } 7.5 \text{ Hz} \), Ar-H), 7.10 (d, 1H, \( J = 15.8 \text{ Hz} \), CH=CH-Ar), 7.07 (dd, 1H, \( J = 7.5 \text{ and } 7.5 \text{ Hz} \), Ar-H), 7.00 (s, 1H, Ar-H), 6.21 (dd, 1H, \( J = 15.8 \text{ and } 5.8 \text{ Hz} \), CH=CH-Ar), 5.80 [d, 1H, \( J = 5.8 \text{ Hz} \), Ar-CH(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): \( \delta = 153.1 \) (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=CH-Ar), 129.5 (d, Ar-CH), 128.9 (d, CH=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-CHOH), 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\(_2\)NaO\(_4\)]\(^+\)=[M+Na]\(^+\): 478.9464; found 478.9464.

![](image)

(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), bromiiodoanisole 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 $R_f(40)=0.60$, $R_f(60f)=0.58$ (petroleum ether/ethyl acetate 50:50, UV detection)].

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

**$^1$H-NMR (CDCl$_3$, 400 MHz):** $\delta=7.37$ (d, 1H, $J=7.9$ Hz, Ar-H), 7.1–6.90 (m, 3H, Ar-H and CH=$CH$-Ar), 6.81 (s, 1H, Ar-H), 6.08 (dd, 1H, $J=15.2$ and 4.7 Hz, CH=$CH$-Ar), 5.79 [s, 1H, Ar-CH(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):** $\delta=159.5$ (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=$CH$-Ar), 124.2 (s, Ar-C), 117.6 (d, CH=$CH$-Ar), 114.1 (d, Ar-CH), 108.6 (s, Ar-C), 106.3 (d, Ar-CH), 73.3 (d, Ar-CHOH), 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$_2$NaO$_5$]$^+=[M+Na]$^+$. 508.9570; found 508.9575.

![Image](image-url)

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)$_3$NCl (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\(^{-1}\)): \(\nu_{\text{max}}\)
\[3409, 3061, 2923, 2856, 1688, 1592, 1462, 1197, 1018, 746 \text{ cm}^{-1}\].

\(^1H\)-NMR (CDCl\(_3\), 400 MHz): \(\delta=\)
10.23 (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=CH-Ar), 7.44 (d, 1H, \(J=5.2\) Hz, Ar-H), 5.82 [d, 1H, \(J=5.5\) Hz, Ar-CH(OH)-CH=CH], 3.10 (br. s, 1H, OH) ppm.

\(^{13}C\)-NMR (CDCl\(_3\), 100 MHz): \(\delta=\)
192.4 (s, Ar-CHO), 141.3 (s, Ar-C), 139.5 (s, Ar-C), 135.4 (d, CH=CH-Ar), 133.7 (d, Ar-CH), 132.9 (s, Ar-C), 132.8 (d, CH=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-CHOH) ppm.

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

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)\(_3\)NCl (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\(^{-1}\)): \(\nu_{\text{max}}\)
\[3468, 2926, 1690, 1500, 1255, 1203, 1032, 967, 759 \text{ cm}^{-1}\].

\(^1H\)-NMR (CDCl\(_3\), 400 MHz): \(\delta=\)
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=CH-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, CH=CH-Ar), 5.69 [dd, 1H, J=5.8 and 1.1 Hz, Ar-CH(OH)-CH=CH], 3.81 (s, 3H, Ar-OCH₃), 3.78 (s, 3H, Ar-OCH₃), 2.79 (br. s, 1H, OH) ppm.

**¹³C-NMR (CDCl₃, 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=CH-Ar), 112.2 (s, Ar-C), 110.2 (d, CH=CH-Ar), 73.1 (d, Ar-CHOH), 56.2 (q, Ar-OCH₃), 56.1 (q, Ar-OCH₃) ppm.

**HR-MS (ESI+):** m/z calculated for [C₁₈H₁₇BrNaO₄]⁺=[M+Na]⁺: 399.0202; found 399.0206.

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), NaHCO₃ (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 Rₚ(4o)=0.60, Rₚ(6oh)=0.40 (petroleum ether/ethyl acetate 50:50, UV detection)].

**IR (MIR-ATR, 4000–600 cm⁻¹):** νmax=3452, 2933, 2851, 1691, 1567, 1473, 1389, 1101, 758 cm⁻¹.

**¹H-NMR (CDCl₃, 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=CH-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, CH=CH-Ar), 5.76
[d, 1H, J=5.4 Hz, Ar-CH(OH)-CH=CH], 3.82 (s, 3H, Ar-OCH₃), 3.80 (s, 6H, 2 × Ar-OCH₃), 2.74 (br. s, 1H, -OH) ppm.

¹³C-NMR (CDCl₃, 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=CH-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, CH=CH-Ar), 108.6 (s, Ar-C), 106.3 (d, Ar-CH), 73.2 (d, Ar-CHOH), 61.1 (q, Ar-OCH₃), 61.1 (q, Ar-OCH₃), 56.2 (q, Ar-OCH₃) ppm.

HR-MS (ESI⁺): m/z calculated for [C₁₉H₁₉BrNNaO₅]⁺=[M+Na]⁺: 429.0314; found 429.0314.

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), NaHCO₃ (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): νmax=3021, 2932, 2845, 1672, 1593, 1470, 1450, 1242, 1022, 981, 751 cm⁻¹.

¹H-NMR (CDCl₃, 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-OCH₃), 3.31 (t, 2H, J=7.3 Hz, ArCOCH₂), 3.03 [t, 2H, J=7.3 Hz, Ar(CO)CH₂CH₂] ppm.
\textbf{\textsuperscript{13}C-NMR (CDCl$_3$, 100 MHz)}: $\delta$=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.

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 \textbf{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$^{-1}$):** $\nu_{\text{max}}$=3385, 3026, 2928, 1593, 1489, 1453, 1238, 1022, 967, 745 cm$^{-1}$.

**\textsuperscript{1}H-NMR (CDCl$_3$, 400 MHz):** $\delta$=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=CH-Ph), 6.45 (dd, 1H, $J$=16.0 and 6.0 Hz, CH=CH-Ph), 5.55 [br. s, 1H, Ar-CH(OH)], 3.84 (s, 3H, Ar-OCH$_3$), 2.95 (br. s, 1H, -OH) ppm.

**\textsuperscript{13}C-NMR (CDCl$_3$, 100 MHz):** $\delta$= 156.7 (s, Ar-C), 137.0 (s, Ar-C), 130.9 (d, Ar-CH), 130.8 (s, Ar-C), 130.0 (d, CH=CH-Ph), 128.9 (d, CH=CH-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.
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)$_3$NCl (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 ºC 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$^{-1}$):** $\nu_{max}$=2941, 2839, 1672, 1592, 1477, 1449, 1247, 1032, 983, 758 cm$^{-1}$.

**$^1$H-NMR (CDCl$_3$, 400 MHz):** $\delta$=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, ArCOCH$_2$) ppm.

**$^{13}$C-NMR (CDCl$_3$, 100 MHz):** $\delta$=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.
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(6pb)=0.20 (petroleum ether/ethyl acetate 80:20, UV detection)].

For compound 6pe:

IR (MIR-ATR, 4000–600 cm⁻¹): νmax=3431, 3003, 2931, 2839, 1590, 1481, 1451, 1239, 1035, 966, 752 cm⁻¹.

¹H-NMR (CDCl₃, 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=CHAr), 6.36 (dd, 1H, J=15.9 and 5.9 Hz, CH=CHAr), 5.48 [d, 1H, J=5.9, Ar-CH(OH)-CH=CH], 3.74 (s, 3H, Ar-OCH₃), 3.67 (s, 3H, Ar-OCH₃), 2.98 (br. s, 1H, OH) ppm.

¹³C-NMR (CDCl₃, 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=CHAr), 129.5 (d, Ar-CH), 128.9 (d, CH=CHAr), 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-CH(OH)), 55.5 (q, Ar-OCH₃), 55.2 (q, Ar-OCH₃) ppm.

HR-MS (ESI⁺): m/z calculated for [C₁₇H₁₈NaO₃]⁺=[M+Na]⁺: 293.1148; found 293.1147.

[Diagram of 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), NaHCO₃ (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 colorless 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): νₘₐₓ=3065, 2941, 2845, 1676, 1596, 1472, 1293, 1027, 756 cm⁻¹.

¹H-NMR (CDCl₃, 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-OC₃H₃), 3.32 [t, 2H, J=7.5 Hz, Ar(CO)CH₂], 3.14 [t, 2H, J=7.5 Hz, Ar(CO)CH₂CH₂] ppm.

¹³C-NMR (CDCl₃, 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-OCH₃), 43.4 (t, Ar-CO-CH₂), 30.9 (t, Ar-CO-CH₂CH₂) ppm.

HR-MS (ESI+): m/z calculated for [C₁₆H₁₅BrNaO₂]⁺=[M+Na]⁺: 341.0148; found 341.01451.

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 Rₜ(4p)=0.30, Rₜ(7pe)=0.6 and Rₜ(6pe)=0.20 (petroleum ether/ethyl acetate 80:20, UV detection)].

For compound 6pe:
IR (MIR-ATR, 4000–600 cm⁻¹): $\nu_{\text{max}}$=3381, 2927, 2844, 1593, 1460, 1238, 1022, 746 cm⁻¹.

$^1$H-NMR (CDCl₃, 400 MHz): $\delta$=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=CH-Ar), 6.39 (dd, 1H, $J$=15.8 and 5.5 Hz, CH=CH-Ar), 5.61 [dd, 1H, $J$=5.5 and 5.5 Hz, Ar-CH(OH)-CH=CH], 3.88 (s, 3H, Ar-CH$_2$), 3.00 (d, 1H, $J$=5.5 Hz, OH) ppm.

$^{13}$C-NMR (CDCl₃, 100 MHz): $\delta$=156.7 (s, Ar-C), 136.8 (s, Ar-C), 133.9 (d, Ar-CH), 132.8 (d, CH=CH-Ar), 130.5 (s, Ar-C), 128.9 (d, CH=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-CHOH), 55.4 (q, Ar-CH$_2$) ppm.

HR-MS (ESI⁺): m/z calculated for [C$_{16}$H$_{15}$BrNaO$_2$]$^+$=[M+Na]$^+$: 341.0147; found 341.0147.

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)$_3$NCl (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): $\nu_{\text{max}}$=3068, 2923, 2851, 1672, 1597, 1484, 1242, 1030, 756 cm⁻¹.
$^1$H-NMR (CDCl$_3$, 400 MHz): $\delta=7.59$ (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$_2$H$_2$-], 2.99 [t, 2H, Ar(CO)-CH$_2$-CH$_2$] ppm.

$^{13}$C-NMR (CDCl$_3$, 100 MHz): $\delta=201.7$ (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), 125.3 (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$_2$-CH$_2$) ppm.

HR-MS (ESI$^+$): m/z calculated for [C$_{17}$H$_{17}$BrNaO$_3$]$^+$=[M+Na]$^+$: 371.0253; found 371.0259.

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$^{-1}$): $\nu_{max}$=3407, 2930, 2843, 1594, 1481, 1237, 1025, 750 cm$^{-1}$.

$^1$H-NMR (CDCl$_3$, 400 MHz): $\delta=7.33$ (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=CH-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, CH=CH-Ar), 5.49 [d, 1H, $J=6.0$ Hz, Ar-CH(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): $\delta=159.6$ (s, Ar-C), 156.7 (s, Ar-C), 131.9 (d, CH=CH-Ar), 130.8 (s, Ar-C), 130.0 (s, Ar-C), 128.8 (d, CH=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-CH), 55.6 (q, Ar-OCH₃), 55.5 ppm.

**HR-MS (ESI⁺):** m/z calculated for [C₁₇H₁₈BrO₃]⁺=[M+H]⁺: 349.0434; found 349.0258 and [C₁₇H₁₆BrO₃]⁺=[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)$_3$NCl (138 mg, 0.60 mmol), NaHCO$_3$ (102 mg, 1.20 mmol), 2-bromobenzaldehyde 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 (CDCl₃, 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-OCH₃), 3.35 [t, 2H, J=7.3 Hz Ar(CO)CH₂], 3.24 [t, 2H, J=7.3 Hz, Ar(CO)CH₂CH₂] ppm.
$^{13}$C-NMR (CDCl$_3$, 100 MHz): $\delta$=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)CH$_2$], 27.2 [t, $J$=7.3 and 6.8 Hz, Ar(CO)-CH$_2$CH$_2$] ppm.

HR-MS (ESI+): m/z calculated for [C$_{17}$H$_{16}$NaO$_3$]$^+\text{=[M+Na]}^+$: 291.0991; found 291.0992.

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$^{-1}$): $\nu_{max}$=3421, 2927, 2847, 2745, 1686, 1592, 1475, 1238, 1026, 748 cm$^{-1}$.

$^1$H-NMR (CDCl$_3$, 400 MHz): $\delta$=10.18 (s, 1H, Ar-CHO), 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=CH-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, CH=CH-Ar), 5.56 [d, 1H, $J$=5.7 Hz, Ar-CH(OH)-CH=CH], 3.8 (s, 3H, Ar-OCH$_3$), 3.08 (br. s, 1H, OH) ppm.

$^{13}$C-NMR (CDCl$_3$, 100 MHz): $\delta$=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=CH-Ar), 130.5 (s, Ar-C), 129.0 (d, CH=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-CHOH), 55.5 (q, Ar-OCH$_3$) ppm.
HR-MS (ESI+): m/z calculated for [C\textsubscript{17}H\textsubscript{16}NaO\textsubscript{3}]\textsuperscript{+}=[M+Na]\textsuperscript{+}: 291.0991; found 291.0992.

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)\textsubscript{2} (7.5 mg, 5 mol%), Bn (Et)\textsubscript{3}NCl (153 mg, 0.67 mmol), NaHCO\textsubscript{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\textsuperscript{-1}): \(\nu_{\text{max}}=2926, 1684, 1492, 1450, 1205, 746, 700\) cm\textsuperscript{-1}.

\(^1\)H-NMR (CDCl\textsubscript{3}, 400 MHz): \(\delta=7.50\) (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\textsubscript{2}), 2.95 [t, 2H, \(J=7.4\) Hz, Ar(CO)CH\textsubscript{2}CH\textsubscript{2}], 2.38 (s, 3H, Ar-CH\textsubscript{3}) ppm.

\(^{13}\)C-NMR (CDCl\textsubscript{3}, 100 MHz): \(\delta=203.4\) (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 \(\times\) Ar-CH), 128.4 (d, 2C, 2 \(\times\) Ar-CH), 128.4 (d, Ar-CH), 126.2 (d, Ar-CH), 125.7 (d, Ar-CH), 43.2 [t, Ar(CO)-CH\textsubscript{2}], 30.4 (t, Ar(CO)-CH\textsubscript{2}-CH\textsubscript{2}), 21.3 (s, Ar-CH\textsubscript{3}) ppm.

HR-MS (ESI\textsuperscript{+}): m/z calculated for [C\textsubscript{16}H\textsubscript{17}O]\textsuperscript{+}=[M+H]\textsuperscript{+}: 225.1274; found 225.1274.
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$^{-1}$): $\nu_{\text{max}}=3337, 3026, 2923, 1598, 1486, 1450, 966, 742$ cm$^{-1}$.

$^1$H-NMR (CDCl$_3$, 400 MHz): $\delta=7.57$ (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=CH-Ar), 6.39 (dd, 1H, $J=15.8$ and 6.3 Hz, CH=CH-Ar), 5.61 [d, 1H, $J=6.3$ Hz, Ar-CH(OH)], 2.42 (s, 3H, Ar-CH$_3$), 2.06 (br. s, 1H, -OH) ppm.

$^{13}$C-NMR (CDCl$_3$, 100 MHz): $\delta=140.7$ (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=CH-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, CH=CH-Ar), 71.89 (d, Ar-CHOH), 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.

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)$_3$NCl (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):** \( \nu_{\text{max}} = 2941, 2837, 1683, 1593, 1448, 1255, 1155, 1043, 971, 756, 697 \text{ cm}^{-1} \).

\(^1\text{H-NMR (CDCl}_3, 400 \text{ MHz}): \delta = 7.51 (d, 1H, J=8.0 \text{ Hz, Ar-H}), 7.26 (dd, 1H, J=7.1 \text{ and } 7.8 \text{ Hz, Ar-H}), 7.13 (dd, 2H, J=7.5 \text{ and } 8.0 \text{ Hz, Ar-H}), 7.09 (s, 1H, Ar-H), 6.73 (d, 1H, J=7.6 \text{ Hz, Ar-H}), 6.69 (s, 1H, Ar-H), 6.65 (dd, 1H, J=2.2 \text{ and } 2.2 \text{ Hz, Ar-H}), 3.69 (s, 3H, Ar-OC\text{H}_3), 3.13 (t, 2H, J=7.3 \text{ Hz, ArCOCH}_2), 2.93 [t, 2H, J=7.4 \text{ Hz, Ar(CO)CH}_2CH_2], 2.39 (s, 3H, Ar-CH_3) \text{ ppm}.

\(^{13}\text{C-NMR (CDCl}_3, 100 \text{ MHz}): \delta = 203.3 (s, Ar-CO), 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-OCH_3), 43.1 (t, Ar-CO-CH_2), 30.4 (t, Ar-CO-CH_2-CH_2-), 21.3 (q, Ar-CH_3) \text{ ppm}.

**HR-MS (ESI⁺):** m/z calculated for [C\text{17}H\text{18}NaO_2]^⁺=[M+Na]^⁺: 277.1199; found 277.1197.

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):** \( \nu_{\text{max}} = 3376, 2933, 1591, 1479, 1265, 1160, 1041, 970, 765, 689 \text{ cm}^{-1} \).

\(^1\text{H-NMR (CDCl}_3, 400 \text{ MHz}): \delta = 7.44 (d, 1H, J=7.3 \text{ Hz, Ar-H}), 7.25–7.00 \text{ (m, 4H, Ar-H)}, 6.88 (d, 1H, J=7.6 \text{ 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=CH-Ar), 6.26 (dd, 1H, J=15.8 and 6.2 Hz, CH=CH-Ar), 5.48 [d, 1H, J=6.2 Hz, Ar-CH(OH)-CH=CH], 3.71 (s, 3H, Ar-OCH₃), 2.30 (s, 3H, Ar-CH₃), 1.97 (br. s, 1H, -OH) ppm.

¹³C-NMR (CDCl₃, 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=CH-Ar), 126.4 (d, CH=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-CHOH), 55.3 (q, Ar-OCH₃), 19.26 (q, Ar-C₃H₃) ppm.

HR-MS (ESI⁺): m/z calculated for [C₁₇H₁₈NaO₂]⁺=[M+Na]⁺: 277.1199; found 277.1200.

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), NaHCO₃ (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): νmax=2937, 2836, 1683, 1513, 1453, 1250, 1145, 1028, 756 cm⁻¹.

¹H-NMR (CDCl₃, 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-OCH₃), 3.75 (s, 3H, Ar-OCH₃), 3.11 (t, 2H, J=7.4 Hz, Ar-CO-CH₂⁻), 2.90 [t, 2H, J=7.4 Hz, Ar(CO)CH₂CH₂], 2.37 (s, 3H, Ar-CH₃) ppm.
**13C-NMR (CDCl₃, 100 MHz):** δ=203.6 (s, Ar-CO), 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-OCH₃), 55.8 (q, Ar-OCH₃), 43.5 (t, Ar-CO-CH₂), 29.9 [t, Ar(CO)CH₂CH₂], 21.3 (t, Ar-CH₃) ppm.

**HR-MS (ESI⁺):** m/z calculated for [C₁₈H₂₀NaO₃]⁺=[M+Na]⁺: 307.1305; found 307.1306.

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 Rₚ(4q)=0.60, Rₚ(7qc)=0.70 and Rₚ(6qc)=0.40 (petroleum ether/ethyl acetate 70:30, UV detection)].

For compound 6qc:

**IR (MIR-ATR, 4000–600 cm⁻¹):** νmax=3501, 2932, 2841, 1593, 1510, 1456, 1254, 1141, 1021, 965, 739 cm⁻¹.

**1H-NMR (CDCl₃, 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=CH-Ar), 6.24 (dd, 1H, J=15.8 and 6.5 Hz, CH=CH-Ar), 5.58 [d, 1H, J=6.5 Hz, Ar-CH(OH)-CH=CH], 3.89 (s, 6H, 2 × Ar-OCH₃), 2.40 (s, 3H, Ar-CH₃), 2.05 (br. s, 1H, -OH) ppm.

**13C-NMR (CDCl₃, 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=CH-Ar), 126.4 (d, Ar-CH), 125.8 (d, CH=CH-Ar), 119.9 (d, Ar-CH), 111.0 (d, Ar-CH), 108.8 (d, Ar-CH), 71.9 (d, Ar-C(OH)), 55.9 (q, Ar-OCH₃), 55.8(q, Ar-OCH₃), 19.3 (q, Ar-CH₃) ppm.

**HR-MS (ESI⁺):** m/z calculated for [C₁₈H₂₀KO₃]⁺=[M+K]⁺: 323.1044; found 323.1047.
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)$_3$NCl (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$^{-1}$): $\nu_{max}$=3061, 2967, 1684, 1448, 1291, 1025, 970, 746 cm$^{-1}$.

**$^1$H-NMR** (CDCl$_3$, 400 MHz): $\delta$=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$_2$CH$_2$], 2.41 (s, 3H, Ar-CH$_3$) ppm.

**$^{13}$C-NMR** (CDCl$_3$, 100 MHz): $\delta$=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$_2$CH$_2$], 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.
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$^{-1}$):** $\nu_{max}$=3325, 3057, 2925, 1589, 1458, 1257, 1018, 964, 745 cm$^{-1}$.

**$^1$H-NMR (CDCl$_3$, 400 MHz):** $\delta$=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=CH-Ar), 6.24 (dd, 1H, $J$=15.8 and 6.3 Hz, CH=CH-Ar), 5.58 [d, 1H, $J$=6.3 Hz, Ar-CH(OH)-CH=CH], 2.38 (s, 3H, Ar-CH$_3$), 2.22 (br. s, 1H, OH) ppm.

**$^{13}$C-NMR (CDCl$_3$, 100 MHz):** $\delta$=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=CH-Ar), 127.4 (d, Ar-CH), 127.2 (d, Ar-CH), 126.4 (d, Ar-CH), 125.8 (d, CH=CH-Ar), 123.7 (s, Ar-C), 71.7 (s, Ar-CHOH), 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.

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)$_3$Cl (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): νmax=3065, 2930, 2846, 1685, 1594, 1484, 1287, 1236, 1034, 845, 749 cm⁻¹.

¹H-NMR (CDCl₃, 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-OCH₃), 3.12 [t, 2H, J=7.6 Hz, Ar(CO)CH₂], 3.01 [t, 2H, J=7.6 Hz, Ar(CO)CH₂CH₂], 2.41 (s, 3H, Ar-CH₃) ppm.

¹³C-NMR (CDCl₃, 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-OCH₃), 41.7 (t, Ar(CO)-CH₂), 30.0 (t, Ar(CO)-CH₂CH₂), 21.32 (q, Ar-CH₃) ppm.

HR-MS (ESI⁺): m/z calculated for [C₁₇H₁₇BrNaO₂]+=[M+Na]⁺: 355.0304; found 355.0311.

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 Rf(4q)=0.50, Rf(7qf)=0.70 and Rf(6qf)=0.50 and (petroleum ether/ethyl acetate 70:30, UV detection)].

For compound 6qf:

IR (MIR-ATR, 4000–600 cm⁻¹): νmax=3373, 3018, 2926, 2847, 1599, 1485, 1242, 1027, 966, 850, 750 cm⁻¹.
$^1$H-NMR (CDCl$_3$, 400 MHz): $\delta=7.44$ (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=CH-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, CH=CH-Ar), 5.47 [d, 1H, $J=6.7$ Hz, Ar-CH(OH)-CH=CH], 3.67 (s, 3H, Ar-OC$_3$H$_5$), 2.29 (s, 3H, Ar-CH$_3$), 2.20 (br. s, 1H, OH) ppm.

$^{13}$C-NMR (CDCl$_3$, 100 MHz): $\delta=159.5$ (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=CH-Ar), 125.7 (d, CH=CH-Ar), 124.2 (d, Ar-CH), 117.6 (d, Ar-CH), 114.1 (d, Ar-CH), 71.9 (d, Ar-CH(OH)), 55.6 (s, Ar-OC$_3$H$_5$), 19.3 (s, Ar-CH$_3$) 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)$_3$NCl (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$_4$Cl solution and extracted with ethyl acetate (3 × 20 mL). The organic layer was washed with saturated NaCl solution, dried over anhydrous Na$_2$SO$_4$ 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$_2$O (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$_2$SO$_4$, 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%).

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), NaHCO₃ (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. NaBH₄ (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. BF₃·Et₂O (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 R̃₉(5h)=0.80, R̃₉(4h)=0.70 and R̃₉(11hh)=0.85 (petroleum ether/ethyl acetate 95:5, UV detection)]

IR (MIR-ATR, 4000–600 cm⁻¹): νmax=2922, 2852, 1588, 1465, 1437, 1357, 1284, 1246, 1158, 1122, 1107, 1021, 963, 747, 698, 665 cm⁻¹.

¹H-NMR (CDCl₃, 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, ArCH=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=CH), 5.80 [d, 1H, J=7.8 Hz, PhCH(O)CH=CH], 5.22 (d, 1H, J=11.7 Hz, PhCH₃H₈OCHCH=CH), 5.14 (d, 1H, J=11.7 Hz, PhCH₃H₈OCHCH=CH) ppm.

¹³C-NMR (CDCl₃, 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=CH-Ar), 129.1 (d, Ar-CH=CH=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-CHCH=CH), 72.9 (t, Ph-CH2OCHCH=CH) ppm.

**HR-MS (ESI⁺):** m/z calculated for [C₁₆H₁₃BrNaO]⁺=[M+Na]⁺: 323.0042; found 323.0041.

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), NaHCO₃ (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. NaBH₄ (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. BF₃.Et₂O (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, Rf(5h)=0.80, Rf(4i)=0.50 and Rf(11ih)=0.65 UV detection)]

**IR (MIR-ATR, 4000–600 cm⁻¹):** νmax= 2922, 2852, 1590, 1563, 1459, 1286, 1238, 1173, 1028, 1013, 963, 739, 697 cm⁻¹.

**¹H-NMR (CDCl₃, 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, ArCH=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=CH), 5.80 [d, 1H, J=7.3 Hz, PhCH(O)CH=CH], 5.22 (dd, 1H, J=12.2 and 2.4 Hz, PhCH₃H₃OCHCH=CH), 5.13 (dd, 1H, J=12.2 and 1.0 Hz, PhCH₃H₃OCHCH=CH), 4.98 (s, 2H, PhCH₂O) ppm.
**13**C-NMR (CDCl₃, 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=Ar), 127.8 (d, Ar-CH=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-CHCH=CH), 72.8 (t, Ph-CH₂OCHCH=CH) 70.1 (t, PhCH₂O) ppm.


![11jh](image)

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), NaHCO₃ (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. NaBH₄ (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. BF₃·Et₂O (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, Rₜ(5h)=0.75, Rₜ(4j)=0.35 and Rₜ(11jh)=0.50 UV detection)].

**IR (MIR-ATR, 4000–600 cm⁻¹):** vₘₐₓ=2959, 2929, 1592, 1571, 1464, 1287, 1236, 1161, 1014, 802, 754, 733, 599 cm⁻¹.

**1H-NMR (CDCl₃, 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, ArCH=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=CH), 5.74 [d, 1H, J=7.5 Hz, PhCH(O)CH=CH], 5.16 (dd, 1H, J=12.3 and 2.2 Hz, PhCHCH=CH=CH), 5.08 (d, 1H, J=12.3 Hz, PhCHCH=CH=CH), 3.68 (s, 3H, Ar-OCH₃) ppm.

^{13}\text{C-NMR (CDCl}_3, 100\text{MHz}): \delta=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=CH-Ar), 127.5 (d, Ar-CH-CH=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-CHCH=CH), 72.9 (t, Ph-CH₂OCHCH=CH), 55.4 (q, Ar-OCH₃) ppm.

HR-MS (ESI⁺): m/z calculated for [C_{17}H_{14}BrO]^+=[(M+H)–H₂O]^+: 313.0223; found 313.0212, [C_{17}H_{14}^{81}\text{BrO}]^+=[(M+H)–H₂O]^+: 315.0202; found 315.0189 and [C_{17}H_{19}BrNO₂]^+=[M+NH₄]^+: 348.0594; found 348.0587.

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)$_3$NCl (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$_2$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 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\(^{-1}\)):** \(\nu_{max}=2918, 2850, 1595, 1502, 1461, 1385, 1260, 1200, 1166, 1024, 750, 697\ cm\(^{-1}\).**

**\(^1\)H-NMR (CDCl\(_3\), 400 MHz):** \(\delta=7.43\) (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, ArCH=CH), \(6.13\) (dd, 1H, \(J=15.6\) and 7.8 Hz, ArCH=CH), 5.81 (d, 1H, \(J=7.8\) Hz, PhCH(O)CH=CH), 5.25 (dd, 1H, \(J=12.2\) Hz, \(J=12.2\) and 2.4 Hz, PhCH\(_2\)OCHCH=CH), 5.14 (d, 1H, \(J=12.2\) Hz, PhCH\(_2\)OCHCH=CH), 5.10 (s, 2H, PhCH\(_2\)O) 3.83 (s, 3H, Ar-OCH\(_3\)) ppm.

**\(^{13}\)C-NMR (CDCl\(_3\), 100 MHz):** \(\delta=149.1\) (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=CH-Ar), 130.0 (d, Ar-CH-CH=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-CHCH=CH), 72.8 (t, Ph-CH\(_2\)OCHCH=CH), 71.1 (t, PhCH\(_2\)O), 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.

![1-{(E)-2-[4-(Benzyloxy)-2-bromo-5-methoxyphenyl]vinyl}-1,3-dihydro-2-benzofuran (11h)](image_url)

\(1\-{(E)-2-[4-(Benzyloxy)-2-bromo-5-methoxyphenyl]vinyl}-1,3\)-dihydro-2-benzofuran (11h): 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 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. NaBH₄ (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. BF₃·Et₂O (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):** \( \nu_{max} = 2957, 2920, 2851, 1503, 1462, 1441, 1379, 1261, 1206, 1163, 1026, 743 \text{ cm}^{-1} \).

**\(^1\)H-NMR (CDCl₃, 400 MHz):** \( \delta = 7.40 \) (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, ArCH=CH), 6.02 (dd, 1H, J=15.6 and 7.8 Hz, ArCH=CH), 5.78 [d, 1H, J=7.8 Hz, PhCH(O)CH=CH], 5.23 (dd, 1H, J=12.2 and 2.4 Hz, PhCH₃H₅OCHCH=CH), 5.13 (d, 1H, J=12.2 Hz, PhCH₃H₅OCHCH=CH), 5.06 (s, 2H, PhCH₂O) 3.86 (s, 3H, Ar-OCH₃) ppm.

**\(^{13}\)C-NMR (CDCl₃, 100 MHz):** \( \delta = 150.2 \) (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=CH-Ar), 129.9 (d, Ar-CH-CH=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-CHCH=CH), 72.9 (t, Ph-CH₂OCHCH=CH), 71.3 (t, PhCH₂O), 56.2 (q, Ar-OCH₃) ppm.

**HR-MS (ESI⁺):** m/z calculated for \([\text{C}_{24}\text{H}_{22}\text{BrO}_3]^+ = [\text{M}+\text{H}]^+\): 437.0747; found 437.0735 and \([\text{C}_{24}\text{H}_{22}{^81}\text{BrO}_3]^+ = [\text{M}+\text{H}]^+\): 439.0726; found 439.0732.
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)$_3$NCl (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$_2$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 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$^{-1}$):** $\nu_{max}$=2901, 2852, 1502, 1474, 1412, 1247, 1229, 1116, 1034, 978, 961, 933, 863, 838, 750 cm$^{-1}$.

$^1$H-NMR (CDCl$_3$, 400 MHz): $\delta$=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, ArCH=CH), 6.99 (d, 2H, $J$=2.4 Hz, Ar-H), 6.07 (dd, 1H, $J$=15.5 and 7.8 Hz, ArCH=CH), 5.94 (s, 2H, OCH$_2$O), 5.78 [d, 1H, $J$=7.8 Hz, PhCH(O)CH=CH], 5.22 (dd, 1H, $J$=12.2 and 2.4 Hz, PhCH$_2$H$_5$OCHCH=CH), 5.13 (d, 1H, $J$=12.2 Hz, PhCH$_2$H$_5$OCHCH=CH) ppm.

$^{13}$C-NMR (CDCl$_3$, 100 MHz): $\delta$=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=CH-Ar), 130.3 (d, Ar-CH-CH=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-CHCH=CH), 72.8 (t, Ph-CH$_2$OCHCH=CH) ppm.
**HR-MS (ESI⁺):** m/z calculated for \([\text{C}_{17}\text{H}_{13}\text{BrNaO}_3]⁺=[\text{M+Na}]⁺\): 366.9940; found 366.9938 and \([\text{C}_{17}\text{H}_{13}{^8}\text{BrNaO}_3]⁺=[\text{M+Na}]⁺\): 368.9920; found 368.9918.

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), NaHCO₃ (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. NaBH₄ (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. BF₃·Et₂O (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):** \(\nu_{\text{max}}\)=2928, 2847, 1502, 1462, 1439, 1380, 1256, 1160, 1024, 751 cm⁻¹.

**\(^1\text{H-NMR} (\text{CDCl}_3, 400 \text{ MHz}):** δ=7.30–7.15 (m, 4H, Ar-H), 7.00 (d, 1H, \(J=15.6\) Hz, ArCH=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=CH), 5.78 [d, 1H, \(J=7.8\) Hz, PhCH(O)CH=CH], 5.21 (dd, 1H, \(J=12.2\) and 2.4 Hz, PhCH=CH), 5.13 (d, 1H, \(J=12.2\) Hz, PhCH=CH), 3.83 (s, 3H, Ar-OCH₃), 3.81 (s, 3H, Ar-OCH₃) ppm.

**\(^{13}\text{C-NMR} (\text{CDCl}_3, 100 \text{ 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=CH-Ar), 129.8 (d, Ar-CH-CH=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-CHCH=CH), 72.8 (t, Ph-CH2OCHCH=CH), 56.0 (q, Ar-OCH3), 56.9 (q, Ar-OCH3) ppm.

**HR-MS (ESI⁺):** m/z calculated for \([\text{C}_{18}\text{H}_{17}\text{BrNaO}_3]^+=[\text{M}+\text{Na}]^+\): 383.0253; found 383.0254.

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)\(_3\)NCl (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\(_2\)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 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\(^{-1}\)):** \(v_{max}\)=2923, 2851, 1559, 1480, 1426, 1391, 1325, 1201, 1166, 1106, 1009, 926, 753 cm\(^{-1}\).

\(^1\)H-NMR (CDCl\(_3\), 400 MHz): \(\delta=7.45–7.15\) (m, 4H, Ar-H), 7.10 (d, 1H, \(J=15.6\) Hz, ArCH=CH), 6.87 (s, 1H, Ar-H), 6.13 (dd, 1H, \(J=15.6\) and 7.8 Hz, ArCH=CH), 5.81 [d, 1H, \(J=7.8\) Hz, PhCH(O)CH=CH], 5.23 (dd, 1H, \(J=12.2\) and 2.4 Hz, 214
PhCH$_2$H$_2$OCHCH=CH), 5.14 (d, 1H, $J$=12.2 Hz, PhCH$_2$H$_2$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): $\delta$=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=CH=CH-Ar), 130.9 (d, Ar-CH-CH=CH=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-CH=CH=CH), 72.9 (t, Ph-CH$_2$OCHCH=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$_2$O]$^+$: 373.0434; found 373.0416 and [C$_{19}$H$_{18}$S$_1$BrO$_3$]$^+$=[(M+H)–H$_2$O]$^+$: 375.0413; found 375.0401.

**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)$_3$NCl (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$_2$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 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$^{-1}$):** $\nu_{max}$=2956, 2922, 2852, 1600, 1500, 1455, 1383, 1260, 1166, 1025, 737, 697 cm$^{-1}$.
$^1$H-NMR (CDCl$_3$, 400 MHz): $\delta=7.50–7.25$ (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, ArCH=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=CH), 5.75 [d, 1H, $J=7.8$ Hz, ArCH(O)CH=CH], 5.18 (dd, 1H, $J=12.7$ and 2.0 Hz, ArCH$_2$H$_6$OCHCH=CH), 5.12 (d, 1H, $J=12.7$ Hz, ArCH$_4$H$_6$OCHCH=CH), 5.10 (s, 2H, PhCH$_2$O), 5.08 (s, 2H, PhCH$_2$O), 3.83 (s, 3H, Ar- OCH$_3$) ppm.

$^{13}$C-NMR (CDCl$_3$, 100 MHz): $\delta=159.1$ (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=CH-Ar), 130.3 (d, Ar-CH-CH=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-CH=CH), 72.7 (t, Ar-CH$_2$OCHCH=CH), 71.1 (t, PhCH$_2$O), 70.3 (t, PhCH$_2$O), 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$_{28}$Br$_{65}$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$_{28}$Br$_{65}$BrNaO$_4$]$^+$=[M+Na]$^+$: 567.0964; found 567.0977.

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)$_3$NCl (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 °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. BF₃·Et₂O (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 11i (119 mg, 44%) as brown viscous liquid. [TLC control (petroleum ether/ethyl acetate 90:10, Rᵣ(5i)=0.70, Rᵣ(4i)=0.30 and Rᵣ(11i)=0.55 UV detection)].

IR (MIR-ATR, 4000–600 cm⁻¹): νmax=2923, 2852, 1600, 1502, 1455, 1439, 1380, 1259, 1163, 1026, 737, 697 cm⁻¹.

¹H-NMR (CDCl₃, 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, ArCH=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=CH), 5.74 (d, 1H, J=7.8 Hz, ArCH(O)CH=CH), 5.17 (dd, 1H, J=12.2 and 2.0 Hz, ArCH₂H₆OCHCH=CH), 5.10 (d, 1H, J=12.2 Hz, ArCH₆H₆OCHCH=CH), 5.07 (s, 2H, PhCH₂O), 5.07 (s, 2H, PhCH₂O), 3.83 (s, 3H, Ar-OCH₃) ppm.

¹³C-NMR (CDCl₃, 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=CH=CH=CH=CH=CH=CH=CH=CH=CH=CH=CH=CH=CH=CH=CH=CH=CH), 130.2 (d, Ar-CH=CH=CH=CH=CH=CH=CH=CH=CH=CH=CH=CH=CH=CH=CH=CH=CH), 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-CH=CH=CH=CH=CH=CH=CH=CH=CH=CH=CH=CH=CH=CH=CH=CH=CH=CH), 71.1 (t, PhCH₂O), 70.3 (t, PhCH₂O), 56.1 (s, 3H, Ar-OCH₃) ppm.

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)$_3$NCl (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$_2$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 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$^{-1}$): $\nu_{\text{max}}$=2922, 2851, 1600, 1503, 1462, 1439, 1259, 1162, 1027, 801, 737, 697 cm$^{-1}$.

$^1$H-NMR (CDCl$_3$, 400 MHz): $\delta$=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, ArCH=CH), 7.01 (s, 1H, Ar-H), 7.00 (s, 1H, Ar-H), 6.91 (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=CH), 5.75 [d, 1H, $J$=7.8 Hz, ArCH(O)CH=CH], 5.18 (dd, 1H, $J$=12.2 and 2.4 Hz, ArCH$_2$H$_2$OCHCH=CH), 5.09 (d, 1H, $J$=12.2 Hz, ArCH$_2$H$_2$OCHCH=CH), 5.07 (s, 2H, PhCH$_2$O), 3.86 (s, 3H, Ar-OCH$_3$), 3.83 (s, 3H, Ar-OCH$_3$) ppm.

$^{13}$C-NMR (CDCl$_3$, 100 MHz): $\delta$=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=CH-Ar),
130.1 (d, Ar-CH-CH=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-CHCH=CH), 72.7 (t, Ar-CH₂OCHCH=CH), 70.3 (t, PhCH₂O), 56.1 (q, Ar-OCH₃), 55.9 (q, Ar-OCH₃) ppm.

**HR-MS (ESI⁺):** m/z calculated for [C₂₅H₂₄BrO₄]⁺=[M+H]⁺: 467.0852; found 467.0824 and [C₂₅H₂₄⁸¹BrO₄]⁺=[M+H]⁺: 469.0832; found 469.0817, [C₂₅H₂₃BrNaO₄]⁺=[M+Na]⁺: 489.0672; found 489.0646 and [C₂₅H₂₃⁸¹BrNaO₄]⁺=[M+Na]⁺: 491.0651; found 491.0649.

**1H-NMR (CDCl₃, 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, 1H, J=7.8 and 1.5 Hz, Ar-H), 7.15–7.00 (m, 3H,
Ar-H and ArCH=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=CH), 5.75 [d, 1H, J=7.8 Hz, ArCH(O)CH=CH], 5.18 (dd, 1H, J=12.2 and 2.4 Hz, ArCH$_2$H$_5$OCHCH=CH), 5.09 (d, 1H, J=12.2 Hz, ArCH$_2$H$_5$OCHCH=CH), 3.81 (s, 3H, Ar-OC$_3$H$_3$) 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=CH-Ar), 129.0 (d, Ar-CH=CH=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-CHCH=CH), 72.8 (t, Ar-CH$_2$OCHCH=CH), 55.6 (q, Ar-OC$_3$H$_3$) ppm.

HR-MS (ESI$^+$) m/z calculated for [C$_{17}$H$_{15}$BrNaO$_2$]$^+=[M+Na]: 353.0148; found 353.0164.

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)$_3$NCl (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$_2$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 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\(^{-1}\)): \(\nu_{max} = 2957, 2922, 2852, 1594, 1465, 1284, 1241, 1016, 804\) cm\(^{-1}\).

\(^1\)H-NMR (CDCl\(_3\), 400 MHz): \(\delta = 7.42\) (d, 1H, \(J = 8.8\) Hz, Ar-H), \(\delta = 7.10\) (d, 1H, \(J = 8.3\) Hz, Ar-H), \(\delta = 7.04\) (d, 1H, \(J = 3.3\) Hz, Ar-H), \(7.02\) (d, 1H, \(J = 15.6\) Hz, ArCH=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=CH), 5.75 [d, 1H, \(J = 7.8\) Hz, ArCH(O)CH=CH], 5.19 (dd, 1H, \(J = 12.2\) and 2.4 Hz, ArCH\(_2\)H\(_0\)OCHCH=CH), 5.10 (d, 1H, \(J = 12.2\) Hz, ArCH\(_2\)H\(_0\)OCHCH=CH), 3.81 (s, 3H, Ar-OCH\(_3\)), 3.76 (s, 3H, Ar-OCH\(_3\)) ppm.

\(^{13}\)C-NMR (CDCl\(_3\), 100 MHz): \(\delta = 160.0\) (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=CH-Ar), 130.5 (d, Ar-CH-CH=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-CHCH=CH), 72.8 (t, Ar-CH\(_2\)OCHCH=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.

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\(_3\))NCl (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 \(^\circ\)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\(_2\)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 8:20), furnished the product 11kj (103 mg, 44%) as brown viscous liquid. [TLC control (petroleum ether/ethyl acetate 90:10, Rf(5j)=0.70, Rf(4k)=0.30 and Rf(11kj)=0.40 UV detection)].

**IR (MIR-ATR, 4000–600 cm⁻¹):** \( \nu_{max} = 2924, 2853, 1597, 1497, 1465, 1261, 1201, 1166, 1117, 1029, 813, 743, 698 \text{ cm}^{-1} \).  

**\(^1\text{H}-\text{NMR (CDCl}_3, \text{ 400 MHz):****} \( \delta = 7.42 \) (d, 2H, \( J = 7.3 \text{ Hz, Ar-H} \)), 7.37 (dd, 2H, \( J = 7.8 \text{ and 7.3 Hz, Ar-H} \)), 7.31 (t, 1H, \( J = 7.3 \text{ Hz, Ar-H} \)), 7.10 (d, 1H, \( J = 8.3 \text{ Hz, Ar-H} \)), 7.06 (s, 1H, Ar-H), 7.04 (s, 1H, Ar-H), 6.99 (d, 1H, \( J = 15.6 \text{ Hz, ArCH=CH} \)), 6.84 (dd, 1H, \( J = 8.3 \text{ and 2.0 Hz, Ar-H} \)), 6.79 (d, 1H, \( J = 2.0 \text{ Hz, Ar-H} \)), 6.10 (dd, 1H, \( J = 15.6 \text{ and 7.8 Hz, ArCH=CH} \)), 5.75 (d, 1H, \( J = 7.8 \text{ Hz, ArCH(O)CH=CH} \)), 5.19 (dd, 1H, \( J = 12.2 \text{ and 2.4 Hz, ArCH}_2\text{H}_6\text{OCHCH=CH} \)), 5.10 (s, 2H, PhCH=O), 5.09 (d, 1H, \( J = 12.2 \text{ Hz, ArCH}_2\text{H}_6\text{OCHCH=CH} \)), 3.83 (s, 3H, Ar-OCH), 3.81 (s, 3H, Ar-OCH) ppm.

**\(^{13}\text{C}-\text{NMR (CDCl}_3, \text{ 100 MHz):****} \( \delta = 159.9 \) (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=CH=Ar), 130.3 (d, Ar-CH-CH=CH=Ar), 128.8 (s, Ar-C), 128.6 (d, 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-CH=CH=CH), 72.7 (t, Ar-CH=CH=CH), 71.1 (t, PhCH=O), 56.1 (q, Ar-OCH), 55.5 (q, Ar-OCH) ppm.

**HR-MS (ESI⁺):** m/z calculated for \([\text{C}_{25}\text{H}_{24}\text{BrO}_{4}]^{+} = [\text{M+H}]^{+}\): 467.0852; found 467.0826 and \([\text{C}_{25}\text{H}_{24}\text{BrO}_{4}]^{+} = [\text{M+H}]^{+}\): 469.0832; found 469.0812.

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)$_3$NCl (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$_2$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 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$^{-1}$):** $\nu_{max}$=2921, 2852, 1605, 1500, 1474, 1235, 1106, 1036, 932, 870, 822 cm$^{-1}$.

$^1$H-NMR (CDCl$_3$, 400 MHz): $\delta$=7.07 (d, 1H, $J$=8.3 Hz, Ar-H), 6.99 (s, 2H, Ar-H), 6.98 (d, 1H, $J$=15.6 Hz, ArCH=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=CH), 5.94 (s, 2H, OCH$_2$O), 5.72 [d, 1H, $J$=7.8 Hz, ArCH(O)CH=CH], 5.17 (dd, 1H, $J$=12.2 and 2.4 Hz, ArCH$_2$H$_b$OCHCH=CH), 5.08 (d, 1H, $J$=12.2 Hz, ArCH$_a$H$_b$OCHCH=CH), 3.81 (s, 3H, Ar-OCH$_3$) ppm.

$^{13}$C-NMR (CDCl$_3$, 100 MHz): $\delta$=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=CH-Ar), 130.2 (d, Ar-CH-CH=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$_2$O), 84.7 (d, Ar-CHCH=CH), 72.7 (t, Ar-CH$_2$OCHCH=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.
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)$_3$NCl (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$_2$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 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$^{-1}$):** $\nu_{max}$=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):** $\delta$=7.08 (d, 1H, $J$=8.8 Hz, Ar-H), 7.06 (d, 1H, $J$=15.6 Hz, ArCH=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=CH), 5.75 (d, 1H, $J$=7.8 Hz, ArCH(O)CH=CH), 5.18 (dd, 1H, $J$=12.2 and 2.4 Hz, ArCH$_2$H$_6$OCHCH=CH), 5.09 (d, 1H, $J$=12.2 Hz, ArCH$_2$H$_6$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):** $\delta$=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=CH-Ar), 130.6 (d, Ar-CH-CH=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-CHCH=CH), 72.7 (t, Ar-
CH₂OCHCH=CH), 61.1 (q, Ar-OCH₃), 60.9 (q, Ar-OCH₃), 56.1 (q, Ar-OCH₃), 55.5 (q, Ar-OCH₃) ppm.

**HR-MS (ESI⁺):** m/z calculated for [C₂₀H₂₁BrNaO₅]⁺=[M+Na]⁺: 443.0465; found 443.0448.

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), Bu(NH)₃Cl (114.0 mg, 0.50 mmol), NaHCO₃ (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. NaBH₄ (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. BF₃·Et₂O (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.

**¹H-NMR (CDCl₃, 400 MHz):** δ=5.50–7.27 (m, 6H, Ar-H), 7.14 (d, 1H, J=2.9 Hz, Ar-H), 7.01 (d, 1H, J=15.6 Hz, ArCH=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=CH), 5.97 (d, 1H, J=2.9 Hz, OCH₃H₆O), 5.97 (d, 1H, J=2.9 Hz, OCH₃H₆O), 5.70 (d, 1H, J=7.8 Hz, ArCH(O)CH=CH), 5.12 (dd, 1H, J=11.7 and 2.9 Hz,
ArCH₃H₉OCHCH=CH), 5.04 (d, 1H, J=11.7 Hz, ArCH₃H₉OCHCH=CH), 5.01 (s, 2H, PhCH₂O) ppm.

**¹³C-NMR (CDCl₃, 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=CH-Ar), 133.4 (s, Ar-C), 132.3 (d, Ar-CH-CH=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, OCH₂O), 84.9 (d, Ar-CHCH=CH), 72.9 (t, Ar-CH₂OCHCH=CH), 70.2 (t, PhCH₂O) ppm.

**HR-MS (ESI⁺):** m/z calculated for [C₂₄H₁₉BrNaO₄]⁺=[M+Na]⁺: 473.0359; found 473.0330 and [C₂₄H₁₉BrNaO₄]⁺=[M+Na]⁺: 475.0338; found 475.0317.

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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)₃NCl (114.0 mg, 0.50 mmol), NaHCO₃ (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. NaBH₄ (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. BF₃·Et₂O (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, Rₗ(5m)=0.70, Rₗ(4l)=0.30 and Rₗ(11lm)=0.50 UV detection)].
IR (MIR-ATR, 4000–600 cm⁻¹): $\nu_{\text{max}}$=2956, 2924, 2853, 1598, 1502, 1439, 1259, 1162, 1033, 852, 803, 735, 698 cm⁻¹.

$^1$H-NMR (CDCl₃, 400 MHz): $\delta$=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, ArCH=CH), 6.88 (s, 1H, Ar-H), 6.68 (s, 1H, Ar-H), 6.60 (s, 1H, Ar-H), 6.96 (dd, 1H, $J$=15.6 and 7.8 Hz, ArCH=CH), 5.97 (d, 2H, OCH₂O), 5.67 (d, 1H, $J$=7.8 Hz, ArCH(O)CH=CH), 5.11 (dd, 1H, $J$=11.7 and 2.9 Hz, ArCH₃H₆OCHCH=CH), 5.07 (s, 2H, PhCH₂O), 5.02 (dd, 1H, $J$=11.7 and 2.9 Hz, ArCH₃H₆OCHCH=CH), 3.85 (s, 3H, Ar-OCH₃) ppm.

$^{13}$C-NMR (CDCl₃, 100 MHz): $\delta$=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=CH-Ar), 130.0 (d, Ar-CH-CH=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, OCH₂O), 85.1 (d, Ar-CHCH=CH), 72.8 (t, Ar-CH₂OCHCH=CH), 71.2 (t, PhCH₂O), 56.2 (q, Ar-OCH₃) ppm.

HR-MS (ESI⁺): m/z calculated for [C₂₅H₂₂BrO₅]⁺=[M+H]⁺: 481.0645; found 481.0615 and [C₂₅H₂₂BrO₅]⁺=[M+H]⁺: 483.0625; found 483.0602, [C₂₅H₂₁BrNaO₃]⁺=[M+Na]⁺: 503.0465; found 503.0438 and [C₂₅H₂₁BrO₅Na₂]⁺=[M+Na]⁺: 505.0444; found 505.0422.

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), NaHCO₃ (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. NaBH₄ (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. BF₃.Et₂O (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, Rᶠ(5m)=0.70, Rᶠ(4n)=0.30 and Rᶠ(11nm)=0.55 UV detection)].

IR (MIR-ATR, 4000–600 cm⁻¹): \( ν_{max} = 2924, 2852, 1600, 1503, 1473, 1380, 1261, 1208, 1163, 1035, 937, 860, 736, 698, 665 \text{ cm}^{-1} \).

¹H-NMR (CDCl₃, 400 MHz): \( δ = 7.00 \text{ (s, 2H, Ar-H), 6.98 (d, 1H, } J = 15.6 \text{ Hz, ArCH=CH), 6.67 (s, 1H, Ar-H), 6.63 (s, 1H, Ar-H), 6.06 (dd, 1H, } J = 15.6 \text{ and 7.8 Hz, ArCH=CH), 5.97 (d, 1H, } J = 2.9 \text{ Hz, OCH₃H₂O), 5.96 (d, 1H, } J = 2.9 \text{ Hz, OCH₃H₆O), 5.69 (d, 1H, } J = 7.8 \text{ Hz, ArCH(O)CH=CH), 5.11 (dd, 1H, } J = 11.7 \text{ and 2.0 Hz, ArCH₃H₆OCHCH=CH), 5.02 (dd, 1H, } J = 11.7 \text{ and 2.0 Hz, ArCH₃H₆OCHCH=CH), 3.86 (s, 3H, Ar-OCH₃), 3.83 (s, 3H, Ar-OCH₃) \text{ ppm.}

¹³C-NMR (CDCl₃, 100 MHz): \( δ = 149.5 \text{ (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=CH=CH=CH=CH), 130.0 (d, Ar-CH-CH=CH=CH=CH=CH), 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, OCH₂O), 85.2 (d, Ar-CHCH=CH), 72.8 (t, Ar-CH₂OCHCH=CH), 56.1 (q, Ar-OCH₃), 56.0 (q, Ar-OCH₃) \text{ ppm.}

HR-MS (ESI⁺): m/z calculated for [C₁₉H₁₇BrNaO₅]⁺=[M+Na]⁺: 427.0152; found 427.0127 and [C₁₉H₁₇¹⁸BrNaO₅]⁺=[M+Na]⁺: 429.0137; found 429.0121, HR-MS (ESI⁺) m/z calculated for [C₁₉H₁₈BrO₅]⁺=[M+H]⁺: 405.0332; found 405.0304 and [C₁₉H₁₈¹⁸BrO₅]⁺=[M+H]⁺: 407.0312; found 407.0294.
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)$_3$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 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$_2$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 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$^{-1}$): $\nu_{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): $\delta=7.05$ (d, 1H, $J=15.6$ Hz, ArCH=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=CH), 5.96 (d, 1H, $J=2.9$ Hz, OCH$_3$H$_2$O), 5.95 (d, 1H, $J=2.9$ Hz, OCH$_3$H$_2$O), 5.69 (d, 1H, $J=7.8$ Hz, ArCH(O)CH=CH), 5.11 (dd, 1H, $J=11.7$ and 2.9 Hz, ArCH$_3$H$_2$OCHCH=CH), 5.03 (dd, 1H, $J=11.7$ and 2.9 Hz, ArCH$_3$H$_2$OCHCH=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): $\delta=152.6$ (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=CH-Ar), 130.8 (d, Ar-CH-CH=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$_3$O), 85.0 (d, Ar-
(CHCH=CH), 72.9 (t, Ar-CH₂OCHCH=CH), 61.1 (q, Ar-OCH₃), 60.9 (q, Ar-OCH₃), 56.1 (q, Ar-OCH₃) ppm.

**HR-MS (ESI⁺):** m/z calculated for [C₂₀H₁₉BrNaO₆]⁺=[M+Na]⁺: 457.0257; found 457.0257 and [C₂₀H₁₉BrNaO₆]⁺=[M+Na]⁺: 459.0237; found 459.0236.

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), NaHCO₃ (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. NaBH₄ (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. BF₃·Et₂O (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.

**¹H-NMR (CDCl₃, 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, ArCH=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=CH), 5.75 (d, 1H, J=8.3 Hz, ArCH(O)CH=CH), 5.18 (dd, 1H, J=11.7 and 2.0 Hz, ArCH₂H₆OCHCH=CH), 5.10 (s, 2H, PhCH₂O), 5.07 (dd, 1H,
\( J = 11.2 \) and 2.9 Hz, \( \text{ArCH}_2H_2\text{OCHCH}=\text{CH} \), 3.88 (s, 3H, \( \text{Ar-OCH}_3 \)), 3.86 (s, 3H, \( \text{Ar-OCH}_3 \)), 3.83 (s, 3H, \( \text{Ar-OCH}_3 \)) ppm.

\( ^{13}\text{C}-\text{NMR (CDCl}_3, 100 \text{ MHz}): \delta = 149.3 \) (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-CH=CH=CH), 73.0 (t, Ar-CH=CH=CH=CH), 71.1 (t, PhCH2O), 56.2 (q, Ar-OCH3), 56.1 (q, Ar-OCH3), 56.0 (q, Ar-OCH3) ppm.

\( \text{HR-MS (ESI}^+): \) m/z calculated for \([\text{C}_{26}\text{H}_{25}\text{BrNaO}_5]^+=[\text{M+Na}]^+: \) 519.0778; found 519.0753 and \([\text{C}_{26}\text{H}_{25}\text{NaO}_5]^+=[\text{M+Na}]^+: \) 521.0757; found 521.0735.

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), \( \text{Bn(Et)}_3\text{NCl} \) (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 \( ^\circ \)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\(_2\)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 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): \( \nu_{\text{max}} = 2924, 2852, 1600, 1504, 1462, 1264, 1210, 1163, 1121, 1029, 863 \) cm⁻¹.

\(^1\)H-NMR (CDCl₃, 400 MHz): \( \delta = 7.02 \) (s, 1H, Ar-H), 7.01 (d, 1H, \( J = 15.6 \) Hz, ArCH=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=CH), 5.74 (d, 1H, \( J = 7.8 \) Hz, ArCH(O)CH=CH), 5.17 (dd, 1H, \( J = 11.2 \) and 2.9 Hz, ArCH₃OCHCH=CH), 3.88 (s, 3H, Ar-OCH₃), 3.86 (s, 6H, Ar-OCH₃), 3.83 (s, 3H, Ar-OCH₃) ppm.

\(^13\)C-NMR (CDCl₃, 100 MHz): \( \delta = 149.5 \) (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=CH-Ar), 130.1 (d, Ar-CH-CH=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-CHCH=CH), 73.0 (t, Ar-CH₂OCHCH=CH), 56.2 (q, Ar-OCH₃), 56.1 (q, Ar-OCH₃), 56.0 (q, Ar-OCH₃), 55.9 (q, Ar-OCH₃) ppm.

HR-MS (ESI⁺): m/z calculated for \([\text{C}_{20}\text{H}_{21}\text{BrNaO}_5]^+ = [\text{M+Na}]^+\): 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), NaHCO₃ (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. NH₄Cl 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 NaBH₄ (1.50 mmol), stirred for two hours at rt. The reaction mixture was quenched with saturated aq. NH₄Cl solution and extracted with ethyl acetate (3 × 20 mL). The organic layer was washed with saturated NaCl solution, dried over anhydrous Na₂SO₄ 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 \(-40\, ^\circ\text{C}\), BF$_3$Et$_2$O (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 \times 20 \, \text{mL}).

The organic layers were dried over anhydrous Na$_2$SO$_4$, 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%).

(2E)-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$^{-1}$):** $\nu_{\max}$=3330, 1485, 1459, 1006, 967, 753, 564 cm$^{-1}$.

**$^1$H-NMR (CDCl$_3$, 400 MHz):** $\delta$=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, ArCH=CH), 6.21 (dd, 1H, $J$=15.6 and 5.9 Hz, ArCH=CH), 5.47 [d, 1H, $J$=5.9 Hz, PhCH(OH)CH=CH], 4.63 (d, 1H, $J$=12.2 Hz, PhCH$_2$H$_2$OH), 4.62 (d, 1H, $J$=12.2 Hz, PhCH$_2$H$_2$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):** $\delta$=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=CH-Ar), 130.4 (d, Ar-CH), 128.7 (d, Ar-CH-CH=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 $\times$ d, 2C, Ar-CH), 125.9 (d, Ar-CH), 71.4 (d, Ph-CHCH=CH), 63.1 (t, Ph-CH$_2$OH), 19.1 (q, Ar-CH$_3$) ppm.

**HR-MS (ESI$^+$):** m/z calculated for [C$_{17}$H$_{18}$NaO$_2$]$^+$=[M+Na]$^+$: 277.1199; found d277.1197.
(2E)-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$^{-1}$):** $\nu_{\text{max}}=3320, 1597, 1489, 1461, 1244, 1023, 753$ cm$^{-1}$.  

**$^1$H-NMR (CDCl$_3$, 400 MHz):** $\delta=7.39$ (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, ArCH=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=CH), 5.52 [d, 1H, $J=5.9$ Hz, PhCH(OH)CH=CH], 4.66 (s, 2H, ArCH$_2$OH), 3.77 (s, 3H, Ar-OCH$_3$), 3.64 (br.s, 2H, 2 $\times$ OH) ppm.

**$^{13}$C-NMR (CDCl$_3$, 100 MHz):** $\delta=156.7$ (s, Ar-C), 141.1 (s, Ar-C), 138.5 (s, Ar-C), 131.0 (d, Ar-CH-CH=CH-Ar), 130.0 (d, Ar-CH), 128.8 (d, Ar-CH-CH=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-CHCH=CH), 63.5 (t, Ph-CH$_2$OH), 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.
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$^{-1}$):** $v_{max}$=2924, 2853, 1731, 1460, 1029, 965, 747, 697 cm$^{-1}$.

**$^1$H-NMR (CDCl$_3$, 400 MHz):** $\delta$=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, ArCH=CH), 6.16 (dd, 1H, $J=15.6$ and 7.8 Hz, ArCH=CH), 5.79 [d, 1H, $J=7.8$ Hz, PhCH(O)CH=CH], 5.23 (dd, 1H, $J=12.2$ and 2.4 Hz, PhCH$_a$H$_b$OCHCH=CH), 5.14 (d, 1H, $J=12.2$ Hz, PhCH$_a$H$_b$OCHCH=CH), 2.39 (s, 3H, Ar-CH$_3$) ppm.

**$^{13}$C-NMR (CDCl$_3$, 100 MHz):** $\delta$=141.0 (s, Ar-C), 139.2 (s, Ar-C), 135.7 (s, Ar-C), 135.5 (s, Ar-C), 130.3 (2 $\times$ d, 2C, Ar-CH=CH=CH-Ar and Ar-CH), 129.9 (d, Ar-CH), 127.7 (2 $\times$ d, 2C, Ar-CH=CH=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-CHCH=CH), 72.8 (t, Ph-CH$_2$OCHCH=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.

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$^{-1}$):** $v_{max}$=2904, 2838, 1489, 1461, 1244, 1028, 749, 697 cm$^{-1}$.
1H-NMR (CDCl₃, 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, ArCH=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=CH), 5.78 [d, 1H, J=7.8 Hz, PhCH(O)CH=CH], 5.23 (dd, 1H, J=12.2 and 2.4 Hz, PhCH₄H₄OCHCH=CH), 5.13 (d, 1H, J=12.2 Hz, PhCH₄H₄OCHCH=CH), 3.86 (s, 3H, Ar-OCH₃) ppm.

13C-NMR (CDCl₃, 100 MHz):  δ=156.9 (s, Ar-C), 141.2 (s, Ar-C), 139.2 (s, Ar-C), 129.4 (d, Ar-CH-CH=CH=Ar), 128.9 (d, Ar-CH), 127.6 (d, Ar-CH-CH=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-CHCH=CH), 72.7 (t, Ph-CH₂OCHCH=CH), 55.4 (q, Ar-OCH₃) ppm.

HR-MS (ESI+): m/z calculated for [C₁₇H₁₇O₂]⁺=[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.1.1: $^1$H-NMR (400 MHz) spectrum of 6ne in CDCl$_3$

Figure II.1.2: $^{13}$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. In literature, molecules containing (Z)-enediyynes 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.\textsuperscript{71,72,73}

Usually, this reaction was performed by using either Pd(PPh\textsubscript{3})\textsubscript{2}Cl\textsubscript{2} or Pd(PPh\textsubscript{3})\textsubscript{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.\textsuperscript{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,\textsuperscript{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,\textsuperscript{76} performing the reaction in aqueous medium,\textsuperscript{77} solvent-free
reaction conditions etc.,\textsuperscript{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.

\textbf{III.2 BACKGROUND:}

In the year 1975, three research groups independently developed a method for
the synthesis of bi-aryl acetylenes \textsuperscript{20} by Heck,\textsuperscript{79} Cassar\textsuperscript{80} Sonogashira and Hagihara\textsuperscript{81}
Heck’s strategy was based on the known Mizoroki-Heck reaction and by using \( \text{Pd(OAc)}_2 \) and \( \text{Ph}_3\text{P} \) as a catalytic system and triethylamine as a base as well as a solvent, whereas Cassar’s process involved the use of \( \text{Pd(PPh}_3)_4 \) 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).
Ryu et al. disclosed a novel copper-free Sonogashira coupling reaction for the synthesis of bi-aryl substituted acetylenes 20 by using ionic liquid ([BMI][PF₆]) and the products were obtained in very good to excellent yields (Scheme III.3).³³

Matthias Beller and co-workers presented a very convenient and novel strategy for the synthesis of bi-aryl acetylenes 20 directly from aromatic anis signals 5 and terminal aryl acetylene 8 by in-situ generated arenediazonium salts (Scheme III.4).³⁴
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

\[
\begin{align*}
\text{R}^1 & \quad \text{H} \quad \text{R}^1 \quad \text{R}^1
\end{align*}
\]

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

\[
\begin{align*}
\text{R}^1 & \quad \text{COOH} \\
\text{R}^2 & \quad \text{X} & \quad \text{X} & \quad \text{X}
\end{align*}
\]

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

\[
\begin{align*}
\text{R}^1 & \quad \text{COOH} \\
\text{R}^2 & \quad \text{X} & \quad \text{X}
\end{align*}
\]
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

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
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).\textsuperscript{90}

\begin{align*}
\text{Scheme III.10}
\end{align*}

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).\textsuperscript{91}

\begin{align*}
\text{Scheme III.11}
\end{align*}

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). \(^9\)

$$\text{R}_{14} + \text{R}_{7} \xrightarrow{\text{Cul (15 mol%), \text{8-hydroxy quinoline (30 mol%)}, \text{K}_{2}\text{CO}_{3}, \text{DMF, 110 °C, 24 h}}} \text{R}_{20} (17-73\%)$$

**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). \(^9\)

$$\text{R}_{1} + \text{H} = \text{H} \xrightarrow{\text{PdCl}_{2}(\text{PPh}_{3})_{2}, \text{Cul, \text{Piperidine/CH}_{3}\text{CN reflux}}} \text{R}_{20} (65\%)$$

**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). \(^9\)

$$\text{R}_{2} + \text{R}_{16} \xrightarrow{\text{PdCl}_{2}(\text{PPh}_{3})_{2} (6 \text{~mol\%}), \text{Cul (10 mol\%)}, \text{amidine base, benzene, H}_{2}\text{O rt or 60-80 °C, 18 h}}} \text{R}_{20} (80-95\%)$$

**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). \(^9\)
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).  

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.  

In this regard, as described above, many research groups used different alkyne sources such as terminal aryl alkyne, 2-methylbut-3-yn-2-ol 12, propiolic acid 9 or 2-ccetylenedicarboxylic acid 11, gaseous acetylene 15, trimethylsilyl acetylene 16, bis(trimethylsilyl)acetylene 17, bis(tributylstannyl)acetylene 18. 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 and ionic liquids. As a part of our ongoing research interest on transition-metal mediated organic transformations in one-pot
fashion, 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).

Thus, the domino Sonogashira cross-coupling of lithium acetylide \( \text{19} \) with aryl halide \( \text{1/2} \) 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 \( \text{Pd(OAc)}_2 \) (2 mol\%) and \( \text{PPh}_3 \) (4 mol\%), in DMA and using \( \text{K}_2\text{CO}_3 \) as the base at 100 °C furnished product \( \text{20i} \) 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)\( \text{3} \) (15%, Table III.1, entry 2). Interestingly, the yield was improved to 66% with the \( \text{Pd(PPh}_3)_2\text{Cl}_2 \) (Table III.1, entry 3). Similarly, with other ligands such as Diphos, Mephos and dpephos, furnished the product \( \text{20i} \) 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 \( \text{CH}_3\text{CN} \) at 80 °C (50%, Table III.1, entry 7). Interestingly, by switching the solvent to DMF, it delivered the product \( \text{20i} \) in very good yield (80%, Table III.1, entry 8). Also, the ligand dpf proved to be good in DMA solvent (79%, Table III.1, entry 9). Interestingly, using Xantphos in DMA furnished the product \( \text{20i} \) in excellent yield (95%, Table III.1, entry 10). The other variation with different bases furnished the product \( \text{20i} \) in poor to moderate yields (Table III.1, entries 11 to 13). However, the reaction with excess of aryl bromide \( \text{1i} \) gave the product \( \text{20i} \) 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.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst (mol%)</th>
<th>Ligand (mol%)</th>
<th>Base (2 equiv)</th>
<th>Solvent (2 mL)</th>
<th>Temp (°C)</th>
<th>Time (h)</th>
<th>Yield of 20i (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Pd(OAc)₂ (5)</td>
<td>PPh₃ (10)</td>
<td>K₂CO₃</td>
<td>DMA</td>
<td>100</td>
<td>3</td>
<td>42</td>
</tr>
<tr>
<td>2.</td>
<td>Pd(OAc)₂ (2)</td>
<td>P(2-furyl)₃ (4)</td>
<td>K₂CO₃</td>
<td>DMA</td>
<td>100</td>
<td>2</td>
<td>15</td>
</tr>
<tr>
<td>3.</td>
<td>Pd (PPh₃)₂Cl₂ (2)</td>
<td>-</td>
<td>K₂CO₃</td>
<td>DMA</td>
<td>100</td>
<td>3</td>
<td>66</td>
</tr>
<tr>
<td>4.</td>
<td>Pd(OAc)₂ (2)</td>
<td>DiPhos (4)</td>
<td>K₂CO₃</td>
<td>DMA</td>
<td>100</td>
<td>3</td>
<td>50</td>
</tr>
<tr>
<td>5.</td>
<td>Pd(OAc)₂ (2)</td>
<td>MePhos (4)</td>
<td>K₂CO₃</td>
<td>DMA</td>
<td>100</td>
<td>2</td>
<td>58</td>
</tr>
<tr>
<td>6.</td>
<td>Pd(OAc)₂ (2)</td>
<td>DPEPhos (4)</td>
<td>K₂CO₃</td>
<td>DMA</td>
<td>100</td>
<td>2</td>
<td>68</td>
</tr>
<tr>
<td>7.</td>
<td>Pd(OAc)₂ (2)</td>
<td>Xantphos (4)</td>
<td>K₂CO₃</td>
<td>CH₃CN</td>
<td>80</td>
<td>12</td>
<td>50</td>
</tr>
<tr>
<td>8.</td>
<td>Pd(OAc)₂ (2)</td>
<td>Xantphos (4)</td>
<td>K₂CO₃</td>
<td>DMF</td>
<td>100</td>
<td>3</td>
<td>80</td>
</tr>
<tr>
<td>9.</td>
<td>Pd(OAc)₂ (2)</td>
<td>dppf (4)</td>
<td>K₂CO₃</td>
<td>DMA</td>
<td>100</td>
<td>3</td>
<td>79</td>
</tr>
<tr>
<td>10.</td>
<td>Pd(OAc)₂ (2)</td>
<td>Xantphos (4)</td>
<td>K₂CO₃</td>
<td>DMA</td>
<td>100</td>
<td>3</td>
<td>95</td>
</tr>
<tr>
<td>11.</td>
<td>Pd(OAc)₂ (2)</td>
<td>Xanthos (4)</td>
<td>TEA</td>
<td>DMA</td>
<td>100</td>
<td>2</td>
<td>52</td>
</tr>
<tr>
<td>12.</td>
<td>Pd(OAc)₂ (2)</td>
<td>Xanthos (4)</td>
<td>DIPEA</td>
<td>DMA</td>
<td>100</td>
<td>2</td>
<td>30</td>
</tr>
<tr>
<td>13.</td>
<td>Pd(OAc)₂ (2)</td>
<td>Xanthos (4)</td>
<td>Cy₂NMe</td>
<td>DMA</td>
<td>100</td>
<td>2</td>
<td>41</td>
</tr>
<tr>
<td>14.</td>
<td>Pd(OAc)₂ (2)</td>
<td>Xanthos (4)</td>
<td>K₂CO₃</td>
<td>DMA</td>
<td>100</td>
<td>3</td>
<td>30</td>
</tr>
<tr>
<td>15.</td>
<td>Pd(OAc)₂ (2)</td>
<td>Xanthos (4)</td>
<td>K₂CO₃</td>
<td>DMA</td>
<td>100</td>
<td>3</td>
<td>55</td>
</tr>
</tbody>
</table>

*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$_2$CO$_3$, in DMA as a solvent at 100 °C]. 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 $\delta$ 8.39 having $J$=1.5 and 1.5 Hz accounts for two aromatic protons, doublet of a doublet at $\delta$ 8.22 having $J$=8.3 and 1.5 Hz accounts for two aromatic protons, doublet at $\delta$ 7.85 having $J$=7.8 Hz accounts for two aromatic protons, doublet of a doublet at $\delta$ 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 $\delta$ 148.2 (2C), 124.0 (2C) were due to four aromatic carbon, the presence of eight aromatic methine carbons resonates at $\delta$ 137.4 (2C), 129.6 (2C), 126.6 (2C) and 123.6 (2C) and presence $\delta$ 89.1 ppm was due to acetylenic carbons. The presence of the [M+Na]$^+$ peak at m/z [C_{14}H_{8}N_{2}NaO_{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.

![Chemical Reaction Diagram]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrates (1a-1m)</th>
<th>Products (20a-20m)</th>
<th>Time (h)</th>
<th>Yield (%)$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>1a</td>
<td>20a</td>
<td>0.25</td>
<td>75</td>
</tr>
<tr>
<td>2.</td>
<td>1b</td>
<td>20b</td>
<td>1.0</td>
<td>88</td>
</tr>
<tr>
<td>3.</td>
<td>1c</td>
<td>20c</td>
<td>1.0</td>
<td>83</td>
</tr>
<tr>
<td>4.</td>
<td>1d</td>
<td>20d</td>
<td>1.0</td>
<td>76</td>
</tr>
<tr>
<td>5.</td>
<td>1e</td>
<td>20e</td>
<td>1.0</td>
<td>70</td>
</tr>
<tr>
<td>6.</td>
<td>1f</td>
<td>20f</td>
<td>0.5</td>
<td>72</td>
</tr>
<tr>
<td>7.</td>
<td>1g</td>
<td>20g</td>
<td>0.25</td>
<td>74</td>
</tr>
<tr>
<td>8.</td>
<td>1h</td>
<td>20h</td>
<td>0.25</td>
<td>69</td>
</tr>
<tr>
<td>9.</td>
<td>1i</td>
<td>20i</td>
<td>3.0</td>
<td>95</td>
</tr>
<tr>
<td>10.</td>
<td>1j</td>
<td>20j</td>
<td>0.5</td>
<td>70</td>
</tr>
<tr>
<td>11.</td>
<td>1k</td>
<td>20k</td>
<td>0.25</td>
<td>60</td>
</tr>
<tr>
<td>12.</td>
<td>1l</td>
<td>20l</td>
<td>12.0</td>
<td>73</td>
</tr>
<tr>
<td>13.</td>
<td>1m</td>
<td>20m</td>
<td>1.0</td>
<td>80</td>
</tr>
</tbody>
</table>
All reactions were carried out on 0.5 mmol scale of 1 in 2 mL of DMA (0.25 M). Isolated yields of chromatographically pure products. 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 acetylenes 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-j.

\[
\begin{align*}
\text{Entry} & \quad \text{Substrates (2a-j)} & \quad \text{Products (20a-20r)} & \quad \text{Time (h)} & \quad \text{Yield (%)} \\
1 & \quad \begin{array}{c}
\text{O}_2\text{N} \\
\begin{array}{c}
\text{CH}_2\text{I} \\
\text{MeO} \\
\text{MeO}
\end{array}
\end{array} & \quad \begin{array}{c}
\text{O}_2\text{N} \\
\begin{array}{c}
\text{CH}_2\text{I} \\
\text{MeO} \\
\text{MeO}
\end{array}
\end{array} & \quad 20a & \quad 0.25 & \quad 69 \\
2 & \quad \begin{array}{c}
\text{Br} \\
\begin{array}{c}
\text{CH}_2\text{I} \\
\text{MeO} \\
\text{MeO}
\end{array}
\end{array} & \quad \begin{array}{c}
\text{Br} \\
\begin{array}{c}
\text{CH}_2\text{I} \\
\text{MeO} \\
\text{MeO}
\end{array}
\end{array} & \quad 20b & \quad 0.25 & \quad 70 \\
3 & \quad \begin{array}{c}
\text{Br} \\
\begin{array}{c}
\text{CH}_2\text{I} \\
\text{MeO} \\
\text{MeO}
\end{array}
\end{array} & \quad \begin{array}{c}
\text{Br} \\
\begin{array}{c}
\text{CH}_2\text{I} \\
\text{MeO} \\
\text{MeO}
\end{array}
\end{array} & \quad 20n & \quad 0.25 & \quad 73 \\
4 & \quad \begin{array}{c}
\text{CF}_3 \\
\begin{array}{c}
\text{CH}_2\text{I} \\
\text{MeO} \\
\text{MeO}
\end{array}
\end{array} & \quad \begin{array}{c}
\text{CF}_3 \\
\begin{array}{c}
\text{CH}_2\text{I} \\
\text{MeO} \\
\text{MeO}
\end{array}
\end{array} & \quad 20o & \quad 0.25 & \quad 65 \\
5 & \quad \begin{array}{c}
\text{OMe} \\
\begin{array}{c}
\text{CH}_2\text{I} \\
\text{MeO} \\
\text{MeO}
\end{array}
\end{array} & \quad \begin{array}{c}
\text{OMe} \\
\begin{array}{c}
\text{CH}_2\text{I} \\
\text{MeO} \\
\text{MeO}
\end{array}
\end{array} & \quad 20f & \quad 0.25 & \quad 65 \\
6 & \quad \begin{array}{c}
\text{MeO} \\
\begin{array}{c}
\text{CH}_2\text{I} \\
\text{MeO} \\
\text{MeO}
\end{array}
\end{array} & \quad \begin{array}{c}
\text{MeO} \\
\begin{array}{c}
\text{CH}_2\text{I} \\
\text{MeO} \\
\text{MeO}
\end{array}
\end{array} & \quad 20p & \quad 0.5 & \quad 75 \\
7 & \quad \begin{array}{c}
\text{MeO} \\
\begin{array}{c}
\text{CH}_2\text{I} \\
\text{MeO} \\
\text{MeO}
\end{array}
\end{array} & \quad \begin{array}{c}
\text{MeO} \\
\begin{array}{c}
\text{CH}_2\text{I} \\
\text{MeO} \\
\text{MeO}
\end{array}
\end{array} & \quad 20i & \quad 0.5 & \quad 78 \\
8 & \quad \begin{array}{c}
\text{MeO} \\
\begin{array}{c}
\text{CH}_2\text{I} \\
\text{MeO} \\
\text{MeO}
\end{array}
\end{array} & \quad \begin{array}{c}
\text{MeO} \\
\begin{array}{c}
\text{CH}_2\text{I} \\
\text{MeO} \\
\text{MeO}
\end{array}
\end{array} & \quad 20j & \quad 0.25 & \quad 68 \\
9 & \quad \begin{array}{c}
\text{MeO} \\
\begin{array}{c}
\text{CH}_2\text{I} \\
\text{MeO} \\
\text{MeO}
\end{array}
\end{array} & \quad \begin{array}{c}
\text{MeO} \\
\begin{array}{c}
\text{CH}_2\text{I} \\
\text{MeO} \\
\text{MeO}
\end{array}
\end{array} & \quad 20q & \quad 1.0 & \quad 75 \\
10 & \quad \begin{array}{c}
\text{MeO} \\
\begin{array}{c}
\text{CH}_2\text{I} \\
\text{MeO} \\
\text{MeO}
\end{array}
\end{array} & \quad \begin{array}{c}
\text{MeO} \\
\begin{array}{c}
\text{CH}_2\text{I} \\
\text{MeO} \\
\text{MeO}
\end{array}
\end{array} & \quad 20r & \quad 1.0 & \quad 78
\end{align*}
\]

\(^a\)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 acetylene under domino [Pd]-catalysis. This method is applicable to a wide range of bromo or iodoarenes bearing electron withdrawing, neutral, electron rich substituents.

\[
\text{Scheme III.19}
\]

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 (\(\delta\) in ppm) and coupling constants (\(J\) in Hz) are reported in standard fashion with reference to either internal standard tetramethylsilane (TMS) (\(\delta_H=0.00\) ppm) or CHCl\(_3\) (\(\delta_H=7.25\) ppm). \(^{13}\)C-NMR spectra were recorded on Bruker Avance 400 (100 MHz) spectrometer at RT in CDCl\(_3\); chemical shifts (\(\delta\) in ppm) are reported relative to CHCl\(_3\) [\(\delta_C=77.00\) 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 (dpf) (with purity 97%), triphenylphosphine (PPh$_3$) (with purity 99%), Tri(2-furyl)phosphine (with purity 99%), Ethylenebis(diphenylphosphine)( Diphos ) (with purity 99%), Pd(PPh$_3$)$_2$Cl$_2$ (with purity 98%), 2-Dicyclohexylphosphino-2’-methylbiphenyl,2-Methyl-2’-dicyclohexylphosphinobiphenyl (MePhos) (with purity 97%), (Oxydi-2,1-phenylene)bis(diphenylphosphate) (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$_2$CO$_3$ (with purity 99%) purchased from Sigma-Aldrich were used without further purification. The base K$_2$CO$_3$ was dried at 150-170 °C over an oil bath. DMF and DMA dried over calcium hydride. Acetonitrile dried over P$_2$O$_5$. 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,\textsuperscript{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$_2$CO$_3$ (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 NH₄Cl solution and the aqueous layer was extracted with ethyl acetate (3 × 20 mL). The organic layers were dried over anhydrous Na₂SO₄, 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%).

![Image of 1-Nitro-3-[(3-nitrophenyl)ethynyl]benzene (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%), K₂CO₃ (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):** \( v_{max}=3082, 2958, 2922, 2853, 1529, 1402, 1352, 1236, 904, 823, 805, 734, 670 \) cm⁻¹.

**¹H-NMR (CDCl₃, 400 MHz):** \( \delta=8.39 \) (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.

**¹³C-NMR (CDCl₃, 100 MHz):** \( \delta=148.1 \) (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 [C₁₄H₈N₂NaO₄]⁺=[M+Na]⁺: 291.0376; found 291.0368.

(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%), K₂CO₃ (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 Rₚ(1b)=0.80, Rₚ(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 Rₚ(2b)=0.85, Rₚ(20b)=0.80 (petroleum ether, UV detection)].

IR (MIR-ATR, 4000–600 cm⁻¹): νmax=2957, 2922, 2852, 1602, 1498, 1442, 1260, 1069, 1025, 799, 753, 688 cm⁻¹.

¹H-NMR (CDCl₃, 400 MHz): δ=7.57 (m, 4H, Ar-H), 7.36 (m, 6H, Ar-H) ppm.

¹³C-NMR (CDCl₃, 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.

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%), K₂CO₃ (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\(^{-1}\)): \(v_{\text{max}}=3053, 2955, 2923, 2852, 1700, 1585, 1504, 1404, 1213, 1017, 796, 770\) cm\(^{-1}\).

\(^1\)H-NMR (CDCl\(_3\), 400 MHz): \(\delta=8.58\) (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): \(\delta=133.3\) (s, 4C, 4 \(\times\) Ar-C), 130.6 (d, 2C, 2 \(\times\) Ar-CH), 128.9 (d, 2C, 2 \(\times\) Ar-CH), 128.4 (d, 2C, 2 \(\times\) Ar-CH), 126.9 (d, 2C, 2 \(\times\) Ar-CH), 126.5 (d, 2C, 2 \(\times\) Ar-CH), 125.3 (d, 2C, 2 \(\times\) Ar-CH), 121.1 (s, 2C, 2 \(\times\) Ar-C), 92.4 (s, 2C, 2 \(\times\) Ar-C\(=\)) ppm.

HR-MS (ESI\(^+\)): m/z calculated for \([\text{C}_{22}\text{H}_{15}]^+=[\text{M+H}]^+\): 279.1168; found 279.1172.

\[\text{Me} \quad \equiv \quad \text{Me} \]

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\(_2\)CO\(_3\) (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\(^{-1}\)): \(v_{\text{max}}=3059, 3021, 2923, 2853, 1601, 1491, 1457, 1404, 1238, 1116, 755, 716\) cm\(^{-1}\).

\(^1\)H-NMR (CDCl\(_3\), 400 MHz): \(\delta=7.52\) (d, 2H, \(J=8.3\) Hz, 2 \(\times\) Ar-H), 7.30–7.10 (m, 6H, 2 \(\times\) Ar-H) 2.54 (s, 6H, 2 \(\times\) Ar-CH\(_3\)) ppm.
\textbf{13C-NMR (CDCl$_3$, 100 MHz):} \delta=139.9 \text{ (s, } 2\text{C, } 2 \times \text{Ar-C}), 131.8 \text{ (d, } 2\text{C, } 2 \times \text{Ar-CH}), 129.5 \text{ (d, } 2\text{C, } 2 \times \text{Ar-CH}), 128.2 \text{ (d, } 2\text{C, } 2 \times \text{Ar-CH}), 125.6 \text{ (d, } 2\text{C, } 2 \times \text{Ar-CH}), 123.3 \text{ (s, } 2\text{C, } 2 \times \text{Ar-C}), 92.3 \text{ (s, } 2\text{C, } 2 \times \text{Ar-}C\equiv\text{)}, 20.9 \text{ (q, } 2\text{C, } 2 \times \text{Ar-CH$_3$)} \text{ ppm.}

\textbf{HR-MS (ESI$^+$):} \ 	ext{m/z} \text{ calculated for } [\text{C}_{16}\text{H}_{15}]^+=[\text{M+H}]^+: 207.1168; \text{ found 207.1164.}

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\textbf{1-Methyl-3-[(3-methylphenyl)ethynyl]benzene (20e):} \textbf{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$_2$CO$_3$ (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 $\degree$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)].

\textbf{IR (MIR-ATR, 4000–600 cm$^{-1}$):} $\nu_{\text{max}}$=3037, 2956, 2923, 2853, 1603, 1489, 1458, 1404, 1240, 1120, 999, 783, 691 cm$^{-1}$.

\textbf{1H-NMR (CDCl$_3$, 400 MHz):} $\delta$=7.37–7.27 (m, 4H, 4 $\times$ Ar-H), 7.22 (dd, 2H, $J$=7.8 ad 7.3 Hz, 2 $\times$ Ar-H), 7.13 (d, 2H, $J$=7.3 Hz, 2 $\times$ Ar-H), 2.34 (s, 6H, 2 $\times$ Ar-CH$_3$) ppm.

\textbf{13C-NMR (CDCl$_3$, 100 MHz):} $\delta$=138.0 (s, 2C, 2 $\times$ Ar-C), 131.1 (d, 2C, 2 $\times$ Ar-CH), 129.1 (d, 2C, 2 $\times$ Ar-CH), 128.6 (d, 2C, 2 $\times$ Ar-CH), 128.2 (d, 2C, 2 $\times$ Ar-CH), 123.1 (s, 2C, 2 $\times$ Ar-C), 89.2 (s, 2C, 2 $\times$ Ar-C≡), 21.2 (q, 2C, 2 $\times$ Ar-CH$_3$) ppm.

\textbf{HR-MS (ESI$^+$):} \text{m/z} \text{ calculated for } [\text{C}_{16}\text{H}_{15}]^+=[\text{M+H}]^+: 207.1168; \text{ found 207.1171.}

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\textbf{1-(Trifluoromethyl)-3-[[3-(trifluoromethyl)phenyl]ethynyl]benzene (20f):} \textbf{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%), K₂CO₃ (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 Rₖ(1f)=0.90, Rₖ(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 Rₖ(2e)=0.90, Rₖ(20f)=0.80 (petroleum ether, UV detection)].

**IR (MIR-ATR, 4000–600 cm⁻¹):** νₘₐₓ=2931, 1622, 1450, 1396, 1264, 1188, 1013 cm⁻¹.

**¹H-NMR (CDCl₃, 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.

**¹³C-NMR (CDCl₃, 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 [C₁₆H₀F₆]⁺=[M+H]⁺: 315.0603; found 315.0581.

![1-Chloro-2-[(2-chlorophenyl)ethynyl]benzene (20g)](image)

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%), K₂CO₃ (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 Rₖ(1g)=0.90, Rₖ(20g)=0.80 (petroleum ether, UV detection)].

**IR (MIR-ATR, 4000–600 cm⁻¹):** νₘₐₓ=2931, 1622, 1450, 1396, 1264, 1188, 1013 cm⁻¹.
1H-NMR (CDCl₃, 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.

13C-NMR (CDCl₃, 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 [C₁₄H₉Cl₂]⁺=[M+H]⁺: 247.0076; found 247.0076.

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$_2$CO$_3$ (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): $\nu_{max}$=3058, 2923, 2853, 1598, 1493, 1402, 1234 1089, 829, 749, 695 cm⁻¹.

1H-NMR (CDCl₃, 400 MHz): δ=7.50–7.40 (m, 4H, Ar-H), 7.37–7.27 (m, 4H, Ar-H) ppm.

13C-NMR (CDCl₃, 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 [C₁₄H₉Cl₂]⁺=[M+H]⁺: 247.0076; found 247.0076.
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\(^{-1}\)): \(\nu_{\text{max}}=2957, 2922, 2852, 1563, 1462, 1403, 1237 \text{ cm}^{-1}\).

\(^1\text{H}-\text{NMR} (\text{CDCl}_3, 400 \text{ MHz}): \delta=7.25 (dd, 2H, J=7.8 \text{ and } 7.8 \text{ Hz, } 2 \times \text{Ar-H}), 7.13 (ddd, 2H, J=7.8, 2.4 \text{ and } 1.5 \text{ Hz, } 2 \times \text{Ar-H}), 7.07–7.02 (m, 2H, J=Hz, 2 \times \text{Ar-H}), 6.89 (dd, 2H, J=2.4 \text{ and } 1.0 \text{ Hz, } 2 \times \text{Ar-H}) \text{ ppm}.

\(^{13}\text{C}-\text{NMR} (\text{CDCl}_3, 100 \text{ MHz}): \delta=159.3 (s, 2C, 2 \times \text{Ar-C}), 129.4 (d, 2C, 2 \times \text{Ar-CH}), 124.2 (d, 2C, 2 \times \text{Ar-CH}), 124.1 (s, 2C, 2 \times \text{Ar-C}), 116.3 (d, 2C, 2 \times \text{Ar-CH}), 115.0 (s, 2C, 2 \times \text{Ar-C}), 89.1 (s, 2C, 2 \times \text{Ar-C}), 55.3 (q, 2C, 2 \times \text{Ar-OCH}_3) \text{ ppm}.

HR-MS (ESI\(^+\)): m/z calculated for [C_{16}H_{15}O_2]^+=[M+H]^+: 239.1067; found 239.1068.

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$^{-1}$):** $\nu_{\text{max}}=2957, 2921, 2851, 1607, 1511, 1462, 1403, 1248, 1172, 1026, 834, 750$ cm$^{-1}$.

**$^1$H-NMR (CDCl$_3$, 400 MHz):** $\delta=7.46$ (d, 4H, $J=8.8$ Hz, $4 \times$ Ar-H), 6.87 (d, 4H, $J=8.8$ Hz, $4 \times$ Ar-H), 3.81 (s, 6H, $2 \times$ Ar-OCH$_3$) ppm.

**$^{13}$C-NMR (CDCl$_3$, 100 MHz):** $\delta=159.3$ (s, 2C, $2 \times$ Ar-C), 132.8 (d, 4C, $4 \times$ Ar-CH), 115.6 (s, 2C, $2 \times$ Ar-C), 113.9 (d, 4C, $4 \times$ Ar-CH), 87.9 (s, 2C, $2 \times$ Ar-C≡), 55.2 (q, 2C, $2 \times$ Ar-OCH$_3$) ppm.

**HR-MS (ESI$^+$):** m/z calculated for [C$_{16}$H$_{15}$O$_2$]$^+=[M+H]$^+$: 239.1067; found 239.1068.

[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$_2$CO$_3$ (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$^{-1}$):** $\nu_{\text{max}}=2957, 2923, 2853, 1536, 1433, 1408, 1199, 1041, 851, 826, 700$ cm$^{-1}$.

**$^1$H-NMR (CDCl$_3$, 400 MHz):** $\delta=7.30$ (dd, 2H, $J=5.4$ and 1.5 Hz, $2 \times$ Ar-H), 7.27 (dd, 2H, $J=3.9$ and 1.5 Hz, $2 \times$ Ar-H), 7.00 (dd, 2H, $J=5.4$ and 3.9 Hz, Ar-H) ppm.
13C-NMR (CDCl₃, 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 [C₁₀H₇S₂⁺]=[M+H⁺]: 190.9984; found 190.9980.

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%), K₂CO₃ (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 Rₛ(1l)=0.70, Rₛ(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.

1H-NMR (CDCl₃, 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-CH₃) ppm.

13C-NMR (CDCl₃, 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 × ArCH₃) ppm.

HR-MS (ESI⁺): m/z calculated for [C₂₀H₁₇N₂⁺]=[M+H⁺]: 285.1386; found 285.1389.
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$_2$CO$_3$ (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$^{-1}$): $\nu_{max}$ = 3001, 2922, 2852, 1600, 1510, 1462, 1352, 1232, 1125, 1031, 860, 748 cm$^{-1}$.

$^1$H-NMR (CDCl$_3$, 400 MHz): $\delta$=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): $\delta$=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.

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$_2$CO$_3$ (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$^{-1}$): $\nu_{max}$=2922, 2852, 1556, 1479, 1434, 1400, 1237, 1048, 750 cm$^{-1}$.
\(^1\)H-NMR (CDCl\(_3\), 400 MHz): \(\delta = 7.62\) (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): \(\delta = 133.6\) (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\(_9\)Br\(_2\)]\(^+\) = [M]\(^+\): 333.8987; found 333.8986.

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\(_2\)CO\(_3\) (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\(^{-1}\)): \(\nu_{max} = 2922, 2852, 1589, 1493, 1463, 1391, 1074, 1009, 824\) cm\(^{-1}\).

\(^1\)H-NMR (CDCl\(_3\), 400 MHz): \(\delta = 7.48\) (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): \(\delta = 133.0\) (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\(_9\)Br\(_2\)]\(^+\) = [M+H]\(^+\): 334.9066; found 334.9057.
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$_2$CO$_3$ (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$^{-1}$):** $\nu_{max}$=2958, 2923, 2852, 1596, 1462, 1435, 1275, 1245, 1024, 751 cm$^{-1}$.

**$^1$H-NMR (CDCl$_3$, 400 MHz):** $\delta$=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):** $\delta$=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-OC$_3$) ppm.

**HR-MS (ESI$^+$):** m/z calculated for [C$_{16}$H$_{15}$O$_2$]$^+$=[M+H]$^+$: 239.1067; found 239.1063.

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$_2$CO$_3$ (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\(^{-1}\)): \(\nu_{\text{max}}=2956, 2921, 2851, 1597, 1514, 1464, 1246, 1138, 1025, 765\ cm^{-1}\).

\(^1\)H-NMR (CDCl\(_3\), 400 MHz): \(\delta=7.11\) (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): \(\delta=149.3\) (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.

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\(_2\)CO\(_3\) (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): \(\delta=7.19\) (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): \(\delta=154.6\) (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\(^{-1}\)): \(\nu_{\text{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 CDCl₃

Figure III.2.1: \(^{13}\)C-NMR (100 MHz) spectrum of 20l in CDCl₃
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11. Sequential one-pot method for oxy-Michael addition, Heck coupling and degradation followed by condensation: Facile synthesis of 2-benzoexepin-3(1$H$)-


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