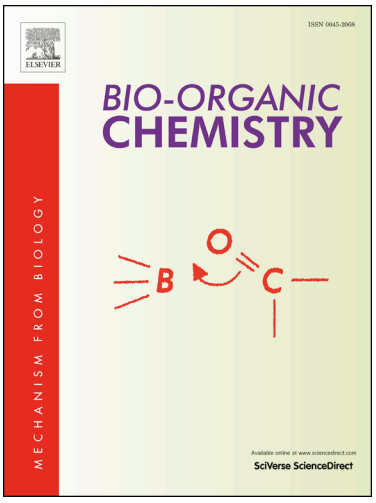

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Synthesis, in vitro and in silico Evaluation of Diaryl Heptanones as Potential 5LOX Enzyme Inhibitors

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Abstract: A new series of diaryl heptanones (**12a-q**) were synthesized and their structures were confirmed by its ^{1}H, ^{13}C NMR and Mass spectral data. These analogs were evaluated for their anti-oxidant activity and potential to inhibit 5-lipoxygenase. Compounds **12k** and **12o** showed potent in vitro 5-lipoxygenase enzyme inhibitory activity with IC_{50} values of 22.2, 21.5 μM, which are comparable to curcumin (24.4 μM). Further they also have shown significant antioxidant activity. Molecular docking studies clearly showed correlation between binding energy and potency of these compounds.

Key words: Diarylheptanones, 5-lipoxygenase, anti-inflammatory, anti-oxidant, molecular docking.

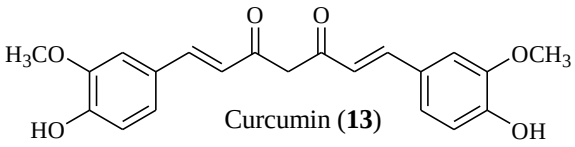
Abbreviations: 5-LOX, 5-lipoxygenase; IBX, iodoxy benzoic acid; DCM, dichloromethane; LaH, lithium aluminum hydride.

Introduction:

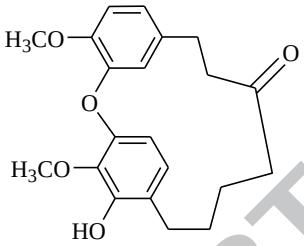
Inflammation is a complex biological response in vascular tissues against the harmful stimuli, such as pathogens, damaged cells, or irritants [1]. It is a protective mechanism adopted by the organisms to remove the injurious stimuli and to initiate the healing process. Hence, inflammation is considered as an essential survival strategy adopted by the body to ward off major damage. However, inflammation can also lead to a host of diseases, such as hay fever, atherosclerosis, rheumatoid arthritis and even cancer [2].

In acute inflammation, the cellular phospholipases are activated to break down membrane phospholipids into arachidonic acid, which in turn is metabolized to inflammatory prostaglandins and leucotrienes respectively by the enzymes cyclooxygenase (COX) and lipoxygenase (LOX). The search for inhibitors of these enzymes thus forms the basis for development of new anti-inflammatory agents. In the enzyme family of cyclooxygenases, inhibition of cyclooxygenase-2 (COX-2) is more desirable. However, recent studies revealed that selective inhibition of COX-2 does reduce inflammation, but causes side effects, particularly those leading to cardiovascular complications [3]. On the contrary, the inhibition of the 5-lipoxygenase (5-LOX) enzyme of the alternative pathway of inflammation not only reduces inflammation but also improves cardiac health by reducing risk of atherosclerosis [4]. The alternative pathway mediated by 5-LOX has thus become an important target for the development of new anti-inflammatory drugs.

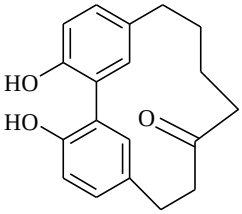
Diarylheptanoids are a class of plant secondary metabolites, which are structurally made up of two aromatic rings connected by a seven carbon aliphatic chain. There are two major categories of diarylheptanoids, linear diarylheptanoids and cyclic diarylheptanoids [5-14] were depicted in figure 1. Several natural and synthetic diarylheptanoid derivatives are known to possess a broad spectrum of biological activities. Some of them are well known for their anti-inflammatory, anti-oxidant and anti-cancer potentials [15-22]. Few synthetic methodologies are reported for diarylheptanoids and structurally related diarylnonanones, which are also reported to be effective cytotoxic and anti-inflammatory agents [16, 18, 23]. In view of the biological potential of diarylheptanoids and diarylnonanones, we report herein the synthesis, anti-oxidant and anti-inflammatory activities of several new diarylheptanoids. The anti-inflammatory activity of the synthesized compounds was also evaluated *in silico* using molecular docking studies.



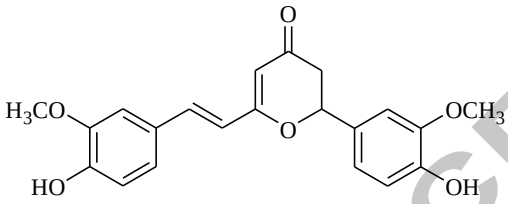
Curcumin (**13**)



Juglanin A (**14**)



Acerogenin E (**15**)

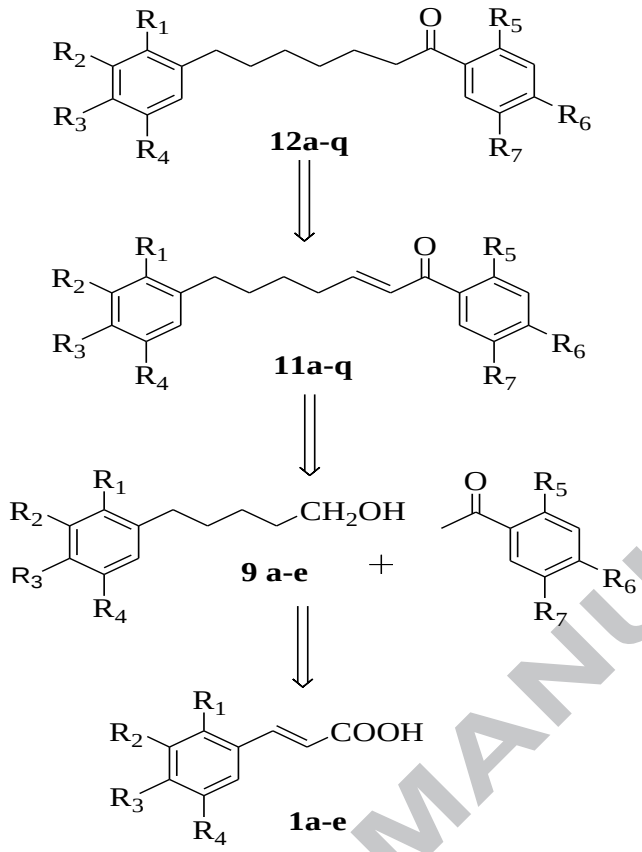


Cyclocurcumin (**16**)

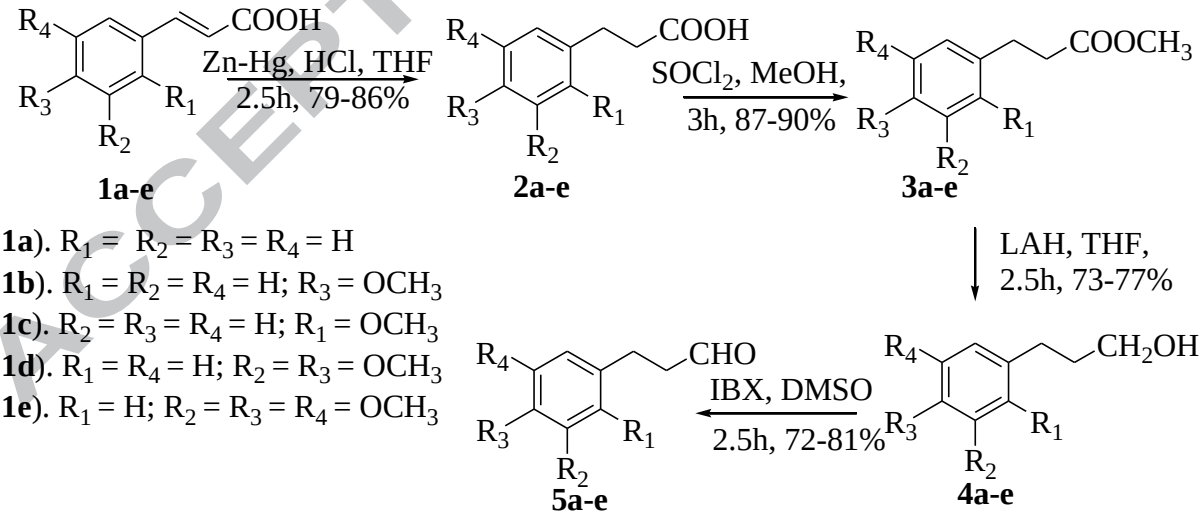
Figure 1: Some of the natural heptanones.

Result and discussion: The synthetic approach for diaryl heptanones summarized in Scheme 2 and Scheme 3 were comprehended based on the disconnection approach as depicted in Scheme 1. Here, the enone intermediate moiety (**11**) could be the precursor for substituted diarylheptanone compounds. The disconnection of this precursor between the olefinic carbons α and β to the keto group leads to 5-(substituted phenyl)-pentanal (**9**) and commercially available substituted acetophenone as the most advanced precursors. Further disconnection analysis as described in Scheme 1 manifested that 5-(substituted phenyl)-pentanal (**9**) can be produced from substituted cinnamic acid.

Based on the disconnection approach summarized in Scheme 1 the key intermediate **11a-q** of diarylheptanones synthesis was achieved by adopting the Scheme 2. The intermediates 3-(substituted-phenyl)-propanoic acid (**2a-e**) was obtained by the reduction of substituted cinnamic acid with Zn-Hg amalgam, which were methylated with MeOH/HCl to get 3(substituted-phenyl)-propnoic acid methyl ester (**3a-e**). These methyl esters upon reduction with lithium aluminum hydride followed by mild oxidation with IBX yielded the aldehyde compounds 3-(substituted phenyl) propan-1-al (**5a-e,** 72-81 %). The aldehyde compounds **5a-e** were treated with triphenylcarbethoxymethylene phosphorane [24] under modified Wittig reaction conditions to obtain compounds 5-(substituted-phenyl)-pent-2-en-oic acid ethyl esters **6a-e** in good yields (60-66 %).

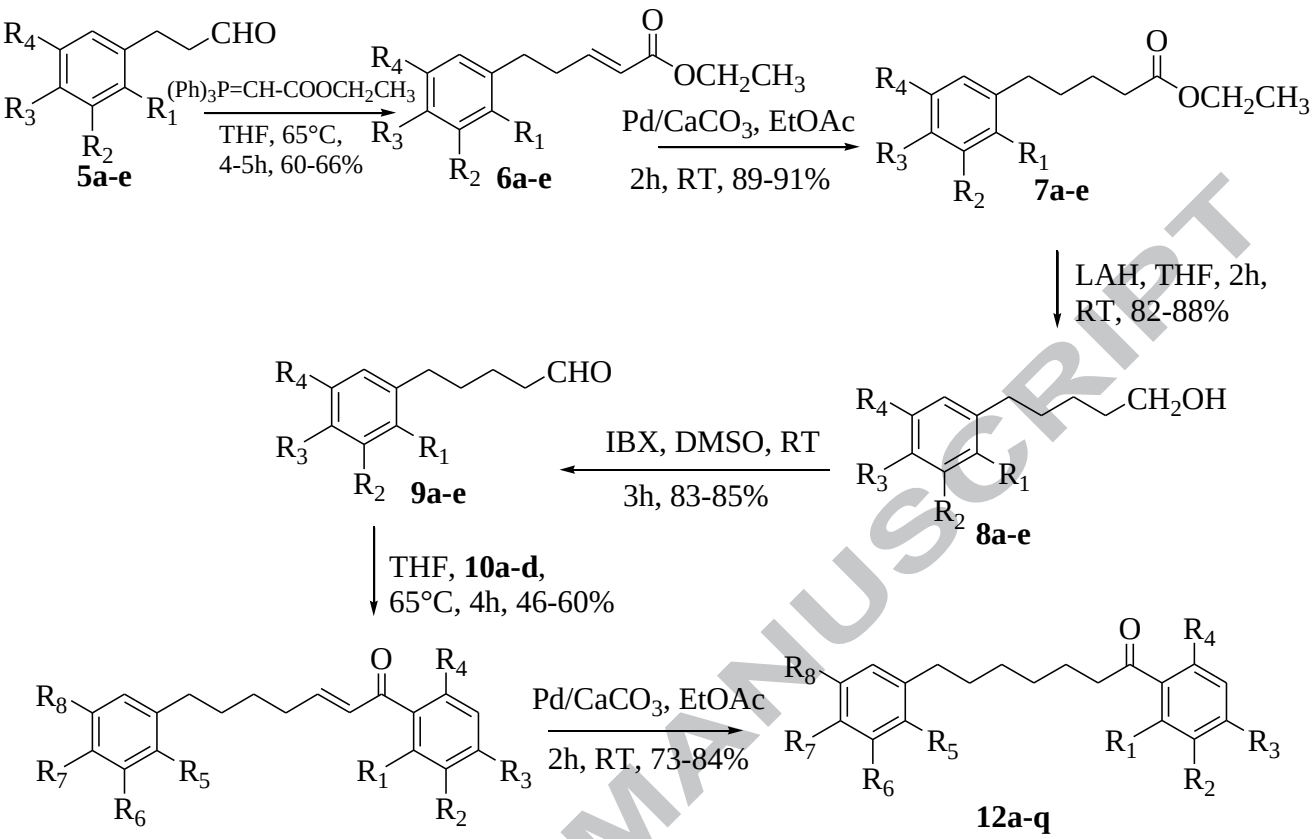


Scheme 1: Retro-synthetic analysis of diarylheptanones (**12a-12q**)

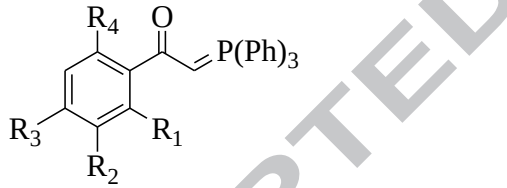


1a). $R_1 = R_2 = R_3 = R_4 = H$
1b). $R_1 = R_2 = R_4 = H$; $R_3 = OCH_3$
1c). $R_2 = R_3 = R_4 = H$; $R_1 = OCH_3$
1d). $R_1 = R_4 = H$; $R_2 = R_3 = OCH_3$
1e). $R_1 = H$; $R_2 = R_3 = R_4 = OCH_3$

Scheme 2: Synthesis of phenyl propanaldehyde precursors **5a-e**.



5a-e **6a-e** **7a-e** **8a-e** **9a-e** **11a-q** **12a-q**



10a-d

10a). $R_1 = R_2 = R_3 = R_4 = H$
10b). $R_1 = R_3 = OCH_3$; $R_2 = R_4 = H$
10c). $R_2 = R_3 = OCH_3$; $R_1 = R_4 = H$
10d). $R_2 = R_4 = OCH_3$; $R_1 = R_3 = H$

12a). $R_1 = R_4 = R_5 = R_6 = R_7 = R_8 = H$; $R_2 = R_3 = OCH_3$
12b). $R_1 = R_3 = R_5 = R_6 = R_7 = R_8 = H$; $R_2 = R_4 = OCH_3$
12c). $R_1 = R_2 = R_3 = R_4 = R_5 = R_6 = R_8 = H$; $R_7 = OCH_3$
12d). $R_2 = R_4 = R_5 = R_6 = R_8 = H$; $R_1 = R_3 = R_7 = OCH_3$
12e). $R_2 = R_3 = R_6 = R_7 = R_8 = H$; $R_1 = R_4 = R_5 = OCH_3$
12f). $R_1 = R_2 = R_3 = R_4 = R_6 = R_7 = R_8 = H$; $R_5 = OCH_3$
12g). $R_1 = R_4 = R_6 = R_7 = R_8 = H$; $R_1 = R_3 = R_5 = OCH_3$
12h). $R_1 = R_4 = R_6 = R_7 = R_8 = H$; $R_2 = R_3 = R_5 = OCH_3$
12i). $R_2 = R_3 = R_6 = R_7 = R_8 = H$; $R_1 = R_4 = R_5 = OCH_3$
12j). $R_1 = R_2 = R_3 = R_4 = R_5 = R_8 = H$; $R_6 = R_7 = OCH_3$
12k). $R_1 = OH$; $R_2 = R_4 = R_5 = R_8 = H$; $R_3 = R_6 = R_7 = OCH_3$
12l). $R_1 = R_4 = R_5 = R_8 = H$; $R_2 = R_3 = R_6 = R_7 = OCH_3$
12m). $R_2 = R_3 = R_5 = R_8 = H$; $R_1 = R_4 = R_6 = R_7 = OCH_3$
12n). $R_1 = R_2 = R_3 = R_4 = R_5 = H$; $R_6 = R_7 = R_8 = OCH_3$
12o). $R_1 = OH$; $R_2 = R_4 = R_5 = H$; $R_3 = R_6 = R_7 = R_8 = OCH_3$
12p). $R_1 = R_4 = R_5 = H$; $R_2 = R_3 = R_6 = R_7 = R_8 = OCH_3$
12q). $R_2 = R_3 = R_5 = H$; $R_1 = R_4 = R_6 = R_7 = R_8 = OCH_3$

Scheme 3: Synthesis of diarylheptanones **12a-q**.

The compounds 5-(substituted-phenyl)-pent-2-enoic acid ethyl esters (**6a-e**) were subjected to catalytic reduction under hydrogen atmosphere with 5% $Pd/CaCO_3$ to obtain ethyl 5-(substituted phenyl)-pentanoates (**7a-e**) with yields in the range of 89-91%, which upon reduction with LAH yielded 5-(substituted phenyl)-pentan-1-ol compounds (**8a-e**) in 82-88% yield. The compounds **8a-e** were treated with IBX in DMSO to obtain 5-(substituted-phenyl) pentan-1-al compounds (**9a-e**) in good yields (83 - 85%).

In final condensation, the 5-(substituted-phenyl)-pentan-1-al compounds **(9a-e)** were treated with substituted acetophenone phosphoranes **10a-d** via modified Wittig reaction to obtain 7-(substituted-phenyl)-1-(substituted-phenyl)-hept-2-ene-1-ones (**11a-q)** with yields in the range of 46-60%, which on catalytic hydrogenation with 5% $Pd/CaCO_3$ yielded the corresponding 7-(substituted-phenyl)-1-(substituted-phenyl)-heptan-1-one compounds (**12a-q**) in 73-84 % yields.

Biological activities of diarylheptanones:

The synthesized compounds **12a-q** were evaluated for their efficacy in inhibiting 5-lipoxygenase, an enzyme known to be involved in the mediation of inflammation. The analogs **12k** and **12o** showed potent 5-lipoxygenase inhibition with IC_{50} values of 22.2 and 21.5 μM respectively and are comparable with the positive control curcumin (IC_{50} 24.4 μM). Except **12D**, the remaining compounds showed moderate inhibitory activity (IC_{50}) in the range 75-150 μM. These results clearly showed that 2-hydroxy group on the benzoyl ring is essential for bioactivity. Further **12k** also has shown appreciable anti-oxidant activity (IC_{50} 16.7 μM), when compared with gallic acid (IC_{50} 13.7 μM). Substitution of either of the benzene rings present in the heptanone pharmacophore with $–OCH_3$ groups failed to show any influence on bioactivity profile of these compounds. To have better insight on the inhibitory profile of these compounds, docking simulations were conducted.

Table 1: *In-vitro* activities of diarylheptanone analogs **12a-q**

S.No	Compound	5-LOX inhibition ($IC_{50}\mu M$)	Anti-oxidant NBT ($IC_{50}\mu M$)
1	**12a**	139.9	83.3
2	**12b**	118.1	33.1
3	**12c**	145.1	>300
4	**12d**	>300	>300
5	**12e**	104.2	>300
6	**12f**	148.5	>300
7	**12g**	115.8	>300
8	**12h**	117.3	>300
9	**12i**	104.2	>300
10	**12j**	134.9	43.4
11	**12k**	22.22	16.7
12	**12l**	106.8	>300
13	**12m**	96.1	36.4
14	**12n**	95.4	28.5
15	**12o**	21.5	26.1
16	**12p**	75.2	>300
17	**12q**	108.4	>300
18	**Gallic acid**	------	13.7
19	**Curcumin**	24.4	------

Docking studies:

Here, the docking simulations were initiated by defining the region containing active site residues as the receptor site. Partial flexibility was allowed for the amino acids present close to the active site. The docking simulations were performed with the help of AutoDockVina. In our computational study, curcumin scored exceptionally well with a score of -11.7 Kcal/mol and it also showed highest in vitro 5-LOX inhibitory activity (24.4 μM). This compound showed several interactions with the active site residues His551, Asn555 and nearby lipophilic amino

acids Ala672, Val673. The diketo (or keto-enol) group showed very strong salt-bridge interactions with Asn426, another important amino acid essential for ligand recognition and its transit to catalytic site. Docking simulations were also performed with zileuton®, an approved 5-lox inhibitor. The hydroxyurea moiety showed several interactions with the catalytic site amino acids Asn555, His551, His373 and the benzothiofuran ring filled the lipophilic pocket of 5-lox enzyme with a score of -8.9 Kcal/mol. The synthesized compounds were also found to fit very well into the active site with benzoyl "head" first pose. The tail containing the lipophilic chain tipped with substituted benzene ring was found to make several lipid-lipid interactions with the receptor site residues, aiding in further stabilizing the ligand inside the receptor pocket. All the active compounds are found to interact with at least one histidine present in the catalytic site, Gln558 and Asn555. Among the synthesized compounds, **12k** showed best docking score (-10.8 Kcal) and has shown highest in vitro 5-LOX inhibitory activity followed by **12o** (-10.5 Kcal). The 2-hydroxy group and benzoyl carbonyl showed several interactions with the histidine residues present in the active site, supporting the bioactivity profile observed for these compounds. The docking scores for the synthesized compounds and along with their corresponding 5-LOX inhibition activities are summarized in Table 2. Curcumin as well as the heptanones did not fit well in the receptor pocket of either COX-I or COX-II (docking scores <8 Kcal/mol) and were often found to dock away from the catalytic site.

One of the reasons for 5-LOX selectivity could be the shape and flexibility of receptor pocket. In case of 5-LOX, the receptor pocket is relatively large and flexible. The catalytic Fe in this enzyme is held into place by coordination with side chains of three conserved His residues (numbered 368, 373 and 551) and the main chain carboxyl group of the C-terminal Ile674 [25]. It may be also aided in this by the residue Asn 555, which is not close enough to be present in the actual coordination sphere. Whereas COX-I and COX-II are cytochrome oxidase enzymes with catalytic iron present in rigid heme ring and the receptor pocket is relatively rigid [26]. This could be the reason for absence of COX inhibitory activity for curcumin and also heptanones in this present study.

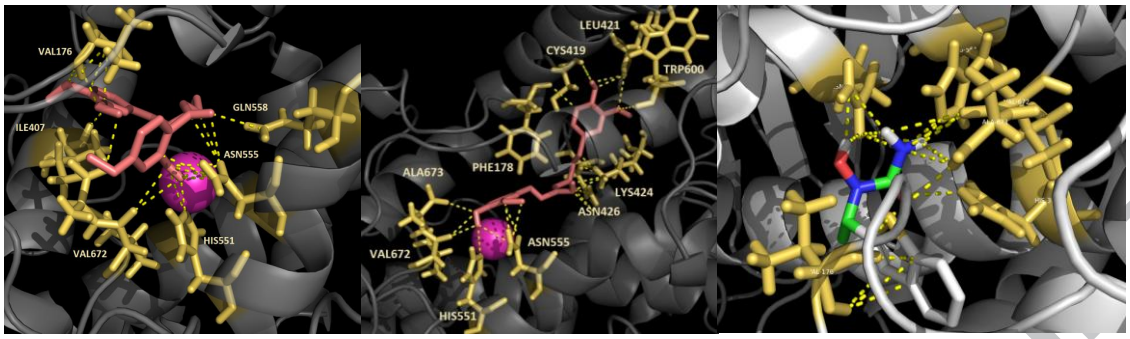


Figure 02: Docking poses of the compound **12k**, Curcumin and zileuton® at the receptor pocket. Ligand (salmon red), Fe (magenta) and active site residues making polar contacts (light yellow orange)

Computational studies: The protein X-ray crystal structureof the enzyme 5-LOX (3V99.pdb), COX-I (3KK6) and COX-II (5KIR.pdb) were obtained from www.rcsb.org. The protein structures was thoroughly analysed for misalignments, atom clashes and protein breaks. 5-LOX protein lacked a major loop near the active site. It was repaired by HOMOLOGY modelling using expasy server (https://swissmodel.expasy.org/) [27] molecular dynamics simulation was performed on the modelled protein by MDWeb server (http://mmb.irbbarcelona.org/MDWeb/index.php) using AMBER forcefield [28]. 3D Ligand database was prepared using Chemoffice and AutoDock software tools. Protein preparation was also done using AutoDock tools using default protocol. Docking simulations were performed with the help of Autodock Vina [29]. The amino acids near the active site were defined as flexible for optimal interactions. Receptor-ligand interactions were analyzed by PyMol software [30]. LIGPLOT interactions were plotted by using LigPlot+ software (http://www.ebi.ac.uk/thornton-srv/software/LIGPLOT/).

Table 2: Results of the docking simulations of synthesized compounds and curcumin

Compound Code	Amino acid interactions	Docking score Kcal/mol	5-LOX IC_{50} μM
12a	Asn426, Gln364, Leu608, His373	-9.8	139.9
12b	Gln364, His368, Asn555, Leu608, Ala673	-9.2	118.1
12c	Gln364, Gln558, Lys424, Asn426, Leu421	-8.7	145.1
12d	Asn426, Gln364, His368, Ala673	-8.9	>300
12e	Glu615, Ala673, Lys174	-7.9	104.2
12f	Gln364, His368, Asn555, Leu608, Ala673	-9.2	148.5
12g	Asn426, Gln364, His368, Ala673	-8.9	115.8
12h	Glu615, Ala673, Lys174	-7.9	117.3
12i	Glu615, Ala673, Lys174	-7.9	104.2
12j	Glu613, Ala673, His373, Asn555	-8.5	134.9
12k	Ile407, Val176, Val672, His368, His551, Asn555, Gln558	-10.8	22.2
12l	Ala673, Asn555, Gln558, His368, Gln364, Lys424, Asn426	-8.5	106.8
12m	Gln364, Gln558, sn426, Asp423, Leu421	-8.7	96.1
12n	Val672, His551, Asn555, Gln364, Asn426	-8.7	95.4
12o	Ile407, Val176, Val672, His368, His551, Asn555, Gln558	-10.5	21.5
12p	Ala673, Gln558, Leu608, His368, Gln364,	-9.5	75.2
12q	Gln364, Gln558, Lys424, Asn426, Leu421	-8.7	108.4
Curcumin	Leu421, Trp600, His551, His368, Asn555, Ala673, Val672, Lys424, Asn426, Cys419	-11.7	24.4
Zileuton®	His551, His373, Asn555, Val176, Ala673	-8.9	Not tested

Conclusions

The diarylheptanone analogs were prepared with a view to obtain potent anti-inflammatory compounds with 5-LOX inhibitory activity and to probe structure activity relationships of diaryl heptanoids. A total of 17 new compounds were synthesized and screened for *in vitro* 5-LOX enzyme inhibition. An attempt was made to investigate selective inhibitory profile of diaryl heptanoids towards 5-LOX using docking simulations. The studies showed that, diaryl heptanoids snugly fits the active site of 5-LOX and showed no-fitment at all in the active pockets of COX-1 and COX-2. Compounds **12k** and **12o** showed potent in vitro 5-lipoxygenase enzyme inhibitory activity with IC_{50} values of 22.2, 21.5 μM, which are comparable to curcumin (24.4 μM). Further they also have shown significant anti-oxidant activity. Molecular docking studies clearly showed correlation between binding energy and potency of these compounds. The compounds containing hydroxyl group adjacent to the keto functional group and also compounds with few number of methoxy groups exhibited reasonable anti-inflammatory activity.

Experimental:

General experimental procedures: The ^{1}H NMR spectra were recorded on Bruker Avance AV 400 MHz NMR spectrometer and ^{13}C NMR spectra were recorded on Bruker Avance AV 100 MHz NMR spectrometer. Mass studies were performed on LC-MS system equipped with Agilent 1100 series LC/ MSD detector and 1100 series Agilent HPLC pump. Exact mass was measured on Water's Q-Tof instrument. Normal phase silica gel (ACME, 100-200 mesh) was used for column chromatography. Silica gel pre-coated plates (AlugramSil G/UV254) were used for thin layer chromatography. The plates were eluted with a solvent system containing hexane/ethyl acetate (9:1) and visualized by immersing the plate in sulfuric acid/methanol reagent followed by heating at 110°C. Nitro blue tetrazolium (NBT) was obtained from Sigma Chemicals (USA). The solvents and other chemicals used were of AR grade and were procured from Qualigens Fine Chemicals, Mumbai (India).

General procedure for preparation of 3-(substituted phenyl)-propionic acid (2a-e):

A mixture of zinc powder (25 g, 0.384 mol) and mercuric chloride (3.1 g, 0.0114 mol) was suspended in 100 ml of water in a 250 ml beaker. The mixture was treated with 50 ml of con. HCl slowly drop wise and after completion of addition, the stirring was continued for 15 min.

The mixture was decanted to separate the solution and the remaining Zn-Hg amalgam was used for reduction.

To a mixture of substituted cinnamic acid (**1a-e**, 0.134 mol), THF (150 mL) and 5N HCl (100 mL) was added above freshly prepared Zn-Hg amalgam slowly portion wise. An additional 5N HCl (50 mL) added and the stirring continued for 2 h. After completion of reaction, as monitored by TLC hexane/ethyl acetate (8:2), the reaction mixture was poured into water (200 mL) and extracted with chloroform (2 × 400 mL), The organic layer was washed with brine solution, dried over Na_2SO_4 and concentrated. The crude residue was subjected to column chromatography on silica gel using hexane/ethyl acetate mixtures as eluents. The fractions were monitored using TLC and pure compound was obtained from the fractions eluted with ethyl acetate in hexane, 5 % / 95 % (v/v). These fractions were combined and concentrated to obtained 3-(substituted-phenyl)-propionic acids (**2a-e**) as oily compounds with yields of 79 %-86 %.

*3-(Phenyl)-propionic acid (**2a**)*: Weight: 16.1 g; % yield: 79.4 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 12.2 (1H, s, COOH), 7.34 (2H, t, J = 7.6 Hz, H-3′, 5′), 7.18 (2H, d, J = 7.2 Hz, H-2′, 6′), 7.11 (1H, d, J = 7.2 Hz, H-4′), 2.88 (2H, t, J = 7.2 Hz, H-3), 2.54 (2H, t, J = 7.6 Hz, H-2); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 178.4 (C=O), 146.2 (C-1′), 132.8 (C-3′, 5′), 132.6 (C-2′, 6′), 122.4 (C-4′), 38.4 (C-2), 32.6 (C-3); LC-MS: *m/*z 149.3 $(M-H)^-$.

*3-(4-Methoxy-phenyl)-propionic acid (**2b**)*: Weight: 17.4 g; % yield: 86.1 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 12.1 (1H, s, COOH), 7.24 (2H, d, J = 7.6 Hz, H-2′, 6′), 6.88 (2H, d, J = 7.2 Hz, H-3′, 5′), 3.82 (3H, s, OCH_3), 2.89 (2H, t, J = 8.0 Hz, H-3), 2.52 (2H, t, J = 8.0 Hz, H-2); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 178.8 (C=O), 168.4 (C-4′), 136.3 (C-1′), 132.6 (C-2′, 6′), 118.4 (C-3′, 5′), 55.2 (OCH_3), 38.6 (C-2), 33.2 (C-3); LC-MS: *m/z* 179.2 $(M-H)^-$.

*3-(2-Methoxy-phenyl)-propionic acid (**2c**)*: Weight: 17.2 g; % yield: 85.1 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 11.8 (1H, s, COOH), 7.21 (1H, dd, J = 7.6, 2.4 Hz, H-6′), 7.08 (1H, td, J = 8.0, 3.2 Hz, H-4′), 6.92 (1H, td, J = 8.0, 3.2 Hz, H-5′), 6.86 (1H, dd, J = 7.6, 2.4 Hz, H-3′), 3.78 (3H, s, OCH_3), 2.92 (2H, t, J = 7.2 Hz, H-3), 2.62 (2H, t, J = 8.0 Hz, H-2); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 178.6 (C=O), 166.4 (C-2′), 132.8 (C-6′), 130.8 (C-4′), 128.4 (C-1′), 122.8 (C-5′), 118.6 (C-3′), 55.8 (OCH_3), 38.6 (C-2), 24.8 (C-3); LC-MS: *m/*z 203.5 $(M+Na)^+$.

*3-(3,4-Dimethoxy-phenyl)-propionic acid (**2d**)*: Weight: 16.8 g; % yield: 83.3 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 11.8 (1H, s, COOH), 6.78 (1H, d, J = 7.6 Hz, H-5′), 6.72 (1H, dd, J = 7.6, 3.2 Hz, H-6′), 6.58 (1H, d, J = 3.2 Hz, H-2′), 3.78 (3H, s, OCH_3), 3.72 (3H, s, OCH_3), 2.88 (2H,

t, *J* = 7.6 Hz, H-3), 2.66 (2H, t, *J* = 7.6 Hz, H-2); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 178.2 (C=O), 156.4 (C-3′), 154.2 (C-4′), 138.4 (C-1′), 128.6 (C-6′), 118.6 (C-5′), 116.8 (C-2′), 55.8 (OCH_3), 55.6 (OCH_3), 38.9 (C-2), 30.9 (C-3); LC-MS: *m/*z 233.3 $(M+Na)^+$.

*3-(3, 4, 5-Tri methoxy-phenyl)-propionic acid (**2e**)*: Weight: 16.5 g; % yield: 81.8 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 11.8 (1H, s, COOH), 6.12 (2H, s, H-2′, 6′), 3.73 (9H, s, OCH_3), 2.98 (2H, t, *J* = 7.6 Hz, H-3), 2.54 (2H, t, *J* = 7.6 Hz, H-2); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 178.2 (C=O), 156.4 (C-3′, 5′), 138.9 (C-4′), 134.8 (C-1′), 108.8 (C-2′, 6′), 55.8 (OCH_3), 55.6 (OCH_3), 55.4 (OCH_3), 38.4 (C-2), 31.8 (C-3); LC-MS: *m/*z 263.2$(M+Na)^+$.

*General procedure for preparation of 3-(substituted-phenyl)-propionic acid methyl ester (**3a-e**):*
A mixture of substituted dihydrocinnamic acid (**2a-e**, 0.133 mol) in methanol (350 mL) was treated slowly with thionyl chloride (20 mL, 0.275 mol) drop wise during 1 h. After completion of addition, the reaction mixture was stirred for another 2 h at rt. After completion of reaction, which was monitored by TLC hexane/ethyl acetate (8:2), the reaction mixture was poured into water (200 mL), extract with ethyl acetate (2 × 400 mL). The extract was washed with water, brine solution, dried over Na_2SO_4 and concentrated. The crude compound was subjected to column chromatography on silica gel using hexane/ethyl acetate mixtures. The fractions were monitored and the fractions eluted with ethyl acetate in hexane, 3 % / 97 % (v/v) were combined and concentrated to obtained 3-(substituted phenyl)-propionic acid methyl esters (**3a-e**) as oily compounds with yields in the range of 87 %-90 %.

*3-(Phenyl)-propionic acid methyl ester (**3a**)*: Weight: 15.6 g; % yield: 89.6 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.34 (2H, d, *J* = 8.0 Hz, H-3′, 5′), 7.21 (2H, d, *J* = 7.6 Hz, H-2′, 6′), 7.11 (1H, d, *J* = 7.2 Hz, H-4′), 3.68 (3H, s, OCH_3), 2.98 (2H, t, *J* = 7.6 Hz, H-3), 2.62 (2H, t, *J* = 7.6 Hz, H-2); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 176.2 (C=O), 146.2 (C-1′), 132.6 (C-3′, 5′), 130.8 (C-2′, 6′), 128.3 (C-4′), 50.6 (OCH_3), 36.8 (C-2), 30.9 (C-3); LC-MS: *m/*z 165.2 $(M+H)^+$.

*3-(4-Methoxy-phenyl)-propionic acid methyl ester (**3b**)*: Weight: 15.6 g; % yield: 90.7 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.14 (2H, d, *J* = 8.0 Hz, H-2′, 6′), 6.84 (2H, d, *J* = 7.6 Hz, H-3′, 5′), 3.78 (3H, s, OCH_3), 3.72 (3H, s, OCH_3), 2.98 (2H, t, *J* = 8.0 Hz, H-3), 2.61 (2H, t, *J* = 7.6 Hz, H-2); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 176.2 (C=O), 164.2 (C-4′), 138.4 (C-1′), 130.2 (C-2′, 6′), 118.8 (C-3′, 5′), 55.8 (OCH_3), 51.2 (OCH_3), 36.2 (C-2), 30.9 (C-3); LC-MS: *m/*z 193.3 $(M-H)^-$.

*3-(2-Methoxy-phenyl)-propionic acid methyl ester (**3c**)*: Weight: 15.1 g; % yield: 87.8 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.12 (1H, dd, *J* = 8.0, 3.2 Hz, H-6′), 6.98 (1H, td, *J* = 8.0, 3.2 Hz, H-4′), 6.86 (1H, td, *J* = 8.0, 2.4 Hz, H-5′), 6.72 (1H, dd, *J* = 8.0, 3.2 Hz, H-3′), 3.78 (3H, s, OCH_3), 3.66 (3H, s, OCH_3), 2.98 (2H, t, *J* = 7.6 Hz, H-3), 2.61 (2H, t, *J* = 7.2 Hz, H-2); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 174.2 (C=O), 168.2 (C-2′), 132.9 (C-6′), 128.6 (C-4′), 126.9 (C-1′), 120.8 (C-5′), 116.4 (C-3′), 55.8 (OCH_3), 50.6 (OCH_3), 36.9 (C-2), 22.1 (C-3); LC-MS: *m/z* 193.2 $(M-H)^-$.

*3-(3, 4-Dimethoxy-phenyl)-propionic acid methyl ester (**3d**)*: Weight: 15.30 g; % yield: 89.7 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.72 (1H, d, *J* = 8.0 Hz, H-5′), 6.64 (1H, dd, *J* = 8.0, 3.2 Hz, H-6′), 6.56 (1H, d, *J* = 3.2 Hz, H-2′), 3.78 (6H, s, OCH_3), 3.66 (3H, s, OCH_3), 2.98 (2H, t, *J* = 7.6 Hz, H-3), 2.66 (2H, t, *J* = 7.6 Hz, H-2); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 174.4 (C=O), 158.4 (C-3′), 156.3 (C-4′), 138.2 (C-1′), 126.8 (C-6′), 118.4 (C-5′), 116.8 (C-2′), 55.8 (OCH_3), 55.6 (OCH_3), 50.1 (OCH_3), 38.4 (C-2), 31.8 (C-3); LC-MS: *m/z* 225.5 $(M+H)^+$, 243.3 $(M+Na)^+$.

*3-(3, 4, 5-Trimethoxy-phenyl)-propionic acid methyl ester (**3e**)*: Weight: 15.10 g; **%** yield: 89.3 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.22 (2H, s, H-2′, 6′), 3.86 (6H, s, OCH_3), 3.78 (3H, s, OCH_3), 3.66 (3H, s, OCH_3), 2.96 (2H, t, *J* = 8.0 Hz, H-3), 2.62 (2H, t, *J* = 7.6 Hz, H-2); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 172.4 (C=O), 156.4 (C-3′, 5′), 142.8 (C-4′), 136.2 (C-1′), 108.6 (C-2′, 6′), 56.4 (OCH_3), 56.3 (OCH_3), 55.9 (OCH_3), 50.9 (OCH_3), 38.2 (C-2), 31.6 (C-3); LC-MS: *m/z* 255.2 $(M+H)^+$, 277.5 $(M+Na)^+$.

*General procedure for preparation of 3-(substituted-phenyl)-propan-1-ol (**4a-e**):*

A mixture of Lithium aluminum hydride (9.5 g, 0.250 mol), dry THF (250 mL), to it add substituted dihydrocinnamic acid methyl ester (**3a-e**, 0.127 mol), in THF (50 mL) was added slowly drop wise during 30 min. After completion of addition the reaction mixture was stirred for 2 h at rt, after completion of reaction as monitored by TLC hexane/ethyl acetate (8:2), the reaction mixture was poured in water (200 mL), acidified with 5N HCl, extract with chloroform (2 × 400mL), extract was wash with water, brine solution, dried over Na_2SO_4 and concentrated. The crude residue was subjected to column chromatography on silica gel, column was eluted with hexane/ethyl acetate mixtures, pure compound was eluted in ethyl acetate in hexane, 10 % / 90 % (v/v) which was monitored by TLC, pure fractions were combined and concentrated to obtained 3-(substituted phenyl)- propan-1-ol as oily compounds with yields of 73 %-77 %.

*3-(Phenyl)-propan-1-ol (**4a**)*: Weight: 9.10 g; % yield: 73.2 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.32-7.28 (2H, m, H-3′, 5′), 7.14 (2H, d, J = 8.0 Hz, H-2′, 6′), 7.06 (1H, d, J = 7.2 Hz, H-4′), 3.56 (2H, d, J = 8.0 Hz, CH_2), 2.56 (2H, t, J = 7.2 Hz, H-3), 2.43 (1H, s, OH), 1.86 (2H, d, J = 7.6 Hz, H-2); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 146.2 (C-1′), 132.8 (C-3′, 5′), 130.2 (C-2′, 6′), 126.8 (C-4′), 65.8 (C-1), 38.3 (C-2), 31.9 (C-3); LC-MS: *m/z* 135.2 $(M-H)^-$.

*3-(4-Methoxy-Phenyl)-propan-1-ol (**4b**)*: Weight: 9.90 g; % yield: 77.2 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.11 (2H, d, J = 7.6 Hz, H-2′, 6′), 6.88 (2H, d, J = 8.0 Hz, H-3′, 5′), 3.78 (3H, s, OCH_3), 3.56 (2H, s, CH_2), 2.61 (2H, t, J = 7.2 Hz, H-3), 2.51 (1H, s, OH), 1.88 (2H, t, J = 7.6 Hz, H-2); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 156.4 (C-4′), 136.5 (C-1′), 130.8 (C-2′, 6′), 118.2 (C-3′, 5′), 64.8 (C-1), 56.2 (OCH_3), 38.6 (C-2), 31.8 (C-3); LC-MS: *m/z* 165.5 $(M-H)^-$.

*3-(2-Methoxy-Phenyl)-propan-1-ol (**4c**)*: Weight: 9.50 g; % yield: 74.0 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.12 (1H, dd, J = 8.0, 3.2 Hz, H-6′), 6.98 (1H, td, J = 7.6, 3.2 Hz, H-4′), 6.79 (1H, td, J = 7.6, 2.4 Hz, H-5′), 6.68 (1H, dd, J = 7.6, 3.2 Hz, H-3′), 3.78 (3H, s, OCH_3), 3.56 (2H, s, CH_2), 2.84 (2H, t, J = 7.2 Hz, H-3), 2.42 (1H, s, OH), 1.86 (2H, t, J = 7.6 Hz, H-2); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.2 (C-2′), 132.8 (C-6′), 128.4 (C-4′), 126.2 (C-1′), 121.9 (C-5′), 16.8 (C-3′), 66.4 (CH_2), 55.8 (OCH_3), 38.2 (C-2), 23.9 (C-3); LC-MS: *m/z* 167.2 $(M+H)^+$.

***3-(3, 4-Dimethoxy-Phenyl)-propan-1-ol (4d)*:** Weight: 9.80 g; % yield: 74.8 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.68 (1H, d, J = 7.6 Hz, H-5′), 6.62 (1H, dd, J = 7.6, 3.2 Hz, H-6′), 6.54 (1H, d, J = 3.2 Hz, H-2′), 3.78 (3H, s, OCH_3), 3.62 (2H, s, CH_2), 2.68 (2H, t, J = 7.6 Hz, H-3), 2.12 (1H, s, OH), 1.88 (2H, t, J = 7.6 Hz, H-2); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 156.4 (C-3′), 154.2 (C-4′), 138.6 (C-1′), 126.4 (C-6′), 118.6 (C-5′), 116.8 (C-2′), 66.3 (C-1), 55.8 (OCH_3), 55.6 (OCH_3), 38.2 (C-2), 30.9 (C-3); LC-MS: *m/*z 217.5 $(M+Na)^+$.

*3-(3, 4, 5-Trimethoxy-Phenyl)-propan-1-ol (**4e**)*: Weight: 10.20 g; % yield: 76.5 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.12 (2H, s, H-2′, 6′), 3.78 (6H, s, OCH_3), 3.76 (3H, s, OCH_3), 3.56 (2H, s, CH_2), 2.68 (2H, t, J = 7.6 Hz, H-3), 2.12 (1H, s, OH), 1.88 (2H, t, J = 7.2 Hz, H-2); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 156.8 (C-3′, 5′), 138.6 (C-1′), 133.8 (C-4′), 109.8 (C-2′, 6′), 66.8 (C-1), 55.8 (OCH_3), 55.6 (OCH_3), 55.5 (OCH_3), 38.2 (C-2), 31.8 (C-3); LC-MS: *m/z* 249.2 $(M+Na)^+$.

*General procedure for 3-(substituted-phenyl)-propan-1-al (**5a-e**):* Suitable 3-(substituted-phenyl)-propan-1-ol (**4a-e**, 0.02727 mol) compound was dissolved in DMSO (150 mL) and to the mixture IBX (28 g, 0.02727 mol) was added portion wise during 45 min. After completion of

addition, the reaction mixture was stirred for 2 h. at room temperature. After completion of reaction which was monitored by TLC hexane/ethyl acetate (8:2), the reaction mixture was poured into water (200 mL). The mixture was filter off; the filter bed was washed with chloroform (200 mL). The filtrate was taken in to a separating funnel, separated the organic layer and the aqueous layer was extracted with chloroform (200 mL). The combined organic layer was washed with water, brine solution, dried over Na_2SO_4 and concentrated under vacuum. The crude residue was subjected to column chromatography on silica gel, using ethyl acetate in hexane, 15 % / 85 % (v/v) eluents as monitored by TLC, pure fractions were combined and concentrated to obtained 3-(substituted-phenyl)-propan-1-al as oily compounds with yields of (**5a-e**, 73 -81 %).

*3-(Phenyl)-propan-1-al (**5a**)*: Weight: 6.50 g; % yield: 73.4 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.82 (1H, s, CHO), 7.34 (2H, d, J = 7.6 Hz, H-3′, 5′), 7.21 (2H, d, J = 8.0 Hz, H-2′, 6′), 7.09 (1H, t, J = 7.2 Hz, H-4′), 2.98 (2H, t, J = 7.6 Hz, H-3), 2.79 (2H, t, J = 7.2 Hz, H-2); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 201.4 (C=O), 148.2 (C-1′), 136.9 (C-3′, 5′), 136.2 (C-2′, 6′), 129.6 (C-4′), 48.6 (C-2), 29.2 (C-3); LC-MS: *m/z* 157.3 $(M+Na)^+$.

*3-(4-Methoxy phenyl)-propan-1-al (**5b**)*: Weight: 7.20 g; % yield: 81.0 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.82 (1H, s, CHO), 7.14 (2H, d, J = 8.0 Hz, H-2′, 6′), 6.82 (2H, d, J = 7.6 Hz, H-3′, 5′), 3.72 (3H, s, OCH_3), 2.98 (2H, t, J = 7.6 Hz, H-3), 2.72 (2H, t, J = 7.6 HZ, H-2); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 201.4 (C=O), 168.2 (C-4′), 136.8 (C-1′), 130.8 (C-2′, 6′), 116.8 (C-3′, 5′), 55.8 (OCH_3), 48.6(C-2), 28.9 (C-3); LC-MS: *m/z* 187.2 $(M+Na)^+$.

*3-(2-Methoxy Phenyl)-propan-1-al (**5c**)*: Weight: 6.80 g; % yield: 76.5 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.72 (1H, s, CHO), 7.12 (1H, dd, J = 7.6, 3.2 Hz, H-6′), 6.98 (1H, td, J = 7.6, 3.2 Hz, H-4′), 6.88 (1H, td, J = 7.6, 2.4 Hz, H-5′), 6.76 (1H, dd, J = 7.6, 3.2 Hz, H-3′), 3.78 (3H, s, OCH_3), 2.98 (2H, t, J = 7.6 Hz, H-3), 2.76 (2H, t, J = 7.2 Hz, H-2); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 202.1 (C=O), 168.9 (C-2′), 132.6 (C-6′), 128.2 (C-4′), 126.4 (C-1′), 121.5 (C-5′), 118.4 (C-3′), 56.3 (OCH_3), 46.8 (C-2), 19.8 (C-3); LC-MS: *m/z* 203.3 $(M+K)^+$.

*3-(3, 4-Dimethoxy phenyl)-propan-1-al (**5d**)*: Weight: 6.90 g; % yield: 77.4 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.72 (1H, s, CHO), 6.79 (1H, d, J = 8.0 Hz, H-5′), 6.66 (1H, dd, J = 7.6, 3.2 Hz, H-6′), 6.58 (1H, d, J = 3.2 Hz, H-2′), 3.78 (6H, s, OCH_3), 2.98 (2H, t, J = 8.0 Hz, H-3), 2.76 (2H, t, J = 7.6 Hz, H-2); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 202.1 (C=O), 156.4 (C-3′), 148.6 (C-4′), 138.6 (C-1′), 126.9 (c-6′), 118.6 (C-5′), 116.8 (C-2′), 55.8 (OCH_3), 55.6 (OCH_3), 48.3 (C-2), 28.9 (C-3); LC-MS: *m/z* 195.2 $(M+H)^+$, 217.3 $(M+Na)^+$.

*3-(3, 4, 5-Trimethoxy phenyl)-propan-1-al (**5e**)*: Weight: 7.10 g; % yield: 79.6 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.72 (1H, s, CHO), 6.12 (2H, s, H-2′, 6′), 3.78 (6H, s, OCH_3), 3.76 (3H, s, OCH_3), 2.98 (2H, t, J = 7.6 Hz, H-3), 2.7 6(2H, t, J = 7.2 Hz, H-2); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 202.1 (C=O), 152.4 (C-3′, 5′), 144.6 (C-1′),138.6 (C-4′), 106.8 (C-2′, 6′), 55.8 (OCH_3), 55.6 (OCH_3), 55.5 (OCH_3), 48.2 (C-2), 30.1 (C-3); LC-MS: *m/z* 225.3 $(M+H)^+$.

*General procedure for 5-(Substituted-phenyl)-pent-2-enoic acid ethylester (**6a-e**):* A mixture of suitable 3-(substituted phenyl)-propan-1-al (**5a-e**, 0.02038 mol), dry THF (50 mL) and ethyl triphenylphosphorane (7.1 g, 0.02038 mol) was refluxed for 4-5 h. After completion of reaction, the reaction mixture was concentrated under vacuum. The crude residue was purified by column chromatography on silica gel (ethyl acetate in hexane, 5 % / 95 % - 10 % / 90 % (v/v)) to yield the corresponding 5-(substituted phenyl)-pent-2-enoic acid ethyl ester (**6a-e**, 60-66%).

*5-(Phenyl)-pent-2-enoic acid ethyl ester (**6a**)*:Weight: 5.54 g; % yield: 60.7 %;^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.26 (2H, d, J = 7.6 Hz, H-3′, 5′), 7.18 (2H, d, J = 8.0 Hz, H-2′, 6′), 7.08 (1H, d, J = 8.0 Hz, H-4′), 6.98 (1H, d, J = 16.4 Hz, H-3), 5.92 (1H, d, J = 16.0 Hz, H-2), 4.28 (2H, q, J = 7.6 Hz, OCH_2), 2.68 (2H, t, J = 7.6 Hz, H-5), 2.36 (2H, t, J = 8.0 Hz, H-4), 1.42 (3H, s, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.2 (C=O), 148.5 (C-3), 142.8 (C-1′), 136.5 (C-3′, 5′), 132.4 (C-2′, 6′), 128.7 (C-4′), 124.6 (C-2), 62.3 (OCH_2), 38.4 (C-5), 35.8 (C-4), 14.6 (CH_3); LC-MS: *m/z* 227.2 $(M+Na)^+$.

*5-(4-Methoxy-phenyl)-pent-2-enoic acid ethyl ester (**6b**)*: Weight: 5.61 g; % yield: 65.5 %;^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.28 (2H, d, J = 8.0 Hz, H-2′, 6′), 7.04 (1H, d, J = 16.0 Hz, H-3), 6.86 (2H, d, J = 8.0 Hz, H-3′, 5′), 4.52 (2H, q, J = 7.6 Hz, OCH_2), 3.78 (3H, s, OCH_3), 2.68 (2H, t, J = 7.6 Hz, H-5), 2.36 (2H, t, J = 8.0 Hz, H-4), 1.42 (3H, s, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.2 (C=O), 161.2 (C-4′), 148.5 (C-3), 138.6 (C-1′), 132.4 (C-2′, 6′), 122.6 (C-2), 116.8 (C-3′, 5′), 62.1 (OCH_2), 56.8 (OCH_3), 38.3 (C-5), 35.4 (C-4), 14.6 (CH_3); LC-MS: *m/z* 235.5 $(M+H)^+$, 257.2 $(M+Na)^+$.

*5-(2-Methoxy-Phenyl)-Pent-2-enoic acid ethyl ester (**6c**)*: Weight: 5.42 g; % yield: 63.3 %;^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.26 (1H, dd, J = 7.6, 2.4 Hz, H-6′), 7.08 (1H, td, J = 8.0, 2.4 Hz, H-4′), 6.98 (1H, d, J = 16.4 Hz, H-3), 6.86 (1H, td, J = 8.0, 3.2 Hz, H-5′), 6.78(1H, dd, J = 7.6, 2.4 Hz, H-3′), 5.88 (1H, d, J = 16.0 Hz, H-2), 4.32 (2H, t, J = 7.6 Hz, OCH_2), 3.78 (3H, s, OCH_3), 2.68 (2H, t, J = 7.6 Hz, H-5), 2.36 (2H, t, J = 8.0 Hz, H-4), 1.42 (3H, s, CH_3); ^{13}C NMR ($CDCl_3$,

100 MHz): δ 168.2 (C=O), 164.6 (C-2′), 148.6 (C-3), 136.4 (C-6′), 132.8 (C-4′), 132.6 (C-1′), 128.4 (C-5′), 126.4 (C-2), 116.8 (C-3′), 61.6 (OCH_2), 55.8 (OCH_3), 36.8 (C-4), 28.4 (C-5), 14.3 (CH_3); LC-MS: *m/*z 235.3 $(M+H)^+$.

*5-(3, 4-Dimethoxy-phenyl)-pent-2-enoic acid ethyl ester (**6d**)*: Weight: 5.1 g; % yield: 62.5 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.08 (1H, d, *J* = 16.0 Hz, H-3), 6.84 (1H, d, *J* = 7.6 Hz, H-5′), 6.72 (1H, dd, *J* = 3.2, 7.6 Hz, H-6′), 6.68 (1H, d, *J* = 3.2 Hz, H-2′), 5.92 (1H, d, *J* = 16.4 Hz, H-2), 4.34 (2H, q, *J* = 7.6 Hz, OCH_2), 3.78 (6H, s, OCH_3), 2.64 (2H, t, *J* = 8.0 Hz, H-5), 2.32 (2H, t, *J* = 8.0 Hz, H-4), 1.46 (3H, s, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.4 (C=O), 158.6 (C-3′), 156.8 (C-4′), 148.2 (C-3), 138.6 (C-1′), 126.4 (C-6′), 124.3 (C-2), 118.2 (C-5′), 116.5 (C-2′), 61.8 (OCH_2), 55.8 (OCH_3), 55.7 (OCH_3), 38.6 (C-5), 34.8 (C-4), 14.2 (CH_3); LC-MS: *m/z* 265.5 $(M+H)^+$, 287.3 $(M+Na)^+$.

*5-(3, 4, 5-Trimethoxy-Phenyl)-Pent-2-enoic acid ethyl ester (**6e**)*: Weight: 5.20 g; % yield: 66.1 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.12 (1H, d, *J* = 16.4 Hz, H-3), 6.28 (2H, s, H-2′, 6′) , 5.92 (1H, d, *J* = 16.0 Hz, H-2), 4.36 (2H, q, *J* = 7.6 Hz, OCH_2), 3.86 (9H, s, OCH_3), 2.68 (2H, t, *J* = 8.0 Hz, H-5), 2.31 (2H, t, *J* = 7.6 Hz, H-4), 1.28 (3H, s, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.2 (C=O), 156.2 (C-3′, 5′), 152.8 (C-3), 136.4 (C-1′), 134.9 (C-4′), 128.4 (C-2), 114.6 (C-2′, 6′), 61.8 (OCH_2), 56.8 (OCH_3), 56.5 (OCH_3), 55.8 (OCH_3), 38.1 (C-5), 34.6 (C-4), 14.3 (CH_3); LC-MS: *m/z* 295.3 $(M+Na)^+$.

*General procedure for 5-(substituted-phenyl)-pentanoic acid ethyl ester (**7a-e**)*: A mixture of suitable 5-(substituted phenyl)-pent-2-enoic acid ethyl esters (**6a-e**, 0.01 mol), ethyl acetate (40 mL) and palladium on $CaCO_3$ (10 mg) was taken in a RB flask and contents were vigorously stirred under H_2 atmosphere for 2 h. After completion of reaction, the reaction mixture was filtered on celite, washed with ethyl acetate and the filtrate was concentrated under vacuum to obtain the corresponding 5-(substituted phenyl)-pentanoic acid ethyl ester (**7a-e**, 89-91%).

*5-(Phenyl)-Pentanoic acid ethyl ester (**7a**)*: Weight: 4.55 g; % yield: 90.3 %;^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.32 (2H, d, *J* = 7.2 Hz, H-3′, 5′), 7.16 (2H, s, H-2′, 6′), 7.06 (1H, d, *J* = 7.6 Hz, H-4′), 4.31 (2H, q, *J* = 7.2 Hz, OCH_2), 2.68 (2H, t, *J* = 8.0 Hz, H-5), 2.31 (2H, t, *J* = 7.6 Hz, H-2), 1.78-1.64 (4H, m, H-3, 4), 1.46 (3H, s, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 181.6 (C=O), 146.5 (C-1′), 128.9 (C-2′, 6′), 128.3 (C-3′, 5′), 126.8 (C-4′), 63.1 (OCH_2), 36.8 (C-5), 33.9 (C-2), 32.1 (C-4), 26.8 (C-3), 14.5 (CH_3); LC-MS: *m/z* 205.4 $(M-H)^-$.

*5-(4-Methoxy-phenyl)-pentanoic acid ethyl ester (**7b**)*: Weight: 4.58 g; % yield: 90.9 %;^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.12 (2H, d, J = 7.2 Hz, H-2′, 6′), 6.88 (2H, d, J = 7.6 Hz, H-3′, 5′), 4.37 (2H, q, J = 8.0 Hz, OCH_2), 3.78 (3H, s, OCH_3), 2.66 (2H, t, J = 7.2 Hz, H-5), 2.31 (2H, t, J = 7.6 Hz, H-2), 1.76-1.74 (2H, m, H-3), 1.62-1.56 (2H, m, H-4), 1.41 (3H, s, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 184.1 (C=O), 166.2 (C-4′), 136.3 (C-1′), 129.8 (C-2′, 6′), 116.4 (C-3′, 5′), 62.6 (OCH_2), 56.8 (OCH_3), 39.6 (C-5), 36.8 (C-2), 32.4 (C-4), 28.4 (C-3), 14.5 (CH_3); LC-MS: *m/*z 259.3 $(M+H)^+$.

*5-(2-Methoxy-Phenyl)-Pentanoic acid ethyl ester (**7c**)*: Weight: 4.52 g; % yield: 89.7 %;^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.28 (1H, dd, J = 7.2, 2.4 Hz, H-6′), 7.12 (2H, td, J = 7.6, 3.2 Hz, H-4′, 5′), 7.01 (1H, dd, J = 7.2, 2.4 Hz, H-3′), 4.31 (2H, q, J = 8.0 Hz, OCH_2), 3.72 (3H, s, OCH_3), 2.74 (2H, t, J = 7.2 Hz, H-5), 2.38 (2H, t, J = 7.6 Hz, H-2), 1.72-1.66 (4H, m, H-3, 4), 1.42 (3H, s, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 182.4 (C=O), 168.4 (C-2′), 136.8 (C-6′), 132.4 (C-4′), 1245.9 (C-1′), 122.8 (C-5′), 116.4 (C-3′), 62.6 (OCH_2), 56.2(OCH_3), 36.4 (C-2), 32.8 (C-4), 26.4 (C-5), 25.1 (C-3), 14.2 (CH_3); LC-MS: *m/*z 237.5 $(M+H)^+$.

*5-(3, 4-Dimethoxy-Phenyl)-Pentanoic acid ethyl ester (**7d**)*: Weight: 4.54 g; % yield: 90.3 %;^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.86 (1H, d, J = 7.6 Hz, H-5′), 6.72 (1H, dd, J = 7.6, 2.4 Hz, H-6′), 6.58 (1H, d, J = 2.4 Hz, H-2′), 4.38 (2H, q, J = 7.2 Hz, OCH_2), 3.82 (6H, s, OCH_3), 2.76 (2H, t, J = 7.6 Hz, H-5), 2.37 (2H, t, J = 8.0 Hz, H-2), 1.76-1.72 (2H, m, H-3), 1.66-1.59 (2H, m, H-4), 1.46 (3H, s, OCH_3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 184.1 (C=O), 154.1 (C-3′), 152.6 (C-4′), 138.6 (C-1′), 130.1 (C-6′), 116.2 (C-5′), 114.8 (C-2′), 62.3 (OCH_2), 56.8 (OCH_3), 56.6 (OCH_3), 38.6 (C-5), 36.4 (C-2), 31.9 (C-4), 28.3 (C-3), 14.2 (CH_3); LC-MS: *m/*z 267.2 $(M+H)^+$, 289.3 $(M+Na)^+$.

*5-(3, 4, 5-Trimethoxy-Phenyl)-Pentanoic acid ethyl ester (**7e**)*: Weight: 4.60 g; % yield: 91.4%;^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.28 (2H, s, H-2′, 6′), 4.48 (2H, q, J = 7.6 Hz, OCH_2), 3.78 (6H, s, OCH_3), 3.72 (3H, s, OCH_3), 2.68 (2H, t, J = 8.0 Hz, H-5), 2.36 (2H, t, J = 7.6 Hz, H-2), 1.76-1.72 (4H, m, H-3,4), 1.48(3H, s, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 182.2 (C=O), 156.8 (C-3′, 5′), 146.2 (C-1′), 138.6 (C-4′), 110.6 (C-2′, 6′), 63.1 (OCH_2), 55.8 (OCH_3), 55.6 (OCH_3), 55.5 (OCH_3), 41.4 (C-5), 36.4 (C-2), 32.8 (C-4), 28.1 (C-3), 14.6 (CH_3); LC-MS: *m/*z 297.2 $(M+H)^+$, 319.4 $(M+Na)^+$.

*General procedure for 5-(substituted-phenyl)-pentan-1-ol (**8a-e**)*: Lithium aluminum hydride (1.1 g, 0.02898 mol) was suspended in dry THF (20 mL) and treated with a solution of suitable

5-(substituted phenyl)-pentanoic acid ethyl esters (**7a-e**, 0.01449 mol) in THF (5 mL) was added slowly drop wise for 15 min. Then the reaction mixture was stirred for 2 h at r.t. After completion of reaction, the reaction mixture was poured into water (100 mL), acidified with 2N HCl and extracted with chloroform (2 × 250 mL). The combined organic layer was washed with brine solution, dried over Na_2SO_4 and concentrated under vacuum. The crude residue was purified by column chromatography on silica gel (ethyl acetate in hexane, 20 % / 80 % (v/v)) to yield the corresponding 5-(substituted -phenyl)-pentan-1-ol (**8a-e**, 82-88 %).

*5-(Phenyl)-Pentan-1-ol (**8a**)*: Weight: 3.08 g; % yield: 86.0 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.42 (2H, d, J = 7.6 Hz, H-3′, 5′), 7.26 (2H, d, J = 8.0 Hz, H-2′, 6′), 7.08 (1H, s, H-4′), 3.58 (2H, t, J = 7.2 Hz, H-1), 2.66 (2H, t, J = 7.6 Hz, H-5), 1.78-1.74 (2H, m, H-4), 1.52-1.49 (2H, m, H-2), 1.29-1.27 (2H, m, H-3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 142.6 (C-1′), 129.4 (C-2′, 6′), 128.4 (C-3′, 5′), 126.8 (C-4′), 66.4 (C-1), 38.6 (C-5), 34.6 (C-2), 32.7 (C-4), 28.9 (C-3); LC-MS: *m/*z 165.2 $(M+H)^+$.

*5-(4-Methoxy-Phenyl)-Pentan-1-ol (**8b**)*: Weight: 3.25 g; % yield: 87.9 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.12 (2H, d, J = 8.0 Hz, H-2′, 6′), 6.84 (2H, d, J = 7.6 Hz, H-3′, 5′), 3.88 (2H, t, J = 7.2 Hz, H-1), 3.72 (3H, s, OCH_3), 2.72 (2H, t, J = 7.6 Hz, H-5), 2.08 (1H, s, OH), 1.74-1.71 (2H, m, H-4), 1.51-1.48 (2H, m, H-2), 1.33-1.31 (2H, m, H-3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 162.8 (C-4′), 134.6 (C-1′), 132.8 (C-2′, 6′), 114.6 (C-3′, 5′), 66.2 (C-1), 56.1 (OCH_3), 38.6 (C-5), 33.7 (C-2), 32.9 (C-4), 26.1 (C-3); LC-MS: *m/*z 217.3 $(M+Na)^+$.

*5-(2-Methoxy-Phenyl)-Pentan-1-ol (**8c**)*: Weight: 3.16 g; % yield: 85.4 %;^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.16 (1H, dd, J = 7.2, 2.4 Hz, H-6′), 7.08 (1H, td, J = 7.6, 3.2 Hz, H-4′), 6.88 (1H, td, J = 8.0, 2.4 Hz, H-5′), 6.72 (1H, dd, J = 7.6, 3.2 Hz, H-3′), 3.72 (3H, s, OCH_3), 3.68 (2H, t, J = 7.2 Hz, H-1), 2.74 (2H, t, J = 7.6 Hz, H-5), 2.08 (1H, s, OH), 1.76-1.72 (2H, m, H-4), 1.48-1.46 (2H, m, H-2), 1.34-1.29 (2H, m, H-3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 164.9 (C-2′), 136.5 (C-6′), 128.4 (C-4′), 125.8 (C-1′), 122.6 (C-5′), 116.8 (C-3′), 66.2 (C-1), 55.8 (OCH_3), 36.4 (C-2), 32.9 (C-4), 26.4 (C-5), 25.9 (C-3); LC-MS: *m/*z 217.3 $(M+Na)^+$.

*5-(3, 4-Dimethoxy-Phenyl)-Pentan-1-ol (**8d**)*: Weight: 3.10 g; % yield: 82.0 %;^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.86 (1H, d, J = 7.6 Hz, H-5′), 6.72 (1H, dd, J = 7.2, 3.2 Hz, H-6′), 6.58 (1H, d, J = 3.2 Hz, H-2′), 3.81 (2H, t, J = 7.6 Hz, H-1), 2.76 (2H, t, J = 8.0 Hz, H-5), 2.08 (1H, s, OH), 1.83-1.79 (2H, m, H-4), 1.56-1.52 (2H, m, H-2), 1.35-1.33 (2H, m, H-3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 156.3 (C-3′), 154.2 (C-4′), 136.4 (C-1′), 128.6 (C-6′), 116.8 (C-2′), 114.2 (C-5′), 66.8

(C-1), 55.9 (OCH_3), 55.8 (OCH_3), 38.5 (C-5), 36.8 (C-2), 32.9 (C-4), 26.4 (C-3); LC-MS: *m/*z 247.6 $(M+Na)^+$.

*5-(3, 4, 5-Trimethoxy-Phenyl)-Pentan-1-ol (**8e**)*: Weight: 3.21 g; % yield: 83.2 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.28 (2H, s, H-2′, 6′), 3.86 (6H, s, OCH_3), 3.78 (3H, s, OCH_3), 3.62 (2H, t, *J* = 7.6 Hz, H-1), 2.68 (2H, t, *J* = 7.2 Hz, H-5), 2.07 (1H, s, OH), 1.81-1.79 (2H, m, H-4), 1.56-1.53 (2H, m, H-2), 1.32-1.27 (2H, m, H-3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 156.3 (C-3′, 5′), 138.6 (C-1′), 132.4 (C-4′), 114.3 (C-2′,6′), 68.2 (C-1), 55.8 (OCH_3), 55.7 (OCH_3), 55.6 (OCH_3), 39.2 (C-5), 36.1 (C-2), 32.7 (C-4), 26.5 (C-3); LC-MS: *m/*z 255.4 $(M+H)^+$, 277.2 $(M+Na)^+$.

*General procedure for 5-(substituted-phenyl)-pentan-1-al (**9a-e**)*: To a mixture of 9-(substituted phenyl)-pentan-1-ol compounds (**8a-e**, 0.01 mol) in DMSO (20 mL) in a 100 mL R.B flask was added IBX (0.01 mol) slowly portion wise and the reaction mixture was then stirred for 3 h at r.t . After completion of reaction, the reaction mixture was poured into water (100 mL) and chloroform (100 mL).The mixture was kept under stirring for 10 minutes and then filtered, and the filter bed washed with chloroform (100 mL). The organic layer was separated. The aqueous layer was extracted with chloroform (100 mL) and the combined the organic layer was washed with water, brine solution, dried over Na_2SO_4 and concentrated under vacuum. The crude residue was purified by column chromatography on silica gel (ethyl acetate in hexane, 15 % / 85 % (v/v) as eluent) to obtain the corresponding 5-(substituted phenyl)-pentan-1-al (**9a-e**, 83-85%).

*5-(Phenyl)-pentan-1-al (**9a**)*: Weight: 2.46 g; % yield: 83.0 %;^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.71 (1H, s, CHO), 7.38 (2H, s, H-3′, 5′), 7.21 (2H, d, *J* = 7.6 Hz, H-2′, 6′), 7.08 (1H, d, *J* = 8.0 Hz, H-4′), 2.66 (2H, t, *J* = 8.0 Hz, H-5), 2.46 (2H, t, *J* = 7.2 Hz, H-2), 1.711-1.68 (4H, m, H-3, 4); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 202.6 (C=O), 142.3 (C-1′), 129.8 (C-2′, 6′), 128.2 (C-3′, 5′), 126.3 (C-4′), 46.9 (C-2), 36.8 (C-5), 32.6 (C-4), 22.8 (C-3); LC-MS: *m/*z 161.4 $(M-H)^-$.

*5-(4-Methoxy-phenyl)-pentan-1-al (**9b**)*: Weight: 2.50 g; % yield: 84.2 %;^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.76 (1H, s, CHO), 7.12 (2H, d, *J* = 7.6 Hz, H-2′, 6′), 6.88 (2H, d, *J* = 7.2 Hz, H-3′, 5′), 3.72 (6H, s, OCH_3), 2.68(2H, t, *J* = 8.0 Hz, H-5), 2.52 (2H, t, *J* = 7.6 Hz, H-2), 1.74-1.69(4H, m, H-3, 4); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 202.6 (C=O), 166.4 (C-4′), 136.2 (C-1′), 129.8 (C-2′, 6′), 114.8 (C-3′, 5′), 56.3 (OCH_3), 46.2 (C-2), 38.3 (C-5), 33.6 (C-4), 22.6 (C-3); LC-MS: *m/z* 193.2 $(M+H)^+$, 369.3 $(M+Na)^+$.

*5-(2-Methoxy-phenyl)-pentan-1-al (**9c**)*: Weight: 2.52g; % yield: 84.9 %;^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.72 (1H, s, CHO), 7.12 (1H, dd, *J* = 7.6, 2.4 Hz, H-6′), 6.99 (1H, td, *J* = 8.0, 3.2 Hz, H-

4′), 6.78 (1H, td, *J* = 7.6, 3.2 Hz, H-5′), 6.68 (1H, dd, *J* = 7.2, 2.4 Hz, H-3′), 3.76 (3H, s, OCH_3), 2.68 (2H, t, *J* = 8.0 Hz, H-5), 2.46 (2H, t, *J* = 8.0 Hz, H-2), 1.72-1.69 (4H, m, H-3, 4); ^{13}C NMR ($CDCl_3$, 100 MHz): *δ* 202.6 (C=O), 166.8 (C-2′), 136.8 (C-6′), 128.6 (C-4′), 126.9 (C-1′), 122.4 (C-5′), 114.8 (C-3′), 56.6 (OCH_3), 46.8 (C-2), 33.8 (C-4), 26.4 (C-5), 22.8 (C-3); LC-MS: *m/*z 215.6$(M+Na)^+$.

*5-(3, 4-Dimethoxy-phenyl)-pentan-1-al (**9d**)*: Weight: 2.48 g; % yield: 83.6 %;^{1}H NMR ($CDCl_3$, 400 MHz): *δ* 9.76 (1H, s, CHO), 6.68 (1H, d, *J* = 8.0 Hz, H-5′), 6.57 (1H, dd, *J* = 7.2, 2.4 Hz, H-6′), 6.52 (1H, d, *J* = 3.2 Hz, H-2′), 3.78 (6H, s, OCH_3), 3.72 (3H, s, OCH_3), 2.68 (2H, t, *J* = 7.6 Hz, H-5), 2.46 (2H, t, *J* = 7.2 Hz, H-2), 1.72-1.68 (4H, m, H-3, 4); ^{13}C NMR ($CDCl_3$, 100 MHz): *δ* 202.4 (C=O), 156.8 (C-3′), 152.8 (C-4′), 136.7 (C-1′), 128.6 (C-6′), 116.4 (C-2′), 114.2 (C-5′), 56.3 (OCH_3), 55.9 (OCH_3), 46.3 (C-2), 36.9 (C-5), 34.6 (C-4), 26.9 (C-3); LC-MS: *m/*z 223.5 $(M+H)^+$, 245.2 $(M+Na)^+$.

*5-(3, 4, 5-Trimethoxy-phenyl)-pentan-1-al (**9e**)*: Weight: 2.51 g; % yield: 84.5 %;^{1}H NMR ($CDCl_3$, 400 MHz): *δ* 9.74 (1H, s, CHO), 6.26 (2H, s, H-2′, 6′), 3.86 (6H, s, OCH_3), 3.72 (9H, s, OCH_3), 2.58 (2H, t, *J* = 7.2 Hz, H-5), 2.42 (2H, t, *J* = 8.0 Hz, H-2), 1.74-1.69 (4H, m, H-3, 4); ^{13}C NMR ($CDCl_3$, 100 MHz): *δ* 202.1 (C-1), 156.8 (C-3′, 5′), 138.4 (C-1′), 132.6 (C-4′), 110.5 (C-2′, 6′), 56.3 (OCH_3), 55.8 (OCH_3), 55.7 (OCH_3), 46.8 (C-2), 38.2 (C-5), 32.8 (C-4), 28.6 (C-3); LC-MS: *m/*z 253.6 $(M+H)^+$, 275.4 $(M+Na)^+$.

*General procedure for preparation of 7-(substituted-phenyl)-1-(substituted-phenyl)-hept-2-en-1-one (**11a-q**)*: A mixture of any one of 5-(substituted-phenyl)-propan-1-al (**9a-e**, 0.0016mol), any one of 1-(substituted-phenyl)-2-(triphenylphosphonyllidiene)-ethanone (**10a-d**, 0.0016 mol), dry THF (20 mL), was refluxed for 4 h. After completion of reaction which was monitored by TLC hexane/ethyl acetate (9:1), the reaction mixture was concentrated under vacuum. The crude residue was subjected to column chromatography on silica gel, column was eluted with hexane/ethyl acetate mixtures. Pure compound was eluted in ethyl acetate in hexane, 5 % / 95 % (v/v) which were monitored by TLC and pure fractions were combined and concentrated under vacuum obtained 7-(substituted phenyl)-1-(substituted phenyl)-hept-2en-1-one (**11a-q**) with yields of 46-60 %.

*7-(Phenyl)-1-(3,4-dimethoxy-phenyl)-hept-2-en-1-one (**11a**)*: Weight: 472 mg; % yield: 47.2 %; ^{1}H NMR ($CDCl_3$, 400 MHz): *δ* 7.42 (1H, dd, *J* = 7.6, 2.4 Hz, H-6′), 7.24 (2H, d, *J* = 7.2 Hz, H-

3″, 5″), 7.21 (1H, d, *J* = 2.4 Hz, H-2′), 7.14 (2H, d, *J* = 8.0 Hz, H-2″, 6″), 7.08 (1H, d, *J* = 7.6 Hz, H-4″), 7.02 (1H, d, *J* = 17.2 Hz, H-2), 6.99 (2H, d, *J* = 16.4 Hz, H-3), 6.88 (1H, d, *J* = 7.6 Hz, H-5′), 3.78 (6H, s, OCH_3), 2.66 (2H, t, *J* = 8.0 Hz, H-7), 2.03 (2H, t, *J* = 7.6 Hz, H-4), 1.69-1.66 (2H, m, H-6), 1.33-1.31 (2H, m, H-5); ^{13}C NMR ($CDCl_3$, 100 MHz): *δ* 187.2 (C=O), 156.8 (C-4′), 149.6 (C-3′), 147.8 (C-3), 139.6 (C-1″), 132.1 (C-1′), 129.3 (C-2″, 6″), 128.1 (C-3″, 5″), 126.7 (C-4″), 126.2 (C-2), 123.7 (C-6′), 118.2 (C-2′), 115.8 (C-5′), 56.3 (OCH_3), 56.2 (OCH_3), 36.2 (C-7), 32.9 (C-4), 32.6 (C-6), 29.7 (C-5); LC-MS: *m/z* 325.3 $(M+H)^+$.

*7-(Phenyl)-1-(2,5-dimethoxy-phenyl)-hept-2-en-1-one (**11b**)*: Weight: 469 mg; % yield: 46.9 %;^{1}H NMR ($CDCl_3$, 400 MHz): *δ* 7.38 (1H, d, *J* = 2.4 Hz, H-6′), 7.21 (2H, s, H-3″, 5″), 7.14-7.12 (2H, m, H-2″, 6″), 7.06 (1H, s, H-4″), 7.01 (1H, d, *J* = 17.2 Hz, H-2), 6.99 (1H, d, *J* = 16.4 Hz, H-3), 6.92 (1H, dd, *J* = 7.6, 2.4 Hz, H-4′), 6.86 (1H, d, *J* = 7.6 Hz, H-3′), 3.78 (3H, s, OCH_3), 3.76 (3H, s, OCH_3), 2.68 (2H, t, *J* = 7.6 Hz, H-7), 2.02 (2H, t, *J* = 8.0 Hz, H-4), 1.68-1.64 (2H, m, H-6), 1.33-1.31 (2H, m, H-5); ^{13}C NMR ($CDCl_3$, 100 MHz): *δ* 187.4 (C=O), 158.6 (C-2′), 156.7 (C-5′), 149.6 (C-3), 142.6 (C-1″), 129.6 (C-2″, 6″), 129.5 (C-3″, 5″), 126.8 (C-4″), 125.8 (C-2), 123.7 (C-1′), 121.6 (C-4′), 118.6 (C-6′), 115.4 (C-3′), 56.8 (OCH_3), 56.7 (OCH_3), 55.9 (OCH_3), 36.1 (C-7), 32.8 (C-4), 32.1 (C-6), 29.5 (C-5); LC-MS: *m/z* 325.3 $(M+H)^+$, 347.4 $(M+Na)^+$.

*7-(4-Methoxy-phenyl)-1-(phenyl)-hept-2-en-1-one (**11c**)*: Weight: 415 mg; % yield: 54.2 %; ^{1}H NMR ($CDCl_3$, 400 MHz): *δ* 7.88 (2H, d, *J* = 7.2 Hz, H-2′, 6′), 7.62 (1H, d, *J* = 8.0 Hz, H-4′), 7.46 (2H, d, *J* = 7.6 Hz, H-3′, 5′), 7.04 (1H, d, *J* = 17.2 Hz, H-2), 7.01 (2H, d, *J* = 7.6 Hz, H-2″, 6″), 6.99 (1H, d, *J* = 16.4 Hz, H-3), 6.78 (2H, d, *J* = 7.6 Hz, H-3″, 5″), 3.82 (3H, s, OCH_3), 2.68 (2H, t, *J* = 7.2 Hz, H-7), 2.01 (2H, t, *J* = 7.6 Hz, H-4), 1.76-1.72 (2H, m, H-6), 1.33-1.29 (2H, m, H-5); ^{13}C NMR ($CDCl_3$, 100 MHz): *δ* 187.1 (C=O), 164.2 (C-4″), 149.5 (C-3), 139.6 (C-1′), 136.4 (C-4′), 132.7 (C-1″), 130.8 (C-2′, 6′), 129.4 (C-2″, 6″), 128.6 (C-3′, 5′), 125.6 (C-2), 114.8 (C-3″, 5″), 56.3 (OCH_3), 36.1 (C-7), 32.9 (C-4), 32.3 (C-6), 29.8 (C-5); LC-MS: *m/z* 295.3 $(M+H)^+$, 317.3 $(M+Na)^+$.

*7-(4-Methoxy-phenyl)-1-(2,4-dimethoxy-phenyl)-hept-2-en-1-one (**11d**)*: Weight: 455 mg; % yield: 49.3 %; ^{1}H NMR ($CDCl_3$, 400 MHz): *δ* 7.68 (1H, d, *J* = 7.2 Hz, H-6′), 7.03 (1H, d, *J* = 17.2 Hz, H-2), 7.01 (2H, d, *J* = 7.2 Hz, H-2″, 6″), 6.99 (1H, d, *J* = 16.4 Hz, H-3), 6.78 (2H, d, *J* = 7.6 Hz, H-3″, 5″), 6.56 (1H, dd, *J* = 7.2, 3.2 Hz, H-5′), 6.46 (1H, d, *J* = 3.2 Hz, H-3′), 3.88 (6H, s, OCH_3), 3.84 (3H, s, OCH_3), 2.66 (2H, t, *J* = 7.6 Hz, H-7), 2.02 (2H, t, *J* = 7.6 Hz, H-4), 1.72-

1.68 (2H, m, H-6), 1.3-1.31 (2H, m, H-5); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 187.2 (C=O), 174.3 (C-4′), 168.6 (C-2′), 160.8 (C-4″), 148.9 (C-3), 136.8 (C-1″), 132.7 (C-6′), 129.6 (C-2″, 6″), 126.5 (C-2), 116.4 (C-1′), 114.8 (C-3″, 5″), 108.6 (C-5′), 101.3 (C-3′), 56.6 (OCH_3), 56.4 (OCH_3), 56.3 (OCH_3), 36.8 (C-7), 32.7 (C-4), 32.1 (C-6), 29.7 (C-5); LC-MS: *m/z* 355.3 $(M+H)^+$, 377.3 $(M+Na)^+$.

7-(4-Methoxy-phenyl)-1-(2,5-dimethoxy-phenyl)-hept-2-en-1-one ***(11e)***: Weight: 415 mg; % yield: 54.2 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.38 (1H, d, *J* = 3.2 Hz, H-6′), 7.04 (1H, d, *J* = 17.2 Hz, H-2), 7.01 (2H, d, *J* = 7.2 Hz, H-2″, 6″), 6.99 (1H, d, *J* = 16.4 Hz, H-3), 6.92 (1H, dd, *J* = 7.6, 3.2 Hz, H-4′), 6.86 (1H, d, *J* = 7.6 Hz, H-3′), 6.74 (2H, d, *J* = 7.2 Hz, H-3″, 5″), 3.78 (6H, s, OCH_3), 3.72 (3H, s, OCH_3), 2.68 (2H, t, *J* = 8.0 Hz, H-7), 2.01 (2H, t, *J* = 7.6 Hz, H-4), 1.72-1.69 (2H, m, H-6), 1.33-1.29 (2H, m, H-5); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 187.2 (C=O), 168.6 (C-4″), 158.6 (C-2′), 158.1 (C-2′), 148.6 (C-3), 132.7 (C-1″), 129.6 (C-2″, 6″), 126.5 (C-2), 123.7 (C-1′), 121.6 (C-4′), 118.4 (C-6′), 116.3 (C-3′), 114.7 (C-3″, 5″), 56.3 (OCH_3), 56.2 (OCH_3), 55.8 (OCH_3), 36.3 (C-7), 32.8 (C-4), 32.1 (C-6), 29.9 (C-5); LC-MS: *m/z* 355.3 $(M+H)^+$, 377.2 $(M+Na)^+$.

7-(2-Methoxy-phenyl)-1-(phenyl)-hept-2-en-1-one ***(11f)***: Weight: 425 mg; % yield: 55.5 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.88 (2H, d, *J* = 8.0 Hz, H-2′, 6′), 7.62 (1H, d, *J* = 8.0 Hz, H-4′), 7.48 (2H, d, *J* = 7.2 Hz, H-3′, 5′), 7.06 (1H, d, *J* = 17.2 Hz, H-2),7.02 (1H, dd, *J* = 7.6, 3.2 Hz, H-6′), 6.98 (1H, d, *J* = 16.4 Hz, H-3), 6.96 (1H, td, *J* = 8.0, 2.4 Hz, H-4″), 6.82 (1H, td, *J* = 7.6, 3.2 Hz, H-5″), 6.74 (1H, dd, *J* = 7.6, 3.2 Hz, H-3″), 3.72 (3H, s, OCH_3), 2.66 (2H, t, *J* = 8.0 Hz, H-7), 2.08 (2H, t, *J* = 7.6 Hz, H-4), 1.71-1.68 (2H, m, H-6), 1.33-1.31 (2H, m, H-5); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 187.2 (C=O), 166.2 (C-2″), 148.9 (C-3), 138.6 (C-1′), 136.2 (C-4′), 129.9 (C-2′, 6′), 129.7 (C-6″), 129.3 (C-3′, 5′), 128.4 (C-4″), 126.5 (C-2), 125.9 (C-1″), 121.6 (C-5″), 114.8 (C-3″), 56.3 (OCH_3), 32.9 (C-6), 32.6 (C-4), 29.8 (C-5), 26.2 (C-7); LC-MS: *m/z* 295.3 $(M+H)^+$, 317.3 $(M+Na)^+$.

7-(2-Methoxy-phenyl)-1-(2,4-dimethoxy-phenyl)-hept-2-en-1-one ***(11g)***: Weight: 462 mg; % yield: 50.1 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.68 (1H, d, *J* = 8.0 Hz, H-6′), 7.12 (1H, dd, *J* = 7.6, 3.2 Hz, H-6″), 7.02 (1H, d, *J* = 17.2 Hz, H-2), 6.99 (1H, d, *J* = 16.4 Hz, H-3), 6.96 (1H, td, *J* = 8.0, 3.2 Hz, H-4″), 6.88 (1H, td, *J* = 8.0, 3.2 Hz, H-5″), 6.74 (1H, dd, *J* = 7.6, 2.4 Hz, H-3″), 6.58 (1H, dd, *J* = 7.6, 2.4 Hz, H-5′), 6.46 (1H, d, *J* = 2.4 Hz, H-3′), 3.82 (3H, s, OCH_3), 3.78 (6H, s, OCH_3), 2.66 (2H, t, *J* = 8.0 Hz, H-7), 2.03 (2H, t, *J* = 7.2 Hz, H-4), 1.66-1.63 (2H, m, H-6),

1.33-1.31 (2H, m, H-5); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 187.2 (C=O), 172.8 (C-4′), 166.4 (C-2′), 162.8 (C-2″), 148.7 (C-3), 132.8 (C-6′), 129.4 (C-6″), 126.8 (C-4″), 126.3 (C-2), 125.6 (C-1″), 122.6 (C-5″), 118.6 (C-1′), 114.3 (C-3″), 108.3 (C-5′), 101.8 (C-3′), 56.3 (OCH_3), 55.8 (OCH_3), 55.6 (OCH_3), 32.8 (C-4), 32.4 (C-6), 29.8 (C-5), 26.2 (C-7); LC-MS: *m/z* 355.4 $(M+H)^+$, 377.2 $(M+Na)^+$.

7-(2-Methoxy-phenyl)-1-(3,4-dimethoxy-phenyl)-hept-2-en-1-one ***(11h)***: Weight: 465 mg; % yield: 50.4 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.38 (1H, dd, *J* = 7.2, 2.4 Hz, H-6′), 7.26 (1H, d, *J* = 2.4 Hz, H-2′), 7.04 (1H, dd, *J* = 8.0, 3.2 Hz, H-6″), 7.01 (1H, d, *J* = 16.4 Hz, H-2), 6.99 (1H, d, *J* = 16.4 Hz, H-3), 6.94 (1H, td, *J* = 7.6, 3.2 Hz, H-4″), 6.88 (1H, d, *J* = 7.2 Hz, H-5′), 6.79 (1H, td, *J* = 8.0, 3.2 Hz, H-5″), 6.72 (1H, dd, *J* = 7.6, 2.4 Hz, H-3″), 3.82 (3H, s, OCH_3), 3.78 (6H, s, OCH_3), 2.67 (2H, t, *J* = 8.0 Hz, H-7), 2.06 (2H, t, *J* = 8.0 Hz, H-4), 1.66-1.62 (2H, m, H-6), 1.33-1.31 (2H, m, H-5); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 187.2 (C=O), 166.2 (C-2″), 158.3 (C-4′), 150.8 (C-3′), 148.5 (C-3), 132.6 (C-1′), 129.6 (C-6″), 128.4 (C-4″), 125.8 (C-2), 125.1 (C-1″), 123.8 (C-6′), 120.6 (C-5″), 118.3 (C-2′), 116.8 (C-5′), 114.3 (C-3″), 56.3 (OCH_3), 56.1 (OCH_3), 56.0 (OCH_3), 32.8 (C-4), 32.6 (C-6), 29.8 (C-5), 26.3 (C-7); LC-MS: *m/z* 377.4 $(M+Na)^+$.

7-(2-Methoxy-phenyl)-1-(2,5-dimethoxy-phenyl)-hept-2-en-1-one ***(11i)***: Weight: 460 mg; % yield: 49.9 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.32 (1H, d, *J* = 3.2 Hz, H-6′), 7.08 (1H, dd, *J* = 7.6, 3.2 Hz, H-6″), 7.02 (1H, d, *J* = 16.4 Hz, H-2), 6.99 (1H, d, *J* = 16.0 Hz, H-3), 6.96 (1H, td, *J* = 8.0, 3.2 Hz, H-4′), 6.94 (1H, dd, *J* = 7.2, 2.4 Hz, H-4″), 6.88 (1H, d, *J* = 7.2 Hz, H-3′), 6.79 (1H, td, *J* = 8.0, 3.2 Hz, H-5″), 6.69 (1H, dd, *J* = 7.6, 2.4 Hz ,H-3″), 3.82 (6H, s, OCH_3), 3.78 (3H, s, OCH_3), 2.67 (2H, t, *J* = 8.0 Hz, H-7), 2.03 (2H, t, *J* = 7.6 Hz, H-4), 1.73-1.68 (2H, m, H-6), 1.33-1.30 (2H, m, H-5); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 187.2 (C=O), 168.5 (C-2″), 158.2 (C-2′), 156.9 (C-5′), 149.5 (C-3), 130.3 (C-6″), 128.6 (C-4″), 126.4 (C-2), 126.1 (C-1″), 123.9 (C-1′), 121.8 (C-4′), 120.8 (C-5″), 18.4 (C-6′), 116.3 (C-3′),114.8 (C-3″), 56.5 (OCH_3), 56.3 (OCH_3), 55.8 (OCH_3), 32.9 (C-4), 32.6 (C-6), 29.8 (C-5), 26.3 (C-7); LC-MS: *m/z* 355.3 $(M+H)^+$, 377.3 $(M+Na)^+$.

7-(3, 4-Dimethoxy-phenyl)-1-(phenyl)-hept-2-en-1-one ***(11j)***: Weight: 440 mg; % yield: 60.3 %;^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.88 (2H, d, *J* = 7.2 Hz, H-2′, 6′), 7.56 (1H, d, *J* = 8.0 Hz, H-4′), 7.48 (2H, d, *J* = 7.6 Hz, H-3′, 5′), 7.08 (1H, d, *J* = 17.2 Hz, H-2), 6.99 (1H, d, *J* = 16.4 Hz, H-3), 6.83 (1H, d, *J* = 8.0 Hz, H-5″), 6.68 (1H, dd, *J* = 7.6, 3.2 Hz, H-6″), 6.52 (1H, d, *J* = 2.4 Hz, H-2″), 3.78 (3H, s, OCH_3), 3.76 (3H, s, OCH_3), 2.66 (2H, t, *J* = 7.2 Hz, H-7), 2.08 (2H, t, *J* =

7.6 Hz, H-4), 166-1.62 (2H, m, H-6), 133-1.31 (2H, m, H-5); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 187.6 (C=O), 151.2 (C-3″), 148.9 (C-3), 146.8 (C-4″), 142.8 (C-1′), 138.1 (C-4′), 134.8 (C-1″), 132.6 (C-2′, 6′), 130.8 (C-3′, 5′), 128.4 (C-2), 126.3 (C-6″), 116.3 (C-2″), 116.1 (C-5″), 56.3 (OCH_3), 56.1 (OCH_3), 36.8 (C-7), 32.8 (C-4), 32.1 (C-6), 29.6 (C-5); LC-MS: *m/z* 325.4 $(M+H)^+$, 347.3 $(M+Na)^+$.

*7-(3, 4-Dimethoxy-phenyl)-1-(2-hydroxy-4-methoxy-phenyl)-hept-2-en-1-one (**11k**)*: Weight: 445 mg; % yield: 53.4 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.68 (1H, d, *J* = 7.2 Hz, H-6′), 7.04 (1H, d, *J* = 17.2 Hz, H-2), 6.99 (1H, d, *J* = 16.4 Hz, H-3), 6.81 (1H, d, *J* = 8.0 Hz, H-5″), 6.61 (1H, dd, *J* = 7.6, 2.4 Hz, H-6″), 6.56 (1H, d, *J* = 2.4 Hz, H-2″), 6.53 (1H, dd, *J* = 7.6, 3.2 Hz, H-5′), 6.44 (1H, d, *J* = 8.0 Hz, H-3′), 3.82 (3H, s, OCH_3), 3.78 (6H, s, OCH_3), 2.68 (2H, t, *J* = 8.0 Hz, H-7), 2.08 (2H, t, *J* = 7.6 Hz, H-4), 1.76-1.74 (2H, m, H-6), 133-1.28 (2H, m, H-5); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 187.3 (C=O), 172.4 (C-4′), 166.2 (C-2′), 156.8 (C-3), 156.3 (C-3″), 148.9 (C-4″), 136.3 (C-1″), 134.8 (C-6′), 128.5 (C-2), 126.2 (C-6″), 118.9 (C-1′), 116.8 (C-2″), 116.1 (C-5″), 108.3 (C-5′), 101.8 (C-3′), 55.8 (OCH_3), 55.6 (OCH_3), 55.3 (OCH_3), 36.9 (C-7), 31.9 (C-4), 31.3 (C-6), 29.1 (C-5); LC-MS: *m/z* 371.2 $(M+H)^+$, 393.3 $(M+Na)^+$.

*7-(3, 4-Dimethoxy-phenyl)-1-(3,4-dimethoxy-phenyl)-hept-2-en-1-one (**11l**)*: Weight: 445 mg; % yield: 51.4 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.26 (1H, dd, *J* = 8.0, 3.2 Hz, H-6′), 7.21 (1H, d, *J* = 3.2 Hz, H-2′), 7.03 (1H, d, *J* = 17.2 Hz, H-2), 6.98 (1H, d, *J* = 16.4 Hz, H-3), 6.91 (1H, d, *J* = 7.6 Hz, H-5′), 6.66 (1H, d, *J* = 7.6 Hz, H-5″), 6.59 (1H, dd, *J* = 7.6, 2.4 Hz, H-6″), 6.48 (1H, d, *J* = 2.4 Hz, H-2″), 3.78 (6H, s, OCH_3), 3.72 (6H, s, OCH_3), 2.68 (2H, t, *J* = 7.6 Hz, H-7), 2.13 (2H, t, *J* = 8.0 Hz, H-4), 1.72-1.69 (2H, m, H-6), 1.33-1.31 (2H, m, H-5); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 187.3 (C=O), 156.5 (C-4′), 148.6 (C-3′), 147.9 (C-3″), 144.9 (C-4″), 136.5 (C-1″), 132.3 (C-1′), 128.6 (C-2), 126.1 (C-6′), 121.8 (C-6″), 118.9 (C-2′), 116.8 (C-5′), 116.2 (C-2″), 114.9 (C-5″), 36.8 (C-7), 32.9 (C-4), 32.6 (C-6), 29.7 (C-5); LC-MS: *m/z* 385.4 $(M+H)^+$, 407.3 $(M+Na)^+$.

*7-(3, 4-Dimethoxy-phenyl)-1-(2,5-dimethoxy-phenyl)-hept-2-en-1-one (**11m**)*: Weight: 450 mg; % yield: 52.0 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.28 (1H, d, *J* = 3.2 Hz, H-6′), 7.03 (1H, d, *J* = 17.2 Hz, H-2), 6.99 (1H, d, *J* = 16.4 Hz, H-3), 6.96 (1H, dd, *J* = 7.6, 2.4 Hz, H-4′), 6.88 (1H, d, *J* = 7.6 Hz, H-3′), 6.63 (1H, d, *J* = 8.0 Hz, H-5″), 6.58 (1H, dd, *J* = 8.0, 3.2 Hz, H-6″), 6.52 (1H, d, *J* = 3.2 Hz, H-2″), 3.82 (6H, s, OCH_3), 3.78 (6H, s, OCH_3), 2.68 (2H, t, *J* = 7.2 Hz, H-7), 2.03 (2H, t, *J* = 7.6 Hz, H-4), 1.68-1.63 (2H, m, H-6), 1.33-1.31 (2H, m, H-5); ^{13}C NMR ($CDCl_3$, 100

MHz): δ 187.3 (C=O), 168.4 (C-5′), 166.7 (C-2′), 149.4 (C-3), 148.3 (C-3″), 144.9 (C-4″), 136.4 (C-1″), 128.6 (C-2), 126.2(C-1′), 121.9 (C-6″), 121.3 (C-4′), 118.9 (C-6′), 116.4 (C-3′), 114.9 (C-5″), 114.8 (C-2″), 56.3 (OCH_3), 56.2 (OCH_3), 55.8 (OCH_3), 36.9 (C-7), 32.7 (C-4), 32.1 (C-6), 29.7 (C-5); LC-MS: *m/z* 385.3 $(M+H)^+$, 407.3 $(M+Na)^+$.

*7-(3, 4, 5-Trimethoxy-phenyl)-1-(phenyl)-hept-2-en-1-one (**11n**)*: Weight: 410 mg; % yield: 58.4 %;^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.92 (2H, d, *J* = 7.2 Hz, H-2′, 6′), 7.58 (1H, d, *J* = 7.6 Hz, H-4′), 7.46 (2H, d, *J* = 7.6 Hz, H-3′, 5′), 6.99 (1H, d, *J* = 16.4 Hz, H-2), 6.94 (1H, d, *J* = 16.0 Hz, H-3), 6.18 (2H, s, H-2″, 6″), 3.78 (6H, s, OCH_3), 3.72 (3H, s, OCH_3), 2.68 (2H, t, *J* = 7.6 Hz, H-7), 2.11 (2H, t, *J* = 7.2 Hz, H-4), 1.66-1.62 (2H, m, H-6), 1.38-1.33 (2H, m, H-5); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 188.2 (C=O), 154.2 (C-3″, 5″), 148.6 (C-3), 133.9 (C-1′), 137.5 (C-6′), 136.8 (C-1″), 132.6 (C-4″), 129.8 (C-2′, 6′), 129.2 (C-3′, 5′), 126.4 (C-2), 110.7 (C-2″,6″), 56.8 (OCH_3), 56.6 (OCH_3), 55.8(OCH_3), 36.9 (C-7), 33.6 (C-4), 32.4 (C-6), 29.8 (C-5); LC-MS: *m/z* 355.3 $(M+H)^+$, 377.2 $(M+Na)^+$.

*7-(3, 4, 5-Trimethoxy-phenyl)-1-(2-hydroxy-4-methoxy-phenyl)-hept-2-en-1-one(**11o**)*: Weight: 435 mg; % yield: 54.9 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.62 (1H, d, *J* = 7.2 Hz, H-6′), 7.01 (1H, d, *J* = 16.4 Hz, H-2), 6.98 (1H, d, *J* = 16.0 Hz, H-3), 6.68 (1H, dd, *J* = 7.2, 3.2 Hz, H-5′), 6.48 (1H, d, *J* = 3.2 Hz, H-3′), 6.14 (2H, s, H-2″, 6″), 3.78 (6H, s, OCH_3), 3.72 (3H, s, OCH_3), 2.72 (2H, t, *J* = 7.6 Hz, H-7), 2.01 (2H, t, *J* = 7.2 Hz, H-4), 1.68-1.62 (2H, m, H-6), 1.48-1.42 (2H, m, H-5); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 188.2 (C=O), 169.8 (C-4′), 159.6 (C-2′), 152.2 (C-3″, 5″), 148.6 (C-3), 138.2 (C-1″), 136.3 (C-6′), 132.8 (C-4″), 128.2 (C-2), 118.5 (C-1′), 110.6 (C-2″, 6″), 108.4 (C-5′), 103.6 (C-3′), 56.8 (OCH_3), 56.7 (OCH_3), 55.9 (OCH_3), 38.5(C-7), 33.7 (C-4), 32.8 (C-6), 29.8 (C-5); LC-MS: *m/z* 401.3 $(M+H)^+$, 423.4 $(M+Na)^+$.

*7-(3, 4, 5-Trimethoxy-phenyl)-1-(3, 4-dimethoxy-phenyl)-hept-2-en-1-one (**11p**)*: Weight: 440 mg ; % yield: 53.6 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.38 (1H, dd, *J* = 8.0, 3.2 Hz, H-6′), 7.21 (1H, d, *J* = 3.2 Hz, H-2′), 7.08 (1H, d, *J* = 16.4 Hz, H-2), 6.99 (1H, d, *J* = 16.0 Hz, H-3), 6.91 (1H, d, *J* = 8.0 Hz, H-5′), 6.14 (2H, s, H-2″, 6″), 3.86 (6H, s, OCH_3), 3.78 (3H, s, OCH_3), 3.72 (6H, s, OCH_3), 2.68 (2H, t, *J* = 8.0 Hz, H-7), 2.06 (2H, t, *J* = 7.6 Hz, H-4), 1.68-1.63 (2H, m, H-6), 1.31-1.33 (2H, m, H-5); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 187.6 (C=O), 159.2 (C-4′), 152.6 (C-3″, 5″), 152.8 (C-3′), 149.5 (C-3), 136.1 (C-1″), 132.8 (C-4″), 132.1 (C-1′), 128. (C-2), 126.3 (C-6′), 118.6 (C-2′), 115.7 (C-5′), 108.5 (C-2″, 6″), 56.8 (OCH_3), 56.7 (OCH_3), 56.4 (OCH_3), 55.6

(OCH_3), 55.3 (OCH_3), 36.8 (C-7), 32.9 (C-4), 32.6 (C-6), 29.6 (C-5); LC-MS: *m/z* 415.4 $(M+H)^+$, 437.2 $(M+Na)^+$.

*7-(3, 4, 5-trimethoxy-phenyl)-1-(2, 5-dimethoxy-phenyl)-hept-2-en-1-one (**11q**)*: Weight: 430 mg; % yield: 52.2 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.24 (1H, d, *J* =3.2 Hz, H-6′), 7.02 (1H, d, *J* = 17.2 Hz, H-2), 6.99 (1H, d, *J* = 16.4 Hz, H-3), 6.96 (1H, dd, *J* = 7.2, 2.4 Hz, H-4′), 6.88 (1H, d, *J* = 7.2 Hz, H-3′), 6.09 (2H, s, H-2″, 6″), 3.78 (9H, s, OCH_3), 3.76 (6H, s, OCH_3), 2.68 (2H, t, *J* = 7.6 Hz, H-7), 2.04 (2H, t, *J* = 8.0 Hz, H-4), 1.78-1.73 (2H, m, H-6), 1.43-1.38 (2H, m, H-5); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 187.6 (C=O), 159.4 (C-2′), 156.3 (C-5′), 152.6 (C-3″, 5″), 148.9 (C-3), 136.4 (C-1″), 132.4 (C-4″), 128.6 (C-2), 126.5 (C-1′), 122.8 (C-4′), 118.6 (C-6′), 116.5 (C-3′), 108.3 (C-2″, 6″), 56.3 (OCH_3), 56.2 (OCH_3), 56.1 (OCH_3), 55.8 (OCH_3), 38.6 (C-7), 33.7 (C-4), 32.8 (C-6), 29.8 (C-5); LC-MS: *m/z* 415.3 $(M+H)^+$, 437.4 $(M+Na)^+$.

*General procedure for 7-(substituted-phenyl)-1-(substituted-phenyl)-hept-1-one (**12a-q**):*

A mixture of any one of 7-(substituted-phenyl)-1-(substituted-phenyl)-hept-2-en-1-one (**11a-q**, 0.0015 mol), ethyl acetate (20 mL), and catalytic amount of palladium on $CaCO_3$ then hydrogen gas was passed through the reaction mixture for 1h. After completion of reaction which was monitored by TLC hexane/ethyl acetate (8:2), the reaction mixture was filtered off on celite, and was wash with ethyl acetate, the filtrate was concentrated. The crude residue was subjected to column chromatography on silica gel; column was eluted with hexane/ethyl acetate mixtures. Pure compound was eluted in ethyl acetate in hexane, 10 % / 90 % (v/v), which were monitored by TLC and pure fractions were combined, concentrated to obtained 7-(substituted-phenyl)-1-(substituted-phenyl)-hept-1-one (**12a-q**) with yields of 73 % - 84 % respectively.

*7-(Phenyl)-1-(3, 4-dimethoxy-phenyl)-heptan-1-one (**12a**)*: Weight: 240 mg; % yield: 79.5 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.57 (1H, dd, *J* = 1.6, 8.0 Hz, H-6′), 7.53 (1H, d, *J* = 2.0 Hz, H-2′), 7.26 (2H, d, *J* = 7.2 Hz, H-3″, 5″), 7.16 (3H, d, *J* = 7.6 Hz, H-2″, 4″, 6″), 6.87 (1H, d, *J* = 8.4 Hz, H-5′), 3.93 (6H, s, OCH_3), 2.91 (2H, t, *J* = 7.6 Hz, H-7), 2.61 (2H, t, *J* = 7.6 Hz, H-2), 1.76-1.69 (2H, m, H-6), 1.67-1.59 (2H, m, H-3), 1.41-1.39 (4H, m, H-4, 5); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 199.1 (C=O), 153.2 (C-4′), 149.1 (C-3′), 142.7 (C-1″), 130.4 (C-1′), 128.4 (C-2″), 128.3 (C-6″), 128.2 (C-3″, 5″), 125.6 (C-4″), 122.7 (C-6′), 110.3 (C-2′), 110.0 (C-5′), 56.0 (OCH_3), 55.9 (OCH_3), 38.1 (C-2), 35.9 (C-7), 31.3 (C-6), 29.2 (C-4), 29.1 (C-5), 24.7 (C-3); LC-MS: *m/z*

327.4 $(M+H)^+$, 349.4 $(M+Na)^+$. Q-Tof: *m/z* 327.1965 $[M+H]^+$ (Calculated for $C_{21}H_{27}O_3$, 327.1960).

*7-(Phenyl)-1-(2,5-dimethoxy-phenyl)-heptan-1-one (**12b**)*: Weight: 225 mg; % yield: 74.5 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.26 (2H, q, *J* = 4.0 Hz, H-3″, 5″), 7.21 (1H, d, *J* = 2.8 Hz, H-6′), 7.18 (3H, d, *J* = 6.0 Hz, H-2″, 4″, 6″), 6.99 (1H, dd, *J* = 3.2, 8.8 Hz, H-4′), 6.88 (1H, d, *J* = 9.2 Hz, H-3′), 3.84 (3H, s, OCH_3), 3.78 (3H, s, OCH_3), 2.95 (2H, t, *J* = 7.6 Hz, H-7), 2.59 (2H, t, *J* = 8.0 Hz, H-2), 1.71-1.60 (4H, m, H-3, 6), 1.37-1.36 (4H, m, H-4, 5); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 202.7 (C=O), 153.5 (C-2′), 152.8 (C-5′), 142.8 (C-1″), 129.1 (C-2″, 6″), 128.4 (C-3″, 5″), 128.2 (C-4″), 125.6 (C-1′), 119.5 (C-4′), 114.0 (C-6′), 113.2 (C-3′), 56.1 (OCH_3), 55.8 (OCH_3), 43.7 (C-2), 35.9 (C-7), 31.3 (C-6), 29.2 (C-4), 29.1 (C-5), 24.3 (C-3); LC-MS: *m/z* 327.3 $(M+H)^+$, 349.4 $(M+Na)^+$. Q-Tof: *m/z* 327.1965 $[M+H]^+$ (Calculated for $C_{21}H_{27}O_3$, 327.1960).

*7-(4-Methoxy-phenyl)-1-(phenyl)-heptan-1-one (**12c**)*: Weight: 235 mg; % yield: 77.8 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.85 (2H, d, *J* = 7.2 Hz, H-2′, 6′), 7.45 (1H, t, *J* = 7.2 Hz, H-4′), 7.35 (2H, t, *J* = 7.6 Hz, H-3′, 5′), 6.98 (2H, d, *J* = 8.4 Hz, H-2″, 6″), 6.72 (2H, d, *J* = 8.8 Hz, H-3″,5″), 3.67 (3H, s, OCH_3), 2.85 (2H, t, *J* = 7.2 Hz, H-7), 2.45 (2H, t, *J* = 8.0 Hz, H-2), 1.68-1.61 (2H, m, H-6), 1.54-1.47 (2H, m, H-3), 1.31-1.25 (4H, m, H-4, 5); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 200.3 (C=O), 157.6 (C-4″), 137.1 (C-1′), 134.7 (C-4′), 132.7 (C-1″), 129.2 (C-2″, 6″), 128.5 (C-2′, 6′), 127.9 (C-3′, 5′), 113.6 (C-3″, 5″), 55.2 (OCH_3), 38.5 (C-2), 34.9 (C-7), 31.4 (C-6), 29.1 (C-4), 28.9 (C-5), 24.2 (C-3); LC-MS: *m/z* 297.3 $(M+H)^+$. Q-Tof: *m/z* 297.1866 $[M+H]^+$ (Calculated for $C_{20}H_{25}O_2$, 297.1855).

*7-(4-Methoxy-phenyl)-1-(2, 4-dimethoxy-phenyl)-heptan-1-one (**12d**)*: Weight: 240 mg; % yield: 79.7 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.56 (1H, dd, *J* = 1.2, 8.0 Hz, H-5′), 7.53 (1H, s, H-3′), 7.07 (2H, d, *J* = 8.4 Hz, H-2″, 6″), 6.87 (1H, d, *J* = 8.4 Hz, H-6′), 6.81 (2H, d, *J* = 8.4 Hz, H-3″, 5″), 3.94 (6H, s, OCH_3), 3.78 (3H, s, OCH_3), 2.90 (2H, t, *J* = 7.2 Hz, H-7), 2.55 (2H, t, *J* = 7.6 Hz, H-2), 1.76-1.69 (2H, m, H-6), 1.64-1.56 (2H, m, H-3), 1.39-1.36 (4H, m, H-4, 5); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 199.2 (C=O), 157.6 (C-2′), 153.2 (C-4′), 149.1 (C-4″), 134.8 (C-1″), 129.2 (C-6′), 122.6 (C-2″, 6″), 113.7 (C-1′), 110.3 (C-3″, 5″), 110.0 (C-5′), 101.4 (C-3′), 56.0 (OCH_3), 55.9 (OCH_3), 55.2 (OCH_3), 38.1 (C-2), 34.9 (C-7), 31.5 (C-6), 29.3 (C-4), 29.0 (C-5), 24.6 (C-3);

LC-MS: *m/z* 357.3 $(M+H)^+$, 379.4 $(M+Na)^+$. Q-Tof: *m/z* 357.2069 $[M+H]^+$ (Calculated for $C_{22}H_{29}O_4$, 357.2066).

*7-(4-Methoxy-phenyl)-1-(2, 5-dimethoxy-phenyl)-heptan-1-one (**12e**)*: Weight: 242 mg; % yield: 80.4 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.21 (1H, d, *J* = 3.2 Hz, H-6′), 7.07 (2H, d, *J* = 8.4 Hz, H-2″, 6″), 6.99 (1H, dd, *J* = 3.2, 8.4 Hz, H-4′), 6.88 (1H, d, *J* = 8.8 Hz, H-3′), 6.80 (2H, d, *J* = 8.4 Hz, H-3″, 5″), 3.83 (3H, s, OCH_3), 3.77 (6H, s, OCH_3), 2.95 (2H, t, *J* = 7.2 Hz, H-7), 2.54 (2H, t, *J* = 8.0 Hz, H-2), 1.68-1.56 (4H, m, H-3, 6), 1.36-1.34 (4H, m, H-4, 5); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 202.7 (C=O), 157.6 (C-4″), 153.5 (C-2′), 152.8 (C-5′), 134.9 (C-1″), 129.2 (C-2″, 6″), 119.4 (C-1′), 114.0 (C-6′), 113.7 (C-3′), 113.2 (C-3″, 5″), 56.1 (OCH_3), 55.8 (OCH_3), 55.2 (OCH_3), 43.7 (C-2), 34.9 (C-7), 31.5 (C-6), 29.2 (C-4), 29.0 (C-5), 24.3 (C-3); LC-MS: *m/z* 357.4 $(M+H)^+$. Q-Tof: *m/z* 357.2069 $[M+H]^+$ (Calculated for $C_{22}H_{29}O_4$, 357. 2066).

*7-(2-Methoxy-phenyl)-1-(phenyl)-heptan-1-one (**12f**)*: Weight: 240 mg; % yield: 79.4 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.94 (2H, d, *J* = 7.2 Hz, H-2′, 6′), 7.53 (1H, t, *J* = 7.2 Hz, H-4′), 7.43 (2H, t, *J* = 7.6 Hz, H-3′, 5′), 7.17-7.09 (2H, m, H-4″, 6″), 6.88-6.80 (2H, m, H-3″, 5″), 3.79 (3H, s, OCH_3), 2.94 (2H, t, *J* = 7.2 Hz, H-13), 2.60 (2H, t, *J* = 7.6 Hz, H-8), 1.77-1.69 (2H, m, H-12), 1.63-1.56 (2H, m, H-9), 1.41-1.39 (4H, m, H-10, 11); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 200.5 (C=O), 157.5 (C-2″), 137.2 (C-1′), 132.8 (C-4′), 131.2 (C-6″), 129.8 (C-2′, 6′), 129.7 (C-3′, 5′), 128.5 (C-4″), 126.8 (C-1″), 120.4 (C-5″), 110.3 (C-3″), 55.3 (OCH_3), 38.6 (C-8), 30.1 (C-12), 29.7 (C-10), 29.4 (C-11), 29.3 (C-13), 24.4 (C-9); LC-MS: *m/z* 297.4 $(M+H)^+$, 319.3 $(M+Na)^+$. Q-Tof: *m/z* 297.1866 $[M+H]^+$ (Calculated for $C_{20}H_{25}O_2$, 297.1855).

*7-(2-Methoxy-phenyl)-1-(2,4-dimethoxy-phenyl)-heptan-1-one (**12g**)*: Weight: 245 mg; % yield: 81.4 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.76 (1H, d, *J* = 8.8 Hz, H-6′), 7.15 (1H, d, *J* = 7.6 Hz, H-6″), 7.11 (1H, d, *J* = 7.2 Hz, H-4″), 6.87 (1H, d, *J* = 7.2 Hz, H-5″), 6.82 (1H, d, *J* = 8.0 Hz, H-3″), 6.51 (1H, dd, *J* = 2.4, 8.8 Hz, H-5′), 6.44 (1H, d, *J* = 2.0 Hz, H-3′), 3.85 (3H, s, OCH_3), 3.83 (3H, s, OCH_3), 3.79 (3H, s, OCH_3), 2.91 (2H, t, *J* = 7.2 Hz, H-7), 2.59 (2H, t, *J* = 8.0 Hz, H-2), 1.69-1.64 (2H, m, H-6), 1.59-1.54 (2H, m, H-3), 1.39-1.36 (4H, m, H-4, 5); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 200.9 (C=O), 164.1 (C-2′), 160.6 (C-4′), 157.5 (C-2″), 132.5 (C-6′), 131.3 (C-6″), 129.7 (C-4″), 126.7 (C-1″), 121.6 (C-5″), 120.3 (C-1′), 110.3 (C-3″), 105.1 (C-5′), 98.4 (C-3′), 55.8 (OCH_3), 55.4 (OCH_3), 55.3 (OCH_3), 43.6 (C-2), 30.1 (C-6), 29.7 (C-4), 29.5 (C-5), 29.4 (C-

7), 24.6 (C-3); LC-MS: *m/z* 357.4 $(M+H)^+$, 379.4 $(M+Na)^+$. Q-Tof: *m/z* 357.2069 $[M+H]^+$ (Calculated for $C_{22}H_{29}O_4$, 357.2066).

*7-(2-Methoxy-phenyl)-1-(3,4-dimethoxy-phenyl)-heptan-1-one (**12h**)*: Weight: 250 mg; % yield: 83.1 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.57 (1H, dd, *J* = 1.6, 8.4 Hz, H-6′), 7.53 (1H, d, *J* = 1.6 Hz, H-2′), 7.16 (1H, dd, *J* = 1.2, 7.6 Hz, H-6″), 7.11 (1H, d, *J* = 6.0 Hz, H-4″), 6.87 (2H, d, *J* = 8.0 Hz, H-3″, 5″), 6.83 (1H, d, *J* = 8.4 Hz, H-5′), 3.93 (6H, s, OCH_3), 3.80 (3H, s, OCH_3), 2.91 (2H, t, *J* = 7.2 Hz, H-7), 2.60 (2H, t, J = 7.6 Hz, H-2), 1.77-1.69 (2H, m, H-6), 1.63-1.56 (2H, m, H-3), 1.41-1.40 (4H, m, H-4, 5); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 199.2 (C=O), 157.5 (C-2″), 153.1 (C-4′), 149.1 (C-3′), 131.2 (C-1′), 130.4 (C-6″), 129.7 (C-4″), 126.8 (C-1″), 122.6 (C-6′), 120.3 (C-5″), 110.3 (C-2′), 110.2 (C-5′), 110.1 (C-3″), 56.0 (OCH_3), 55.9 (OCH_3), 55.2 (OCH_3), 38.2 (C-2), 30.1 (C-6), 29.7 (C-4), 29.4 (C-5), 29.3 (C-7), 24.7 (C-3); LC-MS: *m/z* 357.4 $(M+H)^+$. Q-Tof: *m/z* 357.2069 $[M+H]^+$ (Calculated for $C_{22}H_{29}O_4$, 357.2066).

*7-(2-Methoxy-phenyl)-1-(2,5-dimethoxy-phenyl)-heptan-1-one (**12i**)*: Weight: 252 mg; % yield: 83.7 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.21 (1H, d, *J* = 3.2 Hz, H-6′), 7.13 (2H, q, *J* = 8.0 Hz, H-4″, 5″), 6.98 (1H, dd, *J* = 2.8, 8.8 Hz, H-6″), 6.87-6.81 (3H, m, H-3′, 4′, 3″), 3.79 (9H, s, OCH_3), 2.95 (2H, t, *J* = 7.2 Hz, H-7), 2.59 (2H, t, *J* = 7.2 Hz, H-2), 1.69-1.56 (4H, m, H-3, 6), 1.37-1.31 (4H, m, H-4, 5); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 202.7 (C=O), 157.4 (C-2″), 153.5 (C-2′), 152.7 (C-5′), 131.1 (C-6″), 129.6 (C-4″), 129.0 (C-1″), 126.7 (C-1′), 120.2 (C-5″), 119.3 (C-4′), 113.9 (C-6′), 113.1 (C-3′), 110.2 (C-3″), 56.0 (OCH_3), 55.7 (OCH_3), 55.2 (OCH_3), 43.7 (C-2), 30.0 (C-6), 29.6 (C-4), 29.3 (C-5), 29.2 (C-7), 24.3 (C-3); LC-MS: *m/z* 357.4 $(M+H)^+$, 379.0 $(M+Na)^+$. Q-Tof: *m/z* 357.2069 $[M+H]^+$ (Calculated for $C_{22}H_{29}O_4$, 357.2066).

*7-(3, 4-Dimethoxy-phenyl)-1-(phenyl)-heptan-1-one (**12j**)*: Weight: 235mg; % yield: 78.1 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.95 (2H, d, *J* = 7.2 Hz, H-2′, 6′), 7.54 (1H, t, *J* = 7.6 Hz, H-4′), 7.45 (2H, t, *J* = 7.6 Hz, H-3′, 5′), 6.78 (1H, d, *J* = 8.8 Hz, H-5″), 6.70 (2H, d, *J* = 5.2 Hz, H-2″, 6″), 3.85 (6H, s, OCH_3), 2.95 (2H, t, *J* = 7.2 Hz, H-7), 2.55 (2H, t, *J* = 8.0 Hz, H-2), 1.78-1.70 (2H, m, H-6), 1.65-1.58 (2H, m, H-3), 1.42-1.38 (4H, m, H-4, 5); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 200.4 (C=O), 148.8 (C-3″), 147.1 (C-4″), 137.2 (C-1′), 135.5 (C-4′), 132.8 (C-1″), 128.5 (C-2′,6′), 128.0 (C-3′, 5′), 120.2 (C-6″), 111.9 (C-2″), 111.4 (C-5″), 55.9 (OCH_3), 55.8 (OCH_3), 38.5 (C-2), 35.5 (C-7), 31.4 (C-6), 29.2 (C-4), 29.1 (C-5), 24.3 (C-3); LC-MS: *m/z* 327.3 $(M+H)^+$, 349.2 $(M+Na)^+$, 365.2 $(M+K)^+$. Q-Tof: *m/z* 327.1965 $[M+H]^+$ (Calculated for $C_{21}H_{27}O_3$, 327.1960).

*7-(3, 4-Dimethoxy-phenyl)-1-(2-hydroxy-4-methoxy-phenyl)-heptan-1-one (**12k**)*: Weight: 220 mg; % yield: 73.1 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 12.9 (1H, s, OH), 7.64 (1H, d, J = 9.2 Hz, H-6′), 6.78 (1H, d, J = 7.6 Hz, H-5″), 6.71 (2H, d, J = 6.0 Hz, H-2″, 6″), 6.43 (2H, t, J = 7.6 Hz, H-3′, 5′), 3.87 (3H, s, OCH_3), 3.85 (3H, s, OCH_3), 3.83 (3H, s, OCH_3), 2.88 (2H, t, J = 7.2 Hz, H-7), 2.55 (2H, t, J = 7.6 Hz, H-2), 1.76-1.69 (2H, m, H-6), 1.65-1.57 (2H, m, H-3), 1.42-1.37 (4H, m, H-4, 5); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 205.1 (C=O), 165.9 (C-4′), 165.5 (C-2′), 148.8 (C-3″), 147.1 (C-4″), 135.3 (C-1″), 131.6 (C-6′), 120.1 (C-6″), 113.5 (C-1′), 111.8 (C-2″), 111.3 (C-5″), 107.5 (C-5′), 100.9 (C-3′), 55.9 (OCH_3), 55.8 (OCH_3), 55.5 (OCH_3), 43.7 (C-2), 35.5 (C-7), 32.5 (C-6), 29.2 (C-4), 29.0 (C-5), 24.7 (C-3); LC-MS: *m/z* 373.2 $(M+H)^+$, 395.2 $(M+Na)^+$, 411.1 $(M+K)^+$. Q-Tof: *m/z* 373.2042 $[M+H]^+$ (Calculated for $C_{22}H_{29}O_5$, 373.2015).

*7-(3, 4-Dimethoxy-phenyl)-1-(3, 4-dimethoxy-phenyl)-heptan-1-one (**12l**)*: Weight: 246 mg; % yield: 81.7 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.57 (1H, dd, J = 1.6, 8.4 Hz, H-6′), 7.53 (1H, d, J = 1.6 Hz, H-2′), 6.88 (1H, d, J = 8.4 Hz, H-5′), 6.78 (1H, d, J = 8.4 Hz, H-5″), 6.72-6.70 (2H, m, H-2″, 6″), 3.94 (6H, s, OCH_3), 3.86 (6H, s, OCH_3), 2.91 (2H, t, J = 7.2 Hz, H-7), 2.55 (2H, t, J = 7.6 Hz, H-2), 1.7-1.70 (2H, m, H-6), 1.65-1.58 (2H, m, H-3), 1.42-1.38 (4H, m, H-4, 5); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 199.1 (C=O), 153.2 (C-4′), 149.1 (C-3′), 148.8 (C-3″), 147.1 (C-4″), 135.5 (C-1″), 130.4 (C-1′), 122.6 (C-6′), 120.2 (C-6″), 111.9 (C-2′), 111.3 (C-5′), 110.3 (C-2″), 110.0 (C-5″), 56.0 (OCH_3), 55.9 (OCH_3), 55.9 (OCH_3), 55.8 (OCH_3), 38.1 (C-2), 35.5 (C-7), 31.5 (C-6), 29.2 (C-4), 29.1 (C-5), 24.7 (C-3); LC-MS: *m/z* 387.3 $(M+H)^+$, 409.3 $(M+Na)^+$, 425.2 $(M+K)^+$. Q-Tof : *m/z* 387.2165 $[M+H]^+$ (Calculated for $C_{23}H_{31}O_5$, 387.2171).

*7-(3, 4-Dimethoxy-phenyl)-1-(2, 5-dimethoxy-phenyl)-heptan-1-one (**12m**)*: Weight: 240 mg; % yield: 79.7 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.21 (1H, d, J = 3.2 Hz, H-6′), 6.99 (1H, dd, J = 3.2, 8.8 Hz, H-4′), 6.88 (1H, d, J = 9.2 Hz, H-3′), 6.78 (1H, d, J = 8.8 Hz, H-5″), 6.71-6.69 (2H, m, H-2″, 6″), 3.86 (3H, s, OCH_3), 3.84 (6H, s, OCH_3), 3.78 (3H, s, OCH_3), 2.96 (2H, t, J = 7.6 Hz, H-7), 2.54 (2H, t, J = 8.0 Hz, H-2), 1.71-1.66 (2H, m, H-6), 1.64-1.56 (2H, m, H-3), 1.38-1.36 (4H, m, H-4, 5); ^{13}C NMR ($CDCl_3$, 100 MHz): - δ202.6(C=O), 153.5(C-2′), 152.8(C-5′), 148.8(C-3″), 147.1(C-4″), 135.5(C-1″), 129.0(C-1′), 120.1(C-6″), 119.5(C-4′), 114.0(C-6′), 113.2(C-3′), 111.9(C-2″), 111.3(C-5″), 56.1(OCH3), 55.9(OCH3), 55.8(OCH3), 43.7(C-2), 35.5(C-7), 31.5(C-6), 29.2(C-4), 29.1(C-5), 24.3(C-3); LC-MS: *m/z* 387.3 $(M+H)^+$, 409.3 $(M+Na)^+$, 425.4 $(M+K)^+$. Q-Tof : *m/z* 387.2165$[M+H]^+$ (Calculated for $C_{23}H_{31}O_5$, 387.2171).

*7-(3, 4, 5-Trimethoxy-phenyl)-1-(phenyl)-heptan-1-one (**12n**)*: Weight: 240 mg; % yield: 79.7 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.95 (2H, d, J = 7.2 Hz, H-2′, 6′), 7.55 (1H, t, J = 7.2 Hz, H-4′), 7.45 (2H, d, J = 7.6 Hz, H-3′, 5′), 6.39 (2H, s, H-2″, 6″), 3.84 (6H, s, OCH_3), 3.82 (3H, s, OCH_3), 2.96 (2H, t, J = 7.2 Hz, H-7), 2.55 (2H, t, J = 7.6 Hz, H-2), 1.79-1.59 (4H, m, H-3, 6), 1.43-1.40 (4H, m, H-4, 5); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 200.4 (C=O), 153.1 (C-3″, 5″), 138.5 (C-4″), 137.1 (C-1′), 136.2 (C-1″), 132.8 (C-4′), 128.5 (C-2′, 6′), 128.0 (C-3′, 5′), 105.5 (C-2″, 6″), 60.8 (OCH_3), 56.1 (OCH_3), 38.5 (C-2), 36.3 (C-7), 31.3 (C-6), 29.2 (C-4), 29.1 (C-5), 24.2 (C-3); LC-MS: *m/z* 357.3 $(M+H)^+$, 379.2 $(M+Na)^+$. Q-Tof: *m/z* 357.2046 $[M+H]^+$ (Calculated for $C_{22}H_{29}O_4$, 357.2066).

*7-(3, 4, 5-Trimethoxy-phenyl)-1-(2-hydroxy-4-methoxy-phenyl)-heptan-1-one (**12o**)*: Weight: 220 mg; % yield: 73.1 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.64 (1H, d, J = 9.6 Hz, H-6′), 6.44-6.39 (4H, m, H-3′, 5′, 2″, 6″), 3.85 (6H, s, OCH_3), 3.82 (6H, s, OCH_3), 2.89 (2H, t, J = 7.2 Hz, H-7), 2.55 (2H, t, J = 8.0 Hz, H-2), 1.77-1.59 (4H, m, H-3, 6), 1.42-1.41 (4H, m, H-4, 5); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 204.9 (C=O), 165.9 (C-4′), 165.5 (C-2′), 153.1 (C-3″, 5″), 138.4 (C-4″), 136.2 (C-1″), 131.5 (C-6′), 113.5 (C-1′), 107.5 (C-2″, 6″), 105.5 (C-5′), 101.0 (C-3′), 60.8 (OCH_3), 56.1 (OCH_3), 55.5 (OCH_3), 37.9 (C-2), 36.3 (C-7), 31.3 (C-6), 29.2 (C-4), 29.1 (C-5), 24.7 (C-3); LC-MS: *m/z* 403.4 $(M+H)^+$, 425.3 $(M+Na)^+$, 441.3 $(M+K)^+$, 827.6 $(2M+Na)^+$. Q-Tof: *m/z* 403.2108 $[M+H]^+$ (Calculated for $C_{23}H_{31}O_6$, 403.2121).

*7-(3, 4, 5-Trimethoxy-phenyl)-1-(3,4-dimethoxy-phenyl)-heptan-1-one (**12p**)*: Weight: 230 mg; % yield: 76.4 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.57 (1H, dd, J = 1.6, 8.4 Hz, H-6′), 7.53 (1H, d, J = 1.6 Hz, H-2′), 6.88 (1H, d, J = 8.4 Hz, H-5′), 6.39 (2H, s, H-2″, 6″), 3.94 (6H, s, OCH_3), 3.85 (6H, s, OCH_3), 3.82 (3H, s, OCH_3), 2.92 (2H, t, J = 7.2 Hz, H-7), 2.55 (2H, t, J = 8.0 Hz, H-2), 1.78-1.71 (2H, m, H-6), 1.67-1.59 (2H, m, H-3), 1.43-1.41 (4H, m, H-4, 5); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 199.1 (C=O), 153.2 (C-4′), 153.1 (C-3″, 5″), 149.1 (C-3′), 138.5 (C-4″), 136.1 (C-1″), 130.3 (C-1′), 122.6 (C-6′), 110.3 (C-2′), 110.1 (C-5′), 105.4 (C-2″, 6″), 60.8 (OCH_3), 56.1 (OCH_3), 56.0 (OCH_3), 55.9 (OCH_3), 38.0 (C-2), 36.3 (C-7), 31.3 (C-6), 29.2 (C-4), 29.1 (C-5), 24.6 (C-3); LC-MS: *m/z* 417.3 $(M+H)^+$, 439.4 $(M+Na)^+$. Q-Tof: *m/z* 417.2291 $[M+H]^+$ (Calculated for $C_{24}H_{33}O_6$, 417.2277).

*7-(3, 4, 5-Trimethoxy-phenyl)-1-(2, 5-dimethoxy-phenyl)-heptan-1-one (**12q**)*: Weight: 245 mg; % yield: 81.4 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.21 (1H, d, J = 3.2 Hz, H-6′), 7.00 (1H, dd, J = 3.2, 9.2 Hz, H-4′), 6.89 (1H, d, J = 9.2 Hz, H-3′), 6.39 (2H, s, H-2″, 6″), 3.85 (9H, s, OCH_3),

3.82 (3H, s, OCH_3), 3.78 (3H, s, OCH_3), 2.98 (2H, t, J = 7.2 Hz, H-7), 2.54 (2H, t, J = 8.0 Hz, H-2), 1.70-1.65 (2H, m, H-6), 1.63-1.60 (2H, m, H-3), 1.39-1.37 (4H, m, H-4, 5); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 202.6 (C=O), 153.5 (C-2′), 153.1 (C-5′), 152.8 (C-3″, 5″), 138.6 (C-4″), 136.1 (C-1″), 129.1 (C-1′), 119.5 (C-4′), 114.1 (C-6′), 113.2 (C-3′), 105.4 (C-2″, 6″), 60.8 (OCH_3), 56.1 (OCH_3), 56.0 (OCH_3), 55.8 (OCH_3), 43.7 (C-2), 36.3 (C-7), 31.4 (C-6), 29.2 (C-4), 29.0 (C-5), 24.3 (C-3); LC-MS: *m/z* 417.4 $(M+H)^+$, 439.3 $(M+Na)^+$, 455.3 $(M+K)^+$. Q-Tof: *m/z* 417.2291 $[M+H]^+$ (Calculated for $C_{24}H_{33}O_6$, 417.2277).

5-Lipoxygenase inhibitory activity: 5-Lipoxygenase enzyme inhibitory activity was measured using the method of Schewe, *et al*. [31] modified by Reddanna, *et al*. [32]. The assay mixture contained 80 μM linoleic acid (5 μL) and potato 5-lipoxygenase (5 μL) in 50 mM phosphate buffer (175 μL, pH 6.3). The reaction was initiated by the addition of enzyme buffer mix to linoleic acid and the enzyme activity was monitored as the increase in absorbance at 234 nm. The reaction was monitored for 120 sec and the inhibitory potential of the test substances **12a-q** were measured by incubating various concentrations (20 μL) of test substances for two minutes before the addition of linoleic acid. All assays were performed in triplicate. Percentage inhibition was calculated by comparing slope of the curve obtained for test substances with that of the control and plot diagrams are presented in supplementary data. The results are summarized in Table 1

Superoxide radical scavenging activity: Superoxide radical scavenging activity of compounds **12a-q** were determined spectrophotometrically (560 nm) by following the nitro blue tetrazolium (NBT) photo reduction method of McCord and Fridovich [33]. The assay mixture contained EDTA (6.6 μM), NaCN (3 μg), riboflavin (2 μM), NBT (50 μM), test substance and phosphate buffer (58 mmol, pH 7.8) in a final volume of 3 mL. Each mixture in a tube was shaken well, and the optical density was measured at 560 nm. Each tube was then uniformly illuminated with an incandescent lamp for 15 min, and the optical density was measured again at 560 nm. The percentage inhibition of superoxide radical-generation was measured by comparing the absorbance values of the control and that of the test substance. The IC50 values were obtained from a plot drawn between concentrations (μM) versus the percentage inhibition. The super-oxide radical's inhibitions exhibited by compounds **12a-q** have been summarized in Table 1.

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Refferences:

1. Inflammation Research perspectives, Editors: Giocomo T. Romano.
2. http://en Wikipedia.org/wiki/Inflammation.
3. De Caterina R, Zampolli A. From asthma to atherosclerosis-5-lipoxygenase, leukotrienes, and inflammation. N. Engl. J. Med 2004; 350: 4-7.
4. Reynolds Jf, Noakes TD, Schwellnus MP, et al. Non-steroidal anti-inflammatory drugs fail to enhancehealing of acute hamstring injuries treated with physiotherapy. S. Afr. Med. J 1995; 85: 517-22.
5. Keseru GM, Nogradi M. The chemistry of natural diarylheptanoids. part D, Studies in Natural Products Chemistry 1995; 17: 357-94.
6. Claeson P, Claeson UP, Tuchinda P, et al. Occurrence, structure and bioactivity of 1, 7-diarylheptanoids. Studies in Natural Products Chemistry 2002; 26: 881-08.
7. Lv HN, She GM. Naturally occurring diarylheptanoids. Nat. prod. Commun 2010; 5: 1687-08.
8. Tezuka Y, Gewali MB, Ali MS, et al. Eleven Novel Diarylheptanoids and Two Unusual Diarylheptanoid Derivatives from the Seeds of Alpinia blepharocalyx. J. Nat. Prod 2001; 64: 208-13.
9. Morihara M, Sakurai N, Inoue T, et al. Two Novel Diarylheptanoid Glucosides from Myrica gale var. tomentosa and Absolute Structure of Plane-Chiral Galeon. Chem. Pharm. Bull 1997; 45: 820-23.
10. Akazawa H, Fujita Y, Banno N, et al. Three new cyclic diarylheptanoids and Other Phenolic Compounds from the Bark of Myrica rubra and Their melanogenesis Inhibitory and Radical Scavenging Activities. J. Oleo. Sci 2010; 59: 213-21.
11. Sekiguchi M, Shigemori H, Ohsaki A. Renealtins A and B, New Diarylheptanoids with a Tetrahydrofuran Ring from the Seeds of Renealmia exaltata. J. Nat. Prod 2002; 65: 375-76.

12. Ali MS, Tezuka Y, Banskota AH, et al. Blepharocalyxins C−E, Three New Dimeric Diarylheptanoids, and Related Compounds from the Seeds of Alpinia blepharocalyx. J. Nat. Prod 2001; 64: 491-96.
13. Kikuzaki H, Nakatani N. Cyclic diarylheptanoids from rhizomes of Zingiber officinale. Phytochemistry 1996; 43: 273-77.
14. Shishodia S, Sethi G, Aggarwal BB. Curcumin: getting back to the roots. Ann N Y Acad Sci 2005; 1056: 206-17.
15. Egan ME, Pearson MS, Weiner A, et al. Caplan, Curcumin, a major constituent of turmeric, corrects cystic fibrosis defects. Science 2004; 304: 600-02.
16. Anto RJ, George J, Dinesh Babu KV, et al. Antimutagenic and anticarcinogenic activity of natural and synthetic curcuminoids. Mutat. Res 1996; 370: 127-31.
17. Yang H, Sung SH, Kim J, et al. Neuroprotective Diarylheptanoids from the Leaves and Twigs of Juglans sinensis against Glutamate-Induced Toxicity in HT22 Cells. Planta Med 2011; 77: 841-45.
18. Esatbeyoglu T, Huebbe P, Ernst IMA, et al. Curcumin--from molecule to biological function. Angew. Chem., Int. Ed 2012; 51: 5308-32.
19. Priyadarsini KI, Maity DK, Naik GH, et al. Role of phenolic O-H and methylene hydrogen on the free radical reactions and antioxidant activity of curcumin. Free Radic. Biol. Med 2003; 35: 475-84.
20. Tung NH, Kim SK, Ra JC, et al. Antioxidative and Hepatoprotective Diarylheptanoids from the Bark of Alnus japonica. Planta Med 2010; 76: 626-29.
21. Tao QF, Xu Y, Lam RYY,et al. Diarylheptanoids and a Monoterpenoid from the Rhizomes of Zingiber officinale: Antioxidant and Cytoprotective Properties. J. Nat. prod 2008; 71: 12-17.
22. Akazawa H, Akihisa T, Taguchi Y, et al. Melanogenesis Inhibitory and Free Radical Scavenging Activities of Diarylheptanoids and Other Phenolic Compounds from the Bark of Acer nikoense. Biol. Pharm. Bull 2006; 29: 1970-72.
23. Kyung-Seon Lee, Gao Li, Sung Hwan Kim, et al. Cytotoxic Diarylheptanoids from the Roots of *Juglans mandshurica.* J. Nat. Prod., 2002, 65 (11), 1707–1708.
24. Denney DB, Ross ST. The preparation and reactions of some halophosphoranes. J. Org. Chem 1962; 27: 998-1000.

25. Gilbert NC, Bartlett SG, Waight MT *et al*. The structure of human 5-lipoxygenase. Science. 2011; 331(6014): 217-9

26. Shimokawa T and Smith WL. Essential histidines of prostaglandin endoperoxide synthase. His-309 is involved in heme binding. J. Biol. Chem., 1991, 266, 6168-6173.

27. Biasina M, Bienert S, Waterhouse A, et al. SWISS-MODEL: modelling protein tertiary and quaternary structure using evolutionary information. T. Nucleic acids research 2014; 42: 252-58.

28. Hospital A, Andrio P, Fenollosa C, et al. MDWeb and MDMoby: an integrated web-based platform for molecular dynamics simulations. Bioinformatics 2012; 28: 1278-79.

29. Trott O, Olson AJ. AutoDock Vina: improving the speed and accuracy of docking with a new scoring function, efficient optimization and multithreading. Journal of Computational Chemistry, 2010; 31: 455-61.

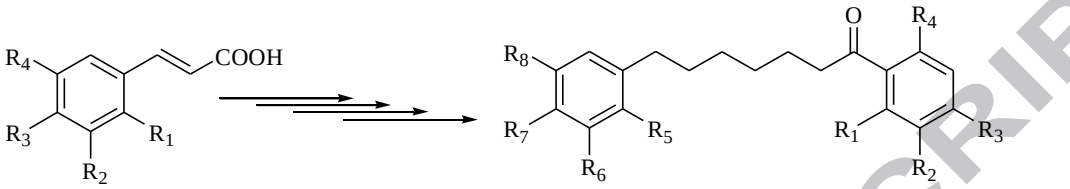
30. The PyMOL Molecular Graphics System, Version 1.8 Schrödinger, LLC

31. Schewe T, Rapaport SM, Kuhn H. Enzymology and physiology of reticulocyte lipoxygenase: comparison with other lipoxygenases. Adv.Enzymol. Mol. Biol 1986; 58: 191-72.

32. Reddenna P, Whelan J, Maddipati KR, et al. Purification of arachidonate 5-lipoxygenase from potato tubers. Methods Enzymol 1990; 187: 268-77.

33. Mc Cord JM and Fridovich I; Superoxide dismutase: An enzymatic function for erythrocuperin. *J. Biol. Chem.*, 1969, 244, 6049 - 6055.

Graphical abstract:



12a). $R_1 = R_4 = R_5 = R_6 = R_7 = R_8 = H$; $R_2 = R_3 = OCH_3$
12b). $R_1 = R_3 = R_5 = R_6 = R_7 = R_8 = H$; $R_2 = R_4 = OCH_3$
12k). $R_1 = OH$; $R_2 = R_4 = R_5 = R_8 = H$; $R_3 = R_6 = R_7 = OCH_3$
12m). $R_1 = R_3 = R_5 = R_8 = H$; $R_2 = R_4 = R_6 = R_7 = OCH_3$
12p). $R_1 = R_4 = R_5 = H$; $R_2 = R_3 = R_6 = R_7 = R_8 = OCH_3$

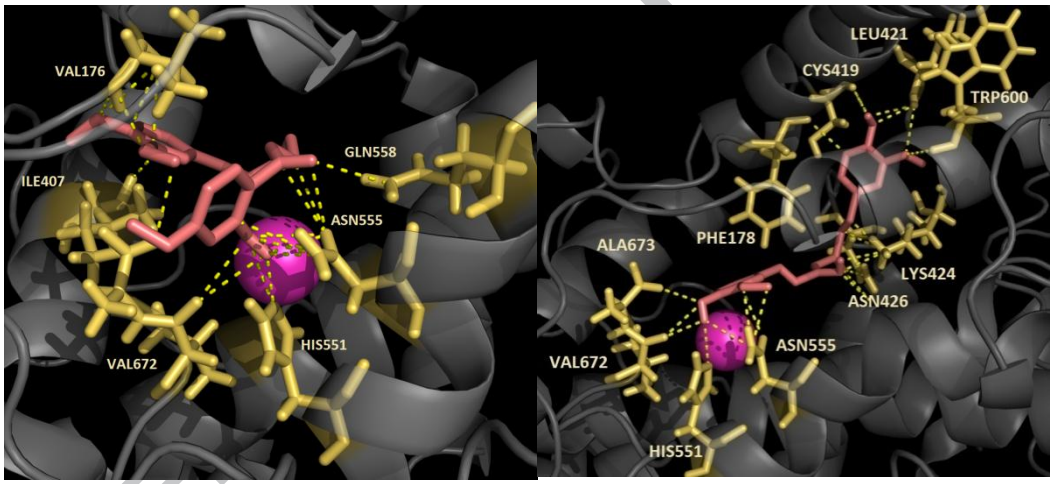


Figure: Docking poses of the compound **12k** and Curcumin at the receptor pocket. Ligand (salmon red), Fe (magenta) and active site residues making polar contacts (light yellow orange)

Highlights:

1. Synthesized novel diarylheptanones
2. *In vitro* 5-LOX inhibiting assay
3. Molecular docking
4. Compounds **12k**, **12o** showed potent activity in both *In vitro* & *In silico*