Chapter 3

Synthesis and Anticancer Activity
Evaluation of Curcumin Analogues
3.1 Introduction

Cells are the main building blocks of living organisms. Cell division is essential for growth, repair and reproduction. It is tightly controlled by genes inside the cell. A change in the DNA causes a special gene called oncogene (stimulate production of growth-stimulating chemicals that trigger cell division) to be switched on. This leads to uncontrolled growth and multiplication of cells. The most common form of cell division is called mitosis, during this process an exact copy of the cell is made and split into two new cells. However, there is also a second type of cell division called meiosis. This is a specialized process that produces the sex cells: eggs and sperm. When meiosis goes wrong it leads to inherited disorder (e.g. Down's syndrome). But the uncontrolled growth of cells by mitosis forms a lump called a tumour. Some tumour are benign and may not cause any problem, others however are malignant. They can invade into other body tissues and cause severe damage. It is these malignant tumours that we call cancer.

There are more than 200 different types of cancer which can develop in almost any organ or tissue, such as the lung, colon, breast, skin, bones or nerve tissue. Cancer may be caused due to environmental toxins, genetic problems, radiation, viruses, obesity, excessive exposure to sunlight, intake of excess alcohol and exposure to toxic chemicals. According to WHO, about 7.6 million people died due to cancer worldwide in 2008 and it is estimated that approximately 12 million cancer deaths will occur by 2030 worldwide.

All forms of cancers together account for approximately 13% of all deaths each year, the most common being: lung cancer (1.3 million deaths), stomach cancer (803,000 deaths), colorectal cancer (639,000 deaths), liver cancer (610,000 deaths) and breast cancer (519,000 deaths).


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3.2 Cancer: Drugs and Treatment

Cancer is a dreadful human disease, increasing with changing life style, nutrition, and global warming. The chemotherapeutic drugs are classified as alkylating agents (cis-platin, carboplatin, oxaliplatin, mechloretamine, cyclophosphamide, chlorambucil, ifosfamide), antimetabolites (azathiopurine, mercaptopurine), topoisomerase inhibitors (amascrine, etoposide, teniposide), plant alkaloids (vincristine, vinblastine, vinorelbine, vindesine, paclitaxel, docetaxel), antibiotics (actinomycin, anthracyclines, doxorubicin, daunorubicin) and tyrosine kinase inhibitors (imatinib mesylate).

Figure 3.1: Mechanism of action of anticancer drugs

Based on the mechanism of action an anticancer drug may be categorized as DNA (deoxyribonucleic acid) damaging agent, DNA synthesis inhibitor or mitotic disrupter. Folic acid, heterocyclic bases and nucleotides are the main building blocks of DNA. Compounds such as methotrexate, mercaptopurine, fluorouracil, hydroxyurea block some
steps in the formation of nucleotide or deoxyribonucleotides which are necessary for making DNA thus in turn prevent replication of cancerous cells. Some anticancer agents like cis-platin, daunorubicin, doxorubicin, etoposide damage DNA and RNA (ribonucleic acid) by disrupting replication of DNA. An anticancer agent (vinblastine, vincristine, paclitaxel) can act as a mitotic disrupter by disturbing the formation of spindles required for cell division (figure 3.1).  

The most common side effects of chemotherapy are hair loss, heart damage, appetite loss, weight loss, nervous system changes, taste changes, lung damage, stomatitis, esophagitis, nausea, vomiting, liver damage, constipation, urinary system damage, diarrhea, fatigue etc.

Traditionally many plants and their parts have been used for the treatment of diseases and healing wounds. According to the WHO, 80% of the world’s population primarily those of developing countries rely on plant-derived medicines for the health care. During the last 50 years about 500 000 natural and synthetic chemical compounds have been tested for their anticancer activity but only 25 of them are in use today. Over 62% of the anticancer drugs approved between 1983-1994, belongs to natural products or natural product analogues. Some example includes vinblastine (1) and vincristine (2, Catharanthus roseus), podophyllotoxin (3, Podophyllum peltatum roots), paclitaxel (4, Taxus baccata, T. brevifolia, T. canadensis), camptothecin (5, Camptotheca acuminata), homoharringtonine (6, Cephalotaxus harringtonia var. drupacea), flavopiridol (7, Dysoxylum binectariferum), etoposide (8, semisynthetic) and combrestatin A4 (9, Combretum caffrum). The two plant-derived natural products, paclitaxel and camptothecin were estimated to account for nearly one-third of the global anticancer market, about $3 and $9 billion, respectively in the year 2002. Numerous types of bioactive compounds have been isolated from plant sources. Several of them are
currently in clinical trials or preclinical trials or undergoing further investigation. Among them curcumin (10) which is present in spices, is of great interest for the treatment of cancer because of its superior safety profile.

3.3 Curcumin: Synthesis and Properties

The roots of turmeric (Curcuma longa Linn) have been used as a yellow dye for food and as a spice in South East Asia. For many centuries, turmeric has also been used for the treatment of wounds, inflammation and tumours in Eastern medicine. The three important constituents of turmeric are curcumin (10), demethoxycurcumin (11, DMC) and bisdemethoxycurcumin (12, BDMC). Commercially available curcumin mixture contains 77% curcumin, 17% DMC and 3% BDMC. A lesser known curcuminoid from
turmeric is cyclocurcumin (13), first isolated and characterized by Kiuchi et al.\textsuperscript{18} Over two centuries ago, the active ingredient of turmeric contributing for its biological properties was isolated and identified as curcumin. It is soluble in ethanol, alkali, ketone, acetic acid and chloroform but insoluble in water.\textsuperscript{19} The chemical structure of curumin ([\((E,E)-1,7\text{-bis}(4\text{-hydroxy}-3\text{-methoxy-phenyl})-1,6\text{-heptadiene}-3,5\text{-ione})\]) was determined by Roughley and Whiting in 1973.\textsuperscript{20}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{structures.png}
\caption{Structures of curcumin and its analogues.}
\end{figure}

In 1937, Paban et al reported its first synthesis from the chloride of the carbometoxyferuloic acid, and later same authors reported modified simple procedure for its synthesis.\textsuperscript{21} In this method the methylene group of acetyl acetone was blocked with boric anhydride and reacted with vanillin (figure 3.2) and the product formation takes place via Knoevenagel condensation. Boron-based reagents such as boron oxide, boric acid and tributoxyboron complex act as Lewis acids with the $\beta$-diketone system and consequently, reduce the nucleophilicity of the C-3 position. The two terminal methyl groups then undergo di-aldol condensation with two vanillin molecules. Hydrolysis of the intermediate in acid medium results in the formation of curcumin (figure 3.2).\textsuperscript{22}

Curcuminoids are synthesized in the biological system via sequence of reactions catalyzed by two type III polyketide synthases (PKSs), named diketide-CoA synthase
(DCS) and curcumin synthase (CURS). DCS catalyzes the condensation of malonyl-CoA on to feruloyl-CoA to give feruloyldiketide-CoA. CURS catalyzes the formation of curcumin from feruloyl-CoA and the feruloyl diketide-CoA synthesized by DCS (figure 3.3).\textsuperscript{23,24}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{synthesis_of_curcumin.png}
\caption{Synthesis of curcumin\textsuperscript{25}}
\end{figure}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{biosynthesis_of_curcuminoids.png}
\caption{Biosynthesis of curcuminoids}
\end{figure}
Both double bonds of curcumin have $E$ configuration and the keto form is preferred in solid phase and the enol form in solution. The bis-keto form predominates in acidic and neutral aqueous solutions (figure 3.4). Curcumin acts as a pH indicator, in acidic solutions ($\text{pH} < 7.4$) it turns yellow, whereas in basic ($\text{pH} > 8.6$) solutions it turns bright red.

![Figure 3.4: Keto-enol tautomerism in curcumin](image)

Curcumin has low bioavailability and lot of research is going to develop a related molecule with increased bioavailability, better potency and less toxicity. The reasons for low bioavailability of any compound within the body are poor absorption, high rate of metabolism, inactivity of metabolic products and/or rapid elimination and clearance from the body. Thus the main problems with curcumin are water insolubility, low serum levels, limited tissue distribution, apparent rapid metabolism and short half-life. Curcumin gets metabolized to curcuminglucuronide (14), curcumin sulfate (15), dihydrocurcumin (16, DHC), tetrahydrocurcumin (17, THC), hexahydrocurcumin (18, HHC) and hexahydrocurcuminol (19) in vivo (figure 3.5) and gets degraded into ferulic acid (20) and dihydroferulic acid (21) and this is the main reason of its low bioavailability.
Curcumin is a dietary phytochemical having low toxicity. Curcumin is used for the treatment of cancer (leukemia, colon, liver, breast and prostate), Alzheimer’s disease, HIV, chronic inflammations, oxidative stress and cystic fibrosis. Curcumin exhibits anti-inflammatory, anti-oxidant, anti-viral and anti-angiogenic...
properties.\textsuperscript{38,39} It also causes hypocholesterolemic effects in diabetic patients. Preclinical studies have revealed the chemopreventive potential of curcumin in several different animal tumor bioassay systems, including colon,\textsuperscript{40,41} duodenal,\textsuperscript{42} stomach,\textsuperscript{43} prostate,\textsuperscript{44} and breast\textsuperscript{45} carcinogenesis, both \textit{in vitro} and \textit{in vivo}. Clinical trials are going to test the efficacy of curcumin, against Alzheimer’s disease and cystic fibrosis. Three, phase I clinical trials have demonstrated tolerances as high as 12 g per day.\textsuperscript{46-48}

Curcumin’s biological effect includes modulation of several cellular receptors (EGFR and HER2), signal transcription factors (NF-κB, AP-1, Egr-1, β-catenin and PPAR-γ),\textsuperscript{49} various oxygenases \{cyclooxygenase-2 (COX-2) and 5-lipoxygenase (5-LOX)\},\textsuperscript{50} inducible nitric oxide synthase (iNOS), cell cycle proteins (cyclin D1p21), cytokines (TNF, IL-1, IL-6, chemokines),\textsuperscript{51} as well as cell surface adhesion molecules. Among the transcription factors affected by curcumin, NF-κB is the most important one as it plays a pivotal role in various inflammatory responses leading to host defense and activation of many gene expressions.\textsuperscript{52} Inappropriate regulation of NF-κB has been shown to give rise to various pathological disorders including inflammation, viral replication, atherosclerosis and growth of almost all types of tumors.\textsuperscript{53,54} Cyclooxygenase-2, which is overexpressed in colorectal cancers through NF-κB or activator protein-1 transactivation, is also suppressed by curcumin\textsuperscript{55} and other cyclooxygenase-2 inhibitors are known to have chemopreventive and antiangiogenic properties.\textsuperscript{56} Curcumin arrest the cell cycle at G\textsubscript{0}-G\textsubscript{1} or G\textsubscript{2}-M through up-regulation of the cyclin-dependent kinase inhibitors p21 and p27 and down-regulation of Cdc2 and cyclin B1.\textsuperscript{57} Curcumin blocks growth factor signaling \textit{via} inhibition of tyrosine kinase activity or depletion of ErbB-2.\textsuperscript{58} The ability of curcumin to cleave β-catenin for degradation is considered to be the basis of the chemopreventive effect of curcumin in colorectal cancer.\textsuperscript{59-62} It was found that curcumin treatment reduced the incidence of adenoma formation in the familial adenomatous polyposis mouse model to 40% of control.\textsuperscript{41}
Sharma et al observed that the phenolic hydroxyl groups are needed for antioxidant activity and that the presence of more than one of these groups, confers better activity than that of curcumin itself. The role of β-diketone moiety for the anti-oxidant activity was suggested by Sugiyama et al based on their observations using dimethyltetrahydrocurcumin.

Saturation of the alkene and reduction of the carbonyl functions in the C-7 linker of curcumin appears to reduce its anti-inflammatory activity by suppressing activation of NF-κB through inhibition of I-κB kinase activity. Initial studies indicate the importance of hydroxyphenyl in curcumin for its anti-inflammatory activity since acylation and alkylation of the phenolic hydroxy group of curcumin were found to drastically reduce its anti-inflammatory activity.

The significance of phenolic hydroxyl group for the inhibition of COX-1 activity was reported by Hong et al. However, recent studies reveal that many analogues of curcumin lacking a 4-hydroxyphenyl unit, such as 1,7-di-(2,3,4-trimethoxyphenyl)-1,6-heptadien-3,5-dione (22; COX-1: IC$_{50}$ = 0.06 µM,) and 4-[7-(4-methoxycarbonyl)phenyl]-3,5-dioxo-1,6-heptadienyl]benzoatedimethyl ester (23; COX-1: IC$_{50}$ = 0.05 µM), were more potent COX-1 inhibitors than curcumin (COX-1: IC$_{50}$ = 50 µM). Also the replacement of the β-diketone moiety by pyrazole (24) or isoxazole (25) unit leads to compounds with COX-inhibitory activity similar to curcumin. Replacing the “ene-[1,3-dioxol]-ene” C-7 linker of curcumin by C-5 “ene-oxoene,” as in 1,4-pentadiene-3-ones
(26) and their cyclopenta- (27) and cyclohexa- (28-29) analogues, has been reported to improve the inhibition of LPS-induced TNF-α and interleukin-6 expression.\(^{70}\)

![Chemical structures of 26-29](image)

The anticarcinogenic properties have been demonstrated in curcumin,\(^{71,72}\) and it has been suggested that the presence of a hydroxyphenyl group in compounds analogous to curcumin, especially in the 2-position (30; \(\mathrm{CD} = 0.3 \ \mu\mathrm{M}\), Curcumin; \(\mathrm{CD} = 7.3 \ \mu\mathrm{M}\)), is supportive of the chemoprotective activity through the ability to induce Phase II detoxification enzymes. The necessity of the ‘‘ene-[1,3-dioxo]-ene’’ C-7 linker, however, could not be firmly established. An early report by Markaverich et al\(^{73}\) suggests that the Michael acceptor type 2,6-bis(3,4-dihydroxybenzylidene)cyclohexanones (31), having only a ‘‘ene-oxo-ene’’ motif, could inhibit cancer cell proliferation \textit{in vitro} and \textit{in vivo}.

![Chemical structures of 30 and 31](image)

Ishida et al\(^{74}\) observed that diarylheptanoids of curcumin type with 3,4-dihydroxyphenyl (32a), 3,4-dimethoxyphenyl (32b), 2-fluorophenyl (33) and the
pyrazole (24) analogue of curcumin were cytotoxic, whereas the reduced curcumin types were inactive.

\[\text{Ohtsu et al}^{75} \text{ found that introduction of a CH}_2\text{CH}_2\text{COOEt group into the 1,3-diketo unit (34) affords a new type of antiandrogen agent.}\]

\[\text{34}\]

3.5 Present Investigation

In order to search potent curcumin analogues possessing favourable biological activity, different types of curcuminoids were designed. Both in vitro and in vivo studies show that curcumin gets metabolised via oxidation, reduction, glucuronidation and sulfation.\textsuperscript{76,77} Since glucuronidation and sulfation occurs at 4′-OH group of curcumin,\textsuperscript{78} it was assumed that modification at the 4′-OH could be beneficial for its activity by reducing the rate of metabolism. Thus some C-7 curcuminoids were synthesized with halogen, alkyl and nitrogen containing heterocycles at the 4′ position (scheme 3.2).

Moreover the poor absorption and fast metabolism under physiological conditions of the β-diketo compound restricts its use for the treatment of various diseases.\textsuperscript{79-82} The β-diketone moiety renders curcumin to be rapidly metabolized by aldo-keto reductase in liver.\textsuperscript{70} Thus, the seven carbon β-dicarbonyl linker of curcumin is the main cause of the instability. Now more emphasis is being given to the synthesis of modified curcumin
analogues with more stability and better pharmacokinetics.\textsuperscript{25,83,84} Omitting the methylene group and one carbonyl group a series of mono-carbonyl curcumin analogues (1,5-diaryl-1,4-pentadiene-3-ones) were synthesized and evaluated for their bioactivity by the research groups of Markaverich,\textsuperscript{73} Artico\textsuperscript{85} and El-Subbagh.\textsuperscript{86} The result that the mono-carbonyl analogues exhibit more powerful inhibition in a variety of cancer cells than curcumin indicated that the central methylene group which had been considered the main active group of curcuminoids in antitumor property may be of decreasing importance. In 2008, G. Liang et al synthesized mono-carbonyl curcumin analogues and tested for their anti-inflammatory activity \textit{in vitro}. Amongst the several analogues synthesized three compounds (figure 3.6) showed an enhanced ability to inhibit lipopolysaccharide (LPS)-induced TNF-\alpha and IL-6 in macrophages.\textsuperscript{70} Keeping in mind the biological potential of C-5 curcuminoids, such compounds were synthesized under schemes 3.4, 3.5 and 3.6.

![Figure 3.6: 1,5-Diaryl-1,4-pentadiene-3-ones structurally related to curcumin](image)

Hence, the present investigation deals with the synthesis and characterization of C-7 curcuminoids (with halo, alkyl and heterocyclic ring), C-5 monocarbonyl curcuminoids (with ether linkage and terminal ethyl ester group) and C-5 curcumin-oxazines derivatives (figure 3.7).
3.6 Results and Discussion

We started our work with the synthesis of some benzaldehydes with heterocyclic ring at para position (35-41) by reacting para-fluorobenzaldehyde with heterocyclic amines as depicted in scheme 3.1. These compounds were characterized by various spectroscopic techniques and data corresponds to literature reports.

![Scheme 3.1](image)

In the $^1$H NMR spectrum of compound 37 (figure 3.8) triplets at $\delta$ 3.33 and 3.84 were assigned to the eight protons of the morpholine nucleus. Doublets were observed at
δ 6.90 and 7.76 for the aromatic ring protons. A singlet at δ 9.79 was assigned to the aldehydic proton.

![Figure 3.8: 1H NMR spectrum of compound 37](image)

The classical 1,3-diketones (42-54) were synthesized using acetylacetone as a starting material by literature reported procedure with slight modification (scheme 3.2). To protect the C-3 of acetylacetone from an unwanted Knoevenagel reaction, a boric acetylacetone anhydride complex was prepared first by reacting acetylacetone with boric oxide in dry DMF. The methyl groups of protected acetyl acetone then underwent aldol condensation with different benzaldehydes in presence of 1,2,3,4-tetrahydroquinoline as a catalyst (scheme 3.2). Finally, the boron complex was decomposed using acetic acid to get the desired curcuminoids (42-54). Compounds 42-47 contain alkyl, halo or alkoxy substituents. While, compounds 48-54 containing heterocyclic moiety were synthesized using benzaldehydes 35-41 which were prepared according to scheme 3.1.
In the IR spectrum of compound 50 (figure 3.9), a broad peak around 3300 cm\(^{-1}\) was observed for enolic O–H stretch. The \(^1\)H NMR of compound 50 (figure 3.10) showed two triplets at \(\delta 3.25\) and \(3.86\) for eight hydrogens each of the morpholine nucleus. Doublets at \(\delta 6.88\) and \(7.48\) were assigned to the aromatic protons. Two doublets at \(\delta 6.47\) and \(7.59\) with \(J\) value 15.4 Hz, were assigned to the protons \(\alpha\) and \(\beta\) to carbonyl group.
Based on the coupling constants of the olefinic protons in the $^1$H NMR it was confirmed that the compounds 42-54 have $E$ stereochemistry. Compound 50 exist exclusively in its enolic form in solution phase which was confirmed by a singlet at $\delta 5.76$ due to enolic CH proton. Moreover, the enolic hydroxyl proton also appeared as a broad signal at $\delta 16.17$. The enolic form was further confirmed by the absence of any signal due to the two protons of COCH$_2$CO linkage. In the $^{13}$C NMR of compound 50 (figure 3.11) total ten signals appeared. The upfield peaks at $\delta 48.05$ and 66.62 were assigned to the carbons attached to nitrogen and oxygen atoms of morpholine nucleus. Appearance of the peak at $\delta 101.23$ due to enolic CH and absence of any signal due to methylene carbon of keto form supports that the compound 50 exist exclusively as enol form.

![Figure 3.10: $^1$H NMR spectrum of compound 50](image-url)
Figure 3.11: $^{13}$C NMR spectrum of compound 50

Figure 3.12: ESI-MS of compound 50
The signals for carbonyl carbons appeared at δ 183.25. The carbons α and β to carbonyl group appeared at δ 120.81 and 140.13, respectively. Remaining four signals at δ 114.69, 126.10, 129.59 and 152.28 were assigned to the aromatic carbons. ESI-MS of compound 50 (figure 3.12) showed molecular ion peak at \( m/z \) 447.32 \([M + H]^+\).

Under physiological pH β-diketone moiety leads to instability of curcumin, hence the β-diketone was replaced and mono-keto curcumin analogues were designed. These derivatives (69-100) were synthesized in order to examine the role of ethyl ester and ethereal linkages towards the biological activity of curcuminoids. Eight curcuminoids having a free hydroxyl group at para position of the aromatic ring (61-68) were synthesized as starting material under acidic conditions (scheme 3.3). These C-5 curcuminoids were characterized by various spectroscopic techniques and data corresponds to literature reported values.\(^{91-93}\)

Scheme 3.3

Etherification of hydroxyl group of compounds 61-68 was carried out using bromoesters (scheme 3.4 and 3.5). The four α-bromoesters namely ethyl-2-bromoacetate, ethyl-2-bromopropanoate, ethyl-2-bromobutanoate and ethyl-2-bromopentanoate were treated with compounds 61-68 containing a free phenolic hydroxyl group. The reaction was carried in the presence of anhydrous potassium carbonate and dry DMF as solvent to get monocarbonyl curcuminoids 69-100 as depicted in scheme 3.4.
Scheme 3.4

In the IR spectrum of compound 69 (figure 3.13) band at 1764 cm\(^{-1}\) was due to the C=O stretching of the ester group. In the \(^1\)H NMR spectrum of compound 69 (figure 3.14) triplet and quartet at \(\delta\) 1.31 and 4.29 were observed for the ethyl group of the ester linkage. The quartet for methylene appeared downfield due to its proximity to electronegative oxygen atom. The four methylene protons of the cyclopentanone ring appeared as singlet at \(\delta\) 3.08 due to symmetry in the molecule. The signal at \(\delta\) 4.67 was assigned to the four methylene protons of the ether linked to aromatic ring. The doublets at \(\delta\) 6.97 and 7.57 with coupling constant 8.8 Hz were assigned to the aromatic protons. The signal appearing at \(\delta\) 7.54 was for the alkene protons of the \(\alpha,\beta\)-unsaturated system.
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Figure 3.13: IR spectrum of compound 69

Figure 3.14: $^1$H NMR spectrum of compound 69
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Figure 3.15: $^{13}$C NMR spectrum of compound 69

Figure 3.16: ESI-MS of compound 69
In the $^{13}$C NMR spectrum of compound 69 (figure 3.15), the primary and secondary carbons of the ethyl group of the ester appeared at δ 14.12 and 61.50. The signal at δ 65.22 was assigned to the methylene carbon between etheral oxygen and carbonyl group of ester. The two secondary carbons of the cyclic ring appeared together at δ 26.38. Amongst the four aromatic carbons the two secondary carbons appeared at δ 114.87 and 132.44, while the quarternary carbons appeared at δ 129.65 and 158.56. Signals at δ 133.05 and 135.68 were assigned to the β and α carbons, respectively of the α,β-unsaturated system. The quarternary carbon of the ester appeared at δ 168.47. The most downfield signal at δ 196.17 was due to the carbonyl carbon of the cyclopentanone ring. ESI-MS of compound 69 (figure 3.16) showed molecular ion peak at $m/z$ 465.27 [M + H]$^+$. 

\[ \text{Scheme 3.5} \]
The compounds 61-68 were also reacted with ethyl-4-bromobutanoate, ethyl-5-
bromopentanoate and ethyl-6-bromohexanoate to get derivatives 101-124 with C-3 to C-5
linker between the phenolic oxygen atom and ethyl ester group. These compounds were
synthesized to study the influence of the length of carbon chain on the biological activity
of such compounds.

In the IR spectrum of compound 112 (figure 3.17) band at 1733 cm\(^{-1}\) was due to
C=O stretch of the ester group. In the \(^1\)H NMR spectrum of compound 112 (figure 3.18)
triplet and quartet at \(\delta 1.25\) and 4.13 were assigned to the ethyl group of ester moiety. The
methylene protons of five carbon chain linker appeared at \(\delta 1.48-1.56\), 1.71 and 1.88.
Triplet at \(\delta 2.34\) was for the four protons of the two COCH\(_2\) groups. Multiplet at \(\delta 1.80-
1.84\) and signal at \(\delta 2.94\) were assigned to the six hydrogens of the cyclohexyl system. A
singlet at \(\delta 3.89\) was assigned to the six protons of the two methoxy groups. The triplet at
\(\delta 4.06\) was assigned to the two OCH\(_2\) groups. Peaks at \(\delta 6.89\), 7.02 and 7.08 were
assigned to the aromatic protons. Singlet at \(\delta 7.74\) was assigned to the \(\beta\) carbons of the
unsaturated system. In the \(^{13}\)C NMR of compound 112 (figure 3.19) total twenty signals
appeared. The signals at \(\delta 14.21\) and 60.23 were assigned to the ethyl group. The two
terminal carbons of the five carbon chain linker appeared at \(\delta 34.18\) and 68.59 while the
remaining three carbons appeared at \(\delta 22.99\), 25.52 and 28.76. The methylene carbons of
the ring appeared at \(\delta 24.67\) and 28.49. The methoxy carbon appears at \(\delta 55.99\). Peaks at
\(\delta 112.23\), 114.15, 123.90, 128.88, 148.90 and 149.08 were assigned to the aromatic
carbons. The \(\beta\) and \(\alpha\) carbons of the unsaturated system appeared at \(\delta 134.37\) and 136.82.
The peaks at \(\delta 173.60\) and 190.06 were assigned to the carbonyl carbons of the
cyclohexanone and ester part. ESI-MS of compound 112 (figure 3.20) showed molecular
ion peak at \(m/z 651.52 [M + H]^+\).
Figure 3.17: IR spectrum of compound 112

Figure 3.18: $^1$H NMR spectrum of compound 112
Compound 112

Figure 3.19: $^{13}$C NMR spectrum of compound 112

Figure 3.20: ESI-MS of compound 112
Compounds containing dihydro-1,3-oxazine ring show anti-tumor, anti-bacterial, anti-HIV, antimalarial, analgesics and anticonvulsant activities. The 1,3-oxazine are generally prepared by Mannich condensation of phenol and a primary amine with formaldehyde. This reaction involves the C-C bond formation by attack of the ortho phenol position on the amine Mannich adduct. Thus, a few curcuminoid-oxazine (125-127) were synthesized according to literature reported methods as depicted in scheme 3.6.

![Scheme 3.6](image)

(R = CH₃, n = 0, 125; R = CH₃, n = 1, 126; R = Br, n = 1, 127)

In the IR spectrum of compound 127 (figure 3.21) peaks at 1234 and 1118 cm⁻¹ were due to asymmetric and symmetric C–O–C stretch. In the ¹H NMR of compound 127 (figure 3.22) pentet and triplet at δ 1.78 and 2.87 were assigned to the methylene protons of cyclohexanone ring. The singlets at δ 4.62 and 5.35 were characteristic of the methylene protons adjacent to nitrogen and oxygen atoms of the oxazine ring. Signals at δ 6.82, 6.99, 7.13, 7.26-7.29 and 7.35 were assigned to the aromatic protons. The most downfield signal at δ 7.68 was assigned to alkene CH. In the ¹³C NMR of compound 127...
(figure 3.23) total seventeen signals appeared. The most upfield signals at δ 22.91 and 28.47 were assigned to the methylene carbons of the cyclohexanone ring. Peaks at δ 50.65 and 79.53 were characteristic of the methylene carbons attached to nitrogen and oxygen atoms of the oxazine nucleus. The peaks at δ 134.51 and 136.37 were characteristic of the carbons of α,β-unsaturated system. The signals at δ 147.22 and 154.63 were assigned to the aromatic carbons attached to nitrogen and oxygen atoms. The most downfield signal at δ 189.95 was due to the carbonyl carbon. The peaks at δ 114.18, 117.02, 120.11, 120.37, 128.95, 129.35, 130.59 and 132.15 were assigned to the remaining aromatic carbons.

Figure 3.21: IR spectrum of compound 127
Figure 3.22: $^1$H NMR spectrum of compound 127

Figure 3.23: $^{13}$C NMR spectrum of compound 127
3.7 In vitro Cytotoxicity Screening

HeLa cells were cultured in DMEM medium with 10% fetal bovine serum and 1% penicillin/streptomycin. For the cytotoxicity assays, cells were seeded into 96-well plate (2.5 x 10^4 in 100 µL per well). Test compounds were suspended in DMSO to make 10 mM stock solutions and diluted by DMEM. Addition of compounds was performed after adherent cells reached 40-50% confluence. After incubation for 48 h at 37 °C in humidified atmosphere with 5% CO₂, 10 µL of MTT (5 mg/mL in PBS) was added to each well and incubated for another 4 h. The culture medium was then aspirated and 100 µL of DMSO was added to each well. The 96-well plate was read by microarray reader for optical density at 490 nm. All tests were performed in triplicates and every time Doxorubicin was used as standard.

Some of the synthesized compounds were screened for their cytotoxicity against Hela cell line at 50 µM concentration. Amongst the C-7 curcuminoids (42-54) two compounds 52 and 53 with N-Me and N-Et piperazinyl groups exhibited some cytotoxicity (figure 3.24). Screening of other compounds is under progress.

![Figure 3.24: Cytotoxicity screening](image-url)
3.8 Experimental Section

3.8.1 Analytical Methods

All of the chemicals used in the synthesis were purchased from Sigma-Aldrich and were used as such. The solvents used were of analytical grade and were used as supplied unless otherwise stated. The melting point of the compounds, were determined on EZ-Melt automated melting point apparatus, Stanford Research Systems and are uncorrected. IR (film/KBr) spectra were recorded using Perkin-Elmer FT-IR spectrophotometer and the values are expressed as $\nu_{\text{max}}$ cm$^{-1}$. NMR spectra were recorded on a Jeol ECX spectrospin instrument in CDCl$_3$ or DMSO-$d_6$ solutions, with TMS as an internal reference. The letters s, brs, d, t, and q refer to singlet, broad singlet, doublet, triplet and quartet, respectively. Chemical shifts ($\delta$ values) and coupling constants ($J$ values) are given in ppm and hertz, respectively. Mass data were recorded in Jeol-AccuTOF JMS-T100LC mass spectrometer. Silica gel (60-120 mesh) was used for column chromatography.

3.8.2 Synthesis and Characterization of Compounds

Typical procedure: Synthesis of 4-morpholinobenzaldehyde (37) and related compounds (35-41): To a well stirred solution of morpholine (1.05 g, 12.08 mmol) in dry DMF (15 mL) anhydrous potassium carbonate (1.66 g, 12.08 mmol) was added. After 15 min para-fluorobenzaldehyde (500 mg, 4.02 mmol) was added and the reaction mixture was stirred at 80 °C for 8-10 h. After completion of the reaction as indicated by TLC, the temperature of the reaction mixture was dropped to room temperature and partitioned between cold water and chloroform. The organic layer was washed with cold water thrice to remove DMF. The crude product was purified using column chromatography to obtain compound 37. Yield 68%; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 3.33
(t, J = 4.5 Hz, 4H), 3.84 (t, J = 4.8 Hz, 4H), 6.90 (d, J = 8.7 Hz, 2H, ArH), 7.76 (d, J = 8.5 Hz, 2H, ArH), 9.79 (s, 1H, CHO).

**General procedure for the synthesis of (1E,6E)-1,7-bis(4-morpholinophenyl)hepta-1,6-diene-3,5-dione (50) and related compounds (42-54):**

To a well-stirred solution of acetyl acetone (200 mg, 1.2 mmol) in dry DMF, boric oxide (140 mg, 1.2 mmol) and tributyl borate (552 mg, 2.4 mmol) were added at 65 °C and stirred for 15 min. To the in situ formed borate complex, 4-morpholinobenzaldehyde (37; 459 mg, 2.4 mmol) was added and stirred for 5 min. After that a mixture of 1,2,3,4-tetrahydroquinoline (0.1 mL) and acetic acid (0.3 mL) in DMF (1 mL) was added to the reaction mixture and heated to 95 °C for 4 h. After cooling to 15 °C, 20% acetic acid (20 mL) was added with stirring and again the reaction mixture was stirred at 70 °C for another 1 h. Then it was cooled to 15 °C and solid was filtered, washed with water and dried. The crude curcumin obtained was purified by column chromatography to obtain compound 50. Yield 58% (red solid); mp 123-124 °C; IR (film, cm⁻¹): 2967, 2921, 2852, 1600, 1516, 1449, 1334, 1239, 1188, 1125; ′H NMR (400 MHz, CDCl₃) δ: 3.25 (t, J = 5.1 Hz, 8H, 4NCH₂), 3.86 (t, J = 5.1 Hz, 8H, 4OCH₂), 5.76 (s, 1H), 6.47 (d, J = 15.4 Hz, 2H, 2CH=CHCO), 6.88 (d, J = 8.8 Hz, 4H, ArH), 7.48 (d, J = 8.8 Hz, 4H, ArH), 7.59 (d, J = 15.4 Hz, 2H, 2CH=CHCO), 16.17 (brs, 1H, OH); ′C NMR (100 MHz, CDCl₃) δ: 49.05, 66.62, 101.23, 114.69, 120.81, 126.10, 129.59, 140.13, 152.28, 183.25; ESI-MS (m/z): 447.32 [M + H]⁺.

(1E,6E)-1,7-Bis(4-ethylphenyl)hepta-1,6-diene-3,5-dione (42): Yield 64% (yellow solid); mp 167-168 °C; IR (film, KBr): 2965, 2928, 1626 (C=O), 1575, 1418, 1138, 976; ′H NMR (400 MHz, CDCl₃) δ: 1.25 (t, J = 7.3 Hz, 6H, 2CH₃CH₂), 2.68 (q, J = 7.3 Hz, 4H, 2CH₂CH₃), 5.83 (s, 1H), 6.59 (d, J = 16.1 Hz, 2H, 2CH=CHCO), 7.23 (d, J = 8.0 Hz,
4H, ArH), 7.48 (d, J = 8.0 Hz, 4H, ArH), 7.65 (d, J = 16.1 Hz, 2H, 2CH=CHCO), 15.98 (brs, 1H, OH); ESI-MS (m/z): 333.52 [M + H]⁺.

**(1E,6E)-1,7-Bis(4-iso-propylphenyl)hepta-1,6-diene-3,5-dione (43):** Yield 77% (yellow solid); mp 134-135 °C; IR (film, cm⁻¹): 3429, 2960, 2924, 1628 (C=O), 1603, 1417, 1139, 1054; ¹H NMR (400 MHz, CDCl₃) δ: 1.26 (d, J = 6.6 Hz, 12H, 2CH₂(CH₃)₂), 2.93 (septet, J = 6.6 Hz, 2H, 2CH₂(CH₃)₂), 5.83 (s, 1H), 6.59 (d, J = 15.4 Hz, 2H, 2CH=CHCO), 7.25-7.27 (m, 4H, ArH), 7.49 (d, J = 8.0 Hz, 4H, ArH), 7.65 (d, J = 15.4 Hz, 2H, 2CH=CHCO), 15.98 (brs, 1H, OH); ESI-MS (m/z): 361.31 [M + H]⁺.

**(1E,6E)-1,7-Bis(4-propylphenyl)hepta-1,6-diene-3,5-dione (44):** Yield 65% (yellow solid); mp 121-122 °C; IR (film, cm⁻¹): 2955, 2926, 2869, 1627 (C=O), 1181, 1140, 976; ¹H NMR (400 MHz, CDCl₃) δ: 0.95 (t, J = 7.3 Hz, 6H, 2CH₂CH₂CH₂), 1.65 (sextet, J = 7.3 Hz, 4H, 2CH₂CH₂CH₂), 2.61 (t, J = 7.3 Hz, 4H, 2CH₂CH₂CH₂), 5.82 (s, 1H), 6.59 (d, J = 16.1 Hz, 2H, 2CH=CHCO), 7.20 (d, J = 8.0 Hz, 4H, ArH), 7.48 (d, J = 8.0 Hz, 4H, ArH), 7.64 (d, J = 16.1 Hz, 2H, 2CH=CHCO), 15.97 (brs, 1H, OH); ESI-MS (m/z): 361.35 [M + H]⁺.

**(1E,6E)-1,7-Bis(4-chlorophenyl)hepta-1,6-diene-3,5-dione (45):** Yield 68% (yellow solid); mp 200-201 °C; IR (film, cm⁻¹): 2926, 2854, 1636 (C=O), 1562, 1489, 1404, 1091, 972; ¹H NMR (400 MHz, CDCl₃) δ: 5.83 (s, 1H), 6.59 (d, J = 15.4 Hz, 2H, 2CH=CHCO), 7.37 (d, J = 8.0 Hz, 4H, ArH), 7.49 (d, J = 8.0 Hz, 4H, ArH), 7.61 (d, J = 15.4 Hz, 2H, 2CH=CHCO), 15.81 (brs, 1H, OH); ¹³C NMR (100 MHz, CDCl₃) δ: 102.06, 124.43, 129.21, 129.24, 133.41, 136.02, 139.31, 183.03; ESI-MS (m/z): ESI-MS (m/z): 345.12 [M + H]⁺, 347.14 [M + 2]⁺, 349.14 [M + 4]⁺.

**(1E,6E)-1,7-Bis(4-bromophenyl)hepta-1,6-diene-3,5-dione (46):** Yield 58% (yellow solid); IR (film, cm⁻¹): 3421, 2926, 1582, 1486, 1400, 1072, 1009; ¹H NMR (400 MHz,
CDCl$_3$ $\delta$: 5.82 (s, 1H), 6.60 (d, $J$ = 15.4 Hz, 2H, 2CH=CHCO), 7.41 (d, $J$ = 8.8 Hz, 4H, ArH), 7.53 (d, $J$ = 8.8 Hz, 4H, ArH), 7.59 (d, $J$ = 15.4 Hz, 2H, 2CH=CHCO), 15.81 (s, 1H, OH). ESI-MS ($m/z$): 432.88 [M + H]$^+$, 434.76 [M + 2]$^+$, 436.76 [M + 4]$^+$.

(1E,6E)-1,7-Bis(4-(2-bromoethoxy)phenyl)hepta-1,6-diene-3,5-dione (47): Yield 67% (orange solid); mp 125-126 $^\circ$C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 3.65 (t, $J$ = 6.6 Hz, 4H, 2CH$_2$Br), 4.33 (t, $J$ = 6.6 Hz, 4H, 2OCH$_2$), 5.79 (s, 1H), 6.51 (d, $J$ = 16.1 Hz, 2H, 2CH=CHCO), 6.93 (d, $J$ = 8.8 Hz, 4H, ArH), 7.52 (d, $J$ = 8.8 Hz, 4H, ArH), 7.62 (d, $J$ = 16.1 Hz, 2H, 2CH=CHCO), 16.03 (brs, 1H, OH); ESI-MS ($m/z$): 520.87 [M + H]$^+$, 524.92 [M + 2]$^+$, 526.91 [M + 4]$^+$.

(1E,6E)-1,7-Bis(4-(pyrrolidin-1-yl)phenyl)hepta-1,6-diene-3,5-dione (48): Yield 54% (red solid); IR (film, cm$^{-1}$): 3421, 2920, 1601, 1462, 1384, 1327, 1137; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 2.01-2.05 (m, 8H), 3.33-3.36 (m, 8H), 5.71 (s, 1H), 6.39 (d, $J$ = 16.1 Hz, 2H, 2CH=CHCO), 6.53 (d, $J$ = 8.8 Hz, 4H, ArH), 7.44 (d, $J$ = 8.8 Hz, 4H, ArH), 7.59 (d, $J$ = 16.1 Hz, 2H, 2CH=CHCO); ESI-MS ($m/z$): 415.34 [M + H]$^+$.

(1E,6E)-1,7-Bis(4-(piperidin-1-yl)phenyl)hepta-1,6-diene-3,5-dione (49): Yield 52%; IR (film, cm$^{-1}$): 2928, 2850, 1624 (C=O), 1598, 1437, 1302, 1242, 1191, 1159, 1125; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 1.61 (br, 4H), 2.13 (s, 4H), 3.25-3.29 (m, 8H), 3.39-3.41 (m, 4H), 5.59 (s, 1H), 6.29 (d, $J$ = 15.4 Hz, 2H, COCH=CH), 6.82-6.90 (m, 8H, ArH), 7.54 (d, $J$ = 15.4 Hz, 2H, COCH=CH), 15.61 (brs, 1H, OH); ESI-MS ($m/z$): 443.12 [M + H]$^+$.

(1E,6E)-1,7-Bis(4-(piperazin-1-yl)phenyl)hepta-1,6-diene-3,5-dione (51): Yield 59% (orange solid); mp 179-180 $^\circ$C; IR (film, cm$^{-1}$): 2919, 2850, 1663 (C=O), 1601, 1438, 1281, 1234, 1186, 1136, 1009; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 3.25-3.28 (m, 4H), 3.29-3.32 (m, 4H), 3.52-3.55 (m, 3H), 3.61-3.64 (m, 1H), 3.69-3.72 (m, 3H), 3.76-3.78 (m,
1H), 5.76 (s, 1H), 6.48 (d, J = 16.1 Hz, 2H, 2CH=CHCO), 6.90 (d, J = 8.8 Hz, 4H, ArH), 7.48 (d, J = 8.8 Hz, 4H, ArH), 7.59 (d, J = 16.1 Hz, 2H, 2CH=CHCO), 8.11 (s, 2H, NH), 16.14 (brs, 1H, OH); ESI-MS (m/z): 445.35 [M + H]^+.

(1E,6E)-1,7-Bis(4-(4-methylpiperazin-1-yl)phenyl)hepta-1,6-diene-3,5-dione (52): Yield 46% (orange solid); mp 112-114 °C; IR (film, cm\(^{-1}\)): 2925, 1600, 1159, 818; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 2.35 (s, 6H, 2NCH\(_3\)), 2.55-2.58 (m, 8H), 3.30-3.32 (m, 8H), 5.61 (s, 1H), 6.31 (d, J = 15.4 Hz, 2H, 2CH=CHCO), 6.88 (d, J = 8.8 Hz, 4H, ArH), 7.44 (d, J = 8.8 Hz, 4H, ArH), 7.54 (d, J = 15.4 Hz, 2H, 2CH=CHCO), 15.58 (brs, 1H, OH); ESI-MS (m/z): 473.13 [M + H]^+.

(1E,6E)-1,7-Bis(4-(4-ethylpiperazin-1-yl)phenyl)hepta-1,6-diene-3,5-dione (53): Yield 47% (red solid); IR (film, cm\(^{-1}\)): 2923, 2851, 1601, 1239, 1186, 1126; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 1.13 (t, J = 7.3 Hz, 6H, 2CH\(_2\)CH\(_3\)), 2.48 (q, J = 7.3 Hz, 4H, 2CH\(_2\)CH\(_3\)), 2.60 (t, J = 5.1 Hz, 8H), 3.32 (t, J = 5.1 Hz, 8H), 5.61 (s, 1H), 6.31 (d, J = 15.4 Hz, 2H, 2CH=CHCO), 6.88 (d, J = 8.8 Hz, 4H, ArH), 7.43 (d, J = 8.8 Hz, 4H, ArH), 7.54 (d, J = 15.4 Hz, 2H, 2CH=CHCO), 15.59 (brs, 1H, OH); ESI-MS (m/z): 501.22 [M + H]^+.

(1E,6E)-1,7-Bis(4-(4-phenylpiperazin-1-yl)phenyl)hepta-1,6-diene-3,5-dione (54): Yield 60% (orange solid); mp 179-180 °C; IR (film, cm\(^{-1}\)): 2918, 2849, 1601, 1492, 1231, 1156, 980; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 3.34 (t, J = 4.4 Hz, 8H), 3.46 (t, J = 4.4 Hz, 8H), 5.77 (s, 1H), 6.48 (d, J = 16.1 Hz, 2H, 2CH=CHCO), 6.89-6.99 (m, 10H, ArH), 7.28-7.32 (m, 4H, ArH), 7.49 (d, J = 8.8 Hz, 4H, ArH), 7.60 (d, J = 16.1 Hz, 2H, 2CH=CHCO), 16.18 (brs, 1H, OH); ESI-MS (m/z): 597.44 [M + H]^+.

**Typical procedure for the synthesis of (2\(E\),6\(E\))-2,6-bis(4-hydroxybenzylidene) cyclohexanone (63) and related compounds (61-68):** To a well stirred solution of cyclohexanone (56; 2 g, 0.02 mol) in glacial acetic acid (20 mL) and Conc. HCl (20 mL)
maintained at 0 °C, 4-hydroxy benzaldehyde (59; 4.97 g, 0.04 mol) was added. The reaction mixture was stirred at 35-40 °C for 2 h. After standing the reaction mixture overnight at 0 °C temperature it was treated with water (20 mL). The solid thus obtained was filtered and recrystallised with ethanol to get compound 63 in good yield.

**Typical procedure for the synthesis of diethyl-2,2'-(4,4'-(1\(E\),1'\(E\))-2-oxocyclopentane-1,3-diylidene)-bis(methan-1-yl-1-ylidene)bis(4,1-phenylene))bis(oxy) diacetate (69) and related compounds (70-100):** To a stirred solution of (\(E\))-2-(4-hydroxybenzyl)-5-(4-hydroxybenzylidene)cyclopentanone (61; 200 mg, 0.67 mmol) in dry DMF (10 mL), anhydrous K\(_2\)CO\(_3\) (281 mg, 2.03 mmol) was added and stirred for 15 min. To this ethylbromoacetate (226 mg, 1.35 mmol) was added and stirred at 35-40 °C for 10-12 h. After completion of reaction, water (20 mL) was added and extracted with chloroform (3 x 10 mL). The organic layer was washed by water several times. The organic layer was dried over sodium sulphate and purified by column chromatography to obtain compound 69. Yield 76% (yellow solid); mp 157-158 °C; IR (film, cm\(^{-1}\)): 2990, 2921, 2853, 1764 (OC=O), 1693 (OC=O), 1595, 1510, 1304, 1261 (C–O–C), 1211, 1181, 1120, 1077 (C–O–C); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 1.31 (t, \(J = 7.3\) Hz, 6H, 2COOCH\(_2\)CH\(_3\)), 3.08 (s, 4H, CH\(_2\)CH\(_2\)), 4.29 (q, \(J = 7.3\) Hz, 4H, 2COOCH\(_2\)CH\(_3\)), 4.67 (s, 4H, OCH\(_2\)), 6.97 (d, \(J = 8.8\) Hz, 4H, ArH), 7.54 (s, 2H, 2CH=CH=C), 7.57 (d, \(J = 8.8\) Hz, 4H, ArH); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\): 14.12, 26.38, 61.50, 65.22, 114.87, 129.65, 132.44, 133.01, 135.68, 158.56, 168.47, 196.17; ESI-MS (m/z): 465.27 [M + H]+.

**Diethyl-2,2'-(4,4'-(1\(E\),1'\(E\))-2-oxocyclopentane-1,3-diylidene)bis(methan-1-yl-1-ylidene)-bis-(4,1-phenylene))bis(oxy)dipropanoate (70):** Yield 73% (yellow solid); mp 153-154 °C; IR (film, KBr): 2986, 2939, 1746 (OC=O), 1603, 1505, 1249 (C–O–C), 1173, 1134, 1097, 1047 (C–O–C), 1016; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 1.26 (t, \(J = 7.3\) Hz, 6H,
2COOCH\textsubscript{2}CH\textsubscript{3}), 1.65 (d, $J = 7.3$ Hz, 6H, 2CH\textsubscript{2}CH\textsubscript{3}), 3.07 (s, 4H, CH\textsubscript{2}CH\textsubscript{2}), 4.23 (q, $J = 7.3$ Hz, 4H, 2COOCH\textsubscript{2}CH\textsubscript{3}), 4.80 (q, $J = 7.3$ Hz, 2H, 2CH\textsubscript{2}CH\textsubscript{3}), 6.93 (d, $J = 8.8$ Hz, 4H, Ar\textsubscript{H}), 7.53 (s, 4H, Ar\textsubscript{H}), 13\textsuperscript{C} NMR (100 MHz, CDCl\textsubscript{3}) $\delta$: 14.10, 18.44, 26.39, 61.43, 72.49, 115.19, 129.44, 132.45, 133.06, 135.58, 158.40, 171.75, 196.19; ESI-MS ($m$/$z$): 493.32 [M + H]$^+$.  

Diethyl-2,2'-((4,4'-(1\textsuperscript{E},1'\textsuperscript{E})-(2-oxocyclopentane-1,3-diylidene)-bis-(methan-1-yl-1-ylidene)-bis(4,1-phenylene))bis(oxy)dibutanoate (71): Yield 82\% (yellow solid); mp 105-106 °C; IR (film, cm\textsuperscript{-1}): 2977, 2937, 2879, 1752 (OC=O), 1664, 1601, 1569, 1508, 1372, 1246 (C–O–C), 1191, 1160, 1059, 1024 (C–O–C–C); \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) $\delta$: 1.09 (t, $J = 7.3$ Hz, 6H, 2CH\textsubscript{2}CH\textsubscript{2}CH\textsubscript{3}), 1.26 (t, $J = 7.3$ Hz, 6H, 2COOCH\textsubscript{2}CH\textsubscript{3}), 2.01 (pentet, $J = 6.6$ Hz, 4H, 2CH\textsubscript{2}CH\textsubscript{2}CH\textsubscript{3}), 3.07 (s, 4H, CH\textsubscript{2}CH\textsubscript{2}CH\textsubscript{3}), 4.23 (q, $J = 7.3$ Hz, 4H, 2COOCH\textsubscript{2}CH\textsubscript{3}), 4.60 (t, $J = 6.6$ Hz, 2H, 2OCH\textsubscript{2}), 6.93 (d, $J = 8.8$ Hz, 4H, Ar\textsubscript{H}), 7.53 (s, 4H, Ar\textsubscript{H}), 7.55 (s, 2H, 2CH=CH); 13\textsuperscript{C} NMR (100 MHz, CDCl\textsubscript{3}) $\delta$: 9.61, 14.17, 26.08, 26.41, 61.32, 115.24, 129.43, 132.46, 133.11, 135.58, 158.80, 171.27, 196.23; ESI-MS ($m$/$z$): 521.33 [M + H]$^+$.  

Diethyl-2,2'-((4,4'-(1\textsuperscript{E},1'\textsuperscript{E})-(2-oxocyclopentane-1,3-diylidene)-bis-(methan-1-yl-1-ylidene)-bis(2-methoxy-4,1-phenylene))bis(oxy)diacetate (73): Yield 74\% (yellow solid); mp 140-141 °C; IR (film, cm\textsuperscript{-1}): 2922, 2851, 1752 (C=O), 1597, 1510, 1277 (C–O–C), 1215,
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1144, 1072, 1032 (C–O–C); $^1$H NMR (400 MHz, CDCl$_3$) δ: 1.29 (t, $J = 7.3$ Hz, 6H, 2COOCH$_2$CH$_3$), 3.10 (s, 4H, $CH_2CH_2$), 3.94 (s, 6H, 2OCH$_3$), 4.27 (q, $J = 7.3$ Hz, 4H, 2COOCH$_2$CH$_3$), 4.74 (s, 4H), 6.85 (d, $J = 8.0$ Hz, 2H, ArH), 7.15 (d, $J = 2.2$ Hz, 2H, ArH), 7.18 (d, $J = 8.8$ Hz, 2H, ArH), 7.53 (s, 2H, 2CH=C); ESI-MS (m/z): 525.33 [M + H]$^+$.

Diethyl-2,2'-(4,4'-(1$E$,1'-$E$)-(2-oxocyclopentane-1,3-diylidene)-bis(methan-1-yl-1-ylidene)bis(2-methoxy-4,1-phenylene))bis(oxy)dipropanoate (74): Yield 70% (yellow solid); mp 107-108 °C; IR (film, cm$^{-1}$): 2923, 2852, 1751 (C=O), 1598, 1508, 1273 (C–O–C), 1242, 1143, 1095, 1033 (C–O–C); $^1$H NMR (400 MHz, CDCl$_3$) δ: 1.26 (t, $J = 7.3$ Hz, 6H, 2COOCH$_2$CH$_3$), 1.68 (d, $J = 6.6$ Hz, 6H, 2CHCH$_3$), 3.10 (s, 4H, $CH_2CH_2$), 3.92 (s, 6H, 2OCH$_3$), 4.21-4.23 (m, 4H), 4.82 (q, $J = 6.6$ Hz, 2H, 2OCH$_3$), 6.86 (d, $J = 8.0$ Hz, 2H, ArH), 7.14-7.17 (m, 4H, ArH), 7.52 (s, 2H, 2CH=C); ESI-MS (m/z): 553.34 [M + H]$^+$.

Diethyl-2,2'-(4,4'-(1$E$,1'-$E$)-(2-oxocyclopentane-1,3-diylidene)bis(methan-1-yl-1-ylidene)bis(2-methoxy-4,1-phenylene))bis(oxy) dibutanoate (75): Yield 62% (yellow solid); IR (film, cm$^{-1}$): 2976, 2936, 1751 (C=O), 1618, 1595, 1510, 1273, 1241 (C–O–C), 1143, 1027 (C–O–C); $^1$H NMR (400 MHz, CDCl$_3$) δ: 1.09-1.13 (m, 6H), 1.23-1.27 (m, 6H), 2.03-2.09 (m, 4H), 3.09 (s, 4H), 3.91 (s, 6H, 2OCH$_3$), 4.20-4.26 (m, 4H), 4.62 (t, $J = 6.6$ Hz, 2H, 2OCH$_3$), 6.87 (d, $J = 6.6$ Hz, 2H, ArH), 7.14-7.17 (m, 4H, ArH), 7.52 (s, 2H, 2CH=C); ESI-MS (m/z): 581.37 [M + H]$^+$.

Diethyl-2,2'-(4,4'-(1$E$,1'-$E$)-(2-oxocyclopentane-1,3-diylidene)bis(methan-1-yl-1-ylidene)bis(2-methoxy-4,1-phenylene))bis(oxy) dipentanoate (76): Yield 60% (yellow solid); mp 80-81 °C; IR (film, cm$^{-1}$): 2960, 2925, 2852, 1752 (OC=O), 1735, 1618, 1595, 1509, 1274, 1241 (C–O–C), 1143, 1030 (C–O–C); $^1$H NMR (400 MHz, CDCl$_3$) δ: 0.99 (t, $J = 7.3$ Hz, 6H, 2CH$_2$CH$_2$CH$_3$), 1.25 (t, $J = 6.6$ Hz, 6H, 2COOCH$_2$CH$_3$), 1.52-1.63 (m, 4H),
1.93-2.04 (m, 4H), 3.09 (s, 4H, \(\text{CH}_2\text{CH}_2\)), 3.91 (s, 6H, 2O\(\text{CH}_3\)), 4.19-4.25 (m, 4H), 4.67 (t, \(J = 5.1\) Hz, 2H, 2O\(\text{CH}\)), 6.86 (d, \(J = 8.0\) Hz, 2H, Ar\(\text{H}\)), 7.14-7.17 (m, 4H, 4H, Ar\(\text{H}\)), 7.52 (s, 2H, 2CH=C); ESI-MS (m/z): 609.32 [M + H]$^+$. 

**Diethyl-2,2'-(4,4'-(1E,1'\(E\))-(2-oxocyclohexane-1,3-diylidene)bis(methan-1-yl-1-ylidene)bis(4,1-phenylene))bis(oxy)diacetate (77):** Yield 72% (yellow solid); mp 127-128 °C; IR (film, cm$^{-1}$): 2984, 2936, 2872, 1759 (OC=O), 1657, 1599, 1558, 1510, 1296, 1278, 1212 (C–O–C), 1164, 1080 (C–O–C); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 1.28-1.32 (m, 6H, 2COO\(\text{CH}_2\text{CH}_3\)), 1.79 (pentet, \(J = 5.9\) Hz, 2H), 2.89-2.92 (m, 4H), 4.29 (q, \(J = 7.3\) Hz, 4H, 2COO\(\text{CH}_2\text{CH}_3\)), 4.65 (s, 4H, 2O\(\text{CH}_2\)), 6.92-6.95 (m, 4H, Ar\(\text{H}\)), 7.44 (d, \(J = 8.8\) Hz, 4H, Ar\(\text{H}\)), 7.74 (s, 2H, 2CH=C); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 14.13, 22.95, 28.44, 61.47, 65.29, 114.53, 129.70, 132.16, 134.75, 136.25, 158.01, 168.59, 190.15; ESI-MS (m/z): 479.28 [M + H]$^+$. 

**Diethyl-2,2'-(4,4'-(1E,1'\(E\))-(2-oxocyclohexane-1,3-diylidene)bis(methan-1-yl-1-ylidene)bis(4,1-phenylene))bis(oxy)dipropanoate (78):** Yield 62% (yellow solid); mp 95-97 °C; IR (film, cm$^{-1}$): 2985, 2935, 2871, 1751 (OC=O), 1664, 1601, 1569, 1508, 1274, 1248 (C–O–C), 1199, 1161, 1134, 1098, 1051 (C–O–C); $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$: 1.17 (t, \(J = 7.3\) Hz, 6H, 2COO\(\text{CH}_2\text{CH}_3\)), 1.52 (d, \(J = 6.6\) Hz, 6H, 2CH\(\text{CH}_3\)), 1.69-1.72 (m, 2H), 2.84-2.87 (m, 4H), 4.14 (q, \(J = 7.3\) Hz, 4H, 2COO\(\text{CH}_2\text{CH}_3\)), 5.03 (q, \(J = 7.3\) Hz, 2H, 2O\(\text{CH}\)), 6.94 (d, \(J = 8.8\) Hz, 4H, Ar\(\text{H}\)), 7.49 (d, \(J = 8.8\) Hz, 4H, Ar\(\text{H}\)), 7.56 (s, 2H, C=CH\(\text{H}\)); $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$: 13.97, 18.16, 22.42, 27.87, 60.87, 71.57, 114.90, 128.52, 132.19, 134.50, 135.23, 157.64, 171.23, 188.59; ESI-MS (m/z): 507.32 [M + H]$^+$. 

**Diethyl-2,2'-(4,4'-(1E,1'\(E\))-(2-oxocyclohexane-1,3-diylidene)bis(methan-1-yl-1-ylidene)bis(4,1-phenylene))bis(oxy)dbutanoate (79):** Yield 67% (yellow solid); mp 101-102 °C; IR (film, cm$^{-1}$): 2988, 2937, 1732 (OC=O), 1601, 1505, 1278, 1246 (C–O–C), 1137,
1023 (C–O–C); $^1$H NMR (400 MHz, CDCl$_3$) δ: 1.10 (t, $J = 7.3$ Hz, 6H, 2CH$_2$CH$_3$), 1.24 (t, $J = 7.3$ Hz, 6H, 2COOCH$_2$CH$_3$), 1.79 (pentet, $J = 5.9$ Hz, 2H), 2.0 (pentet, $J = 7.3$ Hz, 4H, 2CHCH$_2$CH$_3$), 2.90 (t, $J = 5.1$ Hz, 4H), 4.23 (q, $J = 6.6$ Hz, 4H, 2COOCH$_2$CH$_3$), 4.58 (t, $J = 6.6$ Hz, 2H, 2OCH), 6.90 (d, $J = 8.8$ Hz, 4H, ArH), 7.42 (d, $J = 8.8$ Hz, 4H, ArH), 7.73 (s, 2H, C=CH); ESI-MS (m/z): 535.38 [M + H]$^+$.  

Diethyl-2,2'-(4,4'-(1$^E$,1'$^E$)-(2-oxocyclohexane-1,3-diylidene)bis(methan-1-yl-1-ylidene)bis(4,1-phenylene))bis(oxy)dipentanoate (80): Yield 64% (yellow viscous oil); IR (film, cm$^{-1}$): 2961, 2933, 2873, 1752 (OC=O), 1735, 1601, 1508, 1246 (C–O–C), 1185, 1160, 1136, 1112, 1025 (C–O–C); $^1$H NMR (400 MHz, CDCl$_3$) δ: 0.99 (t, $J = 7.3$ Hz, 6H, 2CH$_2$CH$_3$), 1.25 (t, $J = 6.6$ Hz, 6H, 2COOCH$_2$CH$_3$), 1.47-1.55 (m, 4H), 1.79 (pentet, $J = 5.9$ Hz, 2H, 2CHCH$_2$CH$_2$CH$_3$), 1.90-1.98 (m, 4H), 2.88 (t, $J = 5.9$ Hz, 4H), 4.27 (q, $J = 6.6$ Hz, 4H, 2COOCH$_2$CH$_3$), 4.62-4.65 (m, 2H), 6.89 (d, $J = 8.8$ Hz, 4H, ArH), 7.42 (d, $J = 8.8$ Hz, 4H, ArH), 7.73 (s, 2H, 2CH=CH); ESI-MS (m/z): 563.40 [M + H]$^+$.  

Diethyl-2,2'-(4,4'-(1$^E$,1'$^E$)-(2-oxocyclohexane-1,3-diylidene)bis(methan-1-yl-1-ylidene)bis(2-methoxy-4,1-phenylene))bis(oxy)diacetate (81): Yield 79% (yellow solid); IR (film, cm$^{-1}$): 3478, 2962, 2873, 1754 (OC=O), 1735, 1601, 1508, 1246 (C–O–C), 1185, 1160, 1136, 1112, 1025 (C–O–C); $^1$H NMR (400 MHz, CDCl$_3$) δ: 1.32 (t, $J = 7.3$ Hz, 6H, 2COOCH$_2$CH$_3$), 1.81 (pentet, $J = 5.9$ Hz, 2H), 2.93 (t, $J = 5.1$ Hz, 4H), 3.91 (s, 6H, 2OCH$_3$), 4.27 (q, $J = 7.3$ Hz, 4H, 2COOCH$_2$CH$_3$), 4.72 (s, 4H, OCH$_2$), 6.82 (d, $J = 8.0$ Hz, 2H, ArH), 7.03-7.06 (m, 4H, ArH), 7.73 (s, 2H, 2CH=CH); $^{13}$C NMR (100 MHz, CDCl$_3$) δ: 14.14, 22.94, 28.44, 55.98, 61.41, 66.22, 113.42, 114.42, 123.47, 130.37, 134.94, 136.58, 147.71, 149.14, 168.65, 189.99; ESI-MS (m/z): 539.34 [M + H]$^+$.  

Diethyl-2,2'-(4,4'-(1$^E$,1'$^E$)-(2-oxocyclohexane-1,3-diylidene)bis(methan-1-yl-1-ylidene)bis(2-methoxy-4,1-phenylene))bis(oxy)dipropanoate (82): Yield 75% (yellow solid); IR (film, cm$^{-1}$): 2922, 2851, 1735 (OC=O), 1508, 1247 (C–O–C), 1194, 1141, 1094, 1033
Diethyl-2,2'-(4,4'-(1E,1'E)-(2-oxocyclohexane-1,3-diylidene)bis(methan-1-yl-1-ylidene)bis(2-methoxy-4,1-phenylene))bis(oxy)diacetate (85): Yield 82% (yellow solid); mp 123-124 °C; IR (film, cm⁻¹): 2961, 2924, 1757 (OC=O), 1601, 1570, 1508, 1240 (C–O–C), 1201, 1177, 1148, 1081, 1029 (C–O–C); ¹H NMR (400 MHz, CDCl₃) δ:
Diethyl-2,2′-(4,4′-(1E,1′E)-(5-ethyl-2-oxocyclohexane-1,3-diylidene)bis(methan-1-yl-1-ylidene)bis(4,1-phenylene))bis(oxy)dipropanoate (86): Yield 79% (yellow viscous oil);
IR (film, cm⁻¹): 2961, 2925, 2874, 1751 (OC=O), 1601, 1508, 1294, 1247 (C–O–C), 1195, 1177; ¹H NMR (400 MHz, CDCl₃) δ: 0.89 (t, J = 7.3 Hz, 3H, CH₂CH₃), 1.26 (t, J = 7.3 Hz, 6H, 2COOCH₂CH₃), 1.42 (pentet, J = 7.3 Hz, 2H, CH–CH₂CH₃), 1.64 (d, J = 6.6 Hz, 2H, 2OCH₂CH₃), 1.63-1.65 (m, 1H, CH), 2.44-2.51 (m, 2H), 3.05-3.08 (m, 2H), 4.20-4.26 (m, 4H, 2COOCH₂CH₃), 4.79 (q, J = 6.6 Hz, 2OCH₂CH₃), 6.90 (d, J = 8 Hz, 4H, ArH), 7.41-7.43 (d, J = 8.8 Hz, 4H, ArH), 7.73 (s, 2H, 2CH=CH); ESI-MS (m/z): 535.38 [M + H]^+.

Diethyl-2,2′-(4,4′-(1E,1′E)-(5-ethyl-2-oxocyclohexane-1,3-diylidene)bis(methan-1-yl-1-ylidene)bis(4,1-phenylene))bis(oxy) dibutanoate (87): Yield 76% (yellow viscous oil);
IR (film, cm⁻¹): 2972, 2935, 2368, 1752 (OC=O), 1734, 1601, 1508, 1293, 1245 (C–O–C), 1177, 1136, 1057, 1023 (C–O–C); ¹H NMR (400 MHz, CDCl₃) δ: 0.89 (t, J = 7.3 Hz, 3H, CH₂CH₃), 1.09 (t, J = 7.3 Hz, 6H, 2CHCH₂CH₃), 1.25 (t, J = 7.3 Hz, 6H, 2COOCH₂CH₃), 1.42 (pentet, J = 7.3 Hz, 2H, CH–CH₂CH₃), 1.61 (brs, 1H), 2.01 (pentet, J = 7.3 Hz, 4H), 2.47 (t, J = 13.5 Hz, 2H), 3.07 (dd, J = 15.4 Hz, 3.7 Hz, 2H), 4.20-4.26 (m, 4H), 4.59 (t, J = 5.6 Hz, 2H, 2OCH), 6.91 (d, J = 8.8 Hz, 4H, ArH), 7.42 (d, J = 8.8 Hz, 4H, ArH), 7.73 (s, 2H, 2CH=C); ESI-MS (m/z): 563.35 [M + H]^+.

Diethyl-2,2′-(4,4′-(1E,1′E)-(5-ethyl-2-oxocyclohexane-1,3-diylidene)bis(methan-1-yl-1-ylidene)bis(4,1-phenylene))bis(oxy)dipentanoate (88): Yield 72% (yellow viscous oil);
IR (film, cm$^{-1}$): 2925, 2365, 1750 (OC=O), 1601, 1507, 1244 (C–O), 1178, 1144, 1026 (C–O–C); $^1$H NMR (400 MHz, CDCl$_3$) δ: 0.89 (t, $J = 7.3$ Hz, 3H, CH$_2$CH$_3$), 0.98 (t, $J = 7.3$ Hz, 6H, 2CH$_2$CH$_3$), 1.25 (t, $J = 7.3$ Hz, 6H, 2COOCH$_2$CH$_3$), 1.42 (pentet, $J = 7.3$ Hz, 2H, CH-CH$_2$CH$_3$), 1.51-1.57 (m, 5H), 1.90-1.96 (m, 4H), 2.47 (t, $J = 13.2$ Hz, 2H), 2.40-2.45 (m, 4H), 4.65 (t, $J = 7.3$ Hz, 2H, 2OCH), 6.90 (d, $J = 8.8$ Hz, 4H, ArH), 7.42 (d, $J = 8.8$ Hz, 4H, ArH), 7.73 (s, 2H, 2CH=C); ESI-MS (m/z): 591.15 [M + H]$^+$. 

Diethyl-2,2'-(4,4'-(1E,1'E)-(5-ethyl-2-oxocyclohexane-1,3-diylidene)bis(methan-1-yl-1-ylidene)bis(2-methoxy-4,1-phenylene))bis(oxy)diacetate (89): Yield 78% (yellow solid); mp 121-122 °C; IR (film, cm$^{-1}$): 2960, 2934, 1758 (OC=O), 1663, 1598, 1512, 1261 (C–O–C), 1216, 1143, 1033 (C–O–C); $^1$H NMR (400 MHz, CDCl$_3$) δ: 0.90 (t, $J = 7.3$ Hz, 3H, CH-CH$_2$CH$_3$), 1.29 (t, $J = 7.3$ Hz, 6H, 2COOCH$_2$CH$_3$), 1.43 (pentet, $J = 7.3$ Hz, 2H, CH-CH$_2$CH$_3$), 1.63-1.68 (m, 1H, CH), 2.45-2.53 (m, 2H), 3.11 (dd, $J = 16.1$, 3.7 Hz, 2H), 3.91 (s, 6H, 2OCH$_3$), 4.27 (q, $J = 7.3$ Hz, 4H, 2COOCH$_2$CH$_3$), 4.73 (s, 4H, 2OCH$_2$), 6.83 (d, $J = 8$ Hz, 2H, ArH), 7.04-7.07 (m, 4H, ArH), 7.73 (s, 2H, 2CH=C); ESI-MS (m/z): 567.37 [M + H]$^+$. 

Diethyl-2,2'-(4,4'-(1E,1'E)-(5-ethyl-2-oxocyclohexane-1,3-diylidene)bis(methan-1-yl-1-ylidene)bis(2-methoxy-4,1-phenylene))bis(oxy)dipropanoate (90): Yield 64% (yellow viscous oil); IR (film, cm$^{-1}$): 2917, 2849, 1751 (OC=O), 1589, 1508, 1262 (C–O–C), 1143, 1096, 1035 (C–O–C); $^1$H NMR (400 MHz, CDCl$_3$) δ: 0.90 (t, $J = 7.3$ Hz, 3H, CH-CH$_2$CH$_3$), 1.25 (t, $J = 8.0$ Hz, 6H, 2COOCH$_2$CH$_3$), 1.44 (pentet, $J = 7.3$ Hz, 2H, CH-CH$_2$CH$_3$), 1.51-1.53 (m, 1H, CH), 1.68 (d, $J = 6.6$ Hz, 6H, 2CH$_2$CH$_3$), 2.44-2.51 (m, 2H), 3.08-3.11 (m, 2H), 3.89 (s, 6H, 2OCH$_3$), 4.19-4.26 (m, 4H), 4.80 (q, $J = 6.6$ Hz, 2H, 2CH$_2$CH$_3$), 6.84 (d, $J = 8.8$ Hz, 2H, ArH), 7.02-7.04 (m, 4H, ArH), 7.72 (s, 2H, 2CH=C); ESI-MS (m/z): 595.39 [M + H]$^+$. 

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Diethyl-2,2′-(4,4′-(1E,1′E)-(5-ethyl-2-oxocyclohexane-1,3-diylidene)bis(methan-1-yl-1-ylidene)bis(2-methoxy-4,1-phenylene)bis(oxy)dibutanoate (91): Yield 77% (yellow viscous oil); IR (film, cm\(^{-1}\)): 2968, 2936, 2878, 1752 (OC=O), 1735, 1598, 1509, 1465, 1263 (C–O–C), 1193, 1142, 1028 (C–O–C); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 0.90 (t, \(J = 7.3\) Hz, 3H, CH-CH\(_2\)CH\(_3\)), 1.15 (t, \(J = 7.3\) Hz, 6H, 2CH\(_2\)CH\(_3\)), 1.25 (t, \(J = 7.3\) Hz, 6H, 2COOCH\(_2\)CH\(_3\)), 1.43 (pentet, \(J = 7.3\) Hz, 2H, CH-CH\(_2\)CH\(_3\)), 1.64 (brs, 1H, CH), 2.04 (pentet, \(J = 7.3\) Hz, 4H, 2CH\(_2\)CH\(_3\)), 2.45-2.51 (m, 2H), 3.10 (dd, \(J = 16.1\) Hz, 2.9 Hz, 2H), 3.88 (s, 6H, 2OCH\(_3\)), 4.18-4.26 (m, 4H), 4.60 (t, \(J = 6.6\) Hz, 2H, 2OCHCH\(_2\)), 6.84 (d, \(J = 8.8\) Hz, 2H, ArH), 7.02-7.04 (m, 4H, ArH), 7.72 (s, 2H, CH=C); ESI-MS (m/z): 623.34 \([M + H]^+\).

Diethyl-2,2′-(4,4′-(1E,1′E)-(5-ethyl-2-oxocyclohexane-1,3-diylidene)bis(methan-1-yl-1-ylidene)bis(2-methoxy-4,1-phenylene)bis(oxy)dipentanoate (92): Yield 87% (yellow viscous oil); IR (film, cm\(^{-1}\)): 2961, 2874, 1752 (OC=O), 1598, 1508, 1262 (C–O–C), 1235, 1190, 1142, 1031 (C–O–C); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 0.90 (t, \(J = 7.3\) Hz, 3H, CH-CH\(_2\)CH\(_3\)), 0.99 (t, \(J = 7.3\) Hz, 6H, 2CH\(_2\)CH\(_2\)CH\(_3\)), 1.25 (t, \(J = 7.3\) Hz, 6H), 1.43 (pentet, \(J = 7.3\) Hz, 2H, CH-CH\(_2\)CH\(_3\)), 1.52-1.65 (m, 5H), 1.89-2.06 (m, 4H), 2.44-2.51 (m, 2H), 3.10 (dd, \(J = 16.1\) Hz, 2.9 Hz, 2H), 3.88 (s, 6H, 2OCH\(_3\)), 4.18-4.25 (m, 4H), 4.64-4.67 (m, 2H, 2CH), 6.84 (d, \(J = 8.8\) Hz, 2H, ArH), 7.02-7.04 (m, 4H, ArH), 7.72 (s, 2H, CH=C); ESI-MS (m/z): 651.45 \([M + H]^+\).

Diethyl-2,2′-(4,4′-(1E,1′E)-(5-tert-butyl-2-oxocyclohexane-1,3-diylidene)bis(methan-1-yl-1-ylidene)bis(4,1-phenylene)bis(oxy)diacetate (93): Yield 87% (yellow solid); mp 138-140 °C; IR (film, cm\(^{-1}\)): 2961, 2869, 1758 (OC=O), 1602, 1508, 1201, 1175, 1081; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 0.96 (s, 9H, C(CH\(_3\))\(_3\)), 1.30 (t, \(J = 7.3\) Hz, 6H, 2COOCH\(_2\)CH\(_3\)), 1.44-1.50 (m, 1H, CH), 2.42 (t, \(J = 13.2\) Hz, 2H), 3.13 (d, \(J = 13.2\) Hz, 2H), 4.28 (q, \(J = 7.3\) Hz, 4H, 2COOCH\(_2\)CH\(_3\)), 4.66 (s, 4H, 2OCH\(_2\)), 6.95 (d, \(J = 8.8\) Hz,
Diethyl-2,2’-(4,4’-(1E,1’E)-(5-tert-butyl-2-oxocyclohexane-1,3-diylidene)bis(methan-1-yl-1-ylidene)bis(4,1-phenylene)bis(oxy))dipropionate (94): Yield 65% (yellow viscous oil); IR (film, cm⁻¹): 2962, 2871, 1751 (OC=O), 1601, 1508, 1248 (C–O–C), 1175, 1133, 1097, 1051 (C–O–C); ¹H NMR (400 MHz, CDCl₃) δ: 0.95 (s, 9H, C(CH₃)₃), 1.25 (t, J = 8 Hz, 6H, 2COOCH₂CH₃, 1.64 (d, J = 6.6 Hz, 6H, 2CHCH₂), 2.38-2.44 (m, 2H), 3.12 (d, J = 13.2 Hz, 2H), 4.20-4.27 (m, 4H), 4.79 (q, J = 6.6 Hz, 2H, 2OCHCH₂), 6.91 (d, J = 8 Hz, 4H, ArH), 7.42 (d, J = 8 Hz, 4H, ArH), 7.70 (s, 2H, C=CH); ESI-MS (m/z): 535.34 [M + H]⁺.

Diethyl-2,2’-(4,4’-(1E,1’E)-(5-tert-butyl-2-oxocyclohexane-1,3-diylidene)bis(methan-1-yl-1-ylidene)bis(4,1-phenylene)bis(oxy))dibutanoate (95): Yield 64% (yellow viscous oil); IR (film, cm⁻¹): 2966, 1752 (OC=O), 1735, 1602, 1246 (C–O–C), 1175, 1132, 1109, 1057 (C–O–C); ¹H NMR (400 MHz, CDCl₃) δ: 0.96 (s, 9H, C(CH₃)₃), 1.09 (t, J = 7.3 Hz, 6H, 2CH₂CH₃), 1.25 (t, J = 7.3 Hz, 6H, 2COOCH₂CH₂), 1.42-1.46 (m, 1H, CH), 2.01 (pentet, J = 7.3 Hz, 4H, 2CH₂CH₃), 2.38-2.45 (m, 2H), 3.11-3.14 (m, 2H), 4.20-4.26 (m, 4H, 2COOCH₂CH₂), 4.60 (t, J = 5.9 Hz, 2H, OCH), 6.91 (d, J = 8 Hz, 4H, ArH), 7.42 (d, J = 8.8 Hz, 4H, ArH), 7.70 (s, 2H, C=CH); ESI-MS (m/z): 591.32 [M + H]⁺.

Diethyl-2,2’-(4,4’-(1E,1’E)-(5-tert-butyl-2-oxocyclohexane-1,3-diylidene)bis(methan-1-yl-1-ylidene)bis(4,1-phenylene)bis(oxy))dipentanoate (96): Yield 63% (yellow viscous oil); IR (film, cm⁻¹): 2962, 2874, 1755 (OC=O), 1734, 1602, 1507, 1247 (C–O–C), 1175, 1136, 1024 (C–O–C); ¹H NMR (400 MHz, CDCl₃) δ: 0.93 (s, 9H, C(CH₃)₃), 0.98 (t, J = 7.3 Hz, 6H, 2CH₂CH₂CH₃), 1.23-1.26 (m, 6H, 2COOCH₂CH₂), 1.43-1.46 (m, 1H, CH), 1.53-1.62 (m, 4H), 1.87-1.99 (m, 4H, 2CH₂CH₂CH₃), 2.38-2.45 (m, 2H), 3.10-3.14 (m, 2H), 4.19-4.26 (m, 4H, 2COOCH₂), 4.63-4.66 (m, 2H, 2OCH), 6.90 (d, J = 8 Hz, 4H,
ArH), 7.42 (d, J = 8.8 Hz, 4H, ArH), 7.70 (s, 2H, C=CH); ESI-MS (m/z): 619.44 [M + H]+.

**Diethyl-2,2′-(4,4′-(1E,1′E)-(5-tert-butyl-2-oxocyclohexane-1,3-diylidene)bis(methan-1-yl-1-ylidene)bis(2-methoxy-4,1-phenylene)bis(oxy))diacetate (97):** Yield 74% (yellow solid); mp 125-126 °C; IR (film, cm−1): 2924, 2851, 1757 (OC=O), 1508, 1271, 1234 (C–O–C), 1202, 1145, 1033 (C–O–C); 1H NMR (400 MHz, CDCl3) δ: 0.97 (s, 9H, C(CH3)3), 1.29 (t, J = 7.3 Hz, 6H, 2COOCH2CH3), 1.49-1.52 (m, 1H, CHC(CH3)3), 2.40-2.47 (m, 2H), 3.18 (dd, J = 15.4, 2.2 Hz, 2H), 3.91 (s, 6H, 2OCH3), 4.27 (q, J = 7.3 Hz, 4H, 2COOCH2CH3), 473 (s, 4H, 2OCH3), 6.84 (d, J = 8.8 Hz, 2H, ArH), 7.05-7.06 (m, 4H, ArH), 7.71 (s, 2H, 2CH=C); ESI-MS (m/z): 595.42 [M + H]+.

**Diethyl-2,2′-(4,4′-(1E,1′E)-(5-tert-butyl-2-oxocyclohexane-1,3-diylidene)bis(methan-1-yl-1-ylidene)bis(2-methoxy-4,1-phenylene)bis(oxy))dipropanoate (98):** Yield 64% (yellow solid); mp 126-128 °C; IR (film, cm−1): 2961, 1751 (OC=O), 1598, 1581, 1510, 1267 (C–O–C), 1244, 1097, 1035 (C–O–C); 1H NMR (400 MHz, CDCl3) δ: 0.96 (s, 9H, C(CH3)3), 1.25 (t, J = 7.3 Hz, 6H, 2COOCH2CH3), 1.49-1.52 (m, 1H, CHC(CH3)3), 2.40-2.47 (m, 2H), 3.18 (dd, J = 15.4, 2.2 Hz, 2H), 3.91 (s, 6H, 2OCH3), 4.27 (q, J = 7.3 Hz, 4H, 2COOCH2CH3), 473 (s, 4H, 2OCH3), 6.84 (d, J = 8.8 Hz, 2H, ArH), 7.05-7.06 (m, 4H, ArH), 7.71 (s, 2H, 2CH=C); ESI-MS (m/z): 623.48 [M + H]+.

**Diethyl-2,2′-(4,4′-(1E,1′E)-(5-tert-butyl-2-oxocyclohexane-1,3-diylidene)bis(methan-1-yl-1-ylidene)bis(2-methoxy-4,1-phenylene)bis(oxy))dibutanoate (99):** Yield 70% (yellow solid); mp 118-119 °C; IR (film, cm−1): 2964, 2878, 1752 (OC=O), 1734, 1597, 1509, 1465, 1269, 1241 (C–O–C), 1193, 1144, 1026 (C–O–C), 1003; 1H NMR (400 MHz, CDCl3) δ: 0.96 (s, 9H, C(CH3)3), 1.11 (t, J = 7.3 Hz, 6H, 2CH2CH3), 1.25 (t, J = 7.3 Hz, 6H, 2COOCH2CH3), 1.48 (t, J = 13.1 Hz, 1H), 2.04 (pentet, J = 7.3 Hz, 4H, 2CHCH2CH3), 2.43 (t, J = 13.9 Hz, 2H), 3.16 (d, J = 13.9 Hz, 2H), 3.88 (s, 6H, 2OCH3), 7.02-7.04 (m, 4H, ArH), 7.70 (s, 2H, 2CH=C); ESI-MS (m/z): 651.50 [M + H]+.
Diethyl-2,2'-((4,4'-(1E,1'E)-(5-tert-butyl-2-oxocyclohexane-1,3-diylidene)bis(methan-1-yl-1-ylidene)bis(2-methoxy-4,1-phenylene)bis(oxy))dipentanoate (100): Yield 60% (yellow solid); IR (film, cm⁻¹): 2961, 2873, 1751 (OC=O), 1590, 1508, 1270, 1240 (C–O–C), 1189, 1143, 1029 (C–O–C); ¹H NMR (400 MHz, CDCl₃) δ: 0.96 (s, 9H, C(CH₃)₃), 0.99 (t, J = 7.3 Hz, 6H, 2COOCH₂CH₃), 1.24 (t, J = 7.3 Hz, 6H, 2COOCH₂CH₃), 1.44-1.49 (m, 1H, CH), 1.54-1.63 (m, 4H, 2CH₂CH₂CH₃), 1.90-2.05 (m, 4H, 2CH₂CH₂CH₃), 2.39-2.46 (m, 2H), 3.15-3.18 (m, 2H), 3.88 (s, 6H, 2OCH₃), 4.19-4.24 (m, 4H, 2COOCH₂CH₃), 4.65-4.68 (m, 2H, 2OCH), 6.84 (d, J = 8.8 Hz, 2H, ArH), 7.0-7.03 (m, 4H, ArH), 7.69 (s, 2H, C=CH); ESI-MS (m/z): 679.53 [M + H]⁺.

Typical procedure for the synthesis of diethyl-4,4'-(4,4'-(1E,1'E)-(2-oxocyclopentane-1,3-diylidene)bis(methan-1-yl-1-ylidene)bis(4,1-phenylene))bis(oxy) dibutanoate (101) and related compounds (102-124): To a vigorously stirred solution of (E)-2-(4-hydroxybenzyl)-5-(4-hydroxybenzylidene)cyclopentanone (61; 200 mg, 0.67 mol) in dry DMF (10 mL), anhydrous K₂CO₃ (281 mg, 1.35 mmol) was added and stirred for 15 min, then ethyl-4-bromobutanoate (265 mg, 1.35 mmol) was added. The reaction mixture was stirred for 10-12 h at 35-40 °C. After completion of reaction, product was extracted with CHCl₃ and crude product was purified by column chromatography. Yield 88% (yellow solid); mp 116-117 °C; IR (film, cm⁻¹): 2962, 2922, 2852, 1738 (OC=O), 1697, 1599, 1509, 1376, 1271, 1257 (C–O–C), 1174, 1020 (C–O–C); ¹H NMR (400 MHz, CDCl₃) δ: 1.26 (t, J = 7.3 Hz, 6H), 2.13 (pentet, J = 7.3 Hz, 4H), 2.53 (t, J = 7.3 Hz, 4H), 3.08 (s, 4H, CH₂CH₂), 4.06 (t, J = 5.9 Hz, 4H, 2OCH₂), 4.15 (q, J = 7.3 Hz, 4H, 2COOCH₂CH₃), 6.94 (d, J = 8.8 Hz, 4H), 7.55 (d, J = 8.8 Hz, 6H); ESI-MS (m/z): 521.38 [M + H]⁺.
**Diethyl-5,5’-(4,4’-(1E,1’E)-(2-oxocyclopentane-1,3-diylidene)bis(methan-1-yl-1-ylidene))bis(4,1-phenylene))bis(oxy)dipentanoate (102):** Yield 83% (yellow solid); mp 148-149 °C; IR (film, cm\(^{-1}\)): 2924, 2852, 1733 (OC=O), 1595, 1510, 1250 (C–O–C), 1161, 1138, 1032 (C–O–C); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 1.26 (t, \(J = 7.3 \text{ Hz}, 6\text{H}, 2\text{COOCH}_2\text{CH}_3\)), 1.84-1.85 (m, 8H), 2.39 (t, \(J = 5.9 \text{ Hz}, 4\text{H}, 2\text{CH}_2\text{CO}\)), 3.08 (s, 4H, \(\text{CH}_2\text{CH}_2\)), 4.01-4.02 (m, 4H, O\(\text{CH}_2\)), 4.13 (q, \(J = 7.3 \text{ Hz}, 4\text{H}, 2\text{COOCH}_2\text{CH}_3\)), 6.94 (d, \(J = 8.8 \text{ Hz}, 4\text{H}, \text{ArH}\)), 7.55 (d, \(J = 8.0 \text{ Hz}, 6\text{H}\)); ESI-MS (\(m/z\)): 549.38 \([\text{M + H}]^+\).

**Diethyl-6,6’-(4,4’-(1E,1’E)-(2-oxocyclopentane-1,3-diylidene)bis(methan-1-yl-1-ylidene))bis(4,1-phenylene))bis(oxy)dihexanoate (103):** Yield 85% (yellow solid); mp 126-128 °C; IR (film, cm\(^{-1}\)): 2923, 1735 (OC=O), 1625, 1601, 1510, 1252 (C–O–C), 1175, 1097, 1037 (C–O–C); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 1.26 (t, \(J = 7.3 \text{ Hz}, 6\text{H}, 2\text{COOCH}_2\text{CH}_3\)), 1.48-1.56 (m, 4H), 1.71 (pentet, \(J = 7.3 \text{ Hz}, 4\text{H}\)), 1.82 (pentet, \(J = 7.3 \text{ Hz}, 4\text{H}\)), 2.34 (t, \(J = 7.3 \text{ Hz}, 4\text{H}, 2\text{CH}_2\text{CO}\)), 3.08 (s, 4H, \(\text{CH}_2\text{CH}_2\)), 4.01 (t, \(J = 6.6 \text{ Hz}, 4\text{H}, \text{OCH}_2\text{CH}_2\)), 4.13 (q, \(J = 7.3 \text{ Hz}, 4\text{H}, 2\text{COOCH}_2\text{CH}_3\)), 6.94 (d, \(J = 8.8 \text{ Hz}, 4\text{H}, \text{ArH}\)), 7.54 (s, 2H, C=CH), 7.55 (d, \(J = 8.8 \text{ Hz}, 2\text{H}, \text{ArH}\)); ESI-MS (\(m/z\)): 577.45 \([\text{M + H}]^+\).

**Diethyl-4,4’-(4,4’-(1E,1’E)-(2-oxocyclopentane-1,3-diylidene)bis(methan-1-yl-1-ylidene))bis(2-methoxy-4,1-phenylene))bis(oxy) dibutanoate (104):** Yield 80% (yellow solid); mp 109-110 °C; IR (film, cm\(^{-1}\)): 2924, 2852, 1732 (OC=O), 1618, 1593, 1514, 1466, 1332, 1273, 1247 (C–O–C), 1182, 1140, 1032 (C–O–C); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 1.26 (t, \(J = 7.3 \text{ Hz}, 6\text{H}, 2\text{COOCH}_2\text{CH}_3\)), 2.18 (pentet, \(J = 6.6 \text{ Hz}, 4\text{H}, 2\text{OCH}_2\text{CH}_2\text{CH}_2\)), 2.54 (t, \(J = 7.3 \text{ Hz}, 4\text{H}, 2\text{COCH}_2\)), 3.11 (s, 4H, \(\text{CH}_2\text{CH}_2\)), 3.91 (s, 6H, \(2\text{OCH}_3\)), 4.11-4.17 (m, 8H), 6.95 (d, \(J = 8.0 \text{ Hz}, 2\text{H}, \text{ArH}\)), 7.13 (d, \(J = 2.2 \text{ Hz}, 2\text{H}, \text{ArH}\)), 7.21 (dd, \(J = 6.6, 2.2 \text{ Hz}, 2\text{H}, \text{ArH}\)), 7.54 (s 2H, 2\(\text{CH}=\text{C}\)); ESI-MS (\(m/z\)): 581.34 \([\text{M + H}]^+\).
Diethyl-5,5'-(4,4'-(1E,1'\)E)\((2\)-oxocyclopentane-1,3-diylidene)bis(methan-1-yl-1-ylidene)bis(2-methoxy-4,1-phenylene))bis(oxy)dipentanoate (105): Yield 60% (yellow solid); mp 143-145 °C; IR (film, cm⁻¹): 2924, 1734 (OC=O), 1591, 1509, 1272, 1245 (C–O–C), 1217, 1161, 1139, 1033 (C–O–C); ¹H NMR (400 MHz, CDCl₃) δ: 1.26 (t, J = 7.3 Hz, 6H, 2COOCH₂CH₃), 1.81-1.87 (m, 4H), 1.89-1.93 (m, 4H), 2.40 (t, J = 7.3 Hz, 4H, 2COCH₂), 3.11 (s, 4H), 3.91 (s, 6H, 2OCH₃), 4.09 (t, J = 6.6 Hz, 4H, 2OCH₂), 4.14 (t, J = 7.3 Hz, 4H, 2COOCH₂CH₃), 6.92 (d, J = 8.8 Hz, 2H, ArH), 7.13 (d, J = 2.2 Hz, 2H, ArH), 7.21 (dd, J = 8.0, 2.2 Hz, 2H, ArH), 7.54 (s, 2H, 2CH=C); ESI-MS (m/z): 609.44 [M + H]^+.

Diethyl-6,6'-(4,4'-(1E,1'\)E)\((2\)-oxocyclopentane-1,3-diylidene)bis(methan-1-yl-1-ylidene)bis(2-methoxy-4,1-phenylene))bis(oxy)dihexanoate (106): Yield 65% (yellow solid); mp 98-99 °C; IR (film, cm⁻¹): 2924, 2852, 1734 (OC=O), 1594, 1509, 1272, 1245 (C–O–C), 1217, 1139, 1032 (C–O–C); ¹H NMR (400 MHz, CDCl₃) δ: 1.25 (t, J = 7.3 Hz, 6H, 2COOCH₂CH₃), 1.50-1.55 (m, 4H), 1.71 (pentet, J = 7.3 Hz, 4H), 1.89 (pentet, J = 6.6 Hz, 4H, 2COCH₂), 3.11 (s, 4H, CH₂CH₂), 3.91 (s, 6H, 2OCH₃), 4.08 (t, J = 6.6 Hz, 4H, 2OCH₂), 4.14 (q, J = 7.3 Hz, 4H, 2COOCH₂CH₃), 6.92 (d, J = 8.8 Hz, 2H, ArH), 7.13 (d, J = 2.2 Hz, 2H, ArH), 7.21 (dd, J = 8.8, 2.2 Hz, 2H, ArH), 7.54 (s, 2H, 2CH=C); ESI-MS (m/z): 637.51 [M + H]^+.

Diethyl-4,4'-(4,4'-(1E,1'\)E)\((2\)-oxocyclohexane-1,3-diylidene)bis(methan-1-yl-1-ylidene)bis(4,1-phenylene))bis(oxy)diglutinoate (107): Yield 63% (yellow solid); mp 108-109 °C; IR (film, cm⁻¹): 2948, 2929, 2872, 1728 (OC=O), 1662, 1601, 1509, 1473, 1296, 1254 (C–O–C), 1177, 1165, 1049 (C–O–C); ¹H NMR (400 MHz, CDCl₃) δ: 1.26 (t, J = 6.6 Hz, 6H, 2COOCH₂CH₃), 1.80 (pentet, J = 5.9 Hz, 2H), 2.13 (pentet, J = 7.3 Hz, 4H), 2.52 (t, J = 7.3 Hz, 4H, COCH₂), 2.91 (t, J = 5.9 Hz, 4H), 4.04 (t, J = 5.9 Hz, 4H, 2OCH₂), 4.15
Diethyl-5,5’-(4,4’-(1E,1’E)-(2-oxocyclohexane-1,3-diyldiene)bis(methan-1-yl-1-ylidene)
bis(4,1-phenylene))bis(oxy)dipentanoate (108): Yield 80% (yellow solid); IR (film, cm\(^{-1}\)):
2946, 2875, 1737 (OC=O), 1667, 1604, 1510, 1261 (C–O–C), 1163, 1057 (C–O–C),
1010; \(^1\)H NMR (400 MHz, CDCl\(_3\) \(\delta\)): 1.26 (t, \(J = 7.3\) Hz, 6H, 2OCH\(_2\)CH\(_3\)), 1.79-1.80 (m, 2H), 1.82-1.84 (m, 8H), 2.39 (t, \(J = 7.3\) Hz, 4H), 2.91 (t, \(J = 5.9\) Hz, 4H), 4.01 (t, \(J = 5.9\) Hz, 4H, 2OCH\(_2\)), 2.92 (t, \(J = 5.9\) Hz, 4H), 2.34 (t, \(J = 6.6\) Hz, 4H), 2.54 (t, \(J = 6.6\) Hz, 4H, 2OCH\(_2\)), 3.88 (s, 6H, 2OCH\(_3\)), 4.10 (t, \(J = 6.6\) Hz, 4H, 2OCH\(_2\)), 4.13 (q, \(J = 7.3\) Hz, 4H, 2COOCH\(_2\)CH\(_3\)), 6.91 (d, \(J = 8.8\) Hz, 4H, ArH), 7.43 (d, \(J = 8.8\) Hz, 4H, ArH), 7.75 (s, 2H, 2CH=CH), ESI-MS (m/z): 563.34 [M + H]\(^+\).

Diethyl-6,6’-(4,4’-(1E,1’E)-(2-oxocyclohexane-1,3-diyldiene)bis(methan-1-yl-1-ylidene)
bis(4,1-phenylene))bis(oxy)dihexanoate (109): Yield 82% (yellow solid); mp 89-90 °C; IR (film, cm\(^{-1}\)):
2924, 2866, 1735 (OC=O), 1596, 1578, 1519, 1258 (C–O–C), 1165, 1031
(C–O–C); \(^1\)H NMR (400 MHz, CDCl\(_3\) \(\delta\)): 1.26 (t, \(J = 7.3\) Hz, 6H, 2OCH\(_2\)CH\(_3\)), 1.49-1.55 (m, 4H), 1.71 (pentet, \(J = 7.3\) Hz, 4H), 1.82 (pentet, \(J = 7.3\) Hz, 6H), 2.34 (t, \(J = 7.3\) Hz, 4H), 2.17 (pentet, \(J = 6.6\) Hz, 4H, 2OCH\(_2\)), 4.13 (q, \(J = 7.3\) Hz, 4H, 2COOCH\(_2\)CH\(_3\)), 3.99 (t, \(J = 6.6\) Hz, 4H, 2OCH\(_2\)), 4.10 (t, \(J = 6.6\) Hz, 4H, 2OCH\(_2\)), 4.10 (t, \(J = 6.6\) Hz, 4H, 2OCH\(_2\)), 4.15 (q, \(J = 7.3\) Hz, 4H, 2COOCH\(_2\)CH\(_3\)), 6.91 (d, \(J = 8.8\) Hz, 4H, ArH), 7.43 (d, \(J = 8.8\) Hz, 4H, ArH), 7.75 (s, 2H, 2CH=CH), ESI-MS (m/z): 591.47 [M + H]\(^+\).

Diethyl-4,4’-(4,4’-(1E,1’E)-(2-oxocyclohexane-1,3-diyldiene)bis(methan-1-yl-1-ylidene)
bis(2-methoxy-4,1-phenylene))bis(oxy) dibutanoate (110): Yield 73% (yellow solid); mp 120-121 °C; IR (film, cm\(^{-1}\)):
2940, 1735 (OC=O), 1596, 1578, 1519, 1258 (C–O–C), 1168, 1139, 1031 (C–O–C); \(^1\)H NMR (400 MHz, CDCl\(_3\) \(\delta\)): 1.26 (t, \(J = 7.3\) Hz, 6H, 2COOCH\(_2\)CH\(_3\)), 1.82 (pentet, \(J = 5.9\) Hz, 2H), 2.17 (pentet, \(J = 6.6\) Hz, 4H), 2.54 (t, \(J = 6.6\) Hz, 4H, 2OCH\(_2\)), 3.88 (s, 6H, 2OCH\(_3\)), 4.10 (t, \(J = 6.6\) Hz, 4H, 2OCH\(_2\)), 4.15 (q, \(J = 7.3\) Hz, 4H, 2COOCH\(_2\)CH\(_3\)), 6.91 (d, \(J = 8.0\) Hz, 2H, ArH), 7.75 (s, 2H, 2CH=CH), ESI-MS (m/z): 591.47 [M + H]\(^+\).
7.02 (d, \( J = 1.5 \) Hz, 2H, Ar\( H \)), 7.08 (d, \( J = 8.8 \) Hz, 2H, Ar\( H \)), 7.74 (s, 2H, 2\( CH=\)C); ESI-MS (\( m/z \)): 595.21 [M + H]\(^+\).

**Diethyl-5,5'-(4,4'-\((1E,1'E)-(2\text{-oxocyclohexane-1,3-diyldiene})\)bis(methan-1-yl-1-ylidene)bis(2-methoxy-4,1-phenylene))bis(oxy)dipentanoate (111):** Yield 79% (yellow solid); mp 85-87 °C; IR (film, cm\(^{-1}\)): 2938, 2872, 1734 (OC=O), 1656, 1594, 1577, 1515, 1466, 1416, 1255, 1230 (C–O–C), 1164, 1138, 1033 (C–O–C); \(^1\)H NMR (400 MHz, CDCl\(_3\)) δ: 1.28 (t, \( J = 7.3 \) Hz, 6H, 2COOCH\(_2\)CH\(_3\)), 1.79-1.85 (m, 6H), 1.86-1.94 (m, 4H), 2.39 (t, \( J = 7.3 \) Hz, 4H), 2.94 (t, \( J = 5.9 \) Hz, 4H), 3.89 (s, 6H, 2OCH\(_3\)), 4.07 (t, \( J = 6.6 \) Hz, 4H, 2OCH\(_2\)), 4.13 (q, \( J = 7.3 \) Hz, 4H, 2H, Ar\( H \)), 6.89 (d, \( J = 8.0 \) Hz, 2H, Ar\( H \)), 7.02 (d, \( J = 1.5 \) Hz, 2H, Ar\( H \)), 7.08 (dd, \( J = 8.8, 2 \) Hz, 2H, Ar\( H \)), 7.74 (s, 2H, 2CH=\( C \)); ESI-MS (\( m/z \)): 623.47 [M + H]\(^+\).

**Diethyl-6,6'-(4,4'-\((1E,1'E)-(2\text{-oxocyclohexane-1,3-diyldiene})\)bis(methan-1-yl-1-ylidene)bis(4,1-phenylene))bis(oxy)dihexanoate (112):** Yield 65% (yellow solid); mp 80-81 °C; IR (film, cm\(^{-1}\)): 2938, 2867, 1733 (OC=O), 1686, 1596, 1578, 1513, 1466, 1251 (C–O–C), 1161, 1140, 1034 (C–O–C); \(^1\)H NMR (400 MHz, CDCl\(_3\)) δ: 1.28 (t, \( J = 7.3 \) Hz, 6H, 2COOCH\(_2\)CH\(_3\)), 1.48-1.56 (m, 4H), 1.71 (pentet, \( J = 7.3 \) Hz, 4H), 1.80-1.84 (m, 2H), 1.88 (pentet, \( J = 7.3 \) Hz, 4H), 2.34 (t, \( J = 7.3 \) Hz, 4H, 2COCH\(_3\)), 2.94 (t, \( J = 5.9 \) Hz, 4H), 3.89 (s, 6H, 2OCH\(_3\)), 4.06 (t, \( J = 6.6 \) Hz, 4H, 2OCH\(_2\)), 4.13 (q, \( J = 7.3 \) Hz, 4H, 2COOCH\(_2\)CH\(_3\)), 6.89 (d, \( J = 8.0 \) Hz, 2H, Ar\( H \)), 7.02 (d, \( J = 1.5 \) Hz, 2H, Ar\( H \)), 7.08 (dd, \( J = 8.8, 2 \) Hz, 2H, Ar\( H \)), 7.74 (s, 2H, 2CH=\( C \)); ESI-MS (\( m/z \)): 651.52 [M + H]\(^+\).

**Diethyl-4,4'-(4,4'-\((1E,1'E)-(5\text{-ethyl-2-oxocyclohexane-1,3-diyldiene})\)bis(methan-1-yl-1-ylidene)bis(4,1-phenylene))bis(oxy) dibutanoate (113):** Yield 61% (yellow solid); mp 66-68 °C; IR (film, cm\(^{-1}\)): 2960, 2926, 2874, 1733 (OC=O), 1686, 1600, 1509, 1253
Diethyl-5,5′-(4,4′-(1,1′E,1′E)-5-ethyl-2-oxocyclohexane-1,3-diylidene)bis(methan-1-yl-1-ylidene)bis(4,1-phenylene))bis(oxy)dipentanoate (114): Yield 88% (yellow solid); mp 88-89 °C; IR (film, cm⁻¹): 2921, 2851, 1733 (OC=O), 1599, 1508, 1250 (C–O–C), 1173, 1032 (C–O–C); ¹H NMR (400 MHz, CDCl₃) δ: 0.90 (t, J = 7.3 Hz, 3H, CH₂CH₃), 1.26 (t, J = 7.3 Hz, 6H, 2COOCH₂CH₃), 1.43 (pentet, J = 7.3 Hz, 2H, CH–CH₂CH₃), 1.62-1.67 (m, 1H, CH), 2.13 (pentet, J = 6.6 Hz, 4H), 2.41-2.49 (m, 2H), 2.52 (t, J = 5.9 Hz, 4H, 2COCH₂), 3.09 (dd, J = 15.4, 3.7 Hz, 2H), 4.05 (t, J = 5.9 Hz, 4H, 2OCH₂), 4.15 (q, J = 7.3 Hz, 4H, 2COOCH₂CH₃), 6.92 (d, J = 8.8 Hz, 4H, ArH), 7.44 (d, J = 8.8 Hz, 4H, ArH), 7.75 (s, 2H, 2CH=C); ESI-MS (m/z): 563.38 [M + H]^⁺.

Diethyl-6,6′-(4,4′-(1,1′E,1′E)-5-ethyl-2-oxocyclohexane-1,3-diylidene)bis(methan-1-yl-1-ylidene)bis(4,1-phenylene))bis(oxy)dihexanoate (115): Yield 81% (yellow viscous oil); IR (film, cm⁻¹): 2934, 2871, 1734 (OC=O), 1600, 1509, 1252 (C–O–C), 1174, 1148, 1031 (C–O–C); ¹H NMR (400 MHz, CDCl₃) δ: 0.90 (t, J = 7.3 Hz, 3H, CH₂CH₂CH₃), 1.24-1.28 (m, 6H, 2COOCH₂CH₃), 1.43 (q, J = 7.3 Hz, 2H), 1.50-1.55 (m, 5H), 1.71 (pentet, J = 7.3 Hz, 4H), 1.82 (pentet, J = 7.3 Hz, 4H), 2.32-2.36 (m, 4H), 2.49 (t, J = 13.9 Hz, 2H), 3.09 (d, J = 12.5 Hz, 2H), 4.0 (t, J = 6.6 Hz, 4H, 2OCH₂), 4.10-4.16 (m, 4H), 6.91-6.93 (m, 4H, ArH), 7.44 (d, J = 8.8 Hz, 4H, ArH), 7.75 (s, 2H, 2CH=C); ESI-MS (m/z): 619.51[M + H]^⁺.
Diethyl-4,4’-(4,4’-(1E,1’E)-(5-ethyl-2-oxocyclohexane-1,3-diylidene)bis(methan-1-yl-1-ylidene)bis(2-methoxy-4,1-phenylene))bis(oxy)dibutanoate (116): Yield 81% (yellow solid); mp 87-88 °C; IR (film, cm$^{-1}$): 2934, 1734 (OC=O), 1596, 1511, 1466, 1245 (C–O–C), 1139, 1033 (C–O–C); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 0.91 (t, $J = 7.3$ Hz, 3H, CH-CH$_2$CH$_3$), 1.26 (t, $J = 7.3$ Hz, 6H, COOCH$_2$CH$_3$), 1.44 (pentet, $J = 7.3$ Hz, 2H, CH-CH$_2$CH$_3$), 1.63 (brs, 1H, CH), 2.14-2.21 (m, 4H), 2.47-2.51 (m, 2H), 2.54 (t, $J = 7.3$ Hz, 4H, 2COCH$_2$), 3.12 (dd, $J = 16.1, 2.9$ Hz, 2H), 3.88 (s, 6H, 2OCH$_3$), 4.08-4.17 (m, 8H), 6.92 (d, $J = 8.0$ Hz, 2H, ArH), 7.02 (d, $J = 1.5$ Hz, 2H, ArH), 7.08-7.10 (m, 2H, ArH), 7.74 (s, 2H, CH=C); ESI-MS (m/z): 623.40 [M + H]$^+$.  

Diethyl-5,5’-(4,4’-(1E,1’E)-(5-ethyl-2-oxocyclohexane-1,3-diylidene)bis(methan-1-yl-1-ylidene)bis(2-methoxy-4,1-phenylene))bis(oxy)dipentanoate (117): Yield 75% (yellow solid); mp 87-88 °C; IR (film, cm$^{-1}$): 2925, 2873, 1733 (OC=O), 1596, 1510, 1466, 1260, 1243 (C–O–C), 1163, 1139, 1034 (C–O–C); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 0.91 (t, $J = 7.3$ Hz, 3H, CH-CH$_2$CH$_3$), 1.26 (t, $J = 7.3$ Hz, 6H, 2COOCH$_2$CH$_3$), 1.43 (pentet, $J = 7.3$ Hz, 2H, CH-CH$_2$CH$_3$), 1.53 (s, 1H, CH), 1.81-1.85 (m, 4H), 1.89-1.92 (m, 4H), 2.40 (t, $J = 7.3$ Hz, 4H, 2COCH$_2$), 2.47-2.53 (m, 2H), 3.13 (dd, $J = 16.1, 3.0$ Hz, 2H), 3.89 (s, 6H, 2OCH$_3$), 4.08 (t, $J = 6.6$ Hz, 4H, 2OCH$_2$), 4.13 (q, $J = 7.3$ Hz, 4H, 2COOCH$_2$CH$_3$), 6.90 (d, $J = 8.8$ Hz, 2H, ArH), 7.02 (d, $J = 2.2$ Hz, 2H, ArH), 7.09 (dd, $J = 8.8, 2.2$ Hz, 2H, ArH), 7.74 (s, 2H, 2CH=C); ESI-MS (m/z): 651.46 [M + H]$^+$.  

Diethyl-6,6’-(4,4’-(1E,1’E)-(5-ethyl-2-oxocyclohexane-1,3-diylidene)bis(methan-1-yl-1-ylidene)bis(2-methoxy-4,1-phenylene))bis(oxy)dihexanoate (118): Yield 76% (yellow solid); mp 62-64 °C; IR (film, cm$^{-1}$): 2926, 1734 (OC=O), 1584, 1508, 1243 (C–O–C), 1138, 1033 (C–O–C); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 0.91 (t, $J = 7.3$ Hz, 3H, CH-CH$_2$CH$_3$), 1.28 (t, $J = 7.3$ Hz, 6H, 2COOCH$_2$CH$_3$), 1.44 (pentet, $J = 7.3$ Hz, 2H, CH-CH$_2$CH$_3$), 1.50-1.56 (m, 4H), 1.62-1.65 (m, 1H, CH), 1.71 (pentet, $J = 7.3$ Hz, 4H), 1.88
(pentet, \(J = 7.3\) Hz, 4H), 2.34 (t, \(J = 7.3\) Hz, 4H, 2CO\(CH_2\)), 2.46-2.53 (m, 2H), 3.12 (dd, \(J = 15.4\), 2.9 Hz, 2H), 3.89 (s, 6H, 2O\(CH_3\)), 4.06 (t, \(J = 6.6\) Hz, 4H, 2O\(CH_2\)), 4.13 (q, \(J = 7.3\) Hz, 4H, 2COO\(CH_2CH_3\)), 6.90 (d, \(J = 8.8\) Hz, 2H, Ar\(H\)), 7.02 (d, \(J = 1.5\) Hz, 2H, Ar\(H\), 7.09 (d, \(J = 8.8\) Hz, 2H, Ar\(H\)), 7.74 (s, 2H, \(CH=C\)); ESI-MS (\(m/z\)): 679.45 [M + H]^+.

**Diethyl-4,4'-(1E,1'E)-(5-tert-butyl-2-oxocyclohexane-1,3-diylidene)bis(methan-1-yl-1-ylidene)bis(4,1-phenylene)bis(oxy))dibutanoate (119):** Yield 63% (yellow solid); mp 87-88 °C; IR (film, cm\(^{-1}\)): 2926, 1735 (OC=O), 1601, 1508, 1297, 1253 (C–O–C), 1174, 1051 (C–O–C); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 0.97 (s, 9H, C(CH\(_3\))\(_3\)), 1.26 (t, \(J = 7.3\) Hz, 6H, 2COO\(CH_2CH_3\)), 1.53-1.54 (m, 1H, CH), 2.13 (pentet, \(J = 7.3\) Hz, 4H), 2.43 (t, \(J = 12.5\) Hz, 2H), 2.53 (t, \(J = 7.3\) Hz, 4H), 3.14 (dd, \(J = 12.5\) Hz, 2.9 Hz, 2H), 4.05 (q, \(J = 6.6\) Hz, 4H, 2O\(CH_2\)), 4.15 (q, \(J = 7.3\) Hz, 4H, 2COO\(CH_2CH_3\)), 6.93 (d, \(J = 8.8\) Hz, 4H, Ar\(H\)), 7.43 (d, \(J = 8.8\) Hz, 4H, Ar\(H\)), 7.72 (s, 2H, \(2CH=C\)); ESI-MS (\(m/z\)): 591.42 [M + H]^+.

**Diethyl-5,5'-(1E,1'E)-(5-tert-butyl-2-oxocyclohexane-1,3-diylidene)bis(methan-1-yl-1-ylidene)bis(4,1-phenylene)bis(oxy))dipentanoate (120):** Yield 74% (yellow solid); mp 120-121 °C; IR (film, cm\(^{-1}\)): 2955, 2905, 2870, 1741 (OC=O), 1661, 1596, 1512, 1333, 1254 (C–O–C), 1160, 1117, 1050 (C–O–C); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 0.97 (s, 9H, C(CH\(_3\))\(_3\)), 1.26 (t, \(J = 7.3\) Hz, 6H, 2COO\(CH_2CH_3\)), 1.44-1.52 (m, 1H, CH), 1.82-1.85 (m, 8H, 2\(CH_2CH_2CO\)), 2.39 (t, \(J = 7.3\) Hz, 4H), 2.43-2.46 (m, 2H), 3.15 (d, \(J = 15.4\) Hz, 2H), 3.98-4.02 (m, 4H), 4.13 (q, \(J = 7.3\) Hz, 4H, 2COO\(CH_2CH_3\)), 6.92 (d, \(J = 8.8\) Hz, 4H, Ar\(H\)), 7.44 (d, \(J = 8.8\) Hz, 4H, Ar\(H\)), 7.73 (s, 2H, \(2CH=C\)); ESI-MS (\(m/z\)): 619.42 [M + H]^+.

**Diethyl-6,6'-(1E,1'E)-(5-tert-butyl-2-oxocyclohexane-1,3-diylidene)bis(methan-1-yl-1-ylidene)bis(4,1-phenylene)bis(oxy))dihexanoate (121):** Yield 66% (yellow solid);
mp 79-80 °C; IR (film, cm⁻¹): 2925, 2867, 1735 (OC=O), 1702, 1601, 1508, 1491, 1296, 1252 (C–O–C), 1173, 1158, 1115, 1030 (C–O–C); ¹H NMR (400 MHz, CDCl₃) δ: 0.97 (s, 9H, C(CH₃)₃), 1.25 (t, J = 7.3 Hz, 6H, 2COOCH₂CH₃), 1.47-1.55 (m, 5H), 1.67-1.73 (m, 4H), 1.82 (pentet, J = 7.3 Hz, 4H), 2.34 (t, J = 7.3 Hz, 4H), 2.43 (d, J = 13.1 Hz, 2H), 3.14 (dd, J = 15.4 Hz, 2.2 Hz, 2H), 4.00 (t, J = 6.6 Hz, 4H, 2OCH₂), 4.13 (q, J = 7.3 Hz, 4H, 2COOCH₂CH₃), 6.92 (d, J = 8.8 Hz, 4H, ArH), 7.43 (d, J = 8.8 Hz, 4H, ArH), 7.73 (s, 2H, 2CH=C); ESI-MS (m/z): 647.45 [M + H]⁺.

**Diethyl-4,4'-(4,4'-((1E,1'E)-5-tert-butyl-2-oxocyclohexane-1,3-diylidene)bis(methan-1-yl-1-ylidene)bis(2-methoxy-4,1-phenylene)bis(ox))dibutanoate (122):** Yield 61% (yellow solid); mp 115-116 °C; IR (film, cm⁻¹): 2959, 1733 (OC=O), 1663, 1596, 1512, 1247 (C–O–C), 1162, 1141, 1034 (C–O–C); ¹H NMR (400 MHz, CDCl₃) δ: 0.97 (s, 9H, C(CH₃)₃), 1.26 (t, J = 7.3 Hz, 6H, 2COOCH₂CH₃), 1.48-1.54 (m, 1H, CH), 2.18 (pentet, J = 6.6 Hz, 4H, 2CH₂CH₂CH₂CO), 2.41-2.48 (m, 2H), 2.54 (t, J = 7.3 Hz, 4H, 2OCH₂), 3.19 (dd, J = 15.4 Hz, 2.2 Hz, 2H), 3.89 (s, 6H, 2OCH₃), 4.14-4.17 (m, 8H), 6.93 (d, J = 8.8 Hz, 2H, ArH), 7.03 (d, J = 2.2 Hz, 2H, ArH), 7.09 (dd, J = 8.8 Hz, 2.2 Hz, 2H, ArH), 7.71 (s, 2H, 2CH=C); ESI-MS (m/z): 651.44 [M + H]⁺.

**Diethyl-5,5'-(4,4'-(1E,1'E)-5-tert-butyl-2-oxocyclohexane-1,3-diylidene)bis(methan-1-yl-1-ylidene)bis(2-methoxy-4,1-phenylene)bis(ox))dipentanoate (123):** Yield 69% (yellow solid); IR (film, cm⁻¹): 2956, 2871, 1733 (OC=O), 1596, 1510, 1246 (C–O–C), 1161, 1140, 1034 (C–O–C); ¹H NMR (400 MHz, CDCl₃) δ: 0.97 (s, 9H, C(CH₃)₃), 1.26 (t, J = 7.3 Hz, 6H, 2COOCH₂CH₃), 1.47-1.53 (m, 1H, CH), 1.79-1.85 (m, 4H), 1.86-1.94 (m, 4H), 2.40 (t, J = 7.3 Hz, 4H, 2CH₂CO), 2.45-2.48 (m, 2H), 3.20 (dd, J = 15.4 Hz, 2.9 Hz, 2H), 3.89 (s, 6H, 2OCH₃), 4.08 (t, J = 6.6 Hz, 4H, 2OCH₂), 4.13 (q, J = 7.3 Hz, 4H, 2COOCH₂CH₃), 6.91 (d, J = 8 Hz, 2H, ArH), 7.04 (d, J = 2.2 Hz, 2H, ArH), 7.09 (dd, J = 8.8, 2.2 Hz, 2H, ArH), 7.71 (s, 2H, 2CH=C); ESI-MS (m/z): 679.49 [M + H]⁺.
Diethyl-6,6’-(4,4’-(1E,1’E)-(5-tert-butyl-2-oxocyclohexane-1,3-diylidene)bis(methan-1-yl-1-ylidene)bis(2-methoxy-4,1-phenylene)bis(oxy))dihexanoate (124): Yield 60% (yellow solid); mp 84-85 °C; IR (film, cm⁻¹): 2930, 2868, 1733 (OC=O), 1596, 1512, 1466, 1246 (C-O-C), 1159, 1141, 1034 (C-O-C); ¹H NMR (400 MHz, CDCl₃) δ: 0.98 (s, 9H, C(CH₃)₃), 1.25 (t, J = 7.3 Hz, 6H, 2COOCH₂CH₃), 1.48-1.55 (m, 4H), 1.71 (pentet, J = 7.3 Hz, 4H, 2OCH₂CH₂CH₂), 1.89 (pentet, J = 7.3 Hz, 4H, 2OCH₂CH₂CH₂), 2.34 (t, J = 7.3 Hz, 4H, 2COCH₂), 2.41-2.48 (m, 2H), 3.17-3.21 (m, 2H), 3.89 (s, 6H, 2OCH₃), 4.06 (t, J = 6.6 Hz, 4H, 2OCH₂CH₂), 4.13 (q, J = 7.3 Hz, 2COOCH₂CH₃), 6.91 (d, J = 8 Hz, 2H, ArH), 7.04 (s, 2H, ArH), 7.07-7.10 (m, 2H, ArH), 7.13 (s, 2H, ArH); ESI-MS (m/z): 707.54 [M + H]+.

Typical procedure for the synthesis of (2E,6E)-2,6-bis((3-(4-bromophenyl)-3,4-dihydro-2H-benzo[e][1,3]oxazin-6-yl)methylene)cyclohexanone (127) and related compounds (125-126): The 4-bromoaniline (224 mg, 1.30 mmol) and formaldehyde solution (41%, 5 mL), compound 63 ((2E,6E)-2,6-bis(4-hydroxybenzylidene)cyclohexanone) (200 mg, 0.65 mmol) were added to 5 mL of 1,4-dioxane and the reaction mixture was refluxed at 100 °C for 24 h. After completion of the reaction chloroform (20 mL) was added to it and washed with 2M NaOH solution (20 mL), and finally it was washed with water (20 mL). The organic layer was dried over anhydrous sodium sulphate and concentrated to dryness and purified by column chromatography. Yield 50% (yellow solid); mp 151-152 °C; IR (film, cm⁻¹): 3011, 2925, 1656, 1597, 1493, 1278, 1234, 1165, 1118, 940; ¹H NMR (400 MHz, CDCl₃) δ: 1.78 (pentet, J = 5.8 Hz, 2H), 2.87 (t, J = 5.1 Hz, 4H), 4.62 (s, 4H, 2NCH₂), 5.35 (s, 4H, 2OCH₂), 6.82 (d, J = 8.8 Hz, 2H, ArH), 6.99 (d, J = 8.8 Hz, 4H, ArH), 7.13 (s, 2H, ArH), 7.26-7.29 (m, 2H, ArH), 7.35 (d, J = 9.5 Hz, 4H, ArH), 7.68 (s, 2H, 2C=CH); ¹³C NMR (100 MHz, CDCl₃) δ: 22.91, 28.47, 30.59, 30.65, 79.53, 114.18, 117.02, 120.11, 120.37, 128.95, 129.35, 130.59, 132.15, 134.51, 136.37, 147.22, 154.63, 189.95.
(2E,5E)-2,5-Bis((3-p-tolyl-3,4-dihydro-2H-benzo[e][1,3]oxazin-6-yl)methylene)cyclopentanone (125): Yield 45% (yellow solid); mp 152-153 °C; IR (film, KBr): 2924, 2855, 1605, 1572, 1514, 1498, 1232, 1209, 1195, 1114, 928; $^1$H NMR (400 MHz, CDCl$_3$) δ: 2.26 (s, 6H, $2CH_3$), 3.04 (s, 4H, $CH_2CH_2$), 4.63 (s, 4H, $2NCH_2$), 5.38 (s, 4H, $2OCH_2$), 6.84 (d, $J = 8$ Hz, 2H, ArH), 7.02 (d, $J = 8$ Hz, 4H, ArH), 7.07 (d, $J = 8.8$ Hz, 4H, ArH), 7.24 (s, 2H, ArH), 7.37-7.40 (m, 2H, ArH), 7.48 (s, 2H, $2C=CH$).

(2E,6E)-2,6-Bis((3-p-tolyl-3,4-dihydro-2H-benzo[e][1,3]oxazin-6-yl)methylene)cyclohexanone (126): Yield 48% (yellow solid); mp 98-99 °C; IR (film, cm$^{-1}$): 3345, 2923, 2853, 1597, 1412, 1234, 1116; $^1$H NMR (400 MHz, CDCl$_3$) δ: 1.76-1.79 (m, 2H), 2.26 (s, 6H, $2CH_3$), 2.86-2.89 (m, 4H), 4.61 (s, 4H, $2NCH_2$), 5.36 (s, 4H, $2OCH_2$), 6.81 (d, $J = 8$ Hz, 2H, ArH), 7.01 (d, $J = 8$ Hz, 4H, ArH), 7.07 (d, $J = 8$ Hz, 4H, ArH), 7.14 (s, 2H, ArH), 7.27 (s, 2H, ArH), 7.68 (s, 2H, $2C=CH$).
References


Chapter 3  Synthesis and Anticancer Activity evaluation of curcumin analogues


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