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NOTES

# Novel bisbenzopyronopyran derivatives: photochemical synthesis and their in-vitro antimicrobial studies

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**Abstract**

The present research work describes the productive synthesis of novel bisbenzopyronopyran derivatives **4(a-h)** and **5(a-h)** via the photocyclization reactions of bischromones **3(a-h)** under the inert conditions. The latter compounds have been realized efficiently through the *O*-alkylation reactions of the 3-hydroxychromone **2** with suitable dihalogenated aliphatic/aromatic/hetero-aromatic reagents in the presence of dry acetone/anhydrous $K_2CO_3/Bu_4N^+I^-$ (PTC). The cyclization reaction of chalcone **1** under the Algar-Flynn-Oyamada reaction conditions ($KOH/H_2O_2$) could results in the formation of compound **2** in the good yield. The structural scaffolds of the newly prepared bischromones and resultant bisbenzopyronopyrans have been certified from the meticulous analysis of their various spectroscopic parameters such as UV-Vis, IR, $^1H/^{13}C$-NMR, and ESI-MS. It was found that *o/m/p*-xylene and pyridine-linked final symmetrical bistetracycles exhibited higher antimicrobial potencies as compared to alkyl chain-linked cyclized products. The bischromones **3(a-h)** could be able to endow modest level of antimicrobial behavior.

## 1 | INTRODUCTION

The study of synthetic photochemistry has provided a competent and environment-friendly opportunity to obtain together chemically and biologically significant scaffolds. The photochemical pathways also contribute a great prosperity in the preparations of many novel products which are not feasible through the normal thermal routes.[1] The prospect of employing photoreactions in the generations of diverse classes of organic compounds has been the scientifically sound area of research for the chemists.[2] The photoradiative processes are found to occur without using any composite catalysts, specific reagents, noxious solvents while the nonoccurrence of multistep strategies have prevented the formation of byproducts. These characteristics have made them more attractive protocols in the hands of synthetic chemists.[3,4] The photochemical reactions of α,β-unsaturated carbonyl compounds have been well understood geometrically and these are the powerful tool for the efficient preparations of large variety of potent carbocyclic and heterocyclic products. Different types of oxygenated heterocyclic products having conjugated enone moiety in their cyclic scaffold play a fundamental role in the both synthetic and natural systems because of their enormous and beneficial photochemical transformations.[5–8]

Over the previous few decades, the studies on six-membered oxygen heterocycles, such as pyrans and their benzo derivatives, have become the subject of considerable interest in the field of organic syntheses owing to their broad spectrum of pharmacological profiles.[9–11] These molecules form the structural motif of several synthetic as well as naturally occurring biologically active products including antibiotics, pheromones, alkaloids, and iridoids.[12–14] The pyran ring systems are extensively dispersed in the plants and animal kingdom. These are

utilized as the fragrant preservatives in cosmetics and food stuffs.[15,16] This family of compounds has been synthetically developed due to their prevailing commercial applications.[17,18] In addition, their derivatives can be used as an essential controller for photochemical activities and potassium cation channel. Benzopyran derivatives are usually exploited as the potential biologically active products.[19]

Chromones (benzo-γ-pyrones or 4*H*-chromen-4-one) are the privileged class of heterocyclic compounds containing two chromophoric entities in their structures that is, C=C and C=O which make them photochemically highly reactive molecules.[20–22] The structural heterogeneity pertaining to the position, number, and nature of various substituents associated to the central nucleus are specifically consistent to their physical, chemical, and biological properties.[23] They are omnipresent in nature particularly in plants realm and usually found as the mother fragment in numerous flavonoids, that is, flavones, flavonols, and isoflavones.[24,25] They are also studied as pivotal intermediates in the generations of bioactive heterocyclic systems. These substrates have engrossed much attention in the field of synthetic chemistry due to their wide range of bioactivities.[26–30] They are also found to be associated with the array of physiological processes. Furthermore, the chromone moiety is found to be present in the various therapeutic drugs such as baicalin (anti-inflammatory), nedocromil sodium (anti-allergic), puerarin (alcohol abuse), iguratimod (anti-rheumatic), and cromolyn (anti-inflammatory)[31,32] (Figure 1).

Literature observations suggest that molecules encompassing coalesced chromen-4-one and pyran moieties together in their frameworks are found to exhibit noticeable bioactivities due to their unique physicochemical properties.[33] Fused chromeno-pyran derivatives like brosimone, cycloartocarpin, and ophioglonin are the well-known products due to their tyrosinase inhibitory and anti-HBV activity, respectively[34] (Figure 2).

The chromone derivatives have been found to exhibit many interesting photoreactions like photodimerization, phototautomerization, photo-oxidation, photorearrang ements, photoreduction, and photoisomerization reactions.[35] Among these photoreactions, intramolecular hydrogen-abstractions have been successfully utilized for the generations of some unique polyheterocyclic compounds. The exhilarated interest in the syntheses and photochemistry of variously substituted chromone systems has frequently enthralled the organic photochemists in the past decades. This vast field remains an attractive and challenging thrust area for the development of oxygen containing tri- and tetracyclic compounds which could be realized through the Norrish type-II reactions.[36–39] The tethering of two chromone moieties together by using different types of spacers (aliphatic/aromatic/heteroaromatic) lead to the generations of bichromophoric molecules called as bischromones **3(a-h)**.

With aforesaid literature knowledge in mind and by following our earlier results dealing with the photo-transformations of 3-alkoxychromones/bischrom ones,[40–44] now we wish to report herein the detailed

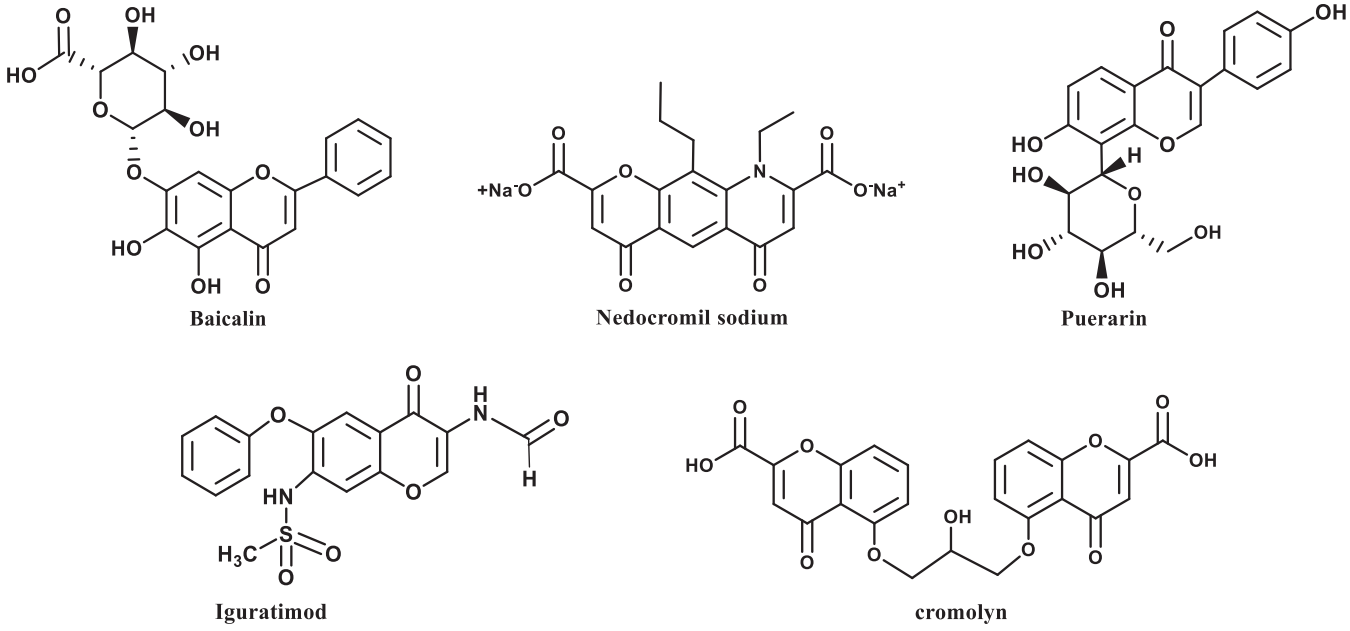



**FIGURE 1** Examples of chromone based therapeutic drugs

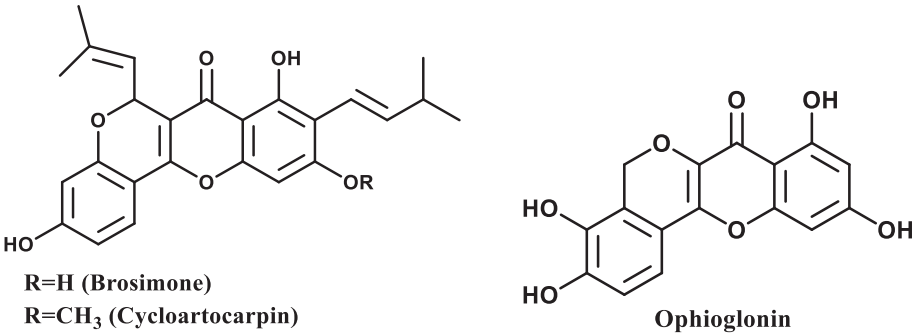



**FIGURE 2** Examples of bioactive chromeno-pyrans

photochemical cyclization reactions of alkyl/aromatic/heteroaromatic chain linked bischromones **3(a-h)**. The foremost objective of this study was to establish a straightforward photochemical protocol for the syntheses of novel bisbenzopyronopyrans (bis-isochromeno-chromenones) **4(a-h)/5(a-h)**. The major interest in these researches was also to unravel the impact of the intervening units (aliphatic/aromatic/heteroaromatic) upon the formations and antimicrobial portrait of the final bistetracyclic products.

## 2 | RESULTS AND DISCUSSION

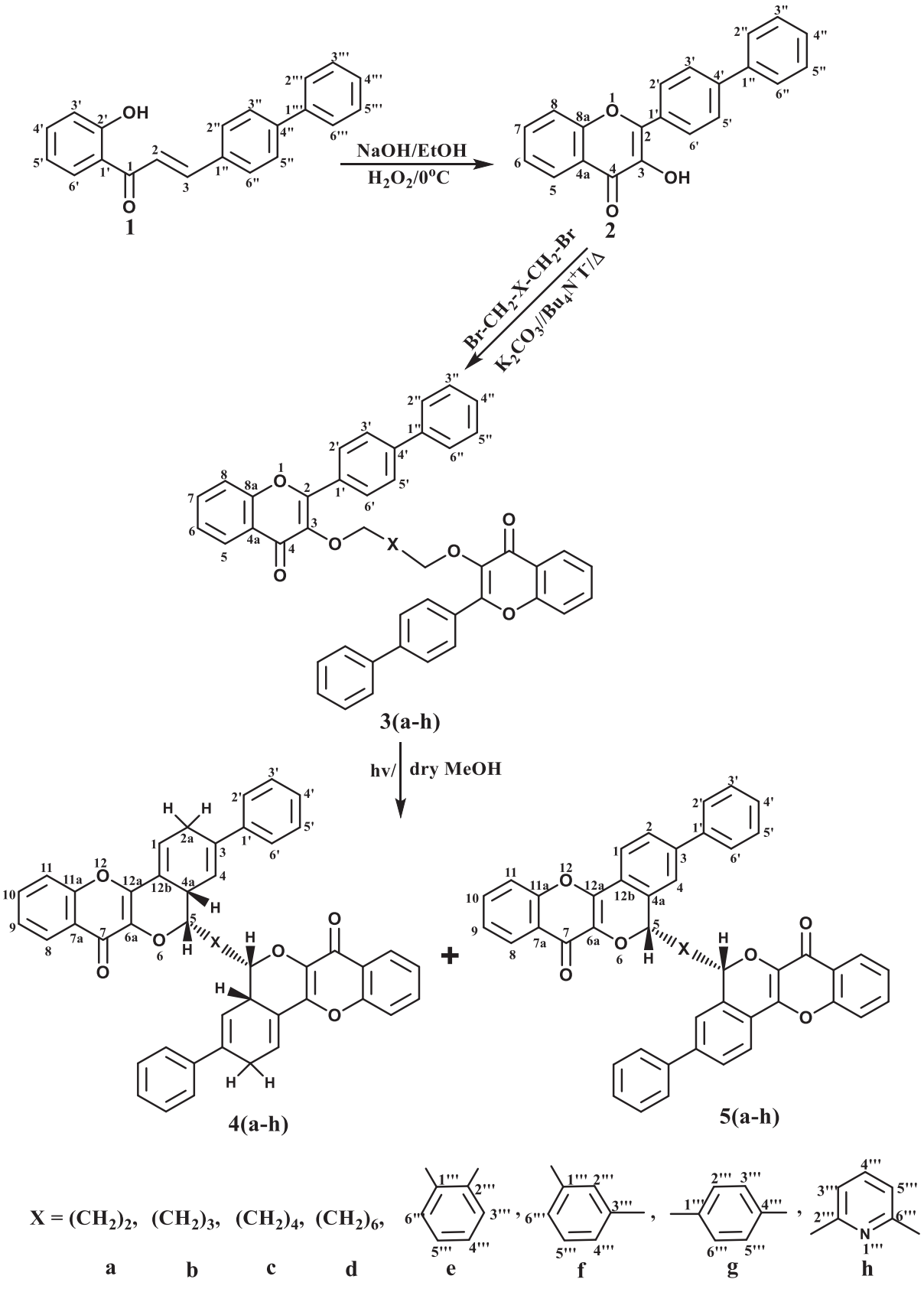
Our approach to the target bisbenzopyronopyrans (bis-isochromeno-chromenones) **4(a-h)** and **5(a-h)** has been initially started (Scheme 1) from the synthesis of 3-hydroxy-2-biphenyl-4*H*-chromen-4-one **2** which was realized from the reaction of chalcone **1** under the Algar-Flynn-Oyamada reaction conditions ($KOH/H_2O_2$). The subsequent *O*-alkylation reactions of the **2** with suitable di-brominated reagents (1,4-dibromobutane, 1,5-dibromo pentane, 1,6-dibromohexane, 1,8-dibromooctane, α,α′-di bromo-*o*-xylene, α,α′-dibromo-*m*-xylene, α,α′-dibromo-*p*-xylene, and 2,2′-bisbromomethyl-pyridine) in the presence of dry acetone/freshly dried $K_2CO_3$/tetra butyl ammonium iodide (phase transfer catalyst) escorted the formations of bis-chromen-4-ones **3(a-h)** in good yields. The application of $Bu_4N^+I^-$ in these reactions certainly improved the yields of bichromophoric products **3(a-h)**. The chalcone **1** was easily prepared according to the previously reported procedure in the literature.[45]

Bischromen-4-ones **3(a-h)** were extensively photolyzed in dry MeOH with pyrex-filtered light by means of Hg arc lamp (125 W) under the dry nitrogen atmosphere. The durations of these photoreactions were carefully optimized by using the TLC analyses of the photolytic mixtures at the regular intervals of 30 min. After the photoirradiations of about 4-5 h, most of the starting materials could be able to convert themselves into two types of new photoproducts (TLC). Upon prolonged photoirradiations, the TLC started to exhibit the spot of some polymeric stuff at the bottom along with two spots of products. At this stage photoirradiations were switched off, and then solvent was distilled off under the reduced pressure to obtain the gummy mixtures of photolysates. The latter were separated on the silica gel (100-200 mesh) columns to provide two new products in each case [**3(a-h)**]. These compounds were further crystallized from $CHCl_3$ to furnish the pure bisbenzopyronopyran derivatives **4(a-h)** and **5(a-h)**.

The structures of these products could be unequivocally established through the contrasting of their UV-Vis/IR/ESI-MS/$^1$H-NMR/$^{13}$C-NMR spectra with those of starting compounds **3(a-h)**. The elemental analysis results proved very helpful to establish the purity of the newly prepared compounds. The synthetic route espoused to attain the target products **4(a-h)** and **5(a-h)** has been portrayed in Scheme 1 and the prospective mechanism for their photochemical formations have been revealed in Scheme 2.

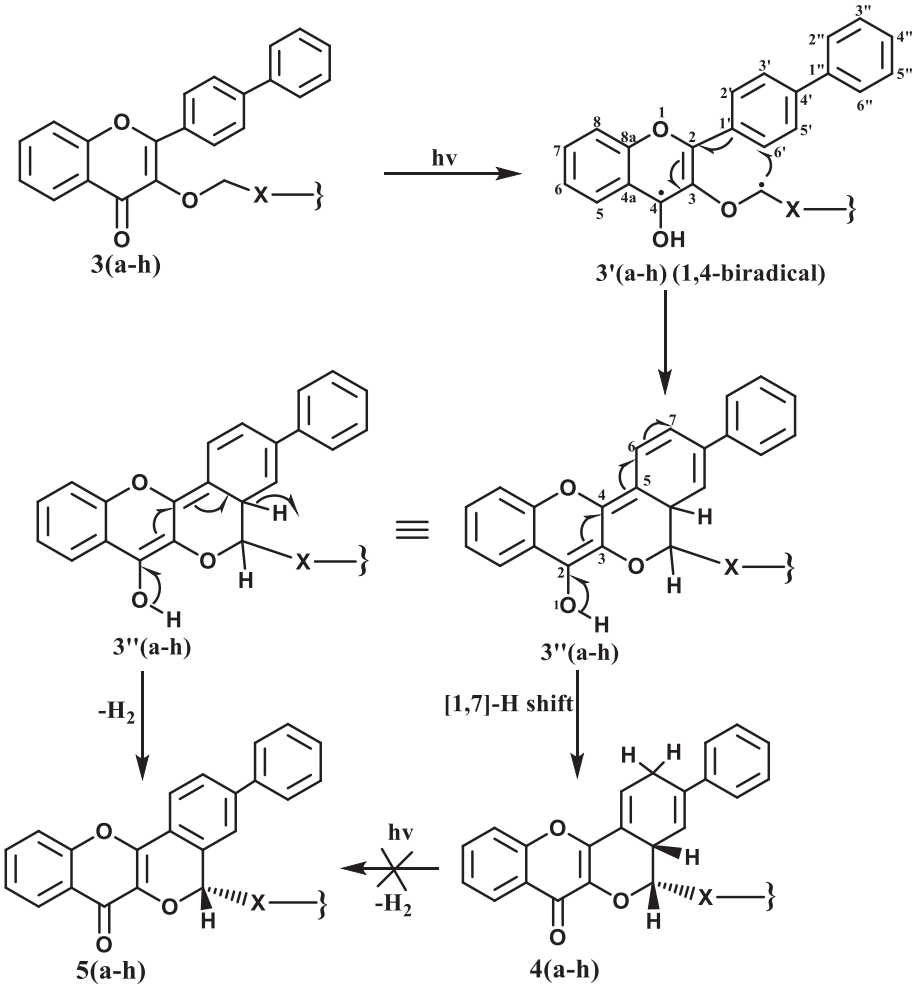
IR spectrum of compound **2** demonstrated a broad band at 3174 $cm^{-1}$ that could be easily allotted to the stretching frequency of O-H group. Its UV-Vis spectrum exhibited two maxima at 340 and 238 nm due to $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ transition, respectively. In its $^1$H-NMR (500 MHz, $CDCl_3$) spectrum, the prevalence of $C_3$-O***H*** group was certified by the materialization of one proton broad singlet (exchangeable with $D_2O$) at $\delta$ 7.07. In the aromatic region, the four benzenoid ring protons (H-5, 6, 7, 8) and nine biphenyl ring hydrogens (H-2′ to H-6′ and H-2″ to H-6″) furnished their respective signals in the region at $\delta$ 8.35-7.42 (see Section 5).

UV-Vis spectra of **3(a-h)** exhibited two peaks at 312-302 and 245-236 nm which may be produced by $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ transition, respectively. IR spectra of bischromones **3(a-h)** were very supportive to analyze their proposed structures. They did not concede any absorption frequency in O-H group region, which definitely represented the involvement of this functionality during the course of *O*-alkylation reactions. Here, intense bands emerged at 1638-1630 $cm^{-1}$ due to the conjugated




**SCHEME 1** Synthesis of bisbenzopyronopyrans **4(a-h)** and **5(a-h)**

**SCHEME 2** Proposed mechanism for the formations of **4(a-h)** and **5(a-h)**




C=O group of the pyrone moiety while C=C stretching frequency aroused at 1614-1601 $cm^{-1}$.

On the other hand in the 500 MHz $^1$H-NMR spectra (DMSO-$d_6$) of **3(a-h)**, the $D_2O$ exchangeable O-***H*** proton signal of **2** was found to be absent which again substantiated the formation of bischromone via the ether linkages. The $C_3$-OC***H₂*** group protons in compounds **3(a-d)** produced well defined triplets at $\delta$ 4.07-4.04 ($J_{vic}$ = 6.7-6.0 Hz); whereas, same hydrogens in **3(e-h)** resonated in the form of sharp singlets at $\delta$ 5.39-5.04. The downfield resonances in case of the latter could be occurring due to the benzylic nature of these hydrogens (OC***H₂***). The remaining methylene group [(C***H₂***)$_n$] hydrogens in **3(a-d)** engendered their suitable quintet or multiplet in the region at $\delta$ 1.77-1.33. The protons of intervening *o/m/p*-xylene/pyridine rings as well as benzenoid/$C_2$-biphenyl rings generated the signals of suitable multiplicity in the region at $\delta$ 8.18-7.35 (see Section 5).

In the $^{13}$C-NMR (125 MHz, C*D*Cl$_3$) spectra of bischromones **3(a-h)**, the C=O groups of pyrone moiety were responsible to divulge the most downfield resonances at $\delta$ 175.62-174.38. Other recognizable signals realized at $\delta$ 143.92-142.86 could be easily relegated to C-3 due to its presence in the double bond along with coalition with an oxygen atom. The signals ensued in the aliphatic region at $\delta$ 74.68-71.27 may be equipped to $C_3$-O***C***H$_2$ group carbon atoms while rest of the carbon atoms related to interior groups [(***C***H$_2$)$_n$] in **3(a-d)** were found to be located in the upfield region at $\delta$ 29.42-22.82. The carbon atoms of internal aromatic rings (*o/m/p*-xylene/pyridine) in **3(e-h)** along with benzenoid (C-4a, C-5, C-6 C-7, C-8, C-8a) and biphenyl ring carbons (C-1′ to C-6′ and C-1″ to C-6″) fomented their signals in the aromatic region at $\delta$ 140.73-117.32 (see Section 5).

IR spectra of symmetrical bisheterocycles **4(a-h)** and **5(a-h)** possessed strong absorptions in the carbonyl group region at 1646-1632 $cm^{-1}$ which clearly pronounced that both side chromophoric units of bischromones **3(a-h)** have been involved in the formations of tetracyclic products. This observation also suggests the subsistence of symmetry in their structural frameworks. UV-Vis spectra of these products displayed two maxima at 354-322 and 291-232 nm which were easily assignable to $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ transition, respectively.

The structures of novel bisbenzopyronopyrans **4(a-h)** and **5(a-h)** have been derived from their 500 MHz $^1$H-NMR ($CDCl_3$/DMSO-$d_6$) spectra. The contrast of $^1$H-NMR spectra of **3(a-h)** with those of **4(a-h)** and **5(a-h)** showed that triplets present at $\delta$ 4.07-4.04 in **3(a-d)** and singlets in **3(e-h)** at $\delta$ 5.39-5.04 were found to be absent in case of the latter which clearly illustrated that the internal chain $C_3$-OC***H*****$_2$** group has participated in the photoproducts formations. The salient attribute in the $^1$H-NMR spectra of **4(a-h)** were the signals of dihydrophenyl ring protons. Two significant resonances present at $\delta$ 5.08-4.22 and $\delta$ 3.85-3.64 were easily dispensed to H-5 and bridgehead proton H-4a, respectively. The coupling value of $J_{5,4a}$ = 12.8-12.0 Hz manifested the *cis* dispositions of H-4a and H-5, respectively. The H-1 and H-4 hydrogens appeared themselves as a broad singlet or doublet at $\delta$ 6.38-6.14 and another doublet at $\delta$ 6.03-5.72, respectively. The appearance of four protons multiplet at $\delta$ 2.95-2.74 could be straightforwardly elected to H-2a. At the extreme right of the spectra, the protons belonging to middle groups [(C***H*****$_2$)$_n$] in products **4(a-d)** could be able to impart relevant signals in the region at $\delta$ 1.79-1.42. The lowest field of the spectra included suitable signals of benzenoid, internal *o/m/p*-xylene/pyridine and $C_3$-aryl ring protons at $\delta$ 8.28-7.30 (see Section 5). In their 125 MHz $^{13}$C-NMR ($CDCl_3$/DMSO-$d_6$) spectra, the four perceptible resonances positioned at $\delta$ 179.53-177.16, 156.76-154.22, 150.59-146.24, and 143.82-142.29 were easily appointed to C-7, C-11a, C-12a, and C-6a, respectively. The dihydrophenyl ring carbon atoms were clearly situated at $\delta$ 139.38-133.31 (C-12b), 130.73-129.14 (C-3), 124.63-124.06 (C-1), 123.56-121.15 (C-4), 78.03-73.16 (C-5), 40.92-39.26 (C-4a), and 35.72-32.06 (C-2a). The intervening group [(***C***H$_2$)$_n$] carbon atoms in compounds **4(a-d)** exhibited recognizable signals in aliphatic region at $\delta$ 30.64-18.52. The carbon atoms of the remaining rings rigged the predictable pattern of resonances in the aromatic region at $\delta$ 140.91-116.58 (see Section 5).

$^1$H-NMR spectra (500 MHz, $CDCl_3$/DMSO-$d_6$) of bistetracyclic products **5(a-h)** were quite elementary that contributed the majority of signals in aromatic region at $\delta$ 8.27-7.36. The ring junction protons H-4a located in photoproducts **4(a-h)** were found to be absent altogether in these $^1$H-NMR spectra which fully supported the formation of dehydrogenated products **5(a-h)**. The emergence of well-defined triplets at $\delta$ 4.94-4.90 ($J_{vic}$ = 12.8-12.0 Hz) in **5(a-d)** while sharp singlets at $\delta$ 6.00-5.91 in **5(e-h)** could be easily imputed to H-5 proton of pyran ring. In compounds **5(a-d)**, the hydrogens of interior groups [(C***H*****$_2$)$_n$] afforded their respective signals of the suitable multiplicities in the upfield region at $\delta$ 2.04-1.51. $^{13}$C-NMR spectra (125 MHz, $CDCl_3$) of these compounds displayed four downfield signals which were located at $\delta$ 182.09-180.16 (C-7), 157.33-155.28 (C-11a), 156.35-155.04 (C-12a), and 143.92-143.13 (C-6a) while rest of the aromatic ring carbon atoms were resonating in the downfield region at $\delta$ 140.73-117.62 (see Section 5). The pyran ring carbon atoms C-5 appeared easily at $\delta$ 80.73-74.16 while the upfield resonances situated at $\delta$ 32.88-20.54 in compounds **5(a-d)** may be assigned to the carbon atoms of the interior methylene groups [(***C***H$_2$)$_n$].

The ESI-MS spectral fragmentation data of newly synthesized bischromones **3(a-h)** and resulting bistetracyclic photoproducts **4(a-h)** and **5(a-h)** displayed good obedience with their prospective structures (see Section 5).

## 2.1 | Mechanistic considerations

The above described photochemical cyclizations of bischromen-4-ones **3(a-h)** may be occurring through the Norrish Type-II-H-abstraction from the $C_3$-OC***H*****$_2$** group by the photoexcited C=O chromophore of the pyrone moiety which could lead to the generations of 1,4-diradicals **3′(a-h)**. The resulting diradicals may undergo cyclizations through the clipping of -O-ĊH- radical with 6′-position of $C_2$-biphenyl ring to afford the tetracyclic intermediates **3″(a-h)** in situ (Scheme 2**)**. The latter further follow (1,7)-H-sigmatropic reactions to provide the dihydrocyclized products **4(a-h)** while the dehydrogenations of **3″(a-h)** could results in the formations of aromatized products **5(a-h)**.

It is mentioned hereby that photolysis of these bischromones **3(a-h)** in dry THF also yielded the similar cyclohydrogenated **4(a-h)** and cyclodehydrogenated **5(a-h)** products. Thus, hydrogen donating capability of the solvent (protic and aprotic) did not have any significant affect upon the outcome of these photochemical reactions which describes the involvement of the intramolecular H-abstractions in these syntheses. When products **4(a-h)** were separately photolyzed, they did not yield any product similar to **5(a-h)** rather some polymeric materials were always obtained. This observation proves that **5(a-h)** are not the dehydrogenated products of **4(a-h)**, rather both types of photoproducts have been realized independently from the same intermediates **3″(a-h)**. It is evident from these molecules that $C_3$-OC***H*****$_2$** group hydrogens are benzylic in case of **3(e-h)** which could lead to the formation of more stabilized benzyloxy $C_3$-OĊH- radical as compared to alkoxyl radicals which are involved in **3(a-d)**. This aspect was corroborated from our experimental observation that alkyl chains linked bischromones **3(a-d)** produced the yields of both photoproducts in the range of 40-52% while chemical efficiency of 60-74% was furnished by the aromatic (*o/m/p*-xylene) and heteroaromatic units based compounds **3(e-h)**. Thus

**TABLE 1** In vitro antimicrobial data of bischromones (MIC in μg $mL^{-1}$)

| | Gram-negative bacteria | | | | Gram-positive bacteria | | | Fungi | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Compound No.** | ***Escherichia coli*** | ***Klebsiella pneumoniae*** | ***Pseudomonas aeruginosa*** | ***Pseudomonas fluorescens*** | ***Staphylococcus aureus*** | ***Bacillus subtilis*** | ***Streptococcus pyogenes*** | ***Aspergillus janus*** | ***Penicillium glabrum*** | ***Aspergillus niger*** | ***Fusarium oxysporum*** | ***Aspergillus sclerotiorum*** |
| **3a** | 32 | 32 | 64 | **16** | 32 | 32 | 32 | **16** | 32 | 32 | 32 | 32 |
| **3b** | **16** | **16** | 32 | 32 | 32 | 32 | **16** | 32 | 32 | 32 | 32 | 32 |
| **3c** | 32 | 32 | 32 | **8** | 32 | **16** | 32 | 32 | 32 | 32 | **16** | 32 |
| **3d** | 32 | **16** | 64 | 32 | **16** | 32 | 32 | 32 | **16** | 32 | 32 | 32 |
| **3e** | **16** | 32 | **8** | 32 | **16** | 32 | **16** | 32 | 32 | **16** | 32 | 32 |
| **3f** | 32 | **16** | 32 | **16** | 32 | **16** | 32 | 32 | 32 | 32 | **16** | **16** |
| **3g** | **16** | 32 | 32 | **16** | 32 | 32 | 32 | **16** | 32 | 32 | 32 | **8** |
| **3h** | 32 | **16** | 32 | 32 | **8** | 32 | 32 | 32 | **8** | 32 | **16** | 32 |
| **Amoxicillin** | **4** | **4** | **4** | **4** | **2** | **2** | **4** | — | — | — | — | — |
| **Fluconazole** | — | — | — | — | — | — | — | **2** | **2** | **2** | **2** | **2** |

*Note*: Bold values are indicated the significant antimicrobial activity of the tested compounds.

**TABLE 2** In vitro antimicrobial data of photoinduced compounds (MIC in μg $mL^{-1}$)

| | Gram-negative bacteria | | | | Gram-positive bacteria | | | Fungi | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Compound No.** | ***Escherichia coli*** | ***Klebsiella pneumoniae*** | ***Pseudomonas aeruginosa*** | ***Pseudomonas fluorescens*** | ***Staphylococcus aureus*** | ***Bacillus subtilis*** | ***Streptococcus pyogenes*** | ***Aspergillus janus*** | ***Penicillium glabrum*** | ***Aspergillus niger*** | ***Fusarium oxysporum*** | ***Aspergillus sclerotiorum*** |
| **4a** | **16** | 32 | 32 | 32 | 32 | **8** | 32 | 32 | 32 | **16** | 32 | 32 |
| **5a** | 32 | **8** | 32 | 32 | **16** | 32 | 32 | **16** | **16** | 32 | **8** | 32 |
| **4b** | **8** | 32 | 32 | **16** | 32 | 32 | **16** | 32 | 32 | 32 | 32 | 32 |
| **5b** | 32 | **16** | 32 | **8** | **8** | 32 | 32 | 32 | 32 | **16** | 32 | 32 |
| **4c** | **16** | 32 | **16** | 32 | 32 | **16** | **16** | 32 | **16** | 32 | 32 | **16** |
| **5c** | 32 | **8** | 32 | **16** | **16** | 32 | 32 | 32 | 32 | 32 | **8** | **8** |
| **4d** | **16** | 32 | **16** | 32 | 32 | **16** | **8** | 32 | 32 | **16** | 32 | 32 |
| **5d** | **8** | **16** | 32 | **16** | **16** | 32 | 32 | 32 | **16** | **8** | 32 | 32 |
| **4e** | 32 | 32 | **8** | 32 | 32 | **8** | **16** | **16** | 32 | 32 | **16** | **8** |
| **5e** | **16** | **8** | 32 | **8** | **8** | 32 | 32 | 32 | **8** | **16** | 32 | **16** |
| **4f** | 32 | **16** | **16** | 32 | 32 | 32 | **8** | **16** | 32 | 32 | **8** | **16** |
| **5f** | **16** | **16** | **8** | **8** | **16** | 32 | 32 | 32 | 32 | **8** | **16** | 32 |
| **4g** | 32 | **8** | 32 | 32 | 32 | **8** | **16** | **16** | **16** | 32 | 32 | **8** |
| **5g** | **8** | 32 | **16** | **8** | **8** | 32 | 32 | **8** | 32 | **16** | **16** | 32 |
| **4h** | **16** | **16** | **8** | 32 | **16** | 32 | **8** | 32 | 32 | **16** | **8** | **16** |
| **5h** | **8** | **8** | 32 | **16** | 32 | **8** | 32 | **16** | **16** | **8** | **16** | **8** |
| **Amoxicillin** | **4** | **4** | **4** | **4** | **2** | **2** | **4** | — | — | — | — | — |
| **Fluconazole** | — | — | — | — | — | — | — | **2** | **2** | **2** | **2** | **2** |

*Note:* Bold values are indicated the significant antimicrobial activity of the tested compounds.

chemical efficiency of final bisbenzopyronopyrans in these reactions has been found to be dependent upon the nature of intervening spacer units (alkyl and benzyl).

## 3 | ANTIMICROBIAL STUDIES

The in vitro antibacterial and antifungal evaluations of newly prepared bischromones **3(a-h)** and bisbenzopyro nopyrans **4(a-h)**/**5(a-h)** have been executed by adopting the serial tube dilution procedures.[46] Four Gram-negative bacterium species (*Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Escherichia coli*, and *Pseudomonas fluorescens*) and three Gram-positive pathogens (*Bacillus subtilis*, *Streptococcus pyogenes*, and *Staphylococcus aureus*) were used for the antibacterial activity. Five fungal strains (*Aspergillus janus*, *Aspergillus sclerotiorum*, *Aspergillus niger*, *Penicillium glabrum*, and *Fusarium oxysporum*) were taken for carrying out the antifungal analysis. The recorded minimal inhibitory concentrations (MICs-μg $mL^{-1}$) values are defined as the least concentrations of inspected antimicrobial agents, that is, *bactericidal* or *fungicidal* agents which completely arrested the visible growth of tested pathogenic microbes. The stockpile solutions have been obtained by dissolving 10 mg of tested samples and reference drugs (*Amoxicillin* and *Fluconazole*) in 10.0 mL of DMSO (1.0 mg $mL^{-1}$) subsequently these solutions were diluted in successions by means of sterilized micropipette to provide the different concentrations of 128, 64, 32, 16, 8, and 4 μg $mL^{-1}$. Further, the bacterial and fungal suspensions prepared in saline medium were injected to the serially diluted test tubes. The chosen bacterial and fungal pathogens were nourished in sterilized nutrient broth and malt extract medium, respectively. The bacterial pathogens vaccinated test tubes were carefully sustained in the incubator at 37°C for 24 h; whereas, fungal strains immunized tubes have been incubated at 28°C for 72 h and the reference drugs were also reserved under the similar conditions for correlating the results. After the appropriate incubation periods, the immunized test tubes were examined visually for turbidity appearance. The tubes showing no noticeable growth of tested organisms (*bacteria* and *fungi*) and having the smallest amount of reference drug were measured as the minimal inhibitory concentrations (MICs). The results achieved from these screenings have been compiled in Tables 1 and 2. The attained MIC values of bischromones **3(a-h)** and symmetrical bistetracycles **4(a-h)** and **5(a-h)** have been compared among each other as well as with reference drugs (lower MIC values depicts the higher activity of the tested products).

It is conspicuous from Table 1 that bischromones **3a** and **3b** showed prudent response (MIC-16 μg $mL^{-1}$) against the *P. fluorescens*, *A. janus*, and *E. coli*, *K. pneumoniae*, *S. pyogenes*, respectively. Compound **3c** was found to be exceedingly potent (MIC-8 μg $mL^{-1}$) against *P. fluorescens*; whereas, it exhibited the MIC value of 16 μg $mL^{-1}$ against *B. subtilis* and *F. oxysporum*. Compound **3d** furnished modest level of activity (MIC-16 μg $mL^{-1}$) against bacterial species *K. pneumoniae*, *S. aureus* and fungal pathogen *P. glabrum*. Compound **3e** was found to suppress the growth of *P. aeruginosa* and *E. coli*, *S. aureus*, *S. pyogenes*, *A. niger* at the MIC value of 8 and 16 μg $mL^{-1}$, respectively. Bischromone **3f** revealed sensible level of actions against *K. pneumoniae*, *P. fluorescens*, *B. subtilis*, *F. oxysporum*, and *A. sclerotiorum*. The compound **3g** demonstrated potent behavior (MIC-8 μg $mL^{-1}$) against *A. sclerotiorum* and it also furnished the modest potency (MIC-16 μg $mL^{-1}$) against *E. coli*, *P. fluorescens*, and *A. janus*. Bischromone **3h** was found to reveal the MIC value of 8 and 16 μg $mL^{-1}$ against *S. aureus*, *P. glabrum*, and *K. pneumoniae*, *F. oxysporum*, respectively.

Table 2 construed that most of the bisbenzo pyronopyrans **4(a-h)** and **5 (a-h)** evinced the modest to potent activities (MIC-16 and 8 μg $mL^{-1}$) against the tested bacterial and fungal strains. Compound **4a** showed noteworthy response against *B. subtilis* at the MIC value of 8 μg $mL^{-1}$; whereas product **5a** could be able to achieve substantial activity (MIC-8 μg $mL^{-1}$) against the *K. pneumoniae* and *F. oxysporum*. The product **4b** enacted significant result (MIC-8 μg $mL^{-1}$) against *E. coli*. Compound **5b** impeded the growth of bacterial pathogens namely *P. fluorescens* and *S. aureus* at the MIC value of 8 μg $mL^{-1}$. Product **4c** was found to be equipped with sensible performance (MIC-16 μg $mL^{-1}$) against *E. coli*, *P. aeruginosa*, *B. subtilis*, *S. pyogenes*, *P. glabrum*, and *A. sclerotiorum*. Bisbenzopyronopyrans **5c** and **4d** were found to be fabulously powerful (MIC-8 μg $mL^{-1}$) against *K. pneumoniae*, *F. oxysporum*, *A. sclerotiorum*, and *S. pyogenes*, respectively. Compound **5d** manifested efficient response against *E. coli* and *A. niger* at the MIC value of 8 μg $mL^{-1}$, while product **4e** conquered astonishing actions against *P. aeruginosa*, *B. subtilis*, and *A. sclerotiorum* at the similar MIC value. Bisheterocycle **5e** could access perceptible activity (MIC-8 μg $mL^{-1}$) against *K. pneumoniae*, *P. fluorescens*, *S. aureus*, and *P. glabrum*. The compounds **4f** and **5f** exhibited noticeable response (MIC-8 μg $mL^{-1}$) against *S. pyogenes*, *F. oxysporum* and *P. aeruginosa*, *P. fluorescens*, *A. niger*, respectively. Compound **4g** displayed appreciable potency (MIC-8 μg $mL^{-1}$) against *K. pneumoniae*, *B. subtilis*, and *A. sclerotiorum*. The product **5g** revealed the momentous

behavior (MIC-8 μg $mL^{-1}$) against *E. coli*, *P. fluorescens*, *S. aureus*, and *A. janus*, while bisheterocycle **4h** engendered incredible outcome (MIC-8 μg $mL^{-1}$) against *P. aeruginosa*, *S. pyogenes*, and *F. oxysporum*. Bistetracyclic product **5h** furnished potent behavior against *E. coli*, *K. pneumoniae*, *B. subtilis*, *A. niger*, and *A. sclerotiorum* at the MIC value of 8 μg $mL^{-1}$.

It is discernible from the above described antimicrobial results that *o/m/p*-xylene and pyridine linked bisbenzopyronopyrans **4(e-h)** and **5(e-h)** seems to be behaving as the promising antifungal and antibacterial agents as compared to other bisheterocycles **4(a-d)** and **5 (a-d)** which are assembled around the four, five, six and eight methylene groups.

## 4 | CONCLUSION

It may be concluded that the present investigations have been able to develop the efficient photochemical method for the syntheses of novel aliphatic/aromatic/heteroaromatic chains linked bisbenzopyronopyrans. These products have been obtained by using the environmentally benevolent protocol in which light has been used as the reagent. Here, intramolecular H-abstraction reactions have been exploited to yield novel symmetrical bisbenzopyronopyrans. Furthermore, the nature of the intervening spacer displayed profound influence on the photochemical efficiency as well as antimicrobial performances of the newly prepared bisbenzopyronopyrans. The antimicrobial examinations revealed that resulting photoproducts demonstrated significant efficacy against the tested microorganisms than their intermediate analogs. This aspect has vindicated our target toward the photocyclization reactions of bischromones. It was found that final bisheterocycles linked through aromatic and heteroaromatic chains showed enhanced antimicrobial activities as compared to other products which are built around the varying length aliphatic chains. In general, the bistetracyclic scaffolds seems to be the interesting template for the recognition of potential antimicrobial agents.

## 5 | EXPERIMENTAL

### 5.1 | Materials and method

All the solvents and fine chemicals utilized to perform the present research work have been purchased from the various commercial suppliers such as Loba Chemie, S. D. Fine, TCI, and Sigma-Aldrich chemical companies, and these chemicals have been used as such without any further purification. The melting point ranges of prepared compounds were recorded in paraffin wax using open glass capillaries and hence are uncorrected. XEVO G2-XS QTOF spectrometer (I.I.T. Ropar, Punjab, India) was used for scrutinizing the Positive-ion mode ESI Mass Spectra; whereas, Infrared Spectra were run on a Perkin Elmer FT-IR Spectrophotometer as neat samples (Department of Chemistry, Punjabi University, Patiala, India) with frequencies recorded in reciprocal centimeters ($cm^{-1}$). Proton ($^{1}H$) and carbon ($^{13}C$) Nuclear Magnetic Resonance Spectra have been obtained in DMSO-$d_6$ or $CDCl_3$ solvent on a Bruker Advance 500 MHz (125 MHz for $^{13}C$ NMR) Neo Spectrometer (RSIC, Panjab University, Chandigarh, India) using $SiMe_4$ as the reference material. The chemical shifts have been accounted on the $\delta$ scale while the coupling constants ($J$) are revealed in Hertz. The spin multiplicities in the $^{1}H$-NMR spectra have been designated by using their standard abbreviations such as m (multiplet), td (triplet of doublet), dt (doublet of triplet), dd (doublet of doublet), q (quartet), t (triplet), d (doublet), brs (broad singlet), and s (singlet). The photochemical reactions have been operated in the pyrex reactor under the dry nitrogen atmosphere. Thin-layer chromatography (TLC) plates encrusted with silica gel G suspended in MeOH-$CHCl_3$ (2:1) have been exploited at appropriate interval of times for optimizing the durations of the photoreactions. For TLC analyses, the mixture of hexane-EtOAc (9:1) has been thoroughly employed as a mobile phase and spots were carefully visualized by their exposure to the $I_2$ fumes in the glass chamber. The separations as well as purification of the photolytic mixtures have been carried out by using the silica-gel (100-200 mesh) column chromatography where hexane/ethylacetate (1:3) has been used as the eluents. Chalcone **1** was prepared and analyzed in the similar manner as reported in literature.[45]

### 5.2 | Synthesis of 2-([1,1′-Biphenyl]-4-yl)-3-hydroxy-4*H*-chromen-4-one 2

A mixture of chalcone **1** (2.0 g, 0.006 mol), powdered KOH (1.0 g, 0.018 mol) and MeOH (20.0 mL) was vigorously stirred for 30 min at 0°C, thereafter $H_2O_2$ (1.5 g, 0.044 mol) was added drop-wise to this well stirred solution. As the addition of $H_2O_2$ completed, the stirring of the reaction mixture was further continued until initially formed reddish-orange solution was transformed into an intense yellow mass which depicted the accomplishment of reaction. The ensued reaction mixture was poured onto crushed iced and subsequently neutralized with diluted hydrochloric acid to achieve a solid substance which was filtered off and dried under suction. The crude

product was purified by its crystallization in MeOH: $CHCl_3$ (1:1) to furnish the pure compound **2**.

Light yellow solid; yield 70%; m.p. 220-222°C; IR (KBr) $\upsilon_{max}$ ($cm^{-1}$): 3174 (O-H), 3079 (aromatic C-H), 1628 (C=O) and 1594 $cm^{-1}$ (C=C); UV-Vis (MeOH): $\lambda_{max}$ (nm) 340, 238; $^1$H-NMR (500 MHz, $CDCl_3$): $\delta$ 8.35 (2H, dt, $J_{m,o}$ = 2.0, 7.0 Hz, H-2′, 6′), 8.28 (1H, dd, $J_{m,o}$ = 2.1, 8.0 Hz, H-5), 7.78 (2H, dt, $J_{m.o}$ = 2.0, 8.0 Hz, H-3′, 5′), 7.73 (1H, td, $J_{m,o}$ = 2.2, 7.0 Hz, H-8), 7.68 (2H, dt, $J_{m,o}$ = 2.5, 8.5, H-2″, 6″), 7.63 (1H, d, $J_o$ = 8.5 Hz, H-7), 7.49 (2H, td, $J_{m,o}$ = 2.0, 7.5, H-3″, 5″), 7.42 (2H, m, H-6, 4″), 7.07 (1H, brs, O***H***); $^{13}$C-NMR (100 MHz, DMSO-$d_6$): $\delta$ 172.84 (***C***=O), 154.52 (C-8a), 144.74 (C-2), 141.19 (C-3), 139.20 (C-1′), 133.50 (C-4′), 130.25 (C-1″), 129.84 (C-7), 128.87 (C-2′, 6′), 128.07 (C-3′, 5′), 127.84 (C-2″, 6″), 126.82 (C-3″, 5″), 126.66 (C-4″), 126.54 (C-5), 124.73 (C-4a), 121.28 (C-6), 118.22 (C-8); ESI-MS: *m/z* Calculated for $C_{21}H_{14}O_3$: 314.09 $[M]^+$; Found: 315.14 $[M + 1]^+$ (100%), 316.15 $[M + 2]^+$ (22%); Anal. calc. for $C_{21}H_{14}O_3$: C, 80.24%; H, 4.49%; Found: C, 80.56%; H, 4.51%.

## 5.3 | General procedure for the synthesis of bischromones 3(a-h)

To the well stirred suspension of chromone **2** (0.006 mol), freshly ignited $K_2CO_3$ (0.012 mol), $Bu_4N^+I^-$ (0.002 mol), and dry acetone (25.0 mL) was added the suitable dibrominated reagents (1,4-dibromobutane, 1,5-dibromo pentane, 1,6-dibromohexane, 1,8-dibromooctane, α,α′-dibromo-*o*-xylene, α,α′-dibromo-*m*-xylene, α,α′-dibromo-*p*-xylene, and 2,2′-bisbromomethyl-pyridine, 0.003 mol) slowly and slowly. The resulting mixtures were allowed to stir under refluxing for 3-4 h. The consumption of starting substrate was monitored by means of TLC (hexane/ethyl acetate—9:1). After the completion, the reactions mixtures were turned from orange-red to colorless masses which were further decomposed into ice-HCl with intense shaking to endow the solid substances. The accessed crude products were crystallized by using methanol/chloroform (1:1) which yielded the pure bischromones **3(a-h)**.

### 5.3.1 | 3,3′-(Butane-1,4-diylbis[oxy])bis (2-[[1,1′-biphenyl]-4-yl]-4H-chromen-4-one) 3a

Off white solid; yield 59%; m.p. 210-212°C; IR (KBr) $cm^{-1}$:3062 (aromatic C-H), 2929, 2876 (aliphatic C-H), 1630 (C=O) and 1611 (C=C); UV-Vis (MeOH): $\lambda_{max}$(nm) 308, 242; $^1$H-NMR (500 MHz, DMSO-$d_6$): $\delta$ 8.18 (4H, d, $J_o$ = 8.4 Hz, H-2′, 6′), 8.12 (2H, dd, $J_{m,o}$ = 2.4, 7.9 Hz, H-5), 7.91 (4H, d, $J_o$ = 8.5 Hz, H-3′, 5′), 7.85 (2H, td, $J_{m,o}$ = 2.0, 8.3 Hz, H-7), 7.80 (4H, d, $J_o$ = 7.0 Hz, H-2″, 6″), 7.53 (2H, t, $J_o$ = 7.4 Hz, H-8), 7.50 (4H, d, $J_o$ = 7.3 Hz, H-3″, 5″), 7.44 (4H, m, H-6, 4″), 4.07 (4H, t, $J_{vic}$ = 6.1 Hz, OC***H***$_2$), 1.77 (4H, quintet, $J_{vic}$ = 6.3 Hz, $OCH_2C$***H***$_2$); $^{13}$C-NMR (125 MHz, $CDCl_3$): $\delta$ 175.13 (***C***=O), 155.54 (C-8a), 155.27 (C-2), 143.48 (C-3), 140.73 (C-1′), 133.52 (C-4′), 133.39 (C-1″), 129.87 (C-7), 129.79 (C-2′, 6′), 129.08 (C-3′, 5′), 128.92 (C-2″, 6″), 127.97 (C-3″, 5″), 127.11 (C-4″), 125.83 (C-5), 124.64 (C-4a), 124.24 (C-6), 118.04 (C-8), 72.31 (O***C***$H_2$), 26.71 ($OCH_2$***C***$H_2$); ESI-MS: *m/z* Calculated for $C_{46}H_{34}O_6$: 682.24 $[M]^+$; Found: 683.34 $[M + 1]^+$ (27%), 684.34 $[M + 2]^+$ (12%), 706.32 $[M + Na + 1]^+$ (8%); Anal. calc. for $C_{46}H_{34}O_6$: C, 80.92%; H, 5.02%; Found: C, 81.24%; H, 5.04%.

### 5.3.2 | 3,3′-(Pentane-1,5-diylbis[oxy])bis (2-[[1,1′-biphenyl]-4-yl]-4H-chromen-4-one) 3b

Off white solid; yield 63%; m.p. 138-140°C; IR (KBr) $cm^{-1}$:3065 (aromatic C-H), 2936, 2872 (aliphatic C-H), 1632 (C=O) and 1608 (C=C); UV-Vis (MeOH): $\lambda_{max}$(nm) 306, 237; $^1$H-NMR (500 MHz, DMSO-$d_6$): $\delta$ 8.16 (4H, d, $J_o$ = 7.6 Hz, H-2′, 6′), 8.10 (2H, dd, $J_{m,o}$ = 2.2, 7.3 Hz, H-5), 7.93 (4H, d, $J_o$ = 8.2 Hz, H-3′, 5′), 7.88 (4H, d, $J_o$ = 7.8 Hz, H-2″, 6″), 7.84 (2H, td, $J_{m,o}$ = 2.6, 8.0 Hz, H-7), 7.55 (2H, t, $J_o$ = 7.5 Hz, H-8), 7.50 (4H, d, $J_o$ = 7.0 Hz, H-3″, 5″), 7.45 (4H, m, H-6, 4″), 4.06 (4H, t, $J_{vic}$ = 6.7 Hz, OC***H***$_2$), 1.73 (4H, quintet, $J_{vic}$ = 6.8 Hz, $OCH_2C$***H***$_2$), 1.56 (2H, m, $OCH_2CH_2C$***H***$_2$); $^{13}$C-NMR (125 MHz, $CDCl_3$): $\delta$ 174.46 (***C***=O), 155.96 (C-8a), 155.34 (C-2), 142.86 (C-3), 139.08 (C-1′), 134.66 (C-4′), 133.43 (C-1″), 130.56 (C-7), 129.84 (C-2′, 6′), 129.14 (C-3′, 5′), 128.33 (C-2″, 6″), 127.68 (C-3″, 5″), 127.24 (C-4″), 125.57 (C-5), 124.43 (C-4a), 123.95 (C-6), 117.32 (C-8), 72.20 (O***C***$H_2$), 29.42 ($OCH_2$***C***$H_2$), 24.14 ($OCH_2CH_2$***C***$H_2$); ESI-MS: *m/z* Calculated for $C_{47}H_{36}O_6$: 696.25 $[M]^+$; Found: 697.36 $[M + 1]^+$ (32%), 698.36 $[M + 2]^+$ (24%), 719.34 $[M + Na]^+$ (10%); Anal. calc. for $C_{47}H_{36}O_6$: C, 81.02%; H, 5.21%; Found: C, 81.34%; H, 5.18%.

### 5.3.3 | 3,3′-(Hexane-1,6-diylbis[oxy])bis (2-[[1,1′-biphenyl]-4-yl]-4H-chromen-4-one) 3c

Off white solid; yield 66%; m.p. 130-132°C; IR (KBr) $cm^{-1}$:3068 (aromatic C-H), 2922, 2868 (aliphatic C-H), 1634 (C=O) and 1614 (C=C); UV-Vis (MeOH): $\lambda_{max}$(nm) 310, 240; $^1$H-NMR (500 MHz, DMSO-$d_6$): $\delta$ 8.18

(2H, d, $J_o$ = 8.5 Hz, H-5), 8.12 (4H, td, $J_{m,o}$ = 2.0, 8.5 Hz, H-2′, 6′), 7.90 (4H, d, $J_o$ = 7.0 Hz, H-3′, 5′), 7.82 (6H, m, H-7, 2″, 6″), 7.70 (2H, t, $J_o$ = 8.4 Hz, H-8), 7.52 (2H, t, $J_o$ = 7.3 Hz, H-6), 7.48 (4H, m, H-3″, 5″), 7.36 (2H, d, $J_o$ = 7.3 Hz, H-4‴), 4.05 (4H, t, $J_{vic}$ = 6.4 Hz, OC***H₂***), 1.71 (4H, quintet, $J_{vic}$ = 6.4 Hz, $OCH_2C$***H₂***), 1.45 (4H, m, $OCH_2CH_2C$***H₂***); $^{13}$C-NMR (125 MHz, $CDCl_3$): $\delta$ 174.94 (***C***=O), 155.52 (C-8a), 155.12 (C-2), 143.35 (C-3), 140.13 (C-1′), 135.86 (C-4′), 134.27 (C-1″), 129.98 (C-7), 129.68 (C-2′, 6′), 129.02 (C-3′, 5′), 128.47 (C-2″, 6″), 128.30 (C-3″, 5″), 127.99 (C-4″), 125.38 (C-5), 124.74 (C-4a), 124.36 (C-6), 118.53 (C-8), 72.08 (O***C***$H_2$), 29.18 ($OCH_2$***C***$H_2$), 26.32 ($OCH_2CH_2$***C***$H_2$); ESI-MS: *m/z* Calculated for $C_{48}H_{38}O_6$: 710.27 $[M]^+$; Found: 710.40 $[M]^+$ (100%), 712.42 $[M + 2]^+$ (36%); Anal. calc. for $C_{48}H_{38}O_6$: C, 81.11%; H, 5.39%; Found: C, 80.78%; H, 5.41%.

### 5.3.4 | 3,3′-(Octane-1,8-diylbis[oxy])bis (2-[[1,1′-biphenyl]-4-yl]-4H-chromen-4-one) 3d

Off white solid; yield 68%; m.p. 148-150°C; IR (KBr) $cm^{-1}$:3064 (aromatic C-H), 2930, 2879 (aliphatic C-H), 1638 (C=O) and 1610 (C=C); UV-Vis (MeOH): $\lambda_{max}$(nm) 302, 245; $^1$H-NMR (500 MHz, DMSO-$d_6$): $\delta$ 8.17 (2H, d, $J_o$ = 8.5 Hz, H-5), 8.11 (4H, td, $J_{m,o}$ = 2.3, 8.7 Hz, H-2′, 6′), 7.91 (4H, d, $J_o$ = 8.6 Hz, H-3′, 5′), 7.83 (4H, td, $J_{m,o}$ = 2.6, 8.6 Hz, H-2″, 6″), 7.78 (2H, td, $J_{m,o}$ = 2.0, 7.0 Hz, H-7), 7.73 (2H, d, $J_o$ = 7.2 Hz, H-8), 7.50 (6H, m, H-3″, 4″, 5″), 7.44 (2H, dd, $J_{m,o}$ = 1.6, 7.0 Hz, H-6), 4.04 (4H, t, $J_{vic}$ = 6.0 Hz, OC***H₂***), 1.68 (4H, quintet, $J_{vic}$ = 6.8 Hz, $OCH_2C$***H₂***), 1.42 (4H, m, $OCH_2CH_2C$***H₂***), 1.33 (4H, m, $OCH_2CH_2CH_2C$***H₂***); $^{13}$C-NMR (125 MHz, $CDCl_3$): $\delta$ 175.62 (***C***=O), 155.87 (C-8a), 155.53 (C-2), 143.16 (C-3), 140.38 (C-1′), 133.91 (C-4′), 133.06 (C-1″), 129.77 (C-7), 129.48 (C-2′, 6′), 129.26 (C-3′, 5′), 128.69 (C-2″, 6″), 127.82 (C-3″, 5″), 127.40 (C-4″), 125.59 (C-5), 124.88 (C-4a), 124.23 (C-6), 118.41 (C-8), 71.94 (O***C***$H_2$), 29.02 ($OCH_2$***C***$H_2$), 26.14 ($OCH_2CH_2$***C***$H_2$), 22.82 ($OCH_2CH_2CH_2$***C***$H_2$); ESI-MS: *m/z* Calculated for $C_{50}H_{42}O_6$: 738.30 $[M]^+$; Found: 738.41 $[M]^+$ (96%), 762.38 $[M + Na + 1]^+$ (25%); Anal. calc. for $C_{50}H_{42}O_6$: C, 81.28%; H, 5.73%; Found: C, 81.60%; H, 5.75%.

### 5.3.5 | 3,3′-((1,2-Phenylenebis [methylene])bis(oxy))bis(2-[[1,1′-biphenyl]-4-yl]-4H-chromen-4-one) 3e

Off white solid; yield 75%; m.p. 118-120°C; IR (KBr) $cm^{-1}$:3058, 3028 (aromatic C-H), 2950, 2880 (aliphatic C-H), 1637 (C=O) and 1605 (C=C); UV-Vis (MeOH): $\lambda_{max}$(nm) 304, 236; $^1$H-NMR (500 MHz, DMSO-$d_6$): $\delta$ 8.06 (2H, dd, $J_{m,o}$ = 2.5, 7.9 Hz, H-5), 7.93 (4H, dd, $J_{m,o}$ = 2.2, 8.5 Hz, H-2′, 6′), 7.82 (2H, td, $J_{m,o}$ = 2.7, 7.1 Hz, H-7), 7.71 (2H, d, $J_o$ = 8.1 Hz, H-8), 7.63 (4H, dd, $J_{m,o}$ = 2.8, 8.5 Hz, H-3′, 5′), 7.54 (4H, dd, $J_{m,o}$ = 2.6, 8.2 Hz, H-2″, 6″), 7.48 (2H, td, $J_{m,o}$ = 2.4, 7.9 Hz, H-6) 7.43 (8H, m, H-3″, 4″, 5″, 3‴, 6‴), 7.35 (2H, dd, $J_{m,o}$ = 2.2, 8.2 Hz, H-4‴), 5.04 (4H, s, OC***H₂***); $^{13}$C-NMR (125 MHz, $CDCl_3$): $\delta$ 174.90 (***C***=O), 156.14 (C-8a), 155.23 (C-2), 143.04 (C-3), 139.99 (C-1‴, 2‴), 139.85 (C-1′), 135.72 (C-4′), 133.37 (C-1″), 130.69 (C-7), 129.71 (C-2′, 6′), 129.22 (C-3′, 5′), 128.90 (C-2″, 6″), 128.66 (C-3″, 5″), 127.95 (C-3‴, 6‴), 127.04 (C-4″), 126.75 (C-4‴, 5‴), 125.83 (C-5), 124.64 (C-4a), 124.22 (C-6), 117.99 (C-8), 71.27 (O***C***$H_2$); ESI-MS: *m/z* Calculated for $C_{50}H_{34}O_6$: 730.24 $[M]^+$; Found: 731.34 $[M + 1]^+$ (100%), 732.35 $[M + 2]^+$ (52%), 753.33 $[M + Na]^+$ (42%), 754.33 $[M + Na + 1]^+$ (21%); Anal. calc. for $C_{50}H_{34}O_6$: C, 82.18%; H, 4.69%; Found: C, 82.51%; H, 4.71%.

### 5.3.6 | 3,3′-((1,3-Phenylenebis [methylene])bis(oxy))bis(2-[[1,1′-biphenyl]-4-yl]-4H-chromen-4-one) 3f

Off white solid; yield 76%; m.p. 126-128°C; IR (KBr) $cm^{-1}$:3054, 3026 (aromatic C-H), 2950, 2845 (aliphatic C-H), 1635 (C=O) and 1613 (C=C); UV-Vis (MeOH): $\lambda_{max}$(nm) 307, 244; $^1$H-NMR (500 MHz, DMSO-$d_6$): $\delta$ 8.12 (2H, dd, $J_{m,o}$ = 2.3, 7.9 Hz, H-5), 7.99 (4H, d, $J_o$ = 8.3 Hz, H-2′, 6′), 7.84 (2H, td, $J_{m,o}$ = 2.4, 7.2 Hz, H-7), 7.72 (2H, d, $J_o$ = 7.9 Hz, H-8), 7.65 (8H, m, H-3′, 5′, 2″, 6″), 7.58 (6H, m, H-6, 3″, 5″), 7.48 (3H, m, H-4″, 5‴), 7.42 (2H, d, $J_o$ = 7.3 Hz, H-4‴, 6‴), 7.36 (1H, s, H-2‴), 5.28 (4H, s, OC***H₂***); $^{13}$C-NMR (125 MHz, $CDCl_3$): $\delta$ 174.38 (***C***=O), 156.30 (C-8a), 155.82 (C-2), 143.92 (C-3), 140.26 (C-1‴, 3‴), 139.67 (C-1′), 134.45 (C-4′), 133.17 (C-1″), 130.65 (C-7), 129.50 (C-2′, 6′), 129.36 (C-3′, 5′), 129.03 (C-5‴), 128.28 (C-2″, 6″), 127.97 (C-3″, 5″), 127.39 (C-4″), 126.81 (C-4‴, 6‴), 125.76 (C-5), 125.16 (C-2‴), 124.48 (C-4a), 124.06 (C-6), 118.57 (C-8), 72.56 (O***C***$H_2$); ESI-MS: *m/z* Calculated for $C_{50}H_{34}O_6$: 730.24 $[M]^+$; Found: 730.36 $[M]^+$ (100%), 731.36 $[M + 1]^+$ (74%); Anal. calc. for $C_{50}H_{34}O_6$: C, 82.18%; H, 4.69%; Found: C, 81.85%; H, 4.71%.

### 5.3.7 | 3,3′-((1,4-Phenylenebis [methylene])bis(oxy))bis(2-([1,1′-biphenyl]-4-yl)-4H-chromen-4-one 3g

Off white solid; yield 74%; m.p. 132-134°C; IR (KBr) $cm^{-1}$:3052, 3024 (aromatic C-H), 2948, 2883 (aliphatic C-H), 1632 (C=O) and 1609 (C=C); UV-Vis (MeOH): $\lambda_{max}$(nm) 312, 238; $^1$H-NMR (500 MHz, DMSO-$d_6$): $\delta$ 8.17

(2H, dd, $J_{m,o}$ = 2.6, 7.9 Hz, H-5), 8.06 (4H, td, $J_{m,o}$ = 2.4, 8.4 Hz, H-2′, 6′), 7.84 (8H, td, $J_{m,o}$ = 2.3, 7.1 Hz, H-3′, 5′, 2″, 6″), 7.79 (2H, q, $J_o$ = 7.0 Hz, H-7), 7.74 (2H, m, H-8), 7.53 (2H, td, $J_{m,o}$ = 2.4, 7.1 Hz, H-5), 7.45 (6H, m, H-3″, 4″, 5″), 7.40 (4H, s, H-2‴, 3‴, 4‴, 5‴), 5.39 (4H, s, OC***H₂***); $^{13}$C-NMR (125 MHz, $CDCl_3$): $\delta$ 175.22 (***C***=O), 156.49 (C-8a), 155.69 (C-2), 142.88 (C-3), 140.55 (C-1‴, 4‴), 139.32 (C-1′), 135.20 (C-4′), 134.31 (C-1″), 129.94 (C-7), 129.88 (C-2′, 6′), 129.19 (C-3′, 5′), 128.86 (C-2″, 6″), 128.51 (C-3″, 5″), 127.56 (C-4″), 127.42 (C-2‴, 3‴, 5‴, 6‴), 125.63 (C-5), 124.13 (C-4a), 123.81 (C-6), 117.92 (C-8), 72.84 (O***C***H$_2$); ESI-MS: *m/z* Calculated for $C_{50}H_{34}O_6$: 730.24 $[M]^+$; Found: 731.33 $[M + 1]^+$ (56%), 753.30 $[M + Na]^+$ (27%); Anal. calc. for $C_{50}H_{34}O_6$: C, 82.18%; H, 4.69%; Found: C, 81.70%; H, 4.67%.

### 5.3.8 | 3,3′-((Pyridine-2,6-diylbis [methylene])bis(oxy))bis(2-([1,1′-biphenyl]-4-yl)-4H-chromen-4-one) 3h

Light yellow solid; yield 77%; m.p. 179-180°C; IR (KBr) $cm^{-1}$:3062, 3037 (aromatic C-H), 2918, 2854 (aliphatic C-H), 1636 (C=O) and 1601 (C=C); UV-Vis (MeOH): $\lambda_{max}$(nm) 303, 243; $^1$H-NMR (500 MHz, DMSO-$d_6$): $\delta$ 8.13 (3H, m, H-5, 4‴), 7.84 (4H, td, $J_{m,o}$ = 2.7, 8.5 Hz, H-2′, 6′), 7.76 (6H, m, H-7, 3′, 5′), 7.69 (2H, d, $J_m$ = 2.4 Hz, H-8), 7.67 (2H, brs, H-3‴, 5‴), 7.52 (4H, td, $J_{p,o}$ = 0.8, 8.0 Hz, H-2″, 6″), 7.42 (6H, t, $J_o$ = 7.7 Hz, H-3″, 4″, 5″), 7.38 (2H, d, $J_o$ = 7.2 Hz, H-6), 5.16 (4H, s, OC***H₂***); $^{13}$C-NMR (125 MHz, $CDCl_3$): $\delta$ 174.90 (***C***=O), 156.19 (C-8a), 155.92 (C-2), 155.28 (C-2‴, 6‴), 143.29 (C-3), 140.18 (C-1′), 139.95 (C-4′), 137.16 (C-1″), 133.51 (C-4‴), 129.59 (C-7), 129.22 (C-2′, 6′), 128.90 (C-3′, 5′), 127.95 (C-2″, 6″), 127.14 (C-3″, 5″), 126.99 (C-4″), 125.84 (C-5), 124.76 (C-4a), 124.21 (C-3‴, 5‴), 121.64 (C-6), 118.06 (C-8), 74.68 (O***C***H$_2$); ESI-MS: *m/z* Calculated for $C_{49}H_{33}NO_6$: 731.23 $[M]^+$; Found: 732.34 $[M + 1]^+$ (29%), 733.35 $[M + 2]^+$ (15%), 754.33 $[M + Na]^+$ (8%), 755.33 $[M + Na + 1]^+$ (5%); Anal. calc. for $C_{49}H_{33}NO_6$: C, 80.42%; H, 4.55%, N, 1.91%; Found: C, 80.74%; H, 4.53%, N, 1.92%.

## 5.4 | General protocol for the photolysis of bischromones 3(a-h)

The bischromones **3(a-h)** (0.001 mol) were dissolved in dry MeOH (50.0 mL) by taking in pyrex vessel and the dry nitrogen was bubbled through these solutions for 30 min. These solutions were further photoirradiated for 4-6 h by using light from 125-W mercury arc lamp by maintaining the dry $N_2$ atmosphere during these reactions. The TLC plates (hexane/ethyl acetate: 9:1) were utilized to scrutinize the progress of these photoreactions and consumption of their starting materials. The photolysis of **3(a-h)** after the appropriate intervals exhibited the developments of two new photoproducts below the $R_f$ values (TLC) of their starting materials. After the completion of these reactions, the solvent was distilled off under the reduced pressure and the photolysates thus acquired were loaded on silica gel columns (100-200 mesh) stuffed in pure hexane. The elution of columns with hexane-ethyl acetate (1:3) solvent systems afforded two new products which were further crystallizations from $CH_2Cl_2$ to yield the pure bistetracyclic compounds **4(a-h)** and **5(a-h)**.

### 5.4.1 | (4aS,5S)-5-(2-((4aR,5R)-7-Oxo-3-phenyl-2,4a,5,7-tetrahydroisochromeno [4,3-b]chromen-5-yl)ethyl)-3-phenyl-4a,5-dihydroisochromeno[4,3-b]chromen-7 (2H)-one 4a

Light yellow solid; yield 15%; m.p. 182-184°C; IR (KBr) $cm^{-1}$:3058 (aromatic C-H), 2990, 2918, 2896, 2846 (aliphatic C-H), 1644 (C=O) and 1610 (C=C); UV-Vis (MeOH): $\lambda_{max}$(nm) 322, 241; $^1$H-NMR (500 MHz, DMSO-$d_6$): $\delta$ 8.25 (2H, d, $J_o$ = 8.2 Hz, H-8), 7.87 (2H, d, $J_o$ = 7.8 Hz, H-10), 7.57 (4H, m, H-9, 11), 7.45 (4H, d, $J_o$ = 8.2 Hz, H-2′, 6′), 7.40 (6H, td, $J_{p,o}$ = 0.9, 7.9 Hz, H-3′, 4′, 5′), 6.14 (2H, brs, H-1), 6.03 (2H, d, $J_{vic}$ = 3.1 Hz, H-4), 4.30 (2H, d, $J_{5,4a}$ = 12.7 Hz, H-5), 3.66 (2H, m, H-4a), 2.92 (4H, m, H-2a), 1.79 (4H, m, C***H₂***); $^{13}$C-NMR (125 MHz, DMSO-$d_6$): $\delta$ 177.28 (***C***=O), 154.35 (C-11a), 147.23 (C-12a), 142.57 (C-6a), 139.73 (C-7a), 139.30 (C-12b), 133.19 (C-1′), 130.65 (C-3), 129.44 (C-10), 128.08 (C-2′, 6′), 127.89 (C-3′, 5′), 126.73 (C-4′), 126.39 (C-8), 124.23 (C-9), 124.06 (C-1), 121.89 (C-4), 117.47 (C-11), 73.90 (C-5), 40.73 (C-4a), 32.06 (C-2a), 28.79 (***C***H$_2$); ESI-MS: *m/z* Calculated for $C_{46}H_{34}O_6$: 682.24 $[M]^+$; Found: 682.14 $[M]^+$ (100%), 683.14 $[M + 1]^+$ (28%), 705.23 $[M + Na]^+$ (53%); Anal. calc. for $C_{46}H_{34}O_6$: C, 80.92%; H, 5.02%; Found: C, 81.24%; H, 5.04%.

### 5.4.2 | (S)-5-(2-((R)-7-Oxo-3-phenyl-5,7-dihydroisochromeno[4,3-b]chromen-5-yl)ethyl)-3-phenylisochromeno[4,3-b] chromen-7(5H)-one 5a

Brown solid; yield 25%; m.p. 244-246°C; IR (KBr) $cm^{-1}$:3028 (aromatic C-H), 2918, 2846 (aliphatic C-H), 1639 (C=O) and 1599 (C=C); UV-Vis (MeOH): $\lambda_{max}$(nm) 348, 285; $^1$H-NMR (500 MHz, DMSO-$d_6$): $\delta$ 8.13 (2H, d, $J_o$ = 8.0 Hz, H-8), 7.92 (4H, td, $J_{m,o}$ = 2.2, 8.4 Hz, H-1, 2), 7.81 (2H, t, $J_o$ = 7.0 Hz, H-10), 7.74 (4H, m, H-4, 11), 7.63 (4H, d, $J_o$ = 7.8 Hz, H-2′, 6′), 7.56 (2H, td, $J_{m,o}$ = 1.6, 7.1 Hz, H-9), 7.46 (6H, q, $J_o$ = 7.0 Hz, H-3′, 4′, 5′), 4.93

(2H, t, $J_{vic}$ = 6.2 Hz, H-5), 2.04 (4H, m, C***H₂***); $^{13}$C-NMR (125 MHz, $CDCl_3$): $\delta$ 180.78 (***C***=O), 157.23 (C-11a), 156.14 (C-12a), 143.66 (C-6a), 139.92 (C-4a), 139.59 (C-7a), 133.91 (C-12b), 130.38 (C-1′), 129.78 (C-3), 129.46 (C-10), 128.39 (C-4), 128.27 (C-1), 127.91 (C-2), 127.77 (C-2′, 6′), 126.89 (C-3′, 5′), 125.50 (C-8), 124.99 (C-4′), 124.59 (C-9), 117.62 (C-11), 74.45 (C-5), 30.15 (***C***$H_2$); ESI-MS: *m/z* Calculated for $C_{46}H_{30}O_6$: 678.20 $[M]^+$; Found: 678.23 $[M]^+$ (100%), 679.23 $[M + 1]^+$ (63%), 680.23 $[M + 2]^+$ (22%); Anal. calc. for $C_{46}H_{30}O_6$: C, 81.40%; H, 4.46%; Found: C, 81.07%; H, 4.44%.

### 5.4.3 | (4aS,5S)-5-(3-((4aR,5R)-7-Oxo-3-phenyl-2,4a,5,7-tetrahydroisochromeno[4,3-b]chromen-5-yl)propyl)-3-phenyl-4a,5-dihydroisochromeno[4,3-b]chromen-7(2H)-one 4b

Light yellow solid; yield 16%; m.p. 160-162°C; IR (KBr) $cm^{-1}$:3056 (aromatic C-H), 2995, 2916, 2882, 2829 (aliphatic C-H), 1640 (C=O) and 1608 (C=C); UV-Vis (MeOH): $\lambda_{max}$(nm) 326, 236; $^1$H-NMR (500 MHz, DMSO-$d_6$): $\delta$ 8.24 (2H, d, $J_o$ = 7.5 Hz, H-8), 7.88 (2H, d, $J_o$ = 8.1 Hz, H-10), 7.58 (4H, m, H-9, 11), 7.44 (4H, d, $J_o$ = 7.8 Hz, H-2′, 6′), 7.38 (6H, td, $J_{p,o}$ = 0.5, 7.7 Hz, H-3′, 4′, 5′), 6.18 (2H, d, $J_{vic}$ = 2.8 Hz, H-1), 6.00 (2H, d, $J_{vic}$ = 2.8 Hz, H-4), 4.28 (2H, d, $J_{5,4a}$ = 12.4 Hz, H-5), 3.82 (2H, m, H-4a), 2.95 (4H, m, H-2a), 1.76 (4H, m, C***H₂***), 1.48 (2H, quintet, $J_{vic}$ = 6.4 Hz, $CH_2$C***H₂***); $^{13}$C-NMR (125 MHz, DMSO-$d_6$): $\delta$ 177.16 (***C***=O), 155.14 (C-11a), 146.48 (C-12a), 142.39 (C-6a), 139.82 (C-7a), 139.14 (C-12b), 132.26 (C-1′), 130.73 (C-3), 129.86 (C-10), 127.64 (C-2′, 6′), 127.36 (C-3′, 5′), 126.43 (C-4′), 126.19 (C-8), 125.75 (C-9), 124.63 (C-1), 123.40 (C-4), 118.16 (C-11), 73.16 (C-5), 39.28 (C-4a), 32.54 (C-2a), 30.64 (***C***$H_2$), 18.52 ($CH_2$***C***$H_2$); ESI-MS: *m/z* Calculated for $C_{47}H_{36}O_6$: 696.25 $[M]^+$; Found: 696.38 $[M]^+$ (100%), 697.38 $[M + 1]^+$ (38%), 698.38 $[M + 2]^+$ (14%); Anal. calc. for $C_{47}H_{36}O_6$: C, 81.02%; H, 5.21%; Found: C, 81.34%; H, 5.18%.

### 5.4.4 | (S)-5-(3-((R)-7-Oxo-3-phenyl-5,7-dihydroisochromeno[4,3-b]chromen-5-yl)propyl)-3-phenylisochromeno[4,3-b]chromen-7(5H)-one 5b

Brown solid; yield 28%; m.p. 216-218°C; IR (KBr) $cm^{-1}$:3041 (aromatic C-H), 2920, 2845 (aliphatic C-H), 1633 (C=O) and 1603 (C=C); UV-Vis (MeOH): $\lambda_{max}$(nm) 352, 280; $^1$H-NMR (500 MHz, $CDCl_3$): $\delta$ 8.12 (2H, dd, $J_{m,o}$ = 2.6, 8.2 Hz, H-8), 7.94 (4H, d, $J_o$ = 7.7 Hz, H-1, 2), 7.83 (2H, d, $J_o$ = 7.8 Hz, H-10), 7.75 (4H, m, H-4, 11), 7.62 (4H, d, $J_o$ = 7.5 Hz, H-2′, 6′), 7.55 (2H, dd, $J_{m,o}$ = 2.0, 7.2 Hz, H-9), 7.45 (6H, t, $J_o$ = 7.5 Hz, H-3′, 4′, 5′), 4.90 (2H, t, $J_{vic}$ = 6.6 Hz, H-5), 2.00 (4H, m, C***H₂***), 1.58 (2H, quintet, $J_{vic}$ = 6.3 Hz, $CH_2$C***H₂***); $^{13}$C-NMR (125 MHz, $CDCl_3$): $\delta$ 180.34 (***C***=O), 156.82 (C-11a), 155.12 (C-12a), 143.45 (C-6a), 140.58 (C-4a), 139.26 (C-7a), 132.74 (C-12b), 130.44 (C-1′), 129.89 (C-3), 129.21 (C-10), 128.56 (C-4), 128.11 (C-1), 127.53 (C-2), 126.94 (C-2′, 6′), 126.14 (C-3′, 5′), 125.61 (C-8), 124.68 (C-4′), 123.18 (C-9), 118.25 (C-11), 74.23 (C-5), 32.88 (***C***$H_2$), 20.54 ($CH_2$***C***$H_2$); ESI-MS: *m/z* Calculated for $C_{47}H_{32}O_6$: 692.22 $[M]^+$; Found: 692.16 $[M]^+$ (100%), 715.32 $[M + Na]^+$ (44%), 716.32 $[M + Na + 1]^+$ (20%); Anal. calc. for $C_{47}H_{32}O_6$: C, 81.49%; H, 4.66%; Found: C, 81.81%; H, 4.68%.

### 5.4.5 | (4aS,5S)-5-(4-((4aR,5R)-7-Oxo-3-phenyl-2,4a,5,7-tetrahydroisochromeno[4,3-b]chromen-5-yl)butyl)-3-phenyl-4a,5-dihydroisochromeno[4,3-b]chromen-7(2H)-one 4c

Light yellow solid; yield 18%; m.p. 173-175°C; IR (KBr) $cm^{-1}$:3052 (aromatic C-H), 2983, 2912, 2895, 2841 (aliphatic C-H), 1642 (C=O) and 1616 (C=C); UV-Vis (MeOH): $\lambda_{max}$(nm) 331, 244; $^1$H-NMR (500 MHz, $CDCl_3$): $\delta$ 8.26 (2H, dd, $J_{m,o}$ = 2.1, 7.4 Hz, H-8), 7.86 (2H, t, $J_o$ = 7.3 Hz, H-10), 7.60 (4H, m, H-9, 11), 7.46 (4H, d, $J_o$ = 8.0 Hz, H-2′, 6′), 7.41 (6H, m, H-3′, 4′, 5′), 6.16 (2H, brs, H-1), 5.98 (2H, d, $J_{vic}$ = 2.6 Hz, H-4), 4.26 (2H, d, $J_{5,4a}$ = 12.2 Hz, H-5), 3.69 (2H, m, H-4a), 2.89 (4H, m, H-2a), 1.78 (4H, m, C***H₂***), 1.46 (4H, quintet, $J_{vic}$ = 6.2 Hz, $CH_2$C***H₂***); $^{13}$C-NMR (125 MHz, DMSO-$d_6$): $\delta$ 178.36 (***C***=O), 154.22 (C-11a), 146.71 (C-12a), 143.60 (C-6a), 139.65 (C-7a), 139.07 (C-12b), 133.92 (C-1′), 130.40 (C-3), 129.26 (C-10), 128.11 (C-2′, 6′), 127.25 (C-3′, 5′), 126.35 (C-4′), 126.24 (C-8), 125.82 (C-9), 124.54 (C-1), 122.38 (C-4), 118.67 (C-11), 73.68 (C-5), 39.36 (C-4a), 33.82 (C-2a), 30.48 (***C***$H_2$), 26.20 ($CH_2$***C***$H_2$); ESI-MS: *m/z* Calculated for $C_{48}H_{38}O_6$: 710.27 $[M]^+$; Found: 710.38 $[M]^+$ (100%), 733.32 $[M + Na]^+$ (56%); Anal. calc. for $C_{48}H_{38}O_6$: C, 81.11%; H, 5.39%; Found: C, 81.43%; H, 5.41%.

### 5.4.6 | (S)-5-(4-((R)-7-Oxo-3-phenyl-5,7-dihydroisochromeno[4,3-b]chromen-5-yl)butyl)-3-phenylisochromeno[4,3-b]chromen-7(5H)-one 4c

Brown solid; yield 29%; m.p. 238-240°C; IR (KBr) $cm^{-1}$:3026 (aromatic C-H), 2912, 2839 (aliphatic C-H), 1641 (C=O) and 1607 (C=C); UV-Vis (MeOH): $\lambda_{max}$(nm) 349, 288; $^1$H-NMR (500 MHz, DMSO-$d_6$): $\delta$ 8.15 (2H, t, $J_o$ = 7.4 Hz, H-8), 7.91 (4H, dd, $J_{p,o}$ = 0.7, 8.1 Hz, H-1, 2), 7.81 (2H, td, $J_{m,o}$ = 2.2, 7.3 Hz, H-10), 7.76

(4H, m, H-4, 11), 7.64 (4H, t, $J_o$ = 7.6 Hz, H-2′, 6′), 7.58 (2H, dd, $J_{m,o}$ = 1.8, 7.2 Hz, H-9), 7.47 (6H, m, H-3′, 4′, 5′), 4.92 (2H, t, $J_{vic}$ = 6.3 Hz, H-5), 2.03 (4H, m, C***H₂***), 1.56 (4H, quintet, $J_{vic}$ = 6.9 Hz, $CH_2CH_2$***H₂***); $^{13}$C-NMR (125 MHz, $CDCl_3$): δ 181.26 (***C***=O), 156.94 (C-11a), 155.48 (C-12a), 143.13 (C-6a), 139.73 (C-4a), 139.12 (C-7a), 133.19 (C-12b), 129.76 (C-1′), 129.64 (C-3), 129.34 (C-10), 129.02 (C-4), 128.46 (C-1, 2), 127.85 (C-2′, 6′), 126.51 (C-3′, 5′), 125.83 (C-8), 124.48 (C-4′), 123.86 (C-9), 117.91 (C-11), 74.16 (C-5), 32.62 (***C***$H_2$), 28.34 ($CH_2$***C***$H_2$); ESI-MS: *m/z* Calculated for $C_{48}H_{34}O_6$: 706.24 $[M]^+$; Found: 706.40 $[M]^+$ (100%), 708.40 $[M + 2]^+$ (79%); Anal. calc. for $C_{48}H_{34}O_6$: C, 81.57%; H, 4.85%; Found: C, 81.24%; H, 4.87%.

### 5.4.7 | (4aS,5S)-5-(6-((4aR,5R)-7-Oxo-3-phenyl-2,4a,5,7-tetrahydroisochromeno[4,3-b]chromen-5-yl)hexyl)-3-phenyl-4a,5-dihydroisochromeno[4,3-b]chromen-7(2H)-one 4d

Light yellow solid; yield 20%; m.p. 169-171°C; IR (KBr) $cm^{-1}$:3060 (aromatic C-H), 2986, 2920, 2898, 2830 (aliphatic C-H), 1638 (C=O) and 1611 (C=C); UV-Vis (MeOH): $\lambda_{max}$(nm) 329, 232; $^1$H-NMR (500 MHz, DMSO-$d_6$): δ 8.22 (2H, td, $J_{m,o}$ = 2.5, 7.6 Hz, H-8), 7.85 (2H, d, $J_o$ = 7.4 Hz, H-10), 7.59 (4H, m, H-9, 11), 7.47 (4H, t, $J_o$ = 8.3 Hz, H-2′, 6′), 7.37 (6H, dd, $J_{m,o}$ = 2.0, 8.1 Hz, H-3′, 4′, 5′), 6.20 (2H, brs, H-1), 6.02 (2H, d, $J_{vic}$ = 3.2 Hz, H-4), 4.22 (2H, d, $J_{5,4a}$ = 12.0 Hz, H-5), 3.75 (2H, m, H-4a), 2.93 (4H, m, H-2a), 1.75 (4H, m, C***H₂***), 1.49 (4H, quintet, $J_{vic}$ = 6.0 Hz, $CH_2$C***H₂***), 1.42 (4H, m, $CH_2CH_2$C***H₂***); $^{13}$C-NMR (125 MHz, DMSO-$d_6$): δ 178.45 (***C***=O), 155.86 (C-11a), 147.84 (C-12a), 142.29 (C-6a), 139.76 (C-7a), 139.28 (C-12b), 132.54 (C-1′), 129.88 (C-3), 129.75 (C-10), 128.46 (C-2′, 6′), 127.78 (C-3′, 5′), 126.86 (C-4′), 126.36 (C-8), 124.79 (C-9), 124.22 (C-1), 121.15 (C-4), 117.86 (C-11), 73.32 (C-5), 40.58 (C-4a), 32.95 (C-2a), 30.26 (***C***$H_2$), 26.04 ($CH_2$***C***$H_2$), 22.72 ($CH_2CH_2$***C***$H_2$); ESI-MS: *m/z* Calculated for $C_{50}H_{42}O_6$: 738.30 $[M]^+$; Found: 739.18 $[M + 1]^+$ (100%), 762.12 $[M + Na + 1]^+$ (25%); Anal. calc. for $C_{50}H_{42}O_6$: C, 81.28%; H, 5.73%; Found: C, 81.60%; H, 5.75%.

### 5.4.8 | (S)-5-(6-((R)-7-Oxo-3-phenyl-5,7-dihydroisochromeno[4,3-b]chromen-5-yl)hexyl)-3-phenylisochromeno[4,3-b]chromen-7(5H)-one 5d

Brown solid; yield 32%; m.p. 220-222°C; IR (KBr) $cm^{-1}$:3023 (aromatic C-H), 2926, 2850 (aliphatic C-H), 1634 (C=O) and 1600 (C=C); UV-Vis (MeOH): $\lambda_{max}$(nm) 352, 286; $^1$H-NMR (500 MHz, DMSO-$d_6$): δ 8.16 (2H, td, $J_{m,o}$ = 2,3, 7.9 Hz, H-8), 7.93 (4H, m, H-1, 2), 7.88 (2H, t, $J_o$ = 7.3 Hz, H-10), 7.75 (4H, m, H-4, 11), 7.66 (4H, d, $J_o$ = 7.1 Hz, H-2′, 6′), 7.54 (2H, dd, $J_{m,o}$ = 2.3, 7.0 Hz, H-9), 7.44 (6H, t, $J_o$ = 7.4 Hz, H-3′, 4′, 5′), 4.94 (2H, t, $J_{vic}$ = 6.8 Hz, H-5), 2.01 (4H, m, C***H₂***), 1.57 (4H, quintet, $J_{vic}$ = 6.4 Hz, $CH_2$C***H₂***), 1.51 (4H, m, $CH_2CH_2$C***H₂***); $^{13}$C-NMR (125 MHz, $CDCl_3$): δ 180.49 (***C***=O), 157.31 (C-11a), 156.04 (C-12a), 143.24 (C-6a), 139.84 (C-4a), 138.96 (C-7a), 133.67 (C-12b), 129.91 (C-1′), 129.43 (C-3), 129.05 (C-10), 128.96 (C-4), 128.49 (C-1), 127.64 (C-2), 127.43 (C-2′, 6′), 126.68 (C-3′, 5′), 125.22 (C-8), 124.74 (C-4′), 124.19 (C-9), 118.34 (C-11), 74.64 (C-5), 32.50 (***C***$H_2$), 28.18 ($CH_2$***C***$H_2$), 24.74 ($CH_2CH_2$***C***$H_2$); ESI-MS: *m/z* Calculated for $C_{50}H_{38}O_6$: 734.27 $[M]^+$; Found: 735.34 $[M + 1]^+$ (100%), 757.36 $[M + Na]^+$ (33%); Anal. calc. for $C_{50}H_{38}O_6$: C, 81.72%; H, 5.21%; Found: C, 82.04%; H, 5.23%.

### 5.4.9 | (4aS,5R)-5-(2-((4aR,5S)-7-Oxo-3-phenyl-2,4a,5,7-tetrahydroisochromeno[4,3-b]chromen-5-yl)phenyl)-3-phenyl-4a,5-dihydroisochromeno[4,3-b]chromen-7(2H)-one 4e

Light yellow solid; yield 25%; m.p. 194-196°C; IR (KBr) $cm^{-1}$:3063, 3033 (aromatic C-H), 2956, 2918, 2849 (aliphatic C-H), 1635 (C=O) and 1614 (C=C); UV-Vis (MeOH): $\lambda_{max}$(nm) 328, 246; $^1$H-NMR (500 MHz, DMSO-$d_6$): δ 8.26 (2H, d, $J_o$ = 8.1 Hz, H-8), 7.89 (2H, dd, $J_{m,o}$ = 2.0, 7.8 Hz, H-10), 7.72 (2H, d, $J_o$ = 8.4 Hz, H-11), 7.56 (2H, td, $J_{m,o}$ = 2.3, 8.3 Hz, H-9), 7.47 (4H, d, $J_o$ = 8.1 Hz, H-2′, 6′), 7.40 (6H, td, $J_{m,o}$ = 2.0, 7.9 Hz, H-3′, 4′, 5′), 7.35 (2H, d, $J_o$ = 7.3 Hz, H-3‴, 6‴), 7.33 (2H, t, $J_o$ = 7.2 Hz, H-4‴, 5‴), 6.38 (2H, d, $J_{vic}$ = 2.6 Hz, H-1), 5.88 (2H, d, $J_{vic}$ = 2.1 Hz, H-4), 4.99 (2H, d, $J_{5,4a}$ = 12.6 Hz, H-5), 3.64 (2H, m, H-4a), 2.90 (4H, m, H-2a); $^{13}$C-NMR (125 MHz, DMSO-$d_6$): δ 178.07 (***C***=O), 155.92 (C-11a), 146.67 (C-12a), 143.33 (C-6a), 139.68 (C-1‴, 2‴), 139.59 (C-7a), 133.31 (C-12b), 130.19 (C-1′), 129.14 (C-3), 128.39 (C-10), 128.23 (C-3‴, 6‴), 127.02 (C-4‴, 5‴), 126.43 (C-2′, 6′), 126.13 (C-3′, 4′, 5′), 126.08 (C-8), 124.53 (C-9), 124.28 (C-1), 123.16 (C-4), 119.47 (C-11), 74.54 (C-5), 40.92 (C-4a), 34.28 (C-2a); ESI-MS: *m/z* Calculated for $C_{50}H_{34}O_6$: 730.24 $[M]^+$; Found: 730.06 $[M]^+$ (100%), 731.06 $[M + 1]^+$ (58%), 732.06 $[M + 2]^+$ (22%), 754.38 $[M + Na + 1]^+$ (20%); Anal. calc. for $C_{50}H_{34}O_6$: C, 82.18%; H, 4.69%; Found: C, 82.50%; H, 4.71%.

### 5.4.10 | (S)-5-(2-(((R)-7-Oxo-3-phenyl-5,7-dihydroisochromeno[4,3-b]chromen-5-yl)methyl)benzyl)-3-phenylisochromeno[4,3-b]chromen-7(5H)-one 5e

Light brown solid; yield 35%; m.p. 232-234°C; IR (KBr) $cm^{-1}$:3058, 3028 (aromatic C-H), 2946, 2880 (aliphatic

C-H), 1637 (C=O) and 1602 (C=C); UV-Vis (MeOH): $\lambda_{max}$(nm) 350, 289; $^1$H-NMR (500 MHz, DMSO-$d_6$): $\delta$ 8.18 (2H, d, $J_o$ = 8.5 Hz, H-8), 7.93 (4H, td, $J_{m,o}$ = 2.2, 8.4 Hz, H-1, 2), 7.81 (2H, t, $J_o$ = 7.0 Hz, H-10), 7.77 (4H, m, H-4, 11), 7.64 (4H, td, $J_{m,o}$ = 2.3, 8.0 Hz, H-2′, 6′), 7.56 (2H, td, $J_{m,o}$ = 1.3, 7.0 Hz, H-9), 7.45 (6H, m, H-3′, 4′, 5′), 7.37 (2H, dd, $J_{m,o}$ = 2.4, 8.0 Hz, H-3‴, 6‴), 7.33 (2H, t, $J_o$ = 7.2 Hz, H-4‴, 5‴), 5.92 (2H, s, H-5); $^{13}$C-NMR (125 MHz, $CDCl_3$): $\delta$ 181.58 (***C***=O), 155.35 (C-11a), 155.07 (C-12a), 143.91 (C-6a), 140.73 (C-4a), 139.41 (C-7a), 137.74 (C-1‴, 2‴), 133.68 (C-12b), 133.55 (C-3, 1′), 129.52 (C-10), 129.30 (C-4), 128.25 (C-3‴, 6‴), 127.90 (C-4‴, 5‴), 127.17 (C-1, 2), 126.01 (C-2′, 6′), 125.52 (C-3′, 5′), 124.96 (C-8), 124.45 (C-4′), 121.65 (C-9), 118.10 (C-11), 76.48 (C-5); ESI-MS: *m/z* Calculated for $C_{50}H_{30}O_6$: 726.20 $[M]^+$; Found: 727.42 $[M + 1]^+$ (100%), 728.42 $[M + 2]^+$ (52%), 749.18 $[M + Na]^+$ (30%), 750.18 $[M + Na + 1]^+$ (19%); Anal. calc. for $C_{50}H_{30}O_6$: C, 82.63%; H, 4.16%; Found: C, 82.96%; H, 4.18%.

### 5.4.11 | (4aS,5R)-5-(3-((4aR,5S)-7-Oxo-3-phenyl-2,4a,5,7-tetrahydroisochromeno[4,3-b]chromen-5-yl)phenyl)-3-phenyl-4a,5-dihydroisochromeno[4,3-b]chromen-7(2H)-one 4f

Light yellow solid; yield 26%; m.p. 188-190°C; IR (KBr) $cm^{-1}$:3075, 3028 (aromatic C-H), 2940, 2848 (aliphatic C-H), 1646 (C=O) and 1615 (C=C); UV-Vis (MeOH): $\lambda_{max}$(nm) 325, 240; $^1$H-NMR (500 MHz, DMSO-$d_6$): $\delta$ 8.21 (2H, d, $J_o$ = 7.9 Hz, H-8), 7.90 (2H, td, $J_{m,o}$ = 2.2, 7.6 Hz, H-10), 7.73 (2H, t, $J_o$ = 8.2 Hz, H-11), 7.55 (2H, dd, $J_{m,o}$ = 2.4, 7.0 Hz, H-9), 7.49 (5H, m, H-2′, 6′, 5‴), 7.42 (6H, dd, $J_{m,o}$ = 2.4, 8.1 Hz, H-3′, 4′, 5′), 7.34 (2H, d, $J_o$ = 7.0 Hz, H-4‴, 6‴), 7.30 (1H, s, H-2‴), 6.32 (2H, brs, H-1), 5.79 (2H, d, $J_{vic}$ = 3.3 Hz, H-4), 4.98 (2H, d, $J_{5,4a}$ = 12.8 Hz, H-5), 3.78 (2H, m, H-4a), 2.79 (4H, m, H-2a); $^{13}$C-NMR (125 MHz, DMSO-$d_6$): $\delta$ 178.56 (***C***=O), 156.76 (C-11a), 146.24 (C-12a), 142.43 (C-6a), 139.68 (C-7a), 138.78 (C-1‴, 3‴), 133.56 (C-12b), 133.03 (C-1′), 130.64 (C-3), 129.51 (C-5‴), 128.98 (C-10), 127.95 (C-2′, 6′), 127.66 (C-3′, 5′), 126.72 (C-4′), 126.39 (C-8), 126.11 (C-4‴, 6‴), 125.19 (C-9), 125.02 (C-2‴), 124.31 (C-1), 122.72 (C-4), 118.24 (C-11), 74.96 (C-5), 39.26 (C-4a), 35.64 (C-2a); ESI-MS: *m/z* Calculated for $C_{50}H_{34}O_6$: 730.24 $[M]^+$; Found: 730.44 $[M]^+$ (100%), 731.44 $[M + 1]^+$ (74%); Anal. calc. for $C_{50}H_{34}O_6$: C, 82.18%; H, 4.69%; Found: C, 81.85%; H, 4.71%.

### 5.4.12 | (S)-5-(3-(((R)-7-Oxo-3-phenyl-5,7-dihydroisochromeno[4,3-b]chromen-5-yl)methyl)benzyl)-3-phenylisochromeno[4,3-b]chromen-7(5H)-one 5f

Light brown solid; yield 37%; m.p. 250-252°C; IR (KBr) $cm^{-1}$:3056, 3022 (aromatic C-H), 2953, 2876 (aliphatic C-H), 1645 (C=O) and 1606 (C=C); UV-Vis (MeOH): $\lambda_{max}$(nm) 354, 284; $^1$H-NMR (500 MHz, $CDCl_3$): $\delta$ 8.16 (2H, dd, $J_{m,o}$ = 2.2, 8.0 Hz, H-8), 7.95 (4H, m, H-1, 2), 7.84 (2H, d, $J_o$ = 7.2 Hz, H-10), 7.76 (4H, m, H-4, 11), 7.69 (4H, d, $J_o$ = 8.2 Hz, H-2′, 6′), 7.54 (2H, dd, $J_{m,o}$ = 2.4, 7.3 Hz, H-9), 7.47 (7H, m, H-3′, 4′, 5′, 5‴), 7.38 (2H, d, $J_o$ = 7.6 Hz, H-4‴, 6‴), 7.32 (1H, s, H-2‴), 5.91 (2H, s, H-5); $^{13}$C-NMR (125 MHz, $CDCl_3$): $\delta$ 180.16 (***C***=O), 156.20 (C-11a), 155.33 (C-12a), 143.72 (C-6a), 139.98 (C-4a), 139.01 (C-7a), 138.67 (C-1‴, 3‴), 132.86 (C-12b), 130.18 (C-1′), 129.66 (C-3), 129.34 (C-10), 129.23 (C-4), 129.16 (C-5‴), 128.46 (C-1), 127.13 (C-2), 126.84 (C-2′, 6′), 126.29 (C-3′, 5′), 126.03 (C-4‴, 6‴), 125.33 (C-8), 125.21 (C-2‴), 124.89 (C-4′), 123.38 (C-9), 119.41 (C-11), 76.52 (C-5); ESI-MS: *m/z* Calculated for $C_{50}H_{30}O_6$: 726.20 $[M]^+$; Found: 726.04 $[M]^+$ (100%), 727.04 $[M + 1]^+$ (86%); Anal. calc. for $C_{50}H_{30}O_6$: C, 82.63%; H, 4.16%; Found: C, 82.96%; H, 4.14%.

### 5.4.13 | (4aS,5R)-5-(4-((4aR,5S)-7-Oxo-3-phenyl-2,4a,5,7-tetrahydroisochromeno[4,3-b]chromen-5-yl)phenyl)-3-phenyl-4a,5-dihydroisochromeno[4,3-b]chromen-7(2H)-one 4g

Light yellow solid; yield 28%; m.p. 164-166°C; IR (KBr) $cm^{-1}$:3068, 3021 (aromatic C-H), 2954, 2844 (aliphatic C-H), 1643 (C=O) and 1616 (C=C); UV-Vis (MeOH): $\lambda_{max}$(nm) 334, 238; $^1$H-NMR (500 MHz, $CDCl_3$): $\delta$ 8.28 (2H, d, $J_o$ = 8.4 Hz, H-8), 7.86 (2H, dd, $J_{m,o}$ = 2.5, 7.9 Hz, H-10), 7.74 (2H, d, $J_o$ = 8.0 Hz, H-11), 7.59 (2H, td, $J_{m,o}$ = 1.8, 7.6 Hz, H-9), 7.50 (4H, t, $J_o$ = 7.4 Hz, H-2′, 6′), 7.44 (6H, m, H-3′, 4′, 5′), 7.38 (4H, s, H-2‴, 3‴, 4‴, 5‴), 6.30 (2H, brs, H-1), 5.81 (2H, d, $J_{vic}$ = 2.5 Hz, H-4), 5.00 (2H, d, $J_{5,4a}$ = 12.3 Hz, H-5), 3.80 (2H, m, H-4a), 2.82 (4H, m, H-2a); $^{13}$C-NMR (125 MHz, DMSO-$d_6$): $\delta$ 178.72 (***C***=O), 155.44 (C-11a), 147.65 (C-12a), 143.82 (C-6a), 139.30 (C-7a), 138.66 (C-1‴, 4‴), 133.42 (C-12b), 131.23 (C-1′), 129.75 (C-3), 129.05 (C-10), 127.82 (C-2′, 6′), 127.34 (C-2‴, 3‴, 5‴, 6‴), 126.93 (C-3′, 5′), 126.89 (C-4′), 126.16 (C-8), 124.83 (C-9), 124.09 (C-1), 123.56 (C-4), 119.23 (C-11), 74.64 (C-5), 40.15 (C-4a), 34.39 (C-2a); ESI-MS: *m/z* Calculated for $C_{50}H_{34}O_6$: 730.24 $[M]^+$; Found:

731.36 $[M + 1]^+$ (100%), 732.36 $[M + 2]^+$ (66%); Anal. calc. for $C_{50}H_{34}O_6$: C, 82.18%; H, 4.69%; Found: C, 82.50%; H, 4.67%.

### 5.4.14 | (S)-5-(4-(((R)-7-Oxo-3-phenyl-5,7-dihydroisochromeno[4,3-b]chromen-5-yl)methyl)benzyl)-3-phenylisochromeno[4,3-b]chromen-7(5H)-one 5g

Light brown solid; yield 40%; m.p. 215-217°C; IR (KBr) $cm^{-1}$:3052, 3026 (aromatic C-H), 2958, 2882 (aliphatic C-H), 1632 (C=O) and 1598 (C=C); UV-Vis (MeOH): $\lambda_{max}$(nm) 350, 291; $^1$H-NMR (500 MHz, $CDCl_3$): $\delta$ 8.22 (2H, d, $J_o$ = 8.2 Hz, H-8), 7.99 (4H, dd, $J_{p,o}$ = 0.8, 7.3 Hz, H-1, 2), 7.80 (2H, td, $J_{m,o}$ = 2.8, 7.5 Hz, H-10), 7.75 (4H, m, H-4, 11), 7.67 (4H, dd, $J_{m,o}$ = 2.1, 8.0 Hz, H-2′, 6′), 7.56 (2H, t, $J_o$ = 7.6 Hz, H-9), 7.46 (6H, m, H-3′, 4′, 5′), 7.36 (4H, s, H-2‴, 3‴, 4‴, 5‴), 5.94 (2H, s, H-5); $^{13}$C-NMR (125 MHz, $CDCl_3$): $\delta$ 180.99 (***C***=O), 155.28 (C-11a), 155.04 (C-12a), 143.64 (C-6a), 140.22 (C-4a), 139.85 (C-7a), 137.55 (C-1‴, 4‴), 133.52 (C-12b), 130.55 (C-1′), 129.27 (C-3), 129.08 (C-10), 128.31 (C-4), 127.73 (C-1, 2), 127.59 (C-2′, 6′), 127.26 (C-2‴, 3‴, 5‴, 6‴), 125.73 (C-3′, 5′), 124.97 (C-8), 124.28 (C-4′), 122.97 (C-9), 118.76 (C-11), 76.92 (C-5); ESI-MS: *m/z* Calculated for $C_{50}H_{30}O_6$: 726.20 $[M]^+$; Found: 726.38 $[M]^+$ (100%), 727.38 $[M + 1]^+$ (71%), 728.38 $[M + 2]^+$ (34%); Anal. calc. for $C_{50}H_{30}O_6$: C, 82.63%; H, 4.16%; Found: C, 82.96%; H, 4.18%.

### 5.4.15 | (4aS,5R)-5-(6-((4aR,5S)-7-Oxo-3-phenyl-2,4a,5,7-tetrahydroisochromeno[4,3-b]chromen-5-yl)pyridine-2-yl)-3-phenyl-4a,5-dihydroisochromeno[4,3-b]chromen-7(2H)-one 4h

Light yellow solid; yield 30%; m.p. 200-202°C; IR (KBr) $cm^{-1}$:3062, 3015 (aromatic C-H), 2938, 2850 (aliphatic C-H), 1635 (C=O) and 1613 (C=C); UV-Vis (MeOH): $\lambda_{max}$(nm) 324, 243; $^1$H-NMR (500 MHz, DMSO-$d_6$): $\delta$ 8.26 (3H, m, H-8, 4‴), 7.82 (2H, d, $J_o$ = 7.0 Hz, H-10), 7.75 (2H, td, $J_{m,o}$ = 2.3, 8.0 Hz, H-11), 7.66 (2H, d, $J_o$ = 7.6 Hz, H-3‴, 5‴), 7.56 (2H, m, H-9), 7.46 (4H, d, $J_o$ = 7.7 Hz, H-2′, 6′), 7.40 (6H, t, $J_o$ = 7.7 Hz, H-3′, 4′, 5′), 6.26 (2H, brs, H-1), 5.72 (2H, d, $J_{vic}$ = 3.0 Hz, H-4), 5.08 (2H, d, $J_{5,4a}$ = 12.6 Hz, H-5), 3.85 (2H, m, H-4a), 2.74 (4H, m, H-2a); $^{13}$C-NMR (125 MHz, $CDCl_3$): $\delta$ 179.53 (***C***=O), 156.66 (C-11a), 155.92 (C-2‴, 6‴), 150.59 (C-12a), 142.85 (C-6a), 140.91 (C-7a), 139.38 (C-12b), 137.78 (C-4‴), 133.46 (C-1′), 129.99 (C-3), 129.70 (C-10), 128.91 (C-2′, 6′), 127.97 (C-3′, 5′), 127.58 (C-4′), 126.50 (C-8), 125.59 (C-9), 124.99 (C-3‴, 5‴), 124.62 (C-1), 121.22 (C-4), 116.58 (C-11), 78.03 (C-5), 39.73 (C-4a), 35.72 (C-2a); ESI-MS: *m/z* Calculated for $C_{49}H_{33}NO_6$: 731.23 $[M]^+$; Found: 732.58 $[M + 1]^+$ (100%), 754.46 $[M + Na]^+$ (49%), 755.46 $[M + Na + 1]^+$ (38%); Anal. calc. for $C_{49}H_{33}NO_6$: C, 80.42%; H, 4.55%, N, 1.91%; Found: C, 80.74%; H, 4.57%, N, 1.90%.

### 5.4.16 | (S)-5-((6-(((R)-7-Oxo-3-phenyl-5,7-dihydroisochromeno[4,3-b]chromen-5-yl)methyl)pyridine-2-yl)methyl)-3-phenylisochromeno[4,3-b]chromen-7(5H)-one 5h

Light brown solid; yield 44%; m.p. 228-230°C; IR (KBr) $cm^{-1}$:3058, 3037 (aromatic C-H), 2944, 2879 (aliphatic C-H), 1646 (C=O) and 1605 (C=C); UV-Vis (MeOH): $\lambda_{max}$(nm) 348, 282; $^1$H-NMR (500 MHz, DMSO-$d_6$): $\delta$ 8.27 (2H, dd, $J_{m,o}$ = 2.8, 8.2 Hz, H-8), 7.94 (4H, d, $J_o$ = 8.0 Hz, H-1, 2), 7.83 (2H, td, $J_{m,o}$ = 2.0, 8.6 Hz, H-10), 7.78 (4H, m, H-4, 11), 7.69 (4H, d, $J_o$ = 8.2 Hz, H-2′, 6′), 7.64 (3H, m, H-9, 4‴), 7.57 (6H, dd, $J_{m,o}$ = 2.9, 8.6 Hz, H-3′, 4′, 5′), 7.47 (2H, d, $J_o$ = 8.0 Hz, H-3‴, 5‴), 6.00 (2H, s, H-5); $^{13}$C-NMR (125 MHz, $CDCl_3$): $\delta$ 182.09 (***C***=O), 157.33 (C-11a), 156.35 (C-12a), 155.90 (C-2‴, 6‴), 143.73 (C-6a), 140.56 (C-4a), 140.48 (C-7a), 133.39 (C-12b), 133.23 (C-4‴), 129.83 (C-1′), 129.67 (C-3), 129.21 (C-10), 129.00 (C-4), 128.63 (C-1), 128.27 (C-2), 127.72 (C-2′, 6′), 127.40 (C-3′, 5′), 127.07 (C-4′), 125.88 (C-8), 124.63 (C-9), 124.30 (C-3‴, 5‴), 118.24 (C-11), 80.73 (C-5); ESI-MS: *m/z* Calculated for $C_{49}H_{29}NO_6$: 727.20 $[M]^+$; Found: 728.32 $[M + 1]^+$ (100%), 729.32 $[M + 2]^+$ (28%), 751.14 $[M + Na + 1]^+$ (22%); Anal. calc. for $C_{49}H_{29}NO_6$: C, 80.87%; H, 4.02%, N, 1.92%; Found: C, 80.54%; H, 4.04%, N, 1.93%.

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