Organic & Biomolecular Chemistry

PAPER

Cite this: *Org. Biomol. Chem.*, 2017, **15**, 4554

Divergent synthesis of biflavonoids yields novel inhibitors of the aggregation of amyloid β (1–42)†

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Received 30th March 2017,
Accepted 8th May 2017

DOI: 10.1039/c7ob00804j

rsc.li/obc

Biflavonoids are associated with a variety of biologically useful properties. However, synthetic biflavonoids are poorly explored within drug discovery. There is considerable structural diversity possible within this compound class and large regions of potentially biologically relevant biflavonoid chemical space remain untapped or underexplored. Herein, we report the development of a modular and divergent strategy towards biflavonoid derivatives which enabled the step-economical preparation of a structurally diverse collection of novel unnatural biflavonoids. Preliminary studies established that the strategy could also be successfully extended to the preparation of very rare triflavonoids, which are also expected to be useful tools for biological intervention. Prompted by previous inhibitory studies with flavonoid libraries, amyloid anti-aggregation screening was performed, which led to the identification of several structurally novel inhibitors of the aggregation of the amyloid β peptide ($A\beta_{42}$). Aggregated $A\beta_{42}$ is a pathological hallmark of Alzheimer's disease and the use of small molecules to inhibit the aggregation process has been identified as a potentially valuable therapeutic strategy for disease treatment. Methylated biaurones were associated with highest levels of potency (the most active compound had an IC_{50} value of 16 μM), establishing this scaffold as a starting point for inhibitor development.

Introduction

Biflavonoids are a family of polyphenolic compounds characterised by the presence of two flavonoid units conjoined through an alkyl or alkoxy-based linker.[1] Natural biflavonoids, found in many fruits, vegetables and plants, are associated with a variety of biologically useful properties[1,2] (such as anti-cancer,[3] anti-inflammatory,[4] anti-microbial,[5] anti-viral,[6] anti-clotting,[7] anti-bacterial,[8] anti-fungal[9] and anti-oxidant[10] activities) and in many cases the bioactivity of a biflavonoid is greater than that of the constituent monomer(s)[9,11] (Fig. 1). *Synthetic* biflavonoids have also been found to exhibit interesting biological activities, similar to their aforementioned natural analogues.[1,9,11–13] However, despite these attractive features, synthetic biflavonoids represent a poorly explored compound family within drug discovery.[1] The variation possible in flavonoid units, coupled with a large number of possible permutations in the position and nature of the inter-flavonoid linkage, means that there is considerable structural diversity possible within the biflavonoid compound class.[1] Whilst there exist a number of different approaches for the production of biflavonoids, these typically generate compound collections that are based around a limited range of structures.[1] Indeed, there remain large regions of potentially biologically relevant biflavonoid chemical space that are underexplored.[1,14] Thus, there is a need for new and robust strategies for the generation of collections of unnatural biflavonoids with higher levels of structural diversity so that the biological potential of this compound class can be more fully explored and exploited.[1] Herein, we report the development of a divergent strategy towards biflavonoid derivatives. Application of this strategy enabled the step-economical preparation of a structurally diverse collection of novel biflavonoids, with variation in the nature of both the flavonoid units (substituted aurone and flavone) and linker moiety, from readily-accessible starting materials. In addition, the strategy was also successfully extended to the preparation of very rare triflavonoid analogues, which are also expected to have interesting biological properties. Screening of the library compounds in anti-aggregation assays with amyloid β peptide 1–42 ($A\beta_{42}$), a pathological hallmark of Alzheimer's disease (AD), led to the identification of several structurally novel aggregation inhibitors.[15] The use of small molecules to prevent this aggregation process is considered a potential strategy for the development of new

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†Electronic supplementary information (ESI) available: ThT assay data and ^{1}H and ^{13}C NMR spectra of biflavonoids and triflavonoids. See DOI: 10.1039/c7ob00804j

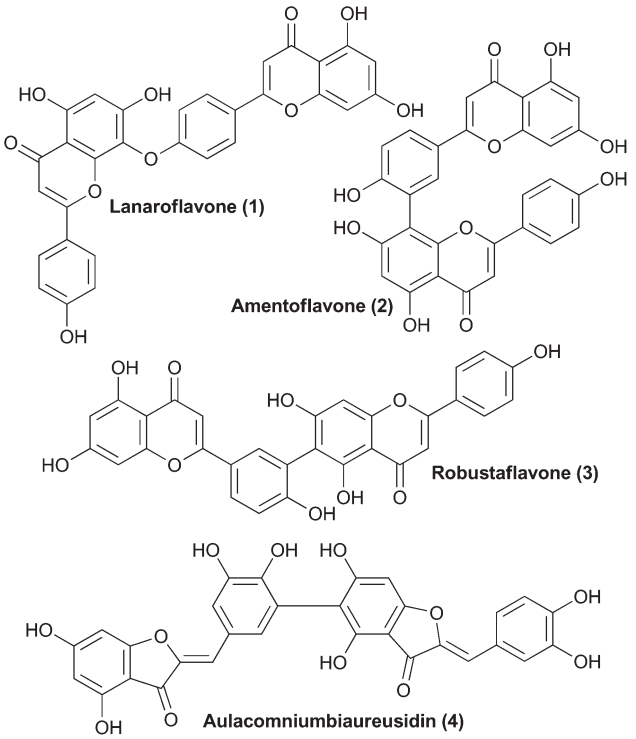


Fig. 1 Examples of naturally occurring biflavonoids. Amongst the *biflavones* (compounds of the general form **8**, see Scheme 1) amentoflavone (**2**) exhibits both anti-fungal and anti-inflammatory activities,[20] robustaflavone (**3**) is a potent inhibitor of the Hepatitis B virus[21] while lanaroflavone (**1**) displays anti-malarial properties.[22] The *biaurone* (a compound of the general form **9**, see Scheme 1) aulacomniumbiaureusidin (**4**) was isolated from *Aulacomnium palustre*.[23]

therapies for AD.[16,17] Of the compounds examined, methylated biaurones were associated with the highest levels of potency; the most active of these had an IC_{50} value comparable to epigallocatechin gallate (EGCG), an AD treatment candidate which has reached phase III clinical trials.[18,19] The methylated biaurone scaffold could therefore represent a potentially valuable starting point for further studies into the development of new inhibitors or probe molecules to target $A\beta_{42}$ aggregation.

Results and discussion

Outline of the divergent synthetic strategy

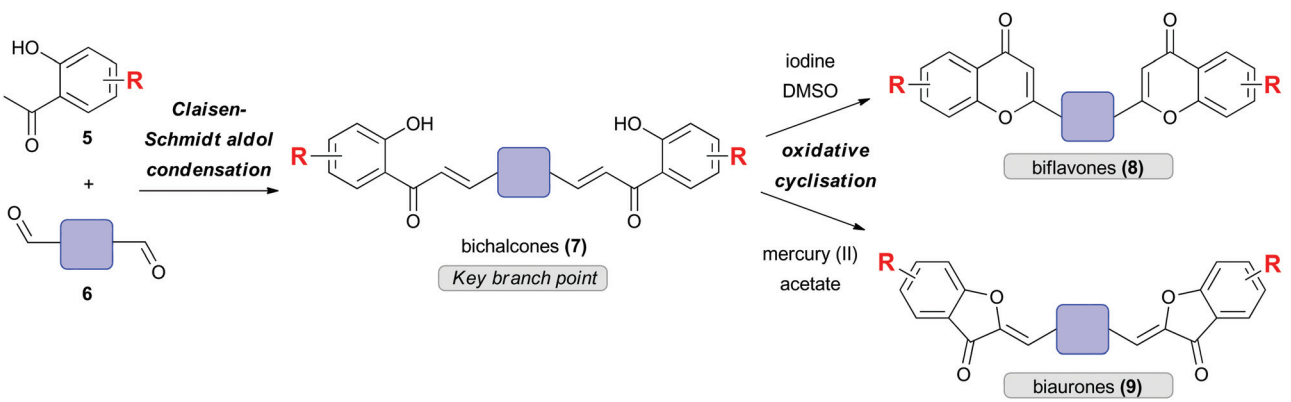
Inspired by our previous studies on flavonoid synthesis,[24,25] we envisaged a divergent strategy for the synthesis of biflavones **8** and biaurones **9** that centered on the use of a bichalcone scaffold **7** as the key branching point (Scheme 1). It was anticipated that application of different oxidative cyclisation methods would provide access to both target dimeric frameworks; iodine-mediated oxidation of **7**[26] would furnish the biflavones **8**, whereas mercury(II) acetate-mediated oxidative cyclisation[27] would yield biaurones **9**. It was presumed that bichalcones **7** could be readily accessed *via* the Claisen–Schmidt aldol condensation[28] between bialdehydes **6** and the corresponding acetophenones **5**.

Divergent synthesis of diverse biflavones and biaurones

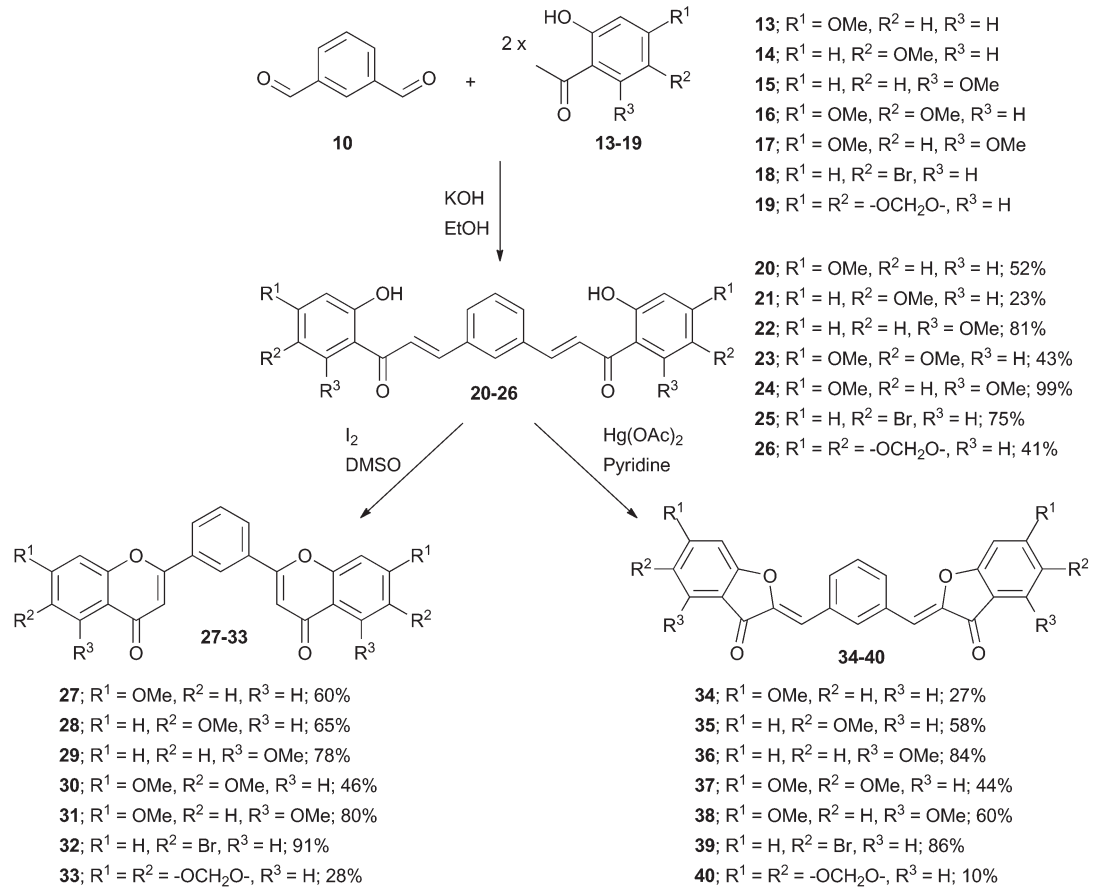
In this study, three commercially available bialdehyde building blocks were selected for use: isophthalaldehyde (**10**), terephthaldehyde (**11**) and 4,4′-biphenyldicarboxaldehyde (**12**). These were combined with a range of acetophenone derivatives to yield bichalcones, which could then be readily converted into the desired biflavones and biaurones by oxidative cyclisation (Schemes 2–4). Yields at each stage were generally moderate-to-good. Overall, this route enabled concise, modular and step-efficient access to a library of 34 unnatural substituted biflavonoids (17 biflavones and 17 biaurones, 29 of which are previously unreported) based around a diverse range of structures from a small set of readily available building blocks. Crucially, variation in the substitution pattern around the flavonoid units and the position and nature of the aryl linkage unit between them was achieved. The library compounds contain potential biomolecular-interacting elements (for example, hydrogen-bonding groups) and several compounds contain an aryl-bromide group, which could provide a synthetic handle for further elaboration or diversification.

Preliminary studies into the synthesis of triflavonoids

We were interested in the possibility that our divergent approach could be extended to the preparation of triflavonoids.



Scheme 1 Outline of divergent synthetic strategies towards biflavones and biaurones.



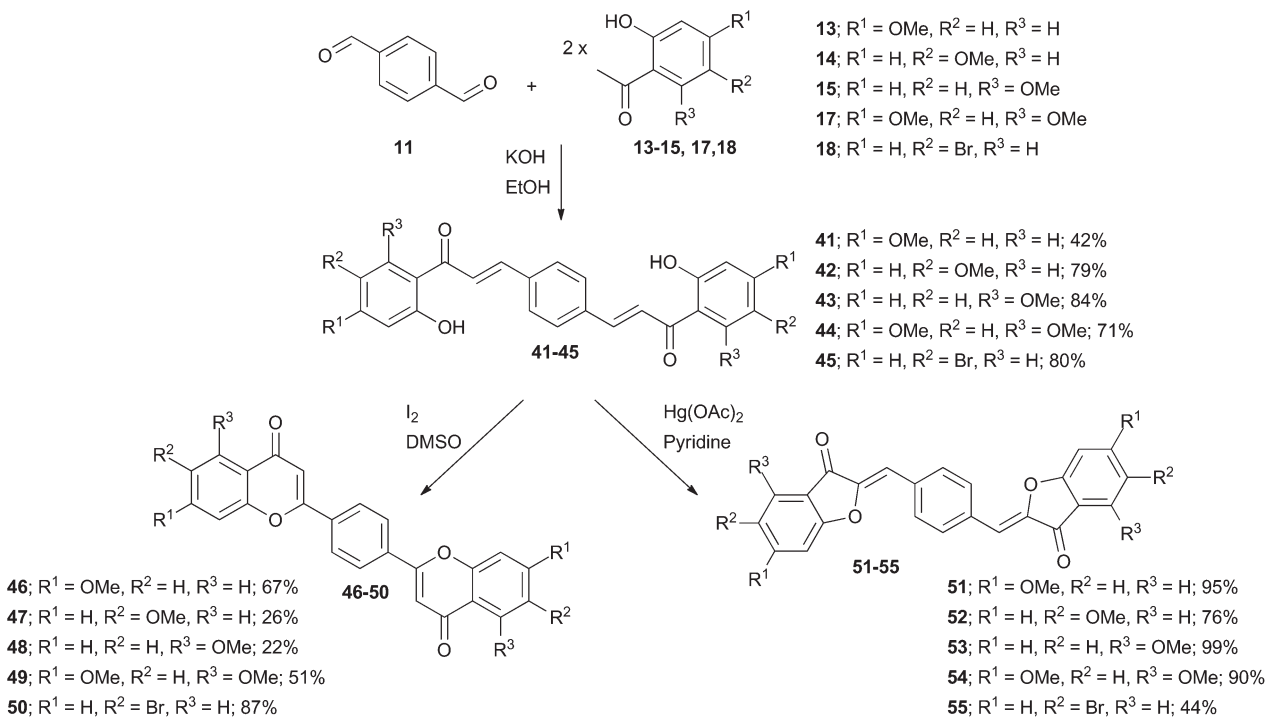
13; R^1 = OMe, R^2 = H, R^3 = H
14; R^1 = H, R^2 = OMe, R^3 = H
15; R^1 = H, R^2 = H, R^3 = OMe
16; R^1 = OMe, R^2 = OMe, R^3 = H
17; R^1 = OMe, R^2 = H, R^3 = OMe
18; R^1 = H, R^2 = Br, R^3 = H
19; R^1 = R^2 = -OCH_2O-, R^3 = H

20; R^1 = OMe, R^2 = H, R^3 = H; 52%
21; R^1 = H, R^2 = OMe, R^3 = H; 23%
22; R^1 = H, R^2 = H, R^3 = OMe; 81%
23; R^1 = OMe, R^2 = OMe, R^3 = H; 43%
24; R^1 = OMe, R^2 = H, R^3 = OMe; 99%
25; R^1 = H, R^2 = Br, R^3 = H; 75%
26; R^1 = R^2 = -OCH_2O-, R^3 = H; 41%

27; R^1 = OMe, R^2 = H, R^3 = H; 60%
28; R^1 = H, R^2 = OMe, R^3 = H; 65%
29; R^1 = H, R^2 = H, R^3 = OMe; 78%
30; R^1 = OMe, R^2 = OMe, R^3 = H; 46%
31; R^1 = OMe, R^2 = H, R^3 = OMe; 80%
32; R^1 = H, R^2 = Br, R^3 = H; 91%
33; R^1 = R^2 = -OCH_2O-, R^3 = H; 28%

34; R^1 = OMe, R^2 = H, R^3 = H; 27%
35; R^1 = H, R^2 = OMe, R^3 = H; 58%
36; R^1 = H, R^2 = H, R^3 = OMe; 84%
37; R^1 = OMe, R^2 = OMe, R^3 = H; 44%
38; R^1 = OMe, R^2 = H, R^3 = OMe; 60%
39; R^1 = H, R^2 = Br, R^3 = H; 86%
40; R^1 = R^2 = -OCH_2O-, R^3 = H; 10%

Scheme 2 Divergent synthesis using bialdehdye **10** as building block.



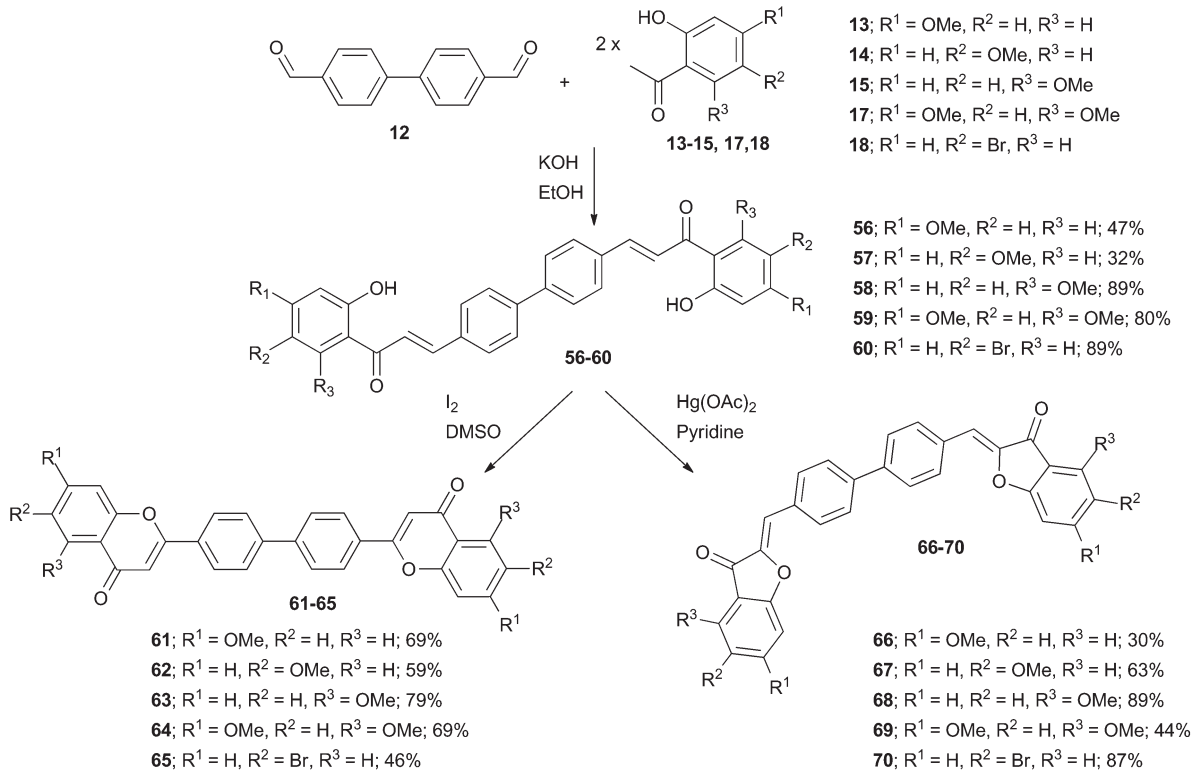
13; R^1 = OMe, R^2 = H, R^3 = H
14; R^1 = H, R^2 = OMe, R^3 = H
15; R^1 = H, R^2 = H, R^3 = OMe
17; R^1 = OMe, R^2 = H, R^3 = OMe
18; R^1 = H, R^2 = Br, R^3 = H

41; R^1 = OMe, R^2 = H, R^3 = H; 42%
42; R^1 = H, R^2 = OMe, R^3 = H; 79%
43; R^1 = H, R^2 = H, R^3 = OMe; 84%
44; R^1 = OMe, R^2 = H, R^3 = OMe; 71%
45; R^1 = H, R^2 = Br, R^3 = H; 80%

46; R^1 = OMe, R^2 = H, R^3 = H; 67%
47; R^1 = H, R^2 = OMe, R^3 = H; 26%
48; R^1 = H, R^2 = H, R^3 = OMe; 22%
49; R^1 = OMe, R^2 = H, R^3 = OMe; 51%
50; R^1 = H, R^2 = Br, R^3 = H; 87%

51; R^1 = OMe, R^2 = H, R^3 = H; 95%
52; R^1 = H, R^2 = OMe, R^3 = H; 76%
53; R^1 = H, R^2 = H, R^3 = OMe; 99%
54; R^1 = OMe, R^2 = H, R^3 = OMe; 90%
55; R^1 = H, R^2 = Br, R^3 = H; 44%

Scheme 3 Divergent synthesis using bialdehdye **11** as building block.



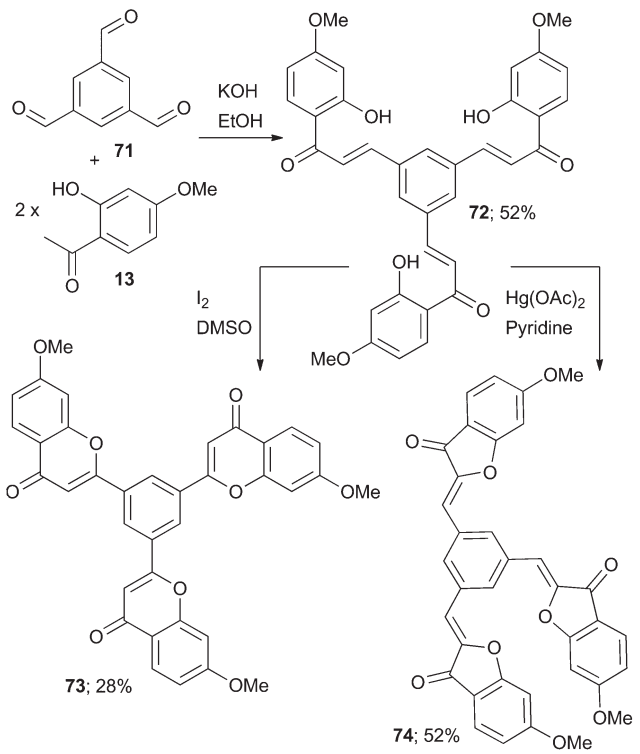
Scheme 4 Divergent synthesis using bialdehdye **12** as building block.

Thus, it was envisaged that the use of tri-aldehyde building blocks would enable access to trichalcones, which could then be divergently converted to triflavones or triaurones by application of iodine- or mercury(II) acetate-based oxidative conditions respectively. As proof-of-principle, we targeted the generation of triflavone **73** and triaurone **74**. These could both be readily accessed from tricarbaldehyde **71** and acetophenone **13** (Scheme 5). This establishes the general feasibility of our approach for the synthesis of triflavonoids, a structurally rare and biologically interesting compound class.

Inhibition of $A\beta_{42}$ aggregation

The inhibitory activity of the compound library against the aggregation of amyloid beta (1–42) ($A\beta_{42}$), a principal neuropathic agent in Alzheimer's disease (AD),[15] was investigated. Although inhibition of $A\beta_{42}$ aggregation has long been acknowledged as a promising strategy for the development of AD therapeutics,[16] drug candidates have frequently failed in clinical trials,[29,30] so the need for further candidates remains. A variety of chalcone and flavonoid derivatives,[31–33] as well as several naturally occurring biflavonoids,[11] have shown amyloid anti-aggregation activity, thereby prompting investigation of the inhibitory effects of our biflavonoid library.

A Thioflavin T (ThT) assay was used to assess the anti-aggregation activity of the library compounds (Fig. 2A). An enhancement in fluorescence intensity of this dye is observed upon binding to amyloid fibrils, giving a characteristic time course of amyloid aggregation (Fig. 2A) in association with fibril



Scheme 5 Divergent synthesis of triflavone **73** and triaurone **74**.

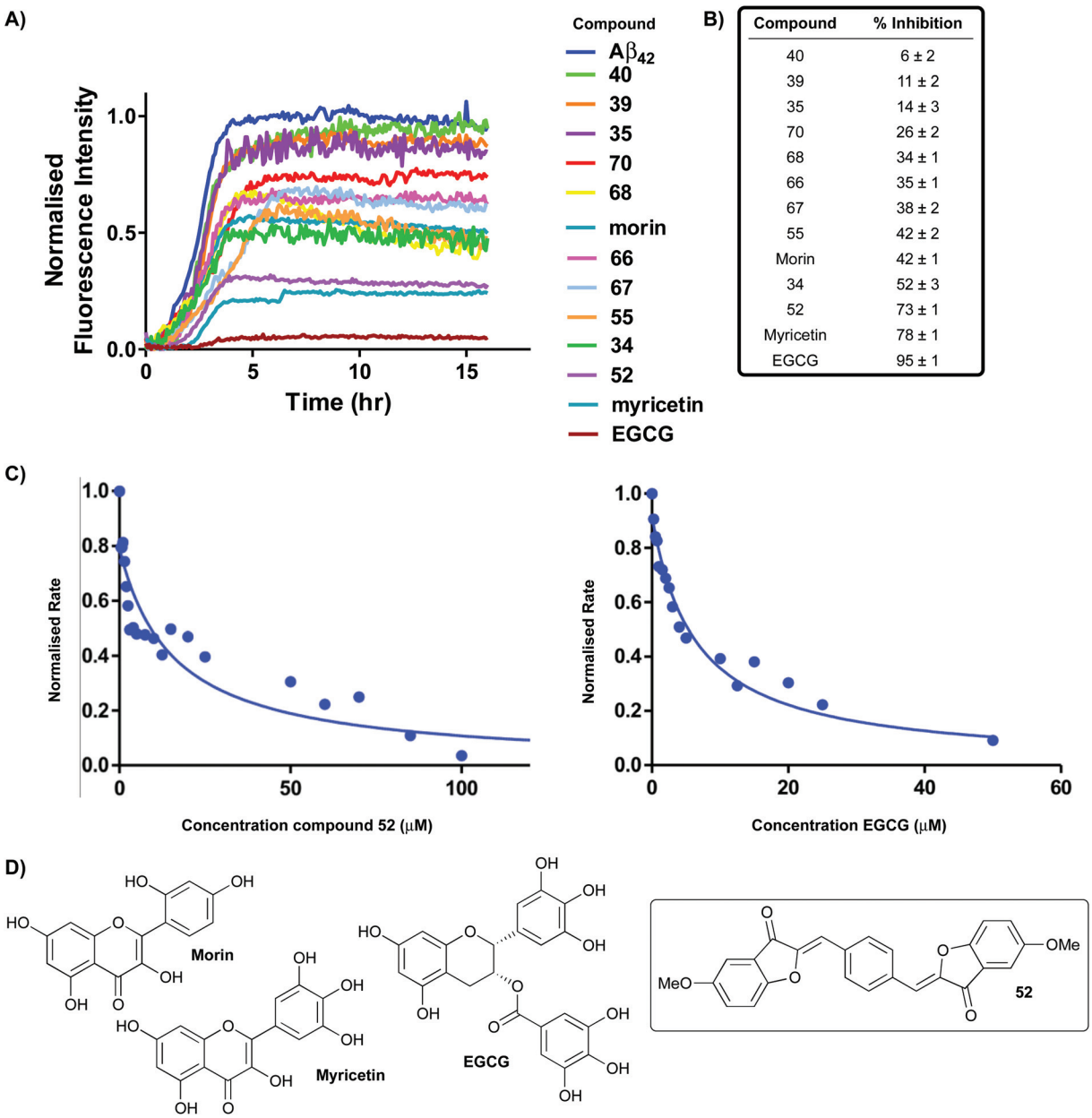


Fig. 2 (A) $A\beta_{42}$ aggregation profiles with the addition of biflavonoids, by means of ThT fluorescence. The curve for $A\beta_{42}$ (blue) represents the time course of $A\beta_{42}$ aggregation (initial concentration of 10 μM $A\beta_{42}$ peptide) in the absence of inhibitors. Inhibited aggregation is observed with the addition of small molecules (concentration of 50 μM). See the Experimental Section for full details. Data represent the average results of three independent biological repeats. (B) Percentage inhibition of $A\beta_{42}$ aggregation achieved by a selection of the biaurones (50 μM concentration), morin, myricetin and EGCG relative to that of $A\beta_{42}$ alone (10 μM), calculated from the saturation phase of the $A\beta_{42}$ aggregation profiles shown in panel (A). 100% represents complete aggregation inhibition and 0% shows no inhibition. (C) Variation in aggregation rate with compound concentration for compound **52** and EGCG. IC_{50} values calculated by taking the slope of the ThT aggregation curve (as in panel A) to represent the aggregation rate. The aggregation rate with a range of inhibitor concentrations (0.5 to 100 μM) was plotted using GraphPad®. (D) Structures of the reference chalcones used in the ThT fluorescence assay and **52**, the most active compound identified in this study.

formation. Changes in the aggregation kinetics and final fluorescence intensity value, upon addition of small molecules, are indicative of inhibitory or modulatory effects on the aggregation process. Of the 34 compounds examined, 24 were either inactive, insoluble or overly fluorescent under the assay conditions (see ESI† for details). For 10 compounds the aggregation time courses could be recorded (Fig. 2A) and the methylated biaurones were observed to show the greatest inhibitory activities. For reference three chalcone derivatives known to exert an inhibitory effect, EGCG,[34,35] myricetin[36,37] and morin,[38] were assayed simultaneously, and their percentage inhibition values are shown in Fig. 2B.

Compound **52** was found to be the most potent, with an inhibitory activity comparable to that of myricetin and greater than that of morin (Fig. 2B, structures shown in Fig. 2D). An IC_{50} value of 15.8 ± 3.7 μM was calculated based on the concentration dependence of inhibition for **52**. The apparent affinity of biaurone **52** was comparable to that measured for the phase III clinical trial drug EGCG (IC_{50} 6.4 ± 0.7 μM) (Fig. 2C).

All of the biaurone derivatives examined have the same general structure, being composed of two aurone ring systems connected through a linker moiety. Reinke and Gestwicki have previously reported a structure–activity relationship (SAR) study on amyloid-beta aggregation inhibition by a structurally related series of compounds that contain two interconnected phenyl ring systems.[39] They postulated that there are two docking sites on the Aβ surface that can accommodate the aromatic end groups of such ligands and it was found that compound activity was affected by the substitution pattern of the aromatic ring systems and the length and flexibility of the linker region. Our screening data for the biaurones is broadly consistent with these observations. For more detailed structure–activity information the number of compounds tested is too small. However, based on the limited evidence available, a *para*-substituted phenyl linker is consistently associated with higher levels of inhibitory activity than a *meta*-substituted phenyl linker, with the di-phenyl linker in-between these extremes (compare *e.g.* **35** *vs.* **52** and **67**, and **55** *vs.* **70**). It is not readily apparent why all biflavones were largely inactive in the ThT assay. Several biaurones were better inhibitors than their biflavone equivalents (that is, biflavones incorporating the same linker moiety and the same substituents around the aromatic end groups; compare *e.g.* **52** *vs.* **47**, **55** *vs.* **50** and **34** *vs.* **27**). This observation may imply that flavone groups are relatively poorly accommodated by any docking sites on the Aβ surface. Starting from the trends observed here on $Aβ_{42}$ aggregation inhibition in the biaurone series, systematic exploration of the effects identified by Reinke and Gestwicki[39] (namely linker length, flexibility and orientation) may lead to more potent compounds. It would also be interesting to investigate the effects of heteroaromatic linkers upon inhibitory activity and physicochemical properties.

Blood brain barrier (BBB) penetration is an important consideration in Alzheimer's drug research.[40] Thus far, the degree of BBB permeation achieved by **52**, the most potent compound identified in this study, has not been experimentally determined, due to known difficulties in pertaining accurate data.[41] However, comparison of its physiochemical properties with those associated with optimal brain exposure (molecular weight ≤360; topological polar surface area between 40 and 90 $Å^2$; lipophilicity calculated partition coefficient ≤3; number of hydrogen bond donors ≤0.5)[42] suggests that the compound fits a selection of the criteria (molecular weight = 366; topological polar surface area = 52.6; lipophilicity calculated partition coefficient = 4.9–5.6; number of hydrogen bond donors = 0),[43] with scope for improvement in future lead optimisation studies. It is worth noting that such parameters focus on the ability of small molecules to passively diffuse into the brain, whereas other factors such as active or facilitated transport may be at play.[44] In employing these guidelines, BBB permeability can therefore be underestimated, and further experiments would be required to further probe this issue.

Conclusions

Herein, we have reported the successful development of a modular and divergent strategy towards structurally diverse biflavonoid derivatives from readily-accessible bialdehyde and acetophenone building blocks. Our strategy therefore enables the probing of underexplored regions of biflavonoid chemical space, which could facilitate greater exploration and exploitation of the biological potential of this compound class. A total of 34 substituted biflavonoids (17 biflavones and 17 biaurones) based around a diverse range of structures was generated in this study, of which 29 are previously unreported. Conceivably, the synthetic strategy could be applied on a larger scale using a greater range of building blocks. Preliminary studies also demonstrated that this approach could be successfully extended to the preparation of very rare triflavonoid analogues that are also expected to be of biological interest. Amyloid anti-aggregation screening was performed, which led to the identification of several structurally novel inhibitors of the aggregation of $Aβ_{42}$, which has long been acknowledged as a promising strategy for the development of Alzheimer's disease therapeutics.[16] This work adds to the repertoire of inhibitors: all active compounds were biaurones, while biflavones were all found to lack inhibitory properties. Methylated biaurones were associated with the highest levels of potency, highlighting the potential value of this scaffold as a starting point for the development of next-generation inhibitors or probe molecules that target $Aβ_{42}$ aggregation. Notably, one library compound was found to have an IC_{50} value which is comparable to EGCG, an Alzheimer's and Parkinson's disease treatment candidate that reached phase II and III clinical trials.

Experimental section

Chemical synthesis

General information and materials. All reagents and solvents were purchased from commercial sources and used without further purification unless otherwise stated. All the experiments were carried out under a nitrogen atmosphere unless otherwise stated. Melting points were measured using a Büchi B545 melting point apparatus and are uncorrected. Thin layer chromatography (TLC) was performed on precoated Merck silica gel GF_{254} plates. IR spectra were recorded on a PerkinElmer Spectrum One (FT-IR) spectrophotometer. Flash column chromatography was performed on silica gel (230–400 mesh). ^1H NMR and ^{13}C NMR were recorded on a Bruker Avance 500 MHz instrument in $CDCl_3$ and DMSO-d_6. HRMS was recorded on a Micromass Q-TOF mass spectro-

meter or a Waters LCT Premier Time of Flight mass spectrometer.

General procedure A: Synthesis of bichalcones or trichalcone (GP-A). To a stirred solution of KOH (12.0 equiv.) in absolute EtOH (100 mL) cooled to 0 °C in an ice-bath was added dropwise a solution of the corresponding bialdehyde or trialdehyde (1.0 equiv.) and acetophenone (2.0 equiv. or 3.0 equiv.). The reaction mixture was stirred at 0 °C for 1 h and then at room temperature for 72 h under nitrogen or until TLC analysis indicated complete consumption of starting material. The resulting mixture was then poured into ice-water (200 mL) and acidified to pH 3–4 with 3 M HCl. The aqueous solution was extracted with $CHCl_3$ (3 × 100 mL) and the combined organic layer was washed with satd $NaHCO_3$ (2 × 100 mL), brine (2 × 100 mL), dried over anhydrous $MgSO_4$, filtered and the solvent removed under reduced pressure. The crude residue was purified by flash column chromatography over silica or successive recrystallization from hot MeOH or $CHCl_3$ to afford the corresponding bichalcones or trichalcone.

General procedure B: Synthesis of biflavones or triflavone (GP-B). To a stirred solution of the corresponding bichalcone or trichalcone (1.0 equiv.) in DMSO (10 mL) was added iodine (0.1 equiv.). The reaction mixture was stirred at 120 °C for 24 h under a nitrogen atmosphere. The resulting mixture was allowed to cool to room temperature and then poured into ice-water (50 mL). The aqueous solution was extracted with $CHCl_3$ (3 × 50 mL) and the combined organic layer was washed with H_2O (2 × 50 mL), brine (2 × 50 mL), dried over anhydrous $MgSO_4$, filtered and the solvent removed under reduced pressure. The crude residue was purified by flash column chromatography over silica to afford the corresponding biflavones or triflavone.

General procedure C: Synthesis of biaurones or triaurone (GP-C). To a stirred solution of the corresponding bichalcone or trichalcone (1.0 equiv.) in pyridine (10 mL) was added mercury(II) acetate (2.0 equiv. or 3.0 equiv.). The reaction mixture was stirred at 110 °C for 1 h under a nitrogen atmosphere. The resulting mixture was allowed to cool to room temperature and then poured into ice-water (50 mL) and acidified to pH 3–4 with 3 M HCl. The aqueous solution was extracted with $CHCl_3$ (3 × 50 mL) and the combined organic layer was washed with H_2O (2 × 50 mL), brine (2 × 50 mL), dried over anhydrous $MgSO_4$, filtered and the solvent removed under reduced pressure. The crude residue was purified by flash column chromatography over silica and/or recrystallization from $CHCl_3$ or MeOH to afford the corresponding biaurones or triaurone.

Synthesis of bichalcones and trichalcone

(2*E*,2′*E*)-3,3′-(1,3-Phenylene)bis(1-(2-hydroxy-4-methoxyphenyl) prop-2-en-1-one) (20). A mixture of acetophenone **13** (1.28 g, 7.70 mmol), bialdehyde **10** (500 mg, 3.73 mmol) and KOH (2.67 g, 44.7 mmol) in absolute EtOH (100 mL) was reacted according to GP-A. The crude residue was purified by recrystallization from MeOH to afford bichalcone **20** (639 mg, 40%) as a bright yellow powdery solid. **m.p.** 290–292 °C. **TLC** R_f = 0.47 (CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 3003w (C–H str), 2844w (C–H str), 1638m (C=O str), 1620m, 1571s (C=C str), 1507m, 1478w, 1467w, 1444m, 1362s, 1327w, 1302w, 1292w, 1231s, 1219s, 1210s, 1133s, 1019s. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 3.89 (6H, s, 2 × –OCH_3), 6.51–6.55 (4H, m, ArH), 7.52 (1H, t, *J* 8.0 Hz, ArH), 7.64 (2H, d, *J* 15.2 Hz, 2 × –C*H*=CHCO–), 7.72 (2H, d, *J* 7.6 Hz, ArH), 7.87 (2H, d, *J* 8.8 Hz, ArH), 7.89 (1H, br s, ArH), 7.92 (2H, d, *J* 15.6 Hz, 2 × –CH=C*H*CO–), 13.38 (2H, s, 2 × OH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 55.6, 101.1, 107.9, 114.0, 121.4, 128.5, 129.7, 130.1, 131.3, 135.7, 143.3, 166.4, 166.8, 191.5. **LCMS** (ES+) *m*/*z* = 431.2 ($[M + H]^+$, t_r = 5.26 min). **HRMS** (ESI+) *m*/*z* = 431.1486 $[M + H]^+$ found, $C_{26}H_{23}O_6^+$ required 431.1489.

(2*E*,2′*E*)-3,3′-(1,3-Phenylene)bis(1-(2-hydroxy-5-methoxyphenyl) prop-2-en-1-one) (21). A mixture of acetophenone **14** (2.52 g, 15.2 mmol), bialdehyde **10** (1.03 g, 7.68 mmol) and KOH (5.37 g, 95.7 mmol) in absolute EtOH (100 mL) was reacted according to GP-A. The crude residue was purified by flash column chromatography (SiO_2, PE/EtOAc; 5 : 1) to afford bichalcone **21** (750 mg, 23%) as a bright orange fluffy solid. **m.p.** 138–140 °C. **TLC** R_f = 0.48 (PE/EtOAc; 2 : 1). **IR** ν_{max} (neat)/cm^{-1}: 2913w (C–H str), 2834w (C–H str), 1644m (C=O str), 1570s (C=C str), 1485s, 1411w, 1350s, 1278m, 1266m, 1244m, 1222w, 1196s, 1175m, 1165s, 1035m, 1020s. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 3.84 (6H, s, 2 × –OCH_3), 6.96 (2H, d, *J* 9.2 Hz, ArH), 7.14 (2H, dd, *J* 9.2, 3.2 Hz, ArH), 7.34 (2H, d, *J* 2.8 Hz, ArH), 7.49 (1H, t, *J* 7.6 Hz, ArH), 7.59 (2H, d, *J* 15.6 Hz, 2 × –C*H*=CHCO–), 7.69 (2H, dd, *J* 7.6, 1.2 Hz, ArH), 7.82 (1H, br s, ArH), 7.88 (2H, d, *J* 15.2 Hz, 2 × –CH=C*H*CO–), 12.32 (2H, s, 2 × OH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 56.0, 112.7, 119.3, 119.4, 121.0, 124.1, 129.0, 129.6, 130.3, 135.3, 144.2, 151.7, 157.9, 192.9. **LCMS** (ES+) *m*/*z* = 431.2 ($[M + H]^+$, t_r = 2.19 min). **HRMS** (ESI+) *m*/*z* = 431.1486 $[M + H]^+$ found, $C_{26}H_{23}O_6^+$ required 431.1489.

(2*E*,2′*E*)-3,3′-(1,3-Phenylene)bis(1-(2-hydroxy-6-methoxyphenyl) prop-2-en-1-one) (22). A mixture of acetophenone **15** (2.79 g, 16.8 mmol), bialdehyde **10** (1.12 g, 8.35 mmol) and KOH (5.35 g, 95.3 mmol) in absolute EtOH (100 mL) was reacted according to GP-A. The crude residue was purified by recrystallization from MeOH to afford bichalcone **22** (2.93 g, 81%) as a bright yellow-orange powdery solid. **m.p.** 168–170 °C. **TLC** R_f = 0.48 (CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 2940w (C–H str), 2844w (C–H str), 1632s (C=O str), 1608m, 1559s (C=C str), 1476w, 1457s, 1432s, 1347m, 1321w, 1299w, 1276w, 1228s, 1199w, 1182w, 1168m, 1086s, 1034m. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 3.98 (6H, s, 2 × –OCH_3), 6.46 (2H, dd, *J* 8.5, 1.0 Hz, ArH), 6.64 (2H, dd, *J* 8.5, 1.0 Hz, ArH), 7.39 (2H, t, *J* 8.5 Hz, ArH), 7.48 (1H, t, *J* 7.5 Hz, ArH), 7.67 (2H, dd, *J* 7.5, 1.5 Hz, ArH), 7.79 (1H, br s, ArH), 7.82 (2H, d, *J* 15.5 Hz, 2 × –C*H*=CHCO–), 7.90 (2H, d, *J* 16.0 Hz, 2 × –CH=C*H*CO–), 13.08 (2H, s, 2 × OH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 56.0, 101.6, 111.0, 111.9, 128.4, 128.9, 129.5, 129.6, 136.1, 136.1, 141.9, 161.0, 164.9, 194.3. **LCMS** (ES+) *m*/*z* = 431.2 ($[M + H]^+$, t_r = 1.84 min). **HRMS** (ESI+) *m*/*z* = 431.1471 $[M + H]^+$ found, $C_{26}H_{23}O_6^+$ required 431.1489.

(2*E*,2′*E*)-3,3′-(1,3-Phenylene)bis(1-(2-hydroxy-4,5-dimethoxyphenyl)prop-2-en-1-one) (23). A mixture of acetophenone **16**

(1.46 g, 7.44 mmol), bialdehyde **10** (530 mg, 3.95 mmol) and KOH (2.85 g, 50.8 mmol) in absolute EtOH (100 mL) was reacted according to GP-A. The crude residue was purified by recrystallization from MeOH to afford bichalcone **23** (837 mg, 43%) as a bright orange powdery solid. **m.p.** 226–228 °C. **TLC** R_f = 0.46 (PE/EtOAc; 1 : 1). **IR** ν_{max} (neat)/cm^{-1}: 2940w (C–H str), 2830w (C–H str), 1633s (C=O str), 1560s (C=C str), 1510s (C=C str), 1445m, 1436m, 1396s, 1354s, 1277s, 1247m, 1233m, 1203s, 1156s, 1043m, 1028s. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 3.95 (6H, s, 2 × –OCH_3), 3.96 (6H, s, 2 × –OCH_3), 6.53 (2H, s, ArH), 7.27 (2H, s, ArH, overlain by $CDCl_3$), 7.53 (1H, d, *J* 8.0 Hz, ArH), 7.57 (2H, d, *J* 15.2 Hz, 2 × –C*H*=CHCO–), 7.74 (2H, dd, *J* 7.6, 1.2 Hz, ArH), 7.88 (1H, br s, ArH), 7.94 (2H, d, *J* 15.6 Hz, 2 × –CH=C*H*CO–), 13.34 (2H, s, 2 × OH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 56.2, 57.0, 100.9, 110.8, 111.9, 121.4, 129.0, 129.6, 130.0, 135.7, 142.1, 143.4, 157.3, 162.0, 191.1. **LCMS** (ES+) *m*/*z* = 491.3 ([M + H]$^+$, t_r = 2.06 min). **HRMS** (ESI+) *m*/*z* = 491.1723 [M + H]$^+$ found, $C_{28}H_{27}O_8^+$ required 491.1706.

(2*E*,2′*E*)-3,3′-(1,3-Phenylene)bis(1-(2-hydroxy-4,6-dimethoxyphenyl)prop-2-en-1-one) (24). A mixture of acetophenone **17** (2.95 g, 15.0 mmol), bialdehyde **10** (1.07 g, 7.98 mmol) and KOH (5.37 g, 95.7 mmol) in absolute EtOH (100 mL) was reacted according to GP-A. The crude residue was purified by recrystallization from MeOH and $CHCl_3$ to afford bichalcone **24** (3.29 g, 99%) as a bright yellow powdery solid. **m.p.** 250–252 °C. **TLC** R_f = 0.38 (CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 2946w (C–H str), 2847w (C–H str), 1623s (C=O str), 1584s (C=C str), 1552s (C=C str), 1487w, 1452m, 1439m, 1414w, 1344s, 1319w, 1278s, 1218s, 1212s, 1162s, 1113s, 1036m. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 3.86 (6H, s, 2 × –OCH_3), 3.95 (6H, s, 2 × –OCH_3), 5.99 (2H, d, *J* 2.4 Hz, ArH), 6.13 (2H, d, *J* 2.0 Hz, ArH), 7.47 (1H, t, *J* 7.6 Hz, ArH), 7.64 (2H, d, *J* 8.4 Hz, ArH), 7.78 (1H, br s, ArH), 7.80 (2H, d, *J* 16.0 Hz, 2 × –C*H*=CHCO–), 7.94 (2H, d, *J* 15.6 Hz, 2 × –CH=C*H*CO–), 14.23 (2H, s, 2 × OH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 55.6, 56.0, 91.4, 93.8, 106.3, 128.4, 128.7, 129.3, 129.4, 136.3, 141.4, 162.5, 166.4, 168.4, 192.5. **LCMS** (ES+) *m*/*z* = 491.3 ([M + H]$^+$, t_r = 1.91 min). **HRMS** (ESI+) *m*/*z* = 491.1696 [M + H]$^+$ found, $C_{28}H_{27}O_8^+$ required 491.1700.

(2*E*,2′*E*)-3,3′-(1,3-Phenylene)bis(1-(5-bromo-2-hydroxyphenyl)prop-2-en-1-one) (25). A mixture of acetophenone **18** (3.26, 15.2 mmol), bialdehyde **10** (1.07 g, 7.98 mmol) and KOH (5.38 g, 95.9 mmol) in absolute EtOH (100 mL) was reacted according to GP-A. The crude residue was purified by recrystallization from MeOH to afford bichalcone **25** (3.16 g, 75%) as a bright yellow powdery solid. **m.p.** 248–250 °C. **TLC** R_f = 0.65 (CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 2950w (C–H str), 1740w, 1639s (C=O str), 1570s (C=C str), 1468s, 1436w, 1400w, 1356m, 1337m, 1310w, 1291w, 1279w, 1263m, 1232m, 1192s, 1168s, 1084w, 1021m. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 6.98 (2H, d, *J* 8.8 Hz, ArH), 7.56–7.62 (3H, m, ArH), 7.65 (2H, d, *J* 15.6 Hz, 2 × –C*H*=CHCO–), 7.80 (2H, dd, *J* 8.0, 1.6 Hz, ArH), 7.94 (1H, br s, ArH), 8.00 (2H, d, *J* 15.6 Hz, 2 × –CH=C*H*CO–), 8.05 (2H, d, *J* 2.4 Hz, ArH), 12.67 (2H, s, 2 × OH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 110.5, 120.5, 120.7, 121.1, 129.3, 129.9, 130.8, 131.8, 135.3, 139.2, 145.2, 162.5, 192.5. **LCMS** (ES+) *m*/*z* = 528.9 ([M + H]$^+$, t_r = 2.20 min). **HRMS** (ESI+) *m*/*z* = 526.9486 [M + H]$^+$ found, $C_{24}H_{17}O_4Br_2^+$ required 526.9494.

(2*E*,2′*E*)-3,3′-(1,3-Phenylene)bis(1-(6-hydroxybenzo[*d*][1,3]dioxol-5-yl)prop-2-en-1-one) (26). A mixture of acetophenone **19** (1.36 g, 7.55 mmol), bialdehyde **10** (530 mg, 3.95 mmol) and KOH (2.88 g, 51.3 mmol) in absolute EtOH (100 mL) was reacted according to GP-A. The crude residue was purified by flash column chromatography (SiO_2, CH_2Cl_2) to afford bichalcone **26** (747 mg, 41%) as a bright orange powdery solid. **m.p.** 246–248 °C. **TLC** R_f = 0.43 (CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 2921w (C–H str), 1636s (C=O str), 1617s, 1578s (C=C str), 1502m (C=C str), 1477s, 1422s, 1343s, 1264s, 1221s, 1180m, 1168m, 1106s, 1035s. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 6.04 (4H, s, 2 × –OCH_2O–), 6.53 (2H, s, ArH), 7.29 (2H, s, ArH), 7.52 (1H, t, *J* 7.6 Hz, ArH), 7.54 (2H, d, *J* 15.6 Hz, 2 × –C*H*=CHCO–), 7.72 (2H, dd, *J* 7.6, 1.2 Hz, ArH), 7.87 (1H, br s, ArH), 7.92 (2H, d, *J* 15.6 Hz, 2 × –CH=C*H*CO–), 13.76 (2H, s, 2 × OH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 99.0, 102.0, 106.1, 112.5, 121.4, 128.7, 129.7, 130.1, 135.6, 140.7, 143.5, 154.8, 163.9, 191.0. **LCMS** (ES+) *m*/*z* = 459.1 ([M + H]$^+$, t_r = 1.82 min). **HRMS** (ESI+) *m*/*z* = 481.0877 [M + Na]$^+$ found, $C_{26}H_{18}O_8Na^+$ required 481.0894.

(2*E*,2′*E*)-3,3′-(1,4-Phenylene)bis(1-(2-hydroxy-4-methoxyphenyl)prop-2-en-1-one) (41). A mixture of acetophenone **13** (2.52 g, 15.2 mmol), bialdehyde **11** (1.05 g, 7.83 mmol) and KOH (5.40 g, 96.2 mmol) in absolute EtOH (100 mL) was reacted according to GP-A. The crude residue was purified by recrystallization from MeOH to afford bichalcone **41** (1.40 g, 42%) as a bright yellow powdery solid. **m.p.** 264–266 °C. **TLC** R_f = 0.38 (CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 2949w (C–H str), 2848w (C–H str), 1641s (C=O str), 1563s (C=C str), 1513s (C=C str), 1447w, 1421s, 1376s, 1351s, 1312s, 1289s, 1242s, 1223m, 1195m, 1152s, 1035s, 1019s. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 3.89 (6H, s, 2 × –OCH_3), 6.51–6.53 (4H, m, ArH), 7.64 (2H, d, *J* 15.6 Hz, 2 × –C*H*=CHCO–), 7.72 (4H, s, ArH), 7.85 (2H, d, *J* 8.8 Hz, ArH), 7.90 (2H, d, *J* 15.2 Hz, 2 × –CH=C*H*CO–), 13.39 (2H, s, 2 × OH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 55.6, 101.1, 107.9, 114.1, 121.5, 129.1, 131.2, 136.9, 143.1, 166.4, 166.8, 191.5. **LCMS** (ES+) *m*/*z* = 431.2 ([M + H]$^+$, t_r = 1.87 min). These characterisation data are in accordance with that previously reported in the literature.[45]

(2*E*,2′*E*)-3,3′-(1,4-Phenylene)bis(1-(2-hydroxy-5-methoxyphenyl)prop-2-en-1-one) (42). A mixture of acetophenone **14** (2.54 g, 15.3 mmol), bialdehyde **11** (1.05 g, 7.83 mmol) and KOH (5.40 g, 96.2 mmol) in absolute EtOH (100 mL) was reacted according to GP-A. The crude residue was purified by recrystallization from MeOH to afford bichalcone **42** (2.66 g, 79%) as a dark orange powdery solid. **m.p.** 246–248 °C. **TLC** R_f = 0.41 (CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 2961w (C–H str), 2836w (C–H str), 1643m (C=O str), 1568s (C=C str), 1485s, 1416m, 1357m, 1303w, 1286w, 1266s, 1201m, 1175s, 1035m, 1020s. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 3.87 (6H, s, 2 × –OCH_3), 7.01 (2H, d, *J* 9.2 Hz, ArH), 7.18 (2H, dd, *J* 9.2, 3.2 Hz, ArH), 7.38 (2H, d, *J* 2.8 Hz, ArH), 7.67 (2H, d, *J* 15.6 Hz, 2 × –C*H*=CHCO–), 7.75 (4H, s, ArH), 7.94 (2H, d, *J* 15.6 Hz, 2 × –CH=C*H*CO–), 12.31 (2H, s, 2 × OH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 56.2, 113.0, 119.5, 119.6, 121.4, 124.0, 129.2, 136.9, 144.1, 151.8, 158.0,

193.1. **LCMS** (ES+) m/z = 431.2 ($[M + H]^+$, t_r = 1.85 min). These characterisation data are in accordance with that previously reported in the literature.[46]

(2*E*,2′*E*)-3,3′-(1,4-Phenylene)bis(1-(2-hydroxy-6-methoxyphenyl) prop-2-en-1-one) (43). A mixture of acetophenone **15** (2.50 g, 15.0 mmol), bialdehyde **11** (1.02 g, 7.60 mmol) and KOH (5.43 g, 96.8 mmol) in absolute EtOH (100 mL) was reacted according to GP-A. The crude residue was purified by recrystallization from MeOH to afford bichalcone **43** (2.76 g, 84%) as a bright yellow powdery solid. **m.p.** 228–230 °C. **TLC** R_f = 0.43 (CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 2947w (C–H str), 2843w (C–H str), 1634m (C═O str), 1587m (C═C str), 1563s (C═C str), 1476m, 1456m, 1435w, 1418m, 1361m, 1332w, 1238s, 1206m, 1200m, 1168m, 1088s, 1038m. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 3.98 (6H, s, 2 × –OCH_3), 6.45 (2H, dd, J 8.5, 1.0 Hz, ArH), 6.64 (2H, dd, J 8.5, 1.0 Hz, ArH), 7.38 (2H, t, J 8.5 Hz, ArH), 7.66 (4H, s, ArH), 7.80 (2H, d, J 15.5 Hz, 2 × –C*H*═CHCO–), 7.91 (2H, d, J 15.5 Hz, 2 × –CH═C*H*CO–), 13.11 (2H, s, 2 × OH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 56.0, 101.5, 111.0, 111.9, 128.5, 128.9, 136.1, 137.1, 141.7, 161.0, 164.9, 194.2. **LCMS** (ES+) m/z = 431.2 ($[M + H]^+$, t_r = 1.84 min). These characterisation data are in accordance with that previously reported in the literature.[47]

(2*E*,2′*E*)-3,3′-(1,4-Phenylene)bis(1-(2-hydroxy-4,6-dimethoxyphenyl)prop-2-en-1-one) (44). A mixture of acetophenone **17** (2.82 g, 14.4 mmol), bialdehyde **11** (1.05 g, 7.83 mmol) and KOH (5.42 g, 96.6 mmol) in absolute EtOH (100 mL) was reacted according to GP-A. The crude residue was purified by recrystallization from MeOH to afford bichalcone **44** (2.73 g, 71%) as a dull yellow powdery solid. **m.p.** 288–290 °C. **TLC** R_f = 0.34 (CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 2944w (C–H str), 2843w (C–H str), 1619s (C═O str), 1588s (C═C str), 1565s (C═C str), 1489w, 1449w, 1438m, 1415m, 1346s, 1287w, 1216s, 1159s, 1110s, 1033w. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 3.86 (6H, s, 2 × –OCH_3), 3.95 (6H, s, 2 × –OCH_3), 5.99 (2H, d, J 2.4 Hz, ArH), 6.13 (2H, d, J 2.4 Hz, ArH), 7.65 (4H, s, ArH), 7.79 (2H, d, J 15.6 Hz, 2 × –C*H*═CHCO–), 7.96 (2H, d, J 15.6 Hz, 2 × –CH═C*H*CO–), 14.26 (2H, s, 2 × OH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 55.6, 55.9, 91.3, 93.8, 106.4, 128.4, 128.8, 137.2, 141.2, 162.5, 166.4, 168.5, 192.3. **LCMS** (ES+) m/z = 491.2 ($[M + H]^+$, t_r = 1.94 min). **HRMS** (ESI+) m/z = 491.1685 $[M + H]^+$ found, $C_{28}H_{27}O_8^+$ required 491.1700.

(2*E*,2′*E*)-3,3′-(1,4-Phenylene)bis(1-(5-bromo-2-hydroxyphenyl) prop-2-en-1-one) (45). A mixture of acetophenone **18** (3.30 g, 15.3 mmol), bialdehyde **11** (1.09 g, 8.13 mmol) and KOH (5.37 g, 95.7 mmol) in absolute EtOH (100 mL) was reacted according to GP-A. The crude residue was purified by recrystallization from MeOH to afford bichalcone **45** (3.43 g, 80%) as a bright yellow-orange powdery solid. **m.p.** >300 °C. **TLC** R_f = 0.68 (CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 2969w (C–H str), 1738w, 1639s (C═O str), 1568s (C═C str), 1468s, 1415m, 1398w, 1367m, 1336m, 1303w, 1289w, 1269m, 1234w, 1194s, 1086w, 1023s. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 6.98 (2H, d, J 8.8 Hz, ArH), 7.61 (2H, dd, J 8.8, 2.4 Hz, ArH), 7.65 (2H, d, J 15.6 Hz, 2 × –C*H*═CHCO–), 7.79 (4H, s, ArH), 7.97 (2H, d, J 15.6 Hz, 2 × –CH═C*H*CO–), 8.04 (2H, d, J 2.4 Hz, ArH), 12.68 (2H, s, 2 × OH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 110.5, 120.8, 120.8, 121.2, 129.5, 131.8, 136.8, 139.2, 145.0, 162.6, 192.4. **LCMS** (ES–) m/z = 527.0 ($[M - H]^-$, t_r = 2.52 min). These characterisation data are in accordance with that previously reported in the literature.[46]

(2*E*,2′*E*)-3,3′-([1,1′-Biphenyl]-4,4′-diyl)bis(1-(2-hydroxy-4-methoxyphenyl)prop-2-en-1-one) (56). A mixture of acetophenone **13** (1.63 g, 9.81 mmol), bialdehyde **12** (1.02 g, 4.85 mmol) and KOH (3.53 g, 62.9 mmol) in absolute EtOH (100 mL) was reacted according to GP-A. The crude residue was purified by recrystallization from MeOH to afford bichalcone **56** (1.15 g, 47%) as a bright yellow powdery solid. **m.p.** 248–250 °C. **TLC** R_f = 0.41 (CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 2968w (C–H str), 2843w (C–H str), 1635s (C═O str), 1574s (C═C str), 1552m (C═C str), 1508m (C═C str), 1500w, 1432m, 1363s, 1286m, 1216s, 1203s, 1123s, 1025m, 1017m, 1002m. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 3.89 (6H, s, 2 × –OCH_3), 6.50–6.54 (4H, m, ArH), 7.65 (2H, d, J 15.6 Hz, 2 × –C*H*═CHCO–), 7.72 (4H, d, J 8.4 Hz, ArH), 7.77 (4H, d, J 8.4 Hz, ArH), 7.87 (2H, d, J 8.8 Hz, ArH), 7.95 (2H, d, J 15.6 Hz, 2 × –CH═C*H*CO–), 13.45 (2H, s, 2 × OH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 55.6, 101.1, 107.9, 114.1, 120.5, 127.5, 129.2, 131.2, 134.4, 142.1, 143.6, 166.3, 166.8, 191.7. **LCMS** (ES+) m/z = 507.3 ($[M + H]^+$, t_r = 2.04 min). These characterisation data are in accordance with that previously reported in the literature.[48]

(2*E*,2′*E*)-3,3′-([1,1′-Biphenyl]-4,4′-diyl)bis(1-(2-hydroxy-5-methoxyphenyl)prop-2-en-1-one) (57). A mixture of acetophenone **14** (1.60 g, 9.63 mmol), bialdehyde **12** (1.00 g, 4.76 mmol) and KOH (3.46 g, 61.2 mmol) in absolute EtOH (100 mL) was reacted according to GP-A. The crude residue was purified by recrystallization from MeOH to afford bichalcone **57** (780 mg, 32%) as a bright orange powdery solid. **m.p.** 214–216 °C. **TLC** R_f = 0.11 (CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 2970w (C–H str), 2839w (C–H str), 1636m (C═O str), 1568s (C═C str), 1548m (C═C str), 1486s, 1461w, 1410m, 1353s, 1309m, 1275m, 1261s, 1241w, 1180s, 1040m, 1013w, 1002m. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 3.88 (6H, s, 2 × –OCH_3), 7.01 (2H, d, J 8.8 Hz, ArH), 7.18 (2H, dd, J 9.2, 2.8 Hz, ArH), 7.41 (2H, d, J 2.8 Hz, ArH), 7.67 (2H, d, J 15.2 Hz, 2 × –C*H*═CHCO–), 7.74 (4H, d, J 8.4 Hz, ArH), 7.79 (4H, d, J 8.4 Hz, ArH), 7.98 (2H, d, J 15.6 Hz, 2 × –CH═C*H*CO–), 12.38 (2H, s, 2 × OH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 56.2, 113.0, 119.4, 119.7, 120.4, 123.9, 127.6, 129.3, 134.2, 142.4, 144.8, 151.7, 158.0, 193.2. **LCMS** (ES+) m/z = 507.2 ($[M + H]^+$, t_r = 2.00 min). **HRMS** (ESI+) m/z = 529.1607 $[M + Na]^+$ found, $C_{32}H_{26}O_6Na^+$ required 529.1622.

(2*E*,2′*E*)-3,3′-([1,1′-Biphenyl]-4,4′-diyl)bis(1-(2-hydroxy-6-methoxyphenyl)prop-2-en-1-one) (58). A mixture of acetophenone **15** (1.62 g, 9.75 mmol), bialdehyde **12** (1.00 g, 4.76 mmol) and KOH (3.44 g, 61.3 mmol) in absolute EtOH (100 mL) was reacted according to GP-A. The crude residue was purified by recrystallization from MeOH to afford bichalcone **58** (2.14 g, 89%) as a bright yellow-orange powdery solid. **m.p.** 238–240 °C. **TLC** R_f = 0.43 (CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 2939w (C–H str), 2839w (C–H str), 1627m (C═O str), 1577m (C═C str), 1548s (C═C str), 1474m, 1453s, 1433m, 1354s,

1238s, 1199w, 1183s, 1167m, 1089s, 1037m, 1025m, 1003w. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 3.99 (6H, s, 2 × –OCH_3), 6.46 (2H, dd, *J* 8.5, 1.0 Hz, ArH), 6.65 (2H, dd, *J* 8.5, 1.0 Hz, ArH), 7.39 (2H, t, *J* 8.5 Hz, ArH), 7.70 (4H, d, *J* 8.5 Hz, ArH), 7.73 (4H, d, *J* 8.5 Hz, ArH), 7.86 (2H, d, *J* 15.5 Hz, 2 × –C*H*=CHCO–), 7.93 (2H, d, *J* 15.5 Hz, 2 × –CH=C*H*CO–), 13.15 (2H, s, 2 × OH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 56.0, 101.6, 111.0, 112.0, 127.4, 127.8, 129.1, 134.9, 136.0, 141.9, 142.2, 161.0, 164.9, 194.3. **LCMS** (ES+) *m*/*z* = 507.2 ($[M + H]^+$, t_r = 2.00 min). **HRMS** (ESI+) *m*/*z* = 507.1802 $[M + H]^+$ found, $C_{32}H_{27}O_6^+$ required 507.1802.

(2*E*,2′*E*)-3,3′-([1,1′-Biphenyl]-4,4′-diyl)bis(1-(2-hydroxy-4,6-dimethoxyphenyl)prop-2-en-1-one) (59). A mixture of 2-hydroxy-4,6-dimethoxyacetophenone **17** (1.88 g, 9.58 mmol), bialdehyde **12** (1.01 g, 4.80 mmol) and KOH (3.45 g, 61.5 mmol) in absolute EtOH (100 mL) was reacted according to GP-A. The crude residue was purified by recrystallization from MeOH to afford bichalcone **59** (2.17 g, 80%) as a bright yellow powdery solid. **m.p.** 268–270 °C. **TLC** R_f = 0.17 (CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 2938w (C–H str), 2838w (C–H str), 1608s (C=O str), 1579s (C=C str), 1547s (C=C str), 1498w, 1481w, 1440m, 1406m, 1343s, 1295m, 1214s, 1186m, 1153s, 1114s, 1035m, 1023w, 1002w. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 3.86 (6H, s, 2 × –OCH_3), 3.96 (6H, s, 2 × –OCH_3), 6.00 (2H, d, *J* 2.4 Hz, ArH), 6.14 (2H, d, *J* 2.4 Hz, ArH), 7.68–7.73 (8H, m, ArH), 7.84 (2H, d, *J* 15.6 Hz, 2 × –C*H*=CHCO–), 7.97 (2H, d, *J* 15.6 Hz, 2 × –CH=C*H*CO–), 14.31 (2H, br s, 2 × OH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 55.6, 55.9, 91.3, 93.8, 106.4, 127.4, 127.7, 129.0, 135.1, 141.7, 141.7, 162.5, 166.3, 168.5, 192.5. **LCMS** (ES+) *m*/*z* = 567.2 ($[M + H]^+$, t_r = 2.10 min). These characterisation data are in accordance with that previously reported in the literature.[48]

(2*E*,2′*E*)-3,3′-([1,1′-Biphenyl]-4,4′-diyl)bis(1-(5-bromo-2-hydroxyphenyl)prop-2-en-1-one) (60). A mixture of acetophenone **18** (2.12 g, 9.86 mmol), bialdehyde **12** (1.08 g, 5.14 mmol) and KOH (3.50 g, 62.4 mmol) in absolute EtOH (100 mL) was reacted according to GP-A. The crude residue was purified by recrystallization from MeOH to afford bichalcone **60** (2.77 g, 89%) as a bright yellow-orange powdery solid. **m.p.** 258–260 °C. **TLC** R_f = 0.65 (CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 2938w (C–H str), 1738w, 1637s (C=O str), 1563s (C=C str), 1496w, 1465s, 1398m, 1362m, 1335s, 1308m, 1289m, 1279m, 1264m, 1232w, 1179s, 1085w, 1015m, 1003m. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 6.97 (2H, d, *J* 8.8 Hz, ArH), 7.60 (2H, dd, *J* 9.2, 2.4 Hz, ArH), 7.64 (2H, d, *J* 16.0 Hz, 2 × –C*H*=CHCO–), 7.75 (4H, d, *J* 8.4 Hz, ArH), 7.81 (4H, d, *J* 8.4 Hz, ArH), 8.01 (2H, d, *J* 15.6 Hz, 2 × –CH=C*H*CO–), 8.05 (2H, d, *J* 2.4 Hz, ArH), 12.76 (2H, s, 2 × OH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 110.5, 119.6, 120.7, 121.3, 127.7, 129.5, 131.8, 134.0, 139.0, 142.6, 145.8, 162.5, 192.6. **LCMS** (ES–) *m*/*z* = 603.0 ($[M - H]^-$, t_r = 2.42 min). **HRMS** (ESI–) *m*/*z* = 600.9658 $[M - H]^-$ found, $C_{30}H_{19}O_4Br_2^+$ required 600.9656.

(2*E*,2′*E*,2″*E*)-3,3′,3″-(Benzene-1,3,5-triyl)tris(1-(2-hydroxy-4-methoxyphenyl)prop-2-en-1-one) (72). A mixture of 2-hydroxy-4-methoxyacetophenone **13** (1.56 g, 9.39 mmol), benzene-1,3,5-tricarbaldehyde **71** (503 mg, 3.10 mmol) and KOH (2.32 g, 41.3 mmol) in absolute EtOH (100 mL) was reacted according to GP-A. The crude residue was purified by recrystallization from MeOH to afford trichalcone **72** (972 mg, 52%) as a bright yellow powdery solid. **m.p.** 278–280 °C. **TLC** R_f = 0.50 (CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 2926w (C–H str), 2843w (C–H str), 1714w, 1637m (C=O str), 1619m, 1572s (C=C str), 1508m (C=C str), 1443w, 1360s, 1280w, 1265w, 1212s, 1154w, 1128s, 1021m. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 3.90 (9H, s, 3 × –OCH_3), 6.52 (3H, d, *J* 2.4 Hz, ArH), 6.56 (3H, dd, *J* 8.8, 2.4 Hz, ArH), 7.69 (3H, d, *J* 15.2 Hz, 3 × –C*H*=CHCO–), 7.91 (3H, d, *J* 9.2 Hz, ArH), 7.92 (3H, s, ArH), 7.94 (3H, d, *J* 16.0 Hz, 3 × –CH=C*H*CO–), 13.34 (3H, s, 3 × OH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 55.7, 101.1, 108.1, 114.0, 122.4, 129.6, 131.3, 136.5, 142.4, 166.6, 166.9, 191.2. **LCMS** (ES+) *m*/*z* = 607.2 ($[M + H]^+$, t_r = 2.17 min). **HRMS** (ESI+) *m*/*z* = 629.1764 $[M + Na]^+$ found, $C_{36}H_{30}O_9Na^+$ required 629.1782.

Synthesis of biflavones and triflavone

2,2′-(1,3-Phenylene)bis(7-methoxy-4*H*-chromen-4-one) (27). A mixture of bichalcone **20** (207 mg, 0.482 mmol) and I_2 (81.2 mg, 0.314 mmol) in DMSO (10 mL) was reacted according to GP-B. The crude residue was purified by flash column chromatography (SiO_2, 1–5% MeOH/CH_2Cl_2) to afford biflavone **27** (123 mg, 60%) as a pale yellow-white powdery solid. **m.p.** 288–290 °C. **TLC** R_f = 0.31 (5% MeOH/CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 2931w (C–H str), 2838w (C–H str), 1626s (C=O str), 1602s, 1578m (C=C str), 1501w (C=C str), 1481w, 1436s, 1373m, 1359s, 1276w, 1260m, 1235w, 1202w, 1164m, 1128w, 1088m, 1037w, 1026m. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 3.98 (6H, s, 2 × –OCH_3), 6.87 (2H, s, 2 × –C=CH), 7.00–7.02 (4H, m, ArH), 7.67 (1H, t, *J* 8.0 Hz, ArH), 8.03 (2H, dd, *J* 8.0, 1.2 Hz, ArH), 8.13 (2H, d, *J* 8.4 Hz, ArH), 8.41 (1H, br s, ArH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 56.0, 100.3, 108.1, 114.9, 117.7, 123.6, 127.0, 128.6, 129.8, 132.8, 158.0, 161.6, 164.4, 177.6. **LCMS** (ES+) *m*/*z* = 427.2 ($[M + H]^+$, t_r = 1.75 min). **HRMS** (ESI+) *m*/*z* = 427.1161 $[M + H]^+$ found, $C_{26}H_{19}O_6^+$ required 427.1176.

2,2′-(1,3-Phenylene)bis(6-methoxy-4*H*-chromen-4-one) (28). A mixture of bichalcone **21** (203 mg, 0.472 mmol) and I_2 (30.6 mg, 0.121 mmol) in DMSO (10 mL) was reacted according to GP-B. The crude residue was purified by flash column chromatography (SiO_2, 1–10% MeOH/CH_2Cl_2) to afford biflavone **28** (131 mg, 65%) as a pale yellow-white powdery solid. **m.p.** >300 °C. **TLC** R_f = 0.36 (5% MeOH/CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 3075w (C–H str), 2834w (C–H str), 1630s (C=O str), 1611s, 1578m (C=C str), 1565m (C=C str), 1484s, 1464s, 1434m, 1362s, 1293m, 1281m, 1244m, 1205s, 1132w, 1079m, 1023s. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 3.95 (6H, s, 2 × –OCH_3), 6.93 (2H, s, 2 × –C=CH), 7.36 (2H, dd, *J* 9.0, 3.0 Hz, ArH), 7.59 (2H, d, *J* 9.0 Hz, ArH), 7.63 (2H, d, *J* 3.0 Hz, ArH), 7.71 (1H, t, *J* 8.0 Hz, ArH), 8.08 (2H, dd, *J* 8.0, 2.0 Hz, ArH), 8.49 (1H, t, *J* 1.5 Hz, ArH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 56.0, 104.9, 107.5, 119.6, 123.9, 124.1, 124.6, 128.9, 129.9, 133.0, 151.1, 157.2, 161.9, 178.2. **LCMS** (ES+) *m*/*z* = 427.2 ($[M + H]^+$, t_r = 1.96 min). **HRMS** (ESI+) *m*/*z* = 427.1168 $[M + H]^+$ found, $C_{26}H_{19}O_6^+$ required 427.1176.

2,2′-(1,3-Phenylene)bis(5-methoxy-4*H*-chromen-4-one) (29). A mixture of bichalcone **22** (307 mg, 0.714 mmol) and I_2

(33.8 mg, 0.133 mmol) in DMSO (10 mL) was reacted according to GP-B. The crude residue was purified by flash column chromatography (SiO_2, 1–5% MeOH/CH_2Cl_2) to afford biflavone **29** (237 mg, 78%) as a white powdery solid. **m.p.** >300 °C. **TLC** R_f = 0.55 (10% MeOH/CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 3019w (C–H str), 2842w (C–H str), 1633s (C=O str), 1600s (C=C str), 1568m (C=C str), 1477s, 1459m, 1437m, 1382s, 1316s, 1267s, 1214m, 1191w, 1089s, 1072m, 1042m, 1026s. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 4.04 (6H, s, 2 × –OCH_3), 6.85 (2H, s, 2 × –C=CH), 6.88 (2H, d, J 8.4 Hz, ArH), 7.23 (2H, d, J 8.4 Hz, ArH), 7.62–7.70 (3H, m, ArH), 8.04 (2H, dd, J 8.0, 1.6 Hz, ArH), 8.44 (1H, br s, ArH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 56.6, 106.7, 109.8, 110.2, 114.6, 123.5, 128.7, 129.8, 132.5, 134.1, 158.3, 159.8, 159.9, 178.2. **LCMS** (ES+) m/z = 427.1 ($[M + H]^+$, t_r = 1.49 min). **HRMS** (ESI+) m/z = 427.1164 $[M + H]^+$ found, $C_{26}H_{19}O_6^+$ required 427.1176.

2,2′-(1,3-Phenylene)bis(6,7-dimethoxy-4*H*-chromen-4-one) (30). A mixture of bichalcone **23** (61.6 mg, 0.126 mmol) and I_2 (21.1 mg, 0.0831 mmol) in DMSO (10 mL) was reacted according to GP-B. The crude residue was purified by flash column chromatography (SiO_2, 1–5% MeOH/CH_2Cl_2) to afford biflavone **30** (28.3 mg, 46%) as a pale yellow-white powdery solid. **m.p.** >300 °C. **TLC** R_f = 0.38 (5% MeOH/CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 2924w (C–H str), 2837w (C–H str), 1739w, 1627s (C=O str), 1594s (C=C str), 1507s (C=C str), 1475s, 1456s, 1431s, 1365m, 1346s, 1264s, 1217s, 1198s, 1166m, 1081s, 1027w. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 4.00 (6H, s, 2 × –OCH_3), 4.08 (6H, s, 2 × –OCH_3), 6.91 (2H, s, 2 × –C=CH), 7.07 (2H, s, ArH), 7.55 (2H, s, ArH), 7.66 (1H, t, J 7.0 Hz, ArH), 8.03 (2H, dd, J 7.6, 1.2 Hz, ArH), 8.41 (1H, br s, ArH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 56.4, 56.7, 99.8, 104.2, 107.6, 117.3, 123.4, 128.4, 129.8, 132.8, 147.9, 152.3, 154.8, 161.4, 177.5. **LCMS** (ES+) m/z = 487.2 ($[M + H]^+$, t_r = 1.57 min). **HRMS** (ESI+) m/z = 487.1414 $[M + H]^+$ found, $C_{28}H_{23}O_8^+$ required 487.1393.

2,2′-(1,3-Phenylene)bis(5,7-dimethoxy-4*H*-chromen-4-one) (31). A mixture of bichalcone **24** (303 mg, 0.618 mmol) and I_2 (26.7 mg, 0.105 mmol) in DMSO (10 mL) was reacted according to GP-B. The crude residue was purified by flash column chromatography (SiO_2, 1–5% MeOH/CH_2Cl_2) to afford biflavone **31** (239 mg, 80%) as a pale yellow-white powdery solid. **m.p.** 288–290 °C. **TLC** R_f = 0.56 (10% MeOH/CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 2989w (C–H str), 2948w (C–H str), 1640s (C=O str), 1596s (C=C str), 1572s (C=C str), 1489m, 1457m, 1424m, 1395w, 1339s, 1273m, 1216m, 1203s, 1162s, 1110s, 1059m, 1034w. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 3.98 (6H, s, 2 × –OCH_3), 3.98 (6H, s, 2 × –OCH_3), 6.42 (2H, d, J 2.0 Hz, ArH), 6.68 (2H, d, J 2.0 Hz, ArH), 6.81 (2H, s, 2 × –C=CH), 7.64 (1H, t, J 8.0 Hz, ArH), 8.00 (2H, dd, J 8.0, 2.0 Hz, ArH), 8.37 (1H, t, J 2.0 Hz, ArH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 56.0, 56.5, 92.9, 96.5, 109.3, 109.6, 123.1, 128.3, 129.7, 132.4, 159.4, 159.9, 160.9, 164.3, 177.5. **LCMS** (ES+) m/z = 487.2 ($[M + H]^+$, t_r = 1.72 min). **HRMS** (ESI+) m/z = 487.1384 $[M + H]^+$ found, $C_{28}H_{23}O_8^+$ required 487.1387.

2,2′-(1,3-Phenylene)bis(6-bromo-4*H*-chromen-4-one) (32). A mixture of bichalcone **25** (222 mg, 0.421 mmol) and I_2 (95.1 mg, 0.375 mmol) in DMSO (10 mL) was reacted according to GP-B. The crude residue was purified by flash column chromatography (SiO_2, 1–5% MeOH/CH_2Cl_2) to afford biflavone **32** (191 mg, 87%) as a pale yellow-white powdery solid. **m.p.** >300 °C. **TLC** R_f = 0.25 (1% MeOH/CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 2919w (C–H str), 2851w (C–H str), 1738w, 1631s (C=O str), 1602s, 1559m (C=C str), 1478w, 1460s, 1435m, 1354m, 1328w, 1288w, 1245w, 1212w, 1138w, 1119w, 1092w, 1037m. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 6.95 (2H, s, 2 × –C=CH), 7.56 (2H, d, J 8.8 Hz, ArH), 7.74 (1H, t, J 8.0 Hz, ArH), 7.86 (2H, dd, J 8.8, 2.4 Hz, ArH), 8.10 (2H, dd, J 8.0, 1.6 Hz, ArH), 8.40 (2H, d, J 2.4 Hz, ArH), 8.46 (1H, br s, ArH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 108.4, 119.1, 120.1, 124.0, 125.3, 128.5, 129.3, 130.1, 132.7, 137.1, 155.0, 162.3, 176.8. **LCMS** (ES+) m/z = 525.0 ($[M + H]^+$, t_r = 2.19 min). **HRMS** (ESI+) m/z = 522.9181 $[M + H]^+$ found, $C_{24}H_{13}O_4Br_2^+$ required 522.9175.

6,6′-(1,3-Phenylene)bis(8*H*-[1,3]dioxolo[4,5-*g*]chromen-8-one) (33). A mixture of bichalcone **26** (167 mg, 0.365 mmol) and I_2 (96.7 mg, 0.381 mmol) in DMSO (10 mL) was reacted according to GP-B. The crude residue was purified by flash column chromatography (SiO_2, 1–5% MeOH/CH_2Cl_2) to afford biflavone **33** (46.4 mg, 28%) as a pale yellow-white powdery solid. **m.p.** >300 °C. **TLC** R_f = 0.35 (5% MeOH/CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 3051w (C–H str), 2916w (C–H str), 1739w, 1636s (C=O str), 1611s, 1502w (C=C str), 1457s, 1437m, 1361s, 1252s, 1174m, 1140m, 1032s. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 6.16 (4H, s, 2 × –OCH_2O–), 6.87 (2H, s, 2 × –C=CH), 7.05 (2H, s, ArH), 7.58 (2H, s, ArH), 7.69 (1H, t, J 8.0 Hz, ArH), 8.03 (2H, dd, J 8.0, 1.6 Hz, ArH), 8.41 (1H, br s, ArH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 98.1, 102.4, 102.6, 107.8, 119.1, 123.6, 128.6, 129.9, 132.9, 146.5, 153.1, 153.6, 161.5, 177.2. **LCMS** (ES+) m/z = 455.1 ($[M + H]^+$, t_r = 1.67 min). **HRMS** (ESI+) m/z = 455.0787 $[M + H]^+$ found, $C_{26}H_{15}O_8^+$ required 455.0767.

2,2′-(1,4-Phenylene)bis(7-methoxy-4*H*-chromen-4-one) (46). A mixture of bichalcone **41** (205 mg, 0.476 mmol) and I_2 (93.2 mg, 0.367 mmol) in DMSO (10 mL) was reacted according to GP-B. The crude residue was purified by flash column chromatography (SiO_2, 1–5% MeOH/CH_2Cl_2) to afford biflavone **46** (136 mg, 67%) as a pale yellow powdery solid. **m.p.** >300 °C. **TLC** R_f = 0.32 (5% MeOH/CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 3066w (C–H str), 2844w (C–H str), 1622s (C=O str), 1588s (C=C str), 1502w (C=C str), 1438s, 1421m, 1376m, 1354s, 1301w, 1286m, 1257s, 1238s, 1203m, 1166m, 1129m, 1092m, 1047w, 1019m. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 3.97 (6H, s, 2 × –OCH_3), 6.85 (2H, s, 2 × –C=CH), 7.00–7.03 (4H, m, ArH), 8.06 (4H, s, ArH), 8.15 (2H, d, J 8.5 Hz, ArH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 55.9, 100.5, 108.4, 114.7, 117.8, 126.6, 127.1, 134.4, 158.0, 161.5, 164.4, 177.6. **LCMS** (ES+) m/z = 427.1 ($[M + H]^+$, t_r = 1.69 min). **HRMS** (ESI+) m/z = 449.0980 $[M + Na]^+$ found, $C_{26}H_{18}O_6Na^+$ required 449.0996.

2,2′-(1,4-Phenylene)bis(6-methoxy-4*H*-chromen-4-one) (47). A mixture of bichalcone **42** (214 mg, 0.498 mmol) and I_2 (70.5 mg, 0.278 mmol) in DMSO (10 mL) was reacted according to GP-B. The crude residue was purified by flash column chromatography (SiO_2, 1–5% MeOH/CH_2Cl_2) to afford biflavone **47** (55.7 mg, 26%) as a pale yellow-white powdery solid. **m.p.** >300 °C. **TLC** R_f = 0.38 (5% MeOH/CH_2Cl_2). **IR** ν_{max}

(neat)/cm^{-1}: 2921w (C–H str), 1737w, 1647s (C═O str), 1615s, 1580m (C═C str), 1510w (C═C str), 1484s, 1459m, 1426m, 1413w, 1359s, 1352s, 1294m, 1258w, 1201s, 1125m, 1074s, 1048m, 1020s, 1010m. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 3.94 (6H, s, 2 × –OCH_3), 6.92 (2H, s, 2 × –C═CH), 7.34 (2H, dd, *J* 9.6, 2.4 Hz, ArH), 7.56 (2H, d, *J* 9.6 Hz, ArH), 7.63 (2H, d, *J* 2.4 Hz, ArH), 8.10 (4H, s, ArH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 56.0, 104.9, 107.7, 119.6, 124.2, 124.6, 126.8, 134.5, 151.1, 157.2, 161.7, 178.1. **LCMS** (ES+) *m*/*z* = 427.2 ([M + H]$^+$, t_r = 1.91 min). These characterisation data are in accordance with that previously reported in the literature.[46]

2,2′-(1,4-Phenylene)bis(5-methoxy-4*H*-chromen-4-one) (48). A mixture of bichalcone **43** (227 mg, 0.526 mmol) and I_2 (88.0 mg, 0.347 mmol) in DMSO (10 mL) was reacted according to GP-B. The crude residue was purified by flash column chromatography (SiO_2, 1–5% MeOH/CH_2Cl_2) to afford biflavone **48** (151 mg, 22%) as a pale yellow-white powdery solid. **m.p.** >300 °C. **TLC** R_f = 0.50 (10% MeOH/CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 2935w (C–H str), 2842w (C–H str), 1739w, 1633s (C═O str), 1599s (C═C str), 1513w (C═C str), 1476s, 1437m, 1417s, 1374s, 1327m, 1286m, 1268s, 1092s, 1070m, 1030s, 1011w. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 4.03 (6H, s, 2 × –OCH_3), 6.83 (2H, s, 2 × –C═CH), 6.87 (2H, d, *J* 8.5 Hz, ArH), 7.18 (2H, d, *J* 8.5 Hz, ArH), 7.62 (2H, t, *J* 8.5 Hz, ArH), 8.05 (4H, s, ArH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 56.5, 106.7, 110.0, 110.1, 114.7, 126.6, 134.0, 158.2, 159.7, 159.8, 178.1. **LCMS** (ES+) *m*/*z* = 427.2 ([M + H]$^+$, t_r = 1.53 min). **HRMS** (ESI+) *m*/*z* = 427.1166 [M + H]$^+$ found, $C_{26}H_{19}O_6^+$ required 427.1176.

2,2′-(1,4-Phenylene)bis(5,7-dimethoxy-4*H*-chromen-4-one) (49). A mixture of bichalcone **44** (212 mg, 0.432 mmol) and I_2 (77.4 mg, 0.305 mmol) in DMSO (10 mL) was reacted according to GP-B. The crude residue was purified by flash column chromatography (SiO_2, 1–5% MeOH/CH_2Cl_2) to afford biflavone **49** (107 mg, 51%) as a pale yellow-white powdery solid. **m.p.** >300 °C. **TLC** R_f = 0.44 (10% MeOH/CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 2981w (C–H str), 2844w (C–H str), 1633s (C═O str), 1588s (C═C str), 1566s (C═C str), 1491m, 1462m, 1418s, 1346s, 1292m, 1264w, 1216m, 1202s, 1162s, 1117s, 1107s, 1058m, 1029w. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 3.95 (6H, s, 2 × –OCH_3), 3.99 (6H, s, 2 × –OCH_3), 6.42 (2H, d, *J* 2.0 Hz, ArH), 6.62 (2H, d, *J* 2.0 Hz, ArH), 6.77 (2H, s, 2 × –C═CH), 8.02 (4H, s, ArH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 55.8, 56.5, 92.9, 96.4, 109.4, 109.9, 126.4, 134.0, 159.3, 159.9, 161.0, 164.3, 177.4. **LCMS** (ES+) *m*/*z* = 487.1 ([M + H]$^+$, t_r = 1.53 min). **HRMS** (ESI+) *m*/*z* = 487.1376 [M + H]$^+$ found, $C_{28}H_{23}O_8^+$ required 487.1387.

2,2′-(1,4-Phenylene)bis(6-bromo-4*H*-chromen-4-one) (50). A mixture of bichalcone **45** (221 mg, 0.418 mmol) and I_2 (97.9 mg, 0.386 mmol) in DMSO (10 mL) was reacted according to GP-B. The crude residue was purified by flash column chromatography (SiO_2, 1–5% MeOH/CH_2Cl_2) to afford biflavone **50** (191 mg, 87%) as a pale yellow-white powdery solid. **m.p.** >300 °C. **TLC** R_f = 0.40 (3% MeOH/CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 3039w (C–H str), 2922w (C–H str), 1738w, 1629s (C═O str), 1600s, 1564m (C═C str), 1515m (C═C str), 1461m, 1438s, 1355m, 1328w, 1295w, 1252m, 1213w, 1133m, 1094w, 1042s, 1014w. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 6.94 (2H, s, 2 × –C═CH), 7.53 (2H, d, *J* 8.8 Hz, ArH), 7.84 (2H, dd, *J* 8.8, 2.4 Hz, ArH), 8.10 (4H, s, ArH), 8.40 (2H, d, *J* 2.0 Hz, ArH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 108.6, 119.0, 120.1, 125.3, 126.9, 128.5, 134.4, 137.1, 155.0, 162.0, 176.8. **LCMS** (ES+) *m*/*z* = 524.9 ([M + H]$^+$, t_r = 2.17 min). These characterisation data are in accordance with that previously reported in the literature.[46]

2,2′-([1,1′-Biphenyl]-4,4′-diyl)bis(7-methoxy-4*H*-chromen-4-one) (61). A mixture of bichalcone **56** (215 mg, 0.423 mmol) and I_2 (46.8 mg, 0.184 mmol) in DMSO (10 mL) was reacted according to GP-B. The crude residue was purified by flash column chromatography (SiO_2, 1–5% MeOH/CH_2Cl_2) to afford biflavone **61** (147 mg, 69%) as a pale yellow-green powdery solid. **m.p.** >300 °C. **TLC** R_f = 0.28 (5% MeOH/CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 2922w (C–H str), 2849w (C–H str), 1625s (C═O str), 1607s, 1570s (C═C str), 1499m, 1439s, 1405m, 1377s, 1358m, 1319w, 1275m, 1252m, 1199m, 1163s, 1134m, 1091s, 1016m, 1004m. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 3.97 (6H, s, 2 × –OCH_3), 6.85 (2H, s, 2 × –C═CH), 7.02–7.04 (4H, m, ArH), 7.83 (4H, d, *J* 8.5 Hz, ArH), 8.05 (4H, d, *J* 8.5 Hz, ArH), 8.17 (2H, d, *J* 9.0 Hz, ArH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 55.9, 100.5, 107.7, 114.5, 117.9, 126.8, 127.1, 127.7, 131.5, 142.7, 158.0, 162.4, 164.3, 177.8. **LCMS** (ES+) *m*/*z* = 503.2 ([M + H]$^+$, t_r = 1.80 min). **HRMS** (ESI+) *m*/*z* = 503.1506 [M + H]$^+$ found, $C_{32}H_{23}O_6^+$ required 503.1489.

2,2′-([1,1′-Biphenyl]-4,4′-diyl)bis(6-methoxy-4*H*-chromen-4-one) (62). A mixture of bichalcone **57** (231 mg, 0.455 mmol) and I_2 (91.4 mg, 0.360 mmol) in DMSO (10 mL) was reacted according to GP-B. The crude residue was purified by flash column chromatography (SiO_2, 1–5% MeOH/CH_2Cl_2) to afford biflavone **62** (134 mg, 59%) as a pale yellow-white powdery solid. **m.p.** >300 °C. **TLC** R_f = 0.39 (5% MeOH/CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 3066w (C–H str), 2937w (C–H str), 1736w, 1635s (C═O str), 1615s, 1576s (C═C str), 1483s, 1452w, 1434m, 1405m, 1361s, 1320m, 1287m, 1252m, 1205m, 1127m, 1079s, 1049m, 1014m, 1002w. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 3.94 (6H, s, 2 × –OCH_3), 6.90 (2H, s, 2 × –C═CH), 7.33 (2H, d, *J* 8.8 Hz, ArH), 7.56 (2H, d, *J* 9.2 Hz, ArH), 7.63 (2H, s, ArH), 7.83 (4H, d, *J* 8.0 Hz, ArH), 8.06 (4H, d, *J* 8.0 Hz, ArH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 56.0, 104.9, 107.0, 119.5, 123.9, 124.6, 126.9, 127.7, 131.5, 142.7, 151.1, 157.1, 162.6, 178.3. **LCMS** (ES+) *m*/*z* = 503.2 ([M + H]$^+$, t_r = 1.94 min). **HRMS** (ESI+) *m*/*z* = 503.1470 [M + H]$^+$ found, $C_{32}H_{23}O_6^+$ required 503.1489.

2,2′-([1,1′-Biphenyl]-4,4′-diyl)bis(5-methoxy-4*H*-chromen-4-one) (63). A mixture of bichalcone **58** (206 mg, 0.407 mmol) and I_2 (12.8 mg, 0.0504 mmol) in DMSO (10 mL) was reacted according to GP-B. The crude residue was purified by flash column chromatography (SiO_2, 1–5% MeOH/CH_2Cl_2) to afford biflavone **63** (162 mg, 79%) as a pale yellow powdery solid. **m.p.** >300 °C. **TLC** R_f = 0.50 (10% MeOH/CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 3020w (C–H str), 2843w (C–H str), 1631s (C═O str), 1601s, 1573m (C═C str), 1498w, 1476s, 1459m, 1438m, 1405m, 1377s, 1330w, 1309s, 1269s, 1094s, 1071m, 1036m, 1018m, 1000w. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 4.03 (6H, s, 2 × –OCH_3), 6.81 (2H, s, 2 × –C═CH), 6.86 (2H, d, *J* 8.0 Hz, ArH), 7.18 (2H, dd, *J* 8.5, 1.0 Hz, ArH), 7.61 (2H, t, *J* 8.5 Hz, ArH), 7.80 (4H, d, *J* 8.5 Hz, ArH), 8.02 (4H, d, *J* 8.5 Hz, ArH).

^{13}C NMR (500 MHz, $CDCl_3$): δ 56.5, 106.5, 109.2, 110.2, 114.6, 126.7, 127.6, 131.1, 133.8, 142.6, 158.3, 159.8, 160.5, 178.3. **LCMS** (ES+) m/z = 503.2 ($[M + H]^+$, t_r = 1.64 min). **HRMS** (ESI+) m/z = 503.1485 $[M + H]^+$ found, $C_{32}H_{23}O_6^+$ required 503.1489.

2,2′-([1,1′-Biphenyl]-4,4′-diyl)bis(5,7-dimethoxy-4*H*-chromen-4-one) (64). A mixture of bichalcone **59** (201 mg, 0.355 mmol) and I_2 (57.0 mg, 0.225 mmol) in DMSO (10 mL) was reacted according to GP-B. The crude residue was purified by flash column chromatography (SiO_2, 1–5% MeOH/CH_2Cl_2) to afford biflavone **64** (138 mg, 69%) as a pale yellow-white powdery solid. **m.p.** >300 °C. **TLC** R_f = 0.46 (10% MeOH/CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 2915w (C–H str), 2837w (C–H str), 1635s (C═O str), 1603s, 1571s (C═C str), 1491m, 1458m, 1420w, 1404w, 1348s, 1315s, 1271m, 1215s, 1202m, 1159s, 1116s, 1056s, 1034w, 1002w. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 3.95 (6H, s, 2 × –OCH_3), 3.99 (6H, s, 2 × –OCH_3), 6.42 (2H, s, ArH), 6.62 (2H, s, ArH), 6.76 (2H, s, 2 × –C═CH), 7.80 (4H, d, J 8.0 Hz, ArH), 8.00 (4H, d, J 8.0 Hz, ArH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 55.8, 56.5, 92.9, 96.2, 109.2, 109.4, 126.6, 127.6, 131.1, 142.5, 159.9, 160.1, 161.0, 164.1, 177.5. **LCMS** (ES+) m/z = 563.2 ($[M + H]^+$, t_r = 1.85 min). **HRMS** (ESI+) m/z = 563.1691 $[M + H]^+$ found, $C_{34}H_{27}O_8^+$ required 563.1700.

2,2′-([1,1′-Biphenyl]-4,4′-diyl)bis(6-bromo-4*H*-chromen-4-one) (65). A mixture of bichalcone **60** (203 mg, 0.335 mmol) and I_2 (55.2 mg, 0.217 mmol) in DMSO (10 mL) was reacted according to GP-B. The crude residue was purified by flash column chromatography (SiO_2, 1–5% MeOH/CH_2Cl_2) to afford biflavone **65** (92.0 mg, 46%) as a pale yellow-green powdery solid. **m.p.** >300 °C. **TLC** R_f = 0.39 (5% MeOH/CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 2955w (C–H str), 2868w (C–H str), 1731w, 1636s (C═O str), 1607s, 1567s (C═C str), 1549m (C═C str), 1496m, 1461s, 1430s, 1350s, 1316s, 1277w, 1232w, 1156m, 1137w, 1040w, 1002w. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 6.92 (2H, s, 2 × –C═CH), 7.53 (2H, d, J 8.8 Hz, ArH), 7.81–7.85 (6H, m, ArH), 8.06 (4H, d, J 8.0 Hz, ArH), 8.40 (2H, d, J 2.4 Hz, ArH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 107.8, 118.8, 120.0, 125.4, 127.0, 127.8, 128.5, 131.1, 136.9, 143.0, 155.0, 163.0, 177.0. **LCMS** (ES+) m/z = 601.0 ($[M + H]^+$, t_r = 2.22 min). **HRMS** (ESI+) m/z = 598.9488 $[M + H]^+$ found, $C_{30}H_{17}Br_2O_4^+$ required 598.9494.

2,2′,2″-(Benzene-1,3,5-triyl)tris(7-methoxy-4*H*-chromen-4-one) (73). A mixture of trichalcone **72** (205 mg, 0.338 mmol) and I_2 (88.4 mg, 0.348 mmol) in DMSO (10 mL) was reacted according to GP-B. The crude residue was purified by flash column chromatography (SiO_2, 1–10% MeOH/$CHCl_3$) to afford triflavone **73** (57.6 mg, 28%) as a pale yellow powdery solid. **m.p.** >300 °C. **TLC** R_f = 0.38 (3% MeOH/CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 3076w (C–H str), 2932w (C–H str), 2842w (C–H str), 1739w, 1625s (C═O str), 1603s, 1503m (C═C str), 1436s, 1371s, 1354s, 1275m, 1262m, 1236m, 1199m, 1160s, 1129m, 1087s, 1020m. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 4.05 (9H, s, 3 × –OCH_3), 7.06–7.09 (6H, m, 3 × –C═CH and ArH), 7.14 (3H, d, J 2.4 Hz, ArH), 8.19 (3H, d, J 8.8 Hz, ArH), 8.60 (3H, s, ArH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 56.2, 100.2, 108.8, 115.6, 117.7, 125.7, 127.1, 133.9, 158.1, 160.5, 164.8, 177.6. **LCMS** (ES+) m/z = 601.1 ($[M + H]^+$, t_r = 2.00 min). **HRMS** (ESI+) m/z = 601.1477 $[M + H]^+$ found, $C_{36}H_{25}O_9^+$ required 601.1493.

Synthesis of biaurones and triaurone

(2*Z*,2′*Z*)-2,2′-(1,3-Phenylenebis(methanylylidene))bis(6-methoxybenzofuran-3(2*H*)-one) (34). A mixture of bichalcone **20** (102 mg, 0.237 mmol) and $Hg(OAc)_2$ (151 mg, 0.474 mmol) in pyridine (10 mL) was reacted according to GP-C. The crude residue was purified by flash column chromatography (SiO_2, 1% MeOH/CH_2Cl_2) to afford biaurone **34** (27.0 mg, 27%) as a pale yellow-white powdery solid. **m.p.** 228–230 °C. **TLC** R_f = 0.25 (1% MeOH/CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 2919w (C–H str), 2842w (C–H str), 1700m (C═O str), 1651m (C═C str), 1591s (C═C str), 1498m, 1440s, 1339m, 1324m, 1265s, 1193m, 1150s, 1124s, 1112s, 1093s, 1018m. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 3.98 (6H, s, 2 × –OCH_3), 6.80 (2H, dd, J 8.4, 2.0 Hz, ArH), 6.87 (2H, d, J 2.0 Hz, ArH), 6.89 (2H, s, 2 × –C═CH), 7.55 (1H, t, J 7.6 Hz, ArH), 7.75 (2H, d, J 8.8 Hz, ArH), 7.94 (2H, dd, J 8.0, 1.6 Hz, ArH), 8.45 (1H, br s, ArH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 56.1, 96.7, 111.1, 112.4, 114.7, 126.0, 129.4, 132.0, 133.1, 134.0, 148.2, 167.7, 168.7, 183.0. **LCMS** (ES+) m/z = 427.1 ($[M + H]^+$, t_r = 1.89 min). **HRMS** (ESI+) m/z = 427.1183 $[M + H]^+$ found, $C_{26}H_{19}O_6^+$ required 427.1176.

(2*Z*,2′*Z*)-2,2′-(1,3-Phenylenebis(methanylylidene))bis(5-methoxybenzofuran-3(2*H*)-one) (35). A mixture of bichalcone **21** (202 mg, 0.470 mmol) and $Hg(OAc)_2$ (303 mg, 0.949 mmol) in pyridine (10 mL) was reacted according to GP-C. The crude residue was purified by recrystallization from $CHCl_3$ to afford biaurone **35** (117 mg, 58%) as a bright yellow powdery solid. **m.p.** 278–280 °C. **TLC** R_f = 0.34 (0.5% MeOH/CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 3076w (C–H str), 2837w (C–H str), 1706s (C═O str), 1648s (C═C str), 1600s (C═C str), 1489s, 1434m, 1318m, 1297m, 1276s, 1253w, 1196s, 1182m, 1172m, 1115s, 1020s. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 3.87 (6H, s, 2 × –OCH_3), 6.94 (2H, s, 2 × –C═CH), 7.26–7.31 (6H, m, ArH, overlain by $CDCl_3$), 7.57 (1H, t, J 7.6 Hz, ArH), 7.97 (2H, d, J 7.6 Hz, ArH), 8.43 (1H, br s, ArH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 56.0, 105.4, 112.2, 113.8, 121.7, 126.5, 129.5, 132.5, 133.1, 134.3, 148.1, 156.2, 161.4, 185.0. **LCMS** (ES+) m/z = 427.2 ($[M + H]^+$, t_r = 2.01 min). **HRMS** (ESI+) m/z = 427.1162 $[M + H]^+$ found, $C_{26}H_{19}O_6^+$ required 427.1176.

(2*Z*,2′*Z*)-2,2′-(1,3-Phenylenebis(methanylylidene))bis(4-methoxybenzofuran-3(2*H*)-one) (36). A mixture of bichalcone **22** (207 mg, 0.480 mmol) and $Hg(OAc)_2$ (319 mg, 0.999 mmol) in pyridine (10 mL) was reacted according to GP-C. The crude residue was purified by flash column chromatography (SiO_2, 0.5% MeOH/CH_2Cl_2) to afford biaurone **36** (172 mg, 84%) as a bright yellow powdery solid. **m.p.** 248–250 °C. **TLC** R_f = 0.45 (2% MeOH/CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 2938w (C–H str), 2840w (C–H str), 1702s (C═O str), 1643s (C═C str), 1594s (C═C str), 1491s, 1422m, 1348m, 1324m, 1284m, 1250s, 1213w, 1158w, 1136w, 1076s, 1061s. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 4.03 (6H, s, 2 × –OCH_3), 6.66 (2H, d, J 8.4 Hz, ArH), 6.89 (2H, s, 2 × –C═CH), 6.95 (2H, d, J 8.0 Hz, ArH), 7.53 (1H, t, J 8.0 Hz, ArH), 7.62 (2H, d, J 8.0 Hz, ArH), 7.92 (2H, dd, J 8.0, 1.6 Hz, ArH), 8.42 (1H, br s, ArH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 56.3, 104.8, 105.3, 110.8, 111.1, 129.3, 132.1, 133.1, 133.9, 138.6, 147.2, 158.6, 167.1, 182.4. **LCMS** (ES+) m/z = 427.1

([M + H]$^+$, t_r = 1.80 min). **HRMS** (ESI+) m/z = 427.1164 [M + H]$^+$ found, $C_{26}H_{19}O_6^+$ required 427.1176.

(2*Z*,2′*Z*)-2,2′-(1,3-Phenylenebis(methanylylidene))bis(5,6-dimethoxybenzofuran-3(2*H*)-one) (37). A mixture of bichalcone **23** (95.6 mg, 0.195 mmol) and $Hg(OAc)_2$ (142 mg, 0.446 mmol) in pyridine (10 mL) was reacted according to GP-C. The crude residue was purified by flash column chromatography (SiO_2, 0.5% MeOH/CH_2Cl_2) to afford biaurone **37** (42.0 mg, 44%) as a bright yellow powdery solid. **m.p.** >300 °C. **TLC** R_f = 0.40 (3% MeOH/CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 2937w (C–H str), 2835w (C–H str), 1687m (C=O str), 1647m (C=C str), 1605s (C=C str), 1496s, 1477s, 1437s, 1328m, 1278s, 1240m, 1221s, 1192s, 1130s, 1103s, 1027w, 1001m. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 3.93 (6H, s, 2 × –OCH_3), 4.06 (6H, s, 2 × –OCH_3), 6.89 (2H, s, 2 × –C=CH), 6.90 (2H, s, ArH), 7.20 (2H, s, ArH), 7.53 (1H, t, J 7.6 Hz, ArH), 7.95 (2H, dd, J 7.6, 1.2 Hz, ArH), 8.36 (1H, br s, ArH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 56.4, 56.8, 95.7, 104.1, 111.2, 112.9, 129.4, 131.9, 133.1, 134.3, 146.7, 148.3, 157.9, 163.6, 183.5. **LCMS** (ES+) m/z = 487.3 ([M + H]$^+$, t_r = 1.79 min). **HRMS** (ESI+) m/z = 487.1371 [M + H]$^+$ found, $C_{28}H_{23}O_8^+$ required 487.1387.

(2*Z*,2′*Z*)-2,2′-(1,3-Phenylenebis(methanylylidene))bis(4,6-dimethoxybenzofuran-3(2*H*)-one) (38). A mixture of bichalcone **24** (105 mg, 0.213 mmol) and $Hg(OAc)_2$ (134 mg, 0.421 mmol) in pyridine (10 mL) was reacted according to GP-C. The crude residue was purified by flash column chromatography (SiO_2, 1% MeOH/CH_2Cl_2) to afford biaurone **38** (62.1 mg, 60%) as a pale yellow-white powdery solid. **m.p.** 296–298 °C. **TLC** R_f = 0.45 (5% MeOH/CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 2938w (C–H str), 2842w (C–H str), 1697m (C=O str), 1650w (C=C str), 1588s (C=C str), 1503m (C=C str), 1468m, 1423m, 1363w, 1346m, 1241m, 1215s, 1154s, 1087s, 1037w. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 3.96 (6H, s, 2 × –OCH_3), 3.98 (6H, s, 2 × –OCH_3), 6.17 (2H, d, J 1.6 Hz, ArH), 6.49 (2H, d, J 1.6 Hz, ArH), 6.83 (2H, s, 2 × –C=CH), 7.50 (1H, t, J 8.0 Hz, ArH), 7.88 (2H, dd, J 7.6, 1.2 Hz, ArH), 8.39 (1H, br s, ArH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 56.2, 56.3, 89.4, 94.2, 105.2, 110.1, 129.2, 131.6, 133.2, 133.7, 148.2, 159.5, 169.2, 180.7. **LCMS** (ES+) m/z = 487.1 ([M + H]$^+$, t_r = 1.75 min). These characterisation data are in accordance with that previously reported in the literature.[49]

(2*Z*,2′*Z*)-2,2′-(1,3-Phenylenebis(methanylylidene))bis(5-bromobenzofuran-3(2*H*)-one) (39). A mixture of bichalcone **25** (203 mg, 0.384 mmol) and $Hg(OAc)_2$ (265 mg, 0.832 mmol) in pyridine (10 mL) was reacted according to GP-C. The crude residue was purified by recrystallization from $CHCl_3$ to afford biaurone **39** (173 mg, 86%) as a pale yellow-brown powdery solid. **m.p.** >300 °C. **TLC** R_f = 0.27 (CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 3066w (C–H str), 1713s (C=O str), 1649s, 1602s (C=C str), 1596s (C=C str), 1456s, 1424m, 1336w, 1291m, 1259s, 1193m, 1180s, 1171s, 1134m, 1116s, 1052w. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 6.98 (2H, s, 2 × –C=CH), 7.31 (2H, d, J 8.8 Hz, ArH), 7.59 (1H, t, J 8.0 Hz, ArH), 7.81 (2H, dd, J 8.8, 2.0 Hz, ArH), 7.97 (2H, d, J 2.0 Hz, ArH), 8.00 (2H, dd, J 8.0, 1.2 Hz, ArH), 8.40 (1H, br s, ArH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 113.1, 114.7, 116.6, 123.2, 127.5, 129.6, 132.8, 132.9, 134.6, 139.7, 147.2, 164.8, 183.3. **LCMS** (ES+) m/z = 525.1 ([M + H]$^+$, t_r = 2.30 min). **HRMS** (ESI+) m/z = 522.9162 [M + H]$^+$ found, $C_{24}H_{13}O_4Br_2^+$ required 522.9181.

(6*Z*,6′*Z*)-6,6′-(1,3-Phenylenebis(methanylylidene))bis([1,3]dioxolo[4,5-*f*]benzofuran-7(6*H*)-one) (40). A mixture of bichalcone **26** (105 mg, 0.229 mmol) and $Hg(OAc)_2$ (150 mg, 0.470 mmol) in pyridine (10 mL) was reacted according to GP-C. The crude residue was purified by flash column chromatography (SiO_2, 0.5% MeOH/CH_2Cl_2) and recrystallized from $CHCl_3$ to afford biaurone **40** (10.2 mg, 10%) as a bright yellow powdery solid. **m.p.** >300 °C. **TLC** R_f = 0.38 (1% MeOH/CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 3051w (C–H str), 2917w (C–H str), 1702m (C=O str), 1652m, 1615s (C=C str), 1488m, 1460s, 1325w, 1300m, 1280m, 1228w, 1189w, 1178m, 1115s, 1034m. **^{1}H NMR** (500 MHz, DMSO-d_6): δ 6.23 (4H, s, 2 × –OCH_2O–), 6.87 (2H, s, 2 × –C=CH), 7.21 (2H, s, ArH), 7.25 (2H, s, ArH), 7.63 (1H, t, J 8.0 Hz, ArH), 8.04 (2H, dd, J 8.0, 1.6 Hz, ArH), 8.39 (1H, br s, ArH). **^{13}C NMR** (500 MHz, DMSO-d_6): δ 94.9, 101.2, 103.3, 110.5, 113.7, 129.7, 132.1, 132.7, 145.3, 147.9, 156.2, 156.3, 164.4, 181.9. **LCMS** (ES+) m/z = 455.1 ([M + H]$^+$, t_r = 2.02 min). **HRMS** (ESI+) m/z = 455.0763 [M + H]$^+$ found, $C_{26}H_{15}O_8^+$ required 455.0761.

(2*Z*,2′*Z*)-2,2′-(1,4-Phenylenebis(methanylylidene))bis(6-methoxybenzofuran-3(2*H*)-one) (51). A mixture of bichalcone **41** (49.4 mg, 0.115 mmol) and $Hg(OAc)_2$ (84.4 mg, 0.265 mmol) in pyridine (10 mL) was reacted according to GP-C. The crude residue was purified by flash column chromatography (SiO_2, 1% MeOH/CH_2Cl_2) to afford biaurone **51** (47.0 mg, 95%) as a bright yellow-orange powdery solid. **m.p.** 288–290 °C. **TLC** R_f = 0.55 (1% MeOH/CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 2941w (C–H str), 2848w (C–H str), 1693m (C=O str), 1642m (C=C str), 1605s (C=C str), 1585s (C=C str), 1498m, 1440m, 1350m, 1323w, 1296w, 1267s, 1192m, 1116s, 1093s, 1015m. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 3.95 (6H, s, 2 × –OCH_3), 6.76–6.79 (4H, m, ArH), 6.81 (2H, s, 2 × –C=CH), 7.72 (2H, d, J 8.4 Hz, ArH), 7.95 (4H, s, ArH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 56.1, 96.7, 110.9, 112.2, 114.7, 125.9, 131.6, 133.5, 148.4, 167.6, 168.5, 182.8. **LCMS** (ES+) m/z = 427.0 ([M + H]$^+$, t_r = 5.25 min). **HRMS** (ESI+) m/z = 427.1178 [M + H]$^+$ found, $C_{26}H_{19}O_6^+$ required 427.1176.

(2*Z*,2′*Z*)-2,2′-(1,4-Phenylenebis(methanylylidene))bis(5-methoxybenzofuran-3(2*H*)-one) (52). A mixture of bichalcone **42** (106 mg, 0.245 mmol) and $Hg(OAc)_2$ (153 mg, 0.481 mmol) in pyridine (10 mL) was reacted according to GP-C. The crude residue was purified by flash column chromatography (SiO_2, 1% MeOH/CH_2Cl_2) and recrystallized from MeOH to afford biaurone **52** (79.0 mg, 76%) as a bright orange powdery solid. **m.p.** >300 °C. **TLC** R_f = 0.47 (1% MeOH/CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 3072w (C–H str), 2950w (C–H str), 1704s (C=O str), 1647s, 1620w (C=C str), 1599s (C=C str), 1489s, 1435m, 1421m, 1322m, 1281m, 1190m, 1164m, 1129m, 1110s, 1098s, 1023s. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 3.87 (6H, s, 2 × –OCH_3), 6.90 (2H, s, 2 × –C=CH), 7.25 (2H, t, J 2.0 Hz, ArH), 7.29 (4H, t, J 1.2 Hz, ArH), 8.01 (4H, s, ArH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 56.0, 105.4, 112.0, 113.8, 126.4, 131.8, 146.1, 147.3, 148.3, 156.2, 161.2, 184.9. **LCMS** (ES+) m/z = 427.1 ([M + H]$^+$, t_r = 1.96 min). **HRMS** (ESI+) m/z = 426.1111 [M + H]$^+$ found, $C_{26}H_{19}O_6^+$ required 426.1098.

(2*Z*,2′*Z*)-2,2′-(1,4-Phenylenebis(methanylylidene))bis(4-methoxybenzofuran-3(2*H*)-one) (53). A mixture of bichalcone **43** (202 mg, 0.470 mmol) and $Hg(OAc)_2$ (309 mg, 0.969 mmol) in pyridine (10 mL) was reacted according to GP-C. The crude residue was purified by recrystallization from $CHCl_3$ to afford biaurone **53** (199 mg, 99%) as a bright yellow-orange powdery solid. **m.p.** >300 °C. **TLC** R_f = 0.21 (1% MeOH/CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 2968w (C–H str), 2840w (C–H str), 1698s (C=O str), 1652s, 1594s (C=C str), 1509w (C=C str), 1495s (C=C str), 1458w, 1355w, 1300w, 1280w, 1251s, 1165m, 1073s. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 4.03 (6H, s, 2 × –OCH_3), 6.66 (2H, d, *J* 8.4 Hz, ArH), 6.86 (2H, s, 2 × –C=CH), 6.92 (2H, d, *J* 8.0 Hz, ArH), 7.61 (2H, t, *J* 8.0 Hz, ArH), 7.99 (4H, s, ArH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 56.3, 104.8, 105.4, 110.8, 111.0, 131.6, 133.6, 138.6, 147.5, 158.6, 167.0, 182.3. **LCMS** (ES+) *m*/*z* = 427.1 ($[M + H]^+$, t_r = 1.83 min). **HRMS** (ESI+) *m*/*z* = 427.1165 $[M + H]^+$ found, $C_{26}H_{19}O_6^+$ required 427.1176.

(2*Z*,2′*Z*)-2,2′-(1,4-Phenylenebis(methanylylidene))bis(4,6-dimethoxybenzofuran-3(2*H*)-one) (54). A mixture of bichalcone **44** (204 mg, 0.415 mmol) and $Hg(OAc)_2$ (283 mg, 0.888 mmol) in pyridine (10 mL) was reacted according to GP-C. The crude residue was purified by recrystallization from $CHCl_3$ to afford biaurone **54** (181 mg, 90%) as a bright yellow powdery solid. **m.p.** >300 °C. **TLC** R_f = 0.30 (3% MeOH/CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 2999w (C–H str), 2843w (C–H str), 1694m (C=O str), 1647w, 1609s (C=C str), 1590s (C=C str), 1502w (C=C str), 1466w, 1428w, 1362m, 1327w, 1248m, 1211s, 1153s, 1085s, 1038w. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 3.95 (6H, s, 2 × –OCH_3), 3.98 (6H, s, 2 × –OCH_3), 6.17 (2H, d, *J* 1.6 Hz, ArH), 6.43 (2H, d, *J* 1.6 Hz, ArH), 6.79 (2H, s, 2 × –C=CH), 7.94 (4H, s, ArH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 56.2, 56.3, 89.3, 94.1, 105.2, 110.0, 131.4, 133.5, 148.4, 159.5, 169.0, 169.1, 180.5. **LCMS** (ES+) *m*/*z* = 487.2 ($[M + H]^+$, t_r = 1.75 min). These characterisation data are in accordance with that previously reported in the literature.[49]

(2*Z*,2′*Z*)-2,2′-(1,4-Phenylenebis(methanylylidene))bis(5-bromobenzofuran-3(2*H*)-one) (55). A mixture of bichalcone **45** (208 mg, 0.393 mmol) and $Hg(OAc)_2$ (266 mg, 0.835 mmol) in pyridine (10 mL) was reacted according to GP-C. The crude residue was purified by recrystallization from $CHCl_3$ to afford biaurone **55** (90.5 mg, 44%) as a bright orange powdery solid. **m.p.** >300 °C. **TLC** R_f = 0.40 (PE/CH_2Cl_2; 2 : 1). **IR** ν_{max} (neat)/cm^{-1}: 3081w (C–H str), 1702s (C=O str), 1639s, 1591s (C=C str), 1509w (C=C str), 1449s, 1422m, 1347w, 1293m, 1259s, 1196m, 1174s, 1132m, 1110s, 1046w. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 6.94 (2H, s, 2 × –C=CH), 7.29 (2H, s, ArH), 7.79 (2H, dd, *J* 8.8, 2.0 Hz, ArH), 7.96 (2H, d, *J* 2.0 Hz, ArH), 8.01 (4H, s, ArH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 112.9, 114.7, 116.6, 123.2, 127.5, 132.0, 133.6, 139.6, 147.5, 164.7, 183.1. **LCMS** (ES−) *m*/*z* = 523.9 ($[M - H]^-$, t_r = 2.28 min). **HRMS** (ESI+) *m*/*z* = 522.9180 $[M + H]^+$ found, $C_{24}H_{13}O_4Br_2^+$ required 522.9181.

(2*Z*,2′*Z*)-2,2′-([1,1′-Biphenyl]-4,4′-diylbis(methanylylidene))bis(6-methoxybenzofuran-3(2*H*)-one) (66). A mixture of bichalcone **56** (153 mg, 0.302 mmol) and $Hg(OAc)_2$ (208 mg, 0.653 mmol) in pyridine (10 mL) was reacted according to GP-C. The crude residue was purified by flash column chromatography (SiO_2, 0.5% MeOH/CH_2Cl_2) and recrystallized from $CHCl_3$ to afford biaurone **66** (45.7 mg, 30%) as a bright yellow-orange powdery solid. **m.p.** 264–266 °C. **TLC** R_f = 0.44 (1% MeOH/CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 2921w (C–H str), 2835w (C–H str), 1688m (C=O str), 1644m, 1589s (C=C str), 1551m (C=C str), 1495m (C=C str), 1443m, 1347w, 1321m, 1271m, 1191m, 1129s, 1112s, 1099s, 1014m, 1003m. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 3.96 (6H, s, 2 × –OCH_3), 6.78–6.82 (4H, m, ArH), 6.88 (2H, s, 2 × –C=CH), 7.73–7.76 (6H, m, ArH), 8.01 (4H, d, *J* 8.4 Hz, ArH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 56.1, 96.7, 111.3, 112.2, 114.9, 125.9, 127.4, 131.9, 132.0, 141.1, 148.1, 167.5, 168.5, 182.9. **LCMS** (ES+) *m*/*z* = 503.2 ($[M + H]^+$, t_r = 2.11 min). **HRMS** (ESI+) *m*/*z* = 503.1487 $[M + H]^+$ found, $C_{32}H_{23}O_6^+$ required 503.1489.

(2*Z*,2′*Z*)-2,2′-([1,1′-Biphenyl]-4,4′-diylbis(methanylylidene))bis(5-methoxybenzofuran-3(2*H*)-one) (67). A mixture of bichalcone **57** (206 mg, 0.406 mmol) and $Hg(OAc)_2$ (265 mg, 0.832 mmol) in pyridine (10 mL) was reacted according to GP-C. The crude residue was purified by recrystallization from $CHCl_3$ to afford biaurone **67** (128 mg, 63%) as a bright yellow-orange powdery solid. **m.p.** 284–286 °C. **TLC** R_f = 0.56 (0.5% MeOH/CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 3072w (C–H str), 2948w (C–H str), 1705s (C=O str), 1645s, 1597s (C=C str), 1491s (C=C str), 1437w, 1317m, 1282m, 1201s, 1162m, 1122m, 1112s, 1102m, 1025m, 1004w. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 3.87 (6H, s, 2 × –OCH_3), 6.95 (2H, s, 2 × –C=CH), 7.26–7.30 (6H, m, ArH), 7.77 (4H, d, *J* 8.4 Hz, ArH), 8.04 (4H, d, *J* 8.4 Hz, ArH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 56.0, 105.3, 112.5, 113.8, 121.8, 126.3, 127.4, 132.0, 132.1, 141.3, 148.0, 156.2, 161.2, 184.9. **LCMS** (ES+) *m*/*z* = 503.2 ($[M + H]^+$, t_r = 2.18 min). **HRMS** (ESI+) *m*/*z* = 525.1293 $[M + Na]^+$ found, $C_{32}H_{22}O_6Na^+$ required 525.1309.

(2*Z*,2′*Z*)-2,2′-([1,1′-Biphenyl]-4,4′-diylbis(methanylylidene))bis(4-methoxybenzofuran-3(2*H*)-one) (68). A mixture of bichalcone **58** (100 mg, 0.197 mmol) and $Hg(OAc)_2$ (137 mg, 0.428 mmol) in pyridine (10 mL) was reacted according to GP-C. The crude residue was purified by flash column chromatography (SiO_2, 1% MeOH/CH_2Cl_2) and recrystallized from MeOH to afford biaurone **68** (88.5 mg, 89%) as a bright yellow powdery solid. **m.p.** 298–300 °C. **TLC** R_f = 0.37 (2% MeOH/CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 2944w (C–H str), 2841w (C–H str), 1698m (C=O str), 1648m, 1594s (C=C str), 1492s (C=C str), 1439w, 1353w, 1317m, 1281m, 1251s, 1197m, 1163m, 1074s, 1002w. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 4.04 (6H, s, 2 × –OCH_3), 6.66 (2H, d, *J* 8.0 Hz, ArH), 6.90 (2H, s, 2 × –C=CH), 6.93 (2H, d, *J* 8.0 Hz, ArH), 7.61 (2H, t, *J* 8.0 Hz, ArH), 7.75 (4H, d, *J* 8.4 Hz, ArH), 8.01 (4H, d, *J* 8.4 Hz, ArH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 56.3, 104.8, 105.2, 110.9, 111.4, 127.4, 131.9, 132.1, 138.4, 141.1, 147.1, 158.6, 167.0, 182.3. **LCMS** (ES+) *m*/*z* = 503.2 ($[M + H]^+$, t_r = 1.91 min). **HRMS** (ESI+) *m*/*z* = 503.1486 $[M + H]^+$ found, $C_{32}H_{23}O_6^+$ required 503.1489.

(2*Z*,2′*Z*)-2,2′-([1,1′-Biphenyl]-4,4′-diylbis(methanylylidene))bis(4,6-dimethoxybenzofuran-3(2*H*)-one) (69). A mixture of bichalcone **59** (102 mg, 0.180 mmol) and $Hg(OAc)_2$ (114 mg, 0.359 mmol) in pyridine (10 mL) was reacted according to GP-C. The crude residue was purified by flash column

chromatography (SiO_2, 0.5% MeOH/CH_2Cl_2) to afford biaurone **69** (45.0 mg, 44%) as a bright yellow powdery solid. **m.p.** >300 °C. **TLC** R_f = 0.24 (3% MeOH/CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 3004w (C–H str), 2841w (C–H str), 1694m (C=O str), 1648m, 1587s (C=C str), 1500m (C=C str), 1457m, 1416w, 1360m, 1330m, 1255s, 1208s, 1146s, 1084s, 1037m, 1002w. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 3.95 (6H, s, 2 × –OCH_3), 3.98 (6H, s, 2 × –OCH_3), 6.17 (2H, d, *J* 1.6 Hz, ArH), 6.44 (2H, d, *J* 1.6 Hz, ArH), 6.83 (2H, s, 2 × –C=CH), 7.73 (4H, d, *J* 8.4 Hz, ArH), 7.98 (2H, d, *J* 8.4 Hz, ArH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 56.2, 56.3, 89.3, 94.1, 105.3, 110.2, 127.3, 131.7, 132.2, 140.9, 148.1, 159.5, 169.0, 180.6. **LCMS** (ES+) *m*/*z* = 563.1 ($[M + H]^+$, t_r = 1.87 min). These characterisation data are in accordance with that previously reported in the literature.[49]

(2*Z*,2′*Z*)-2,2′-([1,1′-Biphenyl]-4,4′-diylbis(methanylylidene))bis(5-bromobenzofuran-3(2*H*)-one) (70). A mixture of bichalcone **60** (210 mg, 0.348 mmol) and $Hg(OAc)_2$ (220 mg, 0.689 mmol) in pyridine (10 mL) was reacted according to GP-C. The crude residue was purified by recrystallization from $CHCl_3$ to afford biaurone **70** (182 mg, 87%) as a bright yellow-orange powdery solid. **m.p.** >300 °C. **TLC** R_f = 0.38 (CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 3021w (C–H str), 1706s (C=O str), 1698s, 1639s (C=C str), 1588s (C=C str), 1497w (C=C str), 1455s, 1322w, 1296w, 1259s, 1207w, 1172s, 1119s, 1047w, 1002w. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 6.99 (2H, s, 2 × –C=CH), 7.30 (2H, d, *J* 8.8 Hz, ArH), 7.77–7.80 (6H, m, ArH), 7.96 (2H, d, *J* 2.0 Hz, ArH), 8.03 (4H, d, *J* 8.4 Hz, ArH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 113.5, 114.7, 116.5, 123.4, 127.4, 127.5, 131.7, 132.3, 139.4, 141.6, 147.1, 164.7, 183.2. **LCMS** (ES+) *m*/*z* = 602.1 ($[M + H]^+$, t_r = 2.67 min). **HRMS** (ESI+) *m*/*z* = 598.9500 $[M + H]^+$ found, $C_{30}H_{17}O_4Br_2^+$ required 598.9494.

(2*Z*,2′*Z*,2″*Z*)-2,2′,2″-(Benzene-1,3,5-triyltris(methanylylidene))tris(6-methoxybenzofuran-3(2*H*)-one) (74). A mixture of trichalcone **72** (102 mg, 0.168 mmol) and $Hg(OAc)_2$ (160 mg, 0.502 mmol) in pyridine (10 mL) was reacted according to GP-C. The crude residue was purified by flash column chromatography (SiO_2, 1–5% MeOH/$CHCl_3$) and recrystallized from $CHCl_3$ to afford triaurone **74** (53.1 mg, 52%) as a pale yellow-brown powdery solid. **m.p.** >300 °C. **TLC** R_f = 0.40 (2% MeOH/CH_2Cl_2). **IR** ν_{max} (neat)/cm^{-1}: 3074w (C–H str), 2947w (C–H str), 2842w (C–H str), 1698m (C=O str), 1649m, 1591s (C=C str), 1499m (C=C str), 1440s, 1346m, 1328m, 1265s, 1194m, 1151m, 1124s, 1112s, 1095s, 1015m. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 4.01 (9H, s, 3 × –OCH_3), 6.82 (3H, dd, *J* 8.4, 2.0 Hz, ArH), 6.94 (3H, d, *J* 1.6 Hz, ArH), 6.96 (3H, s, 3 × –C=CH), 7.76 (3H, d, *J* 8.4 Hz, ArH), 8.46 (3H, s, ArH). **^{13}C NMR** (500 MHz, $CDCl_3$): δ 56.2, 96.7, 110.5, 112.7, 114.6, 126.0, 133.7, 134.3, 148.6, 167.9, 168.8, 183.0. **LCMS** (ES+) *m*/*z* = 601.1 ($[M + H]^+$, t_r = 2.18 min). **HRMS** (ESI+) *m*/*z* = 601.1511 $[M + H]^+$ found, $C_{36}H_{25}O_9^+$ required 601.1493.

Biological screening

Aβ preparation. $A\beta_{42}$ was prepared as previously described.[33] Briefly, $A\beta_{42}$ (1 mg) was purchased from Eurogentec Ltd as a lyophilised powder. The peptide was dissolved in trifluroacetic acid (TFA, 1 mL), sonicated in an ice-water bath for 60 s, then lyophilised. Ice cold 1,1,1,3,3,3-hexafluro-2-propanol (HFIP, 1 mL) was added to re-suspend the peptide. The sample was sonicated for 60 s at 0 °C, then aliquoted into 20 μL portions. The HFIP was removed in the vacuum desiccator overnight and the lyophilised samples were stored at −80 °C until use. The required concentration of $A\beta_{42}$ was prepared by dissolving the sample in dimethyl sulfoxide (DMSO) (5% of total solvent volume), then adding sodium phosphate buffer (50 mM, pH 7.4). The solution was sonicated at 0 °C for 3 min, then centrifuged at 13 400 rpm for 30 min at 0 °C to separate any aggregated species.

Thioflavin T assay. ThT was purchased from AbCam (Cambridge). Final concentrations of 10 μM $A\beta_{42}$, 20 μM ThT and 50 μM compound in sodium phosphate buffer (50 mM, pH 7.4) were used for all samples. The assay samples (100 μL) were mixed in a black non-binding 96-well plate (Greiner Bio-One, Switzerland) which was sealed (Nunc, polyolefin acrylate film) and loaded into the fluorescence plate reader (Tecan, Switzerland) at 37 °C. Fluorescence kinetics were measured at 5 min reading intervals, with 15 s shaking before each read. The excitation and emission wavelengths were 440 and 480 nm, respectively.

Acknowledgements

We thank the Cambridge Commonwealth Trust and Cambridge Home and European Scholarship Scheme for the awards of scholarships to T. H. S., T. J. S and S. C. The research leading to these results has received funding from the European Research Council under the European Union's Seventh Framework Programme (FP7/2007-2013)/ERC grant agreements no. [279337/DOS and 695669 & 665631/FH]. The authors also thank AstraZeneca, the European Union (EU), the Engineering and Physical Sciences Research Council (EPSRC), the Biotechnology and Biological Sciences Research Council (BBSRC), the Medical Research Council (MRC), and the Wellcome Trust for funding. Data accessibility: all data supporting this study are included in the paper and provided as ESI† accompanying this paper.

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