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Synthesis of ten membered di-oxa-carbocyclic annulated flavones and olefin tethered bisflavone derivatives–olefin ring closing / cross metathesis

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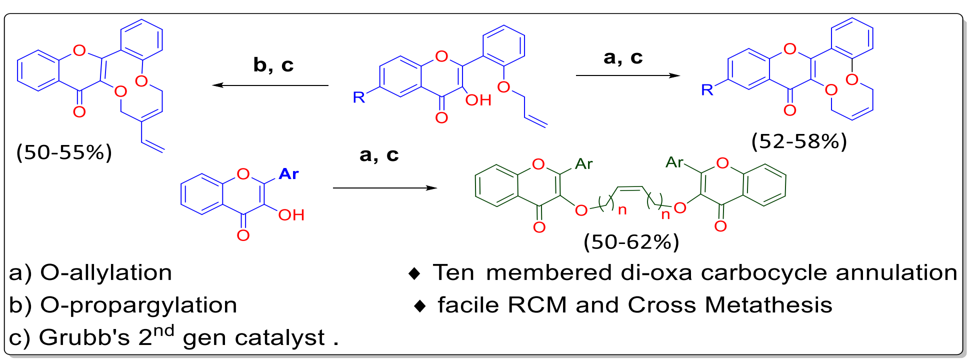
Abstract

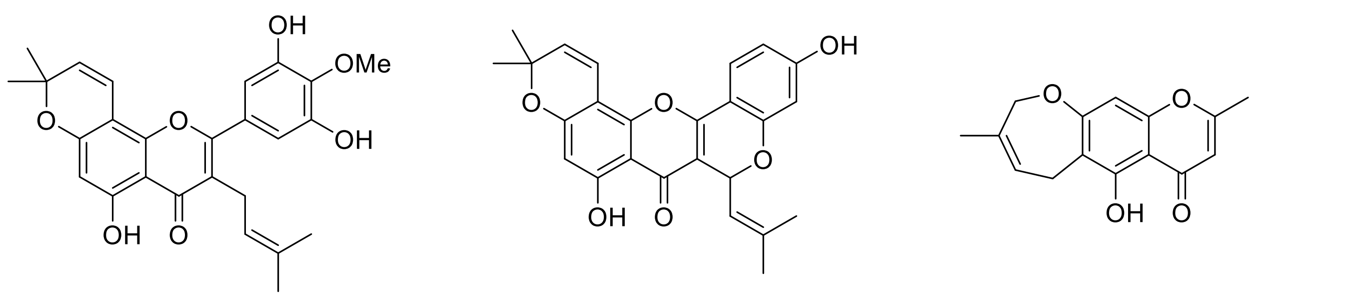
A practical and efficient synthetic strategy to a series of unique ten membered dioxa carbocycle annulated 6-6-10-6 tetracyclic flavones (52-58%) and oxa-olefin bridged bisflavone/ chromone derivatives (50-62%) has been developed in this scheme. 3-Hydroxyflavone and C-2 styryl/heteryl chromones were synthesized and utilized as scaffolds for oxacarbocycle annulations and homocouplings at pyran ring through olefin ring-closing and cross metathesis using Grubbs' 2nd generation catalyst. The potential application of flavones and chromone derivatives in new drug discovery discriminates the importance of powerful synthetic pathways to obtain such diverse heterocyclic derivatives.



Keywords: Flavonols, olefin metathesis, Grubbs' 2nd gen. catalyst, annulation, bisflavones/chromones

Introduction

Flavonoids are naturally occurring polyphenolic secondary metabolites predominantly found in the plant kingdom.[1,2] These are essential constituents of the human diet and possess a therapeutic potential.[3] Flavones and related chromones are known to exhibit health through their biological activities such as anti-inflammatory,[4,5] anti-allergy,[6] anti-tumor,[7] anti-oxidant,[8] anti-viral,[9] anti-microbial,[10] anti-bacterial,[11] anti-platelet aggregation effects,[12] ion transport effects,[13] cardiovascular disease protection[14,15] and vascular fragility.[16] Flavonoids also proved as chemo preventive and chemo therapeutic agents.[17] The interesting structural features and diverse biological activities of these oxygen heterocycles attracted synthetic and medicinal chemists in the construction of new flavone/ chromone embedded bioactive heterocyclic compounds.[18] Some of the biologically significant oxa carbocyclic linear and angular ring fused natural flavone/ chromone derivatives cyclomorusin, artoflavone and Ptaeroxylin[19,20,21] are shown in Figure 1.



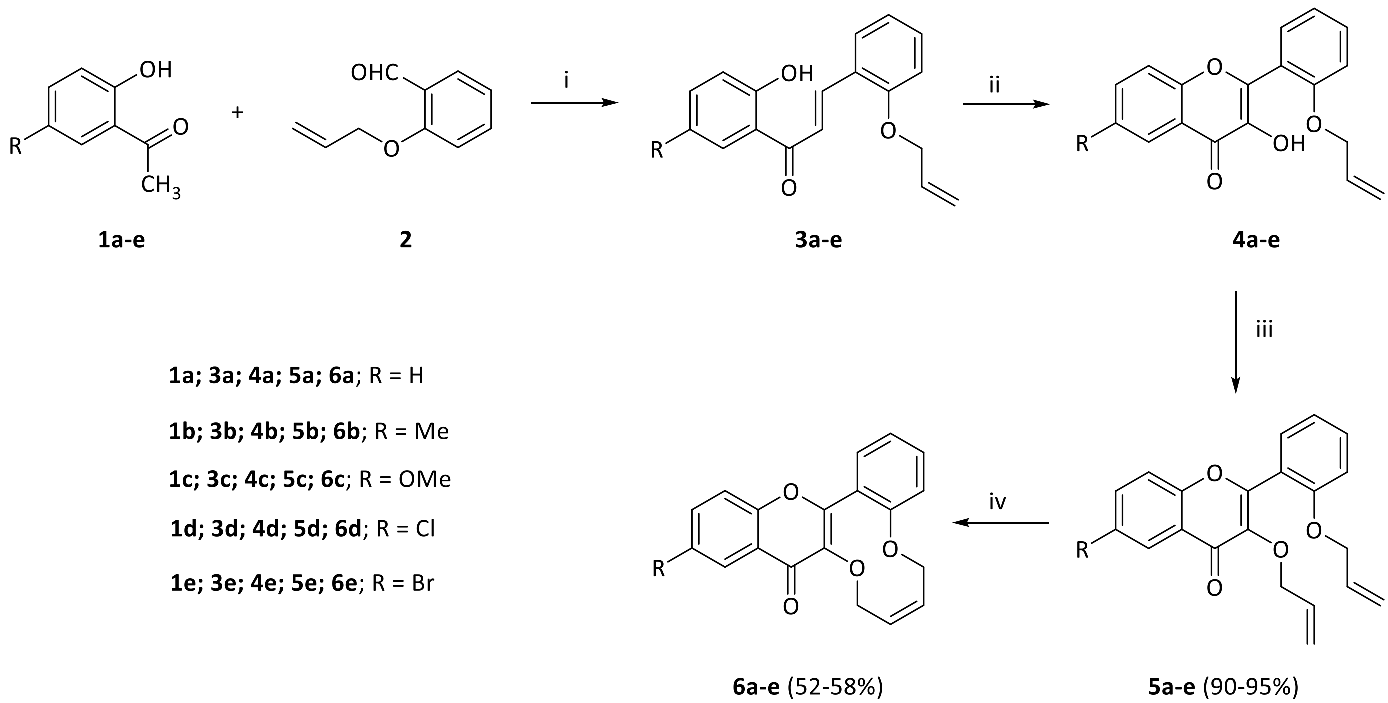
(antioxidant) Artoflavone A (antioxidant) Cyclomorusin (antithelminthic activity) Ptaeroxylin

Figure 1. Pharmacologically active flavone/ chromone natural products.

Developing cyclic frame work is the basic strategy in organic synthesis. Generally, well known cyclization reactions involve radical, cationic and anionic intermediates. With these methods 5 to 7-membered common rings are easy to construct, however formation of 8-11 membered to large rings is difficult due to disfavoured inherent ring strain. Ring closing metathesis has become one of the most powerful methodologies in organic synthesis for the construction of diverse heterocyclic and carbocyclic ring systems, especially for medium to large rings from spatially closer dienes and ene-yne precursors.[22,23,24] Some of the pharmacologically important heterocyclic ring-fused flavones and dioxocin ring containing biologically active natural products were efficiently synthesised by applying RCM.[25,26] Ruthenium based Grubbs' 1st and 2nd generation catalysts have been widely used in ring closing (RCM)[27,28] and cross metathesis (CM).[29,30] Most of the previously reported examples carbocyclic and oxacarbocyclic annulations are at 7/8 and 6/7 positions of flavones.[31] The present study is mainly focused on the synthesis of 10-membered ring-fused flavones at C-3 position and symmetrical bis-flavones involving RCM and CM strategy using Grubbs' 2nd gen catalyst. This is the first reported procedure for the synthesis of 10-membered dioxa-carbocyclic annulated flavone derivatives by adopting the RCM strategies.

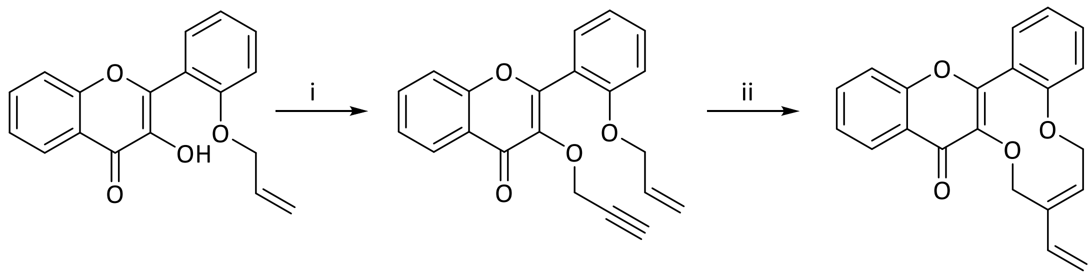
Results and Discussion

2-Hydroxyacetophenones (**1a-e**) when condensed with 2-(allyloxy) benzaldehyde (**2**) in presence of KOH in ethanol at room temperature for 12 h yielded 2-hydroxychalcones **3a-e** (90-92%).[32,33] Hydroxychalcones **3a-e** were treated with H_2O_2 /NaOH in methanol (Algar-Flynn-Oyamada cyclisation) to provide corresponding 3-hydroxy flavones (**4a-e**). The allylation of **4a-e** with allyl bromide in presence of K_2CO_3/acetone under reflux gave diene key intermediates **5a-e**. The dienes **5a-e** were subjected to ring-closing metathesis (RCM) in presence of Grubbs' 2nd gen catalyst in DCM under reflux to form ten membered dioxacarbocycle annulated flavone derivatives **6a-e** in satisfactory yields (Scheme 1). In the ^{1}H NMR spectra of **6a**, the newly formed ring protons appeared at δ 6.21 – 6.08 (m, 2H), δ 4.88 (d, *J* 2.9 Hz, 4H) and ^{13}C NMR of **6a**, ring carbons appeared at δ 131.64 (=CH), 131.41 (=CH), 62.8 (OCH_2), 68.9 (OCH_2)



Scheme 1. Synthesis of **6a-e.** Reagents and conditions: i) KOH, EtOH, rt, 12 h; ii) H_2O_2, NaOH, MeOH, rt, 4 h; iii) Allyl bromide, K_2CO_3, acetone, reflux, 4 h; iv) Grubbs' 2nd gen catalyst (10 mole%), DCM, reflux, 6 h.

In order to prepare vinyl dioxa carbocycle annulated flavone (**8a**), intermediate **4a** was treated with propargyl bromide in presence of K_2CO_3/acetone under reflux to give (**7a**) an ene-yne intermediate which underwent ring-closing metathesis in the presence of Grubbs' 2nd gen. catalyst in CH_2Cl_2 under reflux to form 10-membered ene-yne ring closing product **8a** with a satisfactory yield of 50-55% (Scheme 2). In the ^{1}H NMR spectra of **8a**, the characteristic signal of newly formed vinyl dioxepine appeared at δ 6.04 – 5.90 (m, 1H), δ 5.32 (dd, *J* 17.3, 3.2 Hz, 2H), δ 5.19 (dd, *J* 10.6, 2.9 Hz, 2H), δ 4.89 (d, *J* 2.4 Hz, 2H), δ 4.62 (dt, *J* 4.9, 1.6 Hz, 1H). In ^{13}C NMR of compound **8a** characteristic carbons appeared at δ 59.2 (OCH_2), δ 69.2 (OCH_2), 112.7 ($=CH_2$), 120.4 (=CH), 139.2 (=CH).

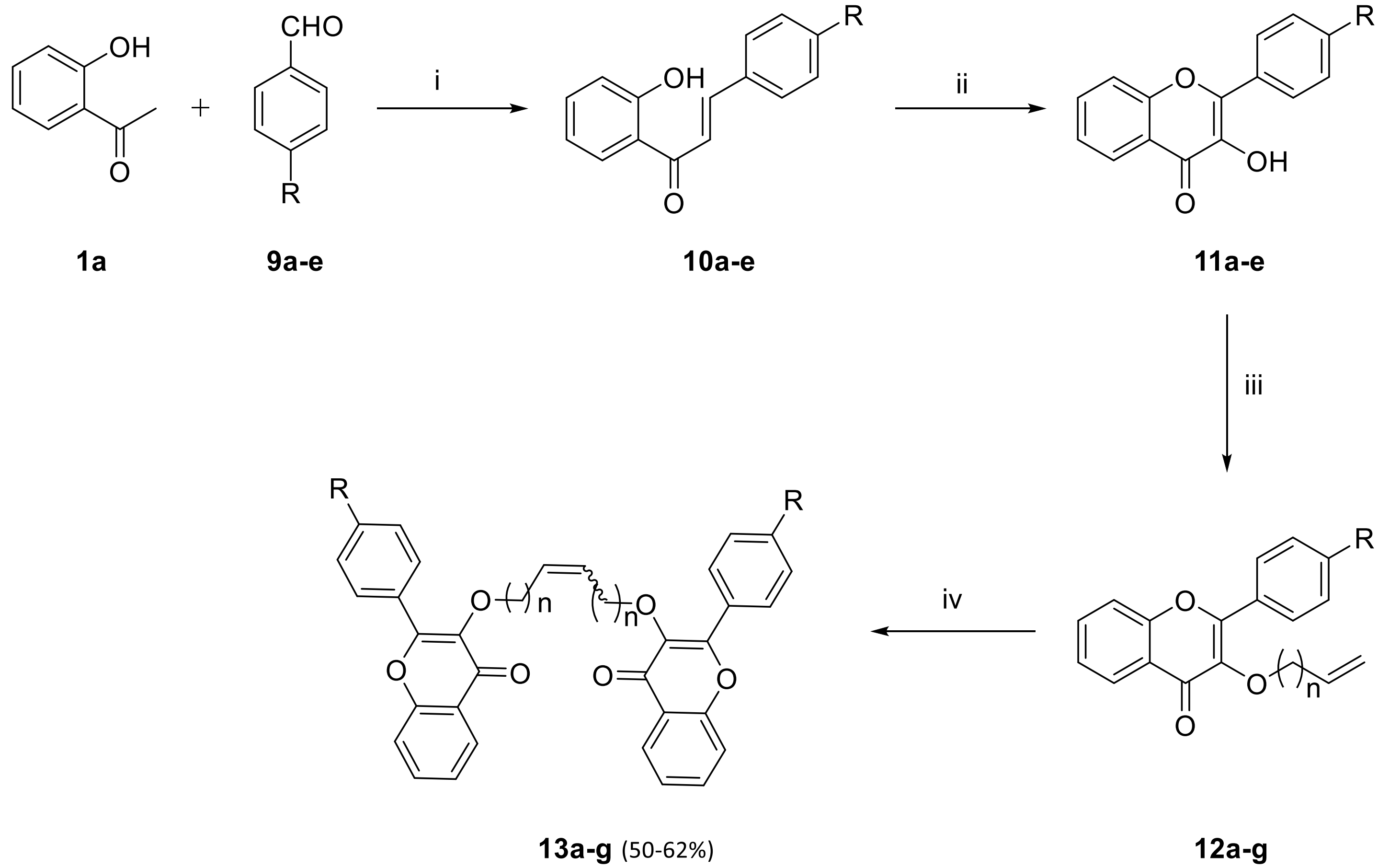


4a **7a** (90-91%) **8a** (50-55%)

Scheme 2. Synthesis of 10-membered vinyl dioxacarbocycle annulated derivative (**8a).** Reagents and conditions: i) Propargyl bromide, K_2CO_3, acetone, reflux, 4 h; ii) Grubbs' 2nd gen. catalyst (10 mole%), DCM, reflux, 6 h.

To further expand the scope of the olefin metathesis strategy, we concentrated on preparing cross metathesis product bisflavone **13a-g**. 3-hydroxyflavones (**11a-e**) on treating with alkenyl bromides and K_2CO_3 / acetone at 70 ^oC gave 3-alkenyloxy flavones (**12a-g**). The intermediates **12a-g** were subjected to olefin cross metathesis using Grubbs' 2nd gen. catalyst (10 mol%, 6 h) under reflux in CH_2Cl_2 to give olefin cross metathesis products oxa-alkenyl chain tethered bis-flavones (**13a-g**) with 45 – 50% yields (Scheme 3). In the ^1H NMR spectra of **13a,** the protons of newly formed olefin appeared at δ 5.79 (=CH) (d, *J* 10.5 Hz, 2H), δ 4.68 – 4.50 (m, 4H) and in ^{13}C NMR carbons resonated at δ 67.7 (OCH_2), 128.4 (=CH).

We next gave attention to extend cross metathesis to styryl chromones and 2- furyl/thiophenyl chromones to prepare the corresponding olefin tethered bis derivatives. In the first step, cinnamaldehyde **14** was condensed with 2-hydroxyacetophenone **1a** in presence of KOH in ethanol to give 2-hydroxychalcones **15**, In the second step, **15** was converted to the respective (E)-3-hydroxy-2-styryl-4H-chromen-4-one **16** by treating with hydrogen peroxide and NaOH in methanol. To the solution of compound **16,** K_2CO_3 and allyl bromide was added in presence of acetone at 70 ^oC to give C-3 allyloxy compound **17**. The allyloxy precursor **17** on treating with Grubbs' 2nd gen. catalyst under reflux in DCM gave cross coupled product **18** in 45 – 50% yield (Scheme 4). Cross metathesis product was selectively formed instead of the expected competitive ring closing metathesis product. In the ^1H NMR spectra of **18**, the protons of newly formed olefin appeared at δ 6.17 (dd, *J* 10.1, 4.9 Hz, 2H), δ 4.96 – 4.80 (m, 4H).



12a; **13a**; n = 1, R = H

12b; **13b**; n = 1, R = CH_3

12c; **13c**; n = 1, R = OCH_3

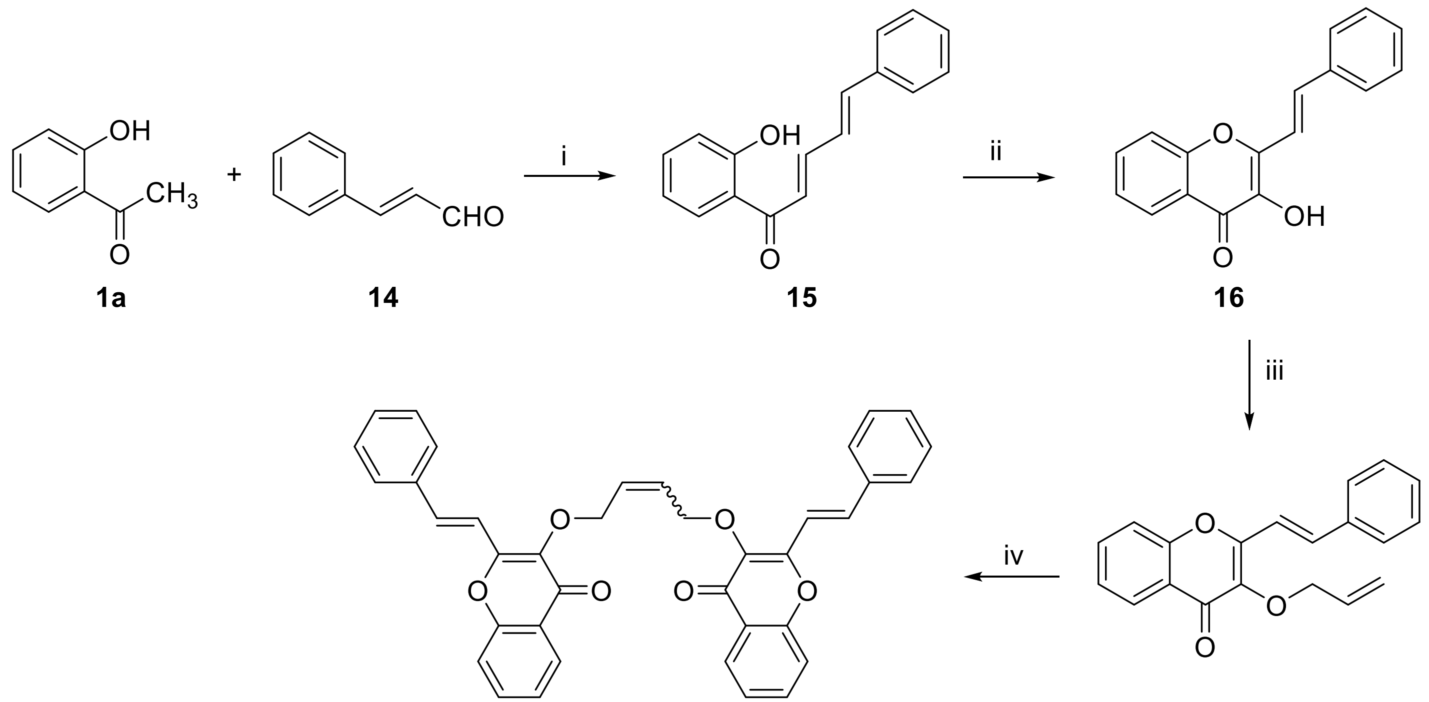
12d; **13d**; n = 1, R = Br

12e; **13e**; n = 1, R = Cl

12f; **13f**; n = 2, R = H

12g; **13g**; n = 3, R = H

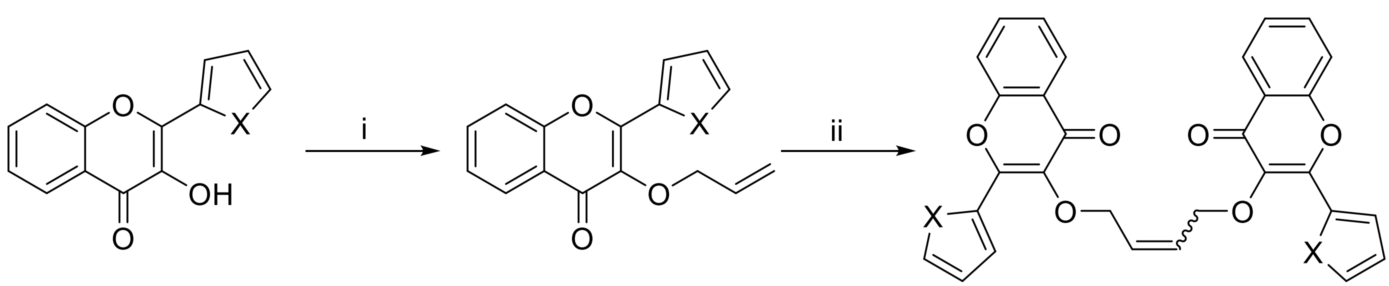
Scheme 3. Synthesis of bis-flavones **13a-g.** Reagents and conditions: i) KOH, EtOH, rt, 12 h; ii) H_2O_2, NaOH, MeOH, rt, 4 h; iii) Akenyl bromide, K_2CO_3, acetone, reflux, 4 h; iv) Grubbs' 2[nd] gen catalyst (10 mole%), DCM, reflux, 6 h.



18 (50-55%) **17**

Scheme 4. Synthesis of bis-styryl flavone (**18**). Reagents and conditions: i) KOH, EtOH, rt, 12 h; ii) H_2O_2, NaOH, MeOH, rt, 4 h; iii) Allyl bromide, K_2CO_3, acetone, 70 °C, 4 h; iv) Grubbs' 2nd gen catalyst (10 mole%), DCM, reflux, 6 h.

Compound **19a-b** reacted with allyl bromide in acetone and K_2CO_3 at 70 °C to give intermediates **20a-b**. The allyloxy compounds **20a-b** on treating with Grubbs' 2nd gen. catalyst under reflux in DCM exclusively gave cross metathesis product bis-thiophenyl/furyl chromones (**21a-b**) in 52 – 56% yields (Scheme 5). In the ^{1}H NMR spectra of **21a**, the characteristic signal at δ 6.25 – 6.16 (m, 2H), δ 4.91 (dd, *J* 3.2, 1.5 Hz, 4H) δ and in **21b**, the signal at δ 6.13 (m, 2H), δ 4.84 (dd, *J* 3.0, 1.2 Hz, 4H) suggest the formation of the olefinic bond.



19a-b **20a-b** **21a-b** (43-45%)

19a; 20a; 21a; X = S
19b; 20b; 21b; X = O

Scheme 5. Synthesis of bisfuryl/thiophenyl chromones (**21a-b**) Reagent and condition: i) Allyl bromide, K_2CO_3, acetone, 70 °C, 4 h; ii) Grubbs' 2nd gen. catalyst (10 mol %), DCM, reflux, 6 h.

Conclusions

We report a simple and practicable synthesis of potentially bioactive 10-membered dioxacarbocycle-annulated flavones and bisflavones and furyl/thiophenyl chromones by adopting Grubbs' (2nd gen. catalyst) ring closing metathesis (RCM) and cross metathesis (CM) strategy. It is key to understand the requirements for effective olefin CM and RCM in order to achieve and manipulate successful reactions to afford flavonoid molecular architectures.

Experimental Section

General. Unless otherwise specified, all solvents and reagents were obtained from commercial suppliers. Solvents were purified as per the procedures given in the *Text book of practical organic chemistry* by Vogel, 6th Edition. All reactions were performed under nitrogen atmosphere unless otherwise noted. Column chromatography was performed using Merck silica gel 60-120 mesh. ^{1}H NMR and ^{13}C NMR spectra were recorded on bruker spectrometer at 400 MHz and 100 MHz respectively, tetramethylsilane (TMS) as internal standard, chemical shift (δ) are reported in parts per million (ppm). Multiplicity singlet (s), doublet (d), doublet of doublet (dd), triplet of doublet (td) doublet of doublet of doublet (ddd), doublet of doublet of triplet (ddt) and multiplet (m) coupling constant (*J* in Hz). Mass spectral analysis was accomplished using electro spray ionization (ESI) techniques.

General procedure for the synthesis of 2-(2-(allyloxy)phenyl)-3-hydroxy-4H-chromen-4-ones (4a-e). 5 Molar aq. KOH solution (5 mL) was added to 2-hydroxyacetophenone (**1a**) (3.0 g, 0.021 mmol) and 2-(allyloxy) benzaldehyde (**2**) (5.0 g, 0.003 mmol) in ethanol and the reaction mixture was stirred for 12h at room temperature. After completion of reaction, indicated by TLC the reaction mixture was acidified with aq. HCl to pH 4-6. Pale yellow solid was filtered and dried to get 5.0 g of 2-hydroxychalcone (**3a**). It was used for further reaction without column chromatography. To 2-hydroxychalcone (**3a**) (3.0 g, 0.010 mmol) H_2O_2 (15 mL), NaOH (3.0 g) in methanol was added. This mixture was stirred for 4 h at room temperature, then acidified with 2 M HCl to P^H 4-6 and ice cold water (200 mL) was added to get white colour solid, it was filtered and purified with column chromatography (60-120) to yield 4.5 g of 2-(2-(allyloxy)phenyl)-3-hydroxy-4*H*-chromen-4-one (**4a**).

2-(2-(Allyloxy) phenyl)-3-hydroxy-4H-chromen-4-one (4a). White solid; Yield 90%; mp: 80-82 °C. IR (solid, KBr, $v_{max,}$ cm^{-1}): 1625 (C=O, ketone). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, *J* 7.2 Hz, 1H), 7.71 – 7.65 (m, 1H), 7.62 (dd, *J* 7.6, 1.2 Hz, 1H), 7.53 – 7.44 (m, 1H), 7.41 (t, *J* 7.5 Hz, 1H), 7.11 (t, *J* 7.5 Hz, 1H), 7.05 (d, *J* 8.4 Hz, 1H), 5.98 (dd, *J* 15.6, 10.2 Hz, 1H), 5.40 – 5.28 (m, 1H), 5.23 – 5.14 (m, 1H), 4.62 (t, *J* 10.6 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.38, 156.46, 156.00, 146.20, 138.83, 133.39, 132.80, 131.97, 131.05, 125.54, 124.38, 121.38, 120.81, 120.05, 119.22, 118.42, 117.30, 113.25, 69.34. MS (ESI): *m/z* 294 [M+H]$^+$.

2-(2-(Allyloxy) phenyl)-3-hydroxy-6-methyl-4*H*-chromen-4-one (4b). Yellow solid; Yield 92%; mp: 84-87 °C. IR (solid, KBr, $v_{max,}$ cm^{-1}): 1623 (C=O, ketone). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (dd, *J* 25.9, 12.2 Hz, 1H), 7.61 (td, *J* 7.8, 1.6 Hz, 1H), 7.50 – 7.42 (m, 1H), 7.33 – 7.27 (m, 1H), 7.24 – 7.19 (m, 1H), 7.15 – 6.98 (m, 1H), 6.59 – 6.31 (m, 1H), 6.16 – 5.90 (m, 1H), 5.40 – 5.28 (m, 1H), 5.27 – 5.13 (m, 1H), 4.71 – 4.58 (m, 2H), 2.43 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.16, 156.45, 156.23, 145.37, 144.73, 138.61, 132.86, 131.82, 131.02, 126.07, 125.22, 120.97, 120.80, 120.23, 119.09, 118.01, 117.25, 113.28, 69.37, 21.9. MS (ESI): *m/z* 308 [M+H]$^+$.

2-(2-(Allyloxy)phenyl)-3-hydroxy-6-methoxy-4*H*-chromen-4-one (4c). Golden red solid; Yield 95%; mp: 86-88 °C. IR (solid, KBr, $v_{max,}$ cm^{-1}): 1626 (C=O, ketone). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 – 7.59 (m, 1H), 7.50 – 7.46

(m, 1H), 7.46 – 7.42 (m, 1H), 7.29 (dd, *J* 9.2, 3.1 Hz, 1H), 7.11 (td, *J* 7.5, 0.9 Hz, 1H), 7.05 (d, *J* 8.4 Hz, 1H), 6.49 (s, 1H), 6.05 – 5.92 (m, 1H), 5.37 – 5.29 (m, 1H), 5.23 – 5.17 (m, 1H), 4.66 – 4.60 (m, 2H), 3.93 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 172.96, 156.43, 156.38, 151.14, 145.99, 138.48, 132.80, 131.91, 131.05, 124.23, 121.81, 120.80, 120.13, 119.87, 117.25, 113.23, 103.83, 69.32, 55.97. MS (ESI): *m/z* 324 [M+H]$^+$.

2-(2-(Allyloxy)phenyl)-6-chloro-3-hydroxy-4*H*-chromen-4-one (4d). White solid; Yield 88%; mp: 90-95 ^{o}C. IR (solid, KBr, $\nu_{max,}$ cm^{-1}): 1628 (C=O, ketone). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J* 2.4 Hz, 1H), 7.64 – 7.58 (m, 2H), 7.52 – 7.42 (m, 1H), 7.10 (dd, *J* 14.4, 6.9 Hz, 1H), 7.05 (d, *J* 8.4 Hz, 1H), 6.05 – 5.91 (m, 1H), 5.31 (dt, *J* 16.3, 8.1 Hz, 1H), 5.20 (dd, *J* 10.6, 1.2 Hz, 1H), 4.64 (t, *J* 8.6 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.32, 156.43, 154.25, 146.66, 138.97, 133.66, 132.73, 132.18, 131.02, 130.30, 124.75, 122.30, 120.83, 120.13, 119.67, 117.38, 113.21, 69.34. MS (ESI): *m/z* 328 [M+H]$^+$.

2-(2-(Allyloxy)phenyl)-6-bromo-3-hydroxy-4*H*-chromen-4-one (4e). Light yellow solid; Yield 86%; mp: 93-96 ^{o}C. IR (solid, KBr, $\nu_{max,}$ cm^{-1}): 1635 (C=O, ketone). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (d, *J* 2.4 Hz, 1H), 7.77 – 7.71 (m, 1H), 7.61 (dd, *J* 7.6, 1.7 Hz, 1H), 7.48 (ddd, *J* 8.5, 7.5, 1.8 Hz, 1H), 7.40 (d, *J* 9.0 Hz, 1H), 7.11 (td, *J* 7.5, 0.9 Hz, 1H), 7.05 (d, *J* 8.4 Hz, 1H), 6.50 (s, 1H), 5.98 (ddt, *J* 17.3, 10.5, 4.9 Hz, 1H), 5.37 – 5.29 (m, 1H), 5.20 (dq, *J* 10.6, 1.5 Hz, 1H), 4.63 (dt, *J* 4.9, 1.6 Hz, 2H).^{13}C NMR (101 MHz, $CDCl_3$) δ 172.12, 156.43, 154.67, 146.43, 138.96, 136.34, 132.71, 132.18, 131.00, 127.99, 122.70, 120.84, 120.35, 119.65, 117.68, 117.39, 113.20, 69.33. MS (ESI): *m/z* 371 [M+H]$^+$.

General procedure for the synthesis of 3-(allyloxy)-2-(2-(allyloxy) phenyl)-4H-chromen-4-ones (5a-e). To the solution of compounds **4a-e** (1.0 g, 0.003 mmol) in dry acetone (30 mL) was added at room temperature in presence of K_2CO_3 (0.9 g, 0.005 mmol) and allyl bromide (0.6 mL, 0.005 mmol). The reaction mixture was refluxed for 4 h at 70 ^{o}C then mixture was cooled to rt. The solvent was evaporated and extracted with ethyl acetate (50 mL). The organic layer was washed with brine solution (30 mL) and (**5a-e**)solvent was removed in *vacuo*. The crude product 3-(allyloxy)-2-(2-(allyloxy)phenyl)-4H-chromen-4-one was purified by column chromatography on silica gel (Ethylacetate/hexane 1:3).

3-(Allyloxy)-2-(2-(allyloxy)phenyl)-4*H*-chromen-4-one (5a). White solid; Yield 93%; mp: 58-60 ^{o}C. IR (solid, KBr, $\nu_{max,}$ cm^{-1}): 1634 (C=O, ketone). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (dd, *J* 8.0, 1.5 Hz, 1H), 7.64 (ddd, *J* 8.6, 7.1, 1.7 Hz, 1H), 7.51 – 7.43 (m, 3H), 7.42 – 7.36 (m, 1H), 7.07 (td, *J* 7.5, 0.9 Hz, 1H), 7.01 (d, *J* 8.4 Hz, 1H), 6.02 – 5.90 (m, 1H), 5.84 – 5.73 (m, 1H), 5.34 – 5.27 (m, 1H), 5.18 (dq, *J* 10.6, 1.4 Hz, 1H), 5.12 (ddd, *J* 17.2, 3.2, 1.6 Hz, 1H), 5.07 – 5.02 (m, 1H), 4.58 (tdd, *J* 5.9, 4.0, 2.6 Hz, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.03, 156.68, 156.45, 155.74, 140.61, 133.90, 133.23, 132.79, 131.80, 131.16, 125.84, 124.55, 124.49, 120.60, 120.47, 118.15, 117.70, 117.53, 117.35, 112.72, 73.31, 69.17. MS (ESI): *m/z* 334 [M+H]$^+$.

3-(Allyloxy)-2-(2-(allyloxy)phenyl)-6-methyl-4H-chromen-4-one (5b). Light yellow solid; Yield 96%; mp: 60-62 ^{o}C. IR (solid, KBr, $\nu_{max,}$ cm^{-1}): 1622 (C=O, ketone). IR (solid, KBr, $\nu_{max,}$ cm^{-1}): 1630 (C=O, ketone). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, *J* 8.1 Hz, 1H), 7.49 – 7.41 (m, 2H), 7.25 – 7.18 (m, 2H), 7.10 – 7.04 (m, 1H), 7.01 (d, *J* 8.2 Hz, 1H), 6.01 – 5.91 (m, 1H), 5.77 (ddt, *J* 16.2, 10.4, 5.9 Hz, 1H), 5.34 – 5.28 (m, 1H), 5.18 (ddd, *J* 10.5, 2.9, 1.4 Hz, 1H), 5.11 (ddd, *J* 17.2, 3.2, 1.5 Hz, 1H), 5.03 (dd, *J* 10.4, 1.5 Hz, 1H), 4.60 (dt, *J* 4.9, 1.6 Hz, 2H), 4.56 (dt, *J* 5.9, 1.2 Hz, 2H), 2.48 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 174.94, 156.45, 155.91, 144.48, 140.50, 133.98, 132.85, 131.67, 131.17, 126.10, 125.60, 122.33, 120.78, 120.45, 117.80, 117.59, 117.33, 112.72, 73.31, 69.19, 21.80. MS (ESI): *m/z* 348 [M+H]$^+$.

3-(Allyloxy)-2-(2-(allyloxy)phenyl)-6-methoxy-4*H*-chromen-4-one (5c). Yellow solid; Yield 95%; mp: 62-64 ^{o}C. IR (solid, KBr, $\nu_{max,}$ cm^{-1}): 1638 (C=O, ketone). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* 3.1 Hz, 1H), 7.49 – 7.46 (m, 1H), 7.46 – 7.42 (m, 1H), 7.39 (d, *J* 9.2 Hz, 1H), 7.27 – 7.23 (m, 1H), 7.07 (td, *J* 7.5, 0.9 Hz, 1H), 7.01 (d, *J* 8.3 Hz, 1H), 6.02 – 5.89 (m, 1H), 5.78 (ddt, *J* 17.1, 10.4, 5.9 Hz, 1H), 5.30 (ddd, *J* 17.3, 3.3, 1.7 Hz, 1H), 5.18 (dq, *J* 10.6, 1.5 Hz, 1H), 5.11 (ddd, *J* 17.2, 3.2, 1.6 Hz, 1H), 5.04 (ddd, *J* 10.4, 2.8, 1.2 Hz, 1H), 4.59 (dt, *J* 4.9, 1.6 Hz, 2H), 4.56 (dt, *J* 5.9, 1.3 Hz, 2H), 3.92 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 174.74, 156.51, 156.49, 156.45, 150.72, 140.18, 133.94, 132.80, 131.74, 131.16, 125.13, 123.64, 120.70, 120.46, 119.58, 117.66, 117.30, 112.72, 104.55, 73.32, 69.16, 55.93. MS (ESI): *m/z* 364 [M+H]$^+$.

3-(Allyloxy)-2-(2-(allyloxy) phenyl)-6-chloro-4*H*-chromen-4-one (5d). White solid; Yield 92%; mp: 60-65 °C. IR (solid, KBr, $v_{max,}$ cm^{-1}): 1643 (C=O, ketone). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, *J* 2.5 Hz, 1H), 7.58 (dd, *J* 8.9, 2.6 Hz, 2H), 7.49 – 7.44 (m, 1H), 7.43 – 7.39 (m, 1H), 7.07 (tt, *J* 6.7, 3.3 Hz, 1H), 7.04 – 6.99 (m, 1H), 6.01 – 5.88 (m, 1H), 5.76 (dt, *J* 17.1, 10.4 Hz, 1H), 5.33 – 5.25 (m, 1H), 5.19 (dq, *J* 10.6, 1.5 Hz, 1H), 5.11 (dd, *J* 17.2, 3.1 Hz, 1H), 5.04 (dd, *J* 10.4, 2.8 Hz, 1H), 4.59 (dt, *J* 4.9, 1.6 Hz, 2H), 4.55 (dt, *J* 5.9, 1.3 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.88, 156.99, 156.45, 154.06, 140.62, 133.68, 133.45, 132.72, 131.99, 131.13, 130.47, 125.52, 125.17, 120.50, 120.24, 119.87, 117.91, 117.40, 112.71, 73.32, 69.17. MS (ESI): *m/z* 368 [M+H]$^+$.

3-(Allyloxy)-2-(2-(allyloxy) phenyl)-6-bromo-4*H*-chromen-4-one (5e). White solid; Yield 90%; mp: 65-67 °C. IR (solid, KBr, $v_{max,}$ cm^{-1}): 1649 (C=O, ketone). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (d, *J* 2.4 Hz, 1H), 7.72 (dd, *J* 8.9, 2.4 Hz, 1H), 7.47 (dd, *J* 7.3, 4.3 Hz, 2H), 7.35 (d, *J* 8.9 Hz, 1H), 7.11 – 7.04 (m, 1H), 7.02 (d, *J* 8.5 Hz, 1H), 5.95 (ddt, *J* 17.2, 10.2, 5.0 Hz, 1H), 5.76 (ddt, *J* 16.3, 10.4, 5.9 Hz, 1H), 5.35 – 5.25 (m, 1H), 5.19 (dd, *J* 10.6, 1.4 Hz, 1H), 5.15 – 5.07 (m, 1H), 5.05 (dd, *J* 10.3, 1.3 Hz, 1H), 4.59 (dt, *J* 4.8, 1.4 Hz, 2H), 4.55 (dt, *J* 4.8, 1.1 Hz, 2H).^{13}C NMR (101 MHz, $CDCl_3$) δ 173.76, 157.03, 156.43, 154.47, 140.65, 136.19, 133.65, 132.70, 132.01, 131.13, 128.39, 125.92, 120.50, 120.19, 120.12, 117.96, 117.91, 117.42, 112.68, 73.32, 69.15. MS (ESI): *m/z* 412 [M+H]$^+$.

General procedure for the synthesis of (*Z*)-6,9-dihydro-11*H*-benzo[4,5][1,6]dioxecino[3,2-b]chromen-11-ones (6a-e). 3-(allyloxy)-2-(2-(allyloxy) phenyl)-4H-chromen-4-one (**5a**) (0.15 g, 0.004 mmol) was dissolved in CH_2Cl_2 (20 mL) and Grubbs 2nd gen catalyst (10mol %) was added under N_2 atmosphere and the reaction mixture was heated at 45 °C for 6 h (**6a-e**). The solvent was concentrated in *vacuo* and the products **6a-e** were purified by the column chromatography on silica gel (AcOEt/hexane1:3).

(*Z*)-6,9-Dihydro-11*H*-benzo[4,5][1,6]dioxecino[3,2-*b*]chromen-11-one (6a). White solid; Yield 55%; mp: 60-62 °C. IR (solid, KBr, $v_{max,}$ cm^{-1}): 1622 (C=O, ketone). 1H NMR (400 MHz, $CDCl_3$) δ 8.30 (dd, *J* 8.0, 1.2 Hz, 1H), 7.72 – 7.62 (m, 1H), 7.56 – 7.47 (m, 2H), 7.43 (dd, *J* 11.7, 9.3 Hz, 2H), 7.12 (dd, *J* 16.7, 8.2 Hz, 2H), 6.21 – 6.08 (m, 2H), 4.88 (d, *J* 2.9 Hz, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.21, 155.89, 155.84, 154.83, 141.90, 133.14, 132.15, 131.64, 131.41, 130.04, 125.83, 124.66, 124.61, 122.43, 121.36, 118.19, 112.81, 68.91, 62.85. HRMS (ESI, *m/z*) Calcd for $C_{19}H_{15}O_4$ [M+H]$^+$: 307.0959, Found: 307.0964.

(*Z*)-13-Methyl-6,9-dihydro-11*H*-benzo[4,5][1,6]dioxecino[3,2-b]chromen-11-one (6b). Brown solid; Yield 57%; mp: 60-64 °C. IR (solid, KBr, $v_{max,}$ cm^{-1}): 1624 (C=O, ketone). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, *J* 8.2 Hz, 1H), 7.54 (dd, *J* 7.6, 1.7 Hz, 1H), 7.43 (ddd, *J* 13.5, 7.6, 3.9 Hz, 1H), 7.30 (s, 1H), 7.22 (dd, *J* 8.2, 1.1 Hz, 1H), 7.11 (dd, *J* 9.1, 8.4, 4.5 Hz, 2H), 6.21 – 6.09 (m, 2H), 4.87 (dd, *J* 5.3, 3.9 Hz, 4H), 2.49 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.16, 156.05, 155.82, 144.43, 132.09, 131.68, 131.30, 130.03, 126.21, 125.55, 122.56, 121.33, 117.88, 112.80, 77.34, 77.02, 76.70, 68.90, 62.85, 21.80. HRMS (ESI, *m/z*) Calcd for $C_{20}H_{16}O_4$ [M+H]$^+$: 321.10821, Found: 321.11214.

(*Z*)-13-Methoxy-6,9-dihydro-11*H*-benzo[4,5][1,6]dioxecino[3,2-b]chromen-11-one (6c). White solid; Yield 54%; mp: 65-67 °C. IR (solid, KBr, $v_{max,}$ cm^{-1}): 1625 (C=O, ketone). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* 3.1 Hz, 1H), 7.54 (dd, *J* 7.6, 1.6 Hz, 1H), 7.43 (dd, *J* 10.8, 5.3 Hz, 2H), 7.26 (dd, *J* 8.6, 3.6 Hz, 1H), 7.16 – 7.08 (m, 2H), 6.24 – 5.98 (m, 2H), 5.03 – 4.77 (m, 4H), 3.92 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.91, 156.59, 155.78, 154.70, 150.86, 141.50, 132.15, 131.66, 131.36, 130.07, 125.25, 123.51, 122.50, 121.35, 119.63, 112.78, 104.56, 68.90, 62.81, 55.95. HRMS (ESI, *m/z*) Calcd for $C_{20}H_{16}O_5$ [M+H]$^+$: 337.10313, Found: 337.10705.

(Z)-13-Chloro-6,9-dihydro-11*H*-benzo[4,5][1,6]dioxecino[3,2-b]chromen-11-one (6d). White solid; Yield 58%; mp: 70-75 °C. IR (solid, KBr, $v_{max,}$ cm^{-1}): 1627 (C=O, ketone). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, *J* 2.5 Hz, 1H), 7.59 (dt, *J* 12.4, 6.2 Hz, 1H), 7.54 (dd, *J* 7.6, 1.6 Hz, 1H), 7.48 – 7.41 (m, 2H), 7.18 – 7.08 (m, 2H), 6.18 – 6.09 (m, 2H), 4.94 – 4.81 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.04, 155.84, 155.19, 154.20, 141.91, 133.37, 132.27, 131.63, 131.50, 130.60, 129.98, 125.64, 125.14, 122.05, 121.40, 119.93, 112.83, 68.93, 62.84. HRMS (ESI, *m/z*) Calcd for $C_{19}H_{13}ClO_4$ [M+Na]$^+$: 341.04729, Found: 341.05751.

(*Z*)-13-Bromo-6,9-dihydro-11*H*-benzo[4,5][1,6]dioxecino[3,2-b]chromen-11-one (6e). Light green solid; Yield 52%; mp: 65-70 °C. IR (solid, KBr, $\nu_{max,}$ cm^{-1}): 1630 (C=O, ketone). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (d, *J* 2.4 Hz, 1H), 7.75 – 7.71 (m, 2H), 7.33 (dd, *J* 14.4, 5.5 Hz, 2H), 7.00 (d, *J* 7.2 Hz, 1H), 6.87 (d, *J* 4.1 Hz, 1H), 5.90 (d, *J* 14.4 Hz, 2H), 4.58 (d, *J* 26.1 Hz, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.54, 157.15, 156.76, 155.71, 154.47, 140.36, 136.11, 132.08, 131.84, 131.17, 129.28, 128.46, 128.14, 125.76, 120.60, 120.26, 120.09, 117.90, 112.38, 71.83, 67.81, 29.70. HRMS (ESI, *m/z*) Calcd for $C_{19}H_{13}BrO_4$ [M+H]$^+$: 385.99769, Found: 385.29322.

General procedure for the synthesis of 2-(2-(allyloxy) phenyl)-3-(prop-2-yn-1-yloxy)-4*H*-chromen-4-one (7a). 2-(2-(allyloxy)phenyl)-3-hydroxy-4*H*-chromen-4-one (**4a**) (0.9 g, 0.003 mmol) was dissolved in solvent acetone (30 mL) then K_2CO_3 (0.84 g, 0.006 mmol) and propargyl bromide (0.4 mL, 0.004 mmol)were added. The reaction mixture was refluxed for 4 h, concentrated in *vacuo* and the crude product **7a** was purified by column chromatography on silica gel (AcOEt/hexane1:3).

2-(2-(Allyloxy)phenyl)-3-(prop-2-yn-1-yloxy)-4*H*-chromen-4-one (7a). White solid; Yield (90-91%); mp: 80-82 °C. IR (solid, KBr, $\nu_{max,}$ cm^{-1}): 1632 (C=O, ketone). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (dd, *J* 8.0, 1.6 Hz, 1H), 7.67 (dd, *J* 8.6, 7.1 Hz, 1H), 7.55 (dd, *J* 7.6, 1.7 Hz, 1H), 7.50 – 7.44 (m, 2H), 7.44 – 7.39 (m, 1H), 7.08 (td, *J* 7.5, 0.9 Hz, 1H), 7.02 (d, *J* 8.4 Hz, 1H), 5.97 (ddd, *J* 17.2, 10.2, 5.0 Hz, 1H), 5.32 (dd, *J* 17.3, 3.2 Hz, 1H), 5.19 (dq, *J* 10.6, 1.4 Hz, 1H), 4.89 (d, *J* 2.4 Hz, 2H), 4.62 (dt, *J* 5.0, 1.6 Hz, 2H), 2.33 (t, *J* 2.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.76, 157.12, 156.58, 155.78, 139.29, 133.38, 132.84, 131.91, 131.37, 125.86, 124.65, 124.46, 120.45, 118.19, 117.44, 112.75, 79.04, 75.58, 69.24, 59.29. MS (ESI): *m/z* 332 [M+H]$^+$.

General procedure for the synthesis of (*Z*)-8-vinyl-6,9-dihydro-11*H*-benzo[4,5][1,6]dioxecino[3,2-*b*]chromen-11-one (8a). 2-(2-(Allyloxy)phenyl)-3-(prop-2-yn-1-yloxy)-4*H*-chromen-4-one **(7a)** (0.2 g, 0.004 mmol) was dissolved in CH_2Cl_2 (20 mL) and Grubbs' 2nd gen catalyst (10 mol %) was added under N_2 atmosphere and the reaction mixture was heated at 45 °C for 6 h to give ene-yne metathesis product **8a,** a white solid. The solvent was concentrated in *vacuo* and purified by the column chromatography on silica gel (AcOEt/hexane 1:3)

(Z)-8-Vinyl-6,9-dihydro-11*H*-benzo[4,5][1,6]dioxecino[3,2-b]chromen-11-one (8a). White solid; Yield 51%; mp: 80-85 °C. IR (solid, KBr, $\nu_{max,}$ cm^{-1}): 1635 (C=O, ketone). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (dd, *J* 8.0, 1.5 Hz, 1H), 7.67 (dd, *J* 8.6, 7.1 Hz, 1H), 7.55 (dd, *J* 7.6, 1.7 Hz, 2H), 7.49 – 7.44 (m, 1H), 7.44 – 7.39 (m, 1H), 7.12 – 7.04 (m, 1H), 7.02 (d, *J* 8.4 Hz, 1H), 6.04 – 5.90 (m, 1H), 5.32 (dd, *J* 17.3, 3.2 Hz, 1H), 5.19 (dd, *J* 10.6, 2.9 Hz, 2H), 4.89 (d, *J* 2.4 Hz, 2H), 4.62 (dt, *J* 4.9, 1.6 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.83, 157.08, 156.57, 155.77, 139.28, 133.35, 132.83, 131.88, 131.35, 125.84, 124.61, 124.44, 124.41, 120.42, 118.16, 117.40, 112.72, 69.21, 59.26. MS (ESI): *m/z* 333 [M+H]$^+$. Anal. Calcd for $C_{21}H_{16}O_4$: C, 75.89; H, 4.85. Found: C, 75.85, H, 4.80%.

General procedure for the synthesis of (*Z*)-3,3'-(but-2-ene-1,4-diylbis(oxy))bis(2-phenyl-4*H*-chromen-4-ones (13a-g). The allyloxy flavones **12a-g** were dissolved in CH_2Cl_2 (20 mL) and Grubbs' 2nd gen. catalyst (10 mol-%) was added . The mixture was refluxed for 6 h to give cross metathesis products **13a-g**. The crude was purified by the column chromatography on silica gel (AcOEt/hexane 1:3).

(*Z*)-3,3'-(but-2-ene-1,4-diylbis(oxy))bis(2-phenyl-4*H*-chromen-4-one) (13a). White solid; Yield 54%; mp: 85-87 °C. IR (solid, KBr, $\nu_{max,}$ cm^{-1}): 1633 (C=O, ketone). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (dd, *J* 16.5, 7.8 Hz, 2H), 8.07 – 7.99 (m, 4H), 7.68 (dd, *J* 15.0, 7.4 Hz, 2H), 7.58 – 7.49 (m, 2H), 7.48 – 7.42 (m, 4H), 7.38 (dd, *J* 11.2, 7.5 Hz, 4H), 5.79 (d, *J* 10.5 Hz, 2H), 4.68 – 4.50 (m, 4H).^{13}C NMR (101 MHz, $CDCl_3$) δ 175.08, 155.29, 139.88, 133.43, 133.39, 130.98, 130.69, 130.64, 129.70, 129.21, 128.68, 128.40, 125.84, 124.68, 124.64, 124.16, 118.01, 117.97, 72.10, 67.76. HRMS (ESI, *m/z*) Calcd for $C_{34}H_{24}O_6$ [M+H]$^+$: 529.16064, Found: 529.16518.

(*Z*)-3, 3'-(but-2-ene-1,4-diylbis(oxy))bis(2-(*p*-tolyl)-4*H*-chromen-4-one) (13b). White solid; Yield 52%; mp: 82-85 °C. IR (solid, KBr, $\nu_{max,}$ cm^{-1}): 1636 (C=O, ketone). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J* 5.9 Hz, 2H), 7.95 (d, *J* 5.8 Hz, 4H), 7.68 (s, 2H), 7.53 (d, *J* 6.9 Hz, 2H), 7.40 (s, 2H), 5.82 (d, *J* 14.2 Hz, 2H), 4.59 (d, *J* 21.5 Hz, 4H), 2.40 (d, *J* 10.9 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.05, 156.33, 155.24, 141.17, 139.64, 133.32, 129.73, 129.18, 128.59, 128.11, 125.80, 124.60, 124.14, 117.99, 77.34, 77.03, 76.71, 72.04, 21.56. HRMS (ESI, *m/z*) Calcd for $C_{36}H_{28}O_6$ [M+H]$^+$: 557.19194, Found: 557.19769.

(*Z*)-3, 3'-(but-2-ene-1,4-diylbis(oxy))bis(2-(4-methoxyphenyl)-4*H*-chromen-4-one) (13c). White solid; Yield 62%; mp: 82-85 °C. IR (solid, KBr, $\nu_{max,}$ cm^{-1}): 1639 (C=O, ketone). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 – 8.15 (m, 2H), 8.09 – 8.00 (m, 4H), 7.74 – 7.59 (m, 2H), 7.58 – 7.43 (m, 2H), 7.45 – 7.32 (m, 2H), 7.02 – 6.89 (m, 4H), 5.87 (dd, *J* 25.4, 5.7 Hz, 2H), 4.60 (dd, *J* 7.7, 4.7 Hz, 4H), 3.95 – 3.79 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.95, 161.50, 156.13, 155.17, 139.24, 133.26, 132.31, 130.43, 129.79, 129.26, 125.79, 124.59, 124.14, 123.28, 117.93, 113.92, 113.75, 71.99, 67.66, 55.43, 29.72. HRMS (ESI, *m/z*) Calcd for $C_{36}H_{28}O_8$ [M+H]$^+$: 589.18177, Found: 589.18569.

(*Z*)-3, 3'-(but-2-ene-1, 4-diylbis(oxy))bis(2-(4-chlorophenyl)-4*H*-chromen-4-one) (13d). White solid; Yield 55%; mp: 102-108 °C. IR (solid, KBr, $\nu_{max,}$ cm^{-1}): 1641 (C=O, ketone). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (t, *J* 9.4 Hz, 2H), 8.00 (d, *J* 8.2 Hz, 4H), 7.70 (t, *J* 7.7 Hz, 2H), 7.52 (t, *J* 8.0 Hz, 2H), 7.42 (t, *J* 7.8 Hz, 6H), 5.82 (d, *J* 22.5 Hz, 2H), 4.69 – 4.57 (m, 4H).^{13}C NMR (101 MHz, $CDCl_3$) δ 174.95, 155.15, 139.92, 133.65, 133.60, 131.73, 130.17, 130.14, 129.84, 129.75, 129.30, 125.86, 125.34, 124.87, 124.82, 124.05, 117.99, 117.95, 71.96, 67.68. HRMS (ESI, *m/z*) Calcd for $C_{34}H_{22}Cl_2O_6$ [M+H]$^+$: 596.4440, Found: 596.08749.

(*Z*)-3, 3'-(but-2-ene-1,4-diylbis(oxy))bis(2-(4-bromophenyl)-4*H*-chromen-4-one) (13e). White solid; Yield 50%; mp: 105-110 °C. IR (solid, KBr, $\nu_{max,}$ cm^{-1}): 1639 (C=O, ketone). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (dd, *J* 18.9, 7.0 Hz, 2H), 7.96 – 7.89 (m, 4H), 7.69 (dd, *J* 15.5, 7.1 Hz, 2H), 7.58 (dd, *J* 8.6, 2.7 Hz, 4H), 7.50 (dd, *J* 16.4, 8.3 Hz, 2H), 7.46 – 7.34 (m, 2H), 5.92 – 5.71 (m, 2H), 4.76 – 4.51 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.95, 155.15, 139.92, 133.65, 133.60, 131.73, 130.17, 130.14, 129.84, 129.75, 129.30, 125.86, 125.34, 124.87, 124.82, 124.05, 117.99, 117.95, 71.96, 67.68. HRMS (ESI, *m/z*) Calcd for $C_{34}H_{22}Br_2O_6$ [M+H]$^+$: 686.35200, Found: 686.98468.

(*Z*)-3, 3'-(Hex-3-ene-1, 6-diylbis(oxy))bis(2-phenyl-4*H*-chromen-4-one) (13f). White solid; Yield 52%; mp: 70-75 °C. IR (solid, KBr, $\nu_{max,}$ cm^{-1}): 1627 (C=O, ketone). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 – 8.24 (m, 2H), 8.11 – 8.06 (m, 4H), 7.67 (ddd, *J* 8.6, 7.1, 1.7 Hz, 2H), 7.55 – 7.51 (m, 2H), 7.50 – 7.45 (m, 6H), 7.43 – 7.37 (m, 2H), 5.46 – 5.35 (m, 2H), 4.03 (t, *J* 6.8 Hz, 4H), 2.38 (dq, *J* 16.1, 5.4 Hz, 4H).^{13}C NMR (101 MHz, $CDCl_3$) δ 175.13, 156.25, 155.25, 141.16, 139.77, 133.68, 133.32, 129.17, 128.65, 128.23, 125.80, 124.59, 124.15, 118.44, 117.97, 76.74, 73.19, 21.55. HRMS (ESI, *m/z*) Calcd for $C_{36}H_{29}O_6$ [M+H]$^+$: 557.19194, Found: 557.19587.

(*Z*)-3, 3'-(Oct-4-ene-1,8-diylbis(oxy))bis(2-phenyl-4*H*-chromen-4-one) (13g). White solid; Yield 56%; mp: 72-76 °C. IR (solid, KBr, $\nu_{max,}$ cm^{-1}): 1621 (C=O, ketone). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, *J* 7.7 Hz, 2H), 8.08 (d, *J* 3.9 Hz, 4H), 7.67 (t, *J* 7.2 Hz, 2H), 7.56 – 7.45 (m, 8H), 7.39 (t, *J* 7.4 Hz, 2H), 5.34 – 5.15 (m, 2H), 4.00 (t, *J* 6.4 Hz, 4H), 1.95 (d, *J* 36.5 Hz, 4H), 1.82 – 1.63 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.19, 155.83, 155.29, 140.66, 133.35, 131.11, 130.63, 129.89, 128.74, 128.39, 125.83, 124.60, 124.24, 117.99, 72.19, 29.84, 28.78. MS (ESI): *m/z* 585 [M+H]$^+$. Anal. Calcd for $C_{38}H_{32}O_6$: C, 78.06; H, 5.52. Found: C, 78.10, H, 5.56%.

General procedure for the synthesis of 3,3'-(((*Z*)-but-2-ene-1,4-diyl)bis(oxy))bis(2-((E)-styryl)-4*H*-chromen-4-one) (18). (E)-3-(allyloxy)-2-styryl-4H-chromen-4-one (**17**) (0.2 g, 0.006 mmol) was dissolved in CH_2Cl_2 (20 mL) and Grubbs' 2nd catalyst (10 mol %) was added under N_2 condition and the reaction mixture was heated at 45 °C for 6 h to yield cross metathesis product **18**. The solvent was concentrated in *vacuo* and purified by the column chromatography on silica gel (AcOEt/hexane 1:3).

3,3'-(((*Z*)-But-2-ene-1,4-diyl)bis(oxy))bis(2-((*E*)-styryl)-4*H*-chromen-4-one) (18). Brown solid; Yield (50-55%); mp: 122-126 °C. IR (solid, KBr, v_{max}, cm^{-1}): 1637 (C=O, ketone). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (dd, J 8.0, 1.6 Hz, 2H), 7.62 (ddd, J 8.6, 7.1, 1.7 Hz, 2H), 7.42 (t, J 7.4 Hz, 2H), 7.36 (ddd, J 8.1, 7.1, 1.0 Hz, 2H), 6.49 – 6.31 (m, 2H), 6.17 (ddd, J 10.1, 4.9, 2.7 Hz, 2H), 4.96 – 4.80 (m, 4H). ^{13}C NMR (101 MHz) δ 171.15, 154.48, 148.54, 137.15, 133.09, 129.44, 125.99, 124.63, 124.55, 119.94, 118.43, 117.95, 77.39, 77.07, 76.76, 65.57. MS (ESI): *m/z* 581 $[M+H]^+$. Anal. Calcd for $C_{38}H_{28}O_6$: C, 78.61; H, 4.86. Found: C, 78.65, H, 4.90%.

General procedure for the synthesis of (*Z*)-3,3'-(but-2-ene-1,4-diylbis(oxy))bis(2-(furan/thiophene-2-yl)-4*H*-chromen-4-one) (21a-b). 3-(allyloxy)-2-(furan /thophine-2-yl)-4H-chromen-4-one (**20a-b**) (0.2 g, 0.007 mmol) was dissolved in CH_2Cl_2 (20 mL) and Grubbs' 2nd gen catalyst (10 mol %) was added under N_2 medium and the reaction mixture was heated at 45 °C for 6 h to give pure cross metathesis product (**21a-b**). The solvent concentrated in *vacuo* and purified by the column chromatography on silica gel (AcOEt/hexane).

(*Z*)-3, 3'-(But-2-ene-1,4-diylbis(oxy))bis(2-(thiophen-2-yl)-4*H*-chromen-4-one) (21a). White solid; Yield (43-45%); mp: 90-95 °C. IR (solid, KBr, v_{max}, cm^{-1}): 1631 (C=O, ketone). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (dd, *J* 8.0, 1.5 Hz, 2H), 7.91 (dd, *J* 3.8, 1.1 Hz, 2H), 7.72 – 7.67 (m, 2H), 7.57 – 7.44 (m, 4H), 7.38 (t, *J* 7.5 Hz, 2H), 7.16 (dd, *J* 5.0, 3.9 Hz, 2H), 6.25 – 6.16 (m, 2H), 4.91 (dd, *J* 3.2, 1.5 Hz, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.63, 154.77, 133.35, 133.35, 131.50, 130.08, 129.67, 127.39, 125.79, 124.66, 117.78, 77.29, 77.04, 76.78, 71.50. MS (ESI): *m/z* 541 $[M+H]^+$. Anal. Calcd for $C_{30}H_{20}O_6S_2$: C, 66.65; H, 3.73. Found: C, 66.69, H, 3.79%.

(*Z*)-3, 3'-(But-2-ene-1,4-diylbis(oxy))bis(2-(furan-2-yl)-4*H*-chromen-4-one) (21b). White solid; Yield (43-45%); mp: 88-91 °C. IR (solid, KBr, v_{max}, cm^{-1}): 1638 (C=O, ketone). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, *J* 8.1 Hz, 2H), 7.64 (t, *J* 18.9 Hz, 5H), 7.57 (d, *J* 8.8 Hz, 2H), 7.44 – 7.32 (m, 5H), 6.13 (m, 2H), 4.84 (dd, *J* 3.0, 1.2 Hz, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.12, 145.10, 133.42, 129.94, 125.73, 124.79, 118.04, 116.87, 112.69, 77.35, 77.04, 76.72, 71.59, 29.72. MS (ESI): *m/z* 509 $[M+H]^+$. Anal. Calcd for $C_{30}H_{20}O_8$: C, 70.86; H, 3.96. Found: C, 70.80, H, 3.91%.

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Supplementary Material

The experimental procedures (^{1}H NMR, ^{13}C NMR, and HRMS spectrum of the compounds **4a-e, 5a-e, 6a-e, 13a-g, 18** and **21a-b**) associated with this article can be found in the website.

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