RSC Advances

PAPER

View Article Online
View Journal | View Issue

Cite this: *RSC Adv.*, 2018, **8**, 16802

Diastereoselective synthesis of novel spiro indanone fused pyrano[3,2-*c*]chromene derivatives following hetero-Diels–Alder reaction and *in vitro* anticancer studies†

Pravati Panda,[a] Sabita Nayak,*[a] Susanta Ku. Sahoo,[a] Seetaram Mohapatra,[a] Deepika Nayak,[b] Rajalaxmi Pradhan[b] and Chanakya Nath Kundu*[b]

The development of concise methods for the synthesis of small functionalised spirocyclic molecules is important in the search of new bioactive molecules. To contribute this, here we represent a diastereoselective oxa-hetero-Diels–Alder reaction for the synthesis of novel spiro indanone fused pyrano[3,2-*c*]chromene derivatives and studied their *in vitro* anticancer activities. Using previously less explored cyclic ketone *i.e.* indane-1,3-dione and 3-vinyl-2*H*-chromene derivatives, we obtained novel spiro-heterocyclic frameworks at the interphase between "drug-like" molecules and natural products. Various spiro indanone fused pyrano[3,2-*c*]chromene derivatives were synthesized regiospecifically bearing a quaternary stereocenter in high yields (up to 85%) with excellent diastereoselectivity in toluene using 4 Å MS as additive under reflux condition at 120 °C. *In vitro* cytotoxic studies of these compounds against MCF-7 (breast cancer), HCT-116 (colon cancer), H-357 (oral cancer), MD-MB-231(Breast cancer) cell lines were evaluated by MTT {3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide} assay *in vitro*. The screening results revealed that many of the compounds are showing moderate to high levels of anticancer activities against the tested cancer cell lines and some displayed potent inhibitory activities in comparison to the commercial anticancer drug 5-fluorouracil (5-FU). Among the series, compound **3′c** showed most potent cytotoxicity (15.0–27.5 μM) in three cancer cell lines (MCF-7, HCT-116 and MD-MB-231).

Received 29th March 2018
Accepted 23rd April 2018

DOI: 10.1039/c8ra02729c

rsc.li/rsc-advances

Introduction

Chiral indane frameworks, particularly indanone subunits, constitute a unique group of desirable targets in organic synthesis and attracted the attention of organic chemists and biologists because of their broad distribution in biologically active natural products and pharmaceutically active compounds such as fredericamycin, colephomone-D, raddenone and yenhusomidine.[1,2] Due to their synthetic utility and application in pharmaceuticals, a variety of synthetic protocols have been developed for the synthesis of optically pure indanone skeleton.[3] Of particular interest are methods for stereoselective formation of medicinally important spirocyclic indanone frameworks, such as those that enantioselectively generate a quaternary stereocenter, considered a challenging transformation.[4–8] Organocatalyst mediated synthesis of oxa spirocyclic indanone scaffold was reported in the literature in 2013 by Peng *et al.*[1] following Morita–Baylis–Hillman reaction. Although good stereoselectivity was observed in product formation, however the synthetic method suffers from drawbacks in reaction conditions and yields. Efficient cost effective synthesis methods of the oxa spirocyclic indanone backbone are needed in order to expand the usefulness of this intriguing combination of pharmacologically interesting pyran and indanone motifs.

On the other hand, the pyran ring is among one of the most widely investigated heterocycles.[9] It is the core unit of benzopyran, chromene, flavonoids, coumaroin, xanthones and naphthoquinones, which exhibit diverse pharmacological activities.[10–15] The benzopyran or chromene cores are prevalent in many natural products show fascinating therapeutic activities.[16–22] In recent years, chromeno fused pyran based heterocyclic natural products such as Ethuliacoumarion and its derivatives, spiro oxindole fused pyranochromene, dihydropyranochromene *etc.*[23,24] have attracted tremendous interest among researchers because they possess both a chromene and pyran moiety which has potential applications in medicinal

[a]*Department of Chemistry, Ravenshaw University, Cuttack, Odisha, India. E-mail: sabitanayak18@gmail.com*

[b]*Cancer Biology Division, School of Biotechnology, Kalinga Institutue of Industrial Technology, Campus-11, Patia, Bhubaneswar, Odisha-751024, India. E-mail: cnkundu@kiitbiotech.ac.in*

† Electronic supplementary information (ESI) available. See DOI: 10.1039/c8ra02729c

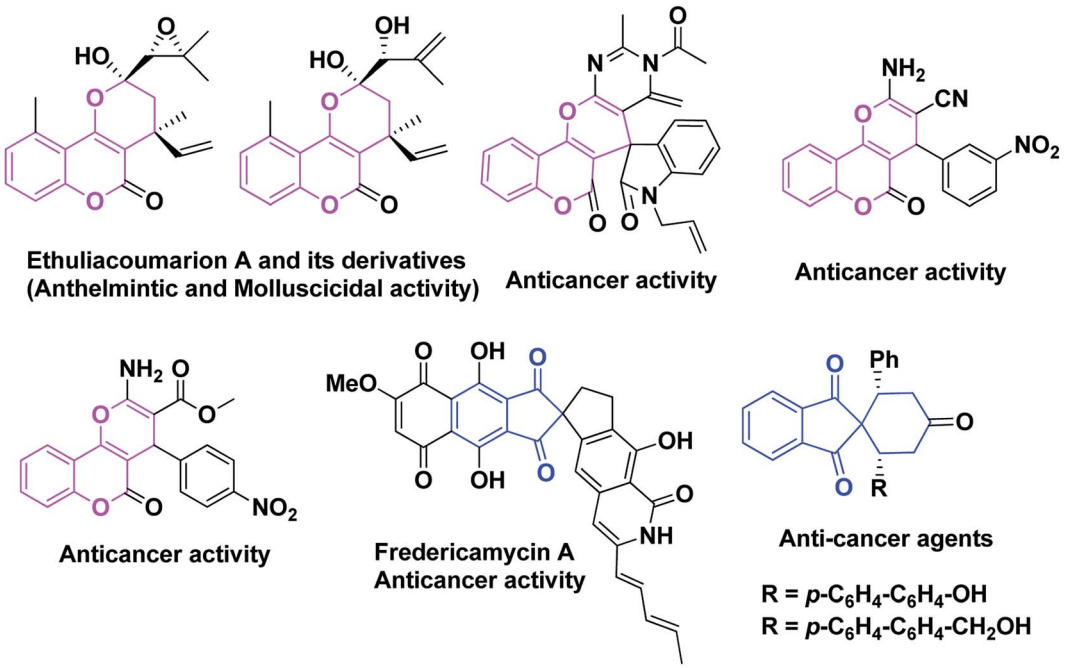
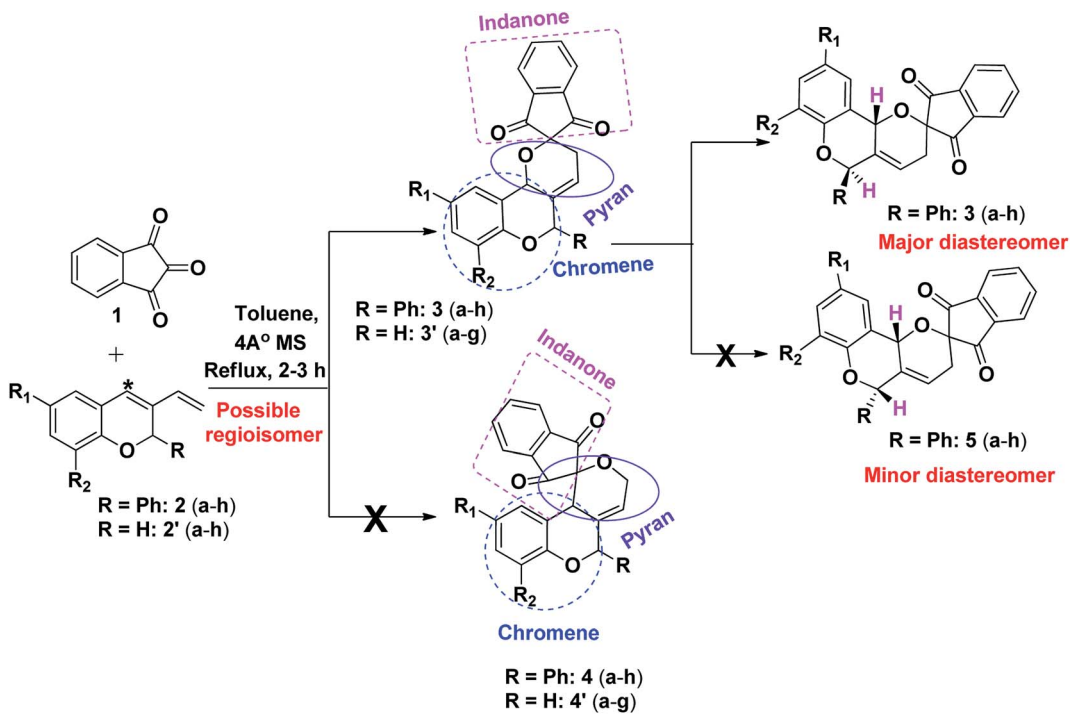


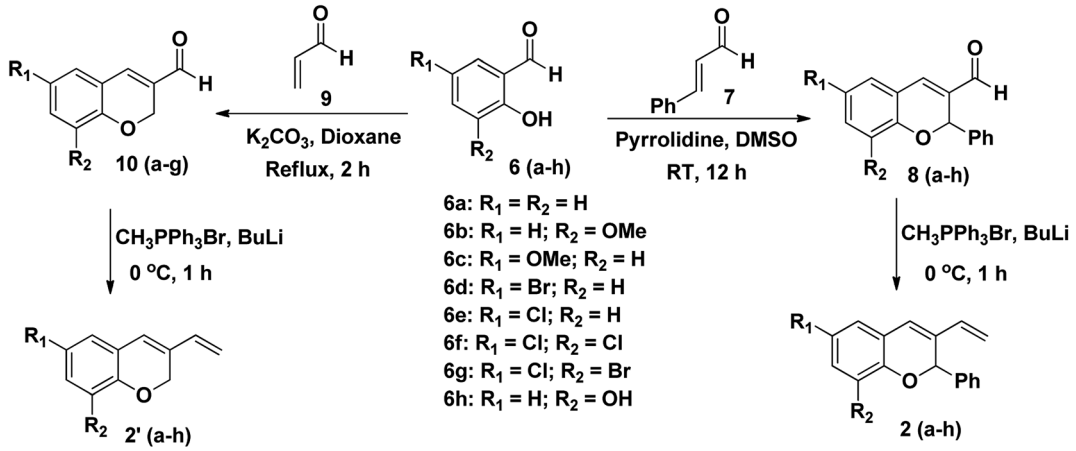
Fig. 1 Various natural and synthetic products based on biologically active indanone and pyranochromene scaffolds.

chemistry and exhibit significant biological activities, such as anticancer, anthelmintic and molluscicidal activity (Fig. 1).

Due to the biomedical importance of chromeno fused pyran and spiro-indane-1,3-dione skeletons, combination of these two units in one molecule may benefit diversity of structure and drug discovery. The hetero-Diels–Alder (HDA) reaction is arguably the most powerful way of constructing six-membered heterocycles bearing a chiral tertiary or quaternary carbon centre in a single step from commercially available substrates.[25] Although asymmetric HDA reactions of aldehydes as dienophile have been extensively studied,[23] ketone substrates, in contrast, are much less reactive in HDA reactions due to electronic and steric properties, and are still challenging substrates for chemists.[26]



Scheme 1 Model for synthesis of spiro indanone fused pyrano chromene.

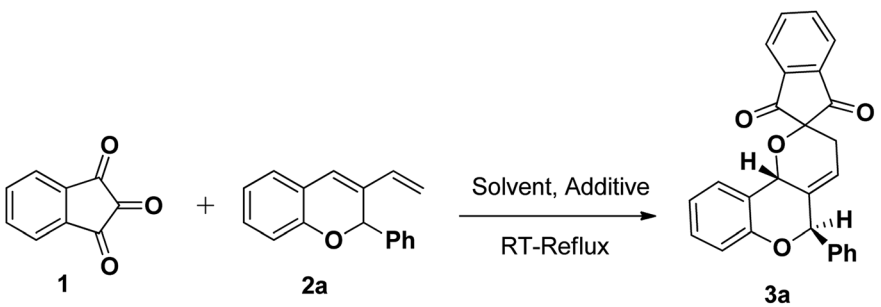


Scheme 2 Synthesis of 2*H*-chromene-3-carbaldehyde **8(a–h)** and **10(a–g)** and 3-vinyl-2*H*-chromene **2(a–h)** and **2′(a–h)**.

As a part of our continuing efforts for the synthesis of heterocycles, to combine the interesting and remarkable biological activities of both indanone and chromeno fused pyran derivatives we sought a synthesis of spiro indanone fused pyrano[3,2-*c*]chromene skeleton. Literature survey disclosed number of reports describing the synthesis of spiro pyran derivatives using isatin backbone.[26–29] However, to the best of our knowledge only a very few reports are there for the synthesis of oxa spirocyclic indanone scaffold.[30] In this study, we present our contribution to the successful discovery of new potent anticancer candidates through concise construction of novel chiral spiro indanone fused pyrano[3,2-*c*]chromene exhibiting a unique profile of biological activities *via* hetero Diels Alder reaction. Furthermore, we hope this new type of spiro pyrano chromene can serve as a potential anticancer agent.

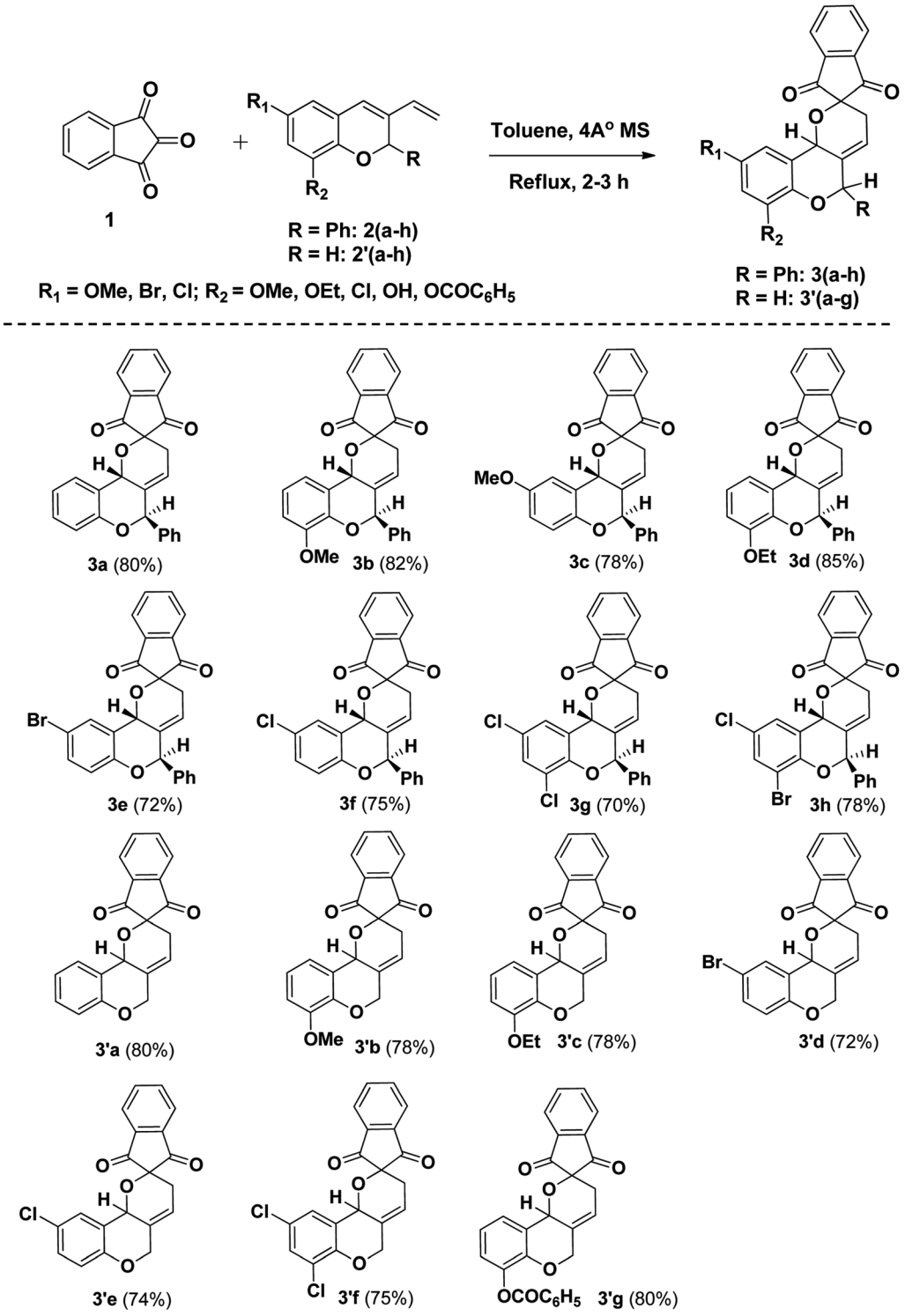
A novel synthetic approach for the regiospecific and diastereoselective synthesis of spiro indanone fused pyrano[3,2-*c*] chromene **3(a–h)** by the reaction of indane-1,3-dione **1** and 3-vinyl-2*H*-chromene **2(a–h)** and **2′(a–h)** in toluene *via* hetero Diels Alder reaction was reported (Scheme 1). It was interesting

Table 1 Optimisation for the synthesis of **3a**



Entry	Solvent	Additive	Temp. (°C)	Time (h)	Yield[a] (%)
1	Toluene	_	RT	12 h	n.r
2	Toluene	_	Reflux	12 h	40%
3	Toluene	4 Å MS	Reflux	2 h	80%
4	Benzene	4 Å MS	RT	12 h	n.r
5	Benzene	4 Å MS	Reflux	4 h	50%
6	CH_3CN	4 Å MS	RT	12 h	n.r
7	CH_3CN	4 Å MS	Reflux	6 h	40%
8	DCM	4 Å MS	RT	12 h	n.r
9	DCM	4 Å MS	Reflux	6 h	20%

[a] Indane-1,3-dione **1** (1 mmol) and 3-vinyl-2*H*-chromene **2a** (1 mmol) at reflux in toluene for 3 h in the presence of 4 Å MS.

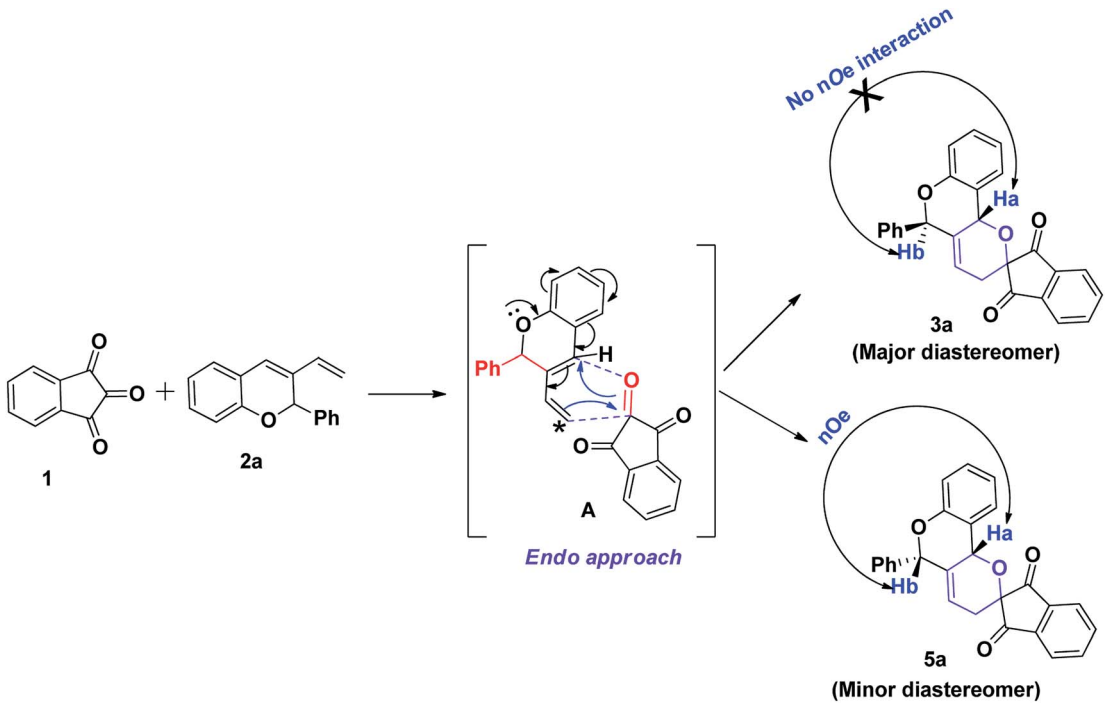


Scheme 3 Synthesis of spiro indanone fused pyrano chromene 3(a–h) and 3′(a–g).

that regioisomer **3(a–h)** and **3′(a–g)** were formed regiospecifically whereas regioisomers **4(a–h)** and **4′(a–g)** were not observed might be due to the non-interaction of *C orbital of the diene (lower orbital co-efficient) with carbonyl carbon orbital of the dienophile (Scheme 1).

Results and discussion

Initially, 2*H*-chromene-3-carbaldehydes **8(a–h)** and **10(a–g)** were prepared by the reaction of salicylaldehyde **6(a–g)** with cinnamaldehyde **7** or acrolein **9** following Oxa–Michael–Aldol



Scheme 4 A plausible mechanism for the formation of compound **3a**.

reaction in good yields (Scheme 2).[31,32] 2*H*-Chromene-3-carbaldehyde derivatives **8(a–h)** and **10(a–g)** were completely characterised using their analytical and spectral data. For example, the ^{1}H NMR spectrum of **8a** and **10a** exhibited a singlet at 9.66 and 9.59 ppm due to CHO, also the characteristic olefinic protons came at 7.42 and 7.26 ppm. The 2*H*-protons of chromene aldehyde appeared as singlet at 6.35 and 5.11 ppm in **8a** and **10a** which indicates the formation of chromene aldehydes.

Wittig reaction of **8(a–h)** and **10(a–g)** with methyl triphenyl phosphonium bromide in BuLi afforded 3-vinyl-2*H*-chromene derivatives **2(a–h)** and **2′(a–h)** in good yield.[33] Compounds **2(a–h)** and **2′(a–f)** were successfully characterised by ^{1}H, ^{13}C NMR and IR. For example, the aldehydic proton which appears at 9.66 ppm for compound **8a** vanishes in the ^{1}H NMR of compound **2a**. The olefinic protons of compound **2a** appeared as double doublet at 6.52 ppm (J = 11.2 Hz, 17.6 Hz, CH) and 5.09 ppm (J = 11.2 Hz, 18.8 Hz, CH_2) which indicates the formation of compound **2a**.

Literature reports revealed that dienes can undergo hetero Diels Alder reaction with aldehyde or ketone to form an oxa spirocyclic scaffold. Prompted by the literature findings we planned to synthesize spiro indanone fused pyranochromene derivatives by the reaction of indane-1,3-dione and 3-vinyl-2*H*-chromene.

To optimise the reaction conditions, we screened the hetero Diels–Alder reaction of indane-1,3-dione **1** (1 mmol) and 3-vinyl-2*H*-chromene **2a** (1 mmol) as a model. The effect of several solvents and additive were studied (Table 1). Using toluene as solvent at room temperature under additive free condition for 12 h, no product formation was observed (entry 1). When the reaction was put under reflux condition at 120 °C for 12 h, 40% conversion was observed and the starting material remains unreacted (entry 2). The same reaction was again repeated using 4 Å MS as additive. Gratifyingly, the addition of 4 Å MS increased the yield of the product to 80% and decreased the time of reaction to 2 h (entry 3). From this we come to the point that additives have significant influence to the yield of the product. The effect of other solvents such as benzene, CH_3CN and DCM in the presence of 4 Å MS were also studied to improve the yield. No product formation was observed under room temperature stirring for 12 h in all cases (entries 4, 6 and 8). Also refluxing in various solvents such as benzene, CH_3CN and DCM did not give significant influence to the yield of the product (entries 5, 7 and 9). So we conclude that the greatest reaction efficacy and stereocontrol in the product formation was obtained using toluene and 4 Å MS (entry 3). In all cases regiospecifically a single diastereoisomer was formed as major isomer.

Results of experiments under the optimised conditions for probing the scope of the reaction are summarized in Scheme 3. A range of 3-vinyl-2*H*-chromene **2(a–h)** and **2′(a–h)** derivatives were examined with indane-1,3-dione **1** in toluene using 4 Å MS as additives under reflux condition at 120 °C for the construction of spiro indanone fused pyranochromene derivatives **3(a–h)** and **3′(a–g)** (Scheme 3).

The results showed that, in general variation of the electronic properties of the substituent at different positions of the 3-vinyl-2*H*-chromene **2(a–h)** and **2′(a–g)** was well tolerated giving the spiro indanone fused pyranochromene derivatives **3(a–h)** and **3′(a–g)** with excellent yields with diastereoselectivity albeit with a slight low yield for **3g**. Additionally, dienes substituted with halogen groups took a slight longer reaction

Table 2 IC50 values of compound **3(a–h)** and **3′(a–g)** in MCF-7, HCT-116, H-357 and MD-MB-231 cell line[a]

Compound name	MCF-7 (μM)	HCT-116 (μM)	H-357 (μM)	MD-MB-231 (μM)
3a	**31.5 ± 2.0**	**35.5 ± 3.0**	64.5 ± 10.0	**38 ± 1.0**
3b	52.5 ± 4.0	**41.5 ± 3.6**	68 ± 10.0	63 ± 5.6
3c	91 ± 6.2	**41 ± 3.0**	66 ± 8.0	78 ± 8.0
3d	**32 ± 3.2**	**36 ± 1.0**	67 ± 6.0	**19 ± 1.0**
3e	**34 ± 2.2**	**40 ± 4.0**	65.5 ± 2.8	**37.5 ± 2.0**
3f	**40 ± 1.0**	50 ± 8.2	54.5 ± 8.0	**36 ± 1.2**
3g	**32.5 ± 3.0**	**38 ± 2.0**	63.5 ± 6.0	**33.5 ± 1.8**
3h	48 ± 2.2	**35 ± 1.0**	69 ± 6.0	51 ± 4.0
3′a	65 ± 7.2	43 ± 1.0	76.5 ± 7.0	72.5 ± 6.2
3′b	41 ± 2.1	**40 ± 4.0**	74 ± 11.3	52.5 ± 4.0
3′c	**20 ± 1.0**	**27.5 ± 1.0**	55 ± 4.0	**15 ± 1.0**
3′d	41.5 ± 6.0	44 ± 3.0	73 ± 6.3	47 ± 4.0
3′e	65 ± 4.8	**39.5 ± 1.8**	71 ± 5.8	69 ± 6.0
3′f	**38.5 ± 2.1**	50 ± 8.0	75 ± 7.4	**31 ± 2.0**
3′g	50 ± 8.0	54 ± 8.0	70 ± 8.1	**27 ± 1.0**
5-FU	40 ± 6.0	42 ± 1.0	48 ± 1.0	40 ± 2.0

[a] The data was presented as mean ± SD of 4 different experiments.

time might be due to the negative inductive effect of halogens. Dienes containing benzoate group **2′g** also underwent the reaction smoothly affording good yield of the product with excellent diastereoselectivity. Unexpectedly, dienes containing hydroxyl groups **2′h** and nitro group when treated with indane-1,3-dione do not provide the Diels Alder adduct. Presence of –I effecting group (NO_2, –OH) in diene might be decreasing HOMO energy level causing higher HOMO–LUMO energy gap. The applied thermal energy is not sufficient enough to crossover the energy gap, causing no interaction between diene and dienophile to give the product. The structures of the products **3(a–h)** and **3′(a–g)** were established on the basis of their spectral data (^{1}H and ^{13}C NMR) as well as HRMS analysis. The regiospecific formation of the products **3(a–h)** and **3′(a–g)** were confirmed by ^{1}H NMR. For instance, the allylic –CH_2 of newly formed pyran ring in all cases comes at 2–3 ppm which indicates the formation of **3(a–h)** and **3′(a–g)**. The regiospecific product formation **3a** might be obtained due to the flow of electron from oxygen atom of the chromene ring to the olefinic *C of the diene which results the interaction of highest negative charge density *C of the diene with the lowest positive charge density carbonyl carbon of the dienophile. The stereochemistry of the major isomer **3a** was determined by 2D NMR (NOESY). In the NOESY spectra of compound **3a** (Major) the benzylic proton and 2*H*-chromene proton do not show interaction with each other whereas in case of minor isomer both the protons shows interaction from which we come to the point that the *trans*-isomer is major where as *syn*- is minor. Only in two cases we are able to separate out the minor *cis*-isomer whereas in other cases we failed. Diastereoselective *trans*-isomer is formed as the major isomer in all cases.

A plausible mechanism for the hetero-Diels–Alder reaction of indane-1,3-dione **1** and 3-vinyl-2*H*-chromene **2a** is shown in Scheme 4. The stereochemistry of the product depends on the endo-orientation of the dienophile as well as by the stereochemistry of the diene in the transition state. Here we assume that the cycloadducts **3a** could form *via* an endo-transition state A *i.e.* the dienophile approaches from the opposite face to the Ph group giving the anti product (major isomer), where Ha and Hb show no NOESY interaction, and the dienophile approaches from the same face to the Ph group *i.e.* more hindered side giving syn product *i.e.* **5a** (minor isomer) as represented in Scheme 4. The diastereoisomeric ratio remains high throughout the course of the reaction.

Literature report reveals that indanone based natural products such as Fredericamycin and related synthetic derivatives are showing anticancer activity. Similarly pyranochromene based molecules also shows potent anticancer activity. The synthesized spiro indanone fused pyrano[3,2-*c*]chromene molecules **3(a–h)** and **3′(a–g)** were explored for *in vitro* cytotoxicity activity in various human cancer cell lines such as MCF-7 (breast cancer), HCT-116 (colon cancer), H-357 (oral cancer), MD-MB-231(breast cancer) using MTT assay as shown in Table 2. The results exhibited that compounds **3′c** shows most potent cytotoxic activity [IC50 (fifty percent cell death in culture) 15.0–27.5 μM] against MCF-7 (breast cancer), HCT-116 (colon cancer), MD-MB-231 (breast cancer) cell lines. Compounds **3a**, **3d**, **3e**, **3f**, **3g**, **3′f** (IC50: 31.5–40.1 μM) shows better activity in MCF7 cell line comparison to standard drug 5-FU. Compounds **3a**, **3b**, **3c**, **3d**, **3e**, **3h**, **3′b**, **3′e**, (IC50: 35.5–41.5 μM) shows better activity in HCT-116 cell line comparison to standard drug 5-FU. Compounds **3a**, **3d**, **3e**, **3f**, **3g**, **3′f**, **3′g** (IC50: 19.0–38.0 μM) shows better activity in MD-MB-231 cell line comparison to standard drug 5-FU. However none of the compounds in the series shows better activity in H-357 cancer cell line. SAR showed that possibly, the ethoxy group present in **3′c** could be responsible for more cytotoxic activity. Though compound **3′c** and **3d**, both having ethoxy group but absence of phenyl group in **3′c** might increase the cytotoxic activities.

Conclusion

In summary, we have developed a novel protocol for regiospecific and diastereoselective synthesis of spiro indanone fused pyrano chromene frameworks containing indanone, pyran and chromene moieties through oxa-hetero Diels–Alder approach by the reaction of indane-1,3-dione and 3-vinyl-2*H*-chromene in good to excellent yields with a wide substrate scope. Several advantages associated with this protocol such as cost effective, high yields, easy accessibility, wide substrate scope and short reaction time. The synthesized products were evaluated for their potential anticancer activities. Most of these compounds showed potent activities. Compound **3′c** is significantly more potent. The possible mechanism of this kind of spiro indanone fused pyrano[3,2-*c*]chromene as an anticancer agent will be studied in future.

Experimental section

General methods

^{1}H NMR spectra were recorded on 400 MHz (100 MHz for ^{13}C NMR) JEOL NMR spectrometer with $CDCl_3$ as solvent and tetramethylsilane (TMS) as internal standard. Chemical shifts were reported in parts per million (ppm, δ scale) downfield from TMS at 0.00 ppm and referenced to the $CDCl_3$ at 7.26 ppm (for ^{1}H NMR) or 77.0 ppm (for ^{13}C NMR). Melting points are uncorrected and were determined with SMP10 digital melting point apparatus using open capillary tubes. All reagents and solvents used in this study were commercially available (from Sigma-Aldrich) and were used without further purification.

General procedure for the synthesis of 8(a–h)

Salicylaldehyde (1 mmole) and cinnamaldehyde (1.1 mmole) were taken in a round bottom flask and 3 ml of dry DMSO was added to it followed by pyrrolidine (0.2 mmol). Then it was stirred at room temperature in argon atmosphere. The progress of the reaction was monitored by TLC and was found to be completed after 12 h. After completion of reaction, 50 ml of water was added to it and then extracted with ethyl acetate. The combined organic layers were washed with brine (30 mL). The organic layers were dried over Na_2SO_4 and concentrated in rotavapor. The crude product was crystallised in isopropanol at 0 °C provided aldehyde compound in pure form. In some cases column chromatography has been done in order to purify the compound. Synthesized chromene aldehydes were successfully characterised by ^{1}H, ^{13}C NMR, IR and mass analysis.

2-Phenyl-2*H*-chromene-3-carboxaldehyde (8a). Yellow solid (88%); mp 72–74 °C. IR (KBr) (ν_{max}/cm^{-1}): 3048, 2820, 2707, 1670, 1570, 1457, 1216, 1102, 996, 768, 612, 520. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.66 (1H, s, CHO), 7.42 (1H, s, CH), 7.37–7.35 (2H, m, H–Ar), 7.30–7.25 (5H, m, H–Ar), 6.96–6.87 (2H, m, H–Ar), 6.35 (1H, s, CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 190.1, 154.9, 140.8, 139.1, 133.7, 129.5, 128.7, 126.8, 121.8, 120.0, 117.1, 74.2. ESI-HRMS [M + Na]$^+$: calcd for $C_{16}H_{12}O_2$: 259.0730, found: 259.0730. Anal. calcd for $C_{16}H_{12}O_2$: C, 81.34; H, 5.12. Found: C, 81.35; H, 5.15.

8-Methoxy-2-phenyl-2*H*-chromene-3-carboxaldehyde (8b). Yellow solid (85%); mp 117–119 °C. IR (KBr) (ν_{max}/cm^{-1}): 3051, 2908, 2811, 2720, 1657, 1631, 1573, 1378, 1255, 1210, 1093, 964, 892, 763, 723, 691, 581, 510. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.67 (1H, s, CHO), 7.40 (1H, s, CH), 7.38–7.36 (2H, m, H–Ar), 7.28–7.24 (3H, m, H–Ar), 6.94–6.88 (3H, m, H–Ar), 6.44 (1H, s, CH), 3.84 (3H, s, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 190.3, 148.6, 144.2, 141.1, 139.1, 134.1, 128.7, 128.6, 126.7, 121.7, 121.4, 120.9, 116.2, 74.3, 56.4. ESI-HRMS [M + Na]$^+$: calcd for $C_{17}H_{14}O_3$: 289.0835, found: 289.0837. Anal. calcd for $C_{17}H_{14}O_3$: C, 76.68; H, 5.30. Found: C, 76.69; H, 5.33.

7-Methoxy-2-phenyl-2*H*-chromene-3-carboxaldehyde (8c). Yellow solid (75%); mp 121–123 °C. IR (KBr) (ν_{max}/cm^{-1}): 3051, 2908, 2811, 2720, 1657, 1631, 1573, 1378, 1255, 1210, 1093, 964, 892, 763, 723, 691, 581, 510. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.59 (1H, s, CHO), 7.40 (1H, s, CH), 7.38–7.36 (2H, m, H–Ar), 7.32–7.25 (5H, m, H–Ar), 6.53 (1H, dd, J = 8.0 Hz, 4.0 Hz, H–Ar), 6.34 (1H, s, CH), 3.80 (3H, s, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 189.7, 164.5, 156.7, 141.0, 139.3, 131.0, 128.5, 126.7, 113.4, 108.9, 105.8, 102.0, 98.0, 74.6, 55.5. ESI-HRMS [M + Na]$^+$: calcd for $C_{17}H_{14}O_3$: 289.0835, found: 289.0837. Anal. calcd for $C_{17}H_{14}O_3$: C, 76.68; H, 5.30. Found: C, 76.72; H, 5.34.

8-Ethoxy-2-phenyl-2*H*-chromene-3-carboxaldehyde (8d). Yellow solid (85%); mp 98–100 °C. IR (KBr) (ν_{max}/cm^{-1}): 2974, 2807, 1748, 1664, 1627, 1609, 1469, 1376, 1256, 1218, 1098, 1005, 902, 754, 689, 642, 615, 521. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.70 (1H, s, CHO), 7.41 (1H, s, CH), 7.40–7.37 (2H, m, H–Ar), 7.30–7.26 (3H, m, H–Ar), 6.96–6.88 (3H, m, H–Ar), 6.46 (1H, s, CH), 4.08 (2H, q, J = 8.0 Hz, CH_2), 1.40 (3H, t, J = 8.0 Hz, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 190.4, 147.9, 144.7, 141.3, 139.1, 134.1, 128.6, 128.5, 126.6, 121.7, 121.5, 121.2, 118.1, 73.9, 65.1, 14.9. ESI-HRMS [M + Na]$^+$: calcd for $C_{18}H_{16}O_3$: 303.0992, found: 303.0985. Anal. calcd for $C_{18}H_{16}O_3$: C, 77.12; H, 5.75. Found: C, 77.15; H, 5.77.

6-Bromo-2-phenyl-2*H*-chromene-3-carboxaldehyde (8e). Pale yellow solid (80%); mp 137–139 °C. IR (KBr) (ν_{max}/cm^{-1}): 3058, 2934, 2824, 2714, 1891, 1819, 1677, 1631, 1586, 1560, 1482, 1411, 1384, 1307, 1203, 1158, 1132, 1067, 957, 814, 691, 626, 522. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.66 (1H, s, CHO), 7.39–7.27 (8H, m, CH, H–Ar), 6.78 (1H, d, J = 8.0 Hz, H–Ar), 6.34 (1H, s, CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 189.9, 153.9, 139.2, 138.6, 136.2, 134.7, 131.6, 129.1, 128.8, 126.9, 121.9, 119.2, 113.8, 74.6. ESI-HRMS [M + Na]$^+$: calcd for $C_{16}H_{11}BrO_2$: 336.9835, found: 336.9833. Anal. calcd for $C_{16}H_{11}BrO_2$: C, 60.98; H, 3.52. Found: C, 61.01; H, 3.54.

6-Chloro-2-phenyl-2*H*-chromene-3-carboxaldehyde (8f). Faint yellow solid (81%); mp 129–131 °C. IR (KBr) (ν_{max}/cm^{-1}): 3058, 2934, 2824, 2714, 1891, 1819, 1677, 1631, 1586, 1560, 1482, 1411, 1384, 1307, 1203, 1158, 1132, 1067, 957, 814, 691, 626, 522. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.67 (1H, s, CHO), 7.36 (1H, s, CH), 7.34–7.22 (7H, m, H–Ar), 6.82 (1H, d, J = 8.0 Hz, H–Ar), 6.34 (1H, s, CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 189.8, 153.3, 139.3, 138.5, 134.6, 133.1, 128.9, 128.7, 128.5, 126.8, 126.7, 121.2, 118.6, 74.5. ESI-HRMS [M + Na]$^+$: calcd for $C_{16}H_{11}ClO_2$: 293.0340, found: 293.0338. Anal. calcd for $C_{16}H_{11}ClO_2$: C, 70.99; H, 4.10. Found: C, 71.02; H, 4.13.

6,8-Dichloro-2-phenyl-2*H*-chromene-3-carboxaldehyde (8g). Golden yellow solid (82%); mp 136–138 °C. IR (KBr) (ν_{max}/cm^{-1}): 3071, 2811, 1683, 1631, 1462, 1398, 1333, 1242, 1171, 1086, 88, 883, 723, 652, 555, 451. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.73 (1H, s, CHO), 7.35–7.27 (7H, m, H–Ar), 7.17 (1H, s, CH), 6.48 (1H, s, CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 189.8, 149.3, 138.7, 138.0, 135.4, 133.0, 129.1, 128.8, 127.1, 126.6, 123.3, 122.4, 74.8. ESI-HRMS $[M + Na]^+$: calcd for $C_{16}H_{10}Cl_2O_2$: 326.9950, found: 326.9947. Anal. calcd for $C_{16}H_{10}Cl_2O_2$: C, 62.97; H, 3.30. Found: C, 62.99; H, 3.28.

6-Bromo-8-chloro-2-phenyl-2*H*-chromene-3-carboxaldehyde (8h). Yellow solid (81%); mp 132–134 °C. IR (KBr) (ν_{max}/cm^{-1}): 3071, 2811, 1683, 1631, 1462, 1398, 1333, 1242, 1171, 1086, 88, 883, 723, 652, 555, 451. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.75 (1H, s, CHO), 7.53 (1H, s, CH), 7.36–7.31 (6H, m, H–Ar), 7.22 (1H, d, J = 4.0 Hz, H–Ar), 6.51 (1H, s, CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 189.9, 149.3, 138.7, 138.0, 135.4, 133.0, 131.6, 129.5, 126.9, 121.9, 119.2, 117.1, 113.8, 74.5. Anal. calcd for $C_{16}H_{10}BrClO_2$: C, 54.97; H, 2.88. Found: C, 54.95; H, 2.89.

General procedure for the synthesis of 10(a–f)

To a solution of salicylaldehyde (1 mmol) in dioxane (100 ml) was added K_2CO_3 (4–5 mmol) and acrolein (2 mmol). The reaction mixture was refluxed for 2 h. The progress of the reaction was monitored by TLC checking. After 2 h the reaction completed, the reaction mixture was then poured into water (100 ml). The solution was extracted with ethyl acetate (30 mL × 3). The combined organic layers were washed with brine (30 mL). Then the organic layers were dried over anhydrous Na_2SO_4 and evaporated under vaccum. The residue was crystallised from $CHCl_3$/*n*-hexane to give 2*H*-chromene-3-carbaldehyde as solid. Synthesized chromene aldehydes were successfully characterised by ^{1}H, ^{13}C NMR, IR and mass analysis.

2*H*-chromene-3-carbaldehyde (10a). Yellow solid (90%); mp 64–66 °C. IR (KBr) (ν_{max}/cm^{-1}): 3045, 2818, 2708, 2312, 1683, 1631, 1462, 1398, 1242, 1171, 1086, 886, 833, 723, 652. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.59 (1H, s, CHO), 7.33–7.29 (2H, m, CH, H–Ar), 7.22 (1H, dd, J = 8.0 Hz, 4.0 Hz, H–Ar), 6.97 (1H, td, J = 8.0 Hz, 2.0 Hz, H–Ar), 6.88 (1H, d, J = 8.0 Hz, H–Ar), 5.04 (2H, s, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 189.9, 156.1, 141.3, 133.3, 131.8, 129.4, 122.0, 120.5, 116.6, 63.3. ESI-HRMS $[M + H]^+$: calcd for $C_{10}H_8O_2$: 161.0558, found: 161.0594. Anal. alcd for $C_{10}H_8O_2$: C, 74.99; H, 5.03. Found: C, 75.02; H, 5.06.

8-Methoxy-2*H*-chromene-3-carbaldehyde (10b). Yellow solid (87%); mp 82–84 °C. IR (KBr) (ν_{max}/cm^{-1}): 2974, 2883, 2818, 2733, 2364, 2325, 1663, 1560, 1475, 1339, 1216, 1093, 1002, 886, 782, 723, 704, 594, 490. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.59 (1H, s, CHO), 7.26 (1H, s, CH), 6.97–6.92 (2H, m, H–Ar), 6.86 (1H, dd, J = 8.0 Hz, 4.0 Hz, H–Ar), 5.11 (2H, s, CH_2), 3.90 (3H, s, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 189.9, 148.1, 145.0, 141.3, 131.8, 121.7, 121.3, 121.1, 115.5, 63.7, 56.2. GCMS *m*/*z*: calcd for $C_{11}H_{10}O_3$: 190.0, found: 190.2. Anal. calcd for $C_{11}H_{10}O_3$: C, 69.46; H, 5.30. Found: C, 69.49; H, 5.32.

8-Ethoxy-2*H*-chromene-3-carbaldehyde (10c). Yellow solid (85%); mp 89–91 °C. IR (KBr) (ν_{max}/cm^{-1}): 2974, 2883, 2818, 2733, 2364, 2325, 1663, 1560, 1475, 1339, 1216, 1093, 1002, 886, 782, 723, 704, 594, 490. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.60 (1H, s, CHO), 7.26 (1H, s, CH), 6.96 (1H, dd, J = 8.0 Hz, 4.0 Hz, H–Ar), 6.91 (1H, t, J = 8.0 Hz, H–Ar), 6.85 (1H, dd, J = 4.0 Hz, 4.8 Hz, H–Ar), 5.11 (2H, s, CH_2), 4.12 (2H, q, J = 4.0 Hz, CH_2), 1.47 (3H, t, J = 4.8 Hz, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 189.9, 147.4, 145.4, 141.5, 131.7, 121.6, 121.3, 117.0, 64.7, 63.6, 14.8. MS *m*/*z*: calcd for $C_{12}H_{12}O_3$: 204.0, found: 204.1. Anal. calcd for $C_{12}H_{12}O_3$: C, 70.57; H, 5.92. Found: C, 70.59; H, 5.95.

6-Bromo-2*H*-chromene-3-carbaldehyde (10d). Straw yellow solid (79%); mp 104–106 °C. IR (KBr) (ν_{max}/cm^{-1}): 3058, 2934, 2824, 2714, 1891, 1819, 1677, 1631, 1586, 1560, 1482, 1411, 1384, 1307, 1203, 1158, 1132, 1067, 957, 814, 691, 626, 522. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.58(1H, s, CHO), 7.37–7.35(1H, m, H–Ar), 7.31(1H, d, J = 1.6 Hz, H–Ar), 7.16(1H, s, CH), 6.75(1H, d, J = 6.8 Hz, H–Ar), 5.02(2H, s, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 189.8, 155.2, 139.7, 135.8, 132.7, 131.7, 122.4, 118.6, 114.0, 63.7. ESI-HRMS $[M + H]^+$: calcd for $C_{10}H_7BrO_2$: 238.9702, found: 239.9736. Anal. calcd for $C_{10}H_7BrO_2$: C, 50.24; H, 2.95. Found: C, 50.22; H, 2.97.

6-Chloro-2*H*-chromene-3-carbaldehyde (10e). Yellow solid (82%); mp 93–95 °C. IR (KBr) (ν_{max}/cm^{-1}): 3058, 2934, 2824, 2714, 1891, 1819, 1677, 1631, 1586, 1560, 1482, 1411, 1384, 1307, 1203, 1158, 1132, 1067, 957, 814, 691, 626, 522. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.52(1H, s, CHO), 7.15(1H, dd, J = 8.0 Hz, 4.0 Hz, H–Ar), 7.10(2H, m, CH, H–Ar), 6.74(1H, d, J = 8.0 Hz, H–Ar), 4.95(2H, s, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 189.6, 154.5, 139.6, 132.7, 132.6, 128.5, 126.7, 121.7, 118.0, 63.5. GCMS *m*/*z*: calcd for $C_{10}H_7ClO_2$: 194.0, found: 194.0. Anal. calcd for $C_{10}H_7ClO_2$: C, 61.72; H, 3.63. Found: C, 61.73; H, 3.65.

6,8-Dichloro-2*H*-chromene-3-carbaldehyde (10f). Yellow solid (80%); mp 127–129 °C. IR (KBr) (ν_{max}/cm^{-1}): 3077, 2857, 1683, 1631, 1553, 1456, 1339, 1210, 1152, 1093, 970, 866, 847, 717, 645, 568. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.55(1H, s, CHO), 7.27 (1H, s, CH), 7.09 (1H, s, H–Ar), 7.03(1H, s, H–Ar), 5.06(2H, s, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 189.3, 150.3, 138.6, 133.0, 132.7, 127.1, 126.6, 122.6, 122.4, 64.3. GCMS *m*/*z*: calcd for $C_{10}H_6Cl_2O_2$: 227.9, found: 228.0. Anal. calcd for $C_{10}H_6Cl_2O_2$: C, 52.43; H, 2.64. Found: C, 52.45; H, 2.67.

6-Hydroxy-2*H*-chromene-3-carbaldehyde (10g). Straw yellow solid (68%); mp 170–172 °C. IR (KBr) (ν_{max}/cm^{-1}): 3206, 2954, 2837, 2714, 1650, 1573, 1482, 1405, 1346, 1294, 1287, 1216, 1145, 1106, 1021, 898, 814, 717, 626, 568. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.58 (1H, s, CHO), 7.19 (1H, s, CH), 6.82–6.71 (3H, m, H–Ar), 4.97 (2H, s, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 189.9, 150.3, 150.1, 141.2, 132.6, 121.3, 120.2, 117.4, 115.0, 63.2. GCMS *m*/*z*: calcd for $C_{10}H_8O_3$: 176.0, found: 176.0. Anal. calcd for $C_{10}H_8O_3$: C, 68.18; H, 4.58. Found: C, 68.19; H, 4.61.

General procedure for the synthesis of 2(a–h) and 2′(a–h)

Wittig salt methyl triphenylphosphonium bromide (3 mmol) dissolved in dry THF was taken in a round bottom flask and stirred at 0 °C in argon atmosphere. To it BuLi(1.6 M) (3 mmol) was added in a drop wise manner. After half an hour the previously prepared 2-phenyl-2*H*-chromene aldehyde (1 mmol) in dry THF was added slowly at −20 °C and stirred for 1 h. The progress of the reaction was monitored by TLC checking. After

completion of the reaction, the reaction mixture was quenched by saturated ammonium chloride and extracted with ethyl acetate. The organic layers were washed with brine, dried over anhydrous Na_2SO_4 and evaporated in vaccum. The crude product was purified by column chromatography to afford the pure product. Most of the purified compounds are amorphous solid.

2-Phenyl-3-vinyl-2*H*-chromene (2a). White solid (70%); IR (KBr) (ν_{max}/cm^{-1}): 3058, 2824, 2727, 1663, 1573, 1462, 1333, 1314, 1152, 1093, 996, 879, 763, 691, 607, 522. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.40–7.38 (2H, m, H–Ar), 7.28–7.26 (3H, m, H–Ar), 7.06–7.03 (2H, m, H–Ar), 6.85–6.81 (1H, t, J = 8.0 Hz, H–Ar), 6.73 (1H, d, J = 8.0 Hz, H–Ar), 6.66 (1H, s, CH), 6.52 (1H, dd, J = 11.2 Hz, 17.6 Hz, CH), 6.10 (1H, s, CH), 5.09 (2H, dd, J = 11.2 Hz, 18.8 Hz, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 152.0, 138.6, 135.2, 132.4, 129.5, 128.5, 127.6, 126.1, 124.4, 122.3, 121.3, 116.4, 114.9, 76.3. EI-HRMS m/z: calcd for $C_{17}H_{14}O$: 234.1045, found: 234.9634. Anal. calcd for $C_{17}H_{14}O$: C, 87.15; H, 6.02. Found: C, 87.12; H, 6.05.

8-Methoxy-2-phenyl-3-vinyl-2*H*-chromene (2b). White solid (68%); IR (KBr) (ν_{max}/cm^{-1}): 2928, 1627, 1488, 1442, 1311, 1209, 1153, 1014, 884, 819, 763, 689, 568. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.44–7.42 (2H, m, H–Ar), 7.24–7.16 (3H, m, H–Ar), 6.75–6.71 (1H, m, H–Ar), 6.66–6.59 (3H, m, H–Ar, CH), 6.49 (1H, dd, J = 11.2 Hz, 17.6 Hz, CH), 6.18 (1H, s, CH), 5.07 (2H, dd, J = 6.4 Hz, 11.2 Hz, CH_2), 3.65 (3H, s, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 148.0, 140.8, 138.2, 135.0, 132.4, 128.3, 128.2, 127.3, 124.1, 123.0, 120.8, 119.0, 114.7, 112.6, 75.8, 55.9. EI-HRMS m/z: calcd for $C_{18}H_{16}O_2$: 264.1150, found: 264.9737. Anal. calcd for $C_{18}H_{16}O_2$: C, 81.79; H, 6.10. Found: C, 81.80; H, 6.14.

6-Methoxy-2-phenyl-3-vinyl-2*H*-chromene (2c). White solid (70%); IR (KBr) (ν_{max}/cm^{-1}): 2928, 1627, 1488, 1442, 1311, 1209, 1153, 1014, 884, 819, 763, 689, 568. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.31–7.29 (2H, m, H–Ar), 7.21–7.14 (3H, m, H–Ar), 6.59–6.50 (4H, m, H–Ar, CH), 6.45 (1H, dd, J = 10.8 Hz, 17.2 Hz, CH), 5.97 (1H, s, CH), 5.04 (2H, dd, J = 10.8 Hz, 16.4 Hz, CH_2), 3.65 (3H, s, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 154.0, 145.8, 138.4, 135.1, 133.3, 128.4, 127.6, 124.4, 122.9, 116.9, 115.0, 114.8, 111.5, 76.0, 55.6. Anal. calcd for $C_{18}H_{16}O_2$: C, 81.79; H, 6.10. Found: C, 81.75; H, 6.09.

8-Ethoxy-2-phenyl-3-vinyl-2*H*-chromene (2d). Orange liquid (67%); IR (ν_{max}/cm^{-1}): 2928, 1627, 1488, 1442, 1311, 1209, 1153, 1014, 884, 819, 763, 689, 568. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.45 (2H, d, J = 8.8 Hz, H–Ar), 7.25–7.23 (3H, m, H–Ar), 6.77–6.63 (3H, m, H–Ar), 6.55 (2H, dd, J = 11.2 Hz, 18.0 Hz, CH), 6.19 (1H, s, CH), 5.13–5.06 (2H, m, CH_2), 3.95 (2H, q, J = 11.2 Hz, CH_2), 1.29 (3H, t, J = 6.8 Hz, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 147.3, 141.5, 138.4, 135.3, 132.6, 128.3, 128.2, 127.5, 124.4, 123.5, 121.0, 119.4, 115.0, 114.8, 75.6, 65.0, 14.8. Anal. calcd for $C_{19}H_{18}O_2$: C, 81.99; H, 6.52. Found: C, 81.97; H, 6.53.

6-Bromo-2-phenyl-3-vinyl-2*H*-chromene (2e). White solid (70%); IR (KBr) (ν_{max}/cm^{-1}): 3018, 2915, 1631, 1579, 1475, 1417, 1249, 1210, 1106, 1080, 989, 898, 814, 704, 626, 542. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.35–7.27 (5H, m, H–Ar), 7.19–7.13 (2H, m, H–Ar), 6.61–6.58 (2H, m, H–Ar, CH), 6.49 (1H, dd, J = 11.2 Hz, 17.6 Hz, CH), 6.09 (1H, s, CH), 5.15 (2H, dd, J = 10.8 Hz, 24.8 Hz, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 150.9, 137.9, 134.7, 133.5, 131.9, 129.0, 128.7, 128.5, 127.6, 124.2, 123.0, 118.2, 115.9, 113.2, 76.4. EI-HRMS $[M + H]^+$: calcd for $C_{17}H_{13}BrO$: 313.1885, found: 314.3597. Anal. calcd for $C_{17}H_{13}BrO$: C, 65.19; H, 4.18. Found: C, 65.17; H, 4.21.

6-Chloro-2-phenyl-3-vinyl-2*H*-chromene (2f). White solid (66%); IR (KBr) (ν_{max}/cm^{-1}): 3018, 2915, 1631, 1579, 1475, 1417, 1249, 1210, 1106, 1080, 989, 898, 814, 704, 626, 542. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.37–7.35 (2H, m, H–Ar), 7.32–7.28 (3H, m, H–Ar), 7.03–6.97 (2H, m, H–Ar), 6.66 (1H, d, J = 8.4 Hz, H–Ar), 6.59 (1H, s, CH), 6.50 (1H, dd, J = 10.8 Hz, 16.8 Hz, CH), 6.09 (1H, s, CH), 5.15 (2H, dd, J = 11.2 Hz, 24.0 Hz, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 150.4, 138.0, 134.7, 133.6, 129.0, 128.7, 128.5, 128.4, 127.6, 126.1, 126.0, 123.7, 123.2, 117.7, 115.9, 76.4. EI-HRMS m/z: calcd for $C_{17}H_{13}ClO$: 268.0655, found: 268.9242. Anal. calcd for $C_{17}H_{13}ClO$: C, 75.98; H, 4.88. Found: C, 75.95; H, 4.88.

6,8-Dichloro-2-phenyl-3-vinyl-2*H*-chromene (2g). White solid (65%); IR (KBr) (ν_{max}/cm^{-1}): 3071, 2928, 1819, 1637, 1612, 1560, 1462, 1262, 1210, 1048, 976, 905, 873, 840, 723, 685, 658, 588. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.42–7.27 (5H, m, H–Ar), 7.09 (1H, d, J = 2.0 Hz, H–Ar), 6.93 (1H, d, J = 2.8 Hz, H–Ar), 6.58–6.50 (2H, m, CH), 6.24 (1H, s, CH), 5.24 (2H, dd, J = 11.2 Hz, 26.4 Hz, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 146.5, 137.4, 134.6, 134.5, 129.0, 128.8, 128.5, 127.4, 126.0, 125.0, 124.7, 122.7, 122.2, 116.9, 76.4. Anal. calcd for $C_{17}H_{12}Cl_2O$: C, 67.35; H, 3.99. Found: C, 67.38; H, 3.97.

8-Bromo-6-chloro-2-phenyl-3-vinyl-2*H*-chromene (2h). Orange liquid (69%); IR (KBr) (ν_{max}/cm^{-1}): 3071, 2928, 1819, 1637, 1612, 1560, 1462, 1262, 1210, 1048, 976, 905, 873, 840, 723, 685, 658, 588. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.42–7.40 (2H, m, H–Ar), 7.27–7.22 (4H, m, H–Ar), 6.94 (1H, d, J = 2.4 Hz, H–Ar), 6.56–6.49 (2H, m, CH), 6.24 (1H, s, CH), 5.21 (2H, dd, J = 11.2 Hz, 24.8 Hz, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 147.5, 137.3, 134.5, 134.4, 131.6, 128.8, 128.4, 127.4, 126.3, 125.3, 124.9, 122.8, 116.8, 111.0, 76.4. Anal. calcd for $C_{17}H_{12}BrClO$: C, 58.73; H, 3.48. Found: C, 58.75; H, 3.45.

3-Vinyl-2*H*-chromene (2′a). Orange liquid (65%); IR (ν_{max}/cm^{-1}): 2974, 2928, 1722, 1605, 1586, 1469, 1405, 1255, 1210, 1086, 976, 782, 730, 658. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.09–7.05 (1H, m, H–Ar), 6.98 (1H, d, J = 6.0 Hz, H–Ar), 6.86–6.78 (2H, m, H–Ar), 6.43 (1H, dd, J = 10.8 Hz, 26.8 Hz, CH), 6.35 (1H, s, CH), 5.14 (2H, dd, J = 10.8 Hz, 20.4 Hz, CH_2), 4.94 (2H, s, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 153.7, 134.6, 130.7, 129.1, 127.0, 123.6, 122.3, 121.3, 115.3, 113.3, 65.1. Anal. calcd for $C_{11}H_{10}O$: C, 83.51; H, 6.37. Found: C, 83.53; H, 6.34.

8-Methoxy-3-vinyl-2*H*-chromene (2′b). Orange liquid (68%); IR (ν_{max}/cm^{-1}): 2974, 2928, 1722, 1605, 1586, 1469, 1405, 1255, 1210, 1086, 976, 782, 730, 658. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 6.83–6.75 (2H, m, H–Ar), 6.60–6.64 (1H, m, H–Ar), 6.58–6.36 (2H, m, CH), 5.16 (2H, dd, J = 9.2 Hz, 17.8 Hz, CH_2), 5.02 (2H, s, CH_2), 3.86 (3H, s, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 147.4, 142.3, 134.4, 130.7, 123.4, 123.0, 121.0, 119.3, 113.6, 112.0, 65.3, 56.0. Anal. calcd for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43. Found: C, 76.59; H, 6.40.

8-Ethoxy-3-vinyl-2*H*-chromene (2′c). Orange liquid (70%); IR (ν_{max}/cm^{-1}): 2974, 2928, 1722, 1605, 1586, 1469, 1405, 1255, 1210, 1086, 976, 782, 730, 658. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H

6.78–6.74 (2H, m, H–Ar), 6.64–6.62 (1H, m, H–Ar), 6.45–6.35 (2H, m, CH), 5.15 (2H, dd, J = 10.8 Hz, 16.4 Hz, CH_2), 5.01 (2H, s, CH_2), 4.07 (2H, q, J = 14.0 Hz, CH_2), 1.44 (3H, t, J = 8.8 Hz, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 146.6, 142.7, 134.4, 130.5, 123.5, 123.1, 120.8, 119.2, 113.6, 113.4, 65.2, 64.3, 14.7. Anal. calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. Found: C, 77.19; H, 6.97.

6-Bromo-3-vinyl-2*H*-chromene (2′d). White solid (65%); IR (KBr) (ν_{max}/cm^{-1}): 3018, 2915, 1631, 1579, 1475, 1417, 1249, 1210, 1106, 1080, 989, 898, 814, 704, 626, 542. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.10–7.02 (2H, m, H–Ar), 6.61 (1H, d, J = 9.2 Hz, H–Ar), 6.38–6.30 (1H, m, CH), 6.22 (1H, s, CH), 5.13 (2H, dd, J = 11.2 Hz, 26.0 Hz, CH_2), 4.88 (2H, s, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 152.7, 134.2, 131.7, 131.5, 129.2, 124.2, 122.3, 117.1, 114.4, 113.3, 65.2. EI-HRMS $[M + H]^+$: calcd for $C_{11}H_9BrO$: 237.0926, found: 238.9675. Anal. calcd for $C_{11}H_9BrO$: C, 55.72; H, 3.83. Found: C, 55.74; H, 3.85.

6-Chloro-3-vinyl-2*H*-chromene (2′e). White solid (67%); IR (KBr) (ν_{max}/cm^{-1}): 3018, 2915, 1631, 1579, 1475, 1417, 1249, 1210, 1106, 1080, 989, 898, 814, 704, 626, 542. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.10–6.98 (2H, m, H–Ar), 6.72 (1H, d, J = 9.2 Hz, H–Ar), 6.48–6.39 (1H, m, CH), 6.28 (1H, s, CH), 5.27 (2H, dd, J = 11.4 Hz, 26.2 Hz, CH_2), 4.98 (2H, s, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 152.2, 134.3, 131.9, 128.9, 126.9, 126.2, 123.9, 122.8, 116.9, 114.4, 65.2. Anal. calcd for $C_{11}H_9ClO$: C, 68.58; H, 4.71; found: C, 68.57; H, 4.73.

6,8-Dichloro-3-vinyl-2*H*-chromene (2′f). White solid (70%); IR (KBr) (ν_{max}/cm^{-1}): 3071, 2928, 1819, 1637, 1612, 1560, 1462, 1262, 1210, 1048, 976, 905, 873, 840, 723, 685, 658, 588. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.14 (1H, d, J = 2.0 Hz, H–Ar), 6.88 (1H, d, J = 2.0 Hz, H–Ar), 6.45 (1H, dd, J = 11.2 Hz, 18.0 Hz, CH), 6.30 (1H, s, CH), 5.27 (2H, dd, J = 10.8 Hz, 29.6 Hz, CH_2), 5.07 (2H, s, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 148.0, 133.9, 132.3, 128.8, 125.9, 125.0, 124.5, 121.9, 121.2, 115.4, 65.9. GCMS $[M + H]^+$: calcd for $C_{11}H_8Cl_2O$: 227.0, found: 228.0. Anal. calcd for $C_{11}H_8Cl_2O$: C, 58.18; H, 3.55. Found: C, 58.20; H, 3.58.

3-Vinyl-2*H*-chromen-8-yl benzoate (2′g). Colour less liquid (65%); IR (ν_{max}/cm^{-1}): 3071, 1800, 1722, 1683, 1593, 1437, 1268, 1216, 1171, 983, 769, 685, 626, 555. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.23–8.20 (2H, m, H–Ar), 7.82–7.48 (3H, m, H–Ar), 7.28–6.82 (3H, m, H–Ar), 6.46–6.38 (2H, m, CH), 5.14 (2H, dd, J = 11.2 Hz, 31.6 Hz, CH_2), 4.94 (2H, s, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 164.4, 145.6, 138.3, 134.3, 133.4, 131.3, 130.2, 129.4, 129.2, 128.4, 128.2, 124.4, 124.2, 123.1, 122.5, 121.1, 113.9, 65.3. Anal. calcd for $C_{18}H_{14}O_3$: C, 77.68; H, 5.07. Found: C, 77.69; H, 5.09.

3-Vinyl-2*H*-chromen-8-ol (2′h). Yellow liquid (60%); IR (ν_{max}/cm^{-1}): 3206, 1650, 1573, 1482, 1405, 1346, 1294, 1287, 1216, 1145, 1106, 1021, 898, 814, 717, 626, 568. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 6.78–6.73 (2H, m, H–Ar), 6.59–6.56 (1H, m, H–Ar), 6.43 (1H, dd, J = 10.8 Hz, 18.4 Hz, CH), 6.37 (1H, s, CH), 5.65 (1H, broad singlet, CH), 5.15 (2H, dd, J = 10.8 Hz, 26.8 Hz, CH_2), 4.97 (2H, s, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 143.7, 139.9, 134.5, 130.6, 123.5, 122.5, 121.5, 118.4, 115.4, 113.5, 65.4. Anal. calcd for $C_{11}H_{10}O_2$: C, 75.84; H, 5.79. Found: C, 75.86; H, 5.77.

General procedure for the synthesis of 3(a–h) and 3′(a–f)

Ninhydrin (1 mmol) was taken in dry toluene (5 mL) to it 4 Å MS was added and stirred at 120 °C for 10 min till the colour change observed. Then 3-vinyl-2*H*-chromene (1 mmol) was added to it. The progress of the reaction was monitored by TLC checking. The reaction was completed in 2–3 h. The reaction mixture was cooled, 4 Å MS were filtered and the toluene was removed under vaccum. The crude reaction mixture was purified by flash column chromatography to get the pure product. After column purification most of the compounds obtained as amorphous solid.

(5′*R*,10*b*′*R*)-5′-Phenyl-5′,10*b*′-dihydro-3′*H*-spiro[indene-2,2′-pyrano[3,2-*c*]chromene]-1,3-dione (3a). White solid (80%); IR (KBr) (ν_{max}/cm^{-1}): 3058, 2921, 2863, 1735, 1715, 1573, 1482, 1287, 1229, 1035, 996, 892, 756, 704, 652, 594. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04–8.02 (2H, m, H–Ar), 7.93–7.90 (2H, m, H–Ar), 7.58 (2H, d, J = 8.4 Hz, H–Ar), 7.40–7.36 (2H, m, H–Ar), 7.28–7.16 (3H, m, H–Ar), 7.00 (1H, d, J = 8.4 Hz, H–Ar), 6.86–6.82 (1H, m, H–Ar), 6.27–6.25 (1H, m, CH), 5.82 (1H, s, CH), 5.52 (1H, s, CH), 2.87–2.81 (1H, m, CH_2), 2.33–2.26 (1H, m, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.9, 196.6, 152.8, 140.5, 140.4, 139.1, 136.6, 136.4, 132.5, 129.1, 128.5, 127.6, 127.4, 125.8, 124.3, 124.1, 121.8, 121.0, 119.8, 116.6, 79.8, 74.3, 66.1, 25.9. HRMS $[M + H]^+$ calcd for $C_{26}H_{18}O_4$: 394.4187, found: 395.1326. Anal. calcd for $C_{26}H_{18}O_4$: C, 79.17; H, 4.60. Found: C, 79.19; H, 4.59.

(5′*S*,10*b*′*R*)-5′-Phenyl-5′,10*b*′-dihydro-3′*H*-spiro[indene-2,2′-pyrano[3,2-*c*]chromene]-1,3-dione (5a). White solid (70%); IR (KBr) (ν_{max}/cm^{-1}): 3058, 2921, 2863, 1735, 1715, 1573, 1482, 1287, 1229, 1035, 996, 892, 756, 704, 652, 594. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.04–8.02 (2H, m, H–Ar), 7.95–7.91 (2H, m, H–Ar), 7.50–7.38 (6H, m, H–Ar), 7.22–7.17 (1H, m, H–Ar), 6.94–6.89 (2H, m, H–Ar), 6.07 (1H, s, CH), 5.71 (1H, s, CH), 5.28–5.25 (1H, m, CH), 2.65–2.59 (1H, m, CH_2), 2.13–2.04 (1H, m, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 198.3, 196.8, 154.1, 140.1, 136.6, 136.5, 129.1, 128.4, 128.3, 127.9, 127.6, 124.2, 124.1, 121.1, 119.3, 116.5, 78.4, 74.3, 68.8, 26.1. Anal. calcd for $C_{26}H_{18}O_4$: C, 79.17; H, 4.60. Found: C, 79.18; H, 4.57.

7′-Methoxy-5′-phenyl-5′,10*b*′-dihydro-3′*H*-spiro[indene-2,2′-pyrano[3,2-*c*]chromene]-1,3-dione (3b). White solid (82%); IR (KBr) (ν_{max}/cm^{-1}): 2921, 2863, 1761, 1696, 1586, 1475, 1346, 1255, 1210, 1086, 989, 924, 873, 710, 645. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.03–8.01 (2H, m, H–Ar), 7.91–7.87 (2H, m, H–Ar), 7.58 (2H, d, J = 7.6 Hz, H–Ar), 7.39–7.37 (2H, m, H–Ar), 7.28–7.23 (1H, m, H–Ar), 6.82–6.78 (3H, m, H–Ar), 6.28 (1H, d, J = 4.8 Hz, CH), 5.93 (1H, s, CH), 5.52 (1H, s, CH), 3.92 (3H, s, CH_3), 2.85–2.80 (1H, m, CH_2), 2.31–2.25 (1H, m, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 197.8, 196.4, 148.1, 142.2, 140.3, 140.2, 138.6, 136.5, 136.4, 132.1, 128.4, 127.6, 125.5, 124.1, 124.0, 122.4, 120.6, 119.9, 119.1, 110.7, 80.0, 74.3, 66.0, 56.0, 25.8. HRMS calcd for $C_{27}H_{20}O_5$: 424.4447, found: 425.1440. Anal. calcd for $C_{27}H_{20}O_5$: C, 76.40; H, 4.75. Found: C, 76.42; H, 4.73.

9′-Methoxy-5′-phenyl-5′,10*b*′-dihydro-3′*H*-spiro[indene-2,2′-pyrano[3,2-*c*]chromene]-1,3-dione (3c). White solid (78%); IR (KBr) (ν_{max}/cm^{-1}): 2921, 2863, 1761, 1696, 1586, 1475, 1346, 1255, 1210, 1086, 989, 924, 873, 710, 645. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.04–8.00 (2H, m, H–Ar), 7.92–7.87 (2H, m, H–Ar),

7.56–7.54 (2H, m, H–Ar), 7.38–7.29 (3H, m, H–Ar), 6.92–6.90 (1H, m, H–Ar), 6.76–6.70 (2H, m, H–Ar), 6.23–6.22 (1H, m, CH), 5.76 (1H, s, CH), 5.51 (1H, s, CH), 3.62 (3H, s, CH_3), 2.84–2.79 (1H, m, CH_2), 2.32–2.25 (1H, m, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 197.9, 196.6, 153.9, 146.8, 140.4, 140.3, 139.2, 136.6, 136.5, 132.7, 128.4, 127.5, 125.9, 124.2, 124.1, 122.2, 119.7, 119.5, 117.4, 115.9, 115.8, 111.2, 79.7, 74.3, 66.3, 55.6, 26.0. HRMS calcd for $C_{27}H_{20}O_5$: 424.4447, found: 425.1480. Anal. calcd for $C_{27}H_{20}O_5$: C, 76.40; H, 4.75. Found: C, 76.39; H, 4.76.

7′-Ethoxy-5′-phenyl-5′,10*b*′-dihydro-3′*H*-spiro[indene-2,2′-pyrano[3,2-*c*]chromene]-1,3-dione (3d). White solid (85%); IR (KBr) (ν_{max}/cm^{-1}): 2980, 2902, 1741, 1709, 1579, 1489, 1249, 1203, 1074, 1054, 892, 736, 710. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.06–8.02 (2H, m, H–Ar), 7.92–7.89 (2H, m, H–Ar), 7.59–7.56 (2H, m, H–Ar), 7.42–7.36 (2H, m, H–Ar), 7.32–7.28 (1H, m, H–Ar), 6.82–6.72 (3H, m, H–Ar), 6.28–6.22 (1H, m, CH), 5.94 (1H, s, CH), 5.51 (1H, s, CH), 4.18 (2H, q, J = 14.0 Hz, CH_2), 2.86–2.81 (1H, m, CH_2), 2.32–2.30 (1H, m, CH_2), 1.50 (3H, t, J = 6.8 Hz, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 197.9, 196.6, 147.4, 142.6, 140.4, 140.3, 138.8, 136.6, 136.4, 132.2, 128.4, 127.6, 125.6, 124.2, 124.0, 122.5, 120.6, 119.9, 119.1, 112.2, 80.0, 74.4, 66.2, 64.4, 25.9, 14.8. HRMS calcd for $C_{28}H_{22}O_5$: 438.4713, found: 439.1497. Anal. calcd for $C_{28}H_{22}O_5$: C, 76.70; H, 5.06. Found: C, 76.72; H, 5.09.

9′-Bromo-5′-phenyl-5′,10*b*′-dihydro-3′*H*-spiro[indene-2,2′-pyrano[3,2-*c*]chromene]-1,3-dione (3e). White solid (72%); IR (KBr) (ν_{max}/cm^{-1}): 3064, 2941, 2853, 1761, 1709, 1586, 1469, 1405, 1287, 1203, 1132, 989, 866, 743, 691, 600. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.06–8.01 (2H, m, H–Ar), 7.93–7.90 (2H, m, H–Ar), 7.53–7.52 (2H, m, H–Ar), 7.42–7.36 (2H, m, H–Ar), 7.38–7.31 (3H, m, H–Ar), 6.88 (1H, d, J = 8.8 Hz, H–Ar), 6.28–6.27 (1H, m, CH), 5.82 (1H, s, CH), 5.47 (1H, s, CH), 2.86–2.80 (1H, m, CH_2), 2.33–2.27 (1H, m, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 197.6, 196.4, 151.9, 140.3, 138.5, 136.7, 136.6, 132.0, 131.5, 130.1, 128.5, 127.8, 125.7, 124.3, 124.1, 123.8, 120.4, 118.5, 113.2, 79.9, 74.2, 65.7, 25.8. HRMS $[M + H]^+$ calcd for $C_{26}H_{17}BrO_4$: 472.0310, found: 473.0364. Anal. calcd for $C_{26}H_{17}BrO_4$: C, 65.98; H, 3.62. Found: C, 65.96; H, 3.65.

9′-Chloro-5′-phenyl-5′,10*b*′-dihydro-3′*H*-spiro[indene-2,2′-pyrano[3,2-*c*]chromene]-1,3-dione (3f). White solid (75%); IR (KBr) (ν_{max}/cm^{-1}): 2910, 1739, 1701, 1600, 1469, 1414, 1274, 1218, 1098, 986, 884, 735, 698, 596, 466. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.06–8.01 (2H, m, H–Ar), 7.98–7.90 (2H, m, H–Ar), 7.53–7.52 (2H, m, H–Ar), 7.42–7.36 (2H, m, H–Ar), 7.38–7.21 (3H, m, H–Ar), 6.98 (1H, d, J = 8.8 Hz, H–Ar), 6.38–6.32 (1H, m, CH), 5.82 (1H, s, CH), 5.48 (1H, s, CH), 2.86–2.80 (1H, m, CH_2), 2.38–2.26 (1H, m, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 197.7, 196.4, 151.4, 140.4, 140.3, 138.6, 136.7, 136.6, 131.7, 129.2, 128.6, 127.8, 127.2, 126.0, 125.9, 124.4, 124.1, 123.3, 120.4, 118.0, 79.9, 74.2, 65.8, 25.9. HRMS calcd for $C_{26}H_{17}ClO_4$: 428.8638, found: 429.0905. Anal. calcd for $C_{26}H_{17}ClO_4$: C, 72.82; H, 4.00. Found: C, 72.84; H, 4.03.

7′,9′-Dichloro-5′-phenyl-5′,10*b*′-dihydro-3′*H*-spiro[indene-2,2′-pyrano[3,2-*c*]chromene]-1,3-dione (3g). White solid (70%); IR (KBr) (ν_{max}/cm^{-1}): 2919, 2853, 1748, 1701, 1609, 1460, 1367, 1284, 1227, 1190, 1126, 995, 931, 745, 707, 587. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07–8.03 (2H, m, H–Ar), 7.94–7.92 (2H, m, H–Ar), 7.56 (2H, d, J = 8.0 Hz, H–Ar), 7.43–7.39 (2H, m, H–Ar), 7.32–7.25 (2H, m, H–Ar), 7.11 (1H, d, J = 4.0 Hz, H–Ar), 6.37–6.31 (1H, m, CH), 5.98 (1H, s, CH), 5.51 (1H, s, CH), 2.88–2.82 (1H, m, CH_2), 2.36–2.30 (1H, m, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 197.6, 196.2, 147.4, 140.3, 137.7, 136.8, 136.7, 130.7, 129.3, 128.7, 128.1, 126.0, 125.8, 125.6, 124.5, 124.4, 124.2, 122.3, 121.3, 80.6, 74.3, 65.8, 25.9. HRMS $[M + H]^+$ calcd for $C_{26}H_{16}Cl_2O_4$: 462.0426, found: 463.0390. Anal. calcd for $C_{26}H_{16}Cl_2O_4$: C, 67.40; H, 3.48. Found: C, 67.42; H, 3.52.

9′-Bromo-7′-chloro-5′-phenyl-5′,10*b*′-dihydro-3′*H*-spiro[indene-2,2′-pyrano[3,2-*c*]chromene]-1,3-dione (3h). White solid (78%); IR (KBr) (ν_{max}/cm^{-1}): 2919, 2853, 1748, 1701, 1609, 1460, 1367, 1284, 1227, 1190, 1126, 995, 931, 745, 707, 587. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.99–7.96 (2H, m, H–Ar), 7.88–7.85 (2H, m, H–Ar), 7.49 (2H, d, J = 6.8 Hz, H–Ar), 7.36–7.32 (3H, m, H–Ar), 7.28–7.22 (1H, m, H–Ar), 7.08–7.07 (1H, m, H–Ar), 6.27–6.25 (1H, m, CH), 5.91 (1H, s, CH), 5.44–5.40 (1H, m, CH), 2.80–2.74 (1H, m, CH_2), 2.28–2.22 (1H, m, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 197.6, 196.2, 148.2, 140.3, 137.7, 136.8, 136.7, 132.1, 130.7, 128.7, 128.0, 126.7, 126.2, 125.6, 124.4, 124.3, 124.2, 121.3, 111.2, 80.8, 74.3, 65.8, 25.9. HRMS $[M + H]^+$ calcd for $C_{26}H_{16}BrClO_4$: 507.7598, found: 508.9917. Anal. calcd for $C_{26}H_{16}BrClO_4$: C, 61.50; H, 3.18. Found: C, 61.53; H, 3.17.

5′,10*b*′-Dihydro-3′*H*-spiro[indene-2,2′-pyrano[3,2-*c*]chromene]-1,3-dione (3′a). White solid (80%); IR (KBr) (ν_{max}/cm^{-1}): 2974, 2908, 1754, 1709, 1579, 1469, 1262, 1210, 1086, 989, 879, 769, 710, 645. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.06–8.04 (2H, m, H–Ar), 7.96–7.91 (2H, m, H–Ar), 7.34–7.32 (1H, m, H–Ar), 7.19–7.13 (1H, m, H–Ar), 6.90–6.80 (2H, m, H–Ar), 6.08–6.05 (1H, m, CH), 5.88 (1H, d, J = 2.4 Hz, CH), 4.73–4.58 (2H, m, CH_2), 2.78–2.73 (1H, m, CH_2), 2.24–2.18 (1H, m, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 198.2, 196.6, 154.1, 140.3, 136.6, 136.5, 130.7, 128.9, 127.7, 124.3, 124.1, 122.1, 120.9, 118.4, 116.4, 74.5, 68.3, 67.6, 25.7. HRMS $[M + H]^+$ calcd for $C_{20}H_{14}O_4$: 318.3228, found: 319.1013. Anal. calcd for $C_{20}H_{14}O_4$: C, 75.46; H, 4.43. Found: C, 75.47; H, 4.41.

7′-Methoxy-5′,10*b*′-dihydro-3′*H*-spiro[indene-2,2′-pyrano[3,2-*c*]chromene]-1,3-dione (3′b). White solid (78%); IR (KBr) (ν_{max}/cm^{-1}): 2928, 2844, 1748, 1701, 1581, 1478, 1357, 1274, 1227, 1107, 1051, 1014, 874, 745, 707, 652. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.06–8.04 (2H, m, H–Ar), 7.94–7.93 (2H, m, H–Ar), 6.96 (1H, d, J = 8.0 Hz, H–Ar), 6.85–6.76 (2H, m, H–Ar), 6.07 (1H, s, CH), 5.88 (1H, s, CH), 4.77–4.70 (2H, m, CH_2), 3.86 (3H, s, CH_3), 2.78–2.73 (1H, m, CH_2), 2.22–2.15 (1H, m, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 198.3, 196.4, 148.1, 143.9, 140.5, 136.8, 136.7, 130.5, 124.4, 124.2, 122.9, 120.7, 119.4, 118.7, 110.7, 78.8, 68.8, 68.2, 56.0, 25.9. HRMS calcd for $C_{21}H_{16}O_5$: 348.3487, found: 349.1124. Anal. calcd for $C_{21}H_{16}O_5$: C, 72.41; H, 4.63. Found: 72.43; H, 4.61.

7′-Ethoxy-5′,10*b*′-dihydro-3′*H*-spiro[indene-2,2′-pyrano[3,2-*c*]chromene]-1,3-dione (3′c). White solid (78%); IR (KBr) (ν_{max}/cm^{-1}): 2974, 2908, 1754, 1709, 1579, 1469, 1262, 1210, 1086, 989, 879, 769, 710, 645. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.08–8.04 (2H, m, H–Ar), 7.96–7.93 (2H, m, H–Ar), 6.92–6.90 (1H, m, H–Ar), 6.87–6.79 (2H, m, H–Ar), 6.12 (1H, s, CH), 5.83 (1H, s, CH), 4.77 (2H, s, CH_2), 4.12 (2H, q, J = 8.0 Hz, CH_2), 2.80 (1H, d, J = 28.8 Hz, CH_2), 2.25 (1H, d, J = 20.8 Hz, CH_2), 1.48 (3H, t, J =

8.0 Hz, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 198.2, 196.6, 147.2, 144.0, 140.3, 136.6, 136.5, 130.5, 124.3, 124.1, 122.9, 120.5, 119.3, 118.8, 118.4, 112.1,74.5, 68.7, 67.7, 64.3, 25.7, 14.7. HRMS $[M + H]^+$ calcd for $C_{22}H_{18}O_5$: 362.3753, found: 363.1278. Anal. calcd for $C_{22}H_{18}O_5$: C, 72.92; H, 5.01. Found: C, 72.90; H, 5.03.

9′-bBomo-5′,10*b*′-dihydro-3′*H*-spiro[indene-2,2′-pyrano[3,2-*c*]chromene]-1,3-dione (3′d). White solid (72%); IR (KBr) (ν_{max}/cm^{-1}): 2921, 2843, 1748, 1715, 1593, 1469, 1411, 1287, 1229, 1177, 1048, 989, 853, 820, 691, 626, 548. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.00–7.97 (2H, m, H–Ar), 7.88–7.86 (2H, m, H–Ar), 7.36 (1H, d, J = 2.8 Hz, H–Ar), 7.29–7.12 (1H, m, H–Ar), 6.63 (1H, d, J = 8.8 Hz, H–Ar), 6.00 (1H, s, CH), 5.74 (1H, s, CH), 4.63–4.51 (2H, m, CH_2), 2.71–2.65 (1H, m, CH_2), 2.16–2.10 (1H, m, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 198.0, 196.4, 153.2, 140.3, 136.7, 136.6, 131.8, 130.2, 129.7, 124.4, 124.2, 124.0, 119.0, 118.2, 113.1, 74.4, 68.4, 67.2, 25.7. HRMS $[M + H]^+$ calcd for $C_{20}H_{13}BrO_4$: 397.2188, found: 398.9998. Anal. calcd for $C_{20}H_{13}BrO_4$: C, 60.47; H, 3.30. Found: C, 60.49; H, 3.27.

9′-Chloro-5′,10*b*′-dihydro-3′H-spiro[indene-2,2′-pyrano[3,2-*c*]chromene]-1,3-dione (3′e). White solid (74%); IR (KBr) (ν_{max}/cm^{-1}): 2915, 2857, 1741, 1722, 1579, 1469, 1417, 1287, 1229, 1190, 96, 866, 820, 704, 633, 561. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.06–8.02 (2H, m, H–Ar), 7.94–7.92 (2H, m, H–Ar), 7.28–7.27 (1H, m, H–Ar), 7.19–7.06 (1H, m, H–Ar), 6.72 (1H, d, J = 8.8 Hz, H–Ar), 6.07–6.06 (1H, m, CH), 5.81 (1H, d, J = 2.4 Hz, CH), 4.70–4.57 (2H, m, CH_2), 2.77–2.71 (1H, m, CH_2), 2.23–2.16 (1H, m, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 198.0, 196.4, 152.7, 140.3, 136.7, 136.6, 129.7, 128.9, 127.3, 125.7, 124.3, 124.1, 123.5, 118.9, 117.8, 74.4, 68.4, 67.3, 25.7. HRMS calcd for $C_{20}H_{13}ClO_4$: 352.7678, found: 353.0492. Anal. calcd for $C_{20}H_{13}ClO_4$: C, 68.09; H, 3.71. Found: C, 68.07; H, 3.74.

7′,9′-Dichloro-5′,10*b*′-dihydro-3′*H*-spiro[indene-2,2′-pyrano[3,2-*c*]chromene]-1,3-dione (3′f). White solid (75%); IR (KBr) (ν_{max}/cm^{-1}): 3103, 2934, 2857, 1748, 1709, 1586, 1489, 1462, 1352, 1274, 1223, 1177, 1093, 976, 918, 860, 704, 626, 535. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.08–8.04 (2H, m, H–Ar), 7.96–7.93 (2H, m, H–Ar), 7.27–7.20 (2H, m, H–Ar), 6.12 (1H, s, CH), 5.83 (1H, s, CH), 4.77 (2H, s, CH_2), 2.80 (1H, d, J = 28.8 Hz, CH_2), 2.25 (1H, d, J = 20.8 Hz, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 197.9, 196.2, 148.6, 140.2, 136.8, 136.7, 129.2, 128.9, 125.9, 125.6, 124.7, 124.4, 124.2, 121.9, 119.6, 74.4, 68.9, 67.2, 25.7. HRMS $[M + H]^+$ calcd for $C_{20}H_{12}Cl_2O_4$: 386.0113, found: 387.0100. Anal. calcd for $C_{20}H_{12}Cl_2O_4$: C, 62.04; H, 3.12. Found: C, 62.02; H, 3.15.

(*R*)-1,3-Dioxo-1,3,5′,10*b*′-tetrahydro-3′*H*-spiro[indene-2,2′-pyrano[3,2-*c*]chromen]-7′-yl benzoate (3′g). White solid (75%); IR (KBr) (ν_{max}/cm^{-1}): 2919, 2844, 1757, 1710, 1600, 1478, 1265, 1089, 986, 865, 773, 707, 642, 540. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.22–8.20 (2H, m, H–Ar), 8.06–8.04 (2H, m, H–Ar), 7.94–7.92 (2H, m, H–Ar), 7.64–7.60 (1H, m, H–Ar), 7.52–7.48 (2H, m, H–Ar), 7.28–7.26 (1H, m, H–Ar), 7.05–7.03 (1H, d, J = 8.0 Hz, H–Ar), 6.91 (1H, t, J = 8.0 Hz, H–Ar), 6.05 (1H, s, CH), 5.91 (1H, s, CH), 4.73 (1H, d, J = 12.0 Hz, CH_2), 4.61 (1H, d, J = 12.0 Hz, CH_2), 2.79–2.74 (1H, m, CH_2), 2.21–2.16 (1H, m, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 198.1, 196.5, 164.6, 146.2, 140.3, 138.7, 136.6, 136.5, 133.4, 130.3, 130.3, 129.3, 128.4, 125.1, 124.3, 124.1, 124.0, 122.2, 120.6, 118.9, 74.5, 68.7, 67.6, 25.8. Anal. calcd for $C_{27}H_{18}O_6$: C, 73.97; H, 4.14. Found: C, 73.99; H, 4.11.

Methodology for biological experiments

Cell culture and reagents

Breast cancer (MDA-MB-231, MCF-7), colon cancer (HCT-116) and oral squamous cell carcinoma (H357) cells were grown and cultured in DMEM supplemented with 10% FBS, 1.5 mM L-glutamine and 1% antibiotic (100 U ml^{-1} of penicillin, 10 mg ml^{-1} of streptomycin) at 37 °C in a humidified atmosphere of 5% CO_2. Cell culture reagents and other growth supplements were procured from Himedia, India.

Cell viability assay

The anchorage dependant cell viability of the investigational compounds, parent compound and 5-FU (commonly used anti-cancer agent) were measured using MTT cell viability assay. In brief, 8000–10 000 cells per well were seeded in 96 well flat bottom tissue culture plates and grown to 70–80% confluence. Then cells were treated with increasing concentrations of the compounds for 48 h prior to harvest. Then media was aspirated and washed once with 1XPBS. Then 0.05% MTT solution was added to each well and incubated in 37 °C for 5–6 h to allow formation of formazan crystals. The formazan crystals were dissolved by adding 100 μL of 0.2% NP-40 detergent solution and incubated in dark for 1 h. The colour intensity was measured spectrophotometrically at 570 nm by using micro-plate reader (Mithras LB 940, Berthold Germany). Each data point was calculated in triplicate and all the assays were performed at least thrice.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

SN and SRM are thankful to CSIR New Delhi [02(0218)/14/EMR-II] and DRDO New Delhi ERIP/ER/1203083/M/01 for providing research grant. SN thanks to CSIR, New Delhi for providing research grant. PP thanks to DST, Odisha for providing research fellowship. Authors are also thankful to DST, FIST, New Delhi for providing NMR facility in Ravenshaw University.

Notes and references

1 X. Li, L. Yang, C. Peng, X. Xie, H.-J. Leng, B. Wang, Z.-W. Tang, G. He, L. Ouyang, W. Huang and B. Han, *Chem. Commun.*, 2013, **49**, 8692–8694.

2 (*a*) T. Chanda and M. S. Singh, *Org. Biomol. Chem.*, 2016, **14**, 8895–8910; (*b*) D. Pizzirani, M. Roberti, S. Grimaudo, A. D. Cristina, R. M. Pipitone, M. Tolomeo and M. Recanatini, *J. Med. Chem.*, 2009, **52**, 6936–6940; (*c*)

R. Misra and R. C. Pandey, *J. Am. Chem. Soc.*, 1982, **104**, 4478–4479.
3 N. C. Dige and D. M. Pore, *Synth. Commun.*, 2015, 1532–2432.
4 Y. Yang, D. Philips and S. Pan, *J. Org. Chem.*, 2011, **76**, 1902–1905.
5 S. Mahajan, P. Chauhan, M. Blümel, R. Puttreddy, K. Rissanen, G. Raabe and D. Enders, *Synthesis*, 2016, **48**, 1131–1138.
6 J. Duan, J. Cheng, Y. Cheng and P. Li, *Asian J. Org. Chem.*, 2016, **5**, 477–480.
7 S. A. Patil, R. Patil and S. A. Patil, *Eur. J. Med. Chem.*, 2017, **138**, 182–198.
8 S. Asadi and G. M. Ziarani, *Mol. Diversity*, 2016, **20**, 111–152.
9 D. Kumar, P. Sharma, H. Singh, K. Nepali, G. K. Gupta, S. K. Jain and F. Ntie-Kang, *RSC Adv.*, 2017, **7**, 36977–36999.
10 S. S. Mansoor, K. Logaiya, K. Aswin and P. N. Sudhan, *J. Taibah Uni. Sci.*, 2015, **9**, 213–226.
11 J. Madda, A. Venkatesham, N. K. Bejjanki, N. Kommu, S. Pombala, C. G. Kumar, T. P. Rao and J. B. Nanubolu, *Bioorg. Med. Chem. Lett.*, 2014, **24**, 4428–4434.
12 N. Jain, R. M. Kanojia, J. Xu, G. Jian-Zhong, E. Pacia, M.-T. Lai, F. Du, A. Musto, G. Allan, D. W. Hahn, S. Lundeen and Z. Sui, *J. Med. Chem.*, 2006, **49**, 3056–3059.
13 A. Saha, S. Payra and S. Banerjee, *RSC Adv.*, 2015, **5**, 101664–101671.
14 B. D. Rupnar, T. R. Kachave, P. D. Jawale, S. U. Shisodia and R. P. Pawar, *Pharma Chem.*, 2017, **9**, 120–124.
15 S. Kanakaraju, B. Prasanna, S. Basavoju and G. V. P. Chandramouli, *Arabian J. Chem.*, 2017, **10**, 2705–2713.
16 J. Liu, S.-S. Wen, J. Wang, J.-A. Xiao, S.-J. Huang and H. Yang, *Tetrahedron*, 2015, **71**, 4629–4634.
17 N. J. Parmar, R. A. Patel, S. B. Teraiya, D. Sharma and V. K. Gupta, *RSC Adv.*, 2012, **2**, 3069–3075.
18 S. Khodabakhshi, B. Karami, K. Eskandari and M. Farahi, *Tetrahedron Lett.*, 2014, **55**, 3753–3755.
19 M. S. Singh, G. C. Nandi and S. Samai, *Green Chem.*, 2012, **14**, 447–455.
20 N. A. Al-Masoudi, H. H. Mohammed, A. M. Hamdy, O. A. Akrawi, N. Eleya, A. Spannenberg, C. Pannecouque and P. Langer, *Z. Naturforsch.*, 2013, **68b**, 229–238.
21 S. Ahadi, M. Zolghadr, H. R. Khavasi and A. Bazgir, *Org. Biomol. Chem.*, 2013, **11**, 279–286.
22 A. Venkatesham, R. Srinivasa Rao, K. Nagaiah, J. S. Yadav, G. RoopaJones, S. J. Basha, B. Sridhar and A. Addlagatta, *Med. Chem. Commun.*, 2012, **3**, 652–658.
23 (*a*) M. M. Heravi, T. Ahmadi, M. Ghavidel, B. Heidari and H. Hamidi, *RSC Adv.*, 2015, **5**, 101999–102075; (*b*) S. Vodnala, A. K. D. Bhavani, R. Kamutam, V. G. M. Naidu and P. C. Prabhakar, *Bioorg. Med. Chem. Lett.*, 2016, **26**, 3973–3977; (*c*) R. Rahimi, M. Mahdavi, S. Pejman, P. Zare and S. Balalaei, *Acta Biochim. Pol.*, 2015, **62**, 83–88.
24 (*a*) P. Parenti, A. Pizzigoni, G. Hanozet, E. H. Hakim, L. Makmur, S. A. Achmad and B. Giordana, *Biochem. Biophys. Res. Commun.*, 1998, **244**, 445–448; (*b*) Y. ; Sun, J. Liu, X. Jiang, T. Sun, L. Liu, X. Zhang, S. Ding, J. Li, Y. Zhuang, Y. Wang and R. Wang, *Sci. Rep.*, 2015, **5**, 13699.
25 L. Liu, H. Kim, Y. Xie, C. Farès, P. S. J. Kaib, R. Goddard and B. List, *J. Am. Chem. Soc.*, 2017, **139**, 13656–13659.
26 T. Liang, G. Li, L. Wojtas and J. C. Antilla, *Chem. Commun.*, 2014, **50**, 14187–14190.
27 H.-L. Cui and F. Tanaka, *Chem.–Eur. J.*, 2013, **19**, 6213–6216.
28 H.-L. Cui, P. V. Chouthaiwale, F. Yin and F. Tanaka, *Org. Biomol. Chem.*, 2016, **14**, 1777–1783.
29 T.-P. Gao, J.-B. Lin, X.-Q. Hu and P.-F. Xu, *Chem. Commun.*, 2014, **50**, 8934–8936.
30 G. B. Gill, M. S. H. ldris and K. S. Kirollos, *J. Chem. Soc., Perkin Trans. 1*, 1992, **1**, 2355–2365.
31 S. Nayak, S. Chakroborty, S. Bhakta, P. Panda, S. Mohapatra, S. Kumar, P. K. Jena and C. Purohit, *Lett. Org. Chem.*, 2015, **12**, 352–358.
32 J. Zhang, C. Lou, Z. Hu and M. Yan, *ARKIVOC*, 2009, **xiv**, 362–375.
33 P. T. Parvatkar, P. S. Torney and S. G. Tilve, *Curr. Org. Synth.*, 2013, **10**, 288–317.

