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Synthesis of novel acrylyl pyranochromen-2-one derivatives and their antibacterial activity evaluation

Suchita Prasad, Ayushi Mittal & Sunil K Sharma*

Department of Chemistry, University of Delhi, Delhi 110 007, India

E-mail: sksharma@chemistry.du.ac.in

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A series of fourteen pyranochromen-2-one acrylate derivatives has been synthesized by acid-catalyzed esterification reaction of the corresponding pyranochromen-2-one acrylic acids with various alcohols under reflux conditions. In order to have comparison of the activity profiles of esters and amides, the synthesis of ten pyranochromen-2-one acrylamides from corresponding acrylic acids using different coupling agents has also been carried out. All of the synthesized compounds have been fully characterized from their spectral data and evaluated for antibacterial activity against both Gram-positive (*Bacillus cereus* and *Staphylococcus aureus*) and Gram-negative bacteria (*Pseudomonas aeruginosa* and *Escherichia coli*). It is inferred form the results that the presence of hydroxyl group along with longer hydrophobic alkyl chain is favorable for a compound to inhibit bacterial growth, which can be used to design and develop the next generation of compounds with higher antibacterial efficacy.

Keywords: Acrylates, acrylamides, antibacterial activity, pyranochromen-2-ones, Gram positive, Gram negative

Heterocyclic compounds with their origins rooted in medicinal chemistry, are one of the most complex and intriguing division of organic chemistry. They constitute the largest and most varied family of organic compounds that make up for about two-thirds of all known organic compounds[1]. Drug pipeline research is deeply based on mimicking nature's compounds and thus medicinal chemistry efforts have evolved around a simulation of heterocycles as these structural motifs are the core elements of a wide repertoire of natural products such as nucleic acids, amino acids, carbohydrates, vitamins, and alkaloids. Their intrinsic versatility and inimitable physico-chemical properties, have poised them as true cornerstones of medicinal chemistry which is evident from their presence in most currently marketed pharmaceuticals. Four of the top five US small molecule drug retail sales in 2014, were or contained heterocyclic fragments in their structure and accounted for almost 80% of the total revenue generated from the top five prescription drugs[2]. The one reason behind such high inclusion of heterocycles in therapeutics is their inherent ability to manifest substituents around a core scaffold and to provide fertile grounds for optimization of drug candidates through modulation of drug properties such as potency and selectivity through bioisosteric replacements, lipophilicity, polarity and aqueous solubility[3,4].

Oxygen-containing heterocycles have acquired substantial attention which stems from the fact that these are important synthetic targets due to their ubiquity in natural products, their wide range of biological activities, and their utility as versatile intermediates in organic synthesis[5]. About 8% of all heterocycles with anticancer properties approved by FDA since 2010 are oxygen-based heterocycles[6]. The synthesis of coumarin derivatives fused with other heterocycles is an attractive domain in organic chemistry because of their exciting biological and photodynamic properties[7]. Of the various fused coumarin derivatives, pyranocoumarins are privileged structural motifs in natural as well as synthetic molecules exhibiting a wide array of biological activities such as antifungal[8], antibacterial[9], anti-hyperglycaemic and anti-dyslipidemic[10], anti-cancer[11], cytotoxic[12], anti-HIV[13], anti-HBV[14], antiviral[15], antiproliferative[16], anti-inflammatory[17], antinocice ptive[18] and antituberculosis[19] activities. Decursin (**1**) isolated from *Streptomyces* sp. GMT-8, an endophyte in *Zingiber officinale* Rosc., was found to inhibit the growth of Gram-positive bacteria (*Staphylococcus aureus*, *Bacillus cereus*, *Bacillus subtilis*) with the minimum inhibitory concentrations (MICs) within the

range of 32 to 256 µg mL^{-1} (Ref 20). Decursin (**1**) and decursinol angelate (**2**) from *Angelica gigas* roots were also found to display antibacterial activity against *Bacillus subtilis* with MIC of 12.5 and 50 µg mL^{-1}, respectively[21]. Aegelinol (**3**) and agasyllin (**4**) from the roots of *Ferulago campestris* showed significant antibacterial effect against both Gram-negative and Gram-positive bacteria at a concentration between 16 and 125 µg mL^{-1} (Figure 1)[22].

Our research group is extensively involved in the synthesis of an array of oxygen and nitrogen containing heterocyclic compounds *e.g.* 2-pyridones, coumarins, quinolones, benzofurans, chromones, *etc.* which have been evaluated for various bioactivities such as antioxidant, antimicrobial, antiplatelet, anti-inflammatory, anticancer, *etc.* Earlier, C-3 alkylated (**5**)[23], quaternary ammonium (**6** and **7**)[24] and triazolyl (**8**)[25] pyranocoumarins have been synthesized by our group and screened for their anti-proliferative, Src kinase inhibitory and antimicrobial potential (Figure 1). Further exploration of the chemical diversity space around pyranocoumarin skeleton prompted us to undertake the following work.

Moreover, numerous chromen-4-one based acrylates and acrylamides synthesized by our group have been screened for anti-inflammatory, antiproliferative and c-Src kinase inhibitory activities[26,27]. Further, the antimicrobial activity of various cinnamic-related molecules was reported in literature with most of the cinnamate and 4-coumarate esters and cinnamoyl and 4-coumaroyl amides worth mentioning[28]. A remarkable antimicrobial activity against a broad spectrum of pathogens including yeasts, Gram-positive and Gram-negative bacteria was detected for isobutyl cinnamate with MIC values in the micromolar range[28]. The essence of all these facts and our search for developing newer antimicrobial agents with improved therapeutic efficacy laid the rationale for designing and synthesizing acrylyl pyranochromen-2-ones (Figure 2). The antibacterial screening of all the synthesized derivatives was carried out against both

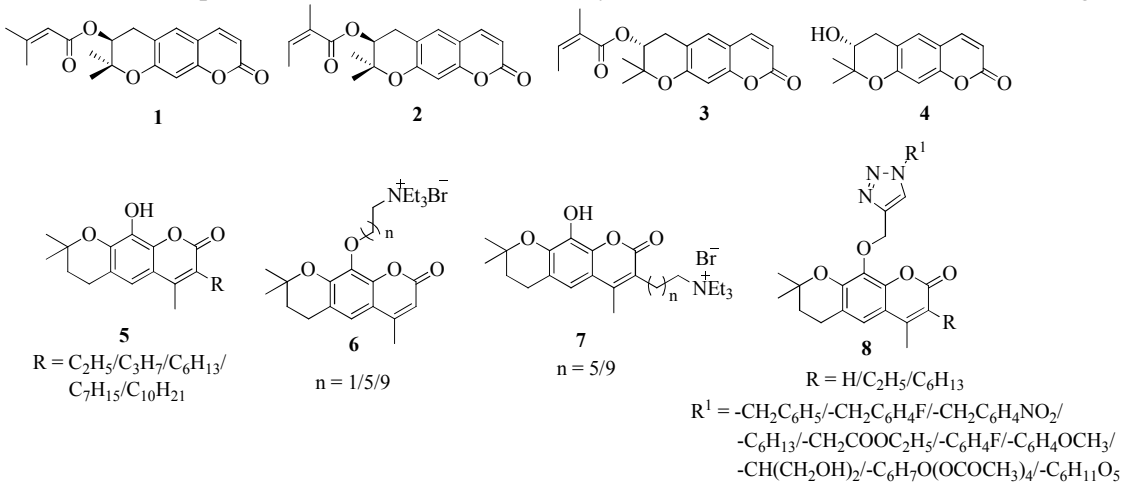


Figure 1 — Naturally isolated and chemically synthesized pyranocoumarin derivatives

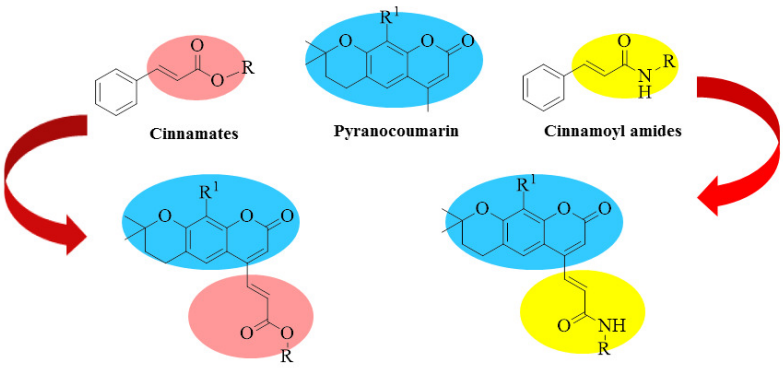


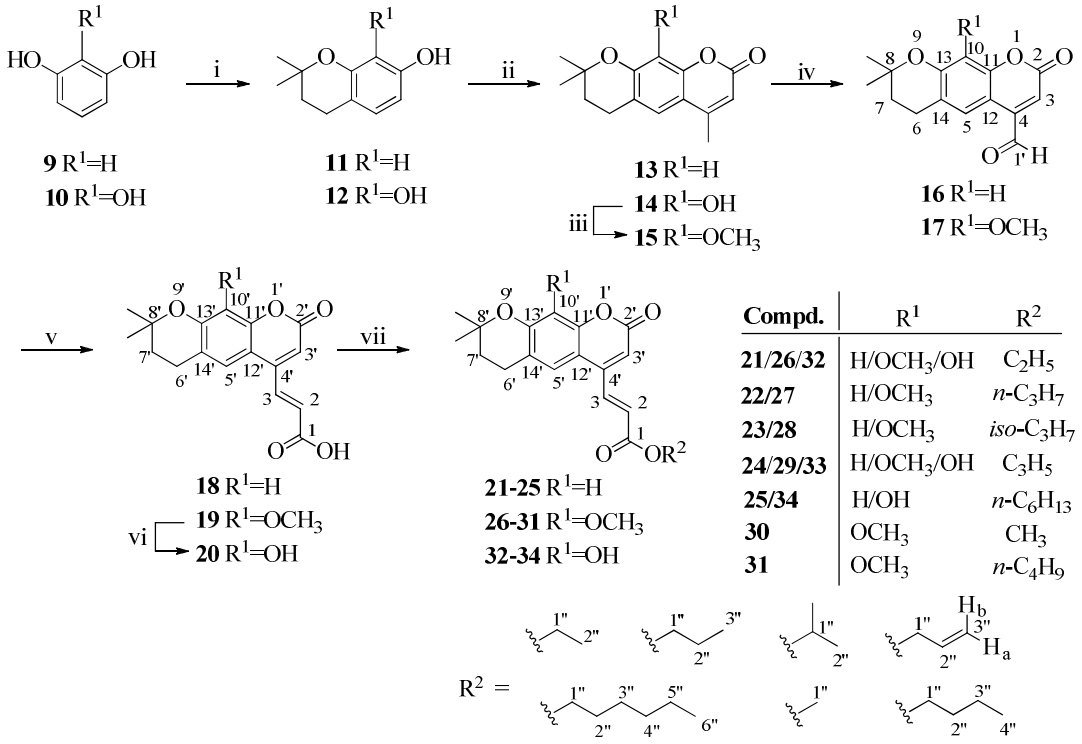
Figure 2 — Designed acrylyl pyranochromen-2-ones

Gram-positive and Gram-negative bacteria using Gentamicin as a standard.

Results and Discussion

Chemistry

A series of fourteen pyranochromen-2-one acrylate derivatives (**21**-**34**) has been synthesized by acid-catalyzed esterification reaction of the corresponding pyranochromen-2-one acrylic acids (**18**-**20**) with various alcohols under reflux conditions (Scheme I). The desired acrylic acid precursors (**18/19**) were synthesized from Knoevenagel condensation of 8,8-dimethyl-2-oxo-2,6,7,8-tetrahydropyrano[3,2-*g*]chromene-4-carbaldehydes (**16/17**) with malonic acid using pyridine as a base. The acrylic acid bearing hydroxyl group at C-10 position of pyranochromen-2-one *i.e.* (*E*)-3-(10-hydroxy-8,8-dimethyl-2-oxo-2,6,7,8-tetrahydropyrano[3,2-*g*]chromen-4-yl)acrylic acid (**20**) was obtained from the demethylation reaction of its corresponding methoxy analog (**19**) using hydrobromic acid and acetic acid. The carbaldehydes (**16/17**) in turn, were prepared from the oxidation of C-4 methyl derivatives of pyranochromen-2-one (**13/15**) using selenium dioxide as an oxidizing agent. An attempt of directly synthesizing acrylic acid (**20**) from pyranochromen-2-one having hydroxyl group at C-10 (**14**) involved selenium dioxide oxidation of compound **14** to its corresponding carbaldehyde followed by Knoevenagel condensation. However, the oxidation of compound **14** resulted in a very poor yield of the desired C_{10}-OH carbaldehyde, therefore, pyranochromen-2-one (**14**) was converted to its corresponding methoxy compound (**15**) employing dimethyl sulphate as a methylating agent in the presence of potassium carbonate as a base[29]. The synthesis of compounds **13/14** was achieved starting from easily available commercial starting materials *i.e.* resorcinol (**9**) / pyrogallol (**10**) in two steps. In the first step, resorcinol (**9**) / pyrogallol (**10**) was made to undergo reaction with 2-methylbuta-1,3-diene (isoprene) in the presence of orthophosphoric acid using xylene as a solvent to yield 2,2-dimethylchroman-7-ol (**11**) / 2,2-dimethylchroman-7,8-diol (**12**)[30]. In order to minimize the self-condensation of isoprene, the chief difficulty encountered while working with dienes, the addition of isoprene to a stirred solution of resorcinol (**9**) / pyrogallol (**10**) in xylene and orthophosphoric acid was done very slowly. The second step involved



Compd.	R^1	R^2
21/26/32	H/OCH_3/OH	C_2H_5
22/27	H/OCH_3	*n*-C_3H_7
23/28	H/OCH_3	*iso*-C_3H_7
24/29/33	H/OCH_3/OH	C_3H_5
25/34	H/OH	*n*-C_6H_{13}
30	OCH_3	CH_3
31	OCH_3	*n*-C_4H_9

Scheme I — Synthesis of pyranochromen-2-one acrylates: (i) isoprene, H_3PO_4, xylene, 25°C, 15 h; (ii) ethyl acetoacetate, conc. H_2SO_4, 25°C, 12 h; (iii) dimethyl sulphate, K_2CO_3, acetone, 25°C, 12 h; (iv) SeO_2, dioxane, reflux, 30 h; (v) $CH_2(COOH)_2$, pyridine, reflux, 6 h; (vi) HBr-CH_3COOH, 110°C, 24 h; (vii) R^2OH, conc. H_2SO_4, reflux, 12 h.

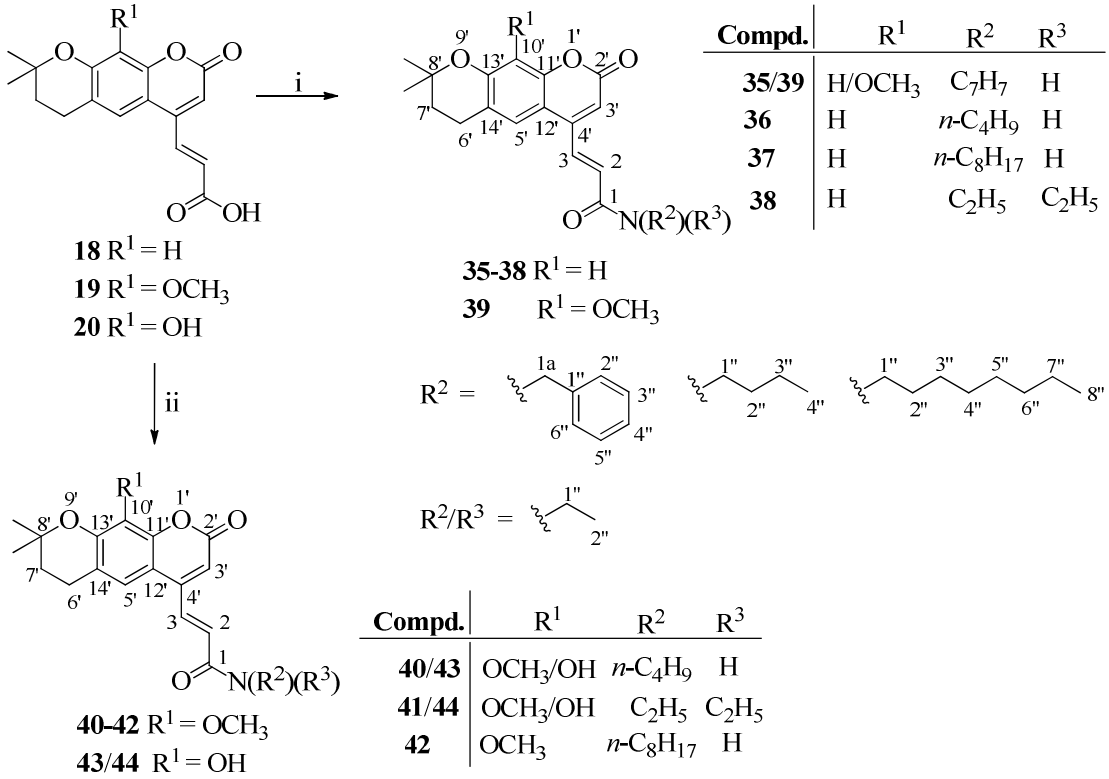
Pechmann condensation of compounds **11/12** with ethyl acetoacetate in the presence of sulphuric acid to afford the pyranochromen-2-ones **13/14 (Ref** 29).

In order to have a comparison of the activity profiles of esters and amides, the synthesis of ten pyranochromen-2-one acrylamides (**35**-**44**) from corresponding acrylic acids (**18**-**20**) using dicyclohexylcarbodiimide (DCC) or benzotriazol-1-yloxy-tris(dimethylamino) phosphonium hexa fluorophosphate (BOP) has also been carried out following the strategy as outlined in Scheme II. (*E*)-3-(8,8-Dimethyl-2-oxo-2,6,7,8-tetrahydropyrano[3,2-*g*] chromen-4-yl)-*N*-alkyl/-*N*,*N*-dialkylacrylamides **35**-**39** were synthesized by reacting (*E*)-3-(8,8-dimethyl-2-oxo-2,6,7,8-tetrahydropyrano[3,2-*g*]chromen-4-yl)acrylic acids **18/19** with appropriate amines in the presence of BOP as a coupling reagent and triethylamine as a base for the generation of carboxylate anion. In another reaction sequence, DCC and 1-hydroxybenzotriazole (HOBt) were used as coupling agent and additive, respectively, to yield the acrylamides **40**-**44**. The structure of all the synthesized compounds was characterized by using various spectroscopic techniques. The structural characterization of the known compounds was achieved by comparison of their melting point and spectral data with those reported in the literature.

Antibacterial activity

All of the synthesized acrylyl pyranochromen-2-one derivatives (**21**-**44**) were screened for antibacterial activity against two Gram-positive pathogenic strains namely *B. cereus* and *S. aureus* and two Gram-negative bacterial strains *i.e*. *P. aeruginosa* and *E. coli* using Kirby-Bauer disc susceptibility test with some minor modifications at a concentration of 250 μg/disc[31,32]. Of all the tested compounds, three pyranochromen-2-one derivatives bearing hydroxyl group at C-10' of pyranochromen-2-one (**33**, **34** and **43**) exhibit moderate activity against *B. cereus*, *S. aureus* and *P. aeruginosa* with no growth inhibitory effect shown on *E. coli* (Table I).

The results reveal that the presence of hydroxyl group is essential to inhibit bacterial growth as the corresponding analogs having either no substitution (**24**, **25** and **36**) or methoxyl group at C-10' of pyranochromen-2-one (**29** and **40**) do not develop any zone of inhibition against the tested bacteria. Furthermore, comparison of the activity profiles of



Compd.	R^1	R^2	R^3
35/39	H/OCH_3	C_7H_7	H
36	H	*n*-C_4H_9	H
37	H	*n*-C_8H_{17}	H
38	H	C_2H_5	C_2H_5

Compd.	R^1	R^2	R^3
40/43	OCH_3/OH	*n*-C_4H_9	H
41/44	OCH_3/OH	C_2H_5	C_2H_5
42	OCH_3	*n*-C_8H_{17}	H

Scheme II — Synthesis of pyranochromen-2-one acrylamides: (i) $NH(R^2)(R^3)$, BOP, NEt_3, DMF, 25°C, 15 h; (ii) $NH(R^2)(R^3)$, DCC, HOBt, DMF, 25°C, 15 h.

Table I — Zone of inhibition (mm) of compounds 33, 34 and 43 against pathogenic bacterial strains using gentamicin as a positive control

Compd	Gram-positive		Gram-negative	
	B. cereus	*S. aureus*	*P. aeruginosa*	*E. coli*
33	– [a]	12	– [a]	– [a]
34	12	17	12	– [a]
43	– [a]	13	12	– [a]
Gentamicin	24	25	26	23

Diameter of zone of inhibition (mm) including disc diameter of 6 mm; Concentration of compound = 250 µg/disc. [a]No zone of inhibition at the tested concentration.

derivatives bearing hydroxyl group at C-10' position (**32**, **33**, **34**, **43** and **44**) demonstrates that the elongation of the alkyl chain of ester or amide leads to the enhancement in bacterial growth inhibitory potency as compound **34** having *n*-hexyl chain is found to be the most potent.

Experimental Section

Chemistry

Materials and Methods

All of the chemicals and reagents used for the synthesis of compounds were procured from Spectrochem Pvt. Ltd., India, SD Fine Chemicals Pvt. Ltd., India and Sigma-Aldrich Chemicals, USA. The organic solvents were dried and distilled prior to their use. The progress of the reactions was monitored using pre-coated TLC plates (Merck silica gel $60F_{254}$); the spots were visualized with UV light and ninhydrin stain. All the synthesized compounds were purified by column chromatography using silica gel (100-200 mesh). Melting points were measured on a Buchi M-560 equipment and are uncorrected. Perkin-Elmer 2000 FT-IR spectrophotometer was used to record the infrared spectra. The characterization of compounds by ^{1}H, ^{13}C and ^{2}D HETCOR NMR was achieved by recording the spectra on JEOL ECX-400P (400 MHz, 100.5 MHz) NMR spectrometer using tetramethylsilane (TMS) as internal standard. The chemical shift values are on a δ scale and the coupling constant values (*J*) are in Hertz. The UV spectra were recorded on Cary 300 UV-Vis spectrophotometer, Agilent Technologies. The HRMS data was obtained on Q-TOF LCMS-Agilent Technology-6530.

General procedure for the synthesis of 2,2-dimethylchroman-7-ol, 11 / 2,2-dimethylchroman-7,8-diol, 12

In a round-bottom flask, resorcinol **9**/pyrogallol **10** (10 g, 1 equiv.) was dissolved in 55 mL of xylene followed by addition of H_3PO_4 (17 mL) with constant stirring. After stirring the reaction mixture for 15 min at 25°C, 2-methyl-1,3-butadiene (isoprene) (1.2 equiv.) dissolved in 50 mL of xylene was added slowly to the reaction mixture and allowed to stir for another 15 h at 25°C. On completion of the reaction as monitored by TLC (MeOH:$CHCl_3$ :: 1:49), the reaction mixture was neutralized using 5% aqueous $NaHCO_3$ and extracted with ethyl acetate (4 × 150 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure. The crude product so obtained was purified by column chromatography to afford the desired compound **11/12** as an off-white solid in 92/90% isolated yield[30].

General procedure for the synthesis of 4,8,8-trimethyl-7,8-dihydropyrano[3,2-*g*] chromen-2(6*H*)-one (13)/10-hydroxy-4,8,8-trimethyl-7,8-dihydropyrano[3,2-*g*]chromen-2(6*H*)-one, 14

To a stirred and cooled solution (0°C) of compound **11/12** (5 g, 1 equiv.) and ethyl acetoacetate (1.2 equiv.), conc. H_2SO_4 (25 mL) was added drop-wise maintaining the temperature of the reaction mixture at 0°C, followed by stirring at 25°C for 12 h. The progress of the reaction was monitored by TLC (MeOH:$CHCl_3$ :: 1:49) and on completion of the reaction, the contents of the flask were poured over crushed ice. The solid product so obtained was filtered, washed with water and hexane and dried under vacuum which on column purification gave the desired product **13/14** as a white solid in 91/90% isolated yield[29].

General procedure for the synthesis of 10-methoxy-4,8,8-trimethyl-7,8-dihydropyrano[3,2-*g*]chromen-2(6*H*)-one, 15

To a stirred solution of 10-hydroxy-4,8,8-trimethyl-7,8-dihydropyrano[3,2-*g*] chromen-2(6*H*)-one **14** (2 g, 1 equiv., 7.68 mmol) in acetone (40 mL), anhydrous potassium carbonate (3.18 g, 3 equiv., 23.04 mmol) was added and stirred for 15 min. This was followed by the addition of dimethyl sulphate (1.45g, 1.5 equiv., 11.52 mmol) with an additional stirring of the reaction mixture for 12 h at 25°C. On completion of the reaction as monitored by TLC (ethyl acetate:petroleum ether :: 1:4), the contents of the flask were poured over crushed ice with continuous stirring. After filtration, washing with water and hexane and drying under vacuum, the crude

solid so obtained was subjected to column chromatography to afford the desired compound **15** as a white solid in 85% isolated yield[29].

General procedure for the synthesis of 8,8-dimethyl-2-oxo-2,6,7,8-tetrahydro pyrano[3,2-*g*chromene-4-carbaldehyde, 16 / 10-methoxy-8,8-dimethyl-2-oxo-2,6,7,8-tetrahydropyrano[3,2-*g*]chromene-4-carbaldehyde, 17

Selenium dioxide (1.7 equiv.) was added to compound **13/15** (1 g, 1 equiv.) dissolved in anhydrous 1,4-dioxane (30 mL) and the reaction mixture was refluxed for 30 h. The progress of the reaction was monitored by TLC (ethyl acetate:petroleum ether :: 3:7). On completion of the reaction, the dark brown solution was filtered through a funnel plugged with cotton followed by evaporation of the solvent *in vacuo*. The purification of the crude product through column chromatography gave the desired carbaldehyde **16/17** as yellow solid in 75/76% isolated yield.

8,8-Dimethyl-2-oxo-2,6,7,8-tetrahydro pyrano [3,2-*g*]chromene-4-carbaldehyde, 16 (Ref34): The title compound **16** was obtained from the reaction of 4,8,8-trimethyl-7,8-dihydropy rano[3,2-*g*]chromen-2(6*H*)-one **13** (1 g, 1 equiv., 4.09 mmol) with selenium dioxide (0.77 g, 1.7 equiv., 6.95 mmol) as a yellow solid (0.8 g, 75%) by following the general procedure. m.p.153.0-153.6°C. UV (MeOH) λ_{max}: 335 nm; IR (KBr): 2973, 2939, 2865, 1718 (C=O), 1618, 1559, 1383, 1289, 1157, 1119, 1049, 854, 749 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.37 (s, 6H, 2 × C-8 CH_3), 1.86 (t, 2H, *J* = 6.6 Hz, H-7), 2.86 (t, 2H, *J* = 6.6 Hz, H-6), 6.65 (s, 1H, H-3), 6.76 (s, 1H, H-10), 8.29 (s, 1H, H-5), 10.04 (s, 1H, H-1'); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 22.30 (C-6), 27.08 (2 × C-8 *C*H_3), 32.57 (C-7), 76.37 (C-8), 104.94 (C-10), 107.66 (C-12), 119.57 (C-14), 122.19 (C-3), 127.09 (C-5), 143.82 (C-11), 154.67 & 158.64 (C-4 & C-13), 161.08 (C-2), 192.37 (C-1'); HRMS: *m/z* Calcd for $C_{15}H_{14}O_4$; $(M + H)^+$ 259.0970. Found: 259.0967.

10-Methoxy-8,8-dimethyl-2-oxo-2,6,7,8-tetrahydropyrano[3,2-*g*]chromene-4-carbaldehyde, 17: The title compound **17** was obtained from the reaction of 10-methoxy-4,8,8-trimethyl-7,8-dihydro pyrano [3,2-*g*]chromen-2(6*H*)-one **15** (1 g, 1 equiv., 3.65 mmol) with selenium dioxide (0.69 g, 1.7 equiv., 6.21 mmol) as a yellow solid (0.8 g, 76%) by following the general procedure; m.p: 140.3-141.0°C. UV (MeOH) λ_{max}: 334 nm; IR (KBr): 2942, 2847, 1719 (C=O), 1705 (C=O), 1609, 1412, 1390, 1112, 1057, 892, 764 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.41 (s, 6H, 2 × C-8 CH_3), 1.86 (t, 2H, *J* = 6.6 Hz, H-7), 2.86 (t, 2H, *J* = 6.6 Hz, H-6), 3.92 (s, 3H, OCH_3), 6.66 (s, 1H, H-3), 8.03 (s, 1H, H-5), 10.04 (s, 1H, H-1'); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 22.49 (C-6), 27.07 (2 × C-8 *C*H_3), 32.44 (C-7), 61.38 (OCH_3), 76.54 (C-8), 107.88 (C-12), 120.04 (C-14), 121.08 (C-5), 122.15 (C-3), 135.89 (C-10), 143.94 & 147.30 (C-11 & C-13), 151.85 (C-4), 160.72 (C-2), 192.19 (C-1'); HRMS: *m/z* Calcd for $C_{16}H_{16}O_5$; $(M + H)^+$ 289.1076. Found: 289.1074.

General procedure for the synthesis of (*E*)-3-(8,8-dimethyl-2-oxo-2,6,7,8-tetrahydro pyrano[3,2-*g*]chromen-4-yl)acrylic acid 18 / (*E*)-3-(10-methoxy-8,8-dimethyl-2-oxo-2,6,7,8-tetrahydropyrano[3,2-*g*]chromen-4-yl)acrylic acid, 19

The synthesis of acrylic acid derivatives **18** and **19** was achieved *via* Knoevenagel condensation. A mixture of carbaldehyde **16/17** (1 g, 1 equiv.), malonic acid (2 equiv.) and pyridine (10 drops) was heated at 110°C. After 1 h, additional malonic acid (0.5 equiv.) was added to the reaction mixture. After stirring for 6 h, the reaction mixture was poured over ice and neutralized with 30% HCl solution. The obtained yellow coloured precipitate was filtered and washed with water. Column purification of the dried crude solid gave the desired acrylic acid derivative **18/19** as a yellow/light yellow solid in 90/87% isolated yield.

(*E*)-3-(8,8-Dimethyl-2-oxo-2,6,7,8-tetrahyd ropyrano[3,2-*g*]chromen-4-yl) acrylic acid, 18 (Ref 33): The title compound **18** was obtained from the reaction of 8,8-dimethyl-2-oxo-2,6,7,8-tetrahydropyrano[3,2-*g*]chromene-4-carbaldehyde **16** (1 g, 1 equiv., 3.87 mmol) with malonic acid (0.81 g, 2 equiv., 7.74 mmol) as a yellow solid (1.04 g, 90%) by following the general procedure. m.p.223.7-224.6°C. UV (MeOH) λ_{max}: 240, 268 and 353 nm; IR (KBr): 3420 (O-H str), 2978, 1716 (C=O), 1692 (C=O), 1624, 1558, 1420, 1377, 1292, 1162, 1121, 968, 845 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.38 (s, 6H, 2 × C-8' CH_3), 1.87 (t, 2H, *J* = 6.9 Hz, H-7'), 2.86 (t, 2H, *J* = 6.6 Hz, H-6'), 6.38 (s, 1H, H-3'), 6.57 (d, 1H, *J* = 16.1

Hz, H-2), 6.78 (s, 1H, H-10'), 7.36 (s, 1H, H-5'), 7.98 (d, 1H, *J* = 16.1 Hz, H-3); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 22.27 (C-6'), 27.08 (2 × C-8' *C*H_3), 32.57 (C-7'), 76.27 (C-8'), 105.38 (C-10'), 110.33 (C-3'), 110.90 (C-12'), 118.82 (C-14'), 125.12 (C-5'), 125.61 (C-2), 139.75 (C-3), 147.63 (C-11'), 153.99 & 158.51 (C-4' & C-13'), 161.33 & 169.53 (C-2' & C-1)ppm; HRMS: *m/z* Calcd for $C_{17}H_{16}O_5$; $(M + H)^+$ 301.1076. Found: 301.1080.

(*E*)-3-(10-Methoxy-8,8-dimethyl-2-oxo-2,6,7,8-tetra hydropyrano[3,2-*g*] chromen-4-yl)acrylic acid, 19: The title compound **19** was obtained from the reaction of 10-methoxy-8,8-dimethyl-2-oxo-2,6,7,8-tetrahy dropyrano[3,2-*g*]chromene-4-carbaldehyde **17** (1 g, 1 equiv., 3.47 mmol) with malonic acid (0.72 g, 2 equiv., 6.94 mmol) as a light yellow solid (1 g, 87%) by following the general procedure. m.p.221.0-221.6°C. UV (MeOH) λ_{max}: 263 and 349 nm; IR (KBr): 2974, 2944, 1718 (C=O), 1675 (C=O), 1645, 1612, 1566, 1409, 1385, 1281, 1248, 1189, 1109, 1053, 924, 848 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.43 (s, 6H, 2 × C-8' CH_3), 1.88 (t, 2H, *J* = 6.6 Hz, H-7'), 2.87 (t, 2H, *J* = 6.6 Hz, H-6'), 3.95 (s, 3H, OCH_3), 6.39 (s, 1H, H-3'), 6.56 (d, 1H, *J* = 15.4 Hz, H-2), 7.13 (s, 1H, H-5'), 7.98 (d, 1H, *J* = 16.1 Hz, H-3); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 22.50 (C-6'), 27.08 (2 × C-8' *C*H_3), 32.48 (C-7'), 61.43 (OCH_3), 76.46 (C-8'), 110.49 (C-3'), 111.04 (C-12'), 119.14 & 119.36 (C-5' & C-14'), 125.74 (C-2), 136.26 (C-10'), 139.84 (C-3), 146.49, 147.88 & 151.39 (C-4', C-11' & C-13'), 160.77 & 169.68 (C-2' & C-1); HRMS: *m/z* Calcd for $C_{18}H_{18}O_6$; $(M + H)^+$ 331.1182. Found: 331.1178.

General procedure for the synthesis of (*E*)-3-(10-hydroxy-8,8-dimethyl-2-oxo-2,6,7,8-tetrahydrop yrano[3,2-*g*]chromen-4-yl)acrylic acid, 20

In case of 10-hydroxy acrylic acid derivative **20**, the condensation reaction product **19** *i.e.* (*E*)-3-(10-methoxy-8,8-dimethyl-2-oxo-2,6,7,8-tetrahydropyrano[3,2-*g*]chromen-4-yl)acrylic acid (1 g, 3.03 mmol) was further subjected to demethylation reaction using HBr:AcOH (7:3, 10 mL) at 120°C. After 48 h, the reaction mixture was poured over crushed ice with stirring. The precipitate so obtained was filtered, washed with water, dried and purified by column chromatography to afford the acrylic acid derivative **20** as a yellow solid in 73% (0.7 g) isolated yield. m.p.: 266.1-267.0°C. UV (MeOH) λ_{max}: 261 and 354 nm; IR (KBr): 3352 (O-H str), 2933, 1718 (C=O), 1716 (C=O), 1638, 1400, 1284, 1246, 1184, 1122, 1044, 978, 839 cm^{-1}; ^{1}H NMR (400 MHz, Acetone-d_6): δ 1.37 (s, 6H, 2 × C-8' CH_3), 1.90 (t, 2H, *J* = 6.6 Hz, H-7'), 2.91 (t, 2H, *J* = 6.6 Hz, H-6'), 6.45 (s, 1H, H-3'), 6.70 (d, 1H, *J* = 16.1 Hz, H-2), 7.13 (s, 1H, H-5'), 7.91 (d, 1H, *J* = 16.1 Hz, H-3); ^{13}C NMR (100.5 MHz, Acetone-d_6): δ 22.59 (C-6'), 27.01 (2 × C-8' *C*H_3), 33.15 (C-7'), 76.95 (C-8'), 110.65 (C-3'), 112.05 (C-12'), 115.55 (C-5'), 119.21 (C-14'), 127.75 (C-2), 134.40 (C-10'), 138.22 (C-3), 141.84, 146.53 & 149.18 (C-4', C-11' & C-13'), 160.80 & 166.70 (C-2' & C-1); HRMS: *m/z* Calcd for $C_{17}H_{16}O_6$; $(M + H)^+$ 317.1025. Found: 317.1033.

General procedure for the synthesis of pyranochromen-2-one acrylates, 21-34

In a round-bottom flask, acrylic acid **18**-**20** (1 g) and appropriate alcohol (50 mL) were taken. Conc. H_2SO_4 (3-4 drops) was added and the reaction mixture was refluxed for 12-15 h. After the reaction was over as indicated by TLC (ethyl acetate:petroleum ether :: 3:7), the reaction mixture was allowed to cool to RT. The alcohol was evaporated under reduced pressure followed by the addition of ice cold water (50 mL) and extraction with ethyl acetate (3 × 50 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and evaporated *in vacuo* to obtain the crude product which on purification by column chromatography afforded the desired acrylate **21**-**34** in 70-80% isolated yield.

(*E*)-Ethyl 3-(8,8-dimethyl-2-oxo-2,6,7,8-tetrahy drop yrano[3,2-*g*]chromen-4-yl)acrylate, 21 (Ref 33): The title compound **21** was obtained from the reaction of (*E*)-3-(8,8-dimethyl-2-oxo-2,6,7,8-tetrahydropyrano [3,2-*g*]chromen-4-yl)acrylic acid **18** (1 g, 3.33 mmol) with ethanol (50 mL) as a yellow solid (0.87 g, 80%) by following the general procedure. m.p.148.0-149.0°C. UV (MeOH) λ_{max}: 253, 271 and 349 nm; IR (KBr): 2981, 2937, 1698 (C=O), 1638, 1620, 1553, 1381, 1292, 1186, 1160, 1122, 1050, 974, 871, 565 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.33-1.39 (m, 9H, 2 × C-8' CH_3 & H-2''), 1.86 (t, 2H, *J* = 6.6 Hz, H-7'), 2.84 (t, 2H, *J* = 6.6 Hz, H-6'), 4.31 (q, 2H, *J* = 7.3 Hz, H-1''), 6.33 (s, 1H, H-3'), 6.53 (d, 1H, *J* = 16.1 Hz, H-2), 6.76 (s, 1H, H-10'), 7.37 (s, 1H, H-5'), 7.88 (d, 1H, *J* = 16.1 Hz, H-3); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 14.41 (C-2''), 22.22 (C-6'), 27.06 (2 × C-8' *C*H_3), 32.57 (C-7'), 61.51 (C-1''), 76.18 (C-8'), 105.25 (C-10'), 109.88 (C-3'), 111.09 (C-12'), 118.77 (C-14'),

125.26 (C-5'), 126.77 (C-2), 137.47 (C-3), 148.08 (C-11'), 153.94 & 158.35 (C-4' & C-13'), 161.38 & 165.72 (C-2' & C-1); HRMS: *m/z* Calcd for $C_{19}H_{20}O_5$; $(M + H)^+$ 329.1389. Found: 329.1384.

(*E*)-*n*-Propyl 3-(8,8-dimethyl-2-oxo-2,6,7,8-tetrahydropyrano [3,2-*g*]chromen-4-yl)acrylate, 22: The title compound **22** was obtained from the reaction of (*E*)-3-(8,8-dimethyl-2-oxo-2,6,7,8-tetrahydropyrano[3,2-*g*]chromen-4-yl)acrylic acid (**18**) (1 g, 3.33 mmol) with propan-1-ol (50 mL) as a yellow solid (0.89 g, 78%) by following the general procedure; m.p: 142.0-143.2°C. UV (MeOH) λ_{max}: 252, 270 and 348 nm; IR (KBr): 2972, 2933, 1699 (C=O), 1638, 1621, 1552, 1382, 1328, 1291, 1186, 1160, 1123, 1050, 975, 871, 566 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.01 (t, 3H, *J* = 7.3 Hz, H-3''), 1.37 (s, 6H, 2 × C-8' CH_3), 1.71-1.79 (m, 2H, H-2''), 1.86 (t, 2H, *J* = 6.6 Hz, H-7'), 2.85 (t, 2H, *J* = 6.6 Hz, H-6'), 4.22 (t, 2H, *J* = 7.0 Hz, H-1''), 6.34 (s, 1H, H-3'), 6.55 (d, 1H, *J* = 16.1 Hz, H-2), 6.76 (s, 1H, H-10'), 7.37 (s, 1H, H-5'), 7.89 (d, 1H, *J* = 16.1 Hz, H-3); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 10.58 (C-3''), 22.16 & 22.22 (C-2'' & C-6'), 27.06 (2 × C-8' *C*H_3), 32.57 (C-7'), 67.09 (C-1''), 76.17 (C-8'), 105.25 (C-10'), 109.89 (C-3'), 111.10 (C-12'), 118.76 (C-14'), 125.26 (C-5'), 126.76 (C-2), 137.48 (C-3), 148.08 (C-11'), 153.95 & 158.35 (C-4' & C-13'), 161.36 & 165.81 (C-2' & C-1); HRMS: *m/z* Calcd for $C_{20}H_{22}O_5$; $(M + H)^+$ 343.1545. Found: 343.1540.

(*E*)-Isopropyl 3-(8,8-dimethyl-2-oxo-2,6,7,8-tetrahydropyrano [3,2-*g*] chromen-4-yl)acrylate, 23: The title compound **23** was obtained from the reaction of (*E*)-3-(8,8-dimethyl-2-oxo-2,6,7,8-tetrahydropyrano[3,2-*g*]chromen-4-yl)acrylic acid (**18**) (1 g, 3.33 mmol) with propan-2-ol (50 mL) as a yellow solid (0.89 g, 78%) by following the general procedure. m.p.152.8-154.1°C. UV (MeOH) λ_{max}: 249, 272 and 344 nm; IR (KBr): 2978, 2929, 1708 (C=O), 1618, 1381, 1326, 1294, 1182, 1157, 1118, 1048, 975, 873, 564 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.34 (d, 6H, *J* = 6.6 Hz, H-2''), 1.37 (s, 6H, 2 × C-8' CH_3), 1.86 (t, 2H, *J* = 6.6 Hz, H-7'), 2.85 (t, 2H, *J* = 6.6 Hz, H-6'), 5.13-5.21 (m, 1H, H-1''), 6.33 (s, 1H, H-3'), 6.51 (d, 1H, *J* = 15.4 Hz, H-2), 6.76 (s, 1H, H-10'), 7.37 (s, 1H, H-5'), 7.86 (d, 1H, *J* = 15.4 Hz, H-3); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 22.01 (C-2''), 22.21 (C-6'), 27.04 (2 × C-8' *C*H_3), 32.56 (C-7'), 69.11 (C-1''), 76.15 (C-8'), 105.21 (C-10'), 109.82 (C-3'), 111.10 (C-12'), 118.73 (C-14'), 125.27 (C-5'), 127.28 (C-2), 137.17 (C-3), 148.14 (C-11'), 153.92 & 158.31 (C-4' & C-13'), 161.37 & 165.23 (C-2' & C-1); HRMS: *m/z* Calcd for $C_{20}H_{22}O_5$; $(M + H)^+$ 343.1545. Found: 343.1560.

(*E*)-Allyl 3-(8,8-dimethyl-2-oxo-2,6,7,8-tetrahydropyrano[3,2-*g*]chromen-4-yl)acrylate, 24: The title compound **24** was obtained from the reaction of (*E*)-3-(8,8-dimethyl-2-oxo-2,6,7,8-tetrahydropyr ano[3,2-*g*]chromen-4-yl)acrylic acid (**18**) (1 g, 3.33 mmol) with prop-2-en-1-ol (50 mL) as a yellow solid (0.85 g, 75%) by following the general procedure. m.p.137.7-139.1°C. UV (MeOH) λ_{max}: 253 and 348 nm; IR (KBr): 2927, 1701 (C=O), 1618, 1552, 1382, 1329, 1292, 1182, 1160, 1122, 1049, 976, 872, 564 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.37 (s, 6H, 2 × C-8' CH_3), 1.86 (t, 2H, *J* = 7.0 Hz, H-7'), 2.84 (t, 2H, *J* = 6.6 Hz, H-6'), 4.76 (d, 2H, *J* = 5.8 Hz, H-1''), 5.32 (dd, 1H, *J* = 1.4 & 9.5 Hz, H-a), 5.40 (dd, 1H, *J* = 1.4 & 16.9 Hz, H-b), 5.94-6.05 (m, 1H, H-2''), 6.34 (s, 1H, H-3'), 6.56 (d, 1H, *J* = 16.1 Hz, H-2), 6.76 (s, 1H, H-10'), 7.36 (s, 1H, H-5'), 7.91 (d, 1H, *J* = 16.1 Hz, H-3); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 22.21 (C-6'), 27.05 (2 × C-8' *C*H_3), 32.55 (C-7'), 66.11 (C-1''), 76.18 (C-8'), 105.25 (C-10'), 109.96 (C-3'), 111.02 (C-12'), 118.78 (C-14'), 119.17 (C-3''), 125.24 (C-5'), 126.37 (C-2), 131.83 (C-2''), 137.93 (C-3), 147.95 (C-11'), 153.94 & 158.37 (C-4' & C-13'), 161.30 & 165.33 (C-2' & C-1); HRMS: *m/z* Calcd for $C_{20}H_{20}O_5$; $(M + H)^+$ 341.1389. Found: 341.1387.

(*E*)-*n*-Hexyl 3-(8,8-dimethyl-2-oxo-2,6,7,8-tetrahydropyrano [3,2-*g*]chromen-4-yl)acrylate, 25: The title compound **25** was obtained from the reaction of (*E*)-3-(8,8-dimethyl-2-oxo-2,6,7,8-tetrahydropyrano[3,2-*g*]chromen-4-yl)acrylic acid (**18**) (1 g, 3.33 mmol) with hexan-1-ol (50 mL) as a yellow solid (0.92 g, 72%) by following the general procedure. m.p.106.1-106.5°C. UV (MeOH) λ_{max}: 253, 270 and 357 nm; IR (KBr): 2956, 2928, 1701 (C=O), 1618, 1553, 1388, 1326, 1294, 1183, 1157, 1120, 1052, 976, 874, 565 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 0.91 (t, 3H, *J* = 7.3 Hz, H-6''), 1.31-1.45 (m, 12H, 2 × C-8' CH_3 & H-3'' - H-5''), 1.68-1.77 (m, 2H, H-2''), 1.86 (t, 2H, *J* = 6.6 Hz, H-7'), 2.84 (t, 2H, *J* = 6.6 Hz, H-6'), 4.25 (t, 2H, *J* = 7.3 Hz, H-1''), 6.34 (s, 1H, H-3'), 6.54 (d, 1H, *J* = 15.4 Hz, H-2), 6.76 (s, 1H, H-10'), 7.37 (s, 1H, H-5'), 7.88 (d, 1H, *J* = 15.4 Hz, H-3); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 14.20 (C-6''), 22.21 (C-6'), 22.72 (C-5''), 25.77 (C-4''), 27.07 (2 × C-8' *C*H_3),

28.74 (C-3''), 31.60 (C-2''), 32.59 (C-7'), 65.71 (C-1''), 76.18 (C-8'), 105.27 (C-10'), 109.89 (C-3'), 111.10 (C-12'), 118.76 (C-14'), 125.26 (C-5'), 126.79 (C-2), 137.47 (C-3), 148.09 (C-11'), 153.97 & 158.36 (C-4' & C-13'), 161.38 & 165.83 (C-2' & C-1); HRMS: *m/z* Calcd for $C_{23}H_{28}O_5$; $(M + H)^+$ 385.2015. Found: 385.2010.

(*E*)-Ethyl 3-(10-methoxy-8,8-dimethyl-2-oxo-2,6, 7,8-tetrahydrop yrano[3,2-*g*] chromen-4-yl)acrylate, 26: The title compound **26** was obtained from the reaction of (*E*)-3-(10-methoxy-8,8-dimethyl-2-oxo-2,6,7,8-tetrahydropyrano[3,2-*g*]chromen-4-yl)acrylic acid (**19**) (1 g, 3.03 mmol) with ethanol (50 mL) as a yellow solid (0.86 g, 79%) by following the general procedure. m.p.163.4-164.7°C. UV (MeOH) λ_{max}: 255 and 355 nm; IR (KBr): 2978, 2943, 1697 (C=O), 1640, 1609, 1560, 1389, 1294, 1180, 1167, 1124, 1059, 976, 867, 570 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.37 (t, 3H, *J* = 7.3 Hz, H-2''), 1.42 (s, 6H, 2 × C-8' CH_3), 1.87 (t, 2H, *J* = 7.3 Hz, H-7'), 2.85 (t, 2H, *J* = 7.0 Hz, H-6'), 3.94 (s, 3H, OCH_3), 4.31 (q, 2H, *J* = 7.3 Hz, H-1''), 6.35 (s, 1H, H-3'), 6.53 (d, 1H, *J* = 16.1 Hz, H-2), 7.14 (s, 1H, H-5'), 7.87 (d, 1H, *J* = 16.1 Hz, H-3); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 14.41 (C-2''), 22.46 (C-6'), 27.08 (2 × C-8' *C*H_3), 32.49 (C-7'), 61.39 (OCH_3), 61.51 (C-1''), 76.37 (C-8'), 110.08 (C-3'), 111.23 (C-12'), 119.20 & 119.23 (C-5' & C-14'), 126.76 (C-2), 136.11 (C-10'), 137.51 (C-3), 146.49, 148.31 & 151.28 (C-4', C-11' & C-13'), 160.86 & 165.72 (C-2' & C-1); HRMS: *m/z* Calcd for $C_{20}H_{22}O_6$; $(M + H)^+$ 359.1495. Found: 359.1492.

(*E*)-*n*-Propyl 3-(10-methoxy-8,8-dimethyl-2-oxo-2,6,7,8-tetrah ydropyrano [3,2-*g*]chromen-4-yl)acrylate, 27: The title compound **27** was obtained from the reaction of (*E*)-3-(10-methoxy-8,8-dimethyl-2-oxo-2,6,7,8-tetrahy dropyrano[3,2-*g*]chromen-4-yl)acrylic acid (**19**) (1 g, 3.03 mmol) with propan-1-ol (50 mL) as a yellow solid (0.87 g, 77%) by following the general procedure. m.p.122.3-123.9°C. UV (MeOH) λ_{max}: 256 and 353 nm; IR (KBr): 2975, 2940, 1697 (C=O), 1610, 1561, 1399, 1295, 1168, 1125, 1057, 975, 868, 572 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 0.99 (t, 3H, *J* = 7.0 Hz, H-3''), 1.41 (s, 6H, 2 × C-8' CH_3), 1.69-1.79 (m, 2H, H-2''), 1.86 (t, 2H, *J* = 6.6 Hz, H-7'), 2.85 (t, 2H, *J* = 6.6 Hz, H-6'), 3.92 (s, 3H, OCH_3), 4.20 (t, 2H, *J* = 6.6 Hz, H-1''), 6.34 (s, 1H, H-3'), 6.53 (d, 1H, *J* = 16.1 Hz, H-2), 7.13 (s, 1H, H-5'), 7.86 (d, 1H, *J* = 16.1 Hz, H-3); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 10.56 (C-3''), 22.11 (C-2''), 22.41 (C-6'), 27.03 (2 × C-8' *C*H_3), 32.42 (C-7'), 61.35 (OCH_3), 67.06 (C-1''), 76.34 (C-8'), 109.99 (C-3'), 111.17 (C-12'), 119.18 & 119.22 (C-5' & C-14'), 126.70 (C-2), 136.14 (C-10'), 137.46 (C-3), 146.55, 148.28 & 151.41 (C-4', C-11' & C-13'), 160.83 & 165.77 (C-2' & C-1); HRMS: *m/z* Calcd for $C_{21}H_{24}O_6$; $(M + H)^+$ 373.1651. Found: 373.1673.

(*E*)-Isopropyl 3-(10-methoxy-8,8-dimethyl-2-oxo-2,6,7,8-tetrahydropyrano [3,2-*g*]chromen-4-yl)acry late, 28: The title compound **28** was obtained from the reaction of (*E*)-3-(10-methoxy-8,8-dimethyl-2-oxo-2,6,7,8-tetrahydropyrano[3,2-*g*]chromen-4-yl)acrylic acid (**19**) (1 g, 3.03 mmol) with propan-2-ol (50 mL) as a yellow solid (0.88 g, 78%) by following the general procedure. m.p.117.4-118.3°C. UV (MeOH) λ_{max}: 255 and 349 nm; IR (KBr): 2984, 2936, 1702 (C=O), 1609, 1390, 1292, 1172, 1121, 1058, 973, 868 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.33 (d, 6H, *J* = 6.6 Hz, H-2''), 1.41 (s, 6H, 2 × C-8' CH_3), 1.87 (t, 2H, *J* = 6.6 Hz, H-7'), 2.85 (t, 2H, *J* = 6.6 Hz, H-6'), 3.93 (s, 3H, OCH_3), 5.11-5.21 (m, 1H, H-1''), 6.34 (s, 1H, H-3'), 6.50 (d, 1H, *J* = 15.4 Hz, H-2), 7.14 (s, 1H, H-5'), 7.85 (d, 1H, *J* = 15.4 Hz, H-3); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 22.01 (C-2''), 22.44 (C-6'), 27.06 (2 × C-8' *C*H_3), 32.45 (C-7'), 61.38 (OCH_3), 69.12 (C-1''), 76.34 (C-8'), 109.99 (C-3'), 111.23 (C-12'), 119.17 & 119.25 (C-5' & C-14'), 127.25 (C-2), 136.17 (C-10'), 137.21 (C-3), 146.57, 148.38 & 151.41 (C-4', C-11' & C-13'), 160.88 & 165.24 (C-2' & C-1); HRMS: *m/z* Calcd for $C_{21}H_{24}O_6$; $(M + H)^+$ 373.1651. Found: 373.1671.

(*E*)-Allyl 3-(10-methoxy-8,8-dimethyl-2-oxo-2,6, 7,8-tetrahydropyrano[3,2-*g*] chromen-4-yl)acrylate, 29: The title compound **29** was obtained from the reaction of (*E*)-3-(10-methoxy-8,8-dimethyl-2-oxo-2,6,7,8-tetrahyd ropyrano[3,2-*g*]chromen-4-yl)acrylic acid (**19**) (1 g, 3.03 mmol) with prop-2-en-1-ol (50 mL) as a yellow solid (0.84 g, 75%) by following the general procedure. m.p.138.9-139.2°C. UV (MeOH) λ_{max}: 256 and 356 nm; IR (KBr): 2978, 2937, 1706 (C=O), 1609, 1561, 1450, 1393, 1295, 1180, 1163, 1111, 1052, 973, 874, 772, 571 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.42 (s, 6H, 2 × C-8' CH_3), 1.87 (t, 2H, *J* = 6.6 Hz, H-7'), 2.86 (t, 2H, *J* = 6.6 Hz, H-6'), 3.94 (s, 3H, OCH_3), 4.75 (d, 2H, *J* = 5.9 Hz, H-1''), 5.32 (d, 1H, *J* = 10.2 Hz, H-a), 5.40 (dd, 1H, *J* = 1.5 & 17.6 Hz, H-b), 5.94-6.06 (m, 1H, H-2''), 6.35 (s,

1H, H-3'), 6.55 (d, 1H, *J* = 16.1 Hz, H-2), 7.13 (s, 1H, H-5'), 7.90 (d, 1H, *J* = 16.1 Hz, H-3); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 22.46 (C-6'), 27.07 (2 × C-8' CH_3), 32.48 (C-7'), 61.39 (OCH_3), 66.12 (C-1''), 76.38 (C-8'), 110.15 (C-3'), 111.18 (C-12'), 119.20 (C-5', C-14' & C-3''), 126.37 (C-2), 131.83 (C-2''), 136.24 (C-10'), 137.97 (C-3), 146.60, 148.19 & 151.47 (C-4', C-11' & C-13'), 160.80 & 165.34 (C-2' & C-1); HRMS: *m/z* Calcd for $C_{21}H_{22}O_6$; $(M + H)^+$ 371.1495. Found: 371.1503.

(*E*)-Methyl 3-(10-methoxy-8,8-dimethyl-2-oxo-2,6,7,8-tetrahydropyrano[3,2-*g*]chromen-4-yl)acrylate, 30: The title compound **30** was obtained from the reaction of (*E*)-3-(10-methoxy-8,8-dimethyl-2-oxo-2,6,7,8-tetrahy dropyrano[3,2-*g*]chromen-4-yl)acrylic acid (**19**) (1 g, 3.03 mmol) with methanol (50 mL) as a yellow solid (0.83 g, 80%) by following the general procedure. m.p.196.7-197.8°C. UV (MeOH) λ_{max}: 255 and 355 nm; IR (KBr): 2976, 2950, 1700 (C=O), 1610, 1431, 1389, 1297, 1207, 1170, 1125, 1060, 978, 865 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.42 (s, 6H, 2 × C-8' CH_3), 1.87 (t, 2H, *J* = 6.6 Hz, H-7'), 2.85 (t, 2H, *J* = 7.0 Hz, H-6'), 3.86 (s, 3H, H-1''), 3.93 (s, 3H, OCH_3), 6.34 (s, 1H, H-3'), 6.53 (d, 1H, *J* = 16.1 Hz, H-2), 7.13 (s, 1H, H-5'), 7.88 (d, 1H, *J* = 16.1 Hz, H-3); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 22.46 (C-6'), 27.08 (2 × C-8' CH_3), 32.48 (C-7'), 52.47 (C-1''), 61.39 (OCH_3), 76.38 (C-8'), 110.12 (C-3'), 111.19 (C-12'), 119.21 (C-5' & C-14'), 126.27 (C-2), 136.24 (C-10'), 137.79 (C-3), 146.60, 148.21 & 151.47 (C-4', C-11' & C-13'), 160.82 & 166.13 (C-2' & C-1); HRMS: *m/z* Calcd for $C_{19}H_{20}O_6$; $(M + H)^+$ 345.1338. Found: 345.1336.

(*E*)-*n*-Butyl 3-(10-methoxy-8,8-dimethyl-2-oxo-2,6,7,8-tetrahydropyrano[3,2-*g*]chromen-4-yl)acrylate, 31: The title compound **31** was obtained from the reaction of (*E*)-3-(10-methoxy-8,8-dimethyl-2-oxo-2,6,7,8-tetrahy dropyrano[3,2-*g*]chromen-4-yl)acrylic acid (**19**) (1 g, 3.03 mmol) with butan-1-ol (50 mL) as a yellow solid (0.92 g, 79%) by following the general procedure. m.p.127.6-128.6°C. UV (MeOH) λ_{max}: 256 and 356 nm; IR (KBr): 2961, 2938, 1697 (C=O), 1638, 1610, 1561, 1458, 1398, 1295, 1181, 1169, 1125, 1108, 1057, 976, 868, 572 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.97 (t, 3H, *J* = 7.3 Hz, H-4''), 1.42 (s, 6H, 2 × C-8' CH_3), 1.43-1.48 (m, 2H, H-3''), 1.67-1.75 (m, 2H, H-2''), 1.87 (t, 2H, *J* = 6.6 Hz, H-7'), 2.85 (t, 2H, *J* = 6.6 Hz, H-6'), 3.94 (s, 3H, OCH_3), 4.26 (t, 2H, *J* = 7.0 Hz, H-1''), 6.35 (s, 1H, H-3'), 6.52 (d, 1H, *J* = 15.4 Hz, H-2), 7.14 (s, 1H, H-5'), 7.87 (d, 1H, *J* = 15.4 Hz, H-3); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 13.90 (C-4''), 19.33 (C-3''), 22.47 (C-6'), 27.09 (2 × C-8' CH_3), 30.81 (C-2''), 32.50 (C-7'), 61.40 (OCH_3), 65.42 (C-1''), 76.37 (C-8'), 110.08 (C-3'), 111.25 (C-12'), 119.20 & 119.23 (C-5' & C-14'), 126.76 (C-2), 136.25 (C-10'), 137.52 (C-3), 146.62, 148.32 & 151.46 (C-4', C-11' & C-13'), 160.85 & 165.83 (C-2' & C-1); HRMS: *m/z* Calcd for $C_{22}H_{26}O_6$; $(M + H)^+$ 387.1808. Found: 387.1807.

(*E*)-Ethyl 3-(10-hydroxy-8,8-dimethyl-2-oxo-2,6,7,8-tetrahyd ropyrano[3,2-*g*] chromen-4-yl)acrylate, 32: The title compound **32** was obtained from the reaction of (*E*)-3-(10-hydroxy-8,8-dimethyl-2-oxo-2,6,7,8-tetrahydropyrano[3,2-*g*]chromen-4-yl)acrylic acid (**20**) (1 g, 3.16 mmol) with ethanol (50 mL) as a yellow solid (0.85 g, 78%) by following the general procedure. m.p.152.2-153.1°C. UV (MeOH) λ_{max}: 262 and 361 nm; IR (KBr): 3392 (O-H str), 2983, 2932, 1716 (C=O), 1619, 1567, 1500, 1451, 1412, 1375, 1286, 1243, 1184, 1163, 1123, 1103, 1034, 979, 849, 757, 614 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.36 (t, 3H, *J* = 7.3 Hz, H-2''), 1.42 (s, 6H, 2 × C-8' CH_3), 1.89 (t, 2H, *J* = 7.0 Hz, H-7'), 2.85 (t, 2H, *J* = 6.6 Hz, H-6'), 4.31 (q, 2H, *J* = 7.3 Hz, H-1''), 5.74 (*brs*, 1H, OH), 6.35 (s, 1H, H-3'), 6.53 (d, 1H, *J* = 15.4 Hz, H-2), 6.98 (s, 1H, H-5'), 7.87 (d, 1H, *J* = 16.1 Hz, H-3); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 14.41 (C-2''), 22.15 (C-6'), 27.06 (2 × C-8' CH_3), 32.70 (C-7'), 61.51 (C-1''), 77.07 (C-8'), 110.14 (C-3'), 111.26 (C-12'), 115.23 (C-5'), 118.35 (C-14'), 126.76 (C-2), 132.75 (C-10'), 137.47 (C-3), 140.49, 145.18 & 148.49 (C-4', C-11' & C-13'), 160.48 & 165.71 (C-2' & C-1); HRMS: *m/z* Calcd for $C_{19}H_{20}O_6$; $(M + H)^+$ 345.1338. Found: 345.1345.

(*E*)-Allyl 3-(10-hydroxy-8,8-dimethyl-2-oxo-2,6,7,8-tetrahydro pyrano[3,2-*g*] chromen-4-yl)acrylate, 33: The title compound **33** was obtained from the reaction of (*E*)-3-(10-hydroxy-8,8-dimethyl-2-oxo-2,6,7,8-tetrahyd ropyrano[3,2-*g*]chromen-4-yl)acrylic acid (**20**) (1 g, 3.16 mmol) with prop-2-en-1-ol (50 mL) as a yellow solid (0.82 g, 73%) by following the general procedure. m.p.140.9-142.1°C. UV (MeOH) λ_{max}: 263 and 360 nm; IR (KBr): 3276 (O-H str), 2978, 2940, 1702 (C=O), 1617, 1576, 1465, 1399, 1288, 1163, 1118, 1096, 1039, 978, 938, 849, 707 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.42 (s, 6H, 2 × C-8' CH_3), 1.89 (t, 2H, *J* = 6.6 Hz, H-7'), 2.86 (t,

2H, *J* = 6.6 Hz, H-6'), 4.76 (d, 2H, *J* = 5.9 Hz, H-1''), 5.32 (dd, 1H, *J* = 1.4 & 10.3 Hz, H-a), 5.40 (dd, 1H, *J* = 1.5 & 16.8 Hz, H-b), 5.68 (s, 1H, OH), 5.95-6.05 (m, 1H, H-2''), 6.36 (s, 1H, H-3'), 6.57 (d, 1H, *J* = 16.1 Hz, H-2), 6.98 (s, 1H, H-5'), 7.90 (d, 1H, *J* = 16.1 Hz, H-3); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 22.15 (C-6'), 27.06 (2 × C-8' *C*H_3), 32.69 (C-7'), 66.12 (C-1''), 77.09 (C-8'), 110.24 (C-3'), 111.21 (C-12'), 115.22 (C-5'), 118.36 (C-14'), 119.18 (C-3''), 126.37 (C-2), 131.83 (C-2''), 132.76 (C-10'), 137.94 (C-3), 140.43, 145.20 & 148.37 (C-4', C-11' & C-13'), 160.42 & 165.34 (C-2' & C-1); HRMS: *m/z* Calcd for $C_{20}H_{20}O_6$; $(M + H)^+$ 357.1338. Found: 357.1348.

(*E*)-*n*-Hexyl 3-(10-hydroxy-8,8-dimethyl-2-oxo-2,6, 7,8-tetrahy dropyrano[3,2-*g*]chromen-4-yl) acrylate, 34: The title com pound **34** was obtained from the reaction of (*E*)-3-(10-hydroxy-8,8-dimethyl-2-oxo-2,6,7,8-tetrahydropyrano[3,2-*g*]chromen-4-yl)acrylic acid (**20**) (1 g, 3.16 mmol) with hexan-1-ol (50 mL) as a yellow solid (0.89 g, 70%) by following the general procedure. m.p.149.2-149.9°C. UV (MeOH) λ_{max}: 262 and 358 nm; IR (KBr): 3544 (O-H str), 3078, 2959, 2930, 1699 (C=O), 1624, 1570, 1450, 1403, 1300, 1189, 1170, 1119, 1094, 1034, 976, 875, 700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.90 (t, 3H, *J* = 7.3 Hz, H-6''), 1.29-1.45 (m, 12H, 2 × C-8' CH_3 & H-3'' - H-5''), 1.67-1.76 (m, 2H, H-2''), 1.88 (t, 2H, *J* = 6.6 Hz, H-7'), 2.85 (t, 2H, *J* = 7.0 Hz, H-6'), 4.24 (t, 2H, *J* = 6.6 Hz, H-1''), 5.74 (s, 1H, OH), 6.35 (s, 1H, H-3'), 6.54 (d, 1H, *J* = 15.4 Hz, H-2), 6.97 (s, 1H, H-5'), 7.86 (d, 1H, *J* = 15.4 Hz, H-3); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 14.18 (C-6''), 22.13 (C-6'), 22.70 (C-5''), 25.74 (C-4''), 27.05 (2 × C-8' *C*H_3), 28.71 (C-3''), 31.58 (C-2''), 32.68 (C-7'), 65.69 (C-1''), 77.05 (C-8'), 110.13 (C-3'), 111.25 (C-12'), 115.22 (C-5'), 118.32 (C-14'), 126.76 (C-2), 132.74 (C-10'), 137.43 (C-3), 140.48, 145.16 & 148.45 (C-4', C-11' & C-13'), 160.44 & 165.80 (C-2' & C-1); HRMS: *m/z* Calcd for $C_{23}H_{28}O_6$; $(M + H)^+$ 401.1964. Found: 401.1976.

General procedure for the synthesis of pyranochromen-2-one acrylamides, 35-39

To a stirred solution of acrylic acid (**18/19**) (1 g, 1 equiv.) in DMF (10 mL), triethylamine (1 equiv.) was added. The resulting solution was cooled to 0°C followed by the addition of an appropriate amine (1 equiv.) and solution of BOP (1 equiv.) in DCM (10 mL). After stirring the reaction mixture at 0°C for 30 min, it was allowed to come to RT (25°C) and stirred for additional 15 h at 25°C. The progress of the reaction was monitored by TLC (ethyl acetate:petroleum ether :: 3:7). On completion of the reaction, DMF and DCM were removed under reduced pressure followed by extraction of the compound using ethyl acetate (3 × 50 mL). The ethyl acetate layer was then successfully washed with 1N HCl (3 × 20 mL), water (3 × 20 mL), 1M $NaHCO_3$ solution (3 × 20 mL) and water (3 × 20 mL). The organic layer was dried over anhydrous Na_2SO_4 and the solvent was removed *in vacuo* to provide the crude product which on column purification gave the desired acrylamide (**35**-**39**) in 73-78 % isolated yield.

(*E*)-*N*-Benzyl-3-(8,8-dimethyl-2-oxo-2,6,7,8-tetrahy dropyrano [3,2-*g*] chromen-4-yl)acrylamide, 35: The title compound **35** was obtained from the reaction of (*E*)-3-(8,8-dimethyl-2-oxo-2,6,7,8-tetrahydro pyrano[3,2-*g*]chromen-4-yl)acrylic acid (**18**) (1 g, 1 equiv., 3.33 mmol) with phenylmethanamine (0.36 g, 1 equiv., 3.33 mmol) as a yellow solid (0.96 g, 74%) by following the general procedure. m.p.207.8-209.0°C. UV (MeOH) λ_{max}: 250, 271 and 349 nm; IR (KBr): 3373 (N-H str), 2972, 2927, 1700 (C=O), 1683 (NH*CO*), 1618, 1546, 1380, 1290, 1158, 1120, 1035, 977, 844, 729, 565 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.37 (s, 6H, 2 × C-8' CH_3), 1.85 (t, 2H, *J* = 7.0 Hz, H-7'), 2.83 (t, 2H, *J* = 6.6 Hz, H-6'), 4.60 (d, 2H, *J* = 5.1 Hz, H-1a), 6.29 (s, 1H, H-3'), 6.32 (*brs*, 1H, NH), 6.55 (d, 1H, *J* = 15.4 Hz, H-2), 6.74 (s, 1H, H-10'), 7.29-7.37 (m, 5H, H-2'' - H-6''), 7.44 (s, 1H, H-5'), 7.93 (d, 1H, *J* = 15.4 Hz, H-3); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 22.18 (C-6'), 27.06 (2 × C-8' *C*H_3), 32.57 (C-7'), 44.28 (C-1a), 76.19 (C-8'), 105.11 (C-10'), 108.99 (C-3'), 111.21 (C-12'), 118.84 (C-14'), 125.48 (C-5'), 127.97 (C-2), 128.17 (C-2'' & C-6''), 128.78 (C-4''), 129.02 (C-3'' & C-5''), 134.52 (C-3), 137.66 (C-1''), 148.81 (C-11'), 153.65 & 158.24 (C-4' & C-13'), 161.63 & 164.00 (C-2' & C-1); HRMS: *m/z* Calcd for $C_{24}H_{23}NO_4$; $(M + H)^+$ 390.1705. Found: 390.1704.

(*E*)-*N*-Butyl-3-(8,8-dimethyl-2-oxo-2,6,7,8-tetrahyd ropyrano [3,2-*g*]chromen-4-yl)acrylamide, 36: The title compound **36** was obtained from the reaction of (*E*)-3-(8,8-dimethyl-2-oxo-2,6,7,8-tetrahydropyrano [3,2-*g*]chromen-4-yl)acrylic acid (**18**) (1 g, 1 equiv., 3.33 mmol) with butan-1-amine (0.24 g, 1 equiv., 3.33 mmol) as a yellow solid (0.85 g, 72%) by

following the general procedure. m.p.170.6-172.3°C. UV (MeOH) λ_{max}: 250, 273 and 354 nm; IR (KBr): 3392 (N-H str), 2929, 2856, 1685 (NH*CO*), 1382, 1292, 1237, 1156, 1118, 967, 847, 565 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 0.96 (t, 3H, *J* = 7.3 Hz, H-4''), 1.36 (s, 6H, 2 × C-8' CH_3), 1.38-1.46 (m, 2H, H-3''), 1.55-1.62 (m, 2H, H-2''), 1.85 (t, 2H, *J* = 6.6 Hz, H-7'), 2.83 (t, 2H, *J* = 6.6 Hz, H-6'), 3.39-3.46 (m, 2H, H-1''), 6.02 (*brs*, 1H, NH), 6.30 (s, 1H, H-3'), 6.53 (d, 1H, *J* = 15.4 Hz, H-2), 6.74 (s, 1H, H-10'), 7.44 (s, 1H, H-5'), 7.88 (d, 1H, *J* = 15.4 Hz, H-3); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 13.92 (C-4''), 20.29 (C-3''), 22.17 (C-6'), 27.06 (2 × C-8' *C*H_3), 31.72 (C-2''), 32.57 (C-7'), 39.92 (C-1''), 76.18 (C-8'), 105.08 (C-10'), 108.84 (C-3'), 111.33 (C-12'), 118.84 (C-14'), 125.52 (C-5'), 129.21 (C-2), 133.87 (C-3), 149.11 (C-11'), 153.79 & 158.26 (C-4' & C-13'), 161.74 & 164.30 (C-2' & C-1); HRMS: *m/z* Calcd for $C_{21}H_{25}NO_4$; $(M + H)^+$ 356.1862. Found: 356.1855.

(*E*)-3-(8,8-Dimethyl-2-oxo-2,6,7,8-tetrahydro pyr ano[3,2-*g*] chromen-4-yl)-*N*-octylacrylamide, 37: The title compound **37** was obtained from the reaction of (*E*)-3-(8,8-dimethyl-2-oxo-2,6,7,8-tetrahydropyra no[3,2-*g*]chromen-4-yl)acrylic acid (**18**) (1 g, 1 equiv., 3.33 mmol) with octan-1-amine (0.43 g, 1 equiv., 3.33 mmol) as a yellow solid (1 g, 73%) by following the general procedure. m.p.289.3-290.5°C. UV (MeOH) λ_{max}: 274 and 353 nm; IR (KBr): 3389 (N-H str), 2927, 2855, 1697 (C=O), 1683 (NH*CO*), 1383, 1289, 1236, 1158, 1118, 977, 844, 565 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 0.88 (t, 3H, *J* = 7.0 Hz, H-8''), 1.26-1.40 (m, 16H, 2 × C-8' CH_3 & H-3'' - H-7''), 1.59-1.63 (m, 2H, H-2''), 1.85 (t, 2H, *J* = 6.6 Hz, H-7'), 2.83 (t, 2H, *J* = 7.0 Hz, H-6'), 3.37-3.45 (m, 2H, H-1''), 5.89 (*brs*, 1H, NH), 6.31 (s, 1H, H-3'), 6.51 (d, 1H, *J* = 15.4 Hz, H-2), 6.75 (s, 1H, H-10'), 7.44 (s, 1H, H-5'), 7.88 (d, 1H, *J* = 15.4 Hz, H-3); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 14.29 (C-8''), 22.17 (C-6'), 22.82 (C-7''), 27.07 (2 × C-8' *C*H_3), 27.14, 29.38, 29.44, 29.68 & 31.98 (C-2'' - C-6''), 32.57 (C-7'), 40.25 (C-1''), 76.18 (C-8'), 105.09 (C-10'), 108.88 (C-3'), 111.42 (C-12'), 118.77 (C-14'), 125.52 (C-5'), 129.15 (C-2), 133.94 (C-3), 149.10 (C-11'), 153.88 & 158.32 (C-4' & C-13'), 161.85 & 164.24 (C-2' & C-1); HRMS: *m/z* Calcd for $C_{25}H_{33}NO_4$; $(M + H)^+$ 412.2488. Found: 412.2479.

(*E*)-3-(8,8-Dimethyl-2-oxo-2,6,7,8-tetrahydropyran o[3,2-*g*]chr omen-4-yl)-*N*,*N*-diethylacrylamide, 38: The title compound **38** was obtained from the reaction of (*E*)-3-(8,8-dimethyl-2-oxo-2,6,7,8-tetrahydropyra no[3,2-*g*]chromen-4-yl)acrylic acid (**18**) (1 g, 1 equiv., 3.33 mmol) with diethylamine (0.24 g, 1 equiv., 3.33 mmol) as a yellow solid (0.89 g, 75%) by following the general procedure. m.p.174.9-175.6°C. UV (MeOH) λ_{max}: 249, 273 and 355 nm; IR (KBr): 2981, 2931, 1720 (C=O), 1649 (NH*CO*), 1618, 1554, 1458, 1374, 1149, 1121, 970, 874, 562 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.19-1.29 (m, 6H, H-2'' & H-2'''), 1.36 (s, 6H, 2 × C-8' CH_3), 1.84 (t, 2H, *J* = 6.6 Hz, H-7'), 2.82 (t, 2H, *J* = 6.6 Hz, H-6'), 3.43-3.55 (m, 4H, H-1'' & H-1'''), 6.33 (s, 1H, H-3'), 6.75 (s, 1H, H-10'), 6.95 (d, 1H, *J* = 14.6 Hz, H-2), 7.45 (s, 1H, H-5'), 7.93 (d, 1H, *J* = 15.4 Hz, H-3); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 13.27 & 15.40 (C-2'' & C-2'''), 22.15 (C-6'), 27.05 (2 × C-8' *C*H_3), 32.57 (C-7'), 41.57 & 42.66 (C-1'' & C-1'''), 76.12 (C-8'), 105.09 (C-10'), 108.99 (C-3'), 111.47 (C-12'), 118.72 (C-14'), 125.54 (C-5'), 126.13 (C-2), 135.34 (C-3), 149.47 (C-11'), 153.89 & 158.26 (C-4' & C-13'), 161.77 & 164.22 (C-2' & C-1); HRMS: *m/z* Calcd for $C_{21}H_{25}NO_4$; $(M + H)^+$ 356.1862. Found: 356.1857.

(*E*)-*N*-Benzyl-3-(10-methoxy-8,8-dimethyl-2-oxo-2,6,7,8-tetra hydropyrano [3,2-*g*]chromen-4-yl)acr ylamide, 39: The title compound **39** was obtained from the reaction of (*E*)-3-(10-methoxy-8,8-dimethyl-2-oxo-2,6,7,8-tetrahydropyrano[3,2-*g*]chromen-4-yl)acrylic acid (**19**) (1 g, 1 equiv., 3.03 mmol) with phenylmethanamine (0.32 g, 1 equiv., 3.03 mmol) as a yellow solid (0.97 g, 76%) by following the general procedure. m.p.225.4-226.1°C. UV (MeOH) λ_{max}: 255 and 354 nm; IR (KBr): 3355 (N-H str), 2975, 2933, 1710 (C=O), 1670 (NH*CO*), 1605, 1560, 1542, 1449, 1389, 1183, 1121, 1106, 1046, 970, 852, 753, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.41 (s, 6H, 2 × C-8' CH_3), 1.86 (t, 2H, *J* = 6.6 Hz, H-7'), 2.84 (t, 2H, *J* = 6.6 Hz, H-6'), 3.92 (s, 3H, OCH_3), 4.60 (d, 2H, *J* = 5.9 Hz, H-1a), 6.29 (*brs*, 2H, H-3' & NH), 6.53 (d, 1H, *J* = 15.4 Hz, H-2), 7.21 (s, 1H, H-5'), 7.28-7.38 (m, 5H, H-2'' - H-6''), 7.91 (d, 1H, *J* = 14.6 Hz, H-3); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 22.41 (C-6'), 27.09 (2 × C-8' *C*H_3), 32.49 (C-7'), 44.31 (C-1''), 61.37 (OCH_3), 76.39 (C-8'), 109.23 (C-3'), 111.49 (C-12'), 119.28 & 119.48 (C-5' & C-14'), 127.99 (C-2), 128.18 (C-2'' & C-6''), 128.73 (C-4''), 129.04 (C-3'' & C-5''), 134.61 (C-3), 136.11 & 137.74 (C-10' & C-1''), 146.53, 149.10 & 151.43 (C-4', C-11' & C-13'), 161.16 & 164.16 (C-2' & C-1); HRMS: *m/z* Calcd for $C_{25}H_{25}NO_5$; $(M + H)^+$ 420.1811. Found: 420.1811.

General procedure for the synthesis of pyranochromen-2-one acrylamides, 40-44

In a round-bottom flask containing a solution of acrylic acid (**19/20**) (1 g, 1 equiv.) in DMF (20 mL), HOBt (1.2 equiv.) and DCC (1.2 equiv.) were added. After the addition of appropriate amine (1.02 equiv.), the resulting reaction mixture was stirred at 25°C for 15 h. On completion of the reaction as indicated by TLC (ethyl acetate:petroleum ether :: 3:7), the reaction mixture was cooled to 0°C and filtered. The filtrate was evaporated under reduced pressure, followed by the addition of DCM (30 mL) with subsequent filtration. The DCM layer was evaporated in a rotary evaporator and the crude solid so obtained was subjected to column chromatography affording the desired acrylamide (**40**-**44**) in 72-74 % isolated yield.

(*E*)-*N*-Butyl-3-(10-methoxy-8,8-dimethyl-2-oxo-2,6,7,8-tetrah ydropyrano[3,2-*g*] chromen-4-yl) acrylam ide, 40: The title compound **40** was obtained from the reaction of (*E*)-3-(10-methoxy-8,8-dimethyl-2-oxo-2,6,7,8-tetrahydropyrano[3,2-*g*]chromen-4-yl)acrylic acid (**19**) (1 g, 1 equiv., 3.03 mmol) with butan-1-amine (0.23 g, 1.02 equiv., 3.09 mmol) as a yellow solid (0.86 g, 74%) by following the general procedure. m.p.164.2-165.5°C. UV (MeOH) λ_{max}: 263 and 354 nm; IR (KBr): 3276 (N-H str), 2972, 2938, 2867, 1686 (NH*CO*), 1610, 1560, 1449, 1391, 1157, 1117, 1054, 973, 846, 706, 572 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.96 (t, 3H, *J* = 7.3 Hz, H-4''), 1.36-1.46 (m, 8H, 2 × C-8' CH_3 & H-3''), 1.55-1.64 (m, 2H, H-2''), 1.86 (t, 2H, *J* = 7.0 Hz, H-7'), 2.84 (t, 2H, *J* = 6.6 Hz, H-6'), 3.39-3.46 (m, 2H, H-1''), 3.92 (s, 3H, OCH_3), 6.25 (*brs*, 1H, NH), 6.32 (s, 1H, H-3'), 6.57 (d, 1H, *J* = 15.4 Hz, H-2), 7.23 (s, 1H, H-5'), 7.88 (d, 1H, *J* = 14.6 Hz, H-3); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 13.92 (C-4''), 20.28 (C-3''), 22.36 (C-6'), 27.05 (2 × C-8' *C*H_3), 31.63 (C-2''), 32.43 (C-7'), 39.90 (C-1''), 61.33 (OCH_3), 76.39 (C-8'), 108.82 (C-3'), 111.53 (C-12'), 119.33 & 119.57 (C-5' & C-14'), 129.58 (C-2), 133.43 (C-3), 135.98 (C-10'), 146.43, 149.60 & 151.40 (C-4', C-11' & C-13'), 161.45 & 164.44 (C-2' & C-1); HRMS: *m/z* Calcd for $C_{22}H_{27}NO_5$; $(M + H)^+$ 386.1967. Found: 386.1993.

(*E*)-*N*,*N*-Diethyl-3-(10-methoxy-8,8-dimethyl-2-oxo-2,6,7,8-te trahydropyrano[3,2-*g*]chromen-4-yl) acrylamide, 41: The tit le compound **41** was obtained from the reaction of (*E*)-3-(10-methoxy-8,8-dimethyl-2-oxo-2,6,7,8-tetrahydropyrano[3,2-*g*]chromen-4-yl)acrylic acid (**19**) (1 g, 1 equiv., 3.03 mmol) with diethylamine (0.23 g, 1.02 equiv., 3.09 mmol) as a yellow solid (0.85 g, 73%) by following the general procedure. m.p.158.2-159.5°C. UV (MeOH) λ_{max}: 264 and 346 nm; IR (KBr): 2975, 2932, 1718 (C=O), 1648 (NH*CO*), 1610, 1450, 1385, 1120, 1106, 1053, 978, 865, 777, 572 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.18-1.29 (m, 6H, H-2'' & H-2'''), 1.41 (s, 6H, 2 × C-8' CH_3), 1.86 (t, 2H, *J* = 7.0 Hz, H-7'), 2.84 (t, 2H, *J* = 6.6 Hz, H-6'), 3.43-3.55 (m, 4H, H-1'' & H-1'''), 3.94 (s, 3H, OCH_3), 6.34 (s, 1H, H-3'), 6.94 (d, 1H, *J* = 14.6 Hz, H-2), 7.23 (s, 1H, H-5'), 7.91 (d, 1H, *J* = 14.6 Hz, H-3); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 13.25 & 15.37 (C-2'' & C-2'''), 22.39 (C-6'), 27.07 (2 × C-8' *C*H_3), 32.50 (C-7'), 41.62 & 42.71 (C-1'' & C-1'''), 61.37 (OCH_3), 76.33 (C-8'), 109.18 (C-3'), 111.59 (C-12'), 119.22 & 119.53 (C-5' & C-14'), 126.08 (C-2), 135.46 (C-3), 136.12 (C-10'), 146.53, 149.70 & 151.38 (C-4', C-11' & C-13'), 161.29 & 164.32 (C-2' & C-1); HRMS: *m/z* Calcd for $C_{22}H_{27}NO_5$; $(M + H)^+$ 386.1967. Found: 386.1966.

(*E*)-3-(10-Methoxy-8,8-dimethyl-2-oxo-2,6,7,8-tet rahydrop yrano[3,2-*g*]chromen-4-yl)-*N*-octylacry lamide, 42: The title compound **42** was obtained from the reaction of (*E*)-3-(10-methoxy-8,8-dimethyl-2-oxo-2,6,7,8-tetrahydropyrano[3,2-*g*]chromen-4-yl)acrylic acid (**19**) (1 g, 1 equiv., 3.03 mmol) with octan-1-amine (0.4 g, 1.02 equiv., 3.09 mmol) as a yellow solid (0.99 g, 74%) by following the general procedure. m.p.79.2-79.7°C. UV (MeOH) λ_{max}: 260 and 349 nm; IR (KBr): 3310 (N-H str), 2928, 2854, 1718 (C=O), 1609, 1394, 1124, 1110, 1053, 966, 577 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.88 (t, 3H, *J* = 6.6 Hz, H-8''), 1.24-1.44 (m, 16H, 2 × C-8' CH_3 & & H-3'' - H-7''), 1.55-1.65 (m, 2H, H-2''), 1.86 (t, 2H, *J* = 6.6 Hz, H-7'), 2.84 (t, 2H, *J* = 7.0 Hz, H-6'), 3.37-3.45 (m, 2H, H-1''), 3.93 (s, 3H, OCH_3), 6.03 (*brs*, 1H, NH), 6.32 (s, 1H, H-3'), 6.53 (d, 1H, *J* = 15.4 Hz, H-2), 7.22 (s, 1H, H-5'), 7.87 (d, 1H, *J* = 14.6 Hz, H-3); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 14.08 (C-8''), 22.20 (C-6'), 22.61 (C-7''), 26.88 (2 × C-8' *C*H_3), 26.94, 29.17, 29.22, 29.45 & 31.77 (C-2'' - C-6''), 32.28 (C-7'), 40.07 (C-1''), 61.18 (OCH_3), 76.19 (C-8'), 108.84 (C-3'), 111.34 (C-12'), 119.10 & 119.34 (C-5' & C-14'), 129.03 (C-2), 133.52 (C-3), 135.91 (C-10'), 146.30, 149.09 & 151.16 (C-4', C-11' & C-13'), 161.01 & 164.12 (C-2' & C-1); HRMS: *m/z* Calcd for $C_{26}H_{35}NO_5$; $(M + H)^+$ 442.2593. Found: 442.2583.

(*E*)-*N*-Butyl-3-(10-hydroxy-8,8-dimethyl-2-oxo-2,6,7,8-tetrah ydropyrano[3,2-*g*] chromen-4-yl)acry lamide, 43: The title compound **43** was obtained from the reaction of (*E*)-3-(10-hydroxy-8,8-dimethyl-2-oxo-2,6,7,8-tetrahydropyrano[3,2-*g*]chromen-4-yl)acrylic acid (**20**) (1 g, 1 equiv., 3.16 mmol) with butan-1-amine (0.24 g, 1.02 equiv., 3.22 mmol) as a yellow solid (0.86 g, 73%) by following the general procedure. m.p.181.2-182.0°C. UV (MeOH) λ_{max}: 263 and 359 nm; IR (KBr): 3270 (N-H str), 3088 (O-H str), 2939, 2875, 1715 (C=O), 1659 (NH*CO*), 1619, 1567, 1445, 1368, 1200, 1120, 1038, 855, 659 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.96 (t, 3H, *J* = 7.3 Hz, H-4''), 1.36-1.45 (m, 8H, 2 × C-8' CH_3 & H-3''), 1.55-1.60 (m, 2H, H-2''), 1.88 (t, 2H, *J* = 6.6 Hz, H-7'), 2.84 (t, 2H, *J* = 6.6 Hz, H-6'), 3.38-3.46 (m, 2H, H-1''), 5.72 (s, 1H, OH), 5.94 (*brs*, 1H, NH), 6.33 (s, 1H, H-3'), 6.52 (d, 1H, *J* = 15.4 Hz, H-2), 7.05 (s, 1H, H-5'), 7.87 (d, 1H, *J* = 15.4 Hz, H-3); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 13.93 (C-4''), 20.30 (C-3''), 22.09 (C-6'), 27.08 (2 × C-8' *C*H_3), 31.75 (C-2''), 32.72 (C-7'), 39.94 (C-1''), 77.09 (C-8'), 109.24 (C-3'), 111.59 (C-12'), 115.48 (C-5'), 118.36 (C-14'), 129.08 (C-2), 132.65 (C-10'), 134.05 (C-3), 140.44, 145.13 & 149.39 (C-4', C-11' & C-13'), 160.88 & 164.26 (C-2' & C-1); HRMS: *m/z* Calcd for $C_{21}H_{25}NO_5$; $(M + H)^+$ 372.1811. Found: 372.1804.

(*E*)-*N*,*N*-Diethyl-3-(10-hydroxy-8,8-dimethyl-2-oxo-2,6,7,8-te trahydropyrano [3,2-*g*]chromen-4-yl)acr ylamide, 44: The title compound **44** was obtained from the reaction of (*E*)-3-(10-hydroxy-8,8-dimethyl-2-oxo-2,6,7,8-tetrah ydropyrano[3,2-*g*]chromen-4-yl)acrylic acid (**20**) (1 g, 1 equiv., 3.16 mmol) with diethylamine (0.24 g, 1.02 equiv., 3.22 mmol) as a yellow solid (0.85 g, 72%) by following the general procedure. m.p.207.4-208.1°C. UV (MeOH) λ_{max}: 264 and 355 nm; IR (KBr): 3076 (O-H str), 2978, 2934, 1702 (C=O), 1645 (NH*CO*), 1613, 1587, 1463, 1396, 1360, 1192, 1154, 1101, 1042, 970, 850 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.18-1.29 (m, 6H, H-2'' & H-2'''), 1.41 (s, 6H, 2 × C-8' CH_3), 1.87 (t, 2H, *J* = 6.6 Hz, H-7'), 2.82 (t, 2H, *J* = 6.6 Hz, H-6'), 3.43-3.55 (m, 4H, H-1'' & H-1'''), 5.78 (s, 1H, OH), 6.35 (s, 1H, H-3'), 6.95 (d, 1H, *J* = 14.6 Hz, H-2), 7.05 (s, 1H, H-5'), 7.91 (d, 1H, *J* = 15.4 Hz, H-3); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 13.27 & 15.40 (C-2'' & C-2'''), 22.08 (C-6'), 27.06 (2 × C-8' *C*H_3), 32.72 (C-7'), 41.58 & 42.68 (C-1'' & C-1'''), 77.01 (C-8'), 109.26 (C-3'), 111.64 (C-12'), 115.51 (C-5'), 118.31 (C-14'), 126.14 (C-2), 132.67 (C-10'), 135.38 (C-3), 140.36, 145.11 & 149.88 (C-4', C-11' & C-13'), 160.88 & 164.25 (C-2' & C-1); HRMS: *m/z* Calcd for $C_{21}H_{25}NO_5$; $(M + H)^+$ 372.1811. Found: 372.1810.

Biology

Pathogens

The pathogenic strains of bacteria used in the antibacterial assay namely, *Bacillus cereus* (MTCC 430), *Staphylococcus aureus* (MTCC 740), *Pseudomonas aeruginosa* (MTCC 741) and *Escherichia coli* (MTCC 1586) were procured from Institute of Microbial Technology, Chandigarh (India).

Materials

Mueller Hinton agar, nutrient broth and sterile filter paper discs (6 mm) were procured from HiMedia, Mumbai, India. Gentamicin and DMSO were purchased from Sigma-Aldrich Chemicals, USA.

Antibacterial activity assay

Kirby-Bauer disc susceptibility test with some minor modifications was used to assess the antibacterial activity profile of the synthesized compounds[31,32]. The test organisms to be used in the assay were inoculated in Nutrient broth (NB) and placed in an orbital shaker (Climo Shaker IsF-1-X) at 200 rpm min^{-1} at 37°C for 14-16 h. The optical density of the overnight grown culture was adjusted 0.5 at a transmission wavelength of 600 nm. The samples at a concentration of 250 µg/disc were impregnated on a 6 mm sterile filter paper discs placed in the respective grid of each Mueller Hinton agar plates already seeded with the target test organisms followed by overnight incubation at 37°C. Gentamicin was used as a positive control in the assay. HiMedia Antibiotic Zonescale was used to measure the zone of inhibition. All the assays were carried out in triplicates.

Conclusions

In conclusion, a series of fourteen pyranochromen-2-one acrylates and ten pyranochromen-2-one acrylamides has been synthesized and completely characterized by ^{1}H and ^{13}C NMR, ^{2}D heteronuclear correlation (HETCOR) spectroscopy, FT-IR, UV spectroscopy and high resolution mass spectroscopy (HRMS). Of these, twenty compounds **22**-**44** are new and reported for the first time. Although compound **21** is known in literature[33], neither its complete spectral data nor any biological evaluation was reported. Herein, the spectral data for all the compounds has been reported in the Experimental Section. All the

synthesized acrylyl pyranochromen-2one derivatives **21**-**44** were evaluated for their antibacterial activity against both Gram-positive (*B. cereus* and *S. aureus*) and Gram-negative bacteria (*P. aeruginosa* and *E. coli*) using gentamicin as a positive control. Out of twenty four compounds screened, three pyranochromen-2-one derivatives (**33**, **34** and **43**) are found to exhibit moderate activity against *B. cereus*, *S. aureus* and *P. aeruginosa*. From the results, it is inferred that the presence of hydroxyl group along with the longer hydrophobic alkyl chain is favorable for a compound to inhibit bacterial growth.

Supplementary Information

Supplementary information is available in the website http://nopr.niscair.res.in/handle/123456789/60.

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