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Three Component Solvent-free Synthesis of Chroman-2,4-dione-based Heterocyclic Ketene Aminal (HKA) Derivatives by "GAP" Chemistry

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A concise and efficient one-pot synthesis of chroman-2,4-dione-based HKA derivatives by three component reaction of HKAs, triethoxymethane and 4-hydroxycoumarin derivatives under solvent-free and catalyst-free conditions is described. This protocol has many advantages, in that the GAP (Group-Assistant-Purification) chemistry process is involved in this method. As a result, the experimenter can avoid cumbersome process steps such as traditional chromatography and recrystallization purifications. The desired products can be easily obtained by washing the crude products with 95% EtOH.

Key Words : GAP chemistry, Heterocyclic ketene aminals (HKAs), 4-Hydroxycoumarin, Chroman-2,4-dione

Introduction

With the development of green chemistry and the enhancement of people's awareness of environmental protection in recent years, chemists have paid much attention to the development of GAP chemistry in organic synthesis.[1] It is well-known that the development of efficient processes can avoid time-consuming and costly syntheses involving tedious workup such as purification-chromatography or recrystallization.[1] In addition, these reactions often give excellent chemo- and regioselectivity.[2]

Heterocycles containing the chromanone ring are important targets in synthetic and medicinal chemistry because this fragment is a key moiety in numerous biologically active compounds. For example, such prominent drug molecules as 4-hydroxycoumarin, hymecromone, armichromone, procaterol, carbocromen, warfarin, phenpro-coumon and PD099560 (Fig. 1) offer anti-HIV,[3] antioxidant,[4] anti-microbial,[5] antitumor,[6] anticancer,[7] anti-coagulant[8] and so on.[9]

Consequently, development of efficient cascade strategies that provide maximum structural complexity and diversity with a minimum number of synthetic steps became very important in chemistry.

In the past several years, our group has established a series of one-pot reactions with heterocylic ketene aminal (HKAs)[10] to synthesize a variety of biologically active heterocyclic compounds.[11] We have also developed solvent-free conditions (SFC) that have been used with great success, providing a series of highly substituted bicyclic pyridines,[12] tetrahydroimidazo[1,2-*a*]pyridines[13] and 1*H*-pyrazol-5(4*H*)-one-based HKAs.[14] During our continuous efforts on the development of SFC reactions, we have also been interested in developing chroman-2,4-dione derivatives based on HKA building blocks. Therefore, here we would like to report another green approach to the rapid construction of a library of chroman-2,4-dione-based HKA derivatives, starting with 4-hydroxycoumarin derivatives. High yields were obtained in a short period of time without purification (Scheme 1).

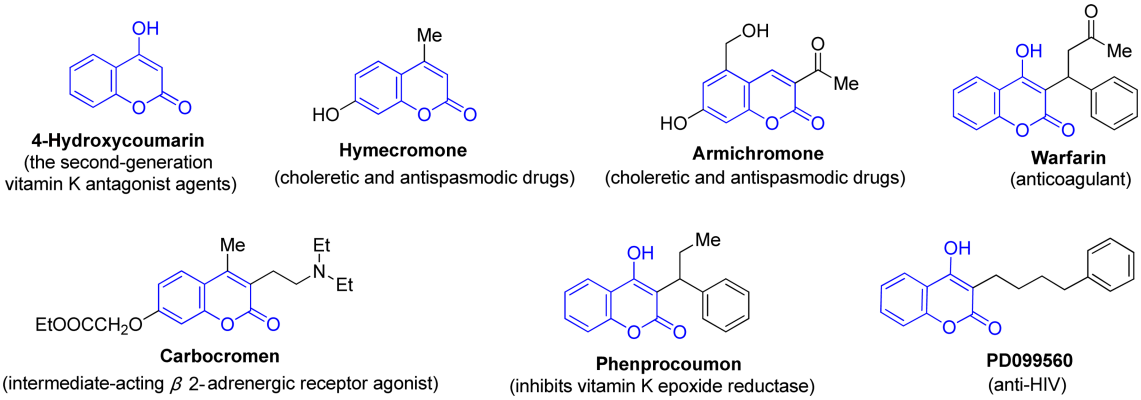
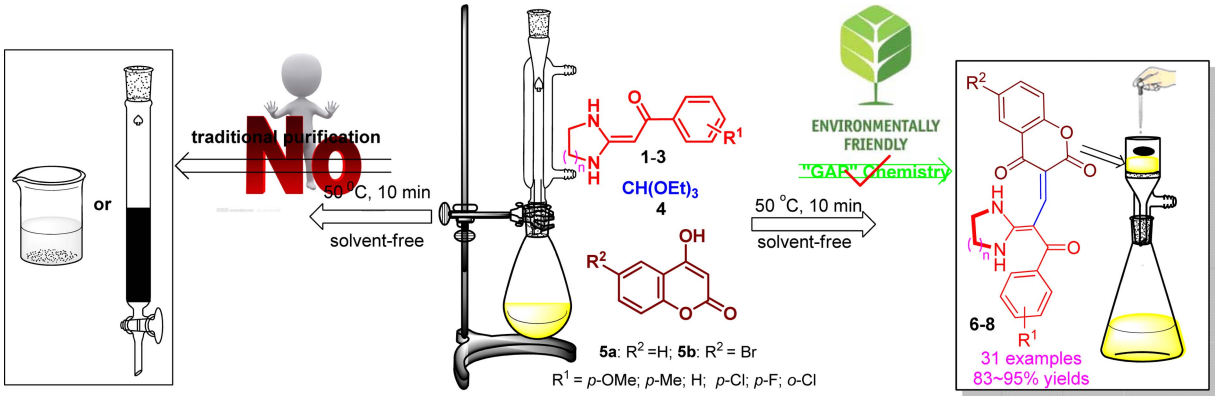


Figure 1. Some biologically active 3-substituted chromanones.



Scheme 1. This work: synthesis of chroman-2,4-dione-based HKAs.

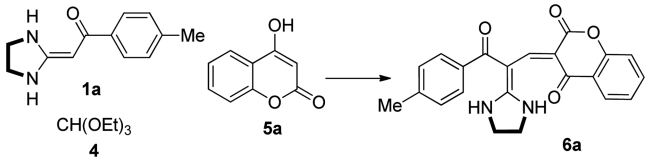
Results and Discussion

The choice of an appropriate reaction media is of crucial importance for successful synthesis. Initially, to get chroman-2,4-dione-based HKA derivative **6a**, we tested the reaction of HKA **1a**, triethoxymethane **4**, 4-hydroxy-coumarin **5a** as a simple model substrate under various reaction conditions. The results are shown in Table 1.

To begin with, the model reaction was employed without any catalyst and solvent at 110 °C (previously successful in our laboratory) (Table 1, entry 1). Unfortunately, it was found that the color of the reaction mixture immediately became darker. As a result, the reaction led to many by-products and the yield of the product was very low (Table 1, entry 1). To improve the yield, we examined this reaction at a lower temperature (Table 1, entry 2-4). To our delight, a lower temperature greatly improved the yield of the desired product (Table 1, entries 1 *vs.* 2 & 3). However, the reaction did not proceed at room temperature (Table 1, entries 4). The results showed that 50 °C afforded the highest yields (Table 1, entries 1 *vs.* 2 & 3). In order to identify the ideal catalyst-solvent pair conditions for the transformation, this model reaction was also investigated in the presence of potassium carbonate, triethylamine, potassium *tert*-butylate and acetic acid (Table 1, entries 5-8) and solvents such as water, ethanol, acetonitrile and 1,4-dioxane (Table 1, entries 9-12), The data in Table 1 show that without a catalyst, this transformation proceeded more efficiently than with other catalysts (Table 1, entry 1). Among the solvents, protonic solvents inhibited the reaction and aprotic solvents had no impact on the reaction. Although this cascade reaction proceeded well in acetonitrile and 1,4- dioxane (Table 1, entries 1, 11-12), the solvent-free process was chosen as the final conditions for this method due to the advantage of being environment friendly.

After optimization of the conditions, the scope and limitations of the method to construct a compound library were examined. To our delight, under the above optimized conditions, the reactions proceeded smoothly, and a variety of

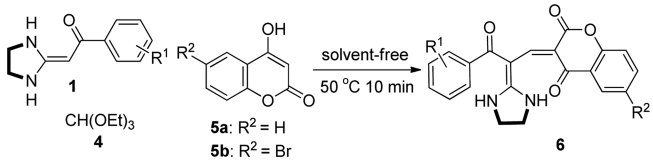
Table 1. Optimization of reaction conditions[a]



Entry	solvent	Catalyst	Temp. (°C)	Time (min)	Yield[b] (%)
1	-	-	110	10	35
2	-	-	80	10	57
3	**-**	**-**	**50**	**10**	**92**
4	-	-	r.t.	10	NR[c]
5	-	K_2CO_3	50	10	68
6	-	Et_3N	50	10	45
7	-	*t*-BuOK	50	10	30
8	-	AcOH	50	10	73
9	water	-	50	10	NR[c]
10	EtOH	-	50	10	trace
11	MeCN	-	50	10	90
12	1,4-dioxane	-	50	10	86

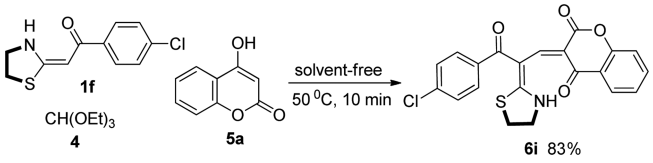
[a]The reaction was performed with **1a** (0.5 mmol), **4**(1.0 mmol), **5a** (0.6 mmol) and the solvent (5 mL) under reflux. [b]isolated yield based on HKA **1a**; [c]NR = no reaction.

Table 2. Preparation of chroman-2,4-dione-based HKA derivatives **6**[a]



Entry	R^1	R^2	**6**	Yield[b] (%)
1	*p*-Me (**1a**)	H (**5a**)	**6a**	92
2	*p*-Cl (**1c**)	H (**5a**)	**6b**	90
3	*o*-Cl (**1d**)	H (**5a**)	**6c**	89
4	*p*-Me (**1a**)	Br (**5b**)	**6d**	93
5	H (**1b**)	Br (**5b**)	**6e**	92
6	*p*-Cl (**1c**)	Br (**5b**)	**6f**	90
7	*o*-Cl (**1d**)	Br (**5b**)	**6g**	90
8	*p*-F (**1e**)	Br (**5b**)	**6h**	88

[a]The reaction was performed with HKA **1** (0.5 mmol), **4** (1.0 mmol), **5** (0.6 mmol). [b]Isolated yield based on HKAs **1**.



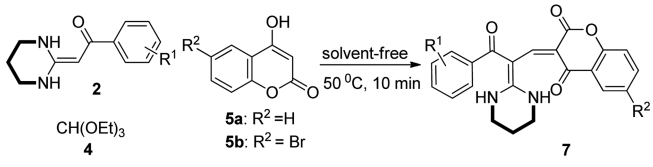
Scheme 2. One-pot synthesis of HKA derivatives **6i**.

desired products **6-8** were obtained in excellent yields (83%-95%, Table 2-4 & Scheme 2).

As shown in Table 2, a number of five-membered ring HKAs **1a-1e** were treated with triethoxymethane **4** and 4-hydroxycoumarin derivatives **5a-5b** to afford the products in good yields (88%-93%, Table 2, entries 1-8). The results demonstrated that the reactions between a series of differently substituted five-membered ring HKAs and 4-hydroxycoumarin derivatives proceeded smoothly. In general, the five-membered ring HKAs with electron-donating groups had slightly higher yields than with electron-with-drawing groups, and 4-hydroxycoumarin had a slightly lower yield than 6-bromo-4-hydroxycoumarin. Based on this, five-membered HKA **1f** was reacted with triethoxymethane **4** and 4-hydroxycoumarin **5a** under the same conditions (Scheme 2) to give the target compounds also in good yields (83%).

After these successful results, the ring size was also investigated in order to show the versatility of this protocol. The results showed that the cascade reaction of **2a-2f** or **3a-3f**, **4** & **5a-5b** provided easy access to the products in good yields under the same conditions (87%-95%, Tables 3-4). The capacity of the reaction was fruitfully proved for a wide range of HKAs. On the whole, the seven-membered HKAs were more favorable in terms of yields than the five-membered or six-membered HKAs (Table 4 *vs.* Table 2 & Table 3).

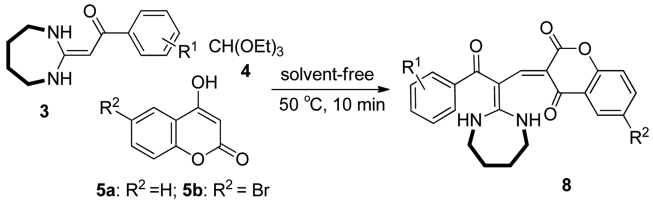
Table 3. Preparation of chroman-2,4-dione-based HKA derivatives **7**[a]



Entry	R^1	R^2	7	Yield[b] (%)
1	*p*-OMe (**2a**)	H (**5a**)	**7a**	93
2	*p*-Me (**2b**)	H (**5a**)	**7b**	92
3	H (**2c**)	H (**5a**)	**7c**	90
4	*p*-Cl (**2d**)	H (**5a**)	**7d**	88
5	*o*-Cl (**2e**)	H (**5a**)	**7e**	88
6	*p*-F (**2f**)	H (**5a**)	**7f**	87
7	*p*-OMe (**2a**)	Br (**5b**)	**7g**	94
8	*p*-Me (**2b**)	Br (**5b**)	**7h**	93
9	H (**2c**)	Br (**5b**)	**7i**	90
10	*p*-Cl (**2d**)	Br (**5b**)	**7j**	89
11	*o*-Cl (**2e**)	Br (**5b**)	**7k**	88

[a]The reaction was performed with HKA **2** (0.5 mmol), **4** (1.0 mmol), **5** (0.6 mmol). [b]Isolated yield based on HKAs **2**.

Table 4. Preparation of chroman-2,4-dione-based HKA derivatives **8**[a]



Entry	R^1	R^2	8	Yield[b] (%)
1	*p*-OMe (**3a**)	H (**5a**)	**8a**	93
2	*p*-Me (**3b**)	H (**5a**)	**8b**	92
3	H (**3c**)	H (**5a**)	**8c**	91
4	*p*-Cl (**3d**)	H (**5a**)	**8d**	89
5	*o*-Cl (**3e**)	H (**5a**)	**8e**	88
6	*p*-F (**3f**)	H (**5a**)	**8f**	87
7	*p*-OMe (**3a**)	Br (**5b**)	**8g**	95
8	*p*-Me (**3b**)	Br (**5b**)	**8h**	95
9	H (**3c**)	Br (**5b**)	**8i**	93
10	*o*-Cl (**3e**)	Br (**5b**)	**8j**	91
11	*p*-F (**3f**)	Br (**5b**)	**8k**	90

[a]The reaction was performed with HKA **3** (0.5 mmol), **4**(1.0 mmol), **5** (0.6 mmol). [b]Isolated yield based on HKAs **3**.

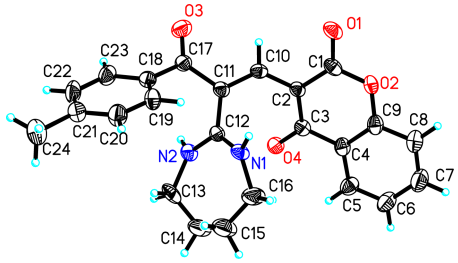


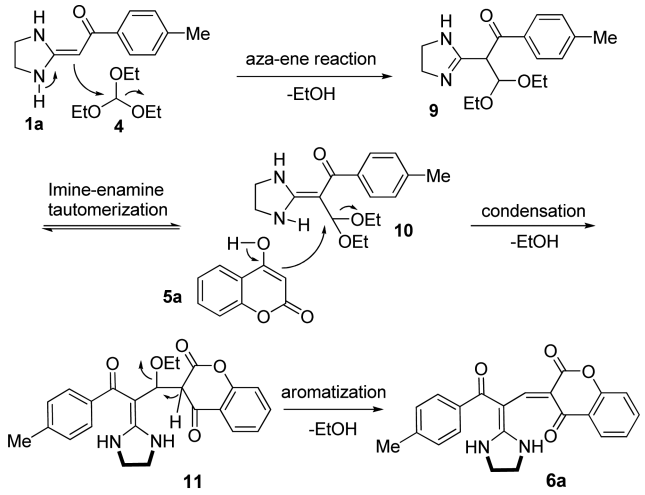
Figure 2. X-ray crystal structures of **8b**; ellipsoids are drawn at the 30% probability level.

To verify the structure of the product chroman-2,4-dione-based HKAs, **8b** was selected as a representative compound and characterized by X-ray crystallography, as shown in Figure 2 (CCDC 965292).[15]

A proposed mechanism for the cascade reaction is depicted in Scheme 3. HKA **1a** reacted with triethoxymethane **4** to form intermediate **9** *via* an aza-ene reaction mechanism[16] and lost one molecular ethanol. Then, **9** underwent a process of imine–enamine tautomerization to obtain compound **10**. Intermediate **10** reacted with 4-hydroxycoumarin **5a** to from compound **11** *via* aldol condensation accompanied by losing one molecular ethanol. Finally, **11** was transformed into the final product **6a** by an aromatization mechanism.

Conclusion

In summary, a new GAP synthesis of chroman-2,4-dione-based HKA derivatives was achieved by the cascade reac-



Scheme 3. Proposed mechanism for the three-component reaction.

tion of HKAs, triethoxymethane and 4-hydroxy-coumarin derivatives at 50 °C without catalyst and solvent. The reaction finished within 10 min and gave the desired products with good to excellent yields and complete regioselectivity. This work is a nice addition to the GAP chemistry in which purification *via* chromatography and recrystallization can be avoided.

Experimental Section

All compounds were fully characterized by spectroscopic data. The NMR spectra were recorded on the Bruker DRX400 or DRX500; chemical shifts (δ) are expressed in ppm, and J values are given in Hz, DMSO-d_6 and $CDCl_3$ were used as the solvents. The IR spectra were recorded on a FT-IR Thermo Nicolet Avatar 360 using a KBr pellet. The reactions were monitored by thin-layer chromatography (TLC) using silica gel GF_{254}. The melting points were determined on an XT-4A melting point apparatus and are uncorrected. HRMs were performed on an Agilent LC/Msd TOF and Monosiotopic Mass instrument. All chemicals and solvents were used as received without further purification unless otherwise stated. The raw material **1-3** was synthesized according to the literature.[17] Materials **3a-b** were purchased from Aldrich Corporation Limited.

General Procedure. HKA **1-3** (0.5 mmol), triethoxymethane **4** (1.0 mmol) and 4-hydroxycoumarin derivatives **5** (0.6 mmol) were charged into a 25 mL round-bottom flask and the mixture was heated to 50 °C for about 10 minutes and monitored by TLC. Until the substrate HKA had been used up. Then reaction mixture was cooled to room temperature, filtered and washed with 95% EtOH to give the pure product in 83-95% yield. The products were further identified by FTIR, NMR and HRMS, and were in good agreement with the assigned structures.

(*Z*)-3-(2-(Imidazolidin-2-ylidene)-3-oxo-3-*p*-tolylpropylidene)chroman-2,4-dione (6a): Orange solid; mp 176-178.5 °C; IR (KBr): 3391, 3178, 3091, 2955, 2904, 1662, 1613, 1580, 1519, 1461, 1402, 1368, 1289, 1205, 1090, 1031, 950, 755 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 2.32 (s, 3H, CH_3), 3.73-3.74 (m, 4H, NCH_2CH_2N), 7.07-7.10 (m, 1H, ArH), 7.14-7.19 (m, 2H, ArH), 7.28-7.29 (m, 2H, ArH), 7.41-7.42 (m, 2H, ArH), 7.83-7.86 (m, 1H, ArH), 8.03 (s, 1H, CH), 9.43 (br, 2H, 2NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 21.1, 38.7, 38.7, 98.1, 110.7, 116.2, 121.4, 123.1, 125.7, 128.4, 128.9, 129.0, 132.8, 136.5, 141.5, 148.9, 153.8, 162.5, 167.5, 175.7, 192.9; HRMS (TOF ES^+): *m/z* calcd for $C_{22}H_{19}N_2O_4$ [$(M+H)^+$], 375.1339; found, 375.1342.

(*Z*)-3-(3-(4-Chlorophenyl)-2-(imidazolidin-2-ylidene)-3-oxopropylidene)chroman-2,4-dione (6b): Yellow solid; mp 171-173 °C; IR (KBr): 3375, 3187, 3094, 2958, 1662, 1605, 1581, 1513, 1466, 1405, 1359, 1288, 1203, 1087, 1031, 949, 754 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 3.89-3.93 (m, 2H, CH_2), 4.07-4.10 (m, 2H, CH_2), 6.82-6.88 (m, 2H, ArH), 7.32-7.37 (m, 2H, ArH), 7.53-7.56 (m, 4H, ArH), 7.82 (s, 1H, CH), 9.49 (br, 1H, NH), 10.65 (br, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6) δ 43.5, 43.8, 97.5, 114.8, 116.8, 119.0, 125.2, 128.9, 128.9, 130.3, 130.3, 131.3, 133.6, 136.1, 137.7, 148.1, 157.3, 158.1, 158.3, 190.1, 194.1; HRMS (TOF ES^+): *m/z* calcd for $C_{21}H_{16}ClN_2O_4$ [$(M+H)^+$], 395.0793; found, 395.0797.

(*Z*)-3-(3-(2-Chlorophenyl)-2-(imidazolidin-2-ylidene)-3-oxopropylidene)chroman-2,4-dione (6c): Orange solid; mp 154-156 °C; IR (KBr): 3200, 2967, 1712, 1670, 1614, 1507, 1468, 1386, 1281, 1236, 1095, 1046, 910, 751 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 3.90-3.95 (m, 2H, CH_2), 4.06-4.10 (m, 2H, CH_2), 6.77-6.82 (m, 2H, ArH), 7.31-7.52 (m, 7H, CH and ArH), 9.47 (br, 1H, NH), 10.62 (br, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 43.0, 43.4, 97.6, 115.1, 116.5, 118.3, 124.0, 127.2, 128.5, 129.4, 129.6, 130.9, 133.5, 137.9, 146.7, 156.3, 157.9, 158.3, 188.9, 194.1; HRMS (TOF ES^+): *m/z* calcd for $C_{21}H_{16}ClN_2O_4$ [$(M+H)^+$], 395.0793; found, 395.0795.

(*Z*)-6-Bromo-3-(2-(imidazolidin-2-ylidene)-3-oxo-3-*p*-tolylpropylidene)chroman-2,4-dione (6d): Orange solid; mp 186-188 °C; IR (KBr): 3119, 2960, 2794, 1661, 1607, 1546, 1511, 1437, 1372, 1297, 1250, 1116, 1057, 930, 746 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 2.38 (s, 3H, CH_3), 3.75-3.82 (m, 4H, NCH_2CH_2N), 7.16-7.19 (m, 1H, ArH), 7.29-7.32 (m, 2H, ArH), 7.46-7.48 (m, 2H, ArH), 7.65-7.68 (m, 1H, ArH), 7.89-7.90 (m, 1H, ArH), 7.97 (s, 1H, CH), 9.48 (br, 2H, 2NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 21.1, 43.8, 43.8, 97.8, 111.5, 115.0, 115.1, 117.9, 123.3, 127.8, 128.4, 128.9, 129.0, 135.0, 136.3, 148.3, 152.8, 166.2, 167.4, 173.9, 192.8; HRMS (TOF ES^+): *m/z* calcd for $C_{22}H_{18}BrN_2O_4$ [$(M+H)^+$], 453.0444; found, 453.0449.

(*Z*)-6-Bromo-3-(2-(imidazolidin-2-ylidene)-3-oxo-3-phenylpropylidene)chroman-2,4-dione (6e): Orange solid; mp 168-170 °C; IR (KBr): 3370, 3211, 2970, 1694, 1603, 1563, 1511, 1434, 1370, 1266, 1114, 1077, 922, 730 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 3.89-3.92 (m, 2H, CH_2), 4.04-4.08 (m, 2H, CH_2), 6.80-6.82 (m, 1H, ArH), 7.31-7.32 (m, 1H, ArH), 7.39-7.41 (m, 1H, ArH), 7.50-7.58 (m, 5H, ArH), 7.97 (s, 1H, CH), 9.54 (br, 1H, NH), 10.34 (s, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6) δ 43.4, 43.8, 98.1, 109.9, 114.1, 118.7, 128.3, 128.3, 128.8, 128.8, 130.0, 131.4, 131.8, 134.4,

138.9, 148.9, 155.7, 157.5, 158.4, 190.8, 191.5; HRMS (TOF ES$^+$): *m/z* calcd for $C_{21}H_{16}BrN_2O_4$ [(M+H)$^+$], 439.0288; found, 439.0294.

(*Z*)-6-Bromo-3-(3-(4-chlorophenyl)-2-(imidazolidin-2-ylidene)-3-oxopropylidene)chroman-2,4-dione (6f): Yellow solid; mp 185-187 °C; IR (KBr): 3118, 2958, 1663, 1606, 1548, 1504, 1437, 1372, 1297, 1248, 1203, 1115, 933, 742 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.82-3.90 (m, 2H, CH_2), 3.96-4.06 (m, 2H, CH_2), 6.81-6.83 (m, 1H, ArH), 7.26-7.29 (m, 1H, ArH), 7.37-7.40 (m, 1H, ArH), 7.54-7.57 (m, 3H, ArH), 7.96 (s, 1H, CH), 9.53 (br, 1H, NH), 10.36 (br, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 43.1, 43.5, 97.6, 109.6, 113.9, 118.3, 128.8, 128.8, 130.0, 130.0, 131.4, 134.0, 135.8, 137.3, 148.3, 155.2, 157.0, 158.1, 189.8, 190.3; HRMS (TOF ES$^+$): *m/z* calcd for $C_{21}H_{15}BrClN_2O_4$ [(M+H)$^+$], 472.9898; found, 472.9896.

(*Z*)-6-Bromo-3-(3-(2-chlorophenyl)-2-(imidazolidin-2-ylidene)-3-oxopropylidene)chroman-2,4-dione (6g): Yellow solid; mp 191-193 °C; IR (KBr): 2971, 1677, 1605, 1521, 1434, 1377, 1243, 1199, 1127, 1049, 934, 730 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) δ 3.90-3.94 (m, 2H, CH_2), 4.03-4.07 (m, 2H, CH_2), 6.75-6.77 (m, 1H, ArH), 7.26-7.27 (m, 1H, ArH), 7.37-7.41 (m, 2H, ArH), 7.46-7.49 (m, 1H, ArH), 7.50-7.54 (m, 1H, ArH), 7.56 (s, 1H, ArH), 7.58 (s, 1H, CH), 9.66 (br, 1H, NH), 10.25 (br, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6) δ 43.3, 43.9, 98.6, 109.8, 115.1, 118.6, 127.8, 128.9, 129.8, 130.1, 131.5, 131.5, 134.4, 138.3, 147.8, 153.7, 155.7, 156.8, 158.5, 189.5, 190.7; HRMS (TOF ES$^+$): *m/z* calcd for $C_{21}H_{15}BrClN_2O_4$ [(M+H)$^+$], 472.9898; found, 472.9897.

(*Z*)-6-Bromo-3-(3-(4-fluorophenyl)-2-(imidazolidin-2-ylidene)-3-oxopropylidene)chroman-2,4-dione (6h): Orange solid; mp 286-289 °C; IR (KBr): 3246, 2919, 1720, 1647, 1595, 1511, 1406, 1296, 1256, 1225, 1187, 1151, 1090, 775 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.96-4.01 (m, 2H, CH_2), 4.63-4.67 (m, 2H, CH_2), 7.30-7.34 (m, 2H, ArH), 7.42-7.45 (m, 1H, ArH), 7.57 (s, 1H, ArH), 7.89-7.93 (m, 3H, ArH), 8.37 (s, 1H, CH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 49.6, 54.7, 99.8, 115.0, 115.5, 115.8, 116.2, 120.3, 125.5, 128.7, 132.2, 132.2, 132.3, 135.4, 136.2, 146.7, 147.4, 152.7, 153.7, 157.9, 190.4; HRMS (TOF ES$^+$): *m/z* calcd for $C_{21}H_{15}BrFN_2O_4$ [(M+H)$^+$], 439.0088; found, 439.0092.

(*Z*)-3-((*Z*)-3-(4-Chlorophenyl)-3-oxo-2-(thiazolidin-2-ylidene)propylidene)chroman-2,4-dione (6i): Yellow solid; mp 279-281 °C; IR (KBr): 3078, 1663, 1622, 1582, 1450, 1383, 1290, 1242, 1189, 1162, 1080, 1011, 837, 758 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) δ 3.49-3.52 (m, 2H, CH_2), 4.45-4.47 (m, 2H, CH_2), 6.89-6.95 (m, 2H, ArH), 7.43-7.47 (m, 1H, ArH), 7.52-7.54 (m, 1H, ArH), 7.58-7.64 (m, 4H, ArH), 7.86 (s, 1H, CH), 10.85 (br, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6) δ 28.2, 51.0, 110.5, 117.2, 119.4, 122.4, 123.7, 129.1, 129.1, 130.8, 130.8, 132.0, 135.1, 136.3, 137.0, 143.5, 158.2, 159.1, 164.1, 189.9, 195.2; HRMS (TOF ES$^+$): *m/z* calcd for $C_{21}H_{14}ClNNaO_4S$ [(M+Na)$^+$], 434.0224; found, 434.0229.

(*Z*)-3-(3-(4-Methoxyphenyl)-3-oxo-2-(tetrahydropyrimidin-2(1*H*)-ylidene)propylidene)chroman-2,4-dione (7a): Yellow solid; mp 171-173 °C; IR (KBr): 3185, 3014, 2965, 1605, 1557, 1511, 1453, 1409, 1316, 1252, 1209, 1175, 1113, 1085, 1021, 947, 756 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.94-1.98 (m, 2H, CH_2), 3.26-3.29 (m, 4H, NCH_2CH_2N), 3.82 (s, 3H, OCH_3), 7.02-7.04 (m, 2H, ArH), 7.14-7.19 (m, 2H, ArH), 7.48-7.51 (m, 1H, ArH), 7.55-7.57 (m, 2H, ArH), 7.82-7.84 (m, 1H, ArH), 7.94 (s, 1H, CH), 9.04 (br, 2H, 2NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 17.4, 38.1, 38.1, 55.4, 97.1, 113.5, 113.5, 116.1, 117.5, 121.5, 123.0, 125.6, 131.2, 131.2, 131.7, 132.5, 146.3, 153.8, 160.9, 161.8, 162.5, 175.4, 192.5; HRMS (TOF ES$^+$): *m/z* calcd for $C_{23}H_{21}N_2O_5$ [(M+H)$^+$], 405.1445; found, 405.1446.

(*Z*)-3-(3-Oxo-2-(tetrahydropyrimidin-2(1*H*)-ylidene)-3-*p*-tolylpropylidene)chroman-2,4-dione (7b): Yellow solid; mp 160-162 °C; IR (KBr): 3179, 3022, 1638, 1605, 1552, 1519, 1467, 1411, 1317, 1253, 1209, 1032, 951, 753 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.97-2.01 (m, 2H, CH_2), 2.39 (s, 3H, CH_3), 3.31-3.33 (m, 4H, NCH_2CH_2N), 7.16-7.22 (m, 2H, ArH), 7.30-7.32 (m, 2H, ArH), 7.47-7.54 (m, 3H, ArH), 7.84-7.87 (m, 1H, ArH), 8.00 (s, 1H, CH), 9.07 (br, 2H, 2NH); ^{13}C NMR (125 MHz, DMSO-d_6) δ 17.4, 21.0, 38.1, 38.1, 97.1, 116.0, 117.2, 121.4, 122.9, 125.5, 128.6, 128.6, 128.9, 128.9, 132.4, 136.8, 141.0, 146.8, 153.8, 160.8, 193.3; HRMS (TOF ES$^+$): *m/z* calcd for $C_{23}H_{21}N_2O_4$ [(M+H)$^+$], 389.1496; found, 389.1495.

(*Z*)-3-(3-Oxo-3-phenyl-2-(tetrahydropyrimidin-2(1*H*)-ylidene)propylidene)chroman-2,4-dione (7c): Yellow solid; mp 200-202 °C; IR (KBr): 3179, 3012, 2962, 1696, 1646, 1604, 1547, 1504, 1461, 1407, 1316, 1255, 1200, 1084, 935, 748 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.94-1.97 (m, 2H, CH_2), 3.27-3.30 (m, 4H, NCH_2CH_2N), 7.14-7.19 (m, 2H, ArH), 7.46-7.55 (m, 6H, ArH), 7.82-7.83 (m, 1H, ArH), 7.98 (s, 1H, CH), 9.08 (br, 2H, 2NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 17.4, 38.1, 38.1, 97.3, 116.2, 117.2, 121.4, 123.0, 125.6, 128.2, 128.2, 128.7, 128.7, 131.0, 132.6, 139.7, 147.2, 153.8, 160.8, 162.4, 175.6, 193.7; HRMS (TOF ES$^+$): *m/z* calcd for $C_{22}H_{19}N_2O_4$ [(M+H)$^+$], 375.1339; found, 375.1343.

(*Z*)-3-(3-(4-Chlorophenyl)-3-oxo-2-(tetrahydropyrimidin-2(1*H*)-ylidene)propylidene)chroman-2,4-dione (7d): Yellow solid; mp 171-173 °C; IR (KBr): 3256, 3174, 3015, 1603, 1556, 1515, 1466, 1401, 1376, 1256, 1208, 1088, 939, 756 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.94-1.97 (m, 2H, CH_2), 3.28-3.31 (m, 4H, NCH_2CH_2N), 7.15-7.20 (m, 2H, ArH), 7.49-7.56 (m, 5H, ArH), 7.76-7.84 (m, 1H, ArH), 7.95-7.96 (m, 1H, CH), 9.11 (br, 2H, 2NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 17.4, 38.1, 38.1, 97.6, 116.2, 116.7, 121.3, 123.1, 125.7, 128.3, 128.3, 130.5, 130.5, 132.7, 135.8, 138.4, 147.3, 153.8, 160.6, 162.4, 175.7, 192.4; HRMS (TOF ES$^+$): *m/z* calcd for $C_{22}H_{18}ClN_2O_4$ [(M+H)$^+$], 409.0950; found, 409.0952.

(*Z*)-3-(3-(2-Chlorophenyl)-3-oxo-2-(tetrahydropyrimidin-2(1*H*)-ylidene)propylidene)chroman-2,4-dione (7e): Yellow solid; mp 183-185 °C; IR (KBr): 3194, 3027, 1636, 1605, 1567, 1519, 1459, 1406, 1320, 1279, 1251, 1206, 1149, 1098, 0140, 932, 758 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.98-2.01 (m, 2H, CH_2), 3.85-3.88 (m, 4H, NCH_2CH_2N),

6.76-6.79 (m, 2H, ArH), 7.26-7.52 (m, 7H, CH and ArH), 10.51 (br, 1H, NH), 10.84 (br, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 18.3, 38.5, 38.7, 98.3, 113.0, 116.4, 118.5, 125.0, 127.5, 128.6, 129.4, 129.7, 130.6, 131.0, 133.2, 138.3, 146.6, 154.7, 157.7, 158.6, 190.8, 193.8; HRMS (TOF ES$^+$): *m/z* calcd for $C_{22}H_{18}ClN_2O_4$ [(M+H)$^+$], 409.0950; found, 409.0954.

(*Z*)-3-(3-(4-Fluorophenyl)-3-oxo-2-(tetrahydropyrimidin-2(1*H*)-ylidene)propylidene)chroman-2,4-dione (7f): Yellow solid; mp 166-168 °C; IR (KBr): 3178, 3016, 2958, 1642, 1601, 1547, 1504, 1463, 1409, 1376, 1315, 1253, 1205, 1151, 1085, 940, 755 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.94-1.95 (m, 2H, CH_2), 3.26-3.29 (m, 4H, NCH_2CH_2N), 7.13-7.18 (m, 2H, ArH), 7.29-7.33 (m, 2H, ArH), 7.48-7.50 (m, 1H, ArH), 7.58-7.61 (m, 2H, ArH), 7.80-7.83 (m, 1H, ArH), 7.95 (s, 1H, CH), 9.08 (br, 2H, 2NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 17.4, 38.1, 38.1, 97.4, 115.1, 115.3, 116.2, 117.0, 121.4, 123.1, 125.6, 131.4, 131.4, 132.6, 136.1, 147.1, 153.8, 160.7, 162.4, 164.9, 175.7, 192.3; HRMS (TOF ES$^+$): *m/z* calcd for $C_{22}H_{18}FN_2O_4$ [(M+H)$^+$], 393.1245; found, 393.1249.

(*Z*)-6-Bromo-3-(3-(4-methoxyphenyl)-3-oxo-2-(tetrahydropyrimidin-2(1*H*)-ylidene)propylidene)chroman-2,4-dione (7g): Yellow solid; mp 202-204 °C; IR (KBr): 3180, 3009, 1633, 1600, 1556, 1512, 1437, 1366, 1311, 1249, 1206, 1169, 1072, 934, 754 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.97-1.99 (m, 2H, CH_2), 3.30-3.30 (m, 4H, NCH_2CH_2N), 3.85 (s, 3H, OCH_3), 7.04-7.07 (m, 2H, ArH), 7.17-7.19 (m, 1H, ArH), 7.59-7.61 (m, 2H, ArH), 7.65-7.67 (m, 1H, ArH), 7.90-7.91 (m, 2H, CH and ArH), 9.10 (br, 2H, 2NH); ^{13}C NMR (125 MHz, DMSO-d_6) δ 17.8, 38.5, 38.5, 55.8, 97.2, 113.9, 113.9, 115.3, 118.6, 119.1, 123.8, 128.0, 131.6, 131.6, 131.8, 135.1, 146.1, 153.1, 161.1, 162.2, 174.0, 192.8; HRMS (TOF ES$^+$): *m/z* calcd for $C_{23}H_{20}BrN_2O_5$ [(M+H)$^+$], 483.0550; found, 483.0548.

(*Z*)-6-Bromo-3-(3-oxo-2-(tetrahydropyrimidin-2(1*H*)-ylidene)-3-*p*-tolylpropylidene)chroman-2,4-dione (7h): Yellow solid; mp 200-202 °C; IR (KBr): 3182, 3012, 1654, 1601, 1549, 1509, 1439, 1371, 1311, 1249, 1203, 1120, 1070, 936, 821 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.95-1.97 (m, 2H, CH_2), 2.49 (s, 3H, CH_3), 3.28-3.30 (m, 4H, NCH_2CH_2N), 7.14-7.19 (m, 2H, ArH), 7.26-7.30 (m, 2H, ArH), 7.46-7.48 (m, 2H, ArH), 7.63-7.65 (m, 1H, ArH), 7.89 (s, 1H, CH), 9.10 (br, 2H, 2NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 17.4, 21.1, 38.1, 38.1, 96.9, 115.0, 118.2, 118.8, 125.9, 127.7, 128.8, 128.8, 129.1, 129.1, 134.9, 136.5, 141.4, 146.4, 152.7, 160.6, 173.8, 193.4; HRMS (TOF ES$^+$): *m/z* calcd for $C_{23}H_{20}BrN_2O_4$ [(M+H)$^+$], 467.0601; found, 467.0599.

(*Z*)-6-Bromo-3-(3-oxo-3-phenyl-2-(tetrahydropyrimidin-2(1*H*)-ylidene)propylidene)chroman-2,4-dione (7i): Yellow solid; mp 199-201 °C; IR (KBr): 3179, 3023, 1648, 1597, 1563, 1528, 1477, 1435, 1318, 1252, 1206, 1149, 1082, 779, 700 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.98-1.99 (m, 2H, CH_2), 3.31-3.33 (m, 4H, NCH_2CH_2N), 7.18-7.19 (m, 1H, ArH), 7.51-7.53 (m, 2H, ArH), 7.56-7.58 (m, 3H, ArH), 7.67-7.69 (m, 1H, ArH), 7.91 (m, 1H, ArH), 7.94 (s, 1H, CH), 9.14 (br, 2H, 2NH); ^{13}C NMR (125 MHz, DMSO-d_6) δ 17.7, 38.5, 38.5, 97.4, 115.3, 118.3, 119.2, 123.7, 128.0, 128.5, 128.5, 129.0, 129.0, 131.5, 135.2, 139.8, 147.0, 153.1, 161.0, 162.4, 174.2, 193.9; HRMS (TOF ES$^+$): *m/z* calcd for $C_{22}H_{18}BrN_2O_4$ [(M+H)$^+$], 453.0444; found, 453.0442.

(*Z*)-6-Bromo-3-(3-(4-chlorophenyl)-3-oxo-2-(tetrahydropyrimidin-2(1*H*)-ylidene)propylidene)chroman-2,4-dione (7j): Yellow solid; mp 203-205 °C; IR (KBr): 3256, 3165, 3019, 1631, 1604, 1556, 1437, 1367, 1313, 1251, 1204, 1086, 935, 743 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.94-1.96 (m, 2H, CH_2), 3.28-3.30 (m, 4H, NCH_2CH_2N), 7.15-7.17 (m, 1H, ArH), 7.53-7.58 (m, 4H, ArH), 7.64-7.67 (m, 1H, ArH), 7.87-7.88 (m, 2H, CH and ArH), 9.13 (br, 2H, 2NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 17.4, 38.1, 38.1, 97.2, 115.1, 117.6, 118.9, 123.2, 127.7, 128.4, 128.4, 130.6, 130.6, 135.1, 135.9, 138.2, 146.8, 152.8, 160.4, 162.1, 174.0, 192.4; HRMS (TOF ES$^+$): *m/z* calcd for $C_{22}H_{17}BrClN_2O_4$ [(M+H)$^+$], 487.0055; found, 487.0059.

(*Z*)-6-Bromo-3-(3-(2-chlorophenyl)-3-oxo-2-(tetrahydropyrimidin-2(1*H*)-ylidene)propylidene)chroman-2,4-dione (7k): Yellow solid; mp 204-206.5 °C; IR (KBr): 3211, 3031, 1678, 1643, 1606, 1567, 1529, 1435, 1372, 1316, 1241, 1201, 1149, 1084, 939, 736 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.96-1.98 (m, 2H, CH_2), 3.32-3.33 (m, 4H, NCH_2CH_2N), 7.14-7.17 (m, 1H, ArH), 7.14-7.19 (m, 2H, ArH), 7.35-7.37 (m, 1H, ArH), 7.43-7.48 (m, 2H, ArH), 7.53-7.55 (m, 1H, ArH), 7.64-7.67 (m, 1H, ArH), 7.77 (s, 1H, CH), 7.85-7.86 (m, 1H, ArH), 9.11 (br, 2H, 2NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 17.4, 38.2, 38.2, 97.5, 115.1, 117.8, 118.9, 123.0, 127.0, 127.8, 129.1, 129.7, 129.8, 130.8, 135.2, 139.3, 148.0, 152.8, 159.6, 162.0, 174.2, 192.0; HRMS (TOF ES$^+$): *m/z* calcd for $C_{22}H_{17}BrClN_2O_4$ [(M+H)$^+$], 487.0055; found, 487.0051.

(*Z*)-3-(2-(1,3-Diazepan-2-ylidene)-3-(4-methoxyphenyl)-3-oxopropylidene)chroman-2,4-dione (8a): Yellow solid; mp 180-182 °C; IR (KBr): 3196, 3020, 2951, 1604, 1557, 1505, 1410, 1368, 1322, 1253, 1213, 1174, 1109, 1080, 948, 756 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.82-1.84 (m, 4H, CH_2CH_2), 3.34-3.35 (m, 4H, NCH_2 and CH_2N), 3.81 (s, 3H, OCH_3), 7.01-7.03 (m, 2H, ArH), 7.14-7.19 (m, 2H, ArH), 7.48-7.51 (m, 1H, ArH), 7.54-7.56 (m, 2H, ArH), 7.83-7.85 (m, 1H, ArH), 7.93 (s, 1H, CH), 8.91 (br, 2H, 2NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 26.2, 26.2, 43.5, 43.5, 55.4, 97.3, 113.4, 113.4, 116.2, 119.2, 121.5, 123.0, 125.6, 131.1, 131.1, 131.9, 132.5, 146.8, 153.8, 161.7, 162.7, 166.8, 175.5, 193.0; HRMS (TOF ES$^+$): *m/z* calcd for $C_{24}H_{23}N_2O_5$ [(M+H)$^+$], 419.1601; found, 419.1601.

(*Z*)-3-(2-(1,3-Diazepan-2-ylidene)-3-oxo-3-*p*-tolylpropylidene)chroman-2,4-dione (8b): Yellow solid; mp 184-186 °C; IR (KBr): 3426, 3199, 3020, 1660, 1640, 1605, 1555, 1500, 1460, 1410, 1376, 1252, 1204, 1110, 1073, 751 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.82-1.83 (m, 4H, CH_2CH_2), 2.36 (s, 3H, CH_3), 3.55-3.56 (m, 4H, NCH_2 and CH_2N), 7.14-7.20 (m, 2H, ArH), 7.27-7.29 (m, 2H, ArH), 7.44-7.52 (m, 3H, ArH), 7.82-7.84 (m, 1H, ArH), 7.95 (s, 1H, CH), 8.92 (br, 2H, 2NH); ^{13}C NMR (100 MHz, DMSO-

d_6) δ 21.1, 26.2, 26.2, 43.5, 43.5, 97.4, 116.2, 119.0, 121.5, 123.0, 125.6, 128.7, 128.7, 128.9, 128.9, 132.6, 136.9, 141.1, 147.2, 153.8, 162.6, 166.7, 175.6, 193.8; HRMS (TOF ES$^+$): *m/z* calcd for $C_{24}H_{23}N_2O_4$ [(M+H)$^+$], 403.1652; found, 403.1655.

(*Z*)-3-(2-(1,3-Diazepan-2-ylidene)-3-oxo-3-phenylpropylidene)chroman-2,4-dione (8c): Yellow solid; mp 199-201 °C; IR (KBr): 3200, 3007, 2955, 1634, 1602, 1496, 1413, 1324, 1260, 1207, 1135, 1095, 1059, 754, 714 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.81-1.82 (m, 4H, CH_2CH_2), 3.34-3.35 (m, 4H, NCH_2 and CH_2N), 7.15-7.21 (m, 2H, ArH), 7.46-7.54 (m, 6H, ArH), 7.83-7.85 (m, 1H, ArH), 7.98 (s, 1H, CH), 8.95 (br, 2H, 2NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 26.2, 26.2, 43.5, 43.5, 97.6, 116.2, 118.8, 121.4, 123.1, 125.7, 128.2, 128.2, 128.6, 128.6, 130.9, 132.7, 139.8, 147.4, 153.8, 162.6, 166.6, 175.6, 194.0; HRMS (TOF ES$^+$): *m/z* calcd for $C_{23}H_{21}N_2O_4$ [(M+H)$^+$], 389.1496; found, 389.1494.

(*Z*)-3-(3-(4-Chlorophenyl)-2-(1,3-diazepan-2-ylidene)-3-oxopropylidene)chroman-2,4-dione (8d): Yellow solid; mp 163-165 °C; IR (KBr): 3251, 1604, 1562, 1466, 1401, 1366, 1257, 1212, 1091, 1000, 755 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.81-1.83 (m, 4H, CH_2CH_2), 3.54-3.55 (m, 4H, NCH_2 and CH_2N), 3.82 (s, 3H, OCH_3), 7.15-7.21 (m, 2H, ArH), 7.43-7.58 (m, 5H, ArH), 7.82-7.84 (m, 1H, ArH), 7.95 (s, 1H, CH), 8.97 (s, 2H, 2NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 26.2, 26.2, 43.5, 43.5, 97.8, 110.9, 118.4, 121.3, 123.1, 125.7, 128.3, 128.3, 130.4, 130.4, 132.8, 135.7, 138.6, 147.6, 153.8, 162.6, 166.4, 175.8, 192.8; HRMS (TOF ES$^+$): *m/z* calcd for $C_{23}H_{20}ClN_2O_4$ [(M+H)$^+$], 423.1106; found, 423.1106.

(*Z*)-3-(3-(2-Chlorophenyl)-2-(1,3-diazepan-2-ylidene)-3-oxopropylidene)chroman-2,4-dione (8e): Yellow solid; mp 290-192 °C; IR (KBr): 3200, 3039, 2947, 1607, 1566, 1523, 1466, 1402, 1322, 1280, 1244, 1208, 1138, 1092, 932, 753 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.84-1.85 (m, 4H, CH_2CH_2), 3,41-3.42 (m, 4H, NCH_2 and CH_2N), 7.14-7.18 (m, 2H, ArH), 7.39-7.54 (m, 5H, ArH), 7.80-7.82 (m, 1H, ArH), 7.85 (s, 1H, CH), 8.92 (br, 2H, 2NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 26.2, 26.2, 43.4, 43.4, 98.0, 116.3, 118.6, 121.2, 123.2, 125.7, 126.9, 129.2, 129.8, 130.7, 132.9, 139.6, 148.1, 153.8, 165.6, 175.9, 192.1; HRMS (TOF ES$^+$): *m/z* calcd for $C_{23}H_{20}ClN_2O_4$ [(M+H)$^+$], 423.1106; found, 423.1104.

(*Z*)-3-(2-(1,3-Diazepan-2-ylidene)-3-(4-fluorophenyl)-3-oxopropylidene)chroman-2,4-dione (8f): Yellow solid; mp 226-228 °C; IR (KBr): 3243, 3023, 2957, 1604, 1566, 1506, 1469, 1408, 1326, 1260, 1143, 1081, 852, 754 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.82-1.83 (m, 4H, CH_2CH_2), 3.36-3.37 (m, 4H, NCH_2 and CH_2N), 7.16-7.21 (m, 2H, ArH), 7.31-7.36 (m, 2H, ArH), 7.49-7.51 (m, 1H, ArH), 7.59-7.62 (m, 2H, ArH), 7.83-7.85 (m, 1H, ArH), 7.96 (s, 1H, CH), 8.97 (br, 2H, 2NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 26.3, 26.3, 43.5, 43.5, 97.6, 115.1, 115.3, 116.2, 118.5, 121.4, 123.1, 125.7, 131.2, 131.3, 132.6, 136.4, 147.4, 153.9, 162.4, 164.8, 166.6, 176.6, 192.6; HRMS (TOF ES$^+$): *m/z* calcd for $C_{23}H_{20}FN_2O_4$ [(M+H)$^+$], 407.1402; found, 407.1403.

(*Z*)-3-(2-(1,3-Diazepan-2-ylidene)-3-(4-methoxyphenyl)-3-oxopropylidene)-6-bromochroman-2,4-dione (8g): Yellow solid; mp 214-216 °C; IR (KBr): 3260, 3049, 2929, 1641, 1603, 1436, 1367, 1249, 1173, 746 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.84-1.85 (m, 4H, CH_2CH_2), 3.36-3.37 (m, 4H, NCH_2 and CH_2N), 3.82 (s, 3H, OCH_3), 7.03-7.09 (m, 2H, ArH), 7.16-7.18 (m, 1H, ArH), 7.55-7.58 (m, 2H, ArH), 7.64-7.67 (m, 1H, ArH), 7.87-7.89 (m, 2H, CH and ArH), 8.95 (br, 2H, 2NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 26.3, 26.3, 43.5, 43.5 55.4, 97.0, 113.5, 113.5, 115.0, 118.9, 120.0, 123.4, 127.6, 131.2, 131.2, 131.6, 134.8, 146.2, 152.8, 161.8, 162.2, 166.6, 173.7, 192.9; HRMS (TOF ES$^+$): *m/z* calcd for $C_{24}H_{22}BrN_2O_5$ [(M+H)$^+$], 497.0707; found, 497.0712.

(*Z*)-3-(2-(1,3-Diazepan-2-ylidene)-3-oxo-3-*p*-tolylpropylidene)-6-bromochroman-2,4-dione (8h): Yellow solid; mp 217-219 °C; IR (KBr): 3256, 3047, 2916, 1640, 1605, 1537, 1436, 1368, 1320, 1246, 1206, 1126, 742 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.83-1.84 (m, 4H, CH_2CH_2), 2.37 (s, 3H, CH_3), 3.36-3.37 (m, 4H, NCH_2 and CH_2N), 7.16-7.18 (m, 1H, ArH), 7.29-7.30 (m, 2H, ArH), 7.46-7.47 (m, 2H, ArH), 7.64-7.67 (m, 1H, ArH), 7.86-7.89 (m, 2H, CH and ArH), 8.97 (br, 2H, 2NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 21.1, 26.3, 26.3, 43.5, 43.5, 97.1, 115.0, 118.9, 119.8, 123.4, 127.7, 128.7, 128.7, 129.0, 129.0, 134.9, 136.7, 141.2, 146.7, 152.8, 162.2, 166.5, 173.8, 193.8; HRMS (TOF ES$^+$): *m/z* calcd for $C_{24}H_{22}BrN_2O_4$ [(M+H)$^+$], 481.0757; found, 481.0760.

(*Z*)-3-(2-(1,3-Diazepan-2-ylidene)-3-oxo-3-phenylpropylidene)-6-bromochroman-2,4-dione (8i): Yellow solid; mp 219-221 °C; IR (KBr): 3335, 3251, 3043, 1667, 1603, 1564, 1520, 1436, 1365, 1251, 1202, 1134, 934, 722 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.82-1.83 (m, 4H, CH_2CH_2), 3.37-3.38 (m, 4H, NCH_2 and CH_2N), 7.16-7.18 (m, 1H, ArH), 7.47-7.55 (m, 5H, ArH), 7.65-7.69 (m, 1H, ArH), 7.89-7.92 (m, 2H, CH and ArH), 8.99 (br, 2H, 2NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 26.2, 26.2, 43.5, 43.5, 97.3, 115.1, 118.9, 119.6, 123.3, 127.7, 128.2, 128.2, 128.6, 128.6, 131.1, 135.0, 139.6, 146.9, 152.8, 162.2, 166.4, 173.9, 194.0; HRMS (TOF ES$^+$): *m/z* calcd for $C_{23}H_{20}BrN_2O_4$ [(M+H)$^+$], 467.0601; found, 467.0603.

(*Z*)-6-Bromo-3-(3-(2-chlorophenyl)-2-(1,3-diazepan-2-ylidene)-3-oxopropylidene)chroman-2,4-dione (8j): Yellow solid; mp 208-210 °C; IR (KBr): 3243, 3039, 1678, 1640, 1607, 1567, 1530, 1436, 1367, 1240, 1202, 1134, 746 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.85-1.86 (m, 4H, CH_2CH_2), 3.33-3.43 (m, 4H, NCH_2 and CH_2N), 7.16-7.18 (m, 1H, ArH), 7.38-7.48 (m, 3H, ArH), 7.53-7.55 (m, 1H, ArH), 7.65-7.68 (m, 1H, ArH), 7.79 (s, 1H, CH), 7.76-7.87 (m, 1H, ArH), 8.97 (br, 2H, 2NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 26.2, 26.2, 43.4, 43.4, 97.6, 115.1, 119.0, 123.1, 126.9, 127.8, 129.2, 129.7, 129.8, 130.7, 135.2, 139.5, 147.7, 152.8, 165.3, 174.0, 192.1; HRMS (TOF ES$^+$): *m/z* calcd for $C_{23}H_{19}BrClN_2O_4$ [(M+H)$^+$], 501.0211; found, 501.0215.

(*Z*)-3-(2-(1,3-Diazepan-2-ylidene)-3-(4-fluorophenyl)-3-oxopropylidene)-6-bromochroman-2,4-dione (8k): Yellow solid; mp 226-228 °C; IR (KBr): 3328, 3256, 3035, 1668,

1601, 1564, 1512, 1438, 1366, 1323, 1240, 1130, 956, 754 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 1.83-1.84 (m, 4H, CH_2CH_2), 3.36-3.37 (m, 4H, NCH_2 and CH_2N), 7.16-7.20 (m, 1H, ArH), 7.32-7.36 (m, 2H, ArH), 7.60-7.68 (m, 3H, ArH), 7.89-7.90 (m, 2H, CH and ArH), 9.00 (br, 2H, 2NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 26.6, 26.6, 43.9, 43.9, 97.7, 115.5, 115.5, 115.8, 119.3, 119.8, 123.7, 128.1, 131.7, 131.8, 135.4, 136.5, 136.5, 147.3, 153.2, 162.9, 165.3, 166.7, 174.3, 193.0; HRMS (TOF ES^+): *m/z* calcd for $C_{23}H_{19}BrFN_2O_4$ [$(M+H)^+$], 485.0507; found, 485.0510.

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15. CCDC 965292 contains the supplementary crystallographic data for compound **8b**. These data can be obtained free of charge from The Cambridge Crystallographic Data Center *via* www.ccdc.cam.ac.uk/data_request/cif
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