Design, Synthesis, Molecular docking and Biological studies of Novel Phytoestrogen-Tanaproget hybrids

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SUPPORTING INFORMATION

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General Information

Unless otherwise noted, chemicals were purchased from commercial suppliers at the highest purity grade available and were used without further purification. Solvents were distilled by standard methods. Thin layer chromatography was performed on Merck precoated 0.25 mm silica gel plates (60F-254) using UV light as visualizing agent and/or iodine as developing agent. Silica gel (100-200 mesh) was used for column chromatography. Melting points were performed with Ambassador® and Digital Melting point apparatus (Nutronics), Popular India. IR spectra were recorded on FT-IR spectrometer and expressed as wave numbers (cm⁻¹). ¹H and ¹³C NMR spectra were recorded on a Brüker Avance (500 MHz & 125 MHz) & Jeol Resonance ECX (400 MHz & 100 MHz) spectrometer. Spectra were referenced internally to the residual proton resonance in CDCl₃ (δ 7.26 ppm), DMSO-d₆ (δ 2.50ppm) or with tetramethylsilane (TMS, δ 0.00 ppm) as the internal standard. Spectra were referenced internally to the residual proton resonance in CDCl₃ (δ 7.26 ppm), DMSO-d₆ (δ 2.50ppm) or with tetramethylsilane (TMS, δ 0.00 ppm) as the internal standard. Spectra were processed using Bruker Topspin® 3.0.b.8. Chemical shifts (δ) were reported as part per million (ppm) in δ scale downfield from TMS. ¹³C NMR spectra were referenced to CDCl₃ (δ 77.23 ppm, the middle peak) and DMSO-d₆ (δ 39.5 ppm, the middle peak). Coupling constants are expressed in Hz. The following abbreviations are used to explain the multiplicities: s = singlet, d = doublet, t = triplet, dt = doublet of triplet, m = multiplet, br = broad. High-resolution mass spectra (HRMS) were obtained on a BrükermicroTOF™-Q II mass spectrometer (ESIMS).

General procedures

Synthesis of Starting Material :

1. General procedure for synthesis of compounds (1a-1c, 2a-2c, 5, 6, 7a, 7b, 8a-8c, 10).

The synthesis followed the literature procedure.

2. General procedure for synthesis of compounds (3a-3c)

The synthesis followed the literature procedure.

3. General procedure for synthesis of compounds (4a-4r, 5a-5c, 6a-6c, 9a-9o, 10a-10c).¹

To a G-4 process vial capped with Teflon septum was added 3-bromo flavone (0.5 mmol), boronic acid (0.6 mmol), Pd-complex (0.2 mol%, 1.0 mg), TBAB (0.12 mmol), K₂CO₃ (1.2 mmol) and 6 ml of ethanol. After a pre-stirring for one minute, the vial was subjected to microwave irradiation time of 18-20 minute at 60 °C. It was then cooled to room temperature, diluted with water, and extracted with EtOAc for three times. The organic phase was dried with Na₂SO₄ and concentrated to yield the product. The crude material was chromatographed on a silica gel column eluting with a mixture of hexane and ethyl acetate (8:2) to afford the product in (81-95%) yield. The purified products were identified by FTIR, NMR and HRMS spectra.

Docking Data :

Table 1. Autodock binding energy, no. of hydrogen bonds and residues involved in H-bonding interactions of most potent compounds for Estrogen receptor (PDB Code: 3EQM).

Entry	Comp. no.	Binding energy (kcal/mol)	K _i (nM)	No. of Hydrogen bonding	Residues involved in Hydrogen bonding interaction
1	4a	-10.75	13.09	2	Pro429, Val370
2	4b	-11.10	7.31	2	Pro429, Val370
3	4c	-10.77	12.68	1	Arg115
4	4d	-11.07	7.70	1	Pro429
5	4e	-11.47	3.89	1	Pro429
6	4f	-11.24	-13.32	1	Pro429
7	4g	-11.20	6.13	1	Arg115
8	4h	-11.24	5.73	1	Arg115
9	4i	-11.17	6.45	2 or 1	Arg115 or Pro429, Val370
10	4j	-10.77	14.0	1	Ser314
11	4k	-10.92	9.83	2	Pro429, Val370
12	4l	-10.73	13.61	2	Pro429, Val370
13	4m	-10.91	10.12	2	Pro429, Val370
14	4n	-11.27	5.50	2	Pro429, Val370
15	4o	-11.17	6.50	2	Pro429, Val370
16	4p	-11.12	7.08	2	Arg115, Thr310
17	4q	-10.98	8.89	2	Arg115, Thr310
18	4r	-11.26	5.62	1	Arg115
19	5a	-10.07	41.31	1	Val370
20	5b	-10.25	30.48	2	Pro429, Val370
21	5c	-10.60	16.94	1	Ser314
22	6a	-10.53	19.17	1	Ser314
23	6b	-10.52	19.44	1	Ser314
24	6c	-11.03	8.25	1	Ser314
25	9a	-11.75	2.43	3	Met364, Arg145, Arg435
26	9b	-11.28	5.37	0	--

27	9c	-11.79	2.29	2	Arg435, Gln367
28	9d	-11.45	4.04	1	Thr310
29	9e	-11.97	1.67	1	Arg435
30	9f	-11.87	2.0	0	--
31	9g	-12.01	1.58	1	Arg435
32	9h	-12.09	1.37	1	Arg145
33	9i	12.02	1.55	2	Arg145, Met364
34	9j	-11.88	1.96	1	Gln367, Ala438
35	9k	-11.37	4.67	0	--
36	9l	-11.33	4.93	0	--
37	9m	-11.53	3.54	2	Met364, Arg145
38	9n	-11.90	1.88	1	Arg145
39	9o	-11.08	7.50	2	Ser199, Met374
40	10a	-11.11	7.14	0	--
41	10b	-11.30	5.18	0	--
42	10c	-11.71	2.60	0	--
43	Flavone	-9.31	150.34	1	Met364
44	5-FU	-5.37	115.16	1	Arg192
45	CYC-PHO	-6.19	29.26	3	Ser314, Pro429, Ser314
46	CYC-HEXI	-9.0	254.88	2	Met364, Pro429

Flavone = 6-bromo-3-butyl-2-(4-hydroxyphenyl)-4H-chromen-4-one, 5-FU = 5-fluorouracil, CYC-PHO = cyclophosphamide, CYC-HEXI = cycloheximide.

Table 2. Autodock binding energy, no. of hydrogen bonds and residues involved in H-bonding interactions of most potent compounds forProgesterone (PDB Code: 1ZUC).

Entry	Compound no.	Binding energy (kcal/mol)	Ki (nM)	No of Hydrogen bonding	Residues involved in Hydrogen bonding interaction
1	4a	-9.55	100.14	1	Tyr777
2	4b	-9.58	94.58	1	Tyr777
3	4c	-9.57	97.30	0	--
4	4d	-10.18	34.52	1	Tyr777
5	4e	-10.21	32.66	1	Tyr777
6	4f	-9.73	73.99	1	Tyr777
7	4g	-9.32	148.20	1	Tyr777
8	4h	-9.21	176.34	2	Tyr777, his770
9	4i	-8.91	293.92	1	Ile699
10	4j	-9.56	98.40	1	Tyr777
11	4k	-9.44	121.30	1	Tyr777
12	4l	-9.34	168.88	1	Ile699
13	4m	-9.76	70.03	1	Tyr777
14	4n	-9.20	181.67	2	Tyr777, his770
15	4o	-9.26	163.71	1	Ile699
16	4 p	-9.18	186.89	2	Ile699, his770
17	4q	-8.71	411.34	1	Ile699
18	4r	-8.82	341.01	1	Ile699
19	5a	-10.44	22.10	0	--
20	5b	-10.77	12.86	0	--
21	5c	-10.03	25.36	0	--
22	6a	-10.35	25.99	0	--
23	6b	-10.46	21.42	0	--
24	6c	-10.21	32.65	0	--
25	9a	-9.32	146.53	1	Lys769
26	9b	-9.40	129.72	0	--

27	9c	-9.63	87.99	0	--
28	9d	-9.53	103.09	0	--
29	9e	-9.96	49.85	0	--
30	9f	-9.92	53.33	0	--
31	9g	-9.34	143.20	1	Lys769
32	9h	-9.21	176.78	1	Lys769
33	9i	-9.05	232.18	1	Lys769
34	9j	-9.40	128.42	1	Le699
35	9k	-9.42	124.98	0	--
36	9l	-9.35	140.83	0	--
37	9m	-10.01	45.80	0	--
38	9n	-10.35	25.88	0	--
39	9o	-9.94	51.75	0	--
40	10a	-9.32	148.27	0	--
41	10b	-9.50	109.12	1	Lys769
42	10c	-10.02	44.98	1	Ser728
43	Tanaproget	-10.39	24.20	1	Gln725
44	5-FU	-4.67	378.20	1	Gln725
45	CYC-PHO	-5.75	61.31	0	--
46	CYC-HEXI	-9.04	236.31	3	Gln725, Ser728, Arg766

Table 3. Comparative data of Progesterone (PDB Code: 1ZUC) and Estrogens receptor (PDB Code: 3EQM) of Binding energy and Ki.

Entry	Compound no.	Progesterone receptor (PDB Code: Z1UC)		Estrogens receptor (PDB Code: 3EQM)	
		Binding energy (kcal/mol)	Ki (nM)	Binding energy (kcal/mol)	Ki (nM)
1	4a	-9.55	100.14	-10.75	13.09
2	4b	-9.58	94.58	-11.10	7.31
3	4c	-9.57	97.30	-10.77	12.68
4	4d	-10.18	34.52	-11.07	7.70
5	4e	-10.21	32.66	-11.47	3.89
6	4f	-9.73	73.99	-11.24	-13.32
7	4g	-9.32	148.20	-11.20	6.13
8	4h	-9.21	176.34	-11.24	5.73
9	4i	-8.91	293.92	-11.17	6.45
10	4j	-9.56	98.40	-10.77	14.0
11	4k	-9.44	121.30	-10.92	9.83
12	4l	-9.34	168.88	-10.73	13.61
13	4m	-9.76	70.03	-10.91	10.12
14	4n	-9.20	181.67	-11.27	5.50
15	4o	-9.26	163.71	-11.17	6.50
16	4p	-9.18	186.89	-11.12	7.08
17	4q	-8.71	411.34	-10.98	8.89
18	4r	-8.82	341.01	-11.26	5.62
19	5a	-10.44	22.10	-10.07	41.31
20	5b	-10.77	12.86	-10.25	30.48
21	5c	-10.03	25.36	-10.60	16.94
22	6a	-10.35	25.99	-10.53	19.17
23	6b	-10.46	21.42	-10.52	19.44
24	6c	-10.21	32.65	-11.03	8.25
25	9a	-9.32	146.53	-11.75	2.43

26	9b	-9.40	129.72	-11.28	5.37
27	9c	-9.63	87.99	-11.79	2.29
28	9d	-9.53	103.09	-11.45	4.04
29	9e	-9.96	49.85	-11.97	1.67
30	9f	-9.92	53.33	-11.87	2.0
31	9g	-9.34	143.20	-12.01	1.58
32	9h	-9.21	176.78	-12.09	1.37
33	9i	-9.05	232.18	-12.02	1.55
34	9j	-9.40	128.42	-11.88	1.96
35	9k	-9.42	124.98	-11.37	4.67
36	9l	-9.35	140.83	-11.33	4.93
37	9m	-10.01	45.80	-11.53	3.54
38	9n	-10.35	25.88	-11.90	1.88
39	9o	-9.94	51.75	-11.08	7.50
40	10a	-9.32	148.27	-11.11	7.14
41	10b	-9.50	109.12	-11.30	5.18
42	10c	-10.02	44.98	-11.71	2.60
43	Tanaproget	-10.39	24.20	-	-
44	Flavone	-	-	-9.31	150.34
45	5-FU	-4.67	378.20	-5.37	115.16
46	CYC-PHO	-5.75	61.31	-6.19	29.26
47	CYC-HEXI	-9.04	236.31	-9.0	254.88

Flavone = 6-bromo-3-butyl-2-(4-hydroxyphenyl)-4H-chromen-4-one, 5-FU = 5-fluorouracil, CYC-PHO = cyclophosphamide, CYC-HEXI = cycloheximide.

Fig 1. Docked poses of some potent compounds complex with Progesterone (PDB Code: 1ZUC) and Estrogen receptor (PDB Code: 3EQM).

Characterization Data:

3-bromo-2-(4-methoxyphenyl)-4H-chromen-4-one (1a)

Yield: 89%; ^1H NMR (400 MHz, CDCl_3 , ppm): δ 8.27 (d, $J = 7$ Hz, 1H), 7.8 (d, $J = 8.5$ Hz, 2H), 7.70 (t, $J = 7.5$ Hz, 1H), 7.49-7.43 (m, 2H), 7.03 (d, $J = 8.5$ Hz, 2H), 3.90 (s, 3H).

3-bromo-2-(3,4,5-trimethoxyphenyl)-4H-chromen-4-one (1c)

Yield: 91%; ^1H NMR (400 MHz, CDCl_3 , ppm): δ 8.39 (dd, $J = 1.5, 10$ Hz, 1H), 7.89-7.85 (m, 1H), 7.75 (d, $J = 10$ Hz, 1H), 7.61-7.57 (m, 1H), 7.30

(s, 1H), 6.94 (s, 1H), 4.12 (s, 6H), 4.09 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3 , ppm): δ 178.6, 163.4, 156.3, 153.7, 133.9, 127.1, 126.7, 125.8, 125.5, 118.2, 107.5, 107.1, 103.8, 61.2, 56.5.

3-bromo-2-(4-methoxyphenyl)quinolin-4(1H)-one (2a)

Yield: 85%; ^1H NMR (400 MHz, CDCl_3 , ppm): δ 11.39 (s, 1H, D_2O exchangeable), 8.61 (d, $J = 5\text{ Hz}$, 1H), 8.07 (m, 2H), 7.61-7.56 (m, 1H), 7.42 (d, $J = 10\text{ Hz}$, 2H), 6.72 (d, $J = 10.5\text{ Hz}$, 2H), 3.68 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3 , ppm): δ 174.0, 160.8, 150.3, 148.1, 139.2, 132.3, 130.7, 126.9, 126.0, 124.5, 123.3, 118.8, 113.6, 55.4.

3-bromo-2-(3,4-dimethoxyphenyl)quinolin-4(1H)-one (2b)

Yield: 81%; ^1H NMR (400 MHz, CDCl_3 , ppm): δ 10.3 (s, 1H, D_2O exchangeable), 8.60 (s, 1H,), 8.18 (d, $J = 10\text{ Hz}$, 1H), 7.72 (t, $J = 10\text{ Hz}$, 1H), 7.66-7.62 (m, 1H), 7.34 (t, $J = 9.5\text{ Hz}$, 1H), 7.09 (s, 1H), 6.78 (d, $J = 10.5\text{ Hz}$, 1H), 3.85 (s, 6H).

3-bromo-2-(3,4,5-trimethoxyphenyl)quinolin-4(1H)-one (2c)

Yield: 79%; ^1H NMR (400 MHz, CDCl_3 , ppm): δ 11.2 (s, 1H, D_2O exchangeable), 8.13 (t, $J = 9.5\text{ Hz}$, 1H), 7.89 (t, $J = 10.5\text{ Hz}$, 1H), 7.67-7.63 (m, 1H), 7.33 (t, $J = 10\text{ Hz}$, 1H), 6.7 (s, 2H), 3.79 (s, 3H), 3.75 (s, 6H). ^{13}C NMR (100 MHz, CDCl_3 , ppm): δ 173.9, 152.9, 150.2, 139.1, 138.7, 132.4, 130.5, 126.1, 124.5, 123.3, 118.7, 106.3, 103.5, 60.9, 56.2.

3-bromo-2-(furan-2-yl)-4H-chromen-4-one (5)

Yield: 83%; ^1H NMR (400 MHz, CDCl_3 , ppm): δ 8.25-8.17 (m, 1H), 7.72-7.64 (m, 2H), 7.54-7.46 (m, 1H), 7.44-7.36 (m, 1H), 7.13 (d, $J = 4.5\text{ Hz}$, 1H), 6.67-6.59 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3 , ppm): δ 172.9, 155.2, 152.1, 146.1, 134.3, 126.5, 125.8, 125.3, 119.2, 117.9, 112.7, 106.0, 105.6.

3-bromo-2-(furan-2-yl)quinolin-4(1H)-one (6)

Yield: 85%; ^1H NMR (400 MHz, CDCl_3 , ppm): δ 8.25 (t, J = 10 Hz, 1H), 7.77-7.69 (m, 3H), 7.55 (t, J = 9.5, 1H), 6.70-6.66 (m, 2H), 1.74 (s, 1H, D_2O exchangeable).

6-bromo-3-butyl-2-(4-hydroxyphenyl)-4H-chromen-4-one (7a)

Yield: 0.877g (60%) as white solid; ^1H NMR (500 MHz, $\text{DMSO}-d_6$, ppm): δ 10.08 (s, 1H, D_2O exchangeable), 8.11 (d, J = 2.5 Hz, 1H), 7.89 (dd, J = 2.5, 9Hz, 1H), 7.58 (d, J = 9Hz, 1H), 7.48 (dd, J = 2, 7Hz, 2H), 6.92 (dd, J = 2, 6.5Hz, 2H), 2.45 (t, J = 8Hz, 2H), 1.45-1.41 (m, 2H), 1.27-1.20 (m, 2H), 0.80 (t, J = 7.5Hz, 3H). ^{13}C NMR (125 MHz, $\text{DMSO}-d_6$, ppm): δ 175.8, 162.0, 159.4, 154.3, 136.2, 130.2, 127.0, 123.5, 123.1, 120.8, 120.6, 117.2, 115.3, 30.4, 25.0, 22.2, 13.5. FTIR (KBr, $\nu = \text{cm}^{-1}$): 3474, 2953, 2910, 2850, 1640, 1626, 1550, 1435, 1368, 1277, 1217, 1132, 830, 660. HRMS (ESI+): m/z calcd for $\text{C}_{19}\text{H}_{17}\text{BrO}_3\text{K}$ $[\text{M}+\text{K}]^+$: 410.9992 found: 410.9991.

6-bromo-3-butyl-2-(4-methoxyphenyl)-4H-chromen-4-one (7b)

Yield: 1.52 g (92%) as yellow solid; ^1H NMR (500 MHz, CDCl_3 , ppm): δ 8.35 (s, 1H), 7.70 (d, J = 8Hz, 1H), 7.54 (d, J = 8.5Hz, 2H), 7.32 (d, J = 9Hz, 1H), 7.02 (d, J = 8.5Hz, 2H), 3.89 (s, 3H), 2.55 (t, J = 7.5Hz, 2H), 1.55-1.51 (m, 2H), 1.35-1.30 (m, 2H), 0.864 (t, J = 7.5Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3 , ppm): δ 177.2, 161.8, 161.0, 154.7, 136.1, 130.1, 128.4, 125.5, 124.2, 122.1, 119.8, 117.8, 113.9, 55.4, 31.2, 25.6, 22.8, 13.8. FTIR (KBr, $\nu = \text{cm}^{-1}$): 2953, 2923, 2856, 1645, 1628, 1598, 1519, 1446, 1362, 1253, 1107, 1035, 811, 727, 660, 533. HRMS (ESI+): m/z calcd for $\text{C}_{20}\text{H}_{20}\text{BrO}_3$ $[\text{M}+\text{H}]^+$: 387.0590 found: 387.0588.

6-bromo-3-butyl-2-(4-methoxyphenyl)chroman-4-one (10)

Yield: 1.66 g (90%) as pale yellow solid; ^1H NMR (500 MHz, CDCl_3 , ppm): δ 7.97 (d, J = 2.5Hz, 1H), 7.50 (dd, J = 2.5, 9Hz, 1H),

7.34 (d, $J = 8.5\text{Hz}$, 2H), 6.92 (d, $J = 8.5\text{Hz}$, 2H), 6.86 (d, $J = 8.5\text{Hz}$, 1H), 5.25 (d, $J = 10\text{Hz}$, 1H), 3.81 (s, 3H), 2.99-2.95 (m, 1H), 1.63-1.56 (m, 2H), 1.24-1.18 (m, 4H), 0.80 (t, $J = 7\text{Hz}$, 3H). ^{13}C NMR (125 MHz, CDCl_3 , ppm): δ 193.4, 160.1, 159.7, 138.6, 129.7, 129.6, 128.8, 122.2, 120.2, 114.3, 114.1, 83.3, 55.5, 50.6, 28.8, 26.0, 22.9, 13.9. FTIR (KBr, $\nu = \text{cm}^{-1}$): 2953, 2917, 2850, 1695, 1592, 1513, 1465, 1410, 1247, 1174, 1029, 823, 648, 533. HRMS (ESI+): m/z calcd. for $\text{C}_{20}\text{H}_{22}\text{BrO}_3$ $[\text{M}+\text{H}]^+$: 389.0746 found: 389.0745.

6-bromo-3-butyl-2-(4-hydroxyphenyl)quinolin-4(1H)-one (8a)

Yield: 1.5 g (60%) as white solid; ^1H NMR (500 MHz, DMSO-d_6 , ppm): δ 11.75 (s, 1H, D_2O exchangeable), 9.85 (s, 1H, D_2O exchangeable), 8.17 (d, $J = 2.5\text{Hz}$, 1H), 7.72 (dd, $J = 2.5, 9\text{Hz}$, 1H), 7.54 (d, $J = 9\text{Hz}$, 1H), 7.30 (d, $J = 8.5\text{Hz}$, 2H), 6.89 (d, $J = 8.5\text{Hz}$, 2H), 2.33 (t, $J = 8\text{Hz}$, 2H), 1.33-1.26 (m, 2H), 1.14-1.01 (m, 2H), 0.69 (t, $J = 7.5\text{Hz}$, 3H). ^{13}C NMR (125 MHz, DMSO-d_6 , ppm): δ 173.7, 158.6, 149.8, 137.9, 134.1, 131.3, 130.1, 126.8, 124.9, 120.9, 120.1, 115.8, 115.2, 30.7, 25.4, 22.1, 13.6. FTIR (KBr, $\nu = \text{cm}^{-1}$): 3277, 3158, 2956, 2928, 1665, 1651, 1517, 1495, 1366, 1273, 1170, 890, 824, 648, 588. HRMS (ESI+): m/z calcd for $\text{C}_{19}\text{H}_{19}\text{BrNO}_2$ $[\text{M}+\text{H}]^+$: 372.0593 found: 372.0590.

6-bromo-3-butyl-2-(4-methoxyphenyl)quinolin-4(1H)-one (8b)

Yield: 2.6 g (95%) as brown solid; ^1H NMR (500 MHz, DMSO-d_6 , ppm): δ 11.66 (s, 1H, D_2O exchangeable), 8.18 (s, 1H), 7.74 (d, $J = 8\text{Hz}$, 1H), 7.55 (d, $J = 9\text{Hz}$, 1H), 7.45 (d, $J = 7.5\text{Hz}$, 2H), 7.11 (d, $J = 7.5\text{Hz}$, 2H), 3.83 (s, 3H), 2.33 (t, $J = 7.5\text{Hz}$, 2H), 1.37-1.30 (m, 2H), 1.15-1.11 (m, 2H), 0.72 (t, $J = 7.5\text{Hz}$, 3H). ^{13}C NMR (125 MHz, DMSO-d_6 , ppm): δ 175.1, 160.0, 148.3, 138.2, 133.9, 131.3, 130.1, 127.1, 124.8, 120.7, 120.0, 115.1, 113.9, 55.4, 30.8, 25.4, 22.2, 13.6. FTIR (KBr, $\nu = \text{cm}^{-1}$): 3256, 2940, 2856, 1663, 1647, 1500, 1296, 1252, 1171, 1035. HRMS (ESI+): m/z calcd for $\text{C}_{20}\text{H}_{21}\text{BrNO}_2$ $[\text{M}+\text{H}]^+$: 386.0750 found: 386.0750.

2-(4-aminophenyl)-6-bromo-3-butyl-4H-chromen-4-one (8c)

Yield: 1.3 g (95%) as brown solid; ^1H NMR (500 MHz, DMSO- d_6 , ppm): δ 11.65 (s, 1H, D_2O exchangeable), 8.18 (d, $J = 2\text{ Hz}$, 1H), 7.73 (dd, $J = 2, 8.5\text{ Hz}$, 1H), 7.56 (d, $J = 9\text{ Hz}$, 1H), 7.29 (d, $J = 8\text{ Hz}$, 2H), 6.92 (d, $J = 7.5\text{ Hz}$, 2H), 2.36 (t, $J = 8.5\text{ Hz}$, 2H), 1.38-1.32 (m, 2H), 1.19-1.13 (m, 2H), 0.75 (t, $J = 7, 3\text{ Hz}$). ^{13}C NMR (125 MHz, DMSO- d_6 , ppm): δ 175.9, 149.6, 138.6, 137.2, 135.3, 131.9, 131.0, 127.7, 125.1, 121.7, 121.5, 121.1, 116.9, 31.4, 25.9, 22.7, 14.3. FTIR (KBr, $\nu = \text{cm}^{-1}$): 3416, 3351, 3185, 2955, 2926, 2855, 1650, 1633, 1601, 1577, 1508, 1393, 1289, 1263, 1240, 1182, 835, 759, 688. HRMS (ESI $^{+}$): m/z calcd. for $\text{C}_{19}\text{H}_{19}\text{BrN}_2\text{NaO}$ $[\text{M}+\text{Na}]^{+}$: 393.0572 found: 393.0573.

(4-methyl-2-oxo-4-vinyl-2,4-dihydro-1H-benzo[d][1,3]oxazin-6-yl)boronic acid (3a)

Yield: 1.45 g (81%) as white solid; ^1H NMR (500 MHz, DMSO- d_6 , ppm): δ 10.29 (s, 1H, D_2O exchangeable), 7.97 (s, 2H, D_2O exchangeable), 7.68 (d, $J = 10\text{ Hz}$, 2H), 6.83 (d, $J = 8\text{ Hz}$, 1H), 6.01 (dd, $J = 10.5, 18\text{ Hz}$, 1H), 5.16 (d, $J = 10.5\text{ Hz}$, 1H), 4.98 (d, $J = 17\text{ Hz}$, 1H), 1.73 (s, 3H). ^{13}C NMR (100 MHz, DMSO- d_6 , ppm): δ 153.4, 140.6, 137.4, 136.5, 131.4, 128.9, 123.9, 116.2, 115.0, 85.1, 26.3. FTIR (KBr, $\nu = \text{cm}^{-1}$): 3408, 3279, 2978, 2930, 1718, 1645, 1513, 1355, 1248, 1088, 925. HRMS (ESI $^{+}$): m/z calcd for $\text{C}_{11}\text{H}_{13}\text{BNO}_4$ $[\text{M}+\text{H}]^{+}$: 234.0932 found: 234.0930.

(4-allyl-4-methyl-2-oxo-2,4-dihydro-1H-benzo[d][1,3]oxazin-6-yl)boronic acid (3b)

Yield: 1.5 g (80%) as white solid; ^1H NMR (500 MHz, DMSO- d_6 , ppm): δ 10.16 (s, 1H, D_2O exchangeable), 7.92 (s, 2H, D_2O exchangeable), 7.61 (t, $J = 3.5\text{ Hz}$, 2H), 6.77 (d, $J = 8.5\text{ Hz}$, 1H), 5.62-5.56 (m, 1H), 5.07-5.02 (m, 2H), 2.66-2.62 (m, 1H), 2.55-2.51 (m, 1H), 1.55 (s, 3H). ^{13}C NMR (100 MHz, DMSO- d_6 , ppm): δ 153.2, 137.3, 136.1, 132.8, 131.2, 128.7, 124.6, 121.2,

114.9, 85.9, 45.1, 27.7. FTIR (KBr, $\nu = \text{cm}^{-1}$): 3430, 3158, 2978, 2934, 1720, 1656, 1383, 1342, 1257, 1109, 1042. HRMS (ESI+): m/z calcd for $\text{C}_{12}\text{H}_{16}\text{BNO}_4$ $[\text{M}+\text{H}]^+$: 248.1088 found: 248.1087.

(4-methyl-2-oxo-4-pentyl-2,4-dihydro-1H-benzo[d][1,3]oxazin-6-yl)boronic acid (3c)

Yield: 1.28g (95%) as yellow solid; ^1H NMR (500 MHz, CDCl_3 , ppm): δ 9.76 (s, 1H, D_2O exchangeable), 7.41 (d, $J = 8.5$ Hz, 1H), 7.18 (s, 1H), 6.86 (d, $J = 8.5$ Hz, 1H), 2.03-1.98 (m, 2H), 1.75 (s, 3H), 1.49-1.35 (m, 6H), 0.94 (t, $J = 7$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3 , ppm): δ 153.0, 133.6, 131.8, 127.0, 126.9, 116.5, 115.8, 85.5, 41.1, 31.9, 27.2, 23.3, 22.6, 14.8. HRMS (ESI+): m/z calcd. for $\text{C}_{14}\text{H}_{21}\text{BNO}_4$ $[\text{M}+\text{H}]^+$: 278.1558.

6-(2-(4-methoxyphenyl)-4-oxo-4H-chromen-3-yl)-4-methyl-4-vinyl-1H-benzo[d][1,3]oxazin-2(4H)-one (4a)

Yield: 79% as brown solid, mp 160-168 $^{\circ}\text{C}$; ^1H NMR (500 MHz, CDCl_3 , ppm): δ 9.08 (s, 1H, D_2O exchangeable), 8.27 (d, $J = 8$ Hz, 1H), 7.80 (d, $J = 9$ Hz, 1H), 7.7 (t, $J = 8.5$ Hz, 1H), 7.48 (d, $J = 8$ Hz, 1H), 7.44 (t, $J = 7.5$ Hz, 1H), 7.37 (dd, $J = 1.5, 8.5$ Hz, 1H), 7.13 (d, $J = 8$ Hz, 1H), 7.08-7.02 (m, 3H), 6.87 (d, $J = 8$ Hz, 1H), 6.06-5.97 (m, 1H), 5.26-5.06 (m, 2H), 3.90 (s, 3H), 1.82 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3 , ppm): δ 174.8, 164.5, 161.8, 155.9, 153.0, 139.4, 134.2, 132.3, 131.5, 129.4, 127.5, 127.3, 126.8, 125.9, 124.5, 123.6, 120.0, 117.7, 115.7, 114.8, 113.8, 113.7, 87.7, 55.6, 25.7. FTIR (KBr, $\nu = \text{cm}^{-1}$): 3256, 2955, 1709, 1655, 1615, 1587, 1505, 1463, 1345, 1333, 1306. HRMS (ESI+): m/z calcd. for $\text{C}_{27}\text{H}_{22}\text{NO}_5$ $[\text{M}+\text{H}]^+$: 440.1492 found: 440.1495.

6-(2-(3,4-dimethoxyphenyl)-4-oxo-4H-chromen-3-yl)-4-methyl-4-vinyl-1H-benzo[d][1,3]oxazin-2(4H)-one (4b)

Yield: 77% as brown solid, mp 139-143 $^{\circ}\text{C}$; ^1H NMR (500 MHz, CDCl_3 , ppm): δ 8.93 (s, 1H, D_2O exchangeable), 8.28 (d, $J = 8$ Hz, 1H),

7.70 (t, $J = 8$ Hz, 1H), 7.51 (t, $J = 8$ Hz, 2H), 7.46 (d, $J = 7.5$ Hz, 1H), 7.35 (dd, $J = 1.5, 8$ Hz, 1H), 7.13 (d, $J = 7.5$ Hz, 1H), 7.06 (t, $J = 7.5$ Hz, 1H), 7.00 (d, $J = 8.5$ Hz, 1H), 6.87 (d, $J = 7.5$ Hz, 1H), 6.05-5.96 (m, 1H), 5.25-5.05 (m, 2H), 3.95 (s, 6H), 1.81 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3 , ppm): δ 173.4, 161.9, 155.7, 151.6, 148.6, 139.4, 134.6, 134.2, 132.3, 129.4, 127.5, 126.7, 125.8, 125.2, 124.5, 123.8, 123.5, 123.3, 121.9, 117.9, 114.8, 112.6, 110.7, 108.7, 83.8, 56.2, 25.7. FTIR (KBr, $\nu = \text{cm}^{-1}$): 3267, 2975, 1713, 1652, 1611, 1557, 1505, 1463, 1350, 1328, 1306. HRMS (ESI+): m/z calcd. for $\text{C}_{28}\text{H}_{23}\text{NNaO}_6$ $[\text{M}+\text{Na}]^+$: 492.1417 found : 492.1431.

4-methyl-6-(4-oxo-2-(3,4,5-trimethoxyphenyl)-4H-chromen-3-yl)-4-vinyl-1H-benzo[d][1,3]oxazin-2(4H)-one (4c)

Yield: 80% as brown solid, mp 140-145 °C; ^1H NMR (500 MHz, CDCl_3 , ppm): δ 8.95 (s, 1H, D_2O exchangeable), 8.28 (d, $J = 8$ Hz, 1H), 7.72-7.68 (m, 1H), 7.51 (s, 1H), 7.36 (dd, $J = 2, 8.5$ Hz, 1H), 7.12 (d, $J = 7.5$ Hz, 1H), 7.06 (t, $J = 7.5$ Hz, 1H), 7.00 (d, $J = 8.5$ Hz, 1H), 6.87 (d, $J = 8$ Hz, 1H), 6.04-5.96 (m, 1H), 5.25-5.05 (m, 2H), 3.96 (s, 3H), 3.95 (s, 6H), 1.81 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3 , ppm): δ 173.3, 161.9, 155.6, 153.1, 139.4, 134.4, 132.3, 129.4, 127.9, 127.5, 126.7, 125.9, 124.5, 123.5, 118.0, 115.7, 114.7, 107.1, 82.4, 61.2, 56.5, 25.7. FTIR (KBr, $\nu = \text{cm}^{-1}$): 3269, 2959, 1713, 1690, 1652, 1621, 1555, 1513, 1473, 1359, 1336, 1321. HRMS (ESI+): m/z calcd. for $\text{C}_{29}\text{H}_{26}\text{NO}_7$ $[\text{M}+\text{H}]^+$: 522.1523 found : 522.1501.

4-allyl-6-(2-(4-methoxyphenyl)-4-oxo-4H-chromen-3-yl)-4-methyl-1H-benzo[d][1,3]oxazin-2(4H)-one (4d)

Yield: 82% as brown solid, mp 124-125 °C; ^1H NMR (500 MHz, CDCl_3 , ppm): δ 9.74 (s, 1H, D_2O exchangeable), 8.27 (d, $J = 8$ Hz, 1H), 7.72 (s, 1H), 7.53-7.50 (m, 1H), 7.46-7.42 (m, 1H), 7.31 (d, $J = 8.5$ Hz, 2H), 7.17 (s, 1H), 7.01 (s, 2H), 7.00 (d, $J = 8.5$ Hz, 1H), 6.78 (d, $J = 8.5$ Hz, 1H), 5.75-5.66

(m, 1H), 5.13-5.01 (m, 2H), 3.9 (s, 3H), 2.69-2.60 (m, 2H), 1.67 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3 , ppm): δ 173.5, 162.0, 155.7, 152.5, 151.6, 148.6, 135.2, 134.3, 133.7, 132.0, 131.1, 127.1, 125.9, 123.3, 121.8, 120.5, 117.9, 116.4, 115.7, 112.5, 110.6, 108.6, 84.3, 56.3, 45.5, 26.3. FTIR (KBr, $\nu = \text{cm}^{-1}$): 3267, 2975, 1713, 1692, 1652, 1611, 1557, 1505, 1463, 1350, 1328, 1306. HRMS (ESI+): m/z calcd. for $\text{C}_{28}\text{H}_{24}\text{NO}_5$ $[\text{M}+\text{H}]^+$: 454.1648 found : 454.1636.

4-allyl-6-(2-(3,4-dimethoxyphenyl)-4-oxo-4H-chromen-3-yl)-4-methyl-1H-

benzo[d][1,3]oxazin-2(4H)-one (4e)

Yield: 84% as brown solid, mp 117-119 °C; ^1H NMR (500 MHz, CDCl_3 , ppm): δ 9.40 (s, 1H, D_2O exchangeable), 8.29 (d, $J = 8\text{ Hz}$, 1H), 7.91 (s, 1H), 7.27 (t, $J = 8\text{ Hz}$, 1H), 7.53-7.45 (m, 2H), 7.32 (d, $J = 8\text{ Hz}$, 1H), 7.18 (s, 1H), 7.10 (d, $J = 18\text{ Hz}$, 2H), 6.79 (d, $J = 8.5\text{ Hz}$, 1H), 5.73-5.65 (m, 1H), 5.14-5.09 (m, 2H), 3.93 (d, 6H), 2.67-2.63 (m, 2H), 1.68 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3 , ppm): δ 173.5, 162.0, 155.7, 152.6, 151.6, 148.6, 135.2, 134.3, 133.7, 132.0, 131.1, 127.1, 126.6, 125.9, 125.1, 123.4, 121.8, 120.5, 118.0, 116.4, 115.7, 112.5, 110.7, 108.7, 84.6, 56.3, 56.2, 45.5, 26.3. FTIR (KBr, $\nu = \text{cm}^{-1}$): 3265, 2975, 1713, 1652, 1641, 1555, 1513, 1473, 1349, 1331, 1311. HRMS (ESI+): m/z calcd. for $\text{C}_{29}\text{H}_{25}\text{NNaO}_6$ $[\text{M}+\text{Na}]^+$: 506.1574 found: 506.1575.

4-allyl-4-methyl-6-(4-oxo-2-(3,4,5-trimethoxyphenyl)-4H-chromen-3-yl)-1H-

benzo[d][1,3]oxazin-2(4H)-one (4f)

Yield: 83% as brown solid, mp 118-120 °C; ^1H NMR (500 MHz, CDCl_3 , ppm): δ 10.08 (s, 1H, D_2O exchangeable), 8.19 (dd, $J = 8\text{ Hz}$, 1H), 7.75 (s, 1H), 7.69-7.64 (m, 1H), 7.55-7.47 (m, 1H), 7.43-7.35 (m, 1H), 7.12-7.10 (m, 2H), 7.04 (s, 1H), 6.80-6.78 (m, 1H), 5.68-5.60 (m, 1H), 5.08-5.04 (m, 2H), 3.90 (s, 6H), 3.8 (s, 3H), 2.64-2.54 (m, 2H), 1.62 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3 , ppm): δ 173.4, 162.0, 153.1, 152.4, 140.6, 135.0, 134.4, 133.7, 132.0, 131.1, 127.9, 127.2,

126.7, 126.6, 126.0, 121.8, 121.4, 120.5, 118.0, 116.4, 115.7, 107.2, 84.4, 61.2, 56.6, 45.5, 26.3. FTIR (KBr, $\nu = \text{cm}^{-1}$): 3235, 2934, 1716, 1686, 1645, 1592, 1463, 1406. HRMS (ESI⁺): m/z calcd. for $\text{C}_{30}\text{H}_{27}\text{NNaO}_7$ $[\text{M}+\text{Na}]^+$: 536.1679 found : 536.1678.

6-(2-(4-methoxyphenyl)-4-oxo-4H-chromen-3-yl)-4-methyl-4-pentyl-1H-benzo

[d][1,3]oxazin-2(4H)-one (4g)

Yield: 81% as white solid, mp 113-114 °C; ^1H NMR (500 MHz, CDCl_3 , ppm): δ 9.90 (s, 1H, D_2O exchangeable), 8.14 (dd, $J = 8$ Hz, 1H), 7.78 (d, $J = 8.5$ Hz, 1H), 7.67 (t, $J = 8$ Hz, 1H), 7.42 (m, 2H), 7.28 (d, $J = 8.5$ Hz, 1H), 7.15 (s, 2H), 6.99 (d, $J = 8.5$ Hz, 2H), 6.79 (d, $J = 8.5$ Hz, 1H), 3.86 (s, 3H), 1.91-1.87 (m, 2H), 1.64 (s, 3H), 1.37-1.24 (m, 6H), 0.82 (t, $J = 8$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3 , ppm): δ 178.0, 155.9, 155.4, 152.8, 146.4, 146.0, 133.9, 133.7, 131.7, 127.0, 126.9, 125.8, 125.3, 124.2, 118.0, 116.5, 115.7, 113.3, 112.6, 105.5, 85.4, 41.0, 31.8, 27.1, 23.2, 22.5, 14.1. FTIR (KBr, $\nu = \text{cm}^{-1}$): 3228, 2934, 2869, 1705, 1687, 1615, 1463, 1406, 1352. HRMS (ESI⁺): m/z calcd. for $\text{C}_{30}\text{H}_{29}\text{NNaO}_5$ $[\text{M}+\text{Na}]^+$: 506.1937 found : 506.1921.

6-(2-(3,4-dimethoxyphenyl)-4-oxo-4H-chromen-3-yl)-4-methyl-4-pentyl-1H-

benzo[d][1,3]oxazin-2(4H)-one (4h)

Yield: 86% as white solid, mp 109-110 °C; ^1H NMR (500 MHz, CDCl_3 , ppm): δ 9.61 (s, 1H, D_2O exchangeable), 7.80-7.69 (m, 1H), 7.51 (t, $J = 7.5$ Hz, 1H), 7.46-7.41 (m, 1H), 7.31 (d, $J = 8.5$ Hz, 1H), 7.15 (s, 1H), 6.78 (d, $J = 8$ Hz, 1H), 3.95-3.96 (d, 6H), 1.92-1.88 (m, 2H), 1.65 (s, 3H), 1.37-1.28 (m, 8H), 0.84 (t, $J = 8$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3 , ppm): δ 173.4, 161.9, 152.7, 152.9, 151.6, 148.6, 134.2, 133.6, 131.8, 127.0, 126.9, 126.7, 125.8, 125.2, 123.3, 121.8, 117.9, 116.5, 115.8, 112.6, 110.7, 108.7, 85.5, 56.3, 56.2, 41.0, 31.9, 27.2, 23.3, 22.5, 14.1. HRMS (ESI⁺): m/z calcd. for $\text{C}_{31}\text{H}_{31}\text{NNaO}_6$ $[\text{M}+\text{Na}]^+$: 536.2043 found: 536.2034.

4-methyl-6-(4-oxo-2-(3,4,5-trimethoxyphenyl)-4H-chromen-3-yl)-4-pentyl-1H-benzo[d][1,3]oxazin-2(4H)-one (4i)

Yield: 80% as white solid, mp 155-158 °C; ^1H NMR (500 MHz, CDCl_3 , ppm): δ 9.63 (s, 1H, D_2O exchangeable), 8.28 (d, $J = 8\text{ Hz}$, 1H), 7.72 (t, $J = 8\text{ Hz}$, 1H), 7.52-7.44 (m, 2H), 7.31 (d, $J = 8.5\text{ Hz}$, 1H), 7.16 (s, 1H), 7.09 (s, 2H), 6.79 (d, $J = 8\text{ Hz}$, 1H), 3.93 (d, 9H), 1.92-1.89 (m, 2H), 1.65 (s, 3H), 1.31-1.23 (m, 6H), 0.83 (t, $J = 7\text{ Hz}$, 3H). ^{13}C NMR (125 MHz, CDCl_3 , ppm): δ 173.3, 161.9, 155.6, 153.1, 152.9, 140.6, 134.4, 133.6, 131.8, 127.9, 127.0, 126.9, 126.7, 126.0, 121.8, 118.0, 116.5, 115.8, 109.1, 107.2, 85.5, 61.1, 56.5, 41.0, 31.8, 27.2, 23.2, 22.5, 14.1. HRMS (ESI $^+$): m/z calcd. for $\text{C}_{32}\text{H}_{33}\text{NNaO}_7$ $[\text{M}+\text{Na}]^+$: 566.2149 found: 566.2151.

6-(2-(4-methoxyphenyl)-4-oxo-1,4-dihydroquinolin-3-yl)-4-methyl-4-vinyl-1H-benzo[d][1,3]oxazin-2(4H)-one (4j)

Yield: 83% as brown solid, mp 159-161 °C; ^1H NMR (500 MHz, CDCl_3 , ppm): δ 9.49 (s, 1H, D_2O exchangeable), 9.08 (s, 1H, D_2O exchangeable), 8.28 (d, $J = 8\text{ Hz}$, 1H), 7.79 (d, $J = 9\text{ Hz}$, 1H), 7.70 (t, $J = 8.5\text{ Hz}$, 1H), 7.37 (dd, $J = 1.5, 8.5\text{ Hz}$, 1H), 7.13 (d, $J = 8\text{ Hz}$, 1H), 7.08-7.02 (m, 2H), 6.87 (d, $J = 8\text{ Hz}$, 1H), 6.84 (d, $J = 8\text{ Hz}$, 1H), 6.06-6.00 (m, 1H), 5.26-5.06 (m, 2H), 3.90 (s, 3H), 1.82 (t, $J = 8\text{ Hz}$, 3H). ^{13}C NMR (125 MHz, CDCl_3 , ppm): δ 174.8, 164.5, 161.8, 155.9, 139.4, 138.7, 134.6, 134.2, 132.3, 131.5, 129.4, 127.5, 123.6, 120.0, 117.7, 115.7, 114.8, 113.7, 87.7, 55.6, 25.7. FTIR (KBr, $\nu = \text{cm}^{-1}$): 3305, 3267, 2975, 1714, 1692, 1641, 1557, 1505, 1463. HRMS (ESI $^+$): m/z calcd. for $\text{C}_{27}\text{H}_{22}\text{N}_2\text{NaO}_4$ $[\text{M}+\text{Na}]^+$: 461.1471 found: 461.1467.

6-(2-(3,4-dimethoxyphenyl)-4-oxo-1,4-dihydroquinolin-3-yl)-4-methyl-4-vinyl-1H-benzo[d][1,3]oxazin-2(4H)-one (4k)

Yield: 85% as Brown solid, mp 147-150 °C; ^1H NMR (500 MHz, CDCl_3 , ppm): δ 9.31 (s, 1H, D_2O exchangeable), 8.93 (s, 1H, D_2O

exchangeable), 8.28 (d, $J = 8$ Hz, 1H), 7.70 (t, $J = 8$ Hz, 1H), 7.51 (t, $J = 8.5$ Hz, 2H), 7.46 (d, $J = 8$ Hz, 1H), 7.36 (dd, $J = 1.5, 8.5$ Hz, 1H), 7.13 (d, $J = 7.5$ Hz, 1H), 7.06 (t, $J = 7.5$ Hz, 1H), 6.99 (d, $J = 8.5$ Hz, 1H), 6.87 (d, $J = 7.5$ Hz, 1H), 6.05-5.98 (m, 1H), 5.20-5.05 (m, 2H), 3.95 (s, 6H), 1.81 (t, $J = 8$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3 , ppm): δ 174.8, 164.5, 161.8, 156.0, 153.2, 139.4, 138.7, 134.6, 134.2, 133.8, 132.3, 131.5, 129.4, 127.5, 126.9, 125.9, 124.5, 123.8, 123.6, 120.1, 117.7, 115.8, 114.8, 113.7, 84.3, 55.8, 25.8. HRMS (ESI⁺): m/z calcd. for $\text{C}_{28}\text{H}_{24}\text{N}_2\text{NaO}_5$ $[\text{M}+\text{Na}]^+$: 491.1577 found : 491.1572.

4-methyl-6-(4-oxo-2-(3,4,5-trimethoxyphenyl)-1,4-dihydroquinolin-3-yl)-4-vinyl-1H-benzo[d][1,3]oxazin-2(4H)-one (4l)

Yield: 87% as Brown solid, mp 112-115 °C; ^1H NMR (500 MHz, CDCl_3 , ppm): δ 9.31 (s, 1H, D_2O exchangeable), 8.93 (s, 1H, D_2O exchangeable), 8.26 (d, $J = 8$ Hz, 1H), 7.70-7.68 (m, 1H), 7.50 (s, 1H), 7.34 (dd, $J = 2, 8.5$ Hz, 1H), 7.11 (d, $J = 7.5$ Hz, 1H), 7.04 (t, $J = 7.5$ Hz, 1H), 6.98 (d, $J = 8.5$ Hz, 1H), 6.86 (d, $J = 8$ Hz, 1H), 6.03-5.94 (m, 1H), 5.23-5.03 (m, 2H), 3.95 (s, 3H), 3.94 (s, 6H), 1.79 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3 , ppm): δ 174.7, 164.1, 161.5, 156.5, 153.6, 139.1, 138.5, 134.1, 134.0, 133.6, 132.2, 131.4, 129.3, 127.4, 126.8, 125.4, 124.2, 123.7, 123.5, 120.1, 117.5, 115.7, 84.3, 60.5, 55.8, 25.7. HRMS (ESI⁺): m/z calcd. for $\text{C}_{29}\text{H}_{26}\text{N}_2\text{NaO}_6$ $[\text{M}+\text{Na}]^+$: 521.1683 found : 521.1682.

4-allyl-6-(2-(4-methoxyphenyl)-4-oxo-1,4-dihydroquinolin-3-yl)-4-methyl-1H-benzo[d][1,3]oxazin-2(4H)-one (4m)

Yield: 76% as Brown solid, mp 138-141 °C; ^1H NMR (500 MHz, CDCl_3 , ppm): δ 9.61 (s, 1H, D_2O exchangeable), 8.26 (dd, $J = 1, 8$ Hz, 1H), 7.80 (d, $J = 8.5$ Hz, 2H), 7.68 (t, $J = 7.5$ Hz, 1H), 7.48 (d, $J = 8.5$ Hz, 1H), 7.43 (t, $J = 7$ Hz, 1H), 7.32 (dd, $J = 1.5, 8.5$ Hz, 1H), 7.18 (s, 1H), 7.02 (d, $J = 8.5$ Hz, 2H), 6.77 (d, $J = 8.5$ Hz, 1H), 6.23 (s, 1H, D_2O exchangeable), 5.72-5.65 (m, 1H), 5.14-5.09 (m,

2H), 3.89 (s, 3H, 2.70-2.62 (m, 2H), 1.68 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3 , ppm): δ 175.0, 164.6, 161.8, 155.9, 152.5, 134.3, 133.7, 132.0, 131.9, 131.5, 131.1, 127.2, 127.1, 126.8, 126.6, 125.9, 120.5, 120.0, 117.7, 116.6, 115.7, 113.7, 84.3, 55.6, 45.5, 26.3. FTIR (KBr, $\nu = \text{cm}^{-1}$): 3394, 3293, 2957, 2930, 1712, 1686, 1646, 1610, 1572, 1355. HRMS (ESI $^{+}$): m/z calcd. for $\text{C}_{28}\text{H}_{24}\text{N}_2\text{NaO}_4$ $[\text{M}+\text{Na}]^{+}$: 475.1628 found : 475.1631.

4-allyl-6-(2-(3,4-dimethoxyphenyl)-4-oxo-1,4-dihydroquinolin-3-yl)-4-methyl-1H-benzo[d][1,3]oxazin-2(4H)-one (4n)

Yield: 77% as Brown solid, mp 160-165 °C; ^1H NMR (500 MHz, CDCl_3 , ppm): δ 9.66 (s, 1H, D_2O exchangeable), 8.28 (dd, $J = 1, 8$ Hz, 1H), 7.74-7.71 (m, 2H), 7.52 (d, $J = 8$ Hz, 1H), 7.46 (t, $J = 7$ Hz, 1H), 7.31 (dd, $J = 1.5, 8$ Hz, 1H), 7.17 (d, $J = 1.5$ Hz, 1H), 7.09 (s, 2H), 6.78 (d, $J = 8.5$ Hz, 1H), 5.71-5.67 (m, 1H), 5.52 (s, 1H, D_2O exchangeable), 5.13-5.09 (m, 2H), 3.94 (s, 3H), 2.69-2.60 (m, 2H), 1.67 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3 , ppm): δ 174.1, 152.4, 150.5, 150.3, 148.5, 139.4, 135.2, 133.7, 132.2, 132.0, 131.1, 127.2, 126.6, 124.4, 123.5, 122.3, 121.9, 120.5, 116.4, 115.7, 114.2, 113.4, 112.6, 110.6, 84.3, 56.1, 56.0, 45.5, 26.3. FTIR (KBr, $\nu = \text{cm}^{-1}$): 3375, 3290, 2987, 2927, 1713, 1677, 1648, 1601, 1407, 1352. HRMS (ESI $^{+}$): m/z calcd. for $\text{C}_{29}\text{H}_{26}\text{N}_2\text{NaO}_5$ $[\text{M}+\text{Na}]^{+}$: 505.1733 found : 505.1733.

4-allyl-4-methyl-6-(4-oxo-2-(3,4,5-trimethoxyphenyl)-1,4-dihydroquinolin-3-yl)-1H-benzo[d][1,3]oxazin-2(4H)-one (4o)

Yield: 78% as Brown solid, mp 178-180 °C; ^1H NMR (500 MHz, CDCl_3 , ppm): δ 9.71 (s, 1H, D_2O exchangeable), 9.20 (s, 1H, D_2O exchangeable), 8.24 (d, $J = 8$ Hz, 1H), 7.83 (d, $J = 8$ Hz, 1H), 7.63-7.58 (m, 2H), 7.34-7.28 (m, 2H), 7.15 (s, 1H), 7.03 (s, 1H), 6.78 (d, $J = 8.5$ Hz, 1H), 5.71-5.63 (m, 1H), 5.12-5.07 (m, 2H), 3.77 (s, 9H), 2.67-2.58 (m, 2H), 1.65 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3 , ppm): δ 173.9, 152.8, 152.3, 150.5, 139.4, 138.9, 135.1, 133.7, 131.9, 131.1, 130.3, 127.1,

126.5, 126.0, 124.5, 123.4, 121.7, 120.4, 118.7, 116.4, 115.6, 106.8, 84.2, 60.9, 56.3, 45.5, 26.3. HRMS (ESI⁺): m/z calcd. for $C_{30}H_{28}N_2NaO_6$ $[M+Na]^+$: 535.1839 found: 535.1841.

6-(2-(4-methoxyphenyl)-4-oxo-1,4-dihydroquinolin-3-yl)-4-methyl-4-pentyl-1H-

benzo[d][1,3]oxazin-2(4H)-one (4p)

Yield: 79% as white solid, mp 145-148 °C; ¹H NMR (500 MHz, CDCl₃, ppm): δ 9.90 (s, 1H, D₂O exchangeable), 8.24 (d, J = 8 Hz, 1H), 7.78 (d, J = 8.5 Hz, 1H), 7.65 (t, J = 7.5 Hz, 1H), 7.46-7.39 (m, 2H), 7.29 (d, J = 8.5 Hz, 1H), 7.15 (s, 2H), 7.00 (d, J = 8.5 Hz, 2H), 6.80 (d, J = 8.5 Hz, 1H), 5.82 (s, 1H, D₂O exchangeable), 3.86 (s, 3H), 1.92-1.87 (m, 2H), 1.64 (s, 3H), 1.37-1.29 (m, 6H), 0.82 (s, 3H). ¹³C NMR (125 MHz, CDCl₃, ppm): δ 174.9, 164.5, 161.8, 155.9, 153.0, 145.1, 134.2, 131.7, 131.5, 127.2, 127.0, 126.9, 126.8, 125.9, 120.0, 117.6, 116.5, 115.7, 113.7, 85.4, 55.6, 41.0, 31.8, 27.1, 23.2, 22.5, 14.0. FTIR (KBr, ν = cm⁻¹): 3375, 3290, 2987, 2927, 1710, 1677, 1643, 1407, 1352. HRMS (ESI⁺): m/z calcd. for $C_{30}H_{30}N_2NaO_4$ $[M+Na]^+$: 505.2097 found : 505.2096.

6-(2-(3,4-dimethoxyphenyl)-4-oxo-1,4-dihydroquinolin-3-yl)-4-methyl-4-pentyl-1H-

benzo[d][1,3]oxazin-2(4H)-one (4q)

Yield: 77% as white solid, mp 117-118 °C; ¹H NMR (500 MHz, DMSO, ppm): δ 12.18, (s, 1H, D₂O exchangeable), 10.28 (s, 1H, D₂O exchangeable), 8.16 (d, J = 8 Hz, 1H), 7.68 (d, J = 3.5 Hz, 2H), 7.41-7.38 (m, 3H), 7.23-7.13 (m, 2H), 7.02 (s, 1H), 6.82 (d, J = 8.5 Hz, 1H), 3.84 (s, 3H), 3.82 (s, 3H), 1.91 (t, J = 13 Hz, 2H), 1.56 (s, 3H), 1.28-0.80 (m, 6H), 0.79 (t, J = 7 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃, ppm): δ 173.4, 161.9, 155.6, 152.9, 151.6, 148.6, 134.2, 133.6, 131.8, 126.9, 126.6, 125.8, 125.2, 123.3, 121.8, 121.1, 117.9, 116.5, 115.8, 112.5, 110.7, 108.7, 85.5, 56.3, 56.2, 41.0, 31.8, 27.2, 23.2, 22.5, 14.1. HRMS (ESI⁺): m/z calcd. for $C_{31}H_{32}N_2NaO_5$ $[M+Na]^+$: 535.2203 found: 535.2170.

4-methyl-6-(4-oxo-2-(3,4,5-trimethoxyphenyl)-1,4-dihydroquinolin-3-yl)-4-pentyl-1H-benzo[d][1,3]oxazin-2(4H)-one (4r)

Yield: 75% as white solid, mp 110-113 °C; ^1H NMR (500 MHz, DMSO, ppm): δ 12.25 (s, 1H, D₂O exchangeable), 10.27 (s, 1H, D₂O exchangeable), 8.29-8.22 (m, 1H), 8.15 (t, J = 8 Hz, 1H), 7.41-7.38 (m, 4H), 7.28 (s, 1H), 6.93 (d, J = 21.5 Hz, 1H), 6.82 (d, J = 8.5 Hz, 1H), 3.83 (s, 6H), 3.74 (s, 3H), 1.93-1.74 (m, 2H), 1.56 (s, 3H), 1.27-1.16 (m, 6H), 0.79 (t, J = 10 Hz, 3H). ^{13}C NMR (125 MHz, CDCl₃, ppm): δ 173.3, 161.9, 155.6, 153.1, 152.9, 140.6, 134.4, 133.6, 131.8, 127.9, 127.0, 126.9, 126.7, 126.0, 121.8, 118.0, 116.5, 115.8, 109.1, 107.2, 85.5, 61.1, 56.5, 41.0, 31.8, 27.2, 23.2, 22.5, 14.1. HRMS (ESI⁺): m/z calcd. for C₃₂H₃₄N₂NaO₆ [M+Na]⁺ : 565.2309 found : 565.2304.

6-(2-(furan-2-yl)-4-oxo-4H-chromen-3-yl)-4-methyl-4-vinyl-1H-benzo[d][1,3]oxazin-2(4H)-one (5a)

Yield: 76% as brown solid, mp 97-99 °C; ^1H NMR (500 MHz, CDCl₃, ppm): δ 8.75 (s, 1H, D₂O exchangeable), 8.19 (d, J = 7.5 Hz, 1H), 7.65 (t, J = 8 Hz, 1H), 7.61 (m, 2H), 7.48 (d, J = 8.5 Hz, 2H), 7.38 (t, J = 7.5 Hz, 1H), 7.12 (d, J = 2.5 Hz, 1H), 6.78 (s, 1H), 6.59 (s, 1H), 6.04-5.96 (m, 1H), 5.24-5.05 (m, 2H), 1.81 (s, 3H). ^{13}C NMR (100 MHz, CDCl₃, ppm): δ 178.0, 155.9, 155.3, 145.9, 139.4, 138.7, 133.9, 132.2, 129.3, 127.4, 125.8, 125.3, 124.5, 123.5, 118.0, 116.5, 115.7, 114.7, 113.3, 112.7, 105.57, 84.2. FTIR (KBr, ν = cm⁻¹): 3290, 2987, 1712, 1677, 1652, 1635, 1586, 1422, 1352. HRMS (ESI⁺): m/z calcd. for C₂₄H₁₇NNaO₅ [M+Na]⁺ : 422.0998 found : 422.0995.

4-allyl-6-(2-(furan-2-yl)-4-oxo-4H-chromen-3-yl)-4-methyl-1H-benzo[d][1,3]oxazin-2(4H)-one (5b)

Yield: 73% as brown solid, mp 95-97 °C; ^1H NMR (500 MHz, CDCl_3 , ppm): δ 9.82 (s, 1H, D_2O exchangeable), 8.17 (d, $J = 8\text{ Hz}$, 1H), 7.76 (s, 1H), 7.65 (t, $J = 7.5\text{ Hz}$, 1H), 7.59 (s, 1H), 7.47 (d, $J = 8.5\text{ Hz}$, 1H), 7.37 (t, $J = 7\text{ Hz}$, 1H), 7.30 (d, $J = 8.5\text{ Hz}$, 1H), 7.16 (s, 1H), 7.12 (d, $J = 8.5\text{ Hz}$, 1H), 6.80 (d, $J = 8\text{ Hz}$, 1H), 5.73-5.65 (m, 1H), 5.13-5.08 (m, 2H), 2.66-2.62 (m, 2H), 1.66 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3 , ppm): δ 178.2, 156.0, 155.5, 152.5, 146.5, 146.1, 134.0, 132.0, 131.2, 127.1, 126.6, 125.9, 125.4, 124.3, 121.8, 120.5, 118.1, 116.5, 115.7, 113.4, 112.8, 105.5, 84.3, 45.6, 26.3. FTIR (KBr, $\nu = \text{cm}^{-1}$): 3284, 1713, 1697, 1609, 1556, 1372, 1303, 1236. HRMS (ESI $^{+}$): m/z calcd. for $\text{C}_{25}\text{H}_{19}\text{NNaO}_5$ $[\text{M}+\text{Na}]^{+}$: 436.1155 found: 436.1142.

6-(2-(furan-2-yl)-4-oxo-4H-chromen-3-yl)-4-methyl-4-pentyl-1H-benzo[d][1,3]oxazin-2(4H)-one (5c)

Yield: 80% as brown solid, mp 96-99 °C; ^1H NMR (500 MHz, CDCl_3 , ppm): δ 9.69 (s, 1H, D_2O exchangeable), 8.17 (d, $J = 6.5\text{ Hz}$, 1H), 7.64-7.59 (m, 2H), 7.46 (d, $J = 7.5\text{ Hz}$, 1H), 7.36 (t, $J = 8\text{ Hz}$, 1H), 7.29 (d, $J = 7\text{ Hz}$, 1H), 7.12 (d, $J = 20\text{ Hz}$, 2H), 6.79 (d, $J = 8\text{ Hz}$, 1H), 6.58 (s, 1H), 1.91-1.86 (m, 2H), 1.64 (s, 3H), 1.37-1.23 (m, 6H), 0.82 (t, $J = 8\text{ Hz}$, 3H). ^{13}C NMR (125 MHz, CDCl_3 , ppm): δ 178.0, 155.9, 155.4, 152.8, 146.4, 146.0, 133.9, 133.7, 131.7, 127.0, 126.9, 125.8, 125.3, 124.2, 118.0, 116.5, 115.7, 113.3, 112.6, 105.5, 85.4, 41.0, 31.8, 27.1, 23.2, 22.5, 14.1. HRMS (ESI $^{+}$): m/z calcd. for $\text{C}_{27}\text{H}_{25}\text{NNaO}_5$ $[\text{M}+\text{Na}]^{+}$: 466.1624 found: 466.1636.

6-(2-(furan-2-yl)-4-oxo-1,4-dihydroquinolin-3-yl)-4-methyl-4-vinyl-1H-benzo[d][1,3]oxazin-2(4H)-one (6a)

Yield: 79% as brown solid, mp 127-130 °C; ^1H NMR (500 MHz, CDCl_3 , ppm): δ 9.17 (s, 1H, D_2O exchangeable), 8.75 (s, 1H, D_2O

exchangeable), 8.19 (d, $J = 9$ Hz, 1H), 7.66 (t, $J = 7.5$ Hz, 1H), 7.61 (m, 2H), 7.48 (d, $J = 8.5$ Hz, 2H), 7.38 (t, $J = 7.5$ Hz, 1H), 7.12 (d, $J = 2.5$ Hz, 1H), 6.78 (s, 1H), 6.59 (s, 1H), 6.04-5.96 (m, 1H), 5.24-5.05 (m, 2H), 1.81 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3 , ppm): δ 178.1, 155.8, 155.3, 145.9, 139.4, 138.7, 133.9, 132.2, 129.3, 127.4, 125.8, 125.3, 124.5, 123.5, 118.0, 116.5, 115.7, 114.7, 113.3, 112.7, 105.57, 84.2. FTIR (KBr, $\nu = \text{cm}^{-1}$): 3486, 3229, 2869, 1717, 1693, 1645, 1546, 1462, 1341, 1259. HRMS (ESI $^{+}$): m/z calcd. for $\text{C}_{24}\text{H}_{18}\text{N}_2\text{NaO}_4$ $[\text{M}+\text{Na}]^{+}$: 421.1158 found : 421.1152.

4-allyl-6-(2-(furan-2-yl)-4-oxo-1,4-dihydroquinolin-3-yl)-4-methyl-1H-benzo[d][1,3]oxazin-2(4H)-one (6b)

Yield: 78% as brown solid, mp 146-148 °C; ^1H NMR (400 MHz, CDCl_3 , ppm): δ 9.90 (s, 1H, D_2O exchangeable), 8.17 (dd, $J = 2, 10$ Hz, 1H), 7.67-7.63 (m, 1H), 7.59 (d, $J = 1$ Hz, 1H), 7.47 (d, $J = 10$ Hz, 1H), 7.39-7.35 (m, 1H), 7.30-7.27 (m, 1H), 7.15 (d, $J = 2.5$ Hz, 1H), 7.11 (d, $J = 4.5$ Hz, 1H), 6.80 (d, $J = 10.5$ Hz, 1H), 6.59-6.57 (m, 1H), 6.24 (s, 1H, D_2O exchangeable), 5.73-5.63 (m, 1H), 5.12-5.07 (m, 2H), 2.69-2.58 (m, 2H), 1.66 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3 , ppm): δ 178.2, 156.1, 155.4, 152.5, 146.5, 146.1, 134.0, 132.0, 131.2, 127.1, 126.6, 125.9, 125.4, 124.3, 121.8, 120.5, 118.1, 116.5, 115.7, 113.4, 112.8, 105.5, 84.3, 45.6, 26.3. FTIR (KBr, $\nu = \text{cm}^{-1}$): 3492, 3278, 2849, 1715, 1689, 1665, 1609, 1565, 1412, 1343, 1259. HRMS (ESI $^{+}$): m/z calcd. for $\text{C}_{25}\text{H}_{20}\text{N}_2\text{NaO}_4$ $[\text{M}+\text{Na}]^{+}$: 435.1315 found : 435.1314.

6-(2-(furan-2-yl)-4-oxo-1,4-dihydroquinolin-3-yl)-4-methyl-4-pentyl-1H-benzo[d][1,3]oxazin-2(4H)-one (6c)

Yield: 76% as brown solid, mp 153-157 °C; ^1H NMR (500 MHz, CDCl_3 , ppm): δ 9.69 (s, 1H, D_2O exchangeable), 8.17 (d, $J = 6.5$ Hz, 1H), 7.64-7.59 (m, 2H), 7.46 (d, $J = 7.5$ Hz, 1H), 7.36 (t, $J = 8$ Hz, 1H), 7.29 (d, $J = 7$ Hz, 1H), 7.12 (d, $J = 20$ Hz, 2H), 6.79 (d, $J = 8$ Hz, 1H), 6.58 (s, 1H), 4.23 (s, 1H, D_2O exchangeable), 1.91-

1.86 (m, 2H), 1.64 (s, 3H), 1.37-1.23 (m, 6H), 0.82 (t, $J = 7\text{ Hz}$, 3H). ^{13}C NMR (125 MHz, CDCl_3 , ppm): δ 178.0, 155.9, 155.4, 152.8, 146.4, 146.0, 133.9, 133.7, 131.8, 127.1, 126.9, 125.8, 125.3, 124.3, 118.0, 116.5, 115.7, 113.3, 112.7, 105.5, 85.4, 41.0, 31.8, 27.2, 23.2, 22.5, 14.1. HRMS (ESI⁺): m/z calcd. for $\text{C}_{27}\text{H}_{26}\text{N}_2\text{NaO}_4$ $[\text{M}+\text{Na}]^+$: 465.1784 found : 465.1781.

6-(3-butyl-2-(4-hydroxyphenyl)-4-oxo-4H-chromen-6-yl)-4-methyl-4-vinyl-1H-

benzo[d][1,3]oxazin-2(4H)-one (9a)

Yield: 81% as white solid, mp 161-164 °C; ^1H NMR (500 MHz, CDCl_3 , ppm): δ 8.67 (s, 1H, D_2O exchangeable), 8.35 (s, 1H, D_2O exchangeable), 7.71 (d, $J = 9\text{ Hz}$, 1H), 7.48 (d, $J = 8\text{ Hz}$, 2H), 7.38-

7.32 (m, 2H), 7.14 (d, $J = 7.5\text{ Hz}$, 1H), 7.07 (t, $J = 7.5\text{ Hz}$, 1H), 7.01 (d, $J = 7.5\text{ Hz}$, 2H), 6.86-6.76 (m, 1H), 6.05-5.97 (m, 1H), 5.29-5.06 (m, 2H), 2.57 (t, $J = 7\text{ Hz}$, 2H), 1.82 (s, 3H), 1.57-1.50 (m, 2H), 1.33-1.29 (m, 2H), 0.85 (t, $J = 7.5\text{ Hz}$, 3H). ^{13}C NMR (125 MHz, CDCl_3 , ppm): δ 177.6, 162.5, 159.0, 155.0, 153.0, 139.4, 138.7, 136.3, 132.3, 130.4, 129.4, 128.6, 127.5, 124.5, 123.6, 122.1, 120.0, 118.0, 116.5, 116.3, 115.8, 114.8, 84.3, 31.3, 25.8, 25.7, 23.0, 14.0. FTIR (KBr, $\nu = \text{cm}^{-1}$): 3474, 3251, 2953, 2910, 2850, 1710, 1695, 1640, 1626, 1550. HRMS (ESI⁺): m/z calcd. for $\text{C}_{30}\text{H}_{27}\text{NNaO}_5$ $[\text{M}+\text{Na}]^+$: 504.1775 found : 504.1769.

6-(3-butyl-2-(4-methoxyphenyl)-4-oxo-4H-chromen-6-yl)-4-methyl-4-vinyl-1H-

benzo[d][1,3]oxazin-2(4H)-one (9b)

Yield: 86% as white solid, mp 174-176 °C; ^1H NMR (500 MHz, CDCl_3 , ppm): δ 9.0 (s, 1H, D_2O exchangeable), 8.34 (d, $J = 2\text{ Hz}$, 1H), 7.69 (dd, $J = 2, 8.5\text{ Hz}$, 1H), 7.54 (d, $J = 9\text{ Hz}$, 2H), 7.31 (d, J

$= 8.5\text{ Hz}$, 1H), 7.13 (d, $J = 7.5\text{ Hz}$, 1H), 7.06 (t, $J = 7.5\text{ Hz}$, 1H), 7.02 (d, $J = 8.5\text{ Hz}$, 2H), 6.82 (d, $J = 8, 1\text{ Hz}$), 6.06-5.96 (m, 1H), 5.96-5.05 (m, 2H), 3.88 (s, 3H), 2.55 (t, $J = 7.5\text{ Hz}$, 2H), 1.81 (s, 3H), 1.56-1.50 (m, 2H), 1.34-1.28 (m, 2H), 0.85 (t, $J = 7.5\text{ Hz}$, 3H). ^{13}C NMR (125

MHz, CDCl₃, ppm): δ 177.4, 162.0, 161.2, 155.0, 153.0, 139.4, 138.7, 136.3, 132.3, 130.3, 129.4, 128.6, 127.5, 125.7, 124.5, 123.8, 123.5, 122.3, 120.0, 115.8, 114.8, 114.1, 84.3, 55.6, 31.3, 25.8, 25.7, 23.0, 14.0. FTIR (KBr, $\nu = \text{cm}^{-1}$): 3305, 2953, 2923, 2856, 1709, 1680, 1645, 1628, 1598, 1519, 1446, 1362. HRMS (ESI⁺): m/z calcd. for C₃₁H₂₉NNaO₅ [M+Na]⁺ : 518.1937 found : 518.1935.

4-allyl-6-(3-butyl-2-(4-hydroxyphenyl)-4-oxo-4H-chromen-6-yl)-4-methyl-1H-

benzo[d][1,3]oxazin-2(4H)-one (9c)

Yield: 83% as white solid, mp 196-197 °C; ¹H NMR (500 MHz, CDCl₃, ppm): δ 9.69 (s, 1H, D₂O exchangeable), 8.33 (s, 1H, D₂O exchangeable), 7.72 (s, 1H), 7.45 (d, $J = 8$ Hz, 1H), 7.32 (d, $J = 8.5$ Hz, 2H), 7.18 (s, 1H), 7.11 (s, 2H), 7.03 (d, $J = 8$ Hz, 1H), 6.77 (d, $J = 8.5$ Hz, 1H), 6.54 (s, 1H), 5.73-5.65 (m, 1H), 5.14-5.10 (m, 2H), 2.70-2.56 (m, 4H), 1.68 (s, 3H), 1.59-1.52 (m, 2H), 1.33-1.28 (m, 2H), 0.84 (t, $J = 7$ Hz, 3H). FTIR (KBr, $\nu = \text{cm}^{-1}$): 3423, 3273, 2922, 2856, 1710, 1680, 1665, 1634, 1563. HRMS (ESI⁺): m/z calcd. for C₃₁H₂₉NNaO₅ [M+Na]⁺ : 518.1937 found : 518.1937.

4-allyl-6-(3-butyl-2-(4-methoxyphenyl)-4-oxo-4H-chromen-6-yl)-4-methyl-1H-

benzo[d][1,3]oxazin-2(4H)-one (9d)

Yield: 76% as white solid, mp 192-193 °C; ¹H NMR (500 MHz, CDCl₃, ppm): δ 9.49 (s, 1H, D₂O exchangeable), 8.33 (d, $J = 1.5$ Hz, 1H), 7.69 (d, $J = 6$ Hz, 1H), 7.53 (d, $J = 8.5$ Hz, 2H), 7.31 (d, $J = 8.5$ Hz, 2H), 7.17 (d, $J = 1.5$ Hz, 1H), 7.01 (d, $J = 8.5$ Hz, 2H), 6.76 (d, $J = 8.5$ Hz, 1H), 5.72-5.65 (m, 1H), 5.14-5.09 (m, 2H), 3.88 (s, 3H), 2.68-2.60 (m, 2H), 2.54 (t, $J = 8$ Hz, 2H), 1.67 (s, 3H), 1.55-1.49 (m, 2H), 1.32-1.28 (m, 2H), 0.84 (t, $J = 7.5$ Hz, 3H). ¹³C NMR (125 MHz, CDCl₃, ppm): δ 177.5, 162.1, 161.2, 155.0, 152.3, 136.3, 133.7, 132.0, 131.1, 130.3, 128.6, 127.2, 126.6, 125.7, 124.3, 122.2, 120.5, 120.0, 118.0, 116.4, 115.6, 114.1, 84.3, 55.6, 45.5, 31.3, 26.3,

25.8, 22.9, 13.9. FTIR (KBr, $\nu = \text{cm}^{-1}$): 3271, 2952, 2860, 1706, 1695, 1643, 1633, 1564, 1513, 1334, 1259. HRMS (ESI⁺): m/z calcd. for $\text{C}_{32}\text{H}_{31}\text{NNaO}_5$ $[\text{M}+\text{Na}]^+$: 532.2094 found : 532.2094.

6-(3-butyl-2-(4-hydroxyphenyl)-4-oxo-4H-chromen-6-yl)-4-methyl-4-pentyl-1H-benzo[d][1,3]oxazin-2(4H)-one (9e)

Yield: 75% as white solid, mp 197-199 °C; ¹H NMR (500 MHz, CDCl_3 , ppm): δ 9.46 (s, 1H, D_2O exchangeable), 8.34 (s, 1H, D_2O exchangeable), 7.81 (s, 1H), 7.70 (d, $J = 8.5$ Hz, 1H), 7.47 (d, $J = 8$ Hz, 2H), 7.32 (d, $J = 8.5$ Hz, 2H), 7.17 (s, 2H), 7.02 (d, $J = 8$ Hz, 1H), 6.77 (d, $J = 8$ Hz, 1H), 1.92-1.89 (m, 2H), 1.66 (s, 3H), 1.53-1.49 (m, 2H), 1.38-1.26 (m, 8H), 0.86 (m, 6H). ¹³C NMR (100 MHz, CDCl_3 , ppm): δ 177.7, 162.7, 159.4, 155.0, 153.0, 136.3, 133.5, 131.8, 130.4, 128.5, 126.9, 124.5, 124.3, 122.0, 121.8, 120.0, 119.1, 118.0, 116.5, 115.9, 185.6, 31.8, 31.3, 27.2, 25.9, 23.3, 23.0, 22.6, 14.1, 14.0. FTIR (KBr, $\nu = \text{cm}^{-1}$): 3474, 3251, 2953, 2910, 2850, 1685, 1640, 1626. HRMS (ESI⁺): m/z calcd. for $\text{C}_{33}\text{H}_{35}\text{NNaO}_5$ $[\text{M}+\text{Na}]^+$: 548.2407 found : 548.2412.

6-(3-butyl-2-(4-methoxyphenyl)-4-oxo-4H-chromen-6-yl)-4-methyl-4-pentyl-1H-benzo[d][1,3]oxazin-2(4H)-one (9f)

Yield: 74% as white solid, mp 199-202 °C; ¹H NMR (500 MHz, CDCl_3 , ppm): δ 9.42 (s, 1H, D_2O exchangeable), 8.34 (s, 1H), 7.69 (d, $J = 8$ Hz, 1H), 7.54 (d, $J = 8$ Hz, 2H), 7.31 (d, $J = 8.5$ Hz, 1H), 7.16 (s, 1H), 7.09 (s, 1H), 7.02 (d, $J = 8$ Hz, 2H), 6.76 (d, $J = 8.5$ Hz, 1H), 3.88 (s, 3H), 2.55 (t, $J = 7$ Hz, 2H), 1.94-1.89 (m, 2H), 1.66 (s, 3H), 1.56-1.50 (m, 2H), 1.38-1.26 (m, 8H), 0.86-0.84 (m, 6H). ¹³C NMR (125 MHz, CDCl_3 , ppm): δ 177.4, 162.0, 161.2, 155.0, 152.7, 136.3, 133.7, 131.8, 130.3, 128.6, 127.1, 127.0, 125.7, 124.4, 122.3, 120.0, 118.0, 116.4, 115.8, 114.1, 85.5, 55.6, 41.0, 31.9, 31.3, 27.2, 25.8, 23.3, 22.9, 22.5, 14.1, 13.9. FTIR (KBr, $\nu = \text{cm}^{-1}$): 3251, 2953,

2910, 2850, 1713, 1685, 1640, 1626, 1560, 1370. HRMS (ESI⁺): *m/z* calcd. for C₃₄H₃₇NNaO₅ [M+Na]⁺: 562.2561 found: 562.2550.

6-(3-butyl-2-(4-hydroxyphenyl)-4-oxo-1,4-dihydroquinolin-6-yl)-4-methyl-4-vinyl-1H-benzo[d][1,3]oxazin-2(4H)-one (9g)

Yield: 81% as white solid, mp 115-117 °; ¹H NMR (500 MHz, CDCl₃, ppm): δ 9.67 (s, 1H, D₂O exchangeable), 8.31 (s, 1H, D₂O exchangeable), 7.71 (s, 1H), 7.43 (d, *J* = 8 Hz, 1H), 7.32 (d, *J* =

8.5 Hz, 2H), 7.20 (s, 1H), 7.10 (s, 2H), 7.02 (d, *J* = 8 Hz, 1H), 6.78 (d, *J* = 8.5 Hz, 1H), 6.53 (s, 1H), 5.75-5.66 (m, 1H), 5.45 (s, 1H, D₂O exchangeable), 5.14-5.10 (m, 2H), 2.70-2.56 (m, 4H), 1.68 (s, 3H), 1.59-1.52 (m, 2H), 1.33-1.28 (m, 2H), 0.85 (t, *J* = 7 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃, ppm): δ 177.1, 160.4, 153.1, 148.6, 139.4, 138.7, 138.0, 134.5, 132.3, 129.9, 129.4, 128.6, 127.5, 125.8, 125.5, 124.6, 123.6, 121.8, 119.7, 115.8, 114.8, 114.0, 84.4, 31.6, 26.3, 25.7, 23.0, 14.0. HRMS (ESI⁺): *m/z* calcd. for C₃₀H₂₈N₂NaO₄ [M+Na]⁺: 503.1941 found: 503.1936.

6-(3-butyl-2-(4-methoxyphenyl)-4-oxo-1,4-dihydroquinolin-6-yl)-4-methyl-4-vinyl-1H-benzo[d][1,3]oxazin-2(4H)-one (9h)

Yield: 87% as white solid, mp 135-136 °C; ¹H NMR (500 MHz, CDCl₃, ppm): δ 10.07 (s, 1H, D₂O exchangeable), 8.35 (s, 1H, D₂O exchangeable), 8.03 (d, *J* = 5.5 Hz, 1H), 7.57 (d, *J* =

8.5 Hz, 1H), 7.44 (d, *J* = 8.5 Hz, 1H), 7.31 (d, *J* = 8.5 Hz, 2H), 7.13 (d, *J* = 7.5 Hz, 1H), 7.07 (t, *J* = 7 Hz, 1H), 6.92 (d, *J* = 8.5 Hz, 1H), 6.84 (d, *J* = 8.5 Hz, 2H), 6.04-5.96 (m, 1H), 5.25-5.04 (m, 2H), 3.77 (s, 3H), 2.42-2.39 (m, 2H), 1.81 (s, 3H), 1.41-1.36 (m, 2H), 1.26-1.13 (m, 4H), 0.73 (t, *J* = 7.5 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃, ppm): δ 177.1, 160.4, 153.1, 148.6, 139.4, 138.7, 138.0, 134.5, 132.3, 129.9, 129.4, 128.6, 127.5, 124.6, 123.6, 121.8, 119.7, 116.6, 115.8, 114.8, 114.0, 113.8, 84.4, 55.4, 31.6, 26.3, 25.7, 22.9, 14.0. FTIR

(KBr, $\nu = \text{cm}^{-1}$): 3315, 3256, 2940, 2856, 1716, 1685, 1663, 1647, 1560, 1396, 1252. HRMS

(ESI⁺): m/z calcd. for $\text{C}_{31}\text{H}_{30}\text{N}_2\text{NaO}_4$ $[\text{M}+\text{Na}]^+$: 517.2097 found: 517.2095.

6-(2-(4-aminophenyl)-3-butyl-4-oxo-1,4-dihydroquinolin-6-yl)-4-methyl-4-vinyl-1H-

benzo[d][1,3]oxazin-2(4H)-one (9i)

Yield: 78% as white solid, mp 193-196 °C; ^1H NMR (500 MHz,

CDCl_3 , ppm): δ 9.06 (s, 1H, D_2O exchangeable), 8.67 (s, 1H,

D_2O exchangeable), 8.35 (s, 1H), 7.70 (d, $J = 9$ Hz, 1H), 7.48 (d,

$J = 8$ Hz, 2H), 7.31 (d, $J = 9$ Hz, 1H), 7.15-7.06 (m, 2H), 7.01 (d, $J = 8.5$ Hz, 2H), 6.86 (d, $J = 8$ Hz, 1H), 6.06-5.97 (m, 1H), 5.26-5.06 (m, 2H), 4.11 (s, 2H, D_2O exchangeable), 2.57 (t, $J = 7$ Hz, 2H), 1.82 (s, 3H), 1.57-1.50 (m, 2H), 1.34-1.27 (m, 2H), 0.85 (t, $J = 7.5$ Hz, 3H).

FTIR (KBr, $\nu = \text{cm}^{-1}$): 3416, 3351, 3270, 3185, 2955, 2926, 2855, 1705, 1685, 1633, 1601, 1577, 1508, 1393, 1289. HRMS (ESI⁺): m/z calcd. for $\text{C}_{30}\text{H}_{29}\text{N}_3\text{NaO}_3$ $[\text{M}+\text{Na}]^+$: 502.2101 found: 502.2106.

4-allyl-6-(3-butyl-2-(4-methoxyphenyl)-4-oxo-1,4-dihydroquinolin-6-yl)-4-methyl-1H-

benzo[d][1,3]oxazin-2(4H)-one (9k)

Yield: 80% as white solid, mp 191-193 °C; ^1H NMR (500

MHz, CDCl_3 , ppm): δ 10.09 (s, 1H, D_2O exchangeable), 9.34

(s, 1H, D_2O exchangeable), 8.19 (s, 1H), 7.86 (d, $J = 8$ Hz,

1H), 7.40 (d, $J = 8$ Hz, 1H), 7.30 (d, $J = 8.5$ Hz, 1H), 7.29-7.10 (m, 2H), 7.02 (s, 1H), 6.68 (d, $J = 8$ Hz, 2H), 6.63 (d, $J = 8.5$ Hz, 1H), 5.58-5.49 (m, 1H), 4.99-4.94 (m, 2H), 3.61 (s, 3H), 2.26 (t, $J = 7.5$ Hz, 2H), 1.52 (m, 5H), 1.27-1.20 (m, 2H), 1.00 (t, $J = 8$ Hz, 2H), 0.72 (t, $J = 8$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3 , ppm): δ 177.0, 160.2, 152.7, 138.4, 135.2, 134.3, 133.7, 131.8, 131.4, 130.0, 128.1, 127.3, 126.9, 126.4, 125.4, 121.7, 120.4, 120.0, 116.6, 115.5, 113.8, 84.2, 55.3, 45.4, 31.5, 29.7, 26.2, 22.8, 13.9. FTIR (KBr, $\nu = \text{cm}^{-1}$): 3293, 3161,

2931, 1712, 1688, 1635, 1564, 1493 1408, 1348, 1288. HRMS (ESI⁺): *m/z* calcd. for C₃₂H₃₂N₂NaO₄ [M+Na]⁺ : 531.2256 found : 531.2255.

4-allyl-6-(2-(4-aminophenyl)-3-butyl-4-oxo-1,4-dihydroquinolin-6-yl)-4-methyl-1H-benzo[d][1,3]oxazin-2(4H)-one (9l)

Yield: 82% as white solid, mp 186-187 °C; ¹H NMR (500 MHz, DMSO, ppm): δ 10.35 (s, 1H, D₂O exchangeable), 8.15 (d, *J* = 8.5 Hz, 2H), 7.64-7.57 (m, 1H), 7.43 (s, 1H), 7.39 (d, *J* = 8 Hz, 1H), 7.24 (s, 2H), 7.16 (d, *J* = 8 Hz, 1H), 6.84 (d, *J* = 8.5 Hz, 1H), 6.70 (d, *J* = 8 Hz, 1H), 5.67-5.58 (m, 1H), 5.09-5.06 (m, 5H, 3H D₂O exchangeable), 2.72-2.69 (m, 1H), 2.59-2.55 (m, 1H), 2.38 (t, *J* = 8 Hz, 2H), 1.58 (s, 3H), 1.38-1.32 (m, 2H), 1.18-1.13 (m, 2H), 0.73 (t, *J* = 8 Hz, 3H). ¹³C NMR (125 MHz, DMSO, ppm): δ 175.1, 149.9, 149.4, 138.2, 134.5, 133.6, 131.8, 131.4, 129.5, 127.0, 126.9, 126.5, 124.7, 121.7, 120.9, 120.7, 119.7, 119.6, 116.1, 114.8, 113.2, 83.0, 44.4, 30.8, 26.2, 25.6, 22.3, 13.7. FTIR (KBr, ν = cm⁻¹): 3444, 3321, 3237, 3140, 2960, 1713, 1683, 1645, 1624, 1572, 1492, 1400. HRMS (ESI⁺): *m/z* calcd. for C₃₁H₃₁N₃NaO₃ [M+Na]⁺ : 516.2257 found : 516.2254.

6-(3-butyl-2-(4-hydroxyphenyl)-4-oxo-1,4-dihydroquinolin-6-yl)-4-methyl-4-pentyl-1H-benzo[d][1,3]oxazin-2(4H)-one (9m)

Yield: 78% as pale yellow solid, mp 180-182 °C; ¹H NMR (500 MHz, CDCl₃, ppm): δ 9.40 (s, 1H, D₂O exchangeable), 8.51 (s, 1H, D₂O exchangeable), 8.33 (s, 1H), 7.69 (d, *J* = 8 Hz, 1H), 7.53 (d, *J* = 8 Hz, 2H), 7.32 (d, *J* = 8.5 Hz, 1H), 7.16 (s, 1H), 7.10 (s, 1H), 7.01 (d, *J* = 8 Hz, 2H), 6.77 (d, *J* = 8.5 Hz, 1H), 4.20 (s, 1H, D₂O exchangeable), 2.55 (t, *J* = 7 Hz, 2H), 1.94-1.89 (m, 2H), 1.66 (s, 3H), 1.56-1.50 (m, 2H), 1.38-1.26 (m, 8H), 0.86-0.84 (m, 6H). ¹³C NMR (125 MHz, CDCl₃, ppm): δ 177.4, 162.0, 161.2, 155.0, 152.7, 136.3, 133.7, 131.8, 130.3, 128.6, 127.1, 127.0, 125.7, 124.4, 122.3, 120.0, 118.0, 116.4, 115.8, 114.1, 85.5, 55.6,

41.0, 31.9, 31.3, 27.2, 25.8, 23.3, 22.9, 22.5, 14.1, 13.9. HRMS (ESI⁺): m/z calcd. for $C_{33}H_{36}N_2NaO_4$ $[M+Na]^+$: 547.2573 found : 547.2574.

6-(3-butyl-2-(4-methoxyphenyl)-4-oxo-1,4-dihydroquinolin-6-yl)-4-methyl-4-pentyl-1H-benzo[d][1,3]oxazin-2(4H)-one (9n)

Yield: 79% as white solid, mp 132-133 °C; ¹H NMR (500 MHz, CDCl₃, ppm): δ 10.58 (s, 1H, D₂O exchangeable), 9.65 (s, 1H, D₂O exchangeable), 8.38 (s, 1H), 7.59-7.56 (m, 1H), 7.45 (d, J = 8.5 Hz, 1H), 7.31 (d, J = 8.5 Hz, 2H), 7.16 (s, 2H), 7.04 (s, 1H), 6.86 (d, J = 8 Hz, 1H), 6.77 (d, J = 8.5 Hz, 1H), 3.77 (s, 3H), 2.44-2.41 (m, 1H), 1.91-1.88 (m, 2H), 1.65 (s, 3H), 1.38-1.25 (m, 11H), 0.84 (t, J = 5 Hz, 3H), 0.72 (t, J = 7 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃, ppm): δ 177.1, 160.4, 152.9, 148.7, 138.2, 134.4, 133.7, 131.8, 130.0, 128.6, 127.6, 127.0, 126.9, 125.5, 121.7, 119.7, 116.6, 116.5, 115.8, 114.0, 85.5, 55.4, 41.0, 31.9, 31.6, 27.2, 26.3, 23.2, 22.9, 22.5, 14.1, 14.0. HRMS (ESI⁺): m/z calcd. for $C_{34}H_{38}N_2NaO_4$ $[M+Na]^+$: 561.2723 found : 561.2723.

6-(2-(4-aminophenyl)-3-butyl-4-oxo-1,4-dihydroquinolin-6-yl)-4-methyl-4-pentyl-1H-benzo[d][1,3]oxazin-2(4H)-one (9o)

Yield: 85% as brown solid, mp 175-177 °C; ¹H NMR (500 MHz, CDCl₃, ppm): δ 10.53 (s, 1H, D₂O exchangeable), 9.66 (s, 1H, D₂O exchangeable), 8.35 (s, 1H), 7.56 (d, J = 6.5 Hz, 1H), 7.41 (s, 2H), 7.31 (d, J = 8 Hz, 2H), 7.15 (s, 1H), 6.80 (d, J = 8.5 Hz, 2H), 6.58 (d, J = 7.5 Hz, 1H), 4.69 (s, 2H, D₂O exchangeable), 2.44 (t, J = 7.5 Hz, 1H), 1.92-1.87 (m, 2H), 1.64 (s, 3H), 1.38-1.25 (m, 11H), 0.83 (t, J = 6.5 Hz, 3H), 0.71 (t, J = 7 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃, ppm): δ 177.2, 160.3, 152.9, 148.8, 138.1, 134.5, 133.7, 131.8, 130.1, 128.7, 127.6, 127.1, 126.9, 125.5, 121.8, 119.8, 116.6, 116.5, 115.8, 114.1, 85.5, 41.1, 31.9, 31.6, 27.2, 26.3, 23.3, 22.9, 22.6, 14.1, 14.0. HRMS (ESI⁺): m/z calcd. for $C_{33}H_{37}N_3NaO_3$ $[M+Na]^+$: 546.2727 found : 546.2730.

6-(3-butyl-2-(4-methoxyphenyl)-4-oxochroman-6-yl)-4-methyl-4-vinyl-1H-benzo[d][1,3]oxazin-2(4H)-one (10a)

Yield: 76% as yellow solid, mp 180-182 °C; ¹H NMR (500 MHz, CDCl₃, ppm): δ9.08 (s, 1H, D₂O exchangeable), 7.97 (d, *J* = 2Hz, 1H), 7.50 (dd, *J* = 2, 8.5 Hz, 1H), 7.34 (d, *J* = 8.5 Hz, 2H), 7.25 (s, 1H), 7.13 (d, *J* = 7.5 Hz, 1H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.91 (d, *J* = 8.5 Hz, 2H), 6.86 (d, *J* = 8.5 Hz, 1H), 6.05-6.00 (m, 1H), 5.54-5.05 (m, 3H), 3.81 (s, 3H), 2.99-2.95 (m, 1H), 1.82 (s, 3H), 1.62-1.53 (m, 2H), 1.28-1.19 (m, 4H), 0.80 (t, *J* = 6.5 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃, ppm): δ193.5, 160.2, 159.7, 153.0, 139.4, 138.6, 134.6, 132.3, 129.8, 129.4, 128.8, 127.5, 127.1, 124.5, 123.5, 122.2, 120.2, 115.7, 114.8, 114.3, 84.3, 83.3, 55.5, 50.6, 28.8, 26.1, 25.7, 22.9, 13.9. FTIR (KBr, ν = cm⁻¹): 3275, 2953, 2917, 2850, 1711, 1695, 1665, 1625, 1513, 1465, 1410, 1390. HRMS (ESI⁺): *m/z* calcd. for C₃₁H₃₁NNaO₅ [M+Na]⁺ : 520.2094 found : 520.2091.

4-allyl-6-(3-butyl-2-(4-methoxyphenyl)-4-oxochroman-6-yl)-4-methyl-1H-benzo[d][1,3]oxazin-2(4H)-one (10b)

Yield: 75% as yellow solid, mp 141-142 °C; ¹H NMR (500 MHz, CDCl₃, ppm): δ9.89 (s, 1H, D₂O exchangeable), 8.04 (d, *J* = 2Hz, 1H), 7.75 (s, 1H), 7.58 (dd, *J* = 2, 8.5 Hz, 1H), 7.41 (d, *J* = 3 Hz, 2H), 7.16 (s, 1H), 6.99 (d, *J* = 8.5 Hz, 2H), 6.93 (d, *J* = 8.5 Hz, 1H), 6.84 (d, *J* = 8.5 Hz, 1H), 5.80-5.73 (m, 1H), 5.32 (d, *J* = 10 Hz, 1H), 5.22-5.17 (m, 2H), 3.88 (s, 3H), 3.06-3.02 (m, 1H), 2.77-2.68 (m, 2H), 1.75 (s, 3H), 1.69-1.63 (m, 2H), 1.35-1.26 (m, 4H), 0.86 (t, *J* = 6.5 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃, ppm): δ193.5, 160.1, 159.6, 138.6, 135.2, 133.7, 132.0, 131.1, 129.8, 129.7, 128.8, 127.2, 127.1, 126.6, 122.2, 120.5, 120.2, 116.4, 115.7, 84.3, 83.2, 55.4, 50.6, 45.5, 28.7, 26.3, 26.0, 22.9, 13.9. FTIR (KBr, ν = cm⁻¹):

3240, 2956, 1710, 1702, 1638, 1598, 1414, 1351, 1253. HRMS (ESI⁺): m/z calcd. for C₃₂H₃₃NNaO₅ [M+Na]⁺ : 534.2250 found :534.2238.

6-(3-butyl-2-(4-methoxyphenyl)-4-oxochroman-6-yl)-4-methyl-4-pentyl-1H-

benzo[d][1,3]oxazin-2(4H)-one (10c)

Yield: 84% as yellow solid, mp 150-152 °C; ¹H NMR (500 MHz, CDCl₃, ppm): δ9.58 (s, 1H, D₂O exchangeable), 7.96 (s,

1H), 7.51 (d, *J* = 8.5 Hz, 1H), 7.33-7.30 (m, 3H), 7.16 (s, 1H), 7.11-7.05 (m, 1H), 6.90 (d, *J* = 7.5 Hz, 2H), 6.85 (d, *J* = 8.5 Hz, 1H), 6.76 (d, *J* = 8.5 Hz, 1H), 5.24 (d, *J* = 10 Hz, 1H), 3.80 (s, 3H), 2.96 (q, 1H), 2.94-1.89 (m, 2H), 1.65 (s, 3H), 1.61-1.58 (m, 2H), 1.30-1.18 (m, 10H), 0.84 (t, *J* = 6 Hz, 3H), 0.777 (t, *J* = 7 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃, ppm): δ193.5, 160.1, 159.7, 152.8, 138.6, 133.7, 131.8, 129.8, 129.7, 128.8, 127.1, 126.9, 122.2, 120.2, 116.4, 115.7, 114.3, 114.1, 85.4, 83.3, 55.4, 50.6, 41.0, 31.8, 28.8, 27.2, 26.1, 23.2, 22.9, 22.5, 14.1, 13.9. HRMS (ESI⁺): m/z calcd. for C₃₄H₃₉NNaO₅ [M+Na]⁺ : 564.2720 found : 564.2715.

References:

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- [2] Cárdenas, M.; Marder, M.; Blank, V. C.; Roguin, L. P. *Bioorg. Med. Chem.* **2006**, *14*, 2966-71.
- [3] Zhang, P.; Zhang, P.; Terefenko, E. A.; Fensome, A.; Wrobel, J.; Winneker, R.; Lundeen, S.; Marschke, K. B.; Zhang, Z. *J. Med. Chem.* **2002**, *45*, 4379-82.

¹H and ¹³C Spectra

skj-6-45

skj-6-45

SKJ-6-29

skj-6-30

SKJ-6-30C13

skj-6-31

SKJ-6-16 C13

SKJ-6-18

skj-6-18

SKJ-6-49

SKJ-6-49C13

SKJ-6-39C13

skj-6-40

skj-6-36

skj-6-36

SKJ-6-53

SKJ-6-54

—12.258

—10.279

8.296
8.267
8.253
8.227
8.170
8.154
8.104
7.412
7.385
7.287
6.951
6.908
6.830
6.613

4.081
3.835
3.745
2.498
1.936
1.913
1.892
1.799
1.778
1.747
1.566
1.270
1.251
1.231
1.220
1.212
1.203
1.188
1.169
0.817
0.797
0.778

Chemical Shift (ppm)	Integration
12.258	0.81
10.279	1.00
8.296	1.28
8.267	0.54
8.253	3.69
8.227	0.86
8.170	0.82
8.154	1.10
4.081	6.01
3.835	2.96
3.745	2.18
2.498	3.12
1.936	6.21
1.913	3.15

SKJ-6-54 C13

—173.35

161.97

155.69

153.12

152.93

140.67

134.40

133.66

131.83

127.91

127.06

126.94

126.71

126.00

121.86

118.02

116.54

115.82

109.16

107.25

85.54

77.46

77.22

76.95

61.18

56.59

41.06

31.88

27.22

23.28

22.57

14.12

Chemical Shift (ppm)	Integration
173.35	0.81
161.97	1.00
155.69	1.28
153.12	0.54
152.93	3.69
140.67	0.86
134.40	0.82
133.66	1.10
131.83	6.01
127.91	2.96
127.06	2.18
126.94	3.12
126.71	6.21
126.00	3.15
121.86	2.18
118.02	3.12
116.54	6.21
115.82	3.15
109.16	2.18
107.25	3.12
85.54	6.01
77.46	2.96
77.22	2.18
76.95	3.12
61.18	6.21
56.59	3.15
41.06	2.18
31.88	3.12
27.22	6.21
23.28	3.15
22.57	2.18
14.12	3.12

SKJ-6-47

skj-6-32

SKJ-6-32A

SKJ-6-50

SKJ-6-50C13

SKJ-6-55

SKJ-6-55 C13

SKJ-6-19

SKJ-6-19

SKJ-6-6

SKJ-6-6

SKJ-6-7

SKJ-6-7

SKJ-6-11

SKJ-6-10

SKJ-6-10

¹³C NMR spectrum (400 MHz, CDCl₃) of compound 10. The spectrum shows peaks in the aromatic region (114.08 to 177.17 ppm) and aliphatic region (14.04 to 31.63 ppm). The chemical structure of compound 10 is shown in the inset.

Chemical structure of compound 10: CC(C)(C)C1=CC=C(C=C1C2=CC=CC=C2C(=O)N3C(=O)C(=C(C=C3)C(=O)N4C(=O)C(=CC=C4)O)CC)C(=O)O

¹³C NMR peaks (ppm): 177.17, 170.45, 160.45, 153.16, 148.69, 139.42, 138.77, 138.09, 134.55, 132.37, 129.99, 129.45, 128.67, 127.59, 125.88, 125.53, 124.62, 123.68, 121.86, 119.77, 115.85, 114.84, 114.08, 84.41, 77.49, 77.23, 76.98, 31.63, 26.36, 25.76, 23.01, 14.04.

Chemical structure of compound 10: CCOC1=CC=C(C=C1)C2=CC(=CC=C2)C(=O)N(C2=CC=C(C=C2)C3=CC(=CC=C3)C(=O)N(C)C)C2

¹H NMR spectrum (CDCl₃):

Chemical Shift (ppm)	Integration
10.077	0.82
8.996	0.81
8.042	1.14
8.025	1.01
7.579	2.09
7.562	0.96
7.454	0.96
7.436	1.14
7.319	1.01
7.302	2.16
7.260	1.21
7.139	1.30
7.124	1.15
7.086	2.07
7.071	3.00
7.056	3.10
6.929	2.26
6.912	2.07
6.856	2.07
6.839	2.07
5.987	2.07
5.980	2.07
5.958	2.07
5.234	2.07
5.210	2.07
5.162	2.07
5.147	2.07
5.131	2.07
5.113	2.07
5.097	2.07
5.080	2.07
5.045	2.07
3.772	2.07
2.456	2.07
2.410	2.07
2.394	2.07
1.810	2.07
1.425	2.07
1.410	2.07
1.395	2.07
1.380	2.07
1.364	2.07
1.348	2.07
1.333	2.07
1.317	2.07
1.162	2.07
1.147	2.07
1.133	2.07
1.118	2.07
0.741	2.07
0.726	2.07
0.711	2.07

skj-6-23 c13

SKJ-6-8 c13

SKJ-6-15

skj-6-15 c13

Chemical structure of compound 10 is shown above the spectrum. The structure is a complex molecule with a central benzene ring substituted with a 4-methoxyphenyl group, a 4-propylphenyl group, and a 4-allylphenyl group. The central benzene ring is also substituted with a 4-allylphenyl group.

¹³C NMR spectrum (CDCl₃) of compound 10. The spectrum shows peaks at the following chemical shifts (ppm): 193.50, 160.20, 159.71, 153.09, 139.44, 138.62, 134.66, 132.32, 129.81, 129.41, 128.85, 127.56, 127.16, 124.57, 123.59, 122.26, 120.22, 115.79, 114.82, 114.34, 84.34, 83.32, 77.49, 77.23, 76.98, 55.50, 50.65, 28.82, 26.12, 25.76, 22.95, and 13.95.

Chemical Structure of 10: CCCCC1=C(C2=CC=CC=C2C(=O)C1=CC=CC=C2)C(=O)C3=CC=CC=C3C(=O)N4C(=O)C(C)C(C)C4

¹H NMR Spectrum (CDCl₃):

Chemical Shift (ppm)	Integration
7.419, 7.403	2.30
7.597, 7.593, 7.580, 7.576	1.00
7.752	0.66
8.046, 8.042	0.92
7.162, 7.155, 7.141, 7.126, 7.112, 7.104, 7.096, 7.088, 7.080, 7.072, 7.064, 7.056, 7.048, 7.040, 7.032, 7.024, 7.016, 7.008, 7.000, 6.992, 6.984, 6.976, 6.968, 6.960, 6.952, 6.944, 6.936, 6.928, 6.920, 6.912, 6.904, 6.896, 6.888, 6.880, 6.872, 6.864, 6.856, 6.848, 6.840, 6.832, 6.824, 6.816, 6.808, 6.800, 6.792, 6.784, 6.776, 6.768, 6.760, 6.752, 6.744, 6.736, 6.728, 6.720, 6.712, 6.704, 6.696, 6.688, 6.680, 6.672, 6.664, 6.656, 6.648, 6.640, 6.632, 6.624, 6.616, 6.608, 6.600, 6.592, 6.584, 6.576, 6.568, 6.560, 6.552, 6.544, 6.536, 6.528, 6.520, 6.512, 6.504, 6.496, 6.488, 6.480, 6.472, 6.464, 6.456, 6.448, 6.440, 6.432, 6.424, 6.416, 6.408, 6.400, 6.392, 6.384, 6.376, 6.368, 6.360, 6.352, 6.344, 6.336, 6.328, 6.320, 6.312, 6.304, 6.296, 6.288, 6.280, 6.272, 6.264, 6.256, 6.248, 6.240, 6.232, 6.224, 6.216, 6.208, 6.200, 6.192, 6.184, 6.176, 6.168, 6.160, 6.152, 6.144, 6.136, 6.128, 6.120, 6.112, 6.104, 6.096, 6.088, 6.080, 6.072, 6.064, 6.056, 6.048, 6.040, 6.032, 6.024, 6.016, 6.008, 6.000, 5.992, 5.984, 5.976, 5.968, 5.960, 5.952, 5.944, 5.936, 5.928, 5.920, 5.912, 5.904, 5.896, 5.888, 5.880, 5.872, 5.864, 5.856, 5.848, 5.840, 5.832, 5.824, 5.816, 5.808, 5.800, 5.792, 5.784, 5.776, 5.768, 5.760, 5.752, 5.744, 5.736, 5.728, 5.720, 5.712, 5.704, 5.696, 5.688, 5.680, 5.672, 5.664, 5.656, 5.648, 5.640, 5.632, 5.624, 5.616, 5.608, 5.600, 5.592, 5.584, 5.576, 5.568, 5.560, 5.552, 5.544, 5.536, 5.528, 5.520, 5.512, 5.504, 5.496, 5.488, 5.480, 5.472, 5.464, 5.456, 5.448, 5.440, 5.432, 5.424, 5.416, 5.408, 5.400, 5.392, 5.384, 5.376, 5.368, 5.360, 5.352, 5.344, 5.336, 5.328, 5.320, 5.312, 5.304, 5.296, 5.288, 5.280, 5.272, 5.264, 5.256, 5.248, 5.240, 5.232, 5.224, 5.216, 5.208, 5.200, 5.192, 5.184, 5.176, 5.168, 5.160, 5.152, 5.144, 5.136, 5.128, 5.120, 5.112, 5.104, 5.096, 5.088, 5.080, 5.072, 5.064, 5.056, 5.048, 5.040, 5.032, 5.024, 5.016, 5.008, 5.000, 4.992, 4.984, 4.976, 4.968, 4.960, 4.952, 4.944, 4.936, 4.928, 4.920, 4.912, 4.904, 4.896, 4.888, 4.880, 4.872, 4.864, 4.856, 4.848, 4.840, 4.832, 4.824, 4.816, 4.808, 4.800, 4.792, 4.784, 4.776, 4.768, 4.760, 4.752, 4.744, 4.736, 4.728, 4.720, 4.712, 4.704, 4.696, 4.688, 4.680, 4.672, 4.664, 4.656, 4.648, 4.640, 4.632, 4.624, 4.616, 4.608, 4.600, 4.592, 4.584, 4.576, 4.568, 4.560, 4.552, 4.544, 4.536, 4.528, 4.520, 4.512, 4.504, 4.496, 4.488, 4.480, 4.472, 4.464, 4.456, 4.448, 4.440, 4.432, 4.424, 4.416, 4.408, 4.400, 4.392, 4.384, 4.376, 4.368, 4.360, 4.352, 4.344, 4.336, 4.328, 4.320, 4.312, 4.304, 4.296, 4.288, 4.280, 4.272, 4.264, 4.256, 4.248, 4.240, 4.232, 4.224, 4.216, 4.208, 4.200, 4.192, 4.184, 4.176, 4.168, 4.160, 4.152, 4.144, 4.136, 4.128, 4.120, 4.112, 4.104, 4.096, 4.088, 4.080, 4.072, 4.064, 4.056, 4.048, 4.040, 4.032, 4.024, 4.016, 4.008, 4.000, 3.992, 3.984, 3.976, 3.968, 3.960, 3.952, 3.944, 3.936, 3.928, 3.920, 3.912, 3.904, 3.896, 3.888, 3.880, 3.872, 3.864, 3.856, 3.848, 3.840, 3.832, 3.824, 3.816, 3.808, 3.800, 3.792, 3.784, 3.776, 3.768, 3.760, 3.752, 3.744, 3.736, 3.728, 3.720, 3.712, 3.704, 3.696, 3.688, 3.680, 3.672, 3.664, 3.656, 3.648, 3.640, 3.632, 3.624, 3.616, 3.608, 3.600, 3.592, 3.584, 3.576, 3.568, 3.560, 3.552, 3.544, 3.536, 3.528, 3.520, 3.512, 3.504, 3.496, 3.488, 3.480, 3.472, 3.464, 3.456, 3.448, 3.440, 3.432, 3.424, 3.416, 3.408, 3.400, 3.392, 3.384, 3.376, 3.368, 3.360, 3.352, 3.344, 3.336, 3.328, 3.320, 3.312, 3.304, 3.296, 3.288, 3.280, 3.272, 3.264, 3.256, 3.248, 3.240, 3.232, 3.224, 3.216, 3.208, 3.200, 3.192, 3.184, 3.176, 3.168, 3.160, 3.152, 3.144, 3.136, 3.128, 3.120, 3.112, 3.104, 3.096, 3.088, 3.080, 3.072, 3.064, 3.056, 3.048, 3.040, 3.032, 3.024, 3.016, 3.008, 3.000, 2.992, 2.984, 2.976, 2.968, 2.960, 2.952, 2.944, 2.936, 2.928, 2.920, 2.912, 2.904, 2.896, 2.888, 2.88	

¹H NMR (400 MHz, CDCl₃)

8.36, 8.28, 7.78, 7.73, 7.69, 5.58, 5.01, 4.56, 2.87, 2.63, 2.60, 2.29, 1.93

¹³C NMR (100 MHz, CDCl₃)

193.55, 138.62, 135.28, 133.74, 132.00, 131.12, 129.76, 129.71, 128.82, 127.18, 127.13, 126.60, 122.21, 122.02, 120.53, 120.20, 116.40, 115.71, 26.33, 26.08

Chemical structure of compound 10 is shown.

SKJ-6-12C13