Electronic Supplementary Material (ESI) for MedChemComm.

Synthesis of novel 1-substituted triazole linked 1,2-benzothiazine 1,1-dioxido propenone derivatives as potent anti-inflammatory agents and inhibitors of monocyte-to-macrophage differentiation

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Supporting information

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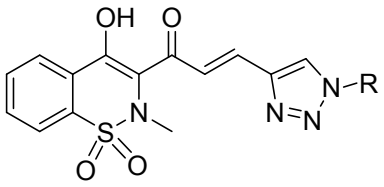
1. **Table-S1:** Physicochemical properties of compounds **8a-s**



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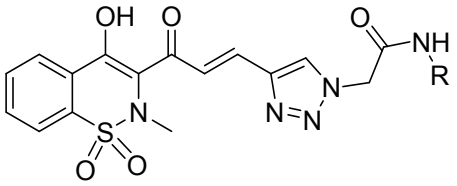
Entry	Compound	R	Yield%	m.p. ˚C	Purity (%)
1	**8a**	$-(CH_2)_9-CH_3$	63	104-106	96.2
2	**8b**	$-(CH_2)_7-CH_3$	69	111-113	95.2
3	**8c**	C_6H_5	84	257-259	99.8
4	**8d**	$4-CH_3C_6H_4$	76	213-215	97.2
5	**8e**	$4-CF_3C_6H_4$	78	258-260	96.9
6	**8f**	$4-OCH_3C_6H_4$	68	197-199	95.8
7	**8g**	$4-NO_2C_6H_4$	81	>260	98.9
8	**8h**	$4-FC_6H_4$	82	250-252	96.7
9	**8i**	$3-Cl,4-FC_6H_3$	62	258-260	98.7
10	**8j**	$3-ClC_6H_4$	84	124-126	97.6
11	**8k**	$3-CF_3C_6H_4$	72	177-179	96.6
12	**8l**	$2-Cl,5-NO_2C_6H_3$	74	121-123	96.2
13	**8m**	$2,4-F_2C_6H_3$	90	244-246	99.5
14	**8n**	$2-BrC_6H_4$	78	114-116	97.4
15	**8o**	$-(CH_2)_2-C_6F_{13}$	72	109-111	96.6
16	**8p**	$3-FC_6H_4$	81	199-201	95.7
17	**8q**	$3-OCH_3C_6H_4$	81	>260	98.8
18	**8r**	$3-NO_2C_6H_4$	68	252-254	96.1
19	**8s**	$2-FC_6H_4$	65	231-233	98.8

2. Table-S2: Physicochemical properties of compounds **12a-l**



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Entry	Compound	R	Yield %	m.p. ˚C	Purity %
1	**12a**	C_6H_5	70	171-173	98.8
2	**12b**	4-FC_6H_4	68	237-239	96.3
3	**12c**	Cyclo hexyl	75	199-201	99.6
4	**12d**	2-Br,4-FC_6H_3	73	223-225	96.6
5	**12e**	4-$CF_3C_6H_4$	69	207-209	97.8
6	**12f**	4-$OCH_3C_6H_4$	71	243-245	98.9
7	**12g**	3-ClC_6H_4	63	126-128	96.7
8	**12h**	2,6-$F_2C_6H_3$	66	197-199	98.6
9	**12i**	4-$CH_3C_6H_4$	73	221-223	98.3
10	**12j**	3-FC_6H_4	75	231-233	99.8
11	**12k**	3-CF_3,4-ClC_6H_3	62	258-260	96.7
12	**12l**	3-$CF_3C_6H_4$	71	244-246	99.5

3. Experimental procedure, spectroscopic data of all the compounds:

General:

Melting points were recorded on Casia-Siamia (VMP-AM) melting point apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer FT-IR 240-C spectrophotometer using KBr optics. ^{1}H NMR spectra were recorded on Bruker AV 300MHz in $CDCl_3$, DMSO- d_6, TFA, ^{13}C NMR spectra were recorded on Bruker AV 75 MHz in DMSO- d_6 using TMS as an internal standard. Electron impact (EI) chemical ionization mass spectra were recorded on a VG 7070 H instrument at 70 eV. All the reactions were monitored by thin layer chromatography (TLC) on precoated silica gel 60 F_{254} (mesh); spots were visualized with UV light. Merck silica gel (60-120 mesh) was used for column chromatography. All the final compounds were analyzed by HPLC to evaluate purity using SHIMADZU LC-20 instrument. Separation was carried out by using a mobile phase of acetonitrile: 0.1% formic acid (60:40) on Zodiac C_{18} Column (150 mm ×

4.6 mm, 5 μM) in an isocratic mode at a flow rate of 1.0 ml/min with Photo-diode Array (PDA) detection at 254 nm and purity exceeded 95%.

2-(2-Oxopropyl)benzo[d]isothiazol-3(2H)-one 1,1-dioxide (**S2**):[1]

The sodium salt of saccharin **S1** (1.03 g, 5 mmol) (commercially available) was dissolved in DMF (10 mL) then chloroacetone (0.49 mL, 6 mmol) was added. The reaction mixture was heated to 100 °C for 4 h while stirring. After 4 h, it was cooled to room temperature and added to ice cold water. Then the solid was filtered and washed with cool water more times and dried.

1-(4-Hydroxy-1,1-dioxido-2H-benzo[e][1,2]thiazin-3-yl) ethanone (**S3**):[1]

The activated sodium metal (0.57 g, 25 mmol) was dissolved in ethanol (10 mL) at room temperature. Then *N*-alkylated product **S2** (1.19 g, 5 mmol) was added to sodium methoxide-ethanol solution in one portion and stirred at room temperature for 5 min. While addition the reaction mixture was turned to tick red color solution which indicated Gabriel-Colman rearrangement. After 5 min, the solvent was removed under vacuum then ice cold water was added and neutralized with 1N HCl. Consequently, the solid was filtered and washed with water then dried.

1-(4-Hydroxy-2-methyl-1,1-dioxido-2H-benzo[e][1,2]thiazin-3-yl)ethanone (**S4**):[1]

A mixture of rearranged product (**S3**) (20.9mmol), 20% aqueous sodium hydroxide (8.4 mL) and acetone (50 mL) was stirred at room temperature for 5min. Dimethyl sulfate (5.9 mL) was added to the mixture drop wise over a period of 5 min. The mixture was stirred for further half an hour followed by the careful addition of dilute HCl (20 mL; 5%) to get the white precipitates which were filtered, washed with water and dried.

Preparation of azide derivatives

General procedure:

Alipahatic azides:[2] Iodo alkane (10.0 mmol) and sodium azide (30.0 mmol) were taken in a round bottom flask and was added 40 mL acetone: water (3:1) as a result homogeneous solution was obtained. The solution was heated to 60 °C for 8 h. After completion of reaction, cooled to room temperature and excess solvent was removed under vacuum. To the aqueous residue was added hexane three times (30 mL each time) while extracting. The combined extracts were washed with water then organic layer was separated, dried over anhydrous sodium sulphate and excess solvent was removed under vaccum to obtain alkyl azide in quantitative yield.

Aromatic azides:[3] Substituted aniline was (13.6 mmol) dissolved in 50 mL HCl: H_2O (1:1) and cooled at -5 °C by ice-salt mixture. Then a solution of sodium nitrite (1.87 g, 27.2 mmol) dissolved in water (15 mL) was added slowly at -5 °C. After completion of addition, the reaction mixture was stirred at -5°C for 60 min. Then the reaction mixture was neutralized with sodium acetate (22.3 g, 272 mmol). Following this, a solution of NaN_3 (1.77 g, 27.2 mmol) in water (15 mL) was added slowly over the period of 30 min by maintaining the temp at -5 to 0 °C. After stirring for 30 min, the solution was allowed to warm at room temperature. Extracted with ethyl acetate, dried the organic layer over sodium sulphate and evaporated to yield substituted phenyl azide.

Preparation of 2-azido-N-(sustituted)acetamide derivatives (**9a-l**)[4]

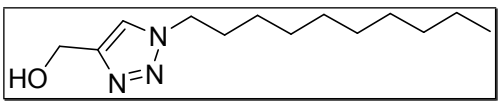
Substituted aniline (13.6 mmol) and triethylamine (1.9 mL, 13.6 mmol) were dissolved in DMF (10 mL) and cooled to 0 °C then chloroacetylchloride (1.08 mL, 13.6 mmol) was added drop wise over 10 min. After completion of addition, the reaction mixture was stirred at 0 °C for 2 h. Then the reaction mixture was allowed to warm at room temperature and stirred for 1 h. Following this, NaN_3 (1.33 g, 20.4 mmol) was added in one portion to reaction mixture which was in viscous solid. This reaction mixture stirred at room temperature for 12 h. After completion of reaction, the solution was added to ice cold water then the solid was filtered and washed with water more times and dried.

Preparation of 1-substituted(1,2,3)triazol-4-yl-methanol (5) and 2-(4-(hydroxymethyl)-1H-1,2,3-triazol-1-yl)-N-substituted-acetamide (**10**):

General procedure:

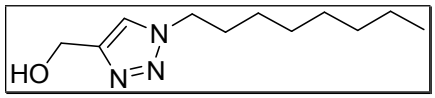
In an argon atmosphere, alkylazide /alkyl amide azide **9** (5.4 mmol), propargyl alcohol (8 mmol), and t-BuOH (5 mL) were taken sequentially into a round bottom flask followed by addition of an aqueous $Cu(OAc)_2$ solution (5 mol%, 1 mL). The reaction was stirred for 18 h at room temperature and the reaction was monitored by TLC. The resulting mixture was extracted with dichloromethane twice, combined organic layer was washed with water, dried over sodium sulphate and purified by passing through a column packing with silica gel using petroleum ether/EtOAc (6:4) as eluents.

(1-Decyl-1H-(1,2,3)triazol-4-yl)methanol (**5a**):[2]



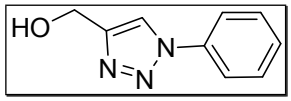
White solid, Yield: 91%, I.R. (KBr, cm^{-1}): 3395 (OH), 1550 (C=C); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 0.89 (t, 3H, CH_3), 1.24-1.32 (m, 14H, CH_2), 1.85-1.88 (m, 2H, -CH_2), 4.31 (t, 2H, CH_2), 4.59 (s, 2H, CH_2-O), 4.95 (brs, 1H, OH), 7.76 (s, 1H, Ar-H); MS (ESI, 70eV): m/z: 240 (M+1).

(1-Octyl-1H-(1,2,3)triazol-4-yl)methanol (**5b**):



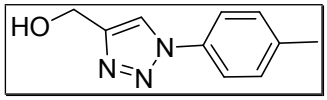
White solid, Yield: 93%, I.R. (KBr, cm^{-1}): 3387 (OH), 1528 (C=C); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 0.88 (t, 3H, CH_3), 1.25-1.30 (m, 10H, CH_2), 1.84-1.88 (m, 2H, -CH_2), 4.32 (t, 2H, CH_2), 4.61 (s, 2H, CH_2-O), 4.97 (brs, 1H, OH), 7.78 (s, 1H, Ar-H); MS (ESI, 70eV): m/z: 212 (M+1).

(1-Phenyl-1H-1,2,3-triazol-4-yl)methanol (**5c**):[5]



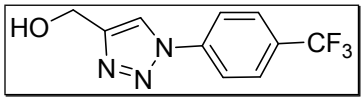
White solid, Yield: 90%, I.R. (KBr, cm^{-1}): 3379 (OH), 1594 (C=C); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 4.72 (s, 2H, CH_2), 5.13 (brs, 1H, OH), 7.31-7.33 (m, 1H, Ar-H), 7.45-7.54 (m, 2H,Ar-H), 7.74-7.82 (m, 2H, Ar-H), 8.27 (s, 1H, triazol-H); MS (ESI, 70eV): m/z: 176 (M+1).

(1-p-Tolyl-1H-(1,2,3)triazol-4-yl)methanol (**5d**):[5]



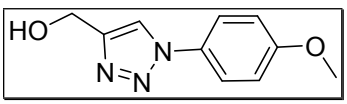
Brown solid, Yield: 78%, I.R. (KBr, cm^{-1}): 3426 (OH), 1517 (C=C); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 2.40 (s, 3H, CH_3), 4.71 (s, 2H, CH_2), 5.15 (brs, 1H, OH), 7.28 (d, 2H, Ar-H, J = 7.81 Hz), 7.64 (d, 2H, Ar-H, J = 7.81 Hz), 8.25 (s, 1H, triazol-H); MS (ESI, 70eV): m/z: 190 (M+1).

(1-(4-(Trifluoromethyl)phenyl)-1H-(1,2,3)triazol-4-yl)methanol (**5e**):



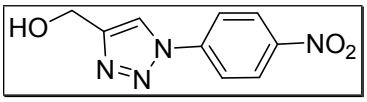
White solid, Yield: 84%, I.R. (KBr, cm^{-1}): 3295 (OH), 1522 (C=C); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 4.74 (s, 2H, CH_2), 5.06 (brs, 1H, OH), 7.80 (d, 2H, Ar-H, J = 8.31 Hz), 8.05 (d, 2H, Ar-H, J = 8.31 Hz), 8.43 (s, 1H, triazol-H); MS (ESI, 70eV): m/z: 244 (M+1).

(1-(4-Methoxyphenyl)-1H-(1,2,3)triazol-4-yl)methanol (**5f**):[5]



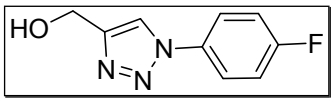
Brown solid, Yield: 82%, I.R. (KBr, cm^{-1}): 3421 (OH), 1584 (C=C); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 3.85 (s, 3H, OCH_3), 4.67 (s, 2H, CH_2), 5.11 (brs, 1H, OH), 7.01 (d, 2H, Ar-H, J = 8.87 Hz), 7.70 (d, 2H, Ar-H, J = 8.87 Hz), 8.26 (s, 1H, triazol-H); MS (ESI, 70eV): m/z: 206 (M+1).

(1-(4-Nitrophenyl)-1H-(1,2,3)triazol-4-yl)methanol (**5g**):[5]



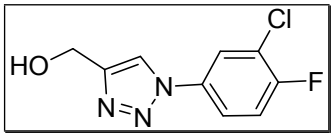
Yellow solid, Yield: 86%, I.R. (KBr, cm^{-1}): 3283 (OH), 1583 (C=C); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 4.68 (s, 2H, CH_2), 5.25 (brs, 1H, OH), 8.22 (d, 2H, Ar-H, J = 9.06 Hz), 8.40 (d, 2H, Ar-H, J = 9.06 Hz), 8.71-8.75 (m, 1H, triazol-H); MS (ESI, 70eV): m/z: 221 (M+1).

(1-(4-Fluoro-phenyl)-1H-(1,2,3)triazol-4-yl)methanol (**5h**):[5]



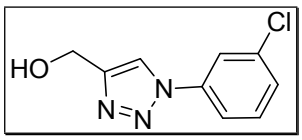
White solid, Yield: 92%, I.R. (KBr, cm^{-1}): 3325 (OH), 1526 (C=C); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 4.70 (s, 2H, CH_2), 5.11 (brs, 1H, OH), 7.32 (d, 2H, Ar-H), 7.90 (d, 2H,Ar-H), 8.30 (s, 1H, Ar-H); MS (ESI, 70eV): m/z: 194 (M+1).

(1-(3-Chloro-4-fluorophenyl)-1H-(1,2,3)triazol-4-yl)methanol (**5i**)**:**



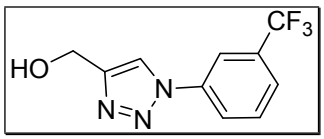
White solid, Yield: 91%, I.R. (KBr, cm^{-1}): 3263 (OH), 1583 (C=C); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 4.68 (s, 2H, CH_2), 5.18 (brs, 1H, OH), 7.39 (m, 1H, Ar-H, J = 8.69 Hz), 7.80-7.90 (m, 1H, Ar-H), 8.02-8.09 (m, 1H, Ar-H), 8.48 (s, 1H, triazol-H); MS (ESI, 70eV): m/z: 228 (M+1).

(1-(3-Chlorophenyl)-1H-(1,2,3)triazol-4-yl)methanol (**5j**):[5]



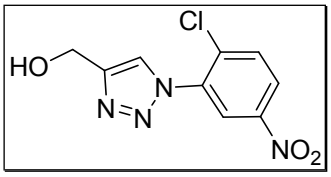
White solid, Yield: 93%, I.R. (KBr, cm^{-1}): 3263 (OH), 1593 (C=C); ^{1}H NMR (DMSO-d_6, 400 MHz): δ 4.67-4.72 (m, 2H, CH_2), 5.07-5.15 (m, 1H, OH), 7.39 (d, 1H, Ar-H, J = 7.93 Hz), 7.50 (t, 1H, Ar-H, J = 8.12 Hz), 7.78 (d, 1H, Ar-H, J = 7.93 Hz), 7.90-7.93 (m, 1H, Ar-H), 8.37-8.42 (m, 1H, triazol-H); MS (ESI, 70eV): m/z: 210 (M+1).

(1-(3-(Trifluoromethyl)phenyl)-1H-(1,2,3)triazol-4-yl)methanol (**5k**):



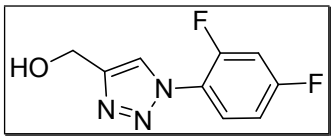
White solid, Yield: 87%, I.R. (KBr, cm^{-1}): 3288 (OH), 1520 (C=C); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 4.86 (s, 2H, CH_2), 5.09 (brs, 1H, OH), 7.62-7.70 (m, 2H, Ar-H), 7.95-8.02 (m, 2H, Ar-H), 8.04 (s, 1H, triazol-H); MS (ESI, 70eV): m/z: 244 (M+1).

(1-(2-Chloro-5-nitrophenyl)-1H-(1,2,3)triazol-4-yl)methanol (**5l**):



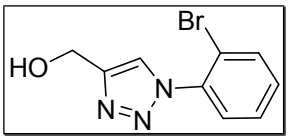
White solid, Yield: 88%, I.R. (KBr, cm^{-1}): 3294 (OH), 1516 (C=C); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 4.75 (s, 2H, CH_2), 5.19 (brs, 1H, OH), 7.88-7.95 (m, 1H, Ar-H), 8.21-8.28 (m, 1H, Ar-H), 8.34-8.42 (m, 1H, Ar-H), 8.49 (s, 1H, triazol-H); MS (ESI, 70eV): m/z: 255 (M+1).

(1-(2,4-Difluorophenyl)-1H-(1,2,3)triazol-4-yl)methanol (**5m**):



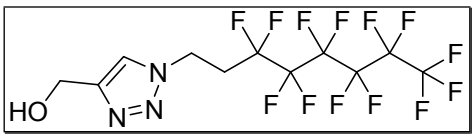
White solid, Yield: 88%, I.R. (KBr, cm^{-1}): 3325 (OH), 1526 (C=C); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 4.67 (s, 2H, CH_2), 5.11 (brs, 1H, OH), 7.14-7.25 (m, 1H, Ar-H), 7.27-7.39 (m, 1H, Ar-H),7.82-7.93 (m, 1H, Ar-H), 8.19 (s, 1H, triazol-H); MS (ESI, 70eV): m/z: 212 (M+1).

(1-(2-Bromophenyl)-1H-(1,2,3)triazol-4-yl)methanol (**5n**):



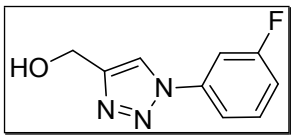
White solid, Yield: 62%, I.R. (KBr, cm^{-1}): 3304 (OH), 1514 (C=C); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 4.68-4.74 (m, 2H, CH_2), 5.08 (brs, 1H, OH), 7.42-7.50 (m, 1H, Ar-H), 7.52-7.58 (m, 2H, Ar-H), 7.78-7.84 (d, 1H, Ar-H, J = 7.85 Hz), 8.04 (s, 1H, triazol-H); MS (ESI, 70eV): m/z: 254 (M+1).

(1-(3,3,4,4,5,5,6,6,7,7,8,8,8-Tridecafluorooctyl)-1H-1,2,3-triazol-4-yl)methanol (**5o**):



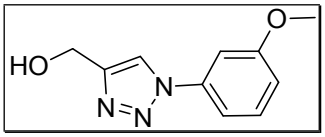
White solid, Yield: 62%, I.R. (KBr, cm^{-1}): 3387 (OH), 1528 (C=C); ^1H NMR (DMSO-d_6, 500 MHz): δ 2.86-2.96 (m, 2H, -CH_2), 4.45-4.60 (m, 2H, CH_2), 4.71 (s, 2H, OCH_2), 5.10 (br., s, 1H, OH), 8.01 (s, 1H, Ar-H); MS (ESI, 70eV): m/z: 446 (M+1).

(1-(3-Fluoro-phenyl)-1H-(1,2,3)triazol-4-yl)methanol (**5p**):



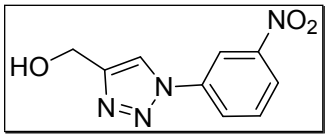
White solid, Yield: 92%, I.R. (KBr, cm^{-1}): 3237 (OH), 1502 (C=C); ^1H NMR (DMSO-d_6, 300 MHz): δ 4.81 (s, 2H, CH_2), 5.01 (brs, 1H, OH), 7.11-7.20 (m, 1H, Ar-H), 7.48-7.64 (m, 3H, Ar-H), 8.20 (s, 1H, Ar-H); MS (ESI, 70eV): m/z: 194 (M+1).

(1-(3-Methoxyphenyl)-1H-(1,2,3)triazol-4-yl)methanol (**5q**):[5]



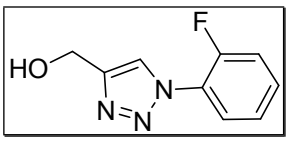
Brown solid, Yield: 80%, I.R. (KBr, cm^{-1}): 3276 (OH), 1503 (C=C); ^1H NMR (DMSO-d_6, 500 MHz): δ 3.87 (s, 3H, OCH_3), 4.82 (s, 2H, CH_2), 5.12 (brs, 1H, OH), 6.94-6.99 (m, 1H, Ar-H), 7.26-7.31 (m, 2H, Ar-H), 7.33-7.36 (m, 2H, Ar-H), 7.39-7.44 (m, 2H, Ar-H), 8.12 (s, 1H, triazol-H); MS (ESI, 70eV): m/z: 206 (M+1).

(1-(3-Nitrophenyl)-1H-(1,2,3)triazol-4-yl)methanol (**5r**):



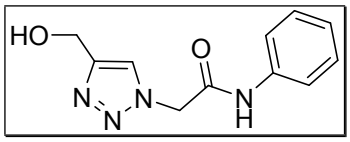
Yellow solid, Yield: 86%, I.R. (KBr, cm^{-1}): 3324 (OH), 1526 (C=C); ^1H NMR (DMSO-d_6, 500 MHz): δ 4.82 (s, 2H, CH_2), 5.11 (brs, 1H, OH), 7.77-7.82 (m, 1H, Ar-H), 8.25 (d, 1H, Ar-H, J = 7.55 Hz), 8.29 (d, 1H, Ar-H, J = 7.55 Hz), 8.45 (s, 1H, Ar-H), 8.71 (s, 1H, triazol-H); MS (ESI, 70eV): m/z: 221 (M+1).

(1-(2-Fluoro-phenyl)-1H-(1,2,3)triazol-4-yl)-methanol (**5s**):



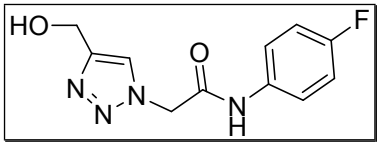
White solid, Yield: 78%, I.R. (KBr, cm^{-1}): 3387 (OH), 1528 (C=C); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 4.82 (s, 2H, CH_2), 5.02 (brs, 1H, OH), 7.31-7.38 (m, 2H, Ar-H), 7.45-7.52 (m, 1H, Ar-H), 7.88 (t, 1H, ArH, J = 8.10 Hz), 8.13 (s, 1H, Ar-H); MS (ESI, 70eV): m/z: 194 (M+1).

2-(4-(Hydroxymethyl)-1H-1,2,3-triazol-1-yl)-N-phenylacetamide (**10a**):



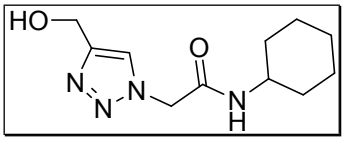
Brown solid, Yield: 80%, I.R. (KBr, cm^{-1}): 3322 (OH), 3144 (CH), 1698 (C=O), 1569 (C=C); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 4.64 (s, 2H, $\underline{CH_2}OH$), 5.23 (s, 2H, NCH_2), 7.01-7.07 (m, 1H, Ar-H), 7.23-7.30 (m, 2H, Ar-H), 7.54-7.60 (m, 2H, Ar-H), 7.91 (s, 1H, triazol-H), 10.26 (brs, 1H, NH); MS (ESI, 70eV): m/z: 233 (M+1).

N-(4-Fluorophenyl)-2-(4-(hydroxymethyl)-1H-1,2,3-triazol-1-yl)acetamide (**10b**):



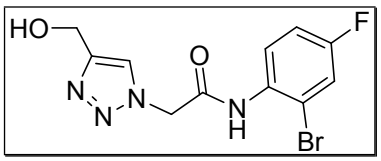
Brown solid, Yield: 82%, I.R. (KBr, cm^{-1}): 3318 (OH), 3144 (CH), 1691 (C=O), 1572 (C=C); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 4.61 (s, 2H, $\underline{CH_2}OH$), 5.23 (s, 2H, NCH_2), 6.95-7.05 (m, 2H, Ar-H), 7.54-7.63 (m, 2H, Ar-H), 7.94 (s, 1H, triazol-H), 10.39 (brs, 1H, NH); MS (ESI, 70eV): m/z: 251 (M+1).

N-Cyclohexyl-2-(4-(hydroxymethyl)-1H-1,2,3-triazol-1-yl)acetamide (**10c**):



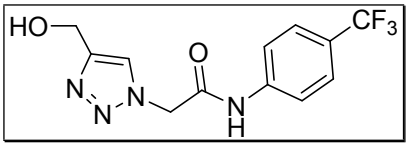
Brown solid, Yield: 84%, I.R. (KBr, cm^{-1}): 3321 (OH), 3135 (CH), 1681 (C=O), 1556 (C=C); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 1.13-1.39 (m, 5H, cyclohexyl-H), 1.56-1.66 (m, 1H, cyclohexyl-H), 1.69-1.88 (m, 4H, cyclohexyl-H), 3.54-3.64 (m, 1H, cyclohexyl-H), 4.64 (brs, 2H, $\underline{CH_2}OH$), 4.98 (s, 2H, NCH_2), 7.81-8.04 (m, 2H, triazol-H & NH); MS (ESI, 70eV): m/z: 239 (M+1).

N-(2-Bromo-4-fluorophenyl)-2-(4-(hydroxymethyl)-1H-1,2,3-triazol-1-yl)acetamide (**10d**):



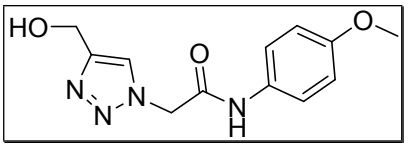
Brown solid, Yield: 86%, I.R. (KBr, cm^{-1}): 3278 (OH), 3144 (CH), 1701 (C=O), 1574 (C=C); ^1H NMR (DMSO-d_6, 500 MHz): δ 4.67 (s, 2H, $\underline{CH_2}OH$), 4.93 (brs, 1H, OH), 5.32 (s, 2H, NCH_2), 7.01-7.08 (m, 1H, Ar-H), 7.30-7.36 (m, 1H, Ar-H), 7.74-7.81 (m, 1H, Ar-H), 7.92 (s, 1H, triazol-H), 9.52 (brs, 1H, NH); MS (ESI, 70eV): m/z: 329 (M+1).

2-(4-(Hydroxymethyl)-1H-1,2,3-triazol-1-yl)-N-(4-(trifluoromethyl)phenyl)acetamide (**10e**):



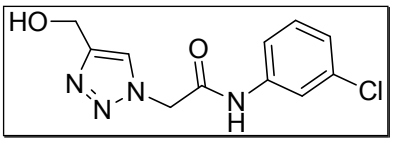
Brown solid, Yield: 79%, I.R. (KBr, cm^{-1}): 3308 (OH), 3114 (CH), 1691 (C=O), 1572 (C=C); ^1H NMR (DMSO-d_6, 500 MHz): δ 4.66-4.73 (m, 2H, $\underline{CH_2}OH$), 5.09 (brs, 1H, OH), 5.31 (s, 2H, NCH_2), 7.54-7.60 (m, 2H, Ar-H), 7.76-7.82 (m, 2H, Ar-H), 7.90 (s, 1H, triazol-H), 10.64 (brs, 1H, NH); MS (ESI, 70eV): m/z: 301 (M+1).

2-(4-(Hydroxymethyl)-1H-1,2,3-triazol-1-yl)-N-(4-methoxyphenyl)acetamide (**10f**):



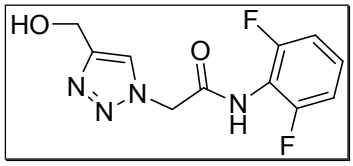
Brown solid, Yield: 83%, I.R. (KBr, cm^{-1}): 3298 (OH), 3116 (CH), 1688 (C=O), 1568 (C=C); ^1H NMR (DMSO-d_6, 500 MHz): δ 3.77 (s, 3H, OCH_3), 4.69 (s, 2H, $\underline{CH_2}OH$), 5.03 (brs, 1H, OH), 5.22 (s, 2H, NCH_2), 6.83 (d, 2H, Ar-H, J = 9.24 Hz), 7.50 (d, 2H, Ar-H, J = 9.24 Hz), 7.88 (s, 1H, triazol-H), 10.13 (brs, 1H, NH); MS (ESI, 70eV): m/z: 263 (M+1).

N-(3-Chlorophenyl)-2-(4-(hydroxymethyl)-1H-1,2,3-triazol-1-yl)acetamide (**10g**):



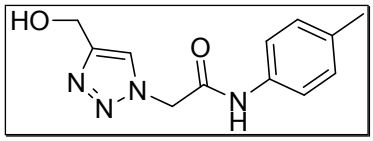
Brown solid, Yield: 86%, I.R. (KBr, cm^{-1}): 3282 (OH), 3112 (CH), 1694 (C=O), 1572 (C=C); ^1H NMR (DMSO-d_6, 500 MHz): δ 4.74 (s, 2H, $\underline{CH_2}OH$), 4.85 (brs, 1H, OH), 5.24 (s, 2H, NCH_2), 7.07 (d, 1H, Ar-H, J = 7.68 Hz), 7.21-7.28 (m, 1H, Ar-H), 7.44 (d, 1H, Ar-H, J = 7.68 Hz), 7.74-7.77 (m, 1H, Ar-H), 7.86 (s, 1H, triazol-H), 10.34 (brs, 1H, NH); MS (ESI, 70eV): m/z: 267 (M+1).

N-(2,6-Difluorophenyl)-2-(4-(hydroxymethyl)-1H-1,2,3-triazol-1-yl)acetamide (**10h**):



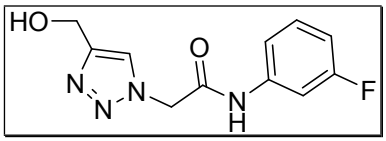
Brown solid, Yield: 88%, I.R. (KBr, cm^{-1}): 3318 (OH), 3104 (CH), 1692 (C=O), 1573 (C=C); ^1H NMR (DMSO-d_6, 300 MHz): δ 4.67-4.78 (m, 2H, $\underline{CH_2}OH$), 4.95 (brs, 1H, OH), 5.34 (s, 2H, NCH_2), 6.93-7.06 (m, 2H, Ar-H), 7.18-7.33 (m, 1H, Ar-H), 7.86 (s, 1H, triazol-H), 10.05 (brs, 1H, NH); MS (ESI, 70eV): m/z: 269 (M+1).

2-(4-(Hydroxymethyl)-1H-1,2,3-triazol-1-yl)-N-(p-tolyl)acetamide (**10i**):



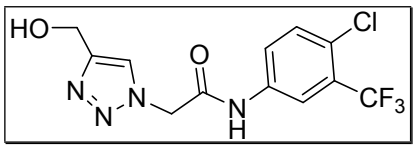
Brown solid, Yield: 82%, I.R. (KBr, cm^{-1}): 3298 (OH), 3142 (CH), 1698 (C=O), 1570 (C=C); ^1H NMR (DMSO-d_6, 500 MHz): δ 2.31 (s, 3H, CH_3), 4.72 (s, 2H, $\underline{CH_2}OH$), 4.85 (brs, 1H, OH), 5.21 (s, 2H, NCH_2), 7.09 (d, 2H, Ar-H, J = 6.21 Hz), 7.45 (d, 2H, Ar-H, J = 6.21 Hz), 7.86 (s, 1H, triazol-H), 10.03 (brs, 1H, NH); MS (ESI, 70eV): m/z: 247 (M+1).

N-(3-Fluorophenyl)-2-(4-(hydroxymethyl)-1H-1,2,3-triazol-1-yl)acetamide (**10j**):



Brown solid, Yield: 80%, I.R. (KBr, cm^{-1}): 3318 (OH), 3104 (CH), 1691 (C=O), 1572 (C=C); ^1H NMR (DMSO-d_6, 500 MHz): δ 4.67 (brs, 1H, OH), 4.75 (s, 2H, $\underline{CH_2}OH$), 5.23 (s, 2H, NCH_2), 6.75-6.83 (m, 1H, Ar-H), 7.21-7.30 (m, 2H, Ar-H), 7.48-7.57 (m, 1H, Ar-H), 7.85 (s, 1H, triazol-H), 10.28 (brs, 1H, NH); MS (ESI, 70eV): m/z: 251 (M+1).

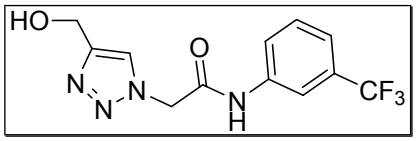
N-(4-Chloro-3-(trifluoromethyl)phenyl)-2-(4-(hydroxymethyl)-1H-1,2,3-triazol-1-yl)acetamide (**10k**):



Brown solid, Yield: 88%, I.R. (KBr, cm^{-1}): 3295 (OH), 3172 (CH), 1668 (C=O), 1573 (C=C); ^1H NMR (DMSO-d_6, 500 MHz): δ 4.67-4.83 (m, 2H, $\underline{CH_2}OH$), 4.91 (brs, 1H, OH), 5.26 (s, 2H,

NCH_2), 7.40-7.51 (m, 1H, Ar-H), 7.73-7.96 (m, 2H, Ar-H), 8.03-8.09 (m, 1H, triazol-H), 10.63 (brs, 1H, NH); MS (ESI, 70eV): m/z: 335 (M+1).

2-(4-(Hydroxymethyl)-1H-1,2,3-triazol-1-yl)-N-(3-(trifluoromethyl)phenyl)acetamide (**10l**):



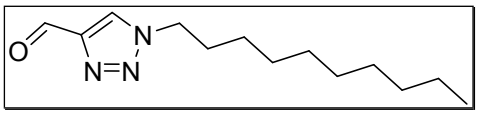
Brown solid, Yield: 82%, I.R. (KBr, cm^{-1}): 3248 (OH), 3140 (CH), 1696 (C=O), 1572 (C=C); ^1H NMR (DMSO-d_6, 500 MHz): δ 4.74 (brs, 2H, $\underline{CH_2}OH$), 4.93 (brs, 1H, OH), 5.27 (s, 2H, NCH_2), 7.30-7.38 (m, 1H, Ar-H), 7.40-7.50 (m, 1H, Ar-H), 7.72-7.80 (m, 1H, Ar-H), 7.87 (s, 1H, Ar-H), 8.01 (s, 1H, triazol-H), 10.55 (brs, 1H, NH); MS (ESI, 70eV): m/z: 298 (M+1).

Preparation of 1-substituted-(1,2,3)triazol-4-carbaldehyde (**6**) *and 2-(4-formyl-1H-1,2,3-triazol-1-yl)-N-substituted-acetamide* (**11**)**:**

General procedure:

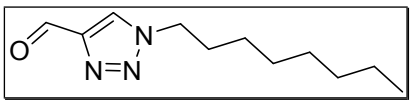
The 1-substituted-(1,2,3)triazol-4-yl-methanol **5** or 2-(4-(hydroxymethyl)-1*H*-1,2,3-triazol-1-yl)-*N*-substituted-acetamide **10** (4 mmol) was taken in dry acetone and cool to 0 ^{0}C and added the Jones reagent (CrO_3/H_2SO_4, acetone) (4 mmol) slowly over 5 min. The reaction mixture was stirred at 0 °C for 15 min. After completion of reaction, the reaction mixture was filtered through the short pad of celite and collected the filtrate, and concentrated under vacuum. The residue was purified by passing through a column packed with silica gel using petroleum ether/EtOAc (8:2) as eluents.

1-Decyl-1H-(1,2,3)triazol-4-carbaldehyde (**6a**):[2]



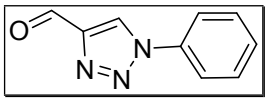
White solid, Yield: 72 %, I.R. (KBr, cm^{-1}): 3127 (CH), 1707 (C=O), 1542 (C=C); ^1H NMR ($CDCl_3$, 300 MHz): δ 0.88 (t, 3H, CH_3), 1.24-1.30 (m, 14H, CH_2), 1.92-1.97 (m, 2H, -CH_2), 4.42 (t, 2H, CH_2), 8.54 (s, 1H, Ar-H), 10.05 (s, 1H, CHO); MS (ESI, 70eV): m/z: 238 (M+1).

1-Octyl-1H-(1,2,3)triazol-4-carbaldehyde (**6b**):



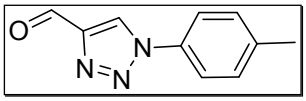
White solid, Yield: 74%, I.R. (KBr, cm^{-1}): 3128 (CH), 1705 (C=O), 1532 (C=C); ^1H NMR ($CDCl_3$, 300 MHz): δ 0.88 (t, 3H, CH_3), 1.25-1.30 (m, 10H, CH_2), 1.92-1.98 (m, 2H, -CH_2), 4.42 (t, 2H, CH_2), 8.54 (s, 1H, Ar-H), 10.06 (s, 1H, CHO); MS (ESI, 70eV): m/z: 210 (M+1).

1-Phenyl-1H-(1,2,3)triazol-4-carbaldehyde (**6c**):[5]



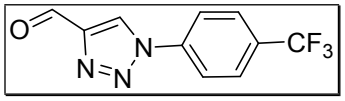
White solid, Yield: 72%, I.R. (KBr, cm^{-1}): 3131 (CH), 1691 (C=O), 1529 (C=C); ^1H NMR ($CDCl_3$, 400 MHz): δ 7.45-7.61 (m, 3H, Ar-H), 7.77-7.82 (m, 2H, Ar-H), 8.55 (s, 1H, Ar-H), 10.19 (s, 1H, -CHO); MS (ESI, 70eV): m/z: 174 (M+1).

1-p-Tolyl-1H-(1,2,3)triazol-4-carbaldehyde (**6d**):[6]



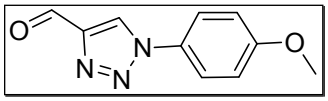
White solid, Yield: 78%, I.R. (KBr, cm^{-1}): 3136 (CH), 1696 (C=O), 1532 (C=C); ^1H NMR ($CDCl_3$, 400 MHz): δ 2.46 (s, 3H, CH_3), 7.35 (d, 2H, Ar-H, J = 8.31 Hz), 7.65 (d, 2H, Ar-H, J = 8.31 Hz), 8.46 (s, 1H, Ar-H), 10.19 (s, 1H, -CHO); MS (ESI, 70eV): m/z: 188 (M+1).

1-(4-(Trifluoromethyl)phenyl)-1H-(1,2,3)triazol-4-carbaldehyde (**6e**):



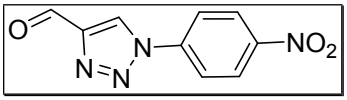
White solid, Yield: 74%, I.R. (KBr, cm^{-1}): 3128 (CH), 1707 (C=O), 1542 (C=C); ^1H NMR ($CDCl_3$, 400 MHz): δ 7.87 (d, 2H, Ar-H, J = 8.58 Hz), 7.99 (d, 1H, Ar-H, J = 8.58 Hz), 8.63 (s, 1H, Ar-H), 10.22 (s, 1H, -CHO); MS (ESI, 70eV): m/z: 242 (M+1).

1-(4-Methoxyphenyl)-1H-(1,2,3)triazol-4-carbaldehyde (**6f**):[6]



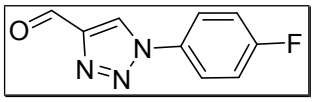
White solid, Yield: 64%, I.R. (KBr, cm^{-1}): 3157 (CH), 1685 (C=O), 1534 (C=C); ^1H NMR ($CDCl_3$, 300 MHz): δ 3.89 (s, 3H, OCH_3), 7.03 (d, 2H, Ar-H, J = 9.06 Hz), 7.67 (d, 2H, Ar-H, J = 9.06 Hz), 8.42 (s, 1H, Ar-H), 10.19 (s, 1H, -CHO); MS (ESI, 70eV): m/z: 204 (M+1).

1-(4-Nitrophenyl)-1H-(1,2,3)triazol-4-carbaldehyde (**6g**):[6]



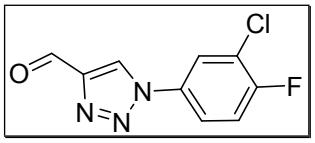
White solid, Yield: 62%, I.R. (KBr, cm^{-1}): 3136 (CH), 1696 (C=O), 1542 (C=C); ^1H NMR ($CDCl_3$, 400 MHz): δ 8.31-8.37 (m, 2H, Ar-H), 8.41-8.48 (m, 2H, Ar-H), 9.75 (s, 1H, Ar-H), 10.17 (s, 1H, -CHO); MS (ESI, 70eV): m/z: 219 (M+1).

1-(4-Fluoro-phenyl)-1H-(1,2,3)triazol-4-carbaldehyde (**6h**):[5]



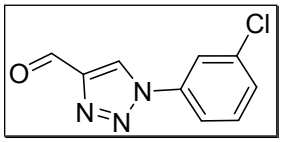
White solid, Yield: 79%, I.R. (KBr, cm^{-1}): 3131 (CH), 1702 (C=O), 1513 (C=C); ^1H NMR ($CDCl_3$, 300 MHz): δ 7.28 (d, 2H, Ar-H), 7.78 (m, 2H, Ar-H), 8.46 (s, 1H, Ar-H), 10.20 (s, 1H, -CHO); MS (ESI, 70eV): m/z: 192 (M+1).

1-(3-Chloro-4-fluorophenyl)-1H-(1,2,3)triazol-4-carbaldehyde (**6i**):



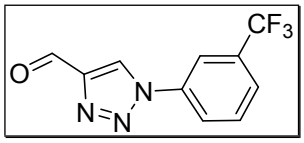
White solid, Yield: 68%, I.R. (KBr, cm^{-1}): 3146 (CH), 1704 (C=O), 1528 (C=C); ^1H NMR ($CDCl_3$, 500 MHz): δ 7.39-7.48 (m, 1H, Ar-H), 8.19-8.24 (m, 1H, Ar-H), 8.19-8.24 (m, 1H, Ar-H), 9.46-9.51 (m, 1H, Ar-H), 10.14 (s, 1H, -CHO); MS (ESI, 70eV): m/z: 226 (M+1).

1-(3-Chloro-phenyl)-1H-(1,2,3)triazol-4-carbaldehyde (**6j**):[6]



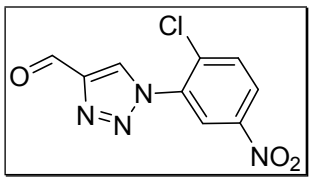
White solid, Yield: 74%, I.R. (KBr, cm^{-1}): 3127 (CH), 1701 (C=O), 1532 (C=C); ^1H NMR ($CDCl_3$, 500 MHz): δ 7.47-7.55 (m, 2H, Ar-H), 7.71 (d, 1H, Ar-H, J = 8.01 Hz), 7.84-7.88 (m, 1H, Ar-H), 8.54 (s, 1H, Ar-H), 10.20 (s, 1H, -CHO); MS (ESI, 70eV): m/z: 208(M+1).

1-(3-(Trifluoromethyl)phenyl)-1H-(1,2,3)triazol-4-carbaldehyde (**6k**):



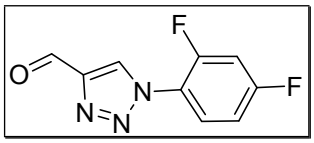
White solid, Yield: 72%, I.R. (KBr, cm^{-1}): 3138 (CH), 1702 (C=O), 1548 (C=C); ^1H NMR ($CDCl_3$, 300 MHz): δ 7.70-7.84 (m, 2H, Ar-H), 8.01-8.12 (m, 1H, Ar-H), 8.59 (s, 1H, Ar-H), 10.22 (s, 1H, -CHO); MS (ESI, 70eV): m/z: 242 (M+1).

1-(2-Chloro-5-nitrophenyl)-1H-(1,2,3)triazol-4-carbaldehyde (**6l**):



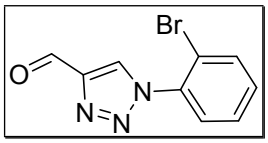
White solid, Yield: 64%, I.R. (KBr, cm^{-1}): 3152 (CH), 1694 (C=O), 1522 (C=C); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.84 (d, 1H, Ar-H, *J* = 9.01 Hz), 8.37-8.41 (m, 1H, Ar-H), 8.58-8.62 (m, 2H, Ar-H), 10.25 (s, 1H, -CHO); MS (ESI, 70eV): m/z: (M+1).

1-(2,4-Difluorophenyl)-1H-(1,2,3)triazol-4-carbaldehyde (**6m**):



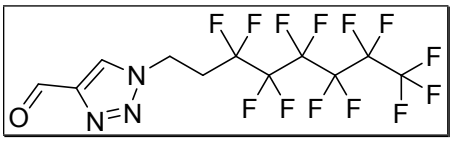
White solid, Yield: 68%, I.R. (KBr, cm^{-1}): 3124 (CH), 1698 (C=O), 1538 (C=C); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.09-7.18 (m, 2H, Ar-H), 8.00-8.07 (m, 1H, Ar-H), 8.54-8.59 (m, 1H, Ar-H), 10.20 (s, 1H, -CHO); MS (ESI, 70eV): m/z: 210 (M+1).

1-(2-Bromo-phenyl)-1H-(1,2,3)triazol-4-carbaldehyde (**6n**):



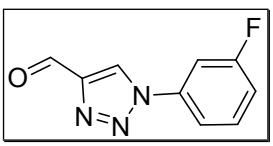
White solid, Yield: 64%, I.R. (KBr, cm^{-1}): 3158 (CH), 1692 (C=O), 1528 (C=C); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.43-7.48 (m, 1H, Ar-H), 7.54 (t, 1H, Ar-H, *J* = 7.91 Hz), 7.61 (d, 1H, Ar-H, *J* = 7.91 Hz), 7.80 (d, 1H, Ar-H, *J* = 7.91), 8.49 (s, 1H, Ar-H), 10.22 (s, 1H, -CHO); MS (ESI, 70eV): m/z: 252 (M+1).

1-(3,3,4,4,5,5,6,6,7,7,8,8,8-Tridecafluorooctyl)-1H-1,2,3-triazole-4-carbaldehyde (**6o**):



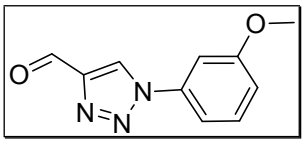
White solid, Yield: 64%, I.R. (KBr, cm^{-1}): 3142 (CH), 1707 (C=O), 1542 (C=C); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.81-2.96 (m, 2H, CH_2), 4.74-4.81 (m, 2H, CH_2), 8.18 (s, 1H, Ar-H), 10.16 (s, 1H, -CHO); MS (ESI, 70eV): m/z: 444 (M+1).

1-(3-Fluoro-phenyl)-1H-(1,2,3)triazol-4-carbaldehyde (**6p**):



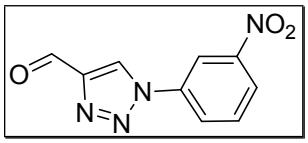
White solid, Yield: 80 %, I.R. (KBr, cm^{-1}): 3128 (CH), 1698 (C=O), 1532 (C=C); ^1H NMR ($CDCl_3$, 300 MHz): δ 7.19-7.29 (m, 1H, Ar-H), 7.53-7.64 (m, 1H, Ar-H), 7.70-7.80 (m, 2H, Ar-H), 9.14 (s, 1H, triazol-H), 10.20 (s, 1H, -CHO); MS (ESI, 70eV): m/z: 192 (M+1).

1-(3-Methoxyphenyl)-1H-(1,2,3)triazol-4-carbaldehyde (**6q**):[5]



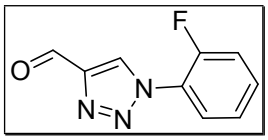
White solid, Yield: 72%, I.R. (KBr, cm^{-1}): 3106 (CH), 1683 (C=O), 1504 (C=C); ^1H NMR ($CDCl_3$, 300 MHz): δ 3.91 (s, 3H, OCH_3), 7.02-7.06 (m, 1H, Ar-H), 7.40-7.50 (m, 3H, Ar-H), 9.00 (s, 1H, triazol-H), 10.19 (s, 1H, -CHO); MS (ESI, 70eV): m/z: 204 (M+1).

1-(3-Nitrophenyl)-1H-(1,2,3)triazol-4-carbaldehyde (**6r**):



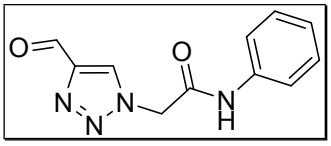
White solid, Yield: 64%, I.R. (KBr, cm^{-1}): 3128 (CH), 1690 (C=O), 1531 (C=C); ^1H NMR ($CDCl_3$, 300 MHz): δ 7.85 (t, 1H, Ar-H, J = 8.50 Hz), 8.34-8.45 (m, 2H, Ar-H), 8.88-8.92 (m, 1H, Ar-H), 9.54 (s, 1H, triazol-H), 10.21 (s, 1H, -CHO); MS (ESI, 70eV): m/z: 219 (M+1).

1-(2-Fluoro-phenyl)-1H-(1,2,3)triazol-4-carbaldehyde (**6s**):



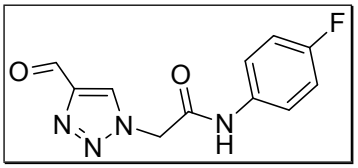
White solid, Yield: 78 %, I.R. (KBr, cm^{-1}): 3108 (CH), 1698 (C=O), 1528 (C=C); ^1H NMR ($CDCl_3$, 300 MHz): δ 7.32-7.44 (m, 2H, Ar-H), 7.48-7.58 (m, 1H, Ar-H), 7.97-8.05 (m, 1H, Ar-H), 8.66 (s, 1H, triazol-H), 10.25 (s, 1H, -CHO); MS (ESI, 70eV): m/z: 192 (M+1).

2-(4-Formyl-1H-1,2,3-triazol-1-yl)-N-phenylacetamide (**11a**):



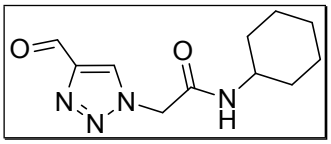
Brown solid, Yield: 58%, I.R. (KBr, cm^{-1}): 3321 (NH), 2941 (CH), 1681 (C=O), 1668 (C=O), 1556 (C=C); ^1H NMR (DMSO-d_6, 500 MHz): δ 5.38 (s, 2H, NCH_2), 7.02-7.09 (m, 1H, Ar-H), 7.24-7.32 (m, 2H, Ar-H), 7.55-7.61 (m, 2H, Ar-H), 8.69 (s, 1H, triazol-H), 10.08 (s, 1H, CHO), 10.26 (brs, 1H, NH); MS (ESI, 70eV): m/z: 231 (M+1).

N-(4-Fluorophenyl)-2-(4-formyl-1H-1,2,3-triazol-1-yl)acetamide (**11b**):



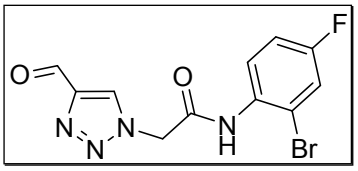
Brown solid, Yield: 60%, I.R. (KBr, cm^{-1}): 3325 (NH), 3101 (CH), 1698 (C=O), 1661 (C=O), 1555 (C=C); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 5.37 (s, 2H, NCH_2), 6.90-7.05 (m, 2H, Ar-H), 7.49-7.65 (m, 2H, Ar-H), 8.67 (s, 1H, triazol-H), 10.09 (s, 1H, CHO), 10.36 (brs, 1H, NH); MS (ESI, 70eV): m/z: 249 (M+1).

N-Cyclohexyl-2-(4-formyl-1H-1,2,3-triazol-1-yl)acetamide (**11c**):



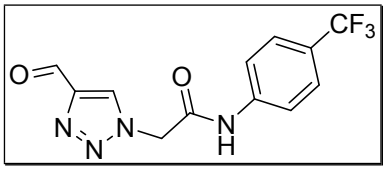
Brown solid, Yield: 68%, I.R. (KBr, cm^{-1}): 3323 (NH), 3108 (CH), 1702 (C=O), 1669 (C=O), 1565 (C=C); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 1.14-1.40 (m, 5H, cyclohexyl-H), 1.57-1.66 (m, 1H, cyclohexyl-H), 1.69-1.78 (m, 2H, cyclohexyl-H), 1.80-1.89 (m, 2H, cyclohexyl-H), 3.56-3.68 (m, 1H, cyclohexyl-H), 5.10 (s, 2H, NCH_2), 8.05 (brs, 1H, NH), 8.53-8.57 (m, 1H, triazol-H), 10.05 (s, 1H, CHO); MS (ESI, 70eV): m/z: 237 (M+1).

N-(2-Bromo-4-fluorophenyl)-2-(4-formyl-1H-1,2,3-triazol-1-yl)acetamide (**11d**):



Brown solid, Yield: 62%, I.R. (KBr, cm^{-1}): 3329 (NH), 3118 (CH), 1706 (C=O), 1674 (C=O), 1556 (C=C); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 5.47 (s, 2H, NCH_2), 7.02-7.10 (m, 1H, Ar-H), 7.30-7.37 (m, 1H, Ar-H), 7.68-7.78 (m, 1H, Ar-H), 8.64 (s, 1H, triazol-H), 9.79 (brs, 1H, NH), 10.08 (s, 1H, CHO); MS (ESI, 70eV): m/z: 327 (M+1).

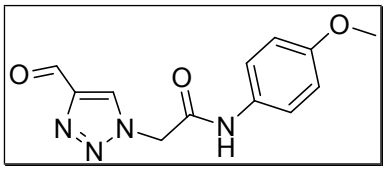
2-(4-Formyl-1H-1,2,3-triazol-1-yl)-N-(4-(trifluoromethyl)phenyl)acetamide (**11e**):



Brown solid, Yield: 56%, I.R. (KBr, cm^{-1}): 3296 (NH), 3108 (CH), 1706 (C=O), 1673 (C=O), 1558 (C=C); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 5.45 (s, 2H, NCH_2), 7.52-7.61 (m, 2H, Ar-H),

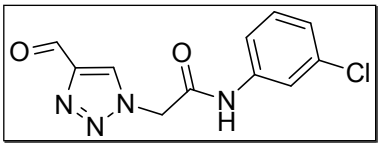
7.72-7.81 (m, 2H, Ar-H), 8.65 (s, 1H, triazol-H), 10.12 (s, 1H, CHO), 10.71 (brs, 1H, NH); MS (ESI, 70eV): m/z: 299 (M+1).

2-(4-Formyl-1H-1,2,3-triazol-1-yl)-N-(4-methoxyphenyl)acetamide (**11f**):



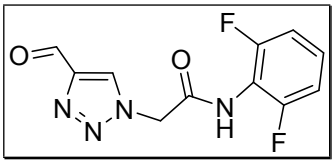
Brown solid, Yield: 58%, I.R. (KBr, cm^{-1}): 3323 (NH), 3109 (CH), 1702 (C=O), 1672 (C=O), 1556 (C=C); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 3.78 (s, 3H, OCH_3), 5.37 (s, 2H, NCH_2), 6.84 (d, 2H, Ar-H, J = 8.87 Hz), 7.50 (d, 2H, Ar-H, J = 8.87 Hz), 8.65 (s, 1H, triazol-H), 10.10 (s, 1H, CHO), 10.25 (brs, 1H, NH); MS (ESI, 70eV): m/z: 261 (M+1).

N-(3-Chlorophenyl)-2-(4-formyl-1H-1,2,3-triazol-1-yl)acetamide (**11g**):



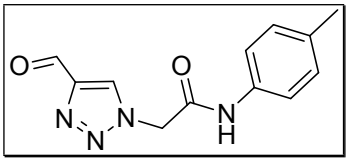
Brown solid, Yield: 59%, I.R. (KBr, cm^{-1}): 3329 (NH), 3101 (CH), 1698 (C=O), 1665 (C=O), 1552 (C=C); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 5.39 (s, 2H, NCH_2), 7.07 (d, 1H, Ar-H, J = 8.07 Hz), 7.25 (t, 1H, Ar-H, J = 8.07 Hz), 7.42 (d, 1H, Ar-H, J = 8.07 Hz), 7.74 (s, 1H, Ar-H), 8.58 (s, 1H, triazol-H), 10.12 (s, 1H, CHO), 10.46 (brs, 1H, NH); MS (ESI, 70eV): m/z: 265 (M+1).

N-(2,6-Difluorophenyl)-2-(4-formyl-1H-1,2,3-triazol-1-yl)acetamide (**11h**):



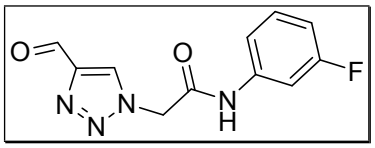
Brown solid, Yield: 62%, I.R. (KBr, cm^{-1}): 3321 (NH), 2941 (CH), 1681 (C=O), 1668 (C=O), 1556 (C=C); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 5.49 (s, 2H, NCH_2), 6.91-7.07 (m, 2H, Ar-H), 7.19-7.34 (m, 1H, Ar-H), 8.59 (s, 1H, triazol-H), 10.12 (s, 1H, CHO), 10.19 (brs, 1H, NH); MS (ESI, 70eV): m/z: 267 (M+1).

2-(4-Formyl-1H-1,2,3-triazol-1-yl)-N-(p-tolyl)acetamide (**11i**):



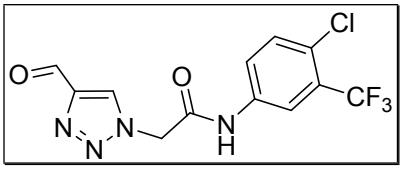
Brown solid, Yield: 65%, I.R. (KBr, cm^{-1}): 3327 (NH), 3108 (CH), 1708 (C=O), 1678 (C=O), 1556 (C=C); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 2.30 (s, 3H, CH_3), 5.38 (s, 2H, NCH_2), 7.07-7.13 (m, 2H, Ar-H), 7.43-7.50 (m, 2H, Ar-H), 8.65 (s, 1H, triazol-H), 10.10 (s, 1H, CHO), 10.29 (brs, 1H, NH); MS (ESI, 70eV): m/z: 245 (M+1).

N-(3-Fluorophenyl)-2-(4-formyl-1H-1,2,3-triazol-1-yl)acetamide (**11j**):



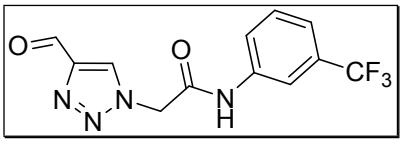
Brown solid, Yield: 58%, I.R. (KBr, cm^{-1}): 3329 (NH), 3115 (CH), 1712 (C=O), 1682 (C=O), 1562 (C=C); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 5.40 (s, 2H, NCH_2), 6.75-6.86 (m, 1H, Ar-H), 7.22-7.34 (m, 1H, Ar-H), 7.49-7.59 (m, 1H, Ar-H), 7.64-7.73 (m, 1H, Ar-H), 8.63 (s, 1H, triazol-H), 10.12 (s, 1H, CHO), 10.53 (brs, 1H, NH); MS (ESI, 70eV): m/z: 249 (M+1).

N-(4-Chloro-3-(trifluoromethyl)phenyl)-2-(4-formyl-1H-1,2,3-triazol-1-yl)acetamide (**11k**):



Brown solid, Yield: 63%, I.R. (KBr, cm^{-1}): 3328 (NH), 3105 (CH), 1708 (C=O), 1672 (C=O), 1556 (C=C); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 5.40 (s, 2H, NCH_2), 7.41-7.52 (m, 1H, Ar-H), 7.76-7.86 (m, 1H, Ar-H), 8.00-8.07 (m, 1H, Ar-H), 8.59 (s, 1H, triazol-H), 10.13 (s, 1H, CHO), 10.71 (brs, 1H, NH); MS (ESI, 70eV): m/z: 333 (M+1).

2-(4-Formyl-1H-1,2,3-triazol-1-yl)-N-(3-(trifluoromethyl)phenyl)acetamide (**11l**):



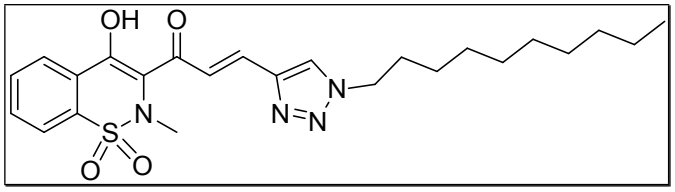
Brown solid, Yield: 53%, I.R. (KBr, cm^{-1}): 3300 (NH), 3108 (CH), 1701 (C=O), 1669 (C=O), 1560 (C=C); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 5.42 (s, 2H, NCH_2), 7.34-7.58 (m, 2H, Ar-H), 7.76-7.87 (m, 1H, Ar-H), 7.99 (m, 1H, Ar-H), 8.58 (s, 1H, triazol-H), 10.15 (s, 1H, CHO), 10.62 (brs, 1H, NH); MS (ESI, 70eV): m/z: 299(M+1).

Preparation of (E)-3-(1-substituted-1H-1,2,3-triazol-4-yl)-1-(4-hydroxy-2-methyl-1,1-dioxido-2H-benzo[e][1,2] thiazin-3-yl)prop-2-en-1-one (**8**) *and (E)-2-(4-(3-(4-hydroxy-2-methyl-1,1-dioxido-2H-benzo[e][1,2]thiazin-3-yl)-3-oxoprop-1-en-1-yl)-1H-1,2,3-triazol-1-yl)-N-substituted acetamide* (**12**):

General procedure:

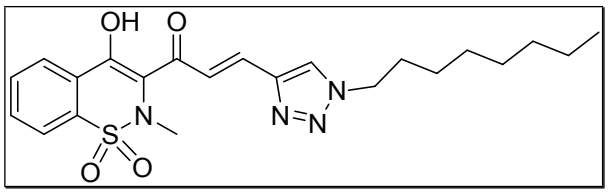
The 1-substituted-(1,2,3)triazol-4-carbaldehyde **7** / 2-(4-formyl-1*H*-1,2,3-triazol-1-yl)-*N*-substituted-acetamide **11** (0.79 mmol) and 1-(4-Hydroxy-2-methyl-1,1-dioxo-1,2-dihydro-1λ^6-benzo[e][1,2]thiazin-3-yl)-ethanone **4** (0.79 mmol) were taken in 10 mL of ethanol then 2 drops of piperidine was added, the total reaction mixture was refluxed for 3-4 h while stirring and the reaction was monitored by TLC. Solvent was removed from resulting mixture, residue was added to cool water and neutralized with 1N HCl then extracted with ethylacetate and concentrated under vacuum. The residue was purified by passing through a column packed with silica gel using petroleum ether/EtOAc (6:4) as eluent.

(E)-3-(1-Decyl-1H-1,2,3-triazol-4-yl)-1-(4-hydroxy-2-methyl-1,1-dioxido-2H-benzo[e][1,2] thiazin-3-yl)prop-2-en-1-one (**8a**):



Yellow solid, Yield: 63%, I.R. (KBr, cm^{-1}): 3445 (OH), 1640 (C=O), 1556 (C=C), 1347 (SO_2asym), 1181 (SO_2sym); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 0.82-0.93 (m, 3H, -$CH_2\underline{CH_3}$), 1.18-1.43 (m, 14H, -C_7H_{14}), 1.87-2.02 (m, 2H, -$NCH_2\underline{CH_2}$), 3.01 (s, 3H, -NCH_3), 4.39 (t, 2H,-$N\underline{CH_2}CH_2$, *J* = 6.80 Hz), 7.44-7.52 (m, 1H, Ar-H), 7.72-7.93 (m, 5H, Ar-H), 8.11-8.18 (m, 1H, Ar-H), 15.57 (brs, 1H, -OH); HRMS m/z Calcd. for $C_{24}H_{33}N_4SO_4$ ([M+H]$^+$): 473.2217, found 473.2215.

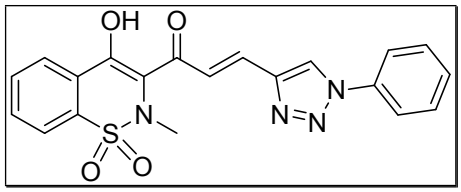
(E)-1-(4-Hydroxy-2-methyl-1,1-dioxido-2H-benzo[e][1,2]thiazin-3-yl)-3-(1-octyl-1H-1,2,3-triazol-4-yl)prop-2-en-1-one (**8b**):



Yellow solid, Yield: 69%, I.R. (KBr, cm^{-1}): 3447 (OH), 1639 (C=O), 1553 (C=C), 1346 (SO_2asym), 1182 (SO_2sym); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 0.82-0.90 (m, 3H, -$CH_2\underline{CH_3}$), 1.20-1.36 (m, 10H, -C_5H_{10}), 1.85-1.95 (m, 2H, $NCH_2\underline{CH_2}$), 2.96 (s, 3H, NCH_3), 4.38 (t, 2H,-$N\underline{CH_2}CH_2$, *J* = 6.93 Hz), 7.43-7.49 (m, 1H, Ar-H), 7.79-7.91 (m, 4H, Ar-H), 8.11-8.17 (m,

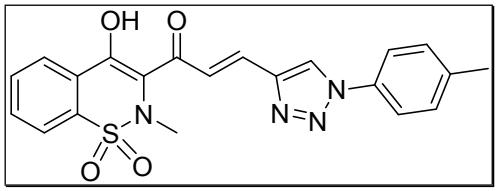
1H, Ar-H), 8.51 (s, 1H, Ar-H); HRMS m/z Calcd. for $C_{22}H_{29}N_4SO_4$ ([M+H]$^+$): 445.1940, found 445.1900.

(E)-1-(4-Hydroxy-2-methyl-1,1-dioxido-2H-benzo[e][1,2]thiazin-3-yl)-3-(1-phenyl-1H-1,2,3-triazol-4-yl)prop-2-en-1-one (**8c**):



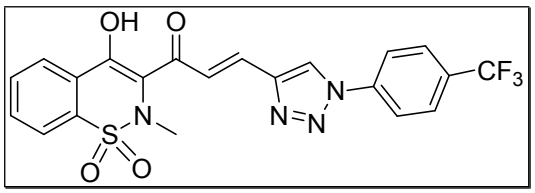
Yellow solid, Yield: 84%, I.R. (KBr, cm^{-1}): 3415 (OH), 1646 (C=O), 1559 (C=C), 1362 (SO_2asym), 1182 (SO_2sym); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 2.98 (s, 3H, NCH_3), 7.52-7.71 (m, 4H, Ar-H), 7.82-8.04 (m, 6H, Ar-H), 8.14-8.21 (m, 1H, Ar-H), 9.51 (s, 1H, Ar-H); HRMS m/z Calcd. for $C_{20}H_{17}N_4SO_4$ ([M+H]$^+$): 409.0965, found 409.0963.

(E)-1-(4-Hydroxy-2-methyl-1,1-dioxido-2H-benzo[e][1,2]thiazin-3-yl)-3-(1-(p-tolyl)-1H-1,2,3-triazol-4-yl)prop-2-en-1-one (**8d**):



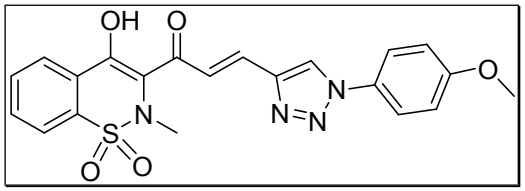
Yellow solid, Yield: 76%, I.R. (KBr, cm^{-1}): 3415 (OH), 1647 (C=O), 1557 (C=C), 1399 (SO_2asym), 1163 (SO_2sym); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 2.43 (s, 3H, CH_3), 2.92 (s, 3H, NCH_3), 7.12-7.40 (m, 4H, Ar-H), 7.82-8.04 (m, 6H, Ar-H), 8.14-8.21 (m, 1H, Ar-H), 9.51 (s, 1H, Ar-H); HRMS m/z Calcd. for $C_{21}H_{19}N_4SO_4$ ([M+H]$^+$): 423.1121, found 423.1119.

(E)-1-(4-Hydroxy-2-methyl-1,1-dioxido-2H-benzo[e][1,2]thiazin-3-yl)-3-(1-(4-(trifluoro methyl)phenyl)-1H-1,2,3-triazol-4-yl)prop-2-en-1-one (**8e**):



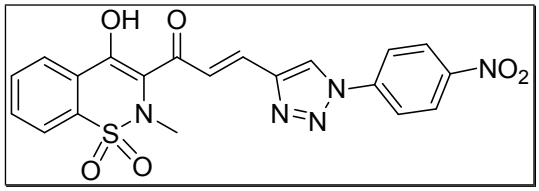
Yellow solid, Yield: 78%, I.R. (KBr, cm^{-1}): 3427 (OH), 1649 (C=O), 1562 (C=C), 1349 (SO_2asym), 1180 (SO_2sym); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 3.00 (s, 3H, -NCH_3), 7.54-7.66 (m, 1H, Ar-H), 7.84-7.95 (m, 6H, Ar-H), 8.12-8.24 (m, 3H, Ar-H), 9.53 (brs, 1H, Ar-H); HRMS m/z Calcd. for $C_{21}H_{15}F_3NaN_4SO_4$ ([M+Na]$^+$): 499.0658, found 499.0664.

(E)-1-(4-Hydroxy-2-methyl-1,1-dioxido-2H-benzo[e][1,2]thiazin-3-yl)-3-(1-(4-methoxy phenyl)-1H-1,2,3-triazol-4-yl)prop-2-en-1-one (**8f**):



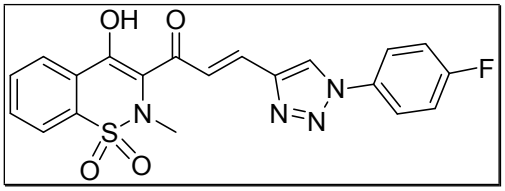
Yellow solid, Yield: 68%, I.R. (KBr, cm^{-1}): 3417 (OH), 1648 (C=O), 1558 (C=C), 1359 (SO_2asym), 1182 (SO_2sym); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 2.98 (s, 3H, -NCH_3), 3.88 (s, 3H, -OCH_3), 7.05 (d, 2H, Ar-H, J = 8.50 Hz), 7.54-7.93 (m, 7H, Ar-H), 8.11-8.22 (m, 1H, Ar-H), 9.03 (brs, 1H, Ar-H); HRMS m/z Calcd. for $C_{21}H_{19}N_4SO_5$ ($[M+H]^+$): 439.1071, found 439.1063.

(E)-1-(4-Hydroxy-2-methyl-1,1-dioxido-2H-benzo[e][1,2]thiazin-3-yl)-3-(1-(4-nitrophenyl)-1H-1,2,3-triazol-4-yl)prop-2-en-1-one (**8g**):



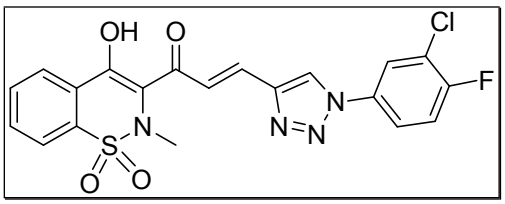
Yellow solid, Yield: 81%, I.R. (KBr, cm^{-1}): 3420 (OH), 1647 (C=O), 1561 (C=C), 1348 (SO_2asym), 1180 (SO_2sym); ^{1}H NMR (TFA+$CDCl_3$, 500 MHz): δ 3.03 (s, 3H, -NCH_3), 7.37-8.28 (m, 9H, Ar-H), 8.45-8.51 (m, 2H, Ar-H); HRMS m/z Calcd. for $C_{20}H_{16}N_5SO_6$ ($[M+H]^+$): 454.0821, found 454.0816.

(E)-3-(1-(4-Fluorophenyl)-1H-1,2,3-triazol-4-yl)-1-(4-hydroxy-2-methyl-1,1-dioxido-2H-benzo [e][1,2]thiazin-3-yl)prop-2-en-1-one (**8h**):



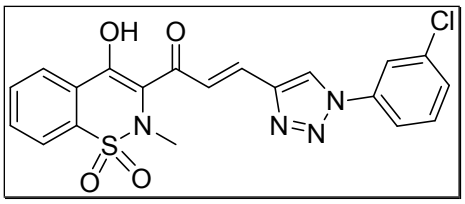
Yellow solid, Yield: 82%, I.R. (KBr, cm^{-1}): 3423 (OH), 1638 (C=O), 1512 (C=C), 1347 (SO_2asym), 1178 (SO_2sym); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 2.94 (s, 3H, -NCH_3), 7.48-7.70 (m, 3H, Ar-H), 7.80-8.22 (m, 7H, Ar-H), 9.42 (brs, 1H, Ar-H); HRMS m/z Calcd. for $C_{20}H_{16}FN_4SO_4$ ($[M+H]^+$): 427.0871, found 427.0866.

(E)-3-(1-(3-Chloro-4-fluorophenyl)-1H-1,2,3-triazol-4-yl)-1-(4-hydroxy-2-methyl-1,1-dioxido-2H-benzo[e][1,2]thiazin-3-yl)prop-2-en-1-one (**8i**):



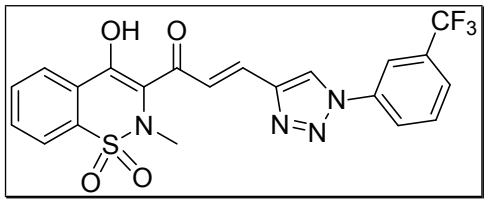
Yellow solid, Yield: 62%, I.R. (KBr, cm^{-1}): 3423 (OH), 1643 (C=O), 1527 (C=C), 1353 (SO_2asym), 1182 (SO_2sym); ^1H NMR (DMSO-d_6, 300 MHz): δ 2.95 (s, 3H, -NCH_3), 7.42-8.30 (m, 10H, Ar-H), 9.51 (brs, 1H, Ar-H); HRMS m/z Calcd. for $C_{20}H_{15}ClFN_4SO_4$ ($[M+H]^+$): 461.0481, found 461.0483.

(E)-3-(1-(3-Chlorophenyl)-1H-1,2,3-triazol-4-yl)-1-(4-hydroxy-2-methyl-1,1-dioxido-2H-benzo[e][1,2]thiazin-3-yl)prop-2-en-1-one (**8j**):



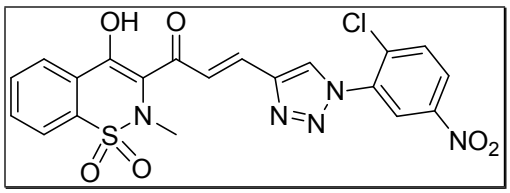
Yellow solid, Yield: 84%, I.R. (KBr, cm^{-1}): 3442 (OH), 1641 (C=O), 1556 (C=C), 1357 (SO_2asym), 1184 (SO_2sym); ^1H NMR (DMSO-d_6, 300 MHz): δ 2.91 (s, 3H, -NCH_3), 7.34-8.14 (m, 10H, Ar-H), 9.18 (brs, 1H, Ar-H); HRMS m/z Calcd. for $C_{20}H_{16}ClN_4SO_4$ ($[M+H]^+$): 443.0575, found 443.0581.

(E)-1-(4-Hydroxy-2-methyl-1,1-dioxido-2H-benzo[e][1,2]thiazin-3-yl)-3-(1-(3-(trifluoro methyl) phenyl)-1H-1,2,3-triazol-4-yl)prop-2-en-1-one (**8k**):



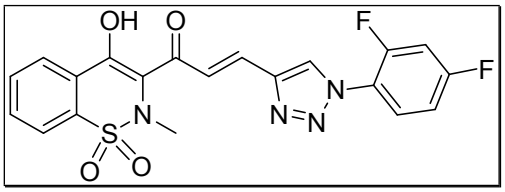
Yellow solid, Yield: 72%, I.R. (KBr, cm^{-1}): 3328 (OH), 1647 (C=O), 1559 (C=C), 1345 (SO_2asym), 1181 (SO_2sym); ^1H NMR (DMSO-d_6, 300 MHz): δ 3.01 (s, 3H, -NCH_3), 7.51-7.63 (m, 1H, Ar-H), 7.71-8.02 (m, 6H, Ar-H), 8.12-8.38 (m, 3H, Ar-H), 9.53 (s, 1H, Ar-H); HRMS m/z Calcd. for $C_{21}H_{16}F_3N_4SO_4$ ($[M+H]^+$): 477.0839, found 477.0843.

(E)-3-(1-(2-Chloro-5-nitrophenyl)-1H-1,2,3-triazol-4-yl)-1-(4-hydroxy-2-methyl-1,1-dioxido-2H-benzo[e][1,2]thiazin-3-yl)prop-2-en-1-one (**8l**):



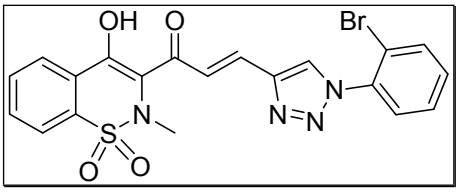
Yellow solid, Yield: 74%, I.R. (KBr, cm^{-1}): 3427 (OH), 1648 (C=O), 1538 (C=C), 1359 (SO_2asym), 1180 (SO_2sym); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 2.93 (s, 3H, -NCH_3), 7.60-8.60 (m, 9H, Ar-H), 8.73 (d, 1H, Ar-H, J = 19.26 Hz); HRMS m/z Calcd. for $C_{20}H_{15}ClN_5SO_6$ ($[M+H]^+$): 488.0431, found 488.0428.

(E)-3-(1-(2,4-Difluorophenyl)-1H-1,2,3-triazol-4-yl)-1-(4-hydroxy-2-methyl-1,1-dioxido-2H-benzo[e][1,2]thiazin-3-yl)prop-2-en-1-one (**8m**):



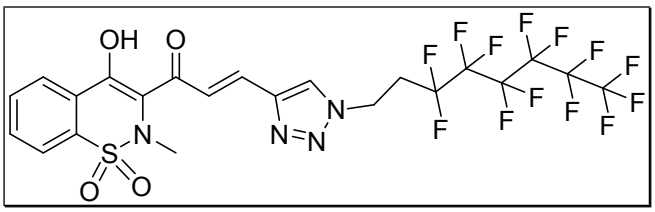
Yellow solid, Yield: 90%, I.R. (KBr, cm^{-1}): 3427 (OH), 1649 (C=O), 1558 (C=C), 1342 (SO_2asym), 1180 (SO_2sym); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 2.97 (s, 3H, -NCH_3), 7.38-7.43 (m, 1H, Ar-H), 7.61 (d, 1H, Ar-H, J = 15.88 Hz), 7.71-7.77 (m,1H, Ar-H), 7.89-8.20 (m, 6H, Ar-H), 9.26 (brs, 1H, Ar-H); HRMS m/z Calcd. for $C_{20}H_{14}F_2NaN_4SO_4$ ($[M+Na]^+$): 467.0596, found 467.0598.

(E)-3-(1-(2-Bromophenyl)-1H-1,2,3-triazol-4-yl)-1-(4-hydroxy-2-methyl-1,1-dioxido-2H-benzo[e][1,2]thiazin-3-yl)prop-2-en-1-one (**8n**):



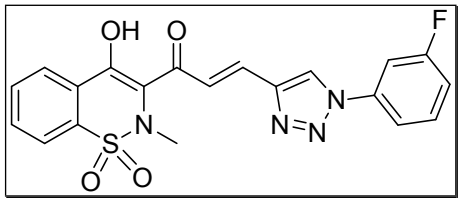
Yellow solid, Yield: 78%, I.R. (KBr, cm^{-1}): 3417 (OH), 1648 (C=O), 1558 (C=C), 1359 (SO_2asym), 1182 (SO_2sym); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 2.92 (s, 3H, -NCH_3), 7.42-7.83 (m, 9H, Ar-H), 8.04-8.13 (m, 1H, Ar-H), 8.48 (s, 1H, Ar-H); HRMS m/z Calcd. for $C_{20}H_{16}BrN_4SO_4$ ($[M+H]^+$): 487.0076, found 487.0072.

(E)-1-(4-Hydroxy-2-methyl-1,1-dioxido-2H-benzo[e][1,2]thiazin-3-yl)-3-(1-(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl)-1H-1,2,3-triazol-4-yl)prop-2-en-1-one (**8o**):



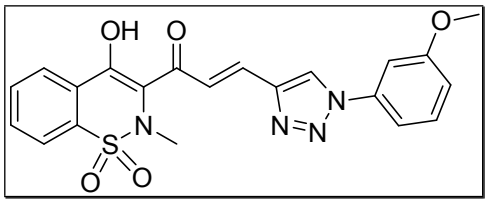
Yellow solid, Yield: 72%, I.R. (KBr, cm^{-1}): 3445 (OH), 1640 (C=O), 1556 (C=C), 1348 (SO_2asym), 1182 (SO_2sym); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 2.53-2.58 (m, 2H, $\underline{CH_2}$-C_6F_{13}), 2.98 (s, 3H, -NCH_3), 4.82 (t, 2H, NCH_2, J = 6.62Hz),7.49-7.56 (m, 1H, Ar-H), 7.84-7.94 (m, 4H, Ar-H), 8.14-8.19 (m, 1H, Ar-H), 8.72 (s, 1H, triazol-H); HRMS m/z Calcd. for $C_{20}H_{16}N_5SO_6$ ($[M+H]^+$): 679.06792, found 679.06787.

(E)-3-(1-(3-Fluorophenyl)-1H-1,2,3-triazol-4-yl)-1-(4-hydroxy-2-methyl-1,1-dioxido-2H-benzo[e][1,2]thiazin-3-yl)prop-2-en-1-one (**8p**):



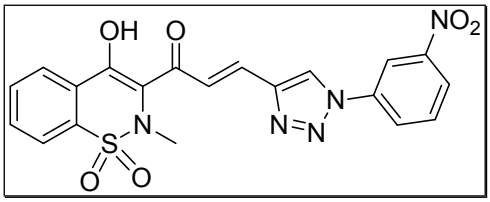
Yellow solid, Yield: 81%, I.R. (KBr, cm^{-1}): 3422 (OH), 1646 (C=O), 1558 (C=C), 1349 (SO_2asym), 1180 (SO_2sym); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 3.00 (s, 3H, -NCH_3), 7.26-7.34 (m, 1H, Ar-H), 7.55-7.68 (m, 2H, Ar-H), 7.79-7.98 (m, 6H, Ar-H), 8.13-8.21 (m, 1H, Ar-H), 9.49 (s, 1H, triazol-H); HRMS m/z Calcd. for $C_{20}H_{16}FN_4SO_4$ ($[M+H]^+$): 427.0871, found 427.0872.

(E)-1-(4-Hydroxy-2-methyl-1,1-dioxido-2H-benzo[e][1,2]thiazin-3-yl)-3-(1-(3-methoxy phenyl)-1H-1,2,3-triazol-4-yl)prop-2-en-1-one (**8q**):



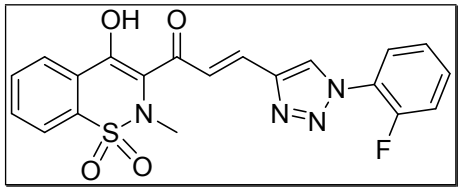
Yellow solid, Yield: 81%, I.R. (KBr, cm^{-1}): 3417 (OH), 1649 (C=O), 1548 (C=C), 1357 (SO_2asym), 1180 (SO_2sym); ^{1}H NMR (TFA+$CDCl_3$, 300 MHz): δ 3.02 (s, 3H, -NCH_3), 3.94 (s, 3H, -OCH_3), 7.12-7.40 (m, 3H, Ar-H), 7.48-7.72 (m, 2H, Ar-H), 7.81-7.98 (m, 4H, Ar-H), 8.15-8.23 (m, 1H, Ar-H), 8.70 (s, 1H, triazol-H); HRMS m/z Calcd. for $C_{21}H_{18}N_4NaSO_5$ ($[M+Na]^+$): 461.089, found 461.0902.

(E)-1-(4-Hydroxy-2-methyl-1,1-dioxido-2H-benzo[e][1,2]thiazin-3-yl)-3-(1-(3-nitrophenyl)-1H-1,2,3-triazol-4-yl)prop-2-en-1-one (**8r**):



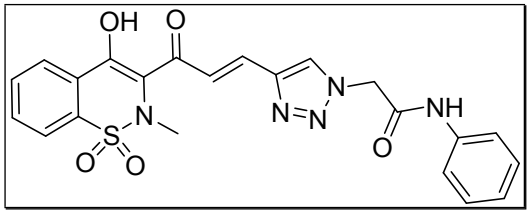
Yellow solid, Yield: 68%, I.R. (KBr, cm^{-1}): 3417 (OH), 1648 (C=O), 1558 (C=C), 1359 (SO_2asym), 1184 (SO_2sym); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 3.01 (s, 3H, -NCH_3), 7.55-7.65 (m, 1H, Ar-H), 7.85-7.98 (m, 5H, Ar-H), 8.10-8.22 (m, 1H, Ar-H), 8.33-8.50 (m, 2H, Ar-H), 8.83-8.89 (m, 1H, Ar-H), 9.70 (s, 1H, triazol-H); HRMS m/z Calcd. for $C_{20}H_{16}N_5SO_6$ ($[M+H]^+$): 454.0821, found 454.0818.

(E)-3-(1-(2-Fluorophenyl)-1H-1,2,3-triazol-4-yl)-1-(4-hydroxy-2-methyl-1,1-dioxido-2H-benzo[e][1,2]thiazin-3-yl)prop-2-en-1-one (**8s**):



Yellow solid, Yield: 65%, I.R. (KBr, cm^{-1}): 3418 (OH), 1642 (C=O), 1542 (C=C), 1349 (SO_2asym), 1181 (SO_2sym); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 3.02 (s, 3H, -NCH_3), 7.35-7.46 (m, 2H, Ar-H), 7.50-7.59 (m, 1H, Ar-H), 7.61-7.74 (m, 2H, Ar-H), 7.81-8.00 (m, 4H, Ar-H), 8.15-8.21 (m, 1H, Ar-H), 8.70 (s, 1H, triazol-H); HRMS m/z Calcd. for $C_{20}H_{16}FN_4SO_4$ ($[M+H]^+$): 427.0870, found 427.0868.

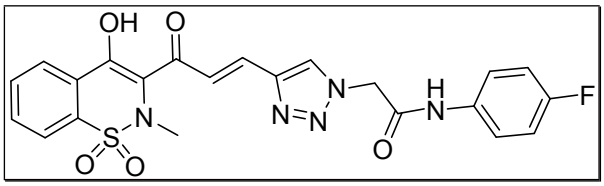
(E)-2-(4-(3-(4-Hydroxy-2-methyl-1,1-dioxido-2H-benzo[e][1,2]thiazin-3-yl)-3-oxoprop-1-en-1-yl)-1H-1,2,3-triazol-1-yl)-N-phenylacetamide (**12a**):



Yellow solid, Yield: 70%, I.R. (KBr, cm^{-1}): 3334 (NH), 1712 (C=O), 1647 (C=O), 1538 (C=C), 1345 (SO_2asym), 1176 (SO_2sym); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 2.99 (s, 3H, NCH_3), 5.34 (s, 2H, NCH_2), 7.06-7.18 (m, 2H, Ar-H), 7.42-7.74 (m, 4H, Ar-H), 7.81-7.99 (m, 5H, Ar-H), 8.11-8.22 (m, 1H, Ar-H), 8.45 (s, 1H, triazol-H), 10.26 (brs, 1H, NH); ^{13}C NMR (DMSO-d_6, 75

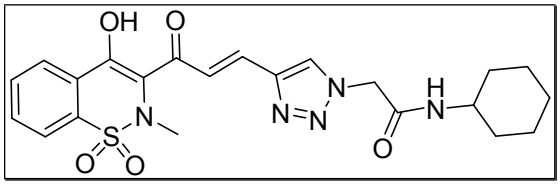
MHz): δ 40.9, 52.1, 117.5, 118.3, 119.1, 123.9, 127.3, 127.5, 128.7, 132.6, 132.8, 132.9, 133.7, 135.2, 135.7, 142.7, 162.9, 173.8, 180.7; HRMS m/z Calcd. for $C_{23}H_{22}N_5SO_5$ ([M+H]$^+$): 466.1180, found 466.1184.

(E)-N-(4-Fluorophenyl)-2-(4-(3-(4-hydroxy-2-methyl-1,1-dioxido-2H-benzo[e][1,2]thiazin-3-yl)-3-oxoprop-1-en-1-yl)-1H-1,2,3-triazol-1-yl)acetamide (**12b**):



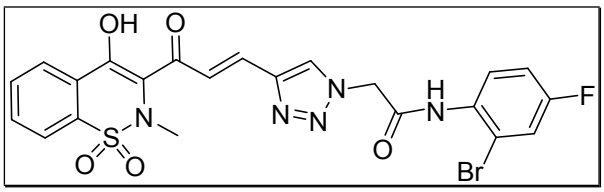
Yellow solid, Yield: 68%, I.R. (KBr, cm^{-1}): 3353 (NH), 1716 (C=O), 1645 (C=O), 1530 (C=C), 1339 (SO_2asym), 1180 (SO_2sym); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 2.98 (s, 3H, NCH_3), 5.30 (s, 2H, NCH_2), 6.92-7.03 (m, 2H, Ar-H), 7.48-7.93 (m, 7H, Ar-H), 8.09-8.19 (m, 1H, Ar-H), 8.51 (s, 1H, triazol-H), 10.33 (brs, 1H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz): δ 40.6, 52.1, 114.4, 117.2, 117.4, 118.2, 123.8, 126.4, 127.4, 128.6, 130.2, 132.5, 133.0, 135.5, 142.2, 160.2 (d, J = 249.14 Hz), 162.8, 172.5, 180.0: HRMS m/z Calcd. for $C_{22}H_{18}N_5FNaSO_5$ ([M+Na]$^+$): 506.0905, found 506.0894.

(E)-N-Cyclohexyl-2-(4-(3-(4-hydroxy-2-methyl-1,1-dioxido-2H-benzo[e][1,2]thiazin-3-yl)-3-oxoprop-1-en-1-yl)-1H-1,2,3-triazol-1-yl)acetamide (**12c**):



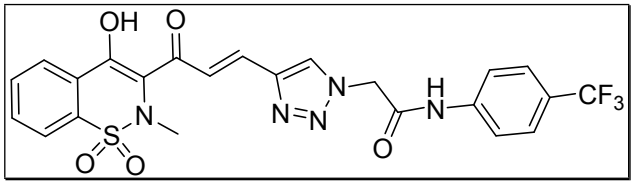
Yellow solid, Yield: 75%, I.R. (KBr, cm^{-1}): 3372 (NH), 1675 (C=O), 1639 (C=O), 1551 (C=C), 1345 (SO_2asym), 1181 (SO_2sym); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 1.15-1.40 (m, 5H, cyclohexyl-H), 1.57-1.65 (m, 1H, cyclohexyl-H), 1.69-1.79 (m, 2H, cyclohexyl-H), 1.81-1.91 (m, 2H, cyclohexyl-H), 3.00 (s, 3H, NCH_3), 3.59-3.69 (m, 1H, cyclohexyl-H), 5.07 (s, 2H, NCH_2), 7.49-7.56 (m, 1H, Ar-H), 7.82-7.92 (m, 4H, Ar-H), 8.02 (br. s, 1H, NH), 8.12-8.18 (m, 1H, Ar-H), 8.44-8.52 (m, 1H, Ar-H); ^{13}C NMR (DMSO-d_6, 75 MHz): δ 24.1, 24.8, 28.8, 31.9, 40.8, 47.8, 51.6, 117.2, 118.2, 123.9, 127.3, 128.7, 132.8, 133.8, 135.7, 142.5, 163.3, 173.7, 180.6; HRMS m/z Calcd. for $C_{22}H_{26}N_5SO_5$ ([M+H]$^+$): 472.1649, found 472.1636.

(E)-N-(2-Bromo-4-fluorophenyl)-2-(4-(3-(4-hydroxy-2-methyl-1,1-dioxido-2H-benzo[e][1,2] thiazin-3-yl)-3-oxoprop-1-en-1-yl)-1H-1,2,3-triazol-1-yl)acetamide (**12d**):



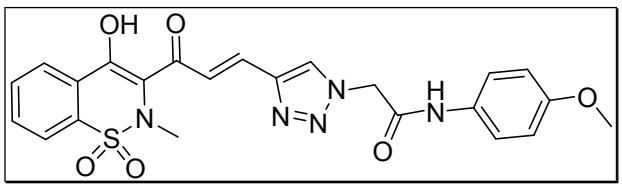
Yellow solid, Yield: 73%, I.R. (KBr, cm^{-1}): 3366 (NH), 1715 (C=O), 1643 (C=O), 1532 (C=C), 1344 (SO_2asym), 1180 (SO_2sym); ^1H NMR (DMSO-d_6, 500 MHz): δ 2.99 (s, 3H, NCH_3), 5.45 (s, 2H, NCH_2), 7.03-7.11 (m, 1H, Ar-H), 7.32-7.39 (m, 1H, Ar-H), 7.55-7.67 (m, 1H, Ar-H), 7.78-7.94 (m, 5H, Ar-H), 8.14-8.22 (m, 1H, Ar-H), 8.34 (s, 1H, triazol-H), 9.58 (brs, 1H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz): δ 40.6, 51.6, 114.0 (d, J = 22.01 Hz), 116.8, 117.6, 118.0, 118.8 (d, J = 25.31Hz), 123.6, 126.4, 126.9, 128.5, 130.9, 131.7, 132.2, 133.1, 135.4, 142.6, 158.7 (d, J = 249.24 Hz), 163.4, 173.5, 180.3; HRMS m/z Calcd. for $C_{22}H_{18}N_5BrFSO_5$ ($[M+H]^+$): 562.0109, found 562.0163.

(E)-2-(4-(3-(4-Hydroxy-2-methyl-1,1-dioxido-2H-benzo[e][1,2]thiazin-3-yl)-3-oxoprop-1-en-1-yl)-1H-1,2,3-triazol-1-yl)-N-(4-(trifluoromethyl)phenyl)acetamide (**12e**):



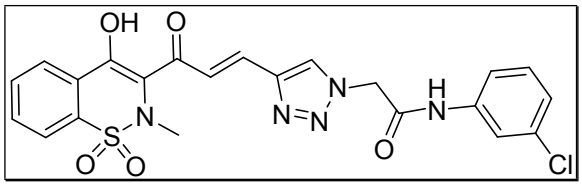
Yellow solid, Yield: 69%, I.R. (KBr, cm^{-1}): 3342 (NH), 1716 (C=O), 1650 (C=O), 1542 (C=C), 1354 (SO_2asym), 1180 (SO_2sym); ^1H NMR (DMSO-d_6, 300 MHz): δ 3.00 (s, 3H, NCH_3), 5.43 (s, 2H, NCH_2), 7.52-7.65 (m, 3H, Ar-H), 7.76-7.99 (m, 6H, Ar-H), 8.11-8.23 (m, 1H, Ar-H), 8.62 (s, 1H, triazol-H), 10.76 (brs, 1H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz): δ 39.9, 51.2, 116.5, 117.4, 117.9, 121.0, 123.1, 124.6, 126.4, 126.9, 127.8, 131.8, 131.9, 132.0, 133.0, 134.8, 140.4, 141.8, 163.0, 172.9, 179.7; HRMS m/z Calcd. for $C_{23}H_{19}N_5F_3SO_5$ ($[M+H]^+$): 534.1029, found 534.1041.

(E)-2-(4-(3-(4-Hydroxy-2-methyl-1,1-dioxido-2H-benzo[e][1,2]thiazin-3-yl)-3-oxoprop-1-en-1-yl)-1H-1,2,3-triazol-1-yl)-N-(4-methoxyphenyl)acetamide (**12f**):



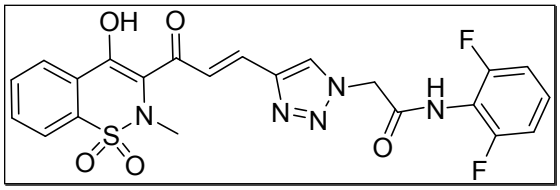
Yellow solid, Yield: 71%, I.R. (KBr, cm^{-1}): 3334 (NH), 1715 (C=O), 1650 (C=O), 1538 (C=C), 1345 (SO_2asym), 1178 (SO_2sym); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 3.00 (s, 3H, NCH_3), 3.79 (s, 3H, OCH_3), 5.32 (s, 2H, NCH_2), 6.81-6.90 (m, 2H, Ar-H), 7.47-7.65 (m, 3H, Ar-H), 7.79-7.94 (m, 4H, Ar-H), 8.13-8.22 (m, 1H, Ar-H), 8.37 (s, 1H, triazol-H), 10.15 (brs, 1H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz): δ 39.8, 51.0, 53.7, 112.3, 116.4, 117.2, 119.5, 122.9, 126.2, 127.7, 129.8, 131.6, 131.7, 132.6, 134.7, 141.7, 154.4, 161.5, 172.7, 179.6; HRMS m/z Calcd. for $C_{23}H_{22}N_5SO_6$ ($[M+H]^+$): 496.1285, found 496.1280.

(E)-N-(3-Chlorophenyl)-2-(4-(3-(4-hydroxy-2-methyl-1,1-dioxido-2H-benzo[e][1,2]thiazin-3-yl)-3-oxoprop-1-en-1-yl)-1H-1,2,3-triazol-1-yl)acetamide (**12g**):



Yellow solid, Yield: 63%, I.R. (KBr, cm^{-1}): 3330 (NH), 1702 (C=O), 1642 (C=O), 1595 (C=C), 1345 (SO_2asym), 1180 (SO_2sym); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 3.00 (s, 3H, NCH_3), 5.34 (s, 2H, NCH_2), 7.05-7.14 (m, 1H, Ar-H), 7.22-7.32 (m, 1H, Ar-H), 7.44-7.66 (m, 2H, Ar-H), 7.73-7.98 (m, 5H, Ar-H), 8.14-8.21 (m, 1H, Ar-H), 8.30 (s, 1H, triazol-H), 10.42 (brs, 1H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz): δ 39.5, 50.7, 115.8, 115.9, 116.9, 117.3, 121.8, 122.7, 126.0, 126.6, 127.3, 128.4, 131.4, 131.6, 131.8, 132.6, 134.2, 137.9, 141.3, 162.3, 172.5, 179.2; HRMS m/z Calcd. for $C_{23}H_{19}ClN_5SO_5$ ($[M+H]^+$): 500.0817, found 500.0822.

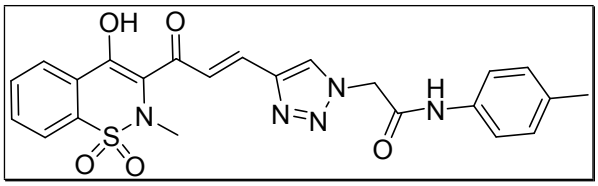
(E)-N-(2,6-Difluorophenyl)-2-(4-(3-(4-hydroxy-2-methyl-1,1-dioxido-2H-benzo[e][1,2] thiazin-3-yl)-3-oxoprop-1-en-1-yl)-1H-1,2,3-triazol-1-yl)acetamide (**12h**):



Yellow solid, Yield: 66%, I.R. (KBr, cm^{-1}): 3346 (NH), 1712 (C=O), 1645 (C=O), 1531 (C=C), 1345 (SO_2asym), 1182 (SO_2sym); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 3.00 (s, 3H, NCH_3), 5.46 (s, 2H, NCH_2), 6.94-7.08 (m, 2H, Ar-H), 7.20-7.34 (m, 1H, Ar-H), 7.54-7.62 (m, 1H, Ar-H), 7.65-7.74 (m, 1H, Ar-H), 7.81-7.97 (m, 3H, Ar-H), 8.13-8.21 (m, 1H, Ar-H), 8.43 (s, 1H, triazol-H), 10.20 (brs, 1H, NH); ^{13}C NMR (DMSO-d_6, 125 MHz): δ 41.2, 51.7, 112.0 (d, J = 21.80Hz),

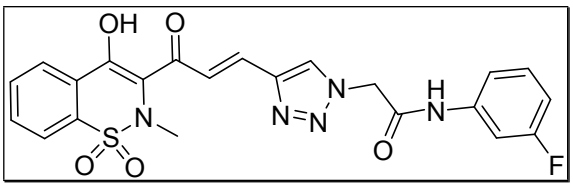
113.6 (t, J = 15.44 Hz), 117.7, 118.7, 124.5, 127.9, 128.5 (t), 128.9, 133.3, 133.8, 134.9, 135.9, 142.9, 157.6 (d, *J* = 249.7 Hz), 164.5, 174.2, 180.9; MS (ESI, 70eV): m/z: 267 (M+1).

(E)-2-(4-(3-(4-Hydroxy-2-methyl-1,1-dioxido-2H-benzo[e][1,2]thiazin-3-yl)-3-oxoprop-1-en-1-yl)-1H-1,2,3-triazol-1-yl)-N-(p-tolyl)acetamide (**12i**):



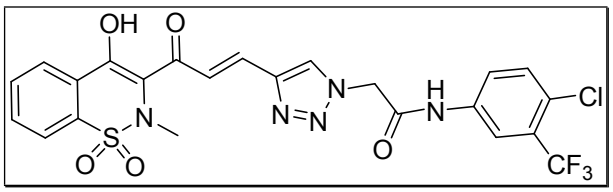
Yellow solid, Yield: 73%, I.R. (KBr, cm^{-1}): 3334 (NH), 1712 (C=O), 1647 (C=O), 1538 (C=C), 1345 (SO_2asym), 1180 (SO_2sym); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 2.31 (s, 3H, CH_3), 2.99 (s, 3H, NCH_3), 5.34 (s, 2H, NCH_2), 7.11 (d, 2H, Ar-H, *J* = 8.12 Hz), 7.48 (d, 2H, Ar-H, *J* = 8.12 Hz), 7.53-7.62 (m, 1H, Ar-H), 7.81-7.96 (m, 4H, Ar-H), 8.13-8.21 (m, 1H, Ar-H), 8.46 (s, 1H, triazol-H), 10.27 (brs, 1H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz): δ 19.2, 39.8, 51.1, 116.4, 117.3, 118.0, 122.9, 126.3, 126.4, 127.7, 131.5, 131.7, 131.8, 132.7, 134.2, 134.7, 141.7, 161.8, 172.7, 179.6; HRMS m/z Calcd. for $C_{23}H_{22}N_5SO_5$ ($[M+H]^+$): 480.1336, found 480.1323.

(E)-N-(3-Fluorophenyl)-2-(4-(3-(4-hydroxy-2-methyl-1,1-dioxido-2H-benzo[e][1,2]thiazin-3-yl)-3-oxoprop-1-en-1-yl)-1H-1,2,3-triazol-1-yl)acetamide (**12j**):



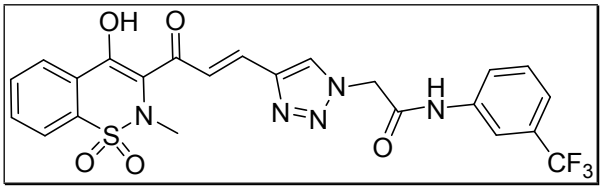
Yellow solid, Yield: 75%, I.R. (KBr, cm^{-1}): 3353 (NH), 1716 (C=O), 1645 (C=O), 1530 (C=C), 1339 (SO_2asym), 1178 (SO_2sym); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 2.99 (s, 3H, NCH_3), 5.38 (s, 2H, NCH_2), 6.76-6.86 (m, 1H, Ar-H), 7.25-7.34 (m, 1H, Ar-H), 7.52-7.63 (m, 2H, Ar-H), 7.78-7.96 (m, 5H, Ar-H), 8.12-8.21 (m, 1H, Ar-H), 8.51-8.57 (m, 1H, triazol-H), 10.57 (brs, 1H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz): δ 40.9, 52.2, 114.6, 117.4, 118.4, 124.0, 127.4, 127.9, 128.7, 129.8 (d, *J* = 9.35 Hz), 132.9 (d, *J* = 18.16 Hz), 134.0, 135.7, 139.6 (d, *J* = 11.00 Hz), 142.7, 162.0 (d, *J* = 243.2 Hz), 163.7, 173.8, 180.7; HRMS m/z Calcd. for $C_{22}H_{18}N_5FNaSO_5$ ($[M+Na]^+$): 506.0905, found 506.0891.

(E)-N-(4-Chloro-3-(trifluoromethyl)phenyl)-2-(4-(3-(4-hydroxy-2-methyl-1,1-dioxido-2H-benzo[e][1,2]thiazin-3-yl)-3-oxoprop-1-en-1-yl)-1H-1,2,3-triazol-1-yl)acetamide (**12k**):



Yellow solid, Yield: 62%, I.R. (KBr, cm^{-1}): 3356 (NH), 1716 (C=O), 1643 (C=O), 1529 (C=C), 1345 (SO_2asym), 1180 (SO_2sym); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 3.00 (s, 3H, NCH_3), 5.39 (s, 2H, NCH_2), 7.43-7.52 (m, 1H, Ar-H), 7.54-7.70 (m, 1H, Ar-H), 7.76-7.96 (m, 5H, Ar-H), 8.06-8.22 (m, 2H, Ar-H), 8.44 (s, 1H, triazol-H), 10.78 (brs, 1H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz): δ 39.7, 50.9, 116.4, 116.6, 117.7, 119.2, 122.2, 122.8, 123.8, 125.8, 126.2, 126.5, 127.6, 130.3, 131.4, 131.7, 132.6, 134.6, 136.0, 141.6, 162.7, 172.7, 179.4; HRMS m/z Calcd. for $C_{23}H_{18}N_5ClF_3SO_5$ ($[M+H]^+$): 568.0664, found 568.0656.

(E)-2-(4-(3-(4-Hydroxy-2-methyl-1,1-dioxido-2H-benzo[e][1,2]thiazin-3-yl)-3-oxoprop-1-en-1-yl)-1H-1,2,3-triazol-1-yl)-N-(3-(trifluoromethyl)phenyl)acetamide (**12l**):



Yellow solid, Yield: 71%, I.R. (KBr, cm^{-1}): 3366 (NH), 1715 (C=O), 1643 (C=O), 1532 (C=C), 1344 (SO_2asym), 1182 (SO_2sym); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 3.00 (s, 3H, NCH_3), 5.36 (s, 2H, NCH_2), 7.31-7.50 (m, 2H, Ar-H), 7.54-7.64 (m, 1H, Ar-H), 7.75-8.02 (m, 6H, Ar-H), 8.12-8.20 (m, 1H, Ar-H), 8.32 (s, 1H, triazol-H), 10.57 (brs, 1H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz): δ 40.3, 51.5, 115.0, 117.1, 117.7, 119.3, 121.7, 122.8 (q, J = 272.34 Hz), 123.3, 126.5, 126.7, 128.2, 128.4, 129.4 (q, J = 31.9 Hz), 131.7, 132.0, 133.0, 135.1, 137.8, 142.3, 162.9, 173.3, 180.0; HRMS m/z Calcd. for $C_{23}H_{19}N_5F_3SO_5$ ($[M+H]^+$): 534.1029, found 534.1040.

4. Biological assays:

Measurement of cell viability

The effect of synthesized compounds on cell viability was determined by Trypan blue dye exclusion assay. THP1 cells were seeded at a density of 2 x 10^5 / ml in 24-well plates in triplicates and were treated with compounds (20 µM) for 48 h. At the end of the treatments, cells were harvested and resuspended in 0.4 % Trypan blue (Sigma) and live/dead cells were counted using cell countess chamber (Invitrogen).

Determination of TNF-α, IL-1β and MCP-1 levels in conditioned medium

To check the inhibitory effects of benzothiazine-1,1-dioxo-3-yl-1,2,3-triazol-4-yl prop 2-en-1-one derivatives (**8a-s** and **12a-l**) on PMA induced inflammation, THP-1 monocytes were seeded at a density of 2 x 10^5 / ml in 12 well plates. Cells were pre-treated with compounds for 2 h before they were stimulated with 100 nM PMA. After 48 h supernatants were centrifuged and assayed for TNF-α, IL-1β and MCP-1 levels using ELISA kit (eBiosciences, San Diego, CA, USA) according to manufacturer's instructions. Concentrations of cytokines released were obtained and the percentage of inhibition of cytokines production was calculated as compared to PMA-stimulated condition. The standard curves were calculated by plotting the pg/ml concentrations *versus* absorbance values from the standards, and were used to quantify the amount of cytokines released by the cells. The results were represented as mean±SD of two independent experiments in duplicates.

Table S3: Effect of PMA on TNF-α, IL-1β and MCP-1 production in THP-1 cells

Treatment Condition	**Secreted levels of cytokines (pg / ml)**		
	TNF-α	**IL-1β**	**MCP-1**
Without PMA	11.5 ± 1.2	5.2 ± 1.6	38.2 ± 3.9
PMA 100 nM	3012.8±145.8	181.3 ±7.8	3261.3 ± 52.8

2 X 10 ^{5}/ml THP-1 monocytes were seeded in 12-well culture plates and stimulated with 100 nM of PMA for a period of 48 h. At the end of the treatment, conditioned media was collected and TNF-α, IL-1β and MCP-1 levels were measured by ELISA as described in Materials and Methods.

Qualitative analysis of monocyte/ macrophage differentiation by light microscopy

THP-1 cells were pretreated with 5-20 μM concentrations of compounds **12e**, **12g**, **12i**, **12j**, **12k** and **12l** for 2 h followed by stimulation with PMA (100 nM). After 48 h, medium was removed and images of monocyte/macrophage adherence and differentiation were taken by phase contrast light microscopy. Data are representative of five different fields of view.

Measurement of inflammatory gene expression levels and monocyte differentiation markers by real time-PCR

For studying expression levels of monocyte differentiation markers and matrix metalloproteinase's at transcript levels, THP-1 monocytes were pretreated for 2 h with 15 μM

concentration of compounds **12g, 12i** and **12l** followed by stimulation with PMA (100 nm). After 24 h, cells were collected in TRIzol (sigma), subsequently total RNA was prepared and performed RT-PCR using respective gene specific primers. Beta-actin was used as a loading control. The primers sequences used are given in Table S4.

Table S4: The sequences of COX-2, LOX-1, CD-36, MMP-1, MMP-9 and β-actin primers

Gene	Forward primer (5'–3')	Reverse primer (5'–3')
COX-2	GGTCCTGGCGCTCAGCCATA	CACCCAAGGGAGTCGGGCAA
LOX-1	ACTCTCCATGGTGGTGCCTGG	ACTCTCCATGGTGGTGCCTGG
CD-36	TGCAAAACGGCTGCAGGTCAA	TGAGGATGACAGGAATGCAGGGC
MMP-1	TGCTGCTGCTGTTCTGGGGTG	TGCTCTTGGCAAATCTGGCGTGT
MMP-9	TTGACAGCGACAAGAAGTGG	GCCATTCACGTCGTCCTTAT
β-actin	ATCCCCCAAAGTTCACAATG	GTGGCTTTTAGGATGGCAAG

Measurement of mitochondrial biogenesis by confocal microscopy

THP-1cells were pretreated with 15 μM concentration of compounds **12g, 12i** and **12l** for 2 h in cover glass bottom dishes (SPL life science) and stimulated with 100 nM PMA. After 48 h, media was removed and cells were stained with 200 nM Mitotracker solution CMXROS (molecular probes) for 60 min followed by counter staining of nucleus with DAPI (sigma). Images of mitochondrial staining were acquired using an Olympus confocal microscope equipped with rhodamine and DAPI filter settings.

Evaluation of lysosomal activity using fluorescence microscopy

THP-1cells were pretreated with 15 μM concentration of compounds **12g, 12i** and **12l** for 2 h in cover glass bottom dishes (SPL life science) and stimulated with PMA (100 nM). After 48 h, media was removed and incubated in 1 ml of HBSS (Hanks balanced salt solution) containing 200 nM lysotracker solution (molecular probes) for 1 h and images were taken using fluorescence microscopy.

MMP-9 activity using gelatin zymography

THP-1 cells were treated with 15 μM concentrations of compounds **12g**, **12i** and **12l** for 2 h followed by stimulation with 100 nM PMA. After 48 h of treatment, 25 μl of conditioned media

freed of cell debris was harvested and mixed with 25 µl of Laemmli buffer without β-mercaptoethanol and ran the 10% SDS-PAGE containing 1mg/ml of gelatin. The gel was incubated for 1 h in Zymogram renaturing Buffer (Triton X 100, 2.5% v/v in water) with gentle agitation at room temperature and allowed to develop using Zymogram developing buffer (50 mM Tris base, 50 mM Tris-HCl, 0.2 mM NaCl, 5 mM $CaCl_2$ and 0.02 % Brij 35) at room temperature for overnight. Gels were stained with 1% Coomassie Blue R-250 solution to get clear bands against a dark blue background where the protease had digested the substrate. Images of gelatinolytic activities were taken and analysis was done.

Invasion assay:

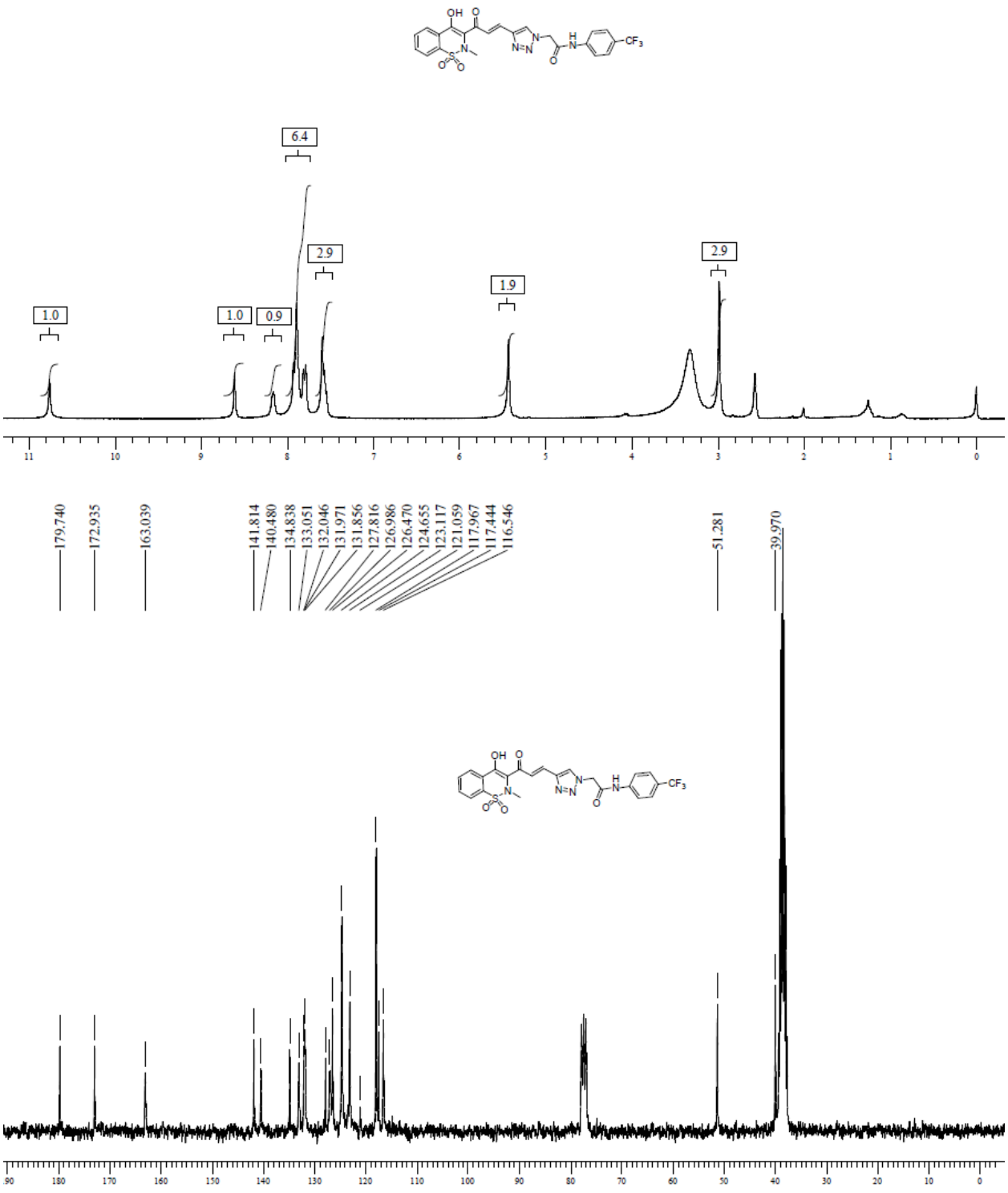
THP-1 cells were pretreated with 15 µM concentration of compounds **12g, 12i** and **12l** for 2 h then transferred into BD matrigel TM invasion chambers of 8 µ pore size with 500 µl of RPMI medium in lower chambers followed by stimulation with 100 nM of PMA. After 48h cells in the transwell chambers were discarded and fixed the migrated cells using 3% glutaraldehyde solution. After 2 h glutaraldehyde was discarded from the chambers and cells were stained with 0.5 % crystal violet for 1 h. Following this images were taken using a fine focusing lens (20 x). After each step, cells were extensively washed with PBS.

Statistical analysis:

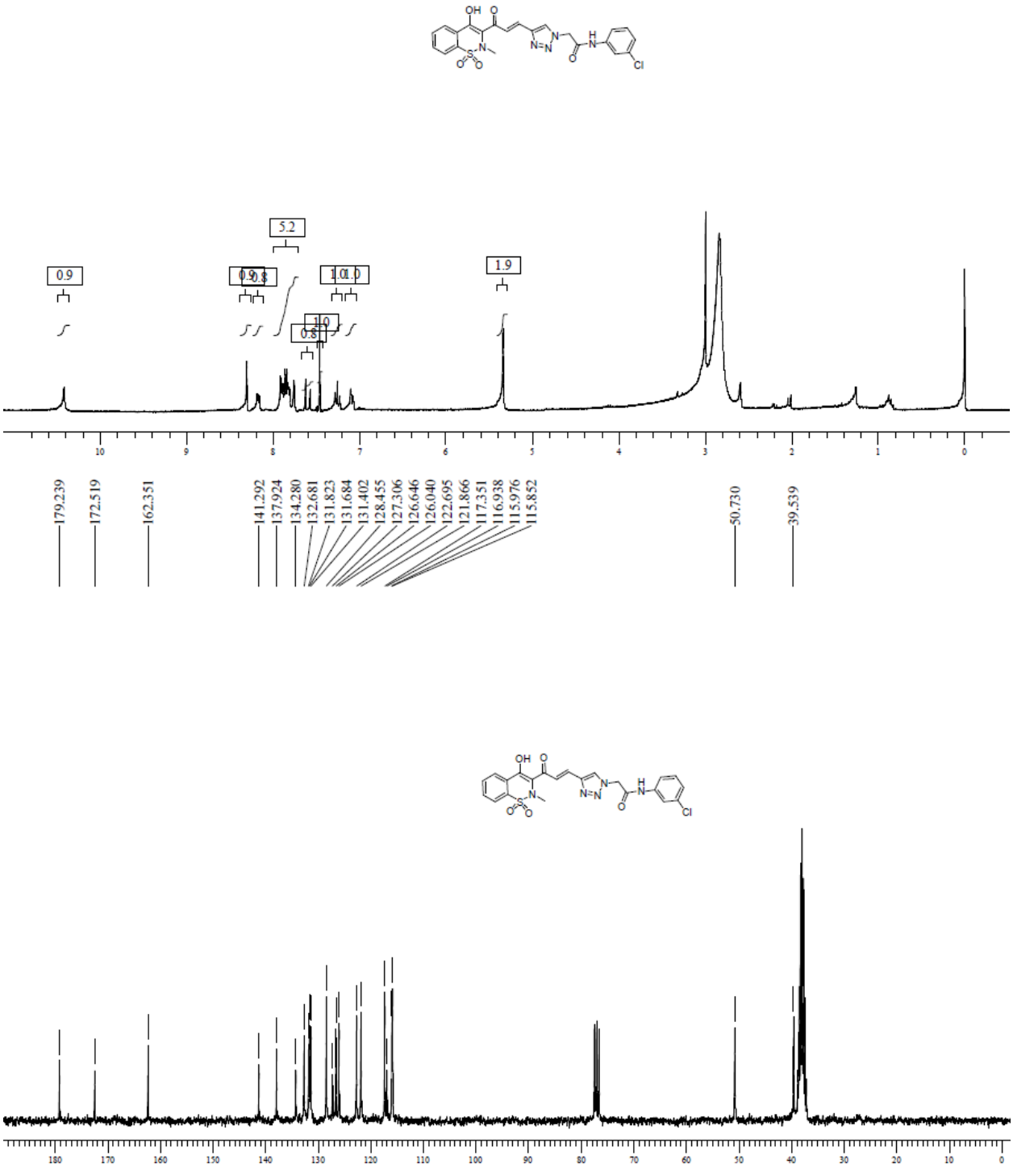
Data are expressed as Mean ± SD. The significance of differences between groups was examined using either Student's t test or ONE-WAY ANOVA as appropriate. P values <0.05 were considered statistically significant.

5. NMR spectra of compounds (12e, 12g, 12i. 12k and 12l):

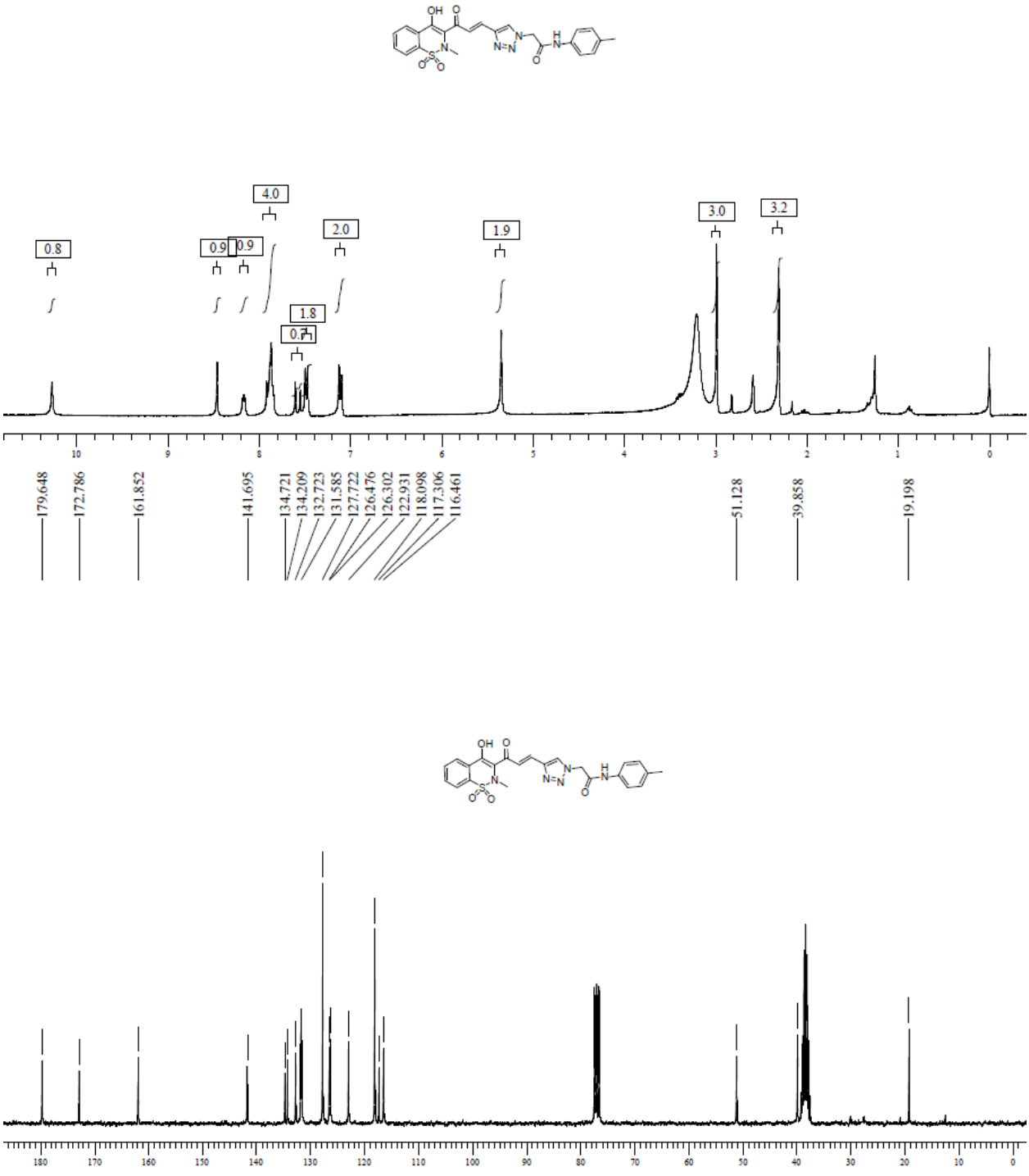
^{1}H NMR (DMSO-d_6, 300 MHz) and ^{13}C NMR (DMSO-d_6, 75MHz) spectra of **12e**:



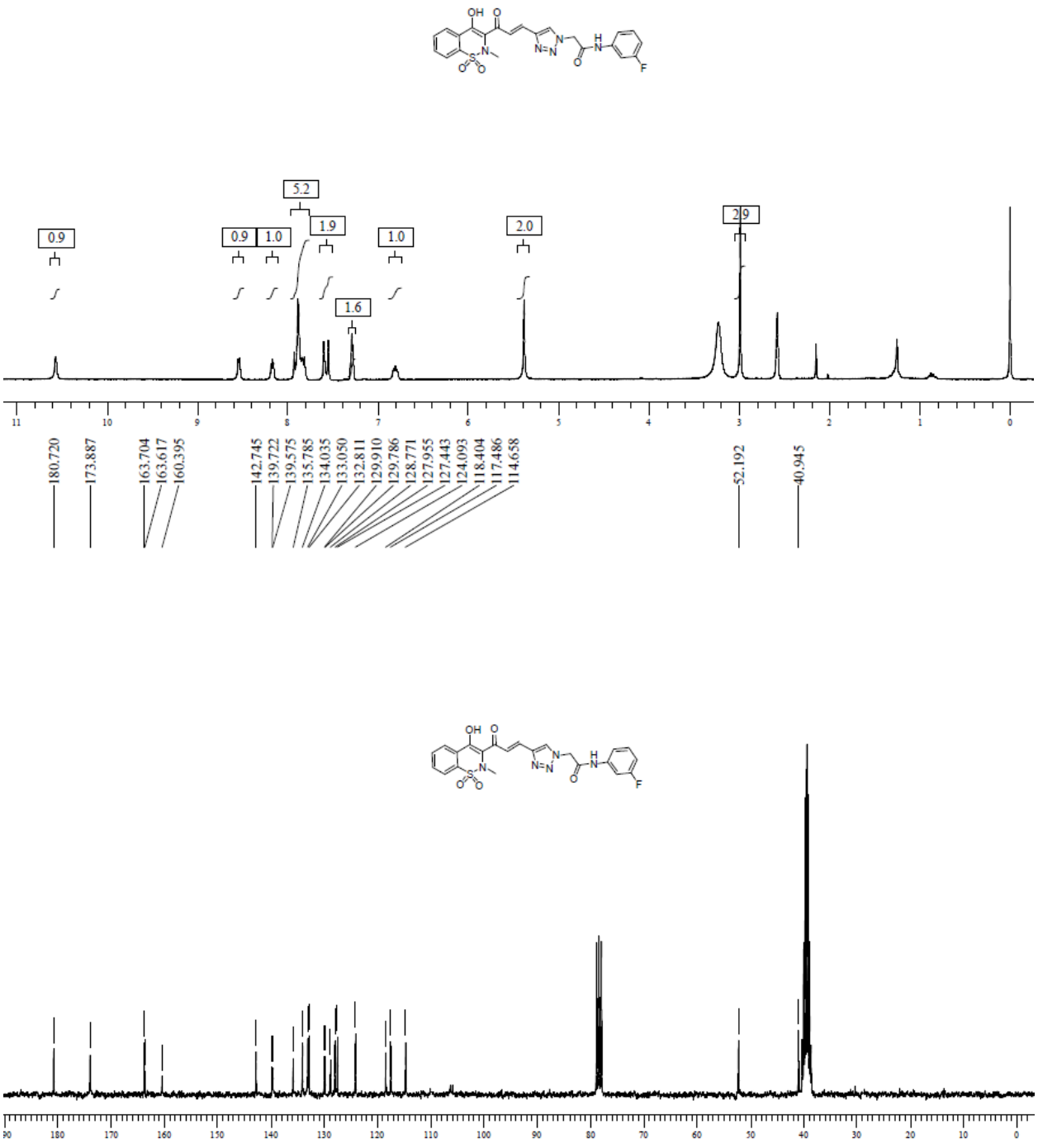
^{1}H NMR (DMSO-d_6, 300 MHz) and ^{13}C NMR (DMSO-d_6, 75MHz) spectra of **12g**:



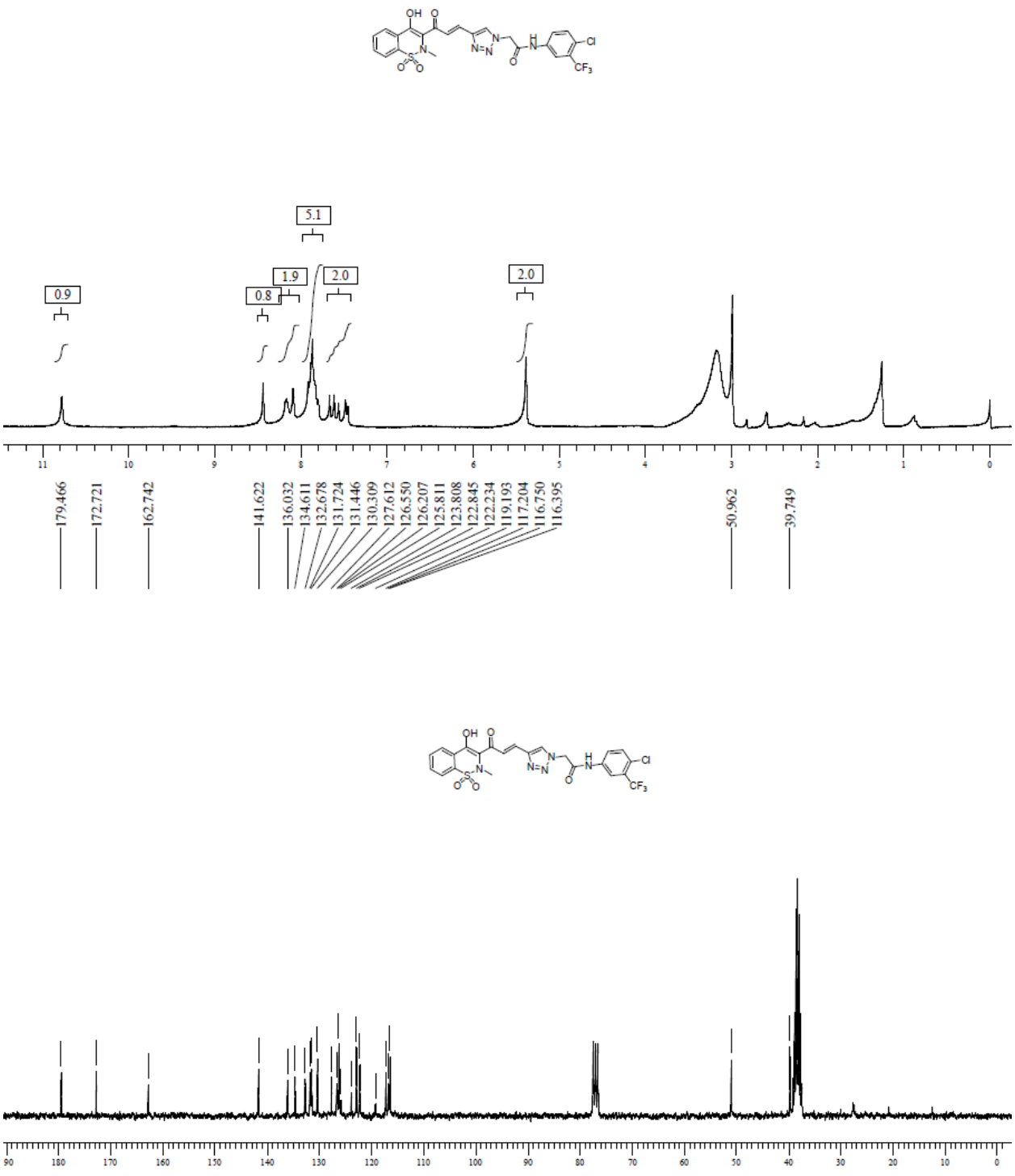
^{1}H NMR (DMSO-d_6, 300 MHz) and ^{13}C NMR (DMSO-d_6, 75MHz) spectra of **12i**:



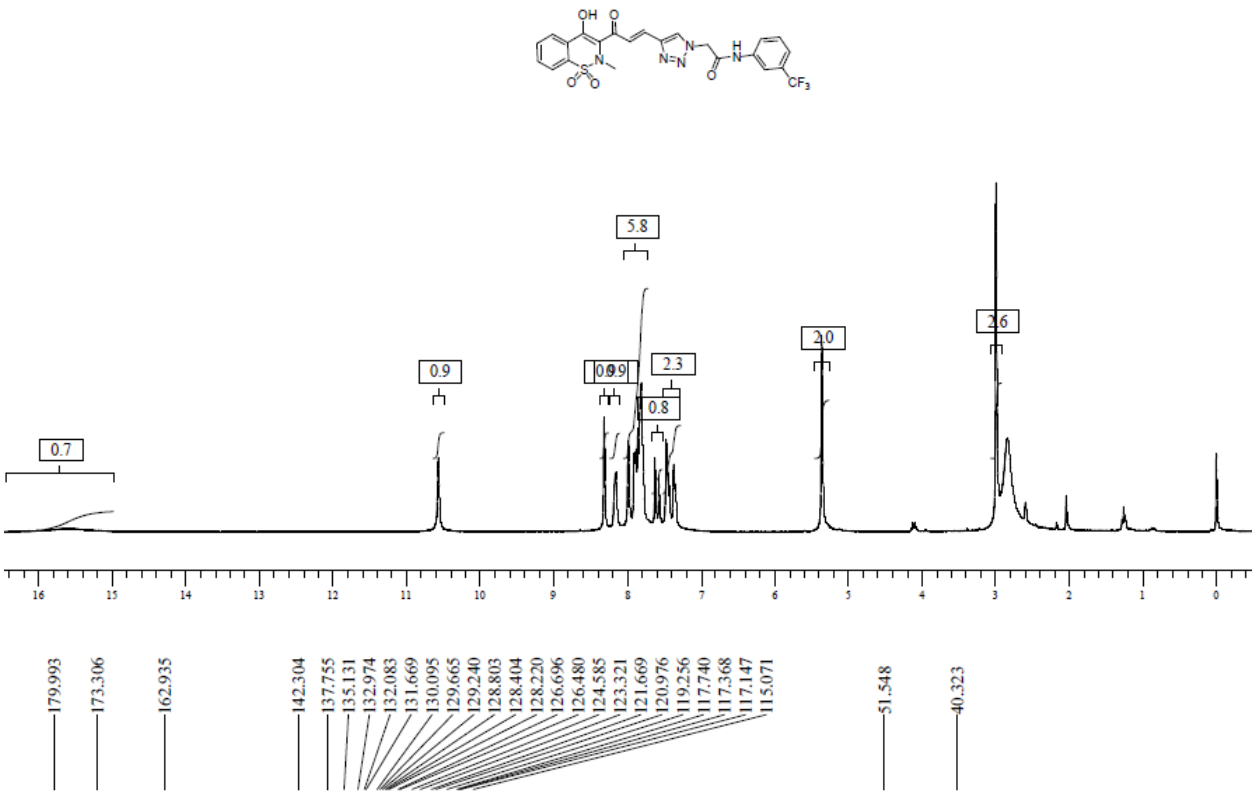
^{1}H NMR (DMSO-d_6, 300 MHz) and ^{13}C NMR (DMSO-d_6, 75MHz) spectra of **12j**:

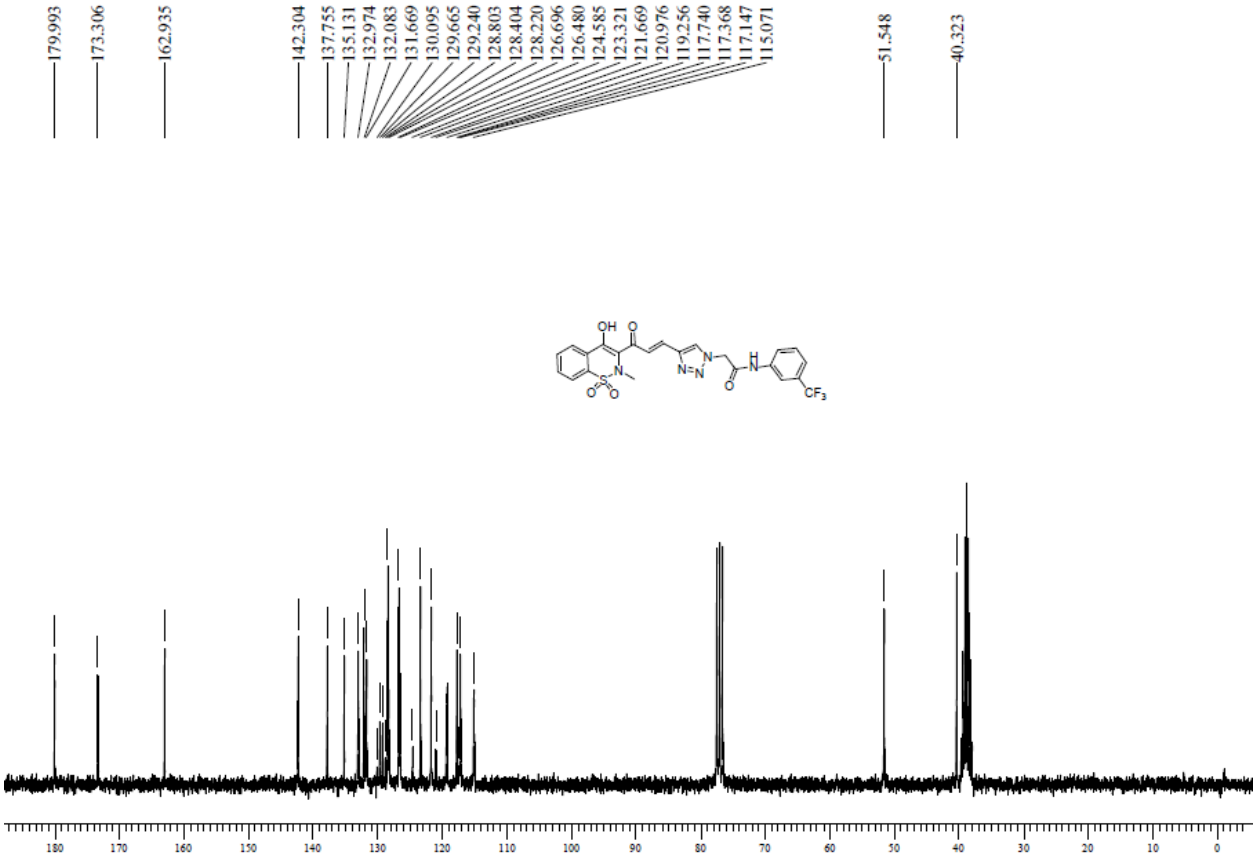


^{1}H NMR (DMSO-d_6, 300 MHz) and ^{13}C NMR (DMSO-d_6, 75MHz) spectra of **12k**:



^{1}H NMR (DMSO-d_6, 300 MHz) and ^{13}C NMR (DMSO-d_6, 75MHz) spectra of **12l**:





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