European Journal of Medicinal Chemistry 46 (2011) 4100–4106

Contents lists available at ScienceDirect

European Journal of Medicinal Chemistry

journal homepage: http://www.elsevier.com/locate/ejmech

Original article

Synthesis, characterization and pharmacological activity of 4-{[1-substituted aminomethyl-4-arylideneamino-5-sulfanyl-4,5-dihydro-1*H*-1,2,4-triazol-3-yl] methyl}-2*H*-1,4-benzothiazin-3(4*H*)-ones

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ARTICLE INFO

Article history:
Received 24 December 2010
Received in revised form
6 June 2011
Accepted 9 June 2011
Available online 17 June 2011

Keywords:
Analgesic activity
Anti-inflammatory activity
1,4-Benzothiazin-3(4*H*)-one

ABSTRACT

A new series of Schiff and Mannich bases derivatives (**6**) of 4-[(4-amino-5-sulfanyl-4*H*-1,2,4-triazol-3-yl) methyl]-2*H*-1,4-benzothiazin-3(4*H*)-one (**4**), derived from (3-oxo-2,3-dihydro-4*H*-1,4-benzothiazin-4-yl) acetic acid (**3**) were synthesized. The structures of all newly synthesized compounds were elucidated by elemental analysis, IR, ^{1}H NMR and mass spectral data. Synthesized compounds were evaluated for their anti-inflammatory and analgesic activity. Among the tested compounds, the (3-oxo-2,3-dihydro-4*H*-1,4-benzothiazin-4-yl)acetic acid (**3**) possess analgesic activity comparable to that of pentazocine; activity decreased on derivatization of the carboxylic acid group. However the anti-inflammatory activity of (3-oxo-2,3-dihydro-4*H*-1,4-benzothiazin-4-yl)acetic acid (**3**) increased by derivatization of the carboxylic acid group and some of the compounds showed anti-inflammatory activity comparable to that of indomethacin.

1. Introduction

In recent years, there has been an upsurge in the synthesis of non-steroidal anti-inflammatory drugs (NSAIDs) with two or more heterocycles to overcome the drawbacks of known non-steroidal anti-inflammatory drugs (NSAIDs) such as asprin, ibuprofen and naproxen. The search for novel analgesic and anti-inflammatory agents devoid of side effects continues to be an active area of research in medicinal chemistry. A number of 2*H*-1,4-benzothiazine derivatives were reported for their biological activities such as antimicrobial [1], antimalarial [2], anti-inflammatory [3], anti-fungal [4] and 15-lipoxygenase inhibition properties [5]. Most of the known non-steroidal anti-inflammatory drugs (NSAIDs) have carboxylic groups in their structures. So we have synthesized (3-oxo-2,3-dihydro-4*H*-1,4-benzothiazin-4-yl)acetic acid (**3**) by a three steps process, which has shown good analgesic activity and mild anti-inflammatory activity.

It is also reported that the derivatization of the carboxyl group of representative NSAIDs, resulted in an increased anti-inflammatory activity with reduced ulcerogenic effect [6–8]. In fact 1,2,4-triazoles and their derivatives have been reported to possess various biological activities such as anti-inflammatory activity and analgesic activity [9–11]. Similarly Mannich bases also possess comprehensive bioactivities like anticancer [12], analgesic [13], anticonvulsant [14,15] antibacterial and antifungal activities [16–18]. So we have synthesized some novel Schiff and Mannich bases (**6**) having triazole as well as 2*H*-1,4-benzothiazin-3(4*H*)-3-one moiety and studied their biological properties.

2. Pharmacology

Some of the selected compounds were evaluated for analgesic and anti-inflammatory activities. The tested compounds were administered in the form of a suspension (1% carboxymethyl cellulose as vehicle). Anti-inflammatory and analgesic activities of the tested compounds were measured with respect to the control and compared with the standard drugs indomethacin and pentazocine respectively. All the pharmacological data are expressed as mean ± SEM; statistical analysis was applied to determine the significance of the difference between the control group and groups of animals tested with the tested compounds.

2.1. Anti-inflammatory activity

Some of the selected compounds were evaluated for their anti-inflammatory activity against carrageenan-induced acute paw

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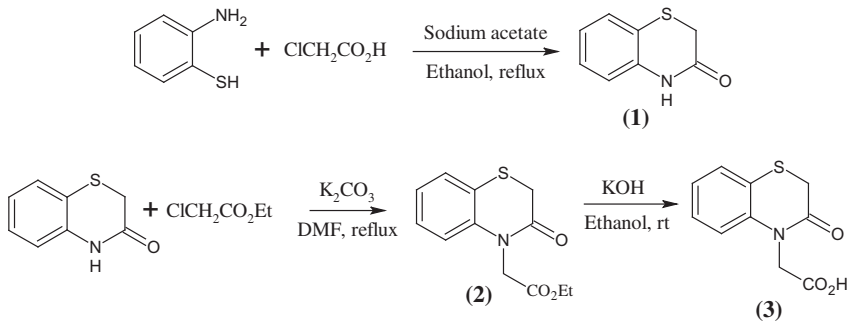
doi:10.1016/j.ejmech.2011.06.010



Scheme 1.

edema method in Wistar albino rats weighing 150–200 g, using Plethysmometer following the method of Winter et al. [20]. The animals were weighed and divided into different groups (control, standard and the test groups) of five rats each. The first group of rats was treated with 1 mL of 1% gum acacia suspension orally (control), the second group was administered with a dose of 20 mg/kg of the indomethacin (standard) and the third group was treated with 20 mg/kg of the suspension of the test compounds. After 30 min, the animals were injected with 0.1 mL of 1% carrageenan in normal saline, subcutaneously to the sub-planar region of right hind paw. The paw volume was measured immediately (0 h) and after 30 min, 60 min and 120 min by using Plethysmometer. Values are expressed as mean, by one way ANOVA analysis followed by dunnet's-t-test and results are tabulated in Table 3.

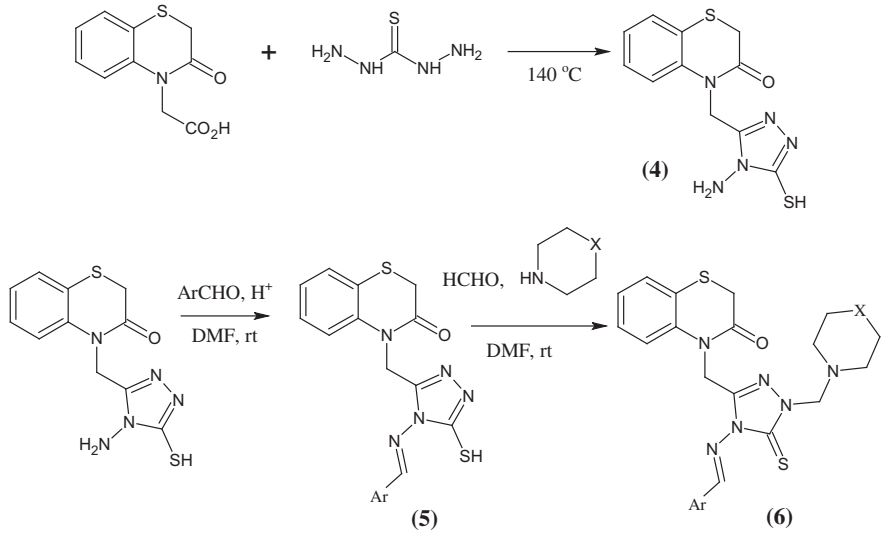
2.2. Analgesic activity

Some of the selected compounds were tested for their analgesic activity using Analgesiometer. Rats of either sex weighing between 150 and 200 g were used for the experiment. The animals were weighed and divided into different groups (control, standard and the test groups) of five rats each. The first group of rats was treated with control, the second group was administered with a dose of 20 mg/kg of the pentazocine (standard) and the third group was treated with 20 mg/kg of the suspension of the test compounds. In this method heat is used as a source of pain. Animals were individually placed on an analgesiometer, so that the tail lies over the nichrome wire of instrument without touching it (i.e., about 1/8 inch above the nichrome wire). Cut off time is 10 s. The end point of the sensation is when rat lifts its tail (i.e. tail flick). Reaction time is noted at an intervals of 30, 60, 90 min after the administration of drug. Values are expressed as mean ± SEM, by one way ANOVA analysis followed by dunnet's-t-test and results are tabulated in Table 4.

3. Results and discussion

3.1. Chemistry

(3-Oxo-2,3-dihydro-4*H*-1,4-benzothiazin-4-yl)acetic acid (**3**) was synthesized by a three step process (Scheme 1) and its structure was confirmed by single crystal XRD study [19]. It was then converted into 4-[(4-amino-5-sulfanyl-4*H*-1,2,4-triazol-3-yl) methyl]-2*H*-1,4-benzothiazin-3(4*H*)-one (**4**) by fusion with thiocarbohydrazide under solvent-free condition (Scheme 2). The triazole obtained was then condensed with suitable aldehydes in the presence of few drops of concentrated sulfuric acid as a catalyst to yield Schiff bases in good yield. These Schiff bases reacted with formaldehyde and secondary amines in DMF medium to give N-Mannich bases (**6**). The structures of the newly synthesized compounds (**6**) were confirmed on the basis of spectral, elemental



Ar = phenyl, *p*-chloro phenyl, *p*-nitro phenyl, *p*-hydroxy phenyl; X = O, CH_2, NMe

Scheme 2.

Table 1
Characterization data of 4-[(4-benzylideneamino-5-sulfanyl-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)methyl]-2*H*-1,4-benzothiazin-3(4*H*)-one **5a-d**.

Compd	R	m.p.(°C) (Yield%)	Mol. formula (Mol. wt)	% Composition, found (Calcd)		
				C	H	N
5a	Phenyl	190 (89)	$C_{18}H_{15}N_5OS_2$ (381.47)	56.56 (56.67	3.99 3.96	18.45 18.36)
5b	*p*-Nitro phenyl	213 (95)	$C_{18}H_{14}N_6O_3S_2$ (426.47)	50.60 (50.69	3.29 3.31	19.78 19.71)
5c	*p*-Chloro phenyl	195 (90)	$C_{18}H_{14}ClN_5OS_2$ (415.91)	51.84 (51.98	3.36 3.39	16.94 16.84)
5d	*p*-Hydroxy phenyl	217 (70)	$C_{18}H_{15}N_5O_2S_2$ (397.47)	54.47 (54.39	3.85 3.80	17.52 17.62)

and crystal structure data. Characterization data of these compounds are tabulated in Table 2.

3.2. Pharmacological screening

The anti-inflammatory activity of the target compounds was evaluated by applying the carrageenan-induced rat paw edema bioassay in rats. Indomethacin was used as a standard drug. Among the tested compounds, the (3-oxo-2,3-dihydro-4*H*-1,4-benzothiazin-4-yl)acetic acid (**3**) showed mild anti-inflammatory activity and its anti-inflammatory activity increased by derivatization of the carboxylic acid group. The compounds **6f** and **6k** showed anti-inflammatory activity comparable to that of indomethacin. The analgesic activity data reveals that (3-oxo-2,3-dihydro-4*H*-1,4-benzothiazin-4-yl)acetic acid (**3**) possesses analgesic activity comparable to that of pentazocine and its analgesic activity decreased by derivatization of the carboxylic acid group. The compounds **6d**, **6e** and **6k** showed very significant activity. The compounds having strong electron releasing group (OH) or strong electron withdrawing group (NO_2) in their structure showed good anti-inflammatory and analgesic activity.

Table 2
Characterization data of 4-{[1-substituted aminomethyl-4-benzylideneamino-5-sulfanyl-4,5-dihydro-1*H*-1,2,4-triazol-3-yl]methyl}-2*H*-1,4-benzothiazin-3(4*H*)-one **6a-l**.

Compd	R	X	m.p. (°C) (Yield%)	Mol. formula (Mol. wt)	%Composition, found (Calcd)		
					C	H	N
6a	Phenyl	NCH_3	185 (85)	$C_{24}H_{27}N_7OS_2$ (493.64)	58.28 (58.39	5.55 5.51	19.92 19.86)
6b	Phenyl	O	173 (75)	$C_{23}H_{24}N_6O_2S_2$ (480.60)	57.56 (57.48	4.99 5.03	17.44 17.49)
6c	Phenyl	CH_2	166 (81)	$C_{24}H_{26}N_6OS_2$ (478.63)	60.13 (60.23	5.52 5.48	17.63 17.56)
6d	*p*-NO_2 phenyl	NCH_3	188 (89)	$C_{24}H_{26}N_8O_3S_2$ (538.64)	53.60 (53.52	4.92 4.87	20.90 20.80)
6e	*p*-NO_2 phenyl	O	192 (79)	$C_{23}H_{23}N_7O_4S_2$ (525.60)	52.47 (52.56	4.38 4.41	18.75 18.65)
6f	*p*-NO_2 phenyl	CH_2	182 (74)	$C_{24}H_{25}N_7O_3S_2$ (523.63)	55.15 (55.05	4.79 4.81	18.64 18.72)
6g	*p*-Cl phenyl	NCH_3	198 (67)	$C_{24}H_{26}ClN_7OS_2$ (528.09)	54.49 (54.58	4.92 4.96	18.68 18.57)
6h	*p*-Cl phenyl	O	184 (83)	$C_{23}H_{23}Cl\ N_6O_2S_2$ (515.05)	53.54 (53.63	4.47 4.50	16.42 16.32)
6i	*p*-Cl phenyl	CH_2	176 (62)	$C_{24}H_{25}ClN_6OS_2$ (513.07)	56.28 (56.18	4.86 4.91	16.33 16.38)
6j	*p*-OH phenyl	NCH_3	155 (58)	$C_{24}H_{27}N_7O_2S_2$ (509.64)	56.62 (56.56	5.32 5.34	19.30 19.24)
6k	*p*-OH phenyl	O	164 (51)	$C_{23}H_{24}N_6O_3S_2$ (496.60)	55.74 (55.63	4.82 4.87	16.99 16.92)
6l	*p*-OH phenyl	CH_2	173 (55)	$C_{24}H_{26}N_6O_2S_2$ (494.63)	58.37 (58.28	5.28 5.30	16.92 16.99)

Table 3
Anti-inflammatory activity data of compound (**3**) and derivatives.

Compounds	Edema volume in mL			Percentage reduction (%)		
	0.5 h	1 h	2 h	0.5 h	1 h	2 h
Control	0.74	0.76	0.77			
Indomethacin	0.24	0.23	0.23	66.89**	70.26**	69.81**
3	0.45	0.53	0.55	38.51**	30.07**	27.93**
6a	0.68	0.69	0.69	8.10*	9.8^{ns}	10.39^{ns}
6b	0.70	0.69	0.69	5.40^{ns}	10.13^{ns}	10.39^{ns}
6c	0.44	0.45	0.45	40.21**	41.18**	41.23**
6d	0.49	0.45	0.48	33.11**	40.53**	37.34**
6e	0.46	0.44	0.52	37.84	42.16**	31.82**
6f	0.35	0.34	0.32	52.71**	55.56**	58.77**
6g	0.45	0.43	0.44	38.51**	44.12**	42.86**
6h	0.53	0.52	0.54	28.04**	32.35**	29.55**
6k	0.34	0.42	0.47	53.38**	45.10**	38.97**

Values are expressed as mean, $^*P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$ and ns statistically not significant.

4. Conclusion

The data of analgesic and anti-inflammatory activity studies indicate the possibility of obtaining a good NSAIDs from (3-oxo-2,3-dihydro-4*H*-1,4-benzothiazin-4-yl)acetic acid by varying the substitution at different positions and derivatives of (3-oxo-2,3-dihydro-4*H*-1,4-benzothiazin-4-yl)acetic acid appear to be suitable moiety in the field of medicine.

5. Experimental section

Melting points were determined in open capillary tubes and are uncorrected. IR spectra (cm^{-1}) were recorded on a Perkin Elmer 577 spectrophotometer in KBr pellets. ^1H NMR spectra were recorded on a Brucker AMX-400 (400 MHz) spectrometer using DMSO-d_6 as solvent and TMS as an internal standard. All chemical shifts values are reported in δ scale downfield from TMS. Mass spectra of Shiff bases were recorded on a Jeol JMS-D300 mass spectrometer operating at 70 eV and mass spectra of Mannich bases were recorded on a Jeol SX-102 (FAB) mass spectrometer. C, H, N analysis was carried out on a Vario-EL (Elementar-III) model. Homogeneity of the compounds was checked by TLC on silica gel plates.

5.1. General procedure for the synthesis of 2H-1,4-benzothiazin-3(4H)-one *1*

Sodium acetate (0.24 mol) was added to a stirred solution of 2-aminothiophenol (0.16 mol) and chloroacetic acid (0.16 mol) in ethanol (200 mL). The resulting reaction mixture was heated under reflux for 6 h and the completion of reaction was checked by TLC (Pet ether:Ethyl acetate, 5:5). The reaction mixture was concentrated by evaporation and then poured into ice-cold water to get 2*H*-1,4-benzothiazin-3(4*H*)-one (**1**) as a white solid. It was then filtered, dried and recrystallized from ethyl acetate. This compound was characterized by its melting point with reference to the literature [21]. Yield 83%; m.p. 177 °C (Lit. m.p. 176–178 °C).

5.2. General procedure for the preparation of ethyl (3-oxo-2,3-dihydro-4H-1,4-benzothiazin-4-yl)acetate *2*

To a solution of 2*H*-1,4-benzothiazin-3(4*H*)-one (0.06 mol) in DMF (50 mL) was added potassium carbonate (0.09 mol) at room temperature. This was followed by the addition of ethyl chloroacetate (0.09 mol). The reaction mixture was heated under reflux for 6 h and the completion of reaction was checked by TLC (Pet ether:Ethyl acetate, 5:5). The reaction mixture cooled to room

Table 4
Analgesic activity data of compound (**3**) and derivatives.

Compound	0 min	30 min	60 min	90 min
Control	3.35 ± 0.048	3.225 ± 0.063	3.340 ± 0.063	3.250 ± 0.06455
Pentazocine	3.4 ± 0.1080	6.400 ± 0.248	7.175 ± 0.111	7.450 ± 0.06455**
3	3.3 ± 0.048	5.775 ± 0.1250**	6.500 ± 0.108**	6.875 ± 0.08539**
6a	3.15 ± 0.1080	3.500 ± 0.1080^{ns}	4.300 ± 0.091*	4.225 ± 0.1493*
6b	3.17 ± 0.125	3.175 ± 0.048^{ns}	3.375 ± 0.103^{ns}	3.400 ± 0.09129^{ns}
6c	3.05 ± 0.048	3.925 ± 0.063**	5.300 ± 0.108**	5.500 ± 0.1581**
6d	3.07 ± 0.125	5.475 ± 0.048**	5.975 ± 0.111**	6.050 ± 0.1190**
6e	3.25 ± 0.063	5.425 ± 0.063**	6.050 ± 0.119**	6.025 ± 0.1109**
6f	3.15 ± 0.125	5.100 ± 0.082**	5.300 ± 0.082**	4.875 ± 0.08539**
6g	3.22 ± 0.103	4.575 ± 0.125**	5.375 ± 0.085**	5.000 ± 0.09129**
6h	3.35 ± 0.12	4.800 ± 0.129**	4.875 ± 0.085**	4.075 ± 0.06292**
6k	3.19 ± 0.12	4.300 ± 0.1225**	5.000 ± 0.091**	6.000 ± 0.1472**

Values are expressed as mean ± SEM, *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$ and ns statistically not significant.

temperature and poured into ice-cold water followed by extraction with ethyl acetate. The combined ethyl acetate layer was evaporated to get ethyl (3-oxo-2,3-dihydro-4H-1,4-benzothiazin-4-yl) acetate as brown liquid, which was directly taken for hydrolysis. Crude yield 64%.

5.3. General procedure for the preparation of (3-oxo-2,3-dihydro-4H-1,4-benzothiazin-4-yl)acetic acid **3**

A solution of potassium hydroxide (58.5 mmol) in water (10 ml) was added to the solution of ethyl (3-oxo-3,4-dihydro-2*H*-1,4-benzothiazin-4-yl)acetate (39 mmol) in ethanol (10 ml). The reaction mixture was stirred at room temperature for 24 h and the completion of reaction was checked by TLC ($CHCl_3$:MeOH, 9:1). It was then evaporated to dryness and dissolved again by adding ice-cold water. The insoluble impurities were separated by filtration. The filtrate was acidified with 4 N HCl (30 mL) to get a solid product (**3**), collected by filtration. The crude product was recrystallized from dichloromethane and structure was confirmed by single crystal XRD study [19]. Yield 63%; m.p. 65 °C.

5.4. General procedure for the preparation of 4-[(4-amino-5-sulfanyl-4H-1,2,4-triazol-3-yl)methyl]-2H-1,4-benzothiazin-3(4H)-one **4**

A mixture of 2-(3-oxo-2,3-dihydro-4*H*-1,4-benzothiazin-4-yl) acetic acid (56.6 mmol) and thiocarbohydrazide (47.1 mmol) was heated at 140 °C in solvent-free condition for 3 h and the completion of reaction was checked by TLC ($CHCl_3$:MeOH, 9:1) [8]. The reaction mixture was cooled to room temperature and the excess of acid was removed by stirring the solid product with saturated solution of sodium bicarbonate. The insoluble solid product (**4**) was then filtered, dried and recrystallized from N,N-Dimethyl formamide. Yield 85%; m.p. 223 °C.

IR (KBr) γ/cm^{-1}: 3317 (N–H), 1675 (C=O), 1279 (C=S); ^{1}H NMR (DMSO-d_6) δ: 3.59 (s, 2H, benzothiazine S-CH_2), 5.17 (s, 2H, N-NH_2), 5.63 (s, 2H, benzothiazine N-CH_2), 7.05–7.08 (t, 1H, J = 7.48 Hz, benzothiazine 6–H), 7.14–7.16 (d, 1H, J = 8.28 Hz, benzothiazine 8–H), 7.23–7.27 (t, 1H, J = 7.38 Hz, benzothiazine 7–H), 7.41–7.43 (d, 1H, J = 8.08 Hz, benzothiazine 5–H), 13.57 (s, 1H, SH/NH); LC-MS (*m*/*z*, %) 294.2 (M$^+$+1, 100).

5.5. General procedure for the preparation of 4-({4-benzylideneamino-5-sulfanyl-4H-1,2,4-triazol-3-yl}methyl)-2H-1,4-benzothiazin-3(4H)-one **5a-d**

A mixture of 4-[(4-amino-5-sulfanyl-4*H*-1,2,4-triazol-3-yl) methyl]-2*H*-1,4-benzothiazin-3(4H)-one (**5**) (3.4 mmol), substituted benzaldehydes (3.4 mmol) and 2-3 drops of concentrated sulfuric acid in N,N-dimethyl formamide (5 mL) medium was stirred at room temperature for 6 h and the completion of reaction was checked by TLC (Pet ether:Ethyl acetate, 5:5) [8]. The reaction mixture was then poured into ice-cold water to give a solid product, which was collected by suction filtration and dried. The crude product was then recrystalilzed from ethyl acetate. The characterization data are given in Table 1.

5.5.1. 4-{[4-benzylideneamino-5-sulfanyl-4,5-dihydro-1H-1,2,4-triazol-3-yl]methyl}-2H-1,4-benzothiazin-3(4H)-one **5a**

IR (KBr) γ/cm^{-1}: 1670 (C=O), 1585 (C=N), 1275 (C=S); ^{1}H NMR (DMSO-d_6) δ: 3.59 (s, 2H, benzothiazine S-CH_2), 5.43 (s, 2H, benzothiazine N-CH_2), 7.03–7.05 (t, 1H, J = 7.1 Hz, benzothiazine 6–H), 7.21–7.23 (t, 1H, J = 7.3 Hz, benzothiazine 7–H), 7.35–7.38 (d, 2H, J = 8.04 Hz, benzothiazine 5-H and 8–H), 7.51–7.62 (m, 3H, protons of phenyl ring),7.89–7.91 (d, 2H, J = 7.60 Hz, protons of phenyl ring *ortho* to the N=CH group), 10.02 (s, 1H, N=CH), 13.70 (s, 1H, SH/NH); LC-MS (*m*/*z*, %) 382.2 (M$^+$+1, 95).

5.5.2. 4-{[4-(p-nitro-benzylideneneamino)-5-sulfanyl-4,5-dihydro-1H-1,2,4-triazol-3-yl]methyl}-2H-1,4-benzothiazin-3(4H)-one **5b**

IR (KBr) γ/cm^{-1}: 1678 (C=O), 1581 (C=N), 1265 (C=S); ^{1}H NMR (DMSO-d_6) δ: 3.60 (s, 2H, benzothiazine S-CH_2), 5.52 (s, 2H, benzothiazine N-CH_2), 7.03–7.06 (t, 1H, J = 7.2 Hz, benzothiazine 6–H), 7.23–7.26 (t, 1H, J = 7.2 Hz, benzothiazine 7–H),7.35–7.37 (d, 2H, J = 7.44 Hz, benzothiazine 5-H and 8–H), 8.17–8.19 (d, 2H, J = 7.76 Hz, protons *meta* to the nitro group), 8.36–8.38 (d, 2H, J = 8.12 Hz, protons *ortho* to the nitro group), 10.40 (s, 1H, N=CH), 13.65 (s, 1H, SH/NH); LC-MS (*m*/*z*, %) 427.1 (M$^+$+1, 93).

5.5.3. 4-{[4-(p-chloro-benzylideneamino)-5-sulfanyl-4,5-dihydro-1H-1,2,4-triazol-3-yl]methyl}-2H-1,4-benzothiazin-3(4H)-one **5c**

IR (KBr) γ/cm^{-1}: 1680 (C=O), 1582 (C=N), 1267 (C=S); ^{1}H NMR (DMSO-d_6) δ: 3.58 (s, 2H, benzothiazine S-CH_2), 5.42 (s, 2H, benzothiazine N-CH_2), 7.01–7.04 (t, 1H, J = 7.3 Hz, benzothiazine 6–H), 7.21–7.24 (t, 1H, J = 7.3 Hz, benzothiazine 7–H),7.35–7.37 (d, 2H, J = 7.44 Hz, benzothiazine 5-H and 8–H), 7.59–7.61 (d, 2H, J = 8.44 Hz, protons *ortho* to the chloro group), 7.92–7.95 (d, 2H, J = 8.5 Hz, protons *meta* to the chloro group), 10.14 (s, 1H, N=CH), 13.68 (s, 1H, SH/NH); LC-MS (*m*/*z*, %) 416.1, 418.3 (M$^+$+1, 92).

5.6. General procedure for the preparation of 4-{[1-substituted aminomethyl-4-benzylideneamino-5-sulfanyl-4,5-dihydro-1H-1,2,4-triazol-3-yl]methyl}-2H-1,4-benzothiazin-3(4H)-one **6a-l**

A mixture of Shiff base (**5**) (2 mmol), formaldehyde (40%) (2 mmol) and appropriate secondary amine (2 mmol) in N,N-dimethyl formamide (5 mL) medium was stirred at room

temperature for 12 h [8]. The precipitated solid was filtered and dried. The crude product was then recrystalilzed from N,N-dimethyl formamide. The characterization data are given in Table 2.

5.6.1. 4-{[1-N-methyl piperazinomethyl-4-benzylideneamino-5-sulfanyl-4,5-dihydro-1H-1,2,4-triazol-3-yl]methyl}-2H-1,4-benzothiazin-3(4H)-one ***6a***

IR (KBr) γ/cm^{-1}: 1678 (C=O), 1583 (C=N), 1265 (C=S); ^{1}H NMR (DMSO-d_6): δ 2.1 (s, 3H, N-CH_3), 2.24 (t, 4H, CH_2N-CH_2), 2.57 (t, 4H, CH_2N-CH_2), 3.55 (s, 2H, benzothiazine S-CH_2), 4.98 (s, 2H, triazole N-CH_2), 5.40 (s, 2H, benzothiazine N-CH_2), 7.04–7.06 (t, 1H, J = 7.36 Hz, benzothiazine 6–H), 7.25–7.27 (t, 1H, J = 7.24 Hz, benzothiazine 7–H), 7.36–7.39 (d, 2H, J = 6.4 & 7.08 Hz, benzothiazine 5-H and 8–H), 7.53–7.57 (m, 2H, protons of phenyl ring *meta* to the N=CH group), 7.61–7.63 (t, 1H, J = 7.2 Hz, protons of phenyl ring *para* to the N=CH group), 7.90–7.92 (d, 2H, J = 7.32 Hz, protons of phenyl ring *ortho* to the N=CH group), 9.86 (s, 1H, N=CH); ^{13}C NMR (DMSO-d_6): δ 30.43 (benzothiazine C-2), 38.86 (C between triazole and benzothiazine), 45.75 (N-CH_3), 49.48 (N-methylpiperazine C-3 and C-5), 54.55 (N-methylpiperazine C-2 and C-6), 68.30 (C between N-methylpiperazine and triazole), 118.72 (benzothiazine C-6), 123.41 (benzothiazine C-7), 123.65 (benzothiazine C-5), 127.08 (benzothiazine C-8), 128.06 (benzothiazine C-10), 131.90 (benzothiazine C-9), 128.81 (phenyl C-3 and C-5), 129.05 (phenyl C-2 and C-6), 132.78 (phenyl C-4), 138.42 (phenyl C-1), 145.67 (C=S), 162.45 (N=CHR), 164.35 (N=CRR), 165.12 (C=O); Direct-MS: m/z, 494.5, 382.05, 101.2 (M^++1).

5.6.2. 4-{[1-morpholinomethyl-4-benzylideneamino-5-sulfanyl-4,5-dihydro-1H-1,2,4-triazol-3-yl]methyl}-2H-1,4-benzothiazin-3(4H)-one ***6b***

IR (KBr) γ/cm^{-1}: 1676.7 (C=O), 1587 (C=N), 1281 (C=S); ^{1}H NMR (DMSO-d_6): δ 2.51 (t, 4H, CH_2N-CH_2), 3.48 (t, 4H, CH_2OCH_2), 3.54 (s, 2H, benzothiazine S-CH_2), 4.98 (s, 2H, triazole N-CH_2), 5.40 (s, 2H, benzothiazine N-CH_2), 7.03–7.05 (t, 1H, J = 7.34 Hz, benzothiazine 6–H), 7.23–7.25 (t, 1H, J = 7.26 Hz, benzothiazine 7–H), 7.35–7.38 (d, 2H, J = 8.07 Hz, benzothiazine 5-H and 8–H), 7.51–7.62 (m, 3H, protons of phenyl ring *meta and para* to the N=CH group), 7.89–7.91 (d, 2H, J = 7.62 Hz, protons of phenyl ring *ortho* to the N=CH group), 9.84 (s, 1H, N=CH); ^{13}C NMR (DMSO-d_6): δ 30.45 (benzothiazine C-2), 38.80 (C between triazole and benzothiazine), 50.02 (morpholine C-3 and C-5), 65.99 (morpholine C-2 and C-6), 68.39 (C between morpholine and triazole), 118.71 (benzothiazine C-6), 123.41 (benzothiazine C-7), 123.65 (benzothiazine C-5), 127.07 (benzothiazine C-8), 128.07 (benzothiazine C-10), 131.92 (benzothiazine C-9), 128.82 (phenyl C-3 and C-5), 129.05 (phenyl C-2 and C-6), 132.78 (phenyl C-4), 138.43 (phenyl C-1), 145.69 (C=S), 162.45 (N=CHR), 164.35 (N=CRR), 165.13 (C=O); Direct-MS: m/z, 481.5, 382.2, 88.5 (M^++1).

5.6.3. 4-{[1-piperidinomethyl-4-benzylideneamino-5-sulfanyl-4,5-dihydro-1H-1,2,4-triazol-3-yl]methyl}-2H-1,4-benzothiazin-3(4H)-one ***6c***

IR (KBr) γ/cm^{-1}: 1682 (C=O), 1584 (C=N), 1265 (C=S); ^{1}H NMR (DMSO-d_6): δ 1.21 (m, 2H, CH_2), 1.36 (m, 4H, CH_2CH_2), 2.44 (t, 4H, CH_2N-CH_2), 3.53 (s, 2H, benzothiazine S-CH_2), 4.97 (s, 2H, triazole N-CH_2), 5.40 (s, 2H, benzothiazine N-CH_2), 7.02–7.04 (t, 1H, J = 7.32 Hz, benzothiazine 6–H), 7.24–7.26 (t, 1H, J = 7.24 Hz, benzothiazine 7–H), 7.34–7.37 (d, 2H, J = 8.06 Hz, benzothiazine 5-H and 8–H), 7.50–7.61 (m, 3H, protons of phenyl ring *meta and para* to the N=CH group), 7.88–7.90 (d, 2H, J = 7.64 Hz, protons of phenyl ring *ortho* to the N=CH group), 9.85 (s, 1H, N=CH); ^{13}C NMR (DMSO-d_6): δ 23.32 (piperidine C-4), 25.40 (piperidine C-3 and C-5), 30.50 (benzothiazine C-2), 38.40 (C between triazole and benzothiazine), 50.04 (piperidine C-2 and C-6), 69.23 (C between piperidine and triazole), 118.71 (benzothiazine C-6), 123.41 (benzothiazine C-7), 123.67 (benzothiazine C-5), 127.07 (benzothiazine C-8), 128.07 (benzothiazine C-10), 131.92 (benzothiazine C-9), 128.82 (phenyl C-3 and C-5), 129.05 (phenyl C-2 and C-6), 132.78 (phenyl C-4), 138.43 (phenyl C-1), 145.69 (C=S), 162.46 (N=CHR), 164.35 (N=CRR), 165.15 (C=O); Direct-MS: m/z, 479.3, 382.2, 86.2 (M^++1).

5.6.4. 4-{[1-N-methyl piperazinomethyl-4-(p-nitro-benzylidenene-amino)-5-sulfanyl-4,5-dihydro-1H-1,2,4-triazol-3-yl]methyl}-2H-1,4-benzothiazin-3(4H)-one ***6d***

IR (KBr) γ/cm^{-1}: 1690 (C=O), 1580 (C=N), 1274 (C=S), 1521 (N=O); ^{1}H NMR (DMSO-d_6): δ 2.2 (s, 3H, N-CH_3), 2.26 (t, 4H, CH_2N-CH_2), 2.60 (t, 4H, CH_2N-CH_2), 3.56 (s, 2H, benzothiazine S-CH_2), 4.99 (s, 2H, triazole N-CH_2), 5.46 (s, 2H, benzothiazine N-CH_2), 7.03–7.04 (t, 1H, J = 7.2 Hz, benzothiazine 6–H), 7.25–7.27 (t, 1H, J = 7.4 Hz, benzothiazine 7–H), 7.35–7.37 (d, 2H, J = 8 Hz, benzothiazine 5-H and 8–H), 8.17–8.21 (m, 2H, J = 7.76 Hz protons *meta* to the nitro group), 8.36–8.39 (d, 2H, J = 8.12 Hz, protons *ortho* to the nitro group), 10.26 (s, 1H, N=CH); ^{13}C NMR (DMSO-d_6): δ 30.42 (benzothiazine C-2), 38.80 (C between triazole and benzothiazine), 45.74 (N-CH_3), 49.47 (N-methylpiperazine C-3 and C-5), 54.50 (N-methylpiperazine C-2 and C-6), 68.36 (C between N-methylpiperazine and triazole), 118.82 (benzothiazine C-6), 124.06 (benzothiazine C-7), 124.06 (benzothiazine C-8), 128.14 (benzothiazine C-5), 129.84 (benzothiazine C-10), 131.19 (benzothiazine C-9), 129.82 (nitrophenyl C-3 and C-5), 123.65 (nitrophenyl C-2 and C-6), 137.99 (nitrophenyl C-4), 149.50 (nitrophenyl C-1), 145.54 (C=S), 160.22 (N=CHR), 162.16 (N=CRR), 165.15 (C=O); Direct-MS: m/z, 539.1, 427.3, 101.1 (M^++1).

5.6.5. 4-{[1- morpholinomethyl-4-(p-nitro-benzylideneneamino)-5-sulfanyl-4,5-dihydro-1H-1,2,4-triazol-3-yl]methyl}-2H-1,4-benzothiazin-3(4H)-one ***6e***

IR (KBr) γ/cm^{-1}: 1679 (C=O), 1583 (C=N), 1279 (C=S), 1530 (N=O); ^{1}H NMR (DMSO-d_6): δ 2.53 (m, 4H, CH_2N-CH_2), 3.55 (t, 4H, CH_2OCH_2), 3.57 (s, 2H, benzothiazine S-CH_2), 4.99 (s, 2H, triazole N-CH_2), 5.47 (s, 2H, benzothiazine N-CH_2), 7.02–7.05 (t, 1H, J = 7.22 Hz, benzothiazine 6–H), 7.23–7.26 (t, 1H, J = 7.24 Hz, benzothiazine 7–H), 7.37–7.39 (d, 2H, J = 8.02 Hz, benzothiazine 5-H and 8–H), 8.17–8.19 (m, 2H, J = 8.04 Hz protons *meta* to the nitro group), 8.35–8.37 (d, 2H, J = 8.16 Hz, protons *ortho* to the nitro group), 10.25 (s, 1H, N=CH); ^{13}C NMR (DMSO-d_6): δ 30.45 (benzothiazine C-2), 38.80 (C between triazole and benzothiazine), 50.02 (morpholine C-3 and C-5), 65.98 (morpholine C-2 and C-6), 68.39 (C between morpholine and triazole), 118.84 (benzothiazine C-6), 124.08 (benzothiazine C-7), 124.08 (benzothiazine C-8), 128.12 (benzothiazine C-5), 129.85 (benzothiazine C-10), 131.18 (benzothiazine C-9), 129.84 (nitrophenyl C-3 and C-5), 123.65 (nitrophenyl C-2 and C-6), 137.98 (nitrophenyl C-4), 149.51 (nitrophenyl C-1), 145.53 (C=S), 160.22 (N=CHR), 162.16 (N=CRR), 165.15 (C=O); Direct-MS: m/z, 526.1, 427.3, 88.1 (M^++1).

5.6.6. 4-{[1- piperidinomethyl-4-(p-nitro-benzylideneneamino)-5-sulfanyl-4,5-dihydro-1H-1,2,4-triazol-3-yl]methyl}-2H-1,4-benzothiazin-3(4H)-one ***6f***

IR (KBr) γ/cm^{-1}: 1675 (C=O), 1579 (C=N), 1267 (C=S), 1523 (N=O); ^{1}H NMR (DMSO-d_6): δ 1.24 (m, 2H, CH_2), 1.39 (m, 4H, CH_2CH_2), 2.46 (t, 4H, CH_2N-CH_2), 3.57 (s, 2H, benzothiazine S-CH_2), 4.96 (s, 2H, triazole N-CH_2), 5.49 (s, 2H, benzothiazine N-CH_2), 7.04–7.05 (t, 1H, J = 7 Hz, benzothiazine 6–H), 7.24–7.26 (t, 1H, J = 7.2 Hz, benzothiazine 7–H), 7.36–7.38 (d, 2H, J = 8.06 Hz, benzothiazine 5-H and 8–H), 8.18–8.20 (m, 2H, J = 7.76 Hz protons *meta* to the nitro group), 8.35–8.37 (d, 2H, J = 8.12 Hz, protons *ortho* to the nitro group), 10.27 (s, 1H, N=CH); ^{13}C NMR (DMSO-d_6): δ 23.32 (piperidine C-4), 25.40 (piperidine C-3 and C-5), 30.48

(benzothiazine C-2), 38.41 (C between triazole and benzothiazine), 50.04 (piperidine C-2 and C-6), 69.23 (C between piperidine and triazole), 118.83 (benzothiazine C-6), 124.09 (benzothiazine C-7), 124.09 (benzothiazine C-8), 128.12 (benzothiazine C-5), 129.85 (benzothiazine C-10), 131.19 (benzothiazine C-9), 129.85 (phenyl C-3 and C-5), 123.65 (phenyl C-2 and C-6), 137.99 (nitrophenyl C-4), 149.52 (nitrophenyl C-1), 145.55 (C=S), 160.22 (N=CHR), 162.16 (N=CRR), 165.14 (C=O). Direct-MS: *m*/*z*, 524.1, 427.3, 86.1 (M^++1).

5.6.7. 4-{[1-N-methyl piperazinomethyl-4-(p-chloro-benzylideneamino)-5-sulfanyl-4,5-dihydro-1H-1,2,4-triazol-3-yl]methyl}-2H-1,4-benzothiazin-3(4H)-one ***6g***

IR (KBr) γ/cm^{-1}: 1674 (C=O), 1575 (C=N), 1264 (C=S); ^{1}H NMR (DMSO-d_6): δ 2.2 (s, 3H, N-CH_3), 2.25 (t, 4H, CH_2N-CH_2), 2.58 (t, 4H, CH_2N-CH_2), 3.55 (s, 2H, benzothiazine S-CH_2), 4.99 (s, 2H, triazole N-CH_2), 5.42 (s, 2H, benzothiazine N-CH_2), 7.01–7.05 (t, 1H, *J* = 7.4 Hz, benzothiazine 6–H), 7.22–7.27 (t, 1H, *J* = 8.40 Hz, benzothiazine 7–H), 7.34–7.36 (d, 2H, *J* = 8.26 Hz, benzothiazine 5-H and 8–H), 7.62–7.64 (m, 2H, *J* = 8.36 Hz protons *ortho* to the chloro group), 7.89–7.92 (d, 2H, *J* = 8.48 Hz, protons *meta* to the chloro group), 9.93 (s, 1H, N=CH); ^{13}C NMR (DMSO-d_6): δ 30.42 (benzothiazine C-2), 38.82 (C between triazole and benzothiazine), 45.74 (N-CH_3), 49.47 (N-methylpiperazine C-3 and C-5), 54.52 (N-methylpiperazine C-2 and C-6), 68.38 (C between N-methylpiperazine and triazole), 118.74 (benzothiazine C-6), 123.46 (benzothiazine C-7), 123.67 (benzothiazine C-5), 127.07 (benzothiazine C-8), 128.10 (benzothiazine C-10), 130.89 (benzothiazine C-9), 129.23 (chlorophenyl C-2 and C-6), 130.46 (chlorophenyl C-3 and C-5), 137.42 (chlorophenyl C-4), 138.34 (chlorophenyl C-1), 145.68 (C=S), 162.42 (N=CHR), 162.64 (N=CRR), 165.13 (C=O). Direct-MS: *m*/*z*, 528.6, 530.6, 416.1, 418.3, 101.3 (M^++1).

5.6.8. 4-{[1- morpholinomethyl-4-(p-chloro-benzylideneamino)-5-sulfanyl-4,5-dihydro-1H-1,2,4-triazol-3-yl]methyl}-2H-1,4-benzothiazin-3(4H)-one ***6h***

IR (KBr) γ/cm^{-1}: 1679 (C=O), 1577 (C=N), 1260 (C=S); ^{1}H NMR (DMSO-d_6): δ 2.52 (m, 4H, CH_2N-CH_2), 3.48 (t, 4H, CH_2OCH_2), 3.54 (s, 2H, benzothiazine S-CH_2), 4.97 (s, 2H, triazole N-CH_2), 5.41 (s, 2H, benzothiazine N-CH_2), 7.00–7.05 (t, 1H, *J* = 7.47 Hz, benzothiazine 6–H), 7.20–7.25 (t, 1H, *J* = 8.43 Hz, benzothiazine 7–H), 7.35–7.37 (d, 2H, *J* = 8.2 Hz, benzothiazine 5-H and 8–H), 7.60–7.62 (m, 2H, *J* = 8.46 Hz protons *ortho* to the chloro group), 7.91–7.94 (d, 2H, *J* = 8.52 Hz, protons *meta* to the chloro group), 9.91 (s, 1H, N=CH); ^{13}C NMR (DMSO-d_6): δ 30.44 (benzothiazine C-2), 38.82 (C between triazole and benzothiazine), 50.04 (morpholine C-3 and C-5), 65.96 (morpholine C-2 and C-6), 68.38 (C between morpholine and triazole), 118.74 (benzothiazine C-6), 123.46 (benzothiazine C-7), 123.67 (benzothiazine C-5), 127.07 (benzothiazine C-8), 128.10 (benzothiazine C-10), 130.89 (benzothiazine C-9), 129.23 (chlorophenyl C-2 and C-6), 130.46 (chlorophenyl C-3 and C-5), 137.42 (chlorophenyl C-4), 138.32 (chlorophenyl C-1), 145.68 (C=S), 162.42 (N=CHR), 162.64 (N=CRR), 165.13 (C=O); Direct-MS: *m*/*z*, 515.3, 517.2, 416.1, 418.3, 88.2 (M^++1).

5.6.9. 4-{[1- piperidinomethyl-4-(p-chloro-benzylideneamino)-5-sulfanyl-4,5-dihydro-1H-1,2,4-triazol-3-yl]methyl}-2H-1,4-benzothiazin-3(4H)-one ***6i***

IR (KBr) γ/cm^{-1}: 1679 (C=O), 1576 (C=N), 1260 (C=S); ^{1}H NMR (DMSO-d_6): δ 1.22 (m, 2H, CH_2), 1.36 (m, 4H, CH_2CH_2), 2.44 (t, 4H, CH_2N-CH_2), 3.54 (s, 2H, benzothiazine S-CH_2), 4.95 (s, 2H, triazole N-CH_2), 5.47 (s, 2H, benzothiazine N-CH_2), 7.03–7.04 (t, 1H, *J* = 7 Hz, benzothiazine 6–H), 7.23–7.25 (t, 1H, *J* = 7.22 Hz, benzothiazine 7–H), 7.35–7.37 (d, 2H, *J* = 8.04 Hz, benzothiazine 5-H and 8–H), 7.61–7.63 (m, 2H, *J* = 8.42 Hz protons *ortho* to the chloro group), 7.91–7.93 (d, 2H, *J* = 8.52 Hz, protons *meta* to the chloro group), 9.92 (s, 1H, N=CH); ^{13}C NMR (DMSO-d_6): δ 23.30 (piperidine C-4), 25.40 (piperidine C-3 and C-5), 30.52 (benzothiazine C-2), 38.42 (C between triazole and benzothiazine), 50.04 (piperidine C-2 and C-6), 69.23 (C between piperidine and triazole), 118.74 (benzothiazine C-6), 123.46 (benzothiazine C-7), 123.67 (benzothiazine C-5), 127.07 (benzothiazine C-8), 128.10 (benzothiazine C-10), 130.89 (benzothiazine C-9), 129.23 (chlorophenyl C-2 and C-6), 130.46 (chlorophenyl C-3 and C-5), 137.42 (chlorophenyl C-4), 138.34 (chlorophenyl C-1), 145.68 (C=S), 162.42 (N=CHR), 162.64 (N=CRR), 165.13 (C=O); Direct-MS: *m*/*z*, 513.2, 515.2, 416.1, 418.3, 86.2 (M^++1).

5.6.10. 4-{[1-N-methyl piperazinomethyl-4-(p-hydroxy-benzylideneamino)-5-sulfanyl-4,5-dihydro-1H-1,2,4-triazol-3-yl]methyl}-2H-1,4-benzothiazin-3(4H)-one ***6j***

IR (KBr) γ/cm^{-1}: 3549 (OH), 1676 (C=O), 1575 (C=N), 1265 (C=S); ^{1}H NMR (DMSO-d_6): δ 2.1 (s, 3H, N-CH_3), 2.23 (t, 4H, CH_2N-CH_2), 2.56 (t, 4H, CH_2N-CH_2), 3.56 (s, 2H, benzothiazine S-CH_2), 4.99 (s, 2H, triazole N-CH_2), 5.41 (s, 2H, benzothiazine N-CH_2), 7.03–7.04 (t, 1H, *J* = 7.2 Hz, benzothiazine 6–H), 7.24–7.26 (t, 1H, *J* = 7.24 Hz, benzothiazine 7–H), 7.36–7.39 (d, 2H, *J* = 6.4 & 7.08 Hz, benzothiazine 5-H and 8–H), 7.66–7.68 (t, 2H, *J* = 7.2 Hz, protons *meta* to the hydroxyl group), 6.85–6.87 (t, 2H, *J* = 7.4 Hz, protons *ortho* to the hydroxyl group), 9.82 (s, 1H, N=CH); ^{13}C NMR (DMSO-d_6): δ 30.42 (benzothiazine C-2), 38.80 (C between triazole and benzothiazine), 45.74 (N-CH_3), 49.44 (N-methylpiperazine C-3 and C-5), 54.52 (N-methylpiperazine C-2 and C-6), 68.38 (C between N-methylpiperazine and triazole), 118.71 (benzothiazine C-6), 123.41 (benzothiazine C-7), 123.65 (benzothiazine C-5), 127.07 (benzothiazine C-8), 128.07 (benzothiazine C-10), 131.92 (benzothiazine C-9), 129.02 (hydroxyphenyl C-3 and C-5), 129.24 (hydroxyphenyl C-2 and C-6), 137.08 (hydroxyphenyl C-4), 138.80 (hydroxyphenyl C-1), 145.70 (C=S), 162.45 (N=CHR), 164.35 (N=CRR), 165.13 (C=O); Direct-MS: *m*/*z*, 510.5, 398.05, 101.2 (M^++1).

5.6.11. 4-{[1- morpholinomethyl-4-(p-hydroxy-benzylideneamino)-5-sulfanyl-4,5-dihydro-1H-1,2,4-triazol-3-yl]methyl}-2H-1,4-benzothiazin-3(4H)-one ***6k***

IR (KBr) γ/cm^{-1}: 3540 (OH), 1676 (C=O), 1575 (C=N), 1265 (C=S); ^{1}H NMR (DMSO-d_6): δ 2.52 (t, 4H, CH_2N-CH_2), 3.46 (t, 4H, CH_2OCH_2), 3.53 (s, 2H, benzothiazine S-CH_2), 4.99 (s, 2H, triazole N-CH_2), 5.41 (s, 2H, benzothiazine N-CH_2), 7.03–7.05 (t, 1H, *J* = 7.34 Hz, benzothiazine 6–H), 7.23–7.25 (t, 1H, *J* = 7.26 Hz, benzothiazine 7–H), 7.35–7.38 (d, 2H, *J* = 8.07 Hz, benzothiazine 5-H and 8–H), 7.67–7.68 (t, 2H, *J* = 7.1 Hz, protons *meta* to the hydroxyl group), 6.85–6.86 (t, 2H, *J* = 7.3 Hz, protons *ortho* to the hydroxyl group), 9.84 (s, 1H, N=CH); ^{13}C NMR (DMSO-d_6): δ 30.45 (benzothiazine C-2), 38.80 (C between triazole and benzothiazine), 50.02 (morpholine C-3 and C-5), 65.99 (morpholine C-2 and C-6), 68.39 (C between morpholine and triazole), 118.71 (benzothiazine C-6), 123.41 (benzothiazine C-7), 123.65 (benzothiazine C-5), 127.07 (benzothiazine C-8), 128.07 (benzothiazine C-10), 131.92 (benzothiazine C-9), 129.04 (hydroxyphenyl C-3 and C-5), 129.26 (hydroxyphenyl C-2 and C-6), 137.06 (hydroxyphenyl C-4), 138.82 (hydroxyphenyl C-1), 145.68 (C=S), 162.45 (N=CHR), 164.35 (N=CRR), 165.13 (C=O); Direct-MS: *m*/*z*, 496.7, 398.05, 88.2 (M^++1).

5.6.12. 4-{[1- piperidinomethyl-4-(p-hydroxy-benzylideneamino)-5-sulfanyl-4,5-dihydro-1H-1,2,4-triazol-3-yl]methyl}-2H-1,4-benzothiazin-3(4H)-one ***6l***

IR (KBr) γ/cm^{-1}: 3545 (OH), 1675 (C=O), 1579 (C=N), 1265 (C=S); ^{1}H NMR (DMSO-d_6): δ 1.22 (m, 2H, CH_2), 1.35 (m, 4H, CH_2CH_2), 2.43 (t, 4H, CH_2N-CH_2), 3.54 (s, 2H, benzothiazine S-CH_2), 4.98 (s, 2H, triazole N-CH_2), 5.41 (s, 2H, benzothiazine N-CH_2), 7.04–7.05 (t, 1H, *J* = 7 Hz, benzothiazine 6–H), 7.24–7.26 (t, 1H, *J* = 7.2 Hz, benzothiazine 7–H), 7.26–7.28 (d, 2H, *J* = 8.06 Hz, benzothiazine 5-

H and 8–H), 7.65–7.67 (t, 2H, J = 7.2 Hz, protons *meta* to the hydroxyl group), 6.84–6.86 (t, 2H, J = 7.4 Hz, protons *ortho* to the hydroxyl group), 9.83 (s, 1H, N=CH); ^{13}C NMR (DMSO-d_6): δ 23.32 (piperidine C-4), 25.40 (piperidine C-3 and C-5), 30.50 (benzothiazine C-2), 38.40 (C between triazole and benzothiazine), 50.04 (piperidine C-2 and C-6), 69.23 (C between piperidine and triazole), 118.71 (benzothiazine C-6), 123.41 (benzothiazine C-7), 123.67 (benzothiazine C-5), 127.07 (benzothiazine C-8), 128.07 (benzothiazine C-10), 131.92 (benzothiazine C-9), 129.02 (hydroxyphenyl C-3 and C-5), 129.22 (hydroxyphenyl C-2 and C-6), 137.08 (hydroxyphenyl C-4), 138.84 (hydroxyl phenyl C-1), 145.69 (C=S), 162.46 (N=CHR), 164.35 (N=CRR), 165.15 (C=O); Direct-MS: m/z, 495.2, 398.05, 86.2 (M^++1).

Acknowledgment

One of the authors, J. Gowda, is thankful to UGC, New Delhi for the financial assistance and to the Head, RSIC, Panjab University, Chandigarh for spectral data.

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