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Synthesis and Antioxidant Activity of a New Series of 2,1-Benzothiazine 2,2-Dioxide Hydrazine Derivatives

MUHAMMAD SHAFIQ[1,2,*], ISLAM ULLAH KHAN[1,*], MUHAMMAD ZIA-UR-REHMAN[3], MUHAMMAD NADEEM ASGHAR[4], ABDULLAH M. ASIRI[5] and MUHAMMAD NADEEM ARSHAD[6]

[1]Materials Chemistry Laboratory, Department of Chemistry, Government College University, Lahore-54000, Pakistan
[2]Department of Chemistry, Government College University, Faisalabad, Pakistan
[3]Applied Chemistry Research Centre, PCSIR Laboratories Complex, Lahore-54600, Pakistan
[4]Department of Chemistry, Forman Christian College University, Lahore-54600, Pakistan
[5]The Center of Excellence for Advanced Materials Research, King Abdul Aziz University, Jeddah, P.O. Box 80203, Saudi Arabia
[6]Department of Chemistry, University of Gujrat, Gujrat, Pakistan

*Corresponding authors: E-mail: hafizshafique@hotmail.com; iukhan@gcu.edu.pk

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A convenient synthesis of a series of new *N*-benzylidene-*N*'-(1-ethyl-2, 2-dioxo-2,3-dihydro-1*H*-2λ^6-benzo[c][1,2]thiazin-4-ylidene)-hydrazines is reported. The starting compound methyl anthranilate was reacted with methane sulfonyl chloride, followed by *N*-ethylation and cyclization reactions. This cyclized 2,1-benzothiazine 2,2-dioxide molecule was then subjected for hydrazinolysis with hydrazine followed by condensation reactions with a number of aromatic aldehydes yielding the 2,1-benzothiazine 2,2-dioxide hydrazine. Structural elucidation was achieved by FT-IR, ^{1}H and ^{13}C NMR and single crystal X-ray diffraction analyses. Crystal structure data for **6a** has been given with a brief structural discussion. The newly synthesized compounds were then screened for their antioxidant activity by ABTS radical cation decolourization assay and metal chelating activity.

Key Words: ABTS radical cation assay, Metal chelating activity, Crystal structure.

INTRODUCTION

2,1-Benzothiazine molecule belongs to an important heterocyclic class of compounds, which possess versatile nature of biological activities. The derivatives of 2,1-benzothiazine 2, 2-dioxide have been reported to possess a number of potent biological activities including lipoxygenase inhibition and are being used as drugs for the treatment of various kinds of heart diseases[1] (Fig. 1).

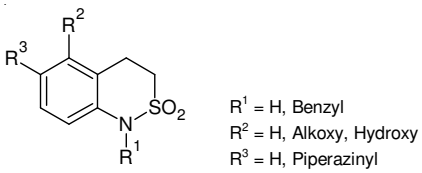


Fig. 1. 3,4-Dihydro-2,1-benzothiazine 2,2-dioxide derivatives

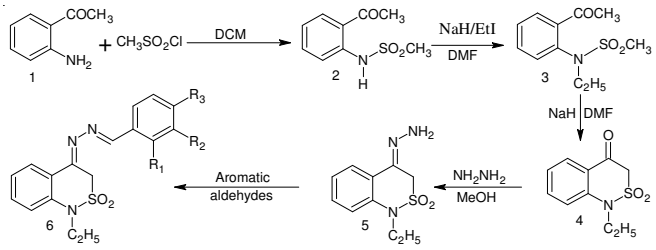
The synthesis of a variety of 2,1-benzothiazines has been reported in literature for their applications as precursors for the preparation of a number of medicinally important natural products such as antituberculosis agents pseudopteroxazole[2,3] and erogorgiaene[4]; S-(+)-curcuphenol, which is an inhibitor of gastric H, K-AT pase with fungicidal and antitumor activities[5-7] and S-(+)-curcumene[8,9]. 2,1-Benzothiazine derivatives have been used as chiral ligands for catalysis and molecular recognition[10]. Recently, literature has shown a tremendous increase in the synthesis and development of new synthetic methodologies for 2,1-benzothiazine derivatives[11-15]. From literature overview, it was observed that there exists a need to explore this ring with respect to its antimicrobial and antioxidant activities.

The main area of our research activity is to explore the reactivity and derivatization of 2,1-benzothiazine 2,2-dioxide nucleus along with the evaluation of its biological potential[16-20]. We have found in our previous work that the reaction of 2,1-benzothiazine 2,2-dioxide molecule with hydrazine and further condensation of this hydrazide with aromatic aldehydes incorporate good antibacterial properties in the target diimine molecules[16]. Herein, we are reporting the antioxidant potential of new *N*-benzylidene-*N*'-(1-ethyl-2, 2-dioxo-2,3-dihydro-1*H*-2λ6-benzo[*c*][1,2]thiazin-4-ylidene)-hydrazines, the homologues of previous diimine derivatives[16].

EXPERIMENTAL

All the chemicals were purchased from E. Merck, BDH or Fluka with highest purity available grades and used without

further purification. However, solvents were purified through distillation. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker DPX-400 instrument at 500 MHz. Chemical shifts values are reported in ppm. Melting points were recorded on an electrothermal (Griffin 1090) apparatus and are reported as uncorrected. IR spectra were recorded on a Perkin-Elmer 1600-FT spectrometer.



Compd.	R_1	R_2	R_3	Compd.	R_1	R_2	R_3
6a	H	H	H	**6f**	H	CH_3	H
6b	H	H	F	**6g**	H	H	$N(CH_3)_2$
6c	Cl	H	H	**6h**	H	OCH_3	OH
6d	H	Cl	H	**6i**	-[a]	-	-
6e	OH	H	H	**6j**	-[b]	-	-

[a]trans-cinnamaldehyde, [b]9-anthranaldehyde

Scheme -I: Synthesis of *N*-benzylidene-*N*'-(1-ethyl-2, 2-dioxo-2, 3-dihydro-1H-2λ^6-benzo[c][1,2]thiazin-4-ylidene)-hydrazines

(1-Ethyl-2,2-dioxo-2,3-dihydro-1H-2λ^6-benzo[*c*][1,2] thiazin-4-ylidene)-hydrazine (5): A mixture of 1-ethyl-2,2-dioxo-2,3-dihydro-1*H*-2λ^6-benzo[*c*][1,2]thiazin-4-one (**4**)[11,17] (11.25 g; 50 mmol), hydrazine hydrate (85 %) (5 mL) and ethanol (200 mL) was allowed to reflux for a period of 6 h. After completion of the reaction, excess hydrazine and solvent was removed under vacuum. The crude product obtained was washed with water and dried. Brown crystalline solid. Yield 91.47 %, m.p. 126-128 ºC. Precursor molecule **5** was characterized by X-ray diffraction data, (CCDC No. for Compound **5** is 859871) which is given as under along with its X-ray structure (Fig. 2). A = 7.7001 (3) Å, B = 10.9276 (4) Å, C = 12.9279 (5) Å, α = 90º, β = 96.601, γ = 90º, V = 1080.59 (7) Å^3.

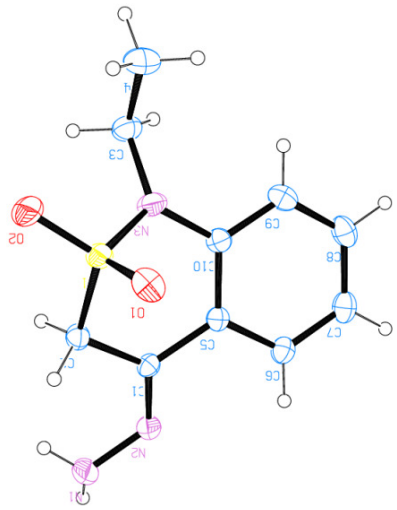


Fig. 2. ORTEP diagram for **5** with the 50 % probability level of the thermal ellipsoids

***N*-Benzylidene-*N*'-(1-ethyl-2,2-dioxo-2,3-dihydro-1*H*-2λ^6-benzo[*c*][1,2]thiazin-4-ylidene)-hydrazines (6a-j):** A mixture of (1-ethyl-2,2-dioxo-2,3-dihydro-1*H*-2λ^6-benzo[*c*][1,2]-thiazin-4-ylidene)-hydrazine (**5**) (2.0 mmol), corresponding aromatic aldehyde (2.1 mmol), methanol (15 mL) and glacial acetic acid (3-4 drops) was refluxed till the completion of reaction (20-120 min) as indicated by TLC. The contents were cooled, filtered and the solids were washed with cold methanol to get the pure title compounds.

***N*-Benzylidene-*N*'-(1-ethyl-2,2-dioxo-2,3-dihydro-1*H*-2λ^6-benzo[*c*][1,2]thiazin-4-ylidene)-hydrazine (6a):** Yellow crystalline solid. Yield 62.86 %, m.p. 154-156 ºC. ^{1}H NMR ($CDCl_3$): δ (ppm) 3-99-4.02 (m, 2H, N-CH_2), 1.35-1.37 (t, 3H, C-CH_3), 4.83 (s, 2H, CH_2), 7.12-7.53 (m, 9H, ArH), 8.60 (s, 1H, NCH); ^{13}C NMR ($CDCl_3$): δ (ppm) 14.33, 42.41, 51.86, 119.50, 141.27, 155.02, 161.88; FT-IR (KBr, ν_{max}, cm^{-1}): 3475, 1640, 1420, 1334, 1140.

***N*-(4-Fluoro-benzylidene)-*N*'-(1-ethyl-2,2-dioxo-2,3-dihydro-1*H*-2λ^6-benzo[*c*][1,2]thiazin-4-ylidene)-hydrazine (6b):** Yellow crystalline solid; Yield 68.59 %; m.p. 149-150 ºC. ^{1}H NMR ($CDCl_3$): δ (ppm) 3-98-4.02 (m, 2H, N-CH_2), 1.34-1.37 (t, 3H, C-CH_3), 4.82 (s, 2H, CH_2), 7.14-7.52 (m, 8H, ArH), 8.58 (s, 1H, NCH); ^{13}C NMR ($CDCl_3$): δ (ppm) 14.32, 42.38, 51.78, 119.45, 141.28, 155.15, 160.63; FT-IR (KBr, ν_{max}, cm^{-1}): 3485, 1642, 1405, 1375, 1234, 1137.

***N*-(2-Chloro-benzylidene)-*N*'-(1-ethyl-2,2-dioxo-2,3-dihydro-1*H*-2λ^6-benzo[*c*][1,2]thiazin-4-ylidene)-hydrazine (6c):** Yellow powder. Yield 73.81 %, m.p. 170-172 ºC. ^{1}H NMR (CDCl3): δ (ppm) 3.98-4.02 (m, 2H, N-CH_2), 1.35-1.37 (t, 3H, C-CH_3), 4.81 (s, 2H, CH_2), 7.18-7.52 (m, 8H, ArH), 9.04 (s, 1H, NCH); ^{13}C NMR ($CDCl_3$): δ (ppm) 14.34, 42.40, 51.84, 119.46, 141.36, 155.62, 158.34; FT-IR (KBr, ν_{max}, cm^{-1}): 3500, 1638, 1394, 1220, 1138.

***N*-(3-Chloro-benzylidene)-*N*'-(1-ethyl-2,2-dioxo-2,3-dihydro-1*H*-2λ^6-benzo[*c*][1,2]thiazin-4-ylidene)-hydrazine (6d):** Yellow powder. Yield 72.17 %, m.p. 117-118 ºC. ^{1}H NMR ($CDCl_3$): δ (ppm) 3.99-4.03 (m, 2H, N-CH_2), 1.35-1.38 (t, 3H, C-CH_3), 4.82 (s, 2H, CH_2), 7.18-7.71 (m, 8H, ArH), 8.55 (s, 1H, NCH); ^{13}C NMR ($CDCl_3$): δ (ppm) 14.34, 42.34, 51.81, 119.41, 141.40, 155.78, 160.35; FT-IR (KBr, ν_{max}, cm^{-1}): 3465, 1640, 1395, 1215, 1125.

***N*-(2-Hydroxy-benzylidene)-*N*'-(1-ethyl-2,2-dioxo-2,3-dihydro-1*H*-2λ^6-benzo[*c*][1,2]thiazin-4-ylidene)-hydrazine (6e):** Yellow powder. Yield 92.91 %, m.p. 206-208 ºC. ^{1}H NMR ($CDCl_3$) δ: 3.99-4.01 (m, 2H, N-CH_2), 1.34-1.36 (t, 3H, C-CH_3), 4.63 (s, 2H, CH_2), 6.98-7.54 (m, 8H, ArH), 8.77 (s, 1H, NCH), 11.12 (s, 1H, OH); ^{13}C NMR ($CDCl_3$): δ (ppm) 14.33, 42.74, 52.21, 119.93, 141.38, 154.45, 159.96; FT-IR (KBr, ν_{max}, cm^{-1}): 3485, 1638, 1360, 1240, 1136.

***N*-(3-Methyl-benzylidene)-*N*'-(1-ethyl-2,2-dioxo-2,3-dihydro-1*H*-2λ^6-benzo[*c*][1,2]thiazin-4-ylidene)-hydrazine (6f):** Yellow solid. Yield 72.88 %, m.p. 108-110 ºC. ^{1}H NMR ($CDCl_3$): δ (ppm) 2.44 (s, 3H, Ar-CH_3) 3.99-4.02 (m, 2H, N-CH_2), 1.33-1.39 (t, 3H, C-CH_3), 4.84 (s, 2H, CH_2), 7.17-7.70 (m, 8H, ArH), 8.57 (s, 1H, NCH); ^{13}C NMR ($CDCl_3$): δ (ppm) 14.32, 42.42, 51.90, 119.51, 141.25, 154.88, 162.06; FT-IR (KBr, ν_{max}, cm^{-1}): 3490, 1640, 1415, 1210, 1190.

{4-[(1-Ethyl-2,2-dioxo-2,3-dihydro-1*H*-2λ^6-benzo[*c*][1,2]thiazin-4-ylidene)-hydrazonomethyl]-

TABLE-1
CRYSTAL DATA AND STRUCTURE REFINEMENT FOR COMPOUND **6a**

Structural formula	$C_{17}H_{17}N_3O_2S$	Cell volume	3223.5(8) Å^3
Formula weight	327.40	Z	8
Crystal system	Monoclinic	Calculated density (g cm^{-3})	1.349
Space group	P2(1)/c	Absorption coefficient (mm^{-1})	0.214
T (K)	296(2) K	Crystal size (mm^3)	0.37 × 0.14 × 0.11
A (Å)	26.211(3)	Reflection collected/unique	7528/3432
B (Å)	7.3703(8)	Range for data collection (º)	0.78-28.46
C (Å)	16.687(3)	Goodness-of-fit on F^2	2.470
α (º)	90.00	F(000)	1375.7
β (º)	90.143(9)	Absorption correction	Multi-scan
γ (º)	90.00	Refinement method	Full-matrix least squares on F^2

phenyl}dimethyl-amine (6g): Fluffy yellow solid. Yield 94.32 %, m.p. 186-190 ºC. ^{1}H NMR ($CDCl_3$): δ (ppm) 3.96-4.00 (m, 2H, N-CH_2), 1.33-1.35 (t, 3H, C-CH_3), 4.87 (s, 2H, CH_2), 7.15-7.73 (m, 8H, ArH), 3.07 (s, 6H, NCH_3), 8.52 (s, 1H, NCH); ^{13}C NMR ($CDCl_3$): δ (ppm) 14.30, 42.58, 51.94, 119.70, 140.87, 152.70, 162.56; FT-IR (KBr, ν_{max}, cm^{-1}): 3520, 1640, 1410, 1388, 1170.

4-[(6-1-Ethyl-2,2-dioxo-2,3-dihydro-1*H*-2λ^6-benzo-[*c*][1,2]thiazin-4-ylidene)-hydrazonomethyl]-2-methoxy-phenol (6h): Yellow solid. Yield 78.79 %, m.p. 156-158 ºC. ^{1}H NMR ($CDCl_3$): δ (ppm) 3.97-4.01 (m, 2H, N-CH_2), 1.35-1.37 (t, 3H, C-CH_3), 4.85 (s, 2H, CH_2), 7.17-7.52 (m, 7H, ArH), 8.52 (s, 1H, NCH) 6.06 (s, 3H, Ar-OCH_3); ^{13}C NMR ($CDCl_3$): δ (ppm) 14.32, 42.48, 51.81, 119.53, 141.08, 153.97, 161.98; FT-IR (KBr, ν_{max}, cm^{-1}): 3490, 1638, 1410, 1330, 1165.

***N*-(1-Ethyl-2,2-dioxo-2,3-dihydro-1*H*-2λ^6-benzo[*c*]-[1,2]thiazin-4-ylidene)-*N*-(3-phenyl-allylidene)-hydrazine (6i):** Deep yellow crystalline solid. Yield 70.35 %, m.p. 152-154 ºC. ^{1}H NMR ($CDCl_3$): δ (ppm) 3.97-4.01 (m, 2H, N-CH_2), 1.34-1.36 (t, 3H, C-CH_3), 4.75 (s, 2H, CH_2), 7.09-7.56 (m, 8H, ArH), 8.39-8.42 (m, 3H, C=CH); ^{13}C NMR ($CDCl_3$): δ (ppm) 14.30, 42.36, 51.74, 119.45, 141.24, 154.39, 163.84; FT-IR (KBr, ν_{max}, cm^{-1}): 3480, 1642, 1328, 1316, 1139.

***N*-Anthracen-9-yl-methylene-*N*-(1-ethyl-2,2-dioxo-2,3-dihydro-1*H*-2λ^6-benzo[*c*][1,2]thiazin-4-ylidene)-hydrazine (6j):** Orange solid. Yield 83.71 %, m.p. 199-201 ºC. ^{1}H NMR ($CDCl_3$): δ (ppm) 4.01-4.05 (m, 2H, N-CH_2), 1.37-1.40 (t, 3H, C-CH_3), 4.91 (s, 2H, CH_2), 7.22-7.65 (m, 13H, ArH), 9.94 (s, 1H, NCH); ^{13}C NMR ($CDCl_3$): δ (ppm) 14.37, 42.49, 52.41, 119.67, 141.43, 155.30, 161.62; FT-IR (KBr, ν_{max}, cm^{-1}): 3515, 1650, 1430, 1316, 1170.

Crystallographic structure determination: X-ray data were collected at 296 K on a Bruker KAPPA APEX II diffractometer using MoK_α X-ray (0.71073 Å) source and a graphite monochromator. The unit cell dimensions were obtained from least-squares fit to setting angles of about 25 reflections. Multi-scan absorption corrections were applied. SAINT[21] was used for the cell refinement and data reduction, while SHELXS-97[22] was used for structure solution and refinement. ORTEP-3 for Windows[23], PLATON[24] and WinGX[25] were used for molecular graphics. In the refinement procedure, all the non-hydrogen atoms were refined with anisotropic displacement parameters. All the $C_{aromatic}$---H and $C_{aliphatic}$---H hydrogen atoms were positioned geometrically and treated as riding atom over their parent carbon atoms. Crystallographic data and refinement details for compound **6a** are given in Table-1 supplementary crystallographic data have been deposited with the CCDC number 842898. These data can be obtained free of charge from Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

Anti-oxidant assay: For antioxidant studies, ABTS (2,2'-azinobis(3-ethylbenzothiazoline-6-sulfonic acid) diammonium salt, potassium persulfate and ferrozine were obtained from Fluka (UK). HPLC grade solvents were used throughout the antioxidative studies. Antioxidant and metal chelation studies were carried out using UV-Visible spectrophotometer, UVD-3200, Labomad, Inc., USA, equipped with temperature controller. Solvent blanks were run for each measurement. All the measurements were taken in triplicate.

ABTS radical cation decolourization assay protocol: $ABTS^{\cdot+}$ (ABTS radical cation) assay protocol[26] was followed for the evaluation of antioxidant activity of the title compounds. ABTS stock solution was prepared by dissolving ABTS disodium salt in double distilled water to a concentration of 7 mM. $ABTS^{\cdot+}$ was produced by reacting 7 mM ABTS stock solution with 2.45 mM potassium persulfate (final concentration) and allowing the mixture to stand in the dark, at room temperature for 12-16 h before use. Antioxidant activity of standard antioxidants and each sample solution was determined by diluting the $ABTS^{\cdot+}$ stock solution with PBS (Phosphate-buffered saline, pH 7.4) to an absorbance of 0.70 (± 0.02) at 734 nm. The solution was allowed to equilibrate at 30 ºC until a steady state of absorbance was achieved. An amount of 10 µL of sample solution was added to 2.99 mL of diluted $ABTS^{\cdot+}$ solution (A = 0.700 ± 0.020), the absorbance was measured at 30 ºC, with exactly 1 min. intervals for 8 min. Solvent blanks were also run in each assay for accurate measurements. The per cent inhibition of absorbance at 734 nm ($I_{734\ nm}$) was calculated by the following formula.

$$I_{734nm} = [1-A_f/A_o] \times 100$$

where, A_o and A_f are the absorbances of radical cation solution before addition and after six minutes of the addition of sample antioxidants, respectively. Percent inhibition for various dilutions of the samples were plotted against the concentrations and a linear curve was obtained. The EC_{50} value, which is the concentration of the sample, which is able to reduce the absorbance value of the radical cation solution to half of its original value, was calculated from the linear equation.

Metal chelating activity: The metal chelating activity of the samples estimated was based on the decrease in the maximal

absorbance of the Fe^{2+}-ferrozine complex according to previously reported method[27]. An aliquot of sample equal to 10 µL was added to 50 µL of freshly prepared ferrous sulphate solution (2 mM). The reaction was initiated by the addition of 200 µL ferrozine (5.0 mM) and adjusting the total volume to 4 mL with ethanol. After the mixture had reached equilibrium (after 10 min), the absorbance at 562 nm was recorded. The control was prepared without the test compound. Fe^{2+} chelating activity of the test molecules was calculated from the following formula:

Percent chelating activity = $[(A_{control} - A_{sample})/A_{sample}] \times 100$

where, A_{sample} and $A_{control}$ are the absorbances of mixture with and without sample at 562 nm, respectively. The comparison of percent chelating activity of the samples was made by incoporating the data in a bar graph.

RESULTS AND DISCUSSION

1-Ethyl-2,2-dioxo-2,3-dihydro-1*H*-2λ⁶-benzo[*c*][1,2]thiazin-4-one (**4**) was synthesized by the condensation of methane sulfonyl chloride with methyl anthranilate followed by *N*-ethylation using ethyl iodide and then cyclization with sodium hydride[11,17]. 1-Ethyl-2,2-dioxo-2,3-dihydro-1H-2λ⁶-benzo[*c*][1,2]thiazin-4-ones (**4**) was then reacted with hydrazine hydrate to get 1-ethyl-2,2-dioxo-2,3-dihydro-1*H*-2λ⁶-benzo[*c*][1,2]thiazin-4-ylidene)-hydrazine (**5**), which was then reacted with different aromatic aldehydes under reflux for appropriate period of time (20-120 min) to get the title compounds (**6a-j**) in good yields.

All of the newly synthesized compounds have been characterized through spectroscopic techniques like FT-IR, ^1H and ^{13}C NMR, the values of which are given in experimental part for each copmpound. Moreover, to determine the stereochemistry (E or Z configuration) of these target molecules, a single crystal of **6a** was studied by X-ray crystallography. The crystal structure indicates E configuration of C=N bond for this specific compound and based upon this finding, it may be supposed that rest of the molecules of this series will have the same *E* configuration.

The compound **6a** was re-crystallized in order to study the three dimensional geometry of the molecules of this series. The crystal structure of the subjected molecule (Fig. 3) revealed that compound was crystalized with two molecules per asymmetric unit. In each molecule C=N linkage adopts an *E* configuration. The non-planer thiazine rings (C1/C6/C7/C8/N1/S1) and (C18/C23/C24/C25/N4/S2) with the r.m.s deviation of 0.2279 Å and 0.2271 Å adopted the sofa shape. The two fused rings *i.e.* aromatic and thiazines are twisted at dihedral angle of 7.68 (91)º and 7.49 (90)º in molecule A and B. No classical hydrogen bonding interaction has been observed in molecules.

ABTS radical cation decolourization assay: The basic principle involved in the $ABTS^{\cdot+}$ decolourization assay is that ABTS, on reaction with $K_2S_2O_8$, forms a greenish blue radical cation with 734 nm as one of its wavelength maxima. Sample solution that are able to transfer an electron to ABTS radical cation reduce the colour of the solution proportionate to its amount. The extent of scavenging of the radical depends upon both the concentration and nature of the compound under analysis. The reducing capacity in terms of EC_{50} value of the synthesized molecules was determined (Fig. 4). The EC_{50} value of the sample molecules was found to decrease in the order **6i > 6g > 6a > 6d > 6f > 6j > 6h > 6e > 5 > 6b**. **5** and **6b** were found to be the most potent scavenger or reducer of the ABTS radical cation. This is also in line with the structure of these compounds. The availability of electrons on nitrogen atom of hydrazine moiety of the molecule is maximum either in the absence of electron withdrawing groups attached to it, as in **5**, or by the donation of electronic pair through resonance by the substituent groups as in the case of **6e** and **6f**.

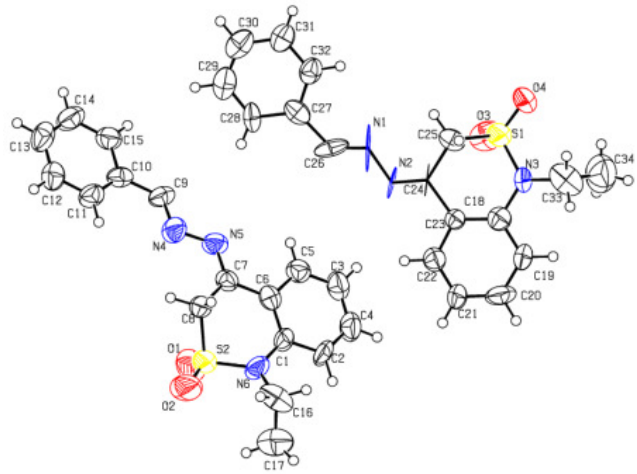


Fig. 3. ORTEP diagram for **6a** with the 50 % probability level of the thermal ellipsoids

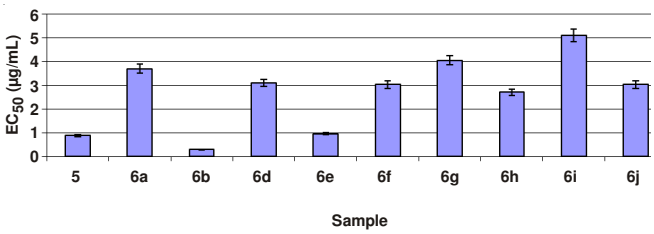


Fig. 4. Comparison of EC_{50} values

Metal chelating activity: The chelation of Fe^{2+} by synthesized molecules was estimated by the method of Dinis *et al.*[27] Ferrozine can quantitatively form complex with Fe^{2+}. However, in the presence of other chelating agents, the complex formation is affected with the result that the intensity of red-coloured Fe^{2+}-ferrozine complex is decreased. Measurement of reduction in colour intensity, therefore, allows estimation of the chelating activity of the co-existing chelator. The transition metal ion, Fe^{2+} possess the ability to move single electrons by virtue of which it can allow the formation and propagation of many radical reactions, even starting with relatively non-reactive radicals. The main strategy to avoid ROS generation that is associated with redox active metal catalysis involves chelating of the metal ions. The sample molecules interfered with the formation of Fe^{2+}-ferrozine complex, suggesting that it has the ability to capture ferrous ion more efficiently than ferrozine. The chelating activity of the sample molecules decrease in the order of **6h > 6j > 6e > 6b > 5 > 6a > 6g > 6f > 6d > 6i** (Fig. 5).

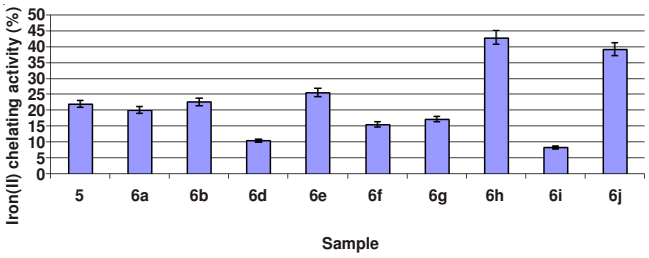


Fig. 5. Comparison of per cent iron(II) chelating activity

Conclusion

Synthesis of *N*-benzylidene-*N*'-(1-ethyl-2,2-dioxo-2,3-dihydro-1*H*-2λ^6-benzo[*c*][1,2]thiazin-4-ylidene)-hydrazines and their evaluation for antioxidant activity is reported. The compounds have been synthesized in good yields with good antioxidant activity. The antibacterial activity of previously described analogues *N*-benzylidene-*N*'-(1-methyl-2,2-dioxo-2,3-dihydro-1*H*-2λ^6-benzo[*c*][1,2]thiazin-4-ylidene)-hydrazines[16] has been already reported with good results. The aim of work was to evaluate the antioxidant potential of this new series of title compounds *N*-benzylidene-*N*'-(1-ethyl-2,2-dioxo-2,3-dihydro-1*H*-2λ^6-benzo[*c*][1,2]thiazin-4-ylidene)-hydrazines. With respect to the established antibacterial as well as antioxidant potential, the compounds of 2,1-benzothiazine 2,2-dioxide hydrazine series could be useful to synthesize more biologically active agents through their further derivatization.

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