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Spectral, DFT and X-ray diffraction studies on regioselective synthesis of thiazolo-quinazoline system

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ABSTRACT

Unsymmetrical quinazoline-3-thione **2**, obtained from one pot condensation of 2-tetralone, p-chlorobenzaldehyde and thiourea in acidic medium, on reaction with α-halo acids afforded thiazolo-quinazoline derivatives **3**, **7** and not their regioisomers **4** and **8** respectively. The cyclised product obtained by the reaction of thione **2** with 1,2-dibromoethane has been assigned structure **5**. Condensation of thione **2** with 3-chloropropionic acid and 1,3-dibromopropane furnished thiazino-quinazoline derivatives **10** and **12** instead of their regioisomers **11** and **13** respectively. The structure of the cyclised products has been established by means of spectral data (IR, NMR and Mass). X-ray diffraction studies of a representative compound supported our claim on structural assignments. DFT studies on regioisomers further validated the claim for assigned structures. The reaction of thione **2** with 3-chloropropionc acid in presence of acetic acid yielded thiazinan-4-one **10.**

1. Introduction

Substituted or fused quinazoline derivatives have proven pharmacological significance [1]. There are enough evidences to suggest that several of them are potentially useful medicinal agents and others are in various stages of development [2]. Quinazoline derivatives have attracted significant attraction due to their diverse pharmacological activities such as antimicrobial [3], anti-malarial [4], anti-inflammatory [5], antihypertensive [6], anticonvulsant [7], anti-diabetic [8], anti-cancer [9], cholinesterase inhibition [10], dihydrofolate reductase inhibition [11], and kinase inhibitory activity [12]. Quinazolines also exhibit a wide variety of biological functions like cellular phosphorylation inhibition [13], ligands for benzodiazepine and GABA receptors in the central nervous system [14], and some of them have acted as DNA binding agents [15]. Quazinone, (3R)-6-chloro-3-methyl-5,10-dihydroimidazo[2,1-*b*] quinazolin-2(3H)-one acts as effective PDE 3 and phospholipase inhibitor [16]. Some of the quinazoline derivatives such as proquazone, 1-isopropyl-7-methyl-4-phenylquinazoline-2(1H)-one [17] and fluoroquazone, 4-(4-fluorophenyl)-7-methyl-1-propan-2-yl-quinazoline-2-one [18] are well known non-steroidal anti-inflammatory drugs. Thiazoles are also endowed with a wide range of pharmaceutical activities. The development of new structures which incorporate various biologically active pharmacophores in a single molecule has attracted much attention in medicinal research. This approach encouraged us to undertake the synthesis of new thiazolo-quinazoline and thiazino-quinazoline derivatives in continuation to our previous work on synthesis of such skeletons [19–21]. The regiochemistry of the cyclised products was established by means of spectral data and verified by X-ray and DFT studies.

2. Result and discussion

A mixture of 2-tetralone **1**, 4-chloro benzaldehyde and thiourea in glacial acetic acid on stirring at 110 °C for 4 h furnished thione **2**. The characterization of this thione was done on the basis of spectral data. The unsymmetrical thione **2,** on condensation with ethyl bromo acetate followed by cyclization of the intermediate in situ was likely to give compound **3** or its isomer **4** or a mixture of both depending upon mode of cyclization (Scheme 1). However, the thione **2,** when treated with ethyl bromo acetate in the presence of anhydrous sodium acetate in absolute ethanol afforded a single product (TLC) **3** or **4** in 82% yield. The appearance of a band at 1713 cm^{-1} (C=O) in the IR spectrum, appearance of peak at δ 170.7 (C=O) in ^{13}C NMR spectrum and exhibition of a quasimolecular ion peak at *m*/*z* 367.2 ($M+H^+$, 100%) in the mass spectrum of the TLC-pure product suggested the formation of thiazolidinone **3** or **4**. The

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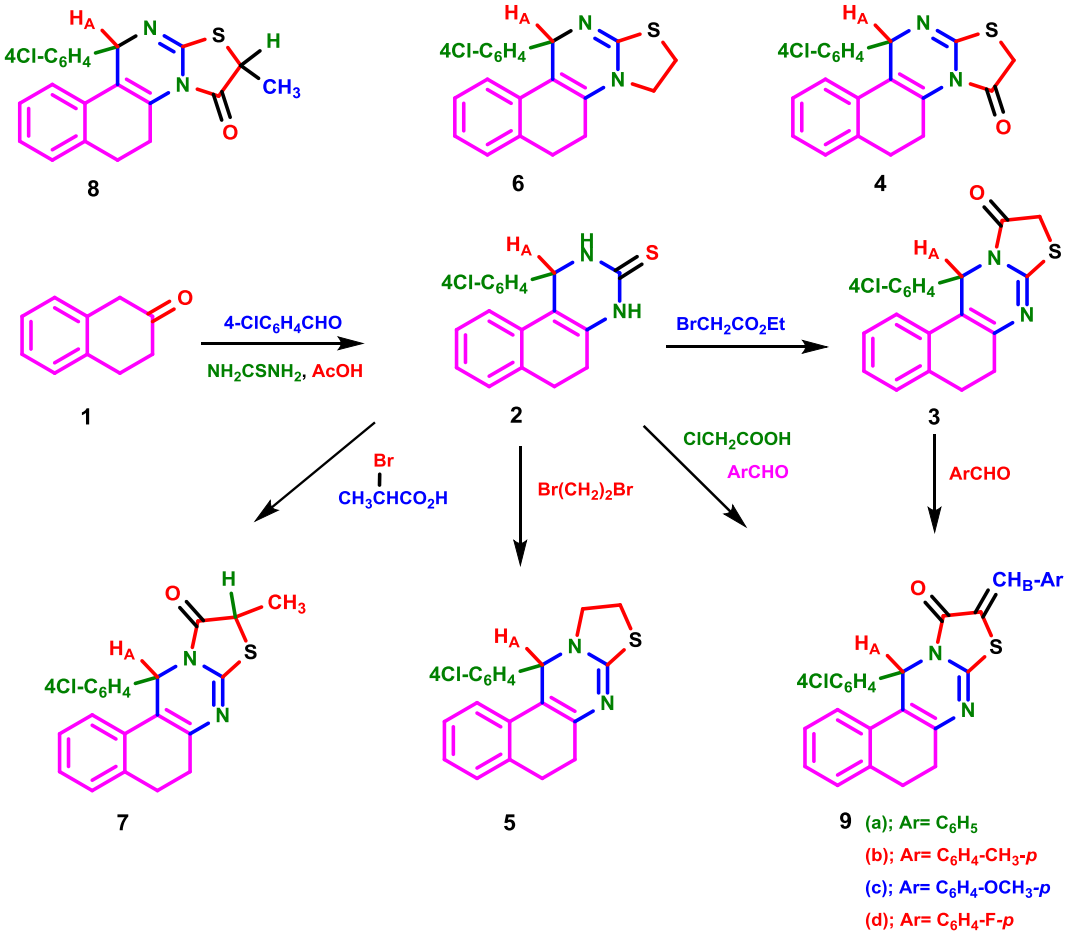


Scheme 1. Synthetic route to thiazolo-quinazoline derivatives.

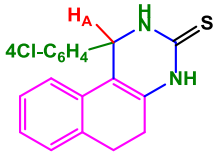
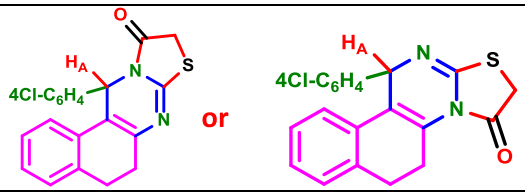
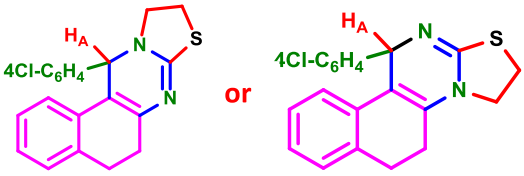
appearance of two multiplets at δ 2.56 and δ 2.83 of two protons each in ^{1}H NMR spectrum of the product have been assigned to tetrahydronaphthalene ring of **3** or **4.** A double doublet of two protons at δ 3.94 (J = 17.4 Hz and 1.7 Hz) assignable to SCH_2 group confirmed the formation of thiazolidinone ring. The IR and mass spectral data were ambivalent on deciding the structure **3** or **4**. However, structure **3** was finally assigned to this cyclization product in preference to the structure **4** on the basis of comparison of chemical shift of H_A proton of **3** or **4** with that of **5** or **6** as discussed below.

The reaction of thione **2** with 1, 2-dibromoethane gave a product which was purified by column chromatography and characterized by its quasimolecular ion peak at m/z 353.2 ($M+H^+$, 100%) as a compound which could be represented by either structure **5** or **6**. In either structure (**5** or **6**), the singlet at δ 6.13 in its ^{1}H NMR spectrum integrating for one proton was assigned to H_A proton. If the structure **4** is correct for the cyclization product, obtained from thione **2** and ethyl bromo acetate, and then H_A would resonate in the same region as that of structure **5** (or **6**). On the other hand if the structure **3** is correct, H_A would be deshielded by the thiazolidinone ring and consequently, H_A would resonate downfield in comparison to H_A in **5** (or **6**). The appearance of a downfield singlet at δ 6.20 for H_A in structure **3** (or **4**) as compared to singlet at δ 6.13 for H_A in structure **5** (or **6**) (Table 1) supported the structure **3** and ruled out the structure **4** because from it such a downfield shift would not be expected [21]. The deshielding effect is due to the magnetic anisotropy of the C=O group and a minor contribution from the rest of the ring.

Whereas the comparison of the chemical shifts of H_A in the structures **3** and **5** (or **6**) is on a better footing as both structures **3** and **5** (or **6**) are tetracyclic compounds. The same conclusion can still be justifiably derived by comparing the chemical shifts of H_A of the thione **2** with that of cyclization product **3**. The H_A proton in thione **2** resonates at δ 5.44 whereas the downfield signal at δ 6.20 (1H, s, H_A) in the cyclised product supported the structure **3** in preference to structure **4**. Arylidene thiazolidinones (**9a-d**) were prepared by two routes. In the first approach, thiazolidinone **3** was condensed with aldehydes to give arylidene thiazolidinones (**9a-d**) while in the second approach compound **9a** was obtained directly by heating compound **2** with chloroacetic acid and benzaldehyde. The structure of **9a-d** was established by IR and ^{1}H NMR spectral data. The parent thiazolidinone **3** exhibited an absorption band at 1713 cm^{-1} (C=O), but the unsaturation at the 2-position being conjugated with the carbonyl group at the 3-position as in arylidene thiazolidinones (**9a-d**) produced a bathochromic shift [22] as expected, the carbonyl absorption band appeared at 1697 cm^{-1} in structure **9a**. The structure of arylidene derivatives **9** has been assigned on the basis of IR and ^{1}H NMR spectral data. ^{1}H NMR spectra of **9a-d** displayed benzylic proton at δ 7.70, 7.68, 7.65 and 7.73 respectively. The structure of compound **9d** was confirmed by X-ray crystallographic studies. X-ray structure of arylidene derivative **9d** also supported our claim for structure **3**.

The downfield shift in the position of H_A in ^{1}H NMR spectrum of the product obtained from reaction of **2** with ethyl bromo acetate may be due to the presence of imine group in structure **4**. If this is the case, then in arylidene derivatives **9a-d**, H_A proton would not be

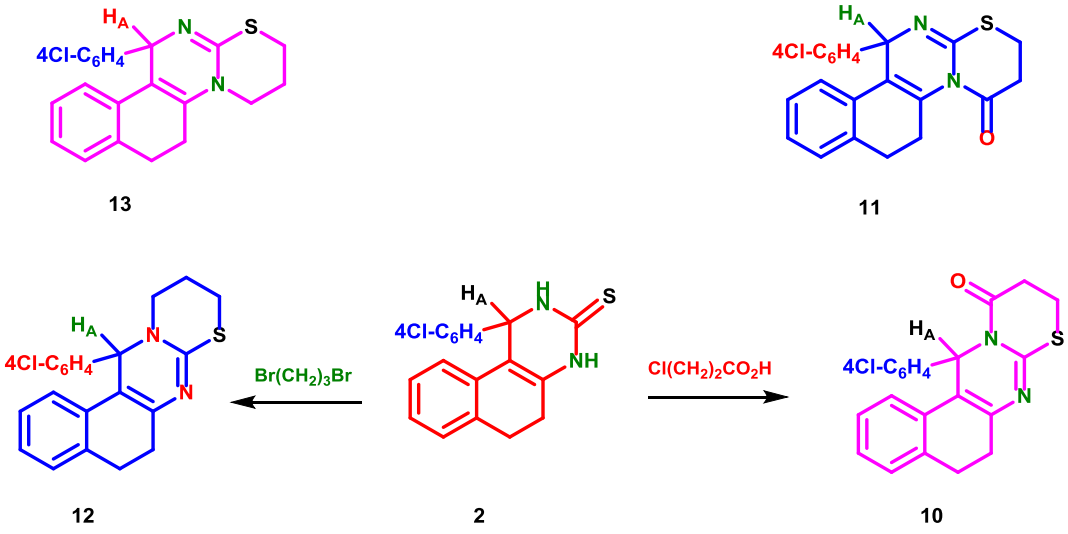
Table 1
Comparison of chemical shift (^{1}H NMR, 400 MHz, DMSO-d_6) of H_A proton in structures 2, 3 and 5.

Entry	Structure	Chemical shift (H_A)
2		δ= 5.44
3 or 4		δ= 6.20
5 or 6		δ= 6.13

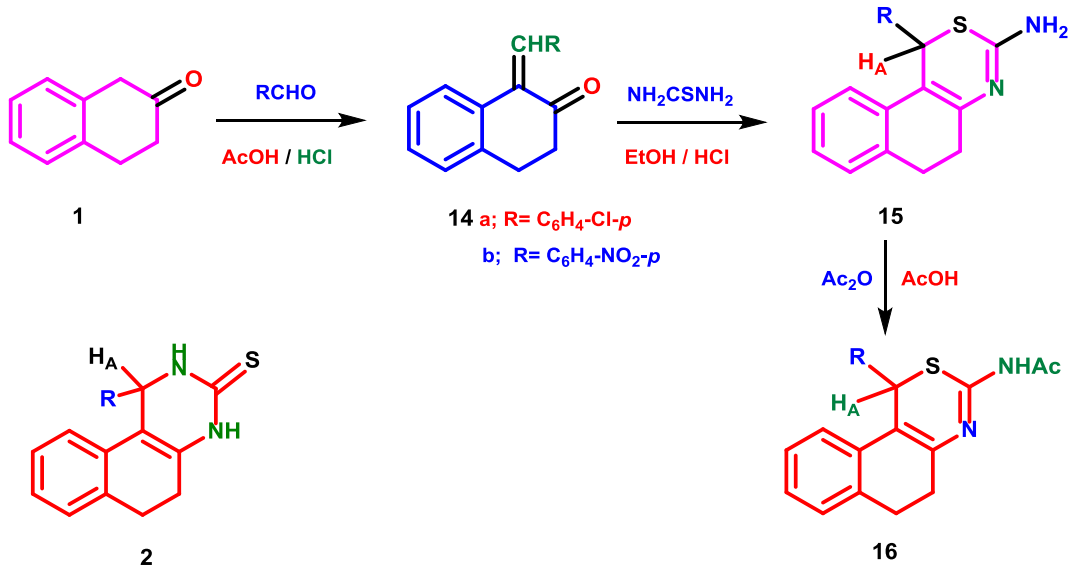
affected further because of the distant position of conjugated carbonyl group from H_A. In case of arylidene derivatives obtained from structure **3,** conjugated carbonyl system, will produce further downfield shift in position of H_A in **9a-d** i.e. δ 6.43, 6.36, 6.40 and δ 6.36. This downfield shift in the position of H_A in arylidene derivatives corroborated by structure **3** and discarded structure **4**. The structure **5** (not **6**) for the product, obtained from the reaction of compound **2** with 1, 2-dibromoethane, was assigned based upon the analogy with structure **3**.

Similarly, structure **7** was assigned to the TLC pure product obtained from the reaction of thione **2** and 2-bromopropionic acid. The analytical and spectral data (IR, NMR and Mass) supported structure **7** and ruled out isomeric structure **8**.

Thione **2**, on condensation with 3-chloropropionic acid in presence of anhydrous sodium acetate furnished a single product (TLC) **10** or **11** in 60% yield. IR spectrum of the product displayed carbonyl group at 1698 cm^{-1}. The mass spectrum of the product exhibited quasimolecular ion peak at *m*/*z* 381.2 (M+H$^+$, 100%) corroborated by structure **10** or **11**. IR and Mass data were of little help in deciding in favour of structure **10** and **11**. The condensation of thione **2** with 1,3-dibromopropane afforded a single product **12** or **13** (Scheme 2), which was purified by column chromatography and characterized by appearance of quasimolecular ion peak at *m*/*z* 367.1 (M+H$^+$, 100%). The comparison of chemical shifts of H_A proton in **10** or **11** and **12** or **13** indicates that H_A proton appeared downfield at δ 6.77 in (**10** or **11**) compared to at δ 6.03 in (**12** or **13**).



Scheme 2. Synthesis of thiazino-quinazoline derivatives.



Scheme 3. Reaction of 1-arylidene-2-tetralone with thiourea in ethanol and HCl.

This is attributed to the anisotropy effect of C=O group of thiazin-4-one ring and supported structure **10**. Finally, structure **10** was assigned to product obtained from the reaction of thione **2** with 3-chloropropionic acid. Based upon above analogy, structure **12** was assigned to the product obtained from reaction of thione **2** with 1,3-dibromopropane.

1-Arylidene-2-tetralone **14** were obtained from reaction of 2-tetralone **1** with aromatic aldehydes in presence of acetic acid at 0–5 °C. The characterization of **14** was done by spectral data. Compound **14**, on condensation with thiourea in ethanol and HCl furnished a product which was different from the thione **2**. This product was identified as **15** (Scheme 3) and its characterization was done by means of analytical and spectral data. IR spectrum of **15a** showed a peak due to C=N group at 1638 cm^{-1}. ^1H NMR spectrum of **15a** displayed a singlet of one proton at δ 5.97 due to H_A proton and two broad signals at δ 9.07 and δ 10.05 assigned to NH protons. Four multiplets of one proton each between δ 2.62–3.02 were assigned to tetrahydronaphthalene ring. The structure of compound **15b** was similarly assigned by spectral data. The structures of 15 were further supported by their acetylation with acetic anhydride to yield compound **16**. IR spectrum of **16a** displayed peaks at 1678 cm^{-1} and 1624 cm^{-1} due to C=O of amide group and C=N group respectively. ^1H NMR spectrum of **16a** showed a singlet of three protons at δ 2.02 due to acetyl group. The structure of **16b** was similarly established.

2.1. Crystallographic study and structural description of compound 9d

X-ray diffraction measurements were performed on X Calibur EOS OXFORD Diffractometer at 293 (2) K. The intensity data were collected using graphite monochromatic Mo-Kα radiation (λ = 0.71073 Å). The structure was solved by direct method using the SHELX-97 software package [23] and refined by full-matrix least-squares procedures on F^2. All non-hydrogen atoms were refined with anisotropic thermal parameters. The compound **9d** crystallizes in the monoclinic space group P21/n, with Z = 4 and cell parameters a = 9.3092(6) Å, b = 16.8078 (10) Å, c = 14.6707(9) Å,, β = 102.134(5). In the compound, C(9)-O and C(7)–C(8) bond distances of 1.208 (3) and 1.344 (4) Å, respectively, indicate the double bond character of these bonds. The bond angles C(8)-C(9)-O and C(7)-C(8)-C(9) are 126.9(3) and 120.2(3) respectively, which is consistent with the sp^2 hybrid character of C9 and C8 atoms. ORTEP diagram of **9d** obtained from X-ray structure is shown in (Fig. 1). The crystallographic data and refinement parameters of **9d** are reported in (Table 2). The selected bond parameters are listed in (Table 3). The crystal packing diagram of **9d** is shown in (Fig. 2) and hydrogen bonding geometry is reported in (Table 4).

Crystallographic data for the structure **9d** has been deposited with the Cambridge Crystallographic Data Centre and its CCDC Number is 1024077.

2.2. Computational studies of compound 3 and regioisomer 4

The molecular geometry optimization, ^1H and ^{13}C NMR spectra calculations were performed with the Gaussian 09 W software package [24] by using DFT methods with B3LYP (Becke three parameter Lee-Yang-Parr) exchange correlation functional, which combines the hybrid exchange functional of Becke [25], with the

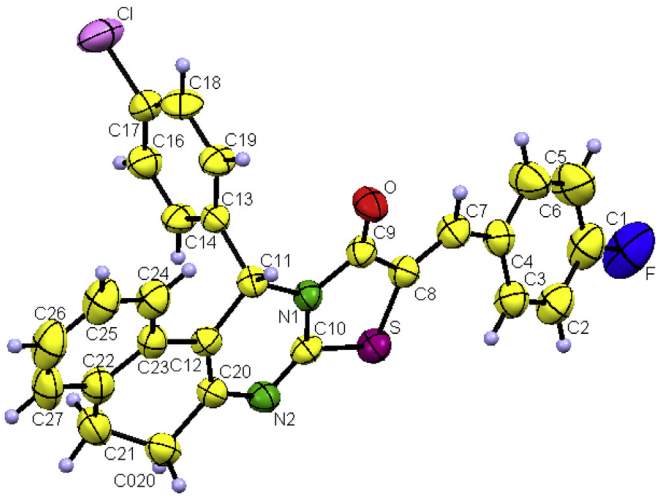


Fig. 1. ORTEP drawing indicating molecular structure and atomic labeling of the (*Z*)-12-(4-chlorophenyl)-9-(4-fluorobenzylidene)-9,12-dihydro-5*H*-benzo[*f*]thiazolo[2,3-*b*]quinazolin-10(6*H*)-one (**9d**).

Table 2
Crystal data and the structure refinement of (*Z*)-12-(4-chlorophenyl)-9-(4-fluorobenzylidene)-9,12-dihydro-5*H*-benzo[*f*]thiazolo[2,3-*b*]quinazolin-10(6*H*)-one (**9d**).

CCDC no.	1024077
Empirical formula	$C_{27}H_{18}ClFN_2OS$
Formula weight	472.94
Temperature (K)	293 (2)
Wavelength (Å)	0.71073 Å
Crystal system	Monoclinic
Space group	P21/n
Unit cell dimensions	
a (Å)	9.3092(6)
b (Å)	16.8078(10)
c (Å)	14.6707(9)
α (°)	90.00
β (°)	102.134(5)
γ (°)	90.00
Volume ($Å^3$)	2244.2(2)
Z	4
Density (calculated) (Mg/m^3)	1.400 Mg/m^3
Absorption coefficient (mm^{-1})	0.295 mm^{-1}
Crystal size	0.22 × 0.20 × 0.16 mm^3
Theta range for data collection	3.1294 to 29.1283
Reflections collected	1429
Independent reflections	2669
Data/restraints/parameters	5125/0/286
Goodness-of-fit on F^2	0.973
Final R indices [I > 2σ(I) = 2591 data]	$R_1 = 0.0629$, $wR_2 = 0.1369$
R indices (all data)	$R_1 = 0.1340$, $wR_2 = 0.1800$
Largest diff. Peak and hole ($eÅ^{-3}$)	−0.381, 0.383

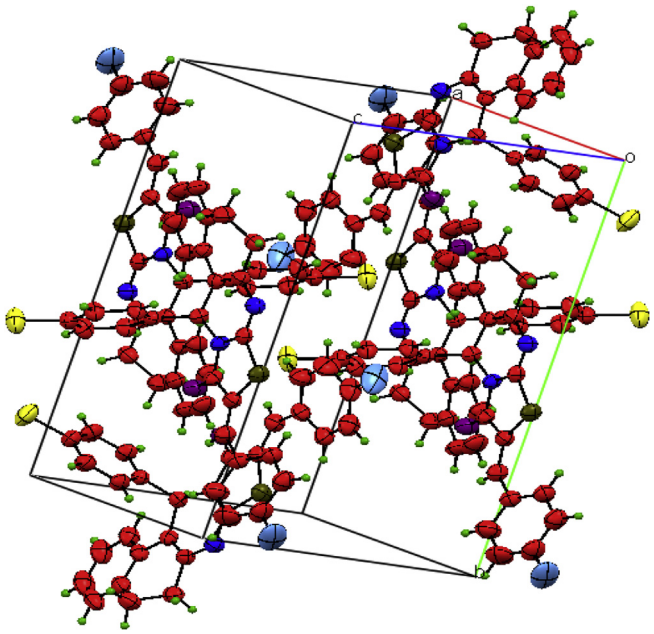


Fig. 2. Crystal packing diagram of 9d along c-axis.

gradient-correlation functional of Lee, Yang and Parr [26]. The 6-31G (d) basic set was used for DFT studies on isomeric pair **3**/**4.** The optimized configurations of compounds **3** and its isomer **4** with atom numbering schemes are shown in (Fig. 3). The optimized bond lengths and bond angles obtained by geometry optimization of structure **3** and **4** are reported in (Table 5). In case of structure **3**, the optimized bond lengths of C=O and C–S bonds in thiazolidinone ring are 1.242 Å and 1.833 Å, which are close to actual bond lengths. The optimized bond angles for O–C–N and S–C–N were observed at 124.15° and 123.77°. In case of structure **4**, the optimized bond lengths of C=O and S–C in thiazolidinone ring are 1.241 Å and 1.839 Å. The optimized bond angles for C–N–C and S–C–N were observed at 116.99° and 122.81°. It may be noted here that slight differences in bond parameters are attributed to the fact that theoretical calculations have been carried out for isolated molecules in gaseous phase.

Shielding tensors of structure **3** and **4** were computed within the GIAO approach [27–29] applying the same methods and basic set as used for geometry optimization. In order to express the chemical shifts in ppm, the geometry of tetramethylsilane (TMS) and chloroform molecules had been optimized and their ^1H and ^{13}C NMR spectra were calculated by the same method using same basis set as in case of the structure **3** and **4**. The calculated isotropic shielding constants σ_i were then transformed to chemical shifts relative to TMS by the equation, $\delta_i = \sigma_{TMS} - \sigma_i$. The experimental and calculated ^1H and ^{13}C NMR chemical shifts (ppm) of compounds **3** and its isomers **4** have been reported in (Table 6). The correlation values of proton chemical shifts are found to be 0.98318 for structure **3** and 0.97375 for its isomer **4** (Fig. 4). Similarly the correlation values of carbon chemical shifts of **3** and **4** are found to be 0.99433 and 0.98835 (Fig. 5). The theoretical and experimental ^1H and ^{13}C data shows good correlation for proposed structures **3**. The total energy obtained for optimized structures **3** and **4** are −1814.29 ha and −1814.28 ha respectively. This shows structure **3** is more stable than isomer **4**.

Table 3
Bond parameters of (*Z*)-12-(4-chlorophenyl)-9-(4-fluoro benzylidene)-9,12-dihydro-5*H*-benzo[*f*]thiazolo[2,3-*b*]quinazolin-10(6*H*)-one (**9d**).

Compound 9d			
Parameters	Experimental	Parameters	Experimental
Bond lengths (Å)		*Bond Angles* (°)	
S–C(8)	1.753(3)	C(8)-S-C(10)	91.59(15)
S–C(10)	1.759(3)	C(9)-N(1)-C(10)	116.9(2)
O–C(9)	1.208(3)	C(10)-N(1)-C(11)	122.0(2)
N(1)–C(10)	1.372(4)	C(9)-N(1)-C(11)	120.9(2)
N(1)–C(9)	1.390(4)	C(7)-C(8)-C(9)	120.2(3)
N(1)–C(11)	1.468(3)	O-C(9)-N(1)	123.3(3)
N(2)–C(10)	1.278(4)	O-C(9)-C(8)	126.9(3)
C(8)–C(9)	1.479(4)	N(1)-C(9)-C(8)	109.7(3)
C(7)–C(8)	1.344(4)	N(1)-C(11)-C(12)	109.2(2)
C(4)–C(7)	1.459(3)	N(2)-C(10)-N(1)	126.7(3)
C(1)–C(6)	1.3900	N(2)-C(10)-S	122.3(2)
C(5)–C(6)	1.3900	N(1)-C(10)-S	111.0(2)

2.3. Antimicrobial activity of compounds *3*, *5*, *7* and *9*

Compounds **3, 5, 7** and **9** were assayed for their *in vitro* antimicrobial activities against *E. coli, Bacillus, Staphylococcus* and *Pseudomonas* by disc diffusion method [30]. Tetracycline was used as the reference standard in each plate. It was observed that among all the tested compounds, compound **5** showed remarkable activity against *E. coli* and *Bacillus.* Compound **7** showed maximum activity against bacteria *Staphylococcus* and *Pseudomonas.* Compound **3** showed moderate activity against all the tested bacteria. Compound **9a** did not show any activity against *E. coli* and *Bacillus.* Compound **9c** was found to be inactive against *Staphylococcus* and *Pseudomonas* (Table 7).

3. Experimental

3.1. Instrumentations

Melting points were determined in sulphuric acid bath and are reported uncorrected. TLC was performed on silica gel G plates

Table 4
Hydrogen bonding geometry of compound **9d**.

D-H··· Å	D-H(Å)	H ··· A(Å)	D ···· A(Å)	D-H ··· A(°)	Symmetry codes
C11-H11-O	0.980	2.705	2.825	86.82	x, y, z
C2-H2-O	0.930	2.812	3.723	166.48	x+1, +y, +z
C3-H3-S	0.930	2.587	3.230	126.66	x, y, z
C21-H21A-O	0.970	2.882	3.547	126.61	-x+1/2, +y-1/2, -z+1/2

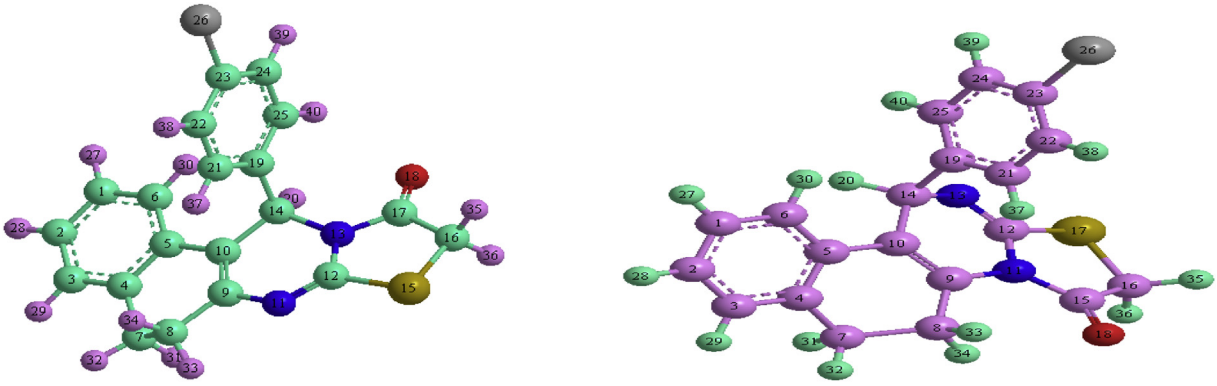


Fig. 3. Optimized structures of compound 3 and its isomer 4.

Table 5
Selected calculated bond parameters of compound **3** and isomer 4.

Compound 3		Isomer 4	
Parameters	Calculated	Parameters	Calculated
Bond lengths (Å)			
S(15)–C(12)	1.833	S(17)-C(12)	1.839
S(15)–C(16)	1.897	C(16)-S(17)	1.889
C(17)–N(13)	1.385	N(11)-C(15)	1.394
C(17)–O(18)	1.242	C(15)-O(18)	1.241
C(12)–N(11)	1.283	N(11)-C(12)	1.423
C(12)–N(13)	1.398	C(12)-N(13)	1.267
C(9)–N(11)	1.417	N(13)-C(14)	1.495
C(14)–H(20)	1.095	C(14)-H(20)	1.096
N(13)–C(14)	1.499	N(13)-C(14)	1.495
C(14)–C(19)	1.536	C(14)-C(19)	1.535
C(9)–C(10)	1.363	C(9)-C(10)	1.359
Bond Angles (°)			
C(16)-S(15)-C(12)	89.80	C(12)-S(17)-C(16)	89.928
C(17)-C(16)-S(15)	107.827	S(17)-C(16)-C(15)	108.418
C(17)-N(13)-C(12)	118.395	C(15)-N(11)-C(12)	116.996
C(17)-N(13)-C(14)	121.472	C(15)-N(11)-C(9))	126.067
C(14)-N(13)-C(12)	119.871	C(14)-N(13)-C(12)	118.895
S(15)-C(12)-N(13)	111.314	S(17)-C(12)-N(11)	111.124
S(15)-C(12)-N(11)	123.770	S(17)-C(12)-N(13)	122.815
N(13)-C(12)-N(11)	124.837	N(13)-C(12)-N(11)	126.060
C(12)-N(11)-C(9)	117.597	C(12)-N(11)-C(9)	116.899
N(11)-C(9)-C(10)	123.089	N(11)-C(9)-C(10)	118.901
N(11)-C(9)-C(8)	115.437	N(11)-C(9)-C(8)	119.153
O(18)-C(17)-N(13)	124.159	O(18)-C(15)-N(11)	125.330

using pet ether-ethyl acetate (4:1) as eluent and iodine vapours as visualizing agent. IR spectra were recorded on ABB FTIR spectrometer and the results are reported in cm^{-1}. ^1H NMR and ^{13}C NMR were recorded in DMSO-d_6 on a BRUKER AVANCE II 400 NMR spectrometer using tetramethylsilane (TMS) as an internal standard (chemical shift in δ, ppm). Mass spectra were recorded on a WATERS, Q- TOF MICROMASS (LC-MS) instrument. The elemental analyses of the compounds were performed on Euro EA 3000 Elemental Analyzer. X-ray diffraction was performed on X Calibur EOS OXFORD Diffractometer.

3.2. General procedure for synthesis of thione **2**

A mixture of 2-tetralone (0.21 g, 0.0016 mol), p-chlorobenzaldehyde (0.22 g, 0.0016 mol) and thiourea (0.12 g, 0.0016 mol) in gl. acetic acid (10 mL) was heated at 110 °C for 4 h. The reaction mixture was then cooled to room temperature. The white solid obtained was filtered, dried and recrystallized from ethanol-DMF (3:1) mixture.

3.2.1. 1-(4-Chlorophenyl)-1,4,5,6-tetrahydrobenzo[f]quinazoline-3(2H)-thione (**2**)

Yellow crystalline solid; yield 78%; mp 190-92 °C. IR (cm^{-1}): 3208 (NH), 1548 (C=C), 1246 (C=S). ^1H NMR (400 MHz, DMSO-d_6): δ 2.44–2.52 (m, 1H, CH_2), 2.58–2.64 (m, 1H, CH_2), 2.84 (t, 2H, CH_2, $J = 7.3$ Hz), 5.44 (d, 1H, H_A, $J = 2.4$ Hz), 6.83 (d, 1H, C_6H_5, $J = 7.0$ Hz), 6.94–7.01 (m, 2H, C_6H_5), 7.06 (d, 1H, C_6H_5, $J = 6.5$ Hz), 7.31 (d, 2H, C_6H_5, $J = 6.7$ Hz), 7.38 (d, 2H, C_6H_5, $J = 6.6$ Hz), 9.19 (br, 1H, NH), 10.06 (br, 1H, NH). Anal. Calcd. (%) for $C_{18}H_{15}ClN_2S$: C, 66.15; H, 4.63; N, 8.57; S, 9.81. Found (%): C, 66.31; H, 4.76; N, 8.69; S, 9.96.

3.3. General procedure for synthesis of thiazolidin-4-ones **3** and **7**

A mixture of thione **2** (0.16 g, 0.5 mmol), ethyl bromo acetate or 2-bromopropionic acid (0.5 mmol), anhydrous sodium acetate (0.082 g, 1.0 mmol) in ethanol (10 mL) was heated under reflux for 5–6 h. The progress of reaction was monitored by TLC. After completion, the volume of the reaction mixture was reduced to half. The cooled reaction mixture was then poured in to ice cold water and filtered the solid obtained. Recrystallization from ethanol–DMF (3:1) mixture furnished pure compounds.

3.3.1. 12-(4-Chlorophenyl)-6,12-dihydro-5H-benzo[f]thiazolo[2,3-b]quinazolin-10(9H)-one (**3**)

Yellow solid; yield 62%; mp 102-04 °C. IR (cm^{-1}): 1713 (C=O), 1612 (C=N). ^1H NMR (400 MHz, DMSO-d_6): δ 2.56–2.67 (m, 2H, CH_2), 2.83–2.87 (m, 2H, CH_2), 3.96 (dd, 1H, SCH_2, $J = 17.4$ Hz, 1.7 Hz), 6.20 (s, 1H, H_A), 6.99–7.05 (m, 2H, C_6H_5), 7.06–7.12 (m, 2H, C_6H_5), 7.32 (d, 2H, C_6H_5, $J = 8.4$ Hz), 7.47 (d, 2H, C_6H_5, $J = 8.4$). ^{13}C NMR

Table 6
Experimental and calculated ^{1}H NMR and ^{13}C NMR chemical shifts of compound 3 and isomer 4.

Compound 3					Isomer 4			
Entry	Expt. chemical shift (ppm)	Calc. shield	Calc. chemical shift (ppm)	Average chemical shift (ppm)	Entry	Calc. shield	Calc. chemical shift (ppm)	Average chemical shift (ppm)
C7	31.9	158.9458	45.89		C7	159.2644	45.56	
C8	28.4	158.8983	45.94		C8	166.1917	38.32	
C12	155.3	38.7043	171.57		C12	43.6228	166.43	
C14	53.9	131.8917	74.17		C14	125.7071	80.63	
C16	36.2	154.4897	50.55		C16	155.3210	49.68	
C17	170.7	28.5259	182.20		C15	31.0622	179.55	
C19	139.9	58.7352	150.63		C19	55.7964	153.70	
C22	138.1	66.6644	142.34		C22	66.9483	142.05	
H31	2.58	29.1584	3.05	2.79	H31	29.2523	2.96	2.98
H32		29.6929	2.54		H32	29.6501	2.58	
H33	2.84	29.8628	2.38	2.64	H33	29.2555	2.96	2.77
H34		29.3113	2.91		H34	29.2060	3.01	
H35	3.95	29.0091	3.20	3.28	H35	28.8620	3.34	3.36
H36		28.8432	3.36		H36	28.8107	3.39	
H20	6.20	26.4525	5.66		H20	26.6735	5.45	
H29	7.01	25.3033	6.76	6.56	H29	25.2637	6.80	6.58
H30		25.7416	6.37		H30	25.7261	6.36	
H27	7.07	25.3818	6.69	6.73	H27	25.3587	6.71	6.77
H28		25.3012	6.77		H28	25.2205	6.84	
H37	7.32	25.0346	7.02	6.95	H37	25.1952	6.87	6.86
H38		25.1884	6.88		H38	25.2195	6.85	
H39	7.46	25.1282	6.93	7.20	H39	25.0509	7.01	7.14
H40		24.5551	7.48		H40	24.7650	7.28	

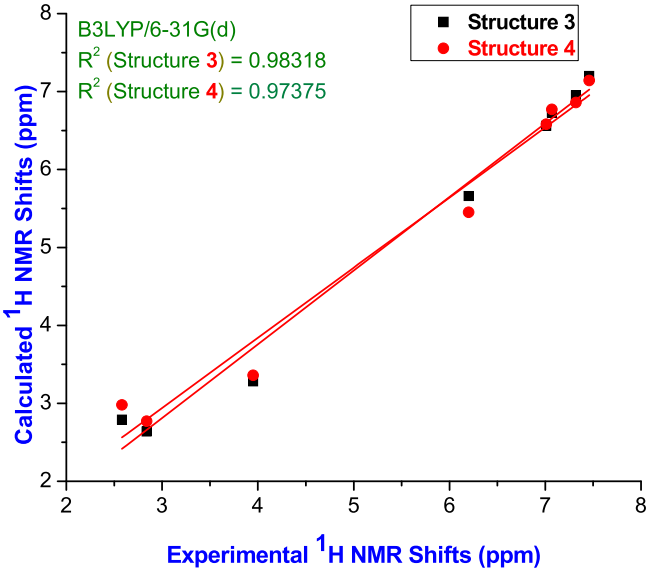


Fig. 4. Plot of the calculated vs. experimental ^{1}H NMR chemical shifts (ppm) of 3 and 4.

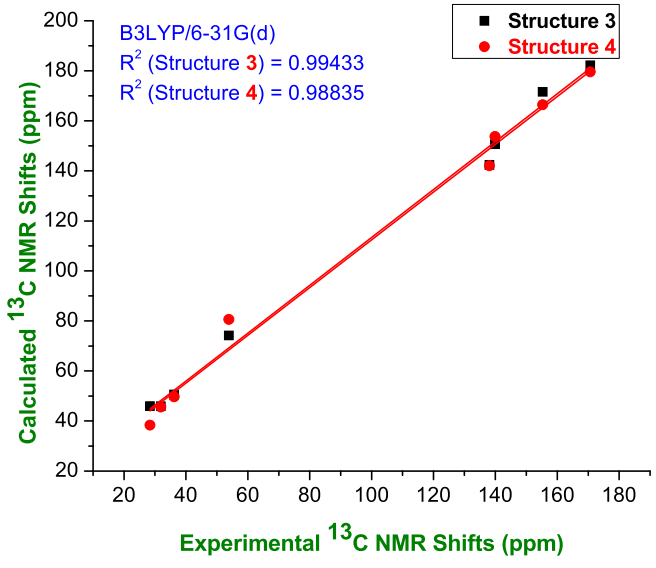
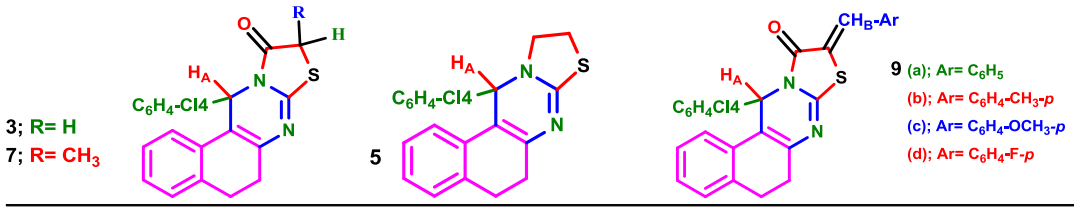


Fig. 5. Plot of the calculated vs. experimental ^{13}C NMR chemical shifts (ppm) of 3 and 4.

Table 7
Antimicrobial activities by disc diffusion method of compounds **3**, **5**, **7** and **9**.



Entry	Compound	Zone of inhibition (mm)			
		Antibacterial Activity			
		Bacillus	*E. coli*	*Staphylococcus*	*Pseudomonas*
1	**3**	7	8	10	7
2	**5**	14	13	12	8
3	**7**	10	10	14	13
4	**9a**	–	–	10	12
5	**9b**	10	8	10	11
6	**9c**	8	7	–	–
7	**9d**	11	11	9	12
	Tetracycline	15	14	24	18
	DMSO	00	00	00	00

(100 MHz, DMSO-d_6) δ: 170.7, 155.3, 139.9, 138.1, 134.7, 133.3, 131.3, 129.7, 128.5, 127.3, 126.1, 121.5, 111.0, 53.9, 36.2, 31.9, 28.4, 27.8, 24.2. MS, *m/z* 367.2 ($M+H^+$, 100%). Anal. Calcd. (%) for $C_{20}H_{15}ClN_2OS$: C, 65.48; H, 4.12; N, 7.64; S, 8.74. found (%): C, 65.62; H, 4.31; N, 7.81; S, 8.92.

*3.3.2. 12-(4-Chlorophenyl)-9-methyl-6,12-dihydro-5H-benzo[f] thiazolo[2,3-b]quinazolin-10(9H)-one (**7**)*

Yellow crystalline solid; yield 68%; mp 182-84 °C. IR (cm^{-1}): 1715 (C=O), 1620 (C=N). ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.34 (d, 3H, CH_3, J = 7.2 Hz), 2.57–2.68 (m, 2H, CH_2), 2.80–2.82 (m, 2H, CH_2), 4.28–4.30 (q, 1H, $SCHCH_3$, J = 7.2 Hz), 6.15 (s, 1H, H_A), 6.99–7.07 (m, 4H, C_6H_5) 7.27 (d, 2H, C_6H_5, J = 8.4 Hz), 7.42 (d, 2H, C_6H_5, J = 8.6 Hz). ^{13}C NMR (100 MHz, DMSO-d_6) δ: 174.1, 154, 139.9, 138.6, 134.7, 133.1, 131.4, 129.8, 128.6, 128.5, 127.3, 126.2, 121.7, 111.6, 54, 53.8, 28.4, 27.7, 18.7. MS, *m/z* 381.2 ($M+H^+$, 100%). Anal. Calcd. (%) for: $C_{21}H_{17}ClN_2OS$: C, 66.22; H, 4.50; N, 7.35; S, 8.42. Found (%): C, 66.39; H, 4.61; N, 7.48; S, 8.53.

*3.4. General procedure for synthesis of thiazinan-4-one **10***

A mixture of thione **2** (0.32 g, 0.001 mol), chloropropionic acid (0.108 g, 0.001 mol), anhydrous sodium acetate (0.16 g, 0.002 mol), gl. acetic acid (10 ml) and acetic anhydride (0.5 ml) was heated under reflux for 10–12 h. The progress of reaction was monitored by TLC. After completion of the reaction, the reaction mixture was kept overnight and then poured in to ice cold water. The solid separated was filtered, dried and recrystallized from ethanol.

*3.4.1. 13-(4-Chlorophenyl)-6,9,10,13-tetrahydro-5H,11H-benzo[f] [1,3]thiazino[2,3-b] quinazolin-11-one (**10**)*

Yellow solid; yield 60%; mp 108-10 °C. IR (cm^{-1}): 1698 (C=O), 1648 (C=N). ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.45–2.51 (m, 1H, CH_2), 2.65–2.73 (m, 1H, CH_2), 2.89–2.98 (m, 2H, CH_2), 3.0–3.1 (m, 4H, SCH_2CH_2), 6.77 (s, 1H, H_A), 6.93–6.96 (m, 1H, C_6H_5), 7.03–7.08 (m, 2H, C_6H_5), 7.11–7.13 (m, 1H, C_6H_5), 7.30–7.36 (q, 4H, C_6H_5, J = 8.6, 7.4 Hz). ^{13}C NMR (100 MHz, DMSO-d_6) δ: 168.8, 151.1, 139.7, 138.0, 134.3, 133.0, 131.8, 129.2, 128.8, 127.5, 126.5, 121.4, 113.0, 61.2, 48.8, 35.4, 27.7, 21.0, 15.0. MS, *m/z* 381.2 ($M+H^+$, 100%). Anal. Calcd. (%) for $C_{21}H_{17}ClN_2OS$: C, 66.22; H, 4.50; N, 7.35; S, 8.42. Found (%): C, 66.36; H, 4.63; N, 7.51; S, 8.68.

*3.5. General procedure for synthesis of arylidene derivatives **9***

Arylidene derivatives **9** were prepared from two routes:

a) A mixture of thione **2** (0.13 g, 0.0004 mol), chloroacetic acid (0.0378 g, 0.0004 mol), aromatic aldehyde (0.0004 mol), anhydrous sodium acetate (0.032 g, 0.0004 mol) in gl. acetic acid (10 ml) and acetic anhydride (0.5 ml) was heated under reflux for 6 h. Reaction mixture was kept overnight and then poured in to ice cold water. The solid obtained was filtered, dried and recrystallized from ethanol.
b) A mixture of thiazolidin-4-one **3** (0.0004 mol), aromatic aldehyde (0.0004 mol) and anhydrous sodium acetate (0.032 g, 0.0004 mol) in gl. acetic acid (10 ml) and acetic anhydride (0.5 ml) was heated under reflux for 3 h. The reaction mixture was then poured in to ice cold water. Filtered the solid obtained, dried and recrystallized from ethanol.

*3.5.1. (Z)-9-Benzylidene-12-(4-chlorophenyl)-6,12-dihydro-5H-benzo[f]thiazolo[2,3-b]quinazolin-10(9H)-one (**9a**)*

Yellow solid; yield 60%; mp 98–100 °C. IR (cm^{-1}): 1694 (C=O), 1624 (C=N). ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.67–2.69 (m, 2H, CH_2), 2.86–2.89 (m, 2H, CH_2), 6.43 (s, 1H, H_A), 7.05–7.08 (m, 2H, C_6H_5), 7.11–7.12 (m, 1H, C_6H_5), 7.23–7.25 (m, 1H, C_6H_5), 7.34–7.37 (m, 2H, C_6H_5), 7.45–7.51 (m, 1H, C_6H_5), 7.53–7.57 (m, 6H, C_6H_5), 7.73 (s, 1H, =CH). Anal. Calcd. (%) for $C_{27}H_{19}ClN_2OS$: C, 71.28; H, 4.21; N, 6.16; S, 7.05. Found (%): C, 71.42; H, 4.38; N, 7.02; S, 7.28.

3.5.2. (Z)-12-(4-Chlorophenyl)-9-(4-methylbenzylidene)-6,12-dihydro-5H-benzo[f] thiazolo[2,3-b]quinazolin-10(9H)-one (9b)

Orange solid; yield 78%; mp 156-58 °C. IR (cm^{-1}): 1698 (C=O), 1612 (C=N). ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.34 (s, 3H, CH_3), 2.55–2.71 (m, 2H, CH_2), 2.80–2.93 (m, 2H, CH_2), 6.36 (s, 1H, H_A), 7.02–7.06 (m, 2H, C_6H_5) 7.08–7.10 (m, 1H, C_6H_5), 7.15–7.17 (m, 1H, C_6H_5), 7.29 (t, 4H, C_6H_5, J = 8.6 Hz), 7.4 (d, 2H, C_6H_5, J = 8.2 Hz), 7.51 (d, 2H, C_6H_5, J = 6.8 Hz), 7.65 (s, 1H, =CH). Anal. Calcd. (%) for $C_{28}H_{21}ClN_2OS$: C, 71.71; H, 4.51; N, 5.97; S, 6.84. Found (%): C, 71.89;

H, 4.68; N, 6.09; S, 7.01.

*3.5.3. (Z)-12-(4-Chlorophenyl)-9-(4-methoxybenzylidene)-6,12-dihydro-5H-benzo[f]thiazolo [2,3-b]quinazolin-10(9H)-one (**9c**)*

Orange solid; yield 79%; mp 138-40 °C. IR (cm^{-1}): 1701 (C=O), 1628 (C=N). ^1H NMR (400 MHz, DMSO-d_6): δ 2.58–2.72 (m, 2H, CH_2), 2.82–2.94 (m, 2H, CH_2), 3.83 (s, 3H, OCH_3), 6.4 (s, 1H, H_A), 7.04–7.07 (m, 4H, C_6H_5), 7.11 (m, 1H, C_6H_5), 7.20–7.22 (m, 1H, C_6H_5), 7.34 (d, 2H, C_6H_5, J = 6.7 Hz), 7.50–7.55 (m, 4H, C_6H_5), 7.68 (s, 1H, =CH). Anal. Calcd. (%) for $C_{28}H_{21}ClN_2O_2S$: C, 69.34; H, 4.36; N, 5.78; S, 6.61. Found (%): C, 69.53; H, 4.51; N, 5.91; S, 6.78.

*3.5.4. (Z)-12-(4-Chlorophenyl)-9-(4-fluorobenzylidene)-6,12-dihydro-5H-benzo[f]thiazolo[2,3-b]quinazolin-10(9H)-one (**9d**)*

Orange solid; yield 73%; mp 194-96 °C. IR (cm^{-1}): 1697 (C=O), 1632 (C=N). ^1H NMR (400 MHz, DMSO-d_6): δ 2.64–2.76 (m, 2H, CH_2), 2.90–2.95 (m, 2H, CH_2), 6.36 (s, 1H, H_A), 7.07–7.10 (m, 4H, C_6H_5), 7.20–7.31 (m, 4H, C_6H_5), 7.48–7.56 (m, 4H, C_6H_5), 7.70 (s, 1H, =CH). MS, m/z 473.0 ($M+H^+$, 100%). Anal. Calcd. (%) for $C_{27}H_{18}ClFN_2OS$: C, 68.57; H, 3.84; N, 5.92; S, 6.78. Found (%): C, 68.72; H, 4.01; N, 6.01; S, 7.98.

*3.6. General procedure for synthesis of **5** and **12***

A mixture of thione **2** (0.26 g, 0.0008 mol), 1,2-dibromo ethane/1,3-dibromo propane (0.0008 mol) in ethanol (5.0 ml) was heated under reflux for 5 h. The volume of the reaction mixture was reduced to half and cooled to room temperature. The reaction mixture was poured in to ice cold water and extracted with ethyl acetate (2 × 25 ml). Gummy solid obtained was purified with column hexane-ethyl acetate (8:2).

*3.6.1. 12-(4-Chlorophenyl)-6,9,10,12-tetrahydro-5H-benzo[f] thiazolo[2,3-b] quinazoline (**5**)*

Yellow solid; yield 52%; mp 178-80 °C. IR (cm^{-1}): 1645 (C=N). ^1H NMR (400 MHz, DMSO-d_6): δ 2.61–2.66 (m, 1H, CH_2), 2.86–3.01 (m, 2H, CH_2), 3.50–3.59 (m, 1H, CH_2), 3.63–3.73 (m, 2H, NCH_2), 4.25–4.31 (m, 1H, SCH_2), 4.46–4.52 (m, 1H, SCH_2), 6.13 (s, 1H, H_A), 7.0–7.16 (m, 4H, C_6H_5), 7.35–7.43 (m, 3H, C_6H_5), 7.58 (d, 1H, C_6H_5, J = 7.9 Hz). MS, m/z 353.2 ($M+H^+$, 100%). Anal. Calcd. (%) for $C_{20}H_{17}ClN_2S$: C, 68.07; H, 4.86; N, 7.94; S, 9.09. Found (%): C, 68.22; H, 5.01; N, 8.01; S, 9.28.

*3.6.2. 13-(4-Chlorophenyl)-6,10,11,13-tetrahydro-5H,9H-benzo[f] [1,3]thiazino[2,3-b] quinazoline (**12**)*

Yellow solid; yield 52%; mp 184-86 °C. IR (cm^{-1}): 1645 (C=N). ^1H NMR (400 MHz, DMSO-d_6): δ 2.55–2.65 (m, 2H, CH_2), 2.87–2.97 (m, 5H, CH_2), 3.18–3.25 (m, 2H, CH_2), 3.81–3.84 (m, 1H, CH_2), 6.03 (s, 1H, H_A), 7.08–7.11 (m, 2H, C_6H_5), 7.13–7.17 (m, 2H, C_6H_5), 7.38–7.54 (m, 2H, C_6H_5), 7.62 (d, 2H, C_6H_5, J = 8.5 Hz). MS, m/z 367.1 ($M+H^+$, 100%). Anal. Calcd. for: $C_{21}H_{19}ClN_2S$: C, 68.75; H, 5.22; N, 7.64; S, 8.74. Found (%): C, 68.92; H, 5.41; N, 7.81; S, 8.98.

*3.7. General procedure for synthesis of 1-arylidene-2-tetralone **14***

A mixture of 2-tetralone (0.05 mol) and aromatic aldehyde (0.05 mol), glacial acetic acid (25 mL) and conc. HCl (15 mL) was kept at 0 °C for 24 h. Filtered the yellow solid obtained, washed with petroleum ether (60–80 °C) and recrystallized from ethanol.

*3.7.1. (E)-1-(4-Chlorobenzylidene)-3,4-dihydronaphthalen-2(1H)-one (**14a**)*

Yellow solid; yield 78%; mp 90–92 °C. IR (cm^{-1}): 1696 (C=O). ^1H NMR (400 MHz, DMSO-d_6): δ 2.56 (t, 2H, CH_2, J = 3.5 Hz), 3.03 (t, 2H, CH_2, J = 6.5 Hz), 7.02–7.06 (m, 1H, C_6H_5), 7.19–7.25 (m, 2H, C_6H_5), 7.31–7.35 (m, 3H, C_6H_5), 7.4 (d, 2H, C_6H_5, J = 8.4 Hz), 7.49 (s, 1H, =CH). Anal. Calcd. (%) for $C_{17}H_{13}ClO$: C, 75.98; H, 4.88. Found (%): C, 76.14; H, 5.08.

3.7.2. (E)-1-(4-Nitrobenzylidene)-3,4-dihydronaphthalen-2(1H)-one (14b)

Yellow solid; yield 85%; mp 120–122 °C. IR (cm^{-1}): 1701 (C=O). ^1H NMR (400 MHz, DMSO-d_6): δ 2.61 (t, 2H, CH_2, J = 6.6 Hz), 3.08 (t, 2H, CH_2, J = 6.5 Hz), 7.02 (t, 1H, C_6H_5, J = 7.3 Hz), 7.13 (d, 1H, C_6H_5, J = 7.5 Hz), 7.26 (t, 1H, C_6H_5, J = 7.4 Hz), 7.34 (d, 1H, C_6H_5, J = 7.4 Hz), 7.58–7.60 (m, 3H, C_6H_5 & = CH), 8.11 (d, 2H, C_6H_5, J = 8.9 Hz). Anal. Calcd. (%) for $C_{17}H_{13}NO_3$: C, 73.11; H, 4.69. Found (%): C, 73.24; H, 4.88.

*3.8. General procedure for synthesis of thiazin-3-amines **15***

To a mixture of arylidene derivative **14** (0.0005 mol), and thiourea (0.038 g, 0.0005 mol) in ethanol (5.0 ml) catalytic amount of conc. HCl (0.5 ml) was added and the mixture was refluxed for 5 h. The solid separated on cooling was filtered, dried and recrystallized from ethanol-DMF (3:1) mixture.

*3.8.1. 1-(4-Chlorophenyl)-5,6-dihydro-1H-naphtho[2,1-d][1,3] thiazin-3-amine (**15a**)*

Light yellow solid; yield 78%; mp 206-08 °C. IR (cm^{-1}): 3214, 3126 (NH), 1645 (C=N). ^1H NMR (400 MHz, DMSO-d_6): δ 2.60–2.66 (m, 1H, CH_2), 2.82–2.88 (m, 1H, CH_2), 2.96–3.0 (m, 2H, CH_2), 5.97 (s, 1H, H_A), 7.07–7.14 (m, 3H, C_6H_5) 7.19–7.21 (m, 1H, C_6H_5), 7.37–7.42 (m, 4H, C_6H_5), 9.07 (br, 1H, NH), 10.05 (br, 1H, NH). Anal. Calcd. (%) for $C_{18}H_{15}ClN_2S$: C, 66.15; H, 4.63; N, 8.57; S, 9.81. Found (%): C, 66.31; H, 4.78; N, 8.71; S, 10.05.

*3.8.2. 1-(4-Nitrophenyl)-5,6-dihydro-1H-naphtho[2,1-d][1,3] thiazin-3-amine (**15b**)*

Green crystalline solid; yield 74%; mp 186-88 °C. IR (cm^{-1}): 3208, 3115 (NH), 1646 (C=N). ^1H NMR (400 MHz, DMSO-d_6): δ 2.62–2.68 (m, 1H, CH_2), 2.83–2.91 (m, 1H, CH_2), 2.98–3.02 (m, 2H, CH_2), 6.15 (s, 1H, H_A), 7.06–7.08 (m, 1H, C_6H_5) 7.11–7.16 (m, 2H, C_6H_5), 7.20–7.23 (m, 1H, C_6H_5), 7.68 (d, 2H, C_6H_5, J = 7.1 Hz), 8.21 (d, 2H, C_6H_5, J = 6.9 Hz), 9.15 (br, 1H, NH), 10.16 (br, 1H, NH). MS, m/z 338.1 ($M+H^+$, 100%). Anal. Calcd. (%) for $C_{18}H_{15}N_3O_2S$: C, 64.08; H, 4.48; N, 12.45; S, 9.50. Found (%): C, 64.21; H, 4.61; N, 12.68; S, 9.71.

*3.9. General procedure for synthesis of thiazin-acetamides **16***

A mixture of thiazin-3-amine derivative **15** (0.0004 mol), anhydrous sodium acetate (0.0008 mol), acetic anhydride (0.5 ml) in acetic acid (5.0 ml) was heated under reflux for 5 h. The reaction mixture cooled to room temperature and poured in to ice cold water. The solid obtained was filtered and recrystallized from dichloro methane-hexane (3:1) mixture.

*3.9.1. N-(1-(4-Chlorophenyl)-5,6-dihydro-1H-naphtho[2,1-d][1,3] thiazin-3-yl)acetamide (**16a**)*

Yellow crystalline solid; yield 58%; mp 178-80 °C. IR (cm^{-1}): 1662 (C=O), 1636 (C=N). ^1H NMR (400 MHz, DMSO-d_6): δ 1.98 (s, 3H, CH_3), 2.56–2.58 (m, 1H, CH_2), 2.82–2.92 (m, 3H, CH_2), 5.24 (s, 1H, H_A), 6.90–6.92 (m, 1H, C_6H_5) 6.98–7.02 (m, 2H, C_6H_5), 7.18–7.22 (m, 1H, C_6H_5), 7.4 (d, 2H, C_6H_5, J = 8.7 Hz), 8.0 (d, 2H, C_6H_5, J = 8.7 Hz), 10.4 (br, 1H, NH). Anal. Calcd. for $C_{20}H_{17}ClN_2OS$: C, 65.12; H, 4.65; N, 7.59; S, 8.69. Found (%): C, 65.24; H, 4.79; N, 7.71; S, 8.81.

*3.9.2. N-(1-(4-Nitrophenyl)-5,6-dihydro-1H-naphtho[2,1-d][1,3] thiazin-3-yl) acetamide (**16b**)*

Orange crystalline solid; yield 60%; mp 154-56 °C. IR (cm^{-1}):

1666 (C=O), 1638 (C=N). ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.0 (s, 3H, CH_3), 2.53–2.56 (m, 1H, CH_2), 2.84–2.98 (m, 3H, CH_2), 5.27 (s, 1H, H_A), 6.92–6.94 (m, 1H, C_6H_5) 7.02–7.07 (m, 2H, C_6H_5), 7.14–7.16 (m, 1H, C_6H_5), 7.46 (d, 2H, C_6H_5, $J = 8.7$ Hz), 8.12 (d, 2H, C_6H_5, $J = 8.7$ Hz), 11.06 (br, 1H, NH). Anal. Calcd. for $C_{20}H_{17}N_3O_3S$: C, 63.31; H, 4.52; N, 11.07; S, 8.45. Found (%): C, 63.54; H, 4.78; N, 11.21; S, 8.61.

Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.molstruc.2017.05.109.

References

[1] (a) B. Maggio, G. Daidone, D. Raffa, S. Plescia, L. Mantione, V.M.C. Cutuli, N.G. Mangano, A. Caruso, Eur. J. Med. Chem. 36 (2001) 737;
(b) G. Grover, S.G. Kini, Eur. J. Med. Chem. 41 (2006) 256.
[2] V. Polshettiwar, R.S. Varma, Curr. Opin. Drug Discov. Dev. 10 (2007) 723.
[3] L.F. Kuyper, D.P. Baccanari, M.L. Jones, R.N. Hunter, R.L. Tansik, S.S. Joyner, C. Boytos, S.K. Rudolph, V. Knick, H.R. Wilson, J.M. Caddell, H.S. Friedman, J.C.W. Comley, J.N. Stables, J. Med. Chem. 39 (1996) 892.
[4] P. Verhaeghe, N. Azas, M. Gasquet, S. Hutter, C. Ducros, M. Laget, S. Rault, P. Rathelot, P. Vanelle, Bioorg. Med. Chem. Lett. 18 (2008) 396.
[5] (a) V. Alagarsamy, V.R. Solomon, R.V. Sheorey, R. Jayakumar, Chem. Biol. Drug Des. 73 (2009) 471;
(b) V. Alagarsamy, R. Solomon, M. Murugan, K. Dhanabal, P. Parthiban, G.V.J. Anjana, J. Enzyme Inhib. Med. Chem. 23 (2008) 839.
[6] V. Alagarsamy, U.S. Pathak, Bioorg. Med. Chem. 15 (2007) 3457.
[7] (a) S.K. Kashaw, V. Kashaw, P. Mishra, N.K. Jain, J.P. Stables, Eur. J. Med. Chem. 44 (2009) 4335;
(b) U. Kabra, C. Chopde, S. Wadodkar, J. Heterocycl. Chem. 48 (2011) 1351.
[8] M.S. Malamas, J. Millen, J. Med. Chem. 34 (1991) 1492.
[9] (a) V. Chandregowda, A.K. Kush, R.G. Chandrasekara, Eur. J. Med. Chem. 44 (2009) 3046;
(b) B. Marvania, P.C. Lee, R. Chaniyara, H.J. Dong, S. Suman, R. Kakadiya, T.C. Chou, T.C. Lee, A. Shah, T.L. Su, Bioorg. Med. Chem. 19 (2011) 1987.
[10] M. Decker, Eur. J. Med. Chem. 40 (2005) 305.
[11] A. Gangjee, M. Kothare, R.L. Kisliuk, J. Heterocycl. Chem. 37 (2000) 1097.
[12] (a) R.D. Li, X. Zhang, Q.Y. Li, Z.M. Ge, R.T. Li, Bioorg. Med. Chem. Lett. 21 (2011) 3637;
(b) A. Foucourt, D. Hedou, C.D. Benard, L. Desire, A.S. Casagrande, B. Leblond, N. Loaec, L. Meijer, T. Besson, Molecules 19 (2014) 15546.
[13] M. Kenji, U. Junko, S. Takashi, I. Michio, A.G. Neil, Y. Jin-Chen, T. Shusuke, O. Shoji, N. Yuji, J. Med. Chem. 46 (2003) 4910.
[14] A. Lewerenz, S. Hentschel, Z. Vissiennon, S. Michael, K. Nieber, Drug Dev. Res. 58 (2003) 420.
[15] N. Malecki, P. Carato, G. Rigo, J.F. Goossens, R. Houssin, C. Bailly, J. P Henichart, Bioorg. Med. Chem. 12 (2004) 641.
[16] M.T. Osinski, K. Schror, Bio. Chem. Pharmacol. 60 (2000) 381.
[17] R.J. VanRyzin, J.H. Trpold, Drug Chem. Toxicol. 3 (1980) 361.
[18] D. Wheathly, Rheumatol. Rehabil. 21 (1982) 98.
[19] R. Gupta, R.P. Chaudhary, J. Mol. Struct. 1049 (2013) 189.
[20] D. Gautam, R.P. Chaudhary, Spectrochim. Acta, Part A. 135 (2015) 219.
[21] R. Gupta, R.P. Chaudhary, J. Heterocycl. Chem. (2014), http://dx.doi.org/10.1002/jhet.2098.
[22] H.M. Randall, R.G. Fowler, N. Fuson, J.R. Dangl, Infrared Determination of Organic Structures, Van Nostrand, New York, 1949.
[23] G.M. Sheldrick, SHELXTL-97, Program for Refinement of Crystal Structure, University of Gottingen, Gottingen, Germany, 1997.
[24] M.J. Frisch, G.W. Trucks, H.B. Schlegel, et al., GAUSSIAN 09, Revision, Gaussian, Inc., Wallingford CT, 2009.
[25] A.D. Becke, Phys. Rev. A 38 (1988) 3098.
[26] C. Lee, W. Yang, R.G. Parr, Phys. Rev. 37 (1988) 785.
[27] K. Wolinski, J.F. Hilton, P. Pulay, J. Am. Chem. Soc. 112 (1990) 8251.
[28] R. Ditchfield, Mol. Phys. 27 (1974) 789.
[29] M. Kaupp, M. Buhl, V.G. Malkin (Eds.), Calculation of NMR and EPR Parameters: Theory and Applications, Wiley-VCH, Weinheim, 2004.
[30] B.A. Arthington-Skaggs, M. Motley, D.W. Warnock, C.J. Morrison, J. Clin. Microbiol. 38 (2000) 2254.