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Synthesis, structure and antimicrobial evaluation of new 3,3a,4,5-tetrahydro-2*H*-benzo[*g*]indazol-2-yl-thiazol-4(5*H*)-ones

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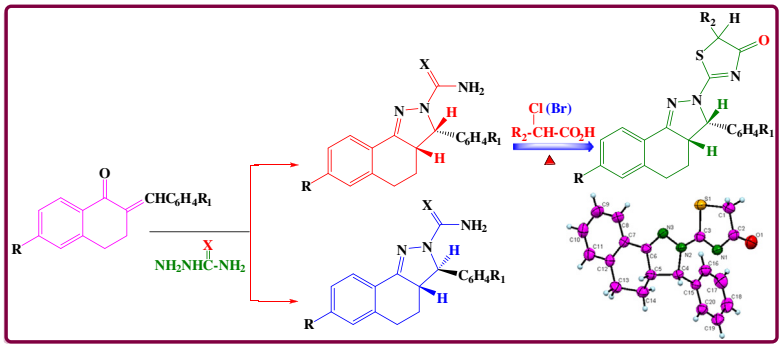
HIGHLIGHTS

- Synthesis of eight new indazolyl-thiazol-4(5*H*)-ones have been accomplished.
- Stereo chemical assignments were made on the basis of spectroscopic experiments.
- X-ray diffraction of one indazolyl-thiazol-4(5*H*)-one derivative has been reported.
- Results of DFT studies on diastereoisomers are correlated with experimental values.
- Newly synthesised compounds exhibit promising antimicrobial activities.

GRAPHICAL ABSTRACT



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ABSTRACT

The reaction of semicarbazide or thiosemicarbazide with 2-arylidene-1-tetralones under alkaline condition affords 3,3a,4,5-tetrahydro-2*H*-benzo[*g*]indazole-2-carbo(thio)amides as a mixture of *cis* and *trans* diastereoisomers of 3-H and 3a-H. The synthesis of new indazolyl-thiazol-4(5*H*)-ones from the condensation of *cis* isomer and α-halo acids is reported. A DFT study along with X-ray single crystal data of a representative compound is presented. All the eight newly synthesised indazolyl-thiazol-4(5*H*)-ones were screened for their antibacterial and antifungal activities and some compounds have shown promising activities.

Introduction

Pyrazoles, in general, and their benzocondensed analogues, tetrahydroindazoles, in particular have been proved to be an effective pharmacophore in medicinal chemistry and constitutes the key sub unit in many biologically active compounds with a broad range of pharmacological activities including anti-inflammatory [1], anti-depressant [2], anticancer [3], antituberculosis [4], and antimicrobial activities [5]. Tetrahydroindazole derivatives have been shown to possess antiproliferative activity against leukaemia cells [6] and lonidamine, an indazole-3-carboxylic acid derivative is a new nonconventional anticancer drug that inhibits the energy metabolism of neoplastic cells and increases the cell membrane permeability [7]. Owing to the immense importance and varied bioactivities exhibited by tetrahydroindazole derivatives, efforts have been made to fuse or couple tetrahydroindazole nucleus with other bioactive scaffolds, possibly for synergic increase in their activity profile [8].

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Also it is well documented that thiazol-4(5*H*)-one nucleus display a variety of pronounced pharmacological activities such as anticonvulsant [9], antimicrobial [10], anti-inflammatory [11], anti cancer [12], anti-HIV [13], and antitumor [14]. Considering the importance of tetrahydroindazole and thiazol-4(5*H*)-one nucleus it was thought worthwhile to design and synthesise some new thiazol-4(5*H*)-one derivatives bearing tetrahydroindazole moiety and screen them for potential biological activities. In continuation to our work on synthesis [15–17] and antimicrobial studies [18,19] of new thiazol-4(5*H*)-ones, we report here the synthesis, X-ray diffraction, DFT and antimicrobial studies of new thiazol-4(5*H*)-ones bearing tetrahydroindazole moiety.

Results and discussion

Chemistry

2-Arylidene-1-tetralones **2a–d** were obtained by condensation of 1-tetralones **1** and substituted aromatic aldehydes in the presence of 5% NaOH in aqueous medium [20]. 2-Arylidene-1-tetralones **2a–d** on condensation with nucleophilic reagents (phenyl hydrazine, semicarbazide and thiosemicarbazide) forms isomeric products. The isomeric composition of products was reported to be influenced by nucleophilic reagents as well as reaction conditions. Lorand et al. [21] have reported that condensation of **2** with thiosemicarbazide afforded only *cis* isomer and its formation is independent of solvent and catalyst used in the reaction. In another communications by the same author [22,23] it has been reported that the condensation of semicarbazide and thiosemicarbazide with 2-arylidene-1-tetralones **2** in acidic medium furnished a mixture of 3-H, 3a-H *cis* and *trans* diastereoisomers in the former case and only one cis diastereoisomer in the latter case. In contrast, Jagtap et al. [24] have reported the formation of mixture of *cis* and *trans* diastereoisomers during the condensation of 2-arylidene-1-tetralones **2** with semicarbazide or thiosemicarbazide in acidic medium. Herein, we found that condensation of 2-arylidene-1-tetralones **2a–d** with semicarbazide or thiosemicarbazide in presence of alc. KOH afforded a readily separable mixture (HPLC) of *cis* and *trans* diastereoisomers (3-H, 3a-H) **3** (*i.e. 3S, 3aS-rel* isomer) and **4** (i.e. *3R, 3aS-rel* isomer) in 42% (X = O) and 58% (X = O) yields. In case of carbothioamides (X = S), *cis* isomer **3** is the major product (90–95%, HPLC) and isomer **4** is only a minor product (5–10%). A mixture of **3a** and **4a** was separated by column chromatography (4:1 pet. ether: ethyl acetate) and the relative configuration of the isomers was established by 2D-COSY, ^{1}H NMR and ^{13}C NMR experiments. The reaction of 2-arylidene-1-tetralones **2** with semicarbazide or thiosemicarbazide proceeds via hydrazone formation resulting from 1,2-addition of semicarbazide or thiosemicarbazide to the carbonyl group and subsequent N—H intramolecular cycloaddition to the double bond of **2**′ as depicted in Scheme 1. In ^{1}H NMR spectrum, the proton H-3 in **3a** and **4a** appeared as a doublet at δ 5.50 and δ 4.79 ppm respectively, with spin–spin H-3 and H-3a vicinal coupling constant values ($^{3}J_{H\text{-}3,3a}$) of 10.9 Hz and 11.1 Hz. The difference in J values is too small to distinguish between *cis* and *trans* isomers. The difference in chemical shifts of H-3 in diastereoisomeric pair **3a** and **4a** is due to the diamagnetic anisotropy of C—(3a)—C-4 bonds and to the orientation of the pendent phenyl group. Firm decision on the configuration of the isomers is made on the basis of ^{13}C NMR spectroscopy. The C-3a chemical shifts for the *cis* and *trans* isomers **3a** and **4a** are 48.1 and 55.1 ppm respectively. The significant up field shift for C-3a in **3a** proved its *cis* configuration unambiguously. Finally, the structure of *cis* diastereoisomer **3b** (X = S) is proved by single crystal X-ray diffraction studies reported in our earlier accepted communication to Journal of Heterocyclic Chemistry. The ortep diagram obtained from X-ray structure of **3b** is shown in Fig. 1. CCDC 935909 contains the supplementary crystallographic data of **3b** and these data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Compounds **3b–e,** with X = S**,** on condensation with chloroacetic acid and α-bromopropionic acid in presence of anhydrous sodium acetate afford substituted 3,3a,4,5-tetrahydro-2*H*-benzo[*g*]indazol-2-yl)thiazol-4(5*H*)-ones (**5a–h**, Scheme 2). Appearance of carbonyl peak at 1697 cm^{-1} in the IR spectrum of **5a** indicates the cyclisation has indeed taken place. In ^{1}H NMR spectrum of **5a**, appearance of singlet of two protons at δ 3.88 is assigned to SCH_2 group of thiazolidinone ring. ^{13}C NMR of **5a** displays carbonyl group at δ 186.5 and C-3a at δ 49.2. The appearance of peak at *m*/*z* 348 $(M+H)^+$ (54%) in mass spectrum supports the cyclised structure **5a**. Similarly, ^{1}H NMR spectrum of **5b** displays a doublet at δ 1.5 of CH_3 group and a quartet of one proton at δ 4.15 due to $SC(H)CH_3$ group confirm the formation of thiazolidinone ring. ^{13}C NMR spectrum of **5b** exhibits C═O and C-3a at δ 189.3 and δ 48.8 respectively. The mass spectrum of **5b**, displays base peak at *m*/*z* 362 $(M+H)^+$ (100%) in support of its cyclised structure. The structure of other derivatives **(5c–h)** has been established in a similar fashion by analytical and spectral data. The analytical data of all the synthesised compounds is in accordance with the assigned structures and is in good agreement with calculated values (within range of ±0.4%).

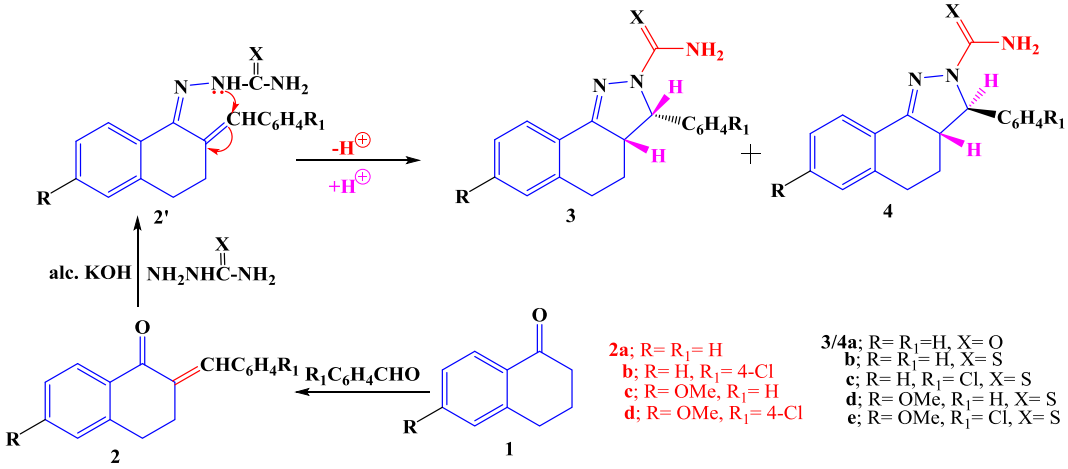
The X-ray crystal structure of compound **5a**, which is reported for the first time in this study, further confirmed the stereochemistry and *cis* orientation of H-3 and H-3a protons (Fig. 2). The crystallographic data and refinement parameters of **5a** are reported in Table 1. CCDC 986834 contains the supplementary crystallographic data and these data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Computational studies

The molecular geometry optimisation and ^{1}H and ^{13}C NMR spectra calculations were performed with the Jaguar software package version 6.5112 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 gradient-correlation functional of Lee et al. [26]. The 6-31G** basis set was used for calculations in the gas phase of *cis* diastereoisomer **5a** and its *trans* isomer **6a.**

A DFT calculation was carried out to predict the geometry of the molecules. The initial coordinates for DFT calculation were obtained from X-ray data. The experimental and optimised bond parameters (bond lengths and bond angles) obtained from X-ray crystallographic study and by geometry optimisation at B3LYP/6-31G** level of theory respectively for structure **5a** is in close agreement and is reported in Table 2. It may be noted here that slight differences in bond parameters can be attributed to the fact that the experimental results are derived from the solid phase whereas the theoretical calculations cater to the gaseous phase. However, the general agreements are good and therefore, the theoretical calculations amply corroborate the solid-state structures. The optimised configurations of **5a** and **6a** with atom numbering schemes are shown in Figs. 3 and 4 respectively.

Shielding tensors of structure **5a** and its *trans* isomer **6a** were evaluated by using B3LYP functional with basis set given above. In order to express the chemical shifts in ppm, the geometry of tetramethylsilane (TMS) and chloroform molecules had been optimised and then their ^{1}H and ^{13}C NMR spectra were calculated by the same method using same basis set as in case of the calculations on structures **5a** and its *trans* isomer **6a**. The shielding of TMS is 32.3379 for ^{1}H NMR and 202.8593 for ^{13}C NMR. The calculated isotropic shielding constants σ_i were then transformed to chemical



Scheme 1. Synthesis of substituted-3,3a,4,5-tetrahydro-2*H*-benzo[*g*]indazol-2-carbothioamides/carboxamides.

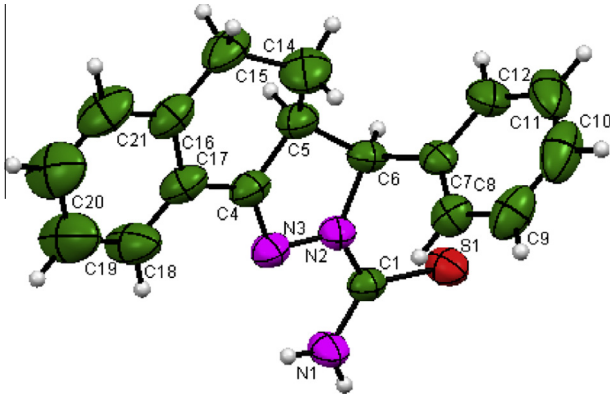


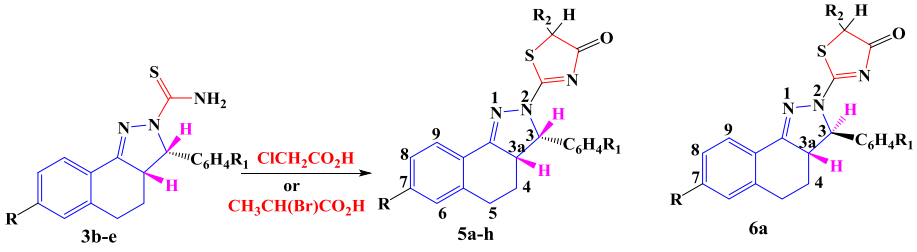
Fig. 1. ORTEP drawing (drawn at 50% probability level) indicating molecular structure and atomic labelling of (3*S*, 3a*S*)-3-phenyl-3,3a,4,5-tetrahydro-2*H*-benzo[*g*]indazole-2-carbothioamide (**3b**).

shifts relative to TMS by the equation $\delta_i = \sigma_{TMS} - \sigma_i$. A comparison between experimental and calculated ^{1}H and ^{13}C NMR chemical shifts (ppm) of compound **5a** and its *trans* isomer **6a** have been reported in Table 3. The correlation values of proton chemical shifts are found to be 0.9561 for structure **5a** and 0.8158 for its *trans* isomer **6a** (Fig. 5). The correlation values of carbon chemical shifts of **5a** and its *trans* isomer **6a** are found to be 0.9898 and 0.9827 respectively (Fig. 6). It may be noted that there is large deviation in correlation values of *trans* isomer **6a**. Based upon comparison of experimental and theoretical NMR studies, ^{1}H and ^{13}C data show good correlations for the proposed *cis* structure **5a.**

Antimicrobial activity

All the newly synthesised indazolyl-thiazol(5*H*)-4-ones **5a–h** were screened for their in vitro antibacterial and antifungal activity. The microorganisms employed for antibacterial studies were *Staphylococcus aureus* (MTCC 096), *Escherichia coli* (MTCC 443) and *Pseudomonas aeruginosa* (MTCC 424). For antifungal screening, *Aspergillus niger* (MTCC 282), *Aspergillus fumigates* (MTCC 343), and *Candida albicans* (MTCC 227) strains were used. Both microbial studies were assessed by Minimum Inhibitory Concentration (MIC) by serial dilution method [27].

Various concentrations (6.25, 12.5, 25, 50, 100, 200, 500 and 1000 μg/ml) of each compound were prepared by serially diluted DMSO from the stock solution. For MIC, a standard drop of the microbial culture, prepared for the assay, was added to the different dilution of compounds in Muller Hilton (MH) broth for bacteria and Sabouraud Dextrose (SD) broth for fungi. Test solutions were then incubated for 16–18 h for bacteria and 28–30 h for fungi at 37 °C. MIC is the minimum concentration of the compound, which inhibits the visible growth of bacteria or fungi. To determine zone of inhibition, inoculated MH agar for bacteria and SD agar for fungi were separately poured into the sterilized petri dishes. The poured material was allowed to set and thereafter the "CUPS" (08 mm diameter) were made by punching into the agar surface with a sterile cork borer and scooping out the punched part of the agar. The test compound solution was added into these cups with the help of a sterile syringe. The plates were incubated at 37 °C for 16–18 h for bacteria and 28–30 h for fungi. Clinically antimicrobial drugs Ciprofloxacin and Miconazole were used as the positive



5	a	b	c	d	e	f	g	h
R	H	H	H	H	OMe	OMe	OMe	OMe
R_1	H	H	4-Cl	4-Cl	H	H	4-Cl	4-Cl
R_2	H	CH_3	H	CH_3	H	CH_3	H	CH_3

Scheme 2. Synthesis of Indazolyl-thiazol-4(5*H*)-ones from substituted-3,3a,4,5-tetrahydro-2*H*-benzo[*g*]indazol-2-carbothioamides.

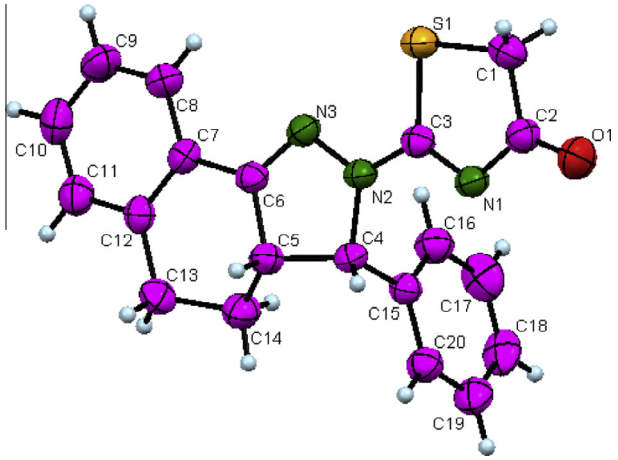


Fig. 2. An ORTEP diagram of 2-((3*S*, 3a*S*)-3-phenyl-3,3a,4,5-tetrahydro-2*H*-benzo[g]indazol-2-yl)thiazol-4(5*H*)-one **5a** with nonhydrogen ellipsoids drawn at 50% probability level.

Table 1
Crystal data and structure refinement parameters of compound **5a**.

CCDC no.	986834
Empirical formula	$C_{20}H_{17}N_3OS$
Formula weight	347.43
Temperature (K)	293 (2)
Wavelength (Å)	0.71073 Å
Crystal system	Triclinic
Space group	*P*−1
Unit cell dimensions	
a (Å)	7.9857 (9)
b (Å)	10.5056 (13)
c (Å)	10.8119 (14)
α (°)	98.293 (11)
β (°)	101.310 (11)
γ (°)	104.388 (11)
Volume (Å^3)	843.58 (18)
Z	2
Density (calculated) (Mg/m^3)	1.368 Mg/m^3
Absorption coefficient (mm^{-1})	0.205 mm^{-1}
Crystal size	0.31 × 0.26 × 0.22 mm^3
Theta range for data collection	2.89–29.05
Reflections collected	6408
Independent reflections	1958
Data/restraints/parameters	3791/0/226
Goodness-of-fit on F^2	1.026
Final *R* indices [$I > 2\sigma(I)$ = 2591 data]	R_1 = 0.0823, wR_2 = 0.1730
R indices (all data)	R_1 = 0.1524, wR_2 = 0.2196
Largest diff. Peak and hole (e Å^{-3})	−0.269, 0.349

control and DMSO was used for blank. The experiments were repeated three times, and the average values are presented in Table 4. Compounds **5d** and **5h** (MIC 12.5 μg/mL) showed good activity against *S. aureus*, *E. coli* and *A. Niger*. Compounds **5f** and **5b** with MIC 6.25 μg/ml displayed excellent antibacterial activity against *S. aureus* and *E. coli* respectively. Compounds **5a** and **5c** exerted wide range of antibacterial and antifungal activities against the entire tested stains. **5b** and **5e** (MIC, 12.5 μg/mL) displayed very good antifungal activities against *C. albicans* and *A. fumigates*.

Experimental

Melting points were determined in sulphuric acid bath and are reported uncorrected. TLC was performed on silica gel G plates using petroleum ether-ethyl acetate (4:1) as eluent and iodine vapours as visualising agent. IR spectra were recorded on ABB FTIR spectrometer and the results are reported in cm^{-1}. ^{1}H NMR and ^{13}C

Table 2
Selected bond parameters of *cis* isomer **5a** and *trans* isomer **6a**.

Parameters	Compound **5a**		Isomer **6a**	
	Experimental	Calculated	Parameters	Calculated
Bond lengths (Å)				
S(1)—C(3)	1.752(4)	1.7838	S(1)—C(7)	1.7731
S(1)—C(1)	1.807(4)	1.8028	S(1)—C(17)	1.8061
N(2)—C(3)	1.335(5)	1.3352	N(3)—C(7)	1.3354
N(2)—C(4)	1.493(4)	1.4707	N(3)—C(10)	1.4738
O(1)—C(2)	1.219(4)	1.1880	O(4)—C(12)	1.1878
N(1)—C(3)	1.324(5)	1.2777	N(5)—C(7)	1.2794
N(1)—C(2)	1.357(5)	1.3757	N(5)—C(12)	1.3790
N(3)—C(6)	1.291(4)	1.2594	N(13)—C(10)	1.2587
N(3)—N(2)	1.403(4)	1.3870	N(3)—N(2)	1.3827
C(6)—C(7)	1.468 (5)	1.4679	C(6)—C(8)	1.4680
C(6)—C(5)	1.511 (5)	1.5058	C(6)—C(13)	1.5014
Bond angles (°)				
C(3)—S(1)—C(1)	88.17(18)	88.8699	C(7)—S(1)—C(17)	88.3798
C(6)—N(3)—N(2)	106.2 (3)	107.7592	C(6)—N(2)—N(3)	108.3699
C(3)—N(2)—N(3)	120.8 (3)	119.9252	C(7)—N(3)—N(2)	119.1699
C(3)—N(2)—C(4)	125.3 (3)	127.6440	C(7)—N(3)—C(10)	123.7635
N(3)—N(2)—C(4)	113.9(3)	112.1809	N(2)—N(3)—C(10)	113.1863
C(3)—N(1)—C(2)	110.9 (3)	112.9312	C(7)—N(5)—C(12)	112.5095
N(3)—C(6)—C(7)	124.6 (3)	124.6650	N(2)—C(6)—C(8)	125.3921
N(3)—C(6)—C(5)	114.9 (3)	114.5100	N(2)—C(6)—C(13)	114.7116
N(1)—C(3)—N(2)	121.7 (3)	124.2106	N(5)—C(7)—N(3)	122.0472
N(1)—C(3)—S(1)	119.4 (3)	118.1553	N(5)—C(7)—S(1)	119.0050
N(2)—C(3)—S(1)	118.9 (3)	117.6207	N(3)—C(7)—S(1)	118.9412
N(2)—C(4)—C(5)	99.4 (3)	99.6568	N(3)—C(10)—C(13)	100.5836

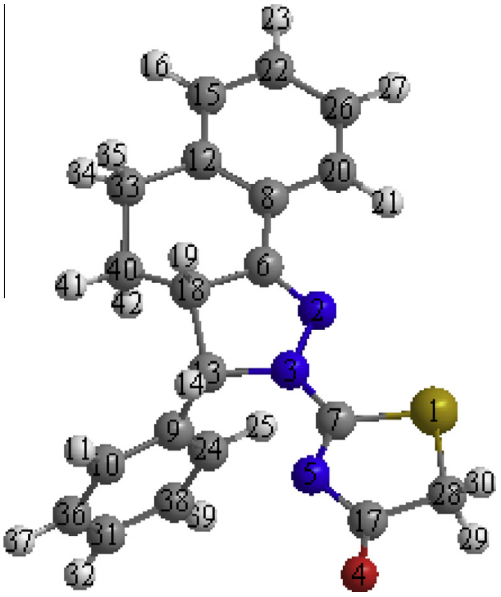


Fig. 3. Optimised structure of **5a.**

NMR were recorded in $CDCl_3$ and DMSO-d_6 on a BRUKER ADVANCE 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. The percentage composition of the mixture of diastereoisomers **3a and b** and **4a and b** was determined by Breeze HPLC system and reported as Fig. S1 of the Supplementary material. The structures were optimised by molecular mechanics using PM3 method based on Hyperchem with version 7.5 packages. 1-Tetralone and 6-methoxy-1-tetralone were procured from Sigma and were used without purification.

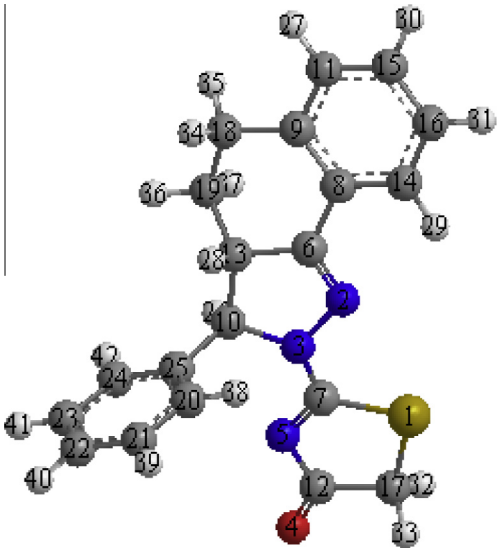


Fig. 4. Optimised structure of **6a.**

General procedure for synthesis of 2

Compound **2** is prepared by refluxing a mixture of 1-tetralone and aromatic aldehyde in aq. NaOH by the reported [20] procedure.

*(E)-2-benzylidene-3,4-dihydronaphthalen-1(2H)-one (**2a**)*

Greyish white solid; yield 82%; mp 103–05 °C; (Lit. [20] mp 105 °C); IR (cm^{-1}): 1705 (C=O); ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.93–2.97 (t, 2H, CH_2, *J* = 6.08 Hz), 3.12–3.16 (t, 2H, CH_2, *J* = 6.88 Hz), 7.24–7.26 (m, 1H, Ar—H), 7.33–7.51 (m, 8H, Ar—H), 7.87 (s, 1H, =CH). MS *m*/*z* 235 ($M+H^+$) 100%.

*(E)-2-(4-chlorobenzylidene)-3,4-dihydronaphthalen-1(2H)-one (**2b**)*

White solid; yield 86%; mp 128–32 °C; (Lit. [20] mp 134 °C); IR (cm^{-1}): 1702 (C=O); ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.92–2.94 (t, 2H, CH_2, *J* = 6.86 Hz), 3.12–3.14 (t, 2H, CH_2, *J* = 6.74 Hz), 7.01–7.03 (d, 2H, C_6H_5, *J* = 7.76 Hz), 7.34–7.42 (m, 5H, Ar—H), 7.92 (s, 1H, =CH), 8.11–8.13 (d, 1H, Ar—H, *J* = 7.34 Hz).

*(E)-2-benzylidene-6-methoxy-3,4-dihydronaphthalen-1(2H)-one (**2c**)*

Light brown solid; yield 88%; mp 100–02 °C; IR (cm^{-1}): 1712 (C=O); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.90–2.93 (t, 2H, CH_2, *J* = 6.76 Hz), 3.09–3.11 (t, 2H, CH_2, *J* = 6.8 Hz), 3.87(s, 3H, OCH_3), 6.70–6.71(d, 1H, Ar—H, *J* = 2.44 Hz), 6.86–6.89 (m, 1H, Ar—H), 7.34–7.42 (m, 5H, Ar—H), 7.83 (s, 1H, =CH), 8.11–8.13 (d, 1H, Ar—H, *J* = 8.7 Hz).

*(E)-2-(4-chlorobenzylidene)-6-methoxy-3,4-dihydronaphthalen-1(2H)-one (**2d**)*

White solid; yield 90%; mp 125–27 °C; IR (cm^{-1}): 1715 (C=O); ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.95–2.98 (t, 2H, CH_2, *J* = 6.84 Hz), 3.10–3.12 (t, 2H, CH_2, *J* = 6.92 Hz), 3.9 (s, 3H, OCH_3), 6.88–6.9 (m, 1H, Ar—H), 7.38–7.44 (m, 5H, Ar—H), 7.86 (s, 1H, =CH), 8.14–8.16 (d, 1H, Ar—H, *J* = 7.86 Hz).

*General procedure for synthesis of (**3a–e**)*

To a solution of 2-benzylidene-3,4-dihydronaphthalen-1(2*H*)-ones **2** (1.0 mol) and semicarbazide or thiosemicarbazide (1.0 mol) in absolute ethanol (20 mL), 1.0 g of KOH was added and the reaction mixture was heated at 70–80 °C for 3–4 h. The progress of the reaction was monitored by TLC. After completion of the reaction, the volume of the reaction mixture was reduced to half and kept overnight. The solid obtained was filtered and washed with ice cold ethanol. Recrystallization from 95% ethanol furnished a pure mixture of two diastereoisomers.

*(3S, 3aS)-3-Phenyl-3,3a,4,5-tetrahydro-2H-benzo[g]indazole-2-carboxamide (**3a**)*

White solid; yield 55%; mp: 238–40 °C; IR (cm^{-1}): 3483, 3276, 3215 (NH), 1684 (C=O), 1571 (C=N); ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.81–0.85 (m, 1H, CH_2), 1.72–1.76 (m, 1H, CH_2), 2.87–2.92 (m, 1H, CH_2), 3.15–3.19 (m, 1H, CH_2), 3.72–3.75 (m, 1H, H-3a), 5.50–5.43 (d, 1H, H-3, *J* = 10.9 Hz), 6.48 (br, 2H, NH_2), 7.0–7.2 (d, 2H, C_6H_5, *J* = 7.16 Hz), 7.17–7.33 (m, 6H, C_6H_5), 7.98–8.0 (m, 1H, C_6H_5); ^{13}C NMR (100 MHz, DMSO-d_6): δ 154.6, 151.6, 139.1, 138.3, 129.8, 128.2, 127.3, 126.4, 125.7, 124.2, 62.8, 61.2, 60.6, 48.1, 28.5, 23.5, 15.3; MS *m*/*z* 292.2 ($M+H^+$) 80%. Anal. Calc. for $C_{18}H_{17}N_3O$: C, 74.20; H, 5.88; N, 14.42; Found: C, 74.36; H, 5.97; N, 14.68%.

*(3S, 3aS)-3-Phenyl-3,3a,4,5-tetrahydro-2H-benzo[g]indazole-2-carbothioamide (**3b**)*

Light yellow crystals; yield 65%; mp: 208–210 °C; IR (cm^{-1}): 3443, 3263, 3144 (NH), 1590 (C=N), 1347(C=S); ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.8–0.91 (m, 1H, CH_2), 1.78–1.82 (m, 1H, CH_2), 2.78–2.94 (m, 2H, CH_2), 3.73–3.80 (m, 1H, H-3a), 6.05–6.08 (d, 1H, H-3, *J* = 10.6 Hz), 7.01–7.03 (d, 2H, C_6H_5, *J* = 7.28 Hz), 7.16–7.35 (m, 6H, C_6H_5), 7.49 (br, 1H, NH_2), 7.81 (br, 1H, NH_2), 8.06–8.08 (d, 1H, C_6H_5, *J* = 7.68 Hz); ^{13}C NMR (100 MHz, DMSO-d_6): δ 178.4, 175.4, 156.1, 155.1, 143.4, 139.8, 137.4, 130.6, 128.9, 126.9, 125.9, 124.8, 69.6, 48.2, 28.6, 27.5, 23.7, 18.3; MS *m*/*z* 308.1 ($M+H^+$) 40%. Anal. Calc. for $C_{18}H_{17}N_3S$: C, 70.33; H, 5.57; N, 13.67; S, 10.43; Found: C, 70.58; H, 5.77; N, 13.87; S, 10.67%.

*(3S,3aS)-3-(4-Chlorophenyl)-3,3a,4,5-tetrahydro-2H-benzo[g]indazole-2-carbothioamide (**3c**)*

Yellow solid; yield 62%; mp: 178–80 °C; IR (cm^{-1}): 3435, 3212, 3119 (NH), 1598 (C=N), 1246 (C=S); ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.81–0.85 (m, 1H, CH_2), 1.77–1.81 (m, 1H, CH_2), 2.82–2.93 (m, 2H, CH_2), 3.76–3.83 (m, 1H, H-3a), 6.03–6.06 (d, 1H, H-3, *J* = 10.7 Hz), 7.01–7.03 (d, 2H, C_6H_5, *J* = 7.76 Hz), 7.17–7.66 (m, 4H, C_6H_5), 7.94 (br, 1H, NH_2), 8.03 (br, 1H, NH_2), 8.06–8.08 (d, 2H, C_6H_5, *J* = 7.68 Hz); ^{13}C NMR (100 MHz, DMSO-d_6): δ 175.4, 156.0, 155.0, 142.3, 139.8, 136.5, 131.8, 130.6, 128.9, 127.5, 126.5, 124.8, 69.0, 65.7, 48.1, 28.6, 27.3, 23.8; MS *m*/*z* 342.1 (M+1) 100%, 344 (M+3) (32%). Anal. Calc. for $C_{18}H_{16}ClN_3S$: C, 63.24; H, 4.72; N, 12.29; S, 9.38; Found: C, 63.46; H, 4.82; N, 12.54; S, 9.49%.

*(3S,3aS)-7-Methoxy-3-phenyl-3,3a,4,5-tetrahydro-2H-benzo[g]indazole-2-carbothioamide (**3d**)*

Light brown solid; yield 72%; mp: 160–62 °C; IR (cm^{-1}): 3470, 3204, 3146 (NH), 1590 (C=N), 1250 (C=S); ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.81–0.86 (m, 1H, CH_2), 1.77–1.80 (m, 1H, CH_2), 2.54–2.56 (m, 2H, CH_2), 3.69–3.75 (m, 1H, H-3a), 3.79 (s, 3H, OCH_3), 6.02–6.04 (d, 1H, H-3, *J* = 10.5 Hz), 6.69 (d, 1H, C_6H_5, *J* = 2.32 Hz), 6.79–6.90 (m, 1H, C_6H_5), 7.01–7.03 (d, 2H, C_6H_5, *J* = 7.28 Hz), 7.19–7.29 (m, 3H, C_6H_5), 7.44 (br, 1H, NH_2), 7.70 (br, 1H, NH_2), 7.98–7.99 (d, 1H, C_6H_5, *J* = 2.96 Hz); ^{13}C NMR (DMSO-d_6): δ 178.3, 161.2, 156.2, 147.8, 142.0, 137.5, 128.2, 126.8, 125.7, 124.4, 119.1, 113.4, 69.4, 66.1, 55, 48.3, 29.2, 25.6, 21.3; MS *m*/*z* 338.1 ($M+H^+$) 100%. Anal. Calc. for $C_{19}H_{19}N_3OS$: C, 67.63; H, 5.68; N, 12.45; S, 9.50; Found: C, 67.91; H, 5.79; N, 12.68; S, 9.63%.

*(3S,3aS)-3-(4-Chlorophenyl)-7-methoxy-3,3a,4,5-tetrahydro-2H-benzo[g]indazole-2-carbothioamide (**3e**)*

White solid; yield 68%; mp: 182–84 °C; IR (cm^{-1}): 3441, 3215, 3125 (NH), 1602 (C=N), 1276 (C=S); ^{1}H NMR (400 MHz,

Table 3
Experimental and calculated ^{1}H NMR and ^{13}C NMR chemical shifts (ppm) of **5a** and **6a.**

Entry	CH_2	CH_2	H-3a	H-3	SCH_2	Ar—H	R^2
^{1}H NMR							
Expt. (**5a**)	0.91	2.80	3.96	5.93	3.88	7.54	
Calcd. (**5a**)	0.97[a]	2.45[a]	2.88	5.15	3.07[a]	7.37[a]	0.9561
Calcd. (**6a**)	1.67[a]	2.55[a]	2.54	4.29	3.04[a]	7.43[a]	0.8158
	C=N	SC=N	C-3	C=O	C-3a	–	R^2
^{13}C NMR							
Expt. (**5a**)	177.19	186.55	66.83	180.75	49.28	–	
Calcd. (**5a**)	166.34	189.55	61.87	185.86	46.09	–	0.9898
Calcd. (**6a**)	164.89	191.80	64.88	186.18	54.55	–	0.9827

[a] Average value.

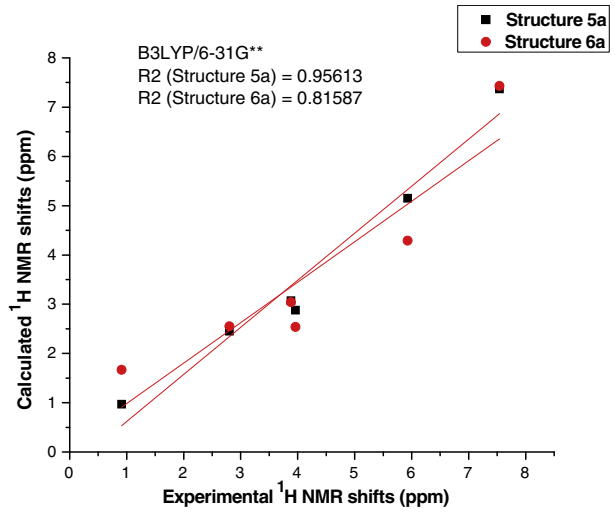


Fig. 5. Plot of the calculated vs. experimental ^{1}H NMR chemical shifts (ppm) of **5a** and its *trans* isomer **6a**.

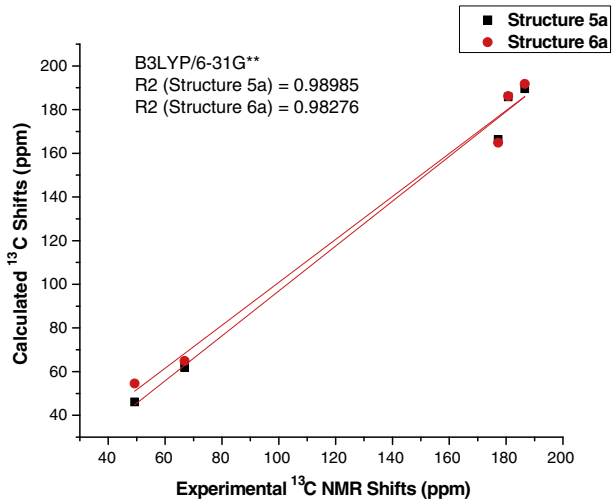


Fig. 6. Plot of the calculated vs. experimental ^{13}C NMR chemical shifts (ppm) of **5a** and its *trans* isomer **6a**.

DMSO-d_6): δ 0.77–0.86 (m, 1H, CH_2), 1.76–1.79 (m, 1H, CH_2), 2.75–2.91 (m, 2H, CH_2), 3.70–3.78 (m, 1H, H-3a), 3.80 (s, 3H, OCH_3), 6.00–6.03 (d, 1H, H-3, *J* = 10.6 Hz), 6.71–6.76 (m, 1H, C_6H_5), 6.83–6.86 (m, 1H, C_6H_5), 7.00–7.02 (d, 2H, C_6H_4, *J* = 7.88 Hz), 7.24–7.33 (m, 2H, C_6H_5), 7.54 (br, 1H, NH_2), 7.91 (br, 1H, NH_2), 7.98–7.99 (d, 1H, C_6H_4, *J* = 3.72 Hz); ^{13}C NMR (100 MHz, DMSO-d_6): δ 175.0, 161.3, 156.1, 142.0, 136.5, 131.8, 128.1, 127.5, 126.6, 119.0, 113.5, 112.7, 65.5, 48.2, 28.9, 23.8; MS *m/z* 372.1 (M+1) 100%, 374 (M+3) (38%). Anal. Calc. for $C_{19}H_{18}ClN_3OS$: C, 61.36; H, 4.88; N, 11.30; S, 8.62; Found: C, 61.68; H, 4.98; N, 11.58; S, 8.76%.

*(3R,3aS)-3-Phenyl-3,3a,4,5-tetrahydro-2H-benzo[g]indazole-2-carboxamide (**4a**)*

White solid; Yield 46%; mp: >250 °C; IR (cm^{-1}): 3476, 3248, 3205 (NH), 1668 (C=O), 1580(C=N); ^{1}H NMR (400 MHz, DMSO-d_6): 1.89–1.93 (m, 1H, CH_2), 2.13–2.16 (m, 1H, CH_2), 2.87–2.92 (m, 2H, CH_2), 3.12–3.19 (m, 1H, H-3a), 4.79–4.82 (d, 1H, H-3, *J* = 11.1 Hz), 6.51 (br, 2H, NH_2), 7.23–7.37 (m, 8H, C_6H_5), 7.90–7.92 (m, 1H, C_6H_5); ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.1, 156.9, 152.1, 143.0, 139.3, 129.1, 128.3, 127.1, 125.8, 124.2, 99.5, 67.8, 61.1, 55.1, 15.0; MS *m/z* 292.2 ($M+H^+$) 80%. Anal. Calc. for $C_{18}H_{17}N_3O$: C, 74.20; H, 5.88; N, 14.42; Found: C, 74.36; H, 5.92; N, 14.68%.

*General procedure for the synthesis of **5(a–h)***

An equimolar mixture of **3b–e** (0.001 mol), chloroacetic acid or 2-bromopropionic acid (0.001 mol) and anhydrous sodium acetate (0.16 g, 0.002 mol) in ethanol (10 mL) was heated under reflux for 4–5 h. The progress of the reaction was monitored by TLC. After completion of the reaction volume of the reaction mixture was reduced to half under vacuum and kept overnight. The solid, thus obtained was filtered, dried and recrystallized from ethanol-DMF mixture (3:1).

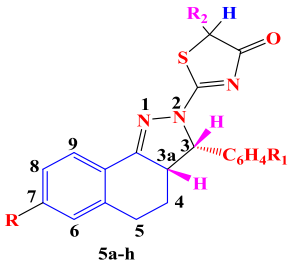
*2-[(3S,3aS)-3-phenyl-3,3a,4,5-tetrahydro-2H-benzo[g]indazol-2-yl]thiazol-4(5H)-one (**5a**)*

Yellow crystalline solid; yield: 64%; mp: 258–60 °C; IR (cm^{-1}): 1697 (C=O), 1589 (C=N); ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.90–0.94 (m,1H, CH_2), 1.80–1.84 (m, 1H, CH_2), 2.79–3.01 (m, 2H, CH_2), 3.88 (s, 2H, SCH_2), 3.95–4.02 (m, 1H, H-3a), 5.92–5.95 (d, 1H, H-3, *J* = 10.5 Hz), 7.06–7.08 (d, 2H, C_6H_5, *J* = 7.12 Hz), 7.25–7.43 (m, 6H, C_6H_5), 8.02–8.04 (dd, 1H, C_6H_5, *J* = 6.68 Hz, *J* = 1.08 Hz); ^{13}C NMR (100 MHz, DMSO-d_6): δ 186.5 (C=N), 180.7 (C=O), 177.1 (C=N), 161.1, 140.3, 135.3, 135.1, 131.5, 129.0, 128.5, 127.7, 126.6, 125.7, 125.1, 66.8, 49.2, 28.5, 23.7; MS *m/z* 348 $(M+H)^+$ (54%). Anal. Calc. for $C_{20}H_{17}N_3SO$: C, 69.14; H, 4.93; N, 12.09; S, 9.23; Found: C, 69.04; H, 4.89; N, 11.98; S, 9.12.

*5-Methyl-2-[(3S,3aS)-3-phenyl-3,3a,4,5-tetrahydro-2H-benzo[g]indazol-2-yl]thiazol-4(5H)-one (**5b**)*

White solid; yield: 62%; mp: 218–20 °C; IR (cm^{-1}): 1705 (C=O), 1594 (C=N); ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.82–0.88 (m,1H, CH_2), 1.48–1.53 (d, 3H, CH_3, *J* = 7.28 Hz), 1.77–1.81 (m, 1H, CH_2), 2.82–2.91 (m, 2H, CH_2), 3.97–4.05 (m, 1H, H-3a), 4.12–4.17 (q, 1H, $SCHCH_3$, *J* = 7.12 Hz), 5.93–5.95 (d, 1H, H-3, *J* = 10.8 Hz), 7.06–7.08 (d, 2H, C_6H_5, *J* = 7.4 Hz), 7.24–7.45 (m, 6H, C_6H_5), 7.98–8.0

Table 4
Antibacterial and antifungal activities of compounds **5(a–h).**



5a-h

5a, R= H, R_1= H, R_2= H
b, R= H, R_1= H, R_2= CH_3
c, R= H, R_1= 4-Cl, R_2= H
d, R= H, R_1= 4-Cl, R_2= CH_3
e, R= OMe, R_1= H, R_2= H
f, R= OMe, R_1= H, R_2= CH_3
g, R= OMe, R_1= 4-Cl, R_2= H
h, R= H, R_1= 4-Cl, R_2= CH_3

Antimicrobial activity (MIC in μg/mL)						
Entry	*S. aureus*	*E. coli*	*P. aeruginosa*	*A. niger*	*C. albicans*	*A. fumigates*
5a	50	50	25	25	25	25
5b	25	6.25	25	12.5	12.5	12.5
5c	25	25	25	12.5	25	50
5d	12.5	12.5	12.5	12.5	12.5	25
5e	25	25	25	25	12.5	12.5
5f	6.25	25	12.5	12.5	50	50
5g	25	25	12.5	12.5	50	50
5h	12.5	12.5	25	12.5	50	50
Cipro	6.25	6.25	6.25	–	–	–
Miconazole	–	–	–	6.25	6.25	6.25

(d, 1H, C_6H_5, J = 7.08 Hz); ^{13}C NMR (100 MHz, DMSO-d_6): δ 189.3 (C=O), 175.4, 160.9 (C=N), 140.5, 135.5, 131.6, 129.1, 128.6, 127.7, 126.7, 125.8, 125.7, 125.0, 66.7, 49.2, 48.8, 28.5, 23.7, 18.8; MS m/z 362 $(M+H)^+$ (100%). Anal. Calc. for $C_{21}H_{19}N_3SO$: C, 69.78; H, 5.30; N, 11.63; S, 8.87; Found: C, 69.88; H, 5.39; N, 11.78; S, 8.98.

*2-[(3S,3aS)-3-(4-chlorophenyl)-3,3a,4,5-tetrahydro-2H-benzo[g]indazol-2-yl]thiazol-4(5H)-one (**5c**)*

Greyish solid; yield: 78%; mp: 238–40 °C; IR (cm^{-1}): 1707 (C=O), 1605 (C=N); ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.89–0.92 (m, 1H, CH_2), 1.79–1.82 (m, 1H, CH_2), 2.51–2.53 (m, 2H, CH_2), 3.85 (s, 2H, SCH_2), 3.98–4.05 (m, 1H, H-3a), 5.94–5.97 (d, 1H, H-3, J = 10.6 Hz), 7.09–7.11 (d, 2H, C_6H_5, J = 8.12 Hz), 7.24–7.45 (m, 5H, C_6H_5), 7.99–8.01 (d, 1H, C_6H_5, J = 6.72 Hz); ^{13}C NMR (100 MHz, DMSO-d_6): δ 186.4 (C=O), 177.1, 160.8 (C=N), 140.4, 134.4, 132.6, 131.6, 129.1, 128.6, 127.7, 126.7, 125.6, 66.1, 49.2, 28.5, 23.7; MS m/z 382 (M + 1) (100%), 384 (M + 3) (28%). Anal. Calc. for $C_{20}H_{16}ClN_3OS$: C, 62.90; H, 4.22; N, 11.00; S, 8.40. Found: C, 62.84; H, 4.19; N, 10.98; S, 8.32.

*2-[(3S,3aS)-3-(4-chlorophenyl)-3,3a,4,5-tetrahydro-2H-benzo[g]indazol-2-yl]-5-methylthiazol-4(5H)-one (**5d**)*

Greyish solid; yield: 72%; mp: 218–20 °C; IR (cm^{-1}): 1695 (C=O), 1595 (C=N); ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.86–0.95 (m,1H, CH_2), 1.49–1.51 (d, 3H, CH_3, J = 7.24 Hz), 1.79–1.83 (m, 1H, CH_2), 2.76–3.00 (m, 2H, CH_2), 3.97–4.05 (m, 1H, H-3a), 4.11–4.18 (q, 1H, $SCHCH_3$, J = 7.68 Hz, J = 7.32 Hz), 5.93–5.97 (d, 1H, H-3, J = 10.6 Hz), 7.08–7.10 (d, 2H, C_6H_5, J = 8.0 Hz), 7.24–7.44 (m, 5H, C_6H_5), 7.98–8.0 (d, 1H, C_6H_5, J = 7.48 Hz); ^{13}C NMR (100 MHz, DMSO-d_6): δ 189.3 (C=O), 175.5, 160.8 (C=N), 140.4, 139.4, 132.6, 131.6, 129.1, 128.6, 127.7, 126.6, 125.6, 65.9, 49.1, 48.9, 28.5, 23.7, 18.7; MS m/z 396 $(M+H)^+$ (100%). Anal. Calc. for $C_{21}H_{18}ClN_3OS$: C, 63.71; H, 4.58; N, 10.61; S, 8.10. Found: C, 63.74; H, 4.49; N, 10.58; S, 8.02.

*2-[(3S,3aS)-7-methoxy-3-phenyl-3,3a,4,5-tetrahydro-2H-benzo[g]indazol-2-yl]thiazol-4(5H)-one (**5e**)*

Light yellow solid; yield: 84%; mp: 208–10 °C; IR (cm^{-1}): 1705 (C=O), 1594 (C=N); ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.86–0.91 (m, 1H, CH_2), 1.79–1.83 (m, 1H, CH_2), 2.76–2.98 (m, 2H, CH_2), 3.77 (s, 3H, OCH_3), 3.82 (s, 2H, SCH_2), 3.89–3.96 (m, 1H, H-3a), 5.88–5.91 (d, 1H, H-3, J = 10.4 Hz), 6.76 (s, 1H, C_6H_5), 6.88–6.91 (m, 1H, C_6H_5), 7.06–7.07 (m, 2H, C_6H_5), 7.27–7.34 (m, 4H, C_6H_5); ^{13}C NMR (100 MHz, DMSO-d_6): δ 186.4 (C=O), 176.5, 161.9 (C=N), 142.6, 135.3, 128.9, 127.6, 125.7, 118.3, 113.8, 112.8, 66.6, 55.1, 49.3, 35.8, 30.7, 28.9, 23.6; MS m/z 378 $(M+H)^+$ (100%). Anal. Calc. for $C_{21}H_{19}N_3O_2S$: C, 66.82; H, 5.07; N, 11.13; S, 8.49. Found: C, 66.74; H, 4.99; N, 11.01; S, 8.32

*2-[(3S,3aS)-7-methoxy-3-phenyl-3,3a,4,5-tetrahydro-2H-benzo[g]indazol-2-yl]-5-methylthiazol-4(5H)-one (**5f**)*

Orange crystalline solid; yield: 80%; mp: 218–20 °C; IR (cm^{-1}): 1697 (C=O), 1602 (C=N); ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.79–0.81 (m,1H, CH_2), 1.49–1.50 (d, 3H, CH_3, J = 7.28 Hz), 1.78–1.82 (m, 1H, CH_2), 2.88–2.94 (m, 2H, CH_2), 3.80 (s, 3H, OCH_3), 3.91–3.98 (m, 1H, H-3a), 4.08–4.13 (q, 1H, $SCHCH_3$, J = 7.24 Hz), 5.89–5.91 (d, 1H, H-3, J = 10.4 Hz), 6.77–6.78 (m, 1H, C_6H_5), 6.89–6.91 (m, 1H, C_6H_5), 7.05–7.07 (m, 2H, C_6H_5), 7.25–7.35(m, 3H, C_6H_5), 7.95–7.95(m, 1H, C_6H_5); ^{13}C NMR (100 MHz, DMSO-d_6): δ 189.2 (C=O), 175.0, 162.0 (C=N), 135.5, 128.5, 127.6, 125.8, 118.3, 113.8, 112.9, 66.4, 55.2, 49.2, 48.8, 35.8, 30.7, 28.9, 23.7, 18.8; MS m/z 392 $(M+H)^+$ (100%). Anal. Calc. for $C_{22}H_{21}N_3O_2S$: C, 67.50; H, 5.41; N, 10.73; S, 8.19. Found: C, 67.48; H, 5.28; N, 10.71; S, 8.08.

*2-[(3S,3aS)-3-(4-chlorophenyl)-7-methoxy-3,3a,4,5-tetrahydro-2H-benzo[g]indazol-2-yl]thiazol-4(5H)-one (**5g**)*

Yellow solid; yield: 68%; mp: 210–12 °C; IR (cm^{-1}): 1702 (C=O), 1610 (C=N); ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.86–0.94 (m, 1H, CH_2), 1.79–1.83 (m, 1H, CH_2), 2.75–2.97 (m, 2H, CH_2), 3.82 (s, 3H, OCH_3), 3.86 (s, 2H, SCH_2), 3.91–3.99 (m, 1H, H-3a), 5.90–5.93 (d, 1H, H-3, J = 10.5 Hz), 6.81–6.82 (m, 1H, C_6H_5), 6.88–6.91 (m, 1H, C_6H_5), 7.07–7.10 (m, 1H, C_6H_5), 7.33–7.40 (m, 2H, C_6H_5), 7.93–7.95 (m, 2H, C_6H_5); ^{13}C NMR (100 MHz, DMSO-d_6): δ 186.3 (C=O), 162.0, 160.6 (C=N), 142.6, 134.4, 132.6, 128.5, 127.6, 118.2, 113.8, 112.9, 65.9, 55.2, 49.2, 35.8, 30.7, 28.9, 23.7; MS m/z 412 (M+1) (100%), 414 (M+3) (38%). Anal. Calc. for $C_{21}H_{18}ClN_3O_2S$: C, 61.23; H, 4.40; N, 10.20; S, 7.78. Found: C, 67.38; H, 5.18; N, 10.68; S, 7.98.

*2-[(3S,3aS)-3-(4-chlorophenyl)-7-methoxy-3,3a,4,5-tetrahydro-2H-benzo[g]indazol-2-yl]-5-methylthiazol-4(5H)-one (**5h**)*

Orange solid; yield: 80%; mp: 162–64 °C. IR (cm^{-1}): 1705 (C=O), 1598 (C=N); ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.84–0.89 (m,1H, CH_2), 1.48–1.49 (d, 3H, CH_3, J = 7.3 Hz), 1.77–1.85 (m, 1H, CH_2), 2.75–2.91 (m, 2H, CH_2), 3.81 (s, 3H, OCH_3), 3.91–3.98 (m, 1H, H-3a), 4.05–4.11 (q, 1H, $SCHCH_3$, J = 7.22 Hz), 5.90–5.93 (d, 1H, H-3, J = 10.4 Hz), 6.71–6.72 (m, 1H, C_6H_5), 6.77–6.80 (m, 1H, C_6H_5), 6.89–6.92(m, 1H, C_6H_5), 7.07–7.09 (d, 1H, C_6H_5, J = 8.08 Hz), 7.35–7.38 (m, 1H, C_6H_5), 7.89–7.92 (d, 1H, C_6H_5, J = 8.72 Hz), 8.02–8.04 (d, 1H, C_6H_5, J = 8.8 Hz); ^{13}C NMR (100 MHz, DMSO-d_6): δ 189.2 (C=O), 176.5, 160.7 (C=N), 142.7, 132.6, 128.6, 126.9, 124.9, 118.2, 112.9, 55.2, 41.6, 29.5, 26.8, 21.8, 18.9; MS m/z 426 (M+1) (100%), 428 (M+3) 32%. Anal. Calc. for $C_{22}H_{20}ClN_3O_2S$: C, 62.04; H, 4.73; N, 9.87; S, 7.53. Found: C, 62.08; H, 4.68; N, 9.78; S, 7.48.

Conclusion

All the newly synthesised indazolyl-thiazol-4(5*H*)-ones have been characterised by ^{1}H NMR, ^{13}C NMR, mass and IR studies.

X-ray diffraction studies of indazolyl-thiazol-4(5*H*)-one **5a** have been reported first time. ^{1}H NMR and ^{13}C NMR spectral data obtained from DFT studies of *cis* and *trans* diastereoisomers was correlated with experimental results. All new compounds were screened for their in *vitro* antibacterial and antifungal activities. It is evidenced that some compounds have emerged as potent antibacterial and antifungal agents endowed with moderate activities.

Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.saa.2014.06.134.

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