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Synthesis, spectroscopic characterization and DFT studies on the novel indeno-thiazolopyrimidine heterocyclic system

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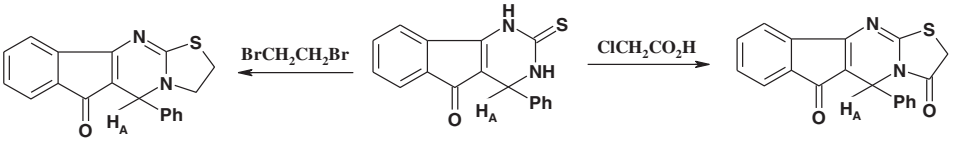
4-Phenyl-2-thioxo-3,4-dihydro-1H-indeno[1,2-d]pyrimidin-5(2H)-one **2**, obtained by stirring a mixture of indane-1,3-dione, benzaldehyde and thiourea in acetic acid at room temperature for 12 h, on reaction with chloroacetic acid and 1,2-dibromoethane furnish compounds **3** (or **6**) and **4** (or **7**), respectively. The regiochemistry of the cyclized products and their structure is established by an elemental analysis, ^{1}H NMR, ^{13}C NMR, IR and mass spectral data. Density functional theory calculations have been carried out for compounds **3** and **4** and their isomers **6** and **7** with Jaguar version 6.5112 using the B3LYP density functional method and LACVP* basis set. ^{1}H and ^{13}C NMR of compounds **3**, **4**, **6** and **7** have been calculated. 2-Arylidene derivatives of **3** were obtained by two routes and their structure was established by spectral data.



Keywords: indane-1,3-dione; regiochemistry; spectral data; arylidene derivatives; DFT

1. Introduction

Thiazolidinone, with a carbonyl group at positions 2, 4, or 5 [1] have been subjected to an extensive study in the recent past. Among them, 4-thiazolidinone is the most important scaffold known to be associated with several biological activities such as antibacterial,[2] antiprotozoal,[3] antifungal,[4] anticonvulsant,[5] anticancer,[6] antituberculosis,[7] antiparasitic,[8] anti-inflammatory,[9] and herbicidal agents.[10] 4-Thiazolidinones have also been reported as novel inhibitors of the bacterial enzyme Mur B, which is a precursor during the biosynthesis of peptidologycan [11] and also non-nucleoside inhibitors of HIV RT [12] and HIV-1 integrase inhibitors.[13]

Indenopyrimidine is an important substructure found in a number of active heterocyclic compounds. The indenopyrimidines have been proved to be a novel class of non-steroidal aromatase inhibitors, which are useful in the treatment of estrogen-dependent diseases.[14] Fused indenopyrimidine heterocycles have been found to exhibit solid-state fluorescent,[15] anticancer,[16] and antiHIV [17] properties.

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In view of the wide spectrum activities of condensed 4-thiazolidinones, it was thought worthwhile to undertake the synthesis of heterocyclic systems in which 4-thiazolidinone nucleus is fused to another biologically active heterocyclic ring. The product is expected to exhibit more biological activity due to the synergic effect. In the present paper, 4-thiazolidinone nucleus is fused with the indenopyrimidine system to yield two novel heterocyclic systems as 5-phenylindeno[1,2-d]thiazolo[3,2-a]pyrimidine-3,6(2H,5H)-dione **3** and 5-phenyl-2,3-dihydroindeno[1,2-d]thiazolo[3,2-a]pyrimidin-6-(5H)-one **4**. The structure and regiochemistry of these compounds are established by spectral and computational methods.

2. Computational studies

The molecular geometry optimization and ^{1}H and ^{13}C NMR spectra calculations were performed with the Jaguar software package version 6.5112 by using density functional theory (DFT) methods with B3LYP (Becke three parameter Lee-Yang-Parr) exchange correlation functional, which combines the hybrid exchange functional of Becke,[18] with the gradient-correlation functional of

Table 1. Selected bond lengths and bond angles of the optimized compound **3**.

	Bond lengths (Å)		Bond angles (°)	
Sr. no.	Entry	Optimized lengths	Entry	Optimized angles
1	C16–H31	1.113	O25–C15–C16	122.5
2	C16–H30	1.113	O25–C15–N11	122.6
3	C15–O25	1.208	C16–C15–N11	118
4	C15–C16	1.509	C12–N13–C9	115
5	C12–S17	1.856	S17–C12–N13	126
6	N11–C15	1.462	N13–C12–N11	126
7	N11–C12	1.462	C15–N11–C12	124
8	C10–C19	1.497	C15–N11–C10	108
9	C10–H18	1.113	C12–N11–C10	108
10	C10–N11	1.47	H18–C10–N11	107.5
11	C9–N13	1.456	N13–C9–C8	120
12	C8–C10	1.497	N13–C9–C5	120
13	C8–C9	1.337	O14–C7–C8	123
14	C7–O14	1.208	O14–C7–C4	123

Table 2. Selected bond lengths and bond angles of the optimized compound **4**.

	Bond lengths (Å)		Bond angles (°)	
Sr. no.	Entry	Optimized lengths	Entry	Optimized angles
1	C(23)–H(37)	1.1130	H(37)–C(23)–H(36)	109.4
2	C(23)–H(36)	1.1130	H(36)–C(23)–C(22)	109.4
3	C(22)–H(35)	1.1130	H(35)–C(22)–H(34)	109.4
4	C(22)–H(34)	1.1130	C(9)–N(13)–C(12)	115
5	S(24)–C(12)	1.8560	S(24)–C(12)–N(13)	126
6	C(23)–S(24)	1.7900	N(13)–C(12)–N(11)	126
7	C(22)–C(23)	1.5230	C(22)–N(11)–C(12)	108
8	N(11)–C(22)	1.4700	C(12)–N(11)–C(10)	108
9	C(10)–H(15)	1.1130	C(16)–C(10)–H(15)	109.3
10	C(7)–O(14)	1.2080	H(15)–C(10)–N(11)	107.5
11	N(13)–C(9)	1.4560	N(13)–C(9)–C(5)	120
12	C(12)–N(13)	1.2600	N(13)–C(9)–C(8)	120
13	N(11)–C(12)	1.4620	O(14)–C(7)–C(8)	123
14	C(10)–N(11)	1.4700	O(14)–C(7)–C(4)	123

Lee *et al.* [19]. The LACVP* basis set was used for calculations in the gas phase of the structures **3** and **4** and their isomers **6** and **7**, respectively. Since the crystal structure of the molecules is not available, a DFT calculation was carried out to predict the geometry of the molecules. The optimized bond lengths and bond angles obtained by geometry optimization at the B3LYP/LACVP* level of theory of structures **3** and **4** are reported in Tables 1 and 2, respectively. In the case of structure **3**, the optimized bond lengths of C=O and C–S in thiazolidinone ring fall in the range of 1.208 Å (1.211 Å) and 1.856 Å (1.768 Å). The optimized bond angles for O–C–N and S–C–N were observed at 122.6° (124.24°) and 126° (124.4°). In the case of structure **4**, the optimized bond lengths of C=O in indanone ring and S–C in thiazolidine ring fall in the range of 1.208 Å (1.211 Å) and 1.856 Å (1.768 Å). The optimized bond angles for C–N–C and S–C–N were observed at 108° (112.6°) and 126° (124.4°). The Z-matrix (*X*, *Y*, *Z* coordinates of minimized structures 3, 4, 6, and 7) are reported as supplementary information (Table S1–S4). The optimized configurations of structures **3** and **4** and their isomers **6** and **7** with atom numbering schemes are shown in Figure 1.

Shielding tensors of structures **3, 4, 6,** and **7** were evaluated using the B3LYP functional with the basis set given above. In order to express the chemical shifts in parts per million (ppm), the geometry of tetramethylsilane (TMS), benzene and chloroform molecules had been optimized and then their ^{1}H and ^{13}C NMR spectra were calculated by the same method using same the basis

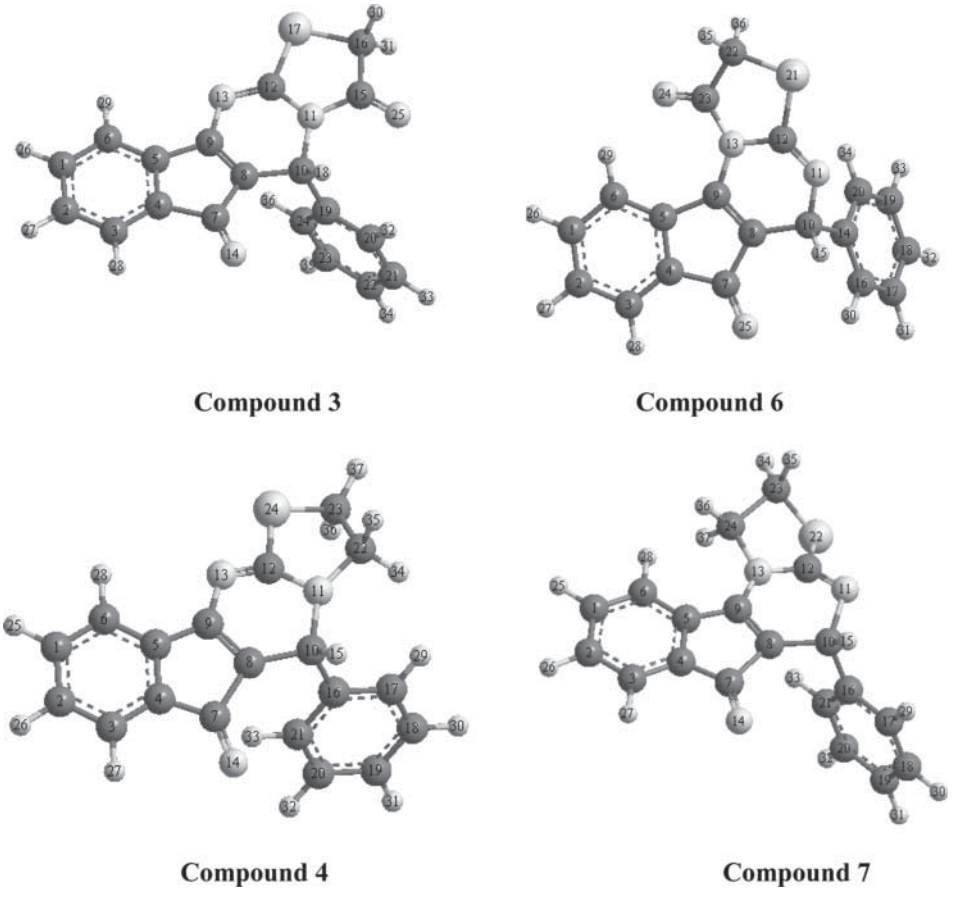


Figure 1. Optimized geometry of compounds 3, 4 and their isomers 6, 7.

Table 3. Experimental and calculated ^{1}H NMR chemical shifts (ppm) of the title compound **3** and its isomer **6**.

Structure **3**					Structure **6**			
Entry	Expt. NMR	Calc. shield	Calc. NMR	Averaged NMR	Entry	Calc. shield	Calc. MR	Averaged NMR
H18	5.96	26.9551	5.73		H15	27.5011	5.21	
H26		24.9244	7.68		H26	25.3692	7.25	
H27	7.28	25.0735	7.54	7.71	H27	25.5140	7.11	7.48
H28		24.7781	7.82		H28	25.0324	7.58	
H29		24.8015	7.80		H29	24.6011	7.99	
H30	4.21	29.2693	3.51		H35	29.4365	3.35	
H31	4.20	29.3701	3.41		H36	29.4485	3.34	
H32		24.7465	7.85		H34	25.8252	6.81	
H33	7.35	25.0724	7.54	7.54	H33	25.4375	7.19	7.21
H34		25.0514	7.56		H32	25.4579	7.17	
H35		25.1962	7.42		H31	25.3546	7.27	
H36		25.2587	7.36		H30	24.9516	7.65	

Table 4. Experimental and calculated ^{1}H NMR chemical shifts (ppm) of the compound **4** and its isomer **7**.

Structure **4**					Structure **7**			
Entry	Expt. NMR	Calc. shield	Calc. NMR	Averaged NMR	Entry	Calc. shield	Calc. NMR	Averaged NMR
H15	5.59	27.1477	5.97		H15	27.086	6.05	
H25		25.524	8.00		H25	25.3629	8.21	
H26	7.24	25.7848	7.68	8.05	H26	25.6811	7.81	8.14
H27		25.101	8.53		H27	25.008	8.65	
H28		25.534	7.99		H28	25.6281	7.87	
H29		24.9237	8.75		H29	24.9905	8.67	
H30		24.9931	8.67		H30	24.9482	8.73	
H31	7.48	25.0989	8.53	8.54	H31	25.0027	8.66	8.82
H32		25.0934	8.54		H32	24.9154	8.77	
H33		25.3355	8.24		H33	24.5192	9.26	
H34	3.85	29.4924	3.05		H36	28.1236	4.76	
H35	3.48	29.0762	3.57		H37	28.0595	4.84	
H36	3.36	28.1222	4.76	4.72	H34	27.7064	5.28	5.35
H37		28.1759	4.69		H35	27.6019	5.41	

set as in the case of the calculations on structures **3, 4, 6,** and **7**. The calculated isotropic shielding constants σ_i were then transformed to chemical shifts relative to TMS by the equation

$$\delta_i = \sigma_{TMS} \quad - \sigma_i$$

Experimental and calculated ^{1}H and ^{13}C NMR chemical shifts (ppm) of compounds **3** and **4** and their isomers **6** and **7** have been compared in Tables 3–6. The correlation values of proton chemical shifts are found to be 0.9990 for structure **3** and 0.9884 for its isomer **6** (Figure 2) and 0.9680 for structure **4** and 0.9464 for its isomer **7** (Figure 3). Similarly, the correlation values of carbon chemical shifts of **3** and **6** are found to be 0.9976 and 0.8779 (Figure 4). ^{13}C chemical shift correlation values of **4** and its isomer **7** are found to be 0.9915 and 0.9770 (Figure 5), respectively. The theoretical and experimental ^{1}H and ^{13}C data show good correlations for proposed structures **3** and **4**. A similar correlation obtained for ^{1}H and ^{13}C data of the related compounds **8**, **9**, **10**, and **11** (Figure 6) validates the claim of structures **3** and **6**. Moreover, the structure of **8** is proved by the X-ray crystallography. This work is unpublished and submitted to another journal for

Table 5. Experimental and calculated ^{13}C NMR chemical shifts (ppm) of the compound **3** and its isomer **6**.

Structure **3**				Structure **6**		
Entry	Expt. NMR	Calc. shield	Calc. NMR	Entry	Calc. shield	Calc. NMR
C1	138.9	70.5965	145.57	C1	63.1448	154.28
C2	132.7	75.1962	140.19	C2	71.342	144.70
C7	167.51	42.2811	178.68	C7	35.9439	186.09
C10	55.8	150.9021	51.66	C10	148.5718	54.38
C12	160.7	54.1587	164.8	C12	23.7274	200.38
C15	170.09	37.1898	184.64	C23	73.6158	142.04
C16	32.5	174.5018	24.06	C22	169.8781	29.46

Table 6. Experimental and calculated ^{13}C NMR chemical shifts (ppm) of the compound **4** and its isomer **7**.

Structure **4**				Structure **7**		
Entry	Expt. NMR	Calc. shield	Calc. NMR	Entry	Calc. shield	Calc. NMR
C1	134	78.5641	134.17	C1	77.3528	135.54
C5	139	72.9833	140.47	C5	71.5582	142.08
C7	190	18.4964	201.94	C7	14.0009	207.01
C12	172	51.4566	164.75	C12	57.3767	158.07
C22	58	150.453	53.07	C24	151.722	51.63
C23	25	186.451	12.45	C23	181.507	18.03

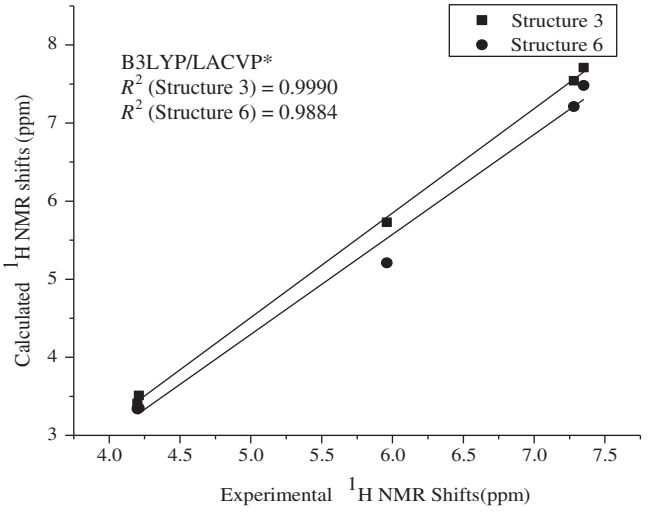


Figure 2. Plot of the calculated vs. the experimental ^{1}H NMR chemical shifts (ppm).

publication. The correlation graphs are reported as supplementary information (Figures S1–S4). Another similar system starting from 2-tetralone has been synthesized and the correlation of ^{1}H and ^{13}C data has shown the similar results, and the work is under preparation for publication. Dispersion corrected energies and zero point energies theoretically obtained for structures **3**, **4**, **6**, and **7** are reported in Table 7.

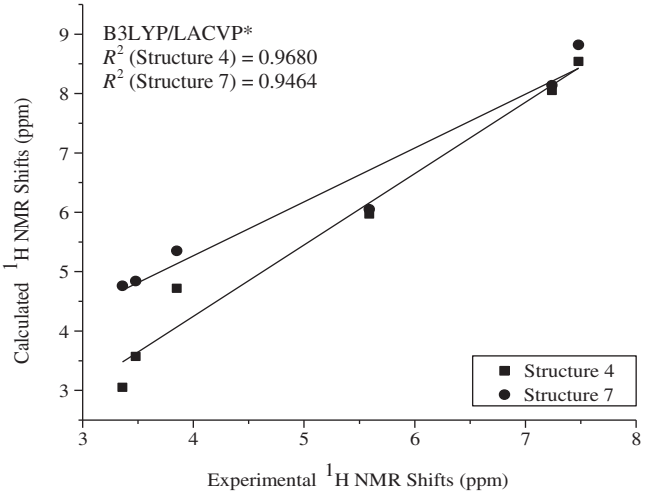


Figure 3. Plot of the calculated vs. the experimental ^{1}H NMR chemical shifts (ppm).

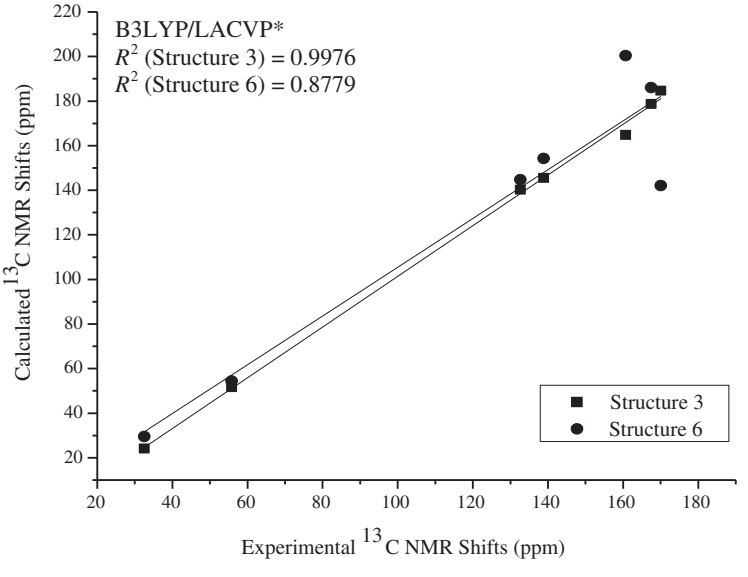


Figure 4. Plot of the calculated vs. the experimental ^{13}C NMR chemical shifts (ppm).

3. Results and discussion

Compound **2** was obtained by our group earlier [20] by stirring a mixture of indane-1,3-dione **1**, benzaldehyde and thiourea in the acetic acid at room temperature for 12 h. IR spectrum of compound **2** shows absorption bands at 1674 (C=O) and 1173 (C=S). In its ^{1}H NMR, H_A proton appears at δ 5.36 and in mass spectrum exhibition of molecular ion peak at m/z 293 [$M^+ + 1$] (12%) confirms its structure. This unsymmetrical thione on reaction with chloroacetic acid followed by the cyclization of the intermediate in situ was likely to furnish compound **3** (or **6**) or both (Scheme 1) depending on the mode of the cyclization. However, the thione **2** when treated with chloroacetic acid in the presence of anhyd. sodium acetate, glacial acetic acid,

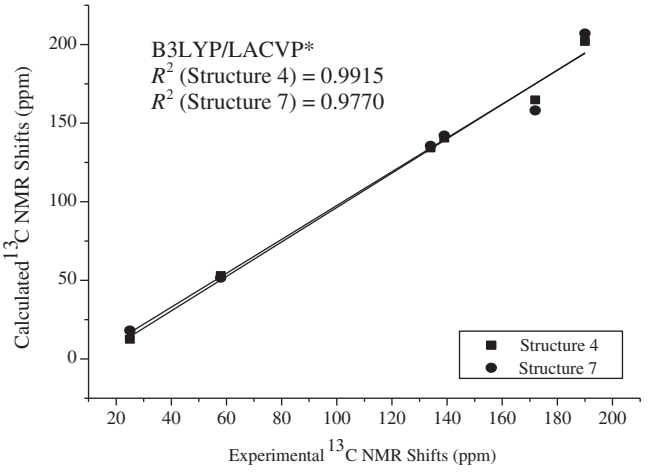
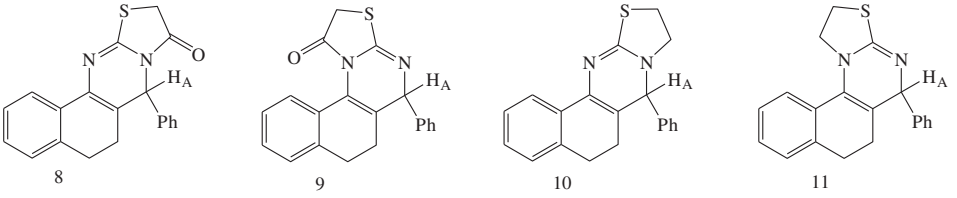


Figure 5. Plot of the calculated vs. the experimental ^{13}C NMR chemical shifts (ppm).



8 9 10 11

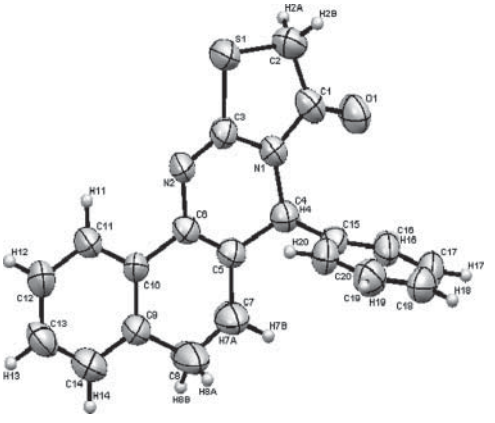


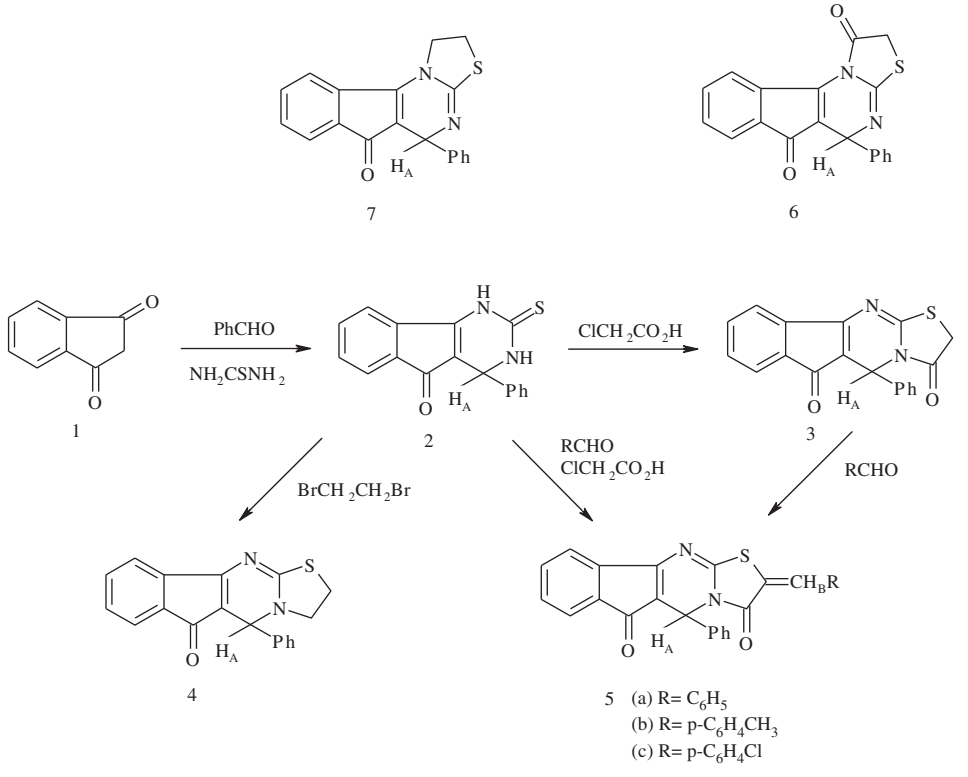
Figure 6. Ortep diagram obtained from X-ray of 7-Phenyl-7,10-dihydro-5*H*-benzo[*h*]thiazolo[2,3-*b*]quinazolin-9(6*H*)-one (**8**).

and acetic anhydride afforded a single product (TLC) **3** or **6** in 85% yield. The appearance of a band at 1736 cm^{-1} (C=O) in the IR spectrum, appearance of peaks at δ 170, 167 (C=O) in ^{13}C NMR spectrum and exhibition of a molecular ion peak at m/z 333 [M$^+$ + 1] (100%) in the mass spectrum of the TLC-pure product suggested that the cyclization had indeed taken place. The IR and mass spectral data were of little help in deciding in the favor of either structure **3** or **6**. However, the structure **3** was finally assigned to this cyclization product in preference to the structure **6** on the basis of ^{1}H NMR spectral data.

The reaction of compound **2** with 1, 2-dibromoethane gave a product which was purified by column chromatography and characterized by its molecular ion peak at m/z 319 [M$^+$ + 1] (100%)

Table 7. Theoretically computed energies for structures **3, 4, 6** and **7**.

Sr. no.	Parameters	Structure **3**	Structure **6**	Structure **4**	Structure **7**
1	Dispersion corrected energies (Kcal/mol)	−871406.74	−871397.32	−824959.19	−824956.68
2	Zero point energy (Kcal/mol)	168.61	181.70	195.72	195.81



Scheme 1. Reaction of 4-phenyl-2-thioxo-3,4-dihydro-1H-indeno[1,2-d]pyrimidin-5(2H)- one **2** with chloroacetic acid and 1,2-dibromoethane.

as a compound which could be represented by either structure **4** or **7**. In either structure (**4** or **7**), the singlet at δ 5.59 in its ^{1}H NMR spectrum integrating for one proton was assignable to H_A. If the structure **6** is correct for the cyclization product, obtained from thione **2** and chloroacetic acid, then H_A will resonate in the same region as that of structure **4** (or **7**). On the other hand, if the structure **3** is correct, H_A will be deshielded by the thiazolidinone ring and consequently, H_A will resonate downfield in comparison to H_A in **4** (or **7**). The appearance of a downfield singlet at δ 5.96 for H_A in structure **3** (or **6**) as compared to singlet at δ 5.59 for H_A in structure **4** (or **7**) supported the structure **3** and ruled out the structure **6** from which such a downfield shift would not be expected. The deshielding effect is due to the magnetic anisotropy of the C=O group with a minor contribution from the rest of the ring.

Although the comparison of the chemical shifts of H_A in the structures **3** and **4** (or **7**) is on a better footing, on the basis that both structures **3** and **4** (or **7**) are tetracyclic compounds, yet the same conclusion is derived by comparing the chemical shifts of H_A of the thione **2** with that of the cyclization product **3**. The H_A proton in thione **2** resonates at δ 5.36, whereas the downfield signal at δ 5.96 (s, 1H, H_A) in the cyclized product also favors the structure **3** in preference to structure **6**.

As expected in **3**, H_A will appear downfield in comparison to its isomer **6** due to the anisotropic effect of carbonyl group of the thiazolidinone ring. H_A (H18) of structure **3** appears at δ 5.96 (calc. δ 5.73), while in structure **6**, the chemical shift of the same proton H_A (H15) is calculated at δ 5.21. The experimental values of chemical shifts of different protons and carbons in structures **3** and **4** are in compliance with calculated values as compared to structures **6** and **7**. ^{13}C NMR spectrum of structure **3** exhibits two peaks at δ 170 and 167 assigned to carbonyl groups of indanone and thiazolidinone rings, respectively. These carbon chemical shifts are in good correlation with theoretical values of **3** but not for its isomer **6**.

Arylidene thiazolidinones (**5**) were prepared by two routes. In the first approach, thiazolidinone **3** was condensed with aldehydes to give arylidene thiazolidinones (**5a–5c**), while in the second approach, compound **5a** was obtained directly by heating compound **2** with chloroacetic acid and benzaldehyde. The structures **5a–5c** were established by IR and ^1H NMR spectral data. The parent thiazolidinone **3** exhibited an absorption band at 1736 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 (**5a–5c**) produced a bathochromic shift [21] as expected. The carbonyl absorption band appeared at 1713, 1705, and 1713 cm^{-1} in structure **5a–5c**, respectively.

Finally, the structure **3** is supported by a further downfield shift in the absorption spectrum of proton H_A (δ 6.21, 6.14, and 6.20, respectively) in arylidene derivatives **5a–5c** as compared to **3** (δ 5.96) due to the extended conjugation of carbonyl group. This could happen only in structure **3** but not possible for structure **6**. It is clear from the total energy obtained from DFT studies that the proposed structure **3** is stable by 5.348 Kcal/mol energy from its isomer **6** (Table 7).

The structure **4** (not **7**) for the product, obtained from the reaction of compound **2** with 1, 2-dibromoethane, was assigned based upon the analogy with compound **3**. The structure **4** is further supported by the fact that its carbon and proton chemical shifts are in good correlation with DFT values rather than of structure **7**. Dispersion corrected DFT calculations were carried out for all the molecules and their dispersion corrected energies obtained supports structures 3 and 4 (Table 7).

4. Experimental

4.1. *Instrumentations*

Melting points were determined in sulfuric acid bath and are uncorrected. TLC was performed on silica gel G plates using pet ether-ethylacetate (4:1) as eluent and iodine vapors as visualizing agent. IR spectra were recorded on ABB FTIR spectrometer and the results are reported in cm^{-1}. ^1H NMR were recorded in DMSO-d_6 on a BRUKER ADVANCE II 400 NMR spectrometer using TMS as an internal standard (chemical shift in δ, ppm). The elemental analysis of compounds was performed on a Carlo Erba-1108 elemental analyzer. The structures were optimized by molecular mechanics using PM3 method based on Hyperchem with version 7.5 packages. Dispersion corrected DFT was carried out using B97-D with Win Gamess version 2009.

4.2. *Procedure for the synthesis of 4-Phenyl-2-thioxo-3,4-dihydro-1H-indeno[1,2-d]pyrimidin-5(2H)-one 2*

This compound was synthesized by a conventional as well as solvent-free method using ionic liquid by our group earlier.[20]

Yield 90%; mp 224–226°C. IR spectrum, ν, cm^{-1}: 1674 (C=O), 1636 (C=C), 1173 (C=S). ^1H NMR spectrum (400 MHz, DMSO-d_6): δ 5.36 (s, 1H, H_A), 7.25–7.39 (m, 8H, C_6H_5), 7.86–7.91

(m, 1H, C_6H_5), 9.77 (br, 1H, NH), 11.68 (br, 1H, NH). Mass spectrum, m/z (I, %): 293 [$M^+ + 1$] (12). $C_{17}H_{12}N_2SO$. Calcd: C, 69.86; H, 4.11; N, 9.59; S, 10.96. Found: C, 69.80; H, 4.18; N, 9.51; S, 10.89.

4.3. *Procedure for synthesis of 5-Phenylindeno[1,2-d]thiazolo[3,2-a]pyrimidine-3,6 (2H,5H)-dione 3*

A mixture of thione **2** (2.92 g, 0.01 mol), chloroacetic acid (0.94 g, 0.01 mol) and anhyd. sodium acetate (0.82 g, 0.01 mol), glacial acetic acid (15 ml) and acetic anhydride (1.0 ml) was refluxed for 5 h. The reaction mixture was kept overnight. The solid thus separated was filtered, washed with cold ethanol, and recrystallized from ethanol to give compound **3** as orange solid.

Yield 85%; mp 202–204°C. IR spectrum, ν, cm^{-1}: 1736 (C=O), 1690 (C=O), 1582 (C=N). ^1H NMR spectrum (400 MHz, DMSO-d_6): δ 4.20–4.21 (m, 2H, SCH_2), 5.96 (s, 1H, H_A), 7.28–7.29 (m, 4H, C_6H_5), 7.34–7.39 (m, 5H, C_6H_5).^{13}C NMR spectrum (100 MHz, DMSO-d_6): δ 170, 167 (C=O), 160 (C=N), 140, 138, 133, 132, 130, 128, 127, 122, 119, 111 (Ph-C), 55, 32, 30. Mass spectrum, m/z (I, %): 333 [$M^+ + 1$] (100). $C_{19}H_{12}N_2O_2S$. Calcd: C, 68.67; H, 3.61; N, 8.43; S, 9.64. Found: C, 68.60; H, 3.69; N, 8.37; S, 9.70.

4.4. *Procedure for the synthesis of 5-Phenyl-2,3-dihydroindeno[1,2-d]thiazolo[3,2-a]pyrimidin-6-(5H)-one 4*

Compound **4** was obtained by stirring a mixture of thione **2** (0.292 g, 0.001 mol) and 1,2-dibromoethane (5.0 ml) at 110°C for 4 h. The crude solid, thus separated, was purified by column chromatography to give compound **4** as orange solid.

Yield 75%; mp 172–174°C. IR spectrum, ν, cm^{-1}: 1690 (C=O), 1643 (C=N). ^1H NMR spectrum (400 MHz, DMSO-d_6): δ 3.30–3.43 (m, 2H, SCH_2), 3.45–3.51 (m, 1H, NCH_2), 3.83–3.86 (m, 1H, NCH_2), 5.59 (s, 1H, H_A), 7.24–7.48 (m, 9H, C_6H_5).^{13}C NMR spectrum (100 MHz, DMSO-d_6): δ 190, 172, 164, 155, 140, 139, 138, 136, 135, 134, 131, 129, 127, 126, 121, 118, 116, 58, 51, 25. Mass spectrum, m/z (I, %): 319 [$M^+ + 1$] (100). $C_{19}H_{14}N_2SO$. Calcd: C, 71.70; H, 4.40; N, 8.81; S, 10.06. Found: C, 71.77; H, 4.48; N, 8.89; S, 10.12.

4.5. *Procedure for synthesis of arylidene derivatives 5a–5c:*

Arylidene derivatives were prepared by two routes:

(i) A mixture of thiazolidinone **3** (0.332 g, 0.001 mol), aromatic aldehydes (0.001 mol), anhyd. sodium acetate (0.082 g, 0.001 mol) and glacial acetic acid (10 ml) was heated under reflux for 4 h. The reaction mixture was cooled at room temperature and filtered the solid thus obtained, crystallized from DMF-ethanol (1:1) mixture to give compounds **5a**–**5c**.

(ii) A mixture of thione **2** (0.292 g, 0.001 mol), aromatic aldehydes (0.001 mol), chloroacetic acid (0.094 g, 0.001 mol) and anhyd. sodium acetate (0.082 g, 0.001 mol) in glacial acetic acid (10 ml) and acetic anhydride (1 ml) was refluxed for 4 h. A similar work up as in (i) gave compounds **5a**–**5c**.

4.5.1. *2-Benzylidene-5-phenylindeno[1,2-d]thiazolo[3,2-a]pyrimidine-3,6(2H,5H)-dione **5a***

Brown solid, yield 70%; mp 124–126°C. IR spectrum, ν, cm^{-1}: 1713, 1690 (C=O), 1605 (C=N). ^1H NMR spectrum (400 MHz, $CDCl_3$): δ 6.21 (s, 1H, H_A), 7.26–7.53 (m, 14H, ArH), 7.82

(s, 1H, H_B). $C_{26}H_{16}N_2O_2S$. Calcd: C, 74.29; H, 3.81; N, 6.67; S, 7.62. Found: C, 74.21; H, 3.88; N, 6.59; S, 7.69.

4.5.2. *(E)-2-(4-methylbezylidene)-5-phenylindeno[1,2-d]thiazolo[3,2-a]pyrimidine-3,6(2H,5H)-dione* ***5b***

Brown solid, yield 68%; mp 252–254°C. IR spectrum, ν, cm^{-1}: 1705, 1680 (C=O), 1582 (C=N). ^1H NMR spectrum (400 MHz, DMSO-d_6): δ 2.53 (s, 3H, CH_3), 6.14 (s, 1H, H_A), 7.25–7.52 (m, 9H, ArH), 7.57–7.64 (m, 2H, ArH), 7.74–7.77 (m, 1H, ArH), 7.82 (s, 1H, H_B), 8.01–8.04 (m, 1H, ArH). $C_{27}H_{18}N_2O_2S$. Calcd: C, 74.65; H, 4.15; N, 6.45; S, 7.37. Found: C, 74.58; H, 4.10; N, 6.52; S, 7.30.

4.5.3. *(E)-2-(4-chlorobenzylidene)-5-phenylindeno[1,2-d]thiazolo[3,2-a]pyrimidine-3,6(2H,5H)-dione* ***5c***

Brown solid, yield 72%; mp 256–258°C. IR spectrum, ν, cm^{-1}: 1713, 1695 (C=O), 1582 (C=N). ^1H NMR spectrum (400 MHz, DMSO-d_6): δ 6.20 (s, 1H, H_A), 7.27–7.31 (m, 4H, ArH), 7.33–8.05 (m, 9H, ArH), 7.51(s, 1H, H_B). $C_{26}H_{15}N_2O_2SCl$. Calcd: C, 68.65; H, 3.30; N, 6.16; S, 7.04. Found: C, 68.72; H, 3.38; N, 6.10; S, 7.10.

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Supplementary online material

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