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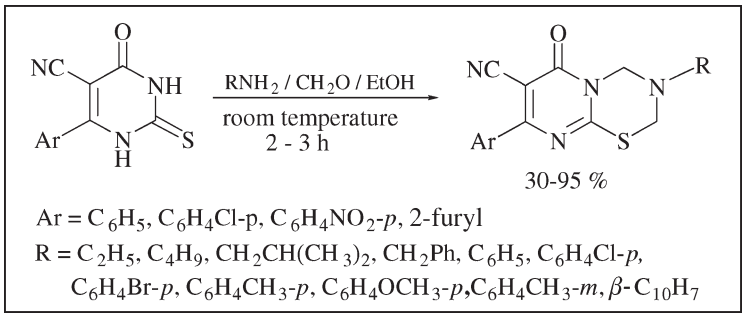

Reaction of 6-aryl-5-cyano-2-mercapto-3,4-dihydropyrimidin-4-ones with formaldehyde and primary amines in suitable solvent via a double Mannich reaction gave the corresponding 8-aryl-7-cyano-3-*N*-substituted-pyrimido[2,1-b]-1,3,5-thiadiazin-6-ones rather than the isomeric products 6-aryl-7-cyano-3-N-substituted-pyrimido[2,1-b]-1,3,5-thiadiazin-8-ones. The cyclization method was found to be the most favored for the formation of the linear products rather than the angular isomers. This was confirmed not only by using spectral analysis and molecular mechanical calculations but also by X-ray single crystal structure determination.

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INTRODUCTION

Although a few publications have been appeared since last 12 years describing the synthesis of 1,3,5-thiadiazines but literature survey on this class of heterocyclic system showed that 1,3,5-thiadiazines and its fused heterocycles possess a broad spectrum of biological interest [1]. It was found that functionalized thiadiazines have insecticidal [2], antibacterial [3], herbicidal [4], and fungicidal [5] effects. The broad biological activities of pyrimidine [6–12] and fused pyrimidine derivatives, prompted us to synthesize new derivative of pyrimidines fused heterocycles. During last decade, we were investigating the behavior of Mannich reaction toward the multifunctional heterocyclic compounds such as 5-mercapto-3-aryl-1,2,4-triazole (Fig. 1). We investigated this reaction in acidic, basic, and neutral mediums, and we concluded that in all cases only one isomeric product **1** was isolated, rather than the other isomeric products **2** [13–15].

Those findings encouraged us to investigate continually the use of functionality factor and the reaction medium. One of the advantages of this reaction is a wide variety to synthesize a number of varieties of poly heterocyclic compounds in one pot reaction which is difficult to obtain by another procedure. Pyrazolothiadiazines [13], Triazolothiadiazines [13,15], and thiadiazinobenzimidazoles [14] were also obtained in high-yields using double or triple Mannich reaction in one pot reaction. We have recently described that similar compounds could be synthesized *via* modification of Mannich reaction using di-functional compounds [13–15]. We found that the cyclization reactions to form the corresponding thiadiazines 1 are different from that reported by Wang and co-workers [16]. They suggested that the thiadiazine derivatives **2** were formed rather than the isomeric derivatives **1**.

In our laboratory, we investigated the Mannich reaction of polyfunctional heterocyclic compounds like 5-mercaptotriazoles, 5-aminopyrazoles, and 2-mercaptobenzimidazoles, which gave the corresponding 1,2,4-triazolo[3,2-b]-1,3,5-thiadiazines **1**, pyrazolo[3,4-d]pyrimidines **3**, and 1,3,5-thiadiazino[3,2-a]benzimidazoles **4**, respectively in high-yield [13–15] (Fig. 2).

RESULTS AND DISCUSSION

In this study, we focused on the susceptibility and selectivity of the cyclization of 6-aryl-5-cyano-2-thioxo-1,2,3,4-tetrahydropyrimidin-4-one (**5a–d**) towards the double Mannich reaction. On treatment of the poly

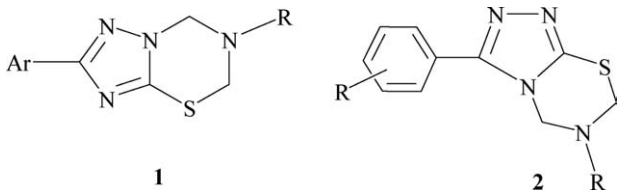


Figure 1. 1,2,4-Triazolo[3,2-b]-1,3,5-thiadiazines **1** and **2**.

functional compounds **5a–d** with one equivalent of variant primary aliphatic and aromatic amines with excess of formaldehyde (37%) in ethanol, ethanol/dioxane and ethanol/acetic acid at room temperature the reaction might proceed to afforded the corresponding 8-aryl-7-cyano-3-N-substituted-pyrimido[2,1-b]-1,3,5-thiadiazin-6-ones (**6–9**) or the other isomeric products 6-aryl-7-cyano-3-N-substituted-pyrimido[2,1-b]-1,3,5-thiadiazin-8-ones (**10–13**) or possible a mixture of both isomeric products. However, based on TLC the reaction gave only single isolable products **6–9** in high-yields, (Scheme 1).

The IR spectra of the products lacked the NH absorption peaks and showed the C≡N and C=O peaks at 2220–2240 and 1650–1700 cm^{-1}, respectively, whereas the ^{1}H-NMR spectra of the reaction products were characterized by the appearance of two signals at δ 5.9–4.8 and 6.1–5.0 attributed to the two methylene groups SCH_2N and NCH_2N respectively in addition to the other protons at the expected chemical shifts. The Mass spectra of the synthesized compounds showed the expected molecular ion peaks and its CHNS analysis were found to be in agreement with the calculated ones. All these data presented here can't confirm which one of these isomers, **6–9** and **10–13** is formed.

We need a solid argument to prove whether the isomeric products formed **6–9** or **10–13**. This directed us to think about the tautomerism of compound **5a–d**, whether their structure existed in the form A or B. For example compound **5a** (R = Ph) is in equilibrium with the two forms A and B as shown in Figure 3.

Based on resonance effect, the tautomer A is more favorable than B as both the CN and CO groups are conjugated with the diene system. Further, this assumption was supported by the molecular mechanics calculations–MMXE, which showed that tautomer A is more stable than B. If double Mannich reaction occurred with tautomer A the product will be the isomeric compounds **6–9**, whereas, the isomeric products **10–13** could be obtained in case of the existence of the tautomer B in the reaction medium (Figure 3).

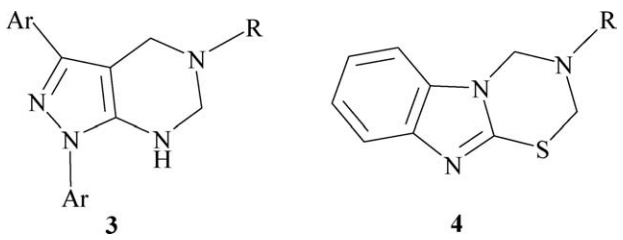
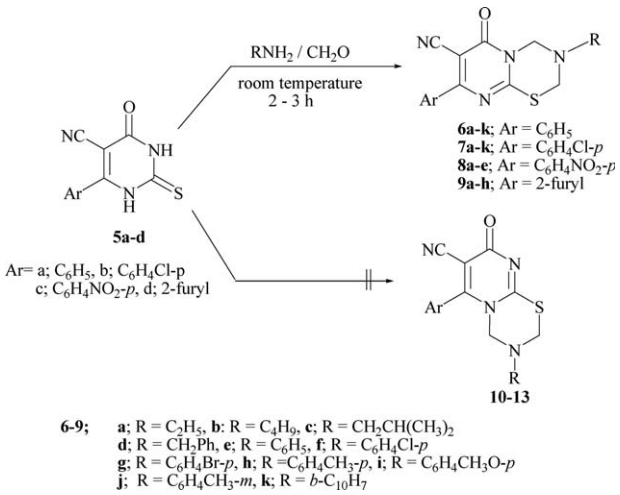


Figure 2. Pyrazolo[3,4-d]pyrimidines **3** and 1,3,5-thiadiazino[3,2-a]benzimidazoles **4**.

Scheme 1. Synthesis of pyrimido[2,1-b]-1,3,5-thiadiazines **6–9**.



Mechanistically, the formation of the cyclized compounds could be explained either by the addition of SH (route a) or NH (route b) group to the formed imines, which resulted from the condensation of formaldehyde with primary amine, (Scheme 2; Table 1). Based on both molecular modeling study and X-ray analysis of **6h** (Figures 4 and 5), the structure of the reaction product was assigned as the isomeric products **6–9** of lower energy rather than the isomeric products **10–13**. The formation of single product only indicates that the reaction is proceeded regioselectively. Recently, similar results were obtained by Dotsenko et al [17].

X-ray analysis of compound **6h** (Ar = C_6H_5, R = $C_6H_4CH_3$-p) $C_{20}H_{16}N_4OS$ VA/01/890 $P2_1/c$ 150K IPDS, Bond Distances (Ångstroms) (see Table 2–4).

BIOLOGICAL ACTIVITY

The antimicrobial activity of some synthesized compounds were determined by the usual disk assay [18] at

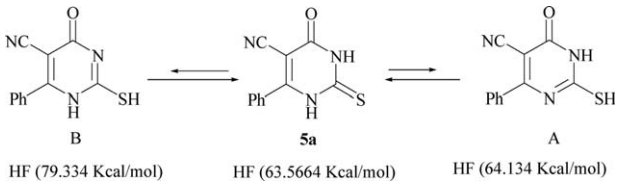
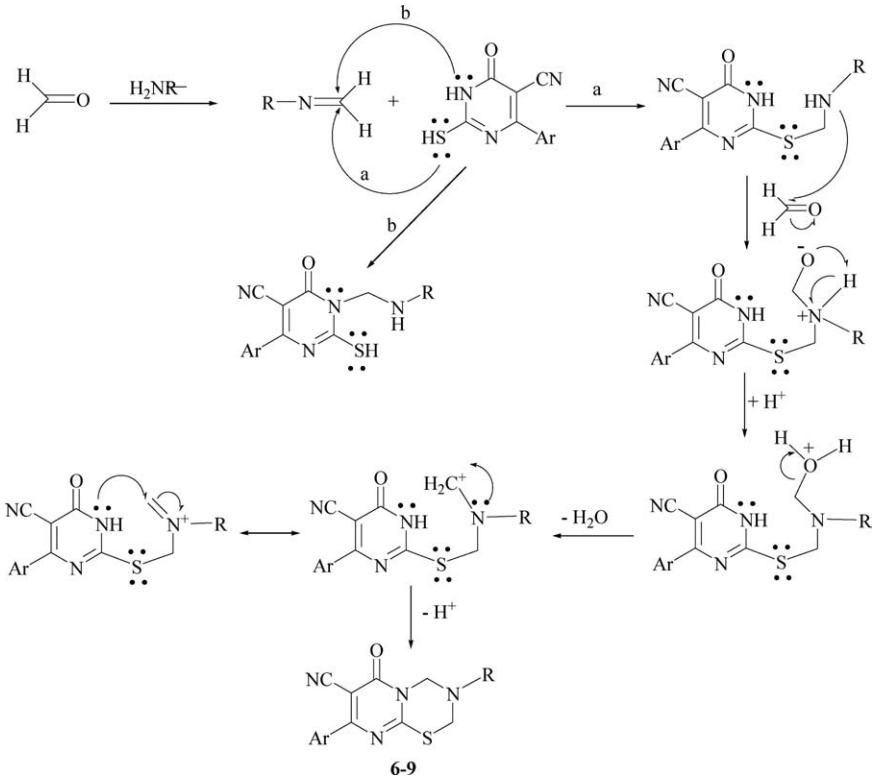


Figure 3. Tautomerism of the thiouracil derivative.

Scheme 2. The suggested mechanism of formation of the isomers **6–9**.



a concentration of (10^{-3} mol) per disk Inhibition zones in (cm) around filter paper disks (3 mm in diameter) were measured and the average of these reading was considered. From the antimicrobial used such as: a, *Bacillus cereus*; b, *E. coli*.

Compound no.	+Ve bacterial *Bacillus*	Diameter of inhibitor (cm)	−Ve bacterial *E. Coli*	Diameter of inhibitor (cm)
6a	+	0.6	+	1.5
6f	+	1	+	2
6h	+	0.2	+	0.9
7c	+	0.7	+	1
7i	+	0.3	+	1
7k	−	−	+	0.8
8b	+	0.7	+	2
8d	+	0.5	+	2.2
9e	−	−	+	1
9g	−	−	+	0.9
DMSO	−	−	−	−
CHL	+	4	+	3.2

CHL, chloramphenicol as standard.

The antimicrobial activity study revealed that all compounds screened showed moderate to weak antimicrobial activity, except compounds **6f**, **8b**, and **8d** have good effect.

EXPERIMENTAL

Melting points were determined using Gallen Camp melting point apparatus and are uncorrected. The IR-spectra were measured on a Shimatzu-470 spectrometer using KBr technique (ν cm^{-1}). The ^{1}H-NMR spectra were measured on a Varian EM-390,90MHz spectrometer (Spectral Unit, Assuit University, Egypt) and dx 500.13 MHz spectrometer (Department of Physical Chemistry, Geneva) using $CDCl_3$, DMSO- d_6 as a solvent and TMS was used as internal standard, δ ppm. The ^{13}C-NMR spectra were measured on dx 125.77 MHz spectrometer. The mass spectra were recorded on Jeol-Jms-600H spectrometer using the direct inlet system. The elemental analyses were performed using Perkin-Elmer elemental analyzer 240-C and the X-ray diffraction analysis from faculty of science, Geneva University.

General procedures for synthesis of 8-Arylpyrimido[2,1-b]-1,3,5-thiadiazine derivatives. A mixture of 5-Cyano-4-oxo-6-aryl-2-thioxo-1,2,3,4-tetrahydropyrimidine (1.0 mmole), primary amines (1.1 mmole) and formaldehyde (2 mL) was stirred in appropriate solvent (20 mL) at room temperature for 2–3 h. The resulting precipitate was collected by filtration, washed with water several times and dried well. The crude product was crystallized from the proper solvent to give the corresponding 8-phenyl-pyrimido[2,1-b]-1,3,5-thiadiazine derivatives.

8-phenylpyrimido [2,1-b]-1,3,5-thiadiazine derivatives (6a-k). These compounds were obtained according to general method using ethanol as solvent.

7-Cyano-3-ethyl-8-phenyl-3,4-dihydro-2H-pyrimido[2,1-b]-1,3,5-thiadiazin-6-one (6a). This compound was obtained as

Table 1

Heat of formations based on the molecular mechanics calculation (MMXE) of compounds **6–13**.

No.	HF	No.	HF	No.	HF	No.	HF
6a	87.700	**10a**	94.335	**7i**	80.360	**11i**	90.103
6b	71.456	**10b**	80.758	**7j**	110.106	**11j**	120.492
6c	124.489	**10c**	134.379	**7k**	136.573	**11k**	147.192
6d	117.719	**10d**	127.728	**8a**	89.755	**12a**	100.910
6e	129.488	**10e**	139.751	**8b**	76.137	**12b**	87.456
6f	116.817	**10f**	126.548	**8c**	79.074	**12c**	89.953
6g	87.322	**10g**	96.342	**8d**	121.659	**12d**	138.179
6h	116.841	**10h**	126.789	**8e**	129.529	**12e**	140.051
6i	143.271	**10i**	152.725	**9a**	69.418	**13a**	77.689
7a	78.220	**11a**	88.028	**9b**	55.812	**13b**	64.038
7b	64.609	**11b**	74.510	**9c**	56.745	**13c**	67.415
7c	67.551	**11c**	77.080	**9d**	102.831	**13d**	113.416
7d	111.687	**11d**	124.945	**9e**	108.786	**13e**	119.086
7e	117.747	**11e**	127.917	**9f**	102.033	**13f**	110.748
7f	110.986	**11f**	121.719	**9g**	113.843	**13g**	122.864
7g	122.764	**11g**	133.586	**9h**	101.168	**13h**	110.01
7h	110.371	**11h**	120.005				

HF, heat of formation (kcal/mol).

colorless crystals from ethanol, yield (0.25 g, 84 %). Mp 148–150°C. IR (KBr): 3050, 2995, 2200, 1660, 1520, 1470 cm^{-1}. ^{1}H-NMR (90 MHz, $CDCl_3$): δ = 1.1 (t, *J* = 2.7 Hz, 3H, NCH_2CH_3), 2.7 (q, *J* = 2.7 Hz, 2H, NCH_2CH_3), 4.6 (s, 2H, SCH_2N), 4.9 (s, 2H, NCH_2N), 7.0–8.1 ppm (m, 5H, arom-H).

Anal. Calcd for $C_{15}H_{14}N_4OS$: C, 60.38; H, 4.73; N, 18.78; S, 10.75. Found: C, 60.12; H, 4.60; N, 18.77; S, 10.76.

3-Butyl-7-cyano-8-phenyl-3,4-dihydro-2H-pyrimido[2,1-b]-1,3,5-thiadiazin-6-one (6b). This compound was obtained as colorless crystals from ethanol, yield (0.23 g, 71%). Mp 155–156°C. IR (KBr): 3080, 2995–2850, 2200, 1670, 1530, 1460 cm^{-1}. ^{1}H-NMR (90 MHz, $CDCl_3$): δ = 0.9 (t, *J* = 1.8 Hz, 3H, CH_2CH_3), 1.4 (m, 2H, CH_2CH_3), 2.3 (m, 2H, NCH_2CH_2), 2.7 (t, *J* = 2.25 Hz, 2H, NCH_2CH_2), 4.7 (s, 2H, SCH_2N), 5.0 (s, NCH_2N), 7.7–8.1 ppm (m, 5H, arom-H).

Anal. Calcd for $C_{17}H_{18}N_4OS$: C, 62.55; H, 5.56; N, 17.16; S, 9.82. Found: C, 62.45; H, 5.50; N, 17.12; S, 9.72.

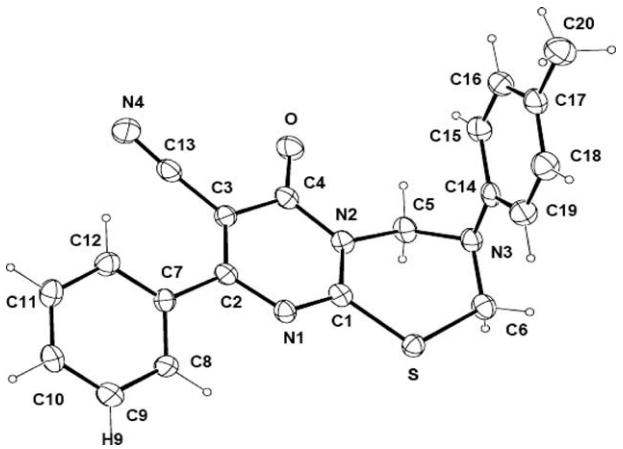


Figure 4. Single crystal X-ray of compound **6h** (Ar = C_6H_5, R = $C_6H_4CH_3$-*p*).

7-Cyano-3-isobutyl-8-phenyl-3,4-dihydro-2H-pyrimido[2,1-b]-1,3,5-thiadiazin-6-one (6c). This compound was obtained as colorless crystals from ethanol, yield (0.15 g, 64%). Mp 156–158°C. IR (KBr): 3080, 2995–2800, 2200, 1680, 1590, 1520 cm^{-1}. ^{1}H-NMR (90 MHz, DMSO-d_6): δ = 0.9 (d, *J* = 2.4 Hz, 6H, CH $(CH_3)_2$), 1.8 (m, 1H, $NCH_2CH(CH_3)_2$), 2.5 (d, *J* = 2.45 Hz, 2H, NCH_2CH), 4.9 (s, 2H, SCH_2N), 5.15 (s, NCH_2N) 7.5–8.1 ppm (m, 4H, arom-H). Anal. Calcd for $C_{17}H_{18}N_4OS$: C, 62.55; H, 5.56; N, 17.16; S, 9.82. Found: C, 62.42; H, 5.49; N, 17.10; S, 9.78.

3-Benzyl-7-cyano-8-phenyl-3,4-dihydro-2H-pyrimido[2,1-b]-1,3,5-thiadiazin-6-one (6d). This compound was obtained as

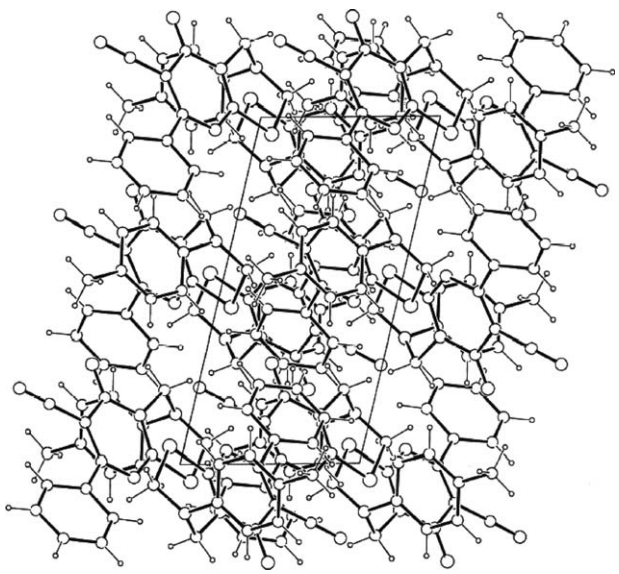


Figure 5. Crystal structure of compound **6h** (Ar = C_6H_5, R = $C_6H_4CH_3$-*p*).

Table 2

Bond distances (Å) of compound **6h**.

Bond	Distance (Å)	Bond	Distance (Å)
S—C6	1.871(2)	S—C1	1.745(2)
N1—C1	1.313(2)	O—C4	1.228(2)
N2—C1	1.369(2)	N1—C2	1.357(2)
N2—C5	1.505(2)	N2—C4	1.405(2)
N3—C6	1.429(2)	N3—C5	1.438(2)
N4—C13	1.159(3)	N3—C14	1.433(3)
C2—C7	1.495(2)	C2—C3	1.398(2)
C3—C13	1.425(3)	C3—C4	1.460(2)
C7—C12	1.393(3)	C7—C8	1.403(2)
C9—C10	1.381(3)	C8—C9	1.392(3)
C11—C12	1.401(3)	C10—C11	1.383(3)
C14—C19	1.402(2)	C14—C15	1.396(3)
C16—C17	1.403(2)	C15—C16	1.384(3)
C17—C20	1.511(3)	C17—C18	1.378(3)
		C18—C19	1.396(3)

Table 3

Bond angles (degrees) of compound **6h**.

Bond	Angle (degree)	Bond	Angle (degree)
C1—S—C6	102.49(8)	C1—N1—C2	119.8(1)
C1—N2—C4	120.7(1)	C1—N2—C5	121.2(2)
C4—N2—C5	118.1(1)	C5—N3—C6	110.9(1)
C5—N3—C14	117.0(2)	C6—N3—C14	119.9(1)
S—C1—N1	113.1(1)	S—C1—N2	122.9(1)
N1—C1—N2	123.9(2)	N1—C2—C3	120.4(2)
N1—C2—C7	114.5(1)	C3—C2—C7	125.1(2)
C2—C3—C4	120.3(2)	C2—C3—C13	126.0(2)
C4—C3—C13	113.7(1)	O—C4—N2	121.2(2)
O—C4—C3	124.2(2)	N2—C4—C3	114.6(1)
N2—C5—N3	111.1(1)	S—C6—N3	113.3(1)
C2—C7—C8	117.0(2)	C2—C7—C12	124.1(2)
C8—C7—C12	118.9(2)	C7—C8—C9	120.5(2)
C8—C9—C10	120.0(2)	C9—C10—C11	120.2(2)
C10—C11—C12	120.3(2)	C7—C12—C11	120.0(2)
N4—C13—C3	176.4(2)	N3—C14—C15	119.8(1)
N3—C14—C19	122.2(2)	C15—C14—C19	117.9(2)
C14—C15—C16	121.1(2)	C15—C16—C17	121.5(2)
C16—C17—C18	116.9(2)	C16—C17—C20	121.0(2)
C18—C17—C20	122.1(2)	C17—C18—C19	122.7(2)
C14—C19—C18	119.8(2)		

colorless crystals from ethanol, yield (0.28 g, 77%). Mp 162–164°C. IR (KBr): 3080, 2985, 2200, 1685, 1590, 1520 cm^{-1}. ^{1}H-NMR (90 MHz, DMSO-d_6): δ = 3.9 (s, 2H, NC$\underline{H}_2$Ph), 4.9 (s, 2H, SC$\underline{H}_2$N), 5.15 (s, 2H, NC$\underline{H}_2$N) 7.1–8.1 ppm (m, 10H, arom-H).

Anal. Calcd for $C_{20}H_{16}N_4OS$: C, 66.65; H, 4.47; N, 15.54; S, 8.90. Found: C, 66.53; H, 4.41; N, 15.50; S, 8.80.

7-Cyano-3,8-diphenyl-3,4-dihydro-2H-pyrimido[2,1-b]-1,3,5-thiadiazin-6-one (6e). This compound was obtained as colorless crystals from ethanol, yield (0.27 g, 80%). Mp 214–216°C. IR (KBr): 3050, 2910, 2200, 1660, 1525, 1475 cm^{-1}. ^{1}H-NMR (90 MHz, DMSO-d_6): δ = 5.0 (s, 2H, SC$\underline{H}_2$N), 5.2

Table 4

Dihedral angles (degrees).

Angle	Degree	Angle	Degree
C6—S—C1—N1	−176.1(1)	C6—S—C1—N2	0.7(2)
C1—S—C6—N3	23.5(2)	C2—N1—C1—S	175.7(1)
C2—N1—C1—N2	−1.0(3)	C1—N1—C2—C3	−4.4(3)
C1—N1—C2—C7	175.5(2)	C4—N2—C1—S	−170.7(1)
C4—N2—C1—N1	5.7(3)	C5—N2—C1—S	10.1(2)
C5—N2—C1—N1	−173.5(2)	C1—N2—C4—O	175.1(2)
C1—N2—C4—C3	−4.7(2)	C5—N2—C4—O	−5.6(3)
C5—N2—C4—C3	174.6(2)	C1—N2—C5—N3	−45.6(2)
C4—N2—C5—N3	135.1(2)	C6—N3—C5—N2	72.5(2)
C14—N3—C5—N2	−70.1(2)	C5—N3—C6—S	−60.4(2)
C14—N3—C6—S	80.9(2)	C5—N3—C14—C15	−41.7(2)
C5—N3—C14—C19	141.0(2)	C6—N3—C14—C15	179.2(2)
C6—N3—C14—C19	1.9(3)	N1—C2—C3—C4	5.0(3)
N1—C2—C3—C13	−175.1(2)	C7—C2—C3—C4	−174.9(2)
C7—C2—C3—C13	4.9(3)	N1—C2—C7—C8	−18.9(2)
N1—C2—C7—C12	161.2(2)	C3—C2—C7—C8	161.0(2)
C3—C2—C7—C12	−18.9(3)	C2—C3—C4—O	179.8(2)
C2—C3—C4—N2	−0.4(3)	C13—C3—C4—O	−0.1(3)
C13—C3—C4—N2	179.7(2)	C2—C7—C8—C9	−177.8(2)
C12—C7—C8—C9	2.1(3)	C2—C7—C12—C11	177.8(2)
C8—C7—C12—C11	−2.1(3)	C7—C8—C9—C10	−0.6(3)
C8—C9—C10—C11	−0.9(3)	C9—C10—C11—C12	1.0(3)
C10—C11—C12—C7	0.5(3)	N3—C14—C15—C16	−176.5(2)
C19—C14—C15—C16	0.9(3)	N3—C14—C19—C18	175.5(2)
C15—C14—C19—C18	−1.8(3)	C14—C15—C16—C17	0.8(3)
C15—C16—C17—C18	−1.7(3)	C15—C16—C17—C20	178.9(2)
C16—C17—C18—C19	0.8(3)	C20—C17—C18—C19	−179.8(2)
C17—C18—C19—C14	0.9(3)		

(s, 2H, NCH_2N), 6.6–7.3 ppm (m, 10H, arom-H). MS (EI, 70Ev): m/z = (%) 345.98 [M^+] (19.5), 285.9 (0.9), 212.91 (3.8), 211.05 (8.6), 180.02 (2.8), 178.0 (2.5), 176.0 (1.2), 169.0 (0.9), 165.0 (2.3), 158.0 (0.7), 154.93 (1.6), 153.93 (1.2), 152.98 (1.1), 149.94 (5.1), 145.94 (1.6), 145.02 (1.0), 142.03 (0.5), 140.99 (10.07), 134.06 (2.6), 133.01 (1.8), 129.06 (8.7), 128.0 (0.4), 127.0 (8.7), 122.0 (5.3), 199.0 (2.5), 118.05 (2.1), 117.04 (4.4), 107.03(2.7), 106 (42.9), 105 (100), 104.02 (93.6), 103 (2.7), 102.08 (0.5), 95.01 (2.1), 93.93 (0.7), 93.01 (4.2), 92.0 (5.3), 90.76 (16.8), 90.02 (3.9), 89.05 (6.0), 88.08 (2.6), 87 (2.2), 85.93 (15.8), 85.04 (1.2), 83.09 (1.8), 82.06 (2.1), 81.06 (1.0), 79.92 (1.1), 79.04 (6.9), 78.02 (13.1), 77.02 (46.2), 76.01 (3.8), 75.00 (4.9).

Anal. Calcd for $C_{19}H_{14}N_4OS$: C, 65.88; H, 4.07; N, 16.17; S, 9.26. Found: C, 65.80; H, 4.00; N, 16.13; S, 9.15.

3-(4-Chlorophenyl)-7-cyano-8-phenyl-3,4-dihydro-2H-pyrimido[2,1-b]-1,3,5-thiadiazin-6-one (6f). This compound was obtained as yellow crystals from ethanol, yield (0.34 g, 90%). Mp 230–232°C. IR (KBr): 3060, 2940, 2200, 1680, 1540, 1470 cm^{-1}. ^{1}H-NMR (90 MHz, DMSO-d_6): δ = 5.5 (s, 2H, SCH_2N), 5.75 (s, 2H, NCH_2N), 7.3–7.95 ppm (m, 9H, arom-H).

Anal. Calcd for $C_{19}H_{13}ClN_4OS$: C, 59.92; H, 3.44; N, 14.71; S, 8.42. Found: C, 59.80; H, 3.41; N, 14.65; S, 8.40.

3-(4-Bromophenyl)-7-cyano-8-phenyl-3,4-dihydro-2H-pyrimido[2,1-b]-1,3,5-thiadiazin-6-one (6g). This compound was obtained as green crystals from ethanol, yield (0.4 g, 95%). Mp 242-244°C. IR (KBr): 3010, 3000, 2200, 1640, 1520, 1490 cm^{-1}. ^{1}H-NMR (500 MHz, DMSO-d_6): δ = 5.5 (s, 2H, SCH_2N), 5.7 (s, NCH_2N), 7.1 (d, J = 10 Hz, 2H, arom-H), 7.5 (m, 5H, arom-H), 7.7 ppm (d, J = 5 Hz, 2H, arom-H). ^{13}C-NMR (125 MHz, DMSO-d_6) δ = 166.0, 164.5, 159.5, 143.0, 134.5, 132.0, 131.5, 128.5, 118.5, 115.0, 114.0, 92.0, 60.0, 53.0.

Anal. Calcd for $C_{19}H_{13}BrN_4OS$: C, 53.66; H, 3.08; N, 13.17; S, 7.54. Found: C, 53.55; H, 2.98; N, 13.12; S, 7.45.

7-Cyano-3-(4-tolyl)-8-phenyl-3,4-dihydro-2H-pyrimido[2,1-b]-1,3,5-thiadiazin-6-one (6h). This compound was obtained as colorless crystals from benzene, yield (0.31 g, 87 %). Mp 210–212°C. IR (KBr): 3050, 2995, 2200, 1650, 1500, 1480 cm^{-1}. ^{1}H-NMR (90 MHz, $CDCl_3$): δ = 2.3 (s, 3H, CH_3), 5.3 (s, 2H, SCH_2N), 5.7 (s, 2H, NCH_2N), 7.1–7.9 ppm (m, 9H, arom-H).

Anal. Calcd for $C_{20}H_{16}N_4OS$: C, 66.65; H, 4.47; N, 15.54; S, 8.90. Found: C, 66.45; H, 4.35; N, 15.50; S, 8.84.

7-Cyano-3-(4-methoxyphenyl)-8-phenyl-3,4-dihydro-2H-pyrimido[2,1-b]-1,3,5–thiadiazin-6-one (6i). This compound was obtained as yellow crystals from (benzene/ cyclohexane), yield (0.35 g, 94 %). Mp 174–176°C. IR (KBr): 3080, 2995, 2200, 1600, 1530, 1480 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 3.74 (s, 3H, OCH_3), 5.19 (s, 2H, SCH_2N), 5.60 (s, 2H, NCH_2N), 6.85 (d, J = 5.1 Hz, 2H, arom-H), 7.00 (d, J = 7 Hz, 2H, arom-H), 7.44–7.52 (m, 3H, arom-H), 7.95 ppm (d, J = 9 MHz 2H, arom-H). ^{13}C-NMR (125 MHz, DMSO-d_6): δ = 166.36, 163.26, 159.66, 155.99, 136.51, 134.32, 132.06, 128.93, 119.10, 115.16, 115.06, 93.01, 61.80, 55.59, 52.26.

Anal. Calcd for $C_{20}H_{16}N_4O_2S$: C, 63.81; H, 4.28; N, 14.88; S, 8.52. Found: C, 63.71; H, 4.14; N, 14.69; S, 8.49.

7-Cyano-3-(3-tolyl)-8-phenyl-3,4-dihydro-2H-pyrimido[2,1-b]-1,3,5-thiadiazin-6-one (6j). This compound was obtained as yellow crystals from ethanol, yield (0.32 g, 89 %). Mp 220–222°C. IR (KBr): 3000, 2990, 2200, 1650, 1520, 1470 cm^{-1}. ^{1}H-NMR (90 MHz, DMSO-d_6): δ = 2.1 (s, 3H, CH_3), 5.3 (s, 2H, SCH_2N), 5.5 (s, 2H, NCH_2N), 7.0–7.8 ppm (m, 9H, arom-H).

Anal. Calcd for $C_{20}H_{16}N_4OS$: C, 66.65; H, 4.47; N, 15.54; S, 8.90. Found: C, 66.50; H, 4.41; N, 15.50; S, 8.88.

7-Cyano-3-(2-naphthyl)-8-phenyl-3,4-dihydro-2H-pyrimido[2,1-b]-1,3,5-thiadiazin-6-one (6k). This compound was obtained as colorless crystals from ethanol, yield (0.38 g, 95 %). Mp 238–240°C. IR (KBr): 3050, 2920, 2200, 1620, 1520, 1480 cm^{-1}. ^{1}H-NMR (90 MHz, DMSO-d_6): δ = 5.7 (s, 2H, SCH_2N), 5.9 (s, 2H, NCH_2N), 7.1–8.15 ppm (m, 12H, arom-H).

Anal. Calcd for $C_{23}H_{16}N_4OS$: C, 69.68; H, 4.07; N, 14.13; S, 8.09. Found: C, 69.58; H, 4.39; N, 14.08; S, 8.00.

8-(4-Chlorophenyl)-Pyrimido[2,1-b]-1,3,5-thiadiazine derivatives (7a-k). These compounds were obtained according to the general method using ethanol/dioxane in a ratio of 1:1 mixture as solvent.

8-(4-Chlorophenyl)-7-cyano-3-ethyl-3,4-dihydro-2H-pyrimido[2,1-b]-1,3,5-thiadiazin-6-one (7a). This compound was obtained as colorless crystals from ethanol, yield (0.32 g, 96 %). Mp 160–162°C. IR (KBr): 3100, 2990, 2200, 1680, 1590, 1520 cm^{-1}. ^{1}H-NMR (90 MHz, $CDCl_3$): δ = 1.3 (t, J = 2.7 Hz, 3H, NCH_2CH_3), 2.9 (q, J = 2.7 Hz, 2H, NCH_2CH_3), 4.9 (s, 2H, SCH_2N), 5.2 (s, 2H, NCH_2N), 7.55–8.1 ppm (m, 4H, arom-H). MS (EI, 70 eV): m/z (%) = 344.97 [M^+ +2] (41.4), 332.97 [M^+] (98.4), 33.98 (30.1), 332.01 (9.8), 330.96 (17.1), 318.05 (5.5), 316.04 (1.8), 299.01 (15.8), 277.93 (27.1), 276.95 (18.7), 275.93 (46.1), 265.92(16.8), 263.93 (27.0), 262.95 (10.4), 260.98 (10.6), 248.97 (17.8), 247.97 (12.8), 246.95 (25.9), 232.02 (11.6), 230.01 (10.5), 219.04 (14.1), 218.04 (10.8), 217.02 (24.5), 215.05 (10.1), 207.03 (10.0), 205.0 (14.4), 194.06 (11.9), 190.03 (12.4), 189.01(11.8), 187.03 (11.1), 185.06 (33.6), 183.04 (10.7), 176.05 (10.9), 130.05 (13.05), 129.05 (19.6), 128.06 (13.0), 127.03 (13.7), 125.2 (14.9), 117.98 (9.48), 116.99 (23.7), 112.99 (15.6), 110.98 (12.2), 110.01 (8.2), 108.98 (5.7), 107.98 (6.6), 106.98 (6.6).

Anal. Calcd for $C_{15}H_{13}ClN_4OS$: C, 54.13; H, 3.94; N, 16.83; S, 9.63. Found: C, 54.02; H, 3.90; N, 16.82; S, 9.58.

3-Butyl-8-(4-chlorophenyl)-7-cyano-3,4-dihydro-2H-pyrimido[2,1-b]-1,3,5-thiadiazin-6-one (7b). This compound was obtained as colorless crystals from ethanol, yield (0.33 g, 94%). Mp 186–188°C. IR (KBr): 3050, 2990–2850, 2200, 1680, 1590, 1520 cm^{-1}. ^{1}H-NMR (90 MHz, $CDCl_3$): δ = 1.0 (t, J = 1.8 Hz, 3H, CH_2CH_3), 1.5 (m, 2H, CH_2CH_3), 1.7 (m, 2H, NCH_2CH_2), 2.9 (t, J = 1.5 Hz, 2H, NCH_2CH_2), 4.8 (s, 2H, SCH_2N), 5.2 (s, 2H, NCH_2N), 7.5–8.1 ppm (m, 4H, arom-H).

Anal. Calcd for $C_{17}H_{17}ClN_4OS$: C, 56.58; H, 4.75; N, 15.53; S, 8.89. Found: C, 56.57; H, 4.70; N, 15.51; S, 8.86.

8-(4-Chlorophenyl)-7-cyano-3-isobutyl-3,4-dihydro-2H-pyrimido[2,1-b]-1,3,5–thiadiazin-6-one (7c). This compound was obtained as colorless crystals from ethanol, yield (0.23 g, 64%). Mp 198–200°C. IR (KBr): 3060, 2985–2800, 2200, 1680, 1590, 1520 cm^{-1}. ^{1}H-NMR (90 MHz, DMSO-d_6): δ = 1.0 (d, J = 1.7 Hz, 6H, $CH(CH_3)_2$), 1.9 (m, 1H, $NCH_2CH(CH_3)_2$), 2.55 (d, J = 2.4 Hz, 2H, NCH_2CH), 5.0 (s, 2H, SCH_2N), 5.2 (s, NCH_2N), 7.7–8.05 ppm (m, 4H, arom-H).

Anal. Calcd for $C_{17}H_{17}ClN_4OS$: C, 56.58; H, 4.75; N, 15.53; S, 8.89. Found: C, 56.49; H, 4.70; N, 15.50; S, 8.80.

3-Benzyl-8-(4-chlorophenyl)-7-cyano-3,4-dihydro-2H-pyrimido[2,1-b]-1,3,5-thiadiazin-6-one (7d). This compound was obtained as colorless crystals from ethanol, yield (0.3 g, 77%). Mp 162–164°C. IR (KBr): 3150, 2985, 2200, 1685, 1590, 1520 cm^{-1}. ^{1}H-NMR (90 MHz, DMSO-d_6): δ = 4.0 (s, 2H, NCH_2Ph), 4.8 (s, 2H, SCH_2N), 5.2 (s, NCH_2N) 7.6–8.15 ppm (m, 9H, arom-H).

Anal. Calcd for $C_{20}H_{15}ClN_4OS$: C, 60.83; H, 3.83; N, 14.19; S, 8.12. Found: C, 60.70; H, 3.74; N, 14.17; S, 8.10.

8-(4-Chlorophenyl)-7-cyano-3-phenyl-3,4-dihydro-2H-pyrimido[2,1-b]-1,3,5- thiadiazin-6-one (7e). This compound was obtained as yellow crystals from ethanol, yield (0.22 g, 60%). Mp 168–170°C. IR (KBr): 3020, 2950, 2200, 1680, 1590, 1520 cm^{-1}. ^{1}H-NMR (90 MHz, DMSO-d_6): δ = 5.5 (s, 2H, SCH_2N), 5.8 (s, 2H, NCH_2N), 7.3–7.9 ppm (m, 9H, arom-H).

Anal. Calcd for $C_{19}H_{13}ClN_4OS$: C, 59.92; H, 3.44; N, 14.71; S, 8.42. Found: C, 59.82; H, 3.41; N, 14.69; S, 8.36.

3,8-Di(4-chlorophenyl)-7-cyano-3,4-dihydro-2H-pyrimido [2,1-b]-1,3,5-thiadiazin-6-one (7f). This compound was obtained as yellow crystals from ethanol, yield (0.3 g, 73%). Mp 222–224°C. IR (KBr): 3020, 2970,2200, 1660, 1590, 1520 cm^{-1}. ^{1}H-NMR (500 MHz, DMSO-d_6): δ = 5.7 (s, 2H, SCH_2N), 5.9 (s, 2H, NCH_2N), 7.1–8.0 ppm (m, 8H, arom-H). ^{13}C-NMR (125 MHz, DMSO-d_6): δ = 165, 164.0, 159.0, 142.0, 137.0, 133.0, 131.0, 130.0, 128.5, 126.0, 118, 115.0, 92.0, 60.0, 53.5. MS (EI, 70Ev): m/z (%) = 418 [M^+ +4] (17.5), 416 [M^+ +2] (36.3), 414 [M^+] (54.8), 383.21 (16.8), 381.21 (21.3), 379.33(2.2), 379.17 (9.8), 280.17 (9.1), 278.14 (13.4), 277.28 (2.9), 277.14 (16.6), 276.15 (8.6), 263.15 (4.0), 262.12 (5.6), 249.11 (5.8), 248.17 (2.5), 247.15 (10.4), 245.115 (10.3), 240.17 (5.4), 217.19 (6.1), 197.16 (2.1), 195.17 (8.5), 193.09 (6.0), 187.12 (3.7), 175.08 (9.1), 169.10 (4.7), 167.06 (5.4), 163.05 (7.0), 162.10 (5.8), 161.08 (29.3), 155.14 (4.3), 153.12 (3.9), 151.09 (6.4), 142.08 (11.6), 141.08 (35.4), 140.08 (44.3), 139.08 (100), 138.22 (2.2), 138.06 (30.4), 137.03 (3.4), 129.07 (5.6), 127.08 (8.1), 126.12 (3.1), 125.08 (12.5), 114.11 (6.2), 113.08 (8.6), 112.09 (2.8), 111.10 (20.3), 105.14 (2.8), 99.07 (4.6), 88.10 (5.1), 86.02 (12.8), 85.06 (2.1), 84.99 (1.2), 80.98 (2.9), 77.07 (6.9), 76.6 (5.9), 75.05 (10.1), 74.05 (1.0).

Anal. Calcd for $C_{19}H_{12}Cl_2N_4OS$: C, 54.95; H, 2.91; N, 13.49; S, 7.72. Found: C, 54.89; H, 2.86; N, 13.40; S, 7.68.

3-(4-Bromophenyl)-8-(4-chlorophenyl)-7-cyano-3,4-dihydro-2H-pyrimido[2,1-b]-1,3,5-thiadiazin-6-one (7g). This compound was obtained as green crystals from benzene, yield (0.21 g, 47%). Mp 224–226°C. IR (KBr): 3020, 2975, 2200, 1660, 1590, 1520 cm^{-1}. ^{1}H-NMR (90 MHz, DMSO-d_6): δ = 5.56 (s, 2H, SCH_2N), 5.8 (s, 2H, NCH_2N), 7.2–8.0 ppm (m, 8H, arom-H).

Anal. Calcd for $C_{19}H_{12}BrClN_4OS$: C, 49.64; H, 2.63; N, 12.19; S, 6.97. Found: C, 49.56; H, 2.59; N, 12.17; S, 6.92.

8-(4-Chlorophenyl)-7-cyano-3-(4-tolyl)-3,4-dihydro-2H-pyrimido[2,1-b]-1,3,5-thiadiazin-6-one (7h). This compound was obtained as colorless crystals from benzene, yield (0.12 g, 30%). Mp 210–212°C. IR (KBr): 3020, 2990, 2200, 1680, 1590, 1520 cm^{-1}. ^{1}H-NMR (90 MHz, DMSO-d_6): δ = 2.2 (s, 3H, CH_3), 5.7 (s, 2H, SCH_2N), 5.8 (s, 2H, NCH_2N), 7.2–8.0 ppm (m, 8H, arom-H).

Anal. Calcd for $C_{20}H_{15}ClN_4OS$: C, 60.83; H, 3.83; N, 14.19; S, 8.12. Found: C, 60.56; H, 3.76; N, 14.16; S, 8.09.

8-(4-Chlorophenyl)-7-cyano-3-(4-methoxyphenyl)-3,4-dihydro-2H-pyrimido-[2,1-b]-1,3,5-thiadiazin-6-one (7i). This compound was obtained as colorless crystals from benzene, yield (0.123 g, 30%). Mp 214–216°C. IR (KBr): 3020, 2990, 2200, 1640, 1590, 1520 cm^{-1}. ^{1}H-NMR (90 MHz, DMSO-d_6) δ = 3.9 (s, 3H, OCH_3), 5.6 (s, 2H, SCH_2N), 5.8 (s, 2H, NCH_2N), 7.2–8.0 ppm (m, 8H, arom-H).

Anal. Calcd for $C_{20}H_{15}ClN_4O_2S$: C, 58.46; H, 3.68; N, 13.64; S, 7.80. Found: C, 58.36; H, 3.60; N, 13.61; S, 7.78.

8-(4-Chlorophenyl)-7-cyano-3-(3-tolyl)-3,4-dihydro-2H-pyrimido[2,1-b]-1,3,5-thiadiazin-6-one (7j). This compound was obtained as colorless crystals from ethanol, yield (0.386 g, 98%). Mp 180–182°C. IR (KBr): 3020, 2990, 2200, 1680, 1590, 1520 cm^{-1}. ^{1}H-NMR (90 MHz, DMSO-d_6): δ = 2.2 (s, 3H, CH_3), 5.4 (s, 2H, SCH_2N), 5.8 (s, NCH_2N), 7.1–8.1 ppm (m, 8H, arom-H).

Anal. Calcd for $C_{20}H_{15}ClN_4OS$: C, 60.83; H, 3.83; N, 14.19; S, 8.12. Found: C, 60.75; H, 3.81; N, 14.09; S, 8.09.

8-(4-Chlorophenyl)-7-cyano-3-(2-naphthyl)-3,4-dihydro-2H-pyrimido[2,1-b]-1,3,5-thiadiazin-6-one (7k). This compound was obtained as green crystals from ethanol, yield (0.344 g, 80%). Mp 216–218°C. IR (KBr): 3050, 2950, 2200, 1620, 1590, 1520 cm^{-1}. ^{1}H-NMR (90 MHz, DMSO-d_6): δ = 5.7 (s, 2H, SCH_2N), 6.0 (s, 2H, NCH_2N), 7.5–8.0 ppm (m, 11H, arom-H).

Anal. Calcd for $C_{23}H_{15}ClN_4OS$: C, 64.11; H, 3.51; N, 13.00; S, 7.44. Found: C, 64.05; H, 3.48; N, 12.97; S, 7.38.

8-(4-Nitrophenyl)-pyrimido[2, 1-b]-1,3,5-thiadiazine derivatives (8a-e). These compounds were obtained according to the general method using ethanol/acetic acid in a ratio of 2:1 as solvent.

7-Cyano-3-ethyl-8-(4-nitrophenyl)-3,4-dihydro-2H-pyrimido [2,1-b]-1,3,5-thiadiazin-6-one(8a). This compound was obtained as colorless crystals from (benzene/cyclohexane), yield (0.137 g, 40 %). Mp 162–164°C. IR (KBr): 3100, 2995, 2200, 1685, 1600, 1520 cm^{-1}. ^{1}H-NMR (90 MHz, $CDCl_3$): δ = 1.3 (t, J = 2.8 Hz, 3H, NCH_2CH_3), 2.9 (q, J = 2.8 Hz, 2H, NCH_2CH_3), 4.9 (s, 2H, SCH_2N), 5.25 (s, 2H, NCH_2N), 8.1–8.3 ppm (m, 4H, arom-H).

Anal. Calcd for $C_{15}H_{13}N_5O_3S$: C, 52.47; H, 3.82; N, 20.40; S, 9.34. Found: C, 52.30; H, 3.79; N, 20.36; S, 9.28.

3-Butyl-7-cyano-8-(4-nitrophenyl)-3,4-dihydro-2H-pyrimido [2,1-b]-1,3,5-thiadiazin-6-one (8b). This compound was obtained as colorless crystals from (benzene/cyclohexane), yield (0.163 g, 44%). Mp 180–182°C. IR (KBr): 3080, 2995-2800, 2200, 1685, 1600, 1520 cm^{-1}. ^{1}H-NMR (90 MHz, $CDCl_3$): δ = 1.0 (t, J = 3.4 Hz, 3H, CH_2CH_3), 1.4 (m, 2H, CH_2CH_3), 2.1 (m, 2H, NCH_2CH_2), 2.8 (t, J = 3.3 Hz, 2H, NCH_2CH_2), 4.85 (s, 2H, SCH_2N), 5.2 (s, 2H, NCH_2N) 8.0–8.2 ppm (m, 4H, arom-H).

Anal. Calcd for $C_{17}H_{17}N_5O_3S$: C, 54.97; H, 4.61; N, 18.86; S, 8.63. Found: C, 54.90; H, 4.51; N, 18.77; S, 8.56.

7-Cyano-3-isobutyl-8-(4-nitrophenyl)-3,4-dihydro-2H-pyrimido [2,1-b]-1,3,5-thiadiazin-6-one (8c). This compound was obtained as colorless crystals from ethanol, yield (0.237 g, 64%). Mp 314–316°C. IR (KBr): 3060, 2985-2800, 2200, 1670, 1550, 1510 cm^{-1}. ^{1}H-NMR (90 MHz, DMSO-d_6): δ = 1.0 (d, J = 2.4 Hz, 6H, $CH(CH_3)_2$), 1.6 (m, 1H, $NCH_2CH(CH_3)_2$), 2.4 (d, J = 2.3 Hz, 2H, NCH_2CH), 4.9 (s, 2H, SCH_2N), 5.2 (s, 2H, NCH_2N) 7.9–8.1 ppm (m, 4H, arom-H).

Anal. Calcd for $C_{17}H_{17}N_5O_3S$: C, 54.97; H, 4.61; N, 18.86; S, 8.63. Found: C, 54.90; H, 4.58; N, 18.82; S, 8.60.

3-Benzyl-7-cyano-8-(4-nitrophenyl)-3,4-dihydro-2H-pyrimido

[2,1-b]-1,3,5-thiadiazin-6-one (8d). This compound was obtained as colorless crystals from (benzene/cyclohexane), yield (0.31 g, 77%). Mp 172–174°C. IR (KBr): 3110, 2975, 2200, 1680, 1590, 1550 cm^{-1}. ^{1}H-NMR (500 MHz, DMSO-d_6): δ = 4.0 (s, 2H, NCH_2Ph), 5.0 (s, 2H, SCH_2N), 5.2 (s, 2H, NCH_2N), 7.4 (m, 6H, arom-H), 8.1 (d, 2H, arom-H), 8.4 ppm (d, 2H, arom-H). ^{13}C-NMR (125 MHz, DMSO-d_6): δ = 166, 164.0, 159.0, 149.0, 140.5, 136.0, 130.0, 128.0, 127.8, 124.0, 115.0, 92, 63.5, 56.5, 53.5. MS (EI, 70Ev): m/z (%) = 405.85 [M^+] (2.2), 375.99 (1.2), 369.11 (1.1), 364.09 (1.1), 348.22 (1.0), 377.15 (1.2), 334.3 (1.3), 298.13 (1.4), 293.12 (1.7), 289.99 (1.2), 280.06 (1.4), 277.02 (1.2), 275.11 (1.7), 271.09 (1.6), 256.11 (6.1), 251.97 (1.5), 244.07 (1.1), 242.13 (1.4), 237.05 (1.1), 228.99 (1.0), 227.10 (1.4), 224.11 (7.8), 221.12 (1.5), 215.18 (1.8), 207.05 (1.8), 207.05 (1.8), 200.11 (19.4), 192.03 (2.0), 191.07 (1.3), 185.09 (45.2), 178.12 (3.0), 173.08 (1.0), 168.08 (1.5), 167.08 (1.5), 166.06 (3.4), 159.10 (1.5), 149.07 (20.9), 145.042 (2.0), 136.10 (2.2), 133.07 (2.9), 127.04 (1.2), 123.06 (2.9), 117.01 (11.0), 113.99 (1.4), 109.02 (11.4), 108.01 (96.3), 106.99 (5.7), 102.99 (3.6), 100.97 (1.2), 98.99 (2.6), 93.01 (100.0), 91.01 (58.0).

Anal. Calcd for $C_{20}H_{15}N_5O_3S$: C, 59.25; H, 3.73; N, 17.27; S, 7.91. Found: C, 59.15; H, 3.68; N, 17.19; S, 7.88.

7-Cyano-8-(4-nitrophenyl)-3-phenyl-3,4-dihydro-2H-pyrimido [2,1-b]-1,3,5-thiadiazin-6-one (8e). This compound was obtained as yellow crystals from (benzene/cyclohexane), yield (0.226 g, 58%). Mp 154–156°C. IR (KBr): 3070, 2920, 2200, 1660, 1530, 1500 cm^{-1}. ^{1}H-NMR (90MHz, DMSO-d_6): δ = 5.6 (s, 2H, SCH_2N), 5.8 (s, 2H, NCH_2N), 7.3–8.3 ppm (m, 9H, arom-H).

Anal. Calcd for $C_{19}H_{13}N_5O_3S$: C, 58.30; H, 3.35; N, 17.89; S, 8.19.Found: C, 58.42; H, 3.23; N, 17.72; S, 8.06.

8-(2-Furyl)-pyrimido[2,1-b]-1,3,5-thiadiazine derivatives (9a-h). These compounds were obtained according to general method using ethanol as solvent.

7-Cyano-3-ethyl-8-(2-furyl)-3,4-dihydro-2H-pyrimido [2,1-b]-1,3,5-thiadiazin-6-one (9a). This compound was obtained as pale yellow crystals from (benzene/cyclohexane), yield (0.17 g, 60 %). Mp 176–178°C. IR (KBr): 3200, 2995, 2200, 1660, 1600, 1520 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.18 (t, J = 1.62 Hz, 3H, NCH_2CH_3), 2.77 (q, J = 1.62 Hz, 2H, NCH_2CH_3), 4.74 (s, 2H, SCH_2N), 5.10 (s, 2H, NCH_2N), 6.60 (q, J = 3.01 Hz, 1H, furan-H), 7.56 (d, J = 3.0 Hz, 1H, furan-H), 7.71 ppm (d, J = 1.0 Hz, 1H, furan-H). ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 159.8, 153.8, 147.2, 118.9, 114.5, 112.9, 77.3, 77.05, 76.7, 63.4, 56.3, 44.46, 12.7. MS (EI, 70Ev): m/z (%) = 288.93 [M^+] (100.0), 287.96 (10.5), 272.97 (2.2), 270.04 (2.1), 264.92 (2.1), 260.89 (1.9), 256.95 (1.7), 246.98 (2.2), 240.97 (5.5), 236.99 (2.7), 231.93 (52.4), 223.04 (2.1), 215.96 (3.1), 214.04 (1.5), 205.99 (1.7), 204.95 (4.3), 202.92 (21.6), 190.98 (2.2), 185.01 (51.4), 183.01 (2.3), 176.01 (5.2), 172.98 (23.1), 171.02 (5.8), 161.98 (8.1), 159.02 (4.6), 153.02 (2.4), 149.01 (13.2), 147.01 (6.7), 144.03 (6.0), 138.05 (9.0), 134.02 (4.1), 129.02 (15.5), 123.01 (4.1), 116.98 (14.4), 114.96 (7.0), 110.98 (4.1), 103.94 (10.2), 101.95 (12.8), 92.97 (76.6), 85.94 (12.2), 78.97 (13.9), 74.99 (30.4), 72.00 (35.2), 70.02 (7.9), 67.01 (1.9).

Anal. Calcd for $C_{13}H_{12}N_4O_2S$: C, 54.15; H, 4.20; N, 19.43; S, 11.12. Found: C, 54.10; H, 4.14; N, 19.39; S, 11.10.

3-Butyl-7-cyano-8-(2-furyl)-3,4-dihydro-2H-pyrimido [2,1-b]- 1,3,5-thiadiazin-6-one (9b). This compound was obtained as colorless crystals from (benzene/cyclohexane), yield (0.129 g, 41 %). Mp 160–162°C. IR (KBr): 3200, 2995, 2200, 1660, 1580, 1520 cm^{-1}. ^{1}H-NMR (90 MHz, $CDCl_3$): δ 1.0 (t, J = 1.8 Hz, 3H, CH_2CH_3), 1.4 (m, 2H, CH_2CH_3), 2.1 (m, 2H, NCH_2CH2), 2.8 (t, J = 1.8 Hz, 2H, NCH2CH2), 4.8 (s, 2H, SCH_2N), 5.05 (s, 2H, NCH_2N), 6.5 (s, 1H, furan-H), 7.4 (s, 1H, furan-H), 7.6 ppm (s, 1H, furan-H).

Anal. Calcd for $C_{15}H_{16}N_4O_2S$: C, 56.94; H, 5.10; N, 17.71; S, 10.14. Found: C, 56.89; H, 5.08; N, 17.69; S, 10.12.

7-Cyano-8-(2-furyl)-3-isobutyl-3,4-dihydro-2H-pyrimido [2,1-b]-1,3,5-thiadiazin-6-one (9c). This compound was obtained as colorless crystals from (benzene/cyclohexane), yield (0.158 g, 50 %). Mp 176–178°C. IR(KBr): 3200, 2995, 2200, 1660, 1600, 1520 cm^{-1}. ^{1}H-NMR (90 MHz, $CDCl_3$): δ = 1.0 (d, J = 3.16 Hz, 6H, $CH(CH_3)_2$), 1.8 (m, 1H, $NCH_2CH(CH_3)_2$), 2.5 (d, J = 3.2 Hz, 2H, NCH2CH), 4.7 (s, 2H, SCH_2N), 5.1 (s, 2H, NCH_2N), 6.5 (s, 1H, furan-H), 7.5 (s, 1H, furan-H), 7.7 ppm (s, 1H, furan-H).

Anal. Calcd for $C_{15}H_{16}N_4O_2S$: C, 56.94; H, 5.10; N, 17.71; S, 10.14. Found: C, 56.88; H, 5.05; N, 17.66; S, 10.10.

3-Benzyl-7-cyano-8-(2-furyl)-3,4-dihydro-2H-pyrimido [2,1-b]-1,3,5-thiadiazin-6-one (9d). This compound was obtained as colorless crystals from ethanol, yield (0.28 g, 80 %). Mp 194–196°C. IR (KBr) 3200, 3030, 2900, 2200, 1650, 1560, 1520 cm^{-1}. ^{1}H-NMR (90 MHz, DMSO-d_6): δ = 3.9 (s, 2H, NCH2Ph), 4.95 (s, 2H, SCH_2N), 5.1 (s, 2H, NCH_2N), 6.9 (s, 1H, furan-H), 7.3 (m, 1H, furan-H), 7.4 (m, 5H, arom-H), 8.15 ppm (s, 1H, furan-H).

Anal. Calcd for $C_{18}H_{14}N_4O_2S$: C, 61.70; H, 4.03; N, 15.99; S, 9.15. Found: C, 61.69; H, 4.01; N, 15.90; S, 9.12.

7-Cyano-8-(2-furyl)-3-phenyl-3,4-dihydro-2H-pyrimido [2,1-b]-1,3,5-thiadiazin-6-one (9e). This compound was obtained as yellow crystals from ethanol, yield (0.289 g, 86 %). Mp 210–212°C. IR (KBr): 3200, 3030, 2940, 2200, 1640, 1580, 1520 cm^{-1}. ^{1}H-NMR (90 MHz, DMSO-d_6): δ = 5.3 (s, 2H, SCH_2N), 5.4 (s, 2H, NCH_2N), 6.6 (s, 1H, furan-H), 7.1 (s, 1H, furan-H), 7.2 (m, 5H, arom-H), 7.9 ppm (s, 1H, furan-H).

Anal. Calcd for $C_{17}H_{12}N_4O_2S$: C, 60.70; H, 3.60; N, 16.66; S, 9.53. Found: C, 60.60; H, 3.55; N, 16.65; S, 9.51.

3-(4-Chlorophenyl)-7-cyano-8-(2-furyl)-3,4-dihydro-2H-pyrimido[2,1-b]-1,3,5-thiadiazin-6-one (9f). This compound was obtained as yellow crystals from ethanol, yield (0.318 g, 86 %). Mp 298–300°C. IR (KBr): 3200, 3030, 2970, 2200, 1640, 1580, 1520 cm^{-1}. ^{1}H-NMR (90 MHz, DMSO-d_6): δ = 5.5 (s, 2H, SCH_2N), 5.7 (s, 2H, NCH_2N), 6.9 (s, 1H, furan-H), 7.3 (s, 1H, furan-H), 7.35 (m, 4H, arom-H), 8.15 ppm (s, 1H, furan-H).

Anal. Calcd for $C_{17}H_{11}ClN_4O_2S$: C, 55.06; H, 2.99; N, 15.11; S, 8.65. Found: C, 54.99; H, 2.90; N, 15.07; S, 8.55.

3-(4-Bromophenyl)-7-cyano-8-(2-furyl)-3,4-dihydro-2H-pyrimido[2,1-b]-1,3,5-thia-diazin-6-one (9g). This compound was obtained as yellow crystals from benzene, yield (0.249 g, 60 %). Mp 270–272°C. IR (KBr): 3200, 3030, 2950, 2200, 1650, 1580, 1520 cm^{-1}. ^{1}H-NMR (500 MHz, DMSO-d_6): δ = 5.45 (s, 2H, SCH_2N), 5.66 (s, 2H, NCH_2N), 6.76 (q, J = 1.0 Hz, 1H, furan-H), 7.09 (d, J = 9.0 Hz, 2H, arom-H.), 7.42 (d, J = 4.0 Hz, 1H, furan-H), 7.46 (d, J = 9.0 Hz, 2H, arom-H), 8.08 ppm (d, J = 1.0 Hz, 1H, furan-H). ^{13}C-NMR (125 MHz, DMSO-d_6): δ = 159.6, 153.4, 448.7, 143.2, 142.5, 134.5, 132.7, 119.3, 119.0, 115.2, 114.6, 113.9, 62.1, 60.2, 53.8. MS (EI, 70Ev): m/z (%) = 416 [M^++2] (100.0), 414 [M^+]

(97.72), 383.2 (27.34), 381.3 (23.49), 371.3 (1.2), 369.2 (1.46), 330.3 (1.72), 328.3 (1.74), 2.33.4 (5.87), 227.3 (2.67), 219.3 (3.45), 203.2 (13.47), 201.3 (8.38), 197.2 (2.85), 185.2 (18.92), 171.2 (3.94), 119.2 (2.38).

Anal. Calcd for $C_{17}H_{11}BrN_4O_2S$: C, 49.17; H, 2.67; N, 13.49; S, 7.72. Found: C, 49.10; H, 2.61; N, 13.48; S, 7.69.

7-Cyano-8-(2-furyl)-3-(4-tolyl)-3,4-dihydro-2H-pyrimido [2,1-b]-1,3,5-thiadiazin-6-one (9h). This compound was obtained as colorless crystals from ethanol, yield (0.269 g, 77 %). Mp 280–282°C. IR (KBr): 3200, 3030, 2900, 2200, 1650, 1560, 1520 cm^{-1}. ^{1}H-NMR (90 MHz, DMSO-d_6): $\delta = 2.1$ (s, 3H, $C\underline{H}_3$), 5.4 (s, 2H, $SC\underline{H}_2N$), 5.5 (s, 2H, $NC\underline{H}_2N$), 7.1 (s, 1H, furan-H), 7.3 (s, 1H, furan-H), 7.36 (m, 4H, arom-H), 8.1 ppm (s, 1H, furan-H).

Anal. Calcd for $C_{18}H_{14}N_4O_2S$: C, 61.70; H, 4.03; N, 15.99; S, 9.15. Found: C, 61.60; H, 3.89; N, 15.91; S, 9.11.

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