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Synthesis and Spectral Investigations of 2,5,7-Triaryl-5*H*-[1,3,4]thiadiazolo[3,2-*a*]pyrimidin-6[7*H*]-ones

METIN KOPARIR*, AHMET CANSIZ and AHMET ÇETIN
Chemistry Department, Faculty of Arts and Sciences
Firat University, 23119 Elazığ, Turkey
E-mail: mkoparir@hotmail.com

A general and convenient route for the synthesis of 5-(aryl)-[1,3,4]thiadiazol-2-ylamines (**2a–d**), Schiff bases of thiadiazoles (**3a–p**) and 2,5,7-triaryl-5*H*-[1,3,4]thiadiazolo[3,2-*a*]pyrimidin-6[7*H*]-one (**4a–p**) is reported. The characterizations of these compounds were obtained by elemental analyses, IR, ^{13}C and ^{1}H NMR techniques.

Key Words: Synthesis, Spectral, 2,5,7-Triaryl-5*H*-[1,3,4]-thiadiazolo[3,2-*a*]pyrimidin-6[7*H*]-ones.

INTRODUCTION

The 1,3,4-thiadiazole ring is associated with diverse biological activities probably by virtue of incorporating a toxophoricts —N=C—S— linkage, the importance of which has been well stressed in many pesticides[1–4]. Various 2-amino/substituted-amino-1,3,4-thiadiazoles and their Schiff bases have recently received significant importance because of their diverse biological properties[5].

The diverse and interesting biological activity reported[6–10] to be shown by the thiadiazolo pyrimidine nucleus led us to synthesize the title compounds 1,3,4-thiadiazolo[3,2-*a*]-pyrimidin-6-ones. The synthesis involves a cycloaddition reaction involving a heterodiene system which is of great potential in the synthesis of heterocyclic compounds[11–13]

RESULTS AND DISCUSSION

In this paper, a [4 + 2] cycloaddition reaction of benzylideneamino-1,3,4-thiadiazole with ketenes is reported. Literature reports show that the cycloaddition of benzylideneamines with phenylacetyl chloride in presence of triethylamine generally gives an azetidinone (β-lactam) ring system[14]. However, the reaction of Schiff base **2** with ketenes, in our case, gives subtituted 2,5,7-triaryl-5*H*-[1,3,4]thiadiazolo[3,2-a]pyrimidin-6[7*H*]-one*s* in good yield (Table-1). The ketene which takes part in the cycloaddition reaction is formed *in-situ* during the reaction of phenylacetyl chloride with triethylamine. In this system, a part of the heterocyclic moiety (1,3,4-thiadiazole) incorporated with the Schiff base comprises a heterodiene system and is the 4π component in the Diels-Alder reaction.

TABLE-1
SPECTROSCOPIC DATA FOR COMPOUNDS (4a–p)

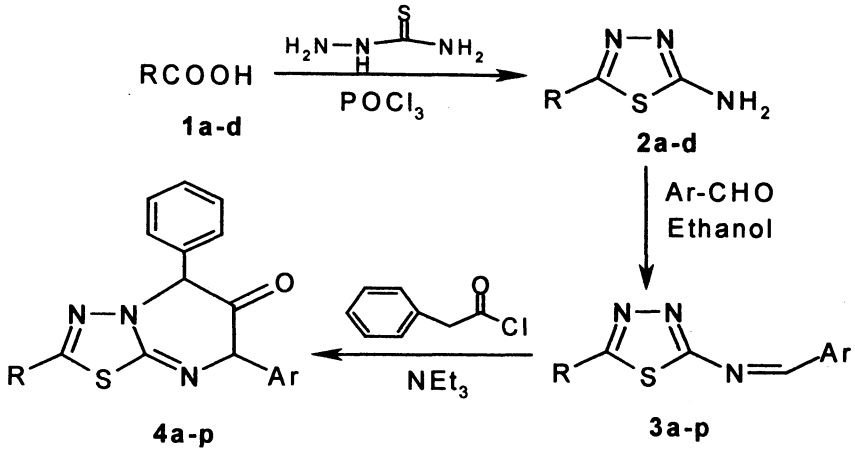
Comp. No.	IR, (KBr, cm^{-1}) ν(C=O)	^1H NMR, δ, ppm	^{13}C NMR, δ, ppm, (C=O; C_5; C_7)
4a	1712	8.33–7.29 (m, 15H, Ar—H), 5.33 (s, 1H, =N—CH—), 5.20 (s, 1H, —N—CH—)	190.98, 73.68, 72.27
4b	1710	8.38–6.83 (m, 14H, Ar—H), 5.34 (s, 1H, =N—CH—), 5.19 (s, 1H, —N—CH—), 3.80 (s, 3H, —OCH_3)	191.33, 73.73, 72.28
4c	1713	8.35–7.29 (m, 14H, Ar—H), 5.32 (s, 1H, =N—CH—), 5.19 (s, 1H, —N—CH—)	190.89, 72.96, 71.99
4d	1715	8.56–7.45 (m, 13H, Ar—H), 5.79 (s, 1H, =N—CH—), 5.23 (s, 1H, —N—CH—)	191.08, 73.01, 72.27
4e	1708	7.97–7.06 (m, 14H, Ar—H), 5.34 (s, 1H, =N—CH—), 5.19 (s, 1H, —N—CH—), 3.79 (s, 3H, —OCH_3)	190.89, 72.96, 71.99
4f	1709	7.96–6.86 (m, 13H, Ar—H), 5.34 (s, 1H, =N—CH—), 5.19 (s, 1H, —N—CH—), 3.82 (s, 3H, —OCH_3), 3.77 (s, 3H, —OCH_3)	191.80, 73.65, 72.21
4g	1710	7.94–7.06 (m, 13H, Ar—H), 5.33 (s, 1H, =N—CH—), 5.18 (s, 1H, —N—CH—), 3.80 (s, 3H, —OCH_3)	190.89, 72.96, 71.99
4h	1715	8.54–7.03 (m, 13H, Ar—H), 5.73 (s, 1H, =N—CH—), 5.18 (s, 1H, —N—CH—), 3.79 (s, 3H, —OCH_3	191.06, 73.70, 72.27
4i	1711	8.19–7.36 (m, 14H, Ar—H), 5.36 (s, 1H, =N—CH—), 5.22 (s, 1H, —N—CH—)	191.36, 73.75, 72.28
4j	1716	8.18–6.86 (m, 13H, Ar—H), 5.35 (s, 1H, =N—CH—), 5.22 (s, 1H, —N—CH—), 3.79 (s, 3H, —OCH_3)	191.80, 73.65, 72.21
4k	1710	8.19–7.29 (m, 13H, Ar—H), 5.35 (s, 1H, =N—CH—), 5.26 (s, 1H, —N—CH—)	191.78, 73.69, 72.27
4l	1708	8.55–7.45 (m, 13H, Ar—H), 5.78 (s, 1H, =N—CH—), 5.22 (s, 1H, —N—CH—)	191.05, 74.23, 72.28
4m	1710	8.51–7.34 (m, 14H, Ar—H), 5.36 (s, 1H, =N—CH—), 5.22 (s, 1H, —N—CH—)	190.89, 72.96, 71.99
4n	1712	8.52–6.84 (m, 13H, Ar—H), 5.35 (s, 1H, =N—CH—), 5.23 (s, 1H, —N—CH—), 3.78 (s, 3H, —OCH_3)	191.34, 73.74, 72.28
4o	1711	8.49–7.29 (m, 13H, Ar—H), 5.34 (s, 1H, =N—CH—), 5.23 (s, 1H, —N—CH—)	191.68, 73.69, 72.27
4p	175	8.53–7.34 (m, 13H, Ar—H), 5.78 (s, 1H, =N—CH—), 5.22 (s, 1H, —N—CH—)	191.06, 73.70, 72.27

TABLE-2
PHYSICAL AND ANALYTICAL DATA OF COMPOUNDS (**4a–p**)

Compd. No.	m.f.	Yield (%)	m.p. (°C)	% Found (calcd.)			
				C	H	N	S
4a	$C_{23}H_{17}N_3OS$	62	171–172	72.01 (72.04)	4.43 (4.47)	10.91 (10.96)	8.33 (8.36)
4b	$C_{24}H_{19}N_3O_2S$	72	163–164	69.69 (69.71)	4.59 (4.63)	10.11 (10.16)	7.72 (7.75)
4c	$C_{23}H_{16}N_3OSCl$	79	181–182	66.09 (66.10)	3.84 (3.86)	10.03 (10.05)	7.65 (7.67)
4d	$C_{23}H_{16}N_4O_3S$	70	159–160	64.39 (64.47)	3.73 (3.76)	12.98 (13.08)	7.45 (7.48)
4e	$C_{24}H_{19}N_3O_2S$	81	149–150	69.58 (69.71)	4.62 (4.63)	10.12 (10.16)	7.71 (7.75)
4f	$C_{25}H_{21}N_3O_3S$	83	155–156	67.68 (67.70)	4.75 (4.77)	9.44 (9.47)	7.19 (7.23)
4g	$C_{24}H_{18}N_3O_2SCl$	74	191–192	64.31 (64.35)	4.03 (4.05)	9.31 (9.38)	7.09 (7.16)
4h	$C_{24}H_{18}N_4O_4S$	65	187–188	62.81 (62.87)	3.94 (3.96)	12.17 (12.22)	7.01 (6.99)
4i	$C_{23}H_{16}N_3OSCl$	86	201–202	66.09 (66.10)	3.84 (3.86)	10.03 (10.05)	7.65 (7.67)
4j	$C_{24}H_{11}N_3O_2SCl$	88	139–140	64.31 (64.35)	3.98 (4.05)	9.33 (9.38)	7.13 (7.16)
4k	$C_{23}H_{15}N_3OSCl_2$	74	127–128	61.05 (61.07)	3.32 (3.34)	9.27 (9.29)	7.10 (7.09)
4l	$C_{23}H_{15}N_4O_3SCl$	76	186–187	59.63 (59.68)	3.25 (3.27)	12.09 (12.10)	6.92 (6.93)
4m	$C_{23}H_{16}N_4O_3S$	70	211–212	64.41 (64.47)	3.75 (3.76)	12.99 (13.08)	7.45 (7.48)
4n	$C_{24}H_{18}N_4O_4S$	66	196–197	62.79 (62.87)	3.97 (3.96)	12.21 (12.22)	7.01 (6.99)
4o	$C_{23}H_{15}N_4O_3SCl$	84	198–199	59.63 (59.68)	3.21 (3.27)	12.09 (12.10)	6.94 (6.93)
4p	$C_{23}H_{15}N_5O_5S$	86	178–179	58.31 (58.35)	3.13 (3.19)	14.78 (14.79)	6.69 (6.77)

We thought, it is worthwhile to synthesize a new series of pyrimidines having 1,3,4-thiadiazole moiety, with the objective of obtaining new biologically active compounds.

The reactions for the synthesis of **(2–4)** are shown in **Scheme-1**. 5-aryl-[1,3,4]thiadiazol-2-ylamines **(2a-d)** has been synthesized by treating thio-semicarbazide with the acids **(1a–d)**. The amines **(2a–d)** on treatment with aromatic aldehydes furnished Schiff bases of thiadiazoles **(3a–p)**, which on reaction with phenylacetyl chloride in presence of triethylamine yield 2,5,7-tri-aryl-5*H*-[1,3,4]thiadiazolo[3,2-*a*]pyrimidin-6[7*H*]-one derivatives **(4a–p)**.



R= a) C_6H_5- b) *p*-CH_3-O-C_6H_4- c) *p*-Cl-C_6H_4- d) *p*-NO_2-C_6H_4-

Ar= a) C_6H_5- b) *p*-CH_3-O-C_6H_4- c) *p*-Cl-C_6H_4- d) m-NO_2-C_6H_4-

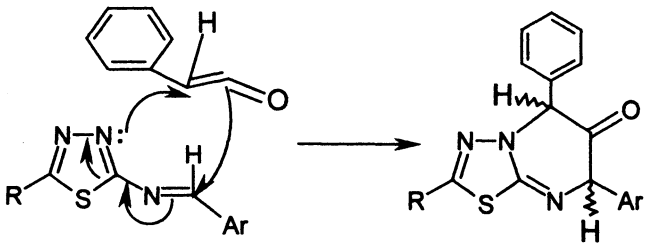
Scheme-1

Compd. No.	R	Ar	Compd. No.	R	Ar	Compd. No.	R	Ar	Compd. No.	R	Ar
3a, 4a	a	a	3e, 4e	b	a	3i, 4i	c	a	3m, 4m	d	a
3b, 4b	a	b	3f, 4f	b	b	3j, 4j	c	b	3n, 4n	d	b
3c, 4c	a	c	3g, 4g	b	c	3k, 4k	c	c	3o, 4o	d	c
3d, 4d	a	d	3h, 4h	b	d	3l, 4l	c	d	3p, 4p	d	d

[1,3,4]thiadiazolo[3,2-*a*]pyrimidin-6-ones are synthesized by a [4 + 2] cycloaddition reaction of benzylideneamino-1,3,4-thiadiazole and aryl ketenes formed *in-situ*. Literature[15] reported the mass fragmentation modes of 1,3,4-thidiazolo[3,2-*a*]pyrimidiones to determine the position of CO in the -5-ones and isometric-7-ones and observed intense ions corresponding to loss of CO from the molecular ion.

In both these types of compounds, a retro-Diels-Alder (RDA) process was observed. This type of intense ion peaks attributed to the loss of CO and RDA process were not observed in the compounds prepared here. It has also been

observed that β-lactam (azetidinone) molecules are less stable and have lower melting points[16] compared to six membered pyrimidinones which have high melting points. In view of these observations compounds **(4)** were proposed to be 2,5,7-triaryl-5*H*-[1,3,4]thiadiazolo[3,2-*a*]pyrimidin-6[7*H*]-ones. A possible-reaction pathway is shown in **Scheme-2**. Finally, we have also partly contributed to this progress by obtaining new 16 derivatives of 2,5,7-triaryl-5*H*-[1,3,4]thiadiazolo[3,2-a]pyrimidin-6[7*H*]-ones.



EXPERIMENTAL

Melting points were determined in open capillary tubes on digital Gallenkamp melting point apparatus and uncorrected. The IR spectra were recorded in KBr with a Mattson 1000 FTIR spectrometer. ^{1}H NMR spectra were recorded on a FX 90 JEOL 90 MHz NMR spectrometer in CDCl + DMSO-d_6 with TMS as an internal standard. Elemental analyses were done on a LECO-CHNS-938. Starting chemicals were obtained from Merck or Aldrich.

General Procedure for (2): A mixture of acid **(1a–d)** (10 mmol), thiosemicarbazide (13 mmol) and phosphorus oxychloride (13 mmol) was warmed at 60°C for 1 h and the temperature was raised to 95°C for an additional 2 h. The contents were then poured on to crushed ice, cooled to 10°C, pH adjusted to 9–10 with 10 M NaOH and the resulting solid was crystallized from DMF to give **(2a–d).**

5-Phenyl-[1,3,4]thidiazol-2-ylamine (2a): Yield 73%, m.p. 222–223°C. IR (KBr, cm^{-1}) ν_{max}: 3420, 1620, 1211, 1074, 982, 876. ^{1}H NMR (DMSO-d_6) δ: 7.85–7.38 (m, 5H, Ar—H), 7.26 (s, 2H, —NH_2); ^{13}C NMR (DMSO, TMS, δ ppm): 170.25, 162.93, 131.46, 127.12, 125.39. Anal. (%), Calcd. for $C_8H_7N_3S$ (177): C, 54.22; H, 3.98; N, 23.71; S, 18.09; Found: C, 54.17; H, 3.91; N, 23.68; S, 17.98.

5-(4-Methoxyphenyl)-[1,3,4]thiadiazol-2-ylamine (2b): Yield 70%, m.p. 201–202°C. IR (KBr, cm^{-1}) ν_{max}: 3428, 1625, 1210, 1075, 980, 875. ^{1}H NMR (DMSO-d_6) δ: 7.71–7.67 (m, 2H, Ar—H), 7.25 (s, 2H, —NH_2), 6.76–6.73 (m, 2H, Ar—H), 3.84 (s, 3H, O-CH_3); ^{13}C NMR (DMSO-d_6, TMS, δ ppm): 171.22, 163.92, 161.03, 128.25, 127.01, 114.88, 55.18. Anal. (%) Calcd. for $C_9H_9N_3OS$ (207): C, 52.16; H, 4.38; N, 20.27; S, 15.47; Found: C, 52.01; H, 4.37; N, 20.19; S, 15.41.

5-(4-Chlorophenyl)-[1,3,4]thiadiazol-2-ylamine (2c) Yield 68%, m.p. 230–231°C. IR (KBr, cm^{-1}) ν_{max}: 3411, 1630, 1211, 1080, 979, 873, 705. ^1H NMR (DMSO-d_6) δ: 7.35–7.22 (m, 6H, Ar—H and —NH_2), ^{13}C NMR (DMSO-d_6, TMS, δ ppm): 171.23, 163.90, 136.11, 131.36, 128.06. Anal. (%) Calcd. for $C_8H_6ClN_3S$ (211): C, 45.39; H, 2.86; N, 19.85; S, 15.15; Found: C, 45.31; H, 2.83; N, 19.79; S, 15.11.

5-(4-Nitrophenyl)-[1,3,4]thiadiazol-2-ylamine (2d): Yield 65%, m.p. 244-245°C. IR (KBr, cm^{-1}) ν_{max}: 3398, 1635, 1213, 1081, 976, 877. ^1H NMR (DMSO-d_6) δ: 8.56–8.53 (m, 2H, Ar—H), 8.30–8.27 (m, 2H, Ar—H), 7.21(s, 2H, —NH_2); ^{13}C NMR (DMSO-d_6, TMS, δ ppm): 171.21, 162.82, 148.82, 137.47, 128.23, 126.77. Anal. (%) Calcd. for $C_8H_6N_4O_2S$ (222): C, 43.24; H, 2.72; N, 25.21; S, 14.43; Found: C, 43.19; H, 2.68; N, 25.17; S, 14.39.

General Procedure for (3): A mixture of 5-aryl-[1,3,4]thiadiazol-2-ylamines **(2a–d)** (10 mmol) and aromatic aldehydes (10 mmol) were added to 100 mL of ethanol : chloroform (7 : 3). Then a few drops of concentrated sulphuric acid were added as a catalyst and the solution was refluxed for 12 h. After removal of the solvent under reduced pressure, the residue was recrystallized from ethanol to give **(3a–p).**

Benzyliedene-(5-phenyl-[1,3,4]thiadiazol-2-ylamine (3a): Yield 72%, m.p. 193–194°C. IR (KBr, cm^{-1}) ν_{max}: 1606 ν(C=N). ^1H NMR (DMSO-d_6) δ: 9.02 (s, 1H, N=CH), 7.89–7.34 (m, 10H, Ar—H); ^{13}C NMR (DMSO-d_6, TMS, δ ppm): 170.15, 168.72, 165.10, 137.59, 133.94, 132.35, 129.92, 132.34, 129.99, 128.99, 128.22, 127.65. Anal. (%) Calcd. for $C_{15}H_{11}N_3S$ (265): C, 67.90; H, 4.18; N, 15.84; S, 12.08; Found: C, 67.89; H, 4.21; N, 15.83; S, 12.10.

(4-Methoxy benzylidene)-(5-phenyl-[1,3,4]thiadiazol-2-yl)amine (3b): Yield 77%, m.p. 208–209°C. IR (KBr, cm^{-1}) 1600 ν(C=N). ^1H NMR (DMSO-d_6) δ: 9.21 (s, 1H, N=CH), 7.86–6.89 (m, 9H, Ar—H), 3.81 (s, 3H, O—CH_3); ^{13}C NMR (DMSO-d_6, TMS, δ ppm): 169.10, 168.27, 165.02, 143.95, 135.94, 134.86, 132.78, 127.63, 116.20, 53.79. Anal. (%) Calcd. for $C_{16}H_{13}N_3OS$ (295): C, 65.06; H, 4.44; N, 14.23; S, 10.86; Found: C, 65.07; H, 4.41; N, 14.29; S, 10.84.

(4-Chloro benzylidene)-(5-phenyl-[1,3,4]thiadiazol-2-yl)amine (3c): Yield 81%, m.p. 251–252°C. IR (KBr, cm^{-1}) 1605 ν(C=N). ^1H NMR (DMSO-d_6) δ: 8.99 (s, 1H, N=CH), 8.06–7.12 (m, 9H, Ar—H); ^{13}C NMR (DMSO-d_6, TMS, δ ppm): 169.16, 166.75, 163.14, 137.82, 136.27, 129.96, 129.48, 128.86, 127.63; Anal. (%) Calcd. for $C_{15}H_{10}ClN_3S$ (299): C, 60.10; H, 3.36; N, 14.02; S, 10.70; Found: C, 60.09; H, 3.31; N, 13.99; S, 10.68.

(3-Nitro benzylidene)-(5-phenyl-[1,3,4]thiadiazol-2-yl)amine (3d): Yield 83%, m.p. 174–175°C. IR (KBr, cm^{-1}) 1610 ν(C=N). ^1H NMR (DMSO-d_6) δ: 9.23 (s, 1H, N=CH), 8.45–7.33 (m, 9H, Ar—H), ^{13}C NMR (DMSO-d_6, TMS, δ ppm): 169.18, 166.87, 165.81, 148.56, 138.36, 135.93, 133.02, 130.14, 129.99, 127.63, 127.13, 123.72, 123.12; Anal. (%) Calcd. for $C_{15}H_{12}N_4O_2S$ (312): C, 57.68; H, 3.87; N, 17.94; S, 10.27; Found: C, 57.61; H, 3.85; N, 18.01; S, 10.29.

Benzylidene-[5-(4-methoxy phenyl)-[1,3,4]thiadiazol-2-yl]amine (3e): Yield 79%; m.p. 188–189°C. IR (KBr, cm^{-1}) 1609 ν(C=N). ^1H NMR (DMSO-d_6) δ: 8.97 (s, 1H, N=CH), 7.80–7.76 (m, 9H, Ar—H), 3.77 (s, 3H, O-CH_3); ^{13}C

NMR (DMSO-d_6, TMS, δ ppm): 169.09, 166.63, 163.09, 161.09, 137.65, 132.35, 128.98, 128.91, 127.31, 116.14, 55.20; Anal. (%) Calcd. for $C_{16}H_{13}N_3OS$ (295): C, 65.06; H, 4.44; N, 14.23; S, 10.8;. Found: C, 64.99; H, 4.47; N, 14.19; S, 10.83.

(4-Methoxy benzylidene)-[5-(4-methoxyphenyl)-[1,3,4]thiadiazol-2-yl]-amine (3f): Yield 88%, m.p. 182–183°C. IR (KBr, cm^{-1}) 1605 ν(C=N). ^1H NMR (DMSO-d_6) δ: 8.98 (s, 1H, N=CH), 7.83–6.76 (m, 8H, Ar—H), 3.82 (s, 3H, O—CH_3), 3.79 (s, 3H, O—CH_3); ^{13}C NMR (DMSO-d_6, TMS, δ ppm): 169.14, 166.73, 163.11, 161.65, 130.91, 130.48, 129.79, 127.32, 116.14, 114.16, 55.21, 53.79; Anal. (%) Calcd. for $C_{17}H_{15}N_3O_2S$ (325): C, 62.75; H, 4.65; N, 12.91; S, 9.85; Found: C, 62.79; H, 4.63; N, 13.00; S, 9.84.

(4-Chloro benzylidene)-[5-(4-methoxyphenyl)-[1,3,4]thiadiazol-2-yl-amine (3g): Yield 90%, m.p. 219–220°C. IR (KBr, cm^{-1}) 1608 ν(C=N). ^1H NMR (DMSO-d_6) δ: 8.98 (s, 1H, N=CH), 8.02–6.75 (m, 8H, Ar—H), 3.75 (s, 3H, O—CH_3), ^{13}C NMR (DMSO-d_6, TMS, δ ppm): 170.01, 166.78, 163.11, 161.08, 137.83, 136.25, 129.49, 128.86, 127.32, 116.15, 55.19; Anal. (%) Calcd. for $C_{16}H_{12}ClN_3OS$ (329): C, 58.27; H, 3.67; N, 12.74; S, 9.72; Found: C, 58.21; H, 3.61; N, 12.79; S, 9.76.

[5-(4-Methoxyphenyl)-[1,3,4]thiadiazol-2-yl]-(3-nitro benzylidene)amine (3h): Yield 92%, m.p. 213–214°C. IR (KBr, cm^{-1}) 1612 ν(C=N). ^1H NMR (DMSO-d_6) δ: 9.19 (s, 1H, N=CH), 8.44-6.75 (m, 8H, Ar-H), 3.77 (s, 3H, O—CH_3;, ^{13}C NMR (DMSO-d_6, TMS, δ ppm): 169.15, 166.78, 165.81, 161.07, 148.51, 138.35, 133.82, 130.16, 127.32, 123.74, 116.14, 55.20; Anal. (%) Calcd. for $C_{16}H_{14}N_4O_3S$ (342): C, 56.13; H, 4.12; N, 16.36; S, 9.37; Found: C, 56.09; H, 4.17; N, 15.35; S, 9.31.

Benzylidene-[5-(4-chloro phenyl)-[1,3,4]thiadiazol-2-yl]amine (3i): Yield 81%, m.p. 239-240°C. IR (KBr, cm^{-1}) 1613 ν(C=N). ^1H NMR (DMSO-d_6) δ: 8.96 (s, 1H, N=CH), 7.86–7.16 (m, 9H, Ar–H), ^{13}C NMR (DMSO-d_6, TMS, δ ppm): 169.13, 166.77, 163.09, 137.65, 130.13, 132.34, 132.31, 128.99, 128.92, 127.10; Anal. (%) Calcd. for $C_{15}H_{10}ClN_3S$ (299): C, 60.10; H, 3.36; N, 14.02; S, 10.70; Found: C, 59.99; H, 3.35; N, 13.98; S, 10.69.

[5-(4-Chloro phenyl)-[1,3,4]thiadiazol-2-yl]-(4-methoxy-benzylidene)-amine (3j): Yield 88%, m.p. 178–179°C. IR (KBr, cm^{-1}) 1606 ν(C=N). ^1H NMR (DMSO-d_6) δ: 8.95 (s, 1H, N=CH), 7.83–6.93 (m, 8H, Ar-H), 3.81 (s, 3H, O-CH_3); ^{13}C NMR (DMSO-d_6, TMS, δ ppm): 169.13, 166.76, 163.13, 136.13, 134.88, 132.31, 130.80, 127.09, 114.13, 53.79; Anal. (%) Calcd. for $C_{16}H_{12}ClN_3OS$ (329): C, 58.27; H, 3.67; N, 12.74; S, 9.72; Found: C, 58.21; H, 3.70; N, 12.75; S, 9.71.

(4-Chloro benzylidene)-[5-(4-chlorophenyl)-[1,3,4]thiadiazol-2-yl]amine (3k): Yield 84%, m.p. 269–270°C. IR (KBr, cm^{-1}) 1600 ν(C=N). ^1H NMR (DMSO-d_6) δ: 8.98 (s, 1H, N=CH), 8.03–7.12 (m, 8H, Ar-H); ^{13}C NMR (DMSO-d_6, TMS, δ ppm): 169.15, 166.78, 163.10, 137.84, 136.25, 136.14, 134.86, 132.31, 129.48, 128.87; Anal. (%) Calcd. for $C_{15}H_9Cl_2N_3S$ (334): C, 53.91; H, 2.71; N, 12.57; S, 9.59; Found: C, 54.00; H, 2.68; N, 12.55; S, 9.60.

[5-(4-chloro-phenyl)-[1,3,4] thiadiazol-2-yl]-(3-nitro-benzylidene)amine

(3l): Yield 79%, m.p. 161–162°C. IR (KBr, cm^{-1}) 1600 ν(C=N). ^1H NMR (DMSO-d_6) δ: 9.21 (s, 1H, N=CH), 8.46–7.14 (m, 8H, Ar—H); ^{13}C NMR (DMSO-d_6, TMS, δ ppm): 169.11, 167.78, 165.82, 148.51, 138.35, 136.14, 133.82, 132.31, 130.16, 127.11, 123.74, 123.13; Anal. (%) Calcd. for $C_{15}H_{11}ClN_4O_2S$ (346): C, 51.95; H, 3.20; N, 16.16; S, 9.25; Found: C, 52.00; H, 3.19; N, 16.15; S, 9.27.

Benzylidene-[5-(4-nitro-phenyl)-[1,3,4]thiadiazol-2-yl]amine (3m): Yield 79%, m.p. 229–230°C. IR (KBr, cm^{-1}) 1613 ν(C=N). ^1H NMR (DMSO-d_6) δ: 8.97 (s, 1H, N=CH), 8.59–7.39 (m, 9H, Ar—H); ^{13}C NMR (DMSO-d_6, TMS, δ ppm): 169.16, 166.77, 163.11, 148.78, 141.97, 140.87, 137.69, 132.25, 128.99, 128.91, 128.47, 125.73; Anal. (%) Calcd. for $C_{15}H_{12}N_4O_2S$ (312): C, 57.68; H, 3.87; N, 17.94; S, 10.27; Found: C, 57.65; H, 3.81; N, 18.00; S, 10.27.

(4-Methoxy-benzylidene)-[5-(4-nitro-phenyl)-[1,3,4]thiadiazol-2-yl]amine (3n): Yield 81%, m.p. 217–218°C. IR (KBr, cm^{-1}) ν: 1603 (C=N). ^1H NMR (DMSO-d_6) δ: 8.98 (s, 1H, N=CH), 8.58–6.94 (m, 8H, Ar—H), 3.81 (s, 3H, O—CH_3; ^{13}C NMR (DMSO-d_6, TMS, δ ppm): 169.11, 166.79, 163.11, 147.87, 141.95, 130.90, 130.80, 128.46, 125.73, 114.16, 53.79; Anal. (%) Calcd. for $C_{16}H_{14}N_4O_3S$ (342): C, 56.13; H, 4.12; N, 16.36; S, 9.37; Found: C, 56.11; H, 4.16; N, 16.30; S, 9.39.

(4-Chloro benzylidene)-[5-(4-nitro-phenyl)-[1,3,4]thiadiazol-2-yl]amine (3o): Yield 91%, m.p. 168–169°C. IR (KBr, cm^{-1}) 1606 ν(C=N). ^1H NMR (DMSO-d_6) δ: 8.95 (s, 1H, N=CH), 8.59–7.12 (m, 8H, Ar—H), ^{13}C NMR (DMSO-d_6, TMS, δ ppm): 169.13, 166.75, 163.09, 147.87, 141.97, 137.83, 136.25, 129.48, 128.87, 128.46, 125.72; Anal. (%) Calcd for $C_{15}H_{11}ClN_4O_2S$ (346): C, 51.95; H, 3.20; N, 16.16; S, 9.25; Found: C, 54.00; H, 3.19; N, 16.11; S, 9.28.

(3-Nitro benzylidene)-[5-(4-nitrophenyl)-[1,3,4]thiadiazol-2-yl]amine (3p): Yield 89%, m.p. 209–210°C. IR (KBr, cm^{-1}) 1611 ν(C=N). ^1H NMR (DMSO-d_6) δ: 9.22 (s, 1H, N=CH), 8.59–7.73 (m, 8H, Ar—H), ^{13}C NMR (DMSO-d_6, TMS, δ ppm): 169.15, 166.77, 165.80, 148.51, 147.88, 141.95, 138.35, 130.81, 130.15, 128.46, 125.72, 123.73, 123.13; Anal. (%) Calcd. for $C_{15}H_{13}N_5O_4S$ (359): C, 50.13; H, 3.65; N, 19.49; S, 8.92; Found: C, 50.15; H, 3.63; N, 19.51; S, 9.00.

General Procedure for (4): Schiff bases **(3a–p)** (1.0 mmol) in dioxane (25 mL) were added to triethylamine (1 mL) and then to this solution was added phenylacetyl chloride (1.0 mmol) in dioxane dropwise at 0°C under stirring during 30 min. The reaction mixture was brought to room temperature and kept stirring for another 6 h at 60°C. The reaction mixture after cooling to room temperature was poured into ice (100 g) and extracted with chloroform (2 × 60 mL) and dried over $MgSO_4$. Removal of the solvent under reduced pressure and recrystallization of the residue were carried out in ethanol to give **(4a–p).** The compounds are characterized (Table-1) and their physical and analytical data are presented in Table-2.

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