

# Synthesis and Antibacterial Activity Studies of Some 2-(Substitutedphenyl)-3-bis2, 4-(4'-methylphenylamino)-s-triazine-6- ylaminobenzoylamino-5-H-4-thiazolidinone

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**Abstract:** Some 4- thiazolidinone derivatives **6(a-l)** have been prepared bearing *s*-triazine moiety by the condensation of Schiff bases from bis-2,4 (4'-methylphenylamino)-*s*-triazine-6-ylaminobenzoyl substituted benzylhydrazone **5(a-l)** with thioglycolic acid. The structures of synthesized compounds have been characterized by IR, <sup>1</sup>HNMR spectral studies. The synthesized compounds **6(a-l)** have been screened for antibacterial activity.

**Keywords:** *s*-Triazine, 4- Thiazolidinone, Antibacterial activity.

## Introduction

The survey of literature related to 4- thiazolidinone derivatives show that compounds with these nuclei have vast medicinal importance. The field ring system is of considerable interest as it is a core structure in various synthetic pharmaceuticals displaying a broad spectrum of biological activities<sup>1</sup>. 4- thiazolidinone a saturated form of thiazole with carbonyl group on fourth carbon, has been considered as a magic moiety (wonder nucleus) which possesses almost all types of biological activities<sup>2</sup> such as anti HIV<sup>3</sup>, anticonvulsant<sup>4</sup>, anticancer<sup>5</sup>, antitubercular<sup>6</sup>, cardioprotective<sup>7</sup>, antiinflammatory<sup>8</sup>, antidiabetic<sup>9</sup> and antimicrobial<sup>10</sup>.

## Experimental

All the melting points were determined in open capillaries and are uncorrected. The reactions were monitored on TLC. The IR spectra were recorded in KBr pellets on a perkin-Elmer 237 spectrophotometer. <sup>1</sup>HNMR spectra on a Bruker Avance DPX 300 MHz spectrometer with CDCl<sub>3</sub> as a solvent, using TMS as internal reference. Elemental analyses were carried out on a carlo Elba 1108 model analyzer.

*Preparation of 2-(4'-methyl phenyl amino)-s-triazine 1*

*p*-Toluidine (0.01 mole) was added slowly to cyanuric chloride (0.01 mole) in dioxane (30 mL) with constant stirring for 4 h at 0 to 5 °C. Then sodium carbonate (0.005 mole) dissolved in water (10 mL) was added drop wise to neutralize HCl evolved during the reaction. Finally the contents were poured into ice. The solid separated out was filtered, washed with water, dried and recrystallized from alcohol. m.p 196 °C, yield 86%.

*Preparation of bis-2,4-(4'-methyl phenyl amino)- s-triazine 2*

*p*-Toluidine (0.01 mole) was added slowly to compound I (0.01 mole) in dioxane (35 mL) with constant stirring for 6 h at room temperature. Then sodium carbonate (0.005 mole) dissolved in water (10 mL) was added drop wise to neutralize HCl evolved during the reaction. Finally the contents were poured into crushed ice. The solid separated out was filtered, washed with water, dried and recrystallized from alcohol. m.p.179 °C.yield 80%.

*Preparation of bis 2,4-(4'-methyl phenyl amino)-s-triazin-6-yl-aminoethyl benzoate 3*

Ethyl *p*-aminobenzoate (0.01 mole) and compound 2 (0.01 mole) were dissolved in dioxane (40 mL). The reaction mixture was refluxed for 6 h, cooled and poured into crushed ice. Then sodium carbonate (0.005 mole) dissolved in water (10 mL) was added to neutralize HCl evolved during the reaction. The solid separated out was filtered, washed with water, dried and recrystallized from alcohol. m.p. 219 °C yield 78%. IR (KBr, cm<sup>-1</sup>), 2956(C-H),3102(Ar-H), 1470(C=N), 806(C-N) 3362(N-H), 1680(C=O).

*Preparation of bis-2,4-(4'-methylphenylamino)-s-triazine-6-ylaminobenzoyl hydrazone 4*

A mixture of compound 3(0.01 mole) in dioxane and hydrazine hydrate (0.01 mole), was refluxed on a water bath for 6 h. The product was isolated with HCl and crystallized from dioxane.m.p.198 yield 79 IR (KBr, cm<sup>-1</sup>), 2908(C-H), 3056(Ar-H), 1498(C=N), 807(C-N), 3356(N-H), 1670(C=O).

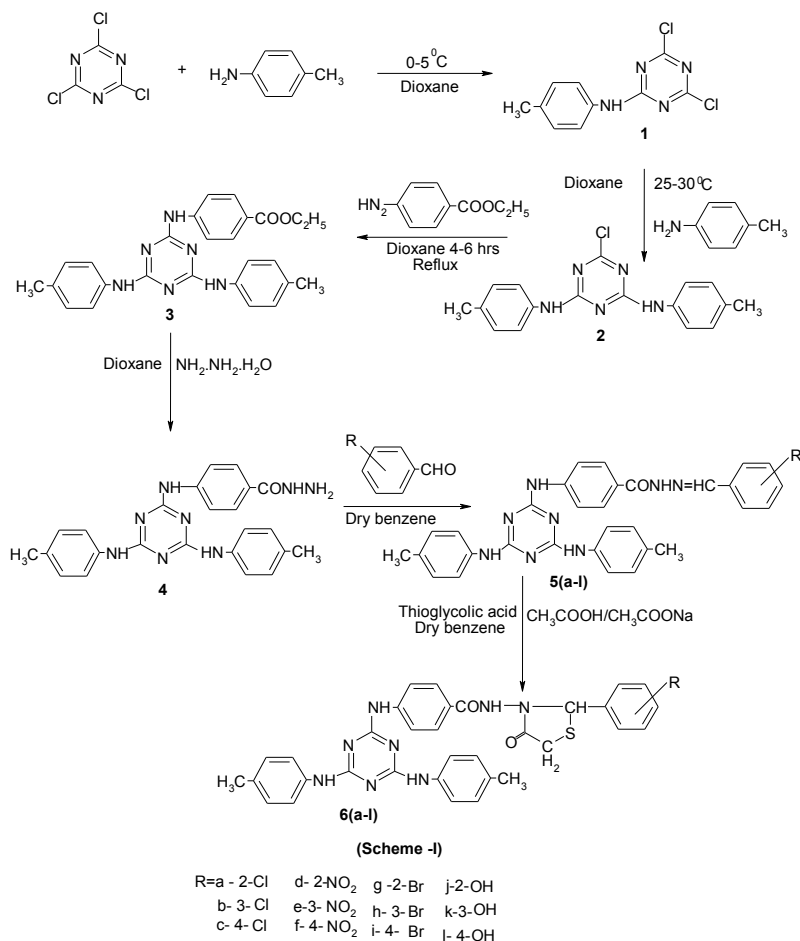
*Preparation of bis-2,4(4'-methylphenylamino)-s-triazine-6-ylaminobenzoyl substituted benzylhydrazone 5*

A mixture of compound 4 (0.01 mole) and substituted aldehyde (0.01 mole) in dioxane (15 mL) was refluxed for 4hrs. The product was isolated and crystallized from methanol. m.p.150 °C.Yield78%. IR (KBr,cm<sup>-1</sup>) 2985(C-H), 3056(Ar-H), 3399(N-H), 1420 (C= N), 1675(C=O), 805(C-N). <sup>1</sup>HNMR (CDCl<sub>3</sub>, δ), 6.45 (Sym.multi. 2CH<sub>3</sub> subs. Benzene ring 8H), 7.68 (S,4N-H,4H), 2.38 (s,2CH<sub>3</sub>,6H), 1.95(s,C-H of thiazolidinone), 6.31 (sym.multi.N-H subs.benzene ring)

*Preparation of 2-substitutedphenyl-3-bis-2,4-(4'-methylphenylamino)-s-triazine-6-ylaminobenzoyl amino-5-H-4- thiazolidinone 6*

Thioglycolic acid (0.01 mole) was added to compound 5 (0.01 mole) in dry benzene (20 mL)and refluxed for 6 h. The product was isolated by washing the upper organic layer with water and sodium bicarbonate solution and crystallized from dioxane. m.p. 197 °C yield 76%. IR(ν<sub>max</sub> in cm<sup>-1</sup>),3456(N-H,3095(Ar-H), 1602(C=C), 1675 (C=O), 750(C-S), 1306 (C=N),802(C-N)675(Ar-Cl). <sup>1</sup>HNMR(CDCl<sub>3</sub>, δ), 6.40 (sym. multi., 8H,2CH<sub>3</sub> subs.benzene ring), 7.45(s,4H,N-H sub. Benzene ring) 2.38(s, 2CH<sub>3</sub>, 6H).

## Reaction Sequence

**Table 1.** Physical characterization data of synthesized compound **6(a-l)**.

Compd	Mol. Formula	Mol. Wgt.	Yield %	m.p. °C	Elemental analysis					
					C %		H %		N %	
					Calcd	Found	Calcd	Found	Calcd	Found
<b>6a</b>	C <sub>33</sub> H <sub>29</sub> N <sub>8</sub> O <sub>2</sub> ClS	637.145	72	146	62.12	62.11	4.58	4.56	17.58	17.55
<b>6b</b>	C <sub>33</sub> H <sub>29</sub> N <sub>8</sub> O <sub>2</sub> ClS	637.145	76	146	62.12	62.10	4.58	4.56	17.58	17.56
<b>6c</b>	C <sub>33</sub> H <sub>29</sub> N <sub>8</sub> O <sub>2</sub> ClS	637.145	74	146	62.12	62.09	4.58	4.55	17.58	17.55
<b>6d</b>	C <sub>33</sub> H <sub>29</sub> N <sub>9</sub> O <sub>4</sub> S	647.682	68	142	61.10	61.08	4.5	4.3	19.46	19.43
<b>6e</b>	C <sub>33</sub> H <sub>29</sub> N <sub>9</sub> O <sub>4</sub> S	647.682	69	142	61.10	61.09	4.5	4.3	19.46	19.44
<b>6f</b>	C <sub>33</sub> H <sub>29</sub> N <sub>9</sub> O <sub>4</sub> S	647.682	78	142	61.10	61.08	4.5	4.4	19.46	19.4
<b>6g</b>	C <sub>33</sub> H <sub>29</sub> N <sub>8</sub> O <sub>2</sub> BrS	681.595	75	147	58.15	58.13	4.28	4.25	16.44	16.42
<b>6h</b>	C <sub>33</sub> H <sub>29</sub> N <sub>8</sub> O <sub>2</sub> BrS	681.595	71	147	58.15	58.12	4.28	4.25	16.44	16.41
<b>6i</b>	C <sub>33</sub> H <sub>29</sub> N <sub>8</sub> O <sub>2</sub> BrS	681.595	73	147	58.15	58.12	4.28	4.25	16.44	16.41
<b>6j</b>	C <sub>33</sub> H <sub>30</sub> N <sub>8</sub> O <sub>3</sub> S	618.693	77	129	64.06	64.03	4.88	4.86	18.11	18.09
<b>6k</b>	C <sub>33</sub> H <sub>30</sub> N <sub>8</sub> O <sub>3</sub> S	618.693	71	129	64.06	64.04	4.88	4.87	18.11	18.09
<b>6l</b>	C <sub>33</sub> H <sub>30</sub> N <sub>8</sub> O <sub>3</sub> S	618.693	78	129	64.06	64.03	4.88	4.86	18.11	18.08

## Results and Discussion

The reaction of *s*-triazine and *p*-toluidine in the dioxane gave bis -2,4 (4'-methyl phenyl amino)-*s*-triazine **2** in two steps. The compound **2** was treated with ethyl *p*-amino benzoate in dioxane to get bis 2,4-(4'-methyl phenyl amino)-*s*-triazine-6'-yl-aminoethylbenzoate **3**. The structure **3** was confirmed by its spectral and analytical studies. The compound **4** was obtained by reaction of **3** with hydrazine hydrate and characterized by its spectral and analytical datas. Its IR spectrum revealed the presence of -NH-, NH<sub>2</sub>, C=O and aromatic ring at 2274, 3356, 1670 and 3056 cm<sup>-1</sup>. The compounds **4** was then condensed with different aromatic aldehydes to get Schiff bases **5**. Which on treatment with thioglycolic acid gave substituted 4- thiazolidinone. Which was characterized by its spectral and analytical datas, its IR spectrum revealed the presence of =C=O group in five membered ring at 1820 cm<sup>-1</sup> the NMR spectrum of **6** in CDCl<sub>3</sub> show one singlet at 7.4 δ due to 3NH protons and one singlet at 2.82 δ due to 2 CH<sub>3</sub> group. The two complex multiplets at 6.2 and 4.2δ were assigned for 8H of two aromatic rings. The thiazolidinone ring characterized by 1H singlet at 3.2ppm and 2H singlet at 3.4 δ. The C, H, N analysis of the compounds **6a** is in good agreement with the proposed molecular formula, C<sub>33</sub>H<sub>29</sub>H<sub>8</sub>O<sub>2</sub>ClS. This was also supported by mass spectrum of the compound which displayed the molecular ion peak at 637.143 and 491.067. All compounds have exhibited good to moderate antibacterial activity.

### Antibacterial activity

The synthesized compounds have been screened for antibacterial activities using filter paper disc diffusion plate<sup>11</sup> method. The testing was carried out at concentration 50 ppm and 100 ppm using bacteria like *E. Coli*, *B. subtilis*, *S. aureus*, *B. fragilis* and *K. pneumonie*, Streptomycin (for bacteria) was used as standard drug. Most of the synthesized compounds have found moderate activity (20-24 zone of inhibition) against different strains of bacteria. Related data have been given in Table 2.

**Table 2.** Antibacterial activity of the synthesized compounds **6(a-l)** against various bacteria at two different concentrations (ppm).

Compd	<i>E. Coli</i>		<i>B.Subtilis</i>		<i>S.aureus</i>		<i>B.Fragilis</i>		<i>K.pneumonie</i>	
	Concd, ppm		Concd, ppm		Concd, ppm		Concd, ppm		Concd, ppm	
	50	100	50	100	50	100	50	100	50	100
<b>6a</b>	+++	++++	+++	++++	++	+++	+	++	+++	++++
<b>6b</b>	+++	++	++	+++	++	+++	++	+++	+++	++++
<b>6c</b>	+++	+++	++++	+++	+	+++	+++	+++	+++	++
<b>6d</b>	++	++	+	+	+	++	+	++	-	-
<b>6e</b>	++	+++	++	+++	++	+++	++	+++	++	+++
<b>6f</b>	++	+++	++	++	+++	+++	+++	++	+++	++
<b>6g</b>	-	+	+	+	+	++	-	-	+	++
<b>6h</b>	++	+++	++	+++	++	+++	++	+++	++	+++
<b>6i</b>	++	+++	++	+++	++	+++	++	+++	++	+++
<b>6j</b>	++	+++	+	++	+	++	++	+++	++	+++
<b>6k</b>	++	+++	++	+++	+++	+++	++++	++	++++	+++
<b>6l</b>	++	+++	++	+++	++	+++	++	+++	++	+++
Std.	+++	++++	++++	++++	+++	++++	+++	++++	+++	++++

Std. streptomycin is used as standard drug. Inhibition diameter in mm:- 0-4(-), 5-9(+), 10-14(++), 15-19(+++), 20-24(++++).

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