

# Convenient method for Synthesis of new derivatives of (1-(4-(2,4-dichlorophenyl)-2-((4-nitrobenzylidene)amino)thiazol-5-yl)ethan-1-one

## Abstracts

The new derivatives of thiazole based Schiff base of (1-(5-(2,3,4-trisubstitutedphenyl)-2-((4-nitrobenzylidene)amino)thiazol-4-yl)ethan-1-one (6) were synthesized by the treatment of 1-(2-amino-5-(2,3,4-trisubstitutedphenyl)thiazol-4-yl)ethan-1-one (4) and corresponding substituted benzaldehyde (5) in low cost easily available non flammable stable and ecofriendly solvent Polyethylene glycol-400 solvent medium. The reactions were performed in the good yield and less time. The structures of all synthesized compounds were established on the basis of elemental analysis, IR, NMR and Mass spectral data.

**Keywords:** new derivative, thiazole Schiff base, Polyethylene glycol-400, low cost, non flammable, ecofriendly solvent

## 1. INTRODUCTION

Thiazole derivative performs the various important pharmacological properties. These thiazole derivatives acts as cytotoxic and antitumor activity and used as therapy to treat to deadly disease as anticancer agent. Dabrafenib and Dasatinib are the derivative of thiazole which is used for cancer therapy with tyrosine kinase inhibitory activity<sup>1-2</sup>. The compound Schiff base is the imines derivative of 2-amino thiazole which is biologically active compounds. The Schiff base is derived from the reaction between the amine and aldehyde in acidic medium. In 2-amino thiazole the terminal amino group is responsible for the formation of Schiff base as thiazole derivatives. Important biological properties of Schiff base fascinated to different scientist and research scholar, as it shows antibacterial<sup>3-4</sup>, antifungal<sup>5</sup>, antimicrobial<sup>6</sup>, anticonvulsant activity<sup>7</sup>, anticancer<sup>8-10</sup>, antitumor<sup>11</sup>, antituberculosis<sup>12</sup>, anti HIV-1<sup>13-14</sup> anti-inflammatory agents<sup>15</sup>, insecticidal<sup>16</sup> and antiviral agent<sup>17</sup>. The Schiff bases have wide range of application in pharmaceutical preparation<sup>18-19</sup>

Above important properties of the thiazole Schiff base compounds attract the researcher to synthesize it in systematic manner. Its first synthesis was carried out by Hugo Schiff in 1864 by interaction of carbonyl group such as aldehydes and ketones with primary amines to produce the substituted imines derivative known as Schiff base<sup>20-21</sup>. After that a number of different derivatives of Schiff bases derived by applying different methods were reported.<sup>22</sup> to synthesized this valuable compounds different catalyst were employed such as copper nitrate<sup>23</sup>, cerium chloride<sup>24</sup>, piperidine<sup>25</sup> etc. these methods reported in the

literature are either low yield producing or solvent or catalyst used are hazardous to the environment. The development of ecofriendly and non hazardous methods of synthesis of target compounds are still in demands. With increasing environmental concerns and the regulatory constraints, the development of environmentally benign organic reactions has become a crucial and demanding area in modern organic chemical research. We wish to report a practical and convenient method for the preparation of newly substituted Schiff base, in PEG 400 a green and ecofriendly solvent medium. Polyethylene glycol 400 is the emerging solvent widely used in various chemical transformations. The increase in the usability of PEG 400 solvent is due to its notable characteristic properties<sup>26</sup> such as nonvolatile, high stability, nonflammable, non-toxic, cost-effective, readily available and safe to use.

Synthesis of (1-(5-(2,3,4-trisubstitutedphenyl)-2-((4-nitrobenzylidene)amino)thiazol-4-yl)ethan-1-one (6) were carried out by the treatment of 1-(2-amino-5-(2,3,4-trisubstitutedphenyl)thiazol-4-yl)ethan-1-one (4) and corresponding substituted benzaldehyde (5) in PEG-400 solvent medium.

## 2. MATERIAL AND METHODS

All chemicals used were of AR grades. The chemical used for all these works were purchased from research lab fine chemical industry, Mumbai. The melting points of all the synthesized compounds

were recorded using hot paraffin bath. The Carbon and Hydrogen analysis were carried out on Carlo-Ebra 1106 analyzer. Nitrogen estimation was carried out on Colman-N-analyzer-29. IR spectra were recorded on Bruker neo. Ltd. spectrometer in the range 4000-400  $\text{cm}^{-1}$  in KBr pellets. NMR spectra were recorded on Bruker AC-500F spectrometer with TMS as internal standard using  $\text{CDCl}_3$  as solvent. Mass spectra were recorded on shimadzu 2010s Mass spectrometer. The purity of compound was checked on silica Gel-G plates by TLC with layer thickness of 0.3 mm.

### 3. RESULTS AND DISCUSSION

#### 3.1 Synthesis of 1-(5-(2,4-dichlorophenyl)-2-((4-nitrobenzylidene)amino)thiazol-4-yl)ethan-1-one (6a)

0.01 mole of 1-(2-amino-5-(2,4-dichlorophenyl)thiazol-4-yl)ethan-1-one (4a) and 0.01 mole of corresponding substituted benzaldehyde were dissolved in 20 ml PEG-400 solvent add 4-5 drops of hydrochloric acid. The reaction mixture was refluxed for 3-4 h. The resinous brown coloured reaction mixture was left to stand at room temperature overnight. The reaction mixture poured in ice cold water to hydrolysed it. The product was extracted in ethyl acetate with the help of separating funnel and drying with  $\text{Na}_2\text{SO}_4$ . Brown coloured solid obtained was recrystallised with ethanol.

The yield of the dried crude product (6a) was found to be 80%, Melting Point: - 102°C,

Molecular Weight: 420.3

m/z: 419.0 (100.0%), 421.0 (63.9%), 420.0 (19.5%), 422.0 (12.4%), 423.0 (10.2%), 421.0 (4.5%), 423.0 (2.9%), 424.0 (2.0%), 421.0 (1.8%), 423.0 (1.1%), 420.0 (1.1%) Analysis: C, 51.44%; H, 2.64%; Cl, 16.87%; N, 10.00%; S, 7.63% IR (KBr,  $\text{cm}^{-1}$ ): 1607.46  $\text{cm}^{-1}$ , 1694.73  $\text{cm}^{-1}$ , 1313.39  $\text{cm}^{-1}$ , 1499.67  $\text{cm}^{-1}$ , 753.24  $\text{cm}^{-1}$ ,  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  2.00 (s,3H, O=C-C-H<sub>3</sub>),  $\delta$  8.91(s,1H, H-C=N),  $\delta$  7.25 -8.0(s, 7H, Ar-H)

#### 3.2 Synthesis of 1-(5-(3-bromo-2,4-dichlorophenyl)-2-((4-nitrobenzylidene)amino)thiazol-4-yl)ethan-1-one (6b)

0.01 mole of 1-(2-amino-5-(3-bromo-2,4-dichlorophenyl)thiazol-4-yl)ethan-1-one (4b) and 0.01 mole of Para-Nitro benzaldehyde(5a) were dissolved in 20 ml PEG-400 solvent add 4-5 drops of hydrochloric acid. The reaction mixture was refluxed for 3-4 h. The resinous brown coloured reaction mixture was left to stand at room temperature overnight. The reaction mixture poured in ice cold water to hydrolysed it. The product was extracted in ethyl acetate with the help of separating funnel and drying with  $\text{Na}_2\text{SO}_4$ . Brown coloured solid obtained was recrystallised with ethanol.

The yield of the dried crude product was found to be 81%, Melting Point: - 136°C

Molecular Weight: 499.2

m/z: 496.9 (100.0%), 498.9 (97.3%), 498.9 (63.9%), 500.9 (62.2%), 499.9 (18.9%), 497.9 (16.2%), 501.9 (12.1%), 499.9 (10.4%), 500.9 (10.2%), 502.9 (9.9%), 498.9 (4.5%), 500.9 (4.4%), 497.9 (3.2%), 500.9 (2.9%), 502.9 (2.8%), 499.9 (2.1%), 501.9 (2.0%), 503.9 (1.9%), 500.9 (1.7%), 500.9 (1.1%), 497.9 (1.1%), 499.9 (1.1%), 498.9 (1.1%),Elemental Analysis: C, 43.37%; H, 2.00%; Br, 16.05%; Cl, 14.10%; N, 8.35%; S, 6.50%,IR (KBr,  $\text{cm}^{-1}$ ): 1699.46  $\text{cm}^{-1}$ , 1694.73  $\text{cm}^{-1}$ ,1313.39  $\text{cm}^{-1}$ , 1499.67  $\text{cm}^{-1}$ , 777.89  $\text{cm}^{-1}$ , 834.95  $\text{cm}^{-1}$ ,  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  2.09 (s,3H, O=C-C-H<sub>3</sub>),  $\delta$  9.84 (s,1H, H-C=N),  $\delta$  6.96 -7.81(s, 7H, Ar-H)

### 3.3 Synthesis of 1-(5-(2,4-dichlorophenyl)-2-((2-hydroxybenzylidene)amino)thiazol-4-yl)ethan-1-one (6c)

0.01 mole of 1-(2-amino-5-(2,4-dichlorophenyl)thiazol-4-yl)ethan-1-one (4a) and 0.01 mole of ortho hydroxy benzaldehyde(5b) were dissolved in 20 ml PEG-400 solvent add 4-5 drops of hydrochloric acid. The reaction mixture was refluxed for 3-4 h. The resinous brown coloured reaction mixture was left to stand at room temperature overnight. The reaction mixture poured in ice cold water to hydrolysed it. The product was extracted in ethyl acetate with the help of separating funnel and drying with Na<sub>2</sub>SO<sub>4</sub>. Brown coloured solid obtained was recrystallised with ethanol.

The yield of the dried crude product was found to be 75%, Melting Point: - 90°C

Molecular Weight: 391.3

m/z: 390.0 (100.0%), 392.0 (63.9%), 391.0 (19.5%), 393.0 (12.4%), 394.0 (10.2%), 392.0 (4.5%), 394.0 (2.9%), 395.0 (2.0%), 392.0 (1.8%), 394.0 (1.1%), Elemental Analysis: C, 55.15%; H, 3.00%; Cl, 18.20%; N, 7.20%; S, 8.20%, IR (KBr, cm<sup>-1</sup>): 1598.65 cm<sup>-1</sup>, 1724.30 cm<sup>-1</sup>, 1283.09 cm<sup>-1</sup>, 1499.67 cm<sup>-1</sup>, 749.66 cm<sup>-1</sup>, 3701.88 cm<sup>-1</sup>, <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 2.69 (s, 3H, O=C-C-H<sub>3</sub>), δ 9.00 (s, 1H, H-C=N), δ 11.11 (s, OH), δ 6.96 - 7.81 (s, 7H, Ar-H)

In the present research work synthesis of 1-(5-(2,3,4-trisubstitutedphenyl)-2-((4-nitrobenzylidene)amino)thiazol-4-yl)ethan-1-one (6) were carried out by the treatment of 1-(2-amino-5-(2,3,4-trisubstitutedphenyl)thiazol-4-yl)ethan-1-one (4) and corresponding substituted benzaldehyde (5) in PEG-400 solvent medium. And the times required for completion of reaction were noted it was observed that the time required for completion of reactions was in between 4 to 5 hours. As well as the solvent medium water are easily available and cost effective. To reduce time duration required for completion of reaction and for maintaining green chemistry parameters and to develop new reaction conditions, the reactions were carried out in PEG 400 mediums. This is an emerging solvent system to carry out various synthetic methods. This solvent is easily available water soluble and easy to handle. The isolation of reaction product is also easy.

Following different 1-(5-(2,3,4-trisubstitutedphenyl)-2-((4-nitrobenzylidene)amino)thiazol-4-yl)ethan-1-one (6) derivative were synthesized using PEG-400 solvent medium, such as

**Table 1. showing the synthesis of different substituted 1-(5-(2,3,4-trisubstitutedphenyl)-2-((4-nitrobenzylidene)amino)thiazol-4-yl)ethan-1-one (6)**

Sr No.	Expt. No.	Compound	Yield %	M.P °C	Colour
1	4	1-(2-((2-bromobenzylidene)amino)-5-(2,4-dichlorophenyl)thiazol-4-yl)ethan-1-one (6d)	80	190	Dark Brown colour solid
2	5	1-(2-((4-bromobenzylidene)amino)-5-(2,4-dichlorophenyl)thiazol-4-yl)ethan-1-one (6e)	82	190-195	Yellow Brown colour solid
3	6	E)-1-(2-((2-chlorobenzylidene)amino)-5-(2,4-dichlorophenyl)thiazol-4-yl)ethan-1-one (6f)	78	135-140	Light Brown colour solid
4	7	1-(2-((4-chlorobenzylidene)amino)-5-(2,4-dichlorophenyl)thiazol-4-yl)ethan-1-one (6g)	80	145-147	Brown colour solid

5	8	1-(5-(naphthalen-2-yl)-2-((4-nitrobenzylidene)amino)thiazol-4-yl)ethan-1-one (6h)	70	85-87	sticky Brown colour solid
6	9	1-(5-(3-hydroxynaphthalen-2-yl)-2-((4-nitrobenzylidene)amino)thiazol-4-yl)ethan-1-one (6i)	75	126-127	Blackish Brown colour solid
7	10	1-(5-(3-hydroxy-8-nitronaphthalen-2-yl)-2-((4-nitrobenzylidene)amino)thiazol-4-yl)ethan-1-one (6j)	70	180-185	Yellow Brown colour solid

#### 4. CONCLUSION

In conclusion, we have shown that the present method of synthesis of title compound by avoiding the hazardous catalyst and hazardous solvent medium. In this work we present a new alternative path by using **easily available environment friendly** solvent medium such as Polyethylene glycol-400. This study will be beneficial for new researcher and scientists among the chemistry worlds.

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