Synthesis of New Substituted Tetrazole and 4-Thiazolidinone from Schiff’s Bases

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Abstract. The present work involved the synthesis of compound (1) (1-amino-4-methyl-6-phenyl pyrimidine-2-(1H)-thione). This compound reacts with different aromatic aldehydes using glacial acetic acid as catalytic on absolute ethanol to give a new series of Schiff’s bases (2-7). New thiazolidine-4-one were prepared from reactions of Schiff’s bases (2,3,4,7) with thioglycolic acid in absolute ethanol giving compounds (8-11). Finally the preparation of new tetrazole derivatives (12-15) by reaction of Schiff’s bases (2,3,4,7) with sodium azide in THF. The structure of the synthesized compounds are confirmed by I.R., 1H-NMR and 13C-NMR spectra and some physical data.

Keywords: tetrazole, thiazolidinone, schiff’s bases

Introduction
Schiff bases are used as substrates in the preparation of number of industrial and biologically active compounds via ring closure, (cyclo addition and replacement reaction) Harika et al. (2014). Thiazolidinone derivatives have various pharmacological activities such as antibacterial (Subdhi et al., 2005), anti fungal (Patel, 2011), anticancer (Srivastava et al., 2002), anticonvulsant (Parekh et al., 2004) and herbicidal actions (Qien et al., 2006). Tetrazoles have been found to exhibit antihistamine (Samadiya and Halve, 2001), antifungal properties (Pradip and Berad, 2008).

Materials and Methods
All reagents and chemicals are from BDH and Fluka, used without purification. Melting points were measured using: electro thermal melting points apparatus type (not corrected). FT spectra were recorded on Shimadzu FT-IR-8400 Infrared Spectrophotometer. 1H-NMR and 13C-NMR spectra were recorded by Geo. 1400(400 MHz) using acetone d6 and CDCl3 as solvent in UK Loughborough.

Synthesis of 1-amino-4-methyl-6-phenyl pyrimidine-2-(1H) thion (1). A mixture of (0.01 mole) of benzoyl acetone and (0.01 mole) of thiosemicarbazide in (50 mL) absolute ethanol containing 3 drops of piperidine, was refluxed for 5 h. The solvent was then removed and the resulting solid was recrystallized from ethanol reported in (Moayed, 2017).

Synthesis of schiff bases (2–7). A mixture of compound (1) (0.01 mole) and different aromatic aldehydes (2-nitro benzaldehyde, 3-nitro benzaldehyde, 4-nitro benzaldehyde, 4-amino benzaldehyde, 4-methoxy benzaldehyde, 4-phthaldehyde (0.01 mole) in absolute ethanol (25 mL) containing 3 drops of glacial acetic acid was stirring for 4 h. The solvent was evaporated under vaccum, the yielded solid crystallized from methanol (Al-Gwady et al., 2018; Natiq and Hussein, 2016). The physical properties are listed in Table 1.

Synthesis of thiazolidinones derivatives (8-11). Mercaptoacetic acid (0.002 mole) in absolute ethanol (10 mL) was added slowly to (0.001 mole) of Schiff bases (2,3,4,7). The mixture was refluxed for 5 h. Excess solvent was evaporated and the residue was treated with potassium bicarbonate to produce compounds (Al-Mosawi, 2014; Lakum et al., 2014; Hussain et al., 2014). The solid precipitates were recrystallized from ethanol. The physical properties are listed in Table 1.

Synthesis of tetrazole derivatives (12-15). The mixture of compound (2,3,4,7) (0.0004 mole) dissolved in (20 mL) tetrahydrofuran and (0.0006 mole) sodium azide was refluxed for 16 h. The precipitate was filtered and recrystallized from absolute ethanol (Mahmoud et al., 2013). The physical properties are listed in Table 1.

Results and Discussion
The new Schiff’s bases were synthesized from the reaction of 1-amino-4-methyl-6-phenyl pyrimidine-2-(1H)-thione (1) with different aromatic aldehyde in
**Table 1. Some physical properties of the compounds (1-15)**

<table>
<thead>
<tr>
<th>Comp. no.</th>
<th>Structure and Name</th>
<th>Molecular formula &amp; M.W.</th>
<th>M.P. °C &amp; colour</th>
<th>Yield (%)</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td><img src="image" alt="" /> 1-Amino-4-methyl-6-phenyl pyrimidine-2-(1H)-thione</td>
<td>C&lt;sub&gt;16&lt;/sub&gt;H&lt;sub&gt;14&lt;/sub&gt;N&lt;sub&gt;4&lt;/sub&gt;O&lt;sub&gt;2&lt;/sub&gt;S 217</td>
<td>160-162 Pale yellow</td>
<td>95</td>
</tr>
<tr>
<td>2</td>
<td><img src="image" alt="" /> 4-methyl-1-[(1E).2-nitrophenyl)methylene]amino]-6-phenyl pyrimidine-2(1H)-thione</td>
<td>C&lt;sub&gt;18&lt;/sub&gt;H&lt;sub&gt;16&lt;/sub&gt;N&lt;sub&gt;4&lt;/sub&gt;O&lt;sub&gt;2&lt;/sub&gt;S 350</td>
<td>228-230 White</td>
<td>74</td>
</tr>
<tr>
<td>3</td>
<td><img src="image" alt="" /> 4-methyl-1-[(1E).3-nitrophenyl)methylene]amino]-6-phenyl pyrimidine-2(1H)-thione</td>
<td>C&lt;sub&gt;18&lt;/sub&gt;H&lt;sub&gt;16&lt;/sub&gt;N&lt;sub&gt;4&lt;/sub&gt;O&lt;sub&gt;2&lt;/sub&gt;S 350</td>
<td>189-190 White</td>
<td>75</td>
</tr>
<tr>
<td>4</td>
<td><img src="image" alt="" /> 4-methyl-1-[(1E).1-(4-nitro phenyl)methylene]amino]-6-phenyl pyrimidine-2(1H)-thione</td>
<td>C&lt;sub&gt;18&lt;/sub&gt;H&lt;sub&gt;16&lt;/sub&gt;N&lt;sub&gt;4&lt;/sub&gt;O&lt;sub&gt;2&lt;/sub&gt;S 350</td>
<td>238-240 Yellow</td>
<td>83</td>
</tr>
<tr>
<td>5</td>
<td><img src="image" alt="" /> 4-methyl-1-[(1E).4-amino phenyl)methylene]amino]-6-phenyl pyrimidine-2(1H)-thione</td>
<td>C&lt;sub&gt;18&lt;/sub&gt;H&lt;sub&gt;16&lt;/sub&gt;N&lt;sub&gt;4&lt;/sub&gt;S 320</td>
<td>99-100 Pale yellow</td>
<td>63</td>
</tr>
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</table>
6  
4-methyl-1-\{[(1E)-1-(4-methoxyphenyl)methylene]amino\}-6-phenyl pyridine-2(1H)-thione

\[\text{C}_{19}\text{H}_{17}\text{N}_{3}\text{OS} \quad 148-150 \quad 51\]
\[335 \quad \text{Light brown}\]

7  
1,1''-((1,4-phenylenebis(methanylylidene))bis(azaneylylidene))bis(4-methyl-6-phenylpyridine-2(1H)-thione)

\[\text{C}_{20}\text{H}_{24}\text{N}_{6}\text{S} \quad 324-326 \quad 65\]
\[533 \quad \text{White}\]

8  
3-(4-methyl-6-phenyl-2-thioxo pyrimidin-1(2H)-yl)-2-(2-nitrophenyl)-1,3-thiazolidin-4-one

\[\text{C}_{20}\text{H}_{16}\text{N}_{4}\text{O}_{3}\text{S}_{2} \quad 181-183 \quad 62\]
\[424 \quad \text{Green}\]

9  
3-(4-methyl-6-phenyl-2-thioxo pyrimidin-1(2H)-yl)-2-(3-nitrophenyl)-1,3-thiazolidin-4-one

\[\text{C}_{20}\text{H}_{16}\text{N}_{4}\text{O}_{3}\text{S}_{2} \quad 186-188 \quad 61\]
\[424 \quad \text{White}\]
3-(4-methyl-6-phenyl-2-thioxo pyrimidin-1(2H)-yl)-2-(4-nitrophenyl)-1,3-thiazolidin-4-one

11

2,2’-(1,4-phenylene)bis(3-(4-methyl-6-phenyl-2-thioxopyrimidin-1(2H)-yl)thiazolidin-4-one)

12

4-methyl-1-[5-(2-nitro phenyl)-2,5-dihydro-1H-tetrazol-1-yl]-6-phenyl pyrimidine-2(1H)-thione

13

4-methyl-1-[5-(3-nitro phenyl)-2,5-dihydro-1H-tetrazol-1-yl]-6-phenyl pyrimidine-2(1H)-thione
4-methyl-1-[5-(4-nitro phenyl)-2,5-dihydro-1H-tetrazol-1-yl]-6-phenyl pyrimidine-2(1H)-thione

1,1’-(1,4-phenylenebis(2,5-dihydro-1H-tetrazole-5,1-diyl))bis(4-methyl-6-phenylpyrimidine-2(1H)-thione)

The 1H NMR & 13C NMR spectrum showed the following bands. **Compound (1)**. 1H NMR (CDCl₃, 400 MHz): δ = 7.30-7.37 (m, 5H, Ar-H), 5.96 (s, 1H, H=C=NC=N), 3.45-3.40 (dd, 2H, NH₂), 2.04 (s, 3H, CH₃). 13C NMR (CDCl₃, 400 MHz): δ = 175.5 (C=S), 155.4 (C=N), 144.1, 128.7, 128.0, 124.0, 95.3 (Ar-H), 55.2 (C=C-H), 16.1 (CH₃) (Selvam et al., 2012).

**Compound (2)**. 1H NMR (acetone-d₆, 400 MHz): δ = 8.61 (s, 1H, H-C=N=NC=N), 8.5-8.1 (m, 4H, Ar-H), 7.5-7.7 (m, 5H, Ar-H), 6.4 (s, 1H, H-C=C=). 2.8 (s, 3H, CH₃). 13C NMR (acetone-d₆, 400 MHz): δ = 180.2 (C=S), 148.9 (C=N), 140.0, 136.4, 133.2, 130.1, 121.3 (Ar-H), 28.4 (CH₃) (Dhanya et al., 2014).

**Compound (4)**. 1H NMR (DMSO-d₆, 400 MHz): δ = 8.4 (s, 1H, H-C=N=NC=N), 8.2-8.1 (m, 4H, Ar-H), 7.4-7.3 (m, 4H, Ar-H), 6.4 (s, 1H, H-C=C=). 3.3 (s, 3H, CH₃). 13C NMR (DMSO-d₆, 400 MHz): δ = 179.9 (C=S), 148.1 (C=N), 142.1, 140.0, 129.8, 125.5, (phenyl ring), 39.5 (CH₃) (Dhanya et al., 2014).
**Compound (5).** $^1$H NMR (DMSO-d$_6$, 400 MHz): $\delta =$ 10.7 (s, 2H, 2NH$_2$), 7.8 (s, 1H, H-C=), 6.8-7.31 (m, 4H, Ar-H), 7.38-7.46 (m, 5H, Ar-H), 1.67 (s, 3H, CH$_3$). $^{13}$C NMR (DMSO-d$_6$, 400 MHz): $\delta =$ 179.7 (C=S), 148.9 (C=N), 140.0, 136.5, 134.1, 131.2, 123.0, 121.0 (phenyl ring). (Dhanya et al., 2014).

**Compound (6).** $^1$H NMR (DMSO-d$_6$, 400 MHz): $\delta =$ 8.9 (s, 1H, H-C=), 8.7 (s, 1H, H-C=), 8.3-8.0 (m, 5H, Ar-H), 7.1-7.7 (m, 5H, Ar-H), 3.8 (s, 3H, OCH$_3$). $^{13}$C NMR (DMSO-d$_6$, 400 MHz): $\delta =$ 160.1 (C=S), 150.3 (C=N), 131, 130, 128, 124, 117, 115 (phenyl ring), 59 (OCH$_3$), 55 (C=C-H). (Dhanya et al., 2014).

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**Scheme (1).** Synthesis of compounds (1-15).
Table 2. Some spectral data for compounds (1-15)

<table>
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<th>Comp. No.</th>
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<th>R-CH</th>
<th>C=N Exo</th>
<th>C=S</th>
<th>N-N</th>
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<td>2960</td>
<td>...</td>
<td>1248</td>
<td>966</td>
<td>(N=N) 1499, 1441</td>
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Fig. 1. FT-IR spectrum of compound (1).

Fig. 2. ¹H-NMR spectrum of compound (1).
Compound (7). $^1$H NMR (acetone-d$_6$, 400 MHz): $\delta$ = 8.68 (s, 1H, H-C=N), 8.08-8.20 (m, 4H, Ar-H), 7.55-7.88 (m, 10H, Ar-H), 5.3 (s, 1H, C=C-H), 2.85 (br, 6H, 2CH$_3$). $^{13}$C NMR (acetone-d$_6$, 400 MHz): $\delta$ = 141.2, 134.6, 133.1, 130.3, 128.8, 128.6, 124.8, 124.5, 122.0 (phenyl ring), 29.5 (CH$_3$). (Dhanya et al., 2014).

Fig. 3. $^{13}$C-NMR spectrum of compound (1).

Fig. 6. FT-IR spectrum of compound (4).

Fig. 4. FT-IR spectrum of compound (2).

Fig. 7. $^1$H-NMR for compound (4).

Fig. 5. $^1$H-NMR spectrum of compound (2).

Fig. 8. FT-IR for compound (5).
Fig. 9. $^1$H-NMR for compound (5).

Fig. 10. $^1$H-NMR for compound (6).

Fig. 11. $^1$H- NMR spectrum of compound (7).

Fig. 12. FT-IR for compound (8).

Fig. 13. FT-IR spectrum for compound (11).

Fig. 14. FT-IR spectrum of compound (12).

**Compound (10).** $^1$H NMR (CDCl$_3$, 400 MHz): $\delta = 8.20 - 8.26$ (m, 4H, Ar-H), 7.52-7.87 (m, 5H, Ar-H), 6.98, (S, 1H, H-C-N), 5.77 (s, 1H, H-C=C), 4.40 (br, 2H, CH$_2$), 2.34 (s, 3H, CH$_3$) (Kumar, 2012).
**Compound (12).** ¹H NMR (DMSO-d⁶, 400 MHz): δ = 11.6 (s, 1H, NH), 8.7 (s, 1H, C=H-N), 8.1-8.4 (m, 4H, Ar-H), 7.2-7.7 (m, 5H, Aa-H), 4.1 (s, 1H, H-C-N). ³¹C NMR (DMSO-d⁶, 400MHz): δ = 179.1 (C=S), 155 (C=N), 149, 140, 135, 134, 129, 128, 129, 124, 122, (phenyl ring), 95 (C=H-C-H), 55 (H-C-N), 16 (CH₃) (Majeed and Saoud, 2013).

**Conclusion**

From the experiment it was concluded that the synthesis of tetrazole and thiazolidinones were prepared on safe and simplicity with a good product yield.

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**Conflict of Interest.** The authors declare have no conflict of interest.

**Reference**


Pradip, D., Berad, B.N. 2008. Synthesis characterization and antimicrobial study of substituted bis-[1,3,4]-oxadizole, bis-[1,3,4]-thiadizole and bis-[1,2,4]-triazole derivaties. *Journal Indian Chemical Society, 85*: 1153-1158.


