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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 aldehyde 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., ^{1}H-NMR and ^{13}C-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), antifungal (Patel, 2011), anticancer (Srivustava *et al*., 2002), anticonvulsant (Parekh *et al*., 2004) and herbicidal actions (Qien *et al*., 2006). Tetrazoles have been found to exhibit antihistamine (Samadhiya 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. ^{1}H-NMR and ^{13}C-NMR spectra were recorded by Geo. 1400(400 MHz) using acetone d^6 and $CDCl_3$ 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).

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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-phthaladehyde (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.

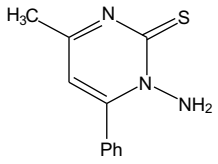
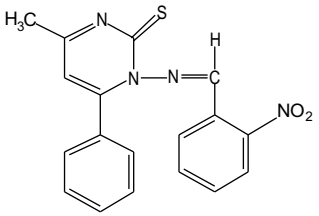
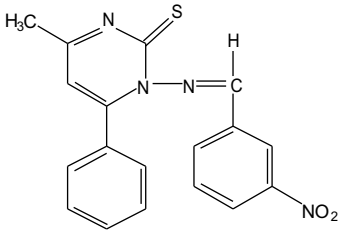
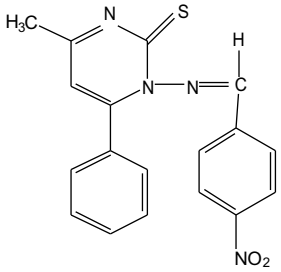
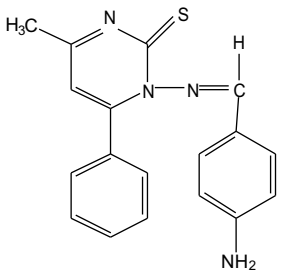
Synthesis of thiazolidinones derivatives (8-11). Mercaptoacetic acid (0.002 mole) in absolute ethanol (10 mL) was added slowly to (0.001 mole) of Schiff bases (**2,3,4,7**). The mixture was refluxed for 5 h. Excess solvent was evaporated and the residue was treated with potassium bicarbonate to produce 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.

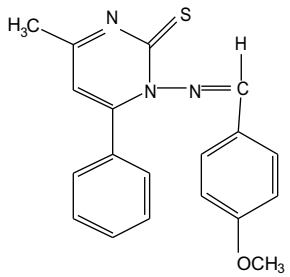
Synthesis of tetrazole derivatives (12-15). The mixture of compound (**2,3,4,7**) (0.0004 mole) dissolved in (20 mL) tetrahydrofuran and (0.0006 mole) sodium azide was refluxed for 16 h. The precipitate was filtered and recrystallized from absolute ethanol (Mahmoud *et al*., 2013). The physical properties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

Results and Discussion

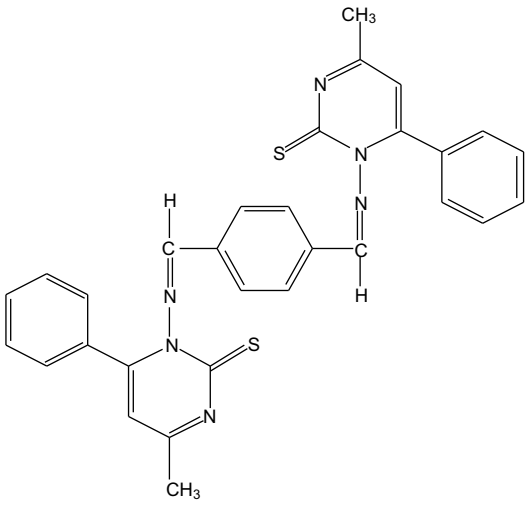
The new Schiff's bases were synthesized from the reaction of 1-amino-4-methyl-6-phenyl pyrimidine-2-(^{1}H)-thione (**1**) with different aromatic aldehyde in

Table 1. Some physical properties of the compounds (**1-15**)

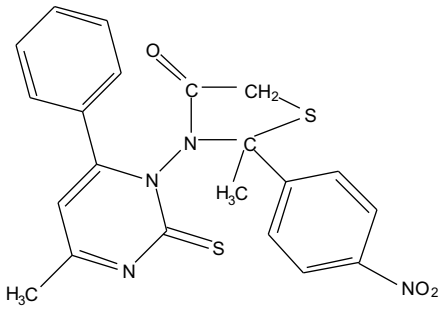
Comp. no.	Structure and Name	Molecular formula & M.W.	M.P. °C & colour	Yield (%)
1		$C_{11}H_{14}N_4O_2S$ 217	160-162 Pale yellow	95
1-Amino-4-methyl-6-phenyl pyrimidine-2-(1H)-thione				
2		$C_{18}H_{14}N_4O_2S$ 350	228-230 White	74
4-methyl-1-{[1E).(2-nitrophenyl) methylene]amino}-6-phenyl pyrimidine-2(1H)-thione				
3		$C_{18}H_{14}N_4O_2S$ 350	189-190 White	75
4-methyl-1-{[1E).(3-nitrophenyl)methylene]amino}-6-phenyl pyrimidine-2(1H)-thione				
4		$C_{18}H_{14}N_4O_2S$ 350	238-240 Yellow	83
4-methyl-1-{[(1E)-1-(4-nitro phenyl)methylene]amino}-6-phenyl pyrimidine-2(1H)-thione				
5		$C_{18}H_{16}N_4S$ 320	99-100 Pale yellow	63
4-methyl-1-{[(1E).(4-amino phenyl)methylene]amino}-6-phenyl pyrimidine-2(1H)-thione				

6		$C_{19}H_{17}N_3OS$ 335	148-150 Light brown	51

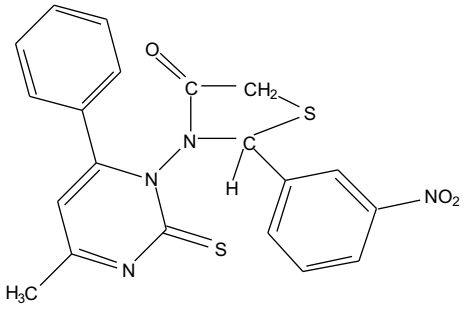
4-methyl-1-{[(1E)-1-(4-methoxyphenyl)methylene]amino}-6-phenyl pyrimidine-2(1H)-thione

7		$C_{30}H_{24}N_6S$ 533	324-326 White	65

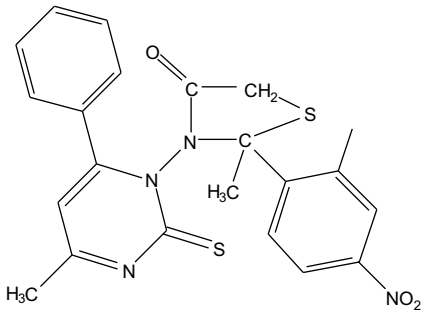
1,1'-((1,4-phenylenebis(methaneylylidene))bis(azaneylylidene))bis(4-methyl-6-phenylpyrimidine-2(1H)-thione)

8		$C_{20}H_{16}N_4O_3S_2$ 424	181-183 Green	62

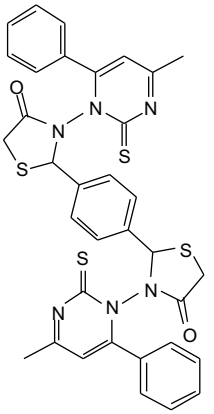
3-(4-methyl-6-phenyl-2-thioxo pyrimidin-1(2H)-yl)-2-(2-nitrophenyl)-1,3-thiazolidin-4-one

9		$C_{20}H_{16}N_4O_3S_2$ 424	186-188 White	61

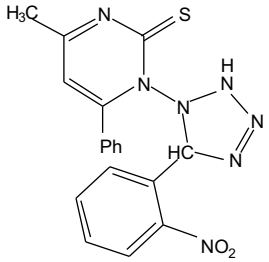
3-(4-methyl-6-phenyl-2-thioxo pyrimidin-1(2H)-yl)-2-(3-nitrophenyl)-1,3-thiazolidin-4-one

10		$C_{20}H_{16}N_4O_3S_2$ 424	244-246 Yellow	86

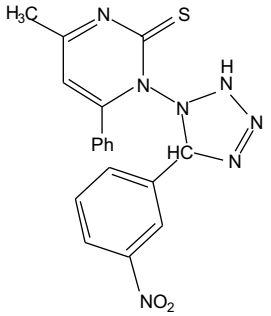
3-(4-methyl-6-phenyl-2-thioxo pyrimidin-1(2H)-yl)-2-(4-nitrophenyl)-1,3-thiazolidin-4-one

11		$C_{34}H_{28}N_6O_2S_4$ 681	318-320 White	71

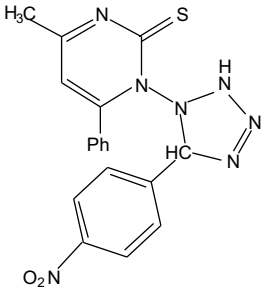
2,2'-(1,4-phenylene)bis(3-(4-methyl-6-phenyl-2-thioxopyrimidin-1(2H)-yl)thiazolidin-4-one)

12		$C_{18}H_{15}N_7O_2S$ 393	200-202 Light brown	51

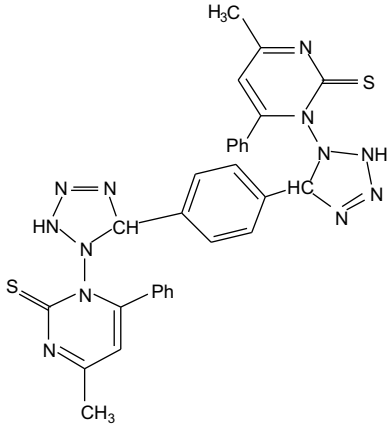
4-methyl-1-[5-(2-nitro phenyl)-2,5-dihydro-1H-tetrazol-1-yl]-6-phyenyl pyrimidine-2(1H)-thione

13		$C_{18}H_{15}N_7O_2S$ 393	228-230 Brown	53

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

14		$C_{18}H_{15}N_7O_2S$ 393	250-252 Yellow	75

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

15		$C_{30}H_{26}N_{122}S_2$ 618.74	268-270 Yellow	69

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

absolute ethanol and in the catalytic amount of glacial acetic acid. The FT-IR spectra of Schiff's bases (**2-7**) showed the absence of peak of carbonyl groups and the new peaks which appeared at 1580-1606 cm^{-1} which are attributed to the new azomethine (C=N) group (Dhanya *et al*., 2014). Some spectral data are listed in Table 2. Thiazolidinoe compounds (**8-11**) were prepared from the reaction of Schiff's bases (**2,3,4,7**) with thioglycolic acid in absolute ethanol. FT-IR spectrum showed sharp peaks at (1724-1700) cm^{-1} due to (C=O) imide stretching frequency, a good evidence for the success of this step of reaction (Kumar *et al*., 2012). Some spectral data are listed in Table 2. Tetrazole compound (**12-15**) were synthesized from the reaction of Schiff's bases (**2,3,4,7**) with sodium azide in THF. The FT-IR absorption bands disappearance at (1580-1599) cm^{-1} is give good evidence for the success step of reaction. These absorption bands due to (C=N) imine group stretching frequency (Saad , 2018). Also FT-IR spectra of tetrazole showed clear absorption bands at (1441-1499) cm^{-1} due to (N=N). Beside this, the FT-IR spectra were appeared of band at (2077-2360) cm^{-1} attributed to the stretching frequency of azide group (Majeed and Saoud, 2013). Some spectral data are listed in Table 2.

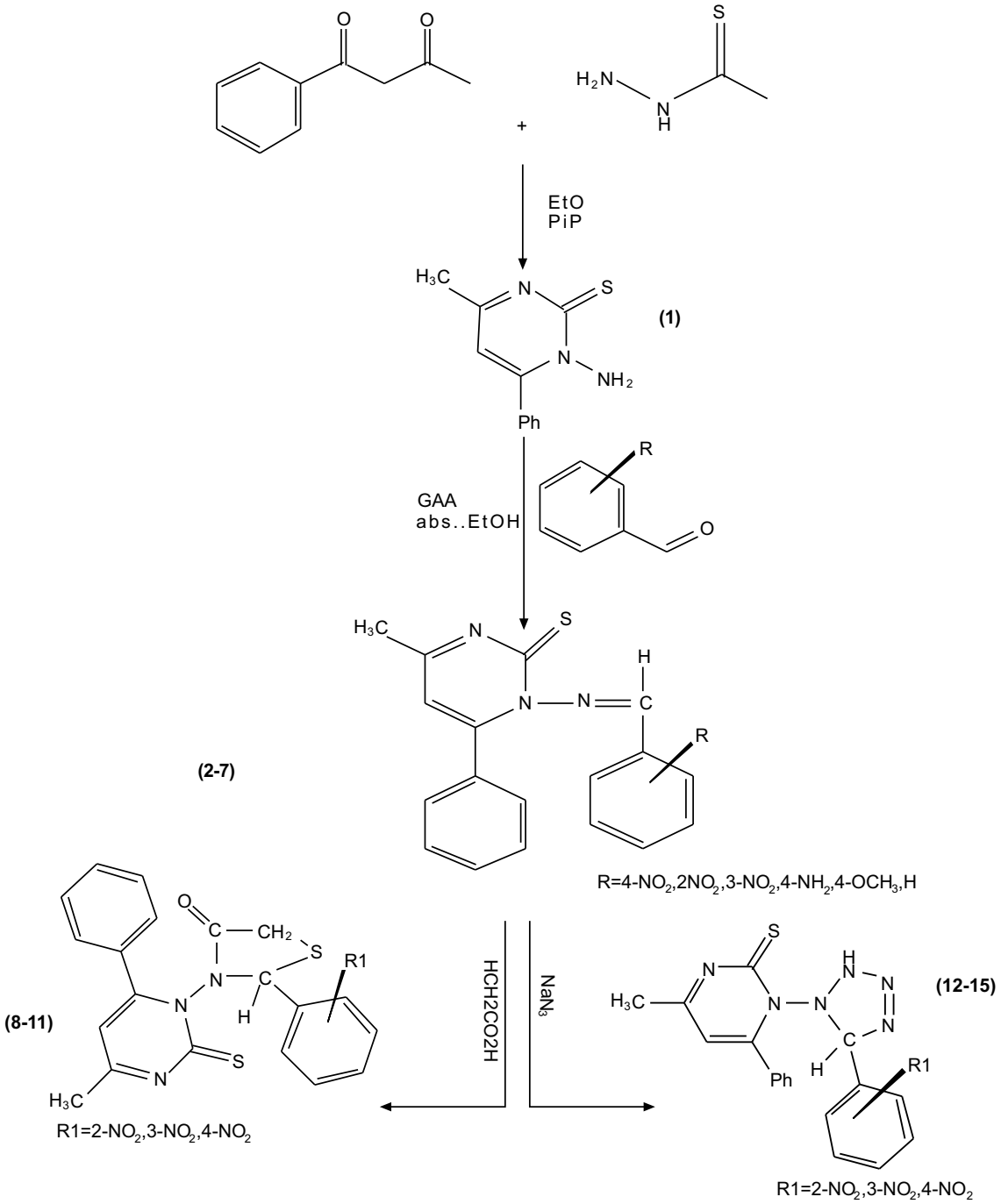
The ^{1}H NMR & ^{13}C NMR spectrum showed the following bands. ***Compound (1).*** ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.30-7.37 (m, 5H, Ar-H), 5.96 (s,^{1}H, H-C=C), 3.45-3.40 (dd, 2H, NH_2), 2.04 (s, 3H,CH_3). ^{13}C NMR ($CDCl_3$, 400 MHz): δ = 175.5 (C=S),155.4 (C=N), 144.1, 128.7, 128.0, 124.0, 95.3 (Ar-H), 55.2 (C=C-H), 16.1 (CH_3) (Selvam *et al*., 2012).

Compound (2). ^{1}H NMR (acetone-d^6, 400 MHz): δ = 8.61 (s,1H, H-C=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, CH_3).^{13}C NMR (acetone -d^6, 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 (CH_3) (Dhanya *et al*., 2014).

Compound (4). ^{1}H NMR (DMSO-d^6, 400 MHz): δ = 8.4 (s,1H, H-C=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, CH_3). ^{13}C NMR (DMSO-d^6 , 400 MHz): δ = 179.9 (C=S), 148.1 (C=N), 142.1, 140.0, 129.8, 125.5, (phenyl ring), 39.5 (CH_3) (Dhanya *et al*., 2014).

Compound (5). ^{1}H NMR (DMSO-d^{6}, 400 MHz): δ = 10.7 (s, 2H, 2NH$_2$), 7.8 (s, 1H, H-C=N), 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): δ = 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): δ = 8.9 (s, 1H, H-C=N), 8.7 (s, 1H, H-C=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): δ = 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).



Scheme (1). Synthesis of compounds **(1-15)**.

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

Comp. no.	V(cm^{-1}) IR						
	N-H tetrazole	=C-H	R-CH	C=N Exo	C=S	N-N	Others
1	…….	3198	2998	1598 Endo	1081	936	3267-3401(NH_2)
2	…….	3145	2981	1596	1227	1062	NO_2(Asy/sym) 1521-1342
3	…….	3141	2977	1599	1221	1064	NO_2(Asy/sym) 1542-1346
4	…….	3089	2986	1580	1270	1085	NO_2(Asy/sym) 1513-1330
5	…….	3076	2963	1606	1214	1103	(NH_2) 3215-3473
6	…….	3113	2986	1585	1284	1084	(C-O-C) 1118-1224
7	…….	3195	2988	1590	1225	1079	……..
8	…….	3139	2975	…….	1216	1064	(C=O) imide 1700 (C-S-C) 810
9	…….	3073	2965	…….	1198	1132	(C=O) imide 1703 (C-S-C)762
10	…….	3024	2982	…….	1207	933	(C=O) imide 1704 (C-S-C)809
11	…….	3081-3154	2977-2910	…….	1291-1220	995-939	(C=O) imide 1724, 1652 (C-S-C) 757
12	3356	3159	2962	…….	1207	911	(N=N) 1447
13	3423	3160	2966	…….	1211	935	(N=N) 1418
14	3359	3088	2962	…….	1174	926	(N=N) 1448
15	3352	3192	2960	…….	1248	966	(N=N) 1499, 1441

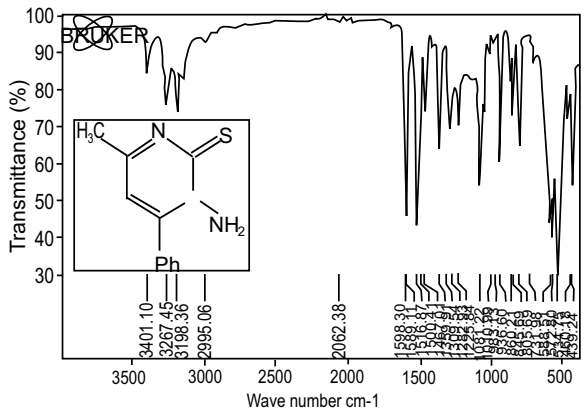


Fig. 1. FT-IR spectrum of compound **(1)**.

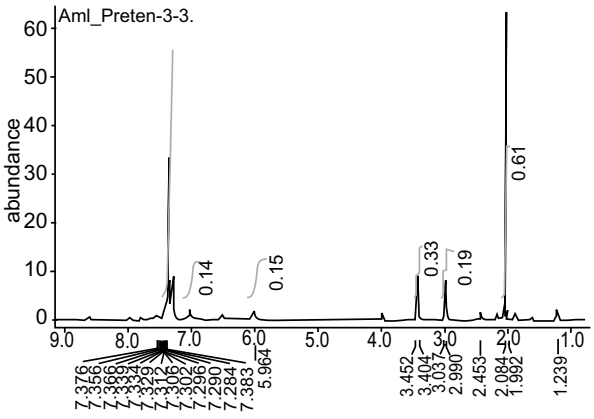


Fig. 2. [1]H-NMR spectrum of compound **(1)**.

Compound (7). ^{1}H NMR (acetone-d^{6}, 400 MHz): δ = 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): δ = 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).

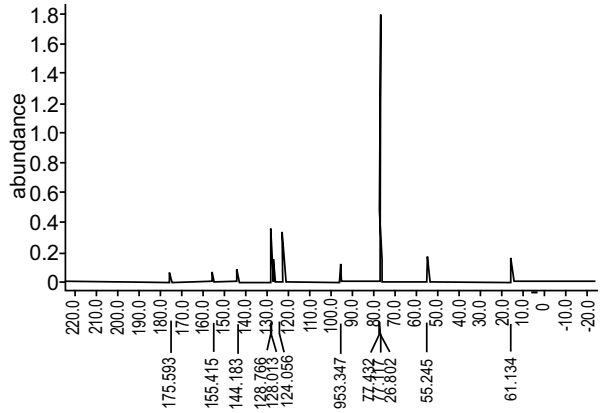


Fig. 3. ^{13}C-NMR spectrum of compound **(1)**.

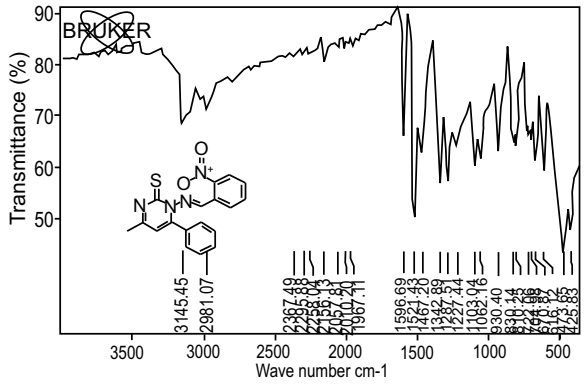


Fig. 4. FT-IR spectrum of compound **(2)**.

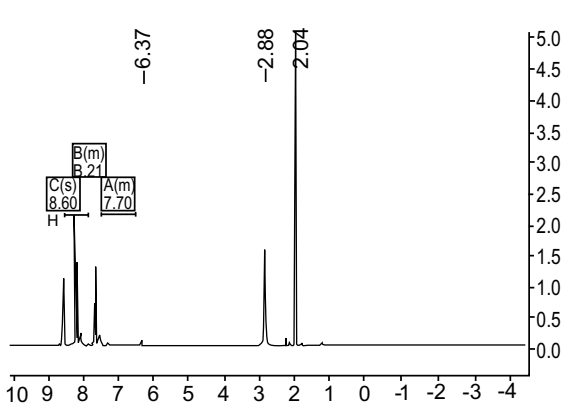


Fig. 5. ^{1}H-NMR spectrum of compound **(2)**.

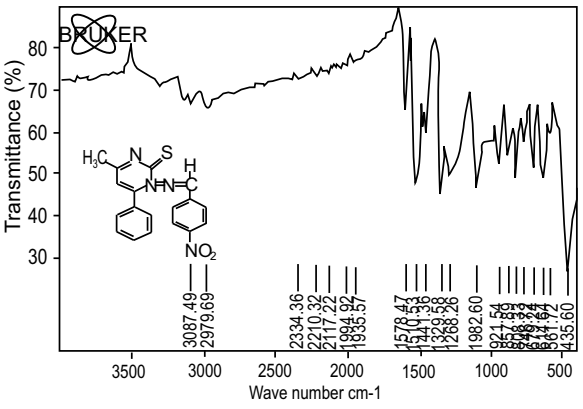


Fig. 6. FT-IR spectrum of compound **(4)**.

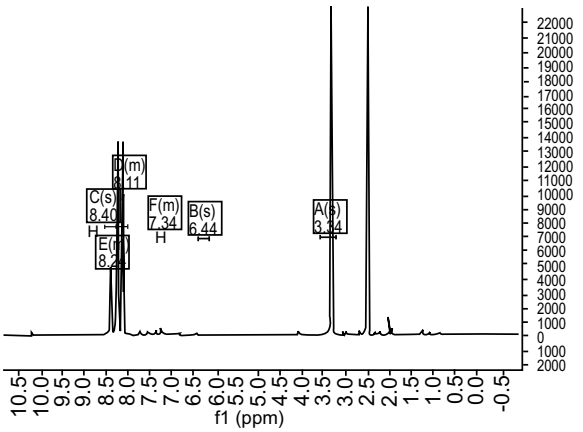


Fig. 7. ^{1}H-NMR for compound **(4)**.

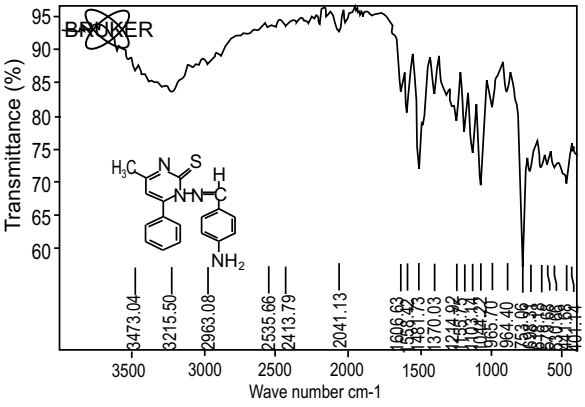


Fig. 8. FT-IR for compound **(5)**.

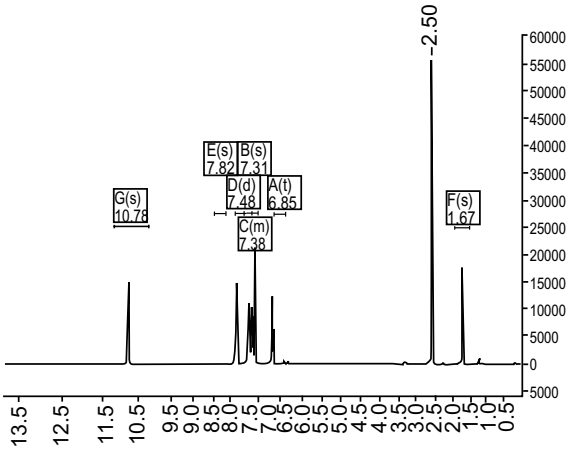


Fig. 9. [1]H-NMR for compound **(5)**.

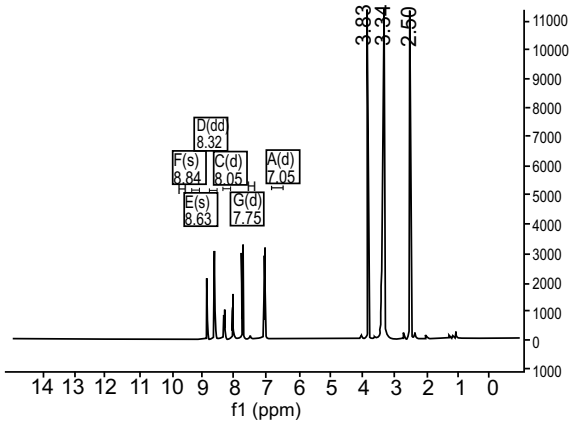


Fig. 10. [1]H-NMR for compound **(6)**.

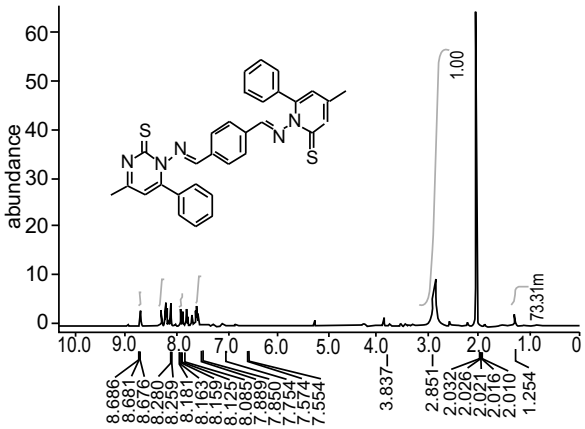


Fig. 11. [1]H- NMR spectrum of compound **(7)**.

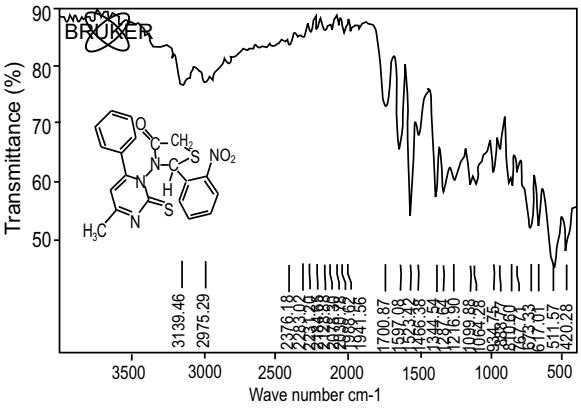


Fig. 12. FT-IR for compound **(8)**.

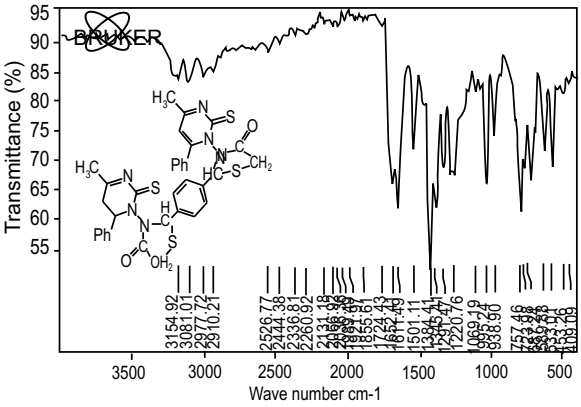


Fig. 13. FT-IR spectrum for compound **(11)**.

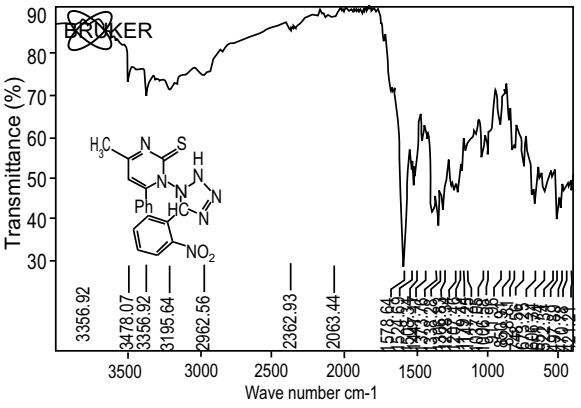


Fig. 14. FT-IR spectrum of compound **(12)**.

Compound (10). [1]H NMR ($CDCl_3$, 400 MHz): δ = 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). ^{1}H NMR (DMSO-d^{6}, 400 MHz): δ = 11.6 (s,1H, NH), 8.7 (s, 1H, C=C-H), 8.1-8.4 (m, 4H, Ar-H), 7.2- 7.7 (m, 5H, Aar-H), 4.1 (s, 1H, H-C-N). 3.4 (s, 3H, CH_3). ^{13}C NMR (DMSO-d^{6}, 400MHz): δ = 179.1 (C=S), 155 (C=N), 149, 140, 135, 134, 131, 129, 128, 129, 124, 122, (phenyl ring), 95 (C=C-H), 55 (H-C-N), 16 (CH_3) (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.

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