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RESEARCH ARTICLE

Synthesis and Characterization of Novel Oxime Derivatives

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ARTICLE HISTORY

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Abstract: ***Background***: The synthesis of effective drugs are very important for the scientist. The various biological effects of the thiazole, oxime and ether functional groups are well known properties by the drug developers. So we have synthesised new molecules which contains three of them on the same molecules.

Methods: The acetophenone derivatives have been used for synthesis new oximes . The synthetic pathway includes mainly four steps. s1. α-Bromination of acetophenone derivatives, s2. Synthesis of thiazole ring using brominated acetophenones, s3. Synthesis of ethers using synthesised thiazole, s4. Synthesis of oximes.

***Results*:** The synthesised molecules characterised using IR,1H-NMR, 13C-NMR and elementel analysis methods.

Conclusion: The new oximes which include thiazole and ether groups have been synthesised using acetophenone derivatives.

Keyword: Thiazole, oxime, ether.

1. INTRODUCTION

Thiazole derivatives have been mostly reported in the literature due to their therapeutic effects such as antifungal [1,2], antimicrobial [3], antitumor [4] and anticancer [5,6] properties. The oximes and it's substitute derivatives have antifungal, antibacterial and antimicrobial effect [7-15] also as thiazole compounds . The molecules which include both oxime and thiazole groups have been widely synthesised in the literature due to their biological activity [16-19]. However, the anti-HIV and anti-inflammatory effects of some molecules containing both ether and oxime groups have been reported in literature [20], Because of the various biological effect of oxime, thiazole and ether functional groups as noticed above we have synthesised new molecules which contains three of them on the same molecules.

2. RESULT AND DISCUSSION

The synthesised oxime derivatives and synhtetic pathway have been given in Table **1** and Fig. (**1**) respectively. The synthetic pathway includes mainly four steps:

s1. α-Bromination of acetophenone derivatives

When 2'-hydroxyacetophenone and 4'-hydroxyacetophenone used:

s1.1. Acetylation of acetophenone derivatives

s1.2. α-Bromination of acetylated acetophenone derivatives

s1.3. Hydrolysis of α-brominated structures

s2. Synthesis of thiazole ring using brominated acetophenones.

s3. Synthesis of ethers using synthesised thiazole derivatives.

s4. Synthesis of oximes.

The alpha brominated acetophenones have been synthesised via two way in the first step of the study. If acetophenone has hydroxyl substituent on benzene ring, we used three steps for bromination reaction as s1.1 to s1.3. Otherwise we used only s1 way which is one step reaction to obtain alpha brominated acetophenones. The details have given in experimental part.

The alpha brominated hydroxyacetophenones have been used for synthesis of the thiazole ring in the second step(s2). The synhtesised thiazole compounds have reacted with other alpha brominated acetophenones which is not include hydroxyl substituent on benzene ring to obtain ethers(s3). The oximes have been synthesised using step 3(s3) products in the last step of the reactions (s4).

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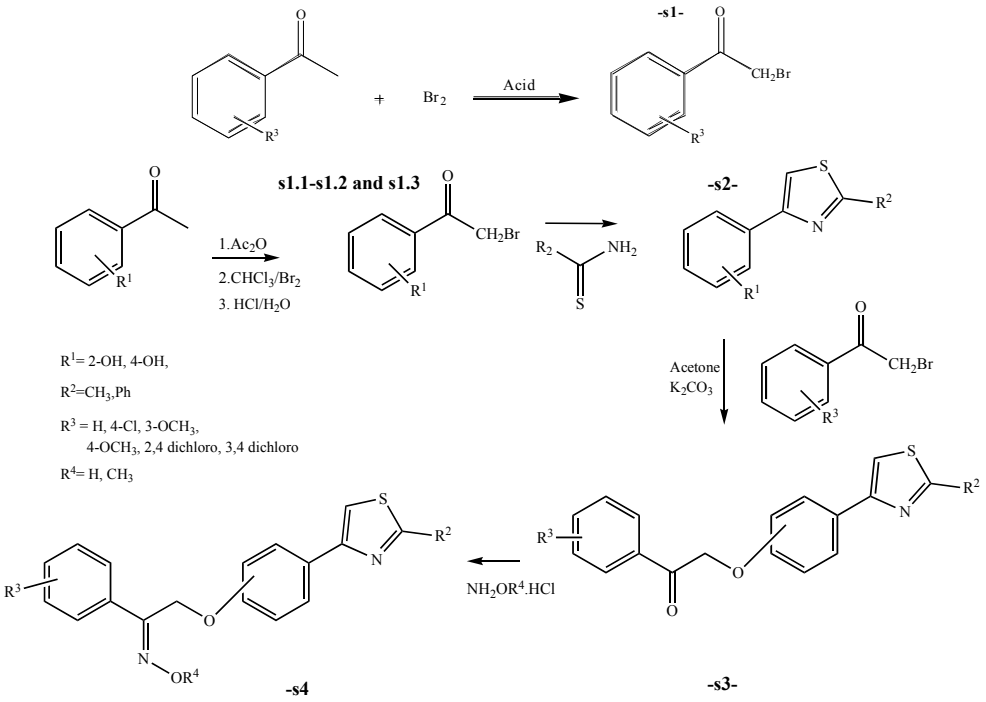
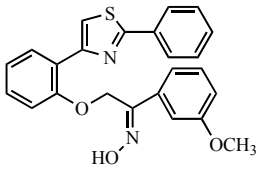
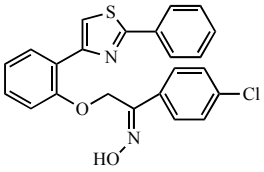
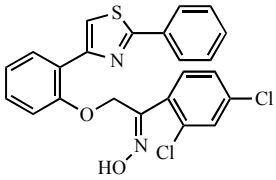
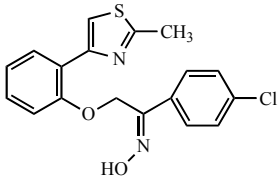
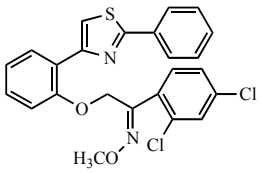
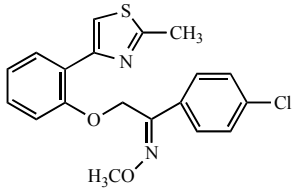
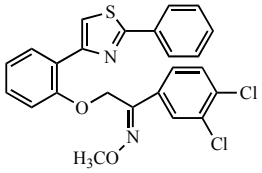
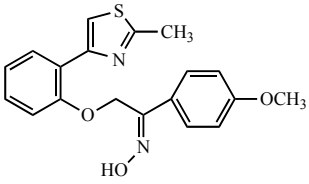
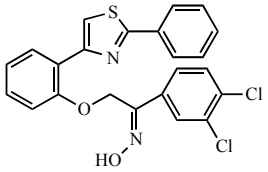
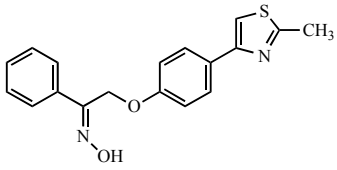


Fig. (1). The synthetic pathway of the studied molecules.

Table 1. The synthesised oxime derivatives.

1		6	
2		7	
3		8	
4		9	
5		10	

The step 1 (s1) has been used for preparing the α–brominated acetophenone derivatives which are used for thiazole synthesis in next step. We have check the bromination products of 4-chlorophenylacetophenone and 2'-hydroxyacetophenone.

α-Bromination of 4-chlorophenylacetophenone

As it seen from the ^{1}H-NMR, 5.0 singlet peak for 2H belongs to CH_2 group hydrogens. The C atom of CH_2 group which is the α- position of 4-chloroacetophenone observed at 34.0 in ^{13}C-NMR also. The experimental elemental analysis result is found very near to theoretical result of ***s1-a***.

α-Bromination of 2'-hydroxy and 4'-hydroxyacetophenone

Because of the strong electron donor effect of -OH group on benzene, the directly bromination of hydroxyacetophenone derivatives also give electrophilic aromatic bromination on benzene ring of hydroxyacetophenone derivatives. So we used acetic anhydride for acetylation to decrease the electron donor effect of -OH group in this step (s1.1). We have checked the OH peak at IR spectrum to confirm the procedure. There is no OH peak observed in the IR spectrum after acetylation process. Two C=O peaks (1690 and 1760 cm^{-1}) have observed also in spectrum. These products have been used for the alpha bromination of acetophenone (s1.2). The brominated ester products converted to alpha brominated hydroxyacetophenones by hydrolysis method (s1.3). In this step the OH peak has been observed at 3360 cm^{-1} in IR spectrum (s1.3.a and s1.3-b). The carbonyl peak also observed at 1600 cm^{-1}. The elemental analysis results confirmed the alpha brominated hydroxyacetophenone structures.

The step 2 (s2) is the synthesis of thiazole group using product of step 1 (s1).

The characteristic thiazole ring peaks for *2-(2-methylthiazol-4-yl)phenol* ***-s2-a*** *and 4-(2-methylthiazol-4-yl)phenol* ***-s2-b*** observed at 7.6 and 7.2 as 1H singlet in the ^{1}H-NMR spectrum respectively. The hydrogen atom of OH observed at 10.7 and 9.65 also for these molecules. The hydrogen peaks of the methyl subtituent on the thiazole ring osberved at 2.5 and 2.7 in the ^{1}H-NMR spectrum of **s2-a and s2-b**. The elemental analysis results also in agreement with theoretical results for the synthesised thiazole compounds.

The step 3 (s3) is the synthesis of ethers using synthesised thiazole derivatives. We have checked the ether group after synthesis the oximes.

The step 4 (s4) is the last step of the synthesis procedure. We have synthesised oximes in this step. All products (Table **1**) characterized using IR,^{1}H-NMR, ^{13}C-NMR and elemental analysis methods.

The OH peaks of oximes which synthesised using hydroxylamine observed between 3420 and 3450 cm^{-1} in the IR spectrums. The characteristic oxime OH peaks have been found between 11.8-12.3 as a singlet peak at ^{1}H-NMR also. The C=N peaks of oxime group observed between 1500-1700 cm^{-1}. The characteristic CH hydrogen of thiazole ring has been observed between 7.1-8.3 at ^{1}H-NMR and C atom observed between 112-115 at ^{13}C-NMR also. The hydrogen peaks of the -O-CH_2 group which is the ether group observed between 5.3 and 5.8 as a singlet 2H. The C-O peaks of ether groups observed between 1200-1290 cm^{-1}at IR spectrum also.

The elemental analysis results also confirmed the all products. After these spectroscopic analysis results we have confirmed the our molecules (1-10) include thiazole ring, oxime and ether functional groups on molecule.

3. EXPERIMENTAL

All the reagents and solvents were used reagent grade and without further purification and melting points (m.p.) were determined in open capillaries on a Gallenkamp apparatus and are uncorrected. The purity of the compounds was checked by thinlayer chromatography (TLC) using silica gel sheets 60 GF_{254} (Fluka). The following instruments have been used for spectrum analysis: BRUKER DPX-400, 400 MHz for 1H-NMR and 100 MHz for ^{13}C-NMR. Perkin Elmer Spectrum100 for FTIR and LECO, CHNS-932 for elemental analysis.

s.1. α-Bromination of Acetophenone Derivatives

The suitable acetophenone (4-Cl; 3-OCH_3; 4-OCH_3; 2,4-dichloro and 3,4-dichloro) and bromine were separately dissolved in aceticacid [15]. Acetophenone derivatives were brominated approx. for 4 h. The reaction mixture was poured into ice-water. The precipitate was filtered. The raw product was recrystallized from ethanol.

s1.1 Acetylation of Acetophenone Derivatives

The suitable hydroxyacetophenone and acetic anhydride were refluxed with 2 drops concentrated sulfuric acid for 3 h. The reaction was checked using TLC. The reaction mixture was poured into ice-water. The crystalline raw product was filtered and recrystallized from ethanol.

s1.2. α-Bromination of Aceticacid Acetylphenylester Derivatives

The suitable aceticacid acetylphenylester derivative and bromine were separately dissolved in chloroform and the reaction was carried out by dropping bromine for 3 h. When the reaction conclude, solvent was evaporated and viscous liquid substance was obtained.

s1.3. Hydrolysis of α-brominated Structures

The viscous liquid which is obtained from step **s1.2** was hydrolysed by the suitable hydrochloric acid in aqueous media for 4 h under reflux condenser. The reaction mixture was poured into ice-water. The crystalline raw product was filtered, washed with water and three times recrystallized from ethanol.

s2. Synthesis of thiazole derivatives

The α-brominated structures which synthesized in previous step (**s1**), were dissolved in ethanol and thioacetamide or thiobenzamid was added to solution. The mixture was boiled for 4 hours under reflux condenser. When the reaction conclude, the reaction vessel became cold to room temperature,

The sodium acetate solution (5M) was added to reaction mixture until neutralize. The crystalline raw product was filtered, washed with water and recrystallized from ethanol 3 times [6].

s3. Synthesis of Ethers Using Synthesised Thiazole Derivatives

In this step, synthesised thiazole derivatives and K_2CO_3 were dissolved in acetone in a reaction vessel. The mixture was boiled about 10 hours under reflux condenser. The product was washed with water and recrystallized from ethanol.

s4. Synthesis of Oximes

The step3 (s3) product, hydroxylamine hydrochloride or methoxylamine hydrochloride and sodium acetate were dissolved in ethanol and boiled for 3 hours under reflux condenser. The reaction mixture was poured into ice-water. The precipitate was filtered and recrystallized from ethanol [15].

2-Bromo-1-(4-chlorophenyl)ethanone - s1-a

Yield % 94.2, M.point 98°C, TLC R_f=0,38 (3: petroleum ether-ethyl acetate),^{1}H-NMR (400 MHz, DMSO). δ= 5.0 (s, 2H, CH_2), 8.0 (d, 2H, *J*=8.6 Hz, H_{Ar}), 7.65 (d, 2H, *J*=8.6 Hz, H_{Ar}). ^{13}C-NMR (DMSO) δ ppm 34.0 (CH_2-Br), 129.42 ($C3_{Ar}$, $C5_{Ar}$), 131.25 ($C2_{Ar}$, $C6_{Ar}$), 133.28 ($C1_{Ar}$), 139.37 ($C4_{Ar}$-Cl), 199.02 (C=O). Theoretical: C:%41.11 H:%2.57 Experimental: C:% 41.68 H:% 2.69.

Aceticacid 2-phenylester - s1.1-a

Yield %95, M.point 91°C, TLC R_f=0.66 (3:1 petroleum ether-ethyl acetate), IR (KBr) υ cm^{-1}: 1690 (C=O), 1760 (C=O), 1000 (C-O), 2980 (CH aliphatic), 3100 (CH aromatic).

2-Bromo-1-(2-hydroxyphenyl)ethanone - s1.3-a

Yield % 70, M.point 46°C, TLC R_f=0,8 (3:1 petroleum ether-ethyl acetate), IR (KBr) υ cm^{-1}: 3360 (OH), 3100 (CH aromatic), 2950 (CH aliphatic), 1600 (C=O), 1190 (C-O).

2-Bromo-1-(4-hydroxyphenyl)ethanone - s1.3-b

Yield% 70, M.point 97°C, TLC R_f=0.65 (3:1 petroleum ether-ethyl acetate), IR (KBr) υ cm^{-1}: 3360 (OH), 3150 (CH aromatic), 2950 (CH aliphatic), 1600 (C=O), 1200 (C-O). Theoretical: C:%44.65 H:%2.26 Experimental: C:%44.31 H:%2.03.

2-(2-methylthiazol-4-yl)phenol -s2-a

Yield % 85, M.point 82°C, TLCR_f=0.79 (toluen), ^{1}H-NMR (400 MHz, DMSO). δ= 10.7 (s, 1H, OH), 7.55 (dd, 1H, $C4_{Ar}$-H), 2.5 (s, 3H, CH_3), 7.2 (s, 1H, $C5_{Thiazole}$-H), 7.1 (d, 1H, $C5_{Ar}$-H), 8.1 (d, 1H, $C2_{Ar}$-H), 8.3 (dd, 1H, $C3_{Ar}$-H). ^{13}C-NMR (DMSO) δ ppm 129.01 ($C4_{Ar}$), 126.67 ($C5_{thiazole}$), 119.78 ($C6_{Ar}$), 130.94 ($C3_{Ar}$), 129.84 ($C2_{Ar}$), 117.01 (CH_3), 166.12 ($C2_{thizaole}$), 152.78 ($C1_{Ar}$), 155.56 ($C4_{thizaole}$), 133.16 ($C5_{Ar}$). IR (KBr) υ cm^{-1}: 3450 (OH), 3100 (CH aromatic), 2900 (CH aliphatic), 1600 (C=N), 1200 (C-O), 700 (C-S). Theoretical: C:%62.82 H:%4.71 N:%7.33 S:%16.75 Experimental: C:%62.80 H:%4.65 N:%7.22 S:%16.61.

4-(2-methylthiazol-4-yl)phenol - s2-b

Yield % 80, M.point 216°C, TLCR_f=0.44 (toluen), ^{1}H-NMR (400 MHz, DMSO). δ= 9.65 (s, 1H, OH), 7.75 (d, 2H, *J*=8.5 Hz, H_{Ar}), 7.6 (s, 1H, $C5_{Thiazole}$-H), 6.8 (d, 2H, *J*=8.5 Hz, H_{Aryl}), 2.7 (s, 3H, CH_3). ^{13}C-NMR (DMSO) δ ppm 19.16 (CH_3), 165.03 ($C2_{thiazole}$), 157.93 ($C1_{Aryl}$), 156.10 ($C4_{Thiazole}$-H), 124.78 ($C4_{Ar}$), 110.00 ($C5_{Thiazole}$), 126.49 ($C2_{Ar}$, $C6_{Ar}$), 114.68 ($C3_{Ar}$, $C5_{Ar}$). IR (KBr) υ cm^{-1}: 3450 (OH), 3100 (CH aromatic), 2900 (CH aliphatic), 1600 (C=N), 1200 (C-O), 750 (C-S).Theoretical: C:%62.82 H:%4.71 N:%7.33 S:% 16.75 Experimental: C:%62.33 H:%4.34 N:%6.88 S:%16.18.

1-(3-methoxyphenyl)-2-[2-(2-phenylthiazole-4-yl)phenoxy]ethanone oxime -1

Yield % 95, M.point 156°C, TLC R_f=0.48 (3:1 petroleum ether-ethyl acetate), ^{1}H-NMR (400 MHz, DMSO). δ= 12.1 (s, 1H, (=N-OH)), 7.55 (s, 1H, $C5_{Thiazole}$-H), 5.5 (s, 2H, $OCH_{2\ ether}$), 3.7 (s, 3H, CH_3), 8.3-6.9 (aromatic). ^{13}C-NMR (DMSO) δ ppm 165.32 ($C5_{Thiazole}$), 159.62 (C=N-OH), 155.59 ($C2_{\ thiazole}$), 153.61 (C_{Ar}), 151.28 (C_{Ar}), 122.80 (C_{Ar}, 130.15 (C_{Ar}), 121.54 (C_{Ar}), 55.5 5(CH_3), 60.06 (O-CH_2), 115.18 ($C3_{\ thiazole}$), 117.74 (C_{Ar}), 119.71 (C_{Ar}), 126.69 (C_{Ar}), 112.60 (C_{Ar}), 129.93 (C_{Ar}), 129.79 (C_{Ar}), 129.72 (C_{Ar}). IR (KBr) υ cm^{-1}: 3450 (OH), 1625 (C=N), 1200 (C-O), 700 (C-S), 2950 (CH aliphatic), 3090 (CH aromatic). UV (DMSO) nm 320, 362. Theoretical: C:%69.23 H:%4.8 N:%6.73 S:%7.69 Experimental: C:%68.73 H:%4.79 N:%6.61 S:%7.60.

1-(2,4-diclorophenyl)-2-[2-(2-phenylthiazole-4-yl)phenoxy]ethanone oxime - 2

Yield % 94, M.point 185°C, TLC R_f=0.50 (3:1 petroleum ether-ethyl acetate), ^{1}H-NMR (400 MHz, DMSO). δ= 12.1 (s, 1H, (=N-OH)), 6.85 (s, 1H, $C5_{Thiazole}$-H), 5.4 (s, 2H, $OCH_{2\ ether}$), 8.3-7.0 (aromatic). ^{13}C-NMR (DMSO) δ ppm 164.54 ($C5_{Thiazole}$), 153.69 (C=N-OH), 152.52 ($C2_{\ thiazole}$), 133.04 (C_{Ar}), 131.93 (C_{Ar}), 115.69 (C_{Ar}), 131.80 (C_{Ar}), 63.20(O-CH_2), 111.59 ($C3_{\ thiazole}$). IR (KBr) υ cm^{-1}: 3430 (OH), 1550 (C=N), 1250 (C-O), 720 (C-S), 2940 (CH aliphatic), 3150 (CH aromatic). UV (DMSO) nm 260, 305. Theoretical: C:%60.66 H:%3.51 N:%6.15 S:%7.03 Experimental: C:%60.44 H:%3.53 N:%5.96 S:%6.69.

1-(2,4-dichlorophenyl)-2-[2-(2-phenylthiazole-4-yl)phenoxy]ethanone O-methyl-oxime - 3

Yield % 80, M.point 130°C, TLCR_f=0.90 (3:1 petroleum ether-ethyl acetate), ^{1}H-NMR (400 MHz, DMSO). δ= 8.3 (s, 1H, $C5_{Thiazole}$-H), 5.6 (s, 2H, $OCH_{2\ ether}$), 2.5 (s, 3H, CH_3), 8.3-7.0 (aromatic). ^{13}C-NMR (DMSO) δ ppm 194.75 ($C5_{Thiazole}$), 163.72 (C=N-OR), 153.51 ($C2_{\ thiazole}$), 149.80 (C_{Ar}), 136.09 (C_{Ar}), 117.27 (C_{Ar}), 132.05 (C_{Ar}), 76.45 (CH_3), 113.22 (O-CH_2), 113.89 ($C3_{\ thiazole}$). IR (KBr) υ cm^{-1}: 1600 (C=N), 1000 (C-O), 720 (C-S), 2940 (CH aliphatic), 3100 (CH aromatic). UV (DMSO) nm 260, 304.Theoretical: C:%61.40 H:%3.83 N:%5.97 S:%6.82 Experimental: C:%62.85 H:%3.47 N:%3.15 S:%6.91.

1-(3,4-dichlorophenyl)-2-[2-(2-phenylthiazole-4-yl)phenoxy]ethanone O-methyl-oxime- 4

Yield % 83, M.point 179°C, TLC R_f=0.875 (3:1 petroleum ether-ethyl acetate), ^{1}H-NMR (400 MHz, DMSO). δ= 7.5 (s, 1H, $C5_{Thiazole}$-H), 5.8 (s, 2H, $OCH_{2\ ether}$), 2.5 (s, 3H, CH_3), 8.3-7.0 (aromatic). ^{13}C-NMR (DMSO) δ ppm 192.69 ($C5_{Thiazole}$), 166.30 (C=N-OR), 156.21 ($C2_{\ thiazole}$), 152.29 (C_{Ar}), 126.41(C_{Ar}), 122.53 (C_{Ar}), 131.37 (C_{Ar}), 130.18(C_{Ar}), 138.79(C_{Ar}), 132.08 (CH), 133.14 (CH), 122.53 (CH), 129.43 (CH), 128.05 (CH), 113.27 ($C3_{\ thiazole}$), 71.41(O-CH_2), 71.48 (CH_3). IR (KBr) υ cm^{-1}: 1700 (C=N), 1220 (C-O), 720 (C-S), 2900 (CH aliphatic), 3100 (CH aromatic). UV (DMSO) nm 258, 301.Theoretical: C:%61.40 H:%3.83 N:% 5,97 S:%6.82 Experimental: C:%61.25 H:%3.58 N:%3.34 S:%6.64.

1-(3,4-dichlorophenyl)-2-[2-(2-phenylthiazole-4-yl)phenoxy]ethanone oxime -5

Yield % 90, M.point 170°C, TLC R_f=0.60 (3:1 petroleum ether-ethyl acetate), ^{1}H-NMR (400 MHz, DMSO). δ= 12.3 (s, 1H, (=N-OH)), 7.7 (s, 1H, $C5_{Thiazole}$-H), 5.5 (s, 2H, $OCH_{2\ ether}$), 8.4-7.0 (aromatic). ^{13}C-NMR (DMSO) δ ppm 166.31 ($C5_{Thiazole}$), 156.05 (C=N-OH), 152.03 ($C2_{\ thiazole}$), 150.70 (C_{Ar}), 131.26 (C_{Ar}), 122.60 (C_{Ar}), 131.65 (C_{Ar}), 133.05 (C_{Ar}), 112.56 ($C3_{\ thiazole}$), 126.94 (C_{Ar}, 122.64 (C_{Ar}), 121.43 (C_{Ar}), 130.44 (C_{Ar}), 126.36 (C_{Ar}), 129.91 (C_{Ar}), 59.57 (O-CH_2). IR (KBr) υ cm^{-1}: 3460 (OH), 1590 (C=N), 1250 (C-O), 770 (C-S), 3100 (CH aromatic). UV (DMSO) nm 259, 308.Theoretical: C:%60.66 H:%3.51 N:%6.15 S:%7.03 Experimental: C:%60.2 H:%3.54 N:%6.07 S:%6.69.

1-(4-chlorophenyl)-2-[2-(2-phenylthiazole-4-yl)phenoxy] ethanone oxime -6

Yield % 90, M.point 147°C, TLC R_f=0.55 (3:1 petroleum ether-ethyl acetate), ^{1}H-NMR (400 MHz, DMSO). δ= 12.15 (s, 1H, (=N-OH)), 7.5 (s, 1H, $C5_{Thiazole}$-H), 5.45 (s, 2H, $OCH_{2\ ether}$), 8.3-7.0 (aromatic). ^{13}C-NMR (DMSO) δ ppm 166.26 ($C5_{Thiazole}$), 155.05 (C=N-OH), 152.56 ($C2_{\ thiazole}$), 150.85 (C_{Ar}), 129.38 (C_{Ar}), 134 (C_{Ar}), 126.5 (C_{Ar}), 129.47 (C_{Ar}), 128.69 (C_{Ar}), 113.41 ($C3_{\ thiazole}$, 130.44 (C_{Ar}), 59.72 (O-CH_2). IR (KBr) υ cm^{-1}: 3420 (OH), 1550 (C=N), 1220 (C-O), 730 (C-S), 2950 (CH aliphatic), 3200 (CH aromatic). UV (DMSO) nm 261, 303.

1-(4-chlorophenyl)-2-[2-(2-methylthiazole-4-yl)phenoxy] ethanone oxime -7

Yield % 95, M.point 185°C, TLC R_f=0.536 (3:1 petroleum ether-ethyl acetate), ^{1}H-NMR (400 MHz, DMSO). δ= 12.1 (s, 1H, (=N-OH)), 7.35 (s, 1H, $C5_{Thiazole}$-H), 5.4 (s, 2H, $OCH_{2\ ether}$), 2.7 (s, 3H, CH_3), 8.2-7.0 (aromatic). ^{13}C-NMR (DMSO) δ ppm 165.01 ($C5_{Thiazole}$), 163.72 (C=N-OH), 155.29 ($C2_{\ thiazole}$), 152.96 (C_{Ar}), 149.73 (C_{Ar}), 130,01 (C_{Ar}), 134.12 (C_{Ar}), 112.71 ($C3_{\ thiazole}$), 129.35 (C_{Ar}), 128.65 (C_{Ar}), 121.51 (C_{Ar}), 123.03 (C_{Ar}), 59.83 (O-CH_2), 55.33 (CH_3). IR (KBr) υ cm^{-1}: 3450 (OH), 1650 (C=N), 1250 (C-O), 790 (C-S), 2900 (CH aliphatic), 3080 (CH aromatic). UV (DMSO) nm 265, 294.Theoretical: C:%60.25 H:%4.18 N:%7.81 S:%8.92 Experimental: C:%59.82 H:%4.14 N:%7.65 S:%8.60.

1-(4-chlorophenyl)-2-[2-(2-methylthiazole-4-yl)phenoxy] ethanone O-methyl-oxime -8

Yield % 80, M.point 165°C, TLC R_f=0.49 (3:1 petroleum ether-ethyl acetate), ^{1}H-NMR (400 MHz, DMSO). δ= 7.1 (s, 1H, $C5_{Thiazole}$-H), 5.75 (s, 2H, $OCH_{2\ ether}$), 2.7 (s, 3H, CH_3), 8.2-7.0 (aromatic). ^{13}C-NMR (DMSO) δ ppm 193.85 ($C5_{Thiazole}$), 163.72 (C=N-OR), 155.26 ($C2_{\ thiazole}$), 150.02 (C_{Ar}), 139.26 (C_{Ar}), 123.08 (C_{Ar}), 129.15(C_{Ar}), 129.46 (C_{Ar}), 130.34 (C_{Ar}), 121.50 (C_{Ar}), 118.21 (C_{Ar}), 113.41 ($C3_{\ thiazole}$), 71.39 (O-CH_2), 19.34 (CH_3). IR (KBr) υ cm^{-1}: 1700 (C=N), 1200 (C-O), 770 (C-S), 2900 (CH aliphatic), 3100 (CH aromatic). UV (DMSO) nm 259, 293.Theoretical: C:%61.20 H:% 4.56 N:%7.51 S:%8.59 Experimental: C:%61.48 H:% 4.68 N:%7.67 S:%9.18.

1-(4-methoxyphenyl)-2-[2-(2-methylthiazole-4-yl)phenoxy] ethanone O-methyl oxime - 9

Yield % 95, M.point 154°C, TLC R_f=0.402 (3:1 petroleum ether-ethyl acetate), ^{1}H-NMR (400 MHz, DMSO). δ= 11.8 (s, 1H), 7.35 (s, 1H, $C5_{Thiazole}$-H), 5.35 (s, 2H, $OCH_{2\ ether}$), 3.7 (s, 3H, CH_3), 2.6 (s, 3H, CH_3), 8.2-6.8 (aromatic). ^{13}C-NMR (DMSO) δ ppm 163.28 ($C5_{Thiazole}$), 160.52 (C=N-OR), 155.12 ($C2_{\ thiazole}$), 155.04 (C_{Ar}), 150.64 (C_{Ar}), 123.85 (C_{Ar}), 121.07 (C_{Ar}), 128.92 (C_{Ar}), 113.93 (C_{Ar}), 130.60 (C_{Ar}), 121.07 (C_{Ar}), 129.01 (C_{Ar}), 113.64 ($C3_{\ thiazole}$), 59.90 (O-CH_2), 55.94 (CH_3), 19.17 (CH_3). IR (KBr) υ cm^{-1}: 3450 (OH), 1600 (C=N), 1250 (C-O), 710 (C-S), 3150 (CH aromatic), 2900 (CH aliphatic). UV (DMSO) nm 265. Theoretical: C:%64.4 H:%5.08 N:%7.90 S:%9.04 Experimental: C:%63.71 H:%4.82 N:%7.18 S:%8.47.

2-[4-(2-methylthiazole-4-yl)phenoxy]-1-phenylethanone oxime -10

Yield % 85, M.point 172°C, TLC R_f=0.68 (3:1 petroleum ether-ethyl acetate), ^{1}H-NMR (400 MHz, DMSO). δ= 12.0 (s, 1H, (=N-OH)), 7.75 (s, 1H, $C5_{Thiazole}$-H), 5.3 (s, 2H, $OCH_{2\ ether}$), 2.7 (s, 3H, CH_3), 7.9-6.9 (aromatic). ^{13}C-NMR (DMSO) δ ppm 165.36 ($C5_{Thiazole}$), 158.96 (C=N-OH), 153.61 ($C2_{\ thiazole}$), 152.94 (C_{Ar}), 129.04 (C_{Ar}), 128.67 (C_{Ar}), 128.17 (C_{Ar}), 126.52 (C_{Ar}), 114.75 ($C3_{\ thiazole}$), 59.07 (O-CH_2), 19.32 (CH_3). IR (KBr) υ cm^{-1}: 3450 (OH), 1600 (C=N), 1290 (C-O), 700 (C-S), 2900 (CH aliphatic), 3100 (CH aromatic). UV (DMSO) nm 260.Theoretical: C:%66.66 H:%4.94 N:%8.64 S:%9.88 Experimental: C:%66.14 H:%4.81 N:%8.11 S:%9.80.

3. CONCLUSION

The new oximes which include thiazole and ether groups have been synthesised using acetophenone derivatives.The synthesised molecules characterised using IR,^{1}H-NMR, ^{13}C-NMR and elementel analysis methods.

CONFLICT OF INTEREST

The author(s) confirm that this article content has no conflict of interest.

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SUPPLEMENTARY MATERIAL

Supplementary material is available on the publisher's web site along with the published article.

REFERENCES

[1] Altintop, M. D.; Ozdemir, A.; Turan-Zitouni, G.; Ilgm, S.; Atli, O.; Demirel, R.; Kaplancikli, Z. A. A novel series of thiazolyl-pyrazoline derivatives: Synthesis and evaluation of antifungal activity, cytotoxicity and genotoxicity. *Eur. J. Med. Chem.,* **2015,** *92*, 342-352.

[2] Ramirez, J.; Svetaz, L.; Quiroga, J.; Abonia, R.; Raimondi, M.; Zacchino, S.; Insuasty, B. Synthesis of novel thiazole-based 8,9-dihydro-7H-pyrimido[4,5-b][1,4]diazepines as potential antitumor and antifungal agents. *Eur. J. Med. Chem.,* **2015,** *92*, 866-875.

[3] Yernale, N. G.; Mathada, M. B. H. Synthesis, Characterization, Antimicrobial, DNA Cleavage, and In Vitro Cytotoxic Studies of Some Metal Complexes of Schiff Base Ligand Derived from Thiazole and Quinoline Moiety. *Bioinorg. Chem. Appl.,* **2014**.

[4] Bao, M. K.; Yang, Y. Q.; Gu, W.; Xu, X.; Cao, M. Z.; Wang, S. F. Synthesis and Antibacterial, Antitumor Activity of 2,6,6-Thrimethyl-bicyclo[3,1,1]heptan-3-(4-aryl-2-thiazoyl)hydrazones. *Chinese J. Org. Chem.,* **2014,** *34*, 2146-2151.

[5] Duran, M.; Demirayak, S. Synthesis of 2-[4,5-dimethyl-1-(phenylamino)-1H-imidazol-2-ylthio]-N-(thiazole-2-yl)acetamide derivatives and their anticancer activities. *Med. Chem. Res.,* **2013,** *22*, 4110-4124.

[6] Kayagil, I.; Demirayak, S. Synthesis and Anticancer Activities of Some Thiazole Derivatives. *Phosphorus Sulfur,* **2009,** *184*, 2197-2207.

[7] Wang, D. L.; Ren, S. X.; Wang, H.; Yan, H.; Feng, J. T.; Zhang, X. Semisynthesis and Antifungal Activity of Novel Oxime Ester Derivatives of Carabrone Modified at C(4) against Botrytis cinerea. *Chem. Biodivers.,* **2014,** *11*, 886-903.

[8] Wang, M. Y.; Qu, Z. Q.; Du, D.; Jiang, L. Synthesis and Antifungal Activity of Novel 1-(3-Indoly)-3-aryl-2-propen-1-one Oxime Ethers. *Chinese J. Org. Chem.,* **2013,** *33*, 1005-1009.

[9] Zhou, S. F.; Li, F. B.; Zhang, P. Z.; Jiang, L. Synthesis and antifungal activity of novel 1-(1H-benzoimidazol-1-yl)propan-2-one oxime-ethers containing the morpholine moiety. *Res. Chem. Intermediat.,* **2013,** *39*, 1735-1743.

[10] Ahluwalia, V.; Garg, N.; Kumar, B.; Walia, S.; Sati, O. P. Synthesis, Antifungal Activity and Structure-Activity Relationships of Vanillin oxime-N-O-alkanoates. *Nat. Prod. Commun.,* **2012,** *7*, 1635-1638.

[11] Yin, A. Q.; Xue, S. J.; Fang, Z. K.; Chen, L.; Xu, Y. Synthesis and Antifungal Activity of 1-Substituted Piperidin-4-one Oxime Ether. *Chinese J. Org. Chem.,* **2009,** *29*, 454-458.

[12] Gaber, A.E.A.M.; Al-Ahmadi, A. A.; Baryyan, A. O. Thermal fragmentation and rearrangement of N-arylbenzamidoxime and O-phenylsulfonyloxime derivatives. *J. Anal. Appl. Pyrol.,* **2008,** *82*, 110-116.

[13] Rossello, A.; Bertini, S.; Lapucci, A.; Macchia, M.; Martinelli, A.; Rapposelli, S.; Herreros, E.; Macchia, B. Synthesis, antifungal activity, and molecular modeling studies of new inverted oxime ethers of oxiconazole. *J. Med. Chem.,* **2002,** *45*, 4903-4912.

[14] Serrano-Wu, M. H.; St Laurent, D. R.; Mazzucco, C. E.; Stickle, T. M.; Barrett, J. F.; Vyas, D. M.; Balasubramanian, B. N. Oxime derivatives of sordaricin as potent antifungal agents. *Bioorg. Med. Chem. Lett.,* **2002,** *12*, 943-946.

[15] Karakurt, A.; Dalkara, S.; Ozalp, M.; Ozbey, S.; Kendi, E.; Stables, J. P. Synthesis of some 1-(2-naphthyl)-2-(imidazole-1-yl)ethanone oxime and oxime ether derivatives and their anticonvulsant and antimicrobial activities. *Eur. J. Med. Chem.,* **2001,** *36*, 421-433.

[16] Dai, H.; Xiao, Y. S.; Li, Z.; Xu, X. Y.; Qian, X. H. The thiazoylmethoxy modification on pyrazole oximes: Synthesis and insecticidal biological evaluation beyond acaricidal activity. *Chinese Chem. Lett.,* **2014,** *25*, 1014-1016.

[17] Dai, H.; Li, S.; Luo, K. P.; Fang, J. X.; Shi, Y. J. 5-(3-Chlorophenylsulfanyl)-1-methyl-3-trifluoromethyl-1H-pyrazole-4-carbaldehyde O-[(2-chloro-1,3-thiazol-5-yl)methyl]oxime. *Acta. Crystallogr. E,* **2012,** *68*.

[18] Dai, H.; Zhang, Y. T.; Shi, Y. J.; Zhang, W. W.; Shen, Y. J. (E)-3-Methyl-5-(4-methylphenoxy)-1-phenyl-1H-pyrazole-4-carbaldehyde O-[(2-chloro-1,3-thiazol-5-yl)methyl]oxime. *Acta. Crystallogr. E,* **2011,** *67*, O727-U2740.

[19] Zhu, X. F.; Shi, D. Q. Synthesis and Biological Activities of Novel Thiophosphoryl Oximates Containing Thiazole and 1,2,3-Triazole Rings. *Chinese J. Chem.,* **2009,** *27*, 565-568.

[20] Zhang, D. W.; Lin, F.; Li, B. C.; Liu, H. W.; Zhao, T. Q.; Zhang, Y. M.; Gu, Q. Efficient synthesis of bis-isoxazole ethers via 1,3-dipolar cycloaddition catalysed by Zn/Zn2+ and their antifungal activities. *Chem. Pap.,* **2015,** *69*, 1500-1511.