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RESEARCH PAPER

Synthesis, Characterization and Biological Evaluation of Some New Heterocyclic Compounds Derived from 2-Naphthol

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A B S T R A C T:

The present study deals with the synthesis, spectroscopic characterization, antibacterial and antifungal activities of novel series five-membered ring heterocyclic compounds containing nitrogen and sulfur heteroatoms. The synthetic routes have been divided into two parts: The first one includes synthesis of compounds (**4a-c**) through one pot operation three component reaction of 2-naphthol **(1)**, substituted benzaldehyde **(2a-c)** and thiourea **(3)** in 1,2-dichloromethane, using a catalytic amount of $ZrOCl_2.8H_2O$ and compound (**6**) was synthesized using semicarbazide (**5)** in absolute ethanol and indium (III) chloride as catalyst. The second part is the hetero-cyclization reactions of the compounds (**4a-c** and **6)** to obtain the heterocyclic compounds (**7a-c, 8**, and **9)**. The structures of the synthesized products are verified on the basis of (FT-IR, ^{1}H-NMR and ^{13}C-NMR) spectroscopy. The synthesized compounds antibacterial activities were screened against *Staphylococcus aureus* (Gram positive) and *Escherichia coli* (Gram negative) bacteria as compared to standard amikacin and antifungal activity against *Candida albicans* fungi as compared to standard Nystatin, well diffusion method is used. The antibacterial and antifungal activities of synthesized compounds **(7a-c, 8** and **9)** were higher than the antibacterial and antifungal activities of synthesized compounds **(4a-c** and **6)**.

KEY WORDS: Three component reaction, Heterocyclic compound, Thiazole, Thiazolidin-4-one, 1,2-dihydro-3*H*-1,2,4-triazol-3-one, antibacterial and antifungal activities.
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1.INTRODUCTION :

Heterocyclic compounds are considered one of the important type of organic compounds due to their applications in industrial and drug design (Taylor et al., 2016). Nitrogen, sulfur and oxygen atoms are the most common heteroatoms because of their important biologically activity (Al-Mulla, 2017).

Three component reactions have gained a special place and vital field of chemistry because they are a process for the achievement of high levels of diversity and brevity, as they allow to be combined as three compounds in a single event to form a single product by one pot operations in a very fast, efficient and time-saving manner without isolation of the intermediates or modification of the reaction conditions (Chunduru and Rao, 2010).

Thiazoles are five membered heterocyclic ring compounds containing sulfur and nitrogen atoms (Toche and Deshmukh, 2017), which have a wide spectrum of biological activities (Ayati *et al*., 2015, Rouf and Tanyeli, 2015). Thiazoledin-4-

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ones are saturated form of thiazole with carbonyl group on the fourth carbon (Kumar and Patil, 2017). The chemistry of thiazolidinones have drawn scientific interest through the years because this particular ring system is the core structure in a variety of synthetic compounds (Abdullah, 2014), an important scaffold known to be associated with a broad spectrum of biological activities (Kapoor *et al*., 2016, Nirwan *et al*., 2019).

1,2-dihydro-3*H*-1,2,4-triazol-3-ones are unsaturated five-membered heterogeneous aromatic rings containing three nitrogen atoms, which possessed a broad spectrum of biological activities (Shneine and Alaraji, 2016, Kaur and Chawla, 2017). Due to the importance of five-membered heterocyclic ring with two hetero atoms, this study achieved the synthesis of some novel heterocyclic compounds with their antibacterial and antifungal activities.

2. Experimental section

2.1. Instruments

Melting points were determined by Stuart Scientific capillary melting point apparatus. The completeness of the reactions are monitored by thin layer chromatography (TLC) on pre-coated silica gel aluminum plates, n-hexane: methanol: chloroform (5:2:3) are used as eluent. Sonication was implemented in ultrasonic cleaner (frequency 40-KHz, normal ultrasonic power 240W). Fourier transform infrared spectroscopy (FT-IR) ranges have been documented on spectrometer (Thermo Fisher FT-IR Model: Nicolet^{TM} iS^{TM}10) were recorded in Raparin University. ^{1}H-NMR and ^{13}C-NMR spectra recorded on a Bruckner (400 MHZ, in Zanjan University/ Iran) using TMS as internal standard and (DMSO-d_6) as solvent, chemical shift are assessed in parts per million (δ ppm), and the abbreviations used were s =singlet, *d*= doublet, *t*= triplet, *m* =multiplet and br =broad.

2.2. Methods

2.2.1. General method of the synthesis of 1-thiocarbamidoalkyl-2-naphthol (4a-c)

(Nagawade and Shinde, 2007, Younis et al., 2012)

In round bottom flask a mixture of 2-naphthol **(1)** (1.44g, 0.01mol), substituted benzaldehyde **(2a-c)** ((1.02 mL) benzaldehyde, (1.51g) 3-nitro benzaldehyde and 4-nitro benzaldehyde, 0.01mol)), thiourea **(3)** (0.91g, 0.012mol), $ZrOCl_2.8H_2O$ (0.032g, 0.1mol) as catalyst in 1,2-dichloromethane (15 mL) were irradiated in an ultrasonic cleaner bath at room temperature for (12-20 min.), the progress of the reactions monitored by TLC. Afterward, the reaction mixture was cooled to the room temperature, H_2O (20 mL) was added and stirred for about (3 min.), the precipitate was filtered off, recrystallized from ethanol. The chemical reactions are shown in the (**Scheme 1**).

Physical properties and Spectral data of ((2-hydroxynaphthalen-1-yl)(phenyl)methyl)thiourea (**4a**)

Chemical formula ($C_{18}H_{16}N_2OS$), m.p: (178-180 ^{o}C), yield: (2.65g, 85.8 %), color: off-white; FT-IR (cm^{-1}): 3338 and 3278 ($NH_{2str.}$), 3175 (N-$H_{str.}$), 3105 (O-$H_{str.}$), 3030 (C-$H_{Ar.\ str.}$), l580 (C=$C_{str.}$), 1235 (C-$O_{str.}$). ^{1}H-NMR (δ ppm) (DMSO-d_6): 10.06 (s, 1H, OH), 9.25 (br. s,1H, NH), 8.16 (br. s, 2H, NH_2), 7.88-7.13 (m, 11$H_{Ar.}$), 5.79 (s, 1H, CH). ^{13}C-NMR (δ ppm) (DMSO-d_6): 183.67 (C=S), 153.70 (C_2), 143.45 (C_1^-), 133.5 (C_{10}), 129.8 (C_3^-, C_5^-), 129.04 (C_5), 128.64 (C_4, C_6), 128.04 (C_2^-, C_6^-), 127.23 (C_8), 126.58 (C_4^-), 126.24 (C_9), 123.21 (C_7), 119.66 (C_3), 119.01 (C_1), 54.26 (CH).

Physical properties and Spectral data of ((2-hydroxynaphthalen-1-yl)(3-nitrophenyl)methyl)thiourea (**4b**)

Chemical formula: ($C_{18}H_{15}N_3O_3S$), m.p: (165-167C^{o}), yield: (3.15g, 89.3 %), color: yellow; FT-IR (cm^{-1}): 3384 and 3362 ($NH_{2str.}$), 3281 (N-$H_{str.}$), 3184 (O-$H_{str.}$), 3027 (C-$H_{Ar.\ str.}$), l590 (C=$C_{str.}$), 1498 ($NO_{2asym.\ str.}$), 1337 ($NO_{2sym.\ str.}$), 1271 (C-$O_{str.}$). ^{1} H-NMR (δ ppm) (DMSO-d_6): 10.26 (s, 1H, OH), 10.1 (br. s, 1H, NH), 9.18 (br. s, 2H, NH_2), 8.14-7.19 (m, 10$H_{Ar.}$), 4.40 (s, 1H, CH). ^{13}C-NMR (δ ppm) (DMSO-d_6): 184.26 (C=S), 153.91 (C_2), 148.22 (C_3^-), 146.34 (C_1^-), 133.06 (C_6^-), 132.83 (C_{10}), 130.60 (C_5^-), 130.11 (C_5), 129.21 (C_4,C_6), 128.74 (C_8), 127.55 (C_2^-), 123.2 (C_9), 121.75 (C_7), 120.71 (C_4^-), 118.84 (C_3), 118.34 (C_1), 53.56 (CH)

Physical properties and Spectral data of ((2-hydroxynaphthalen-1-yl)(4-nitrophenyl)methyl)thiourea (**4c**)

Chemical formula: ($C_{18}H_{15}N_3O_3S$), m.p: (174-176C^{o}), yield (3.3g, 93 %), color: yellow;

FT-IR (cm^{-1}): 3445 and 3414 ($NH_{2str.}$), 3331 (N-$H_{str.}$), 3211 (O-$H_{str.}$), 3051 (C-$H_{Ar.\ str.}$), 1582 (C=$C_{str.}$), 1487 ($NO_{2asym.\ str.}$), 1330 ($NO_{2sym.\ str.}$), 1254 (C-O). ^{1}H-NMR (δ ppm) (DMSO-d_6): 10.17(s, 1H, OH), 10.09 (br. s, 1H, NH), 9.13 (br. s, 2H, NH_2), 8.74-7.18 (m, 10$H_{Ar.}$), 4.77 (s, 1H, CH). ^{13}C-NMR (δ ppm) (DMSO-d_6): 153.85 (C=S), 152.21 (C_2), 146.37 (C_1^-), 146.25 (C_4^-), 132.8 (C_{10}), 130.52 (C_2^-,C_6^-), 129.18 (C_5), 128.75 ($C_{4,6}$), 127.41 (C_8), 123.87 (C_3^-,C_5^-), 123.66 (C_9), 123.14 (C_7), 118.97 (C_3), 118.64 (C_1), 56.53 (CH).

2.2.2. General method of the synthesis of 2-((2-hydroxynaphthalen-1-yl)(4-nitrophenyl) methyl)hydrazine-1-carboxamide (6) (Pouramiri and Kermani, 2017)

A solution of 2-naphthol **(1)** (1.44g, 0.01mol), 4-nitrobenzaldehyde **(2)** (1.51g, 0.01mol), semicarbazide **(5)** (1.226g, 0.011mole) and indium (III) chloride (0.022g, 0.1 mol) in absolute ethanol (15mL) with chloroacetic acid (1.89g, 0.02mol) were irradiated in ultrasonic bath at room temperature for about 15min.. The progress of the reaction was checked by thin layer chromatography, after completion of the reaction, the crude product was filtered off, washed and recrystallized from ethanol. The chemical reaction is shown in the **Scheme (2).**

Physical properties and Spectral data of 2-((2-hydroxynaphthalen-1-yl)(4-nitrophenyl)methyl) hydrazine-1-carboxamide (**6**)

Chemical Formula: ($C_{18}H_{16}N_4O_4$), m.p: (234-236C^o), yield (3.23g, 91.6 %), color: yellow; FT-IR (cm^{-1}): 3445 (N-$H_{str.}$), 3281 and 3169 ($NH_{2str.}$), 3105 (O-$H_{str.}$), 3058 (C-$H_{Ar.\ str.}$), 1681 (C=$O_{str.}$), 1602 (C=$C_{str.}$), 1543 ($NO_{2asym.\ str.}$), 1359 ($NO_{2sym.\ str.}$), 1258 (C-O). ^{1}H-NMR (δ ppm) (DMSO-d_6): 11.29 (br. s, 1H, CH-NH), 10.88 (s, 1H, OH), 10.65 (br. s, 1H, NH-C=O), 8.57-7.65 (m, 10$H_{Ar.}$), 5.16 (s, 1H, CH); ^{13}C-NMR (δ ppm) (DMSO-d_6): 162.25 (C=O), 159.08 (C_2), 143.16 (C_1^-), 138.9 (C_4^-), 133.9 (C_{10}), 132.9 (C_2^-, C_6^-), 132.43 (C_5), 132.37 (C_4, C_6), 122.27 (C_8), 120.16 (C_3^-, C_5^-), 119.84 (C_9), 119.67 (C_7), 119.56 (C_3), 117.14 (C_1), 57.64 (CH).

2.2.3. General method for the synthesis of thaizoles (7a-c) (Kubba and Rahim, 2018)

Phenacyl bromide (0.398g, 0.002 mol) added slowly to solution of compound **(4a-c)** ((0.616g of 4a and 0.706g of 4b, 4c), 0.002 mol) in ethanol in a round bottom flask and refluxed for about (4-6 h). The progress of the reactions monitored by TLC, the mixture was cooled at room temperature then poured into cold water. The precipitate was filtered off and recrystallized from toluene: ethanol (25:75) to afford the pure product. The reactions are shown in the (**Scheme 3**).

Physical properties and Spectral data of (phenyl((5-phenylthiazol-2-yl)amino)methyl)naphthalen-2-ol (**7a**)

Chemical Formula: ($C_{26}H_{20}N_2OS$), m.p: (199-201C^o), yield (0.611g, 74.8 %), color: dark brown; FT-IR (cm^{-1}): 3479 (N-$H_{str.}$), 3350 (O-$H_{str.}$), 3058 (C-$H_{Ar.\ str.}$), l627 (C=$N_{str.}$), 1578 and 1574 (C=$C_{str.}$), 1251 (C-$O_{str.}$). ^{1}H-NMR (δ ppm) (DMSO-d_6): 9.94 (s, 1H, OH), 7.38-6.48 (m, 16H_{Ar} &1H, $CH_{thiazole}$), 5.51 (br. s, 1H, NH), 5.0 (s, 1H, CH); ^{13}C-NMR (δ ppm) (DMSO-d_6): 166.02 (C=$N_{thiazole}$), 158.8 (C_2), 157.36 (C-$N_{thiazole}$), 153.55 (C_1^-), 152.51 (C_{10}), 150.95 ($C_1^=$), 148.4 (C_3^-, C_5^-, $C_3^=$, $C_5^=$), 138.48 (C_5), 130.36 ($C_4^=$), 129.61 (C_4, C_6), 124.29 (C_2^-, C_6^-), 122.94 ($C_2^=$, $C_6^=$), 122.21 (C_8), 120.61 (C_4^-) 119.69 (C_9), 119.34 (C_7), 117.97 (C-$S_{thiazole}$), 116.24 (C_3), 112.65 (C_1), 56.32 (CH).

Physical properties and Spectral data for1-((3-nitrophenyl)((5-phenylthiazol-2yl)amino)methyl) naphthalene-2-ol (**7b**)

Chemical Formula: ($C_{26}H_{19}N_3O_3S$), m.p: (186-188C^o), yield (0.721g, 80 %), color: dark brown; FT-IR (cm^{-1}): 3403 (N-$H_{str.}$), 3271 ($OH_{str.}$), 3056 (C-$H_{Ar.\ str.}$), l600 (C=$N_{str.}$), 1557 (C=$C_{str.}$), 1505 ($NO_{2asym.\ str.}$), 1380 ($NO_{2sym.\ str.}$), 1251 (C-$O_{str.}$); ^{1}H-NMR (δ ppm) (DMSO-d_6): 10.31(s, 1H, OH), 8.75-6.60 (m, 15H_{Ar}), 6.75 (s, 1H $CH_{thiazole}$), 5.45 (br. s, 1H, NH), 5.0(s, 1H, CH). ^{13}C-NMR (δ ppm) (DMSO-d_6): 166.66 (C=$N_{thiazole}$), 166.47 (C_2), 162.90 (C-$N_{thiazole}$), 162.68 (C_3^-), 158.85 (C_1^-), 157.36 (C_6^-), 143.0 (C_{10}), 142.89 ($C_1^=$), 137.08 (C_5^-), 135.36 ($C_3^=$, $C_5^=$), 135.29 (C_5), 135.17 ($C_4^=$), 134.76 (C_4, C_6), 134.47 ($C_2^=$, $C_6^=$) 132.82 (C_8), 131.97 (C_2^-), 129.45 (C_9), 126.79 (C_7), 119.39 (C_4^-), 119.36 (C-$S_{thiazole}$), 118.93 (C_3), 116.28 (C_1), 52.70 (CH).

Physical properties and Spectral data of 1-((4-nitrophenyl)((5-phenylthiazol-2-yl)amino)methyl) naphthalene-2-ol (**7c**)

Chemical Formula: ($C_{26}H_{19}N_3O_3S$), m.p: (193-195C^o), yield (0.76g, 84 %), color: dark brown; FT-IR (cm^{-1}): 3359 (N-$H_{str.}$), 3228 ($OH_{str.}$), 3033 (C-$H_{Ar.\ str.}$), l622 (C=$N_{str.}$), 1597 (C=$C_{str.}$), 1573 ($NO_{2asym.\ str.}$), 1308 ($NO_{2sym.\ str.}$), 1284 (C-$O_{str.}$). ^{1}H-NMR (δ ppm) (DMSO-d_6): 9.90 (s, 1H, OH), 7.91-6.87 (m, 15$H_{Ar.}$), 6.78 (s, 1H, $CH_{thiazole}$), 5.75 (br. s, 1H, NH), 5.15 (s, 1H, CH). ^{13}C-NMR (δ ppm) (DMSO-d_6): 169.41 (C=$N_{thiazole}$), 165.7 (C_2), 152.74 (C-$N_{thiazole}$), 151.47 (C_1^-), 150.95 (C_4^-), 148.61 (C_{10}), 147.92 ($C_1^=$), 144.14 ($C_3^=$, $C_5^=$), 140.59 (C_2^-, C_6^-), 128.24 (C_5), 127.49 ($C_4^=$), 147.75 (C_4, C_6), 125.03 ($C_2^=$, $C_6^=$), 124.30 (C_8), 122.32 (C_3^-, C_5^-), 120.58 (C_9), 119.52 (C_7), 118.02 (C-$S_{thiazole}$), 116.43 (C_3), 112.68 (C_1), 56.21 (CH).

2.2.4. General method for the synthesis of 2-(2-(((2-hydroxynaphthalen-1-yl)(phenyl)methyl) imino)-4-oxothiazolidin-5-yl)acetic acid (8)

(Sushilkumar and Devanand, 2003)

In a 100 mL round bottom flask fitted with reflux condenser, compound **(4a)** (0.616g, 0.002mol) and maleic anhydride (0.196g, 0.002mol) in glacial acetic acid (20 mL) were refluxed with stirring for 12h. The progress of the reactions monitored by TLC, the reaction mixture was minimized to half under reduced pressure, cooled at room temperature and poured on cold water. The precipitate was filtered off, dried and recrystallized from ethanol. The reaction is shown in the (**Scheme 4**).

Physical properties and Spectral data of 2-(2-(((2-hydroxynaphthalen-1-yl)(phenyl)methyl) imino)-4-oxothiazolidin-5-yl)acetic acid **(8)**

Chemical Formula: ($C_{22}H_{18}N_2O_4S$), m.p: (206-208C^o), yield (0.63g, 78 %), color: gray; FT-IR (cm^{-1}): 3276 ($NH_{str.}$), 3083 ($OH_{str.}$), 3042 (C-$H_{Ar.\ str.}$), 1766 (C=$O_{str.\ carboxylic\ acid}$), 1666 (C=$O_{str.\ thiazoledin\text{-}4\text{-}one}$), l581 (C=$N_{str.}$), 1538 (C=$C_{str.}$), 1274 (C-$O_{str.}$). ^{1}H-NMR (δ ppm) (DMSO-d_6): 12.51 (s, 1H, $OH_{carboxylic\ acid}$), 10.98 (br. s, 1H, NH), 9.88 (s, 1H, $OH_{2\text{-}naphthol}$), 7.89-6.78 (m, 11$H_{Ar.}$), 4.14 (t, 1H, CH $_{thizoledin\text{-}4\text{-}one}$), 3.49 (s, 1H, CH), 2.39 (d, 2H, CH_2). ^{13}C-NMR (δ ppm) (DMSO-d_6): 177.95 (C=$O_{carboxylic\ acid}$), 169.57 (C =$O_{thizoledin\text{-}4\text{-}one}$), 148.62 ($C_2$), 145.78 (C-N $_{thiazoledin\text{-}4\text{-}one}$), 143.95 ($C_1^-$), 142.77 ($C_{10}$), 140.08 ($C_3$, C_5^-), 137.20 (C_5), 130.11 (C_2, C_6), 129.50 (C_2^-, C_6^-), 127.51 (C_8), 126.90 (C_4^-), 124.67 (C_9), 121.61 (C_7), 119.69 (C_3), 112.09 (C_1), 60.72 (CH) , 56.55 ($CH_{thiazoledin\text{-}4\text{-}one}$), 48.10 ($CH_2$).

2.2.5. General method of the synthesis of 1-((2-hydroxynaphthalen-1-yl)(4-nitrophenyl) methyl)-5-phenyl-1,2-dihydro-3*H*-1,2,4-triazol-3-one (9) (Shalini et al., 2009)

Benzoyl chloride (0.28g, 0.002mol) and compound (**6**) (0.704g, 0.002mol) were dissolved in ethanol, Potassium carbonate (0.42g, 0.003mol) added , the mixture was refluxed for 6 h. Then heated on water bath on slightly alkaline medium 4% NaOH (20 mL) for around 4 h. the result was neutralized by dilute HCl. The solvent was evaporated and the product was recrystallized from ethanol. The reaction is illustrated in the (**Scheme 5**).

Physical properties and Spectral data of 1-((2-hydroxynaphthalen-1-yl)(4-nitrophenyl) methyl)-5-phenyl-1,2-dihydro-3*H*-1,2,4-triazol-3-one **(9)**

Chemical Formula: ($C_{25}H_{19}N_3O_2$), m.p: (278-280C^o), yield (0.63g, 71.9 %), color: brown; FT-IR (cm^{-1}): 3236 (N-$H_{str.}$), 3137 ($OH_{str.}$), 3035 (C-$H_{Ar.\ str.}$), 1664 (C=$O_{str.}$), l611 (C=$N_{str.}$), 1541 (C=$C_{str.}$), 1509 ($NO_{2asym.\ str.}$), 1342 ($NO_{2sym.\ str.}$), 1245(C-$O_{str.}$). ^{1}H-NMR (δ ppm) (DMSO-d_6): 9.48 (s, 1H, OH), 8.81 (br. s, $NH_{1,2\text{-}dihydro\text{-}3H\text{-}1,2,4\text{-}triazol\text{-}3\text{-}one}$), 8.01-6.72 (m, 15$H_{Ar.}$), 4.54 (s, 1H, CH). ^{13}C-NMR (δ ppm) (DMSO-d_6): 169.56 (C=$O_{1,2\text{-}dihydro\text{-}3H\text{-}1,2,4\text{-}triazol\text{-}3\text{-}one}$), 164.71 (C=$N_{1,2\text{-}dihydro\text{-}3H\text{-}1,2,4\text{-}triazol\text{-}3\text{-}one}$), 144.52 ($C_2$), 142.79 ($C_1^-$), 137.19 ($C_4^-$), 132.51 ($C_{10}$), 130.11 ($C_4^=$), 129.51 ($C_2^-$, C_6^-), 128.80 (C_5, $C_5^=$, $C_3^=$), 127.30 ($C_1^=$), 126.91 (C_4, C_6), 124.65 ($C_2^=$, $C_6^=$), 121.64 (C_8), 119.47 (C_3, C_5^-), 118.90 (C_9), 118.04 (C_7), 115.00 (C_3), 112.07 (C_1^-), 59.00 (CH).

2.2.6. General method of antibacterial activity

(Landage et al., 2019)

An antibacterial activity of synthesized compounds was determined *in vitro* against two bacterial strains Gram-positive (*Staphylococcus aureus*), Gram-negative (*Escherichia coli*) by agar well diffusion method. 20ml of Muller Hinton agar was poured in to sterile petri dish and spread with 100 µl of culture. The well was made in the agar by sterile cork borer of width (6 mm) then 100 µl of synthesized compounds (500ppm and 1000ppm) were loaded in the well along with amikacin as positive control and DMSO as negative control. The plates incubated at 37°C for 24 hours, the zone of inhibition produced by each compound was measured in mm.

2.2.7. General method of antifungal activity
(Pejchal et al., 2015)

Antifungal activity was screened against *Candida albicans* in Muller Hinton agar medium, preparation of nutrient broth, dilution and application were carried out using the same procedure as for antimicrobial testing. The standard antibiotic Nystatin was used as control positive and the plates were incubated at 30 °C for 48 h. The diameters of zone of inhibition observed were measured.

3. RESULTS AND DISCUSSION:

In this study, five membered heterocyclic compounds thaizole, 4-thiazolidinone were synthesized from the reaction of 1-thiocarbamidoalkyl-2-naphthol derivatives **(4a-c)** with phenacyl bromide in ethanol and maleic anhydride in glacial acetic acid, respectively and 1,2-dihydro-3H-1,2,4-triazol-3-one with benzoyl chloride in ethanol. Scheme **(3, 4and 5)**

The FT-IR spectra of the starting materials are changed, when the compounds of (**4a-c**) are cyclized to the compounds (**7a-c** and **8**), two peaks of ($NH_{2str.}$) groups are disappeared, while different new peaks are appeared for ($C=N_{str.}$) functional groups at (1600-1627 cm^{-1}). In compound (**8**) two peaks are appeared for each of the carbonyl group of carboxylic acid and amide (thiazolidin-4-one) at 1766 cm^{-1} and 1666 cm^{-1}, respectively (de Aquino et al., 2008). When compound (**6**) is converted to the compound (**9**) two peaks of ($NH_{2str.}$) at 3169 and 3281 cm^{-1} are disappeared, while ($C=N_{str.}$) peak are appeared at 1611 cm^{-1}, peak of Carbonyl group is shifted from 1681 cm^{-1} to 1664 cm^{-1}.

^{1}H-NMR spectra of the compounds (**4a-c** and **6**) are changed when cyclization occurred and compounds (**7a-c**, **8** and **9**) are obtained. The protons of NH_2 groups are disappeared in the cyclization products, while these two protons are present in the compounds **4a, 4b, 4c** and **6** at 8.16 , 9.18, 9.13 and 6.71 ppm respectively. Singlet band of ($CH_{thiazole}$) are appeared for the compounds **4a, 4b** and **4c** at 6.48, 6.75 and 6.78 ppm, respectively (Bhosale et al., 2012). A singlet band of (OH), doublet bands of (CH_2) and triplet bands of ($CH_{thiazoledin-4-one}$) are appeared at 12.51, 2.39 and 4.14 ppm in compound **8** (Gurumurthi et al., 2009). As described before the two protons of NH_2 group, which appeared at 6.71 ppm are disappeared when compound **6** is cyclized, one proton of the NH-CH that appeared at 11.29 ppm disappeared, while the NH-CO proton band shifted and appeared as a singlet at 8.81 ppm (Ali et al., 2018). Five aromatic protons increased when compounds (**7a-c** and **9**) were formed.

^{13}C-NMR spectra of the synthesized compounds support the formation of new products when the compounds (**4a-c** and **6**) are cyclized to yield (**7a-c**, **8** and **9**). The chemical shifts for carbon of (C=S) group in compound (**4a-c**) are disappeared and the carbon of ($C=N_{thiazole}$) group are formed at 166.02-169.41 ppm, while carbon of ($\underline{C}$-N $_{thiazole}$) and ($\underline{C}$-S $_{thiazole}$) are appeared at 152.74-162.90 ppm and 117.97-119.36 ppm, respectively. This showed that the number of carbons are increased when the compound **4a** is converted to the compound **8**, because of the presence of the carbon $\underline{C}$ =O $_{thizoledin-4-one}$, $\underline{C}$-N $_{thiazoledin-4-one}$, $\underline{C}$-S $_{thiazoledin-4-one,}$ and CH_2 and $C=O_{carboxylic\ acid}$ at 169.57, 145.78, 56.55, 48.10 and 177.95 ppm, respectively. Also, the carbon of (C=S) at 183.67 ppm are disappeared. When the compound **9** is formed from the compound **6** and the chemical shifts for carbon of C=O is shifted from 162.25 to 169.56 ppm and the chemical shift for carbon of ($\underline{C}$=N $_{dihydro\text{-}3\textit{H}\text{-}1,2,4\text{-}triazol\text{-}3\text{-}one}$) group is appeared at 164.71 ppm. Six aromatic carbons are increased in the compounds (**7a-c** and **9**).

All synthesized compounds showed the difference ability for stopping or destroying the growth of bacteria or fungi. Commonly the antibacterial and antifungal activities of the compounds **(4a-c and 6)** are increased when they converted to the heterocyclic compounds **(7a-c, 8 and 9)** and the ability of the synthesized compounds against *Staphylococcus aureus* bacteria, *Escherichia coli* bacteria and *Candida albicans* fungi are increased by increasing their concentrations as shown in the (**Table 1 and Table 2**). The compound **(7a)** was highly active while prepared as 1000 µg/ml.

4. CONCLUSION

As concluded, the useful and simple methods are used for the synthesis of some new heterocyclic compounds in good yields. Nitro group needed less reaction time than Hydrogen. Ultrasound technique is used to save time. The suitable solvent that used for recrystallization of

the products was ethanol. Heterocyclic compounds **(7a-c**, **8** and **9)** are exhibited higher growth inhibition than synthesized compounds (**4a-c** and **6)** against *Staphylococcus aureus*, *Escherichia coli* and *Candida albicans*, increasing the concentration of synthesized compound the growth inhibition are increased.

ACKNOWLEDGEMENT

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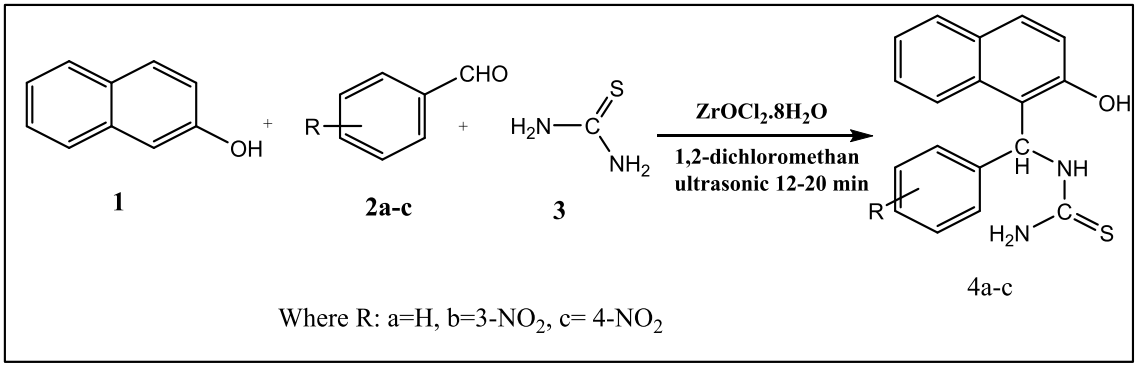
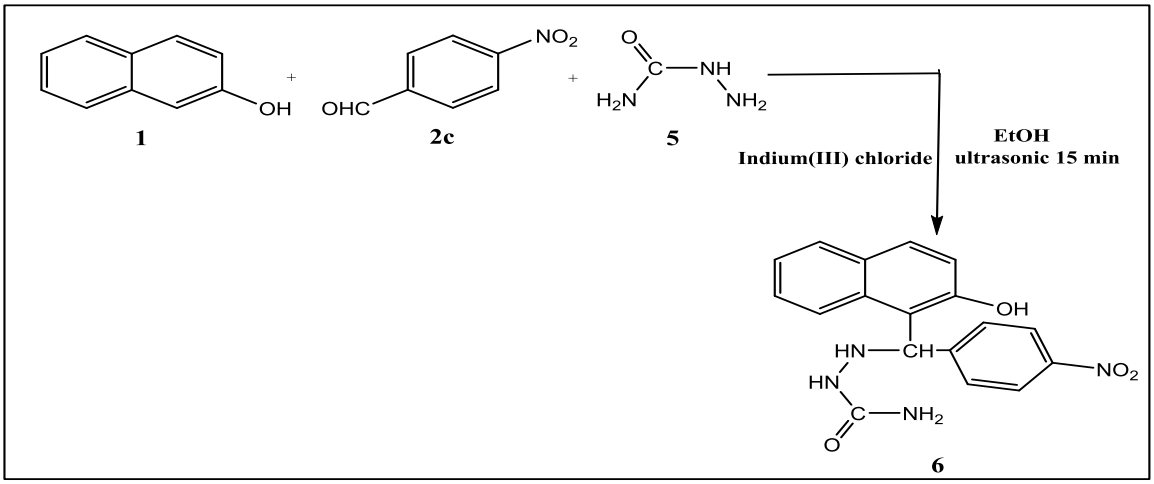


Scheme 1: Synthesis of compounds **(4a-c)**



Scheme 2: Synthesis of compounds **(6)**

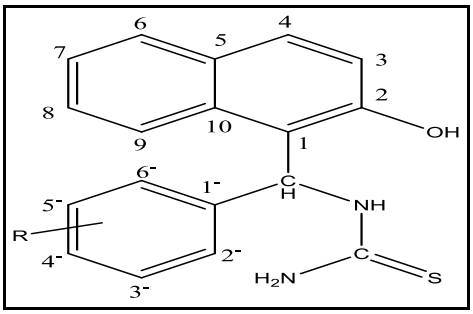


Fig.1: Numbering of compounds (**4a-c**)

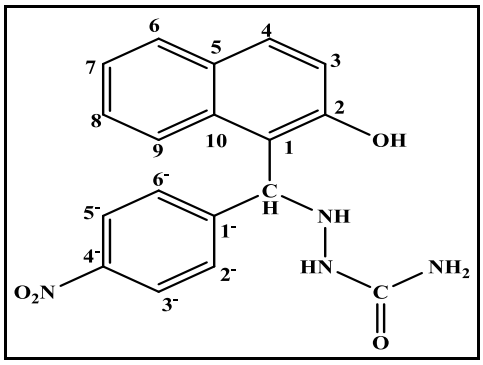
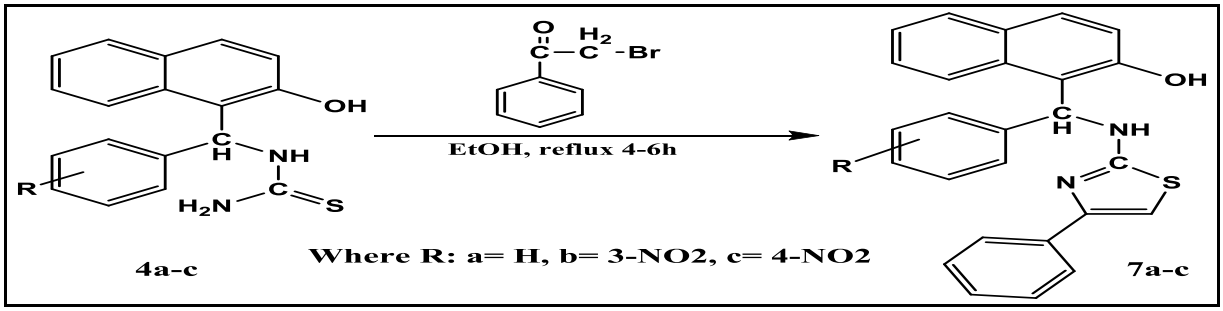


Fig. 2: Numbering of compound (**6**)



Scheme 3: Synthesis of compounds **(7a-c)**

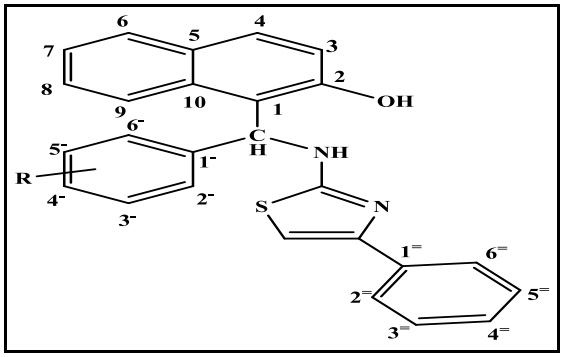
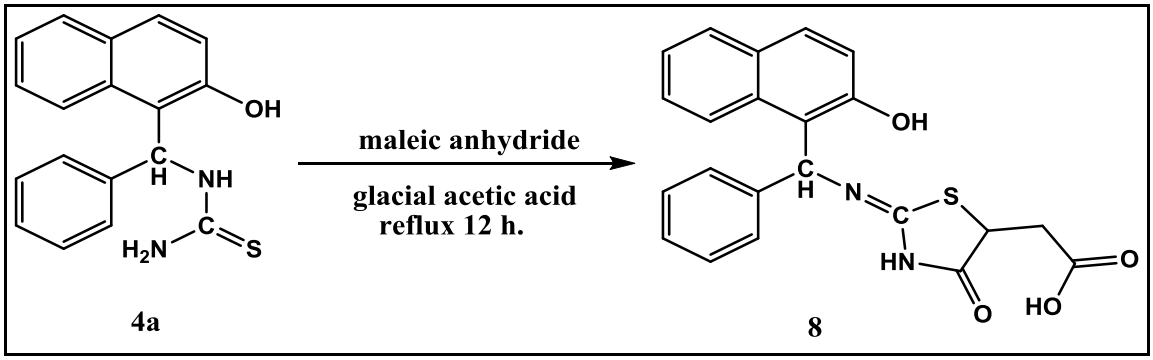


Fig. 3: Numbering compounds (**7a-c**)



Scheme 4: Synthesis of compound **(8)**

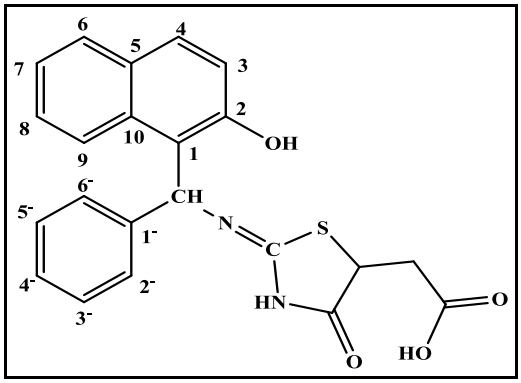
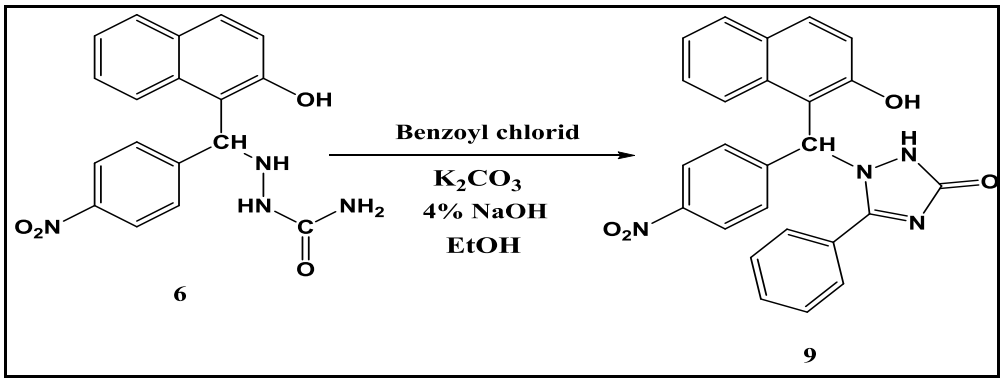


Fig. 4: Numbering of compound (**8**)



Scheme 5: Synthesis of compound **(9)**

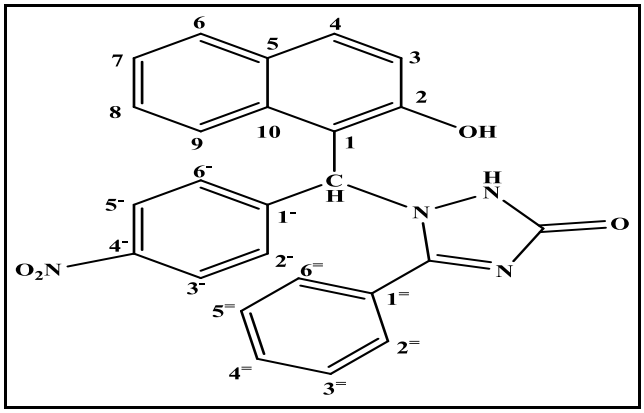


Fig. 5: Numbering of compound **(9)**

Table 1: The antibacterial and antifungal activities of compounds (**4a-c** and **6**)

Variables		Antibacterial Activity			Fig.
		Gram positive	Gram negative	Antifungal	
Compound	Conc.	S. aureus	E. coli	C. albicans	
4a	500ppm	11	11	7	
	1000 ppm	13	12	9	
4b	500 ppm	12	9	9	
	1000 ppm	13	12	11	
4c	500ppm	11	9	9	9
	1000 ppm	12	12	12	10
6	500ppm	13	11	11	11
	1000 ppm	14	12	13	
Amikacin	33			NT	9 and 10
Nystatin	NT			23	11

Table 2. The antibacterial and antifungal activities of compounds (**7a-c** and **9**)

Variables		Antibacterial Activity			Fig.
		Gram positive	Gram negative	Antifungal	
Compound	Conc.	S. aureus	E. coli	C. albicans	
7a	500ppm	25	24	11	9
	1000 ppm	31	29	16	10
7b	500ppm	25	25	13	
	1000 ppm	28	27	17	
7c	500ppm	24	23	15	
	1000 ppm	30	27	20	
8	500ppm	23	24	12	
	1000 ppm	27	28	15	
9	500ppm	26	24	14	11
	1000 ppm	30	29	18	
Amikacin		33		NT	9 and 10
Nystatin		NT		23	11

S. aureus= *Staphylococcus aureus*, E. coli= *Escherichia coli*, C. albicans= *Candida albicans*
NT: not test
For antibacterial:
Highly active (inhibition zone > 30 mm); active (inhibition zone 23-30 mm); moderately active (inhibition Zone 16--23 mm); slightly active (inhibition zone 9-16 mm); inactive (inhibition zone < 9 mm)
For antifungal:
Highly active (inhibition zone > 20 mm); active (inhibition zone 15-20 mm); moderately active (inhibition Zone 10-15 mm); slightly active (inhibition zone 5-10 mm); inactive (inhibition zone < 5 mm)

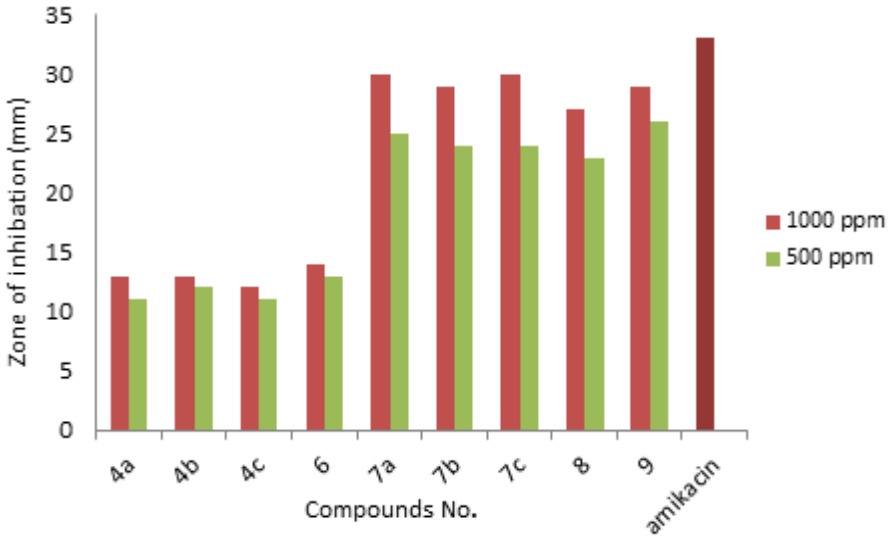


Fig. 6: Antibacterial activity of the synthesized compounds against *Staphylococcus aureus* bacteria.

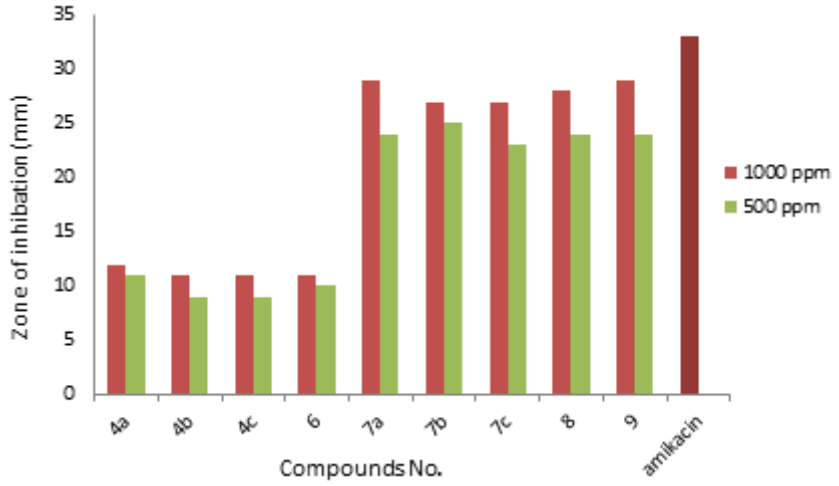


Fig. 7: Antibacterial activity of the all synthesized compounds against *Escherichia coli* bacteria.

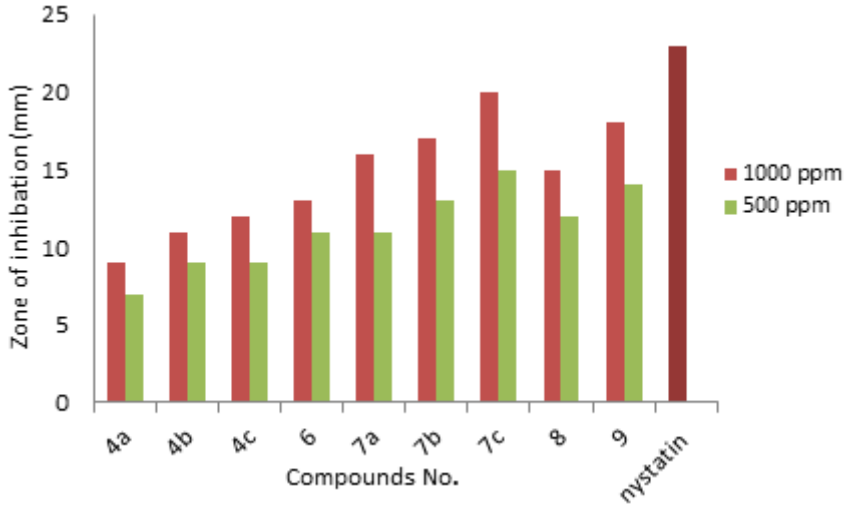


Fig. 8: Antifungal activity of the synthesized compounds against *Candida albicans* fungi

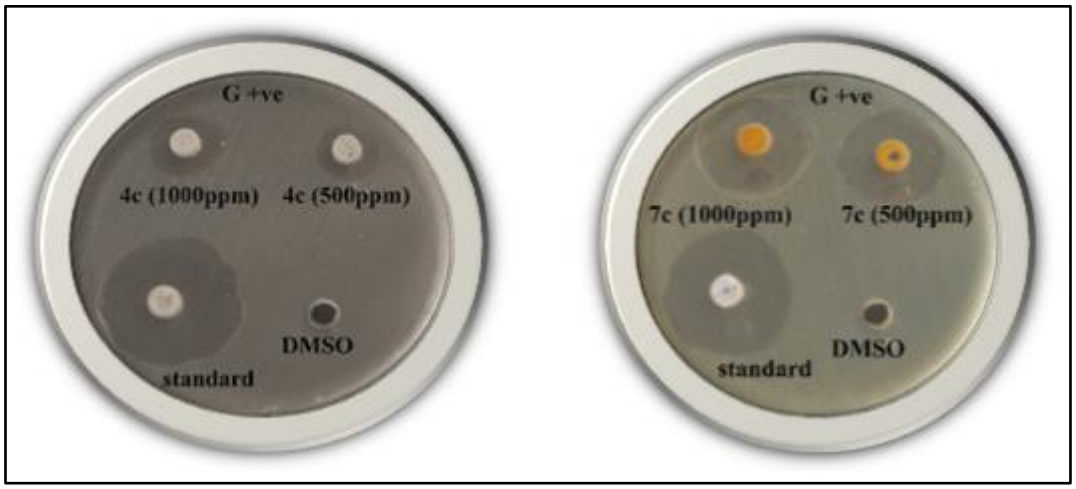


Fig. 9: Anti-bacterial activities of synthesized compounds (**4c** and **7c**) against *Staphylococcus aureus*

Fig. 10: Anti-bacterial activities of synthesized compound **(4c** and **7c)** against *Escherichia coli*

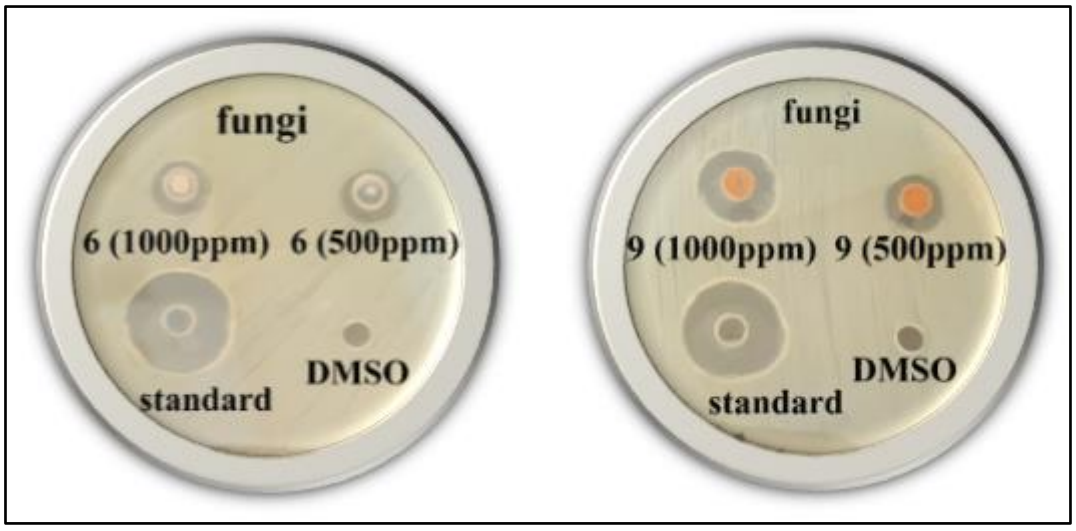


Fig. 11: Antifungal activities of synthesized products **(6** and **9)** against *Candida albicans*

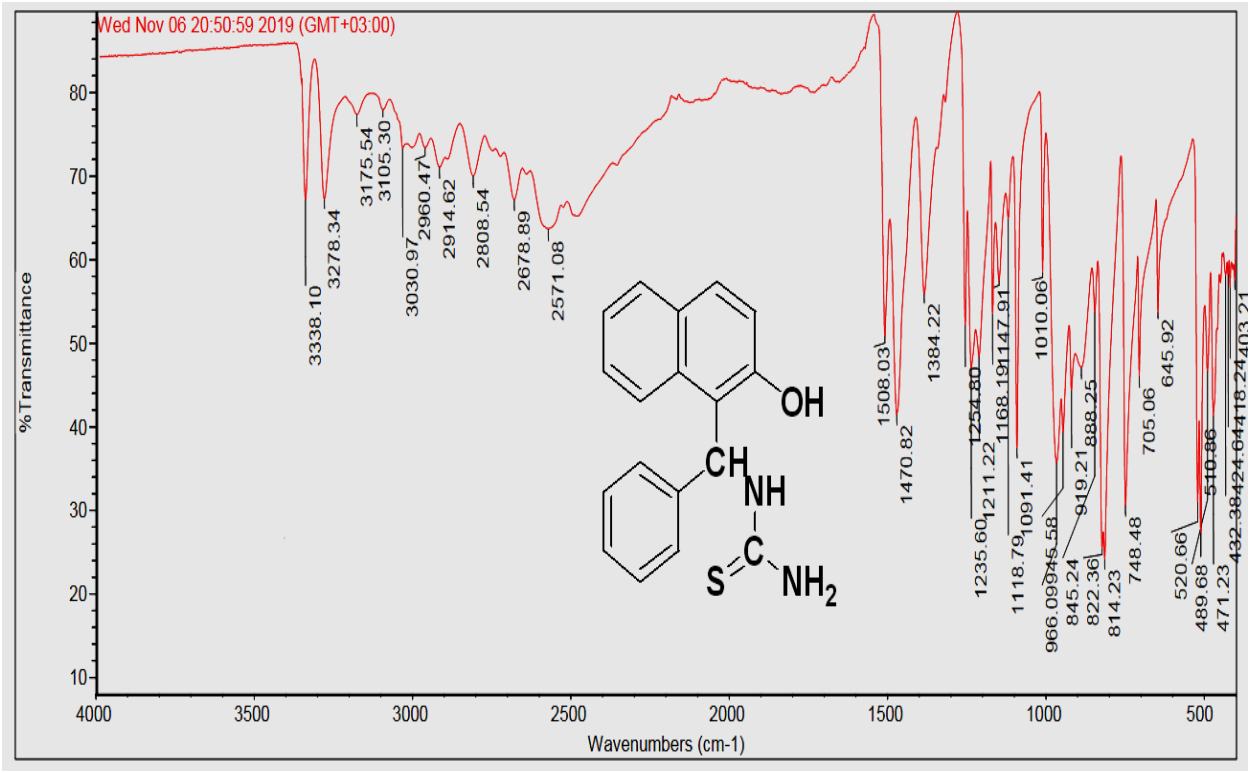


Fig. 12: FT-IR spectrum of ((2-hydroxynaphthalen-1-yl)(phenyl)methyl)thiourea **(4a)**

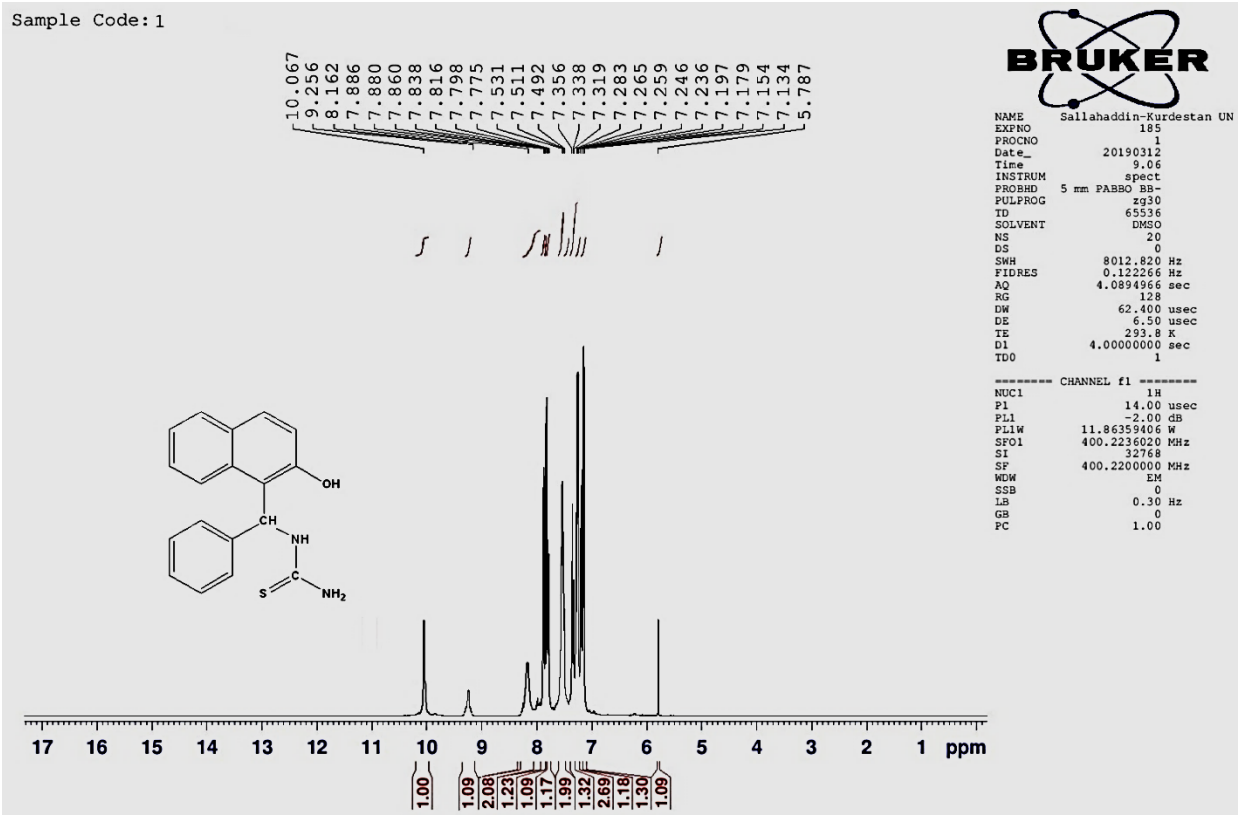


Fig. 13: ^{1}H-NMR Spectrum of ((2-hydroxynaphthalen-1-yl)(phenyl)methyl)thiourea **(4a)**

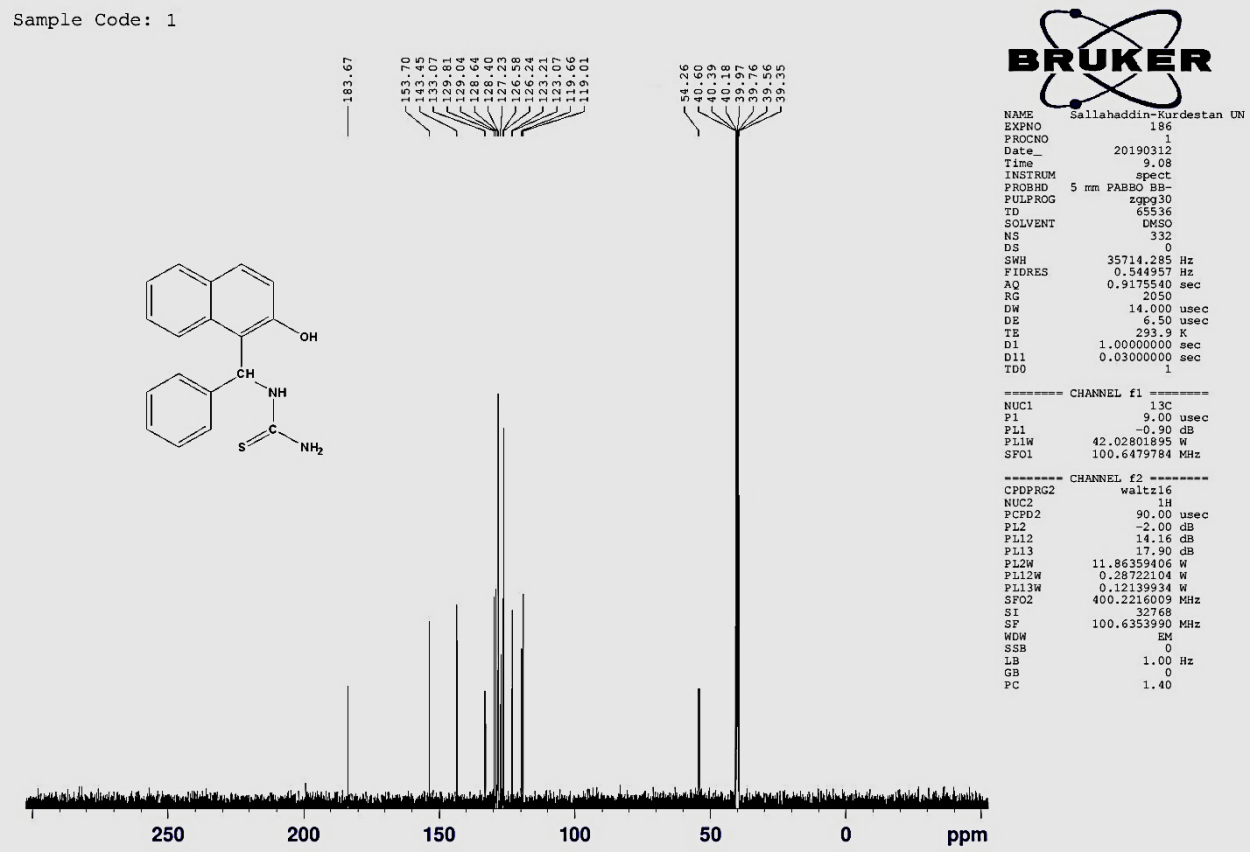


Fig. 14: ^{13}C-NMR spectrum of ((2-hydroxynaphthalen-1-yl)(phenyl)methyl)thiourea **(4a)**

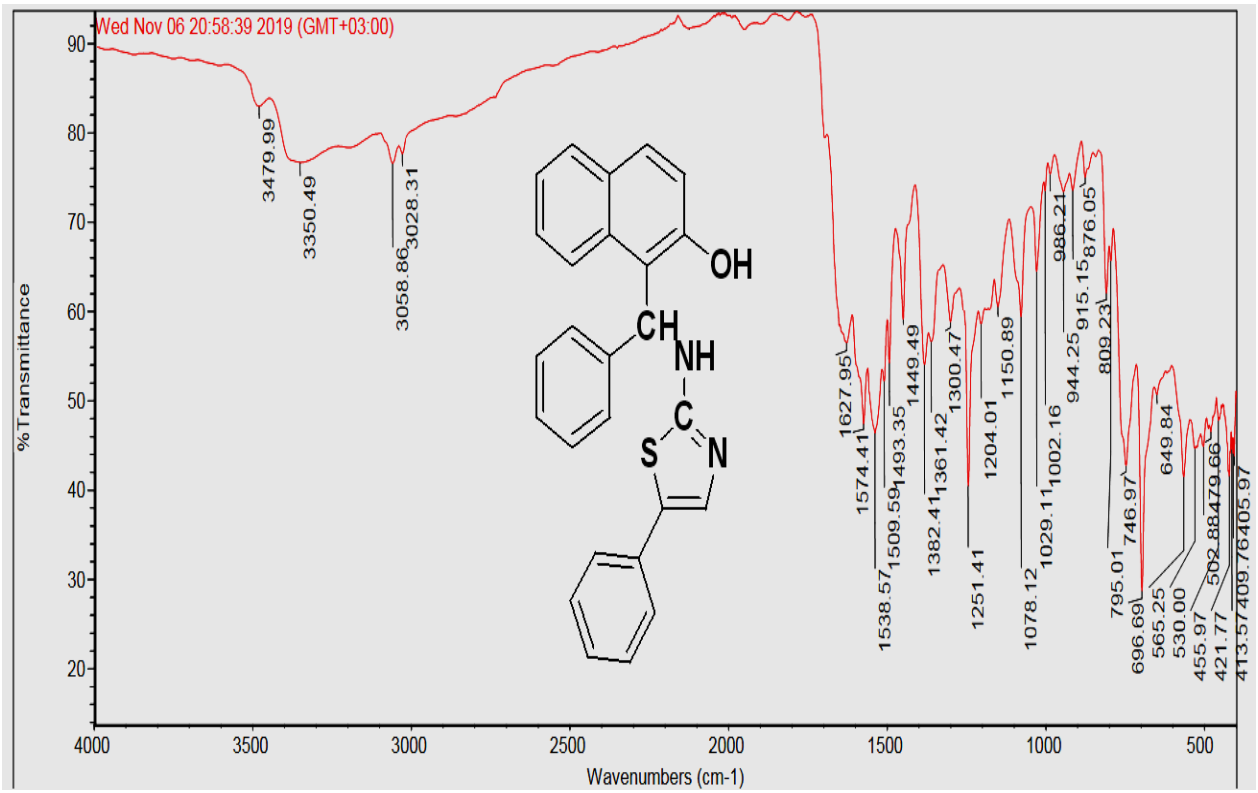


Fig. 15: FT-IR spectrum of (phenyl((5-phenylthiazol-2-yl)amino)methyl)naphthalen-2-ol **(7a)**

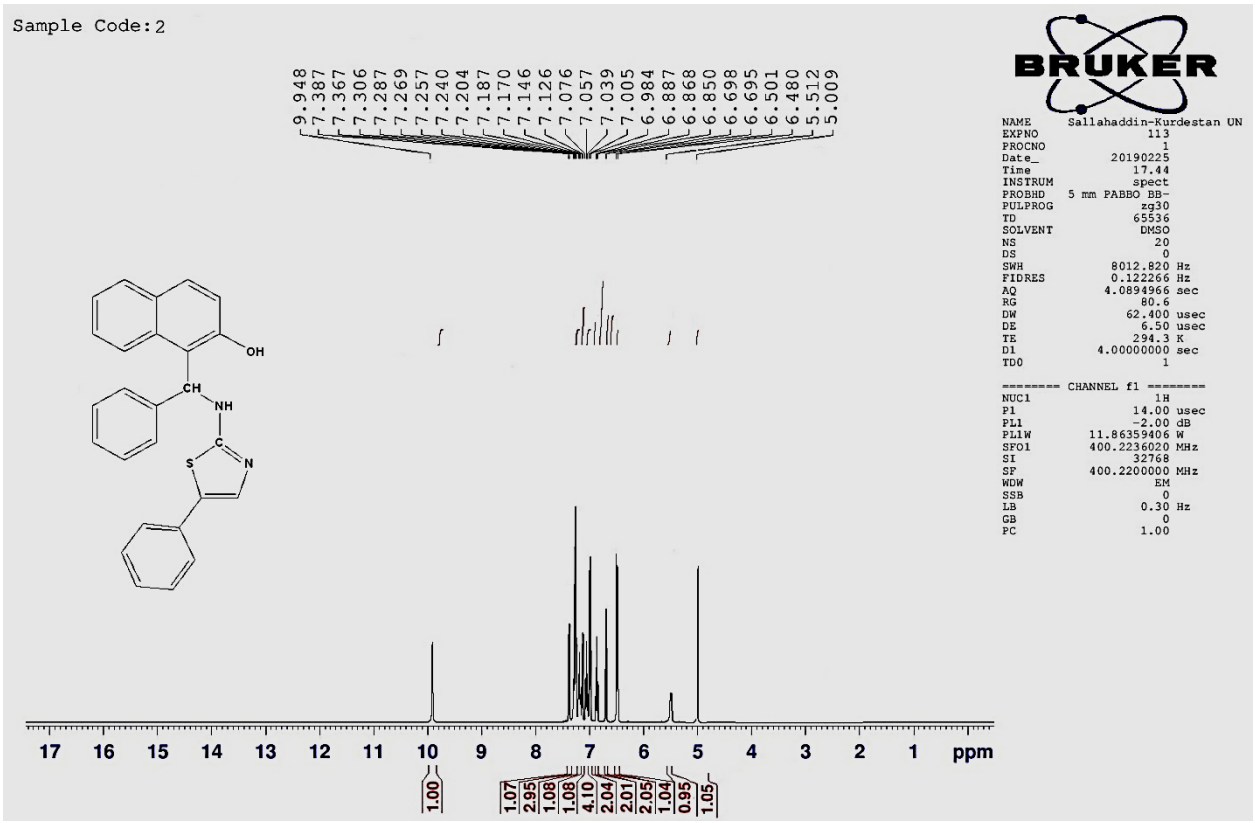


Fig. 16: ^{1}H-NMR Spectrum of (phenyl((5-phenylthiazol-2-yl)amino)methyl)naphthalen-2-ol **(7a)**

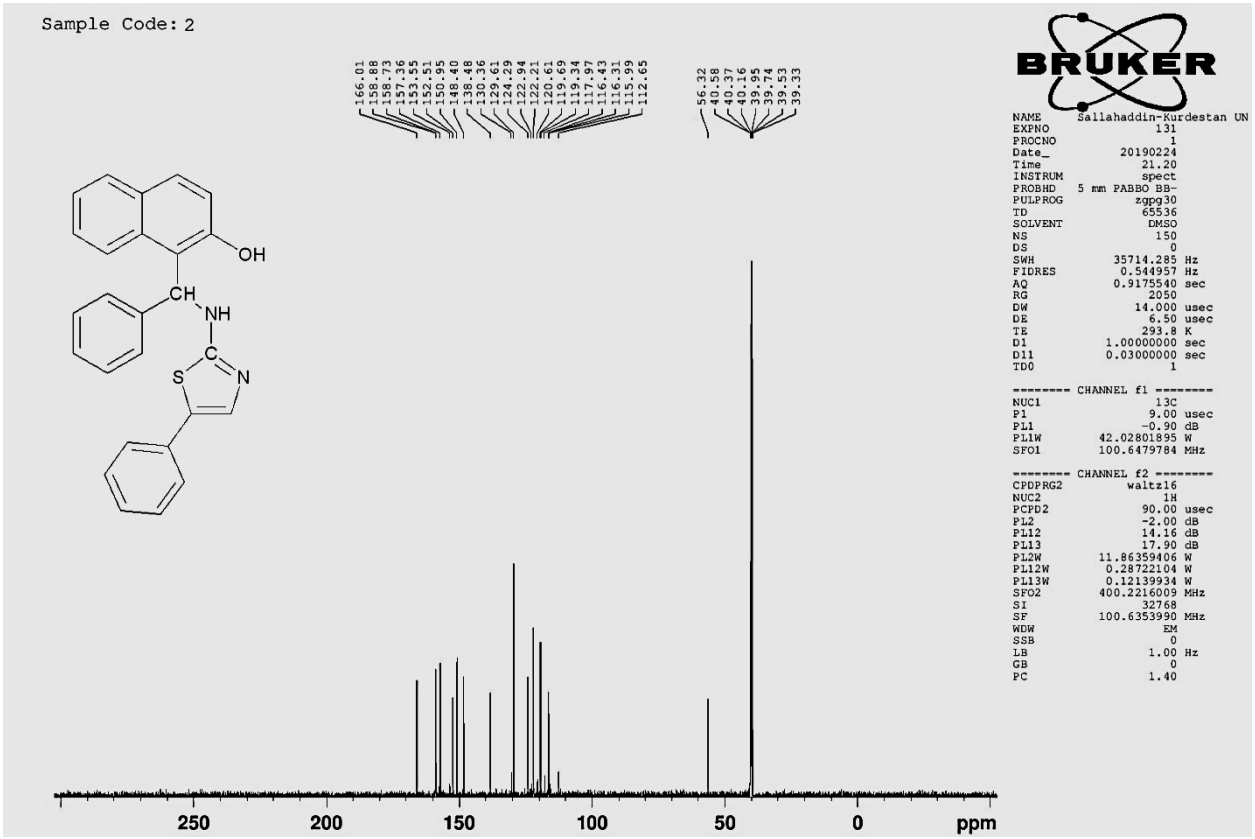


Fig. 17: ^{13}C-NMR spectrum of (phenyl((5-phenylthiazol-2-yl)amino)methyl)naphthalen-2-ol **(7a)**

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