Utility of β-diketones in heterocyclic synthesis: Synthesis of new tetrahydro-
pyrimidinethione, pyrazole, thiophene, dihydropyridine, dihydropyran,
pyridazine derivatives and investigation of their antimicrobial activity

Mohamed Ahmed Mahmoud Abdel Reheim *, Ibrahim Saad Abdel Hafiz and Safaa Mohamed

Department of Chemistry, Faculty of Science, Arish University, Arish 45511, Egypt

* Corresponding author at: Department of Chemistry, Faculty of Science, Arish University, Arish 45511, Egypt.
Tel.: +2.0122.2283357. Fax: +2.068.3350065. E-mail address: dr.mohamedabdulreheim@gmail.com (M.A.M. Reheim).

ABSTRACT

A series of many important diverse number of fused heterocyclic systems were prepared from
the reaction of 1-(2-hydroxynaphthalen-1-yl)-3-phenylpropane-1,3-dione with some
bifunctional nucleophiles, these reactions mainly proceed via condensation of 1-(2-
hydroxynaphthalen-1-yl)-3-phenylpropane-1,3-dione with the aldehydic function followed
by nucleophilic attack. Structures of the new compounds were established by elemental
analyses and spectral data. Some of the products were also screened in vitro for their
antimicrobial activity.

1. Introduction

Among a wide variety of heterocyclic that have been
explored for developing pharmaceutical important molecules
such as pyrazoles, cyanopyridines, pyrimidinethiones and
pyrazines have played an important role in medicinal chemistry.
Various biological applications have been reported for
pyrazoles such as anticaner, antiviral, anti-inflammatory,
antifungal, antimicrobial, antihistaminic, antiplatelet, anal-
gesic, antihyperglycemic, antipyretic, anti-tumor, sedative,
hypnotic activity [1-6], antidepressant [7], anticonvulsant [8].
Cyanopyridine derivatives have attracted considerable atten-
tion as they appeared of interest to possess anticonvulsant [9],
antibacterial [10,11], antitumor [12], antihypertensive [13],
thiones have been found to possess antitubercular [16],
antitumor [17] and hypoglycemc [18] activities. Pyrane and
fused 4H-pyrene derivatives have attracted a great interest
owing to their antimicrobial activity [19-21], inhibition of
influenza, virus sialidases [22], mutagenicity activity [23], anti-
viral [24], antiproliferation agents [25], sex-pheromones [26],
antitumor [27] and anti-inflammatory agents [28]. Moreover,
pyranic derivatives are well known for their antihistaminic
activity [29]. Also, naphthalene is important aryl ring in many
active compounds such as anti-inflammatory, anti-bacterial,
antimicrobial and anti-cancer [30,31]. In view of the above
observations and in continuation of our previous works in
heterocyclic chemistry, we report herein a convenient and
efficient synthesis of new heterocycles based on 1-(2-
hydroxynaphthalen-1-yl)-3-phenylpropane-1,3-dione (1) as
a key starting material. A selected series of these compounds
were investigated for their antimicrobial activities.

2. Experimental

2.1. Instrumentation

All melting points were measured using Akoofler Block
instrument and are uncorrected. IR spectra (KBr) were
recorded on a FTIR 5300 spectrometer (ν, cm⁻¹). The 1H NMR
spectra were recorded in DMSO-d₆ and CDCl₃ at 300 MHz and
400 MHz on a Varian Gemini NMR. 1000 EX mass spec tro-
metry at 70 eV. The purity of synthesized compounds was
checked by thin layer chromatography TLC (aluminum sheets)
using n-hexane, ethyl acetate (9: 1, v:v) eluent.
Elemental analyses were carried out by the Microanalytical Research Center, Faculty of Science, and Microanalytical Unit, Faculty of Pharmacy, Cairo University, Egypt.

2.2. Synthesis

2.2.1. Synthesis of 1-(2-hydroxynaphthalen-1-yl)-3-phenyl propane-1,3-dione (1)

A mixture of ethyl benzoylacetate (0.01 mol) and β-naphthol (0.01 mol) was exposed to microwave irradiation for 4-6 mins, the reaction mixture was allowed to reach room temperature, then diluted with ethanol with stirring and the solid product that formed, was filtered and crystallized from ethanol to give compound 1 (Scheme 1).

2.2.2. General procedure for preparation of benzylidene derivatives (4a-d)

A mixture of compound 1 (0.01 mol), appropriate aryl aldehydes (0.01 mol) in ethanol (30 mL) with catalytic amount of piperidine was heated under reflux for 3 hrs. The reaction mixture was allowed to cool and poured into crushed ice then acidified with HCl. The separated solid was filtered, washed with water and crystallized from ethanol to give compound 4a-d (Scheme 1).

2-Benzylidene-1-(2-hydroxynaphthalen-1-yl)-3-phenyl propane-1,3-dione (4a): Color: Pale green. Yield: 61%. M.p.: 145-147 °C. FT-IR (KBr, ν, cm⁻¹): 3453 (OH), 3057 (CH-Arom). 1H NMR (400 MHz, DMSO-δ, δ, ppm): 6.68 (s, 1H, CH-olefinic), 7.20-8.37 (m, 15H, Ar-H), 9.96 (s, 1H, OH). MS [EI, m/z (%)]: 378 (M⁺, 6). Anal. calcd. for C₂₆H₁₈O₃: C, 82.52; H, 4.79; O, 12.68. Found: C, 82.51; H, 4.78; O, 12.69%.

2-(4-Chlorobenzylidene)-1-(2-hydroxynaphthalen-1-yl)-3-phenylpropane-1,3-dione (4b): Color: Pale yellow. Yield: 72%. M.p.: 170-172 °C. FT-IR (KBr, ν, cm⁻¹): 3434 (OH), 3056 (CH-Arom), 2967 (CH-Aliph), 1727, 1637 (2C=O). 1H NMR (400 MHz, DMSO-δ, δ, ppm): 5.24 (s, 1H, CH-olefinic), 7.06-8.34 (m, 16H, Ar-H), 9.95 (s, 1H, OH). MS [EI, m/z (%)]: 414 (M⁺+2, 80). Anal. calcd. for C₂₆H₁₄ClO₃: C, 75.64; H, 4.15; O, 11.63. Found: C, 75.63; H, 4.14; O, 11.64%.

Scheme 1
2.2.3. General procedure for preparation of tetrahydro pyrimidinethione derivatives (5a-d)

To boiling solution of compound 4a-d (0.01 mol) and thiourea (0.01 mol) in ethanolic potassium hydroxide (30 mL, 10%), was added. The reaction mixture was refluxed for 20 h, then allowed to cool and poured into crushed ice then acidified with HCl. The separated solid was filtered, washed with water and crystallized from ethanol to give compound 5a-d (Scheme 1).

(4,6-Diphenyl-2-thioxo-1,2,3,4-tetrahydropyrimidin-5-yl)-(2-hydroxynaphthalen-1-yl)methanone (5a): Color: Yellow. Yield: 73 %, M.p.: 150-152 °C. FT-IR (KBr, v cm⁻¹): 3447, 3400 (OH/NH), 2971 (CH), 1655 (C=O). ¹H NMR (400 MHz, DMSO-d₆, δ ppm): 7.09 (s, 1H, =CH), 7.11-8.35 (m, 17H, Ar-H), 9.96 (s, 1H, =NH), MS (EI, m/z (%)): 470 (M⁺, 22). Anal. calcld. for C₁₉H₁₂N₂O₂S: C, 76.24; H, 4.42; N, 4.16; S, 9.18.

(2-Hydroxynaphthalen-1-yl)-(4-methoxyphenyl)-6-phenyl-2-thioxo-1,2,3,4-tetrahydropyrimidin-5-yl)methanone (5b): Color: Pale yellow. Yield: 81 %, M.p.: 157-159 °C. FT-IR (KBr, v cm⁻¹): 3444, 3400 (OH/NH), 3057 (CH-Arom.), 2975 (CH-Aliph.), 1655 (C=O). ¹H NMR (400 MHz, DMSO-d₆, δ ppm): 7.20-8.38 (m, 11H, Ar-H), 9.97 (s, 1H, =NH), MS (EI, m/z (%)): 466 (M⁺, 35). Anal. calcld. for C₂₀H₁₅N₂O₃: C, 72.02; H, 4.75; N, 6.00.

(2-Hydroxynaphthalen-1-yl)-(4-methoxyphenyl)-6-phenyl-2-thioxo-1,2,3,4-tetrahydropyrimidin-5-yl)methanone (5c): Color: Pale yellow. Yield: 81 %, M.p.: 157-159 °C. FT-IR (KBr, v cm⁻¹): 3444, 3400 (OH/NH), 3057 (CH-Arom.), 2975 (CH-Aliph.), 1637 (C=O). ¹H NMR (400 MHz, DMSO-d₆, δ ppm): 6.85 (s, 1H, CH-pyrazole), 7.11-8.35 (m, 17H, Ar-H), 9.95 (s, 1H, =NH), MS (EI, m/z (%)): 468 (M⁺, 28). Anal. calcld. for C₂₀H₁₄N₂O₂: C, 72.02; H, 4.70; N, 6.06.

2.2.4. General procedure for preparation of compounds (7a-b)

A mixture of compound 1 (0.01 mol) and hydrazine hydrate or phenyl hydrazine in ethanol (30 mL) was heated under reflux for 12 hrs. The reaction mixture was allowed to cool and poured into crushed ice. The separated solid was filtered, washed with water and crystallized from ethanol to give compound 7a-b (Scheme 1).

(1-(3-Phenyl-1H-pyrazol-5-yl)naphthalen-2-ol) (7a): Color: Pale brown. Yield: 55 %. M.p.: 182-184 °C. FT-IR (KBr, v cm⁻¹): 3441 (OH), 3202 (NH), 3050 (CH-Arom.). ¹H NMR (400 MHz, DMSO-d₆, δ ppm): 6.85 (s, 1H, CH-pyrazole), 9.95 (s, 1H, =NH), 10.10 (hump, 1H, OH), 12.95 (s, 1H, NH). MS (EI, m/z (%)): 286 (M⁺, 50). Anal. calcld. for C₁₉H₁₅N₂O: C, 79.70; H, 4.93; N, 9.78. Found: C, 79.73; H, 4.95; N, 9.80.

(1-(3-phenyl-1H-pyrazol-5-yl)naphthalen-2-ol) (7b): Color: Brown. Yield: 62 %. M.p.: 202-204 °C. FT-IR (KBr, v cm⁻¹): 3417 (OH), 3065 (CH-Arom.). ¹H NMR (400 MHz, DMSO-d₆, δ ppm): 7.11 (s, 1H, CH-pyrazole), 7.21-8.38 (m, 16H, Ar-H), 9.97 (s, 1H, =NH), MS (EI, m/z (%)): 362 (M⁺, 56). Anal. calcld. for C₂₂H₁₈N₂O: C, 82.85; H, 5.01; N, 7.73. Found: C, 82.83; H, 5.09; N, 7.76.

2.2.5. Synthesis of 2-aminoo-5-(2-naphthyl-1-oxo)-4-phenylthiophene-3-carbonitrile (10)

Equimolar amounts of compound 1 (0.01 mol), malononitrile and elemental sulfur (0.01 mol) in ethanol (30 mL) containing piperidine (1.2 mL) were refluxed for 15 hrs, poured onto cold water (30 mL) and acidified with HCl (pH = 3). The solid product thus formed was filtered and crystallized from dioxane (Scheme 1). Color: Yellow. Yield: 86 %, M.p.: 178-180 °C. FT-IR (KBr, v cm⁻¹): 3440 (OH), 3331, 3202 (NH). ¹H NMR (400 MHz, DMSO-d₆, δ ppm): 7.20-8.38 (m, 11H, Ar-H), 9.97 (s, 1H, OH), 12.02 (s, 2H, NH₂). MS (EI, m/z (%)): 372 (M⁺+2, 22). Anal. calcld. for C₂₂H₁₅N₃O: C, 71.33; H, 3.81; N, 7.76. Found: C, 71.35; H, 3.84; N, 7.59.

2.2.6. Synthesis of 6-(2-hydroxynaphthalen-1-yl)-2-oxo-4-phenyl-1,2-dihydropyridine-3-carbonitrile (12)

A mixture of compound 1 (0.01 mol), malononitrile (0.01 mol) in ethanol (30 mL) containing catalytic amount of piperidine was heated under reflux for 24 hrs. The reaction mixture was allowed to cool and poured into crushed ice then acidified with HCl. The separated solid was filtered, washed with water and crystallized from ethanol (Scheme 2). Color: Pale yellow. Yield: 76 %. M.p.: 146-148 °C. FT-IR (KBr, v cm⁻¹): 3408 (OH), 3400 (NH), 3060 (CH-Arom.), 2192 (C≡N), 1636 (C=O). ¹H NMR (300 MHz, DMSO-d₆, δ ppm): 7.09 (s, 1H, =CH), 7.20-8.39 (m, 11H, Ar-H), 9.70 (s, 1H, OH), 9.98 (s, 1H, OH). MS (EI, m/z (%)): 338 (M⁺, 17). Anal. calcld. for C₂₂H₁₈N₃O: C, 78.09; H, 4.17; N, 8.28. Found: C, 78.04; H, 4.13; N, 8.25.

2.2.7. Synthesis of 6-(2-hydroxynaphthalen-1-yl)-2-oxo-4-phenyl-2H-pyran-3-carbonitrile (14)

A mixture of compound 1 (0.01 mol), ethylcyclooctadecane in ethanol (30 mL) containing catalytic amount of piperidine was heated under reflux for 24 hrs. The reaction mixture was allowed to cool and poured into crushed ice then acidified with HCl. The separated solid was filtered, washed with water and crystallized from the ethanol (Scheme 2). Color: Pale yellow. Yield: 83 %. M.p.: 160-162 °C. FT-IR (KBr, v cm⁻¹): 3450 (OH), 3062 (CH-Arom.), 2196 (C≡N), 1658 (C=O). ¹H NMR (400 MHz, DMSO-d₆, δ ppm): 6.92-8.38 (m, 12H, Ar-H), 9.20 (s, 1H, OH). MS (EI, m/z (%)): 339 (M⁺, 27). Anal. calcld. for C₂₂H₁₈N₂O: C, 77.87; H, 3.86; N, 6.13. Found: C, 77.83; H, 3.83; N, 6.10.

2.2.8. General procedure for preparation of pyrano-3-carbonitrile derivatives (19a-d)

A mixture of compound 1 (0.01 mol) and aryldine malononitrile 15a-d (0.01 mol) in ethanol (40 mL) containing catalytic amount of piperidine (1.2 mL) was refluxed for 6 hrs. The reaction mixture was allowed to cool and poured in to cold water (30 mL) and acidified with HCl (pH = 3). The solid product was collected and crystallized from ethanol to give compound 19a-d (Scheme 3).
2-Amino-5-(2-hydroxy-1-naphthoyl)-4,6-diphenyl-4H-pyran-3-carbonitrile (19a): Color: Brown. Yield: 81 %. M.p.: 168-170 °C. FT-IR (KBr, cm⁻¹): 3448 (OH), 3420, 3400 (NH), 3064 (C-H Arom.), 2932 (CH Aliph.), 2197 (C≡N), 1640 (C=O). 1H NMR (400 MHz, DMSO-d₆, δ ppm): 3.83 (s, 3H, OCH₃), 4.40 (hump, 1H, 4H-pyran), 7.07-8.29 (m, 17H, Ar-H + NH₂), 9.93 (s, 1H, OH). MS (EI, m/z (%)): 459 (M⁺, 50). Anal. calcd. for C₂₉H₁₈N₂O₂S: C, 75.96; H, 3.96; N, 6.11. Found: C, 75.93; H, 3.90; N, 6.10%.

A mixture of compound 1 (0.01 mol) and arylidene cyanohydrin derivatives 20a-c (0.01 mol) in ethanol with catalytic amount of piperidine was heated under reflux for 10 hrs. The reaction mixture was allowed to cool and poured into crushed ice then acidified with HCl. The separated solid was filtered, washed with water and crystallized from ethanol to give compound 24a-c (Scheme 3).

2-Amino-5-(2-hydroxy-1-naphthoyl)-4,6-diphenyl-4H-pyran-3-carbonitrile (19b): Color: Pale yellow. Yield: 85 %. M.p.: 216-218 °C. FT-IR (KBr, cm⁻¹): 3450 (OH), 3345, 3210 (NH), 2924 (C-H Arom.), 2193 (C≡N), 1624 (C=O). 1H NMR (400 MHz, DMSO-d₆, δ ppm): 3.83 (s, 3H, OCH₃), 4.40 (hump, 1H, 4H-pyran), 7.07-8.29 (m, 17H, Ar-H+NH₂), 9.93 (s, 1H, OH). MS (EI, m/z (%)): 474 (M⁺, 20). Anal. calcd. for C₃₀H₂₁N₂O₃: C, 75.94; H, 4.67; N, 5.90. Found: C, 75.90; H, 4.63; N, 5.88%.

2-Amino-5-(2-hydroxy-1-naphthoyl)-4,6-diphenyl-4H-pyran-3-carbonitrile (19c): Color: Yellow. Yield: 76 %. M.p.: 173-175 °C. FT-IR (KBr, cm⁻¹): 3434 (OH), 3400 (NH), 3071 (C-H Arom.), 2189 (C≡N), 1634 (C=O). 1H NMR (300 MHz, DMSO-d₆, δ ppm): 7.58-8.36 (m, 17H, Ar-H+NH₂), 9.96 (s, 1H, OH). MS (EI, m/z (%)): 459 (M⁺+1), 50. Anal. calcd. for C₃₀H₁₉N₂O₂: C, 75.96; H, 3.96; N, 6.11. Found: C, 75.93; H, 3.90; N, 6.10%.

2.2.9. General procedure for preparation of dihydropyridine thion derivatives (24a-c)

A mixture of compound 1 (0.01 mol) and arylidene cyanohydrin derivatives 20a-c (0.01 mol) in ethanol with catalytic amount of piperidine was heated under reflux for 10 hrs. The reaction mixture was allowed to cool and poured into crushed ice then acidified with HCl. The separated solid was filtered, washed with water and crystallized from ethanol to give compound 24a-c (Scheme 3).

3-(2-Hydroxy-1-naphthoyl)-4,6-diphenyl-2-thioxo-1,2-dihydropyridine-3-carbonitrile (24a): Color: Yellow. Yield: 76 %. M.p.: 173-175 °C. FT-IR (KBr, cm⁻¹): 3434 (OH), 3400 (NH), 3071 (C-H Arom.), 2189 (C≡N), 1634 (C=O). 1H NMR (300 MHz, DMSO-d₆, δ ppm): 7.58-8.36 (m, 17H, Ar-H+NH₂), 9.96 (s, 1H, OH). MS (EI, m/z (%)): 459 (M⁺+1), 50. Anal. calcd. for C₃₀H₁₉N₂O₂S: C, 75.96; H, 3.96; N, 6.11. Found: C, 75.93; H, 3.90; N, 6.10%.

4-(4-Chlorophenyl)-5-(2-hydroxy-1-naphthoyl)-6-phenyl-2-thioxo-1,2-dihydropyridine-3-carbonitrile (24b): Color: Yellow. Yield: 70 %. M.p.: 173-175 °C. FT-IR (KBr, cm⁻¹): 3434 (OH), 3433 (NH), 3070 (C-H Arom.), 2193 (C≡N), 1634 (C=O). 1H NMR (400 MHz, DMSO-d₆, δ ppm): 7.15-8.32 (m, 16H, Ar-H+NH₂), 9.94 (s, 1H, OH). MS (EI, m/z (%)): 494 ([M⁺+2], 5). Anal. calcd. for C₃₀H₂₁C₂N₂O₃S: C, 70.66; H, 3.48; N, 5.68. Found: C, 70.60; H, 3.44; N, 5.69%.
5-(2-Hydroxy-1-naphthoyl)-4-(4-methoxyphenyl)-6-phenyl-2-thioxo-1,2-dihydropyridine-3-carbonitrile (24c): Color: Yellow. Yield: 69%. M.p.: 178-180 °C. FT-IR (KBr, v, cm\(^{-1}\)): 3408 (OH), 3400 (NH), 3072 (C–H Arom.), 2924 (CH Aliph.), 2190 (C≡N), 1634 (C=O). \(\delta\) ppm: 3.90 (s, 3H, OCH\(_3\)), 7.16-8.33 (m, 16H, Ar–H + NH), 9.95 (s, 1H, OH). MS (EI, m/z (%)): 488 (M\(^+\)), 12. Anal. calcd. for C\(_{30}\)H\(_{20}\)N\(_2\)O\(_3\)S: C, 73.75; H, 4.13; N, 5.73. Found: C, 73.77; H, 4.15; N, 5.77%.

2.2.10. General procedure for preparation of compounds (27a-d)

To a stirred cold solution of aryldiazonium chlorides 25a-d (0.01 mol, prepared by treating aniline derivatives (0.01 mol) with sodium nitrite (0.01 mol) in HCl ethanol (30 mL) and catalytic sodium acetate, the active methylene reagent 1 was added gradually. The stirring was continued for two hrs. The solid product so formed was filtered off, washed with water several times, dried and crystallized from ethanol to give compound 27a-d (Scheme 4).

1-(2-Hydroxynaphthalen-1-yl)-3-phenyl-2-(2-phenylhydrazono)propane-1,3-dione (27a): Color: Red. Yield: 88%. M.p.: 156-158 °C. FT-IR (KBr, v, cm\(^{-1}\)): 3387 (OH), 3300 (NH), 3063 (C–H Arom.), 1743, 1634 (2C=O). \(\delta\) ppm: 7.60-8.37 (m, 17H, Ar–H + NH), 9.97 (s, 1H, OH). MS (EI, m/z (%)): 394 (M\(^+\)), 55. Anal. calcd. for C\(_{25}\)H\(_{18}\)N\(_2\)O\(_3\): C, 76.13; H, 4.60; N, 7.10. Found: C, 76.15; H, 4.63; N, 7.13%.

2-(2-(4-Chlorophenyl)hydrazono)-1-(2-hydroxynaphthalen-1-yl)-3-phenylpropene-1,3-dione (27b): Color: Orange.
1-(2-Hydroxynaphthalen-1-yl)-2-(2-(4-methoxyphenyl) hydrazono)-3-phenylpropane-1,3-dione (27c): Color: Red. Yield: 79%. M.p.: 158-160 °C. FT-IR (KBr, v cm⁻¹): 3387 (OH), 1734, 1634 (C=O). 1H NMR (400 MHz, DMSO-d₆, δ ppm): 7.12-8.70 (m, 16H, Ar-H + NH), 9.97 (s, 1H, OH). MS (EI, m/z [%]): 424 (M⁺, 8). Anal. calcld. for C₂₆H₂₀N₂O₃: C, 73.58; H, 4.74; N, 6.61.

2-(2-Hydroxynaphthalen-1-yl)-2-(2-(p-tolylhydrazono) no)propane-1,3-dione (27d): Color: Red. Yield: 73%. M.p.: 170-172 °C. FT-IR (KBr, v cm⁻¹): 3437 (OH), 3400 (NH), 3072 (C-H Arom.), 2929 (CH Aliph.). MS (EI, m/z ppm): 6.89-8.36 (m, 16H, Ar-H + NH), 9.93 (s, 1H, OH). MS (EI, m/z [%]): 409 (M⁺+1, 17). Anal. calcld. for C₂₆H₂₀N₂O₃: C, 76.46; H, 4.94; N, 6.86.

2.2.11. General procedure for preparation of dihydro pyridazine derivatives (30a-d)

A mixture of compounds 27a-d (0.001 mole), ammonium acetate (1 g) and malononitrile (0.001 mole) was fused in domestic microwave oven for 3 minutes. The solid precipitate so formed was treated with ethanol and filtered out and crystallized from ethanol to give compound 30a-d (Scheme 4).

6-(2-Hydroxy-1-naphthoyl)-3-imino-2-(4-methoxyphenyl)-5-phenyl-2,3-dihydropyridazine-4-carbonitrile (30a): Color: Brown. Yield: 87%. M.p.: 184-186 °C. FT-IR (KBr, v cm⁻¹): 3385 (OH), 3300 (NH), 3071 (CH Arom.), 2924 (CH Aliph.), 2913 (C≡N), 1635 (C=O). 1H NMR (400 MHz, DMSO-d₆, δ ppm): 1.06 (s, 3H, CH₃), 7.17-8.33 (m, 16H, Ar-H + NH), 9.95 (s, 1H, OH). MS (EI, m/z [%]): 456 (M⁺+7, 15). Anal. calcld. for C₂₈H₁₇ClN₄O₂: C, 76.30; H, 4.42; N, 12.27. Found: C, 76.33; H, 4.45; N, 12.29.

2.2.12. General procedure for preparation of pyrazol derivatives (33a-d)

A mixture of compound 4a-d (0.01 mol) and hydrazine hydrate or phenyl hydrazine (0.01 mol) in ethanol (30 mL) was heated under reflux for 12 hrs. The reaction mixture was allowed to cool and poured into crushed ice. The separated solid was filtered, washed with water and crystallized from dioxane to give compound 33a-d (Scheme 5).

(5-(4-Chlorophenyl)-3-phenyl-1H-pyrazol-4-yl) (2-hydroxy naphthalen-1-yl)methanone (33a): Color: Pale yellow. Yield: 68%. M.p.: 186-190 °C. FT-IR (KBr, v cm⁻¹): 3418 (OH), 3204 (NH), 3051 (C-H Arom.), 1618 (C=O). 1H NMR (400 MHz, DMSO-d₆, δ ppm): 6.83-8.08 (m, 15H, Ar-H), 9.97 (s, 1H, OH), 12.93 (s, 1H, NH). MS (EI, m/z [%]): 426 (M⁺+2, 15). Anal. calcld. for C₂₉H₂₁ClN₂O: C, 75.50; H, 4.03; N, 6.59. Found: C, 75.52; H, 4.08; N, 6.60.

(2-Hydroxynaphthalen-1-yl) (5-(4-hydroxyphenyl)-3-phenyl 1H-pyrazol-4-yl)methanone (33b): Color: Brown. Yield: 72%. M.p.: 182-184 °C. FT-IR (KBr, v cm⁻¹): 3446 (OH), 3205 (NH), 3051 (C-H Arom.), 1618 (C=O). 1H NMR (400 MHz, DMSO-d₆, δ ppm): 6.88-8.11 (m, 15H, Ar-H), 10.03 (s, 1H, OH), 12.92 (s, 1H, NH), 13.58 (s, 1H, NH). MS (EI, m/z [%]): 408 (M⁺+2, 10). Anal. calcld. for C₂₉H₂₂N₂O: C, 76.83; H, 4.46; N, 6.89. Found: C, 76.85; H, 4.49; N, 6.91.

(5-(4-Chlorophenyl)-1,3-diphenyl1H-pyrazol-4-yl) (2-hydro xynaphthalen-1-yl)methanone (33c): Color: Pale yellow. Yield: 80%. M.p.: 190-192 °C.
FT-IR (KBr, v, cm⁻¹): 3386 (OH), 3063 (C-H Arom.), 1635 (C=O). ¹H NMR (400 MHz, DMSO-d₆, δ, ppm): 7.18-8.25 (m, 8H, Ar-H), 9.94 (s, 1H, OH). MS (EI, m/z (%)): 502 (M⁺*2, 4). Anal. calcd. for C₂₃H₂₁ClN₂O₂: C, 76.72; H, 4.23; N, 5.59. Found: C, 76.74; H, 4.23; N, 5.61%.

(2-Hydroxynaphthalen-1-yl) (5-(4-hydroxyphenyl)-1-di phenyl-1H-pyrazol-4-yl)methanone (33d): Color: Pale yellow. Yield: 72%. M.p.: 194-196 °C. FT-IR (KBr, v, cm⁻¹): 3450 (OH), 3056 (CH, Arom.). ¹H NMR (400 MHz, DMSO-d₆, δ, ppm): 6.67-8.39 (m, 20H, Ar-H), 9.96 (s, 1H, OH), 9.98 (s, 1H, OH). MS (EI, m/z (%)): 482 (M⁺, 18). Anal. calcd. for C₂₂H₂₀N₂O₂: C, 79.65; H, 4.60; N, 5.81. Found: C, 79.64; H, 4.58; N, 5.80%.

2.2.13. General procedure for preparation of isoxazole derivatives (34a,b)

A mixture of compound 4bd (0.01 mol), hydroxymethyl hydrochloride in glacial acetic acid (30 mL) containing anhydrous sodium acetate (1 g) was heated under reflux for 24 hrs. The reaction mixture was allowed to cool and poured into cold water (60 mL). The separated solid was filtered and crystallized from ethanol to give compound 34a,b (Scheme 5).

(5-(4-Chlorophenyl)-3-phenylisoxazol-4-yl)(2-hydroxy napthalen-1-yl)methanone (34a): Color: Pale yellow. Yield: 71%. M.p.: 158-160 °C. FT-IR (KBr, v, cm⁻¹): 3447 (OH), 3058 (C-H Arom.). ¹H NMR (400 MHz, DMSO-d₆, δ, ppm): 7.16-8.33 (m, 15H, Ar-H), 9.95 (s, 1H, OH). MS (EI, m/z (%)): 427 (M⁺*2, 11). Anal. calcd. for C₂₀H₁₆ClN₅O₂: C, 73.33; H, 3.79; N, 3.29. Found: C, 73.30; H, 3.74; N, 3.27%.

(2-Hydroxynaphthalen-1-yl) (5-(4-hydroxyphenyl)-3-phenyl isoxazol-4-yl)methanone (34b): Color: Pale yellow. Yield: 69%. M.p.: 163-165 °C. FT-IR (KBr, v, cm⁻¹): 3446 (OH), 3060 (C-H Arom.). ¹H NMR (300 MHz, DMSO-d₆, δ, ppm): 7.58-8.36 (m, 15H, Ar-H), 9.94 (s, 1H, OH), 9.97 (s, 1H, OH). MS (EI, m/z (%)): 407 (M⁺, 3). Anal. calcd. for C₂₀H₁₈N₅O₂: C, 76.65; H, 4.21; N, 3.44. Found: C, 76.64; H, 4.23; N, 3.45%.

2.2.14. Synthesis of 2-(ethoxymethylene)-1-(2-hydroxy napthalen-1-yl)-3-phenylpropane-1,3-dione (35)

A mixture of compound 1 (0.01 mol) and triethoxymethane (3 mL) in acetic anhydride (10 mL) was heated under reflux for 6 hrs. The reaction mixture was allowed to cool. The separated solid was filtered, washed with ethanol and crystallized from ethanol (Scheme 6). Color: Brown. Yield: 53%. M.p.: 164-166 °C. FT-IR (KBr, v, cm⁻¹): 3383 (OH), 3068 (CH, Arom.). 2932-2852 (CH, Aliph.), 1739, 1635 (2CO). ¹H NMR (400 MHz, DMSO-d₆, δ, ppm): 1.11 (t, 3H, CH₃), 3.56 (s, 6H, 2CH₃), 3.60 (s, 1H, CH-olefinic), 7.17-8.04 (m, 11H, Ar-H), 9.97 (s, 1H, OH). MS (EI, m/z (%)): 347 (M⁺*1, 13). Anal. calcd. for C₂₂H₂₁O₄: C, 76.29; H, 5.24; O, 18.43%.

2.2.15. Synthesis of 2-((dimethyloximinomethylene)-1-(2 hydroxynaphthalen-1-yl)-3-phenylpropane-1,3-dione (36)

A mixture of compound 1 (0.01 mol) and DMF-DMA (0.01 mol) in dioxane (30 mL) was heated under reflux for 6 hrs. The reaction mixture was allowed to cool. The separated solid was filtered, washed with ethanol and crystallized from ethanol (Scheme 6). Color: Pale yellow. Yield: 57%. M.p.: 158-160 °C. FT-IR (KBr, v, cm⁻¹): 3437 (OH), 3058 (CH, Arom.), 2960-2852 (CH, Aliph.). 1630 (CO). ¹H NMR (300 MHz, DMSO-d₆, δ, ppm): 3.56 (s, 6H, 2CH₃), 7.17 (s, 1H, CH-olefinic), 7.58-8.35 (m, 11H, Ar-H), 9.96 (s, 1H, OH). MS (EI, m/z (%)): 345 (M⁺, 20). Anal. calcd. for C₂₂H₁₈N₂O₃: C, 76.50; H, 5.54; O, 4.11%.

2.2.16. Synthesis of 3-(hydroxymino)-1-(2-hydroxy napthalen-1-yl)-3-phenylpropan-1-one (37)

A mixture of compound 1 (0.01 mol), hydroxylamine hydrochloride in glacial acetic acid (30 mL) containing anhydrous sodium acetate (1 g) was heated under reflux for 24 hrs. The reaction mixture was allowed to cool and poured into cold water (60 mL).
The separated solid was filtered and crystallized from ethanol (Scheme 6). Color: Pale brown. Yield: 76%. M.p.: 145-147 °C. FT-IR (KBr, ν, cm⁻¹): 3427 (OH), 3079 (C-H Arom.), 2925 (CH Aliph.), 1638 (C=O). ¹H NMR (300 MHz, DMSO-d₆, δ, ppm): 4.40 (s, 2H, CH₂), 7.18-8.35 (m, 12H, Ar-H + OH), 9.96 (s, 1H, OH), MS (EI, m/z (%)): 305 (M⁺, 45). Anal. calc. for C₁₂H₁₂NO₅: C, 74.74; H, 4.95; N, 4.59. Found: C, 74.75; H, 4.96; N, 4.61%.

2.3. Pharmacology

2.3.1. In-vitro antimicrobial activity

The newly synthesized compounds and its derivatives have been screened for antibacterial activity against some species of Gram-positive bacteria (Staphylococcus aureus and Bacillus subtilis) and Gram-negative bacteria (Escherichia coli and Pseudomonas aeruginosa). Anti-fungal activities of the compounds were tested against yeast and mycelial fungi; Candida albicans and Aspergillus flavus, respectively. Each tested compound was dissolved in DMSO making a solution concentration of 1.00 mg/mL and loaded separately in paper discs of Whatman filter paper with equal diameter size (10 mm). Paper discs were sterilized in an autoclave. The paper discs loaded with the desired concentration of the complex solution, were placed aseptically in the petri dishes containing nutrient agar medium (agar 20 g + beef extract 3 g + peptone 5 g) inoculated with Staphylococcus aureus, Bacillus subtilis, Escherichia coli, Pseudomonas aeruginosa, Candida albicans and Aspergillus flavus. The petri dishes were incubated at 36 °C. The inhibition zones were recorded after 24 hrs of incubation in case of bacteria and yeast and after 5-6 days in case of mycelial fungi. Each treatment was replicated three times [32]. Ampicillin and clotrimazole, were used as a common standard antibiotic and antifungal agents, respectively. They prepared using the same procedure as above at the same concentration and solvents. The % activity index was calculated for the tested compounds by using the given formula in equation (1).

\[
% \text{Activity Index} = \frac{\text{Zone of inhibition by test compound (diameter)}}{\text{Zone of inhibition by standard (diameter)}} \times 100
\]  

(1)

2.3.2. Minimum inhibitory concentration measurement

The minimum inhibitory concentration (MIC) was determined using the disc diffusion technique by preparing discs containing 1.9-1000 µg/mL of each compound against Gram-positive Staphylococcus aureus, Bacillus subtilis and Gram-negative Escherichia coli, Pseudomonas aeruginosa. The anti-fungal activities of the compounds were tested against two fungi Candida albicans and Aspergillus flavus. The twofold dilutions of the solution were prepared. The microorganism suspensions at 10 CFU/mL (colony forming unit/mL) concentrations were inoculated to the corresponding wells. The plates were incubated at 36 °C for 24 hrs for the bacteria. The standard antibiotic ampicillin and antifungal clotrimazole was also recorded using the same procedure as above at the same concentration and solvents. At the end of the incubation period, the minimum inhibitory concentrations (MIC) values were recorded as the lowest concentration of the substance that had no visible turbidity [33,34]. Control experiments with DMSO and uninoculated media were run parallel to the test compounds under the same condition.

3. Results and discussion

3.1. Synthesis

In continuation of this work and as a part of our biological chemistry program [35-38], we reported here the utility of 1-(2-hydroxynaphthalen-1-yl)-3-phenylpropane-1,3-dione (1) in the synthesis of unique heterocyclic of expected biological interest. Thus, β-diketone (1) is prepared in a quantitative yield in a domestic microwave oven from the reaction of 2-naphthol and ethylbenzoylacetate. β-diketone (1) underwent several chemical transformations aiming at exploring its synthetic potentiality. Thus, β-diketone (1) reacted with aryl aldehydes 3a-d to afford the condensation products 4a-d (Scheme 1). Structures of compounds 4a-d were established using their elemental and spectral data. Compounds 4a-d are allowed to react with thiourea to afford tetrahydropyrimidine thiones 5a-d [39] (Scheme 1). Structures of tetrahydro pyrimidinethiones 5a-d were established using their elemental and spectral data. For example, the IR spectrum of compound 5a revealed an absorption band at 3447 cm⁻¹ corresponding to OH group and a band at 3400 cm⁻¹ corresponding to NH group and a band at 1637 cm⁻¹ corresponding to carbonyl group. The ¹H NMR of the same product revealed to the presence of a signal at δ 4.35 ppm corresponding to aliphatic proton at
pyridine ring, a multiplet signal at δ 7.11-8.37 ppm corresponding to Ar-Hand amino function and a signal at δ 9.93 ppm corresponding to OH function. The mass data of the same product is in accordance with the proposed structure. Furthermore, the behavior of β-diketone (1) toward active methylene was also investigated. Thus, β-diketone (1) reacted with hydrazine and phenylhydrazine to afford substituted pyrazoles 7a,b. Establishing structure pyrazoles 7a,b was based on their elemental and spectral data [40,41] (Scheme 1). In addition to this the behavior of β-diketone (1) toward mixture of active methylene and elemental sulfur was also investigated. Thus, β-diketone (1) reacted with malononitrile and elemental sulfur to afford the thiophene derivative 10 (Scheme 1). The formation of thiophene 10 from the reaction of diketone (1) and malononitrile is believed to be formed via initial addition of malononitrile on the double bond system of carbonyl group of diketone 1 and subsequent elimination of water to afford the non-isolable intermediate 8. The intermediate 8 reacted with elemental sulfur to afford thiophene 10 via intermediacy of compound 9 (Scheme 1). Establishing structure thiophene 10 was based on its elemental analysis and spectral data. The IR spectrum of compound 10 revealed an absorption band at 3440 cm⁻¹ corresponding to OH group and a band at 2212 cm⁻¹ corresponding to CN group and a band at 1638 cm⁻¹ corresponding to carbonyl group. The mass spectrum of the same product is in accordance with the proposed structure.

The behavior of β-diketone (1) toward active methylene reagent was also investigated. Thus, β-diketone reacted with malononitrile to afford the dihydropyridine derivative 12 (Scheme 2). The formation of dihydropyridine derivative 12 from the reaction of diketone (1) and malononitrile is believed to be formed via initial addition of malononitrile on the double bond system of carbonyl group of diketone and subsequent elimination of water to afford the non-isolable intermediate 8. The intermediate 8 tautomerizes and cyclizes under the same reaction condition to afford the non-isolable intermediate 11 which underwent Dimuth rearrangement to afford compound 12 (Scheme 2). Establishing structure 12 was based on its elemental analysis and spectral data. The IR spectrum of compound 12 revealed an absorption band at 2192 cm⁻¹ corresponding to CN group and a band at 1636 cm⁻¹ corresponding to carbonyl group. The mass spectrum of the same product is in accordance with the proposed structure. Thus, it revealed a molecular ion peak at 338 m/z (M⁺) and a number of fragments agree with the proposed structure. The product obtained from the reaction of β-diketone with malononitrile prompted us to investigate further the behavior of β-diketone with ethylcyanoacetate. Thus, when compound 1 is allowed to react with ethylcyanoacetate under the same reaction condition afforded the pyridazine derivative 14 whose structure was based on its spectral analysis. The formation of pyrazine derivative 14 is believed to be formed via initial addition of ethylcyanoacetate on the double bond system of compound 1 and subsequent elimination of water to afford the non-isolable intermediate 13. The intermediate 13 tautomerizes and cyclizes under the same reaction condition to afford the pyrazine derivative 14 (Scheme 2).

On the other hand the behavior of β-diketone (1) toward some electrophilic reagents was also investigated. Thus, β-diketone reacted with arylidinemalononitrile 15a-d under reflux to afford the pyridine derivatives 19a-d (Scheme 3). The formation of pyridine derivatives is believed to be formed via initial addition of active methylene of compound 1 on the double bond system of arylidinemalononitrile to afford the acyclic intermediate 16 which tautomerizes into compound 17 that cyclizes under the same reaction condition to afford compound 18 that tautomerizes into pyrene derivative 19 (Scheme 3). Establishing structure 19a-d were based on their elemental and spectral analysis. Similarly, β-diketone reacted with arylidine cyanothioacetamide 20a-c to afford the dihydropyridinethione derivatives 24a-c (Scheme 3). Establishing structure 24a-c were based on their elemental analysis and spectral data.

Coupling of β-diketone (1) with aryl diazonium salts 25a-d in ethanol containing sodium acetate afforded the hydrazide form compound 27a-d based on spectral data. Compounds 27a-d reacted with malononitrile to afford pyridazine derivatives 30a-d. Establishing structure 30 was based on its elemental and spectral data. For example, the IR spectrum of compound 30c revealed the presence of a band at 3382 cm⁻¹ corresponding to OH group, a band at 3300 cm⁻¹ corresponding to NH group, a band at 2193 cm⁻¹ corresponding to CN group and a band at 1634 cm⁻¹ corresponding to C=O group. 1H NMR of the same product revealed the presence of a signal at δ 3.83 ppm corresponding to OCH₃, a multiplet signal at δ 7.13-8.30 ppm corresponding to Ar-Hand amino function and a singlet signal at δ 9.93 ppm corresponding to OH group. The mass spectrum of the same product is in accordance with the proposed structure. Thus, it revealed a molecular ion peak at 472 m/z (M⁺) beside a number of fragments agree with the proposed structure. Formation of pyridazine derivatives from the reaction of malononitrile and the hydrazo compounds 27 is believed to be formed via initial addition of malononitrile on the double bond of carbonyl group of compound 27 to afford the acyclic intermediate 28, that cyclizes and loses water to give compound 30 under the same reaction condition (Scheme 4).

Once more the behavior of nitrogen nucleophile toward β-diketones 4b,d was also investigated. Thus, when β-diketones 4b,d are allowed to react with hydrazine and phenyl hydrazine pyrazoles derivative 33a-d were obtained via intermediacy of compound 31 and 32 (Scheme 5). Establishing structures of compound 33a-d were based on their elemental and spectral data. Similarly, β-diketones 4b,d reacted with hydroxyl amine hydrochloride to afford isoxazole derivative 34 (Scheme 5). Establishing structures of compound 34a,b were based on their elemental and spectral data.

Refuxing of compound 1 with triethylthiourformate in the presence of acetic anhydride yielded 2-(ethoxymethylenyl)-1-(2-hydroxynaphthalen-1-yl)-3-phenylpropane-1,3-dione, 35. The IR spectrum of compound 35 showed bands at 3383 (OH), 3068 (CH-arom), 2932-2852 (CH-alph) and 1738, 1635 (CO) cm⁻¹. The 1H NMR spectrum of compound 35 in DMSO-d₆ revealed signals at δ 1.11 (t, 3H, CH₃), 4.35 (q, 2H, CH₂), 6.90 (s, 1H, CH-olefinic) and 9.97 (s, 1H, OH). β-diketone 1 react with dimethylformamidimethyl-acetal (DMF-DMA) to yield 2-(dimethylamino) methylene)-1-(2-hydroxynaphthalen-1-yl)-3-phenylpropane-1,3-dione, 36 in excellent yield. The structure of the latter compound was established on the basis of its elemental analysis and spectral data. For example, its 1H NMR spectrum displayed three signals at δ 3.56, 7.17 and 9.96 ppm attributed to magnetically nonequivalent N(CH₃) group, CH-olefinic and OH proton respectively. In addition to this a multiple signals at δ 7.58-8.35 ppm corresponding to aromatic hydrogen atoms. Also hydroxylamine hydrochloride reacted with β-diketone (1) in refluxing glacial acetic acid containing anhydrous sodium acetate to afford 3-(hydroxymimino)-1-(2-hydroxy naphthalen-1-yl)-3-phenylpropan-1-one, 37 in excellent yield (Scheme 6).

3.2. Pharmacology

The newly synthesized compounds have been tested for antibacterial activity against Gram-negative bacteria (Escherichia coli & Pseudomonas aeruginosa) and Gram-positive bacteria (Bacillus subtilis), and antifungal activity against yeast (Candida albicans) and myelial fungi (Aspergillus flavus) by the cup-plate method and agar diffusion disc method for determining MIC (Minimum inhibitory concentration).
Table 1. Antibacterial and antifungal activities of synthesized compounds *.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Gram negative bacteria (-ve)</th>
<th>Gram positive bacteria (+ve)</th>
<th>Fungal species</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>E. coli</td>
<td>P. aeruginosa</td>
<td>S. aureus</td>
</tr>
<tr>
<td></td>
<td>DIZ (mm)</td>
<td>% Activity (index)</td>
<td>DIZ (mm)</td>
</tr>
<tr>
<td>5b</td>
<td>3</td>
<td>14.3</td>
<td>8</td>
</tr>
<tr>
<td>19b</td>
<td>4</td>
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<td>10</td>
</tr>
<tr>
<td>27c</td>
<td>NA</td>
<td>-</td>
<td>NA</td>
</tr>
<tr>
<td>10</td>
<td>17</td>
<td>80.9</td>
<td>21</td>
</tr>
<tr>
<td>33a</td>
<td>13</td>
<td>61.9</td>
<td>17</td>
</tr>
<tr>
<td>19c</td>
<td>2</td>
<td>9.5</td>
<td>5</td>
</tr>
<tr>
<td>33d</td>
<td>6</td>
<td>28.6</td>
<td>11</td>
</tr>
<tr>
<td>33c</td>
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<td>52.4</td>
<td>16</td>
</tr>
<tr>
<td>1</td>
<td>7</td>
<td>33.3</td>
<td>13</td>
</tr>
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<td>5d</td>
<td>14</td>
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<td>19</td>
</tr>
<tr>
<td>4b</td>
<td>9</td>
<td>42.8</td>
<td>14</td>
</tr>
<tr>
<td>34a</td>
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<td>-</td>
<td>3</td>
</tr>
<tr>
<td>4c</td>
<td>10</td>
<td>47.6</td>
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<tr>
<td>34b</td>
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</tr>
<tr>
<td>34b</td>
<td>5</td>
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<td>12</td>
</tr>
<tr>
<td>36</td>
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<tr>
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<td>20</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>21</td>
<td>100</td>
<td>21</td>
</tr>
<tr>
<td>Clotrimazole</td>
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<td>-</td>
<td>NA</td>
</tr>
</tbody>
</table>

* NA: No activity; DIZ: Diameter of inhibition zone.

Table 2. Minimum inhibitory concentrations (MIC) for selected compounds *.

<table>
<thead>
<tr>
<th>Compounds</th>
<th>Minimum inhibitory concentration (MIC) of the synthesized compounds (µg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>E. coli</td>
</tr>
<tr>
<td>5b</td>
<td>750</td>
</tr>
<tr>
<td>19b</td>
<td>750</td>
</tr>
<tr>
<td>27c</td>
<td>NA</td>
</tr>
<tr>
<td>10</td>
<td>93.7</td>
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<tr>
<td>33a</td>
<td>187.5</td>
</tr>
<tr>
<td>19c</td>
<td>NA</td>
</tr>
<tr>
<td>33d</td>
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<td>33c</td>
<td>187.5</td>
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<td>36</td>
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</tr>
<tr>
<td>33b</td>
<td>125</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>125</td>
</tr>
<tr>
<td>Clotrimazole</td>
<td>NA</td>
</tr>
</tbody>
</table>

* NA: No activity.

Ampicillin and clotrimazole were used as standards for comparison of antibacterial and antifungal activity, respectively. Table 1 and 2 illustrated the results of antimicrobial and antifungal activity and its MIC.

The results which are illustrated in Table 1 showed that most of tested compounds were active against most of microorganisms used. Both of compound 24b and 36 showed no antibacterial or antifungal activity. On the other side each of compound 10 and 33b showed maximum antibacterial and antifungal activity. Compound 27c has no antibacterial activity against Gram-negative bacteria only, although it has broad spectrum antibacterial activity against Gram-positive bacteria and antifungal activity against C. albicans and A. flavus. On the other hands, compound 34a showed narrow spectrum antibacterial activity against P. aeruginosa (a Gram-negative bacteria) and S. aureus (a Gram-positive bacteria) and revealed no antibacterial activity against E. coli (a Gram negative bacteria) and B. subtilis (a Gram-positive bacteria), but in case of compound 19c it has no antibacterial activity against B. subtilis only and has narrow range spectrum as antibacterial agent against S. aureus, E. coli and P. aeruginosa with also small range spectrum antibacterial activity. All the other compounds (1, 4b, 4c, 5b, 5d, 19b, 33a, 33c, 33d, 34b) indicated wide range spectrum antibacterial and antifungal activity.

From Table 2, we observed that compounds 10, 5d, 33a, 33b and 33c showed the lowest minimum inhibitory concentrations (MIC) for most tested bacteria and fungi, while compounds 19b, 19c, 33c and 34b exhibited high concentrations of MIC as compared with standard antimicrobial agents used.

4. Conclusion

In conclusion, the results of the present study indicate that the 1-(2-hydroxynaphthalen-1-yl)-3-phenylpropane-1,3-dione (1) was used as an efficient precursor for the synthesis of new heterocycles with expected biological activities.

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References
