SYNTHESIS REACTIONS AND ANTIOXIDANT ACTIVITY OF SOME NEW HETEROCYCLES DERIVED FROM 2-ACETYLNAPHTHALENE

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ABSTRACT:

2-Methyl-4-(1-(naphthalen-2-yl)ethylidene)oxazol-5(4H)-one 2 was used as precursor for the preparation of some novel (1-(4-substituted)-2-methyl-4-(1-naphthalen-2-yl)ethylidene)-1H-imidazol-5(4H)-one derivatives 4a, b and other derivatives 3a,b, 5-12. Furthermore, the preparation of thieno[2,3-d]pyrimidin-4(3H)-one derivative 16, 17 and 4-iminothieno[2,3-d] pyrimidin-3-ylamine derivative 18, 19 is described starting from 2-aminothiophen-3-carbonitrile derivative 15a. Some of the prepared products revealed a promising antioxidant activity by using 1,1-diphenyl-2,2-picryl hydrazyl free radical (DPPH) method.

Keywords: Imidazoles, thienopyrimidines, Antioxidant activity.

INTRODUCTION:

For a long time heterocyclic compounds have constituted one of the largest areas of research in organic chemistry. Heterocyclic compounds are of particular importance as they are associated with a wide variety of physiological activities attributed to heterocyclic systems known today. Among different nitrogen heterocycles, the imidazole ring which acts as a constituent of several important natural products, including purine, histamine, histidine and nucleic acid. Imidazoles and their derivatives have demonstrated a diverse set of biological activities such as antibacterial (Maddila, et al., 2010; Kumari, et al., 2010; Rajasekaran, et al., 2010; Nanda, et al., 2010; Ingle, et al., 2011; Shailesh, et al., 2012), anticancer (Li, et al., 2003, Mahboobi, et al., 2006; Chuu, et al., 2007; Hait, et al. 2009; Kanthou, et al., 2009; De Ryckher, et al., 2009; Sanchila, et al., 2010; Wen-Tai, et al., 2010; Soroor, et al., 2012), anti-inflammatory (Achar, et al., 2010; Shailesh, et al., 2012), antitumor (Liberatore, et al., 2008), antioxidant (Maddila, et al., 2010; Rajasekaran, et al., 2010) activities. Also, prominent biological activities have been reported for fused thienopyrimidine derivatives (Hegab, et al., 2007; Shamrokh, et al., 2010; Marzouk, et al., 2011). In connection with our research program for the synthesis of different heterocyclic compounds, we describe here the synthesis of some new imidazole derivatives hopping to show promising antioxidant activity.

RESULTS AND DISCUSSION

The interaction of 2-acetylnaphthalene 1 with acetyl glycine in acetic anhydride and in the presence of fused sodium acetate effected cyclization and afforded the corresponding 2-methyl-4-(1-(naphthalen-2-yl)ethylidene)oxazol-5(4H)-one 2 (scheme 1). The structure of the oxazolinone derivative 2 was confirmed by elemental analysis and spectral data. The IR spectrum showed absorption band at 1668.9 cm\(^{-1}\) (C=O); moreover, \(^1\)H-NMR spectrum exhibited signals at \(\delta 2.05, 2.70\) ppm for two methyl groups and \(7.60-8.15\) for six aromatic protons, \(8.47\) (s, 1H, \(C\textsubscript{1}naphthyl\)) and its mass spectrum afforded a molecular ion peak M\(^+\) at m/z 251 (3.82%). The behaviour of oxazolinone derivative 2 towards some nucleophilic
reagents was discussed under different conditions, as well as its transformation into the corresponding imidazolinone derivatives. Thus, interaction of 2 with p-nitroaniline or p-chloroaniline in ethanol with boiling led to ring opening and gave the corresponding 2-acetamido-N-substituted-3-(naphthalen-2-y1)but-2-enamides 3a,b which underwent heterocyclization by heating with acetic acid in the presence fused sodium acetate and produced imidazolinone derivatives 4a,b in 70% yield (scheme 1). On the other hand, compound 4a,b could be obtained in one step and better yield by direct reaction of 2 with p-nitroaniline or p-chloroaniline under reflux in acetic acid and fused sodium acetate (89% yield) (scheme 1).

The structures of compounds 3 and 4 were deduced from elemental analysis and spectral data. IR spectra of 3 which showed absorption bands characteristic for 2NH groups while IR spectrum of 4 showed the absence of this absorption bands (c.f. exp.) Similarly, the reaction of oxazolinone 2 with secondary amines in ethanol or acetic acid led to ring opening to produce the corresponding acetamido compounds without transmitting into imidazolinone as in the case of primary amines. When compound 2 was treated with N,N-diethylylamine or morpholine in ethanol under reflux, the corresponding 2-acetamido-N,N-diethyl-3-(naphthalen-2-y1)but-2-enamide 5 and N-1-morphoilino-3-naphthalen-2-y1)-1-oxobut-2-en-2-yl)acetamide 6, were produced, respectively (scheme 1). The IR spectra of 5 and 6 showed characteristic absorption bands for (2C=O) and (NH) groups. Also 1HNMR spectra (δ, ppm) revealed signals at 1.01 (t, J=7.5Hz, 6H, 2CH3), 3.51 (q, J=7.5Hz, 4H, 2CH2) for compound 5 and for compound 6 revealed signals at 3.24-3.70 (m, 8H, 4CH2, morphilino) (c.f. exp.)
Also, the behaviour of oxazolinone ring towards binucleophile reagent such hydrazine hydrate and phenylenediamine was studied hoping to prepare different heterocyclic of five and six membered ring hoping to have good pharmacological activity. Thus, interaction of oxazolinone 2 with hydrazine hydrate in ethanol under stirring at room temperature caused ring opening to give the corresponding hydrazide derivative 7, while the product that isolated from the reaction of 2 with hydrazine hydrate in ethanol with boiling for 2h was formulated as the triazine derivative 8 (scheme 2). The structures of compounds 7 and 8 were deduced from elemental analysis and spectral data. The $^1$H-NMR spectrum of compound 7 (δ, ppm) revealed signals at 3.72 (br, 2H, NH; exchangeable with D$_2$O), while mass spectrum of compound 8 exhibited a molecular ion peak at m/z = 265 (18.67%) (c.f. exp.).

Moreover, interaction of oxazolinone 2 with p-phenylenediamine in ethanol consumed one mole of oxazolinone and produce 2-acetamido-N-(4-aminophenyl)-3-(naphthalen-2-yl)but-2-enamide 9 which under-went heterocyclization by heating with acetic acid in the presence fused sodium acetate and produced imidazolinone derivative 10 (scheme 2). The proposed structures of compounds 9 and 10 was confirmed by elemental analysis and spectral data (c.f. exp.). Treatment of the later compound with p-toluene sulphonyl chloride or p-chlorobenzaldehyde afforded the corresponding sulfonamide derivative 11 and the Schiff base 12, respectively. Inspection of the IR spectrum of the reaction product 11 revealed absorption bands characteristic for (NH), (C=O) groups at 3432, 1671 and (SO$_2$) group at 1187, 1361cm$^{-1}$; $^1$H-NMR spectrum showed signals (δ, ppm) at 1.22, 1.52, 2.57(3s, 9H, 3CH$_3$), and 7.25 (s, 1H, NH, exchangeable with D$_2$O), while for compound 12 the $^1$H-NMR spectrum revealed a signal at 9.83ppm characteristic for (–CH=N–) (c.f. exp.).
It was reported (Hessien, et al., 2009; Hafez, et al., 2010) that various activated nitriles and enaminonitriles were used as intermediates for the syntheses of thieno derivatives and thienopyrimidine derivatives. Thus, condensation of 2-acetyl naphthalene with malononitrile in ethanolic–piperidine solution under reflux gave the corresponding ethyldinemalononitrile derivative 13. IR spectrum showed sharp absorption bands at 2210 and 1589 characteristic for (2C≡N) group and (C=C), respectively and the MS spectrum showed a molecular ion peak at m/z = 218 (M⁺, 100%). Treatment of 13 with elemental sulfur under Gewald reaction conditions (Gewald, 1965) furnished 2-aminothiophene-3-carbonitrile derivatives 15a. The formation of compound 15a occurred via thiation of methyl group in compound 13 to give 14 as an intermediate followed by intramolecular cyclization (scheme 3). Compound 15a was also obtained directly by interaction of ketone 1 with a mixture of malononitrile and elemental sulfur in the presence of few drops of triethylamine. The obtained product 15a throughout the two pathways was checked by TLC and mixed m.p which showed no depression.

Similarly, when compound 1 was treated ethyl cyanoacetate and elemental sulfur under Gewald reaction conditions (Gewald, 1965) gave the corresponding ethyl-2-aminothiophen-3-carboxylate derivative 15b (scheme 3). The IR spectra showed absorption bands (υ, cm⁻¹) at 2206 (C≡N) and 3202 & 3322 (NH₂) groups for 15a while for 15b showed (C=O) at 1721 and NH₂ at 3200, 3321 (c.f. exp.)

The 4-pyrmidonone derivative was prepared by reacting compound 15a with formic acid under reflux to give derivative 16 (scheme 3). Product 16 was formed presumably via intermediacy of the corresponding oxazinimine derivative (Abdelrazek, et al., 1996; Hegab, et al., 2007) which then rearranged under the conditions of the reaction. On the other hand, when compound 15a was refluxed with triethyl orthoformate, it afforded derivative 17. When the ethanolic solution of the later compound was stirred at room temperature with hydrazine hydrate, it afforded 4-iminopyrimidin-3-ylamine derivative 18. the structures of compounds 16-18 were deduced from elemental analysis and spectral data. IR spectra showed the absence of cyano group for 16 and 18, while ¹H-NMR spectrum revealed signals characteristic for ethyl group for 17 (c.f. exp.). However, the pyrimidin-4-ylhydrazine derivative 19 was obtained by treatment of compound 17 with hydrazine hydrate under reflux (scheme 3). Also, compound 18 was isomerized to corresponding more stable 4-hydrazino derivative 19 upon reflux in ethanol in the presence of hydrazine hydrate. Actually, hydrazine hydrate acts as a base in this Dimroth type of rearrangement, which involves a sequence of ring opening and ring closure reaction (Mohamed, et al., 2005; Rashad, et al., 2005; Hegab et al., 2007).
Antioxidant activity.

**RESULTS:**

The provided compounds showed different antioxidant activity using 1,1-diphenyl-2,2-picryl hydrazyl free radical (DPPH) radical scavenging method compared to ascorbic acid standard as shown by the following table:
Table I. Antioxidant activity of some synthesized compounds

<table>
<thead>
<tr>
<th>Compound No.</th>
<th>DDPH radical scavenging Activity</th>
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<tbody>
<tr>
<td>3a</td>
<td>+</td>
</tr>
<tr>
<td>3b</td>
<td>+</td>
</tr>
<tr>
<td>5</td>
<td>+++</td>
</tr>
<tr>
<td>6</td>
<td>+</td>
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<tr>
<td>7</td>
<td>+</td>
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<tr>
<td>8</td>
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<td>9</td>
<td>+</td>
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<tr>
<td>10</td>
<td>+</td>
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<tr>
<td>11</td>
<td>+</td>
</tr>
<tr>
<td>12</td>
<td>+++</td>
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</table>

+ : Weak  
++ : Moderate  
+++ : Good  
++++ : Strong  
- : No activity

Comment: Qualitative analysis are recommended for the promising result.
Table II: Physical data of the new synthesized compounds

<table>
<thead>
<tr>
<th>Compd. No.</th>
<th>M.P.[°C]</th>
<th>Yield[%] solvent</th>
<th>Mol. Formula/Mol.wt.</th>
<th>(Calcd./Found)%</th>
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<td></td>
<td></td>
<td>C</td>
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<td>2</td>
<td>78-79</td>
<td>80</td>
<td>C_{16}H_{13}NO_{2}</td>
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<td>85</td>
<td>C_{22}H_{10}N_{2}O_{4}</td>
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<td>3b</td>
<td>200-202</td>
<td>80</td>
<td>C_{22}H_{16}ClN_{2}O_{2}</td>
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<td>C_{22}H_{17}ClN_{2}O</td>
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<td>C_{17}H_{15}NO_{2}S</td>
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<td>16</td>
<td>220-222</td>
<td>70</td>
<td>C_{16}H_{10}N_{2}OS</td>
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<tr>
<td>17</td>
<td>165-166</td>
<td>70</td>
<td>C_{18}H_{14}N_{2}OS</td>
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<tr>
<td>18</td>
<td>238</td>
<td>75</td>
<td>C_{16}H_{12}N_{2}S</td>
<td>292.36</td>
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<tr>
<td>19</td>
<td>&gt;260</td>
<td>70</td>
<td>C_{16}H_{12}N_{2}S</td>
<td>292.36</td>
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Solvent of crystallization: Pet.E: petroleum ether; B: Benzene; D: dioxan ; M: Methanol ; E: Ethanol
Experimental

Melting points were recorded on an electrothermal IA 9100 digital melting point apparatus and were uncorrected. IR spectra (νmax in cm⁻¹) were recorded on a Shimadzu FT-IR 8300 spectrophotometer using KBr pellets technique. ¹H-NMR and 1³C-NMR spectra were recorded using Bruker WM-400 spectrophotometer using DMSO-d₆ as the solvent and TMS as the internal reference (chemist shifts in ppm). The mass spectra were run at 70 eV with a finnigan SSQ7000 spectrophotometer (thermo-instrument system incorporation, USA) Elemental analysis were operated using Mario El Mentar apparatus, Organic microanalysis unit. Elemental analysis and the above spectra were measured the at National Research Center. Pharmacology was carried out in the Regional Center for Mycology & Biotechnology, Al-Azhar University.

2-Methyl-4-(1-naphthalen-2-yl)ethylidene)oxazol-5-(4H)-one (2).

A mixture of compound 1 (0.01 mol), acetyl glycine (0.01 mol) and 2 gm of fused sodium acetate in (10 mL) of acetic acid and 5 mL of acetic anhydride was refluxed for 1h. The reaction mixture was allowed to cool and then poured into cold water, the product obtained was filtered, dried and recrystallized to give 2. IR (cm⁻¹, ν): 1668.9 (C=O); ¹H-NMR (DMSO-d₆, δ, ppm) 2.05, 2.70 (2s, 6H, 2CH₃), 7.60-8.15 (m, 6H, ArH), 8.47 (s, 1H, C₁ArH); MS: m/z(%): 251[M⁺, 3.82].

General procedure for the preparation of the compounds 3a,b,5,6,8 and 9.

To a solution of oxazolion-5-one (0.01 mol) in ethanol (30 mL), the request amine (p-nitroaniline, p-chloroaniline, diethylamine, morpholine, hydrazine hydrate or p-aminoaniline (0.01 mol) was added. The reaction mixture was heated under reflux for 2h. after cooling precipitate was filtered, dried and recrystallized from the appropriate solvent to give 3a,b, 5,6,8 and 9, respectively

2-Acetamido-N-(4-nitrophenyl)-3-(naphthalen-2-yl)but-2-enamide (3a).

IR(cm⁻¹, ν): 1309, 1552 (NO₂) 1663 (br, 2C=O), 3354, 3472(2NH) groups; ¹H-NMR (CHCl₃, δ, ppm) 2.38, 2.67 (2s, 6H, 2CH₃), 6.59, 6.64 (2s, 2H, 2NH, exchangeable with D₂O), 7.25-8.07 (m,10H,ArH),8.3 (s, 1H, C₁ArH).

2-Acetamido-N-(4-chlorophenyl)-3-(naphthalen-2-yl)but-2-enamid (3b).

IR(cm⁻¹, ν): 1627 (br, 2C=O), 3308, 3476 (2NH) groups; MS: m/z (%)378: [M⁺, 27.11]

2-Acetamido-N,N-diethyl-3-(naphthalen-2-yl)but-2-enamide (5).

IR(cm⁻¹, ν): 1667 (br,2C=O), 3399, (NH + enaolic OH) groups; ¹H-NMR (DMSO-d₆, δ, ppm): 1.01 (t, J=7.5Hz, 6H, 2CH₃), 1.67, 2.72 (2s, 6H, 2CH₃), 3.51 (q, J=7.5 Hz, 4H, 2CH₂),7.60-8.01 (m, 6H, ArH), 8.31 (s, 1H, C₁ArH), 8.96 (s, 1H, NH, exchangeable with D₂O).

N-1-Morpholino-3-(naphthalen-2-yl)-1-oxobut-2-en-2-yl)acetamide (6).

IR(cm⁻¹, ν): 1669 (br, 2C=O), 3389(NH + enolic OH) groups; ¹HNMR (CHCl₃, δ ppm): 2.22, 2.54 (2s, 6H, 2CH₃), 3.24-3.70(m, 8H, 4CH₂, morpholino), 7.55-8.02 (m, 6H, ArH), 8.30 (s, 1H, C₁ArH). 9.43(br, 1H,NH, exchangeable with D₂O).

1,2-Dihydro-3-methyl-5-(1-(naphthalen-2-yl)ethylidene)-1,2,4-triazin-6(5H)-one (8).

IR(cm⁻¹, ν): 1676(C=O), 3123(2NH) groups; MS: m/z(%): 265 [M⁺, 18.67].
2-Acetamido-N-(4-aminophenyl)-3-naphthalen-2-ylbut-2-enamide (9).

IR (cm⁻¹, ν): 1664(br,2C=O), 3167, 3301, 3445(NH₂/NH₂) groups.  
¹H-NMR (CHCl₃, δ, ppm): 2.22, 2.46 (2s, 6H, 2CH₃), 3.48 (s, 2H, NH₂, D₂O exchangeable), 7.55-8.04 (m, 10H, ArH), 8.47 (s, 1H,C₁ArH), 9.44 (s, 2H, 2NH, exchangeable with D₂O).

General procedure for the preparation of the compounds 4a,b and 10.

Procedure 1:
A solution of compound 2 (0.01 mol) in acetic acid (20 mL) was treated with 1gm of fused sodium acetate and (0.01 mol) of (p-nitroaniline, p-chloroaniline, or p-aminoaniline). The mixture was heated for 3h, the solid obtained was collected and recrystallized to give 4a,b and 10.

Procedure 2:
A mixture of (compound 3a,3b, or 9)(0.01 mol) and 1gm of fused sodium acetate in acetic acid (20 mL) was refluxed for 2h. After cooling, the product formed was filtered off, air dried and recrystallized to give 4a,b and 10.

1-(4-Nitrophenyl)-2-methyl-4-(1-naphthalen-2-yl)ethylidene)-1H-imidazole-5(4H)-one (4a).

IR (cm⁻¹, ν): 1677 (C=O), 1619(C=N), 1505, 1332 (NO₂); ¹H-NMR (DMSO-d₆, δ, ppm): 1.86, 2.71 (2s, 6H, 2CH₃), 7.51-8.01 (m, 10H, ArH), 8.11(s, 1H, C₁naphthalene).

1-(4-Chlorophenyl)-2-methyl-4-(1-(naphthalen-2-yl)ethylidene)-1H-imidazol-5(4H)-one (4b).

IR (cm⁻¹, ν): 1629(C=N); 1672(C=O), MS: m/z (%) : 360[M⁺, 5.21].

1-(4-Aminophenyl)-2-methyl-4-(1-(naphthalen-2-yl)ethylidene)-1H-imidazol-5(4H)-one (10).

IR (cm⁻¹, ν) 1632(C=N), 1669 (C=O), 3180, 3305 (NH₂) groups; ¹H-NMR(DMSO-d₆, δ ppm): 1.66, 2.24(2s, 6H, 2CH₃), 7.25(s, 2H, NH₂, exchangeable with D₂O), 7.57-8.02 (m, 10H,ArH), 8.46(s, 1H, C₁naphthalene).

2-Acetamido-3-(naphthalen-2-yl)but-2-enehydrazide (7).

A mixture of oxazolinone 2 (0.01 mol) and hydrazine hydrate (0.015 mol) in ethanol (20 mL) was stirred at room temperature for 2h. The product obtained was filtered and recrystallized to give 7. IR (cm⁻¹, ν): 1691 (br, C=O), 3131, 3210, 3363(NH₂/NH₂) groups; ¹H-NMR (CHCl₃, δppm): 1.63, 2.73 (2s, 6H, 2CH₃), 3.72(s, 2H, NH₂, exchangeable with D₂O). 7.52-7.92 (m, 6H, ArH), 8.25 (s, 1H,C₁ naphthalene).9.25, 9.51(2s, 2H, 2NH, exchangeable with D₂O).

1-[4-(Tolysisulfonamido)phenyl]-2-methyl-4-(1-(naphthalen-2-yl)ethylidene)-1H-imidazol-5(4H)-one (11).

A mixture of compound 10 (0.01 mol) and p-toluene sulphonyl chloride (0.01 mol) in benzene/pyridine (20/10 mL) was heated under reflux for 3h. The reaction mixture was cooled and the product obtained was filtered off, dried and recrystallized to give 11.

IR (cm⁻¹, ν): 1187, 1361 (SO₂-N), 1620 (C=N) 1671 (C=O), 3432(NH₂) groups; ¹H-NMR (CHCl₃, δ, ppm), 1.22, 1.52, 2.57 (3s, 9H, 3CH₃), 7.25 (s, 1H, NH, exchangeable with D₂O), 7.55-7.97 (m, 14H, 3ArH), 8.47 (s,1H, C₁naphthalene).
1-[4-(4-Chlorobenzylidene)aminophenyl]-2-methyl-4-(1-(naphthalen-2-yl) ethylidene)-1H-imidazole-5(4H)-one 12.

To a solution of compound 10 (0.0 mol) in ethanol, 4-chloro-benzaldehyde (0.01 mol) was added followed by addition of 2-3 drops glacial acetic acid, then, the reaction mixture was heated under reflux temperature for 2h, the solid obtained after cooling was filtered, dried and recrystallized to give 12. IR (cm⁻¹, v): 1599(HC=NC=O), 1664(C=O) groups; H-NMR (DMSO-d₆, δ, ppm): 2.00, 2.71 (2H, 6H, 2CH₃), 7.46-7.98 (m, 14H, 3ArH), 8.67 (s, 1H, C₁ naphthalene), 9.83 (s, 1H, CH=NC=O).

1-(Naphthalen-2-yl)ethylidenemalononitrile 13.

A mixture of compound 10 (0.01 mol) and malononitrile was heated under refluxed in ethanolic piperidine for 2h. the solid obtained after cooling was filtered, dried and recrystallized to give 12. IR (cm⁻¹, v): 1589 (C=NC=O), 2210(C=O) groups; H-NMR (DMSO-d₆, δ, ppm): 2.00, 2.71 (2H, 6H, 2CH₃), 7.46-7.98 (m, 14H, 3ArH), 8.67 (s, 1H, C₁ naphthalene), 9.83 (s, 1H, CH=NC=O).

2-Amino-4-(naphthalen-2-yl)thiophen-3-carbonitrile (15a).

Procedure A:

A solution of ethylidenemalononitrile 13 (0.01 mol) and sulfur powder (0.01 mol) in ethanol (30 mL) containing few drops of piperidine, was refluxed for 3h. The solid product was filtered and recrystallized to give 15a.

Procedure B: For preparation of 15a and 15b:

A mixture of compound 1 (0.01 mol), malononitrile or ethyl cyanoacetate (0.01 mol) and sulfur powder (0.01 mol) in ethanol containing few drops of triethylamine for 2h, the solid formed after filtration and cooling was crystallized to give 15a and 15b respectively.

2-Amino-4-(naphthalen-2-yl)thiophen-3-carbonitrile (15a).

IR (cm⁻¹, v): 2206(C=O), 3202, 3322 (NH₂) groups; H-NMR (DMSO-d₆, δ, ppm): 3.74 (br, 2H, NH₂, exchangeable with D₂O), 6.68 (s, 1H, C₅thiophene), 7.15-7.99 (m, 6H, ArH), 8.68 (s, 1H, C₁ naphthalene).

Ethyl-2-amino-4-(naphthalen-2-yl) thiophen-3-carboxylate (15b).

IR (cm⁻¹, v): 1721(C=O), 3200, 3321 (NH₂) groups; H-NMR (DMSO-d₆, δ, ppm): 1.49 (t, = 8.5 Hz, 3H, CH₃), 3.39 (br, 2H, NH₂, exchangeable with D₂O), 3.75 (q, J= 7.5Hz, 2H, CH₂), 6.67 (s, 1H, C₅ thiophene), 7.60-8.01 (m, 6H, ArH), 8.68 (s, 1H, C₁ naphthalene).

5-(Naphthalen-2-yl)thieno[2,3-d]pyrimidin-4(3H)-one (16).

Compound 15a (0.01 mol) was heated under reflux temperature in 20 mL formic acid for 6h. The reaction mixture was cooled, poured into water, filtered and the residue was recrystallized to give 16. IR (cm⁻¹, v): 1596 (C=NC=O), 1697 (C=O), 3211 (NH); H-NMR (DMSO-d₆, δ, ppm): 6.7 (s, 1H, C₄H), 7.20-7.97 (m, 7H, ArH+NH), 8.15 (s, 1H, C₂H), 8.31 (s, 1H, C₁ naphthalene).

Ethyl N-[4-(naphthalen-2-yl)]-3-cyanothieno-2-yl methanimidate (17).

A mixture of compound 15a (0.01 mol) and 20 mL triethyl orthoformate was heated under reflux temperature for 4h, then evaporated and the residue was recrystallized to give compound 17.
IR (cm⁻¹, ν): 2211 (C=N); ¹H-NMR (DMSO-d₆, δ, ppm): 1.23 (t, 8.5Hz, 3H, CH₃), 3.75 (q, J= 7.50, 2H, CH₂), 6.71 (s, 1H, thiophene), 7.25-7.81 (m, 6H, ArH), 8.21 (s, 1H, C-1 naphthalene), 8.51 (s,1H, N= CHOEt).

4-Imino-5-(naphthalen-2yl)thieno[2,3-d]pyrimidin-3-ylamine (18).

A mixture of compound 17 (0.01) dissolved in 20 mL of absolute ethanol and 3 mL of hydrazine hydrate (99%), was stirred for 1h at room temperature. The solid that formed was filtered, washed with a little amount of methanol dried, and recrystallized to give compound 18. IR (cm⁻¹, ν): 1645 (C=N), 3111, 3220, 3250 (NH₂/NH) groups.; MS: m/z (%): 292 (M⁺, 100)

5-(Naphthalene-2-yl)thieno[2,3-d]pyrimidin-4-yl-hydrazine (19):

Method A:

Compound 17 (0.01 mol) was dissolved in 20 mL absolute ethanol, then 2 mL of hydrazine hydrate (99%) were added, and the reaction mixture was heated under reflux temperature for 3h; it was evaporated and the residue was recrystallized to give 19. IR (cm⁻¹, ν): 3180, 3210, 3310 (NH₂/NH).; MS: m/z (%): 292 (M⁺, 71)

Method B: Isomerization of 18 to 19.

Compound 18 (0.01 mol) was dissolved in 20 mL ethanol and then drops of hydrazine hydrate were added, then the reaction mixture was heated under reflux temperature for 2h and evaporated under reduced pressure to give compound 19. Product 19 which was obtained from this isomarization is identical in all respects (physical and spectral data) to those prepared by method A.

Antioxidant Assay:

The antioxidant activity of extract was determined by the DPPH free radical scavenging assay method (Sonia, et al., 2008) in triplicate and average values were considered.

DPPH antioxidant assay

Freshly prepared (0.004%w/v) methanol solution of 2,2-diphenyl-l-picrylhydrazyl (DPPH) radical was prepared and stored at 10°C in the dark. A methanol solution of the test compound was prepared. A 40ul aliquot of the methanol solution was added to 3ml of DPPH solution. Absorbance measurements were recorded immediately with a Milton Roy Spectronic 201 UV-visible spectrophotometer. The decrease in absorbance at 515 nm was determined continuously, with data being recorded at 1 min intervals until the absorbance stabilized (16 min). Tocopherol was used as a reference standard and dissolved in distilled water to make the stock solution with the same concentration. The absorbance of the DPPH radical without antioxidant was also measured as control and 95% methanol was used as blank. All the determinations were performed in three replicates and averaged.

% Scavenging of the DPPH free radical was measured using the following equation:

% DPPH radical-scavenging = [(Absorbance of control - Absorbance of test Sample)/(Absorbance of control)] x 100.
REFERENCES


تشييد، تفاعلات ومضادات الأكسدة لبعض الحلقات الغير متجانسة الحلقة الجديدة المشيدة
من 2- أستيل نفتالين

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في هذا البحث تم استخدام 2-ميثيل-4(1-نفتاليين-2-يل) ايثيليدين أكسازول-(4H)-5(4H)-أون 2 في تحضير بعض
المشتقات 1- (4-مستدمل) 2-ميثيل-4(1-نفتاليين-2-يل) إيثيليدين-1H – إيميدازول– (4H) 5 أون 4،b و بعض
المشتقات الأخرى 12-5،ن 3،. كما تم تحضير مشتق بيريميدين (3H)-2،3-د [بريميدين-3-ديل 18 و 19 من تفاعل مشتق 2- أسينثيونين-3-د-كاربونيتريل. و علاوة على
هذا تم اختبار النشاط المضاد للأكسدة وأعطت بعض هذه المركبات فاعليّة كمضادات للأكسدة.