Academic Sciences International Journal of Pharmacy and Pharmaceutical Sciences

Vol 6, Suppl 2, 2014 ISSN- 0975-1491

Research Article

SYNTHESISOF BIOLOGICALLY AND PHARMACEUTICALLY ACTIVE PYRIMIDINE AND FORMAMIDINE DERIVATIVES FROM 3-AMINO-1H,2H,4H,4AH,5H,10H,10AH-5,10-O-BENZOPYRIMIDINO-[4,5-B]NAPTHALIN-2,4-DIONE

HEMAT MOHAMED DARDEER AND ABOU-BAKR HAREDI ABDEL-MONSEF*

Chemistry Department, Faculty of Science, SouthValley University, 83523 Qena, Egypt. Email: bakooos2004@yahoo.com

Received: 10 Jan 2014, Revised and Accepted: 21 Feb 2014

ABSTRACT

Formamidines are interesting and promising compounds that feature in the biosynthesis of heterocycles and in the catabolism of histidine. In addition, pyrimidine derivatives have occupied a unique position in biological, medicinal and pharmaceutical chemistry.

Objective: According to the importance of these compounds, our interest focused on the synthesis of new series of heterocyclic nitrogen like formamidine and pyrimidine derivatives fused to anthracene ring.

Methods: An efficient synthesis of new formamidine and pyrimidine derivatives attached to anthracene ring in the position 9 and 10 starting from3-amino-1H,-2H,4H,4aH,5H,10H,10aH-5,10-o-benzopyrimidino[4,5-b]-naphthalen-2,4-dione1.

Results: New and several formamidine and pyrimidine derivatives have been prepared.The newly synthesized compounds may possess pharmacological properties and biological effect on insects, bacteria and fungi.

Conclusion: The present study covers the synthesis, reactions and applications of pyrimidine and formamidine compounds.

Keywords: benzopyrimidine,imides, anhydrides, amines,formamidine derivatives, insecticides.

INTRODCTION

Formamidine derivatives are relatively new groups of acaricide-insecticides [1], also they used as a topical acaricide on cattle, sheep, pigs and fruit crops and miticide in the treatment of generalized demodectic mange in dogs. In horses, it causes fatal impaction of the intestine. On the other hand, their biological activities and uses are defined by their toxicity to spider mites, ticks, and certain insects [2]and they are particularly effective against juvenile and resistant forms of these organisms [3-5].They are a group of acaricidal compounds, used as plant sprays and topically on animals. Formamidines have been used as pharmacological agents [6], pesticides like amitraz [7].

Their application as ligands in transition metal complexes and as building blocks in polymers [8], their use as intermediates in synthetic organic chemistry is quite diversified [9], as protecting groups for primary amines [10], and as support linkers in solid phase synthesis [11]. Formamidines are a relatively new class of agricultural chemicals, and there exist diverse types of pesticides activity within the formamidine group such as, compounds active as insecticides and acaricides have been discovered [12]. Also pyrimidines derivatives [13-17]have occupied a unique position in medicinal chemistry. Pyrimidine derivatives have received much attention over the last years because of their interesting biological and pharmacological properties as sedatives [18], anti-bacterials [19-21]and anticancer [22-24].In this study, we have been most interested and aimed to add to this substantial known body of work a novel, convenient and highly efficient synthesis of a variety of pyrimidine and formamidine derivatives by using 3-amino-1H,2H,4H,4aH,5H,10H,-10aH-5,10-o-benzopyrimid-ino[4,5-b]naphthalen-2,-4-dione**1**,these new derivatives may have certain applications in pharmaceutical and medicinal chemistry.

MATERIALS AND METHODS

MATERIALS

All reagents and solvents were purchased from Across Organics and used without further purification. Melting points were uncorrected determined on an electric melting point apparatus (Kofler). The IR spectra (KBr) were recorded on a Shimadzu 408 spectrometer.

The ^{1}H-NMR spectra were recorded by 200 and 400 MHz Varian EM 390 spectrometer; chemical shifts are reported in ppm with TMS as an internal standard and are given in δ units. Electron impact mass spectra were obtained at 70 eV using a GC-MS sp.1000 Shimadzu. Elemental analyses were carried out at Microanalysis Unit at Cairo University.

METHODS

Formation of 3-amino-1H,2H,4H,4aH,5H,10H,10aH-5,10-o-benzopyrimidino-[4,5-b]naphthalen-2,4-dione 1

N-phenylsulfonyloxy-9,10-dihydro-9,10-ethanoanthracen-11,12-dicarboximide (0.5 gm., 1.16 mmol.) and hydrazine hydrate (0.16 gm, 3.48 mmol.) were heated under reflux in a sand bath for 2 hours. The solid formed after cooling was filtered off and recrystallized form benzene to give compound **1** as white crystals. Yield 69%; m.p.302^{o}C; IR spectrum (KBr): indicated the presence of bands due to (νNH and NH_2) at 3400-3300 cm^{-1} and two bands for (νC=O's) at 1740-1700 cm^{-1}; ^{1}H-NMR spectrum: (DMSO-d_6, 400 MHz) indicated at δ3.41 (d, 2H, 2CH sp^3); 4.74 (d, 2H, 2CH sp^3); 4.79 (s, 2H, NH_2); 7.07-7.95 (m, 8H, arom.H) while no signal was appeared due to NH in DMSO.

Synthesis of *N*-(N-maleimidy)-1H,2H,4H,4aH,5H,10H,10aH-5,10-o-benzo-pyrimidino[4,5-b]naphthalen-2,4-dione 2

Compound **1** (0.3 gm., 1.00 mmol.) and maleic anhydride (1.32 gm., 13.46 mmol.) were homogeneously mixed. The solid mixture was heated at 120^{o}C for 1 hour in a 50 ml round bottomed flask equipped with a calcium chloride guard tube. After cooling to room temperature; the residue was treated with petroleum ether (80-100) then the precipitate was isolated by filtration. The crude product was washed with ethanol and recrystallized from chloroform to give *N*-(N-maleimidy)-1H,2H,4H,4aH,-5H,10H,10aH-5,10-o-benzopyrimidino[4,5-b]naphthalen-2,4-dione 2 (0.34 gm.,0.9 mmol.) **2** as white crystals and obtained in 85% yield; m.p.288^{o}C; IR (KBr, cm^{-1}): showed the presence of bands due to (νNH) at 3400cm^{-1} and (ν C=O's) in the region 1770-1700 cm^{-1}; ^{1}H-NMR (200 MHz/DMSO) indicated at δ3.61 (d, 2H, 2CH sp^3); 4.86 (d, 2H, 2CH sp^3); 7.22-7.66 (m, 10H, arom.H+ (CH=CH), 11.22 (s, 1H, NH) ; MS (m/z): 385.3 M$^+$. EA(%C,%H,%N); Calc.: 68.60, 10.90, 3.90; Found,68.59, 11.00, 3.88.

Synthesis of *N*-(N-succinimidyl)-1H,2H,4H,4aH,5H,10H,10aH-5,10-o-benzo-pyrimidino[4,5-b]naphthalen-2,4-dione 3

A mixture of compound **1** (0.5 gm., 1.6 mmol.) and succinic anhydride (3.8 gm., 10.2 mmol.) was heated at 200°C for 2 hours. The residue was treated with dry ether and the crude product was isolated by filtration and crystallized from chloroform to afford (0.52gm., 1.3 mmol.) **3** as white crystals and obtained in 85% yield; m.p. 320 °C; IR (KBr, cm^{-1}) showed the presence of bands due to (νNH) at 3450 cm^{-1} and (νC=O's) in the region 1770-1690 cm^{-1}; ^{1}H-NMR (200 MHz/DMSO) showed at δ2.88 (t, 2H, CH_2); 2.99 (t, 2H, CH_2); 3.68 (d, 2H, 2CH sp^3); 4.88 (d, 2H, 2CH sp^3); 7.11-7.87 (m, 8H, arom.H), 10.88 (s, 1H, NH); MS (m/z): 387.3 M^+. EA(%C,%H,%N); Calc.: 68.20,4.40, 10.80; Found, 68.22, 4.38,10.82.

General procedure for the preparation of compounds 4, 5 and 6

A mixture of 3-amino-1H,2H,4H,4aH,5H,10H,10aH-5,10-o-benzopyrimidino[4,5-b] naphthalen-2,4-dione **1** (0.5 gm., 1.6 mmol.) and the appropriate aromatic anhydrides namely, phthalic, tetrachlorophthalic and/or 9,10-dihydro-9,10-ethanoanthracen-11,12-dicarboxylic anhydrides (1.6 mmol.) in DMF (10 ml) was refluxed for 5-10 hours. After cooling, the reaction mixture was poured on ice-cold water; the crude solid formed was filtered off, dried and crystallized from the appropriate solvent to give compounds **4, 5**and **6**. Compound **6** also can be obtained via cyclo-addition reaction of compound **2** with anthracene in dry xylene.

***N*-(N-phthalimidyl)-1H,2H,4H,4aH,5H,10H,10aH-5,10-o-benzo-pyrimidino[4,5-b]naphthalen-2,4-dione 4**

87% yield; m.p. 305 °C; IR (KBr, cm^{-1}): showed the presence of bands due to (νNH) at 3400 cm^{-1} and (νC=O's)1780, 1720cm^{-1}; ^{1}H-NMR (200 MHz/DMSO) δ (ppm) showed at δ3.67 (d, 2H, 2CH sp^3); 4.89 (d, 2H, 2CH sp^3); 7.17-7.98 (m, 12H, arom. H); while no signal was appeared due to NH in DMSO; MS (m/z): 435.4 M^+. EA(%C,%H, %N): Calc.: 71.70, 3.90, 9.60; Found, 71.66, 4.00, 9.63.

***N*-(N-tetrachlorophthalimidyl)-1H,2H,4H,4aH,5H,10H,10aH-5,10-o-benzo-pyrimidino[4,5-b]naphthalen-2,4-dione 5**

88% yield; m.p. 270 °C; IR (KBr, cm^{-1}): indicated the presence of bands due to (νNH) at 3440 cm^{-1} and (νC=O's) 1790, 1740 cm^{-1}; ^{1}H-NMR (200 MHz/DMSO) δ (ppm) showed at δ3.87 (d, 2H, 2CH sp^3); 4.93 (d, 2H, 2CH sp^3); 7.66-8.11 (m, 8H, arom. H), 11.12 (s, 1H, NH); MS (m/z): 573.2 M^+. EA(%C,%H,%N,%Cl): Calc.: 54.50, 2.30, 7.30, 24.70; Found, 54.53, 2.32, 7.28, 24.73.

***N*-(N-9,10-dihydro-9,10-ethanoanthracen-11,12-dicarboximidyl)-1H,2H,4H,4aH,-5H,10H,10aH-5,10-o-benzopyrimidin[4,5-b]naphthalen-2,4-dione 6**

78% yield; m.p. 310°C; IR (KBr, cm^{-1}): indicated the presence of bands due to (νNH) at 3400 cm^{-1} and (νC=O's) at 1780, 1730; ^{1}H-NMR (200 MHz/DMSO) δ (ppm) showed at δ3.68 (d, 4H, 4CH sp^3); 4.90 (d, 4H, 4CH sp^3); 7.16-7.99 (m, 16H, arom. H), 10.55 (s, 1H, NH); MS (m/z): 563.6 M^+. EA(%C,%H,%N); Calc.:76.71, 4.51, 7.50; Found, 76.74, 4.53,7.46.

Synthesis of 3-(ethoxyformamidine)-1H,2H,4H,4aH,5H,10H-,10aH-5,10-o-benzo-pyrimidino[4,5-b]naphthalen-2,4-dione 7

3-amino-1H,2H,4H,4aH,5H,10H,10aH-5,10-o-benzopyrimidino[4,5-b]naphthalen-2,4-dione **1** (0.3gm., 0.98 mmol.) and triethylorthoformate (0.18 ml, 1.08 mmol.) were refluxed in ethanol for 6 hours. After cooling, the solid formed was filtered off and crystallization from ethanol to give compound **7** (0.32 gm., 0.89 mmol.) as white crystals and obtained in 89 % yield; m.p.210 °C; IR (KBr, cm^{-1}): revealed the presence of a band for (νNH) at 3450 cm^{-1} and two bands for (νC=O's) at 1710, 1680 cm^{-1}; ^{1}H-NMR (400 MHz/DMSO) showed at δ1.19 (t, 3H, CH_3); 3.26 (d, 2H, 2CHsp^3); 4.23 (q, 2H, CH_2); 4.79 (d, 2H, 2CH sp^3); 7.13-7.53 (m, 8H, arom.H); 8.57 (s, 1H, CH) and no signals due to NH in DMSO ; MS (m/z): 361.3 M^+. EA(%C,%H,%N); Calc.: 69.81, 5.26, 11.63; Found, 69.78, 5.29,11.60.

General procedure for the preparation of compounds 8a-c

3-(ethoxyformamidine)-1H,2H,4H,4aH,5H,10H,10aH-5,10-o-benzopyrimidino[4,5-b]naphthalen-2,4-dione **7** (0.5 gm., 1.4 mmol.) and aromatic amines namely, aniline, *p*-toluidine and/or*o*-chloroaniline (1.44 mmol.) were refluxed in ethanol for 8-10 hours. After cooling, the solid formed filtered off and crystallized from appropriate solvent to give the corresponding compounds 8a-c.

***N*-(anilinoformamidine)-1H,2H,4H,4aH,5H,10H,10aH-5,10-o-benzopyrimidino-[4,5-b]naphthalen-2,4-dione 8a**

75% yield; m.p. 240 °C; IR (KBr, cm^{-1}): showed a band for (νNH) at 3350 cm^{-1} and bands for (νC=O's) at 1760, 1700cm^{-1}; ^{1}H-NMR (200 MHz/DMSO) δ (ppm) indicated at δ3.48 (d, 2H, 2CH sp^3); 4.89 (d, 2H, CH sp^3); 7.57-8.44 (m, 14H, arom. H+NH); 8.77 (d, 1H, CH); 11.51 (s, 1H, NH); MS (m/z): 408.5 M^+. EA(%C,%H,%N): Calc.: 73.50, 4.90, 13.70; Found, 73.54, 4.95, 13.67.

***N*-(*p*-toluedinoformamidine)-1H,2H,4H,4aH,5H,10H,10aH-5,10-o-benzopyrimid-ino[4,5-b]naphthalen-2,4-dione 8b**

87% yield; m.p. 282 °C; IR (KBr, cm^{-1}): showed a band for (νNH's) at 3450 cm^{-1} and bands for (νC=O's) at 1770, 1720cm^{-1}; ^{1}H-NMR (200 MHz/DMSO) δ (ppm): indicated at δ1.88 (s, 3H, CH_3); 3.44 (d, 2H, 2CH sp^3); 4.74 (d, 2H, CH sp^3); 7.44-8.11 (m, 13H, arom. H+NH); 8.65 (d, 1H, CH); 10.55 (s, 1H, NH); MS (m/z): 422.5 M^+. EA(%C, %H, %N); Calc.: 73.90, 5.30, 13.30; Found, 73.94, 5.35, 13.22.

***N*-(*o*-chloroanilinoformamidine)-1H,2H,4H,4aH,5H,10H,10aH-5,10-o-benzo-pyrimidino[4,5-b]naphthalen-2,4-dione 8c**

90% yield; m.p. 260 °C; IR (KBr, cm^{-1}): showed a band for (νNH's) at 3500 cm^{-1} and bands for (νC=O's) at 1780, 1710 cm^{-1}; ^{1}H-NMR (200 MHz/DMSO) δ (ppm): indicated at δ3.77 (d, 2H, 2CH sp^3); 4.89 (d, 2H, CH sp^3); 7.88-8.55 (m, 13H, arom. H+NH); 8.89 (d, 1H, CH); 11.12 (s, 1H, NH); MS (m/z): 442.9 M^+. EA(%C,%H,%N,%Cl); Calc.: 67.80, 4.30,12.60, 8.00; Found, 67.75, 4.33, 12.58, 8.11.

General procedure for the preparation of compounds 9, 10 and 11

3-(ethoxyformamidine)-1H,2H,4H,4aH,5H,10H,10aH-5,10-o-benzopyrimidino[4,5-b]naphthalen-2,4-dione **7** (0.5 gm.,1.4 mmol.) and piperidine, morpholine and/or piper-azine (1.44 mmol.) were refluxed in ethanol for 10-12 hours. After cooling; the solid formed filtered off and crystallized from appropriate solvent to give the corresponding compounds **9, 10** and **11** respectively.

***N*-(piperdin-1-ylformamidine)-1H,2H,4H,4aH,5H,10H,10aH-5,10-o-benzo-pyrimidino[4,5-b]naphthalen-2,4-dione 9**

90% yield; m.p. 272 °C; IR(KBr, cm^{-1}): (νCH_2) 2950, 2850 $cm^{-1}$and (νC=O's) 1780, 1710cm^{-1}; ^{1}H-NMR (400 MHz/DMSO) δ(ppm): δ1.44-1.64 (m, 6H, 3CH_2); 3.47 (d, 2H, 2CHsp^3); 3.64 (t,4H,2CH_2); 4.75 (d, 2H, 2CH sp^3); 7.33-7.88 (m, 8H. arom.H) ; 8.66 (s, 1H, CH); 11.34 (s, 1H, NH); MS (m/z): 400.5 M^+. EA(%C,%H,% N): Calc.: 72.00, 6.00, 14.00; Found, 72.23, 5.98, 14.11.

***N*-(morpholin-4-ylformamidine)-1H,2H,4H,4aH,5H,10H,10aH-5,10-o-benzo-pyrimidino[4,5-b]naphthalen-2,4-dione 10**

93% yield; m.p. 230 °C; IR (KBr, cm^{-1}): showed a band for (νNH) at 3450 cm^{-1} and bands for (νCH_2) 2940, 2900 cm^{-1} and bands (νC=O's) 1780, 1700cm^{-1}; ^{1}H-NMR (400 MHz/DMSO) δ (ppm): δ3.22 (t, 4H, 2CH_2); 3.33 (d, 2H, 2CH sp^3); 3.55 (t, 4H, 2CH_2); 4.88 (d, 2H, 2CH sp^3); 7.44-7.89 (m, 8H. arom.H); 8,75 (s, 1H, CH); 11.21 (s, 1H, NH) ; MS (m/z): 402.5 M^+; EA(%C,%H,% N): Calc.: 68.60, 5.50,11.90; Found, 68.56, 5.53, 11.88.

1,4-bis(formamidine-1H,2H,4H,4aH,5H,10H,10aH-5,10-o-benzo-pyrimidino[4,5-b]naphthalen-2,4-dione) piperazine 11

88% yield; m.p. 286 °C; IR(KBr, cm^{-1}): indicated a band for (νNH's) at 3430 cm^{-1} , bands for (νCH_2) 2950, 2900 $acm^{-1}$and band for (νC=O's) at 1770, 1710cm^{-1}; ^{1}H-NMR (400 MHz/DMSO) δ (ppm): δ2.52 (s, 8H, 4CH_2); 3.34 (d, 4H, 4CHsp^3); 4.88 (d, 4H, 4CH sp^3); 7.45-7.88 (m, 16H. arom.H); 8,44 (s, 2H, 2CH); 11.12 (s, 2H, NH·s) ; MS

(m/z): 716.9 M^+. EA(%C, %H, %N); Calc.: 70.40, 5.10, 15.60; Found, 70.44, 4.98, 15.55.

Synthesis of *N*-(dimethylaminoformamidine)-1H,2H,4H,4aH,5H,10H,10aH-5,10-o-benzopyrimidino[4,5-b]naphthalene-2,4-dione 12

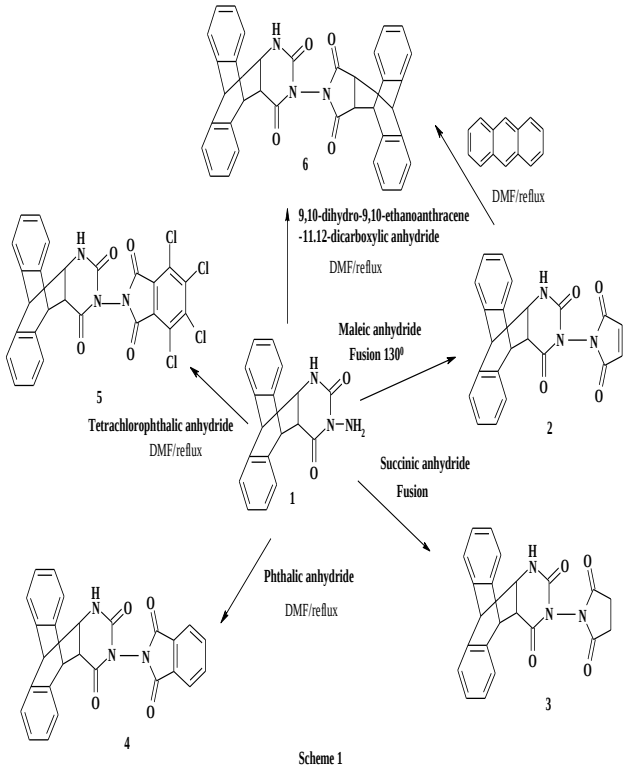
A mixture of compound **7** (0.5 gm., 1.4 mmol.) and dimethylamine (0.2 ml, 4.4 mmol.) was heated under reflux for 6 hours. After Cooling, the white crystals formed were filtered off and crystallized from chloroform to give compound **12** in 85% yield; m.p. 310 ^{o}C; IR(KBr, cm^{-1}): indicated a band for (νNH's) at 3430 cm^{-1} and bands for (νC=O's) at 1740 and 1680cm^{-1}; ^{1}H-NMR spectrum: (DMSO-d$_6$, 200 MHz) showed two singlets at δ2.71 and 2.75 (6H, 2CH$_3$) represent two different methyl protons which due to stereo chemical configuration discussed before; a doublet at 3.27 (2H, 2CH sp^3), a doublet at 4.75 (2H, 2CH sp^3); a multiplet at 7.14-7.77 (8H, arom. H); a singlet at 8.33 (1H, CHsp^2); singlet at δ 11.10 (1H, NH); MS (m/z): 360.4 M^{+}. EA(%C, %H, %N); Calc.:70.00, 5.60, 15.50; Found, 70.31, 5.64, 15.33.

Synthesis of *N*-(2-hydroxyethylaminoformamidine)-1H,2H,4H,4aH,5H,10H,-10aH-5,10-o-benzopyrimidino[4,5-b]naphthalene-2,4-dione 13

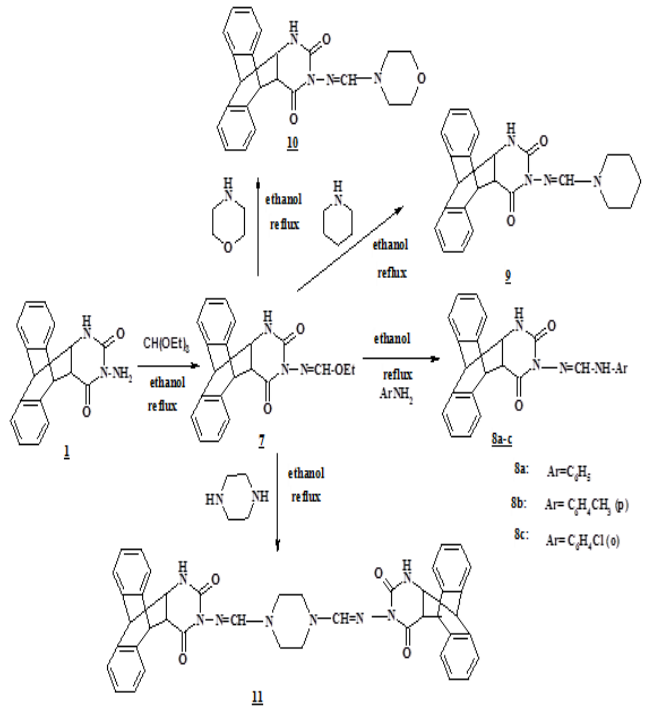
3-(ethoxyformamidine)-1H,2H,4H,4aH,5H,10H,10aH-5,10-o-benzopyrimidino[4,5-b]naphthalen-2,4-dione **7** (0.5 gm,1.4 mmol.); and ethanolamine (0.1 ml, 1.64 mmol.) in ethanol were heated under reflux for 6 hours. After cooling the solid formed was filtered off and crystallized from benzene to give compound **13**as white crystals, in 84% yield; m.p.268^{o}C; IR (KBr, cm^{-1}): showed (νOH) band at 3400 cm^{-1}, characteristic band for (νNH) at 3100 cm^{-1} and two bands for (νC=O's) at 1760, 1690 cm^{-1}; ^{1}H-NMR (200 MHz/DMSO):indicated at δ3.21 (dt, 2H, CH$_2$); 3.32 (d, 2H, 2CH sp^3); 3.45 (dt, 2H, CH$_2$); 4.66 (t, 1H, OH); 4.85 (d, 2H, 2CH sp^3); 7.35-7.88 (m, 9H, arom. H+NH); 8.55 (d, 1H, CH); 11.22 (s, 1H, NH); MS (m/z): 376.4 M^{+}. EA(%C,%H,% N); Calc.: 67.00, 5.40, 12.80; Found, 66.98, 5.45, 12.78.

RESULTS AND DISCUSSION

Fusion of *N*-phenylsulfonyloxy-9,10-dihydro-9,10-ethanoanthracene-11, 12-di-carbo-ximide with hydrazine hydrate in a sand bath gave 3-amino-1H,2H,4H,4aH,5H,-10H,10aH-5,10-o-benzopyrimidino[4,5-b]naphthalen-2,4-dione**1**. Compound **1** was fused with different anhydrides namely, maleic, succinic, phthalic, tetrachlorophthalic and/or 9,10-dihydro-9,10-ethano-anthracen-11,12-dicarboxylic anhydrides to give the corresponding compounds **2-5** as the following; by reaction of compound **1** with maleic anhydride at 120^{o}C gave *N*-(N-maleimidy)-1H,2H,4H,4aH,5H,10H,10aH-5,10-o-benzopyrimidino [4, 5-b] naphthalen-2, 4-dione **2**, reaction with succinic anhydride in the same condition afforded *N*-(succinimidyl)-1H,2H,4H,4aH,5H,10H,-10aH-5,10-o-benzopyrimidino[4,5-b]naphthalen-2,4-dione **3**. The ^{1}H-NMR of compound **3** exhibits two different triplets at δ 2.88 and 2.99 based on the shielding parameters of the methylene protons due to the restricted rotation about N-N bond since a strong repulsion occurs between the nitrogen lone pair and benzene ring. Thus, the stereochemical conformation of the endo-adducts suggested that [25] the lone pair is in anti-orientation while the succinimide moiety is in syn-orientation. The reaction with aromatic anhydride namely, phthalic, tetrachlorophthalic and/or 9,10-dihydro-9,10-ethanoanthracen-11,12-dicarboxylic anhydrides in DMF under reflux gave the corresponding imides **4,5**and **6** (scheme 1). Compound **1** was treated with triethylorthoformate in ethanol under reflux to give 3-(ethoxyformamidine)-1H,2H,4H,4aH,5H,10H,10aH-5,10-o-benzopyrimidino[4,5-b]-naphthalen-2,4-dione**7**,which followed by its reaction with aromatic amines namely aniline, *p*-toluidine and/ or*o*-chloroaniline in ethanol under reflux to give **8a-c**.Also, the action of piperidine, morpholine and/ orpiperazine with 3-(ethoxyformamidine)-1H,2H,4H,4aH-,5H,10H,10aH-5,10-o-benzopyrimidino[4,5-b]naphthalen-2,4-dioneon compound **7**was investigated; where the expected compounds;*N*-(piperdin-1-yl-formamidine)-1H,-2H,4H,4aH,5H,10H,10aH-5,10-o-benzopyrimidino[4,5-b]naph-thalen-2,4-dione **9**, *N*-(morpholin-4-ylformamidine)-1H,2H,4H,4aH,5H,10H,-10aH-5,10-o-benzopyrimid-ino[4,5-b]-naphthalen-2,4-dione **10** and 1,4-bis-(formamidin-1H,2H,4H,4aH,5H,-10H,10aH-5,10-o-benzopyrimidino[4,5-b]-naphthalen-2,4-dione)piperazine**11** were obtained respectively as shown in scheme2.

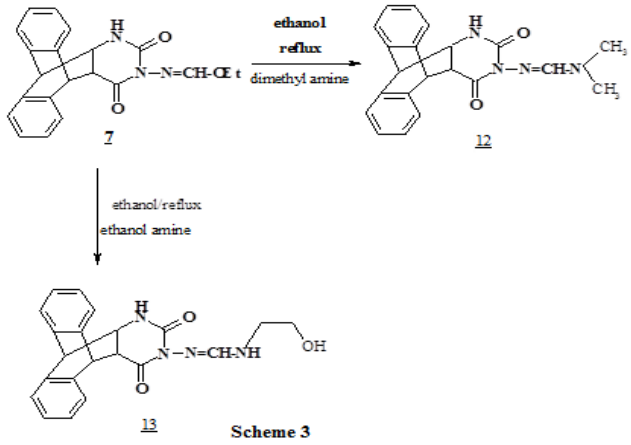


Scheme 1



Sche me 2

Treatment of compound **7** with dimethylamine in ethanol under reflux gave *N*-(dimethylaminoformamidine)-1H,2H,4H,4aH,5H,10H,10aH-5,10-o-benzopyrimidino-[4,5-b]naphthalen-2,4-dione **12**.When ethanolamine was allowed to react with compound **7** in ethanol under reflux; the only product formed was identified as *N*-(2-hydroxyethylaminoformamidine)-1H,2H,4H,4aH,5H,10H,10aH-5,10-o-benzopyrimi-dino[4,5-b]naphthalen-2,4-dione **13** (scheme 3).



7 12 13

Scheme 3

CONCLUSION

We have described a simple, convenient and efficient preparation of new formamidine and pyrimidine derivatives attached to anthracene ring in the position 9 and 10 by using 3-amino-1H,2H,4H,4aH,5H,10H,10aH-5,10-o-benzopyrimidino[4,5-b]-naph-thalen-2,4-dione**1** and 3-(ethoxyformamidine)-1H,2H,4H,4aH,5H,10H,10aH-5,10-o-benzopyrimidino[4,5-b]naphthalen-2,4-dione **7**. These compounds may possess pharmacological properties and biological effect on insects, bacteria and fungi. The structures of these newly compounds was confirmed by using different types of spectroscopic analysis.

ACKNOWLEDGMENT

This work has been supported by the Faculty of Science, South Valley University (Qena). The authors are grateful to Prof. Dr. Mamdouh Adly Hassan for hisguidance and encouragement, and all thanks to Mr. Mohamed Qelay for his encouragement and continuous guidance.

REFERENCES

1. MitsovV: Pharmacological assaying of some compounds of the formamidine group. Nauchni Tr Vissh Med Inst Sofia. 1966; 45(5): 61-67.
2. DittrichV,LoncarevićA:New insecticides for Asiatic rice borer control in paddy rice. J. Econ. Entomol. 1971;64(5): 1225-1229.
3. LingrenPD, WolfenbargeDA,Nosky JB,Diaz M: Response of Campoletis perdistinctus and Apanteles marginiventris to insecticides. J. Econ. Entomol.1972; 65(5):1295-1299.
4. GladneyWJ,Ernst SE,Drummond RO: Chlordimeform: a detachment-stimulating chemical for three-host ticks. J. Med. Entomo. 1974; 11(5): 569-572.
5. KnowlesCO,Roulston WJ: Toxicity to Boophilus microplus of formamidine acaricides and related compounds, and modification of toxicity by certain insecticide synergists.J. Econ.Entomo. 1973;66(6):1245-1251.
6. a) Zieglerskylakakis K, Nill S, Pan JF, Andrae U:Environ. Mol. Mutagen. 1998; 31 (4): 362-373. (b) Kerr SG, Kalman TI: J. Pharm. Sci. 1994; 83 (4): 582-586. (c) CooperRL, Barrett MA, Goldman JM, Rehnberg GR, McelroyWK, Stoker TE:Fundamental Appl. Toxicol. 1994; 22 (3):474-480. (d) Scott MK, Jacoby HJ, Mills JE, BonlioAC, Rasmussen CR: J. Med. Chem. 1983; 26: 535-538.(e) Donetti A, ereda E, Bellora E, Gallazzi A, BazzanoC, Vanoni PC, Del Soldato P, Micheletti R, Pagani F,Giachetti A: J. Med. Chem. 1984; 27: 380-386. (f) BeemanRW, Matsumura F: Nature 1973; 242: 273-274. (g) AzizSA, Knowles CO: Nature 1973; 242: 417-418.
7. a) Leung VKS,Chan TYK, Yeung VTF: J Toxicol.Clinical Toxicol. 1999; 37 (4): 513-514. (b) BaxterGD, Barker SC:Insect Biochem. Mol. Biol. 1999; 29 (5): 461-467. (c) Park JH, Keeley LL:General Comparative Endocrinol. 1998; 110 (1): 88-95. (d) Aydin K, Kurtoglu S,Poyrazoglu MH, Uzum K, Ustunbas HB, Hallac IK:Human Exp. Toxicol. 1997; 16 (11): 680-682. (e) Jorens PG,Zandijk E, Belmans L, Schepens PJC, Bossaert LL:Human Exp. Toxicol. 1997; 16 (10): 600-601. (f) Nakayama A,Sukekawa M, Eguchi Y: Pesticide Sci. 1997; 51 (2): 157-164.(g) Dombrowski JA, Kolmes SA, Dennehy TJ: J. Economic Entomol. 1996; 89 (5): 1130-1136. (h) Moss JI:J. EconomicEntomol. 1996; 89 (5): 1151-1155. (i) Longtine CA, ZehnderGW, Radcliffe EB: J. Entomol. Sci. 1996; 31 (1): 89-101. (j)Kennel O, Prince C, Garnier R:Veterinary Human Toxicol.1996; 38 (1): 28-30. (k) Usmani K A, Abdelghafar SF,Knowles CO: J. Economic Entomol. 1995; 88 (6): 1580-1585.(l) Chen TH, Hsu WH:J. Pharmacol. Exp. Therap. 1994; 271(3): 1240-1245. (m) Shin DH, Hsu WH:Toxicol. Appl. Pharm.1994; 128 (1): 45-49. (n) Queirozneto A, Juang SJ, SouzaKR, Akamatsu A:BrazilianJ. Med. Biol. Res. 1994; 27 (6):1407-1411
8. a) Bohme F, Kunert C, Klinger C, Komber H:Macromol.Symp. 1998; 128: 183-193. (b) Bohme F, Klinger C, KomberH, Haussler L, Jehnichen D: J. Polym. Sci. Part ADPolym.Chem. 1998; 36 (6): 929-938. (c) Komber H, Klinger C,Bohme F: Macromolecules 1997; 30 (25): 8066-8068. (d)Komber H, Klinger C, Bohme F: Polymer 1997; 38 (11):2603-2608. (e) Bohme F, Rillich M, Komber H:Macromol.Chem. Phys. 1995; 196 (10): 3209-3216. (f) Rillich M,Jehnichen D, Komber H, Bohme F:Macromol. Chem. Phys.1995; 196 (5): 1635-1644. (g) Rillich M, Haussler L, JehnichenD, Bohme F: Polym. Bull. 1995; 34 (1): 43-48. (h) Rillich M,Haussler L, Komber H, Wittig F, Bohme F:Polym. Bull. 1994,33 (4), 397-404.
9. a) Streith J, Rudyk H, Tschamber T, Tarnus C, StrehlerC, Deredas D, Frankowski A: Eur. J. Org. Chem. 1999; 4: 893-898. (b) Gorlitzer K, Herbig S, Walter RD: Pharmazie 1997;52 (9): 670-672. (c) Bridges AJ, Zhou HR:J. Heterocycl.Chem. 1997; 34 (4): 1163-1172. (d) Clark GR, Rickard CEF, Surman PWJ, Taylor MJ:J.Chem. Soc., Faraday Trans.1997; 93 (15): 2503-2507. (e) Kapplinger C, Beckert R,Gunther W, Gorls H: Liebigs Annalen 1997; 3: 617-622.(f) Rewcastle GW, Denny WA,winters RT, Colbry NL, Schowalter HDH:J. Chem. Soc., Perkin Trans. 1996; 18:2221-2226. (g) Kim KH, Dumas JP, Germanas JP:J. Org.Chem. 1996; 61 (9): 3138-3144. (h) Streith J, Boiron A,Frankowski A, Lenouen D, Rudyk H, Tschamber T: Synthesis-Stuttgart 1995; 8: 944-946. (i) Takagi K, BajnatiA,Huberthabart M: J.Heterocycl. Chem. 1994; 31 (4): 973-975.(j) Patil SA, Otter BA, Klein RS:Tetrahedron Lett. 1994;35 (30): 5339-5342. (k) Pudlo JS, Wadwani S, Milligan JF,Matteucci MD:Bioorg. and Med. Chem. Lett. 1994; 4 (8): 1025-1028.
10. a) Vincent S, Mons S, Lebeau L, Mioskowski C:Tetrahedron Lett. 1997; 38 (43): 7527-7530. (b) Toste D,Mcnulty J, Still IW: J. Synth. Commun. 1994; 24 (11): 1617-1624.
11. LishingCI, YingH, Sumei R, LiangfuH, Tetrahedron 2000; 56: 8253-8262.
12. HermanJ, BenezetKM, Charles KnowlesOK:Pesticide and Venom Neurotoxicity1978; 189.
13. Hassan AM, Seleem AM, Younes MMA, Taha MM, Abdel-Monsef HA: Synthesis and spectral characterization of some heterocyclic nitrogen compounds. Eur. J. Chem. 2013; 4(2): 121-123
14. Hassan AM, Seleem AM, Younes MMA, Taha MM, Abdel-Monsef HA: Utility of (2,4-Dioxo-1,4-dihydro-2H-quinazolin-3-yl)-acetic acid hydrazide in the synthesis of some heterocyclic nitrogen compounds. Eur. J. Chem. 2013; 4(2): 168-171.
15. Abdel-Monsef HA, Abboudy SM, Taha MM, Younes MMA, Hassan AM: Facile Syntheses of Pharmaceutically Active Quniazolin-2,4-Diones.Int. J. Pharm. Sci. Rev.Res. 2013; 23(2): 65, 405-410.
16. Hassan AM, Younes MMA, Taha MM, Abboudy MS, Abdel-Monsef HA: Applications of 3-Amino-1H-quinazolin-2,4-dione in Heterocyclic Chemistry.Journal of Applicable Chemistry. 2013;2 (6): 1683-1689.
17. 17.Hassan AM, Younes MMA, Taha MM, Abdel-Monsef HA: Synthesis and reactions of 3-aminotetrachloroquinazolin-2,4-dione. Eur. J. Chem. 2011; 2(4): 514-518.
18. KrenitskyTA, RideoutJL,KoszalkaGW, InmonRB, ChaoEY, ElionGB,LatterVS, WilliamsRB:Pyrazolo [3,4-d]pyrimidine ribonucleosides asanticoccidials. 1. Synthesis and activity of somenucleosides of purines and 4-(alkylthio)pyrazolo[3,4-d]pyrimidines. J. Med. Chem.1982; 25: 32-35.

19. RideoutJL, KrenitskTA, ChaoEY, ElionGB, WilliamsRB,LatterVS:Pyrazolo[3,4-d]pyrimidine ribonucleosides as anticoccidials. 3.Synthesis and activity of some nucleosides of 4-[(arylalkenyl)thio]pyrazolo[3,4-d] pyrimidines. J. Med.Chem. 1983; 26(10):1489-1494.
20. YounesMI, AbbasHH, MetwallySA:Synthesis of ethyl-5-amino-1-(5-ethyl-5H-1,2,4-triazino[5,6-b]indol-3-yl)-1H-pyrazole-4-carboxylate and pyrazole-[3,4-d]pyrimidine derivatives.Pharmazie, 1991; 46(2): 98-100.
21. MareiMG, AlyDM, MishrikeyMM:NewSynthesis of Pyrazolo(1,5-c)pyrimidines from Acetylenicβ-Diketones.Bull. Chem. Soc. Jpn. 1992; 65 (12):3419-3422.
22. ShalabyAM, FathallaOA, KassemEMM,ZakiMEA: Synthesis of New 5-N-Pyrazolyl AminoAcids, Pyrazolopyrimidines and PyrazolopyridinesDerivatives. Acta. Chim. Solv. 2000; 47: 187-203.
23. BhuyanPJ, BorahHN, LekhokKC, SanhuJS:Studies on uracils: A facile one-pot synthesis ofpyrazolo[3,4-d]pyrimidines. J. Heterocyclic Chem. 2001;38(2):491-493.
24. El-AfaleqEI,AbubshaitSA:Heterocyclico-Aminonitriles: Preparation of Pyrazolo[3,4-d]pyrimidines with Modification of the Substituents at the 1-Position. Molecules 2001; 6(7):621-638.
25. SrivastavaA,SrivastavaV, VermaSM, Pattabhi V: Stereochemistry of the Addition Product of N-Aminosuccinimide Moiety to an Acetylenic Ester. Bull. Chem. Soc. Jpn. 1994; 67(5): 1386-1389.