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Synthesis and pharmacological activities of C-nucleosides of phenazine derivatives

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ABSTRACT

Several of phenazine derivatives were synthesized from phenazine **(2)** and **(3)** which were synthesized by oxidation of phenylenediamine **(1)** by $FeCl_3$. So by coupling phenazine **(2)** with different aldoses by stirring in the presence of I_2 and acetic acid at room temperature gave compounds **(4)**, **(5)** and **(6)** respectively and by acetylation of compound **(4)** with acetic anhydride and pyridine gave **(7)**. On the other hand, heating of **(1)** or /and **(2)** with aldoses in the presence of hydrazine hydrate, acetic acid, conc. hydrochloric acid and water gave compound **(8)** and **(9)** respectively. Acetylation of compound **(9)** gave **(10)**, while heating compound **(2)** with D-xylose and phenyl hydrazine hydrochloride and diluted acetic acid gave **(11)**. Also, phenazine **(3)** was coupled with xylose by microwave irradiation in the presence of iodine gave oxazole derivative **(12)**. Some of the synthesized compounds have been screened as antibacterial and antifungal. The structures of the synthesized compounds have been deduced from their elemental analysis and spectral data.

KEYWORDS

Phenazine;
O-phenylenediamine;
D-xylose;
Antibacterial.

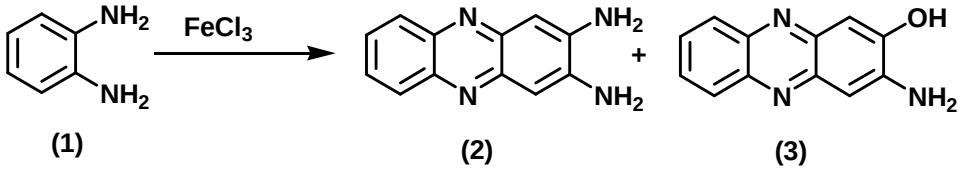
INTRODUCTION

Many of nucleosides have to be active as anticancer, antipyretic and anti-inflammatory[1]. Also, a number of phenazines have demonstrated a broad spectrum of significant biological properties. In continuation of our previous workes on the synthesis of new heterocyclic systems derived from phenazines[2] and pyrazoles for studying their utility as pharmalogical and photoconductive agents, we reported the preparation of a number of C-nuleosides and N-glycosides from different heterocyclic compounds for studying their utility as pharmalogical agents. Structural assignment of all compounds were made on the basis of infrared, nuclear magnetic resonance, mass spectra and elemental analysis and in some cases by comparison with the known properties of the compound or by comparison with samples prepared by unambiguous routes.

RESULT AND DISCUSSION

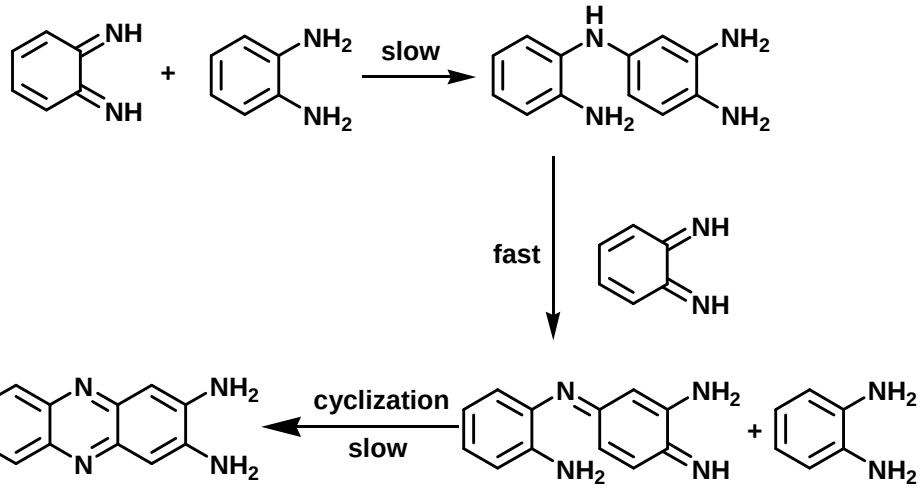
O-Diamino-groups have attracted considerable interest as potential building blocks for much nitrogen containing heterocyclic system. The oxidation of O-phenylenediamine with ferric chloride afforded 2, 3-diaminophenazine **(2)** and 2-amino-3-hydroxyphenazine **(3)**[3] Scheme 1.

The formation of 2, 3-diaminophenazine **(2)** can be illustrated as shown by the following mechanism Scheme 2

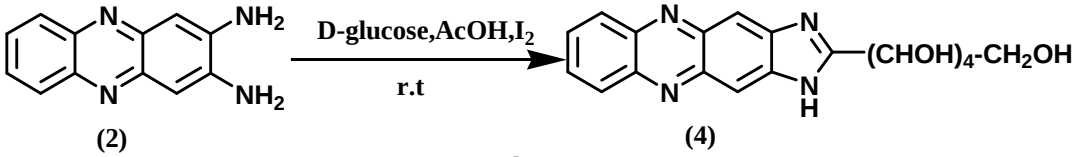


(1) (2) (3)

Scheme 1



Scheme 2



(2) (4)

Scheme 3

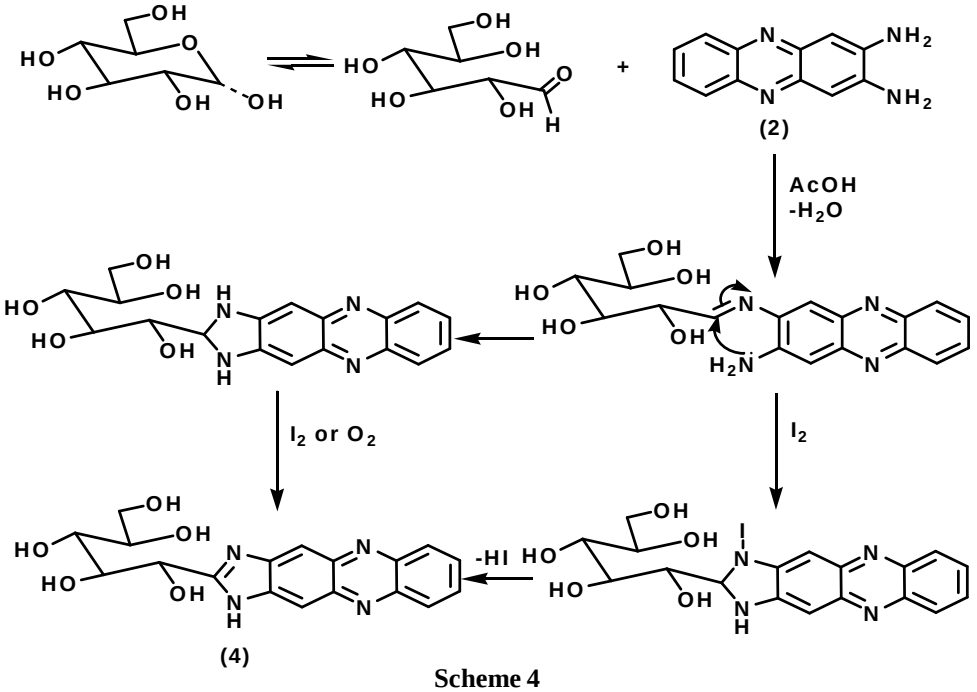
The structure of **(2)**, 3-diaminophenazine **(2)** was confirmed through comparison of its physical data with reported data. The ^{1}HNMR spectrum of **(2)** in DMSO-d_6 exhibited signals at δ 6.26 for $2NH_2$, disappear by deuteration with D_2O.

In recent studies[4] showed that condensation of D-glucose or /and maltose with O-phenylenediamine using iodine as an oxidant or promoter in acetic acid solution to give aldo-benzimidazole in a direct manner. in our study, we tested the direct oxidative condensation of D-glucose with 2,3-diaminophenazine **(2)** in iodine and acetic acid solution gave 2-(D-Gluco-pentitol-1-yl) imidazo [4,5-b] phenazine **(4)** Scheme 3.

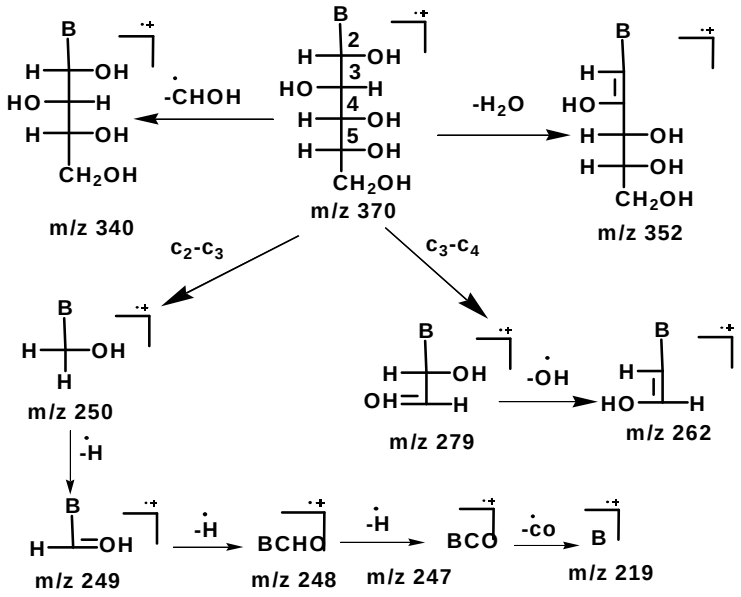
The mechanism of the reaction showed in Scheme 4.

The chemical structure of imidazo [4, 5-b] phenazine derivative **(4)** was confirmed by elemental analysis and spectral data. IR spectrum showed absorption bands at 3396 cm^{-1} due to (OH) groups, 3181 cm^{-1} due to (NH) group, 3080 cm^{-1}due to (CH) aromatic, 2930 cm^{-1}due to (CH) aliphatic, 1645, 1530, 1479 cm^{-1} due to (C=N) and (C=C) groups. The mass spectrum of **(4)** showed molecular ion peak at m/z : 370 (58 %, M), 369 (21 %, M-1), 352 (38 %, M-H_2O), 340 (19 %, M-CHOH), 279 (67 %, BCHOHCHOH) due to cleavage bond at C3-C4 which followed by loss (OH) group gave 262 (25 %, BCHCHOH) and cleavage bond at C2-C3 gave a series of fragmentation at 251 (25 %, BHCH_2OH), 250 (25 %, BCH_2OH), 249 (100 %, BCHOH), 248 (12 %, BCHO), 247 (19 %, BCO) and 219 (56 %, B), where (B)=imidazo [4,5-b] phenazine-2-yl moiety. The formation of the fragments presented in Scheme 5.

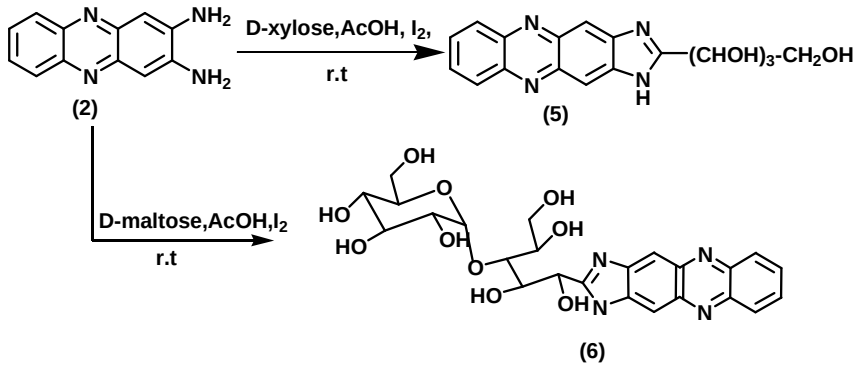
Similarly, treatment of phenazine diamine **(2)** with D-xylose or/and D-maltose after dissolved in aqueous solution of acetic acid and a solution of iodine dissolved in methanol, followed by stirring in open air for **(12)** hours at room temperature gave C-nucleoside of imidazo [4,5-b] phenazines **(5)** and **(6)** respectively as shown in Scheme 6.



Scheme 4



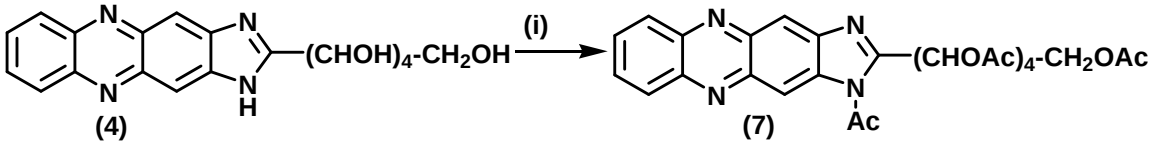
Scheme 5



Scheme 6

The chemical structure of compounds **(5)** and **(6)** are confirmed by elemental analysis and spectral data. The mass spectrum of **(5)** showed molecular ion peaks at 341 (22 %, M+1), 340 (26 %, M), 280 (52 %, BHCHOHCHOH) resulted from cleavage C3-C4 bond, 279 (25 %, BCHOHCHOH) and 261 (25 %, BCHCHO), while cleavage C2-C3 bond showed peaks at m/z :250 (38 %, BCH_2OH), 249 (100 %, BCHOH), 248 (12 %, BCHO), 247 (17 %, BCO), 220 (55 %,BH), 219 (32 %, B), finally cleavage of heterocyclic base fragmentation showed peaks at 193 (38 %, B-CN), 192 (21 %, B-HCN),168(26%,BH_2-HCN-HCN). Where (B)= heterobase moiety. The IR. spectrum of **(6)** showed no absorption band for amino groups and appeared absorption bands at 3394 cm^{-1}due to (OH) groups, 3232 cm^{-1} due to (NH) group, 3180 cm^{-1}due to (CH) aromatic bonds, 2992 cm^{-1} due to (CH) aliphatic bonds, 1672, 1592, 1538 and 1484 cm^{-1} due to (C=N) and (C=C).

Compound **(4)** was treated with acetic anhydride and was boiled under reflux for **(4)** hours afforded acetylated compound **(7)** Scheme 7.



Reacrtion condition: (i) Ac_2O/ pyridine, reflux,4hr.

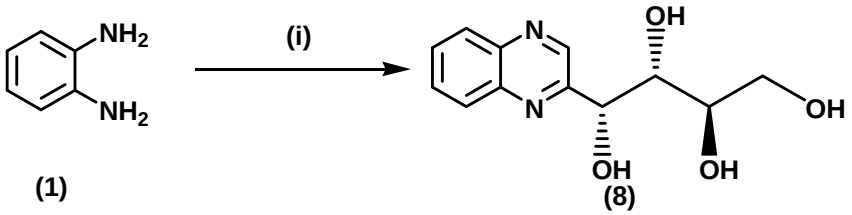
Scheme 7

The IR spectrum of compound **(7)** showed no absorption band for (OH) groups and appeared absorption bands at 3092 cm^{-1} due to (CH) aromatic bonds, 2952 cm^{-1} due to (CH) aliphatic bonds, 1747 cm^{-1} due to (C=O) ester, 1640 cm^{-1} due to (C=O) amide, 1605, 1583,1478 cm^{-1} due to (C=N) and (C=C).

Reaction of phenylenediamine with D-glucose, hydrazine hydrate, hydrochloric acid, acetic acid and water gave **(8)** has been reported[5] Scheme 8

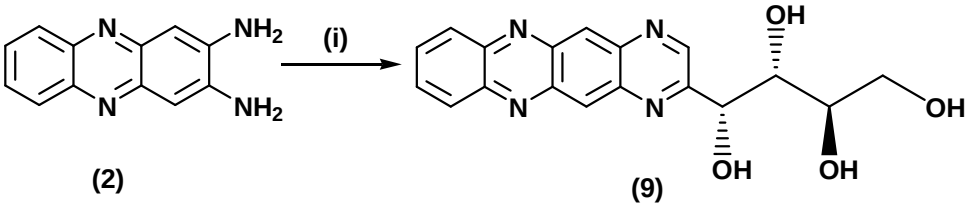
The chemical structure of quinoxaline **(8)** was confirmed by spectral data; the mass spectrum of **(8)** showed molecular ion peaks at m/z; 250 (10%, M), 249 (6%, M-1), 248 (6%, M-2).

Also, the reaction of 2,3-diaminophenazine **(2)** with D-glucose, hydrazine hydrate, hydrochloric acid, acetic acid and water with heating at 100 °C in a sealed flask in water bath for 24 hours gave pyrazino[2,3-b] phenazine derivative **(9)** Scheme 9.



Reaction condition: (i) D-glucose, NH_2NH_2, AcOH, HCl,H_2O,Heat,4hr.

Scheme 8



Reaction condition: (i) D-glucose, NH_2NH_2, AcOH, HCl,H_2O,Heat,24hr.

Scheme 9

The chemical structure of compound **(9)** was confirmed by elemental analysis and spectral data. The I.R. spectrum showed absorption bands at 3462 cm^{-1} due to (OH) groups, 3081 cm^{-1} due to (CH) aromatic,

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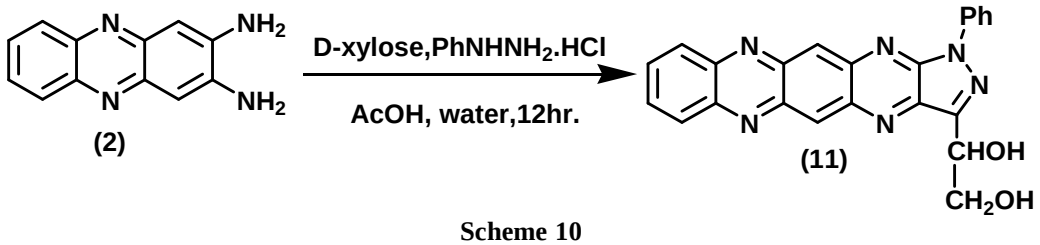
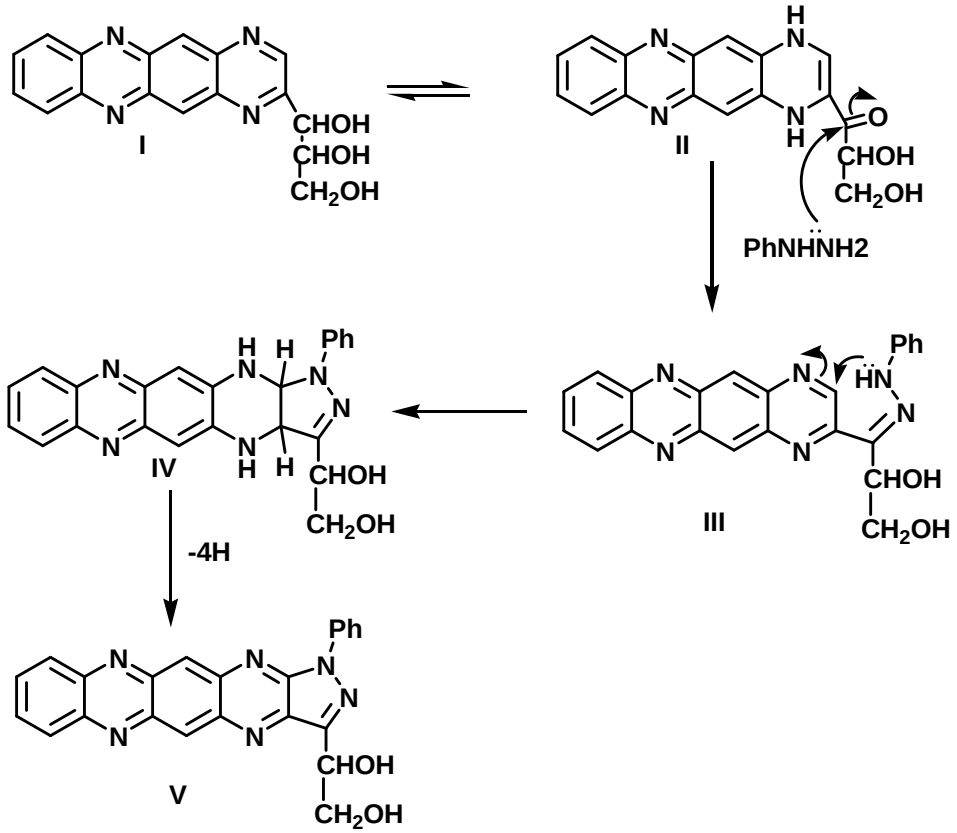
2922 cm^{-1} due to (CH) aliphatic, 1638, 1536, 1500 cm^{-1} due to (C=N) and (C=C) groups. Condensation of one mole of D-xylose and one mole of 2, 3-diaminophenazine **(2)** with five moles of phenylhydrazine hydrochloride in the presence of and acetic acid with heating at 100 °C in a sealed flask in water bath for 12 hours gave compound **(11)** Scheme 10.

The following mechanism has been suggested for the synthesis and indicated that two moles of phenyl hydrazine were reduced during the dehydrogenation of the tetra hydro derivative (IV) which was formed by isomerization of (III) Scheme 11.



Scheme 10



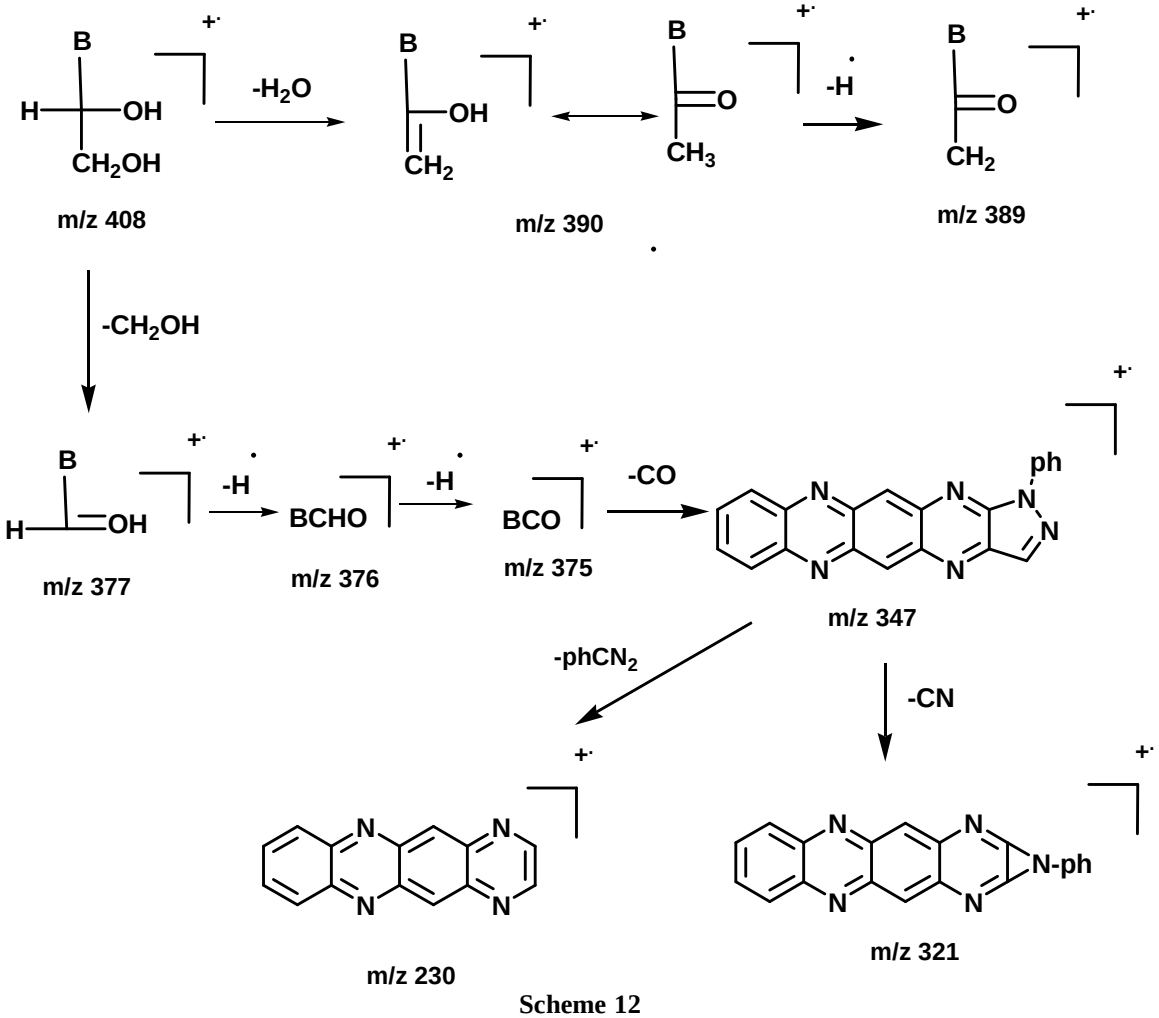
Scheme 11

The chemical structure of compound **(11)** was determined by elemental analysis and the mass spectrum. The mass fragmentation of compound (15) gave ion peaks at m/e: 408 (14%, M), 390 (21 %, M-H_2O), 389 (14 %, BCH_2O), 377 (100 %, BCHOH), 376 (21 %, BCHO) 375 (10 %, BCO), 347 (30 %, B), 321 (24 %, B-CN), 230 (10%, B-phCN_2). The following scheme showed these fragments. Scheme 12

The reaction of 3-amino-2-hydroxyphenazine **(3)** with D-xylose in the presence of iodine as a catalyst solid support and microwave irradiation afforded C-nucleoside of oxazole [4, 5-b] phenazine derivatives **(12)** Scheme 13.

The chemical structure of **(12)** was confirmed by elemental analysis and spectral data. The I.R spectrum showed absorption bands at 3422 cm^{-1} due to (OH) groups,3080 cm^{-1} due to (CH) aromatic bonds, 2920 cm^{-1} due to aliphatic bonds 1636, 1530, 1490 cm^{-1}

due to (C=N) and (C=C) bonds. The mass spectrum of **(12)** showed molecular ion peaks at m/z: 342 (37 %, M+1), 341 (19 %,M), 324 (11 %, M-OH), 311 (39 %, M-CHOH), 280 (64 %, BCHOHCHOH), 265 (39 %, $BH_2CHCHOH$), 263 (8 %, BCHCHOH), 262 (12 %, BCH CHO), 250 (100 %, BCHOH), 249 (16%, BCHO), 220 (22 %, B), 192 (25 %, B-CO), 104 (7 %, PhCNH).



Scheme 12

Scheme 13

ANTIMICROBIAL ACTIVITY

The in vitro antimicrobial activity of the synthesized compounds was investigated against several pathogenic representive Gram-positive bacteria *(Staphylococcus aureus)* and Gram-negative *(Escherichia coli)*, also the synthesized compounds was investigated against two fungus by using the disk diffusion method[6,7].

The medium for cultivation of the test organisms was nutrient agar and each compound dissolved in DMSO of concentration (1mm/1mg). Generally, as showed in TABLE 1 phenazine derivatives **(3)** and **(6)** showed a moderate activity against Gram positive bacteria *(Staphylococcus aureus)*, Gram negative bacteria *(Escherichia coli)* and (*candida albicans*) fungus, while they showed no activity against *(aspergillus flavus)* fungus. On the other hand phenazine deriva-

tives **(3)** and **(5)** showed a moderate activity against Gram positive bacteria (*Staphylococcus aureus*) and (*candida albicans*) fungus while their effect against Gram negative bacteria (*Escherichia coli)* was weak and no activity was showed against (*Aspergillus flavus*) fungs.

Phenazine derivatives **(8)** and **(9)** showed a strong activity against Gram positive bacteria (*Staphylococcus aureus*) with remarkable of compound **(4)**. On the other hand compound **(9)** showed a weak activity against Gram negative bacteria (*Escherichia coli*), while compound **(3)** showed a strong activity. Also compound **(7)** had a moderate activity against (*Candida albicans*) fungus while compound **(9)** had no effect and the both compounds showed no activity against (*Aspergillus flavus*) fungs.

TABLE 1 : Antimicrobial activity of the compounds considered.

Sample	Inhibition zone diameter (mm / mg Sample)			
	Escherichia coli (G^-)	Staphylococcus aureus (G^+)	Aspergillus flavus (Fungus)	Candida Albicans (Fungus)
Control : DMSO	0.0	0.0	0.0	0.0
St. Tetracycline	23	32	12	15
St. Amphotericin B	13	13	17	19
3	6	14	8	12
5	12	15	9	11
6	12	14	0.0	12
7	12	16	11	13
8	12	24	0.0	0.0
9	19	22	5	10

EXPERIMENTAL

All reagents and solvents were purified either by recrystallization or distillation, unless otherwise. Thin layer chromatography was carried out using indicating silica gel. Infrared spectra were recorded as potassium bromide discs on a Perkin-Elmer 383 spectrometer. ^1H and ^{13}C- NMR spectra were obtained on a Brucker AC 200F instrumental at r.t in the solvent idicated chemical shifts are reported in pmm from TMS as the internal standard. The type of signals was indicated by the following letters. Also ^1H and ^{13}C- NMR spectra were measured on a Varian spectrophotometer at 300MHz using DMSO-d6 or CDCl3 as solvent at chemistry department faculty of science, Bardouex University – France. Mass spectra were determined at 70 or 15 electron volt by using AE / MS 30 mass spectrometer. Analytical data were performed by the microanalytical data unit at chemistry department faculty of science, Bardouex university – France and Cairo university, Egypt. All melting points were recorded using thermal melting point apparatus and were uncorrect.

2, 3-Diaminophenazine (2) and 2-amino-3-hydroxyphenazine (3)

O-phenylenediamine **(1)** (5.4 g) was dissolved in Con HCl (8.3 ml) and distilled water (250 ml). A filtered solution of ferric chloride (40 g in water 75 ml) was added slowly with stirring. after standing overnight at room temperature, the red brown colored, crystalline product was filtered off, washed with cold dilute (0.3 N) HCl until free from ferric ions then dissolved in hot water. 2,3-diaminophenazine **(2)** was precipitated by the addition of a concentrated solution of KOH, the product product was filtered off, washed with water and dried at 100-110 °C. The strongly alkaline filterate was heated and acidified (PH 4.5) with glacial acetic acid. After cooling the product **(3)** was collected, washed with water and dried without purification. Compound **(2)** obtained as yellow powder in 48 % yield, m.p. over 300 °C. The ^{1}HNMR in DMSO-d_6 δ 6.26 (s, 4H, $2NH_2$), disappear by deuteration with D_2O, 6.92 (s, 2H, H_{ar}.), 7.53 (m, 2H, Har.) and 7.88 (m, 2H, Har.). The ^{13}C-NMR in DMSO-d_6 exhibited 111.75 (C_8, C_9); 137.25 (C_7, C_{10}, C_4, C_1); 149.67 (C_2, C_3); 151.75 (C_5, C_{12}) and 154.07 (C_6, C_{11}).

Compound **(3)** obtained as orange powder in 45 % yield, m.p. over 300 °C.

2-(D-gluco-pentitol-1-yl) imidazo [4,5-b] phenazine (4)

A mixture of D-glucose (1mmol, 0.180 g) and *O*-diaminophenazine **(2)** (1mmol, 0.210 g) in 7 ml water and (3 ml) acetic acid, then a solution of (1mmol, 0.254 g) of iodine dissolved in (2 ml) of methanol was added, the mixture was stirred at room temperature for 24 hours until the reaction was completed, the reaction mixture quenched by $Na_2S_2O_3$ and the solvent was evaporated, the residue washed with water and co evaporated with ethanol gave **(4)** as a red powder in 65% yield, m.p.

180-182 °C. IR (cm^{-1}, ν): 3396 (OH) groups, 3181(NH) group, 3080 (CH) aromatic, 2930 (CH) aliphatic, 1645, 1530, 1479 (C=N) and (C=C) cm^{-1} groups. MS (m/z %): 370(58 %), 369(21 %,), 352 (38 %), 340 (19 %), 279 (67 %), 262 (25 %), 251(25 %,), 250 (25 %), 249 (100 %), 248 (12 %), 247 (19 %) and 219 (56 %). Anal. Calcd for $C_{18}H_{18}N_4O_5$ (370.36): C, 58.37; H, 4.90; N, 15.13. Found: C, 58.35; H, 4.87; N, 15.11.

2-(D-xylo-tetritol-1-yl) imidazo [4,5-b] phenazine (5)

A mixture of D-xylose (1mml, 0.160 g) and compound **(2)** (1mmol, 0.210 g) dissolved in (4 ml) acetic acid and (8 ml) water, then (1mmol, 0.254 g) of iodine dissolved in (2 ml) of methanol was added, the mixture was stirred at room temperature for 24 hours and the reaction was monitored by TLC then the reaction mixture quenched by $Na_2S_2O_3$ and the solvent was evaporated, the residue washed with water and recrystallized from ethanol gave **(5)** as a reddish brown powder in 60% yield, m.p. 248-250 °C; MS (m/z %): 341 (22 %), 340 (26 %), 280 (52%), 279 (25 %), 261 (25 %), 250 (38 %),249 (100 %), 248 (12 %), 247 (17 %), 220 (55%),219 (32%), 193 (38 %), 192 (21 %),168 (26 %). Anal. Calcd for: $C_{17}H_{16}N_4O_4$, (340.33): C, 59.99; H, 4.74; N, 16.64. Found: C, 59.95; H, 4.72; N, 15.62.

2-[(1,2,4,5-tetrahydroxyl)-3-O-(2,3,4,5-tetrahydroxy-β-D-glucopyranosyl)imidazo [4,5-b]phenazine (6)

A mixture of D-maltose (1mml, 0.342 g) and compound **(2)** (1mmol, 0.210 g) dissolved in (5 ml) acetic acid and (8 ml) water, then (1mmol, 0.254 g) of iodine dissolved in (2 ml) of methanol was added, the mixture was stirred at room temperature for 48 hours and the reaction was monitored by TLC then the reaction mixture quenched by $Na_2S_2O_3$ and the solvent was evaporated, the residue washed with water and recrystallized from ethanol gave **(6)** as a reddish brown powder in 40% yield, m.p. 193-195 °C. IR (cm^{-1}, ν): 3394 (OH), 3232 (NH), 3180 (CH) aromatic bonds, 2992 (CH)aliphatic bonds, 1672,1592,1538 and 1484 cm^{-1}(C=N) and (C=C).MS (m/z %): 534 (60%), 532 (9%), 504 (25%), 477 (49%), 369 (23%), 281(8%), 280 (27%), 279 (5 %), 261 (6 %), 251 (9 %), 250 (15 %), 249(100 %), 234 (15%), 221 (12%), 220 (56%),194(7%) and 193(28%).Anal. Calcd for: $C_{24}H_{28}N_4O_{10}$ (532.50): C, 54.13; H, 5.30; N, 10.52. Found:C, 54.15; H, 5.29; N,10.60.

Synthesis of 1-(N-acetyl)-2-(1,2,3,4,5-penta-O-acetyl-D-glucopentitol-1-yl)imidazo[4,5-b]phenazine (7)

A suspension of compound **(4)** (1mmol, 0.370 g) was boiled with 15ml of acetic anhydride under reflux for 4 hours. The hot solution was poured onto crushed ice the crude product washed successively with water and dried then recrystallized from petroleum ether to gave **(7)** as a red crystals, yield 73%. m.p. 135-137 °C. IR (cm^{-1}, ν): 3092 (CH) aromatic bonds, 2952 (CH) aliphatic bonds, 1747 (C=O) ester, 1640(C=O) amide, 1605, 1583, 1478 cm^{-1} (C=N) and (C=C).

MS (m/z %): 622 (62%), 579(100%), 520(20%), 489(9%), 460 (5%), 447(19%), 418 (29%), 346 (19%), 333 (8%), 304 (15%), 291(63%), 261(19%), 234 (32%). Anal. Calcd for: $C_{30}H_{30}N_4O_{11}$ (622.58): C, 57.88; H, 4.86; N, 9.00. Found: C, 57.84; H, 4.84; N, 8.98.

2-(D-arabino-tetritol-1-yl) quinoxaline (8)

A solution of d-glucose (1mmol, 0.180 g) in water 40 ml was heated with phenylenediamine **(1)** (1mmol, 0.108 g), hydrazine hydrate 0.28 ml, concentrated HCl (0.3 ml) and glacial acetic acid (2 ml) in a sealed flask for 4 hours in a boiling water bath. The flask was cooled, opened and the precipitate obtained was filtered off, wash successively with water, 50% ethanol and ether. Then recrystallized from methanol to give **(8)** as colourless needles, 75% yield m.p. 181-184 °C. MS (m/z %): 250 (10 %), 249 (6 %), 248 (6 %).Anal. Calcd for $C_{12}H_{14}N_2O_4$ (250.25): C, 57.21; H, 5.61; N, 11.32. Found: C, 57.24; H, 5.63; N, 11.34.

2-(D-arabino-tetritol-1-yl) pyrazino [2,3-b] phenazine (9)

A solution of D-glucose (1mmol, 0.180 g) in water (50 ml) was heated at 100 °C with compound **(2)** (1mmol, 0.210 g), hydrazine hydrate (0.3 ml), concentrated HCl (0.28 ml) and glacial acetic acid 3 ml in a sealed flask for 24 hours in water bath. the flask was cooled opened and the precipitate obtained was filtered off, washed successively with water, 50% etha-

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nol and ether, then recrystallized from a mixture of DMF and water gave **(9)** as a faint brown powder, yield 49 %, m.p. 243-245 °C. IR (cm^{-1}, ν): 3462 (OH), 3081 (CH) aromatic, 2922 (CH) aliphatic, 1638, 1536, 1500 cm^{-1} (C=N) and (C=C). MS (m/z%): 352 (27%), 335 (31%), 321 20%), 291 (43%), 276 (20 %), 275 (42 %), 274 (15 %), 273 (57 %),263(63 %),262 (30%), 261 (100%), 260(44%), 259 (12 %), 231 (36 %), 206 (35 %), 205 (11 %), 204 (25 %),179(57 %), 177(26 %), 104 (45 %). Anal. Calcd for: $C_{18}H_{16}N_4O_4$ (352.34): C, 61.36; H,4.58; N,15.90. Found:C, 61.34;H, 4.54; N, 15.91.

2- (1,2,3,4-tetra-O-acetyl-D-arabino-1-yl) pyrazino [2,3-b] phenazine (10)

A suspension of 13 (1mmol, 0.352 g) in acetic anhydride (15 ml) was boiled under reflux for 4 hours. The hot solution was poured onto crushed ice and the acetate was formed, filtered off, washed with water then recrystallized from ethanol gave **(10)** as a pale yelleow powder, 60% yield, m.p. 181-182 °C. IR (cm^{-1}, ν): 3058 (CH) aromatic bonds, 2942 (CH) aliphatic bonds, 1746 (C=O) ester, 1651, 1600, 1560, 1484 cm^{-1} (C=N) and (C=C). The mass fragmention gave ion peaks at m/z: 520(27 %), 460 (18 %), 418 (8%), 400 (4 %), 387(8 %), 358 (16 %), 345 (12 %), 316 (8 %), 303 (7 %), 274 (26 %), 261 (38 %), 245 (9 %), 231 (8 %), 204 (16%), 178 (22%), 104 (13%) and 77 (100 %). Anal. Calcd for $C_{26}H_{24}N_4O_8$ (520.49): C, 60.36; H, 4.65; N, 10.76. Found: C, 60.34; H, 4.64; N, 10.75.

(s)-1-(1-phenyl-1H-1, 2, 4, 6, 11, 13-hexaazacyclopenta [b] naphthacen-3-yl) ethane-1, 2-diol (11)

A portion of 2 (1mmol, 0.210 g), phenylhydrazine hydrochloride (5 mmol, 0.720 g) and glacial acetic acid (4 ml) was added to solution of D-xylose (1mmol, 0.160 g) in (50 ml) water. The mixture was heated in a sealed flask for 12 hours at water bath temperature of 100 °C. After cooling the solid is collected by filteration and washed thoroughly with water then ethanol and finally with ether gave the desired product **(11)** with yield 57% as a brown solid, m.p. 189-191 °C. MS (m/z, %): 408 (14%), 390 (21%), 389 (14%), 377 (100 %), 376 (21%) 375 (10%), 347 (30%), 321(24%), 230 (10%). Anal. Calcd for $C_{23}H_{16}N_6O_2$ (408.41): C, 67.64; H, 3.95; N, 20.58. Found: C, 67.60; H, 3.99; N, 20.57.

2-(D-xylo-tetritol-1-yl) oxazolo [4,5-b] phenazine (12)

A mixture powder of D-xylose (1 mmol, 0.160 g), 3-amino-2-hydroxyphenazine **(3)** (1 mmol, 0.211 g) and iodine (1 mmol, 0.254 g) as a catalyst solid support was grained in (20 ml) glass beaker and irradiated in microwave 400 watt for 4 minutes, the reaction mixture was controlled by TLC until the reaction was completed then the grained powder washed with methanol and ether, filtered off and the product recrystallized from ethanol gave **(12)** as a brown powder, 63% yield, m.p. 200-202°C. IR (cm^{-1}, ν): 3422 (OH) groups, 3080 (CH) aromatic bonds, 2920 aliphatic bonds 1636,1530,1490 cm^{-1} (C=N) and (C=C) bonds. The mass spectrum showed molecular ion peaks at m/z: 342 (37 %), 341(19 %), 324 (11 %), 311 (39 %), 280 (64 %), 265(39 %), 263 (8 %), 262 (12 %), 250 (100 %), 249(16 %), 220(22 %), 192 (25 %) and 104 (7 %). Anal. Calcd for $C_{18}H_{17}N_3O_6$ (. 532.50): C, 58.21; H, 4.6; N, 11.32. Found: C, 58.24; H 4.60; N, 11.34.

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