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Use of Modern Technique for Synthesis of Quinoxaline Derivatives as Potential Anti-Virus Compounds

Mahmoud A. Amin,[1,2,*] Mohamed M. Youssef [1,3]

[1] *Current address: Department of Chemistry, Faculty of Science, Taif University, Taif, Saudi Arabia*
[2]*Department of Chemistry, Faculty of Science, Suez Canal University, Ismailia, Egypt*
[3]*Department Chemistry Department, Faculty of Science, Cairo University, Egypt*

ABSTRACT

*The quinoxaline derivatives **(4a,b)** and **(8)** were synthesized by reaction of pyruvic acid and isatine with o-phenylenediamine and 3,4-diaminophenol. The synthesized quinoxalines were reacted with formaldehyde and 4-aminobenzoic acid to yield Mannch products **(5a,b)** and **(9)**. Condensation of **(5a,b)** and **(9)** with o-phenylenediamine yield the quinoxaline benzimidazole derivatives **(6a,b)** and **(10)**. All reaction carried out by using conventional method and heating by microwave.*

INTRODUCTION

The synthesis and chemistry of quinoxalines have attracted considerable attention in the past ten years.[1,2] Some of them exhibit biological activities including anti-viral,[3] anti-bacterial,[4] anti-inflammatory,[5] anti-protozoal,[6] anti-cancer[7] (colon cancer therapies), anti-depressant,[8] anti-HIV,[9] and as kinase inhibitors.[6] They are also used in the agricultural field as fungicides, herbicides, and insecticides.[10,11] Also, quinoxaline moieties are present in the structure of various antibiotics such as echinomycin, levomycin and actinoleutin, which are known to inhibit the growth of gram positive bacteria and they are active against various transplantable tumors.[12] In addition, quinoxaline derivatives have also found applications in dyes,[13] efficient electron luminescent materials,[14] organic semiconductors,[15,16] chemically controllable switches,[17] building blocks for the synthesis of anion receptors,[18] cavitands,[19] and dehydoannulenes.[20] They also serve as useful rigid subunits in macrocyclic receptors in molecular recognition.[21] Numerous methods are available for the synthesis of quinoxaline derivatives which involve condensation of 1,2-diamines with α-diketones,[14] 1,4-addition of 1,2-diamines to diazenylbutenes,[22] cyclization–oxidation of phenacyl bromides[24] and oxidative coupling of epoxides with ene-1,2-diamines.[25] [26-31]

MATERIALS AND METHODS

Melting points were determined in open glass capillaries on a Stuart digital, MPS melting point apparatus and were uncorrected. I.R. spectra were recorded on a Bruker FTIR- Spectrophotometer. NMR spectra were recorded on a Bruker spectrometers. ^{1}H NMR spectra were recorded at 600.1 MHz and ^{13}C NMR at 150.9 MHz. using TMS as an internal standard. Chemical shifts were expressed as δ (ppm) units. Mass spectra were recorded on Shimadzu GCMS-QP1000EX using an inlet type at 70 eV. The Micro analytical Center of Cairo University performed the microanalyses. Microwave reactions were performed with a Millstone Organic Synthesis Unit (MicroSYNTH with

touch control terminal) with a continuous focused microwave power delivery system in a pressure glass vessels (12mL) and (50mL) sealed with a septum under magnetic stirring. The temperature of the reaction mixture was monitored using a calibrated infrared temperature control under the reaction vessel, and control of the pressure was performed with a pressure sensor connected to the septum of the vessel.

Synthesis of 3,4-diaminophenol (2b). 4-amino-3-nitrophenol (**1**) (3g, 16.3mmol) was added to the 40 ml of concentrated hydrochloric acid solution of stannous chloride (16g, 57.5 mmol) at 75ºC to reduce the nitro groups. After heating in microwave at 120 C for 10 min. The sulution was evaporated ro 15 ml. White crystal of 3,4-diaminophenol hydrochloride (**2b**) was obtained by addition of tetrahydro furan to the solution yield 79%.

Synthesis of 3-methylquinoxaline-2(1H)-one (4a):
Hydrochloric acid 6N (30ml) was added to a mixture of pyruvic (0.88g, 10mmol) acid and o-phenylenediamin (1.08g, 10mmol). The reaction mixture was heated for 10 min on hot plate. The resulting yellow precipitated was poured into water (100 ml) and filtered off, wash by water and dried. The product was recrystallization by using ethanol to give (**4a**) as a yellow crystals, (1.1g, 69.2%) yield, m.p. 253- 254º C. ^{1}H-NMR, ($CDCl_3$); δ 2.6 (s,3H,CH_3), 7.35 (m,2H,H-Ar); 7.5 (dd,1H, J=7.2, 7.8, H-Ar); 7.8 (d,1H, J=8.4,H-Ar), 11.79 (s,1H, NH). ^{13}C-NMR ($CDCl_3$); 21.2 (q,CH_3), 115.3 (d, C-8), 123.6 (d, C-7), 125.8 (d, c-5), 129.2 (d,C-6), 131.7 (s, C-10), 133.7 (s, C-9), 154.6 (s, C-3), 156.1 (s, C-2). IR 3300, 3066, 2951, 1671, 1599, 1519, 1361, 1312, 1228, 1079, 894, 837, 765 cm^{-1}. Anals. $C_9H_8N_2O$ Calc. C: 67.49; H: 5.03; N:17.49. Found: C:67.31; H:5.14 ; N: 17.33.

Synthesis of 6-hydroxy-3-methylquinoxaline-2(1H)-one (4b):
The compound (**4b**) was obtained as a yellow crystals (1.18g, 66% yield) from 1.2g (10mmol) of (**2b**) as described for synthesis of (**4a**), m. p. 210-211ºC. The product was crystallized from ethanol water (1:1). ^{1}H-NMR, ($CDCl_3$); δ 2.6 (s,3H,CH_3), 6.6 (s,1H,H-Ar); 6.84 (d,1H, J=8.3, H-Ar); 7.2 (s,1H,H-Ar), 7.5 (d, 1H, J= 8.3, H-Ar) 11.6 (s,1H, NH). ^{13}C-NMR ($CDCl_3$); 20.3 (q,CH_3), 110.2 (d), 112.6 (d), 117.8 (s), 120.1 (d), 142.9 (s), 161.2 (s), 161.5 (s), 16403 (s). Anals. $C_9H_8N_2O_2$ Calc. C: 61.36, H: 4.58; N:15.90 ;. Found: C:61.25 , H:4.67 ; N: 15.87.

Synthesis of 4-{[-3-methyl-2-oxoquinoxaline-1(2H) methyl]amino-}benzoic acid (5a):
Method (A)
To a mixture of (**4a**) (0.5g, 3.1mml) and formaldehyde (5ml) 4-aminobenzoic acid (0.425g, 3.1mmol) in ethanol (10 ml) was added. The reaction mixture was refluxed 8 hours, pour into water. The precipitated was filtered off and dried. The product was recrystallized by using ethanol to give (**5a**) (0.68g, 70 %) yield, m.p. 237-239ºC.

Method (B)
The same reactants of *Method A* were heated in microwave oven at 500 W and 120ºC for 15 min. The reaction mixture was treated in a similar manner to *Method A* to obtain compounds **5a** in 92% yield.

^{1}H-NMR, ($CDCl_3$ + DMSO-d_6); δ 2.51 (s,3H,CH_3), 3.6 (d, 1H, J= 12.6, CH_2), 3.91 (s, 1H, OH), 4.3 (d, 1H, J= 12.6, CH_2), 7.1 (d, 1H, J= 8.4, H-Ar); 7.3 (t, 1H, J=7.2, H-Ar); 7.34 (d, 1H, J= 7.8, H-Ar), 7.46 (t, 1H, J=7.2. 7.8, H-Ar), 7.78 (d, 1H, J= 7.8, H-Ar), 7.89 (d, 1H, J= 8.4,H-Ar), 12.39 (s,1H, NH). ^{13}C-NMR ($CDCl_3$+ DMSO-d_6); δ 34.96 (q,CH_3), 50.89 (d, CH_2), 114.76 (d, C-Ar), 115.5 (s, C-Ar), 120.87 (d, C-Ar), 123.2 (d, C-Ar), 128.56 (d, C-Ar), 129.79 (s, C-Ar), 131.2 (d, C-Ar), 131.6 (s,C-Ar), 131.97 (s, C-Ar), 152.1 (s, c-Ar), 154.68 (s, C-3Ar), 158.99 (s, C=O), 167.8 (s, C=O). IR 3300-2600 (brs), , 1675, 1597, 1525, 1474, 1367, 1318, 1238, 1087, 897, 827, 775 cm^{-1}. The molecular ion peak at m/z 309 (9.2%). Anals. $C_{17}H_{15}N_3O_3$ Calc. C: 66.01, H: 4.89; N:13.58; Found: C:66.23 , H:5.02 ; N: 13.48.

Synthesis of 4-{[6-hydroxy-3-methyl-2-oxoquinoxaline-1(2H) methyl]amino-}benzoic acid (5b):
Method (A)
The compound (**5b**) was obtained as a white crystals (0.71g, 70% yield) from 0.55g (3.1mmol) of (**4b**) as described for synthesis of (**5a**) by *Method A* and (0.91g, 90% yield) by using *Method B*, m. p. 245-246ºC. The product was crystallized from ethanol.

^{1}H-NMR, (DMSO-d_6); δ 2.51 (s,3H,CH_3), 3.6 (d, 1H, J= 12.5, CH_2), 5.1 (s, 1H, OH), 4.3 (d, 1H, J= 12.5, CH_2), 7.0 (d, 1H, J= 8.4, H-Ar); 7.2 (t, 1H, J=7.2, H-Ar); 7.4 (d, 1H, J= 7.8, H-Ar), 7.7 (d, 1H, J= 7.8, H-Ar), 7.8 (d, 1H, J= 8.4,H-Ar), 12.4 (s,2H, NH,OH). ^{13}C-NMR (DMSO-d_6); δ 34.96 (q,CH_3), 50.89 (d, CH_2), 114.76 (d, C-Ar), 115.5 (s, C-Ar), 120.87 (d, C-Ar), 123.2 (d, C-Ar), 128.56 (d, C-Ar), 129.79 (s, C-Ar), 131.2 (d, C-Ar), 131.6 (s,C-Ar), 131.97 (s, C-Ar), 152.1 (s, c-Ar), 154.68 (s, C-Ar), 158.99 (s, C=O), 167.8 (s, C=O). IR 3300-2600 (brs), 1677, 1647, 1598, 1521, 1473, 1366, 1317, 1230, 1080, 896, 847, 770 cm^{-1}. The molecular ion peak at m/z 323 (12.5%). Anals. $C_{17}H_{15}N_3O_4$ Calc. C: 62.67; H: 4.65; N:12.92; Found: C:62.59; H:5.1; N: 12.86.

Synthesis of 1-({[4-(1H-benzimidazol-2-yl)phenyl]amino}methyl)-3-methylquinoxa-line-2(1H)-one (6a).
Method (A)
To a mixture of (**5a**) (2.0g, 6.5mml), and o-phenylenediamine (0.7g, 6.5mmol), 6N hydrochloric acid (50ml) was added. The reaction mixture was refluxed 7 hours, pour into water and neutralized with a solution of sodium carbonate. The precipitated formed was filtered off. The product was recrystallized by using ethanol to give (**6a**) (1.82g, 74 %) yield, m.p. 289-291º C.

Method (B)
The same reactants of *Method A* were heated in microwave oven at 500 W and 120ºC for 20 min. The reaction mixture was treated in a similar manner to *Method A* to obtain compounds **6a** in 95%.

^{1}H-NMR, (DMSO-d_6); δ 2.51 (s,3H,CH_3), 5.1 (s, 2H, CH_2), 6.5-8.0 (m, 11H, H-Ar); 11.2 (s,1H, NH). ^{13}C-NMR (DMSO-d_6); δ 20.1 (q, CH_3), 24.50 (q,CH_3), 52.23 (d, CH_2), 112.72 (d, C-Ar), 112.9 (d,C-Ar), 113.62 (d, C-Ar), 116.1 (d, C-Ar), 116.2 (d, C-Ar), 122.87 (d, C-Ar), 123.2 (d, C-Ar), 123. 4 (d, C-Ar), 124.8 (d, C-Ar), 126.71 (d, C-Ar), 126.9 (d, C-Ar), 126.9 (s, C-Ar), 127.8 (d, C-Ar), 136.2 (s, C-Ar), 139.6 (s, C-Ar), 139.90 (s, C-Ar), 140.7 (s, C-Ar), 152.2 (s, C-Ar), 157.6 (s, C-Ar), 167.2 (s, C=O). IR 3245, 3082, 2974, 1675, 1601, 1525, 1367, 1315, 1230, 1081, 896, 833, 771 cm^{-1}. The molecular ion peak at m/z 381 (7.9%).Anals. $C_{23}H_{19}N_5O$ Calc. C: 72.42, H: 5.02; N:18.36 ;. Found: C:72.28 , H:5.16 ; N: 18.45.

Synthesis of 1-({[4-(6-hydroxy-1H-benzimidazol-2-yl) phenyl]amino}-methyl)-3-methylquinoxaline-2(1H)-one (6b).
The compound (**6b**) was obtained as a white crystals (1.69g, 69% yield) from 2.0g (6.2mmol) of (**5b**) as described for synthesis of (**6b**) by *Method A* and (2.25g, 92% yield) by using *Method B*, m. p. >300ºC. The product was crystallized from ethanol.

^{1}H-NMR, ($CDCl_3$ + DMSO-d_6); δ 2.3 (s,3H,CH_3), 2.51 (s,3H,CH_3), 4.7 (d, 2H, J= 12.5, CH_2), 4.9 (d, 1H, J= 12.5, CH_2), 7.1 (d, 1H, J= 8.4, H-Ar); 7.2- 7.35 (m, 4H, H-Ar); 7.34 (d, 1H, J= 7.8, H-Ar), 7.46 (t, 1H, J=7.2. 7.8, H-Ar), 7.58-7.61 (m, 2H, H-Ar), 7.78 (d, 1H, J= 7.8, H-Ar), 7.89 (d, 1H, J= 8.4,H-Ar), 12.14 (s,1H, NH). ^{13}C-NMR ($CDCl_3$+ DMSO-d_6); δ 34.96 (q,CH_3), 50.89 (d, CH_2), 114.76 (d, C-Ar), 115.5 (s, C-Ar), 116.1 (d, C-Ar), 120.87 (d, C-Ar), 123.2 (d, C-Ar), 123. 4 (d, C-Ar), 123.5 (d, C-Ar), 128.56 (d, C-Ar), 129.79 (s, C-Ar), 131.2 (d, C-Ar), 131.6 (s,C-Ar), 131.97 (s, C-Ar), 139.7(s, C-Ar), 139.8 (s, C-Ar), 152.1 (s, C-Ar), 154.68 (s, C-Ar), 155.8 (s, C-Ar), 158.99 (s, C=O). IR 3247, 3078, 2976, 1671, 1603, 1518, 1369, 1319, 1230, 1081, 896, 833, 771 cm^{-1}. IR 3245, 3082, 2974, 1675, 1601, 1525, 1367, 1315, 1230, 1083, 897, 835, 773 cm^{-1}. The molecular ion peak at m/z 395 (13.2%).Anals. $C_{24}H_{21}N_5O$ Calc. C: 72.89, H: 5.35; N:17.71 ;. Found: C:72.78 , H:5.46 ; N: 17.60.

Synthesis of 6H-indolo[2,3-b]quinoaxaline (8)
The compound (**8**) was obtained as a yellow crystals (1.4g, 64% yield) from 1.47g (10mmol) of isatine (**7**) as described for synthesis of (**4a**), m. p. 275-276ºC. The product was crystallized from ethanol

The same reactants in synthesis of (**8**) were heated in microwave oven at 500 W and 120ºC for 15 min. The reaction mixture was treated in a similar manner to obtain compounds **4a** in 87% yield.

^{1}H-NMR, (DMSO-d_6); δ 7.0-701 (m,2H,H-indole), 7.5 (d, 1H, J= 8.2,H-indole), 7.8 (d, j=8, 1H, H-quinoxaline), 8.1 (d, 1H, J= 8.2, H- quinoxaline), 10.3 (s,1H, NH). ^{13}C-NMR (DMSO-d_6); δ 116.10, 120.3, 124.6, 124.9, 128.3, 128.9, 129.4, 129.7, 130.3 132.7, 133.2, 133.9, 139.9. IR 3245, 3082, 1675, 1625, 1525, , 1315, 1230, 1081, 896, 833, 771 The molecular ion peak at m/z 219 (8.8%). Anals. $C_{14}H_9N_3$ Calc. C: 76.70, H: 4.14; N:19.17 ;. Found: 76.60, H: 4.21; N:19.20.

Synthesis of 4-(2-(6H-indolo[2,3-b]quinoaxaline-6-yl)methylamino)-benzoic acid (9):
The compound (**10**) was obtained as a yellow crystals (0.75g, 74% yield) from 1.0g (3.01mmol) of (**9**) as described for synthesis of (**5a**) by *Method A* and (0.99g, 90% yield) by using *Method B*, m. p. . >300ºC. The product was crystallized from ethanol.

^{1}H-NMR, (DMSO-d_6); δ 5.76 (s,2H,CH_2), 6.5 (d, 2H, J= 8.7, CH-Ar), 7.2 (s, 1H, OH), 7.4 (t, 1H, J= 8.0, CH-Ar), 7.1 (d, 1H, J= 8.4, H-Ar); 7.4 (m, 2H, H-Ar); 7.5 (t, 1H, J= 8.2, 7.0, H-Ar), 7.6 (m, 2H, H-Ar), 7.7 (d, 1H, J= 8.7, H-Ar), 7.89 (t, 1H, J= 8.2,H-Ar), 8.8 (d, 1H, J=8.0, 11. 9 (s,1H, NH). ^{13}C-NMR (DMSO-d_6); δ 53.54 (d, CH_2), 114.98 (d, C-Ar), 118.5 (d, 2C, C-Ar), 120.77 (d, C-Ar), 121.6 (s), 122.9 (d,CH), 124.8 (d, C-Ar), 127.22 (d, C-Ar), 127.56 (d, C-Ar),129.1 (d, C-Ar), 130.7 (d, C-Ar), 132.8 (d, 2C, C-Ar), 136.3 (s, C-Ar), 137.2 (s, C-Ar), 138 (s, C-Ar), 150.4 (s, C-Ar), 154.68 (s, C-3Ar), 169.78 (s, C=O). IR 3400-2670 (brs.), 1766, 1622, 1527, , 1318, 1230, 1083,

893, 831, 770 cm^{-1}.The molecular ion peak at m/z 368 (11.0%). Anals. $C_{22}H_{16}N_4O_2$ Calc. C: 71.73, H: 4.38; N:15.21 ;. Found: C:71.62 , H:4.50; N: 15.14.

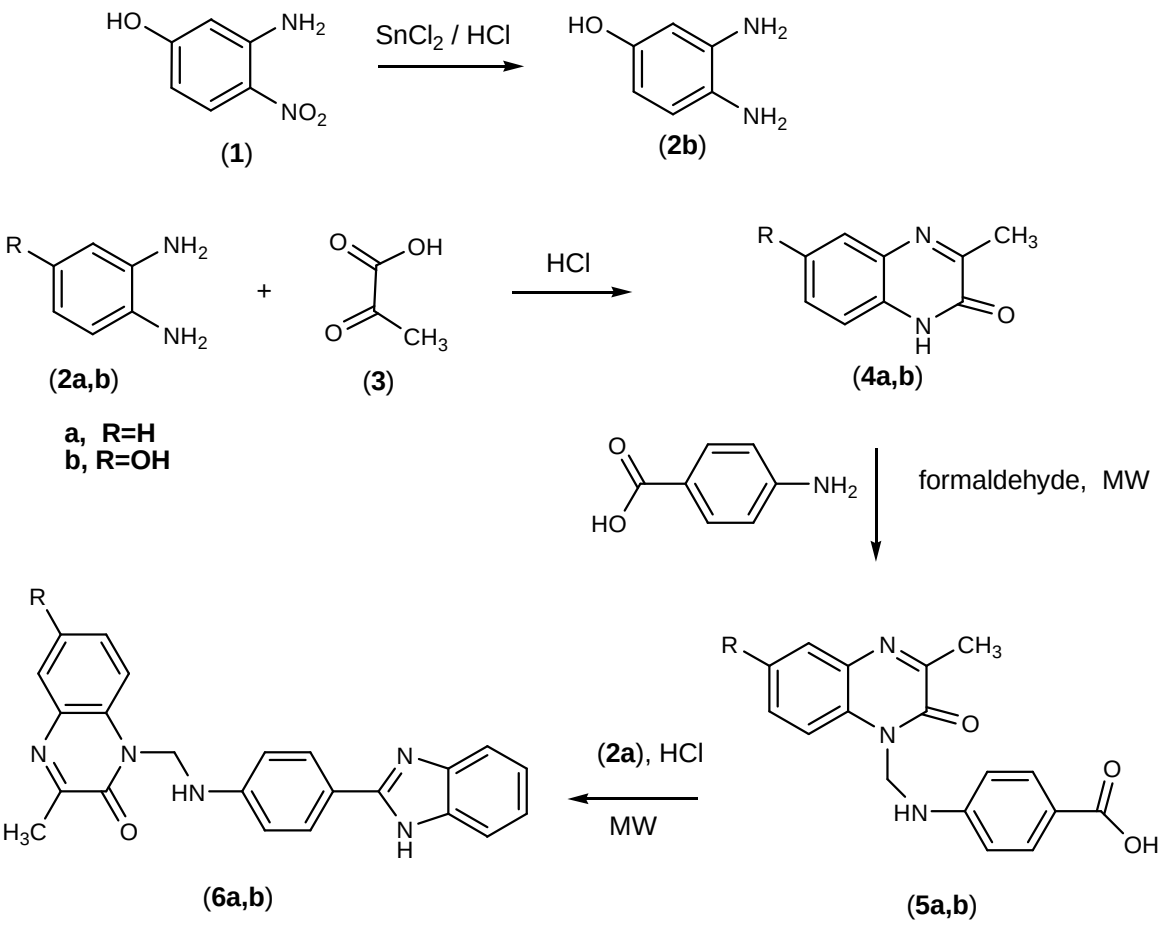
Synthesis of N-((6H-indolo[2,3-b]quinoxaline-6-yl)methyl-4-(1H-benzo[d]imidazo-2-yl)benzenamine (10):
The compound (**9**) was obtained as a white crystals (0.75g, 74% yield) from 0.66g (3.01mmol) of (**8**) as described for synthesis of (**6a**) by *Method A* and (0.99g, 90% yield) by using *Method B*, m. p. . >300ºC. The product was crystallized from ethanol.

^{1}H-NMR, (DMSO-d_6); δ 5.76 (s,2H,CH_2), 6.7-8.3 (m, 16H, CH-Ar), 11. 7 (s,1H, NH). ^{13}C-NMR (DMSO-d_6); δ 53.54 (d, CH_2), 114.5 (d, 2C, C-Ar), 115.6 (d, C-Ar), 116.1 (d, C-Ar),116.2 (d, C-Ar), 120.9 (d, 2C, C-Ar), 122.77 (d, C-Ar), 123.2(d, C-Ar), 123,3(d, C-Ar),124.8 (d, C-Ar),125.2 (s, C-Ar), 126.4 (s), 127.2 (d, C-Ar), 127.3 (d, C-Ar), 127.4 (d, C-Ar),129.3 (d, C-Ar), 130.7 (d, C-Ar), 136.3 (s, C-Ar), 137.4 (s, C-Ar), 137.8 (s, C-Ar), 138.2 (s, C-Ar), 139.7 (s, C-Ar), 139.8 (s, C-Ar), 150.6 (s, C-Ar), 151.3 (s, C-3Ar), 152.1 (s, C-Ar). IR 3251, 3084, 2971, 1620, 1529, , 1315, 1233, 1084, 898, 833, 771 cm^{-1}. The molecular ion peak at m/z 404 (6.6%). Anals. $C_{28}H_{20}N_6$ Calc. C: 76.35, H: 4.58; N:19.08 ;. Found: C:76.5; H:4.6; N: 18.9.

RESULTS AND DISCUSSION

Quinoxaline derivatives form a group of generally less investigated compounds. However, recently growing efforts are made to synthesize and characterize these compounds. Many Quinoxaline derivatives possess very promising properties regarding biological activities as shown in the literature survey. In the present research project, we used the modern microwave technique as well as the conventional methods to prepare some Quinoxaline- compounds with expected biological activity.

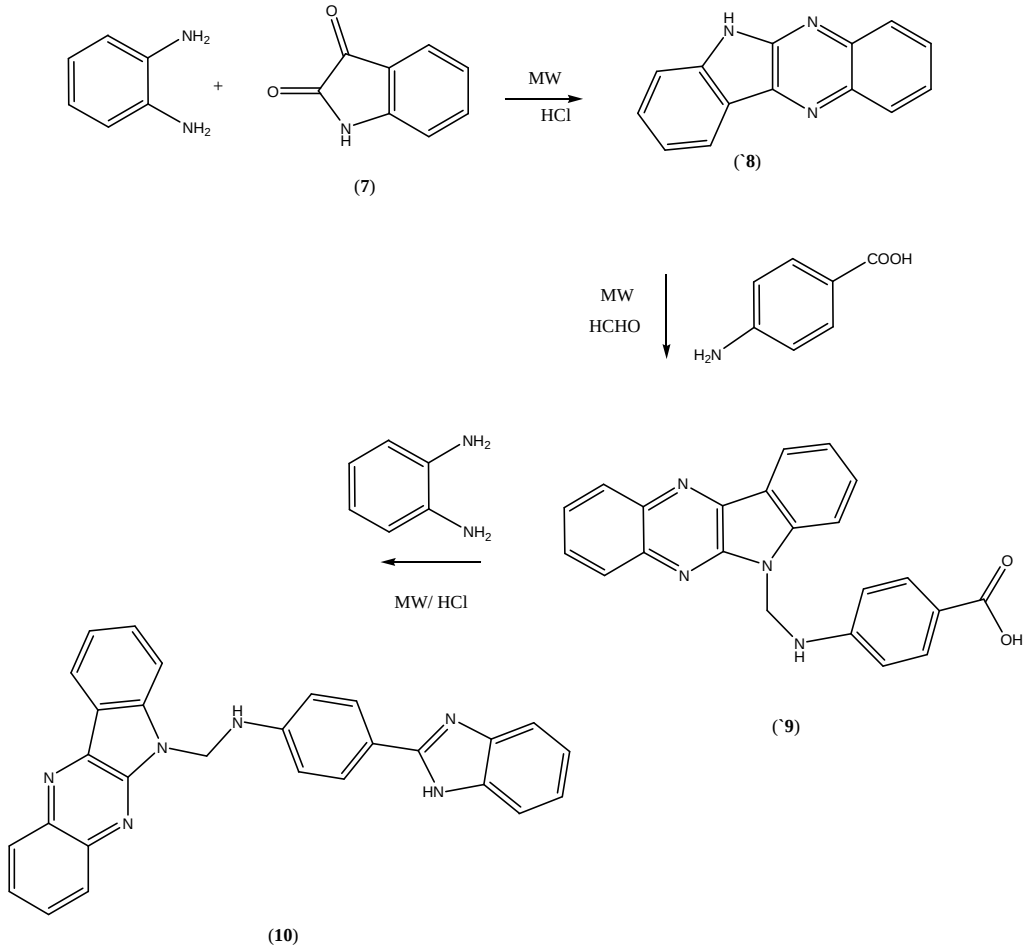
Scheme (1)



Reduction of 4-amino-3-nitrophenol (**1**) was occur by using stannous chloride in the presence of hydrochloric acid to give 3,4-diaminophenol (**2b**). The starting materials 3-methylquinoxaline-2(1H)-one (**4a,b**) was synthesized by the reaction of with o-phenylenediamine (**2a,b**) and pyruvic acid (**3**) in the presence of 6N hydrochloric acid under microwave heating. The 3-methylquinoxaline-2(1H)-one (**4a,b**) was reacted with formaldehyde and 4-aminobenzoic acid using *Mannch* reaction to give 4-{[-3-methyl-2-oxoquinoxaline-1(2H)methyl]amino}benzoic acid (**5a,b**). The 4-{[-3-methyl-2-oxoquinoxaline-1(2H)methyl] amino} benzoic acid (**5,b**) reacted with o-phenylenediamine to give 1-({[4-(1H-benzimidazol-2-yl)phenyl]amino}-methyl)-3-methylquinoxaline-2(1H)-one (**6a,b**), Scheme (1).

Reaction of isatine (**7**) with o-phenylenediamine in the presence of hydrochloric acid give the quinoxaline derivatives (**8**). Condensation of quinoaxaline of (**9**) with o-phenylenediamine in the presence of hydrochloric acid give the quinoxaline benzimidazole derivatives (**10**), Scheme 2.

Scheme (2)



The microwave as a source of heating used for synthesis the above quinoxalines derivatives. Structures of the newly synthesized compounds are proved by using spectroscopic methods such as IR, ^{1}H-NMR and ^{13}C-NMR.

Synthesis of compounds (**6a,b**) and (**10**) were carried out under two different reaction conditions, namely the conventional method and microwave irradiation conditions. Thus, when the reaction of (**4a,b**) was carried out in a refluxing benzoic acid and formaldehyde for 5 hours under TLC control, the product (**5a)** and (**5b**) were obtained in 70% and yield. However, when the same reaction was carried out by heating at 120°C in a microwave oven for 15 minutes, the yields of (**5**a) and (**5**b) were 92%, and 90%, respectively. The condensation of (**5a,b**) with o-phenylenediamine and 3,4-diaminophenol in 6N hydrochloric acid afforded (**6a,b**) in 74 %, 68% yield, respectively. However, when the same reaction was carried out by heating at 120°C in a microwave oven for 15 minutes, the yields of (**6**a) and (**6**b) were 95%, and 92%, respectively. Isatine (**7**) was reacted with (**2a**) in 6N hydrochloric acid afforded (**8**) in 64 % yield, The condensation of (**8**) with o-phenylenediamine in 6N hydrochloric acid afforded (**9**)

in 74 %, 68% yield, respectively. However, when the same reaction was carried out by heating at 100°C in a microwave oven for 10 minutes, the yields of (**6**a) and (**6**b) were 95%, and 90%, respectively. It was then concluded that using microwave as a source of heat not only improves the reaction yield, but also significantly reduces reaction time. IR, Mass and NMR spectra of compounds (**5a,b**), (**6a,b**), (**7**) and (**10**) agreed with the proposed structure.

Antimicrobial activity

The antimicrobial screening procedure of the synthesized compounds as 0.1%solution in DMF was investigated by the disk diffusion method, the antibiotic Assay methods as well as the microbial strains used for the bioassay were illustrated TABLE 1. From the data shown in TABLE2 , it is clear that; the synthesized compounds were generally devoid of activity towards the tested gram negative bacteria (*Klebsiella pneumoniae, Escherichia coli, Pesudomonas aeroginosa and Proteus vulgaris).* Compounds **(6)**, **(7)**, **(9)** and **(10)** are active towards the tested gram-positive bacteria (*Bacillus subtilis, Staphylococcus aureus)* Yeast (*Candida albicans, Candida tropicals).*

TABLL 1 Microbial strains using for investigating the antimicrobial activities

Microbial strain	NRRL strain[a]	Classification	Culture medium
Air-born bacteria			
1- *Bacillus subtilis*	NRS-744	Gram-positive	Nutrient agar medium
Human-pathogenic bacteria			
2-*Staphylococcus aureus*	B-767	Gram-positive	
3-*Klebsiella pneumoniae*	B-17232	Gram-negative	
4- *Escherichia coli*	B-3704	Gram-negative	Nutrient agar medium
5- *Pseudomonas aeroginosa*	B-23	Gram-negative	
6- *Proteus valgaris*	B-123	Gram-negative	
Human-pathogenic yeasts			
7- *Candida albicans*	Y-477	Yeast	Sabaroud dextrose agar
8- *Candida tropicals*		Yeast	

[a]*NRRL= Northern Regional Research Laboratory, U.S. Department of Agriculture, Peoria, Illinois, USA*

TABLE 2 Antimicrobial activities of some synthesis compounds

	Gram-positive		Gram- negative				Yeast	
No	***Bacillus subtili***	***Staphylococcus aureus***	***Klebsiella pneumoniae***	***Escherichia coli***	*Pseudomonas aeroginosa*	*Proteus-valgaris*	*Candida albicans*	*Candida tropicals*
4a	++	++	+	++	+	+	++	++
4b	++	++	++	++	+	+	++	++
5a	+	+	-	-	-	-	+	+
5b	++	++	++	++	++	+	++	++
6a	++	++	-	-	-	-	++	++
6b	++	++	-	-	-	-	++	++
8	+++	+++	++	++	++	++	+++	+++
9	-	-	-	-	-	-	-	-
10	-	-	-	-	-	-	-	-

Date represent zones of inhibition (mm) as follows: - 0 mm, + 1-10 mm, ++ 10-15 mm, +++ 15-10 mm.

CONCLUSION

In summary, this present procedure for the preparation of quinoxalines from aryl- 1,2-diamines and 1,2-diketones by using microwave as a modern technique for heating. The advantages of this method are extremely mild reaction conditions, short reaction times, high yields, simple experimental and isolation procedures, and compliance with the green chemistry protocols.

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