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The synthesis of 2-arylquinoxaline derivatives

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ABSTRACT

A series of new 2-arylquinoxaline derivatives have been synthesized in high yield by condensation of aryl-1,2-diamines with arylglyoxals in DMF at 50-120 ^{o}C.

1. Introduction

Among the various classes of nitrogen-containing heterocyclic compounds, quinoxaline derivatives are an important component of pharmacologically active compounds. Quinoxaline derivatives have various pharamacological activities such as actinoleutin, hinomycin, and levomycin that are known to inhibit growth of gram positive bacteria and are active against various transplantable tumors.[1-6] In addition quinoxaline derivatives are also associated with a wide spectrum of biological activities ranging from antibacterial,[7-10] antifungal,[7,11] antitubercular,[7,12-14] analgesic[9,15] and anti-inflammatory.[15,16] We have reported the synthesis of quinoxaline derivatives from 2-bromo-4-chloro-indanone[17] and arylaminoisoxazol-5(2H)-ones.[18] Here, we report a facile method for the synthesis of 2-arylquinoxalines in good to excellent yields by reaction of 1,2-diaminobenzene derivatives with various arylglyoxals in DMF at 50-120 ^{o}C.

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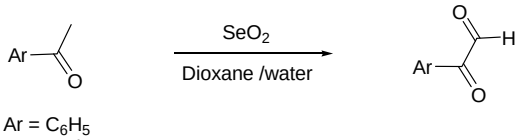
2. Results and Discussion

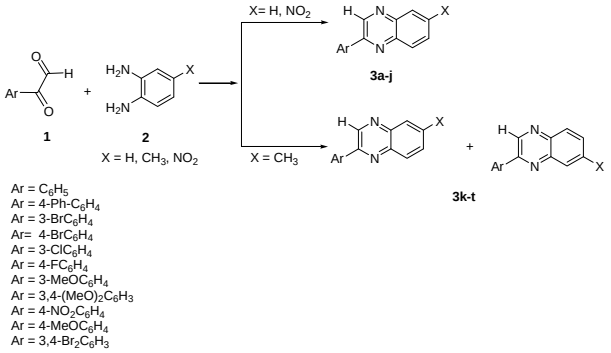
The arylglyoxals were prepared by oxidation of the corresponding acetophenones using SeO_2 (Scheme 1).[19]



Ar = C_6H_5
Ar = 4-Ph-C_6H_4
Ar = 3-BrC_6H_4
Ar= 4-BrC_6H_4
Ar = 3-ClC_6H_4
Ar = 4-FC_6H_4
Ar = 3-MeOC_6H_4
Ar = 3,4-$(MeO)_2C_6H_3$
Ar = 4-$NO_2C_6H_4$
Ar = 4-MeOC_6H_4
Ar = 3,4-$Br_2C_6H_3$

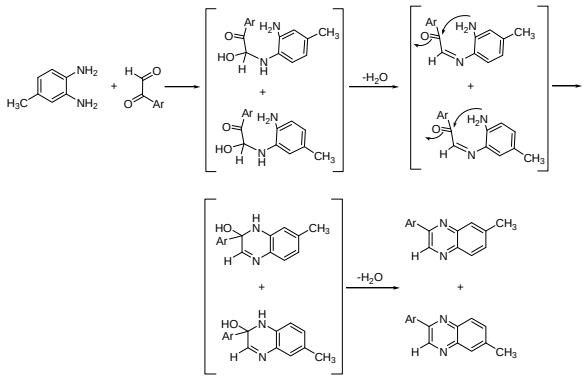
Scheme 1. Synthesis of arylglyoxals

The reaction of arylglyoxals (**1**) with aryl-1,2-diamines (**2**) in DMF at 50-120 ^oC afforded the corresponding 2-arylquinoxalines (**3a-t**) in 68-96% yields (Scheme 2).



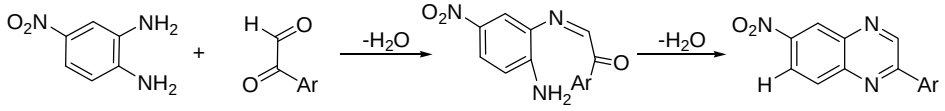
Ar = C_6H_5
Ar = 4-Ph-C_6H_4
Ar = 3-BrC_6H_4
Ar= 4-BrC_6H_4
Ar = 3-ClC_6H_4
Ar = 4-FC_6H_4
Ar = 3-MeOC_6H_4
Ar = 3,4-$(MeO)_2C_6H_3$
Ar = 4-$NO_2C_6H_4$
Ar = 4-MeOC_6H_4
Ar = 3,4-$Br_2C_6H_3$

Scheme 2. Synthesis of 2-arylquinoxalines (**3a-t**)



Scheme 3. Suggested mechanism for synthesis of 2-arylquinoxalines (**3k-t**)

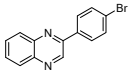
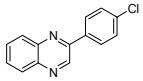
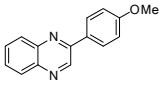
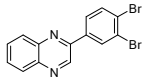
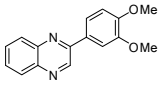
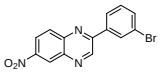
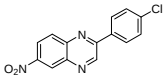
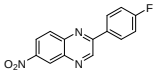
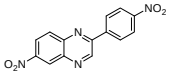
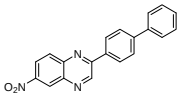
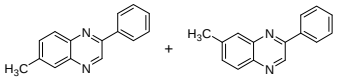
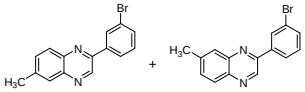
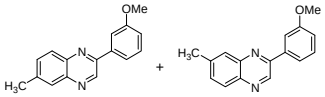
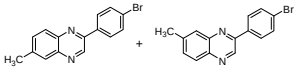
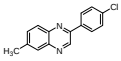
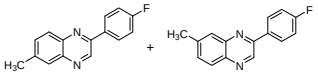
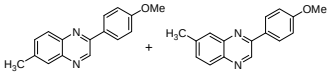
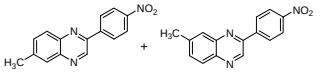
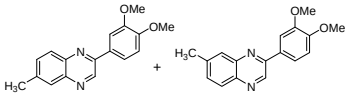
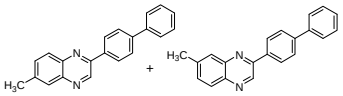
The ^{1}H-NMR spectra of compounds (**3k-t**) show two singlets in the region of δ = 9.23-9.32 ppm, due to the formation of a mixture of two isomers. The proposed mechanism for the synthesis of 2-arylquinoxalines (**3k-t**) is shown in Scheme 3. In case of **3f-j** as the amino group in position 2 is more active than the amino group in position 4 (due to the resonance affect), therefore, it condenses with the formyl group of glyoxals in the first step to form a single product as shown in Scheme 4.



Scheme 4. Suggested mechanism for synthesis of 2-arylquinoxalines (**3f-j**)

It should be mentioned that repeating the reactions at temperatures higher than those mentioned in Table 1 will reduce the yields, due to decomposition.

Table 1. Synthesis of 2-arylquinoxalines (**3a-t**)

Entry	Product (3a-t)	Time (h)	Reaction Temperature (^{o}C)	Yield (%)
a		6	100	81
b		6	90	73
c		6	120	78
d		6	100	79
e		5	120	92
f		4	120	83
g		2	120	74
h		2	50	85
i		8	120	83
j		2	100	84
k		8	100	68
l		4	90	84
m		12	90	87
n		12	80	77
o		8	70	78
p		8	70	72
q		8	90	79
r		9	80	76
s		10	90	96
t		8	80	91

3. Conclusions

The work reported herein provides a highly effective and simple one step method for the synthesis of new 2-arylquinoxalines, which may have pharmaceutical and biological applications.

Acknowledgements

The authors are grateful to the Urmia University for support of this work.

Experimental

General Procedure. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM-300 spectrometer at 300 MHz and 75.5 MHz, respectively. The spectra were measured in $CDCl_3$ or DMSO-d_6 using TMS as the internal standard. Infrared spectra were determined on a Thermo Nicolet (Nexus 670) FT-IR spectrometer, using KBr disks. Microanalyses were performed on a Carlo-Erba Analyzer 1104. Melting points were determined on a digital melting point apparatus (electrothermal) and remain uncorrected.

General Procedure for the Synthesis of 2-Arylquinoxalines (3a-t)
A mixture of arylglyoxal **1** (1 mmol), aryl-1,2-diamine **2** (1 mmol), in DMF (5 ml) were stirred at 50-120 ^{o}C for 2-12 h. The completion of the reactions were monitored with thin-layer chromatography (TLC). After the appropriate time, water was added and the reaction mixture was stirred. The precipitate was then collected, and recrystallized from ethanol to afford pure 2-arylquinoxalines **(3a-t)**.

2-(4-bromophenyl)quinoxaline (3a):
Cream solid; mp: 135 ^{o}C**.** ^{1}H NMR ($CDCl_3$): 7.70-7.84 (m, 4H, ArH), 8.09-8.15 (m, 4H, ArH), 9.32 (s, 1H, ArH) ppm; ^{13}C NMR ($CDCl_3$): δ 125.01, 128.96, 129.09, 129.58, 129.83, 130.50, 132.33, 135.53, 141.53, 142.20,142.65, 150.58 ppm; FT-IR (KBr): ν 3050, 2921, 1586, 1510, 1485, 1312, 1072, 1009, 828, 757 cm^{-1}. Anal. Calc. for $C_{14}H_9BrN_2$: C, 58.97; H, 3.18; N, 9.82. Found: C, 58.74; H, 3.35; N, 9.77%.

2-(4-chlorophenyl)quinoxaline (3b):
Pale yellow solid; mp: 138 ^{o}C. ^{1}H NMR ($CDCl_3$): δ 7.53 (d, J = 8.4 Hz, 2H, ArH), 7.77 (bs, 2H, ArH), 8.13-8.15 (m, 4H, ArH), 9.29 (bs, 1H, ArH) ppm; ^{13}C NMR ($CDCl_3$): δ 128.74, 129.14, 129.37, 129.58, 129.77, 130.46, 135.13, 136.57, 141.60, 142.23, 142.77, 150.55 ppm; FT-IR (KBr): ν 2963, 2936, 2834, 1580, 1489, 1452, 1427, 1313, 1093, 832, 755, 699, 548 cm^{-1}. Anal. Calc. for $C_{14}H_9ClN_2$: C, 69.86; H, 3.77; N, 11.64. Found: C, 69.66; H, 3.81; N, 11.71%.

2-(4-methoxyphenyl)quinoxaline (3c):
Cream solid; mp: 92 ^{o}C. ^{1}H NMR ($CDCl_3$): δ 3.90 (s, 3H, OCH_3),7.08 (d, J =8.4 Hz, 2H, ArH), 7.69-7.78 (m, 2H, ArH), 8.08-8.15 (m, 2H, ArH), 8.18 (d, J = 8.4 Hz, 2H, ArH), 9.30 (s, 1H, ArH) ppm; ^{13}C NMR ($CDCl_3$): δ 55.43, 114.60, 128.98, 129.03, 129.08, 129.22, 129.36, 130.21, 141.14, 142.27, 143.00, 151.40, 161.49 ppm; FT-IR (KBr): ν 3056, 2934, 2833, 1606, 1520, 1324, 1250, 1073, 1029 cm^{-1}. Anal. Calc. for $C_{15}H_{12}N_2O$: C, 76.25; H, 5.12; N, 11.86. Found: C, 76.39; H, 5.01; N, 11.74%.

2-(3,4-dibromophenyl)quinoxaline (3d):
Orang solid; mp: 115 ^{o}C. ^{1}H NMR ($CDCl_3$): δ 7.45 (s, 1H, ArH), 7.66 (d, J = 6.3 Hz, 1H, ArH), 7.81 (bs, 2H, ArH), 8.17 (bs, 2H, ArH), 8.40 (bs, 1H, ArH), 9.31 (bs, 1H, ArH) ppm; ^{13}C NMR ($CDCl_3$): δ 116.30, 116.58, 123.87, 126.03, 128.87, 129.70, 130.27, 130.64, 130.77, 133.25, 138.32, 142.34, 142.57, 150.34 ppm; FT-IR (KBr): ν 3058, 1566, 1549, 1479, 1311, 1080, 960, 758, 687 cm^{-1}. Anal. Calc. for $C_{14}H_8Br_2N_2$: C, 46.19; H, 2.22; N, 7.70. Found: C, 46.01; H, 2.51; N, 7.62%.

2-(3,4-dimethoxyphenyl)quinoxaline (3e):
Yellow solid; mp: 105 ^{o}C. ^{1}H NMR ($CDCl_3$): δ 4.00 (s, 3H, OCH_3), 4.08 (s, 3H, OCH_3), 7.05 (d, *J* = 8.4 Hz, 1H, ArH), 7.74-7.82 (m, 3H, ArH), 7.89 (s, 1H, ArH), 8.11-8.18 (m, 2H, ArH), 9.33 (s, 1H, ArH) ppm; ^{13}C NMR ($CDCl_3$): δ 56.04, 56.10, 110.17, 111.15, 120.50, 129.00, 129.19, 129.27, 129.39, 130.30, 141.12, 142.12, 143.00, 149.74, 151.19, 151.26 ppm; FT-IR (KBr): ν 3057, 2925, 2836, 1598, 1518, 1461, 1430, 1285, 1250, 1026, 764 cm^{-1}. Anal. Calc. for $C_{16}H_{14}N_2O_2$: C, 72.16; H, 5.30; N, 10.52. Found: C, 72.02; H, 5.41; N, 10.63%.

2-(3-bromophenyl)-6-nitroquinoxaline (3f):
Yellow solid; mp: 226-228 ^{o}C. ^{1}H NMR ($CDCl_3$): δ 7.60 (t, *J* = 7.8 Hz, 1H, ArH), 7.82 (d, *J* = 8.1 Hz, 1H, ArH), 8.34-8.43 (m, 2H, ArH), 8.53-8.58 (m, 2H, ArH), 8.92-8.95 (m, 1H, ArH), 9.82 (s, 1H, ArH) ppm; ^{13}C NMR ($CDCl_3$): δ 123.15, 123.91, 124.51, 125.40, 125.74, 127.53, 131.33, 131.86, 134.52, 137.96, 140.79, 144.42, 146.73, 152.57 ppm; FT-IR (KBr): ν 3054, 1551, 1524, 1484, 1350, 1304, 1286, 1193, 1076, 795, 691 cm^{-1}. Anal. Calc. for $C_{14}H_8BrN_3O_2$: C, 50.93; H, 2.44; N, 12.73. Found: C, 50.77; H, 2.32; N, 12.82%.

2-(4-chlorophenyl)-6-nitroquinoxaline (3g):
Cream solid; mp: 261-263 ^{o}C. ^{1}H NMR (DMSO-d_6): δ 7.71 (d, *J* = 8.4 Hz, 2H, ArH), 8.35 (d, *J* = 8.7 Hz, 1H, ArH), 8.45 (d, *J* = 7.8 Hz, 2H, ArH), 8.57 (d, *J* = 8.1 Hz, 1H, ArH), 8.92 (s, 1H, ArH), 9.81 (s, 1H, ArH) ppm; FT-IR (KBr): ν 3052, 2981, 1622, 1592, 1489, 1435, 1311, 834, 780 cm^{-1}. Owing to extreme insolubility, its ^{13}C NMR spectrum could not be measured in any solvent. Anal. Calc. for $C_{14}H_8ClN_3O_2$: C, 58.86; H, 2.82; N, 14.71. Found: C, 58.75; H, 2.78; N, 14.88%.

2-(4-fluorophenyl)-6-nitroquinoxaline (3h):
Yellow solid; mp: 234-236 ^{o}C. ^{1}H NMR (DMSO-d_6): δ 7.48 (t, *J* = 8.7 Hz, 2H, ArH), 8.33 (d, *J* = 9 Hz, 1H, ArH), 8.46-8.51 (m, 3H, ArH), 8.90 (d, *J* = 2.1 Hz, 1H, ArH), 9.79 (s, 1H, ArH) ppm; ^{13}C NMR (DMSO-d_6): δ 116.67, 116.96, 123.53, 124.44, 125.39, 125.52, 130.88, 131.01, 131.13, 131.31, 131.49, 143.84, 146.61, 147.39, 147.64 ppm; FT-IR (KBr): ν 3055, 2925, 2853, 1555, 1524, 1350, 1164, 838 cm^{-1}. Anal. Calc. for $C_{14}H_8FN_3O_2$: C, 62.46; H, 3.00; N, 15.61. Found: C, 62.54; H, 2.98; N, 15.48%.

2-(4-nitrophenyl)-6-nitroquinoxaline (3i):
Cream brown solid; mp: 237-239 ^{o}C. ^{1}H NMR (DMSO-d_6): δ 8.37-8.44 (m, 3H, ArH), 8.57-8.65 (m, 3H, ArH), 8.93 (bs, 1H, ArH), 9.87 (s, 1H, ArH) ppm; ^{13}C NMR (DMSO-d_6): δ 124.66, 125.42, 129.81, 131.40, 131.85, 140.68, 141.47, 146.89, 147.68, 148.22, 149.41, 152.08 ppm; FT-IR (KBr): ν 3093, 2942, 1555, 1519, 1347, 854, 755, 692 cm^{-1}. Anal. Calc. for $C_{14}H_8N_4O_4$: C, 56.76; H, 2.72; N, 18.91. Found: C, 56.66; H, 2.63; N, 18.98%.

2-([1,1'-biphenyl]-4-yl)-6-nitroquinoxaline (3j):
Green yellow; mp: 171-174 ^{o}C. ^{1}H NMR (DMSO-d_6): δ 7.40-7.49 (m, 3H, ArH), 7.77 (d, *J* = 6.8 Hz, 2H, ArH), 7.91 (d, *J* = 7.5 Hz, 2H, ArH), 8.32 (d, *J* = 9.3 Hz, 1H, ArH), 8.48 (bs, 3H, ArH), 8.89 (s, 1H, ArH), 9.82 (s, 1H, ArH); ^{13}C NMR (DMSO-d_6): δ 123.48, 124.42, 125.56, 127.31, 127.90, 128.67, 128.89, 129.11, 129.56, 131.31, 134.54, 139.45, 143.15, 143.97, 147.50, 148.45 ppm; FT-IR (KBr): ν 3055, 2930, 1605, 1547, 1522, 1345, 1191, 1050, 766, 728 cm^{-1}. Anal. Calc. for $C_{20}H_{13}N_3O_4$: C, 73.38; H, 4.00; N, 12.84. Found: C, 73.25; H, 3.88; N, 12.95%.

2-phenyl-6/7-methylquinoxaline (3k):
Cream solid; mp: 89-93 ^{o}C, isomers ratio (67:33). ^{1}H NMR ($CDCl_3$): δ 2.62 (s, 3H, CH_3), 7.55-7.64 (m, 4H, ArH), 7.95-8.03 (m, 2H, ArH), 8.20 (d, *J* = 6.3 Hz, 2H, ArH), 9.27 (s, 1H, H-3, one isomer), 9.29 (s, 1H, H-3, other isomer) ppm; ^{13}C NMR ($CDCl_3$): δ 21.87, 127.43, 127.51, 127.90, 128.46, 128.58, 129.13, 129.99, 130.08, 131.92, 132.67, 138.31, 142.40 ppm; FT-IR (KBr): ν 3055, 2917,

2854, 1540, 1491, 1307, 1026, 827, 766, 688 cm^{-1}. Anal. Calc. for $C_{20}H_{13}N_3O_4$: C, 81.79; H, 5.49; N, 12.72. Found: C, 81.63; H, 5.35; N, 12.95%.

2-(3-bromophenyl)-6/7-methylquinoxaline (3l):
Cream brown solid; mp: 101-104 ^oC, isomers ratio (66:34). ^1H NMR ($CDCl_3$): δ 2.63 (s, 3H, CH_3), 7.44 (t, *J* = 7.8 Hz, 1H, ArH), 7.67-7.69 (m, 2H, ArH), 7.93 (d, *J* = 7.8 Hz, 1H, ArH), 8.05 (d, *J* = 8.1 Hz, 1H, ArH), 8.08-8.11 (m, 1H, ArH), 8.38 (s, 1H, ArH), 9.23 (s, 1H, H-3, one isomer), 9.26 (s, 1H, H-3, other isomer) ppm; ^{13}C NMR ($CDCl_3$): δ 21.92, 123.45, 125.82, 125.92, 127.76, 128.47, 129.13, 130.45, 130.54, 130.59, 138.44, 132.95, 133.02, 141.49, 142.45 ppm; FT-IR (KBr): ν 3058, 2913, 1620, 1538, 1439, 1288, 1058, 966, 822, 774, 689 cm^{-1}. Anal. Calc. for $C_{15}H_{11}BrN_2$: C, 60.22; H, 3.71; N, 9.36. Found: C, 60.39; H, 3.63; N, 9.17%.

2-(3-methoxyphenyl)-6/7-methylquinoxaline (3m):
Cream solid; mp: 84-87 ^oC, isomers ratio (68:32). ^1H NMR ($CDCl_3$): δ 2.61 (s, 3H, CH_3), 3.94 (s, 3H, OCH_3), 7.07 (d, *J* = 8.1 Hz, 1H, ArH), 7.47 (t, *J* = 7.8 Hz, 1H, ArH), 7.72-7.76 (m, 2H, ArH), 7.88-8.07 (m, 2H, ArH), 9.25 (s, 1H, H-3, one isomer), 9.26 (s, 1H, H-3, other isomer) ppm; ^{13}C NMR ($CDCl_3$): δ 21.87, 55.45, 112.50, 112.59, 116.03, 116.12, 119.77, 119.85, 127.88, 128.45, 128.55, 129.12, 130.11, 131.59, 132.65, 138.29, 140.07, 140.25, 140.70, 140.97, 142.28, 142.45, 143.19, 151.52, 160.28 ppm; FT-IR (KBr): ν 2919, 2835, 1607, 1584, 1542, 1507, 1484, 1460, 1041, 829, 784, 625 cm^{-1}. Anal. Calc. for $C_{16}H_{14}N_2O$: C, 76.78; H, 5.64; N, 11.19. Found: C, 76.84; H, 5.52; N, 11.03%.

2-(4-bromophenyl)-6/7-methylquinoxaline (3n):
Cream gray solid: mp: 135-137 ^oC, isomers ratio (66:34). ^1H NMR ($CDCl_3$): δ 2.63 (s, 3H, CH_3), 7.62 (d, *J* = 8.7 Hz, 1H, ArH), 7.70 (d, *J* = 8.7 Hz, 2H, ArH), 7.93 (bs, 1H, ArH), 8.03 (d, *J* = 8.1 Hz, 1H, ArH), 8.09 (d, *J* = 8.7 Hz, 2H, ArH), 9.25 (s, 1H, H-3, one isomer), 9.26 (s, 1H, H-3, other isomer) ppm; ^{13}C NMR ($CDCl_3$): δ 21.80, 21.72, 127.94, 128.10, 128.49, 128.61, 128.93, 128.99, 131.52, 132.16, 132.29, 132.67, 132.83, 135.76, 139.43, 139.81, 140.67, 140.94, 141.82, 141.93, 142.58, 151.23, 161.49 ppm; FT-IR (KBr): ν 3050, 2915, 1621, 1586, 1488, 1072, 833, 823, 777, 492 cm^{-1}. Anal. Calc. for $C_{15}H_{11}BrN_2$: C, 60.22; H, 3.71; N, 9.36. Found: C, 60.32; H, 3.61; N, 9.18%.

2-(4-chlorophenyl)-6-methylquinoxaline (3o) :
Yellow solid; mp: 169-172 ^oC. ^1H NMR ($CDCl_3$): δ 2.63 (s, 3H, CH_3), 7.54 (d, *J* = 8.4 Hz, 2H, ArH), 7.61 (d, *J* = 8.4 Hz, 1H, ArH), 7.94 (s, 1H, ArH), 8.03 (d, *J* = 8.4 Hz, 1H, ArH), 9.16 (d, *J* = 8.4 Hz, 2H, ArH), 9.24 (s, 1H, ArH) ppm; ^{13}C NMR ($CDCl_3$): δ 21.89, 128.39, 128.54, 128.72, 129.09, 129.36, 132.20, 135.27, 136.46, 141.17, 141.80, 142.29, 150.52 ppm; FT-IR (KBr): ν 3052, 2921, 1489, 1435, 1311, 1092, 834, 780 cm^{-1}. Anal. Calc. for $C_{15}H_{11}ClN_2$: C, 70.73; H, 4.35; N, 11.00. Found: C, 70.66; H, 4.22; N, 11.16%.

2-(4-fluorophenyl)-6/7-methylquinoxaline (3p):
Cream solid; mp: 118-121 ^oC, isomers ratio (65:35). ^1H NMR ($CDCl_3$): δ 2.62 (s, 3H, CH_3), 7.23-7.28 (m, 2H, ArH), 7.60 (d, *J* = 8.7 Hz, 1H, ArH), 7.92 (s, 1H, ArH), 8.02 (bd, *J* = 7.5 Hz, 1H, ArH), 8.19 (t, *J* = 6.3 Hz, 2H, ArH), 9.23 (s, 1H, H-3, one isomer, ArH), 9.25 (s, 1H, H-3, other isomer) ppm; ^{13}C NMR ($CDCl_3$): δ 21.90, 116.18, 116.47, 126.88, 127.96, 128.20, 128.99, 129.39, 129.52, 129.64, 132.53, 133.47, 138.83, 140.96, 141.73, 142.27, 150.74, 162.71, 166.03 ppm; FT-IR (KBr): ν 3052, 2921, 1601, 1499, 1225, 838, 721 cm^{-1}. Anal. Calc. for $C_{15}H_{11}FN_2$: C, 75.62; H, 4.65; N, 11.76. Found: C, 75.87; H, 4.54; N, 11.65%.

2-(4-methoxyphenyl)-6/7-methylquinoxaline (3q):
Cream solid; mp: 94-96 ^oC, isomers ratio (60:40). ^1H NMR ($CDCl_3$): δ 2.60 (s, 3H, CH_3), 3.90 (s, 3H, OCH_3), 7.07 (d, *J* = 8.4 Hz, 2H, ArH), 7.52-7.60 (m, 1H, ArH), 7.86-8.02 (m, 2H, ArH), 8.14-8.18 (m, 2H, ArH), 9.23 (s, 1H, H-3, one isomer), 9.24 (s, 1H, H-3, other isomer) ppm; ^{13}C NMR ($CDCl_3$):

δ 21.80, 55.43, 114.55, 127.84, 128.20, 128.50, 128.82, 128.86, 128.93, 129.35, 131.42, 132.54, 139.60, 140.77, 142.07, 142.27, 142.81, 150.64, 151.29, 161.30, 161.40 ppm; FT-IR (KBr): ν 2921, 2852, 1605, 1433, 1325, 1254, 1179, 1027, 831 cm^{-1}. Anal. Calc. for $C_{16}H_{14}N_2O$: C, 76.78; H, 5.64; N, 11.19. Found: C, 76.85; H, 5.55; N, 11.25%.

2-(4-nitrophenyl)-6/7-methylquinoxaline (3r):
Gray solid; mp: 145-148 ^oC, isomers ratio (64:36). ^1H NMR ($CDCl_3$): δ 2.63 (s, 3H, CH_3), 7.65 (d, *J* = 6.9 Hz, 1H, ArH), 7.93 (d, *J* = 9 Hz, 1H, ArH), 8.05 (d, *J* = 7.8 Hz, 1H, ArH), 8.30-8.38 (m, 4H, ArH), 9.30 (s, 1H, H-3, one isomer), 9.32 (s, 1H, H-3, other isomer) ppm; ^{13}C NMR ($CDCl_3$): δ 21.91, 124.25, 128.04, 128.13, 128.24, 128.58, 128.73, 129.33, 133.07, 133.25, 141.58, 141.88, 142.69 ppm; FT-IR (KBr): ν 2922, 1600, 1518, 1490, 1345, 1049, 960, 854, 692 cm^{-1}. Anal. Calc. for $C_{15}H_{11}N_3O_2$: C, 67.92; H, 4.18; N, 15.84. Found: C, 67.85; H, 4.22; N, 15.92%.

2-(3,4-dimethoxyphenyl)-6/7-methylquinoxaline (3s):
Cream brown solid; mp: 97-100 ^oC, isomers ratio (56:44). ^1H NMR ($CDCl_3$): δ 2.61 (s, 3H, CH_3), 3.98 (s, 3H, OCH_3), 4.06 (s, 3H, OCH_3), 7.03 (d, *J* = 8.4 Hz, 1H, ArH), 7.54-7.62 (m, 1H, ArH), 7.72 (d, *J* = 7.2 Hz, 1H, ArH), 7.86 (bs, 2H, ArH), 7.95-8.06 (m, 1H, ArH), 9.24 (s, 1H, H-3, one isomer), 9.26 (s, 1H, H-3, other isomer) ppm; ^{13}C NMR ($CDCl_3$): δ 21.79, 21.86, 56.01, 56.06, 110.02, 110.10, 111.12, 120.23, 120.36, 127.88, 128.16, 128.51, 128.81, 129.60, 131.46, 132.55, 139.65, 139.70, 140.59, 140.79, 141.16, 142.12, 142.88, 149.67, 150.50, 150.93, 151.03, 141.15 ppm; FT-IR (KBr): ν 3081, 2934, 2837, 1600, 1519, 1501, 1288, 1249, 1173, 1023 cm^{-1}. Anal. Calc. for $C_{17}H_{16}N_2O_2$: C, 72.84; H, 5.75; N, 9.99. Found: C, 72.75; H, 5.64; N, 9.78%.

2-([1,1'-biphenyl]-4-yl)-6/7-methylquinoxaline (3t);
Cream solid; mp: 84-87 ^oC, isomers ratio (65:35). ^1H NMR ($CDCl_3$): δ 2.64 (s, 3H, CH_3), 7.42 (d, *J* = 6.9 Hz, 1H, ArH), 7.50 (t, *J* = 6.3 Hz, 2H, ArH), 7.61 (d, *J* = 8.4 Hz, 1H, ArH), 7.69 (d, *J* = 7.2 Hz, 2H, ArH), 7.80-7.99 (m, 3H, ArH), 8.04 (d, *J* = 7.8 Hz, 1H, ArH), 8.29 (d, *J* = 7.8 Hz, 2H, ArH), 9.32 (s, 1H, H-3, one isomer), 9.34 (s, 1H, H-3, other isomer) ppm; ^{13}C NMR ($CDCl_3$): δ 22.04, 126.13, 127.18, 127.46, 127.98, 128.01, 128.13, 128.97, 132.94, 133.92, 134.50, 140.01, 140.58, 142.16, 142.27, 143.55, 151.28 ppm; FT-IR (KBr): ν 3029, 2916, 1602, 1534, 1486, 1052, 845, 764, 689 cm^{-1}. Anal. Calc. for $C_{21}H_{16}N_2$: C, 85.11; H, 5.44; N, 9.45. Found: C, 85.30; H, 5.34; N, 9.32%.

References

1. Zarranz, B., Jaso, A., Aldana, I., and Monge, A. (2004) Synthesis and anticancer activity evaluation of new 2-alkylcarbonyl and 2-benzoyl-3-trifluoromethyl-quinoxaline 1,4-di-N-oxide derivatives, *Bioorg. Med. Chem*., 12, 3711-3721.
2. Lee, H., Cho, S., Namgoong, K., Jung, J. K., and Yang, S. (2004) Synthesis and in vitro evaluation of 7-dialkylaminomethylbenzo[g]quinoxaline-5,10-diones, *Bioorg. Med. Chem. Lett*., 14, 1235-1237.
3. Chung, H. J., Jung, O. J., Chae, M. J., Hong, S. Y., Chung, K. H., and Lee, S. K. (2005) Synthesis and biological evaluation of quinoxaline-5,8-diones that inhibit vascular smooth muscle cell proliferation, *Bioorg. Med. Chem. Lett*., 15, 3380-3384.
4. Amin, K. M., Ismail, M. M. F., Noaman, E., Soliman, D. H., and Ammar, Y. A. (2006) New quinoxaline 1,4-di-N-oxides. Part 1: Hypoxia-selective cytotoxins and anticancer agents derived from quinoxaline 1,4-di-N-oxides, *Bioorg. Med. Chem.,* 14, 6917-6923.
5. Grande, F., Aiello, F., Grazia, O. D., Brizz,i A., Garofalo, A., and Neamati, N. (2007) Synthesis and antitumor activities of a series of novel quinoxalinhydrazides, *Bioorg. Med. Chem.*, 15, 288-294.

6. Diana, P., Martorana, A., Barraja, P., and Montalbaro, A. (2008) Isoindolo[2,1-a]quinoxaline Derivatives, Novel Potent Antitumor Agents with Dual Inhibition of Tubulin Polymerization and Topoisomerase I, *J. Med. Chem*., 51, 2387-2399.
7. Tandon, V. K., Yadav, D. B., Maurya, H. K., Chaturvedi, A. K., and Shukla, P. K. (2006) Design, synthesis, and biological evaluation of 1,2,3-trisubstituted-1,4-dihydrobenzo[g]quinoxaline-5,10-diones and related compounds as antifungal and antibacterial agents, *Bioorg. Med. Chem*., *14*, 6120-6126.
8. Kotharkar, S. A., and Shinde, D. B. (2006) Synthesis of antimicrobial 2,9,10-trisubstituted-6-oxo-7,12-dihydro-chromeno[3,4-b]quinoxalines, *Bioorg. Med. Chem. Lett*., 16, 6181-6184.
9. Mashevskaya, I. V., Makhmudov, R. R., Aleksandrova, G. A., Golovnira, O. V., Duvalov, A. V., and Maslivets, A. N. (2001) Synthesis and Study of the Antibacterial and Analgesic Activity of 3-Acyl-1,2,4,5-tetrahydro-[1,2-a]quinoxaline-1,2,4-triones, *Pharm. Chem. J.*, 35, 196-198.
10. Vyas, D. A., Chauhan, N. A., and Parikh, A. R. (2007) Synthesis and anti microbial activity of quinoxaline based thiazolidinones and azetidinones, *Indian J. Chem*., 46B, 1699-1702.
11. Carta, A., Loriga, M., Paglietti, G., Mattana, A., Fiori, P. L., Mollicotti, P., Sechi, L., and Zanetti, S. Synthesis, anti-mycobacterial, anti-trichomonas and anti-candida in vitro activities of 2-substituted-6,7-difluoro-3-methylquinoxaline 1,4-dioxides, *Eur. J. Med. Chem*., 39, 195-203.
12. Seitz, L. E., Suling, W. J., and Reynolds, R. C. (2002) Synthesis and Antimycobacterial Activity of Pyrazine and Quinoxaline Derivatives, *J. Med. Chem*., 45, 5604-5606.
13. Zarranz, B., Jaso, A., Aldana, I., and Monge, A. (2003) Synthesis and antimycobacterial activity of new quinoxaline-2-carboxamide 1,4-di-N-oxide derivatives, *Bioorg. Med. Chem*., 11, 2149-2156.
14. Jaso, A., Zarranz, B., Aldana, I., and Monge, A.(2005) Synthesis of New Quinoxaline-2-carboxylate 1,4-Dioxide Derivatives as Anti-Mycobacterium tuberculosis Agents, *J. Med. Chem*., *48*, 2019-2025.
15. Burguete, A., Pontiki, E., Litina, D. H., Villar, R., Vicente, E., Solano, B., Ancizu, S., Aldana, I., and Monge, A. (2007) Synthesis and anti-inflammatory/antioxidant activities of some new ring substituted 3-phenyl-1-(1,4-di-N-oxide quinoxalin-2-yl)-2-propen-1-one derivatives and of their 4,5-dihydro-(1H)-pyrazole analogues, *Bioorg. Med. Chem. Lett*., 17, 6439-6443.
16. Wagle, S., Adhikari, A. V., and Kumari, N. S. (2008) Synthesis of Some New 2-(3-Methyl-7-substituted-2-oxoquinoxalinyl)-5-(aryl)-1,3,4-oxadiazoles as Potential Nonsteroidal Antiinflammatory and Analgesic Agents, *Indian J. Chem*., 47B, 439-448.
17. Jasouri, S., Khalafy, J., Badali, M., and Prager, R. H. (2011) Synthesis of 9H-indeno [1,2-b] pyrazine and 11H-indeno[1,2-b]quinoxaline derivatives in one-step reaction from 2-bromo-4-chloro-1-indanone, *S. Afri. J. Chem.*, 64, 105-107.
18. Poursattar Marjani, A., Khalafy, J., and Prager, R. H. (2012) A novel synthesis of imidazo[1,2-a]quinoxalines, *Khim. Geterotsikl. Soedin.,* 48, in press.
19. Riley, H. A., and GraY, A. R. (1943) *Organic Syntheses*, Collect. Vol. II, p. 509 (Wiley & Sons: New York, NY).