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Qinoxaline II. A Practical Efficient And Rapid Synthesis Of New Quinoxalines Catalyzed By Citric Acid As A Trifunctional Bronsted Acid At Room Temperature Under Green Condition

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Abstract: A simple, highly efficient and green procedure for the condensation of aryl and alkyl 1,2-diamines with α-diketones in the presence of catalytic amount of citric acid at room temperature is described. Using this method, quinoxaline derivatives as biologically interesting compounds are produced in high to excellent yields and short reaction times under mild and green condition. In this research, new quinoxaline derivatives were produced (1-12).
Keywords: Quinoxaline synthesis, 1,2-Diamine, α-Diketone, Green chemistry, Citric acid.

1.0 Introduction

Quinoxaline derivatives are a very important class of nitrogen-containing compounds and have been widely used in dyes,[1] pharmaceuticals,[2-3] and electrical/photochemical materials.[4-9] Quinoxaline ring moiety constitute part of the chemical structures of various antibiotics such as Echinomycin, Levomycin and Actinoleutin,[10,11] that are known to inhibit growth of gram positive bacteria and are active against various transplantable tumors. A number of synthetic strategies have been developed for the preparation of substituted quinoxalines.[12-14] By far, the most common method relies on the condensation of an aryl 1,2-diamine with a 1,2-dicarbonyl compound in refluxing ethanol or acetic acid for 2–12h giving 34–85% yields.[15] Recently, Heravi *et al.*[16] and More *et al.* [17] reported greener methods for the synthesis of quinoxaline derivatives in green solvents ($EtOH/H_2O$), using copper sulphate pentahydrate and cerium (IV) ammonium nitrate as catalysts, respectively. 2,3-Disubstituted quinoxalines have also been prepared by Suzuki–Miyaura coupling reaction,[18] condensation of o-phenylenediamines and 1,2-dicarbonyl compounds in MeOH/AcOH under microwave irradiation,[19] iodine catalyzed cyclocondensation of 1,2-dicarbonyl compounds and substituted o-phenylene diamines in DMSO,[20] CH_3CN.[21] Different catalysts used for quinoxaline synthesis such as IBX,[22] Oxalic Acid,[23] SBSSA,[24] Microwave/I_2,[25] $SnCl_2/SiO_2$,[26] I_2,[27] Ultrasound Irradiaton,[28] NH_4Cl,[29] $(NH_4)_6Mo_7O_{24}.4H_2O$,[30] ionic liquid,[31] Bentonit Clay K-10,[32] AcOH,[33] and BSA.[34] However, the critical product isolation procedure, long reaction time and harsh conditions of the above mentioned methods, limit their use in sustainable chemistry.

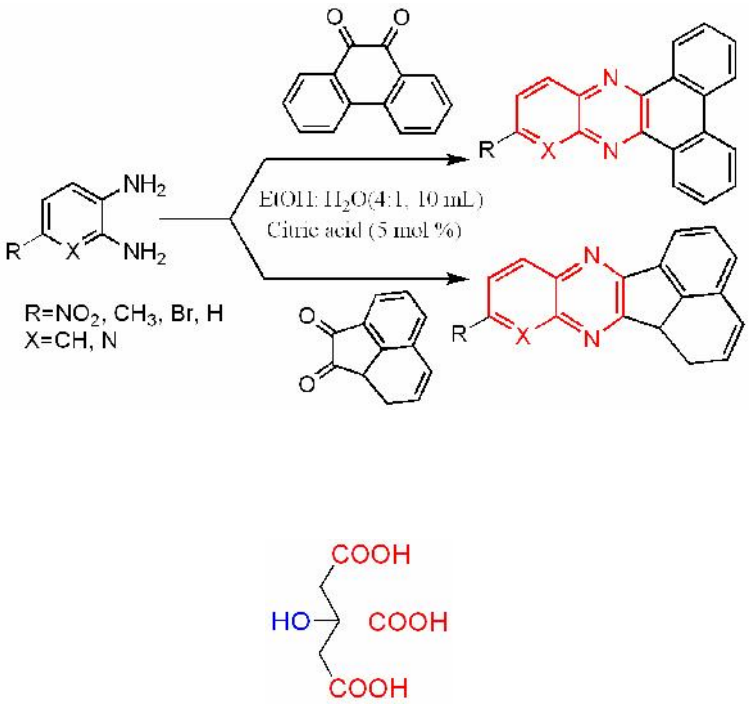


Figure 1- Citric acid structure as a trifunctional Bronsted acid

We disclose herein our results for the synthesis of new quinoxalines using catalytic amounts of citric acid (5 mol%) (**Figure 1**) in mixture of ethanol:water(4:1, 10 mL) as an acidic solution at room temperature.

2.0 Material And Methods

2.1. General

Chemicals were purchased from Merck chemical company. IR spectra of the compounds were obtained on a Frontier FT-IR (Perkin Elmer) spectrometer using a KBr disk. The ^{1}H NMR spectra were recorded on a Bruker AQS 300 Avance instrument at 300 MHz in dimethyl sulfoxide (DMSO-d_6) as solvent and tetramethylsilane (TMS) as an internal standard. The progress of reaction was followed with TLC using silica gel SILG/UV 254 and 365 plates. All products are known compounds and were characterized by comparing the IR, ^{1}H and ^{13}C NMR spectroscopic data (see Supplementary data). All yields refer to isolated products.

2.2. General procedure for the preparation of quinoxaline: A solution of aromatic o-diamine (1mmol) and a 1,2-dicarbonyl compound (1mmol) in ethanol:water (4:1, 10 mL) was stirred at room temperature in the presence of catalytic amount of benzoic acid (5 mol%, 0.0096 g). The progress of the reaction was monitored by TLC (n-hexan-ethylacetate 20:1 or 10:1). After completion of the reaction, water (20 mL) added to the mixture and was allowed to stand at room temperature for 30 min. During this time, crystals of the pure product were formed which were collected by filtration and dried. The products recrystallized from hot ethanol. All the products were confirmed by ^{1}H, ^{13}C NMR, IR and MS.

2Q: Brown liquid, TLC: Rf 0.67 on silica gel eluting with n-hexane :CH3COCH$_2$CH3 (20:1), FT-IR (KBr): 1700, 1622 cm^{-1}(stretching C=N); ^{1}H-NMR (FT-300 MHz, $CDCl_3$/TMS): dppm 1.24(bs, 3H, CH_3) 2.38(bs, 3H, CH_3) 2.55(bs, 3H, CH_3)

2.3. Selected spectral data

2.3.1.-2-Ethyl-3-methyquinoxaline1Q: Brown solid m.p 58-61 ^{o}C, TLC: Rf 0.27 on silica gel eluting with n-hexane:CH3COCH$_2$CH3 (20:1), FT-IR (KBr): 1717, 1609 cm^{-1}(stretching C=N) 1573, 1509, 1346, 1326(stretching nitro group); ^{1}H-NMR (FT-300 MHz, $CDCl_3$/TMS): dppm 1.21(bs, 3H, CH_3) 2.51(s, 3H, CH_3) 2.06(bs, 2H, CH_2); ^{13}C NMR (300 MHz, $CDCl_3$): 11.708, 22.481, 28.731, 128.046, 128.363, 128.517, 128.573, 140.565, 140.954, 152.795, 157.212; MS: m/z = 172 (M+).

2.3.2.-2-Ethyl-3,6-dimethylquinoxaline

2.81(bs, 2H, CH_2) 7.29(bs, 1H, Ar-H) 7.60(s, 1H, Ar-H) 7.72(d, J=5.88, 1H, Ar-H); ^{13}C NMR (300 MHz, $CDCl_3$): 11.798, 21.521, 22.291, 22.365, 28.640, 28.693, 30.688, 126.979, 127.324, 127.559, 127.873, 130.746, 138.795, 138.873, 138.999,

139.411, 140.594, 141.000, 151.777, 152.602, 156.309, 157.128; MS: m/z = 186 (M^+).

2.3.3.-11-Benzoil-dibenzo[a,c]phenazine3Q: Yellow solid m.p 245-247, TLC: Rf 0.85 on silica gel eluting with n-hexane:$CH3COCH_2CH3$ (20:1), FT-IR (KBr): 1653, 1606 cm^{-1}(stretching C=N); ^{1}H-NMR (FT-300 MHz, $CDCl_3$/TMS): dppm 7.27(s, 1H, Ar-H) 7.60(s, 2H, Ar-H) 7.71(s, 2H, Ar-H) 7.79(s, 2H, Ar-H) 7.98(s, 2H, Ar-H) 8.35(s, 1H, Ar-H) 8.52(s, 3H, Ar-H) 8.69(s, 1H, Ar-H) 9.31(s, 1H, Ar-H) 9.44(s, 1H, Ar-H); ^{13}C NMR (300 MHz, $CDCl_3$): 123.048, 128.254, 128.601, 129.450, 130.220, 130.754, 131.056, 132, 916, 140.540, 140.980, 141.323, 141.876, 154.046; MS: m/z = 384 (M+).

2.3.4.-2-Bromopyrido-[2,3-b]dibenzo[5,6-7,8]quinoxaline 4Q: Yellow solid m.p 216-218 ^oC, TLC: Rf 0.77 on silica gel eluting with *n*-hexane :$CH3COCH_2CH3$ (20:1), FT-IR (KBr): 1603 cm^{-1}(stretching C=N); ^{1}H-NMR (FT-300 MHz, $CDCl_3$/TMS): dppm 7.72(bs, 4H, Ar-H) 8.41(bs, 2H, Ar-H) 8.66(s, 1H, Ar-H) 9.06(s, 1H, Ar-H) 9.12(s, 1H, Ar-H) 9.30(s, 1H, Ar-H); ^{13}C NMR (300 MHz, $CDCl_3$): 122.858, 126.519, 127.292, 128.048, 129.026, 131.393, 139.507, 143.815, 155.170; MS: *m/z* = 360 (MH+).

2.3.5.-2,3-Dihydro-2-methyl-5,6-diphenylpyrazine 5Q: Yellow solid, m.p 121-123 ^oC, TLC: Rf 0.22 on silica gel eluting with n-hexane:$CH3COCH_2CH3$ (20:1), FT-IR (KBr): 1615 cm^{-1}(stretching C=N); ^{1}H-NMR (FT-300 MHz, $CDCl_3$/TMS): dppm 1.48(d, J=2.62, 3H, CH_3) 3.17(t, J=14.88, 1H) 3.50(bs, 1H) 4.03(d, J=15.93, 1H) 7.26(bs, 6H, Ar-H) 7.40(bs, 4H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$): 18.883, 50.929, 52.182, 127.896, 128.001, 128.073, 129.453, 129.529, 137.762, 137.945, 159.199, 160.329; $C_{17}H_{16}N_2$, Elem. Anal. Calc.: C, 82.22; H, 6.49; N, 11.28, found: C, 82.19; H, 6.48; N, 11.32; MS: m/z = 186 (M^+).

2.3.6.-2,3-Dihydro-5,6-diphenylpyrazine 6Q: Yellow solid, m.p 161-164 ^oC, TLC: Rf 0.22 on silica gel eluting with n-hexane :$CH3COCH_2CH3$ (20:1), FT-IR (KBr): 1611 cm^{-1}(stretching C=N); ^{1}H-NMR (FT-300 MHz, $CDCl_3$/TMS): dppm 3.70(s, 4H, 2×CH_2) 7.21-7.33(m, 6H, Ar-H) 7.40 (bs, 2H, Ar-H) 7.43(bs, 2H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$): 45.842, 127.915, 128.087, 129.584, 137.823, 160.264; $C_{16}H_{14}N_2$, Elem. Anal. Calc.: C, 82.02; H, 6.02; N, 11.96, found: C, 81.98; H, 6.04; N, 11.94; MS: m/z = 186 (M^+).

2.3.7.-8,9-Dihydro-8-methylacenaphtho[1,2-b]pyrazine 7Q: Brown solid, m.p 68-70 ^oC, TLC: Rf 0.36 on silica gel eluting with n-hexane :$CH3COCH_2CH3$ (20:1), FT-IR (KBr): 1674 cm^{-1}(stretching C=N); ^{1}H-NMR (FT-300 MHz, $CDCl_3$/TMS): dppm 1.41(d, J=3.45, 3H, CH_3) 3.48(bs, 1H) 3.81(bs, 1H) 4.01(bs, 1H) 7.56(bs, 2H, Ar-H) 7.83(bs, 4H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$): 20.282, 49.697, 51.860, 118.493, 118.591, 128.128, 128.300, 130.530, 131.555, 131,680, 141.484, 157.780, 158.173; $C_{15}H_{12}N_2$, Elem. Anal. Calc.: C, 81.79; H, 5.49; N, 12.72, found: C, 81.84; H, 5.48; N, 12.68; MS: m/z = 186 (M^+).

2.3.8.-8,9-Dihydro-acenaphtho[1,2-b]pyrazine 8Q: Yellow solid, m.p 113-116 ^oC, TLC: Rf 0.28 on silica gel eluting with n-hexane :$CH3COCH_2CH3$ (20:1), FT-IR (KBr): 1675 cm^{-1}(stretching C=N); ^{1}H-NMR (FT-300 MHz, $CDCl_3$/TMS): dppm 3.81(s, 4H, 2×CH_2) 7.58(t, J=7.64, 2H, Ar-H) 7.84(d, J=7.65, 4H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$): 44.842, 118. 572, 128.204, 128.330, 130.517, 131.600, 141.309, 158.421; $C_{14}H_{10}N_2$, Elem. Anal. Calc.: C, 81.53; H, 4.89; N, 13.58, found: C, 81.51; H, 4.89; N, 13.60; MS: m/z = 186 (M^+).

2.3.9.-2,3-bis(4-Methoxyphenyl)quinoxaline 13Q: Yellow solid m.p 134-136[lit. 148-150][34], TLC: Rf 0.65 on silica gel eluting with n-hexane :$CH3COCH_2CH3$ (20:1), FT-IR (KBr): 1615 cm^{-1}(stretching C=N); ^{1}H-NMR (FT-300 MHz, $CDCl_3$/TMS): dppm 3.85(s, 6H, 2×CH_3) 6.87(d, J=7.77, 1H, Ar-H) 6.94 (d, J=7.77, 4H, Ar-H) 7.50 (d, J=7.14, 1H, Ar-H) 7.71(s, 1H, Ar-H) 7.93(d, J=7.62, 4H, Ar-H) 8.13(s, 1H, Ar-H); ^{13}C NMR (300 MHz, $CDCl_3$): 55.291, 55.615, 113.786, 114.300, 126.271, 128.875, 129.645, 131.307, 131.449, 132.315, 140.867, 152.926, 160.267, 164.867, 193.506; MS: m/z = 342 (M+).

2.3.10.-6-Nitro-2,3-diphenylquinoxaline 14Q: Red solid m.p 185-187[lit. 185-187][24], TLC: Rf 0.75 on silica gel eluting with n-hexane :$CH3COCH_2CH3$ (20:1), FT-IR (KBr): 1656 cm^{-1}(stretching C=N); ^{1}H-NMR (FT-300 MHz, $CDCl_3$/TMS): dppm 7.38(bs, 6H, Ar-H) 7.56(bs, 4H, Ar-H) 8.28(bs, 1H, Ar-H) 8.45(bs, 1H, Ar-H) 9.02(bs, 1H, Ar-H); ^{13}C NMR (300 MHz, $CDCl_3$):; MS: 123.269, 125.512, 128.450, 129.667, 129.854, 129.953, 130.666, 137..950, 139.870, 143.390, 147.801, 155.621, 156.176; MS: m/z = 327 (M+).

2.3.11.-Acenaphto[1,2-b]quinoxaline 15Q: Yellow solid m.p 241-242 [lit. 238-240][24], TLC: Rf 0.26 on silica gel eluting with n-hexane :$CH3COCH_2CH3$ (20:1), FT-IR (KBr): 1614 cm^{-1}(stretching C=N); ^{1}H-NMR (FT-300 MHz, $CDCl_3$/TMS): dppm 7.74-7.81(m, 4H, Ar-H) 8.05(d, J=8.16, 2H, Ar-H) 8.20-8.23(m, 2H, Ar-H) 8.4(d, J=6.87, 2H, Ar-H); ^{13}C

NMR (300 MHz, $CDCl_3$): 122.328, 128.679, 129.285, 129.442, 129.694, 129.900, 131.248, 136.479, 140.707, 153.595; MS: m/z = 254 (M+).

2.3.12.-9-Methylacenaphto[1,2-b]quinoxaline 16Q: Brown solid m.p 231-242[lit. ≥300 °C][24], TLC: Rf 0.77 on silica gel eluting with n-hexane :$CH3COCH_2CH3$ (20:1), FT-IR (KBr): 1626 cm^{-1}(stretching C=N); ^{1}H-NMR (FT-300 MHz, $CDCl_3$/TMS): dppm 2.56(s, 3H, CH_3) 7.49(d, J=8.31, 1H, Ar-H) 7.70(t, J=7.5, 2H, Ar-H) 7.88(s, 1H, Ar-H) 7.94(d, J=8.07, 2H, Ar-H) 7.99(d, J=8.61, 1H, Ar-H) 8.27(t, J=6.40, 2H, Ar-H); ^{13}C NMR (300 MHz, $CDCl_3$): 21.735, 121.583, 121.785, 128.484, 128.554, 128.938, 129.113, 129.284, 129.799, 131.250, 131.645, 136.097, 139.359, 139.666, 140.915, 153.035, 153.661; MS: m/z = 268 (M+).

2.3.13.-Dibenzo[a,c]phenazine 17Q: Yellow solid m.p 224-226[lit. 223-225][21], TLC: Rf 0.46 on silica gel eluting with n-hexane :$CH3COCH_2CH3$ (20:1), FT-IR (KBr): 1604 cm^{-1}(stretching C=N); ^{1}H-NMR (FT-300 MHz, $CDCl_3$/TMS): dppm 7.71(s, 4H, Ar-H) 7.85(s, 2H, Ar-H) 8.35(s, 2H, Ar-H) 8.43(s, 2H, Ar-H) 9.33(s, 2H, Ar-H); ^{13}C NMR (300 MHz, $CDCl_3$): 122.875, 126.448, 128.023, 128.925, 129.356, 130.205, 130.661, 132.019, 141.323, 141.876; MS: m/z = 280 (M+).

2.3.14.-11-Methyl-dibenzo[a,c]phenazine 18Q: Brown solid m.p 219-221[lit. 208-210][24], TLC: Rf 0.54 on silica gel eluting with n-hexane:$CH3COCH_2CH3$ (20:1), FT-IR (KBr): 1624 cm^{-1}(stretching C=N); ^{1}H-NMR (FT-300 MHz, $CDCl_3$/TMS): dppm 2.65(s, 3H, CH_3) 7.72(bs, 5H, Ar-H) 8.04(s, 1H, Ar-H) 8.15(s, 1H, Ar-H) 8.47(s, 2H, Ar-H) 9.32(bs, 2H, Ar-H); ^{13}C NMR (300 MHz, $CDCl_3$): 20.058, 122.795, 126.032, 126.178, 127.793, 128.797, 129.978, 130.127, 131.727, 131.922, 132.368, 140.393, 140.573, 141.508, 141.971; MS: m/z = 294 (M+).

2.3.15.-2,3-Diphenylquinoxaline 19Q: White solid m.p 125-127[lit. 128-129][22], TLC: Rf 0.20 on silica gel eluting with n-hexane :$CH3COCH_2CH3$ (20:1), FT-IR (KBr): 1556 cm^{-1}; ^{1}H-NMR (FT-300 MHz, $CDCl_3$/TMS): dppm7.33977(bs, 6H, Ar-H) 7.54183(bs, 4H, Ar-H) 7.74584(bs, 2H, Ar-H) 8.20007(bs, 2H, Ar-H) ; ^{13}C NMR (300 MHz, $CDCl_3$): 128.290, 128.896, 129.121, 129.913, 130.066, 138.921, 141.115, 153.384; MS: m/z = 282 (M+).

2.3.16.-6-Methyl-2,3-diphenylquinoxaline 20Q: Brown solid m.p 113-115 [lit. 116-117][24], TLC: Rf 0.25 on silica gel eluting with n-hexane :$CH3COCH_2CH3$ (20:1), FT-IR (KBr): 1619 cm^{-1}(stretching C=N); ^{1}H-NMR (FT-300 MHz, $CDCl_3$/TMS): dppm 2.61(s, 3H, Ar-CH_3) 7.35(s, 6H, Ar-H) 7.55(d, J=6.48, 4H, Ar-H)7.60(s, 1H, Ar-H) 7.98(s, 1H, Ar-H) 8.09(d, J=8.4, 1H, Ar-H); ^{13}C NMR (300 MHz, $CDCl_3$): 21.948, 128.040, 128.244, 128.663, 128.731, 129.903, 129.915, 132.321, 139.246, 139.728, 140.486, 141.289, 152.552, 153.289; MS: m/z = 296 (M+).

3.0 Results And Discussion

In order to find a suitable catalyst for the synthesis of quinoxalines from 1,2-diamines and α-diketones, the condensation of benzene-1,2-diamine with benzil was chosen as a model to provide compound **19Q** (Table 3), and its behavior was studied in the presence of various catalysts in $EtOH/H_2O$ at room temperature. The results are displayed in Table 1. As it can be seen from Table 1, citric acid as an organic catalyst afforded the good results with respect to the inorganic catalysts. Although water is a desirable solvent for chemical reactions for reasons of cost, safety and environmental concerns, use of water in this reaction gave only moderate yields of products (65% after 4h). For chosen better solvent, different solvents were examined (Table 2). H_2O:Ethanol (4:1, 10 mL) was better solvent. Having reaction conditions are optimized, to evaluate this methodology, various o-phenylenediamines were condensed with benzil in the presence of citric acid (5 mol%) at room temperature (Table 3, entries 5,6,19,20). Total reactions are summarized in Table 3. The optimum yields of the products are obtained when 5 mol% of citric acid is used. o-Phenylenediamines and 1,2-dicarbonyl compounds with electron-donating or electron-withdrawing groups were used. As indicated in the Table 3 both electron rich and electron deficient 1,2-dicarbonyl compounds worked pretty well, mostly leading to high yields of products but withdrawing groups had lower yield. Ease of recycling of the catalyst is one of the most advantages of our method. We obtained the catalyst after completing and filtering the reaction and then evaporated the solvent under reduced pressure. For the reaction of benzene-1,2-diamine with benzil no significant loss of the product yield was observed when citric was used after four times recycling.

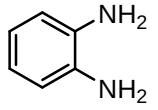
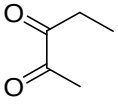
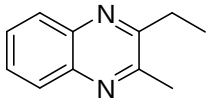
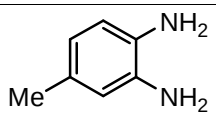
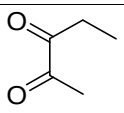
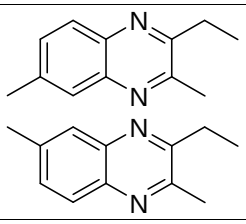
Table 1- The condensation of benzene-1,2-diamine (1 mmol) with benzil (1 mmol) in the presence of different catalysts (0.2 mmol, 5 mol%) in EtOH:H_2O (4:1) at room temperature[23]

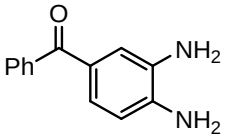
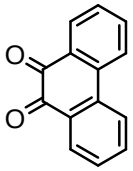
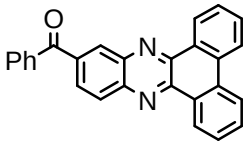
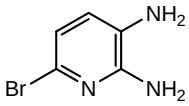
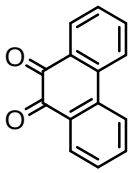
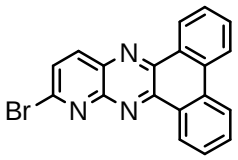
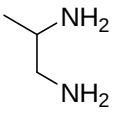
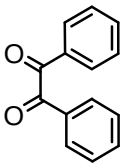
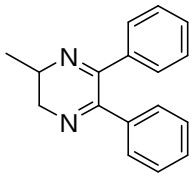
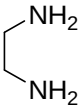
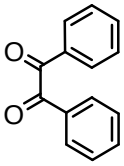
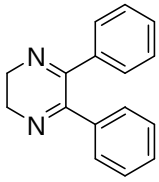
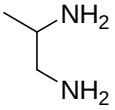
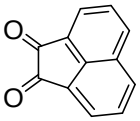
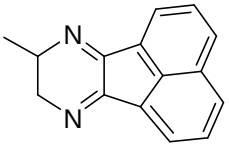
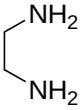
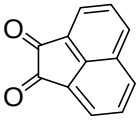
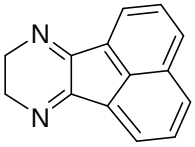
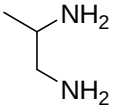
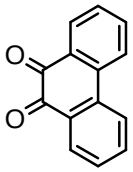
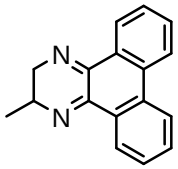
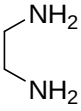
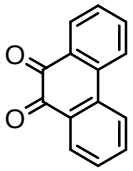
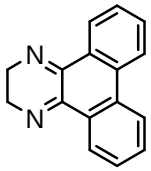
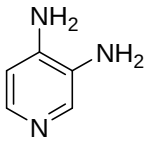
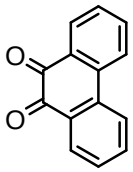
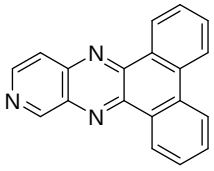
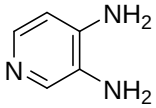
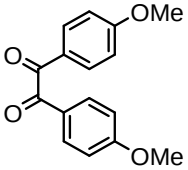
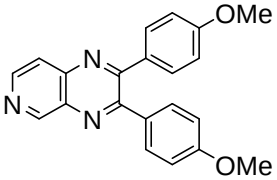
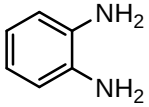
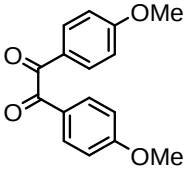
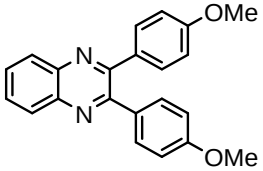
Number	Catalyst name (cat%)	Time (mine)	Yield%[lit]
1	-----	600	----
2	Citric acid (5 mol%)	8	98
2	Phenol(20 mol%)	10	98
3	Oxalic acid(20 mol%)	10	93[23]
4	$ZnCl_2$(20 mol%)	240	70
5	$Mn(OAc)_2$(20 mol%)	240	78
6	$CoCl_2$(20 mol%)	240	81
7	$CuCl_2$((20 mol%))	240	69
8	$Ni(OAc)_2$(20 mol%)	240	68
9	BSA(3 mol%)	5	98[34]

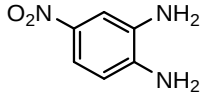
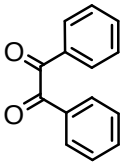
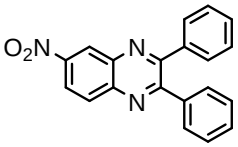
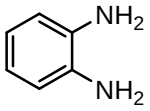
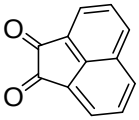
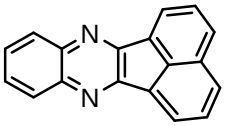
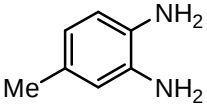
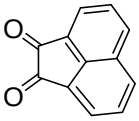
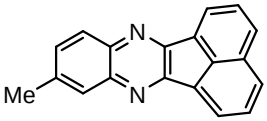
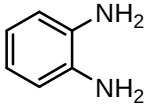
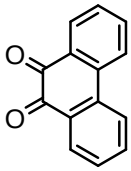
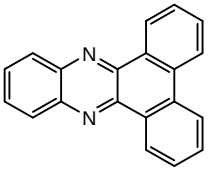
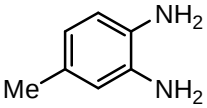
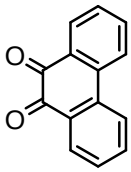
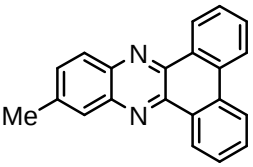
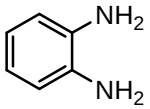
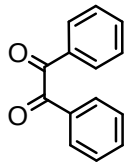
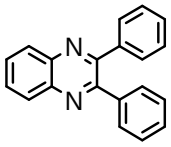
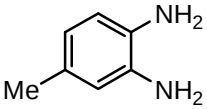
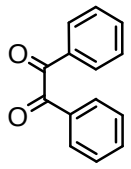
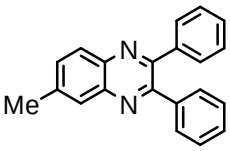
Table 2- Solvent and catalyst optimize in synthesis 2,3-diphenylquinoxaline as a model

Number	Solvent	Cat%	Time (min)	Yield%
1	H_2O(10 mL)	3	240	65
2	H_2O(10 mL)	5	180	67
3	H_2O(10 mL)	10	80	76
4	EtOH:H_2O (1:1, 10 mL)	1	200	70
5	EtOH:H_2O (1:1, 10 mL)	5	150	75
6	EtOH:H_2O (1:1, 10 mL)	10	55	78
7	EtOH:H_2O (4:1, 10 mL)	15	40	80
8	**EtOH:H_2O (4:1, 10 mL)**	**5**	**8**	**98**
9	EtOH:H_2O(7:3, 10mL)	20	45	89
10	EtOH:H_2O(7:3, 10mL)	30	25	92
11	EtOH:H_2O (9:1, 10 mL)	5	100	79
12	EtOH(10 mL)	10	60	81
13	Ethanol(10 mL)	15	35	78
14	Ethanol(10 mL)	20	20	85

Table 3- New quinoxalines synthesis from 1,2-diamines and α-diketones by using Citric acid (5 mol%)

Entry	Diamine (DA)	Diketone (DK)	Product (Q)	Time(h:min) Yield%[a] m.p(Found) m.p[lit.]
1				00:05 99 58-60
2				00:08 89 68-70

3				02:00 98 245 -246
4				00:35 86 215 -216
5				00:05 98 121-123
6				00:05 97 161-164
7				00:10 95 116-118
8				00:05 98 113-116
9				00:05 95 178-181
10				00:05 94 124-126
11				12:00 91 212-215
12				08:00 92 114-116
13				03:20 90 134 -136 148 -150[22]

14				03:15 92 185 -186 185 -187[21]
15				00:15 93 235-236 238-240[21]
16				00:05 97 228 -229 >300[21]
17				00:03 99 225 -226 223 -225[21]
18				00:05 97 218 -220 208 -210[21]
19				00:8 98 125 -126 128 -129[20]
20				00:05 94 113 -115 116 -117[21]

[a]Isolated yield

4.0 Conclusion

In summary, we have developed an efficient method for the synthesis of quinoxaline derivatives via the condensation of 1,2-diamines with α-diketones. This new strategy has several advantages, such as excellent yield, mild reaction conditions, short duration of reaction time, low cost, simple experimental as well as isolation procedures, and finally, it is in agreement with the green chemistry protocols. These advantages will make this method become an attractive greener technique for the construction of quinoxalines and notably similar molecules, compared to the existing methods.

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References

1. Brock E D, Lewis D M, Yousaf T I, Harper H H, WO 9951688, 1999.
2. Gazit A, App H, McMahon G, Chen J, Levitzki A, Bohmer F D, *J. Med. Chem.* 1996, 39, 2170-2177.
3. Sehlstedt U, Aich P, Bergman J, Vallberg H, Norden B, Graslund A., *J. Mol. Biol.* 1998, 278, 31-56.
4. Dailey S, Feast J W, Peace R J, Sage I C, Till, Wood E L, *J. Mater. Chem.* 2001, 11, 2238-2243.
5. O'Brien D, Weaver M S, Lidzey D G, Bradley D D C, *Appl. Phys. Lett.* 1996, 69, 881-883.
6. Yamamoto T, Sugiyama K, Kushida T, Inoue T, Kanbara T, *J. Am. Chem. Soc.* 1996, 118, 3930-3937.
7. Yamamoto T, Zhou Z.-H, Kanbara T, Shimura M, Kizu K, Maruyama, T.; Nakamura, Y.; Fukuda, T.; Lee B.-L, Ooba N, Tomaru S, Kurihara T, Kanno T, Kubota K, Sasaki S, *J. Am. Chem. Soc.* 1996, 118, 10389-10399.
8. Nurulla I, Yamaguchi I, Yamamoto T, *Polym. Bull.* 2000, 44, 231-238.
9. Yamamoto T, Lee B.-L, Kokubo H, Kishida H, Hirota K, Wakabayashi T, Okamoto H, *Macromol. Rapid Commun.* 2003, 24, 440-443.
10. Dell A, William D H, Morris H R, Smith G A, Feeney J, Roberts G C K, *J. Am. Chem. Soc.* 1975, 97, 2497-2502.
11. Bailly C, Echepare S, Gago F, Waring M, J. *Anti-Cancer Drug Des.* 1999, 15, 291-303.
12. Eicher T, Hauptmann S, *The Chemistry of Heterocycles*; Thieme: New York, 1995; 417, 434.
13. Barluenga J, Aznar F, Liz R, Cabal M.-P, *Synthesis* 1985, 313-314.
14. Petukhov P A, Tkachev A V, *Tetrahedron* 1997, 53, 9761-9768.
15. Brown D J *Quinoxalines: Supplement II. In The Chemistry of Heterocyclic Compounds*; Taylor, E. C., Wipf, P., Eds.; John Wiley& Sons: New Jersey, 2004.
16. Heravi M M, Taheri S, Bakhtiari K, *Catal. Commun.* 2007, 8, 211-214.
17. More S V, Sastry M N V, Yao C F, *Green Chem.* 2006, 8, 91-95.
18. Mao L, Sakurai H, Hirao T, *Synthesis* 2004, 2535-2539.
19. Zhao Z, Wisnoski D D, Wolkenberg S E, Leister W H, Wang Y, Lindsley C W, Tetrahedron Lett. 2004, 45, 4873-4876.
20. Bhosale R S, Sarda S R, Ardhapure S S, Jadhav W N, Bhusare S R, Pawar R P, *Tetrahedron Lett.* 2005, 46, 7183-7186.
21. More S V, Sastry M N V, Wang C-C, Yao C.-F, *Tetrahedron Lett.* 2005, 46, 6345-6348.
22. Heravi M M, Bakhtiari K, Tehrani M H, Javadi N M, Oskooie H A, *Arkivoc* 2006, (xvi), 16-22.
23. Hasaninejad A, Zare A, Mohammadizadeh M R, Shekouhy M, *ARKIVOC* 2008 (xiii), 28-35.
24. Niknam K, Saberi D, Mohagheghnejad M, Molecules 2009, 14, 1915-1926.
25. Bandyopadhyay D, Mukherjee S, Rodriguez R R, Banik B K, *Molecules* 2010, 15, 4207-4212.
26. Darabi H R, Aghapoor K, Mohsenzadeh F, Jalali M R, Talebian S, Ebadi-Nia L, Khatamifar E, Aghaee A, *Bull. Korean Chem. Soc.* 2011, 32, 213-218.
27. Bhosale R S, Sarda S R, Ardhapure S S, Jadhav W N, Bhusare S R, Pawar R P, *Tetrahedron Lett.* 2005, 46, 7183–7186.
28. Guo W.-X, Jin H.-L, Chen J.-X, Chen F, Dinga J.-C, Wu H.-Y, *J. Braz. Chem. Soc.* 2009, 20, 1674-1679.
29. Darabi H R, Tahoori F, Aghapoor K, Taala F, Mohsenzadeh F, *J. Braz. Chem. Soc.* 2008, 19, 1646-1652.
30. Hasaninejad A, Zare A, Mohammadizadeh M R, Karami Z, *J. Iran. Chem. Soc.* 2009, *6*, 153-158.
31. Dong F, Kai G, Zhenghao F, Xinli Z, Zuliang L, *Catal. Commun.* 2008, 9, 317–320.
32. Hasaninejad A, Zare A, Shekouhy M, Moosavi-Zare A R, *E-Journal of Chemistry* 2009, 6, 247-253.
33. Islami M R, Hassani Z, *ARKIVOC* 2008, (xv), 280-287.
34. Zolfigol M A, Vahedi H, Massoudi A H, Sajjadifar S, louie O, Moosavi-Zare A R, *3rd International Conference on Drug Discovery & Therapy* February 7– 10, 2011, Dubai Women's College, Dubai, UAE, *Current Medicinal Chemistry* 2011, pp. 202.
35. Hasaninejad A, Zare A, Mohammadizadeh M R, Shekouhy M, *ARKIVOC* 2008, (xiii), 28-35.
36. Kaye I A, *J. Med. Chem.* 1964, 7, 240-241.

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