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Comparative study of microwave assisted and conventional synthesis of novel 2-quinoxalinone-3-hydrazone derivatives and its spectroscopic properties

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A series of novel quinoxalin-2(1*H*)-one-3-hydrazone derivatives, 2a - 8d were synthesized via condensation of 3-hydrazinoquinoxalin-2(1*H*)-one, 1, with the corresponding ketones under microwave irradiation. The microwave assisted reaction was remarkably successful and gave hydrazones in higher yield at less reaction time compared to conventional heating method. The chemical structures of the compounds prepared were confirmed by analytical and spectral data.

Key words: 3-Hydrazinoquinoxalin-2(1*H*)-one, isatin, microwave irradiation, uv-visible, conventional heating.

INTRODUCTION

Microwave-assisted reactions have been intensely investigated since the earliest publication of Gedye and Majetich in 1986 (Gedye et al., 1986; Giguere et al., 1986). It is fast becoming unavoidable technique for the accelerated synthesis of both inorganic (Vanetsev et al., 2005) and organic compounds (Sha et al., 2001), especially in the preparation of various titled heterocycles (Abdellatif et al., 2008; Qingqing et al., 2008; Rodrigo et al., 2008; Outirite et al., 2008) with high bioactivities (Tinh et al., 2008; Muscia et al., 2008).

Based on the experimental data from various studies that have been reported over a decade ago, chemists have found that, microwave-enhanced chemical reaction rates and can be faster than those of conventional heating methods by as much as a thousand-fold (Hayes, 2004).

Microwave technique is of wide application and global relevance in photo and electroluminescent polymers (Bogdal et al., 2002; Sanetra et al., 2004), phase-transfer catalytic reactions (Loupy et al., 2006; Bogdal and Jaskot, 2000; Pathak et al., 2008) and dental stuff (Pieli-chowski et al., 1998). Day by day, the chemistry of C=N

of hydrazone is gradually becoming the back bone of condensation reaction in benzo-fused N-heterocycles (Rashed et al., 1990).

Hydrazone containing azomethine -NHN=CH protons constitutes an important class of compounds for new drug development (Rollas and Kuçukguzel et al., 2007). It plays an essential role in biologically active compounds (Salgin-Goksen et al., 2007; Ragavendran et al., 2007; Mehta et al., 2006; Bijev, 2006) and hence, represents an interesting template for combinatorial (Wenxiang and Jianying, 2001) as well as medicinal chemistry (Rowan et al., 2002; Chang et al., 2003).

In like fashion, quinoxalines including their fused-ring derivatives are relatively easy to prepare (Refaat et al., 2004; Kim and Kim, 2003; Ali et al., 2000) and many of such derivatives have been reported to display diverse pharmacological activities (Su and Bock, 2005; Badran et al., 2003; Jaso et al., 2003).

Many techniques have been employed in the synthesis of hydrazone frameworks (Sridharan et al., 2007; Abd-Elhafez et al., 2003; Vicini et al., 2002; Sridhar and Ramesh, 2001) and quinoxaline moieties (Zhenjiang et al., 2008; Olayiwola et al., 2007; Obafemi and Akinpelu, 2005; Nasr et al., 2002).

However, microwave-assisted approach toward the synthesis of quinoxalinone hydrazone has not been ex-

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Table 1. The result of physical data and elemental analysis of the synthesized compounds 1-8d.

Compound No	M.P. (°C)	R _f ^a Value	Mol. Formula (Mol. Weight)	Elem. Analy. % Calcd. (% Found)		
				C	H	N
1	>360	0.63	C ₈ H ₈ N ₄ O (176)	54.55(54.52)	4.55(4.57)	31.82(31.83)
2a	256 (sharp)	0.65	C ₁₁ H ₁₂ N ₄ O (216)	61.11(61.09)	5.56(5.53)	25.93(25.90)
2b	277 - 278	0.66	C ₁₃ H ₁₆ N ₄ O (244)	63.93(63.95)	6.56(6.54)	22.95(22.93)
2c	268 - 269	0.62	C ₁₂ H ₁₄ N ₄ O(230)	62.61(62.58)	6.09(6.06)	24.35(24.30)
3a	238 - 241	0.58	C ₁₉ H ₁₄ N ₄ O ₃ (346)	65.90(65.94)	4.05(4.08)	16.18(16.21)
3b	265 - 266	0.71	C ₁₉ H ₁₃ N ₄ O ₃ Br(425)	53.65(53.66)	3.06(3.08)	13.18(13.21)
3c	245 - 246	0.73	C ₁₉ H ₁₃ N ₄ O ₃ Cl(380.5)	59.92(59.90)	3.42(3.39)	14.72(14.70)
3d	183 - 185	0.59	C ₂₀ H ₁₆ N ₄ O ₃ (360)	66.67(66.68)	4.44(4.47)	15.56(15.59)
4	249 - 250	0.68	C ₁₃ H ₁₄ N ₄ O(242)	64.46(64.41)	5.79(5.74)	23.14(23.10)
5a	323 - 324	0.57	C ₁₆ H ₁₁ N ₅ O ₂ (305)	62.95(62.95)	3.61(3.64)	22.95(22.90)
5b	328 - 330	0.67	C ₁₆ H ₁₀ N ₅ O ₂ Br(384)	50.00(50.04)	2.60(2.65)	18.23(18.23)
5c	326 (dec.)	0.69	C ₁₆ H ₁₀ N ₅ O ₂ Cl(339.5)	56.55(56.51)	2.95(2.93)	20.62(20.58)
5d	257 - 259	0.60	C ₁₇ H ₁₃ N ₅ O ₂ (319)	63.95(63.99)	4.08(4.04)	21.94(21.90)
6	229 - 231	0.41	C ₂₂ H ₁₅ N ₄ O(351)	75.21(75.17)	4.27(4.22)	15.95(15.91)
7	331 - 333	0.46	C ₁₈ H ₂₂ N ₄ O(310)	69.68(69.71)	7.10(7.14)	18.06(18.09)
8a	201 - 203	0.64	C ₁₄ H ₁₆ N ₄ O(256)	65.63(65.60)	6.25(6.22)	21.88(21.84)
8b	176 - 178	0.70	C ₁₄ H ₁₅ N ₄ OBr(335)	50.15(50.18)	4.48(4.50)	16.72(16.76)
8c	162 - 163	0.61	C ₁₄ H ₁₅ N ₄ OCl(290.5)	57.83(57.88)	5.16(5.20)	19.27(19.31)
8d	282 - 284	0.50	C ₁₅ H ₁₈ N ₄ O(270)	66.67(66.69)	6.67(6.68)	20.74(20.79)

^a Solvent system. Acetone: benzene (2:8) for 1-3d; Acetone: benzene (1:9) for 4-8d.

tensively explored. Thus, it is conceivable to develop a series of quinoxalinyldiazones using microwave irradiation technique and also compare it with traditional method of conventional heating approach.

MATERIALS AND METHODS

General

Melting points were determined with open capillary tube on a Gallenkamp (variable heater) melting point apparatus and were uncorrected. Infra red spectra were recorded as KBr pellets on a buck spectrometer while uv-visible spectra were recorded on a unicam spectrophotometer. ¹H- and ¹³C- NMR were run on a Bruker-AC-250 and JEOL-JNM-GX 300-MHz spectrometer (δ in ppm relative to Me₄Si and H₃PO₄). Mass spectra were run on Finnigan MAT 312 machine. All compounds were routinely checked by TLC on silica gel G plates using acetone: benzene (9:1, v/v) solvent system and the developed plates were visualized by UV light.

The elemental analysis (C, H, N) of compounds were performed using a Carlo Erba-1108 elemental analyzer. Results were found to be in good agreement with the calculated values (Table 1). The microwave-assisted syntheses were carried out in domestic oven, Midea PJ21B-A 400W. Solvents used were of reagent grade and when necessary, were purified and dried by standard methods.

Synthesis of 3-Hydrazinoquinoxalin-2(1H)-one (1)

To a solution of pure 1,2,3,4-tetrahydroquinoxaline-2,3-dione (20.1 g, 124.0 mmole) in hydrazine hydrate (100.0 ml, 2.2 mole) was added water (50 mL) drop wise with constant stirring at 100°C. The resulting mixture was refluxed under continuous stirring for 3 h.

The mixture was allowed to cool and the formed precipitate was filtered, recrystallized from ethanol to give:

1. IR [ν , cm⁻¹, KBr]: 3412(N-H), 3280(N-H), 3175(N-H), 1679(C=O), 1620(C=C). λ_{max} (log ϵ_{max}): 216(4.34), 247(3.75s), 327(3.61s). ¹H-NMR [300 MHz, δ , ppm, DMSO-*d*₆]: 5.81(s-br, 2H, NH₂; D₂O exchangeable), 7.49-7.96(m, 4H, Ar-H), 8.14(s, 1H, NH; D₂O exchangeable), 12.55(s, 1H, NH; D₂O exchangeable). ¹³C-NMR [50 MHz, δ , ppm, DMSO-*d*₆]: 190.5(C=O), 141.9, 134.2, 125.7, 119.6, 117.0, 115.4, 110.4. MS: in m/z[rel. %]: 176[M⁺, 55.5%], 161[92.3%], 146[85.5%], 118[100%], 106[80.1%], 78[40.5%].

General procedure of 3-[2-(1-alkylalkylidene) hydrazino] quinoxalin-2(1H)-one (2a-2c)

Conventional method

To a mixture of 3-hydrazinoquinoxalin-2(1H)-one, 1 (1.0 g, 5.7 mmol) and acyclic ketones (5.7 mmol) was added ethanol (20 mL). The resulting mixture was refluxed under continuous stirring for 5 h and then the solvent was removed by vacuum distillation. The solid product was filtered, dried and recrystallized from ethanol to afford (2a-2c). Completion of the reaction was monitored by TLC.

Microwave method

To a mixture of 3-hydrazinoquinoxalin-2(1H)-one, 1 (1.0 g, 5.7 mmol) and acyclic ketones (5.7 mmol) was added ethanol (20 mL). The reaction mixture was taken in round-bottom flask placed in a microwave oven and irradiated at 400 W for 3 min. And then the solvent was removed by vacuum distillation. The solid product was filtered, dried and recrystallized from ethanol.

3-[2-(1-methylethylidene) hydrazino] quinoxalin-2(1H)-one (2a).

IR [ν , cm^{-1} , KBr]: 3272(N-H), 1673(C=O), 1605(C=C), 1575(C=N), 1271 m, 1223 m. λ_{max} (log ϵ_{max}): 220(3.76), 325(3.23 s), 340(3.43), 350(3.32 s). $^1\text{H-NMR}$ [300 MHz, δ , ppm, DMSO- d_6]: 2.28(s, 3H, CH₃), 2.40(s, 3H, CH₃), 6.13(s, 1H, NH, D₂O exchangeable), 7.37-7.83(m, 4H, Ar-H), 12.42(s-br, 1H, NH, D₂O exchangeable). $^{13}\text{C-NMR}$ [50 MHz, δ , ppm, CH₃OH- d_4]: 155.3(C=O), 151.9, 142.5, 141.9, 129.6, 129.2, 127.6, 126.3, 120.1, 37.0, 35.0. MS: in m/z [rel. %]: 216[M⁺, 25%], 160[95%], 146[82%], 76[12%].

3-[2-(1-ethylpropylidene)hydrazino]quinoxalin-2(1H)-one (2b).

IR [ν , cm^{-1} , KBr]: 3241(N-H), 2928(C-H aliphatic), 1685(C=O), 1612(C=C), 1563(C=N) λ_{max} (log ϵ_{max}): 220(3.71), 345(3.41 s). $^1\text{H-NMR}$ [300 MHz, δ , ppm, DMSO- d_6]: 1.28(s, 6H, 2xCH₃), 2.80(q, 4H, 2xCH₂), 7.02-7.65(m, 4H, Ar-H), 11.59(s-br, 1H, NH, D₂O, exchangeable). $^{13}\text{C-NMR}$ [50 MHz, δ , ppm, CH₃OH- d_4]: 154.1(C=O), 152.5, 148.0, 144.7, 134.2, 132.9, 132.7, 130.4, 125.9, 117.0, 109.3, 13.8, 12.5. MS: in m/z [rel. %]: 244[M⁺, 10 %], 188[65 %], 161[100 %], 146[85 %], 118[75%], 99[15%], 71[17%], 43[8%], 15[3%].

3-[2-(1-methylpropylidene)hydrazino]quinoxalin-2(1H)-one(2c).

IR [ν , cm^{-1} , KBr]: 3275(N-H), 1690(C=O), 1570(C=N), 1220(m). λ_{max} (log ϵ_{max}): 220(3.41), 348(3.62s), 355(3.37). $^1\text{H-NMR}$ [300 MHz, δ , ppm, DMSO- d_6]: 1.50(s, 3H, CH₃), 1.90(s, 3H, CH₃), 2.70(q, 2H, CH₂), 7.11 - 7.78(m, 4H, Ar-H), 11.57(s, 1H, NH, D₂O, exchangeable). $^{13}\text{C-NMR}$ [50 MHz, δ , ppm, DMSO- d_6]: 184.1(C=O), 151.4, 147.3, 145.1, 134.5, 130.1, 129.7, 127.8, 120.6, 70.5, 39.7, 32.2. MS: in m/z [rel. %]: 230[M⁺, 40%], 202[100%], 103[58%], 29[5%].

General Procedure of 3-[2-[1-(6-substituted-2-oxo-2H-chromen-3-yl)ethylidene] hydrazino] quinoxalin-2(1H)-one (3a-3d).**Conventional method**

In a 250 mL round-bottomed flask, unsubstituted or 6-substituted 3-acetylcoumarin (5.7 mmol) and 3-hydrazinoquinoxalin-2(1H)-one, 1 (1.0 g, 5.7 mmol) in dry DMF (20 mL) were taken. The reaction mixture was refluxed at 90 - 95°C for 3 h and the solvent was distilled off. The solid product obtained was filtered, dried and recrystallized from methanol to afford 3a-3d.

Microwave method

In a 250 mL round-bottomed flask, unsubstituted or 6-substituted 3-acetylcoumarin (5.7 mmol) and 3-hydrazinoquinoxalin-2(1H)-one, 1 (1.0 g, 5.7 mmol) in dry DMF (20 mL) were taken. The reaction mixture was irradiated in a microwave oven at 400 W for 1 min. and the solvent was distilled off. The solid product obtained was filtered, dried and recrystallized from methanol to afford 3a-3d.

3-[2-[1-(2-oxo-2H-chromen-3-yl) ethylidene] hydrazino] quinoxalin-2(1H)-one (3a)

IR [ν , cm^{-1} , KBr]: 3140(N-H), 1735(C=O), 1667(C=O), 1575(C=N), 1290(C-O), 1205(m), 1132(m). λ_{max} (log ϵ_{max}): 212(4.58), 327(3.65s), 344(3.68), 350(3.32s), 405(3.13). $^1\text{H-NMR}$ [300 MHz, δ , ppm, DMSO- d_6]: 2.15(s, 3H, CH₃), 5.10(s, 1H, CH), 6.99-7.63 (m, 8H, 2xAr-H), 11.66(s, 1H, NH, D₂O, exchangeable). $^{13}\text{C-NMR}$ [50 MHz, δ , ppm, DMSO- d_6]: 200(C=O), 190.1(C=O), 158.1, 155.2, 153.1, 150.1, 148.7, 148.1, 147.1, 146.1, 145.0, 144.5, 140.1,

139.1, 137.3, 135.3, 130.0, 129.1, 45.1. MS: in m/z [rel. %]: 346[M⁺, 35%], 331[53%], 201[13%], 186[82%], 161[100%], 15[3%].

3-[2-[1-(6-bromo-2-oxo-2H-chromen-3-yl) ethylidene] hydrazine 0] quinoxalin-2(1H)-one (3b)

IR [ν , cm^{-1} , KBr]: 3135(N-H), 1740(C=O), 1665(C=O), 1575(C=N), 1288(m), 1130(m). λ_{max} (log ϵ_{max}): 210(4.10), 325(3.51), 345(3.41), 414(3.32). $^1\text{H-NMR}$ [300 MHz, δ , ppm, DMSO- d_6]: 2.45(s, 3H, CH₃), 5.40(s, 1H, CH), 7.21-7.97(m, 7H, 2xAr-H), 11.56(s, 1H, NH, D₂O, exchangeable). $^{13}\text{C-NMR}$ [50 MHz, δ , ppm, DMSO- d_6]: 200.0(C=O), 184.9(C=O), 158.4, 154.3, 153.0, 150.1, 148.7, 147.3, 146.3, 145.1, 144.7, 140.5, 139.3, 137.5, 135.0, 128.1, 50.4. MS: in m/z [rel. %]: 425[M⁺, 38%], 345[12%], 161[100%], 155[63%], 75[25%].

3-[2-[1-(6-chloro-2-oxo-2H-chromen-3-yl) ethylidene] hydrazine 0] quinoxalin-2(1H)-one (3c)

IR [ν , cm^{-1} , KBr]: 3133(N-H), 1745(C=O), 1666(C=O), 1575(C=N), 1285(m). λ_{max} (log ϵ_{max}): 215(4.11), 328(3.41), 347(3.57), 355(3.84), 360(3.97), 410(3.62). $^1\text{H-NMR}$ [300 MHz, δ , ppm, DMSO- d_6]: 2.58(s, 3H, CH₃), 5.91(s, 1H, CH), 7.59-8.21(m, 7H, 2xAr-H), 12.52(s, 1H, NH, D₂O, exchangeable). $^{13}\text{C-NMR}$ [50 MHz, δ , ppm, DMSO- d_6]: 200.8(C=O), 190.3(C=O), 158.9, 155.1, 153.7, 151.1, 149.7, 147.6, 146.9, 145.1, 144.9, 141.3, 139.3, 137.7, 135.8, 128.6, 52.5. MS: in m/z [rel. %]: 380.5[M⁺, 40%], 345[15%], 161[100%], 15[5%].

3-[2-[1-(6-methyl-2-oxo-2H-chromen-3-yl)ethylidene] hydrazino] quinoxalin-2(1H)-one (3d)

IR [ν , cm^{-1} , KBr]: 3118(N-H), 1742(C=O), 1665(C=O), 1571(C=N), 1273(m). λ_{max} (log ϵ_{max}): 210(3.11), 320(3.67), 342(3.17), 350(3.84), 360(3.51), 408(3.57 %). $^1\text{H-NMR}$ [300 MHz, δ , ppm, DMSO- d_6]: 2.38(s, 3H, CH₃), 3.88(s, 3H, CH₃), 5.03(s, 1H, CH), 6.73-7.43(m, 7H, 2xAr-H), 11.57(s, 1H, NH, D₂O, exchangeable). $^{13}\text{C-NMR}$ [50 MHz, δ , ppm, DMSO- d_6]: 195.0(C=O), 189.2(C=O), 157.3, 154.9, 153.2, 150.3, 149.8, 147.0, 145.9, 145.1, 143.8, 141.0, 138.3, 137.2, 134.6, 127.9, 52.5, 47.5. MS: in m/z [rel. %]: 360[M⁺, 35%], 346[20%], 161[100%], 158[60%], 72[18%], 15[7%].

Cyclopentanone 3-[(3-oxo-3, 4-dihydroquinoxalin-2-yl) hydrazone] 4**Conventional method**

A mixture of 3-hydrazinoquinoxalin-2(1H)-one, 1 (1.0 g, 5.7 mmol) and cyclopentanone (0.50 mL, 5.7 mmol) was dissolved in 50% of aqueous ethanol (20 mL) and then refluxed for 5 h. The reaction mixture was allowed to cool and the formed precipitate was recrystallized from ethanol to give 4.

Microwave method

3-Hydrazinoquinoxalin-2(1H)-one, 1 (1.0 g, 5.7 mmol) was dissolved in cyclopentanone (0.50 mL, 5.7 mmol), followed by the addition of 50% aqueous ethanol (20 mL) in an open beaker over heated alumina. The mixture was irradiated in microwave oven at an emitted power of 400 W for 3 min. to get a clear solution. The clear solution formed was left to stand at room temperature to crystallize. The solid formed was recrystallized from ethanol to give 4.

IR [ν , cm^{-1} , KBr]: 3120(N-H), 1675(C=O). λ_{max} (log ϵ_{max}): 220(3.11), 344(3.89), 350(3.35s). $^1\text{H-NMR}$ [300 MHz, δ , ppm, DMSO- d_6]: 1.75(quintet, 4H, 2xCH₂), 2.87(t, 4H, 2xCH₂), 7.12-

7.93(m, 4H, Ar-H), 11.53(s-br, 1H, NH, D₂O exchangeable). ¹³C-NMR [50 MHz, δ, ppm, DMSO-*d*₆]: 190(C=O), 155.2, 150.7, 149.3, 147.2, 145.3, 144.9, 135.7, 133.8, 98.5, 95.6, 66.3, 61.7. MS: in m/z[rel. %]: 242[M⁺, 75%], 161[100%], 118[68%], 78[10%].

General procedure of 5-substituted-1*H*-indole-2, 3-dione 3-[(3-oxo-3, 4-dihydroquinoxalin-2-yl) hydrazone] (5a-5d).

Conventional method

In a 250 mL round-bottomed flask, 3-hydrazinoquinoxalin-2(1*H*)-one, 1 (1.0 g, 5.7 mmol) and isatin or 5-substituted-isatin (5.7 mmol) in 1:5 of DMF/ethanol (30 mL) were taken. The reaction mixture was refluxed on water bath at 70 - 75 °C for 4 - 5 h and the solvent was distilled off. Then, it was poured into crushed ice and the product was filtered and recrystallized from DMF/water to give 5a-5d.

Microwave method

In a 250 mL round-bottomed flask, 3-hydrazinoquinoxalin-2(1*H*)-one, 1 (1.0 g, 5.7 mmol) and isatin or 5-substituted-isatin (5.7 mmol) in 1:5 of DMF/ethanol (30 mL) were taken. The reaction mixture was irradiated in microwave oven at an emitted power of 400 W for 2 min. Then, it was poured into crushed ice and the product was filtered and recrystallized from DMF/water to give 5a-5d.

1*H*-indole-2, 3-dione 3-[(3-oxo-3, 4-dihydroquinoxalin-2-yl) hydrazone] (5a)

IR [ν, cm⁻¹, KBr]: 3138(N-H), 1705(C=O), 1665(C=O), 1618(C=C), 1533(C=N), 1338, 1290, 1180, 1132. λ_{max} (log ε_{max}): 228(4.13), 272(4.22), 348(3.18s), 370(3.49s), 424(3.56). ¹H-NMR [300 MHz, δ, ppm, DMSO-*d*₆]: 7.10 - 7.65(m, 8H, 2xAr-H), 12.36(s-br, 1H, NH, D₂O exchangeable), 13.55(s-br, 1H, NH, D₂O exchangeable). ¹³C-NMR [50 MHz, δ, ppm, DMSO-*d*₆]: 200.1(C=O), 190.5(C=O), 155.2, 154.6, 154.1, 153.7, 153.1, 152.0, 150.1, 145.7, 143.8, 142.2, 135.1, 130.1, 128.3, 120.7. MS: in m/z[rel. %]: 305[M⁺, 68%], 161[100%], 145[35%], 91[15%].

5-bromo-1*H*-indole-2, 3-dione 3-[(3-oxo-3, 4-dihydroquinoxalin-2-yl) hydrazone] (5b)

IR [ν, cm⁻¹, KBr]: 3140(N-H), 1690(C=O), 1665(C=O), 1531(C=N), 1344, 1298, 1185, 1137. λ_{max} (log ε_{max}): 225(4.10), 270(4.01), 345(3.21), 420(3.71). ¹H-NMR [300 MHz, δ, ppm, DMSO-*d*₆]: 7.21 - 8.15(m, 7H, 2xAr-H), 12.40(s-br, 1H, NH, D₂O exchangeable), 13.57(s-br, 1H, NH, D₂O exchangeable). ¹³C-NMR [50 MHz, δ, ppm, DMSO-*d*₆]: 200.5(C=O), 190.9(C=O), 156.1, 154.9, 154.3, 153.9, 153.1, 152.4, 150.6, 145.9, 144.2, 142.8, 136.0, 130.1, 128.7, 120.9. MS: in m/z[rel. %]: 384[M⁺, 55%], 304[65%], 160[97%], 90[13%].

5-chloro-1*H*-indole-2, 3-dione 3-[(3-oxo-3, 4-dihydroquinoxalin-2-yl) hydrazone] (5c)

IR [ν, cm⁻¹, KBr]: 3145(N-H), 1705(C=O), 1670(C=O), 1533(C=N), 1349, 1188, 1139 cm⁻¹. λ_{max} (log ε_{max}): 210(3.74), 265(3.91), 340(3.46), 421(4.01). ¹H-NMR [300 MHz, δ, ppm, DMSO-*d*₆]: 7.65 - 8.77(m, 7H, 2xAr-H), 12.45(s-br, 1H, NH, D₂O exchangeable), 13.60(s-br, 1H, NH, D₂O exchangeable). ¹³C-NMR [50 MHz, δ, ppm, DMSO-*d*₆]: 201.0(C=O), 190.9(C=O), 156.9, 155.6, 154.8, 153.9, 153.4, 152.7, 150.9, 146.3, 144.1, 143.5, 136.4, 130.6, 129.0, 122.8. MS: in m/z[rel. %]: 339.5[M⁺, 63%], 304[60%], 161[100%], 125.5[18%].

5-methyl-1*H*-indole-2, 3-dione 3-[(3-oxo-3, 4-dihydroquinoxalin-2-yl) hydrazone] (5d)

IR [ν, cm⁻¹, KBr]: 3120(N-H), 1690(C=O), 1665(C=O), 1570(C=N), 1322, 1175. λ_{max} (log ε_{max}): 223(3.11), 267(3.78), 344(3.88), 425(4.12). ¹H-NMR [300 MHz, δ, ppm, DMSO-*d*₆]: 2.41(s, 3H, CH₃), 6.93 - 7.59(m, 7H, 2xAr-H), 11.55(s-br, 1H, NH, D₂O exchangeable), 12.60(s-br, 1H, NH, D₂O exchangeable). ¹³C-NMR [50 MHz, δ, ppm, DMSO-*d*₆]: 198(C=O), 185.1(C=O), 155.8, 155.0, 154.2, 153.5, 152.6, 151.4, 150.2, 145.3, 143.9, 142.1, 134.4, 130.1, 128.3, 120.2. MS: in m/z[rel. %]: 319[M⁺, 73%], 304[51%], 161[100%], 145[29%], 90[10%].

Synthesis of anthrone 3-[(3-oxo-3, 4-dihydroquinoxalin-2-yl) hydrazone], 6

Conventional heating method

3-Hydrazinoquinoxalin-2(1*H*)-one, 1 (1.0 g, 5.7 mmol) and anthrone (1.1 g, 5.7 mmol) were ground together in mortar and quantitatively transferred into a quick fit flask followed by the drop wise addition of 1:4 of DMF/ethanol (20 mL) with continuous stirring. The mixture was refluxed for 3 h. It was then allowed to cool and the formed precipitate was recrystallized from ethanol to afford 6.

Microwave irradiation method

A mixture of 3-hydrazinoquinoxalin-2(1*H*)-one, 1 (1.0 g, 5.7 mmol) and anthrone (1.1 g, 5.7 mmol) were ground together in mortar and quantitatively transferred into a quick fit flask followed by the dropwise addition of 1:4 of DMF/ethanol (20 mL) with continuous stirring. The reaction mixture was irradiated in domestic microwave oven over heated alumina at an emitted power of 400 W for 75s (1.25 min) to give a clear solution. It was then allowed to cool and the formed precipitate was recrystallized from ethanol to afford 6. IR [ν, cm⁻¹, KBr]: 3399(N-H), 1673(C=O), 1588(C=N). λ_{max} (log ε_{max}): 212(3.73), 252(3.50), 269(3.38s), 327(3.14s), 336(3.11s). ¹H-NMR [300 MHz, δ, ppm, DMSO-*d*₆]: 6.99 - 8.13(m, 13H, 4xAr-H), 12.58(s-br, 1H, NH, D₂O exchangeable). MS: in m/z[rel. %]: 351[M⁺, 85%], 174[100%], 76[23%].

Synthesis of 3{2-(1,7,7-trimethylbicyclo [2.2.1] hept-2-yl)hydrazino} quinoxalin-2(1*H*)-one, 7

Conventional method

A solution of camphor (0.9 g, 5.7 mmol) in ethanol (15 mL) was carefully added to 3-hydrazinoquinoxalin-2(1*H*)-one, 1 (1.0 g, 5.7 mmol) in a 250 mL round-bottomed flask. The reaction mixture was refluxed for 3 h. It was then allowed to cool and the formed precipitate was recrystallized from ethanol to afford 7.

Microwave method

A solution of camphor (0.9 g, 5.7 mmol) in ethanol (15 mL) was carefully added to 3-hydrazinoquinoxalin-2(1*H*)-one, 1 (1.0 g, 5.7 mmol) in an open beaker. The reaction mixture was irradiated in microwave oven at an emitted power of 400 W for 1 min. It was then allowed to cool and the formed precipitate was recrystallized from ethanol to afford 7. IR [ν, cm⁻¹, KBr]: 3272(N-H), 1685(C=O), 1588(C=N). λ_{max} (log ε_{max}): 216(4.31), 328(3.59), 350(3.56s). ¹H-NMR [300 MHz, δ, ppm, DMSO-*d*₆]: 1.21(s, 3H, CH₃), 1.52(s, 3H, CH₃), 1.95(s, 3H, CH₃), 2.11(t, 2H, CH₂), 2.36(t, 2H, CH₂), 2.96(t, 2H, CH₂), 3.01(q, 1H, CH), 7.12 - 7.79(m, 4H, Ar-H), 11.58(s-br, 1H, NH, D₂O exchangeable). MS: in m/z[rel. %]: 310[M⁺, 89%], 160[95%], 150[100%], 72[15%], 15[2%].

General procedure of 2-substituted-cyclohexanone 3-[(3-oxo-3,4-dihydroquinoxalin-2-yl)hydrazone] (8a-8d)**Conventional method**

To a pure and dry 3-hydrazinoquinoxalin-2(1*H*)-one, 1 (1.0 g, 5.7 mmol) was added in drop wise manner, cyclohexanone or 2-substituted cyclohexanone (5.7 mmol) with continuous stirring, followed by the addition of ethanol (30 mL). The reaction mixture was refluxed on water bath for 4 h. The reaction mixture was allowed to cool and the formed precipitate was recrystallized from ethanol to give (8a-8d).

Microwave method

To a pure and dry 3-hydrazinoquinoxalin-2(1*H*)-one, 1 (1.0 g, 5.7 mmol) was added in drop wise manner, cyclohexanone or 2-substituted cyclohexanone (5.7 mmol) with continuous stirring, followed by the addition of ethanol (30 mL). The reaction mixture was irradiated in microwave oven at an emitted power of 400 W for 2 min. The reaction mixture was allowed to cool and the formed precipitate was recrystallized from ethanol to give (8a-8d).

Cyclohexanone 3-[(3-oxo-3,4-dihydroquinoxalin-2-yl)hydrazone] (8a)

IR [ν , cm^{-1} , KBr]: 3225(N-H), 1667(C=O), 1575(C=N). λ_{max} (log ϵ_{max}): 220(3.81), 233(4.10), 345(3.52s). $^1\text{H-NMR}$ [300 MHz, δ , ppm, DMSO- d_6]: 1.72(quintet, 2H, CH₂), 2.36(quintet, 4H, 2xCH₂), 2.91(t, 4H, 2xCH₂), 7.03 - 7.89(m, 4H, Ar-H), 12.02(s-br, 1H, NH, D₂O exchangeable). $^{13}\text{C-NMR}$ [50 MHz, δ , ppm, DMSO- d_6]: 189.4(C=O), 145.2, 144.6, 140.7, 138.7, 136.1, 133.2, 130.1, 129.6, 100.7, 98.3, 53.1, 50.5, 47.2. MS: in m/z [rel. %]: 257[M⁺, 37%], 161[92%], 111[100%], 70[28%].

2-bromocyclohexanone 3-[(3-oxo-3,4-dihydroquinoxalin-2-yl)hydrazone] (8b)

IR [ν , cm^{-1} , KBr]: 3235(N-H), 1670(C=O), 1577(C=N). λ_{max} (log ϵ_{max}): 225(3.62), 235(3.96), 346(3.48s). $^1\text{H-NMR}$ [300 MHz, δ , ppm, DMSO- d_6]: 1.89(quintet, 2H, CH₂), 1.95(quintet, 2H, CH₂), 2.81(t, 2H, CH₂), 2.93(t, 2H, CH₂), 3.31(t, 1H, CH), 7.08 - 7.91(m, 4H, Ar-H), 12.35(s-br, 1H, NH, D₂O exchangeable). $^{13}\text{C-NMR}$ [50 MHz, δ , ppm, DMSO- d_6]: 191.0(C=O), 147.1, 145.7, 141.2, 139.5, 137.8, 134.7, 130.9, 129.9, 101.4, 99.5, 55.0, 51.9, 46.7. MS: in m/z [rel. %]: 336[M⁺, 49%], 256[40%], 190[100%], 175[70%].

2-chlorocyclohexanone 3-[(3-oxo-3,4-dihydroquinoxalin-2-yl)hydrazone] (8c)

IR [ν , cm^{-1} , KBr]: 3241(N-H), 1685(C=O), 1577(C=N). λ_{max} (log ϵ_{max}): 225(3.41), 238(3.18), 340(3.73s). $^1\text{H-NMR}$ [300 MHz, δ , ppm, DMSO- d_6]: 1.92(quintet, 2H, CH₂), 1.99(quintet, 2H, CH₂), 2.97(t, 2H, CH₂), 3.06(t, 2H, CH₂), 3.51(t, 1H, CH), 7.22 - 8.07(m, 4H, Ar-H), 12.49(s-br, 1H, NH, D₂O exchangeable). $^{13}\text{C-NMR}$ [50 MHz, δ , ppm, DMSO- d_6]: 196.0(C=O), 148.4, 146.7, 142.5, 140.1, 138.0, 135.4, 131.8, 130.7, 103.6, 99.8, 57.2, 52.8, 49.9. MS: in m/z [rel. %]: 291.5[M⁺, 53%], 256[39%], 145.5[100%], 130.5[73%].

2-methylcyclohexanone 3-[(3-oxo-3,4-dihydroquinoxalin-2-yl)hydrazone] (8d)

IR [ν , cm^{-1} , KBr]: 3205(N-H), 1663(C=O), 1570(C=N). λ_{max} (log ϵ_{max}): 230(3.73), 238(3.41), 350(3.73s). $^1\text{H-NMR}$ [300 MHz, δ , ppm,

DMSO- d_6]: 1.41(d, 3H, CH₃), 1.53(quintet, 2H, CH₂), 1.99(quintet, 2H, CH₂), 2.97(t, 2H, CH₂), 3.06(t, 2H, CH₂), 7.22 - 8.07(m, 4H, Ar-H), 12.49(s-br, 1H, NH, D₂O exchangeable). $^{13}\text{C-NMR}$ [50 MHz, δ , ppm, DMSO- d_6]: 193.2(C=O), 146.8, 145.1, 142.0, 140.1, 137.3, 135.1, 130.4, 130.1, 101.9, 99.1, 55.8, 51.5, 42.2, 13.9. MS: in m/z (rel. %): 271[M⁺, 66%], 256[36%], 125[100%], 84[15%], 15[7%].

RESULTS AND DISCUSSION

In this present work, the reaction of 3-hydrazinoquinoxalin-2(1*H*)-one, 1, with various ketones under microwave assisted technique as well as conventional heating method were studied. The precursor, 3-hydrazinoquinoxalin-2(1*H*)-one, 1, was first synthesized by hydrazinolysis of quinoxaline-2,3-dione with hydrazine hydrate under reflux (Scheme 1). The melting point, R_f values, molecular formula (molecular weight) and the result of elemental analysis of the synthesized compounds 1 - 8d is as shown in Table 1. The melting point ranged between 162°C and > 360°C while the reaction time under microwave was between 1 to 3 min. The products of the reactions were monitored through Thin Layer Chromatography (TLC) spotting using acetone: benzene solvent system.

Each of the reaction gave one spot with the R_f values varying from 0.41 to 0.73. The 6-chloro substituted 3-acetylcoumarin reacted vigorously with 3-hydrazinoquinoxalin-2(1*H*)-one 1 to give 3c in high yield (91%) followed by 6-bromo substituted 3-acetylcoumarin to give 86% of 3b. The 6-methyl substituted 3-acetylcoumarin condensed with 1 to afford 3d in low yield (73.2%), compared with other derivatives of 3 while the unsubstituted 3-acetylcoumarin, upon treatment with 1 gave 84% of 3a.

Hence, electron withdrawing groups (Br and Cl) on C-6 position of 3 favoured the nucleophilic attack on the 3-acetyl carbonyl to form 3b and 3c at high yield respectively whereas the electron donating group (CH₃) on C-6 position retarded the rate of nucleophilicity resulting in low yield (73.2%). In like manner, the chloro substituent on C-2 position of cyclohexanone imposed -I effect on the C-1 carbonyl and made it to be highly electrophilic. It is therefore, readily susceptible to nucleophilic attack from the free NH₂ end of 3-hydrazinoquinoxalin-2(1*H*)-one 1 to give 98.3% of 8c; followed by 2-bromo (being less electronegative than chloro) to give 83.9% yield of 8b. The 2-unsubstituted cyclohexanone gave 71.4% yield of 8a whereas, 2-methyl cyclohexanone, being electron donating in nature (+I effect) retarded the electrophilicity of C-1 carbonyl and made it to be less available to the nucleophilic attack to give low yield (65.2%) of 8d. Mechanistically, the formation of the hydrazones was represented using 7 as a typical example. It was initiated by the nucleophilic attack on the carbonyl of camphor to form the carbanion which subsequently underwent 1, 2-proton shift to afford the corresponding alcohol. Furthermore, the driving force for this reaction is the loss of stable molecule of water from the alcohol to form the expected hydrazone 7 as shown in Scheme 2. Presently,

Table 2. Comparison of conventional and microwave synthesis for the hydrazones 2a-8d.

Compd.	Conventional		Microwave		
	% yield	t/hrs	% yield	t/min	p/watt
2a	55.1	5	78.3	3	400
2b	50.3	5	66.8	3	400
2c	49.9	5	61.9	3	400
3a	59.4	3	84.0	1	400
3b	61.0	3	86.0	1	400
3c	70.2	3	91.0	1	400
3d	51.7	3	73.2	1	400
4	52.2	5	88.9	3	400
5a	70.0	4	90.8	2	400
5b	71.6	5	91.7	2	400
5c	74.0	4	93.4	2	400
5b	63.9	4	88.4	2	400
6	65.7	3	99.5	1.25	400
7	45.2	3	66.0	1	400
8a	52.9	4	71.4	2	400
8b	79.5	4	83.9	2	400
8c	83.2	4	98.3	2	400
8d	48.6	4	65.2	2	400

two ways by which thermally driven organic transformations take place are either by conventional heating or microwave accelerated heating (McLean et al., 2004). Comparative study on the two methods above was carried out and it was observed that all the reactions under microwave irradiation were completed within 1 - 3 min. whereas similar reactions under conventional heating (steam bath) at reflux gave poorer yields after much longer reaction time (Table 2).

For instance, the reaction of equimolar mixture of 3-hydrazinoquinoxalin-2(1*H*)-one **1** and cyclopentanone under microwave oven within 3 min. gave 88.9% of **4** whereas, the same reaction under conventional heating in 5 h of reflux afforded 52.2%. Also, the reaction of equimolar mixture of 3-hydrazinoquinoxalin-2(1*H*)-one and anthrone under microwave irradiation in 1.25 min. gave 99.5% of **6** while the same reaction under conventional heating (reflux) took 3 h to produce 65.7% (Table 2).

The result above indicated that microwave technique gave improved yield in less reaction time than the conventional heating method. This might be because microwaves couple directly with the molecules of the entire reaction mixture, leading to a rapid rise in temperature. Since, the process is not limited by the thermal conductivity of the vessel; the result above is an instantaneous localized superheating of the substance which responds to either dipole rotation or ionic conduction.

However, conventional heating is a slow and inefficient method of transferring heat energy into the reacting system because the heat driven into the substance first passes through the wall of the vessel before reaching the

solvent and reactants (Hayes, 2004). The result of elemental analysis (Table 1) did not only correlate well with the molecular masses of the compounds but also showed a consistent minimum difference of not more than ± 0.05 between % calculated and % found for the carbon, hydrogen and nitrogen of the prepared compounds, 1-8d.

From the spectroscopic studies, the infrared spectra of the compounds 1-8d showed absorption bands due to the stretching vibrations of N-H, C=O, C=C and C=N at 3412 - 3118 cm^{-1} , 1745 - 1663 cm^{-1} , 1620 - 1600 cm^{-1} and 1563 - 1588 cm^{-1} respectively.

Although, the carbonyl of amide present in the quinoxaline nucleus exhibited keto-enol tautomerism as shown in scheme 1, however, there was no infrared absorption band above 3500 cm^{-1} (absence of -OH). This indicated that the compounds existed in keto-form in the solid state. The IR spectrum of **2a** is as shown in Figure 1, where N-H and C=O bands appeared at 3241 and 1685 cm^{-1} respectively. Also, stretching vibration at 1612 and 1563 cm^{-1} depicted C=C aromatic and C=N bands while band at 2928 cm^{-1} is due to presence of CH of aliphatic.

The electronic transition of uv-visible spectra in methanol gave rise to wavelength (λ_{max}) ranging from 210 nm to 425 nm. The first wavelength (λ_{max}) for all the compounds were found between 210 - 230 nm as a result of $n \rightarrow \pi^*$ transition of the compounds indicating the presence of carbonyl of amide. The uv-visible absorption spectrum of the precursor, **1**, showed a peak at $\lambda_{\text{max}} = 216$ nm ($\log \epsilon_{\text{max}} = 4.34$) and two shoulders at $\lambda_{\text{max}} = 247$ nm ($\log \epsilon_{\text{max}} = 3.75\text{s}$) and $\lambda_{\text{max}} = 327$ nm ($\log \epsilon_{\text{max}} = 3.61\text{s}$).

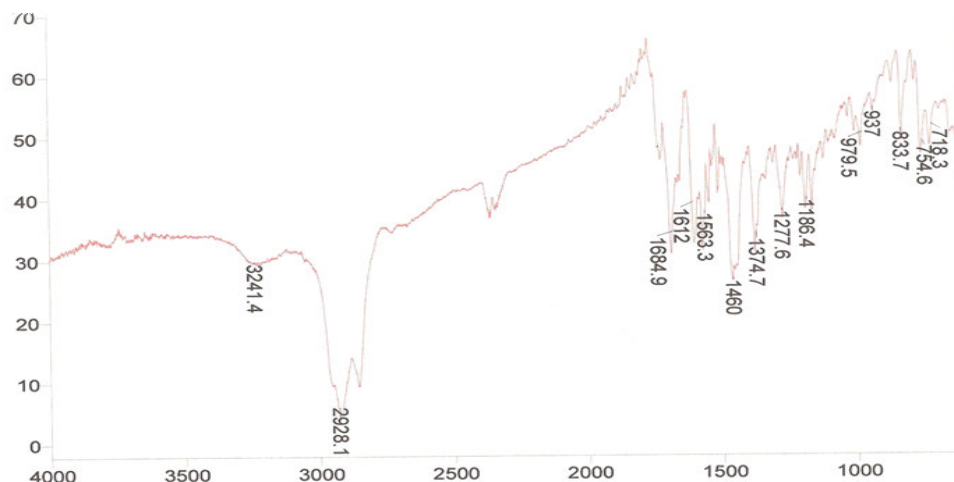
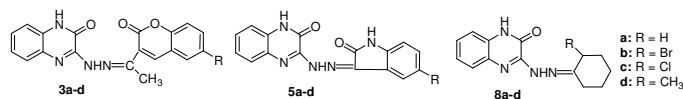


Figure 1. IR spectrum of 3-[2-(1-methylethylidene) hydrazino]quinoxalin-2(1H)-one, 2a.



In contrast, the uv-visible spectra of the hydrazones, 2a-8d, experienced a bathochromic shift of about 15 - 30 nm to give higher λ_{max} values at above 345 nm, which may be ascribed to the chromophoric C=N group; characteristic of K bands of C=N functional group (Komurcu et al., 1995). It may be noted that 2(1H)-quinoxalinone-3-hydrazone derivatives of 3-acetylcoumarin (3a-d) and isatin (5a-d) showed additional wavelength values at above 400 nm. This may be due to the more extensive π conjugation contributed by the additional benzene nuclei.

The chemical shifts and multiplicity patterns of ^1H - and ^{13}C -NMR correlated well with that of the proposed structures. So, the ^1H -NMR spectrum of 2a in $\text{CH}_3\text{OH}-d_4$ exhibited signals at δ 2.28(s, 3H, CH_3), 2.40(s, 3H, CH_3), 6.13(s, 1H, NH, D_2O exchangeable), 7.37 - 7.83(m, 4H, Ar-H) and 12.42(s-br, 1H, NH, D_2O exchangeable). However, no signal was found for methylene proton. Also, ^{13}C -NMR spectrum of 2a showed the presence of ten carbon with the signals ranging from 155.3(C=O) to 35.0 (CH_3) ppm.

The evidences from ^1H - and ^{13}C -NMR spectra of 2a showed that there was no cyclization of the hydrazone side chain to form triazolo-ring under microwave irradiation as well as conventional heating method. The ^1H -NMR spectrum of 2b in deuteriated methanol showed one singlet at δ 1.28(6H), assigned to two methyl groups that were chemically equivalent while one quartet at δ 2.80 (4H) was assigned to two chemically equivalent methylene groups.

The multiplet observed at δ 7.02 - 7.65 downfield of TMS scale was as a result of the presence of four aromatic protons while a broad singlet δ 11.59 (that disappeared

upon D_2O shaking) confirmed the presence of NH proton of the amide. The ^{13}C -NMR of 2b in deuteriated methanol, revealed the presence of thirteen different carbon atoms with C=O having highest signal at δ 154.1 ppm while the two CH_3 carbon atoms appeared to have the least signals at δ 13.8 and 12.5 ppm respectively.

The mass spectrum of 2b showed the molecular ion peak and the base peak at m/z 244 [M^+ , 10%] and 161 [$\text{M}^+ - 2(\text{CH}_2=\text{CH}_2) - (\text{HCN})$, 100%] respectively. Its mass spectrum was also characterized by the occurrence of some daughter fragments at m/z 188 [$\text{M}^+ - 2(\text{CH}_2=\text{CH}_2)$], 146, 118, 99, 71, 43, 15 with relative intensities of 65%, 85%, 75%, 15%, 17%, 8% and 3% respectively (Scheme 3).

The ^1H -NMR spectrum of 5a (unsubstituted isatin nucleus) showed a multiplet corresponding to eight aromatic protons at δ 7.10 - 7.65 while NH proton appeared as broad singlets at δ 12.36(s-br, 1H, NH, D_2O exchangeable) and 13.55(s-br, 1H, NH, D_2O exchangeable). However, 5b (5-bromo substituted) and 5c (5-chloro substituted) showed signals for seven aromatic protons at δ 7.21 - 8.15 and 7.65 - 8.77 respectively while that of 5d (5-methyl substituted) appeared at δ 6.93 - 7.59.

Compared to 5a that had no substituent on the isatin nucleus, the signals observed in the aromatic region of 5b and 5c were more downfield while that of 5d was more up field of TMS scale. The presence of 5-bromo and 5-chloro (electron withdrawing groups) on the isatin nucleus deshielded the aromatic protons thereby causing it to resonate more downfield. Nevertheless, the sigma donating character of 5-methyl in 5d allowed more electron density crowding around the aromatic protons thereby causing a shielding effect. This consequently led to an upfield resonance as so observed in 5d.

Conclusion

It was discovered that microwave-assisted approach is highly efficient procedure for the preparation of various

2(1*H*)-quinoxalinone-3-hydrazone derivatives compared to conventional heating method. The reactions occurred remarkably fast, under mild condition using highly inexpensive reagents and a domestic microwave oven as the irradiation source. The benefits of this environmentally benign and safe protocol include a simple reaction set-up, application of commercially available inexpensive reagents, easy work-up, high product yields, short reaction time as well as the easy elimination of solvents. Thus, this work will be very useful for further studies in terms of toxicity effect and Structural Activity Relationship (SAR) to improve their biological and pharmacological activities.

REFERENCES

- Abd-Elhafez OM, El-khrisy ED, Badria F, Fathy AD (2003). Synthesis and biological Investigations of new thiazolidinone and oxadiazoline coumarin derivatives. *Arch. Pharm. Res.* 26(9): 686-696.
- Abdellatif M, Salabeldin M, Alphy K (2008). Studies with enamionitriles: synthesis and chemical reactivity of 2-phenyl-3-piperidin-1-yl acrylonitrile under microwave heating. *J. Heterocycl. Chem.* 45: 307-310.
- Ali MM, Ismail MMF, El-Gaby MSA, Zahran MA, Ammar YA (2000). Synthesis and anti- microbial activities of some novel quinoxalinone derivatives. *Molecules* 5: 864-873.
- Badran MM, Abouzid KAM, Hussein MHM (2003). Synthesis certain substituted quinoxalines as anti-microbial agent part ii. *Arch. Pharm. Res.* 26: 107-113.
- Bijev A (2006). New heterocyclic hydrazones in the search for antitubercular agents: synthesis and in-vitro evaluations. *Lett. Drug Des. Discov.* 3: 506-512.
- Bogdal D, Jaskot K (2000). Synthesis of vinyl monomers with active azaaromatic groups: phase- transfer catalytic approach. *Synth. Commun.* 38: 3341-3352.
- Bogdal D, Yashchuck V, Pielichowski J, Ogulchansky T, Warzala M, Kudry V (2002). Synthesis and spectral investigation of alkyl methacrylates with halogenated carbazoyl pendant group for photonic application. *J. App. Polym. Sci.* 84: 1650-1656.
- Chang W-J, Yen W-B, Sun C-M (2003). Microwave-assisted soluble polymer-supported synthesis of benzopiperazinones. *Synlett*: 11: 1688-1692.
- Gedye R, Smith F, Westaway K, Ali H, Baldisera L, Laberge L, Roussel J (1986). The use of microwave ovens for rapid organic synthesis. *Tetrahedron Lett.* 27(3): 279 - 282.
- Giguere RJ, Bray TL, Duncan SM, Majetich G (1986). Application of commercial microwave oven to organic synthesis. *Tetrahedron Lett.* 27(41): 4945- 4948.
- Hayes BL (2004). Recent advances in Microwave-assisted synthesis. *Aldrichim. Acta* 37(2): 66-76.
- Jaso A, Zarranz B, Aldana I, Monge A (2003). Synthesis of new 2-acetyl and 2-benzoylquinoxaline 1,4-di-N-oxide derivatives as *antimycobacterium tuberculosis* agents. *Eur. J. Med. Chem.* 38: 791-800.
- Kim SH, Kim JH (2003). Synthesis and tautomerism of novel quinoxalines (part i). *J. Korean Chem. Soc.* 47(3): 241-243.
- Komurcu SG, Rollas S, Uglen M, Gorrod JW (1995). Evaluation of some arylhydrazones of p-amino benzoic acid hydrazide as antimicrobial agents and their *in-vitro* hepatic microsomal metabolism. *Boll. Chim. Farmac.* 134: 375-379.
- Loupy A, Petit A, Bodgal D. *Microwaves and Phase-Transfer Catalysis in : Microwave in organic Synthesis*, Loupy A. (Ed.), 2nd Edition, Wiley-VCH Verlag, Weinheim, 2006.
- McLean NJ, Tye H, Whittaker M (2004). Synthesis of cyclic peptides through hydroxyl side- chain anchoring. *Tetrahedron Lett.* 45: 933.
- Mehta PD, Sengar NPS, Subrahmanyam EVS, Satyanarayana D (2006). Synthesis and biological activity studies of some thiazolidinones and azetidinones. *Indian J. Pharm. Sci.* 68(1): 103-106.
- Muscia GC, Carnevale JP, Bollini M, Asis SE (2008). Microwave-assisted Döbner synthesis of 2- phenylquinoxaline-4-carboxylic acids and their antiparasitic activities. *J. Heterocycl. Chem.* 45: 611-614.
- Nasr MNA (2002). Synthesis and antibacterial activity of fused 1,2,4-triazolo[4,3-a]quinoxaline and oxopyrimido[2,1:5,1]-1,2,4-triazolo[4,3-a]quinoxaline derivatives. *Arch. Pharm. Med. Chem.* 389-394.
- Obafemi CA, Akinpelu DA (2005). Synthesis and antimicrobial activity of some 2(1*H*)- quinoxalinone-6-sulfonyl derivatives. *Phosphorus, Sulfur, Silicon Relat. Elem.* 180: 1795-1807.
- Olayiwola G, Obafemi CA, Taiwo FO (2007). Synthesis and neuropharmacological activity of some quinoxalinone derivatives. *African J. Biotech.* 6(6): 777-786.
- Outirite M, Lebrini M, Lagrenée M, Bentiss F (2008). New one step synthesis of 3,5-disubstituted pyrazoles under microwave irradiation and classical heating. *J. Heterocycl. Chem.* 45: 503-506.
- Pathak VN, Gupta R, Varshney B (2008). A one pot synthesis of 2-aryl-4*H*-1-benzopyran-4-ones under coupled microwave phase transfer catalysis and ultrasonic irradiation. *J. Het. Chem.* 45: 589-592.
- Pielichowski K Bogdal D, Pielichowski J, Boron A (1998). Post-cure effect of long-chain alkylene dimethacrylates. *Angew. Makromol. Chemie.* 257: 59-62.
- Qingqing S, Shuijiang T, Chunmei L, Longji C, Dianxiang Z, Qian W, Bo J, Yan Z.; Wenjuan H (2008). Green and high efficient synthesis of triaza-benzo[b]fluorene-6-one derivatives in water under microwave irradiation. *J. Het. Chem.* 45: 411-416.
- Ragavendran J, Sriam D, Patel S, Reddy I, Bharathwajan N, Stables J, Yogeewari P (2007). Design and synthesis of anticonvulsants from a combined phthalimid-GABA-aniline and hydrazone pharmacophore. *Eur. J. Med. Chem.* 42: 146-151.
- Rashed N, El Massry AM, El Ashry E-SH, Amer A, Zimmer H (1990). A facile synthesis of novel triazoloquinoxalinones and triazinoquinoxalinones. *J. Het. Chem.* 27: 691-694.
- Refaat HM, Moneer AA, Khalil OM (2004). Synthesis and anti-microbial activity of certain novel quinoxalines. *Arch. Pharm. Res.* 27: 1093-1098.
- Rodrigo DP, Faustino MAF, Pinto DCGA, Neve MGPM, Cavaleiro JAS (2008). Kinetic study of meso-tetraphenylporphyrin synthesis under microwave irradiation. *J. Heterocycl. Chem.* 45: 453-460.
- Rollas S, Küçükgüzel ŞG (2007). Biological activities of hydrazone derivatives. *Molecules* 12: 1910-1939.
- Rowan SJ, Cantrill SJ, Cousins GRL, Sanders JKM, Stoddart JF (2002). Dynamic covalent chemistry. *Angew. Chem.* 114: 938-993.
- Salgin-Gökşen U, Gökhan-keleşçi N, Göktaş Ö, Köysal Y, Kiliç E, Işık Ş, Aktay G, Özalp M (2007). 1-Acylothiosemicarbazides, 1,2,4-triazol-5(4*H*)-thiones 1,3,4-thiadiazoles and hydrazones containing 5-methyl-2-benzoxazoline: synthesis, analgesic, anti-inflammatory and antimicrobial activities. *Bioorg. Med. Chem.* 15: 5738-5751.
- Sanetra J, Bogdal D, Warzala M, Boron A (2002). Photo- and electroluminescence properties of polymethacrylates with carbazoyl and fluorescent pendant groups. *Chem. Mat.* 14: 89-95.
- Sha YW, Wang Y, Ge J, Wang X (2001). The rapid synthesis of Schiff-bases without solvent under microwave irradiation. *Chin. J. Org. Chem.* 21: 102.
- Sridhar SK, Ramesh A (2001). Synthesis and pharmacological activities of hydrazones, Schiff and mannich bases of isatin derivatives. *Biol. Pharm. Bull.* 24(10): 1149-1152.
- Sridharan V, Perumal PT, Avendaño C, Menéndez CJ (2007). The first aza Diel-Alder reaction involving an α,β -unsaturated hydrazone as the dienophile : stereoselective synthesis of C-4 functionalized 1,2,3,4-tetrahydroquinolines containing a quaternary stereocenter. *Org. Biomol. Chem.* 5: 1351-1353.
- Su D-S, Bock MG (2005). 2-Quinoxalinone derivatives as bradykinin antagonists and novel compounds. US Patent Appl. (20050020591).
- Tinh DV, Stadlbauer W (2008). Synthesis of 5-mono and 5,7-diamino pyrido[2,3-*d*]pyrimidinediones with potential biological activity by regioselective amination. *J. Heterocycl. Chem.* 45: 821-830.
- Vanetsev AS, Makshina EV, Oleynikov NN, Treť'yakou YD, Romanovskii BV (2005). Microwave Synthesis of Lanthanum Strontium Cobalites and Study of Their Catalytic Activity *Doklady Akademii Nauk* 405(2): 204-207.

Vicini P, Zani F, Cozzini P, Doytchinova I (2003). Hydrazones of 1,2-benzisothiazole hydrazide: synthesis, antimicrobial activities and QSAR investigation. *Eur. J. Med. Chem.* 37(7): 553-564.

Wenxiang H, Jianying W (2001). Combinatorial catalysis with physical, chemical and biological methodologies. *Chem. Mag.* 3(9): 44.

Zhenjiang L, Weisi L, Yingjie S, He H, Pingkai O (2008). Facile synthesis of quinoxaline catalyzed by amidosulfonic acid. *J. Heterocycl. Chem.* 45: 285-288.