Organic Chemistry
Current Research
ISSN: 2161-0401

Baranwal et al. Organic Chem Current Res 2014, S4
DOI: 10.4172/2161-0401.S4-001

Research Article Open Access

A Facile and Efficient Synthesis of Quinoxalines from Phenacyl Bromides and *Ortho* Phenylenediamine Promoted by Zirconium Tungstate

Lingaiah Nagarapu*, Jyothsna Devi Palem, Rama Krishna Reddy Aruva and Rajashaker Bantu

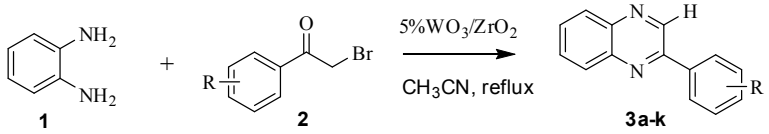
Organic Chemistry Division II, CSIR-Indian Institute of Chemical Technology, Hyderabad, India

Abstract

Quinoxaline derivatives have been synthesized by a simple, efficient, one-pot, two-component condensation of α,β-unsaturated ketones, *o*-phenylenediamine in the presence of a catalytic amount of 5% WO_3/ZrO_2 in excellent yields. The effect of electron releasing and electron with drawing substituent on the aromatic ring of phenacyl bromides on the reaction was investigated. Electron releasing groups and electron withdrawing groups did not affect significantly on the yields and the reaction times. Using 1,2-diamines possessing electron-withdrawing substituent needed longer reaction times and the yields were lower. Environmental acceptability, low cost, high yields and recyclability of the 5%WO_3/ZrO_2 are the important features of this protocol.

Graphical Abstract

Quinoxalines have been synthesized in very good yield from various substituted phenacyl bromides in the presence of 5%WO_3/ZrO_2 as catalyst.



Keywords: Quinoxaline; *o*-phenylenediamine; Zirconium tungstate

Introduction

Quinoxaline derivatives are an important class of nitrogen-containing heterocycles in medicinal chemistry [1-5]. Quinoxaline synthesis and chemistry has attracted considerable attention in the past ten years [6,7]. For example, quinoxaline is a part of various antibiotics such as echinomycin, levomycin, and actinoleutin that are known to inhibit growth of gram positive bacteria, and are active against various transplantable tumors. Some of them exhibit biological activities including anti-viral, anti-bacterial, anti-inflammatory, anti-protozoal, anti-cancer (colon cancer therapies), anti-depressant, anti-HIV, and as kinase inhibitors [8-14]. They are also used in the agricultural field as fungicides, herbicides, and insecticides [1]. In addition, quinoxaline derivatives have also found applications in dyes, efficient electron luminescent materials, organic semiconductors, chemically controllable switches, building blocks for the synthesis of anion receptors, cavitands, and dehydoannulenes [15,16]. They also serve as useful rigid subunits in macrocyclic receptors in molecular recognition.

Several kinds of synthetic routes toward quinoxalines have been developed, which involve condensation of 1,2-diamines with α-diketones [17], Bi-catalyzed oxidative coupling of epoxides with ene-1,2-diamines [18], cyclization-oxidation of phenacyl bromides [19,20]. However, many of these processes suffer from one or more limitations such as drastic reaction conditions, low product yields, the use of toxic metal salts as catalysts, and relatively expensive reagents. Moreover, these reactions are often carried out in polar solvents such as DMSO leading to tedious work-up procedures. We were interested to examine the synthesis of quinoxalines by the condensation of *o*-phenylenediamine and substituted phenacylbromides in the presence of a catalytic amount of 5%WO_3/ZrO_2 [21,22].

Experimental

Melting points were determined by using Fisher John's melting point apparatus and are uncorrected [23,24]. IR spectra were recorded on a Thermo Nicolet Nexus 670 FT-IR spectrometer. Accurate mass measurement was performed on Q STAR mass spectrometer (Applied Biosystems USA). ^1H NMR spectra and ^{13}C NMR were recorded at 300 MHz on a Bruker Avance NMR spectrometer with TMS as an internal standard (chemical shifts in δ, ppm). For column chromatography, silica gel 60-120 mesh was used. For TLC, silica gel $60F_{254}$ (Merck) was used.

General procedure for synthesis of 3a-k

To a solution of *o*-phenylene diamine (**1a,** 1.1 mmol), phenacyl bromide (**2a**, 1.0 mmol) was added 5%WO_3/ZrO_2 (0.3 mmol). The mixture was refluxed for 0.5 h in 3.0 mL of CH_3CN (progress of the reaction was monitored by TLC). After completion, the reaction mass was cooled to room temperature and the solid catalyst was filtered through a Buchner funnel, washed with CH_3CN (2×5 mL). The filtrate was removed under reduced pressure, and the crude product was

***Corresponding author:** Lingaiah Nagarapu, Organic Chemistry Division II, CSIR-Indian Institute of Chemical Technology, Hyderabad 500 007, India, Tel: +91-40-27191509/10/11; Fax: +91-40-27193382; E-mail: nagarapu@iict.res.in

Received January 07, 2014; **Accepted** February 20, 2014; **Published** February 27, 2014

Citation: Nagarapu L, Palem JD, Reddy Aruva RK, Bantu R (2014) A Facile and Efficient Synthesis of Quinoxalines from Phenacyl Bromides and *Ortho* Phenylenediamine Promoted by Zirconium Tungstate. Organic Chem Current Res S4: 001. doi:10.4172/2161-0401.S4-001

purified by column chromatograph. The recovered 5%WO_3/ZrO_2 dried and reused for a number of cycles without significant loss of activity.

2-Phenyl quinoxaline (3a): Solid; Yield 98%; mp 75-78°C; IR (KBr): ν_{max} 2913, 2841, 1916, 1711, 1623, 1521, 1401, 952, 821, 709 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.52-7.61 (s, 3H,Ar-H); 7.73-7.83 (m, 2H, Ar-H); 8.13-8.22 (m, 4H, Ar-H); 9.33 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 127.3, 129.0, 129.1, 129.5, 129.6, 130.1, 130.2, 136.7, 141.5, 142.2, 143.3.; MS(ESI)$^+$: m/z= 207 $[M^+H]^+$.

2-(4-Methylphenyl)quinoxaline (3b): Solid; Yield 96%; mp 84-90°C; IR (KBr): ν_{max} 2923, 2855, 1937, 1727, 1676, 1541, 1426, 954, 825, 712 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 2.47 (s, 3H,-CH_3); 7.31-7.36 (d, *J*=8.30 Hz, 2H, Ar-H); 8.08-8.13 (d, *J*=8.30 Hz, 4H); 9.29 (s, 1H, =CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.32, 127.30, 128.96, 129.16, 129.43, 129.77, 130.07, 140.36, 141.32, 143.19.

2-(4-Methoxyphenyl) quinoxaline (3c): Solid; Yield 97%; mp 94-98°C; IR (KBr): ν_{max} 2925, 1602, 1537, 1483, 1458, 1424, 1177, 953, 845,756 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 3.89 (s, 3H, OCH_3); 7.01-7.09 (d, *J*=9.06 Hz, 2H, Ar-H); 7.6-7.7 (m, 2H, Ar-H); 8.03-8.1 (m, 3H, Ar-H); 8.15-8.21 (d, *J*=8.30Hz, 2H, Ar-H); 9.26 (s, 1H,=CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 29.64, 55.39, 114.53, 128.90, 129.02, 129.25, 129.34, 130.01, 143.06, 161.43. MS(ESI)$^+$: m/z= 237 $[M^+H]^+$.

2-(4-Flourophenyl)quinoxaline (3d): Solid; Yield 92%; mp 112-118°C; IR: ν_{max} 2924, 2855, 1598, 1543, 1419, 1311, 1227, 1118, 956, 835, 754 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.20-7.27 (m, 2H, Ar-H); 7.7-7.8 (m,2H, Ar-H); 8.09-8.11 (m, 2H, Ar-H); 8.21-8.25 (m, 2H, Ar-H); 9.28 (s, 1H, =CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 116.10, 116.39, 129.13, 129.45, 129.60, 130.41, 142.92, 162.59, 165.91.

2-(4-Chlorophenyl) quinoxaline (3e): Solid; Yield 95%; mp-128-130°C; IR: ν_{max} 2924, 1590, 1538, 1485, 1309, 1121, 1045, 955, 830, 753 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.5-7.53 (d, *J*= 7.80Hz, 2H, Ar-H); 7.7-7.79 (m, 2H, Ar-H); 8.09-8.12 (t, *J*= 6.34 Hz, 2H, Ar-H); 8.16-8.19 (d, *J*= 7.806Hz, 2H, Ar-H); 9.29 (s, 1H, =CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 128.76, 129.16, 129.40, 129.57, 129.78, 130.47, 142.84, 142.2,150.55.753. MS(ESI)$^+$: m/z= 241 $[M^+H]^+$.

2-(4-Bromophenyl) quinoxaline (3f): Solid; Yield 94.0%; mp 128-131°C; IR: ν_{max} 2925, 1634, 1583, 1536, 1481, 1421, 1307, 1121, 1070, 954, 827, 710 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.66-7.71 (d, *J*=8.49 Hz, 2H, Ar-H); 7.73-7.80 (t, *J*= 7.81 Hz, 2H, Ar-H); 8.06-8.14 (d, *J*= 8.49 Hz, 4H, Ar-H); 9.29 (s, 1H, =CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 96.17,128.90, 129.481, 129.66, 129.90, 130.15, 132.22, 135.56, 142.46, 156.28. MS(ESI)$^+$: m/z= 287 $[M+H]^+$.

2-(Napthalen-2-yl) quinoxaline (3g): Solid; Yield 96%; mp 127-129°C; IR: ν_{max} 2924, 2855, 1724, 1626, 1542, 1486, 1359, 1193, 963, 859, 746 cm^{-1}.^1H NMR (300 MHz, $CDCl_3$): δ 7.50-7.57 (m, 2H, Ar-H); 7.7-7.81 (m, 2H, Ar-H); 7.86-7.91 (m, 1H, Ar-H); 7.97-802 (d, *J*= 8.30 Hz, 2H, Ar-H); 8.10-8.19(m, 2H, Ar-H); 8.65 (s, 1H, Ar-H); 9.47(s, 1H, =CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 124.57, 126.5, 127.39, 127.77, 128.87,129.22, 129.69, 129.98, 133.38, 134.14, 141.67, 142.87, 143.71. MS(ESI)$^+$: m/z= 257 $[M^+H]^+$.

7-Methyl-2-phenylquinoxaline (3h): Solid; Yield 87%; mp 117-120°C ; IR (KBr): ν_{max} 2923, 2855, 1942, 1725, 1626, 1541, 1426, 954, 825, 712 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 2.44 (s, 3H,-CH_3); 6.69 (d, *J*=8.687Hz, 2H, Ar-H); 7.66-7.7 (m, 2H); 8.1-8.4 (m, 2H), 8.19-8.26 (m, 2H) 9.30 (s, 1H, =CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.32, 128.21, 128.92 129.11, 129.43, 130.9, 131.27, 140.36, 141.42, 143.19. MS(ESI)$^+$: m/z= 221 $[M^+H]^+$.

2-(4-Bromophenyl)-7-methylquinoxaline (3i): Solid; Yield 78%; mp 126-129°C ; IR (KBr): ν_{max} 2923, 2855, 1937, 1727, 1676, 1541, 1426, 954, 825, 712 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 2.49 (s, 3H,-CH_3); 6.69 (d, *J*=8.687Hz, 2H, Ar-H); 7.69-7.71 (m, 2H); 8.04-8.06 (m, 2H), 8.19-8.27 (m, 2H) 9.30 (s, 1H, =CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.32, 128.52, 129.34, 129.43,129.91 130.9, 131.27, 140.36, 141.64, 143.19. MS(ESI)$^+$: m/z= 298 $[M+H]^+$.

7-Bromo-3-(4-methylphenyl)pyrido[2,3-*b*]pyrazine (3j): Solid; Yield 89.0%; mp 118-120°C; IR: ν_{max} 2928, 2855, 1785, 1587, 1432, 1365, 1123, 986, 874, 823, 753 cm^{-1}.; ^1H NMR (300 MHz, $CDCl_3$): δ 2.47 (s, 3H, CH_3); 7.34-7.39 (d, *J*= 8.309Hz,4H, Ar-H); 7.5-7.7 (m, 1H, Ar-H); 8.19-8.26 (d, J=8.30 Hz, 2H, Ar-H); 8.59-8.6 (d, *J*=2.26 Hz, 1H, Ar-H); 9.14-9.16 (d, *J*= 2.26Hz, 1H, Ar-H); ^{13}C NMR (75MHz, $CDCl_3$): δ 21.324, 124.56, 125.32,126.39, 127.89, 28.16, 129.86, 129.91, 131.26, 132.82, 133.14, 124.57, 127.77, 128.87, 129.22, 129.29, 129.69, 133.38, 134.14, 141.67, 142.37, 148, 3.71.

2-(Biphenyl-4-yl) quinoxaline (3k): Solid; Yield 95%; mp 116-118°C; IR: ν_{max} 2924, 1722, 1677, 1533,1417, 1303, 1127, 953, 914, 844, 722 cm^{-1}.^1H NMR (300 MHz, $CDCl_3$): δ 7.36-7.39 (d, *J*=7.16 Hz, 1H, Ar-H); 7.42-7.49 (t, *J*= 7.36 Hz, 2H, Ar-H); 7.61-7.67(d, *J*=7.17 Hz, 2H, Ar-H); 7.7-7.79 (m,4H, Ar-H); 8.1-8.17 (t, *J*=10.9 Hz, 2H, Ar-H); 8.28 -8.33 (d, *J*=8.30 Hz, 2H, Ar-H); 9.36 (s, 1H, =CH).^{13}C NMR (75 MHz, $CDCl_3$): δ 124.57, 127.77, 128.87, 129.22, 129.29, 129.69, 133.38, 134.14, 141.67, 142.37, 143.

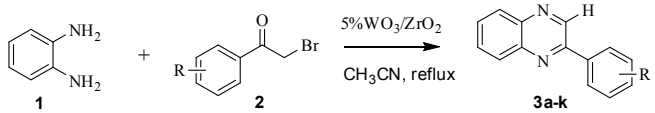
Results and Discussion

In order to optimize the reaction conditions, including solvents and temperature, and a suitable catalyst for the preparation of quinoxalines from *o*-phenylene diamine and α-halo-ketones, the condensation of *o*-phenylenediamine, with phenacyl bromide was chosen as a model reaction, and its behavior was studied in the presence of different catalysts and without catalyst in CH_3CN at reflux temperature. The results are listed in Table 1. As Table 1 indicates, *p*TSA, PMA solid, $FeCl_3$ gave relatively good yields of the product in long reaction times: however by using 5%WO_3/ZrO_2, the product was produced in excellent yield in very short reaction time. Thus, 5%WO_3/ZrO_2 was the catalyst of choice for all the reactions (Scheme 1).

Subsequently, we investigated on the use of different solvents for the purpose. In chlorinated solvents such as dichloromethane and chloroform the reaction was very slow and resulted in lower product yield. Similar results were obtained in coordinating solvents such as

Entry	Catalyst	Solvent	Condition	Time (h)	Time (h)
1	TMSCl	CH_3CN	Reflux	14.0	36
2	PMA solid	CH_3CN	Ref lux	11.0	42
3	FeCl3	C CH_3CN	Ref lux	10.0	45
4	PTSA	CH_3CN	Ref lux	9.0	45
5	5%WO_3/ZrO_2	CH_3CN	R.T	4.6	65
6	5%WO_3/ZrO_2	CH_3CN	Reflux	0.5	94

Table 1: Effect of different reagents and solvents in the condensation of o-phenylenediamine 1, phenacyl bromide 2.

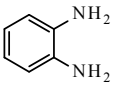
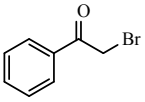
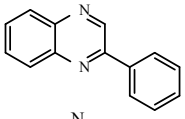
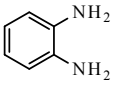
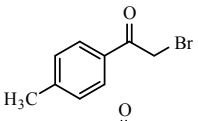
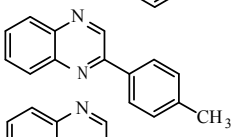
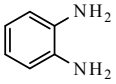
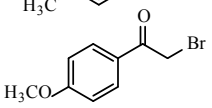
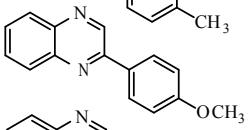
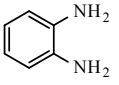
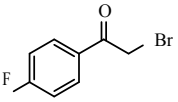
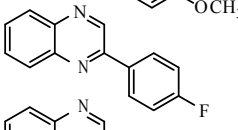
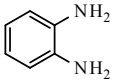
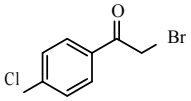
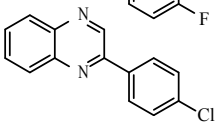
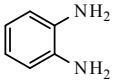
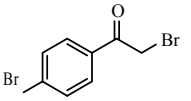
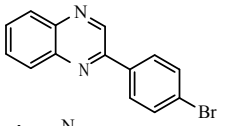
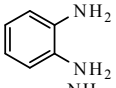
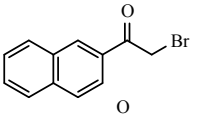
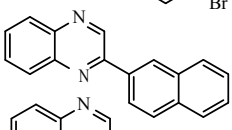
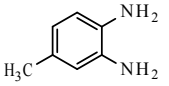
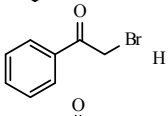
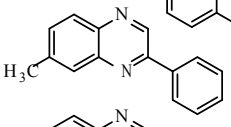
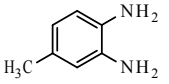
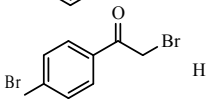
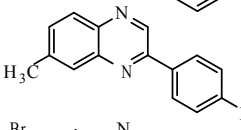
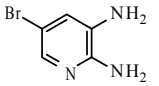
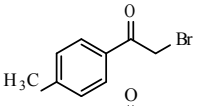
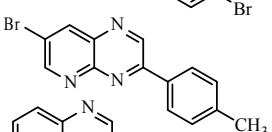
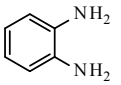
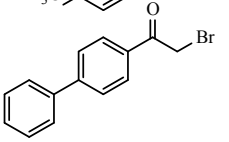
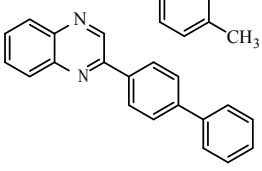


Scheme 1: The condensation of o-phenylenediamine, with phenacyl bromide.

THF, diethyl and dimethyl ether. On the other hand, conducting the reaction in inert solvents such as CH_3CN improved the reaction rates as well as product yields. After screening different solvents, CH_3CN came out as the solvent of choice, which not only afforded the products in good yield, but also with higher reaction rates (90% yield in 0.5 hours) (Table 1). It is also noticed that the condensation using 5% WO_3/ZrO_2 proceeds rapidly and is superior to the different reagents with respect to reaction time, temperature and yield. This claim is justified through the representative examples, illustrated in Table 1, in which the efficiency of 5% WO_3/ZrO_2 has been compared with those of different Lewis/protic acid catalysts (Table 1). The formation of compound **3a** was evident from the appearance of $[M^+H]^+$ peak at *m/z* 221 in mass spectrum (ESI), C-H stretching at 2923 cm^{-1}, C=N stretching at 1727 cm^{-1} in IR and the appearance of methyl protons as singlet at δ 2.45 and the characteristic proton of quinoxalines at δ 9.29 in ^1H NMR.

To establish the generality and scope of our method, various phenacyl bromides have been reacted with *o*-phenylenediamine. The results are displayed in Figure 1. As seen, the reaction proceeds efficiently and the respective quinoxalines were obtained in good to excellent yields and shorter reaction times.

In continuation of our studies [25-30] towards the synthesis of

Entry	Diamine	Haloketone	Product (3a-3k)	Time h	Yield %[a]
1				0.5	98.0
2				0.5	96.0
3				0.5	97.0
4				0.5	92.0
5				0.5	95.0
6				0.5	94.0
7				0.5	96.0
8				0.5	95.0
9				0.5	95.0
10				0.5	89.0
11				0.5	95.0

[a]Isolated yields

Figure 1: Synthesis of quinoxaline derivatives using 5%WO_3/ZrO_2.

novel compounds as useful biologically active compounds, we report in this communication an efficient synthesis of quinoxalines derivatives. To the best of our knowledge, in the literature there appear no reports for the synthesis and screening of quinoxalines derivatives using ZrO_2/WO_3. This fact has prompted us to investigate in depth the utility of 5% WO_3/ZrO_2 for the synthesis of quinoxalines.

The effect of electron releasing and electron with drawing substituent on the aromatic ring of phenacyl bromides on the reaction was investigated. As Figure 1 demonstrates, electron releasing groups and electron withdrawing groups did not affect significantly on the yields and the reaction times (Figure 1, entries 2, 3 and 4, 5, 6). Using 1,2-diamines possessing electron-withdrawing substituent needed longer reaction times and the yields were lower (Table 2, entry 10).

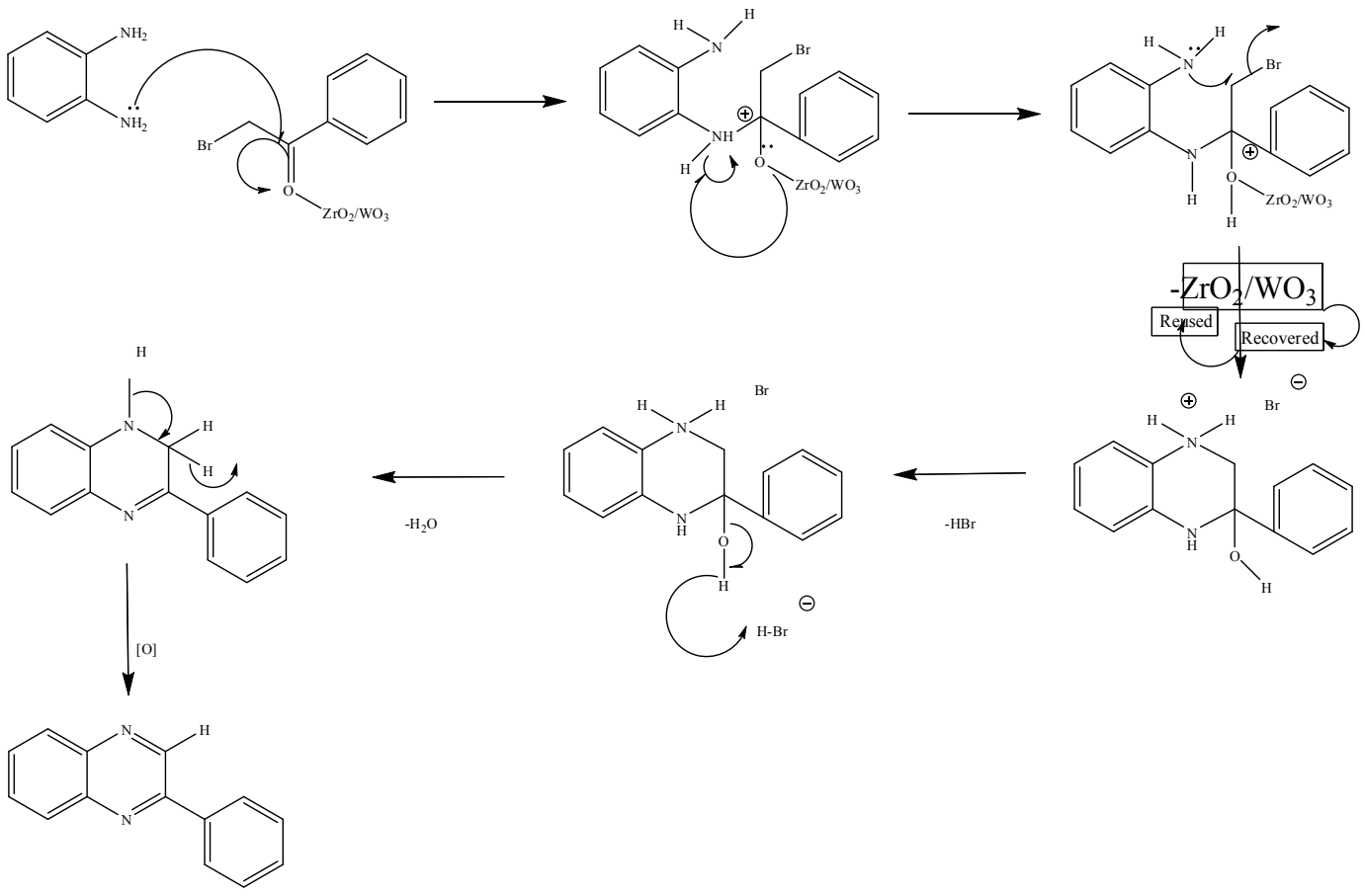
Ease of recycling of the catalyst is one of the most advantages of our method. For the reaction of *o*-phenylenediamine,with phenacyl bromide no significant loss of the product yield was observed when 5%WO_3/ZrO_2 was used after four times recycling (Table 2) (Scheme 2).

Conclusion

In conclusion, we have successfully synthesized and characterized derivatives of substituted quinoxalines using a catalytic amount of 5%WO_3/ZrO_2. This simple procedure is efficient and can be applied to a wide variety of phenacyl bromides. Shorter reaction times and excellent product yields make this catalytic system an alternative method for the synthesis of substituted quinoxaline derivatives. Further application to explore this simple catalytic system for construction of biological molecules is under progress. The remarkable catalytic activity of 5%WO_3/ZrO_2 exhibited is convincingly superior to the recently reported other catalytic methods with respect to reaction time, amount of catalyst used. Easy workup and ready availability of the catalyst makes the procedure superior over the existing methods. Environmental acceptability, low cost, high yields and recyclability of the 5%WO_3/ZrO_2 are the important features of this protocol. Furthermore the present protocol is readily amenable to parallel synthesis and generation of combinatorial substituted quinoxaline libraries.

Entry	Cycle	Time(min)	Yield
1	-	30	94
2	2	30	92
3	3	30	84
4	4	30	78
5	5	30	78

Table 2: The results of the condensation of *o*-Phenylenediamine with phenacyl bromide in the presence of recycled 5%WO_3/ZrO_2.



Scheme 2: Plausible mechanisam for the formation of 2-phenylquinoxaline 3a.

Acknowledgment

The authors are gratefully acknowledged to the DST-SERB/EMEQ-078/2013 for the financial support.

References

1. Sakata G, Makino K, Kurasawa Y (1998) Recent Progress in the Quinoxaline Chemistry. Synthesis and Biological Activity. Heterocycles 27: 2481-2515.
2. Meyers MR ,He W , Hanney B, Sapada A, Blider G, et al. (2003) Potent quinoxaline-Based inhibitors of PDGF receptor tyrosine kinase activity. Part 2: The synthesis and biological activities of RPR127963 an orally bio-available inhibitor. Bioorg Med Chem lett 13: 3097-3100.
3. Kim YB1, Kim YH, Park JY, Kim SK (2004) Synthesis and biological activity of new quinoxaline antibiotics of echinomycin analogues. Bioorg Med Chem Lett 14: 541-544.
4. Jaso A1, Zarranz B, Aldana I, Monge A (2005) Synthesis of new quinoxaline-2-carboxylate 1,4-dioxide derivatives as anti-Mycobacterium tuberculosis agents. J Med Chem 48: 2019-2025.
5. Carta A1, Paglietti G, Rahbar Nikookar ME, Sanna P, Sechi L, et al. (2002) Novel substituted quinoxaline 1,4-dioxides with in vitro antimycobacterial and anticandida activity. Eur J Med Chem 37: 355-366.
6. Katritzky AR, Rees CW (1984) Comprehensive Heterocyclic Chemistry, pergamon: Oxford, Part 2, Vol. 3: p157.
7. Sherman D, Kawakami J, He HY, Dhun F, Rios R, et al. (2007) Synthesis of unsymmetrical and regio-defined 2,3,6-quinoxaline and 2,3,7-pyridopyrazine derivatives. Tetrahedron Lett 48: 8943-8946.
8. Loriga M1, Piras S, Sanna P, Paglietti G (1997) Quinoxaline chemistry. Part 7. 2-[aminobenzoates]- and 2-[aminobenzoylglutamate]-quinoxalines as classical antifolate agents. Synthesis and evaluation of in vitro anticancer, anti-HIV and antifungal activity. Farmaco 52: 157-166.
9. Seitz LE1, Suling WJ, Reynolds RC (2002) Synthesis and antimycobacterial activity of pyrazine and quinoxaline derivatives. J Med Chem 45: 5604-5606.
10. Kim YB1, Kim YH, Park JY, Kim SK (2004) Synthesis and biological activity of new quinoxaline antibiotics of echinomycin analogues. Bioorg Med Chem Lett 14: 541-544.
11. Hui X1, Desrivot J, Bories C, Loiseau PM, Franck X, et al. (2006) Synthesis and antiprotozoal activity of some new synthetic substituted quinoxalines. Bioorg Med Chem Lett 16: 815-820.
12. Lindsley CW1, Zhao Z, Leister WH, Robinson RG, Barnett SF, et al. (2005) Allosteric Akt (PKB) inhibitors: discovery and SAR of isozyme selective inhibitors. Bioorg Med Chem Lett 15: 761-764.
13. Labarbera DV1, Skibo EB (2005) Synthesis of imidazo[1,5,4-de]quinoxalin-9-ones, benzimidazole analogues of pyrroloiminoquinone marine natural products. Bioorg Med Chem 13: 387-395.
14. Sarges R1, Howard HR, Browne RG, Lebel LA, Seymour PA, et al. (1990) 4-Amino[1,2,4]triazolo[4,3-a]quinoxalines. A novel class of potent adenosine receptor antagonists and potential rapid-onset antidepressants. J Med Chem 33: 2240-2254.
15. Thomas KRJ, Velusamy M, Lin JT, Chuen CH, Tao YT (2005) Chromophore-Labeled Quinoxaline Derivatives as efficient Electroluminescent Materials. Chem Mate 1860-1866.
16. Toshima K1, Takano R, Ozawa T, Matsumura S (2002) Molecular design and evaluation of quinoxaline-carbohydrate hybrids as novel and efficient photo-induced GG-selective DNA cleaving agents. Chem Commun (Camb) : 212-213.
17. Kim SY1, Park KH, Chung YK (2005) Manganese(IV) dioxide-catalyzed synthesis of quinoxalines under microwave irradiation. Chem Commun (Camb): 1321-1323.
18. Venkatesh C1, Singh B, Mahata PK, Ila H, Junjappa H (2005) Heteroannulation of nitroketene N,S-arylaminoacetals with POCl3: a novel highly regioselective synthesis of unsymmetrical 2,3-substituted quinoxalines. Org Lett 7: 2169-2172.
19. Wu Z, Ede N J (2001) Solid-phase Synthesis of qunoxalines on Synphase Lanterns. Tetrahedron Lett 42: 8115-8118.
20. Singh SK, Gupta P, Duggineni S, Kundu B (2003) Solid phase synthesis of quinoxalines. Synlett 2147-2150.
21. Sakthivel R, Prescott H, Kemnitz E (2004) WO3 / ZrO2 : a potential catalyst for the acetylation of anisole. J Mol Cat A: Chem 223: 137-142.
22. Nagarapu L, Baseeruddin B, Vijaya Kumari N, Kantevari S, Rudradas AP (2007) Efficient synthesis of aryl -14H- dibenzo[a.j] xanthenes using NaHSO4-SiO2 or 5%WO3/ZrO2 as heterogeneous catalysts under conventional heating in a solvent-free media. Synth. Commns 37(15): 2519-2525.
23. Nagarapu L, Raghu M, Glory A, Yeramanchi L (2010) Polyethylene glycol[PEG-400] mediated synthesis of quinoxalines. Eur J Chem 1(3): 220-231.
24. Das B, Venkateswarlu K, Suneel K, Majhi A (2007) An efficient and convenient protocol for the synthesis of quinoxalines and dihydropyrazines via cyclization-oxidation processes using HClO4-SiO2 as a heterogeneous recyclable catalyst. Tetrahedron Lett 48: 5371-5374.
25. Nagarapu L1, Vanaparthi S, Bantu R, Ganesh Kumar C (2013) Synthesis of novel benzo[4,5]thiazolo[1,2-a]pyrimidine-3-carboxylate derivatives and biological evaluation as potential anticancer agents. Eur J Med Chem 69: 817-822.
26. Nagarapu L1, Yadagiri B2, Bantu R2, Kumar CG3, Pombala S3, et al. (2014) Studies on the synthetic and structural aspects of benzosuberones bearing 2, 4-thiazolidenone moiety as potential anti-cancer agents. Eur J Med Chem 71: 91-97.
27. Nagarapu L, Narsimhaji CH, Shukla Chary K, Rajashakar B (2010) Synthesis of annulated pyrroles: condensation of aldose sugars, arylamines and 1,3-diones using TBAB. Synthesis 3374-3378.
28. Nagarapu L, Chary M V, Satyender A, Supriya B, Rajashakar B (2009) Iron(III) Chloride in Ethanol-Water: Highly Efficient catalytic system for the synthesis of Garcia Gonzalez Polyhydroxyalkyl- and C-Glycosylfurans. Synthesis 2278-2282.
29. Nagarapu L1, Satyender A, Rajashaker B, Srinivas K, Rupa rani P, et al. (2008) Synthesis and antimicrobial activity of novel C-linked imidazole glycoconjugates. Bioorg Med Chem Lett 18: 1167-1171.
30. Nagarapu L1, Paparaju V, Satyender A (2008) Synthesis of novel analogues of (+)-varitriol via olefin cross-metathesis reaction. Bioorg Med Chem Lett 18: 2351-2354.

This article was originally published in a special issue, **Synthetic Organic Chemistry** handled by Editor(s). Dr. Scott T Handy, Middle Tennessee State University, USA