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Catalytic application of recyclable silica-supported bismuth(III) chloride in the benzo[*N*,*N*]-heterocyclic condensation

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ABSTRACT

Silica-supported bismuth(III) chloride ($BiCl_3/SiO_2$) has been successfully employed in the condensation of 1,2-dicarbonyls with a variety of arene-1,2-diamines bearing either electron withdrawing or donating functional groups. The catalyzed reaction proceeded smoothly under ambient temperature in methanol to give the corresponding quinoxaline and pyrido[2,3-*b*]pyrazine compounds in good to excellent yields. The catalyst exhibited remarkable reusable activity and higher catalytic performance than homogeneous $BiCl_3$. A plausible mechanism for the catalytic action of $BiCl_3/SiO_2$ has been introduced. Moreover, the crystal structure of the prepared unsymmetrical benzo[*N*,*N*]-heterocycles has been determined by single crystal X-ray diffraction.

1. Introduction

Due to the detrimental effects of corrosive protic acids and toxic Lewis acids on the environment and stringent environmental laws and regulations set up by the governments, the use of eco-friendly and reusable heterogeneous solid acid catalysts has increased exponentially in the fine and bulk chemical industries during the last couple of decades [1,2]. Immobilization of catalysts on solid support provides an ideal method for combining the advantages of homogeneous catalysts (high activity and selectivity, etc.) with the engineering advantages of heterogeneous catalysts (available active site, easy catalyst separation, long catalytic life, thermal stability, low hygroscopic properties, easy handling and reusability of catalysts). Therefore, use of supported and recoverable catalysts in organic transformations has economic and environmental benefits [3–8].

In the past two decades, bismuth(III) compounds have attracted growing interests as versatile catalysts owing to their remarkable chemical and physical properties e.g. relevant stability, air- and moisture-tolerance, low toxicity. The importance of bismuth(III) salt as homogeneous catalyst in (biologically and pharmaceutically significant) organic transformations has clearly been highlighted in the literature [9–16]. Recently we have successfully incorporated bismuth into the framework of silica, combining the properties such as catalyst selectivity and activity with the ease of separation and catalyst reuse. Synthesis and characterization of silica-supported bismuth(III) chloride ($BiCl_3/SiO_2$) led to the formation of –O–BiOCl species on silica gel and proved to be effective as heterogeneous catalyst for the Paal–Knorr pyrrole cyclo-condensation reaction [17]. It has several advantages such as mild acidity, nontoxic nature, safe, easy to handle and store, stability at temperature and provides experimental simplicity. Considering its effectiveness in *N*-heterocyclic condensation, it was thought that $BiCl_3/SiO_2$ might satisfactorily catalyze benzo[*N*,*N*]-heterocyclic condensation and indeed this was observed.

In the present study, $BiCl_3/SiO_2$ has been investigated for its catalytic activity in acid-catalyzed condensation of various arene-1,2-diamines with 1,2-diketone to give quinoxaline and pyrido[2,3-*b*]pyrazine derivatives (Scheme 1). The biological, pharmaceutical, medicinal, and therapeutic properties of these compounds have been well established in the literature [18–27].

2. Experimental

2.1. Materials and methods

^1H and ^{13}C NMR spectra were recorded on a Bruker-500. All NMR samples were run in $CDCl_3$ and chemical shifts are expressed as ppm relative to internal Me_4Si. Mass spectra were obtained on a

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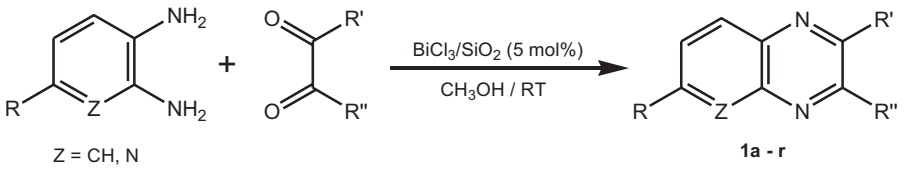


1a: R=H;	R'=R"=Ph; Z=CH	**1h**: R=H;	R'=R"=4-(MeO)-Ph; Z=CH	**1n**: R=H;	R'=Ph; R"=H; Z=CH
1b: R=Me;	R'=R"=Ph; Z=CH	**1i**: R=Me;	R'=R"=4-(MeO)-Ph; Z=CH	**1o**: R=Me;	R'=Ph; R"=H; Z=CH
1c: R=Cl;	R'=R"=Ph; Z=CH	**1j**: R=Cl;	R'=R"=4-(MeO)-Ph; Z=CH	**1p**: R=Cl;	R'=Ph; R"=H; Z=CH
1d: R=NO_2;	R'=R"=Ph; Z=CH	**1k**: R=NO_2;	R'=R"=4-(MeO)-Ph; Z=CH	**1q**: R=NO_2;	R'=Ph; R"=H; Z=CH
1e: R=H;	R'=R"=Ph; Z=N	**1l**: R=H;	R'=R"=4-(MeO)-Ph; Z=N	**1r**: R=H;	R'=Ph; R"=H; Z=N
1f: R=Ph-CO;	R'=R"=Ph; Z=CH	**1m**: R=Ph-CO;	R'=R"=4-(MeO)-Ph; Z=CH		
1g: R=COOH;	R'=R"=Ph; Z=CH				

Scheme 1. Condensation of 1,2-dicarbonyls with 1,2-diamines catalyzed by $BiCl_3/SiO_2$.

Fisons instrument. Substrates are commercially available and used without further purification.

2.2. Preparation of $BiCl_3/SiO_2$ catalyst

A total of 30 g of silica gel (300–400 mesh) were activated by refluxing with 150 mL of 6 mol L^{-1} hydrochloric acid under stirring for 24 h. Then the activated silica gel was filtered and washed with doubly distilled water to neutral and dried under vacuum at 70 °C for 24 h.

Bismuth(III) chloride (1.575 g, 5 mmol) was added to a suspension of activated silica gel (17.5 g) in toluene (30 mL). The mixture was stirred at room temperature overnight and filtered off. The solid was washed with ethanol and filtered off. The obtained solid was dried at 120 °C under vacuum for 5 h to furnish $BiCl_3/SiO_2$ as a white free-flowing powder (6.1 wt% of –O–BiOCl species as determined by TGA and 5.0 mol% of Bi as determined by Atomic Absorption Spectrophotometry). Characterization details of the catalyst are given in our previous work [17].

2.3. General procedure for the acid-catalyzed benzo[N,N]-heterocyclic condensation

A mixture of arene-1,2-diamine (1.2 mmol), 1,2-dicarbonyl (1 mmol), and 0.20 g of $BiCl_3/SiO_2$ (5 mol %) was taken in methanol (5 mL) and stirred at room temperature for the appropriate reaction time (Scheme 1). After completion of the reaction (monitored by TLC using ethyl acetate/hexane (2:8 v/v) or GC), dichloromethane was added to the reaction mixture and the catalyst was recovered by filtration. The organic medium was removed with rotary evaporator under reduced pressure. The crude products were purified by column chromatography using ethyl acetate/hexane (2:8 v/v) [dichloromethane/ethanol (9:1 v/v) for products **1h**–**1m**] to afford pure products for analytical measurements. The products were identified by comparison of their NMR and mass spectra with authentic samples.

2.4. Selected spectroscopic data

2.4.1. 6-Benzoyl-2,3-diphenylquinoxaline (**1f**)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32–7.64 (m, 13H), 7.90 (d, 2H), 8.25–8.30 (AB quartet, 2H), 8.54 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 128.31 (3C), 128.46 (2C), 129.10, 129.24, 129.63, 129.77 (2C), 129.81, 129.84 (2C), 130.18 (2C), 132.40, 132.75, 137.14, 138.24, 138.55, 138.59, 140.14, 142.93, 154.53, 155.07, 195.67; MS (EI), *m*/*z* (rel. intensity %) 386 (M^+, 65), 385 (70), 309 (40), 152 (35), 105 (100), 77 (95).

2.4.2. 6-Carboxylic acid-2,3-diphenylquinoxaline (**1g**)

^{1}H NMR (500 MHz, DMSO/$CDCl_3$) δ 7.30–7.36 (m, 6H), 7.50–7.51 (d, 4H), 8.16–8.17 (d, 1H), 8.34–8.36 (d, 1H), 8.89 (s, 1H), 11.25 (br s, 1H, COOH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 128.22 (2C), 128.23, 128.93, 129.11, 129.76, 129.79 (2C), 131.92, 132.05, 138.63, 140.41, 143.04, 154.17, 154.76, 167.77; MS (EI), *m*/*z* (rel. intensity %) 326 (M^+, 100), 178 (40), 103 (65), 77 (40).

2.4.3. 6-Benzoyl-2,3-bis(4-methoxyphenyl)quinoxaline (**1m**)

^{1}H NMR (500 MHz, $CDCl_3$) δ 3.82 (s, 3H), 3.85 (s, 3H), 6.87 (t, 4H), 7.49–7.55 (m, 6H), 7.60–7.63 (t, 1H), 7.89 (d, 2H), 8.21 (s, 2H), 8.47 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.26 (2C), 113.81 (3C), 128.42 (2C), 129.37 (2C), 129.41 (2C), 130.05, 131.11, 131.16, 131.35 (2C), 132.27 (2C), 132.64, 137.26, 137.71, 139.91, 142.81, 154.06, 154.59, 160.39, 160.54, 195.71; MS (EI), *m*/*z* (rel. intensity %) 446 (M^+, 10), 341 (10), 208 (15), 133 (35), 105 (100), 77 (50).

2.4.4. 6-Chloro-2-phenylquinoxaline (**1p**$_{trans}$)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51–7.58 (m, 3H), 7.71 (dd, *J* 2.3 and 8.95 Hz, 1H), 8.07 (d, *J* 8.8 Hz, 1H), 8.10 (d, *J* 3.15 Hz, 1H), 8.17 (m, 2H), 9.31 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 127.4 (2C), 128.0, 129.1 (2C), 130.4, 130.7, 131.2, 135.2, 136.3, 140.7, 141.7, 144.0, 151.8; MS (EI), *m*/*z* (rel. intensity %) 240 (M^+, 100), 241 (M^+, 25), 242 (M^+, 35), 213 (12), 178 (15), 77 (10).

2.4.5. 7-Chloro-2-phenylquinoxaline (**1p**$_{cis}$)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47–7.54 (m, 3H), 7.60 (dd, *J* 2.2 and 8.9 Hz, 1H), 7.97 (d, *J* 8.9 Hz, 1H), 8.06 (d, *J* 2.2 Hz, 1H), 8.13 (m, 2H), 9.22 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 127.4 (2C), 128.3, 129.0 (2C), 130.1, 130.2, 130.4, 135.8, 136.0, 139.8, 142.4, 143.1, 152.1; MS (EI), *m*/*z* (rel. intensity %) 240 (M^+, 100), 241 (M^+, 27), 242 (M^+, 38), 213 (12), 178 (15), 77 (10).

2.5. Crystal structure analyses of compounds **1o**$_{trans}$, **1p**$_{cis}$, **1q**$_{trans}$ and **1r**$_{cis}$

The selected crystals of 6-methyl-2-phenylquinoxaline (**1o**$_{trans}$), 7-chloro-2-phenylquinoxaline (**1p**$_{cis}$), 6-nitro-2-phenylquinoxaline (**1q**$_{trans}$) and 3-phenylpyrido[2,3-*b*]pyrazine (**1r**$_{cis}$) were covered with perfluorinated oil and mounted on the top of a glass capillary under a flow of cold gaseous nitrogen. The orientation matrix and the unit cell dimensions were determined (Table 1) from *ca.* 1173 (**1o**$_{trans}$, Stoe IPDS I), 7000 (**1p**$_{cis}$, Stoe IPDS II), 2524 (**1q**$_{trans}$, Stoe IPDS I) and 2530 (**1r**$_{cis}$, Stoe IPDS I) reflections (graphite-monochromated Mo-Kα radiation (λ = 71.073 pm). The intensities were corrected for Lorentz and polarizations effects. In addition, absorption corrections were applied for **1p**$_{cis}$ (numerical). The structures were solved by direct methods for all compounds using *SHELXS-97* for **1p**$_{cis}$ and *SIR-92* for **1o**$_{trans}$, **1q**$_{trans}$ and **1r**$_{cis}$. The structures were refined against F^2 by full-matrix least-squares using the program *SHELXL-97*. All hydrogen atoms in all compounds were calculated for ideal positions and were refined with a common displacement parameter. Programs used were *SHELXS-97* [28],

Table 1
Crystallographic data for compounds **1o*trans***, **1p*cis***, **1q*trans*** and **1r*cis***.

Compound	1o*trans*	1p*cis*	1q*trans*	1r*cis*
Empirical formula	$C_{15}H_{12}N_2$	$C_{14}H_9ClN_2$	$C_{14}H_9N_3O_2$	$C_{13}H_9N_3$
Formula mass	220.27	240.68	251.24	207.23
Crystal size [mm]	0.28 × 0.15 × 0.08	0.32 × 0.12 × 0.07	0.56 × 0.12 × 0.11	0.36 × 0.29 × 0.28
Crystal system	Monoclinic	Monoclinic	Triclinic	Monoclinic
Space group	$P2_1$	$P2_1/c$	P-1	$P2_1/c$
a [pm]	954.0(3)	382.1(1)	388.6(1)	552.3(1)
b [pm]	480.4(1)	2602.5(1)	1133.6(2)	1030.3(2)
c [pm]	1260.1(3)	1091.7(1)	1324.4(3)	1741.7(3)
α [°]	90	90	78.36(3)	90
β [°]	103.35(3)	95.65(1)	83.68(3)	92.27(2)
γ [°]	90	90	81.23(2)	90
Volume [$pm^3 \times 10^6$]	561.9(3)	1080.3(3)	562.8(2)	990.3(3)
Z	2	4	2	4
$d_{calcd.}$ [g cm^{-3}]	1.302	1.48	1.482	1.39
Absorp. correction	None	Numerical	None	None
μ [cm^{-1}] (Mo-Kα)	0.78	3.27	1.03	0.86
Temp. [K]	193	100	193	193
$2\theta_{max}$ [°]	52.66	51.78	51.88	52.22
Index range				
h	−11→11	−4→4	−4→4	−6→6
k	−5→5	−31→31	−13→13	−12→12
l	−15→15	−13→13	−16→16	−21→21
Reflections collected	4349	14906	5568	9483
Uniq. reflect. (R_{int})	2097 (0.1786)	2052 (0.0523)	2052 (0.082)	1852 (0.1014)
Reflect. with $F_o > 4\sigma(F_o)$	696	1526	1125	788
Parameters	156	155	173	146
Flack parameter	–	–	–	–
R_1	0.0603	0.0275	0.0406	0.0337
wR_2 (all data)	0.1275[a]	0.0591[b]	0.0969[c]	0.0727[d]
Max. residual electron density [(e pm^{-3})·10^{-6}]	0.255	0.18	0.235	0.136

[a] $w = 1/[\sigma^2(F_o^2)+(0.029P)^2]$; $P = [\max(F_o^2, 0)+2F_c^2]/3$.
[b] $w = 1/[\sigma^2(F_o^2)+(0.0329P)^2]$.
[c] $w = 1/[\sigma^2(F_o^2)+(0.0416P)^2]$.
[d] $w = 1/[\sigma^2(F_o^2)+(0.0257P)^2]$.

SIR-92 [29], *SHELXL-97* [30], *SHELXTL-Plus* [31] and *PLATON* [32]. The Flack Parameter of **1o*trans*** could not be determined reliable because of the use of MoKα radiation.

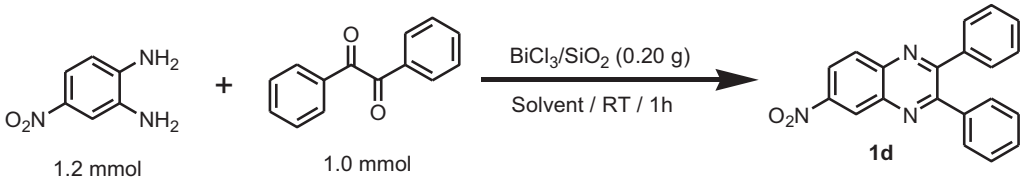
3. Results and discussion

3.1. Optimization of the model reaction

In an initial study to evaluate the catalytic activity of $BiCl_3/SiO_2$, we deliberately chose a strong electron withdrawing group such as nitro on the aromatic ring of benzene-1,2-diamine for the model reaction (Scheme 2). The reason for this judicious choice was that the strong electron withdrawing property of the nitro group in 4-nitrobenzene-1,2-diamine noticeably decreases the nucleophilicity of the amino group, hence longer reaction time is required [33–38]. In order to determine the optimum conditions, the type and amount of solvent, the proportions of catalyst to substrate and the molar ratio of diamine to benzil were examined.

The effect of various solvents on the yield of product is given in Table 2. The reaction did not progress in water (Table 2, entry 1) and gave poor yields in hexane, dichloroethane, dichloromethane and dimethyl sulfoxide (Table 2, entries 6, 9–11). The reaction in *n*-butanol, *n*-propanol, acetonitrile and tetrahydrofuran resulted in 47–74% yield of product (Table 2, entries 4–5, 7–8). Ethanol gave 90% yield of **1d** (Table 2, entry 2), whereas methanol was found to be the most effective solvent (Table 2, entry 3). The optimum amount of methanol was also examined to show that 5 mL would suffice per 1 mmol of benzil to complete the reaction for the synthesis of **1d** (Table 2, entries 3, 12–14).

To investigate the role of $BiCl_3/SiO_2$, the same reaction was carried out in the absence or presence of catalyst. In the absence of $BiCl_3/SiO_2$, low yield of product **1d** was obtained, which indicates that catalyst is obviously necessary for the reaction (Table 3, entries 1–2). A remarkable yield for **1d** was observed (89%) when the reaction was carried out under catalytic influence of homogeneous $BiCl_3$ (Table 3, entry 3), indicating the prominent role of $BiCl_3$ as Lewis acid catalyst. In contrast, heterogeneous $BiCl_3/SiO_2$ proved to



Scheme 2. Condensation of benzil with 4-nitrobenzene-1,2-diamine catalyzed by $BiCl_3/SiO_2$.

Table 2
Solvent effect on the synthesis of **1d** in the presence of $BiCl_3/SiO_2$ as catalyst.

Entry	Solvent	Solvent (mL)	Conversion (%)[a]
1	Water	5	Trace
2	Ethanol	5	90
3	Methanol	5	98
4	*n*-Propanol	5	50
5	*n*-Butanol	5	47
6	Hexane	5	6
7	Acetonitrile	5	72
8	Tetrahydrofuran	5	74
9	Dichloromethane	5	14
10	Dichloroethane	5	6
11	Dimethyl sulfoxide	5	21
12	Methanol	3	96
13	Methanol	10	95
14	Methanol	20	91

[a] Gas chromatography assay (%).

be more effective compared to $BiCl_3$ itself (Table 3, entries 4–7). Therefore, the remarkable efficiency of $BiCl_3/SiO_2$ can be explained by a better synergetic effect of $BiCl_3$ with SiO_2, due to the existence of multiple Lewis acid catalytic centers.

In the study of catalyst loading, the effect of the relative amounts of $BiCl_3/SiO_2$ (i.e., active species of $BiCl_3$) on the outcome of the model reaction was also studied. The optimum amount of $BiCl_3/SiO_2$ was found to be 0.20 g of catalyst containing 0.05 mmol of $BiCl_3$ per 1 mmol of substrate (Table 3, entry 5). The fewer amount gave a lower yield, and the more amounts could not cause the obvious increase for the yield of product.

The study on the molar ratio of 4-nitrobenzene-1,2-diamine to benzil showed that 1.2 mmol of diamine per 1 mmol of benzil in the presence of 0.05 mmol of $BiCl_3/SiO_2$ led to the quantitative conversion of **1d** (Table 4, entry 2).

3.2. Evaluation of the reaction scope

To expand the generality of this novel catalytic method, various aromatic arene-1,2-diamines were tested with 1,2-dicarbonyls under the optimized conditions (Scheme 1) and the results are presented in Table 5. In all cases, the reactions proceeded expeditiously at room temperature, although the yields were highly dependent on the substrate used (Table 5).

Turnover frequency (TOF) as a measure of catalyst activity for this catalytic process has been compared in Table 5 to show the reaction rate is highly dependent on the substrate used. In most cases, moderate to high values of TOF in range of 40–240 h^{-1} have been achieved. Nevertheless, a substantial decrease in the TOF value (6 h^{-1}) is observed for substrates of very low activity (Table 5, entry 11).

The regioselectivity for 4-substituted 1,2-diaminobenzenes on treatment with phenylglyoxal in the presence of $BiCl_3/SiO_2$ was also

Table 3
$BiCl_3/SiO_2$ catalytic effect on the synthesis of **1d** within 1 h.

Entry	Catalyst amount (g)	Loaded $BiCl_3$ (mmol)	Solvent	Conversion (%)[a]
1	–	–	Methanol	11
2	0.50[b]	–	Methanol	28
3	–	0.05	Methanol	89
4	0.10	0.025	Methanol	94
5	0.20	0.05	Methanol	98
6	0.30	0.075	Methanol	98
7	0.40	0.10	Methanol	98

[a] Gas chromatography assay (%).
[b] Activated silica gel in the absence of $BiCl_3$.

Table 4
Optimization of the molar ratio of 4-nitrobenzene-1,2-diamine to benzil on the synthesis of **1d** in the presence of $BiCl_3/SiO_2$ (5 mol%) within 1 h.

Entry	Molar ratio of substrates		Solvent (5 mL)	Conversion (%)[a]
	$4\text{-}O_2N\text{–}C_6H_3(NH_2)_2$	$C_6H_5\text{–}CO\text{–}CO\text{–}C_6H_5$		
1	1	1	Methanol	94
2	1.2	1	Methanol	98
3	1.5	1	Methanol	85
4	2	1	Methanol	78
5	1	1.2	Methanol	92

[a] Gas chromatography assay (%).

investigated (Table 5, entries 15–18). With the exception of 2,3-diaminopyridine, which showed very high selectivity to *cis*-regioisomer **1r** [38,39], the condensation of other 4-substituted 1,2-diaminobenzenes with phenylglyoxal resulted in a mixture of regioisomers **1o**–**1q**, in favor of *trans*-regioisomers [25,40,41]. The regioselectivity was determined by ^1H NMR and also by comparison with known samples. In addition, the molecular structures of compounds $\mathbf{1o}_{trans}$ (Fig. 1), $\mathbf{1p}_{cis}$ (Fig. 2), $\mathbf{1q}_{trans}$ (Fig. 3) and $\mathbf{1r}_{cis}$ (Fig. 4) were determined by X-ray diffraction analysis. On the basis of these molecular structures, the quinoxaline skeleton in all compounds is essentially planar. The molecules of $\mathbf{1o}_{trans}$ and $\mathbf{1r}_{cis}$ are nearly planar, while aryl groups of $\mathbf{1p}_{cis}$ and $\mathbf{1q}_{trans}$ are tilted about 20° and 28°, respectively. The planarity of molecules is directly related to N···H distance of nitrogen of diazacycles and ortho-H of aryl groups. The crystal packing of $\mathbf{1r}_{cis}$ includes four molecules in which quinoxaline units overlap each other not only in a face-to-face interaction, but also in an edge-to-face interaction. In contrast, the crystal packing of $\mathbf{1o}_{trans}$ includes two molecules in which quinoxaline units are arranged in an edge-to-face interaction. The crystal packings of $\mathbf{1p}_{cis}$ and $\mathbf{1q}_{trans}$ show no remarkable intramolecular H bonding forms. The dihedral angles between the best "planes" observed in other compounds and the selected bond distances and bond angles of all compounds are given in Supplementary section.

There are recent reports of carrying out this reaction in the presence of other catalysts under heterogeneous conditions. The data presented in Table 6 show the promising features of this protocol in terms of reaction rate, product yield, low catalyst loading and cost-effectiveness when compared with other protocols.

To evaluate the efficiency of various metal chlorides as catalyst, the synthesis of **1d** was also screened in methanol within 1 h using a catalytic amount of common Lewis acids (5 mol%) at room temperature (Table 7, entries 3–13).

Our investigations revealed that the catalytic activity of various homogeneous metal chlorides was found to be of the order $BiCl_3 > AlCl_3 > ZrCl_4 > FeCl_3 > WCl_6 > CuCl_2 > PtCl_2 > HgCl_2$ while the product **1d** was obtained in low yields when $NiCl_2$, $PdCl_2$ and $ZnCl_2$ were used (Table 7). Clearly, $BiCl_3$ stands out as the homogeneous Lewis acid catalyst of choice, with its higher conversion.

Moreover, the catalytic activity of heterogeneous and homogeneous $BiCl_3$ as Lewis acid was compared (Table 7, entries 2–3) to prove that $BiCl_3/SiO_2$ exhibited the highest catalytic activity with regard to the transformation.

We propose a plausible mechanism for the $BiCl_3/SiO_2$ catalyzed double condensation of benzil with arene-1,2-diamine in Scheme 3. Bismuth sites of the catalyst interact with carbonyl groups of the dicarbonyl compound to form the activated carbonyls of complex **A**. Nucleophilic attack of the diamine on the activated carbonyls in complex **A** produces the intermediate **B**. Eventually, detachment of bismuth ion and subsequent loss of water leads to the formation of the quinoxaline ring.

Table 5
Synthesis of quinoxalines and pyrido[2,3-*b*]pyrazines catalyzed by $BiCl_3/SiO_2$ (5 mol%).

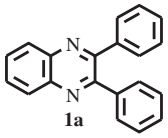
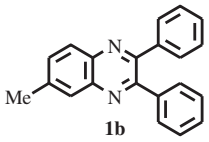
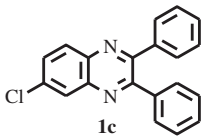
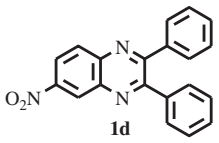
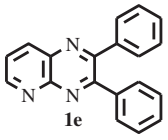
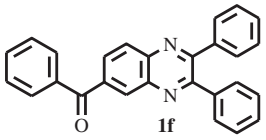
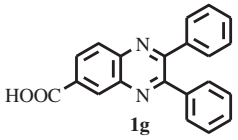
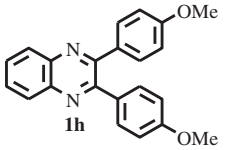
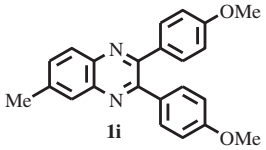
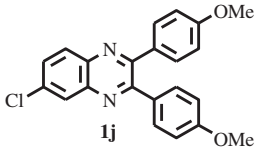
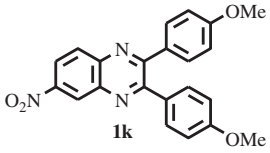
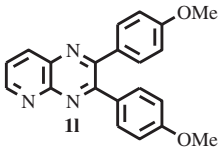
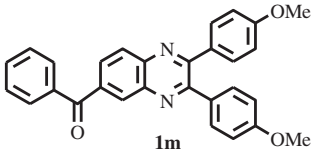
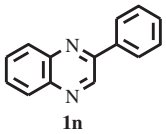
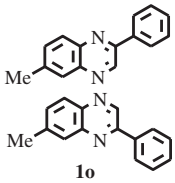
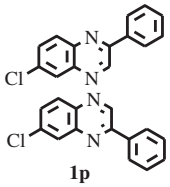
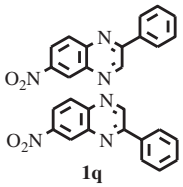
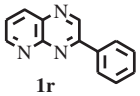
Entry	Product	Time	Conversion (%)	Yield (%)[a]	TOF (h^{-1})[b]
1	 **1a**	5 min	100	100	240
2	 **1b**	5 min	100	97	240
3	 **1c**	8 min	100	97	150
4	 **1d**	60 min	98	94	20
5	 **1e**	30 min	100	98	40
6	 **1f**	90 min	98	82	13
7	 **1g**	90 min	100	72	13
8	 **1h**	30 min	100	98	40
9	 **1i**	30 min	100	92	40
10	 **1j**	90 min	100	95	13

Table 5 (*continued*)

Entry	Product	Time	Conversion (%)	Yield (%)[a]	TOF (h^{-1})[b]
11	 **1k**	180 min	85	80	6
12	 **1l**	180 min	95	87	6
13	 **1m**	90 min	96	81	13
14	 **1n**	5 min	100	98	240
15	 **1o**	5 min	100	98[c] (75/25)[d]	240
16	 **1p**	10 min	100	97[c] (67/33)[d]	120
17	 **1q**	10 min	100	96[c] (80/20)[d]	120
18	 **1r**	10 min	100	98[e]	120

[a] Yields refer to those of pure isolated products characterized by ^{1}H NMR ^{13}C NMR and MS spectral analyses which is consistent with literature values.
[b] TOF: turnover frequency = moles of converted substrate (1,2-dicarbonyl)/(moles of $BiCl_3$ × reaction time in h).
[c] Isolated as a mixture of two regioisomers, i.e. 6-/7-substituted-2-phenylquinoxalines.
[d] Ratio of the 6-/7-substituted products as determined by ^{1}H NMR spectroscopy.
[e] 3-phenylpyrido[2,3-*b*]pyrazine is formed as a sole regioisomer.

3.3. *Recycling of $BiCl_3/SiO_2$*

The reusability of catalyst in methanol was also examined. As shown in Fig. 5, the catalyst was recycled for subsequent runs. It was found that the catalyst is still active in methanol even in 4th run without great loss of activity. The recovery of catalyst was very easy. Product is soluble in methanol, while the catalyst remains insoluble. After completion of the reaction, dichloromethane was added to the reaction mixture and the catalyst was recovered by filtration. It was washed with dichloromethane and ethanol, dried

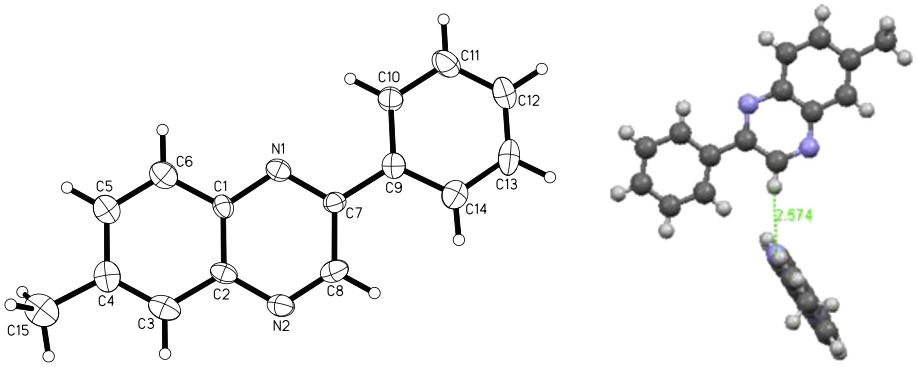


Fig. 1. Molecular and crystal structure of 6-methyl-2-phenylquinoxaline assigned as **1o**$_{trans}$ (thermal ellipsoids at the 40% probability level).

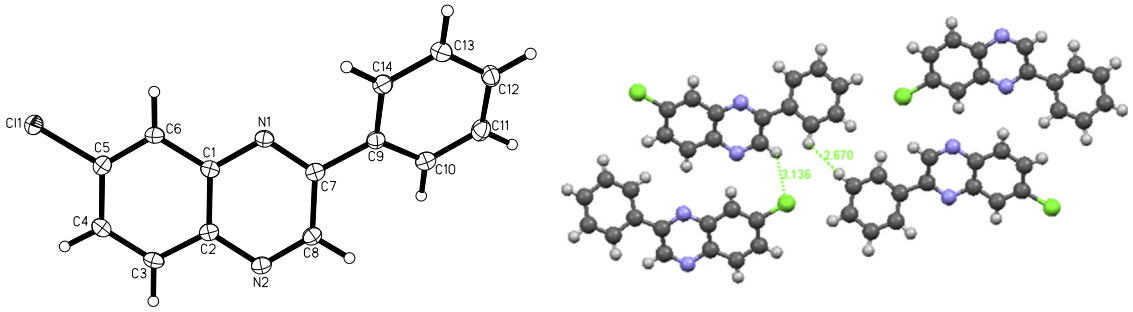


Fig. 2. Molecular and crystal structure of 7-chloro-2-phenylquinoxaline assigned as **1p**$_{cis}$ (thermal ellipsoids at the 40% probability level).

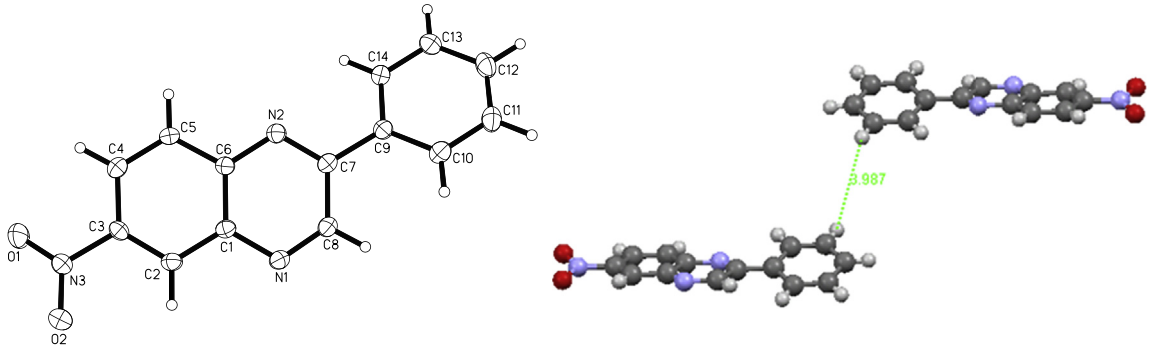


Fig. 3. Molecular and crystal structure of 6-nitro-2-phenylquinoxaline assigned as **1q**$_{trans}$ (thermal ellipsoids at the 40% probability level).

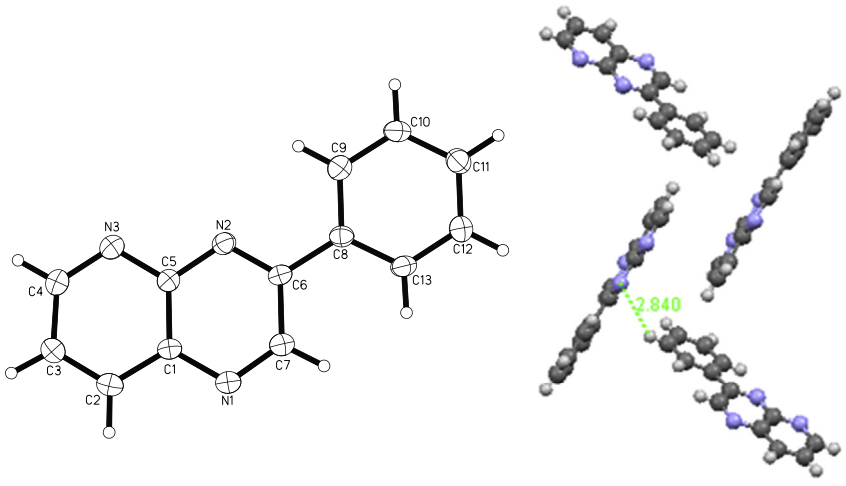


Fig. 4. Molecular and crystal structure of 3-phenylpyrido[2,3-*b*]pyrazine assigned as **1r**$_{cis}$ (thermal ellipsoids at the 40% probability level).

Table 6
Literature results for the synthesis of **1d** under various heterogeneous conditions.

Method	Catalyst (amount), solvent	Conditions	Time (min)	Yield (%)	Ref.
1	Polyaniline - sulfate (5% w/w), $ClCH_2CH_2Cl$	RT	40	90	[42]
2	Montmorillonite K-10 (10% w/w), H_2O	RT	360	70	[43]
3	ZrO_2 (17%)/Ga_2O_3 (4%)/MCM-41 (0.2 g), CH_3CN	RT	120	91	[44]
4	$SbCl_3/SiO_2$ (2.5 mol %), CH_3OH	RT	60	92	[35]
5	Silica bonded S-sulfonic acid (0.1 g), C_2H_5OH/H_2O	RT	200	90	[45]
6	Cellulose sulfuric acid (0.01 g), C_2H_5OH	RT	360	86	[46]
7	Magnetic Fe_3O_4 nanoparticles (10 mol %), H_2O	RT	360	80	[47]
8	Amberlyst-15 (0.05 g), H_2O	70 °C	54	71	[48]
9	Sulfated TiO_2 (5% w/w), C_2H_5OH	RT	120	25	[49]
10	TiO_2 Nanoparticles (2.5 mol %), $ClCH_2CH_2Cl$	RT	90	80	[50]
11	Sulfated TiO_2–P25 (0.1 g), solvent-free	MWI	10	80	[51]
12	Acidic Al_2O_3 (0.2 g), solvent-free	80 °C	25	70	[52]
13	$SnCl_2/SiO_2$ (5 mol %), CH_3OH	RT	60	94	[38]
14	$H_3PW_{12}O_{40}$/MCM-41 (15 mg), C_2H_5OH	RT	300	93	[53]
15	Carbon-doped MoO_3–TiO_2 (0.1 g), C_2H_5OH/H_2O	))))	12	68	[54]
16	$BiCl_3/SiO_2$ (5 mol %), CH_3OH	RT	60	94	This work

RT = room temperature, MWI = microwave irradiation,)))) = ultrasonic irradiation.

Table 7
Catalyst screening of Lewis acids on the synthesis of **1d**.

Entry	Catalyst	Conversion (%)
1	–	11
2	$BiCl_3/SiO_2$	98
3	$BiCl_3$	89
4	$AlCl_3$	86
5	$ZrCl_4$	83
6	WCl_6	77
7	$FeCl_3$	82
8	$CuCl_2$	69
9	$PdCl_2$	18
10	$PtCl_2$	59
11	$NiCl_2$	28
12	$ZnCl_2$	8
13	$HgCl_2$	49

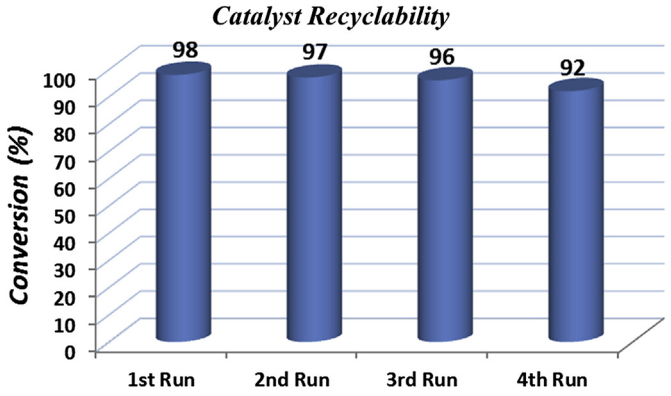
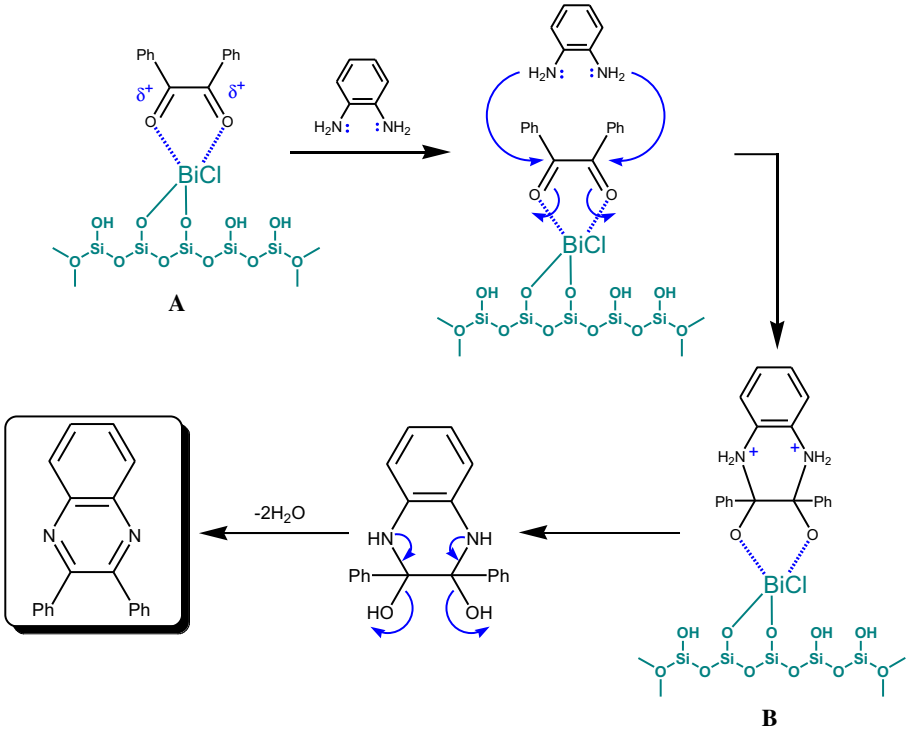


Fig. 5. Recyclability of $BiCl_3/SiO_2$ in methanol for the synthesis of **1d**.



Scheme 3. Plausible mechanism for $BiCl_3/SiO_2$ catalyzed benzo[*N*,*N*]-heterocyclic condensation.

at 120 °C for 2 h and reused in subsequent run. No fresh catalyst was added.

4. Conclusion

In conclusion, $BiCl_3/SiO_2$ is introduced as a novel heterogeneous Lewis acid catalyst for the benzo[*N*,*N*]-heterocyclic condensation. The catalyst showed good to excellent activity for the condensation reaction under ambient conditions.

The procedure offers several advantages including low catalyst loading, operational simplicity, and increased variation of substituents in the product.

The catalyst was stable under the reaction conditions, and its activity in terms of yields slightly decreased with increasing number of cycles of the reaction (conversion: 98% for the first run; 92% for the fourth run) making the procedure a powerful tool from an industrial vantage point.

Appendix A. Supplementary data

The crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre (CCDC) as supplementary publication number CCDC 913262 (**1o**$_{trans}$), 913263 (**1p**$_{cis}$), 913264 (**1q**$_{trans}$), and 913265 (**1r**$_{cis}$). Copies of the data can be obtained, free of charge, by application to CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (Fax: +44-1223-336033; Email: data_request@ccdc.cam.ac.uk or *via* the internet: http://www.ccdc.cam.ac.uk/products/csd/request).

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.jorganchem.2013.06.037.

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