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TFA-Mediated One-Pot Synthesis of Furo-Fused Quinoxalines/ Pyrazines

Kapil Mohan Saini,[a] Sonu Kumar, [a] Monika Patel, [a] Rakesh K. Saunthwal [a] and Akhilesh K. Verma* [a]

Dedication ((optional))

Abstract: Trifluoroacetic acid (TFA) promoted step-economical one-pot approach for the synthesis of furo-fused quinoxalines/pyrazines by the reaction of 2, 3-dichloroquinoxalines/pyrazines with electronically varied alkyne is described. The reaction shows the selective *in-situ* Sonogashira conjoined hydroxylation followed by metal free *5-endo-dig* cyclization. The preliminary experiment depicted the role of TFA as a source of oxygen for oxyarylation and isotopic labeling studies supports the proposed mechanistic pathway goes via activation of alkyne in acidic medium. This methodology tolerates a various kind of substituents, which proves to be valuable for structural and biological assessment.

Introduction

The ubiquity of quinoxaline core in pharmacologically[1] important compounds encouraged the interest of organic chemist to develop an architectural complexity around it. The C-C cross coupling strategy is an efficient tool for the synthesis of a wide variety of biologically active fused *N*- and *O*-heterocycles.[2] For instance, some furano-containing nucleosides possess *in vitro* antiviral and antileukemic activity (Figure 1i).[3] The furo[2,3-*b*]pyrazine and furo[2,3-*b*]quinoxaline derivatives act as potent inhibitors of PDE4B and sirtuins. The significance of alkyl chain at C-2 position of furo[2,3-*b*]quinoxaline showed considerable inhibition in the cell growth against cervical cancer (HeLa) cells (Figure 1 ii and iii).[4] Benthocyanin B control lipid peroxidation induced by free radicals in rat liver microsomes and also inhibits rat erythrocyte hemolysis (Figure 1 iv).[5] Owing to the biological importance of quinoxaline/pyrazine derivatives; functionalization of these heterocycles using cost-effective methodology from easily accessible starting materials is an important area of current research.

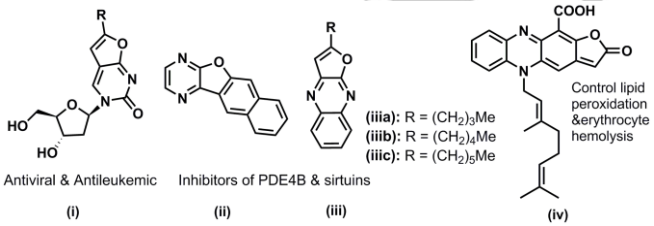
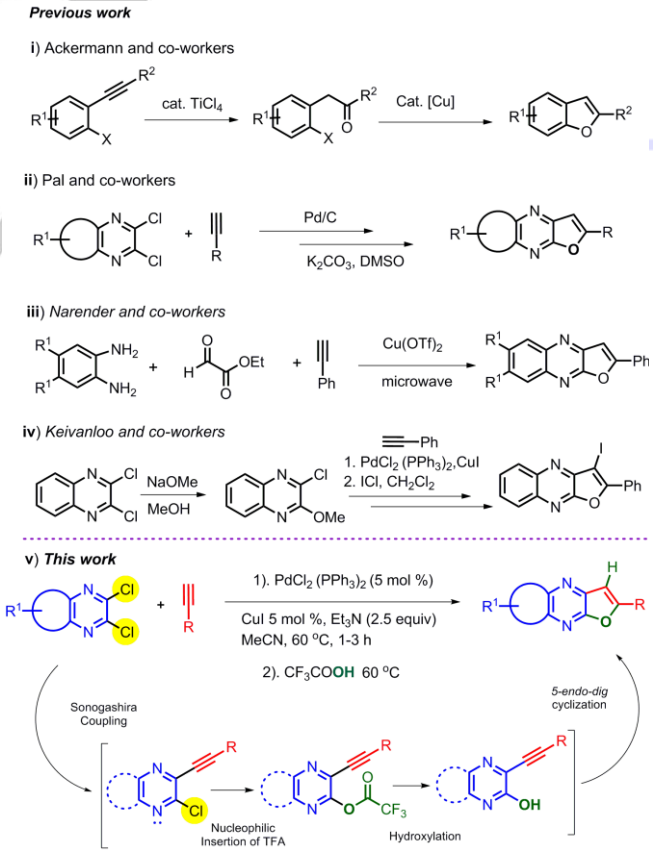


Figure 1. Biologically active furo-fused *N*-heterocyclic derivatives.

Over the past decade, several synthetic approaches for the construction of *N*-heterocyclic scaffolds have been developed.[6,7] Literature survey revealed that majority of reported procedures for the synthesis of furan-fused heterocycles required substrate with pre-installed hydroxyl group.[8] However the metal/ligand/additive and oxidant-free protocol via *in-situ* installation of hydroxyl group for the synthesis furoquinoxaline and pyrazine derivatives has not been much explored. In 2007, Ackermann *et. al.* demonstrated the synthesis of benzo[*b*]furan via anti-Markovnikov hydration of *ortho*-alkynylhaloarenes with concomitant *O*-arylation in presence of Cu-catalyst (Scheme 1, i).[9] Later, Pal and co-workers[4b] investigated a two-step synthesis of furo[2,3-*b*]quinoxaline/pyrazine under basic medium (Scheme 1, ii). A microwave-assisted three component synthesis of furo[2,3-*b*]quinoxaline derivatives using copper catalyst has been reported by Narender group in 2014 (Scheme 1, iii).[10] Subsequently, Keivanloo group designed the multi-step synthesis of iodo substituted furo[2,3-*b*]quinoxaline using ICl as reagent (Scheme 1, iv).[11]



Scheme 1. Designed domino approach for the synthesis of furo-fused *N*-heterocycles.

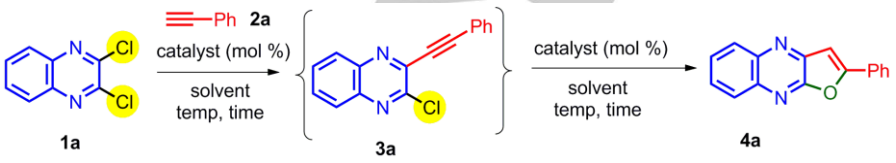
[a] Department of chemistry
University of Delhi, Delhi-110007
E-mail: akverma@acbr.du.ac.in
Supporting information for this article is given via a link at the end of the document.((Please delete this text if not appropriate))

Recently, our group[12] have also explored the Pd-catalyzed hydroarylation of 2-aryl-3-(aryl/alkylethynyl) quinoxaline for the synthesis of benzophenazine. In addition to our existing research on heterocyclic chemistry;[13] herein we have developed a one-pot approach for the synthesis of highly functionalized furo[2,3-b]quinoxaline/pyrazine. The reaction proceeded via a Pd/Cu-catalyzed alkynylation of 2,3-dichloroquinoxaline followed by *5-endo-dig* ring closure in presence of TFA. The present strategy appeared to be attractive as no external oxidant is required. TFA itself act as a source of oxygen for oxyarylation and facilitates the activation of alkyne. The practical utility of one-pot synthesis obviates the tedious purification of the intermediate as well as reduces the cost and efforts for the synthesis of furo-fused quinoxaline/pyrazine.

Results and Discussion

To chase the objective of domino synthesis of 5-*endo-dig* cyclization, we began our investigation using 2,3-dichloroquinoxaline **1a** and phenylacetylene **2a** as a model substrates with a variety of acids. We established a protocol for the Pd/Cu induced C-C coupling reaction for the generation of key intermediate **3a**. As shown in Table 1, the mono Sonogashira intermediate **3a** was isolated in 60% yield when 5 mol % $Pd(OAc)_2$ was employed at 60 °C for 4 h in DMF under inert atmosphere (entry 1). Replacement of $Pd(OAc)_2$ with $PdCl_2(PPh_3)_2$, resulted the formation of intermediate **3a** in higher yield (entry 2). The reaction of **1a** with alkyne **2a** using $PdCl_2(PPh_3)_2$ in MeCN at 60 °C for 1.5 h provided the coupled intermediate **3a** in 90% yield (entry 3). On performing the C-C coupling reaction at room temperature, declines the yield of intermediate **3a** (entry 4). After optimizing the regioselective Sonogashira reaction,[14] we focused our attention towards the tandem cyclization of 2-chloro-3-(phenylethynyl)quinoxaline (**3a**). Inspired from our preliminary results; the sequential one-pot addition of 2 mL of trifluoroacetic provided the desired product **4a** in 65% yield (entry 5). Significant improvement in the yield of the product **4a** was observed on increasing the amount of TFA from 2 mL to 4 mL (entries 6-7). Further elevation in the amount of acid, did not affect the yield of the desire product **4a** (entry 8). Lowering the reaction temperature provided the desire product **4a** in 79% yield (entry 9). In contrast to TFA, glacial acetic acid provided the desire product **4a** in 35% yield (entry 10). However, no product was detected when trifluoromethanesulfonic acid and methanesulfonic acid were employed in the reaction (entries 11 and 12).

Table 1. Optimization of Reaction Conditions [a]

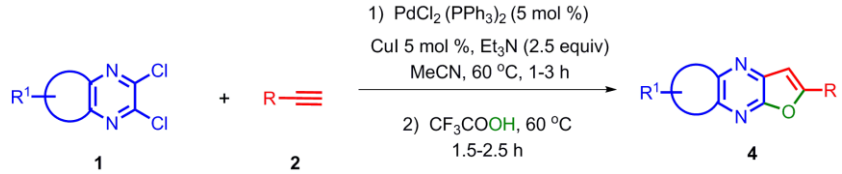


Entry	Catalyst (mol %)	Solvent (mL)	T °C/time (h)	Yield (%)[b]	
				3a[a]	**4a**
1	$Pd(OAc)_2$	DMF	60/4	60	-
2	$PdCl_2(PPh_3)_2$	DMF	60/4	75	-
3	**$PdCl_2(PPh_3)_2$**	**MeCN**	**60/1.5**	**90**	**-**
4	$PdCl_2(PPh_3)_2$	MeCN	25/4	49	-
5	$PdCl_2(PPh_3)_2$	MeCN + CF_3COOH/2	60/1.5 + 60/6	30	65
6	$PdCl_2(PPh_3)_2$	MeCN + CF_3COOH/3	60/1.5 + 60/6	10	69
7	**$PdCl_2(PPh_3)_2$**	**MeCN + CF_3COOH/4**	**60/1.5 + 60/2**	**-**	**86**
8	$PdCl_2(PPh_3)_2$	MeCN + CF_3COOH/5	60/1.5 + 60/2	-	86
9	$PdCl_2(PPh_3)_2$	MeCN + CF_3COOH/4	60/1.5 + 45/2	15	79
10	$PdCl_2(PPh_3)_2$	MeCN + CH_3COOH/4	60/1.5 + 60/2	50	35
11	$PdCl_2(PPh_3)_2$	MeCN + CF_3SO_3H/4	60/1.5 + 60/2	82	-
12	$PdCl_2(PPh_3)_2$	MeCN + CH_3SO_3H/4	60/1.5 + 60/2	86	-

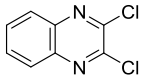
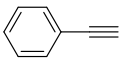
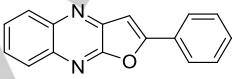
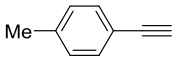
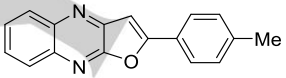
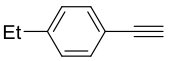
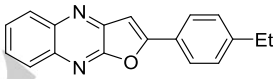
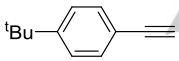
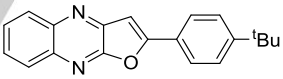
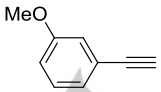
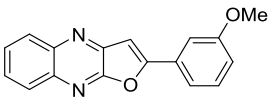
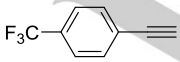
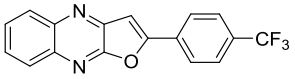
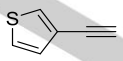
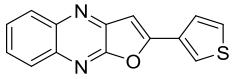
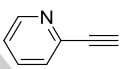
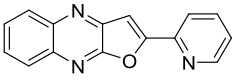
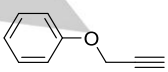
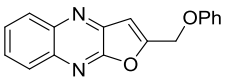
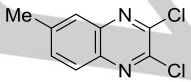
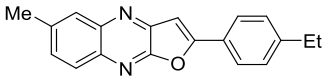
[a]Unless otherwise noted, all Sonogashira reactions were carried out using 0.5 mmol of 2,3-Dichloroquinoxaline **(1a)**, 0.52 mmol of alkyne **(2a)**, catalyst (5 mol %), CuI (5 mol %), Et_3N (2.5 equiv) in 2.0 mL of solvent, under inert atmosphere. [b]Isolated yield.

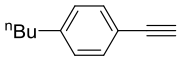
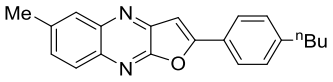
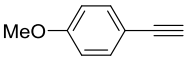
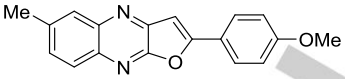
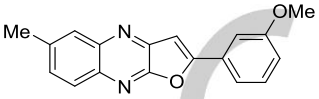
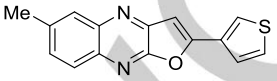
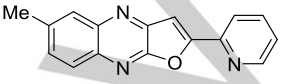
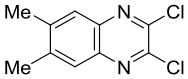
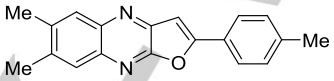
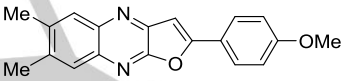
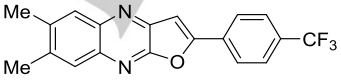
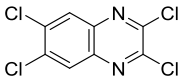
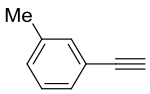
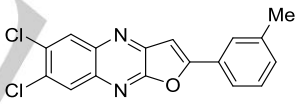
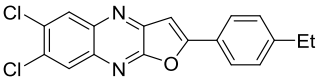
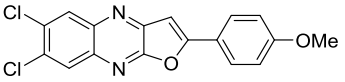
We explored the scope of reaction for the synthesis of furo[2,3-*b*]quinoxaline by allowing highly substituted 2,3-dichloroquinoxaline (**1a-d**) with a variety of electron-neutral, electron-rich and electron-deficient terminal alkynes **2** in the presence of trifluoroacetic acid (Table 2). Both electron-neutral and electron-rich alkynes with **1a** afforded the desired products **4a-c** in excellent yields (entries 1-3). The bulky substitutent 4-^{t}BuPh alkyne **2d** was also capable in providing the cyclized product **4d** in 86% yield (entry 4). Electron deficient alkynes **2e-f** gave the corresponding product **4e-f** in 84 and 80% yields, respectively (entries 5 and 6).The heterocyclic alkynes **2g-h** were successful in providing the fused products **4g-h** in good yields (entries 7 and 8). However, 1-ethynyl-4-(phenoxymethyl)benzene **2i** failed to provide the desired product **4i** probably due to the low reactivity of alkyne (entry 9). Interestingly, when 2,3-dichloro-6-methylquinoxaline **1b** was implemented for tandem cyclization, the desired products **4j-o** were obtained in 83-94% yields (entries 10-15). On increasing the electron density over quinoxaline moiety **1c**, the intriguing cyclized products **4p-r** were obtained in 82-95% yields (entries 16-18). The electronically varied chloro- substituted quinoxaline **1d** afforded the yields of the furo-fused products **4s-u** in 76-79% (entries 19-21). The X-ray crystallographic studies of **4b** further elucidated the formation of cyclized product.[15]

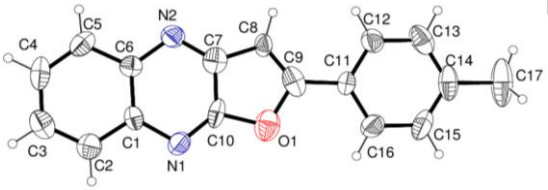
Table 2. Synthesis of furoquinoxaline derivative.[a]



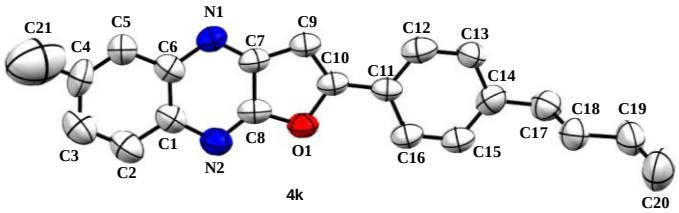
1 2 4

S.No	Quinoxaline	Alkyne		Product		Yield (%)[b]
1	 **1a**		**2a**		**4a**	86
2	**1a**		**2b**		**4b**	88
3	**1a**		**2c**		**4c**	87
4	**1a**		**2d**		**4d**	86
5	**1a**		**2e**		**4e**	84
6	**1a**		**2f**		**4f**	80
7	**1a**		**2g**		**4g**	88
8	**1a**		**2h**		**4h**	82
9	**1a**		**2i**		**4i**	0[c]
10	 **1b**		**2c**		**4j**	88

11	**1b**		**2j**		**4k**	86
12	**1b**		**2k**		**4l**	94
13	**1b**		**2e**		**4m**	86
14	**1b**		**2g**		**4n**	90
15	**1b**		**2h**		**4o**	83
16	 **1c**		**2b**		**4p**	90
17	**1c**		**2k**		**4q**	95
18	**1c**		**2f**		**4r**	82
19	 **1d**		**2l**		**4s**	76
20	**1d**		**2c**		**4t**	78
21	**1d**		**2k**		**4u**	79



4b

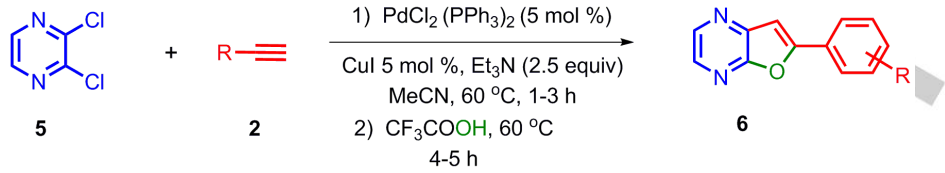


4k

[a] Sonogashira reactions were carried out using 0.5 mmol of 2,3-Dichloroquinoxaline **(1)**, 0.52 mmol of alkyne **(2)**, $PdCl_2(PPh_3)_2$ (5 mol %), CuI (5 mol %), Et_3N (2.5 equiv) in 2.0 mL of MeCN, under inert atmosphere, After completion of Sonogashira reactions 4 mL trifluoroacetic acid (TFA) was added. [b] Isolated yield. [c] 2-chloro-3-(3-phenoxyprop-1-yn-1-yl)quinoxaline was obtained. CCDC number of **4b** and **4k** are 1538954 and 1549438 respectively.

Encouraged from above results, we further extended the chemistry using 2, 3-dichloropyrazine with a variety of terminal alkynes (Table 3). The reaction of 2, 3-dichloropyrazine **5** with electronically varied alkynes **2** afforded the furo-fused pyrazines (**6a-h**) in good yields. The X-ray crystallographic studies[15] of **6b** further supported the synthesis of furo-pyrazine.

Table 3. Synthesis of furo-pyrazine derivative

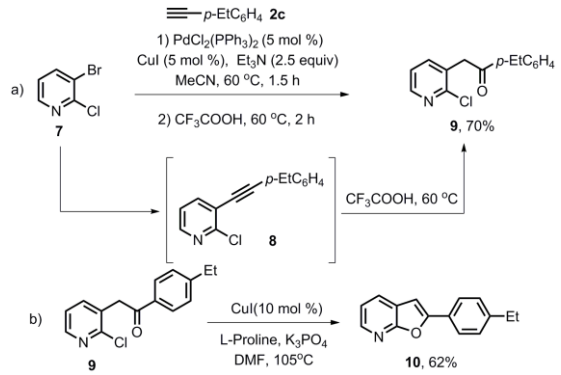


5 + **2** → **6**

S.No	Alkyne	Product	Yield (%)[b]
1	**2a**	**6a**	70
2	**2m**	**6b**	68
3	**2l**	**6c**	72
4	**2b**	**6d**	74
5	**2c**	**6e**	73
6	**2k**	**6f**	76
7	**2j**	**6g**	74
8	**2d**	**6h**	71

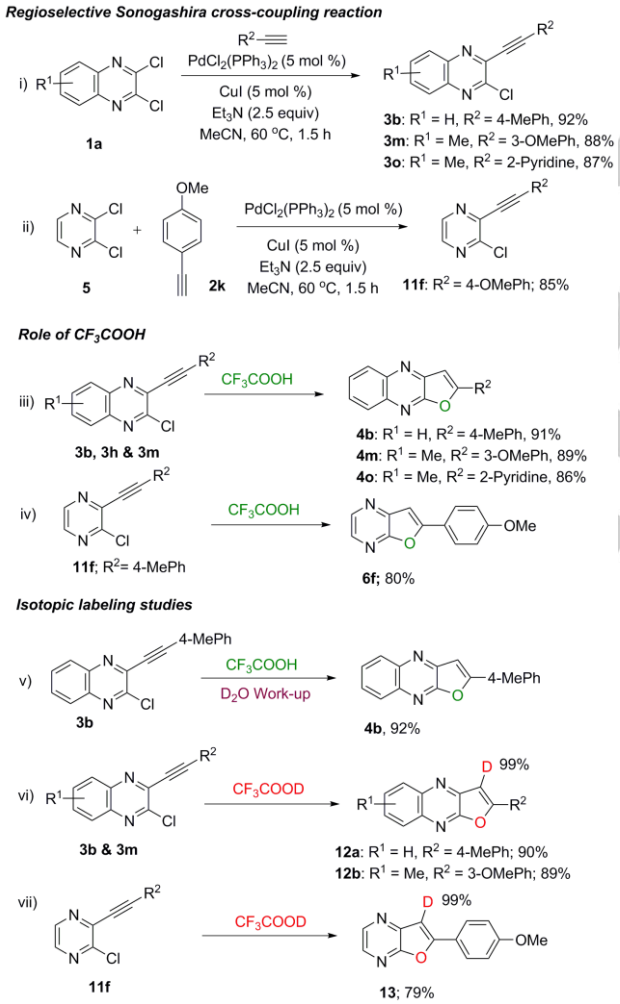
6b

[a] Sonogashira reactions were carried out using 0.5 mmol of 2,3-Dichloropyrazine **(5)**, 0.52 mmol of alkyne **(2)**, $PdCl_2(PPh_3)_2$ (5 mol %), CuI (5 mol %), Et_3N (2.5 equiv) in 2.0 mL of MeCN, under inert atmosphere, After completion of Sonogashira reactions 4 mL trifluoroacetic acid (TFA) was added. [b] Isolated yield. CCDC number of **6b** is 1538955.



Scheme 2. Scope of dihalopyridine

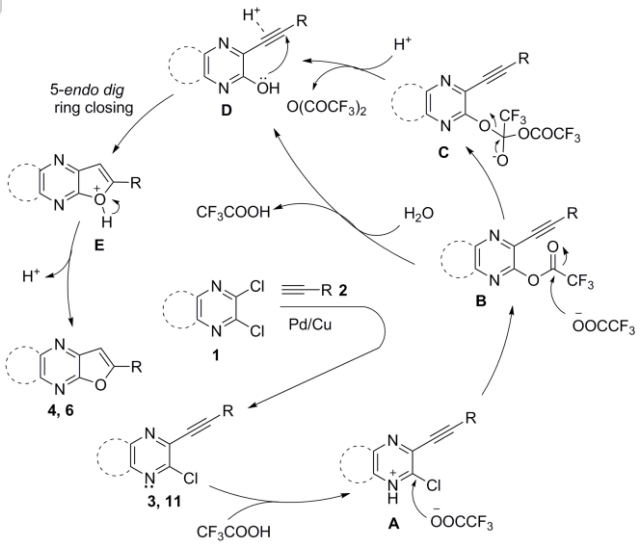
As illustrated in Scheme 2, the reactivity of dihalopyridine was also evaluated, the corresponding uncyclized oxidised product **9** was obtained in 70% yield probably due to the presence of highly activating alkyne **8** (Scheme 4a). When ketone **9** was reacted using CuI (10 mol%), *L*-Proline and K_3PO_4 in DMF provided the cyclized product **10** in 62% yield (Scheme 2b).



Scheme 3. Mechanistic Experiment

In order to propose a mechanistic pathway and role of TFA in one-pot synthesis of furo-fused *N*-heterocycles, an array of preliminary experiments were conducted (Scheme 3). Initially, we performed the regioselective C-C coupling of **1** and **5** with electron-releasing (**2b**, **2k**) and electron-deficient alkyne (**2e, 2h**) under standard reaction condition provided the key intermediate **3b**, **3m**, **3o** and **11f** in good to excellent yields (eq. i, ii). In order to determine the role of TFA, the isolated intermediates were further subjected for domino cyclization by the addition of TFA, afforded the furo-fused quinoxalines (**4b**, **4m** and **4o**) and pyrazine (**6f**) in 80-91% yields (eq. iii, iv). This suggests that Pd-catalyst is not involved in the cyclization. The acidic medium accelerates the formation of furo[2,3-b]quinoxaline/pyrazines. To gain insights into the reaction mechanism, various isotopic labelling experiments were performed. When alkynylquinoxaline **3b** was treated with TFA followed by D_2O work up, no deuterium incorporation was observed in product **4b** (eq. v). This imply that the proton exchange occur *in situ* within the reaction. When deuterated TFA was used as a solvent the desired products **12a**-**b** and **13** were obtained in 90, 89 and 79% yields respectively with 99% D at C-3 position (eq. vi, vii). The formation of deuterated product confirms that the mechanism goes via acid activation of alkyne.

Based on the control experiments and literature studies,[12] we proposed a plausible mechanistic hypothesis as described in Scheme 4. The mechanism was initiated by the Pd-catalyzed Sonogashira coupling reaction of dihalo compound **1** with terminal alkynes **2** which leads to the formation of alkynyl intermediate **3, 11**. The one-pot addition of TFA generates the species **A**. Subsequently, the nucleophilic addition on carbonyl moiety **B** develop species **C** followed by elimination afforded the species **D**. Another possibility for the formation of species **D** is via hydrolysis of species **B**. The acid promoted activation of alkyne with concomitant 5-*endo-dig* ring closer provided the desired cyclized product **4**, **6** via formation of species **E**.



Scheme 4. Plausible Mechanism

Conclusion

In conclusion, we have demonstrated an efficient metal-free one-pot domino approach for the synthesis of diversely substituted furo-fused quinoxalines/pyrazines. The strategy involves the *in situ* alknylation followed by *5-endo-dig* cyclization in the presence of trifluoroacetic acid. The major role of TFA was to provide oxygen for oxyarylation and to facilitate the acidic activation of alkyne for intramolecular cyclization. The preliminary control experiments validate the mechanistic pathway and X-ray crystallographic studies further support the designed chemistry of furo-fused *N*-heterocycles. We anticipate that this protocol is useful for the synthesis of *N*-, *O*- containing polycyclic heterocycles which could find further application, in biologically active compound.

Experimental

General Experimental

All the reactions were performed in an oven-dried Schlenk flask under inert atmosphere. Column chromatography was performed using silica gel (100-200 Mesh). Thin layer chromatography (TLC) was performed on silica gel GF254 plates. Visualization of spots on TLC plate was accomplished with UV light (254 nm) and staining over I_2 chamber. ^{1}H and ^{13}C NMR spectra were recorded at 400 and 100 MHz respectively. Thin-layer chromatography was performed using commercially prepared 60 F_{254} silica gel plates. All melting points are uncorrected.

General Procedure for the Synthesis of furoquinoxalines/Pyrazine: To a solution of substituted 2,3-dichloroquinoxaline/pyrazine **1** (0.5 mmol) in MeCN (2 mL), 5 mol% of $Pd(PPh_3)_2Cl_2$ and CuI were added. The reaction vial was then sealed and flushed with nitrogen. Then, 2.5 equiv of Et_3N and 0.52 mmol of alkyne **2** were added to the reaction mixture. The reaction was then stirred at 60 °C until TLC revealed complete conversion of the starting material. After the completion of the first coupling reaction (monitored by TLC) 4 ml of TFA was added. The reaction was then stirred at 60 °C until TLC revealed complete conversion of mono sonogashira intermediate into final product. The reaction mixture was then allowed to cool, was diluted with H_2O, and was extracted with EtOAc (3 × 10 mL). The combined organic layers were dried over Na_2SO_4, concentrated under vacuum, and purified by column chromatography using 100−200 mesh size silica gels (hexane: ethyl acetate) to afford the corresponding product. The structure and purity of known starting materials (**1a**, **1b**, **1c** and **1d**) were confirmed by comparison of their physical and spectral data (^{1}H NMR, ^{13}C NMR and HRMS).[16]

2-Phenylfuro[2,3-*b*]quinoxaline (**4a**): The product was obtained as a pale yellow needles, mp: 189–190 °C (105.9 mg, 86%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10–8.06 (m, 1H), 8.03–8.01 (m, 1H), 7.94–7.92 (m, 2H), 7.67–7.62 (m, 2H), 7.46–7.41 (m, 3H), 7.19 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.9, 154.3, 144.5, 142.1, 138.7, 131.2, 129.1, 128.72, 128.67, 128.6, 128.4, 128.3, 126.1, 100.7. HRMS (ESI): $[M+H]^+$ Calcd for $[C_{16}H_{10}N_2O]$ 247.0871; found 247.0868.

2-(*p*-Tolyl)furo[2,3-*b*]quinoxaline (**4b**): The product was obtained as a yellow needles, mp: 219–221 °C (table 2: 114.5 mg, 88%; Scheme 5: 118.4 mg, 91%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.19–8.16 (m, 1H), 8.13–8.10 (m, 1H), 7.91 (d, *J* = 8.4 Hz, 2H), 7.76–7.71 (m, 2H), 7.33 (d, *J* = 8.4 Hz, 2H), 7.22 (s, 1H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.3, 154.4, 144.7, 142.2, 141.9, 138.6, 129.9, 128.6, 128.57, 128.2, 126.1, 125.7, 99.9, 21.6. HRMS (ESI): $[M+H]^+$ Calcd for $[C_{17}H_{12}N_2O]$ 261.1028; found 261.1032.

2-(4-Ethylphenyl)furo[2,3-*b*]quinoxaline (**4c**): The product was obtained as a yellow needles, mp: 159–161 °C (119.2 mg, 87%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.18–8.15 (m, 1H), 8.12–8.09 (m, 1H), 7.94 (d, *J* = 8.4 Hz, 2H), 7.75–7.70 (m, 2H), 7.36 (d, *J* = 8.4 Hz, 2H), 7.22 (s, 1H), 2.72 (q, *J* = 7.6 Hz, 2H), 1.28 (t, *J* = 7.6 Hz 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.3, 154.4, 148.2, 144.7, 142.2, 138.6, 128.69, 128.65, 128.62, 128.56, 128.2, 126.2, 125.9, 99.9, 28.9, 15.3. HRMS (ESI): $[M+H]^+$ Calcd for $[C_{18}H_{14}N_2O]$ 275.1184; found 275.1178.

2-(4-(*tert*-butyl)phenyl)furo[2,3-*b*]quinoxaline (**4d**): The product was obtained as a brown needles, mp: 226–228 °C (129.9 mg, 86%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.18–8.15 (m, 1H),8.12–8.10 (m, 1H),7.97 (d, *J* = 7.3 Hz, 2H), 7.75–7.70 (m, 2H),7.56 (d, *J* = 7.3 Hz, 2H), 7.24 (s, 1H), 1.38 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.3, 155.0, 144.7, 142.2, 138.6, 128.7, 128.62, 128.56, 128.2, 126.1, 126.0, 125.7, 100.0, 35.1, 31.1. HRMS (ESI): $[M+H]^+$ Calcd for $[C_{20}H_{18}N_2O]$ 303.1497; found 303.1487.

2-(3-Methoxyphenyl)furo[2,3-*b*]quinoxaline (**4e**): The product was obtained as a pale yellow needles, mp: 154–156 °C (116.1 mg, 84%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.16–8.12 (m, 1H), 8.10–8.06 (m, 1H), 7.73–7.68 (m, 2H), 7.57 (d, *J* = 7.6 Hz, 1H), 7.52–7.51 (m, 1H), 7.40 (t, *J* = 7.6 Hz, 1H), 7.24 (s, 1H), 7.01(dd, *J* = 8.4 and 2.3 Hz, 1H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.7, 160.0, 154.3, 144.5, 142.2, 138.7, 130.2, 129.6, 128.8, 128.7, 128.6, 128.3, 118.7, 117.4, 110.8, 101.0, 55.4. HRMS (ESI): $[M+H]^+$ Calcd for $[C_{17}H_{12}N_2O_2]$ 277.0979; found 277.0956.

2-(4-(Trifluoromethyl)phenyl)furo[2,3-*b*]quinoxaline (**4f**): The product was obtained as a pale yellow needles, mp: 233–235 °C (125.6 mg, 80%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.22–8.18 (m, 1H), 8.15–8.13 (m, 3H), 7.82–7.76 (m, 4H), 7.41 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.9, 154.3, 143.9, 142.4, 139.1, 131.7, 129.3, 128.9, 128.7, 128.6, 126.3, 126.18 (q, *J* = 7.7Hz), 114.1, 102.7. HRMS (ESI): $[M+H]^+$ Calcd for $[C_{17}H_9F_3N_2O]$ 315.0745; found 315.0726.

2-(Thiophen-3-yl)furo[2,3-*b*]quinoxaline (**4g**): The product was obtained as a yellow needles, mp: 177–179 °C (111.0 mg, 88%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17–8.14 (m, 1H), 8.12–8.06 (m, 2H), 7.74–7.71 (m, 2H), 7.59–7.58 (m, 1H), 7.49–7.48 (m, 1H), 7.07 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.1, 154.2, 144.6,

142.2, 138.6, 130.6, 129.1, 128.6, 128.3, 127.6, 126.2, 125.2, 100.2. HRMS (ESI): $[M+H]^+$ Calcd for $[C_{14}H_8N_2OS]$: 253.0436, found 253.0457.

2-(Pyridin-2-yl)furo[2,3-*b*]quinoxaline (**4h**): The product was obtained as a green needles, mp: 140–142 °C (101.3 mg, 82%); ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 8.70 (d, *J* = 3.8 Hz, 1H), 8.58 (s, 1H), 8.20–8.17 (m, 1H), 8.04–8.0 (m, 2H), 7.85–7.78 (m, 3H), 7.36–7.33 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 153.3, 149.3, 148.2, 140.8, 138.1, 137.1, 131.2, 130.4, 129.3, 128.2, 124.2, 121.8, 114.1. HRMS (ESI): $[M+H]^+$ Calcd for $[C_{15}H_9N_3O]$ 248.0824; found 248.0836.

2-(4-Ethylphenyl)-6-methylfuro[2,3-*b*]quinoxaline (**4j**): The product was obtained as a pale yellow needles, mp: 136–138 °C (126.9 mg, 88%); 1H NMR (400 MHz, $CDCl_3$): *δ* 8.05–7.98 (m, 1H), 7.95–7.86 (m, 3H), 7.57–7.54 (m, 1H), 7.36 (d, *J* = 8.4 Hz, 2H), 7.20 (s, 1H), 2.73 (q, *J* = 7.6 Hz, 2H), 2.61 (s, 3H), 1.29 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 163.9, 154.2, 148.0, 144.5, 142.2, 138.5, 130.9, 128.7, 128.1, 127.6, 126.2, 126.1, 100.0, 28.9, 21.7, 15.3. HRMS (ESI): $[M+H]^+$ Calcd for $[C_{19}H_{16}N_2O]$ 289.1341; found 289.1327.

2-(4-Butylphenyl)-6-methylfuro[2,3-*b*]quinoxaline (**4k**): The product was obtained as a pale yellow needles, mp: 153–155 °C (136.1 mg, 86%); ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.99 (d, *J* = 8.4 Hz, 1H), 7.93 (d, *J* = 7.6 Hz, 3H), 7.58–7.54 (m, 1H), 7.34 (d, *J* = 8.4 Hz, 2H), 7.21 (s, 1H), 2.69 (t, *J* = 7.6 Hz, 2H), 2.62 (s, 3H), 1.67–1.61 (m, 2H), 1.43–1.34 (m, 2H), 0.95 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 163.9, 154.6, 146.8, 144.5, 139.3, 138.5, 130.5, 129.2, 128.1, 127.5, 126.0, 100.0, 35.7, 33.3, 22.3, 21.7, 13.9. HRMS (ESI): $[M+H]^+$ Calcd for $[C_{21}H_{20}N_2O]$ 317.1654; found 317.1647.

2-(4-Methoxyphenyl)-6-methylfuro[2,3-*b*]quinoxaline (**4l**): The product was obtained as a pale yellow needles, mp: 241–243 °C (136.5 mg, 94%); ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.92–7.89 (m, 3H), 7.85 (s, 1H), 7.50–7.46 (m, 1H), 7.06 (s, 1H), 6.98 (d, *J* = 9.2 Hz, 2H), 3.83 (s, 3H), 2.54 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 162.0, 155.6, 144.7, 142.2, 139.0, 138.5, 136.8, 130.7, 128.1, 127.9, 127.5, 121.2, 114.6, 98.9, 55.5, 21.7. HRMS (ESI): $[M+H]^+$ Calcd for $[C_{18}H_{14}N_2O_2]$ 291.1134; found 291.1124.

2-(3-Methoxyphenyl)-6-methylfuro[2,3-*b*]quinoxaline (**4m**): The product was obtained as a off white needles, mp: 167–169 °C (Table 2: 124.8 mg, 86%; Scheme 5: 129.1 mg, 89%); ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 8.05–7.96 (m, 1H), 7.91–7.85 (m, 1H), 7.59–7.53 (m, 3H), 7.43 (t, *J* = 7.6 Hz, 1H), 7.25 (s, 1H), 7.03 (d, *J* = 7.6 Hz, 1H), 3.91 (s, 3H), 2.60 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 163.2, 159.9, 153.9, 144.1, 142.1, 139.3, 138.5, 136.9, 131.0, 130.0, 127.9, 127.5, 118.5, 117.1, 100.9, 55.3, 21.5. HRMS (ESI): $[M+H]^+$ Calcd for $[C_{18}H_{14}N_2O_2]$ 291.1134; found 291.1128.

6-Methyl-2-(thiophen-3-yl)furo[2,3-*b*]quinoxaline (**4n**): The product was obtained as a yellow needles, mp: 193–194 °C (119.8 mg, 90%); ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.97–7.78 (m, 3H), 7.50–7.40 (m, 3H), 6.98 (s, 1H), 2.53 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 159.8, 144.3, 143.7, 142.2, 138.6, 131.0, 130.6 , 128.1, 127.5, 126.0, 125.2, 100.3, 21.7. HRMS (ESI): $[M+H]^+$ Calcd for $[C_{15}H_{10}N_2OS]$ 267.0592; found 267.0588.

6-Methyl-2-(pyridin-2-yl)furo[2,3-*b*]quinoxaline (**4o**): The product was obtained as a green needles, mp: 169–171 °C (Table 2: 108.4 mg, 83%; Scheme 5: 112.4 mg, 86%); ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 8.70–8.69 (m, 1H), 8.56 (s, 1H), 8.06–7.99 (m, 1H), 7.94 (s, 1H), 7.90 (d, *J* = 8.4 Hz, 1H), 7.84–7.78 (m, 1H), 7.63–7.60 (m, 1H), 7.35–7.32 (m, 1H), 2.60 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 153.3, 148.0, 146.4, 142.1, 139.2, 137.8, 132.7, 128.8, 128.1, 127.6, 127.0, 121.7, 114.0, 21.8. HRMS (ESI): $[M+H]^+$ Calcd for $[C_{16}H_{11}N_3O]$ 262.0980; found 262.0962.

6,7-Dimethyl-2-(*p*-tolyl)furo[2,3-*b*]quinoxaline (**4p**): The product was obtained as a pale yellow needles, mp: 264–266 °C (129.8 mg, 90%); ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.91–7.89 (m, 3H), 7.84 (s, 1H), 7.33 (d, *J* = 8.4 Hz, 2H), 7.19 (s, 1H), 2.51 (s, 6H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 163.3, 154.3, 143.7, 141.5, 141.1, 139.2, 138.5, 137.4, 129.8, 127.8, 127.7, 126.0, 100.0, 21.6, 20.4, 20.3. HRMS (ESI): $[M+H]^+$ Calcd for $[C_{19}H_{16}N_2O]$ 289.1341; found 289.1334.

2-(4-Methoxyphenyl)-6,7-dimethylfuro[2,3-*b*]quinoxaline (**4q**): The product was obtained as a yellow needles, mp: 204–206 °C (144.6 mg, 95%); ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.97–7.93 (m, 2H), 7.88 (s, 1H), 7.83 (s, 1H), 7.10 (s, 1H), 7.05–7.02 (m, 2H), 3.89 (s, 3H), 2.50 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 163.2, 161.9, 154.3, 143.9, 141.0, 139.0, 138.4, 137.2, 127.7, 127.67, 127.6, 121.3, 114.6, 99.0, 55.5, 20.33, 20.27. HRMS (ESI): $[M+H]^+$ Calcd for $[C_{19}H_{16}N_2O_2]$ 305.1290; found 305.1284.

6,7-Dimethyl-2-(4-(trifluoromethyl)phenyl)furo[2,3-*b*]quinoxaline (**4r**): The product was obtained as a yellow needles, mp: 310–312 °C (140.4 mg, 82%); ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 8.13 (d, *J* = 8.4 Hz, 2H), 7.94 (s, 1H), 7.87 (s, 1H), 7.80 (d, *J* = 8.4 Hz, 2H), 7.39 (s, 1H), 2.53 (d, *J* = 1.9 Hz, 6H); ^{13}C NMR (100 MHz, CF_3COOD): *δ* 172.0, 161.5, 156.9, 149.5, 146.3, 138.8, 135.3, 129.6, 129.0, 128.7, 127.4 (q, *J* = 7.7 Hz, 1C), 97.9, 20.1, 19.6. HRMS (ESI): $[M+H]^+$ Calcd for $[C_{19}H_{13}F_3N_2O]$ 343.1058; found 343.1048.

6,7-Dichloro-2-(*m*-tolyl)furo[2,3-*b*]quinoxaline (**4s**): The product was obtained as a yellow needles, mp: 255–257 °C (124.2 mg, 76%); ^{1}H NMR (400 MHz, CF_3COOD): *δ* 8.38 (d, *J* = 3.1 Hz, 1H) 8.21 (d, *J* = 3.8 Hz, 1H), 7.95–7.92 (m, 2H), 7.52–7.50 (m, 2H), 7.44 (t, *J* = 7.6 Hz, 1H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, CF_3COOD): *δ* 177.8, 158.1, 141.8, 140.9, 138.5, 138.11, 138.08, 137.5, 130.9, 130.6, 129.8, 128.1, 127.0, 126.0, 120.6, 96.4, 20.3. HRMS (ESI): $[M+H]^+$ Calcd for $[C_{17}H_{10}Cl_2N_2O]$ 329.0248; found 329.0241.

6,7-Dichloro-2-(3-ethylphenyl)furo[2,3-*b*]quinoxaline (**4t**): The product was obtained as a yellow needles, mp: 240–242 °C (132.9 mg, 78%); ^{1}H NMR (400 MHz, CF_3COOD): *δ* 8.36–8.35 (m, 1H), 8.18–8.17 (m, 1H), 8.06–8.04 (m, 2H), 7.45–7.41 (m,

3H), 2.70 (q, *J* = 7.6 Hz, 2H), 1.21–1.18 (m, 3H); ^{13}C NMR (100 MHz, CF_3COOD): *δ* 177.9, 158.2, 157.3, 140.7, 138.2, 137.8, 137.1, 130.8, 130.5, 130.1, 128.1, 123.4, 120.5, 95.7, 29.9, 14.0. HRMS (ESI): $[M+H]^+$ Calcd for $[C_{18}H_{12}C_{l2}N_2O]$ 343.0405; found 343.0392.

6,7-Dichloro-2-(4-methoxyphenyl)furo[2,3-*b*]quinoxaline (**4u**): The product was obtained as a yellow needles, mp: 278–280 °C (135.3 mg, 79%); ^{1}H NMR (400 MHz, CF_3COOD): *δ* 8.38–8.37 (m, 1H), 8.19–8.17 (m, 3H), 7.40–7.39 (m, 1H), 7.15 (d, *J* = 9.2 Hz, 2H), 3.95 (s, 3H); ^{13}C NMR (100 MHz, CF_3COOD): *δ* 177.6, 168.3, 158.4, 140.4, 138.4, 137.4, 136.6, 132.8, 130.7, 128.1, 120.3, 118.7, 94.8, 56.0. HRMS (ESI): $[M+H]^+$Calcd for $[C_{17}H_{10}Cl_2N_2O]$ 345.0198; found 345.0169.

6-Phenylfuro[2,3-*b*]pyrazine (**6a**)[3b]: The product was obtained as a off white needles, mp: 99–101 °C (68.7 mg, 70%); ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 8.18 (d, *J* = 2.3 Hz, 1H), 8.16 (d, *J* = 2.3 Hz, 1H), 7.79–7.76 (m, 1H), 7.31–7.26 (m, 4H), 7.18 (s, 1H); HRMS (ESI): $[M+H]^+$ Calcd for $[C_{12}H_8N_2O]$ 197.0715; found 197.0707.

6-(*o*-Tolyl)furo[2,3-*b*]pyrazine (**6b**): The product was obtained as a yellow needles, mp: 81–83 °C (71.5 mg, 68%); ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 8.50 (d, *J* = 3.1 Hz, 1H), 8.22 (d, *J* = 3.1 Hz, 1H), 7.91–7.89 (m, 1H), 7.40–7.27 (m, 3H), 7.11 (s, 1H), 2.61 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 160.3, 155.2, 142.3, 141.5, 137.4, 136.7, 132.0, 130.2, 128.6, 126.4, 105.2, 21.9. HRMS (ESI): $[M+H]^+$ Calcd for $[C_{13}H_{10}N_2O]$ 211.0871; found 211.0864.

6-(*m*-Tolyl)furo[2,3-*b*]pyrazine (**6c**): The product was obtained as a yellow needles, mp: 87–89 °C (75.7 mg, 72%); ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 8.48 (d, *J* = 2.7 Hz, 1H), 8.18 (d, *J* = 2.7 Hz, 1H), 7.75–7.72 (m, 2H), 7.36 (t, *J* = 7.8 Hz, 1H), 7.25 (d, *J* = 7.7 Hz, 1H), 7.18 (s, 1H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 160.5, 155.5, 142.5, 141.5, 138.8, 137.2, 131.3, 128.9, 128.6, 126.2, 122.9, 101.1, 21.4. HRMS (ESI): $[M+H]^+$ Calcd for $[C_{13}H_{10}N_2O]$ 211.0871; found 211.0863.

6-(*p*-Tolyl)furo[2,3-*b*]pyrazine (**6d**): The product was obtained as a yellow needles, mp: 84–86 °C (77.8 mg, 74%); ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 8.48 (dd, *J* = 8.4 and 3.1 Hz, 2H), 8.31 (d, *J* = 3.1 Hz, 1H), 8.19 (d, *J* = 2.3 Hz, 1H), 7.85 (d, *J* = 8.4 Hz, 2H), 7.17(s, 1H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 160.6, 155.5, 142.7, 141.4, 137.7, 133.8, 129.8, 129.2, 125.6, 100.5, 21.5. HRMS (ESI): $[M+H]^+$ Calcd for $[C_{13}H_{10}N_2O]$ 211.0871; found 211.0861.

6-(4-Ethylphenyl)furo[2,3-*b*]pyrazine (**6e**): The product was obtained as a yellow needles, mp: 81–83 °C (81.9 mg, 73%); ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 8.46 (d, *J* = 2.7 Hz, 1H), 8.17 (d, *J* = 3.1 Hz, 1H), 7.85 (d, *J* = 7.6 Hz, 2H), 7.31 (d, *J* = 8.4 Hz, 2H), 7.15 (s, 1H), 2.69 (q, *J* = 6.9 Hz, 2H), 1.25 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 160.6, 155.5, 142.7, 141.5, 136.8, 129.0, 128.4, 128.2, 125.9, 100.2, 28.8, 15.3. HRMS (ESI): $[M+H]^+$ Calcd for $[C_{14}H_{12}N_2O]$ 225.1028; found 225.1017.

6-(4-Methoxyphenyl)furo[2,3-*b*]pyrazine (**6f**): The product was obtained as a yellow needles, mp: 115–117 °C (Table 3: 85.9 mg, 76%; Scheme 5: 90 mg, 80%); ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 8.45 (d, *J* = 3.1 Hz, 1H), 8.16 (d, *J* = 2.3 Hz, 1H), 8.0 (d, *J* = 9.2 Hz, 1H), 7.88 (d, *J* = 8.4 Hz, 1H), 7.08 (s, 1H), 7.02–7.0 (m, 1H), 6.97–6.95 (m, 1H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 161.5, 151.2, 142.4, 142.2, 136.6, 130.7, 127.4, 114.5, 99.4, 55.4. HRMS (ESI): $[M+H]^+$ Calcd for $[C_{13}H_{10}N_2O_2]$ 227.0821; found 227.0810.

6-(4-Butylphenyl)furo[2,3-*b*]pyrazine (**6g**): The product was obtained as a yellow needles, mp: 51–53 °C (93.4 mg, 74%); ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 8.46 (d, *J* = 3.4 Hz, 1H), 8.16 (d, *J* = 3.1 Hz, 1H), 7.83 (d, *J* = 8.4 Hz, 2H), 7.30–7.27 (m, 2H), 7.14 (s, 1H), 2.65 (t, *J* = 8.0 Hz, 2H), 1.63–1.57 (m, 2H), 1.40–1.34 (m, 2H), 0.93–0.89 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 160.7, 155.5, 146.0, 141.4, 136.9, 129.1, 125.7, 100.5, 35.6, 33.3, 22.3, 13.9. HRMS (ESI): $[M+H]^+$ Calcd for $[C_{16}H_{16}N_2O]$ 253.1341; found 253.1329.

6-(4-(tert-Butyl)phenyl)furo[2,3-*b*]pyrazine (**6h**): The product was obtained as a yellow needles, mp: 79–81 °C (89.6 mg, 71%); ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 8.50 (d, *J* = 3.0 Hz, 1H), 8.20 (d, *J* = 2.3 Hz, 1H), 7.91–7.89 (m, 2H), 7.55–7.52 (m, 2H), 7.26 (s, 1H), 1.37 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 160.6, 154.2, 142.8, 141.5, 137.0, 128.3, 125.8, 125.5, 100.6, 35.0, 31.1. HRMS (ESI): $[M+H]^+$ Calcd for $[C_{16}H_{16}N_2O]$ 253.1341; found 253.1331.

2-(2-Chloropyridin-3-yl)-1-(4-ethylphenyl)ethan-1-one (**9**): The product was obtained as a pale yellow semi-solid (90.9 mg, 70%); ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 8.32–8.31 (m, 1H), 7.97 (d, *J* = 8.4 Hz, 2H), 7.61–7.59 (m, 1H), 7.32 (d, *J* = 8.4 Hz, 2H), 7.22–7.20 (m, 1H), 4.41 (s, 2H), 2.72 (q, *J* = 7.6 Hz, 2H), 1.26 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 194.9, 151.6, 150.6, 148.1, 140.4, 133.8, 130.0, 128.4, 128.2, 122.5, 42.4, 28.8, 15.0. HRMS (ESI): $[M+H]^+$ Calcd for $[C_{15}H_{14}ClNO]$: 260.0842, found 260.0840.

2-(4-Ethylphenyl)furo[2,3-*b*]pyridine (**10**): The product was obtained as a off white needles, mp: 130–132 °C (69.22 mg, 62%); ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 8.26–8.24 (m, 1H), 7.86–7.84 (m, 1H), 7.81 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 7.6 Hz, 2H), 7.19–7.16 (m, 1H), 6.93 (s, 1H), 2.68 (q, *J* = 7.6 Hz, 2H), 1.25 (t, *J* = 7.6 Hz 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 161.8, 155.9, 145.8, 143.5, 129.3, 128.4, 127.1, 125.2, 121.6, 119.4, 99.3, 28.8, 15.4. HRMS (ESI): $[M+H]^+$ Calcd for $[C_{15}H_{13}NO]$: 224.1075, found 224.1064.

General Procedure for the Synthesis of 2-chloro-3-(arylethynyl)quinoxaline/Pyrazine: To a solution of substituted 2,3-dichloroquinoxaline/pyrazine **1** (1.0 mmol) in MeCN (2 mL), 5 mol % of $Pd(PPh_3)_2Cl_2$ and CuI were added. The reaction vial was then sealed and flushed with nitrogen. Then, 2.5 equiv of Et_3N and 1.04 mmol of alkyne **2** were added to the reaction mixture. The reaction was then stirred at 60 °C until TLC revealed complete conversion of the starting material. The reaction mixture was then allowed to cool, was diluted with H_2O, and was extracted with EtOAc (3 × 10 mL). The combined organic

layers were dried over Na_2SO_4, concentrated under vacuum, and purified by column chromatography using 100−200 mesh size silica gels (hexane: ethyl acetate) to afford the corresponding product. The structure and purity of compounds were confirmed by comparison of their physical and spectral data (^{1} H NMR, ^{13}C NMR and HRMS).

2-Chloro-3-(*p*-tolylethynyl)quinoxaline (**3b**): The product was obtained as a yellow needles, mp: 179–181 ^{o}C (256.4 mg, 92%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10–8.06 (m, 1H), 8.01–7.97 (m, 1H), 7.79–7.74 (m, 2H), 7.60 (d, *J* = 8.4 Hz, 2H), 7.21 (d, *J* = 8.4 Hz, 2H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.0, 140.7, 140.6, 140.2, 138.7, 132.4, 131.2, 130.6, 129.3, 128.8, 128.2, 118.1, 97.7, 85.1, 21.7. HRMS (ESI): $[M+H]^+$ Calcd for $[C_{17}H_{11}ClN_2]$ 279.0689; found 279.0655.

2-Chloro-3-((3-methoxyphenyl)ethynyl)-6-methylquinoxaline (**3m**): The product was obtained as a pale yellow needles, mp: 167–169 ^{o}C (271.7 mg, 88%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91–7.68 (m, 2H), 7.53 (d, *J* = 8.4 Hz, 1H), 7.28–7.25 (m, 2H), 7.15 (s, 1H), 6.95–6.91 (m, 1H), 3.97 (s, 3H), 2.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.3, 147.0, 141.4, 140.7, 138.7, 138.2, 133.6, 127.60, 127.55, 124.9, 122.2, 122.1, 116.8, 116.7, 96.7, 85.2, 55.3, 21.8. HRMS (ESI): $[M+H]^+$ Calcd for $[C_{18}H_{13}ClN_2O]$: 309.0795, found 309.0819.

2-Chloro-6-methyl-3-(pyridin-2-ylethynyl)quinoxaline (**3o**): The product was obtained as a yellow needles, mp: 146–148 ^{o}C (243.4 mg, 87%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.72 (d, *J* = 4.6 Hz, 1H), 7.91 (d, *J* = 8.4 Hz, 1H), 7.87 (s, 1H), 7.78 – 7.71 (m, 2H), 7.65 – 7.62 (m, 1H), 7.38 – 7.34 (m, 1H), 2.60 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.5, 141.9, 141.6, 140.8, 139.1, 137.6, 136.3, 134.2, 133.1, 128.2, 127.8, 127.7, 124.1, 94.5, 84.2, 21.9. HRMS (ESI): $[M+H]^+$ Calcd for $[C_{16}H_{10}ClN_3]$ 280.0642; found 280.0630.

2-Chloro-3-((4-methoxyphenyl)ethynyl)pyrazine (**11f**): The product was obtained as a yellow needles, mp: 131–133 ^{o}C (207.9 mg, 85%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.47 (d, *J* = 2.3 Hz, 1H), 8.26 (d, *J* = 2.3 Hz, 1H), 7.61–7.59 (m, 2H), 6.93–6.91 (m, 2H), 3.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.9, 150.4, 142.2, 141.2, 139.9, 134.0, 114.2, 113.2, 98.2, 83.8, 55.4. HRMS (ESI): $[M+H]^+$ Calcd for $[C_{17}H_9ClN_2]$ 245.0482; found 245.0477.

***Deuterium Labeling Experiments*.**

2-(*p*-Tolyl)furo[2,3-*b*]quinoxaline-3-d (**12a**): The product was obtained as a yellow needles, mp: 217–219 ^{o}C (117.6 mg, 90%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.12–8.09 (m, 1H), 8.07–8.04 (m, 1H), 7.84 (d, *J* = 8.4 Hz, 2H), 7.70–7.65 (m, 2H), 7.25 (d, *J* = 7.6 Hz, 2H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.1, 154.3, 144.6, 142.1, 141.8, 138.6, 129.8, 128.61, 128.58, 128.49, 128.1, 126.0, 125.6, 99.9–99.37 (m, 1C), 21.6. HRMS (ESI): $[M+H]^+$ Calcd for $[C_{17}H_{11}DN_2O]$ 262.1091; found 262.1086.

2-(3-Methoxyphenyl)-6-methylfuro[2,3-*b*]quinoxaline-3-d (**12b**): The product was obtained as a yellow needles, mp: 161–163 ^{o}C (129.6 mg, 89%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89–7.81 (m, 1H), 7.74–7.69 (m, 1H), 7.40 (t, *J* = 7.6 Hz, 2H), 7.35 (s, 1H), 7.25 (t, *J* = 8.4 Hz, 1H), 6.86 (d, *J* = 8.4 Hz, 1H), 3.75 (s, 3H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.1, 159.9, 153.93, 144.1, 142.2, 139.2, 138.5, 136.9, 130.9, 130.0, 128.0, 127.6, 118.5, 117.1, 100.99–100.93 (m, 1C), 55.3, 21.6. HRMS (ESI): $[M+H]^+$ Calcd for $[C_{18}H_{13}DN_2O_2]$ 292.1196; found 292.1186.

6-(4-Methoxyphenyl)furo[2,3-*b*]pyrazine-7-d (**13**): The product was obtained as a yellow needles, mp: 109–111 ^{o}C (89.8 mg, 79%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.44 (d, *J* = 3.1 Hz, 1H), 8.28 (d, *J* = 2.3 Hz, 1H), 8.0–7.97 (m, 2H), 6.96–6.92 (m, 2H), 3.8 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.9, 151.2, 142.3, 142.2, 136.6, 130.7, 127.4, 113.9, 55.5. HRMS (ESI): $[M+H]^+$ Calcd for $[C_{13}H_9DN_2O_2]$ 228.0883; found 228.0876

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[15] Crystallographic data of compounds **4b, 4k** and **6b** have been deposited at the Cambridge Crystallographic data Centre as a CIF deposit with file number 1538954, 1549438 and 1538955 respectively. Copies of these data can be obtained free of charge on application to CCDC. Email: deposit@ccdc.cam.ac.uk.

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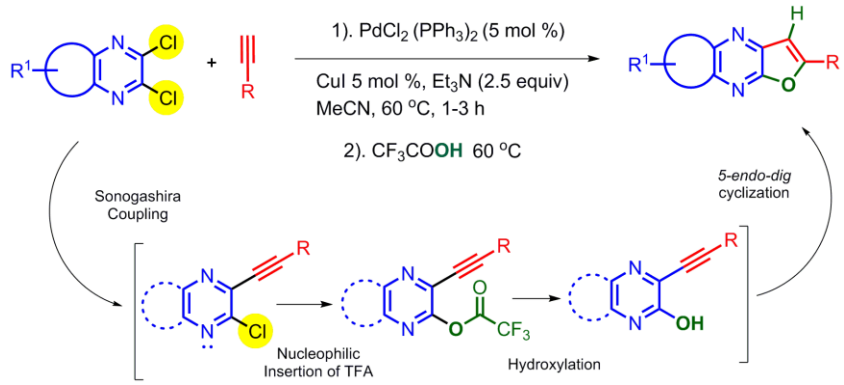

Abstract: Trifluoroacetic acid (TFA) promoted step-economical one-pot approach for the synthesis of furo-fused quinoxalines/pyrazines by the reaction of 2, 3-dichloroquinoxalines/pyrazines with electronically varied alkyne is described. The reaction shows the selective *in-situ* Sonogashira conjoined hydroxylation followed by metal free *5-endo-dig* cyclization. The preliminary experiment depicted the role of TFA as a source of oxygen for oxyarylation and isotopic labeling studies supports the proposed mechanistic pathway goes via activation of alkyne in acidic medium. This methodology tolerates a various kind of substituents, which proves to be valuable for structural and

*Kapil Mohan Saini, Sonu Kumar, Monika Patel, Rakesh K. Saunthwal and Akhilesh K. Verma**

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