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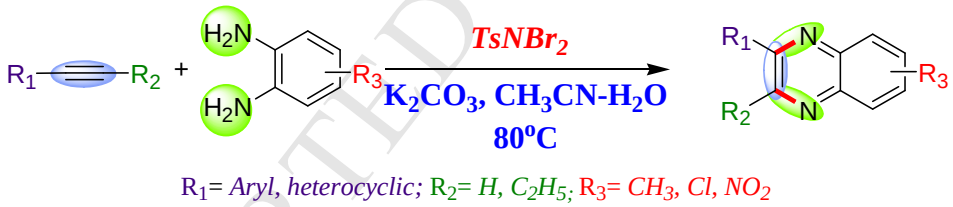
Metal free synthesis of quinoxalines from alkynes via a cascade process using $TsNBr_2$

Debojit Hazarika and Prodeep Phukan*

Department of Chemistry, Gauhati University, Guwahati, 781014, Assam, India
E-mail: pphukan@yahoo.com

Abstract: A metal free protocol for the synthesis of quinoxalines from alkynes has been developed. The reaction was carried out by treating alkynes with $TsNBr_2$ in presence of *O*-phenylenediamines in a mixture of acetonitrile and water (9:1). This one-pot reaction proceeds via an oxidative transformation of alkynes to α,α-dibromoketones in presence of $TsNBr_2$ and eventually to quinoxalines in presence of 1,2-diamines in a cascade process.



R_1= *Aryl, heterocyclic;* R_2= *H, C_2H_5;* R_3= *CH_3, Cl, NO_2*

Keywords: $TsNBr_2$, quinoxalines, alkynes, *O*-phenylenediamine, domino reaction

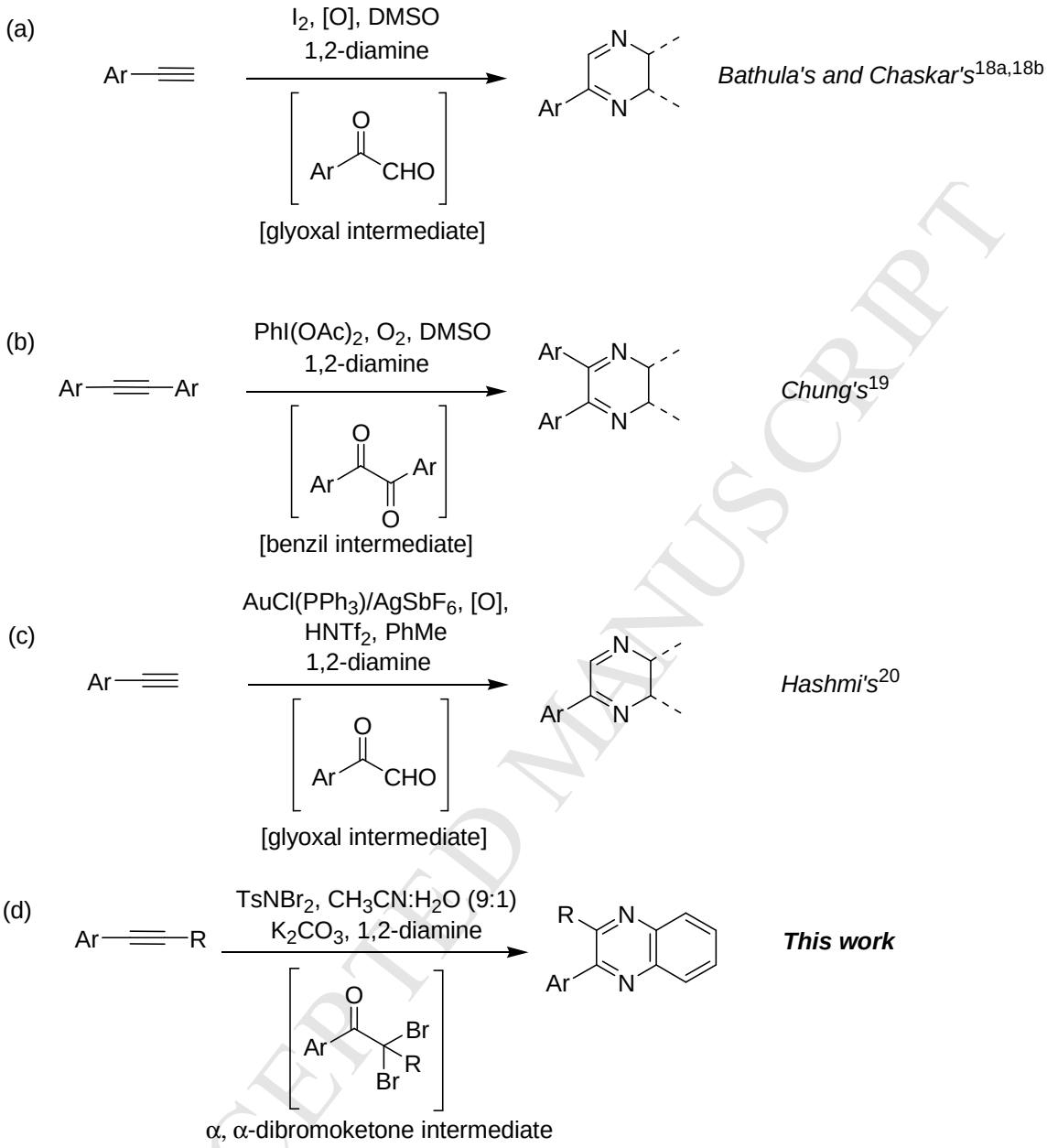
1. Introduction

Biologically active heterocyclic compounds are a boon to pharmacology.[1] Quinoxaline belongs to such an important class of heterocyclic compounds which possess numerous biological activities such as anticancer,[2a] antibacterial,[2b] antiviral,[2c] antifungal,[2d] anti-inflammatory[2e] etc. Quinoxaline also constitute the core of many commercial antibiotics.[3] Moreover they serve as useful synthon for organic synthesis.[4] They have potential application in

the field of organic semiconductors and electroluminescent materials too.[4b,5] Owing to the biological importance and wide variety of applications of quinoxaline, various methods have been developed for the synthesis of this class of heterocyclic compounds. Acid catalyzed condensation of 1,2-diamines with 1,2-dicarbonyl compounds is the most common method for quinoxaline synthesis.[6] However reactions of 1,2-diamines with α-haloketones,[7] epoxides,[8] vicinal diols,[9] α-hydroxy ketones,[10] diazoketones,[11] α-ketocarboxylic acids,[12] hydroxyl acetylenes,[13] α-tosyloxy ketones,[14a] or cinnamic acid,[14b] results in the formation of quinoxaline derivatives. But most of the processes involve harsh reaction condition, use of metal catalyst, multi step synthesis, longer reaction time, low yield and limited substrate scope.

Synthesis of quinoxaline from alkyne has attracted immense interest to the organic chemist.[15] One pot synthesis of quninoxaline via Pd and Ru catalyzed oxidation of internal alkyne to benzil and subsequent treatment with the 1,2-diamine has been developed.[15b,15c,15d] Chen *et al.*[16] synthesized quinoxalines from alkynes and 1,2-diamines in the presence of copper(II) catalyst whereas Minakata *et al.*[17] used hypervalent iodine as the catalyst. These methods also involve more than one step and use of expensive oxidants.

It has been observed that the domino synthesis of quinoxaline using catalytic iodine with a suitable oxidant in DMSO continues to be the common practice for their synthesis from terminal alkynes (**scheme 1a**).[18] Similar protocol has been adopted using ethylenearenes[18a,18b] and ethylarenes[18b] as the suitable synthons. Hypervalent iodine source $PhI(OAc)_2$ have been used as catalyst for domino synthesis of quinoxaline from internal alkyne (**scheme 1b**).[19] Hashmi *et al.* had reported tandem synthesis of quinoxaline via gold catalyzed oxidation of alkynes to glyoxals (**scheme 1c**).[20]



Scheme 1: Domino protocol for the synthesis of quinoxaline from alkyne

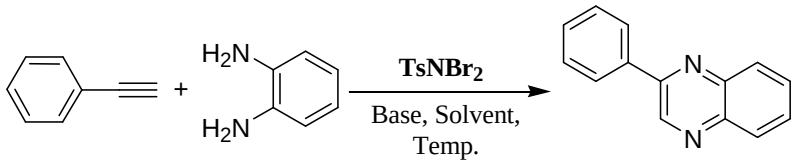
Herein, we are reporting a strategically different domino protocol for the synthesis of quinoxaline from alkynes. While α-bromoketones[7] has been reported to be very effective for preparation of quinoxaline from 1,2-diamine, their synthesis from α,α-dibromoketones is very rare in the literature. From the best of our knowledge only one reaction has been exemplified using α,α-dibromoacetophenones with 1,2-diamine in presence of $Ga(ClO_4)_3$.[21] In continuation

of our work on *N*,*N*-dibromo-*p*-toluene sulfonamide,[22] which is a very interesting and promising brominating reagent that can deliver the synthesis of α-bromoketone[23] and α,α-dibromoketones[24] from alkynes under very mild conditions, we have developed a domino process for the synthesis of quinoxalines from alkynes utilizing α,α-dibromoketones as the synthetic intermediate (**Scheme 1d**).

2. Results and Discussion

N,*N*-dibromo-*p*-toluene sulfonamide was synthesized following a literature procedure.[22e] Initial screening of our work was carried out using phenylacetylene as the model substrate. In a typical reaction, $TsNBr_2$ (1 mmol), *O*-phenylenediamine (0.5 mmol) and K_2CO_3 (1 mmol) was added to a solution of phenylacetylene (0.5 mmol) in a mixture of acetonitrile and water (9:1 ratio, 3 mL) and the reaction was stirred at room temperature. After 24 hours of reaction, the desired product was obtained with 30% yield. When the reaction was studied by varying the amount of base, we have recorded a maximum of 61% of the desired product at room temperature in presence of 4 equivalent K_2CO_3 (**table 1, entry 2-3**). A notable change in the reaction yield and time was observed when the reaction temperature was increased to 60 °C with 77% isolated product within 4 hours (**table 1, entry 5**). Further increment in the temperature to 80 °C led to the improvement of the rate of the reaction to provide 2-phenylquinoxaline in 85% yield within 1 hour (**table 1, entry 6**). Effect of lowering the amount of $TsNBr_2$ on the reaction yield was profound (**table 1, entry 7**). Use of other bases such as Na_2CO_3, Cs_2CO_3, DBU and Et_2NH could not improve the result (**table 1, entry 9-12**). We have also investigated the effect of different solvents on the reaction yield. The use of solvents like DMSO, DMF and acetone-H_2O produced diminishing results (**table 1, entry 13-15**).

Table 1. Optimization of reaction conditions[a]



1 **2** **3**

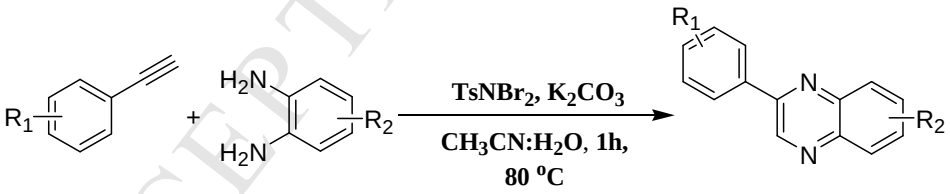
Entry	Base	Equiv. of base	Equiv. of $TsNBr_2$	Solvent	Temp (°C)	Time (hr)	Yield (%)[c]
1	K_2CO_3	2	2	Acetonitrile-H_2O[b]	rt	24	30
2	K_2CO_3	3	2	Acetonitrile-H_2O[b]	rt	18	43
3	K_2CO_3	4	2	Acetonitrile-H_2O[b]	rt	12	61
4	K_2CO_3	5	2	Acetonitrile-H_2O[b]	rt	12	64
5	K_2CO_3	4	2	Acetonitrile-H_2O[b]	60	4	77
6	**K_2CO_3**	**4**	**2**	**Acetonitrile-H_2O[b]**	**80**	**1**	**85**
7	K_2CO_3	4	1	Acetonitrile-H_2O[b]	80	1	35
8	K_2CO_3	4	2.5	Acetonitrile-H_2O[b]	80	1	87
9	Na_2CO_3	4	2	Acetonitrile-H_2O[b]	80	1	44
10	Cs_2CO_3	4	2	Acetonitrile-H_2O[b]	80	1	37
11	DBU	4	2	Acetonitrile-H_2O[b]	80	1	trace
12	Et_2NH	4	2	Acetonitrile-H_2O[b]	80	1	trace

13[d]	K_2CO_3	4	2	DMSO	80	1	39
14	K_2CO_3	4	2	Acetone-H_2O[e]	80	1	51
15	K_2CO_3	4	2	DMF	80	1	24

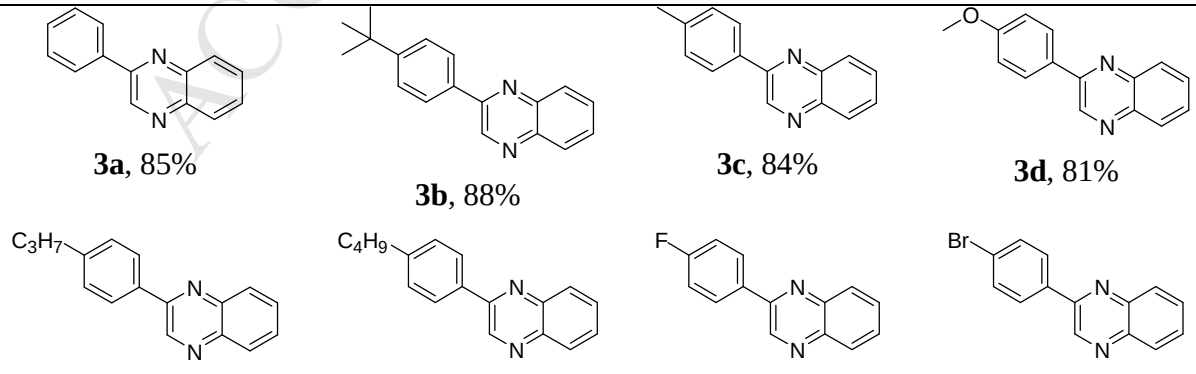
[a]Reaction condition: 1a (0.5 mmol), 2a (0.5 mmol), and solvent (3 mL); [b]MeCN:H_2O = 9:1; [c]Isolated yield. [d]Using DMSO as solvent $TsNBr_2$ was added in ice cold condition. [e]Acetone: H_2O = 30:1.

With the optimized reaction conditions in hand, we have examined the scope of the process for various alkynes (**Table 2**). Terminal alkynes with various substitution patterns on the aromatic ring could provide the desired quinoxalines in high yield (61-88%). Electron donating groups are very effective for this transformation. Halo- functionalities were well tolerable under the reaction conditions (**table 2, 3g**, **3h**) indicating further synthetic utilization of the quinoxaline products. We have successfully transformed an internal alkyne to the corresponding quinoxaline in high yield (**table 2, 3l**, 72%). Heterocyclic alkyne such as 2-ethynyl pyridine was also found to undergo this transformation with relatively lower yield (**table 2, 3m**, 61%). Then we have examined the scope of *O*-phenylenediamines bearing various substitution patterns (**table 2, 3n-3q**). Formation of isomers was detected in case of *mono*-substituted *O*-phenylenediamines, which can be separated by using column chromatography (**table 2, 3o** & **3q**). However in case of 4-methyl-*O*-phenylenediamine, inseparable isomeric mixture was obtained (**3n**).

Table 2: Synthesis of quinoxaline from various alkynes[a]

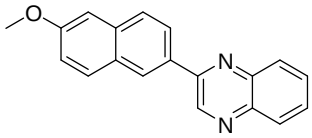
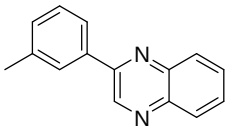
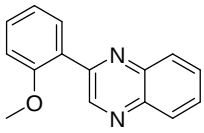
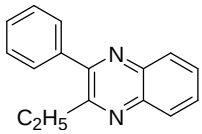


1a-m **2a-e** **3a-q**

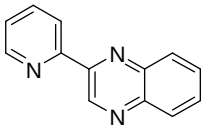
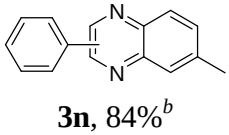
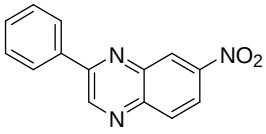
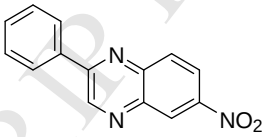


3a, 85% **3b**, 88% **3c**, 84% **3d**, 81%

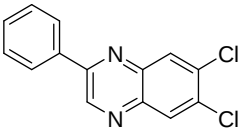
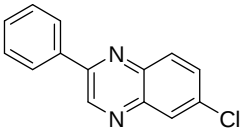
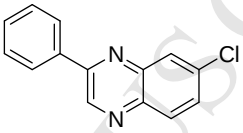
3e, 82% **3f**, 81% **3g**, 83% **3h**, 81%

3i, 79% **3j**, 80% **3k**, 77% **3l**, 72%

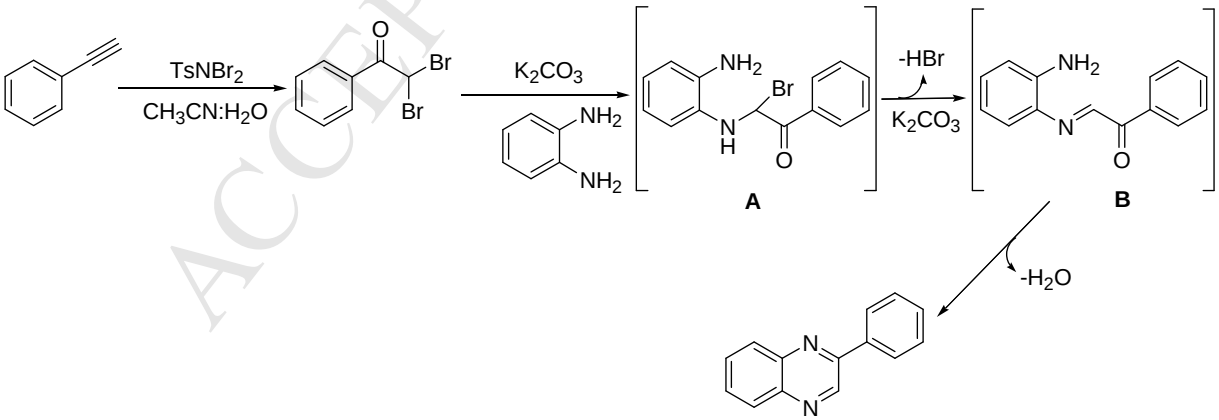
3m, 61% **3n**, 84%[b] **3oa**, 18% **3ob**, 50%

3p, 79% **3qa**, 49% **3qb**, 28%

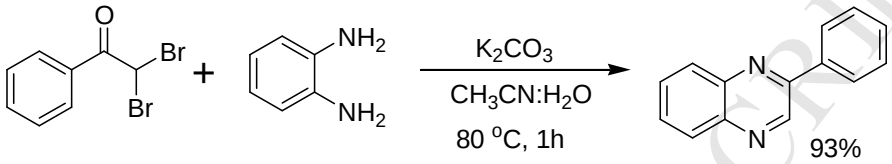
[a]Reaction condition: alkyne (0.5 mmol), 1,2-diamine (0.5 mmol), $TsNBr_2$ (1 mmol), K_2CO_3 (2 mmol), $CH_3CN:H_2O$ (9:1, 3 mL), 80 °C, 1h. [b]Isomeric mixture of 1:1.

A probable mechanistic pathway to explain the reaction is illustrated in **Scheme 2.** Addition of $TsNBr_2$ to alkyne result in the formation of α,α-dibromoketone.[24] In presence of the base, the α,α-dibromoketone undergoes S_N2 attack with the 1,2-diamine forming the intermediate **A** which subsequently releases HBr and form the imine intermediate **B**. Finally condensation takes place resulting in the formation of the desired product.



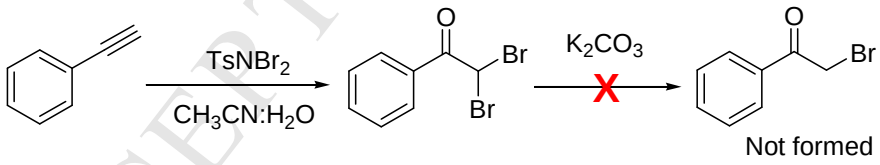
Scheme 2: Proposed mechanism

In order to confirm whether the reaction proceeds via α-bromoketone or α,α-dibromoketone in the reaction, we have performed few control experiments. Initially, α,α-dibromoketone was synthesized from phenyl acetylene using a literature procedure,[24] which was further reacted with *O*-phenylenediamine under the same reaction condition. When 2,2-dibromo-1-phenylethanone was reacted with *O*-phenylenediamine under the same reaction condition, corresponding quinoxalines was formed in 93% yield (**Scheme 3**).



Scheme 3. Quinoxaline synthesis from α,α-dibromoketone

As literature reveals the use of α-bromoketones with 1,2-diamine for the synthesis of quinoxalines,[7] the second experiment was carried out to ensure the absence of α-bromoketone as an intermediate in the reaction mixture. Following our earlier protocol,[24c] a reaction was carried out exactly under the same condition without the addition of *O*-phenylenediamine (**Scheme 4**) in order to confirm whether any α-bromoketone is formed in the course of the reaction. In this case, we could not isolate any specific desired product from the reaction mixture. This nullifies the formation of quinoxaline from alkynes via formation of α-bromoketone intermediate and accordingly the cyclization-oxidation mechanism in presence of $TsNBr_2$.



Scheme 4. Attempt to synthesize α-bromoketone from alkyne

These control experiments definitely indicate the involvement of α,α-dibromoketone as an intermediate in the reaction for the formation of final product quinoxalines.

3. Conclusion

In conclusion, an efficient metal free domino protocol has been developed for direct synthesis of quinoxalines from alkynes. Formation of α,α-dibromoketone intermediate from

alkyne in presence of $TsNBr_2$ and finally to quinoxaline in presence of 1,2-diamine through controlled manipulation of the base and reaction temperature has been successfully achieved. Moreover the reaction works notably under room temperature conditions. Wide substrate scope with good yield and high purity of the desired product can be easily obtained.

4. Experimental Section

4.1 General Remarks

$TsNBr_2$ was prepared using literature procedure.[22e] This reagent can be stored in a refrigerator in a air-tight container. All other reagents and starting materials were purchased from commercial sources. ^{1}H NMR spectra were recorded in Bruker Ultrashield 300 MHz NMR spectrometer and ^{13}C NMR spectra were recorded in Bruker Ultrashield 500 MHz and 300 MHz NMR spectrometer. Chemical shifts are given in δ units relative to the tetramethylsilane (TMS) signal as an internal reference in $CDCl_3$. Coupling constants (*J*) are reported in hertz. IR spectra were recorded in IR Affinity-1 (SHIMADZU) spectrometer. Mass spectra were obtained in a Q-TOF ESI-MS instrument (HAB 273). Chromatographic purification was performed using flash chromatography over a manually packed column containing silica gel (230-400 mesh).

4.2 General procedure for synthesis of quinoxalines (3a-3q)

To a solution of alkyne (0.5 mmol) in a mixture of CH_3CN and H_2O (9:1 ratio, 3 mL), $TsNBr_2$ (1 mmol), 1,2-diamine (0.5 mmol) and K_2CO_3 (2 mmol) was added and the mixture was heated at 80 °C in open air for 1 hour. After completion of the reaction, water was added and the reaction mixture was extracted with EtOAc (3 x 25 mL). The organic layer was separated, dried over

anhydrous Na_2SO_4 and concentrated. The crude product was purified by column chromatography using petroleum ether and ethyl acetate mixture as eluent.

4.2.1. 2-phenylquinoxaline **(3a):**[18a]

Pale yellow solid (87.3 mg, 85%); mp 81-82 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.33 (s, 1H), 8.21-8.12 (m, 4H), 7.80-7.75 (m, 2H), 7.60-7.53 (m, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 151.8, 143.3, 142.1, 141.4, 136.6, 130.3, 130.1, 129.5, 129.5, 129.1, 129.0, 127.4; IR (KBr, cm^{-1}): *v* 3441, 3011, 1630, 1409, 767.

4.2.2. 2-(4-t-Butylphenyl)quinoxaline **(3b):**[18a]

Brown oil (115.7 mg, 88%); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.33 (s, 1H), 8.17-8.10 (m, 4H), 7.76-7.73 (m, 2H), 7.60 (d, *J*= 8.4 Hz, 2H), 1.40 (s, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 153.5, 151.7, 143.3, 142.2, 141.2, 133.8, 130.1, 129.4, 129.3, 128.9, 127.2, 126.1, 34.8, 31.1; IR (KBr, cm^{-1}): *v* 3433, 3022, 1627, 1421, 1210, 761.

4.2.3. 2-(p-Tolyl)quinoxaline **(3c):**[18a]

Pale yellow solid (92.0 mg, 84%); mp 88-89 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.30 (s, 1H), 8.15-8.09 (m, 4H), 7.77-7.72 (m, 2H), 7.36 (d, *J*= 7.5 Hz, 2H), 2.44 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 151.7, 143.2, 142.1, 141.2, 140.4, 133.8, 130.2, 129.8, 129.4, 129.3, 128.9, 127.3, 21.4; IR (KBr, cm^{-1}): *v* 3438, 3022, 1636, 1420, 1039, 766.

4.2.4. 2-(4-Methoxyphenyl)quinoxaline **(3d):**[18a]

Brownish solid (95.1 mg, 81%); mp 100-103 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.27 (s, 1H), 8.17-8.06 (m, 4H), 7.76-7.69 (m, 2H), 7.05 (d, *J*= 8.7 Hz, 2H), 3.87 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 161.2, 151.3, 143.0, 142.1, 141.0, 130.1, 129.2, 129.0, 129.0, 128.9, 128.9, 114.4, 55.3; IR (KBr, cm^{-1}): *v* 3441, 3027, 1609, 1426, 1033, 761.

4.2.5 2-(4-n-Propylphenyl)quinoxaline **(3e):**

Brown solid (101.1 mg, 82%); mp 104-106 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.32 (s, 1H), 8.16-8.10 (m, 4H), 7.80-7.73 (m, 2H), 7.38 (d, *J*= 7.8 Hz, 2H), 2.69 (t, *J*= 7.5 Hz, 2H), 1.74-1.67

(m, 2H), 0.98 (t, *J*= 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 151.8, 145.1, 143.2, 142.2, 141.3, 134.1, 130.1, 129.4, 129.25, 129.21, 128.9, 127.3, 37.7, 24.3, 13.6; IR (KBr, cm^{-1}): *v* 3445, 3009, 1640, 1424, 1208; HRMS (ESI) calculated for $C_{17}H_{16}N_2$ $(M+H)^+$ 249.1313 found 249.1309.

4.2.6. 2-(4-n-Butylphenyl)quinoxaline **(3f):**

Dark brown solid (106.4 mg, 81%); mp 84-85 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.31 (s, 1H), 8.16-8.10 (m, 4H), 7.79-7.72 (m, 2H), 7.38 (d, *J*= 8.4 Hz, 2H), 2.71 (t, *J*= 7.8 Hz, 2H), 1.69-1.61 (m, 2H), 1.43-1.36 (m, 2H), 0.95 (t, *J*= 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 151.8, 145.3, 143.2, 142.2, 141.3, 134.0, 129.4, 129.1, 128.9, 127.3, 35.4, 33.3, 22.2, 13.8; IR (KBr, cm^{-1}): *v* 3016, 1638, 1428, 1217, 953, 755. HRMS (ESI) calculated for $C_{18}H_{18}N_2$ $(M+H)^+$ 263.1470 found 263.1473.

4.2.7. 2-(4-Fluorophenyl)quinoxaline **(3g):**[20]

White solid (92.3 mg, 83%); mp 123-124 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.30 (s, 1H), 8.23-8.12 (m, 4H), 7.80-7.78 (m, 2H), 7.29-7.23 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 164.1(J_{CF} = 249.1Hz), 150.6, 142.8, 142.0, 141.3, 132.8 (J_{CF} = 3.6 Hz), 130.3, 129.5, 129.4 (J_{CF} = 4.75 Hz), 129.0, 116.1 (J_{CF} = 21.6 Hz); IR (KBr, cm^{-1}): *v* 3041, 2361, 1646, 959, 757.

4.2.8. 2-(4-Bromophenyl)quinoxaline **(3h):**[18b]

Pale yellow solid (114.8 mg, 81%); mp 123-125 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.30 (s, 1H), 8.16-8.08 (m, 4H), 7.79-7.69 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 150.5, 142.7, 142.0, 141.5, 135.4, 132.2, 130.4, 129.7, 129.4, 129.0, 128.9, 124.9; IR (KBr, cm^{-1}): *v* 3048, 2354, 1642, 949, 757.

4.2.9. 2-(6-Methoxynapthalen-2-yl)quinoxaline **(3i):**

Yellow solid (112.3 mg, 79%); mp 169-171 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.48 (s, 1H), 8.68-8.64 (m, 1H), 8.43-8.42 (m, 2H), 8.22-8.14 (m, 2H), 8.02 (d, *J*= 9 Hz, 1H), 7.83-7.80 (m,

2H), 7.37 (d, *J*= 9 Hz, 2H), 4.09 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 154.6, 151.0, 143.2, 142.2, 130.4, 130.0, 129.6, 129.47, 129.44, 129.0, 127.4, 127.2, 126.1, 56.8; IR (KBr, cm^{-1}): *v* 3450, 3051, 2355, 1641, 1258, 743; HRMS (ESI) calculated for $C_{19}H_{14}N_2O$ $(M+H)^+$ 287.1106 found 287.1123.

4.2.10. 2-(m-Tolyl)quinoxaline **(3j):**[18b]

White solid (88.2 mg, 80%); mp 82-85 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.32 (s, 1H), 8.15 (t, *J*= 8.7 Hz, 2H), 8.03 (s, 1H), 7.97 (d, *J*= 7.2 Hz, 1H), 7.80-7.75 (m, 2H), 7.47 (t, *J*= 7.5 Hz, 1H), 7.36 (d, *J*= 6.9 Hz, 1H), 2.50 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 151.9, 143.4, 141.4, 138.8, 136.6, 130.8, 130.1, 129.4, 129.3, 129.0, 128.9, 128.0, 124.5, 21.4; IR (KBr, cm^{-1}): *v* 3441, 3033, 1641, 1429, 1227, 1044, 752.

4.2.11. 2-(2-Methoxyphenyl)quinoxaline **(3k):**[2h]

Pale white solid (90.8 mg, 77%); mp 106-108 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.34 (s, 1H), 8.16-8.10 (m, 2H), 7.89 (d, *J* = 7.2 Hz, 1H), 7.75-7.70 (m, 2H), 7.46 (t, *J* = 7.5 Hz, 1H), 7.15 (t, *J* = 7.5 Hz, 1H), 7.04 (d, *J* = 8.4 Hz, 1H) 3.88 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 157.2, 152.0, 147.1, 142.5, 140.8, 131.4, 131.3, 129.6, 129.4, 129.2, 128.9, 126.3, 121.4, 111.2, 55.5; IR (KBr, cm^{-1}): *v* 3450, 3019, 1611, 1444, 771.

4.2.12. 2-Ethyl-3-Phenylquinoxaline **(3l):**[6g]

Brown oil (84.1 mg, 72%); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.13-8.09 (m, 2H), 7.78-7.74 (m, 2H), 7.62-7.57 (m, 2H), 7.53-7.46 (m, 3H), 3.07 (q, *J*= 7.2 Hz, 2H), 1.31 (t, *J*= 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 156.9, 154.8, 141.3, 140.6, 138.9, 129.7, 129.5, 129.1, 128.8, 128.6, 128.5, 128.4, 128.3, 29.2, 12.9; IR (KBr, cm^{-1}): *v* 3441, 3032, 1655, 1264, 751.

4.2.13. 2-(Pyridin-2-yl)quinoxaline **(3m):**[2f]

Brown solid (63.5 mg, 61%); mp 111-113 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.96 (s, 1H), 8.79 (d, *J*= 4.2 Hz, 1H), 8.60 (d, *J*= 8.1 Hz, 1H), 8.18-8.15 (m, 2H), 7.91 (t, *J*= 6 Hz, 1H), 7.81-7.78 (m, 2H), 7.44-7.42 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 154.4, 150.0, 149.3, 144.0, 142.4,

141.6, 137.0, 130.0, 129.9, 129.5, 129.1, 124.5, 121.9; IR (KBr, cm^{-1}): *v* 3051, 1601, 1050, 948, 769.

4.2.14. 6-Methyl-2-phenylquinoxaline and 7-Methyl-2-phenylquinoxaline (1:1) **(3n):**[20]

Yellow solid (92.0 mg, 84%); mp 93-96 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.25 (d, *J*= 7.5 Hz, 1H), 8.17 (d, *J*= 6.6 Hz, 2H), 8.05-7.92 (m, 2H), 7.61-7.53 (m, 4H), 2.61 (d, *J*= 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 151.7, 151.0, 143.2, 142.4, 142.2, 141.4, 140.9, 140.5, 140.1, 139.8, 136.7, 132.6, 131.9, 130.0, 129.6, 129.1, 128.9, 128.4, 128.3, 127.8, 127.4, 127.3, 21.9, 21.8; IR (KBr, cm^{-1}): *v* 3458, 3010, 1637, 1421, 1053, 767.

4.2.15. 7-Nitro-2-phenylquinoxaline **(3oa):**[18b]

Yellow solid (22.4 mg, 18%); mp 199-201 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.49 (s, 1H), 9.04 (d, *J*= 2.4 Hz, 1H), 8.59-8.55 (m, 1H), 8.31-8.26 (m, 3H), 7.63-7.61 (m, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 154.2, 147.3, 145.3, 144.8, 140.2, 135.5, 131.2, 131.0, 129.3, 127.8, 125.5, 123.6; IR (KBr, cm^{-1}): *v* 3447, 3013, 1618, 1429, 771.

4.2.16. 6-Nitro-2-phenylquinoxaline **(3ob):**[18b]

Yellow solid (62.2 mg, 50%); mp 201-203 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.51 (s, 1H), 9.04 (s, 1H), 8.57 (d, *J*= 9Hz, 1H), 8.39-8.21 (m, 3H), 7.63-7.61 (m, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 154.2, 147.3, 145.3, 144.8, 140.2, 135.5, 131.2, 129.8, 129.3, 127.8, 125.5, 123.6; IR (KBr, cm^{-1}): *v* 3010, 1621, 1444, 1327, 778.

4.2.17. 6,7-Dichloro-2-phenylquinoxaline **(3p):**[2g]

Pale yellow solid (62.0 mg, 50%); mp 153-155 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.32 (s, 1H), 8.27-8.17 (m, 4H), 7.58-7.57 (m, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 152.5, 144.2, 140.9, 140.0, 135.7, 134.8, 133.9, 130.7, 130.0, 129.6, 129.2, 127.4; IR (KBr, cm^{-1}): *v* 3422, 3028, 1437, 1077, 755.

4.2.18. 6-Chloro-2-phenylquinoxaline **(3qa):**[2g]

Pale yellow solid (59.5 mg, 49%); mp 147-148 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.33 (s, 1H), 8.21-8.17 (m, 3H), 8.07 (d, *J*= 9 Hz, 1H), 7.70 (d, *J*= 7.5 Hz, 1H), 7.58 (d, *J*= 6.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 151.8, 144.0, 141.7, 140.7, 136.2, 135.1, 131.2, 130.7, 130.3, 129.1, 127.9, 127.4; IR (KBr, cm^{-1}): *v* 3439, 3037, 1633, 1440, 981, 762.

4.2.19. 7-Chloro-2-phenylquinoxaline **(3qb):**[2g]

Pale yellow solid (33.1 mg, 28%); mp 135-137 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.33 (s, 1H), 8.20-8.17 (m, 2H), 8.11-8.08 (m, 2H), 7.73 (d, *J*= 9 Hz, 1H), 7.60-7.52 (m, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 152.4, 143.3, 142.5, 139.9, 136.1, 136.0, 130.5, 130.4, 130.2, 129.1, 128.3, 127.5; IR (KBr, cm^{-1}): *v* 3429, 3031, 1445, 966, 757.

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