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HBTU-CATALYZED SIMPLE AND MILD PROTOCOL FOR THE SYNTHESIS OF QUINOXALINE DERIVATIVES

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Abstract –HBTU-catalyzed, simple, mild, and effective protocol for the synthesis of quinoxalines has been established. The reaction between 1,2-diamines, benzil, and catalytic amount of HBTU in ethanol resulted into quinoxalines. Various aliphatic, aromatic and heterocyclic 1,2-diamines reacted smoothly with benzil to obtained the title compounds in moderate to high overall yield. Use of environmentally benign solvent, high yield of the product, comparably less reaction time and mild reaction condition are advantages of this method.

INTRODUCTION

Quinoxalines are the heterocyclic compounds containing nitrogen as a heteroatom. Quinoxaline scaffold exhibits an important biological properties such as anti-microbial,[1a] anti-malarial,[1b] anti-viral,[1c] anti-oxidant,[1d] anti-HIV activity against anti-HIV_{IIIB} stains,[1e] and potent anti-cancer activities.[1f] In addition to this quinoxaline motif is also used in various fields such as dye industry,[2a,b] optoelectronics,[3a-e] and agricultural chemistry.[4] In the last decade, large number of synthetic methodologies have been established for the synthesis of quinoxalines. Amongst all, the cycloaddition of 1,2-diamines with benzil in ethanol and few drops of concentrated acid in refluxed condition seems to be one of the most prevalent pathway for the synthesis of titled compounds.[5] Beside this, researchers successfully used transition metal based catalysts for the synthesis of aimed product such as $CuSO_4.5H_2O$,[6a] $Zr(DS)_4$,[6b] $NbCl_5$,[6c] $SnCl_2$,[6d] CAN,[6e] ZnI_2,[6f] $SbCl_3$,[6g] $InCl_3$,[6h] $Ga(OTf)_3$,[6i] $Pd(OAc)_2$,[6j] $MnCl_2$,[6k] $Sm(OTf)_3$,[6l] HgI_2,[6m] $NaBH(OAc)_3$ and BH_3·THF,[6n] etc.

In recent past, non-transition metal catalysts like PEG-400 in MW,[7a] PEG–water,[7b] DABCO,[7c] alumina,[7d] $PTSA/H_2O$,[7e] indion 19 resin,[7f] amberlite IR-120H,[7g] grinding,[7h] etc. have also been used for the preparation of quinoxalines. Majority of the known methods have been suffering from some or other drawbacks like substantial use of transition metal based catalysts, refluxed or harsh reaction conditions and introduction of hazardous or toxic organic solvents to obtain the final product in good to high yield.

In the meantime, uronium based coupling agents captured an interest in synthetic organic chemistry for instance TBTU, TATU, COMU, HBPyU *(O*-(benzotriazol-1-yl)-*N,N,N',N'*-bis(tetramethylene)uronium hexafluorophosphate), etc. used extensively for the esterification,[8] amidation,[9a,b] condensation,[10] synthesis of a glycopeptide,[11] etc. Mainly these salts were used for dehydration reaction. Here we found that, the uronium salts can also be used as a Lewis acid catalyst in the synthesis of heterocyclic compounds. Therefore, we intend to report the use of uronium salt (HBTU) as a Lewis acid catalyst to achieve the targeted compounds.

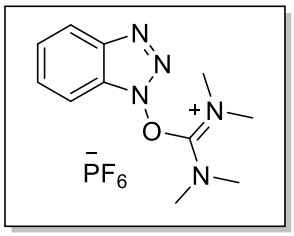


Figure 1. Structure of *O*-benzotriazol-1-yl)-*N,N,N',N'*-tetramethyluronium hexafluorophosphate (HBTU)

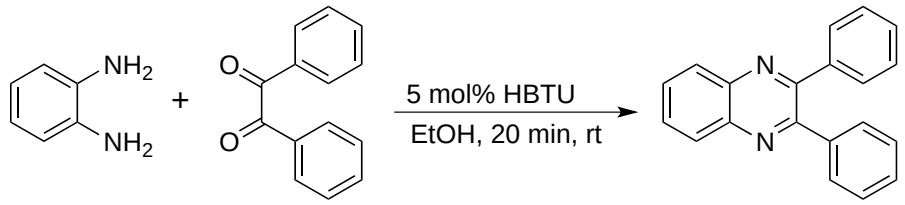
RESULTS AND DISCUSSION

Quinoxaline heterocycles find many applications in various fields, many researchers have been interested in developing new efficient methods for the synthesis of quinoxalines. Therefore, as a part of our ongoing interest in the field of synthesis of heterocyclic compounds, we first time introduced HBTU (Figure 1) as a catalyst for the synthesis of quinoxalines. This condensing agent was found to be an excellent catalyst for the synthesis of quinoxalines. Therefore, we wish to report a simple, easy, green and mild protocol for the synthesis of quinoxalines from 1,2-diamines and benzil. This procedure has advantages over the earlier reported methods like use of non-transition metal based catalyst, mild reaction condition, short reaction time, eco-friendly solvent, and high yield of the product.

Initially, a model reaction between *o*-phenylenediamine **1** (1.0 mmol, 0.108 g), benzil **2** (1.0 mmol, 0.210 g) and HBTU (5 mol%, 0.0215 g), in ethanol (5 mL) was carried out at room temperature. Surprisingly, the reaction completed in 20 min which was confirmed by TLC. Next, the amount of catalyst was kept constant and various solvents screening has been done and examined that, when the solvent polarity was lifted up, the yield of the product increased but required time for the completion of reaction also has been increased. (Table 1, entries 2-5). In case of water, yield get reduced, this may be due to insufficient solubility of the reactants. (Table 1, entry 6). Therefore, ethanol was selected as a solvent for this reaction and, the effect of catalyst was also checked out in the selected solvent. We observed that, when the catalyst amount decreased the chemical yield of the reaction also have been decreased and required time to accomplished the reaction was increased (Table 1, entries 7-10). Lastly, there was no obvious effect on

time and yield of the product if we increase the catalyst amount (Table 1, entry 11). Therefore, an optimal condition for the reaction was selected which was able to give product in 95% yield. (Table 1, entry 1).

Table 1. Effect of various solvents and amount of catalyst on HBTU catalysed reaction of *o*-phenylene-diamine and benzil

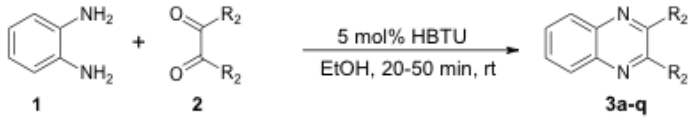


1 **2** **3a**

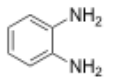
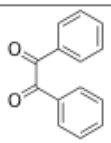
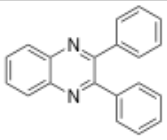
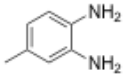
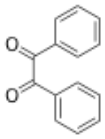
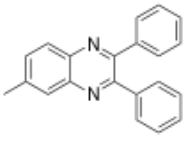
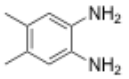
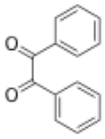
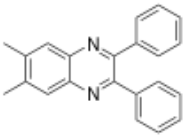
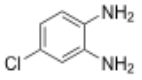
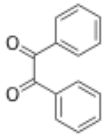
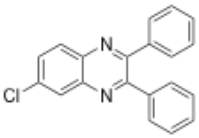
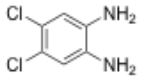
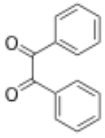
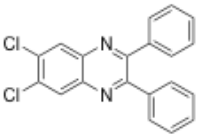
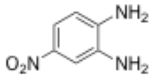
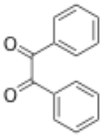
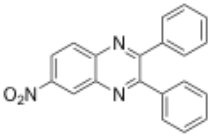
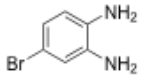
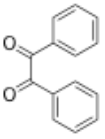
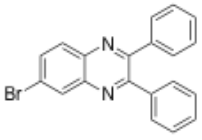
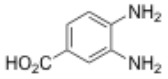
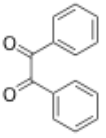
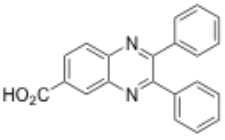
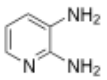
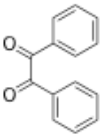
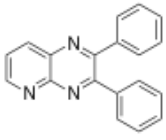
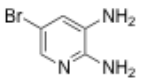
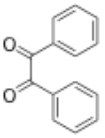
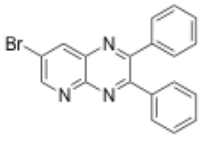
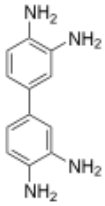
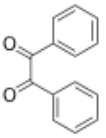
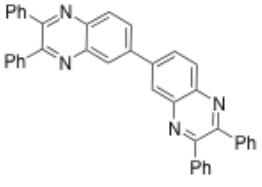
Entry[a]	Solvent	Catalyst (mol%)	Time (min)	Yield[b] (%)
1	EtOH	5	20	95
2	DCM	5	60	60
3	THF	5	45	65
4	DMSO	5	40	70
5	MeCN	5	40	72
6	H_2O	5	>60	50
7	EtOH	4	20	90
8	EtOH	3	25	88
9	EtOH	2	30	85
10	EtOH	1	40	75
11	EtOH	10	20	95

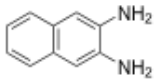
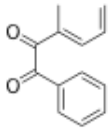
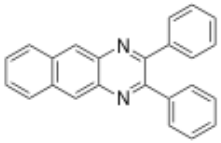
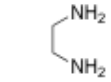
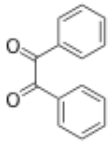
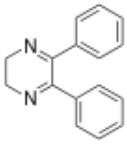
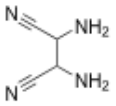
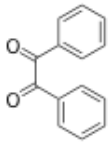
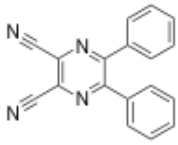
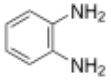
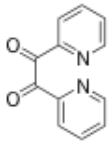
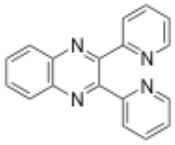
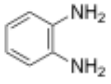
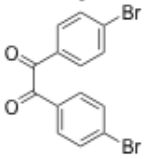
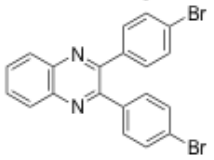
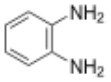
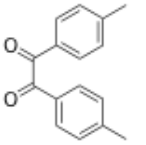
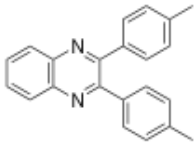
[a]The reaction was carried out at room temperature. [b]Isolated yield of the product.

Table 2. Synthesis of quinoxalines derivatives



1 2 3a-q

Entry[a]	1,2-Diamine	Benzil	Product	Time (min)	Yield[b] (%)
a				20	95
b				18	96
c				15	96
d				30	90
e				35	85
f				45	80
g				35	82
h				50	85
i				25	92
j				30	80
k				20	96

l				22	95
m				25	92
n				40	70
o				25	90
p				30	85
q				20	95

[a] All the products were identified by IR, ^{1}H NMR, ^{13}C NMR and LC-MS spectra.[b]Isolated yield.

For generalization of this protocol and to observe the substrate scope, various aliphatic, aromatic and heterocyclic 1,2-diamines and benzil were reacted under the optimal reaction conditions (Table 2). Out-turn result shows that *o*-phenylenediamine reacts smoothly with benzil to afford final product (Table 2, **3a**). At the same time, electron donating groups attached to the phenyl ring of 1,2-diamine reacted rapidly to form an end product in less time and with more yield of the product (Table 2, **3b-c**). On the contrary, electron withdrawing groups at phenyl ring of 1,2-diamine responded slowly, taken more time and gave less yield the product (Table 2, **3d-g**). However, heterocyclic 1,2-diamine reacted efficiently with benzil to resulted in respective quinoxalines (Table 2, **3h-i**), Similarly, aliphatic 1,2 diamine reacted rapidly with benzil in a given reaction condition and resulted in pyrazine skeleton (Table 2, **3m-n**). Here, 2 mmol of benzil has been taken to afford final product (Table 2, **3k**). Heterocyclic, electron withdrawing and donating benzil also reacted calmly with 1,2-diamine which produces quinoxalines (Table 2, **3o-q**).

The R_f value on TLC plate of synthesized compounds and starting materials were so close in short range UV chamber, and it was difficult to judge the progress of reaction. But in long range, only the product formed showed bright fluorescent spot on TLC plate except for (Table 2, entry **3m-n**). Therefore, it was easy to identify and separate the formed product.

CONCLUSION

We have successfully developed HBTU catalyzed simple, mild and green protocol for the synthesis of quinoxalines. Various aliphatic, aromatic, and heterocyclic 1,2-diamines reacts smoothly with benzil and substituted benzil under an optimized reaction condition and resulted into final product in comparably shorter reaction time (Table 2). Easy handling of catalyst, environment friendly solvent, high yield of the product, and less reaction time are some of the advantages of this procedure.

EXPERIMENTAL

General. All the chemicals, catalyst and reagents were purchased from Sigma-Aldrich and used without any further purification. Solvents were distilled prior to use. The progress of reactions was monitored by thin layer chromatography with TLC Silica gel 60 F_{254} purchased from Merck. Column chromatography was performed on silica gel (60–120 mesh). Melting points were recorded by an open glass capillary sealed at one end melting point tube and are uncorrected. The IR spectra were recorded on PerkinElmer Frontier FT-IR spectrophotometer. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded on Bruker Ultra shield, Avance II model NMR spectrometer. Chemical shifts of ^{1}H and ^{13}C NMR are reported in parts per million (ppm) from tetramethyl silane (TMS) as an internal standard in $CDCl_3$/DMSO-d_6 as a solvent. Mass spectra were recorded on AB SCIEX QTRAP 3200 model LC-MS spectrophotometer.

General procedure for the synthesis of quinoxalines. In an oven dried 50 mL round bottom flask, 1,2-diamine (1.0 mmol), benzil (1.0 mmol) and HBTU (5 mol%) in 5 mL EtOH stirred vigorously at room temperature. The progress of reaction was monitored by TLC. After completion of reaction EtOH was evaporated. Work up was done and the product was extracted with AcOEt thrice (5 mL each), dried over the anhydrous Na_2SO_4, filtered and evaporated under reduced pressure which was purified by silica gel column chromatography (60-120 mesh) using AcOEt-hexane (5:95) to obtain crude product which was recrystallized in hot EtOH to afford the pure product.

2,3-Diphenylquinoxaline (3a): white solid; mp 126-128 ^{o}C; IR (solid, KBr, ν_{max}, cm^{-1}) 3055, 1540, 1441, 1346, 1057, 762, 695, 537; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.32-7.7.35 (6H, m, 6CH aromatic), 7.50-7.54 (4H, m, 4CH aromatic), 7.75 (2H, d, $^{3}J_{HH}$ 3.4 Hz, 2CH aromatic), 8.17 (2H, d, $^{3}J_{HH}$ 3.4 Hz, 2CH aromatic); ^{13}C NMR ($CDCl_3$, 75 MHz) δ_C 128.25, 128.78, 129.20, 129.84, 129.93 (5CH x 15 aromatic), 139.01, 139.08 (CH x 2 aromatic), 141.15, 141.23 (CH x 2 aromatic), 153.45 (C aromatic); LC-MS *m/z* (M+1) 283.7; Anal. Calcd for $C_{20}H_{14}N_2$: C, 85.08; H, 5.00; N, 9.92. Found: C, 84.98; H, 4.90; N, 9.81.

6-Methyl-2,3-diphenylquinoxaline (3b): white solid; mp 120-122 ^{o}C; IR (solid, KBr, ν_{max}, cm^{-1}) 3055, 2921, 2851, 1442, 1344, 1058, 766, 694, 544; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 2.60 (3H, s, Ar-CH_3), 7.33 (5H, s, 5CH aromatic), 7.50-7.51 (4H, d, $^{3}J_{HH}$ 4.8 Hz, 4CH aromatic), 7.67 (2H, d, $^{3}J_{HH}$ 8.4 Hz, 2CH

aromatic), 8.05 (2H, d, $^{3}J_{HH}$ 8.5 Hz, 2CH aromatic); ^{13}C NMR ($CDCl_3$, 75 MHz) δ_C 21.89 (CH_3 aryl), 128.00, 128.19, 128.59, 128.65, 128.81 (5CH x 10 aromatic), 129.81 (CH x 4 aromatic), 139.21, 139.68, 140.43, 141.27 (CH x 4 aromatic), 152.53, 153.28 (CH x 2 aromatic); LC-MS *m/z* (M+1) 297.3; Anal. Calcd for $C_{21}H_{16}N_2$: C, 85.11; H, 5.44; N, 9.4. Found: C, 85.01; H, 5.31; N, 9.34.

6,7-Dimethyl-2,3-diphenylquinoxaline (3c): white solid; mp 170-172 °C; IR (solid, KBr, ν_{max}, cm^{-1}) 2972, 2917, 2849, 1444, 1334, 1022, 870, 699, 555; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 2.51 (6H, s, 2 x Ar-CH_3), 7.30 (2H, dd, $^{3}J_{HH}$ 7.8 Hz, 3.2 Hz, 2CH aromatic), 7.33 (4H, d, $^{4}J_{HH}$ 1.7 Hz, 4CH aromatic), 7.50-7.47 (2H, m, 2CH aromatic), 7.51 (1H, d, $^{4}J_{HH}$ 1.9 Hz, CH aromatic), 7.92 (2H, s, 2CH aromatic); ^{13}C NMR ($CDCl_3$, 75 MHz) δ_C 20.41 (2CH_3 x 2 aryl), 128.17, 128.50, 129.83 (9CH x 9 aromatic), 129.81 (1CH aromatic), 139.38, 140.21, 140.49 (9CH x 9 aromatic), 152.43 (1CH x aromatic); LC-MS *m/z* (M+1) 311.5; Anal. Calcd for $C_{22}H_{18}N_2$: C, 85.13; H, 5.85; N, 9.03. Found: C, 84.99; H, 5.71; N, 8.95.

6-Chloro-2,3-diphenylquinoxaline (3d): yellow solid; mp 119-121 °C; IR (solid, KBr, ν_{max}, cm^{-1}) 3054, 1592, 1551, 1340, 1067, 768, 691, 588; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.32-7.37 (6H, m, 6CH aromatic), 7.50 (4H, d, $^{4}J_{HH}$ 1.6 Hz, 4CH aromatic), 7.68 (1H, d, $^{4}J_{HH}$ 2.3 Hz, CH aromatic), 8.08 (1H, d, $^{3}J_{HH}$ 8.9 Hz, CH aromatic), 8.15 (1H, d, $^{4}J_{HH}$ 2.3 Hz, CH aromatic); ^{13}C NMR ($CDCl_3$, 75 MHz) δ_C 128.03, 128.27 (5CH x 5 aromatic), 128.98, 129.06 (2CH x 2 aromatic), 129.77, 129.81 (4CH x 4 aromatic), 130.38, 130.89 (2CH x 2 aromatic), 135.59, 138.61, 138.68, 139.66, 141.43 (5CH x 5 aromatic), 153.55, 154.22 (2CH x 2 aromatic); LC-MS *m/z* (M+1) 317.6; Anal. Calcd for $C_{20}H_{13}ClN_2$: C, 75.83; H, 4.14; Cl, 11.19; N, 8.84. Found: C, 75.71; H, 3.99; Cl, 11.03, N, 8.73.

6,7-Dichloro-2,3-diphenylquinoxaline (3e): white solid; mp 141-143 °C; IR (solid, KBr, ν_{max}, cm^{-1}) 3055, 1438 1336, 1188, 765, 691, 598; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.30-7.41 (6H, m, 6CH aromatic), 7.48 (2H, d, $^{4}J_{HH}$ 1.8 Hz, 2CH aromatic), 7.50 (2H, d, $^{4}J_{HH}$ 1.4 Hz, 2CH aromatic), 8.26 (2H, s, 2CH aromatic); ^{13}C NMR ($CDCl_3$, 75 MHz) δ_C 128.32 (4CH x 4 aromatic), 129.25 (2CH x 2 aromatic), 129.78 (6CH x 6 aromatic), 134.36 (2CH x 2 aromatic), 138.36 (2CH x 2 aromatic), 139.90(2CH x 2 aromatic), 154.43 (2CH x 2 aromatic); LC-MS *m/z* (M+1) 351.5; Anal. Calcd for $C_{20}H_{12}Cl_2N_2$: C, 68.39; H, 3.44; Cl, 20.19; N, 7.98. Found: C, 68.28; H, 3.55; Cl, 20.11, N, 7.89.

6-Nitro-2,3-diphenylquinoxaline (3f): yellow solid; mp 193-195 °C; IR (solid, KBr, ν_{max}, cm^{-1}) 3089, 3052, 2339, 1641, 1514, 1335, 905, 761, 693, 539; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.34-7.37 (2H, m, 2CH aromatic), 7.42 (4H, d, $^{3}J_{HH}$ 13.0 Hz, 4CH aromatic), 7.54-7.58 (3H, m, 3CH aromatic), 8.28 (1H, d, $^{3}J_{HH}$ 9.2 Hz, CH aromatic), 8.49 (1H, d, $^{4}J_{HH}$ 2.5 Hz, CH aromatic), 8.52 (1H, d, $^{4}J_{HH}$ 2.5 Hz, CH aromatic), 9.06 (1H, d, $^{4}J_{HH}$ 2.4 Hz, CH aromatic); ^{13}C NMR ($CDCl_3$, 75 MHz) δ_C 123.27 (2CH x 2 aromatic), 129.59 (2CH x 2 aromatic), 128.45 (4CH x 4 aromatic), 129.62, 129.82, 129.89 (3CH x 3 aromatic), 130.74 (1CH x aromatic), 138.01, 138.07 (2CH x 2 aromatic), 139.94, 140.53 (2CH x 2 aromatic), 143.55 (1CH x aromatic), 147.84 (1CH x aromatic), 155.66 (1CH x aromatic), 156.28 (1CH x

aromatic); LC-MS *m/z* (M+1) 328.8; Anal. Calcd for $C_{20}H_{13}N_3O_2$: C, 73.38; H, 4.00; N, 12.84. Found: C, 73.21; H, 3.91; N, 12.75.

6-Bromo-2,3-diphenylquinoxaline (3g): brown solid; mp 121-123 °C; IR (solid, KBr, ν_{max}, cm^{-1}) 3055, 1591, 1444, 1337, 1060, 975, 767, 690; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.28-7.40 (6H, m, 6CH aromatic), 7.49 (2H, d, $^4J_{HH}$ 1.9 Hz, 2CH aromatic), 7.52 (2H, d, $^4J_{HH}$ 1.4 Hz, 2CH aromatic), 7.81 (1H, dd, $^3J_{HH}$ 8.9, 2.1CH aromatic), 8.02 (1H, d, $^3J_{HH}$ 8.9 Hz, CH aromatic), 8.34 (1H, d, $^4J_{HH}$ 2.1 Hz, CH aromatic); ^{13}C NMR ($CDCl_3$, 75 MHz) δ_C 123.75 (1CH x aromatic), 128.24, 128.26 (4CH x 4 aromatic), 128.96, 128.98, 129.05 (3CH x 3 aromatic), 129.74, 129.80, 129.84 (4CH x 4 aromatic), 130.44 (1CH x aromatic), 131.40 (1CH x aromatic), 133.39 (1CH x aromatic), 134.80 (1CH x aromatic), 138.56, 138.67 (2CH x 2 aromatic), 139.86 (1CH x aromatic), 141.68 (1CH x aromatic), 153.64 (1CH x aromatic), 154.13 (1CH x aromatic); LC-MS *m/z* (M+1) 361.7; Anal. Calcd for $C_{20}H_{13}BrN_2$: C, 66.50; H, 3.63; Br, 22.12; N, 7.75. Found: C, 66.39; H, 3.54; Br, 22.01, N, 7.64.

2,3-Diphenylquinoxaline-6-carboxylic acid (3h): light brown solid; mp 291-293 °C; IR (solid, KBr, ν_{max}, cm^{-1}) 3310, 2539, 1728, 1683, 1425, 1303, 1056, 913, 692, 538; ^{1}H NMR (300 MHz, DMSO-d_6): δ_H 7.36 (6H, d, $^3J_{HH}$ 7.3 Hz, 6CH aromatic), 7.52 (4H, d, $^3J_{HH}$ 6.4 Hz, 4CH aromatic), 8.16 (1H, d, $^3J_{HH}$ 8.06 Hz, CH aromatic), 8.33 (1H, d, $^3J_{HH}$ 8.6 Hz, CH aromatic), 8.77 (1H, s, CH aromatic); ^{13}C NMR ($CDCl_3$, 75 MHz) δ_C 129.98 (5CH x 5 aromatic), 128.23, 128.93, 128.98 (3CH x 3 aromatic), 129.53, 129.64, 129.68 (4CH x 4 aromatic), 130.87 (1CH x aromatic), 132.57 (1CH x aromatic), 138.38 (2CH x 2 aromatic), 139.58 (1CH x aromatic), 142.37 (1CH x aromatic), 153.77 (1CH x aromatic), 154.36 (1CH x aromatic), 166.85 (1CH x aromatic); LC-MS *m/z* (M+1) 327.5; Anal. Calcd for $C_{21}H_{14}N_2O_2$: C, 77.29; H, 4.32; N, 8.58. Found: C, 77.18; H, 4.21; N, 8.49.

2,3-Di(pyridin-2-yl)quinoxaline (3o): light brown solid; mp 185-186 °C; IR (solid, KBr, ν_{max}, cm^{-1}) 3057, 3005, 1685, 1587, 1350, 1074, 995, 788, 545; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.22-7.27 (2H, m, 2CH aromatic), 7.79-7.84 (4H, m, 4CH aromatic), 7.96 (2H, d, $^3J_{HH}$ 7.8 Hz, 2CH aromatic), 8.24 (2H, d, $^3J_{HH}$ 4.8 Hz, 2CH aromatic), 8.39 (2H, d, $^3J_{HH}$ 4.8 Hz, 2CH aromatic); ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C: 122.98 (3CH x 3 aromatic), 124.25 (3CH x 3 aromatic), 129.39 (3CH x 3 aromatic), 130.50 (2CH x 2 aromatic), 136.64 (2CH x 2 aromatic), 141.158 (1CH x aromatic), 148.61 (2CH x 2 aromatic), 152.47 (1CH x aromatic), 157.41 (1CH x aromatic); LC-MS *m/z* (M+1) 385.1; Anal. Calcd for $C_{18}H_{12}N_4$: C, 76.04; H, 4.25; N, 19.71. Found: C, 75.92; H, 4.17; N, 19.62. C, 76.04; H, 4.25; N, 19.71

2,3-Bis(4-bromophenyl)quinoxaline (3p): yellow solid; mp 193-194 °C; IR (solid, KBr, ν_{max}, cm^{-1}) 3728, 3062, 1661, 1567, 1481, 1326, 1172, 975, 757, 612, 587; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.39 (1H, d, $^4J_{HH}$ 1.9 Hz, CH aromatic), 7.41 (2H, d, $^4J_{HH}$ 2.0 Hz, 2CH aromatic), 7.49 (2H, d, $^4J_{HH}$ 2.0 Hz, 2CH aromatic), 7.52 (2H, d, $^4J_{HH}$ 1.9 Hz, 2CH aromatic), 7.83-7.77 (2H, m, 2CH aromatic), 8.15 (2H, dd, J= 6.4, 3.4 Hz, 2CH aromatic); ^{13}C NMR ($CDCl_3$, 75 MHz) δ_C 123.70 (1CH x aromatic), 129.20 (2CH x 2

aromatic), 130.40 (2CH x 2 aromatic), 131.27, 131.43, 131.51, 131.68, (11CH x 11 aromatic), 132.49 (1CH x aromatic), 137.68 (1CH x aromatic), 141.24 (1CH x aromatic), 151.90 (1CH x aromatic); LC-MS *m/z* (M+1) 441.3; Anal. Calcd for $C_{20}H_{12}Br_2N_2$: C, 54.58; H, 2.75; Br, 36.31; N, 6.36. Found: C, 54.49; H, 2.66; Br, 36.22N, 6.25.

2,3-Di-*p*-tolylquinoxaline (3q): white solid; mp 130-132 ^oC; IR (solid, KBr, ν_{max}, cm^{-1}) 3030, 2919, 2851, 1909, 1661, 1585, 1342, 1184, 1247, 976, 818, 759, 545; ^1H NMR (300 MHz, $CDCl_3$) δ_H 2.36 (6H, s, 6CH Ar-CH_3), 7.14 (4H, d, $^3J_{HH}$ 8.0 Hz, 4CH aromatic), 7.43 (4H, d, $^3J_{HH}$ 8.0 Hz, 4CH aromatic), 7.69-7.75 (2H, m, 2CH aromatic), 8.13-8.17 (2H, m, 2CH aromatic); ^{13}C NMR ($CDCl_3$, 75 MHz) δ_C 21.33 (2CH x 2 aromatic), 128.96, 129.10 (7CH x 7 aromatic), 129.63, 129.72 (8CH x 8 aromatic), 136.38 (1CH x aromatic), 138.72 (1CH x aromatic), 141.14 (1CH x aromatic), 153.46 (1CH x aromatic); LC-MS *m/z* (M+1) 311.5; Anal. Calcd for $C_{22}H_{18}N_2$: C, 85.13; H, 5.85; N, 9.03. Found: C, 85.01; H, 4.76; N, 5.74.

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REFERENCES

1. (a) M. Badran, K. Abouzid, and M. Hussein, *Arch. Pharm. Res*., 2003, **26**, 107; (b) J. Guillon, S. Moreau, E. Mouray, V. Sinou, I. Forfar, B. Fabre, V. Desplat, P. Millet, D. Parzy, C. Jarry, and P. Grellier, *Bioorg. Med. Chem*., 2008, **16**, 9133; (c) M. Shibinskaya, S. Lyakhov, A. Mazepa, S. Andronati, A. Turov, N. Zholobak, and N. Spivak, *Eur. J. Chem*., 2010, **45**, 1237; (d) T. Settypalli, V. Chunduri, A. Maddineni, N. Begari, R. Allagadda, P. Kotha, and A. Chippada, *New J. Chem*., 2019, **43**, 15435; (e) S. Patel, B. Patel, C. Pannecouque, and H. Bhatt, *Eur. J. Med. Chem*., 2016, **117**, 230; (f) T. Kaushal, G. Srivastava, A. Sharma, and A. Negi, *Bioorg. Med. Chem*., 2019, **27**, 16.
2. (a) D. Chang, H. Lee, J. Kim, S. Park, S. Park, L. Dai, and J. Beak, *Org. Lett.*, 2011, **13**, 3880; (b) N. Sonawane and D. Rangnekar, *J. Heterocycl. Chem.*, 2002, **39**, 303.
3. (a) D. Reinhardt, F. Ilgen, D. Kralisch, B. Konig, and G. Kreisel, *Green Chem*., 2008, **10**, 1170; (b) C. Chen, Y. Wei, J. Lin, M. Moturu, W. Chao, Y. Tao, and C. Chien, *J. Am. Chem. Soc*., 2006, **128**, 34; (c) A. Danel, E. Gondek, and I. Kityk, *Opt. Mater*., 2009, **32**, 267; (d) C. Chen, J. Lin, M. Moturu, Y. Lin, W. Yi, Y. Tao, and C. Chien, *Chem. Commun*., 2005, **31**, 3980; (e) A. Shaikh, B. Sharma, S. Chacko, and R. Kamble, *RSC Adv*., 2016, **6**, 60084.
4. D. Govindarajan, C. Chatterjee, G. Shakambari, P. Varalakshmi, K. Jayakumar, and A. Balasubramaniem, *Biocat. Agric. Biotechnol*., 2019, **17**, 702.

5. D. J. Brown, E. C. Taylor, P. Wipf, and J. A. Ellman, 'The Chemistry of Heterocyclic Compounds, Quinoxalines: Supplement II', John Wiley & Sons, New York, 2004.
6. (a) M. Heravi, S. Taheri, K. Bakhtiari, and H. Oskooie, *Catal. Commun*., 2006, **8**, 211; (b) A. Hasaninejad, A. Zare, M. Zolfigol, and M. Shekouhy, *Synth. Commun*., 2009, **39**, 569; (c) J. Hou, Y. Liu, and Z. Zhang, *J. Heterocycl. Chem*., 2010, **47**, 703; (d) D. Shi, G. Dou, S. Ni, J. Shi, and X. Li, *J. Heterocycl. Chem*., 2008, **45**, 1797; (e) S. More, M. Sastry, and C. Yao, *Green Chem*., 2006, **8**, 91; (f) J. Sangshetti, N. Kokare, and D. Shinde, *Russ. J. Org. Chem*., 2009, **45**, 1116; (g) H. Darabi, K. Aghapoor, F. Mohsenzadeh, F. Taala, N. Asadollahnejad, and A. Badiei, *Catal. Lett*., 2009, **133**, 84; (h) P. Hazarika, P. Gogoi, and D. Konwar, *Synth. Commun*., 2007, **37**, 3447; (i) J. Cai, J. Zou, X. Pan, and W. Zhang, *Tetrahedron Lett*., 2008, **49**, 7386; (j) R. Robinson and R. Taylor, *Synlett*, 2005, 1003; (k) M. Heravi, K. Bakhtiari, H. Oskooie, and S. Taheri, *Heteroat. Chem*., 2008, **19**, 218; (l) P. Raghuveerachary and N. Devanna, *Asian J. Chem*., 2011, **23**, 1628; (m) S. Kotharkar and D. Shinde, *Bull. Korean Chem. Soc*., 2006, **27**, 1466; (n) A. Vidal-Albalat, S. Rodriguez, and F. Gonzalez, *Org. Lett*., 2014, **16**, 1752.
7. (a) X. Zhang, J. Wang, and L. Bai, *Synth. Commun*., 2011, **41**, 2053; (b) H. Chavan, L. Adsul, and B. Bandgar, *J. Chem. Sci*., 2011, **123**, 477; (c) C. Qi, H. Jiang, L. Huang, Z. Chen, and H. Chen, *Synthesis*, 2011, 387; (d) M. Jafarpour, A. Rezaeifard, and M. Danehchin, *Appl. Catal. A*., 2011, **394**, 48; (e) A. Kumbhar, S. Kamble, M. Barge, G. Rashinkar, and R. Salunkhe, *Tetrahedron Lett*., 2012, **53**, 2756; (f) G. Meshram, S. Deshpande, V. Vala, and P. Wagh, *Eur. J. Chem*., 2013, **4**, 422; (g) A. Kamal, S. Babu, A. Hussaini, R. Mahesh, and A. Alarifi, *Tetrahedron Lett*., 2015, **56**, 2803; (h) Z. Bhutia, G. Prasannakumar, A. Das, M. Biswas, A. Chatterjee, and M. Banerjee, *ChemistrySelect*, 2017, **2**, 1183.
8. J. Twibanire and T. B. Grindley, *Org. Lett*., 2011, **13**, 2988.
9. (a) C. Montalbetti and V. Falque, *Tetrahedron*, 2005, **61**, 10827; (b) L. Dubey and I. Dubey, *Ukrainica Bioorganica Acta*, 2005, **1**, 13.
10. F. Albericio and A. Faham, *Org. Process Res. Dev*., 2018, **22**, 760.
11. J. Habermann and H. Kunz, *Tetrahedron Lett*., 1998, **39**, 265.