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Note

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Nickel Catalyzed Direct Synthesis of Quinoxalines from 2-Nitroanilines and Vicinal Diols: Identifying Nature of the Active Catalyst

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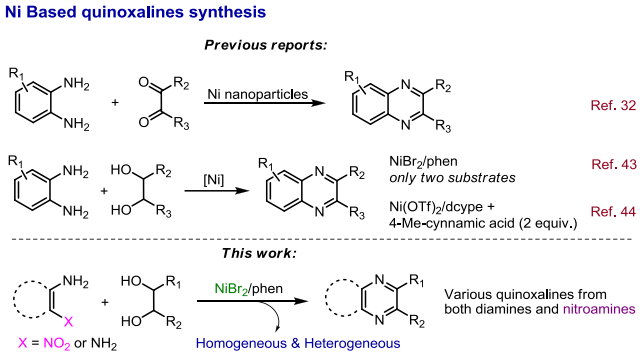
ABSTRACT: Inexpensive and simple $NiBr_2$/1,10-phenanthroline system catalyzed synthesis of a series of quinoxalines from both 2-nitroanilines and 1,2-diamines is demonstrated. The reusability test for this system was performed up to 7th cycle which afforded good yields of the desired product without losing its reactivity significantly. Notably, during the catalytic reaction, formation of heterogeneous Ni-particle was observed which was characterized by PXRD, XPS and TEM techniques.

N-Heterocycles are important bio-active and naturally occurring molecules which have wide range of applications in pharmaceutical, agricultural and material chemistry.[1-4] Multistep synthetic processes, inadequate starting materials and generation of stoichiometric wastages are the major disadvantages for the synthesis of these N-heterocyclic molecules following the classical metal free cyclization or metal catalyzed multicomponent coupling reactions.[5-7] In contrast, hydrogen borrowing methodology or dehydrogenative coupling process are the most elegant sustainable methods for the production of such heterocycles via construction of C-C or C-N bonds.[8,9] Generally, these atom-economical processes circumvent multistep synthetic routes and use of excess reagents. Additionally, water or hydrogen are produced as by-product which makes these protocols environmentally benign and sustainable. Inspired by the pioneering work carried out by Williams,[8,10-13] Beller,[14-16] Milstein,[17-19] Kempe,[20-22] several borrowing hydrogen and dehydrogenative coupling methodologies were developed utilizing alcohols for the synthesis of various organic molecules.[23-26].

Quinoxaline derivatives are important structural motifs present in natural products, pharmacological and biologically active molecules.[27-29] Quinoxalines are widely used in therapeutic drugs, agrochemical, material chemistry and industries.[30,31] Traditional methods for the synthesis of quinoxalines mostly suffered from limited functional group tolerance, generation of salt wastes and in few cases, the requirement of excessive additives. The coupling between 1,2-diketones and 1,2-diamines for the synthesis of quinoxalines is well represented in literature.[32,33] However, utilization of bio-derived readily available alcohols as a coupling partner is one of the attractive routes. For this purpose, various transition metal based homogeneous and heterogeneous catalysts have been explored. Among them, precious 4d and 5d metal based catalysts are mostly common.[34-38] First row transition metal catalyzed few reports are known for the synthesis of quinoxaline derivatives.[39-42] During the preparation of this manuscript, $NiBr_2$/phen catalyzed synthesis of benzimidazoles and quinoxalines was revealed.[43] However, substrate scope for the synthesis of quinoxalines was limited to only two derivatives. Remarkably, Tang *et al*. recently reported a $Ni(OTf)_2$ and 1,2-bis(dicyclohexylphosphino)ethane (dcype) catalyzed synthesis of various N-heterocycles such as tetrahydroquinoxalines, tetrahydro-β-carbolines, piperidines, quinoxalines, etc. However, for this system, additional two equivalents of 4-methyl cinnamic acid was required for the synthesis of quinoxalines.[44]

Scheme 1. Nickel Catalyzed Synthesis of Quinoxalines



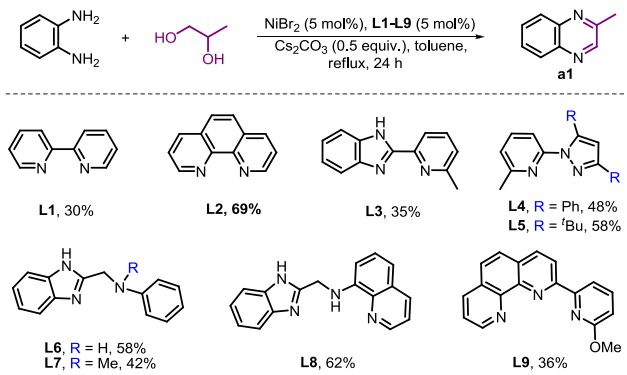
Recently, nickel catalyzed hydrogen borrowing and dehydrogenative coupling strategies have become attractive for sustainable and environmentally benign processes.[24,45] Utilizing these protocols, nickel catalyzed synthesis of pyrroles, pyridines, quinazolin-4(3H)-ones, quinolines, C/N-alkylated products, etc. are well-documented in literature.[46-51] Although, most of the cases, homogeneous Ni complexes were utilized as the pre-catalysts; however, fate of the active catalysts or the materials formed after the catalytic cycle is unknown. To design an efficient catalytic system and to understand the reaction mechanism, identifying the nature of active catalyst (homogeneous, heterogeneous, etc.) during and after the reaction is essential.[52-56]

Herein, we reveal a simple nickel based catalytic system which produced a variety of substituted quinoxalines from dehydrogenative coupling of vicinal diols with 1,2-diamines and 2-nitroaniline derivatives (Scheme **1**).

To optimize the reaction parameters for synthesis of quinoxaline derivatives, initially, 1,2-diaminobenzene and 1,2-propanediol were selected as model substrates. For this purpose, several bidentate and tridentate nitrogen based ligands (5 mol%) in combination with anhydrous $NiBr_2$ (5 mol%) were

screened in presence of 0.5 equiv. Cs_2CO_3 in toluene at oil bath temperature 150 °C (Table **1**). Among all the ligands,

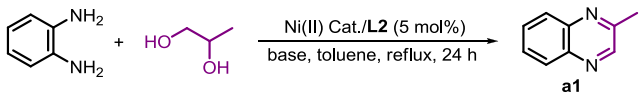
Table 1. Ligand Screening for the Synthesis of Quinoxalines[a]



[a]Reaction conditions: 1,2-diaminobenzene (0.5 mmol), 1,2-propanediol (1.0 mmol), toluene (2 mL), refluxed at 150 °C (oil bath temperature), GC yield (*n*-dodecane was used as internal standard).

1,10-phenanthroline (**L2**) displayed the best result, yielding 69% of **a1**. After getting the optimized ligand system, other common nickel precursors such as $NiCl_2$, $Ni(OAc)_2.4H_2O$, $Ni(COD)_2$, $NiBr_2$(DME) and $NiCl_2$(DME) were screened which showed moderate yields, indicating $NiBr_2$/phen was the best catalytic system for this coupling reaction (Table **2**, entries **1-6**). Increasing the amount of ligand did not alter the product formation significantly; 74% **a1** was formed in presence of 7.5 mol% of **L2** under the reaction conditions (Table **2**, entry **7**). Afterward, various bases and their amount and other reaction parameters were tested in presence of $NiBr_2$/phen system (Table **2**, entries **8-14**). Finally, it was observed that 1:2 ratio of 1,2-diaminobenzene and 1,2-propanediol in presence of 5 mol%

Table 2. Optimization of the Reaction Parameters[a]



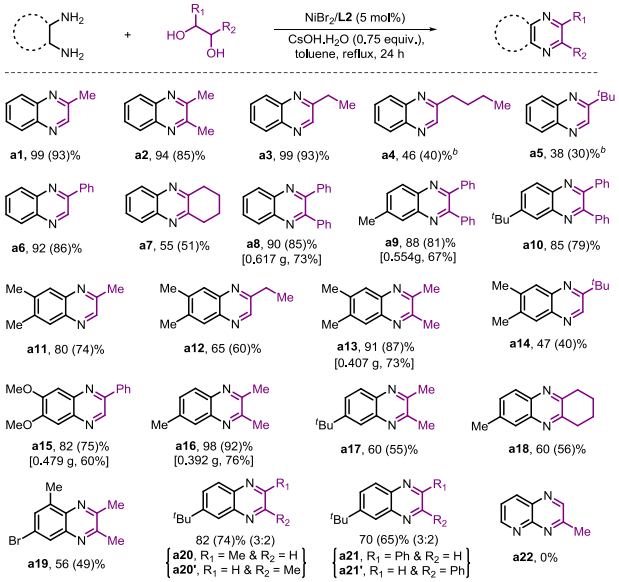
Entry	[Ni] (5 mol%)	Base (0.5 equiv.)	Yield (%)
1	$NiCl_2$	Cs_2CO_3	26
2	$Ni(OAc)_2.4H_2O$	Cs_2CO_3	27
3	$NiBr_2$	Cs_2CO_3	69
4	$Ni(COD)_2$	Cs_2CO_3	61
5	$NiCl_2$(DME)	Cs_2CO_3	60
6	$NiBr_2$(DME)	Cs_2CO_3	65
7[b]	$NiBr_2$	Cs_2CO_3	74
8	$NiBr_2$	KO^{t}Bu	50
9	$NiBr_2$	KOH	60
10	$NiBr_2$	$CsOH.H_2O$	76
11[c]	$NiBr_2$	$CsOH.H_2O$	99
12[d]	$NiBr_2$	$CsOH.H_2O$	78
13[e]	$NiBr_2$	$CsOH.H_2O$	70
14[f]	$NiBr_2$	$CsOH.H_2O$	24
15	-	$CsOH.H_2O$	3

[a]Reaction conditions: 1,2-diaminobenzene (0.5 mmol), 1,2-propanediol (1.0 mmol), $NiBr_2$/**L2** (5 mol%), toluene (2 mL), refluxed at 150 °C (oil bath temperature), GC yield; [b]**L2** (7.5 mol%); [c]$CsOH.H_2O$ (0.75 equiv.); [d]1,2-propanediol (0.75 mmol), $CsOH.H_2O$ (0.75 equiv.); [e]heated at 140 °C; [f]absence of ligand **L2**.

$NiBr_2$/phen and 0.75 equiv. $CsOH.H_2O$ in toluene at 150 °C was the optimal reaction conditions for this dehydrogenative coupling reaction.

With this optimized reaction conditions, next, we explored the scope of the coupling reactions for the synthesis of various substituted quinoxaline derivatives. Reaction of 1,2-diaminobenzene with various unsymmetrical vicinal diols furnished up to 93% isolated yields of the expected quinoxalines (Table **3**, **a1** and **a3-a6**). However, for 1,2-hexanediol and 3,3-dimethylbutane-1,2-diol slightly higher amount of catalyst and 1,2-diol were required to achieve satisfactory yields of the corresponding quinoxalines (Table **3**, **a4** and **a5**). On the other hand, substituted 1,2-diamines with various 1,2-diols also showed moderate to excellent yields. Notably, 1-phenylethanediol and 1,2-diphenylethane-1,2-diol with various 1,2-diamines furnished excellent yields of the desired quinoxalines; probably dehydrogenation of these two diols was relatively more easier than the aliphatic vicinal diols. Both unsymmetrical 1,2-diamines and 1,2-diols produced two regio-isomers with isomeric ratio of 3:2, analyzed by ^{1}H NMR spectroscopy (Table **3**, **a20** and **a21**). Unfortunately, 2,3-diaminopyridine did not lead to the formation of the desired product (Table **3**, **a22**).

Table 3. Ni-Catalyzed Synthesis of Quinoxalines: Scope of 1,2-Diamines[a]

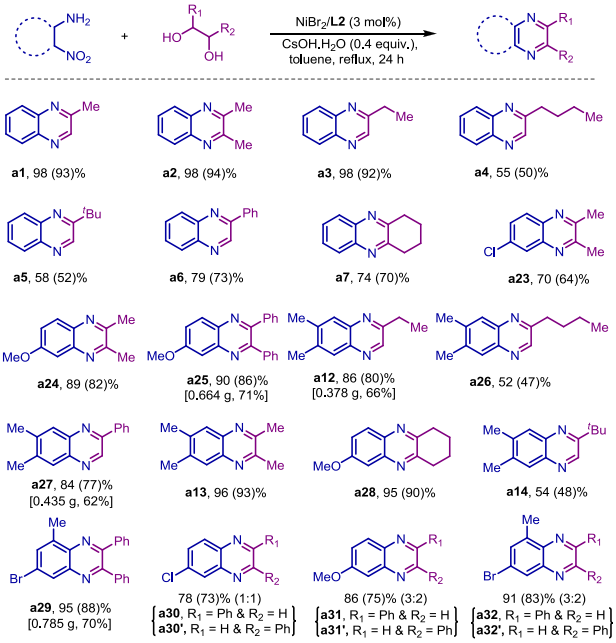


[a]Reaction conditions: 1,2-diamine (0.5 mmol), 1,2-diol (1.0 mmol), toluene (2 mL), refluxed at 150 °C (oil bath temperature), GC yields (isolated yields in parenthesis), preparative scale reactions in third bracket. [b]$NiBr_2$/ **L2** (7.5 mol%), 1,2-diol (1.5 mmol).

Afterward, we explored the scope of this catalytic system for synthesis of quinoxalines from various 2-nitroanilines and vicinal diols. In this scenario, 2-nitroanilines and 1,2-diols acted as hydrogen acceptor and hydrogen donor respectively. This environmental friendly protocol did not require any additional reducing agents for reduction of the nitro group. For this transformation, few other transition metal catalyzed protocols are known in literature.[34,40,57] To establish this methodology, we optimized the reaction parameters by selecting 2-nitroaniline

and 2,3-butanediol as coupling partners (SI, Table **S2**). It was observed that 2-nitroaniline and 2,3-butanediol in 1:3 ratio in presence of 3 mol% $NiBr_2$/**L2** with 0.4 equiv. $CsOH.H_2O$ delivered the best result which produced 98% yield of **a2** (GC yield). Next, we examined the scope of this methodology with various 2-nitroaniline derivatives and 1,2-diols (Table **4**).

Table 4 Ni-Catalyzed Synthesis of Quinoxalines: Scope of 2-Nitroanilines[a]

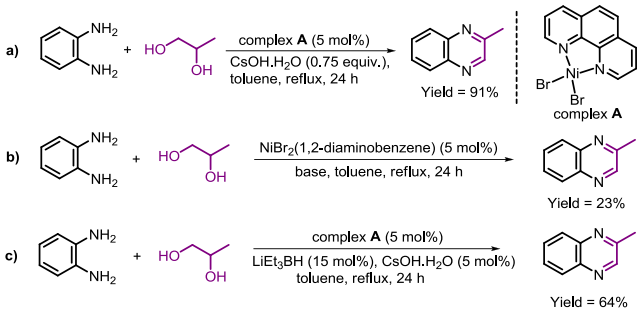


[a]Reaction conditions: 2-nitroarylamine (0.5 mmol), 1,2-diol (1.5 mmol), toluene (2 mL), reflux at 150 °C (oil bath temperature), GC yields (isolated yields in parenthesis), preparative scale reactions in third bracket.

2-Nitroanilines with different symmetrical and also with unsymmetrical vicinal diols furnished good to excellent isolated yields of the quinoxaline products (Table **4**, **a1**-**a7**), while 1,2-hexanediol and 3,3-dimethylbutane-1,2-diol afforded moderate yields (Table **4**, **a4** and **a5**). Different substituted 2-nitroanilines also provided moderate to excellent yields with various vicinal diols. Utilizing this methodology, two regio-isomers 6-chloro-2-phenylquinoxaline and 7-chloro-2-phenylquinoxaline were produced in 1:1 ratio with overall 73% isolated yields by the coupling reaction of 4-chloro-2-nitroaniline and 1-phenylethane-1,2-diol (Table **4**, **a30**). Similarly, the reactions of 6-methoxy-2-phenylquinoxaline and 6-bromo-8-methyl-2-phenylquinoxaline with 1-phenylethane-1,2-diol exhibited a mixture of two regio-isomers in good yields (Table **4**, **a31** and **a32**).

To test the practical applicability of this methodology, we carried out preparative scale reaction for the synthesis of several quinoxaline derivatives from both 1,2-diamine and 2-nitroaniline derivatives which resulted moderate to good isolated yields of the corresponding products (Table **3** and **4**). Synthesis of important drug molecules from the readily available starting materials is highly desirable. Gratifyingly, gram scale synthesis of EGFR tyrosine kinase inhibitor (**a27**), tyrphostin AG 1296 (**a15**) and anti-HIV derivative(**a8**) were performed which furnished up to 73% isolated yields (Table **3** and **4**).[58,59]

Scheme 2. Control Experiments



After getting exciting catalytic activity of this nickel system, next we carried out few control experiments for the mechanistic insight. During the coupling of 1,2-diaminobenzene with 1,2-propanediol, the initial concentration of 1,2-diaminobenzene was high and it can also act as a bidentate ligand. Hence, formation of (1,2-diaminobenzene)$NiBr_2$ during the reaction was quite possible which can behave as the pre-catalyst instead of the *in-situ* generated (phen)$NiBr_2$ (complex **A**). To resolve this issue, we separately prepared (1,2-diaminobenzene)$NiBr_2$ and complex **A** and tested their catalytic activity for 1,2-diaminobenzene and 1,2-propanediol coupling reaction under the optimized conditions (Scheme **2a** and **2b**).[60,61] Interestingly, for synthesis of **a1** from 1,2-diaminobenzene, complex **A** provided excellent yield (91% GC yield) while (1,2-diaminobenzene)$NiBr_2$ produced only 23% yield which was very similar to the result obtained with only $NiBr_2$ in absence of ligand **L2** (Table **2**, entry **14**). This observation confirmed that complex **A** was generated *in-situ* at the beginning of the reaction which performed as the pre-catalyst during the course of this reaction. The reaction of 2-nitroaniline under standard conditions provided slighly lower yield of **a2** in presence of externally added radical scavengers; indicating this Ni system probably did not follow the radical pathway (SI S5).

Additionally, using complex **A** (5 mol%), $LiBEt_3H$ (15 mol%) and 5 mol% $CsOH.H_2O$ under the standard conditions furnished 64% yield of **a1** from 1,2-diaminobenzene (conv. 90%, hydrogenated product of **a1** 26%), indicating dehydrogenation of diol was occurred via formation of Ni-H species (Scheme **2c**). However, all our attempts toward isolation and characterization of the Ni-H species were unsuccessful.

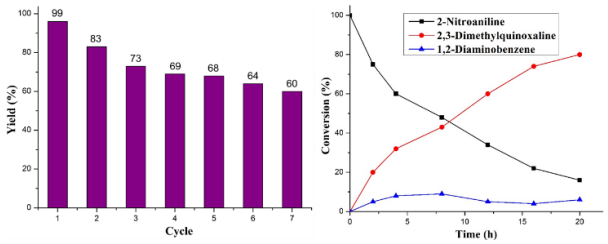


Figure 1. a) Reusability test of Ni-catalyzed synthesis of **a1**; b) Time dependent product distribution study.

Interestingly, this catalytic system did not lose its catalytic activity significantly even after 7th catalytic cycle for synthesis of **a1** from 1,2-diaminobenzene. This demonstrated the reusability and practical applicability of this protocol (Figure **1a**).

In literature, several reports are known for the dehydrogenative coupling reactions of alcohols using phosphine free NiX_2/L (L = nitrogen containing ligands e.g. phen, TMEDA, etc.) system where Ni-H species was proposed

as the active species.[62-67] However, nature of the active catalyst was not clear; with many systems catalytic cycle with homogeneous Ni-complexes were proposed. To check the homogeneity of this Ni system, mercury poisoning experiment was carried out by using 100 equiv. of Hg^0 for the coupling of 1,2-diaminobenzene and 1,2-propanediol, which resulted 71% of **a1** product. This study indicated that this catalytic system was not fully homogeneous and some heterogeneous Ni particles may formed during the reaction. Notably, with our system after the catalytic reaction (24 h), we observed a yellow color solution along with a small quantity of insoluble black particles in the bottom of the reaction tube which was insoluble in the common organic solvents. In order to identify the insoluble particles, we performed the characterization of this materials using PXRD (powder X-ray diffraction), XPS (X-ray photoelectron spectroscopy) and TEM (transmission electron microscope) techniques. The powder XRD pattern of the material revealed the presence of Ni(0) and Ni(II) nanoparticles with 2θ values at 43.44° and 49.30° for Ni(0) and 42.60° and 63.06° for Ni(II) (Figure **2a**).[68] TEM analysis further confirmed that the material was crystalline in form and the presence of metallic Ni with well-resolved lattice spacing of 0.203 nm for (111) plane of cubic Ni- phase (Figure **2b** & **2c**).[69] XPS analysis also revealed that the presence of metallic Ni in the material. In the Ni2p spectra with the peaks at 854.24 and 871.8 eV suggested the presence of metallic Ni and peaks at 855.86 and 873.6 eV represented NiO (Figure **2d**).[70] After the 1st catalytic cycle, we filtered out the solution under inert atmosphere and separately carried out the same reaction using both the homogeneous solution and heterogeneous materials. Considerable amount of **a1** was formed in both the reactions. This clearly suggested that both heterogeneous and homogeneous Ni-materials were catalytically active and participated in this reaction (SI S6). Notably, non-noble metal based nanoparticles are highly valued for chemical synthesis due to their recyclability.[71-73] Quantification of the amount of Ni present in both homogeneous and heterogeneous phases are currently underway in our laboratory.

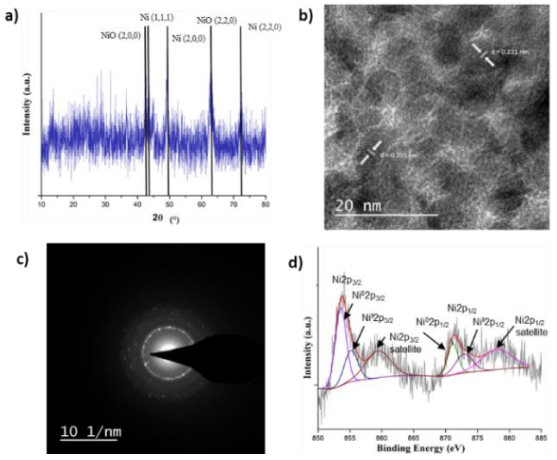


Figure 2. a) PXRD pattern of the materials; b) and c) HRTEM images of the materials; d) XP spectra of Ni2p electrons.

Next, we focused on the mechanism for the synthesis of quinoxalines from 2-nitroanilines and 1,2-diols. From the time dependent product distribution study, a steady formation of 1,2-diamine (maximum 9%) was observed (Figure **1b**). This signified the reaction might preferentially proceed via the 1,2-diamine intermediate (SI, Fig. S3, path **a**). However, imination of amine with ketone followed by the reduction of nitro group and subsequently coupling with carbonyl group generated from 1,2-diol, cannot be ruled out (SI, Fig. S3, path **b**).

In summary, various substituted quinoxaline derivatives were synthesized by applying both hydrogen borrowing and dehydrogenative coupling strategies. Additionally, several biologically active quinoxalines were also effectively synthesized in gram scale. Importantly, utilization of both inexpensive metal precursor ($NiBr_2$) and ligand (1,10-phenanthroline) made this protocol attractive. Remarkably, this catalytic system did not lose its reactivity considerably even after 7th cycle. Notably, formation of some heterogeneous Ni-particles was observed after the reaction. Both the heterogeneous and homogeneous Ni-materials formed during the reaction was found to be catalytically active. The heterogeneous Ni-nanoparticles was characterized by PXRD, XPS and TEM analysis.

EXPERIMENTAL SECTION

General Information: All the experiments were carried out under argon atmosphere either inside the argon filled glove box or using standard Schlenk line technique unless otherwise stated. Glasswares were oven dried prior to use. Solvents were distilled under argon atmosphere according to literature procedures and deoxygenated prior to use. All the commercial reagents, ligands **L1**, **L2** and metal precursors were purchased from Sigma-Aldrich, Alfa-Aesar, Spectrochem, Avra and SD-fine chemical, India. Ligands **L3, L6-L9** were synthesized according to the literature procedures.[40,74-77] All the ^1H and ^{13}C spectra were recorded with $CDCl_3$ and DMSO-D_6 in JEOL Spectrometer. All the GC analysis were performed using Perkein Elmer Clarus 600 and Agilent 7890 B Gas Chromatograph, whereas GC-MS were measured using Agilent 7890 A Gas Chromatograph equipped with Agilent 5890 triple-quadrupole mass system. ESI-MS were recorded on a Waters Micromass Quattro Micro triple-quadrupole mass spectrometer. Chemical states of the heterogeneous material were determined by X-ray photoelectron spectroscopy (XPS) using a PHI 5000 (Versa Probe II, FEI Inc). The morphologies of the material were observed using high resolution transmission electron microscope (HRTEM, FEI Titan G2 60-300 KV). X-ray diffraction (XRD) patterns were obtained by Bruker D8 advance powder X-ray diffractometer using Cu-Kα as X-ray source (1.54 Å). The elemental composition was determined by energy dispersive X-ray spectroscopy (EDX linked to FESEM, Oxford Instrument).

Procedure for Synthesis of 2-(3,5-diphenyl-1*H*-pyrazol-1-yl)-6-methylpyridine (L4): 2-Hydrazinyl-6-methylpyridine was synthesized following the literature procedure.[78] A mixture of 2-hydrazinyl-6-methylpyridine (200 mg, 1.62 mmol) and 1,3-diphenyl-1,3-propanedione (437 mg, 1.95 mmol) were stirred in presence of 1.5 mL glacial acetic acid in 15 mL dry methanol for 16 h. After that the reaction mixture was refluxed for 12 h. The solvent was removed under reduced pressure and the remaining solid was dissolved in dichloromethane. The organic layer was washed with saturated sodium bicarbonate solution, brine solution and finally dried over anhydrous Na_2SO_4. The organic part was removed under reduced pressure. Final product was purified by column chromatography with silica gel using 30% ethyl acetate in hexane. Crystalline white solid was obtained. Yield: 464 mg (92%). ^1H NMR (500 MHz, $CDCl_3$): δ = 7.94 (d, $J_{H,H}$ = 7.15 Hz, 2H), 7.42 (t, $J_{H,H}$ = 7.35 Hz, 2H), 7.35-7.28 (m, 7H), 7.07 (d, $J_{H,H}$ = 7.55 Hz, 1H), 6.82 (s, 1H), 2.39 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 158.1, 152.7, 151.9,

145.3, 138.5, 133.1, 131.3, 129.0, 128.8, 128.3, 128.2, 126.2, 116.1, 106.3, 29.9, 24.2. HRMS (ESI-TOF): calcd. for $C_{21}H_{18}N_3$ $[M+H]^+$: 312.1501; found: 312.1499.

Procedure for Synthesis of 2-(3,5-di-*tert*-butyl-1*H*-pyrazol-1-yl)-6-methylpyridine (L5): A mixture of 2-hydrazinyl-6-methylpyridine (200 mg, 1.62 mmol) and 2,2,6,6-tetramethylheptane-3,5-dione (359 mg, 1.95 mmol) were stirred in presence of 3 mL glacial acetic acid in 15 mL dry methanol for 16 h. After that the reaction mixture was refluxed for 12 h. The solvent was removed under reduced pressure and the remaining solid was dissolved in dichloromethane. The organic layer was washed with saturated sodium bicarbonate solution, brine solution and finally dried over anhydrous Na_2SO_4. The organic part was removed under reduced pressure. Final product was purified by column chromatography with silica gel using 30% ethyl acetate in hexane. Crystalline white solid was obtained. Yield: 378 mg (86%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.67 (t, $J_{H,H}$ = 7.70 Hz, 1H), 7.30 (d, $J_{H,H}$ = 7.85 Hz, 1H), 7.14 (d, $J_{H,H}$ = 7.55 Hz, 1H), 6.04 (s, 1H), 2.55 (s, 3H), 1.31 (s, 9H), 1.26 (s, 9H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 161.4, 157.3, 154.5, 153.5, 138.6, 122.5, 118.9, 101.9, 32.5, 32.2, 30.9, 30.7, 24.1. HRMS (ESI-TOF): calcd. for $C_{17}H_{26}N_3$ $[M+H]^+$: 272.2127; found: 272.2126.

General Procedure for Synthesis of Quinoxalines from 1,2-Diamines and 2-Nitroanilines: 1,2-Diamine/2-nitroaniline (0.5 mmol), vicinal diol (1.0 mmol; 1.5 mmol for 2-nitroaniline), anhydrous $NiBr_2$/**L2** (5 mol%; 3 mol% for 2-nitroaniline), $CsOH.H_2O$ (0.375 mmol; 0.2 mmol for 2-nitroaniline) and 2 mL toluene were taken in a pressure tube and sealed it under argon atmosphere. Then, the tube was placed in a pre-heated oil bath (150 °C) and refluxed for 24 h. The reaction mixture was cooled and 8 mL water was added to the mixture. After that, the organic part was extracted with ethyl acetate (3x8 mL). The combined organic part was dried over anhydrous Na_2SO_4 and solvent was evaporated under reduced pressure. The final product was purified by silica gel column chromatography using ethyl acetate/hexane as eluent.

*2-Methylquinoxaline (**a1**).*[37] Produced following the general procedure as mentioned above by reacting 1,2-diaminobenzene/2-nitroaniline (54.0 mg/69.0 mg, 0.5 mmol, 1 equiv.) and 1,2-propanediol (73.4 μL, 1 mmol, 2 equiv. for diamine; 110.1 μL, 1.5 mmol, 3 equiv. for 2-nitroaniline). The title product was purified by column chromatography with silica gel using 20% EtOAc in hexane as yellow liquid (67 mg; 93% from 1,2-diaminobenzene and 67 mg; 93% from 2-nitroaniline). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.72 (s, 1H), 8.05 (d, $J_{H,H}$ = 7.96 Hz, 1H), 8.00 (d, $J_{H,H}$ = 7.96 Hz, 1H), 7.73-7.65 (m, 2H), 2.75 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 154.0, 146.2, 142.3, 141.2, 130.2, 129.4, 129.1, 128.8, 22.8. GC-MS (M^+): 144.0.

*2,3-Dimethylquinoxaline (**a2**).*[37] Produced following the general procedure as mentioned above by reacting 1,2-diaminobenzene/2-nitroaniline (54.0 mg/69.0 mg, 0.5 mmol, 1 equiv.) and 2,3-butanediol (90.0 μL, 1 mmol, 2 equiv. for diamine; 135.0 μL, 1.5 mmol, 3 equiv. for 2-nitroaniline). The title product was purified by column chromatography with silica gel using 20% EtOAc in hexane as yellow solid (67 mg; 85% from 1,2-diaminobenzene and 74 mg; 94% from 2-nitroaniline). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.96 (dd, $J_{H,H}$ = 6.28, 3.48 Hz, 2H), 7.64 (dd, $J_{H,H}$ = 6.48, 3.60 Hz, 2H), 2.71 (s, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 153.7, 141.3, 129.0, 128.5, 23.4. GC-MS (M^+): 158.0.

*2-Ethylquinoxaline (**a3**).*[37] Produced following the general procedure as mentioned above by reacting 1,2-diaminobenzene/2-nitroaniline (54.0 mg/69.0 mg, 0.5 mmol, 1 equiv.) and 1,2-butanediol (89.5 μL, 1 mmol, 2 equiv. for diamine; 134.3 μL, 1.5 mmol, 3 equiv. for 2-nitroaniline). The title product was purified by column chromatography with silica gel using 20% EtOAc in hexane as yellow liquid (73 mg; 93% from 1,2-diaminobenzene and 72 mg; 92% from 2-nitroaniline). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.74 (s, 1H), 8.06-8.00 (m, 2H), 7.73-7.66 (m, 2H), 3.04 (q, $J_{H,H}$ = 7.52 Hz, 2H), 1.41 (t, $J_{H,H}$ = 7.80 Hz, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 158.7, 145.8, 142.4, 141.4, 130.1, 129.4, 129.1, 129.1, 29.8, 13.6. GC-MS (M^+): 158.1.

*2-Butylquinoxaline (**a4**).*[37] Produced following the general procedure as mentioned above by reacting 1,2-diaminobenzene/2-nitroaniline (54.0 mg/69.0 mg, 0.5 mmol, 1 equiv.) and 1,2-hexanediol (124.2 μL, 1 mmol, 2 equiv. for diamine; 186.3 μL, 1.5 mmol, 3 equiv. for 2-nitroaniline). The title product was purified by column chromatography with silica gel using 20% EtOAc in hexane as yellow dense liquid (37 mg; 40% from 1,2-diaminobenzene and 46.5 mg; 50% from 2-nitroaniline). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.72 (s, 1H), 8.06-8.01 (m, 2H), 7.74-7.66 (m, 2H), 3.00 (t, $J_{H,H}$ = 7.80 Hz, 2H), 1.85-1.78 (m, 2H), 1.49-1.40 (m, 2H), 0.96 (t, $J_{H,H}$ = 7.32 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 157.9, 146.0, 142.4, 141.4, 130.1, 129.4, 129.1, 129.1, 36.4, 31.8, 22.8, 14.1. GC-MS (M^+): 186.1.

*2-tert-Butylquinoxaline (**a5**).*[37] Produced following the general procedure as mentioned above by reacting 1,2-diaminobenzene/2-nitroaniline (54.0 mg/69.0 mg, 0.5 mmol, 1 equiv.) and 3,3-dimethylbutane-1,2-diol (118.1 mg, 1 mmol, 2 equiv. for diamine; 177.1 mg, 1.5 mmol, 3 equiv. for 2-nitroaniline). The title product was purified by column chromatography with silica gel using 20% EtOAc in hexane as yellow dense liquid (28 mg; 30% from 1,2-diaminobenzene and 48 mg; 52% from 2-nitroaniline). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.97 (s, 1H), 8.05-8.02 (m, 2H), 7.73-7.65 (m, 2H), 1.49 (s, 9H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 163.9, 143.6, 141.8, 140.9, 129.8, 129.5, 129.1, 37.4, 29.9. GC-MS (M^+): 186.1.

*2-Phenylquinoxaline (**a6**).*[37] Produced following the general procedure as mentioned above by reacting 1,2-diaminobenzene/2-nitroaniline (54.0 mg/69.0 mg, 0.5 mmol, 1 equiv.) and 1-phenylethane-1,2-diol (138.0 mg, 1 mmol, 2 equiv. for diamine; 207.0 mg, 1.5 mmol, 3 equiv. for 2-nitroaniline). The title product was purified by column chromatography with silica gel using 10% EtOAc in hexane as yellow dense liquid (88 mg; 86% from 1,2-diaminobenzene and 75 mg; 73% from 2-nitroaniline). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.31 (s, 1H), 8.19-8.09 (m, 4H), 7.78-7.70 (m, 2H), 7.57-7.50 (m, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 152.0, 143.5, 142.5, 141.7, 136.9, 130.5, 130.4, 129.8, 129.7, 129.3, 127.7. GC-MS (M^+): 206.0.

*1,2,3,4-Tetrahydrophenazine (**a7**).*[34] Produced following the general procedure as mentioned above by reacting 1,2-diaminobenzene/2-nitroaniline (54.0 mg/69.0 mg, 0.5 mmol, 1 equiv.) and cyclohexane-1,2-diol (116.0 mg, 1 mmol, 2 equiv. for diamine; 174.0 mg, 1.5 mmol, 3 equiv. for 2-nitroaniline). The title product was purified by column chromatography with silica gel using 10% EtOAc in hexane as pale yellow solid (47.0 mg; 51% from 1,2-diaminobenzene and 64 mg; 70% from 2-nitroaniline). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.95-7.91 (m, 2H), 7.64-7.60 (m, 2H), 3.15-3.11 (m, 4H), 2.02-1.99 (m, 4H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 154.3, 141.3, 129.1, 128.5, 33.4, 22.9. GC-MS (M^+): 184.1.

*2,3-Diphenylquinoxaline (**a8**).*[37] Produced following the general procedure as mentioned above by reacting 1,2-diaminobenzene (54.0 mg, 0.5 mmol, 1 equiv.) and 1,2-diphenylethane-1,2-diol (214 mg, 1 mmol, 2 equiv.). The title product was purified by column chromatography with silica gel using 10% EtOAc in hexane as white solid (120 mg; 85%). For 3.0 mmol scale reaction isolated yield was 73% (0.617 g). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.19 (dd, $J_{H,H}$ = 6.48, 3.44 Hz, 2H), 7.77 (dd, $J_{H,H}$ = 6.44, 3.36 Hz, 2H), 7.52-7.50 (m, 4H), 7.35-7.30 (m, 6H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 153.7, 141.4, 139.3, 130.1, 130.0, 129.4, 129.0, 128.5. GC-MS (M^+): 282.0.

*6-Methyl-2,3-diphenylquinoxaline (**a9**).*[41] Produced following the general procedure as mentioned above by reacting 4-methylbenzene-1,2-diamine (61.0 mg, 0.5 mmol, 1 equiv.) and 1,2-diphenylethane-1,2-diol (214 mg, 1 mmol, 2 equiv.). The title product was purified by column chromatography with silica gel using 20% EtOAc in hexane as yellow solid (120 mg; 81%). For 2.8 mmol scale reaction isolated yield was 67% (0.554 g). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.06 (d, $J_{H,H}$ = 8.56 Hz, 1H), 7.94 (s, 1H), 7.60 (d, $J_{H,H}$ = 8.56 Hz, 1H), 7.51-7.49 (m, 4H), 7.34-7.29 (m, 6H), 2.60 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 153.5, 152.7, 141.4, 140.7, 139.9, 139.4, 132.5, 130.0, 128.9, 128.8, 128.4, 128.2, 22.1. GC-MS (M^+): 296.1.

*6-tert-Butyl-2,3-diphenylquinoxaline (**a10**).*[79] Produced following the general procedure as mentioned above by reacting 4-*tert*-butylbenzene-1,2-diamine (82.0 mg, 0.5 mmol, 1 equiv.) and 1,2-diphenylethane-1,2-diol (107 mg, 1 mmol, 2 equiv.). The title product was purified by column chromatography with silica gel using 20% EtOAc in hexane as yellow solid (133 mg; 79%). ^{1}H NMR (400 MHz, $CDCl_3$): δ =8.13 (d, $J_{H,H}$ = 2.12 Hz, 1H), 8.11 (d, $J_{H,H}$ = 8.88 Hz, 1H),7.87 (dd, $J_{H,H}$ = 9.08 Hz, $J_{H,H}$ = 2.36 Hz, 1H), 7.49 (m, 4H), 7.33 (m, 6H), 1.46 (s, 9H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 153.7, 153.6, 153.1, 141.3, 139.9, 139.4, 130.0, 130.0, 129.2, 128.9, 128.7, 128.5, 124.7, 35.6, 31.4. GC-MS (M^+): 338.1.

*2,6,7-Trimethylquinoxaline (**a11**).*[34] Produced following the general procedure as mentioned above by reacting 4,5-dimethylbenzene-1,2-diamine (68.5 mg, 0.5 mmol, 1 equiv.) and 1,2-propanediol (73.4 μL, 1 mmol, 2 equiv.). The title product was purified by column chromatography with silica gel using 20% EtOAc in hexane as pale yellow solid (63 mg; 74%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.61 (s, 1H), 7.77 (s, 1H), 7.73 (s, 1H), 2.71 (s, 3H), 2.46 (s, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 152.9, 145.2, 141.2, 140.7, 140.1, 139.5, 128.4, 128.0, 22.7, 20.6, 20.4. GC-MS (M^+): 172.1.

*2-Ethyl-6,7-dimethylquinoxaline (**a12**).*[80] Produced following the general procedure as mentioned above by reacting 4,5-dimethylbenzene-1,2-diamine/4,5-dimethyl-2-nitroaniline (68.5 mg/83.0 mg, 0.5 mmol, 1 equiv.) and 1,2-butanediol (89.5 μL, 1 mmol, 2 equiv.). The title product was purified by column chromatography with silica gel using 20% EtOAc in hexane as yellow solid (55 mg; 60% from 4,5-dimethylbenzene-1,2-diamine and 74 mg; 80% from 4,5-dimethyl-2-nitroaniline). gel using 20% EtOAc in hexane as yellow solid (120 mg; 81%). For 3.0 mmol scale reaction isolated yield was 66% (0.378 g). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.61 (s, 1H), 7.76 (d, $J_{H,H}$ = 7.40 Hz, 2H), 2.98 (q, $J_{H,H}$ = 7.64 Hz, 2H), 2.43 (s, 6H), 1.38 (t, $J_{H,H}$ = 7.56 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 157.6, 144.7, 141.2, 140.5, 140.3, 139.4, 128.3, 128.1, 29.7, 20.6, 20.4, 13.7. GC-MS (M^+): 186.1.

*2,3,6,7-Tetramethylquinoxaline (**a13**).*[34] Produced following the general procedure as mentioned above by reacting 4,5-dimethylbenzene-1,2-diamine/4,5-dimethyl-2-nitroaniline (68.5 mg/83.0 mg, 0.5 mmol, 1 equiv.) and 2,3-butanediol (89.5 μL, 1 mmol, 2 equiv.). The title product was purified by column chromatography with silica gel using 20% EtOAc in hexane as light yellow solid (81 mg; 87% from 4,5-dimethylbenzene-1,2-diamine and 86 mg; 93% from 4,5-dimethyl-2-nitroaniline). gel using 20% EtOAc in hexane as yellow solid (120 mg; 81%). For 3.0 mmol scale reaction isolated yield was 73% (0.407 g). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.68 (s, 2H), 2.65 (s, 6H), 2.41 (s, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 152.5, 140.1, 139.2, 127.6, 23.2, 20.4. GC-MS (M^+): 186.1.

*2-tert-Butyl-6,7-dimethylquinoxaline (**a14**).*[81] Produced following the general procedure as mentioned above by reacting 4,5-dimethylbenzene-1,2-diamine/4,5-dimethyl-2-nitroaniline (68.5 mg/83.0 mg, 0.5 mmol, 1 equiv.) and 3,3-dimethylbutane-1,2-diol (118.1 mg, 1 mmol, 2 equiv. for diamine; 177.1 mg, 1.5 mmol, 3 equiv. for 2-nitroaniline). The title product was purified by column chromatography with silica gel using 20% EtOAc in hexane as yellow solid (42 mg; 40% from 4,5-dimethylbenzene-1,2-diamine and 51 mg; 48% from 4,5-dimethyl-2-nitroaniline). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.85 (s, 1H), 7.78 (d, $J_{H,H}$ = 6.48 Hz, 2H),2.44 (s, 6H), 1.47 (s, 9H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 162.9, 142.5, 140.7, 140.2, 139.8, 139.3, 128.5, 128.1, 37.2, 30.0, 20.4. GC-MS (M^+): 214.1.

*6,7-Dimethoxy-2-phenylquinoxaline (**a15**).*[58] Produced following the general procedure as mentioned above by reacting 4,5-dimethoxybenzene-1,2-diamine (84.0 mg, 0.5 mmol, 1 equiv.) and 1-phenylethane-1,2-diol (138.0 mg, 1 mmol, 2 equiv.). The title product was purified by column chromatography with silica gel using 20% EtOAc in hexane as yellow solid (99 mg; 75%). gel using 20% EtOAc in hexane as yellow solid (120 mg; 81%). For 3.0 mmol scale reaction isolated yield was 60% (0.479 g). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.10 (s, 1H), 8.11 (d, $J_{H,H}$ = 7.65 Hz, 1H), 7.54-7.51 (m, 2H), 7.48-7.45 (m, 1H), 7.41 (s, 1H), 7.36 (s, 1H), 4.06 (s, 3H), 4.05 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 153.3, 152.8, 150.1, 140.8, 139.7, 138.9, 137.4, 129.8, 129.3, 128.7, 127.4, 126.3, 107.3, 106.8, 56.6, 56.6. GC-MS (M^+): 266.1.

*2,3,6-Trimethylquinoxaline (**a16**).*[82] Produced following the general procedure as mentioned above by reacting 4-methylbenzene-1,2-diamine (61.0 mg, 0.5 mmol, 1 equiv.) and 2,3-butanediol (90.0 μL, 1 mmol, 2 equiv.). The title product was purified by column chromatography with silica gel using 20% EtOAc in hexane as light yellow solid (79 mg; 92%). gel using 20% EtOAc in hexane as yellow solid (120 mg; 81%). For 3.0 mmol scale reaction isolated yield was 76% (0.392 g). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84 (d, $J_{H,H}$ = 8.52 Hz, 1H), 7.72 (s, 1H), 7.47 (d, $J_{H,H}$ = 8.44 Hz, 1H), 2.68 (s, 6H), 2.53 (s, 3H),. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 153.5, 152.6, 141.3, 139.7, 139.3, 131.2, 128.0, 127.5, 23.3, 23.2, 21.9. GC-MS (M^+): 172.0.

*6-tert-Butyl-2,3-dimethylquinoxaline (**a17**).*[43] Produced following the general procedure as mentioned above by reacting 4-*tert*-butylbenzene-1,2-diamine (82.0 mg, 0.5 mmol, 1 equiv.) and 2,3-butanediol (90.0 μL, 1 mmol, 2 equiv.). The title product was purified by column chromatography with silica gel using 20% EtOAc in hexane as yellow solid (58 mg; 55%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91 (d, $J_{H,H}$ = 2.12 Hz, 1H), 7.89 (d, $J_{H,H}$ = 8.80 Hz, 1H), 7.73 (dd, $J_{H,H}$ = 8.76 Hz, $J_{H,H}$ = 2.04 Hz, 1H), 2.68 (s, 6H), 1.39 (s, 9H). ^{13}C{^{1}H} NMR (100 MHz,

$CDCl_3$): δ = 153.4, 152.9, 152.5, 141.1, 139.6, 127.9, 127.8, 123.8, 35.3, 31.4, 23.3, 23.2. GC-MS (M^+): 214.1.

*7-Methyl-1,2,3,4-tetrahydrophenazine (**a18**).*[83] Produced following the general procedure as mentioned above by reacting 4-methylbenzene-1,2-diamine (61.0 mg, 0.5 mmol, 1 equiv.) cyclohexane-1,2-diol (116.0 mg, 1 mmol, 2 equiv.). The title product was purified by column chromatography with silica gel using 15% EtOAc in hexane as pale yellow solid (55.5 mg; 56%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.80 (d, $J_{H,H}$ = 8.56 Hz, 1H), 7.68 (s, 1H), 7.44 (dd, $J_{H,H}$ = 8.56, 1.76 Hz, 1H), 3.19-3.00 (m, 4H), 2.50 (s, 3H), 1.99-1.95 (m, 4H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 154.0, 153.2, 141.4, 139.8, 129.3, 131.3, 127.9, 127.4, 33.3, 33.2, 23.0, 21.9. GC-MS (M^+): 198.1.

*7-Bromo-2,3,5-trimethylquinoxaline (**a19**).*[40] Produced following the general procedure as mentioned above by reacting 5-bromo-3-methylbenzene-1,2-diamine (100.0 mg, 0.5 mmol, 1 equiv.) and 2,3-butanediol (90.0 μL, 1 mmol, 2 equiv.). The title product was purified by column chromatography with silica gel using 20% EtOAc in hexane as yellow solid (61 mg; 49%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.95 (s, 1H), 7.56 (s, 1H), 2.70 (s, 3H), 2.68 (s, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 154.1, 152.8, 141.9, 139.3, 138.9, 132.2, 128.6, 122.3, 23.5, 23.3, 17.1. HRMS (ESI-TOF): calcd. for $C_{11}H_{12}BrN_2[M+H]^+$: 251.0184; found: 251.0182.

*6-tert-Butyl-2-methylquinoxaline (**a20**) and 7-tert-butyl-2-methylquinoxaline (**a20'**).* Produced following the general procedure as mentioned above by reacting 4-*tert*-butylbenzene-1,2-diamine (82.0 mg, 0.5 mmol, 1 equiv.) and 1,2-propanediol (73.4 μL, 1 mmol, 2 equiv.). The title product was purified by column chromatography with silica gel using 15% EtOAc in hexane as yellow solid; Two regio-isomers (3:2) were inseparable in column chromatography (74 mg; 74%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.67-8.65 (s, 1H), 7.97-7.90 (m, 2H), 7.81-7.75 (m, 1H), 2.73-2.72 (s, 3H), 1.40 (s, 9H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 153.7, 153.2, 152.5, 151.2, 146.7, 146.0, 129.1, 128.6, 128.1, 128.0, 124.6, 124.1, 35.4, 35.3, 31.3, 22.7. GC-MS (M^+): 200.0. HRMS (ESI-TOF): calcd. for $C_{13}H_{17}N_2[M+H]^+$: 201.1392; found: 201.1388.

*6-tert-Butyl-2-phenylquinoxaline (**a21**) and 7-tert-butyl-2-phenylquinoxaline (**a21'**).* Produced following the general procedure as mentioned above by reacting 4-*tert*-butylbenzene-1,2-diamine (82.0 mg, 0.5 mmol, 1 equiv.) and , 1-phenylethane-1,2-diol (138.0 mg, 1 mmol, 2 equiv.). The title product was purified by column chromatography with silica gel using 15% EtOAc in hexane as yellow solid; Two regio-isomers (3:2) were inseparable in column chromatography (85 mg; 65%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.28-9.25 (s, 1H), 8.18-8.16 (m, 2H), 8.10-8.03 (m, 2H), 7.88-7.82 (m, 1H), 7.57-7.47 (m, 3H), 1.46-1.45 (s, 9H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 154.0, 152.3, 152.0, 151.5, 143.4, 142.9, 142.4, 141.7, 140.9, 140.2, 137.2, 130.2, 130.2, 129.5, 129.3, 129.1, 128.8, 128.7, 128.6, 128.5, 128.2, 127.7, 127.6, 125.0, 124.5, 35.5, 35.4, 31.3. GC-MS (M^+): 262.1. HRMS (ESI-TOF): calcd. for $C_{18}H_{19}N_2[M+H]^+$: 263.1548; found: 263.1544.

*6-Chloro-2,3-dimethylquinoxaline (**a23**).*[40] Produced following the general procedure as mentioned above by reacting 4-chloro-2-nitroaniline (86.0 mg, 0.5 mmol, 1 equiv.) and 2,3-butanediol (135.0 μL, 1.5 mmol, 3 equiv.). The title product was purified by column chromatography with silica gel using 20% EtOAc in hexane as yellow solid (61 mg; 64%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.92 (d, $J_{H,H}$ = 2.25 Hz, 1H). 7.87 (d, $J_{H,H}$ = 8.85 Hz, 1H), 7.56 (dd, $J_{H,H}$ = 8.85, 2.30, 1H), 2.69 (s, 3H), 2.68 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 154.7, 153.9, 141.6, 139.7, 134.6, 129.9, 129.7, 127.5, 23.4, 23.3. GC-MS (M^+): 192.0.

*6-Methoxy-2,3-dimethylquinoxaline (**a24**).*[84] Produced following the general procedure as mentioned above by reacting 4-methoxy-2-nitroaniline (84.0 mg, 0.5 mmol, 1 equiv.) and 2,3-butanediol (135.0 μL, 1.5 mmol, 3 equiv.). The title product was purified by column chromatography with silica gel using 20% EtOAc in hexane as light yellow solid (77 mg; 82%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.84 (d, $J_{H,H}$ = 8.68 Hz, 1H), 7.30-7.26 (m, 2H), 3.91 (s, 3H), 2.68 (m, 3H), 2.66 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 160.1, 153.5, 150.8, 142.6, 137.2, 129.4, 121.9, 106.3, 55.9, 23.3, 23.0. GC-MS (M^+): 188.0.

*6-Methoxy-2,3-diphenylquinoxaline (**a25**).*[34] Produced following the general procedure as mentioned above by reacting 4-methoxy-2-nitroaniline (84.0 mg, 0.5 mmol, 1 equiv.) and 1,2-diphenylethane-1,2-diol (321.3 mg, 1.5 mmol, 3 equiv.). The title product was purified by column chromatography with silica gel using 10% EtOAc in hexane as pale yellow solid (134 mg; 86%). gel using 20% EtOAc in hexane as yellow solid (120 mg; 81%). For 3.0 mmol scale reaction isolated yield was 71% (0.664 g). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.05 (d, $J_{H,H}$ = 9.16 Hz, 1H), 7.51-7.47 (m, 4H), 7.46 (d, $J_{H,H}$ = 2.84 Hz, 1H), 7.42-7.39 (m, 1H), 7.34-7.30 (m, 6H), 3.97 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 161.1, 153.5, 151.1, 143.0, 139.4, 139.4, 137.6, 130.3, 130.0, 128.9, 128.7, 128.4, 128.4, 123.6, 106.6, 56.0. GC-MS (M^+): 312.1.

*2-Butyl-6,7-dimethylquinoxaline (**a26**).*[80] Produced following the general procedure as mentioned above by reacting 4,5-dimethyl-2-nitroaniline (83.0 mg, 0.5 mmol, 1 equiv.) and 1,2-hexanediol (186.3 μL, 1.5 mmol, 3 equiv.). The title product was purified by column chromatography with silica gel using 20% EtOAc in hexane as yellow solid (50 mg; 47%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.60 (s, 1H), 7.77 (d, $J_{H,H}$ = 6.52 Hz,2H), 2.94 (t, $J_{H,H}$ = 7.76 Hz, 2H), 2.45 (s, 6H), 1.82-1.74 (m, 2H), 1.46-1.37 (m, 2H), 0.94 (t, $J_{H,H}$ = 7.32 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 156.8, 145.0, 141.3, 140.5, 140.3, 139.4, 128.4, 128.1, 36.3, 31.9, 22.7, 20.5, 20.4, 14.1. GC-MS (M^+): 214.1.

*6,7-Dimethyl-2-phenylquinoxaline (**a27**).*[85] Produced following the general procedure as mentioned above by reacting 4,5-dimethyl-2-nitroaniline (83.0 mg, 0.5 mmol, 1 equiv.) and 1-phenylethane-1,2-diol (207.0 mg, 1.5 mmol, 3 equiv.). The title product was purified by column chromatography with silica gel using 20% EtOAc in hexane as yellow solid (90 mg; 77%). gel using 20% EtOAc in hexane as yellow solid (120 mg; 81%). For 3.0 mmol scale reaction isolated yield was 62% (0.435 g). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.19 (s, 1H), 8.15 (d, $J_{H,H}$ = 7.00 Hz, 2H), 7.87 (s, 1H), 7.82 (s, 1H), 7.53 (m, 3H), 2.47 (s, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 151.1, 142.5, 141.4, 140.9, 140.7, 140.3, 137.3 130.0, 129.2, 128.8, 128.3, 127.5, 20.5. GC-MS (M^+): 234.1.

*7-Methoxy-1,2,3,4-tetrahydrophenazine (**a28**).*[34] Produced following the general procedure as mentioned above by reacting 4-methoxy-2-nitroaniline (69.0 mg, 0.5 mmol, 1 equiv.) and cyclohexane-1,2-diol (174.0 mg, 1.5 mmol, 3 equiv.). The title product was purified by column chromatography with silica gel using 30% EtOAc in hexane as pale yellow solid (96 mg; 90%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.83 (d, $J_{H,H}$ = 9.10 Hz, 1H), 7.29 (dd, $J_{H,H}$ = 9.10, 2.70 Hz, 1H), 7.25 (s, 1H), 3.91 (s, 3H), 3.11-3.09 (m, 4H), 2.01-1.99 (m, 4H). ^{13}C{^{1}H} NMR (100

MHz, $CDCl_3$): δ = 160.2, 154.1, 151.4, 142.8, 137.8, 129.5, 122.2, 106.1, 55.8, 33.3, 33.0, 23.1, 23.0. GC-MS (M^+): 214.1.

*7-Bromo-5-methyl-2,3-diphenylquinoxaline (**a29**).*[57] Produced following the general procedure as mentioned above by reacting 4-bromo-2-methyl-6-nitroaniline (115.5 mg, 0.5 mmol, 1 equiv.) and 1,2-diphenylethane-1,2-diol (321.3 mg, 1.5 mmol, 3 equiv.). The title product was purified by column chromatography with silica gel using 20% EtOAc in hexane as yellow solid (164 mg; 88%). gel using 20% EtOAc in hexane as yellow solid (120 mg; 81%). For 3.0 mmol scale reaction isolated yield was 70% (0.785 g). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.18 (s, 1H), 7.68 (s, 1H), 7.56-7.49 (m, 4H), 7.37-7.31 (m, 6H), 2.82 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 153.9, 152.3, 142.0, 139.8, 139.4, 139.2, 133.3, 130.3, 130.0, 129.4, 129.2, 129.1, 128.5, 128.4, 123.8, 17.1. GC-MS (M^+): 374.0.

Two regio-isomers (**a30** and **a30'**) with 1:1 selectivity, were separated by column chromatography. Produced following the general procedure as mentioned above by reacting 4-chloro-2-nitroaniline (86.0 mg, 0.5 mmol, 1 equiv.) and 1-phenylethane-1,2-diol (207.0 mg, 1.5 mmol, 3 equiv.). The title product was was purified by column chromatography with silica gel using 10% EtOAc in hexane as white solid (total yield 87.6 mg, 73%).[57] *6-Chloro-2-phenylquinoxaline (**a30**).* ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.31 (s, 1H), 8.18-8.16 (m, 2H), 8.10-8.06 (m, 2H), 7.72 (dd, $J_{H,H}$ = 8.90, 2.30 Hz, 1H), 7.57-7.52 (m, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 152.2, 144.4, 142.0, 141.1, 136.6, 135.5, 131.5, 131.1, 130.1, 129.4, 128.3, 127.7. GC-MS (M^+): 240.0. *7-Chloro-2-phenylquinoxaline (**a30'**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.29 (s, 1H), 8.18 (dd, $J_{H,H}$ = 8.32, 1.76 Hz, 2H), 8.14 (d, $J_{H,H}$ = 2.28 Hz, 1H), 8.04 (d, $J_{H,H}$ = 9.00 Hz, 1H), 7.67 (dd, $J_{H,H}$ = 9.04, 2.28 Hz, 1H), 7.58-7.52 (m, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 152.7, 143.6, 142.8, 140.3, 136.5, 136.3, 130.8, 130.7, 130.5, 129.4, 128.7, 127.8. GC-MS (M^+): 240.0.

Two regio-isomers (**a31** and **a31'**) with 3:2 selectivity, were separated by column chromatography. Produced following the general procedure as mentioned above by reacting 4-methoxy-2-nitroaniline (84.0 mg, 0.5 mmol, 1 equiv.) and 1-phenylethane-1,2-diol (207.0 mg, 1.5 mmol, 3 equiv.). The title product was was purified by column chromatography with silica gel using 20% EtOAc in hexane as yellow solid (total yield 88 mg, 75%).[34] *7-Methoxy-2-phenylquinoxaline (**a31**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.14 (s, 1H), 8.15 (d, $J_{H,H}$ = 9.96 Hz, 2H), 7.97 (d, $J_{H,H}$ = 9.12 Hz, 1H), 7.55-7.47 (m, 3H), 7.41-7.35 (m, 2H), 3.96 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): 161.2, 152.1, 144.1, 140.9, 137.7, 137.1, 130.2, 130.2, 129.3, 127.7, 123.1, 107.0, 56.0. GC-MS (M^+): 236.0. *6-Methoxy-2-phenylquinoxaline (**a31'**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.23 (s, 1H), 8.15 (d, $J_{H,H}$ = 7.36 Hz, 2H), 8.03 (d, $J_{H,H}$ = 9.12 Hz, 1H), 7.56-7.48 (m, 3H), 7.44-7.39 (m, 2H), 3.98 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 160.8, 149.8, 143.4, 143.3, 138.6, 137.2, 130.8, 129.9, 129.3, 127.4, 123.8, 106.7, 56.0. GC-MS (M^+): 236.0.

*6-Bromo-8-methyl-2-phenylquinoxaline (**a32**) and 7-bromo-8-methyl-2-phenylquinoxaline (**a32'**).* Produced following the general procedure as mentioned above by reacting 4-bromo-2-methyl-6-nitroaniline (115.5 mg, 0.5 mmol, 1 equiv.) and 1-phenylethane-1,2-diol (207.0 mg, 1.5 mmol, 3 equiv.). The title product was was purified by column chromatography with silica gel using 20% EtOAc in hexane as yellow solid; Two regio-isomers (3:2) were inseparable in column chromatography (123 mg; 83%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.29 (s, 1H), 8.23-8.10 (m, 3H), 7.69-7.65 (m, 1H), 7.57-7.51 (m, 3H), 2.83-2.78 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 152.3, 150.6, 143.6, 143.2, 142.4, 142.3, 140.4, 140.1, 139.8, 139.5, 136.8, 136.6, 133.7, 133.0, 130.6, 130.5, 129.9, 129.4, 129.3, 127.7, 127.6, 124.2, 123.4, 17.3, 17.1. GC-MS (M^+): 298.0. HRMS (ESI-TOF): calcd. for $C_{15}H_{12}BrN_2[M+H]^+$: 299.0184; found: 299.0181.

ASSOCIATED CONTENT

Detail reaction optimization, preparative scale reaction, control experiments, reaction kinetics and mechanism, characterization of the material, ^{1}H and ^{13}C spectra of all compounds.

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Notes

The authors declare no competing financial interest.

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