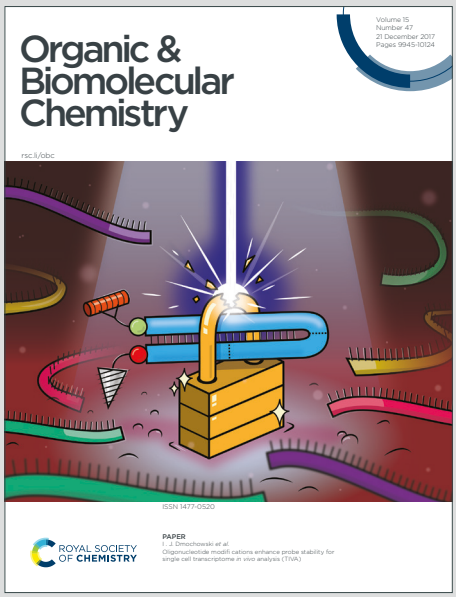
Organic & Biomolecular Chemistry

Accepted Manuscript

This article can be cited before page numbers have been issued, to do this please use: S. Sankararaman and A. Chandrasekhar, *Org. Biomol. Chem.*, 2020, DOI: 10.1039/C9OB02703C.



ROYAL SOCIETY OF CHEMISTRY

rsc.li/obc

View Article Online
DOI: 10.1039/C9OB02703C

ARTICLE

Synthesis of Indolo- and Pyrrolo[1,2-a]quinoxalinones through Palladium-Catalyzed Oxidative Carbonylation of C_2 Position of Indole

Received 00th January 20xx,
Accepted 00th January 20xx

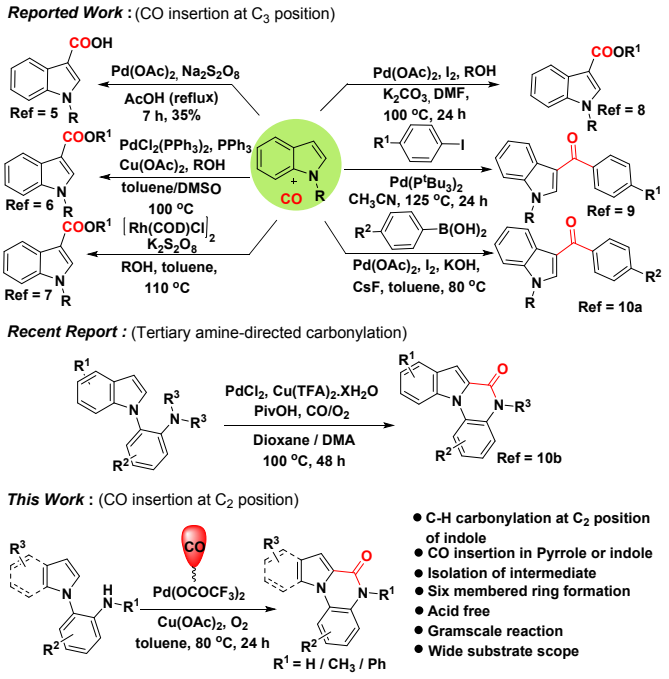
DOI: 10.1039/x0xx00000x

Attoor Chandrasekhar[a] and Sethuraman Sankararaman*[a]

A methodology that involves Pd-catalyzed direct *C*(*sp2*)–*H* bond carbonylation of C_2 position of indole has been introduced for the synthesis of indolo[1,2-a]quinoxalin-6(5*H*)-ones. The methodology developed was used for the synthesis of pyrrolo[1,2-a]quinoxalin-4(5*H*)-ones. The reaction of *N*-subtituted 2-(1*H*-indol-1-yl)anilines or 2-(1*H*-pyrrol-1-yl)anilines and carbon monoxide in presence of $Pd(OCOCF_3)_2$ as a catalyst, $Cu(OAc)_2$ as an oxidant in toluene at 80 °C forms the corresponding quinoxalinones as exclusive products in good yields. The catalytically active C–H activated intermediate Pd complex was isolated and characterized for the *first time* which on exposure to CO gas in toluene at 80 °C gave the corresponding quinoxalinone derivative. On the basis of isolation of the intermediate, a possible mechanism has been proposed for the *C*–*H* activated direct carbonylative annulation of 2-(5-methoxy-1*H*-indol-1-yl)-*N*,4-dimethylaniline.

Introduction

Transition metal catalyzed CO insertion in organic halides or pseudo halides has become a powerful method for the synthesis of carbonyl compounds. A variety of carbonylated heterocyclic compounds were synthesized using methodology that involves Pd-catalyzed carbonylative annulations[1] and they have received considerable attention since the seminal work of Heck.[2] More recently, transition metal catalyzed oxidative carbonylation of a *C*(*sp2*)–*H* bond has become the most atom economic and efficient way to incorporate carbon monoxide in hydrocarbons. The first direct oxidative carbonylation of arenes was introduced by Fujiwara in 1980 which involved electrophilic attack on arene by palladium(II).[3] The concept of Pd-catalyzed carbonylation of *C*(*sp2*)–*H* bond was used to synthesize the various heterocyclic and acyclic compounds,[4] but it is limited to carbonylation of *C*(*sp2*)–*H* of indole derivatives. There are very few reports available based on oxidative carbonylation of C_2 position of indoles (Scheme 1).



Scheme 1. Oxidative carbonylation of indole derivatives

The first direct carbonylation of indoles was reported by Itahara in 1982.[5] 1-Acetylindole was treated with carbon monoxide in the presence of $Pd(OAc)_2$ and $Na_2S_2O_8$ used as an oxidant to give 1-acetylindole-3-carboxylic acid. Lei and co-workers developed direct carbonylation of *N*-substituted and unsubstituted indoles.[6] Rh catalyzed regioselective direct carbonylation of indoles to form indole-3-carboxylates was introduced by Li and his group.[7] Subsequently, Li developed an advanced methodology that uses Pd-

[a] A. Chandrasekhar and Prof. S. Sankararaman
Department of Chemistry
Indian Institute of Technology Madras
Chennai-600036, India
sanka@iitm.ac.in

† Footnotes relating to the title and/or authors should appear here.
Electronic Supplementary Information (ESI) available: Synthesis and spectral data of starting materials, CCDC 1971937 (**3a**), 1971938 (**8a**), 1971939 (**35a**) contain the supplementary crystallographic data. These data can be obtained free of charge from the Cambridge Crystallographic Data Center.See DOI: 10.1039/x0xx00000x

catalyzed direct carbonylation of free and *N*-substituted indoles to produce the corresponding ester derivatives of indoles.[8] A strategy that involves oxidative iodination of indole at C_3 position and subsequent Pd(0)-catalyzed carbonylation to yield indole-3-carboxylate was reported by Arndtsen *et al*.[9] Here they introduced an electrophilic approach to the Pd-catalyzed carbonylative *C–H* functionalization of indole.[9] A new methodology that involves carbonylative Suzuki-Miyaura direct *C–H* carbonylation of indoles in the presence of aromatic boronic acids as a coupling partner was introduced by Guan et *al. in* 2015.[10a] However, till today the direct *C–H* oxidative carbonylation of indoles was demonstrated only at the C_3 position which is more active towards electrophilic reactions. To the best of our knowledge, very few reports are available based on oxidative carbonylation of indoles at C_2 position to date.[10b] Many functional groups are introduced through *C–H* activation at C_2 position of indole[11] while no CO insertion is investigated. Herein we describe a methodology involving Pd-catalyzed direct *C–H* carbonylation of indoles at C_2 position for the synthesis of indolo[1,2,-a]quinoxalin-6(5*H*)-ones. The methodology developed was applied for the synthesis of pyrrolo[1,2-a]quinoxalin-4(5*H*)-ones.

Indole is an important structural motif found in various biologically and pharmaceutically active molecules, agrochemicals, dyes, and essential oils.[12] Since its discovery by Baeyer in 1869, indole has become an important heterocycle in academics and industries. In fact, it is the most widely distributed heterocycle found in nature. Quinoxalinone moiety as core structure has its own importance due to their wide variety of pharmacological properties, such as anticancer, anxiolytic, antimicrobial, analgesic, antiallergic activities, antimicrobial agents, kinases inhibitors, benzodiazepine receptor agonist, anti-inflammatory, antimicrobial, antidiabetic.[13] Some representative examples of biologically active quinoxalinones are shown below (Figure 1).

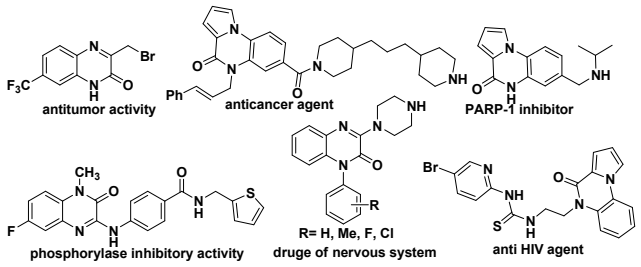
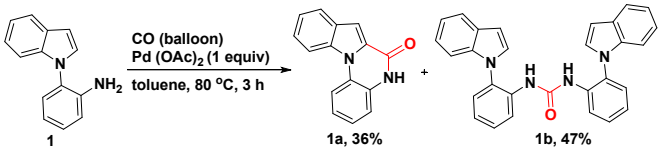


Figure 1. Representative examples of biologically active quinoxalinones.

Beccalli *et al.* reported the synthesis of both pyrrole and indole based quinoxalinones.[14] In 2016 Patel and co-workers developed a methodology for the synthesis of indoloquinoxalin-6-ones from *o*-indolyl-*N,N*-dialkylamines.[15] Zn(II) catalyzed intramolecular *N–H* arylation of indole-2-carboxamide for the synthesis of indoloquinoxalin-6-ones was introduced by Li.[16] Our interest in Pd-catalyzed oxidative carbonylation reactions using CO as a carbon source[4q] led us to investigate the Pd-catalyzed *C–H* carbonylation of indoles for the synthesis of indoloquinoxalin-6-ones. The Pd-catalyzed oxidative carbonylation methodology developed was used to synthesize the pyrroloquinoxalin-4-ones as well.

Results and Discussion

The present investigation started with the reaction of 2-(1*H*-indol-1-yl)aniline (**1**) with carbon monoxide in the presence of the stoichiometric amount of $Pd(OAc)_2$ at 80 °C in toluene (Scheme 2). The reaction proceeded smoothly and 100% conversion was observed within 3h. From the reaction, the anticipated C_2 *C–H* bond carbonylative annulated product (**1a**) was obtained in 36% yield along with 47% of another possible carbonylated product, namely, 1,3(2-(1*H*-indol-1-yl)phenylurea (**1b**) isolated by column chromatography. Both the compounds were characterized by ^{1}H-NMR, ^{13}C-NMR, IR, and HRMS.



Scheme 2. Carbonylation of 2-(1*H*-indol-1-yl)aniline with stoichiometric $Pd(OAc)_2$.

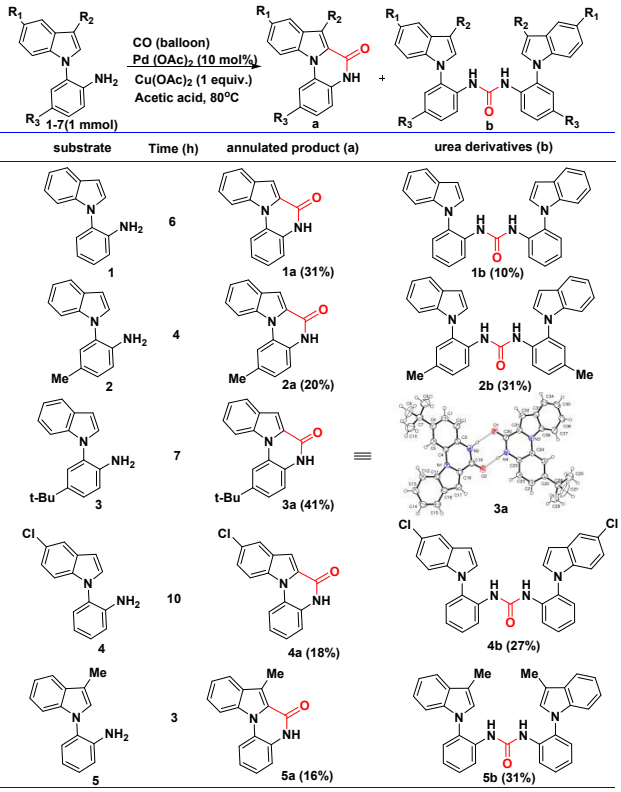
In order to find a suitable catalytic reaction conditions to improve the selectivity of reaction towards the formation of indoloquinoxalinone (**1a**) as a major product, reaction conditions were optimized by changing solvents, oxidants and metal sources. Firstly, **1** was treated with a catalytic amount of $Pd(OAc)_2$ in the presence of $Cu(OAc)_2$ as an oxidant in toluene under balloon pressure of CO at 80 °C. The reaction was stirred for 12 h to obtain the annulated product **1a** in 22% yield. Further reaction conditions were screened and maximum yield (31%) of **1a** was observed when the reaction was performed in AcOH as a solvent (Table-1). The scope of carbonylation was investigated with few examples in AcOH solvent. In all cases, formation of both C_2 *C–H* carbonylative annulated product and urea derivatives were observed and the remaining starting material was decomposed. Surprisingly, no urea derivative was observed in the case of compound **3.** This may be due to lack of hyperconjugation of the *t*-butyl group in **3** unlike methyl group in **2** which reduces the nucleophilicity of the amino group. All the products were purified by column chromatography and thoroughly characterized by spectroscopic data. In addition, the structure of **3a** was established unequivocally by single crystal X-ray data. Due to the strong intermolecular hydrogen bonding **3a** existed as a centrosymmetric hydrogen bonded dimer in the crystal.

Mechanistically, the formation of annulated indoloquinoxalinone(**1a**) and urea derivative (**1b**) presumably results from different processes.[17,4b,4d,4q] In the proposed catalytic cycle for **1b** (Scheme 3), palladium catalyst reacts with amine group to give amino palladium complex **I** by the loss of acetic acid. Subsequently, intermediate **I** reacts with carbon monoxide to form amidopalladium intermediate **II** followed by deprotonation leading to the formation of isocyanate **III**. In the presence of primary amine, **III** afforded the urea derivatives (**1b**). Alternatively, it may be that another molecule of amine (**1**) reacts at the Pd center in (**II**) followed by reductive elimination of

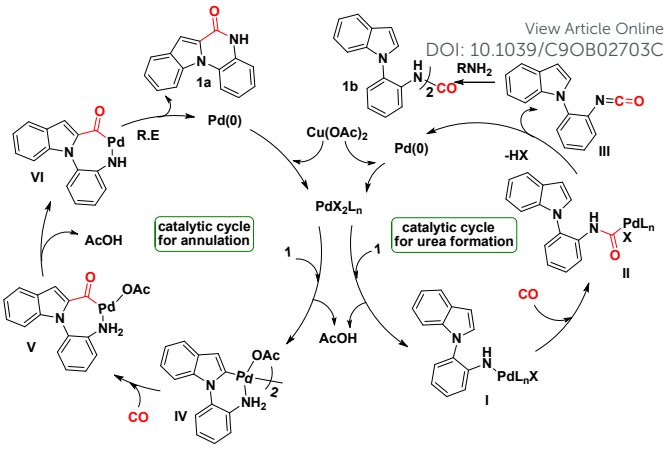
DOI: 10.1039/C9OB02703C

Pd(0) can give the urea derivative (**1b**). On the other hand, for the formation of 1a, Pd catalyst forms a *C–H* activated cyclic complex **IV**. Under the CO atmosphere, complex **IV** reacts to form cyclic acylpalladium intermediate **V** followed by the elimination of AcOH gives complex **VI.** Reductive elimination of **VI** affords the desired annulated product (**1a**).

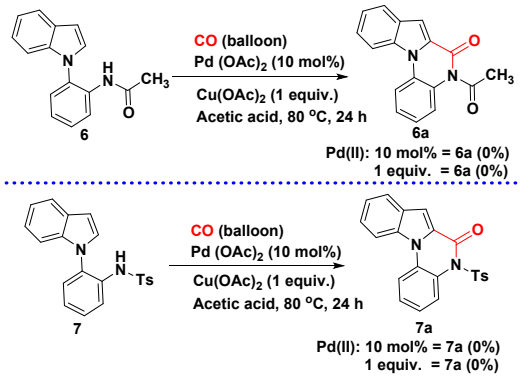
Table 1. Carbonylation of free 2-(1*H*-indol-1-yl)anilines



Our hypothesis that the formation of urea can be controlled by protecting the free amine group, we reasoned that the following advantages accompany the use of secondary amine. (1) Reactivity of primary amine can be reduced by converting it into a secondary amine (steric hindrance). Therefore, the reaction rate of **1** to **I** might be decreased and the problem associated with the formation of the urea might be reduced. (2) Importantly, the formation of isocyanate intermediate (**III**) is not possible with 2° amines. Firstly, 2-(1*H*-indol-1-yl)aniline was converted into *N*-(2-(1*H*-indol-1-yl)phenyl)acetamide (**6**) and *N*-(2-(1*H*-indol-1-yl)phenyl)tosylamide (**7**) by treating with acetyl chloride and tosyl chloride respectively. Both **6** and **7** were treated with carbon monoxide separately under the optimal reaction conditions (Scheme 4). After 24 h only starting material was recovered by column chromatography in both cases. In another set of reactions, both acetyl and tosyl protected indoles (**6** & **7**) were reacted with carbon monoxide separately in the presence of a stoichiometric amount of $Pd(OAc)_2$ under balloon pressure of CO at 80 °C in toluene for 24h. In case of acetyl compound **6,** trace amount of annulated product **1a** was formed instead of **6a** while no reaction was observed with tosyl substrate (**7**).

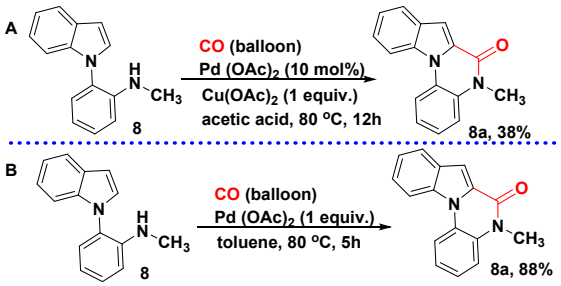


Scheme 3. Speculative mechanism for the formation of mixture of **1a** and **1b.**



Scheme 4. Attempted synthesis of annulated products **6a** & **7a**

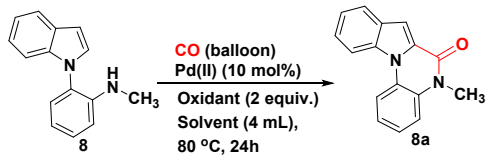
From these observations of the reactions in Scheme 4, we speculated that acetyl or tosyl groups were decreasing the nucleophilicity of amine and resulted in no reaction. We thought electron donating group might help to get carbonylative annulated product by improving nucleophilicity of amine. Therefore, **1** was treated with MeI in the presence of CH_3Li to get 2-(1*H*-indol-1-yl)-*N*-methylaniline (**8**). Compound **8** was subjected to CO under standard reaction conditions (Scheme 5A). Gratifyingly, desired carbonylative annulated indoloquinoxalinone was isolated in 38% yield as an exclusive product. There was no urea formation. In another experiment **8** was treated with carbon monoxide in the presence of a stoichiometric amount of $Pd(OAc)_2$ under balloon pressure of CO at 80 °C in toluene for 24 h (Scheme 5B). Reaction proceeded smoothly to give desired product in 88% yield without any urea formation.



Scheme 5. Selective C_2 oxidative carbonylation of **8**

In order to find a suitable catalytic reaction conditions for Pd-catalyzed carbonylation of 2-(1*H*-indol-1-yl)-*N*-methylaniline, reaction conditions were optimized (Table 2). Initially, compound **8** was treated with CO in presence of 10 mol% of $Pd(OAc)_2$ in toluene at 80 °C. Reaction gave 20% of **8a**. Further reaction conditions were screened with various oxidants. Improvement in reaction yield was not observed. The yield of **8a** was slightly increased when AcOH or TFA was introduced as an additive to the reaction mixture. Complete decomposition of starting material was observed when TFA was used as a solvent. Reaction yield was improved to 70% with more electrophilic metal catalyst $Pd(OCOCF_3)_2$. In the presence of $Pd(OCOCF_3)_2$ as a catalyst, reaction conditions were optimized with different solvents and oxidants. Best reaction yield was obtained with reaction conditions of entry 12. The yield of **8a** decreased to 46% when TFA used as the additive. There is no improvement in yield when different Pd sources were tried. No reaction was observed under Pd free reaction conditions. Under reaction conditions of entry 12, reaction proceeded to give 22% of **8a** at room temperature (entry 20).

Table 2. Optimization of reaction conditions for Pd-catalyzed carbonylation 2-(1*H*-indol-1-yl)-*N*-methylaniline.



S.No	Metal cat.	Solvent	Additive[a]	Oxidant	Yield[b] (%)
1	$Pd(OAc)_2$	Toluene	-	$Cu(OAc)_2$	20
2	$Pd(OAc)_2$	Toluene	-	CuO	15
3	$Pd(OAc)_2$	Toluene	-	O_2	19
4	$Pd(OAc)_2$	Toluene	-	BQ	13
5	$Pd(OAc)_2$	Toluene	-	$Cu(OTf)_2$	13
6	$Pd(OAc)_2$	Toluene	AcOH	$Cu(OAc)_2$	24
7	$Pd(OAc)_2$	Toluene	TFA	$Cu(OAc)_2$	26
8	$Pd(OAc)_2$	TFA	-	$Cu(OAc)_2$	0
9	$Pd(OAc)_2$	Trifluoroethanol	-	$Cu(OAc)_2$	19
10	$Pd(OCOCF_3)_2$	Toluene	-	$Cu(OAc)_2$	70
11	$Pd(OCOCF_3)_2$	AcOH	-	$Cu(OAc)_2$	40
12	$Pd(OCOCF_3)_2$	Toluene	-	$Cu(OAc)_2/O_2$	75
13	$Pd(OCOCF_3)_2$	Toluene	-	$Cu(OAc)_2$(20 mol%)	17
14	$Pd(OCOCF_3)_2$	Toluene	-	O_2	52
15	$Pd(OCOCF_3)_2$	Toluene	TFA	$Cu(OAc)_2/O_2$	46
16	$PdCl_2$	Toluene	-	$Cu(OAc)_2/O_2$	27
17	$PdCl_2(PPh_3)_2$	Toluene	-	$Cu(OAc)_2/O_2$	34
18	$PdCl_2(CH_3CN)_2$	Toluene	-	$Cu(OAc)_2/O_2$	30
19	-	Toluene	-	$Cu(OAc)_2/O_2$	0
20[c]	$Pd(OCOCF_3)_2$	Toluene	-	$Cu(OAc)_2/O_2$	22

[a] = 1 equiv. of additive, [b]= isolated yields, [c]= reaction at room temperature.

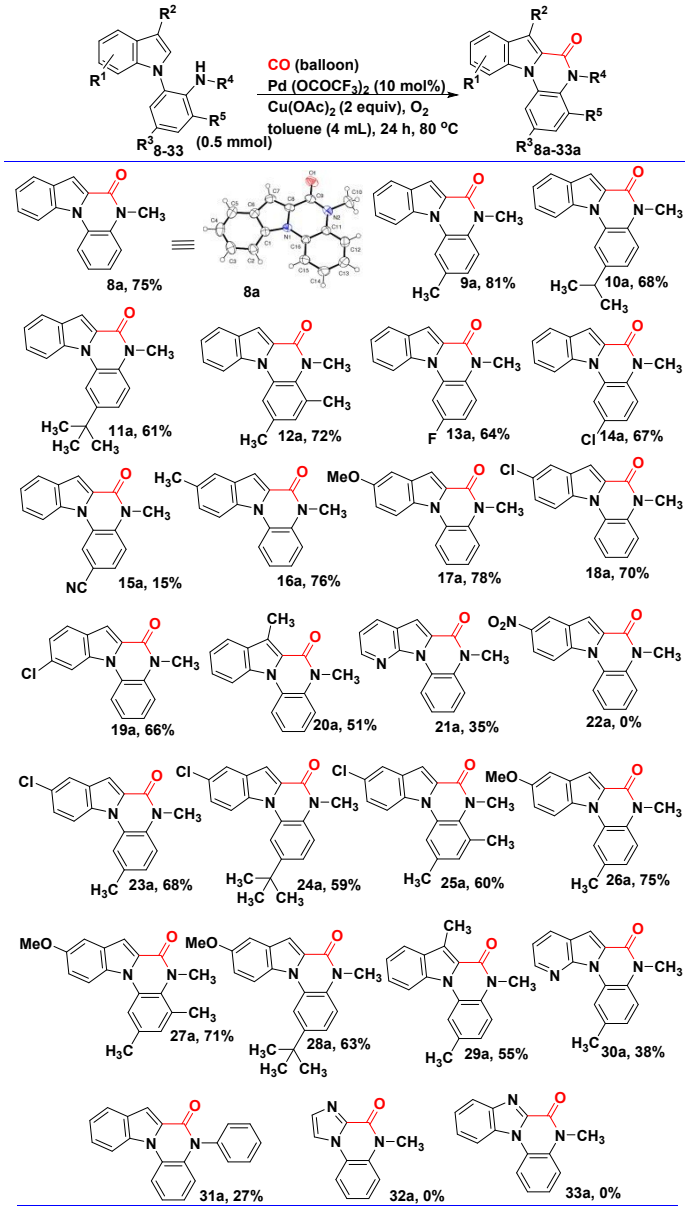
View Article Online DOI: 10.1039/C9OB02703C

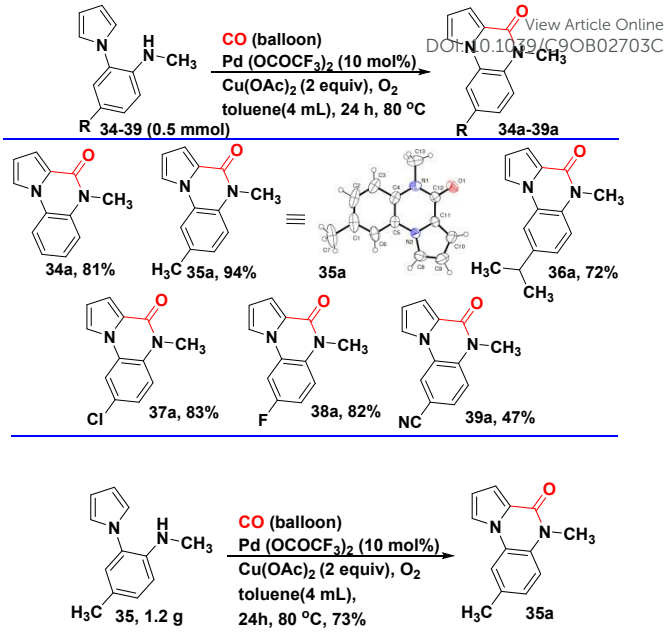
With optimized reaction conditions in hand, the scope of the substrates was demonstrated, and results are summarized in Table 3. Substrates with both electron donating or withdrawing groups are tolerated under optimized reaction conditions. The reaction is more favored to substrate with electron donating group than the ones with electron withdrawing group. Methyl at *para* to amine (**9**) favored the CO insertion to give 81% of the corresponding carbonylative annulated product (**9a**). Fluoro or Chloro substituted substrates also reacted well to produce **13a** and **14a** in 64% 67% yields respectively. Substrate with cyano group at *para* to amine, showed low reactivity and the corresponding carbonylated product (**15a**) was isolated in 15% yields. It might be due to decreased in nucleophilicity of the amine. Electron releasing groups or Chloro attached to indole ring of substrate did not show much difference in reactivity. But indole ring (**22**) with strong electron withdrawing group such as NO_2 did not react at all and only starting material was recovered. Substrates (**20** and **29**) with sterically hindered C_2 position also reacted under standard reaction conditions to give **20a** (51%) and **29a** (55%). Azaindole anilines (**21** & **30**) also reacted with carbon monoxide under optimized reaction conditions. Only 27% of the annulated product (**31a**) was isolated when *N*-Me (**8**) is substituted with *N*-Ph (**31**). Attempted synthesis of imidazoquinoxalinone under standard reaction conditions with **32** and **33** failed to give the annulated product. All the products (**8a-31a)** were purified by column chromatography and thoroughly characterized by spectroscopic data. In addition, the structure of **8a** was established unequivocally by single crystal X-ray data.

Pd-catalyzed carbonylation methodology developed herein was utilized for the synthesis of pyrroloquinoxalin-4-ones (Table 4). 2-(1*H*-pyrrol-1-yl)anilines were found to be more reactive towards oxidative carbonylative annulations under standard reaction conditions than 2-(1*H*-indol-1-yl)anilines and corresponding annulated products were formed in good yields.

Table 3. Selective synthesis of indolo[1,2,-a]quinoxalin-6(5*H*)-ones.

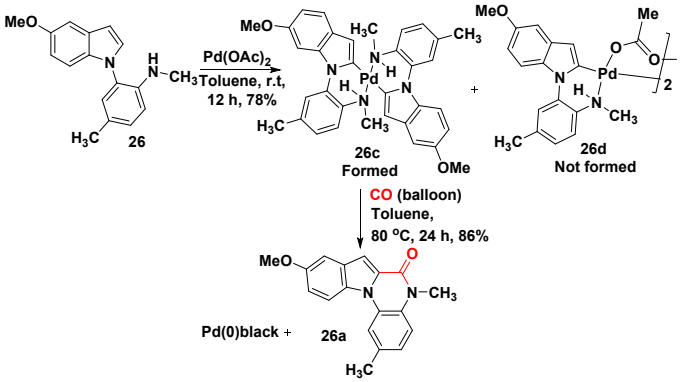
DOI: 10.1039/C9OB02703C





Scheme 6. Synthesis of **35a** in gram scale reaction.

To understand the reaction mechanism, we attempted to isolate the reaction intermediate of the carbonylative annulations reaction by treating **26** with stoichiometric amounts of $Pd(OAc)_2$ in toluene at room temperature for 24h (Scheme 7). We observed the formation of complex **26c** instead of anticipated acetate bridged dinuclear complex **26d**. To confirm the formation of complex **26c** as an intermediate, it was treated with CO in toluene at 80 °C for 24h. Complex **26c** reacted smoothly with CO to form corresponding annulated product (**26a**) in 86% yield. Complex **26c** was characterized by ^{1}H-NMR, ^{13}C-NMR, and HRMS.



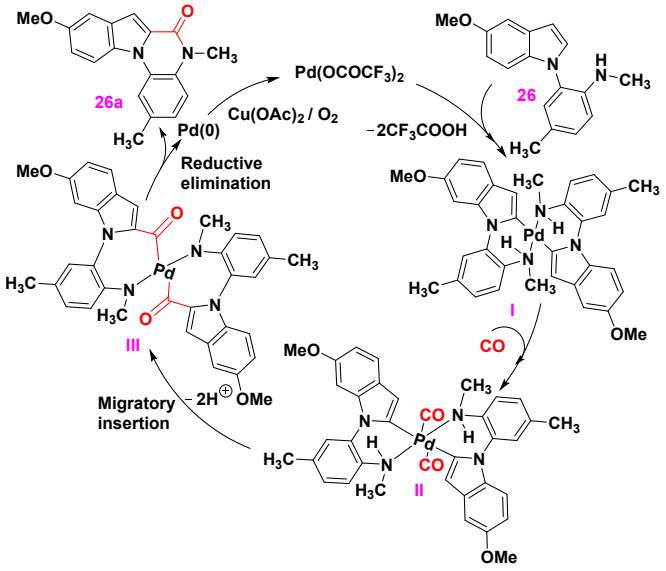
Scheme 7. Isolation and conformation of intermediate complex **26c**.

N-Methyl-2-(1*H*-pyrrol-1-yl)aniline was treated with CO under optimized conditions. The reaction proceeded smoothly to give **34a** in good yield while **35** gave **35a** in 94% yield. Fluoro and Chloro substituted substrates (**37** & **38**) also reacted well. Only 47% of carbonylated product was isolated from cyano substrate (**39**). The products **34a-39a** were purified by column chromatography and thoroughly characterized by spectroscopic data. In addition, the structure of **35a** is established unequivocally by single crystal X-ray data. To test the efficiency of the carbonylation reaction under standard reaction conditions in a gram scale, the reaction was carried out with 1.2 g (6.5 mmol) of *N*,4-dimethyl-2-(1*H*-pyrrol-1-yl)aniline **35** and desired product **35a** was obtained in 73% yield (Scheme 6).

Table 4. Selective synthesis of pyrrolo[1,2,-a]quinoxalin-4(5*H*)-ones

On the basis of the isolation of intermediate **26c** a plausible mechanism for carbonylative annulation of 2-(5-methoxy-1*H*-indol-1-yl)-*N*,4-dimethylaniline is proposed (Scheme 8). Initially, $Pd(OCOCF_3)_2$ reacts with **26** to produce pallado bicyclic complex **I** by the loss of CF_3COOH. Coordination of CO with Pd complex **I** under carbon monoxide atmosphere results in the formation of intermediate **II**. Subsequent migratory insertion of CO followed by de-protonation of complex **II** produces cyclic acyl palladium intermediate (**III**). The reductive elimination of complex **III** affords

desired carbonylative annulated product **26a** along with metal in the reduced state. Oxidant ($Cu(OAc)_2$) re-oxidizes the Pd(0) to promote the catalytic cycle.



Scheme 8. A plausible mechanism for *C–H* carbonylation of 2-(1*H*-indol-1-yl)anilines.

Conclusion

A methodology based on Pd-catalyzed oxidative carbonylation of C_2 C(*sp2*)-H bond of indole is demonstrated for the synthesis of indolo[1,2-a]quinoxalin-6(5*H*)-ones from corresponding 2-(1*H*-indol-1-yl)anilines. The methodology Pd-catalyzed oxidative carbonylation developed was applied for the synthesis of pyrrolo[1,2-a]quinoxalin-4(5*H*)-ones from 2-(1*H*-pyrrol-1-yl)anilines. 2-(1*H*-pyrrol-1-yl)anilines were found to be more reactive towards oxidative carbonylation than 2-(1*H*-indol-1-yl)anilines. The carbonylation of simple 2-(1*H*-indol-1-yl)anilines produces a mixture of corresponding annulated product (**a**) and urea (**b**). A speculative mechanism for the formation of mixture (**a** & **b**) is proposed. However, the formation of urea derivatives was controlled by protecting the free amine by *N*-methylation. Synthesis of 5,8-dimethylpyrrolo[1,2-a]quinoxalin-4(5*H*)-one was performed in a gram scale. The catalytically active *C–H* activated intermediate Pd complex was isolated and characterized which on exposure to CO gas in toluene at 80 °C gave the corresponding quinoxalinone derivative. On the basis of isolation of the intermediate, a possible mechanism has been proposed for the *C–H* activated direct carbonylative annulations of 2-(5-methoxy-1*H*-indol-1-yl)-*N*,4-dimethylaniline.

Experimental Section

General procedure for the synthesis of indolo[1,2,-a]quinoxalin-6(5*H*)-ones (1a-5a) and urea derivatives (1b, 2b, 4b, 5b):

To a 25 mL oven dried schlenk round bottom flask, was added 2-(1*H*-indol-1-yl)anilines (0.5 mmol) and acetic acid (4 mL). To this clear solution, $Pd(OAc)_2$ (10 mol%) and $Cu(OAc)_2$ (1 equiv.) were added. Reaction mixture was flushed thrice with carbon monoxide from a balloon and stirred at 80°C under CO atmosphere. Progress of the reaction was monitored by TLC. After stirring for required time period (Table **1**) reaction mixture was cooled to room temperature. Solvent was evaporated through rotavapor and crude compound was diluted with AcOEt followed by quenched with bicarbonate solution. Organic layer was dried under Na_2SO_4 and crude compound was purified by column chromatography (eluant: ethyl acetate/ hexane various ratios).

Spectral data

Indolo[1,2-a]quinoxalin-6(5*H*)-one (1a): [18]

Pale yellow solid, yield 31% (72mg), Mp: 212-214 °C (Lit 215-216 °C), ^{1}H NMR (400 MHz, DMSO-d6): δ 11.57 (s, 1H), 8.53 (d, *J* = 8.4 Hz, 1H), 8.50-8.48 (m, 1H), 7.93 (d, *J* = 8.4 Hz,1H), 7.56-7.52 (m, 1H), 7.49 (s, 1H), 7.40-7.36 (m, 2H), 7.33-7.27 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d6): δ 156.2, 134.2, 129.0, 128.8, 128.5, 125.8, 125.3, 124.8, 123.6, 123.3, 122.7, 117.1, 115.9, 115.0, 105.8; IR (KBr): cm^{-1} 1674; HRMS (ESI, m/z) Calcd for $C_{15}H_{10}N_2ONa$ 257.0685 (M+Na), found 257.068.

1,3-bis(2-(1*H*-indol-1-yl)phenyl)urea (1b):

Light brown solid, yield 10% (21 mg), Mp: 152-155 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (d, *J* = 8.4 Hz, 1H), 7.55-7.53 (m, 1H), 7.28-7.23 (m, 1H) , 7.13-7.11 (m, 1H), 7.08-7.01 (m, 3H), 6.88-6.87 (m, 2H), 6.47 (d, *J* = 3.2 Hz,1H), 6.19 (d, *J* = 5.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.2, 136.7, 134.9, 129.2, 129.0, 128.59, 128.52, 128.28, 124.1, 122.9, 122.3, 121.1, 120.7, 110.3, 104.0; IR (KBr): cm^{-1} 3272, 2923, 2855, 1647, 1597, 1546, 1457; HRMS (ESI, m/z) Calcd for $C_{29}H_{23}N_4O$ 443.1866 (M+H), found 443.1866.

2-methylindolo[1,2-a]quinoxalin-6(5*H*)-one (2a): [19]

White solid, yield 20% (50 mg), Mp: 210-222 °C, ^{1}H NMR (400 MHz, DMSO-d6): δ 11.50 (s, 1H), 8.56 (d, *J* = 8.8 Hz 1H), 8.24 (s, 1H), 7.91 (d, *J* = 8 Hz, 1H), 7.55-7.51 (m, 1H), 7.47 (s, 1H), 7.39-7.36 (m, 1H), 7.24 (d, *J* = 8 Hz, 1H), 7.09 (d, *J* = 8 Hz, 1H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d6): δ 155.8, 133.8, 132.9, 128.7, 128.5, 125.8, 125.5 125.2, 124.9, 122.9, 122.4, 116.6, 115.6, 114.9, 105.5, 20.9; IR (KBr): cm^{-1} 1673; HRMS (ESI, m/z) Calcd for $C_{16}H_{13}N_2O$ 249.1028 (M+H), found 249.1043.

1,3-bis(2-(1*H*-indol-1-yl)-4methylphenyl)urea (2b):

Light orange solid, yield 31% (71 mg), Mp: 97- 99 °C, ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.73 (d, *J* = 8 Hz,1H), 7.63-7.61 (m, 1H), 7.15-7.08 (m, 3H), 7.01 (d, *J* = 1.5 Hz, 1H), 6.95-6.94 (m, 2H), 6.55 (d, *J* = 3 Hz, 1H), 6.1 (s, 1H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 125.6, 136.6, 134.4, 131.9, 129.8, 129.4, 128.6, 128.5, 122.8, 121.1, 120.6, 110.3, 103.8, 20.7; IR (KBr): cm^{-1} 3353, 2924, 2853, 1670, 1598, 1524, 1459; HRMS (ESI, m/z) Calcd for $C_{31}H_{26}N_4ONa$ 493.2004 (M+Na), found 493.1984.

***2-tert*-butylmethylindolo[1,2-a]quinoxalin-6(5*H*)-one (3a):**

light brown solid, yield 41% (119 mg), Mp: 200-202 °C, ^{1}H NMR (400 MHz, DMSO-d6): δ 11.49 (s, 1H), 8.33 (d, *J* = 8.8Hz, 1H) 8.26 (s, 1H), 7.91 (s, 8 Hz, 1H), 7.59-7.55 (m, 1H), 7.46 (s, 1H), 7.38-7.29 (m, 3H), 1.38 (s, 9H); ^{13}C NMR (100 MHz, DMSO-d6): δ 156.2, 146.2, 134.0, 129.2, 128.9, 126.2, 126.0, 125.0, 123.4, 122.6, 122.0, 116.9, 114.6,

112.0, 105.8, 34.9, 31.6; IR (KBr): cm^{-1} 1699; HRMS (ESI, m/z) Calcd for $C_{19}H_{18}N_2ONa$ 313.1317 (M+Na), found 313.1299.

9-chloroindolo[1,2-a]quinoxalin-6(5*H*)-one (4a):

Half white solid, yield 18% (48 mg), Mp: 242-245 °C, ^1H NMR (500 MHz, DMSO-d6): δ 11.65 (s,1H), 8.54 (d, *J* = 9.5 Hz, 1H), 8.43-8.41 (m, 1H), 7.98 (d, *J* = 2 Hz, 1H), 7.49 (dd, *J* = 2 Hz, 9 Hz, 1H), 7.45 (s, 1H), 7.38-7.35 (m, 1H), 7.32-7.28 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d6): δ 155.5, 132.1, 129.9, 129.6, 128.1, 126.8, 125.1, 124.8, 124.5, 123.3, 121.8, 116.8, 116.2, 115.5, 104.8; IR (KBr): cm^{-1} 1675; HRMS (ESI, m/z) Calcd for $C_{15}H_{10}N_2OCl$ 269.0476 (M+H), found 269.0474.

1,3-bis(2-(5-chloro-1*H*-indol-1-yl)phenyl)urea (4b):

Light orange solid, yield 27% (67 mg), Mp: 170-175 °C, ^1H NMR (500 MHz, $CDCl_3$): δ 7.81 (d, *J* = 7.5 Hz, 1H), 7.48 (s, 1H), 7.26-7.23 (m, 1H), 7.11-7.05(m, 2H), 6.97 (d, *J* = 9 Hz, 1H), 6.87 (s, 1H), 6.75 (d, *J* = 8.5 Hz, 1H), 6.4 (s, 1H), 6.13 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.1, 135.0, 134.4, 129.8, 129.5, 129.4, 128.7, 128.1, 126.4, 124.4, 123.1, 122.6, 120.6, 111.3, 103.5; IR (KBr): cm^{-1} 3278, 2927, 2855, 1683, 1599, 1530, 1460. HRMS (ESI, m/z) Calcd for $C_{29}H_{21}N_4OCl_2$ 511.1087 (M+H), found 511.1090.

7-methylindolo[1,2-a]quinoxalin-6(5*H*)-one (5a):

Half white solid, yield 16% (40 mg), Mp: 216-220 °C, ^1H NMR (500 MHz, DMSO-d6): δ 11.31 (s, 1H), 8.84 (dd, *J* = 8.5 Hz, 1.6Hz, 1H), 8.38 (d, *J* = 7.5 Hz, 1H), 7.88(dd, *J* = 1.5 Hz, 8 Hz, 1H), 7.55-7.51 (m, 1H), 7.39-7.35 (m, 1H), 7.30-7.29 (m. 1H), 7.26-7.22(m, 2H), 2.76 (d, *J* = 3 Hz, 3H); ^{13}C NMR (125 MHz, DMSO-d6): δ 157.4, 132.5, 129.2, 128.1, 125.9, 125.2, 123.9, 123.2, 123.0, 121.7, 120.8, 117.2, 116.3, 115.2, 114.3, 9.56; IR (KBr): cm^{-1} 1671; HRMS (ESI, m/z) Calcd for $C_{16}H_{13}N_2O$ 249.1022 (M+H), found 249.1027.

1,3-bis(2-(3-methyl-1*H*-indol-1-yl)phenyl)urea (5b):

Yellow solid, yield 31% (70 mg), Mp: 82 - 85 °C, ^1H NMR (400 MHz, $CDCl_3$): δ 7.88 (d, *J* = 7.6 Hz, 1H), 7.47-7.45 (m, 1H), 7.23-7.18 (m, 1H), 7.1-6.98 (m, 4H), 6.82 (dd, *J* = 7.2 Hz, 1.6 Hz, 1H), 6.65 (d, *J* = 1.2 Hz,1H), 6.13 (s, 1H), 2.19 (d, *J* = 1.2Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.2, 137.0, 134.7, 129.3, 129.1, 128.8, 128.2, 125.9, 124.1, 122.8, 122.1, 120.1, 119.3, 113.4, 110.1, 9.7; IR (KBr): cm^{-1} 3346, 2922, 2856, 1681, 1595, 1528, 1455; HRMS (ESI, m/z) Calcd for $C_{31}H_{26}N_4ONa$ 493.2004 (M+Na), found 493.2007.

General procedure for selective synthesis of indolo[1,2,-a]quinoxlin-6(5*H*)-ones (8a-21a, 23a-31a) and pyrrolo[1,2,-a]quinoxlin-4(5*H*)-ones (34a-39a)

To a 25 mL oven dried Schlenk round bottom flask were added 2-(1*H*-indol-1-yl)aniline derivative or 2-(1*H*-pyrrol-1-yl)aniline derivative (0.5 mmol, 1 equiv.) and $Cu(OAc)_2$ (2 equiv.) followed by toluene (4 mL). Then $Pd(OCOCF_3)_2$ (10 mol%) was added. The reaction mixture was flushed thrice with carbon monoxide from a balloon and stirred at 80 °C under a CO/O_2 balloon atmosphere for 24h. The reaction mixture was cooled to room temperature and diluted with EtOAc (10 mL) then passed through a Celite pad, and washed with EtOAc (20 mL). The combined filtrate was concentrated under vacuum, and the crude product was purified by column chromatography on silica gel (eluant: ethyl acetate/hexane).

Spectral data

5-methylindolo[1,2-*a*]quinoxalin-6(5*H*)-one (8a)[16]:

White solid, yield 75% (93 mg), Mp: 157-159 °C, ^1H NMR (400 MHz, $CDCl_3$): δ 8.34-8.32 (m, 1H), 8.25 (dd, *J* = 8.7 Hz, 0.6Hz, 1H), 7.87 (d, *J* = 8 Hz, 1H), 7.57 (d, *J* = 0.8 Hz, 1H), 7.52-7.40 (m, 1H), 7.38-7.30 (m, 4H), 7.18 (s, 1H), 3.69 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.7, 134.3, 129.9, 129.3, 128.2, 126.8, 125.4, 124.3, 123.4, 123.3, 122.5, 115.7, 115.5, 114.3, 107.0, 29.0; IR (KBr): cm^{-1}1651; HRMS (ESI, m/z) Calcd for $C_{16}H_{13}N_2O$ 248.095 (M+H), found 248.0947.

2,5-dimethylindolo[1,2-*a*]quinoxalin-6(5*H*)-one (9a): [16]

White solid, yield 81% (106 mg), Mp: 180-182 °C, ^1H NMR (400 MHz, $CDCl_3$): δ 8.23 (d, *J* = 8.8 Hz, 1H), 8.10 (s, 1H), 7.86 (d, *J* = 7.6 Hz, 1H), 7.54 (s, 1H), 7.51-7.47 (m, 1H), 7.36-7.33 (m, 1H), 7.20 (d, *J* = 8.0 Hz, 1H), 7.08 (d, *J* = 8.4 Hz, 1H), 3.66 (s, 3H), 2.49 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.6, 134.3, 133.2, 129.3, 128.3, 127.6, 126.6, 125.2, 124.8, 123.2, 122.4, 116.0, 115.5, 114.4, 106.8, 29.0, 21.3; IR (KBr): cm^{-1}1647; HRMS (ESI, m/z) Calcd for $C_{17}H_{15}N_2O$ 263.1179 (M+H), found 263.1175.

2-isopropyl-5-methylindolo[1,2-*a*]quinoxalin-6(5*H*)-one (10a):

White crystalline solid, yield 68% (98 mg), Mp: 189-191 °C, ^1H NMR (400 MHz, $CDCl_3$): δ 8.17 (d, *J* = 8.4 Hz, 1H), 8.13 (s, 1H), 7.79 (d, *J* = 8 Hz, 1H), 7.48 (s, 1H), 7.45-7.41 (m, 1H), 7.29-7.25 (m, 1H), 7.18 (d, *J* = 7.6 Hz, 1H), 7.10 (d, *J* = 8.4 Hz, 1H), 3.60 (s, 3H), 3.0 (m, 1H), 1.3 (d, *J* = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.6, 144.4, 134.3, 129.4, 128.4, 127.9, 126.7, 125.3, 123.3, 122.4, 122.2, 115.6, 114.3, 113.6, 106.8, 33.9, 29.0, 24.3; IR (KBr): cm^{-1}1649; HRMS (ESI, m/z) Calcd for $C_{19}H_{19}N_2O$ 291.1492 (M+H), found 291.1489.

2-*tert*-butyl-5-methylindolo[1,2-*a*]quinoxalin-6(5*H*)-one (11a):

White solid, yield 61% (93 mg), Mp: 231-233 °C, ^1H NMR (400 MHz, $CDCl_3$): δ 8.39 (s, 1H), 8.24 (d, *J* = 8.4 Hz, 1H), 7.88 (d, *J* = 8 Hz, 1H), 7.57 (s, 1H), 7.54-7.50 (m, 1H), 7.38-7.29 (m, 3H), 3.69 (s, 3H), 1.4 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.7, 146.7, 134.2, 129.4, 128.4, 127.6, 126.5, 125.3, 123.4, 122.4, 121.3, 115.3, 114.2, 112.7, 106.8, 34.9, 31.6, 29.0; ; IR (KBr): cm^{-1}1654; HRMS (ESI, m/z) Calcd for $C_{20}H_{21}N_2O$ 305.1648(M+H), found 305.1643.

2,4,5-trimethylindolo[1,2-*a*]quinoxalin-6(5*H*)-one (12a):

White solid, yield 72% (99 mg), Mp: 121-123 °C, ^1H NMR (400 MHz, $CDCl_3$): δ 8.15 (d, *J* = 8.8 Hz, 1H), 7.91 (s, 1H), 7.78 (d, *J* = 8 Hz, 1H), 7.44-7.40 (m, 2H), 7.28-7.24 (m, 1H), 6.84 (s, 1H), 3.64 (s, 3H), 2.53 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.7, 134.4, 133.7, 129.6, 129.5, 129.1, 128.3, 128.2, 127.7, 125.2, 123.3, 122.4, 114.6, 114.1, 106.8, 37.5, 23.1, 21.2; ; IR (KBr): cm^{-1}1647; HRMS (ESI, m/z) Calcd for $C_{18}H_{16}N_2ONa$ 299.1155 (M+Na), found 299.1165.

2-fluoro-5-methylindolo[1,2-*a*]quinoxalin-6(5*H*)-one (13a): [16]

White solid, yield 64% (85 mg), Mp: 216-218 °C, ^1H NMR (400 MHz, $CDCl_3$): δ 8.15 (d, *J* = 8.4 Hz, 1H), 8.03 (d, *J* = 10.4 Hz, 1H), 7.87 (d, *J* = 8.0 Hz, 1H), 7.56 (s, 1H), 7.54-7.50 (m, 1H), 7.40-7.36 (m, 1H), 7.30-7.28 (m, 1H), 7.04-7.00 (m, 1H), 3.68 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.8, 157.4, 156.2, 134.2, 129.4, 128.0, 127.3, 127.2, 126.4, 125.8, 123.4, 122.9, 116.6, 116.5, 113.9, 110.6, 110.4, 107.6, 103.4, 103.1, 29.2; IR (KBr): cm^{-1}1655; HRMS (ESI, m/z) Calcd for $C_{16}H_{11}N_2OFNa$ 289.0753 (M+Na), found 289.0757.

2-chloro-5-methylindolo[1,2-*a*]quinoxalin-6(5*H*)-one (14a): [16]

Light orange solid, yield 67% (94 mg), Mp: 261-263 °C, ^1H NMR (400 MHz, $CDCl_3$): δ 8.25 (s, 1H), 8.16 (d, *J* = 8.8 Hz, 1H), 7.87 (d, *J* = 8.0 Hz, 1H), 7.56 (s, 1H), 7.52 (d, *J* = 8.4 Hz, 1H), 7.40-7.36 (m, 1H), 7.26 (s,

2H), 3.67 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.3, 134.2, 129.4, 128.8, 128.7, 127.9, 127.4, 125.9, 124.0, 123.5, 123.0, 116.6, 115.5, 114.1, 107.7, 29.2; ; IR (KBr): cm^{-1}1652; HRMS (ESI, m/z) Calcd for $C_{16}H_{12}N_2OCl$ 283.0638 (M+H), found 283.0627.

5-methyl-6-oxo-5,6-dihydroindolo[1,2-*a*]quinoxaline-2-carbonitrile (15a):

White solid, yield 15% (21 mg), Mp: 240-242 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.53 (s, 1H), 8.18 (d, *J* = 8.8 Hz, 1H), 7.9 (d, *J* = 8.0 Hz, 1H), 7.61-7.58 (m, 3H), 7.45-7.0 (m, 2H), 3.71(s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.3, 134.3, 133.6, 129.4, 128.1, 127.4, 127.0, 126.6, 123.7, 123.4, 118.6, 118.5, 116.2, 114.0, 108.6, 106.5, 29.3; IR (KBr): cm^{-1} 2235, 1669; HRMS (ESI, m/z) Calcd for $C_{17}H_{11}N_3ONa$ 296.0800 (M+Na), found 296.0818.

5,9-dimethylindolo[1,2-*a*]quinoxalin-6(5*H*)-one (16a): [15]

Pale brown solid, yield 76% (99 mg), Mp: 200-202 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.24 (d, *J* = 8.0 Hz, 1H), 8.07 (d, *J* = 8.8 Hz, 1H), 7.61 (s, 1H), 7.46 (s, 1H), 7.32-7.26 (m, 4H), 3.67 (s, 3H), 2.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.73, 132.7, 132.0, 129.8, 129.6, 128.1, 127.2, 126.8, 124.0, 123.3, 122.6, 115.5, 115.3, 113.9, 106.4, 29.0, 21.4; ; IR (KBr): cm^{-1}1649; HRMS (ESI, m/z) Calcd for $C_{17}H_{15}N_2O$ 263.1179 (M+H), found 263.1187.

9-methoxy-5-methylindolo[1,2-*a*]quinoxalin-6(5*H*)-one (17a): [16]

White solid, yield 78% (108 mg), Mp: 166-168 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ δ 8.28 (s, 1H), 8.14 (d, *J* = 8.8 Hz, 1H), 7.50 (s, 1H), 7.37-7.26 (m, 4H), 7.15 (d, *J* = 8.8 Hz, 1H), 3.93 (s, 3H), 3.72 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.5, 155.6, 130.2, 129.8, 129.5, 128.5, 126.6, 124.0, 123.3, 116.4, 115.6, 115.18, 115.10, 106.3, 103.2, 55.7, 29.0; IR (KBr): cm^{-1}1655; HRMS (ESI, m/z) Calcd for $C_{17}H_{15}N_2O_2$ 279.1128 (M+H), found 279.1136.

9-chloro-5-methylindolo[1,2-*a*]quinoxalin-6(5*H*)-one (18a): [16]

White crystalline solid, yield 70% (98 mg), Mp: 206-208 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.19-8.17 (m, 1H), 8.09 (d, *J* = 9.2 Hz, 1H), 7.76 (s, 1H), 7.433 (s, 1H), 7.39 (d, *J* = 9.2 Hz, 1H), 7.34-7.30 (m, 3H), 3.68 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.2, 132.4, 130.2, 129.9, 129.2, 128.2, 126.3, 125.6, 124.6, 123.4, 122.3, 115.8, 115.3, 115.2, 106.1, 29.1; IR (KBr): cm^{-1}1657; HRMS (ESI, m/z) Calcd for $C_{16}H_{11}N_2OClNa$ 305.0452 (M+Na), found 305.0454.

10-chloro-5-methylindolo[1,2-*a*]quinoxalin-6(5*H*)-one (19a):

Light orange solid, yield 66% (93 mg), Mp: 235-237 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.19 (s, 1H), 8.18-8.16 (m, 1H), 7.76 (d, *J* = 8.4 Hz, 1H), 7.50 (s, 1H), 7.34-7.30 (m, 4H), 3.68 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.4, 134.2, 131.2, 130.0, 128.8, 127.7, 126.3, 124.7, 124.0, 123.5, 123.4, 115.8, 115.4, 114.2, 106.8, 29.1; ; IR (KBr): cm^{-1}1656; HRMS (ESI, m/z) Calcd for $C_{16}H_{12}N_2OCl$ 283.0633 (M+H), found 283.0627.

5,7-dimethylindolo[1,2-*a*]quinoxalin-6(5*H*)-one (20a):

White solid, yield 51% (67 mg), Mp: 201-203 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.24-8.22 (m, 1H), 8.18 (d, *J* = 8.4 Hz, 1H), 7.84 (d, *J* = 8 Hz, 1H), 7.52-7.49 (m, 1H), 7.38-7.34 (m, 1H), 7.29-7.26 (m, 3H), 3.63 (s, 3H), 2.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.0, 132.9, 130.2, 130.0, 127.0, 125.7, 123.7, 123.2, 123.1, 121.8, 121.1, 119.1, 115.3, 115.1, 114.1, 28.6, 10.0; IR (KBr): cm^{-1}1639; HRMS (ESI, m/z) Calcd for $C_{17}H_{15}N_2O$ 263.1179 (M+H), found 263.1179.

5-methyl-7-azaindolo[1,2-*a*]quinoxalin-6(5*H*)-one (21a):

White solid, yield 35% (44 mg), Mp: 201-203 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.84 (d, *J* = 8.0 Hz, 1H), 8.63 (d, *J* = 4.4 Hz, 1H), 8.18 (d, *J* = 8 Hz, 1H), 7.47 (s, 1H), 7.39-7.30 (m, 4H), 3.72 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.5, 146.8, 145.8, 131.0, 129.4, 127.3, 125.8, 124.8, 123.8, 121.3, 118.5, 118.4, 115.0, 103.4, 29.1; IR (KBr): cm^{-1}1662; HRMS (ESI, m/z) Calcd for $C_{15}H_{12}N_3O$ 250.0975 (M+H), found 250.0984.

9-chloro-2,5-dimethylindolo[1,2-*a*]quinoxalin-6(5*H*)-one (23a): [15]

White crystalline solid, yield 68% (100 mg), Mp: 236-238 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08 (d, *J* = 8.8 Hz, 1H), 7.95 (s, 1H), 7.76 (d, *J* = 1.6 Hz, 1H), 7.41 (s, 1H), 7.39 (dd, *J* = 2 Hz, 9.2 Hz 1H), 7.21 (d, *J* = 8.4 Hz, 1H), 7.11 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.1, 133.4, 132.4, 130.3, 129.4, 128.1, 127.6, 126.1, 125.4, 125.3, 122.3, 115.8, 115.7, 115.3, 105.9, 29.0, 21.3; IR (KBr): cm^{-1}1654; HRMS (ESI, m/z) Calcd for $C_{17}H_{13}N_2OClNa$ 319.0609 (M+Na), found 319.0621.

2-*tert*-butyl-9-chloro-5-methylindolo[1,2-*a*]quinoxalin-6(5*H*)-one (24a):

Light cream solid, yield 59% (99 mg), Mp: 146-148 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.26 (s, 1H), 8.11 (d, *J* = 9.2 Hz, 1H), 7.79 (s, 1H), 7.45-7.29 (m, 4H), 3.69 (s, 3H), 1.46 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.3, 146.9, 132.4, 130.4, 129.5, 128.1, 127.6, 126.0, 125.6, 122.4, 121.8, 115.5, 115.1, 112.5, 105.9, 34.9, 31.6, 29.0; IR (KBr): cm^{-1}1657; HRMS (ESI, m/z) Calcd for $C_{20}H_{20}N_2OCl$ 339.1259 (M+H), found 339.1265.

9-chloro-2,4,5-trimethylindolo[1,2-*a*]quinoxalin-6(5*H*)-one (25a):

White crtstalline solid, yield 60% (93 mg), Mp: 175-177 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09 (d, *J* = 9.2 Hz, 1H), 7.83 (s, 1H), 7.77 (s, 1H), 7.40-7.38 (m, 2H), 6.92 (s, 1H), 3.70 (s, 3H), 2.60 (s, 3H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.2, 133.8, 132.5, 130.6, 130.1, 129.9, 128.2, 128.0, 127.89, 127.85, 125.4, 122.3, 115.5, 113.9, 105.9, 37.5, 23.1, 21.2; IR (KBr): cm^{-1}1653; HRMS (ESI, m/z) Calcd for $C_{18}H_{16}N_2OCl$ 311.0946 (M+H), found 311.0951.

9-methoxy-2,5-dimethylindolo[1,2-*a*]quinoxalin-6(5*H*)-one (26a):

White solid, yield 75% (109 mg), Mp: 186-188 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09 (d, *J* = 9.2 Hz, 1H), 8.0 (s, 1H), 7.44 (s, 1H), 7.21-7.18 (m, 2H), 7.11 (d, *J* = 9.2 Hz, 1H), 7.07 (d, *J* = 8 Hz, 1H), 3.90 (s, 3H), 3.65 (s, 3H), 2.48 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.4, 155.5, 133.2, 130.2, 129.4, 128.7, 127.5, 126.5, 124.6, 116.2, 115.6, 115.4, 115.2, 106.1, 103.1, 55.7, 28.9, 21.3; IR (KBr): cm^{-1}1649; HRMS (ESI, m/z) Calcd for $C_{18}H_{17}N_2O_2$ 293.1290 (M+H), 293.1260.

9-methoxy-2,4,5-trimethylindolo[1,2-*a*]quinoxalin-6(5*H*)-one (27a):

Pale yellow solid, yield 71% (109 mg), Mp: 151-153 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04 (d, *J* = 9.2 Hz, 1H), 7.83 (s, 1H), 7.36 (s, 1H), 7.18-7.15 (m, 2H), 7.06 (d, *J* = 9.2 Hz, 1H), 6.83 (s, 1H), 3.83 (s, 3H), 3.64 (s, 3H), 2.53 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.5, 155.5, 133.6, 130.5, 129.5, 129.4, 129.3, 128.2, 128.1, 127.6, 116.2, 115.4, 113.7, 106.2, 103.3, 55.7, 37.5, 23.1, 21.1; IR (KBr): cm^{-1}1652; HRMS (ESI, m/z) Calcd for $C_{19}H_{19}N_2O_2$ 307.1447 (M+H), found 307.1442.

2-*tert*-butyl-9-methoxy-4,5-dimethylindolo[1,2-*a*]quinoxalin-6(5*H*)-one (28a):

light orange crystalline solid, yield 63% (105 mg), Mp: 196-198 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.31 (s, 1H), 8.12 (d, *J* = 9.2 Hz, 1H), 7.48 (s,

View Article Online
DOI: 10.1039/C9OB02703C

1H), 7.35-7.28 (m, 2H), 7.26 (s, 1H), 7.16 (dd, *J* = 9.2 Hz, 2.4Hz, 1H), 3.92 (s, 3H), 3.70 (s, 3H), 1.46 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.5, 155.5, 146.7, 130.3, 129.4, 128.8, 127.4, 126.4, 121.1, 116.4, 115.3, 115.0, 112.3, 106.2, 103.3, 55.7, 34.9, 31.6, 28.9; IR (KBr): cm^{-1}1660; HRMS (ESI, m/z) Calcd for $C_{21}H_{23}N_2O$ 335.1754 (M+H), found 335.1758.

2,5,7-trimethylindolo[1,2-*a*]quinoxalin-6(5*H*)-one (29a):

White solid, yield 55% (76 mg), Mp: 181-183 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.4 (d, *J* = 8.4 Hz, 1H), 8.05 (s, 1H), 7.83 (d, *J* = 8 Hz, 1H), 7.52-7.48 (m, 1H), 7.37-7.33 (m, 1H), 7.16 (d, *J* = 8.4 Hz, 1H), 7.04 (d, *J* = 8 Hz, 1H), 3.61 (s, 3H), 2.85 (s, 3H), 2.48 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.0, 133.0, 132.9, 130.3, 127.8, 126.9, 125.6, 124.3, 123.4, 121.7, 121.1, 119.0, 115.7, 115.2, 114.2, 28.6, 21.3, 10.0; IR (KBr): cm^{-1}1635; HRMS (ESI, m/z) Calcd for $C_{18}H_{16}N_2ONa$ 299.1160 (M+Na), found 299.1183.

2,5-dimethyl-7-azaindolo[1,2-*a*]quinoxalin-6(5*H*)-one (30a):

White solid, yield 38% (50 mg), Mp: 216-218 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.66 (s, 1H), 8.64 (d, *J* = 4.4 Hz, 1H),, 8.17 (d, *J* = 8 Hz, 1H), 7.45 (s, 1H), 7.33-7.30 (m, 1H), 7.21 (d, *J* = 8.4 Hz, 1H), 7.12 (d, *J* = 8.4 Hz, 1H), 3.70 (s, 3H), 2.53 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.4, 146.8, 145.7, 133.8, 130.9, 127.5, 127.2, 125.7, 125.5, 121.3, 118.7, 118.4, 114.8, 103.3, 29.0, 21.3; IR (KBr): cm^{-1}1659; HRMS (ESI, m/z) Calcd for $C_{16}H_{14}N_3O$ 264.1137 (M+H), found 264.1145.

5-phenylindolo[1,2-*a*]quinoxalin-6(5*H*)-one (31a): [18]

White solid, yield 27% (42 mg), Mp: 201-203 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.32 (d, *J* = 8.4 Hz, 1H), 8.25 (d, *J* = 8.8 Hz, 1H), 7.83 (d, *J* = 8 Hz, 1H), 7.58 (s, 1H), 7.56-7.52 (m, 2H), 7.48-7.45 (m, 2H), 7.33-7.28 (m, 3H), 7.24-7.20 (m, 1H), 7.03-6.99 (m, 1H), 6.64 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.6, 136.7, 134.6, 131.2, 130.3, 129.45, 129.41, 129.2, 128.4, 126.6, 125.6, 123.9, 123.58, 123.50, 122.6, 117.8, 115.5, 114.3, 107.7; IR (KBr): cm^{-1}1656; HRMS (ESI, m/z) Calcd for $C_{21}H_{15}N_2O$ 311.1184 (M+H), found 311.1166.

5-methylpyrrolo[1,2-*a*]quinoxalin-4(5*H*)-one (34a): [15]

White crystalline solid, yield 81% (80 mg), Mp: 126-128 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, *J* = 8 Hz, 1H), 7.63 (s, 1H), 7.34-7.29 (m, 2H), 7.24-7.21 (m, 2H), 6.65-6.64 (m, 1H), 3.65 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.7, 130.4, 125.6, 124.1, 123.4, 122.9, 116.0, 115.7, 114.5, 113.3, 112.7, 28.5; IR (KBr): cm^{-1}1645; HRMS (ESI, m/z) Calcd for $C_{12}H_{11}N_2O$ 199.0871 (M+H), found 199.0856.

5,8-dimethylpyrrolo[1,2-*a*]quinoxalin-4(5*H*)-one (35a): [15]

White crystalline solid, yield 94% (97 mg), Mp: 152-154 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62-7.61 (m, 1H), 7.47 (d, *J* = 0.8 Hz, 1H), 7.21-7.18 (m, 2H), 7.13-7.11 (m, 1H), 6.64-6.63 (m, 1H), 3.64 (s, 3H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.6, 132.9, 128.1, 126.4, 123.8, 123.5, 115.9, 115.6, 114.9, 113.1, 112.5, 28.5, 21.0; IR (KBr): cm^{-1}1641; HRMS (ESI, m/z) Calcd for $C_{13}H_{13}N_2O$ 213.1028 (M+H), found 213.1038.

8-isopropyl-5-methylpyrrolo[1,2-*a*]quinoxalin-4(5*H*)-one (36a):

Color less oil, yield 72% (86 mg), Mp: 100-102 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (dd, *J* = 1.6 Hz, 2.4 Hz 1H), 7.51 (d, *J* = 1.6 Hz, 1H), 7.23 (s, 1H), 7.21-7.18 (m, 2H), 6.65-6.64 (m, 1H), 3.65 (s, 3H), 3.01 (m, 1H), 1.31 (d, *J* = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.6, 144.1, 128.4, 123.9, 123.8, 123.5, 115.9, 115.7, 113.1, 112.6, 112.4, 33.8, 28.5, 2.1; IR (KBr): cm^{-1}1640; HRMS (ESI, m/z) Calcd for $C_{15}H_{17}N_2O$ 241.1341 (M+H), found 241.1367.

8-chloro-5-methylpyrrolo[1,2-*a*]quinoxalin-4(5*H*)-one (37a): [15]

White solid, yield 83% (96 mg), Mp: 196-198 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61 (d, *J* = 2.0 Hz, 1H), 7.56-7.55 (m, 1H), 7.28-7.26 (m, 1H), 7.22-7.20 (m, 2H), 6.67-6.65 (m, 1H), 3.63 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.3, 129.1, 128.4, 125.5, 124.7, 123.3, 116.8, 116.3, 114.7, 113.8, 113.4, 28.6; IR (KBr): cm^{-1}1647; HRMS (ESI, m/z) Calcd for $C_{12}H_{10}N_2OCl$ 233.0476 (M+H), found 233.0481.

8-fluoro-5-methylpyrrolo[1,2-*a*]quinoxalin-4(5*H*)-one (38a):

White crystalline solid, yield 82% (88 mg), Mp: 213-215 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53 (s, 1H), 7.37 (dd, *J* = 2.8 Hz, 9.2 Hz 1H), 7.27-7.21 (m, 2H), 7.06-7.01 (m, 1H), 6.67-6.66 (m, 1H), 3.64 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.7, 157.2, 155.3, 126.9, 124.8, 124.7, 123.4, 117.0, 116.9, 116.3, 113.8, 113.3, 112.5, 112.3, 102.2, 101.9, 28.7; IR (KBr): cm^{-1}1649; HRMS (ESI, m/z) Calcd for $C_{12}H_{10}N_2OF$ 217.0777 (M+H), found 217.0778.

5-methyl-4-oxo-4,5-dihydropyrrolo[1,2-*a*]quinoxaline-8-carbonitrile (39a):

White solid, yield 47% (52 mg), Mp: 221-223 °C, ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.63 (s, 1H), 8.24 (s, 1H), 7.77 (d, *J* = 6.4 Hz, 1H), 7.59 (s, 1H), 7.07 (s, 1H), 6.71 (s, 1H), 3.54 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 154.3, 133.5, 129.4, 123.6, 122.3, 119.0, 118.7, 118.6, 117.1, 113.7, 112.8, 104.7, 28.5; IR (KBr): cm^{-1} 2232, 1665; HRMS (ESI, m/z) Calcd for $C_{13}H_{10}N_3O$ 224.0824 (M+H), found 224.0821.

Isolation of intermediate complex 26c

To a 10 mL oven dried reaction tube were added 2-(5-methoxy-1*H*-indol-1-yl)-N,4-dimethylaniline **26** (0.75 mmol, 200 mg) and toluene (4 mL). Then $Pd(OAc)_2$ (1 equiv., 168 mg) was added. The reaction mixture was stirred at room temperature. After 24 h, yellow precipitate was formed in reaction medium. Precipitate was filtered through Whatman filter paper and washed with hexane. Collected yellow solid (**26c**) was dried at room temperature. To isolate the total amount of complex **26c,** filtrate (mother liquor) was concentrated using rotavapor. Concentrated crude mixture was dissolved in minimum amount of toluene and 10 mL of hexane was added to obtain complex **26c** as a yellow color precipitate. Then filtered through Whatman filter paper and washed with hexane. Collected yellow solid (**26c**) was dried at room temperature and finally combined yellow precipitate **26c** dried under high vacuum. The complex **26c** was isolated in 78% yield (186 mg).

Spectral data

Intermediate complex (26c):

Yellow solid, yield 78% (186 mg), Mp: 197-199 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.22 (d, *J* = 5.6 Hz, 1H), 7.52 (d, *J* = 9.2 Hz, 1H), 7.34 (d, *J* = 2.4 Hz, 1H), 7.29 (s, 1H), 7.14 (d, *J* = 8.0 Hz, 1H), 6.99 (dd, *J* = 9.2 Hz, 2.4 Hz, 1H), 6.86 (d, *J* = 8.0 Hz, 1H), 6.75 (s, 1H), 3.90 (s, 3H), 2.70 (d, *J* = 5.2 Hz, 3H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.0, 139.0, 137.3, 136.2, 135.6, 134.0, 126.4, 123.8, 123.3, 120.7, 114.6, 111.6, 105.6, 88.4, 56.0, 43.2, 21.4; HRMS (ESI, m/z) Calcd for $C_{34}H_{35}N_4O_2Pd$ 637.1795 (M+H), found 637.1768.

CO insertion and conversion of Intermediate complex 26c to 26a :

Complex **26c** (0.292 mmol, 186 mg) was taken in a 25 mL oven dried Schlenk round bottom flask and toluene (3 mL) was added. The

reaction mixture was flushed three times with 'CO' from the balloon and stirred at 80 °C under a CO balloon. After 24h the reaction mixture was cooled to room temperature and diluted with EtOAc (10 mL) then passed through a Celite pad, and washed with EtOAc (20 mL). The combined filtrate was concentrated under vacuum, and the crude product was purified by column chromatography on silica gel to get **26a** in 86% yield (147 mg).

Conflicts of interest

There are no conflicts to declare

Acknowledgements

We thank the Department of Chemistry, IIT Madras for infrastructure and SAIF, IIT Madras for XRD data, and IIT Madras for financial support. AC thanks the UGC, New Delhi for a fellowship.

Notes and references

1. A) Reviews on carbonylation: a) M. D. Mihovilovic, P. Stanetty, *Angew. Chem., Int. Ed*. **2007**, *46*, 3612; b) C. F. T. Barnard, *Organometallics*. **2008**, *27*, 5402; c) A. Brennfuhrer, H. Neumann, M. Beller, *ChemCatChem.* **2009**, *1*, 28; d) A. Brunnführer, H. Newmann, M. Beller, *Angew. Chem., Int. Ed.,* **2009**, *48*, 4114; e) R. Grigg, S. P. Mutton, *Tetrahedron*. **2010**, *66*, 5515; f) Q. Liu, H. Zhang, A. Lei, *Angew. Chem., Int. Ed*. **2011**, *50*, 10788; g) X. -F. Wu, H. Neumann, M. Beller, *Chem. Soc. Rev*. **2011**, *40*, 4986; h) X. -F. Wu, H. Neumann, M. Beller, *Chem. Rev*. **2013**, *113*, 1; i) S. T. Gadge, B. M. Bhanage, *RSC Adv*. **2014**, *4*, 10367; j) C. Shen, X. -F. Wu, *Chem. Eur. J*. **2017**, *23*, 2973; k) M. Beller, Carbonylation of Benzyl- and Aryl-X Compounds. In Applied Homogeneous Catalysis with Organometallic Compounds, 2nd ed.; B. Cornils, W. A. Herrmann, Eds; Wiley-VCH: Weinheim, **2002**; l) C. S. Cho, J. W. Lee, D. Y. Lee, S. C. Shim, T. J. Kim, *Chem. Commun*. **1996**, 2115; m) S. C. Shim, L. H. Jiang, D. Y. Lee, C. S. Cho, *Bull. Korean. Chem. Soc.* **1995,** *16*, 1064; n) A. Chandrasekhar, V. Ramkumar, S. Sankararaman, *Eur. J. Org. Chem.* **2016**, *2016*, 4041; o) A. Dosgupta, V. Ramkumar, S. Sankararaman, *Eur. J. Org. Chem*. **2016**, *2016*, 4817; p) A. Chandrasekhar, S. Sankararaman, *J. Org. Chem*. **2017**, *82*, 11487. q) S. Guo, J. Zhai, F. Wang, X. Fan, *Org. Biomol. Chem*. **2017**, *15*, 3674. r) S. Guo, F. Wang, Y. Liu, X. Fan, *Tetrahedron.* **2019**, *75*, 3355.
2. a) R. K. Heck, D. S. Breslow, *J. Am. Chem. Soc.* **1963**, *85*, 2779; b) A. Schoenberg, R. K. Heck, *J. Org. Chem.* **1974**, *39*, 3327.
3. a) Y. Fujiwara, T. Kawauchi, H. Taniguchi, *J. Chem. Soc. Chem. Commun.* **1980**, 220; b) T. Jintoku, H. Taniguchi, Y. Fujiwara, *Chem. Lett*. **1987**, 1159; c) W. Lu, Y. Yamaoka, Y. Taniguchi, T. Kitamura, K. Takaki, Y. Fujiwara, *J. Organomet. Chem*. **1999**, *580*, 290.
4. a) K. Orito, A. Horibata, T. Nakamura, H. Ushito, H. Nagasaki, M. Yuguchi, S. Yamashita, M. Tokuda, *J. Am. Chem. Soc*. **2004**, *126*, 14342; b) R. Giri, J. -Q. Yu, *J. Am. Chem. Soc*. **2008**, *130*, 14082; c) Z. -H. Guan, Z. -H. Ren, S. M. Spinella, S. Yu, Y. -M. Liang, X. Zhang, *J. Am. Chem. Soc.* **2009**, *131*, 729; d) R. Giri, J. K. Lam, J. -Q. Yu, *J. Am. Chem. Soc.* **2010**, *132*, 686; e) Q. Liu, H. Zhang, A. Lei, *Angew. Chem., Int. Ed*. **2011**, *50*, 10788; f) Z. -H. Guan, M. Chen, Z. -H. Ren, *J. Am. Chem. Soc*. **2012**, *134*, 17490; g) M. Chen, Z. -H. Ren, Y. -Y. Wang, Z. -H. Guan, *Angew. Chem., Int. Ed*. **2013**, *52*, 14196; h) V. Rajeshkumar, T. -H. Lee, S. -C. Chuang, *Org. Lett*. **2013**, *15*, 1468; i) L. Wang, A. Lei, *Angew. Chem., Int. Ed*. **2014**, *53*, 5657; j) W. Li, Z. Duan, R. Jiang, A. Lei, *Org. Lett*. **2015**, *17*, 1397; k) S. Li, F. Li, J. Gong, Z. Yang, *Org. Lett*. **2015**, *17*, 1240; l) W. Li, Z. Duan, X. Zhang, H. Zhang, M. Wang, R. Jiang, H. Zeng, C. Liu, A. Lei, *Angew. Chem., Int. Ed.***2015**, *54*, 1893; m) J. -R. Chen, X. -Q. Hu, L. -Q. Lu, W. -J. Xiao, *Chem. Rev*. **2015**, *115*, 5301; n) S. T. Gadge, P. Gautam, B. M. Bhanage, *Chem. Rec*. **2016**, *16*, 835; o) Y. He, F. Wang, X. Zhang, X. Fan, *Chem. Common*. **2017**, *53*, 4002; p) J. Wen, S. Tang, F. Zhang, R. Shi, A. Lei, *Org. Lett*. **2017**, *19*, 94; q) A. Chandrasekhar, V. Ramkumar, S. Sankararaman, *Org. Biomol. Chem*. **2018**, *16*, 8629. r) S. Guo, F. Wang, L. Sun, X. Zhang, X. Fan, *Adv. Synth. Catal*. **2018**, *360*, 2537.
5. T. Itahara, *Chem. Lett*. **1982**, 1151.
6. H. Zhang, D. Liu, C. Chan, C. Liu, A. Lie, *Chem. Eur. J.* **2011**, *17*, 9581.
7. R. Lang, J. Wu, L. Shi, C. Xia, F. Li, *Chem. Commun.* **2011***, 47,* 12553.
8. R. Lang, L. Shi, D. Li, C. Xia, F. Li, *Org. Lett*. **2012**, *14*, 4130.
9. J. Tjutrins, B. Arndtsen, *J. Am. Chem. Soc.* **2015***, 137,* 12050.
10. a) M. N. Zhao, L. Ran, M. Chen, Z. H. Ren, X. Y. Wang, Z. H. Guan, *ACS Catal*. **2015**, *5*, 1210; b) During the preparation of this MS a paper has appeared on a similar theme: Q. -C. Mu, Y. -X. Nie, X. –F. Bai, J. Chen, L. Yang, -Z. Xu, L. Li, C. –G. Xia, L. –W. Yu, *Chem. Sci*., **2019**, *10*, 9292.
11. a) Review: A. H. Sandtorv, *Adv. Synth. Catal*. **2015**, *357*, 2403; b) X. Wang, B. S. Lane, D. Sames, *J. Am. Chem. Soc*. **2005**, *127*, 4996; c) N. P. Grimster, C. Gauntlett, C. R. A. Godfrey, M. J. Gaunt, *Angew. Chem., Int. Ed*. **2005**, *44*, 3125; d) B. S. Lane, M. A. Brown, D. Sames, *J. Am. Chem. Soc*. **2005**, *127*, 8050; e) N. R. Deprez, D. Kalyani, A. Krause, M. S. Sanford, *J. Am. Chem. Soc*. **2006**, *128*, 4972; f) D. R. Stuart, E. Villemure, K. Fagnou, *J. Am. Chem. Soc.* **2007**, *129*, 12072; g) R. J. Phipps, N. P. Grimster, M. J. Gaunt, *J. Am. Chem. Soc.* **2008**, *130*, 8172; h) N. Lebrasseur, I. Larrosa, *J. Am. Chem. Soc*. **2008**, *130*, 2926; i) S. Kirchberg, R. Fröhlich, A. Studer, *Angew. Chem., Int. Ed*. **2009**, *48*, 4235.
12. a) N. K. Kaushik, N. Kaushik, P. Attri, N. Kumar, C. H. Kim, A. K. Verma, E. H. Choi, *Molecules* **2013,** *18*, 6620; b) R. D.

View Article Online
DOI: 10.1039/C9OB02703C

Taylor, M. MacCoss, A. D. G Lawson, *J. Med. Chem*. **2014**, *57*, 5845; c) C. V. Galliford, K. A. Scheidt, *Angew. Chem., Int. Ed.* **2007**, *46*, 8748; d) M. -Z. Zhang, Q. Chen, G. -F. Yang, *Eur. J. Med. Chem*. **2015**, *89*, 421; e) A. W. Woodward, B. Bartel, *Ann. Bot*. **2005**, *95*, 707.

13. a) X. Li, K. Yang, W. Li, W. Xu, *Drugs Future* **2006**, *31*, 979; b) A. Carta, S. Piras, G. Loriga, G. Paglietti, *Mini-Rev. Med. Chem.* **2006**, *6*, 1179; c) P. Sanna, A. Carta, M. Loriga, S. Zanetti, L. Sechi, Il *Farmaco* **1999**, *54*, 169; d) J. Dudash, Y. Z. Zhang, J. B. Moore, R. Look, Y. Liang, M. P. Beavers, B. R. Conway, P. J. Rybczynski, K. T. Demarest, *Bioorg. Med. Chem. Lett*. **2005**, *15*, 4790; e) J. A. Willardsen, D. A. Dudley, W. L. Cody, L. G. Chi, T. B. McClanahan, T. E. Mertz, R. E. Potoczak, L. S. Narasimhan, D. R. Holland, S. T. Rapundalo, *J. Edmunds, J Med. Chem.* **2004**, *47*, 4089;
14. G. Abbiati, E. M. Beccalli, G. Broggini, G. Paladino, E. Rossi, *Synthesis*. **2005**, *17*, 2881.
15. A. Gogoi, P. Sau, W. Ali, S. Guin, B. K. Patel, *Eur. J. Org. Chem*. **2016**, *2016*, 1449.
16. L. Kong, Y. Sun, Z. Zheng, R. Tang, M. Wang, Y. Li, *Org. Lett*. **2018**, *20*, 5251.
17. a) D. J. Diaz, A. K. Darko, L. McElwee-White, *Eur. J. Org. Chem*. **2007**, *2007*, 4453; b) D. Liang, Z. Hu, J. Peng. J. Huang, Q. Zhu. *Chem. Commun*. 2013, *49*, 173; c) Z. Xie, S. Luo, Q. Zhu, *Chem. Commun*. **2016**, *52*, 12873; d) T. V. Thikekar, C. M. Sun, *Adv. Synth. Catal.* **2017**, *359,* 3388; e) B. Gabriele, R. Mancuso, G. Salerno, M. Costa, *Chem. Commun*. **2003**, 486; f) K. Hiwatari, Y. Kayaki, K. Okita, T. Ukai, I. Shimizu, A. Yamamoto, *Bull. Chem. Soc. Jpn*. **2004**, *77*, 2237.
18. W. Liu, J. Bang, Y. Zhang, L. Ackermann, *Angew. Chem., Int. Ed*. **2015**, *54*, 14137.
19. Q. Yuan, D. Ma, *J. Org. Chem*. **2008**, *73*, 5159.