JOC The Journal of Organic Chemistry

Note

Oxidant-Controlled C-sp2/sp3 – H Cross-dehydrogenative Coupling of N-Heterocycles with Benzylamines

Rohit Sharma, Mohd Abdullaha, and Sandip B. Bharate

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.7b00856 • Publication Date (Web): 18 Aug 2017

Just Accepted

ACS Publications

The Journal of Organic Chemistry is published by the American Chemical Society.
1155 Sixteenth Street N.W., Washington, DC 20036

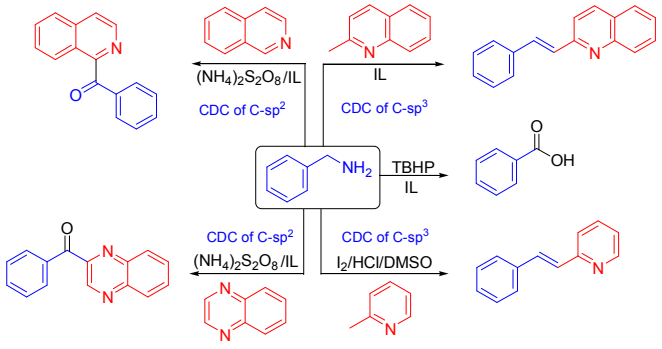
Oxidant-Controlled C-sp^2/sp^3 – H Cross-dehydrogenative Coupling of *N*-Heterocycles with Benzylamines

Rohit Sharma,[†‡] *Mohd Abdullaha,*[†‡] *Sandip B. Bharate*[†‡]*

[†]Medicinal Chemistry Division, CSIR-Indian Institute of Integrative Medicine, Canal Road, Jammu-180001, India

[‡] Academy of Scientific & Innovative Research, CSIR-Indian Institute of Integrative Medicine, Canal Road, Jammu-180001, India

TOC



- New method for CDC coupling of *N*-heterocycles
- No use of metal or ligand
- Use of ionic liquid
- CDC coupling with *N*-heterocycles having C-sp^2 and sp^3 carbon

ABSTRACT. Oxidant controlled ionic liquid mediated cross-dehydrogenative coupling (CDC) of benzylamines with *N*-heterocycles having sp^2 or sp^3 carbon resulted in the formation of *C*-benzoylated or alkenylated products. Benzoylation of *N*-heterocycles occurs via $(NH_4)_2S_2O_8$ catalyzed benzoyl radical formation. An oxidative alkenylation of *N*-heterocycles having *C*-sp^3 carbon (2-methylaza-arenes) occurs via deamination of benzylamine followed by Csp^3-H bond activation in high

stereoselectivity. Both benzoylation and alkenylation protocols are metal-free, green, simple, efficient and tolerates wide variety of functional groups.

KEYWORDS. Cross-dehydrogenative coupling, *N*-heterocycles, sp^3 C-H bond functionalization, ionic liquid, oxidative coupling, oxidative alkenylation

In recent years, oxidative cross coupling reaction has gained tremendous importance in synthetic organic chemistry.[1,2] Organic transformations for direct conversion of C-H bonds to C-C bonds is a hot area in organic chemistry because they are atom economical and provide short route for construction of C-C bonds.[3-7] Formation of C-C bonds from two different C-H bonds is known as 'cross dehydrogenative coupling (CDC)' reaction and it does not require pre-functionalized starting materials.[4,8 9] In this context, the activation of C-H bonds (sp^2, sp^3) remains a challenging task for synthetic organic chemists.[10,11]

The CDC reaction of *N*-heterocycles with wide range of substrates has emerged as a powerful tool in organic chemistry.[12,13] Direct C-H bond functionalization of *N*-heterocycles requires metal catalyst to precede the reaction. The benzoyl derivatives of *N*-heterocycles possess various biological activities and are also present among various natural products.[14-17] There are few reports available in literature where C-H functionalizations of electron deficient arenes are described.[18-21] Formation of benzoylated product in electron deficient arenes is done in Minisci type fashion by generation of acyl radical *in situ* from aldehydes[19,21-23] and toluene,[20] but these methods suffers from various drawbacks such as harsh reaction conditions and involves the use of additives/ oxidants.[11] In last few decades, lot of work has been done on transition metal catalyzed or metal-free aerobic C–X (X = C, N, O etc) bond activation,[24] C–C bond cleavage and functionalization.[25] However, to the best of our knowledge, direct C–N bond cleavage[26] of benzyl amines utilizing an ionic liquid (IL) oxidation strategy under metal-free conditions has not yet been established. Furthermore, benzoylation of *N*-heterocycles from benzylamine has never been reported.

ILs have received considerable attention in organic synthesis,[27,28] because of their fascinating physiochemical properties such as non-volatility, non-flammability and recyclability.[28] 1-Butyl-3-methylimidazolium tetrafluoroborate ([Bmim]BF_4)[27] has been utilized in various reactions such as Michael reaction,[29] cleavage of ethers,[30] halogenations of alkenes,[31] and in olefin metathesis.[32] Based on these reports we explored the use of [Bmim]BF_4 as a solvent for our proposed C-H functionalization. In continuation to our interest in using benzylamine for *N*-heterocycle synthesis,[33,34] herein we report ammonium persulfate catalyzed IL-mediated CDC reaction of *N*-heterocycles with benzylamine. Here, the benzylamine gets oxidized to aldehyde and then in presence of IL, it gets coupled with *N*-heterocycles having C-sp^2 and C-sp^3 carbon.

The benzoylation of isoquinoline/ quinoxaline is reported via $AlCl_3$ catalyzed Minisci type reaction with toluene,[20] or TBHP/TFA[19] or $PhI(OCOCF_3)_2$/$TMSN_3$[21] catalyzed coupling with benzaldehydes (Figure 1). The palladium acetate catalyzed coupling of isoquinoline N-oxides with nitroalkenes also produces benzoylated isoquinolines.[35] Furthermore, there are only three reports on the alkenylation of 2-substituted azaarenes.[36-38] Amongst these, only Qian *et al*[37] reported alkyenylation of both 2-methyl pyridines and 2-methyl quinolines, which is an iron-catalyzed reaction. These methods requires either use of metal catalyst[37] or an external oxidant[36,38] and longer reaction times.[36] The present work describes metal-free IL or iodine-mediated alkenylation of 2-substituted azaarenes.

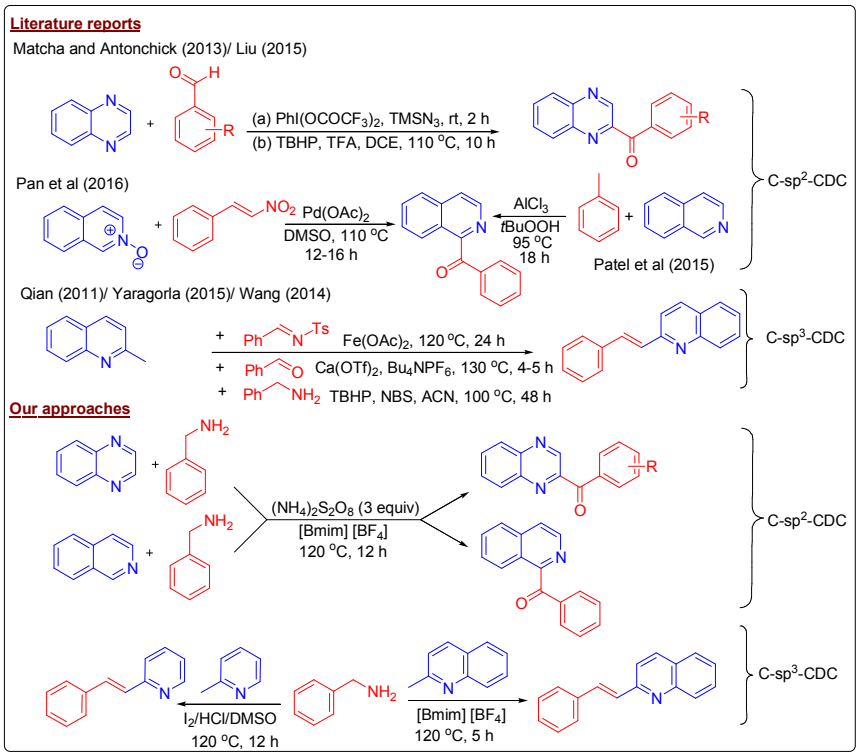
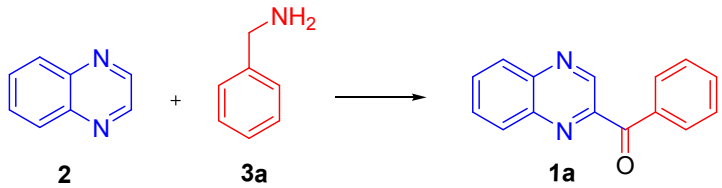


Figure 1. Literature reports and current approaches for C-sp^2/C-sp^3 CDC coupling of *N*-heterocycles

The study was initiated with preliminary reaction of quinoxaline **2** with benzylamine **3a** in presence of $K_2S_2O_8$ and ionic liquid (1-n-butyl-3-methyl imidazolium tetrafluroborate) (Table 1). The benzoylated product **1a** was obtained but only in 10% yield (entry 1). Then, we screened various oxidants including TBHP, DTBP, $(NH_4)_2S_2O_8$, TBAI, iodine (entries 2-18), solvents (ionic liquid, DMSO, DCE), out of which $(NH_4)_2S_2O_8$ (ammonium persulfate) was found to be the best oxidant in combination with IL as a reaction medium for this coupling reaction yielding the product **1a** in 80% yield (entry 6).

Table 1. Optimization of reaction conditions for CDC coupling of quinoxaline **2** with benzylamine **3a**



Entry	Oxidant(equiv.)	Solvent	Temp(°C)	Time (h)	**1a**, % yield[a]
1	$K_2S_2O_8$ (3)	Bmim[BF_4]	100	10	10
2	$K_2S_2O_8$ (4)	Bmim[BF_4]	120	12	15
3[a]	TBHP (3)	Bmim[BF_4]	120	12	traces
4	DTBP (3)	Bmim[BF_4]	120	12	0
5	O_2	Bmim[BF_4]	120	24	0
6[b]	**$(NH_4)_2S_2O_8$ (3)**	**Bmim[BF_4]**	**120**	**12**	**80**
7	$(NH_4)_2S_2O_8$ (3)	Bmim[BF_4]	100	12	70
8	$(NH_4)_2S_2O_8$ (3)	Bmim[BF_4]	140	12	80
9	TBAI (0.5)	Bmim[BF_4]	120	12	0
10	Iodine (0.8)	DMSO	120	12	0
11	$K_2S_2O_8$ (3)	DMSO	120	12	traces
12	$K_2S_2O_8$ (3)	DCE	120	12	traces
13	TBHP (3)	DCE	120	12	traces
14	DTBP (3)	DCE	120	12	traces
15	$(NH_4)_2S_2O_8$ (3)	DMSO	120	12	traces
16	$(NH_4)_2S_2O_8$ (3)	DCE	120	12	10
17	TBAI (0.5)	DCE	120	12	0
18	Iodine (0.8)	DCE	120	12	0

[a]The benzoic acid was obtained as the only product (~90% yield) in this reaction. [b]For 100 mg of reaction: **2** (1 equiv.), **3a** (2 equiv.), $(NH_4)_2S_2O_8$ (3 equiv.) and 1 ml of ionic liquid.

During the course of oxidant optimization studies, we surprisingly obtained benzoic acid **3aa** from benzylamine **3a** under TBHP/IL condition (entry 3 of Table 1). After conducting literature search, it was observed that conversion of benzyl amine **3a** to benzoic acid **3aa** requires metal catalyst,[39-41] dual oxidant,[42] or bio-oxidation.[43] Therefore, we explored the scope of this transformation for various

substituted benzylamines. The reaction of electron-withdrawing (**3ac, 3ad, 3af, 3ag, 3aj**) as well as electron-donating (**3ab, 3ae, 3ai, 3ak**) groups containing benzyl amines participated well in this transformation giving corresponding benzoic acids **3aa-ak** in good yields (Figure 2).

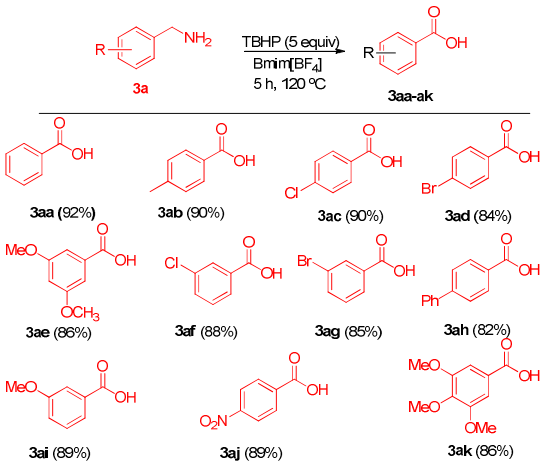


Figure 2. TBHP catalyzed conversion of benzylamines to benzoic acids (all reactions were carried out at 50 mg scale).

Next, we moved towards our primary goal of performing a CDC reaction of *N*-heterocycles with benzylamines. Under optimized reaction conditions, the scope of the reaction was explored for CDC reaction of various *N*-heterocycles such as quinoxalines, isoquinolines and quinolines with substituted benzylamines. Reaction works well with all three N-heterocycles resulting in regioselective benzoylation. Various substituted benzylamines participated well in this reaction. Reaction works well with benzylamines substituted with electron withdrawing as well as electron donating groups. No particular electronic effect was seen but in case of electron donating groups (example **1g**), the yields are slightly less in comparison to electron withdrawing groups (examples **1b, 1c, 1d, 1e, 1f**). In case of isoquinoline heterocycle, C1-benzoylated products **5a-d** were obtained but in comparatively lower yields than quinoxalines (Figure 3). In case of quinoline heterocycle, benzoylation occurred specifically at C4-position (examples **7a, 7b**). In order to get C1-acylated product for quinoline, we conducted a CDC reaction of 4-chloroquinoline (where C4-position is blocked) with benzyl amine, but the reaction does

not proceed at all. This indicated that benzoylation reaction is regiospecific. For benzoylation of quinoline, the optimized condition for this reaction of 2 equivalents of benzylamine, where generally only a C4-acylated product gets formed, without formation of C2-benzoylation product, even in traces. Further in order to understand whether this reaction takes place to some extent at C2 position, we used excess of benzylamine. In this case also, only C4-benzoylation product was formed, and there was no formation of C2-benzoylated product (not even in traces). This observation is indicative of the fact that this reaction is highly regiospecific. Further, we also performed the reaction of isoquinoline **5b** (where the C1-position is already blocked by benzoyl group) with benzyl amine **3** under optimized reaction condition, in order to check whether further benzoylation occurs at C4 or any other position. Reaction does not proceed at all, and starting material **5b** was recovered as such.

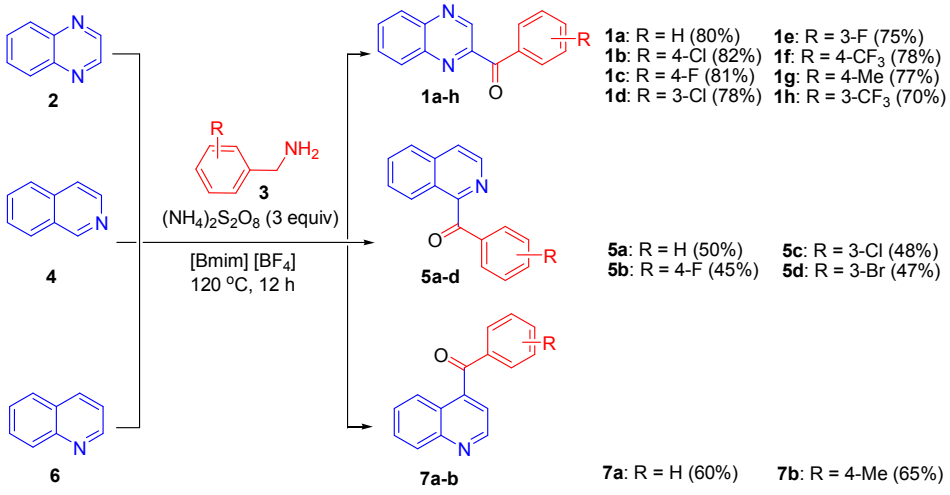


Figure 3. Substrate scope for oxidative CDC reaction of *N*-heterocycles having sp^2 carbon.

The proposed mechanism of the reaction is depicted in Figure 4. When the reaction was monitored at intermediate stage, the formation of benzaldehyde **I** was noticed, indicating that benzylamine **3a** first gets converted to benzaldehyde. Here, the aerial oxygen may be playing role for conversion of benzylamine to benzaldehyde. Ammonium persulfate generates the benzoyl radical **II** which attacks C2 position of **III** resulting in formation of intermediate **IV**. The [Bmim]BF_4 helps in radical formation. Finally, aromatization of **IV** leads to formation of **1a**.

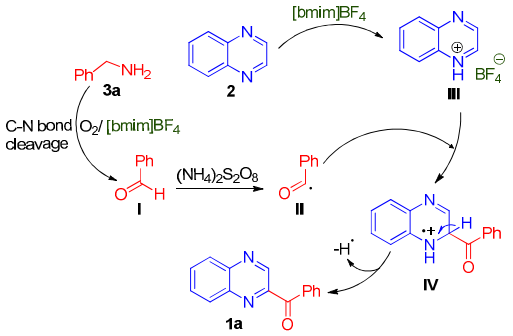


Figure 4. Proposed reaction mechanism for direct metal-free benzoylation of *N*-heterocycle

Next, we thought to conduct a CDC reaction for *N*-heterocycles having C-sp^3 carbon. In case of cyclic carbon containing C-sp^3 carbon (for example: 1,2,3,4-tetrahydroquinoline) reaction does not proceed. Then, we conducted the reaction of 2-methylquinoline **8** (which contain C-sp^3 carbon outside the ring) with benzylamine **3a** under optimized reaction condition (entry 6 of Table 1), where reaction worked well giving 2-styrylquinoline **9a** as a major product (Figure 5). The alkenylation of quinoline occurred via deamination of benzylamine. The C-sp^3-H proton of 2-methylquinoline **8** is more acidic as the resulting carbanion is stabilized by resonance. Therefore, next we performed reaction only in IL, without using any oxidant. To our surprise, the 2-styrylquinoline **9a** was still obtained in good yield. Further, the substrate scope of the reaction for substituted benzylamines was explored. Reaction works well with all type of groups on benzylamines. Also electronic substituents at *otho*, *meta* and *para* position are well tolerated in this alkenylation reaction. The recyclability of IL was also investigated using a model reaction between **8** and benzylamine **3a**. After completion of reaction, reaction mixture was extracted with diethyl ether and remaining ionic liquid was dried under reduced pressure for its reuse. Ionic liquid was reused up to five times yielding 60, 58, 58, 56, 54% yield of **9a**. There is no appreciable loss of activity of ionic liquid. Small decrease in yields might be due to loss of ionic liquid during work up.

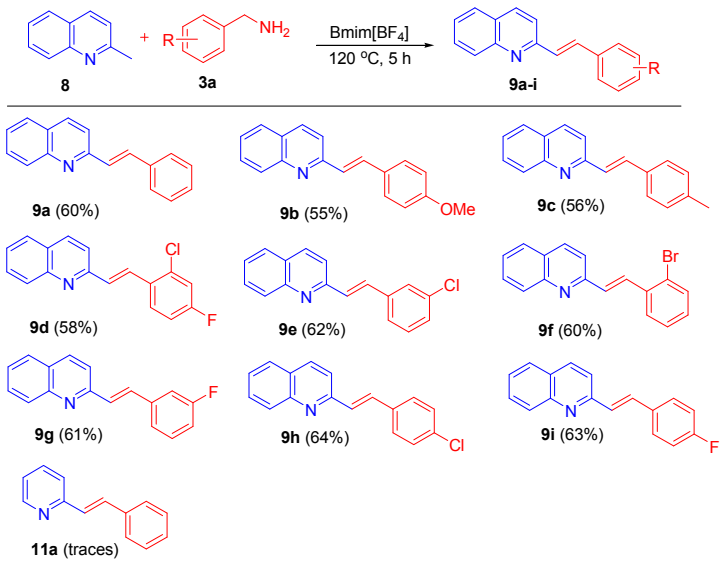


Figure 5. Substrate scope for oxidative CDC reaction of 2-methyl quinoline having sp^3 carbon

Next, we investigated another C-sp^3 carbon containing azaarene (i.e. 2-methyl pyridine) for this CDC reaction. When reaction of 2-methylpyridine (**10**) was performed with benzylamine **3a** under optimized reaction condition (entry 6 of Table 1), the 2-styryl pyridine **11a** was formed, but only in traces. Further, on performing this reaction only in Bmim[BF_4], the 2-styryl pyridine **11a** was not formed at all. All further optimization efforts in IL does not led to improvement in the product yield. This might be due to the difference in reactivity of 2-methyl pyridine **10** and 2-methyl quinoline **8** which is also reported in the literature.[44] Further, we explored variation in the reaction conditions, other than IL, and it was observed that in presence of iodine (80 mol%), HCl (20 µl) in DMSO solvent under reflux conditions, 2-styryl pyridine **11a** was formed in 40% yield. Using these reaction conditions, substrate scope of the reaction was explored. Reaction works well with electron withdrawing groups (**11d, 11e, 11f**) and neutral groups (**11a, 11b, 11c**) substituted benzylamines. Also in case of substituted 2-methyl pyridines, reaction works better than simple 2-methyl pyridines, giving better yields (Figure 6).

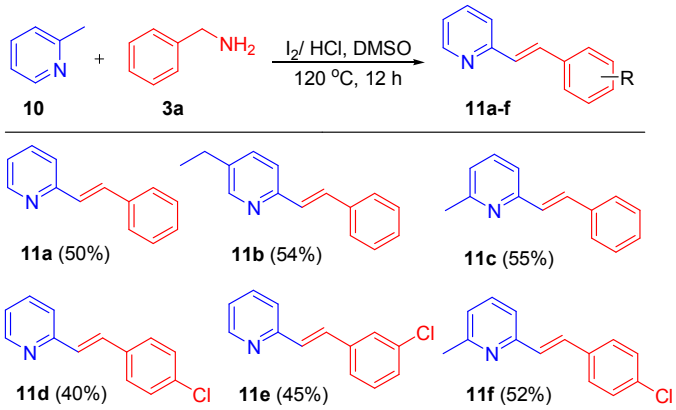


Figure 6. Substrate scope for oxidative CDC reaction of 2-methyl pyridine having sp^3 carbon

In conclusion, we have developed oxidant controlled ionic liquid mediated conversion of benzylamine to carboxylic acid followed by application towards CDC reaction of *N*-heterocycles having C-sp^2/sp^3 carbon atom producing C_1-acylated/ alkenylated products.

EXPERIMENTAL SECTION

General information. ^{1}H, ^{13}C and DEPT NMR spectra were recorded on FT-NMR 500 and 400 MHz instruments. Chemical data for protons are reported in parts per million (ppm) downfield from tetramethylsilane and are referenced to the residual proton in the NMR solvent ($CDCl_3$: 7.26, CD_3OD: 3.28 and DMSO-d_6: 2.5 ppm). Carbon nuclear magnetic resonance spectra (^{13}C NMR) were recorded at 125 MHz or 100 MHz. The chemical shift values for carbons are reported in parts per million (ppm, δ scale) downfield from tetramethylsilane and are referenced to the carbon resonance of the solvent ($CDCl_3$: 77, CD_3OD: 49 and DMSO-d_6: 39.5 ppm). IR spectra were recorded on IR spectrophotometer. Melting points were recorded on digital melting point apparatus.

General procedure for synthesis of benzoic acid 3aa-ak from benzylamines. To the solution of benzyl amine **3a-k** (50 mg, 1 equiv.) in 1 mL of ionic liquid was added 5 equiv. of TBHP and the reaction mixture was heated at 120 °C for 5 h. After completion of the reaction, the resultant reaction

mixture was extracted with ethyl acetate and diethyl ether. Ether layer was collected and dried over rotavapor so as to recover ionic liquid for further use. Ethyl acetate layer was separated and concentrated on rotavapor to get crude product. Purification of crude products using silica gel chromatography (hexane: EtOAc - 10: 1) gave benzoic acids **3aa-ak**.

*Benzoic acid (**3aa**).*[45] Figure 2; white solid (52 mg, 92%); m.p. 120-125 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (d, *J* = 8.0 Hz, 1H), 7.63 (t, *J* = 8.0 Hz, 1H), 7.50 (t, *J* = 12.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.3, 133.8, 130.2, 129.5, 128.5; IR ($CHCl_3$): ν_{max} 3342, 2922, 2322, 1645, 1253, 1254 cm^{-1}; ESI-MS: *m/z* 121.10 [M-H]$^{-}$.

*4-Methylbenzoic acid (**3ab**).*[46] Figure 2; white solid (57.5 mg, 90%); m.p. 175-180 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (d, *J* = 8.0 Hz, 1H), 7.25-7.20 (m, 2H), 7.16 (d, *J* = 8.0 Hz, 1H) 2.38 (s, 3H); IR ($CHCl_3$): ν_{max} 3314, 2924, 2354, 1639, 1454, 1254 cm^{-1}; ESI-MS: *m/z* 135.10 [M-H]$^{-}$.

*4-Chlorobenzoic acid (**3ac**).*[46] Figure 2; white solid (77 mg, 90%); m.p. 240-245 ^{o}C; ^{1}H NMR (400 MHz, acetone-d_6): δ 8.05 (d, *J* = 8.0 Hz, 2H), 7.56 (d, *J* = 8.0 Hz, 2H); IR ($CHCl_3$): ν_{max} 3093, 2917, 2845, 2678, 1932, 1683, 1594, 1425, 1295, 1282, 1129, 1016.18 cm^{-1}; ESI-MS: *m/z* 155.10 [M-H]$^{-}$.

*4-Bromobenzoic acid (**3ad**).*[46] Figure 2; white solid (77 mg, 84%); m.p. 140-145 ^{o}C; ^{1}H NMR (400 MHz, acetone-d_6): δ 7.97 (d, *J* = 8.0 Hz, 2H), 7.72 (d, *J* = 8.0 Hz, 2H); ESI-MS: *m/z* 199.10 [M-H]$^{-}$.

*3,5-Dimethoxybenzoic acid (**3ae**).*[47] Figure 2; white solid (73 mg, 86%); m.p. 182-186 ^{o}C; ^{1}H NMR (400 MHz, acetone-d_6): δ 7.17 (d, *J* = 4.0 Hz, 2H), 6.73 (t, *J* = 4.0 Hz, 1H), 3.84 (s, 3H); IR ($CHCl_3$): ν_{max} 3418, 2957, 2645, 1762, 1599, 1348, 1212, 1070 cm^{-1}; ESI-MS: *m/z* 181.20 [M-H]$^{-}$.

*3-Chlorobenzoic acid (**3af**).*[46] Figure 2; yellow solid (63 mg, 88%); m.p. 155-158 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10 (s, 1H), 8.02-7.99 (m, 1H), 7.61-7.58 (m, 1H), 7.45 (t, *J* = 8.0 Hz, 1H); ESI-MS: *m/z* 155.10 [M-H]$^{-}$.

*3-Bromobenzoic acid (**3ag**).*[46] Figure 2; yellow solid (78 mg, 85%); m.p. 150-155 ^{o}C; ^{1}H NMR (400 MHz, acetone-d_6): δ 8.15 (s, 1H), 8.03 (d, *J* = 8.0 Hz, 1H), 7.82-7.79 (m, 1H), 7.50 (t, *J* = 8.0 Hz, 1H); IR ($CHCl_3$): ν_{max} 2842, 2657, 2552, 1682, 1568, 1437, 1313, 1261, 1083 cm^{-1}; ESI-MS: *m/z* 199.10 [M-H]$^{-}$.

*[1,1'-Biphenyl]-4-carboxylic acid (**3ah**).*[46] Figure 2; yellow solid (76 mg, 82%); m.p. 150-155 ^{o}C; ^{1}H NMR (400 MHz, acetone-d_6): δ 8.14 (d, *J* = 8.0 Hz, 2H), 7.81 (d, *J* = 4.0 Hz, 2H), 7.55 (d, *J* = 8.0 Hz, 2H) 7.53 (d, *J* = 8.0 Hz, 2H), 7.44 (t, *J* = 8.0 Hz, 1H); IR ($CHCl_3$): ν_{max} 2846, 2557, 2552, 2442, 2362, 1680, 15580 1437, 1261, 1261, 1040 cm^{-1}; ESI-MS: *m/z* 197.10 [M-H]$^{-}$.

*3-Methoxybenzoic acid (**3ai**).*[48] Figure 2; white solid (64 mg, 89%); m.p. 100-102 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 (d, *J* = 8.0 Hz, 1H), 7.62 (s, 1H), 7.38 (t, *J* = 8.0 Hz, 1H), 7.15 (d, *J* = 8.0 Hz, 1H), 3.85 (s, 3H); IR ($CHCl_3$): ν_{max} 3392, 2922, 2850, 1681, 1584, 1456, 1439, 1414, 1281, 1233, 1193, 1047 cm^{-1}; ESI-MS: *m/z* 151.20 [M-H]$^{-}$.

*4-Nitrobenzoic acid (**3aj**).*[46] Figure 2; yellow solid (64 mg, 89%); ^{1}H NMR (400 MHz, acetone-d_6): δ 8.37-8.35 (m, 2H), 8.29-8.27 (m, 2H); IR ($CHCl_3$): ν_{max} 3113, 2918, 1959, 1691, 1605, 1520, 1495, 1430, 1293, 1128, 1109, 1014 cm^{-1}; ESI-MS: *m/z* 166.1000 [M-H]$^{-}$.

*3,4,5-Trimethoxybenzoic acid (**3ak**).*[49] Figure 2; white solid (87 mg, 86%); m.p. 170-175 ^{o}C; ^{1}H NMR (400 MHz, acetone-d_6): δ 7.32 (s, 2H), 3.88 (s, 6H), 3.80 (s, 3H); IR ($CHCl_3$): ν_{max}3419, 3018, 2836, 2645, 1682, 1586, 1416, 1325, 1269, 1224, 1123, 1001 cm^{-1}; ESI-MS: *m/z* 211.2000 [M-H]$^{-}$.

General procedure for synthesis of C-1 acylated products 1a-h, 5a-d and 7a-b by coupling of N-heterocycles and benzylamine. To the solution of *N*-heterocycles **2**, **4** or **6** (100 mg, 1 equiv.) in 1 mL of ionic liquid was added 2 equiv of benzylamine **3** followed by addition of $(NH_4)_2S_2O_8$ (3 equiv.). Reaction mixture was then heated at 120 ^{o}C for 12 h. After completion of the reaction, resulting reaction mixture was extracted with ethyl acetate and diethyl ether. Ether layer was collected and dried over rotary evaporator so as to recover ionic liquid for further use. Ethyl acetate layer was separated and concentrated on rotavapor to get crude product. Purification by using silica gel chromatography (hexane: EtOAc - 10:1) yielded pure products **1a-h**, **5a-d** and **7a-b**.

*Phenyl(quinoxalin-2-yl)methanone (**1a**).*[20] Figure 3; yellow solid (143 mg, 80%); m.p. 80-85 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.50 (s, 1H), 8.26-8.20 (m, 4H), 7.91-7.86 (m, 2H), 7.67-7.65 (m, 1H), 7.57-5.53 (m, 2H); IR ($CHCl_3$): ν_{max} 3399, 2923, 2955, 2852, 1730, 1659, 1597, 1491, 1464, 1447, 1322, 1310, 1207, 1184, 1163, 1126, 1080 cm^{-1}; ESI-MS: *m/z* 235.1057 [M+H]$^{+}$.

*(4-Chlorophenyl)(quinoxalin-2-yl)methanone (**1b**).*[20] Figure 3; yellow solid (168 mg, 82%); m.p. 110-115 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.51 (s, 1H), 8.27-8.19 (m, 4H), 7.94-7.87 (m, 2H), 7.54-7.50 (m, 2H);); IR ($CHCl_3$):ν_{max} 3444, 2918, 2346, 1668, 1590, 1463, 1317, 1167, 1127, 1090, 1014 cm^{-1}; ESI-MS: *m/z* 269.0715 $[M+H]^+$.

*(4-Fluorophenyl)(quinoxalin-2-yl)methanone (**1c**).* Figure 3; yellow oil (155 mg, 81%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.48 (s, 1H), 8.35-8.31 (m, 2H), 8.21-8.17 (m, 2H), 7.92-7.83 (m, 2H), 7.22 (t, *J* = 8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.3, 171.2, 168.7, 152.2, 149.1, 147, 144.1, 137.9, 137.8, 135.9, 135.7, 134.7, 134.2, 133.2, 119.5, 119.3; IR ($CHCl_3$): ν_{max} 3428, 1957, 2923, 2852, 1643, 1598, 1505, 1414, 1294, 1233, 1159, 1133 cm^{-1}; ESI-MS: *m/z* 253.0640 $[M+H]^+$; TOF-HRMS calcd for $C_{15}H_{10}FN_2O$ $[M+H]^+$ 253.0772, found 253.0770.

*(3-Chlorophenyl)(quinoxalin-2-yl)methanone (**1d**).*[50] Figure 3; yellow oil (160 mg, 78%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.52 (s, 1H), 8.28-8.15 (m, 4H), 7.93-7.88 (m, 2H), 7.65-7.64 (m, 1H), 7.63-7.47 (m, 1H); IR ($CHCl_3$): ν_{max} 3584, 3419, 3068, 2924, 2957, 2853, 1725, 1666, 1568, 1493, 1465, 1422, 1363, 1312, 1207, 1166, 1081 cm^{-1}; ESI-MS: *m/z* 269.03 $[M+H]^+$.

*(3-Fluorophenyl)(quinoxalin-2-yl)methanone (**1e**).* Figure 3; yellow oil (145 mg, 75%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.50 (s, 1H), 8.21 (d, *J* = 8.0 Hz, 2H), 8.07-8.04 (m, 1H), 8.01-7.98 (m, 1H), 7.93-7.86 (m, 2H), 7.54-7.48 (m, 1H), 7.38-7.33 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.7, 167.5, 151.8, 149.1, 147.1, 144.2, 136.1, 134.8, 134.3, 133.9, 133.3, 130.9, 128.2, 127.8, 124.5, 122.0; IR ($CHCl_3$): ν_{max} 3386, 2923, 2852, 1738, 1674, 1585, 1435, 1363, 1240, 1209, 1184, 1080 cm^{-1}; ESI-MS: *m/z* 253.09 $[M+H]^+$; TOF-HRMS calcd for $C_{15}H_{10}FN_2O$ $[M+H]^+$ 253.0772, found 253.0772.

*Quinoxalin-2-yl(4-(trifluoromethyl)phenyl)methanone (**1f**).* Figure 3; yellow oil (180 mg, 78%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.58 (s, 1H), 8.39 (d, *J* = 8 Hz, 2H), 8.25-8.19 (m, 2H), 7.97-7.88 (m, 2H), 7.83 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.4, 147.6, 147.1, 145.1, 143.4, 140.4, 138.5, 132.5, 131.5, 130.5, 129.5, 125.4, 125.3, 124.5, 123.9, 119.1; IR ($CHCl_3$): ν_{max} 3444, 2099, 1658, 1650, 1644, 1633, 1318 cm^{-1}; ESI-MS: *m/z* 303.1067 $[M+H]^+$; TOF-HRMS calcd for $C_{16}H_{10}F_3N_2O$ $[M+H]^+$ 303.0740, found 303.0735.

*Quinoxalin-2-yl(p-tolyl)methanone (**1g**).*[21] Figure 3; yellow solid (134 mg, 77%); m.p. 102-105 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.45 (s, 1H), 8.20 (d, *J* = 8 Hz, 2H), 8.15 (d, *J* = 8 Hz, 2H), 7.89-7.84 (m, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.4, 152.6, 148.9, 148.2, 146.7, 144, 136.5, 135.4, 134.9, 134.2, 133.9, 132.9, 132.7, 25.4; IR ($CHCl_3$): ν_{max} 3421, 2954, 2928, 2851, 1731, 1658, 1606, 1571, 1464, 1491, 1319, 1233, 1209, 1185, 1161 cm^{-1}; ESI-MS: *m/z* 249.11 $[M+H]^+$.

*Quinoxalin-2-yl(3-(trifluoromethyl)phenyl)methanone (**1h**).* Figure 3; yellow oil (163 mg, 70%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.58 (s, 1H), 8.62 (s, 1H), 8.49 (d, *J* = 8 Hz, 1H), 8.25-8.19 (m, 2H), 7.97-7.89 (m, 3H), 7.72 (t, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.6, 151.5, 149, 147.3, 144.2, 140, 138.2, 136.3, 134.9, 134.3, 133.6, 133.3, 132.8, 132.1, 132.0; IR ($CHCl_3$): ν_{max} 3398, 2923, 2851, 1730, 1666, 1611, 1339, 1304, 1283, 1228, 1161, 1128, 1073, 1013 cm^{-1}; ESI-MS: *m/z* 303.10 $[M+H]^+$; TOF-HRMS calcd for $C_{16}H_9F_3N_2OH$ $[M+H]^+$ 303.0740, found 303.0736.

*Isoquinolin-1-yl(phenyl)methanone (**5a**).*[20] Figure 3; white solid (90 mg, 50%); m.p. 72-75 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.64 (d, *J* = 4.0 Hz, 1H), 8.22 (d, *J* = 8.0 Hz, 1H), 8.08 (d, *J* = 8.0 Hz, 1H), 7.97-7.95 (m, 1H), 7.92 (d, *J* = 8.0 Hz, 1H), 7.82 (d, *J* = 8.0 Hz, 1H), 7.74-7.73 (m, 1H), 7.62-7.58 (m, 1H), 7.48-7.43 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198, 160.2, 144.8, 140.6, 140.4, 137.6, 137.5, 137.2, 134.7, 134.5, 133.9, 133.6, 132.3, 132.2, 132, 130.9, 130.2, 130, 126.6, 126.5; IR ($CHCl_3$): ν_{max} 3058, 2924, 2623, 1918, 1672, 1622, 1597, 1418, 1389, 1214, 1278, 1249, 1227, 1156 cm^{-1}; ESI-MS: *m/z* 234.11 $[M+H]^+$.

*(4-Fluorophenyl)(isoquinolin-1-yl)methanone (**5b**).*[35] Figure 3; yellow solid (88 mg, 45%); m.p. 92-95 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.61 (d, *J* = 8.0 Hz, 1H), 8.22 (d, *J* = 8.0 Hz, 1H), 8.03-7.98 (m, 2H), 7.91 (d, *J* = 8.0 Hz, 1H), 7.81 (d, *J* = 4.0 Hz, 1H), 7.73-7.70 (m, 1H), 7.61-7.59 (m, 1H), 7.15 (t, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.6, 171.2, 159.7, 144.7, 140.6, 137.4, 137.3, 136.5, 134.7, 132.3, 131, 130.2, 129.9, 126.2, 119.6, 119.3, 119.1; IR ($CHCl_3$): ν_{max} 3421, 3057, 2928, 2609, 1922, 1668, 1597, 1504, 1412, 1387, 1279, 148, 1231, 1151, 1049 cm^{-1}; ESI-MS: *m/z* 252.11 $[M+H]^+$.

*(3-Chlorophenyl)(isoquinolin-1-yl)methanone (**5c**).*[35] Figure 3; yellow oil (100 mg, 48%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.61 (d, *J* = 4.0 Hz, 1H), 8.28 (d, *J* = 8.0 Hz, 1H), 7.96 (s, 1H), 7.94 (d, *J* = 8.0 Hz, 1H), 7.85-7.82 (m, 2H), 7.77-7.73 (m, 1H), 7.66-7.64 (m, 1H), 7.58-7.56 (m, 1H), 7.43 (t, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.6, 159.1, 144.9, 142.2, 140.7, 138.5, 137.3, 134.7, 134.5, 133.6, 132.8, 132.4, 131, 130.3, 129.8, 126.9; IR ($CHCl_3$): ν_{max} 3585, 3056, 2925, 2853, 1667, 1570, 1425, 1245, 1157, 1018, 1050 cm^{-1}; ESI-MS: *m/z* 268.08 $[M+H]^+$.

*(3-Bromophenyl)(isoquinolin-1-yl)methanone (**5d**).*[35] Figure 3; yellow oil (145 mg, 47%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.61 (d, *J* = 4.0 Hz, 1H), 8.28 (d, *J* = 8.0 Hz, 1H), 8.11 (s, 1H), 7.94 (d, *J* = 8.0 Hz, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.84 (d, *J* = 4.0 Hz, 1H), 7.78-7.72 (m, 2H), 7.65 (t, *J* = 8.0 Hz, 1H), 7.37 (t, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.6, 159.1, 144.9, 142.4, 140.7, 140.1, 137.4, 134.7, 133.8, 133.2, 132.4, 131.0, 130.3, 129.9, 126.9, 126.5; IR ($CHCl_3$): ν_{max}3419, 3057, 2922, 2850, 1672, 1563, 1423, 1278, 1244, 1155, 1070, 1017 cm^{-1}; ESI-MS: *m/z* 312.04 $[M+H]^+$.

*Phenyl(quinolin-4-yl)methanone (**7a**).*[51] Figure 3; yellow oil (108 mg, 80%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.04 (d, *J* = 4.0 Hz, 1H), 8.23 (d, *J* = 8.0 Hz, 1H), 7.88-7.85 (m, 3H), 7.79 (t, *J* = 8.0 Hz, 1H), 7.66 (t, *J* = 8.0 Hz, 1H), 7.56-7.53 (m, 1H), 7.52 (t, *J* = 8.0 Hz, 2H), 7.46 (d, *J* = 8.0 Hz, 1H); ESI-MS: *m/z* 234.08 $[M+H]^+$.

*Quinolin-4-yl(p-tolyl)methanone (**7b**).* Figure 3; yellow oil (125 mg, 65%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.01 (d, *J* = 4.0 Hz, 1H), 8.20 (d, *J* = 8.0 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 3H), 7.53 (t, *J* = 8.0 Hz, 1H), 7.23 (d, *J* = 8.0 Hz, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 195, 149.5, 148.5, 145.4, 144.9, 134.2, 130.4, 130, 129.9, 129.5, 129.2, 127.6, 125.5, 119.4, 21.8; IR ($CHCl_3$): ν_{max} 3583, 3283, 2923, 3054, 2345, 1730, 1651, 1604, 1505, 1463, 1312, 1276, 1178, 1155 cm^{-1}; ESI-MS: *m/z* 248.08 $[M+H]^+$; TOF-HRMS calcd for $C_{17}H_{14}NO$ $[M+H]^+$ 248.1070, found 248.1077.

General procedure for synthesis of (E)-2-styrylquinolines 9a-i. To the solution of 2-methylquinoline (**8**, 100 mg, 1 equiv.) in 1 mL of ionic liquid was added 2 equiv of benzylamine **3** and reaction mixture was heated at 120 ^{o}C for 5 h. After completion of the reaction, the resultant reaction

mixture was extracted with ethyl acetate and diethyl ether. Ether layer was collected and dried over rotavapor so as to recover ionic liquid for further use. Ethyl acetate layer was separated and concentrated on rotavapor to get crude product. The crude products were purified by using silica gel chromatography (hexane: EtOAc - 10:1) to get pure products **9a-i**.

*(E)-2-Styrylquinoline (**9a**).*[52] Figure 5; off-white solid (96 mg, 60%); m.p. 95-100 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09 (d, *J* = 8.0 Hz, 2H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.69-7.62 (m, 5H), 7.49-7.37 (m, 4H), 7.33-7.29 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 157.4, 149.7, 137.8, 131.2, 130.6, 130.4, 130.3, 130.1, 128.9, 128.7, 127.6, 120.7; IR ($CHCl_3$): ν_{max} 3387, 3057, 2919, 2849, 1633, 1611, 1593, 1551, 1502, 1446, 1426, 1345, 1316, 1203, 1181, 1140, 1013 cm^{-1}; ESI-MS: *m/z* 232.00 $[M+H]^+$.

*(E)-2-(4-Methoxystyryl)quinoline (**9b**).*[52] Figure 5; off-white solid (100 mg, 55%); m.p. 120-123 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.16 (d, *J* = 8.8 Hz, 1H), 8.07 (d, *J* = 8.8 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.70-7.58 (m, 5H), 7.50-7.48 (m, 1H), 7.30 (d, *J* = 16.8 Hz, 1H), 6.95-6.93 (m, 2H), 3.85 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.2, 156.4, 148.3, 136.2, 134.1, 129.7, 129.4, 129.1, 128.7, 127.5, 127.2, 126.9, 125.9, 119.2, 114.3, 55.4; IR ($CHCl_3$): ν_{max} 3745, 3416, 2917, 2849, 1632, 1596, 1554, 1455, 1429, 1328, 1303, 1258, 1175, 1111, 1027 cm^{-1}; ESI-MS: *m/z* 262.20 $[M+H]^+$.

*(E)-2-(4-Methylstyryl)quinoline (**9c**).*[53] Figure 5; off-white solid (95 mg, 56%); m.p. 140-143 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.13-8.07 (m, 2H), 7.79 (d, *J* = 6.4 Hz, 1H), 7.71-7.65 (m,3H), 7.56 (d, *J* = 6.4 Hz, 2H), 7.50-7.48 (m, 1H), 7.39 (d, *J* = 13.2 Hz, 1H), 7.23 (d, *J* = 6.4 Hz, 2H), 2.39 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 136.2, 134.5, 129.7, 129.6, 129.1, 128, 127.5, 127.2, 126, 119.2, 21.4; IR ($CHCl_3$): ν_{max} 3587, 3420, 2919, 2354, 2346, 1637, 1591, 1502, 1425, 1177, 1118, 1016 cm^{-1}; ESI-MS: *m/z* 245.80 $[M+H]^+$.

*(E)-2-(2-Chloro-4-fluorostyryl)quinoline (**9d**).* Figure 5; yellow oil (115 mg, 58%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17 (d, *J* = 7.2 Hz, 1H), 8.10 (d, *J* = 6.8 Hz, 1H), 7.99 (d, *J* = 13.2 Hz, 1H), 7.81-7.71 (m, 4H), 7.54-7.51 (m, 1H), 7.36 (d, *J* = 13.2, 1H), 7.20-7.18 (m, 1H), 7.07-7.03 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.7, 157.0, 149.6, 137.9, 132.9, 131.3, 130.7, 130.6, 129.5, 128.9, 127.9, 120.4, 118.5, 116.0; IR ($CHCl_3$): ν_{max} 3393, 3061, 3031, 2922, 2851, 1593, 1490, 1504, 1428, 1407, 1272,

1247, 1229, 1120, 1044 cm^{-1}: ESI-MS: *m/z* 284.70 $[M+H]^+$; TOF-HRMS calcd for $C_{17}H_{12}ClFN$ $[M+H]^+$ 284.0637, found 284.0622.

*(E)-2-(3-Chlorostyryl)quinoline (**9e**)*.[52] Figure 5; off-white solid (115 mg, 62%); m.p. 95-100 ^oC;^1H NMR (400 MHz, $CDCl_3$): δ 8.16 (d, *J* = 6.8 Hz, 1H), 8.10 (d, *J* = 6.8 Hz, 1H), 7.81 (d, *J* = 6.4, 1H), 7.73 (m, 1H), 7.67-7.63 (m, 3H), 7.53-7.50 (m, 2H), 7.42-7.27 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 155.4, 148.2, 136.5, 130, 129.9, 129.2, 128.5, 127.5, 127.1, 126.4, 125.4, 119.5; IR ($CHCl_3$): ν_{max} 3392, 3058, 2955, 2924, 2853, 1931, 1732, 1613, 1562, 1594, 1504, 1465, 1376, 1311, 1202, 1118, 1096, 1077 cm^{-1}; ESI-MS: *m/z* 265.90 $[M+H]^+$.

*(E)-2-(2-Bromostyryl)quinoline (**9f**)*.[52] Figure 5; off-white solid (130 mg, 60%); m.p. 58-60 ^oC; ^1H NMR (500 MHz, $CDCl_3$): δ 8.16 (d, *J* = 9.0 Hz, 1H), 8.11 (d, *J* = 8.5 Hz, 1H), 8.01 (d, *J* = 16 Hz, 1H), 7.82-7.70 (m, 4H), 7.64 (d, *J* = 8.0 Hz, 1H), 7.53-7.50 (m, 1H), 7.40-7.34 (m, 2H), 7.19-7.17 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 155.7, 148.2, 133.2, 132.9, 129.8, 129.7, 129.3, 127.7, 127.5, 127.1, 126.4, 118.8; IR ($CHCl_3$): ν_{max} 3585, 3381, 3056, 2955, 2923, 2851, 1952, 1726, 1614, 1555, 1595, 1504, 1467, 1437, 1427, 1376, 1347, 1312, 1182, 1118, 1080 cm^{-1}; ESI-MS: *m/z* 311.80 $[M+H]^+$.

*(E)-2-(3-Fluorostyryl)quinoline (**9g**)*.[44] Figure 5; off-white solid (107 mg, 61%); m.p. 245-248 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ 8.16 (d, *J* = 8.8 Hz, 1H), 8.10 (d, *J* = 8.4 Hz, 1H), 7.81 (d, *J* = 8.0 Hz, 1H), 7.74-7.65 (m, 3H), 7.54-7.50 (m, 1H), 7.42-7.34 (m, 4H), 7.05-7.00 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.6, 156.9, 149.7, 140.2, 137.9, 134.5, 134.5, 131.7, 131.6, 131.3, 130.7, 128.9, 128.8, 127.8, 124.6, 120.9, 116.8, 114.9; IR ($CHCl_3$): ν_{max} 3585, 3299, 3059, 3034, 2920, 2850, 1731, 1637, 1606, 1593, 1582, 1504, 1446, 1428, 1350, 1313, 1268, 1142, 1122, 1018 cm^{-1}; ESI-MS: *m/z* 250.20 $[M+H]^+$.

*(E)-2-(4-Chlorostyryl)quinoline (**9h**)*.[52] Figure 5; off-white solid (120 mg, 64%); m.p. 140-145 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ 8.12-8.07 (m, 2H), 7.82 (d, *J* = 6.4 Hz, 1H), 7.72-7.70 (m, 1H), 7.64-7.60 (m, 2H), 7.55-7.49 (m, 3H), 7.37-7.34 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 155.6, 148.2, 136.5, 133, 129.9, 129.5, 129.2, 129, 128.4, 127.5, 126.3, 119.3; IR ($CHCl_3$): ν_{max} 3585, 3363, 3045, 3028,

2918, 2850, 1903, 1613, 1591, 1504, 1492, 1428, 1404, 1315, 1106, 1096, 1079, 1009 cm^{-1}; ESI-MS: *m/z* 265.80 $[M+H]^+$.

*(E)-2-(4-Fluorostyryl)quinoline (**9i**)*.[52] Figure 5; off-white solid (110 mg, 63%); m.p. 121-125 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ 8.14 (d, *J* = 6.8 Hz, 1H), 8.09 (d, *J* = 6.8 Hz, 1H), 7.79 (d, *J* = 6.4 Hz, 1H), 7.71-7.60 (m, 5H), 7.52 (t, *J* = 5.6 Hz, 1H), 7.34 (d, *J* = 12.8 Hz, 1H), 7.11 (t, *J* = 7.2 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.9, 161.9, 155.8, 148.2, 136.4, 133.1, 132.7, 129.8, 129.1, 128.9, 128.8, 128.6, 127.5, 126.2, 119.2, 115.9, 115.7; IR ($CHCl_3$): ν_{max} 3421, 3035, 2920, 1613, 1555, 1509, 1429, 1413, 1316, 1297, 1220, 1165, 1102, 1121, 1015 cm^{-1}; ESI-MS: *m/z* 250.00 $[M+H]^+$.

General procedure for synthesis of (E)-2-styrylpyridines 11a-f. To the solution of 2-methylpyridine (**10**, 100 mg, 1 equiv.) in 2 mL of DMSO was added 2 equiv of benzylamine **3**, 80 mol% of iodine and 20 µl of HCl. Reaction mixture was then heated at 120 ^oC for 12 h. After completion of the reaction, resultant reaction mixture was extracted with ethyl acetate and water. Ethyl acetate layer was separated and concentrated on rotavapor to get crude product. The crude products were purified by using silica gel chromatography (hexane: EtOAc - 10: 1) to get pure products **11a-f**.

*(E)-2-Styrylpyridine (**11a**)*.[54] Figure 6; yellow oil (97 mg, 50%); ^1H NMR (400 MHz, $CDCl_3$): δ 8.62 (d, *J* = 4.0 Hz, 1H), 7.69-7.65 (m, 1H), 7.61-7.58 (m, 3H), 7.41-7.36 (m, 3H), 7.32-7.28 (m, 1H), 7.17-7.14 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157, 151, 138.1, 138, 134.2, 130.2, 129.8, 128.2, 128.6, 123.6, 123.5; IR ($CHCl_3$): ν_{max} 3361, 2921, 2850, 1734, 1638, 1584, 1562, 1494, 1468, 1429, 1186, 1149, 1080, 1019 cm^{-1}; ESI-MS: *m/z* 181.90 $[M+H]^+$.

*(E)-5-Ethyl-2-styrylpyridine (**11b**)*. Figure 6; yellow oil (105 mg, 54%); ^1H NMR (400 MHz, $CDCl_3$): δ 8.45 (s, 1H), 7.58-7.54 (m, 3H), 7.46-7.44 (m, 1H), 7.37-7.26 (m, 4H), 7.18 (d, *J* = 16.0 Hz, 1H), 2.65 (dd, *J* = 8.0, 16.0 Hz, 2H), 1.25 (t, *J* = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.2, 149.3, 137.9, 136.9, 135.9, 131.8, 128.7, 128.1, 127.9, 127, 121.7, 25.9, 15.3; IR ($CHCl_3$): ν_{max} 3380, 3036, 2966, 2929, 2874, 1608, 1583, 1487, 1445, 1395, 1324, 1270, 1242, 1188, 1076, 1024 cm^{-1}; ESI-MS: *m/z* 209.90 $[M+H]^+$; TOF-HRMS calcd for $C_{15}H_{16}N$ $[M+H]^+$ 210.1277, found 210.1259.

*(E)-2-Methyl-6-styrylpyridine (**11c**)*.[55] Figure 6; yellow oil (100 mg, 55%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64-7.55 (m, 3H), 7.39 (t, *J* = 6.0 Hz, 2H), 7.31-7.17 (m, 4H), 7.04 (d, *J* = 6.0 Hz, 1H), 2.60 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.7, 156.5, 138.1, 133.8, 130.6, 130.1, 129.6, 128.5, 128.2, 123.2, 120.2, 24.4; IR ($CHCl_3$): ν_{max} 3335, 3060, 3027, 2958, 2924, 2852, 1725, 1638, 1583, 1567, 1537, 1453, 1326, 1188, 1157, 1074, 1028 cm^{-1}; ESI-MS: *m/z* 195.90 $[M+H]^+$.

(*E)-2-(4-Chlorostyryl)pyridine (**11d**)*.[56] Figure 6; yellow oil (93 mg, 40%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.62-8.60 (m, 1H), 7.69-7.64 (m, 1H), 7.60 (d, *J* = 16.0 Hz, 1H), 7.51-7.48 (m, 2H), 7.39-7.26 (m, 3H), 7.18-7.12 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 156.6, 151.1, 138.2, 136.6, 135.4, 132.9, 130.4, 129.8, 129.7, 123.8, 123.7; IR ($CHCl_3$): ν_{max} 3416, 3045, 3001, 2956, 2924, 2852, 2359, 1714, 1636, 1560, 1582, 1491, 1469, 1326, 1274, 1186, 1148, 1090, 1046 cm^{-1}; ESI-MS: *m/z* 215.90 $[M+H]^+$.

*(E)-2-(3-Chlorostyryl)pyridine (**11e**)*.[57] Figure 6; off-white solid (105 mg, 45%); Yield, 45%; 105 mg; m.p. >300 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.63-8.62 (m, 1H), 7.69-7.67 (m, 1H), 7.60 (d, *J* = 12.8 Hz, 2H), 7.45-7.37 (m, 2H), 7.32-7.27 (m, 2H), 7.19-7.15 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 156.5, 151.2, 139.9, 138.1, 136.1, 132.7, 131.4, 130.6, 129.7, 128.2, 126.9, 123.9; IR ($CHCl_3$): ν_{max} 3385, 3057, 2919, 2850, 1954, 1690, 1663, 1729, 1635, 1611, 1551, 1593, 1502, 1446, 1426, 1345, 1316, 1182, 1117, 1140, 1071 cm^{-1}; ESI-MS: *m/z* 215.90 $[M+H]^+$.

*(E)-2-(4-Chlorostyryl)-6-methylpyridine (**11f**)*. Figure 6; yellow oil (112 mg, 52%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58-7.49 (m, 4H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.23 (d, *J* = 8.0 Hz, 1H), 7.15 (d, *J* = 16.4 Hz, 1H), 7.04 (d, *J* = 7.6 Hz, 1H), 2.59 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.4, 154.7, 136.8, 135.3, 133.8, 131, 130.9, 128.9, 128.2, 122, 119, 24.7; IR ($CHCl_3$): ν_{max} 3417, 2958, 2924, 2851, 2346, 1725, 1639, 1582, 1491, 1451, 1404, 1375, 1286, 1121, 1089, 1074, 1012 cm^{-1}; ESI-MS: *m/z* 229.80 $[M+H]^+$; TOF-HRMS calcd for $C_{14}H_{13}ClN$ $[M+H]^+$ 230.0731, found 230.0721.

ACKNOWLEDGEMENT. R.S is thankful to DST for award of INSPIRE fellowship. Authors thank analytical department, IIIM for NMR and MS analysis of our compounds. This work was supported by SERB project (grant no SR/FT/CS-168/2011).

AUTHOR INFORMATION.

Corresponding Author

*Tel: +91-191-2586333; Tel: +91-191-2585006 (Extn. 345). E-mail: sbharate@iiim.ac.in, sandipbharate@gmail.com (S.B.B.)

ORCID: 0000-0001-6081-5787

Notes

The authors declare no competing financial interest.

SUPPORTING INFORMATION AVAILABLE: NMR spectra scans. This material is available free of charge via the Internet at http://pubs.acs.org.

REFERENCES

(1) Yeung, C. S.; Dong, V. M. *Chem. Rev.* **2011**, *111*, 1215.

(2) Murahashi, S.-I.; Zhang, D. *Chem. Soc. Rev.* **2008**, *37*, 1490.

(3) Girard, S. A.; Knauber, T.; Li, C. J. *Angew. Chem. Int. Ed. Engl.* **2014**, *53*, 74.

(4) Li, C.-J. *Acc. Chem. Res.* **2009**, *42*, 335.

(5) Han, W.; Mayer, P.; Ofial, A. R. *Angew. Chem. Int. Ed.* **2011**, *50*, 2178.

(6) Kitahara, M.; Umeda, N.; Hirano, K.; Satoh, T.; Miura, M. *J. Am. Chem. Soc.* **2011**, *133*, 2160.

(7) Le Bras, J.; Muzart, J. *Chem. Rev.* **2011**, *111*, 1170.

(8) Mousseau, J. J.; Charette, A. B. *Acc. Chem. Res.* **2013**, *46*, 412.

(9) Ashenhurst, J. A. *Chem. Soc. Rev.* **2010**, *39*, 540.

(10) Li, B.; Dixneuf, P. H. *Chem. Soc. Rev.* **2013**, *42*, 5744.

(11) Shi, Z.; Zhang, C.; Tang, C.; Jiao, N. *Chem. Soc. Rev.* **2012**, *41*, 3381.

(12) Li, Y.; Wang, M.; Fan, W.; Qian, F.; Li, G.; Lu, H. *J. Org. Chem.* **2016**, *81*, 11743.

(13) Song, G.; Wang, F.; Li, X. *Chem. Soc. Rev.* **2012**, *41*, 3651.

(14) Chen; Zhu, Y.-F.; Liu, X.-J.; Lu, Z.-X.; Xie, Q.; Ling, N. *J. Med. Chem.* **2001**, *44*, 4001.

(15) Duncton, M. A. J. *Med. Chem. Commun.* **2011**, *2*, 1135.

(16) Al-Khalil, S.; Schiff, P. L. *J. Nat. Prod.* **1985**, *48*, 989.

(17) Baser, K. H. C. *J. Nat. Prod.* **1982**, *45*, 704.

(18) Pruet, J. M.; Robertus, J. D.; Anslyn, E. V. *Tetrahedron Lett.* **2010**, *51*, 2539.

(19) Chen, J.; Wan, M.; Hua, J.; Sun, Y.; Lv, Z.; Li, W.; Liu, L. *Org. Biomol. Chem.* **2015**, *13*, 11561.

(20) Ali, W.; Behera, A.; Guin, S.; Patel, B. K. *J. Org. Chem.* **2015**, *80*, 5625.

(21) Matcha, K.; Antonchick, A. P. *Angew. Chem. Int. Ed.* **2013**, *52*, 2082.

(22) Siddaraju, Y.; Lamani, M.; Prabhu, K. R. *J. Org. Chem.* **2014**, *79*, 3856.

(23) Baslé, O.; Bidange, J.; Shuai, Q.; Li, C.-J. *Adv. Synth. Catal.* **2010**, *352*, 1145.

(24) Wang, Q.; Su, Y.; Li, L.; Huang, H. *Chem. Soc. Rev.* **2016**, *45*, 1257.

(25) Beccalli, E. M.; Broggini, G.; Martinelli, M.; Sottocornola, S. *Chem. Rev.* **2007**, *107*, 5318.

(26) Wu, K.; Huang, Z.; Liu, C.; Zhang, H.; Lei, A. *Chem. Commun.* **2015**, *51*, 2286.

(27) Bharate, J. B.; Bharate, S. B.; Vishwakarma, R. A. *ACS Comb. Sci.* **2014**, *16*, 624.

(28) Wagh, K. V.; Bhanage, B. M. *Green Chem.* **2015**, *17*, 4446.

(29) Dell'Anna, M. M.; Gallo, V.; Mastrorilli, P.; Nobile, C. F.; Romanazzi, G.; Suranna, G. P. *Chem. Commun.* **2002**, 434.

(30) Boovanahalli, S. K.; Kim, D. W.; Chi, D. Y. *J. Org. Chem.* **2004**, *69*, 3340.

(31) Chiappe, C.; Capraro, D.; Conte, V.; Pieraccini, D. *Org. Lett.* **2001**, *3*, 1061.

(32) Mayo, K. G.; Nearhoof, E. H.; Kiddle, J. J. *Org. Lett.* **2002**, *4*, 1567.

(33) Sharma, R.; Vishwakarma, R. A.; Bharate, S. B. *Adv. Synth. Catal.* **2016**, *358*, 3027.

(34) Sharma, R.; Vishwakarma, R. A.; Bharate, S. B. *Eur. J. Org. Chem.* **2016**, *2016*, 5227.

(35) Li, J.-l.; Li, W.-z.; Wang, Y.-c.; Ren, Q.; Wang, H.-s.; Pan, Y.-m. *Chem. Commun.* **2016**, *52*, 10028.

(36) Gong, L.; Xing, L.-J.; Xu, T.; Zhu, X.-P.; Zhou, W.; Kang, N.; Wang, B. *Org. Biomol. Chem.* **2014**, *12*, 6557.

(37) Qian, B.; Xie, P.; Xie, Y.; Huang, H. *Org. Lett.* **2011**, *13*, 2580.

(38) Yaragorla, S.; Singh, G.; Dada, R. *Tetrahedron Lett.* **2015**, *56*, 5924.

(39) Rajalakshmi, V.; Vijayaraghavan, V. R.; Varghese, B.; Raghavan, A. *Inorg. Chem.* **2008**, *47*, 5821.

(40) Sharma, S.; Barooah, N.; Baruah, J. B. *J. Mol. Catal. A: Chem.* **2005**, *229*, 171.

(41) Barooah, N.; Sharma, S.; Sarma, B. C.; Baruah, J. B. *Appl. Organomet. Chem.* **2004**, *18*, 440.

(42) Naik, R.; Pasha, M. A. *Synth. Commun.* **2006**, *36*, 165.

(43) Galletti, P.; Funiciello, F.; Soldati, R.; Giacomini, D. *Adv. Synth. Catal.* **2015**, *357*, 1840.

(44) Mao, D.; Hong, G.; Wu, S.; Liu, X.; Yu, J.; Wang, L. *Eur. J. Org. Chem.* **2014**, *2014*, 3009.

(45) Goldbach, M.; Danieli, E.; Perlo, J.; Kaptein, B.; Litvinov, V. M.; Blümich, B.; Casanova, F.; Duchateau, A. L. L. *Tetrahedron Lett.* **2016**, *57*, 122.

(46) Karimi, B.; Naderi, Z.; Khorasani, M.; Mirzaei, H. M.; Vali, H. *Chem. Cat. Chem.* **2016**, *8*, 906.

(47) Cvengros, J.; Neufeind, S.; Becker, A.; Schmalz, H.-G. *Synlett.* **2008**, *2008*, 1993.

(48) Sultane, P. R.; Mete, T. B.; Bhat, R. G. *Tetrahedron Lett.* **2015**, *56*, 2067.

(49) Hirose, T.; Takai, H.; Watabe, M.; Minamikawa, H.; Tachikawa, T.; Kodama, K.; Yasutake, M. *Tetrahedron.* **2014**, *70*, 5100.

(50) Mukhopadhyay, R.; Kundu, N. G. *Tetrahedron Lett.* **2000**, *41*, 9927.

(51) Kuriyama, M.; Hamaguchi, N.; Sakata, K.; Onomura, O. *Eur. J. Org. Chem.* **2013**, *2013*, 3378.

(52) Crisenza, G. E. M.; Dauncey, E. M.; Bower, J. F. *Org. Biomol. Chem.* **2016**, *14*, 5820.

(53) Yan, Y.; Xu, K.; Fang, Y.; Wang, Z. *J. Org. Chem.* **2011**, *76*, 6849.

(54) Goggins, S.; Rosevere, E.; Bellini, C.; Allen, J. C.; Marsh, B. J.; Mahon, M. F.; Frost, C. G. *Org. Biomol. Chem.* **2014**, *12*, 47.

(55) Chen, Z.; Luo, M.; Wen, Y.; Luo, G.; Liu, L. *Org. Lett.* **2014**, *16*, 3020.

(56) Chen, S.; Zhang, X.; Chu, M.; Gan, X.; Lv, X.; Yu, J. *Synlett.* **2015**, *26*, 791.

(57) Hepburn, H. B.; Melchiorre, P. *Chem. Commun.* **2016**, *52*, 3520.