MnO_2 mediated sequential oxidation/olefination of alkyl-substituted heteroarenes with alcohols

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0.Graphical Abstract

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MnO_2 Mediated Sequential Oxidation/ Olefination of Alkyl-Substituted Heteroarenes with Alcohols

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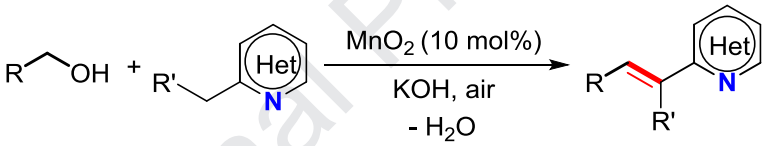

· **Phosphine ligand free** · **Air as mild oxidant** up to 94% yield

· **Nitrogen ligand free** · **Recyclable** 40 examples

Pergamon

MnO_2 Mediated Sequential Oxidation/Olefination of Alkyl-Substituted Heteroarenes with Alcohols

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ABSTRACT

A practical and efficient ligand-free MnO_2 mediated sequential oxidation and olefination has been developed for the facile synthesis of a broad range of unsaturated *N*-heteroazaarenes from simple alkyl-substituted heteroarenes and alcohols. The procedure tolerates a series of functional groups, such as methoxyl, chloro, bromo, iodo, vinyl, phenolic and hetero groups, providing the olefination products in moderate to good yields.The protocol could be conducted at mild conditions and used environmentally friendly air as the clear oxidant.

1. Introduction

As one of the most important fundamental structural motifs, unsaturated *N*-heteroaromatic compounds has been considered as a privileged structure in natural products, pharmaceuticals and functional materials (Figure 1).[1] As such, the development of efficient methods toward these complex molecules is of great significance to chemical, medicinal and material science and has attracted a great deal of attention over the past decades.[2] Plenty of powerful synthetic routes, including many named reactions,[3] catalytic coupling[4] or olefin metathesis,[5] have been developed to access such kinds of molecules. However, multi-step functional group manipulations and unavoidable generation of stoichiometric amount of undesired waste are the few shortcomings in these reactions.

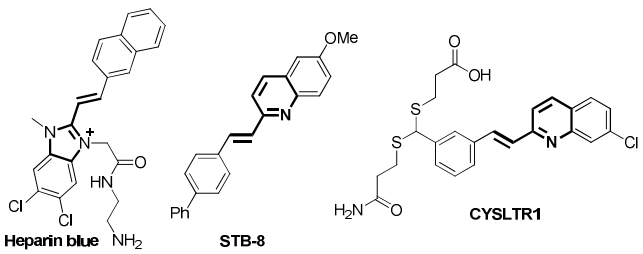
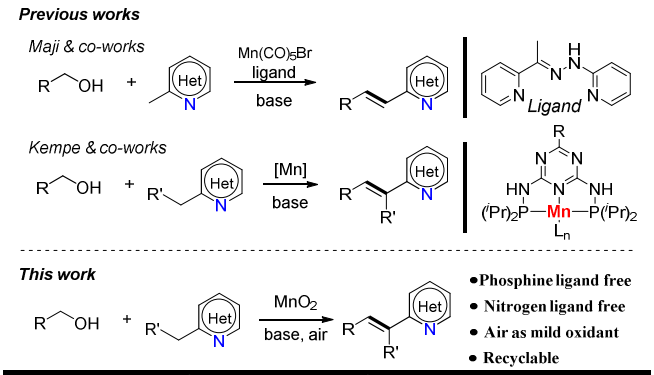


Figure 1. Selected bioactive compounds with unsaturated *N*-heteroarene moiety.

An attractive approach to circumvent these problems is abundantly available metal catalyzed acceptorless dehydrogenative condensation (ADC),[6] which enables the synthesis of di-substituted alkenes compounds from alcohols combination of catalytic dehydrogenation and condensation steps. Moreover, alcohols can be obtained from indigestible and abundantly available lignocellulose biomass.[7] Kempe[8] and Maji group[9] pioneered a novel manganese-catalyzed reaction leading to di-substituted olefins synthesis using alcohols with *N*-heteroarenes at the same time, the reaction proceeds via ADC process,



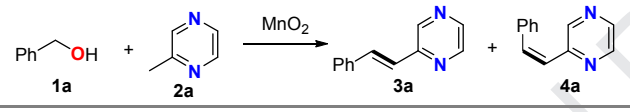
Scheme 1. Methods for Mn-catalyzed olefination.

producing only water and hydrogen as green coproducts (Scheme 1, top). However, metal complexes or addition of capricious ligands for catalyst activation are generally required to maintain the catalytic cycle, thereby limiting the potential scope of this environmentally benign transformation. These results together with our progress on the use of alcohols as green partners for metal catalyzed coupling reactions,[10] prompted us to envision that alcohols might be oxidized in MnO_2/air catalytic system and condensed with methylazaarenes for the synthesis of di-substituted olefins. Moreover, to the best of our knowledge, MnO_2 catalyzed oxidation/olefination of alcohols and methylazaarenes to synthesis unsaturated *N*-heteroaromatic has not been reported. Herein, we present on the first protocol for successful implementation of the MnO_2 catalyzed oxidation of alcohols with a variety of alkyl-substituted azaarenes via olefination process, which allows for synthesis of various multiple-substituted alkenes under mild condition.

2. Results and discussion

As an initial attempt, the reaction between phenylmethanol (**1a**) and 2-methylpyrazine (**2a**) was chosen as the model reaction for optimization of the reaction conditions (Table 1).

Table 1. Optimization of the reaction conditions [a]

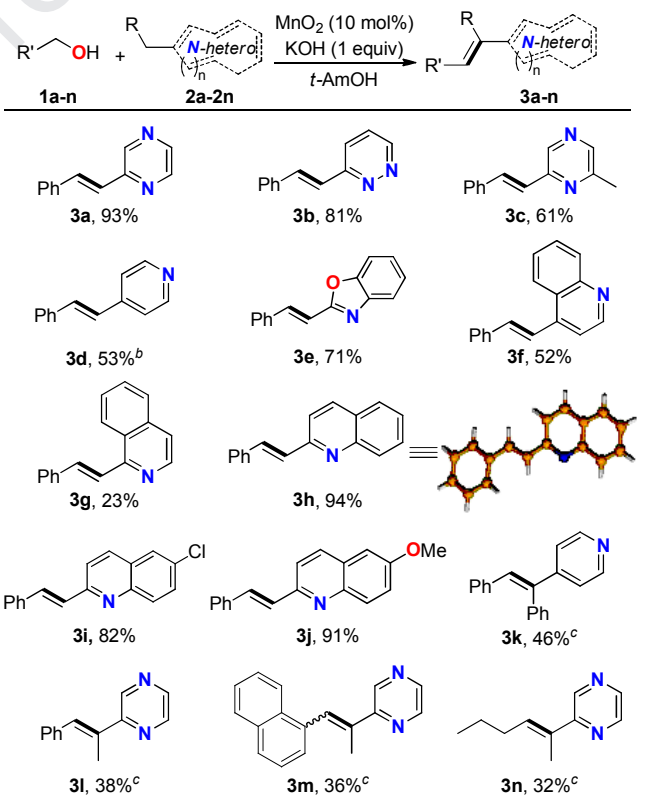


Entry	Base	Solvent	**3a** (%)	**3a**/**4a**
1	Cs_2CO_3	*t*-AmOH	12	> 20:1
2	K_2CO_3	*t*-AmOH	< 5	-
3	Na_2CO_3	*t*-AmOH	< 5	-
4	CsOH	*t*-AmOH	83	19:1
5	KOH	*t*-AmOH	96 (72)[b]	> 20:1
6	NaOH	*t*-AmOH	53	17:1
7	*t*-BuOLi	*t*-AmOH	< 5	-
8	*t*-BuONa	*t*-AmOH	63	16:1
9	*t*-BuOK	*t*-AmOH	89	18:1
10	KOH	*t*-BuOH	88	19:1
11	KOH	*i*-PrOH	12	> 20:1
12	KOH	EtOH	0	-
13	KOH	THF	32	> 20:1
14	KOH	Diglyme	90	16:1
15	KOH	Toluene	19	> 20:1
16	-	*t*-AmOH	0	-
17	KOH	*t*-AmOH	11[c] (10)[d]	> 20:1
18	KOH	*t*-AmOH	< 5[e]	-

[a] General conditions: **1a** (0.55 mmol), **2a** (0.5 mmol), MnO_2 (0.05 mmol), base (0.5 mmol), solvent (1.0 mL), 120 °C, 21 h. Yield of **3a** and the ratio of **3a**/**4a** determined by GC-analysis using *n*-cetane as an internal standard. [b] Under oxygen. [c] No MnO_2. [d] No MnO_2, 48 h. [e] Under nitrogen.

Because manganese precatalyst has shown to be highly effective for the dehydragenation/olefination of methylazaarenes with alcohols,[8,9] we initially focused on exploring conditions using MnO_2 as readily available catalyst at 120 °C. The desired (*E*)-2-styrylpyrazine (**3a**) was obtained in 12% yield, when the reaction was conducted in the presence of Cs_2CO_3 under an air atomsphere (Table 1, entry 1). This result indicated that our proposed sequential oxidation/olefination reactions of methylazaarene with alcohol was indeed possible. Base screening indicated that when the reaction was ran in presence of KOH, the desired product was obtained best yield and the high regioselective (Table 1, entry 5). The reaction still worked even under oxygen atmosphere (oxygen balloon) and **3a** was obtained in good yield. Other inorganic bases or organic bases, did not improve the reactivity (Table 1, entries 2-9). Further investigation of the solvents revealed that the reactivity was affected by the nature of the solvents, and the best result was achieved with *t*-AmOH as the solvent. Meanwhile, reaction in other alcohol solvents, such as *t*-BuOH, *i*-PrOH and EtOH resulted in lower yield or no reaction (Table 1, entries 10-12). This reactivity trend(*t*-AmOH > *t*-BuOH > *i*-PrOH > EtOH) is that sterically hindered alcohols suppress the competing aldol reaction with benzaldehyde intermediate, revealing that the mechanism may via aldehyde species. No appreciable increase in yield of olefination product was obtained in ether solvents or non-polar solvent. Finally, control reactions demonstrated that the low yield of **3a** was obtained under nitrogen atmosphere or in the absence of catalyst or base (Table 1, entries 16-18).

Table 2. Substrate scope of *N*-heteroaromatics [a]



[a] General conditions: **1a** (0.55 mmol), **2** (0.5 mmol), MnO_2 (10 mol%), KOH (0.5 mmol), *t*-AmOH (1.0 mL), air, 120 °C, 21 h. Isolated yield, unless otherwise noted. [b] **1a** (2.0 mmol), 140 °C, 36 h. [c] **1a** (2.0 mmol), KOH (1.0 mmol), 140 °C, 48 h.

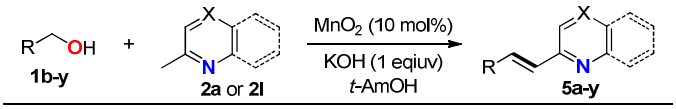
Taken together, we can conclude that the oxidation/olefination was carried out by stirring *t*-AmOH solution of phenylmethanol, 2-methylpyrazine, 10 mol% of MnO_2, and an equivalent of KOH at

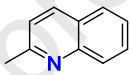
120°C under an air for 21 hours to give the olefination product **3a** in the best yield.

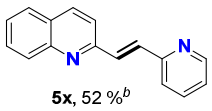
On the basis of the results described above, a variety of *N*-heteroaromatics were submitted to the MnO_2-catalyzed oxidant/olefination reaction to investigate its substrate scope and generality (Table 2). 2-Methylpyrazine and 3-methylpyridazine substrates gave the corresponding products in high yields (**3a**-**3b**). The oxidation/olefiantion reaction of 2,6-dimethylpyrazine or 4-methylpyridine (lower acidity of methyl) reacted with phenylmethanol resulted in modearate yields of the desired products **3c**-**3d**. When the pyrazine core was replaced with benzo[d]oxazole, the olefination reaction still took place to give **3e** in 71% yield. Although the reaction of 4-methylquinoline and 1-methylisoquinoline offered **3f** and **3g** in moderate yields, the reaction with 2-methylquinoline proceeded smoothy to produce the desired adduct **3h** in excellent yield. The yield of product is likely related to the stability of the enamine intermediate, which increases in the order **3g** < **3f** < **3h**. This result showing that the olefination mechanism may via enamine intermediate. Methyl-substituted *N*-heteroarenes derived from 2-methylquinoline were effective substrates and smoothly reacted with benzyl alcohol to provide the corresponding products **3i** and **3j** in 82 and 91% yield, respectively. Ethyl or benzyl substituted azaarenes were less reactive, and the olefination products **3k**-**3n** were isolated in moderate yields when the reaction temperature and time were increased. These results may be due to large steric hindrance of the methylenyl of the azaarenes.

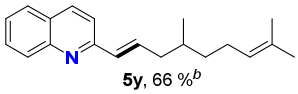
Furthermore, the scope of the alcohols was also explored and the results are shown in Table 3. The procedure tolerated well some functional groups, such as methyl, phenyl, methoxy, halogen and heteroarene, with good yields. The electronic effects of substituent in alcohol had some effect on the reaction. Generally, the alcohols with electron-withdrawing groups gave slightly lower yields than those electron-donating analogues (**5a** *vs* **5b**-**c** and **5g**, **5i**, **5l** *vs* **5n**-**5p**). An obvious steric hindrance effect on the reactivity was observed, which was demonstrated by the reactivities of **5e** *vs* **5g** and **5m** *vs* **5n**. It is worth noting that the tolerance of halogen group on the aromatic ring in this olefination protocol offers an opportunity for subsequent transformations, which facilitates expedient synthesis of complex unsaturate *N*-heteroarenes (**5b**-**5c**, **5m**-**5p**). Naphthyl-substituted alcohol was also compatible with this process, furnishing the desired product **5q** in 87% yield. In addition to aromatic-substituted alcohols, although the reaction of furan-2-ylmethanol gave the corresponding product **5r** in moderate yield, the reaction with thiophen-2-ylmethanol proceeded smoothy to give **5s** in good yield. Pyridin-2-ylmethanol was also a good reaction partner, and (*E*)-2-(2-(pyridin-2-yl)vinyl)quinoline **5x** was isolated in 52% yield. To extend the scope of our catalytic system, we also tested more challenging aliphatic alcohols under the standard procedure. 2-Ethylbutan-1-ol was initially surveyed and the reaction proceeded smoothly to give the desired olefination **5t** in moderate yield. Furthermore, similar results were obtained in the reactions of aliphatic alcohols with different substituted to deliver the desired adducts **5u**-**5w** efficiently in good yields. And importantly, unsaturate alcohol substrates, citronellol, was also good reaction partner, providing the corresponding product **5y** in 66% yield, while the internal double bond remained intact.

Table 3. Substrate scope of alcohols [a]



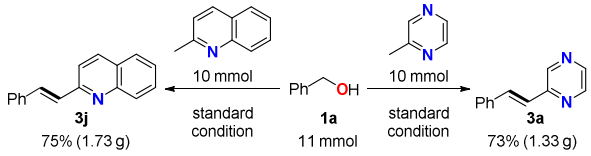
Entry		1	R	Yield (%)
1		**1d**	4-$CH_3C_6H_4$	**5a**, 89
2		**1k**	4-ClC_6H_4	**5b**, 81
3		**1l**	4-BrC_6H_4	**5c**, 73
4	**2a**	**1p**	2-thienyl	**5d**, 68
5		**1b**	2-$CH_3C_6H_4$	**5e**, 66
6		**1c**	3-$CH_3C_6H_4$	**5f**, 84
7		**1d**	4-$CH_3C_6H_4$	**5g**, 93
8		**1e**	2,4,6-$(CH_3)_3C_6H_2$	**5h**, 64
9		**1f**	4-*t*-BuC_6H_4	**5i**, 91
10		**1g**	4-PhC_6H_4	**5j**, 83
11		**1h**	2-$CH_3OC_6H_4$	**5k**, 71
12		**1i**	4-$CH_3OC_6H_4$	**5l**, 92
13		**1j**	2-ClC_6H_4	**5m**, 57
14		**1k**	4-ClC_6H_4	**5n**, 84
15	**2l**	**1l**	4-BrC_6H_4	**5o**, 66
16		**1m**	4-IC_6H_4	**5p**, 48
17		**1n**	1-Naphthyl	**5q**, 77
18		**1o**	2-furyl	**5r**, 58
19		**1p**	2-thienyl	**5s**, 74
20		**1q**	Et_2CH	**5t**, 53[b]
21[b]		**1r**	*t*-Bu	**5u**, 61[b]
22[b]		**1s**	Cyclopropyl	**5v**, 56[b]
23[b]		**1t**	Cyclohexyl	**5w**, 68[b]


5x, 52 %[b]


5y, 66 %[b]

[a] General conditions: **1** (0.55 mmol), **2a** or **2l** (0.5 mmol), MnO_2 (10 mol%), KOH (0.5 mmol), *t*-AmOH (1.0 mL), air, 120 °C, 21 h. Isolated yield. [b] **1** (2.0 mmol), KOH (1.0 mmol), 140 °C, 48 h.

To further demonstrate the robustness of our system, we were able to run experiments on gram scale in the presence of 10 mol% of MnO_2 to produce the olefination adducts **3a** and **3j** in 73% (1.33 g) and 75% (1.73 g) yield, respectively.



Scheme 2. Gram scale experiments.

To validate the recyclability of current oxidant/olefination, the reuse investigation was performed in the model reaction of **1a** with **2a** in presence of 10 mol% of MnO_2. After the completion of reaction, a small aliquot of the reaction mixture was analyzed by

GC to monitor product **3a** formation. Then the reaction mixture was filtered, washed with ethyl acetate, water and ethanol, dried on vacuum, the catalyst of MnO_2 was recovered and continued to catalyze for another reaction. It is shown in Figure. 2 that the olefination could be repeated at least five times with the fifth run giving a 81% yield of **3a**. And the catalytic activity of the recovered MnO_2 dried on the oxygen atmosphere better than argon (see the Supporting Information for details), these results indicate that the catalyst MnO_2 can can be re-generated by oxygen or air.

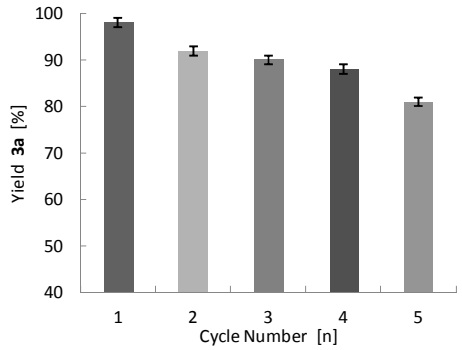
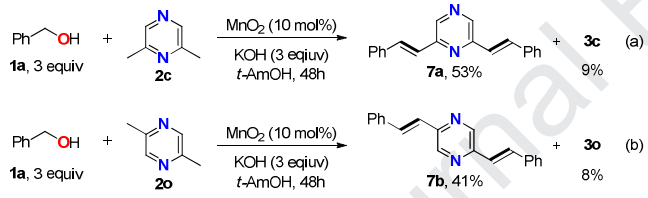


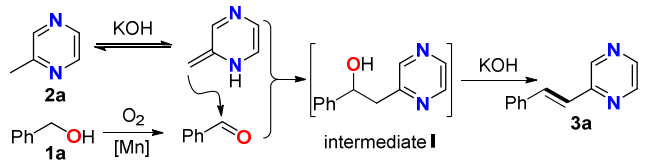
Figure 2. Reusability of MnO_2 Catalyst

The practice and convenience of this proceed to unsaturated *N*-heteroaromatics can be di-olefination of substrates containing two methyl groups as well, the corresponding products **7a** and **7b** were isolated in reasonable yields, respectively.



Scheme 3. MnO_2 catalyzed di-olefination.

On the basis of the results we obtained here and previous reports,[7,8] a plausible mechanism for the present process can be proposed. In this scenario, initial alcohol is oxidized by air in the presence of MnO_2 to generate aldehyde. After enamine was formed under the base condition, nucleophilic attack of the enamine into the C=O bond of aldehyde gained the intermediate **I**. Subsequent elimination releases water in the presence of base and give rise to the unsaturated *N*-heteroaromatic product.



Scheme 4. Possible mechanism of olefination.

3. Conclusion

In summary, we have developed an efficient MnO_2/air catalytic system that allows the direct formation of unsaturated *N*-heteroaromatics from commercially available alcohols and alkylazaarenes via oxidation/olefination under the aerobic conditions. The method is compatible with a variety of functional groups and can be used to prepare a range of 1,2-disubstitued unsaturated *N*-heteroaromatics. Further investigations to gain a detailed mechanistic understanding as well as application of this aerobic oxidative catalytic system to other oxidation/olefination reactions are currently in progress.

4. Experimental section

4.1 General Information

^1H and ^{13}C spectra were obtained on a Brüker AVIII300 (300 MHz) or AVII (500 MHz) spectrometer. Proton-decoupled spectra are denoted as {^1H}. Chemical shifts (δ) were reported in parts per million (ppm) using the residual solvent signal as an internal standard ($CDCl_3$: δ_H = 7.26 ppm, δ_C = 77.16 ppm). All coupling constants (*J* values) were reported in Hertz (Hz). Multiplicities were reported as follows: s, singlet; d, doublet; t, triplet; m, multiplet. High-resolution mass spectrometry (HRMS) measurements were recorded on a Bruker Daltronics microTOF (ESI) spectrometer. Flash chromatography was carried out using matrix 60 silica.

*4.2 General procedure for synthesis of products (1)substrates General procedure for MnO2 catalyzed oxidation/olefination reaction (**3a-3n, 5a-5y, 7a-7a**)*

Using a nitrogen-filled glove box, an oven-dried Schlenk tube (100 mL volume) was charged with a magnetic stirring bar, MnO_2 (0.05 mmol), KOH (0.5 mmol), alcohols (**1**) (0.55 mmol), heteroarenes (**2**) (0.5 mmol) and *t*-AmOH (1 mL). Then the Schlenk tube was closed tightly with a teflon cap, removed from the glove box. A reflux condenser was evacuated and refilled with dry air and then attached to the Schlenk tube maintaining dry air stream. A bubble counter was attached to the top of the condenser and the whole system was purged with dry air for 15 seconds. The Schlenk tube was immersed into a pre-heated oil bath (design temperature). After design time the reaction was cooled, a small aliquot of the organic phase was analyzed by GC or GC-MS to monitor product formation. Purification of the remainder by column chromatography on silica gel (petroleum ether/ethyl acetate = 20/1 – 5/1) gave the corresponding products in the reported yield.

4.2.1 (E)-2-styrylpyrazine (3a)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 169 mg, 93% yield. ^1H NMR (300 MHz, $CDCl_3$): δ 8.59 (s, 1H), 8.49 (s, 1H), 8.35 (d, *J* = 2.3 Hz, 1H), 7.70 (d, *J* = 16.1 Hz, 1H), 7.55 (d, *J* = 8.1 Hz, 2H), 7.38 – 7.28 (m, 3H), 7.11 (d, *J* = 16.1 Hz, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 151.3, 144.4, 143.8, 142.8, 136.0, 135.2, 129.0, 128.9, 127.3, 124.0. HRMS (ESI) calcd. for $C_{12}H_{11}N_2$ [M+H]: 183.0922, found: 183.0931.

4.2.2 (E)-3-styrylpyridazine (3b)

The title compound was prepared according to the general procedure and purified by column chromatography to give a yellow solid, 147 mg, 81% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.98 (d, *J* = 4.8 Hz, 1H), 7.63 (d, *J* = 16.4 Hz, 1H), 7.55 (t, *J* = 4.9 Hz, 2H), 7.52 (s, 1H), 7.40 – 7.36 (m, 1H), 7.31 (dd, *J* = 8.7, 4.6 Hz, 3H), 7.26 (d, *J* = 5.2 Hz, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 158.3, 149.7, 135.9, 135.2, 129.1, 128.9, 127.4, 126.4, 125.2, 123.9 ppm. HRMS (ESI) calcd. for $C_{12}H_{11}N_2$ [M+H]: 183.0922, found: 183.0928.

4.2.3 (E)-2-methyl-6-styrylpyrazine (3c)

The title compound was prepared according to the general procedure and purified by column chromatography to give the colorless oil 119 mg, 61% yield.
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.46 (s, 1H), 8.29 (s, 1H), 7.73 (d, *J* = 16.1 Hz, 1H), 7.59 (d, *J* = 7.1 Hz, 2H), 7.37 (dt, *J* = 13.9, 6.9 Hz, 3H), 7.14 (d, *J* = 16.1 Hz, 1H), 2.59 (s, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 153.3, 150.1, 142.6, 140.5, 136.2, 134.7, 128.8, 127.3, 124.5, 21.8 ppm. HRMS (ESI) calcd. for $C_{13}H_{13}N_2$ [M+H]: 197.1079, found: 197.1082.

4.2.4 (E)-4-styrylpyridine (3d)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 95 mg, 53% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.59 (d, *J* = 4.4 Hz, 2H), 7.65 – 7.49 (m, 2H), 7.38 (dt, *J* = 15.3, 6.3 Hz, 5H), 7.34 – 7.26 (m, 2H), 7.03 (d, *J* = 16.3 Hz, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 150.0, 144.7, 136.1, 133.2, 128.8, 128.7, 127.0, 125.9, 120.8 ppm. HRMS (ESI) calcd. for $C_{13}H_{12}N$ [M+H]: 182.0970, found: 182.0978.

4.2.5 General (E)-2-styrylbenzo[d]oxazole (3e)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 156 mg, 71% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.06 (d, *J* = 8.5 Hz, 1H), 8.01 (d, *J* = 8.5 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.69 – 7.62 (m, 1H), 7.57 – 7.48 (m, 2H), 7.44 (dt, *J* = 8.0, 4.0 Hz, 2H), 7.22 (d, *J* = 2.1 Hz, 1H), 6.51 (d, *J* = 2.8 Hz, 1H), 6.43 (dd, *J* = 3.3, 1.8 Hz, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 162.8, 150.4, 142.2, 139.4, 135.1, 129.7, 128.9, 127.5, 125.2, 124.5, 119.8, 113.9, 110.3 ppm. HRMS (ESI) calcd. for $C_{15}H_{12}NO$ [M+H]: 222.0919, found: 222.0908.

4.2.6 (E)-4-styrylquinoline (3f)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 120 mg, 52% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.96 (s, 1H), 8.24 (t, *J* = 8.2 Hz, 2H), 7.88 – 7.74 (m, 2H), 7.71 – 7.57 (m, 4H), 7.44 (dt, *J* = 26.5, 11.5 Hz, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 149.9, 148.4, 143.0, 136.4, 135.1, 129.8, 129.3, 128.8, 128.7, 127.0, 126.5, 126.3, 123.4, 122.7, 116.9 ppm. HRMS (ESI) calcd. for $C_{17}H_{14}N$ [M+H]: 232.1126, found: 232.1128.

4.2.7 (E)-1-styrylisoquinoline (3g)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 53mg, 23% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.57 (d, *J* = 5.6 Hz, 1H), 8.39 (d, *J* = 8.4 Hz, 1H), 8.01 (s, 2H), 7.84 (d, *J* = 8.2 Hz, 1H), 7.67 (ddd, *J* = 15.3, 14.8, 7.1 Hz, 4H), 7.58 (d, *J* = 5.6 Hz, 1H), 7.43 (dd, *J* = 10.9, 4.4 Hz, 2H), 7.38 – 7.29 (m, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 154.6, 142.5, 136.9, 136.8, 135.8, 129.9, 128.8, 128.6, 127.5, 127.3, 127.2, 124.5, 122.9, 120.0 ppm. HRMS (ESI) calcd. for $C_{17}H_{14}N$ [M+H]: 232.1126, found: 232.1141.

4.2.8 (E)-2-styrylquinoline (3h)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 217 mg, 94% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.20 – 8.07 (m, 2H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.69 (ddd, *J* = 15.4, 6.3, 4.5 Hz, 5H), 7.50 (t, *J* = 7.5 Hz, 1H), 7.47 – 7.38 (m, 3H), 7.37 – 7.30 (m, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.9, 148.1, 136.4, 136.3, 134.4, 129.7, 129.1, 128.9, 128.7, 128.6, 127.4, 127.2, 126.1, 119.2 ppm. HRMS (ESI) calcd. for $C_{17}H_{14}N$ [M+H]: 232.1126, found: 232.1133.

4.2.9 (E)-6-chloro-2-styrylquinoline (3i)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 217 mg, 82% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.11 – 7.94 (m, 2H), 7.76 (d, *J* = 2.1 Hz, 1H), 7.71 (d, *J* = 11.8 Hz, 1H), 7.68 – 7.58 (m, 4H), 7.42 (d, *J* = 8.2 Hz, 2H), 7.40 – 7.30 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.1, 146.5, 136.3, 135.4, 134.9, 131.8, 130.6, 128.8, 128.4, 127.8, 127.3, 126.2, 120.2 ppm. HRMS (ESI) calcd. for $C_{17}H_{13}ClN$ [M+H]: 266.0736, found: 266.0736.

4.2.10 (E)-6-methoxy-2-styrylquinoline (3j)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 237 mg, 91% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.01 (s, 1H), 7.98 (s, 1H), 7.63 (d, *J* = 5.9 Hz, 2H), 7.62 – 7.58 (m, 2H), 7.43 – 7.37 (m, 3H), 7.36 – 7.26 (m, 2H), 7.04 (d, *J* = 2.8 Hz, 1H), 3.91 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.6, 153.6, 144.0, 136.6, 135.1, 133.3, 130.5, 128.8, 128.7, 128.4, 128.2, 127.1, 122.3, 119.5, 105.2, 55.5 ppm. HRMS (ESI) calcd. for $C_{18}H_{16}NO$ [M+H]: 262.1232, found: 262.1241.

4.2.11 (E)-4-(1,2-diphenylvinyl)pyridine (3k)

The title compound was prepared according to the general procedure and purified by column chromatography to give a yellow solid 118mg, 46% yield. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.82 (s, 2H), 7.77 (dd, *J* = 23.0, 11.7 Hz, 6H), 7.52 – 7.28 (m, 7H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ 148.4, 142.5, 135.8, 133.3, 128.2, 128.0, 126.6, 124.3 ppm. HRMS (ESI) calcd. for $C_{19}H_{16}N$ [M+H]: 258.1283, found: 258.1291.

4.2.12 (E)-2-(1-phenylprop-1-en-2-yl)pyrazine (3l)

The title compound was prepared according to the general procedure and purified by column chromatography to give

the colorless oil 74 mg, 38% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.86 (s, 1H), 8.56 (s, 1H), 8.45 (d, *J* = 2.1 Hz, 1H), 7.50 (s, 1H), 7.45 – 7.36 (m, 4H), 7.34 – 7.27 (m, 1H), 2.38 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.4, 142.6, 141.9, 137.1, 1321, 129.4, 128.3, 127.4, 15.4 ppm. HRMS (ESI) calcd. for $C_{13}H_{13}N_2$ [M+H]: 197.1079, found: 197.1075.

4.2.13 2-(1-(naphthalen-1-yl)prop-1-en-2-yl)pyrazine (3m) (E:Z= 7:1)

The title compound was prepared according to the general procedure and purified by column chromatography to give a yellow solid 89 mg, 36% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.95 (s, 1H), 8.62 (s, 1H), 8.51 (s, 1H), 8.21 (s, 0.19H), 8.09-8.07 (m, 0.35H), 8.03-8.00 (m, 2H), 7.92-7.86 (m, 1H), 7.86-7.83 (m, 1.27H), 7.72-7.69 (m, 0.25H), 7.55-7.46 (m, 5.05H), 7.32 (s, 0.18H), 7.22-7.21 (2, 0.22H), 6.97 -6.95 (m, 0.15H), 2.45 (s, 0.48H), 2.25 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 154.7, 143.6, 142.8, 141.9, 135.5, 134.4, 133.6, 131.9, 130.3, 128.5, 127.9, 126.8, 126.2, 126.0, 125.3, 125.0, 15.6 ppm. HRMS (ESI) calcd. for $C_{17}H_{15}N_2$ [M+H]: 247.1235, found: 247.1241.

4.2.14 (E)-2-(hex-2-en-2-yl)pyrazine (3n)

The title compound was prepared according to the general procedure and purified by column chromatography to give a yellow solid 53 mg, 32% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.64 (s, 1H), 8.45 (s, 1H), 8.33 (s, 1H), 5.90 (d, *J* = 10.0 Hz, 1H), 2.23 (s, 3H), 1.81 – 1.69 (m, 1H), 0.96 – 0.89 (m, 2H), 0.59 (dd, *J* = 5.6, 3.5 Hz, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.2, 141.6, 141.1, 138.6, 130.4, 129.8, 13.9, 11.7, 7.9 ppm. HRMS (ESI) calcd. for $C_{10}H_{15}N_2$ [M+H]: 163.1235, found: 163.1241.

4.2.15 (E)-2-(4-methylstyryl)pyrazine (5a)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 174 mg, 89% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.59 (d, *J* = 31.0 Hz, 2H), 8.40 (s, 1H), 7.73 (d, *J* = 16.1 Hz, 1H), 7.50 (d, *J* = 7.9 Hz, 2H), 7.21 (d, *J* = 7.8 Hz, 2H), 7.12 (d, *J* = 16.1 Hz, 1H), 2.39 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 151.5, 144.2, 143.7, 142.5, 139.2, 135.2, 133.3, 129.6, 127.3, 123.0, 21.4 ppm. HRMS (ESI) calcd. for $C_{13}H_{13}N_2$ [M+H]: 197.1079, found: 197.1082.

4.2.16 (E)-2-(4-chlorostyryl)pyrazine (5b)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 174 mg, 81% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.63 (s, 1H), 8.54 (s, 1H), 8.43 (s, 1H), 7.69 (d, *J* = 16.1 Hz, 1H), 7.52 (d, *J* = 8.5 Hz, 2H), 7.45 (d, *J* = 8.4 Hz, 2H), 7.14 (d, *J* = 16.1 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 150.8, 144.3, 143.7, 142.9, 134.6, 134.4, 133.7, 128.9, 128.4, 124.4 ppm. HRMS (ESI) calcd. for $C_{12}H_{10}ClN_2$ [M+H]: 217.0532, found: 217.0541.

4.2.17 (E)-2-(4-bromostyryl)pyrazine (5c)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 189 mg, 73% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.63 (s, 1H), 8.54 (s, 1H), 8.43 (s, 1H), 7.69 (d, *J* = 16.1 Hz, 1H), 7.52 (d, *J* = 8.5 Hz, 2H), 7.45 (d, *J* = 8.4 Hz, 2H), 7.14 (d, *J* = 16.1 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.4, 143.9, 143.0, 135.0, 133.9, 132.0, 128.7, 124.64, 123.0 ppm. HRMS (ESI) calcd. for $C_{12}H_{10}BrN_2$ [M+H]: 261.0027, found: 261.0032.

4.2.18 (E)-2-(2-(thiophen-2-yl)vinyl)pyrazine (5d)

The title compound was prepared according to the general procedure and purified by column chromatography to give a yellow solid, 127 mg, 68% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.53 (d, *J* = 17.7 Hz, 2H), 8.38 (s, 1H), 7.88 (d, *J* = 15.8 Hz, 1H), 7.30 (d, *J* = 5.0 Hz, 1H), 7.21 (d, *J* = 3.0 Hz, 1H), 7.04 (dt, *J* = 5.0, 3.4 Hz, 1H), 6.94 (d, *J* = 15.8 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 150.8, 144.2, 143.5, 142.5, 141.5, 128.6, 127.9, 127.8, 126.3, 123.0 ppm. HRMS (ESI) calcd. for $C_{10}H_9N_2S$ [M+H]: 189.0486, found: 189.0492.

4.2.19 (E)-2-(2-methylstyryl)quinoline (5e)

The title compound was prepared according to the general procedure and purified by column chromatography to give the colorless oil, 162 mg, 66% yield.^{1}H NMR (300 MHz, $CDCl_3$): δ 8.16 (t, *J* = 8.5 Hz, 2H), 8.00 (d, *J* = 16.2 Hz, 1H), 7.85 – 7.71 (m, 4H), 7.54 (dd, *J* = 8.1, 7.0 Hz, 1H), 7.37 (d, *J* = 16.2 Hz, 1H), 7.33 – 7.29 (m, 1H), 2.57 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.1, 148.2, 136.5, 136.2, 135.1, 132.0, 130.5, 130.1, 129.6, 129.2, 128.4, 127.4, 127.2, 126.2, 126.1, 125.7, 119.2, 19.9 ppm.HRMS (ESI) calcd. for $C_{18}H_{16}N$ [M+H]: 246.1283, found: 246.1289.

4.2.20 (E)-2-(3-methylstyryl)quinoline (5f)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 205 mg, 84% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.13 (d, *J* = 8.6 Hz, 1H), 8.08 (d, *J* = 8.5 Hz, 1H), 7.79 (d, *J* = 8.1 Hz, 1H), 7.75 – 7.67 (m, 2H), 7.65 (d, *J* = 7.8 Hz, 1H), 7.47 (dt, *J* = 28.9, 11.8 Hz, 4H), 7.29 (d, *J* = 7.5 Hz, 1H), 7.15 (d, *J* = 7.4 Hz, 1H), 2.41 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.1, 148.3, 138.4, 136.5, 136.3, 134.5, 129.7, 129.5, 129.2, 128.9, 128.7, 123.0, 127.5, 126.1, 124.5, 119.2, 21.5 ppm. HRMS (ESI) calcd. for $C_{18}H_{16}N$ [M+H]: 246.1283, found: 246.1291.

4.2.21 (E)-2-(4-methylstyryl)quinolines (5g)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 227 mg, 93% yield.^{1}H NMR (300 MHz, $CDCl_3$): δ 8.12 (d, *J* = 8.6 Hz, 1H), 8.07 (d, *J* = 8.5 Hz, 1H), 7.78 (d, *J* = 8.1 Hz, 1H), 7.70 (dt, *J* = 5.3, 4.7 Hz, 2H), 7.65 (d, *J* = 5.0 Hz, 1H), 7.55 (d, *J* = 8.0 Hz, 2H), 7.49 (dd, *J* = 8.0, 7.0 Hz, 1H), 7.37 (d, *J* = 16.3 Hz, 1H), 7.22 (d, *J* = 8.0 Hz, 2H), 2.39 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.1, 148.2, 138.7, 136.2, 134.3, 133.7, 129.6, 129.5, 129.1, 128.0, 127.4, 127.2, 127.2, 126.0, 119.1, 21.3 ppm. HRMS (ESI) calcd. for $C_{18}H_{16}N$ [M+H]: 246.1283, found: 246.1285.

4.2.22 (E)-2-(2,4,6-trimethylstyryl)quinoline(5h)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 175mg, 64% yield.
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.12 (dd, *J* = 12.2, 8.6 Hz, 2H), 7.83 – 7.66 (m, 4H), 7.50 (dd, *J* = 8.1, 6.9 Hz, 1H), 6.94 (dd, *J* = 11.1, 5.5 Hz, 3H), 2.44 (s, 6H), 2.32 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.3, 148.3, 137.0, 136.5, 136.5, 136.3, 134.1, 133.1, 132.9, 129.7, 129.3, 129.0, 127.5, 127.4, 126.1, 119.0, 21.3, 21.1 ppm. HRMS (ESI) calcd. for $C_{20}H_{20}N$ [M+H]: 274.1596, found: 274.1599.

4.2.23 (E)-2-(4-(tert-butyl)styryl)quinoline (5i)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 261mg, 91% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.12 (d, *J* = 8.6 Hz, 1H), 8.08 (d, *J* = 8.5 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.69 (dd, *J* = 17.2, 8.8 Hz, 3H), 7.59 (d, *J* = 8.3 Hz, 2H), 7.49 (dd, *J* = 7.9, 7.0 Hz, 1H), 7.46 – 7.34 (m, 3H), 1.35 (s, 9H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.3, 152.0, 148.3, 136.3, 134.3, 133.8, 129.7, 129.2, 128.3, 127.5, 127.3, 127.1, 126.1, 125.8, 119.2, 34.8, 31.3 ppm. HRMS (ESI) calcd. for $C_{21}H_{22}N$ [M+H]: 288.1752, found: 288.1763.

4.2.24 (E)-2-(2-([1,1'-biphenyl]-4-yl)vinyl)quinoline (5j)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 254 mg, 83% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.15 (d, *J* = 8.5 Hz, 1H), 8.10 (d, *J* = 8.5 Hz, 1H), 7.80 (d, *J* = 8.1 Hz, 1H), 7.78 – 7.71 (m, 4H), 7.70 – 7.59 (m, 5H), 7.54 – 7.48 (m, 2H), 7.45 (d, *J* = 7.2 Hz, 2H), 7.37 (dd, *J* = 11.2, 4.6 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.9, 148.2, 141.3, 140.4, 136.3, 135.5, 133.9, 129.7, 129.1, 128.9, 128.8, 127.7, 127.5, 127.4, 127.3, 126.9, 126.1, 119.3 ppm. HRMS (ESI) calcd. for $C_{23}H_{18}N$ [M+H]: 308.1439, found: 308.1442.

4.2.25 (E)-2-(2-methoxystyryl)quinoline (5k)

The title compound was prepared according to the general procedure and purified by column chromatography to give the colorless oil, 185 mg, 71% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.10 (t, *J* = 8.0 Hz, 2H), 8.03 (d, *J* = 16.6 Hz, 1H), 7.79 – 7.66 (m, 4H), 7.52 – 7.41 (m, 2H), 7.36 – 7.27 (m, 1H), 7.01 (t, *J* = 7.5 Hz, 1H), 6.94 (d, *J* = 8.3 Hz, 1H), 3.93 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.4, 156.7, 148.2, 136.1, 129.7, 129.6, 129.3, 129.2, 127.4, 127.2, 127.2, 126.0, 125.5, 120.8, 119.0, 111.0, 55.5 ppm. HRMS (ESI) calcd. for $C_{18}H_{16}NO$ [M+H]: 262.1232, found: 262.1241.

4.2.26 (E)-2-(4-methoxystyryl)quinoline (5l)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 240 mg, 92% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.14 (d, *J* = 8.5 Hz, 1H), 8.09 (d, *J* = 8.5 Hz, 1H), 7.81 (d, *J* = 8.1 Hz, 1H), 7.77 – 7.69 (m, 2H), 7.64 (dd, *J* = 11.4, 6.7 Hz, 3H), 7.51 (t, *J* = 7.4 Hz, 1H), 7.34 (s, 1H), 7.29 (d, *J* = 1.7 Hz, 2H), 6.97 (d, *J* = 7.3 Hz, 2H), 3.88 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.1, 156.3, 148.3, 136.2, 134.0, 129.7, 129.3, 129.1, 128.7, 127.5, 127.2, 126.9, 125.9, 119.2, 114.3, 55.4 ppm. HRMS (ESI) calcd. for $C_{18}H_{16}NO$ [M+H]: 262.1232, found: 262.1238.

4.2.27 (E)-2-(2-chlorostyryl)quinolines (5m)

The title compound was prepared according to the general procedure and purified by column chromatography to give the colorless oil, 151 mg, 57% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.13 (dd, *J* = 25.6, 12.7 Hz, 2H), 7.93 – 7.68 (m, 3H), 7.57 – 7.41 (m, 2H), 7.35 – 7.28 (m, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.7, 148.1, 136.3, 134.5, 134.0, 131.7, 130.1, 129.9, 129.7, 129.4, 129.2, 127.4, 127.4, 127.0, 126.9, 126.33, 118.9 ppm. HRMS (ESI) calcd. for $C_{17}H_{13}ClN$ [M+H]: 266.0736, found: 266.0742.

4.2.28 (E)-2-(4-chlorostyryl)quinolines (5n)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 222 mg, 84% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.14 (d, *J* = 8.5 Hz, 1H), 8.08 (d, *J* = 8.5 Hz, 1H), 7.79 (d, *J* = 8.1 Hz, 1H), 7.75 – 7.62 (m, 3H), 7.60 – 7.48 (m, 3H), 7.37 (dd, *J* = 12.1, 3.7 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.5, 148.2, 136.3, 135.0, 134.2, 132.9, 129.8, 129.4, 129.2, 128.9, 128.3, 127.5, 127.3, 126.2, 119.3 ppm. HRMS (ESI) calcd. for $C_{17}H_{13}ClN$ [M+H]: 266.0736, found: 266.0739.

4.2.29 (E)-2-(4-bromostyryl)quinolines (5o)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 204 mg, 66% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.14 (d, *J* = 8.6 Hz, 1H), 8.08 (d, *J* = 8.5 Hz, 1H), 7.79 (d, *J* = 8.1 Hz, 1H), 7.71 (dd, *J* = 8.4, 7.0 Hz, 1H), 7.66 (d, *J* = 1.3 Hz, 1H), 7.62 (d, *J* = 5.8 Hz, 1H), 7.55 – 7.48 (m, 5H), 7.38 (d, *J* = 16.3 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.5, 148.1, 136.5, 135.4, 133.1, 131.9, 129.8, 129.5, 129.1, 128.6, 127.5, 127.4, 126.3, 122.5, 119.3 ppm. HRMS (ESI) calcd. for $C_{17}H_{13}BrN$ [M+H]: 310.0231, found: 310.0242.

4.2.30 (E)-2-(4-iodostyryl)quinolines (5p)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 171 mg, 48% yield.^{1}H NMR (300 MHz, $CDCl_3$): δ 8.14 (d, *J* = 8.5 Hz, 1H), 8.08 (d, *J* = 8.9 Hz, 1H), 7.79 (d, *J* = 8.1 Hz, 1H), 7.72 (t, *J* = 8.4 Hz, 3H), 7.63 (dd, *J* = 12.4, 7.3 Hz, 2H), 7.51 (t, *J* = 7.5 Hz, 1H), 7.43 – 7.35 (m, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.5, 148.2, 137.9, 136.4, 136.0, 133.1, 129.8, 129.7, 129.2, 128.8, 127.5, 127.4, 126.3, 119.4, 94.2 ppm. HRMS (ESI) calcd. for $C_{17}H_{13}IN$ [M+H]: 358.0093, found: 358.0098.

4.2.31 (E)-2-(2-(naphthalen-1-yl)vinyl)quinolines (5q)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 217 mg, 77% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.54 (d, *J* = 16.0 Hz, 1H), 8.36 (d, *J* = 8.2 Hz, 1H), 8.16 (t, *J* = 8.8 Hz, 2H), 7.97 – 7.84 (m, 3H), 7.81 (d, *J* = 8.1 Hz, 1H), 7.78 – 7.68 (m, 2H), 7.62 – 7.53 (m, 3H),

7.53 – 7.45 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.0, 148.3, 136.5, 136.4, 134.0, 133.7, 133.7, 131.8, 131.7, 131.5, 131.3, 129.7, 129.3, 128.9, 128.6, 127.6, 127.5, 127.4, 126.4, 126.3, 126.2, 125.9, 125.7, 124.2, 123.7, 119.5, 117.4 ppm. HRMS (ESI) calcd. for $C_{21}H_{16}N$ [M+H]: 282.1283, found: 282.1283.

4.2.32 (E)-2-(2-(furan-2-yl)vinyl)quinolines (5r)

The title compound was prepared according to the general procedure and purified by column chromatography to give a yellow solid, 128 mg, 58% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.80 (d, *J* = 16.4 Hz, 1H), 7.76 – 7.68 (m, 1H), 7.63 – 7.59 (m, 2H), 7.54 (dd, *J* = 5.0, 4.2 Hz, 1H), 7.48 – 7.37 (m, 3H), 7.34 (dd, *J* = 6.2, 3.3 Hz, 2H), 7.09 (d, *J* = 15.7 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.6, 152.8, 148.3, 143.1, 136.3, 129.7, 129.2, 127.5, 127.3, 126.8, 126.0, 121.7, 119.9, 111.9, 111.1 ppm. HRMS (ESI) calcd. for $C_{15}H_{12}NO$ [M+H]: 222.0919, found: 222.0921.

4.2.33 (E)-2-(2-(thiophen-2-yl)vinyl)quinolines (5s)

The title compound was prepared according to the general procedure and purified by column chromatography to give a yellow solid, 175 mg, 74% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.92 (dd, *J* = 14.8, 8.5 Hz, 2H), 7.69 (d, *J* = 16.1 Hz, 1H), 7.61 – 7.51 (m, 2H), 7.37 (d, *J* = 8.5 Hz, 1H), 7.33 (dt, *J* = 8.0, 3.9 Hz, 1H), 7.13 (d, *J* = 5.1 Hz, 1H), 7.07 (dd, *J* = 9.8, 6.2 Hz, 2H), 6.96 – 6.86 (m, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.4, 148.1, 141.9, 136.1, 129.6, 129.0, 128.1, 128.0, 127.7, 127.4, 127.1, 125.9, 125.9, 119.2 ppm. HRMS (ESI) calcd. for $C_{15}H_{12}NS$ [M+H]: 238.0690, found: 238.0687.

4.2.34 (E)-2-(3-ethylpent-1-en-1-yl)quinolines (5t)

The title compound was prepared according to the general procedure and purified by column chromatography to give the colorless oil, 139 mg, 53% yield.^{1}H NMR (300 MHz, $CDCl_3$): δ 8.04 (dd, *J* = 8.5, 5.4 Hz, 2H), 7.74 (d, *J* = 8.1 Hz, 1H), 7.66 (dd, *J* = 8.4, 7.0 Hz, 1H), 7.56 (d, *J* = 8.6 Hz, 1H), 7.45 (dd, *J* = 8.1, 6.9 Hz, 1H), 6.70 (d, *J* = 16.0 Hz, 1H), 6.55 (dd, *J* = 16.0, 8.6 Hz, 1H), 2.09 (ddt, *J* = 13.4, 8.8, 4.4 Hz, 1H), 1.49 (ddt, *J* = 21.0, 13.6, 6.8 Hz, 4H), 0.92 (t, *J* = 7.4 Hz, 6H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.5, 148.0, 141.8, 136.0, 131.3, 129.4, 129.1, 127.4, 127.1 125.8, 118.5, 46.8, 27.5, 11.9 ppm. HRMS (ESI) calcd. for $C_{16}H_{20}N$ [M+H]: 263.1310, found: 263.1310.

4.2.35 (E)-2-(3,3-dimethylbut-1-en-1-yl)quinolines (5u)

The title compound was prepared according to the general procedure and purified by column chromatography to give the colorless oil, 128 mg, 61% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.95 (d, *J* = 8.5 Hz, 2H), 7.64 (d, *J* = 8.1 Hz, 1H), 7.57 (t, *J* = 7.7 Hz, 1H), 7.46 (d, *J* = 8.7 Hz, 1H), 7.36 (t, *J* = 7.5 Hz, 1H), 6.74 (d, *J* = 16.2 Hz, 1H), 6.57 (d, *J* = 16.3 Hz, 1H), 1.11 (s, 10H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.8, 148.1, 148.0, 136.0, 129.4, 129.0, 127.3, 127.0, 126.4, 125.7, 118.5, 33.8, 29.4 ppm. HRMS (ESI) calcd. for $C_{15}H_{18}N$ [M+H]: 212.1439, found: 212.1442.

4.2.36 (E)-2-(2-cyclopropylvinyl)quinolines (5v)

The title compound was prepared according to the general procedure and purified by column chromatography to give the colorless oil, 109 mg, 56% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.92 (dd, *J* = 8.6, 2.7 Hz, 2H), 7.63 (d, *J* = 8.1 Hz, 1H), 7.56 (ddd, *J* = 8.3, 7.0, 1.3 Hz, 1H), 7.44 – 7.25 (m, 2H), 6.69 (d, *J* = 15.7 Hz, 1H), 6.30 (dd, *J* = 15.7, 9.3 Hz, 1H), 1.76 – 1.48 (m, 1H), 0.88 – 0.80 (m, 2H), 0.61 – 0.48 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.1, 148.1, 142.0, 136.0, 129.4, 128.9, 128.2, 127.3, 126.9, 125.6, 118.8 , 14.9, 8.0 ppm. HRMS (ESI) calcd. for $C_{14}H_{14}N$ [M+H]: 196.1126, found: 196.1126.

4.2.37 (E)-2-(2-cyclohexylvinyl)quinolines (5w)

The title compound was prepared according to the general procedure and purified by column chromatography to give the colorless oil, 161 mg, 68% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.03 (d, *J* = 8.5 Hz, 2H), 7.73 (d, *J* = 8.1 Hz, 1H), 7.66 (t, *J* = 7.7 Hz, 1H), 7.51 (d, *J* = 8.5 Hz, 1H), 7.45 (dd, *J* = 11.4, 4.3 Hz, 1H), 6.78 (dd, *J* = 16.1, 6.2 Hz, 1H), 6.67 (d, *J* = 16.1 Hz, 1H), 2.24 (s, 1H), 1.92 – 1.69 (m, 5H), 1.40 – 1.19 (m, 5H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.7, 148.0, 143.3, 136.0, 129.4, 129.0, 128.6, 127.3, 127.0, 125.7, 118.6, 41.1, 32.5, 26.1, 25.9 ppm. HRMS (ESI) calcd. for $C_{17}H_{20}N$ [M+H]: 238.1596, found: 238.1596.

4.2.37 (E)-2-(2-(pyridin-2-yl)vinyl)quinolines (5x)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 121 mg, 52% yield.^{1}H NMR (300 MHz, $CDCl_3$): δ 8.68 – 8.51 (m, 1H), 8.11 (t, *J* = 8.5 Hz, 2H), 7.81 (dd, *J* = 4.0, 2.3 Hz, 2H), 7.74 (d, *J* = 8.1 Hz, 1H), 7.66 (ddd, *J* = 13.0, 8.1, 5.0 Hz, 3H), 7.54 (d, *J* = 6.9 Hz, 1H), 7.47 (t, *J* = 7.5 Hz, 1H), 7.16 (dd, *J* = 7.0, 3.8 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.1, 154.9, 149.7, 136.8, 136.7, 134.0, 132.1, 130.0, 129.0, 127.5, 126.6, 122.9, 122.8, 120.3, 109.9 ppm. HRMS (ESI) calcd. for $C_{16}H_{13}N_2$ [M+H]: 233.1079, found: 233.1079.

4.2.38 (E)-2-(4,8-dimethylnona-1,7-dien-1-yl)quinolines (5y)

The title compound was prepared according to the general procedure and purified by column chromatography to give the colorless oil, 184 mg, 66% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.97 (t, *J* = 8.5 Hz, 2H), 7.67 (d, *J* = 8.1 Hz, 1H), 7.59 (t, *J* = 7.7 Hz, 1H), 7.45 (d, *J* = 8.7 Hz, 1H), 7.38 (t, *J* = 7.5 Hz, 1H), 6.71 (dt, *J* = 30.0, 11.4 Hz, 2H), 5.04 (t, *J* = 6.3 Hz, 1H), 2.39 – 2.19 (m, 1H), 2.10 (dt, *J* = 14.3, 7.1 Hz, 1H), 1.96 (dt, *J* = 15.6, 7.6 Hz, 2H), 1.61 (s, 3H), 1.54 (s, 3H), 1.37 (ddd, *J* = 9.1, 6.4, 3.2 Hz, 1H), 1.23 – 1.13 (m, 1H), 0.90 (d, *J* = 6.7 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.3, 136.2, 132.1, 131.2, 129.5, 129.0, 127.4, 127.1, 125.8, 124.6, 118.6, 40.6, 36.8, 32.7, 25.7, 25.6, 19.6, 17.7 ppm. HRMS (ESI) calcd. for $C_{20}H_{26}N$ [M+H]: 280.2065, found: 280.2071.

4.2.39 (E)-2,6-di((E)-styryl)pyrazine (7a)

The title compound was prepared according to the general procedure and purified by column chromatography to give a yellow solid 150 mg, 53% yield.^{1}H NMR (300 MHz, DMSO-d_6): δ 8.76 (s, 2H), 7.79 (s, 1H), 7.73 (s, 1H), 7.69 (d, *J* = 7.4 Hz, 4H), 7.43 (d, *J* = 6.4 Hz, 4H), 7.39 (s, 2H),

7.35 (d, *J* = 7.3 Hz, 2H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ 149.3, 141.4, 135.5, 133.9, 128.4, 126.8, 124.1, 109.0 ppm. HRMS (ESI) calcd. for $C_{20}H_{17}N_2$ [M+H]: 285.1392, found: 285.1387.

4.2.40 (E)-2,5-di((E)-styryl)pyrazine (7b)

The title compound was prepared according to the general procedure and purified by column chromatography to give a yellow solid 116 mg, 41% yield.^{1}H NMR (300 MHz, DMSO-d_6): δ 8.61 (s, 2H), 7.84 (d, *J* = 16.2 Hz, 2H), 7.69 (d, *J* = 7.8 Hz, 4H), 7.40 (t, *J* = 7.5 Hz, 5H), 7.35 – 7.25 (m, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ 147.9, 142.3, 135.4, 133.0, 127.9, 126.3, 123.8 ppm. HRMS (ESI) calcd. for $C_{20}H_{17}N_2$ [M+H]: 285.1392, found: 285.1390.

Notes

The authors declare no competing financial interest.

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Supplementary Material

Supplementary data associated with this article can be found, in the online version, at

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Pergamon

MnO_2 Mediated Sequential Oxidation/Olefination of Alkyl-Substituted Heteroarenes with Alcohols

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ABSTRACT

A practical and efficient ligand-free MnO_2 mediated sequential oxidation and olefination has been developed for the facile synthesis of a broad range of unsaturated *N*-heteroazaarenes from simple alkyl-substituted heteroarenes and alcohols. The procedure tolerates a series of functional groups, such as methoxyl, chloro, bromo, iodo, vinyl, phenolic and hetero groups, providing the olefination products in moderate to good yields.The protocol could be conducted at mild conditions and used environmentally friendly air as the clear oxidant.

1. Introduction

As one of the most important fundamental structural motifs, unsaturated *N*-heteroaromatic compounds has been considered as a privileged structure in natural products, pharmaceuticals and functional materials (Figure 1).[1] As such, the development of efficient methods toward these complex molecules is of great significance to chemical, medicinal and material science and has attracted a great deal of attention over the past decades.[2] Plenty of powerful synthetic routes, including many named reactions,[3] catalytic coupling[4] or olefin metathesis,[5] have been developed to access such kinds of molecules. However, multi-step functional group manipulations and unavoidable generation of stoichiometric amount of undesired waste are the few shortcomings in these reactions.

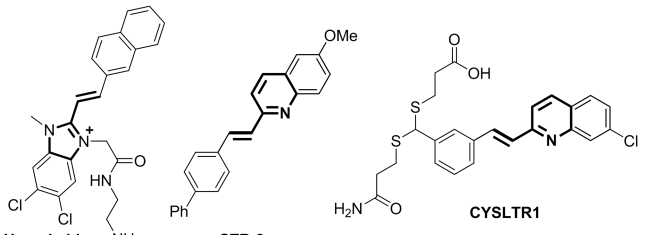
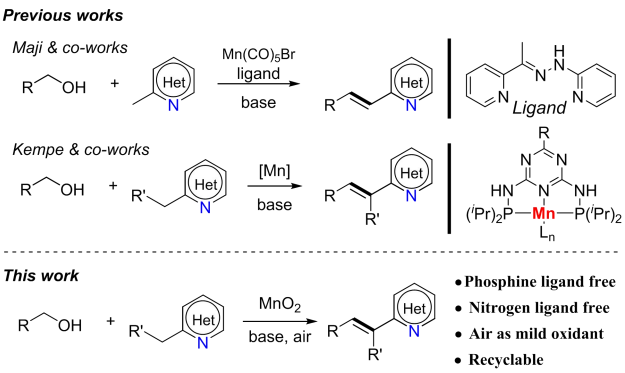


Figure 1. Selected bioactive compounds with unsaturated *N*-heteroarene moiety.

An attractive approach to circumvent these problems is abundantly available metal catalyzed acceptorless dehydrogenative condensation (ADC),[6] which enables the synthesis of di-substituted alkenes compounds from alcohols combination of catalytic dehydrogenation and condensation steps. Moreover, alcohols can be obtained from indigestible and abundantly available lignocellulose biomass.[7] Kempe[8] and Maji group[9] pioneered a novel manganese-catalyzed reaction leading to di-substituted olefins synthesis using alcohols with *N*-heteroarenes at the same time, the reaction proceeds via ADC process,



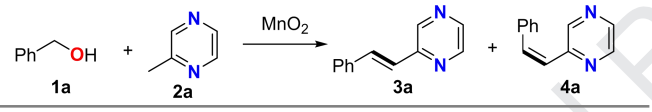
Scheme 1. Methods for Mn-catalyzed olefination.

producing only water and hydrogen as green coproducts (Scheme 1, top). However, metal complexes or addition of capricious ligands for catalyst activation are generally required to maintain the catalytic cycle, thereby limiting the potential scope of this environmentally benign transformation. These results together with our progress on the use of alcohols as green partners for metal catalyzed coupling reactions,[10] prompted us to envision that alcohols might be oxidized in MnO_2/air catalytic system and condensed with methylazaarenes for the synthesis of di-substituted olefins. Moreover, to the best of our knowledge, MnO_2 catalyzed oxidation/olefination of alcohols and methylazaarenes to synthesis unsaturated *N*-heteroaromatic has not been reported. Herein, we present on the first protocol for successful implementation of the MnO_2 catalyzed oxidation of alcohols with a variety of alkyl-substituted azaarenes via olefination process, which allows for synthesis of various multiple-substituted alkenes under mild condition.

2. Results and discussion

As an initial attempt, the reaction between phenylmethanol (**1a**) and 2-methylpyrazine (**2a**) was chosen as the model reaction for optimization of the reaction conditions (Table 1).

Table 1. Optimization of the reaction conditions [a]

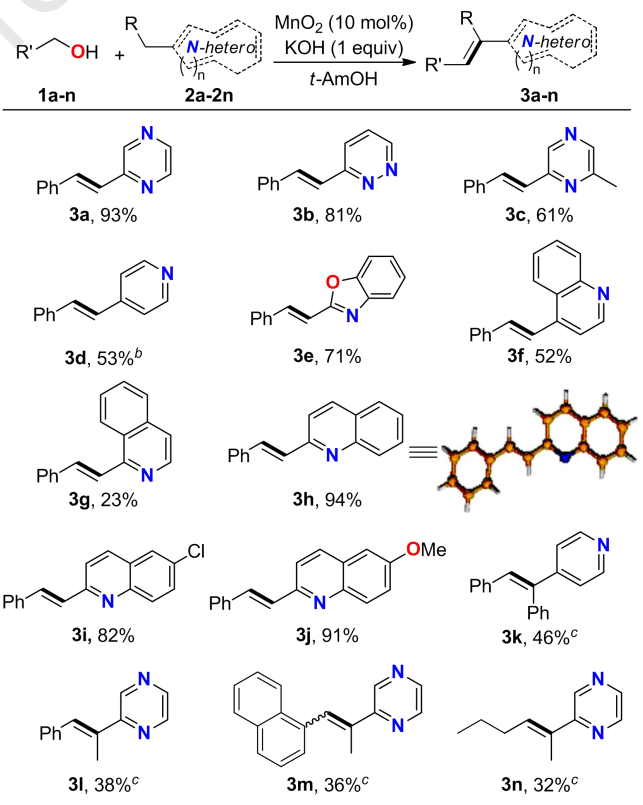


Entry	Base	Solvent	**3a** (%)	**3a**/**4a**
1	Cs_2CO_3	*t*-AmOH	12	> 20:1
2	K_2CO_3	*t*-AmOH	< 5	-
3	Na_2CO_3	*t*-AmOH	< 5	-
4	CsOH	*t*-AmOH	83	19:1
5	KOH	*t*-AmOH	96 (72)[b]	> 20:1
6	NaOH	*t*-AmOH	53	17:1
7	*t*-BuOLi	*t*-AmOH	< 5	-
8	*t*-BuONa	*t*-AmOH	63	16:1
9	*t*-BuOK	*t*-AmOH	89	18:1
10	KOH	*t*-BuOH	88	19:1
11	KOH	*i*-PrOH	12	> 20:1
12	KOH	EtOH	0	-
13	KOH	THF	32	> 20:1
14	KOH	Diglyme	90	16:1
15	KOH	Toluene	19	> 20:1
16	-	*t*-AmOH	0	-
17	KOH	*t*-AmOH	11[c] (10)[d]	> 20:1
18	KOH	*t*-AmOH	< 5[e]	-

[a] General conditions: **1a** (0.55 mmol), **2a** (0.5 mmol), MnO_2 (0.05 mmol), base (0.5 mmol), solvent (1.0 mL), 120 °C, 21 h. Yield of **3a** and the ratio of **3a**/**4a** determined by GC-analysis using *n*-cetane as an internal standard. [b] Under oxygen. [c] No MnO_2. [d] No MnO_2, 48 h. [e] Under nitrogen.

Because manganese precatalyst has shown to be highly effective for the dehydragenation/olefination of methylazaarenes with alcohols,[8,9] we initially focused on exploring conditions using MnO_2 as readily available catalyst at 120 °C. The desired (*E*)-2-styrylpyrazine (**3a**) was obtained in 12% yield, when the reaction was conducted in the presence of Cs_2CO_3 under an air atomsphere (Table 1, entry 1). This result indicated that our proposed sequential oxidation/olefination reactions of methylazaarene with alcohol was indeed possible. Base screening indicated that when the reaction was ran in presence of KOH, the desired product was obtained best yield and the high regioselective (Table 1, entry 5). The reaction still worked even under oxygen atmosphere (oxygen balloon) and **3a** was obtained in good yield. Other inorganic bases or organic bases, did not improve the reactivity (Table 1, entries 2-9). Further investigation of the solvents revealed that the reactivity was affected by the nature of the solvents, and the best result was achieved with *t*-AmOH as the solvent. Meanwhile, reaction in other alcohol solvents, such as *t*-BuOH, *i*-PrOH and EtOH resulted in lower yield or no reaction (Table 1, entries 10-12). This reactivity trend(*t*-AmOH > *t*-BuOH > *i*-PrOH > EtOH) is that sterically hindered alcohols suppress the competing aldol reaction with benzaldehyde intermediate, revealing that the mechanism may via aldehyde species. No appreciable increase in yield of olefination product was obtained in ether solvents or non-polar solvent. Finally, control reactions demonstrated that the low yield of **3a** was obtained under nitrogen atmosphere or in the absence of catalyst or base (Table 1, entries 16-18).

Table 2. Substrate scope of *N*-heteroaromatics [a]



[a] General conditions: **1a** (0.55 mmol), **2** (0.5 mmol), MnO_2 (10 mol%), KOH (0.5 mmol), *t*-AmOH (1.0 mL), air, 120 °C, 21 h. Isolated yield, unless otherwise noted. [b] **1a** (2.0 mmol), 140 °C, 36 h. [c] **1a** (2.0 mmol), KOH (1.0 mmol), 140 °C, 48 h.

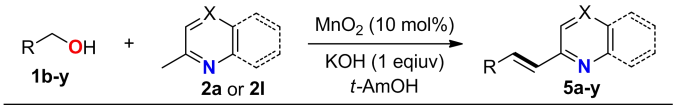
Taken together, we can conclude that the oxidation/olefination was carried out by stirring *t*-AmOH solution of phenylmethanol, 2-methylpyrazine, 10 mol% of MnO_2, and an equivalent of KOH at

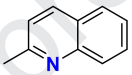
120°C under an air for 21 hours to give the olefination product **3a** in the best yield.

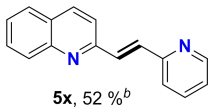
On the basis of the results described above, a variety of *N*-heteroaromatics were submitted to the MnO_2-catalyzed oxidant/olefination reaction to investigate its substrate scope and generality (Table 2). 2-Methylpyrazine and 3-methylpyridazine substrates gave the corresponding products in high yields (**3a-3b**). The oxidation/olefiantion reaction of 2,6-dimethylpyrazine or 4-methylpyridine (lower acidity of methyl) reacted with phenylmethanol resulted in modearate yields of the desired products **3c-3d**. When the pyrazine core was replaced with benzo[d]oxazole, the olefination reaction still took place to give **3e** in 71% yield. Although the reaction of 4-methylquinoline and 1-methylisoquinoline offered **3f** and **3g** in moderate yields, the reaction with 2-methylquinoline proceeded smoothy to produce the desired adduct **3h** in excellent yield. The yield of product is likely related to the stability of the enamine intermediate, which increases in the order **3g** < **3f** < **3h**. This result showing that the olefination mechanism may via enamine intermediate. Methyl-substituted *N*-heteroarenes derived from 2-methylquinoline were effective substrates and smoothly reacted with benzyl alcohol to provide the corresponding products **3i** and **3j** in 82 and 91% yield, respectively. Ethyl or benzyl substituted azaarenes were less reactive, and the olefination products **3k-3n** were isolated in moderate yields when the reaction temperature and time were increased. These results may be due to large steric hindrance of the methylenyl of the azaarenes.

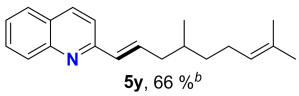
Furthermore, the scope of the alcohols was also explored and the results are shown in Table 3. The procedure tolerated well some functional groups, such as methyl, phenyl, methoxy, halogen and heteroarene, with good yields. The electronic effects of substituent in alcohol had some effect on the reaction. Generally, the alcohols with electron-withdrawing groups gave slightly lower yields than those electron-donating analogues (**5a** *vs* **5b-c** and **5g**, **5i**, **5l** *vs* **5n-5p**). An obvious steric hindrance effect on the reactivity was observed, which was demonstrated by the reactivities of **5e** *vs* **5g** and **5m** *vs* **5n**. It is worth noting that the tolerance of halogen group on the aromatic ring in this olefination protocol offers an opportunity for subsequent transformations, which facilitates expedient synthesis of complex unsaturate *N*-heteroarenes (**5b-5c**, **5m-5p**). Naphthyl-substituted alcohol was also compatible with this process, furnishing the desired product **5q** in 87% yield. In addition to aromatic-substituted alcohols, although the reaction of furan-2-ylmethanol gave the corresponding product **5r** in moderate yield, the reaction with thiophen-2-ylmethanol proceeded smoothy to give **5s** in good yield. Pyridin-2-ylmethanol was also a good reaction partner, and (*E*)-2-(2-(pyridin-2-yl)vinyl)quinoline **5x** was isolated in 52% yield. To extend the scope of our catalytic system, we also tested more challenging aliphatic alcohols under the standard procedure. 2-Ethylbutan-1-ol was initially surveyed and the reaction proceeded smoothly to give the desired olefination **5t** in moderate yield. Furthermore, similar results were obtained in the reactions of aliphatic alcohols with different substituted to deliver the desired adducts **5u-5w** efficiently in good yields. And importantly, unsaturate alcohol substrates, citronellol, was also good reaction partner, providing the corresponding product **5y** in 66% yield, while the internal double bond remained intact.

Table 3. Substrate scope of alcohols [a]



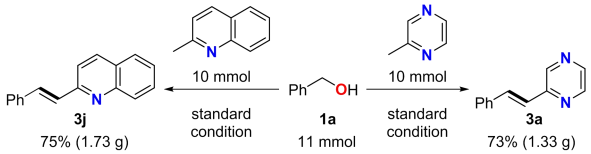
Entry		1	R	Yield (%)
1		**1d**	4-$CH_3C_6H_4$	**5a**, 89
2		**1k**	4-ClC_6H_4	**5b**, 81
3		**1l**	4-BrC_6H_4	**5c**, 73
4	**2a**	**1p**	2-thienyl	**5d**, 68
5		**1b**	2-$CH_3C_6H_4$	**5e**, 66
6		**1c**	3-$CH_3C_6H_4$	**5f**, 84
7		**1d**	4-$CH_3C_6H_4$	**5g**, 93
8		**1e**	2,4,6-$(CH_3)_3C_6H_2$	**5h**, 64
9		**1f**	4-*t*-BuC_6H_4	**5i**, 91
10		**1g**	4-PhC_6H_4	**5j**, 83
11		**1h**	2-$CH_3OC_6H_4$	**5k**, 71
12		**1i**	4-$CH_3OC_6H_4$	**5l**, 92
13		**1j**	2-ClC_6H_4	**5m**, 57
14		**1k**	4-ClC_6H_4	**5n**, 84
15	**2l**	**1l**	4-BrC_6H_4	**5o**, 66
16		**1m**	4-IC_6H_4	**5p**, 48
17		**1n**	1-Naphthyl	**5q**, 77
18		**1o**	2-furyl	**5r**, 58
19		**1p**	2-thienyl	**5s**, 74
20		**1q**	Et_2CH	**5t**, 53[b]
21[b]		**1r**	*t*-Bu	**5u**, 61[b]
22[b]		**1s**	Cyclopropyl	**5v**, 56[b]
23[b]		**1t**	Cyclohexyl	**5w**, 68[b]


5x, 52 %[b]


5y, 66 %[b]

[a] General conditions: **1** (0.55 mmol), **2a** or **2l** (0.5 mmol), MnO_2 (10 mol%), KOH (0.5 mmol), *t*-AmOH (1.0 mL), air, 120 °C, 21 h. Isolated yield. [b] **1** (2.0 mmol), KOH (1.0 mmol), 140 °C, 48 h.

To further demonstrate the robustness of our system, we were able to run experiments on gram scale in the presence of 10 mol% of MnO_2 to produce the olefination adducts **3a** and **3j** in 73% (1.33 g) and 75% (1.73 g) yield, respectively.



Scheme 2. Gram scale experiments.

To validate the recyclability of current oxidant/olefination, the reuse investigation was performed in the model reaction of **1a** with **2a** in presence of 10 mol% of MnO_2. After the completion of reaction, a small aliquot of the reaction mixture was analyzed by

GC to monitor product **3a** formation. Then the reaction mixture was filtered, washed with ethyl acetate, water and ethanol, dried on vacuum, the catalyst of MnO_2 was recovered and continued to catalyze for another reaction. It is shown in Figure. 2 that the olefination could be repeated at least five times with the fifth run giving a 81% yield of **3a**. And the catalytic activity of the recovered MnO_2 dried on the oxygen atmosphere better than argon (see the Supporting Information for details), these results indicate that the catalyst MnO_2 can can be re-generated by oxygen or air.

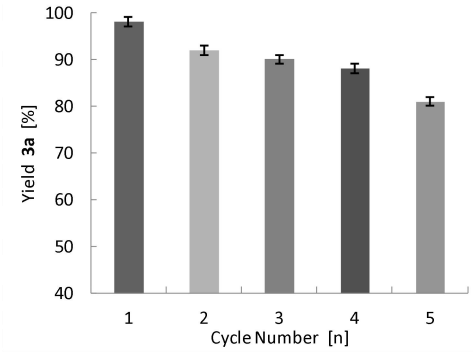
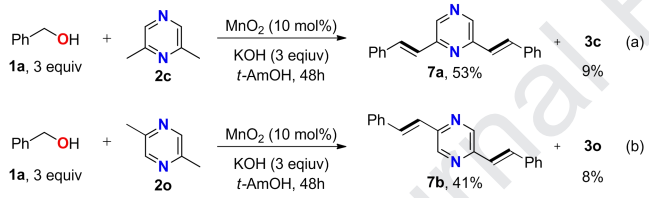


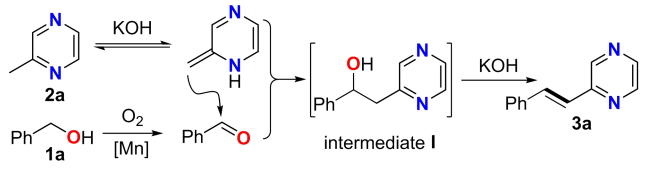
Figure 2. Reusability of MnO_2 Catalyst

The practice and convenience of this proceed to unsaturated *N*-heteroaromatics can be di-olefination of substrates containing two methyl groups as well, the corresponding products **7a** and **7b** were isolated in reasonable yields, respectively.



Scheme 3. MnO_2 catalyzed di-olefination.

On the basis of the results we obtained here and previous reports,[7,8] a plausible mechanism for the present process can be proposed. In this scenario, initial alcohol is oxidized by air in the presence of MnO_2 to generate aldehyde. After enamine was formed under the base condition, nucleophilic attack of the enamine into the C=O bond of aldehyde gained the intermediate **I**. Subsequent elimination releases water in the presence of base and give rise to the unsaturated *N*-heteroaromatic product.



Scheme 4. Possible mechanism of olefination.

3. Conclusion

In summary, we have developed an efficient MnO_2/air catalytic system that allows the direct formation of unsaturated *N*-heteroaromatics from commercially available alcohols and alkylazaarenes via oxidation/olefination under the aerobic conditions. The method is compatible with a variety of functional groups and can be used to prepare a range of 1,2-disubstitued unsaturated *N*-heteroaromatics. Further investigations to gain a detailed mechanistic understanding as well as application of this aerobic oxidative catalytic system to other oxidation/olefination reactions are currently in progress.

4. Experimental section

4.1 General Information

^1H and ^{13}C spectra were obtained on a Brüker AVIII300 (300 MHz) or AVII (500 MHz) spectrometer. Proton-decoupled spectra are denoted as $\{^1H\}$. Chemical shifts (δ) were reported in parts per million (ppm) using the residual solvent signal as an internal standard ($CDCl_3$: δ_H = 7.26 ppm, δ_C = 77.16 ppm). All coupling constants (*J* values) were reported in Hertz (Hz). Multiplicities were reported as follows: s, singlet; d, doublet; t, triplet; m, multiplet. High-resolution mass spectrometry (HRMS) measurements were recorded on a Bruker Daltronics microTOF (ESI) spectrometer. Flash chromatography was carried out using matrix 60 silica.

*4.2 General procedure for synthesis of products (1)substrates General procedure for MnO2 catalyzed oxidation/olefination reaction (**3a-3n, 5a-5y, 7a-7a**)*

Using a nitrogen-filled glove box, an oven-dried Schlenk tube (100 mL volume) was charged with a magnetic stirring bar, MnO_2 (0.05 mmol), KOH (0.5 mmol), alcohols (**1**) (0.55 mmol), heteroarenes (**2**) (0.5 mmol) and *t*-AmOH (1 mL). Then the Schlenk tube was closed tightly with a teflon cap, removed from the glove box. A reflux condenser was evacuated and refilled with dry air and then attached to the Schlenk tube maintaining dry air stream. A bubble counter was attached to the top of the condenser and the whole system was purged with dry air for 15 seconds. The Schlenk tube was immersed into a pre-heated oil bath (design temperature). After design time the reaction was cooled, a small aliquot of the organic phase was analyzed by GC or GC-MS to monitor product formation. Purification of the remainder by column chromatography on silica gel (petroleum ether/ethyl acetate = 20/1 – 5/1) gave the corresponding products in the reported yield.

4.2.1 (E)-2-styrylpyrazine (3a)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 169 mg, 93% yield. ^1H NMR (300 MHz, $CDCl_3$): δ 8.59 (s, 1H), 8.49 (s, 1H), 8.35 (d, *J* = 2.3 Hz, 1H), 7.70 (d, *J* = 16.1 Hz, 1H), 7.55 (d, *J* = 8.1 Hz, 2H), 7.38 – 7.28 (m, 3H), 7.11 (d, *J* = 16.1 Hz, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 151.3, 144.4, 143.8, 142.8, 136.0, 135.2, 129.0, 128.9, 127.3, 124.0. HRMS (ESI) calcd. for $C_{12}H_{11}N_2$ [M+H]: 183.0922, found: 183.0931.

4.2.2 (E)-3-styrylpyridazine (3b)

The title compound was prepared according to the general procedure and purified by column chromatography to give a yellow solid, 147 mg, 81% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.98 (d, *J* = 4.8 Hz, 1H), 7.63 (d, *J* = 16.4 Hz, 1H), 7.55 (t, *J* = 4.9 Hz, 2H), 7.52 (s, 1H), 7.40 – 7.36 (m, 1H), 7.31 (dd, *J* = 8.7, 4.6 Hz, 3H), 7.26 (d, *J* = 5.2 Hz, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 158.3, 149.7, 135.9, 135.2, 129.1, 128.9, 127.4, 126.4, 125.2, 123.9 ppm. HRMS (ESI) calcd. for $C_{12}H_{11}N_2$ [M+H]: 183.0922, found: 183.0928.

4.2.3 (E)-2-methyl-6-styrylpyrazine (3c)

The title compound was prepared according to the general procedure and purified by column chromatography to give the colorless oil 119 mg, 61% yield.
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.46 (s, 1H), 8.29 (s, 1H), 7.73 (d, *J* = 16.1 Hz, 1H), 7.59 (d, *J* = 7.1 Hz, 2H), 7.37 (dt, *J* = 13.9, 6.9 Hz, 3H), 7.14 (d, *J* = 16.1 Hz, 1H), 2.59 (s, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 153.3, 150.1, 142.6, 140.5, 136.2, 134.7, 128.8, 127.3, 124.5, 21.8 ppm. HRMS (ESI) calcd. for $C_{13}H_{13}N_2$ [M+H]: 197.1079, found: 197.1082.

4.2.4 (E)-4-styrylpyridine (3d)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 95 mg, 53% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.59 (d, *J* = 4.4 Hz, 2H), 7.65 – 7.49 (m, 2H), 7.38 (dt, *J* = 15.3, 6.3 Hz, 5H), 7.34 – 7.26 (m, 2H), 7.03 (d, *J* = 16.3 Hz, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 150.0, 144.7, 136.1, 133.2, 128.8, 128.7, 127.0, 125.9, 120.8 ppm. HRMS (ESI) calcd. for $C_{13}H_{12}N$ [M+H]: 182.0970, found: 182.0978.

4.2.5 General (E)-2-styrylbenzo[d]oxazole (3e)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 156 mg, 71% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.06 (d, *J* = 8.5 Hz, 1H), 8.01 (d, *J* = 8.5 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.69 – 7.62 (m, 1H), 7.57 – 7.48 (m, 2H), 7.44 (dt, *J* = 8.0, 4.0 Hz, 2H), 7.22 (d, *J* = 2.1 Hz, 1H), 6.51 (d, *J* = 2.8 Hz, 1H), 6.43 (dd, *J* = 3.3, 1.8 Hz, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 162.8, 150.4, 142.2, 139.4, 135.1, 129.7, 128.9, 127.5, 125.2, 124.5, 119.8, 113.9, 110.3 ppm. HRMS (ESI) calcd. for $C_{15}H_{12}NO$ [M+H]: 222.0919, found: 222.0908.

4.2.6 (E)-4-styrylquinoline (3f)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 120 mg, 52% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.96 (s, 1H), 8.24 (t, *J* = 8.2 Hz, 2H), 7.88 – 7.74 (m, 2H), 7.71 – 7.57 (m, 4H), 7.44 (dt, *J* = 26.5, 11.5 Hz, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 149.9, 148.4, 143.0, 136.4, 135.1, 129.8, 129.3, 128.8, 128.7, 127.0, 126.5, 126.3, 123.4, 122.7, 116.9 ppm. HRMS (ESI) calcd. for $C_{17}H_{14}N$ [M+H]: 232.1126, found: 232.1128.

4.2.7 (E)-1-styrylisoquinoline (3g)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 53mg, 23% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.57 (d, *J* = 5.6 Hz, 1H), 8.39 (d, *J* = 8.4 Hz, 1H), 8.01 (s, 2H), 7.84 (d, *J* = 8.2 Hz, 1H), 7.67 (ddd, *J* = 15.3, 14.8, 7.1 Hz, 4H), 7.58 (d, *J* = 5.6 Hz, 1H), 7.43 (dd, *J* = 10.9, 4.4 Hz, 2H), 7.38 – 7.29 (m, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 154.6, 142.5, 136.9, 136.8, 135.8, 129.9, 128.8, 128.6, 127.5, 127.3, 127.2, 124.5, 122.9, 120.0 ppm. HRMS (ESI) calcd. for $C_{17}H_{14}N$ [M+H]: 232.1126, found: 232.1141.

4.2.8 (E)-2-styrylquinoline (3h)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 217 mg, 94% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.20 – 8.07 (m, 2H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.69 (ddd, *J* = 15.4, 6.3, 4.5 Hz, 5H), 7.50 (t, *J* = 7.5 Hz, 1H), 7.47 – 7.38 (m, 3H), 7.37 – 7.30 (m, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.9, 148.1, 136.4, 136.3, 134.4, 129.7, 129.1, 128.9, 128.7, 128.6, 127.4, 127.2, 126.1, 119.2 ppm. HRMS (ESI) calcd. for $C_{17}H_{14}N$ [M+H]: 232.1126, found: 232.1133.

4.2.9 (E)-6-chloro-2-styrylquinoline (3i)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 217 mg, 82% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.11 – 7.94 (m, 2H), 7.76 (d, *J* = 2.1 Hz, 1H), 7.71 (d, *J* = 11.8 Hz, 1H), 7.68 – 7.58 (m, 4H), 7.42 (d, *J* = 8.2 Hz, 2H), 7.40 – 7.30 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.1, 146.5, 136.3, 135.4, 134.9, 131.8, 130.6, 128.8, 128.4, 127.8, 127.3, 126.2, 120.2 ppm. HRMS (ESI) calcd. for $C_{17}H_{13}ClN$ [M+H]: 266.0736, found: 266.0736.

4.2.10 (E)-6-methoxy-2-styrylquinoline (3j)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 237 mg, 91% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.01 (s, 1H), 7.98 (s, 1H), 7.63 (d, *J* = 5.9 Hz, 2H), 7.62 – 7.58 (m, 2H), 7.43 – 7.37 (m, 3H), 7.36 – 7.26 (m, 2H), 7.04 (d, *J* = 2.8 Hz, 1H), 3.91 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.6, 153.6, 144.0, 136.6, 135.1, 133.3, 130.5, 128.8, 128.7, 128.4, 128.2, 127.1, 122.3, 119.5, 105.2, 55.5 ppm. HRMS (ESI) calcd. for $C_{18}H_{16}NO$ [M+H]: 262.1232, found: 262.1241.

4.2.11 (E)-4-(1,2-diphenylvinyl)pyridine (3k)

The title compound was prepared according to the general procedure and purified by column chromatography to give a yellow solid 118mg, 46% yield. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.82 (s, 2H), 7.77 (dd, *J* = 23.0, 11.7 Hz, 6H), 7.52 – 7.28 (m, 7H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ 148.4, 142.5, 135.8, 133.3, 128.2, 128.0, 126.6, 124.3 ppm. HRMS (ESI) calcd. for $C_{19}H_{16}N$ [M+H]: 258.1283, found: 258.1291.

4.2.12 (E)-2-(1-phenylprop-1-en-2-yl)pyrazine (3l)

The title compound was prepared according to the general procedure and purified by column chromatography to give

the colorless oil 74 mg, 38% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.86 (s, 1H), 8.56 (s, 1H), 8.45 (d, *J* = 2.1 Hz, 1H), 7.50 (s, 1H), 7.45 – 7.36 (m, 4H), 7.34 – 7.27 (m, 1H), 2.38 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.4, 142.6, 141.9, 137.1, 1321, 129.4, 128.3, 127.4, 15.4 ppm. HRMS (ESI) calcd. for $C_{13}H_{13}N_2$ [M+H]: 197.1079, found: 197.1075.

4.2.13 2-(1-(naphthalen-1-yl)prop-1-en-2-yl)pyrazine (3m) (E:Z= 7:1)

The title compound was prepared according to the general procedure and purified by column chromatography to give a yellow solid 89 mg, 36% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.95 (s, 1H), 8.62 (s, 1H), 8.51 (s, 1H), 8.21 (s, 0.19H), 8.09-8.07 (m, 0.35H), 8.03-8.00 (m, 2H), 7.92-7.86 (m, 1H), 7.86-7.83 (m, 1.27H), 7.72-7.69 (m, 0.25H), 7.55-7.46 (m, 5.05H), 7.32 (s, 0.18H), 7.22-7.21 (2, 0.22H), 6.97 -6.95 (m, 0.15H), 2.45 (s, 0.48H), 2.25 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 154.7, 143.6, 142.8, 141.9, 135.5, 134.4, 133.6, 131.9, 130.3, 128.5, 127.9, 126.8, 126.2, 126.0, 125.3, 125.0, 15.6 ppm. HRMS (ESI) calcd. for $C_{17}H_{15}N_2$ [M+H]: 247.1235, found: 247.1241.

4.2.14 (E)-2-(hex-2-en-2-yl)pyrazine (3n)

The title compound was prepared according to the general procedure and purified by column chromatography to give a yellow solid 53 mg, 32% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.64 (s, 1H), 8.45 (s, 1H), 8.33 (s, 1H), 5.90 (d, *J* = 10.0 Hz, 1H), 2.23 (s, 3H), 1.81 – 1.69 (m, 1H), 0.96 – 0.89 (m, 2H), 0.59 (dd, *J* = 5.6, 3.5 Hz, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.2, 141.6, 141.1, 138.6, 130.4, 129.8, 13.9, 11.7, 7.9 ppm. HRMS (ESI) calcd. for $C_{10}H_{15}N_2$ [M+H]: 163.1235, found: 163.1241.

4.2.15 (E)-2-(4-methylstyryl)pyrazine (5a)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 174 mg, 89% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.59 (d, *J* = 31.0 Hz, 2H), 8.40 (s, 1H), 7.73 (d, *J* = 16.1 Hz, 1H), 7.50 (d, *J* = 7.9 Hz, 2H), 7.21 (d, *J* = 7.8 Hz, 2H), 7.12 (d, *J* = 16.1 Hz, 1H), 2.39 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 151.5, 144.2, 143.7, 142.5, 139.2, 135.2, 133.3, 129.6, 127.3, 123.0, 21.4 ppm. HRMS (ESI) calcd. for $C_{13}H_{13}N_2$ [M+H]: 197.1079, found: 197.1082.

4.2.16 (E)-2-(4-chlorostyryl)pyrazine (5b)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 174 mg, 81% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.63 (s, 1H), 8.54 (s, 1H), 8.43 (s, 1H), 7.69 (d, *J* = 16.1 Hz, 1H), 7.52 (d, *J* = 8.5 Hz, 2H), 7.45 (d, *J* = 8.4 Hz, 2H), 7.14 (d, *J* = 16.1 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 150.8, 144.3, 143.7, 142.9, 134.6, 134.4, 133.7, 128.9, 128.4, 124.4 ppm. HRMS (ESI) calcd. for $C_{12}H_{10}ClN_2$ [M+H]: 217.0532, found: 217.0541.

4.2.17 (E)-2-(4-bromostyryl)pyrazine (5c)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 189 mg, 73% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.63 (s, 1H), 8.54 (s, 1H), 8.43 (s, 1H), 7.69 (d, *J* = 16.1 Hz, 1H), 7.52 (d, *J* = 8.5 Hz, 2H), 7.45 (d, *J* = 8.4 Hz, 2H), 7.14 (d, *J* = 16.1 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.4, 143.9, 143.0, 135.0, 133.9, 132.0, 128.7, 124.64, 123.0 ppm. HRMS (ESI) calcd. for $C_{12}H_{10}BrN_2$ [M+H]: 261.0027, found: 261.0032.

4.2.18 (E)-2-(2-(thiophen-2-yl)vinyl)pyrazine (5d)

The title compound was prepared according to the general procedure and purified by column chromatography to give a yellow solid, 127 mg, 68% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.53 (d, *J* = 17.7 Hz, 2H), 8.38 (s, 1H), 7.88 (d, *J* = 15.8 Hz, 1H), 7.30 (d, *J* = 5.0 Hz, 1H), 7.21 (d, *J* = 3.0 Hz, 1H), 7.04 (dt, *J* = 5.0, 3.4 Hz, 1H), 6.94 (d, *J* = 15.8 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 150.8, 144.2, 143.5, 142.5, 141.5, 128.6, 127.9, 127.8, 126.3, 123.0 ppm. HRMS (ESI) calcd. for $C_{10}H_9N_2S$ [M+H]: 189.0486, found: 189.0492.

4.2.19 (E)-2-(2-methylstyryl)quinoline (5e)

The title compound was prepared according to the general procedure and purified by column chromatography to give the colorless oil, 162 mg, 66% yield.^{1}H NMR (300 MHz, $CDCl_3$): δ 8.16 (t, *J* = 8.5 Hz, 2H), 8.00 (d, *J* = 16.2 Hz, 1H), 7.85 – 7.71 (m, 4H), 7.54 (dd, *J* = 8.1, 7.0 Hz, 1H), 7.37 (d, *J* = 16.2 Hz, 1H), 7.33 – 7.29 (m, 1H), 2.57 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.1, 148.2, 136.5, 136.2, 135.1, 132.0, 130.5, 130.1, 129.6, 129.2, 128.4, 127.4, 127.2, 126.2, 126.1, 125.7, 119.2, 19.9 ppm.HRMS (ESI) calcd. for $C_{18}H_{16}N$ [M+H]: 246.1283, found: 246.1289.

4.2.20 (E)-2-(3-methylstyryl)quinoline (5f)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 205 mg, 84% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.13 (d, *J* = 8.6 Hz, 1H), 8.08 (d, *J* = 8.5 Hz, 1H), 7.79 (d, *J* = 8.1 Hz, 1H), 7.75 – 7.67 (m, 2H), 7.65 (d, *J* = 7.8 Hz, 1H), 7.47 (dt, *J* = 28.9, 11.8 Hz, 4H), 7.29 (d, *J* = 7.5 Hz, 1H), 7.15 (d, *J* = 7.4 Hz, 1H), 2.41 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.1, 148.3, 138.4, 136.5, 136.3, 134.5, 129.7, 129.5, 129.2, 128.9, 128.7, 123.0, 127.5, 126.1, 124.5, 119.2, 21.5 ppm. HRMS (ESI) calcd. for $C_{18}H_{16}N$ [M+H]: 246.1283, found: 246.1291.

4.2.21 (E)-2-(4-methylstyryl)quinolines (5g)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 227 mg, 93% yield.^{1}H NMR (300 MHz, $CDCl_3$): δ 8.12 (d, *J* = 8.6 Hz, 1H), 8.07 (d, *J* = 8.5 Hz, 1H), 7.78 (d, *J* = 8.1 Hz, 1H), 7.70 (dt, *J* = 5.3, 4.7 Hz, 2H), 7.65 (d, *J* = 5.0 Hz, 1H), 7.55 (d, *J* = 8.0 Hz, 2H), 7.49 (dd, *J* = 8.0, 7.0 Hz, 1H), 7.37 (d, *J* = 16.3 Hz, 1H), 7.22 (d, *J* = 8.0 Hz, 2H), 2.39 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.1, 148.2, 138.7, 136.2, 134.3, 133.7, 129.6, 129.5, 129.1, 128.0, 127.4, 127.2, 127.2, 126.0, 119.1, 21.3 ppm. HRMS (ESI) calcd. for $C_{18}H_{16}N$ [M+H]: 246.1283, found: 246.1285.

4.2.22 (E)-2-(2,4,6-trimethylstyryl)quinoline(5h)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 175mg, 64% yield.
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.12 (dd, *J* = 12.2, 8.6 Hz, 2H), 7.83 – 7.66 (m, 4H), 7.50 (dd, *J* = 8.1, 6.9 Hz, 1H), 6.94 (dd, *J* = 11.1, 5.5 Hz, 3H), 2.44 (s, 6H), 2.32 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.3, 148.3, 137.0, 136.5, 136.5, 136.3, 134.1, 133.1, 132.9, 129.7, 129.3, 129.0, 127.5, 127.4, 126.1, 119.0, 21.3, 21.1 ppm. HRMS (ESI) calcd. for $C_{20}H_{20}N$ [M+H]: 274.1596, found: 274.1599.

4.2.23 (E)-2-(4-(tert-butyl)styryl)quinoline (5i)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 261mg, 91% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.12 (d, *J* = 8.6 Hz, 1H), 8.08 (d, *J* = 8.5 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.69 (dd, *J* = 17.2, 8.8 Hz, 3H), 7.59 (d, *J* = 8.3 Hz, 2H), 7.49 (dd, *J* = 7.9, 7.0 Hz, 1H), 7.46 – 7.34 (m, 3H), 1.35 (s, 9H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.3, 152.0, 148.3, 136.3, 134.3, 133.8, 129.7, 129.2, 128.3, 127.5, 127.3, 127.1, 126.1, 125.8, 119.2, 34.8, 31.3 ppm. HRMS (ESI) calcd. for $C_{21}H_{22}N$ [M+H]: 288.1752, found: 288.1763.

4.2.24 (E)-2-(2-([1,1'-biphenyl]-4-yl)vinyl)quinoline (5j)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 254 mg, 83% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.15 (d, *J* = 8.5 Hz, 1H), 8.10 (d, *J* = 8.5 Hz, 1H), 7.80 (d, *J* = 8.1 Hz, 1H), 7.78 – 7.71 (m, 4H), 7.70 – 7.59 (m, 5H), 7.54 – 7.48 (m, 2H), 7.45 (d, *J* = 7.2 Hz, 2H), 7.37 (dd, *J* = 11.2, 4.6 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.9, 148.2, 141.3, 140.4, 136.3, 135.5, 133.9, 129.7, 129.1, 128.9, 128.8, 127.7, 127.5, 127.4, 127.3, 126.9, 126.1, 119.3 ppm. HRMS (ESI) calcd. for $C_{23}H_{18}N$ [M+H]: 308.1439, found: 308.1442.

4.2.25 (E)-2-(2-methoxystyryl)quinoline (5k)

The title compound was prepared according to the general procedure and purified by column chromatography to give the colorless oil, 185 mg, 71% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.10 (t, *J* = 8.0 Hz, 2H), 8.03 (d, *J* = 16.6 Hz, 1H), 7.79 – 7.66 (m, 4H), 7.52 – 7.41 (m, 2H), 7.36 – 7.27 (m, 1H), 7.01 (t, *J* = 7.5 Hz, 1H), 6.94 (d, *J* = 8.3 Hz, 1H), 3.93 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.4, 156.7, 148.2, 136.1, 129.7, 129.6, 129.3, 129.2, 127.4, 127.2, 127.2, 126.0, 125.5, 120.8, 119.0, 111.0, 55.5 ppm. HRMS (ESI) calcd. for $C_{18}H_{16}NO$ [M+H]: 262.1232, found: 262.1241.

4.2.26 (E)-2-(4-methoxystyryl)quinoline (5l)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 240 mg, 92% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.14 (d, *J* = 8.5 Hz, 1H), 8.09 (d, *J* = 8.5 Hz, 1H), 7.81 (d, *J* = 8.1 Hz, 1H), 7.77 – 7.69 (m, 2H), 7.64 (dd, *J* = 11.4, 6.7 Hz, 3H), 7.51 (t, *J* = 7.4 Hz, 1H), 7.34 (s, 1H), 7.29 (d, *J* = 1.7 Hz, 2H), 6.97 (d, *J* = 7.3 Hz, 2H), 3.88 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.1, 156.3, 148.3, 136.2, 134.0, 129.7, 129.3, 129.1, 128.7, 127.5, 127.2, 126.9, 125.9, 119.2, 114.3, 55.4 ppm. HRMS (ESI) calcd. for $C_{18}H_{16}NO$ [M+H]: 262.1232, found: 262.1238.

4.2.27 (E)-2-(2-chlorostyryl)quinolines (5m)

The title compound was prepared according to the general procedure and purified by column chromatography to give the colorless oil, 151 mg, 57% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.13 (dd, *J* = 25.6, 12.7 Hz, 2H), 7.93 – 7.68 (m, 3H), 7.57 – 7.41 (m, 2H), 7.35 – 7.28 (m, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.7, 148.1, 136.3, 134.5, 134.0, 131.7, 130.1, 129.9, 129.7, 129.4, 129.2, 127.4, 127.4, 127.0, 126.9, 126.33, 118.9 ppm. HRMS (ESI) calcd. for $C_{17}H_{13}ClN$ [M+H]: 266.0736, found: 266.0742.

4.2.28 (E)-2-(4-chlorostyryl)quinolines (5n)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 222 mg, 84% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.14 (d, *J* = 8.5 Hz, 1H), 8.08 (d, *J* = 8.5 Hz, 1H), 7.79 (d, *J* = 8.1 Hz, 1H), 7.75 – 7.62 (m, 3H), 7.60 – 7.48 (m, 3H), 7.37 (dd, *J* = 12.1, 3.7 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.5, 148.2, 136.3, 135.0, 134.2, 132.9, 129.8, 129.4, 129.2, 128.9, 128.3, 127.5, 127.3, 126.2, 119.3 ppm. HRMS (ESI) calcd. for $C_{17}H_{13}ClN$ [M+H]: 266.0736, found: 266.0739.

4.2.29 (E)-2-(4-bromostyryl)quinolines (5o)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 204 mg, 66% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.14 (d, *J* = 8.6 Hz, 1H), 8.08 (d, *J* = 8.5 Hz, 1H), 7.79 (d, *J* = 8.1 Hz, 1H), 7.71 (dd, *J* = 8.4, 7.0 Hz, 1H), 7.66 (d, *J* = 1.3 Hz, 1H), 7.62 (d, *J* = 5.8 Hz, 1H), 7.55 – 7.48 (m, 5H), 7.38 (d, *J* = 16.3 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.5, 148.1, 136.5, 135.4, 133.1, 131.9, 129.8, 129.5, 129.1, 128.6, 127.5, 127.4, 126.3, 122.5, 119.3 ppm. HRMS (ESI) calcd. for $C_{17}H_{13}BrN$ [M+H]: 310.0231, found: 310.0242.

4.2.30 (E)-2-(4-iodostyryl)quinolines (5p)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 171 mg, 48% yield.^{1}H NMR (300 MHz, $CDCl_3$): δ 8.14 (d, *J* = 8.5 Hz, 1H), 8.08 (d, *J* = 8.9 Hz, 1H), 7.79 (d, *J* = 8.1 Hz, 1H), 7.72 (t, *J* = 8.4 Hz, 3H), 7.63 (dd, *J* = 12.4, 7.3 Hz, 2H), 7.51 (t, *J* = 7.5 Hz, 1H), 7.43 – 7.35 (m, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.5, 148.2, 137.9, 136.4, 136.0, 133.1, 129.8, 129.7, 129.2, 128.8, 127.5, 127.4, 126.3, 119.4, 94.2 ppm. HRMS (ESI) calcd. for $C_{17}H_{13}IN$ [M+H]: 358.0093, found: 358.0098.

4.2.31 (E)-2-(2-(naphthalen-1-yl)vinyl)quinolines (5q)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 217 mg, 77% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.54 (d, *J* = 16.0 Hz, 1H), 8.36 (d, *J* = 8.2 Hz, 1H), 8.16 (t, *J* = 8.8 Hz, 2H), 7.97 – 7.84 (m, 3H), 7.81 (d, *J* = 8.1 Hz, 1H), 7.78 – 7.68 (m, 2H), 7.62 – 7.53 (m, 3H),

7.53 – 7.45 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.0, 148.3, 136.5, 136.4, 134.0, 133.7, 133.7, 131.8, 131.7, 131.5, 131.3, 129.7, 129.3, 128.9, 128.6, 127.6, 127.5, 127.4, 126.4, 126.3, 126.2, 125.9, 125.7, 124.2, 123.7, 119.5, 117.4 ppm. HRMS (ESI) calcd. for $C_{21}H_{16}N$ [M+H]: 282.1283, found: 282.1283.

4.2.32 (E)-2-(2-(furan-2-yl)vinyl)quinolines (5r)

The title compound was prepared according to the general procedure and purified by column chromatography to give a yellow solid, 128 mg, 58% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.80 (d, *J* = 16.4 Hz, 1H), 7.76 – 7.68 (m, 1H), 7.63 – 7.59 (m, 2H), 7.54 (dd, *J* = 5.0, 4.2 Hz, 1H), 7.48 – 7.37 (m, 3H), 7.34 (dd, *J* = 6.2, 3.3 Hz, 2H), 7.09 (d, *J* = 15.7 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.6, 152.8, 148.3, 143.1, 136.3, 129.7, 129.2, 127.5, 127.3, 126.8, 126.0, 121.7, 119.9, 111.9, 111.1 ppm. HRMS (ESI) calcd. for $C_{15}H_{12}NO$ [M+H]: 222.0919, found: 222.0921.

4.2.33 (E)-2-(2-(thiophen-2-yl)vinyl)quinolines (5s)

The title compound was prepared according to the general procedure and purified by column chromatography to give a yellow solid, 175 mg, 74% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.92 (dd, *J* = 14.8, 8.5 Hz, 2H), 7.69 (d, *J* = 16.1 Hz, 1H), 7.61 – 7.51 (m, 2H), 7.37 (d, *J* = 8.5 Hz, 1H), 7.33 (dt, *J* = 8.0, 3.9 Hz, 1H), 7.13 (d, *J* = 5.1 Hz, 1H), 7.07 (dd, *J* = 9.8, 6.2 Hz, 2H), 6.96 – 6.86 (m, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.4, 148.1, 141.9, 136.1, 129.6, 129.0, 128.1, 128.0, 127.7, 127.4, 127.1, 125.9, 125.9, 119.2 ppm. HRMS (ESI) calcd. for $C_{15}H_{12}NS$ [M+H]: 238.0690, found: 238.0687.

4.2.34 (E)-2-(3-ethylpent-1-en-1-yl)quinolines (5t)

The title compound was prepared according to the general procedure and purified by column chromatography to give the colorless oil, 139 mg, 53% yield.^{1}H NMR (300 MHz, $CDCl_3$): δ 8.04 (dd, *J* = 8.5, 5.4 Hz, 2H), 7.74 (d, *J* = 8.1 Hz, 1H), 7.66 (dd, *J* = 8.4, 7.0 Hz, 1H), 7.56 (d, *J* = 8.6 Hz, 1H), 7.45 (dd, *J* = 8.1, 6.9 Hz, 1H), 6.70 (d, *J* = 16.0 Hz, 1H), 6.55 (dd, *J* = 16.0, 8.6 Hz, 1H), 2.09 (ddt, *J* = 13.4, 8.8, 4.4 Hz, 1H), 1.49 (ddt, *J* = 21.0, 13.6, 6.8 Hz, 4H), 0.92 (t, *J* = 7.4 Hz, 6H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.5, 148.0, 141.8, 136.0, 131.3, 129.4, 129.1, 127.4, 127.1 125.8, 118.5, 46.8, 27.5, 11.9 ppm. HRMS (ESI) calcd. for $C_{16}H_{20}N$ [M+H]: 263.1310, found: 263.1310.

4.2.35 (E)-2-(3,3-dimethylbut-1-en-1-yl)quinolines (5u)

The title compound was prepared according to the general procedure and purified by column chromatography to give the colorless oil, 128 mg, 61% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.95 (d, *J* = 8.5 Hz, 2H), 7.64 (d, *J* = 8.1 Hz, 1H), 7.57 (t, *J* = 7.7 Hz, 1H), 7.46 (d, *J* = 8.7 Hz, 1H), 7.36 (t, *J* = 7.5 Hz, 1H), 6.74 (d, *J* = 16.2 Hz, 1H), 6.57 (d, *J* = 16.3 Hz, 1H), 1.11 (s, 10H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.8, 148.1, 148.0, 136.0, 129.4, 129.0, 127.3, 127.0, 126.4, 125.7, 118.5, 33.8, 29.4 ppm. HRMS (ESI) calcd. for $C_{15}H_{18}N$ [M+H]: 212.1439, found: 212.1442.

4.2.36 (E)-2-(2-cyclopropylvinyl)quinolines (5v)

The title compound was prepared according to the general procedure and purified by column chromatography to give the colorless oil, 109 mg, 56% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.92 (dd, *J* = 8.6, 2.7 Hz, 2H), 7.63 (d, *J* = 8.1 Hz, 1H), 7.56 (ddd, *J* = 8.3, 7.0, 1.3 Hz, 1H), 7.44 – 7.25 (m, 2H), 6.69 (d, *J* = 15.7 Hz, 1H), 6.30 (dd, *J* = 15.7, 9.3 Hz, 1H), 1.76 – 1.48 (m, 1H), 0.88 – 0.80 (m, 2H), 0.61 – 0.48 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.1, 148.1, 142.0, 136.0, 129.4, 128.9, 128.2, 127.3, 126.9, 125.6, 118.8 , 14.9, 8.0 ppm. HRMS (ESI) calcd. for $C_{14}H_{14}N$ [M+H]: 196.1126, found: 196.1126.

4.2.37 (E)-2-(2-cyclohexylvinyl)quinolines (5w)

The title compound was prepared according to the general procedure and purified by column chromatography to give the colorless oil, 161 mg, 68% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.03 (d, *J* = 8.5 Hz, 2H), 7.73 (d, *J* = 8.1 Hz, 1H), 7.66 (t, *J* = 7.7 Hz, 1H), 7.51 (d, *J* = 8.5 Hz, 1H), 7.45 (dd, *J* = 11.4, 4.3 Hz, 1H), 6.78 (dd, *J* = 16.1, 6.2 Hz, 1H), 6.67 (d, *J* = 16.1 Hz, 1H), 2.24 (s, 1H), 1.92 – 1.69 (m, 5H), 1.40 – 1.19 (m, 5H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.7, 148.0, 143.3, 136.0, 129.4, 129.0, 128.6, 127.3, 127.0, 125.7, 118.6, 41.1, 32.5, 26.1, 25.9 ppm. HRMS (ESI) calcd. for $C_{17}H_{20}N$ [M+H]: 238.1596, found: 238.1596.

4.2.37 (E)-2-(2-(pyridin-2-yl)vinyl)quinolines (5x)

The title compound was prepared according to the general procedure and purified by column chromatography to give a white solid, 121 mg, 52% yield.^{1}H NMR (300 MHz, $CDCl_3$): δ 8.68 – 8.51 (m, 1H), 8.11 (t, *J* = 8.5 Hz, 2H), 7.81 (dd, *J* = 4.0, 2.3 Hz, 2H), 7.74 (d, *J* = 8.1 Hz, 1H), 7.66 (ddd, *J* = 13.0, 8.1, 5.0 Hz, 3H), 7.54 (d, *J* = 6.9 Hz, 1H), 7.47 (t, *J* = 7.5 Hz, 1H), 7.16 (dd, *J* = 7.0, 3.8 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.1, 154.9, 149.7, 136.8, 136.7, 134.0, 132.1, 130.0, 129.0, 127.5, 126.6, 122.9, 122.8, 120.3, 109.9 ppm. HRMS (ESI) calcd. for $C_{16}H_{13}N_2$ [M+H]: 233.1079, found: 233.1079.

4.2.38 (E)-2-(4,8-dimethylnona-1,7-dien-1-yl)quinolines (5y)

The title compound was prepared according to the general procedure and purified by column chromatography to give the colorless oil, 184 mg, 66% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.97 (t, *J* = 8.5 Hz, 2H), 7.67 (d, *J* = 8.1 Hz, 1H), 7.59 (t, *J* = 7.7 Hz, 1H), 7.45 (d, *J* = 8.7 Hz, 1H), 7.38 (t, *J* = 7.5 Hz, 1H), 6.71 (dt, *J* = 30.0, 11.4 Hz, 2H), 5.04 (t, *J* = 6.3 Hz, 1H), 2.39 – 2.19 (m, 1H), 2.10 (dt, *J* = 14.3, 7.1 Hz, 1H), 1.96 (dt, *J* = 15.6, 7.6 Hz, 2H), 1.61 (s, 3H), 1.54 (s, 3H), 1.37 (ddd, *J* = 9.1, 6.4, 3.2 Hz, 1H), 1.23 – 1.13 (m, 1H), 0.90 (d, *J* = 6.7 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.3, 136.2, 132.1, 131.2, 129.5, 129.0, 127.4, 127.1, 125.8, 124.6, 118.6, 40.6, 36.8, 32.7, 25.7, 25.6, 19.6, 17.7 ppm. HRMS (ESI) calcd. for $C_{20}H_{26}N$ [M+H]: 280.2065, found: 280.2071.

4.2.39 (E)-2,6-di((E)-styryl)pyrazine (7a)

The title compound was prepared according to the general procedure and purified by column chromatography to give a yellow solid 150 mg, 53% yield.^{1}H NMR (300 MHz, DMSO-d_6): δ 8.76 (s, 2H), 7.79 (s, 1H), 7.73 (s, 1H), 7.69 (d, *J* = 7.4 Hz, 4H), 7.43 (d, *J* = 6.4 Hz, 4H), 7.39 (s, 2H),

7.35 (d, J = 7.3 Hz, 2H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ 149.3, 141.4, 135.5, 133.9, 128.4, 126.8, 124.1, 109.0 ppm. HRMS (ESI) calcd. for $C_{20}H_{17}N_2$ [M+H]: 285.1392, found: 285.1387.

4.2.40 (E)-2,5-di((E)-styryl)pyrazine (7b)

The title compound was prepared according to the general procedure and purified by column chromatography to give a yellow solid 116 mg, 41% yield.^{1}H NMR (300 MHz, DMSO-d_6): δ 8.61 (s, 2H), 7.84 (d, J = 16.2 Hz, 2H), 7.69 (d, J = 7.8 Hz, 4H), 7.40 (t, J = 7.5 Hz, 5H), 7.35 – 7.25 (m, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ 147.9, 142.3, 135.4, 133.0, 127.9, 126.3, 123.8 ppm. HRMS (ESI) calcd. for $C_{20}H_{17}N_2$ [M+H]: 285.1392, found: 285.1390.

Notes

The authors declare no competing financial interest.

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Supplementary Material

Supplementary data associated with this article can be found, in the online version, at

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Declaration of interests

☐ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

The authors declare no competing financial interest.