An Efficient Synthesis of 3-Substituted Isoquinoline and Pyridine Derivatives by Gold Catalyzed Intramolecular Cyclization from *o*-Alkynyloximes

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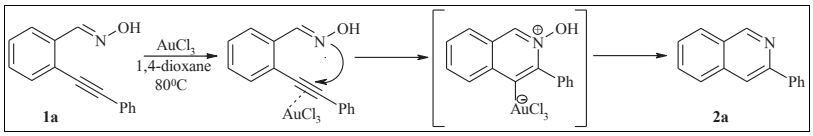

A one-pot reaction was developed efficiently by $AuCl_3$ catalyzed intramolecular cyclization of aromatic *o*-alkynyloximes and 2-alkynylcycloalkene-1-carbaldoximes leading to the formation of isoquinoline and pyridine derivatives with high yields. This methodology has been applied for aromatic as well as aliphatic systems. Aromatic *o*-alkynyloximes are benzene and naphthalene, whereas electron-donating groups are 4-methoxybenzene, 4-methylbenzene, and 4-methoxy-5-methylbenzene. There are electron-withdrawing groups such as chloro and nitrobenzene *o*-alkynyl oximes, and the same methodology has been successfully applied to pyridine and piperonal, which is also extended to aliphatic rings such as five-member, six-member, seven-member, and eight-member 2-alkynylcycloalkene-1-carbaldoximes.

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INTRODUCTION

N-Heterocycles hold an important and special place among pharmaceuticals and natural products. Significant efforts are being carried out to the development of methodologies for the generation of nitrogen-containing heterocycles [1,2]. In the last few decades, an intense attention has been paid continuously to isoquinoline and pyridine derivatives because of their immense biological importance in many natural products and small molecule chemotherapeutics [3–12]. Their biological activities have made them useful in pharmaceutical properties such as antitumor, analgesic, antihistaminic, and antifertility activity [13], and their physical properties make them beneficial as functional materials [10,11].

Accordingly, a number of synthetic methods for isoquinolines have been developed; for example, classic methods, such as the Pomeranz–Fritsch [14], Bischler–Napieralski [15], and Pictet–Spengler [16] reactions, have considerable drawbacks such as the use of strong acids and elevated temperatures. In Bischler–Napieralski and Pictet–Spengler reactions, an additional step involving dehydrogenation is required to complete the synthesis of isoquinoline. Later, the transition metal-catalyzed synthesis of substituted isoquinolines from phenylacetylene substrates [17–23] was reported. In recent studies, Larock *et al* reported the efficient synthesis of isoquinoline derivatives via transition metal-catalyzed cyclization of *ortho*-alkynylaryl aldimines [24,25]. These reactions have proven to be extremely efficient in the synthesis of a wide variety of isoquinolines. However, the development of additional synthetic methods is still highly desirable.

In this paper, we report that $AuCl_3$ catalyzed intramolecular cyclization reaction of *o*-alkynyloximes, in 1,4-dioxane at 80°C, produced isoquinoline and pyridine derivatives with excellent yields.

RESULT AND DISCUSSION

The initial precursor, 2-(phenylethynyl) benzaldehyde oxime (**1a**), is prepared from 2-bromobenzaldehyde and phenylacetylene by Sonogashira coupling reaction, and the resultant compound has been treated with hydroxylamine hydrochloride in the presence of sodium acetate. Our study is initiated with substrate **1a** in the presence of various late transition metal catalysts. Table 1 shows the reaction of **1a** with different reaction conditions. Although substrate **1a** is treated with $AuCl_3$ and $AuCl(PPh_3)/AgSbF_6$ in 1,4-dioxane at room temperature simultaneously for 3 h and 24 h, this has not yielded any reaction product (entries 1–4). However, when the same reaction is heated at 80°C for 2 h, the reaction proceeded smoothly, as the reaction mixture is purified by column chromatography that has resolved one pure product, that is, 3-phenylisoquinoline (**2a**) (entry 5) with 96% yield. In fact, the reaction speed has been accelerated dramatically at high temperatures. Further, the same reaction with $AuCl(PPh_3)/AgSbF_6$ in 1,4-dioxane at 80°C, has been completed within 2 h to obtain exclusively **2a**, albeit with lower yield 91% (entry 6). The compound **2a** is well identified by ^{1}H-NMR, ^{13}C-NMR, and elemental analysis. Of the two catalysts, $AuCl_3$ is the better choice for this intramolecular cyclization reaction (Scheme 1).

The scope and generality of the present reaction is shown in Table 2; further, the reaction has been carried out with 3-(phenylethynyl)-2-naphthaldehyde oxime (**1b**) in 1,4-dioxane at 80°C, which requires longer reaction time 36 h to afford 3-phenylbenzo[g]isoquinoline (**2b**) with

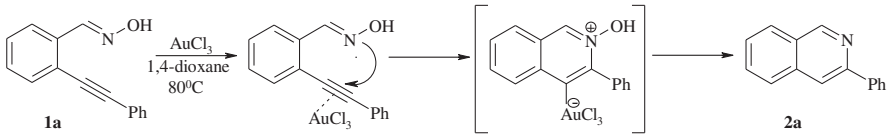
Table 1

Screening of the catalytic activity to cyclize **1a** under various conditions.

Entry	Catalyst (mol%)	Solvent	Time (h)	Temperature (°C)	Product/yield
1	$AuCl_3$ (3)	1,4-Dioxane	3	RT	NR
2	$AuCl(PPh_3)/AgSbF_6$ (3)	1,4-Dioxane	3	RT	NR
3	$AuCl_3$ (3)	1,4-Dioxane	24	RT	NR
4	$AuCl(PPh_3)/AgSbF_6$ (3)	1,4-Dioxane	24	RT	NR
5	$AuCl_3$ (3)	1,4-Dioxane	2	80	**2a**/96
6	$AuCl(PPh_3)/AgSbF_6$ (3)	1,4-Dioxane	2	80	**2a**/91

RT, room temperature; NR, no reaction.

Scheme 1



92% yield (entry 2). It is also noted that the reaction proceeded with substrates that have electron-donating groups such as 4-methoxy-2-(phenylethynyl)benzaldehyde oxime (**1c**), 4-methyl-2-(phenylethynyl) benzaldehyde oxime (**1d**), and 4-methoxy-5-methyl-2-(phenylethynyl) benzaldehyde oxime (**1e**), which produced 6-methoxy-3-phenylisoquinoline (**2c**), 6-methyl-3-phenylisoquinoline (**2d**), and 6-methoxy-7-methyl-3-phenylisoquinoline (**2e**) with 96, 96, and 94% yields, respectively (entries 3–5). On the other hand, the reaction has also been treated with the substrates that have electron-withdrawing groups such as 4-chloro-2-(phenylethynyl)benzaldehyde oxime (**1f**) and 4-nitro-2-(phenylethynyl)benzaldehyde oxime (**1g**) giving 6-chloro-3-phenyl isoquinoline (**2f**) and 6-nitro-3-phenylisoquinoline (**2g**) (entries 6 and 7). It is worth noting that the reaction has good productive yield with 2-(hex-1-yn-1-yl)benzaldehyde oxime (**1h**), 2-(phenylethynyl) nicotinaldehyde oxime (**1i**) was insoluble in 1,4-dioxane, and thus, DMSO was used as solvent in entry 9 and 6-(phenylethynyl)-1,3-benzodioxole-5-carbaldehyde oxime (**1j**) that gave the cyclized products 3-butylisoquinoline (**2 h**) with 61% yield (entry 8), 7-phenyl-1,6-naphthyridine (**2i**) with 91% yield (entry 9), and 7-phenyl-[1,3]dioxolo [4,5-g]isoquinoline (**2j**) with 89% yield (entry 10).

To substantiate further, this methodology has been applied for aliphatic ring systems such as five-member, six-member, seven-member, and eight-member 2-alkynylcycloalkene-1-carbaldoximes. The reaction of 2-(phenylethynyl)cyclopent-1-ene-1-carbaldehyde oxime (**1k**), 2-(phenylethynyl)cyclohex-1-ene-1-carbaldehyde oxime (**1l**), as 2-(phenylethynyl)cyclohept-1-ene-1-carbaldehyde oxime (**1m**), 2-phenylethynyl)cyclooct-1-ene-1-carbaldehyde oxime (**1n**) at 80°C for 6 h gave 3-phenyl-6,7-dihydro-5*H*-cyclopenta [c]pyridine (**2k**), 3-phenyl-5,6,7,8-tetrahydroisoquinoline (**2l**), 3-phenyl-6,7,8,9-tetrahydro-5*H*-cyclohepta[c]pyridine (**2m**), and 3-phenyl-5,6,7,8,9,10-hexahydrocycloocta[c]-pyridine (**2n**), respectively, with excellent yields (entries 11–14). It was observed that the reaction of 2-(phenylethynyl) benzonitrile (**1o**) with $AuCl_3$ at 80°C for 24 h did not yield isoquinoline, and the starting material was recovered. All the compounds (**2a–2n**) (Table 2) were characterized by ^1H, ^{13}C-NMR, and elemental analysis.

CONCLUSION

In conclusion, we have developed a simple and efficient one-pot synthesis to prepare isoquinoline and pyridine derivatives from *o*-alkynyloximes catalyzed by $AuCl_3$. This methodology has been applied to electron-donating and electron-withdrawing groups in aromatic systems. Similar methodology is also applied for aliphatic 2-alkynylcycloalkene-1-carbaldoximes.

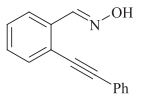
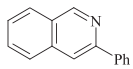
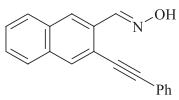
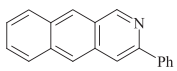
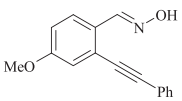
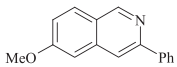
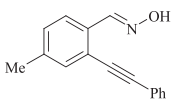
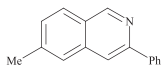
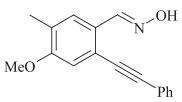
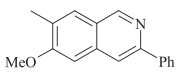
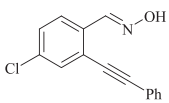
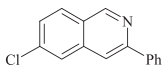
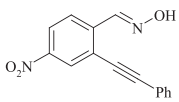
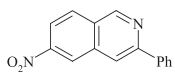
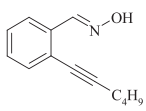
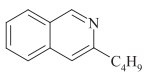
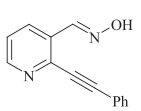
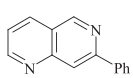
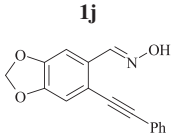
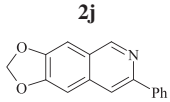
EXPERIMENTAL

Melting points were determined in open capillaries on a Mel-Temp apparatus and are uncorrected. Infrared spectra were measured on a Nicolet Magna-IR 550 spectrometer (Series-II) as KBr pellets, unless otherwise noted. NMR spectra were recorded in $CDCl_3$ on a 400-MHz Varian spectrophotometer. All chemical shifts were reported in parts per million from TMS as an internal standard. The elemental analysis was performed by Perkin Elmer 24°C elemental analyzer. Mass spectra were recorded on a time-of-flight instrument. Starting materials were prepared according to literature procedure [26].

General procedure for the preparation of 2a. In a 5-mL oven-dried test tube, 2-(phenylethynyl)benzaldehyde oxime **1a** (100 mg, 0.45 mmol), $AuCl_3$ (7 mg, 0.0226 mmol), and 1,4-dioxane (1.0 mL) were added at room temperature. The

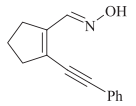
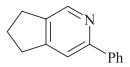
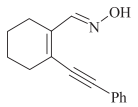
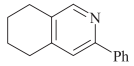
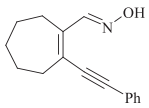
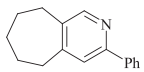
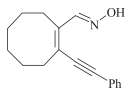
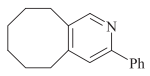
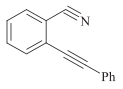
Table 2

Reactions of various *o*-alkynyloximes.[a]

Entry	Substrate	Product	Time (h)	Yield (%)
1	**1a** 	**2a** 	2	96
2	**1b** 	**2b** 	36	92
3	**1c** 	**2c** 	2	96
4	**1d** 	**2d** 	2	96
5	**1e** 	**2e** 	6	94
6	**1f** 	**2f** 	6	92
7	**1g** 	**2g** 	6	90
8	**1h** 	**2h** 	12	61
9	**1i** 	**2i** 	12	91
10	**1j** 	**2j** 	46	89

(*Continues*)

Table 2
(Continued)

Entry	Substrate	Product	Time (h)	Yield (%)
11	**1k** 	**2k** 	6	96
12	**1l** 	**2l** 	6	92
13	**1m** 	**2m** 	6	96
14	**1n** 	**2n** 	6	91
15	**1o** 	NR	24	SM recovered

NR, no reaction; SM, starting material.
[a]All the reactions were carried out at 80°C in 3-mol% $AuCl_3$ and 1,4-dioxane as solvent except entry 9 in DMSO.

resulting mixture was stirred for 2 h at 80°C, and the solvent was removed under vacuum. The crude compound was purified by column chromatography (SiO_2, *n*-hexane/EtOAc = 10:1) to afford the pure product **2a**. The known compounds data were compared with those reported in the literature [27].

3-Phenylisoquinoline (2a). White solid, yield (89 mg, 96%), mp. 96–97°C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.34 (s, 1H), 8.13 (d, J = 7.6 Hz, 2H), 8.07 (s, 1H), 7.99 (d, J = 8.0 Hz, 1H), 7.87 (d, J = 8.0 Hz, 1H), 7.69 (t, J = 7.6 Hz, 1H), 7.58 (t, J = 7.6 Hz, 1H), 7.51 (t, J = 7.6 Hz, 2H), 7.42 (t, J = 7.2 Hz, 1H); ^{13}C-NMR δ 152.40 151.30, 139.60, 136.63, 130.45, 128.77, 128.49, 127.74, 127.54, 127.04, 126.98, 126.89, 116.45. Anal. calcd. for $C_{15}H_{11}N$: C, 87.77; H, 5.40; N, 6.82. Found: C, 87.34; H, 5.56; N, 6.68 %. HRMS [found: m/z 205.0893 (M^+), calcd for $C_{15}H_{11}N$: M, 205.0891].

3-Phenylbenzo[g]isoquinoline (2b). White solid, yield (87 mg, 92%), mp. 110–111°C, ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.31 (s, 1H), 8.83 (s, 1H), 8.78–8.76 (m, 1H), 8.19 (d, J = 7.2 Hz, 2H), 7.95–7.93 (m, 1H), 7.82 (s, 2H), 7.75–7.71 (m, 2H), 7.55 (t, J = 7.2 Hz, 2H), 7.45 (t, J = 7.6 Hz, 1H); ^{13}C NMR δ 153.37, 151.60, 140.05, 135.58, 133.73, 128.85, 128.74, 128.70, 128.68, 128.17, 127.20, 127.12, 125.90, 124.62, 123.17, 112.50. Anal. calcd. for $C_{19}H_{13}N$: C, 89.38; H, 5.13; N, 5.49. Found: C, 89.30; H, 5.19; N, 5.41%. HRMS [found: m/z 255.1050 (M^+), calcd for $C_{19}H_{13}N$: M, 255.1048].

6-Methoxy-3-phenylisoquinoline (2c). White solid, yield (90 mg, 96%), mp. 96–97°C, ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.18 (s, 1H), 8.10 (d, J = 7.2 Hz, 2H), 7.96 (s, 1H), 7.86 (d, J = 8.8 Hz, 1H), 7.50 (t, J = 8.0 Hz, 2H), 7.41 (t, J = 7.2 Hz, 1H), 7.19 (dd, J = 6.8 Hz, 1H) 7.10 (s, 1H), 3.95 (s, 3H); ^{13}C-NMR δ 161.07, 151.75, 151.51, 139.73, 138.57, 129.20, 128.72, 128.44, 126.97, 123.58, 120.14, 115.90, 104.37, 55.45. Anal. calcd. for $C_{16}H_{13}NO$: C, 81.68; H, 5.57; N, 5.95. Found: C, 81.54; H, 5.69; N, 5.91%. HRMS [found: m/z 235.0994 (M^+), calcd for $C_{16}H_{13}NO$: M, 235.0997].

6-Methyl-3-phenylisoquinoline (2d). White solid, yield (89 mg, 96%), mp. 127–128°C, ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.28 (s, 1H), 8.03 (d, J = 7.4 Hz, 2H), 7.99 (s, 1H), 7.95 (d, J = 8.2 Hz, 1H), 7.55 (t, J = 8.4 Hz, 2H), 7.47 (t, J = 7.8 Hz, 1H), 7.24 (d, J = 6.7 Hz, 1H) 7.16 (s, 1H), 2.41 (s, 3H); ^{13}C-NMR δ 152.25, 150.71, 140.23, 137.71, 136.37, 129.91, 129.31, 127.66, 127.48, 127.25, 125.23, 123.86, 116.29, 24.75. Anal. calcd. for $C_{16}H_{13}N$: C, 87.64; H, 5.98; N, 6.39. Found: C, 87.55; H, 6.09; N, 6.43%. HRMS [found: m/z 219.1052 (M^+), calcd for $C_{16}H_{13}N$: M, 219.1048].

6-Methoxy-7-methyl-3-phenylisoquinoline (2e). White solid, yield (89 mg, 94%), mp. 122–123°C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.12 (s, 1H), 8.09 (d, J = 8.0 Hz, 2H), 7.95 (s, 1H), 7.70 (s, 1H), 7.49 (t, J = 7.6 Hz, 2H), 7.39 (t, J = 7.2 Hz, 1H), 7.06 (s, 1H), 3.99 (s, 3H), 2.40 (s, 3H); ^{13}C-NMR δ 160.40,

150.89, 150.70, 139.94, 137.39, 130.24, 128.70, 128.25, 126.90, 123.49, 115.62, 103.11, 55.52, 17.00. Anal. calcd. for $C_{17}H_{15}NO$: C, 81.90; H, 6.06; N, 5.62. Found: C, 82.12; H, 5.94; N, 5.58%. HRMS [found: m/z 249.1158 (M^+), calcd for $C_{17}H_{15}NO$: M, 249.1154].

6-Chloro-3-phenylisoquinoline (2f). White solid, yield (90 mg, 96%), mp. 130–131°C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.29 (s, 1H), 8.11 (d, J = 7.2 Hz, 2H), 7.93 (s, 1H), 8.04 (d, J = 7.8 Hz, 1H), 7.75 (d, J = 7.8 Hz, 1H), 7.84 (s, 1H), 7.52 (t, J = 7.4 Hz, 2H), 7.44 (t, J = 7.1 Hz, 1H); ^{13}C-NMR δ 152.25, 151.12, 138.54, 136.70, 131.36, 128.94, 128.50, 127.71, 127.49, 127.07, 126.77, 126.61, 116.58. Anal. calcd. for $C_{15}H_{10}ClN$: C, 75.16; H, 4.21; N, 5.84. Found: C, 75.24; H, 4.14; N, 5.91%. HRMS [found: m/z 239.0506 (M^+), calcd for $C_{15}H_{10}ClN$: M, 239.0502].

6-Nitro-3-phenylisoquinoline (2g). White solid, yield (84 mg, 90%), mp. 140–141°C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.39 (s, 1H), 8.12 (d, J = 7.2 Hz, 2H), 8.33 (s, 1H), 8.18 (d, J = 7.8 Hz, 1H), 8.25 (d, J = 7.8 Hz, 1H), 7.93 (s, 1H), 7.53 (t, J = 7.4 Hz, 2H), 7.45 (t, J = 7.1 Hz, 1H); ^{13}C-NMR δ 152.45, 151.42, 138.56, 134.70, 150.36, 128.92, 129.50, 121.71, 127.51, 127.11, 124.75, 129.67, 120.42. Anal. calcd. for $C_{15}H_{10}N_2O_2$: C, 71.99; H, 4.03; N, 11.19. Found: C, 72.27; H, 4.12; N, 11.15%. HRMS [found: m/z 250.0745 (M^+), calcd for $C_{15}H_{10}N_2O_2$: M, 250.0742].

3-Butylisoquinoline (2h). Colorless liquid, yield (56 mg, 61%); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.21 (s, 1H), 7.92 (d, J = 8.4 Hz 1H), 7.74 (d, J = 8.4 Hz, 1H), 7.64 (t, J = 7.6 Hz, 1H), 7.52 (t, J = 8.0 Hz, 1H), 7.47 (s, 1H), 2.94 (t, J = 7.2 Hz, 2H), 1.80 (quintet, J = 7.6 Hz, 2H), 1.42 (sextet, J = 7.2 Hz, 2H), 0.96 (t, J = 7.6 Hz, 3H); ^{13}C-NMR δ 155.87, 152.00, 136.51, 130.17, 127.48, 126.24, 126.06, 118.05, 117.89, 37.84, 32.13, 22.47, 13.97. Anal. calcd. for $C_{13}H_{15}N$: C, 84.28; H, 8.16; N, 7.56. Found: C, 84.39; H, 8.05; N, 7.61%. HRMS [found: m/z 185.1207 (M^+), calcd for $C_{13}H_{15}N$: M, 185.1204].

7-Phenyl-1,6-naphthyridine (2i). White solid, yield (85 mg, 91%), mp. 131–132°C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.36 (s, 1H), 9.10 (dd, J = 1.6 Hz, 1H), 8.35 (s, 1H), 8.31 (d, J = 8.0 Hz, 1H), 8.18 (d, J = 7.6 Hz, 2H), 7.56–7.50 (m, 3H), 7.45 (t, J = 6.8 Hz, 1H); ^{13}C-NMR δ 155.92, 155.74, 153.36, 152.08, 139.55, 136.29, 129.86, 129.61, 127.90, 123.37, 122.88, 118.50. Anal. calcd. for $C_{14}H_{10}N_2$: C, 81.53; H, 4.89; N, 13.58. Found: C, 81.64; H, 4.82; N, 13.64%. HRMS [found: m/z 206.0841 (M^+), calcd for $C_{14}H_{10}N_2$: M, 206.0844].

7-Phenyl-[1,3]dioxolo[4,5-g]isoquinoline (2j). Yellow solid, yield (84 mg, 89%), mp. 117–118°C, ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.08 (s, 1H), 8.06 (d, J = 7.6 Hz, 2H), 7.90 (s, 1H), 7.49 (t, J = 7.6 Hz, 2H), 7.40 (t, J = 7.2 Hz, 1H), 7.21 (s, 1H), 7.12 (s, 1H), 6.10 (s, 2H); ^{13}C-NMR δ 151.15, 150.60, 150.13, 148.37, 139.62, 135.11, 128.72, 128.30, 126.82, 125.03, 116.44, 103.13, 102.80, 101.62. Anal. calcd. for $C_{16}H_{11}NO_2$: C, 77.10; H, 4.45; N, 5.62. Found: C, 77.16; H, 4.39; N, 5.64%. HRMS [found: m/z 249.0793 (M^+), calcd for $C_{16}H_{11}NO_2$: M, 249.0790].

3-Phenyl-6,7-dihydro-5H-cyclopenta[c]pyridine (2k). Colorless liquid, yield (89 mg, 96%); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.53 (s, 1H), 7.95 (d, J = 7.6 Hz, 2H), 7.60 (s, 1H), 7.45 (t, J = 7.2 Hz, 2H), 7.38 (t, J = 7.6 Hz, 1H), 2.97 (t, J = 8.0 Hz, 4H), 2.14 (quintet, J = 7.6 Hz, 2H); ^{13}C-NMR δ 155.41, 154.60, 145.34, 139.98, 138.71, 128.59, 128.36, 126.87, 116.81, 32.71, 29.98, 25.07. Anal. calcd. for $C_{14}H_{13}N$: C, 86.12; H, 6.71; N, 7.17. Found: C, 85.98; H, 6.89; N, 7.12%. HRMS [found: m/z 195.1052 (M^+), calcd for $C_{14}H_{13}N$: M, 195.1048].

3-Phenyl-5,6,7,8-tetrahydroisoquinoline (2l). Colorless liquid, yield (68 mg, 92%); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.37 (s, 1H), 7.94 (d, J = 7.2 Hz, 2H), 7.46–7.35 (m, 4H), 2.79 (t, J = 4.8 Hz, 4H), 1.84 (t, J = 3.2 Hz, 4H); ^{13}C-NMR δ 154.38, 150.23, 146.70, 139.71, 131.65, 128.58, 128.32, 126.66, 120.67, 28.94, 26.03, 22.68, 22.46. Anal. calcd. for $C_{15}H_{15}N$: C, 86.08; H, 7.22; N, 6.69. Found: C, 85.94; H, 7.31; N, 6.64%. HRMS [found: m/z 209.1207 (M^+), calcd for $C_{15}H_{15}N$: M, 209.1204].

3-Phenyl-6,7,8,9-tetrahydro-5H-cyclohepta[c]pyridine (2m). Colorless liquid, yield (71 mg, 96%); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.38 (s, 1H), 7.96 (d, J = 6.8 Hz, 2H), 7.47–7.43 (m, 3H), 7.38 (t, J = 7.2 Hz, 1H), 2.82 (dd, J = 7.6 Hz, 4H), 1.89 (quintet, J = 5.6 Hz, 2H), 1.69 (t, J = 4.8 Hz, 4H); ^{13}C-NMR δ 155.61, 152.71, 149.20, 139.57, 137.26, 128.60, 128.44, 126.70, 120.76, 36.55, 32.96, 32.61, 28.04, 27.55. Anal. calcd. for $C_{16}H_{17}N$: C, 86.05; H, 7.67; N, 6.27. Found: C, 86.12; H, 7.59; N, 6.29%. HRMS [found: m/z 223.1358 (M^+), calcd for $C_{16}H_{17}N$: M, 223.1361].

3-Phenyl-5,6,7,8,9,10-hexahydrocycloocta[c]pyridine (2n). Colorless liquid, yield (85 mg, 91%); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.39 (s, 1H), 7.97 (d, J = 7.6 Hz, 2H), 7.47–7.44 (m, 3H), 7.38 (t, J = 7.6 Hz, 1H), 2.79 (sextet, J = 3.6 Hz, 4H), 1.77–1.70 (m, 4H), 1.45–1.35 (m, 4H); ^{13}C-NMR δ 155.43, 150.71, 149.78, 139.53, 135.59, 128.61, 128.43, 126.63, 120.64, 32.08, 31.74, 31.45, 29.09, 25.85, 25.50. Anal. calcd. for $C_{17}H_{19}N$: C, 86.03; H, 8.07; N, 5.90. Found: C, 86.11; H, 8.14; N, 5.85%. HRMS [found: m/z 237.1520 (M^+), calcd for $C_{17}H_{19}N$: 237.1517].

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