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Copper(II) Catalyzed C-H Alkoxylation of 2-Phenyl Pyridines with Aliphatic Diols

Yan Xiao,[a] Juan Li,[a] Yajun Liu, [b] Shuo Wang, [a] Hui Zhang*, [a] and Huaiwei Ding* [a]

Abstract: A very simple copper(II) catalyzed C-O coupling reaction of 2-phenylpyridines and aliphatic diols was achieved using a strategy of C-H functionalization. A series of aroxyl ethanols are easily obtained with the yields of 30-67%. Various functional groups, as well as different length of aliphatic diols are well tolerated in the developed catalytic system. This new protocol is featured by simple reaction system, economical catalyst and good *regio*-selectivity. In addition, a "one-pot" synthesis of 2-phenyl pyridines was developed.

Introduction

Aroxyl aliphatic alcohols are fundamental building blocks in organic synthesis. They are often employed in the construction of chromones， benzofurans and phenols[1]. Aroxyl aliphatic alcohols are traditionally prepared by Buchwald-Hartwig typed C-O coupling reaction, which provides a useful pathway to synthesize aryl alkyl ethers from aryl halides and aliphatic alcohols[2]. However, this protocol always requires pre-halogenation of arenes, additional complex ligands and inorganic bases.

In the past decades, C-H functionalization represents a powerful strategy in the field of organic synthesis [3]. C-H activation/C-O bond coupling reactions have provided various protocols for constructing esters and phenols[4]. It also allows the direct synthesis of aryl alkyl ethers from simple arenes and aliphatic alcohols. As a pioneering work, the Wang group in 2010 reported a $Pd(OAc)_2$ catalyzed *ortho*-alkoxylation of benzamides to provide aryl alkyl ethers[5]. Subsequently, a variety of arenes, including benzamides[6], diarylazo[7], *N*-nitrosoanilines[8], trizoles[9] and 2-phenyl pyridines[10], were successfully coupled with aliphatic alcohols to afford C-O coupled products (Scheme 1). Regarding transition metal catalyst, palladium, copper and cobalt showed their effectiveness in catalyzing direct synthesis of aryl alkyl ethers from arenes and aliphatic alcohols. These reported methods undoubtedly have provided useful pathways to get access to aryl alkyl ethers, however there are still some drawbacks: 1) Expensive palladium was frequently used as catalyst, and a stoichiometric amount of copper salt was often required in the copper mediated conversions; 2) In most cases, excess oxidant was always required. In this context, a simple and economical protocol is highly desirable for the direct coupling of arenes and aliphatic alcohols.

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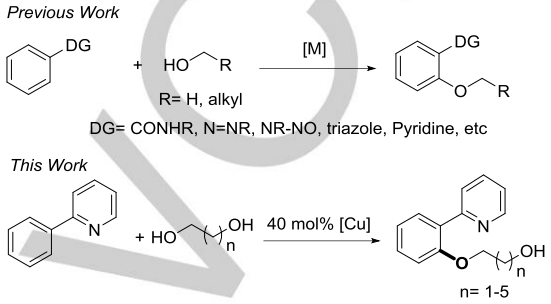
As a continuous study of the synthesis of 2-aryloxyethanols[11], herein, we reported a $CuSO_4 \cdot 5H_2O$ catalyzed direct C-O coupling reaction of 2-phenylpyridines and aliphatic diols. Our work provides an easy access to aroxyl aliphatic alcohols.

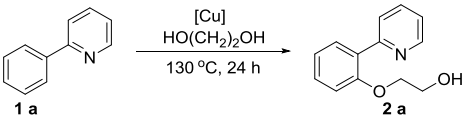


Scheme 1: C-H alkoxylation with aliphatic alcohols

Results and Discussion

Ethylene glycol has wide application in organic synthesis and is often used as solvent and/or ligand for copper catalyzed transformations[12]. We supposed that ethylene glycol also could promote the C-H alkoxylation of arenes with ethylene glycol itself and make the reaction simple. Our study was initiated using 2-phenyl pyridine **1a** and ethylene glycol as model arene and aliphatic diol, respectively. The coupling reaction was carried at 130 °C in the air using 20 mol% of $CuSO_4 \cdot 5H_2O$ as catalyst for 24h. To our delight, the reaction successfully afforded the corresponding product **2a** as sole product with the yield of 47% after column purification (Table 1, entry 1). During the purification process, 51% of starting material was recovered.

Table 1: Effect of copper catalysts and loading amounts[a]



Entry	Cu (mol%)	Yield(%)[b]
1	$CuSO_4 \cdot 5H_2O$(20)	47
2	$CuCl_2$(20)	43
3	$Cu(OAc)_2$(20)	45
4	$Cu(CF_3SO_3)_2$(20)	40
5	$Cu(acac)_2$(20)	41
6	CuBr(20)	15
7	**$CuSO_4 \cdot 5H_2O$(40)**	**57**
8	$CuSO_4 \cdot 5H_2O$(100)	50
9	$CuSO_4 \cdot 5H_2O$(200)	54
10[c]	$CuSO_4 \cdot 5H_2O$(40)	15

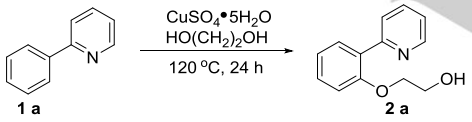
[a] Reaction Conditions: 2-phenyl pyridine (1.0 mmol), ethylene glycol (2 mL), copper salt, 130 °C, 24 h; [b] Isolated yield by silica gel column chromatography; [c] under Argon.

Further screening on copper(II) salts including $CuCl_2$, $Cu(OAc)_2$, $Cu(CF_3SO_3)_2$ and $Cu(acac)_2$ revealed that $CuSO_4 \cdot 5H_2O$ was the

most effective catalyst for this conversion (Table 1, entries 2-5). Copper (I) salt was less effective than copper(II) salts in this conversion as CuBr gave only 15% yield (Table 1, entry 6). In order to get higher yield in this transformation, the loading amount of $CuSO_4 \cdot 5H_2O$ was increased. 40 mol% amount of $CuSO_4 \cdot 5H_2O$ gave higher yield of 57% (Table 1, entry 7). However, it is interesting that further increasing loading amount of copper salt to 1 equiv. or 2 equiv. didn't improve the yield (Table 1, entries 8-9). Only 15% yield was obtained when the reaction was conducted under argon, indicating the importance of oxygen in this conversion (Table 1, entry 10).

Study on reaction temperature showed that lowering reaction temperature to 120 °C gave higher yield of 61%, however the yield of the reaction at 110 °C was dramatically decreased to 44% (Table 2, entry 1). It is to be noted that the reaction was carried out without any additional solvent. Organic solvent, such as DMSO, toluene and 1, 4-dioxane, prevented the C-H alkoxylation of 2-phenyl pyridine (Table 2, entries 2-4). Addition of water into the reaction system also decreased the yield to 32% (Table 2, entry 5). In order to further improve the reaction yields, several classical bidentate ligands for copper catalyst including 8-hydroxyquinoline, 1-hydroxy-2-naphthoic acid, glycine and dibenzoyl ethane were used, but disappointedly, no improvement was observed (Table 2, entries 6-9). On the other hand, the addition of oxidant including $K_2S_2O_8$, Ag_2CO_3, $FeCl_3$, MnO_2 and O_2, to the reaction system also proved fruitless (Table 2, entries 10-14). This result may be attributed to the loss of ethylene glycol due to the oxidation caused by the above oxidants. Thus, we obtained the optimum condition as follows: 2-phenyl pyridine (1.0 mmol), ethylene glycol (2 mL), $CuSO_4 \cdot 5H_2O$ (40 mol%), 120 °C, 24h.

Table 2: Condition screening for $CuSO_4 \cdot 5H_2O$ catalyzed coupling of **1a** and ethylene glycol[a]



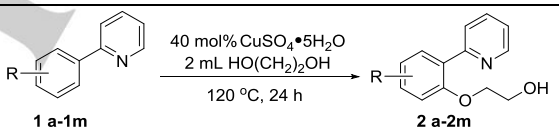
1 a **2 a**

Entry	Solvent[b]	Oxidant[c]	Ligand[d]	Yield(%)[e]
1	-	-	-	**61**, 44[f]
2	DMSO	-	-	30
3	Toluene	-	-	27
4	1,4-dioxane	-	-	24
5	H_2O	-	-	32
6	-	-	8-hydroxyquinoline	29
7	-	-	HNPA[g]	38
8	-	-	Glycine	29
9	-	-	Dibenzoyl ethane	42
10	-	$K_2S_2O_8$	-	<5%
11	-	Ag_2CO_3	-	41
12	-	$FeCl_3$	-	<5%
12	-	MnO_2	-	49
14	-	O_2	-	44

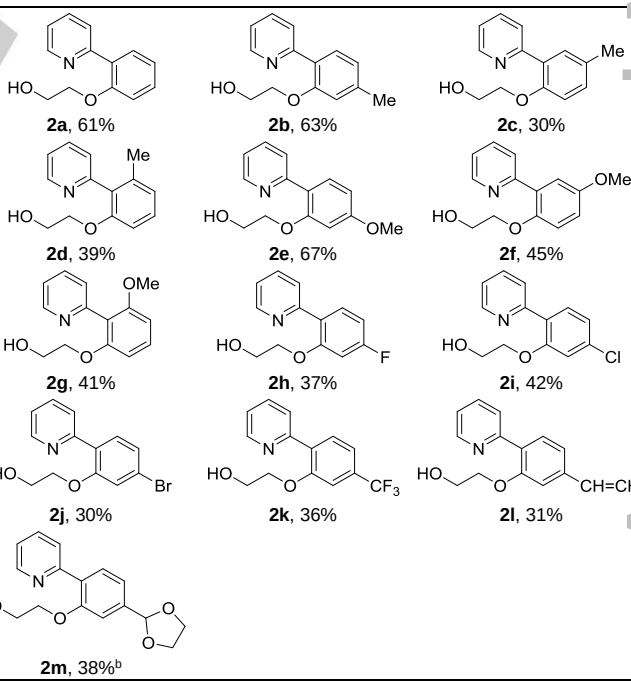
[a] Reaction Conditions: 1.0 mmol of 2-phenyl pyridine, 2.0 mL ethylene glycol, 120 °C, 24 h; [b] 2mL; [c] 2 equiv of oxidants; [d] 40 mol% of ligand; [e] Isolated yield by silica gel column chromatography; [f] 110 °C; [g] HNPA: 1-hydroxy-2-naphthoic acid.

With the optimized reaction condition in hand, the scope of 2-arylpyridines was investigated (Table 3). The reaction of 2-arylpyridines in the presence of 40 mol % of $CuSO_4 \cdot 5H_2O$ in 2 mL ethylene glycol afforded the corresponding C-O coupled products. A broad range of functional groups were compatible with the developed condition. Generally, electron-donating groups at the phenyl ring are beneficial for C-H alkoxylation while electron-withdrawing groups hampered the conversion. *Para*-methyl and methoxyl groups substituted 2-phenyl pyridines gave satisfying yields of 63% and 67%, respectively (**2b** and **2e**). Although *meta*-substituted arenes afforded lower yields, good *regio*-selectivity was observed (**2c** and **2f**). When one *ortho*-carbon was substituted, low yields of the corresponding products were obtained (**2d** and **2g**). Electron-deficient groups (such as halides, vinyl and trifluoromethyl) provided yields of 30-42% yields of products (**2h**-**2l**). It is very interesting that when 4-(pyridin-2-yl)benzaldehyde was used as substrate, the aldehyde was converted to acetal **2m** in 38% yield during the C-H alkoxylation process. To be our best knowledge, copper catalyzed protection of aldehyde with aliphatic alcohols has never been reported, and thus our work provides a new choice for the protection of aldehyde. It should be noted that under the optimum condition, a majority of reactions gave the *ortho*-alkyloxylated product as sole product with good *regio*-selectivity.

Table 3: Substrate scope of 2-arylpyridines[a]



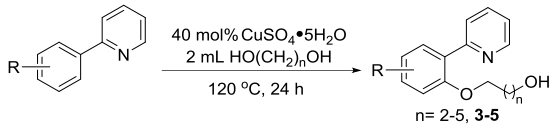
1 a-1m **2 a-2m**



[a] Reaction Conditions: 1.0 mmol of 2-phenyl pyridines, 40 mol% $CuSO_4 \cdot 5H_2O$ and 2.0 mL ethylene glycol, 120 °C for 24 h; [b] 4-pyridin-2-yl)benzaldehyde as starting material.

We next investigated the developed condition toward different length of aliphatic diols (Table 4). Aliphatic diols with length of 3-6 carbons were easily converted to the corresponding aroxyl alcohols. The result summarized in Table 4 unsurprisingly indicated that longer length of aliphatic diols gave lower yields.

Table 4: Substrate scope of aliphatic diols[a]

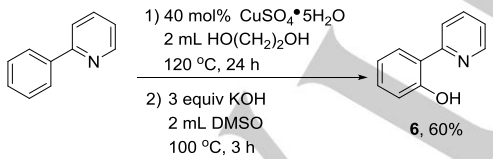


n=2, **3a**, 56%	n=2, **4a**, 59%	n=2, **5a**, 62%
n=3, **3b**, 51%	n=3, **4b**, 56%	n=3, **5b**, 57%
n=4, **3c**, 46%	n=4, **4c**, 50%	n=4, **5c**, 51%
n=5, **3d**, 42%	n=5, **4d**, 47%	n=5, **5d**, 49%

[a] Reactions were carried out using 2-phenylpyridines (1.0 mmol) and $CuSO_4 \cdot 5H_2O$ (40 mol%) in 2.0 mL aliphatic diols at 120 °C for 24 h; isolated yields.

We also tested the reactivity of monohydric alcohol in our developed reaction system, however no reaction was observed when either *n*-butanol or *n*-octanol was used. It should be noted that the reaction became homogeneous within several minutes after heating in the case of aliphatic diols, while precipitate was always observed in the case of monohydric alcohols. It indicated that aliphatic diol can dissolve $CuSO_4 \cdot 5H_2O$ perhaps due to the formation of a Cu(II)-diol complex, which is essential for initiating the reaction.

Our developed condition was further applied in the preparation of phenols (Scheme 2). After the coupling of 2-phenylpyridine and ethylene glycol, the reaction mixture was extracted with CH_2Cl_2 and the organic layer was condensed under vacuum. The crude product without further purification was directly treated with KOH and DMSO. The corresponding phenol **6** was successfully obtained with 60% yield, providing a practical method for the synthesis of phenols from 2-phenyl pyridines.



Scheme 2: One-pot synthesis of 2-(pyridin-2-yl)phenol **6**

Conclusions

In conclusion, a very simple reaction system was developed for the preparation of aroxyl alcohols from 2-phenylpyridnes and aliphatic diols. In this protocol, easily available $CuSO_4 \cdot 5H_2O$ was used as catalyst, and aliphatic alcohols played dual roles of reagent and solvent. Either additives or traditional solvent was not required in this conversion. Furthermore, the reported condition in this work was further successfully applied in the synthesis of phenols. We believe that this simple and practical method will find wide use in both laboratory and industry.

Experimental Section

General information

All chemicals were purchased as reagent grade and used without further purification. Solvents for purification (extraction and chromatography) were purchased as technical grade and distilled on the rotary evaporator prior to use. For column chromatography, SiO_2 (200-300 mesh) was used as stationary phase. The reaction's progress was routinely monitored by thin-layer chromatography (GF254). ^{1}H NMR spectra were recorded on a 600 MHz Bruker NMR spectrometer with tetramethylsilane (TMS) as an internal standard. High resolution mass spectra (HRMS) analysis was performed on Q-TOF Bruker mass spectrometer with ESI as ionization source.

General procedure for the synthesis of aroxyl aliphatic alochols

To a solution of 2-phenylpyridines (1.0 mmol) in aliphatic diols (2 mL), was added $CuSO_4 \cdot 5H_2O$ (40 mol%). After stirring at 120 °C for 24 h, the resulting mixture was cooled to room temperature. Then the mixture was extracted with CH_2Cl_2 and water. The organic layer was dried over anhydrous $MgSO_4$, and evaporated under reduced pressure to afford crude product, which was purified by flash chromatography on silica gel with petroleum ether /ethyl acetate.

2-(2-(pyridin-2-yl)phenoxy)ethan-1-ol (2a)

prepared following the general procedure using 2-phenylpyridine (0.155 g, 1.0 mmol) and ethylene glycol (2 mL) to afford **2a** as white solid (131 mg, 61%). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.65 -8.63 (m, 1H), 8.03 (d, *J* = 8.0 Hz, 1H), 7.81-7.77 (m, 2H), 7.41- 7.36 (m, 1H), 7.30 (ddd, *J* = 7.4, 4.8, 1.0 Hz, 1H), 7.15 (d, *J* = 8.2 Hz, 1H), 7.06 (td, *J* = 7.6, 0.9 Hz, 1H), 4.95 (t, *J* = 5.4 Hz, 1H), 4.11 (t, *J* = 4.9 Hz, 2H), 3.73 (q, *J* = 5.2 Hz, 2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 156.6, 155.4, 149.5, 136.3, 131.2, 130.4, 128.7, 125.3, 122.3, 121.1, 113.6, 70.6, 59.9. HRMS (ESI): calculated for $C_{13}H_{13}NO_2Na$ $(M+Na)^+$: 238.0844; found: 238.0844.

2-(5-methyl-2-(pyridin-2-yl)phenoxy)ethan-1-ol (2b)

prepared following the general procedure using 2- (4-methyl phenyl)pyridine（0.169 g, 1.0 mmol） and ethylene glycol (2 mL) to afford **2b** as white solid (144 mg, 63 %). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.62 - 8.61 (m, 1H), 8.02 (d, *J* = 8.0 Hz, 1H), 7.77 (td, *J* = 7.8, 1.9 Hz, 1H), 7.71 (d, *J* = 7.8 Hz, 1H), 7.27 (ddd, *J* = 7.4, 4.8, 1.0 Hz, 1H), 6.97 (s, 1H), 6.87 (d, *J* = 8.2 Hz, 1H), 4.95 (t, *J* = 5.3 Hz, 1H), 4.09 (t, *J* = 5.0 Hz, 2H), 3.73 (q, *J* = 5.1 Hz, 2H), 2.35 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 156.5, 155.5, 149.4, 140.2, 136.3, 130.9, 125.9, 125.1, 122.0, 121.8, 114.2, 70.5, 59.9, 21.5. HRMS (ESI): calculated for $C_{14}H_{15}NO_2Na$ $(M+Na)^+$: 252.1000; found: 252.0999.

2-(4-methyl-2-(pyridin-2-yl)phenoxy)ethan-1-ol (2c)

prepared following the general procedure using 2- (3-methyl phenyl)pyridine (0.169 g,1.0 mmol) and ethylene glycol (2 mL) to afford **2c** as white solid (68 mg, 30 %). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.63 (d,

J = 4.3 Hz, 1H), 8.02 (d, *J* = 8.0 Hz, 1H), 7.78 (td, *J* = 7.8, 1.7 Hz, 1H), 7.61 (d, *J* = 1.9 Hz, 1H), 7.29 (dd, *J* = 7.0, 5.2 Hz, 1H), 7.17 (dd, *J* = 8.3, 2.0 Hz, 1H), 7.04 (d, *J* = 8.4 Hz, 1H), 4.95 (s, 1H), 4.06 (t, *J* = 4.9 Hz, 2H), 3.71 (t, *J* = 4.9 Hz, 2H), 2.31 (s, 1H), 2.29 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 155.5, 154.6, 149.4, 136.3, 131.6, 130.7, 129.7, 128.4, 125.3, 122.2, 113.74, 70.76, 59.96, 20.51. HRMS (ESI): calculated for $C_{14}H_{15}NO_2Na$ (M+Na)$^+$: 252.1000; found: 252.1003.

2-(3-methyl-2-(pyridin-2-yl)phenoxy)ethan-1-ol (2d)

prepared following the general procedure using 2-(2-methyl phenyl)pyridine（169 mg,1.0 mmol）and ethylene glycol (2 mL) to afford **2d** as white solid (89 mg, 39%). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.62 (ddd, *J* = 4.9, 1.9, 1.0 Hz, 1H), 7.81 (td, *J* = 7.7, 1.9 Hz, 1H), 7.35 (dt, *J* = 7.7, 1.1 Hz, 1H), 7.31 (ddd, *J* = 7.6, 4.9, 1.2 Hz, 1H), 7.26-7.23 (m, 1H), 7.02 -6.85 (m, 2H), 4.75 (d, *J* = 4.9 Hz, 1H), 3.94 (t, *J* = 5.3 Hz, 2H), 3.51 (q, *J* = 4.9 Hz, 2H), 2.00 (s, 3H).^{13}C NMR (151 MHz, DMSO-d_6) δ 155.1, 153.7, 150.8, 149.5, 136.5, 129.6, 125.3, 122.5, 115.8, 115.7, 115.5, 71.4, 60.0, 55.8. HRMS (ESI): calculated for $C_{14}H_{15}NO_2Na$ (M+Na)$^+$: 252.1000; found: 252.0991.

2-(5-methoxy-2-(pyridin-2-yl)phenoxy)ethan-1-ol(2e)

prepared following the general procedure using 2- (4-methoxyphenyl) pyridine (0.185 g,1.0 mmol) and ethylene glycol (2 mL) to afford **2e** as white solid (164 mg, 67%). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.61 (d, *J* = 4.2 Hz, 1H), 8.03 (d, *J* = 8.0 Hz, 1H), 7.82 (d, *J* = 8.6 Hz, 1H), 7.76 (td, *J* = 7.8, 1.8 Hz, 1H), 7.24 (dd, *J* = 6.8, 5.0 Hz, 1H), 6.70 (d, *J* = 2.3 Hz, 1H), 6.66 (dd, *J* = 8.6, 2.3 Hz, 1H), 5.03 (s, 1H), 4.12 (t, *J* = 4.9 Hz, 2H), 3.82 (s, 3H), 3.76 (t, *J* = 4.9 Hz, 2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 161.3, 157.8, 155.3, 149.3, 136.3, 131.9, 124.7, 121.6, 121.4, 106.2, 100.1, 70.7, 59.9, 55.7. HRMS (ESI): calculated for $C_{14}H_{15}NO_3Na$ (M+Na)$^+$: 268.0950; found: 268.0953.

2-(4-methoxy-2-(pyridin-2-yl)phenoxy)ethan-1-ol(2f)

prepared following the general procedure using 2- (3-methoxyphenyl) pyridine (0.185 g,1.0 mmol) and ethylene glycol (2 mL) to afford **2f** as white solid (110 mg, 45 %). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.66 (ddd, *J* = 4.8, 1.9, 0.9 Hz, 1H), 8.07 (dt, *J* = 8.0, 1.1 Hz, 1H), 7.84 – 7.77 (m, 1H), 7.38 (d, *J* = 3.2 Hz, 1H), 7.32 (ddd, *J* = 7.5, 4.8, 1.1 Hz, 1H), 7.10 (d, *J* = 8.9 Hz, 1H), 6.96 (dd, *J* = 8.9, 3.2 Hz, 1H), 4.97 (t, *J* = 5.3 Hz, 1H), 4.04 (t, *J* = 5.0 Hz, 2H), 3.76 (s, 3H), 3.70 (q, *J* = 5.0 Hz, 2H).^{13}C NMR (151 MHz, DMSO-d_6) δ 155.1, 153.7, 150.8, 149.5, 136.5, 129.6, 125.3, 122.5, 115.8, 115.7, 115.5, 71.4, 60.0, 55.8. HRMS (ESI): calculated for $C_{14}H_{15}NO_3Na$ (M+Na)$^+$: 268.0950; found: 268.0961.

2-(3-methoxy-2-(pyridin-2-yl)phenoxy)ethan-1-ol (2g)

prepared following the general procedure using 2- (2-methoxyphenyl) pyridine(0.185 g,1.0 mmol) and ethylene glycol (2 mL) to afford **2g** as white solid (100 mg, 41 %). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.57 (ddd, *J* = 4.9, 1.9, 1.0 Hz, 1H), 7.77 (td, *J* = 7.7, 1.9 Hz, 1H), 7.34 – 7.30 (m, 2H), 7.28 (ddd, *J* = 7.6, 4.9, 1.2 Hz, 1H), 6.76 (ddd, *J* = 24.4, 8.4, 0.8 Hz, 2H), 5.00 (s, 1H), 3.98 (t, *J* = 5.2 Hz, 2H), 3.64 (s, 3H), 3.51 (t, *J* = 5.2 Hz, 2H).^{13}C NMR (151 MHz, DMSO-d_6) δ 157.9, 157.4, 154.4, 149.0, 136.2, 130.1, 126.,7 122.1, 119.8, 107.2, 104.9, 71.2, 59.9, 56.0. HRMS (ESI): calculated for $C_{14}H_{15}NO_3Na$ (M+Na)$^+$: 268.0950; found: 268.0948.

2-(5-fluoro-2-(pyridin-2-yl)phenoxy)ethan-1-ol (2h)

prepared following the general procedure using 2- (4-Fluorophenyl) pyridine（0.173 g,1.0 mmol） and ethylene glycol (2 mL) to afford **2h** as white solid (86 mg, 37 %). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.64 (ddd, *J* = 4.8, 1.8, 0.9 Hz, 1H), 8.02 (dt, *J* = 8.0, 1.1 Hz, 1H), 7.85 (dd, *J* = 8.7, 7.2 Hz, 1H), 7.80 (ddd, *J* = 8.1, 7.5, 1.9 Hz, 1H), 7.30 (ddd, *J* = 7.5, 4.8, 1.1 Hz, 1H), 7.07 (dd, *J* = 11.5, 2.5 Hz, 1H), 6.89 (td, *J* = 8.4, 2.5 Hz, 1H), 4.96 (t, *J* = 5.4 Hz, 1H), 4.13 (t, *J* = 4.8 Hz, 2H), 3.74 (q, *J* = 5.1 Hz, 2H).^{13}C NMR (151 MHz, DMSO-d_6) δ 164.3, 162.7, 157.9, 154.5, 149.5, 136.5, 132.5, 125.0, 122.3, 107.6, 101.4, 71.0, 59.8. HRMS (ESI): calculated for $C_{13}H_{12}FNO_2Na$ (M+Na)$^+$: 256.0750; found: 256.0729.

2-(5-chloro-2-(pyridin-2-yl)phenoxy)ethan-1-ol (2i)

prepared following the general procedure using 2- (4-chlorophenyl) pyridine(0.189 g,1.0 mmol) and ethylene glycol (2 mL) to afford **2i** as white solid (104 mg, 42 %). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.66-8.64 (m, 1H), 8.06-8.03 (m, 1H), 7.85-7.78 (m, 2H), 7.32 (ddt, *J* = 7.3, 4.8, 1.2 Hz, 1H), 7.25 (d, *J* = 1.9 Hz, 1H), 7.12 (ddd, *J* = 8.3, 2.1, 1.0 Hz, 1H), 4.95 (td, *J* = 5.6, 2.3 Hz, 1H), 4.15 (t, *J* = 4.8 Hz, 2H), 3.77-3.70 (m, 2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 156.5, 155.6, 149.5, 140.2, 136.0, 130.9, 125.9, 124.9, 121.8, 113.7, 99.5, 65.4, 57.9, 32.5, 21.5. HRMS (ESI): calculated for $C_{13}H_{12}ClNO_2Na$ (M+Na)$^+$: 272.0454; found: 272.0463.

2-(5-bromo-2-(pyridin-2-yl)phenoxy)ethan-1-ol (2j)

prepared following the general procedure using 2- (4-bromophenyl) pyridine (0.234 g,1.0 mmol) and ethylene glycol (2 mL) to afford **2j** as white solid (88 mg, 30 %). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.65 (ddd, *J* = 4.8, 1.8, 1.0 Hz, 1H), 8.05 (d, *J* = 7.9 Hz, 1H), 7.81 (td, *J* = 7.8, 1.9 Hz, 1H), 7.76 (d, *J* = 8.3 Hz, 1H), 7.37 (d, *J* = 1.9 Hz, 1H), 7.33 (ddt, *J* = 7.4, 4.8, 1.1 Hz, 1H), 7.26 (dd, *J* = 8.3, 1.9 Hz, 1H), 4.96 (tt, *J* = 5.3, 2.1 Hz, 1H), 4.15 (t, *J* = 4.8 Hz, 2H), 3.73 (q, *J* = 4.9 Hz, 2H).^{13}C NMR (151 MHz, DMSO-d_6) δ 157.4, 154.3, 149.6, 136.5, 132.7, 127.9, 125.2, 124.0, 123.0, 122.6, 116.6, 71.2, 59.8. HRMS (ESI): calculated for $C_{13}H_{12}BrNO_2Na$ (M+Na)$^+$: 315.9949; found: 315.9955.

2-(2-(pyridin-2-yl)-5-(trifluoromethyl)phenoxy)ethan-1-ol (2k)

prepared following the general procedure using 2- (4-trifluoromethylphenyl) pyridine（0.223g,1.0 mmol） and ethylene glycol (2 mL) to afford **2l** as white solid (88 mg, 31 %). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.71 (ddd, *J* = 4.8, 1.8, 0.9 Hz, 1H), 8.13 (dt, *J* = 8.0, 1.1 Hz, 1H), 8.04 – 8.00 (m, 1H), 7.86 (td, *J* = 7.8, 1.9 Hz, 1H), 7.48 (d, *J* = 1.7 Hz, 1H), 7.44 -7.36 (m, 2H), 5.04 (s, 1H), 4.24 (t, *J* = 4.8 Hz, 2H), 3.79 (t, *J* = 4.8 Hz, 2H).^{13}C NMR (151 MHz, DMSO-d_6) δ 156.9, 153.9, 149.7, 136.6, 132.5, 132.1, 130.7, 130.5, 125.6, 123.1, 117.6, 110.2, 71.2, 59.8. HRMS (ESI): calculated for $C_{13}H_{12}BrNO_2Na$ (M+Na)$^+$: 306.0718; found: 306.0709.

2-(2-(pyridin-2-yl)-5-vinylphenoxy)ethan-1-ol (2l)

prepared following the general procedure using 2- (4-vinylphenyl) pyridine (0.181g,1.0 mmol) and ethylene glycol (2 mL) to afford **2k** as white solid (87 mg, 36 %). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.65 (ddd, *J* = 4.8, 1.9, 1.0 Hz, 1H), 8.09 (dt, *J* = 8.0, 1.1 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.80 (td, *J* = 7.7, 1.9 Hz, 1H), 7.30 (ddd, *J* = 7.5, 4.8, 1.2 Hz, 1H), 7.25 (d, *J* = 1.6 Hz, 1H), 7.19 (dd, *J* = 8.0, 1.5 Hz, 1H), 6.78 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.95 (dd, *J* = 17.7, 0.9 Hz, 1H), 5.34 (dd, *J* = 10.8, 0.9 Hz, 1H), 5.00 (s, 1H), 4.17 (t, *J* = 4.9 Hz, 2H), 3.77 (t, *J* = 4.9 Hz, 2H).^{13}C NMR (151 MHz, DMSO-d_6) δ 156.9, 155.1, 149.5, 139.4, 136.7, 136.4, 131.3, 128.1, 125.23 122.3, 119.0, 115.6, 111.2, 70.7, 59.9. HRMS (ESI): calculated for $C_{13}H_{12}BrNO_2Na$ (M+Na)$^+$: 264.1000; found: 264.1010.

2-(5-(1,3-dioxolan-2-yl)-2-(pyridin-2-yl)phenoxy)ethan-1-ol (2m)

prepared following the general procedure using 2- (4-formylphenyl) pyridine(0.183g,1.0 mmol) and ethylene glycol (2 mL) to afford **2m** as white solid (109 mg, 38 %). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.67 – 8.66 (m, 1H), 8.07 (d, *J* = 8.0 Hz, 1H), 7.84-7.80 (m, 2H), 7.34-7.31 (m, 1H), 7.22-7.20 (m, 1H), 7.15 (dd, *J* = 7.9, 1.2 Hz, 1H), 5.79 (s, 1H), 5.00 (s, 1H), 4.14 (t, *J* = 4.9 Hz, 2H), 4.11-4.06 (m, 2H), 4.01-3.96 (m, 2H), 3.76 (t, *J* = 4.9 Hz, 2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 156.5, 155.0, 149.5, 140.5, 136.4, 131.1, 129.3, 125.3, 122.5, 119.2, 111.6, 102.9, 70.8, 65.2, 59.9. HRMS (ESI): calculated for $C_{16}H_{17}NO_4$ (M+Na)$^+$: 310.1055; found: 310.1057.

3-(2-(pyridin-2-yl)phenoxy)propan-1-ol (3a)

prepared following the general procedure using 2-phenylpyridine(0.155 g,1.0 mmol)and 1,3-Propanediol (2 mL) to afford **3a** as white solid (128 mg, 56 %). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.66 (d, *J* = 4.6 Hz, 1H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.81 (td, *J* = 7.8, 1.8 Hz, 1H), 7.76 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.39 (td, *J* = 8.5, 1.8 Hz, 1H), 7.31 (ddd, *J* = 7.4, 4.8, 1.0 Hz, 1H), 7.14 (s, 1H), 7.08 – 7.03 (m, 1H), 4.60 (d, *J* = 5.2 Hz, 1H), 4.13 (t, *J* = 6.2 Hz, 2H), 3.55 (t, *J* = 6.2 Hz, 2H), 1.87 (p, *J* = 6.2 Hz, 2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 156.5, 155.5, 149.6, 136.1, 131.1, 130.4, 128.7, 125.1, 122.3, 120.9, 113.0, 65.4, 57.8, 32.5. HRMS (ESI): calculated for $C_{14}H_{15}NO_2Na$ (M+Na)$^+$: 252.1000; found: 252.1003.

4-(2-(pyridin-2-yl)phenoxy)butan-1-ol (3b)

prepared following the general procedure using 2-phenylpyridine (0.155 g,1.0 mmol) and 1,4-Butanediol (2 mL) to afford **3b** as white solid (124 mg, 51 %). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.66 (d, *J* = 3.6 Hz, 1H), 7.90 (d, *J* = 7.9 Hz, 1H), 7.83 -7.74 (m, 2H), 7.41- 7.36 (m, 1H), 7.33-7.29 (m, 1H), 7.14 (d, *J* = 8.1 Hz, 1H), 7.08 -7.03 (m, 1H), 4.45 (t, *J* = 5.2 Hz, 1H), 4.06 (t, *J* = 6.5 Hz, 2H), 3.43 (q, *J* = 6.4 Hz, 2H), 1.76 (dt, *J* = 14.4, 6.6 Hz, 2H), 1.54 (dt, *J* = 13.7, 6.5 Hz, 2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 156.5, 155.5, 149.6, 136.1, 131.1, 130.4, 128.7, 125.1, 122.3, 120.9, 113.1, 68.4, 60.7, 29.4, 25.9. HRMS (ESI): calculated for $C_{15}H_{17}NO_2Na$ (M+Na)$^+$: 266.1157; found: 266.1159.

5-(2-(pyridin-2-yl)phenoxy)pentan-1-ol (3c)

prepared following the general procedure using 2-phenylpyridine (0.155 g,1.0 mmol) and 1,5-Petanediol (2 mL) to afford **3c** as white solid (118 mg, 46 %). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.65 (ddd, *J* = 4.8, 1.7, 0.9 Hz, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.80 (td, *J* = 7.7, 1.9 Hz, 1H), 7.76 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.38 (ddd, *J* = 8.4, 7.4, 1.8 Hz, 1H), 7.30 (ddd, *J* = 7.4, 4.8, 1.1 Hz, 1H), 7.13 (d, *J* = 8.2 Hz, 1H), 7.05 (td, *J* = 7.5, 0.9 Hz, 1H), 4.37 (t, *J* = 5.1 Hz, 1H), 4.04 (t, *J* = 6.4 Hz, 2H), 3.39 (q, *J* = 6.0 Hz, 2H), 1.75 -1.69 (m, 2H), 1.43 (dtd, *J* = 15.4, 8.7, 7.8, 3.4 Hz, 5H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 156.5, 155.5, 149.6, 136.0, 131.1, 130.4, 128.7, 125.2, 122.3, 120.9, 113.2, 32.5, 28.9, 22.5. HRMS (ESI): calculated for $C_{16}H_{20}NO_2$ (M+H)$^+$: 258.1494; found:258.1493.

6-(2-(pyridin-2-yl)phenoxy)hexan-1-ol (3d)

prepared following the general procedure using 2-phenylpyridine (0.155 g,1.0 mmol) and 1,6-Hexanediol (2 mL) to afford **3d** as white solid (114 mg, 42 %). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.67 -8.64 (m, 1H), 7.89-7.87 (m, 1H), 7.80 (td, *J* = 7.7, 1.9 Hz, 1H), 7.75 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.39 - 7.36 (m, 1H), 7.30 (ddd, *J* = 7.4, 4.8, 1.1 Hz, 1H), 7.13 (d, *J* = 7.8 Hz, 1H), 7.05 (td, *J* = 7.5, 1.0 Hz, 1H), 4.33 (t, *J* = 5.0 Hz, 1H), 4.04 (t, *J* = 6.4 Hz, 2H), 3.37 (p, *J* = 6.8, 6.4 Hz, 3H), 1.95 (d, *J* = 45.1 Hz, 2H), 1.70 (dt, *J* = 14.2, 6.5 Hz, 4H), 1.43 - 1.36 (m, 2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 156.5, 155.5, 149.6, 136.0, 131.1, 130.4, 128.8, 125.1, 122.3, 120.9, 113.2, 68.3, 60.9, 32.8, 29.1, 25.9, 25.5. HRMS (ESI): calculated for $C_{17}H_{21}NO_2Na$ (M+Na)$^+$: 294.1470; found:294.1472.

3-(5-methyl-2-(pyridin-2-yl)phenoxy)propan-1-ol(4a)

prepared following the general procedure using 2- (4-methyl phenyl)pyridine (0.169 g,1.0 mmol) and 1,3-Propanediol (2 mL) to afford **4a** as white solid (143 mg, 59%). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.63 (d, *J* = 4.3 Hz, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.78 (td, *J* = 7.7, 1.8 Hz, 1H), 7.67 (d, *J* = 7.8 Hz, 1H), 7.27 (ddd, *J* = 7.4, 4.8, 0.9 Hz, 1H), 6.97 (s, 1H), 6.86 (d, *J* = 7.7 Hz, 1H), 4.55 (t, *J* = 5.2 Hz, 1H), 4.11 (t, *J* = 6.2 Hz, 2H), 3.54 (q, *J* = 6.1 Hz, 2H), 2.35 (s, 3H), 1.86 (p, *J* = 6.2 Hz, 2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 161.4, 157.7, 155.3, 149.45, 136.1, 131.9, 124.5, 121.6, 121.3, 106.0, 99.6, 65.5, 57.8, 55.7, 32.4. HRMS (ESI): calculated for $C_{15}H_{17}NO_2Na$ (M+Na)$^+$: 266.1157; found: 266.1156.

4-(5-methyl-2-(pyridin-2-yl)phenoxy)butan-1-ol(4b)

prepared following the general procedure using 2- (4-methyl phenyl)pyridine (0.169 g,1.0 mmol) and 1,4-Butanediol (2 mL) to afford **4b** as white solid (143 mg, 56%). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.63 (d, *J* = 4.7 Hz, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.77 (td, *J* = 7.8, 1.7 Hz, 1H), 7.69 (d, *J* = 7.8 Hz, 1H), 7.27 (dd, *J* = 7.0, 5.2 Hz, 1H), 6.96 (s, 1H), 6.86 (d, *J* = 7.8 Hz, 1H), 4.45 (t, *J* = 5.1 Hz, 1H), 4.04 (t, *J* = 6.5 Hz, 2H), 3.43 (q, *J* = 6.3 Hz, 2H), 2.35 (s, 3H), 1.78 -1.73 (m, 2H), 1.57-1.51 (m, 2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 156.5, 155.6, 149.5, 140.2, 136.0, 130.9, 125.8, 124.9, 121.9, 121.6, 113.8, 68.3, 60.7, 29.5, 25.9, 21.5. HRMS (ESI): calculated for $C_{16}H_{20}NO_2$ (M+H)$^+$: 258.1494; found: 258.1489.

5-(5-methyl-2-(pyridin-2-yl)phenoxy)pentan-1-ol(4c)

prepared following the general procedure using 2- (4-methyl phenyl)pyridine (0.169 g,1.0 mmol) and 1,5-Petanediol (2 mL) to afford **4c** as white solid (135 mg, 50%). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.63 (d, *J* = 4.5 Hz, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.77 (t, *J* = 7.7 Hz, 1H), 7.69 (d, *J* = 7.8 Hz, 1H), 7.28-7.25 (m, 1H), 6.95 (s, 1H), 6.86 (d, *J* = 7.8 Hz, 1H), 4.39 (t, *J* = 5.0 Hz, 1H), 4.02 (t, *J* = 6.4 Hz, 2H), 3.40 (q, *J* = 5.7 Hz, 2H), 2.35 (s, 3H), 1.72 (p, *J* = 6.6 Hz, 2H), 1.45 (dq, *J* = 16.3, 6.9 Hz, 5H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 156.5, 155.5, 149.5, 140.2, 135.9, 130.9, 125.9, 124.9, 121.9, 121.6, 113.8, 68.3, 61.0, 32.5, 28.9, 22.5, 21.5. HRMS (ESI): calculated for $C_{17}H_{22}NO_2$(M+H)$^+$: 272.1651; found: 272.1650.

6-(5-methyl-2-(pyridin-2-yl)phenoxy)hexan-1-ol(4d)

prepared following the general procedure using 2- (4-methyl phenyl)pyridine (0.169 g,1.0 mmol) and 1,6-Hexanediol (2 mL) to afford **4d** as white solid (133 mg, 47%). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.62 (ddd, *J* = 4.8, 1.7, 0.8 Hz, 1H), 7.87 (d, *J* = 8.0 Hz, 1H), 7.77 (td, *J* = 7.7, 1.9 Hz, 1H), 7.67 (d, *J* = 7.8 Hz, 1H), 7.27 (ddd, *J* = 7.4, 4.8, 1.0 Hz, 1H), 6.98 - 6.84 (m, 2H), 4.34 (t, *J* = 5.2 Hz, 1H), 4.03 (t, *J* = 6.4 Hz, 2H), 2.50 (p, *J* = 1.7 Hz, 3H), 1.75-1.67 (m, 2H), 1.40 (tt, *J* = 14.1, 7.1 Hz, 4H), 1.34-1.28 (m, 2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 156.5, 155.5, 149.5, 140.2, 135.9, 130.9, 125.9, 124.9, 121.9, 121.6, 113.8, 68.2, 61.03, 32.4, 29.1, 25.9, 25.5, 21.5. HRMS (ESI): calculated for $C_{18}H_{24}NO_2$(M+H)$^+$: 286.1807; found: 286.1807.

3-(5-methoxy-2-(pyridin-2-yl)phenoxy)propan-1-ol (5a)

prepared following the general procedure using 2- (4-methoxyphenyl) pyridine (0.185 g, 1.0 mmol) and 1,3-Propanediol (2 mL) to afford **5a** as white solid (160 mg, 62 %). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.63 -8.60 (m, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.79-7.74 (m, 2H), 7.24 (ddd, *J* = 7.4, 4.8, 0.9 Hz, 1H), 6.68 (d, *J* = 2.3 Hz, 1H), 6.65 (dd, *J* = 8.6, 2.4 Hz, 1H), 4.59 (t, *J* = 5.2 Hz, 1H), 4.13 (t, *J* = 6.2 Hz, 2H), 3.82 (s, 3H), 3.56 (t, *J* = 6.2 Hz, 2H), 1.89 (q, *J* = 6.2 Hz, 2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ

161.4, 157.7, 155.4, 149.5, 136.1, 131.9, 124.5, 121.5, 105.9, 99.6, 67.6, 65.9, 57.8, 55.6, 32.4. HRMS (ESI): calculated for $C_{15}H_{17}NO_3Na$ $(M+Na)^+$: 282.1106; found: 282.1107.

4-(5-methoxy-2-(pyridin-2-yl)phenoxy)butan-1-ol (5b)

prepared following the general procedure using 2- (4-methoxyphenyl) pyridine (0.185 g,1.0 mmol) and 1,4-Butanediol (2 mL) to afford **5b** as white solid (143 mg, 57%). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.63-8.60 (m, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.79 -7.74 (m, 2H), 7.23 (dd, *J* = 7.0, 5.2 Hz, 1H), 6.67-6.63 (m, 2H), 4.38 (t, *J* = 5.0 Hz, 1H), 4.06 (t, *J* = 6.5 Hz, 2H), 3.81 (s, 3H), 1.77 (p, *J* = 6.6 Hz, 2H), 1.55 (dt, *J* = 13.6, 6.5 Hz, 2H), 1.45- 1.43 (m, 2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 161.4, 157.7, 155.3, 149.5, 136.1, 131.9, 124.5, 105.9, 99.7, 68.4, 60.9, 55.7, 29.5, 25.8.HRMS (ESI): calculated for $C_{16}H_{19}NO_3Na$ $(M+Na)^+$: 274.1443; found: 274.1444.

5-(5-methoxy-2-(pyridin-2-yl)phenoxy)pentan-1-ol (5c)

prepared following the general procedure using 2- (4-methoxyphenyl) pyridine (0.185 g,1.0 mmol) and1,5-Petanediol (2 mL) to afford **5c** as white solid (146 mg, 51%). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.60 (d, *J* = 4.7 Hz, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.78 - 7.74 (m, 2H), 7.24 (dd, *J* = 7.1, 5.1 Hz, 1H), 6.67-6.63 (m, 2H), 4.36 (s, 1H), 4.05 (t, *J* = 6.4 Hz, 2H), 3.81 (s, 3H), 3.41-3.36 (m, 2H), 1.73 (p, *J* = 6.6 Hz, 2H), 1.44 (tt, *J* = 12.7, 5.6 Hz, 4H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 161.4, 157.8, 155.3, 149.4, 136.1, 131.9, 124.6, 121.5, 105.9, 99.7, 68.4, 60.9, 55.7, 32.5, 28.9, 22.6. HRMS (ESI): calculated for $C_{17}H_{22}NO_3$ $(M+H)^+$: 288.1600; found: 288.1599.

6-(5-methoxy-2-(pyridin-2-yl)phenoxy)hexan-1-ol (5d)

prepared following the general procedure using 2- (4-methoxyphenyl) pyridine (0.185 g,1.0 mmol) and1,6-Hexanediol (2 mL) to afford **5d** as white solid (147 mg, 49%). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.628.60 (m, 1H), 7.87 (d, *J* = 8.0 Hz, 1H), 7.78-7.74 (m, 2H), 7.23 (ddd, *J* = 7.4, 4.8, 1.0 Hz, 1H), 6.66-6.63 (m, 2H), 4.34 (t, *J* = 5.2 Hz, 1H), 4.04 (t, *J* = 6.4 Hz, 2H), 3.81 (s, 3H), 3.38 (q, *J* = 6.4 Hz, 2H), 1.75-1.69 (m, 2H), 1.41 (dt, *J* = 9.5, 5.4 Hz, 4H), 1.33 (td, *J* = 8.6, 8.0, 3.9 Hz, 2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 161.4, 157.8, 155.3, 149.5, 135.97, 131.9, 124.5, 121.6, 121.4, 105.9, 99.7, 68.4, 60.9, 55.7, 32.8, 29.0, 25.9, 25.5.HRMS (ESI): calculated for $C_{18}H_{24}NO_3$ $(M+H)^+$: 302.1756; found: 302.1755.

One-pot synthesis of 2-(pyridin-2-yl)phenol (6)

To a solution of 2-phenylpyridines (1.0 mmol) in ethylene glycol (2 mL), was added $CuSO_4{\cdot}5H_2O$ (40 mol%) at 120 °C. After stirring for 24 h, the resulting mixture was cooled at room temperature. Then the mixture was extracted with CH_2Cl_2 and water. The organic layer was dried over anhydrous $MgSO_4$, and evaporated under reduced pressure to afford crude product. Then potassium hydroxide (84 mg, 1.5 mmol) and DMSO (2 mL) were added. The resulting mixture was stirred at 100 °C for 3 h. The reaction mixture was then acidified to pH= 3 with 1N HCl solution. The aqueous phase was extracted twice with CH_2Cl_2 and the combined organic layers were washed with H_2O and brine, and dried over $MgSO_4$ and concentrated in vacuum. Purification of the crude product by column chromatography afforded 2-(pyridin-2-yl)phenol[13] (**6**) as white solid (102 mg, 60 %).^{1}H NMR (600 MHz, DMSO-d_6) δ 14.15 (s, 1H), 8.64 (d, *J* = 4.9 Hz, 1H), 8.23 (d, *J* = 8.3 Hz, 1H), 8.05 - 8.02 (m, 2H), 7.46 - 7.43 (m, 1H), 7.34 - 7.30 (m, 1H), 6.93 (dd, *J* = 7.6, 5.4 Hz, 2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 159.5, 157.2, 146.6, 138.9, 131.8, 127.3, 122.7, 120.2, 119.2, 119.2, 118.3.

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Keywords: Aroxyl ethanols • Copper • Aliphatic Diol • 2-phenyl pyridine • C-H alkoxylation

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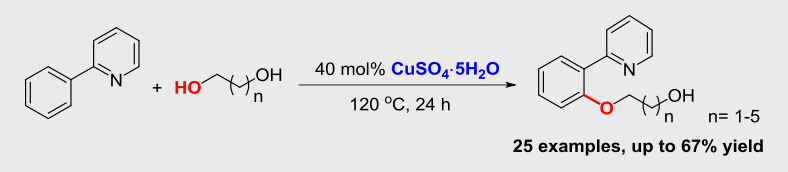

A very simple, economical and *regio*-selective method for the synthesis of aroxyl aliphatic alcohols was developed. 2-Phenyl pyridines and aliphatic diols coupled in the air in the presence of copper(II) salt. Neither additional solvent nor extra oxidant was required for this C-H alkoxylation reaction.

C-H Alkoxylation*

Yan Xiao, Juan Li, Yajun Liu, Shuo Wang, Hui Zhang, and Huaiwei Ding**

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Copper(II) Catalyzed C-H Alkoxylation of 2-Phenyl Pyridines with Aliphatic Diols