

## Supporting Information

### **A Directing Group Free Pd(II)-Catalysed Desulfitative C6-Arylation of 2-Pyridone using Arylsulfonyl Chloride**

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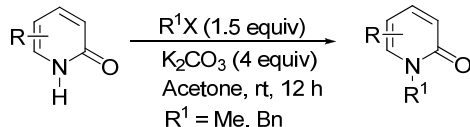
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**General:**

All commercially available compounds were used without further purification. Solvents for elution in column were distilled. Analytical thin layer chromatography (TLC) was performed on pre-coated silica gel 60 F<sub>254</sub>. Visualization on TLC was achieved by the use of UV light (254 nm). Column chromatography was undertaken on silica gel (230-400 mesh). <sup>1</sup>H NMR spectra were recorded on BRUKER ULTRA SHIELD machine (400 MHz, 500 MHz and 600 MHz). <sup>13</sup>C NMR spectra were recorded on BRUKER machine (150, 125 and 100 MHz) and was fully decoupled by broad band proton decoupling. Chemical shifts were quoted in parts per million (ppm) referenced to the appropriate solvent peak or 0.0 ppm for tetramethylsilane. The following abbreviations were used to describe peak splitting patterns when appropriate: s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublet, dt = doublet of triplet, m = multiplet. Coupling constants, *J*, were reported in hertz unit (Hz). Chemical shifts were reported in ppm referenced to the centre of a triplet at 77.16 ppm of CDCl<sub>3</sub>. <sup>19</sup>F NMR spectra was recorded on BRUKER machine (471 MHz). Fourier Transform Infrared Spectroscopy (FT-IR) was obtained with a Bruker Alpha ATR spectrometer and selected absorbance peaks are reported in terms of frequency of absorption (cm<sup>-1</sup>). Gas Chromatography Mass Spectrometry (GCMS) was done in Thermofisher ISQ single quadrupole mass spectrometer (TRACE 1300 series gas chromatograph) by using FID module. High resolution mass spectra (HRMS) were obtained from Agilent 6545XT AdvanceBio LC/Q-TOF by using TOF MS ESI+ method. Materials were obtained from commercial suppliers or prepared according to standard procedures unless otherwise noted.

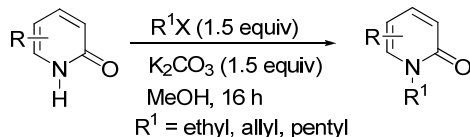
## 1. General procedure for the synthesis of *N*-alkylated 2-pyridones (1a-1c, 1e, 1h-1k):<sup>1</sup>

### (a) Procedure 1:



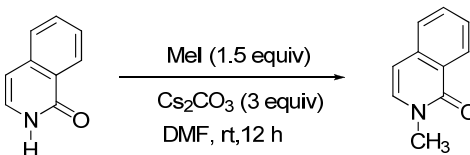
Substituted 2-hydroxy pyridines (5 mmol) were taken in 50 mL dry acetone in a round bottom flask. Then, anhydrous potassium carbonate (20 mmol) and corresponding alkyl halides (7.5 mmol) were added to it step by step. The reaction mixture was allowed to stir at the room temperature for 12 h. After full consumption of the starting materials (as monitored by TLC), acetone was evaporated in vacuum and the residue was partitioned between ethyl acetate and water. The organic layer was extracted, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated under the reduced pressure. The crude product was purified by silica gel column chromatography to obtain the pure *N*-alkylated 2-pyridone products. The analytical data of the compounds were well matched with reported literature values.<sup>1a</sup>

### (b) Procedure 2:



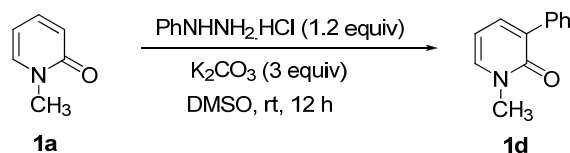
Substituted 2-hydroxypyridine (5 mmol) was taken in 15 mL dry MeOH. To this suspension anhydrous K<sub>2</sub>CO<sub>3</sub> (7.5 mmol) and alkyl halide (7.5 mmol) was added. The resulting reaction mixture was placed in a pre-heated oil bath and refluxed for 16 h. Upon completion of the reaction, the solvent was evaporated. Next, the water and the crude reaction mixture were partitioned between ethyl acetate and water. The organic layer was extracted, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated under the reduced pressure. The crude product was purified by silica gel column chromatography to obtain the pure *N*-alkylated 2-pyridone product. The analytical data of the compounds were well matched with reported literature values.<sup>1b,4a</sup>

## 2. General procedure for the synthesis of *N*-methyl isoquinolone (1g):<sup>2</sup>



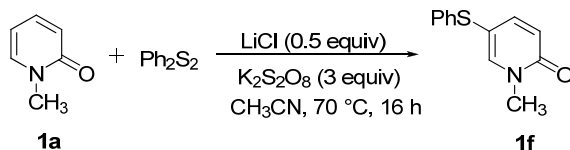
Isoquinolone (5 mmol) was taken in 5 mL dry DMF in a 25 mL round bottom flask. Then, cesium carbonate (7.5 mmol) followed by methyl iodide (7.5 mmol) were added. The reaction mixture was stirred at the room temperature for 12 h. After completion of the reaction (as monitored by TLC), water was added to quench the reaction. The crude reaction mixture was partitioned between ethyl acetate and water. The organic layer was extracted, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated under the reduced pressure. The crude product was loaded to silica gel column chromatography to obtain the pure product. The analytical data of the prepared compounds were matched with reported literature values.<sup>2</sup>

### 3. Procedure for the synthesis of 1-methyl-3-phenylpyridin-2(1H)-one (**1d**):<sup>3</sup>



In a 25 mL round bottom flask equipped with a magnetic stirring bar, **1a** (2 mmol, 1 equiv) was dissolved in 7 mL dry DMSO solvent. Then, K<sub>2</sub>CO<sub>3</sub> (0.3 mmol, 3 equiv) and phenyl hydrazine hydrochloride (0.12 mmol, 1.2 equiv) were added to the reaction mixture. The reaction mixture was allowed to stir at the room temperature for 12 h. After completion of the reaction, saturated NaHCO<sub>3</sub> (20 mL) was added, and the reaction mixture was extracted with ethyl acetate (50 mL). The combined organic layer was washed with saturated sodium chloride solution and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated under the reduced pressure. The crude product was purified by silica gel column chromatography to afford the pure product (**1d**) with 48% isolated yield. The analytical data of the prepared compound was well matched with reported literature data.<sup>3</sup>

### 4. Procedure for the synthesis of 1-methyl-5-(phenylthio)pyridin-2(1H)-one (**1f**):<sup>4</sup>

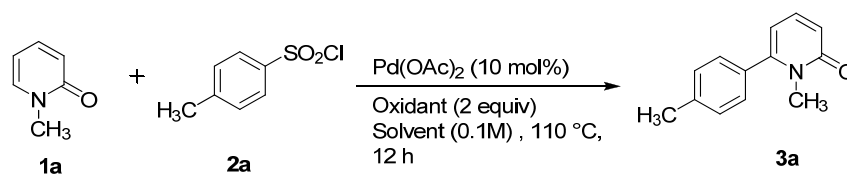


In a 25 mL round bottom flask equipped with a magnetic stirring bar, **1a** (2 mmol, 1 equiv) was dissolved in 8 mL dry acetonitrile. Diphenyl disulfide (3 mmol, 1.5 equiv), lithium chloride (1 mmol, 0.5 equiv) and potassium persulfate (6.0 mmol, 3.0 equiv) were added to this reaction mixture at the room temperature. The round bottom flask was placed in a pre-heated oil bath and stirred at the 70 °C for 16 h. After completion of the reaction as monitored by TLC, saturated NaHCO<sub>3</sub> (20 mL) solution was added and the reaction mixture was extracted with ethyl acetate

(50 mL). The combined organic layers were washed with saturated sodium chloride solution, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated under the reduced pressure. The crude product was purified by silica gel column chromatography to afford the pure C5-thiolated 2-pyridone product (**1f**) with 75% isolated yield. The analytical data of the prepared compound was well matched with reported literature data.<sup>4</sup>

## 5. Optimization:

### i. Optimization table for C6-arylation of 1-methylpyridin-2(1H)-one:



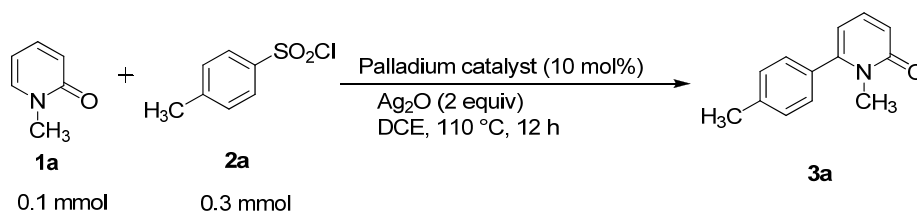
Entries	Solvent	Oxidant (2 equiv)	Additive (mol%)	Yield (%) <sup>b</sup>
1	DCE	-	-	n.d.
2	DCE	Ag <sub>2</sub> O	-	27
3	DCE	Ag <sub>2</sub> O	-	19 <sup>c</sup>
4	DCE	Ag <sub>2</sub> O	-	12 <sup>d</sup>
5	DCE	Ag <sub>2</sub> O	-	11 <sup>e</sup>
6	DCE	Ag <sub>2</sub> O	-	20 <sup>f</sup>
7	toluene	Ag <sub>2</sub> O	-	n.d.
8	dioxane	Ag <sub>2</sub> O	-	12
9	TFE	Ag <sub>2</sub> O	-	n.d.
10	CH <sub>3</sub> CN	Ag <sub>2</sub> O	-	trace
11	DMF	Ag <sub>2</sub> O	-	n.d.
12	Ethanol	Ag <sub>2</sub> O	-	n.d.
13	PhCF <sub>3</sub>	Ag <sub>2</sub> O	-	n.d.
14	DMSO	Ag <sub>2</sub> O	-	n.d.
15	<sup>t</sup> AmOH	Ag <sub>2</sub> O	-	n.d.
16	DCE	K <sub>2</sub> S <sub>2</sub> O <sub>8</sub>	-	trace
17	DCE	AgOAc	-	14
18	DCE	Ag <sub>2</sub> CO <sub>3</sub>	-	trace
19	DCE	Cu(OAc) <sub>2</sub>	-	n.d.
20	DCE	CuI	-	n.d.
21	DCE	-	Li <sub>2</sub> CO <sub>3</sub> (200)	10 <sup>g</sup>

22	DCE	Ag <sub>2</sub> O	Li <sub>2</sub> CO <sub>3</sub> (100)	34
23	DCE	Ag <sub>2</sub> O	NaOAc (100)	30
24	DCE	Ag <sub>2</sub> O	AcOH (50)	n.d.
<b>25</b>	<b>DCE</b>	<b>Ag<sub>2</sub>O</b>	<b>PivOH (50)</b>	<b>52</b>
26	DCE	Ag <sub>2</sub> O	TFA (50)	n.d.
27	DCE	Ag <sub>2</sub> O	BzOH (50)	34
28	DCE	Ag <sub>2</sub> O	4-OMeBzOH (50)	50
29	DCE	Ag <sub>2</sub> O	4-MeBzOH (50)	36
30	DCE	Ag <sub>2</sub> O	2,6-OMeBzOH (50)	30
31	DCE	Ag <sub>2</sub> O	mesitoic acid (50)	22
32	DCE	Ag <sub>2</sub> O	4-NO <sub>2</sub> BzOH (50)	n.d.
33	DCE	Ag <sub>2</sub> O	PivOH (20)	37
34	DCE	Ag <sub>2</sub> O	PivOH (100)	46

<sup>a</sup>Reaction conditions: **1a** (0.1 mmol), **2a** (0.3 mmol), Pd(OAc)<sub>2</sub> (10 mol%), Ag<sub>2</sub>O (0.2 mmol), DCE (0.1 M), 110 °C,

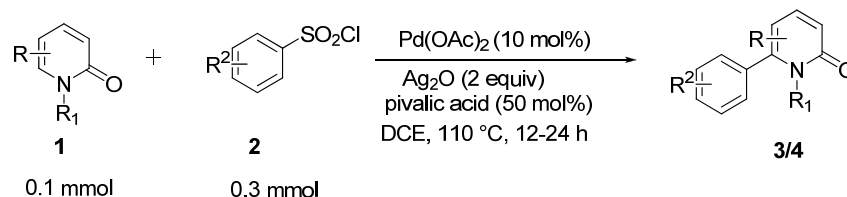
<sup>b</sup>Isolated yield, <sup>c</sup>1.5 equiv Ag<sub>2</sub>O was used, <sup>d</sup>1.1 equiv Ag<sub>2</sub>O was used, <sup>e</sup>1.0 equiv Ag<sub>2</sub>O was used, <sup>f</sup>0.2 mmol **2a** was used, <sup>g</sup>24 h, n.d. = not detected. TFE = trifluoroethanol, <sup>t</sup>AmOH = *tert*-Amyl alcohol.

## ii. Optimization table with various palladium catalysts:



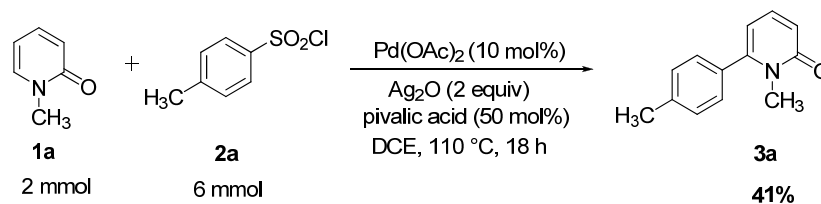
Entry	Pd catalyst (10 mol%)	Yield (%) <sup>b</sup>
1	Pd(OAc) <sub>2</sub>	27
2	PdCl <sub>2</sub>	22
3	PdCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub>	15
4	Pd(TFA) <sub>2</sub>	n.d.
5	Pd(PPh <sub>3</sub> ) <sub>4</sub>	trace

## 6. General procedure for the Pd(OAc)<sub>2</sub>-catalyzed C6-arylation reaction of 2-pyridones:



2-Pyridone derivatives **1** (0.1 mmol) were dissolved in 1 mL dry DCE in 10 mL screw cap vials. Then Pd(OAc)<sub>2</sub> (10 mol%, 2.24 mg), Ag<sub>2</sub>O (2 equiv, 46 mg), pivalic acid (50 mol%, 5.1 mg) and arylsulfonyl chloride (**2**, 0.3 mmol, 3 equiv) were added to the reaction mixture step by step at the room temperature. Next, the reaction mixture was allowed to stir at the 110 °C for 12-24 h. After completion of the reaction, the solvent was evaporated and the crude reaction mixture was partitioned between ethyl acetate and water. Saturated sodium bicarbonate solution was added. The organic layer was separated and dried over anhydrous sodium sulfate and concentrated under the reduced pressure. The crude product was purified by silica gel column chromatography to obtain the pure product with hexane/EtOAc as eluent (60-80% EA/PE).

## 7. Scale up synthesis:



In a 50 mL round bottom flask equipped with a magnetic stirring bar, **1a** (2 mmol, 218 mg) was dissolved in 8 mL dry DCE. Then, Pd(OAc)<sub>2</sub> (10 mol%, 45 mg) followed by Ag<sub>2</sub>O (2 equiv, 924 mg), pivalic acid (50 mol%, 102 mg) and tosyl chloride (**2a**, 3 equiv, 1.14g) were added step by step at the room temperature. Then, the reaction mixture was stirred at the 110 °C in a pre-heated oil bath for 18 h. The reaction mixture was cooled down and the solvent was evaporated. The crude mixture was partitioned between ethyl acetate and water. Saturated sodium bicarbonate solution was added. The organic layer was extracted and dried over anhydrous sodium sulfate and concentrated under reduced pressure. The crude mixture was loaded to silica gel column chromatography using EtOAc/hexane to obtain pure product **3a** in 41% isolated yield (163 mg) as colourless oil.



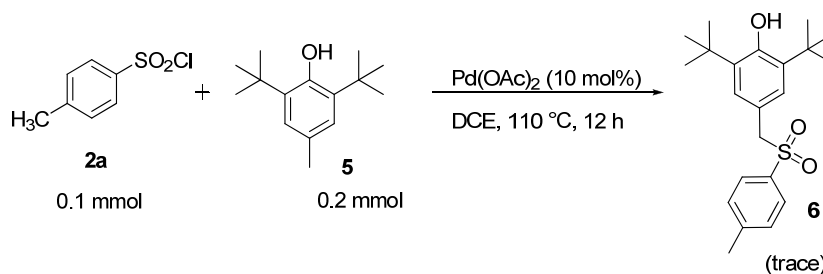
## 8. Control Experiments:

### (a) Radical trapping experiment in the presence of *t*-butylated hydroxytoluene (BHT):



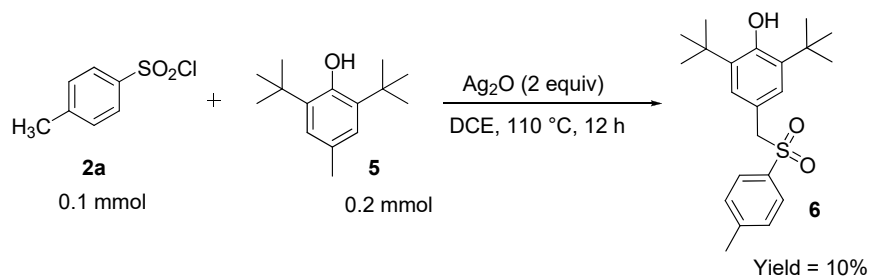
To an oven-dried screw cap vial, **1a** (0.1 mmol, 1 equiv) was dissolved in dry DCE (1 mL). Pd(OAc)<sub>2</sub> (10 mol%) followed by Ag<sub>2</sub>O (2 equiv, 46 mg), pivalic acid (50 mol%, 5.1 mg), *para*-toluenesulfonyl chloride (**2a**, 3 equiv, 57 mg) and BHT (2 equiv, 44 mg) were added step by step to the reaction mixture at the room temperature. After that, the reaction mixture was stirred at the 110 °C for 12 h. After completion of the reaction, the solvent was evaporated and the crude reaction mixture was partitioned between EtOAc and water. The organic layer was extracted and dried over anhydrous sodium sulfate and concentrated under the reduced pressure. The crude mixture was loaded to the column chromatography to purify the product. Trace amount of desired C6-arylated product (**3a**) was obtained with the sulfonated-BHT adduct (**6**) in 77% yield.

### (b) Radical trapping experiment in the presence of catalytic amount of Pd(OAc)<sub>2</sub> (10 mol%):



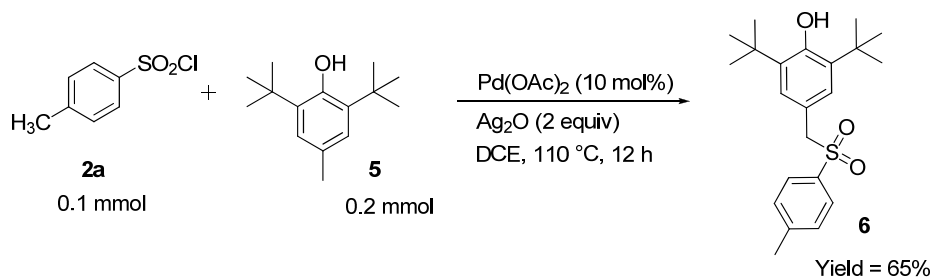
To an oven-dried 10 mL screw cap vial, **2a** (0.1 mmol) was dissolved in dry DCE (1 mL). Then *t*-butylated hydroxytoluene (BHT) (0.2 mmol, 2 equiv) and Pd(OAc)<sub>2</sub> (10 mol%) were added step by step to this reaction mixture at the room temperature. The reaction mixture was stirred at 110 °C for 12 h. After that, the reaction mixture was removed out and it was found that trace amount of **6** was formed and most of the starting material was recovered.

**(c) Radical trapping experiment in the presence of stoichiometric amount of Ag<sub>2</sub>O (2 equiv):**



**2a** (0.1 mmol) was dissolved in dry DCE (1 mL) in a 10 mL screw cap vial. Then, *t*-butylated hydroxytoluene (BHT) (0.2 mmol, 2 equiv) and Ag<sub>2</sub>O (0.2 mmol, 2 equiv) were added to this reaction mixture at the room temperature. The reaction mixture was stirred at the 110 °C for 12 h. After that, the reaction mixture was removed out and the solvent was evaporated under the reduced pressure. The crude reaction mixture was partitioned between ethyl acetate and water. The organic layer was separated and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated under the reduced pressure. The crude mixture was loaded to a column chromatography to obtain the pure product **6** in 10% isolated yield.

**(d) Radical trapping experiment in the presence of both catalytic amount of Pd(OAc)<sub>2</sub> (10 mol%) and stoichiometric amount of Ag<sub>2</sub>O (2 equiv):**



To an oven-dried 10 mL screw cap vial, **2a** (0.1 mmol) was dissolved in dry DCE (1 mL). Then *t*-butylated hydroxytoluene (BHT) (0.2 mmol, 2 equiv) followed by Pd(OAc)<sub>2</sub> (10 mol%) and Ag<sub>2</sub>O (0.2 mmol, 2 equiv) were added to this reaction mixture at the room temperature. It was allowed to stir at the 110 °C for 12 h. Next, the reaction mixture was removed out and the solvent was evaporated under the reduced pressure. The crude reaction mixture was partitioned between ethyl acetate and water. The organic layer was separated and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated under the reduced pressure. The crude mixture was loaded to silica gel column chromatography to obtain the pure product **6** in 65% isolated yield.

## 9. GCMS of the reaction mixture:

The GCMS data of the crude reaction mixture was taken after 2.5 h to identify the intermediate components formed during the course of the reaction. Some of the components were identified. The GCMS spectra with the components were given below,

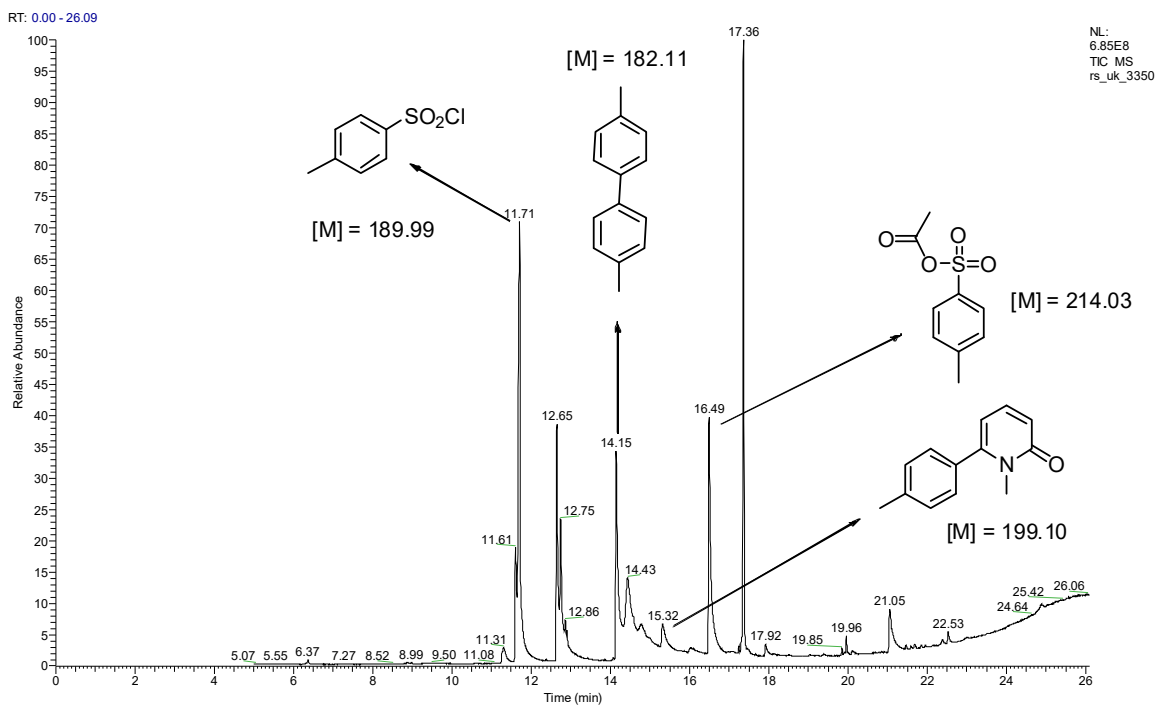
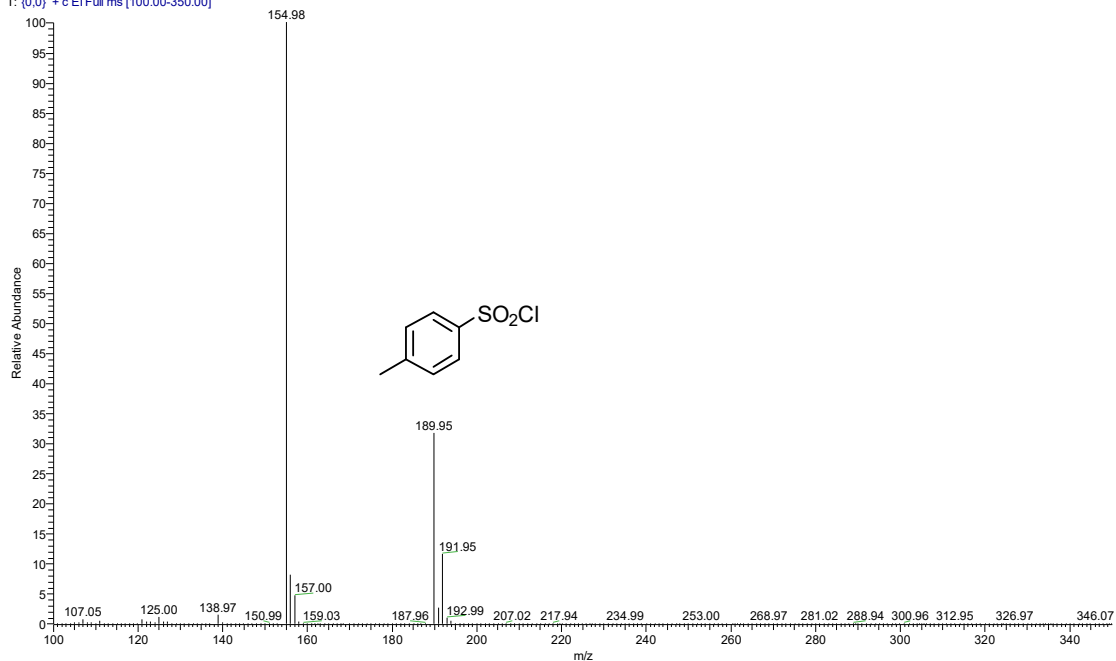
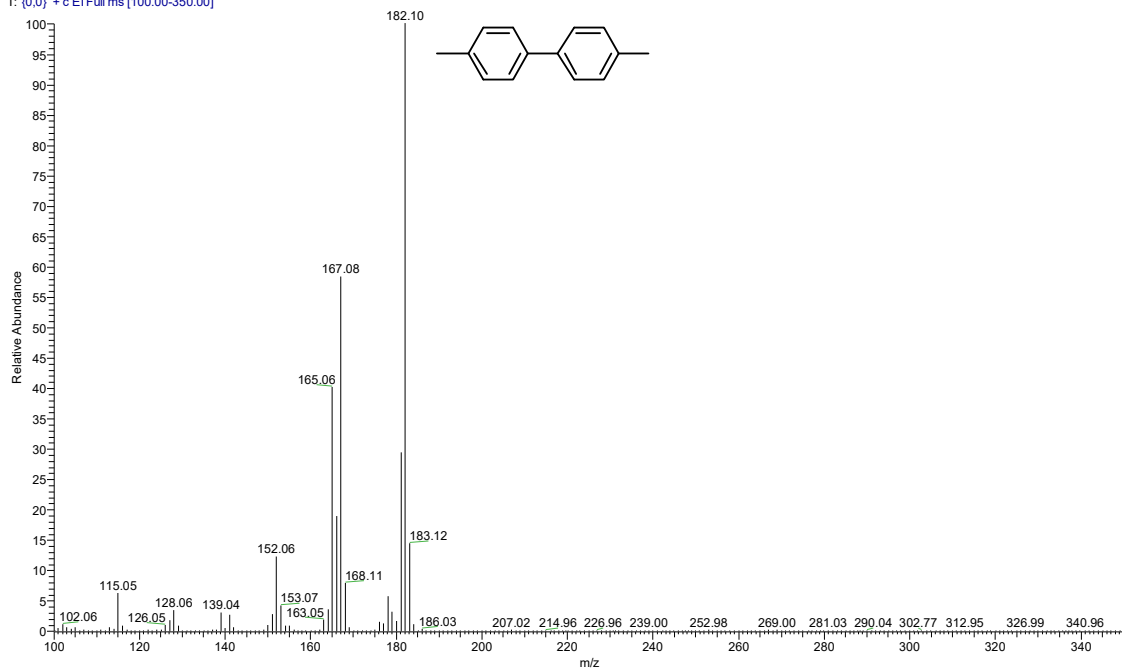


Figure 1: GCMS of the reaction mixture after 2.5 h

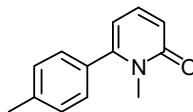
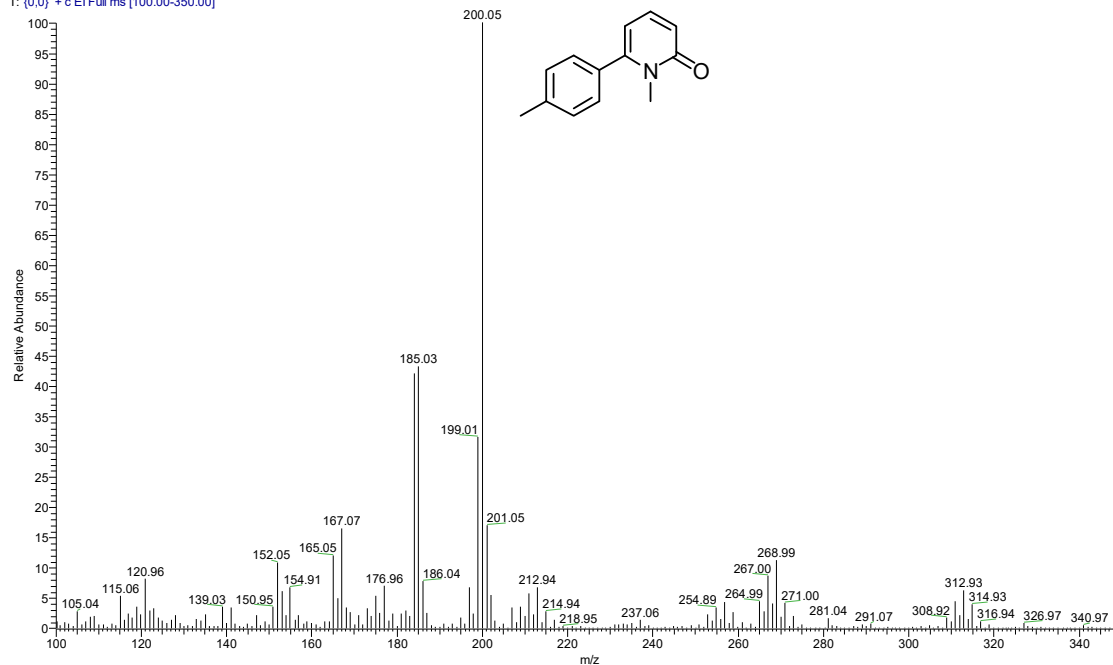
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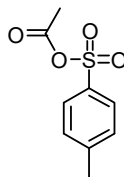
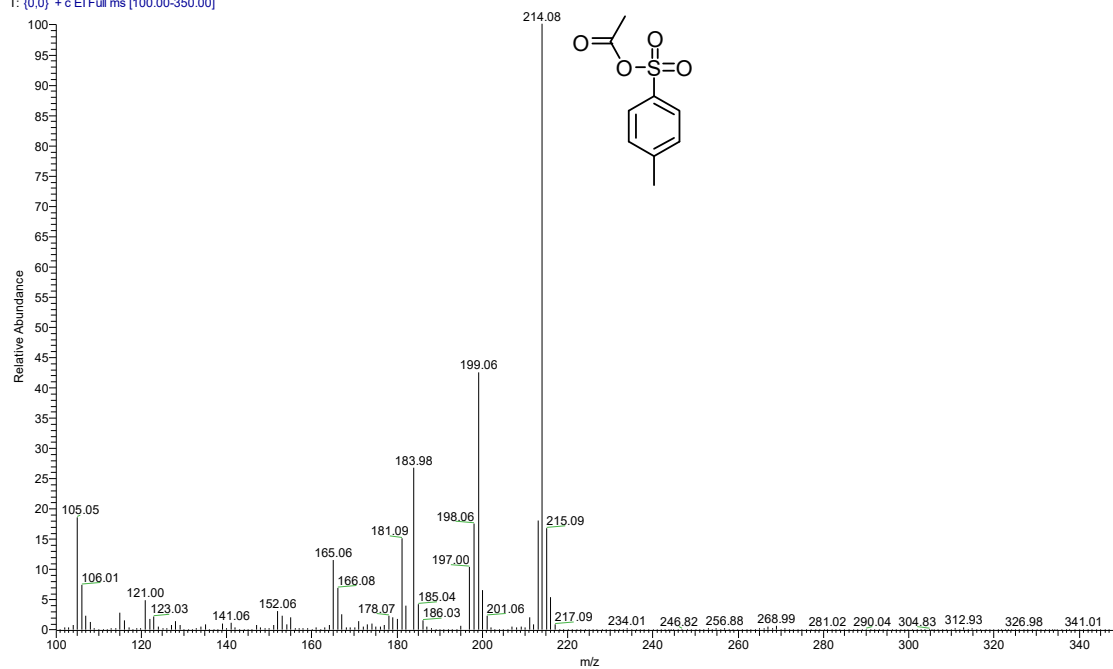
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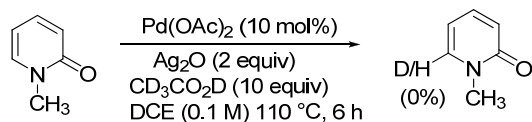
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## 10. Study of deuterium incorporation in the absence of tosyl chloride (2a):



To an oven-dried 10 mL screw cap vial equipped with a magnetic stirring bar, **1a** (0.1 mmol, 1 equiv) was taken in 1 mL dry DCE. Then, Pd(OAc)<sub>2</sub> (10 mol%, 2.24 mg) followed by Ag<sub>2</sub>O (2 equiv, 46 mg), CD<sub>3</sub>CO<sub>2</sub>D (10 equiv, 0.058 mL) were added to the reaction mixture in step by step. The reaction mixture was stirred at the 110 °C for 6 h. The solvent was evaporated under the reduced pressure and the crude reaction mixture was partitioned between ethyl acetate and water. The organic layer was extracted and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated under the reduced pressure. The crude mixture was loaded to the column chromatography to obtain the pure product using EtOAc/hexane. The pure product was subjected to <sup>1</sup>H NMR analysis (400 MHz, DMSO-d<sub>6</sub>). The analysis showed that no deuterium incorporation was observed at the C6-position. The result indicated that presumably, the palladation was irreversible in the absence of coupling partner tosyl chloride.

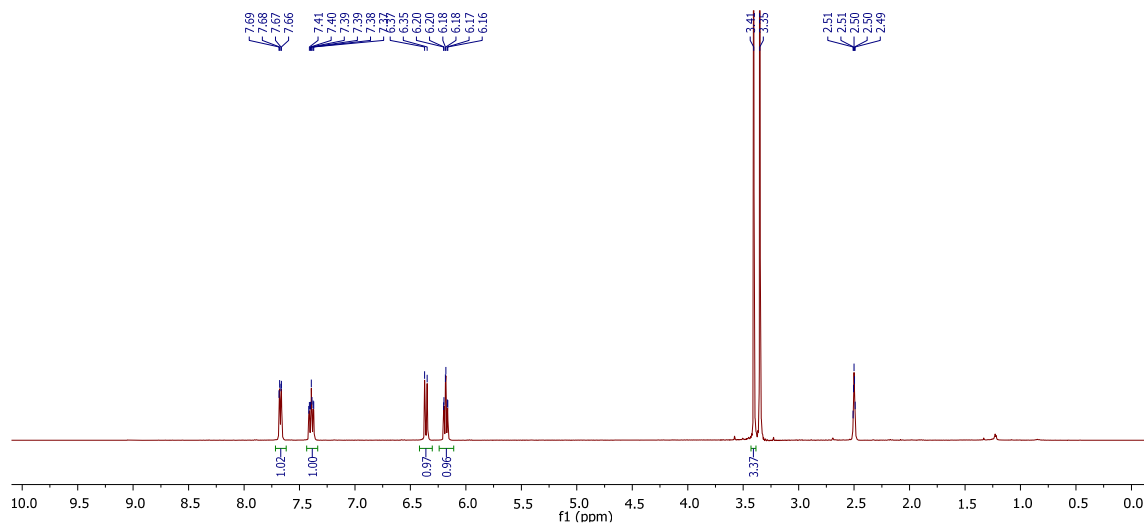
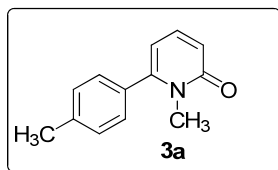
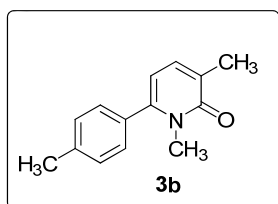


Figure 2: H/D scrambling experiment in the absence of tosyl chloride (400 MHz, DMSO-d<sub>6</sub>)

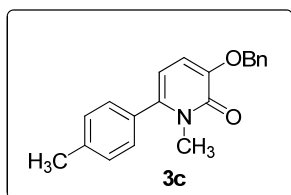
## 11. Analytical data:



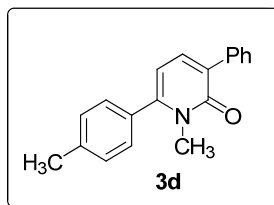
**1-Methyl-6-*p*-tolylpyridin-2(1H)-one (3a):** Colourless oil, yield: 52%,  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.33 (dd,  $J = 9.1, 6.9$  Hz, 1H), 7.27 (d,  $J = 7.4$  Hz, 2H), 7.22 (d,  $J = 8.0$  Hz, 2H), 6.59 (d,  $J = 9.1$  Hz, 1H), 6.09 (d,  $J = 6.9$  Hz, 1H), 3.38 (s, 3H), 2.42 (s, 3H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  164.1, 150.4, 139.5, 138.8, 132.9, 129.5, 128.4, 118.8, 108.0, 34.5, 21.4; FT-IR:  $\tilde{\nu} = 2923, 2854, 1650, 1579, 1550, 1508, 1432, 1378, 1259, 1158, 1063$   $\text{cm}^{-1}$ ; HRMS (ESI): calcd for  $\text{C}_{13}\text{H}_{14}\text{NO}$   $[\text{M}+\text{H}]^+$ : 200.1070, found 200.1075.



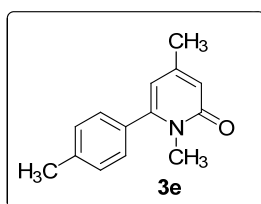
**1,3-Dimethyl-6-*p*-tolylpyridin-2(1H)-one (3b):** Yellow oil, yield: 56%,  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.28 – 7.15 (m, 5H), 6.02 (d,  $J = 6.9$  Hz, 1H), 3.40 (s, 3H), 2.41 (s, 3H), 2.20 (s, 3H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  164.2, 147.7, 139.2, 136.1, 133.2, 129.5, 128.6, 127.7, 107.5, 34.7, 21.4, 17.5; FT-IR:  $\tilde{\nu} = 2924, 2854, 1657, 1581, 1553, 1510, 1436, 1378, 1290, 1158, 1062$   $\text{cm}^{-1}$ ; HRMS (ESI): calcd for  $\text{C}_{14}\text{H}_{16}\text{NO}$   $[\text{M}+\text{H}]^+$ : 214.1226, found 214.1224.



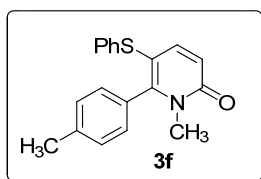
**3-(Benzyloxy)-1-methyl-6-*p*-tolylpyridin-2(1H)-one (3c):** Yellow oil, yield: 55%,  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.46 (d,  $J = 7.4$  Hz, 2H), 7.37 (t,  $J = 7.4$  Hz, 2H), 7.30 (m, 1H), 7.23 (d,  $J = 7.9$  Hz, 2H), 7.18 (d,  $J = 8.1$  Hz, 2H), 6.68 (d,  $J = 7.6$  Hz, 1H), 5.94 (d,  $J = 7.6$  Hz, 1H), 5.18 (s, 2H), 3.42 (s, 3H), 2.40 (s, 3H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  159.3, 147.5, 141.8, 139.1, 136.8, 133.0, 129.4, 128.9, 128.7, 128.1, 127.5, 115.7, 106.2, 70.9, 34.9, 21.4; FT-IR:  $\tilde{\nu} = 2923, 2853, 1651, 1581, 1553, 1510, 1432, 1378, 1290, 1158, 1062$   $\text{cm}^{-1}$ ; HRMS (ESI): calcd for  $\text{C}_{20}\text{H}_{20}\text{NO}_2$   $[\text{M}+\text{H}]^+$ : 306.1489, found 306.1508.



**1-Methyl-3-phenyl-6-*p*-tolylpyridin-2(1*H*)-one (3d):** Colourless oil, yield: 47%,  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.71 (d,  $J = 7.4$  Hz, 2H), 7.55 (d,  $J = 7.2$  Hz, 1H), 7.41 (t,  $J = 7.5$  Hz, 2H), 7.37 – 7.28 (m, 5H), 6.28 (d,  $J = 7.2$  Hz, 1H), 3.50 (s, 3H), 2.44 (s, 3H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  162.7, 149.7, 139.7, 137.3, 137.1, 132.9, 129.7, 129.6, 128.9, 128.6, 128.3, 127.8, 108.6, 35.4, 21.5; FT-IR:  $\tilde{\nu} = 2928, 2858, 1634, 1579, 1515, 1450, 1349, 1220, 1127$   $\text{cm}^{-1}$ ; HRMS (ESI): calcd for  $\text{C}_{19}\text{H}_{18}\text{NO}$   $[\text{M}+\text{H}]^+$ : 276.1383, found 276.1396.

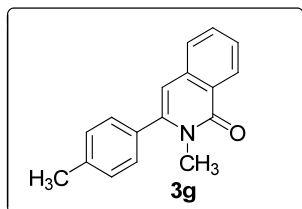


**1,4-Dimethyl-6-*p*-tolylpyridin-2(1*H*)-one (3e):** Colourless oil, yield: 43%,  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.26 (d,  $J = 7.8$  Hz, 2H), 7.21 (d,  $J = 8.0$  Hz, 2H), 6.44 (s, 1H), 5.97 (s, 1H), 3.34 (s, 3H), 2.41 (s, 3H), 2.19 (s, 3H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  163.9, 149.4, 139.7, 132.6, 129.6, 128.5, 117.1, 111.5, 34.4, 21.5, 21.4; FT-IR:  $\tilde{\nu} = 2925, 2852, 1652, 1579, 1553, 1436, 1372, 1287, 1158, 1060$   $\text{cm}^{-1}$ ; HRMS (ESI): calcd for  $\text{C}_{14}\text{H}_{16}\text{NO}$   $[\text{M}+\text{H}]^+$ : 214.1226, found 214.1241.

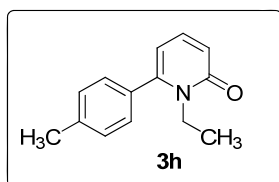


**1-Methyl-5-(phenylthio)-6-*p*-tolylpyridin-2(1*H*)-one (3f):** Reddish oil, yield: 39%,  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.44 (d,  $J = 9.4$  Hz, 1H), 7.25 – 7.20 (m, 5H), 7.13 (t,  $J = 7.0$  Hz, 1H), 7.04 (t,  $J = 7.4$  Hz, 3H), 6.62 (d,  $J = 9.4$  Hz, 1H), 3.27 (s, 3H), 2.40 (s, 3H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  163.0, 153.7, 145.4, 139.7, 138.0, 131.7, 129.7, 129.1, 128.2, 127.9, 126.0, 120.1, 110.3, 35.2, 21.6; FT-IR:  $\tilde{\nu} = 2922, 2842, 1661, 1575, 1536, 1502, 1480, 1419, 1260, 1162, 1023$   $\text{cm}^{-1}$ ; HRMS (ESI): calcd for  $\text{C}_{19}\text{H}_{18}\text{NOS}$   $[\text{M}+\text{H}]^+$ : 308.1104, found 308.1105.

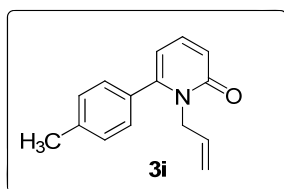




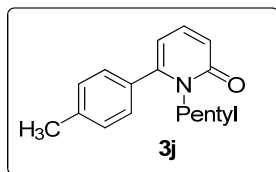
**2-Methyl-3-*p*-tolylisoquinolin-1(2*H*)-one (3g):** Yellow oil, yield: 47%,  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.52 (d,  $J = 7.9$  Hz, 1H), 7.62 – 7.47 (m, 3H), 7.33 – 7.23 (m, 4H), 7.02 (s, 1H), 3.65 (s, 3H), 2.43 (s, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  162.4, 137.6, 136.7, 133.5, 132.0, 131.5, 130.0, 129.5, 128.2, 127.0, 126.1, 124.9, 119.7, 37.2, 21.4; FT-IR:  $\tilde{\nu} = 2925, 2850, 1650, 1626, 1597, 1493, 1351, 1300, 1194, 1057$   $\text{cm}^{-1}$ ; HRMS (ESI): calcd for  $\text{C}_{17}\text{H}_{16}\text{NO}$   $[\text{M}+\text{H}]^+$ : 250.1226, found 250.1233.



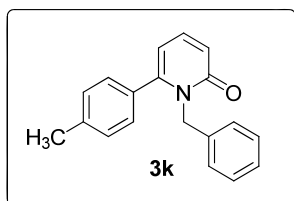
**1-Ethyl-6-*p*-tolylpyridin-2(1*H*)-one (3h):** Yellow oil, yield: 47%,  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.37 – 7.16 (m, 5H), 6.57 (d,  $J = 9.1$  Hz, 1H), 6.02 (d,  $J = 6.8$  Hz, 1H), 3.93 (q,  $J = 7.0$  Hz, 2H), 2.42 (s, 3H), 1.15 (t,  $J = 7.0$  Hz, 3H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  163.3, 150.1, 139.3, 138.5, 133.0, 129.3, 128.6, 119.5, 108.2, 41.2, 21.4, 14.3; FT-IR:  $\tilde{\nu} = 2925, 2853, 1660, 1580, 1550, 1509, 1442, 1352, 1263, 1153, 1064$   $\text{cm}^{-1}$ ; HRMS (ESI): calcd for  $\text{C}_{14}\text{H}_{16}\text{NO}$   $[\text{M}+\text{H}]^+$ : 214.1226, found 214.1232.



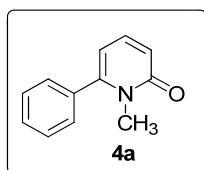
**1-Allyl-6-*p*-tolylpyridin-2(1*H*)-one (3i):** Brownish oil, yield: 61%,  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.32 (m, 2H), 7.27 (d,  $J = 8.0$  Hz, 2H), 7.12 (d,  $J = 7.8$  Hz, 2H), 6.70 – 6.44 (m, 2H), 6.26 (dt,  $J = 15.8, 6.5$  Hz, 1H), 6.17 (dd,  $J = 7.3, 6.1$  Hz, 1H), 4.71 (d,  $J = 6.5$  Hz, 2H), 2.33 (s, 3H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  162.7, 139.6, 138.2, 137.1, 134.3, 133.4, 129.5, 126.7, 122.7, 121.3, 106.3, 50.9, 21.3; FT-IR:  $\tilde{\nu} = 2922, 2856, 1655, 1580, 1541, 1511, 1462, 1343, 1242, 1146, 1023$   $\text{cm}^{-1}$ ; HRMS (ESI): calcd for  $\text{C}_{15}\text{H}_{16}\text{NO}$   $[\text{M}+\text{H}]^+$ : 226.1226, found 226.1234.



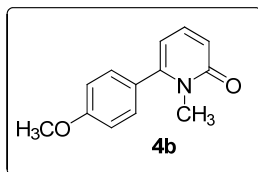
**1-Pentyl-6-*p*-tolylpyridin-2(1*H*)-one (3j):** Colourless oil, yield: 34%,  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.33 – 7.16 (m, 5H), 6.57 (d,  $J = 9.1$  Hz, 1H), 6.02 (dd,  $J = 6.8, 1.2$  Hz, 1H), 3.90 – 3.81 (m, 2H), 2.42 (s, 3H), 1.55 (dt,  $J = 14.9, 7.5$  Hz, 2H), 1.20 – 0.98 (m, 4H), 0.77 (t,  $J = 7.1$  Hz, 3H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  163.5, 150.2, 139.3, 138.5, 133.0, 129.3, 128.6, 119.4, 108.3, 46.0, 29.0, 28.5, 22.2, 21.4, 13.9; FT-IR:  $\tilde{\nu} = 2927, 2857, 1657, 1586, 1551, 1509, 1440, 1261, 1157, 1073$   $\text{cm}^{-1}$ ; HRMS (ESI): calcd for  $\text{C}_{17}\text{H}_{22}\text{NO}$   $[\text{M}+\text{H}]^+$ : 256.1696, found 256.1668.



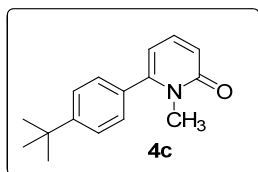
**1-Benzyl-6-*p*-tolylpyridin-2(1*H*)-one (3k):** Reddish oil, yield: 46%,  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.37 (dd,  $J = 9.1, 6.9$  Hz, 1H), 7.23 – 7.16 (m, 3H), 7.12 (d,  $J = 7.8$  Hz, 2H), 7.01 (d,  $J = 7.6$  Hz, 2H), 6.91 (d,  $J = 6.9$  Hz, 2H), 6.68 (d,  $J = 9.1$  Hz, 1H), 6.08 (d,  $J = 6.9$  Hz, 1H), 5.18 (s, 2H), 2.37 (s, 3H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  163.7, 150.7, 139.5, 139.2, 137.3, 132.5, 129.1, 128.8, 128.5, 127.2, 127.0, 119.5, 108.8, 49.1, 21.4; FT-IR:  $\tilde{\nu} = 2923, 2853, 1658, 1585, 1552, 1510, 1458, 1355, 1261, 1142$   $\text{cm}^{-1}$ ; HRMS (ESI): calcd for  $\text{C}_{19}\text{H}_{18}\text{NO}$   $[\text{M}+\text{H}]^+$ : 276.1383, found 276.1381.



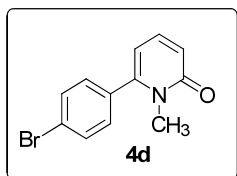
**1-Methyl-6-phenylpyridin-2(1*H*)-one (4a)<sup>5</sup>:** Yellow oil, yield: 45%,  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.49 – 7.45 (m, 3H), 7.37 – 7.32 (m, 3H), 6.61 (d,  $J = 9.1$  Hz, 1H), 6.10 (d,  $J = 6.9$  Hz, 1H), 3.38 (s, 3H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  164.0, 150.3, 138.7, 135.8, 129.4, 128.9, 128.6, 119.1, 107.9, 34.5; FT-IR:  $\tilde{\nu} = 2956, 2852, 1650, 1570, 1547, 1491, 1428, 1378, 1289, 1157, 1057$   $\text{cm}^{-1}$ ; HRMS (ESI): calcd for  $\text{C}_{12}\text{H}_{12}\text{NO}$   $[\text{M}+\text{H}]^+$ : 186.0913, found 186.0922.



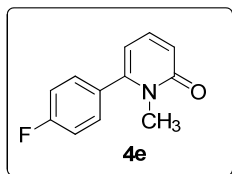
**6-(4-Methoxyphenyl)-1-methylpyridin-2(1H)-one (4b):** Brown oil, yield: 57%,  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.33 (dd,  $J = 9.1, 6.9$  Hz, 1H), 7.29 – 7.24 (m, 2H), 7.07 – 6.88 (m, 2H), 6.59 (d,  $J = 9.1$  Hz, 1H), 6.09 (d,  $J = 6.9$  Hz, 1H), 3.86 (s, 3H), 3.39 (s, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  164.1, 160.4, 150.2, 138.7, 129.9, 128.1, 118.7, 114.3, 108.1, 55.6, 34.6; FT-IR:  $\tilde{\nu} = 2924, 2852, 1660, 1612, 1583, 1556, 1515, 1432, 1378, 1252, 1179, 1034$   $\text{cm}^{-1}$ ; HRMS (ESI): calcd for  $\text{C}_{13}\text{H}_{14}\text{NO}_2$   $[\text{M}+\text{H}]^+$ : 216.1019, found 216.1031.



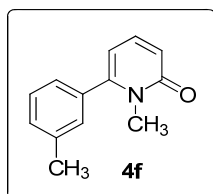
**6-(4-*tert*-Butylphenyl)-1-methylpyridin-2(1H)-one (4c):** Green oil, yield: 47%,  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.47 (d,  $J = 8.2$  Hz, 2H), 7.34 (dd,  $J = 9.1, 6.9$  Hz, 1H), 7.27 (d,  $J = 8.2$  Hz, 2H), 6.60 (d,  $J = 9.1$  Hz, 1H), 6.11 (d,  $J = 6.9$  Hz, 1H), 3.40 (s, 3H), 1.36 (s, 9H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  164.1, 152.7, 150.5, 138.8, 132.7, 128.3, 125.8, 118.7, 108.2, 35.0, 34.7, 31.4; FT-IR:  $\tilde{\nu} = 2962, 2850, 1660, 1583, 1551, 1515, 1430, 1268, 1158, 1109, 1062$   $\text{cm}^{-1}$ ; HRMS (ESI): calcd for  $\text{C}_{16}\text{H}_{20}\text{NO}$   $[\text{M}+\text{H}]^+$ : 242.1539, found 242.1547.



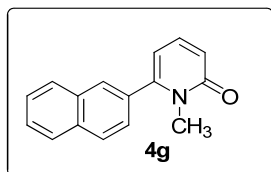
**6-(4-Bromophenyl)-1-methylpyridin-2(1H)-one (4d):** Colourless oil, yield: 46%,  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.62 (d,  $J = 8.4$  Hz, 2H), 7.34 (dd,  $J = 9.1, 6.9$  Hz, 1H), 7.23 (d,  $J = 8.4$  Hz, 2H), 6.62 (d,  $J = 9.1$  Hz, 1H), 6.08 (d,  $J = 6.9$  Hz, 1H), 3.37 (s, 3H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  163.8, 149.0, 138.6, 134.6, 132.2, 130.2, 123.9, 119.6, 107.9, 34.5; FT-IR:  $\tilde{\nu} = 2926, 2856, 1648, 1611, 1573, 1504, 1433, 1378, 1222, 1158, 1062$   $\text{cm}^{-1}$ ; HRMS (ESI): calcd for  $\text{C}_{12}\text{H}_{11}^{79}\text{BrNO}$   $[\text{M}+\text{H}]^+$ : 264.0019, found 264.0034.



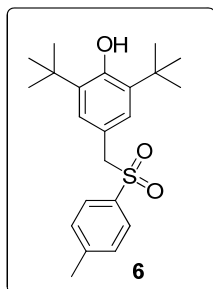
**6-(4-Fluorophenyl)-1-methylpyridin-2(1H)-one (4e):** Yellow oil, yield: 32%,  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.38 – 7.29 (m, 3H), 7.21 – 7.10 (m, 2H), 6.60 (d,  $J = 9.1$  Hz, 1H), 6.07 (d,  $J = 6.9$  Hz, 1H), 3.36 (s, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  163.9, 163.3 ( $J = 249.9$  Hz), 149.1, 138.6, 131.8 (d,  $J = 3.4$  Hz), 130.5 (d,  $J = 8.4$  Hz), 119.4, 116.1 (d,  $J = 21.8$  Hz), 108.1, 34.5;  $^{19}\text{F}$  NMR (471 MHz,  $\text{CDCl}_3$ )  $\delta$  -131.10; FT-IR:  $\tilde{\nu} = 2924, 2852, 1654, 1609, 1578, 1506, 1434, 1379, 1226, 1159, 1062$   $\text{cm}^{-1}$ ; HRMS (ESI): calcd for  $\text{C}_{12}\text{H}_{11}\text{FNO}$   $[\text{M}+\text{H}]^+$ : 204.0819, found 204.0817.



**1-Methyl-6-*m*-tolylpyridin-2(1H)-one (4f):** Brown oil, yield: 51%,  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.38 – 7.29 (m, 2H), 7.26 (dd,  $J = 4.7, 3.1$  Hz, 1H), 7.18 – 7.06 (m, 2H), 6.59 (dd,  $J = 9.1, 1.1$  Hz, 1H), 6.08 (dd,  $J = 6.9, 1.1$  Hz, 1H), 3.37 (s, 3H), 2.41 (s, 3H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  164.0, 150.5, 138.8, 138.7, 135.7, 130.1, 129.1, 128.7, 125.6, 118.9, 107.8, 34.5, 21.5; FT-IR:  $\tilde{\nu} = 2924, 2853, 1660, 1583, 1552, 1487, 1432, 1378, 1218, 1158, 1064$   $\text{cm}^{-1}$ ; HRMS (ESI): calcd for  $\text{C}_{13}\text{H}_{14}\text{NO}$   $[\text{M}+\text{H}]^+$ : 200.1070, found 200.1076.



**1-Methyl-6-(naphthalen-2-yl)pyridin-2(1H)-one (4g):** Brown oil, yield: 48%,  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.97 – 7.87 (m, 3H), 7.85 (s, 1H), 7.63 – 7.53 (m, 2H), 7.47 – 7.33 (m, 2H), 6.67 (d,  $J = 8.5$  Hz, 1H), 6.22 (dd,  $J = 6.8, 1.1$  Hz, 1H), 3.43 (s, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  164.0, 150.3, 138.8, 133.4, 133.1, 133.0, 128.6, 128.4, 128.1, 128.0, 127.4, 127.2, 125.7, 119.2, 108.2, 34.7; FT-IR:  $\tilde{\nu} = 2924, 2853, 1656, 1562, 1429, 1379, 1270, 1158, 1124, 1063$   $\text{cm}^{-1}$ ; HRMS (ESI): calcd for  $\text{C}_{16}\text{H}_{14}\text{NO}$   $[\text{M}+\text{H}]^+$ : 236.1070, found 236.1100.



**2,6-Di-*tert*-butyl-4-(tosylmethyl)phenol (6):** White solid, yield: 77%,  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.44 (d,  $J = 8.1$  Hz, 2H), 7.21 (d,  $J = 8.1$  Hz, 2H), 6.73 (s, 2H), 5.23 (s, 1H), 4.19 (s, 2H), 2.40 (s, 3H), 1.32 (s, 18H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  154.4, 144.4, 136.2, 135.2, 129.4, 129.1, 127.8, 119.2, 63.5, 34.3, 30.2, 21.7; FT-IR:  $\tilde{\nu} = 2957, 2881, 1600, 1435, 1316, 1302, 1220, 1149, 1086$   $\text{cm}^{-1}$ ; HRMS (ESI): calcd for  $\text{C}_{22}\text{H}_{30}\text{NaO}_3\text{S}$   $[\text{M}+\text{Na}]^+$ : 397.1808, found 397.1814.

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# Spectra:

