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Copper(II) Mediated ortho C-H Alkoxylation of Aromatic Amines using Organic Peroxides: Efficient Synthesis of Hindered Ethers

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Supporting Information

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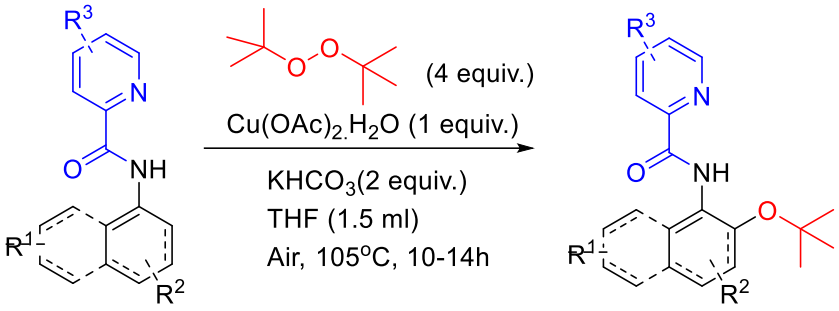
1. General information

All reactions were carried out in oven-dried glassware under standard reaction conditions and all reagents were purchased from Sigma-Aldirch and TCI Chemical and used without further purification unless otherwise noted. All solvents were dried by the standard reported procedures and stored over activated molecular sieves. Reactions were monitored using thin-layer chromatography (TLC) on commercial silica gel plates. Visualization of the developed plates was performed under UV light (254 nm). Flash column chromatography was performed on silica gel (200-400 mesh). ^{1}H and ^{13}C NMR spectra were recorded on Jeol Resonance ECZ 600R spectrometer (600 MHz for ^{1}H NMR, 151 MHz for ^{13}C NMR, 564 MHz for ^{19}F) and Bruker AvanceII 500 spectrometer (500 MHz for ^{1}H NMR, 121 MHz for ^{13}C NMR). EPR data were recorded on magnettech by Freiberg instrument MS-5000. X-ray structure data was recorded by Bruker D8 Quest. Chemical shifts are reported in ppm referenced to an internal tetramethylsilane standard $CDCl_3$ (δ 7.26) for ^{1}H NMR. Chemical shifts of ^{13}C NMR are reported relative to $CDCl_3$ (δ 77.37). The following abbreviations were used to describe peak splitting patterns when appropriate: br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Coupling constants, J, were reported in Hertz unit (Hz). High resolution mass spectra (HRMS) were obtained on an ESI-LC-MS/MS Spectrometer.

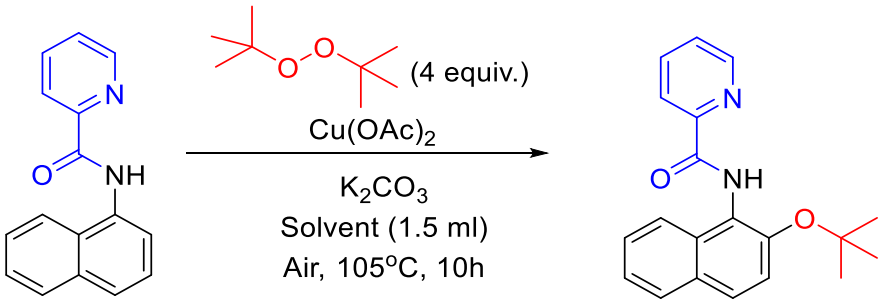
2. Experimental procedure for alkoxylation reaction:



General procedure: A mixture of N-(naphthalen-1-yl)picolinamide (**1a**) (49.6 mg, 0.2 mmol), DTBP (146µL, 0.8 mmol,4 equiv], $Cu(OAc)_2.H_2O$ (39.9 mg, 1equiv.), $KHCO_3$ (40.0 mg, 0.4 mmol) were taken in a pressure reaction tube equipped with stirring bar. The reaction tube was stirred at 105 °C for 10 h under air. After completion the reaction, the reaction mixture was cooled to room temperature and filtered through a plug of celite. The residue was washed with dichloromethane, and the filtrate was concentrated, and evaporated to dryness in rotary evaporator. The crude residue was purified by flash column chromatography (Ethyl acetate: Hexane 10:90) to isolate N-(2-(tert-butoxy)naphthalen-1-yl)picolinamide (50mg, **3a)** in 78% yield.

3. Optimization of reaction condition[a]:

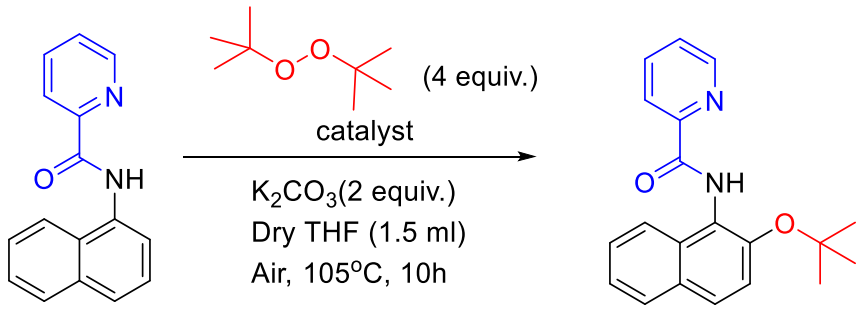
3.1 Table S1: Optimization of Solvent[a]:



Entry	Solvent (ml)	Temp (°C)	Time (h)	Yield (%)
1	PhCl	105	10	26
2	ACN	105	10	N.D.
3	$PhNO_2$	105	10	Trace
4	DCE	105	10	15
5	Toluene	105	10	N.D.
6	**THF**	**105**	**10**	**44**
7	$PhCF_3$	105	10	31
8	Sulfolane	105	10	24

Reaction conditions: [a]1a (0.2 mmol), $Cu(OAc)_2.H_2O$ (20 mol%), DTBP (4 equiv.), K_2CO_3 (2 equiv.) and solvent at 105 °C in a pressure tube under air.

3.2 Table S2: Optimization of Catalyst[a]:

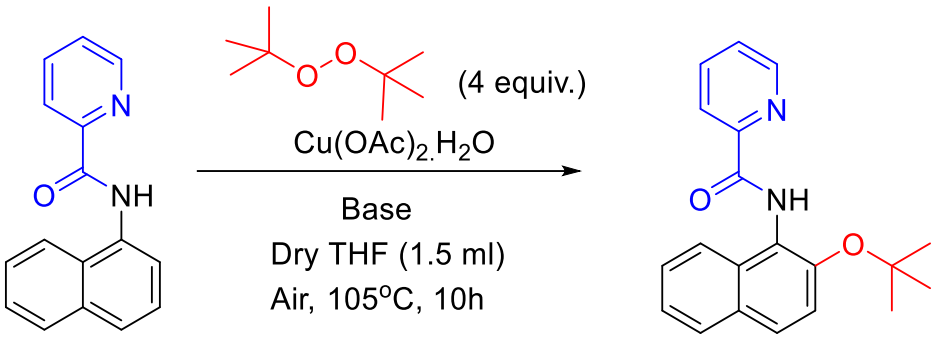


Entry	Catalyst (mol%)	Temp (°C)	Time (h)	Yield (%)

1	-	105	10	ND
2	$Cu(OAc)_2$ (20%)	105	10	38
3	$CuBr_2$ (20%)	105	10	41
4	$Cu(OAc)_2.H_2O$ (20%)	105	10	44
5	$Cu(OTf)_2$ (20%)	105	10	39
6	$Cu(acac)_2$ (20%)	105	10	28
7	CuI (20%)	105	10	22

Reaction conditions: [a]1a (0.2 mmol), DTBP (4 equiv.), K_2CO_3 (2 equiv.), catalyst as mentioned, and THF (1.5ml) at 105 °C in a sealed tube under air.

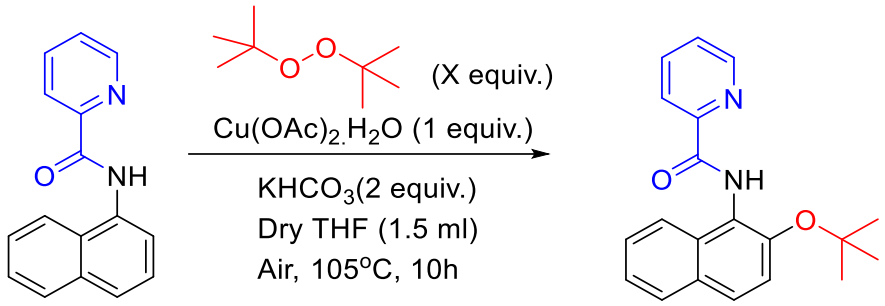
3.3 Table S3: Optimization of Base[a]:



Sr. No.	Base	Temp.(°C)	Time (h)	Yield(%)
1	K_2CO_3(2eq)	105	10	44
2	$KHCO_3$(2eq)	105	10	56
3	Na_2CO_3(2eq)	105	10	46
4	CS_2CO_3(2eq)	105	10	Trace
5	KOAc	105	10	54
6	Li_2CO_3	105	10	29
7	$KHCO_3$(2eq)	105	10	64[b]
8	**$KHCO_3$(2eq)**	**105**	**10**	**78[c]**
9	$KHCO_3$(1eq)	105	10	48
10	$KHCO_3$(2eq)	80	10	50
11	No Base	105	10	30

Reaction conditions: [a]1a (0.2 mmol), DTBP (4 equiv.), $Cu(OAc)_2.H_2O$ (20 mol% or as mentioned), Base (2 equiv.or as mentioned) and THF (1.5ml) at 105°C in a pressure tube under air. [b]$Cu(OAc)_2.H_2O$ (50 mol%) [c]$Cu(OAc)_2.H_2O$ (100 mol%)

3.4 Table S4: Optimization of peroxide[a]:



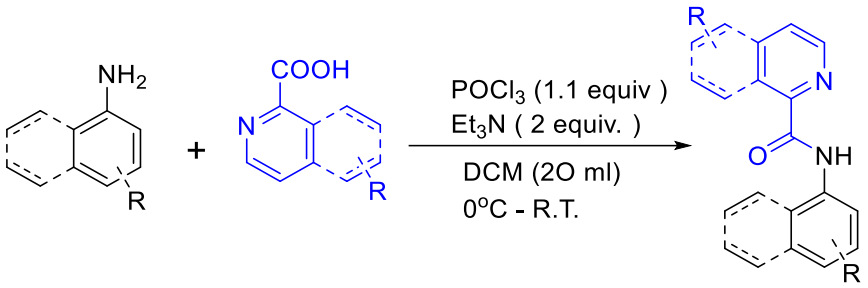
Sr. No.	DTBP (X equiv.)	Temp.(°C)	Time (h)	Yield(%)
1	DTBP (1 equiv.)	105	10	38
2	DTBP (2 equiv.)	105	10	49
3	**DTBP (4 equiv.)**	**105**	**10**	**78**
4	TBHP (5-6M in Decane)	105	10	N.R.
5	TBHP(70% in water)	105	10	N.R.
6	DTBP (4 equiv.)	105	10	62[b]

Reaction conditions: [a]1a (0.2 mmol), $Cu(OAc)_2.H_2O$ (1 equiv.), $KHCO_3$ (2 equiv.) and THF (1.5ml) at 105°C in a pressure tube under air. [b] under nitrogen atmosphere

4. Synthesis of Substrates

4.1 Preparation of Amide Compounds[1]

Picolinic acid or quinoline-2-carboxylic acid (10 mmol), amine (10 mmol), and Et_3N (20 mmol, 2.8 mL) were dissolved in CH_2Cl_2 (20 mL) followed by dropwise addition of $POCl_3$ (1.88 mL) at 0 °C. The resulting mixture was stirred at 0 °C for 0.5 h and warmed to room temperature for 2 h. Then the reaction mixture was cooled to 0 °C. Ice water was added slowly to quench the reaction. The organic layer was collected, and the aqueous phase was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic phase was washed by saturated Na_2CO_3 (2 × 20 mL) and dried over Na_2SO_4. The solvent was evaporated under reduced pressure, and the residue was purified by Flash column chromatography (Ethyl acetate: Hexane 20:80) to isolate the desired product.



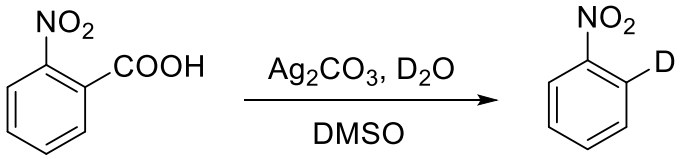
4.2 Preparation of substituted amide compound[2-5].

All other starting materials were prepared according to general procedure.

4.3 Preparation of deuterated amines

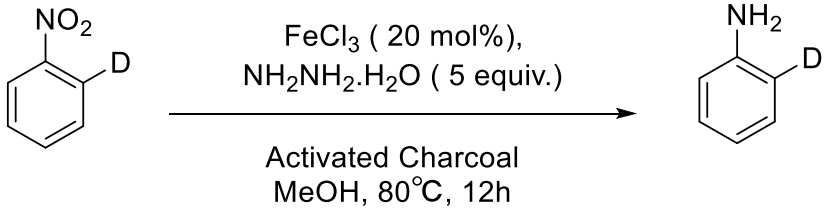
4.3.1 Synthesis of 1-nitrobenzene-2-d[7]:

A mixture of *o*- nitrobenzoic acid (5 mmol), Ag_2CO_3 (140 mg, 0.5 mmol) and D_2O (4.52ml, 250 mmol) was stirred in a pressure tube for 16 hours at 120 ℃ in dry DMSO. After the completion of the reaction, the reaction was washed with ethyl acetate and saturated aqueous $NaHCO_3$. The two layers were separated and the aqueous layer was re-extracted with ethyl acetate (2 x 20 mL). The organic layer was collected and evaporated. The residue was purified by flash chromatography to give deuterated nitrobenzene (372mg, Yield 60%). **^{1}H NMR (600 MHz, $CDCl_3$)**: δ 8.20 (d, *J* = 9.2 Hz, 1H), 7.68 (t, *J* = 7.5 Hz, 1H), 7.56 – 7.50 (m, 2H**).**



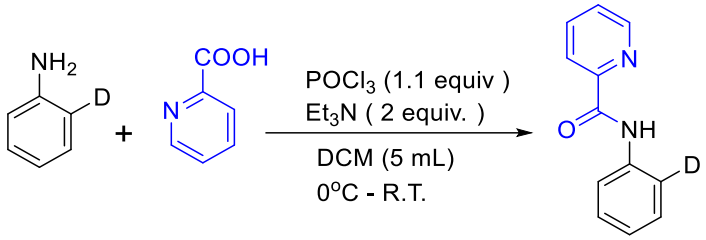
4.3.2 Synthesis of benzen-2-d-amine:

A mixture of benzen-2-d-amine (3 mmol) , activated charcoal (250 mg), $FeCl_3$ (20m mol%, 96 mg), hydrazine monohydrate (5 equiv., 750 µl) and methanol (3 mL) were taken in a pressure tube and was stirred at 80 ℃ for 12 hours. After completion of the reaction, the reaction mixture was filtered through a plug of celite. The solvent was evaporated under reduced pressure and the residue was used for next step without further purification. **^{1}H NMR (500 MHz, $CDCl_3$)** : δ 7.20 – 7.14 (m, 2H), 6.77 (t, *J* = 7.3 Hz, 1H), 6.70 (d, *J* = 8.5 Hz, 1H), 3.64 (s, 2H**).**



4.3.2 Synthesis of N-(phenyl-2-d)picolinamide(2a-D):

Picolinic acid (2 mmol), benzen-2-d-amine (2 mmol), and Et_3N (4 mmol, 0.7 mL) were dissolved in CH_2Cl_2 (5 mL) followed by dropwise addition of $POCl_3$ (0.5 mL) at 0 °C. The resulting mixture was stirred at 0 °C for 0.5 h and warmed to room temperature for 2 h. Then the reaction mixture was cooled to 0 °C. Ice water was added slowly to quench the reaction. The organic layer was collected, and the aqueous phase was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic phase was washed by saturated Na_2CO_3 (2 × 20 mL) and dried over Na_2SO_4. The solvent was evaporated under reduced pressure, and the residue was purified by Flash column chromatography (Ethyl acetate: Hexane 20:80) to isolate the desired product.**^{1}H NMR (600 MHz, $CDCl_3$):** δ 10.02 (s, 1H), 8.61 (dt, *J* = 4.8, 1.3 Hz, 1H), 8.30 (dt, *J* = 8.0, 1.1 Hz, 1H), 7.90 (td, *J* = 7.6, 1.7 Hz, 1H), 7.76 (dd, *J* = 8.7, 1.2 Hz, 1H), 7.47 (ddd, *J* = 7.6, 4.8, 1.2 Hz, 1H), 7.41 – 7.35 (m, 2H), 7.14 (td, *J* = 7.5, 1.2 Hz, 1H).



5. Unreacted substrates:

A series of experiments were carried out under the standard reaction condition with several designed substrates. When naphthalen-1-yl picolinate (8) was examined, which has a N, O bidentate ligand but no alkoxylated product was obtained. It reveals that O is a poor ligand to Cu and the presence of amide group is crucial. Cu(II) is excellent at deprotonating amides to amidates, and that negatively charged amidates are excellent ligands at stabilizing the high-valent Cu(III) oxidation state, which is a key intermediate for the alkoxide transfer. Cu(III) would not be accessible with an O-donor as in compound **8.** N-(naphthalen-1-yl)benzamide (9), N-(naphthalen-1-yl)nicotinamide (10), N-methylnaphthalen-1-amine(11) and N-(naphthalen-1-yl)acetamide(12) were examined under standard condition, no alkoxylated products were obtained. These result indicates that necessity of N,N-bidentate ligand is crucial.

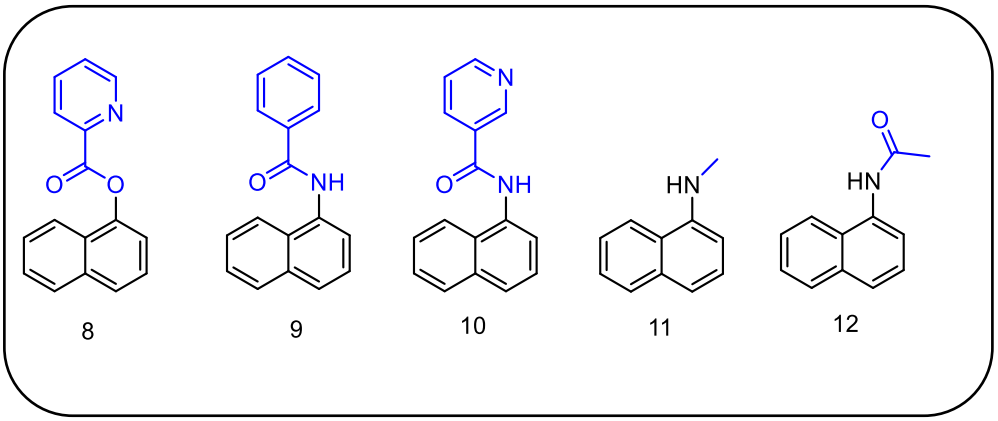


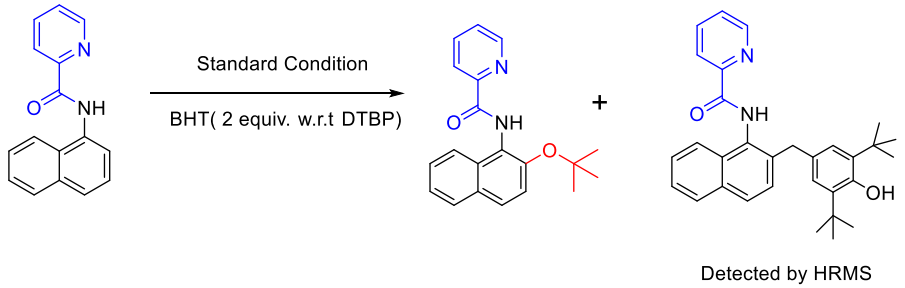
Fig. S1 : Unreactive substrate

6. Control experiments study for the mechanism:

6.1 Control experiment in the presence of radical inhibitor TEMPO and BHT

A mixture of N-(naphthalen-1-yl)picolinamide (**1a)** (49.6 mg, 1equiv. 0.2 mmol), DTBP (146µL, 0.8 mmol,4 equiv], $Cu(OAc)_2.H_2O$ (39.93 mg, 1equiv.), $KHCO_3$ (40.04 mg, 0.4 mmol) and radical inhibitor BHT (8 equiv.) were taken in a sealed reaction tube equipped with stirring bar. The reaction tube stirred at 105 °C for 10 h under air. Reaction was monitored by TLC. Only 20% of **1a** was converted to product.

We have confirmed the *in situ* generated aryl radical species by HRMS. This result indicates that the reaction might be proceed via a radical intermediate means a single electron transfer (SET) pathway.



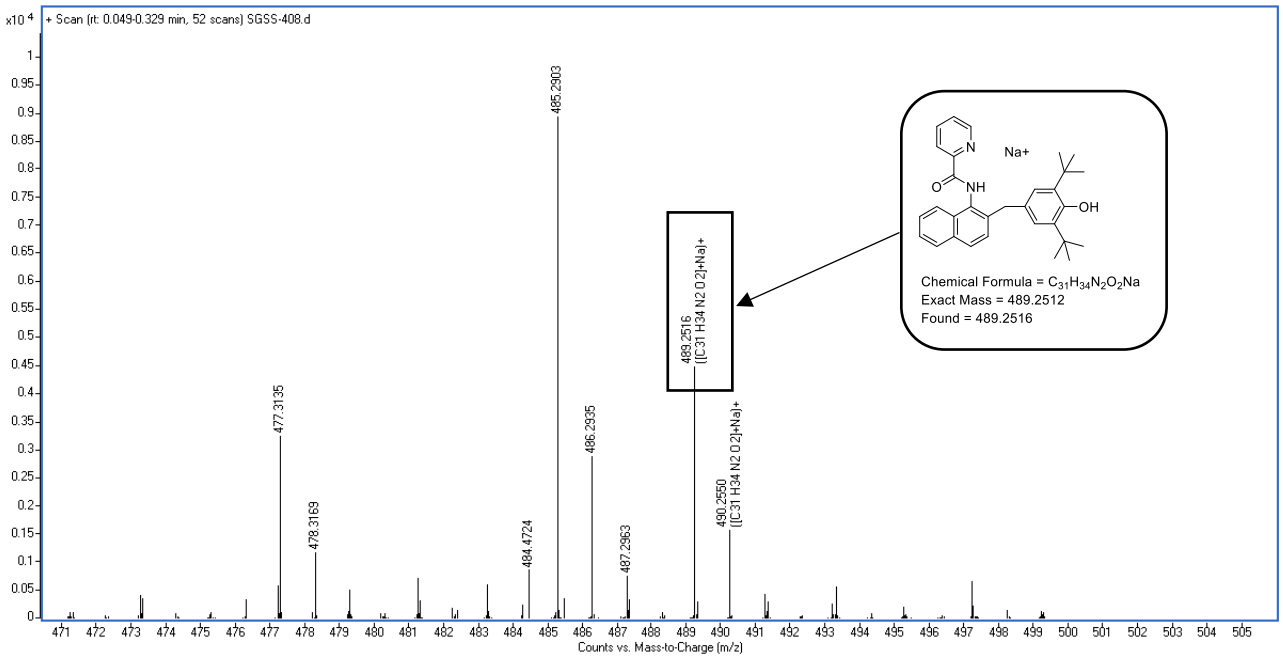
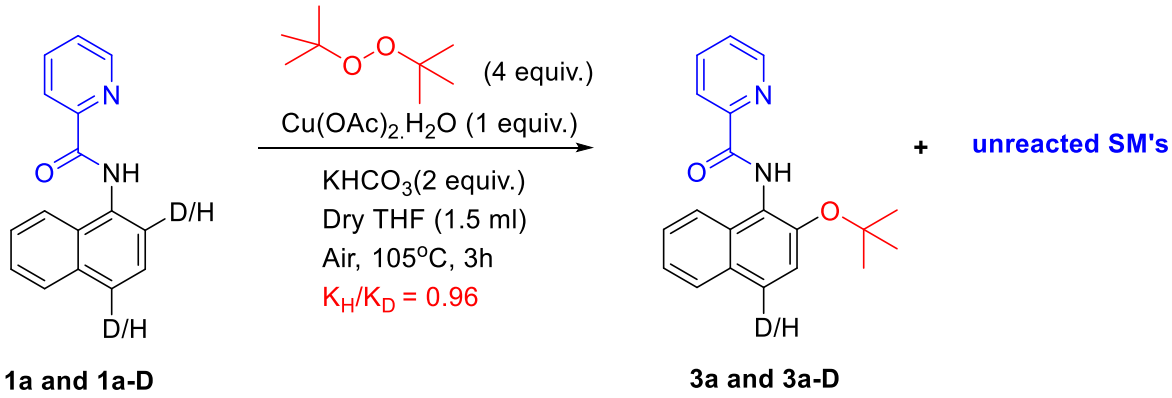


Fig. S2 : BHT trapped intermediates HRMS(ESI) Spectrum

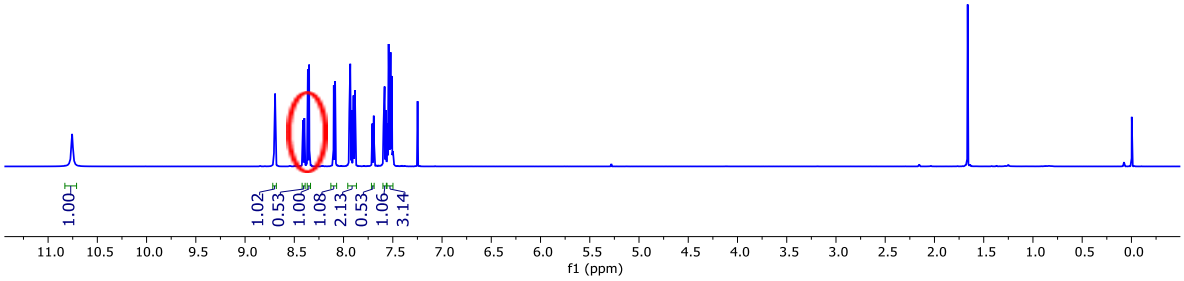
6.2 Kinetic isotope effect (KIE) experiments:

6.2.1 Intermolecular KIE :

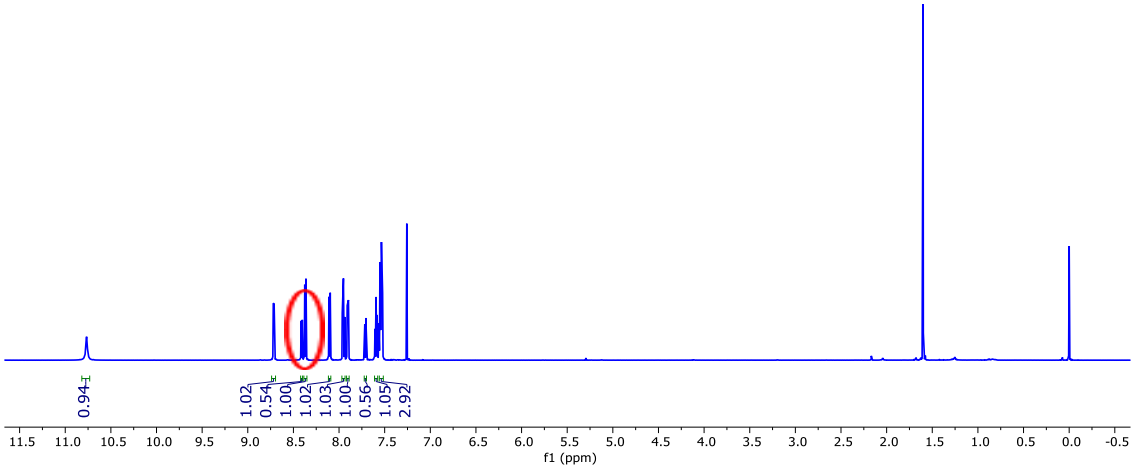
A mixture of N-(naphthalen-1-yl)picolinamide **1a** (0.1 mmol)**, 1a-D (**0.1 mmol), DTBP (146µL, 0.8 mmol,4 equiv], $Cu(OAc)_2.H_2O$(39.9 mg, 1equiv.), $KHCO_3$ (40.0 mg, 0.4 mmol) were taken in a pressure tube equipped with stirring bar. The reaction tube was stirred at 105 °C for 3 h in a pressure tube. The mixture was added into H_2O (10 mL) and extracted with ethyl acetate (10 mL× 3). The organic layer was collected, dried over anhydrous sodium sulfate, and then filtered. After evaporation of the solvent under vacuum, the residue was purified by column chromatography on silica gel (100-200 mesh) using hexane-EtOAc as an eluent (90:10) to recover the unreacted starting materials **1a** and **1a-D.** The mixture was analyzed by ^1H NMR spectrum and the calculated k_H/k_D = 0.96.



Mixture of **1a** and **1a-D** before reaction



Recovered SM (**1a** + **1a-D**) mixture after 3h



With intermolecular KIE experiment, we come to the conclusion that as the k_H/k_D = 0.96 the C-H bond cleavage may not be the rate determining step but intermolecular competition experiment indicates overall KIE and it could be that catalyst-substrate binding is kinetically determinant, therefore it would not clearly inform on the C-H bond cleavage step. So, in order to prove C-H bond cleavage step more precisely we performed an intramolecular KIE experiment

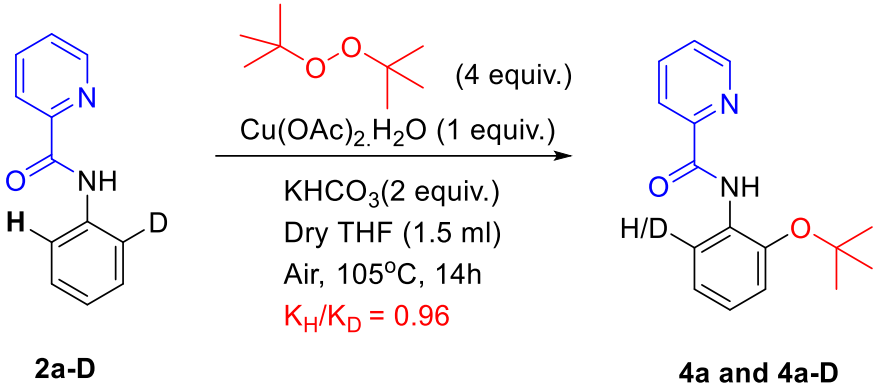
Calculation of intermolecular KIE

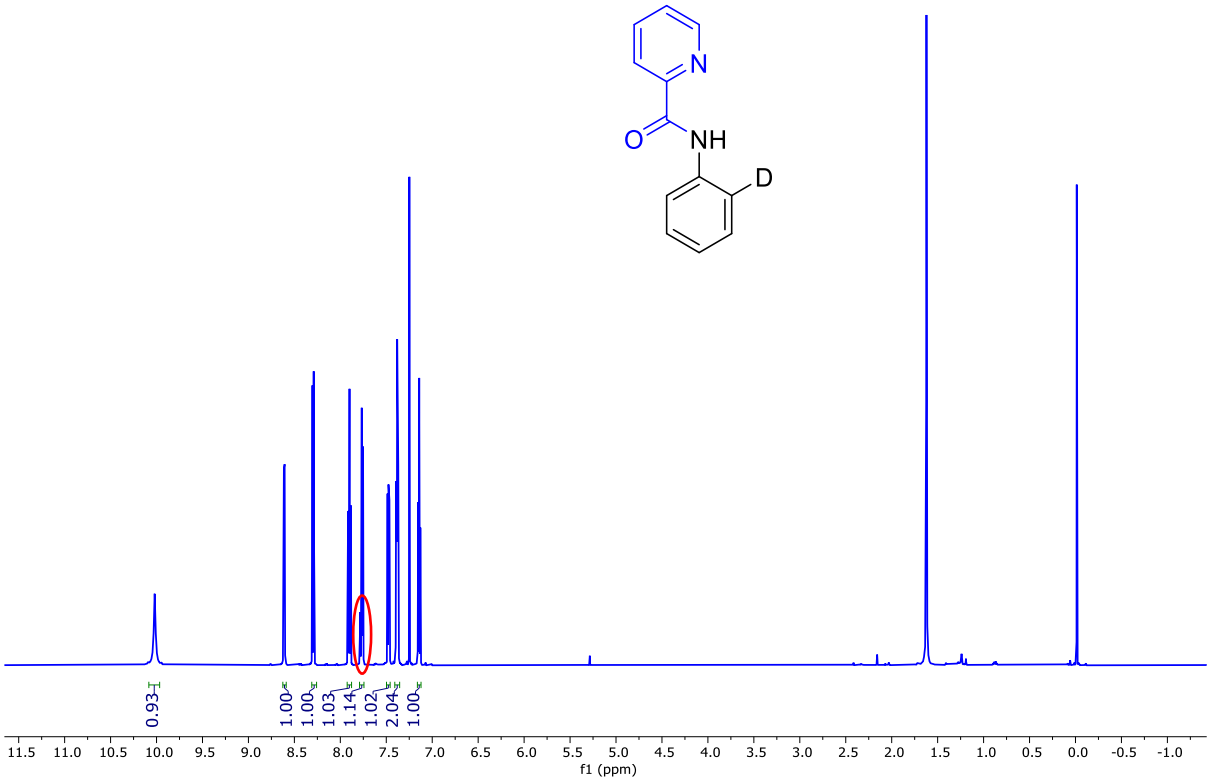
In general, intermolecular KIE from a competitive reaction is calculated either from recover starting material or isolated products (if they are different), taking 50:50 of protonated and deuterated compounds as starting materials for reaction. From the ^{1}H NMR of recovered unreacted starting materials, the ratio of deuterated compound/ protonated compound is the intermolecular KIE.

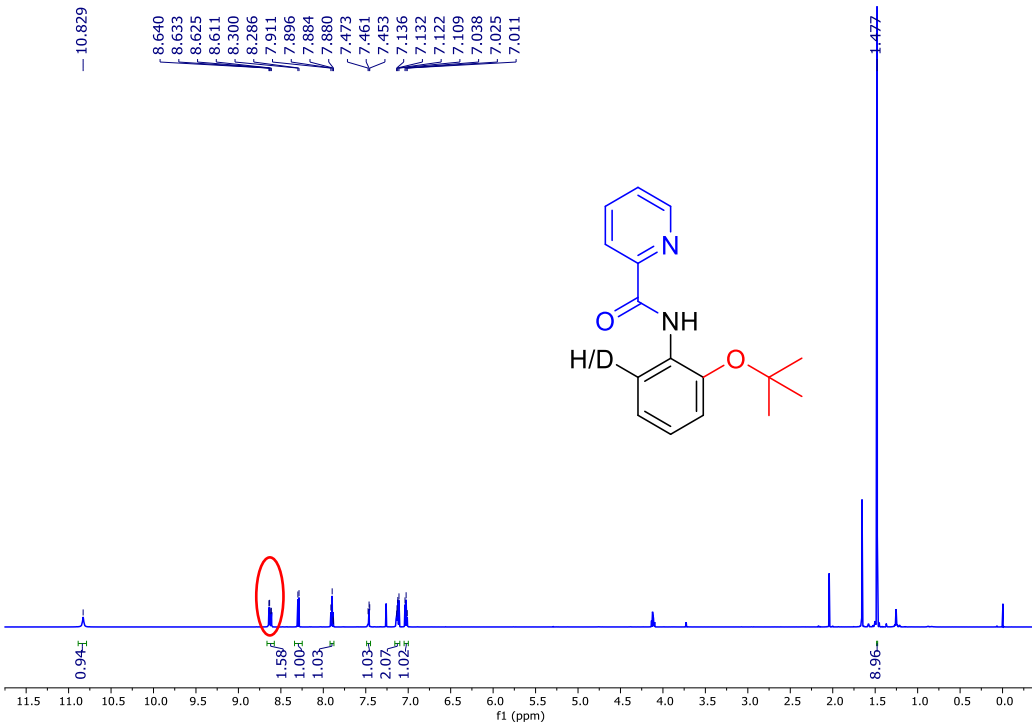
From the ^{1}H NMR (page S-10), in the starting materials the ratio of **1a** and **1a-D** is 0.53: 0.47
After the reaction, in the recovered starting materials (page S-11) the ratio of **1a** and **1a-D** is 0.54: 0.46
NB: For both cases we have taken integration of the proton at 8.41 and 8.37 ppm as marked by red circle.
Ratio of deuterated compound (1a-D)/ protonated compound (1a) in recovered SM
0.46/0.54 = 0.852
Ratio of deuterated compound (1a-D)/ protonated compound (1a) in starting material is
0.47/0.53 = 0.887
Therefore, the KIE = 0.852/0.887 = 0.96 .

6.2.2 Intramolecular KIE :

N-(phenyl-2-d)picolinamide (0.2 mmol) DTBP (146µL, 0.8 mmol,4 equiv], $Cu(OAc)_2.H_2O$ (39.9 mg, 1equiv.), $KHCO_3$ (40.0 mg, 0.4 mmol) were taken in a pressure tube equipped with stirring bar. The reaction tube was stirred at 105 °C for 14 h in a pressure tube. The mixture was added into H_2O (10 mL) and extracted with ethyl acetate (10 mL× 3). The organic layer was collected, dried over anhydrous sodium sulfate, and then filtered. After evaporation of the solvent under vacuum, the residue was purified by column chromatography on silica gel (100-200 mesh) using hexane-EtOAc as an eluent (90:10) to recover the product. The product was characterized by ^1H NMR spectrum and the calculated k_H/k_D = 0.96.







Here we carried out intramolecular KIE experiment to evaluate the competition of functionalization between C-H and C-D bonds. As the k_H/k_D was found to be 0.96, it totally rules out the chance that C-H bond cleavage occurs during the rate determining step.

Calculation of KIE

From the ^{1}H NMR (page S-12), to synthesize **2a-D**, we have found that integration of 1.14 of *ortho* proton, instead of 1.0, it means not all the one side *ortho* proton is deuterated.

We have run the internal KIE experiment with this sample, which contains total available *ortho* proton 1.14 [2a (2H) + 2a-D(1H)] and *ortho* deuterium 0.86 (**2a-D**), the ratio of H: D is 0.57 : 0.43

After the reaction ratio of the *ortho* H in the product is 0.58 (**4a**) and ortho-D product is 0.42 (**4a-D**). (^{1}H NMR, page S-13)

Product **4a-D** is obtained from the reaction of proton (ortho-H) of **2a-D**.

Thus, k_H is 0.42/0.43 = 0.98

In the total **4a** part, some amount of **4a** is contributed by **2a** (both *ortho* proton), as mixture (**2a** and **2a-D**) was there in the starting material.

The amount of **4a** produces from **2a** is (total amount of 2a present in the mixture) x (rate constant, k_H) i.e. (0.57-0.43)x 0.98 = 0.14

So, actual amount of **4a** obtained from **2a-D** (reaction of D) is (total amount of 4a- amount of 4a obtained from 2a) = 0.58-0.14 = 0.44

Thus, k_D = 0.44/0.43 = 1.02

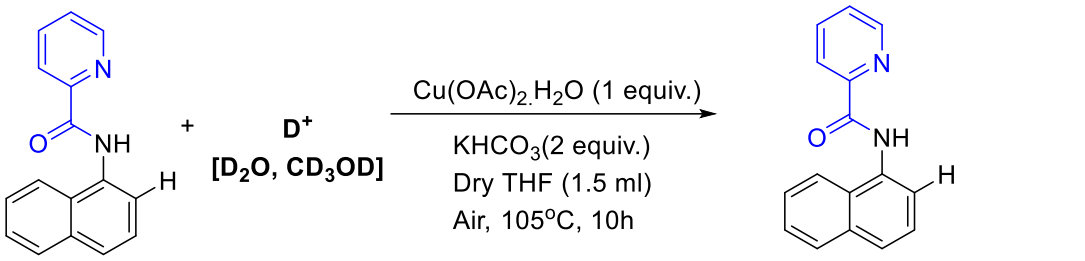
Therefore, KIE, k_H / k_D = 0.96

6.3 Deuterium exchange experiment

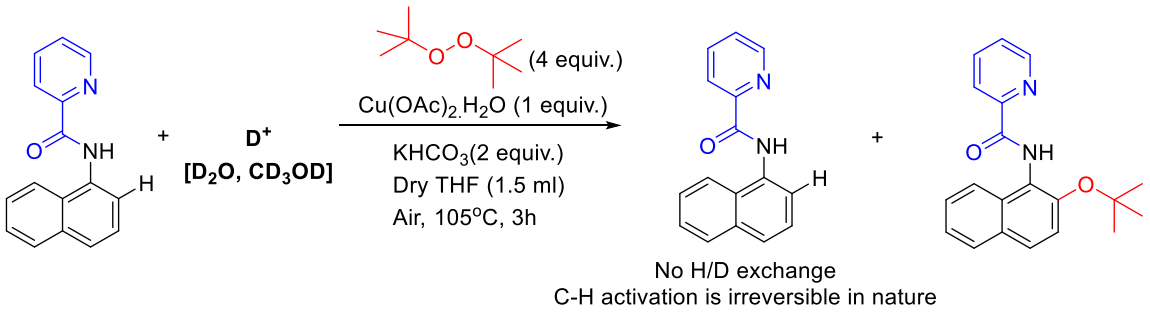
We checked Deuterium exchange experiment to know whether the C-H activation/functionalization is reversible or irreversible in nature. $\mathbf{D}^+$ sources such as $CD_3O\mathbf{D}$ and $\mathbf{D}_2O$ (5 equiv.) were added under the standard condition without the coupling partner. No deuterium incorporation was observed in any of the cases.

In case of $\mathbf{D}_2O$, 94% SM was recovered. Whereas in reaction with $CD_3O\mathbf{D}$, 85% was recovered.

These observations indicate that C-H activation is irreversible in nature.

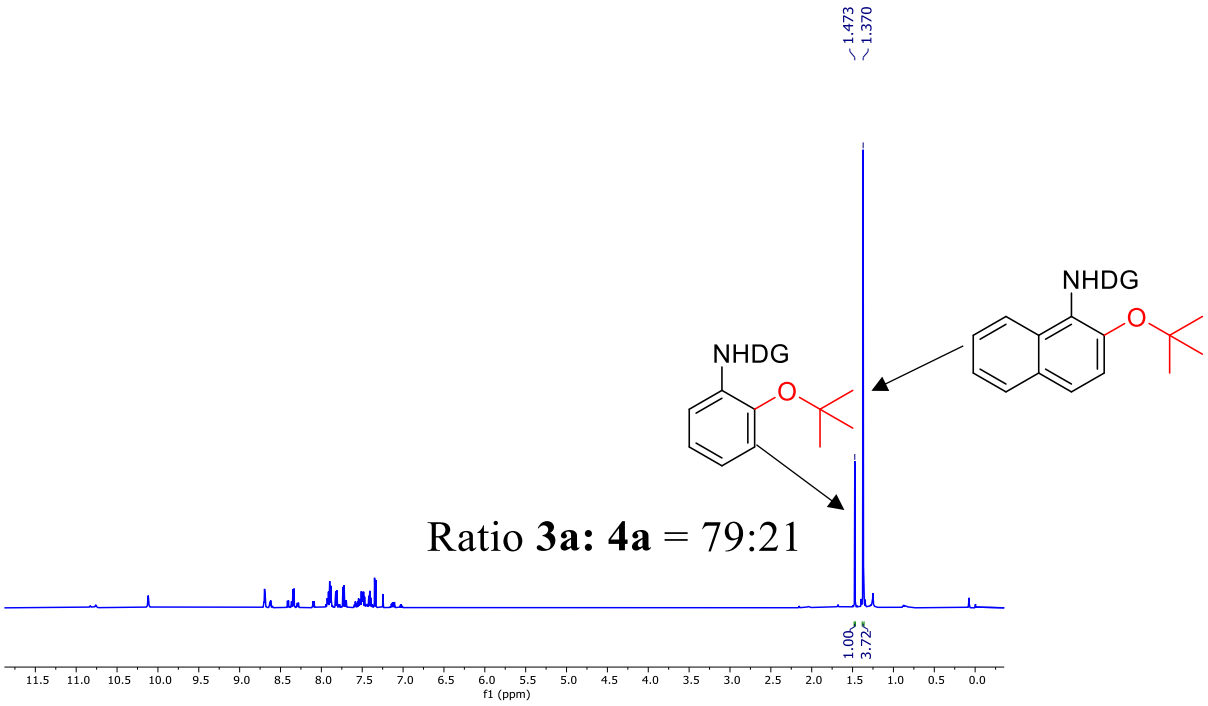


In addition, we also conducted a parallel reaction in presence of DTBP for a shorter reaction time. However, no **D** had not been incorporated in starting material.

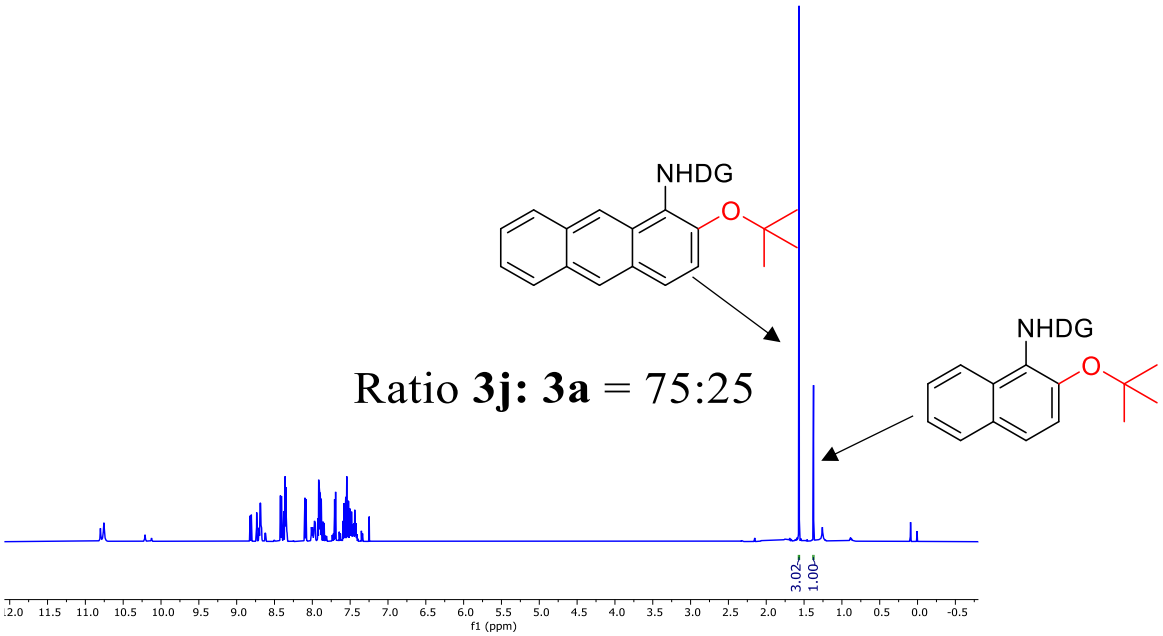


7. Competition experiments:

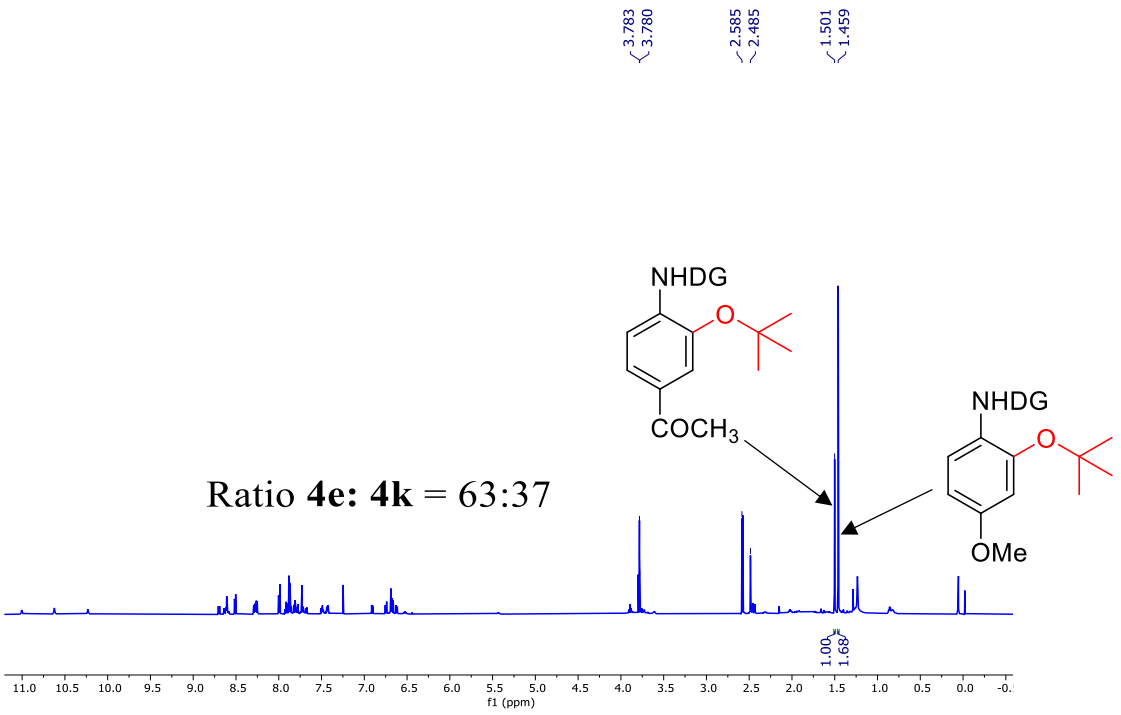
7.1 A equimolar mixture of N-(naphthalen-1-yl)picolinamide (49.6 mg, 0.2 mmol), N-phenylpicolinamide(39.6 mg, 0.2 mmol) DTBP (73µL, 0.4 mmol, 2 equiv], $Cu(OAc)_2.H_2O$ (39.9 mg, 1equiv.), $KHCO_3$ (40.0 mg, 0.4 mmol) were taken in a pressure reaction tube equipped with stirring bar. The reaction tube was stirred at 105 °C for 10 h under air. After that reaction mixture was cooled to room temperature and filtered through a plug of celite, the filtrate was concentrated, and evaporated to dryness in rotary evaporator. The reaction mixture again filtered through a plug of silica gel using eluent ethyl acetate and hexane (10: 90) and examined via ^{1}H-NMR.



7.2 A equimolar mixture of N-(naphthalen-1-yl)picolinamide (49.6 mg, 0.2 mmol), N-(anthracen-1-yl)picolinamide (59.6 mg, 0.2 mmol) DTBP (73µL, 0.4 mmol, 2 equiv], $Cu(OAc)_2.H_2O$ (39.9 mg, 1equiv.), $KHCO_3$ (40.0 mg, 0.4 mmol) were taken in a pressure reaction tube equipped with stirring bar. The reaction tube was stirred at 105 °C for 10 h under air. After that reaction mixture was cooled to room temperature and filtered through a plug of celite, the filtrate was concentrated, and evaporated to dryness in rotary evaporator. The reaction mixture again filtered through a plug of silica gel using eluent ethyl acetate and hexane (10: 90) and examined via ^{1}H-NMR.



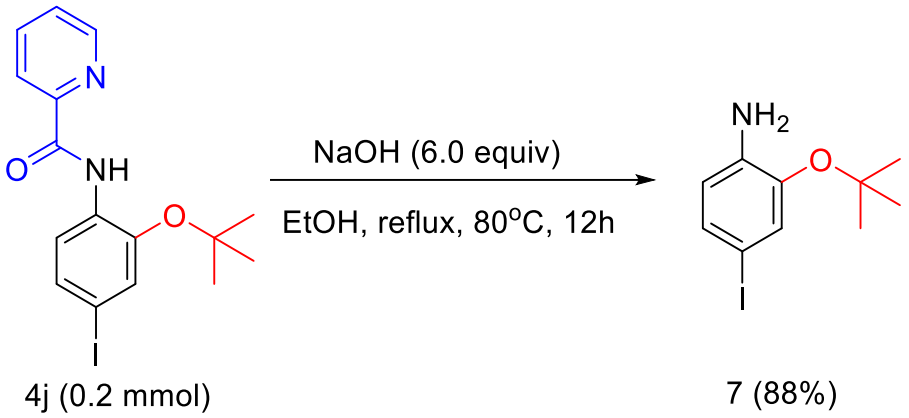
7.3 A equimolar mixture of N-(4-acetylphenyl)picolinamide (48 mg, 0.2 mmol), N-(4-methoxyphenyl)picolinamide (45.6 mg, 0.2 mmol) DTBP (73µL, 0.4 mmol, 2 equiv), $Cu(OAc)_2.H_2O$ (39.9 mg, 1equiv.), $KHCO_3$ (40.0 mg, 0.4 mmol) were taken in a pressure reaction tube equipped with stirring bar. The reaction tube was stirred at 105 °C for 14 h under air. After that reaction mixture was cooled to room temperature and filtered through a plug of celite, the filtrate was concentrated, and evaporated to dryness in rotary evaporator. The reaction mixture again filtered through a plug of silica gel using eluent ethyl acetate and hexane (10: 90) and examined via ^{1}H-NMR.



From the competition experiment re have received some mechanistic insight that favour the electron rich aromatic rings, which is in consistent with the key SET step proposed in reaction mechanism. And this SET step to produce the aryl radical cation is to be the rate limiting step of the reaction.

8. Removal of the directing group:

To a solution of N-(2-(tert-butoxy)-4-iodophenyl)Picolinamide(79.2mg, 0.2 mmol, 1 equiv.) in ethyl alcohol (4 mL), NaOH (48mg, 6equiv.) was added. The mixture was refluxed at 90 °C for 8 h. The solvent was removed by vacuum, then 4 mL of water was added to the residue. The mixture was extracted with dichloromethane (3 x 10 mL). The organic layers were cobined, dried over Na_2SO_4 and the solvent was evaporated under vacuum to provide the product as a yellowish liquid (**7**) (51.2 mg, yield 88%).



4j (0.2 mmol) 7 (88%)

9. EPR Experiment

9.1 A mixture of Amide (**1a**) (49.6 mg, 0.2 mmol), DTBP (146µL, 0.8 mmol,4 equiv], $Cu(OAc)_2.H_2O$ (39.9 mg, 1equiv.), $KHCO_3$ (40.0 mg, 0.4 mmol) were taken in a pressure reaction tube equipped was stirred at 105 °C. An aliquot (200µL) from the reaction mixture was withdrawn typically at 30 min interval starting from the beginning and subjected to EPR analysis at room temperature. A signal appeared at g = 2.096, which was gradually strengthened as the reaction progressed.

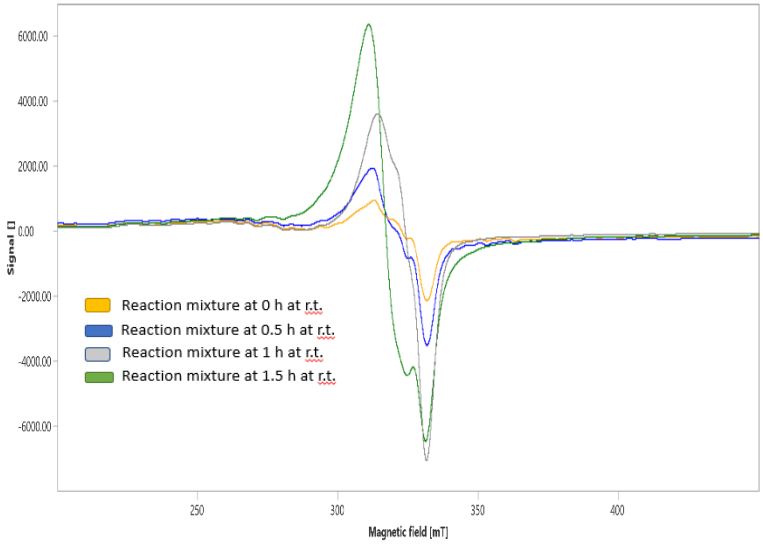


Fig. S3 : EPR Spectrum of reaction mixture at 298 K

9.2 A mixture of Amide (**1a**) (49.6 mg, 0.2 mmol), DTBP (146µL, 0.8 mmol,4 equiv], $Cu(OAc)_2.H_2O$ (39.9 mg, 1equiv.), $KHCO_3$ (40.0 mg, 0.4 mmol) were taken in a pressure reaction tube equipped was stirred at 105 °C. An aliquot (200µL) from the reaction mixture was withdrawn typically at 30 min interval starting from the beginning and subjected to EPR analysis at 113.15K. A signal appeared at g = 2.096, which was gradually strengthened as the reaction progressed.

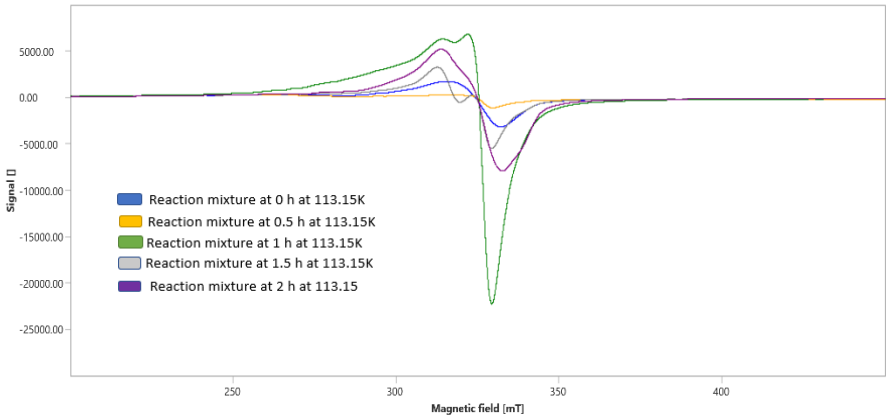


Fig S4 : EPR Spectrum of reaction mixture at 113.15K

9.3 A mixture of Amide (**1a**) (49.6 mg, 0.2 mmol), $Cu(OAc)_2.H_2O$ (39.9 mg, 1equiv.), $KHCO_3$ (40.0 mg, 0.4 mmol) were taken in a pressure reaction tube equipped was stirred at 105 °C. An aliquot (200µL) from the reaction mixture was withdrawn typically at 30 min interval starting from the beginning and subjected to EPR analysis at room temperature. A signal appeared at g = 2.105, which was gradually strengthened as the reaction progressed.

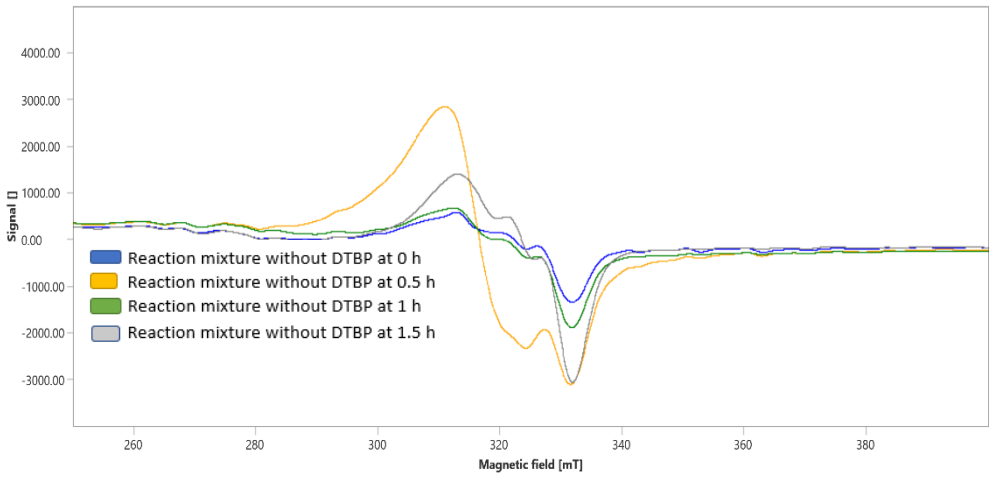


Fig. S5 : EPR Spectrum of reaction mixture without DTBP at 298 K

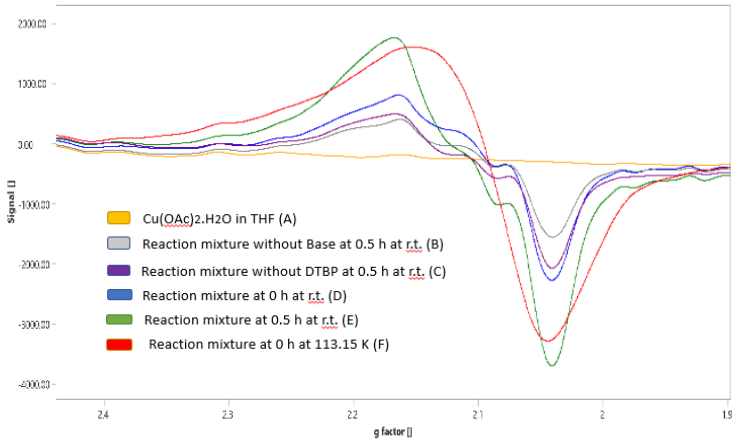


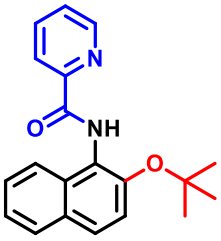
Figure S6 : EPR spectrum in different condition

After performing EPR experiments in different temperature and conditions at regular time intervals which indicates that initially $Cu(OAc)_2.H_2O$ dissolved in THF did not show any signal in EPR due to its dimeric structure. At low temperature it looks like an elongated octahedron geometry of the Cu(II) complex, seems like a square planar Cu(II) complex. But at room temperature the signal is broad, perhaps consistent with exchange happening on the EPR timescale.

10.1 Spectral characterization data:

N-(2-(tert-butoxy)naphthalen-1-yl)Picolinamide(3a):

Yellow oil, (50 mg, 78%) (n-hexane/EtOAc: 90:10)



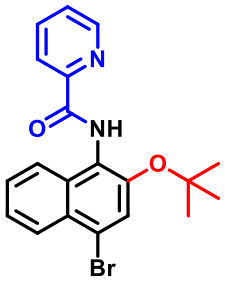
^{1}H NMR (500 MHz, $CDCl_3$): δ 10.13 (s, 1H), 8.71 (d, *J* = 4.0 Hz, 1H), 8.35 (d, *J* = 7.8 Hz, 1H), 7.95 – 7.88 (m, 2H), 7.83 (d, *J* = 8.1 Hz, 1H), 7.74 (d, *J* = 8.9 Hz, 1H), 7.53 – 7.47 (m, 2H), 7.42 (t, *J* = 7.5 Hz, 1H), 7.36 (d, *J* = 8.9 Hz, 1H), 1.38 (s, 9H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$): δ 163.2, 150.1, 148.3, 148.0, 137.6, 130.9, 130.4, 128.0, 127.5, 126.5, 126.2, 126.1, 124.9, 124.6, 123.5, 122.8, 80.9, 29.3.

HRMS-ESI: calcd. For $C_{20}H_{20}N_2O_2Na$ (M+Na)+: 343.1422 Found: 343.1433

N-(4-bromo-2-(tert-butoxy)naphthalen-1-yl)Picolinamide(3b):

Yellow liquid, (44 mg, 52%) (n-hexane/EtOAc: 90:10).



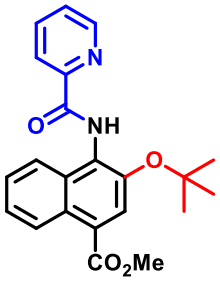
^{1}H NMR (600 MHz, $CDCl_3$): δ 10.05 (s, 1H), 8.70 (d, *J* = 5.1 Hz, 1H), 8.33 (d, *J* = 7.9 Hz, 1H), 8.21 (d, *J* = 5.7 Hz, 1H), 7.97 – 7.88 (m, 2H), 7.69 (s, 1H), 7.56 – 7.51 (m, 3H), 1.38 (s, 9H).

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$): δ 163.3, 149.9, 148.4, 147.9, 137.8, 131.2, 129.5, 127.5, 127.5, 127.1, 126.7, 126.4, 126.2, 125.0, 122.9, 121.1, 81.8, 29.3.

HRMS-ESI: calcd. For $C_{20}H_{19}BrN_2O_2Na$ (M+Na)+: 421.0528 Found: 421.0537

Methyl 3-(tert-butoxy)-4-(picolinamido)-1-naphthoate(3c):

Yellow gummy mass, (48 mg, 60%) (n-hexane/EtOAc: 90:10).



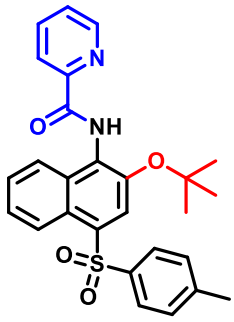
^{1}H NMR (600 MHz, $CDCl_3$): δ 10.26 (s, 1H), 8.90 (d, *J* = 8.7 Hz, 1H), 8.72 (d, *J* = 4.7 Hz, 1H), 8.34 (d, *J* = 7.8 Hz, 1H), 8.06 (s, 1H), 7.95 (t, *J* = 8.5 Hz, 2H), 7.55 (q, *J* = 3.5 Hz, 3H), 4.01 (s, 3H), 1.40 (s, 9H).

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$): δ 167.7, 163.2,149.8, 148.5, 146.4, 137.8, 131.0, 130.7, 129.1, 127.6, 126.8, 126.4, 126.2, 126.0, 125.1, 123.0, 81.6, 52.5, 29.3.

HRMS-ESI: calcd. For $C_{20}H_{22}N_2O_4Na$ (M+Na)+: 401.1477 Found: 401.1459

N-(2-(tert-butoxy)-4-tosylnaphthalen-1-yl)picolinamide (3d)

Brown gummy mass, (62.6 mg, 66%) (n-hexane/EtOAc: 90:10).



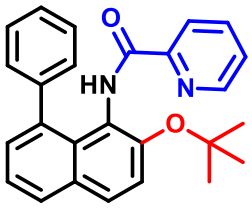
^{1}H NMR (600 MHz, $CDCl_3$): δ 10.31 (s, 1H), 8.72 (d, *J* = 4.7 Hz, 1H), 8.61 (d, *J* = 7.9 Hz, 1H), 8.42 (s, 1H), 8.32 (d, *J* = 8.1 Hz, 1H), 7.95 (t, *J* = 8.1 Hz, 2H), 7.85 (d, *J* = 8.7 Hz, 2H), 7.56 (dd, *J* = 7.4, 4.8 Hz, 1H), 7.50 (dd, *J* = 9.0, 3.0 Hz, 2H), 7.28 (d, *J* = 8.0 Hz, 2H), 2.37 (s, 3H), 1.44 (s, 9H).

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$): δ 163.2, 149.5, 148.5, 146.1, 144.2, 138.8, 137.8, 134.6, 132.4, 130.9, 129.9, 127.6, 127.1, 127.0, 126.9, 126.8, 126.1, 125.8, 124.5, 123.0, 82.4, 29.2, 21.6.

HRMS-ESI: calcd. For $C_{27}H_{26}N_2O_4SNa$ (M+Na)+: 497.1511 Found: 497.1501

N-(2-(tert-butoxy)-8-phenylnaphthalen-1-yl)Picolinamide(3f):

Brown Solid, (52 mg, 62%) (n-hexane/EtOAc: 90:10). M.P.- 118-120°C



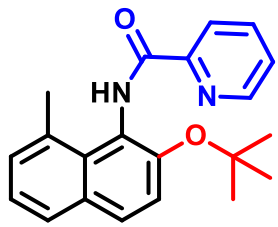
^{1}H NMR (600 MHz, $CDCl_3$): δ 9.04 (s, 1H), 8.33 (d, *J* = 4.7 Hz, 1H), 7.93 (d, *J* = 8.0 Hz, 1H), 7.85 – 7.81 (m, 2H), 7.70 (t, *J* = 8.0 Hz, 1H), 7.43 (s, 1H), 7.39 (t, *J* = 8.0 Hz, 1H), 7.31 (t, *J* = 5.2 Hz, 1H), 7.26 (d, *J* = 6.9 Hz, 3H), 6.91-7.02 (m, 2H), 6.71 (t, *J* = 7.5 Hz, 1H), 1.31 (s, 9H).

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$): δ 162.0, 150.6, 149.9, 147.4, 143.8, 138.5, 136.7, 131.9, 130.5, 129.4, 128.8, 128.4, 128.3, 127.2, 125.6, 125.5, 125.2, 123.9, 123.4, 122.1, 80.6, 29.3.

HRMS-ESI: calcd. For $C_{26}H_{24}N_2O_2Na$ (M+Na)+: 419.1735 Found: 419.1724

N-(2-(tert-butoxy)-8-methylnaphthalen-1-yl)Picolinamide(3g):

Yellow liquid, (50 mg, 70%) (n-hexane/EtOAc: 90:10).



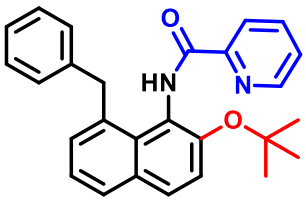
^{1}H NMR (500 MHz, $CDCl_3$): δ 9.79 (s, 1H), 8.69 (d, *J* = 5.6 Hz, 1H), 8.33 (d, *J* = 7.8 Hz, 1H), 7.92 (t, *J* = 8.6 Hz, 1H), 7.74 (d, *J* = 8.9 Hz, 1H), 7.67 (d, *J* = 7.8 Hz, 1H), 7.54 – 7.48 (m, 1H), 7.37 (d, *J* = 8.9 Hz, 1H), 7.26 – 7.22 (m, 2H), 2.75 (s, 3H), 1.34 (s, 9H).

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$): δ 163.9, 150.6, 150.4, 148.5, 137.6, 133.6, 131.9, 131.8, 130.3, 129.0, 127.3, 126.4, 125.5, 124.5, 122.8, 122.5, 80.4, 29.4, 23.8.

HRMS-ESI: calcd. For $C_{21}H_{22}N_2O_2Na$ (M+Na)+: 357.1579 Found: 357.1572

N-(8-benzyl-2-(tert-butoxy)naphthalen-1-yl)Picolinamide(3h):

Yellow liquid, (56.2mg, 65%) (n-hexane/EtOAc: 90:10).



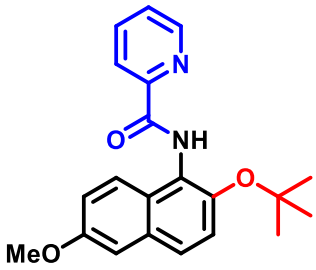
^{1}H NMR (600 MHz, $CDCl_3$): δ 9.38 (s, 1H), 8.52 (d, *J* = 4.9 Hz, 1H), 8.24 (d, *J* = 7.1 Hz, 1H), 7.87 (t, *J* = 7.9 Hz, 1H), 7.78 (dd, *J* = 17.7, 8.6 Hz, 2H), 7.48 – 7.43 (m, 1H), 7.38 (s, 1H), 7.32 (t, *J* = 7.6 Hz, 1H), 7.23 (d, *J* = 6.7 Hz, 1H), 7.13 – 7.11 (m, 3H), 6.82 – 6.79 (m, 2H), 4.89 – 4.17 (m, 2H), 1.24 (s, 9H).

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$): δ 164.1, 150.8, 150.2, 148.1, 141.9, 137.3, 134.8, 132.2, 131.5, 131.4, 129.2, 128.4, 128.2, 126.2, 125.8, 125.1, 124.4, 122.6, 80.4, 41.9, 29.1.

HRMS-ESI: calcd. For $C_{27}H_{26}N_2O_2Na$ (M+Na)+: 433.1892 Found: 433.1873

N-(2-(tert-butoxy)-6-methoxynaphthalen-1-yl)Picolinamide(3i)

Yellow liquid, (61 mg, 82%) (n-hexane/EtOAc: 90:10).



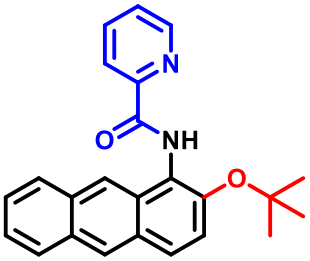
^{1}H NMR (600 MHz, $CDCl_3$): δ 10.14 (s, 1H), 8.70 (d, *J* = 4.4 Hz, 1H), 8.34 (d, *J* = 7.4 Hz, 1H), 7.92 (t, *J* = 7.7 Hz, 1H), 7.80 (d, *J* = 9.2 Hz, 1H), 7.62 (d, *J* = 9.2 Hz, 1H), 7.53 – 7.49 (m, 1H), 7.32 – 7.29 (m, 1H), 7.18 – 7.15 (m, 1H), 7.13 (d, *J* = 2.7 Hz, 1H), 3.91 (s, 3H), 1.36 (s, 9H).

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$): δ 163.2, 157.1, 150.1, 148.4, 146.1, 137.7, 132.2, 126.5, 126.5, 126.4, 126.1, 125.6, 124.3, 122.9, 118.9, 106.2, 80.7, 55.5, 29.2.

HRMS-ESI: calcd. For $C_{21}H_{22}N_2O_3Na$ (M+Na)+: 373.1528 Found 373.1534

N-(2-(tert-butoxy)anthracen-1-yl)picolinamide(3j)

Yellow Solid, (53.4 mg, 68%) (n-hexane/EtOAc: 90:10). M.P.- 150-152°C



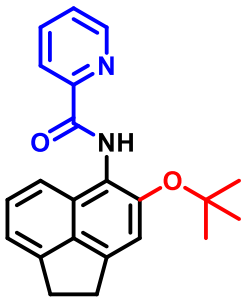
^{1}H NMR (500 MHz, $CDCl_3$): δ 10.81 (s, 1H), 8.81 (d, *J* = 9.2 Hz, 1H), 8.74 (s, 1H), 8.69 (d, *J* = 4.4 Hz, 1H), 8.39 (s, 1H), 8.36 (d, *J* = 7.8 Hz, 1H), 8.00 (dd, *J* = 16.0, 8.2 Hz, 2H), 7.95 – 7.90 (m, 1H), 7.86 (d, *J* = 9.2 Hz, 1H), 7.51 – 7.42 (m, 3H), 1.57 (s, 10H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$): δ 161.8, 150.3, 148.2, 139.8, 137.7, 131.4, 131.0, 130.4, 129.8, 129.1, 128.5, 128.1, 126.4, 126.2, 125.6, 125.3, 124.8, 122.6, 122.3, 120.4, 84.1, 29.9.

HRMS-ESI: calcd. For $C_{24}H_{22}N_2O_2Na$ (M+Na)+: 393.1579 Found: 393.1569

N-(4-(tert-butoxy)-1,2-dihydroacenaphthylen-5-yl)picolinamide(3k)

Brownish Solid, (48.4 mg, 70%) (n-hexane/EtOAc: 90:10). M.P.- 160-162°C



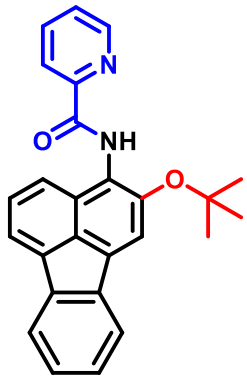
^{1}H NMR (600 MHz, $CDCl_3$): δ 10.18 (s, 1H), 8.69 (d, *J* = 4.2 Hz, 1H), 8.36 (d, *J* = 7.9 Hz, 1H), 7.92 (t, *J* = 7.6 Hz, 1H), 7.59 (d, *J* = 8.2 Hz, 1H), 7.50 (dd, *J* = 7.7, 4.7 Hz, 1H), 7.47 – 7.44 (m, 1H), 7.22 (d, *J* = 6.8 Hz, 1H), 7.15 (s, 1H), 3.43 – 3.36 (m, 4H), 1.39 (s, 9H).

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$): δ 162.7, 150.3, 149.4, 148.3, 145.8, 145.2, 137.6, 136.7, 128.1, 127.8, 126.3, 122.8, 122.7, 120.7, 118.5, 117.4, 80.9, 30.7, 30.2, 29.3.

HRMS-ESI: calcd. For $C_{22}H_{22}N_2O_2Na$ (M+Na)+: 369.1579 Found: 369.1562

N-(2-(tert-butoxy)fluoranthen-3-yl)Picolinamide(3l)

Yellow Solid, (56.7 mg, 72%) (n-hexane/EtOAc: 90:10). M.P.- 140-142°C



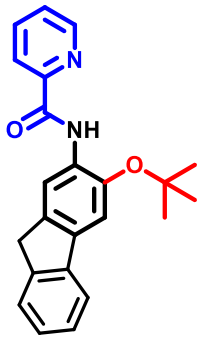
^{1}H NMR (600 MHz, $CDCl_3$): δ 10.46 (s, 1H), 8.72 (d, *J* = 4.6 Hz, 1H), 8.38 (d, *J* = 7.9 Hz, 1H), 8.01 (d, *J* = 8.2 Hz, 1H), 7.96 – 7.93 (m, 1H), 7.86 (q, *J* = 7.4 Hz, 3H), 7.75 (s, 1H), 7.64 – 7.60 (m, 1H), 7.53 (dd, *J* = 7.3, 4.9 Hz, 1H), 7.36 (dd, *J* = 5.6, 3.3 Hz, 2H), 1.46 (s, 9H).

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 162.9, 150.1, 148.9, 148.4, 140.1, 139.0, 137.7, 136.8, 135.6, 129.9, 127.9, 127.6, 127.6, 127.4, 126.6, 126.5, 125.9, 122.9, 121.6, 121.4, 119.5, 118.2, 81.5, 29.3

HRMS-ESI: calcd. For $C_{26}H_{23}N_2O_2$ (M+H)+: 395.1760 Found: 395.1728

N-(3-(tert-butoxy)-9H-fluoren-2-yl)picolinamide(3m)

Yellow liquid, (44 mg, total yield = 62%) (n-hexane/EtOAc: 95 : 5)



Isomers could not be separated.

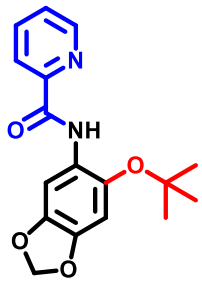
^{1}H NMR (600 MHz, $CDCl_3$): δ 10.94 (s, 1H), 8.85 (s, 1H), 8.66 (d, *J* = 4.6 Hz, 1H), 8.32 (d, *J* = 8.0 Hz, 1H), 7.93 – 7.90 (m, 1H), 7.70 (d, *J* = 6.9 Hz, 1H), 7.53 (d, *J* = 8.0 Hz, 1H), 7.51 (s, 1H), 7.49 – 7.47 (m, 1H), 7.36 (t, *J* = 7.5 Hz, 1H), 7.28 (d, *J* = 6.9 Hz, 1H), 3.92 (s, 2H), 1.54 (s, 9H).

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$): δ 161.8, 150.5, 148.3, 144.5, 144.0, 141.9, 139.1, 137.7, 137.2, 132.0, 126.8, 126.3, 125.1, 122.4, 119.4, 116.2, 114.0, 81.2, 37.1, 29.0.

HRMS-ESI: calcd. For $C_{23}H_{22}N_2O_2Na$ (M+Na)+: 381.1579 Found: 381.1578

N-(6-(tert-butoxy)benzo[d][1,3]dioxol-5-yl)picolinamide(3o)

Yellow sticky liquid, (32.6 mg, 52%) (n-hexane/EtOAc: 90:5).



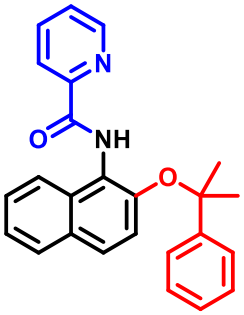
^{1}H NMR (600 MHz, $CDCl_3$): δ 10.66 (s, 1H), 8.62 (d, *J* = 4.6 Hz, 1H), 8.27 (d, *J* = 6.9 Hz, 1H), 8.24 (s, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.46 – 7.42 (m, 1H), 6.67 (s, 1H), 5.95 (s, 2H), 1.43 (s, 9H).

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$): δ 161.3, 150.4, 148.2, 143.4, 143.0, 139.1, 137.7, 127.0, 126.2, 122.3, 104.8, 101.4, 101.3, 81.3, 28.8.

HRMS-ESI: calcd. For $C_{17}H_{18}N_2O_4Na$ (M+Na)+: 337.1164 Found: 337.1154

N-(2-((2-phenylpropan-2-yl)oxy)naphthalen-1-yl)picolinamide(3q):

Yellow sticky liquid, (55.03 mg, 72%) (n-hexane/EtOAc: 90:10).



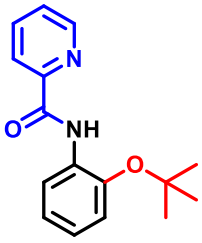
^{1}H NMR (600 MHz, $CDCl_3$) δ 10.04 (s, 1H), 8.71 (d, *J* = 4.8 Hz, 1H), 8.38 (d, *J* = 7.8 Hz, 1H), 7.96 – 7.90 (m, 2H), 7.73 (d, *J* = 8.2 Hz, 1H), 7.57 (d, *J* = 8.0 Hz, 2H), 7.52 (dd, *J* = 7.3, 4.9 Hz, 1H), 7.48 (dd, *J* = 11.2, 8.4 Hz, 2H), 7.37 (q, *J* = 7.2 Hz, 3H), 7.30 (t, *J* = 7.4 Hz, 1H), 6.75 (d, *J* = 9.2 Hz, 1H), 1.72 (s, 6H).

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$) δ 163.4, 150.3, 148.8, 148.4, 146.9, 137.6, 130.8, 129.8, 128.6, 128.0, 127.3, 126.5, 126.4, 125.5, 124.4, 123.7, 122.9, 122.8, 120.1, 81.9, 29.7.

HRMS-ESI: calcd. For $C_{25}H_{22}N_2O_2Na$ (M+Na)+: 405.1579 Found: 405.1574

N-(2-(tert-butoxy)phenyl)Picolinamide(4a):

Yellow liquid, (32.8 mg, 56%) (n-hexane/EtOAc: 95:5).



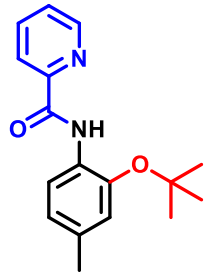
^{1}H NMR (600 MHz, $CDCl_3$): δ 10.83 (s, 1H), 8.66 – 8.59 (m, 2H), 8.29 (d, *J* = 7.9 Hz, 1H), 7.92 – 7.88 (m, 1H), 7.46 (dd, *J* = 7.9, 4.6 Hz, 1H), 7.13 (dd, *J* = 14.3, 7.5 Hz, 2H), 7.03 (t, *J* = 8.0 Hz, 1H), 1.48 (s, 9H).

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$): δ 161.8, 150.4, 148.3, 145.1, 137.6, 132.9, 126.3, 124.0, 123.5, 122.5, 122.4, 119.8, 81.0, 28.9.

HRMS-ESI: calcd. For $C_{16}H_{18}N_2O_2Na$ (M+Na)+: 293.1266 Found: 293.1257

N-(2-(tert-butoxy)-4-methylphenyl)Picolinamide(4b):

Yellow liquid (33.7 mg, 55%) (n-hexane/EtOAc: 95:5).



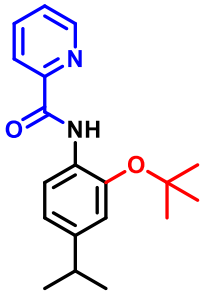
^{1}H NMR (600 MHz, $CDCl_3$): δ 10.73 (s, 1H), 8.63 (d, *J* = 5.0 Hz, 1H), 8.48 (d, *J* = 8.1 Hz, 1H), 8.28 (d, *J* = 8.1 Hz, 1H), 7.91 – 7.87 (m, 1H), 7.47 – 7.43 (m, 1H), 6.96 – 6.91 (m, 2H), 2.32 (s, 3H), 1.47 (s, 9H).

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$): δ 161.6, 150.6, 148.3, 145.0, 137.6, 133.4, 130.4, 126.2, 124.5, 123.3, 122.4, 119.5, 80.9, 29.9, 21.4.

HRMS-ESI: calcd. For $C_{17}H_{20}N_2O_2Na$ (M+Na)+: 307.1422 Found: 307.1431

N-(2-(tert-butoxy)-4-isopropylphenyl)Picolinamide(4c)

Yellow gummy mass, (33.5 mg, 50%) (n-hexane/EtOAc: 95:5).



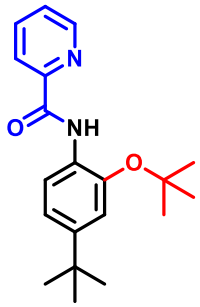
^{1}H NMR (600 MHz, CDCl3): δ 10.73 (s, 1H), 8.63 (d, J = 4.9 Hz, 1H), 8.52 – 8.49 (m, 1H), 8.29 (d, J = 7.9 Hz, 1H), 7.89 (t, J = 7.6 Hz, 1H), 7.45 (dd, J = 7.9, 4.7 Hz, 1H), 7.00 (d, J = 8.4 Hz, 1H), 6.97 (s, 1H), 2.87 (h, J = 6.8 Hz, 1H), 1.47 (s, 9H), 1.24 (d, j = 6.9 Hz 6H).

^{13}C {^{1}H} NMR (151 MHz, CDCl3): δ 161.6, 150.6, 148.3, 145.0, 144.6, 137.6, 130.6, 126.2, 122.4, 121.9, 120.8, 119.6, 80.8, 33.8, 29.0, 24.2.

HRMS-ESI: calcd. For $C_{19}H_{24}N_2O_2Na$ (M+Na)+: 335.1735 Found: 335.1739

N-(2-(tert-butoxy)-4-(tert-butyl)phenyl)picolinamide(4d):

Yellow gummy mass, (35.2 mg, 54%) (n-hexane/EtOAc: 95:5).



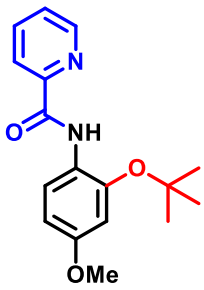
^{1}H NMR (600 MHz, CDCl$_3$): δ 10.72 (s, 1H), 8.63 (d, *J* = 4.6 Hz, 1H), 8.51 (d, *J* = 8.0 Hz, 1H), 8.29 (d, *J* = 8.0 Hz, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.48 – 7.42 (m, 1H), 7.15 (d, *J* = 9.1 Hz, 1H), 7.12 (d, *J* = 4.6 Hz, 1H), 1.47 (s, 9H), 1.32 (s, 9H).

^{13}C NMR (151 MHz, CDCl$_3$): δ 161.6, 150.5, 148.3, 146.9, 144.7, 137.6, 130.2, 126.2, 122.3, 120.7, 120.1, 119.2, 80.8, 34.5, 31.6, 31.5, 29.0, 28.9.

HRMS-ESI: calcd. For $C_{20}H_{26}N_2O_2Na$ (M+Na)+: 349.1892 Found: 349.1891

N-(2-(tert-butoxy)-4-methoxyphenyl)Picolinamide(4e)

Yellow liquid, (30.4 mg, 62%) (n-hexane/EtOAc: 95:5).



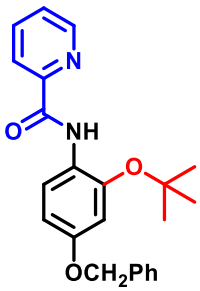
^{1}H NMR (500 MHz, CDCl$_3$): δ 10.64 (s, 1H), 8.63 (d, *J* = 4.4 Hz, 1H), 8.53 (d, *J* = 8.8 Hz, 1H), 8.28 (d, *J* = 7.8 Hz, 1H), 7.89 (td, *J* = 7.7, 1.7 Hz, 1H), 7.48 – 7.42 (m, 1H), 6.72 – 6.68 (m, 2H), 3.81 (s, 3H), 1.48 (s, 9H).

^{13}C {^{1}H} NMR (126 MHz,CDCl$_3$): δ 161.4, 155.8, 150.6, 148.2, 146.2, 137.6, 126.5, 126.1, 122.2, 120.2, 109.5, 108.0, 81.2, 55.6, 28.9.

HRMS-ESI: calcd. For $C_{17}H_{20}N_2O_3Na$ (M+Na)+: 323.1372 Found: 323.1388

N-(4-(benzyloxy)-2-(tert-butoxy)phenyl)picolinamide(4f):

Yellow sticky liquid, (42.8 mg, 57%) (n-hexane/EtOAc: 95:5).



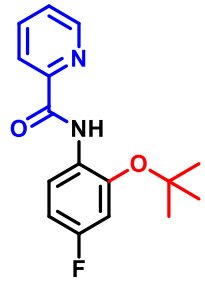
^{1}H NMR (600 MHz, CDCl$_3$): δ 10.65 (s, 1H), 8.62 (d, *J* = 4.5 Hz, 1H), 8.54 (d, *J* = 8.2 Hz, 1H), 8.28 (d, *J* = 7.4 Hz, 1H), 7.89 (t, *J* = 8.0 Hz, 1H), 7.45 (d, *J* = 8.0 Hz, 3H), 7.39 (t, *J* = 7.5 Hz, 2H), 7.33 (t, *J* = 6.9 Hz, 1H), 6.78 (d, *J* = 9.2 Hz, 2H), 5.05 (s, 2H), 1.45 (s, 9H).

^{13}C {^{1}H} NMR (151 MHz, CDCl$_3$): δ 161.4, 155.0, 150.6, 148.2, 146.1, 137.6, 137.1, 128.7, 128.1, 127.7, 126.8, 126.2, 122.3, 120.2, 110.5, 109.2, 81.3, 70.5, 28.9.

HRMS-ESI: calcd. For $C_{23}H_{24}N_2O_3Na$ (M+Na)+: 399.1685 Found: 399.1695

N-(2-(tert-butoxy)-4-fluorophenyl)picolinamide(4g)

Yellow liquid, (20 mg, 32%) (n-hexane/EtOAc: 95:5).



^{1}H NMR (600 MHz, $CDCl_3$): δ 10.71 (s, 1H), 8.63 (d, J = 4.8 Hz, 1H), 8.61 – 8.57 (m, 1H), 8.28 (d, J = 7.9 Hz, 1H), 7.90 (d, J = 13.8 Hz, 1H), 7.47 (dd, J = 8.8, 4.4 Hz, 1H), 6.86 (d, J = 11.0 Hz, 2H), 1.49 (s, 9H)

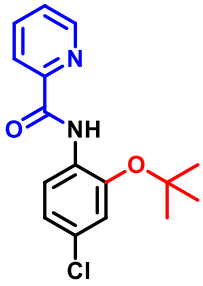
^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$): δ 161.7, 158.5 (d, $^{1}J_{C-F}$ = 244.03 Hz) ,150.3, 148.3, 145.9 (d, $^{3}J_{C-F}$ = 10.9 Hz), 137.7, 129.1, 126.4, 122.4, 120.2 (d, $^{3}J_{C-F}$ = 9.78 Hz), 110.1 (d, $^{2}J_{C-F}$ = 21.8 Hz), 109.8 (d, $^{2}J_{C-F}$ = 23.1Hz), 81.9, 28.9

^{19}F NMR (565 MHz, $CDCl_3$): δ -117.12 - -117.17 (m, $CDCl_3$)

HRMS-ESI: calcd. For $C_{16}H_{17}FN_2O_2Na$ (M+Na)+: 311.1172 Found 311.1183

N-(2-(tert-butoxy)-4-chlorophenyl)Picolinamide(4h)

Yellow sticky liquid, (31.4 mg, 48%) (n-hexane/EtOAc: 95:5).



^{1}H NMR (600 MHz, $CDCl_3$): δ 10.76 (s, 1H), 8.63 (d, J = 5.0 Hz, 1H), 8.58 (d, J = 9.2 Hz, 1H), 8.28 (d, J = 7.6 Hz, 1H), 7.90 (t, J = 7.9 Hz, 1H), 7.47 (dd, J = 7.9, 4.7 Hz, 1H), 7.12 – 7.09 (m, 2H), 1.49 (s, 9H).

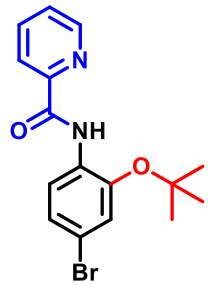
^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$): δ 161.9, 150.2, 148.3, 145.8, 137.8, 131.6, 128.1, 126.5, 123.9, 122.5, 122.4, 120.4, 82.0, 28.9.

HRMS-ESI: calcd. For $C_{16}H_{17}ClN_2O_2Na$ (M+Na)+: 327.0876 Found: 327.0880

N-(4-bromo-2-(tert-butoxy)phenyl)Picolinamide(4i):

Yellow liquid, (37 mg, 53%) (n-hexane/EtOAc: 95:5).

^{1}H NMR (600 MHz, $CDCl_3$): δ 10.77 (s, 1H), 8.63 (d, *J* = 4.6 Hz, 1H), 8.53 (d, *J* = 9.7 Hz, 1H), 8.28 (d, *J* = 7.6 Hz, 1H), 7.93 – 7.88 (m, 1H), 7.48 (dd, *J* = 8.2, 4.4 Hz, 1H), 7.27 – 7.24 (m, 2H), 1.49 (s, 9H)

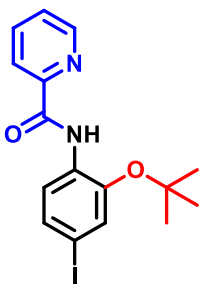


^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$): δ 161.9, 150.2, 148.3, 145.9, 137.8, 132.1, 126.9, 126.5, 125.4, 122.5, 120.7, 115.5, 82.1, 28.9.

HRMS-ESI: calcd. For $C_{16}H_{17}BrN_2O_2Na$ (M+Na)+: 371.0371 Found: 371.0364

N-(2-(tert-butoxy)-4-iodophenyl)picolinamide(4j):

Brown solid, (42 mg, 50%) (n-hexane/EtOAc: 95:5). M.P- 108-110°C



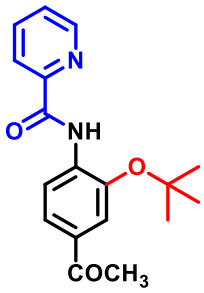
^{1}H NMR (600 MHz, $CDCl_3$): δ 10.77 (s, 1H), 8.64 (d, J = 4.7 Hz, 1H), 8.41 (s, 1H), 8.28 (d, J = 8.0 Hz, 1H), 7.92 – 7.88 (m, 1H), 7.49 – 7.43 (m, 3H), 1.48 (s, 9H).

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$): δ 161.9, 150.2, 148.3, 145.9, 137.8, 133.0, 132.9, 131.2, 126.5, 122.5, 121.2, 85.8, 82.0, 28.9.

HRMS-ESI: calcd. For $C_{16}H_{17}IN_2O_2Na$ (M+Na)+: 419.0232 Found: 419.0212

N-(4-acetyl-2-(tert-butoxy)phenyl)Picolinamide(4k):

White Solid, (30.4 mg, 52%) (n-hexane/EtOAc: 95:5). M.P.- 126-128°C



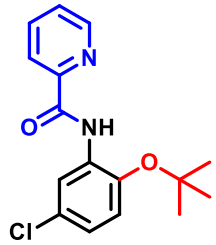
^{1}H NMR (600 MHz, $CDCl_3$): δ 11.02 (s, 1H), 8.71 (d, J = 8.2 Hz, 1H), 8.65 (d, J = 4.6 Hz, 1H), 8.30 (d, J = 8.0 Hz, 1H), 7.92 (t, J = 7.7 Hz, 1H), 7.74 (d, J = 7.6 Hz, 2H), 7.50 (dd, J = 7.5, 4.9 Hz, 1H), 2.59 (s, 3H), 1.52 (s, 9H).

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$): δ 197.1, 162.3, 150.0, 148.4, 145.1, 137.8, 137.2, 132.5, 126.7, 125.3, 122.6, 121.1, 118.7, 81.8, 29.0, 26.6.

HRMS-ESI: calcd. For $C_{18}H_{20}N_2O_3Na$ (M+Na)+: 335.1372 Found: 335.1387

N-(2-(tert-butoxy)-5-chlorophenyl)Picolinamide(4n)

Yellow liquid, (31.4 mg, 48%) (n-hexane/EtOAc: 95:5).



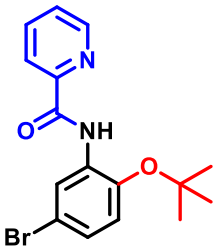
^{1}H NMR (600 MHz, $CDCl_3$): δ 10.80 (s, 1H), 8.69 (d, *J* = 3.1 Hz, 1H), 8.64 (d, *J* = 4.9 Hz, 1H), 8.28 (d, *J* = 8.0 Hz, 1H), 7.91 (t, *J* = 7.6 Hz, 1H), 7.48 (dd, *J* = 7.9, 4.7 Hz, 1H), 7.04 – 6.98 (m, 2H), 1.47 (s, 9H).

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$): δ 161.9, 150.1, 148.4, 143.6, 137.8, 133.8, 129.1, 126.6, 123.3, 123.2, 122.6, 119.8, 81.6, 28.9.

HRMS-ESI: calcd. For $C_{16}H_{17}ClN_2O_2Na$ (M+Na)+: 327.0876 Found: 327.0868

N-(5-bromo-2-(tert-butoxy)phenyl)Picolinamide(4o)

Yellow oil, (33.4 mg, 45%) (n-hexane/EtOAc: 95:5).



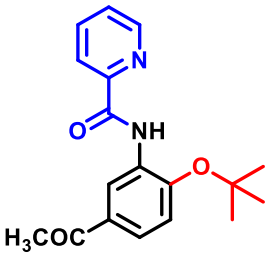
^{1}H NMR (500 MHz, $CDCl_3$): δ 10.79 (s, 1H), 8.84 (d, J = 2.5 Hz, 1H), 8.64 (d, J = 4.7 Hz, 1H), 8.29 (d, J = 7.8 Hz, 1H), 7.96 – 7.88 (m, 1H), 7.52 – 7.46 (m, 1H), 7.14 (dd, J = 8.6, 2.4 Hz, 1H), 6.98 (d, J = 8.6 Hz, 1H), 1.47 (s, 9H).

^{13}C {^{1}H} NMR (121 MHz, $CDCl_3$): δ 161.9, 150.0, 148.3, 144.1, 137.7, 126.5, 126.3, 123.6, 122.5, 116.6, 81.6, 28.9.

HRMS: ESI: calcd. For $C_{16}H_{17}BrN_2O_2$ (M+Na)+:371.0371, Found: 371.0372

N-(5-acetyl-2-(tert-butoxy)phenyl)picolinamide(4p):

Yellow liquid, (36.2 mg, 54%) (n-hexane/EtOAc: 95:5).



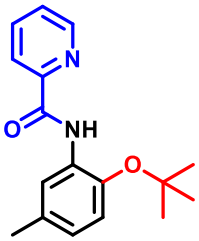
^{1}H NMR (600 MHz, $CDCl_3$): δ 10.86 (s, 1H), 9.28 (s, 1H), 8.65 (d, *J* = 4.8 Hz, 1H), 8.30 (d, *J* = 7.9 Hz, 1H), 7.93 (t, *J* = 7.6 Hz, 1H), 7.72 (d, *J* = 8.3 Hz, 1H), 7.49 (dd, *J* = 8.0, 4.7 Hz, 1H), 7.19 (s, 1H), 2.65 (s, 3H), 1.54 (s, 9H).

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$): δ 197.8, 162.2, 150.1, 149.4, 148.4, 137.8, 132.4, 132.2, 126.6, 123.8, 122.5, 120.8, 120.4, 82.2, 29.1, 26.8.

HRMS-ESI: calcd. For $C_{18}H_{20}N_2O_3Na$ (M+Na)+: 335.1372 Found: 335.1379

N-(2-(tert-butoxy)-5-methylphenyl)picolinamide(4q):

Brown oil, (28.9 mg, total yield = 51%) (n-hexane/EtOAc: 95:5).
Isomers could not be separated.



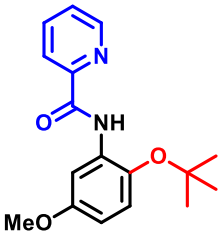
^{1}H NMR (600 MHz, CDCL3): δ 10.78 (s, 1H), 8.63 (d, *J* = 4.8 Hz, 1H), 8.46 (s, 1H), 8.29 (d, *J* = 7.6 Hz, 1H), 7.90 (t, *J* = 8.0 Hz, 1H), 7.47 – 7.44 (m, 1H), 6.99 (d, *J* = 8.0 Hz, 1H), 6.83 (d, *J* = 8.0 Hz, 1H), 2.36 (s, 3H), 1.45 (s, 9H).

^{13}C {^{1}H} NMR (151 MHz, CDCL3): δ 161.8, 150.5, 148.3, 142.7, 137.7, 133.7, 132.6, 126.3, 124.1, 122.4, 120.3, 80.8, 28.9, 21.4.

HRMS-ESI: calcd. For $C_{17}H_{20}N_2O_2Na$ (M+Na)+: 307.1422 Found: 307.1425

N-(2-(tert-butoxy)-5-methoxyphenyl)Picolinamide(4s)

Yellow gummy mass, (36 mg, 60%) (n-hexane/EtOAc: 95:5). Isomers could not be separated.



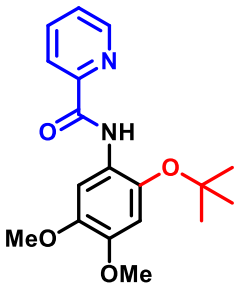
^{1}H NMR (600 MHz, $CDCl_3$): δ 10.80 (s, 1H), 8.63 (d, *J* = 4.6 Hz, 1H), 8.32 (d, *J* = 3.4 Hz, 1H), 8.28 (d, *J* = 8.0 Hz, 1H), 7.89 (t, *J* = 7.5 Hz, 1H), 7.46 (dd, *J* = 8.0, 4.6 Hz, 1H), 7.01 (d, *J* = 9.2 Hz, 1H), 6.58 (dd, *J* = 9.2, 3.4 Hz, 1H), 3.84 (s, 3H), 1.43 (s, 9H).

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$): δ 161.9, 156.0, 150.4, 148.3, 138.5, 137.7, 133.6, 126.4, 123.4, 122.4, 109.5, 104.7, 80.7, 55.7, 28.8.

HRMS: ESI: calcd. For $C_{17}H_{20}N_2O_3Na$ (M+Na)+:323.1372, Found: 323.1360

N-(2-(tert-butoxy)-3,5-dimethoxyphenyl)picolinamide(4u)

Yellow gummy mass, (40.9 mg, 62%) (n-hexane/EtOAc: 95:5).



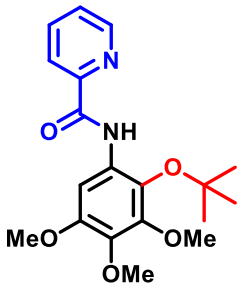
^{1}H NMR (600 MHz, $CDCl_3$): δ 10.65 (s, 1H), 8.62 (d, *J* = 4.6 Hz, 1H), 8.36 (s, 1H), 8.25 (d, *J* = 7.8 Hz, 1H), 7.89 (t, *J* = 7.6 Hz, 1H), 7.49 – 7.42 (m, 1H), 6.68 (s, 1H), 3.94 (s, 3H), 3.84 (s, 3H), 1.43 (s, 9H).

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$): δ 161.4, 150.4, 148.3, 145.2, 144.6, 138.0, 137.7, 126.4, 126.2, 122.2, 108.0, 103.7, 81.0, 56.3, 56.2, 28.8.

HRMS-ESI: calcd. For $C_{18}H_{22}N_2O_4Na$ (M+Na)+: 353.1477 Found: 353.1483

N-(2-(tert-butoxy)-3,4,5-trimethoxyphenyl)Picolinamide(4v)

Yellowish liquid, (34.5 mg, 48%) (n-hexane/EtOAc: 95:5).



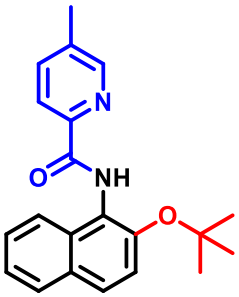
^{1}H NMR (600 MHz, $CDCl_3$): δ 10.62 (s, 1H), 8.62 (d, *J* = 4.5 Hz, 1H), 8.26 (d, *J* = 7.6 Hz, 1H), 8.15 (s, 1H), 7.89 (d, *J* = 6.9 Hz, 1H), 7.47 – 7.44 (m, 1H), 3.91 (s, 3H), 3.87 (s, 6H), 1.45 (s, 9H).

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$): δ 161.8, 150.2, 149.4, 148.5, 148.2, 138.9, 137.7, 133.0, 130.0, 126.4, 122.3, 98.8, 83.3, 61.5, 60.8, 56.2, 29.1.

HRMS-ESI: calcd. For $C_{19}H_{24}N_2O_5Na$ (M+Na)+: 383.1583 Found: 383.1579

N-(2-(tert-butoxy)naphthalen-1-yl)-6-methylpicolinamide(5a):

Yellow gummy mass, (48.5 mg, 68%) (n-hexane/EtOAc: 90:10).



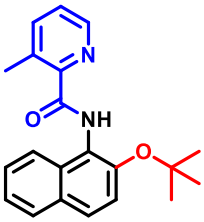
^{1}H NMR (600 MHz, $CDCl_3$): δ 10.21 (s, 1H), 8.54 (d, *J* = 4.4 Hz, 1H), 7.93 (d, *J* = 8.4 Hz, 1H), 7.82 (d, *J* = 8.2 Hz, 1H), 7.72 (d, *J* = 9.0 Hz, 1H), 7.67 (d, *J* = 7.8 Hz, 1H), 7.51 – 7.48 (m, 1H), 7.43 – 7.38 (m, 2H), 7.35 (d, *J* = 8.5 Hz, 1H), 2.81 (s, 3H), 1.39 (s, 9H).

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$): δ 164.8, 148.0, 147.5, 145.7, 141.1, 136.2, 131.0, 130.7, 128.0, 127.2, 126.6, 126.2, 126.0, 124.9, 124.6, 123.7, 80.9, 29.3, 20.8.

HRMS-ESI: calcd. For $C_{21}H_{22}N_2O_2Na$ (M+H)+: 335.1760 Found: 335.1742

N-(2-(tert-butoxy)naphthalen-1-yl)-3-methylpicolinamide(5b):

Brown liquid, (43.5 mg, 61%) (n-hexane/EtOAc: 90:10).



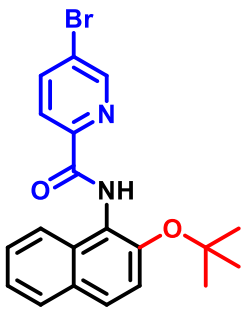
^{1}H NMR (500 MHz, $CDCl_3$): δ 10.19 (s, 1H), 8.06 (d, *J* = 7.6 Hz, 1H), 7.82 (d, *J* = 8.4 Hz, 1H), 7.75 – 7.68 (m, 2H), 7.64 (d, *J* = 8.9 Hz, 1H), 7.43 – 7.38 (m, 1H), 7.35 – 7.30 (m, 1H), 7.26 (d, *J* = 8.7 Hz, 2H), 2.57 (s, 3H), 1.31 (s, 9H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$): δ 163.3, 157.3, 149.4, 147.6, 137.74, 131.0, 130.2, 127.9, 127.2, 126.3, 126.1, 126.0, 124.9, 124.8, 123.4, 119.8, 80.9, 29.2,24.3.

HRMS-ESI: calcd. For $C_{21}H_{23}N_2O$ (M+H)+: 335.1760 Found 335.1757

5-bromo-N-(2-(tert-butoxy)naphthalen-1-yl)Picolinamide(5c)

Yellow liquid, (47.1 mg, 56%) (n-hexane/EtOAc: 90:10).



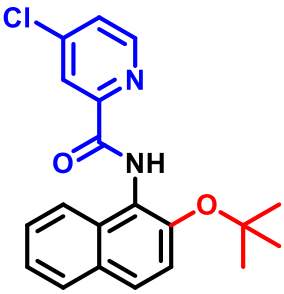
^{1}H NMR (500 MHz, $CDCl_3$): δ 9.94 (s, 1H), 8.76 (d, *J* = 2.1 Hz, 1H), 8.24 (d, *J* = 9.0 Hz, 1H), 8.08 – 8.05 (m, 1H), 7.84 (t, *J* = 9.6 Hz, 2H), 7.75 (d, *J* = 8.9 Hz, 1H), 7.52 – 7.47 (m, 1H), 7.42 (t, *J* = 7.3 Hz, 1H), 7.35 (d, *J* = 8.9 Hz, 1H), 1.38 (s, 9H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$): δ 162.4, 149.6, 148.6, 148.1, 140.3, 130.9, 130.3, 128.1, 127.7, 126.3, 125.6, 124.9, 124.4, 124.3, 124.2, 123.4, 81.0, 29.3.

HRMS-ESI: calcd. For $C_{20}H_{19}BrN_2O_2Na$ (M+Na)+: 421.0528 Found: 421.0519

N-(2-(tert-butoxy)naphthalen-1-yl)-4-chloropicolinamide(5d):

Brown Solid, (39.20 mg, 52%) (n-hexane/EtOAc: 90:10). M.P.-150-152°C



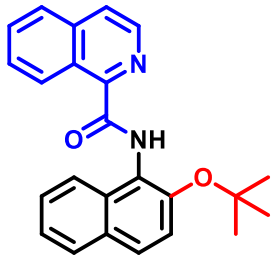
^{1}H NMR (600 MHz, $CDCl_3$): δ 10.02 (s, 1H), 8.59 (d, *J* = 5.2 Hz, 1H), 8.37 (d, *J* = 2.1 Hz, 1H), 7.85 (dd, *J* = 14.3, 8.4 Hz, 2H), 7.75 (d, *J* = 8.9 Hz, 1H), 7.53 – 7.48 (m, 2H), 7.43 (t, *J* = 7.5 Hz, 1H), 7.36 (d, *J* = 8.9 Hz, 1H), 1.39 (s, 9H).

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$): δ 162.0, 151.6, 149.3, 148.1, 146.2, 130.9, 130.3, 128.1, 127.7, 126.7, 126.3, 125.6, 125.0, 124.3, 123.5, 123.4, 81.0, 29.3.

HRMS-ESI: calcd. For $C_{20}H_{19}ClN_2O_2Na$ (M+Na)+: 377.1073 Found: 377.1031

N-(2-(tert-butoxy)naphthalen-1-yl)isoquinoline-1-carboxamide(5e):

Yellow liquid, (51 mg, 65%) (n-hexane/EtOAc: 90:10).



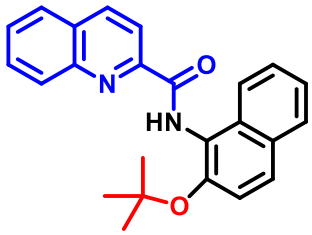
^{1}H NMR (500 MHz, $CDCl_3$): δ 10.38 (s, 1H), 9.72 (d, *J* = 9.1 Hz, 1H), 8.63 (d, *J* = 5.5 Hz, 1H), 8.01 (d, *J* = 8.5 Hz, 1H), 7.91 (t, *J* = 6.5 Hz, 2H), 7.85 (d, *J* = 8.1 Hz, 1H), 7.78 – 7.69 (m, 3H), 7.55 – 7.50 (m, 1H), 7.46 – 7.42 (m, 1H), 7.38 (d, *J* = 8.9 Hz, 1H), 1.42 (s, 9H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$): δ 164.7, 148.2, 148.1, 140.5, 137.7, 131.0, 130.7, 130.5, 129.0, 128.2, 128.1, 127.5, 127.4, 127.0, 126.4, 126.3, 124.9, 124.8, 124.6, 123.7, 81.0,29.3.

HRMS-ESI: calcd. For $C_{24}H_{23}N_2O_2$ (M+H)+: 371.1760 Found: 371.1755

N-(2-(tert-butoxy)naphthalen-1-yl)quinoline-2-carboxamide(5f)

Brown liquid, (44.5 mg, 60%) (n-hexane/EtOAc: 90:10).



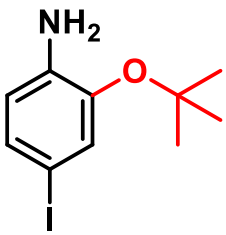
^{1}H NMR (500 MHz, $CDCl_3$): δ 10.44 (s, 1H), 8.47 – 8.38 (m, 2H), 8.24 (d, *J* = 8.5 Hz, 1H), 7.99 – 7.93 (m, 2H), 7.87 – 7.81 (m, 2H), 7.77 (d, *J* = 8.9 Hz, 1H), 7.68 (t, *J* = 7.5 Hz, 1H), 7.52 (t, *J* = 7.7 Hz, 1H), 7.47 – 7.42 (m, 1H), 7.39 (d, *J* = 8.9 Hz, 1H), 1.42 (s, 9H).

^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$): δ 163.3, 149.9, 147.9, 146.7, 137.8, 131.0, 130.3, 129.9, 129.6, 128.2, 128.0, 127.9, 127.4, 126.2, 124.9, 124.7, 123.5, 119.3, 81.1, 29.3.

HRMS-ESI: calcd. For $C_{24}H_{23}N_2O_2$ (M+H)+: 371.1760 Found: 371.1734

2-(tert-butoxy)-4-iodoaniline(7):

Yellow liquid, (51.2 mg, 88%) (n-hexane/EtOAc: 90:10).



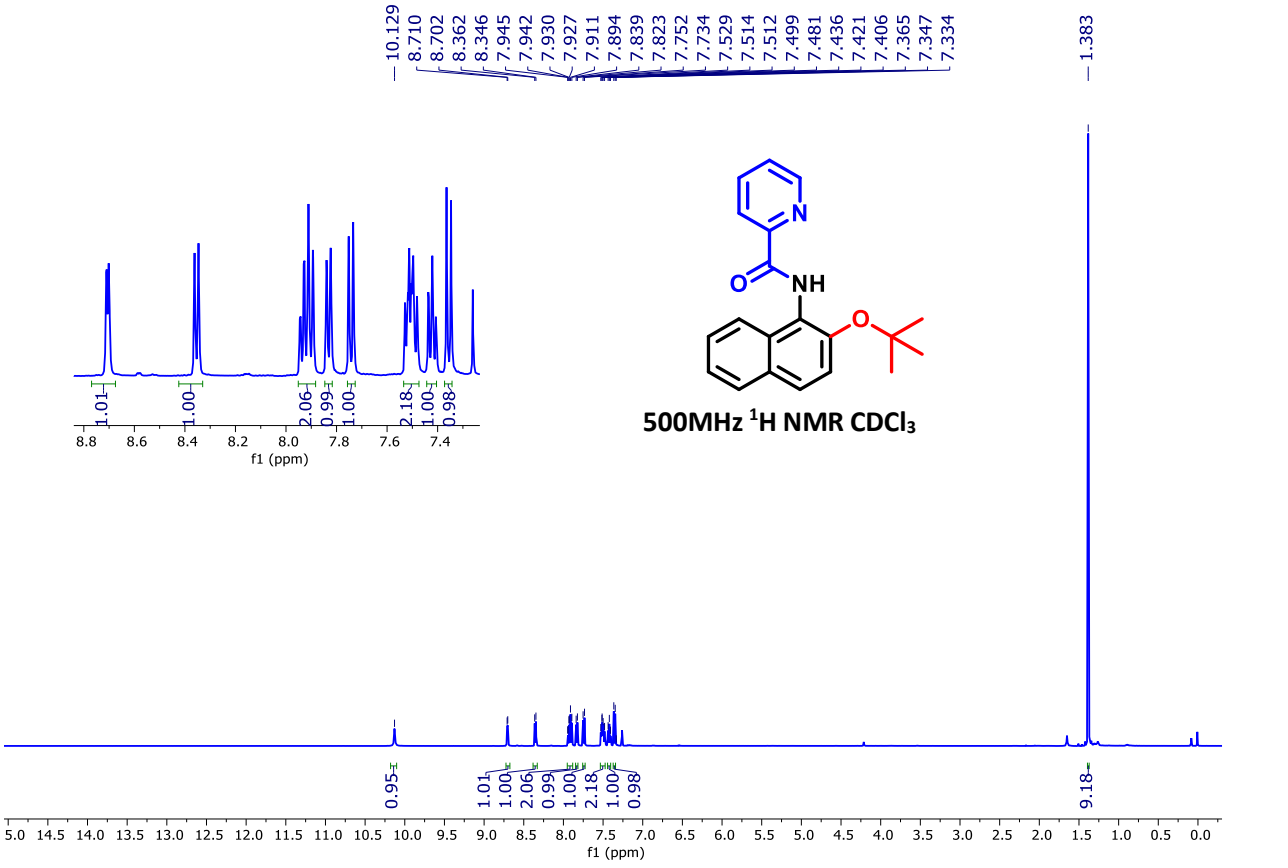
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.23 (d, *J* = 1.7 Hz, 1H), 7.15 (dd, *J* = 8.2, 1.8 Hz, 1H), 6.49 (d, *J* = 8.2 Hz, 1H), 3.81 (s, 2H), 1.40 (s, 9H).

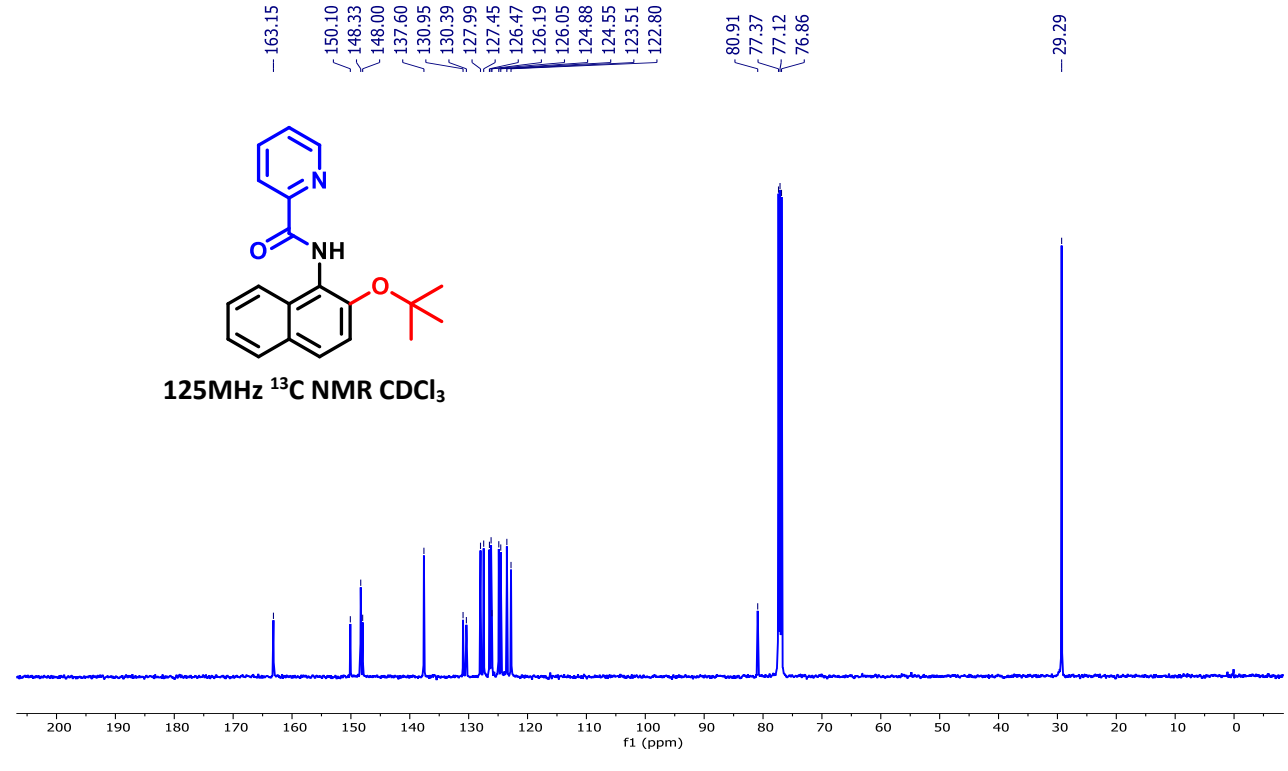
^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$): δ 144.1, 141.2, 132.6, 131.3, 117.3, 80.6, 77.8, 29.0.

HRMS-ESI: calcd. For $C_{10}H_{15}INO$ $(M+H)^+$: 292.0198 Found: 292.0184

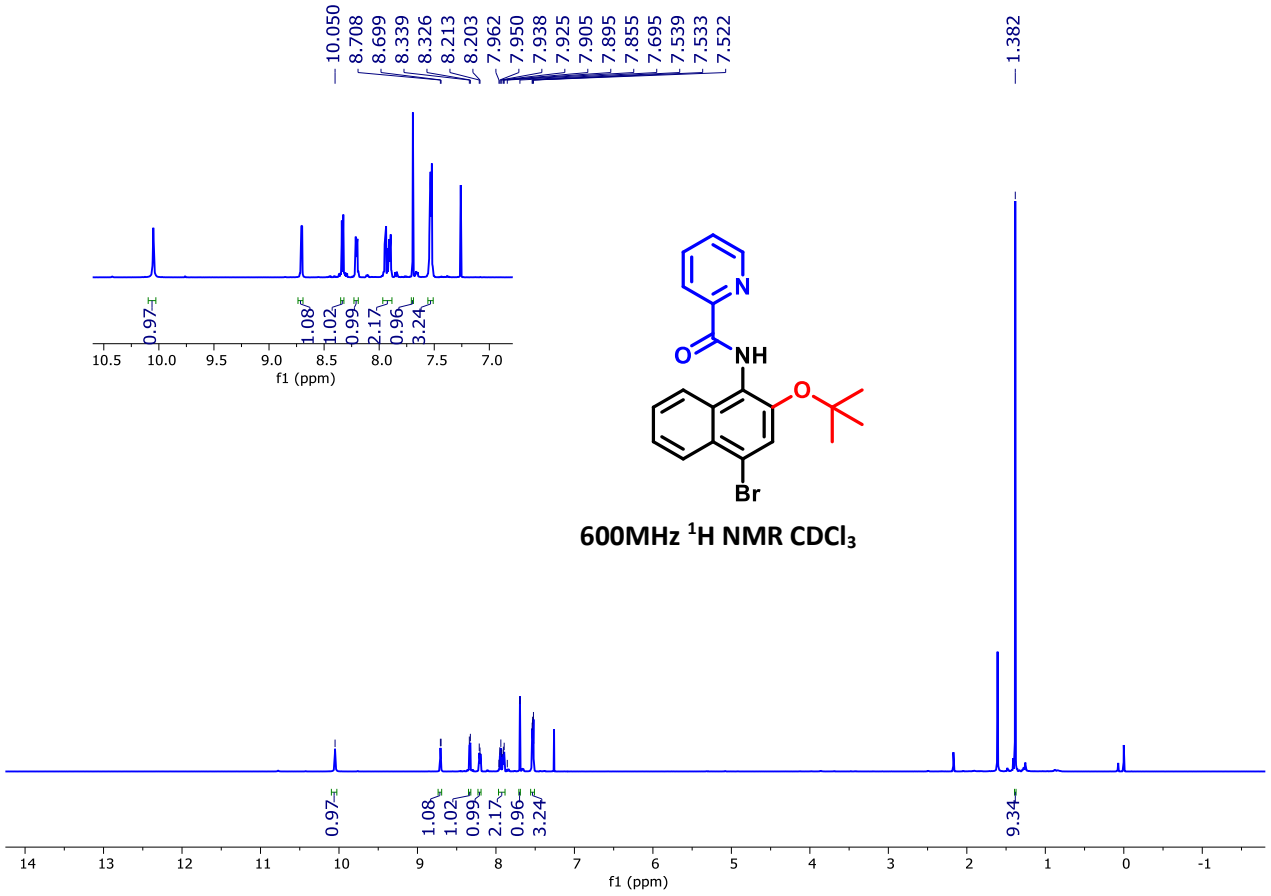
10.2 Copies of ^{1}H NMR , ^{13}C NMR and ^{19}F NMR Spectra :-

N-(2-(tert-butoxy)naphthalen-1-yl)Picolinamide(3a):

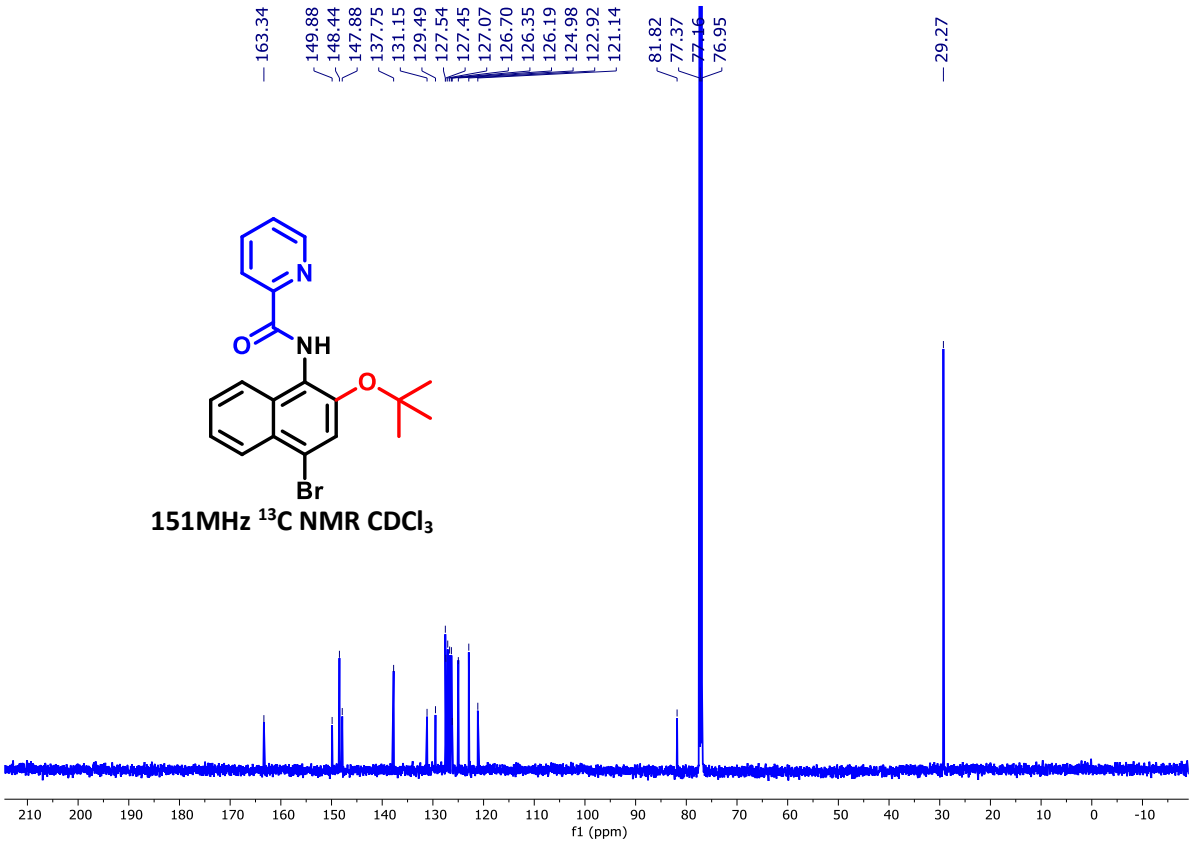




N-(4-bromo-2-(tert-butoxy)naphthalen-1-yl)Picolinamide(3b):

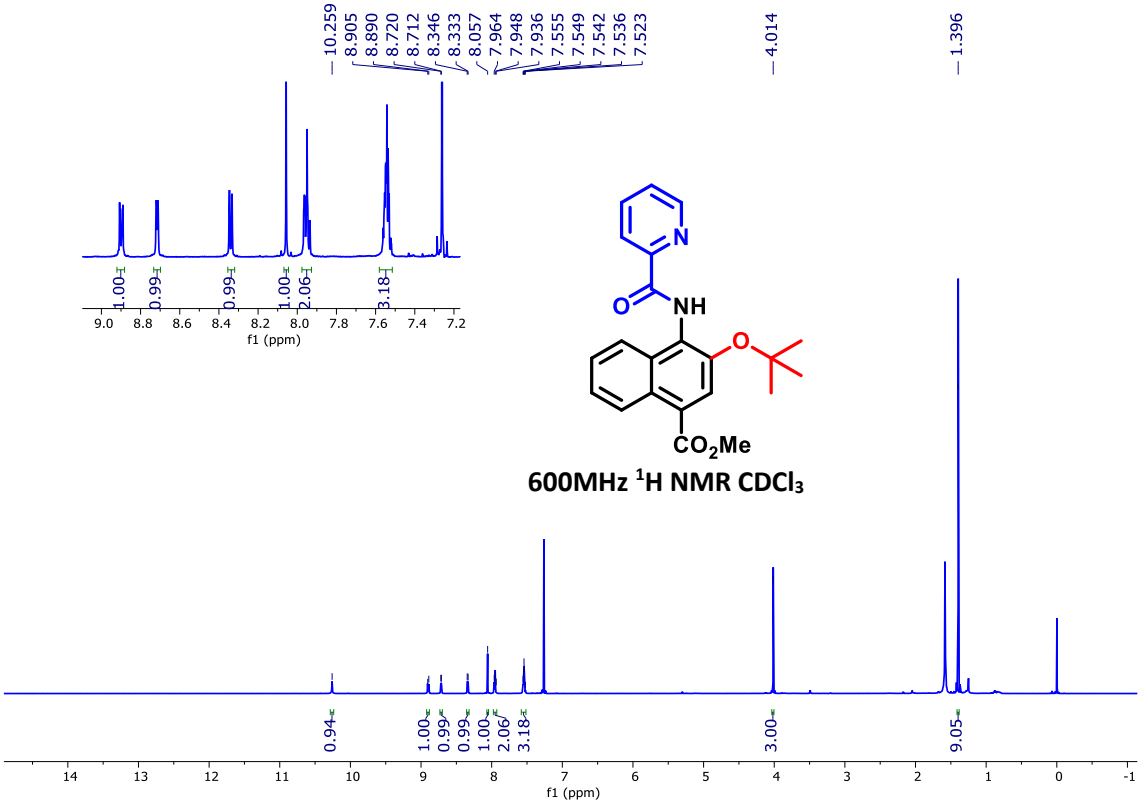


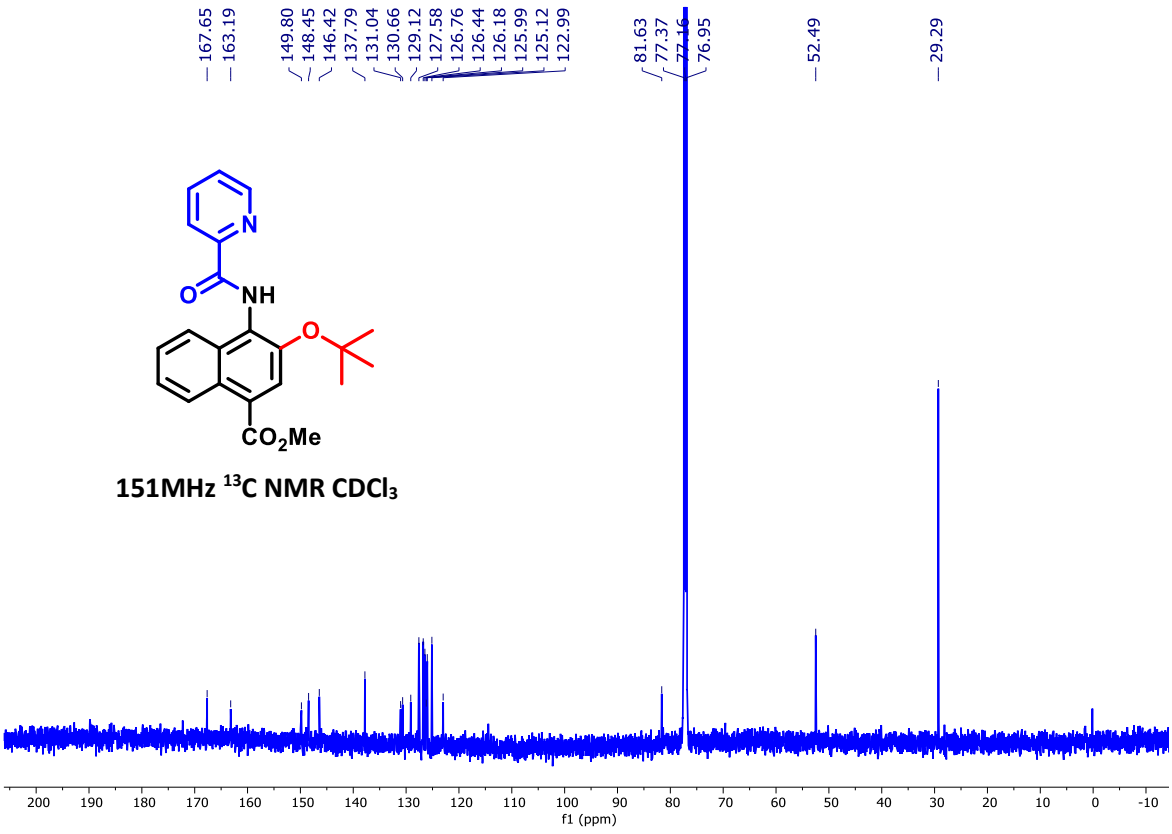
600MHz ^{1}H NMR $CDCl_3$



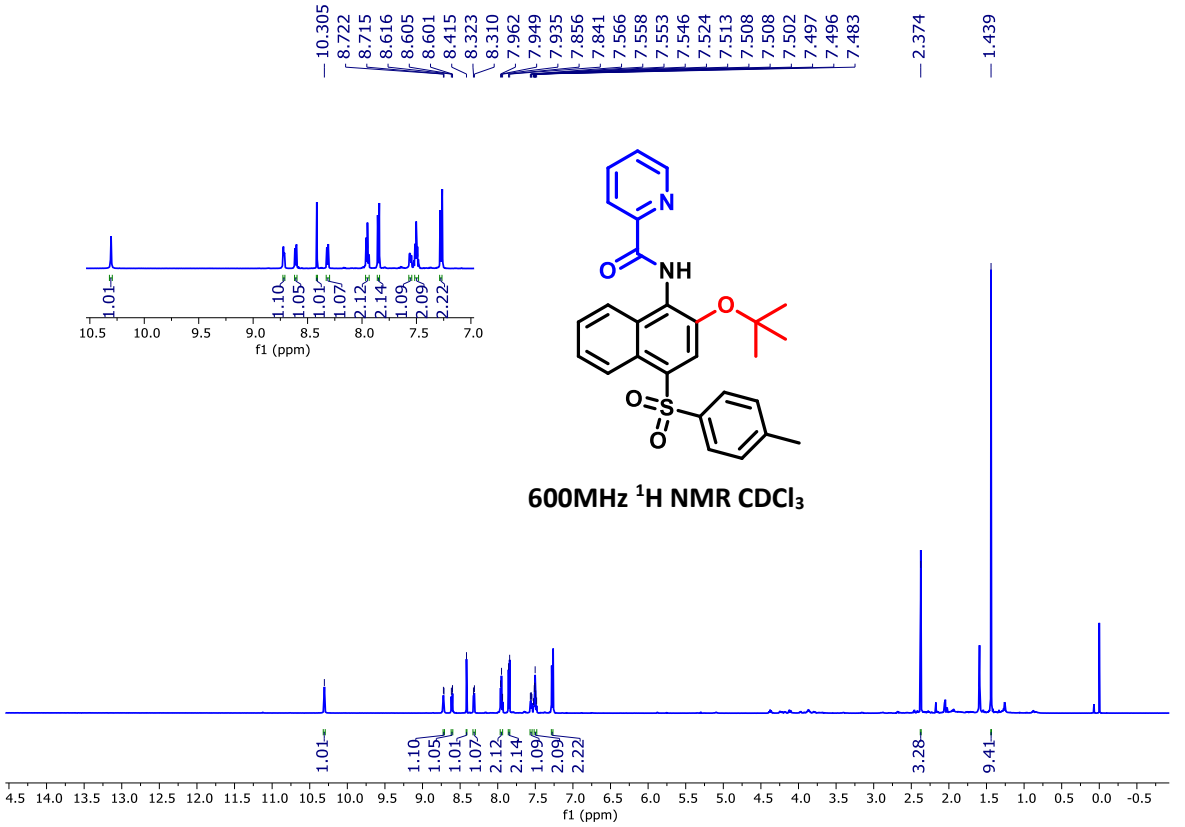
151MHz ^{13}C NMR $CDCl_3$

Methyl 3-(tert-butoxy)-4-(picolinamido)-1-naphthoate(3c):

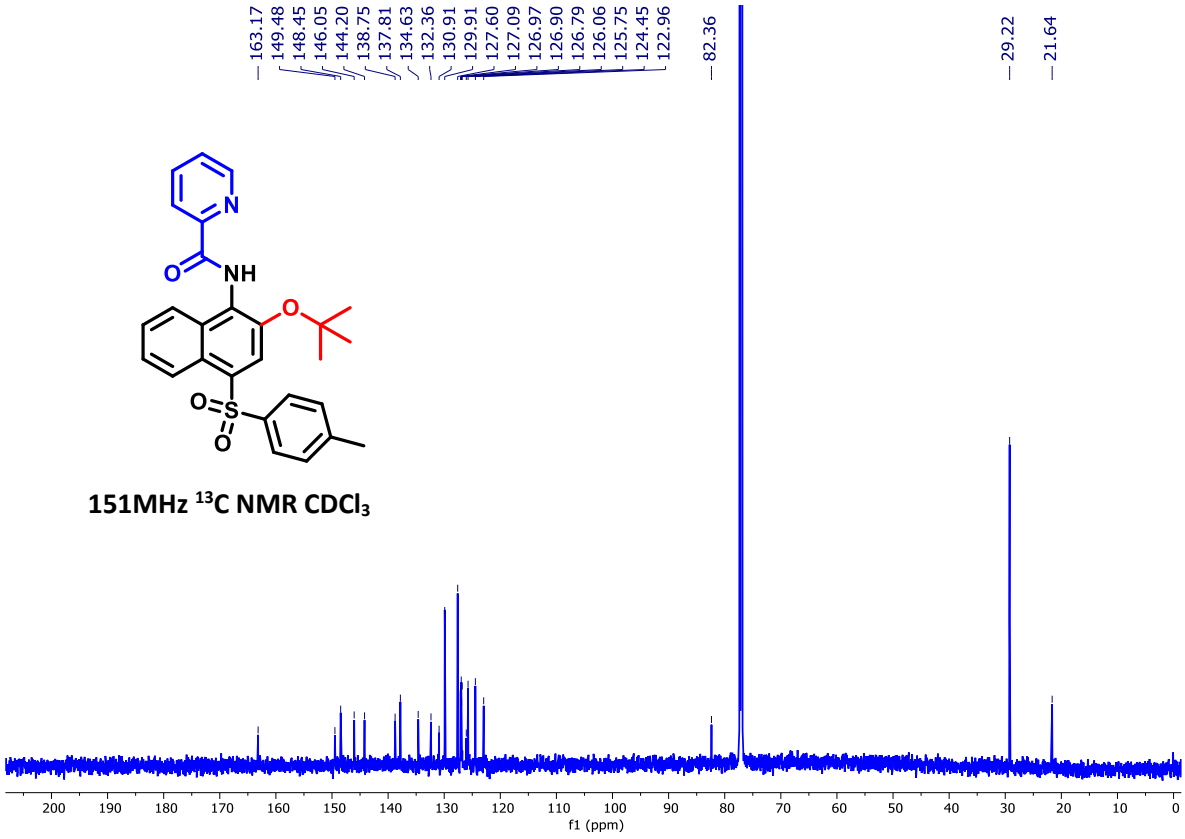




N-(2-(tert-butoxy)-4-tosylnaphthalen-1-yl)picolinamide(3d):

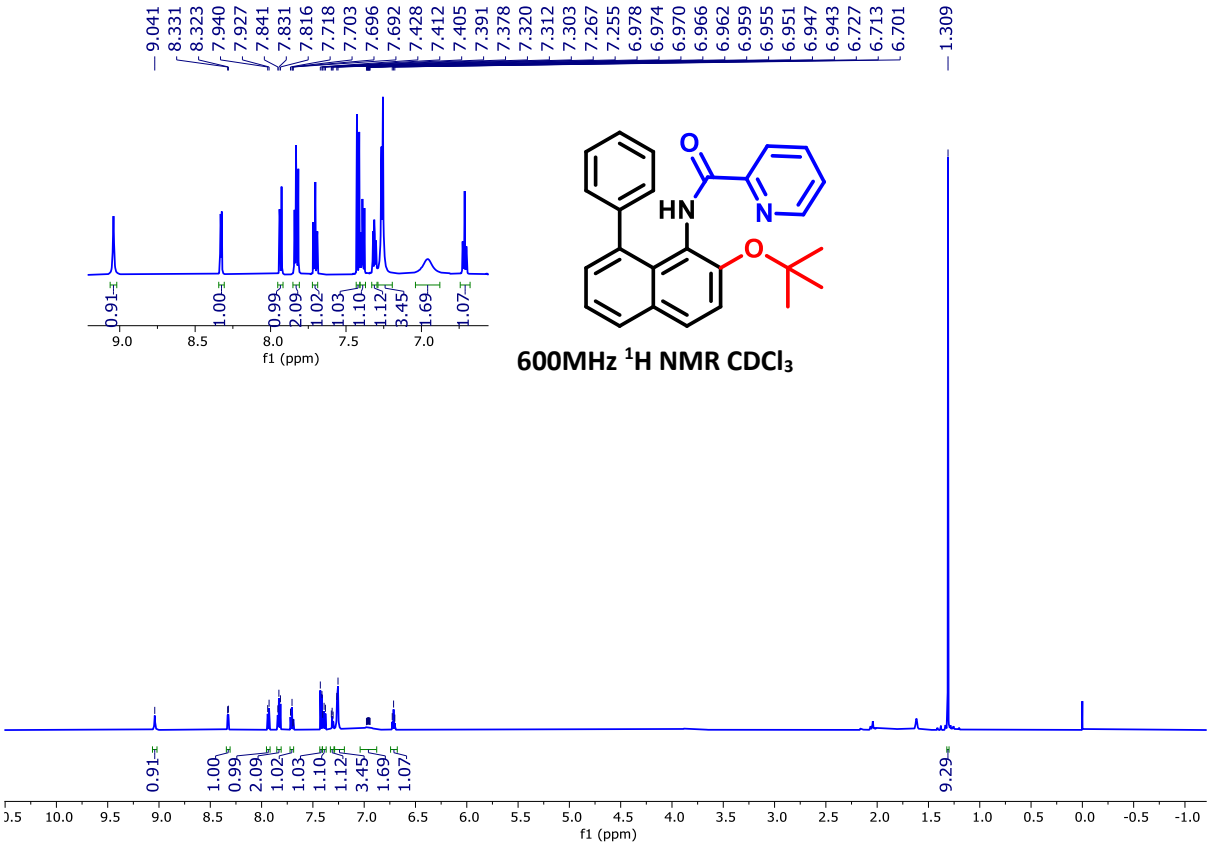


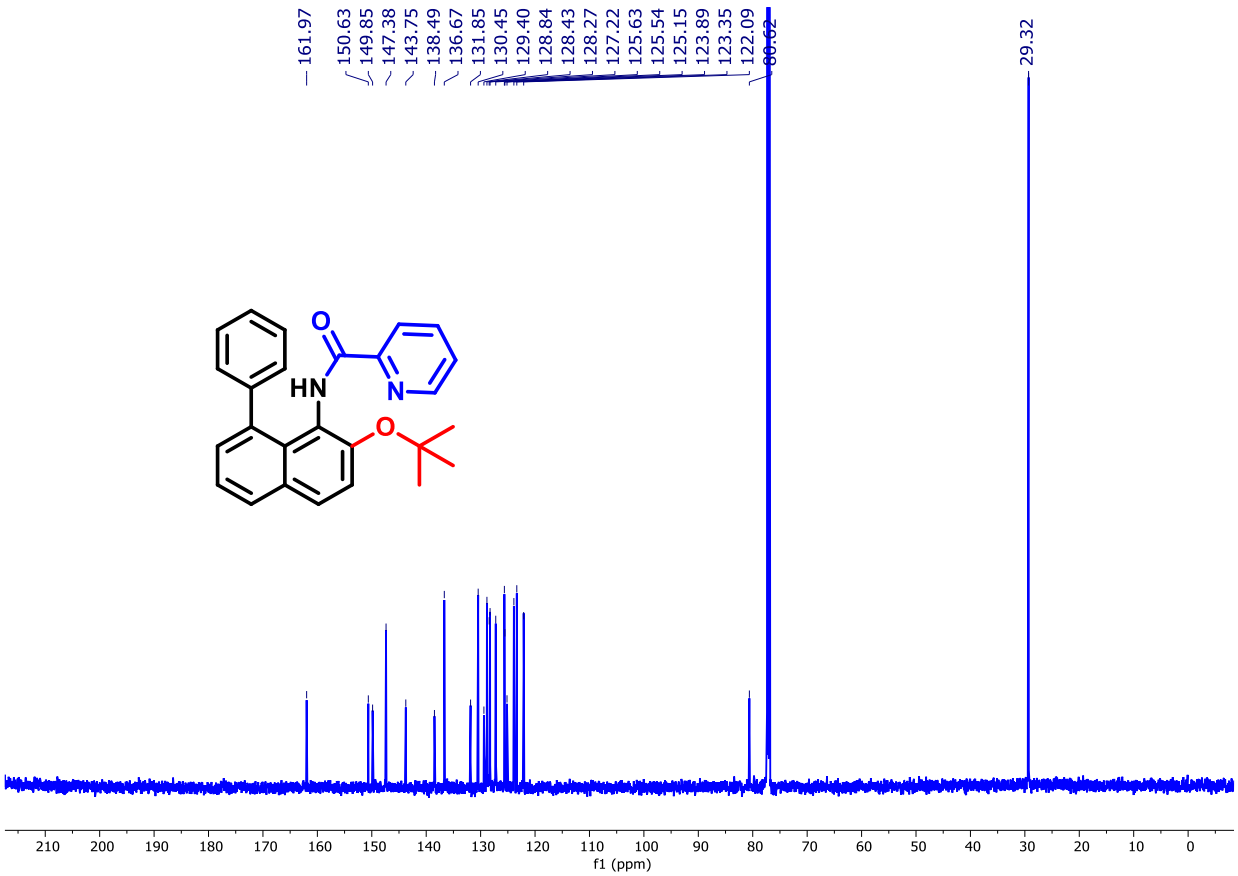
600MHz ^{1}H NMR $CDCl_3$



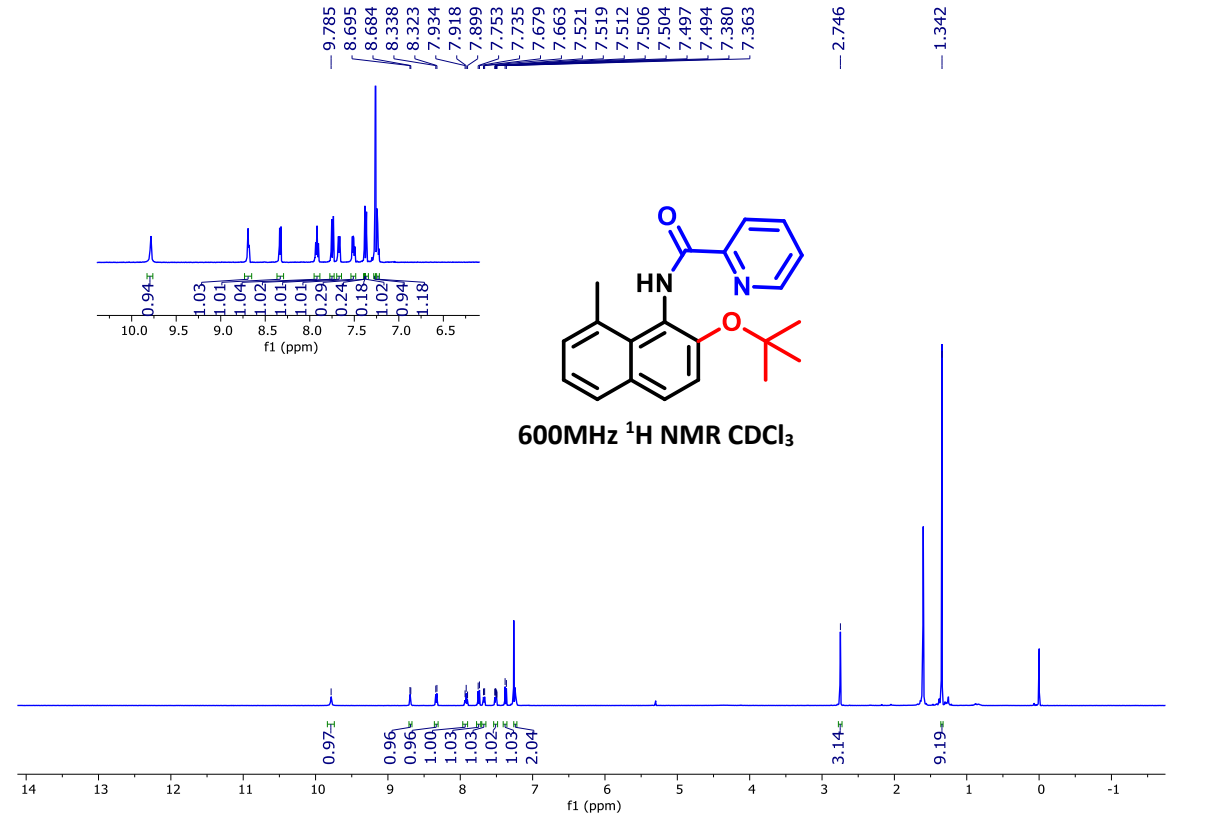
151MHz ^{13}C NMR $CDCl_3$

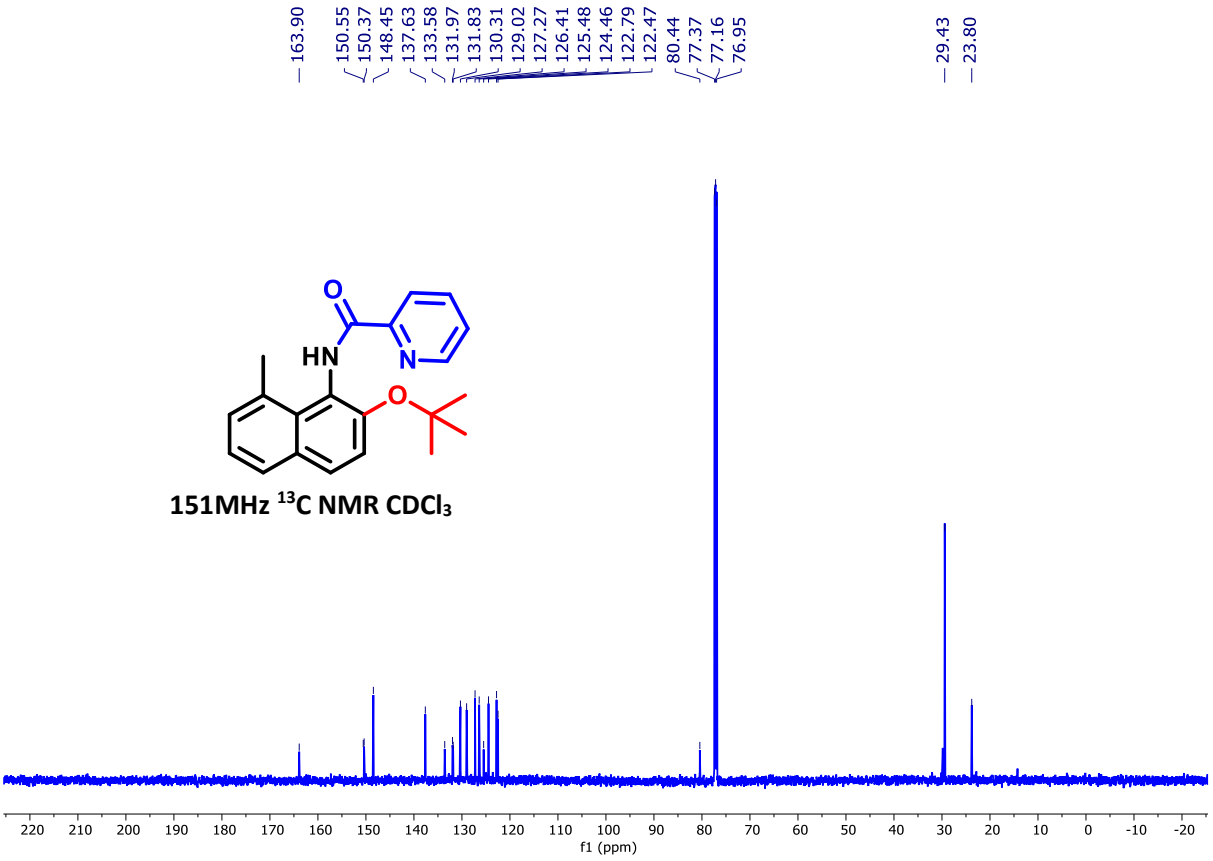
N-(2-(tert-butoxy)-8-phenylnaphthalen-1-yl)Picolinamide(3f):



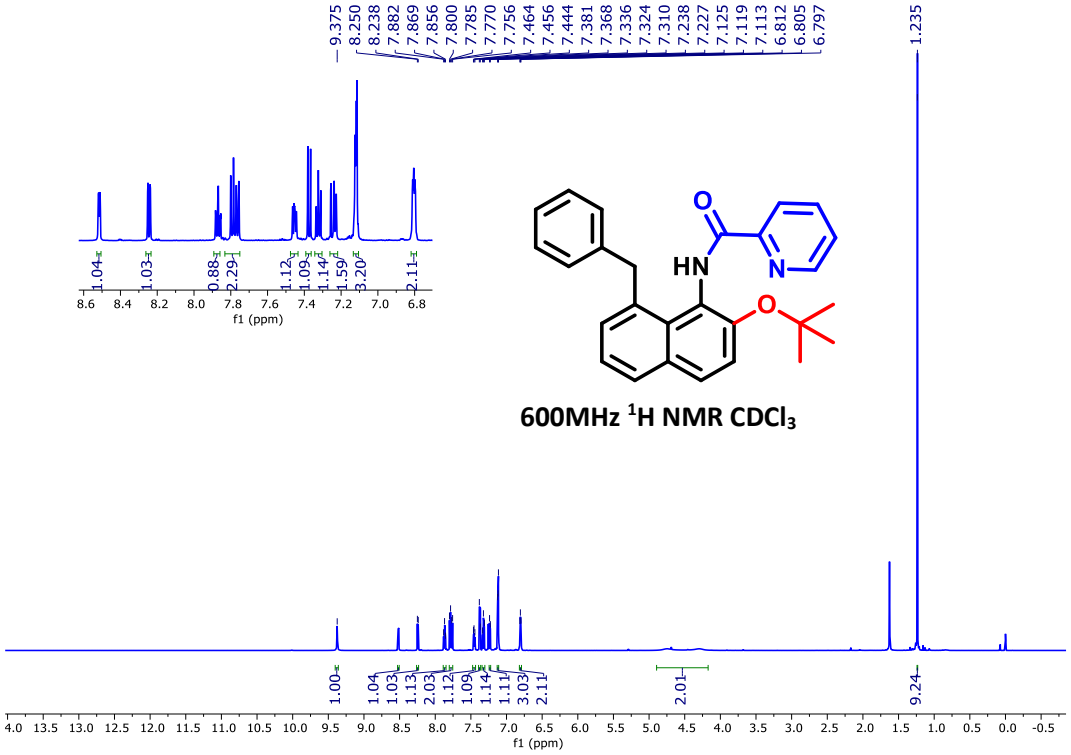


N-(2-(tert-butoxy)-8-methylnaphthalen-1-yl)Picolinamide(3g):

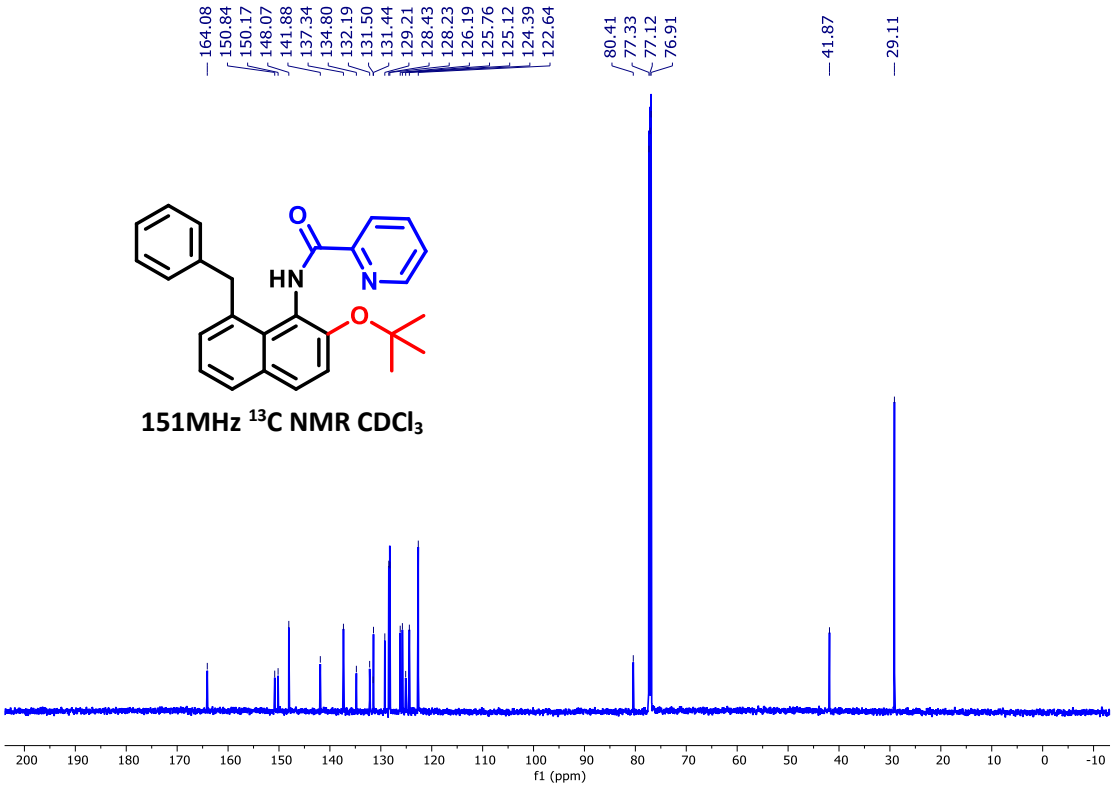




N-(8-benzyl-2-(tert-butoxy)naphthalen-1-yl)Picolinamide(3h):

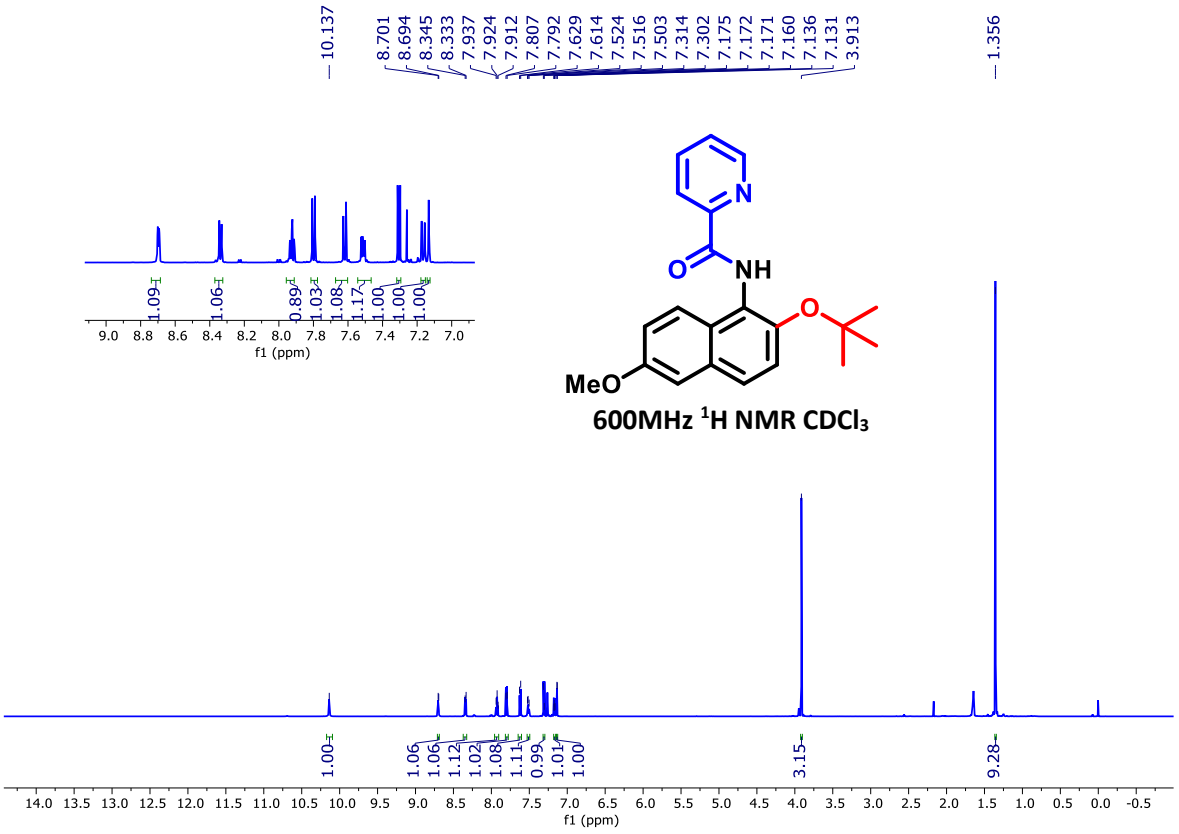


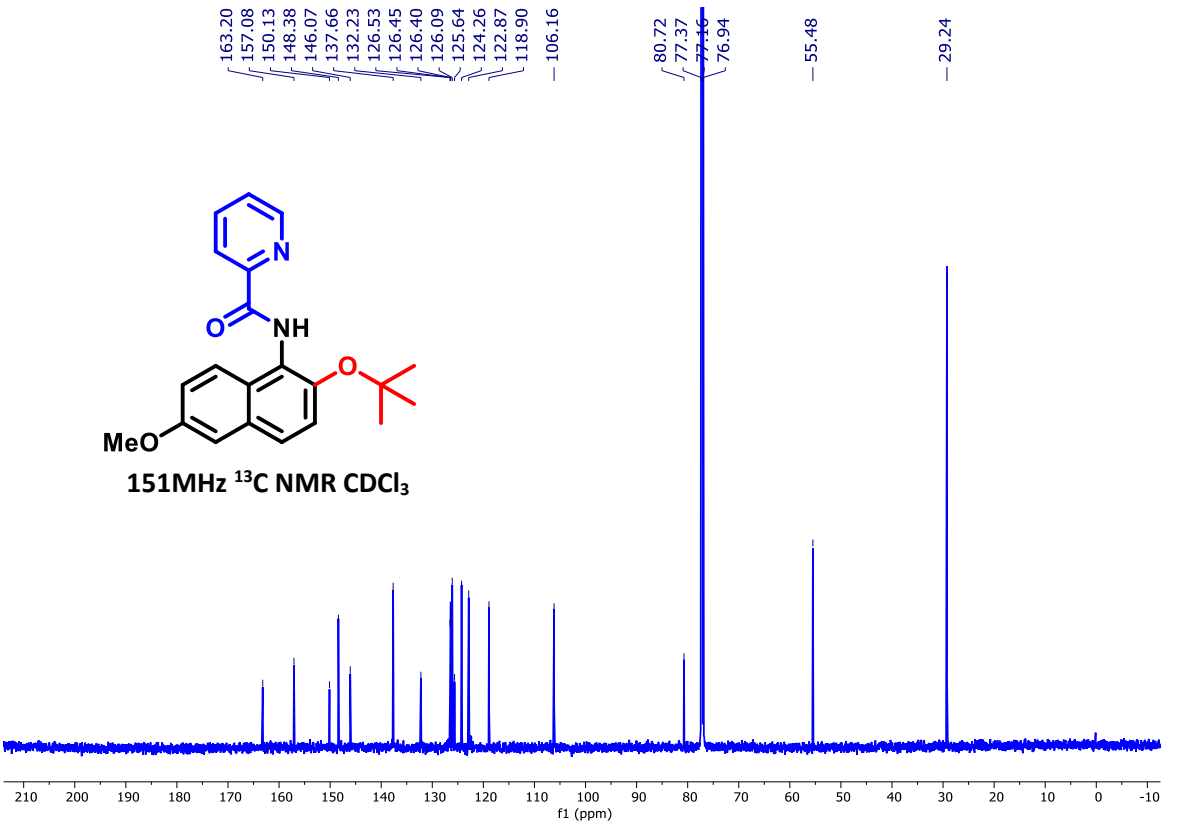
600MHz ^{1}H NMR $CDCl_3$



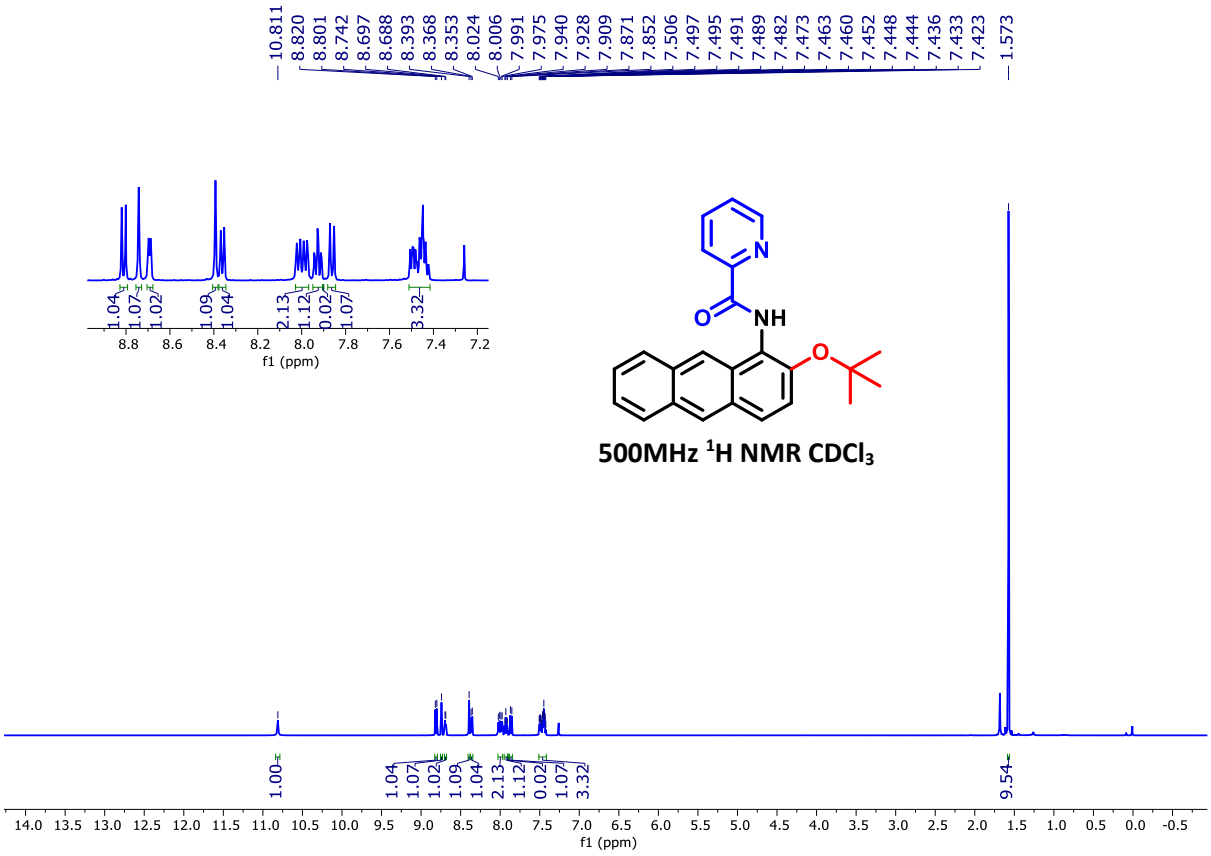
151MHz ^{13}C NMR $CDCl_3$

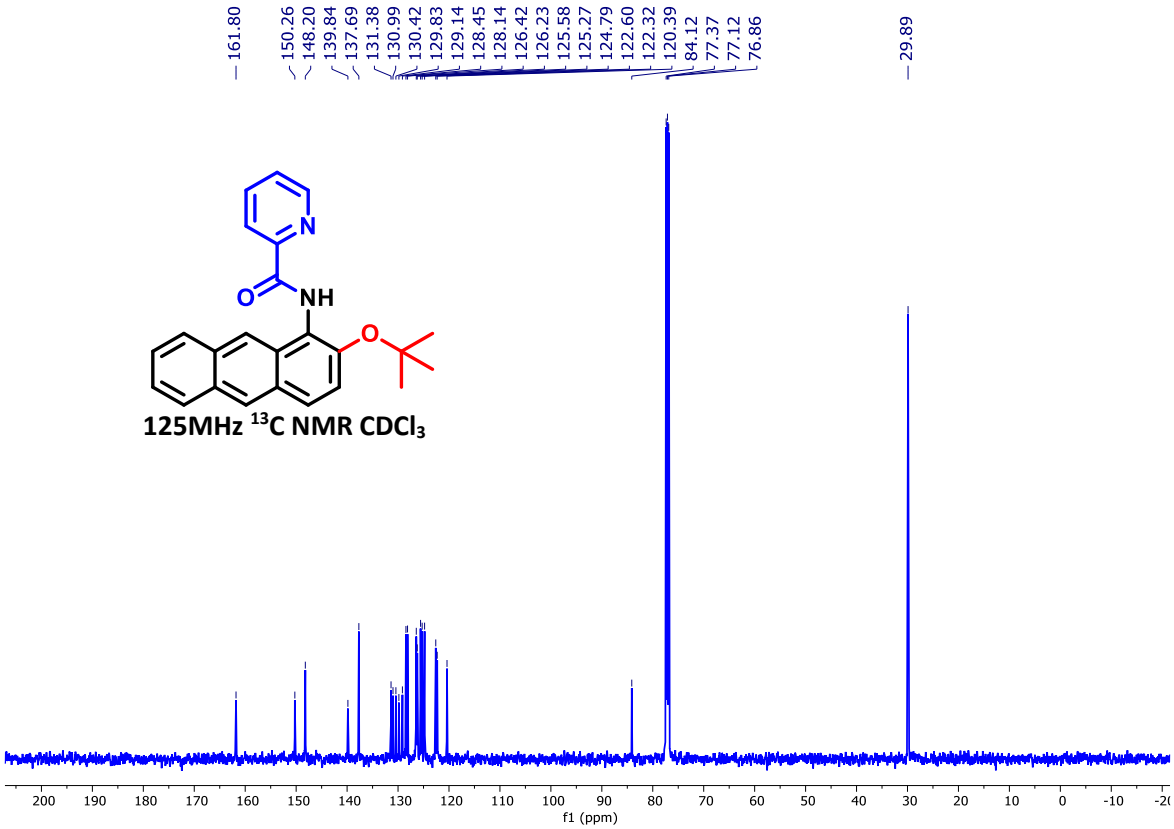
N-(2-(tert-butoxy)-6-methoxynaphthalen-1-yl)Picolinamide(3i)



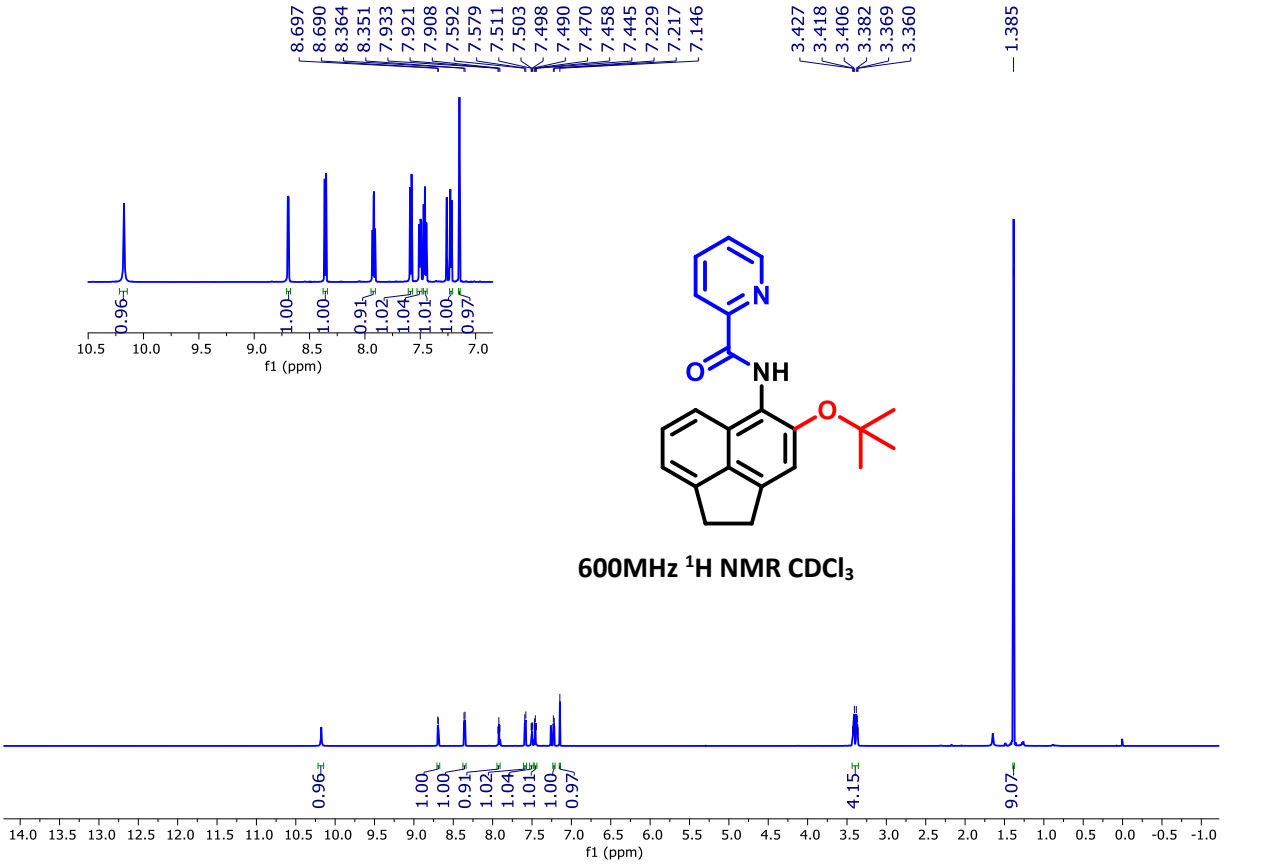


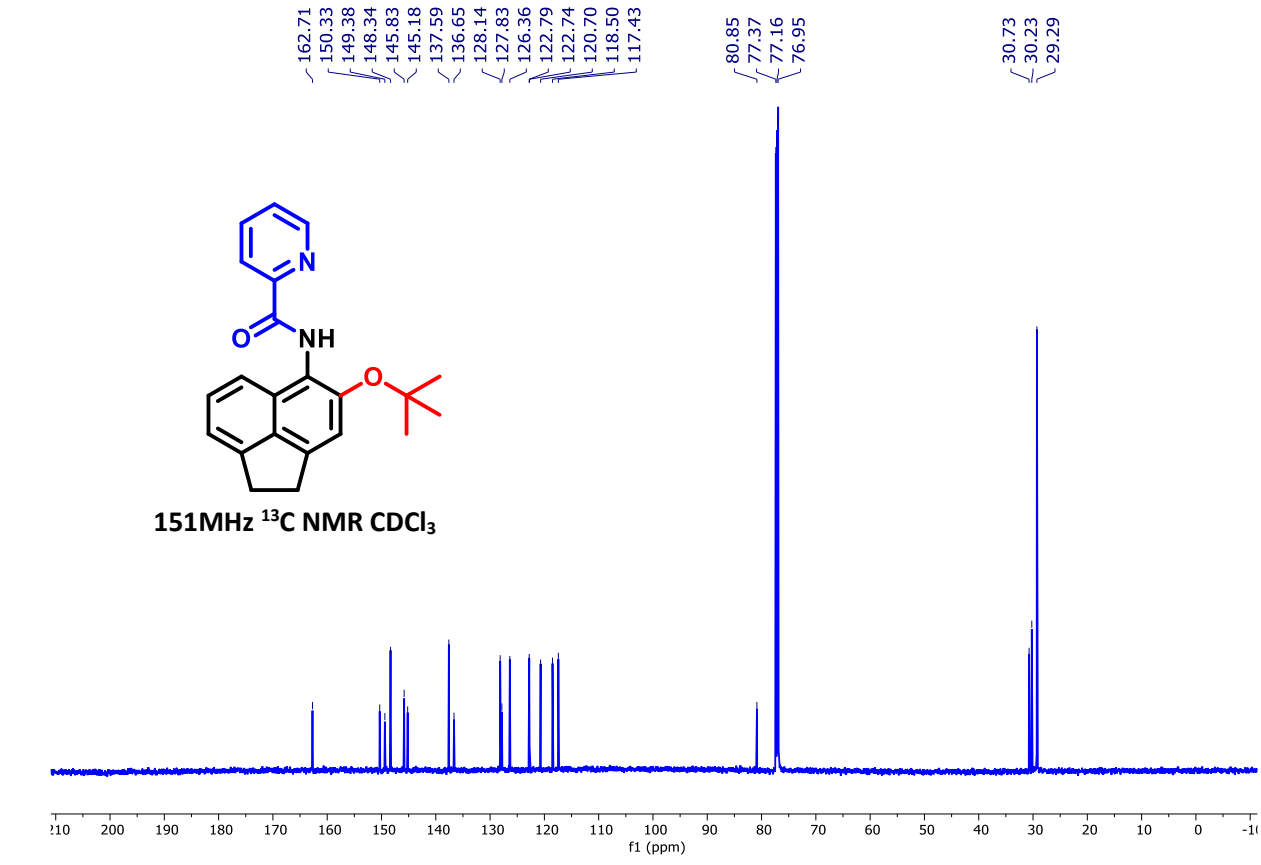
N-(2-(tert-butoxy)anthracen-1-yl)picolinamide(3j)



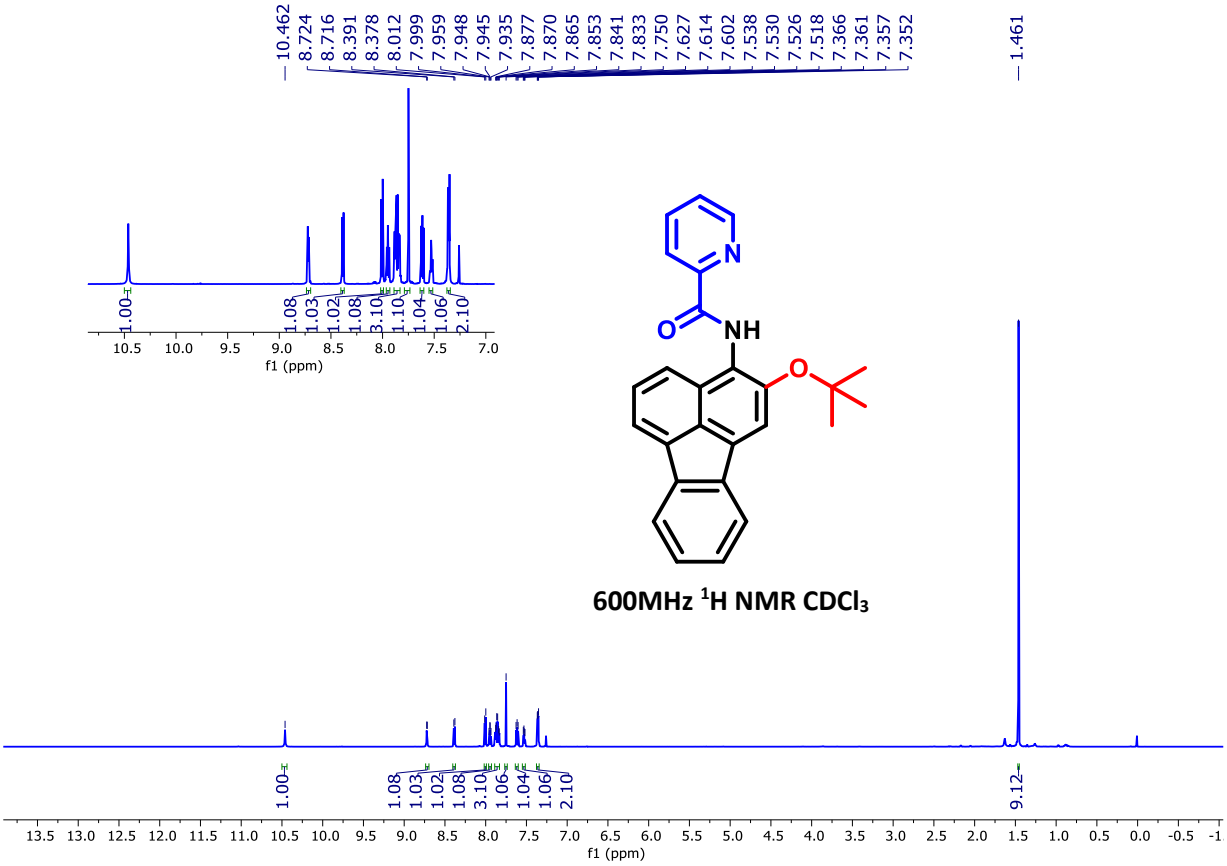


N-(4-(tert-butoxy)-1,2-dihydroacenaphthylen-5-yl)picolinamide(3k)

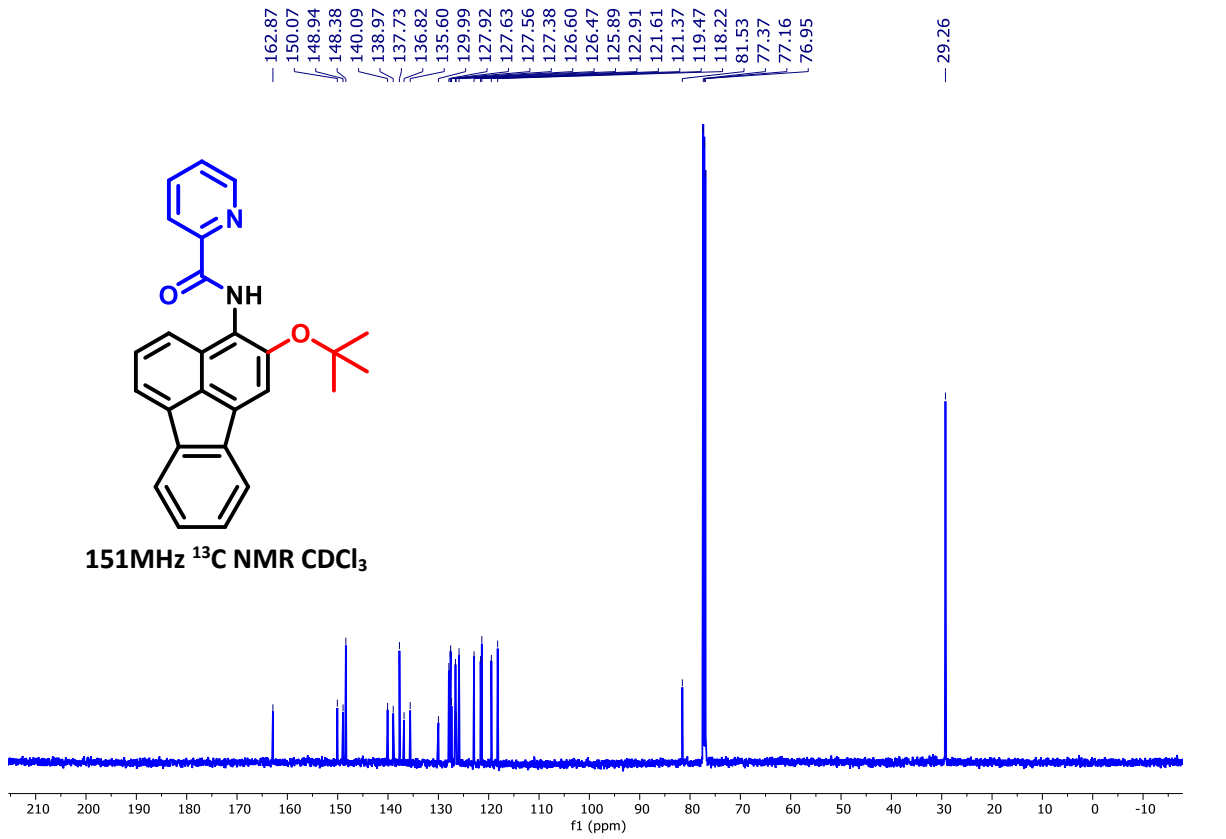




N-(2-(tert-butoxy)fluoranthen-3-yl)Picolinamide(3l)

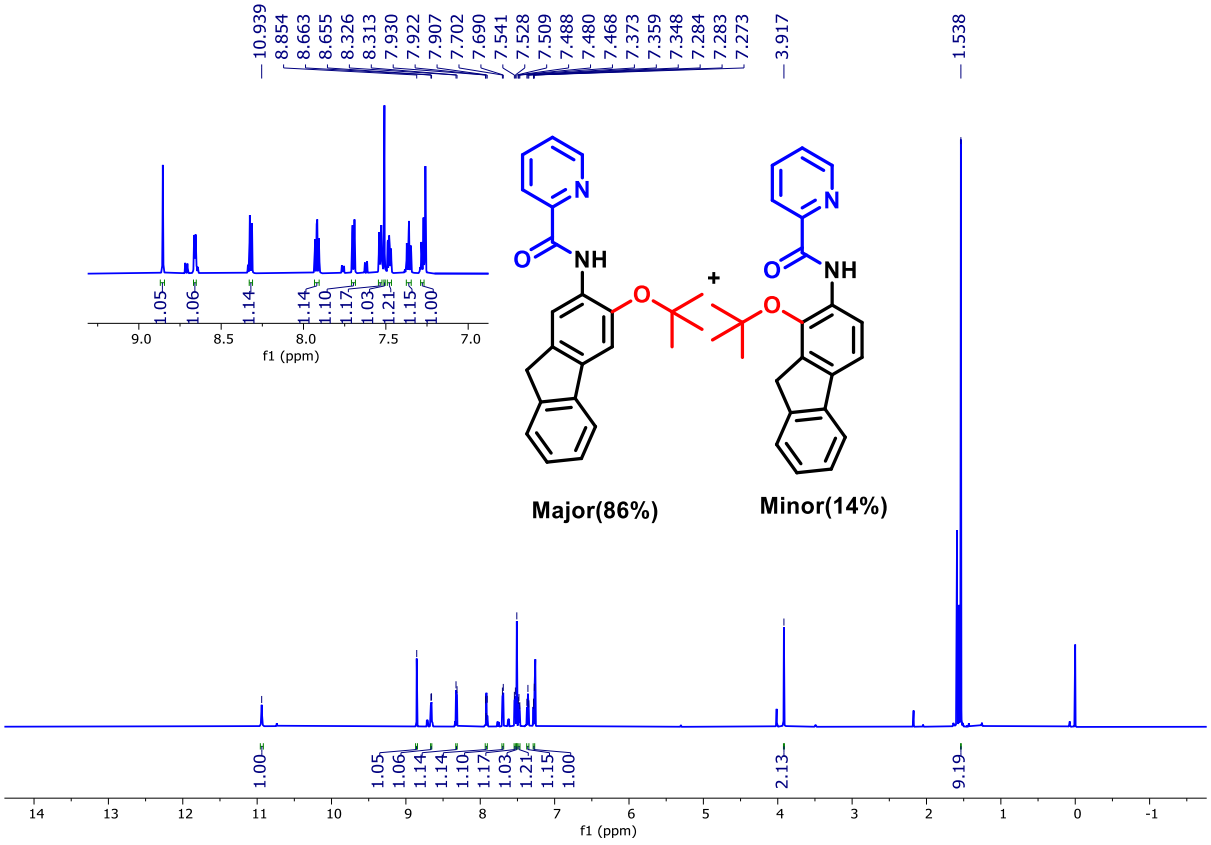


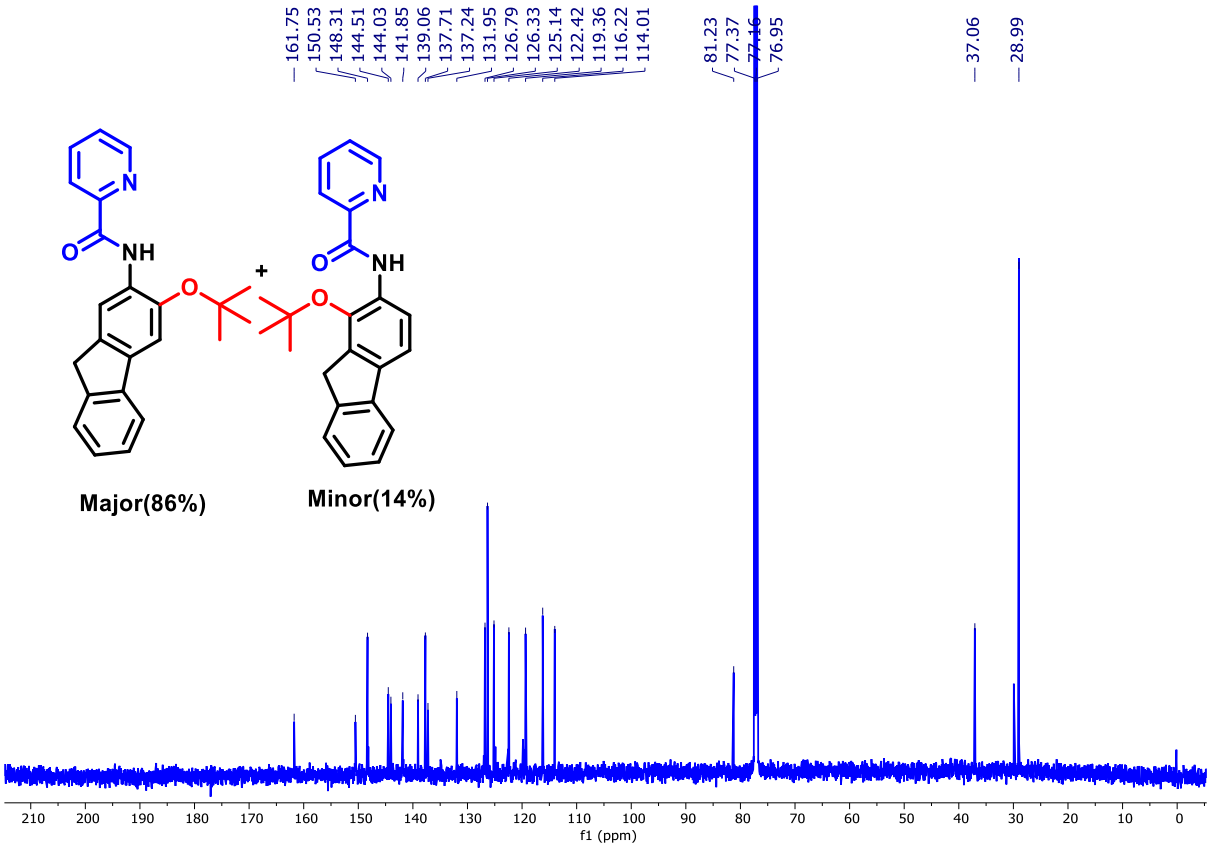
600MHz ^{1}H NMR $CDCl_3$



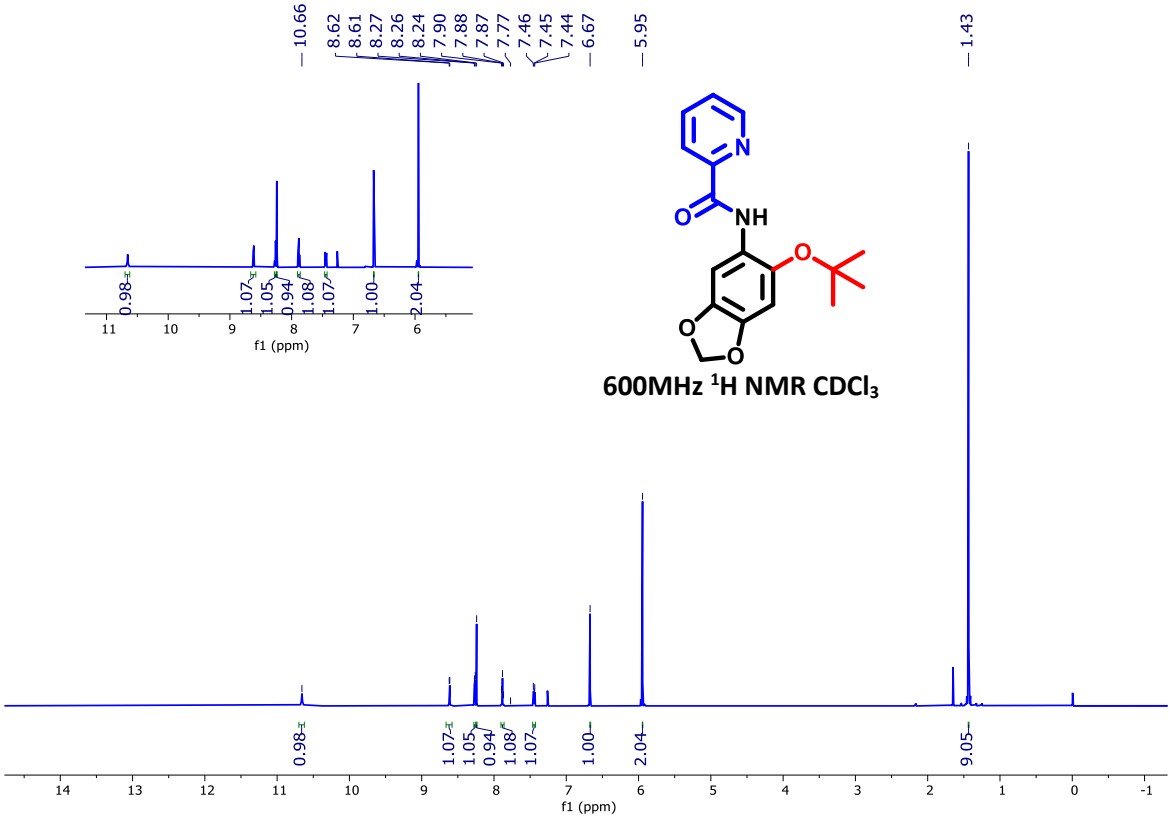
151MHz ^{13}C NMR $CDCl_3$

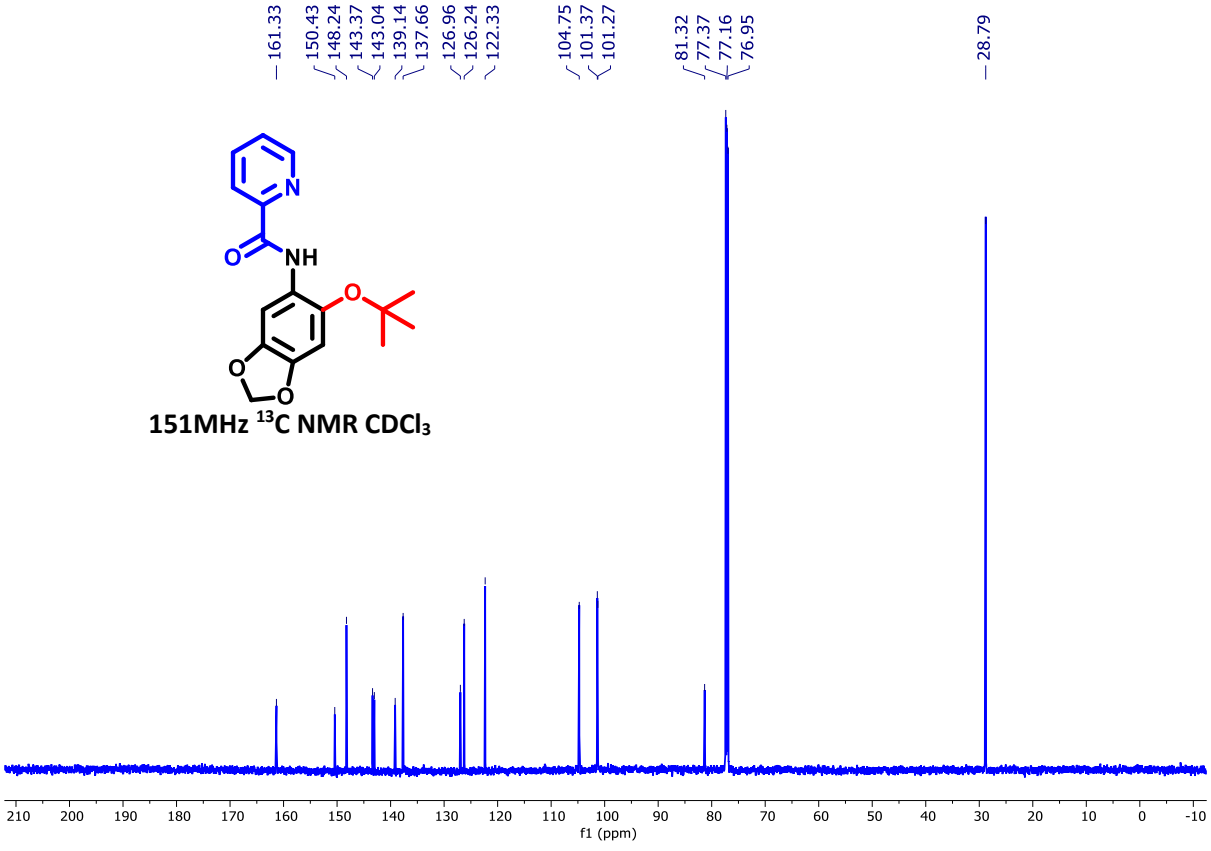
N-(3-(tert-butoxy)-9H-fluoren-2-yl)picolinamide(3n)



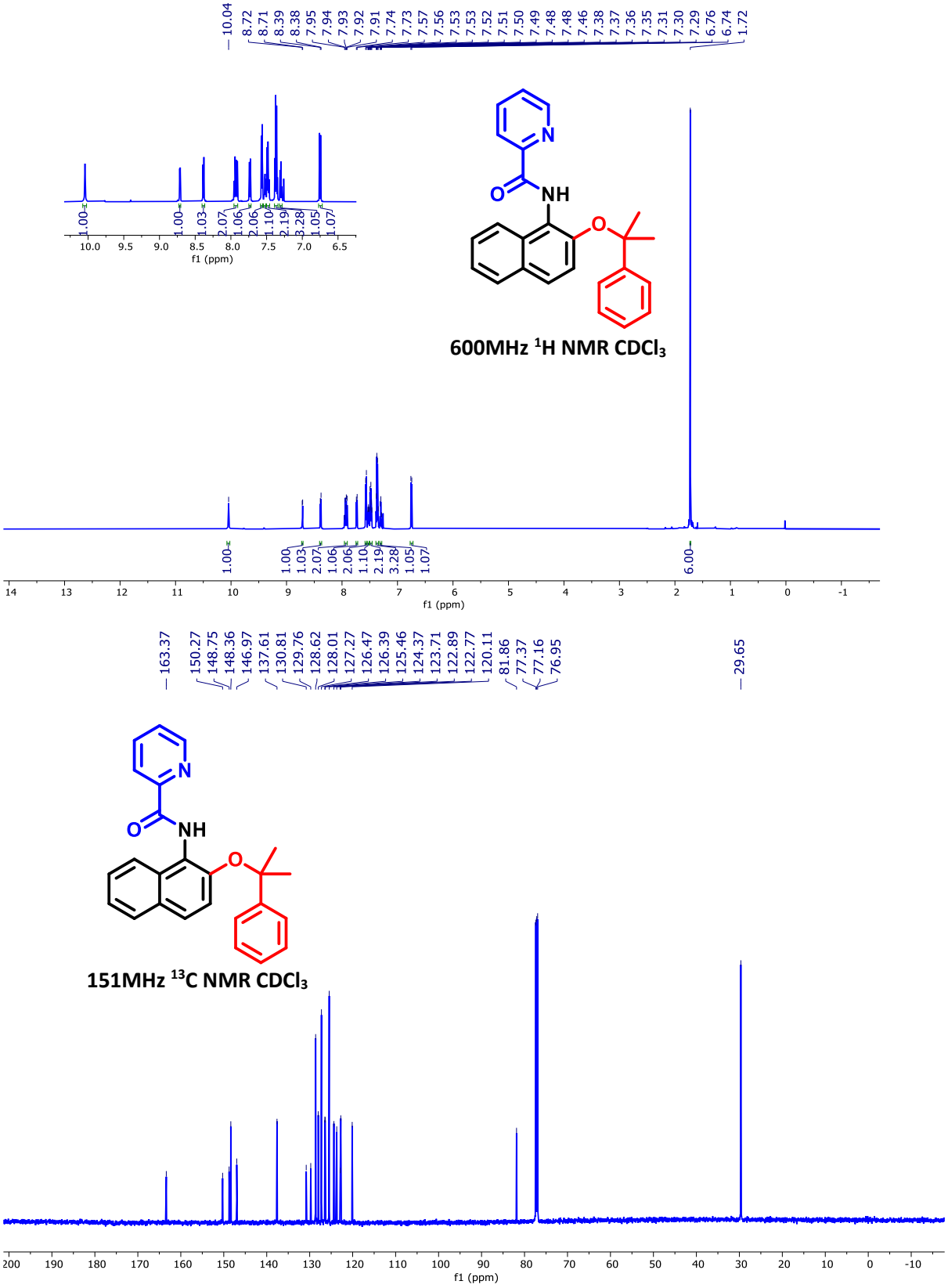


N-(6-(tert-butoxy)benzo[d][1,3]dioxol-5-yl)picolinamide(3o)

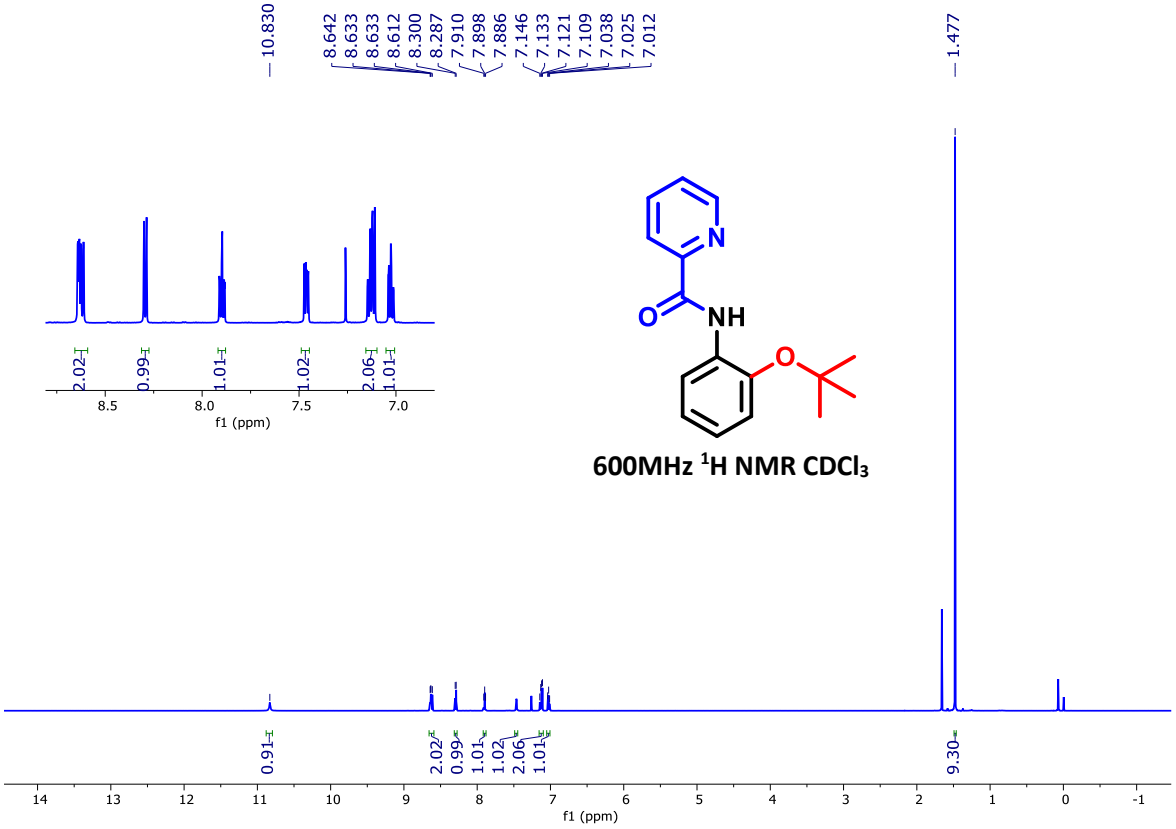


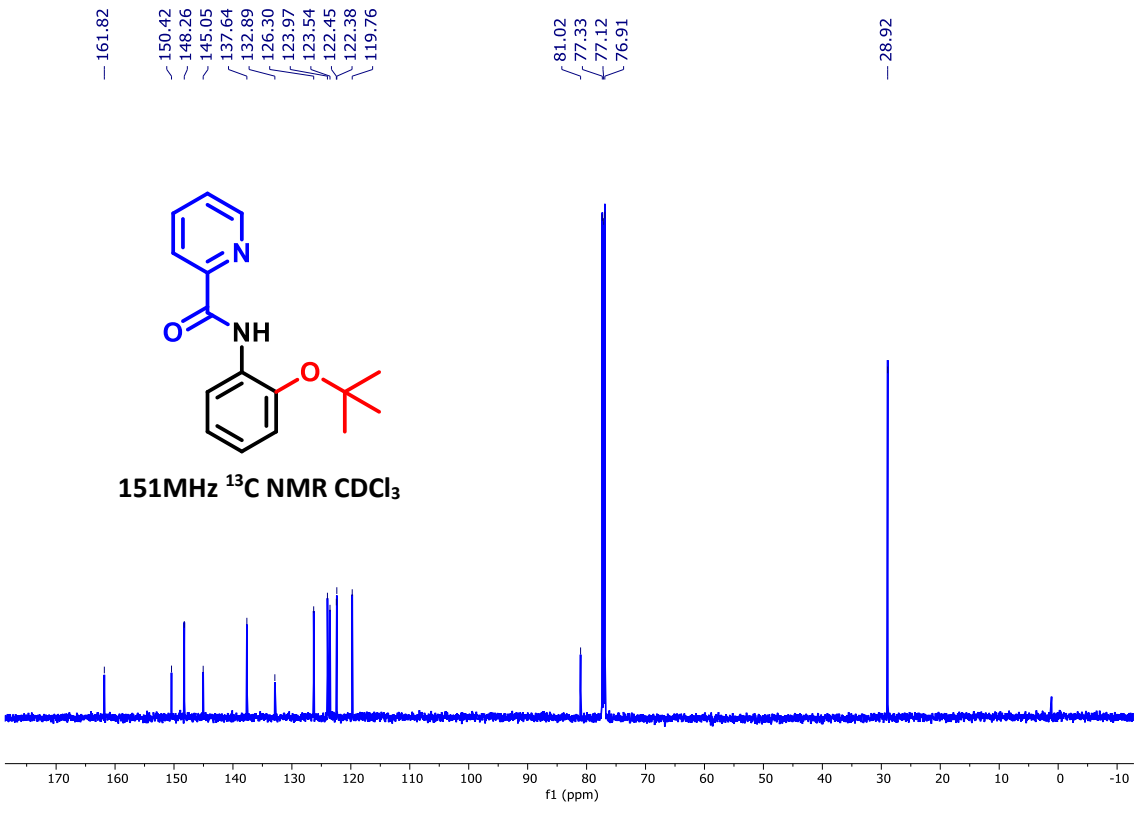


N-(2-((2-phenylpropan-2-yl)oxy)naphthalen-1-yl)picolinamide (3q):

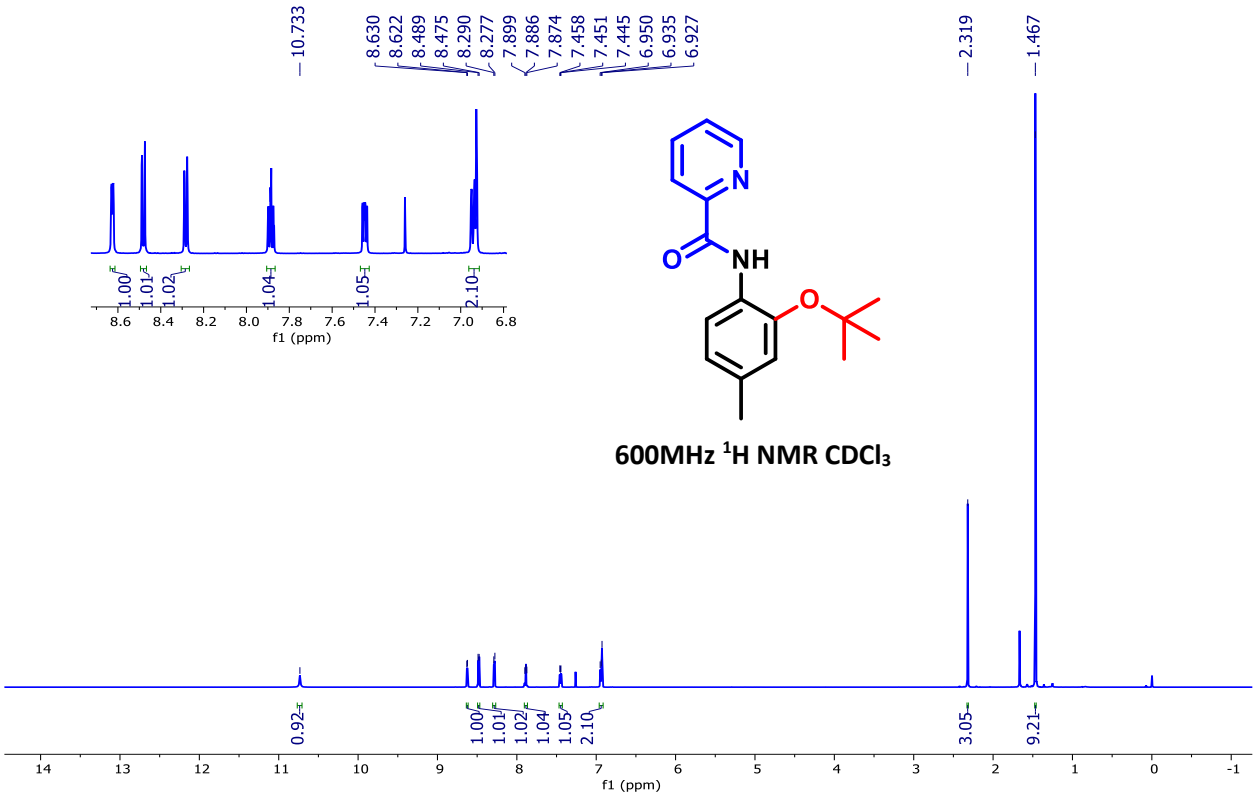


N-(2-(tert-butoxy)phenyl)Picolinamide(4a):

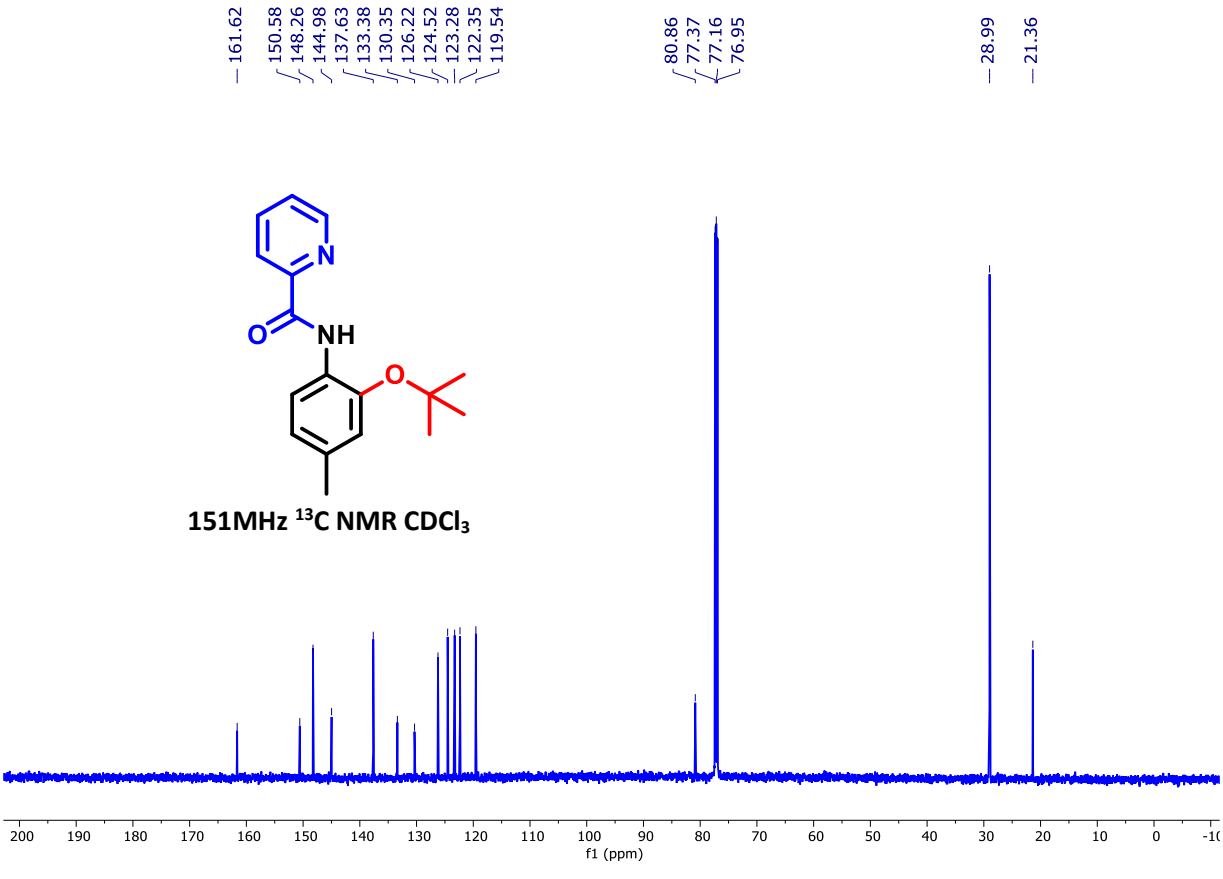




N-(2-(tert-butoxy)-4-methylphenyl)Picolinamide(4b):

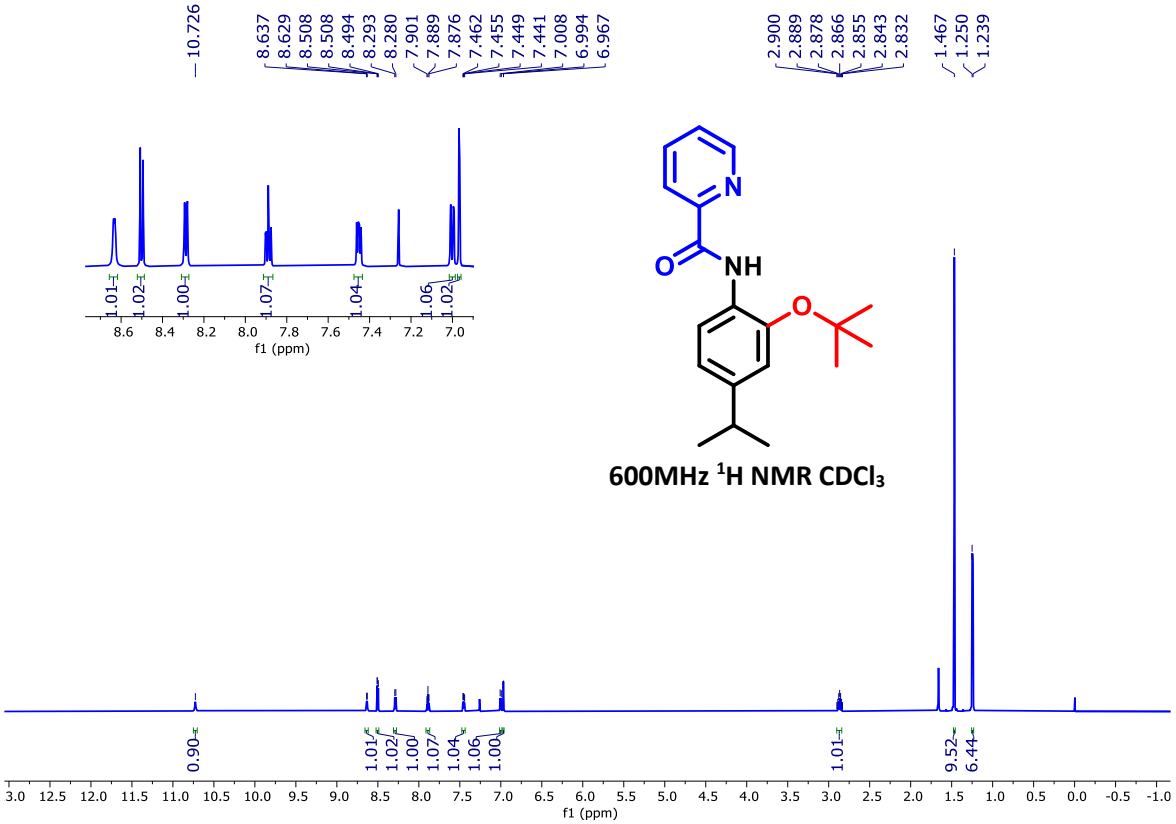


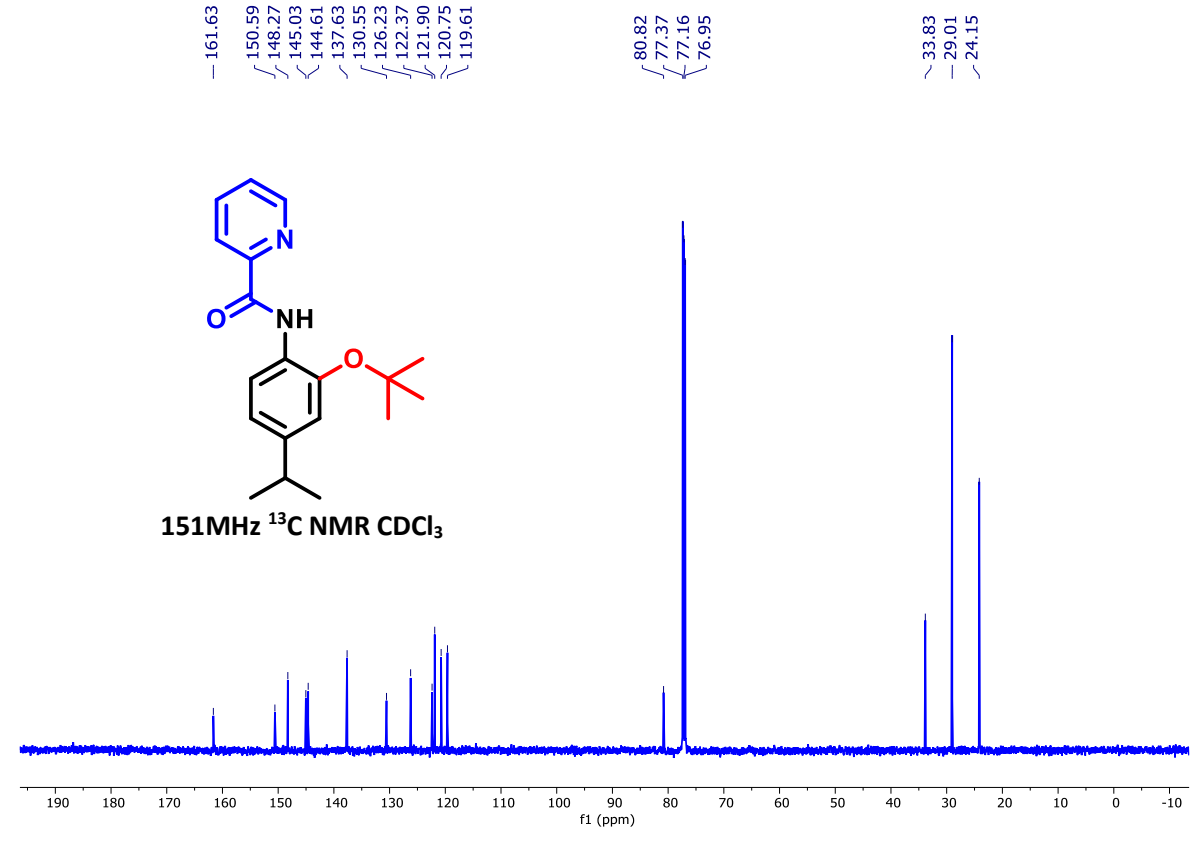
600MHz ^{1}H NMR $CDCl_3$



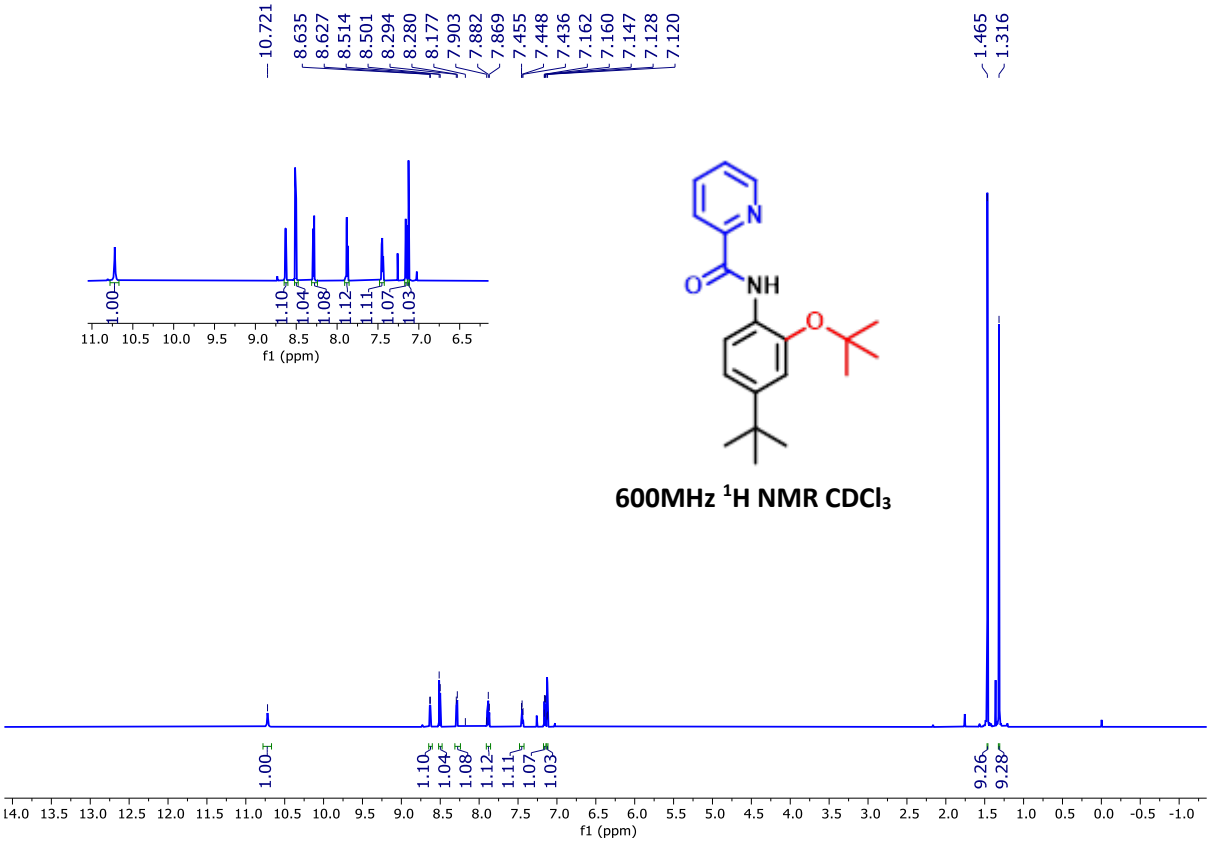
151MHz ^{13}C NMR $CDCl_3$

N-(2-(tert-butoxy)-4-isopropylphenyl)Picolinamide(4c)

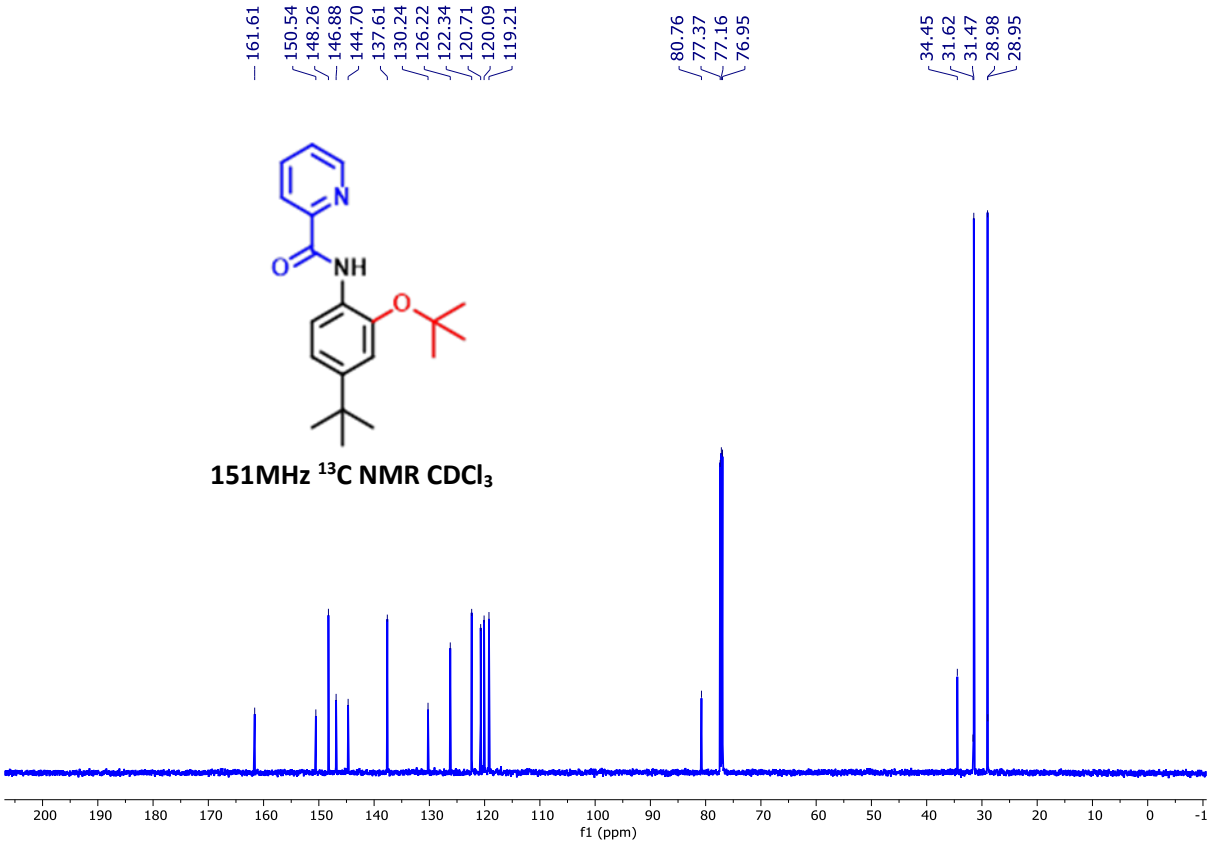




N-(2-(tert-butoxy)-4-(tert-butyl)phenyl)picolinamide(4d):

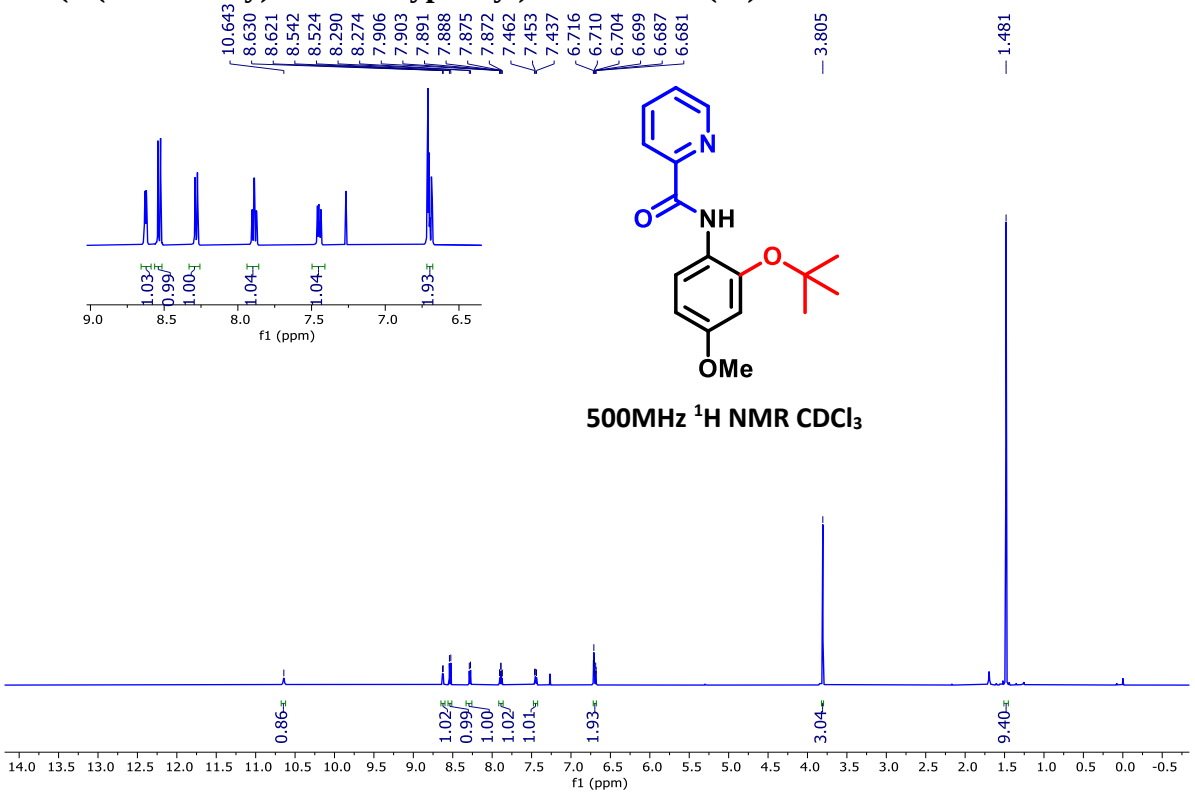


600MHz ^{1}H NMR $CDCl_3$

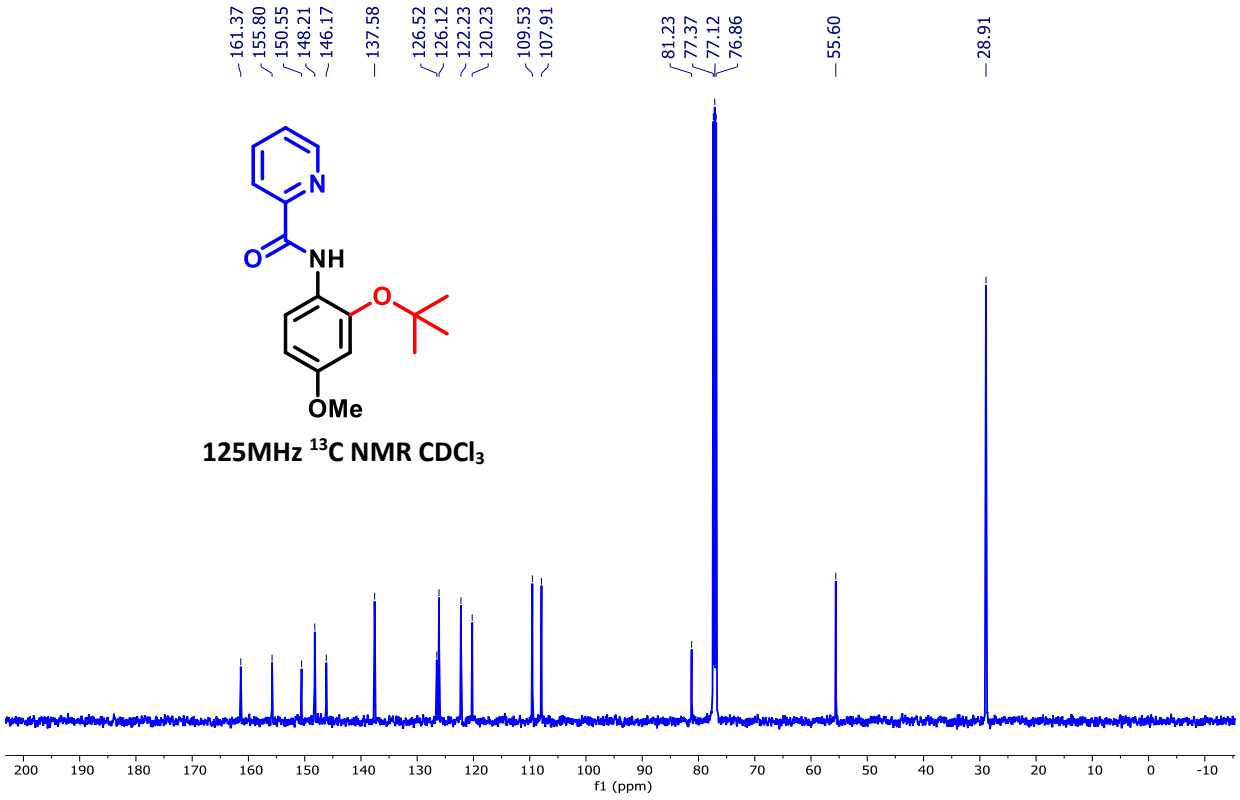


151MHz ^{13}C NMR $CDCl_3$

N-(2-(tert-butoxy)-4-methoxyphenyl)Picolinamide(4e):

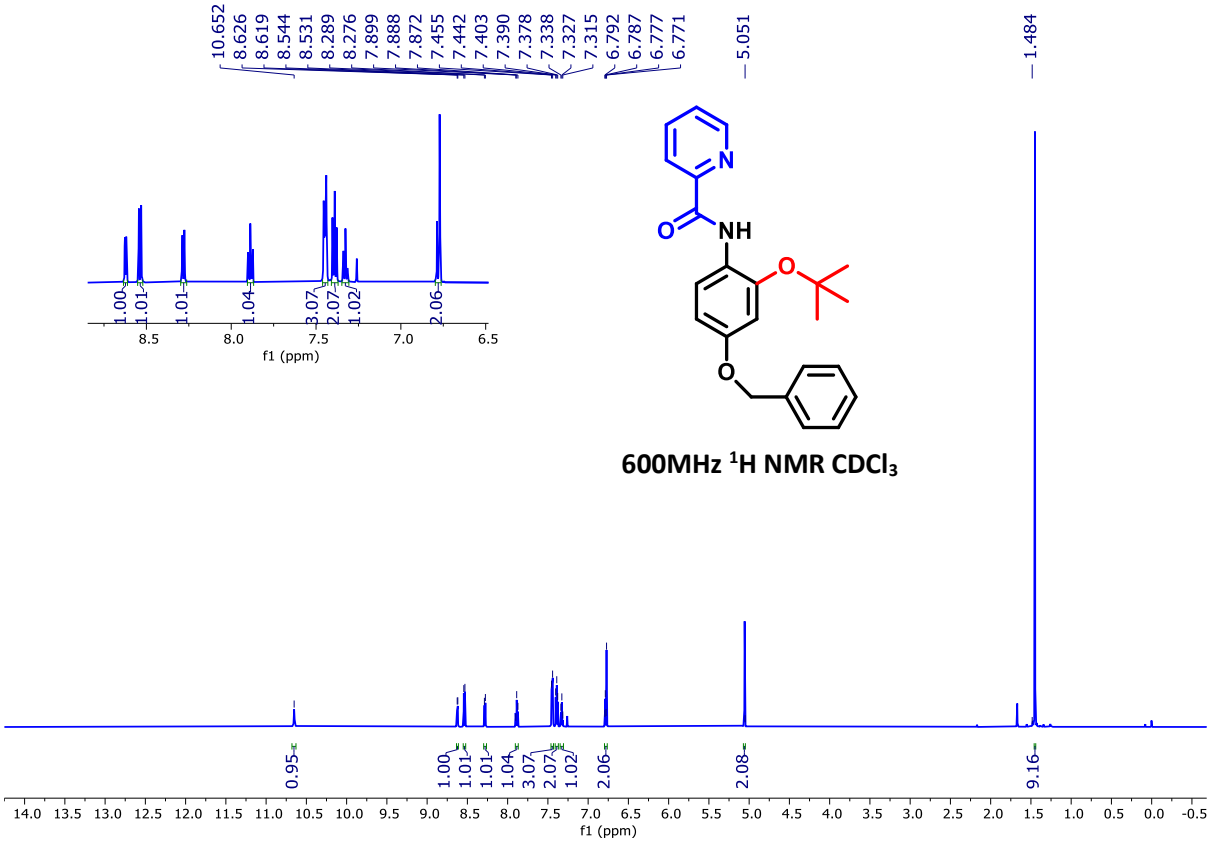


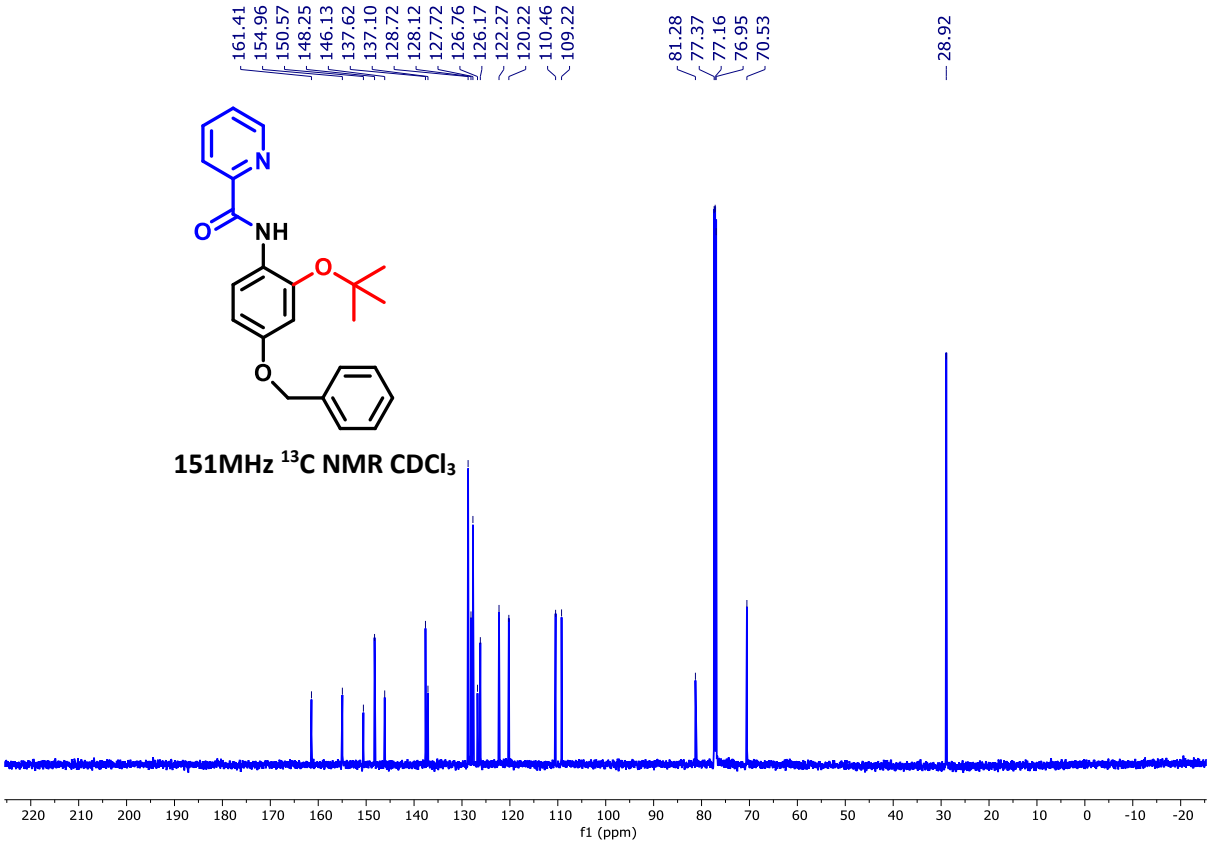
500MHz ^{1}H NMR $CDCl_3$



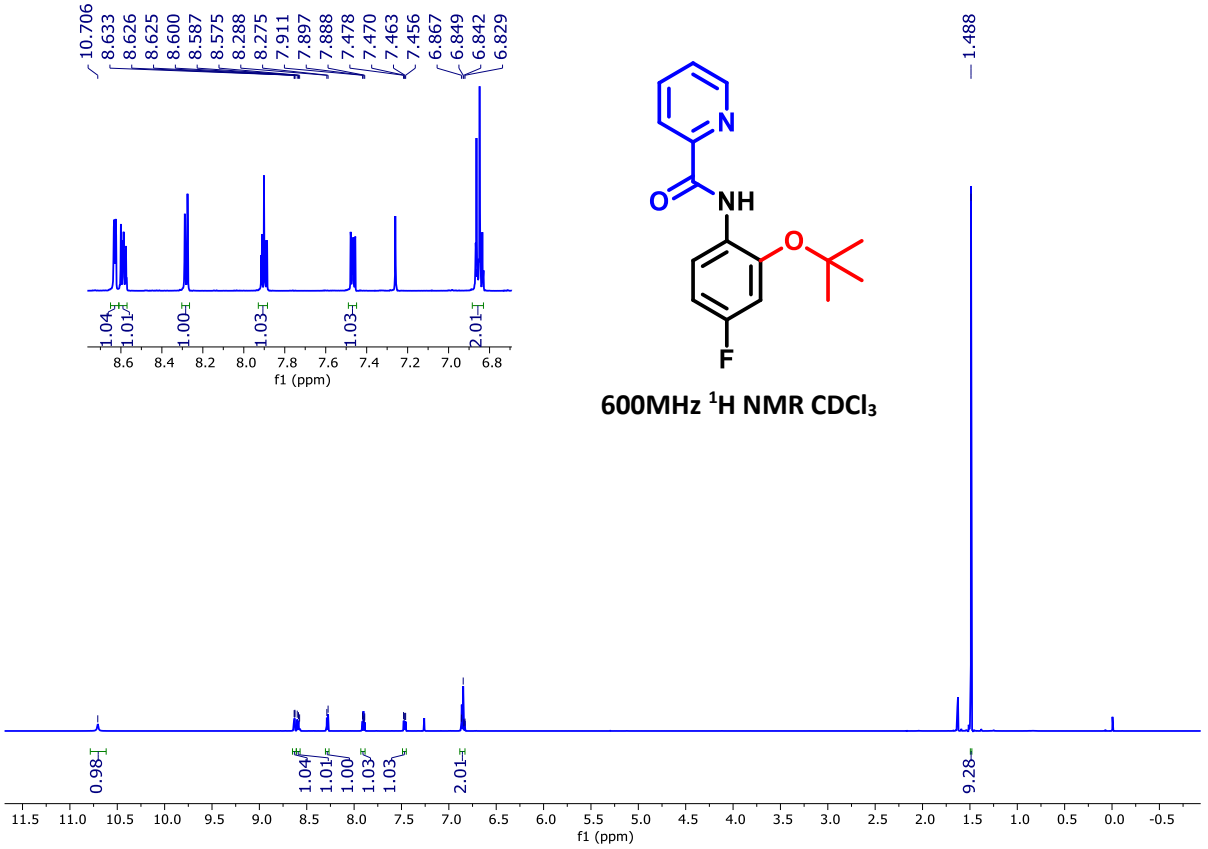
125MHz ^{13}C NMR $CDCl_3$

N-(4-(benzyloxy)-2-(tert-butoxy)phenyl)picolinamide(4f):

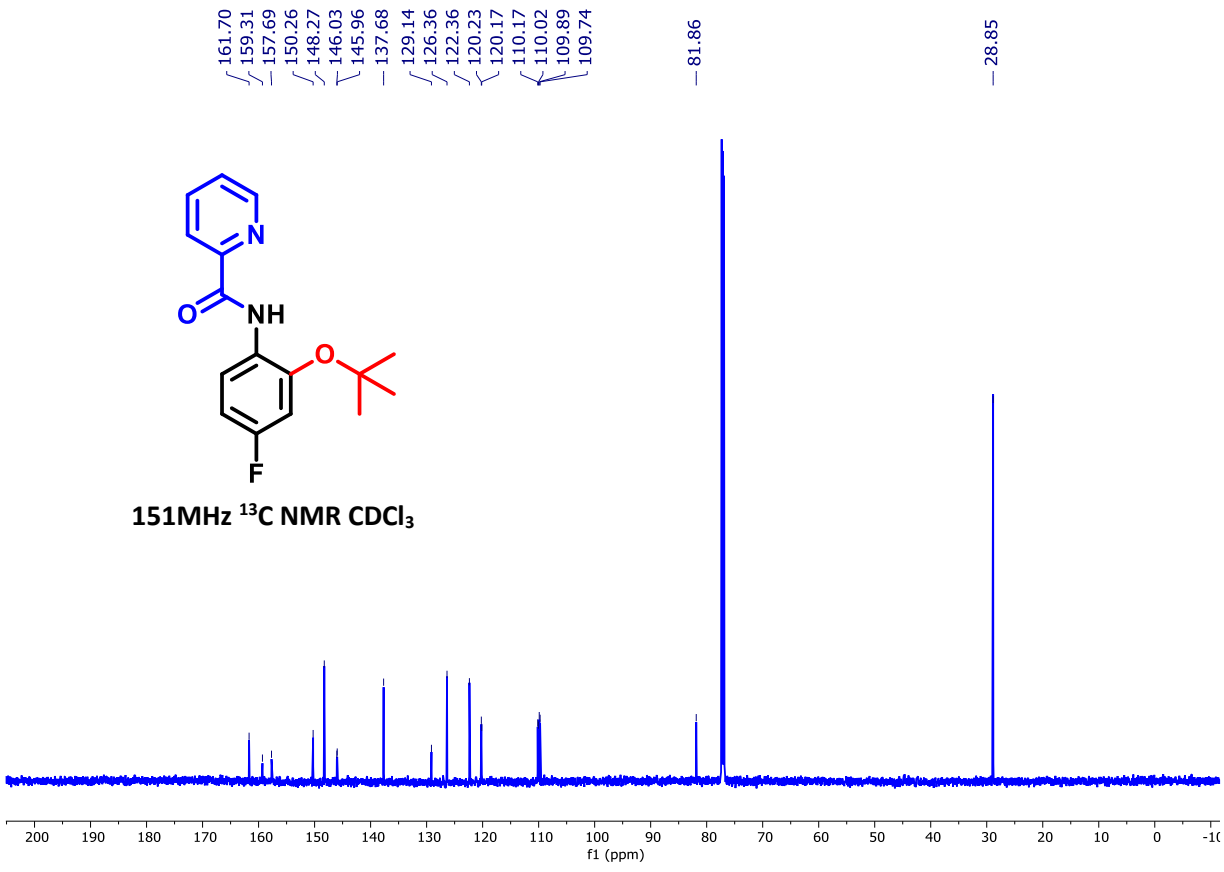




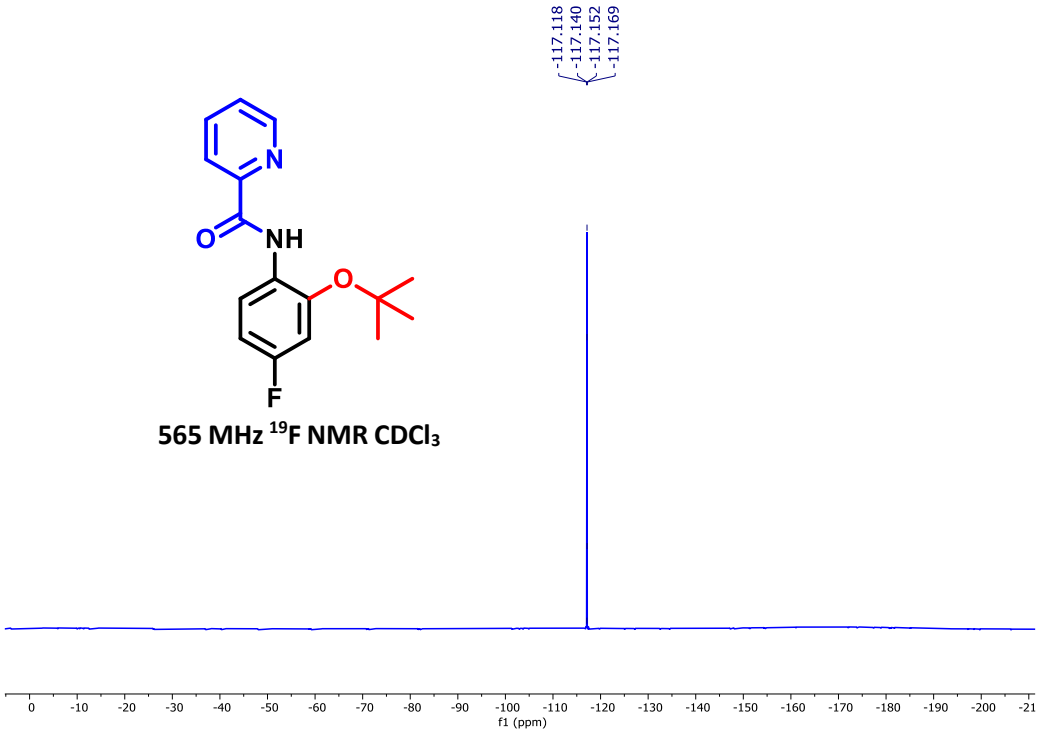
N-(2-(tert-butoxy)-4-fluorophenyl)picolinamide(4g):



600MHz ^{1}H NMR $CDCl_3$

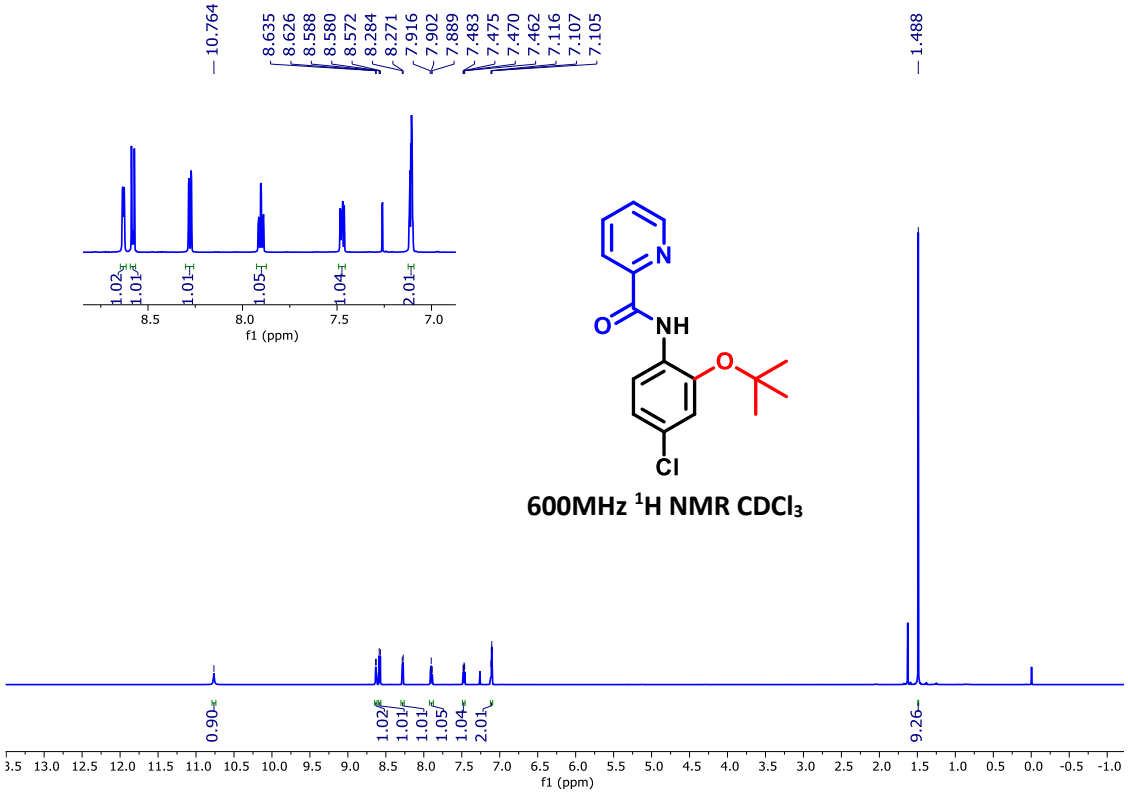


151MHz ^{13}C NMR $CDCl_3$

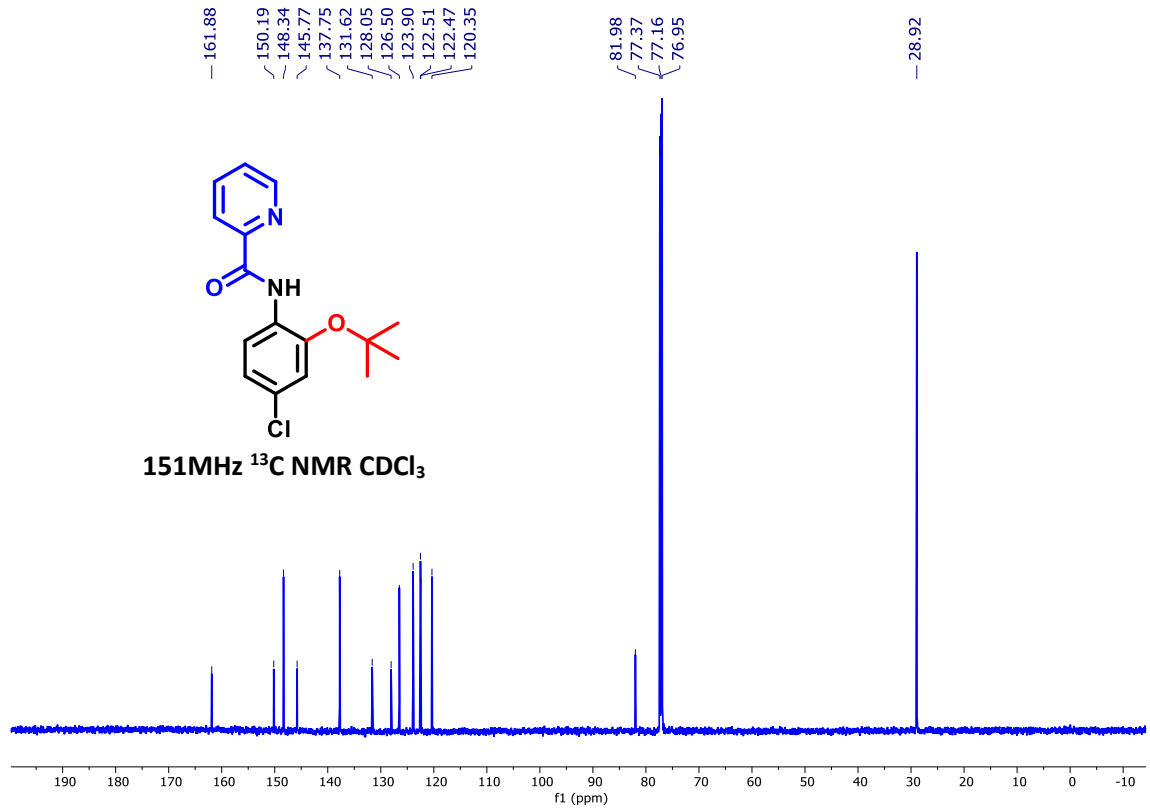


565 MHz ^{19}F NMR $CDCl_3$

N-(2-(tert-butoxy)-4-chlorophenyl)Picolinamide(4h)

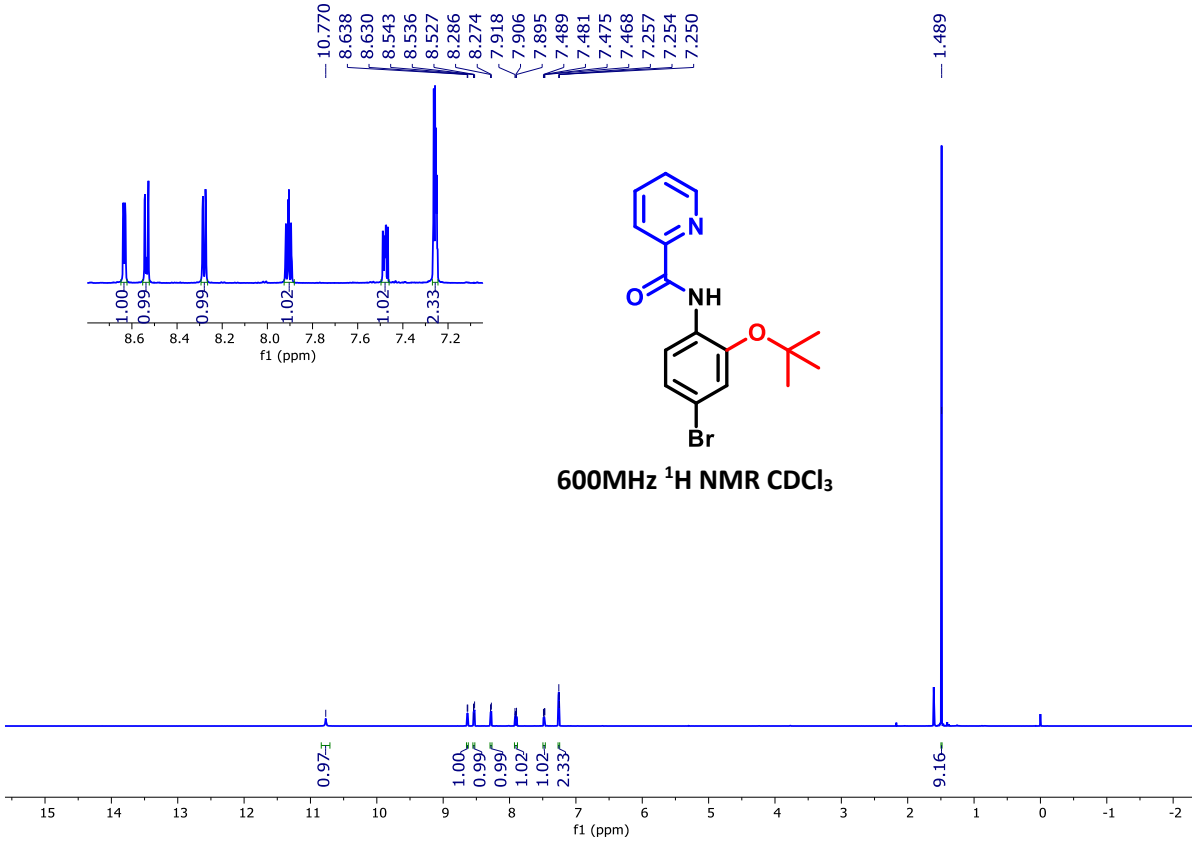


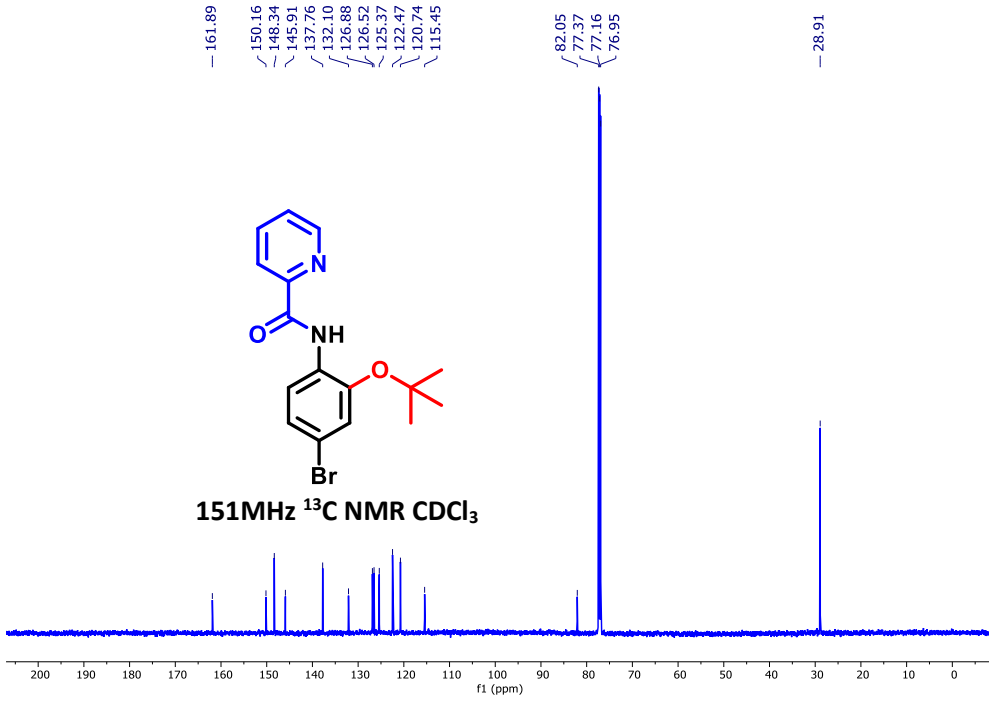
600MHz ^{1}H NMR $CDCl_3$



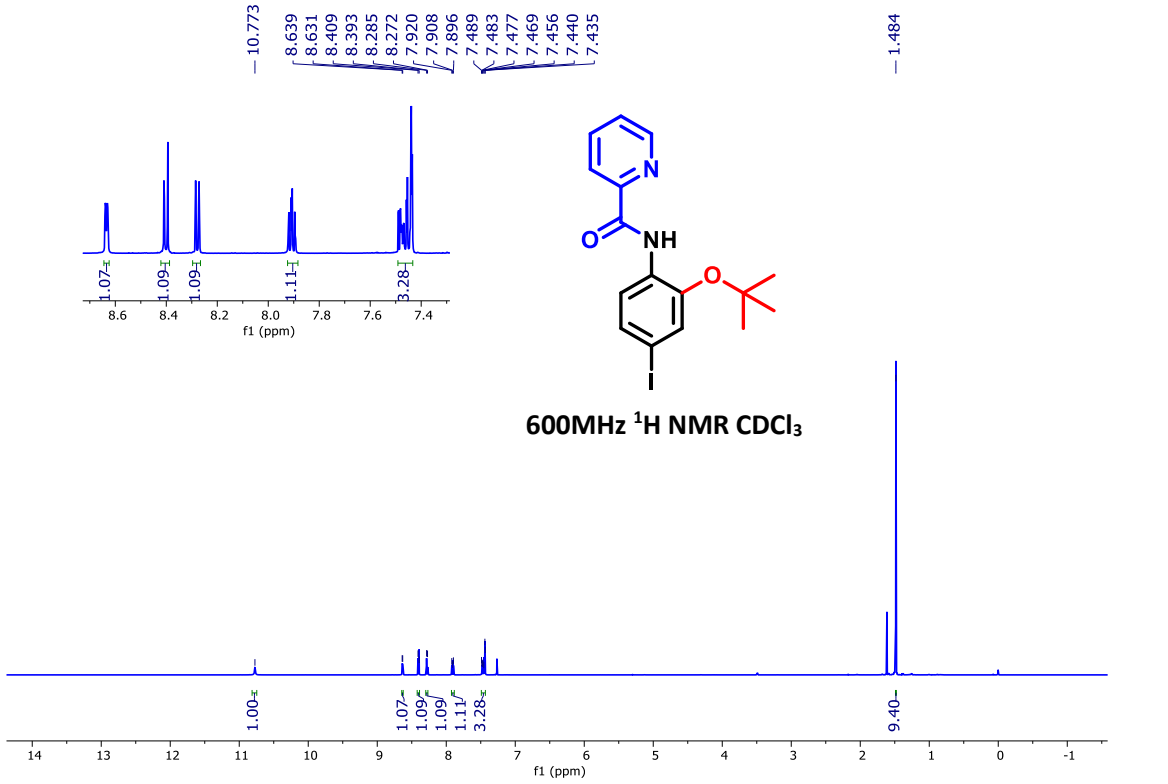
151MHz ^{13}C NMR $CDCl_3$

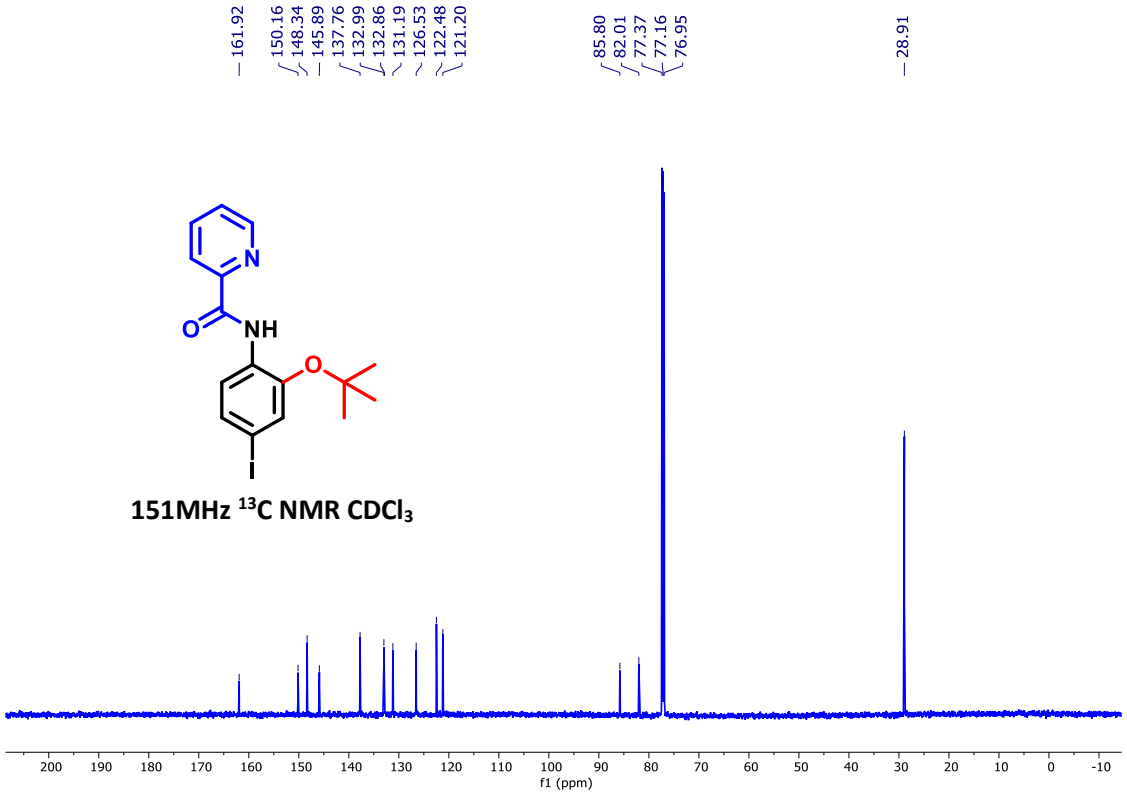
N-(4-bromo-2-(tert-butoxy)phenyl)Picolinamide(4i):



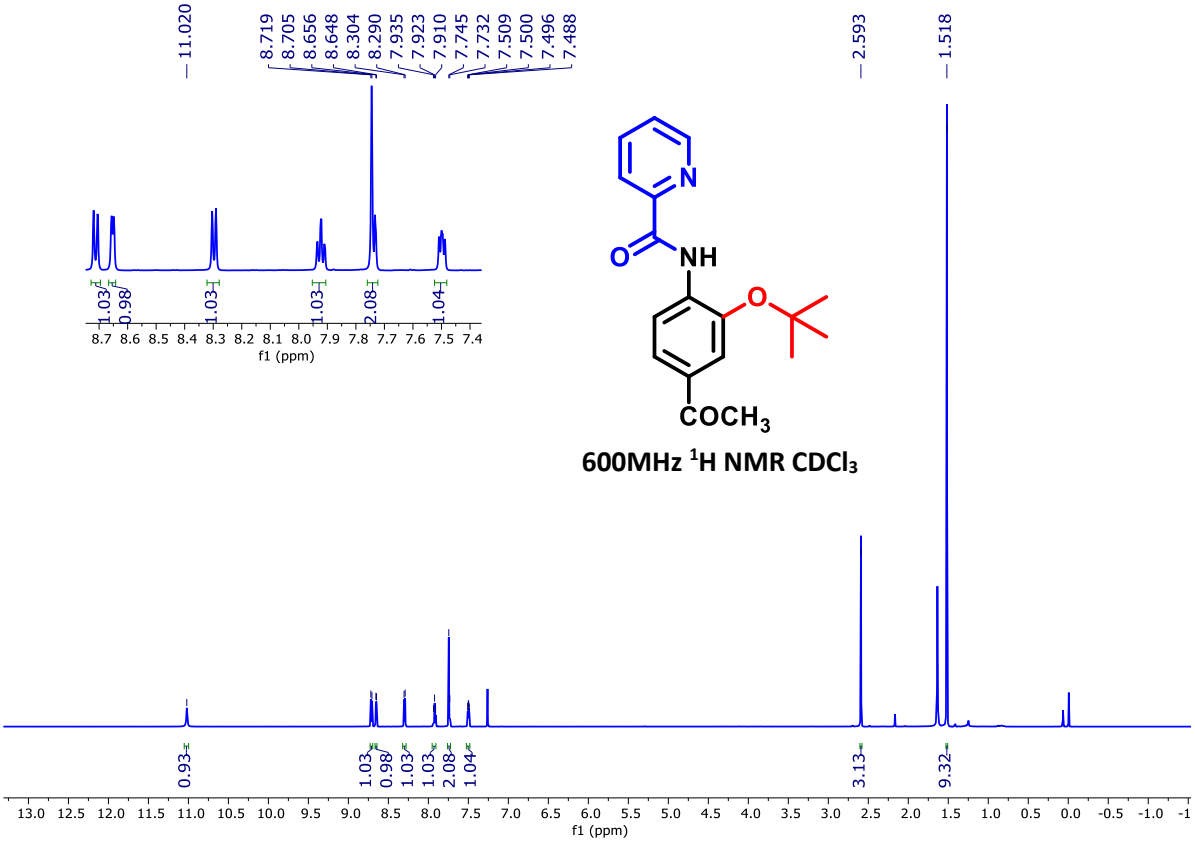


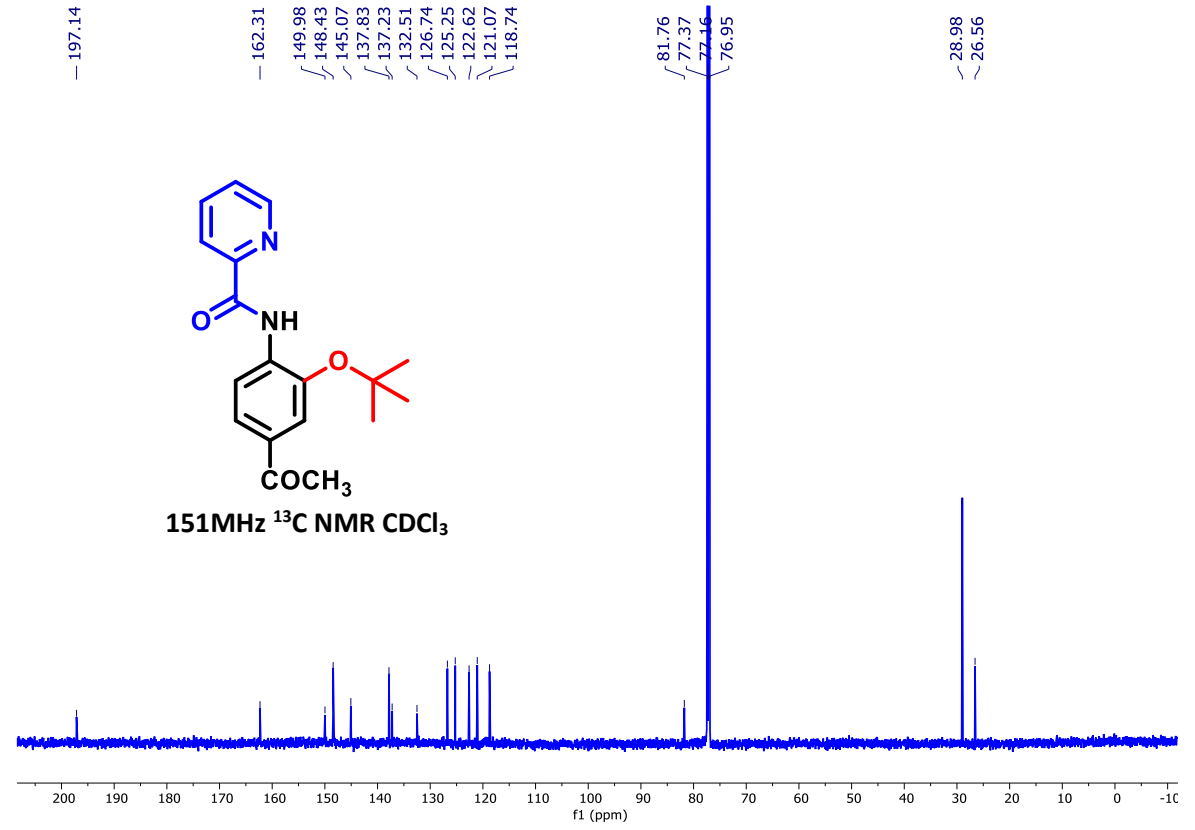
N-(2-(tert-butoxy)-4-iodophenyl)Picolinamide(4j)



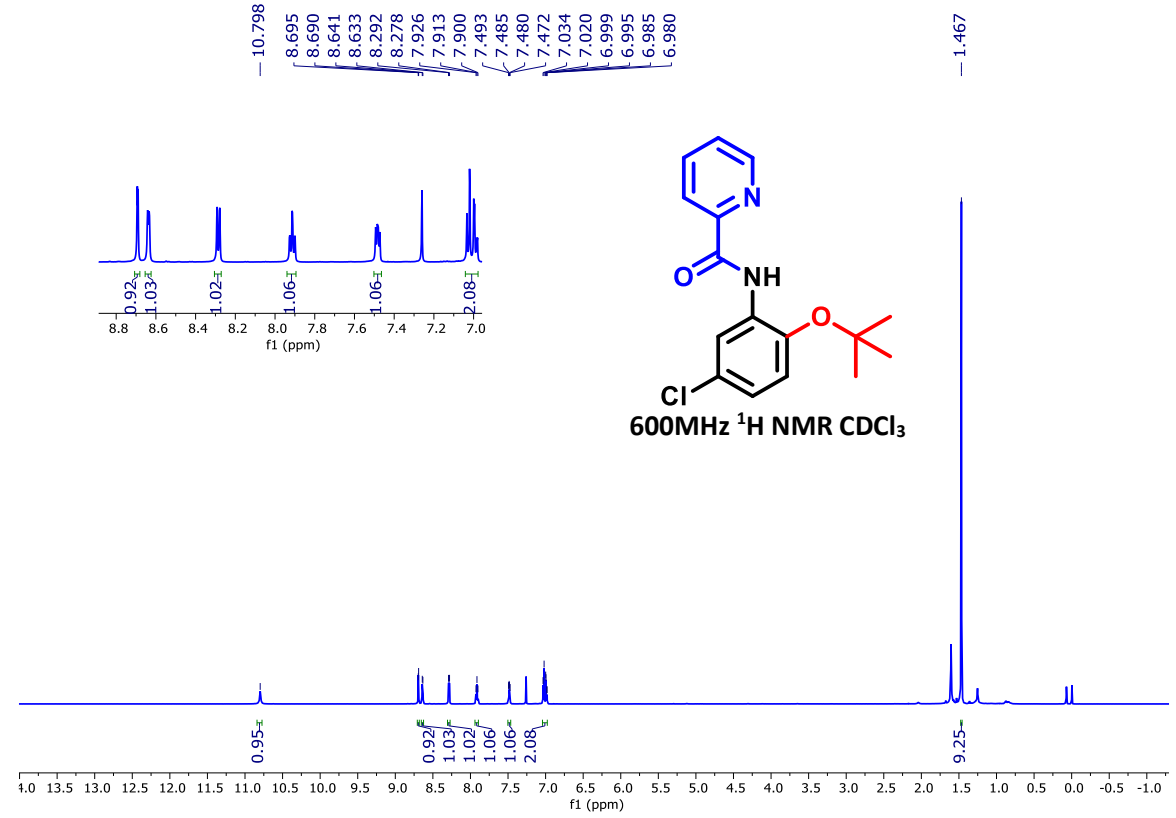


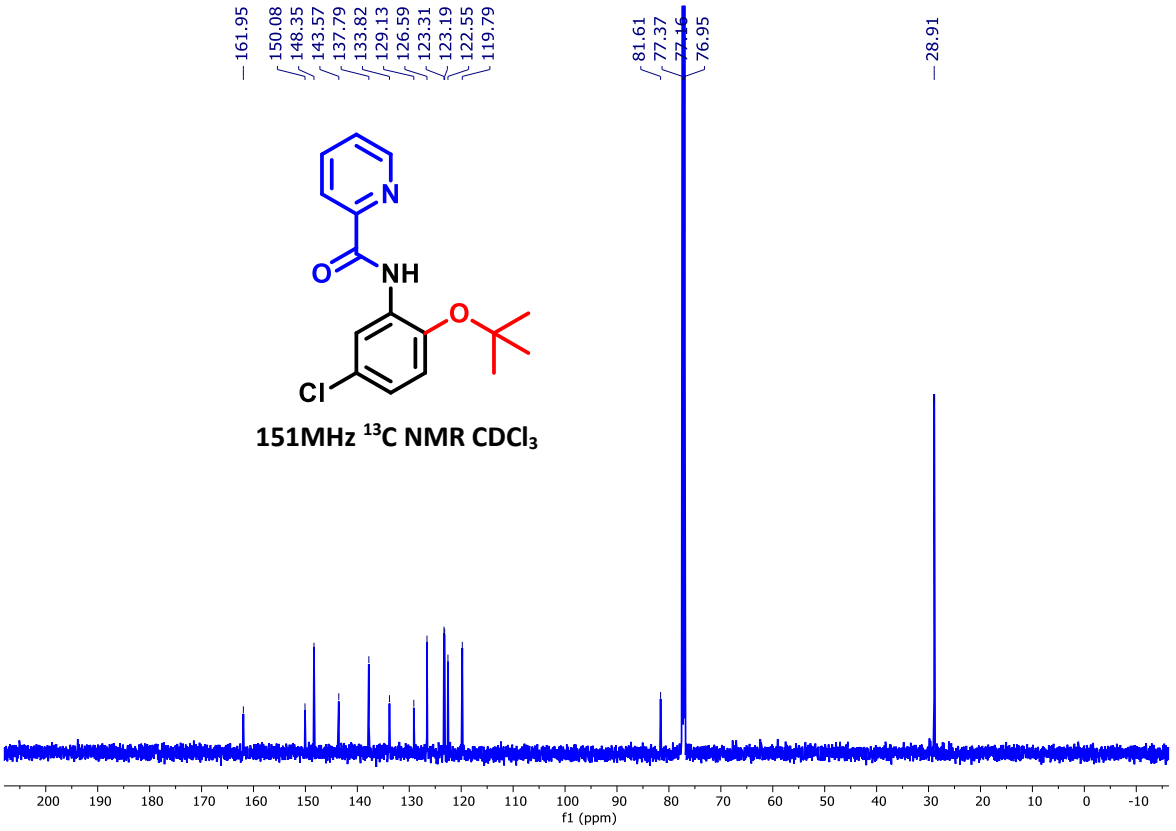
N-(4-acetyl-2-(tert-butoxy)phenyl)Picolinamide(4k):



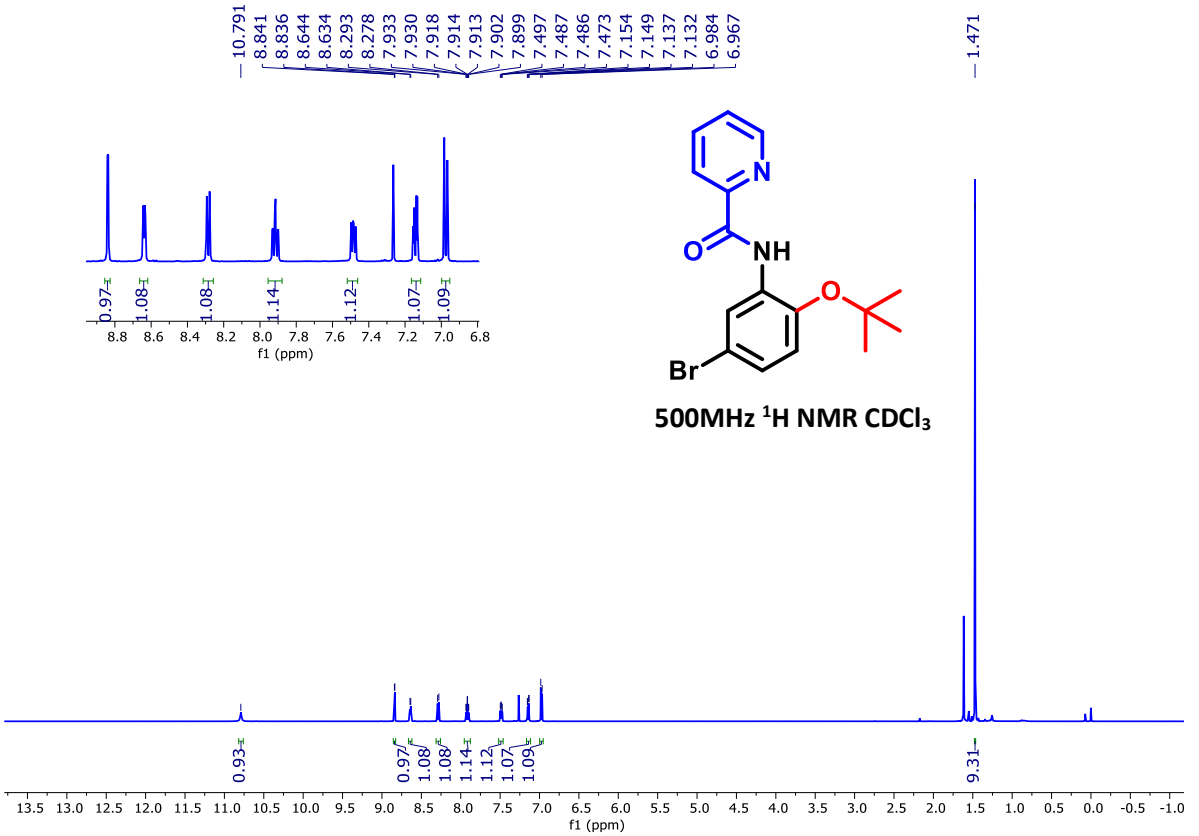


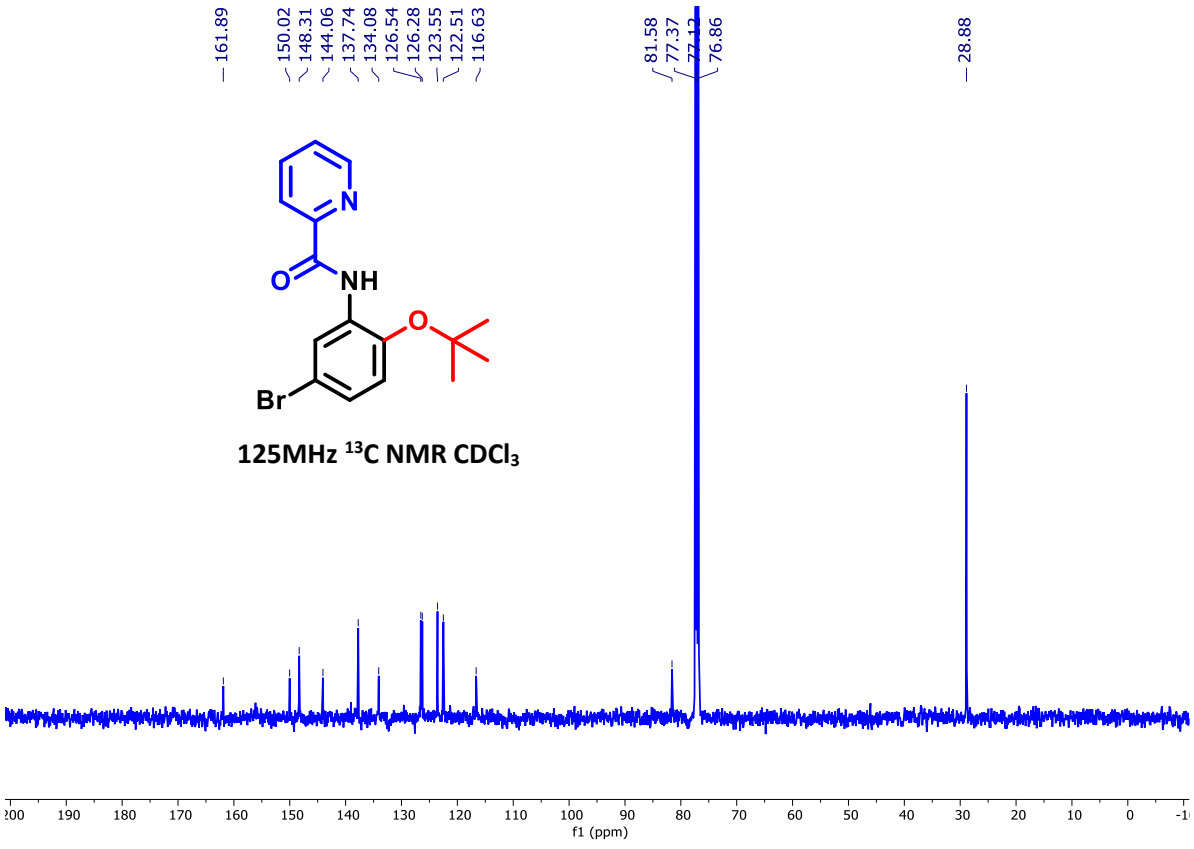
N-(2-(tert-butoxy)-5-chlorophenyl)Picolinamide(4n):



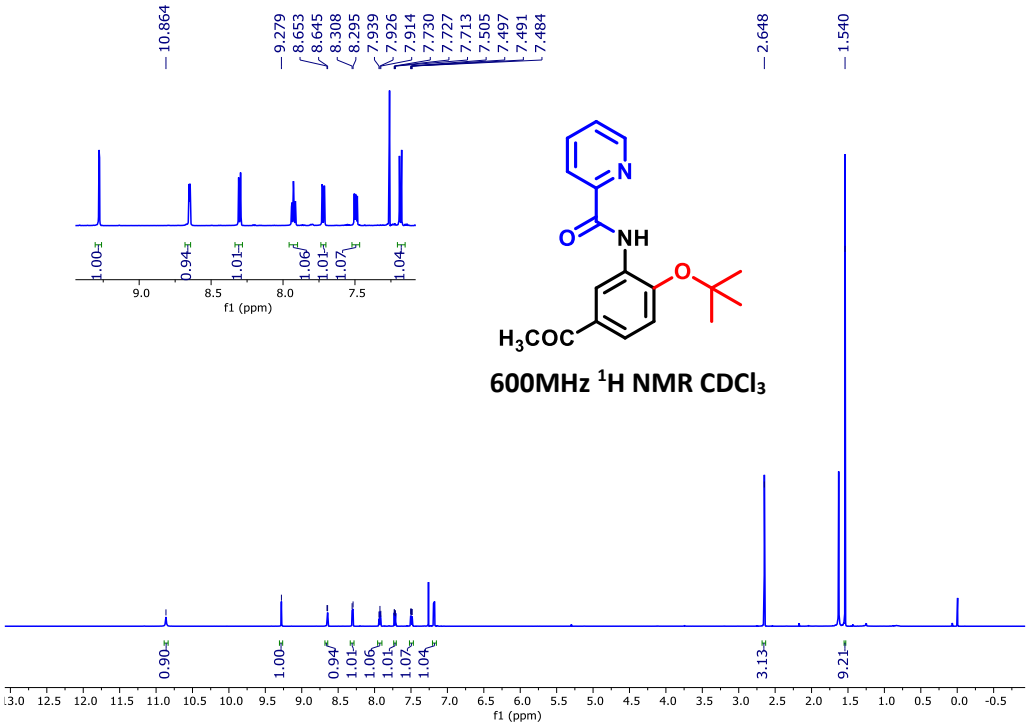


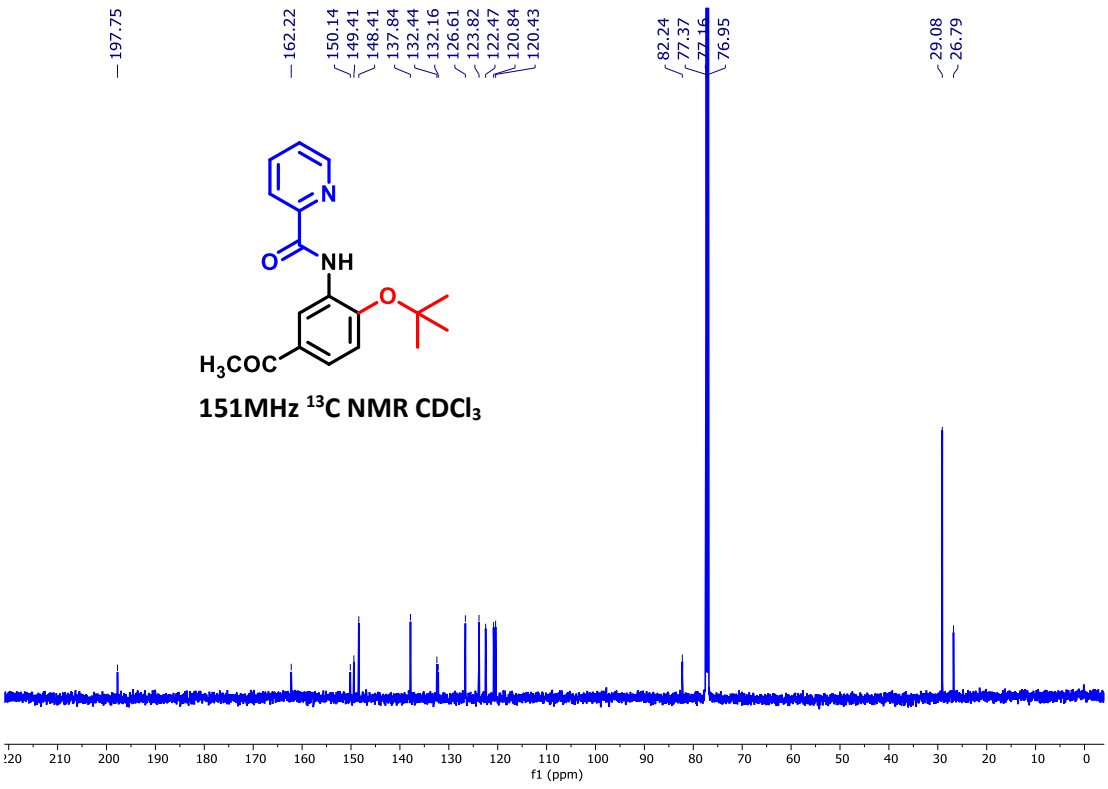
N-(5-bromo-2-(tert-butoxy)phenyl)Picolinamide(4o):



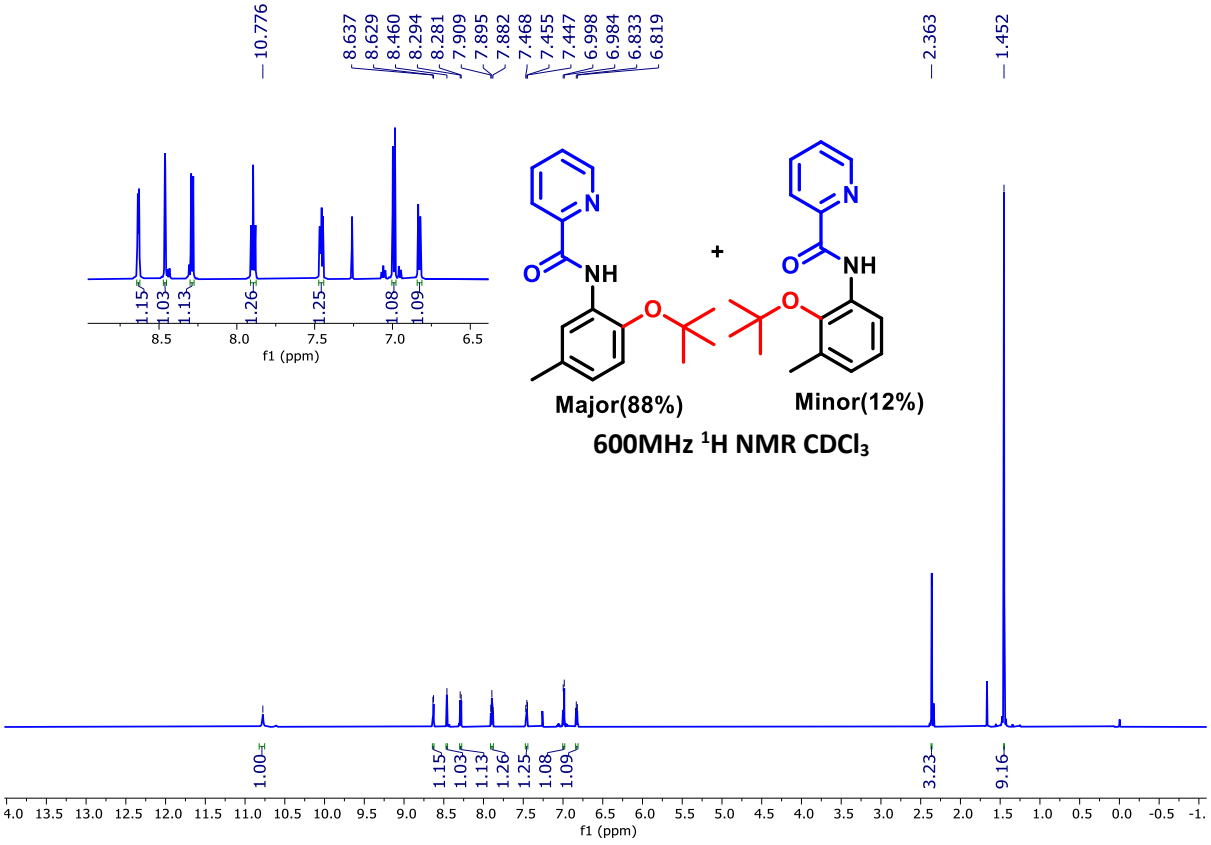


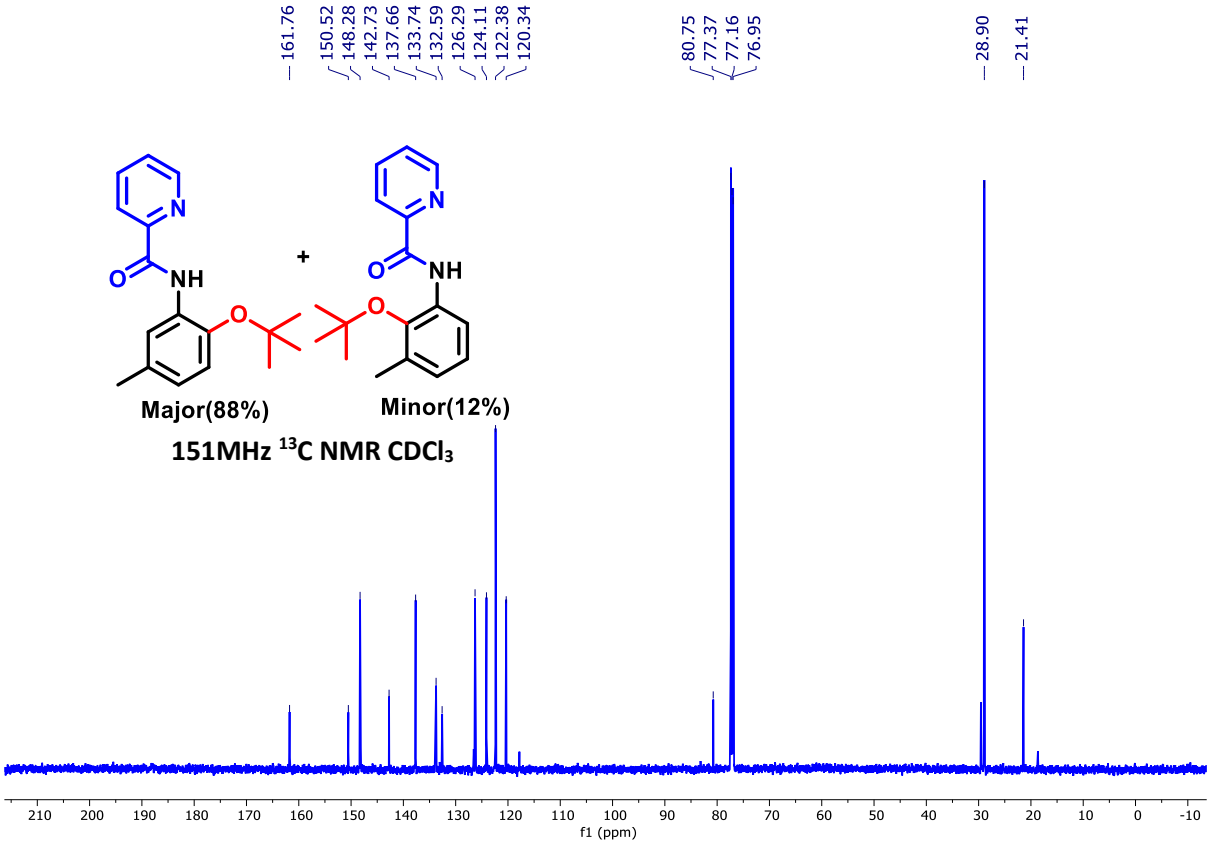
N-(5-acetyl-2-(tert-butoxy)phenyl)picolinamide(4p):



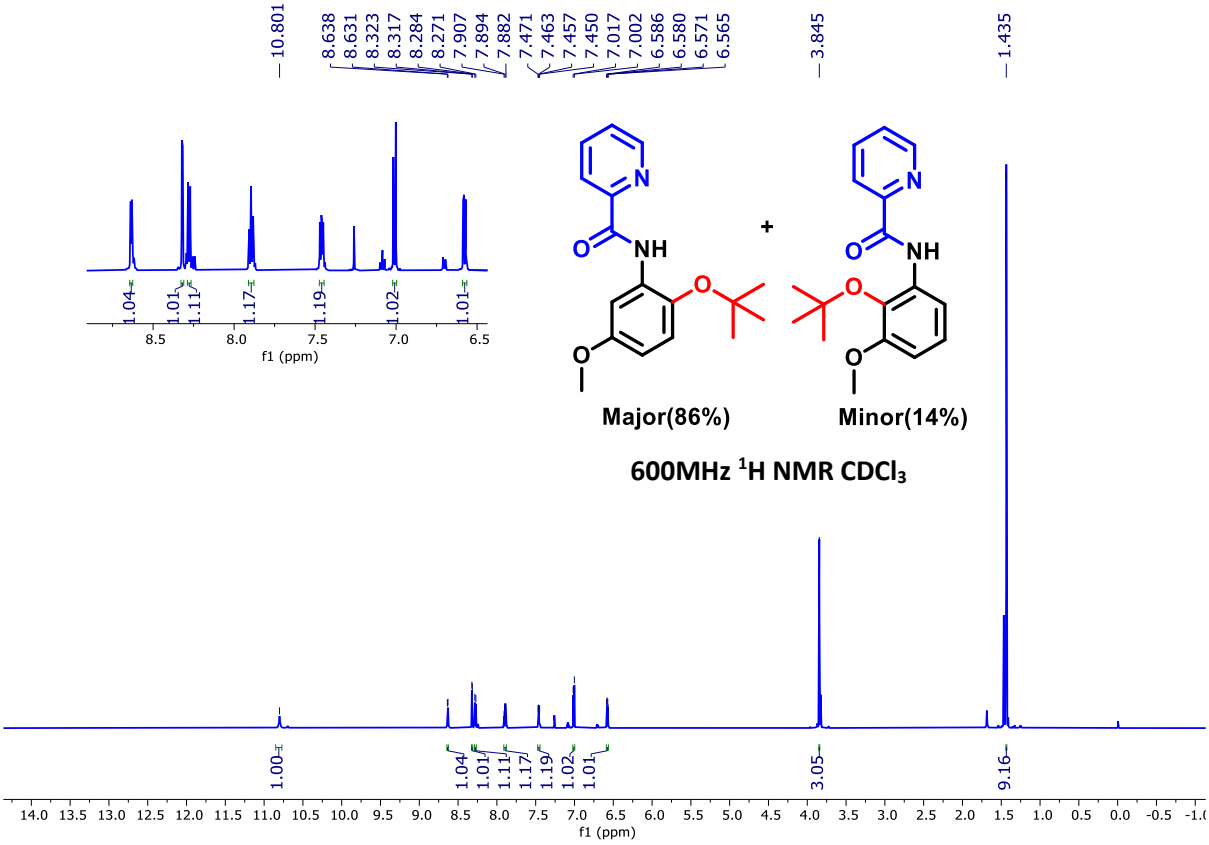


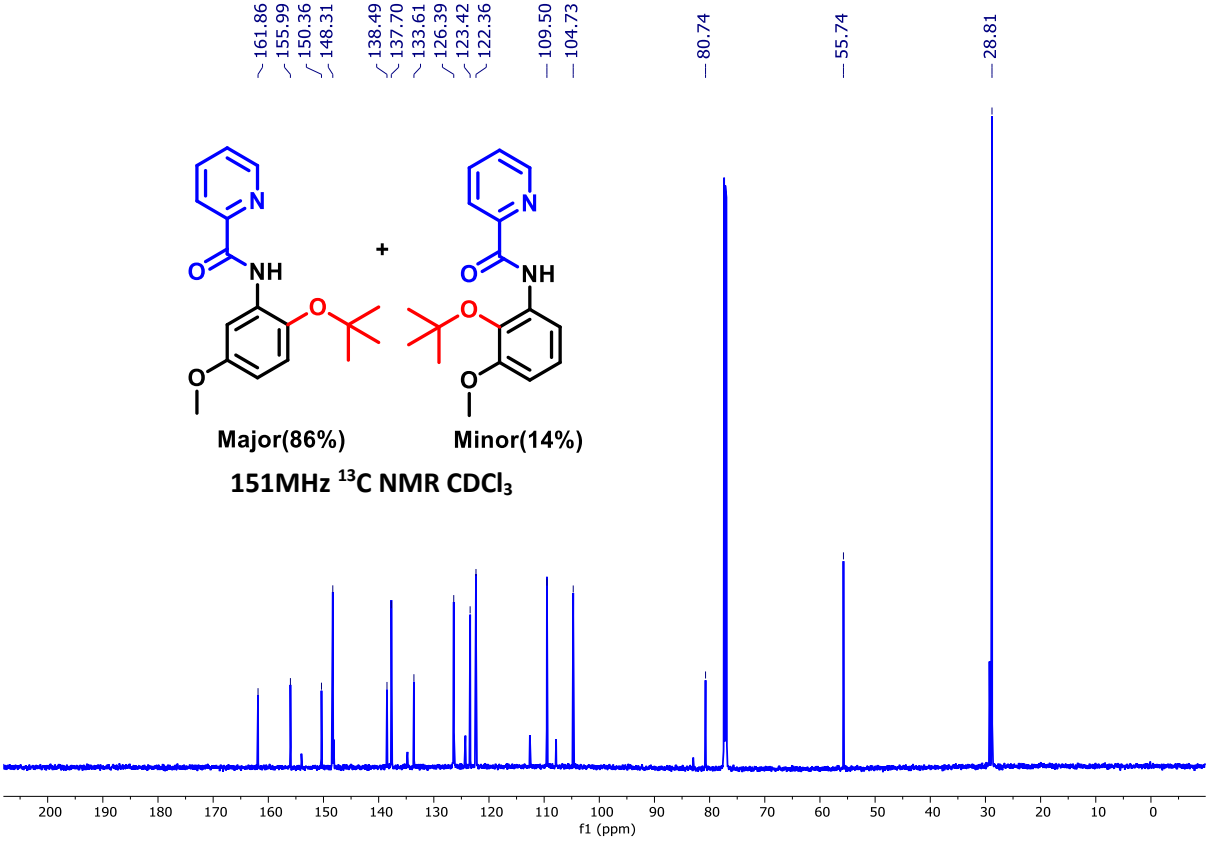
N-(2-(tert-butoxy)-5-methylphenyl)picolinamide(4q)



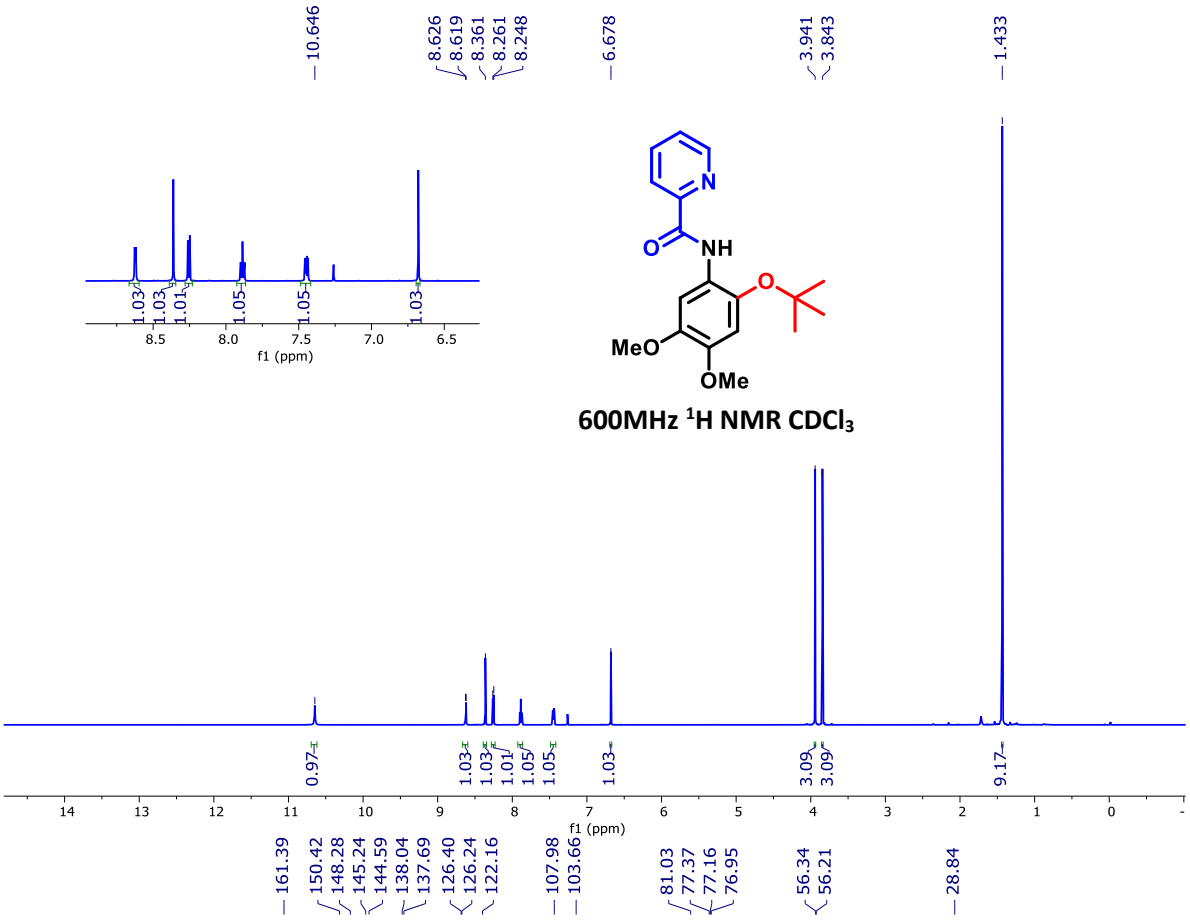


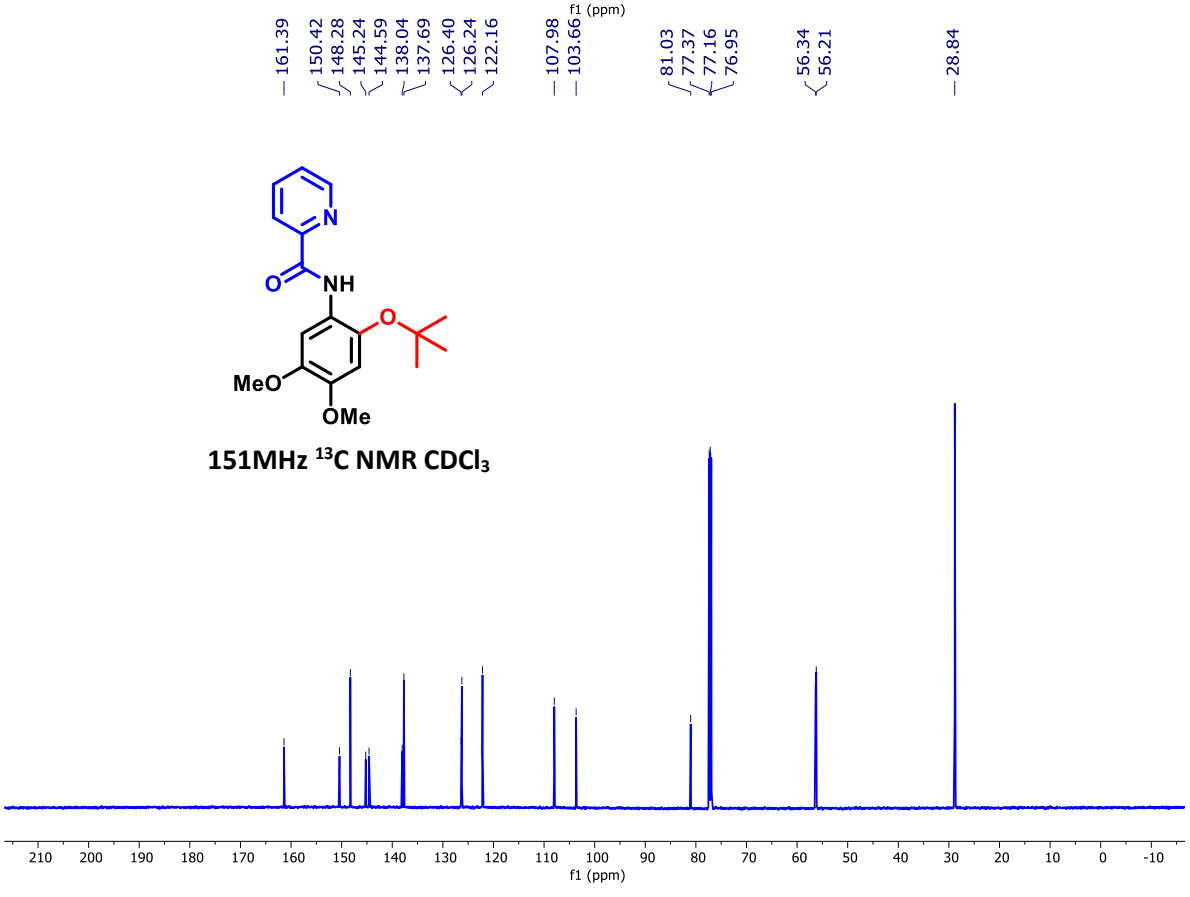
N-(2-(tert-butoxy)-5-methoxyphenyl)Picolinamide(4s)



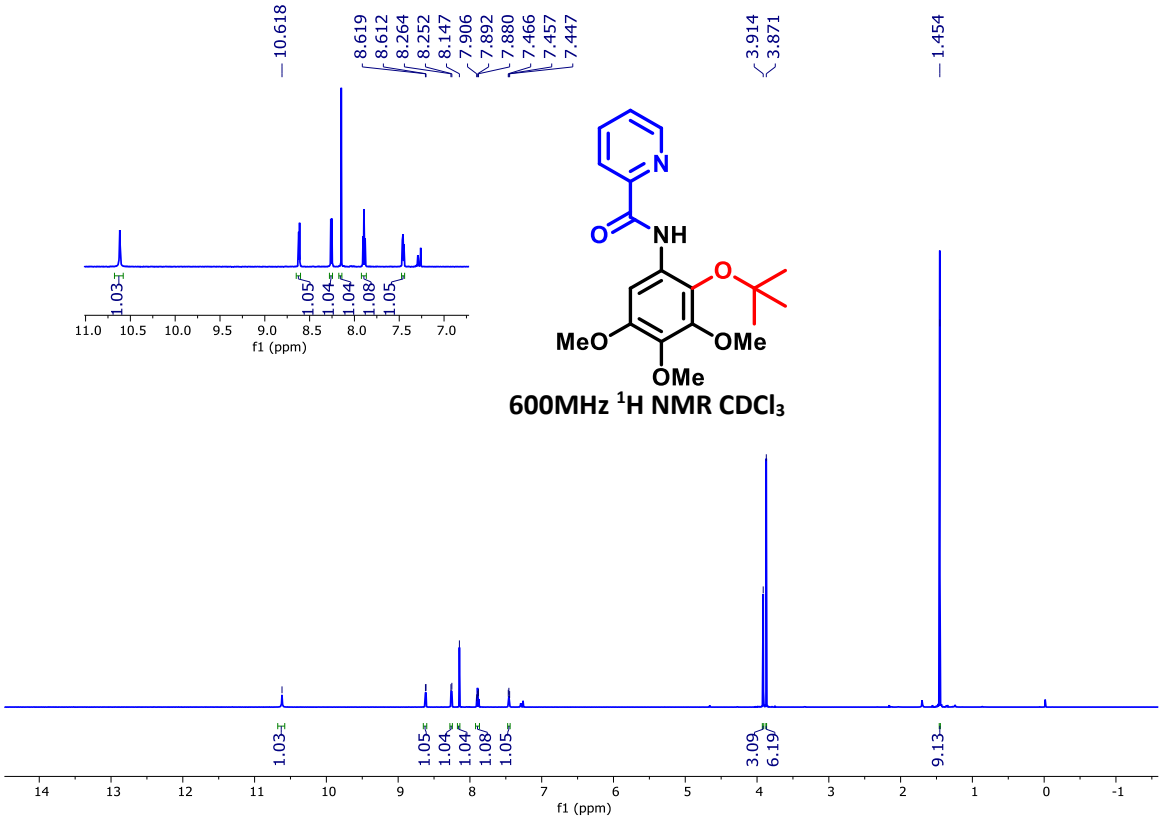


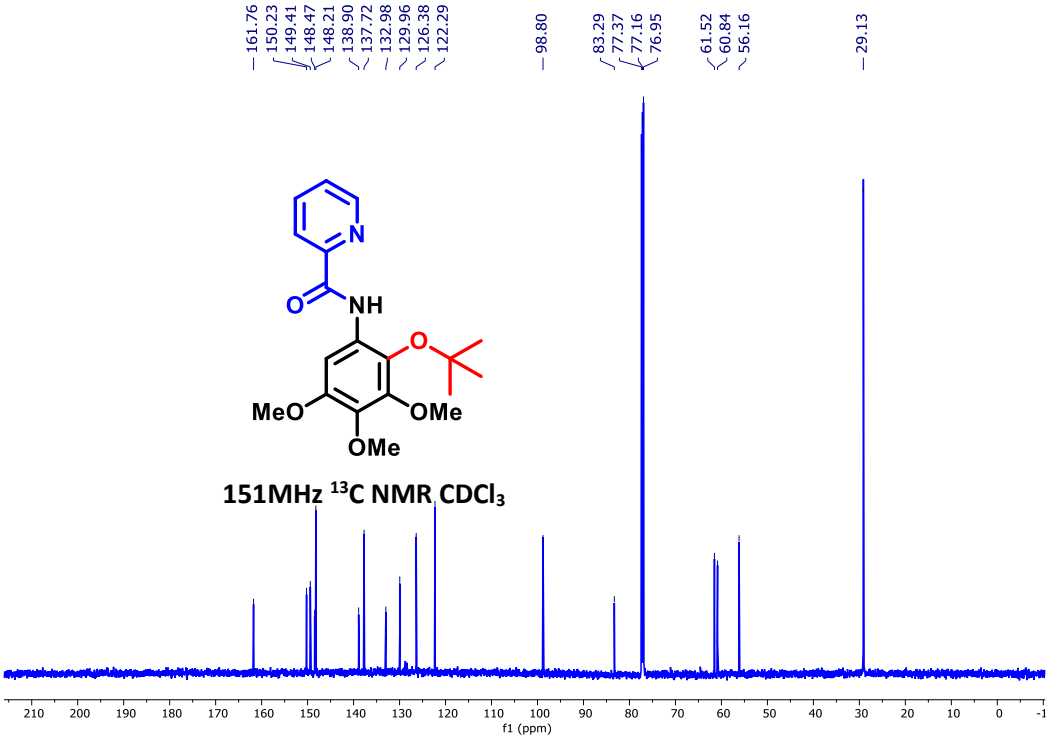
N-(2-(tert-butoxy)-3,5-dimethoxyphenyl)picolinamide(4u)



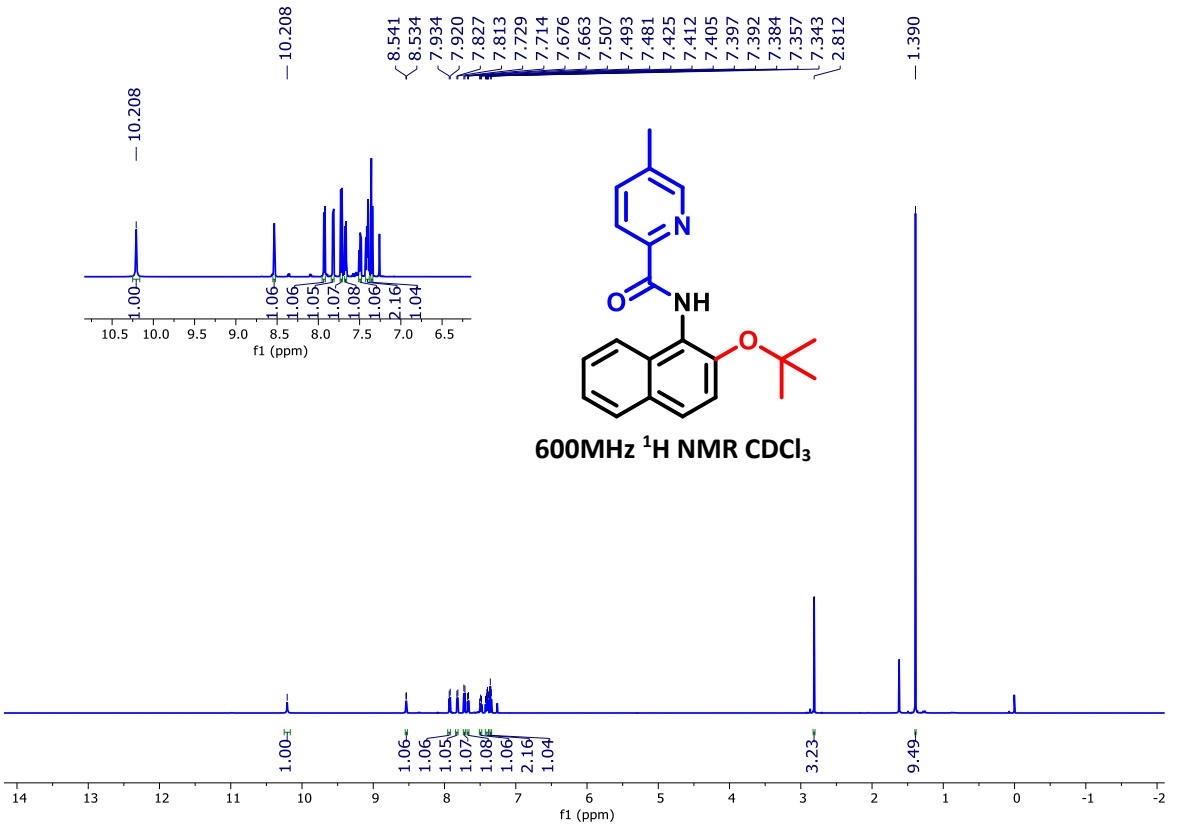


N-(2-(tert-butoxy)-3,4,5-trimethoxyphenyl)picolinamide(4v)

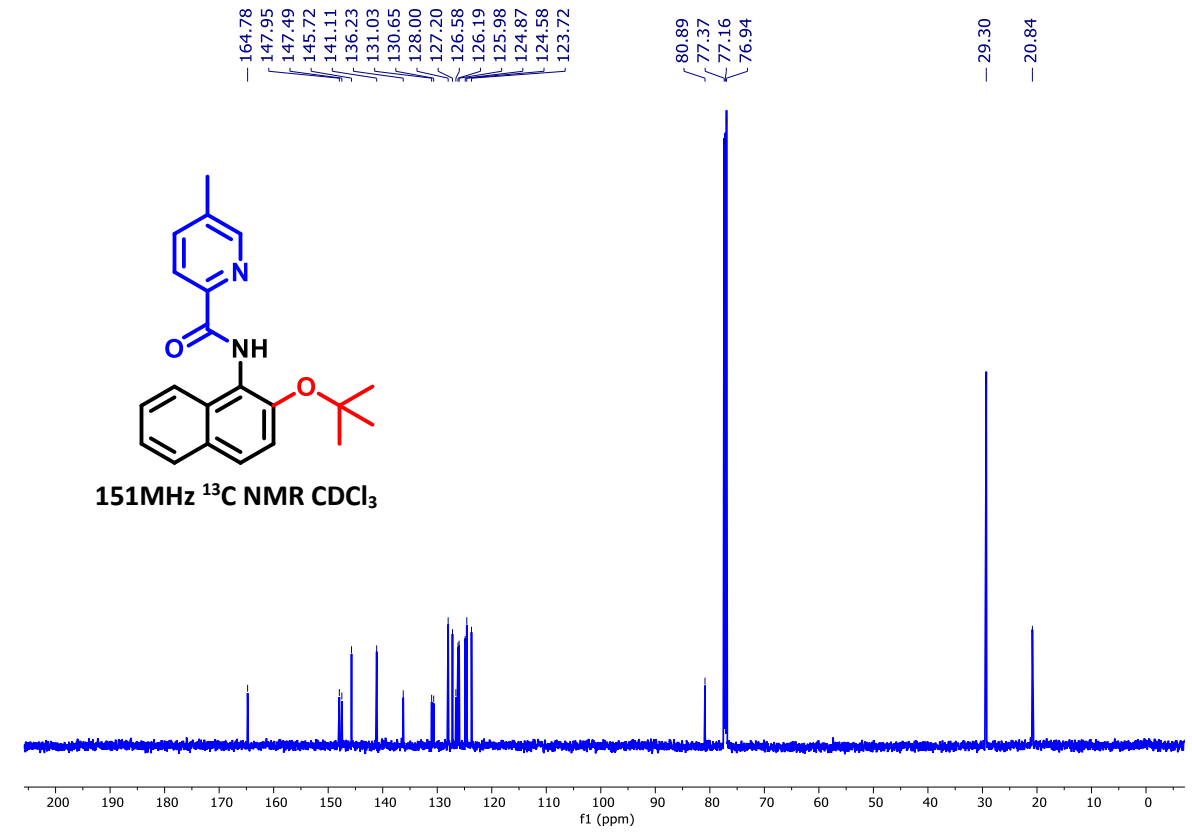




N-(2-(tert-butoxy)naphthalen-1-yl)-6-methylpicolinamide(5a)

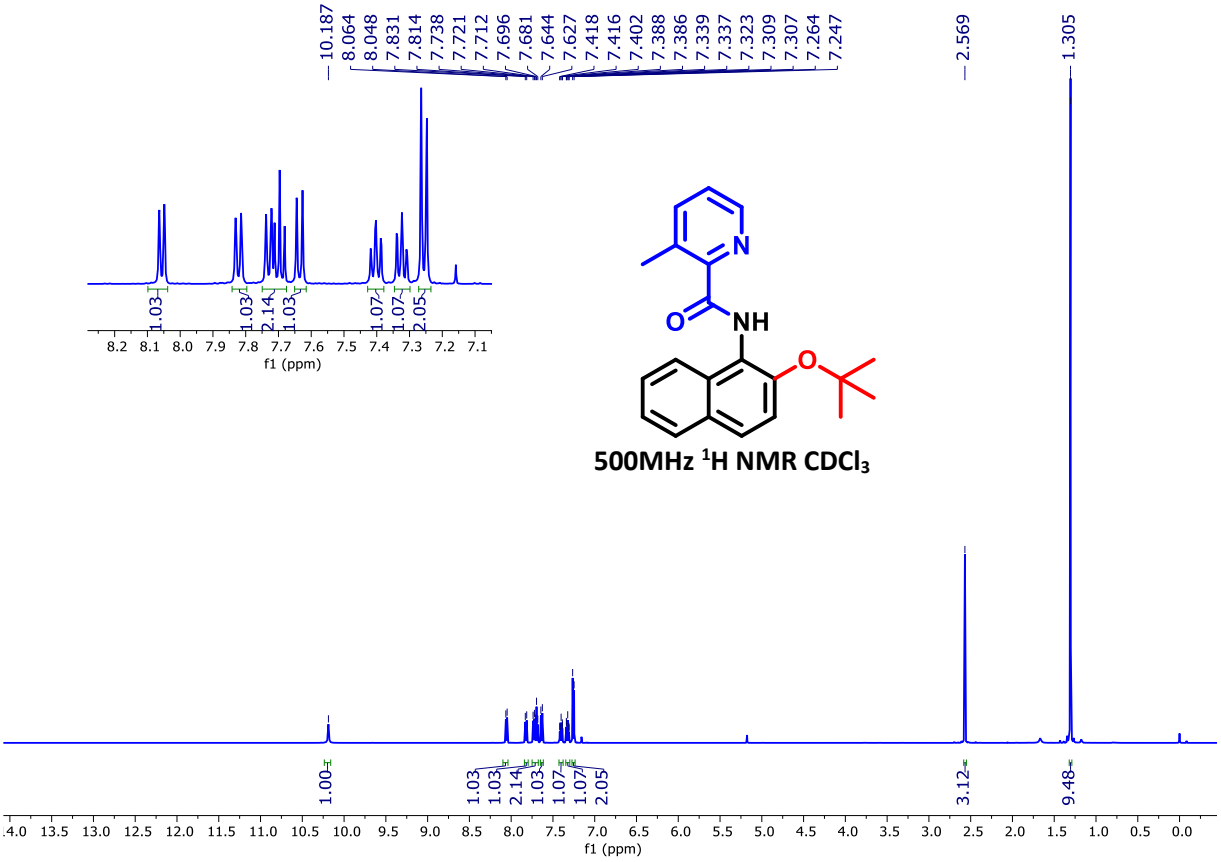


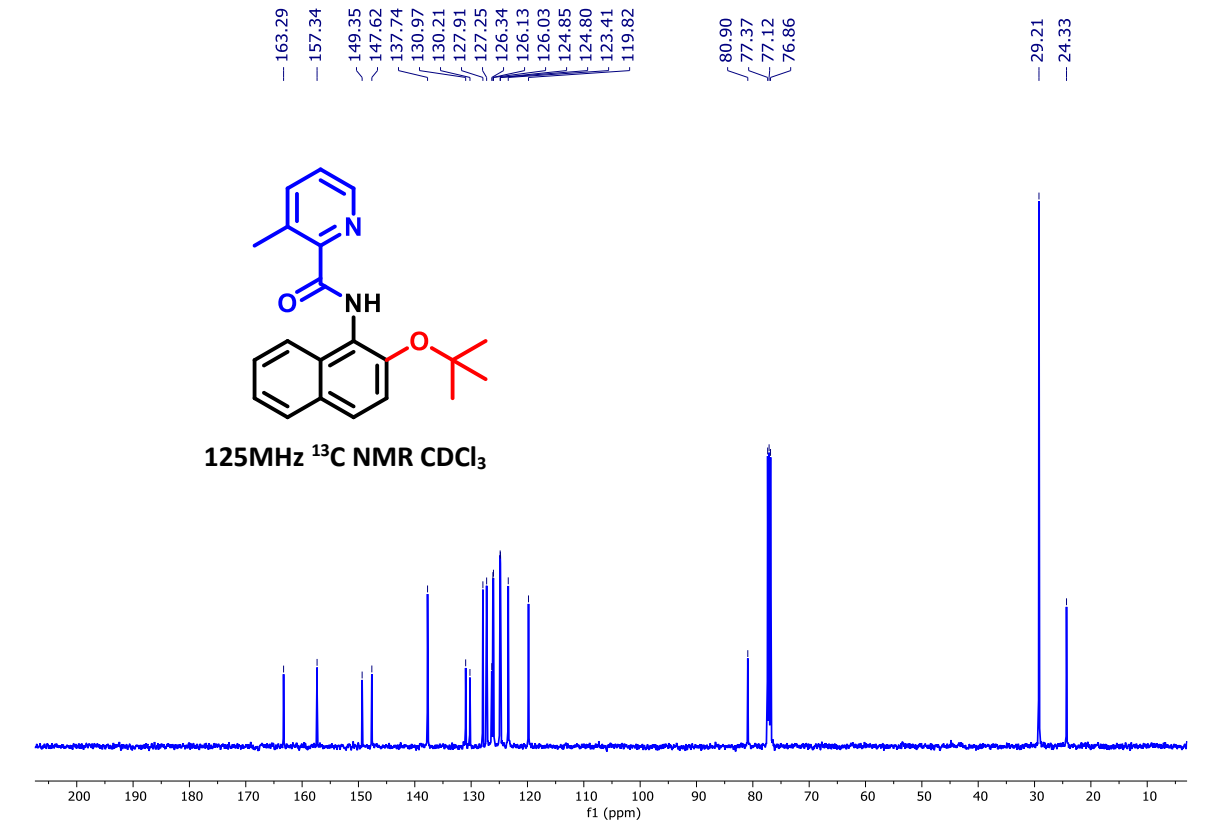
600MHz ^{1}H NMR $CDCl_3$



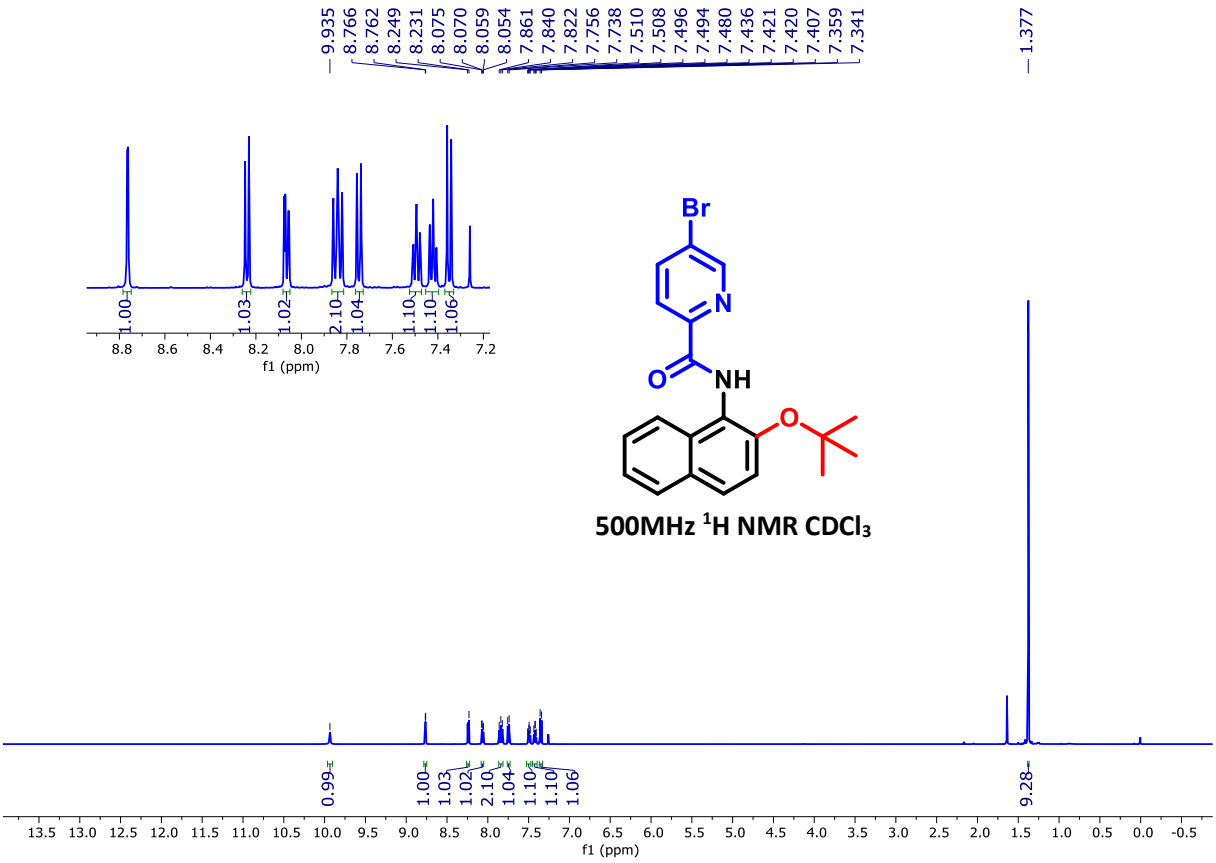
151MHz ^{13}C NMR $CDCl_3$

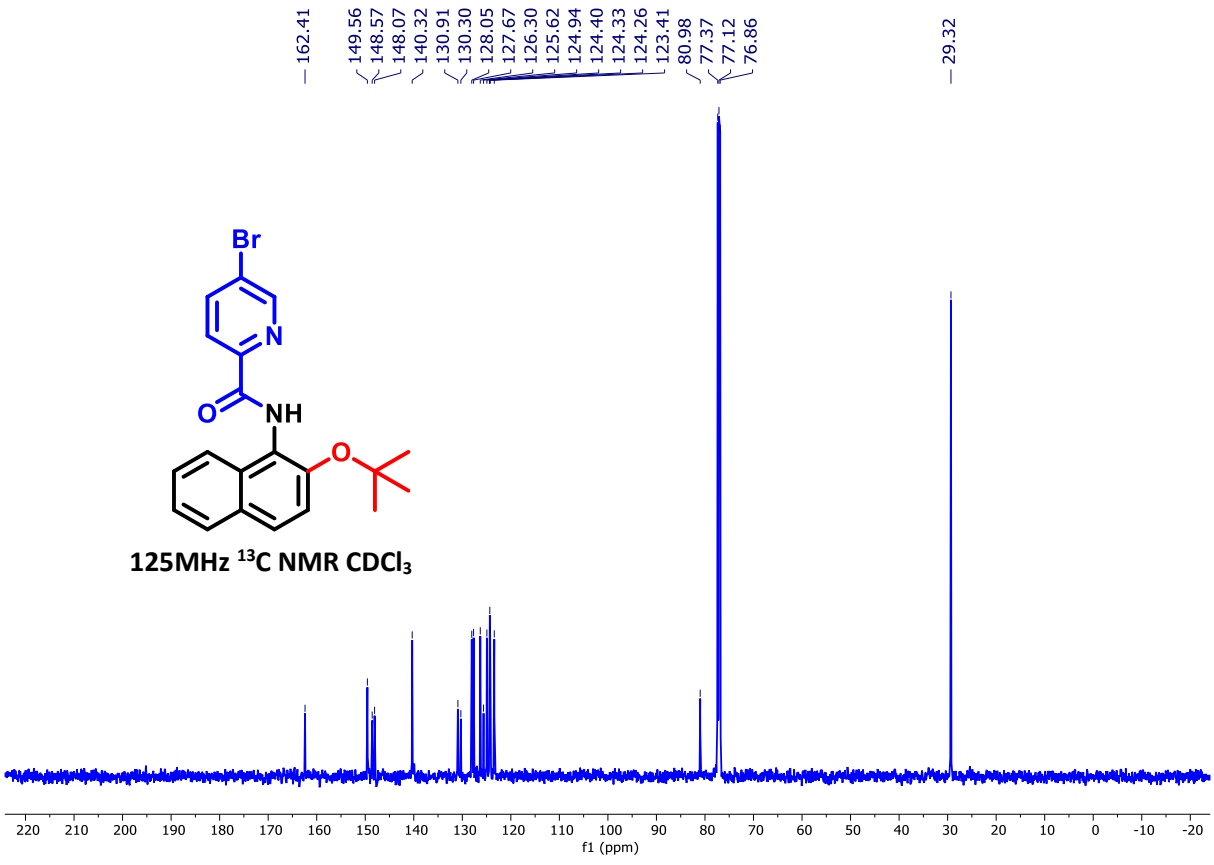
N-(2-(tert-butoxy)naphthalen-1-yl)-3-methylpicolinamide(5b)



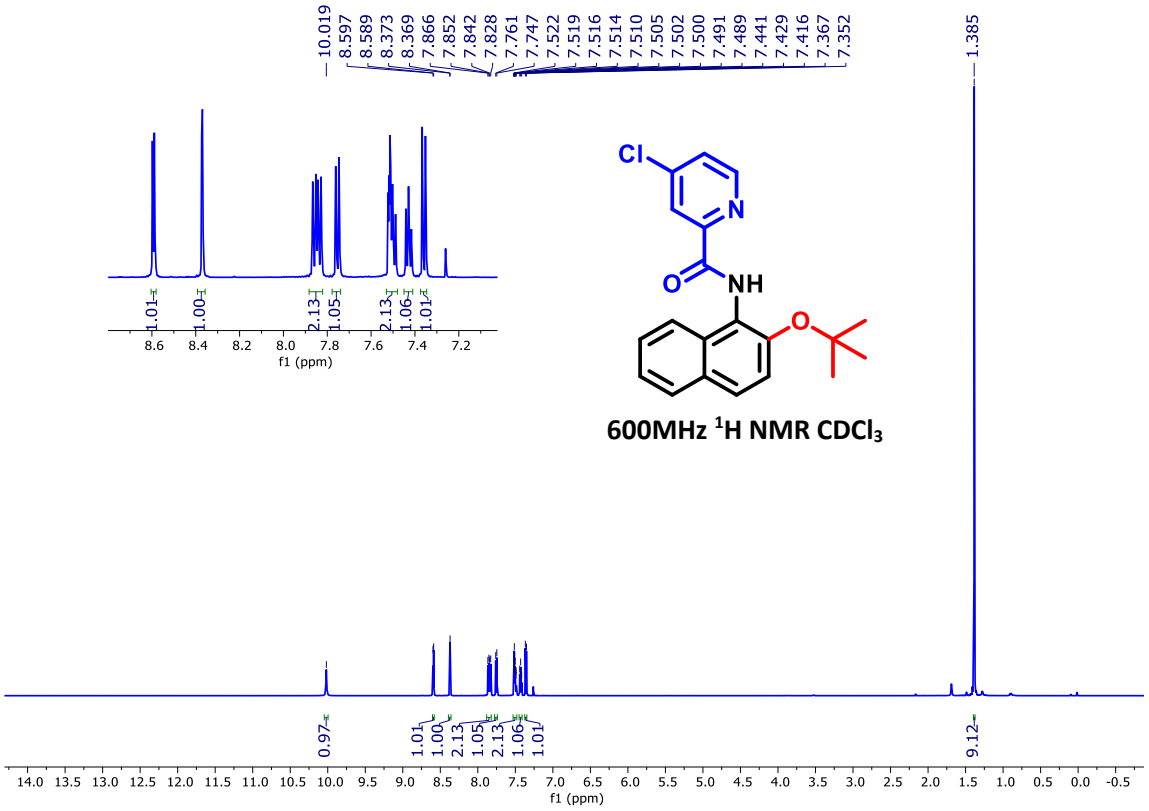


5-bromo-N-(2-(tert-butoxy)naphthalen-1-yl)Picolinamide(5c)

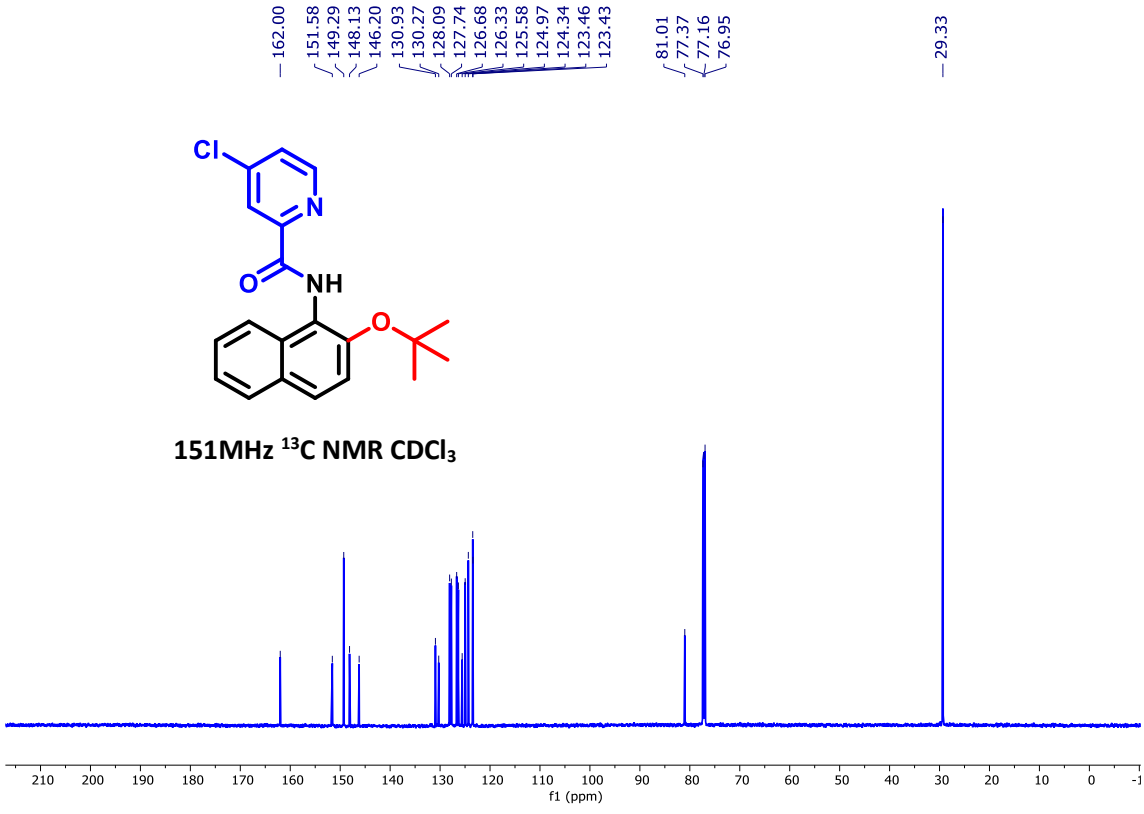




N-(2-(tert-butoxy)naphthalen-1-yl)-5-chloropicolinamide(5d):

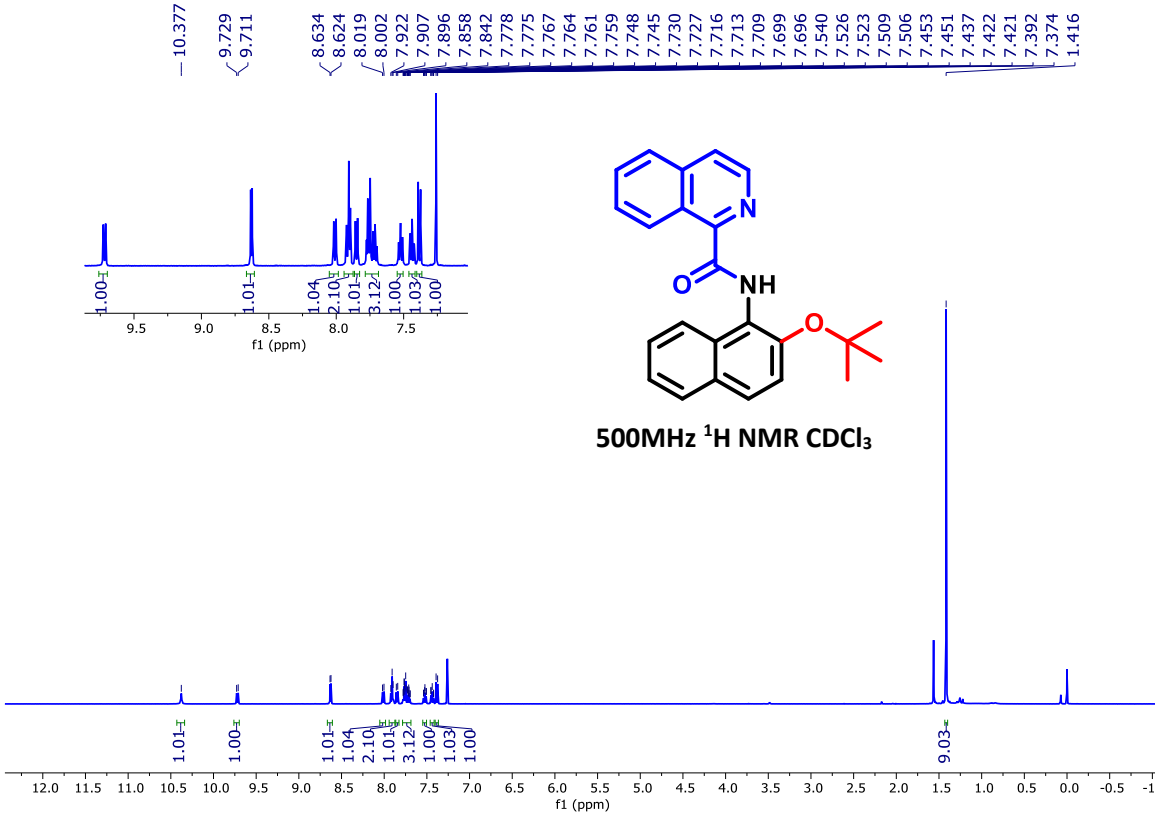


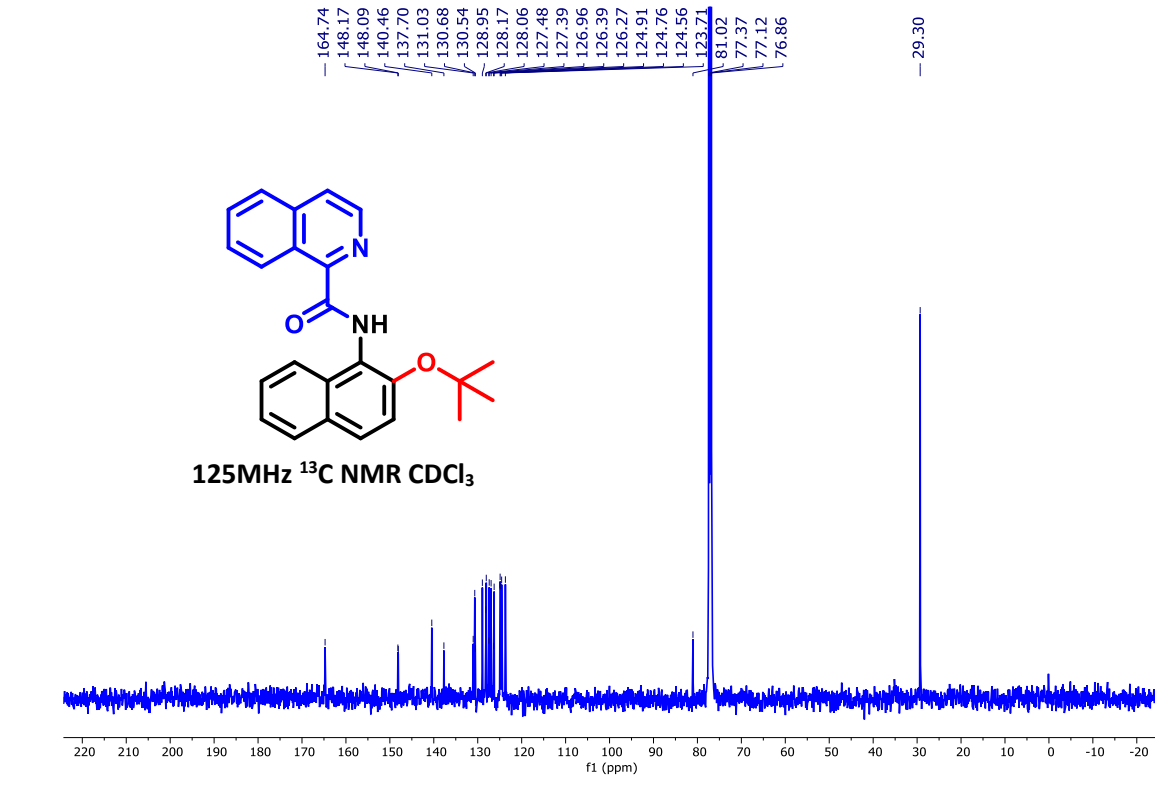
600MHz ^{1}H NMR $CDCl_3$



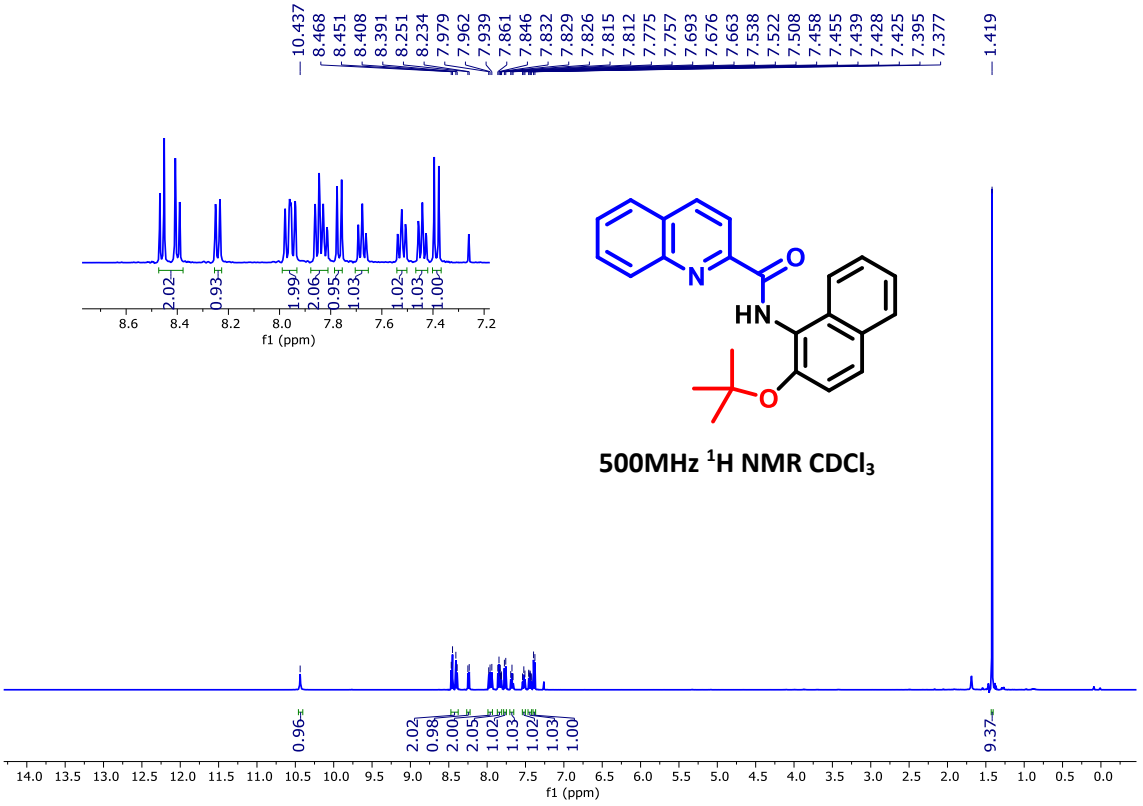
151MHz ^{13}C NMR $CDCl_3$

N-(2-(tert-butoxy)naphthalen-1-yl)isoquinoline-1-carboxamide(5e):

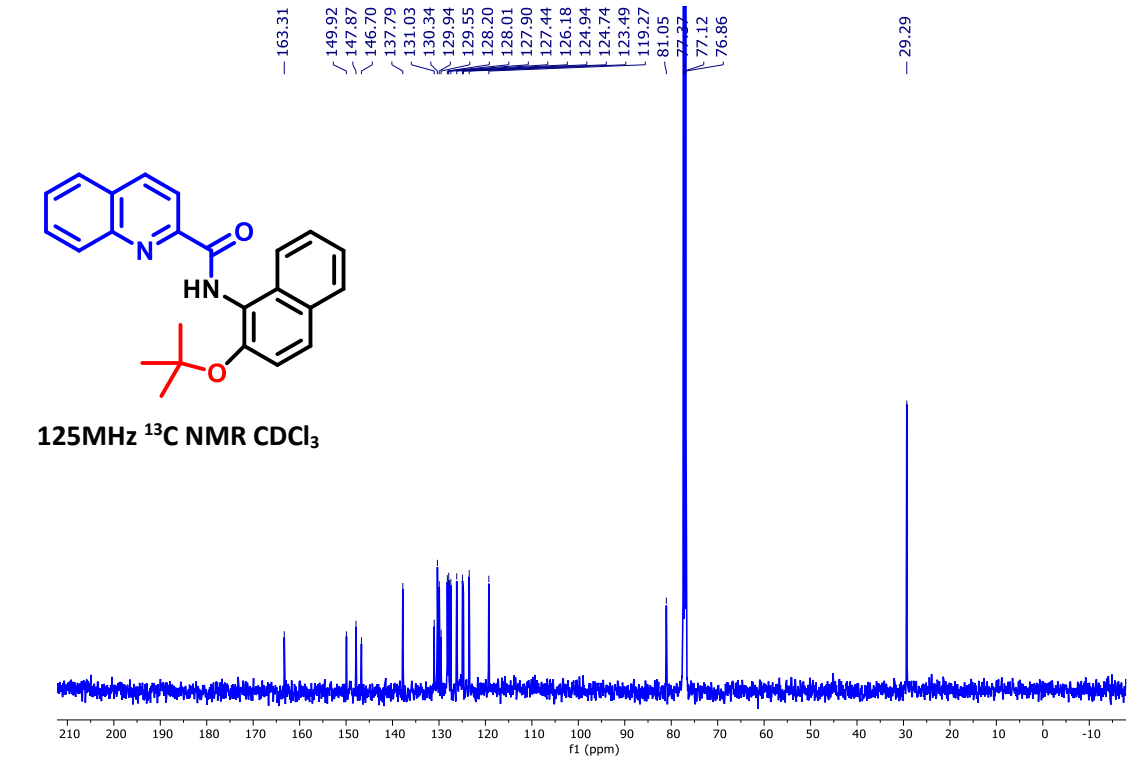




N-(2-(tert-butoxy)naphthalen-1-yl)quinoline-2-carboxamide(5f)

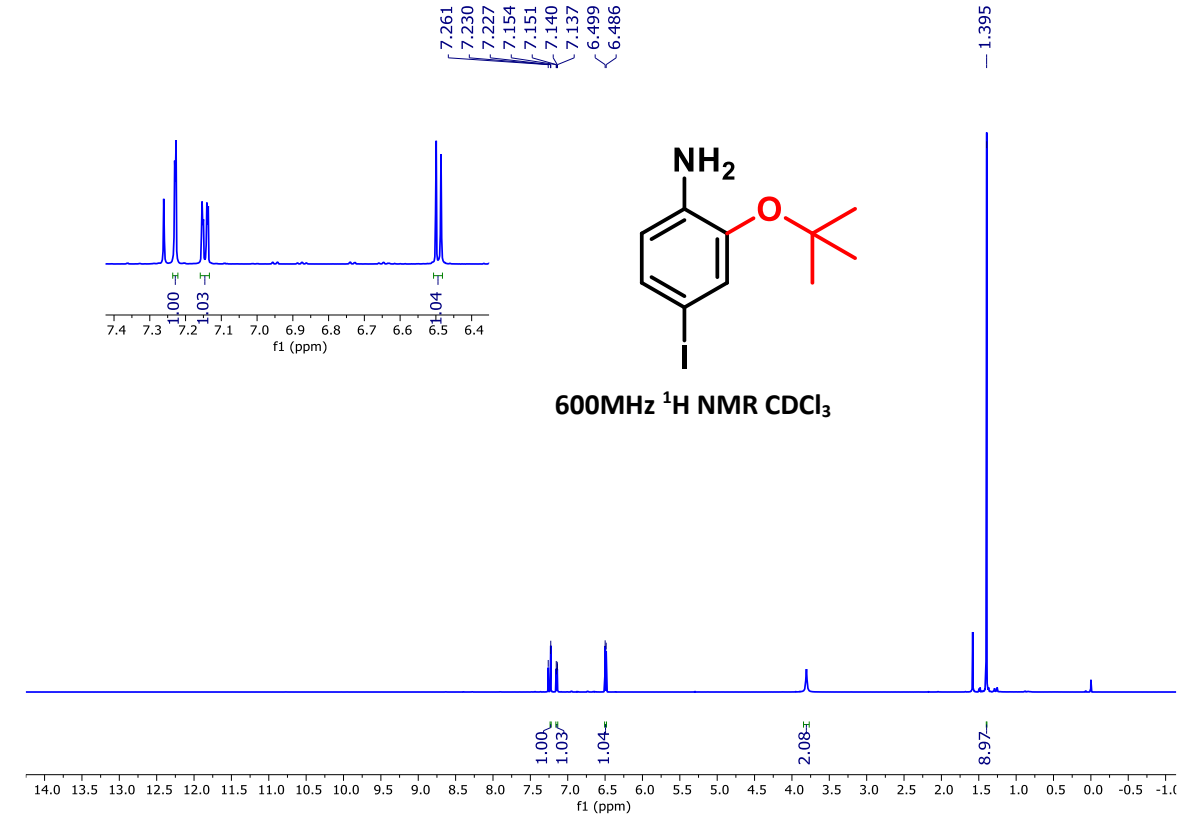


500MHz ^{1}H NMR $CDCl_3$

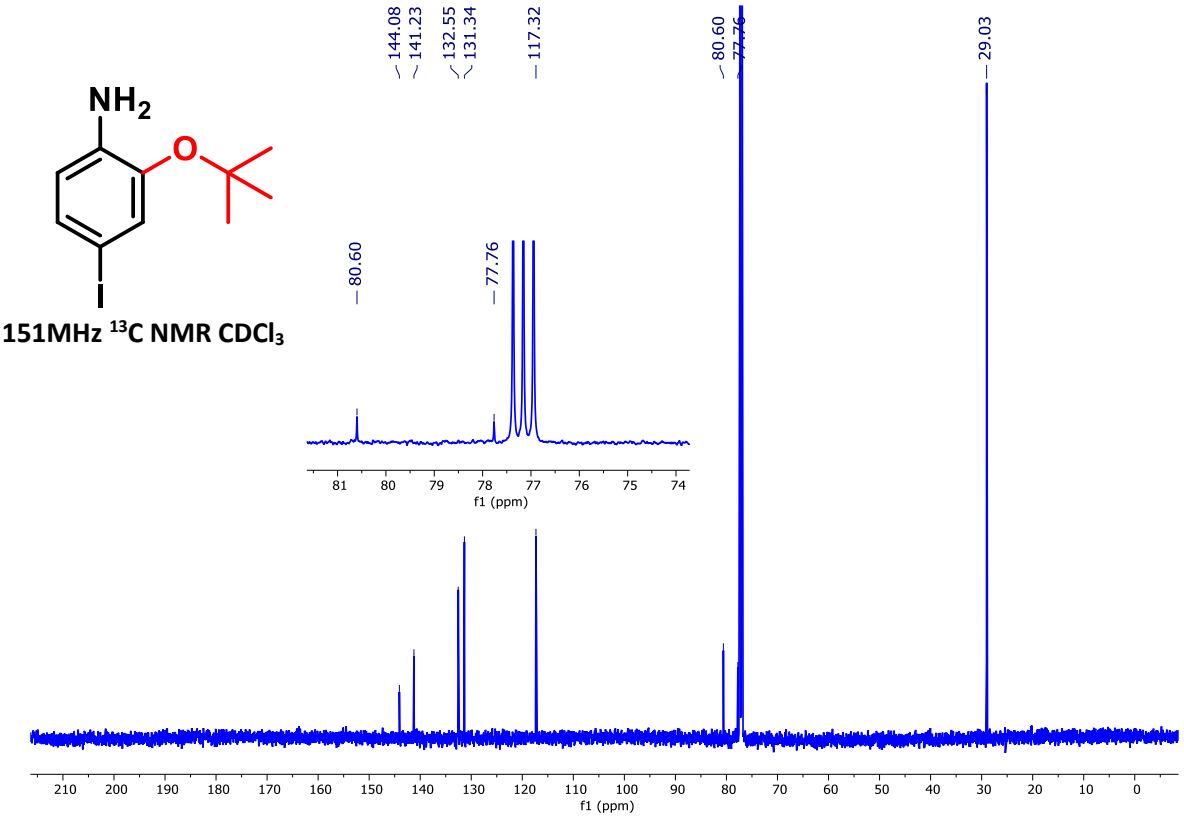


125MHz ^{13}C NMR $CDCl_3$

2-(tert-butoxy)-4-iodoaniline(7):

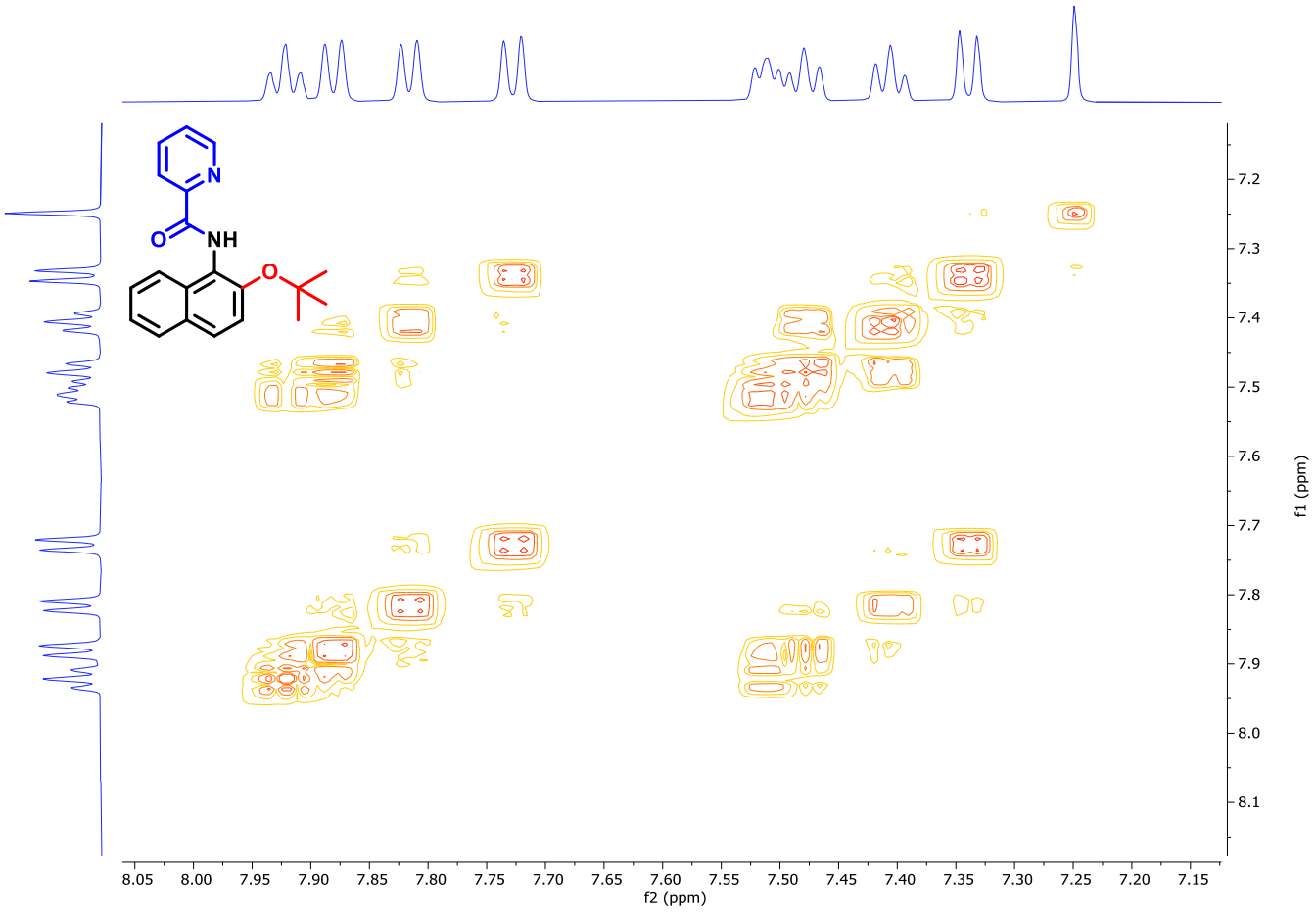


600MHz ^{1}H NMR $CDCl_3$



151MHz ^{13}C NMR $CDCl_3$

2D NMR of 3a


N
O
NH
O
8.05
8.00
7.95
7.90
7.85
7.80
7.75
7.70
7.65
7.60
7.55
7.50
7.45
7.40
7.35
7.30
7.25
7.20
7.15
f2 (ppm)
7.2
7.3
7.4
7.5
7.6
7.7
7.8
7.9
8.0
8.1
f1 (ppm)

11. Crystal Structure and data

Table S5: Crystal Data and Refinement Parameters for **4k**

Identification code	**4k**
Empirical formula	$C_{18}H_{20}N_2O_3$
Formula weight	312.36
Temperature/K	301.(2)
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	7.0141(7)
b/Å	11.0390(11)
c/Å	22.180(2)
α/°	90
β/°	97.678(3)
γ/°	90
Volume/Å^3	1702.0(3)
Z	4
ρ_{calc}g/cm^3	1.219
μ/mm^{-1}	0.084
F(000)	664.0
Crystal size/mm^3	0.510 × 0.107 × 0.095
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	5.24 to 63
Index ranges	$-10 \leq h \leq 10$, $-16 \leq k \leq 16$, $-32 \leq l \leq 32$
Reflections collected	25369
Independent reflections	5626 [R_{int} = 0.0565, R_{sigma} = 0.0565]
Data/restraints/parameters	5626/0/216
Goodness-of-fit on F^2	0.966
Final R indexes [I>=2σ (I)]	R_1 = 0.0866, wR_2 = 0.2518
Final R indexes [all data]	R_1 = 0.1973, wR_2 = 0.3669
Largest diff. peak/hole / e Å^{-3}	0.25/-0.20
CCDC Deposition number	2034533

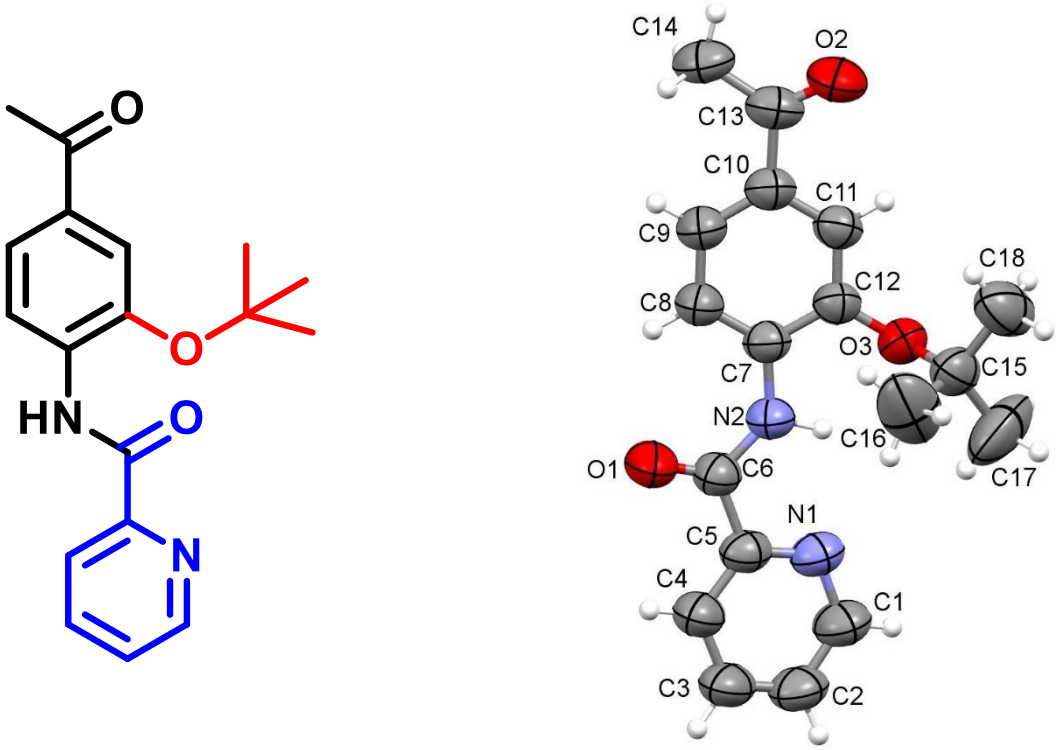


Figure S7. ORTEP diagram of the organic molecule **4k** with atom numbering scheme (45% probability factor for the thermal ellipsoids). Crystal growth from mixed solvent ethyl acetate: hexane (40:60).

12. References

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