Supporting Information

Ruthenium-catalyzed *ortho*-selective C_{Ar}–H amination of heteroaryl arenes with *di*-*tert*-butyldiaziridinone

Xue-Ya Gou,[a‡] Yuke Li,[b‡] Xin-Gang Wang,[a] Hong-Chao Liu,[a] Bo-Sheng Zhang,[a] Jia-Hui Zhao,[a] Zhao-Zhao Zhou,[a] and Yong-Min Liang*[a]

[a] State Key Laboratory of Applied Organic Chemistry, Lanzhou University, Lanzhou 730000, P.R. China
[b] Department of Chemistry and Centre for Scientific Modeling and Computation, Chinese University of Hong Kong, Shatin, Hong Kong, China.

*Corresponding E-mail Address: liangym@lzu.edu.cn

Table of Contents

1. General Methods

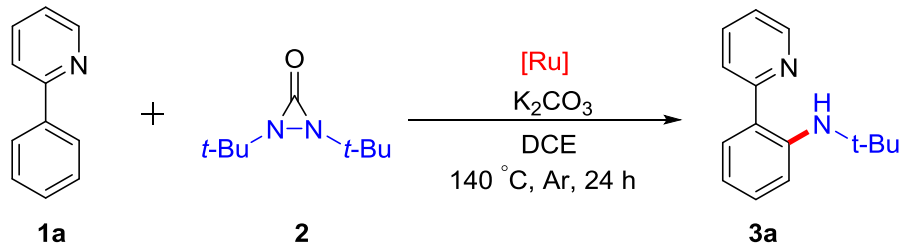
General Procedures. Unless otherwise noted, reactions were performed under Ar atmosphere. Solvent was freshly distilled/degassed prior to use unless otherwise noted. Analytical TLC was performed with silica gel GF254 plates. For column chromatography, a 200-300 mesh silica gel was employed. Organic solutions were concentrated under reduced pressure using a rotary evaporator. Room temperature (r.t.) is 18-22°C.

Materials. Substrate **1a** was commercially available and was not further purified, other substrate **1b-1ag**[1] and **2**[2] were synthesized according to previously described methods. Commercial reagents were purchased from Adamas, Ark, Aladdin, or TCI and used as received with the following exceptions. 1,4-Dioxane and toluene were dried with CaH_2 and freshly distilled, DCE was dried with P_2O_5 and freshly distilled. Other commercially available reagents and solvents were used without further purification.

Instrumentation. Deuterated solvents were purchased from Cambridge Isotope Laboratories. ^{1}H NMR spectra were recorded on Bruker AVANCE III 400 and INOVA instruments with 400 and 600 MHz frequencies, and ^{13}C NMR spectra were recorded on Bruker AVANCE III 400 and INOVA instruments with 400 and 600 MHz with 101 and 151 MHz frequencies. ^{19}F NMR spectra were recorded on a Bruker AVANCE III 400 spectrometer with a ^{19}F operating frequency of 376 MHz. Chemical shifts (δ) were reported in ppm relative to the residual solvent signal ($CDCl_3$ δ = 7.26 for ^{1}H NMR and δ = 77.0 for ^{13}C NMR). Chemical shifts (ppm) were recorded with tetramethyl silane (TMS) as the internal reference standard. Multiplicities are given as s (singlet), d (doublet), t (triplet), dd (doublet of doublets), td (triplet of doublets) or m (multiplet). HRMS was obtained using a Q-TOF instrument equipped with an ESI source. Data collection for crystal structure was performed at room temperature using Mo Kα radiation on a Bruker APEXII diffractometer.

2. Optimization Studies

Table S1. Screening of ruthenium catalyst[a]

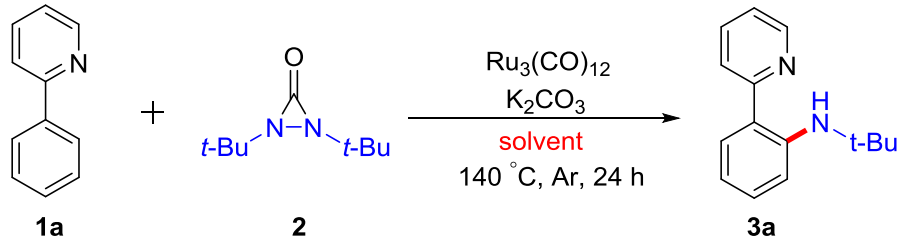


1a **2** **3a**

entry	[Ru]	yield(%)[b]
1	$[RuCl_2(p\text{-cymene})]_2$	n.r.
2	$[Ru(O_2CMes)_2(p\text{-cymene})]$	n.r.
3	$Ru(pph_3)_3Cl_2$	n.r.
4	$Ru_3(CO)_{12}$	35

[a] Reaction conditions: **1a** (0.2 mmol), **2** (0.4 mmol), [Ru] (5 mol %), K_2CO_3 (2.0 equiv.), DCE (2.0 mL), under Ar, 140 °C, 24 h. [b] Isolated yields based on **1a**.

Table S2. Screening of solvent[a]

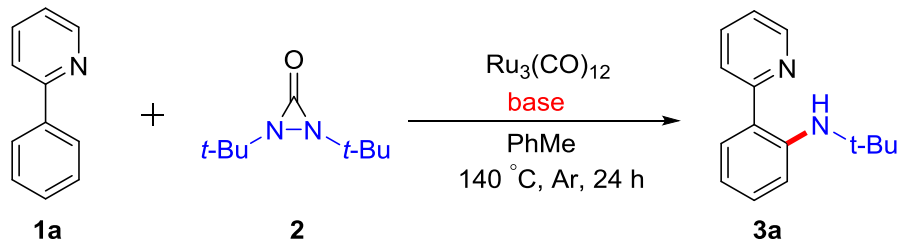


1a **2** **3a**

entry	solvent	yield (%)[b]
1	dioxane	26
2	PhMe	42
3	xylene	31
4	Mesitylene	33
5	THF	34

[a] Reaction conditions: **1a** (0.2 mmol), **2** (0.4 mmol), $Ru_3(CO)_{12}$ (5 mol %), K_2CO_3 (2.0 equiv.), solvent (2.0 mL), under Ar, 140 °C, 24 h. [b] Isolated yields based on **1a**.

Table S3. Screening of base[a]



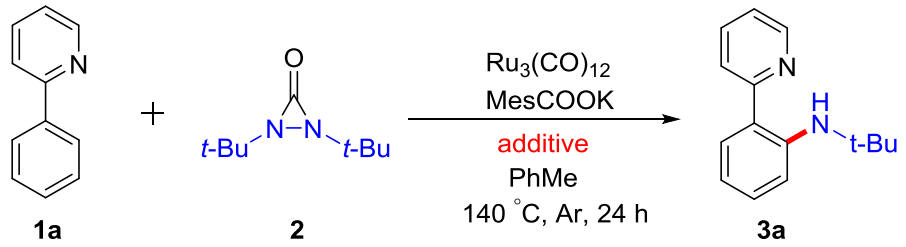
1a **2** **3a**

entry	base	yield (%)[b]
1	$NaCO_3$	21
2	$CsCO_3$	30
3	NaOAc	49

4	KOAC	47
5	CsOAc	45
6	K_3PO_4	43
7	^{t}-BuOK	23
8	PivOK	61
9	MesCOOK	72

[a] Reaction conditions: **1a** (0.2 mmol), **2** (0.4 mmol), $Ru_3(CO)_{12}$ (5 mol%), base (2.0 equiv.), PhMe (2.0 mL), under Ar, 140 °C, 24 h. [b] Isolated yields based on **1a**.

Table S4. Screening of additive[a]

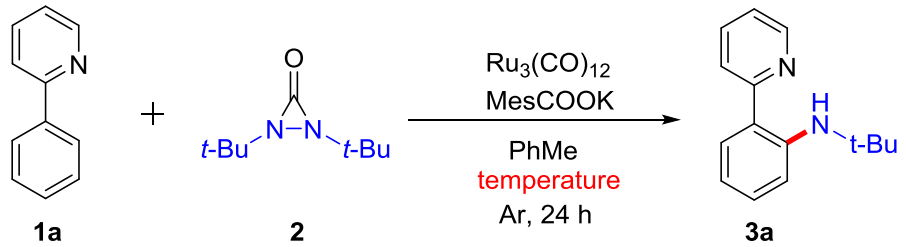


1a **2** **3a**

entry	additive	yield (%)[b]
1	NaOAc	65
2	PivOK	60
3	1-AdCOOH	51
4	MesCOOH	56
5	*N*-Ac-L-Val	41
6	*N*-Piv-Val	40
7	PivOH	44
8	PPh_3	49
9	PCy_3BF_4	42

[a] Reaction conditions: **1a** (0.2 mmol), **2** (0.4 mmol), $Ru_3(CO)_{12}$ (5 mol %), MesCOOK (2.0 equiv.), additive (30 mol%), PhMe (2.0 mL), under Ar, 140 °C, 24 h. [b] Isolated yields based on **1a**.

Table S5. Screening of temperature[a]



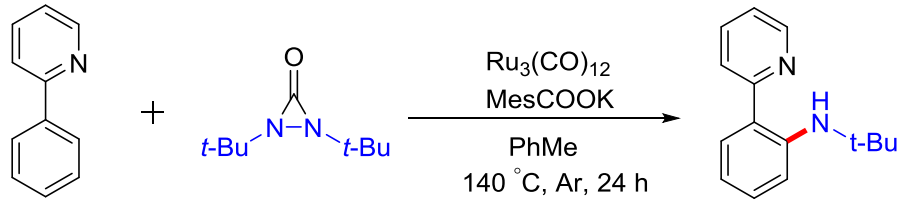
1a **2** **3a**

entry	temperature	yield (%)[b]
1	130°C	65
2	120°C	62
3	110°C	44
4	100°C	31
5	90°C	16
6	80°C	trace

[a] Reaction conditions: **1a** (0.2 mmol), **2** (0.4 mmol), $Ru_3(CO)_{12}$ (5 mol %), MesCOOK (2.0 equiv.),

PhMe (2.0 mL), under Ar, temperature, 24 h. [b] Isolated yields based on **1a**.

Table S6. Black experiments[a]

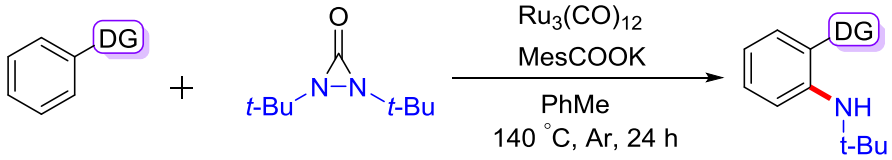


1a **2**

entry	deviation from standard conditions	yield (%)[b]
1	no $Ru_3(CO)_{12}$	n.r.
2	no base	34%

[a] Reaction conditions: **1a** (0.2 mmol), **2** (0.4 mmol), $Ru_3(CO)_{12}$ (5 mol %), MesCOOK (2.0 equiv.), PhMe (2.0 mL), under Ar, 140 °C, 24 h. [b] Isolated yields based on **1a**.

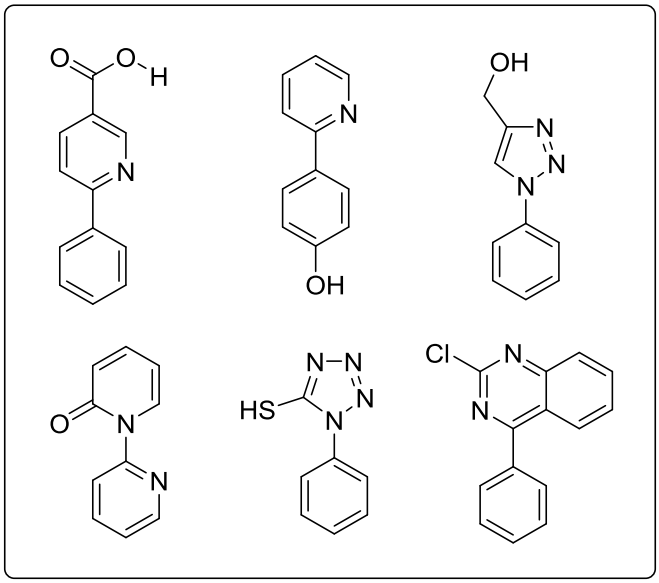
3. General Procedure

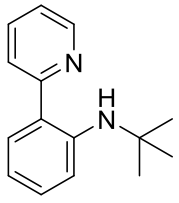


1a-1al **2** **3a-3al**

In a 20 mL tube, a mixture of **1** (0.2 mmol, 1.0 equiv.), $Ru_3(CO)_{12}$ (6.4 mg, 5 mol %), MesCOOK (80 mg, 2.0 equiv. or 120 mg, 3.0 equiv.) were added and charged with argon more than three times. PhMe (2.0 mL) and **2** (80 μL, 68 mg, 2.0 equiv.) were injected into the tube. Afterwards, the reaction tube was then immersed in an oil bath, which was preheated at 140 °C for 24 h. After the reaction was completed, the residue was purified by column chromatography (PE/EA) on silica gel to give the product **3**.

Limited scope:





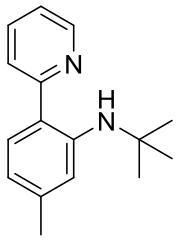
N-(tert-butyl)-2-(pyridin-2-yl)aniline (3a)

32.7 mg, yield: 72%. Light yellow solid. M.p. (from $CHCl_3$): 64-66 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.58 (dd, *J* = 4.8, 1.7 Hz, 1H), 8.06 (s, 1H), 7.73 (td, *J* = 7.8, 1.9 Hz, 1H), 7.62 (d, *J* = 8.1 Hz, 1H), 7.48 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.24 – 7.19 (m, 1H), 7.15 (dd, *J* = 7.4, 4.9 Hz, 1H), 7.03 (d, *J* = 8.4 Hz, 1H), 6.72 (t, *J* = 7.4 Hz, 1H), 1.38 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 160.01, 147.22, 146.47, 136.78, 130.03, 129.41, 123.62, 122.93, 120.67, 115.87, 115.68, 50.77, 29.93.

HRMS (ESI) Calcd for $C_{15}H_{18}N_2$ $[M+H]^+$: 227.1543, found: 227.1547.



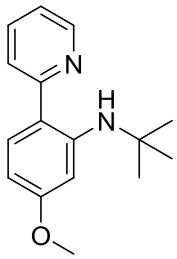
N-(tert-butyl)-5-methyl-2-(pyridin-2-yl)aniline (3b)

27.4 mg, yield: 57%. Yellow liquid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.55 (d, *J* = 4.2 Hz, 1H), 8.18 (s, 1H), 7.70 (td, *J* = 7.7, 1.9 Hz, 1H), 7.59 (d, *J* = 8.1 Hz, 1H), 7.40 (d, *J* = 7.9 Hz, 1H), 7.16 – 7.07 (m, 1H), 6.84 (s, 1H), 6.54 (d, *J* = 7.8 Hz, 1H), 2.34 (s, 3H), 1.39 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 159.92, 147.01, 146.41, 139.28, 136.56, 129.76, 122.46, 120.77, 120.22, 116.79, 116.15, 50.63, 29.87, 21.82.

HRMS (ESI) Calcd for $C_{16}H_{20}N_2$ [M+H]$^+$: 241.1699, found: 241.1703.



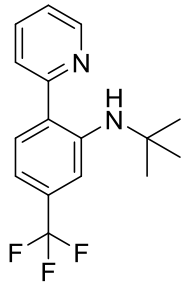
N-(tert-butyl)-5-methoxy-2-(pyridin-2-yl)aniline(3c)

37.6mg, yield: 73%.Yellow liquid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.54 – 8.50 (m, 1H), 7.72 – 7.65 (m, 1H), 7.57 (d, *J* = 8.2 Hz, 1H), 7.46 (d, *J* = 8.7 Hz, 1H), 7.11 – 7.06 (m, 1H), 6.53 (d, *J* = 2.5 Hz, 1H), 6.28 (dd, *J* = 8.6, 2.5 Hz, 1H), 3.83 (s, 3H), 1.42 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 160.75, 159.75, 147.98, 146.95, 136.60, 130.92, 122.01, 119.90, 116.37, 100.89, 100.52, 55.02, 50.60, 29.78.

HRMS (ESI) Calcd for $C_{15}H_{18}N_2$ [M+H]$^+$: 257.1648, found: 257.1653.



N-(tert-butyl)-2-(pyridin-2-yl)-5-(trifluoromethyl)aniline (3d)

42.2 mg, yield: 72%. Light yellow solid. M.p. (from $CHCl_3$): 68-71 °C.

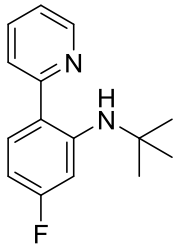
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.63 (d, *J* = 4.1 Hz, 1H), 8.42 (s, 1H), 7.81 (td, *J* = 7.9, 1.8 Hz, 1H), 7.67 (d, *J* = 8.1 Hz, 1H), 7.59 (d, *J* = 8.1 Hz, 1H), 7.31 – 7.24 (m, 1H), 7.24 (s, 1H), 6.94 (d, *J* = 8.0 Hz, 1H), 1.45 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 158.77, 147.34, 146.52, 137.08, 131.14 (q, *J* = 31.7 Hz), 130.21,

125.58(q, *J* = 272.4 Hz), 125.41, 123.09, 121.46, 111.51 (q, *J* = 3.8 Hz), 111.03 (q, *J* = 3.9 Hz), 50.80, 29.70.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -63.03.

HRMS (ESI) Calcd for $C_{16}H_{17}F_3N_2$ [M+H]$^+$: 295.1417, found: 295.1420.



N-(tert-butyl)-5-fluoro-2-(pyridin-2-yl)aniline (**3e**)

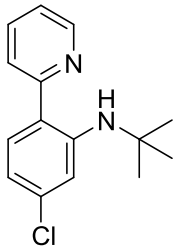
31.7mg, yield: 65%. Light yellow solid. M.p. (from $CHCl_3$): 87-89 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.61 (s, 1H), 8.59 – 8.56 (m, 1H), 7.76 (td, *J* = 8.0, 1.8 Hz, 1H), 7.60 (d, *J* = 8.2 Hz, 1H), 7.48 (dd, *J* = 8.6, 7.0 Hz, 1H), 7.21 – 7.15 (m, 1H), 6.70 (dd, *J* = 12.9, 2.5 Hz, 1H), 6.40 (td, *J* = 8.4, 2.5 Hz, 1H), 1.45 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 163.92 (d, *J* = 244.3 Hz), 159.28, 148.25 (d, *J* = 11.7 Hz), 147.08, 136.85, 131.26 (d, *J* = 11.0 Hz), 122.48, 120.56, 118.68 (d, *J* = 2.1 Hz), 101.90 (d, *J* = 22.1 Hz), 100.95 (d, *J* = 25.6 Hz), 50.65, 29.60.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -111.22.

HRMS (ESI) Calcd for $C_{15}H_{17}FN_2$ [M+H]$^+$: 245.1449, found: 245.1452.



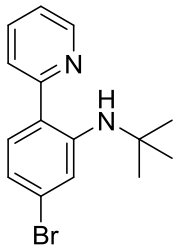
N-(tert-butyl)-5-chloro-2-(pyridin-2-yl)aniline (**3f**)

32.7 mg, yield: 63%. Light yellow solid. M.p. (from $CHCl_3$): 100-102 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.58 – 8.54 (m, 1H), 8.47 (s, 1H), 7.74 (td, *J* = 7.8, 1.8 Hz, 1H), 7.59 (d, *J* = 8.2 Hz, 1H), 7.41 (d, *J* = 8.3 Hz, 1H), 7.19 – 7.14 (m, 1H), 6.95 (d, *J* = 2.0 Hz, 1H), 6.64 (dd, *J* = 8.3, 2.0 Hz, 1H), 1.41 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 159.11, 147.43, 147.16, 136.93, 135.29, 130.84, 122.61, 120.96, 120.88, 115.17, 114.19, 50.71, 29.67.

HRMS (ESI) Calcd for $C_{15}H_{17}ClN_2$ [M+H]$^+$: 261.1153, found: 261.1159.



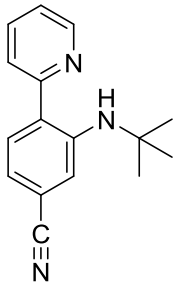
5-bromo-N-(tert-butyl)-2-(pyridin-2-yl)aniline (3g)

31.7 mg, yield: 52%. Light yellow solid. M.p. (from $CHCl_3$): 118-122 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.62 – 8.56 (m, 1H), 8.49 (s, 1H), 7.77 (td, *J* = 8.0, 1.8 Hz, 1H), 7.62 (d, *J* = 8.2 Hz, 1H), 7.37 (d, *J* = 8.3 Hz, 1H), 7.23 – 7.18 (m, 1H), 7.14 (d, *J* = 1.9 Hz, 1H), 6.82 (dd, *J* = 8.3, 1.9 Hz, 1H), 1.44 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 159.14, 147.56, 147.17, 136.93, 131.05, 123.78, 122.58, 121.36, 120.92, 118.08, 117.14, 50.71, 29.68.

HRMS (ESI) Calcd for $C_{15}H_{17}BrN_2$ $[M+H]^+$: 305.0648, found: 305.0648.



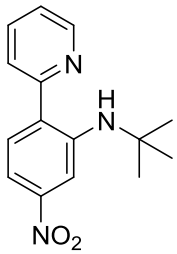
3-(tert-butylamino)-4-(pyridin-2-yl)benzonitrile (3h)

27.2 mg, yield: 54%. Light yellow solid. M.p. (from $CHCl_3$): 150-152 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.63 – 8.59 (m, 1H), 8.54 (s, 1H), 7.83 – 7.77 (m, 1H), 7.62 (d, *J* = 8.1 Hz, 1H), 7.52 (d, *J* = 8.0 Hz, 1H), 7.27 – 7.23 (m, 1H), 7.18 (d, *J* = 1.3 Hz, 1H), 6.95 – 6.88 (m, 1H), 1.41 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 158.15, 147.25, 146.40, 137.17, 130.30, 126.02, 123.06, 121.78, 119.71, 118.02, 116.87, 112.45, 50.66, 29.42.

HRMS (ESI) Calcd for $C_{16}H_{17}N_3$ $[M+H]^+$: 252.1495, found: 252.1500.



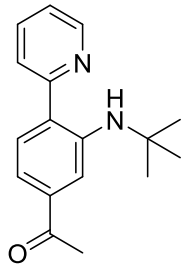
N-(tert-butyl)-5-nitro-2-(pyridin-2-yl)aniline (3i)

35.7 mg, yield: 66%. Red solid. M.p. (from $CHCl_3$): 150-152 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.63 (s, 1H), 8.62 (s, 1H), 7.84 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.80 (d, *J* = 2.2 Hz, 1H), 7.68 (d, *J* = 8.1 Hz, 1H), 7.60 (d, *J* = 8.6 Hz, 1H), 7.48 (dd, *J* = 8.6, 2.2 Hz, 1H), 7.32 – 7.26 (m, 1H), 1.47 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 158.01, 148.62, 147.44, 146.89, 137.28, 130.28, 127.37, 123.38, 122.03, 109.38, 108.28, 50.90, 29.49.

HRMS (ESI) Calcd for $C_{15}H_{17}N_3O_2$ [M+H]$^+$: 272.1394, found: 272.1400.



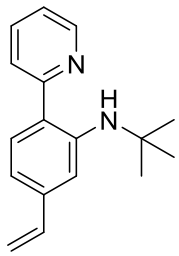
1-(3-(tert-butylamino)-4-(pyridin-2-yl)phenyl)ethan-1-one (3j)

35.0 mg, yield: 65%. Yellow solid. M.p. (from $CHCl_3$): 102-106 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.66 – 8.59 (m, 1H), 8.28 (s, 1H), 7.79 (td, *J* = 7.8, 1.9 Hz, 1H), 7.67 (d, *J* = 8.1 Hz, 1H), 7.64 (d, *J* = 1.6 Hz, 1H), 7.57 (d, *J* = 8.1 Hz, 1H), 7.27 (dd, *J* = 8.1, 1.7 Hz, 1H), 7.25 – 7.21 (m, 1H), 2.62 (s, 3H), 1.45 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 198.41, 158.79, 147.30, 146.40, 137.45, 136.97, 129.96, 126.94, 123.19, 121.43, 115.52, 114.26, 50.76, 29.72, 26.67.

HRMS (ESI) Calcd for $C_{15}H_{17}N_3O_2$ [M+H]$^+$: 269.1648, found: 269.1653.



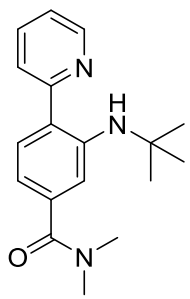
N-(tert-butyl)-2-(pyridin-2-yl)-5-vinylaniline (3k)

32.2 mg, yield: 64%. Yellow liquid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.59 – 8.53 (m, 1H), 8.27 (s, 1H), 7.71 (td, *J* = 7.8, 1.9 Hz, 1H), 7.64 – 7.59 (m, 1H), 7.50 – 7.45 (m, 1H), 7.17 – 7.11 (m, 1H), 7.09 – 7.02 (m, 1H), 6.81 (dd, *J* = 8.0, 1.4 Hz, 1H), 6.71 (dd, *J* = 17.6, 10.8 Hz, 1H), 5.81 – 5.72 (m, 1H), 5.26 (d, *J* = 10.9 Hz, 1H), 1.41 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 159.64, 147.14, 146.71, 138.47, 137.38, 136.71, 130.06, 122.88, 122.65, 120.57, 113.79, 113.74, 113.60, 50.77, 29.97.

HRMS (ESI) Calcd for $C_{17}H_{20}N_2$ [M+H]$^+$: 253.1699, found: 253.1702.



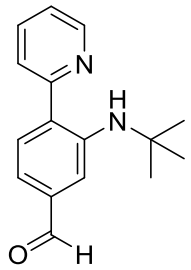
3-(tert-butylamino)-N,N-dimethyl-4-(pyridin-2-yl)benzamide (3l)

29.1 mg, yield: 49%. Yellow solid. M.p. (from $CHCl_3$): 108-110 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.58 (d, *J* = 4.3 Hz, 1H), 8.26 (s, 1H), 7.79 – 7.72 (m, 1H), 7.62 (d, *J* = 8.1 Hz, 1H), 7.50 (d, *J* = 7.9 Hz, 1H), 7.18 (dd, *J* = 7.2, 5.1 Hz, 1H), 7.00 (d, *J* = 1.3 Hz, 1H), 6.72 (dd, *J* = 7.9, 1.3 Hz, 1H), 3.12 (s, 3H), 3.04 (s, 3H), 1.39 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.94, 159.22, 147.16, 146.24, 137.17, 136.86, 129.94, 123.84, 122.86, 120.96, 113.94, 113.31, 50.69, 39.38, 35.12, 29.80.

HRMS (ESI) Calcd for $C_{18}H_{23}N_3O$ $[M+H]^+$: 298.1914, found: 298.1919



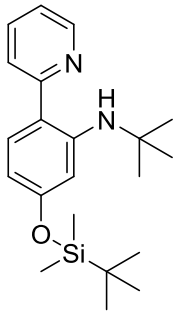
3-(tert-butylamino)-4-(pyridin-2-yl)benzaldehyde (3m)

15.6 mg, yield: 31%. (8.1 mg, yield: 16%) [c]. Yellow solid. M.p. (from $CHCl_3$): 118-121 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.97 (s, 1H), 8.62 (d, *J* = 4.2 Hz, 1H), 8.30 (s, 1H), 7.83 – 7.78 (m, 1H), 7.67 (d, *J* = 8.1 Hz, 1H), 7.63 (d, *J* = 7.9 Hz, 1H), 7.50 – 7.46 (m, 1H), 7.26 – 7.21 (m, 1H), 7.20 – 7.15 (m, 1H), 1.45 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 192.82, 158.78, 147.41, 146.83, 137.09, 136.89, 130.51, 128.17, 123.45, 121.68, 117.11, 114.68, 50.84, 29.70.

HRMS (ESI) Calcd for $C_{16}H_{18}N_2O$ $[M+H]^+$: 255.1492, found: 255.1495.



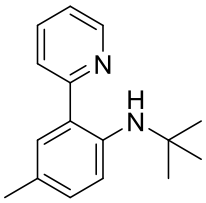
N-(tert-butyl)-5-((tert-butyldimethylsilyl)oxy)-2-(pyridin-2-yl)aniline (3n)

16.4 mg, yield: 23%. Yellow solid. M.p. (from $CHCl_3$): > 340 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.54 – 8.50 (m, 1H), 8.45 (s, 1H), 7.68 (td, *J* = 8.0, 1.8 Hz, 1H), 7.56 (d, *J* = 8.2 Hz, 1H), 7.39 (d, *J* = 8.5 Hz, 1H), 7.11 – 7.05 (m, 1H), 6.49 (d, *J* = 2.3 Hz, 1H), 6.21 (dd, *J* = 8.5, 2.3 Hz, 1H), 1.40 (s, 9H), 1.00 (s, 9H), 0.24 (s, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 159.89, 156.99, 147.95, 146.94, 136.56, 130.85, 122.09, 119.88, 116.79, 107.99, 106.49, 50.57, 29.87, 25.73, 18.28, -4.29.

HRMS (ESI) Calcd for $C_{21}H_{32}N_2OSi$ $[M+H]^+$: 357.2357, found: 357.2362.



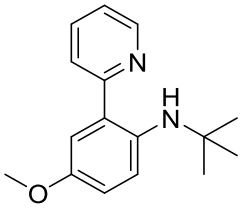
N-(tert-butyl)-4-methyl-2-(pyridin-2-yl)aniline (3o)

22.5 mg, yield: 47%. Yellow liquid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.58 (d, *J* = 4.2 Hz, 1H), 7.73 (td, *J* = 7.9, 1.6 Hz, 1H), 7.60 (d, *J* = 8.1 Hz, 1H), 7.28 (s, 1H), 7.19 – 7.12 (m, 1H), 7.08 – 7.02 (m, 1H), 6.98 (d, *J* = 8.4 Hz, 1H), 2.29 (s, 3H), 1.31 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 159.94, 147.35, 143.87, 136.66, 130.45, 129.92, 125.65, 125.01, 123.00, 120.66, 117.17, 51.00, 29.94, 20.39.

HRMS (ESI) Calcd for $C_{16}H_{20}N_2$ $[M+H]^+$: 241.1699, found: 241.1705.



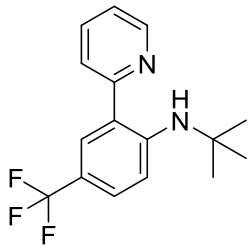
N-(tert-butyl)-4-methoxy-2-(pyridin-2-yl)aniline (3p)

35.9 mg, yield: 70%. Light yellow liquid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.66 – 8.60 (m, 1H), 7.76 (td, *J* = 7.8, 1.8 Hz, 1H), 7.58 (d, *J* = 8.1 Hz, 1H), 7.23 – 7.18 (m, 1H), 7.09 (d, *J* = 8.9 Hz, 1H), 7.05 (d, *J* = 3.0 Hz, 1H), 6.87 (dd, *J* = 8.9, 3.0 Hz, 1H), 3.81 (s, 3H), 1.19 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 159.55, 152.28, 147.58, 139.75, 136.77, 128.71, 123.19, 121.46, 121.03, 115.16, 114.88, 55.61, 51.69, 29.88.

HRMS (ESI) Calcd for $C_{16}H_{20}N_2O$ $[M+H]^+$: 257.1648, found: 257.1653.



N-(tert-butyl)-2-(pyridin-2-yl)-4-(trifluoromethyl)aniline (3q)

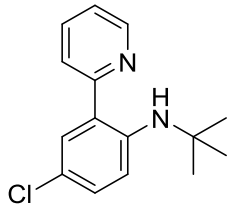
42.0 mg, yield: 71%. Light yellow liquid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.83 (s, 1H), 8.60 – 8.55 (m, 1H), 7.81 – 7.75 (m, 1H), 7.73 (d, *J* = 2.0 Hz, 1H), 7.67 (d, *J* = 8.2 Hz, 1H), 7.42 (dd, *J* = 8.8, 1.8 Hz, 1H), 7.23 – 7.18 (m, 1H), 7.00 (d, *J* = 8.8 Hz, 1H), 1.44 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 158.80, 148.91, 147.13, 137.13, 127.13 – 126.93 (m), 126.43 – 126.24 (m),125.16(q, *J* = 269.9 Hz), 122.70, 121.26, 113.34, 50.72, 29.58.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -60.79.

HRMS (ESI) Calcd for $C_{16}H_{17}F_3N_2$ $[M+H]^+$: 295.1417, found: 295.1415.



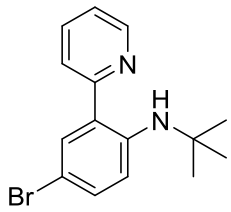
N-(tert-butyl)-4-chloro-2-(pyridin-2-yl)aniline (3r)

40.3 mg, yield: 77%. Light yellow solid. M.p. (from $CHCl_3$): 77-78 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.60 – 8.55 (m, 1H), 8.08 (s, 1H), 7.75 (td, *J* = 7.9, 1.9 Hz, 1H), 7.59 (d, *J* = 8.1 Hz, 1H), 7.45 (d, *J* = 2.6 Hz, 1H), 7.21 – 7.17 (m, 1H), 7.15 (dd, *J* = 8.9, 2.6 Hz, 1H), 6.94 (d, *J* = 9.0 Hz, 1H), 1.36 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 158.68, 147.35, 145.08, 137.02, 129.43, 129.06, 124.64, 122.85, 121.20, 120.43, 116.66, 50.86, 29.82

HRMS (ESI) Calcd for $C_{16}H_{20}N_2O$ $[M+H]^+$: 261.1153, found: 261.1159.



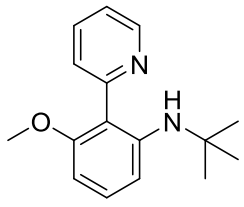
4-bromo-N-(tert-butyl)-2-(pyridin-2-yl)aniline (3s)

36.4 mg, yield: 60%. Light yellow solid. M.p. (from $CHCl_3$): 58-61 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.61 – 8.54 (m, 1H), 8.14 (s, 1H), 7.74 (td, *J* = 7.8, 1.8 Hz, 1H), 7.60 (s, 1H), 7.58 (d, *J* = 2.3 Hz, 1H), 7.29 – 7.25 (m, 1H), 7.21 – 7.16 (m, 1H), 6.89 (d, *J* = 8.9 Hz, 1H), 1.37 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 158.56, 147.32, 145.48, 137.01, 132.25, 131.89, 124.95, 122.83, 121.20, 116.84, 107.30, 50.79, 29.78.

HRMS (ESI) Calcd for $C_{15}H_{17}BrN_2$ $[M+H]^+$: 305.0648, found: 305.0656.



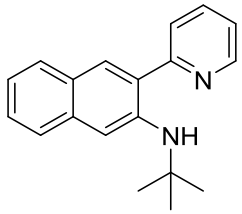
N-(tert-butyl)-3-methoxy-2-(pyridin-2-yl)aniline (3t)

23.2 mg, yield: 45%. Yellow liquid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.69 – 8.65 (m, 1H), 7.71 (td, *J* = 7.8, 1.8 Hz, 1H), 7.49 – 7.44 (m, 1H), 7.20 – 7.17 (m, 1H), 7.16 – 7.13 (m, 1H), 6.73 – 6.69 (m, 1H), 6.39 (d, *J* = 8.2 Hz, 1H), 5.40 (s, 1H), 3.69 (s, 3H), 1.24 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 157.60, 156.10, 148.70, 146.51, 135.98, 129.11, 127.48, 121.33, 116.29, 109.67, 100.45, 55.53, 51.16, 30.02.

HRMS (ESI) Calcd for $C_{16}H_{20}N_2O$ $[M+H]^+$: 257.1648, found: 257.2646.



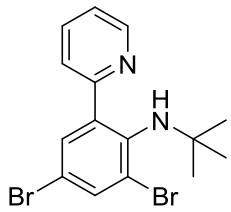
N-(tert-butyl)-3-(pyridin-2-yl)naphthalen-2-amine (**3u**)

38.7 mg, yield: 70%. Yellow liquid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.69 – 8.61 (m, 1H), 7.90 (s, 1H), 7.80 (td, *J* = 7.8, 1.8 Hz, 1H), 7.73 (d, *J* = 8.1 Hz, 1H), 7.70 (d, *J* = 8.1 Hz, 1H), 7.65 (d, *J* = 8.2 Hz, 1H), 7.38 (t, *J* = 7.5 Hz, 1H), 7.28 – 7.22 (m, 2H), 7.19 (t, *J* = 7.5 Hz, 1H), 1.47 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 159.61, 147.61, 143.22, 137.24, 135.01, 130.19, 128.02, 127.90, 126.75, 126.30, 125.60, 124.03, 121.92, 121.59, 108.72, 51.07, 29.42.

HRMS (ESI) Calcd for $C_{19}H_{20}N_2$ $[M+H]^+$: 277.1699, found: 277.1697.



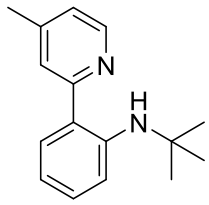
2,4-dibromo-N-(tert-butyl)-6-(pyridin-2-yl)aniline (**3v**)

33.5 mg, yield: 44%. Brown solid. M.p. (from $CHCl_3$):154-156 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.64 (d, *J* = 4.3 Hz, 1H), 7.80 – 7.76 (m, 1H), 7.71 (d, *J* = 2.4 Hz, 1H), 7.68 – 7.64 (m, 1H), 7.61 (d, *J* = 2.4 Hz, 1H), 7.23 – 7.18 (m, 1H), 4.10 (s, 1H), 0.84 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 158.54, 149.17, 142.49, 139.70, 136.03, 134.91, 133.25, 125.16, 124.92, 122.33, 116.51, 56.48, 30.31.

HRMS (ESI) Calcd for $C_{15}H_{16}Br_2N_2$ $[M+H]^+$: 384.9733, found: 384.9730.



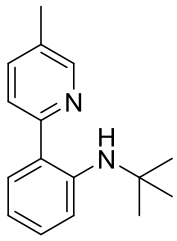
N-(tert-butyl)-2-(4-methylpyridin-2-yl)aniline (**3aa**)

29.0 mg, yield: 60%. Yellow solid. M.p. (from $CHCl_3$): 80-81 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.47 (d, *J* = 5.1 Hz, 1H), 8.02 (s, 1H), 7.50 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.46 (s, 1H), 7.24 (td, *J* = 7.9, 7.3, 1.6 Hz, 1H), 7.06 (d, *J* = 8.3 Hz, 1H), 7.03 (d, *J* = 5.6 Hz, 1H), 6.75 (t, *J* = 7.2 Hz, 1H), 2.42 (s, 3H), 1.41 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 159.78, 147.78, 147.05, 146.37, 129.94, 129.23, 123.98, 123.80, 121.86, 115.89, 115.65, 50.79, 29.89, 21.30.

HRMS (ESI) Calcd for $C_{16}H_{20}N_2$ $[M+H]^+$: 241.1699, found: 241.1703.



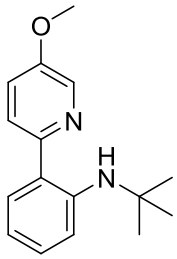
N-(tert-butyl)-2-(5-methylpyridin-2-yl)aniline (3ab)

31.1 mg, yield: 65%. Light yellow solid. M.p. (from $CHCl_3$): 100-102 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.41 (s, 1H), 7.55 (dd, *J* = 8.3, 2.0 Hz, 1H), 7.51 (d, *J* = 8.2 Hz, 1H), 7.46 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.20 (td, *J* = 7.9, 7.3, 1.6 Hz, 1H), 7.03 (d, *J* = 8.2 Hz, 1H), 6.75 – 6.68 (m, 1H), 2.35 (s, 3H), 1.38 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 157.13, 147.44, 146.14, 137.49, 130.08, 129.75, 129.01, 123.81, 122.42, 115.93, 115.70, 50.80, 29.86, 18.06.

HRMS (ESI) Calcd for $C_{16}H_{20}N_2$ $[M+H]^+$: 241.1699, found: 241.1702.



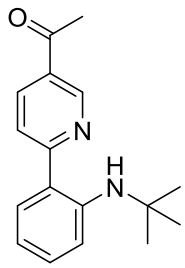
N-(tert-butyl)-2-(5-methoxypyridin-2-yl)aniline (3ac)

36.0 mg, yield: 70%. Yellow liquid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.28 (d, *J* = 3.0 Hz, 1H), 7.55 (d, *J* = 8.8 Hz, 1H), 7.44 – 7.40 (m, 1H), 7.29 (dd, *J* = 8.8, 3.0 Hz, 1H), 7.22 – 7.17 (m, 1H), 7.05 (d, *J* = 7.8 Hz, 1H), 6.73 (t, *J* = 7.1 Hz, 1H), 3.89 (s, 3H), 1.36 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 153.61, 152.50, 145.84, 134.11, 129.59, 128.73, 124.03, 123.60, 122.12, 116.13, 115.87, 55.59, 50.87, 29.90.

HRMS (ESI) Calcd for $C_{16}H_{20}N_2O$ $[M+H]^+$: 257.1648, found: 257.1643.



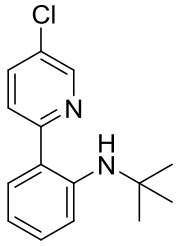
1-(6-(2-(tert-butylamino)phenyl)pyridin-3-yl)ethan-1-one (3ad)

40.2 mg, yield: 75%. Yellow solid. M.p. (from $CHCl_3$): 127-129 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.17 – 9.10 (m, 1H), 8.72 (s, 1H), 8.27 (dd, *J* = 8.6, 2.4 Hz, 1H), 7.79 (d, *J* = 8.5 Hz, 1H), 7.61 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.30 – 7.26 (m, 1H), 7.10 – 7.04 (m, 1H), 6.76 – 6.69 (m, 1H), 2.67 (s, 3H), 1.46 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 196.21, 163.62, 147.70, 147.41, 135.82, 130.70, 130.31, 128.78, 122.00, 120.86, 115.44, 115.31, 50.74, 29.86, 26.54.

HRMS (ESI) Calcd for $C_{17}H_{20}N_2O$ [M+H]$^+$: 269.1648, found: 269.1653.



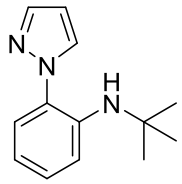
N-(tert-butyl)-2-(5-chloropyridin-2-yl)aniline (3ae)

36.3 mg, yield: 70%. Yellow solid. M.p. (from $CHCl_3$): 99-101 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.58 (d, *J* = 2.1 Hz, 1H), 7.95 (s, 1H), 7.74 (dd, *J* = 8.7, 2.5 Hz, 1H), 7.62 (d, *J* = 8.7 Hz, 1H), 7.49 (d, *J* = 7.7 Hz, 1H), 7.28 (d, *J* = 5.6 Hz, 1H), 7.07 (d, *J* = 8.4 Hz, 1H), 6.75 (t, *J* = 7.4 Hz, 1H), 1.43 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 158.04, 146.37, 145.87, 136.58, 129.97, 129.81, 128.91, 123.75, 122.11, 115.83, 115.57, 50.80, 29.89.

HRMS (ESI) Calcd for $C_{16}H_{20}N_2O$ [M+H]$^+$: 261.1153, found: 261.1159.



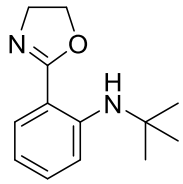
N-(tert-butyl)-2-(1H-pyrazol-1-yl)aniline (3af)

17.8 mg, yield: 41%. Yellow solid. M.p. (from $CHCl_3$): 72-73 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.74 (d, *J* = 1.6 Hz, 1H), 7.63 (d, *J* = 2.2 Hz, 1H), 7.20 (td, *J* = 8.0, 7.5, 1.5 Hz, 1H), 7.14 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.08 (d, *J* = 8.2 Hz, 1H), 6.80 – 6.69 (m, 1H), 6.43 (t, *J* = 2.1 Hz, 1H), 5.50 (s, 1H), 1.29 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 141.69, 140.48, 130.58, 128.33, 128.28, 125.06, 116.65, 106.29, 51.19, 29.74.

HRMS (ESI) Calcd for $C_{13}H_{17}N_3$ [M+H]$^+$: 216.1495, found: 216.1490.



N-(tert-butyl)-2-(1H-pyrazol-1-yl)aniline (3ag)

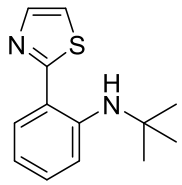
23.2 mg, yield: 53%. Yellow liquid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.64 (s, 1H), 7.75 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.23 (td, *J* = 8.0, 7.3, 1.7 Hz, 1H), 6.93 (d, *J* = 8.5 Hz, 1H), 6.55 (t, *J* = 7.5 Hz, 1H), 4.30 – 4.25 (m, 2H), 4.12 – 4.06 (m, 2H), 1.45 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.23, 148.15, 131.56, 130.39, 113.55, 112.98, 109.16, 65.38,

54.99, 50.58, 29.67.

HRMS (ESI) Calcd for $C_{13}H_{18}N_2O$ $[M+H]^+$: 219.1492, found: 219.1490.



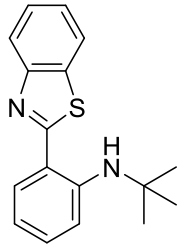
N-(tert-butyl)-2-(thiazol-2-yl)aniline (3ah)

22.7 mg, yield: 49%. Yellow liquid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.81 (s, 1H), 7.76 (d, *J* = 3.3 Hz, 1H), 7.68 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.23 – 7.19 (m, 1H), 7.18 (d, *J* = 3.5 Hz, 1H), 7.01 (d, *J* = 8.5 Hz, 1H), 6.61 (t, *J* = 7.4 Hz, 1H), 1.48 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.37, 145.52, 141.81, 130.25, 130.16, 116.40, 116.03, 114.56, 114.22, 50.72, 29.77.

HRMS (ESI) Calcd for $C_{13}H_{16}N_2S$ $[M+H]^+$: 233.1107, found: 233.1106.



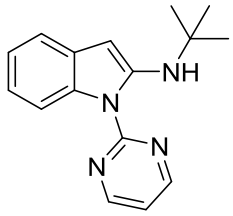
2-(benzo[d]thiazol-2-yl)-N-(tert-butyl)aniline (3ai)

19.8 mg, yield: 35%. Yellow liquid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.30 (s, 1H), 7.92 (d, *J* = 8.0 Hz, 1H), 7.85 (d, *J* = 7.7 Hz, 1H), 7.74 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.47 – 7.41 (m, 1H), 7.36 – 7.31 (m, 1H), 7.25 (dt, *J* = 7.2, 1.5 Hz, 1H), 7.04 (d, *J* = 8.2 Hz, 1H), 6.69 – 6.61 (m, 1H), 1.54 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 169.70, 153.42, 146.63, 133.15, 131.24, 125.88, 124.71, 122.08, 121.02, 115.29, 114.46, 114.08, 50.93, 29.71.

HRMS (ESI) Calcd for $C_{17}H_{18}N_2S$ $[M+H]^+$: 283.1263, found: 283.1262.



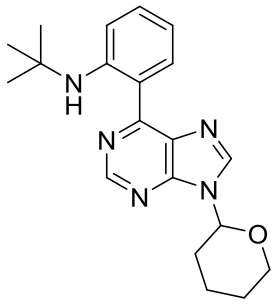
N-(tert-butyl)-1-(pyrimidin-2-yl)-1H-indol-2-amine (3aj)

19.7 mg, yield: 37%. Yellow solid. M.p. (from $CHCl_3$): 108-110 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.71 (s, 1H), 8.70 (s, 1H), 8.41 (d, *J* = 8.2 Hz, 1H), 7.86 (s, 1H), 7.33 – 7.28 (m, 1H), 7.14 – 7.09 (m, 1H), 7.05 (t, *J* = 4.8 Hz, 1H), 7.00 (td, *J* = 7.8, 7.4, 1.3 Hz, 1H), 5.65 (s, 1H), 1.42 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 158.94, 157.39, 145.14, 132.45, 131.37, 122.49, 119.04, 116.76, 115.73, 114.70, 84.47, 51.15, 29.13.

HRMS (ESI) Calcd for $C_{16}H_{18}N_4$ [M+H]$^+$: 267.1604, found: 267.1601.



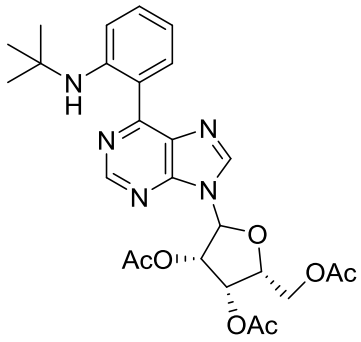
N-(tert-butyl)-2-(9-(tetrahydro-2H-pyran-2-yl)-9H-purin-6-yl)aniline (**3ak**)

43.7 mg, yield: 62%. Yellow liquid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.37 (s, 1H), 8.97 (dd, *J* = 8.0, 1.5 Hz, 1H), 8.91 (s, 1H), 8.31 (s, 1H), 7.34 – 7.29 (m, 1H), 7.07 (d, *J* = 8.5 Hz, 1H), 6.81 (t, *J* = 7.5 Hz, 1H), 5.86 (dd, *J* = 10.1, 2.7 Hz, 1H), 4.24 – 4.18 (m, 1H), 3.83 (td, *J* = 11.7, 2.6 Hz, 1H), 2.17 – 1.69 (m, 6H), 1.49 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 157.86, 150.65, 150.38, 148.60, 140.78, 134.34, 131.49, 130.45, 117.12, 114.87, 114.80, 81.72, 68.82, 50.77, 31.77, 29.88, 24.84, 22.80.

HRMS (ESI) Calcd for $C_{20}H_{25}N_5O$ [M+H]$^+$: 352.2132, found: 352.2130.



(2R,3S,4S)-2-(acetoxymethyl)-5-(6-(2-(tert-butylamino)phenyl)-9H-purin-9-yl)tetrahydrofuran-3,4-diyl diacetate (**3al**)

61.9 mg, yield: 59%. Yellow liquid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.36 (s, 1H), 8.91 (dd, *J* = 8.1, 1.5 Hz, 1H), 8.87 (s, 1H), 8.22 (s, 1H), 7.30 – 7.25 (m, 1H), 7.02 (d, *J* = 8.5 Hz, 1H), 6.75 (t, *J* = 7.5 Hz, 1H), 6.26 (d, *J* = 5.3 Hz, 1H), 5.99 (t, *J* = 5.4 Hz, 1H), 5.72 – 5.64 (m, 1H), 4.44 (dd, *J* = 9.4, 3.2 Hz, 2H), 4.37 (dd, *J* = 12.8, 5.1 Hz, 1H), 2.12 (s, 3H), 2.11 (s, 3H), 2.06 (s, 3H), 1.44 (s, 9H).

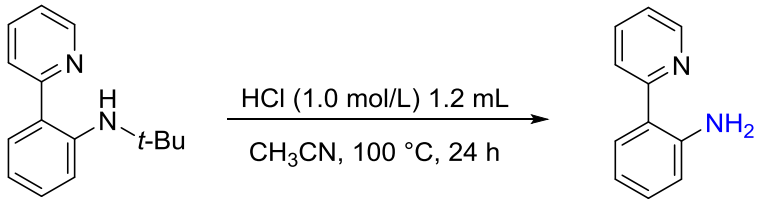
^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.24, 169.49, 169.27, 158.13, 150.90, 150.53, 148.59, 141.26, 134.28, 131.65, 130.84, 116.57, 114.65, 86.17, 80.18, 72.88, 70.51, 62.98, 50.70, 29.75, 20.67, 20.43, 20.29.

HRMS (ESI) Calcd for $C_{26}H_{31}N_5O_7$ [M+H]$^+$: 526.2296, found: 526.2294.

[c] [1,1'-biphenyl]-4-ylmethanol as the substrate.

4. Potential Application of Amination Products

a) Removal of *tert*-butyl group (synthesis of [1,1'-biphenyl]-2-amine 4)



3a (0.2 mmol) **4** 62% yield

In a 20 mL tube, **3a** (0.2 mmol) and 1.0 mol/L HCl (1.2 mL) were added in MeCN (2.0 mL) at 100°C for 24 hours. The reaction was quenched with saturated $NaHCO_3$ solution and extracted with EtOAc. The combined organic layers were washed with brine, dried with Na_2SO_4 and concentrated in vacuo. The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate) to give the corresponding product **4** as light-yellow liquid (17.1 mg, 62%).

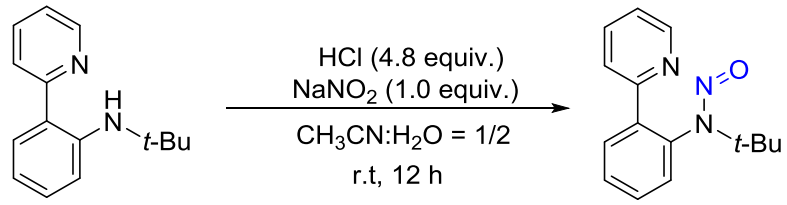
[1,1'-biphenyl]-2-amine (4)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.60 (d, *J* = 4.4 Hz, 1H), 7.75 (td, *J* = 7.8, 1.9 Hz, 1H), 7.64 (d, *J* = 8.1 Hz, 1H), 7.51 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.20 – 7.17 (m, 1H), 7.16 (dd, *J* = 5.7, 1.7 Hz, 1H), 6.83 – 6.77 (m, 1H), 6.76 (d, *J* = 7.9 Hz, 1H), 5.71 (s, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 159.38, 147.82, 146.47, 136.88, 129.85, 129.38, 122.20, 120.93, 117.60, 117.14.

HRMS (ESI) Calcd for $C_{11}H_{10}N_2$ $[M+H]^+$: 171.0917, found: 171.0915.

b) Nitrosation[3] (synthesis of N-(tert-butyl)-N-(2-(pyridin-2-yl)phenyl)nitrous amide 5)



3a (0.2 mmol) **5** 83% yield

3a (0.2 mmol, 1.0 equiv.) was dissolved in a 1:2 mixture of acetonitrile and water (1.4 mL) and cooled to 0 °C (ice bath). Concentrated aqueous HCl (30 µL, 0.96 mmol) was added dropwise. The mixture was stirred vigorously for half an hour, while maintained at 0 °C $NaNO_2$ (13.8 mg, 0.2 mmol) was added to this mixture over the course of 10 min. The reaction was allowed to proceed for 12 h. The mixture was then extracted with CH_2Cl_2. The combined organic layer was washed with brine, dried over Na_2SO_4, concentrated under reduced pressure, and purified by flash silica gel column chromatography (petroleum ether/ethyl acetate) to give the corresponding product **5** as light-yellow liquid (42.2 mg, 83%).

N-(tert-butyl)-N-(2-(pyridin-2-yl)phenyl)nitrous amide (5)

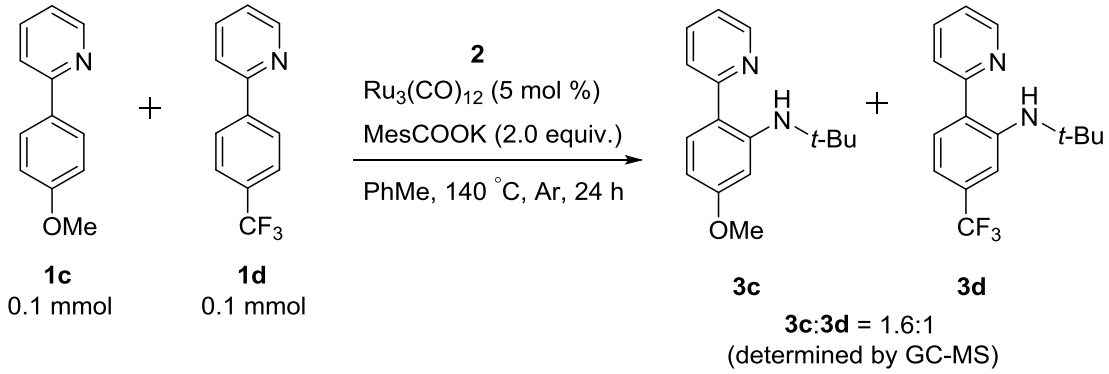
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.73 – 8.62 (m, 1H), 7.73 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.62 (td, *J* = 7.7, 1.8 Hz, 1H), 7.54 (td, *J* = 7.6, 1.4 Hz, 1H), 7.48 (td, *J* = 7.6, 1.7 Hz, 1H), 7.28 – 7.23 (m, 1H), 7.08 (d, *J* = 7.9 Hz, 1H), 6.91 (dd, *J* = 7.7, 1.2 Hz, 1H), 1.28 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 156.27, 149.56, 139.77, 136.30, 136.08, 130.95, 129.69, 129.26, 128.24, 122.87, 122.71, 62.74, 29.77.

HRMS (ESI)Calcd for $C_{15}H_{17}N_3O$ $[M+Na]^+$: 278.1264, found: 278.1257.

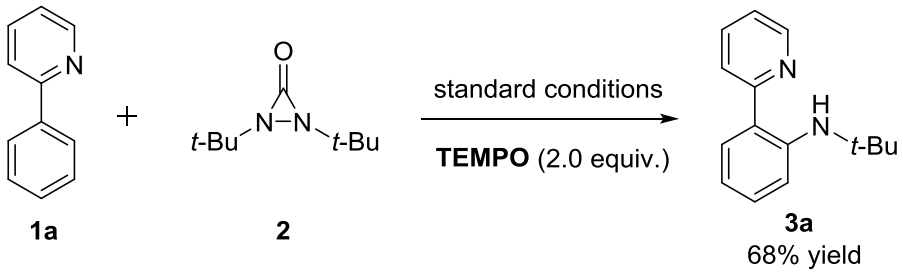
5. Mechanistic Studies

a) Intermolecular competition between differently substituted 2-arylpyridine



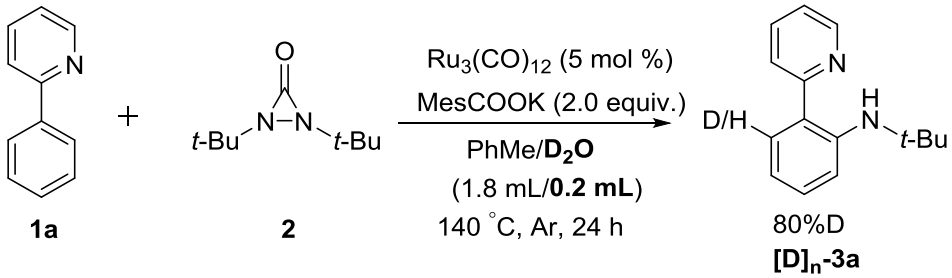
The general procedure was followed, the reaction was run on **1c** (18.5 mg, 0.1 mmol), **1d** (22.3 mg, 0.1 mmol), **2**(40 μL, 34 mg, 0.1 mmol), $Ru_3(CO)_{12}$ (3.2mg, 5 mol %), MesCOOK (40 mg, 2.0 equiv.), PhMe (1.0 mL). After completion of the reaction,the ratio of **3c** and **3d** was detected directly by GC-MS without further purification.

b) Radical trapping experiment

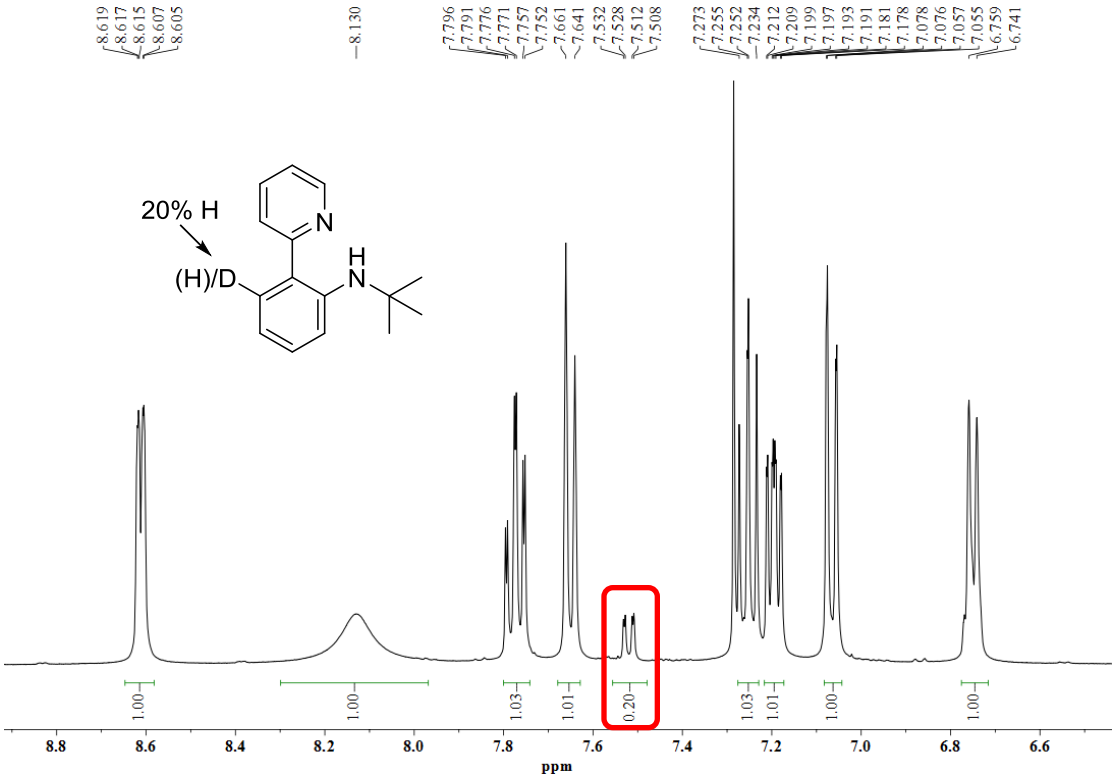


The general procedure was followed, the reaction was run on **1a** (0.2 mmol, 1.0 equiv.), **2** (80 μL, 68 mg, 2.0 equiv.), $Ru_3(CO)_{12}$ (6.4 mg, 5 mol %), MesCOOK (80 mg, 2.0 equiv.), **TEMPO** (62.5 mg, 2.0 equiv.), PhMe (2.0 mL). The residue was purified by column chromatography (PE/EA) on silica gel to give the product **3a**.

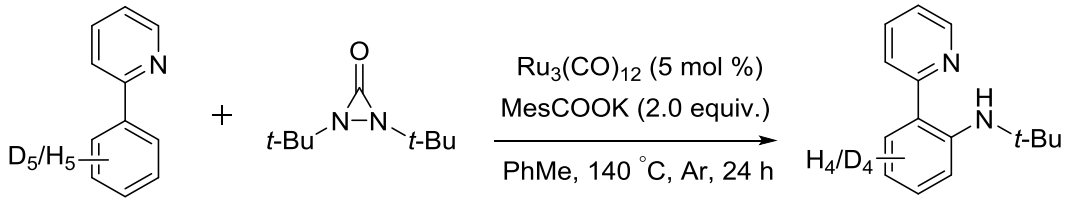
c) H/D exchange experiment



The general procedure was followed, the reaction was run on **1a** (0.2 mmol, 1.0 equiv.), **2** (80 μL, 68 mg, 2.0 equiv.), $Ru_3(CO)_{12}$ (6.4 mg, 5 mol %), MesCOOK (80 mg, 2.0 equiv.), a solvent mixture of PhMe and $\mathbf{D_2O}$ (1.8mL/**0.2 mL**). After evaporation of solvents under reduced pressure, the residue was purified by column chromatography (PE/EA) on silica gel to give the product $\mathbf{[D]_n}$**–3a**. The Dincorporation was determined by ^{1}HNMR spectroscopy. $\mathbf{[D]_n}$**–3a**–80% D incorporation in *ortho*-position.

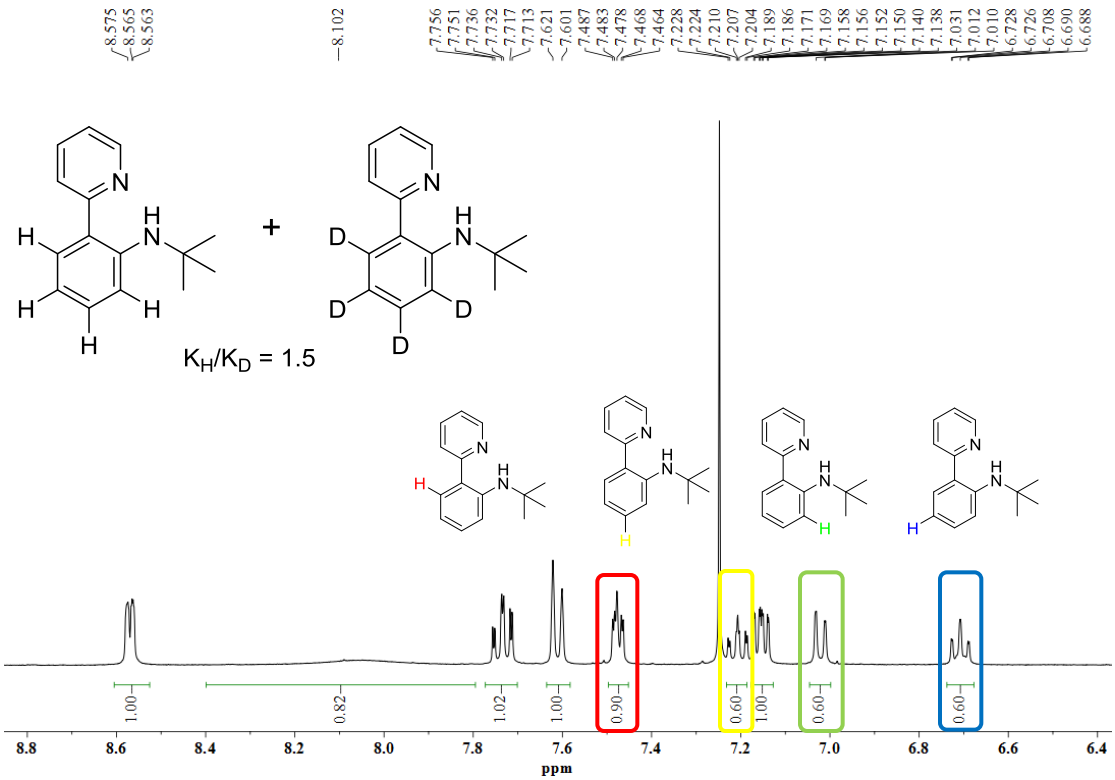


d) KIE study

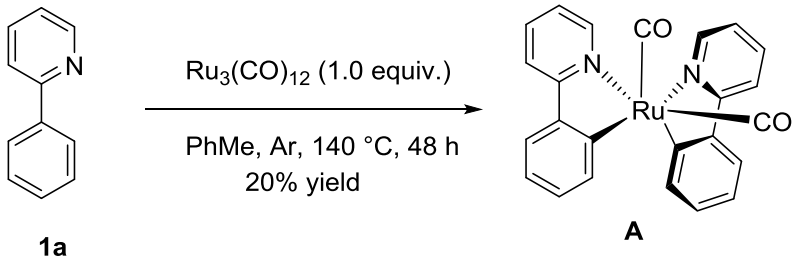


1a/[D]$_5$-1a **2** K_H/K_D **= 1.5** **3a/[D]$_4$-3a**

The general procedure was followed, the reaction was run on **1a** (0.1 mmol, 1.0 equiv.), **[D]$_5$–1a** (0.1 mmol, 1.0 equiv.), **2** (80 μL, 68 mg, 2.0 equiv.), $Ru_3(CO)_{12}$ (6.4 mg, 5 mol %), MesCOOK (80 mg, 2.0 equiv.), PhMe (2.0 mL). The residue was purified by column chromatography (PE/EA) on silica gel to give a mixture of **3a** and **[D]$_4$–3a**, which was analyzed by ^{1}HNMR spectroscopy. Based on the integrations related to different hydrogen resonances, the kinetic isotope effect (*KIE*) was calculated to be k_H/k_D **= 1.5**.



e) Synthesisof the ruthenium(II) intermediate A



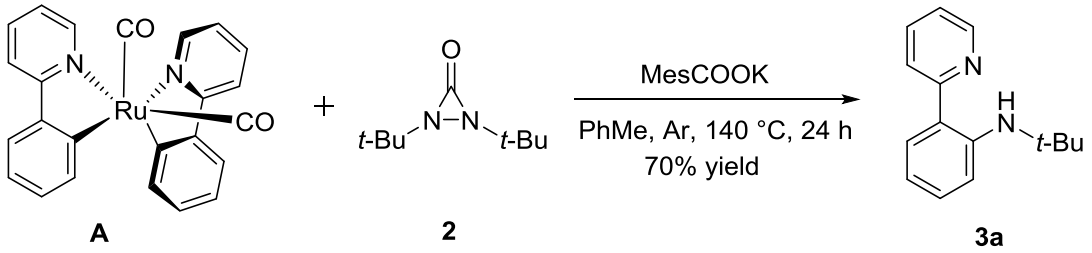
In a 20 mL tube, 2-phenylpyridine (**1a**) (84μL, 0.6mmol) and $Ru_3(CO)_{12}$ (383 mg, 0.6mmol) were added and charged with argon more than three times. PhMe (5.0 mL) was injected into the tube. Afterwards, the reaction tube was then immersed in an oil bath, which was preheated at 140 °C for 48 h. After cooled to room temperature, the reaction mixture was filtered and concentrated. The residue was purified on neutral Al_2O_3 column with petroleum ether/ethyl acetate (10/1) as the eluent to afford the complex **A** as light-yellow solid (55.8 mg, 20%).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 9.04 (d, *J* = 4.5 Hz, 1H), 8.07 (d, *J* = 7.4 Hz, 1H), 7.98 (d, *J* = 8.1 Hz, 1H), 7.90 (d, *J* = 8.1 Hz, 1H), 7.79 (d, *J* = 8.4 Hz, 1H), 7.76 (d, *J* = 7.6 Hz, 1H), 7.65 (d, *J* = 7.3 Hz, 1H), 7.54 (t, *J* = 7.7 Hz, 1H), 7.32 – 7.26 (m, 2H), 7.22 (d, *J* = 5.4 Hz, 1H), 7.13 (t, *J* = 7.1 Hz, 1H), 6.91 (t, *J* = 7.2 Hz, 1H), 6.83 (t, *J* = 7.1 Hz, 1H), 6.76 (d, *J* = 7.2 Hz, 1H), 6.72 (t, *J* = 6.0 Hz, 1H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 202.92, 194.65, 178.36, 177.24, 165.66, 164.67, 153.24, 146.67, 145.51, 142.68, 139.76, 137.75, 137.57, 136.65, 129.70, 129.06, 124.08, 123.48, 123.19, 122.54, 121.50, 120.88, 119.67, 118.94.

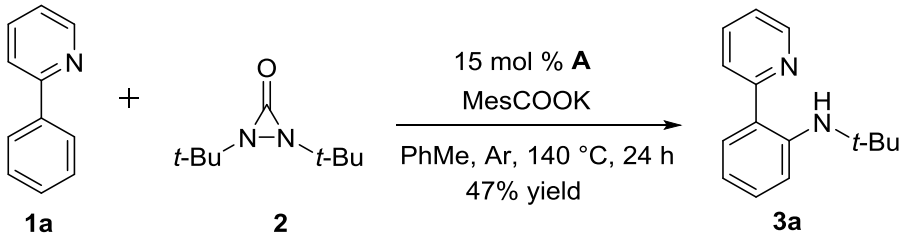
Spectra data was consist with the literature.[4]

f) Stoichiometric reactivity of intermediate A



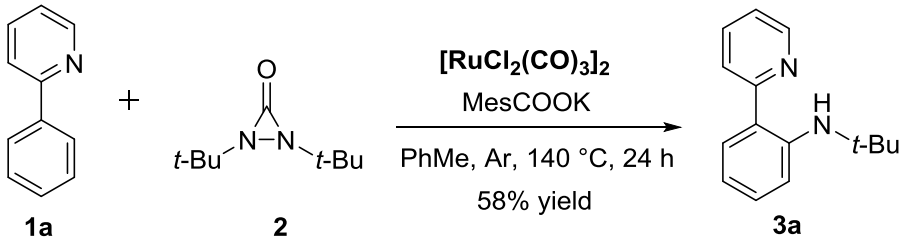
In a 20 mL tube, a mixture of **A** (47 mg, 0.1 mmol, 1.0 equiv.) and MesCOOK (40 mg, 2.0 equiv.) were added and charged with argon more than three times. PhMe (1.0 mL) and **2** (40 μL, 34 mg, 2.0 equiv.) were injected into the tube. Afterwards, the reaction tube was then immersed in an oil bath, which was preheated at 140 °C for 24 h. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 25/1) to **3a** as light-yellow solid (15.8mg, 70%).

g) Catalytic reactivity of intermediate A

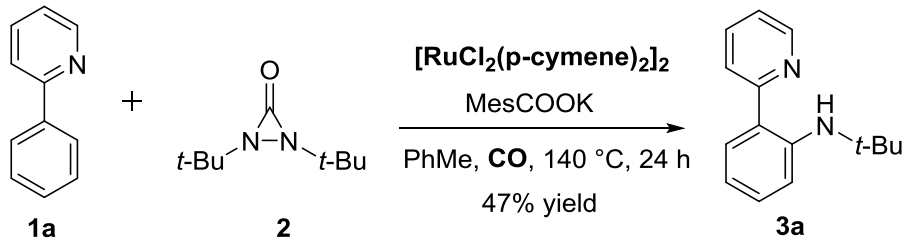


In a 20 mL tube, 2-phenylpyridine (**1a**) (14 μL, 0.1 mmol, 1.0 equiv.), **A** (7.0 mg, 15 mol %) and MesCOOK (40 mg, 2.0 equiv.) were added and charged with argon more than three times. PhMe (1.0 mL) and **2** (40 μL, 34 mg, 2.0 equiv.) were injected into the tube. Afterwards, the reaction tube was then immersed in an oil bath, which was preheated at 140 °C for 24 h. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 25/1) to **3a** as light-yellow solid (13.5 mg, 47 %).

h) CO ligand studies



In a 20 mL tube, a mixture of **1a** (0.2 mmol, 1.0 equiv.), $[RuCl_2(CO)_3]_2$ (5.2 mg, 5 mol %), MesCOOK (80 mg, 2.0 equiv.) were added and charged with argon more than three times. PhMe (2.0 mL) and **2** (80 μL, 68 mg, 2.0 equiv.) were injected into the tube. Afterwards, the reaction tube was then immersed in an oil bath, which was preheated at 140 °C for 24 h. After the reaction was completed, the residue was purified by column chromatography (PE/EA) on silica gel to give the product **3a** in 58% yield.



1a **2** **3a**

In a 20 mL tube, a mixture of **1a** (0.2 mmol, 1.0 equiv.), $[RuCl_2(p\text{-cymene})]_2$ (6.1 mg, 5 mol %), MesCOOK (80 mg, 2.0 equiv.) were added and charged with **CO** more than three times. PhMe (2.0 mL) and **2** (80 μL, 68 mg, 2.0 equiv.) were injected into the tube. Afterwards, the reaction tube was then immersed in an oil bath, which was preheated at 140 °C for 24 h. After the reaction was completed, the residue was purified by column chromatography (PE/EA) on silica gel to give the product **3a** in 47% yield.

6. Computational Details of C-H Activation

a) Computational methods[5]

The density functional theory (DFT) calculations are performed by Gaussian 09 program. All geometries are optimized at the B3LYP level with 6-31G(d,p) basis set (lanl2dz basis set for Ru). Harmonic frequency calculations are performed for stationary points and transition states. Local minima are confirmed without imaginary frequency. Transition states are verified with one imaginary frequency.

b) Results

The density functional theory (DFT) caculation was further employed to investigate the activation of the *ortho*-C-H bond (Figure S1). The barrier of transition state structure TS1 was calculated to be 15.2 kcal/mol, indicated a ruthenium assisted deprotonation of the *ortho*-C–H bond, which was consistent with the experimental result. However, the detailed transformation of A2 to ruthenium (II) complex **A** still needs further study.

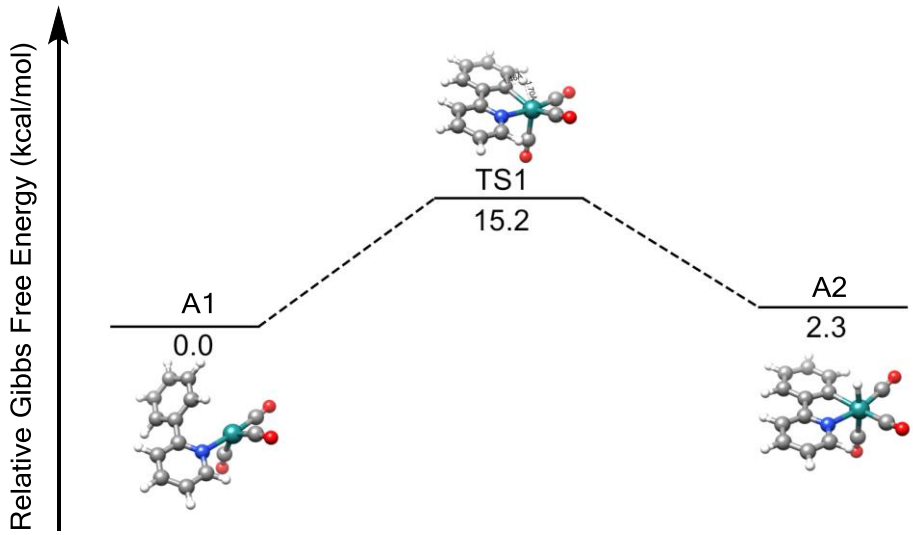


Figure S1. Gibbs free energies of the activation of the *ortho*-C-H bond

c) Results optimized cartesian coordinates at B3LYP level of theory

A1

Atom	X	Y	Z
Ru	-1.239400	-0.009900	0.059100
C	1.775500	-0.787500	-0.169600
C	0.429000	-2.679500	0.024200
C	2.925200	-1.587900	-0.137300
C	1.861100	0.685800	-0.299400
C	1.529200	-3.527400	0.059700
H	-0.580800	-3.066500	0.094100
C	2.804600	-2.968100	-0.017200
H	3.898000	-1.118200	-0.226600
C	1.015700	1.371900	-1.191200
C	2.787900	1.415400	0.461800
H	1.381000	-4.597700	0.148100

H	3.689100	-3.596900	0.005300
C	1.089300	2.763200	-1.300600
H	0.352100	0.813200	-1.847600
C	2.855300	2.803300	0.350000
H	3.433700	0.896600	1.164200
C	2.004100	3.480000	-0.528300
H	0.439000	3.280800	-1.999100
H	3.566700	3.357700	0.954700
H	2.059100	4.561100	-0.613900
N	0.539800	-1.340700	-0.081200
C	-1.001600	0.112000	1.977800
C	-2.656600	1.227000	0.128000
C	-2.202800	-1.062900	-1.232900
O	-0.993900	0.017800	3.134000
O	-3.501700	2.020300	0.149600
O	-2.851800	-1.810800	-1.841100

TS1

Atom	X	Y	Z
Ru	-1.086300	0.062400	-0.083100
C	1.827500	-0.764900	-0.098100
C	0.458100	-2.669600	-0.039000
C	2.966500	-1.593400	-0.074300
C	1.866100	0.693700	-0.138900
C	1.544800	-3.525900	-0.005900
H	-0.555000	-3.053000	-0.026300
C	2.829300	-2.969800	-0.027100
H	3.952800	-1.147000	-0.095900
C	0.618200	1.368600	-0.268500
C	3.063200	1.428400	-0.037500
H	1.386800	-4.597600	0.029900
H	3.708200	-3.606700	-0.008400
C	0.638500	2.779100	-0.322800
H	-0.203500	0.795800	-1.333100
C	3.048200	2.815600	-0.067800
H	4.012700	0.915600	0.081100
C	1.826900	3.490300	-0.212800
H	-0.292400	3.322900	-0.453000
H	3.976600	3.372100	0.014700
H	1.808500	4.576600	-0.239800
N	0.582700	-1.325900	-0.088700
C	-1.339600	-0.194600	1.867700
C	-2.372100	1.463300	-0.187500
C	-2.296300	-1.208900	-0.985400

O	-1.492500	-0.334800	3.001800
O	-3.120000	2.339700	-0.260500
O	-2.966000	-1.956700	-1.554400

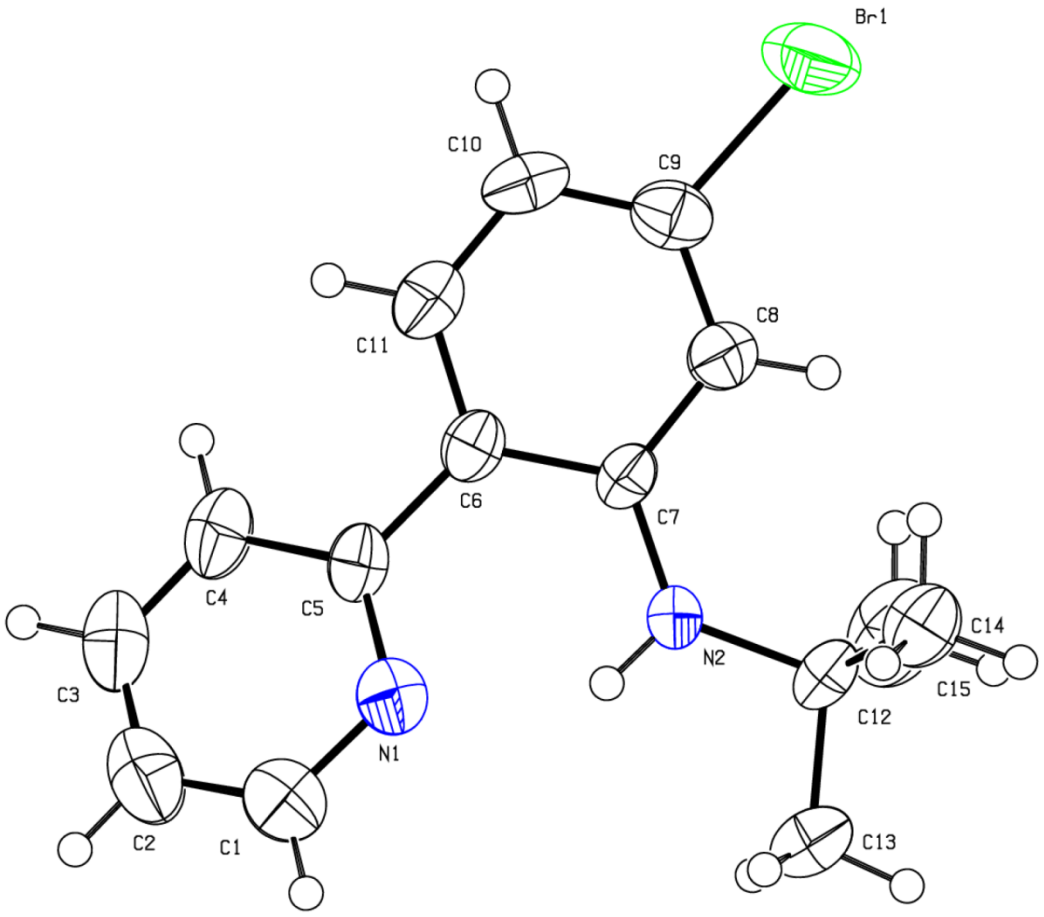
A2

Atom	X	Y	Z
Ru	-1.096100	-0.038000	-0.144000
C	1.855800	-0.684600	-0.116600
C	0.626900	-2.679800	-0.055800
C	3.048600	-1.428900	-0.121300
C	1.783100	0.780500	-0.134800
C	1.772600	-3.461200	-0.056100
H	-0.354600	-3.137400	-0.030300
C	3.010500	-2.814900	-0.092500
H	4.001400	-0.915500	-0.149000
C	0.489300	1.362300	-0.137500
C	2.937900	1.585800	-0.142500
H	1.690700	-4.541600	-0.030600
H	3.933400	-3.386500	-0.097300
C	0.416300	2.763300	-0.143100
H	-0.850900	0.008200	-1.763600
C	2.831000	2.971300	-0.151800
H	3.926600	1.136900	-0.140600
C	1.563100	3.560100	-0.150600
H	-0.551300	3.257300	-0.144100
H	3.725500	3.586900	-0.157800
H	1.467900	4.643000	-0.156200
N	0.657700	-1.334200	-0.087800
C	-1.185200	0.041200	1.866700
C	-2.389800	1.315100	-0.478400
C	-2.386000	-1.504500	-0.490400
O	-1.211400	0.136700	3.010100
O	-3.133800	2.159100	-0.728400
O	-3.106000	-2.355100	-0.775600

7. X-ray Crystallographic Data of 3g and 3m

X-ray crystallographic data of **3g**

Crystals were grown from a mixture of ethyl acetate and n-hexane. The ellipsoid contour percent probability level is 30% in the caption of the thermalellipsoid plot. (CCDC: 1892347)



Bond precision:	C-C = 0.0118 A	Wavelength=0.71000	
Cell:	a=36.666(4)	b=16.9718(19)	c=9.1422(8)
	alpha=90	beta=90	gamma=90
Temperature:	294 K		
	Calculated	Reported	
Volume	5689.1(10)	5689.1(10)	
Space group	F d d 2	F d d 2	
Hall group	F 2 -2d	F 2 -2d	
Moiety formula	C15 H17 Br N2	C15 H17 Br N2	
Sum formula	C15 H17 Br N2	C15 H17 Br N2	
Mr	305.21	305.21	
Dx,g cm-3	1.425	1.425	
Z	16	16	

Mu (mm-1)	2.873	2.875
F000	2496.0	2496.0
F000’	2490.72	
h,k,lmax	44,20,11	45,20,11
Nref	2799[1492]	1977
Tmin,Tmax	0.626,0.708	0.569,1.000
Tmin’	0.568	

Correction method= # Reported T Limits: Tmin=0.569 Tmax=1.000
AbsCorr = MULTI-SCAN

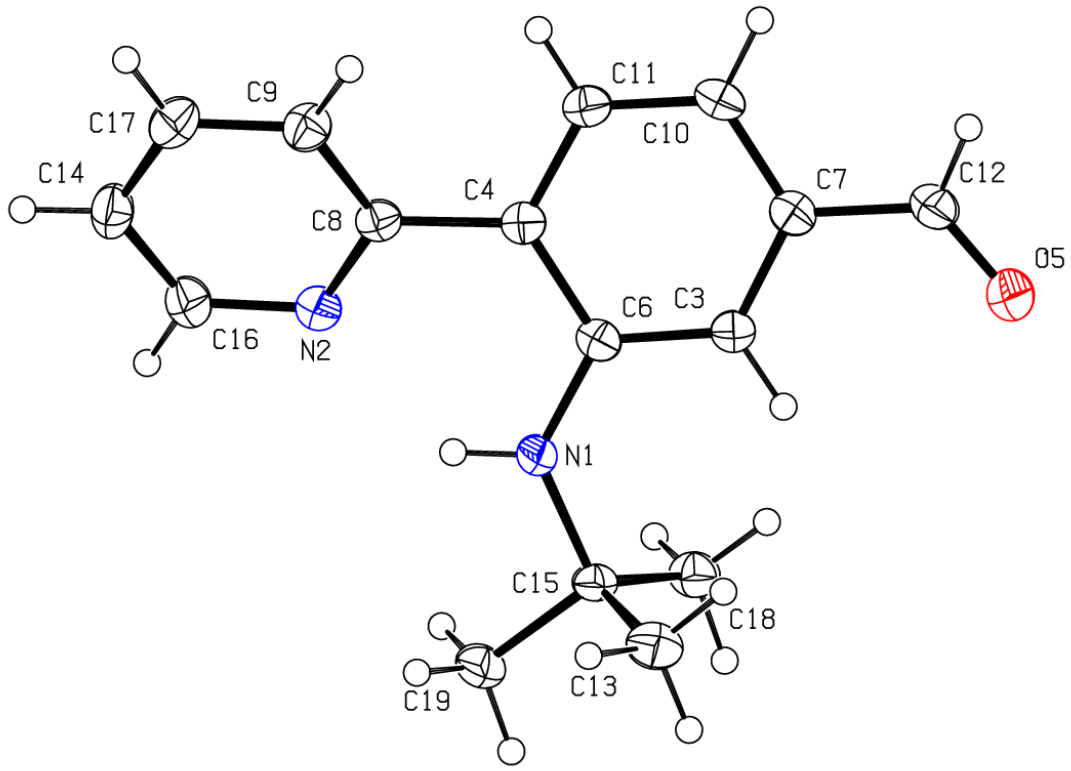
Data completeness= 1.33/0.71 Theta(max)= 25.971

R(reflections)= 0.0545(1504) wR2(reflections)= 0.1349(1977)

S = 1.003 Npar= 166

X-ray crystallographic data of **3m**

Crystals were grown from a mixture of ethyl acetate and n-hexane. The ellipsoid contour percent probability level is 30% in the caption of the thermalellipsoid plot. (CCDC: 1904937)



Bond precision: C-C = 0.0029 A Wavelength=0.71073

Cell:	a=16.2862(10)	b=8.9940(5)	c=18.4405(12)
	alpha=90	beta=91.429(6)	gamma=90
Temperature:	294 K		

	Calculated	Reported
Volume	2700.3(3)	2700.3(3)
Space group	C 2/c	C 1 2/c 1
Hall group	-C 2yc	-C 2yc
Moiety formula	C16 H18 N2 O	C16 H18 N2 O
Sum formula	C16 H18 N2 O	C16 H18 N2 O
Mr	254.32	254.32
Dx,g cm-3	1.251	1.251
Z	8	8
Mu (mm-1)	0.079	0.079
F000	1088.0	1088.0
F000'	1088.40	
h,k,lmax	20,11,22	20,11,22
Nref	2662	2657
Tmin,Tmax	0.986,0.991	0.888,1.000
Tmin'	0.986	

Correction method= # Reported T Limits: Tmin=0.888 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 0.998 Theta(max)= 26.021

R(reflections)= 0.0518(2108) wR2(reflections)= 0.1338(2657)

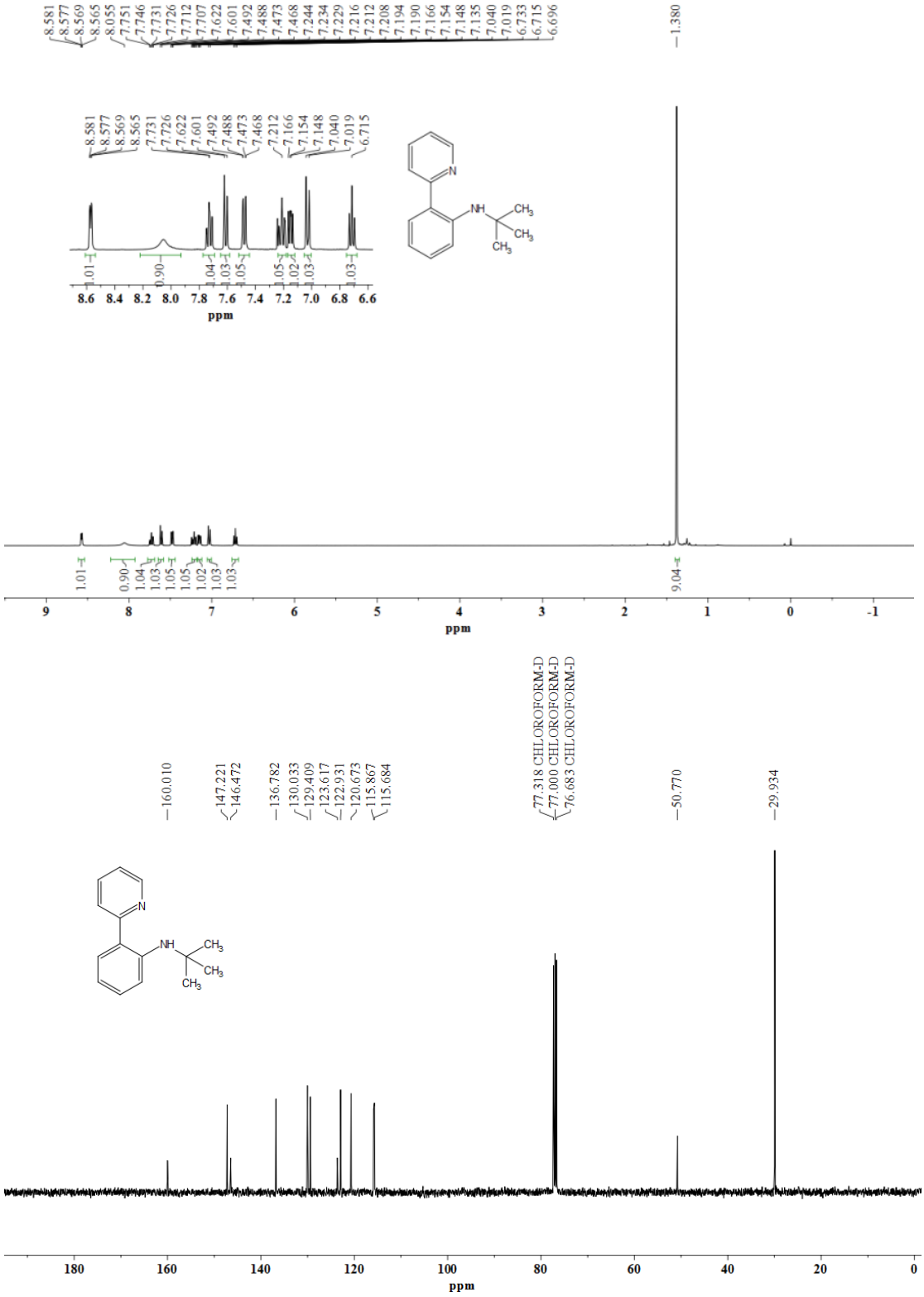
S = 1.054 Npar= 175

8. References

1. H. Kim, J. Park, J. G. Kim and S. Chang, *Org. Lett.*, 2014, 16, 5466-5469.
2. B. Z. Haifeng Du, and Yian Shi, *Org. Synth.*, 2009, 86, 315-324.
3. S. He, G. Tan, A. Luo and J. You, *Chem. Commun.*, 2018, 54, 7794-7797.
4. Z. Fan, J. Ni and A. Zhang, *J. Am. Chem. Soc.*, 2016, 138, 8470-8475.
5. Gaussian 09, Revision D.01, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, G. A. Petersson, H. Nakatsuji, X. Li, M. Caricato, A. Marenich, J. Bloino, B. G. Janesko, R. Gomperts, B. Mennucci, H. P. Hratchian, J. V. Ortiz, A. F. Izmaylov, J. L. Sonnenberg, D. Williams-Young, F. Ding, F. Lipparini, F. Egidi, J. Goings, B. Peng, A. Petrone, T. Henderson, D. Ranasinghe, V. G. Zakrzewski, J. Gao, N. Rega, G. Zheng, W. Liang, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, K. Throssell, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, T. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, J. M. Millam, M. Klene, C. Adamo, R. Cammi, J. W. Ochterski, R. L. Martin, K. Morokuma, O. Farkas, J. B. Foresman, and D. J. Fox, Gaussian, Inc., Wallingford CT, 2016.

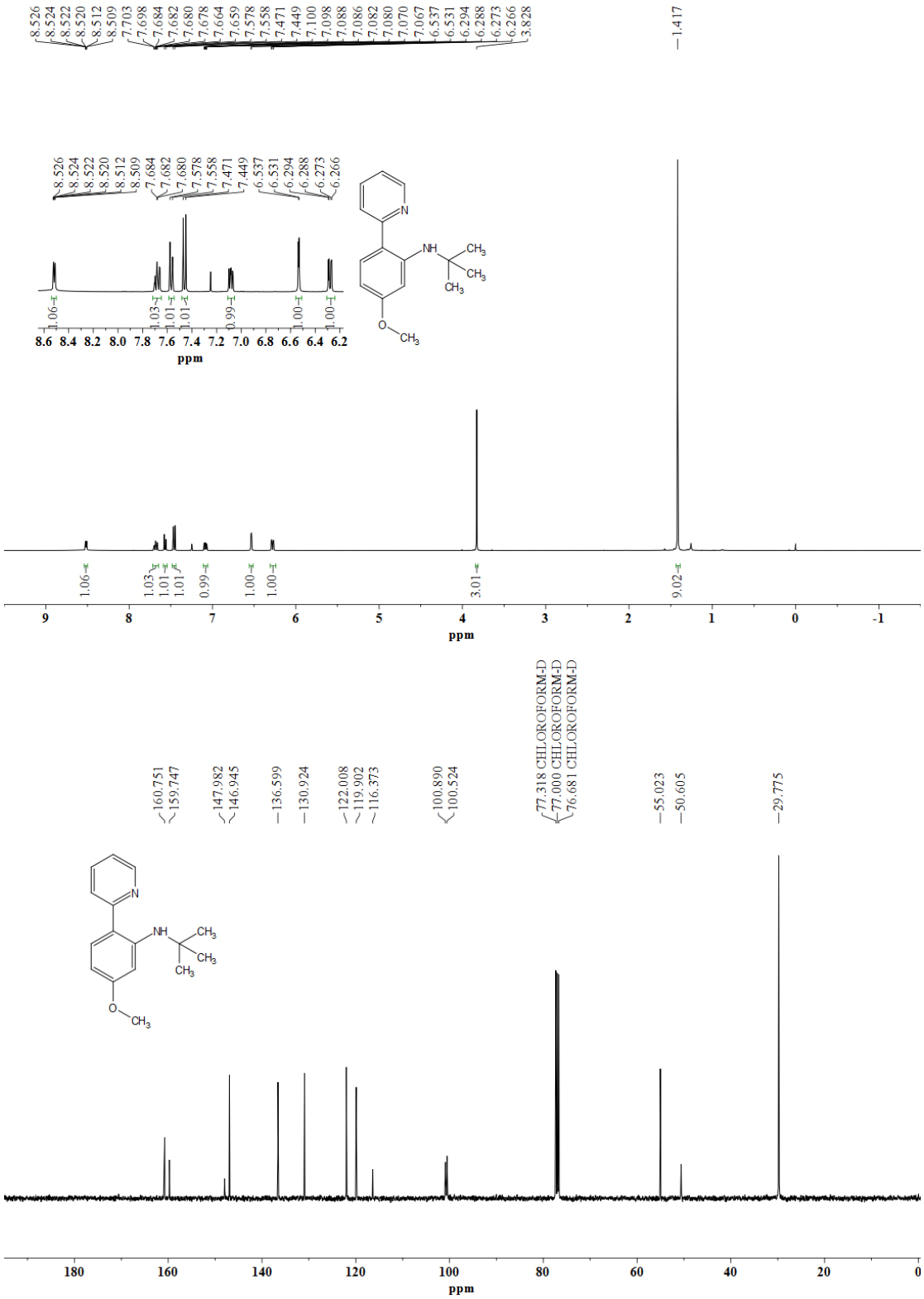
9. NMR spectra

N-(tert-butyl)-2-(pyridin-2-yl)aniline (3a)

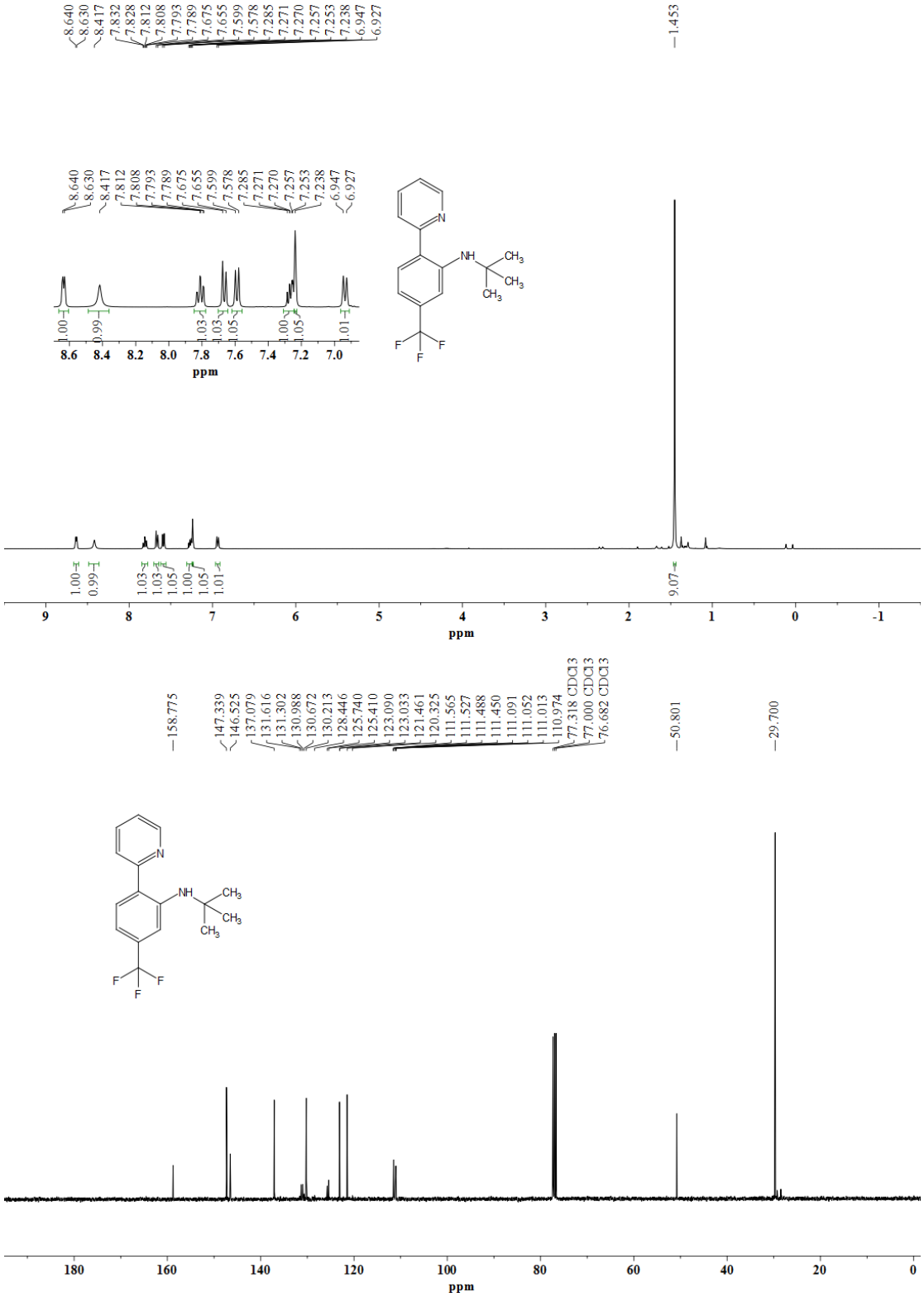


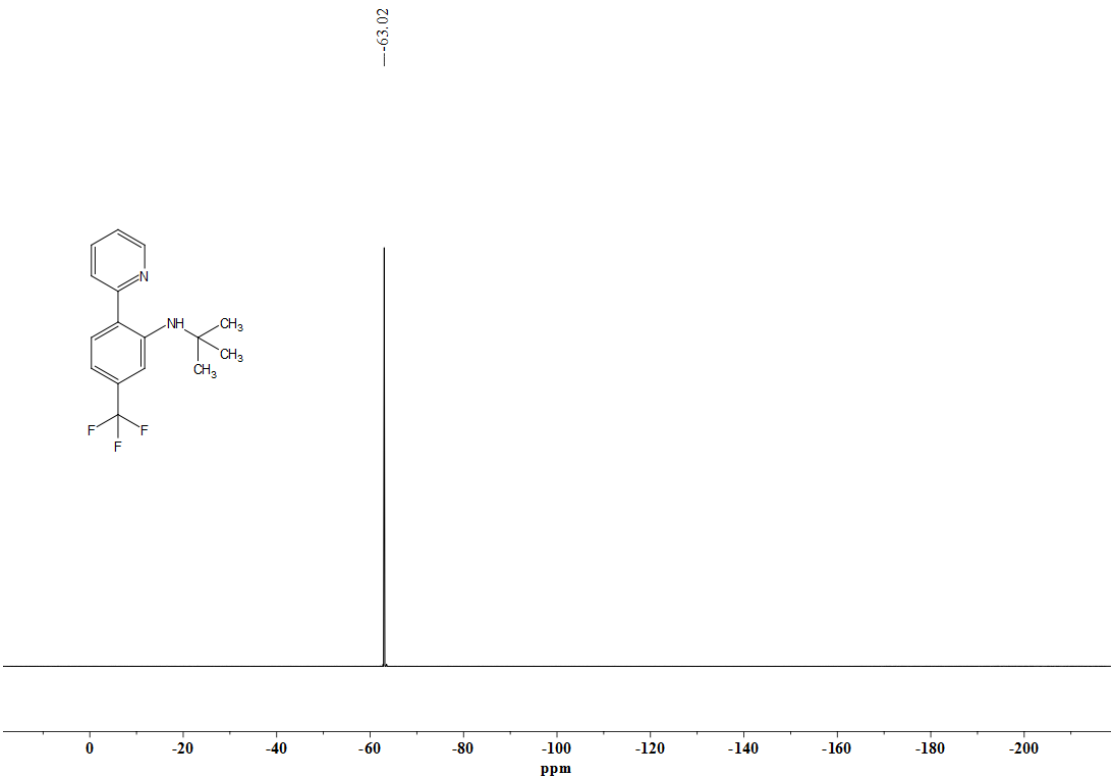
N-(tert-butyl)-5-methyl-2-(pyridin-2-yl)aniline (3b)

N-(tert-butyl)-5-methoxy-2-(pyridin-2-yl)aniline(3c)

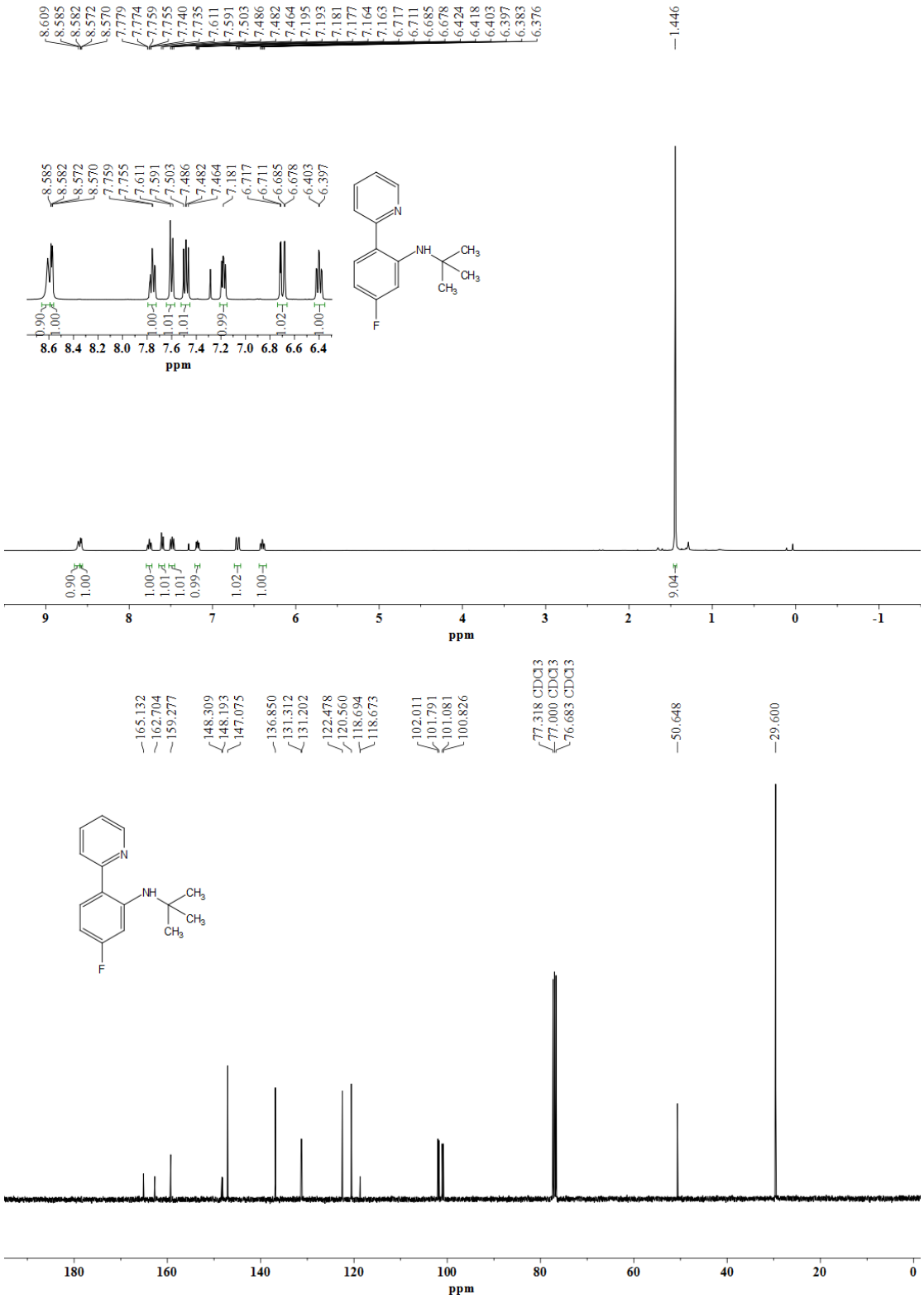


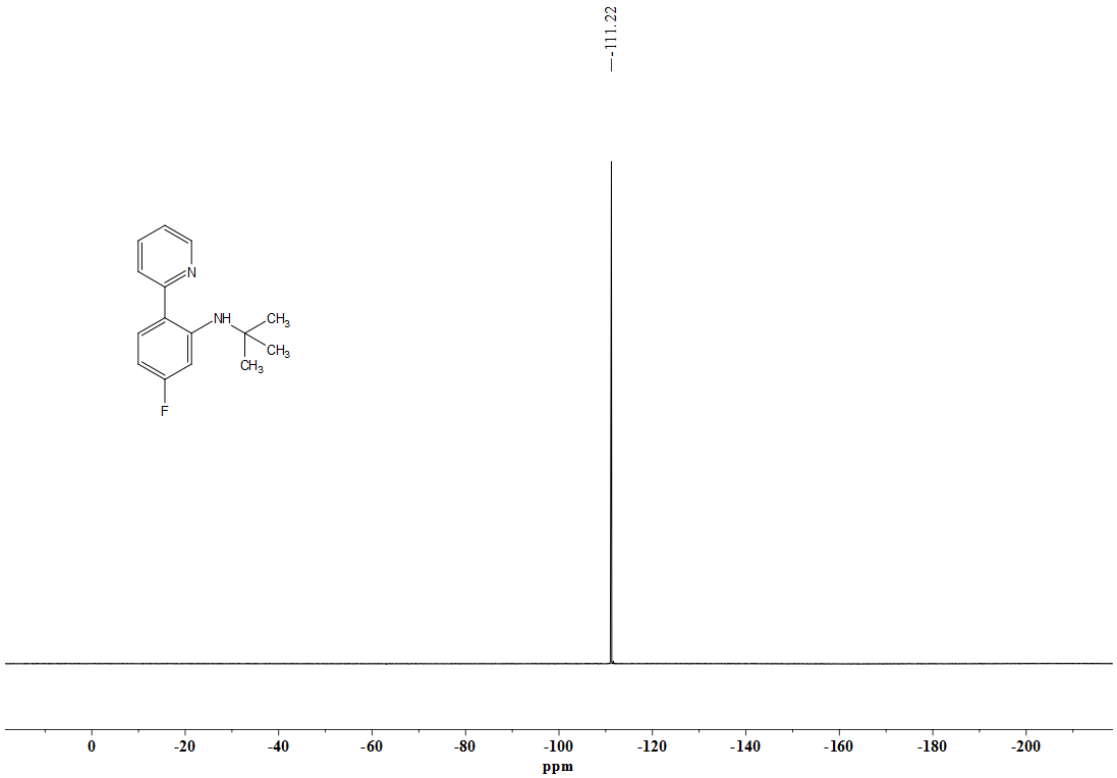
N-(tert-butyl)-2-(pyridin-2-yl)-5-(trifluoromethyl)aniline (3d)



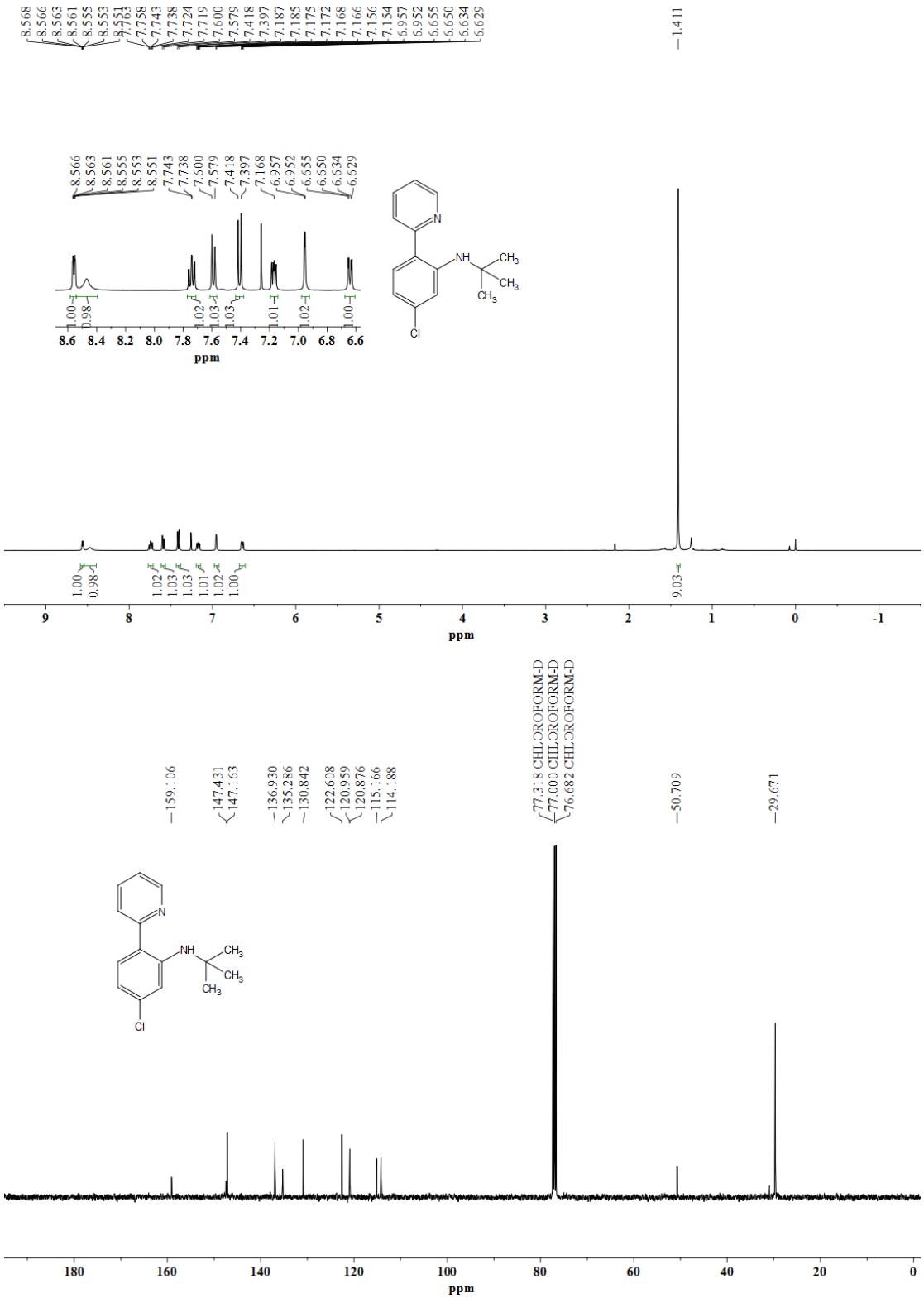

-63.02
N
NH
CH3
CH3
CH3
F
F
F
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm

N-(tert-butyl)-5-fluoro-2-(pyridin-2-yl)aniline (3e)



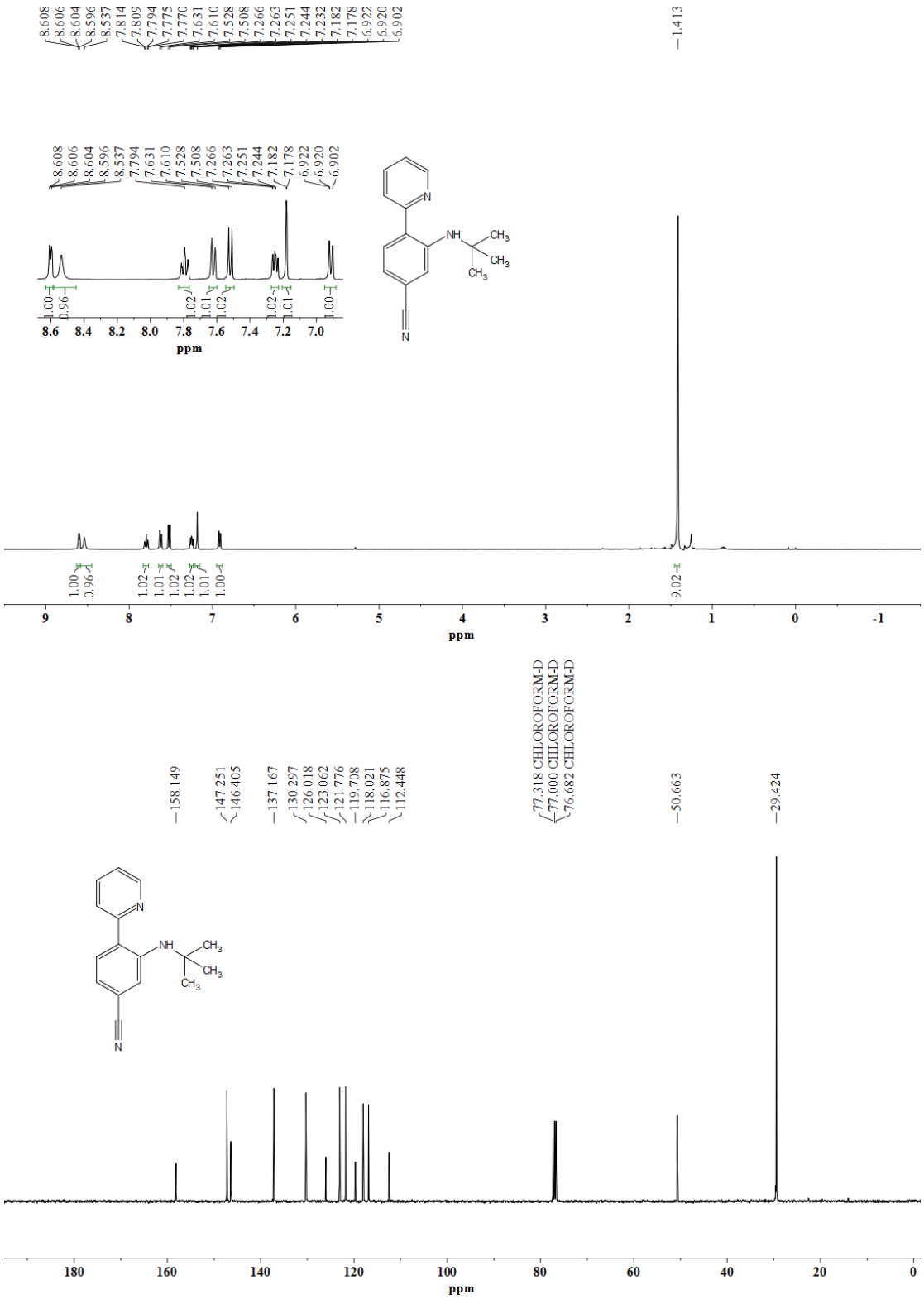

-111.22
N
NH
CH3
CH3
CH3
F
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm

N-(tert-butyl)-5-chloro-2-(pyridin-2-yl)aniline (3f)

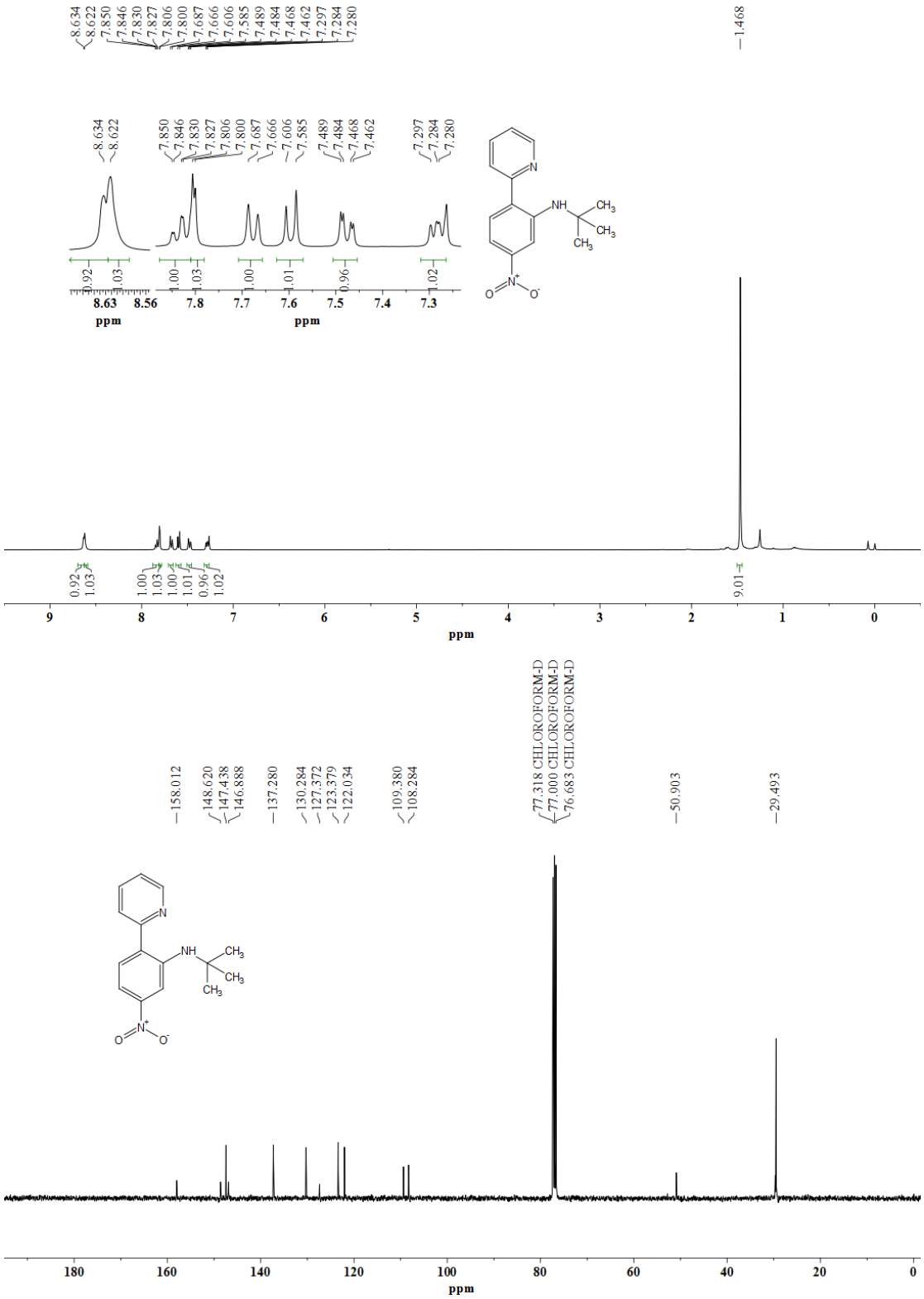


5-bromo-N-(tert-butyl)-2-(pyridin-2-yl)aniline (3g)

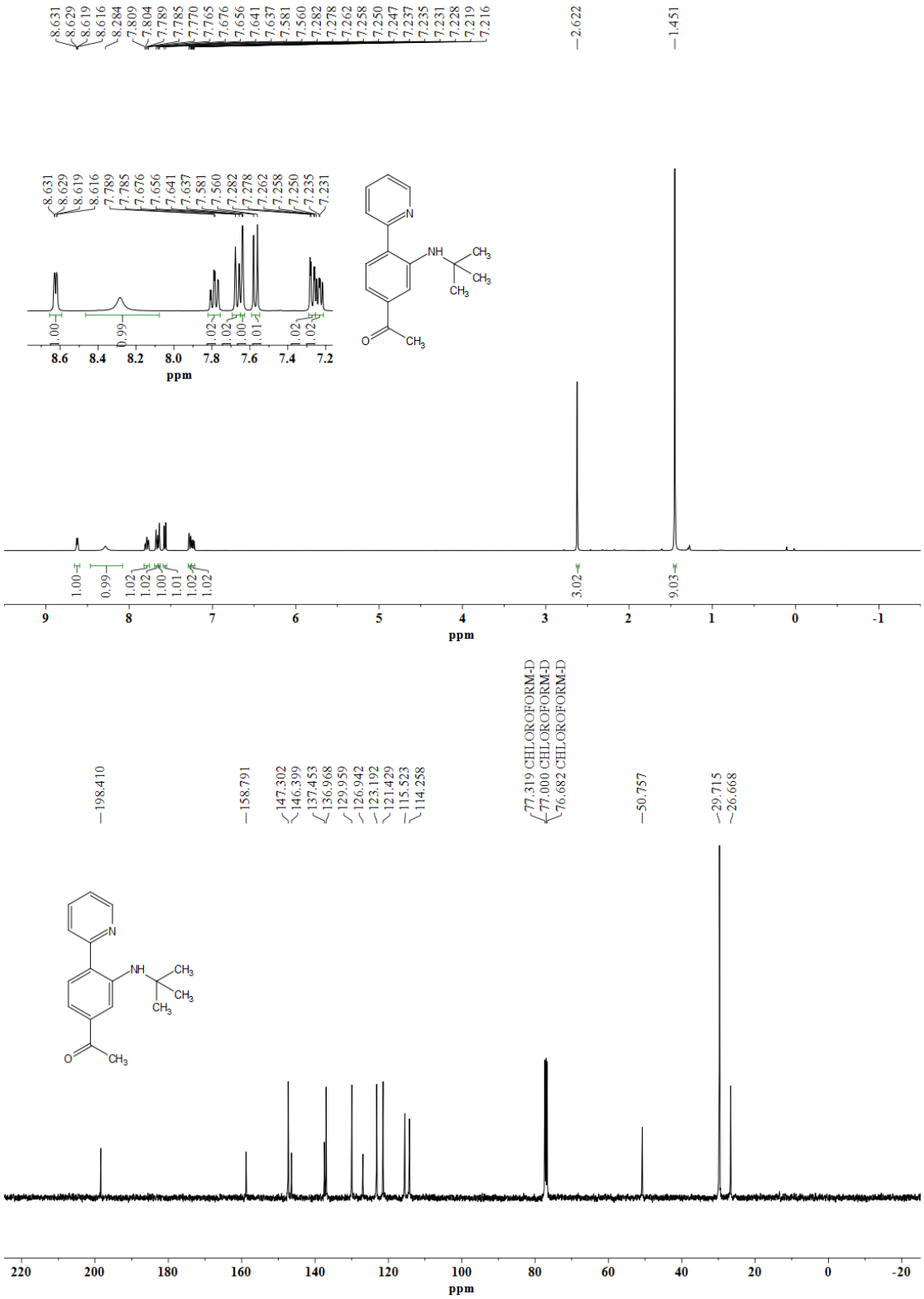
3-(tert-butylamino)-4-(pyridin-2-yl)benzonitrile (3h)



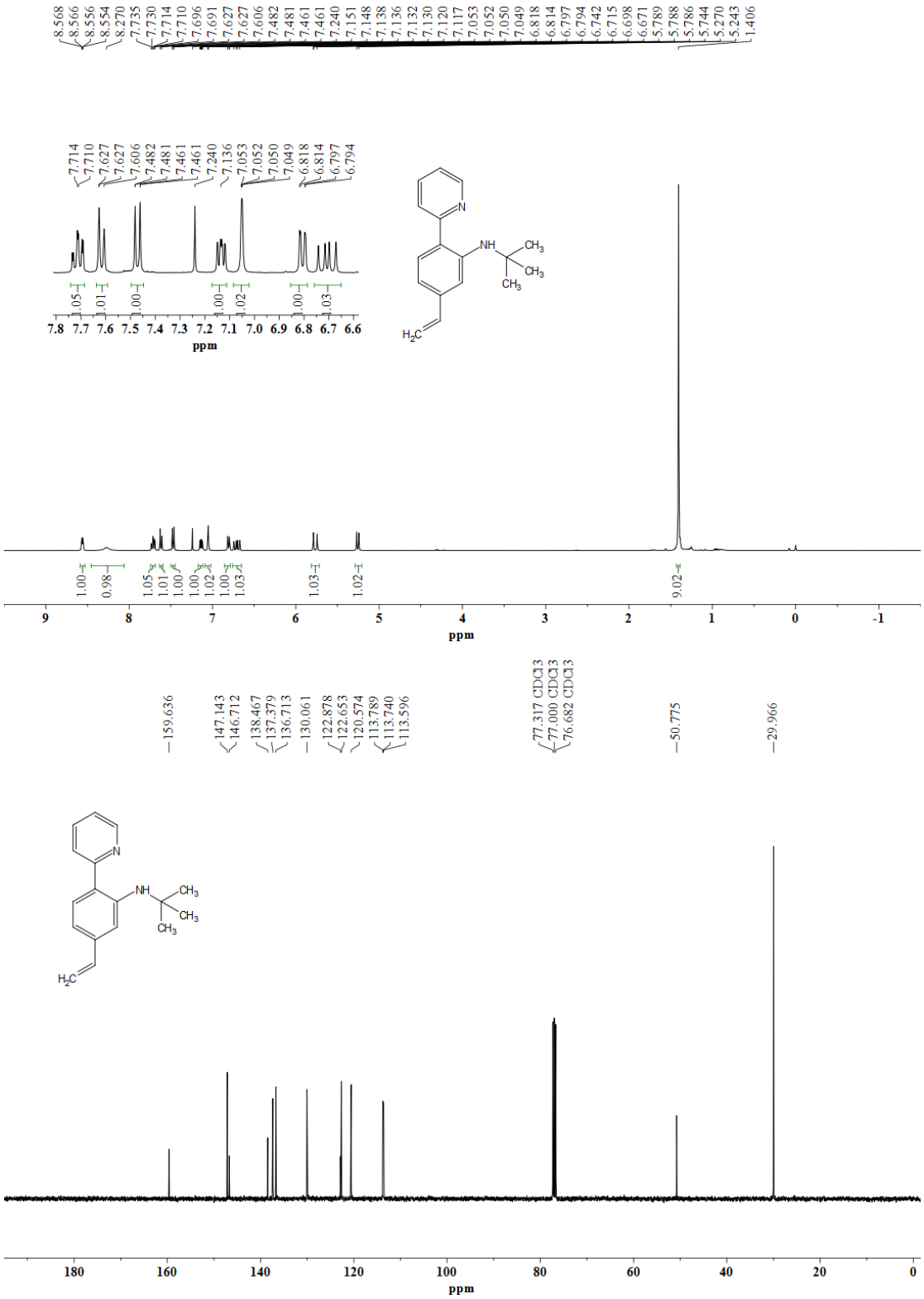
N-(tert-butyl)-5-nitro-2-(pyridin-2-yl)aniline (3i)



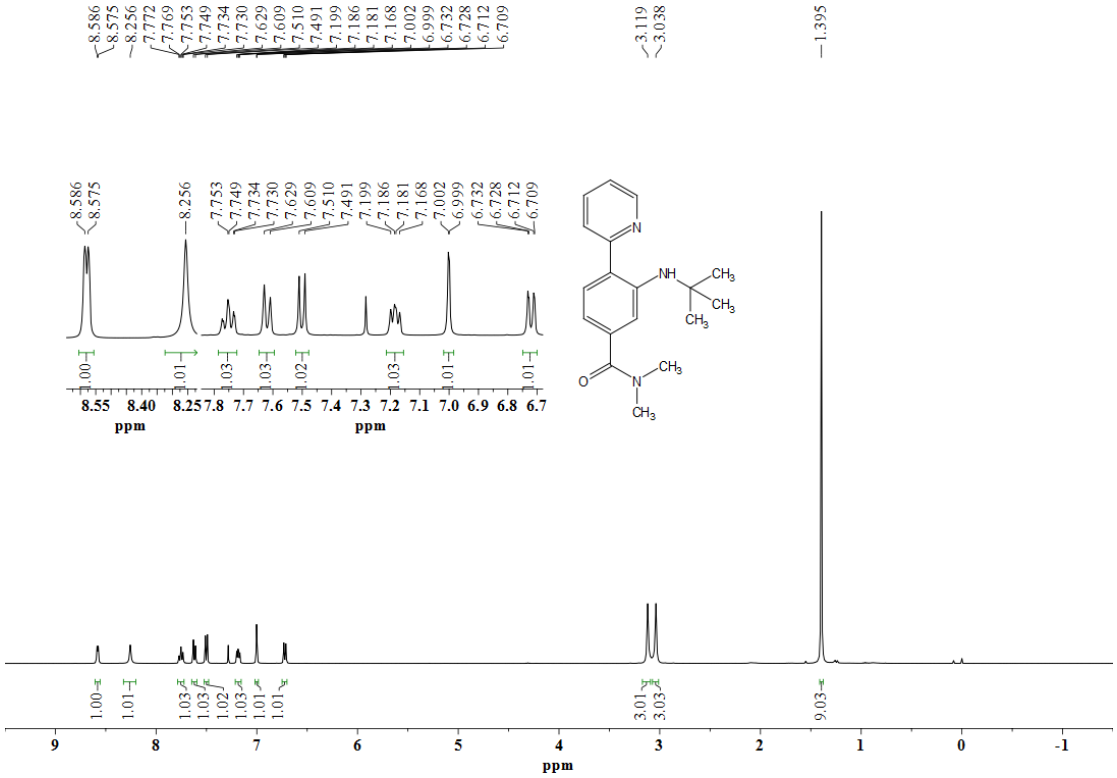
1-(3-(tert-butylamino)-4-(pyridin-2-yl)phenyl)ethan-1-one (3j)

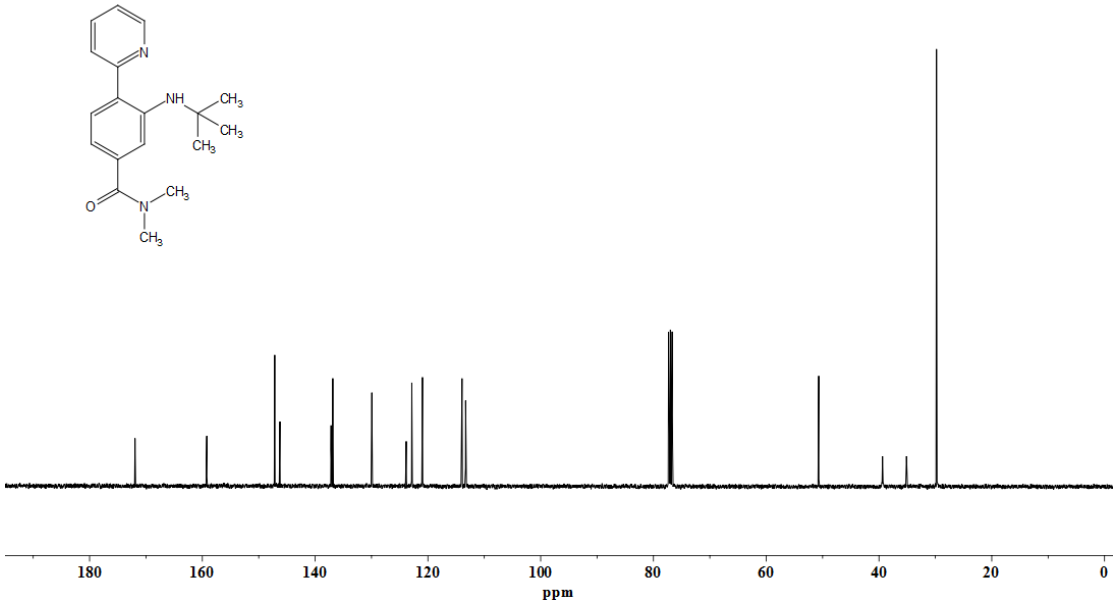


N-(tert-butyl)-2-(pyridin-2-yl)-5-vinylaniline (3k)

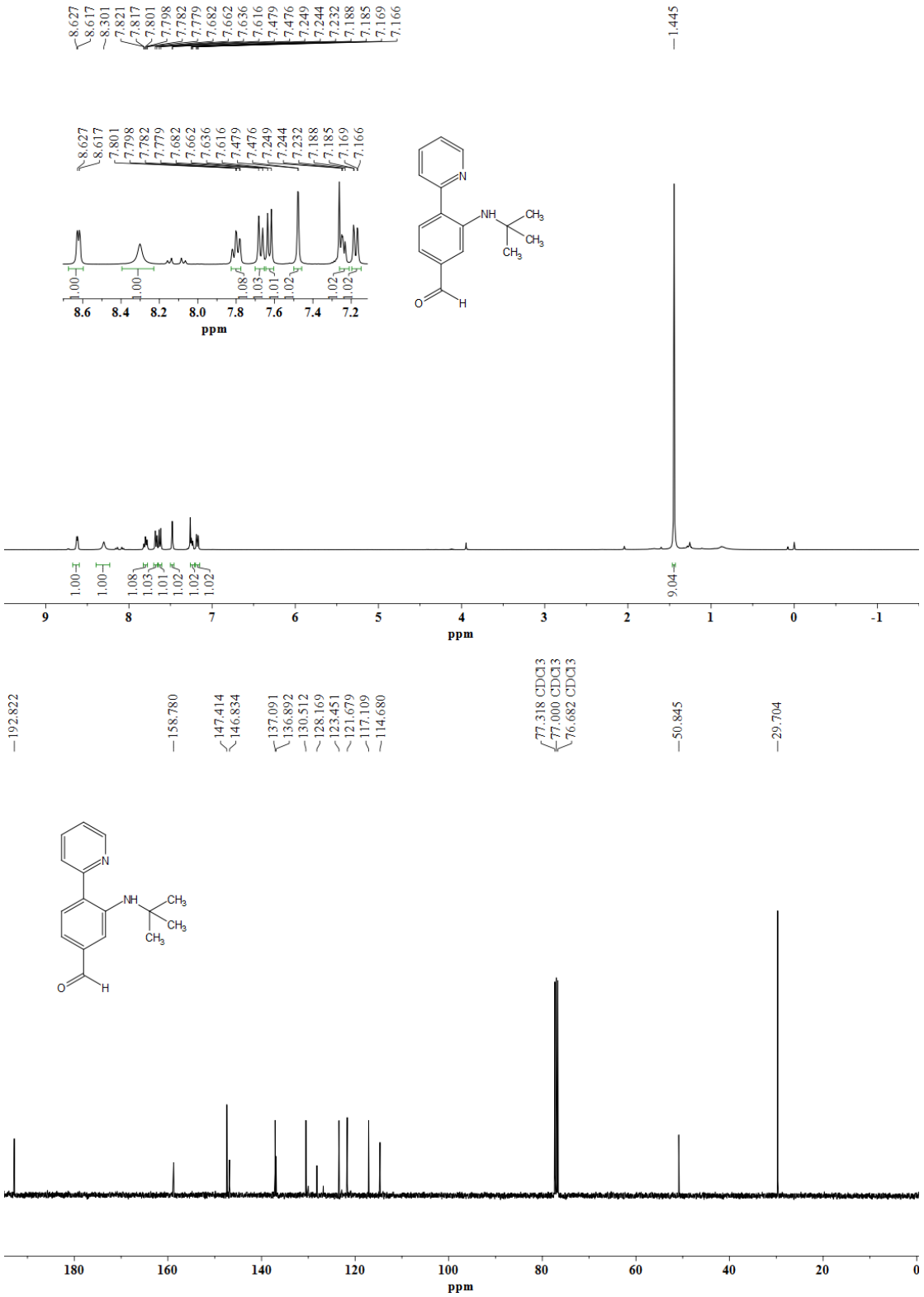


3-(tert-butylamino)-N,N-dimethyl-4-(pyridin-2-yl)benzamide (3l)

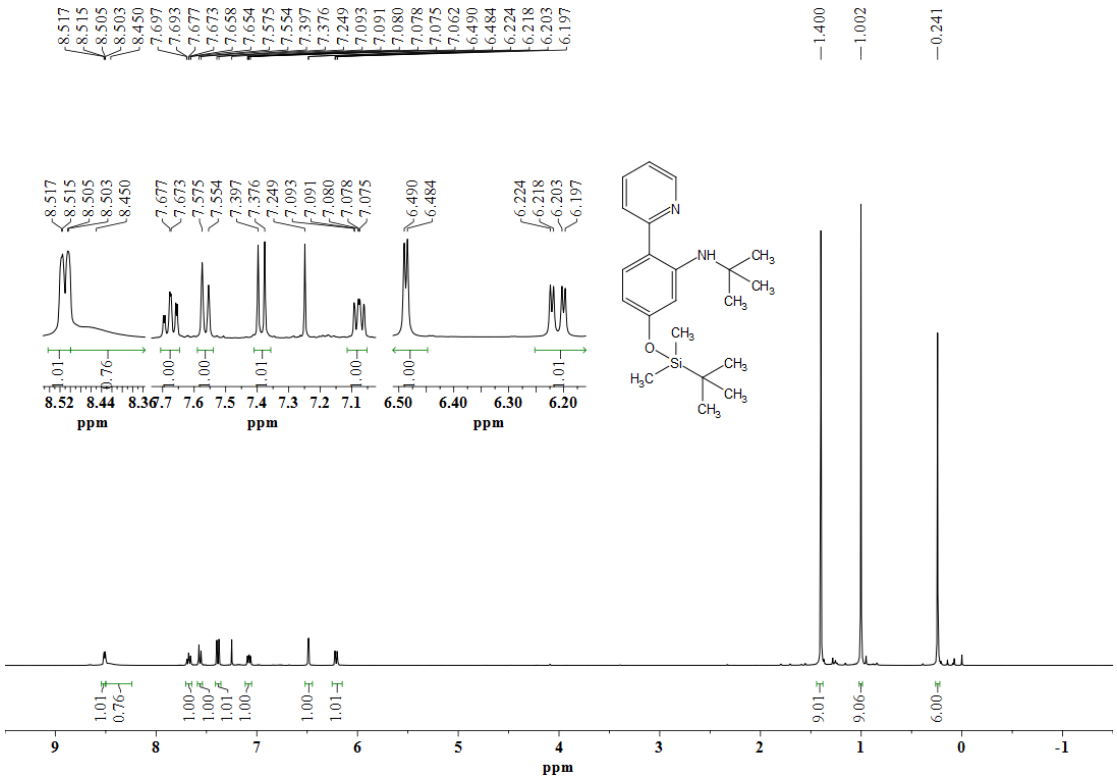


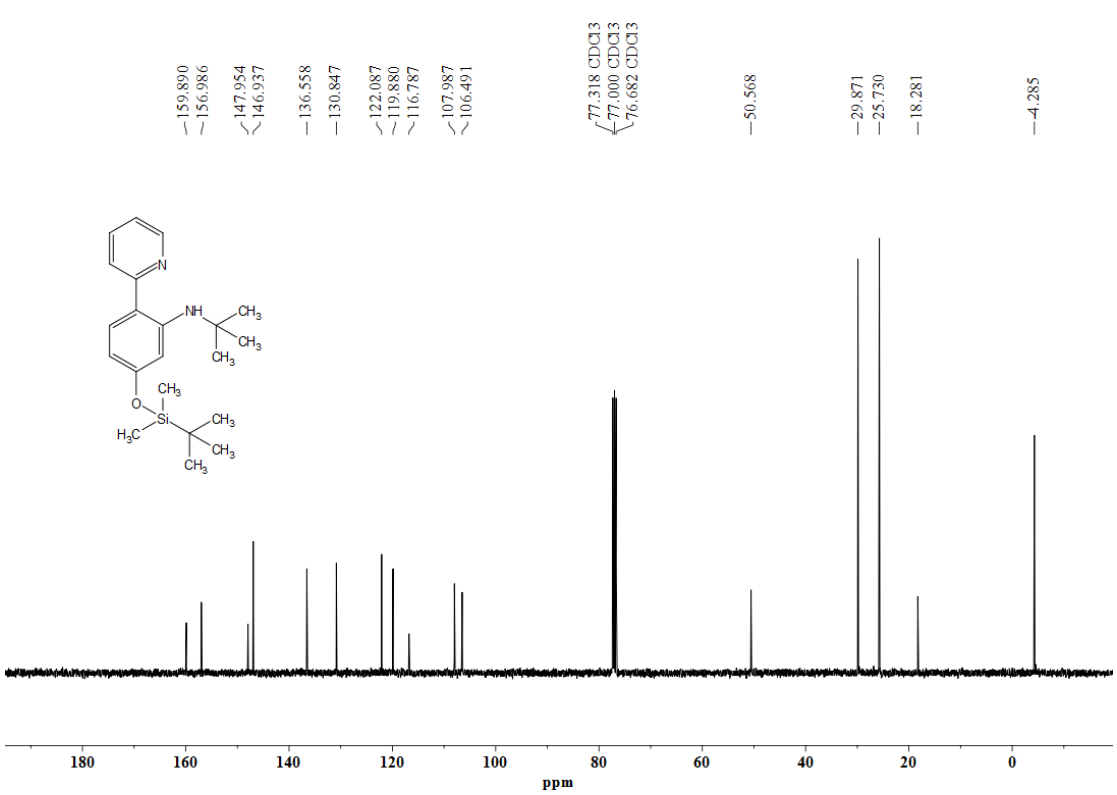


3-(tert-butylamino)-4-(pyridin-2-yl)benzaldehyde (3m)

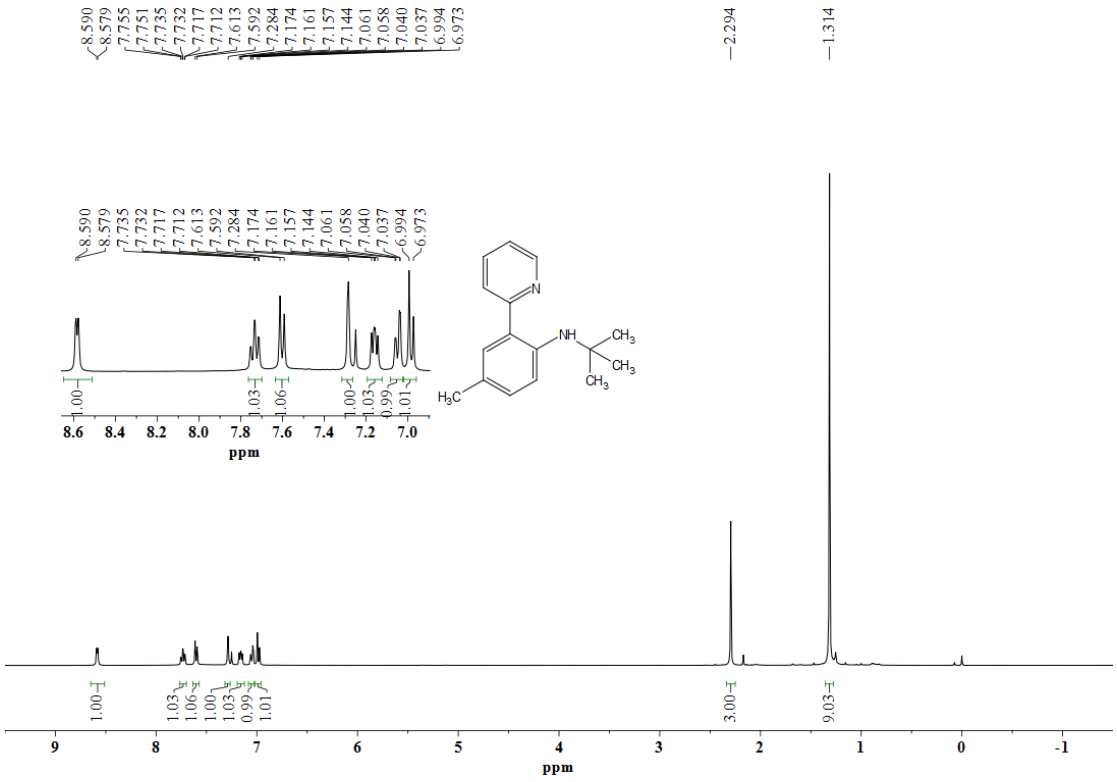


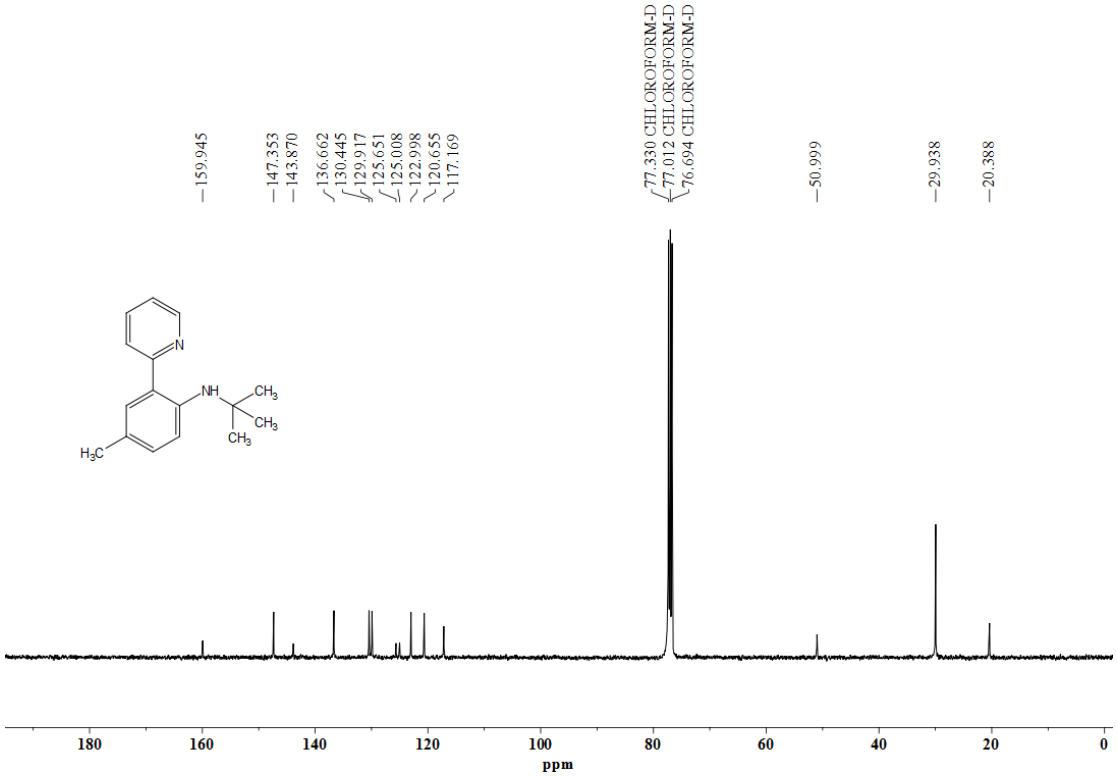
N-(tert-butyl)-5-((tert-butyldimethylsilyl)oxy)-2-(pyridin-2-yl)aniline (3n)



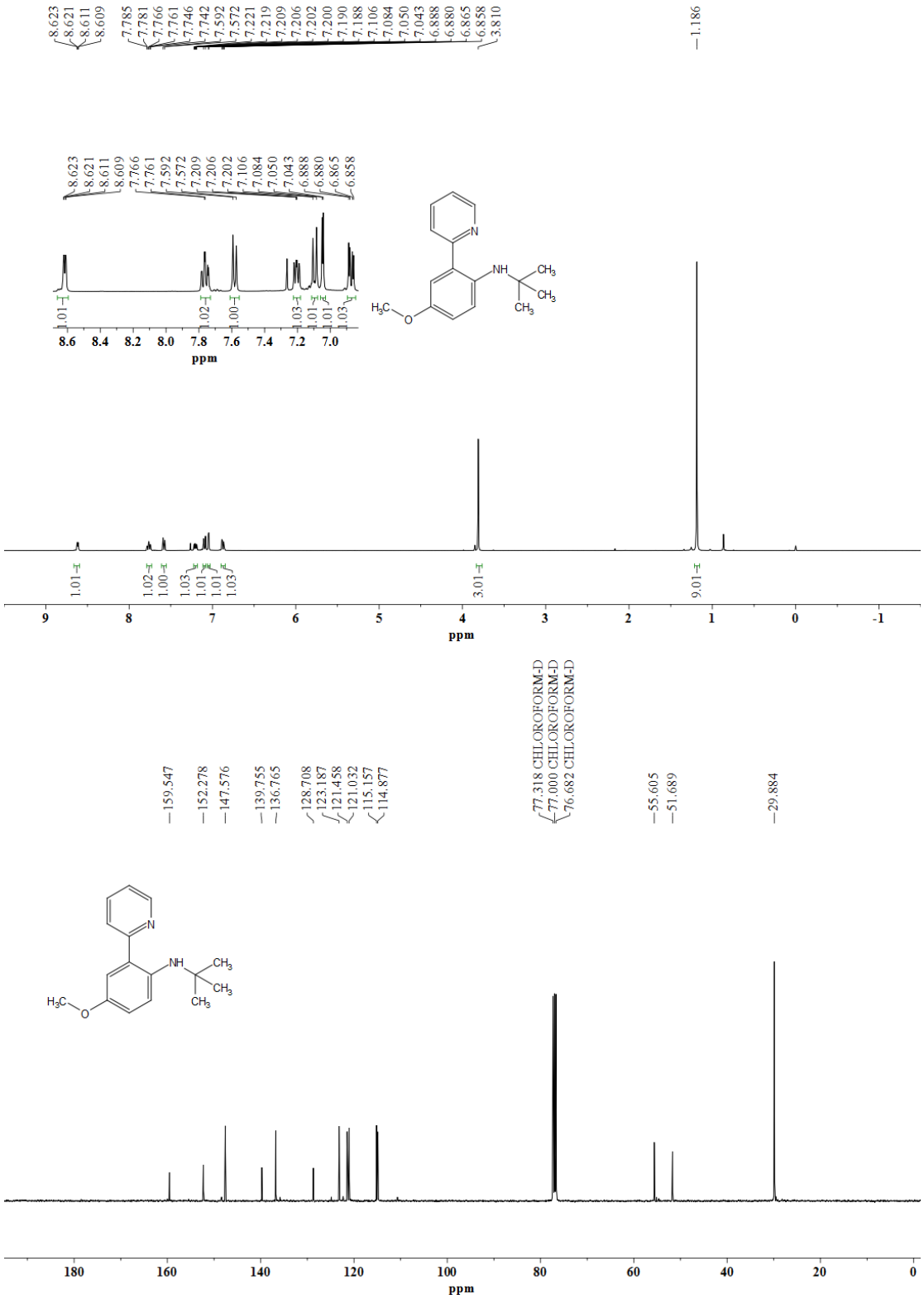


N-(tert-butyl)-4-methyl-2-(pyridin-2-yl)aniline (3o)

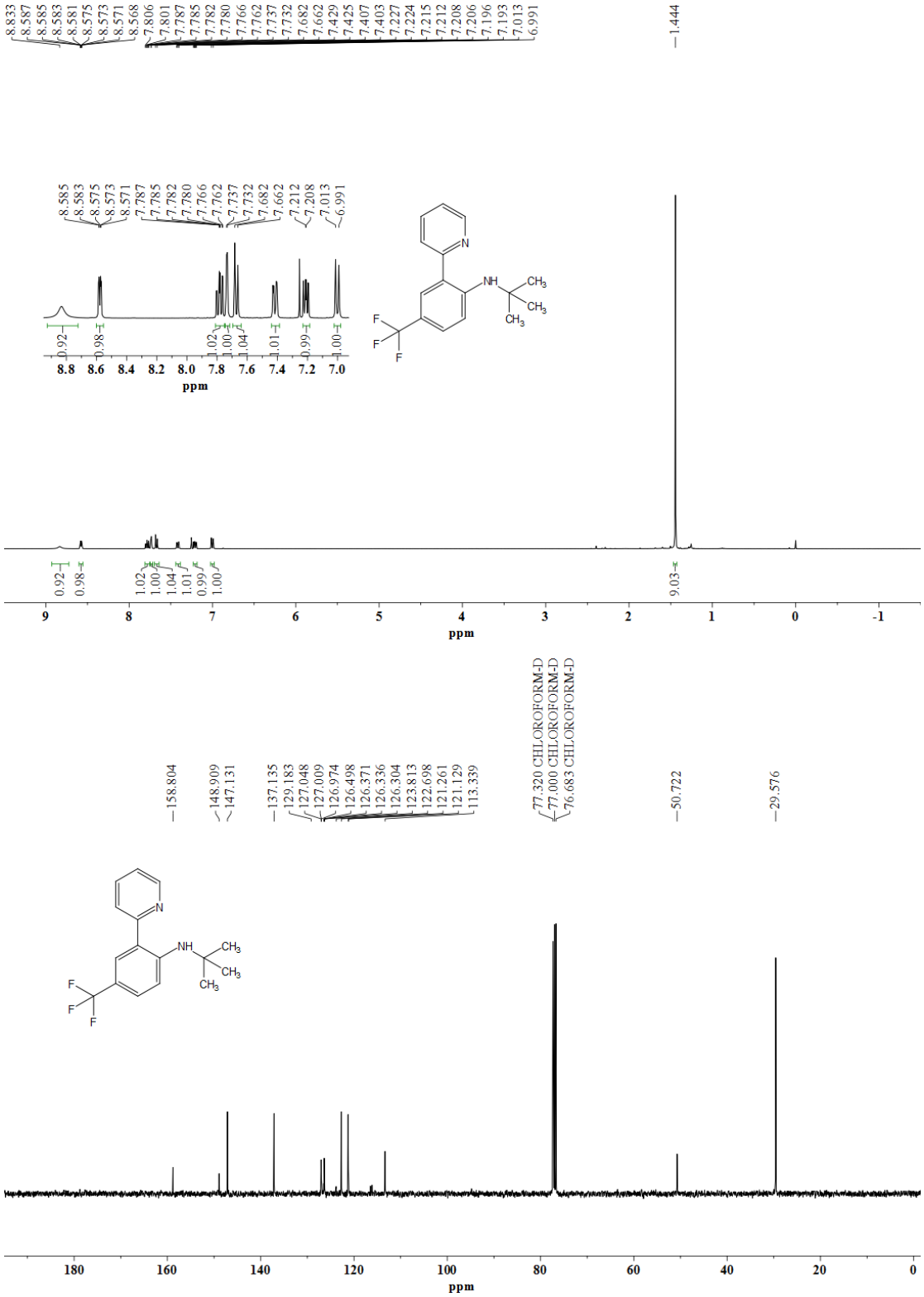


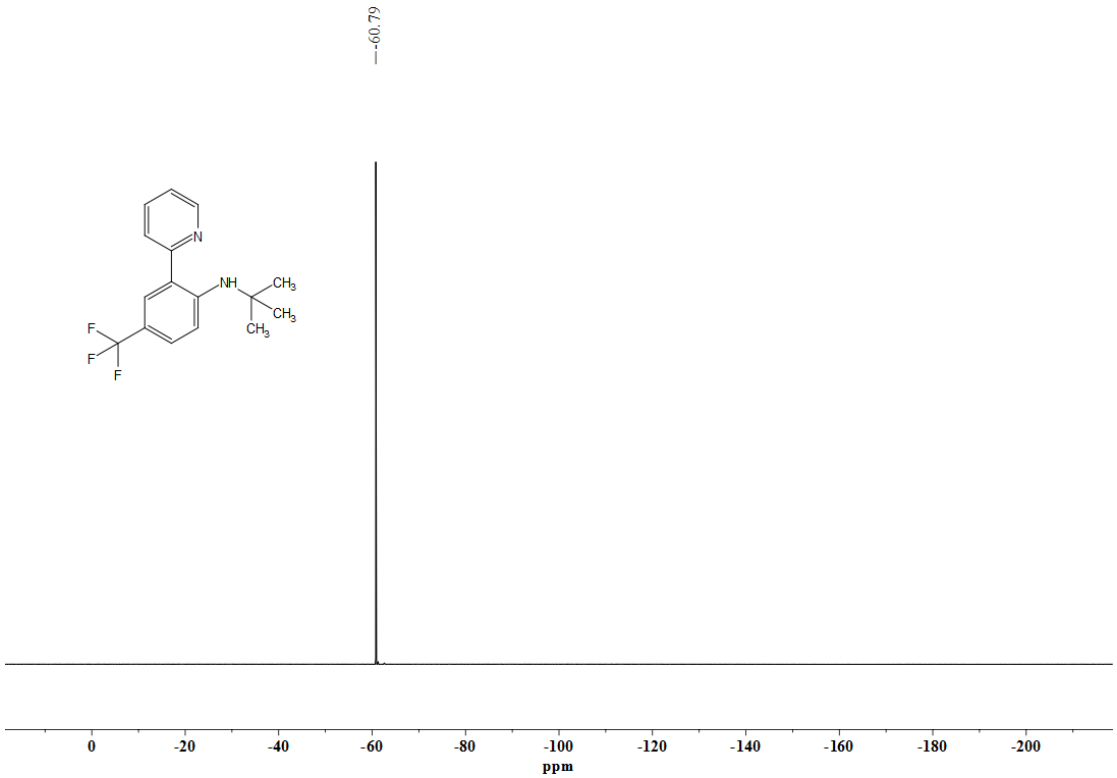


N-(tert-butyl)-4-methoxy-2-(pyridin-2-yl)aniline (3p)

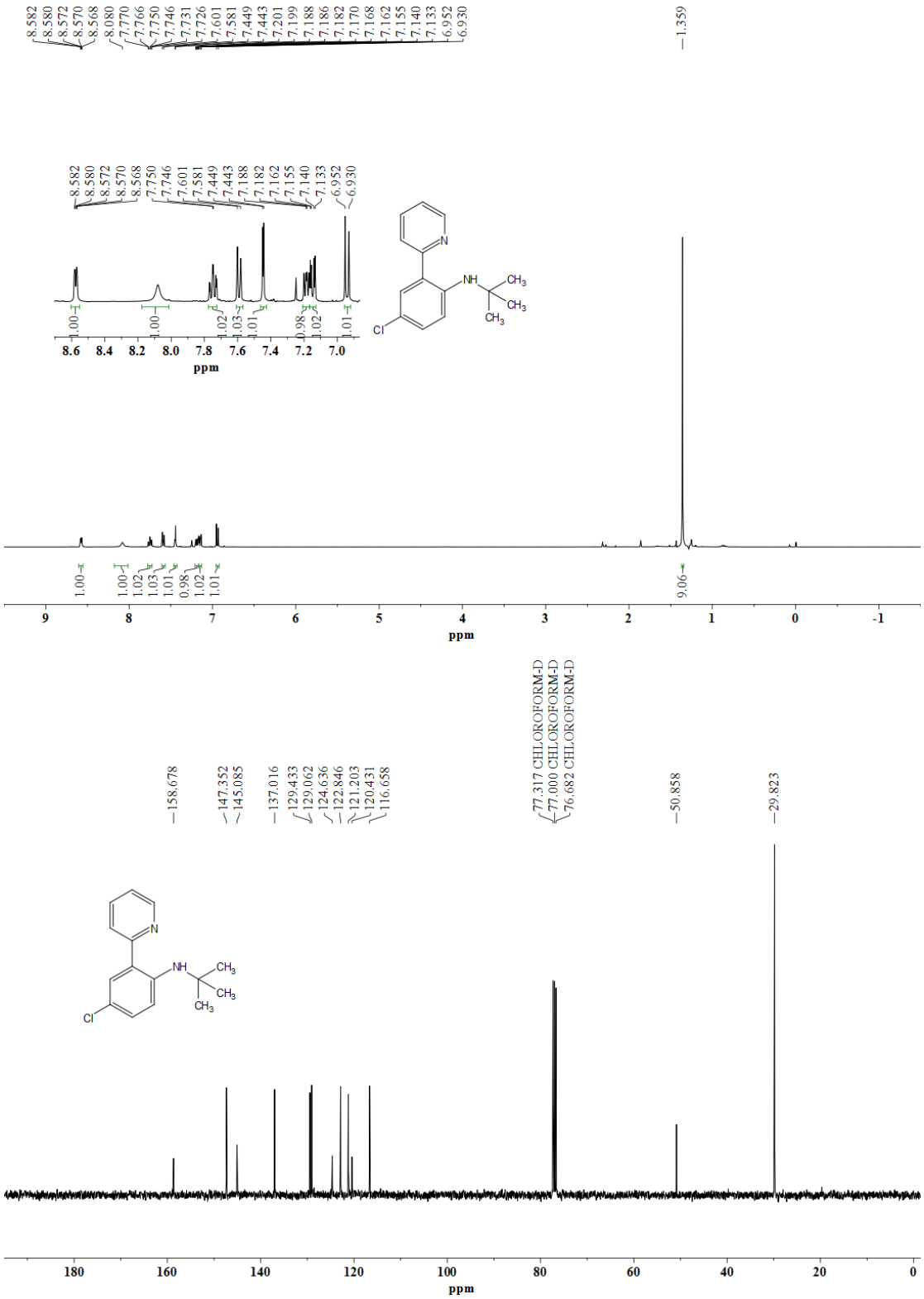


N-(tert-butyl)-2-(pyridin-2-yl)-4-(trifluoromethyl)aniline (3q)

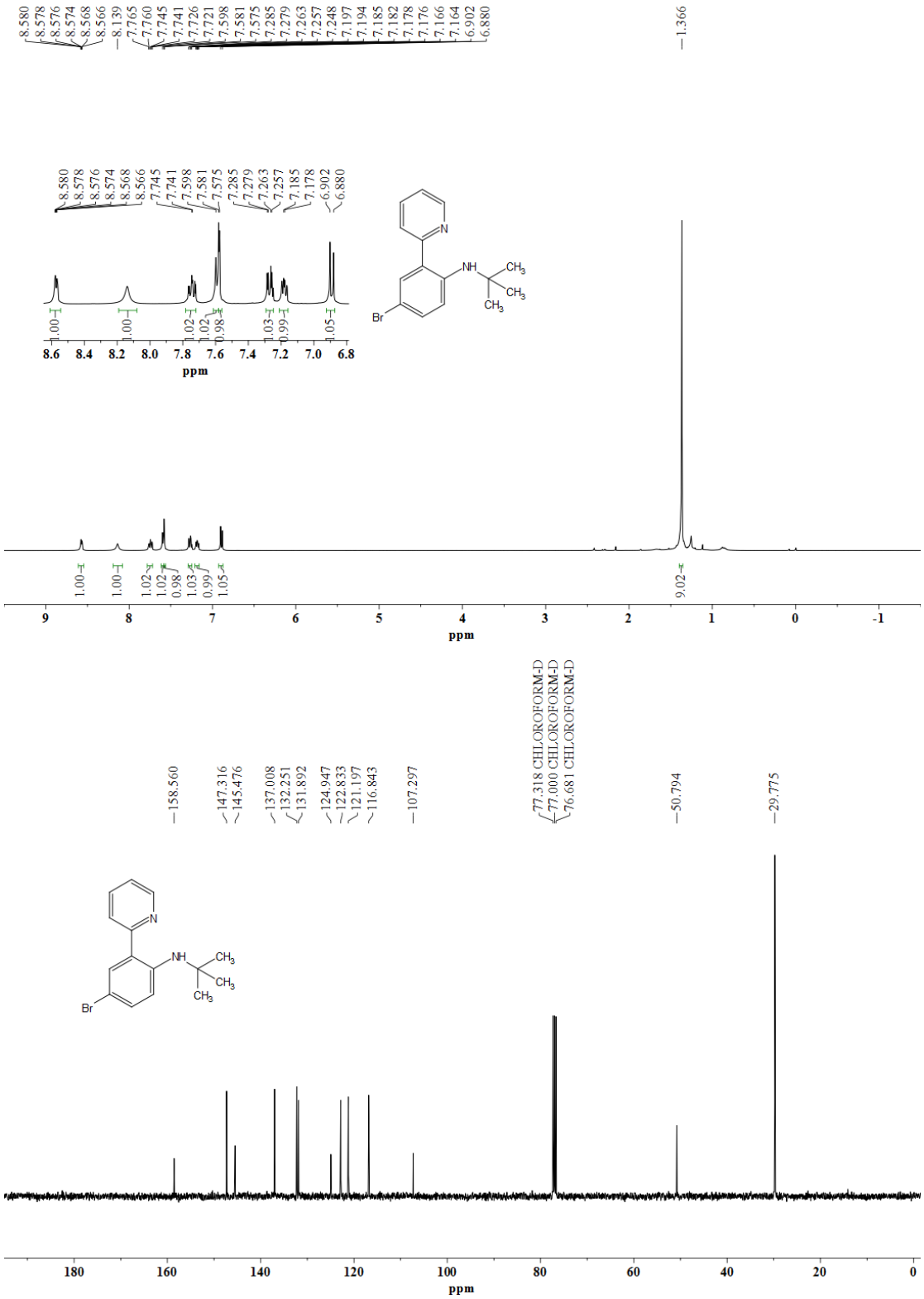



-60.79
N
NH
CH3
CH3
CH3
F
F
F
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm

N-(tert-butyl)-4-chloro-2-(pyridin-2-yl)aniline (3r)

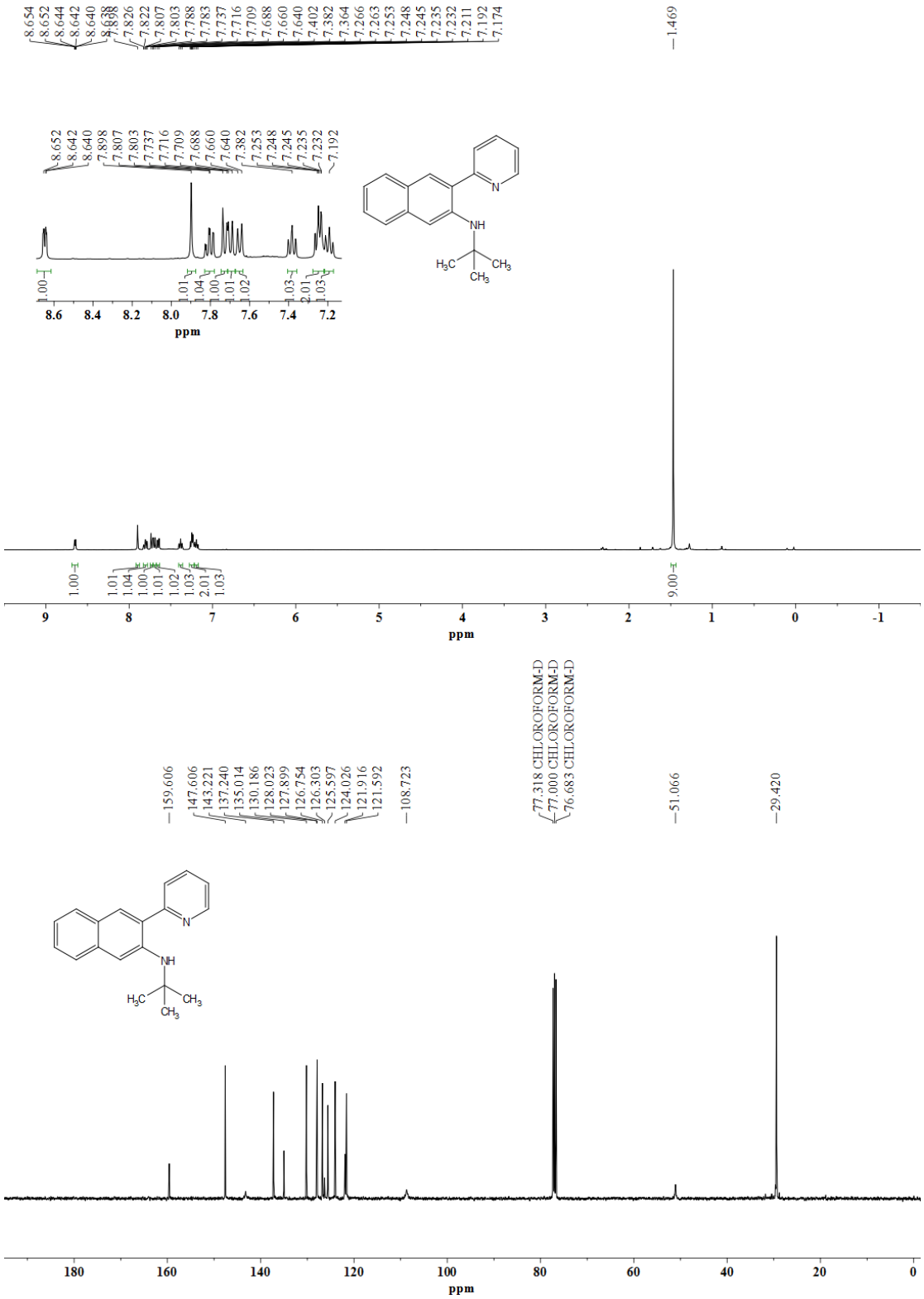


4-bromo-N-(tert-butyl)-2-(pyridin-2-yl)aniline (3s)

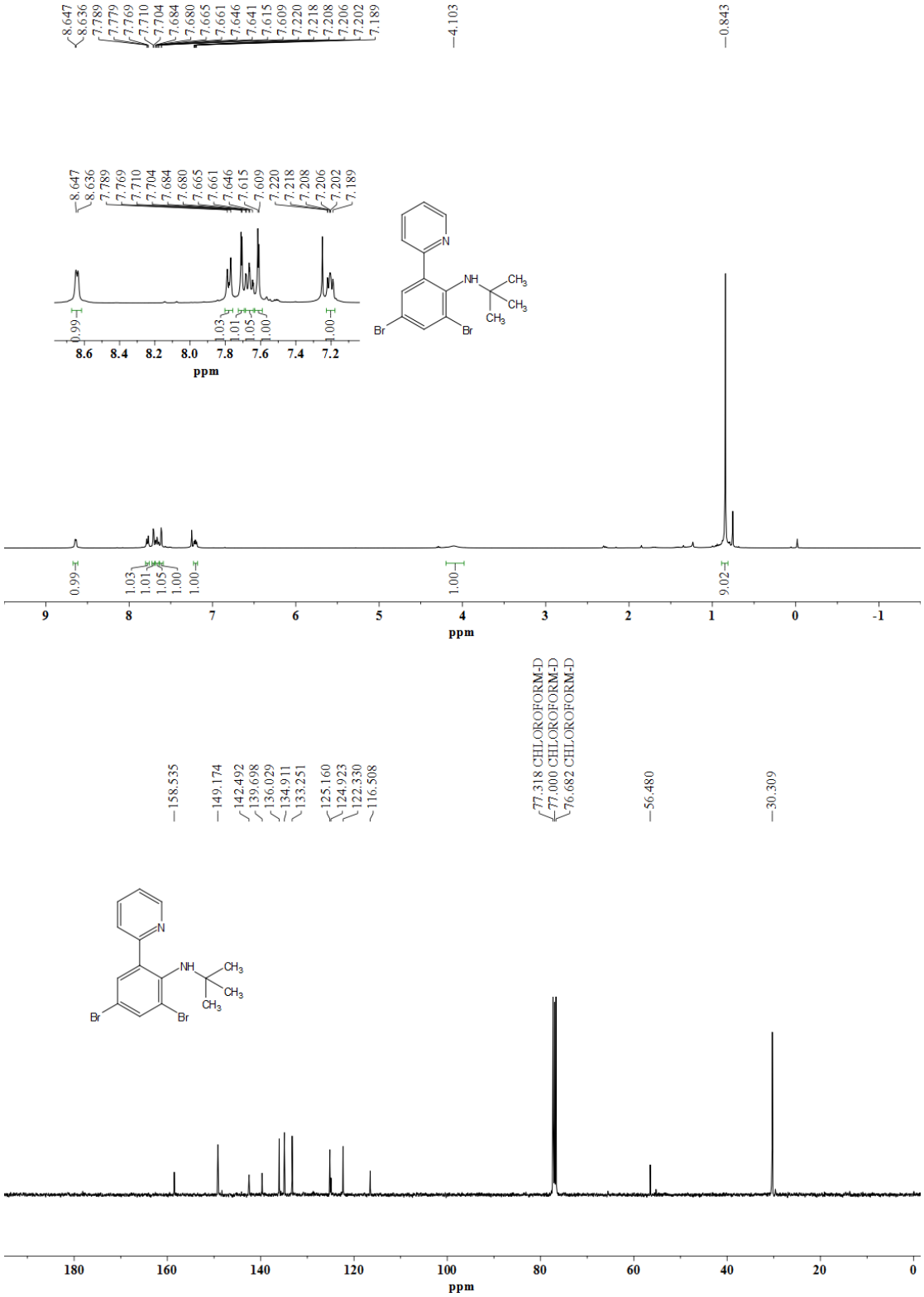


N-(tert-butyl)-3-methoxy-2-(pyridin-2-yl)aniline (3t)

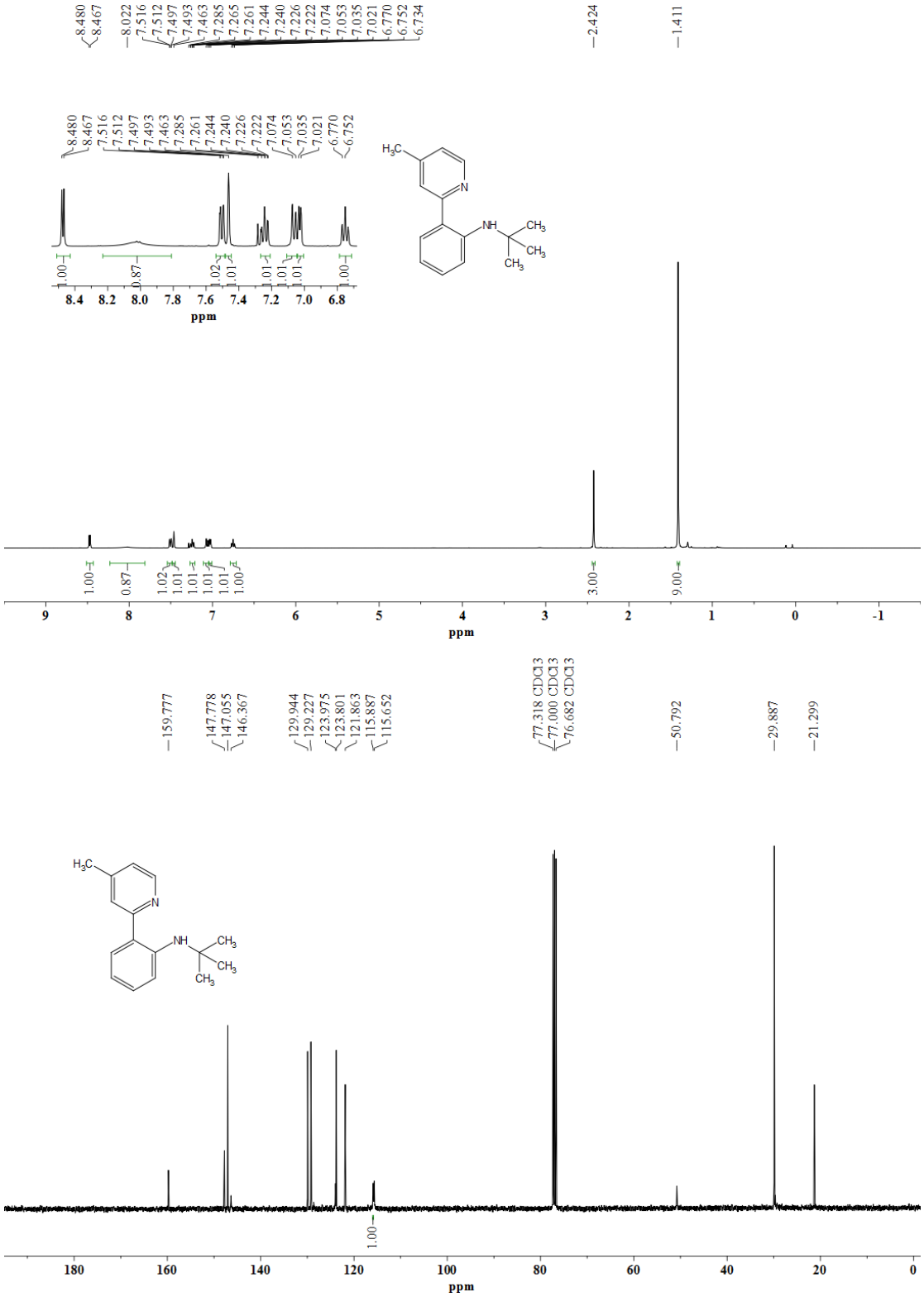
N-(tert-butyl)-3-(pyridin-2-yl)naphthalen-2-amine (3u)



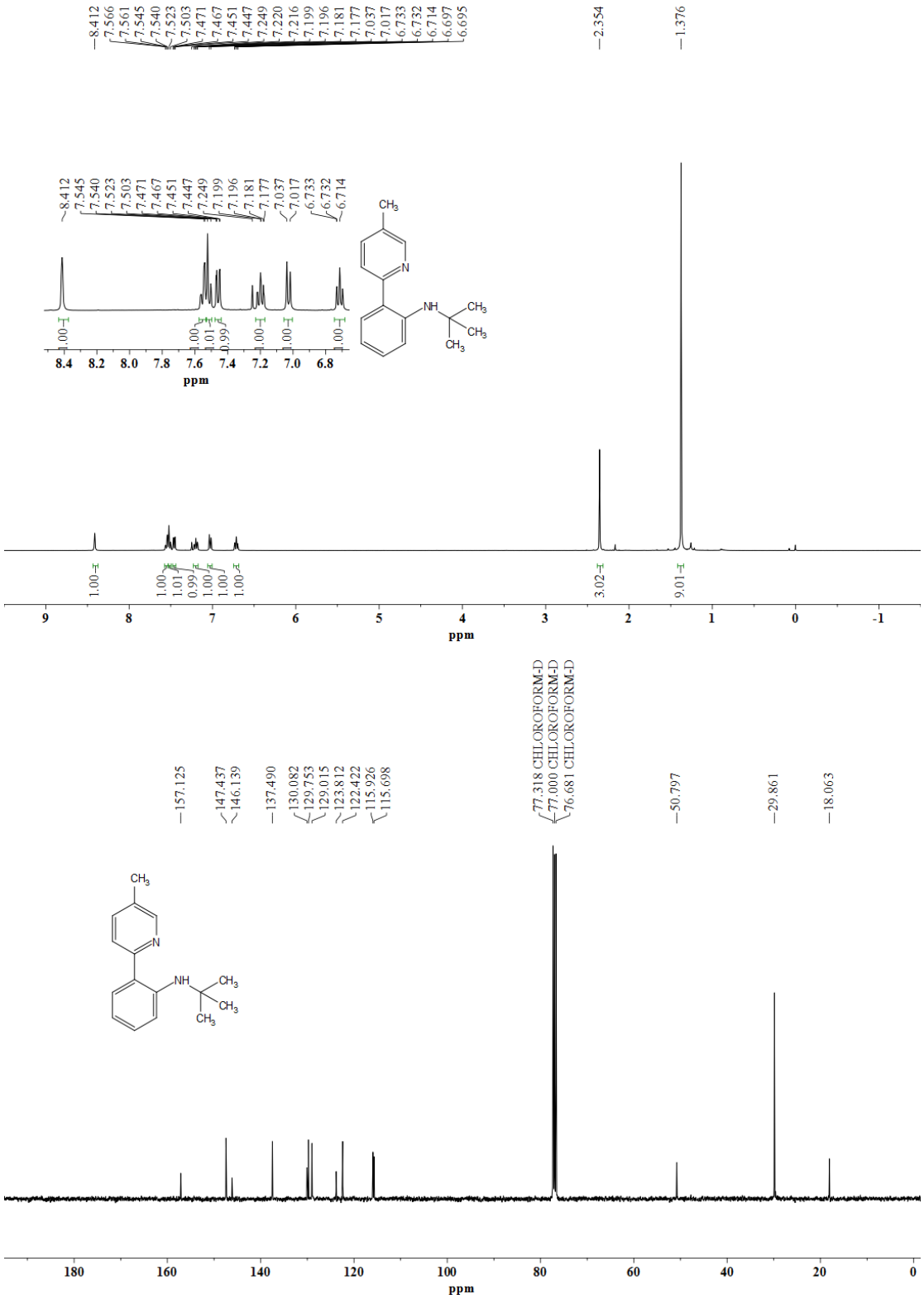
2,4-dibromo-N-(tert-butyl)-6-(pyridin-2-yl)aniline (3v)



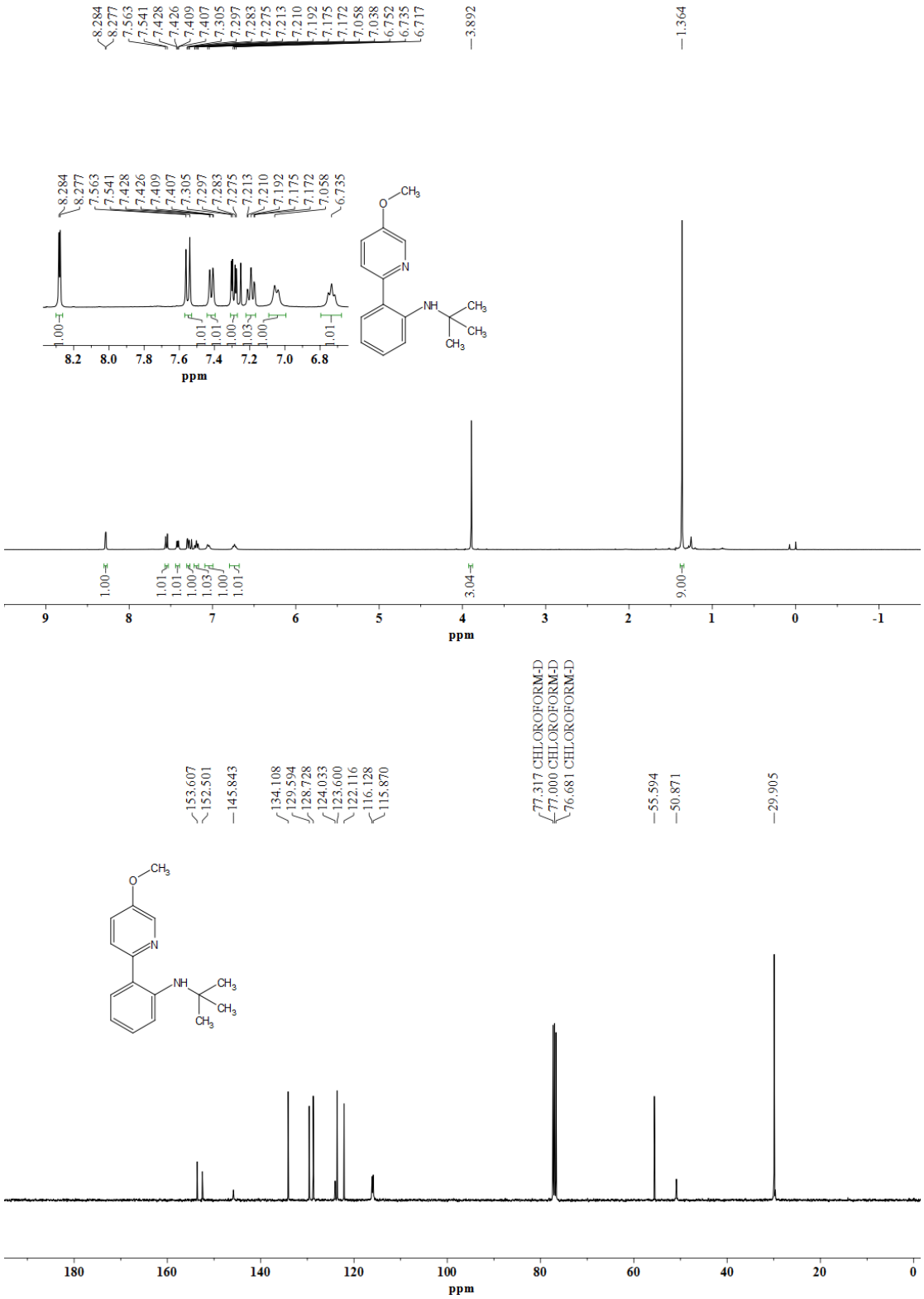
N-(tert-butyl)-2-(4-methylpyridin-2-yl)aniline (3aa)



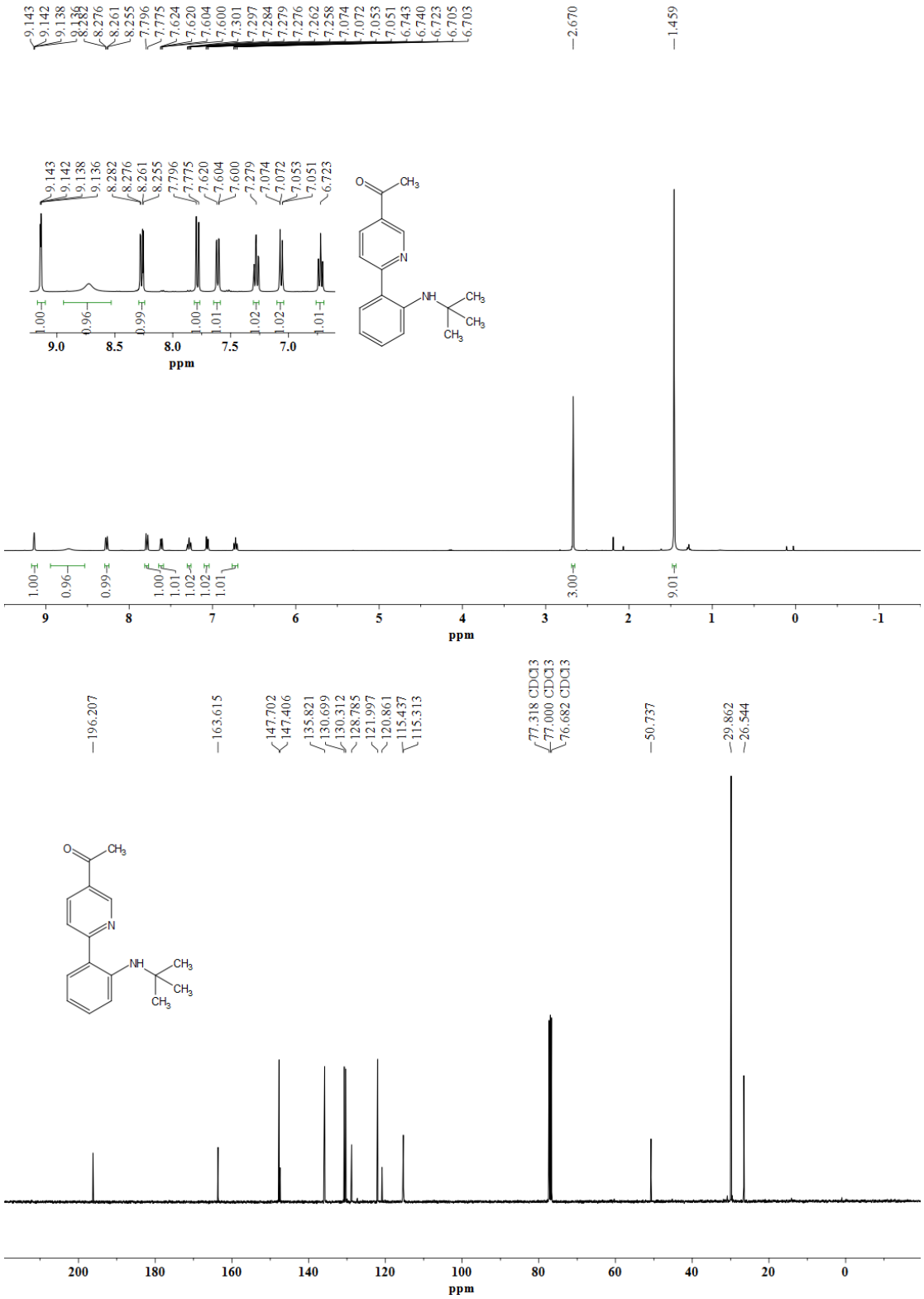
N-(tert-butyl)-2-(5-methylpyridin-2-yl)aniline (3ab)



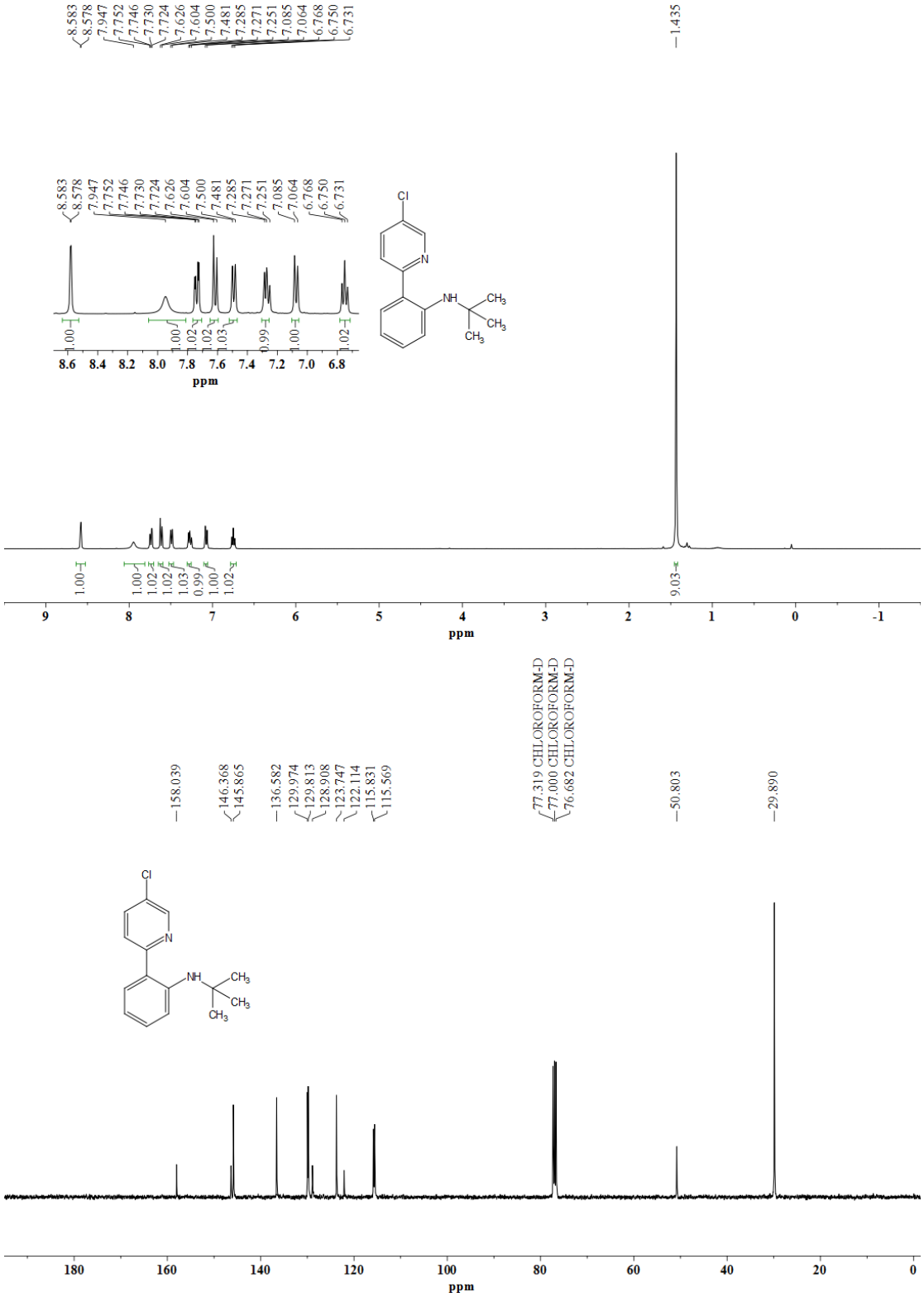
N-(tert-butyl)-2-(5-methoxypyridin-2-yl)aniline (3ac)



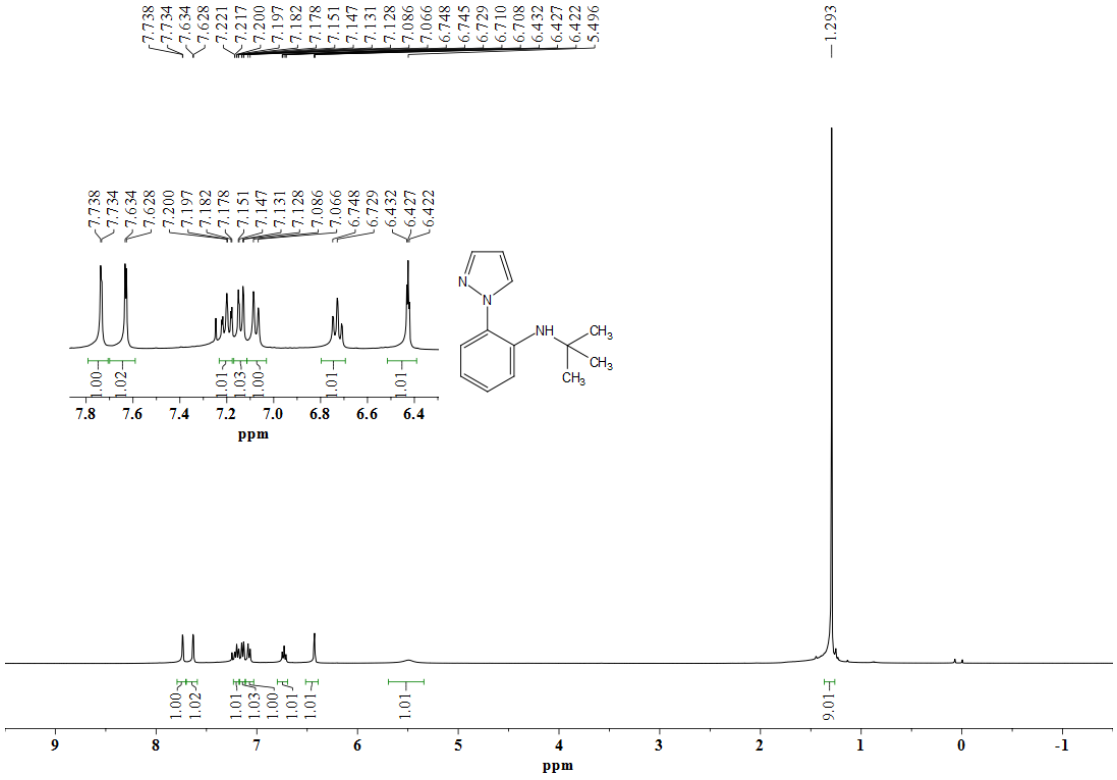
1-(6-(2-(tert-butylamino)phenyl)pyridin-3-yl)ethan-1-one (3ad)

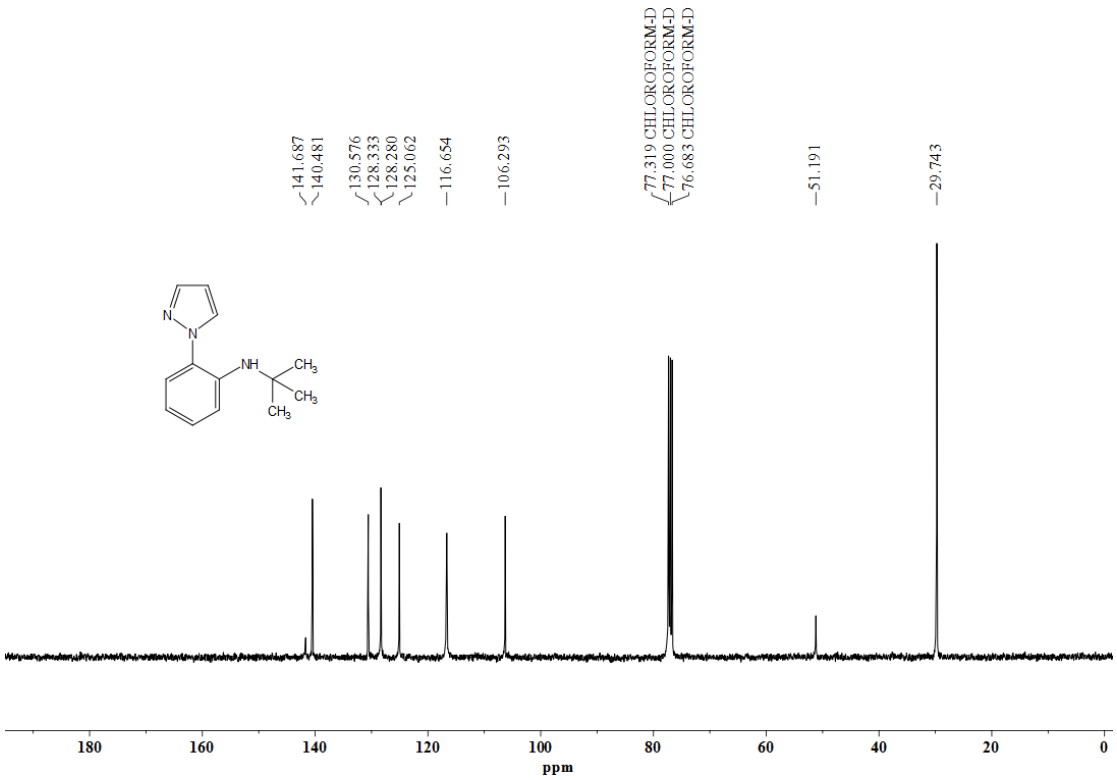


N-(tert-butyl)-2-(5-chloropyridin-2-yl)aniline (3ae)

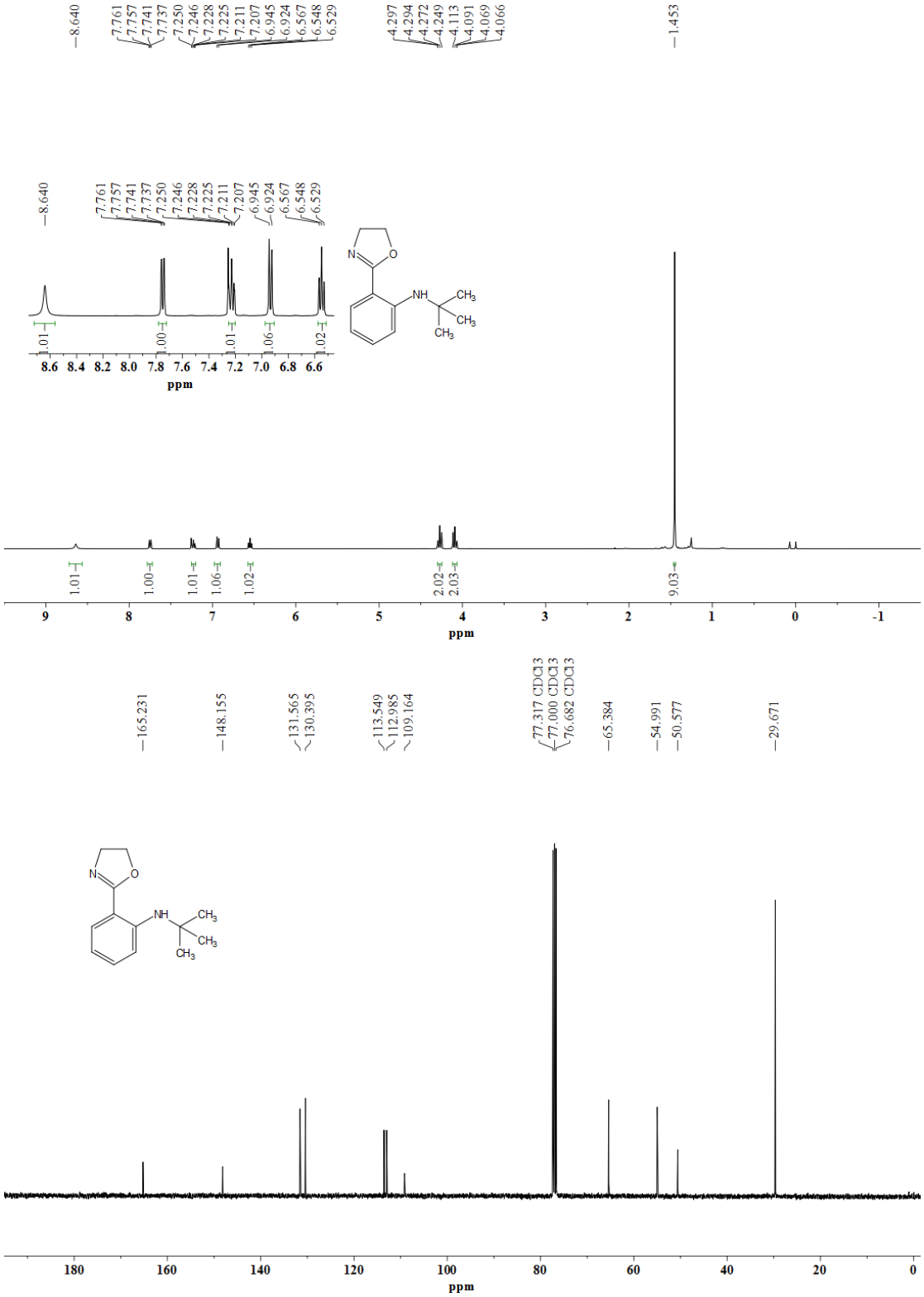


N-(tert-butyl)-2-(1H-pyrazol-1-yl)aniline (3af)

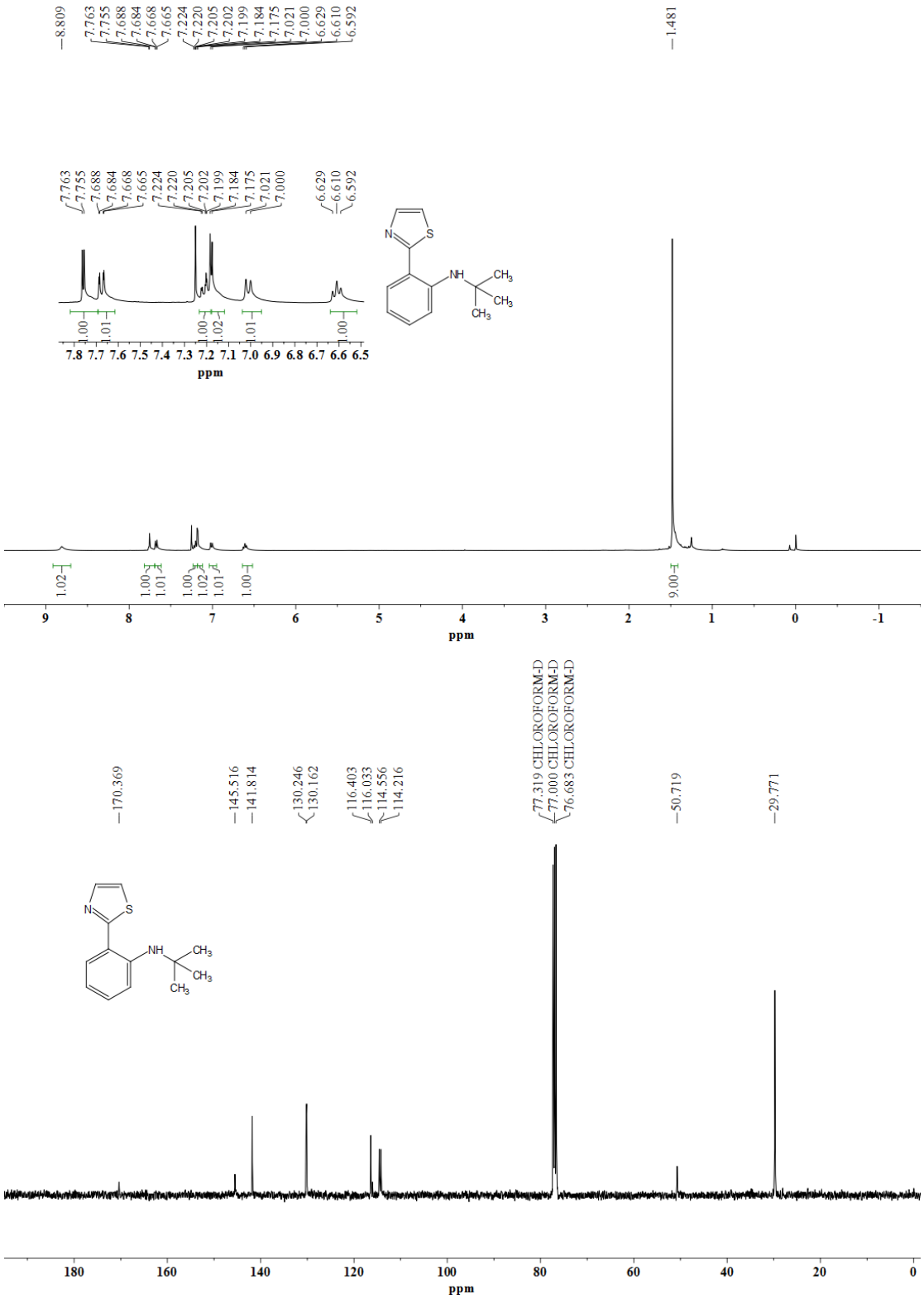




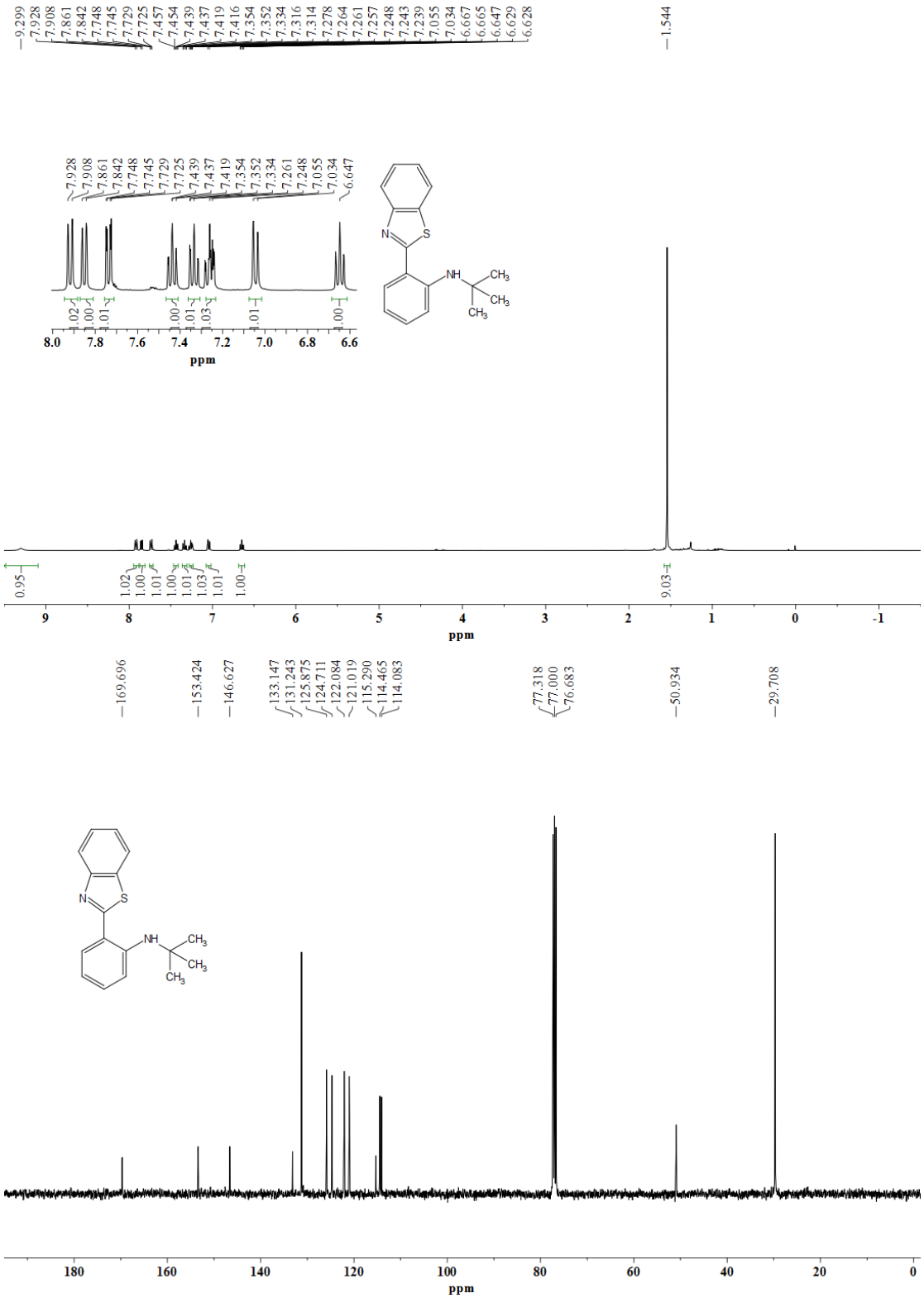
N-(tert-butyl)-2-(1H-pyrazol-1-yl)aniline (3ag)



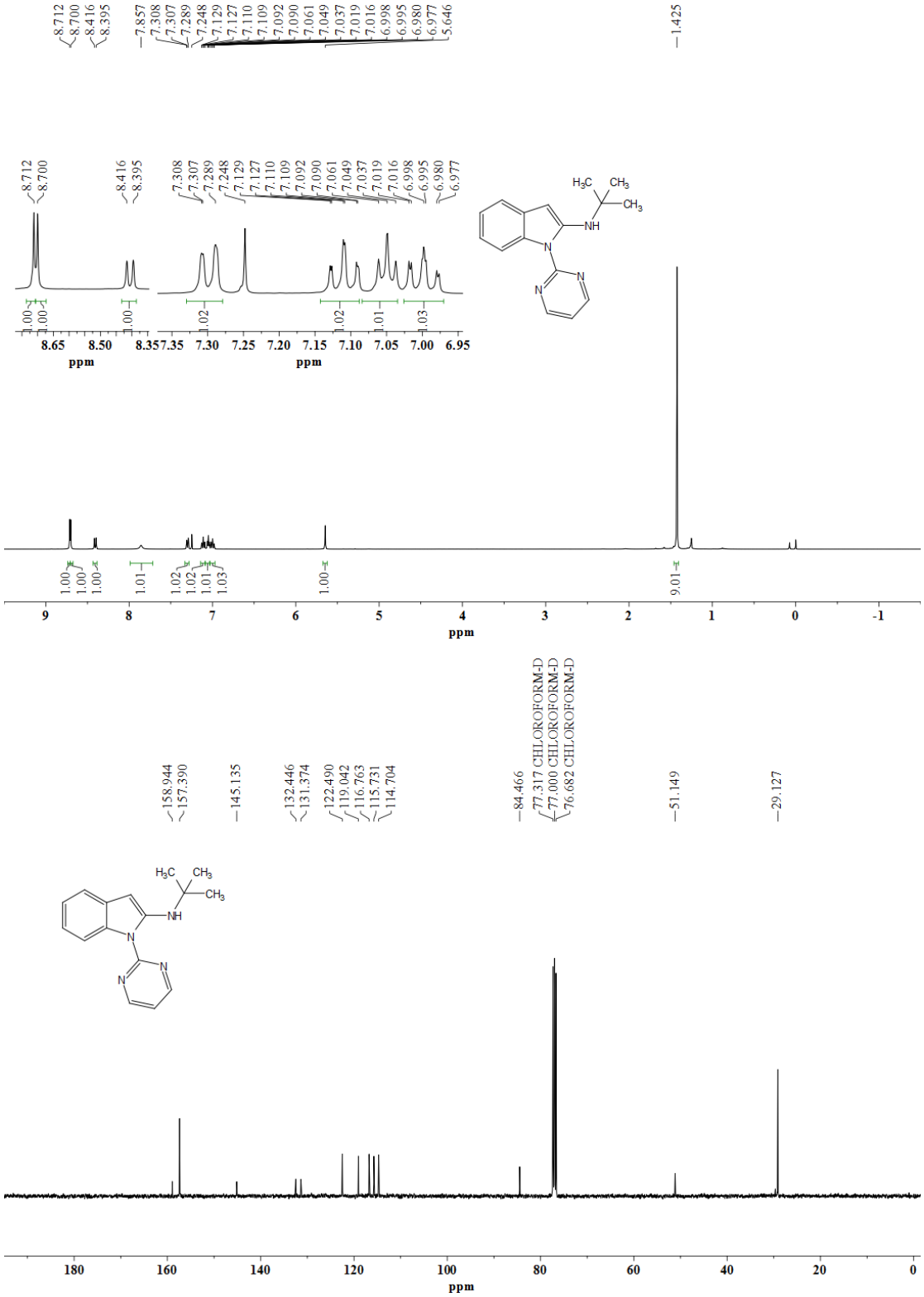
N-(tert-butyl)-2-(thiazol-2-yl)aniline (3ah)



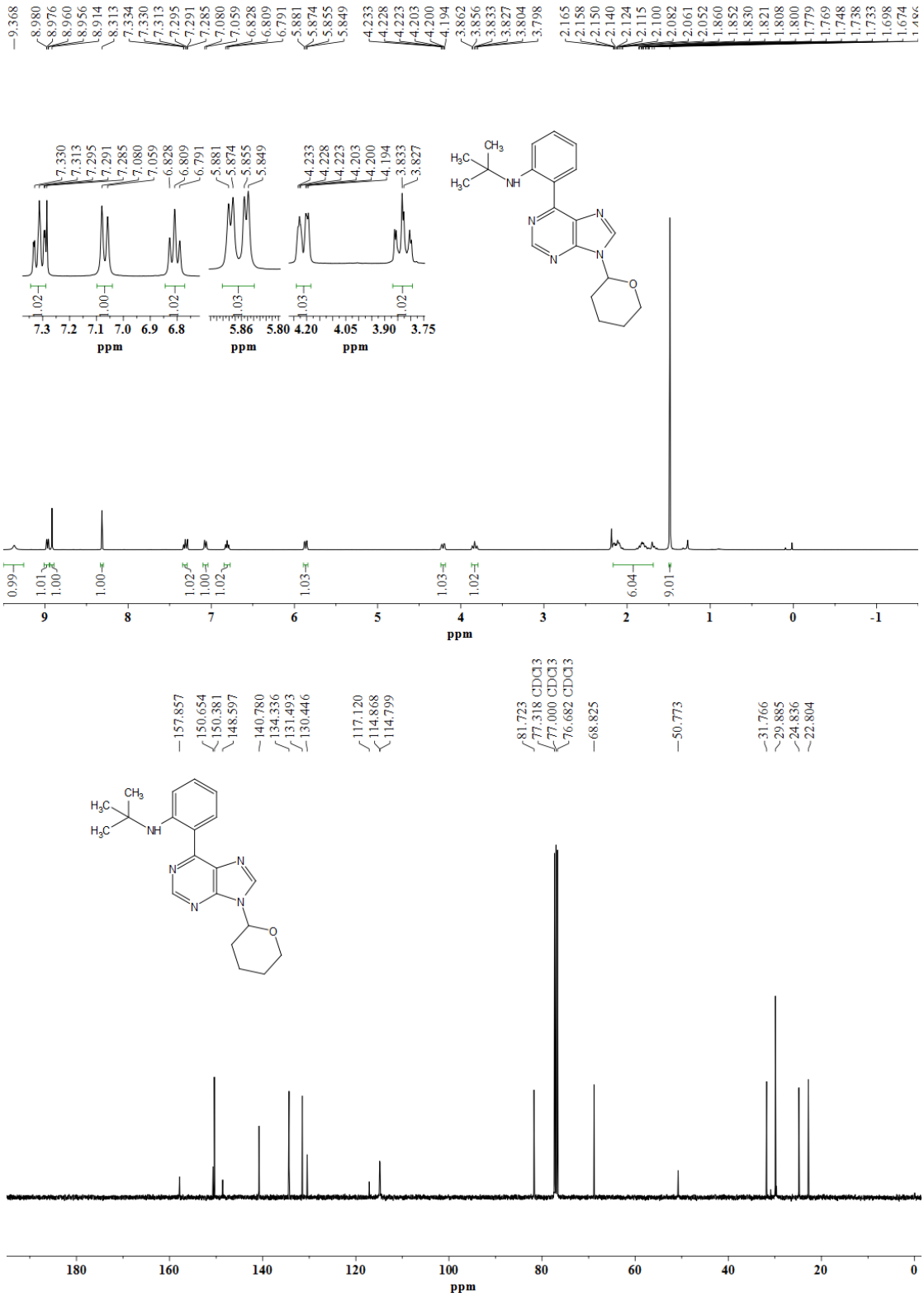
2-(benzo[d]thiazol-2-yl)-N-(tert-butyl)aniline (3ai)



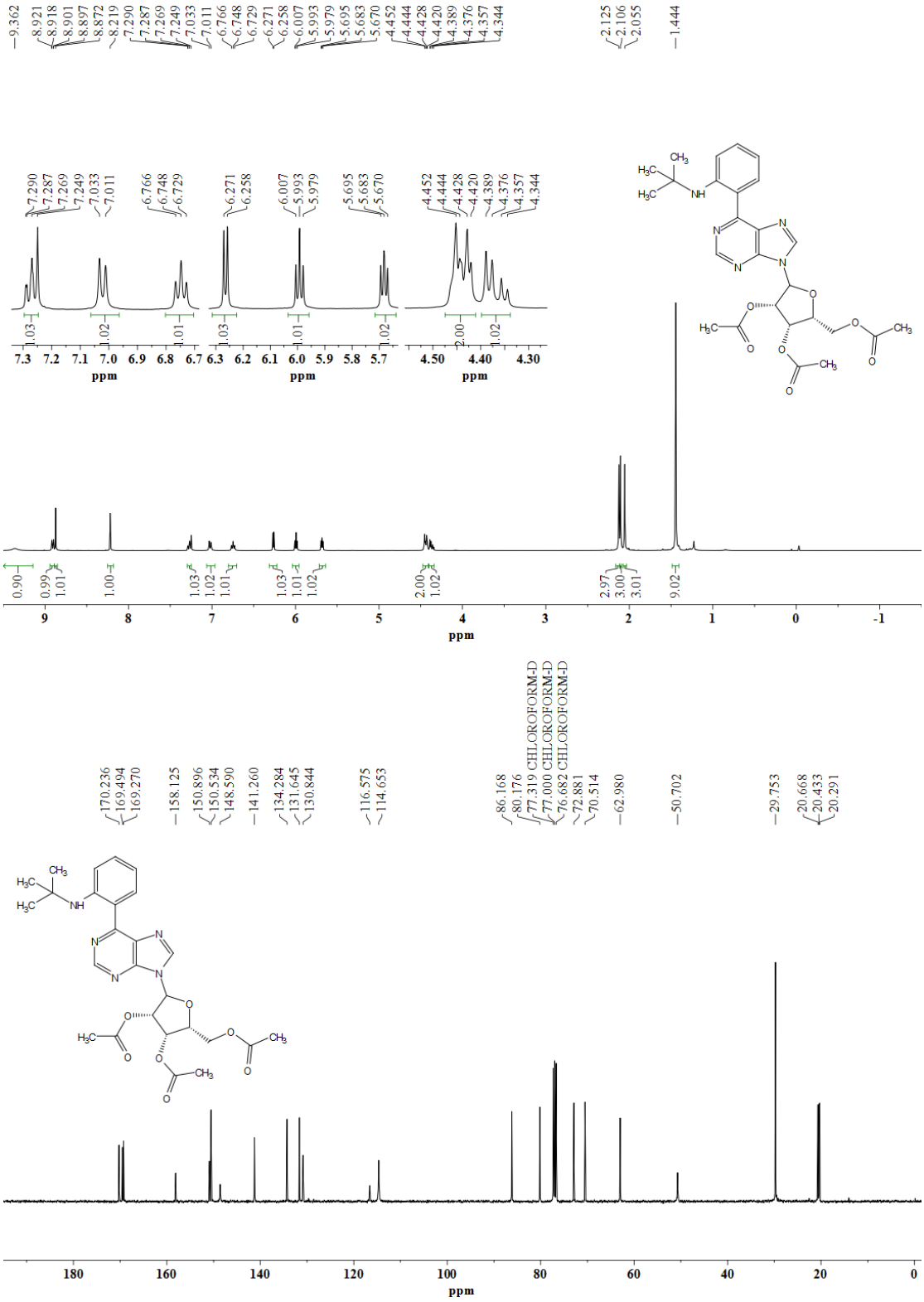
N-(tert-butyl)-1-(pyrimidin-2-yl)-1H-indol-2-amine (3aj)



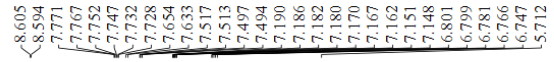
N-(tert-butyl)-2-(9-(tetrahydro-2H-pyran-2-yl)-9H-purin-6-yl)aniline (3ak)

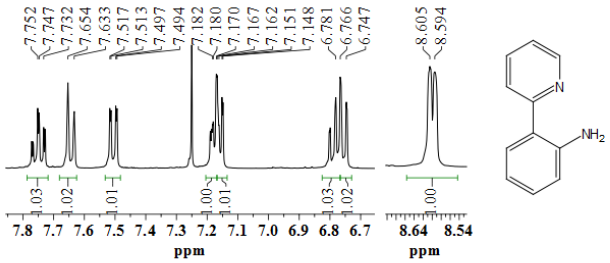


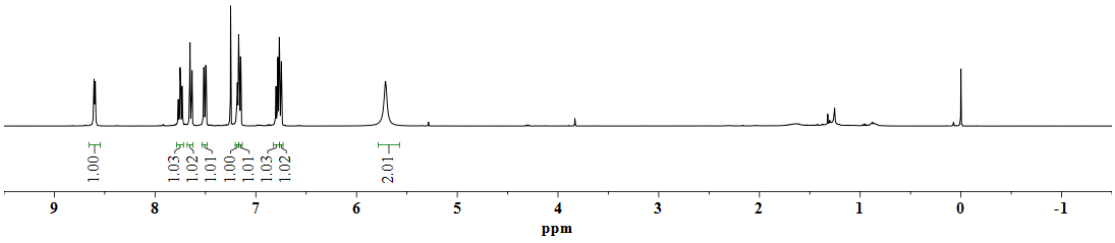
(2R,3S,4S)-2-(acetoxymethyl)-5-(6-(2-(tert-butylamino)phenyl)-9H-purin-9-yl)tetrahydrofuran-3, 4-diyl diacetate (3al)

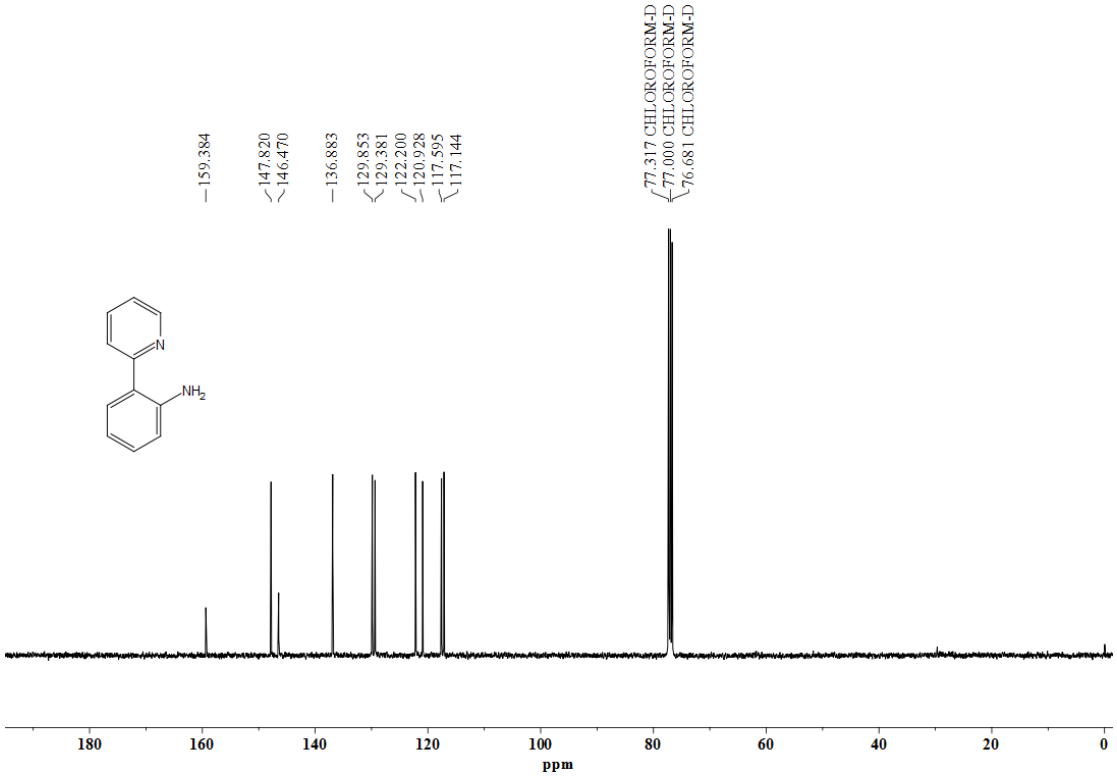


2-(pyridin-2-yl)aniline(4)

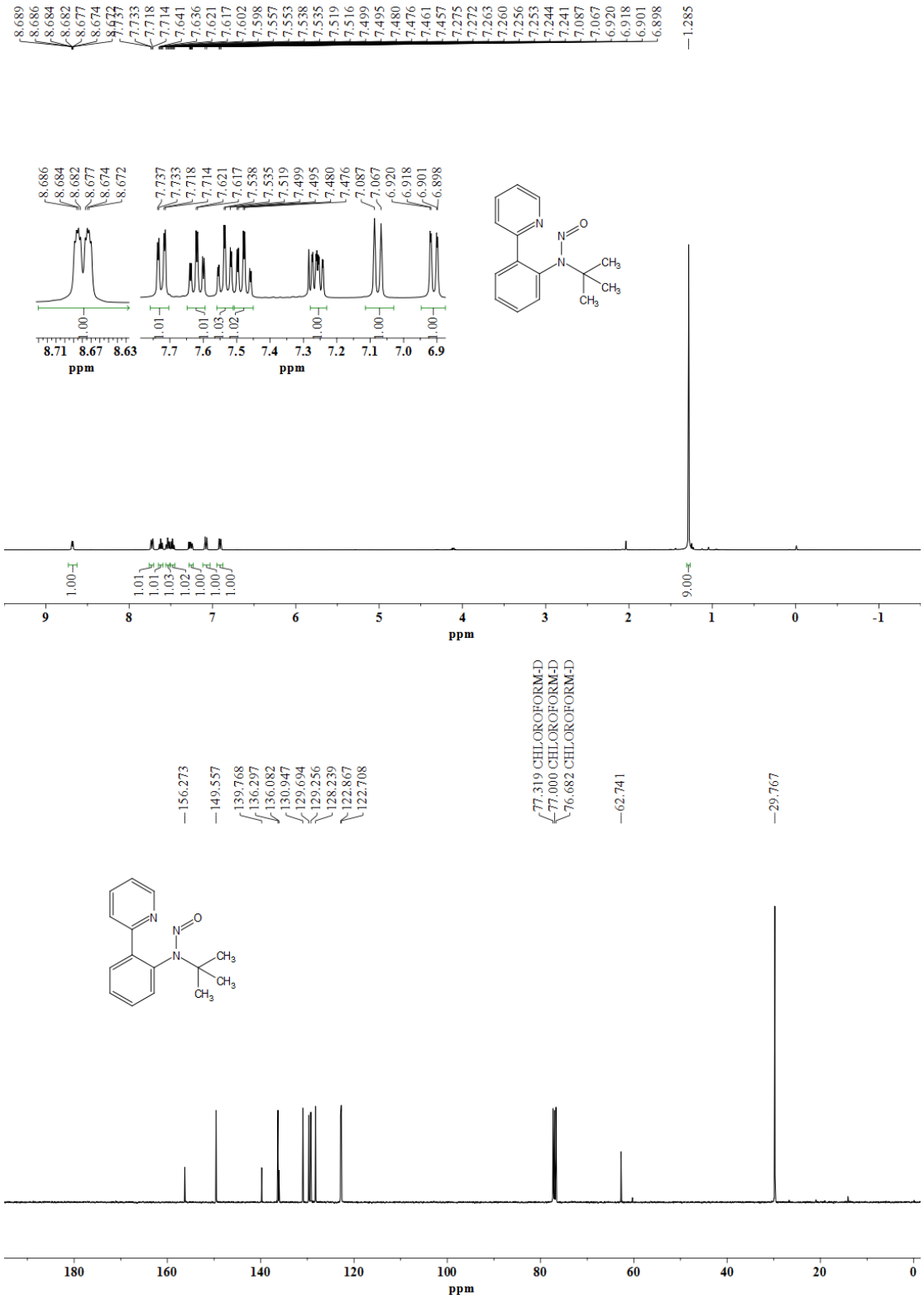








N-(tert-butyl)-N-(2-(pyridin-2-yl)phenyl)nitrous amide (5)



Ruthenium (II) intermediate A