Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting Information for

Rhodium(I)-Catalyzed Directed Trideuteromethylation of (Hetero)arene C–H Bonds with CD_3CO_2D

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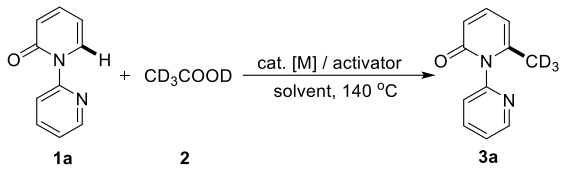
Contents:

1. General information:

Unless otherwise noted, all experiments were carried out in air and all commercially available chemicals, including organic solvents, were used as received from Aldrich, Acros or Strem without further purification. ^{1}H NMR and ^{13}C{^{1}H} NMR spectra were recorded on a Bruker Model Advance DMX 400 Spectrometer (^{1}H 400 MHz and ^{13}C{^{1}H} 101 MHz, respectively), Bruker Model Advance DMX 500 Spectrometer (^{1}H 500 MHz and ^{13}C{^{1}H} 126 MHz, respectively) or Bruker Model Advance DMX 600 Spectrometer (^{1}H 600 MHz and ^{13}C{^{1}H} 151 MHz, respectively). Chemical shifts (δ) are given in ppm and are referenced to residual solvent peaks. Melting points were measured on an X-4 melting point apparatus and are uncorrected. High resolution mass spectra (HRMS) were performed on a VG Autospec-3000 spectrometer. Column chromatography was performed with silica gel (200-300 mesh). 1-(2-pyridyl)-2-pyridones,[1] pyrimidinyl indoles,[2] phenylpyridines and other hereoarenes[3] were prepared according to the previous reports.

2. Optimization of the reaction conditions

Table S1. Optimization of reaction conditions.[a]



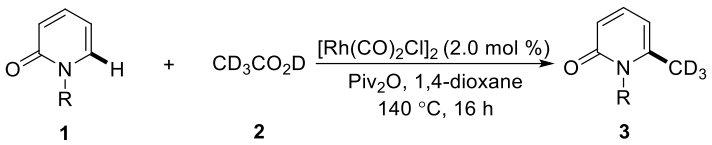
1a 2 3a

Entry	Catalyst	Activator	Additive	Solvent	Yield (%)[b]
1	$[Rh(CO)_2Cl]_2$	Boc_2O	none	1,4-dioxane	21
2	$[Rh(CO)_2Cl]_2$	Boc_2O	PivOH	1,4-dioxane	84
3	$[Rh(CO)_2Cl]_2$	Boc_2O	PivOH	DCE	7
4	$[Rh(CO)_2Cl]_2$	Boc_2O	PivOH	THF	0
5	$[Rh(CO)_2Cl]_2$	Boc_2O	PivOH	acetone	0
6	$[Rh(CO)_2Cl]_2$	Boc_2O	PivOH	toluene	52
7	$[Rh(CO)_2Cl]_2$	Boc_2O	PivOH	PhCl	49
8	$[Rh(CO)_2Cl]_2$	Boc_2O	PivOH	*p*-xylene	41
9	$[Rh(CO)_2Cl]_2$	Boc_2O	PivOH	MeCN	0
10	$[Rh(CO)_2Cl]_2$	Boc_2O	PivOH	MeOH	0
11	$[Rh(CO)_2Cl]_2$	Boc_2O	PivOH	*i*PrOH	0

12	$[Rh(CO)_2Cl]_2$	Boc_2O	PivOH	*t*AmOH	0
13	$[Rh(CO)_2Cl]_2$	Boc_2O	PivOH	DMF	0
14	$[Rh(CO)_2Cl]_2$	Boc_2O	PivOH	DMA	0
15	$[Rh(CO)_2Cl]_2$	Boc_2O	PivOH	DME	0
16	$[Rh(CO)_2Cl]_2$	Boc_2O	PivOH	DMSO	0
17	$[Rh(COD)Cl]_2$	Boc_2O	PivOH	1,4-dioxane	61
18	$[RhCl(PPh_3)_3]$	Boc_2O	PivOH	1,4-dioxane	0
19	$[Rh(CO)_2acac]$	Boc_2O	PivOH	1,4-dioxane	0
20	$[Rh(C_2H_4)_2Cl]_2$	Boc_2O	PivOH	1,4-dioxane	0
21	$[RhCl(1,5\text{-}HD)]_2$	Boc_2O	PivOH	1,4-dioxane	0
22	$[Rh(NBD)Cl]_2$	Boc_2O	PivOH	1,4-dioxane	0
23	$[Rh(NBD)_2]BF_4$	Boc_2O	PivOH	1,4-dioxane	0
24	$[Rh(C_2H_4)_2acac]$	Boc_2O	PivOH	1,4-dioxane	0
25	$[Rh(COD)_2]OTf$	Boc_2O	PivOH	1,4-dioxane	56
26	$[Rh(COD)_2]BF_4$	Boc_2O	PivOH	1,4-dioxane	0
27	$RhCl_3.\ xH_2O$	Boc_2O	PivOH	1,4-dioxane	0
28	$[(p\text{-cymene})_2RuCl_2]_2$	Boc_2O	PivOH	1,4-dioxane	0
29	$[RuCl_2(PPh_3)_3]$	Boc_2O	PivOH	1,4-dioxane	0
30	$[Cp^*IrCl_2]_2$	Boc_2O	PivOH	1,4-dioxane	0
31	$[IrCl(COD)]_2$	Boc_2O	PivOH	1,4-dioxane	0
32	$[Cp^*RhCl_2]_2$	Boc_2O	PivOH	1,4-dioxane	0
33	$[Cp^*Rh(MeCN)_3](SbF_6)_2$	Boc_2O	PivOH	1,4-dioxane	0
34	$Pd(OAc)_2$	Boc_2O	PivOH	1,4-dioxane	0
35	$PdCl_2$	Boc_2O	PivOH	1,4-dioxane	0
36	$[Rh(CO)_2Cl]_2$	$(MeOCO)_2O$	none	1,4-dioxane	13
37	$[Rh(CO)_2Cl]_2$	TFAA	none	1,4-dioxane	0
38	$[Rh(CO)_2Cl]_2$	Tf_2O	none	1,4-dioxane	0
39	**$[Rh(CO)_2Cl]_2$**	**Piv_2O**	**none**	**1,4-dioxane**	**93 (90)[c]**
40	$[Rh(CO)_2Cl]_2$	PivCl	none	1,4-dioxane	10
41[d]	$[Rh(CO)_2Cl]_2$	Piv_2O	none	1,4-dioxane	87
42[e]	$[Rh(CO)_2Cl]_2$	Piv_2O	none	1,4-dioxane	89
43[f]	$[Rh(CO)_2Cl]_2$	Piv_2O	none	1,4-dioxane	92
42[g]	$[Rh(CO)_2Cl]_2$	Piv_2O	none	1,4-dioxane	65
45	none	Piv_2O	none	1,4-dioxane	0
46	$[Rh(CO)_2Cl]_2$	none	none	1,4-dioxane	0

[a]Reaction Conditions: **1a** (0.1 mmol.), **2** (0.11 mmol), cat. [M] (2.0 mol %), activator (1.2 equiv), additive (1.2 equiv), solvent (1.0 mL, 0.1 M), 140 ℃, 16 h, under N_2. [b]Yields were determined by ^1H NMR analysis of unpurified reaction mixtures with internal standard CH_2Br_2. [c]Isolated yield. [d]Reaction temperature 150 ℃. [e]Reaction temperature 130 ℃. [f]Piv_2O (1.5 equiv). [g]$[Rh(CO)_2Cl]_2$ (1.0 mol %) was used. COD: cyclooctadiene; NBD: norbornadiene; HD: hexadiene; Cp*: pentamethylcyclopentadiene.

Table S2. Exploring the effect of directing groups.[a]

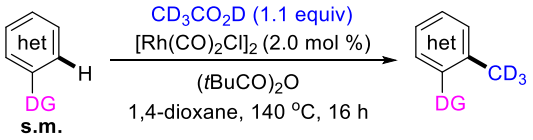


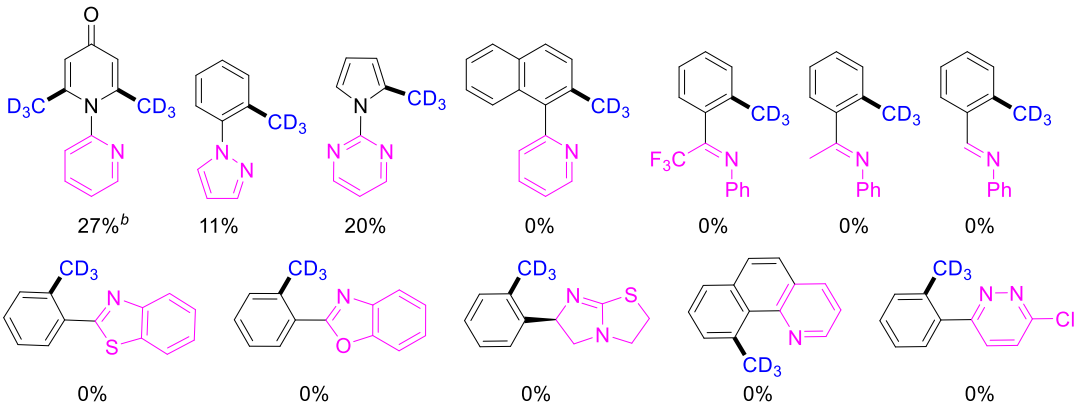
1 **2** **3**

Entry	R	Assay Yield (%)[b]
1	Me	0
2	Et	0
3	Ph	0
4	Bn	0
5	acetyl	0
6	2-pyridyl	93 (90)[c] (**3aa**)
7	2-pyrimidyl	22
8	Ac	0
9	Piv	0
10	Ts	0
11	H	0

[a]Reaction Conditions: **1** (0.1 mmol), **2** (0.11 mmol), $[Rh(CO)_2Cl]_2$ (2.0 mol %), Piv_2O (0.12 mmol, 1.2 equiv), 1,4-dioxane (1.0 mL, 0.1 M), 140 ℃, 16 h, under N_2. [b]Yields were determined by ^1H NMR analysis of unpurified reaction mixtures with internal standard CH_2Br_2. [c]Isolated yield.

Table S3. Minimally effective substrates under the reaction conditions.[a]

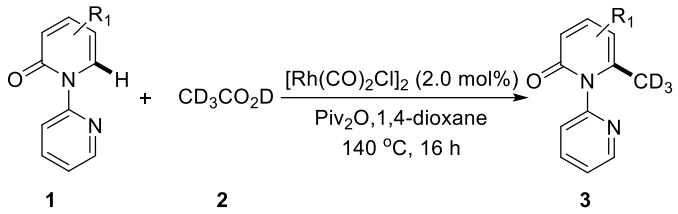




[a]Reaction Conditions: Starting materials (0.3 mmol.), **2** (0.33 mmol), $[Rh(CO)_2Cl]_2$ (2.0 mol%), $(tBuCO)_2O$ (1.2 equiv), 1,4-Dioxane (3 mL, 0.1 M), 140 ℃, 16 h, under N_2. [b]**1u** (0.3 mmol.), **2** (0.66 mmol), $[Rh(CO)_2Cl]_2$ (2.0 mol%),, $(tBuCO)_2O$ (2.4 equiv), 140 ℃, 16 h, under N_2.

3. The general procedures

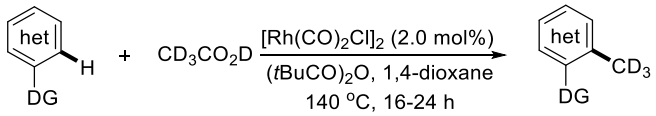
a) Direct trideuteriomethylation of 2-pyridones



1 **2** **3**

To an oven-dried pressure tube with a stir bar were sequentially added 2H-[1,2'-bipyridin]-2-one **1** (0.3 mmol, 1 equiv), $[Rh(CO)_2Cl]_2$ (2.3 mg, 2.0 mol%), CD_3CO_2D (19.0 μL, 0.33 mmol), Piv_2O (73.0 μL, 0.36 mmol) and anhydrous 1,4-dioxane (3.0 mL, 0.1 M). The tube was sealed under N_2 atmosphere and degassed for three times. The reaction mixture was heated and stirred vigorously at 140 °C for 16 h in an oil bath. After that, the color of the reaction mixture changed from light yellow to brown. After the 16 h reaction period, the tube was removed from the oil bath and cooled to room temperature. In a separatory funnel, the mixture was washed with a saturated sodium bicarbonate solution (10 mL) and was extracted with CH_2Cl_2 (5 mL × 3). The combined yellow organic layer was dried over Na_2SO_4, filtered and the volatile materials evaporated under reduced pressure, and the residue was purified by column chromatography on silica gel using a mixture of ethyl acetate and hexanes to give the purified product.

b) Direct C2-trideuteriomethylation of indoles and other (hetero)arene substrates

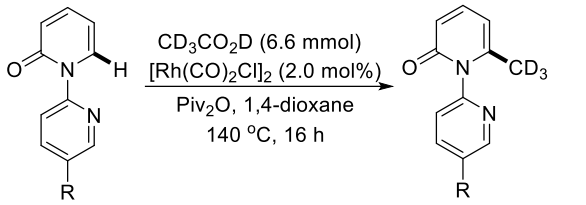


4, 5 **2** **6, 7**

To an oven-dried pressure tube with a stir bar were sequentially added (hetero)arene **4** or **5** (0.3 mmol, 1 equiv), $[Rh(CO)_2Cl]_2$ (2.3 mg, 2.0 mol%), CD_3CO_2D (19.0 μL, 0.33 mmol), (tBuCO)$_2$O (73.0 μL, 0.36 mmol) and anhydrous 1,4-dioxane (3.0 mL, 0.1 M) at rt. The tube was sealed under N_2 atmosphere and degassed three times. The reaction mixture was heated and stirred vigorously at 140 °C for 16-24 h in

the oil bath. After the reaction period, the color of the reaction mixture had changed from light yellow to brown. The tube was removed from the oil bath and cooled to room temperature. The mixture was washed with saturated sodium bicarbonate solution (10 mL) and was extracted with CH_2Cl_2 (5 mL ×3). The combined yellow organic layer was dried over Na_2SO_4, filtered, evaporated under reduced pressure to remove the volatile materials, and the residue was purified by column chromatography on silica gel using a mixture of ethyl acetate and hexanes to give the pure product.

c) Gram-scale synthesis of **3a** and **3p**

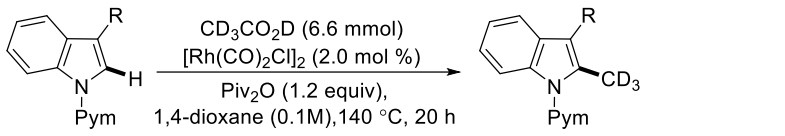


1a, R = H, 6 mmol
1p, R = Me, 6 mmol

3a, R = H, 84%
3p, R = Me, 80%

To a 100 mL round-bottom flask with a stir bar were added 2-pyridones (**1a,** 1.0 g, 6.0 mmol or **1p**, 1.1 g, 6.0 mmol), $[Rh(CO)_2Cl]_2$ (46.8 mg, 2.0 mol%), CD_3CO_2D (380 μL, 6.6 mmol), Piv_2O (1.5 mL, 7.2 mmol) and anhydrous 1,4-dioxane (20 mL) at rt. The flask was connected to the condenser under N_2 flow and degassed three times. The yellow reaction mixture was heated to 140 °C in an oil bath and stirred vigorously for 16 h. At the end of the reaction period, the color of the reaction mixture had changed from yellow to brown. The flask was then removed from the oil bath and cooled to room temperature. The flask was opened to air, the mixture was washed with saturated sodium bicarbonate solution (50 mL) and extracted with CH_2Cl_2 (15 mL × 3). The combined yellow organic layer was dried over Na_2SO_4, filtered and evaporated under reduced pressure to remove the volatile materials. The crude residue was purified by column chromatography on silica gel using a mixture of ethyl acetate/hexanes (2/1, v/v) to give the purified products (**3a**, yellow solid, 953.6 mg, 84% yield; **3p**, yellow solid, 975.6 mg, 80% yield).

d) Gram-scale synthesis of **6a** and **6e**



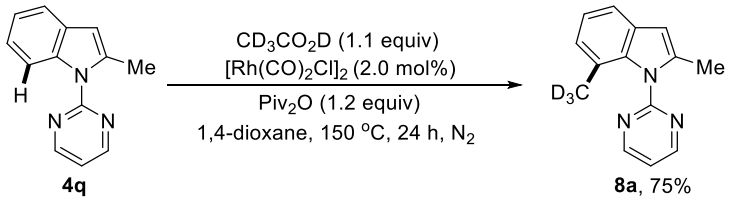
4a, R = H, 6 mmol
4e, R = -$(CH_2)_2$-NH-Boc, 6 mmol

6a, R = H, 81%
6e, R = -$(CH_2)_2$-NH-Boc, 40%

To an oven-dried round-bottom flask with a stir bar were sequentially added indoles (**4a,** 1.2 g, 6.0 mmol; or **4e,** 2.0 g, 6.0 mmol), $[Rh(CO)_2Cl]_2$ (46.8 mg, 2.0 mol%), CD_3CO_2D (380 μL, 6.6 mmol), Piv_2O (1.5 mL, 7.2 mmol) and anhydrous 1,4-dioxane (20 mL) at rt. The tube was sealed under N_2 atmosphere and degassed three times. The reaction mixture was heated and stirred vigorously at 140 °C for 20 h in the oil bath. At the end of the reaction period, the color of the reaction mixture had changed from yellow to dark brown. The flask was then removed from the oil bath and cooled to room temperature. The flask was opened to air, reaction mixture was poured into a separatory funnel, washed with saturated sodium bicarbonate solution (50 mL) and extracted with CH_2Cl_2 (15 mL × 3). The combined yellow organic layer was dried over Na_2SO_4, filtered and the volatile materials evaporated under reduced pressure, and the residue was purified by column chromatography on silica gel using a mixture of ethyl acetate and hexanes (1/4, v/v) to give the purified products (**6a**, yellow solid, 1.0 g, 81% yield; **6e,** yellow solid, 805.1 mg, 40% yield, respectively).

4. Direct trideuteromethylation and di-trideuteromethylation of indoles

a) Direct C7-trideuteriomethylation of indoles

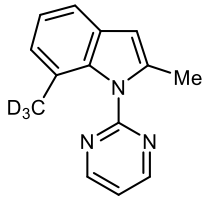


4q **8a**, 75%

To an oven-dried pressure tube with stir bar were sequentially added C2-substuated indole **4q** (62.8 mg, 0.3 mmol), CD_3CO_2D (19.0 μL, 0.33 mmol), $[Rh(CO)_2Cl]_2$ (2.3 mg, 2.0 mol%), (tBuCO)$_2$O (73.0 μL, 0.36 mmol) and anhydrous

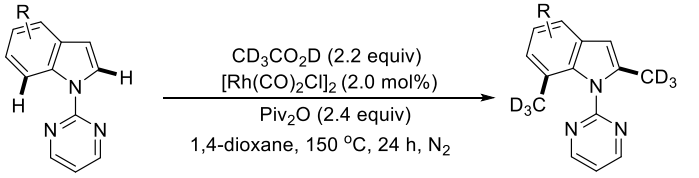
1,4-dioxane (3.0 mL, 0.1 M) at RT. The tube was sealed under a N_2 atmosphere and degassed three times. The mixture was heated and stirred at 150 °C for 24 h in the oil bath. During that time, the color of the reaction mixture changed from light yellow to brown. The tube was removed from the oil bath and cooled to room temperature. The reaction vial was opened to air and the mixture was added to a separatory funnel, washed with saturated sodium bicarbonate solution (10 mL) and extracted with CH_2Cl_2 (5 mL × 3). The combined yellow organic layer was dried over Na_2SO_4, filtered, evaporated under reduced pressure to remove the volatile materials, and the residue was purified by column chromatography on silica gel using a mixture of ethyl acetate/hexanes (1:4, v/v) to give the corresponding product **8a** (50.9 mg, 75% isolated yield).

2-Methyl-7-(methyl-*d*$_3$)-1-(pyrimidin-2-yl)-1H-indole (8a)



The title compound was purified by column chromatography using EtOAc/hexanes (1:3, v/v) and isolated as a yellow semi solid, 50.9 mg, 75%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (d, *J* = 4.9 Hz, 2H), 7.42 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.28 (t, *J* = 4.9 Hz, 1H), 7.08 (t, *J* = 7.5 Hz, 1H), 6.95 (dd, *J* = 7.2, 1.3 Hz, 1H), 6.46 – 6.37 (m, 1H), 2.37 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 158.9, 158.3, 137.7, 136.6, 129.7, 124.8, 121.5, 121.2, 119.0, 117.7, 104.1, 19.2 (h, J = 20.2 Hz), 14.0. HRMS (ESI) calcd. for [$C_{14}H_{11}D_3N_3$(M+H$^+$)]: 277.1371, found: 277.1368.

b) Direct C2,C7-di-trideuteriomethylation of indoles



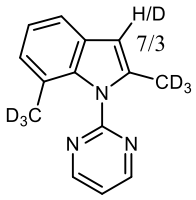
4a, R = H,
4b, R = 3-Me,
4g, R = 5-Me,

8b, R = H, 71%
8c, R = 3-Me, 69%
8d, R = 5-Me, 72%

To an oven-dried pressure tube with a stir bar were sequentially added **4a** (58.6 mg, 0.3 mmol) or **4b** (62.8 mg, 0.3 mmol) or **4g** (62.8 mg, 0.3 mmol), CD_3CO_2D (38.0 μL, 0.66 mmol), $[Rh(CO)_2Cl]_2$ (2.3 mg, 2.0 mol%), (*t*BuCO)$_2$O (146.0 μL, 0.72 mmol) and anhydrous 1,4-dioxane (3.0 mL, 0.1 M) at RT. The tube was sealed under an N_2

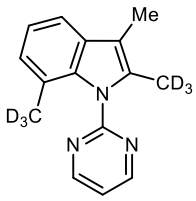
atmosphere and degassed three times. The mixture was heated and stirred at 150 °C for 24 h in the oil bath. During the hearing period, the color of the reaction mixture changed from yellow to dark brown. The tube was removed from the oil bath, cooled to room temperature and opened to air. The mixture was was added to a separatory funnel , washed with saturated sodium bicarbonate solution (10 mL) and extracted with CH_2Cl_2 (5 mL × 3). The combined yellow organic layer was dried over Na_2SO_4, filtered, evaporated under reduced pressure to remove the volatile materials, and the residue was purified by column chromatography on silica gel using a mixture of ethyl acetate/hexanes (1:3, v/v) to give the corresponding products **8b** (48.8 mg, 71%), **8c** (50.4 mg, 69%) and **8d** (52.5 mg, 72%).

2,7-Bis(methyl-*d*$_3$)-1-(pyrimidin-2-yl)-1H-indole (8b)



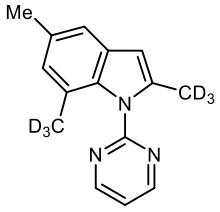
The title compound was purified by column chromatography using EtOAc/hexanes (1:3, v/v) and isolated as a yellow semi solid, 48.8 mg, 71%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (d, *J* = 4.8 Hz, 2H), 7.41 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.29 (t, *J* = 4.8 Hz, 1H), 7.07 (t, *J* = 7.5 Hz, 1H), 6.94 (dd, *J* = 7.2, 1.3 Hz, 1H), 6.41 (s, 0.7H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 158.9, 158.3, 137.7, 136.6, 129.8, 124.8, 121.5, 121.2, 119.0, 117.7, 104.1, 19.2 (h, J = 20.2 Hz), 13.5 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_{14}H_8D_6N_3$($M+H^+$)]: 230.1559, found: 230.1555.

3-Methyl-2,7-bis(methyl-*d*$_3$)-1-(pyrimidin-2-yl)-1H-indole (8c)



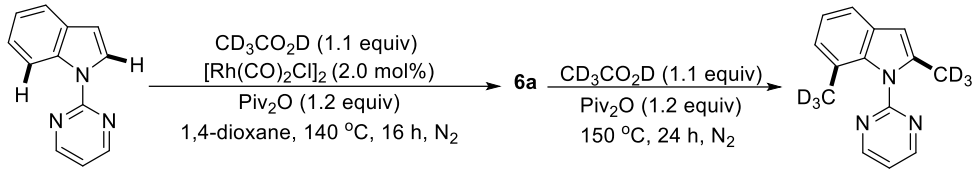
The title compound was purified by column chromatography using EtOAc/hexanes (1:3, v/v) and isolated as a yellow semi solid, 50.4 mg, 69%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.85 (d, *J* = 4.9 Hz, 2H), 7.39 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.27 (t, *J* = 9.7 Hz, 1H), 7.11 (t, *J* = 7.5 Hz, 1H), 6.96 (dd, *J* = 7.2, 1.2 Hz, 1H), 2.28 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 159.2, 158.3, 135.9, 133.3, 130.8, 124.9, 121.4, 120.8, 118.7, 116.0, 110.5, 19.2 (h, J = 20.2 Hz), 10.6 (h, J = 20.2 Hz)，8.9. HRMS (ESI) calcd. for [$C_{15}H_{10}D_6N_3$($M+H^+$)]: 244.1715, found: 244.1712.

5-Methyl-2,7-bis(methyl-*d*$_3$)-1-(pyrimidin-2-yl)-1H-indole (8d)



The title compound was purified by column chromatography using EtOAc/hexanes (1:3, v/v) and isolated as a yellow semi solid, 52.6 mg, 72%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (d, *J* = 4.9 Hz, 2H), 7.31 – 7.25 (m, 2H), 7.22 (dd, *J* = 1.8, 0.9 Hz, 1H), 6.80 (d, *J* = 1.6 Hz, 1H), 6.35 (s, 1H), 2.43 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 158.9, 158.3, 137.8, 135.0, 130.5, 130.2, 126.3, 121.2, 118.7, 117.6, 104.0, 21.2, 19.2 (h, J = 20.2 Hz), 13.4 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_{15}H_{10}D_6N_3$(M+H$^+$)]: 244.1715, found: 244.1712.

c) One-pot sequential C2,C7-di-trideuteriomethylation of indole



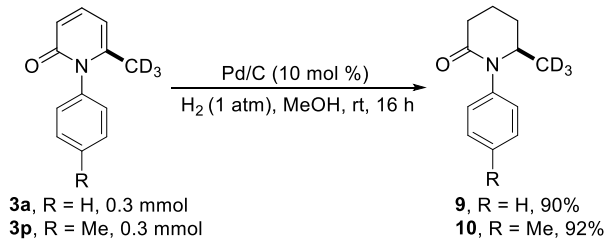
4a **8b**, 51%

To an oven-dried pressure tube with a stir bar were sequentially added **4a** (58.6 mg, 0.3 mmol), CD_3CO_2D (19.0 μL, 0.33 mmol), $[Rh(CO)_2Cl]_2$ (2.3 mg, 2.0 mol%), (*t*BuCO)$_2$O (73.0 μL, 0.36 mmol) and anhydrous 1,4-dioxane (3.0 mL, 0.1 M) at RT. The tube was sealed under an N_2 atmosphere and degassed for three times. The mixture was heated and stirred at 140 °C for 16 h in an oil bath. During the reaction period, the color of the reaction mixture changed from light yellow to brown. The tube was removed from the oil bath and cooled to room temperature. Next, the tube was transferred into the glovebox, was opened under an N_2 atmosphere and then CD_3CO_2D **2** (19.0 μL, 0.33 mmol) and (*t*BuCO)$_2$O (73.0 μL, 0.36 mmol) were sequentially added at RT. The tube was sealed under N_2, taken out of the glove box and degassed three times. The mixture was heated and stirred at 150 °C for 24 h in the oil bath, resulting in a brown solution. After the hearing period, the tube was removed from the oil bath and cooled to room temperature. The reaction vessel was opened to air, added to a separatory funnel, washed with saturated sodium bicarbonate solution (10 mL) and extracted with CH_2Cl_2 (5 mL × 3). The combined yellow organic layer was dried over Na_2SO_4, filtered, the volatile materials removed under reduced pressure, and the residue

was purified by column chromatography on silica gel using a mixture of ethyl acetate/hexanes (1:3, v/v) to give the pure product **8b** (35.1 mg, 51%).

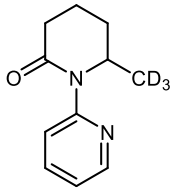
5. Synthetic applications

a) Hydrogenation of **3a** and **3p**



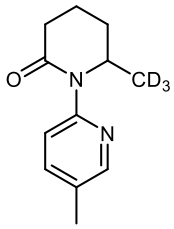
To a 10 mL round-bottomed flask charged with **3a** (56.8 mg, 0.3 mmol) or **3p** (61.0 mg, 0.3 mmol) was added to Pd/C (10 mol %, 42.6 mg (5 wt % Pd on charcoal)) and absolute methanol (2 mL) at RT. The flask was evacuated and refilled with hydrogen three times. The reaction mixture was stirred at room temperature under H_2 (1 atm) for 12 h, opened to air, filtered through a pad of celite and the resulting solution concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel using a mixture of ethyl acetate and hexanes (1/2, v/v) to give the target products as a yellow oil (**9**, 52.2 mg, 90%; **10,** 57.2 mg, 92%, respectively).

6-(Methyl-*d*$_3$)-1-(pyridin-2-yl)piperidin-2-one (9)



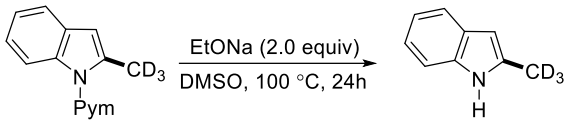
52.2 mg, 90%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 – 8.42 (m, 1H), 7.69 (td, *J* = 7.8, 1.9 Hz, 1H), 7.45 (d, *J* = 8.1 Hz, 1H), 7.13 (dd, *J* = 7.3, 4.9 Hz, 1H), 4.60 (t, *J* = 5.5 Hz, 1H), 2.65 – 2.44 (m, 2H), 2.09 (ddt, *J* = 13.4, 8.8, 4.0 Hz, 1H), 1.98 (ddtd, *J* = 13.2, 9.6, 6.6, 2.8 Hz, 1H), 1.83 (dtd, *J* = 13.3, 6.6, 3.1 Hz, 1H), 1.74 (dtd, *J* = 13.0, 7.5, 6.8, 3.1 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 170.7, 153.9, 148.5, 137.1, 123.5, 121.4, 52.5, 33.0, 30.2, 19.8 (h, J = 20.2 Hz), 17.9. HRMS (ESI) calcd. for [$C_{11}H_{12}D_3N_2O$ (M+H$^+$)]: 194.1367, found: 194.1364.

6-(Methyl-*d*$_3$)-1-(5-methylpyridin-2-yl)piperidin-2-one (10)



57.2 mg, 92%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.26 (d, *J* = 2.4 Hz, 1H), 7.47 (dd, *J* = 8.2, 2.4 Hz, 1H), 7.25 (s, 1H), 4.47 (t, *J* = 5.7 Hz, 1H), 2.49 (qt, *J* = 17.8, 6.7 Hz, 2H), 2.27 (s, 3H), 2.09 – 2.01 (m, 1H), 1.97 – 1.88 (m, 1H), 1.80 (ddh, *J* = 13.6, 6.5, 3.2 Hz, 1H), 1.69 (dddd, *J* = 13.5, 8.4, 5.8, 3.1 Hz, 1H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 169.6, 150.5, 147.7, 136.9, 130.1, 121.9, 51.6, 32.0, 29.2, 18.8 (h, J = 20.2 Hz), 17.0, 16.9. HRMS (ESI) calcd. for [$C_{12}H_{14}D_3N_2O$ (M+H$^+$)]: 208.1524, found: 208.1520.

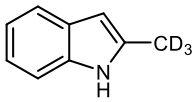
b) Removal of pyrimidinyl group



6a, 0.5 mmol **11**, 73%

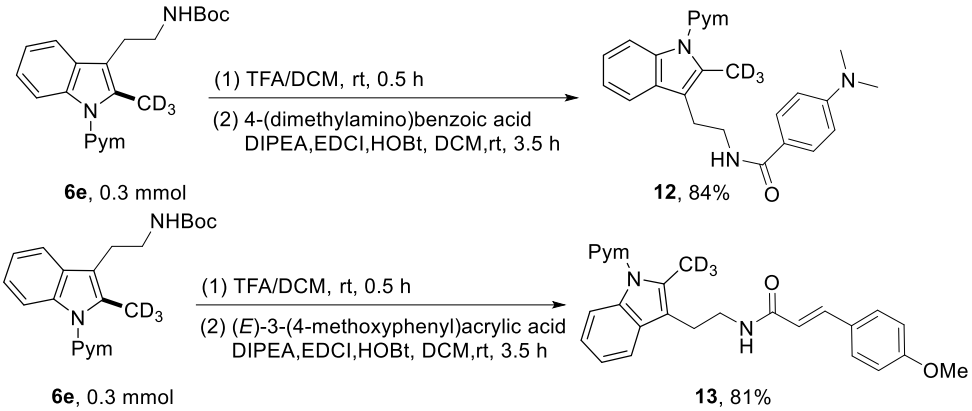
2-(Methyl-*d*$_3$)-1-(pyrimidin-2-yl)-1H-indole (**6a**; 106.1 mg, 0.5 mmol) was placed in a 25 mL two-necked reaction flask that was filled with nitrogen by using a standard Schlenk line. Freshly prepared EtONa (102.1 mg, 1.0 mmol) and dry DMSO (10.0 mL) were added at RT. After being degassed under nitrogen three times, the mixture was heated and stirred vigorously at 100 °C for 24 h. After the heating period, the reaction vessel was cooled to room temperature, the reaction mixture was poured into 15 mL water and extracted with CH_2Cl_2 (15 mL × 3). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue oil was purified by column chromatography on silica gel using a mixture of ethyl acetate/hexanes to give the purified product **11** as a light yellow semi solid in 73% yield.

2-(methyl-*d*$_3$)-1H-indole (11)



49.0 mg, 73%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.72 (dd, *J* = 7.4, 1.4 Hz, 1H), 7.44 (dd, *J* = 7.6, 6.2 Hz, 1H), 7.36 – 7.27 (m, 2H), 6.42 (d, *J* = 2.1 Hz, 1H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 136.1, 135.0, 129.1, 120.9, 120.8, 119.6, 110.2, 100.4, 13.0 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_9H_7D_3N$ (M+H$^+$)]: 135.0996, found: 135.0993.

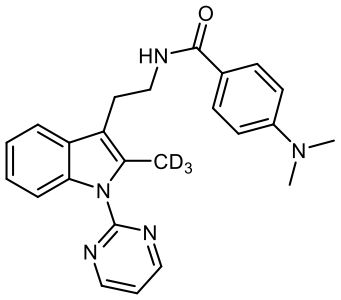
c) Synthesis of deuterated antitumor agent derivatives **12** and **13**



Step 1: To an oven-dried pressure tube with stir bar were sequentially added *tert*-butyl (2-(2-(methyl-d_3)-1-(pyrimidin-2-yl)-1H-indol-3-yl)ethyl)carbamate (**6e**; 106.6 mg, 0.3 mmol), TFA (0.67 mL, 9 mmol) and DCM (3 mL, 0.1M) at ambient temperature for 0.5 h. After stirring for the reaction period, 2 M aqueous NaOH was added until a pH of 7-8 was reached. Next, saturated aqueous $NaHCO_3$ (10 mL) was added to the resulting solution and it was extracted with DCM (3 x 5 mL). The combined organic phases were washed with brine, dried over Na_2SO_4, filtered and concentrate in vacuo to give a yellow semi solid.

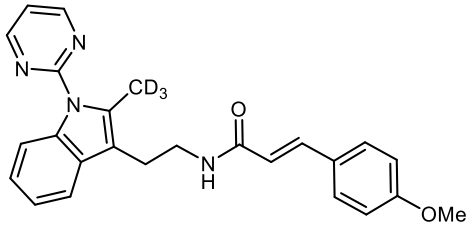
Step 2: To a 25 mL round bottom flask equipped with a stir bar was added 4-dimethylaminobenzoic acid (56.5 mg, 0.36 mmol) or (*E*)-3-(4-methoxyphenyl)acrylic acid (64.1 mg, 0.36 mmol), *N*,*N*-diisopropylethylamine (DIPEA, 116.3 mg, 0.9 mmol), 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDCI, 172.5 mg, 0.9 mmol) and 1-hydroxybenzotriazole (HOBT, 121.6 mg, 0.9 mmol) in DCM (20 mL) at ambient temperature. The resulting solution was stirred for 0.5 h. Next, the crude product of step 1 was added to the reaction vessel and the resulting solution stirred at room temperature for 3 h. After the reaction period, the contents of the flask was added to a separatory funnel and washed with water (10 mL) and extracted with DCM (3 x 10 mL). The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, and filtered. The volatile materials was removed under reduced pressure The crude product was purified by flash column chromatography on silica gel (eluent: hexanes : ethyl acetate = 1:1) to yield the purified product **12** (101.4 mg, 84% yield), **13** (101.0 mg, 81% yield)..

4-(Dimethylamino)-N-(2-(2-(methyl-*d*$_3$)-1-(pyrimidin-2-yl)-1H-indol-3-yl) ethyl) benzamide (12)



Yellow semi solid, 101.4 mg, 84%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 – 8.56 (m, 2H), 8.26 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.71 – 7.48 (m, 3H), 7.26 – 7.17 (m, 2H), 7.11 (dtd, *J* = 4.9, 2.8, 1.4 Hz, 1H), 6.60 (dd, *J* = 8.8, 1.6 Hz, 2H), 6.25 (q, *J* = 6.9, 6.1 Hz, 1H), 3.71 (q, *J* = 6.5 Hz, 2H), 3.09 (t, *J* = 6.7 Hz, 2H), 2.97 (d, *J* = 1.6 Hz, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 167.5, 158.3, 158.1, 152.3, 136.2, 134.3, 129.8, 128.4, 122.8, 121.8, 121.5, 117.9, 117.0, 114.3, 113.7, 111.1, 40.2, 40.1, 24.5, 12.9 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_{24}H_{23}D_3N_5O$ ($M+H^+$)]: 403.2320, found: 403.2316.

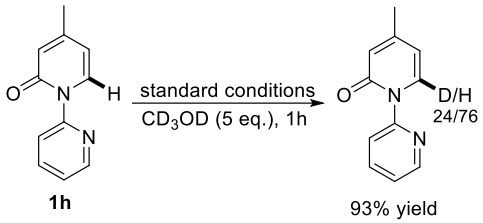
(*E*)-3-(4-Methoxyphenyl)-N-(2-(2-(methyl-d3)-1-(pyrimidin-2-yl)-1H-indol-3-yl)ethyl)acrylamide (13)



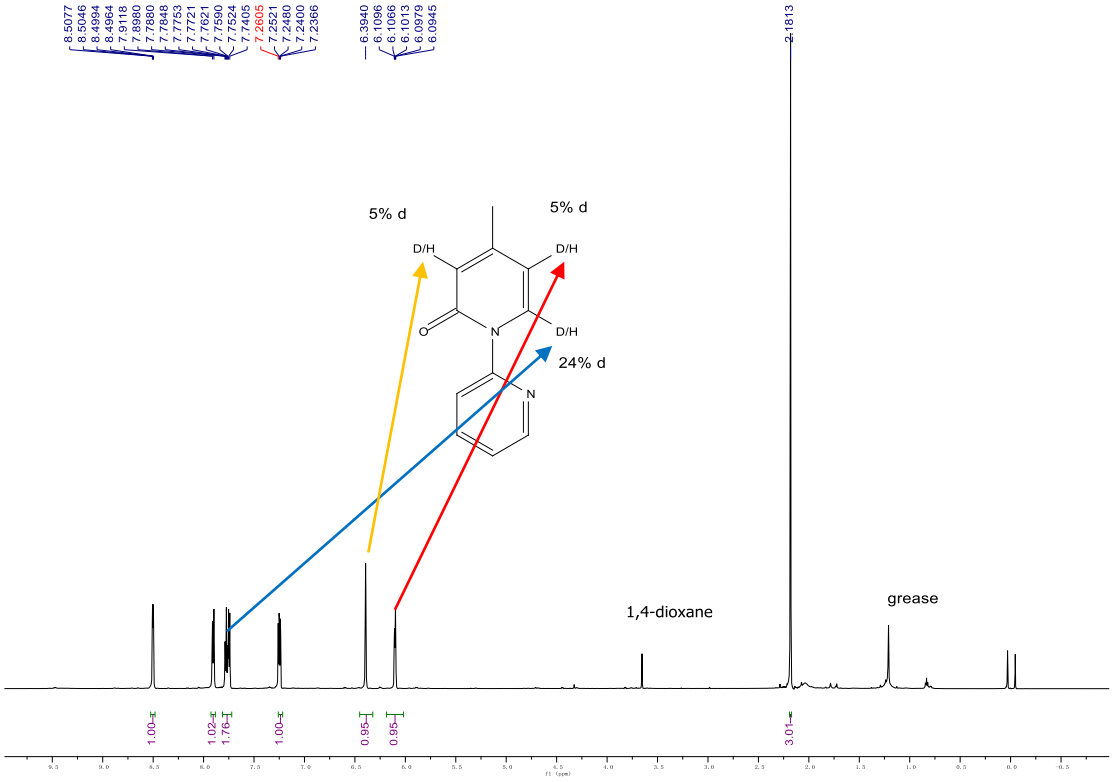
Yellow semi solid, 101.0 mg, 81%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (d, *J* = 4.8 Hz, 2H), 8.24 (d, *J* = 8.1 Hz, 1H), 7.67 – 7.46 (m, 2H), 7.37 (d, *J* = 8.7 Hz, 2H), 7.26 – 7.16 (m, 2H), 7.10 (t, *J* = 4.8 Hz, 1H), 6.82 (d, *J* = 8.7 Hz, 2H), 6.17 (d, *J* = 15.6 Hz, 1H), 5.98 (t, *J* = 5.8 Hz, 1H), 3.78 (s, 3H), 3.61 (q, *J* = 6.5 Hz, 2H), 3.03 (t, *J* = 6.7 Hz, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 166.5, 160.8, 158.3, 158.2, 140.4, 136.2, 134.3, 129.7, 129.4, 127.7, 122.8, 121.8, 118.6, 117.9, 117.1, 114.2, 114.1, 113.7, 55.4, 39.9, 24.4, 12.8 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_{25}H_{22}D_3N_4O_2$ ($M+H^+$)]: 416.2160, found: 416.2158.

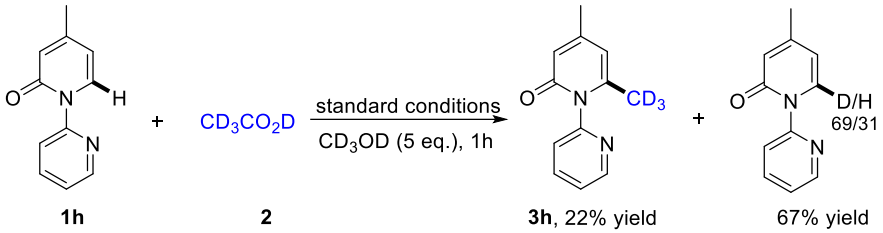
5. The mechanistic study

a) The H/D exchange experiments



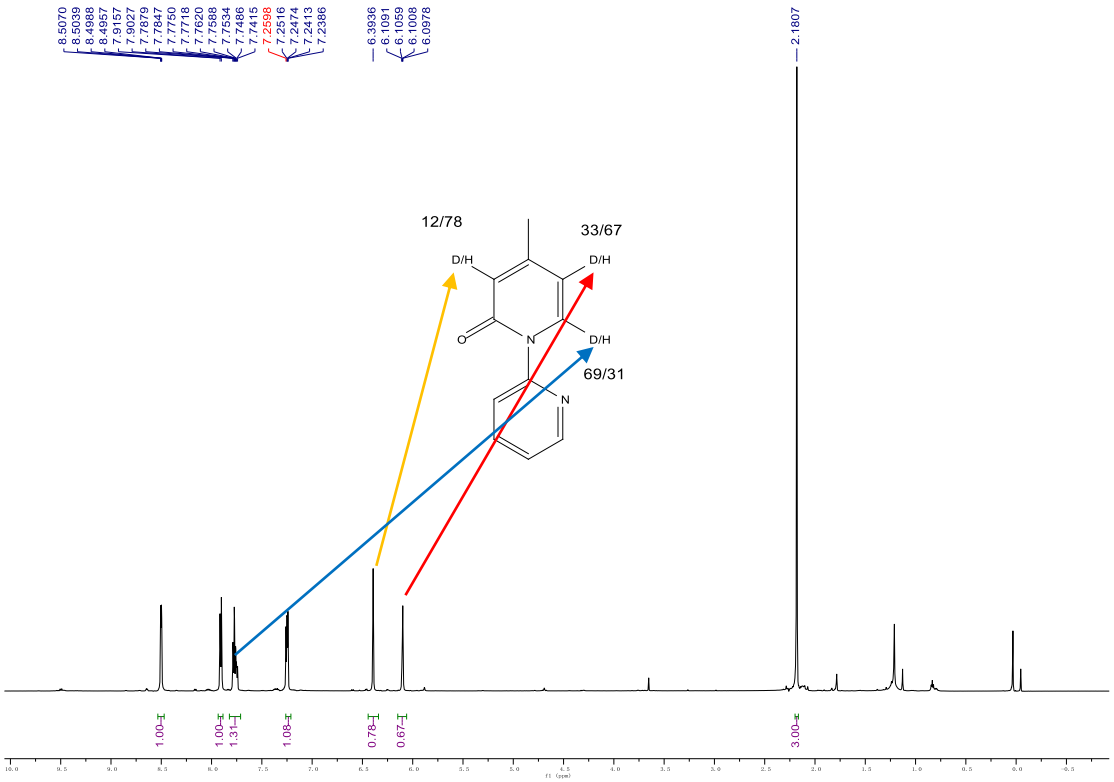
To an oven-dried pressure tube were sequentially added 4-methyl-2H-[1,2'-bipyridin]-2-one **1h** (55.8 mg, 0.3 mmol), $[Rh(CO)_2Cl]_2$ (2.3 mg, 2.0 mol%), CD_3OD (63.9 μL, 1.5 mmol), and 1,4-dioxane (3.0 mL). The tube was sealed under air atmosphere and the reaction mixture was heated and stirred vigorously at 140 °C for 1 h in an oil bath. The tube was then removed from the oil bath, cooled to room temperature and opened to air. The mixture was washed with water (5 mL) and extracted with CH_2Cl_2 (5 mL x 3). The combined organic layer was dried over Na_2SO_4 and filtered. After removal of the volatile materials under reduced pressure to give an inseparable mixture of **1h** (76%) and [D]-**1h** (24%). The ratio of H/D was determined on the basis of ^1H NMR analysis.





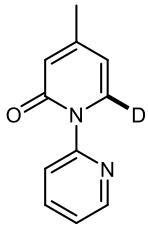
1h **2** **3h**, 22% yield 67% yield

To an oven-dried Schlenk tube with a stirring bar were sequentially added **1h** (55.8 mg, 0.3 mmol), $[Rh(CO)_2Cl]_2$ (2.3 mg, 2.0 mol%), CD_3CO_2D (19.0 μL, 0.33 mmol), Piv_2O (73.0 μL, 0.36 mmol), CD_3OD (63.9 μL, 1.5 mmol) and anhydrous 1,4-dioxane (3.0 mL, 0.1 M). The tube was sealed under air atmosphere and the reaction mixture was heated and stirred vigorously at 140 °C for 1 h in an oil bath. The tube was then removed from the oil bath, cooled to room temperature, opened to air and poured into a separatory funnel. Then the mixture was washed with saturated sodium bicarbonate solution (5 mL) and extracted with CH_2Cl_2 (5 mL x 3). The combined organic layer was dried over Na_2SO_4 and filtered. The volatile materials were removed by vacuum evaporation and the crude residue was purified by column chromatography on silica gel to recover the starting materials as an inseparable mixture of **1h** and [D]-**1h** (37.4 mg, 67%) and isolate the deuterium product **3h** (13.4 mg, 22%) by using ethyl acetate/hexanes = 1:1 and 2:1, respectively. The ratio of H/D was determined by ^1H NMR analysis to be 31/69.

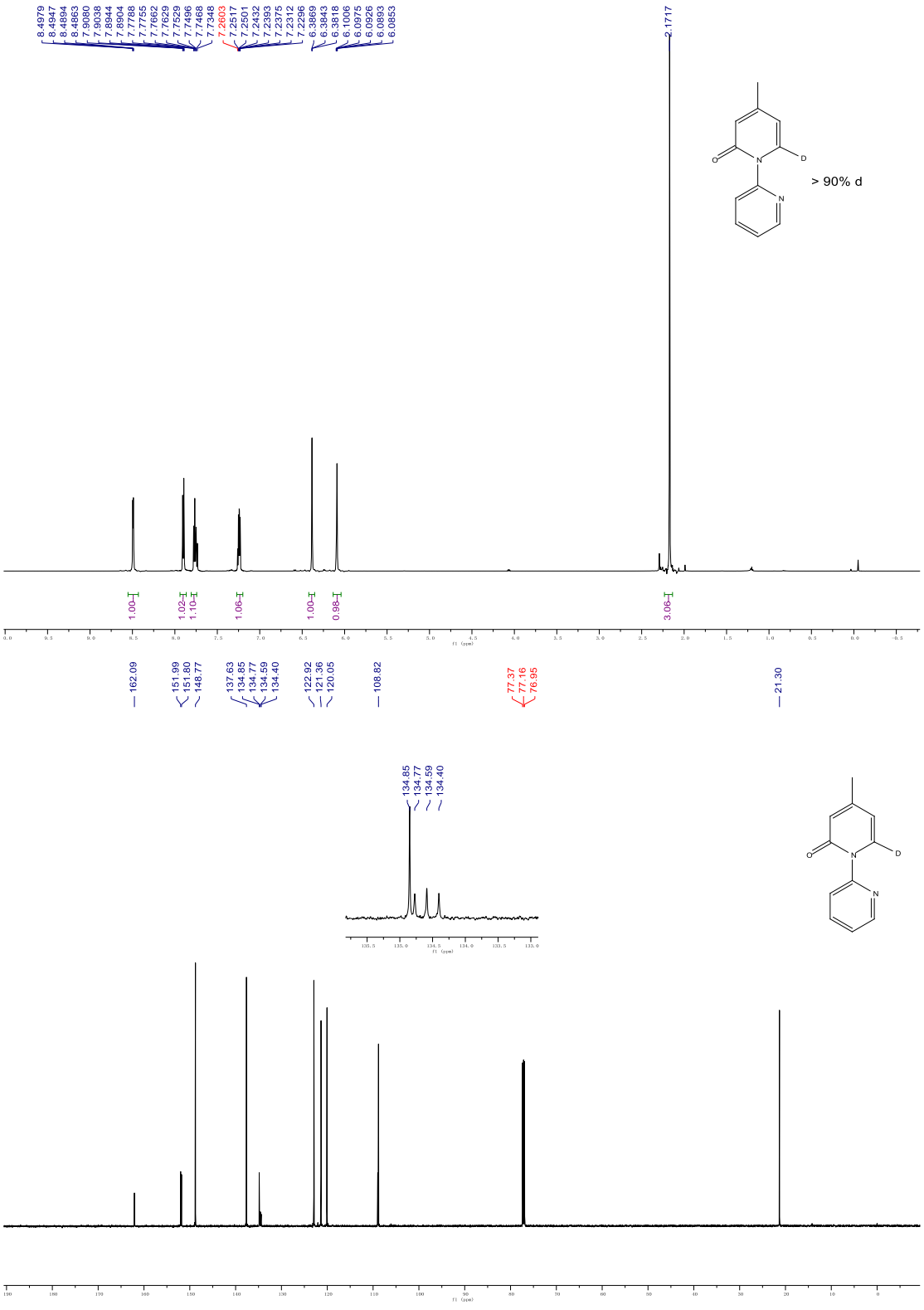


b) Characterization for 4-methyl-2H-[1,2'-bipyridin]-2-one-6-*d* (**1h-D**)

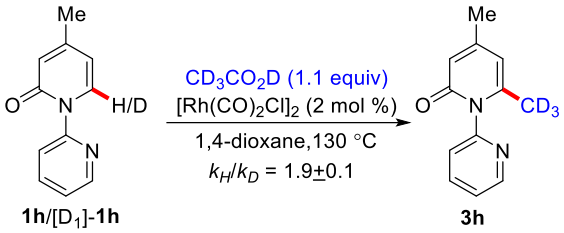
4-Methyl-2H-[1,2'-bipyridin]-2-one-6-d (1h-D)



The title compound was prepared according to the previous report,[4] purified by column chromatography using EtOAc/hexanes (1:1, v/v), and isolated as a yellow semi solid, 95.5 mg, 85%, 0.6 mmol; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.49 (dd, *J* = 5.1, 1.9 Hz, 1H), 7.90 (dd, *J* = 8.1, 2.5 Hz, 1H), 7.78 – 7.73 (m, 1H), 7.27 – 7.20 (m, 1H), 6.38 (t, *J* = 1.5 Hz, 1H), 6.09 (dd, *J* = 4.8, 1.9 Hz, 1H), 2.17 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 162.1, 152.0, 151.8, 148.8, 137.6, 134.8, 134.6 (t, J = 27.2 Hz), 122.9, 121.4, 120.1, 108.8, 21.3. HRMS (ESI) calcd. for [$C_{11}H_{10}DN_2O$ ($M+H^+$)]: 188.0929, found: 188.0923.

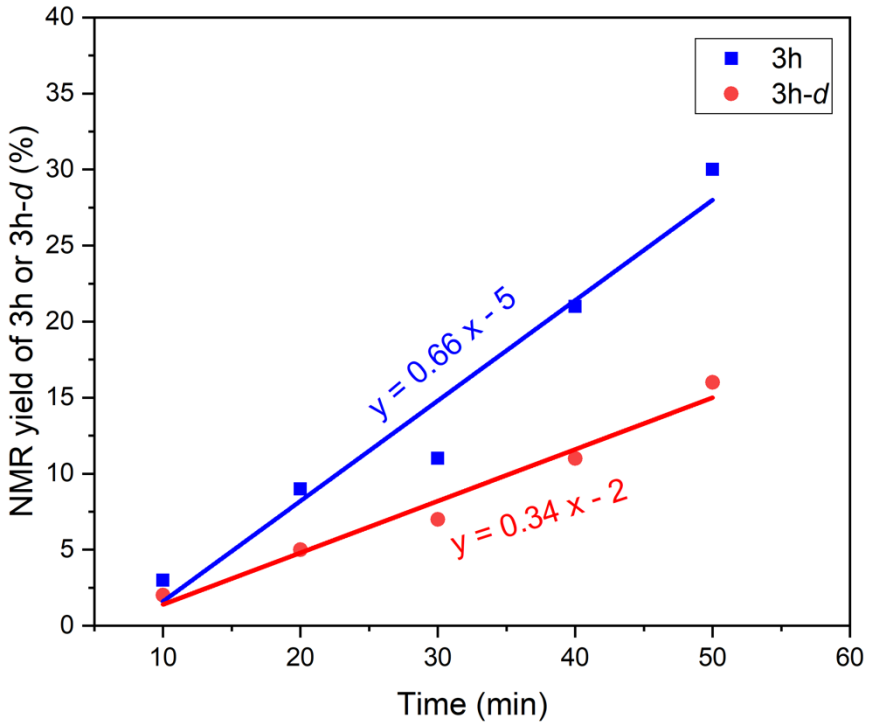


c) Kinetic isotope effect experiments



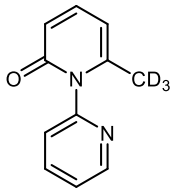
To an oven-dried pressure tube with a stirring bar were sequentially added **1h** (18.6 mg, 0.1 mmol), $[Rh(CO)_2Cl]_2$ (0.8 mg, 2.0 mol%), CD_3CO_2D (6.5 μL, 0.11 mmol), Piv_2O (24.5 μL, 0.12 mmol) and anhydrous 1,4-dioxane (1.0 mL) at RT under an N_2 atmosphere. In another pressure tube, deuterium-labeled compound $[D_1]$-**1h** (18.7 mg, 0.1 mmol) was used instead of **1h** under otherwise identical conditions. The two tubes were sealed, and the reaction mixtures were heated and stirred vigorously at 140 ℃ under N_2. An aliquot of each reaction mixture was taken at times of 10 min, 20 min, 30 min, 40 min and 50 min. The conversions were determined by ^{1}H NMR analysis of the crude reaction mixtures. A value of $k_H/k_D = 1.9 \pm 0.1$ was obtained.

Time (min)		10	20	30	40	50
NMR Yield (%)	**3h**	3	9	11	21	30
	3h-*d*	2	5	7	11	16



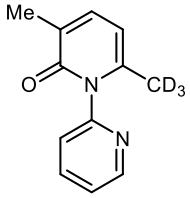
6. Characterization data for products

6-(Methyl-*d*$_3$)-2H-[1,2'-bipyridin]-2-one (3a)



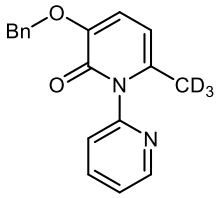
The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (2:1, v/v), and isolated as a yellow solid, m.p. = 102.3~105.6 °C, 51.1 mg, 90%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.65 (ddd, *J* = 4.9, 2.0, 0.9 Hz, 1H), 7.89 (td, *J* = 7.7, 1.9 Hz, 1H), 7.39 (ddd, *J* = 7.6, 4.9, 1.1 Hz, 1H), 7.36 – 7.28 (m, 2H), 6.52 (dd, *J* = 9.3, 1.2 Hz, 1H), 6.09 (dd, *J* = 6.8, 1.2 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 163.9, 152.1, 150.0, 145.8, 140.3, 138.8, 124.1, 123.6, 118.7, 106.3, 19.9 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_{11}H_8D_3N_2O$ ($M+H^+$)]: 190.1054, found: 190.1050.

3-Methyl-6-(methyl-*d*$_3$)-2H-[1,2'-bipyridin]-2-one (3b)



The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (2:1, v/v), and isolated as a yellow solid, m.p. = 107.1~110.4 °C, 54.9 mg, 90%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 – 8.59 (m, 1H), 7.87 (td, *J* = 7.7, 1.9 Hz, 1H), 7.42 – 7.28 (m, 2H), 7.18 (dd, *J* = 6.9, 1.2 Hz, 1H), 6.01 (d, *J* = 6.9 Hz, 1H), 2.11 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 164.1, 152.5, 149.8, 142.5, 138.5, 137.3, 127.3, 123.8, 123.6, 105.7, 19.6 (h, J = 20.2 Hz), 16.8. HRMS (ESI) calcd. for [$C_{12}H_{10}D_3N_2O$ ($M+H^+$)]: 204.1211, found: 204.1208.

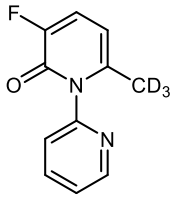
3-(Benzyloxy)-6-(methyl-*d*$_3$)-2H-[1,2'-bipyridin]-2-one (3c)



The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (2:1, v/v), and isolated as a yellow semi solid, 62.0 mg, 70%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (ddd, *J* = 4.9, 2.0, 0.9 Hz, 1H), 7.87 (td, *J* = 7.7, 1.9 Hz, 1H), 7.46 – 7.40 (m, 2H), 7.40 – 7.30 (m, 4H), 7.30 – 7.24 (m, 1H), 6.68 (d, *J* = 7.6 Hz, 1H), 5.91 (d, *J* = 7.5 Hz, 1H), 5.13 (s, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)

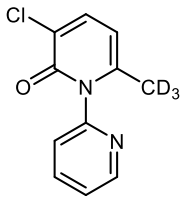
δ 159.5, 152.0, 149.8, 146.9, 138.6, 136.9, 136.7, 128.5, 127.8, 127.4, 124.0, 123.7, 118.1, 104.5, 71.0, 19.2 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_{18}H_{14}D_3N_2O_2$ ($M+H^+$)]: 296.1473, found: 296.1469.

3-Fluoro-6-(methyl-*d*$_3$)-2H-[1,2'-bipyridin]-2-one (3d)



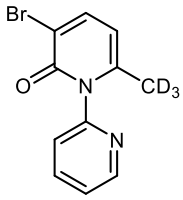
The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (2:1, v/v), and isolated as a yellow semi solid, 47.2 mg, 76%, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 – 8.55 (m, 1H), 7.89 (tt, *J* = 7.8, 1.5 Hz, 1H), 7.52 – 7.29 (m, 2H), 7.06 (ddd, *J* = 8.8, 7.6, 1.1 Hz, 1H), 5.98 (ddd, *J* = 7.7, 4.3, 1.0 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 157.5 (d, $J^2_{C\text{-}F}$ = 25.3 Hz), 152.2 (d, $J^1_{C\text{-}F}$ = 211.1 Hz), 151.1, 140.9, 139.1, 124.5, 123.5, 120.9 (d, $J^3_{C\text{-}F}$ = 17.2 Hz), 103.7, 19.5 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_{11}H_7D_3FN_2O$ ($M+H^+$)]: 208.0960, found: 208.0956.

3-Chloro-6-(methyl-*d*$_3$)-2H-[1,2'-bipyridin]-2-one (3e)



The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (3:1, v/v), and isolated as a yellow solid, m.p. = 117.3~119.4 °C, 54.4 mg, 81%, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (d, *J* = 4.6 Hz, 1H), 7.87 (t, *J* = 7.8 Hz, 1H), 7.47 (d, *J* = 7.5 Hz, 1H), 7.38 (t, *J* = 6.3 Hz, 1H), 7.30 (d, *J* = 8.0 Hz, 1H), 6.04 (d, *J* = 7.4 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 158.8, 150.6, 148.9, 143.6, 137.9, 137.1, 123.4, 122.7, 122.3, 104.6, 18.7 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_{11}H_7D_3ClN_2O$ ($M+H^+$)]: 224.0664, found: 224.0661.

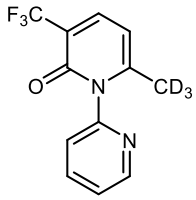
3-Bromo-6-(methyl-*d*$_3$)-2H-[1,2'-bipyridin]-2-one (3f)



The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (2:1, v/v), and isolated as a yellow semi solid, 65.9 mg, 82%, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 – 8.58 (m, 1H), 7.89 (td, *J* = 7.8, 1.9 Hz, 1H), 7.69 (d, *J*

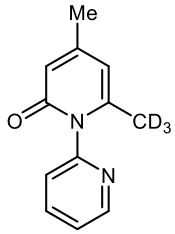
= 7.5 Hz, 1H), 7.47 – 7.29 (m, 2H), 6.02 (d, *J* = 7.5 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 159.9, 151.7, 149.9, 145.6, 142.0, 138.9, 124.4, 123.4, 113.7, 106.4, 19.8 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_{11}H_7D_3BrN_2O$ ($M+H^+$)]: 268.0159, found: 268.0156.

6-(Methyl-*d*$_3$)-3-(trifluoromethyl)-2H-[1,2'-bipyridin]-2-one (3g)



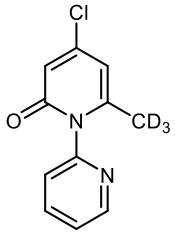
The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (2:1, v/v), and isolated as a yellow semi solid, 53.2 mg, 69%, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (ddd, *J* = 4.9, 1.9, 0.9 Hz, 1H), 7.91 (td, *J* = 7.7, 1.9 Hz, 1H), 7.72 (dt, *J* = 7.3, 0.9 Hz, 1H), 7.48 – 7.33 (m, 2H), 6.25 – 6.11 (m, 1H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 159.5, 150.9, 150.8, 150.1, 139.4 (q, $J^3_{C\text{-}F}$ = 5.0 Hz), 138.9, 126.8 (q, $J^1_{C\text{-}F}$ = 271.7 Hz), 124.5, 123.5, 118.9 (q, $J^2_{C\text{-}F}$ = 31.3 Hz), 104.6, 20.5 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_{12}H_7D_3F_3N_2O$ ($M+H^+$)]: 258.0928, found: 258.0925.

4-Methyl-6-(methyl-*d*$_3$)-2H-[1,2'-bipyridin]-2-one (3h)



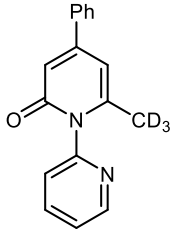
The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (2:1, v/v), and isolated as a yellow solid, m.p. = 109.3~111.9 °C, 50.6 mg, 83%, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (ddd, *J* = 5.0, 1.9, 0.9 Hz, 1H), 7.85 (td, *J* = 7.7, 1.9 Hz, 1H), 7.35 (ddd, *J* = 7.5, 4.9, 1.1 Hz, 1H), 7.30 (dt, *J* = 7.9, 1.0 Hz, 1H), 6.31 (dt, *J* = 1.8, 1.0 Hz, 1H), 5.93 (d, *J* = 1.7 Hz, 1H), 2.15 (s, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 163.8, 152.0, 151.8, 149.8, 144.2, 138.6, 123.9, 123.8, 116.9, 108.9, 21.4, 19.7 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_{12}H_{10}D_3N_2O$ ($M+H^+$)]: 204.1211, found: 204.1207.

4-Chloro-6-(methyl-*d*$_3$)-2H-[1,2'-bipyridin]-2-one (3i)



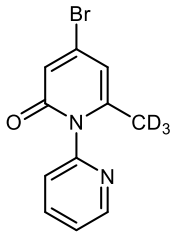
The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (2:1, v/v), and isolated as a yellow solid, m.p. = 114.3~117.1 °C, 53.7 mg, 80%, ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.65 (d, *J* = 4.7 Hz, 1H), 7.90 (tt, *J* = 7.7, 1.7 Hz, 1H), 7.41 (dd, *J* = 7.5, 5.0 Hz, 1H), 7.32 (d, *J* = 7.9 Hz, 1H), 6.57 (t, *J* = 1.7 Hz, 1H), 6.14 (t, *J* = 1.7 Hz, 1H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 162.7, 151.2, 150.0, 147.4, 146.2, 138.8, 124.3, 123.6, 117.1, 108.0, 19.8 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_{11}H_7D_3ClN_2O$ ($M+H^+$)]: 224.0664, found: 224.0661.

6-(Methyl-*d*$_3$)-4-phenyl-2H-[1,2'-bipyridin]-2-one (3j)



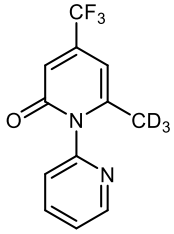
The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (2:1, v/v), and isolated as a yellow semi solid, 62.1 mg, 78%, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (ddd, *J* = 4.8, 1.9, 1.0 Hz, 1H), 7.90 (td, *J* = 7.7, 1.9 Hz, 1H), 7.63 – 7.58 (m, 2H), 7.47 – 7.36 (m, 5H), 6.74 (d, *J* = 1.9 Hz, 1H), 6.38 (d, *J* = 1.9 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 164.0, 152.3, 151.9, 150.0, 145.4, 138.7, 137.8, 129.5, 129.0, 126.8, 124.1, 123.7, 115.0, 106.1, 20.3 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_{17}H_{12}D_3N_2O$ ($M+H^+$)]: 266.1367, found: 266.1364.

4-Bromo-6-(methyl-*d*$_3$)-2H-[1,2'-bipyridin]-2-one (3k)



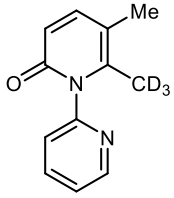
The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (2:1, v/v), and isolated as a yellow semi solid, 62.7 mg, 78%, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (ddd, *J* = 4.9, 1.9, 0.9 Hz, 1H), 7.90 (td, *J* = 7.7, 1.9 Hz, 1H), 7.46 – 7.28 (m, 2H), 6.78 (d, *J* = 2.0 Hz, 1H), 6.28 (d, *J* = 2.1 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 162.4, 151.2, 150.1, 145.9, 138.9, 136.6, 124.3, 123.5, 120.7, 110.6, 19.6 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_{11}H_7D_3BrN_2O$ ($M+H^+$)]: 268.0159, found: 268.0156.

6-(Methyl-*d*$_3$)-4-(trifluoromethyl)-2H-[1,2'-bipyridin]-2-one (3l)



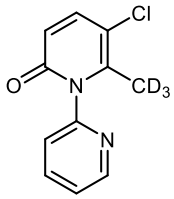
The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (2:1, v/v), and isolated as a yellow solid, m.p. = 147.3~151.0 °C, 54.8 mg, 71%, ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.65 (dd, *J* = 5.1, 1.9 Hz, 1H), 7.91 (td, *J* = 7.7, 1.9 Hz, 1H), 7.42 (ddd, *J* = 7.6, 4.9, 1.1 Hz, 1H), 7.33 (d, *J* = 7.9 Hz, 1H), 6.78 (d, *J* = 2.0 Hz, 1H), 6.22 (d, *J* = 1.9 Hz, 1H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 162.7, 151.1, 150.2, 148.1, 141.9 (q, $J^2_{C\text{-}F}$ = 33.2 Hz), 139.0, 124.9 (q, $J^1_{C\text{-}F}$ = 273.3 Hz), 124.5, 123.3, 116.3 (q, $J^3_{C\text{-}F}$ = 4.5 Hz), 101.3, 20.2 (h, J = 20.2 Hz). ^{19}F NMR (565 MHz, $CDCl_3$) δ -67.07. HRMS (ESI) calcd. for [$C_{12}H_7D_3F_3N_2O$ ($M+H^+$)]: 258.0928, found: 258.0924.

5-Methyl-6-(methyl-*d*$_3$)-2H-[1,2'-bipyridin]-2-one (3m)



The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (2:1, v/v), and isolated as a yellow solid, m.p. = 103.0~105.9 °C, 49.4 mg, 81%, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 – 8.57 (m, 1H), 7.86 (td, *J* = 7.7, 1.9 Hz, 1H), 7.41 – 7.33 (m, 1H), 7.29 (d, *J* = 7.9 Hz, 1H), 7.21 (d, *J* = 9.4 Hz, 1H), 6.44 (d, *J* = 9.4 Hz, 1H), 2.05 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 163.3, 152.6, 149.9, 144.0, 141.8, 138.8, 124.0, 123.7, 118.0, 112.8, 17.4, 16.5 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_{12}H_{10}D_3N_2O$ ($M+H^+$)]: 204.1211, found: 204.1208.

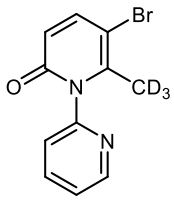
5-Chloro-6-(methyl-*d*$_3$)-2H-[1,2'-bipyridin]-2-one (3n)



The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (2:1, v/v), and isolated as a yellow solid, m.p. = 111.1~113.2 °C, 51.7 mg, 77%, ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.65 (d, *J* = 4.7 Hz, 1H), 7.90 (tt, *J* = 7.7, 1.7 Hz, 1H), 7.41 (dd, *J* = 7.5, 5.0 Hz, 1H), 7.32 (d, *J* = 7.9 Hz, 1H), 6.57 (t, *J* = 1.7 Hz, 1H), 6.14 (t, *J* = 1.7 Hz, 1H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 162.3, 151.9, 150.1,

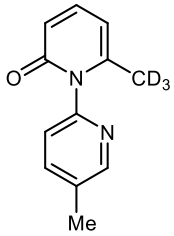
142.4, 141.6, 138.9, 124.3, 123.6, 119.6, 112.1, 17.3 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_{11}H_7D_3ClN_2O$ ($M+H^+$)]: 224.0664, found: 224.0661.

5-Bromo-6-(methyl-*d*$_3$)-2H-[1,2'-bipyridin]-2-one (3o)



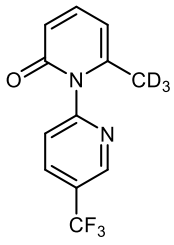
The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (2:1, v/v), and isolated as a yellow semi solid, 60.3 mg, 75%, ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.71 – 8.60 (m, 1H), 7.91 (td, *J* = 7.8, 1.9 Hz, 1H), 7.47 (d, *J* = 9.8 Hz, 1H), 7.41 (ddd, *J* = 7.6, 4.9, 1.0 Hz, 1H), 7.31 (dd, *J* = 7.9, 1.0 Hz, 1H), 6.45 (d, *J* = 9.7 Hz, 1H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 162.6, 152.1, 150.2, 144.0, 143.8, 139.0, 124.4, 123.5, 119.9, 100.0, 20.1 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_{11}H_7D_3BrN_2O$ ($M+H^+$)]: 268.0159, found: 268.0156.

5'-Methyl-6-(methyl-*d*$_3$)-2H-[1,2'-bipyridin]-2-one (3p)



The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (2:1, v/v), and isolated as a yellow solid, m.p. = 101.9~103.5 °C, 54.3 mg, 89%, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (dt, *J* = 2.4, 0.8 Hz, 1H), 7.68 (ddd, *J* = 8.0, 2.4, 0.9 Hz, 1H), 7.29 (dd, *J* = 9.3, 6.8 Hz, 1H), 7.22 (d, *J* = 7.9 Hz, 1H), 6.51 (dd, *J* = 9.3, 1.3 Hz, 1H), 6.07 (dd, *J* = 6.8, 1.3 Hz, 1H), 2.40 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 164.0, 150.2, 149.5, 145.9, 140.1, 139.3, 134.0, 122.7, 118.5, 106.2, 19.9 (h, J = 20.2 Hz), 18.2. HRMS (ESI) calcd. for [$C_{12}H_{10}D_3N_2O$ ($M+H^+$)]: 204.1211, found: 204.1207.

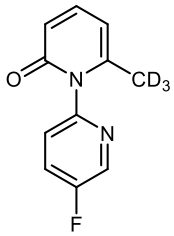
6-(Methyl-*d*$_3$)-5'-(trifluoromethyl)-2H-[1,2'-bipyridin]-2-one (3q)



The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (2:1, v/v), and isolated as a yellow semi solid, 65.6 mg, 85%, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.92 (dt, *J* = 2.5, 0.9 Hz, 1H), 8.13 (dd, *J* = 8.2, 2.4 Hz, 1H),

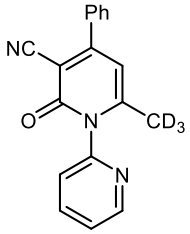
7.52 (d, *J* = 8.2 Hz, 1H), 7.34 (dd, *J* = 9.4, 6.8 Hz, 1H), 6.52 (dd, *J* = 9.3, 1.2 Hz, 1H), 6.12 (dd, *J* = 6.8, 1.2 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 163.6, 154.9, 147.1 (q, $J^3_{C\text{-}F}$ = 4.0 Hz), 145.1, 140.6, 136.1 (q, $J^3_{C\text{-}F}$ = 4.0 Hz), 127.5 (q, $J^2_{C\text{-}F}$ = 33.3 Hz), 127.1 (q, $J^1_{C\text{-}F}$ = 273.7 Hz), 124.0, 118.7, 106.7, 19.9 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_{12}H_7D_3F_3N_2O$ ($M+H^+$)]: 258.0928, found: 258.0925.

5'-Fluoro-6-(methyl-*d*$_3$)-2H-[1,2'-bipyridin]-2-one (3r)



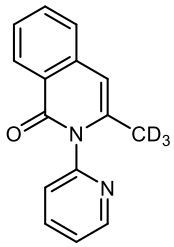
The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (2:1, v/v), and isolated as a yellow semi solid, 49.7 mg, 80%, ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.49 (d, *J* = 3.0 Hz, 1H), 7.61 (ddd, *J* = 8.7, 7.4, 3.0 Hz, 1H), 7.36 (dd, *J* = 8.7, 3.9 Hz, 1H), 7.32 (dd, *J* = 9.3, 6.8 Hz, 1H), 6.52 (dd, *J* = 9.3, 1.3 Hz, 1H), 6.10 (dd, *J* = 6.9, 1.2 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 163.9, 160.0 (d, $J^1_{C\text{-}F}$ = 258.2 Hz), 147.7, 145.7, 140.4, 138.1 (d, $J^2_{C\text{-}F}$ = 25.6 Hz), 125.8 (d, $J^2_{C\text{-}F}$ = 21.1 Hz), 124.8 (d, $J^3_{C\text{-}F}$ = 6.0 Hz), 118.7, 106.4, 19.9 (h, J = 20.2 Hz). ^{19}F NMR (565 MHz, $CDCl_3$) δ -126.18. HRMS (ESI) calcd. for [$C_{11}H_7D_3FN_2O$ ($M+H^+$)]: 208.0960, found: 208.0957.

6-(Methyl-*d*$_3$)-2-oxo-4-phenyl-2H-[1,2'-bipyridine]-3-carbonitrile (3s)



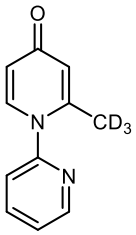
The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (2:1, v/v), and isolated as a yellow semi solid, 72.3 mg, 83%, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (ddd, *J* = 4.9, 1.9, 0.9 Hz, 1H), 7.93 (td, *J* = 7.7, 1.9 Hz, 1H), 7.69 – 7.60 (m, 2H), 7.56 – 7.36 (m, 5H), 6.31 (s, 1H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 161.5, 160.0, 150.9, 150.4, 150.1, 139.1, 135.8, 130.7, 129.0, 128.0, 124.8, 123.4, 115.6, 108.3, 100.3, 20.7 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_{18}H_{11}D_3N_3O$ ($M+H^+$)]: 291.1320, found: 291.1316.

3-(Methyl-*d*$_3$)-2-(pyridin-2-yl)isoquinolin-1(2H)-one (3t)



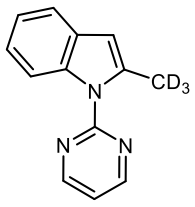
The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (2:1, v/v), and isolated as a yellow solid, m.p. = 121.0~123.4 °C, 46.7 mg, 65%, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (ddd, *J* = 4.9, 2.0, 0.9 Hz, 1H), 8.36 (ddd, *J* = 8.1, 1.4, 0.7 Hz, 1H), 7.91 (td, *J* = 7.7, 2.0 Hz, 1H), 7.63 (ddd, *J* = 8.3, 7.1, 1.4 Hz, 1H), 7.50 – 7.36 (m, 4H), 6.45 – 6.38 (m, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 163.5, 152.4, 149.8, 138.6, 138.5, 137.3, 132.8, 128.0, 126.2, 125.3, 124.9, 124.1, 123.8, 105.8, 19.9 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_{15}H_{10}D_3N_2O$ ($M+H^+$)]: 240.1211, found: 240.1207.

2-(Methyl-*d*$_3$)-4H-[1,2'-bipyridin]-4-one (3u)



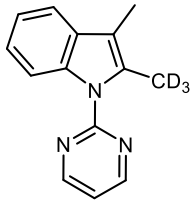
The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (2:1, v/v), and isolated as a yellow semi solid, 38.6 mg, 68%, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (ddd, *J* = 5.0, 2.0, 1.0 Hz, 1H), 7.94 – 7.83 (m, 1H), 7.38 (ddd, *J* = 7.4, 4.9, 1.0 Hz, 1H), 7.36 – 7.27 (m, 2H), 6.50 (dt, *J* = 9.3, 1.1 Hz, 1H), 6.08 (dt, *J* = 6.8, 1.1 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 163.8, 152.0, 149.9, 149.9, 145.7, 140.2, 138.7, 124.0, 123.6, 118.6, 106.2, 19.9 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_{11}H_8D_3N_2O$ ($M+H^+$)]: 190.1054, found: 190.1050.

2-(Methyl-*d*$_3$)-1-(pyrimidin-2-yl)-1H-indole (6a)



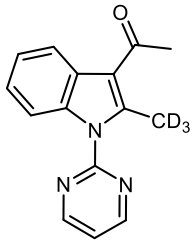
The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (1:4, v/v), and isolated as a yellow solid, m.p. = 112.0~113.9 °C, 57.3 mg, 90%, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, *J* = 4.8 Hz, 2H), 8.34 (dd, *J* = 8.1, 1.3 Hz, 1H), 7.61 – 7.51 (m, 1H), 7.29 – 7.21 (m, 2H), 7.10 (t, *J* = 4.8 Hz, 1H), 6.47 (s, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 158.4, 158.0, 137.7, 136.9, 129.5, 122.4, 121.8, 119.5, 116.9, 114.1, 106.7, 15.9 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_{13}H_9D_3N_3$ ($M+H^+$)]: 213.1214, found: 213.1210.

3-Methyl-2-(methyl-*d*$_3$)-1-(pyrimidin-2-yl)-1H-indole (6b)



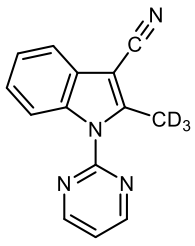
The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (1:4, v/v), and isolated as a yellow semi solid, 58.4 mg, 86%, ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.76 (d, *J* = 4.7 Hz, 2H), 8.29 (dd, *J* = 7.2, 1.8 Hz, 1H), 7.51 (dd, *J* = 7.5, 1.8 Hz, 1H), 7.23 (pd, *J* = 7.1, 1.6 Hz, 2H), 7.09 (t, *J* = 4.8 Hz, 1H), 2.30 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 158.5, 158.0, 136.1, 132.9, 130.7, 122.5, 121.4, 117.8, 116.5, 113.6, 112.8, 12.9 (h, J = 20.2 Hz), 8.9. HRMS (ESI) calcd. for [$C_{14}H_{11}D_3N_3$ (M+H$^+$)]: 227.1371, found: 227.1368.

1-(2-(Methyl-*d*$_3$)-1-(pyrimidin-2-yl)-1H-indol-3-yl)ethan-1-one (6c)



The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (1:4, v/v), and isolated as a yellow semi solid, 61.8 mg, 81%, ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.89 (d, *J* = 4.8 Hz, 2H), 8.06 (d, *J* = 7.9 Hz, 1H), 7.86 (d, *J* = 8.2 Hz, 1H), 7.36 – 7.28 (m, 2H), 7.28 – 7.24 (m, 1H), 2.73 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 195.5, 158.7, 157.1, 144.3, 136.1, 126.9, 123.3, 123.1, 120.7, 119.1, 117.9, 112.5, 32.0, 14.3 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_{15}H_{11}D_3N_3O$ (M+H$^+$)]: 255.1320, found: 255.1317.

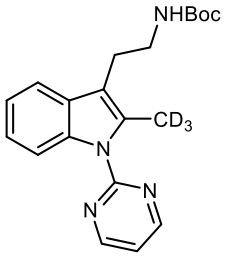
2-(Methyl-*d*$_3$)-1-(pyrimidin-2-yl)-1H-indole-3-carbonitrile (6d)



The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (1:4, v/v), and isolated as a yellow semi solid, 57.7 mg, 81%, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (d, *J* = 4.7 Hz, 2H), 8.28 – 8.14 (m, 1H), 7.74 – 7.62 (m, 1H), 7.32 (q, *J* = 5.4, 5.0 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 157.4, 156.2, 145.8, 134.6, 126.2, 123.4, 122.5, 117.7, 114.7, 113.4, 90.2, 13.9 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_{14}H_8D_3N_4$ (M+H$^+$)]: 238.1167, found:

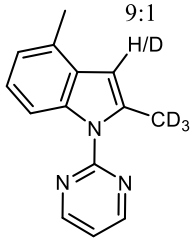
238.1164.

tert-Butyl (2-(2-(methyl-d_3)-1-(pyrimidin-2-yl)-1H-indol-3-yl)ethyl)carbamate (6e)



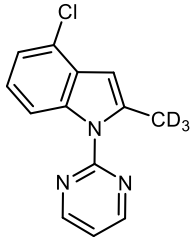
The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (1:4, v/v), and isolated as a yellow solid, m.p. = 102.0~104.1 °C, 51.2 mg, 48%, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (d, J = 4.8 Hz, 2H), 8.31 – 8.18 (m, 1H), 7.59 – 7.46 (m, 1H), 7.26 – 7.16 (m, 2H), 7.13 (t, J = 4.8 Hz, 1H), 4.65 (s, 1H), 3.40 (t, J = 6.5 Hz, 2H), 2.97 (t, J = 6.8 Hz, 2H), 1.45 (s, 9H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 158.3, 158.1, 156.1, 136.2, 134.2, 129.7, 122.7, 121.7, 117.8, 117.0, 114.1, 113.6, 79.1, 40.7, 28.5, 24.7, 12.8 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_{20}H_{22}D_3N_4O_2$ ($M+H^+$)]: 356.2160, found: 356.2157.

4-Methyl-2-(methyl-d_3)-1-(pyrimidin-2-yl)-1H-indole (6f)



The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (1:4, v/v), and isolated as a yellow semi solid, 59.1 mg, 87%, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 – 8.68 (m, 2H), 8.14 (d, J = 8.4 Hz, 1H), 7.20 – 7.08 (m, 2H), 7.01 (d, J = 7.2 Hz, 0.9H), 6.49 (s, 1H), 2.55 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 158.5, 158.1, 137.1, 136.6, 129.0, 128.8, 122.4, 122.2, 116.9, 111.6, 105.1, 18.6, 16.0 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_{14}H_{11}D_3N_3$ ($M+H^+$)]: 227.1371, found: 227.1366.

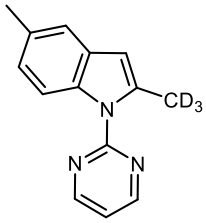
4-Chloro-2-(methyl-d_3)-1-(pyrimidin-2-yl)-1H-indole (6g)



The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (1:4, v/v), and isolated as a yellow semi solid, 62.9 mg, 85%, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (dd, J = 4.8, 1.6 Hz, 2H), 8.27 – 8.14 (m, 1H), 7.20 (dq, J = 7.8, 1.0 Hz, 1H), 7.17 – 7.07 (m, 2H), 6.57 (d, J = 1.6 Hz, 1H).

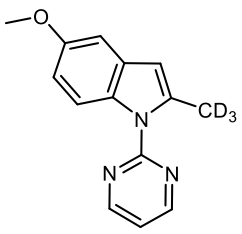
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 158.2, 158.1, 138.7, 137.5, 128.1, 124.6, 122.9, 121.5, 117.4, 112.7, 104.7, 16.0 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_{13}H_8D_3ClN_3$ ($M+H^+$)]: 247.0824, found: 247.0820.

5-Methyl-2-(methyl-*d*$_3$)-1-(pyrimidin-2-yl)-1H-indole (6h)



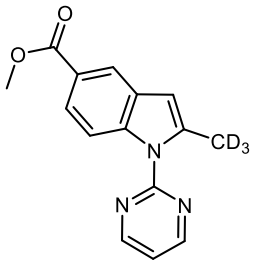
The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (1:4, v/v), and isolated as a yellow semi solid, 57.7 mg, 85%, ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.75 (d, *J* = 4.8 Hz, 2H), 8.24 (d, *J* = 8.4 Hz, 1H), 7.32 (s, 1H), 7.13 – 7.00 (m, 2H), 6.38 (s, 1H), 2.47 (s, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 158.5, 157.9, 137.8, 135.2, 131.1, 129.8, 123.7, 119.4, 116.6, 113.9, 106.6, 21.3, 16.1 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_{14}H_{11}D_3N_3$ ($M+H^+$)]: 227.1371, found: 227.1367.

5-Methoxy-2-(methyl-*d*$_3$)-1-(pyrimidin-2-yl)-1H-indole (6i)



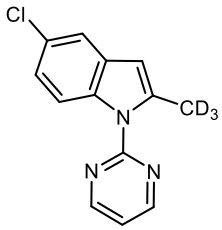
The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (1:4, v/v), and isolated as a yellow semi solid, 59.6 mg, 82%, ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.71 (d, *J* = 4.6 Hz, 2H), 8.29 (d, *J* = 9.0 Hz, 1H), 7.07 – 6.99 (m, 2H), 6.88 (dt, *J* = 9.0, 1.8 Hz, 1H), 6.38 (s, 1H), 3.88 (s, 3H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 158.4, 157.9, 155.4, 138.5, 131.8, 130.3, 116.6, 115.3, 111.1, 106.8, 102.2, 55.7, 16.3 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_{14}H_{11}D_3N_3O$ ($M+H^+$)]: 243.1320, found: 243.1317.

Methyl 2-(methyl-*d*$_3$)-1-(pyrimidin-2-yl)-1H-indole-5-carboxylate (6j)



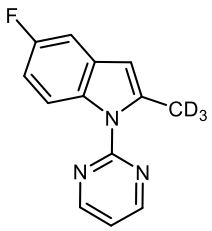
The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (1:4, v/v), and isolated as a yellow semi solid, 64.1 mg, 79%, ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.73 (dd, *J* = 4.8, 1.1 Hz, 2H), 8.33 – 8.17 (m, 2H), 7.91 (dt, *J* = 8.7, 1.5 Hz, 1H), 7.10 (td, *J* = 4.8, 1.1 Hz, 1H), 6.47 (s, 1H), 3.92 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 167.9, 158.1, 158.0, 139.5, 139.3, 129.1, 123.7, 123.6, 121.9, 117.5, 113.6, 107.0, 51.8, 15.8 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_{15}H_{11}D_3N_3O_2$ ($M+H^+$)]: 271.1269, found: 271.1266.

5-Chloro-2-(methyl-*d*$_3$)-1-(pyrimidin-2-yl)-1H-indole (6k)



The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (1:4, v/v), and isolated as a yellow semi solid, 59.9 mg, 81%, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (d, *J* = 4.8 Hz, 2H), 8.25 (d, *J* = 8.9 Hz, 1H), 7.47 (d, *J* = 2.1 Hz, 1H), 7.23 – 7.03 (m, 2H), 6.36 (s, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 158.1, 158.1, 139.3, 135.2, 130.6, 127.2, 122.3, 118.9, 117.2, 115.3, 106.1, 16.1 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_{13}H_8D_3ClN_3$ ($M+H^+$)]: 247.0824, found: 247.0820.

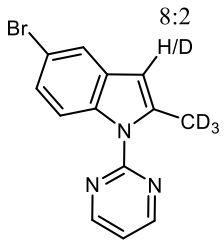
5-Fluoro-2-(methyl-*d*$_3$)-1-(pyrimidin-2-yl)-1H-indole (6l)



The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (1:4, v/v), and isolated as a yellow semi solid, 58.0 mg, 84%, ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.74 (d, *J* = 4.8 Hz, 2H), 8.29 (dd, *J* = 9.1, 4.7 Hz, 1H), 7.24 – 7.05 (m, 2H), 6.96 (td, *J* = 9.1, 2.7 Hz, 1H), 6.39 (s, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 158.8 (d, $J^1_{C\text{-}F}$ = 212.9 Hz), 156.9, 138.5, 132.1, 129.2, 129.1, 115.9, 114.1 (d, $J^3_{C\text{-}F}$ = 8.3 Hz), 108.9 (d, $J^2_{C\text{-}F}$ = 23.9 Hz), 105.5, 103.7 (d, $J^2_{C\text{-}F}$ = 23.9 Hz), 15.1 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_{13}H_8D_3FN_3$

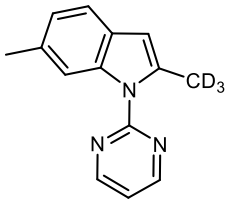
(M+H$^+$)]: 231.1120, found: 231.1117.

5-Bromo-2-(methyl-*d*$_3$)-1-(pyrimidin-2-yl)-1H-indole (6m)



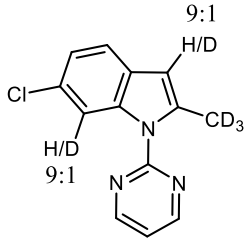
The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (1:4, v/v), and isolated as a yellow semi solid, 71.6 mg, 82%, ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.75 (d, *J* = 4.8 Hz, 2H), 8.20 (d, *J* = 8.8 Hz, 1H), 7.62 (d, *J* = 2.1 Hz, 1H), 7.29 (dd, *J* = 8.9, 2.1 Hz, 1H), 7.12 (t, *J* = 4.8 Hz, 1H), 6.36 (s, 0.8H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 157.0, 157.0, 138.1, 134.4, 130.1, 123.9, 120.9, 116.1, 114.6, 113.9, 104.9, 15.0 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_{13}H_8D_3BrN_3$ (M+H$^+$)]: 291.0319, found: 291.0316.

6-Methyl-2-(methyl-*d*$_3$)-1-(pyrimidin-2-yl)-1H-indole (6n)



The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (1:4, v/v), and isolated as a yellow semi solid, 56.3 mg, 83%, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (d, *J* = 4.8 Hz, 2H), 8.11 (d, *J* = 1.5 Hz, 1H), 7.40 (d, *J* = 7.9 Hz, 1H), 7.11 (t, *J* = 4.8 Hz, 1H), 7.03 (dd, *J* = 7.9, 1.4 Hz, 1H), 6.39 (s, 1H), 2.50 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 158.4, 158.0, 137.2, 137.0, 132.1, 127.2, 123.3, 119.1, 116.8, 114.0, 106.5, 22.0, 15.8 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_{14}H_{11}D_3N_3$ (M+H$^+$)]: 227.1371, found: 227.1367.

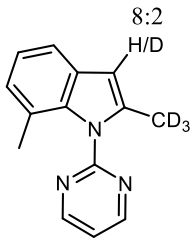
6-Chloro-2-(methyl-*d*$_3$)-1-(pyrimidin-2-yl)-1H-indole (6o)



The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (1:4, v/v), and isolated as a yellow semi solid, 56.2 mg, 76%, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, *J* = 4.8 Hz, 2H), 8.41 – 8.33 (m, 0.9H), 7.40 (d, *J* = 8.3 Hz, 1H), 7.18 – 7.12 (m, 2H), 6.40 (s, 0.9H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 158.3, 158.2, 138.7, 137.2, 128.3, 128.1, 122.4,

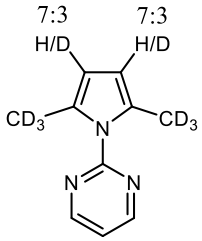
120.2, 117.3, 114.5, 106.6, 16.2 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_{13}H_8D_3ClN_3$ ($M+H^+$)]: 247.0824, found: 247.0820.

7-Methyl-2-(methyl-*d*$_3$)-1-(pyrimidin-2-yl)-1H-indole (6p)



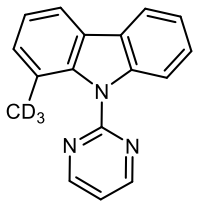
The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (1:4, v/v), and isolated as a yellow semi solid, 52.3 mg, 77%, ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.83 (d, *J* = 4.9 Hz, 2H), 7.46 (d, *J* = 7.8 Hz, 1H), 7.21 (t, *J* = 4.9 Hz, 1H), 7.12 (t, *J* = 7.5 Hz, 1H), 6.99 (d, *J* = 7.2 Hz, 1H), 6.45 (s, 0.8H), 2.01 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 158.8, 158.4, 137.7, 136.6, 129.8, 124.8, 121.7, 121.3, 119.2, 117.8, 104.1, 20.1, 13.3 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_{14}H_{11}D_3N_3$ ($M+H^+$)]: 227.1371, found: 227.1367.

2-(2,5-Bis(methyl-*d*$_3$)-1H-pyrrol-1-yl)pyrimidine (7a)



The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (1:3, v/v), and isolated as a yellow oil, 26.3 mg, 49%, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, *J* = 4.8 Hz, 2H), 7.17 (t, *J* = 4.8 Hz, 1H), 5.90 (s, 1.4H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 158.1, 129.7, 117.9, 108.7, 108.6, 13.9 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_{10}H_6D_6N_3$ ($M+H^+$)]: 180.1402, found: 180.1396.

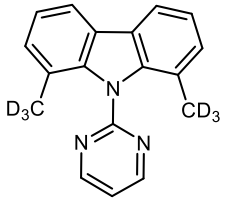
1-(Methyl-*d*$_3$)-9-(pyrimidin-2-yl)-9H-carbazole (7b)



The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (1:5, v/v), and isolated as a yellow semi solid, 56.7 mg, 72%, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.83 (d, *J* = 4.8 Hz, 2H), 8.10 – 7.98 (m, 2H), 7.92 (dd, *J* = 6.4, 2.6 Hz, 1H), 7.38 (ddd, *J* = 8.4, 7.2, 1.4 Hz, 1H), 7.32 – 7.27 (m, 1H), 7.25 – 7.20 (m, 2H), 7.17 (t, *J* = 4.8 Hz, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 158.7, 158.4,

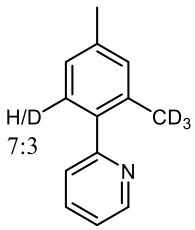
141.3, 139.1, 129.4, 126.4, 126.4, 125.6, 123.9, 122.3, 122.0, 119.9, 117.8, 117.7, 112.3, 20.5 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_{17}H_{11}D_3N_3$ ($M+H^+$)]: 263.1371, found: 263.1368.

1,8-Bis(methyl-*d*$_3$)-9-(pyrimidin-2-yl)-9H-carbazole (7c)



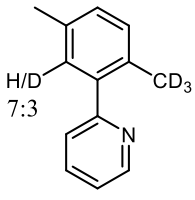
The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (1:2, v/v), and isolated as a yellow semi solid, 55.3 mg, 66%, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.93 (d, *J* = 4.9 Hz, 2H), 7.97 (dd, *J* = 7.7, 1.4 Hz, 2H), 7.46 (t, *J* = 4.9 Hz, 1H), 7.19 (t, *J* = 7.5 Hz, 2H), 7.12 (dd, *J* = 7.3, 1.4 Hz, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 162.0, 158.4, 140.7, 128.8, 124.7, 121.2, 120.8, 120.7, 118.1, 18.0 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_{18}H_{10}D_6N_3$ ($M+H^+$)]: 280.1715, found: 280.1712.

2-(4-Methyl-2-(methyl-*d*$_3$)phenyl)pyridine (7d)



The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (1:2, v/v), and isolated as a light yellow oil, 26.8 mg, 48%, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (ddd, *J* = 4.9, 1.9, 1.0 Hz, 1H), 7.72 (td, *J* = 7.7, 1.9 Hz, 1H), 7.38 (dt, *J* = 7.9, 1.1 Hz, 1H), 7.31 (d, *J* = 7.5 Hz, 0.7H), 7.22 (ddd, *J* = 7.6, 4.9, 1.2 Hz, 1H), 7.09 (d, *J* = 7.9 Hz, 2H), 2.37 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 160.1, 149.2, 138.0, 137.7, 136.0, 135.4, 131.5, 129.6, 126.6, 124.1, 121.4, 21.2, 19.4 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_{13}H_{11}D_3N$ ($M+H^+$)]: 187.1309, found: 187.1306.

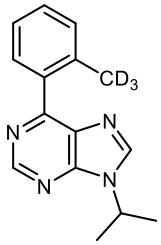
2-(5-Methyl-2-(methyl-*d*$_3$)phenyl)pyridine (7e)



The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (1:2, v/v), and isolated as a light yellow oil, 28.5 mg, 51%, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (ddd, *J* = 4.9, 1.9, 1.0 Hz, 1H), 7.73 (td, *J* = 7.7, 1.8 Hz,

1H), 7.40 (dt, *J* = 7.9, 1.1 Hz, 1H), 7.25 – 7.21 (m, 1.7H), 7.17 (d, *J* = 7.7 Hz, 1H), 7.14 – 7.09 (m, 1H), 2.36 (s, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 160.1, 149.3, 140.3, 136.0, 135.3, 132.4, 130.7, 130.3, 129.0, 124.1, 121.5, 20.9, 19.0 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_{13}H_{11}D_3N$ ($M+H^+$)]: 187.1309, found: 187.1306.

2-(5-Methyl-2-(methyl-*d*$_3$)phenyl)pyridine (7f)



The title compound was prepared following the general procedure, purified by column chromatography using EtOAc/hexanes (1:1, v/v), and isolated as a yellow semi solid, 51.3 mg, 67%, ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.00 (s, 1H), 8.11 (s, 1H), 7.70 – 7.60 (m, 1H), 7.32 (d, *J* = 6.9 Hz, 1H), 7.30 (d, *J* = 8.6 Hz, 2H), 4.93 (p, *J* = 6.8 Hz, 1H), 1.62 (d, *J* = 6.9 Hz, 6H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 158.8, 151.8, 151.4, 142.3, 136.9, 135.1, 132.5, 131.1, 130.6, 129.5, 125.7, 47.4, 22.5, 19.7 (h, J = 20.2 Hz). HRMS (ESI) calcd. for [$C_{15}H_{14}D_3N_4$ ($M+H^+$)]: 256.1636, found: 256.1632.

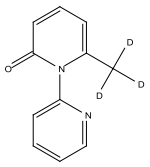
7. References:

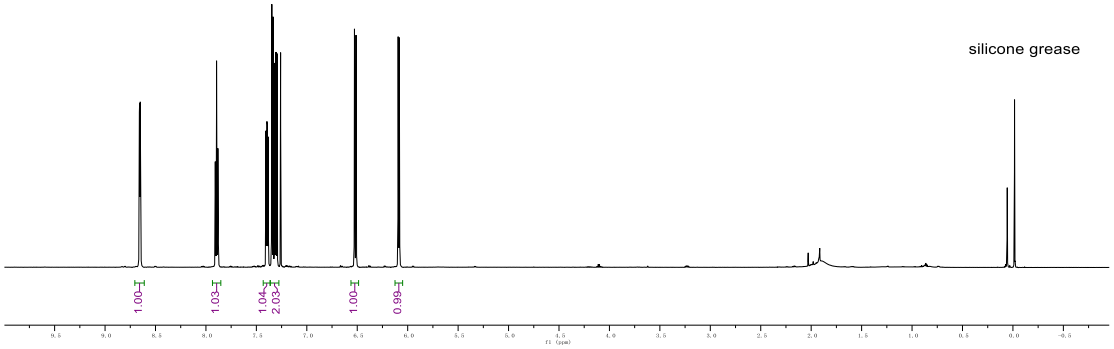
1. H. Zhao, X. Xu, Z. Luo, L. Cao, B. Li, H. Li, L. Xu, Q. Fan and P. J. Walsh, *Chem. Sci.* **2019**, *10*, 10089-10096.
2. H. Yu, H. Zhao, X. Xu, X. Zhang, Z. Yu, L. Li, P. Wang, Q. Shi and Li. Xu, *Asian J. Org. Chem.* **2021**, *10*, 879-885.
3. J. Xu, C. Chen, H. Zhao, C. Xu, Y. Pan, X. Xu, H. Li, L. Xu and B. Fan, *Org. Chem. Front.*, **2018**, *5*, 734–740.
4. W. Miura, K. Hirano and M. Miura, *J. Org. Chem.* **2017,** *82*, 5337-5344.

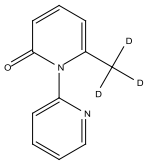
8. Copies of ^{1}H and $^{13}C\{^{1}H\}$ NMR Spectra

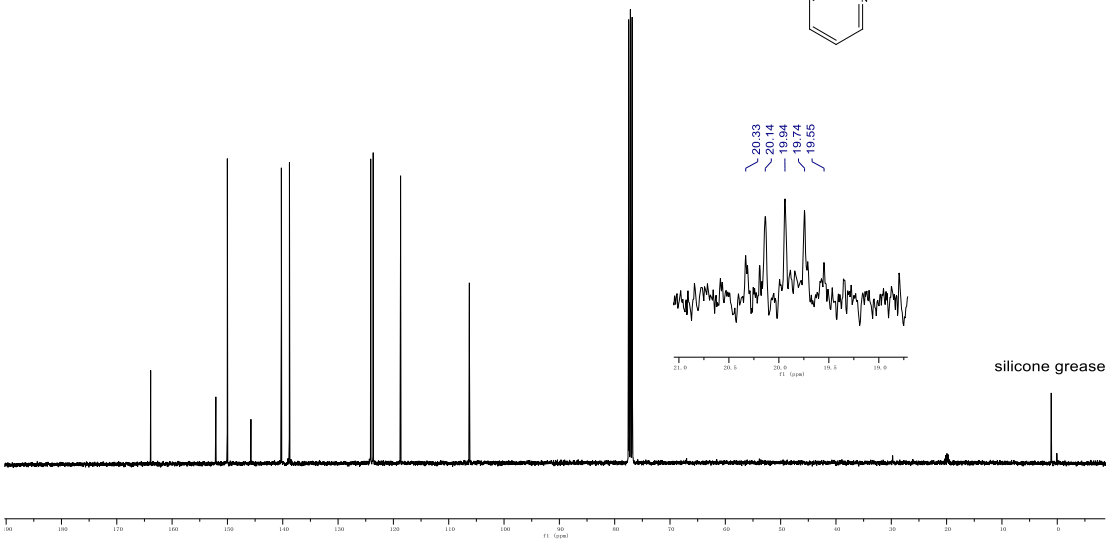
In order to obtain the clear CD_3 splitting picks, most samples were tested for 1024 scans, which leads to untidy baseline of the $^{13}C\{^{1}H\}$ NMR spectrum.

^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **3a** in $CDCl_3$

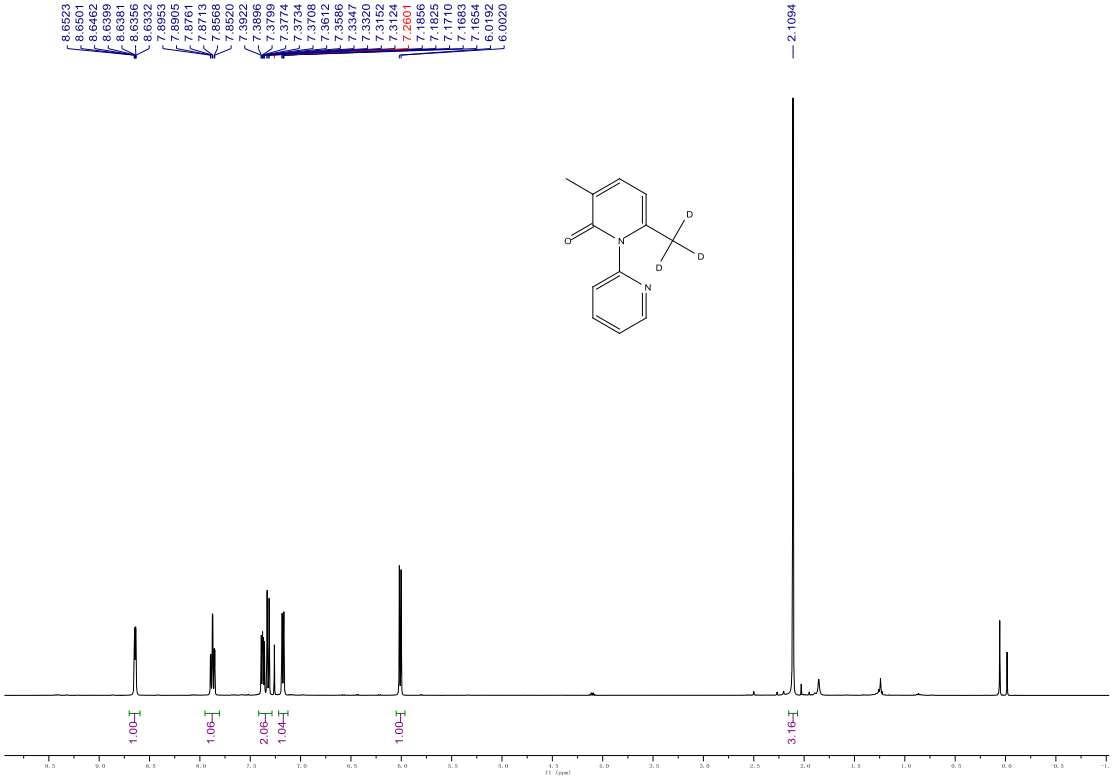


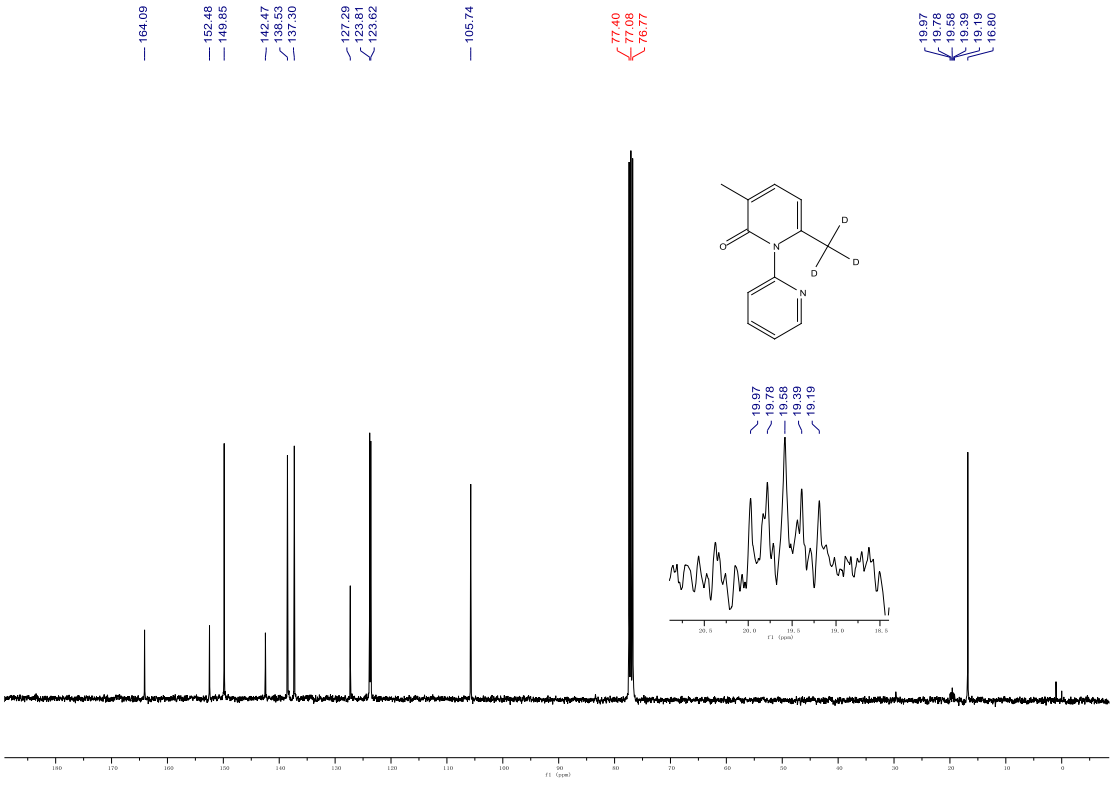




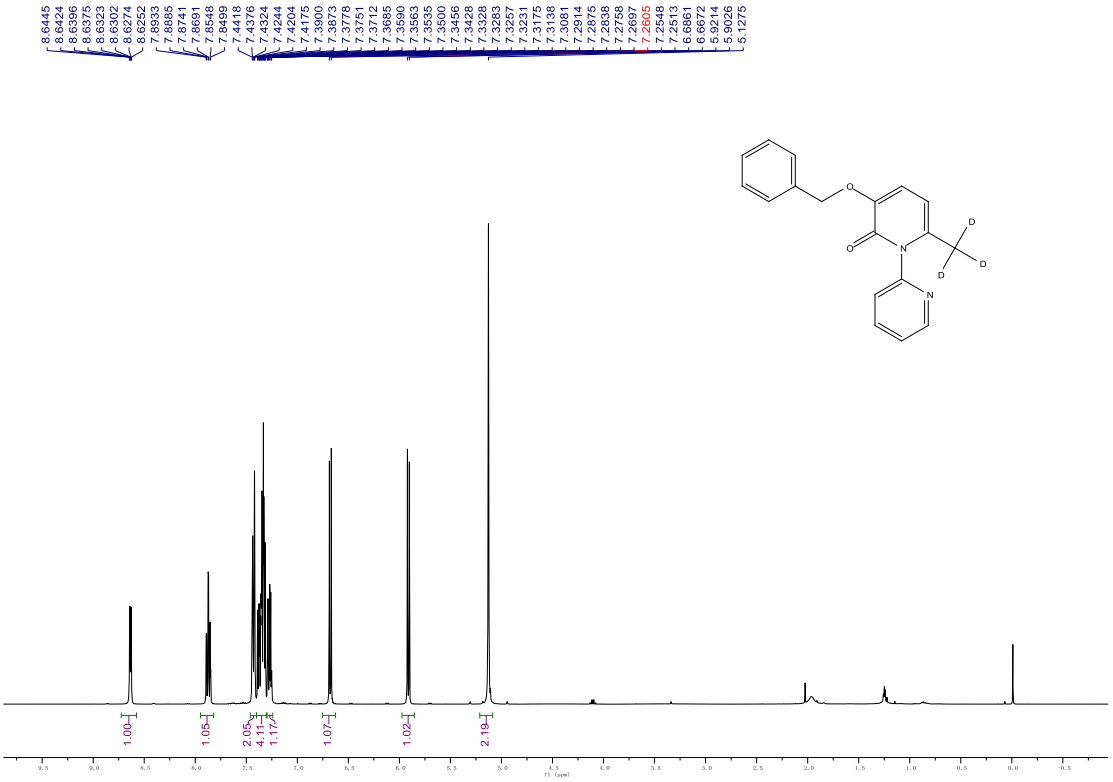


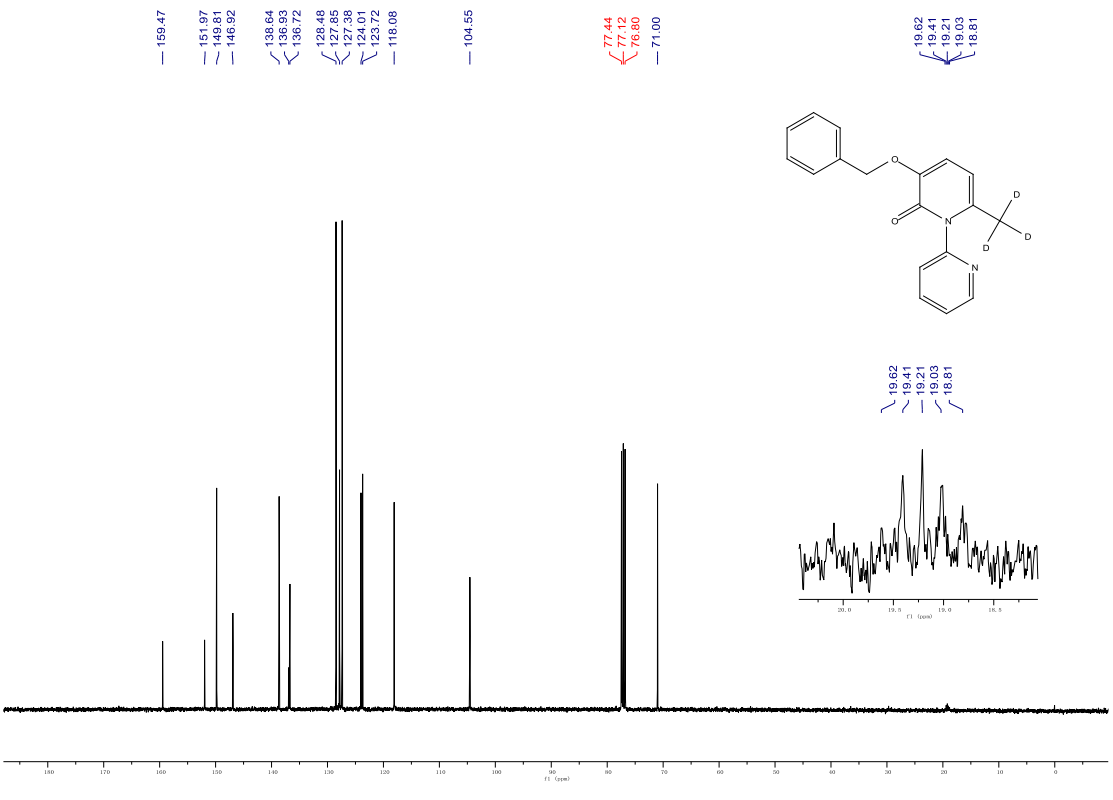
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **3b** in $CDCl_3$



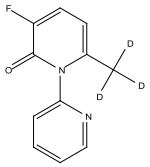


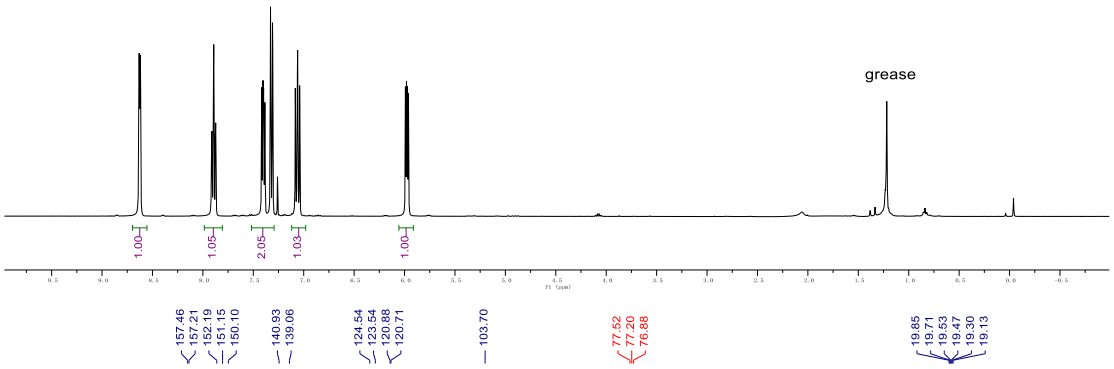
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **3c** in $CDCl_3$



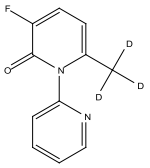


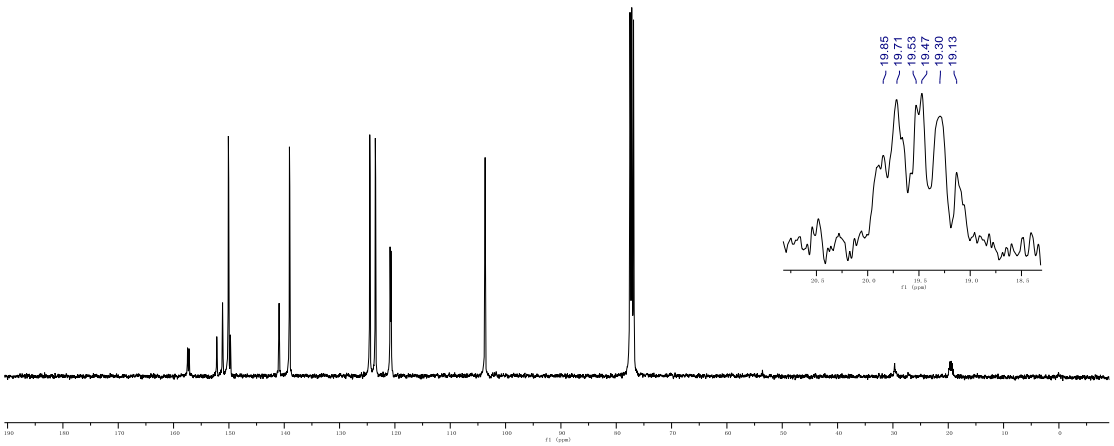
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **3d** in $CDCl_3$



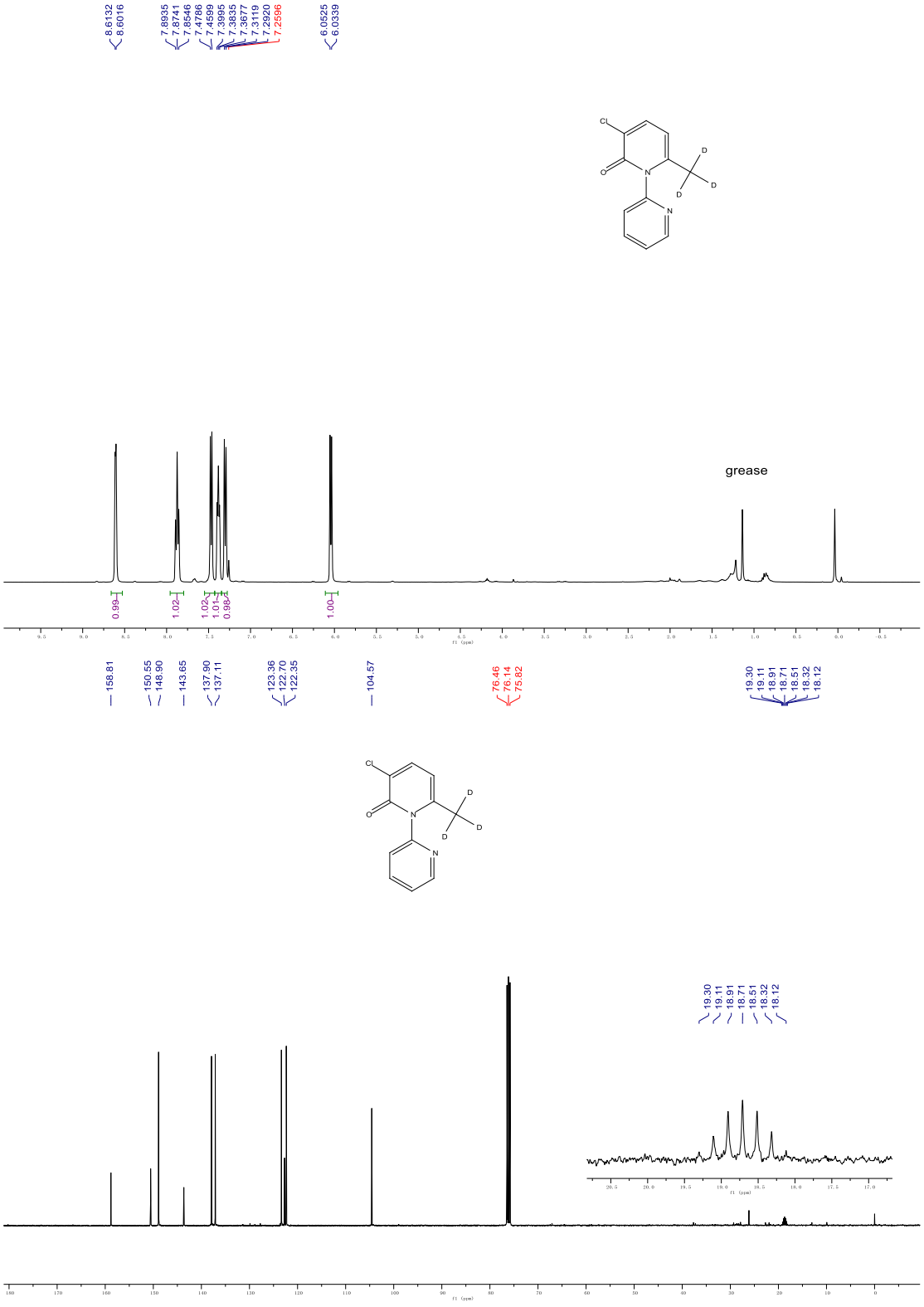


157.46
157.21
152.19
151.15
150.10
140.93
139.06
124.54
123.54
120.88
120.71
103.70
77.52
77.20
76.88
19.85
19.71
19.53
19.47
19.30
19.13

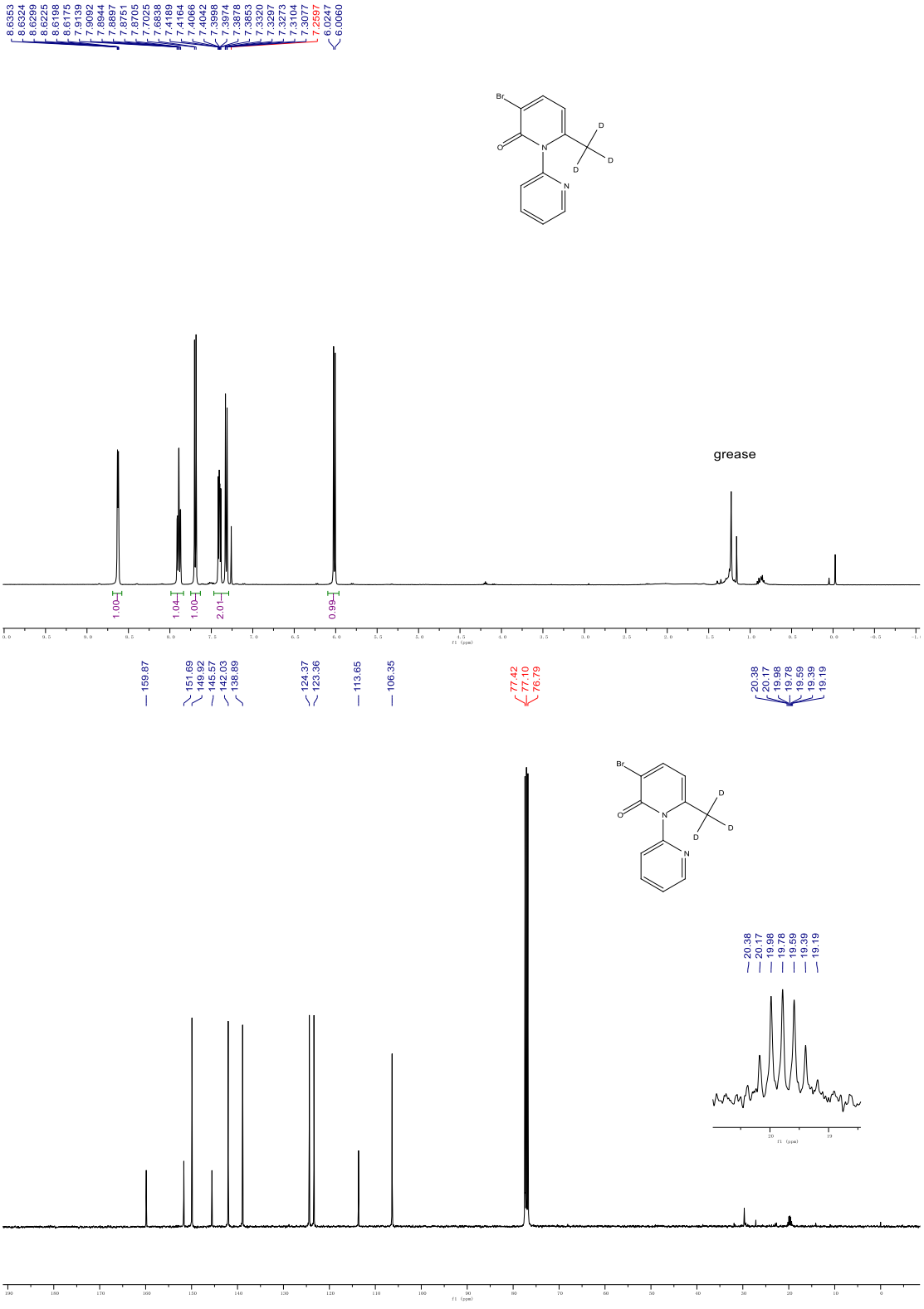




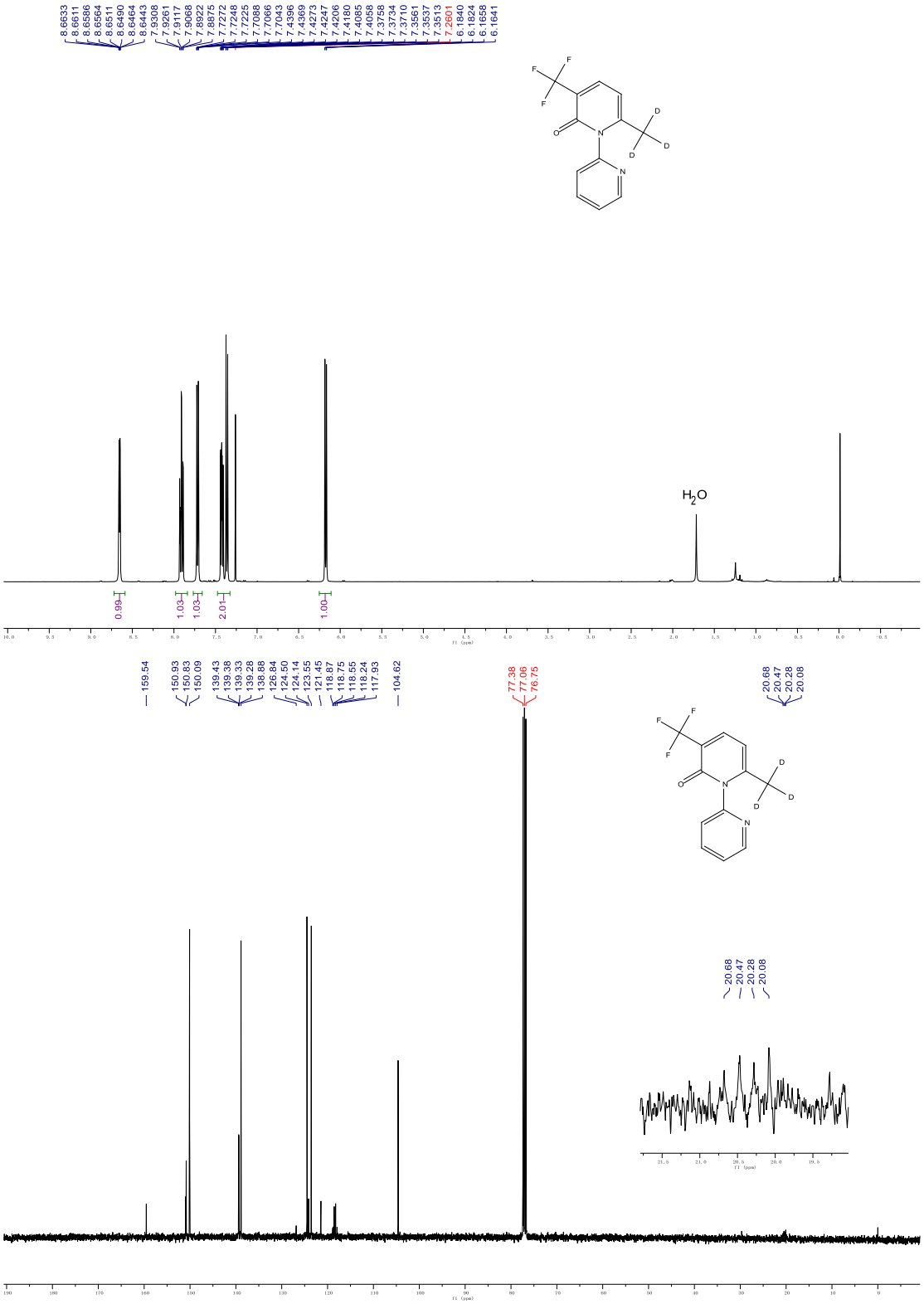
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **3e** in $CDCl_3$



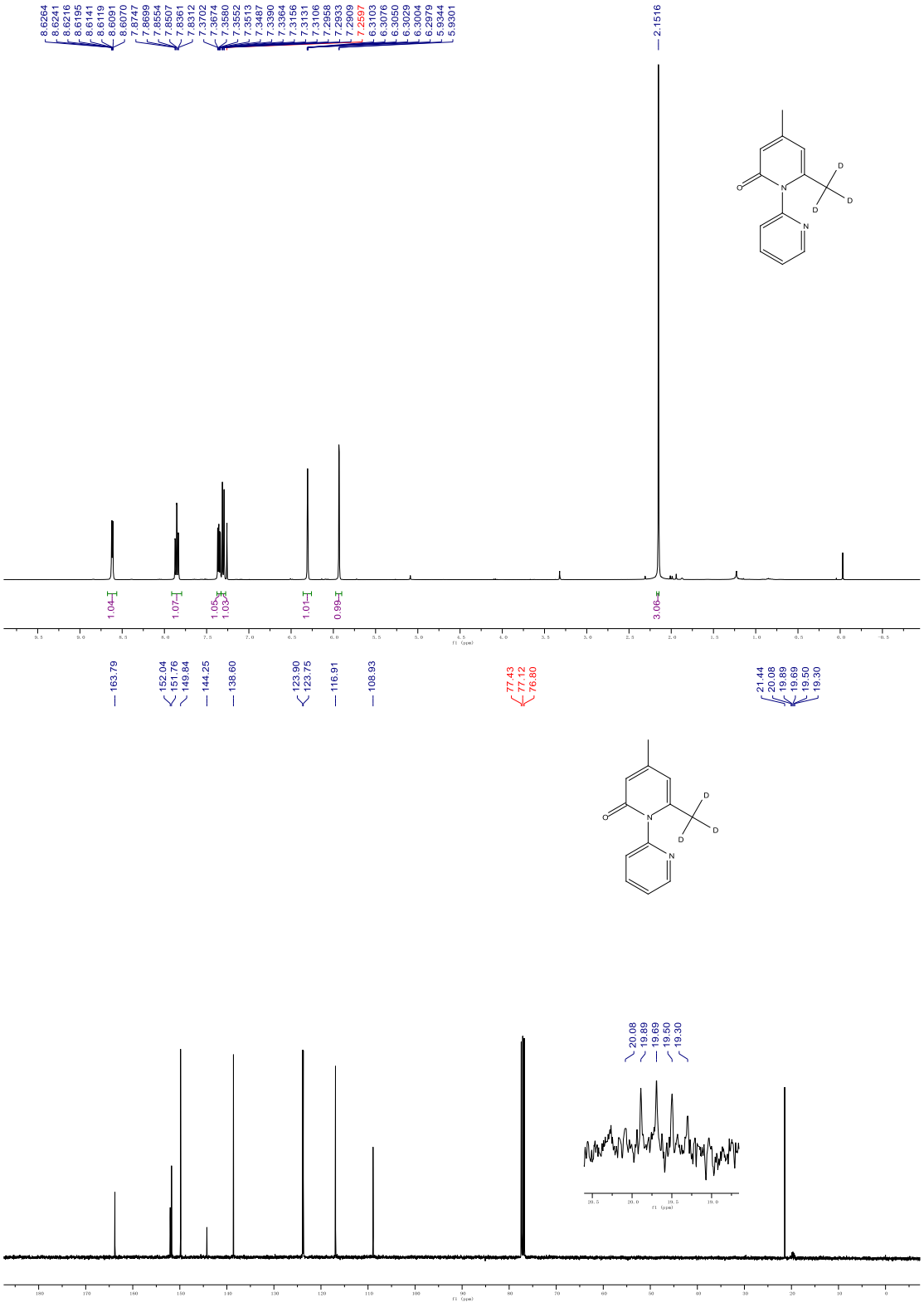
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **3f** in $CDCl_3$



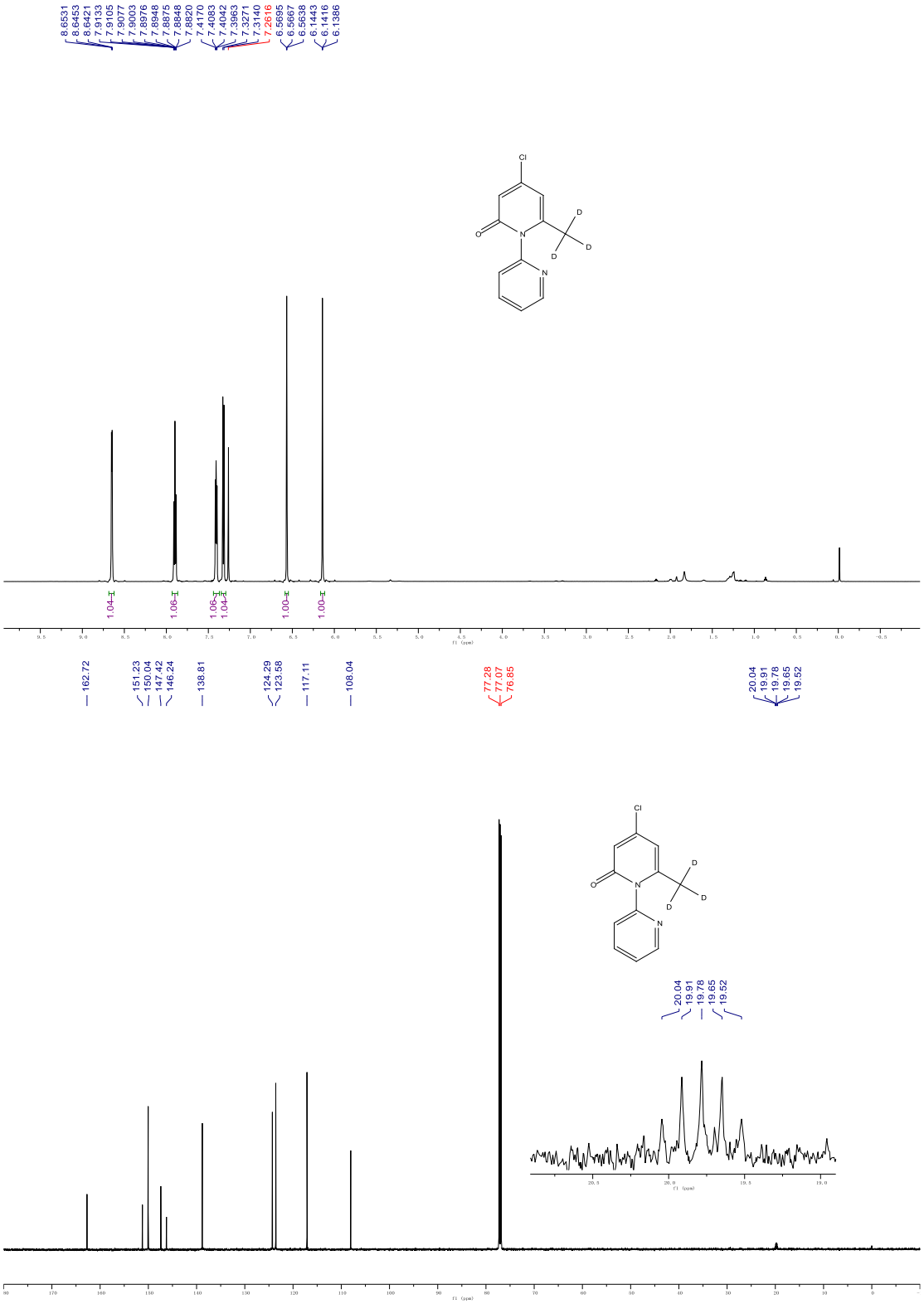
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **3g** in $CDCl_3$



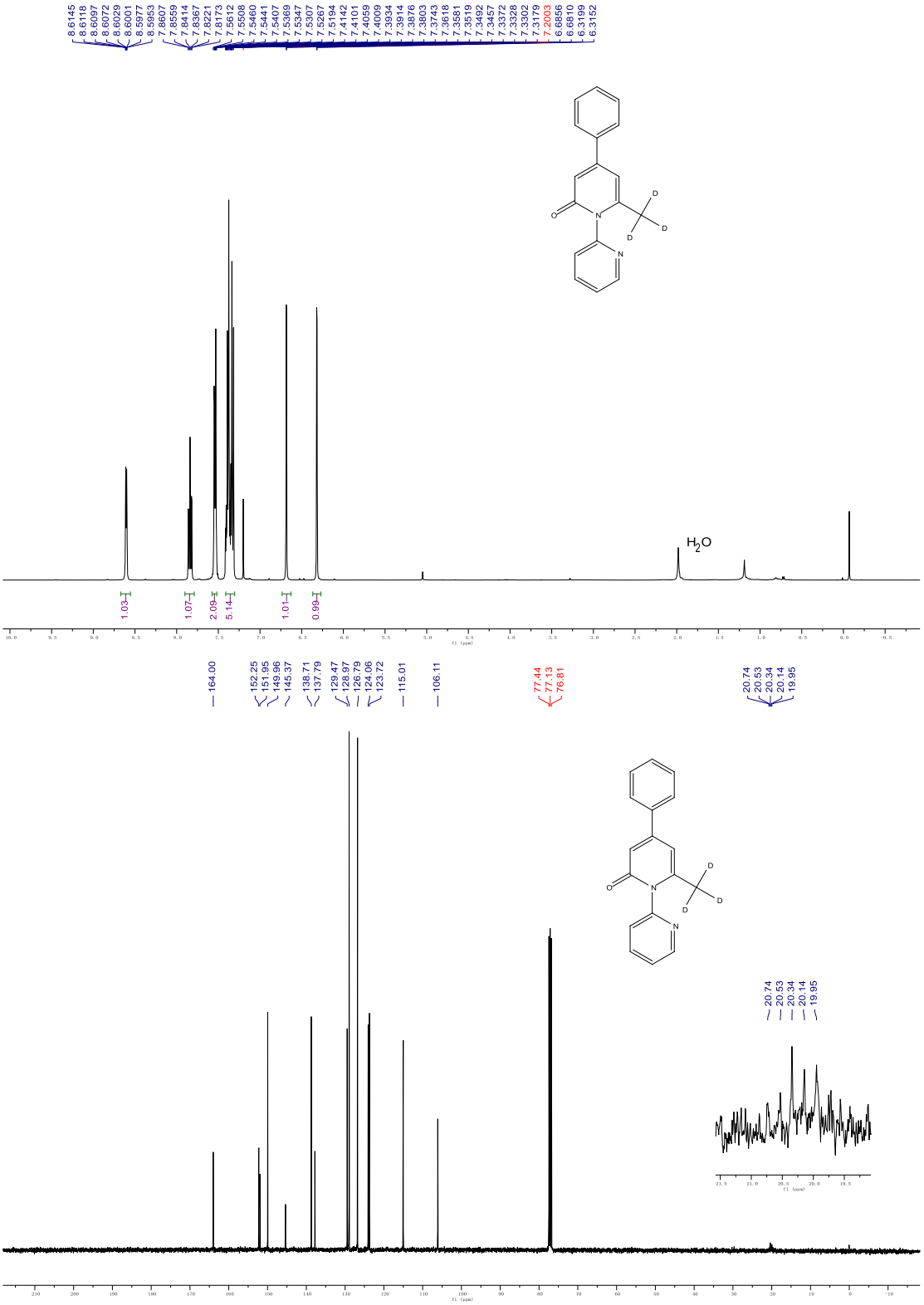
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **3h** in $CDCl_3$



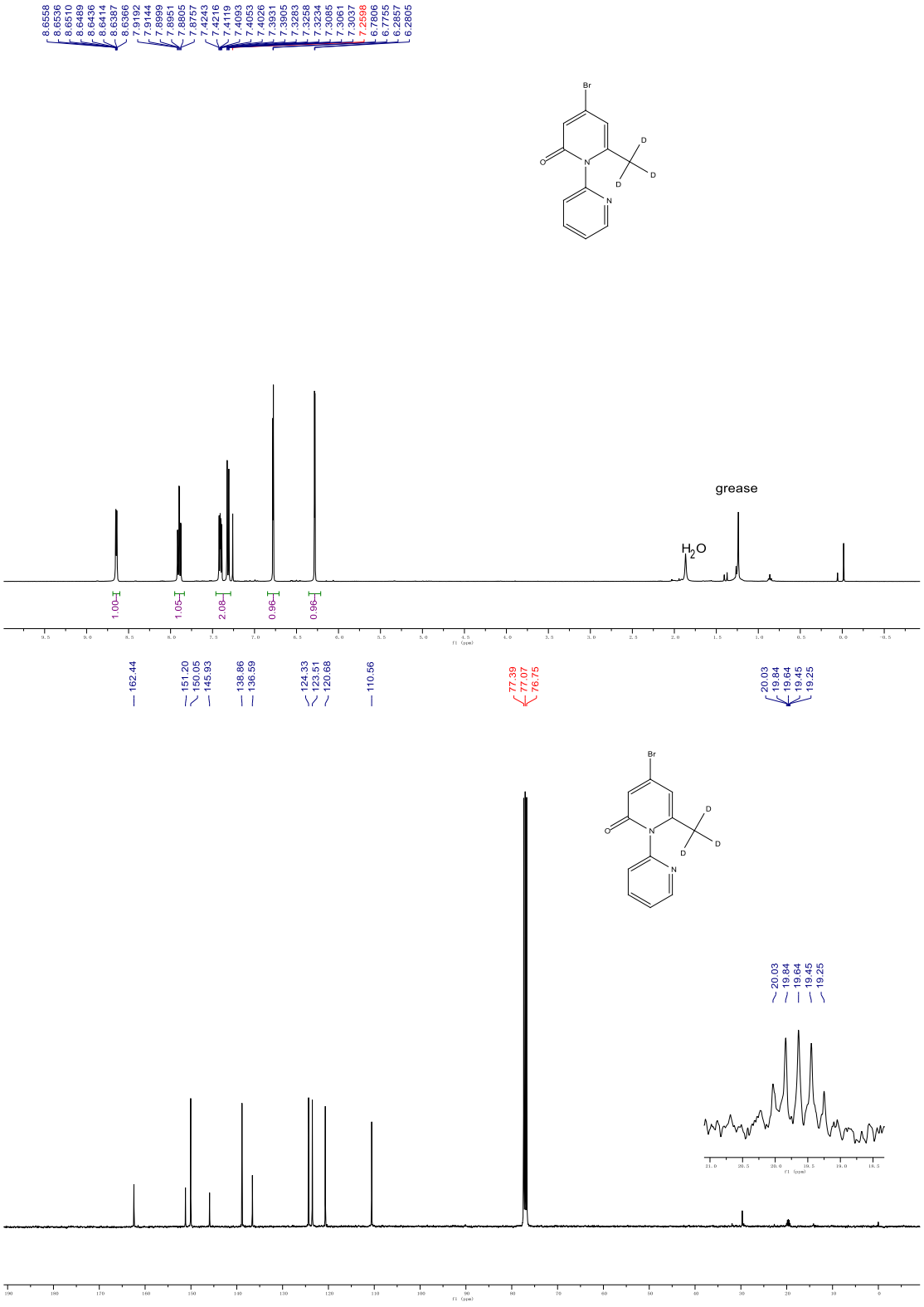
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **3i** in $CDCl_3$



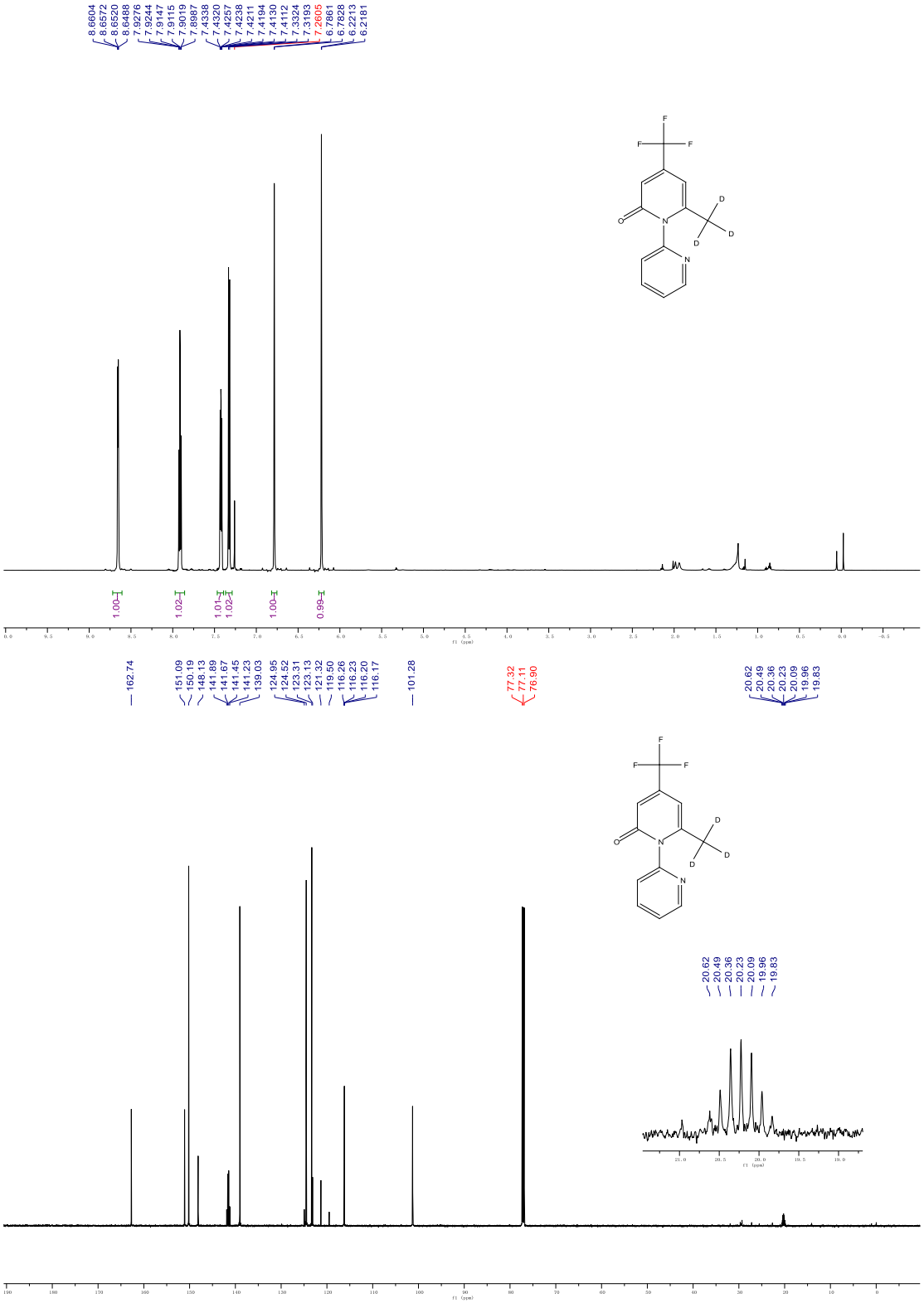
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **3j** in $CDCl_3$



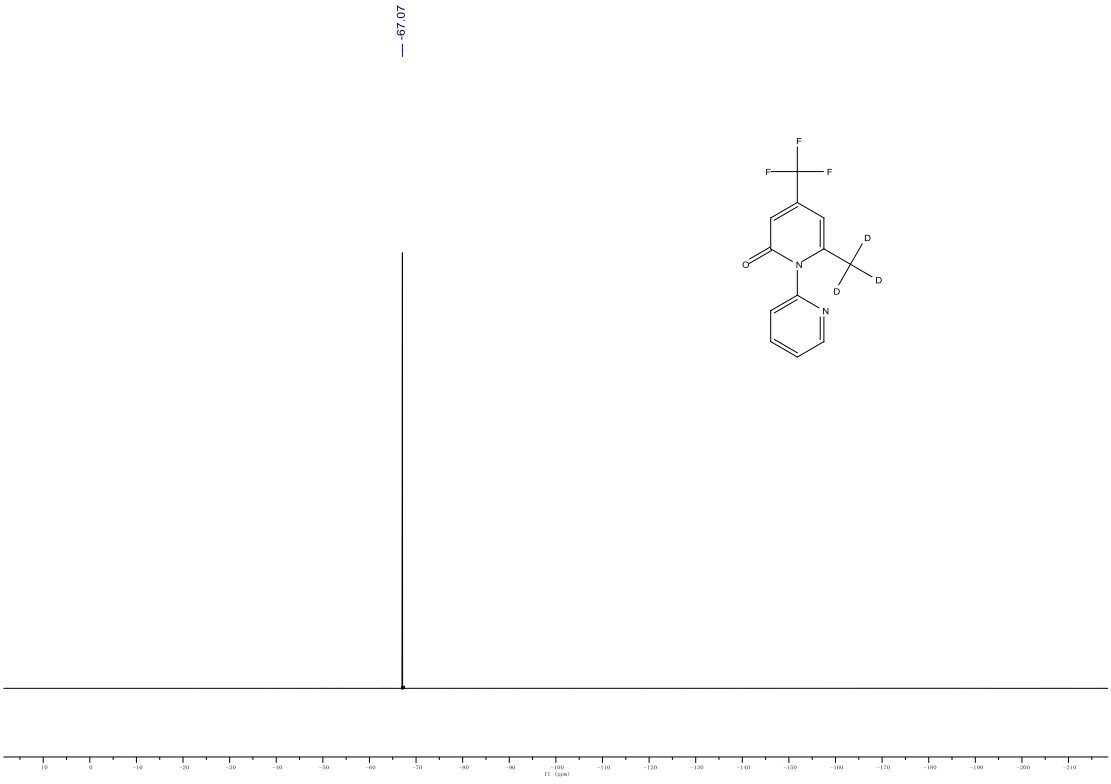
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **3k** in $CDCl_3$



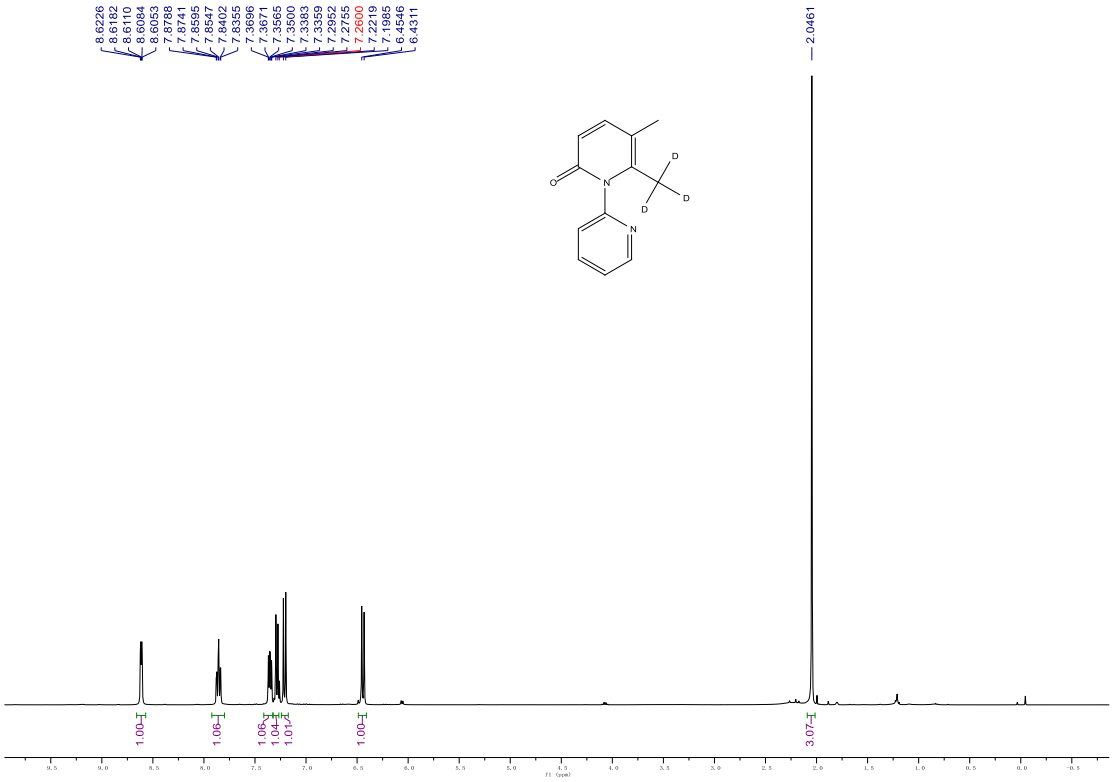
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **3l** in $CDCl_3$

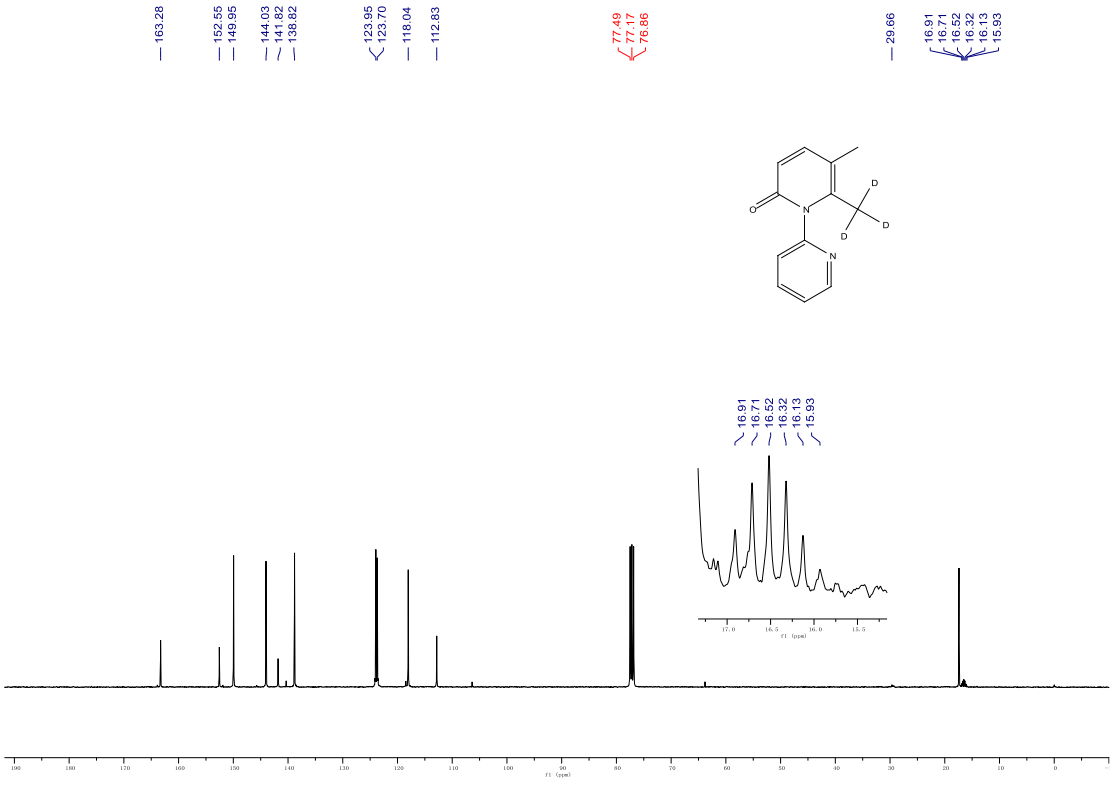


^{19}F NMR spectra of compound **3l** in $CDCl_3$

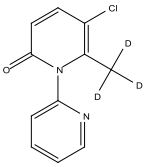


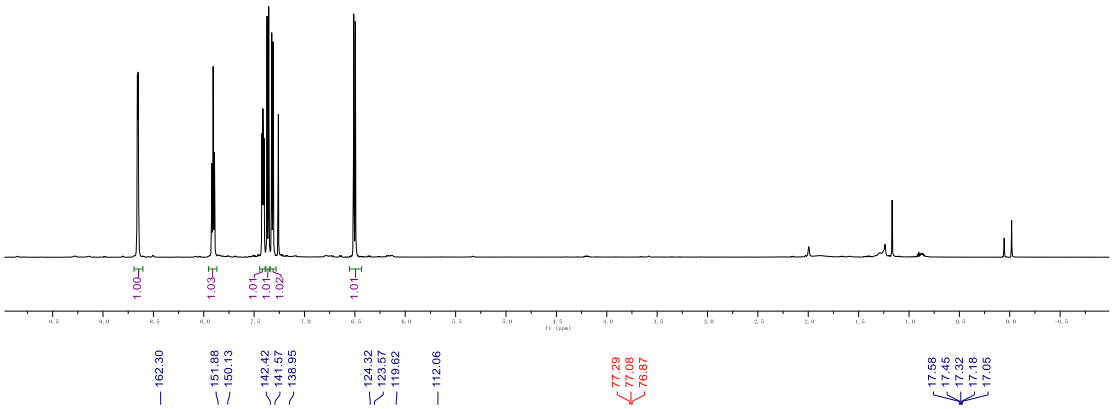
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **3m** in $CDCl_3$

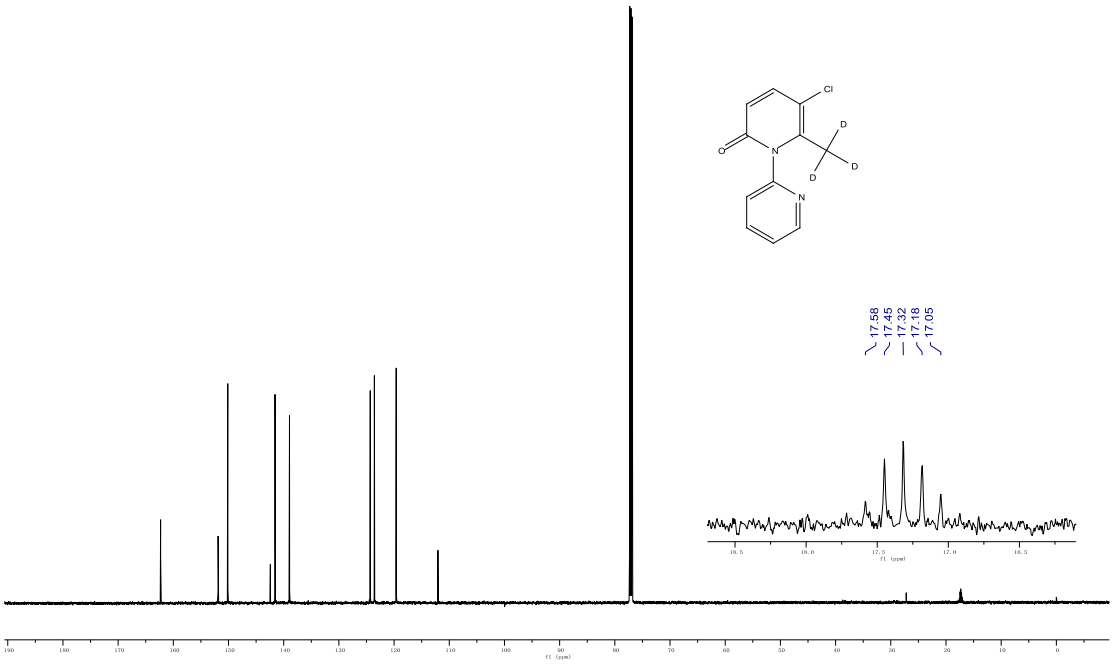




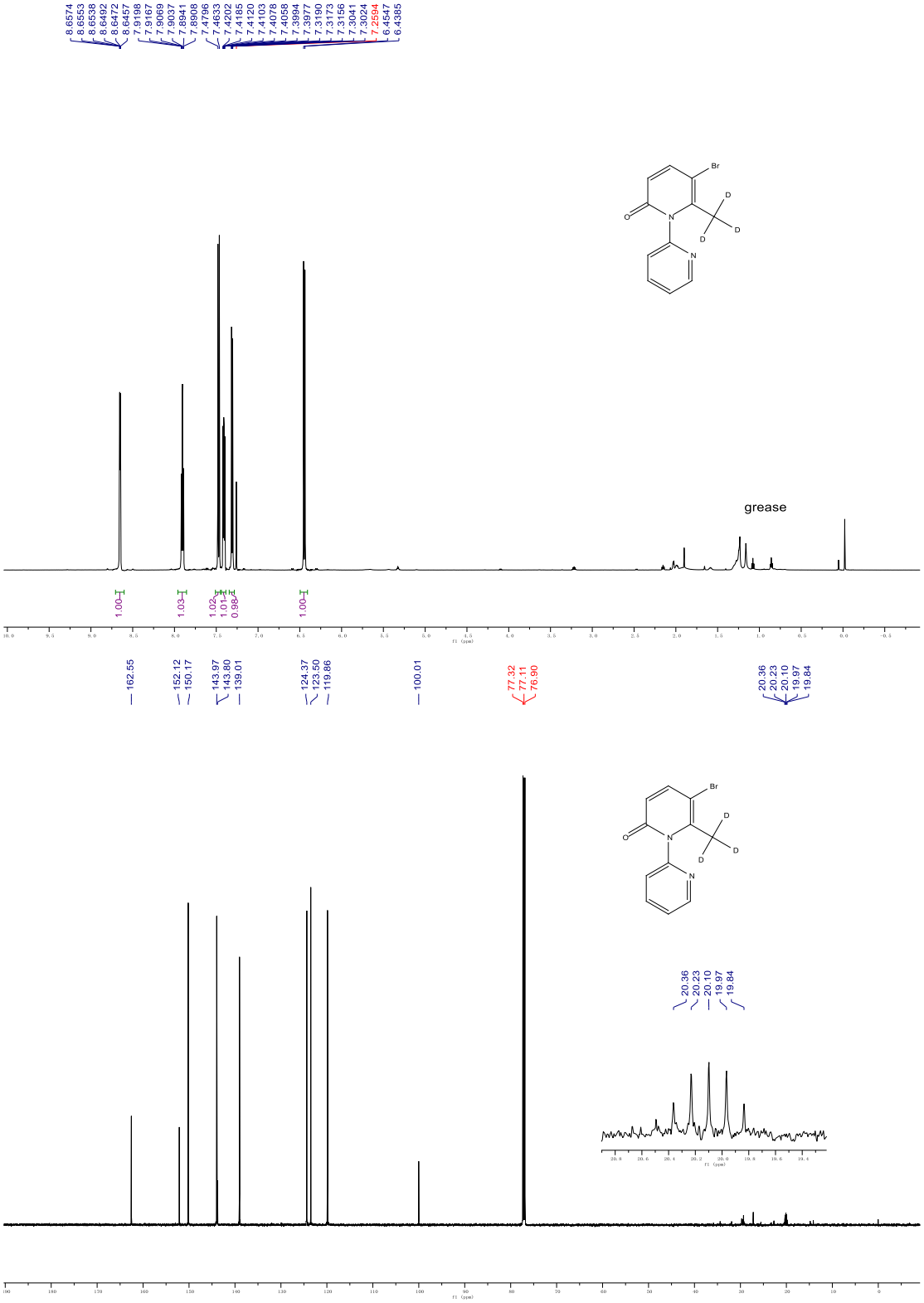
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **3n** in $CDCl_3$



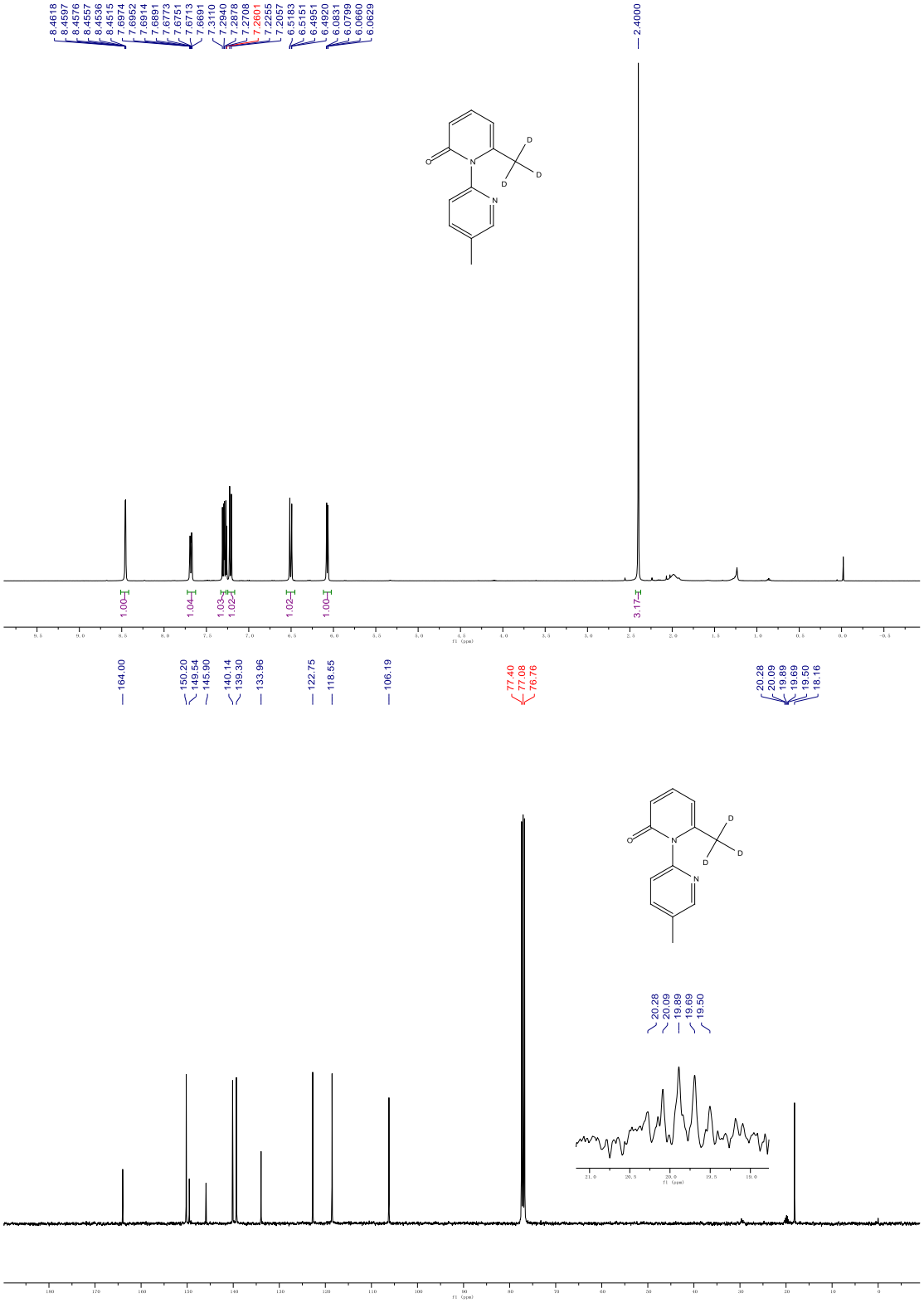




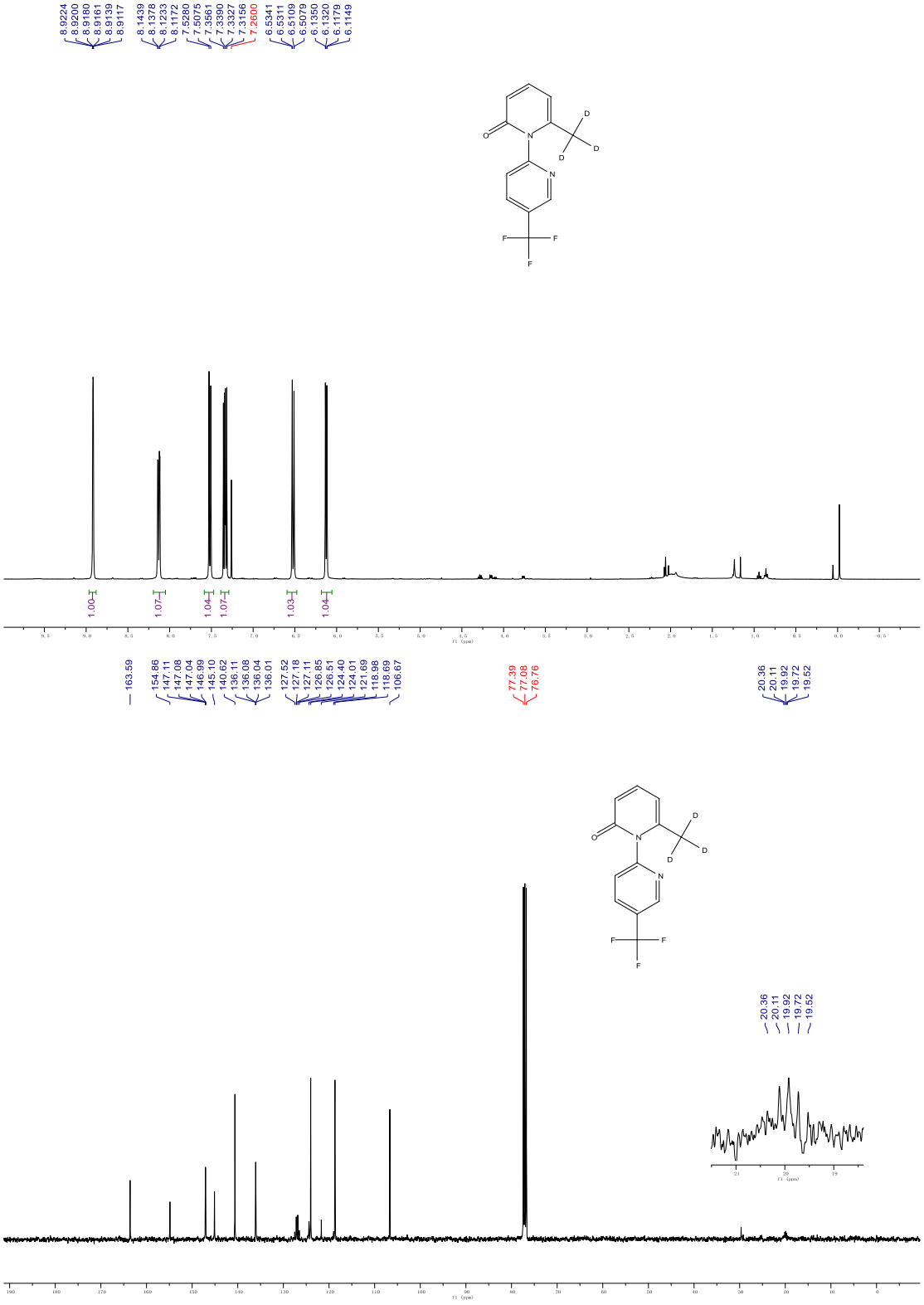
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **3o** in $CDCl_3$



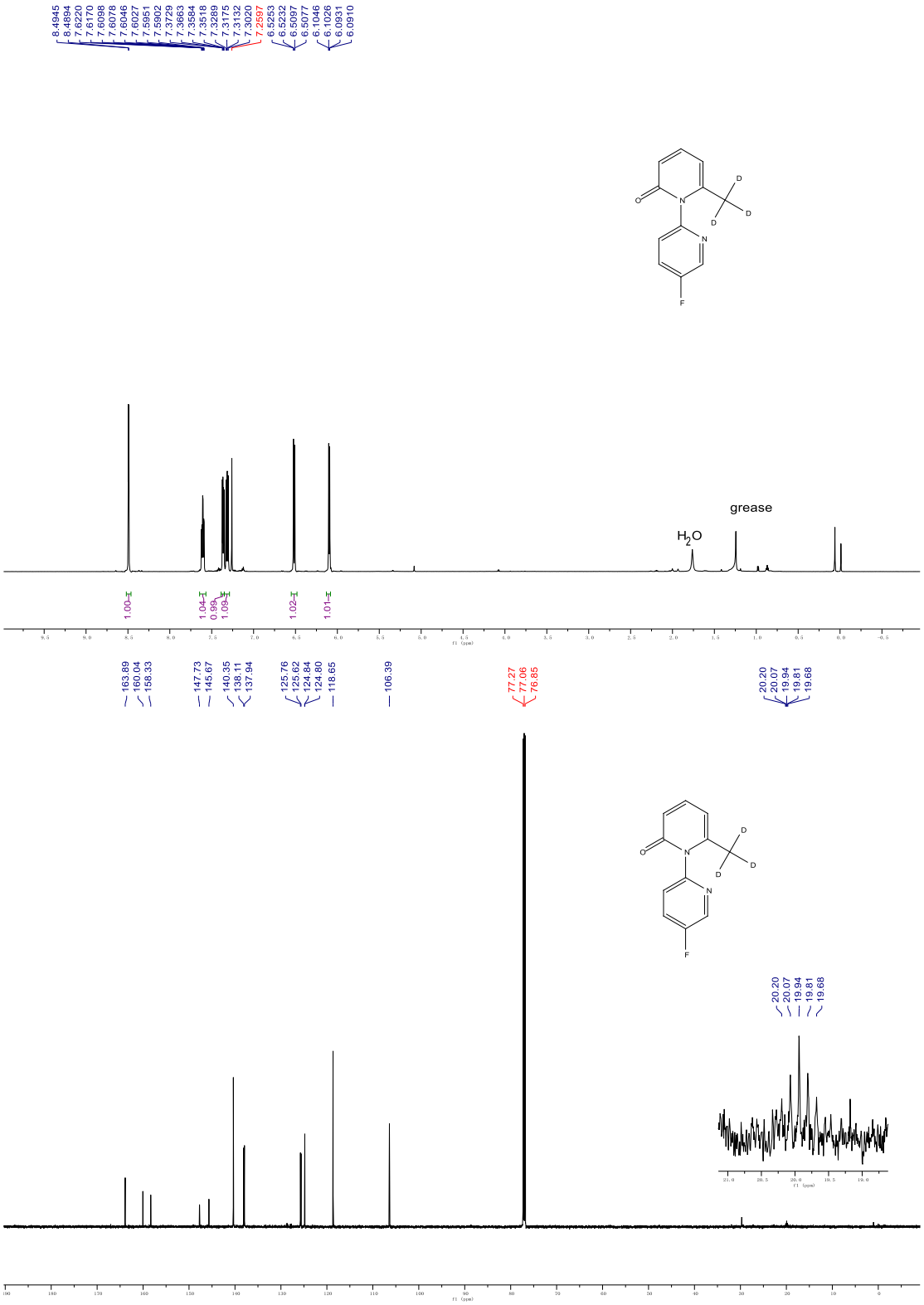
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **3p** in $CDCl_3$



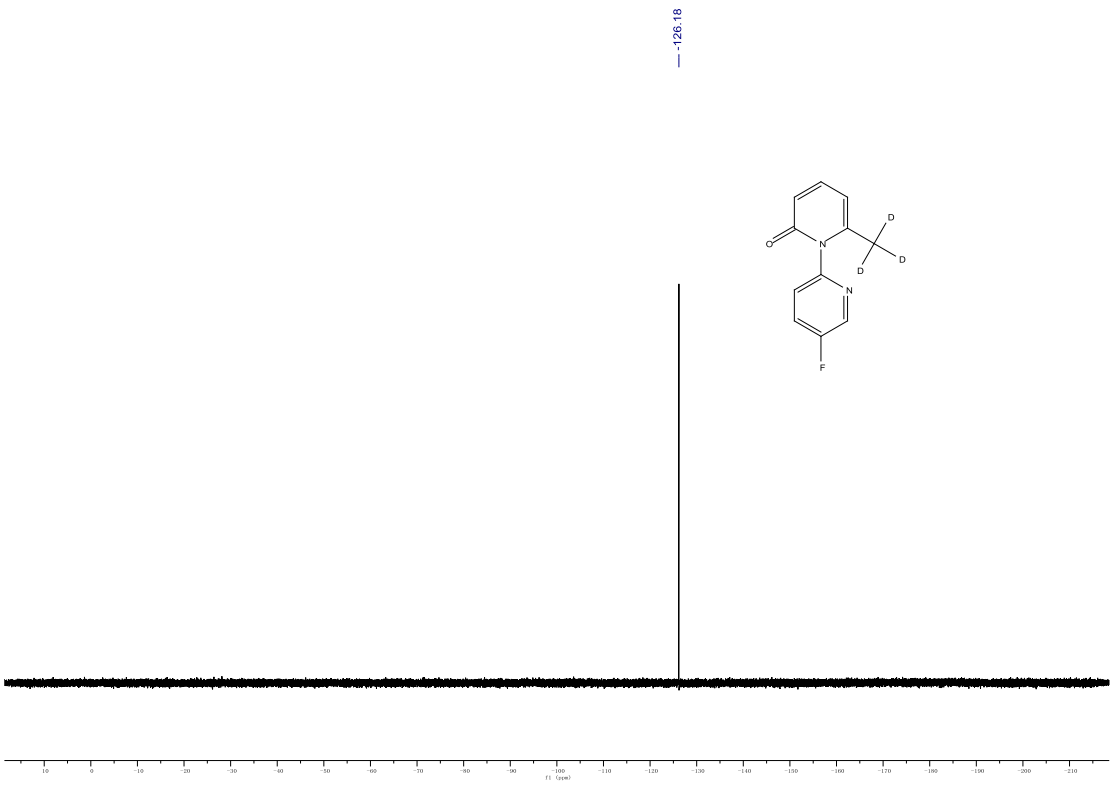
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **3q** in $CDCl_3$



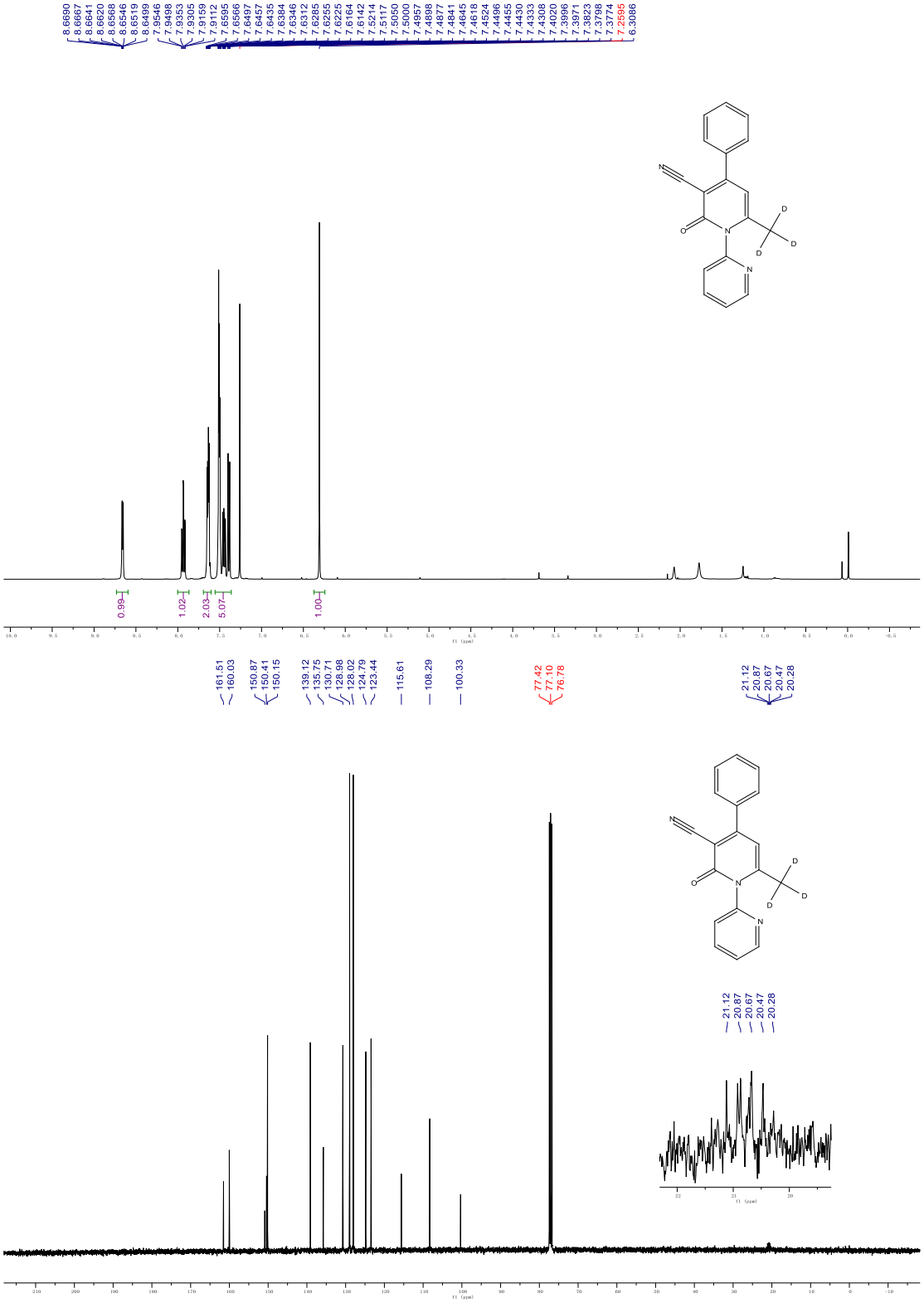
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **3r** in $CDCl_3$



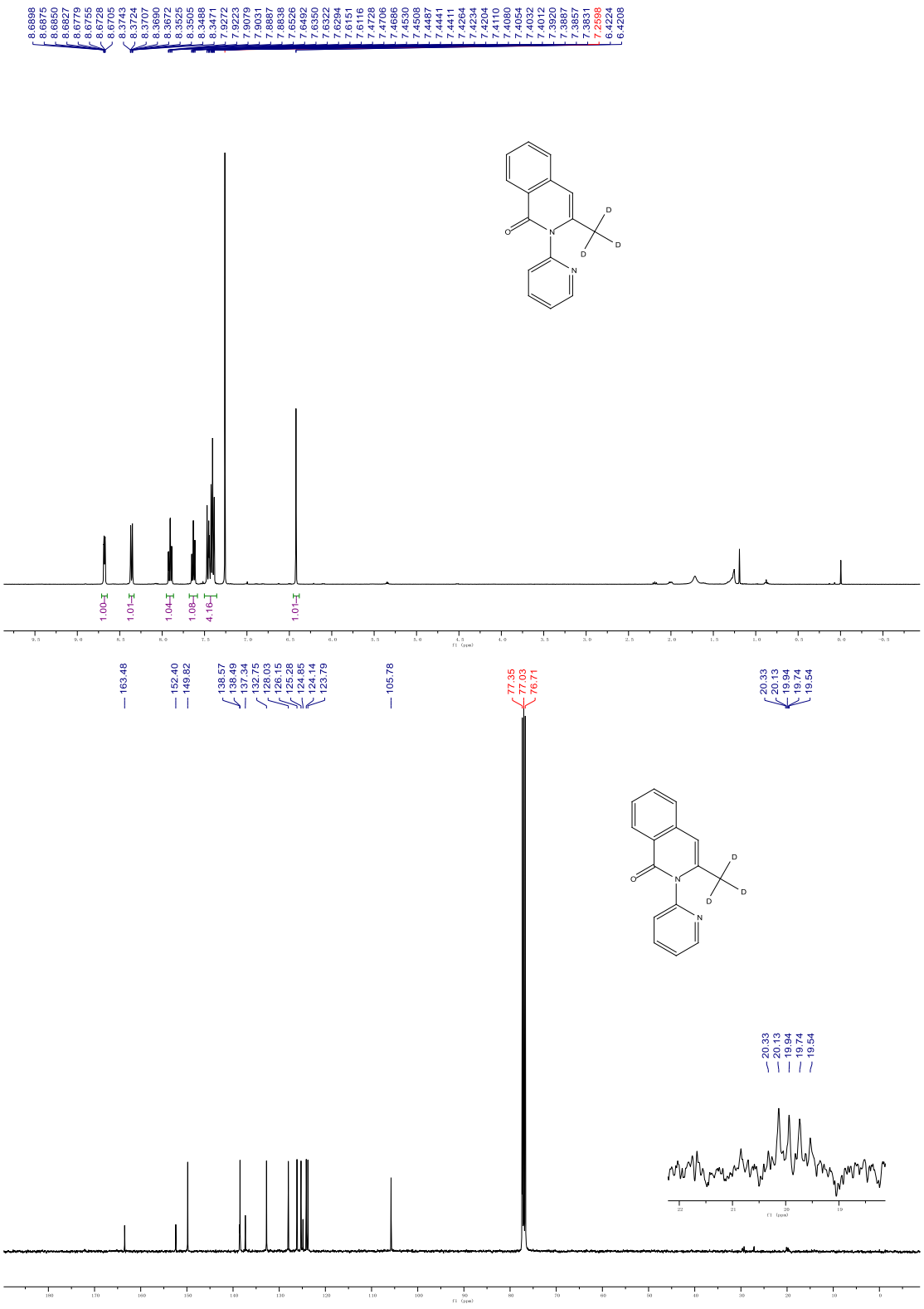
^{19}F NMR spectra of compound **3r** in $CDCl_3$



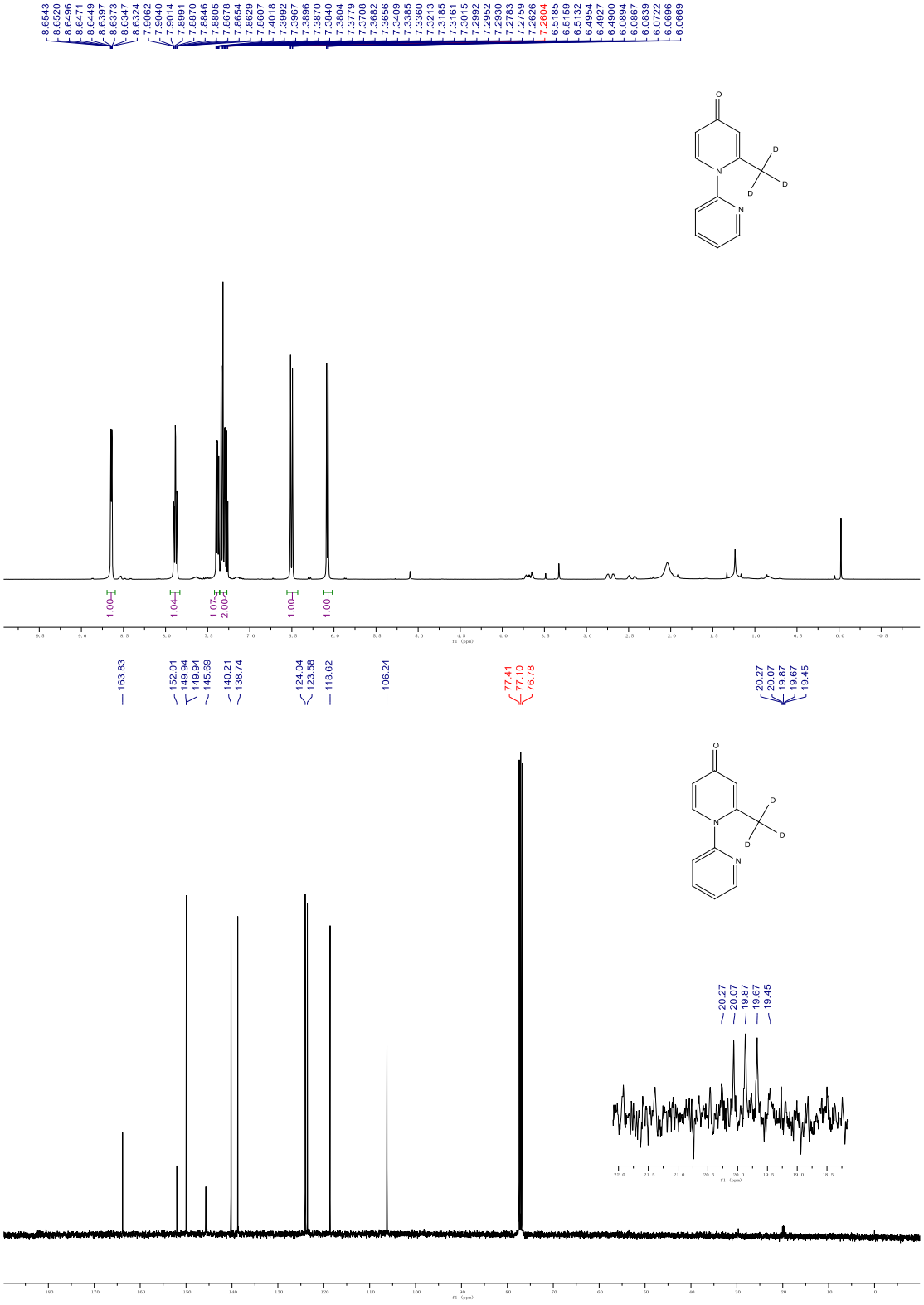
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **3s** in $CDCl_3$



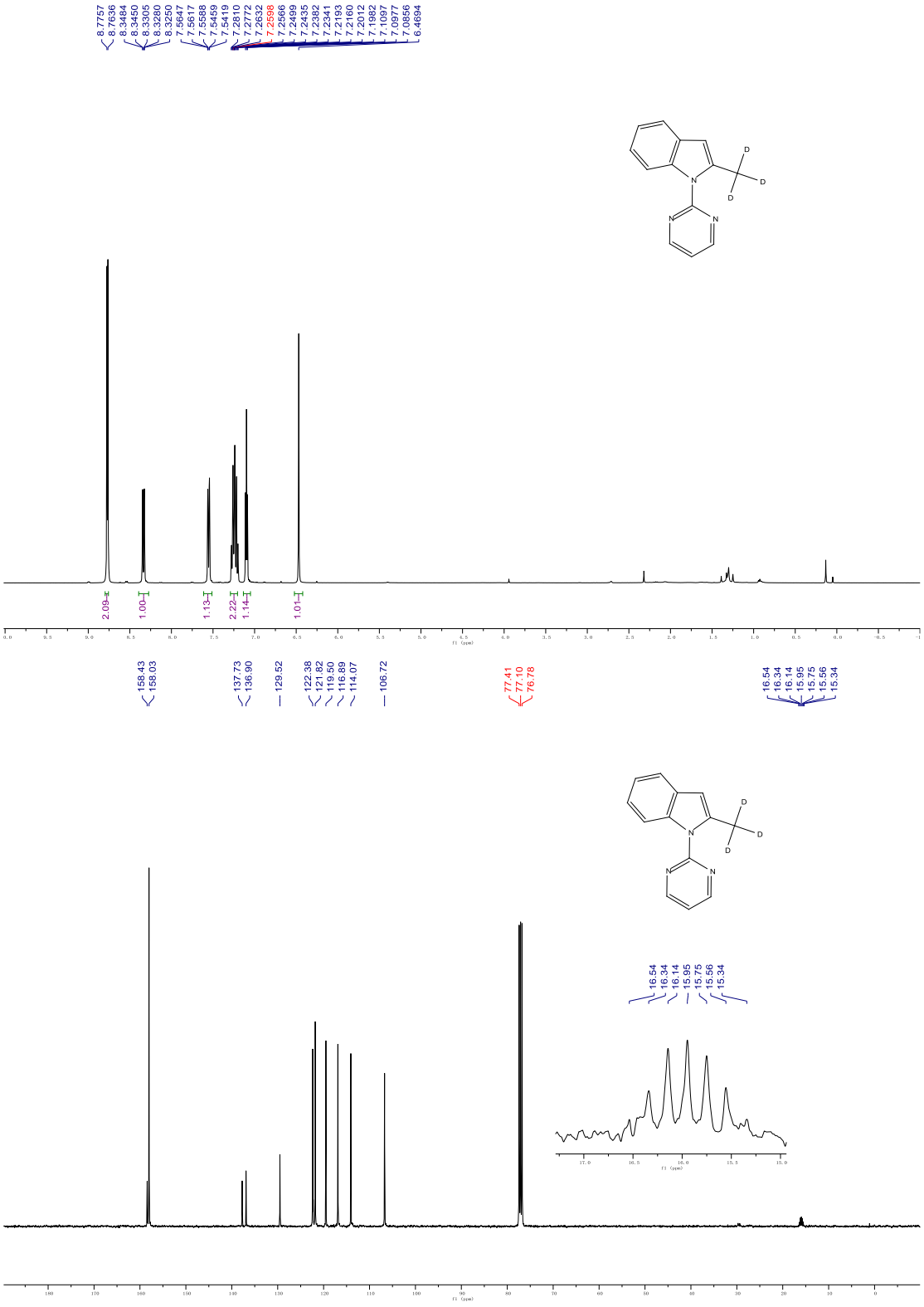
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **3t** in $CDCl_3$



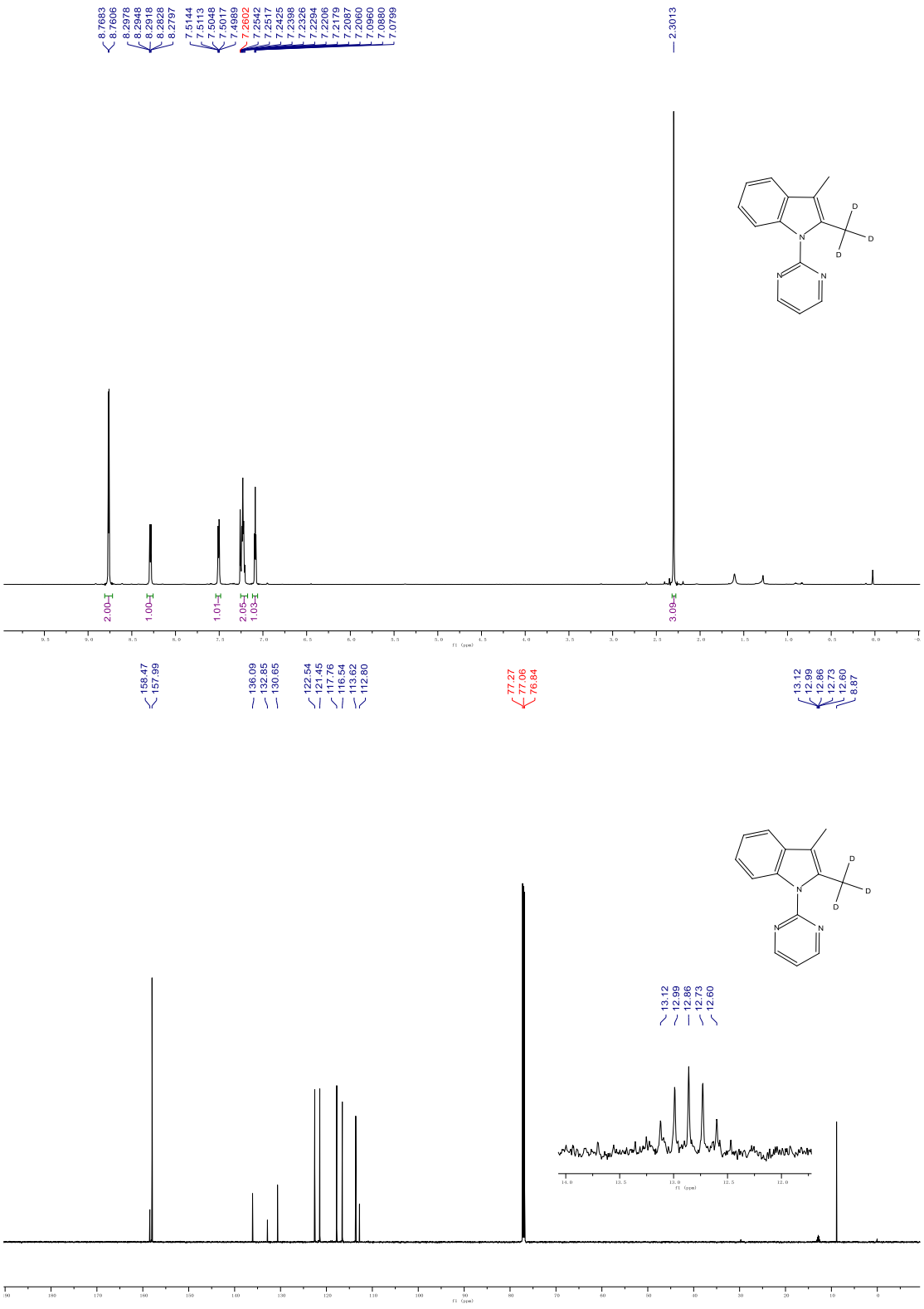
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **3u** in $CDCl_3$



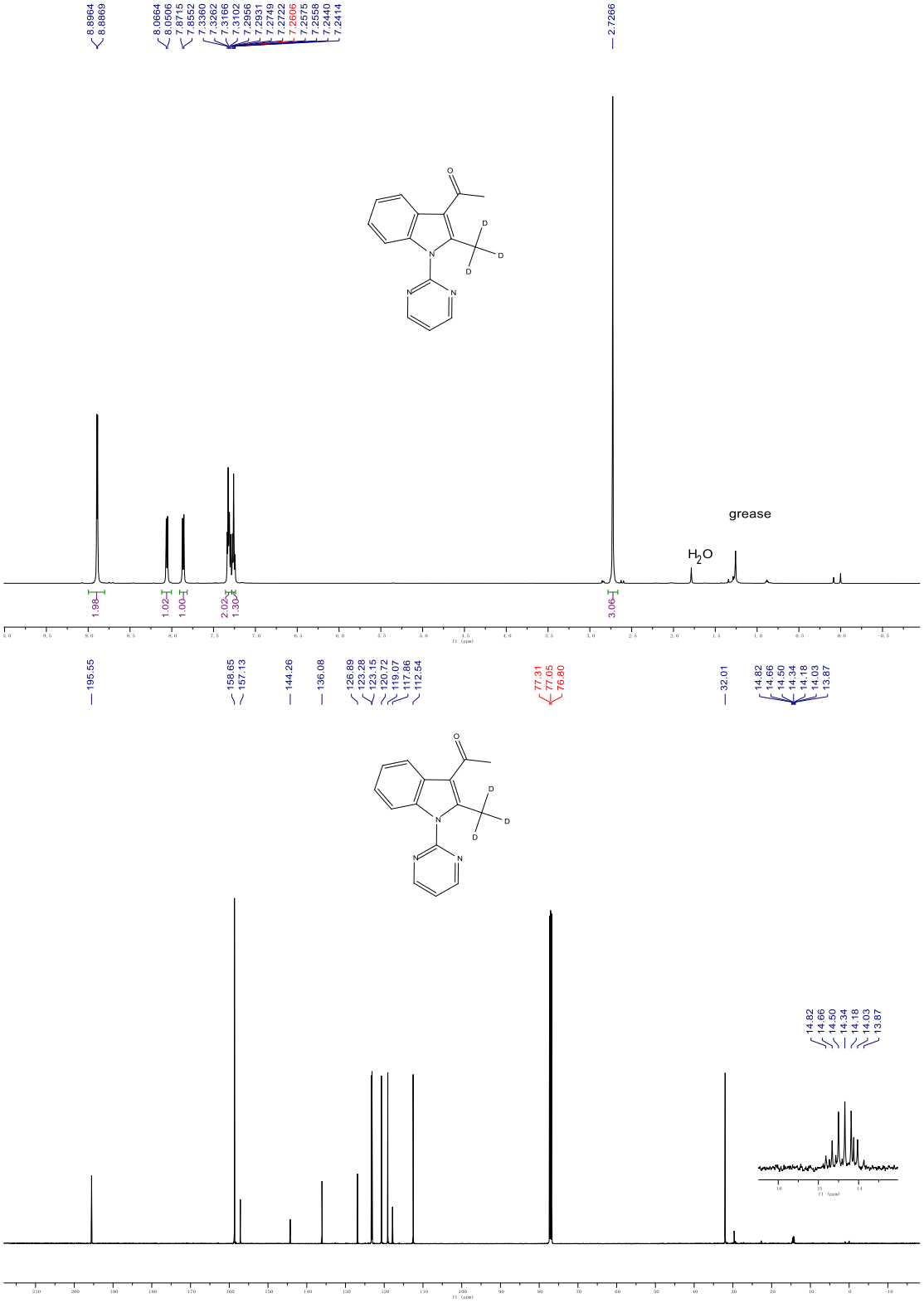
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **6a** in $CDCl_3$



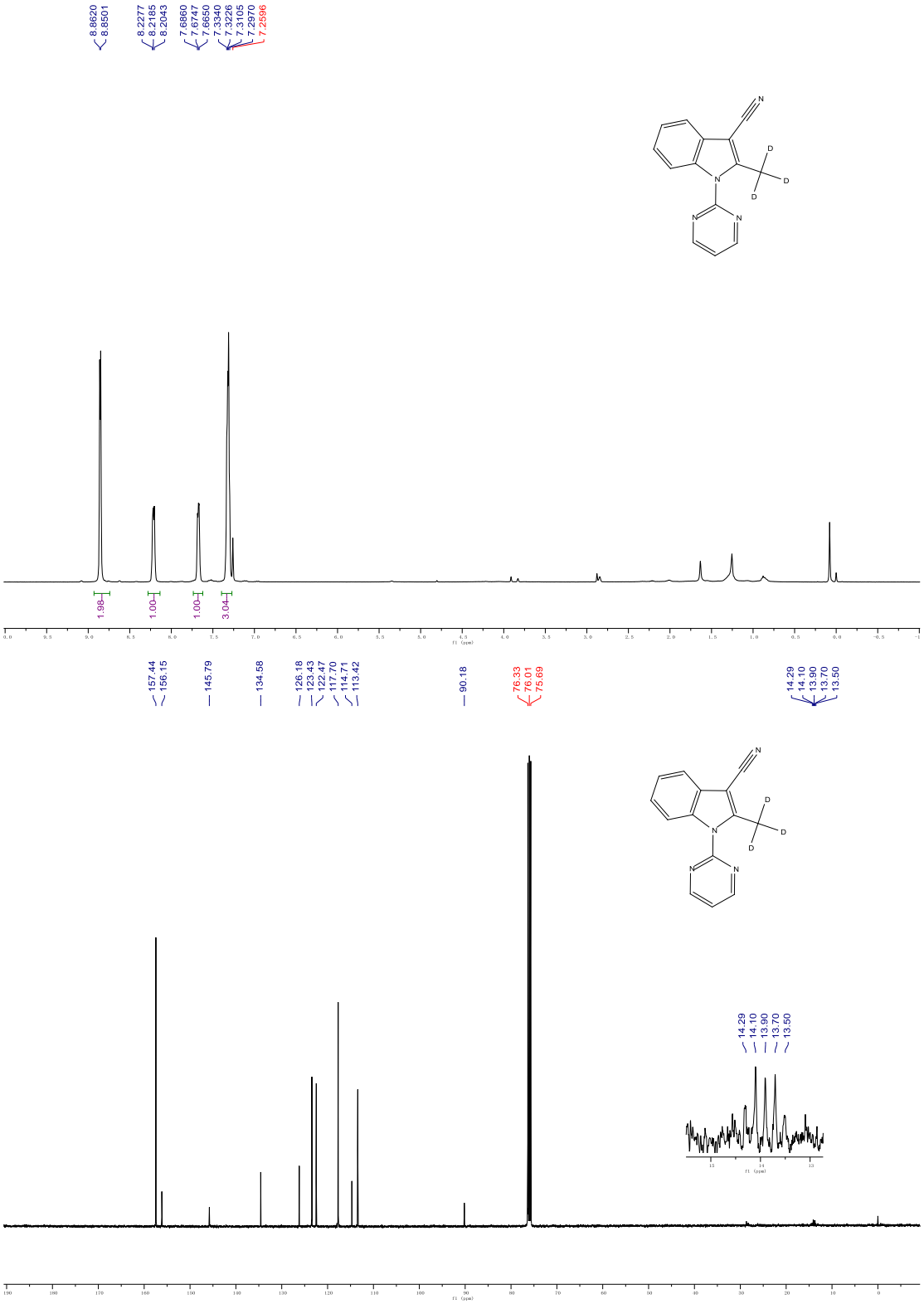
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **6b** in $CDCl_3$



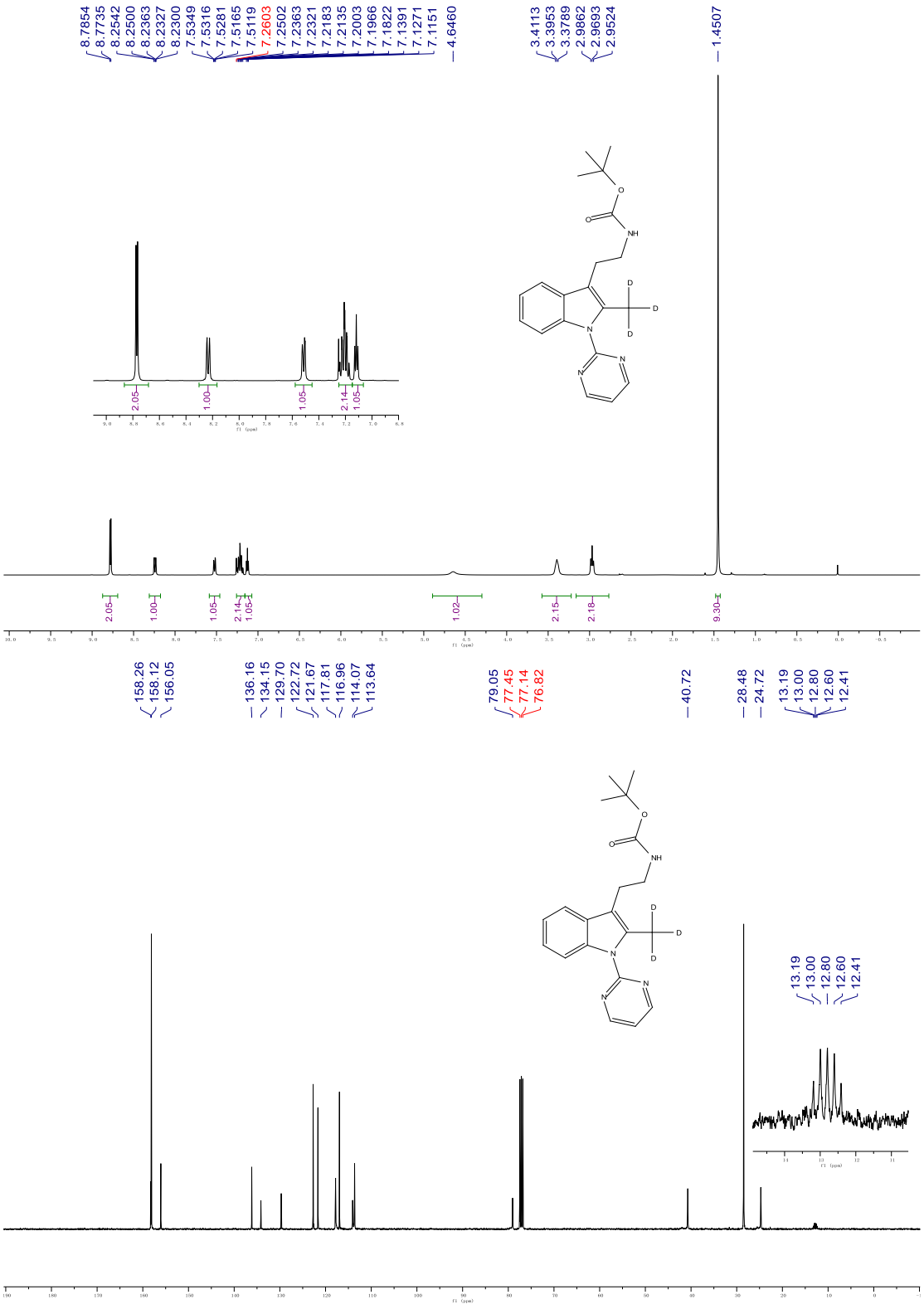
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **6c** in $CDCl_3$



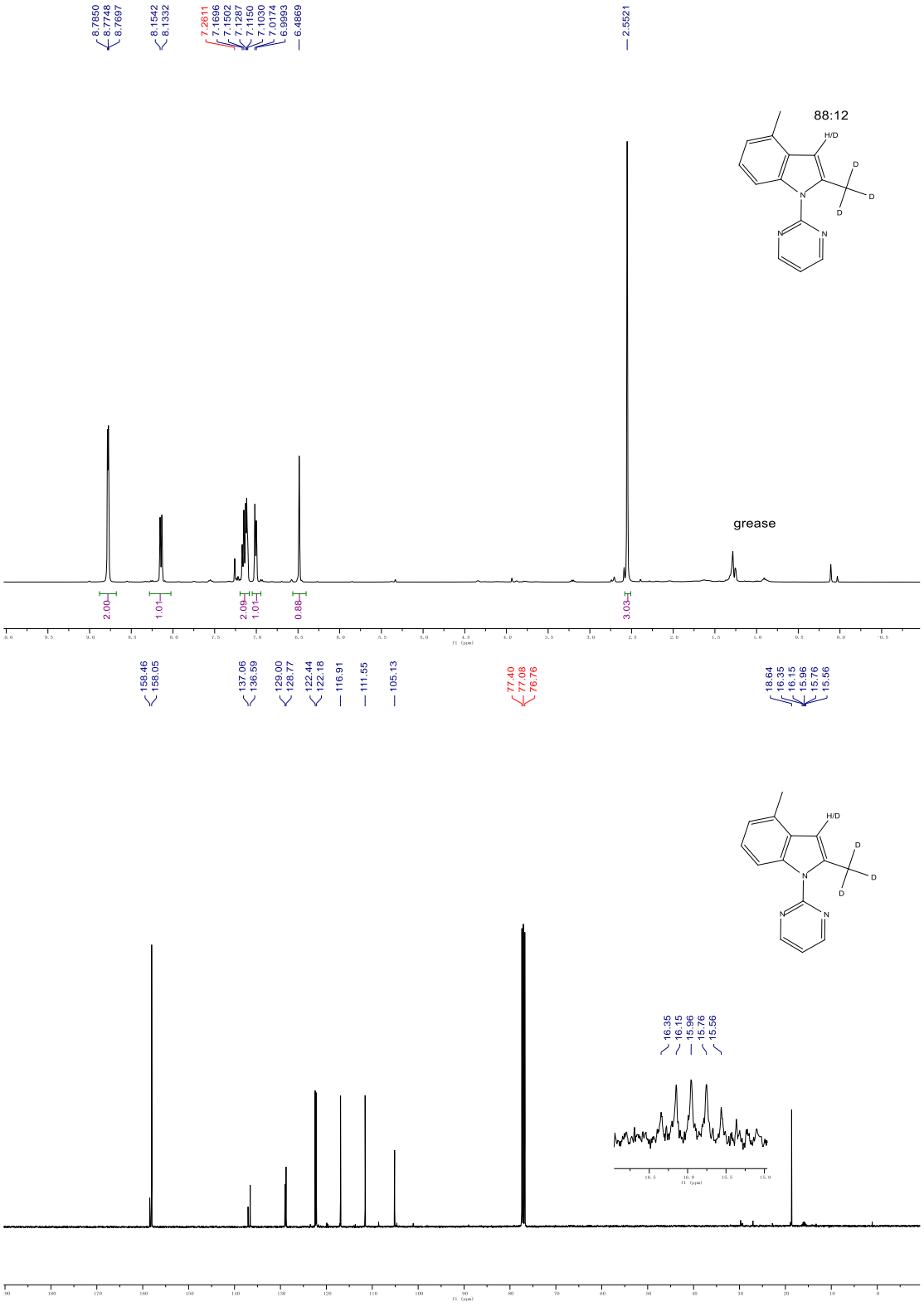
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **6d** in $CDCl_3$



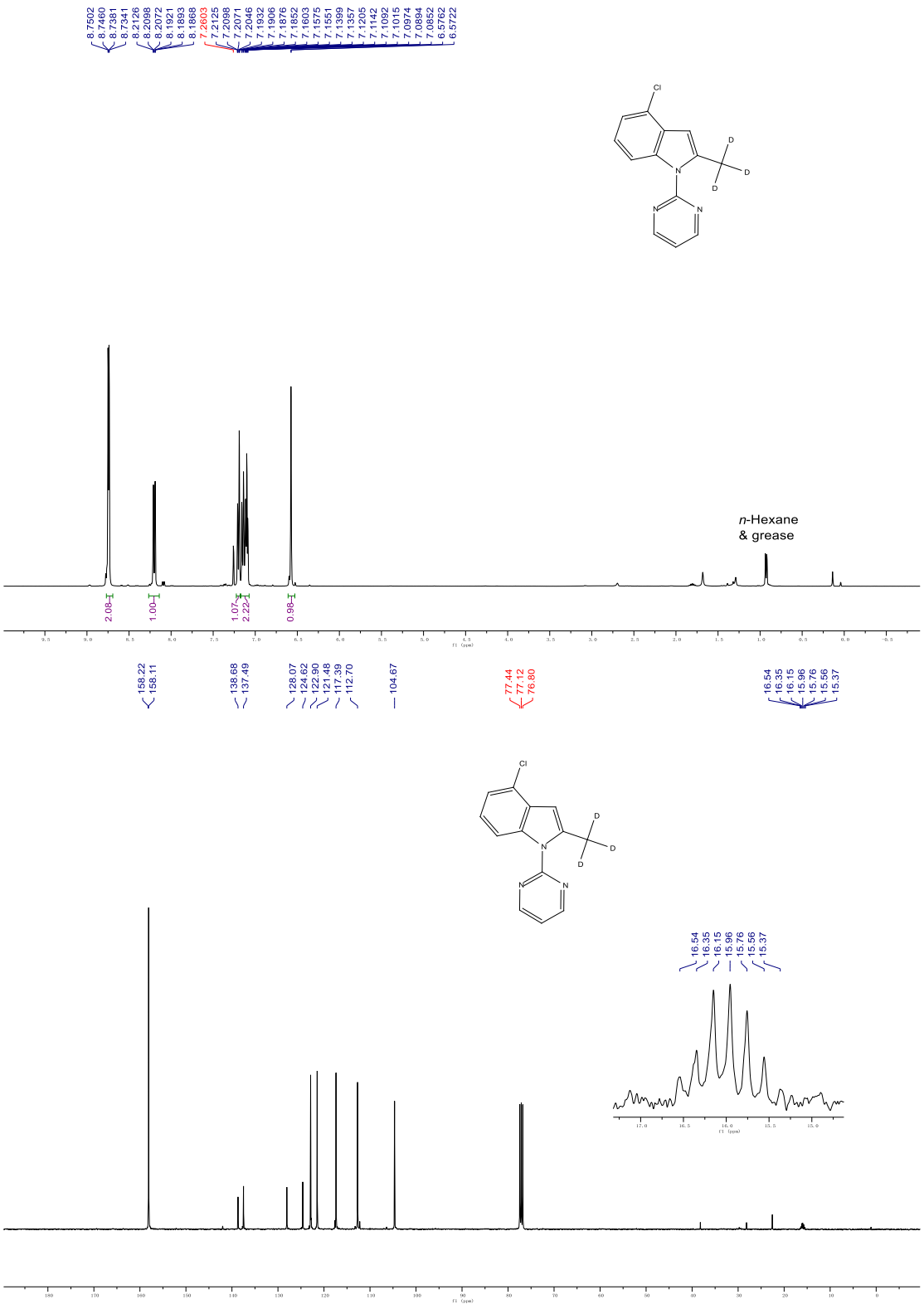
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **6e** in $CDCl_3$



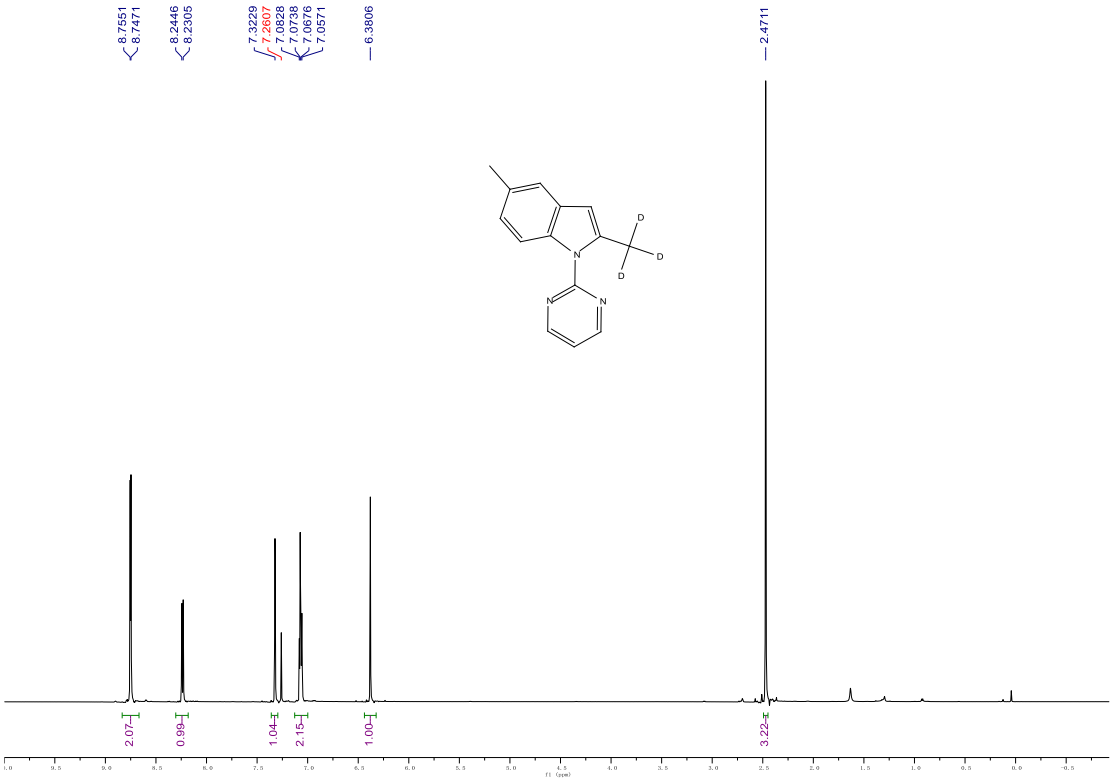
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **6f** in $CDCl_3$

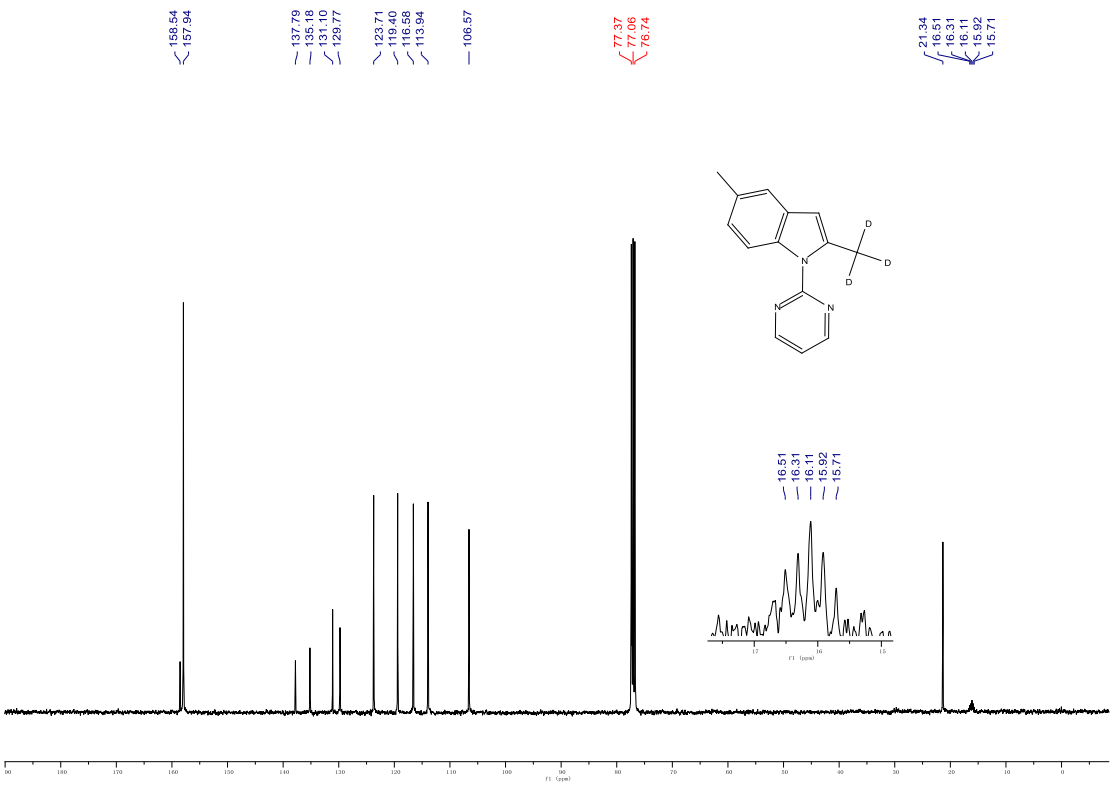


^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **6g** in $CDCl_3$

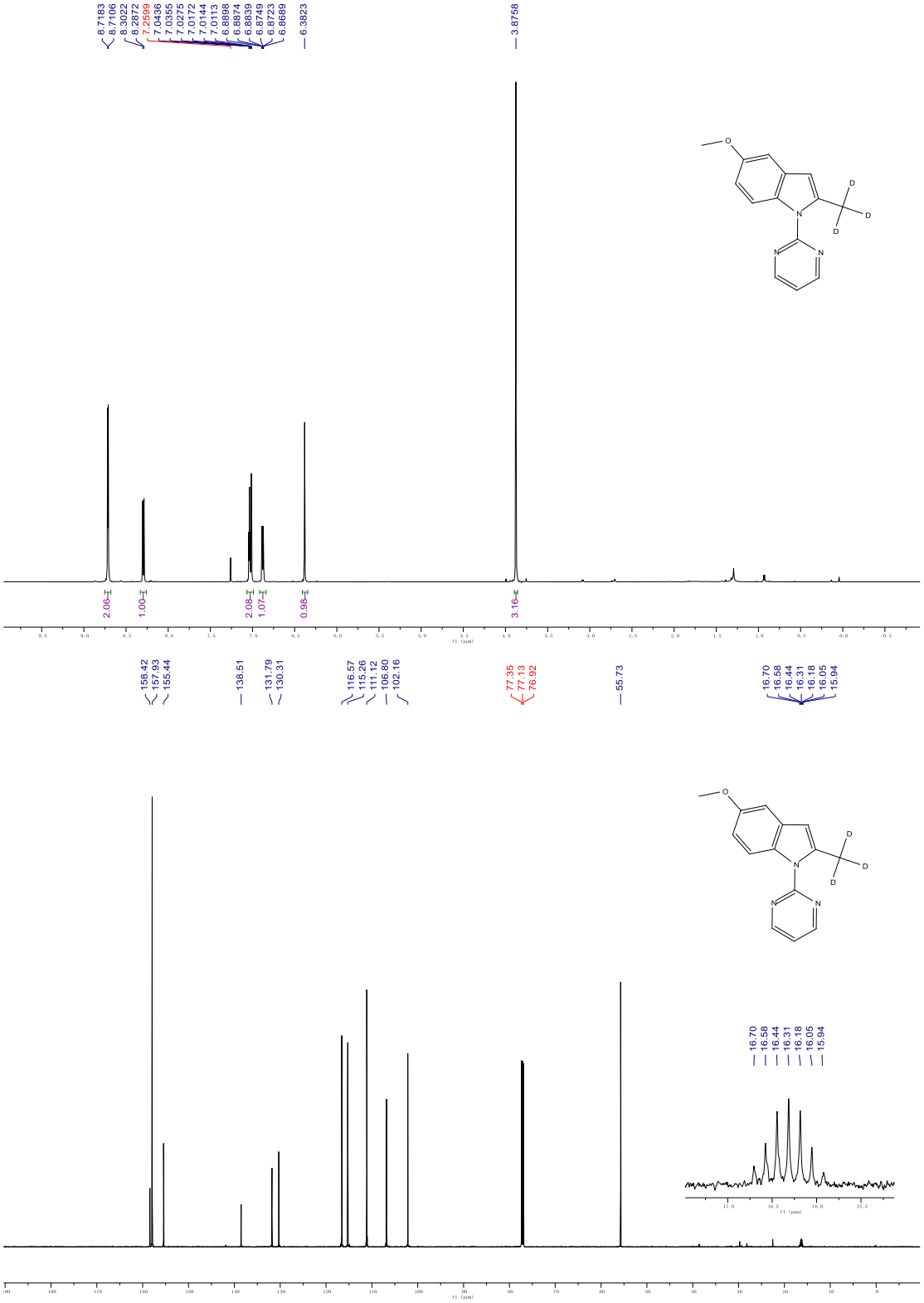


^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **6h** in $CDCl_3$

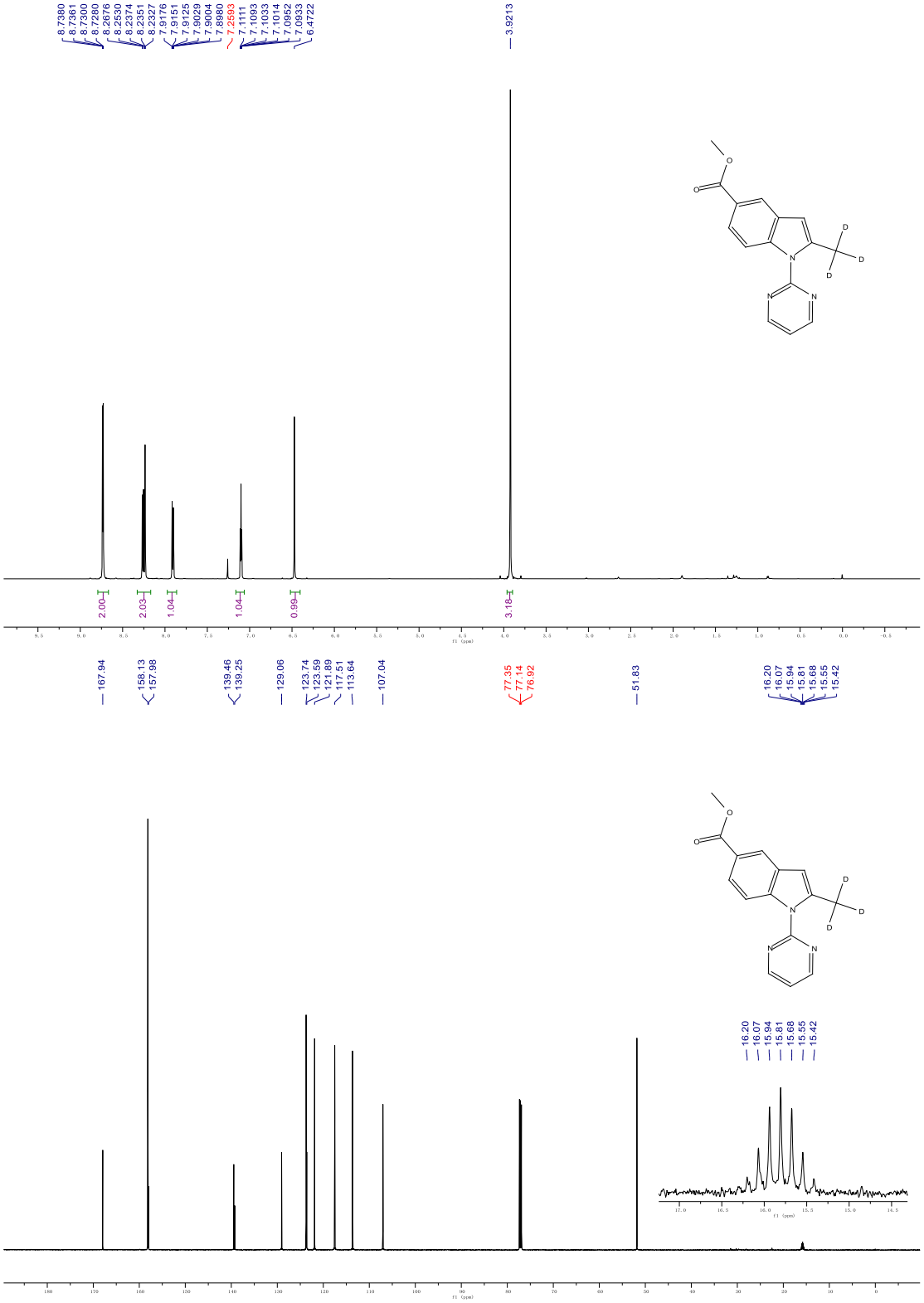




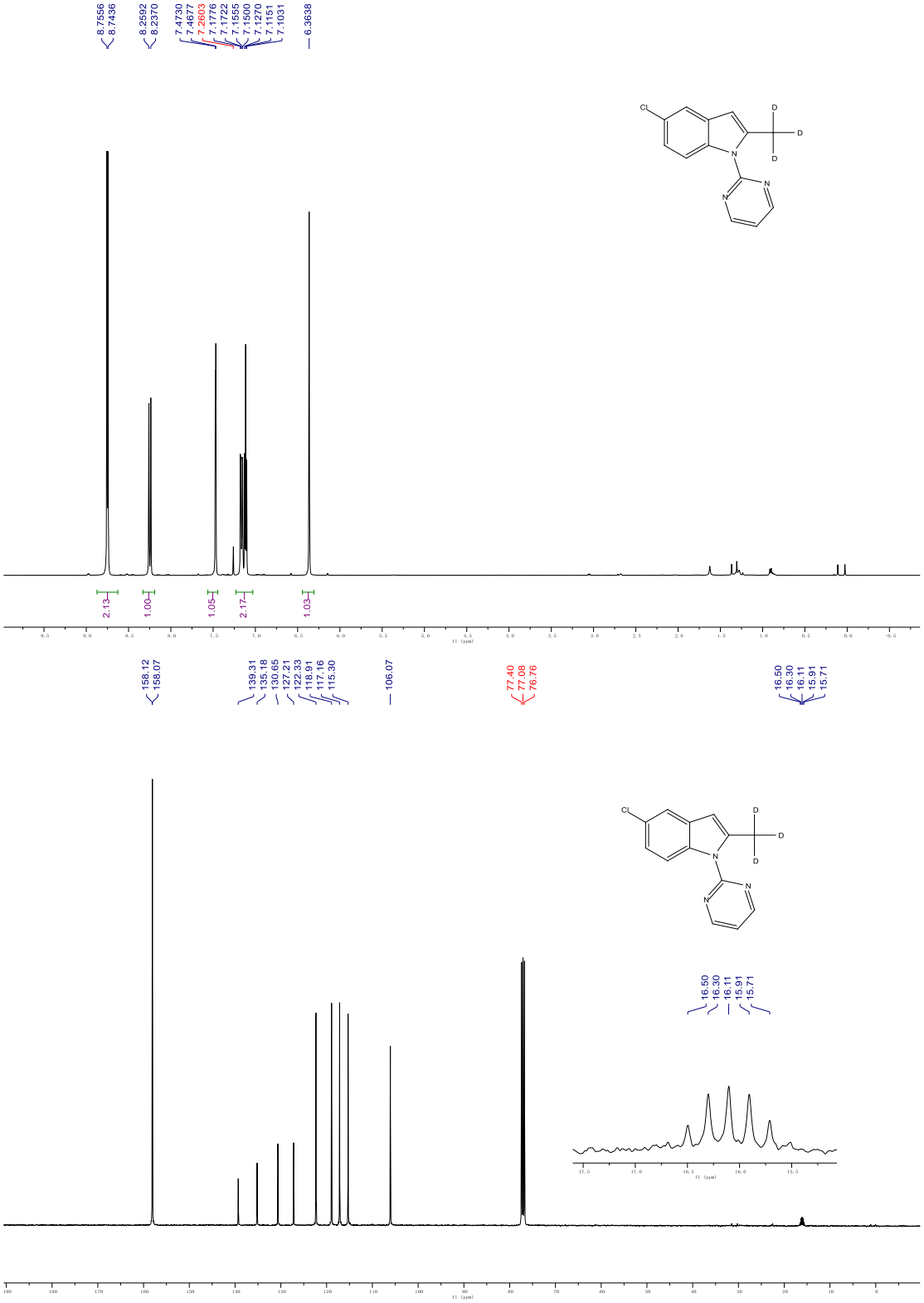
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **6i** in $CDCl_3$



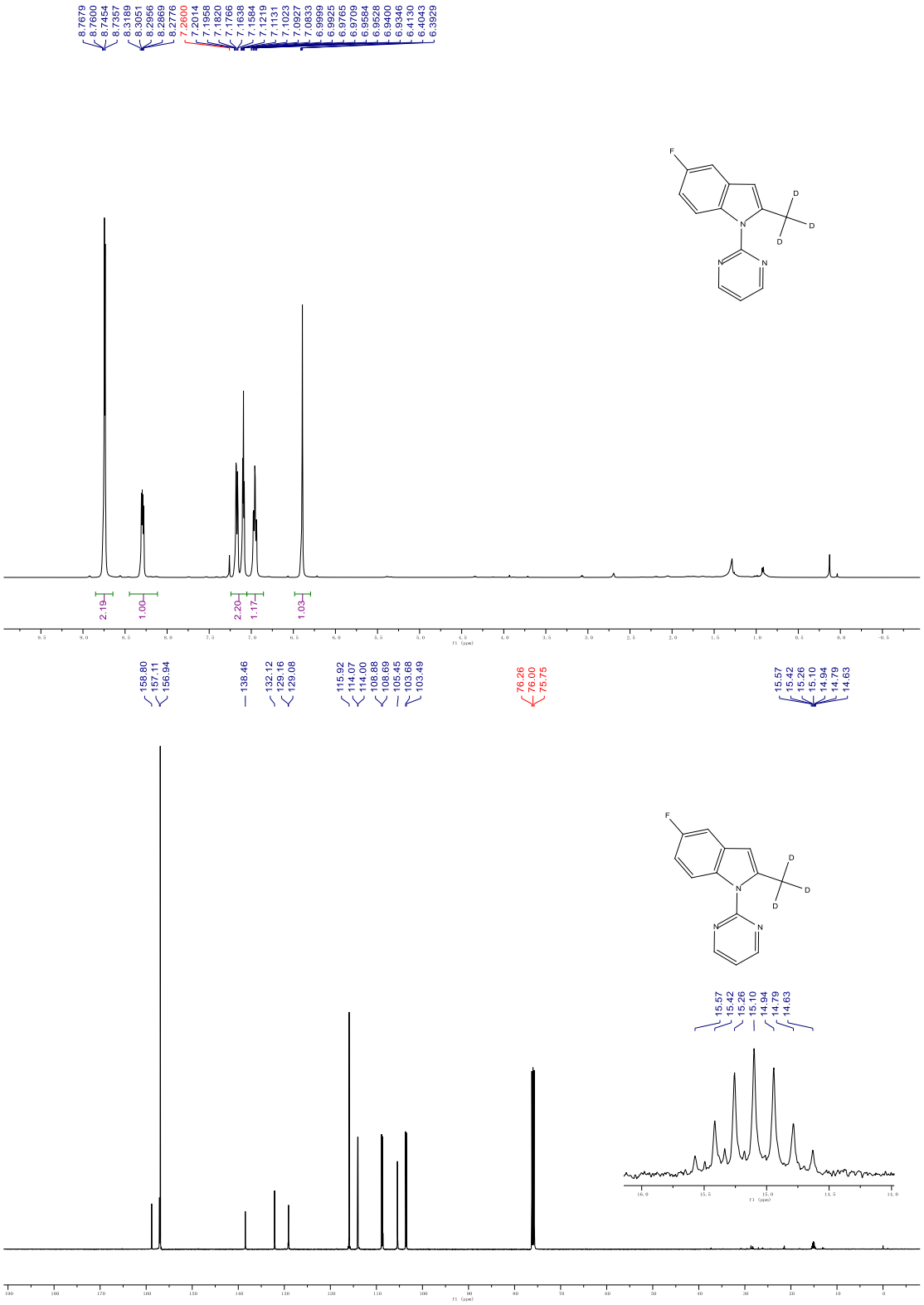
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **6j** in $CDCl_3$



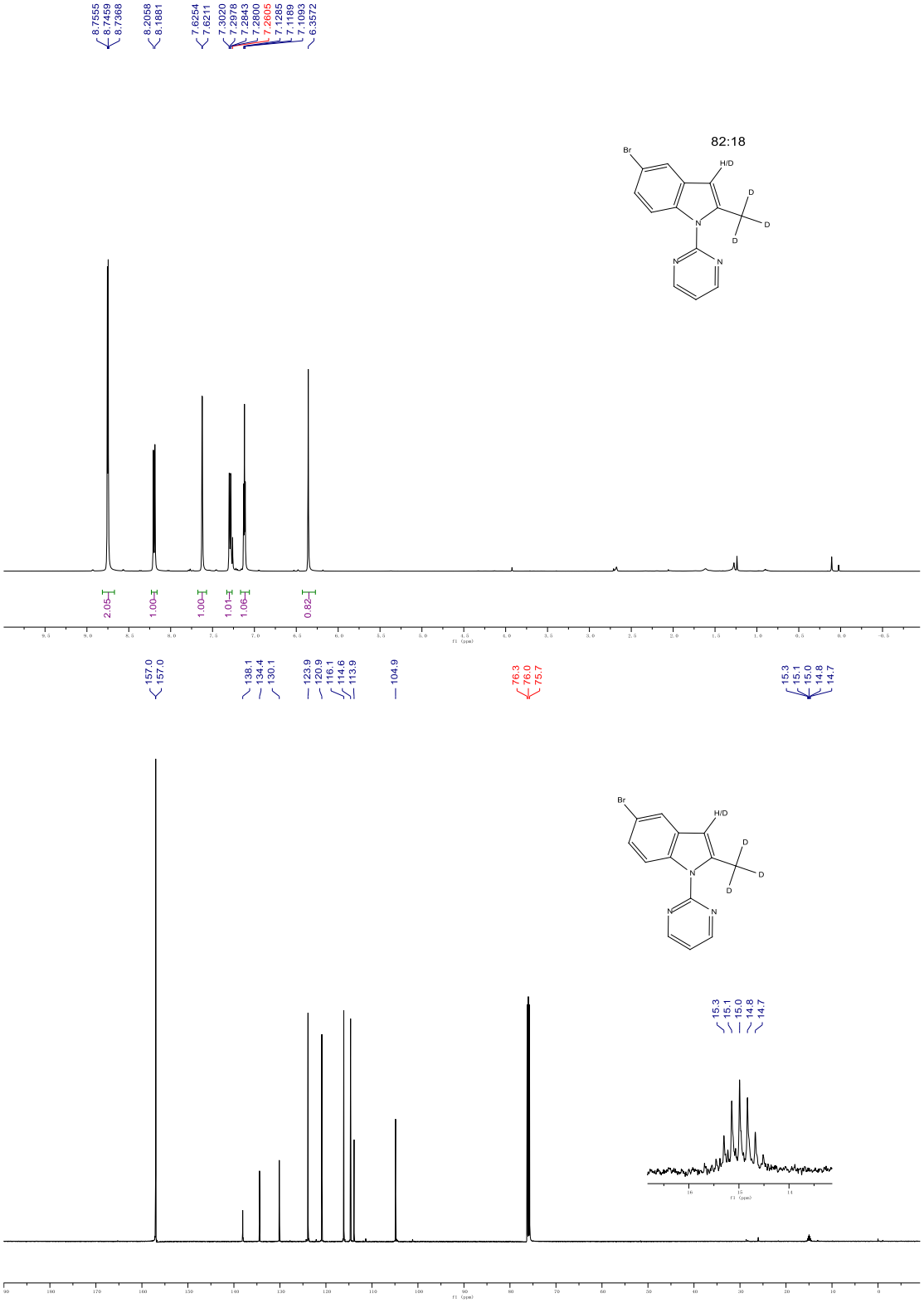
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **6k** in $CDCl_3$



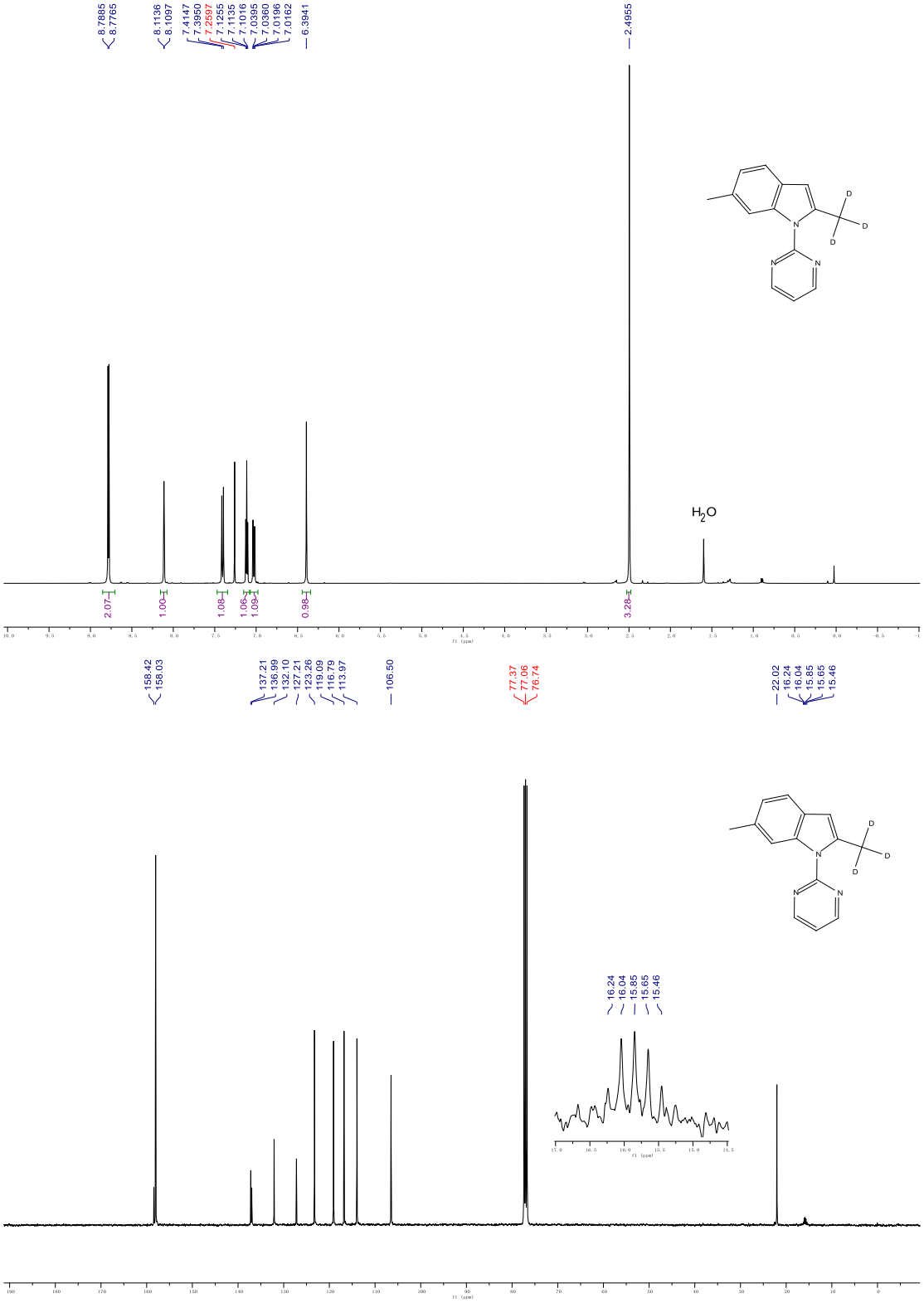
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **6l** in $CDCl_3$



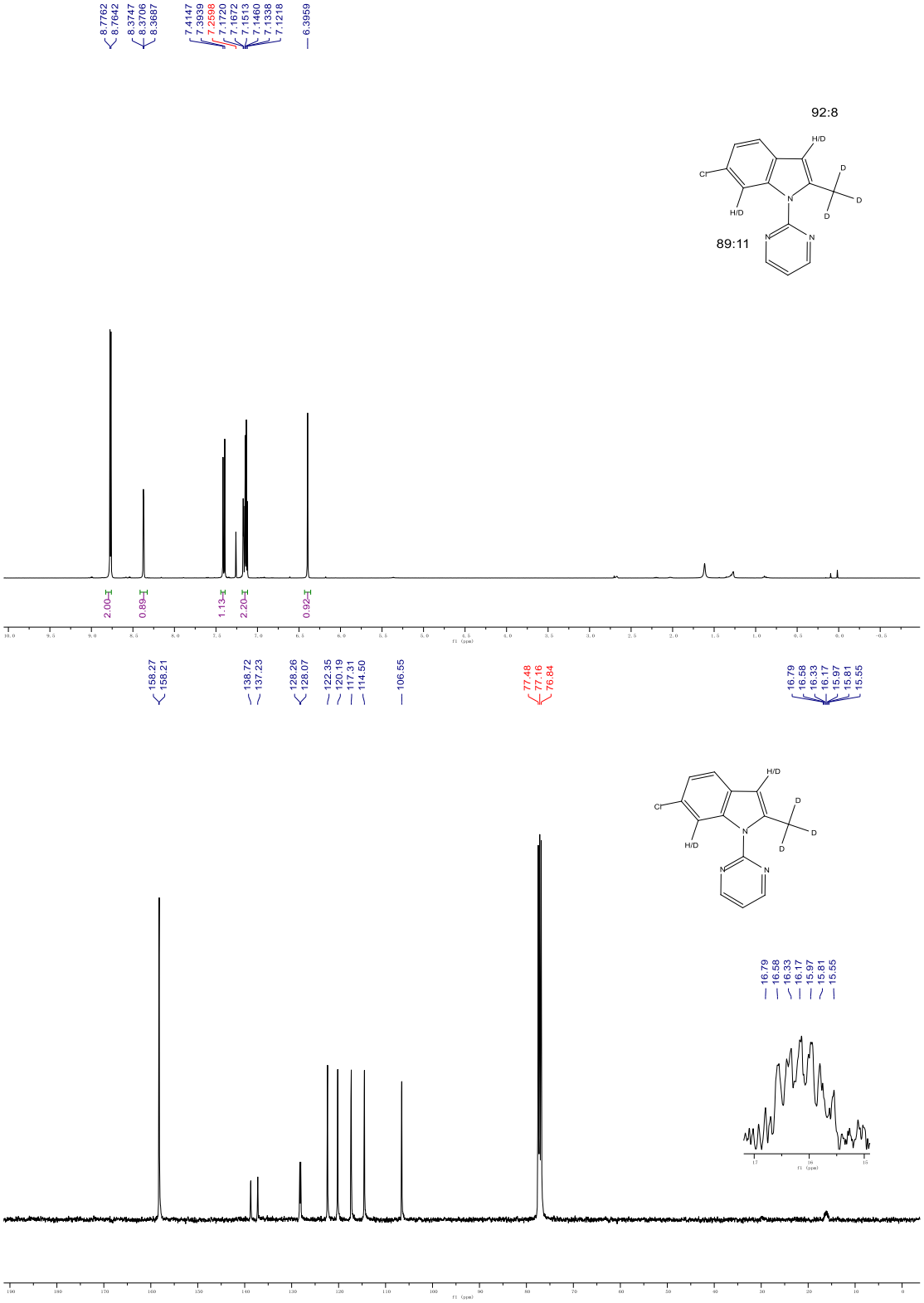
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **6m** in $CDCl_3$



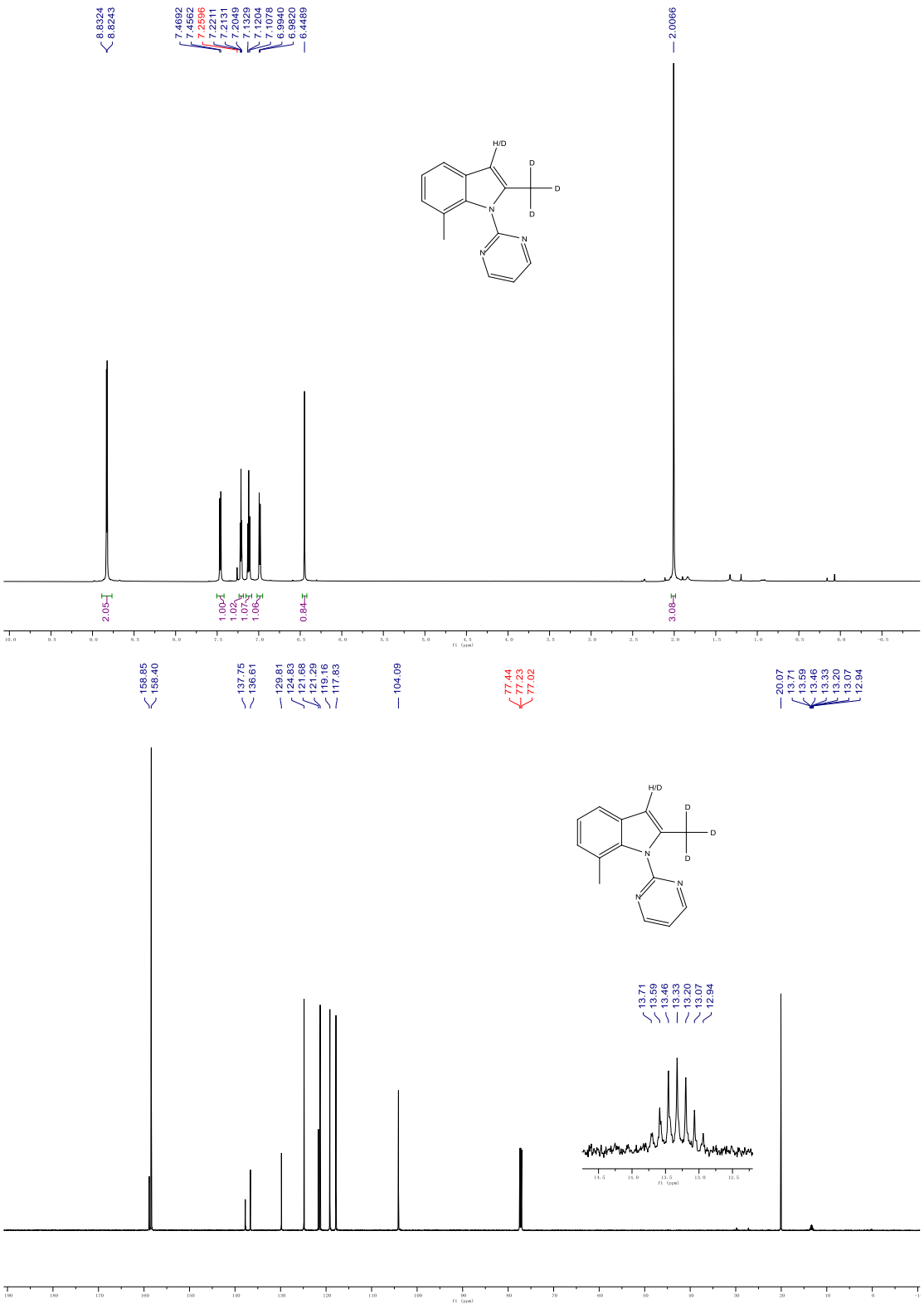
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **6n** in $CDCl_3$



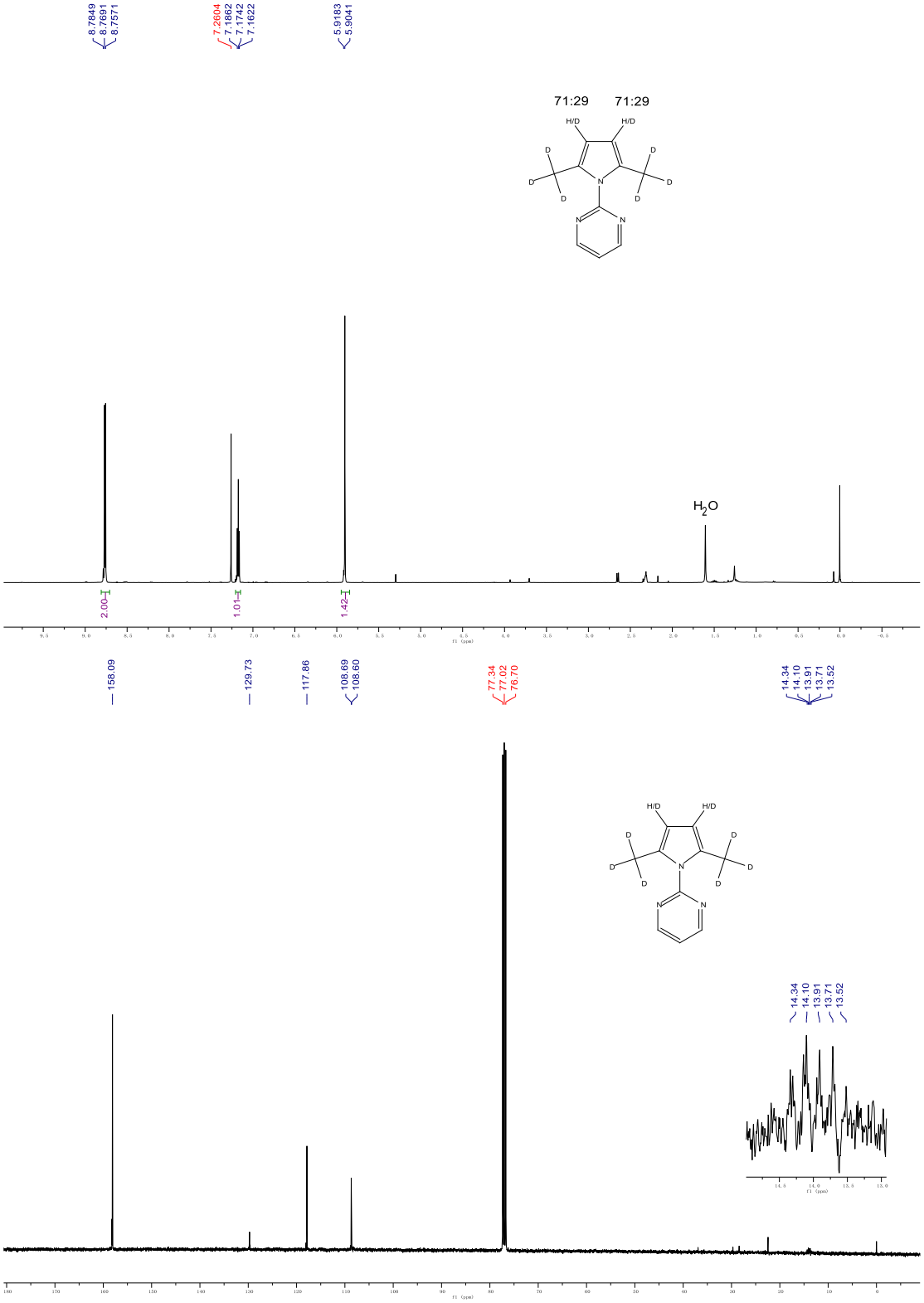
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **6o** in $CDCl_3$



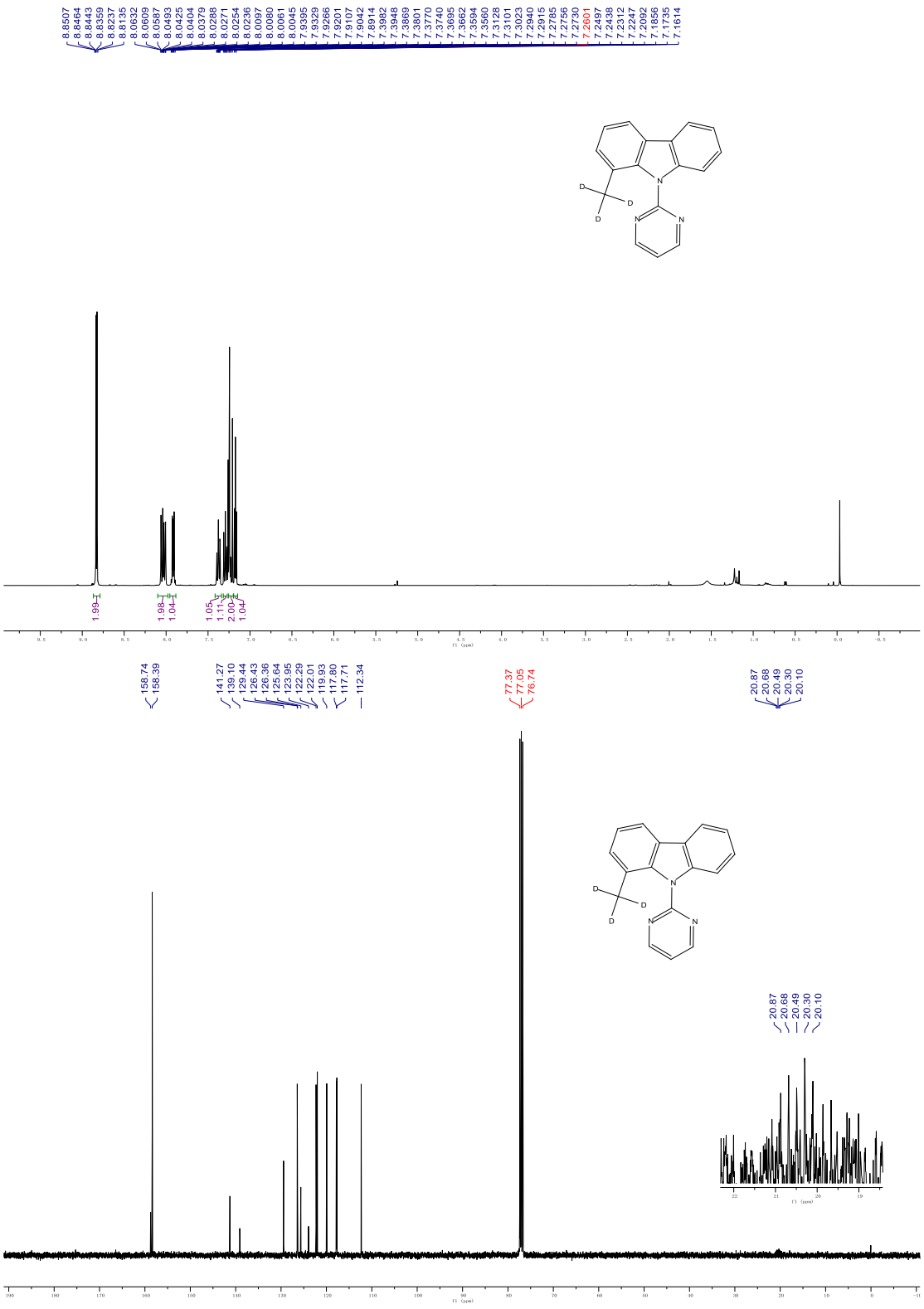
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **6p** in $CDCl_3$



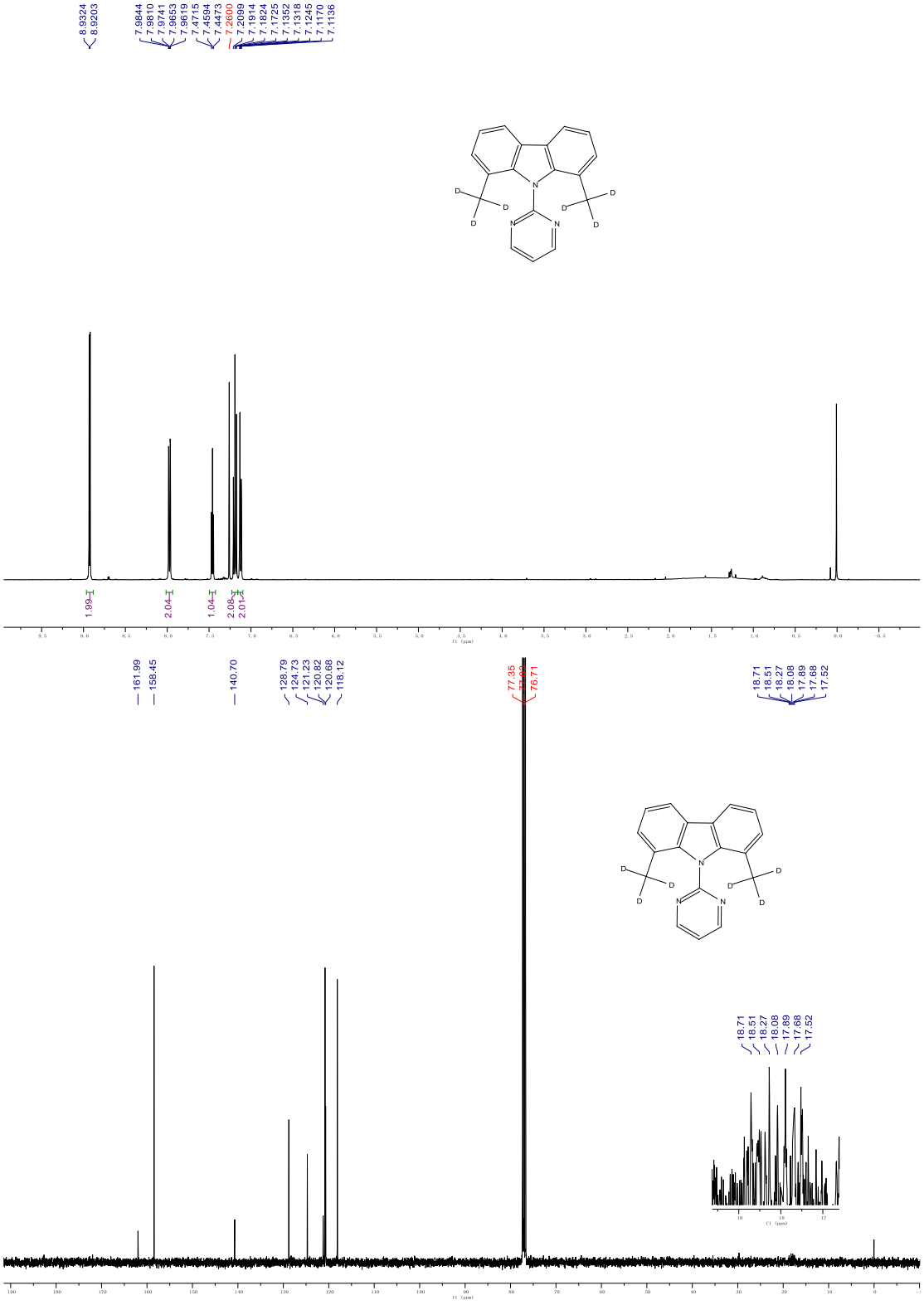
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **7a** in $CDCl_3$



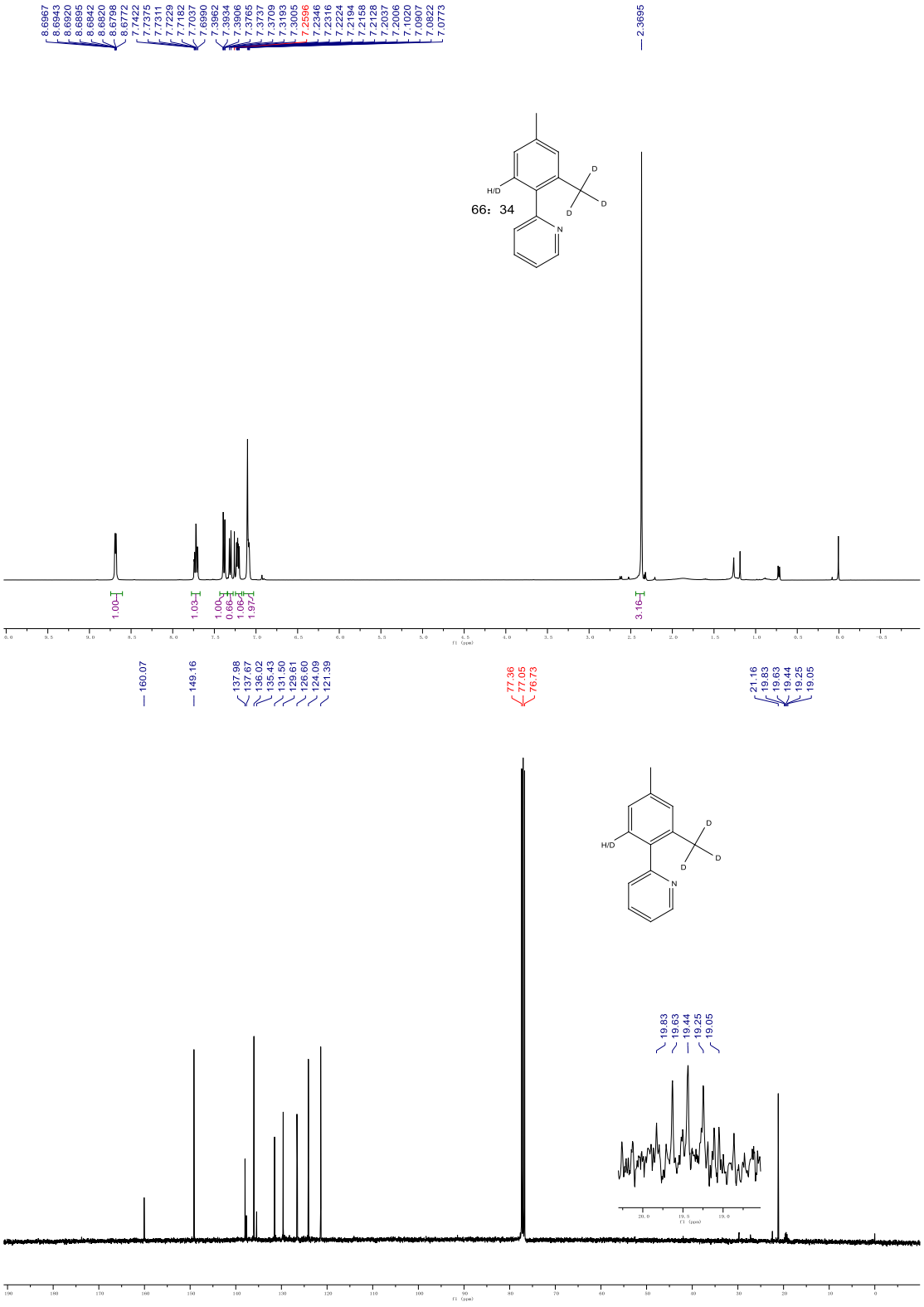
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **7b** in $CDCl_3$



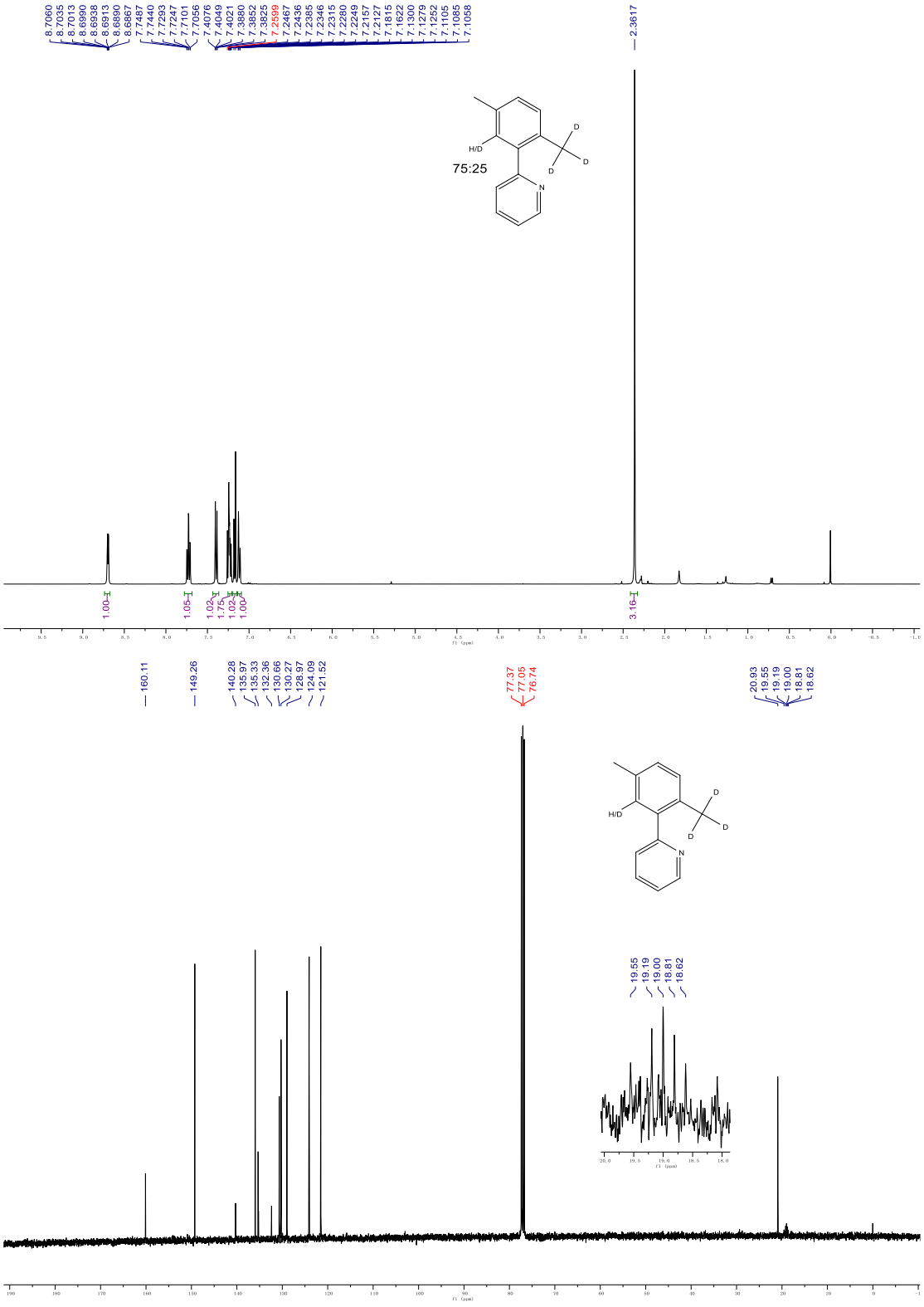
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **7c** in $CDCl_3$



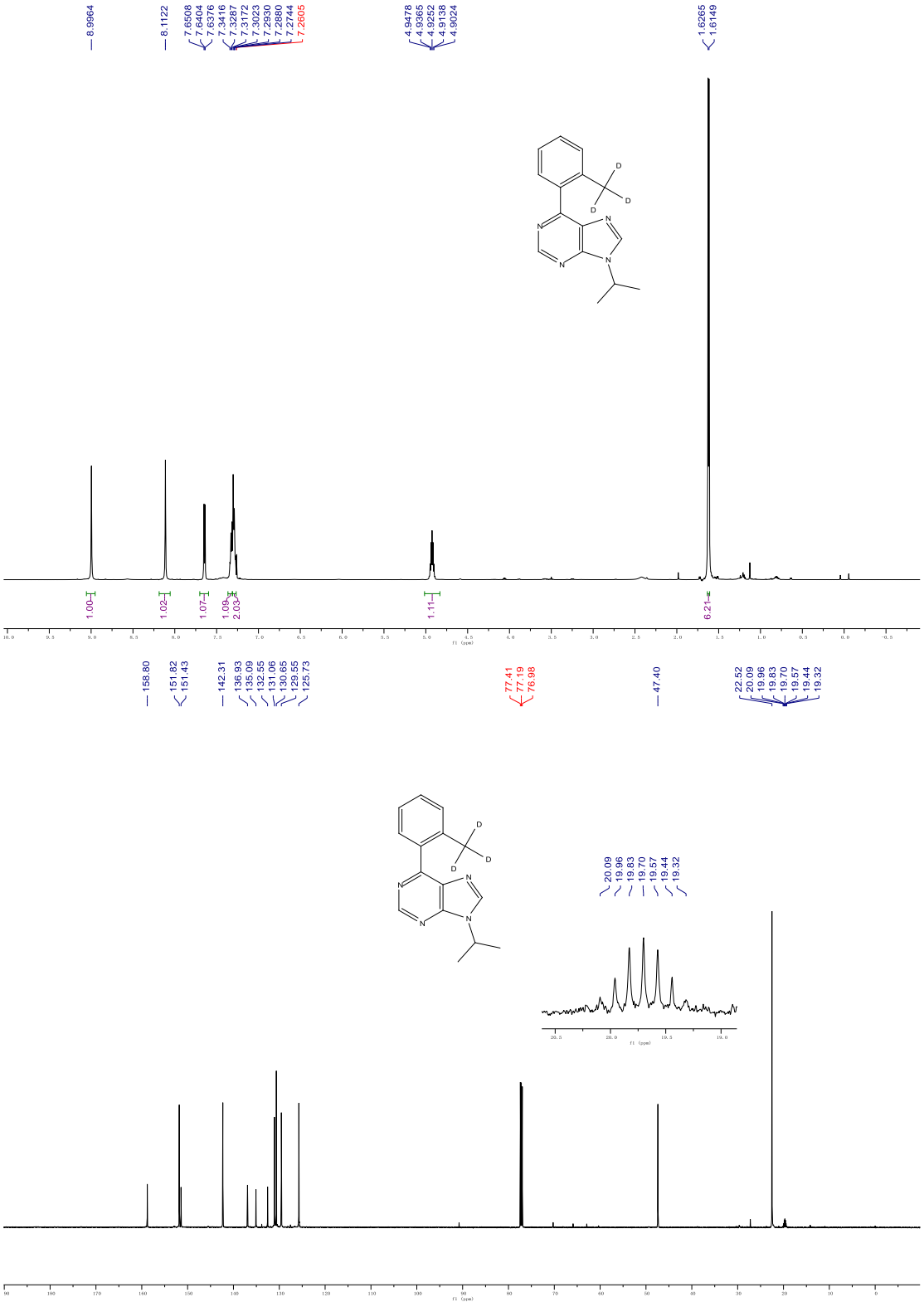
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **7d** in $CDCl_3$



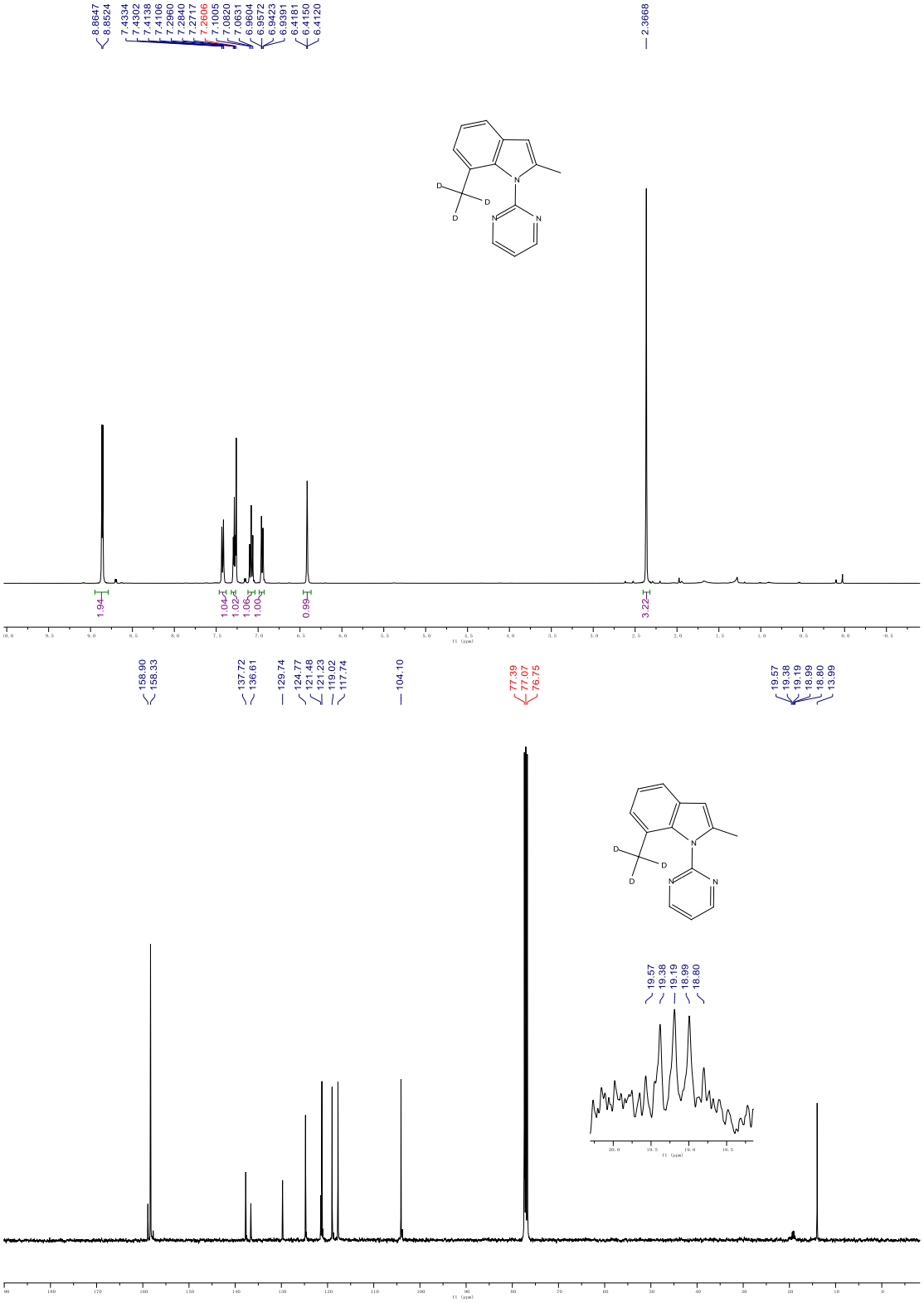
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **7e** in $CDCl_3$



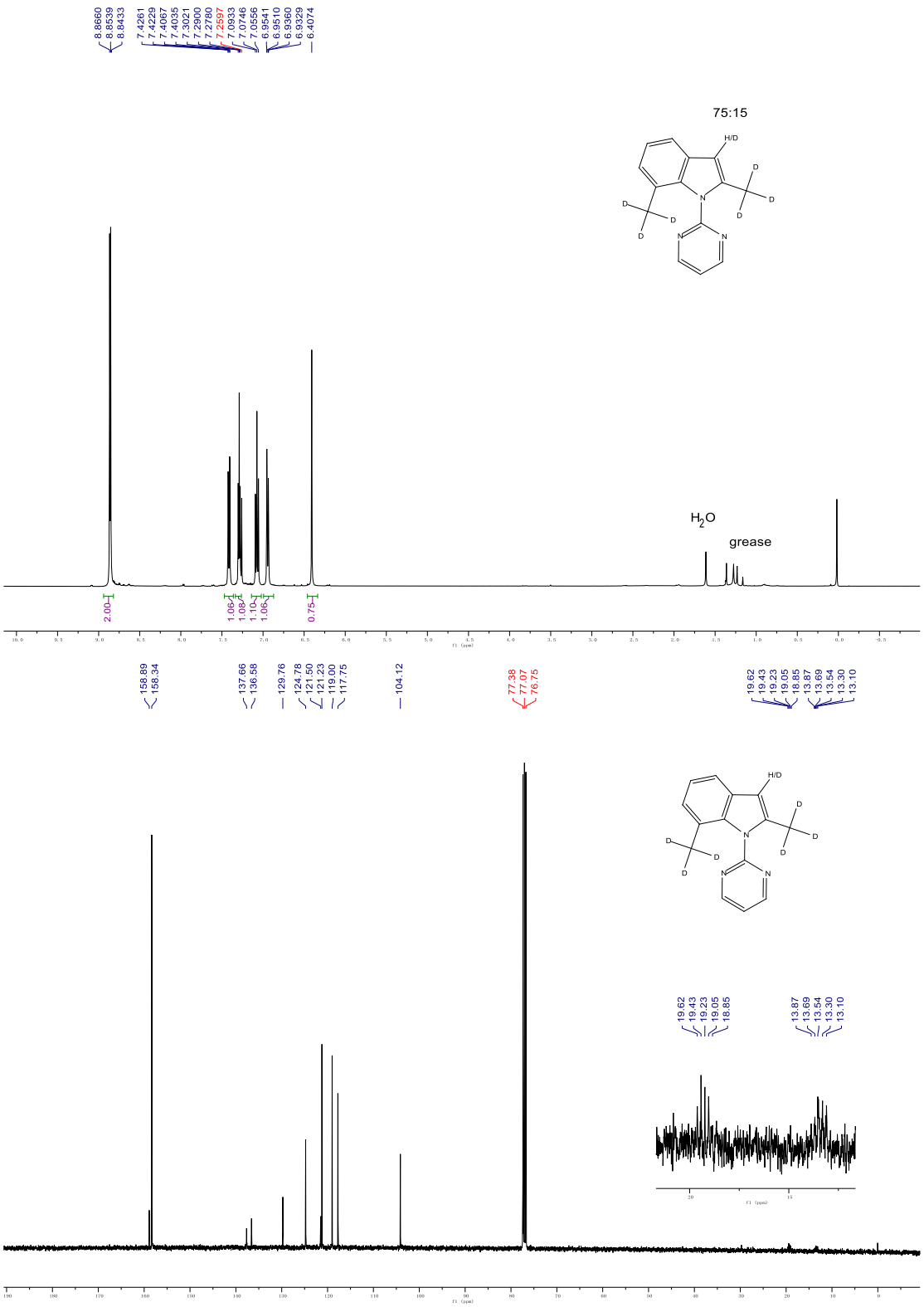
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **7f** in $CDCl_3$



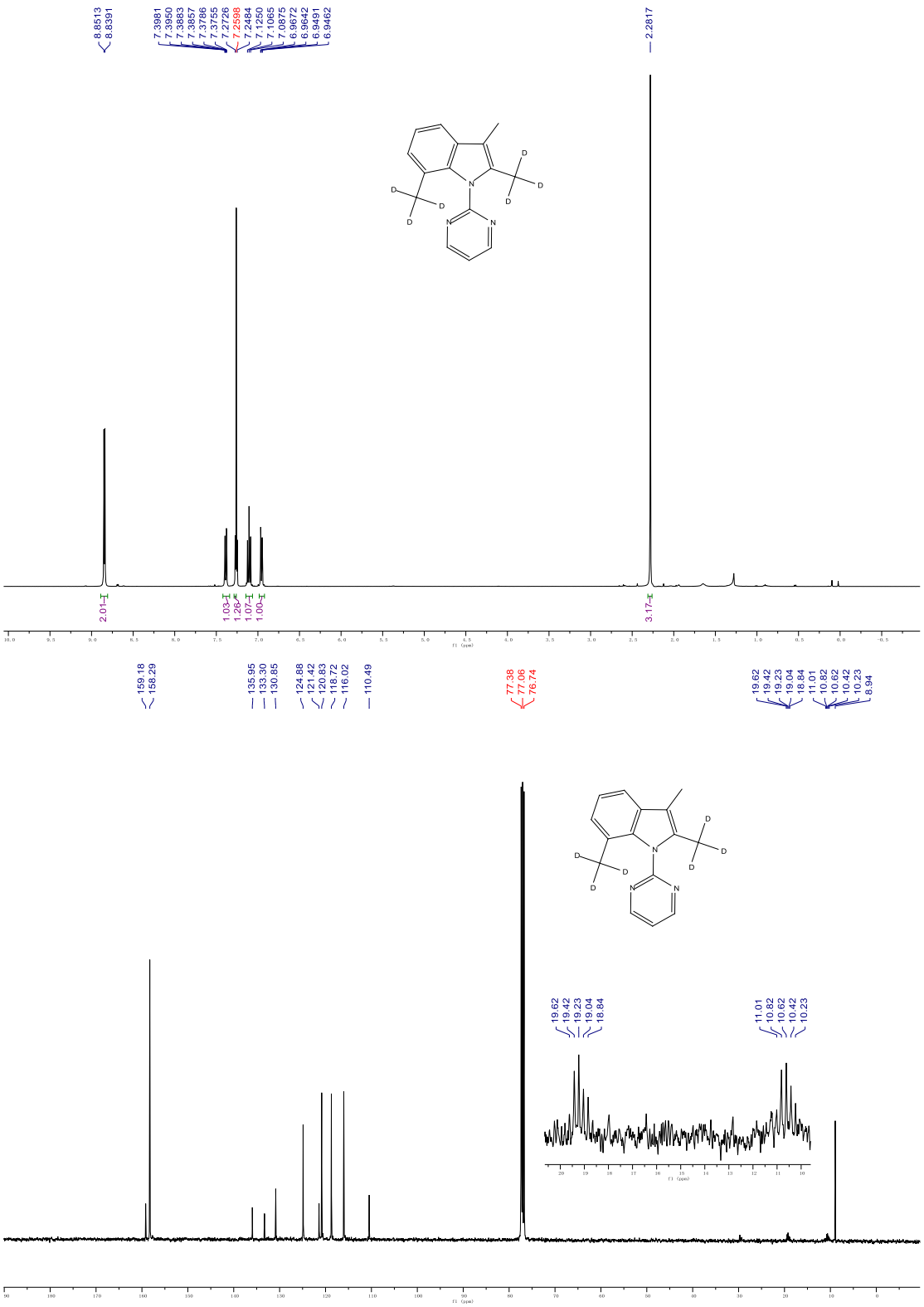
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **8a** in $CDCl_3$



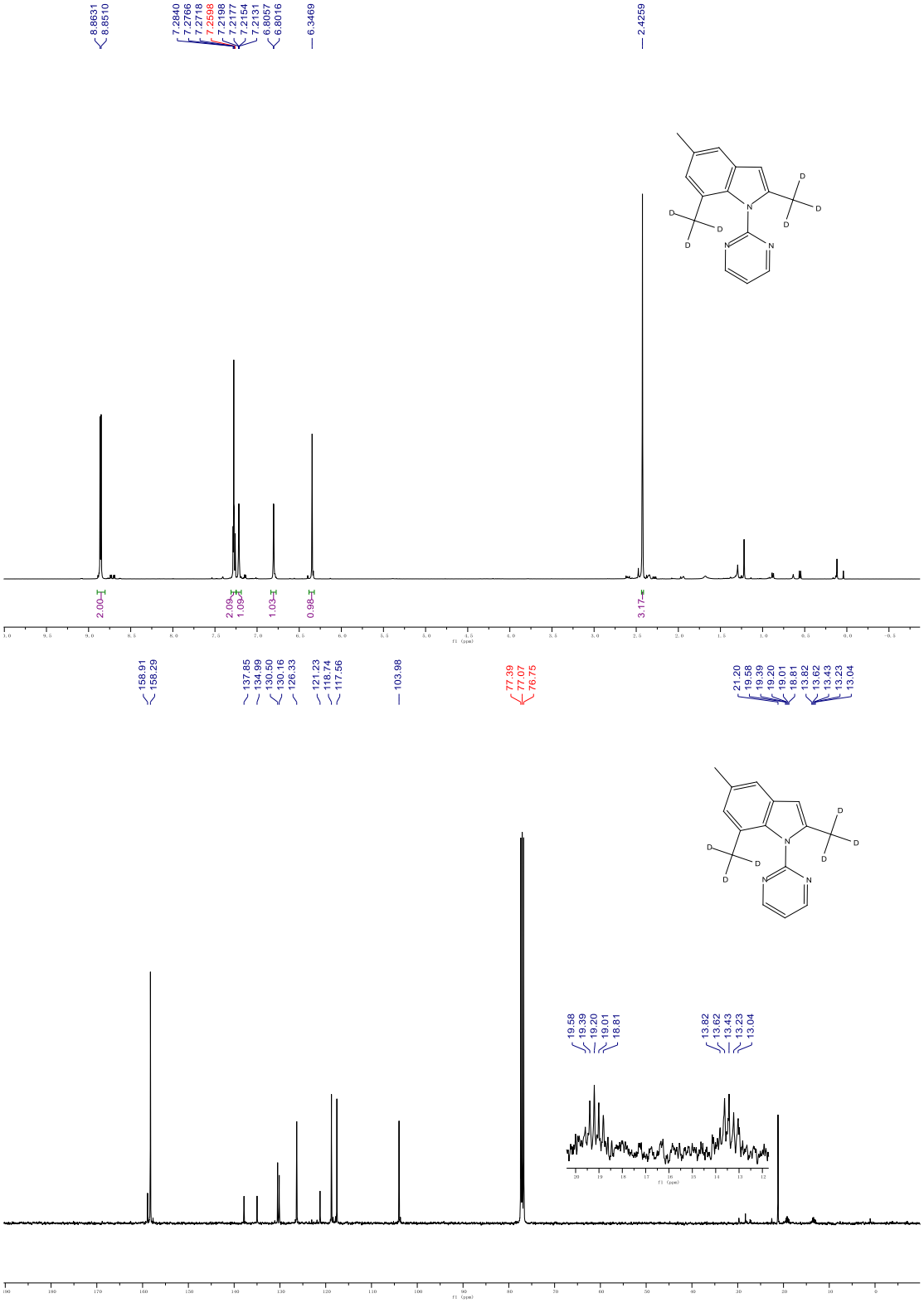
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **8b** in $CDCl_3$



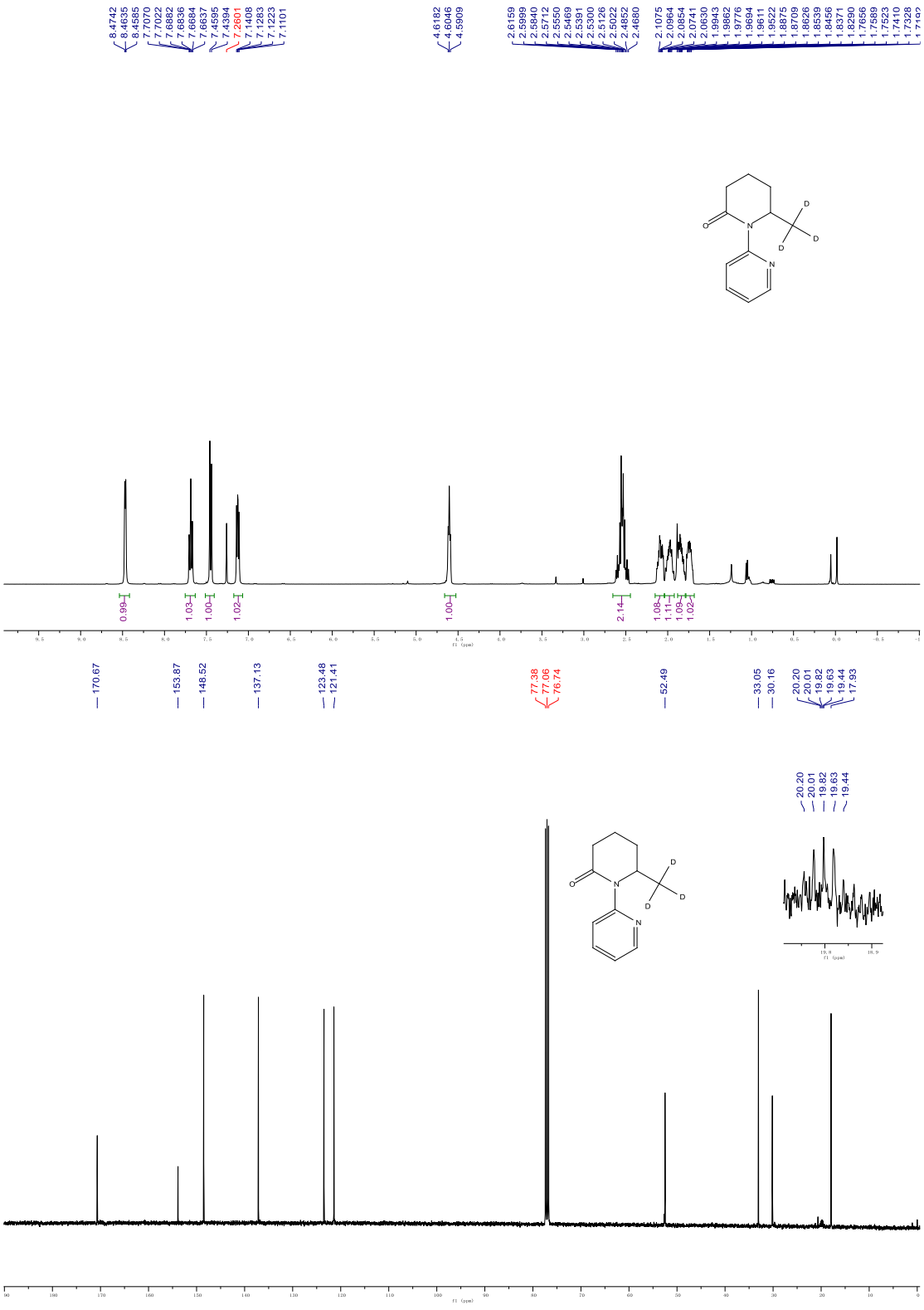
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **8c** in $CDCl_3$



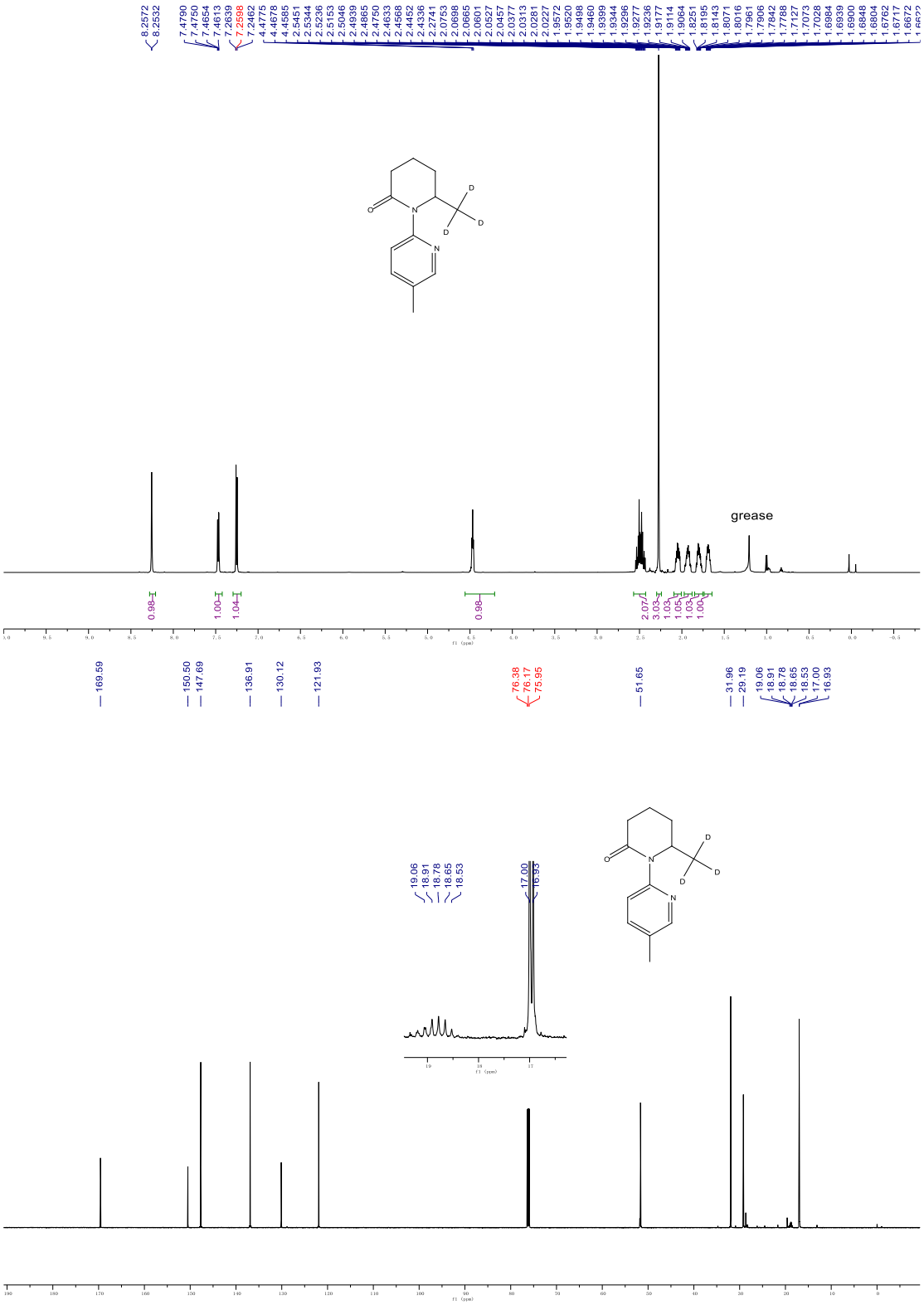
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **8d** in $CDCl_3$



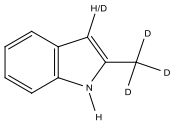
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **9** in $CDCl_3$

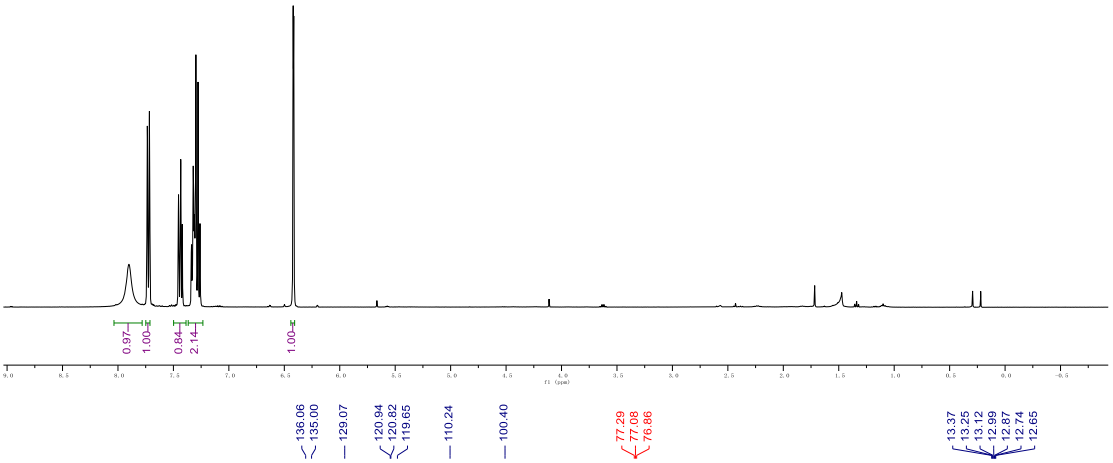


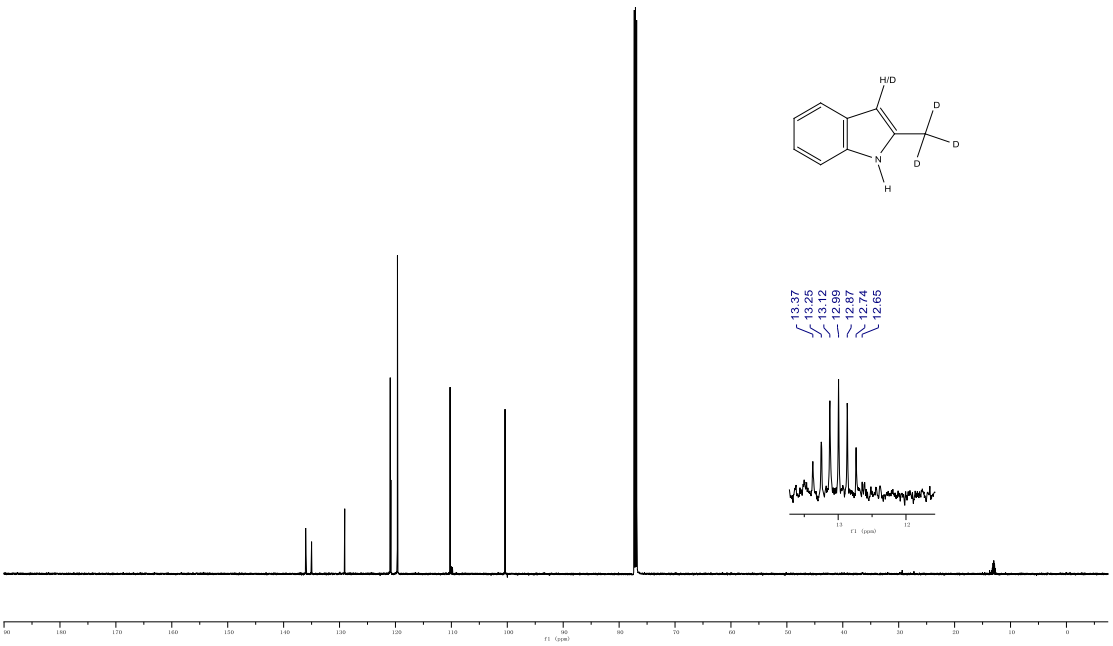
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **10** in $CDCl_3$



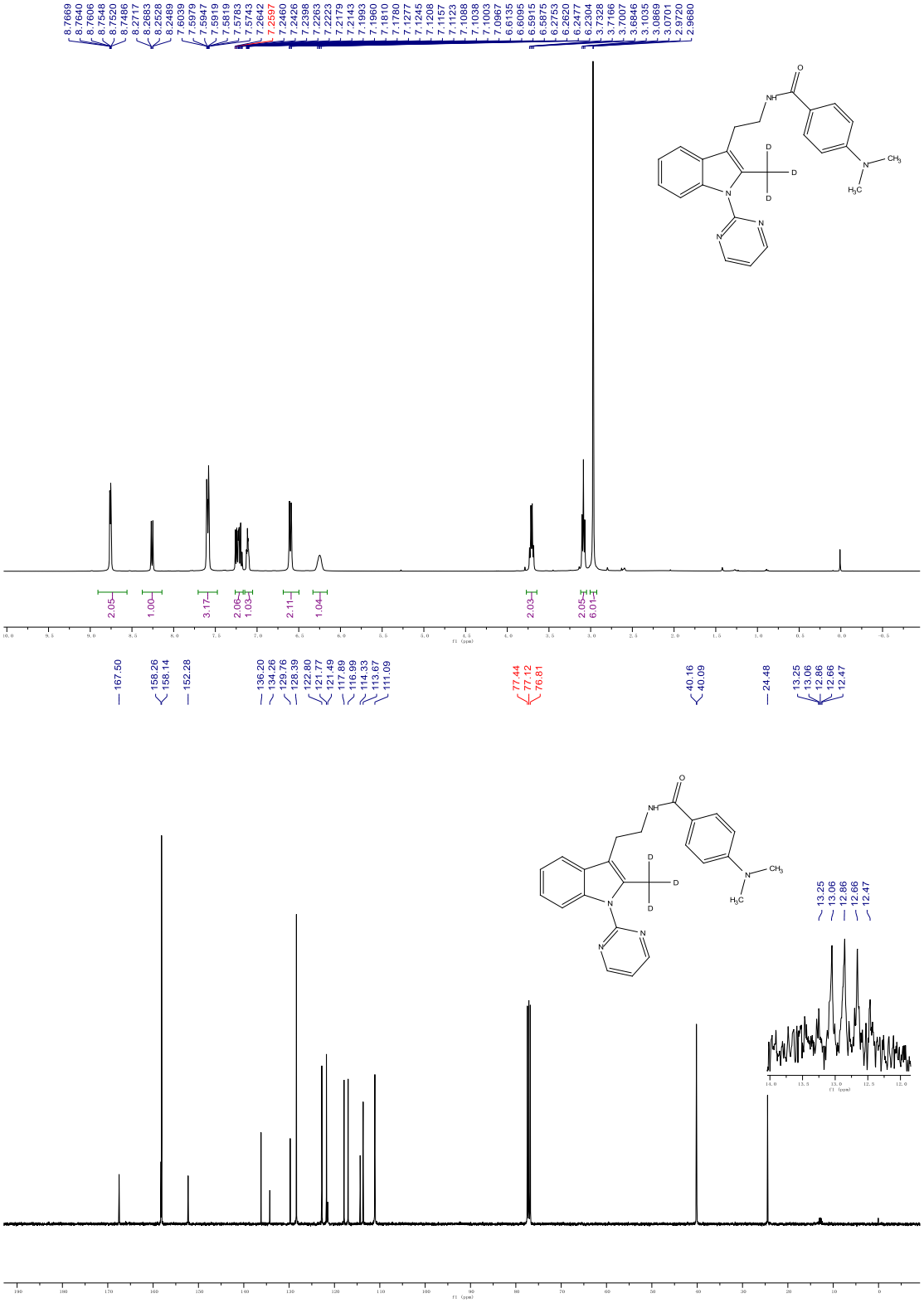
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **11** in $CDCl_3$



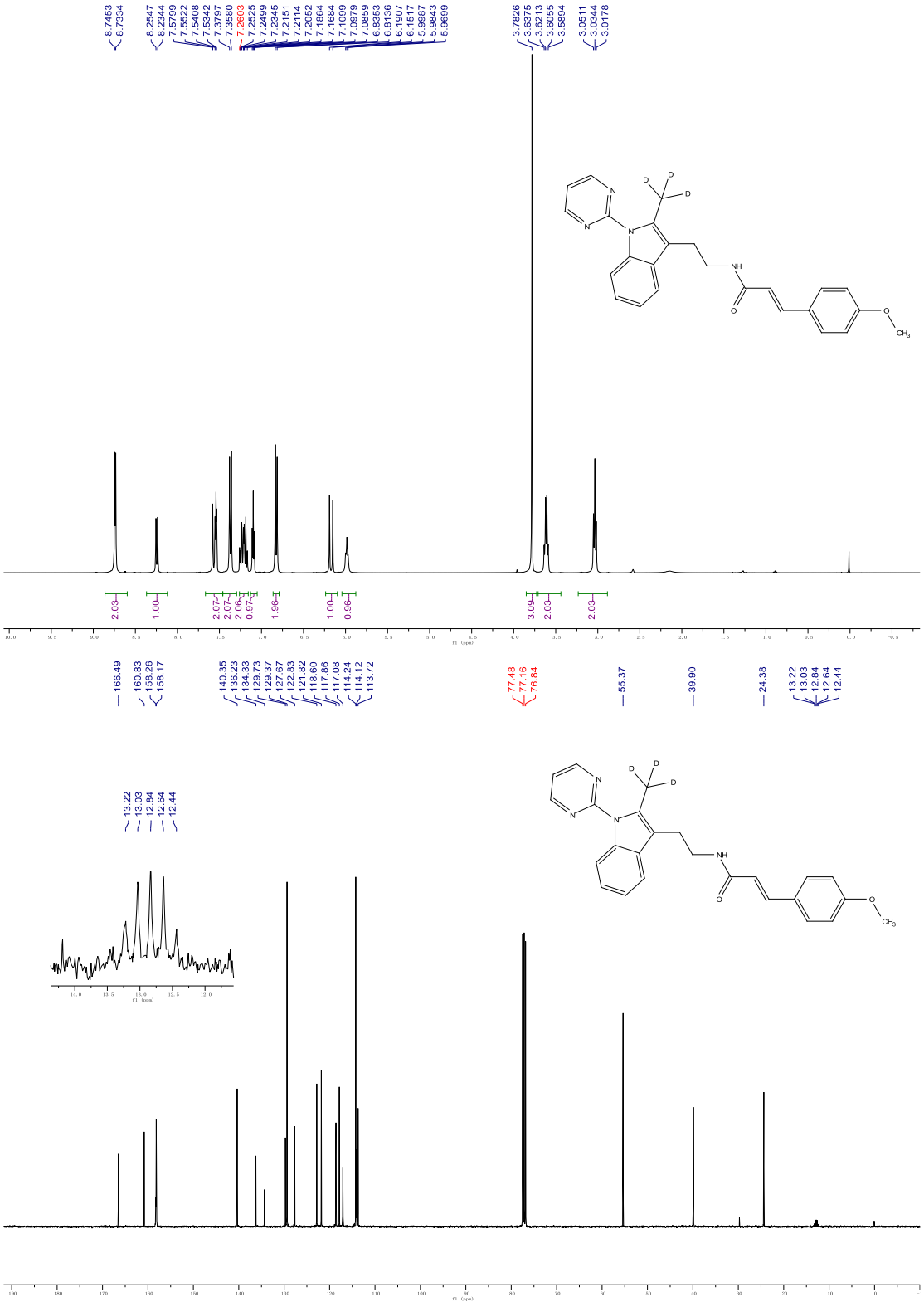




^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **12** in $CDCl_3$



^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compound **13** in $CDCl_3$



9. X-ray Crystal Structure Determination

Single crystals of **3q** (light yellow block-like specimen of $C_{12}H_6D_3F_3N_2O$) and **7f** (light yellow block-like specimen of $C_{15}H_{13}D_3N_4$) was obtained by slow diffusion of hexane into a dichloromethane solution at 0 ℃.

Single crystal diffraction data for **3q** was collected at 200.01 K and **7f** was collected at 293(2) K. All single crystal diffraction data were collected using an IμS micro-focus sealed X-ray tube with Mo Kα radiation (λ = 0.71073 Å) on a Bruker D8 venture Kappa Duo diffractometer equipped with a PHOTON 100 detector. Low-temperature holding was achieved by a Cryostream Cooler (Oxford Cryosystems). All the data were collected 0.5 degree per step and using the ω scan mode. Frames were integrated using the Bruker SAINT software. Semi-empirical absorption correction was applied with the SADABS program.

(1) X-ray crystal structure of **3q**

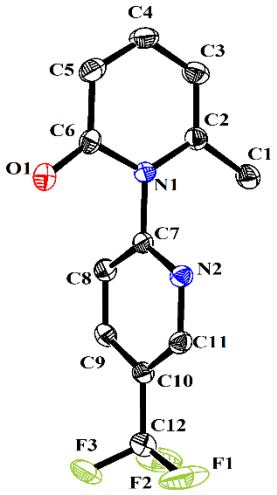


Table 1 Crystal data and structure refinement for 3q.	
Identification code	mo_ZHQ2018100201_0m
Empirical formula	$C_{12}H_9F_3N_2O$
Formula weight	254.21
Temperature/K	200.01
Crystal system	monoclinic
Space group	C2/c
a/Å	21.891(5)
b/Å	11.795(2)
c/Å	8.809(2)
α/°	90

β/°	93.038(8)
γ/°	90
Volume/Å^3	2271.3(8)
Z	8
ρ_{calc}g/cm^3	1.487
μ/mm^{-1}	0.130
F(000)	1040.0
Crystal size/mm^3	0.31 ×0.29 ×0.26
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	5.994 to 55.164
Index ranges	-26 ≤ h ≤ 28, -13 ≤ k ≤ 15, -11 ≤ l ≤ 11
Reflections collected	10800
Independent reflections	2598 [R_{int} = 0.0772, R_{sigma} = 0.0727]
Data/restraints/parameters	2598/6/192
Goodness-of-fit on F^2	0.881
Final R indexes [I>=2σ (I)]	R_1 = 0.0633, wR_2 = 0.1892
Final R indexes [all data]	R_1 = 0.1206, wR_2 = 0.2599
Largest diff. peak/hole / e Å^{-3}	0.26/-0.32

(2) X-ray crystal structure of **7f**

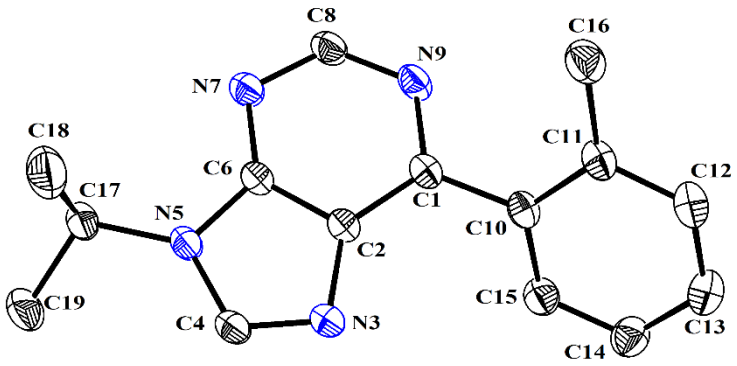


Table 1 Crystal data and structure refinement for 7f.	
Identification code	exp_5929
Empirical formula	$C_{15}H_{17}N_4$
Formula weight	253.32
Temperature/K	293(2)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	12.5969(7)

b/Å	7.4254(3)
c/Å	15.4359(8)
α/°	90
β/°	113.168(7)
γ/°	90
Volume/Å^3	1327.40(13)
Z	4
ρ_{calc}g/cm^3	1.268
μ/mm^{-1}	0.618
F(000)	540.0
Crystal size/mm^3	0.45 × 0.35 × 0.20
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	7.634 to 148.096
Index ranges	-14 ≤ h ≤ 15, -8 ≤ k ≤ 8, -19 ≤ l ≤ 19
Reflections collected	7148
Independent reflections	2547 [R_{int} = 0.0259, R_{sigma} = 0.0301]
Data/restraints/parameters	2547/0/176
Goodness-of-fit on F^2	1.094
Final R indexes [I>=2σ (I)]	R_1 = 0.0435, wR_2 = 0.1257
Final R indexes [all data]	R_1 = 0.0512, wR_2 = 0.1321
Largest diff. peak/hole / e Å^{-3}	0.18/-0.56