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Supporting Information

Potassium *tert*-Butoxide Promoted Regioselective Deuteration of Pyridine

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Contents

1. General Information

Experiments and Reagents

Unless noted otherwise, all experiments were carried out under the protection of nitrogen atmosphere, with oven-*d*ried glassware and magnetic stirring bar. Temperature is reported as the temperature of the metal heating module, with the height of stirring reaction mixture lower than heating module.
Commercially available reagents were purchased from Aladdin, Bidepharm, and Leyan Chemicals, which was used directly without further purification unless stated otherwise. The deuterated solvents were supplied by Ningbo Cuiying Chemicals. The dimethyl sulfoxide-d_6 (DMSO-d_6) for reaction was fetched and transferred to the reaction in glovebox with nitrogen atmosphere.

TLC and Chromatography

Analytic thin-layer chromatography (Leyan chemicals) was used for checking the formation of unexpected side reactions. Visualization was achieved by ultraviolet light (254 nm and 365 nm) and iodine staining. Flash chromatography was performed on silica gel (200-300 mesh) with the indicated solvent systems.

Spectroscopy Analysis

The gas chromatography-mass spectroscopy (GC-MS) are recorded on an Agilent 6890N GC-system with an Agilent 5973Network Mass Selective Detector (electron ionization), and a HP-5MS column (30 m, 0.25 mm × 0.25 μm).
^{1}H NMR (400 MHz) and ^{13}C-NMR (101 MHz) are recorded on a Bruker Ascend 400 spectrometer and chemical shifts are reported in ppm down field from TMS and are referenced to residual proton in $CDCl_3$ or DMSO-d_6. The spectra for deuterated substrates are reported as observed, while the integration difference less than 5% are ignored. The NMR data are reported as: s =singlet, d = doublet, t = triplet, q = quartet, m = multiplet with J = coupling constant in Hz, and the deuterated position are marked as “Labelled”.

Calculation of Deuterium Incorporation

The degree of deuterium-incorporation was calculated based on both GC-MS and ^{1}H-NMR methods, which had been described in our previous work.[1]

2. Condition Optimization

Table S1 Condition optimization [a]

no	base.	equiv.	D-source	time (h)	%D_{MS} [b]	%Recov [c]
1	CH_3COONa	1	DMSO-d_6	18	< 5	- [d]
2	Na_2CO_3	0.5	DMSO-d_6	18	< 5	- [d]
3	NaOH	1	DMSO-d_6	18	9	- [d]
4	NaO^tBu	1	DMSO-d_6	4	48	- [d]
5	LiO^tBu	1	DMSO-d_6	4	13	- [d]
6	K_3PO_4	0.33	DMSO-d_6	18	< 5	- [d]
7	K_2CO_3	0.5	DMSO-d_6	18	< 5	- [d]
8	CH_3COOK	1	DMSO-d_6	18	< 5	- [d]
9	KOH	1	DMSO-d_6	4	202	92
10	KOH	1	DMSO-d_6	18	252	92
11	KO^tBu	1	DMSO-d_6	4	297	94
12	KO^tBu	1	$CDCl_3$ [e]	4	45	- [d]
13	KO^tBu	1	MeOD [e]	4	< 5	- [d]
14	KO^tBu	1	D_2O	4	< 5	- [d]
15	KO^tBu	2.5	DMSO-d_6	4	306	96
16	KO^tBu	1.25	DMSO-d_6	4	305	83
17	KO^tBu	0.5	DMSO-d_6	4	263	97
18	KO^tBu	0.5	DMSO-d_6	18	265	97
19	KO^tBu	0.1	DMSO-d_6	4	106	99
20	KO^tBu	0.1	DMSO-d_6	18	171	99

[a] Reaction condition unless noted otherwise: 2-phenylpyridine **1** (1.0 mmol), Base, DMSO-d_6 (2 mL) in a pressure vessel, 100 °C, N_2, for respective time. [b] %D_{MS} are the deuterium-incorporation detected by GC-MS. (c) %Recov are the recovery ratio of substrate after chromatography separation. [d] The recovery of low deuterium-incorporation conditions had not been determined. [e] 80 °C.

3. Kinetic Profile of Deuteration Progression under Different KO^{t}Bu Loading

Due to the potential negative influence from sampling, all the data of kinetic profile were collected by parallel experiments. The reactions were carried out as general procedure and was stopped at specified time, and was analyzed by GC-MS.

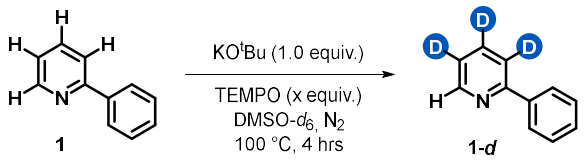
Table S2 Data for kinetic profile of deuteration progression under different KO^{t}Bu loading [a,b]

entry	time (h)	KO^{t}Bu (equiv.)				
		2.5	**1.25**	**1.0**	**0.5**	**0.1**
1	0	0	0	0	0	0
2	1	2.67	2.76	2.69	1.57	0.42
3	2	2.94	2.94	2.95	2.14	0.72
4	3	3.02	3.01	2.93	2.5	0.87
5	4	3.06	3.05	2.97	2.63	1.06
6	5	-	-	-	2.65	1.14
7	7	-	-	-	2.66	1.29
8	19	-	-	-	2.65	1.71

[a] Reaction condition unless noted otherwise: 2-phenylpyridine **1** (1.0 mmol), KO^{t}Bu, DMSO-d_6 (2 mL) in a pressure vessel, 100 °C, N_2, for respective time. [b] $\%D_{MS}$ are the deuterium-incorporation detected by GC-MS.

4. Mechanistic Experiments

Radical capturing experiment



To an oven-*d*ried heavy wall pressure vessel, KOtBu (112 mg, 1.0 mmol, 1.0 equiv.), substrate (1.0 mmol), 2,2,6,6-Tetramethylpiperidine 1-oxyl (TEMPO, 469 mg, 3.0 equiv.), and DMSO-d_6 (2 mL) was added. The vessel was purged with nitrogen stream, and sealed by Teflon bushing with Viton O-ring. The mixture was then heated and stirred for 4 hours at 100 °C in a metallic heating module. The mixture was then diluted with H_2O (30 mL), extracted with dichloromethane (3 x 10 mL), and washed with saturated NaCl solution (2 x 10 mL). The combined organic phase was dried over anhydrous Na_2SO_4, sampled for GC-MS analysis, and then concentrated under reduced pressure. The crude product was then purified by chromatography to afford purified product.

Figure S1 Stacking NMR spectroscopy of radical capturing experiments

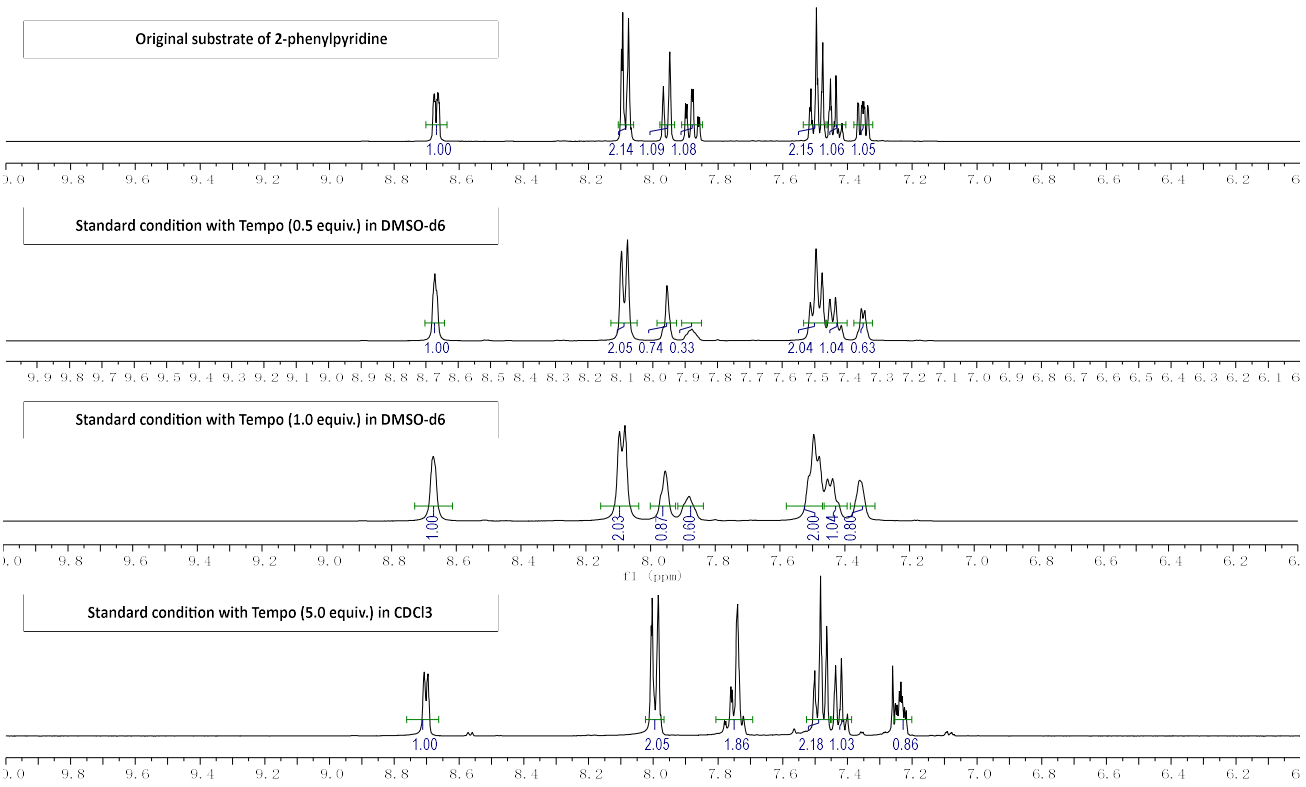
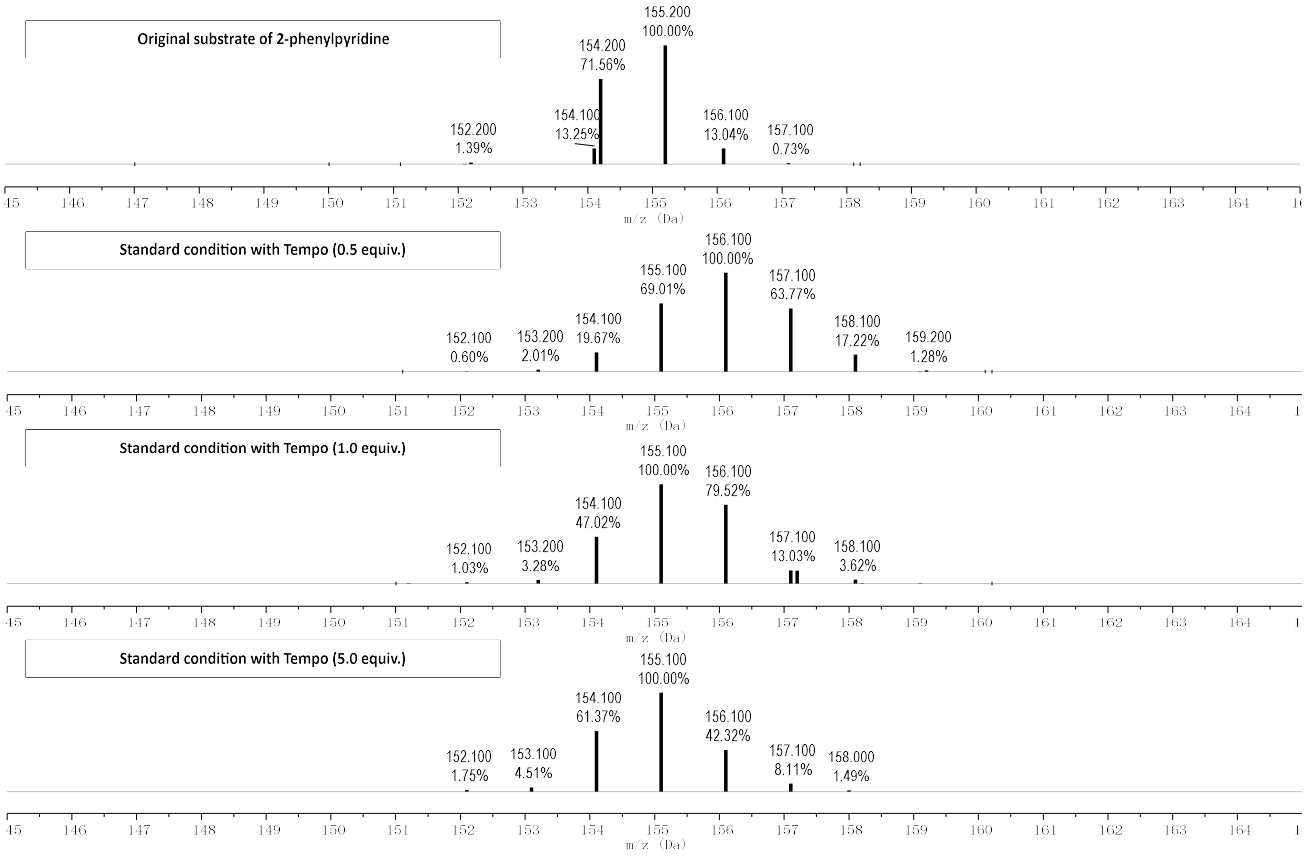
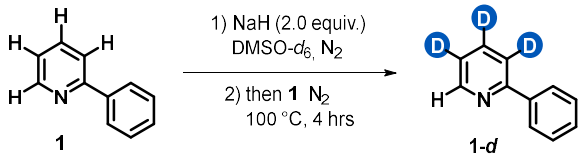


Figure S2 Stacking GC-MS spectroscopy of radical capturing experiments



Dimsyl anion experiment



The preparation of dimsyl anion was carried out as described:[2] To an oven-*d*ried two neck round-bottom flask, NaH (60%, 212 mg) was washed by dry petroleum ether (3 x 2 mL), which was then dried under dry nitrogen blowing. Then DMSO-d_6 (5 mL) was added carefully under the nitrogen gas protection. The mixture was then kept under 50 °C for 2 hours, and then heated to 90 °C until the bubbling finished. Afterward, the 2-phenylpyridine (1.0 equiv.) was added into the mixture and reacted for another 4 hours under 100 °C. The mixture was then diluted with H_2O (30 mL), extracted with dichloromethane (3 x 10 mL), and washed with saturated NaCl solution (2 x 10 mL). The combined organic phase was dried over anhydrous Na_2SO_4, sampled for GC-MS analysis, and then concentrated under reduced pressure. The crude product was then purified by chromatography (petroleum ether/EtOAc = 20/1).

Figure S3 Stacking NMR spectroscopy of dimsyl carbanion experiments

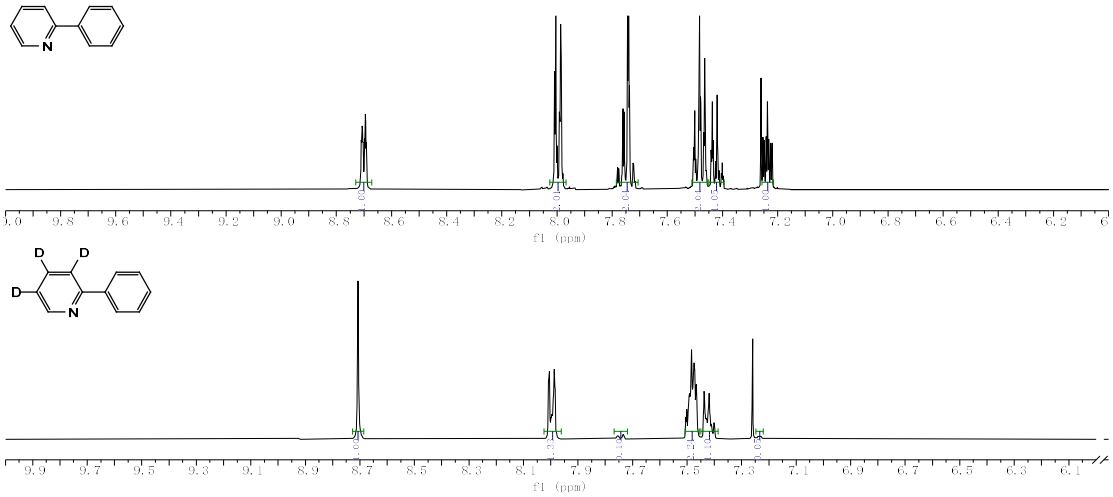
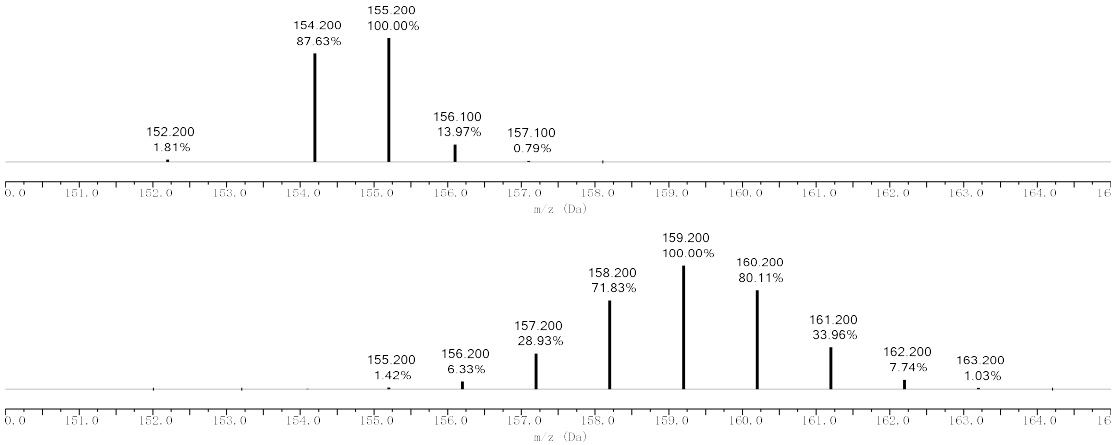
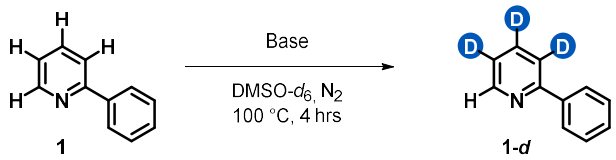


Figure S4 Stacking GC-MS spectroscopy of dimsyl carbanion experiments



5. General Procedure

General procedure for standard condition



To an oven-*d*ried heavy wall pressure vessel, KOtBu (112 mg, 1.0 mmol, 1.0 equiv.), substrate (1.0 mmol), and DMSO-d_6 (2 mL) was added. The vessel was purged with nitrogen stream, and sealed by Teflon bushing with Viton O-ring. The mixture was then heated and stirred for 4 hours at 100 °C in a metallic heating module. The mixture was then diluted with H_2O (30 mL), extracted with dichloromethane (3 x 10 mL), and washed with saturated NaCl solution (2 x 10 mL). The combined organic phase was dried over anhydrous Na_2SO_4, sampled for GC-MS analysis, and then concentrated under reduced pressure. The crude product was then purified by chromatography to afford purified product.

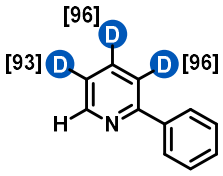
6. References

[1] Junhua Kong, Zhi-Jiang Jiang, Jiayuan Xu, Yan Li, Hong Cao, Yanan Ding, Bencan Tang, Jia Chen, and Zhanghua Gao. Ortho-Deuteration of Aromatic Aldehydes via a Transient Directing Group-Enabled Pd-Catalyzed Hydrogen Isotope Exchange. *The Journal of Organic Chemistry*,**2021**, 86 (19), 13350-13359.

[2] María E. Budén, Javier I. Bardagí, Marcelo Puiatti, and Roberto A. Rossi. Initiation in Photoredox C–H Functionalization Reactions. Is Dimsyl Anion a Key Ingredient? *The Journal of Organic Chemistry*, **2017,** 82 (16), 8325-8333.

7. Results of Substrate deuteration

Deuteration of 2-Phenylpyridine (1)



General procedure to afford **1-*d*** as yellow oil (150.0 mg, 95%) with D-incorporation 93%D at β-position, 96%D at γ-position, 96%D at β'-position and 5%D at *ortho*-Ph-position by ^{1}H NMR; 2.97D by GC-MS; R_f = 0.45 (Petroleum ether/EtOAc = 20/1).

NMR data for starting material:^{1}H NMR (399 MHz, $CDCl_3$) δ 8.73 – 8.67 (m, 1H), 8.03 – 7.97 (m, 2H), 7.79 – 7.71 (m, 2H), 7.51 – 7.45 (m, 2H), 7.45 – 7.39 (m, 1H), 7.24 (ddd, J = 6.7, 4.8, 2.0 Hz, 1H).

NMR data for deuterated product:^{1}H NMR (399 MHz, $CDCl_3$) δ 8.71 (s, 1H), 8.03 – 7.97 (m, 1.97H), 7.77 – 7.73 (m, 0.07H, **Labelled**) 7.52 – 7.45 (m, 2H), 7.45 – 7.39 (m, 0.07 H, **Labelled**).

Figure S5 ^{1}H NMR spectrum comparison

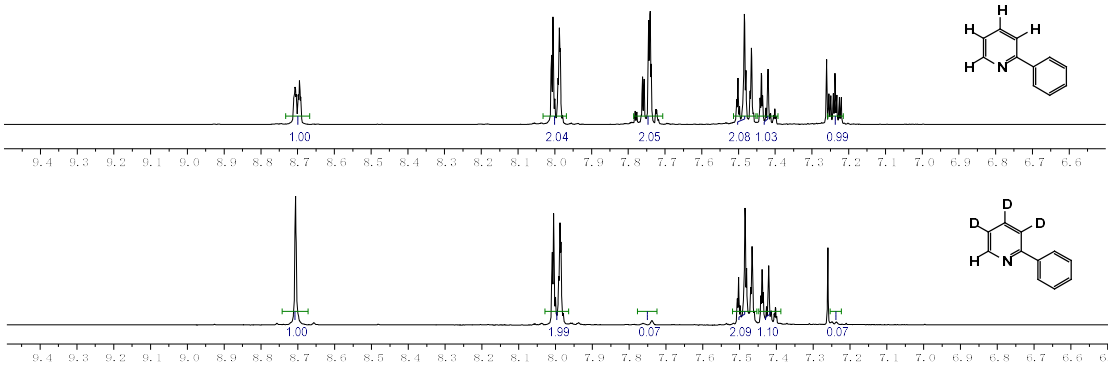


Figure S6 GC-MS spectrum comparison

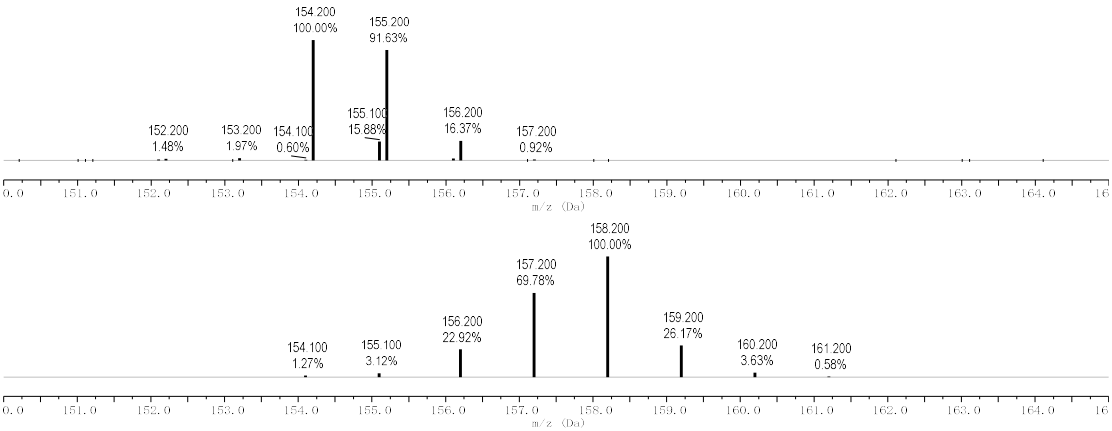


Figure S7 ^{1}H NMR of **1** in chloroform-*d*

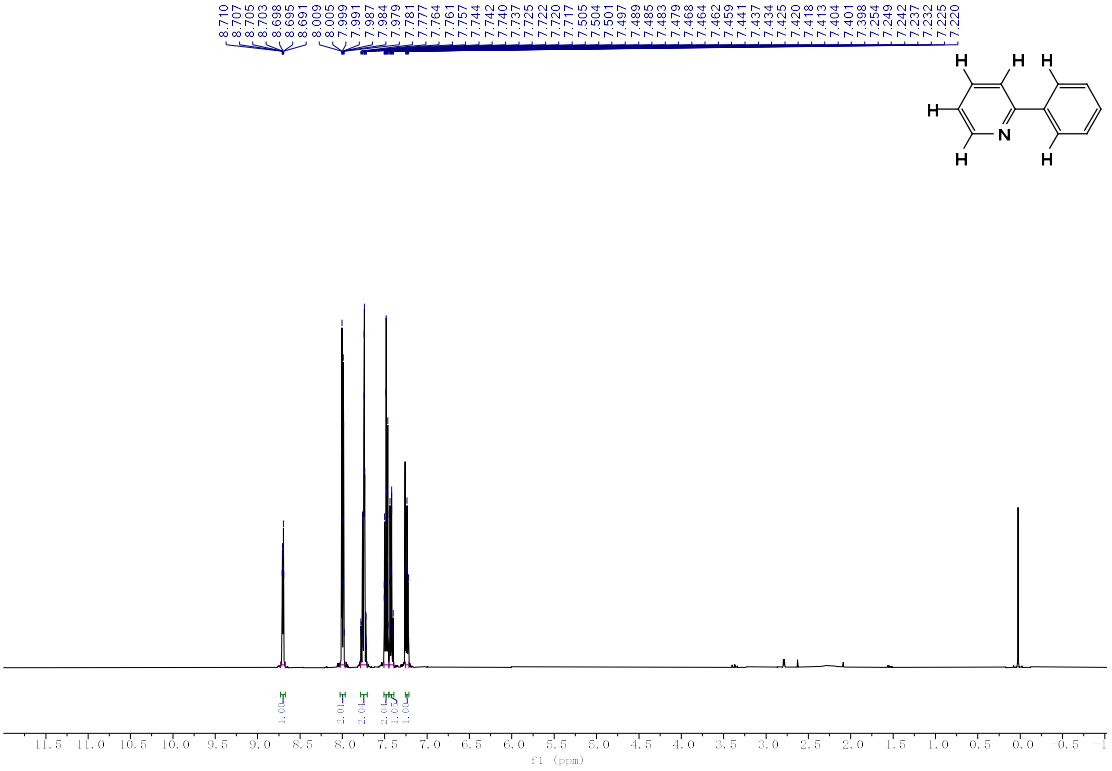
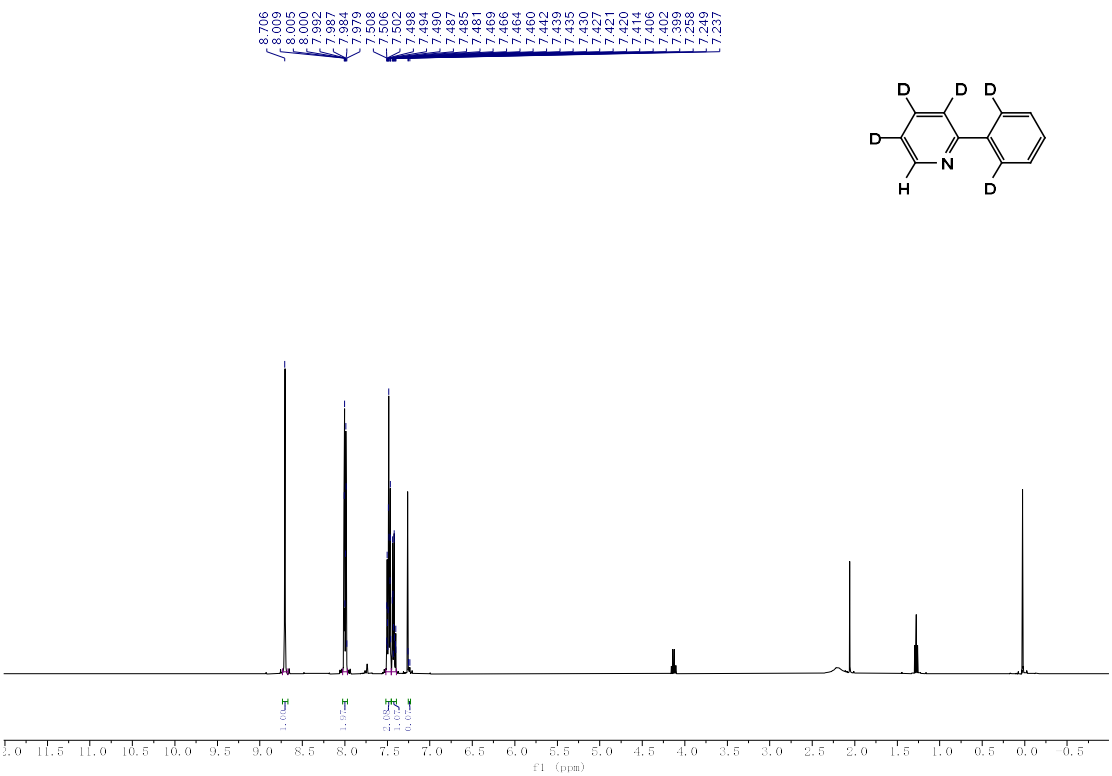
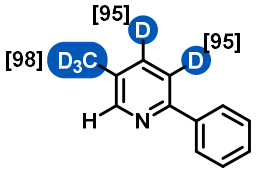


Figure S8 ^{1}H NMR of **1-*d*** in chloroform-*d*



Deuteration of 5-methyl-2-phenylpyridine (2)



General procedure to afford **2-*d*** as colorless oil (169.8 mg, 98%) with D-incorporation 98%D at 5-methyl, 95%D at γ-position, and 95 for β'-position by ^{1}H NMR; 4.72D by GC-MS; R_f = 0.45 (Petroleum ether/EtOAc = 20/1).

NMR data for starting material: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.50 (d, J = 2.2 Hz, 1H), 8.09 – 8.01 (m, 2H), 7.86 (d, J = 8.1 Hz, 1H), 7.69 (dd, J = 8.1, 2.3 Hz, 1H), 7.51 – 7.44 (m, 2H), 7.43 – 7.37 (m, 1H), 2.33 (s, 3H).

NMR data for deuterated product: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.61 (s, 0.93H, **Labelled**), 8.19 – 8.12 (m, 2H), 7.85 (s, 0.06H, **Labelled**), 7.69 (d, J = 2.4 Hz, 0.04H, **Labelled**), 7.61 – 7.54 (m, 2H), 7.54 – 7.46 (m, 1H), 2.32 – 2.28 (m, 0.12H, Labelled).

Figure S9 ^{1}H NMR spectrum comparison

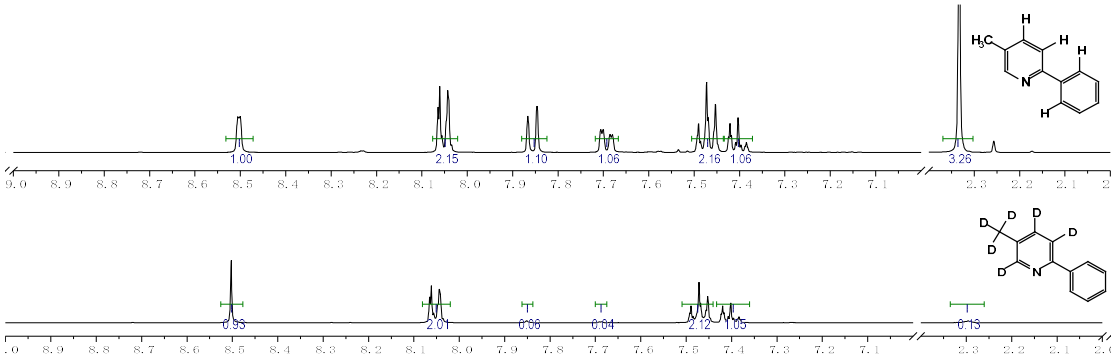


Figure S10 GC-MS spectrum comparison

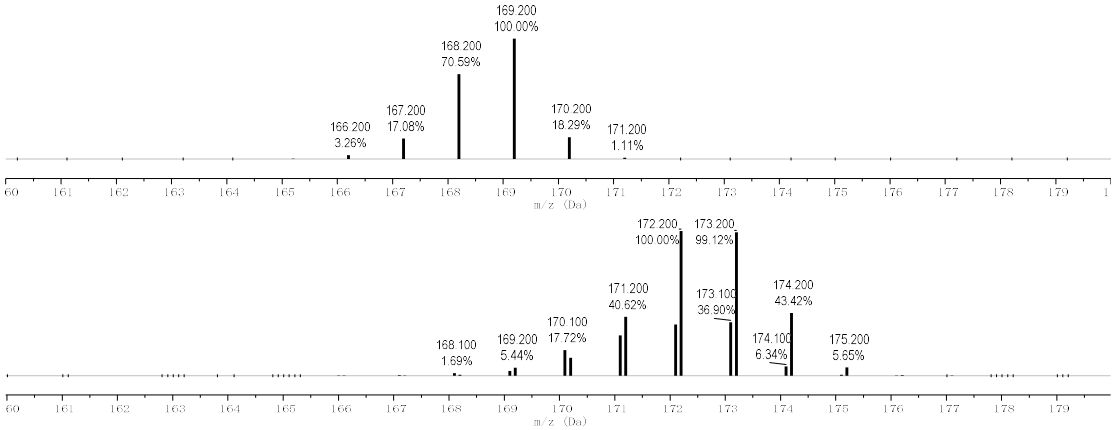


Figure S11 ^{1}H NMR of **2** in DMSO-*d*

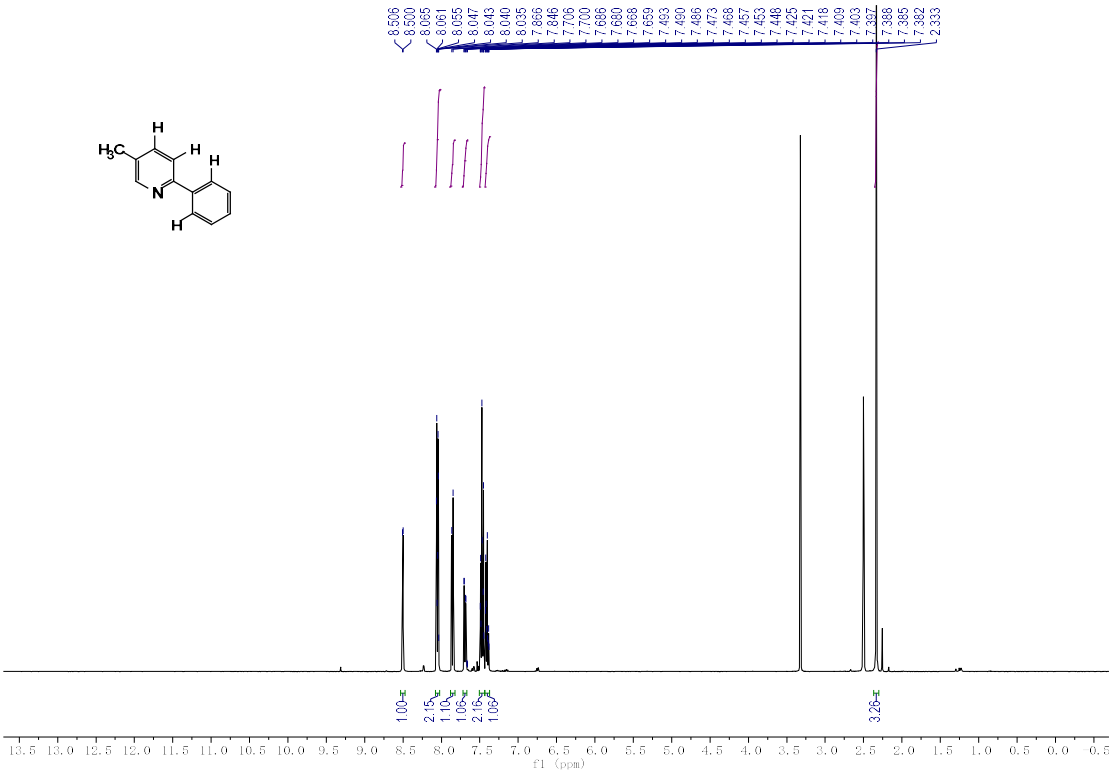
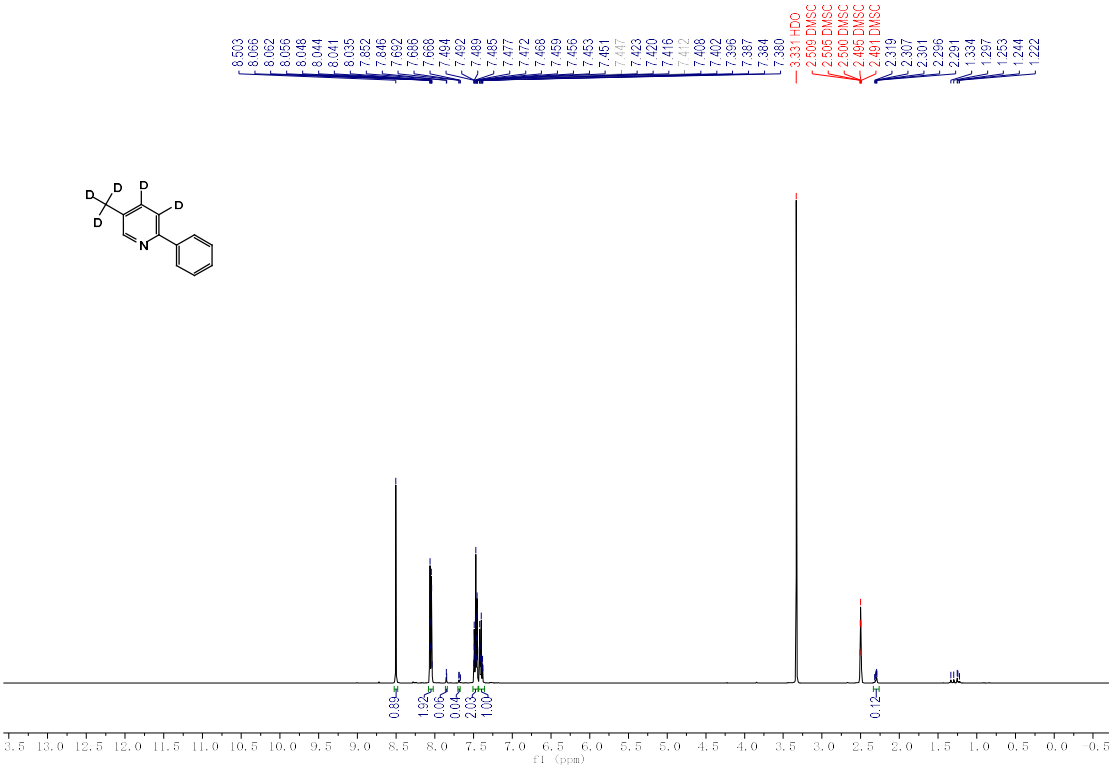
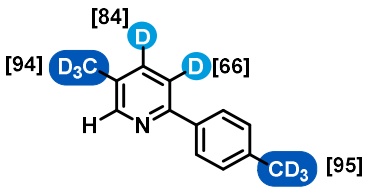


Figure S12 ^{1}H NMR of **2-*d*** in DMSO-d_6



Deuteration of 5-methyl-2-(*p*-tolyl)pyridine (3)



General procedure to afford **3-*d*** as white solid (142.2 mg, 78%) with D-incorporation 94%D at 5-methyl, 95%D at 4'-methyl, 84%D at γ-position, and 66%D at β'-position by ^{1}H NMR; 7.14D by GC-MS; R_f = 0.4 (Petroleum ether/EtOAc = 15/1).

For gram-scale preparation to afford **3-*d*** as white solid (1.803 g, 91%) with D-incorporation 94%D at 5-methyl, 95%D at 4'-methyl, 85%D at γ-position, and 53%D at β'-position by ^{1}H NMR; 6.70D by GC-MS.

NMR data for starting material: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.47 (d, J = 2.3 Hz, 1H), 7.95 (d, J = 8.1 Hz, 2H), 7.79 (d, J = 8.1 Hz, 1H), 7.64 (dd, J = 8.1, 2.3 Hz, 1H), 7.26 (d, J = 7.9 Hz, 2H), 2.34 (s, 3H), 2.30 (s, 3H).

NMR data for deuterated product: ^{1}H NMR (399 MHz, DMSO-d_6) δ 8.46 (s, 1H), 7.97 – 7.90 (m, 2H), 7.81-7.76 (m, 0.34H, **Labelled**), 7.66-7.60 (m, 0.16H, **Labelled**), 7.29 – 7.23 (m, 2H), 2.31 (p, J = 1.97 Hz, 0.17H, **Labelled**), 2.27 (p, J = 2.09 Hz, 0.14H, **Labelled**).

Figure S13 ^{1}H NMR spectrum comparison

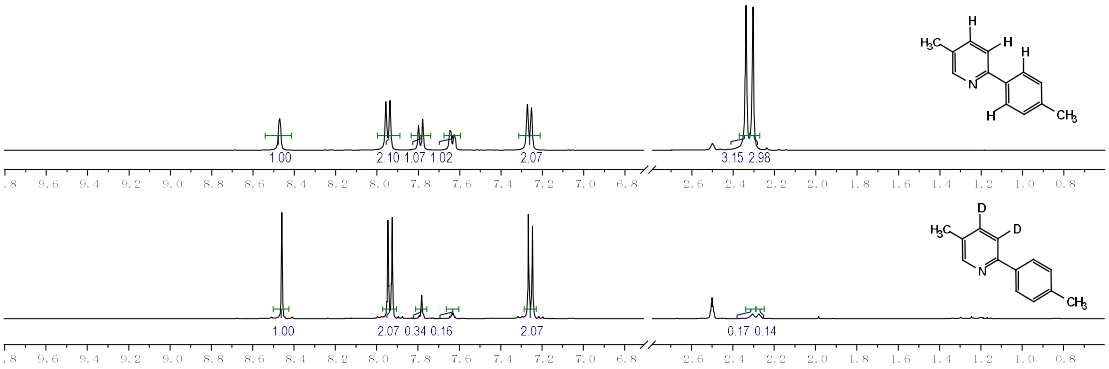


Figure S14 GC-MS spectrum comparison

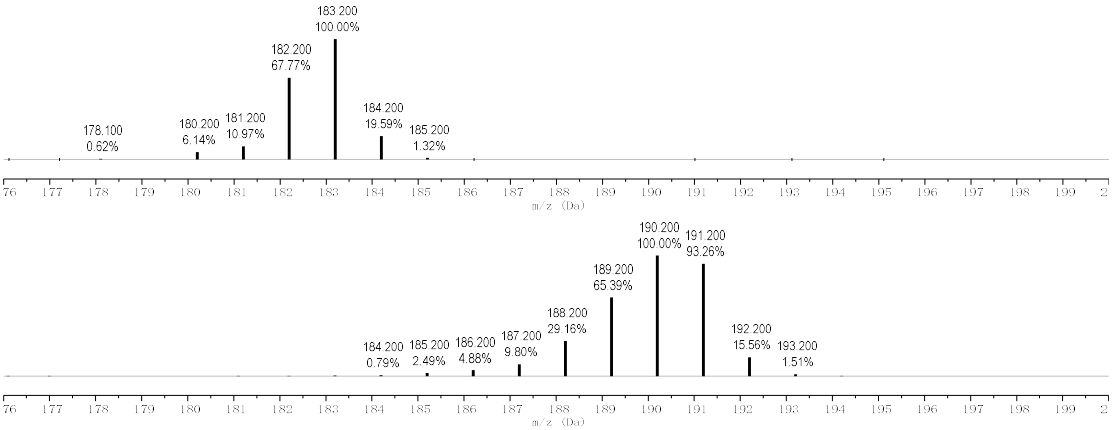


Figure S15 ^{1}H NMR of **3** in DMSO-d_6

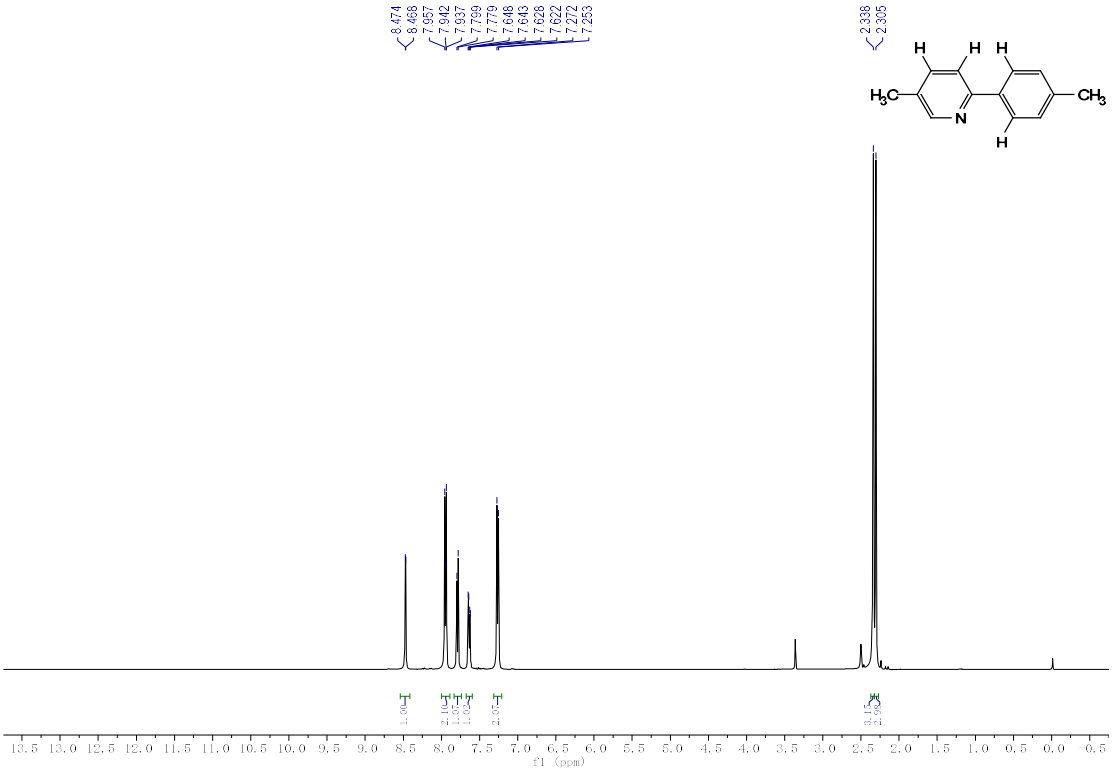
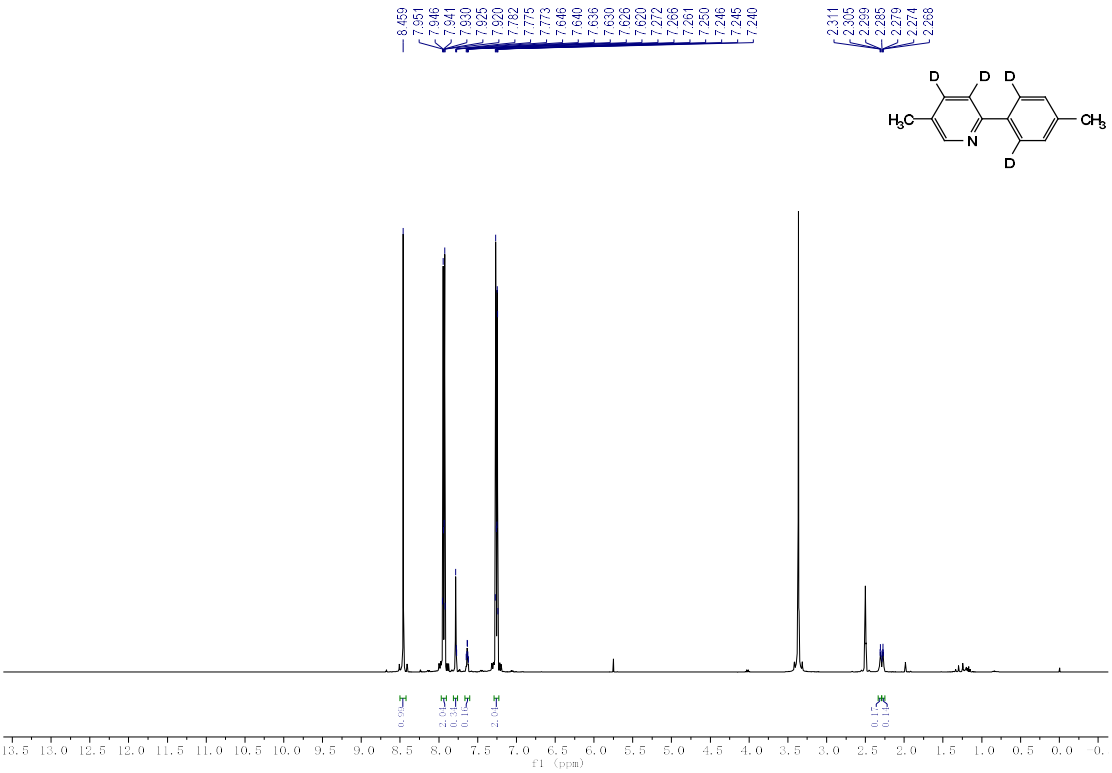
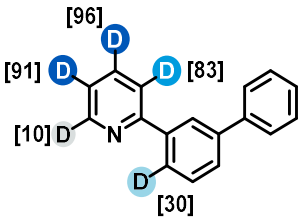


Figure S16 ^{1}H NMR of **3-*d*** in DMSO-d_6



Deuteration of 2-([1,1'-biphenyl]-3-yl)pyridine (4)



General procedure to afford **4-*d*** as yellow oil (103.3 mg, 91%) with D-incorporation 10%D at α-position, 91%D at β-position, 96%D at γ-position, 83%D at β'-position, and 30%D at 6'-phenyl position by ^{1}H NMR; 3.83D by GC-MS; R_f = 0.45 (Petroleum ether/EtOAc = 15/1).

NMR data for starting material: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.70 (ddd, J = 4.9, 1.9, 0.9 Hz, 1H), 8.35 (t, J = 1.9 Hz, 1H), 8.09 (ddt, J = 7.8, 3.1, 1.2 Hz, 2H), 7.91 (td, J = 7.7, 1.8 Hz, 1H), 7.80 – 7.70 (m, 3H), 7.59 (t, J = 7.7 Hz, 1H), 7.50 (dd, J = 8.3, 7.0 Hz, 2H), 7.44 – 7.35 (m, 2H).

NMR data for deuterated product: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.70 (s, 0.90H, **Labelled**), 8.35 (d, J = 1.8 Hz, 1H), 8.12 – 8.05 (m, 0.87H, **Labelled**), 7.91 (s, 0.04H, **Labelled**), 7.79 – 7.70 (m, 3H), 7.63 – 7.55 (m, 1H), 7.50 (t, J = 7.5 Hz, 2H), 7.44 – 7.36 (m, 1.09H, **Labelled**).

Figure S17 ^{1}H NMR spectrum comparison

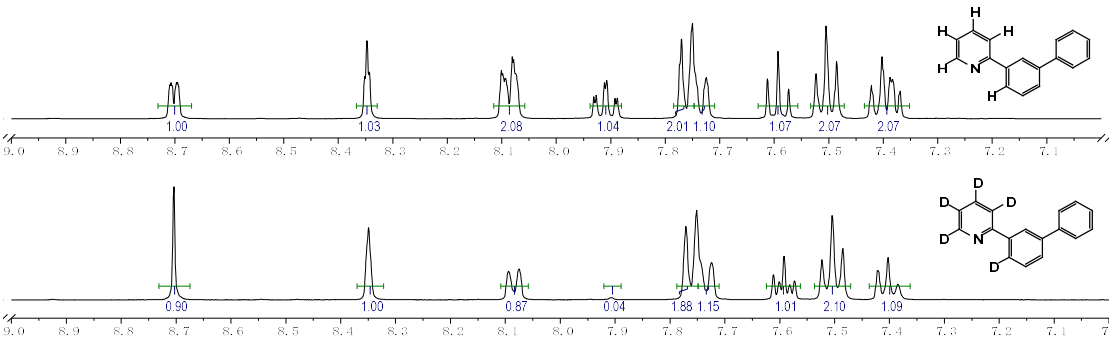


Figure S18 GC-MS spectrum comparison

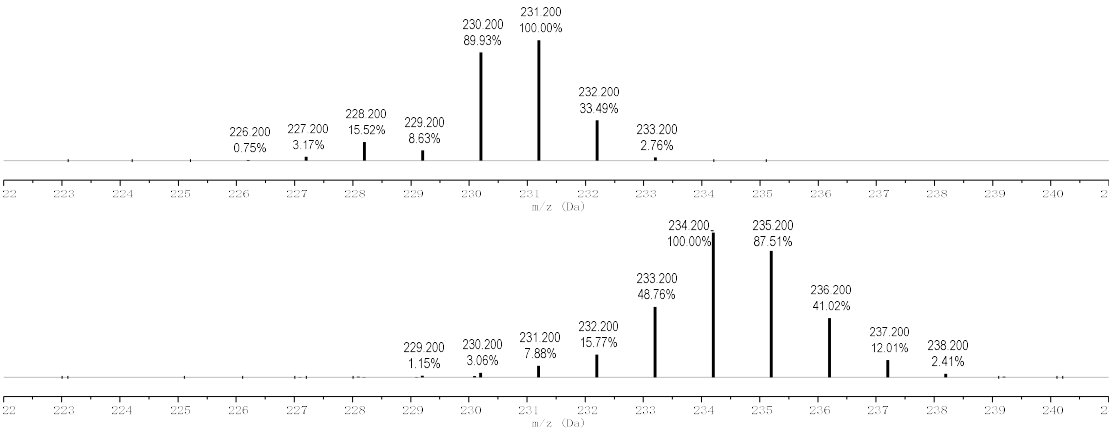


Figure S19 ^{1}H NMR of **4** in DMSO-d_6

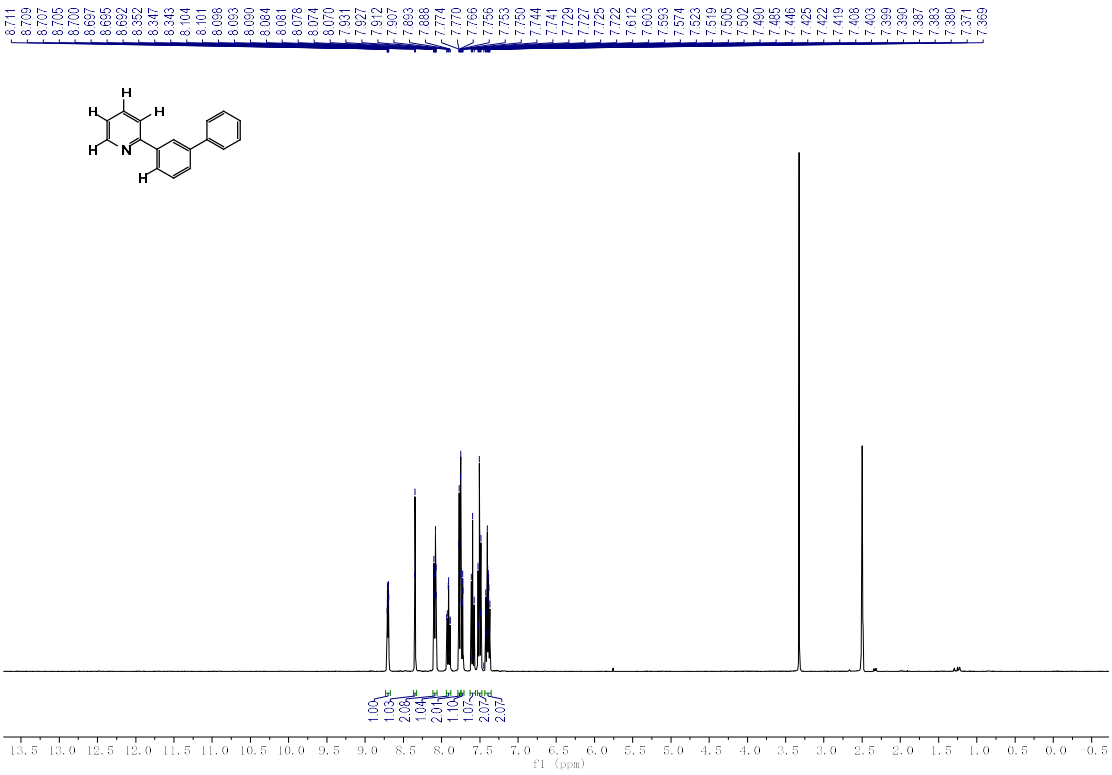
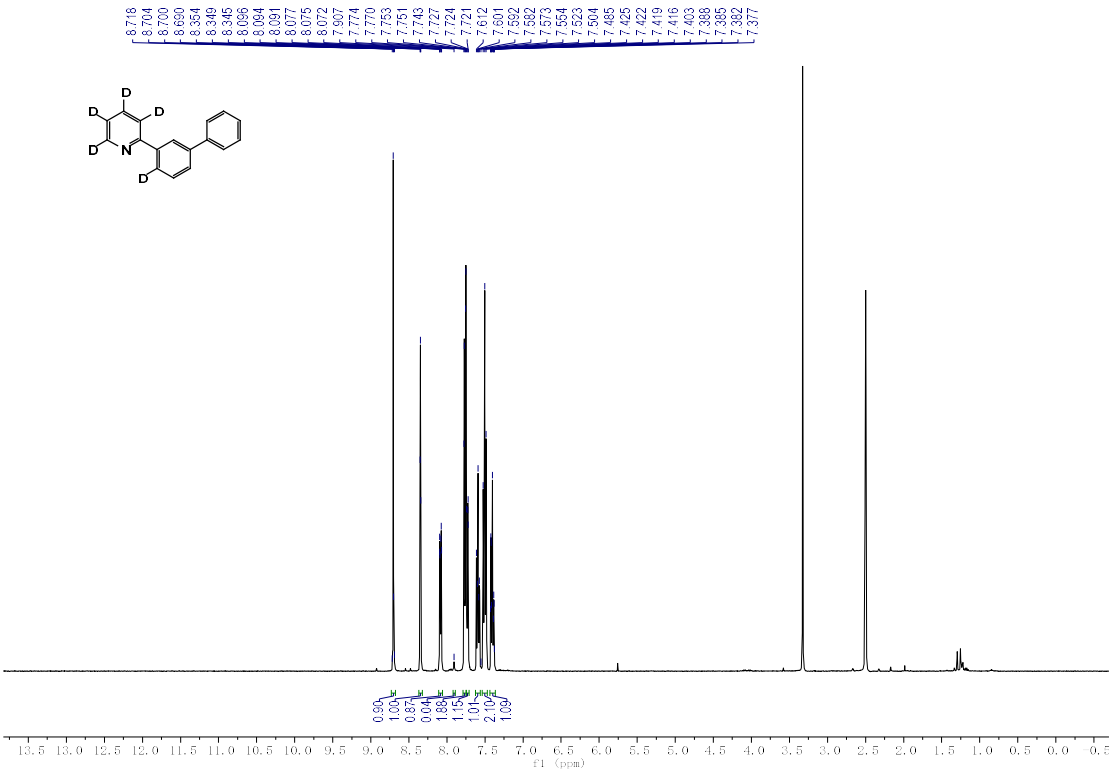
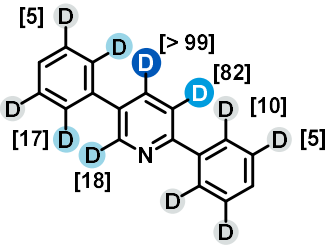


Figure S20 ^{1}H NMR of **4-*d*** in DMSO-d_6



Deuteration of 2,5-diphenylpyridine (5)



General procedure to afford **5-*d*** as yellow oil (117.7 mg, 99%) with D-incorporation 91%D at 18%D at α-position, over 99%D at γ-position, 77%D at β'-position, 17%D at ortho-hydrogen on 5-phenyl group, 10%D at ortho-hydrogen on 2-phenyl group, and an average 5%D at meta-hydrogen on both phenyl ring by ^{1}H NMR; 2.70D by GC-MS; R_f = 0.40 (Petroleum ether/EtOAc = 20/1).

NMR data for starting material: ^{1}H NMR (399 MHz, DMSO-d_6) δ 8.99 (dd, J = 2.4, 0.9 Hz, 1H), 8.17 (dd, J = 8.3, 2.5 Hz, 1H), 8.16 – 8.11 (m, 2H), 8.06 (dd, J = 8.3, 0.8 Hz, 1H), 7.84 – 7.76 (m, 2H), 7.57 – 7.48 (m, 4H), 7.48 – 7.40 (m, 2H).

NMR data for deuterated product: ^{1}H NMR (399 MHz, DMSO-d_6) δ 8.99 (s, 0.81H, **Labelled**), 8.18 – 8.11 (m, 1.80H, **Labelled**), 8.06 – 8.02 (m, 0.23H, **Labelled**), 7.83 – 7.76 (m, 1.66H, **Labelled**), 7.55 – 7.48 (m, 3.81H, **Labelled**), 7.47 – 7.40 (m, 2H).

Figure S21 ^{1}H NMR spectrum comparison

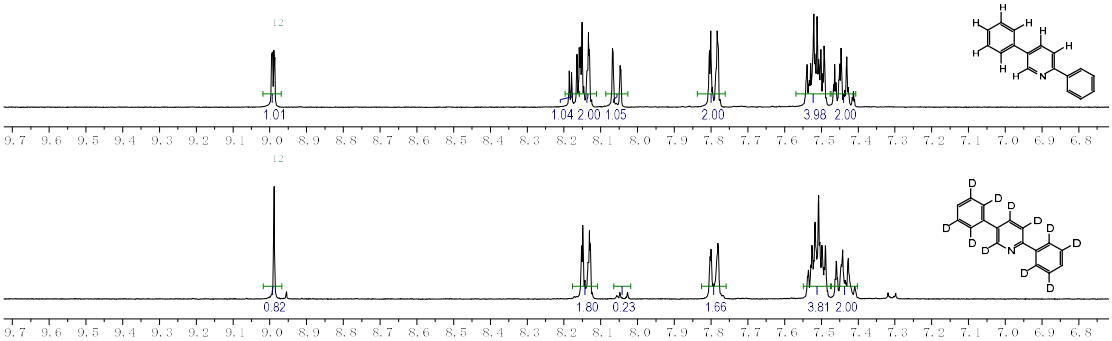


Figure S22 GC-MS spectrum comparison

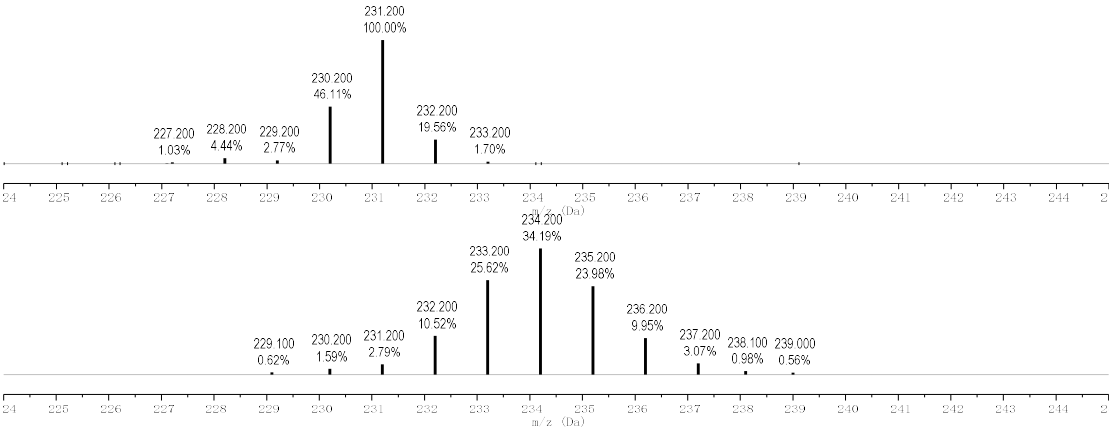


Figure S23 ^{1}H NMR of **5** in Solvent

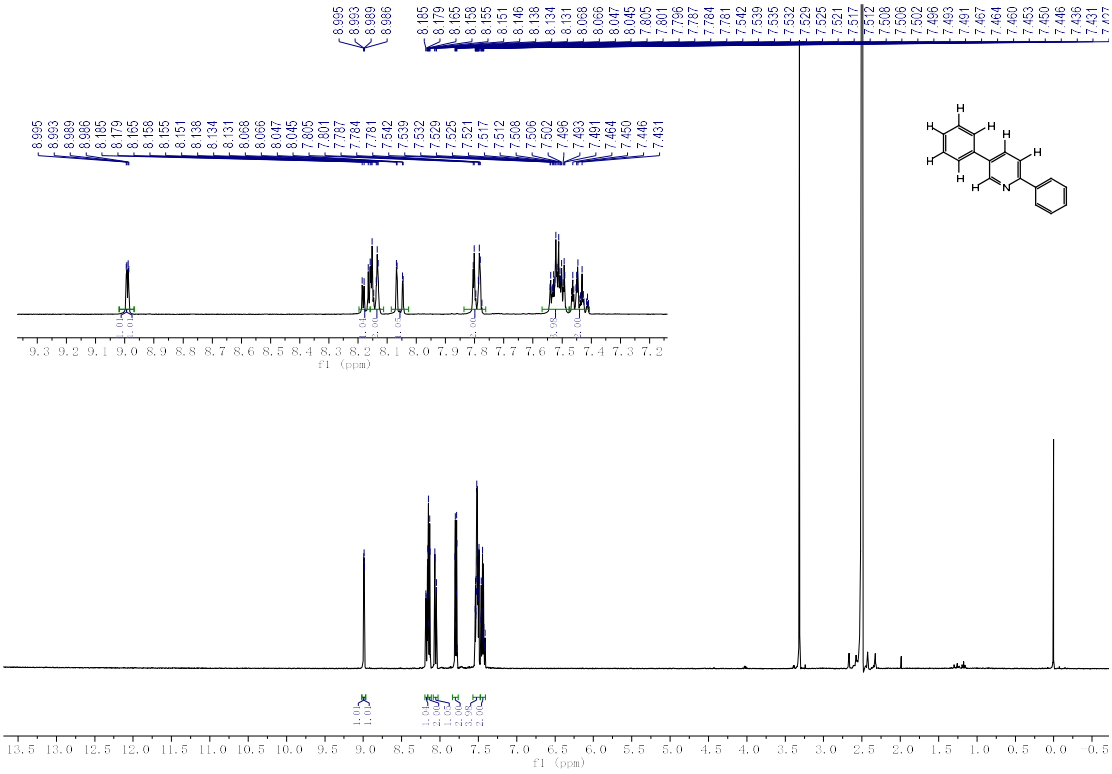
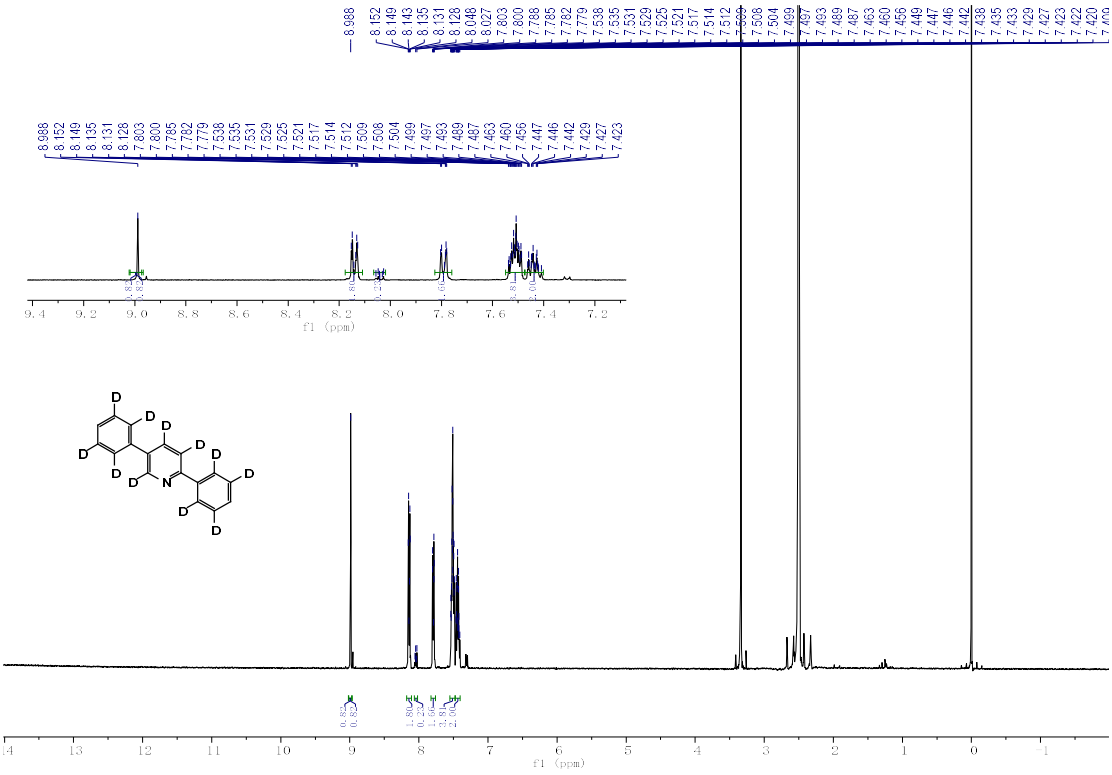
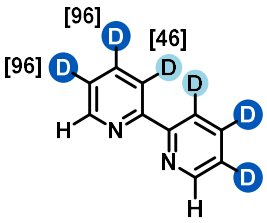


Figure S24 ^{1}H NMR of **5-*d*** in DMSO-d_6



Deuteration of 2,2'-bipyridine (6)



General procedure to afford **6-*d*** as yellow oil (133.5 mg, 84%) with D-incorporation 96%D at β-position, 96%D at γ-position, and 46%D at β'-position by ^{1}H NMR; 4.80D by GC-MS. R_f = 0.45 (Petroleum ether/EtOAc = 2/1)

NMR data for starting material: ^{1}H NMR (399 MHz, DMSO-d_6) δ 8.67 (ddd, J = 4.8, 1.8, 1.0 Hz, 2H), 8.37 (dt, J = 7.9, 1.1 Hz, 2H), 7.93 (ddd, J = 8.0, 7.5, 1.8 Hz, 2H), 7.44 (ddd, J = 7.5, 4.7, 1.2 Hz, 2H).

NMR data for deuterated product: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.69 (d, J = 1.0 Hz, 2H), 8.43 – 8.36 (s, 1.11H, **Labelled**), 7.98 – 7.91 (m, 0.08H, **Labelled**), 7.45 (d, J = 4.6 Hz, 0.08H, **Labelled**).

Figure S25 ^{1}H NMR spectrum comparison

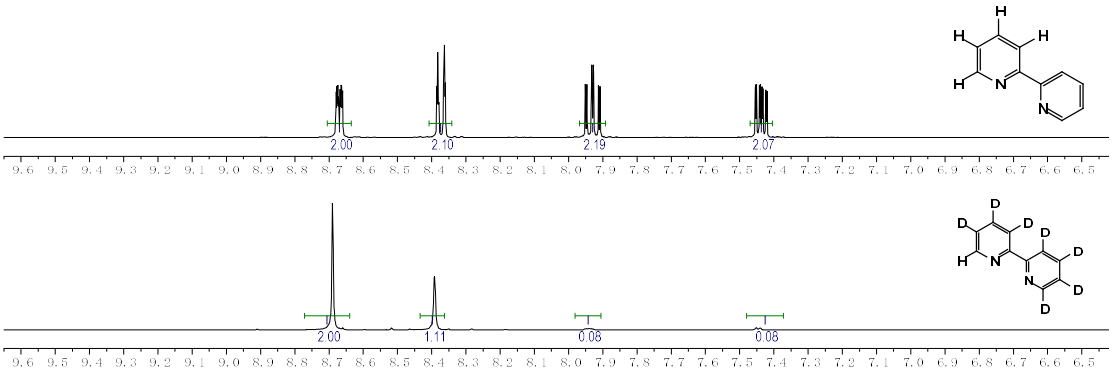


Figure S26 GC-MS spectrum comparison

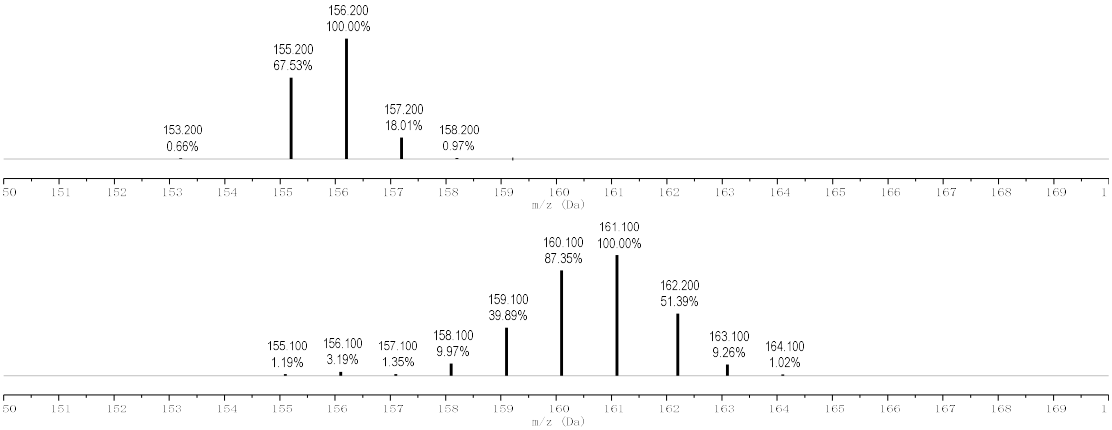


Figure S27 ^{1}H NMR of **6** in DMSO-d_6

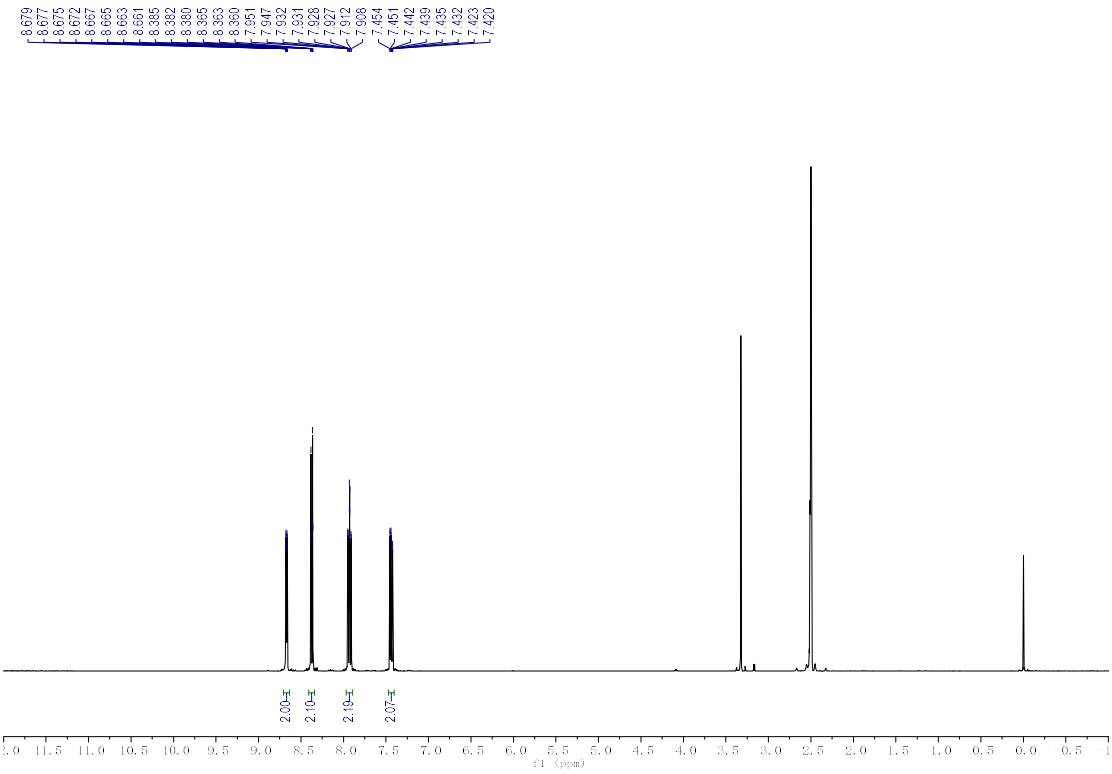
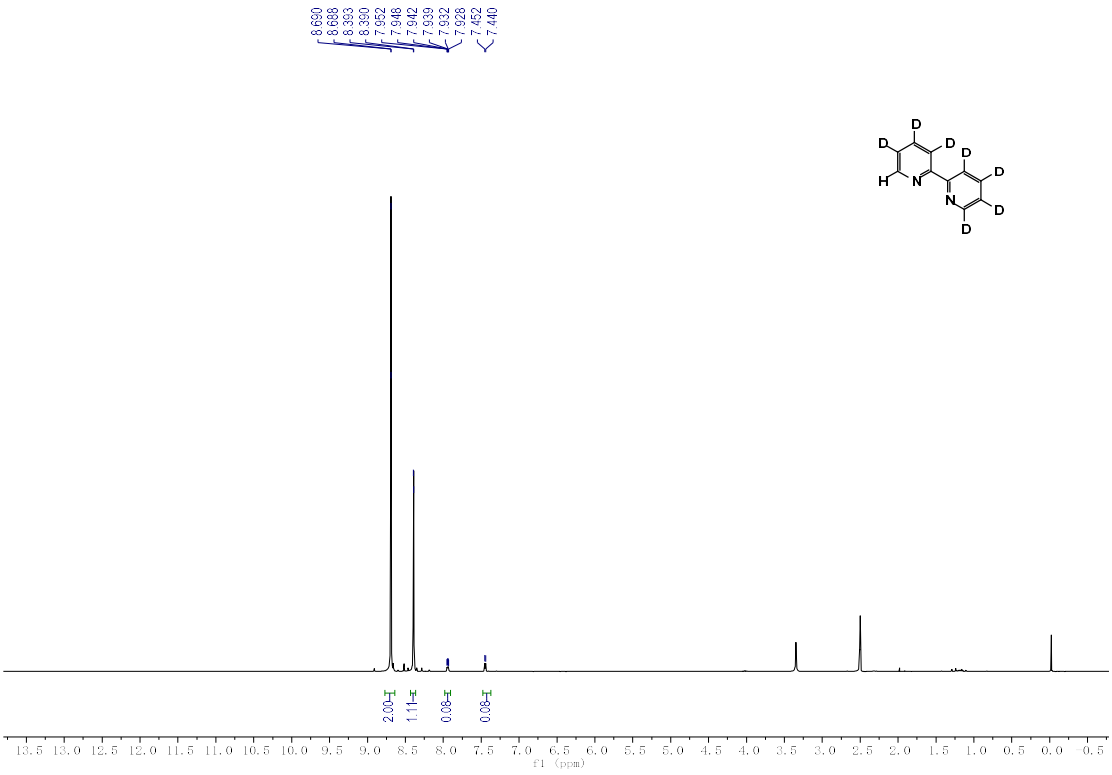
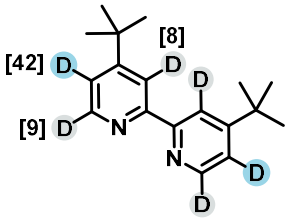


Figure S28 ^{1}H NMR of **6-*d*** in DMSO-d_6



Deuteration of 4,4'-*d*i-tert-butyl-2,2'-bipyridine (7)



General procedure to afford ***7-d*** as white solid (255.8 mg, 96%) with D-incorporation 9% at α-position, 42% at β-position, and 8% at β'-position by ^{1}H NMR; 1.14D by GC-MS. R_f = 0.45 (Petroleum ether/EtOAc = 10/1).

NMR data for starting material: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.60 (d, J = 5.2 Hz, 2H), 8.39 (d, J = 1.9 Hz, 2H), 7.47 (dd, J = 5.2, 2.0 Hz, 2H), 1.34 (s, 18H).

NMR data for deuterated product: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.70 (td, J = 2.6, 0.7 Hz, 1.82H, **Labelled**), 8.49 (d, J = 1.0 Hz, 1.84H, **Labelled**), 7.57 (dd, J = 5.2, 2.0 Hz, 1.16H, **Labelled**), 1.44 (s, 18H).

Figure S29 ^{1}H NMR spectrum comparison

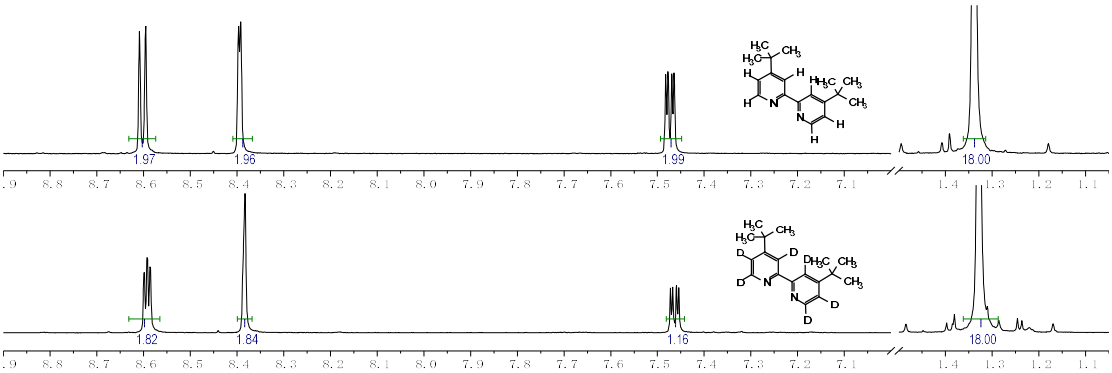


Figure S30 GC-MS spectrum comparison

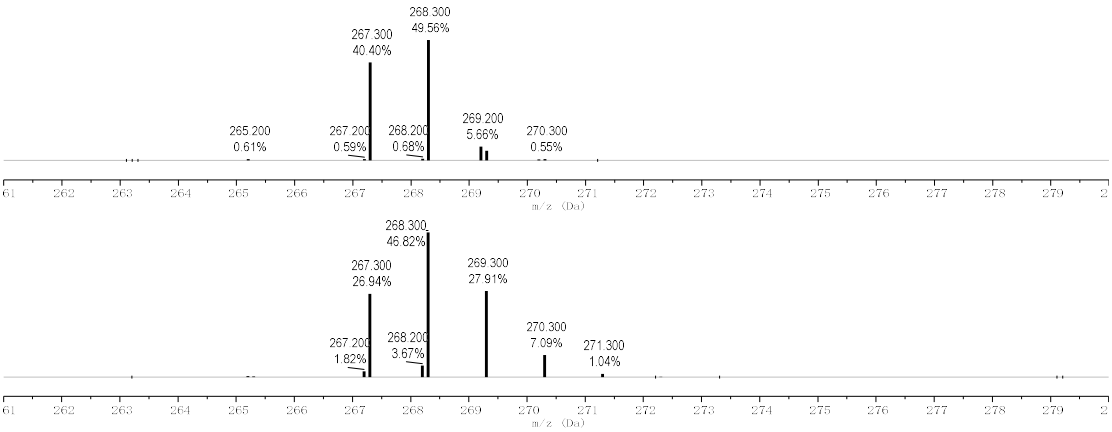


Figure S31 ^{1}H NMR of **7** in DMSO-d_6

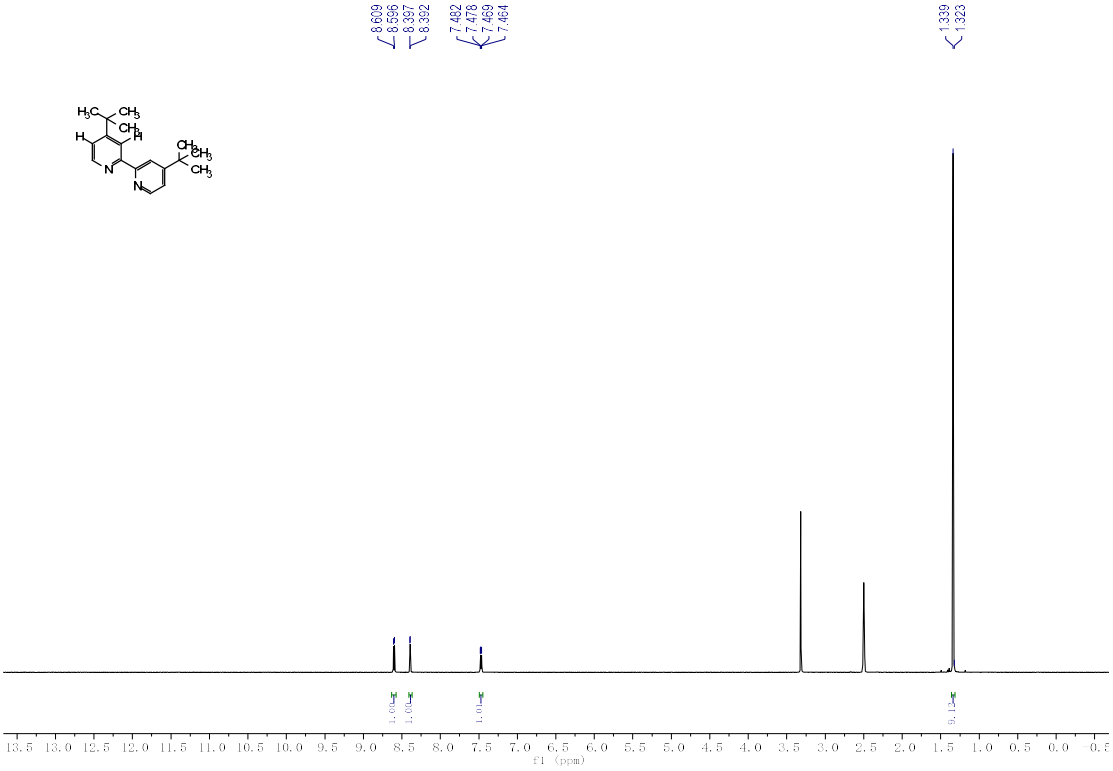
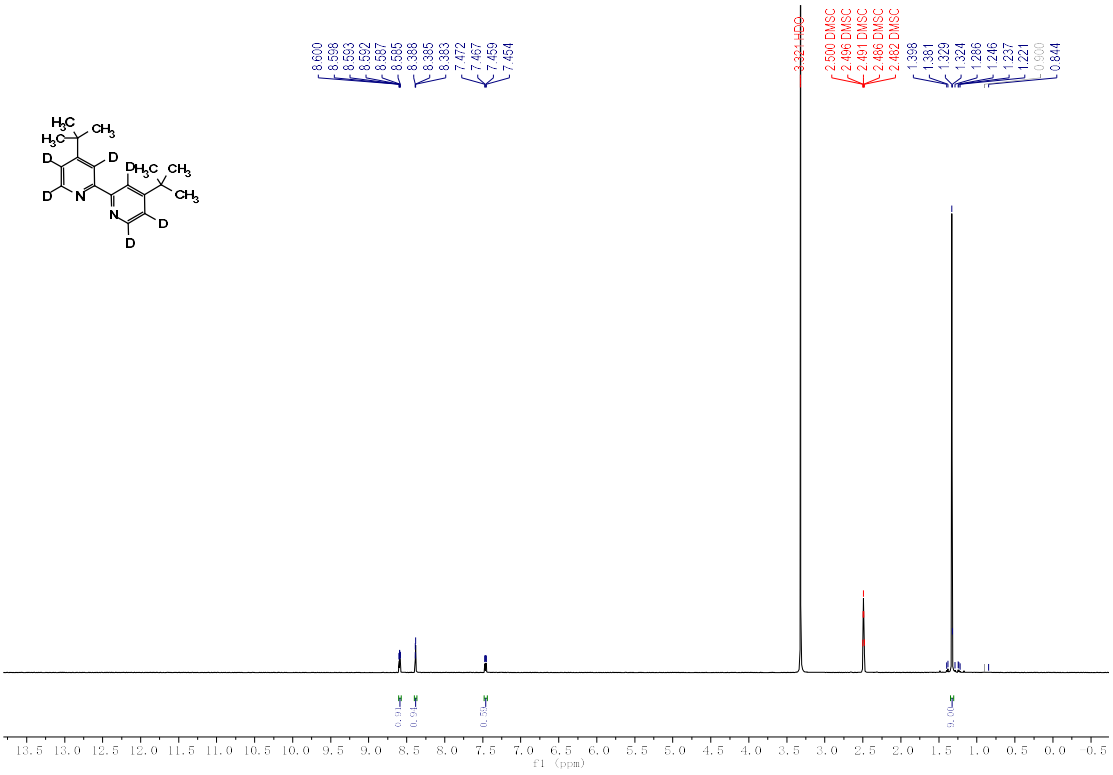
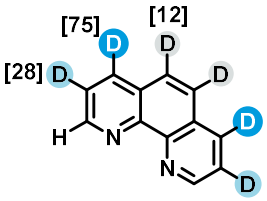


Figure S32 ^{1}H NMR of ***7-d*** in DMSO-d_6



Deuteration of 1,10-phenanthroline (8)



General procedure to afford **8-*d*** as purple oil (145.4 mg, 69%) with D-incorporation 28%D at β-position, 75%D at γ-position, 12%D at olefin bridge by ^{1}H NMR; 2.28D by GC-MS. R_f = 0.45 (dichloromethane/methanol = 30/1).

NMR data for starting material: ^{1}H NMR (399 MHz, DMSO-d_6) δ 9.08 (dd, J = 4.3, 1.8 Hz, 2H), 8.47 (dd, J = 8.1, 1.8 Hz, 2H), 7.97 (s, 2H), 7.76 (dd, J = 8.1, 4.3 Hz, 2H).

NMR data for deuterated product: ^{1}H NMR (399 MHz, DMSO-d_6) δ 9.10 – 9.05 (m, 2H), 8.51 – 8.45 (m, 0.51H, **Labelled**), 7.98 (s, 1.54H, **Labelled**), 7.79 – 7.72 (m, 1.35H, **Labelled**).

Figure S33 ^{1}H NMR spectrum comparison

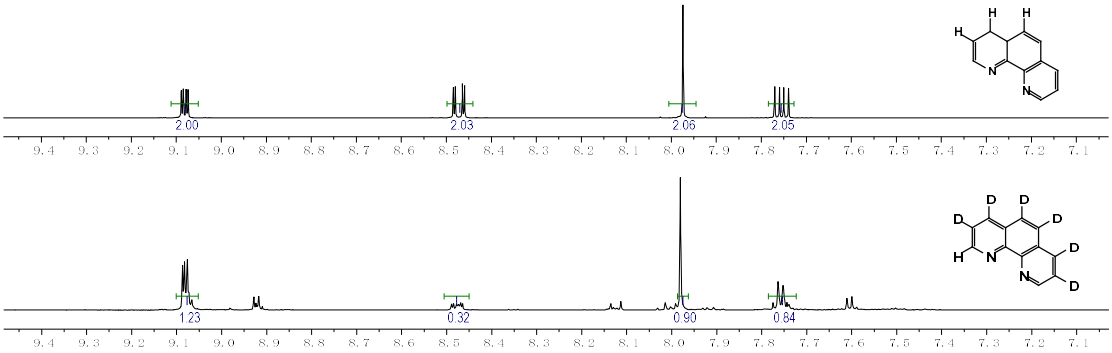


Figure S34 GC-MS spectrum comparison

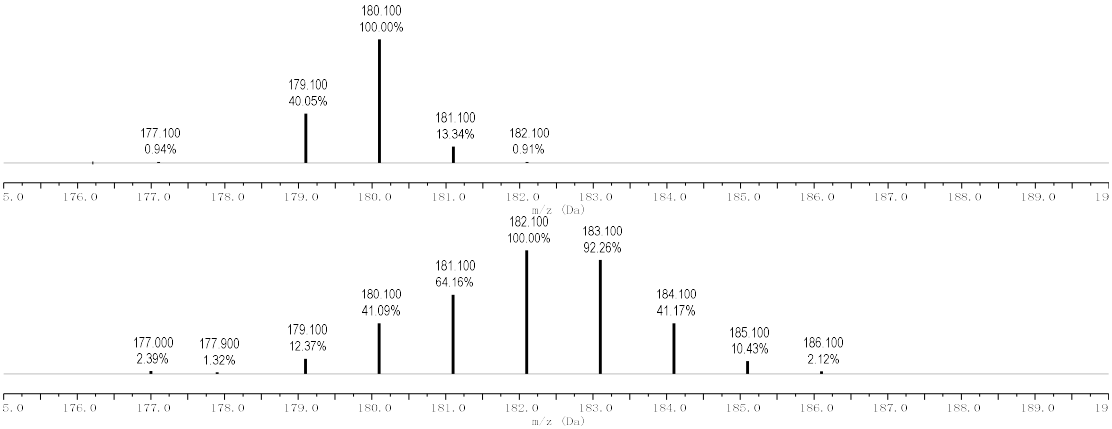


Figure S35 ^{1}H NMR of **8** in DMSO-d_6

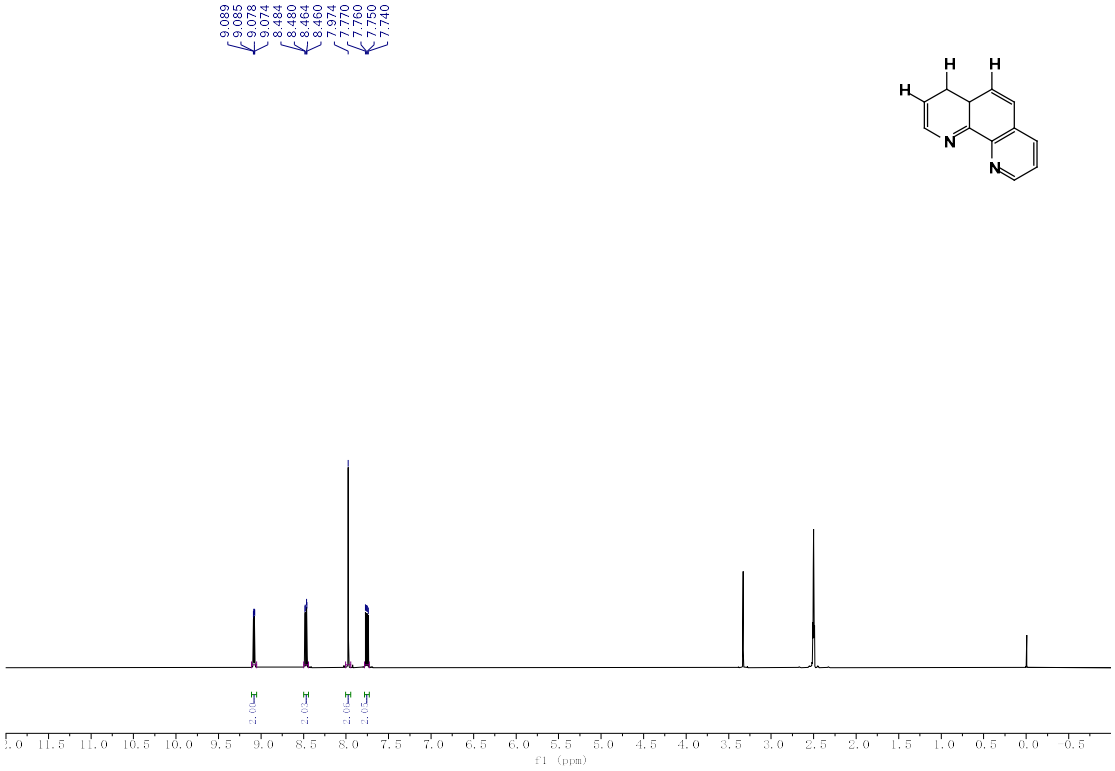
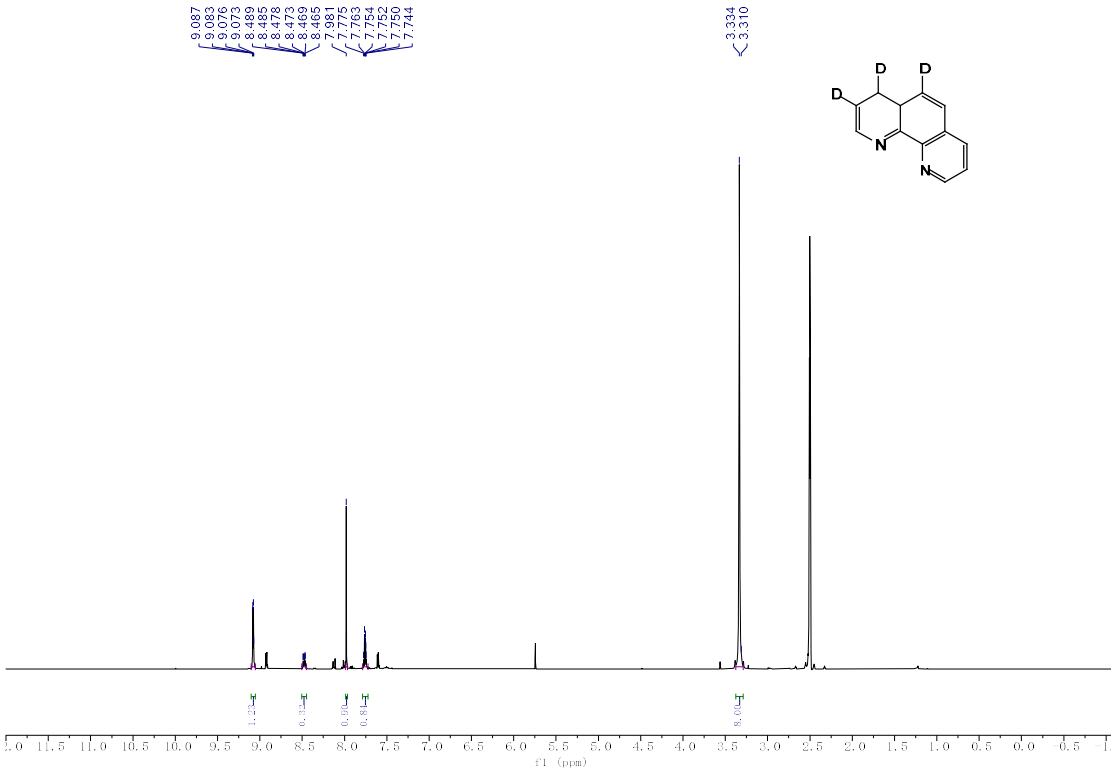
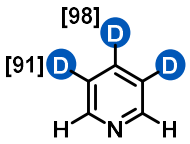


Figure S36 ^{1}H NMR of **8-*d*** in DMSO-d_6



Deuteration of pyridine (9)



General procedure to afford **9-*d*** as yellow oil (90%, determined by GC) with D-incorporation 91%D at β-position and 98%D at γ-position by ^{1}H NMR; 2.74D by GC-MS. R_f = 0.45 (Petroleum ether/EtOAc = 20/1).
NMR data for starting material: ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.58 (dt, J = 4.3, 1.7 Hz, 2H), 7.78 (tt, J = 7.6, 1.8 Hz, 1H), 7.38 (ddd, J = 7.6, 4.2, 1.5 Hz, 2H).
NMR data for deuterated product: ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.58 (s, 2H), 7.80 (s, 0.02H, **Labelled**), 7.39 (dq, J = 4.9, 1.1 Hz, 0.19H, **Labelled**).

Figure S37 ^{1}H NMR spectrum comparison

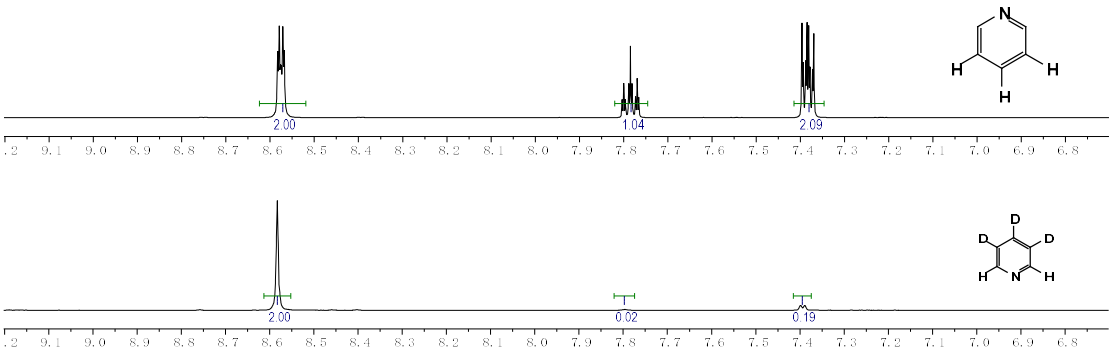


Figure S38 GC-MS spectrum comparison

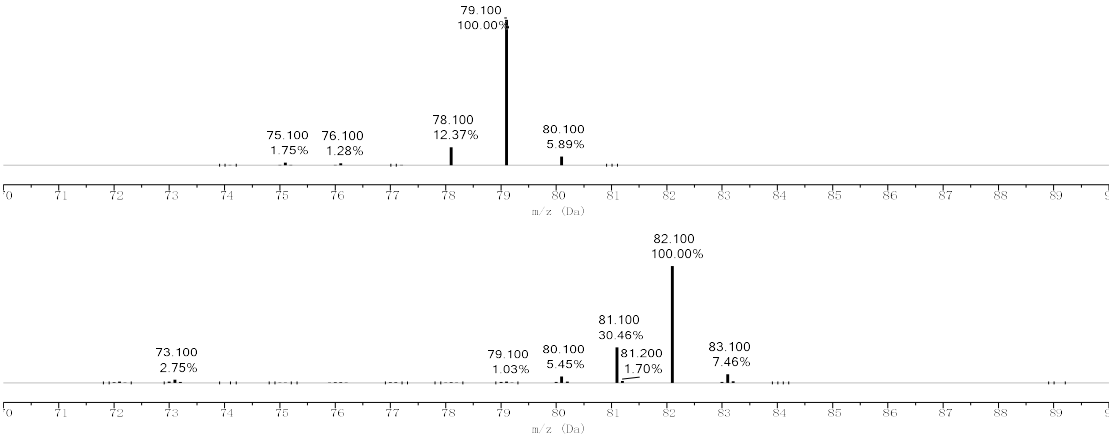


Figure S39 ^{1}H NMR of **9** in Solvent

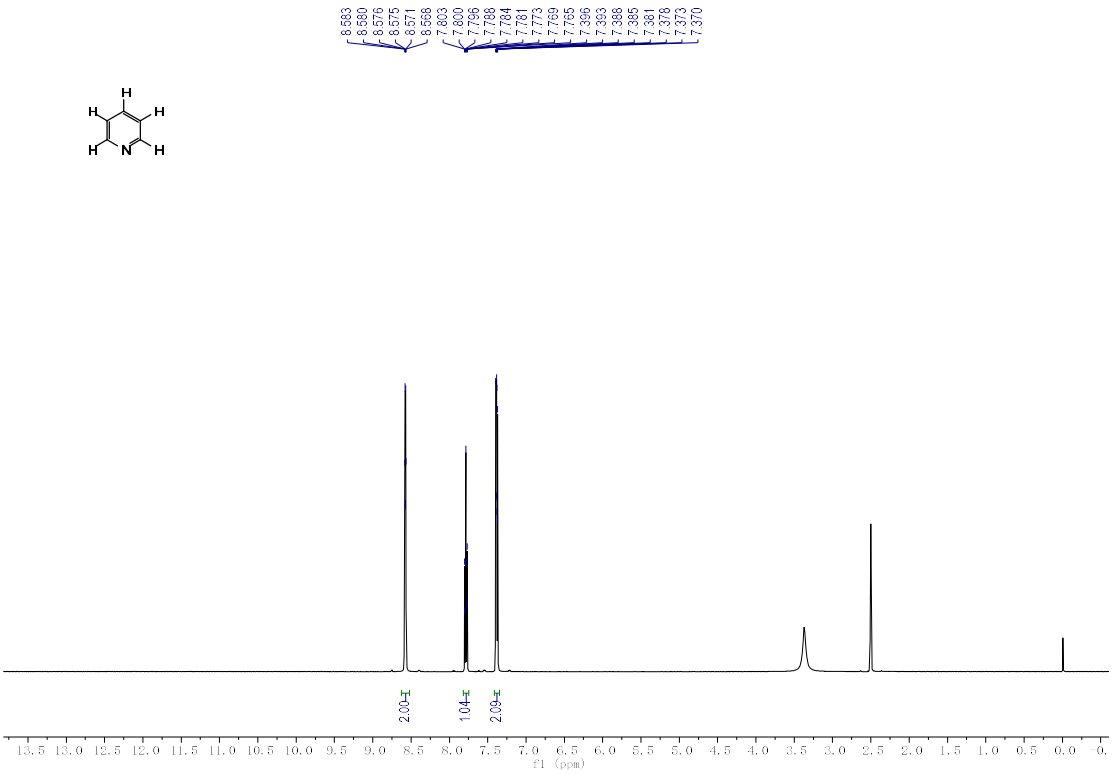
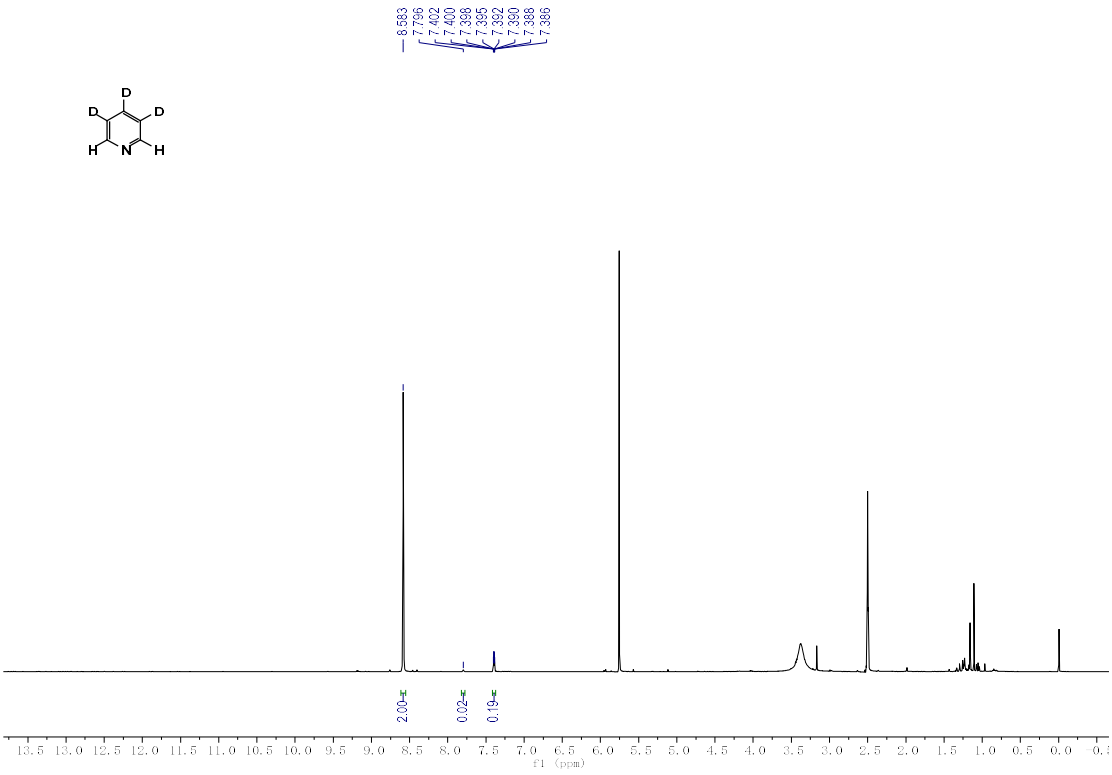
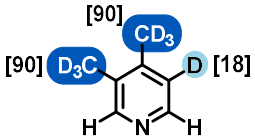


Figure S40 ^{1}H NMR of **9-*d*** in DMSO-d_6



Deuteration of 3,4-*d*imethylpryidine (10)



General procedure to afford **10-*d*** as yellow oil (37.2 mg, 33%) with 90%D at 4-methyl, 90%D at 5-methyl, and 18%D at β-position by ^{1}H NMR; 5.74D by GC-MS; R_f = 0.45 (Petroleum ether/EtOAc = 15/1)

NMR data for starting material: ^{1}H NMR (399 MHz, DMSO-d_6) δ 8.27 (s, 1H), 8.24 (d, J = 4.9 Hz, 1H), 7.13 (d, J = 4.8 Hz, 1H), 2.23 (s, 3H), 2.20 (s, 3H).

NMR data for deuterated product: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.28 (s, 1H), 8.25 (d, J = 4.9 Hz, 1.0H), 7.14 (d, J = 4.9 Hz, 0.82H, **Labelled**), 2.19 (ddt, J = 11.4, 6.7, 2.3 Hz, 0.65H, **Labelled**).

Figure S41 ^{1}H NMR spectrum comparison

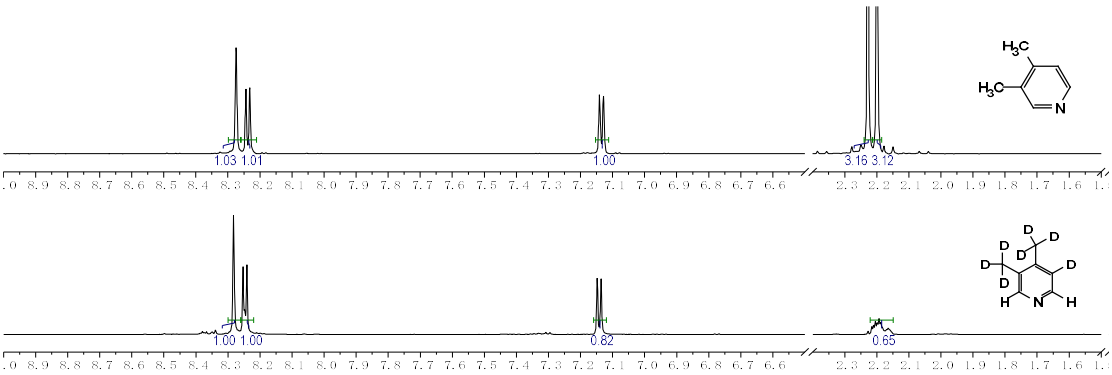


Figure S42 GC-MS spectrum comparison

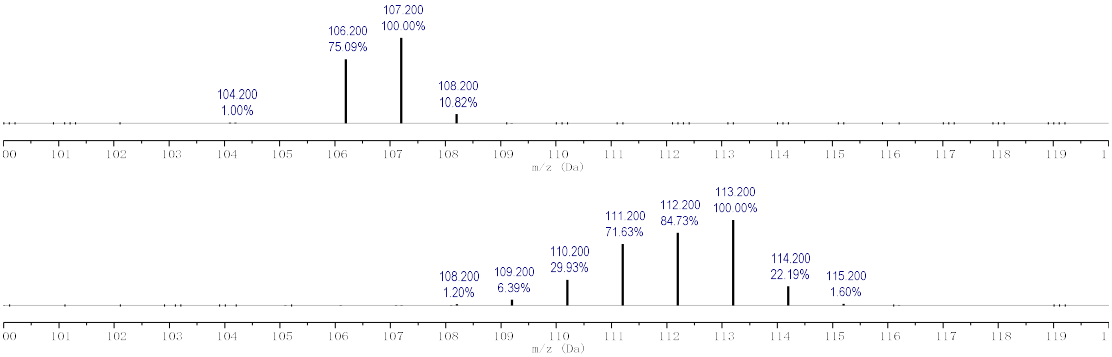


Figure S43 ^{1}H NMR of **10** in DMSO-d_6

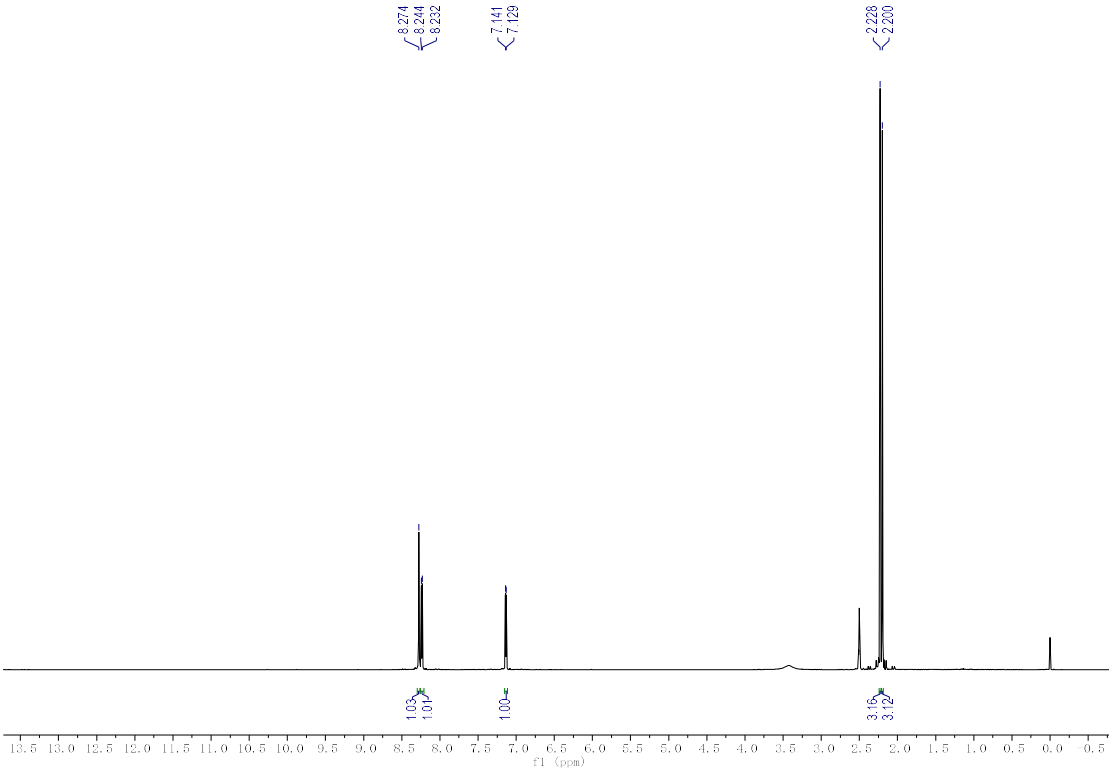
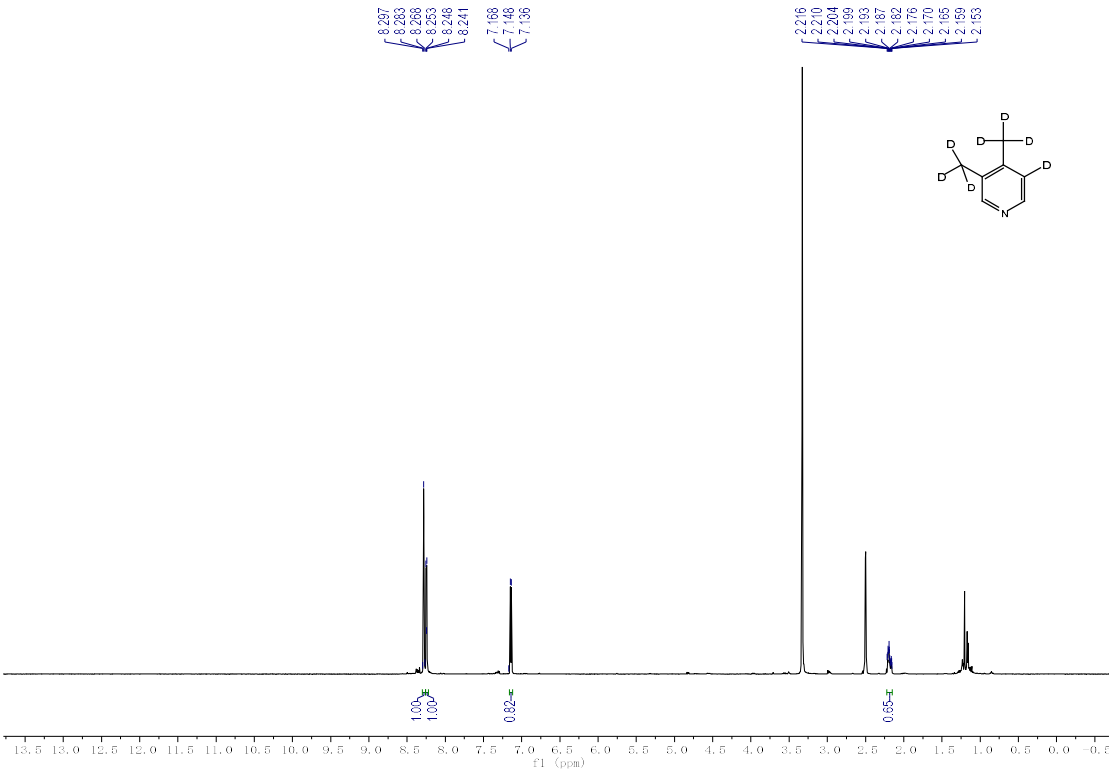
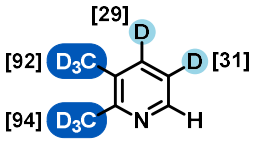


Figure S44 ^{1}H NMR of **10-*d*** in DMSO-d_6



Deuteration of 2,3-*d*imethylpryidine(11)



General procedure to afford **11-*d*** as yellow oil (92.5 mg, 82%) with D-incorporation 31%D at β-position, 29%D at γ-position, 94%D at 5-methyl, and 92%D at 6-methyl by ^{1}H NMR; 6.05D by GC-MS. R_f = 0.45 (Petroleum ether/EtOAc = 20/1)

NMR data for starting material: ^{1}H NMR (399 MHz, DMSO-d_6) δ 8.23 (dd, J = 4.9, 1.7 Hz, 1H), 7.51 – 7.45 (m, 1H), 7.09 (dd, J = 7.5, 4.8 Hz, 1H), 2.40 (s, 3H), 2.23 (s, 3H).

NMR data for deuterated product: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.27 – 8.21 (m, 1H), 7.52 – 7.46 (m, 0.71H, **Labelled**), 7.10 (dd, J = 7.6, 4.8 Hz, 0.69H, **Labelled**), 2.38 (tt, J = 4.5, 2.2 Hz, 0.24H, **Labelled**), 2.20 (p, J = 2.3 Hz, 0.18H, **Labelled**).

Figure S45 ^{1}H NMR spectrum comparison

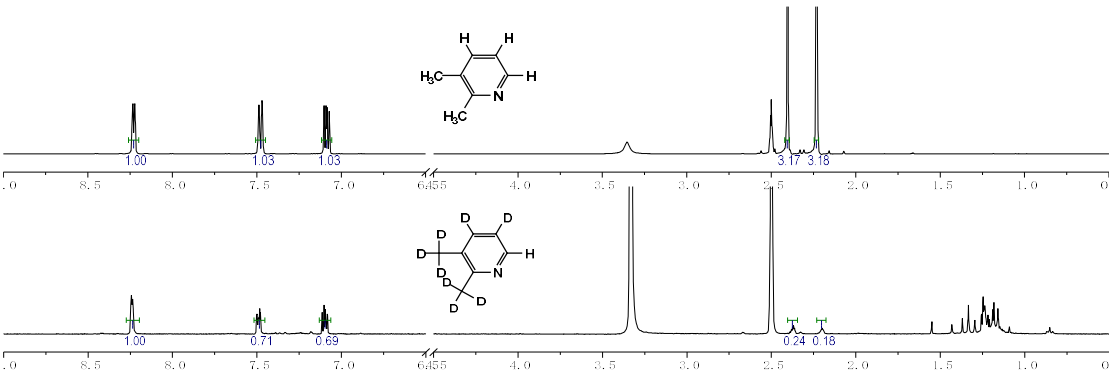


Figure S46 GC-MS spectrum comparison

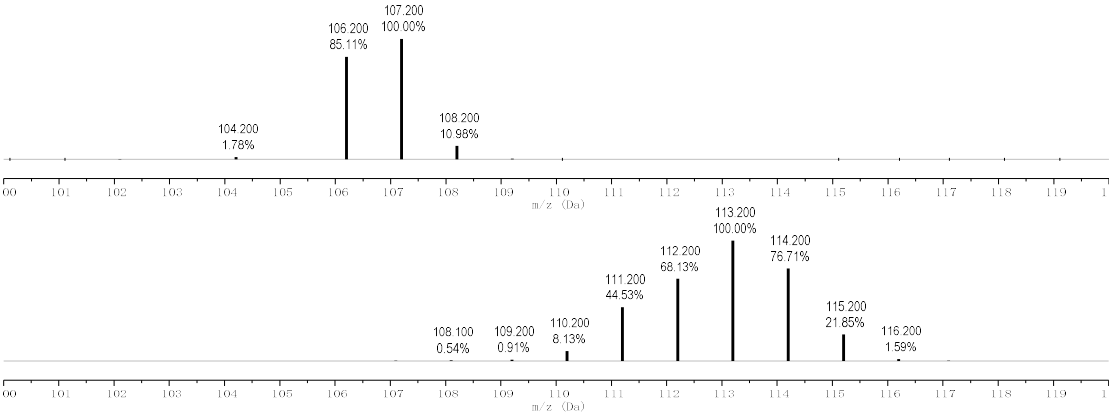


Figure S47 ^{1}H NMR of **11** in DMSO-d_6

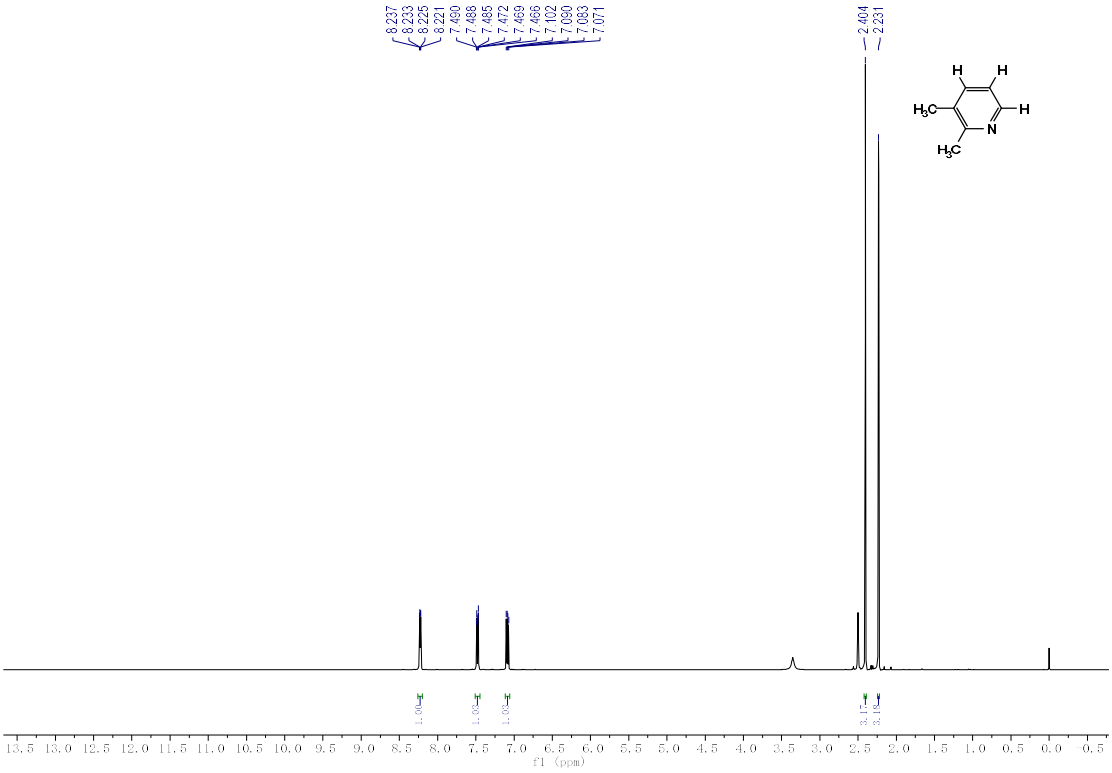
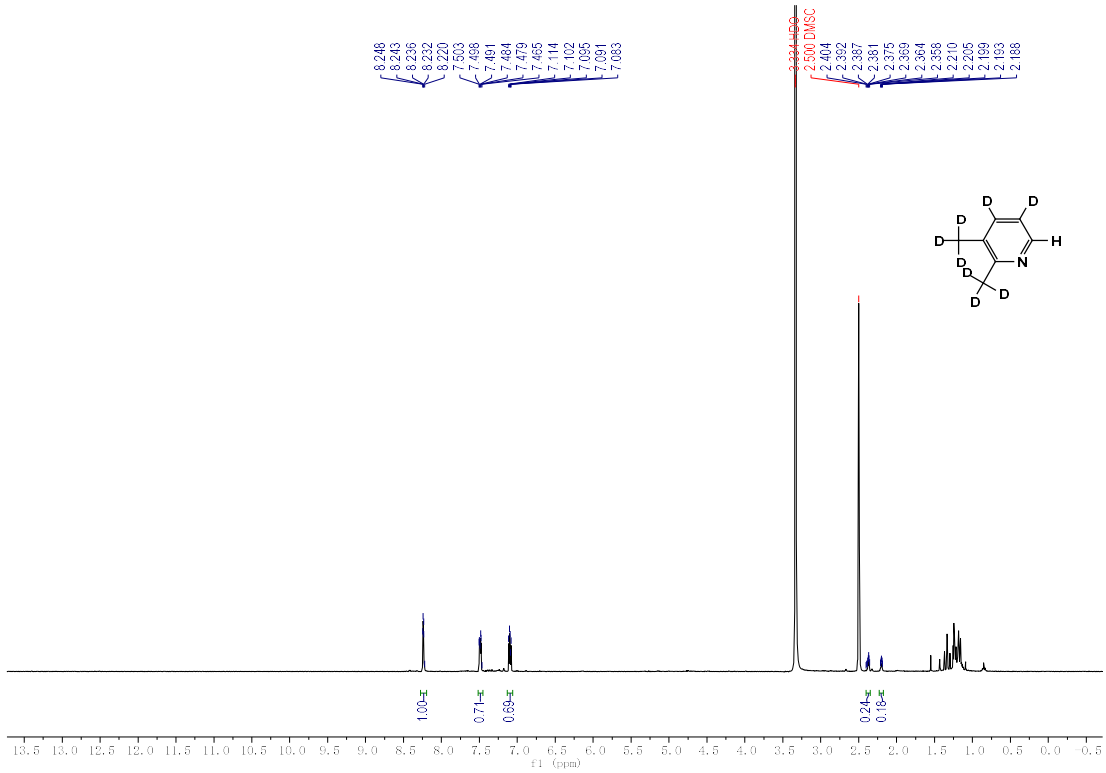
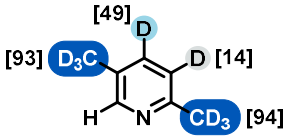


Figure S48 ^{1}H NMR of **11-*d*** in DMSO-d_6



Deuteration of 2,4-*d*imethylpryidine (12)



General procedure to afford **12-*d*** as yellow oil (112.0 mg, 99%) with D-incorporation 94% at 2-methyl, 14%D at β-position, 49%D at γ-position, and 93% at 5-methyl by ^{1}H NMR; 6.29D by GC-MS. R_f = 0.45 (Petroleum ether/EtOAc = 15/1)

NMR data for starting material: ^{1}H NMR (399 MHz, DMSO-d_6) δ 8.25 (dt, J = 2.4, 0.8 Hz, 1H), 7.45 (ddd, J = 7.9, 2.4, 0.8 Hz, 1H), 7.11 (d, J = 7.8 Hz, 1H), 2.40 (s, 3H), 2.23 (s, 3H).

NMR data for deuterated product: ^{1}H NMR (399 MHz, DMSO-d_6) δ 8.25 (d, J = 0.7 Hz, 1.0H), 7.46 (dd, J = 7.8, 2.3 Hz, 0.51H, **Labelled**), 7.14 – 7.08 (m, 0.86H, **Labelled**), 2.37 (p, J = 2.0 Hz, 0.17 H, **Labelled**), 2.23 – 2.18 (m, 0.20 H, **Labelled**).

Figure S459 ^{1}H NMR spectrum comparison

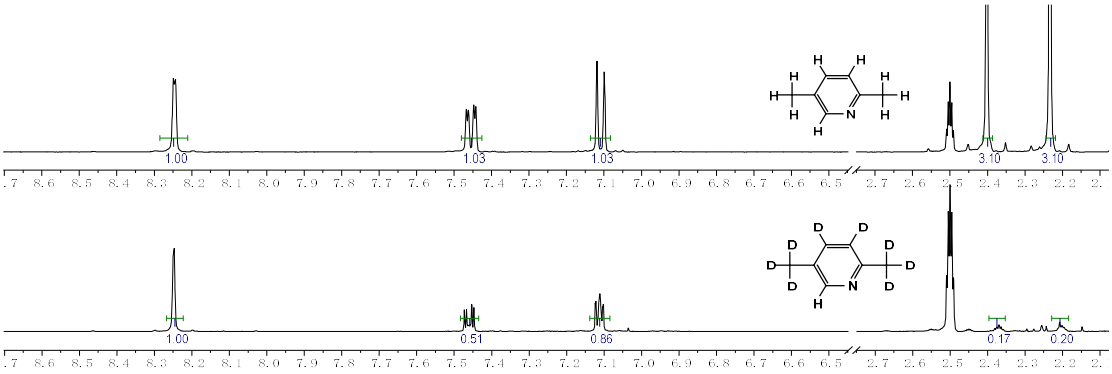


Figure S50 GC-MS spectrum comparison

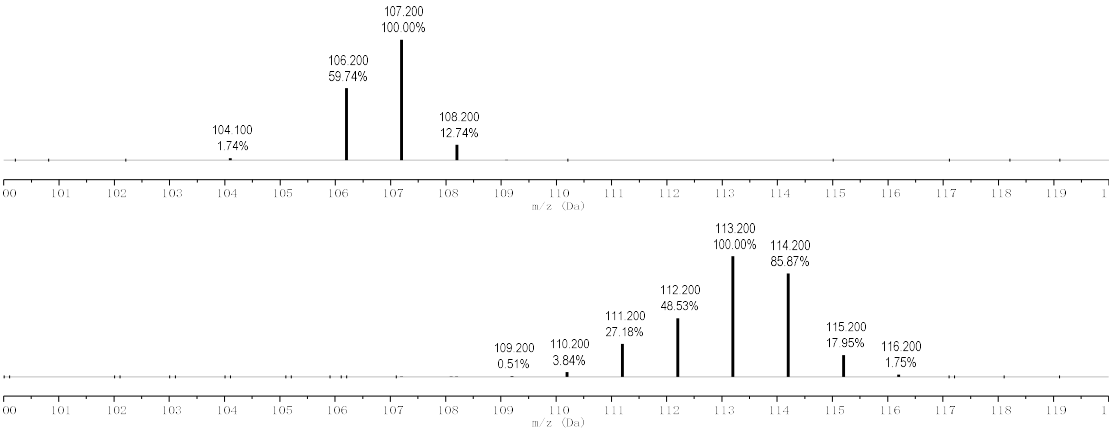


Figure S51 ^{1}H NMR of **12** in DMSO-d_6

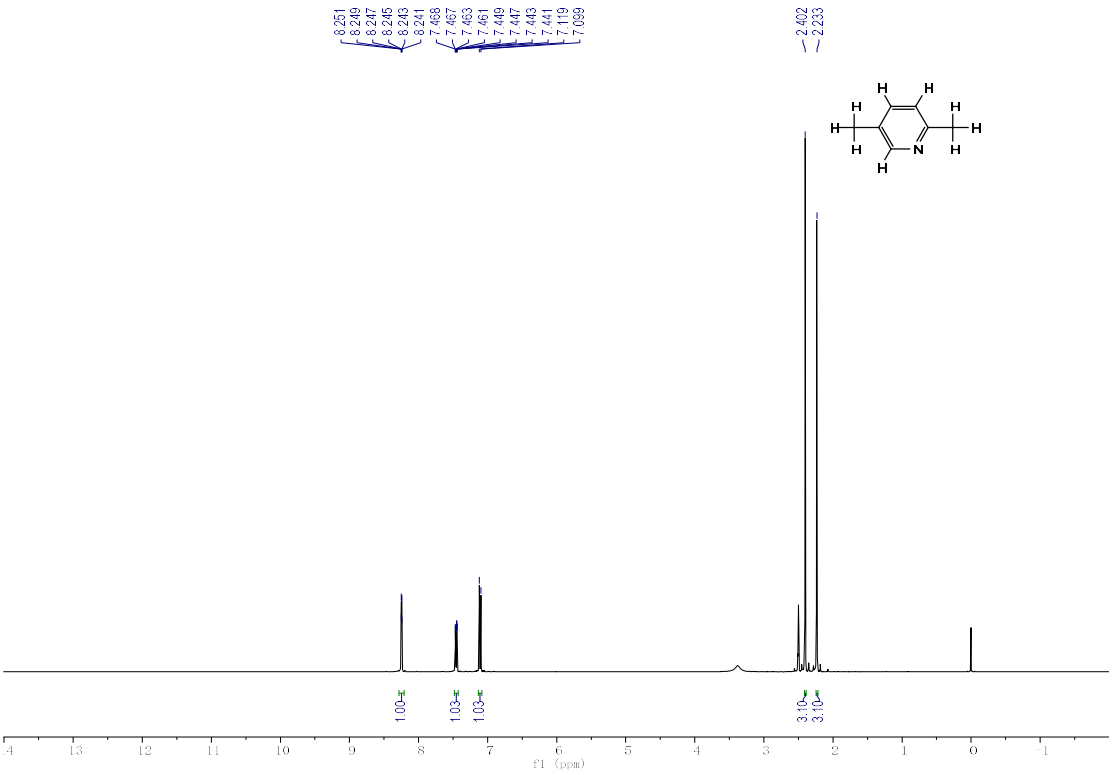
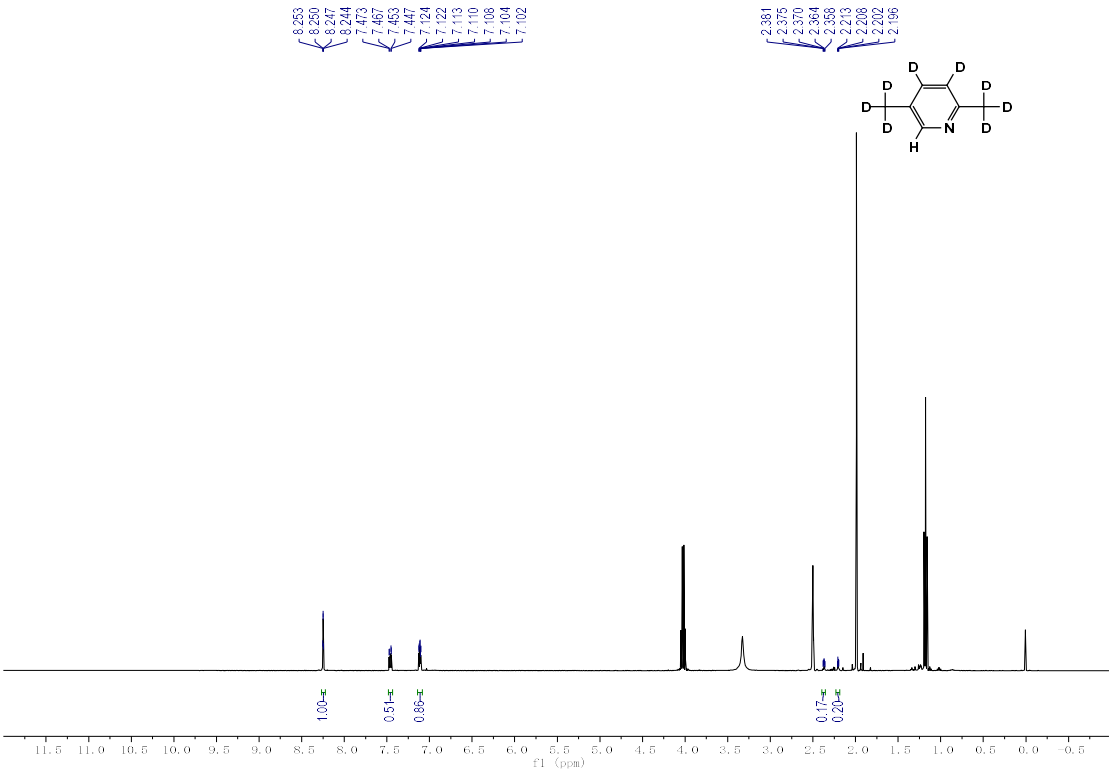
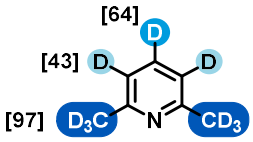


Figure S52 ^{1}H NMR of **12-*d*** in DMSO-d_6



Deuteration of 2,6-*d*imethylpryidine (13)



General procedure to afford **13-*d*** as yellow oil (109.7 mg, 97%, calculated based on internal standard) with D-incorporation 97% at methyl, 43%D at β-position and 64%D at γ-position by ^{1}H NMR based on internal standard; 6.20D by GC-MS. R_f = 0.45 (Petroleum ether/EtOAc = 15/1)

NMR data for starting material with DMT (c =0.00858 mmol/mL) as internal standard: ^{1}H NMR (399 MHz, DMSO-d_6) δ 7.52 (t, J = 7.6 Hz, 1H), 7.00 (dq, J = 7.6, 0.6 Hz, 2H), 3.32 (s, 1H), 2.40 (s, 6H).

NMR data for deuterated product with DMT (c =0.00858 mmol/mL) as internal standard: ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.54 (t, J = 7.6 Hz, 0.36H, **Labelled**), 7.05 – 6.98 (m, 1.13H, **Labelled**). 2.39 – 2.35 (m, 0.18H, **Labelled**).

Figure S46 ^{1}H NMR spectrum comparison

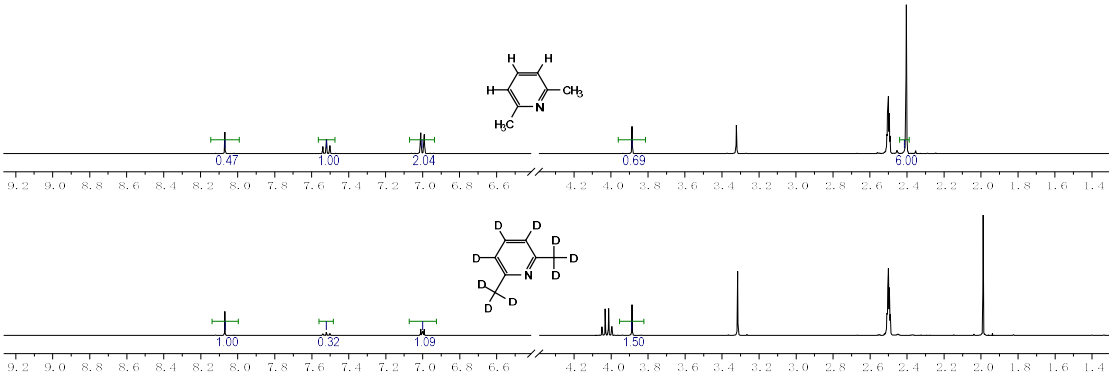


Figure S47 GC-MS spectrum comparison

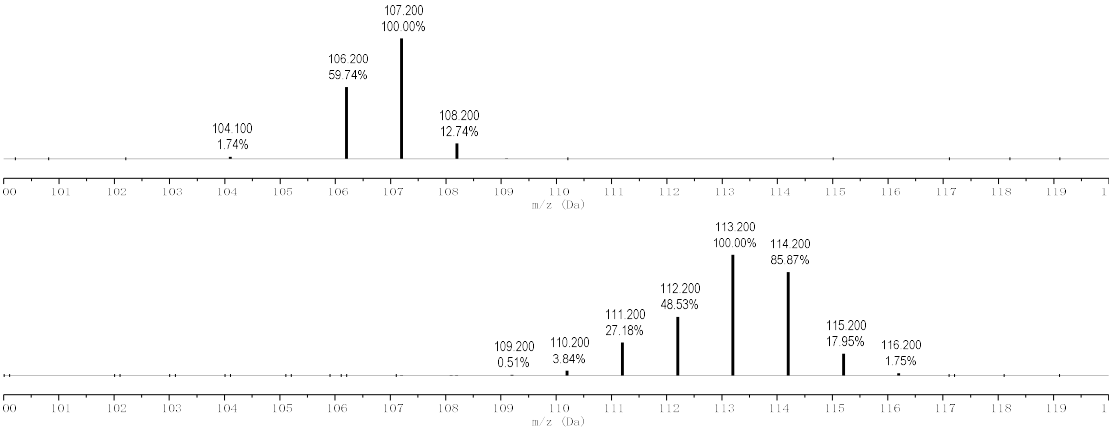


Figure S48 ^{1}H NMR of **13** in Solvent

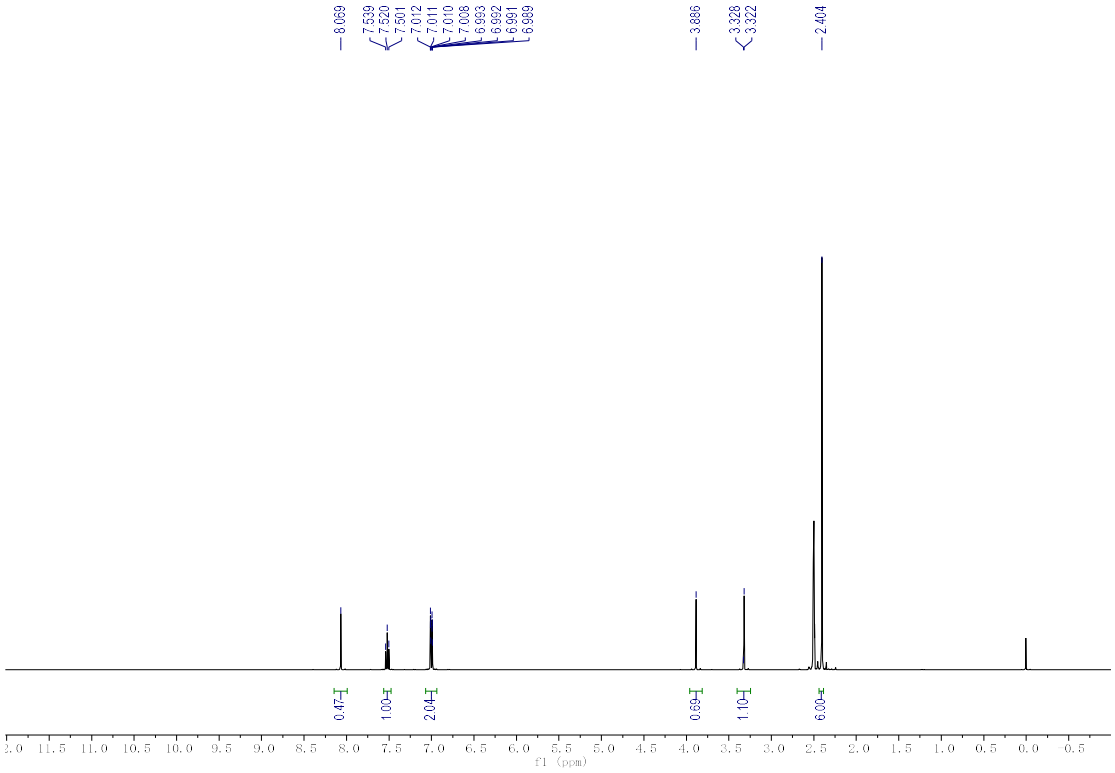
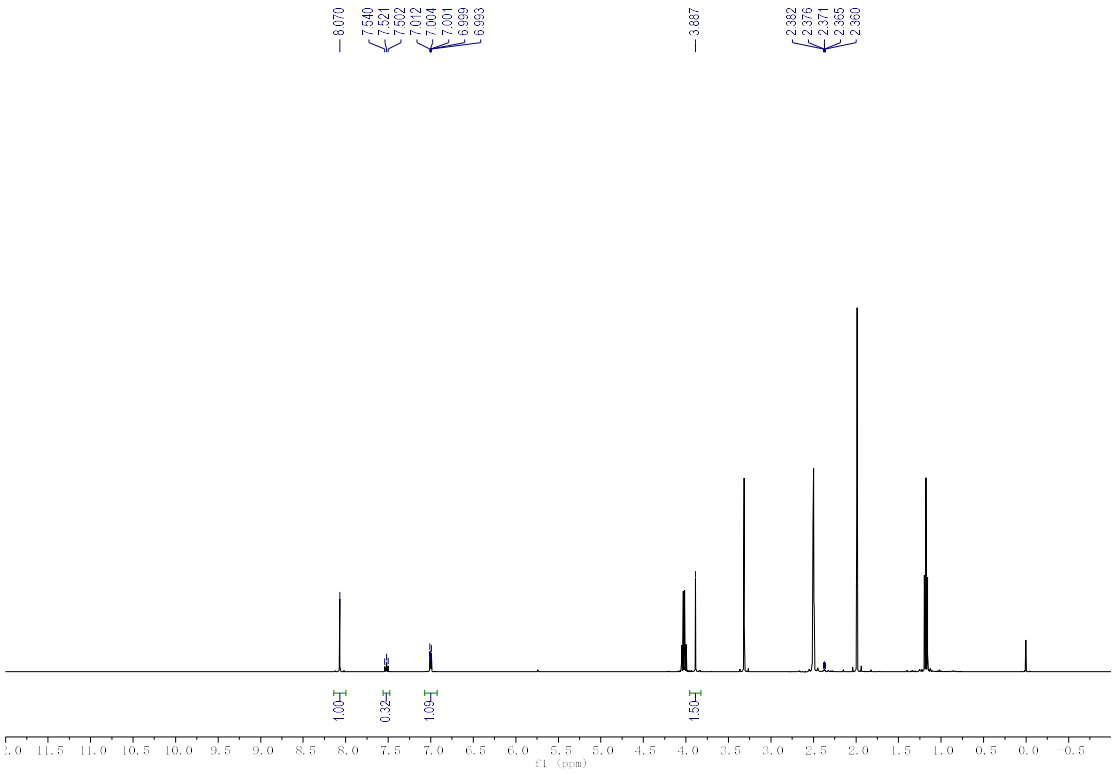
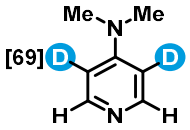


Figure S49 ^{1}H NMR of **13-*d*** in solvent



Deuteration of *N,N-d*imethylpyridin-4-amine (14)



General procedure to afford **14-*d*** as pale-yellow solid (116.1 mg, 95%) with D-incorporation 69%D at β-position by ^{1}H NMR; 1.42D by GC-MS. R_f = 0.45 (dichloromethane/methanol = 10/1)

NMR data for starting material: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.10 (dt, J = 6.0, 1.6 Hz, 2H), 6.57 (dt, J = 6.6, 1.7 Hz, 2H), 2.93 (s, 6H).

NMR data for deuterated product: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.10 (t, J = 2.9 Hz, 2.0H), 6.60 (d, J = 6.2 Hz, 0.60H, **Labelled**), 2.95 (s, 6.02H).

Figure S50 ^{1}H NMR spectrum comparison

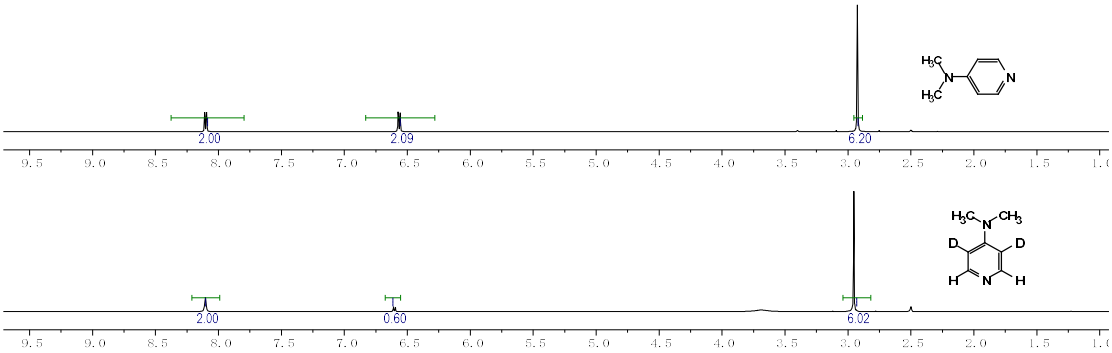


Figure S51 GC-MS spectrum comparison

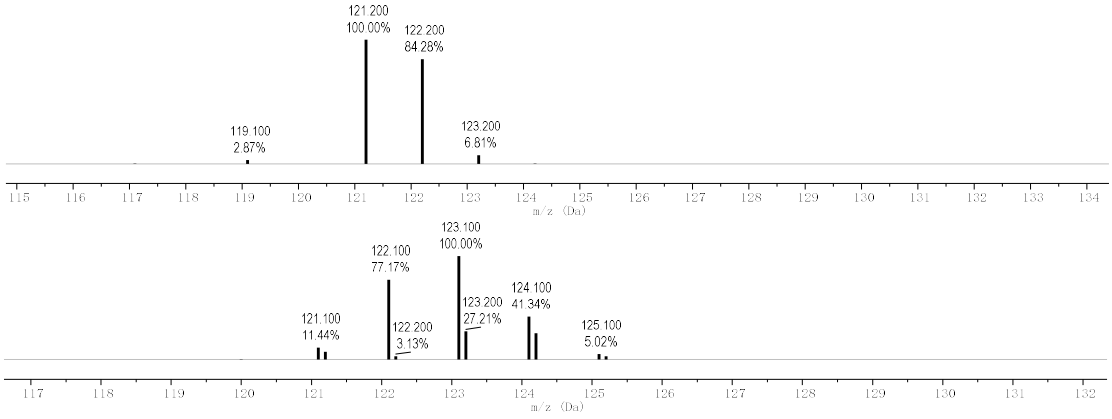


Figure S52 ^{1}H NMR of **14** in DMSO-d_6

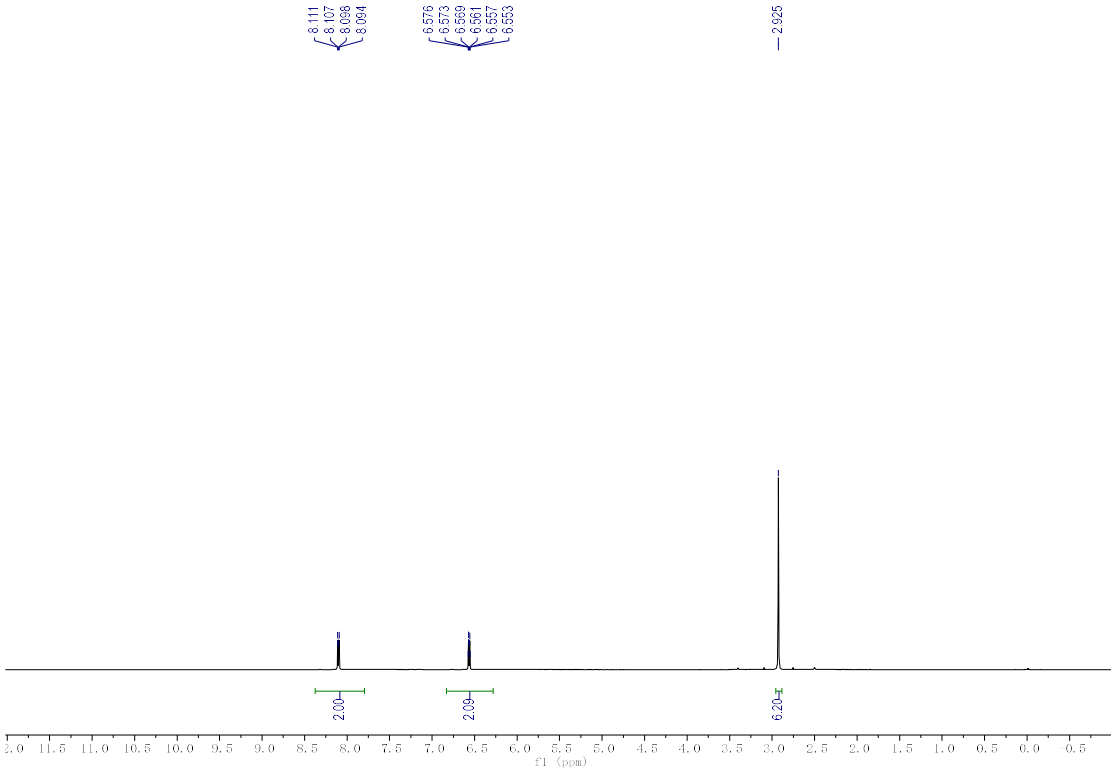
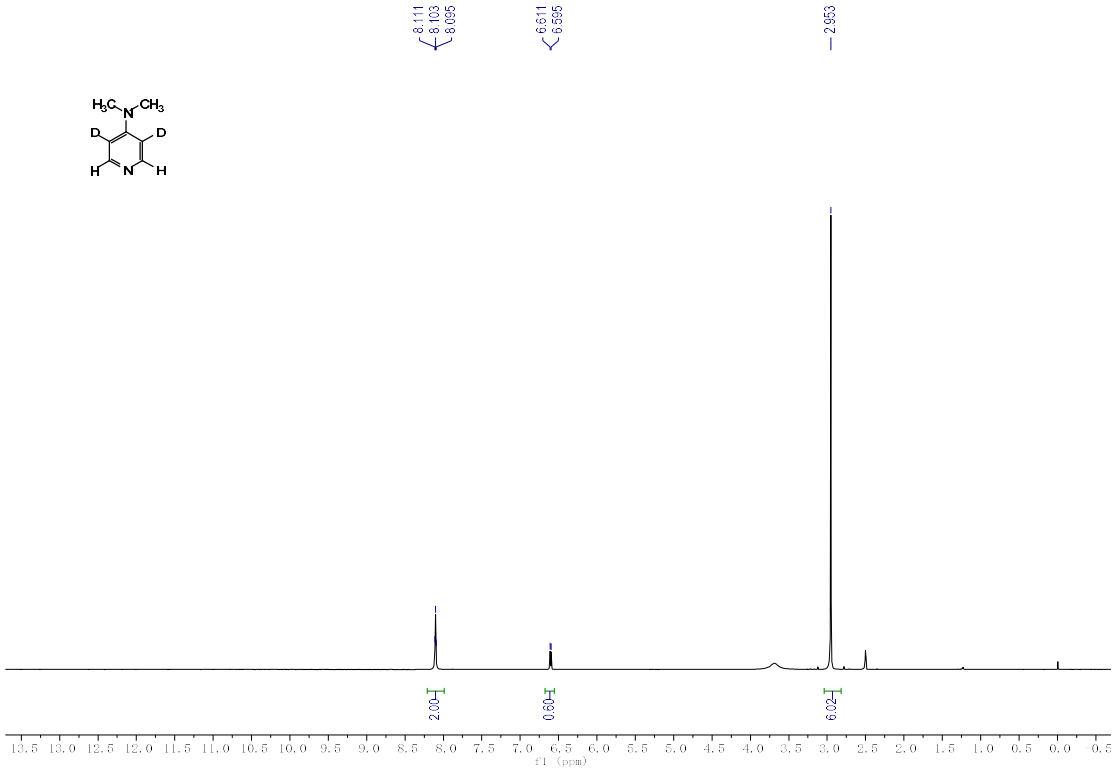
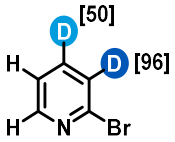


Figure S53 ^{1}H NMR of **14-*d*** in DMSO-d_6



Deuteration of 2-bromopyridine (15)



General procedure to afford **15-*d*** as white solid (112.4 mg, 48%) with D-incorporation 96%D at β'-position and 50%D at γ-position by ^{1}H NMR; 1.51D by GC-MS. R_f = 0.45 (Petroleum ether/EtOAc = 15/1)
NMR data for starting material: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.39 (ddd, J = 4.8, 2.1, 0.8 Hz, 1H), 7.75 (ddd, J = 8.1, 7.4, 2.1 Hz, 1H), 7.64 (dt, J = 8.0, 1.0 Hz, 1H), 7.44 (ddd, J = 7.3, 4.8, 1.0 Hz, 1H).
NMR data for deuterated product: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.40 (dt, J = 4.9, 1.3 Hz, 1.0H), 7.82 – 7.72 (m, 0.49H, **Labelled**), 7.67 – 7.63 (m, 0.04H, **Labelled**), 7.51 – 7.39 (m, 1H).

Figure S54 ^{1}H NMR spectrum comparison

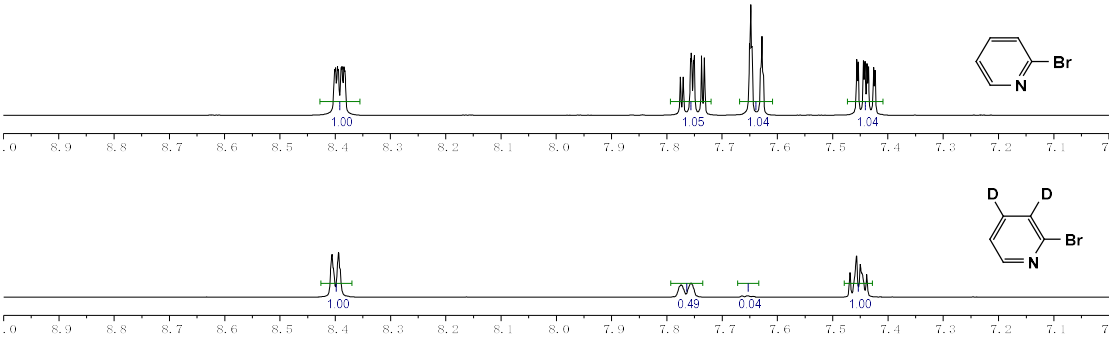


Figure S55 GC-MS spectrum comparison

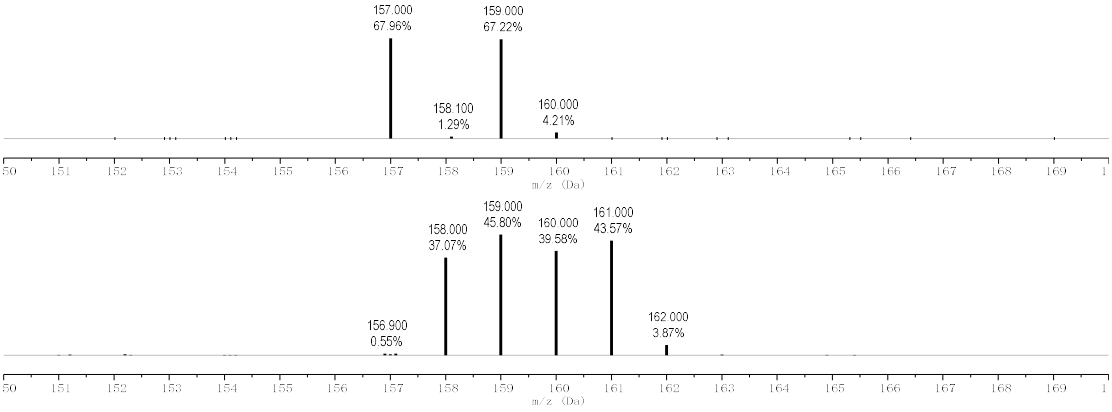


Figure S56 ^{1}H NMR of **15** in DMSO-d_6

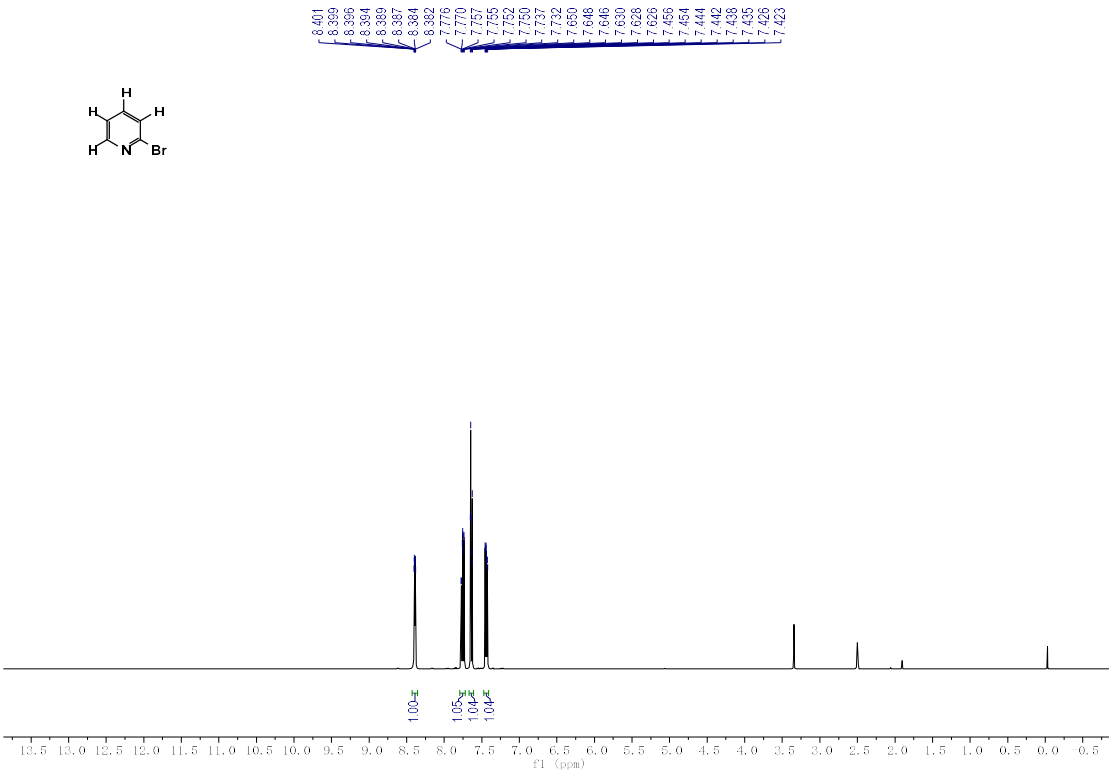
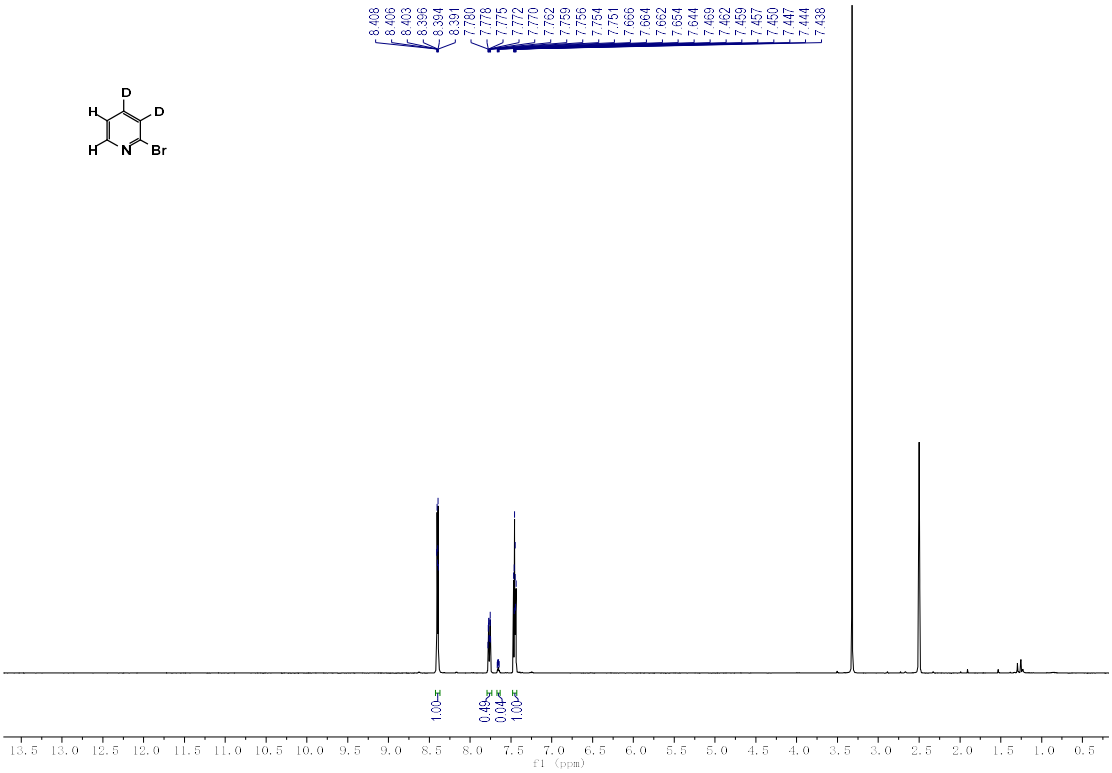
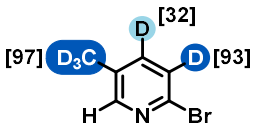


Figure S57 ^{1}H NMR of **15-*d*** in DMSO-d_6



Deuteration of 2-bromo-5-methylpyridine (16)



General procedure to afford **16-*d*** as white solid (147.5 mg, 42%) with D-incorporation 97%D at 5-methyl, 93%D at β'-position, and 32%D at γ-position by ^{1}H NMR; 4.30D by GC-MS. R_f = 0.45 (Petroleum ether/EtOAc = 15/1)

NMR data for starting material with 1,4-dioxane (0.594 mmol/mL): ^{1}H NMR (399 MHz, DMSO-d_6) δ 8.22 (d, J = 2.4 Hz, 1H), 7.57 (dd, J = 8.1, 2.5 Hz, 1H), 7.51 (d, J = 8.1 Hz, 1H), 3.56 (s, 3H), 2.25 (s, 3H).

NMR data for deuterated product with 1,4-dioxane (0.598 mmol/mL)**:** ^{1}H NMR (399 MHz, DMSO-d_6) δ 8.29 – 8.14 (m, 1H), 7.57 (dt, J = 2.2, 1.0 Hz, 0.64H, Labelled), 7.52 – 7.49 (m, 0.06H, Labelled), 2.25 – 2.20 (m, 0.09H, Labelled).

Figure S58 ^{1}H NMR spectrum comparison

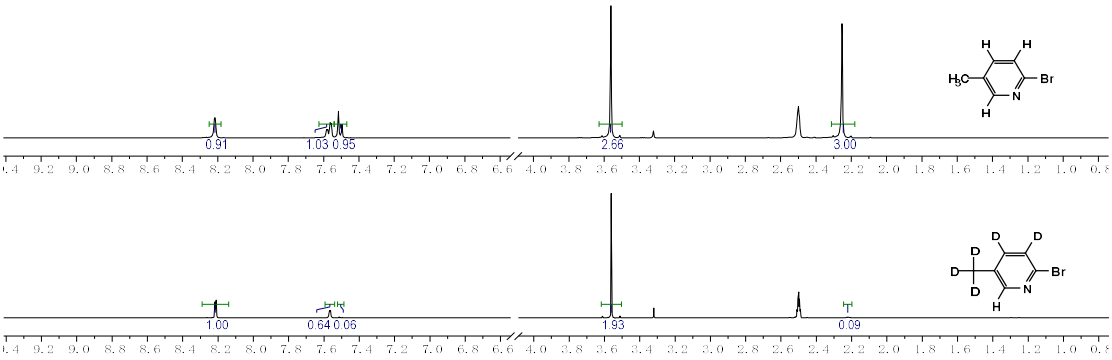


Figure S59 GC-MS spectrum comparison

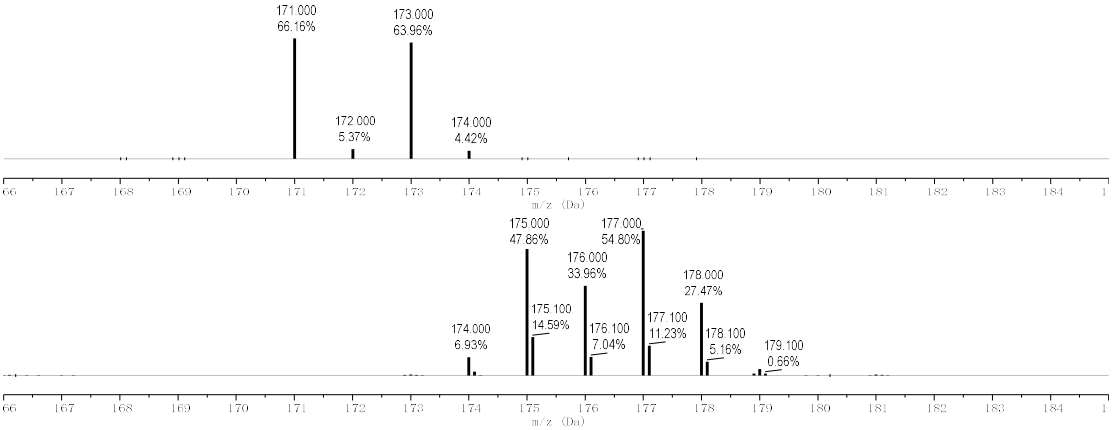


Figure S60 ^{1}H NMR of **16** in DMSO-d_6 with 1,4-dioxane

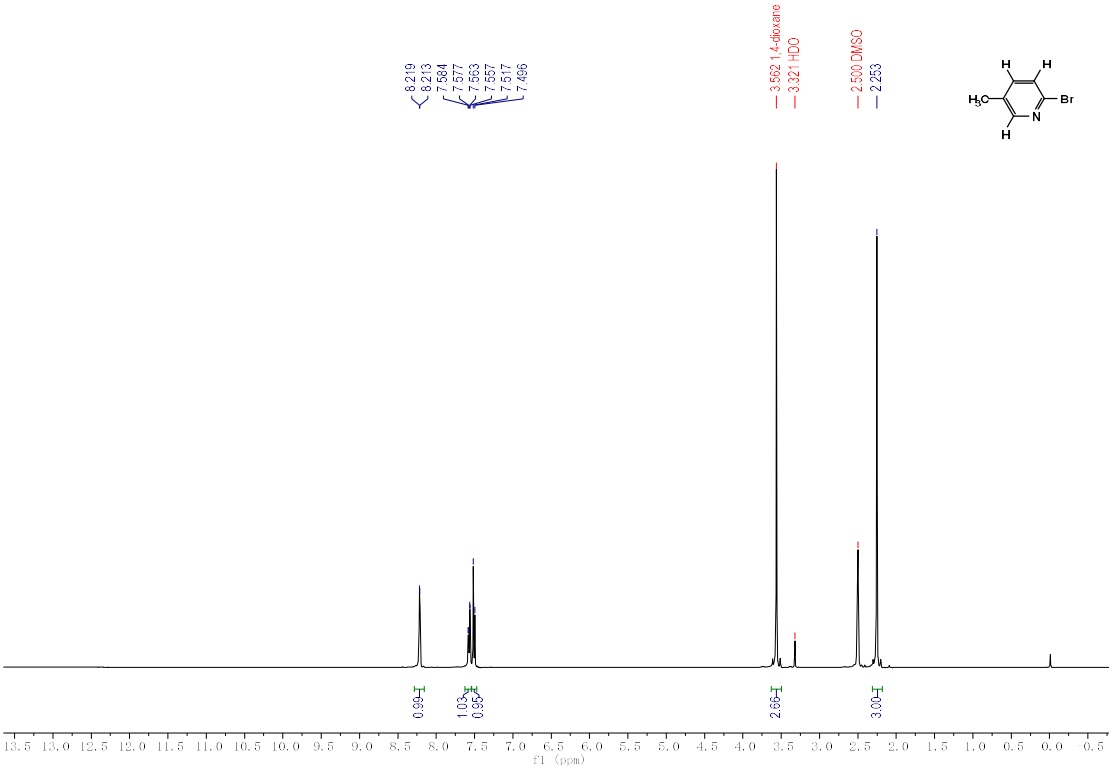
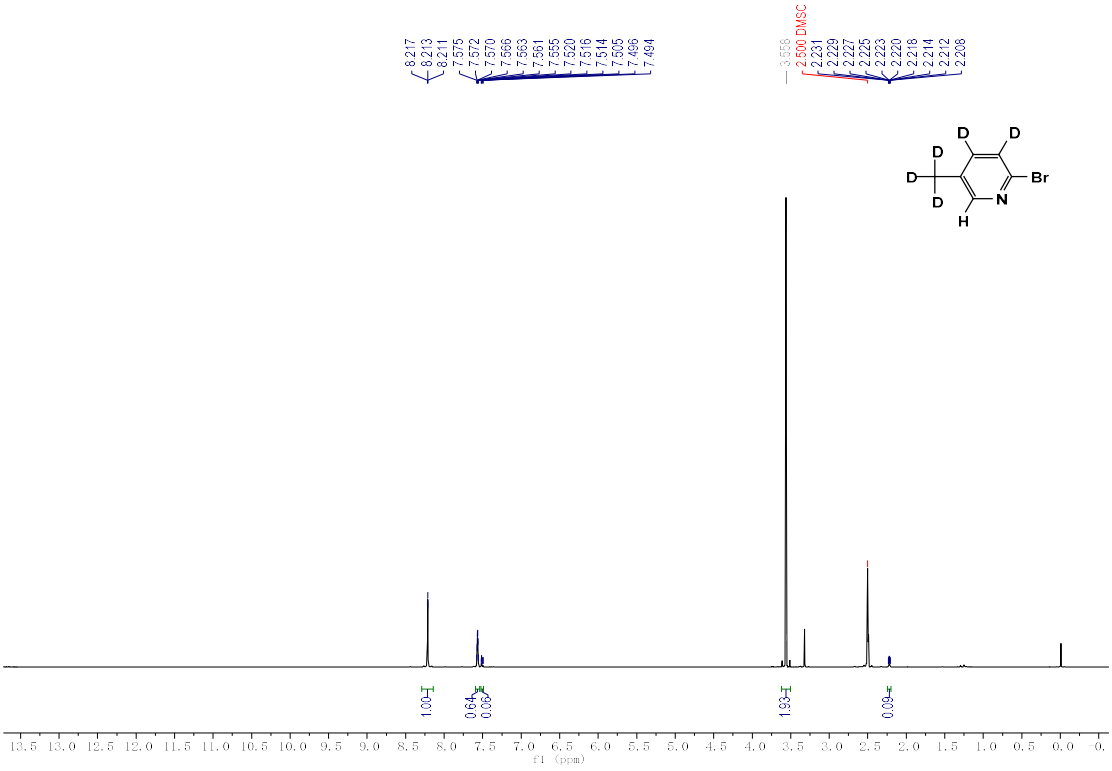
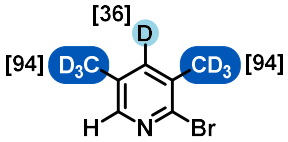


Figure S61 ^{1}H NMR of **16-*d*** in DMSO-d_6 with 1,4-dioxane



Deuteration of 2-bromo-3,5-*d*imethylpyridine (17)



General procedure to afford **17-*d*** as colorless oil (106.7mg, 60%) with D-incorporation 94%D at 3-methyl, 94%D at 5-methyl, and 36%D at γ-position by ^{1}H NMR; 5.89D by GC-MS; R_f = 0.45 (Petroleum ether/EtOAc = 15/1).

NMR data for starting material with dioxane (0.639 mmol/mL)**:** ^{1}H NMR (399 MHz, DMSO-d_6) δ 8.01 (dt, J = 2.4, 0.7 Hz, 1H), 7.55 (dt, J = 2.5, 0.7 Hz, 1H), 2.27 (s, 3H), 2.22 (s, 3H).

NMR data for deuterated product with dioxane (0.628 mmol/mL)**:** ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.07 – 8.02 (m, 1.01H), 7.59 (d, J = 2.4 Hz, 0.64H, **Labelled**), 2.29 – 2.23 (m, 0.19H, **Labelled**), 2.23 – 2.18 (m, 0.19H, **Labelled**).

Figure S62 ^{1}H NMR spectrum comparison

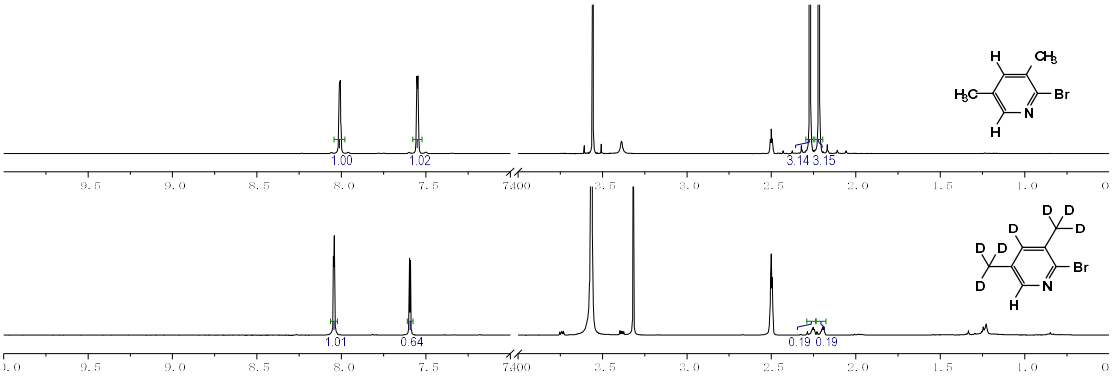


Figure S63 GC-MS spectrum comparison

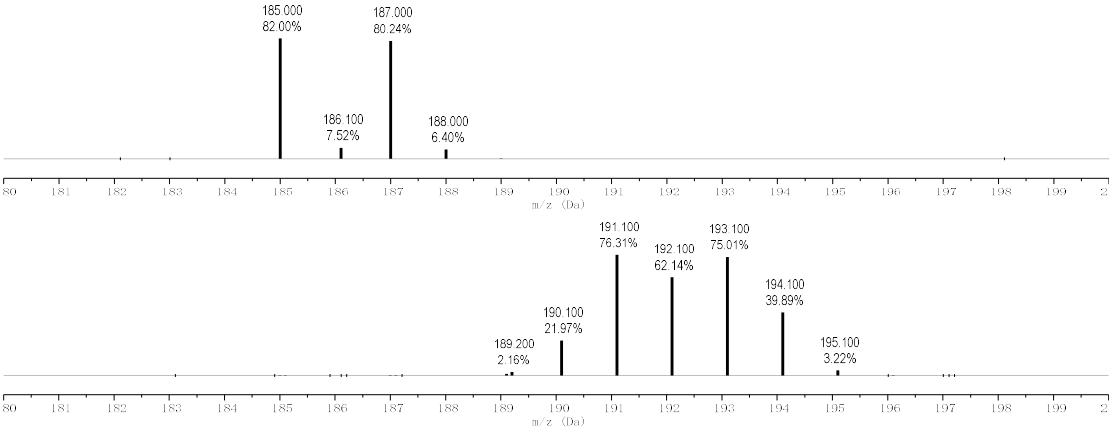


Figure S64 ^{1}H NMR of **17** in DMSO-d_6

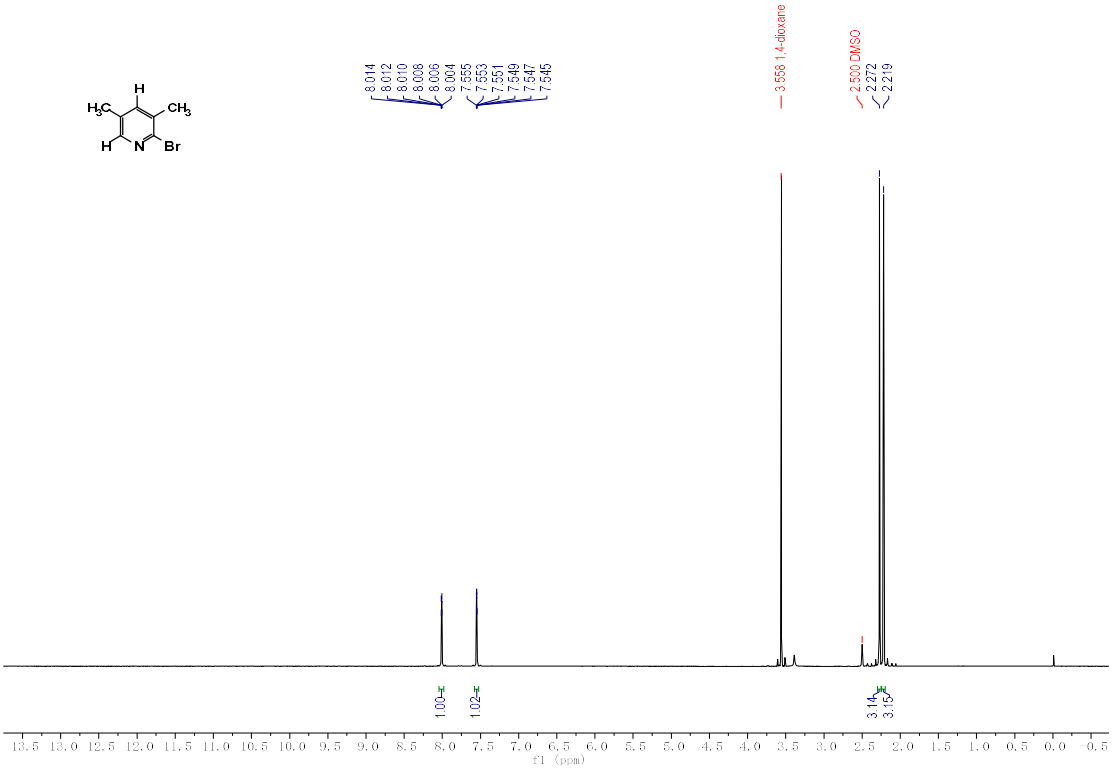
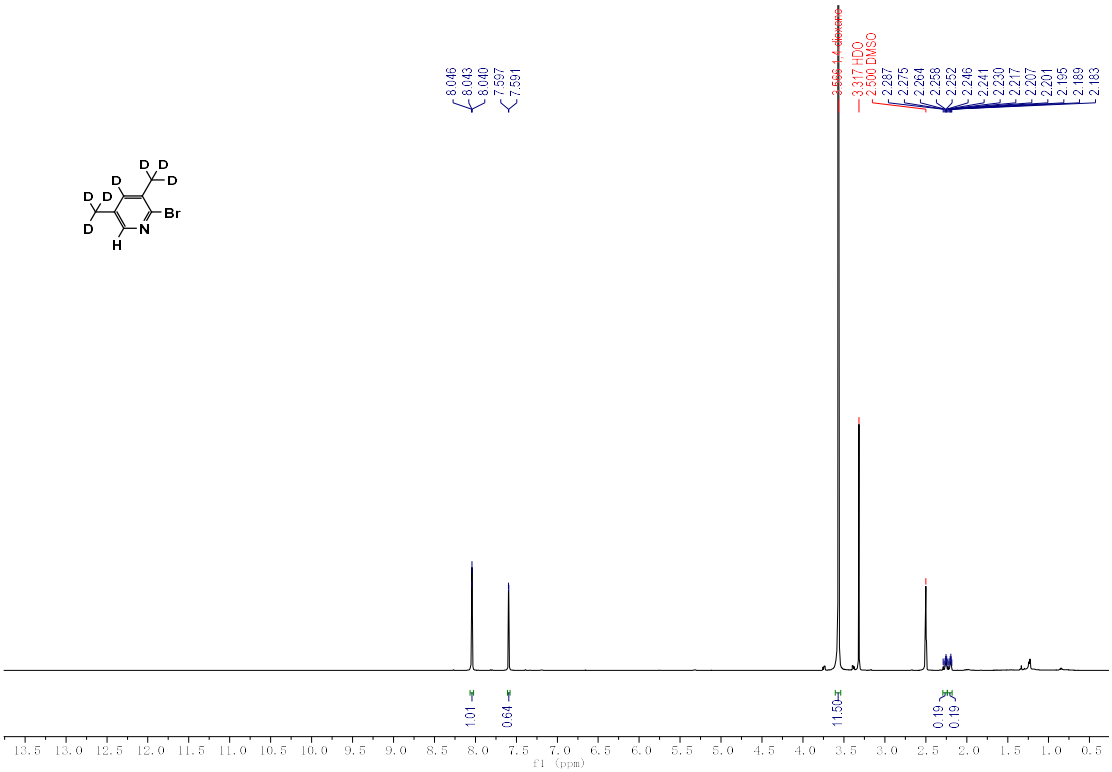
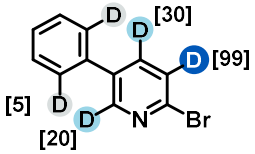


Figure S65 ^{1}H NMR of **17-*d*** in DMSO-d_6



Deuteration of 2-bromo-5-phenylpyridine (18)



General procedure to afford **18-*d*** as white solid (112.4 mg, 48%) with D-incorporation 20%D at α-position, approx. 99%D at β'-position, 30%D at γ-position, and approx. 5%D at 2'-position by ^{1}H NMR; 1.42D by GC-MS; R_f = 0.45 (Petroleum ether/EtOAc = 15/1)

NMR data for starting material with dioxane (0.628 mmol/mL)**:** ^{1}H NMR (399 MHz, DMSO-d_6) δ 8.69 (dd, J = 2.7, 0.7 Hz, 1H), 8.02 (dd, J = 8.3, 2.7 Hz, 1H), 7.74 – 7.68 (m, 3H), 7.52 – 7.46 (m, 2H), 7.46 – 7.40 (m, 1H).

NMR data for deuterated product with dioxane (0.581 mmol/mL): ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.76 – 8.70 (m, 0.95H), 8.06 (d, J = 2.7 Hz, 0.56H, Labelled), 7.77 – 7.72 (m, 2H, Labelled), 7.55 – 7.49 (m, 2H), 7.48 – 7.43 (m, 1.0 H).

Figure S66 ^{1}H NMR spectrum comparison

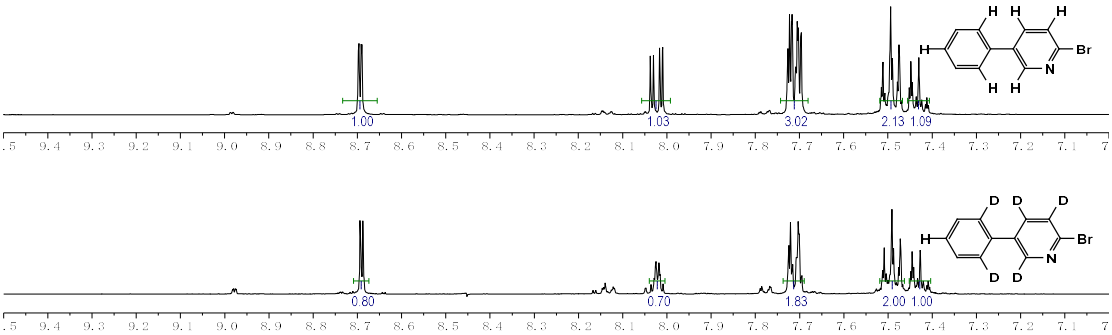


Figure S67 GC-MS spectrum comparison

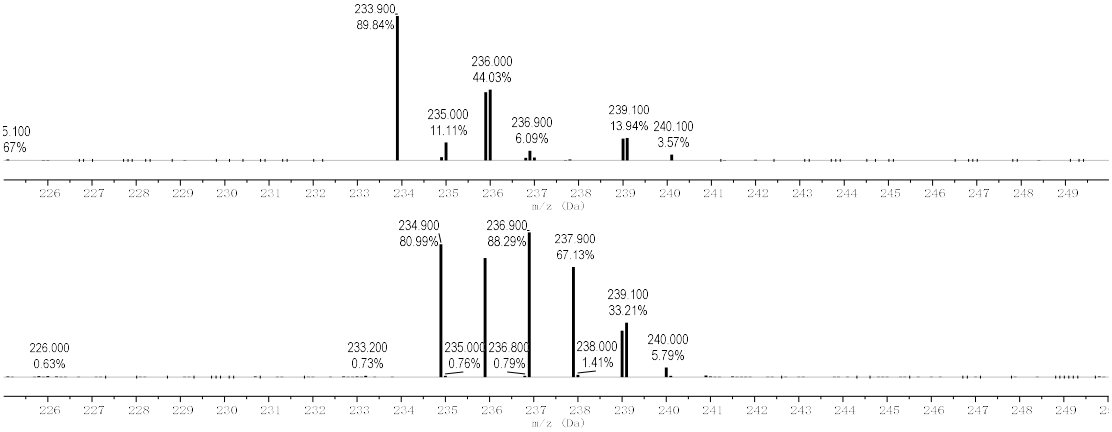


Figure S68 ^{1}H NMR of **18** in Solvent

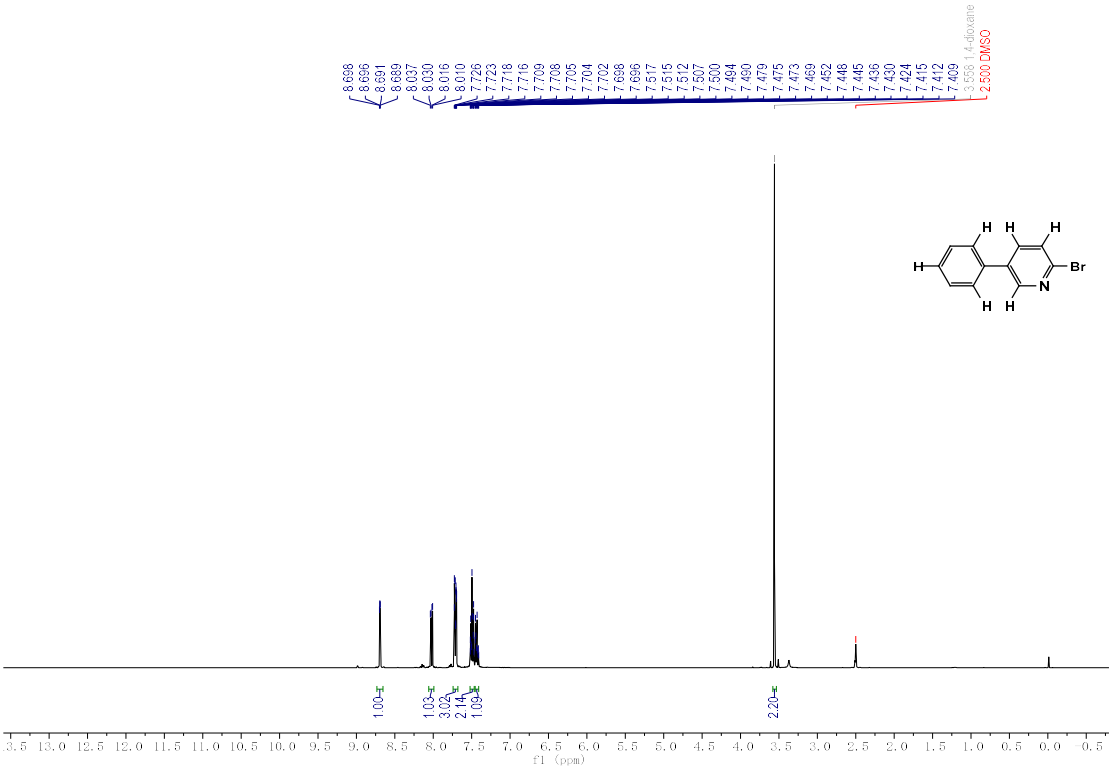
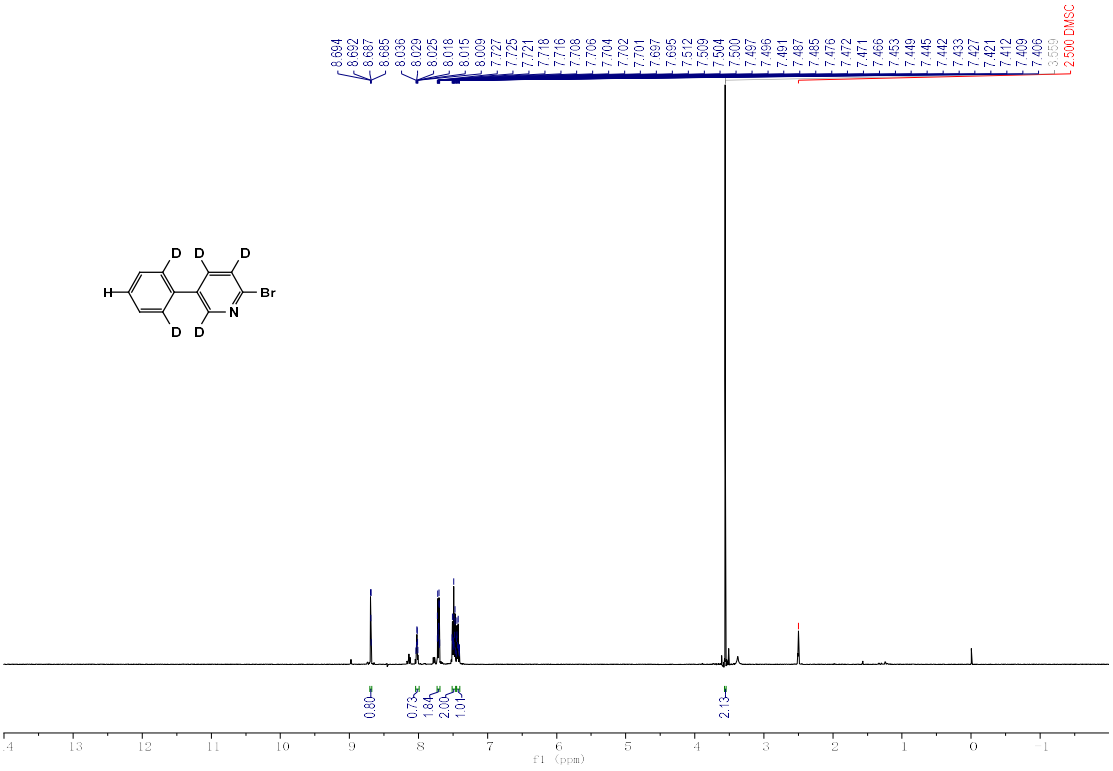
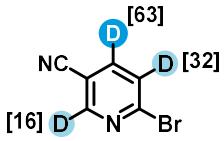


Figure S69 ^{1}H NMR of **18-*d*** in solvent



Deuteration of 6-bromonicotinonitrile (19)



General procedure to afford **19-*d*** as orange oil (101.6 mg, 55%) with D-incorporation 16%D at α-position, β'-position and 63%D at γ-position by ^{1}H NMR; 1.57D by GC-MS. R_f = 0.45 (Petroleum ether/EtOAc = 10/1)

NMR data for starting material with dioxane (c =0.639 mmol/mL): ^{1}H NMR (399 MHz, DMSO-d_6) δ 8.86 (dd, J = 2.4, 0.8 Hz, 1H), 8.24 (dd, J = 8.3, 2.4 Hz, 1H), 7.90 (dd, J = 8.3, 0.8 Hz, 1H), 3.55 (s, 1.23H, internal standard).

NMR data for deuterated product with dioxane (c =0.628 mmol/mL): ^{1}H NMR (399 MHz, DMSO-d_6) δ 8.87 (d, J = 1.0 Hz, 1H), 8.28 – 8.22 (dd, J = 8.0, 2.4 Hz, 0.43 H, **Labelled**), 7.94 – 7.89 (m, 0.81H, **Labelled**).

Figure S70 ^{1}H NMR spectrum comparison

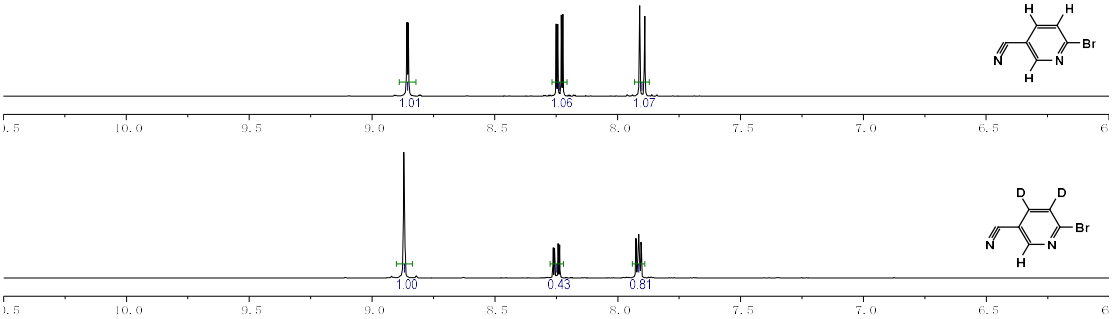


Figure S71 GC-MS spectrum comparison

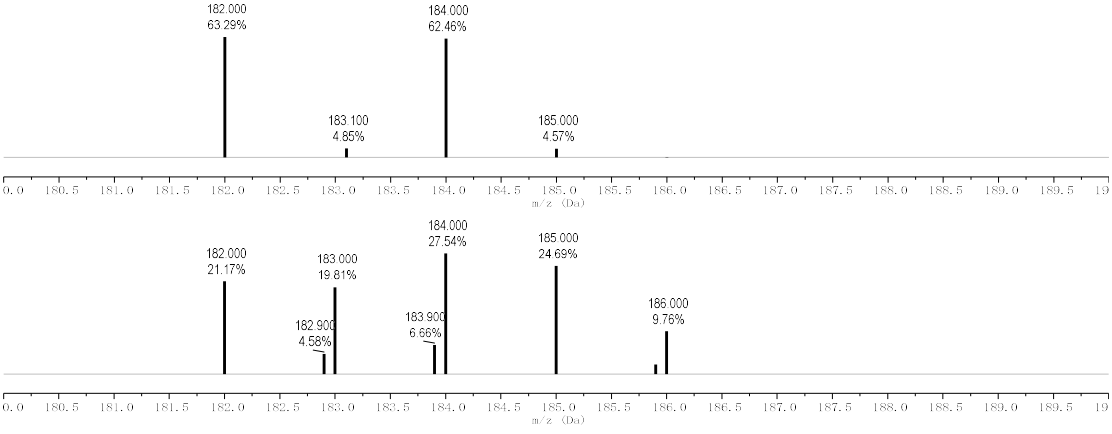


Figure S72 ^{1}H NMR of **19** in DMSO-d_6

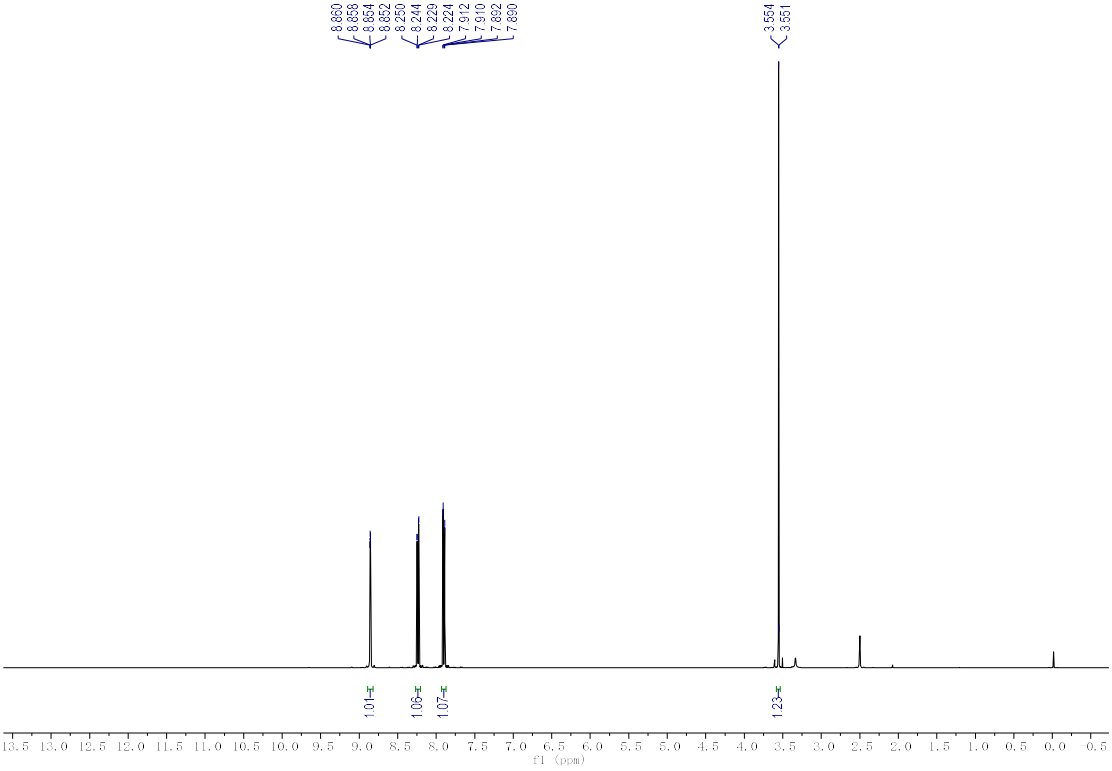
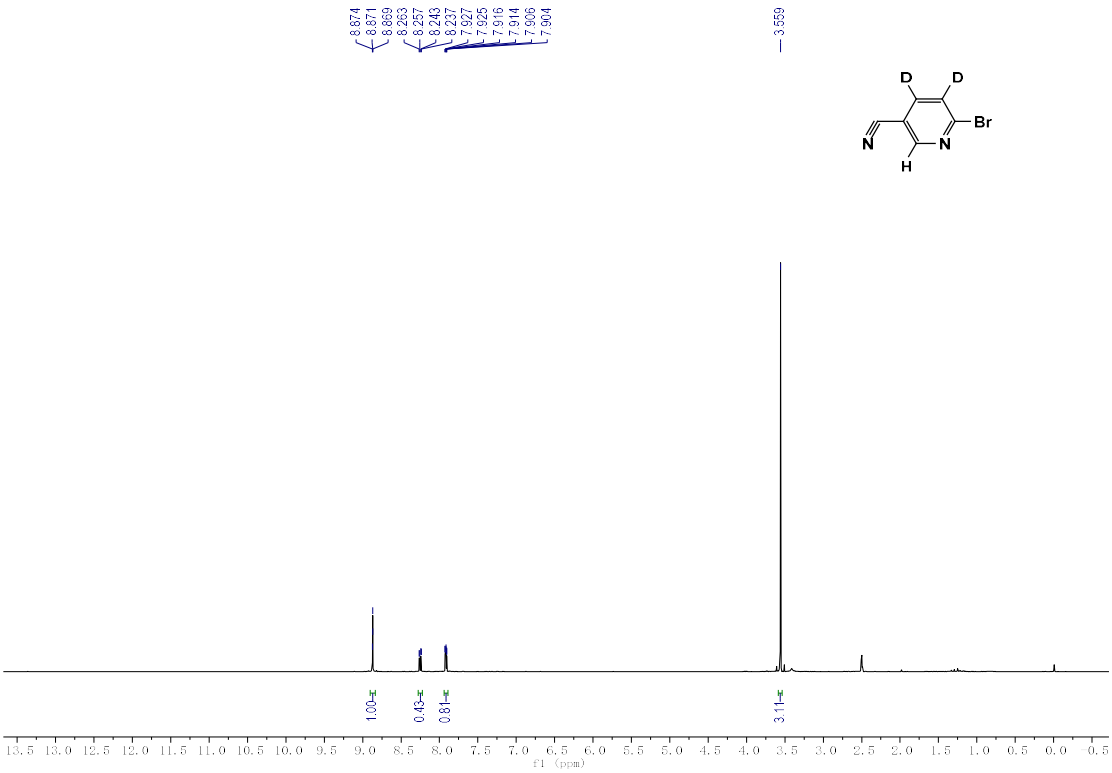
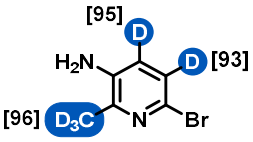


Figure S73 ^{1}H NMR of **19-*d*** in DMSO-d_6



Deuteration of 6-bromo-2-methylpyridin-3-amine (20)



General procedure to afford **20-*d*** as yellow oil (113.9 mg, 59%) with D-incorporation 96%D at 6-methyl, 93%D at β-position, and 95%D at γ-position by ^{1}H NMR; 4.78D by GC-MS. R_f = 0.45 (Petroleum ether/EtOAc = 6/1)

NMR data for starting material with dioxane (c =0.628 mmol/mL): ^{1}H NMR (399 MHz, DMSO-d_6) δ 7.06 (dt, J = 8.3, 0.5 Hz, 1H), 6.87 (d, J = 8.3 Hz, 1H), 5.22 (br, 2H), 2.22 (s, 3H).

NMR data for deuterated product with dioxane (c =0.581 mmol/mL): ^{1}H NMR (399 MHz, DMSO-d_6) δ 7.06 (s, 0.05H, Labelled), 6.90 – 6.82 (m, 0.07H, **Labelled**), 5.21 (br, 2H), 2.18 (p, J = 2.3 Hz, 0.13H, **Labelled**).

Figure S74 ^{1}H NMR spectrum comparison

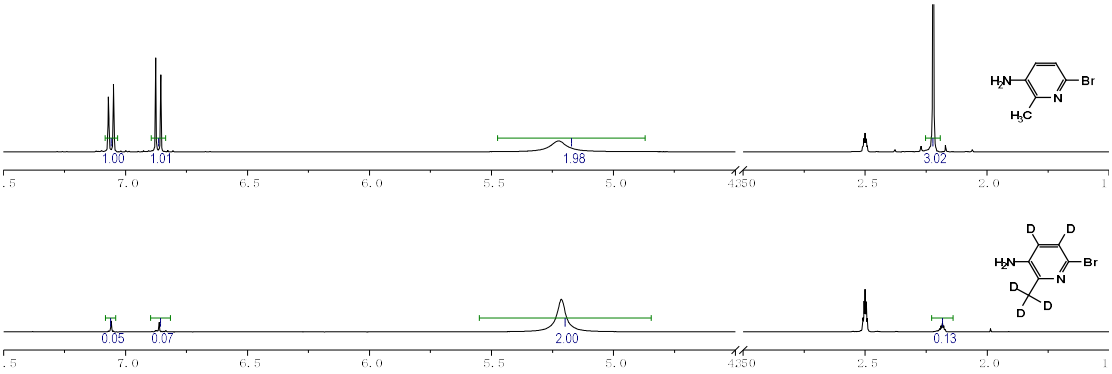


Figure S75 GC-MS spectrum comparison

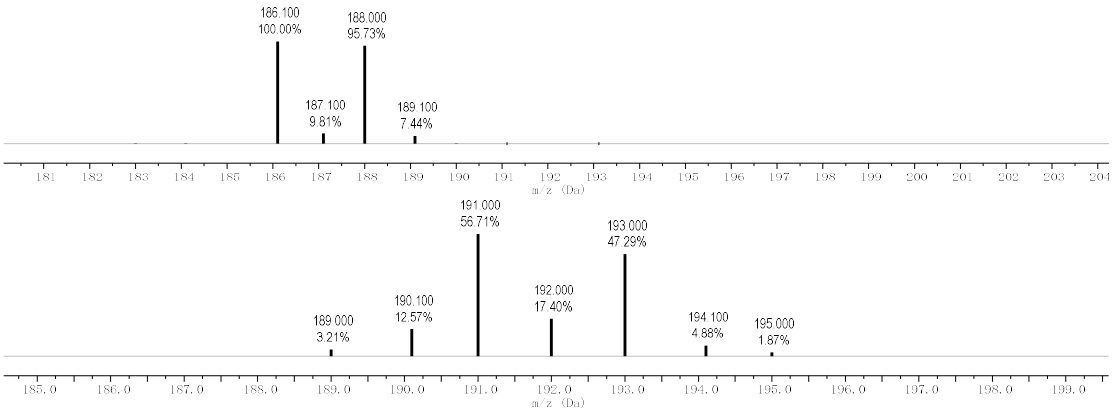


Figure S76 ^{1}H NMR of **20** in DMSO-d_6

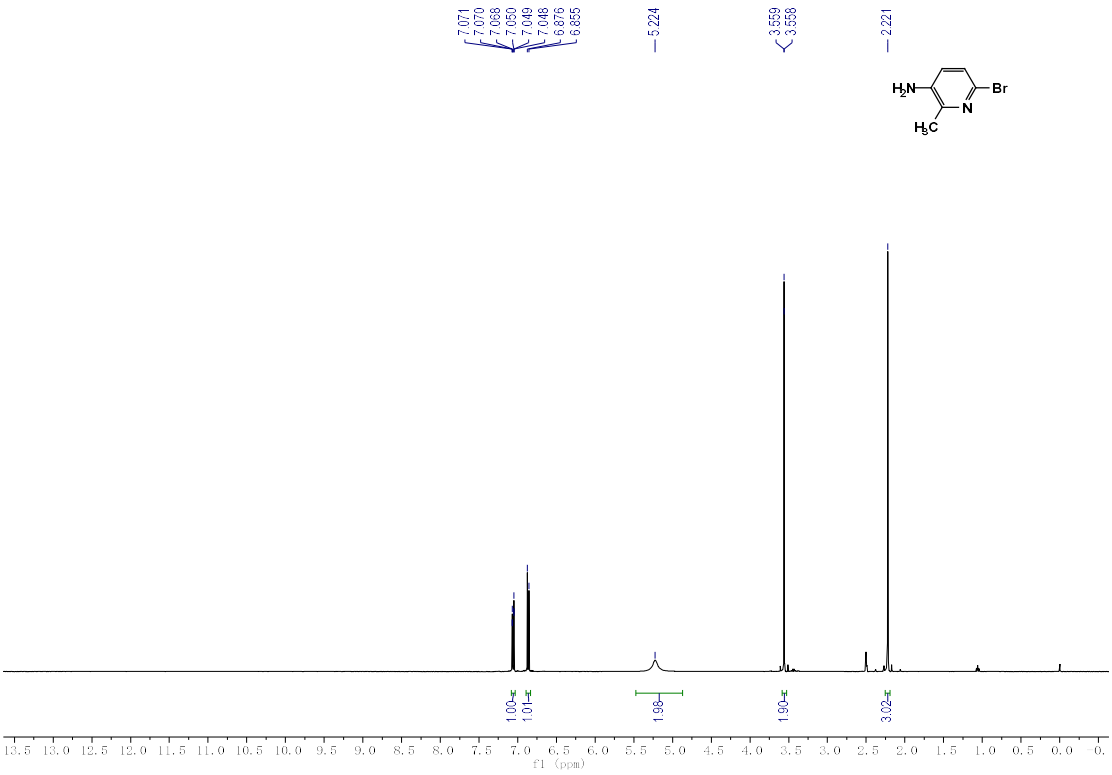
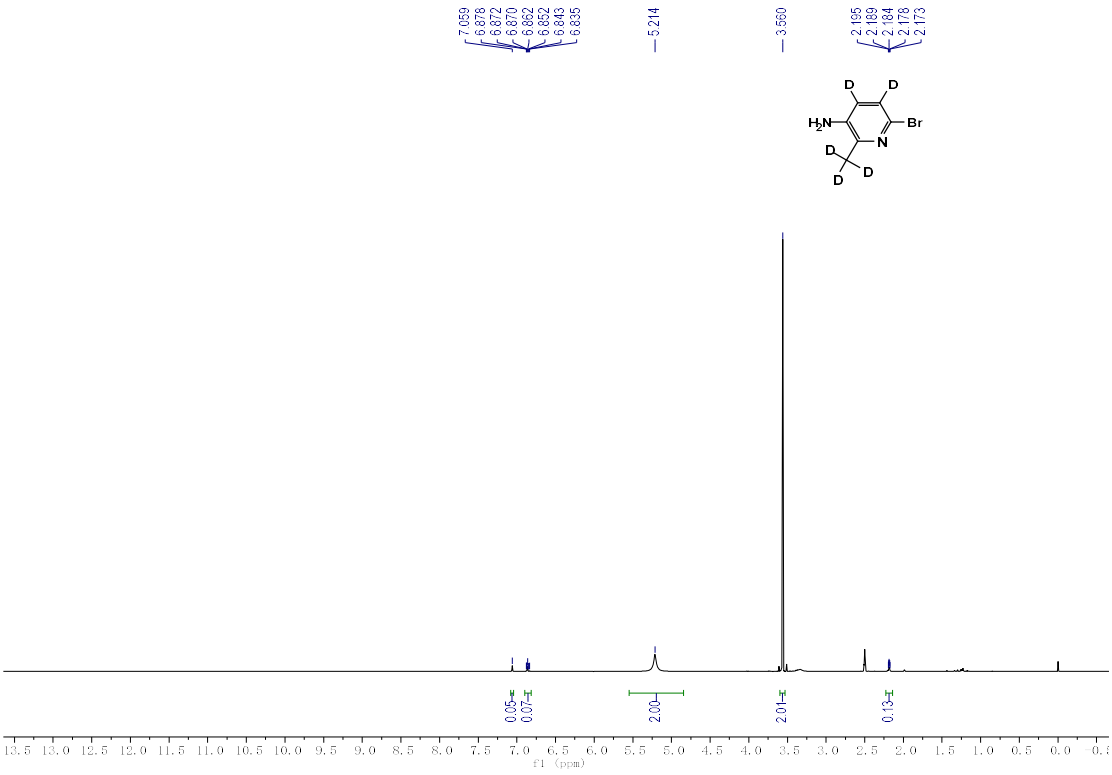
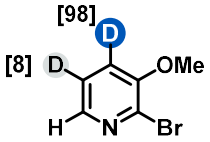


Figure S77 ^{1}H NMR of **20-*d*** in DMSO-d_6



Deuteration of 2-bromo-3-methoxypyridine (21)



General procedure to afford **21-*d*** as yellow oil (61.0 mg, 32%) with D-incorporation 8%D at β-position and 98%D at γ-position by ^{1}H NMR; 0.94D by GC-MS. R_f = 0.45 (Petroleum ether/EtOAc = 6/1)

NMR data for starting material with dioxane (c =0.596 mmol/mL): ^{1}H NMR (399 MHz, DMSO-d_6) δ 7.94 (dd, J = 4.6, 1.5 Hz, 1H), 7.49 (dd, J = 8.1, 1.6 Hz, 1H), 7.39 (dd, J = 8.1, 4.6 Hz, 1H), 3.88 (s, 3H).

NMR data for deuterated product with dioxane (c =0.562 mmol/mL): ^{1}H NMR (399 MHz, DMSO-d_6) δ 7.98 – 7.92 (m, 0.97H), 7.50 (dd, J = 8.0, .1.5 Hz, 0.02H, **Labelled**), 7.40 (d, J = 4.6 Hz, 0.92H, **Labelled**), 3.91 – 3.85 (m, 3.0H).

Figure S78 ^{1}H NMR spectrum comparison

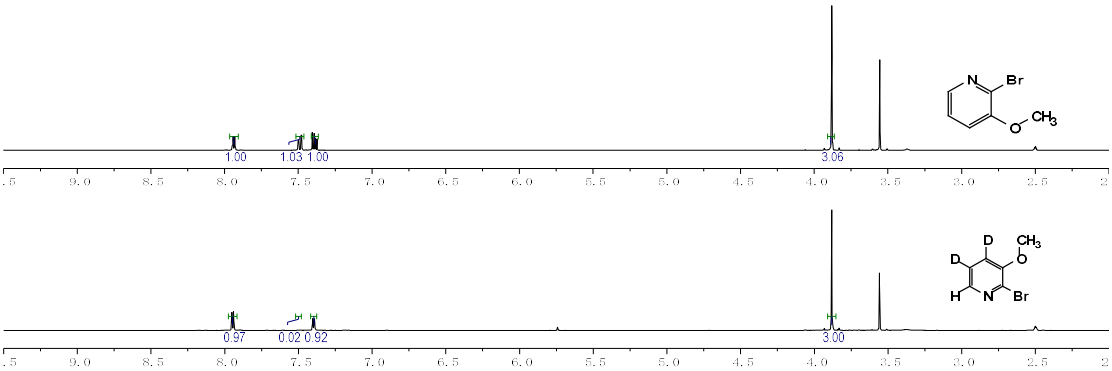


Figure S79 GC-MS spectrum comparison

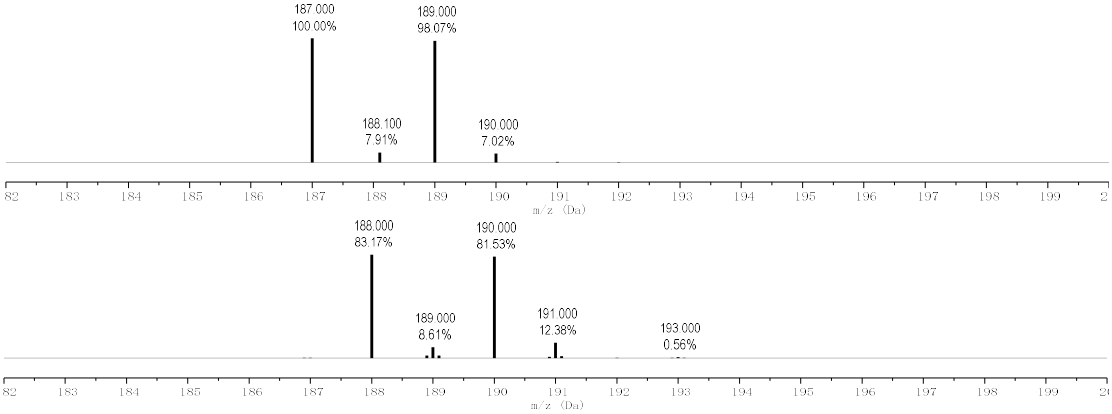


Figure S80 ^{1}H NMR of **21** in DMSO-d_6

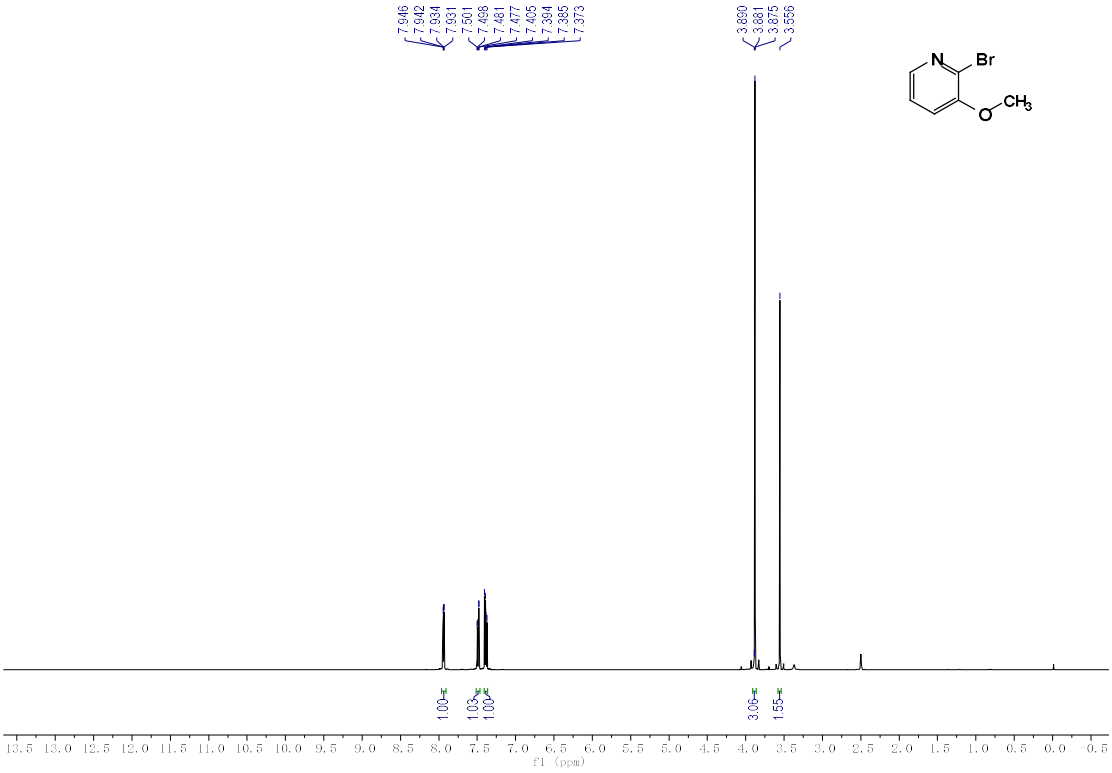
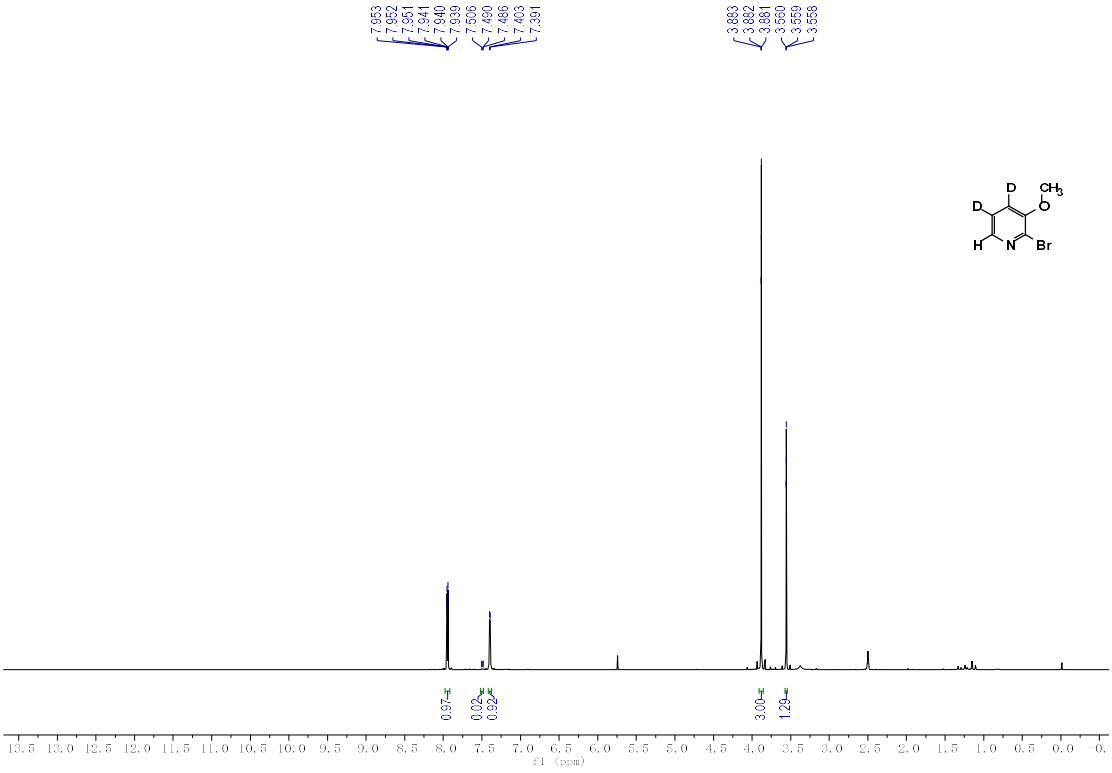
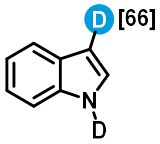


Figure S81 ^{1}H NMR of **21-*d*** in DMSO-d_6



Deuteration of Indole (22)



General procedure to afford **22-*d*** as white solid (103.7 mg, 87%) with D-incorporation 66%D at 3-position by ^{1}H NMR; 0.74D by GC-MS. R_f = 0.45 (Petroleum ether/EtOAc = 8/1).

NMR data for starting material with dioxane (c =0.628 mmol/mL): ^{1}H NMR (399 MHz, DMSO-d_6) δ 11.05 (br, 1H), 7.54 (dq, J = 7.8, 1.0 Hz, 1H), 7.40 (dq, J = 8.1, 1.0 Hz, 1H), 7.32 (t, J = 2.8 Hz, 1H), 7.08 (ddd, J = 8.2, 7.0, 1.3 Hz, 1H), 6.98 (ddd, J = 8.0, 7.0, 1.1 Hz, 1H), 6.42 (ddd, J = 3.0, 2.0, 0.9 Hz, 1H).

NMR data for deuterated product with dioxane (c =0.639 mmol/mL): ^{1}H NMR (399 MHz, DMSO-d_6) δ 11.05 (s, 1H), 7.53 (dd, J = 7.9, 1.0 Hz, 1H), 7.39 (dd, J = 8.1, 1.0 Hz, 1H), 7.32 (t, J = 2.1 Hz, 1H), 7.07 (ddd, J = 8.1, 6.9, 1.2 Hz, 1H), 6.97 (ddd, J = 7.9, 6.9, 1.1 Hz, 1H), 6.44 – 6.38 (m, 0.34H, **Labelled**).

Figure S82 ^{1}H NMR spectrum comparison

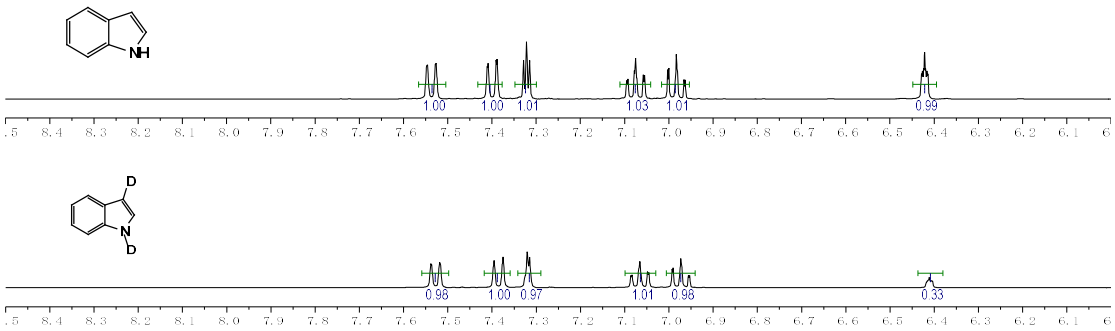


Figure S83 GC-MS spectrum comparison

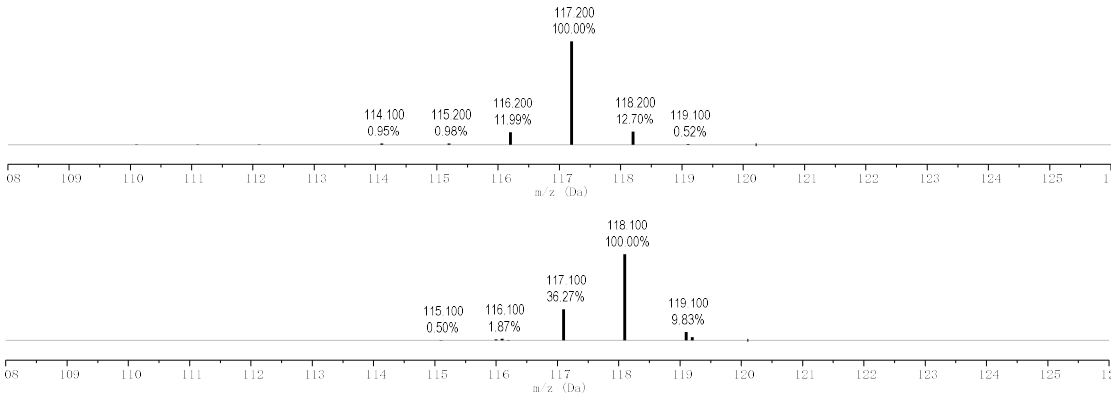


Figure S84 ^{1}H NMR of **22** in DMSO-d_6

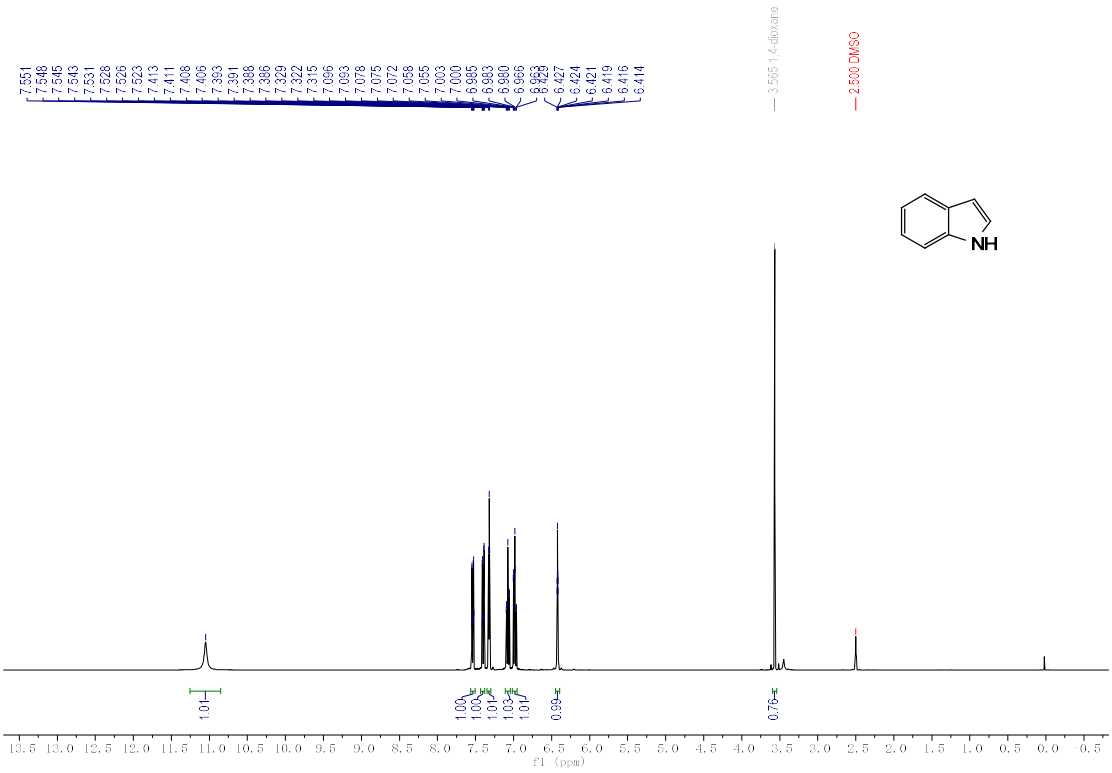
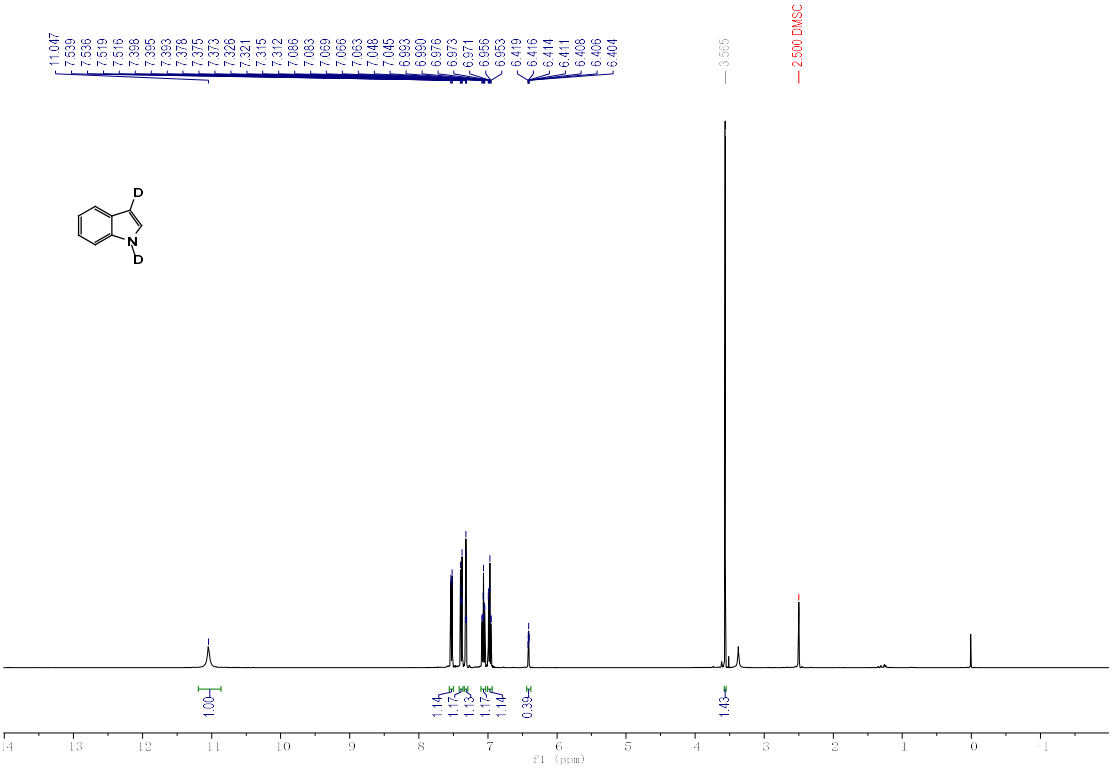
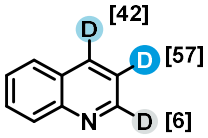


Figure S85 ^{1}H NMR of **22-*d*** in DMSO-d_6



Deuteration of quinoline (23)



General procedure to afford **23-*d*** as yellow oil (96.1 mg, 74%) with D-incorporation 6%D at α-position, 57%D at β-position, and 42%D at γ-position by ^{1}H NMR; 1.05D by GC-MS; R_f = 0.40 (Petroleum ether/EtOAc = 10/1)

NMR data for starting material: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.92 (dd, J = 4.2, 1.8 Hz, 1H), 8.38 (dt, J = 8.3, 1.3 Hz, 1H), 8.03 (dd, J = 8.4, 1.2 Hz, 1H), 7.99 (dd, J = 8.2, 1.4 Hz, 1H), 7.77 (ddd, J = 8.4, 6.8, 1.5 Hz, 1H), 7.62 (ddd, J = 8.0, 6.9, 1.1 Hz, 1H), 7.54 (ddd, J = 8.3, 4.2, 0.9 Hz, 1H).

NMR data for deuterated product: 1H NMR (400 MHz, DMSO-d_6) δ 8.92 (d, J = 1.9 Hz, 0.94H, **Labelled**), 8.38 (t, J = 4.1 Hz, 0.58H, **Labelled**), 8.01 (dd, J = 15.2, 8.3 Hz, 2H), 7.78 (ddd, J = 8.5, 6.8, 1.5 Hz, 1H), 7.62 (td, J = 7.5, 6.8, 1.4 Hz, 1H), 7.54 (qd, J = 4.2, 1.3 Hz, 0.43H, **Labelled**).

Figure S86 ^{1}H NMR spectrum comparison

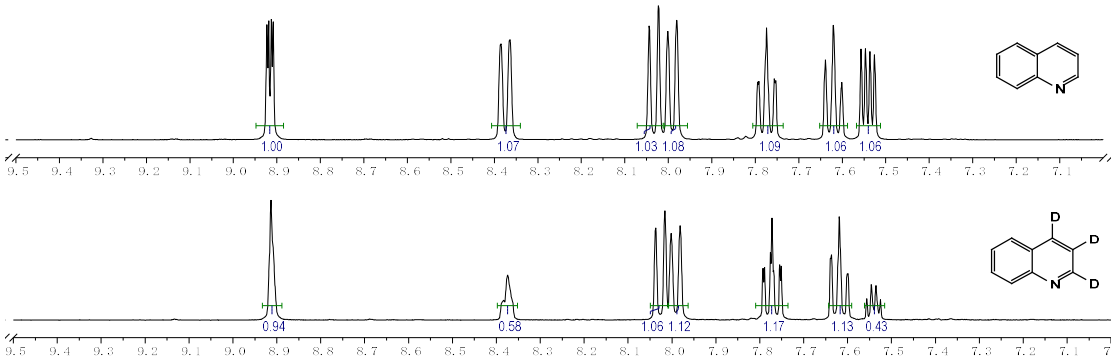


Figure S87 GC-MS spectrum comparison

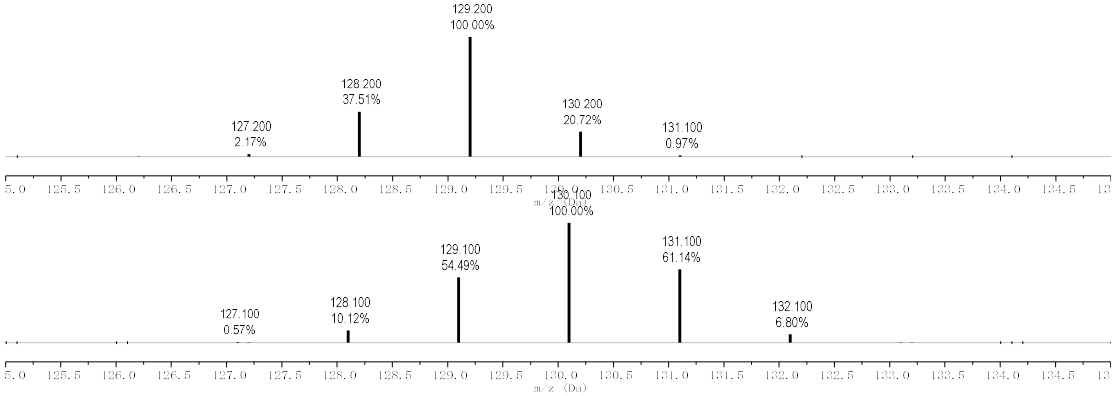


Figure S88 ^{1}H NMR of **23** in Solvent

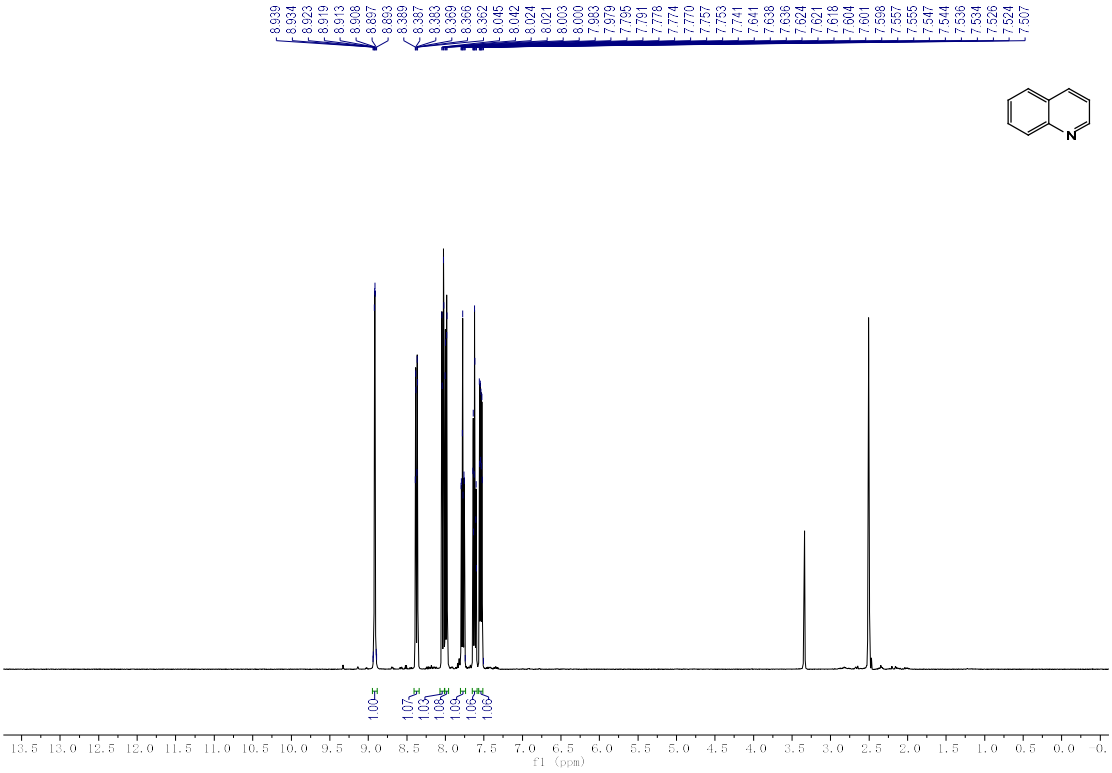
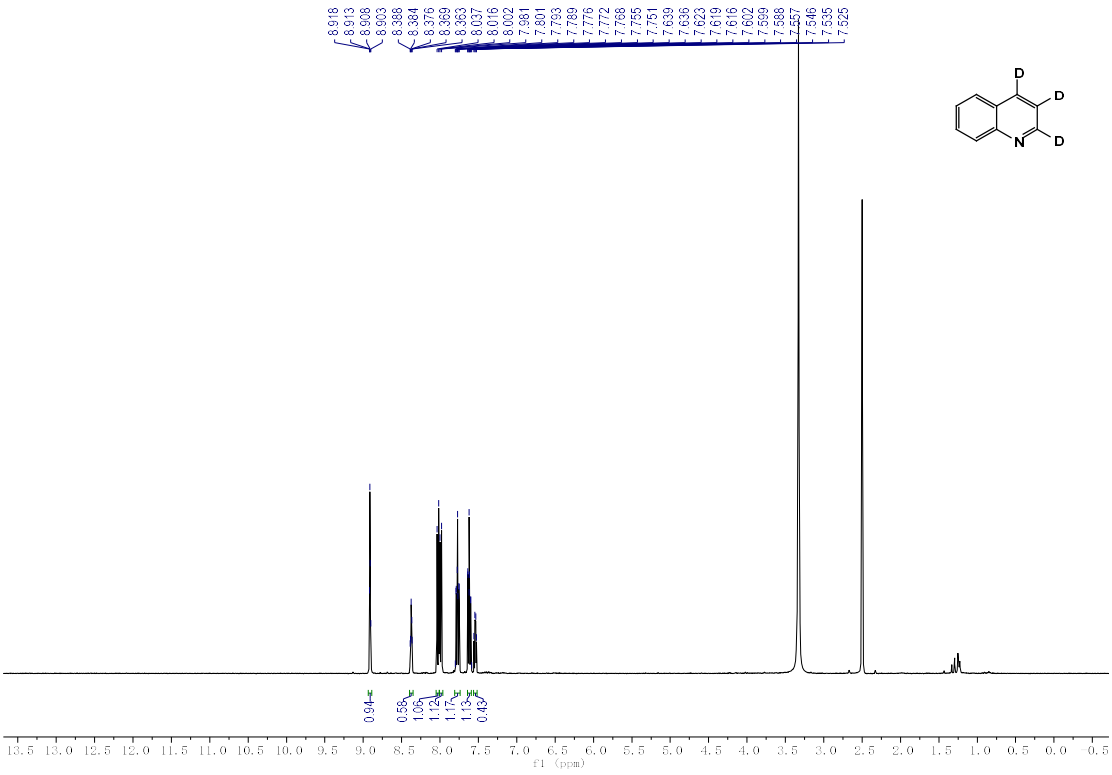
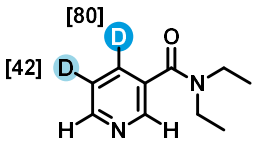


Figure S89 ^{1}H NMR of **23-*d*** in solvent



Deuteration of nikethamide (24)



General procedure to afford **24-*d*** as colourless liquid (151.7 mg, 85%) with D-incorporation 42%D at β-position and 80%D at γ-position by ^{1}H NMR; 1.14D by GC-MS. R_f = 0.45 (Petroleum ether/EtOAc = 1/1).
NMR data for starting material: ^{1}H NMR (400 MHz, Chloroform-*d*) *δ* 8.63 (dd, *J* = 3.3, 1.4 Hz, 2H), 7.72 (dt, *J* = 7.8, 1.9 Hz, 1H), 7.35 (ddd, *J* = 7.8, 4.9, 0.9 Hz, 1H), 3.65 – 3.15 (m, 4H), 1.19 (dt, *J* = 46.9, 7.1 Hz, 6H).
NMR data for deuterated product : ^{1}H NMR (400 MHz, Chloroform-*d*) *δ* 8.65 (q, *J* = 2.2 Hz, 2H), 7.74 (ddq, *J* = 8.2, 6.0, 3.2, 2.6 Hz, 0.2H, **Labelled**), 7.37 (t, *J* = 4.6 Hz, 0.58H, **Labelled),** 3.70 – 3.10 (m, 4H), 1.27 – 1.10 (m, 6H).

Figure S101 ^{1}H NMR spectrum comparison

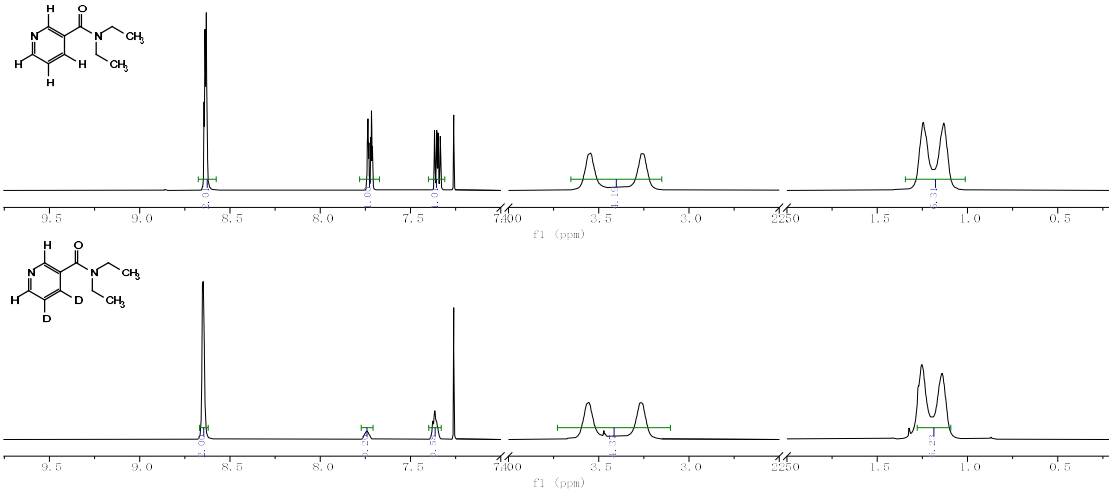


Figure S102 GC-MS spectrum comparison

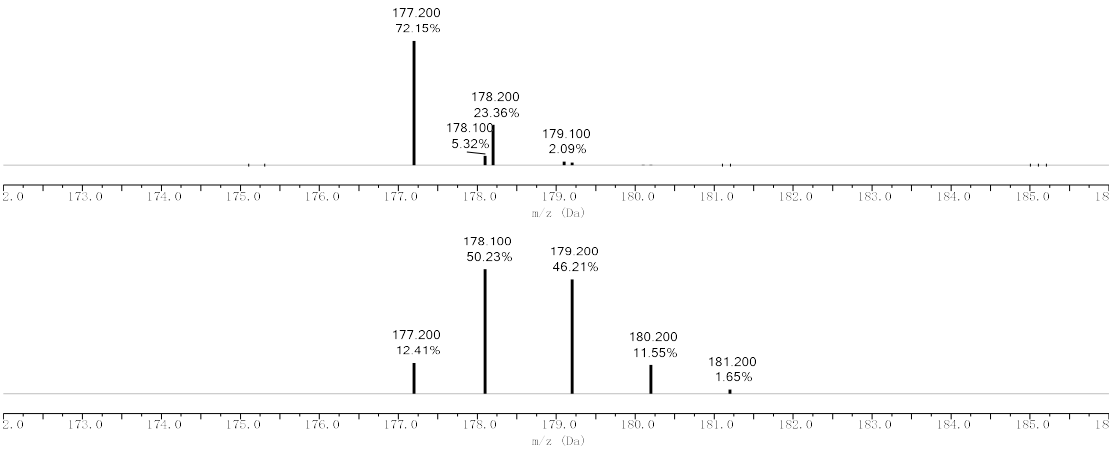


Figure S103 ^{1}H NMR of **24** in Chloroform-*d*

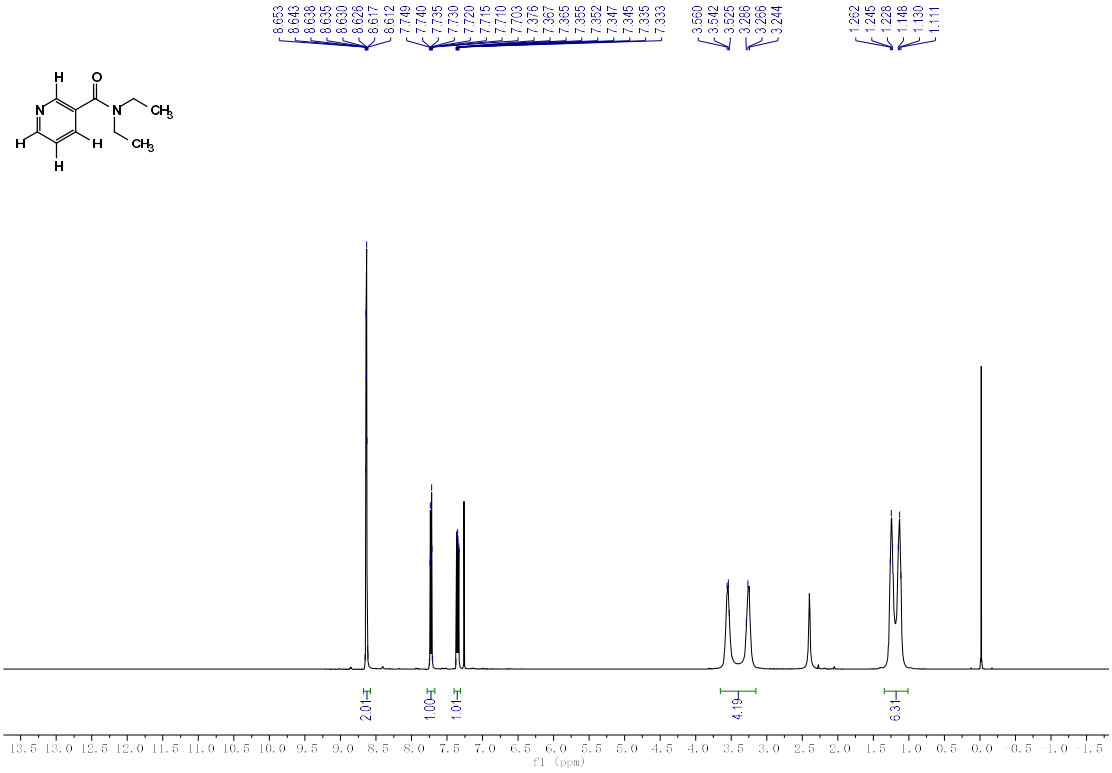
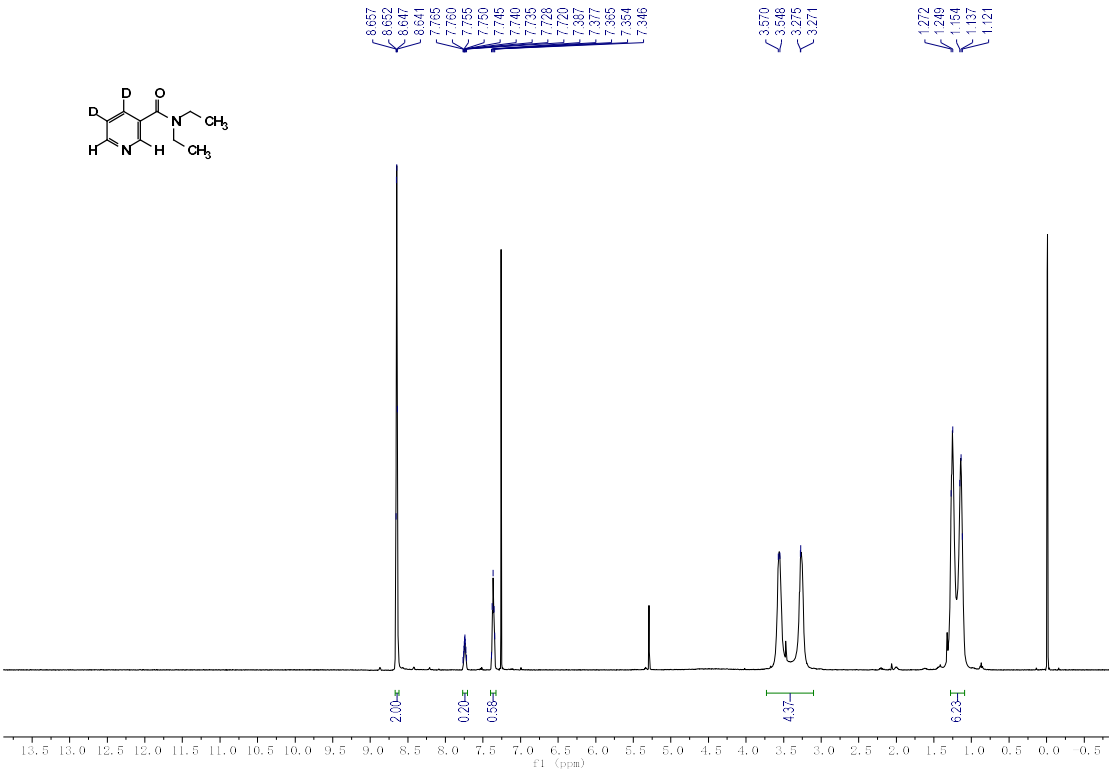
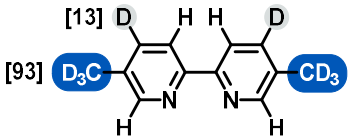


Figure S104 ^{1}H NMR of **24-*d*** in Chloroform-*d*



Deuteration of Abametapir (25)



General procedure to afford **25-*d*** as white solid (82.5 mg, 56%) with D-incorporation 13%D at γ-position and 93%D at 5-methyl by ^{1}H NMR; 5.84D by GC-MS. R_f = 0.45 (Petroleum ether/EtOAc = 15/1).

NMR data for starting material: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.49 (q, J = 1.0 Hz, 1H), 8.24 (dd, J = 8.1, 0.8 Hz, 1H), 7.72 (ddd, J = 8.0, 2.3, 0.8 Hz, 1H), 2.35 (s, 3H).

NMR data for deuterated product : ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.49 (q, J = 0.9 Hz, 2H), 8.28 – 8.21 (m, 2.07H), 7.73 (dd, J = 8.1, 2.3 Hz, 0.75H, **Labelled**), 2.31 (p, J = 2.3 Hz, 0.42H, **Labelled**).

Figure S105 ^{1}H NMR spectrum comparison

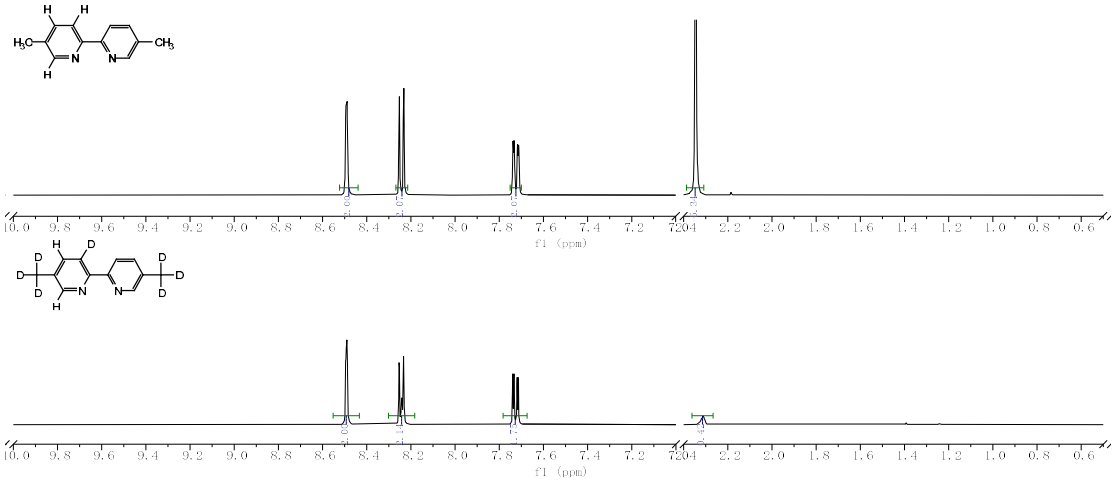


Figure S106 GC-MS spectrum comparison

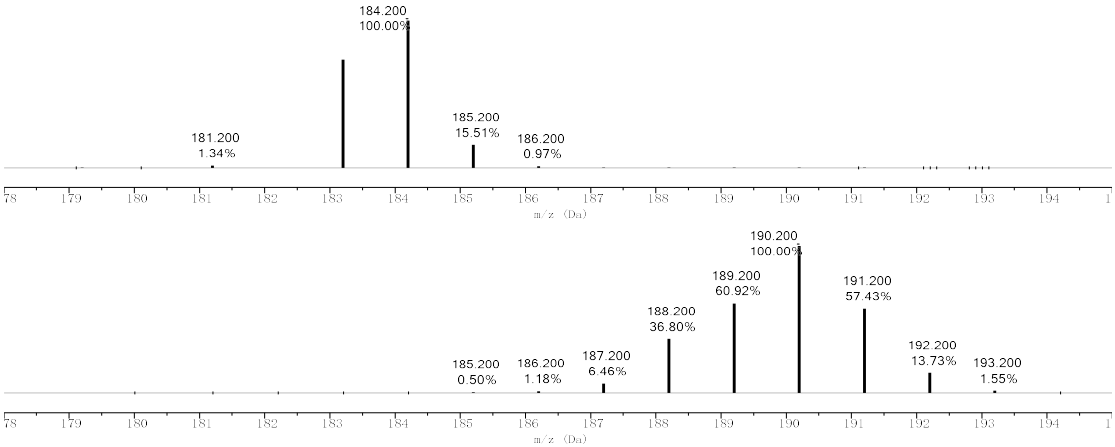


Figure S107 ^{1}H NMR of **25** in DMSO-d_6

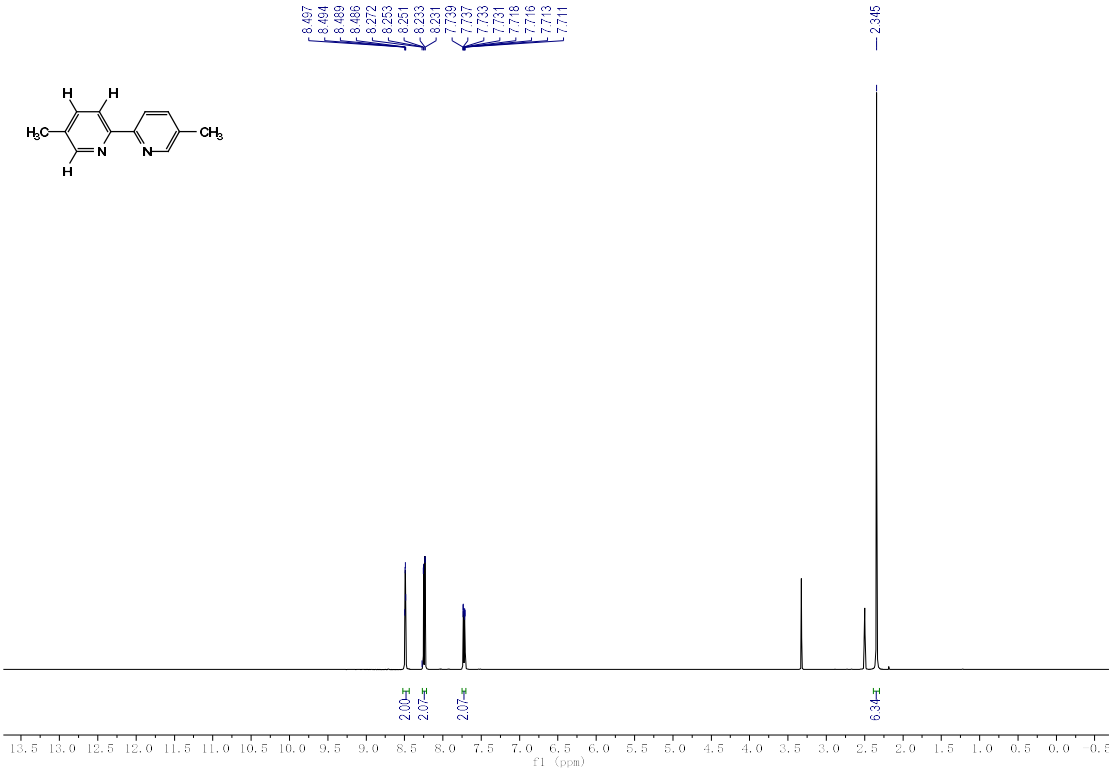
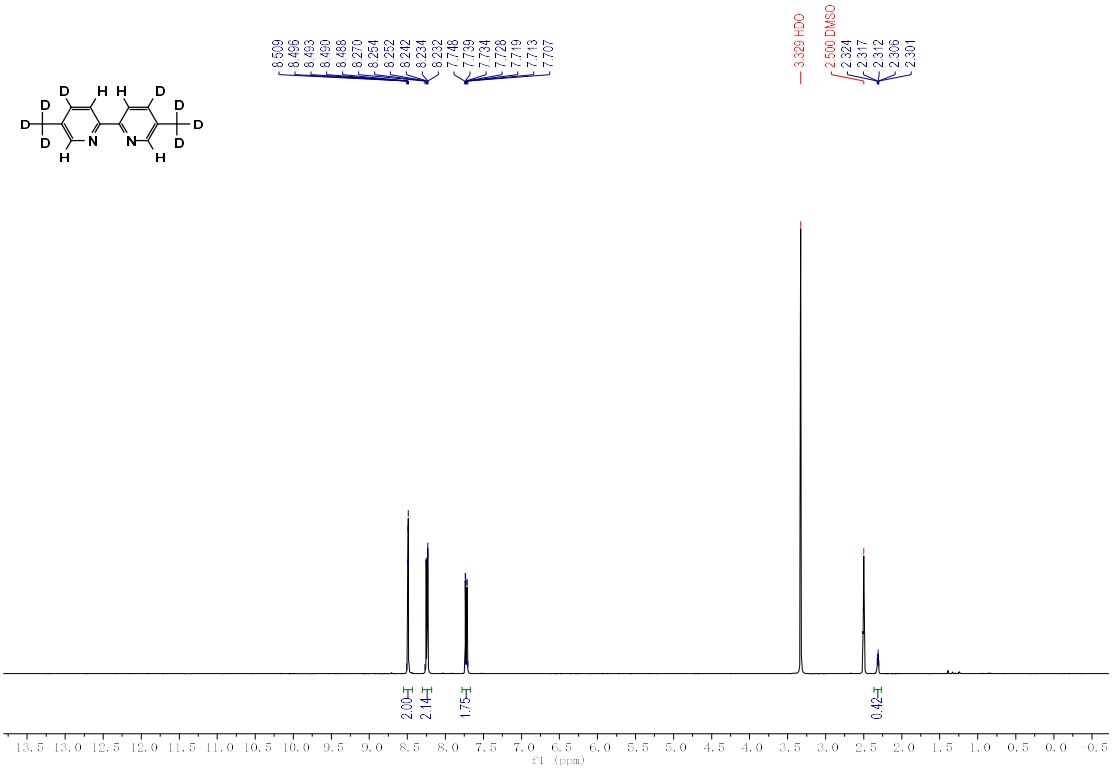
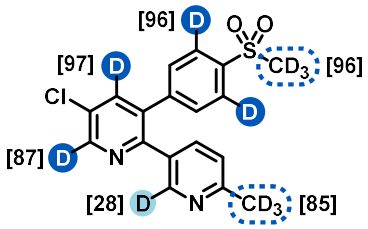


Figure S108 ^{1}H NMR of **25-*d*** in DMSO-d_6



Deuteration of Etoricoxib (26)



General procedure at 0.5 mmol to afford **26-*d*** as orange solid (70 mg, 39%) with D-incorporation 28%D at α-position and 85%D at methyl on 2-methyl-pyridin-4-yl motif, 87%D at α-position and 97%D at γ-position on 3-chloro-pyridyl motif, 96%D at the ortho-position of methylsulfonyl, and 96%D of methylsulfonyl by ^{1}H NMR; R_f = 0.8 (EtOAc).

NMR data for starting material: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.82 (d, *J* = 2.4 Hz, 1H), 8.31 (dd, *J* = 2.4, 0.8 Hz, 1H), 8.11 (d, *J* = 2.3 Hz, 1H), 7.91 (dt, *J* = 8.5, 1.7 Hz, 2H), 7.59 – 7.51 (m, 3H), 7.19 (d, *J* = 8.0 Hz, 1H), 3.25 (s, 3H), 2.44 (s, 3H).

NMR data for deuterated product: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.82 (s, 0.13H, Labelled), 8.35–8.30 (m, 0.72H, Labelled), 8.11 (s, 0.03H, Labelled), 7.91 (d, *J* = 8.5 Hz, 0.03H, Labelled), 7.59 – 7.51 (m, 3H), 7.19 (d, *J* = 8.0 Hz, 1H), 3.22 (s, 0.46H, Labelled), 2.40 (s, 0.13H, Labelled).

Figure S109 ^{1}H NMR spectrum comparison

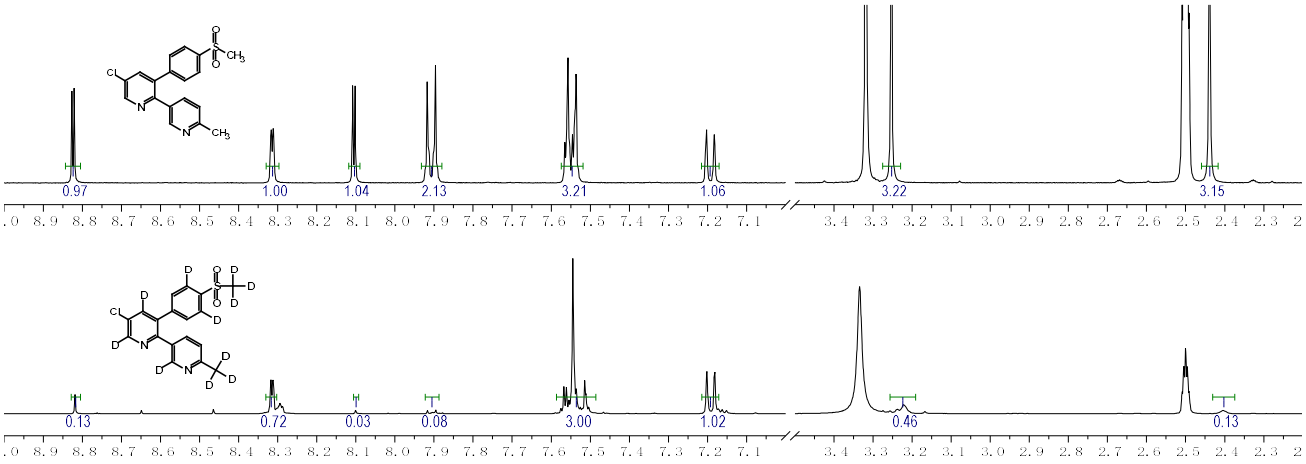


Figure S110 ^{1}H NMR of **26** in DMSO-d_6

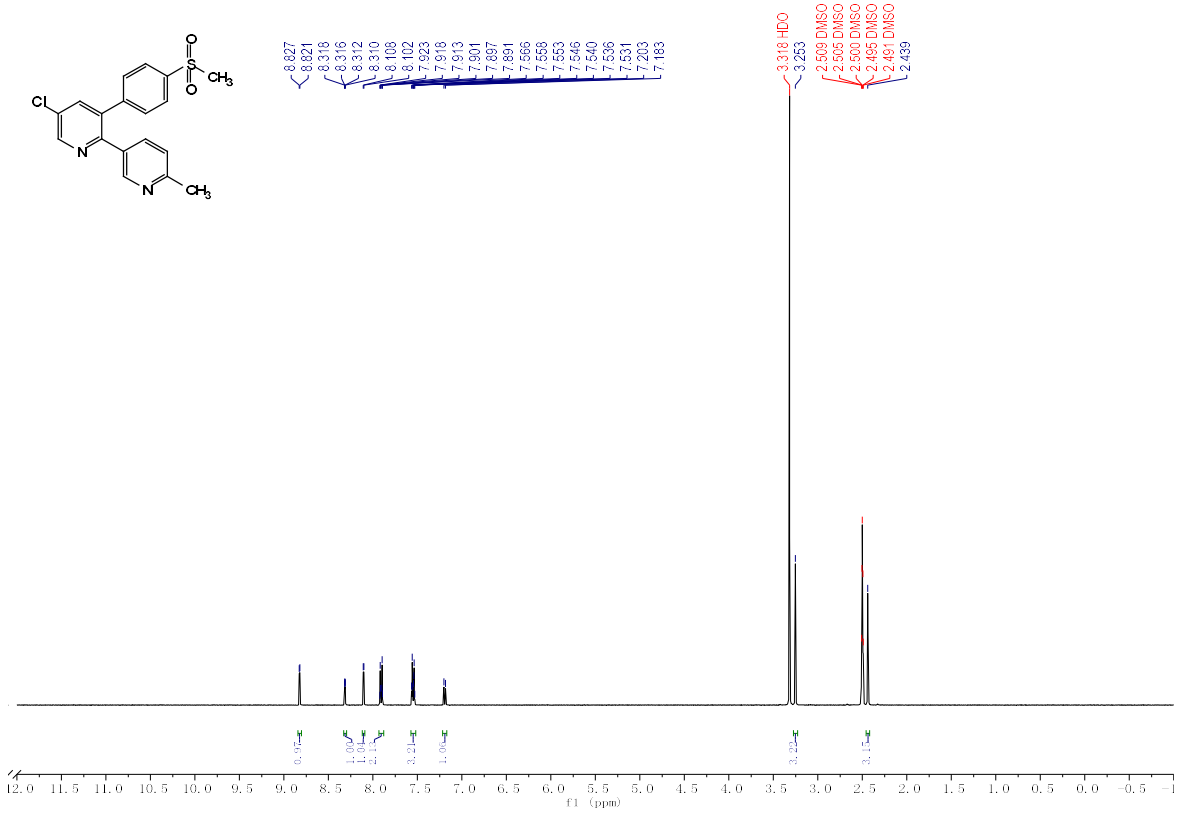


Figure S111 ^{1}H NMR of **26-*d*** in DMSO-d_6