Deuteration of Indole Compounds: Synthesis of Deuterated Auxins, Indole-3-acetic Acid-d5 and Indole-3-butyric Acid-d5

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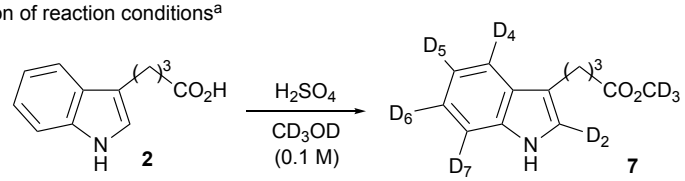
1. Details of Results

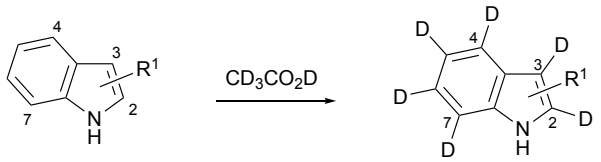
Table S1. Optimization of reaction conditions[a]

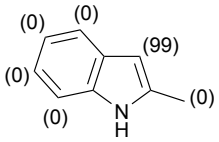
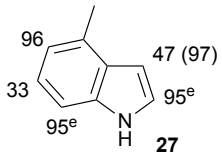
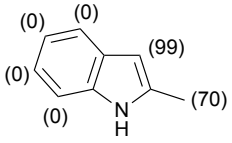
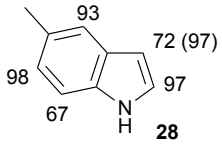
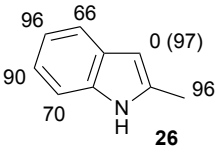
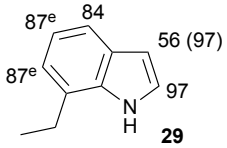
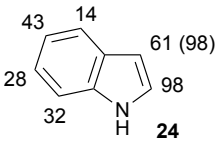
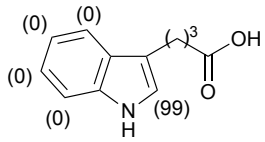
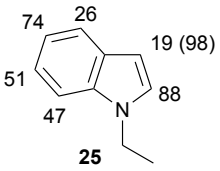


Entry	Acid	Temp. (°C)	Time (h)	Deuterium content (%)[b]						Isolated yield (%)
				D2	D4	D5	D6	D7	Ave. D [c]	
1	2.4 wt% H_2SO_4	rt	3	26[d]	3	26[d]	6	7	14	n.d.[e]
2	2.4 wt% H_2SO_4	60	65	89[d]	55	89[d]	87	68	77	n.d.[e]
3	9.7 wt% H_2SO_4	rt	9	91	5	15	12	7	26	n.d.[e]
4	9.7 wt% H_2SO_4	60	110	91	88	91	92	91	91	n.d.[e]
5	20 wt% H_2SO_4	60	45	83[f]	81[f]	82[f]	83[f]	81[f]	82[f]	98
6[g]	20 wt% H_2SO_4	60	45	82	82	80	81	82	81	n.d.[e]
7	20 wt% D_2SO_4	60	18	98[f]	95[f]	98[f]	98[f]	97[f]	97[f]	99
8[h]	20 wt% D_2SO_4	60	18	94[f]	91[f]	94[f]	93[f]	94[f]	93[f]	93

[a] Reactions were performed in CD_3OD (0.1 M) at 60 °C. [b] Calculated based on ^{1}H NMR spectra of reaction mixture. [c] Indicated as the average D content of D2 and D4-D7. [d] Indicated as the average D content of D2 and D5. [e] Not determined. [f] Calculated based on ^{1}H NMR spectra of isolated product. [g] With light shielding. [h] The reaction was performed in 0.3 M solution

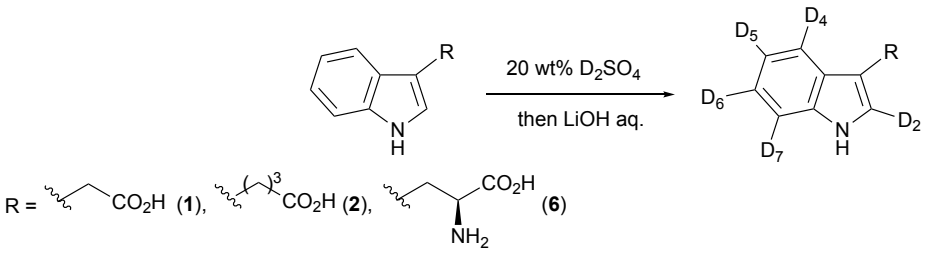
Table S2. H-D exchange reaction of 3-unsubstituted indoles[a]



Entry	Temp.	Time	D Content (%)[b]	Yield	Entry	Temp.	Time	D Content (%)[b]	Yield
1	rt	5 min		n.d.[c]	6	150 °C	110 h		96%
2	80 °C	100 min		n.d.[c]	7	150 °C	110 h		56%
3	150 °C	110 h		92%	8	150 °C	110 h		78%
4[d]	150 °C	110 h		77%	9	100 °C	17 h		n.d.[c]
5	150 °C	110 h		81%					

[a] Reactions were performed in CD_3CO_2D (0.1 M) in a sealed tube. [b] D content was calculated based on ^1H NMR of isolated product. A number in parentheses is a D content of product in reaction mixture. [c] Not determined. [d] D content was calculated based on ^1H NMR spectroscopy after *N*-methylation. [e] Indicated as average D content.

Table S3. Synthesis of polydeuterated IAA, IBA and Trp as an economical way.[a]



Entry	substrate	Solvent	Conc. (M)	Temp. (°C)	Time (h)	Deuterium content (%)						Isolated yield (%)
						D2	D4	D5	D6	D7	Ave. D[b]	
1[c]	**2**	40% CD_3OD/D_2O	0.1	60	38	99	92	93[d]	93[d]	93	94	n.d.[e]
2[c]	**2**	40% CD_3OD/D_2O	0.2	60	38	99	52	59[d]	59[d]	55	65	n.d.[e]
3[c]	**2**	70% CD_3OD/D_2O	0.2	60	38	-[f]	86	-[f]	97	95	-	n.d.[e]
4[g]	**2**	70% CD_3OD/D_2O	0.2	95	5	99	97	97	97	97	97	99
5[g]	**2**	$CH(OCH_3)_3/D_2O$[h,i]	0.2	95	5	97	95	97	97	97	97	95
6[g]	**2**	$CH(OEt)_3/D_2O$[j]	0.1	60	19	71	34	98	98	31	66	71
7[g]	**1**	70% CD_3OD/D_2O	0.2	95	14	98	96	96	95	96	96	99
8[g]	**1**	$CH(OCH_3)_3/D_2O$[h,i]	0.2	95	14	97	97	98	97	97	97	95
9[c]	**6**	70% CD_3OD/D_2O	0.2	95	18	96	96	96	96	96	96	n.d.[e]

[a] Reactions were performed in 20 wt% D_2SO_4 in CD_3OD/D_2O solution. After the reaction completed, the reaction mixture was poured into an aqueous LiOH to hydrolyze. [b] Indicated as the average D content at C2, C4-C7. [c] D content was calculated based on ^1H NMR spectra of product in reaction mixture. [d] Indicated as average D content at C5 and C6. [e] Not determined. [f] Not detemined due to overlaped with D_2SO_4 residual peak. [g] D content was calculated based on ^1H NMR spectra of isolated product. [h] In situ preparation of 20 wt% D_2SO_4 in CH_3OD/D_2O (7/3). [i] Reactions were perfomed on 1 gram scale of substrate. [j] In situ preparation of a mixture of D_2SO_4, C_2H_5OD, D_2O, and $HCO_2C_2H_5$.

Figure S1. ^{1}H NMR (500 MHz) spectra of deuterated IBA CD_3 ester (**7**) in CD_3OD

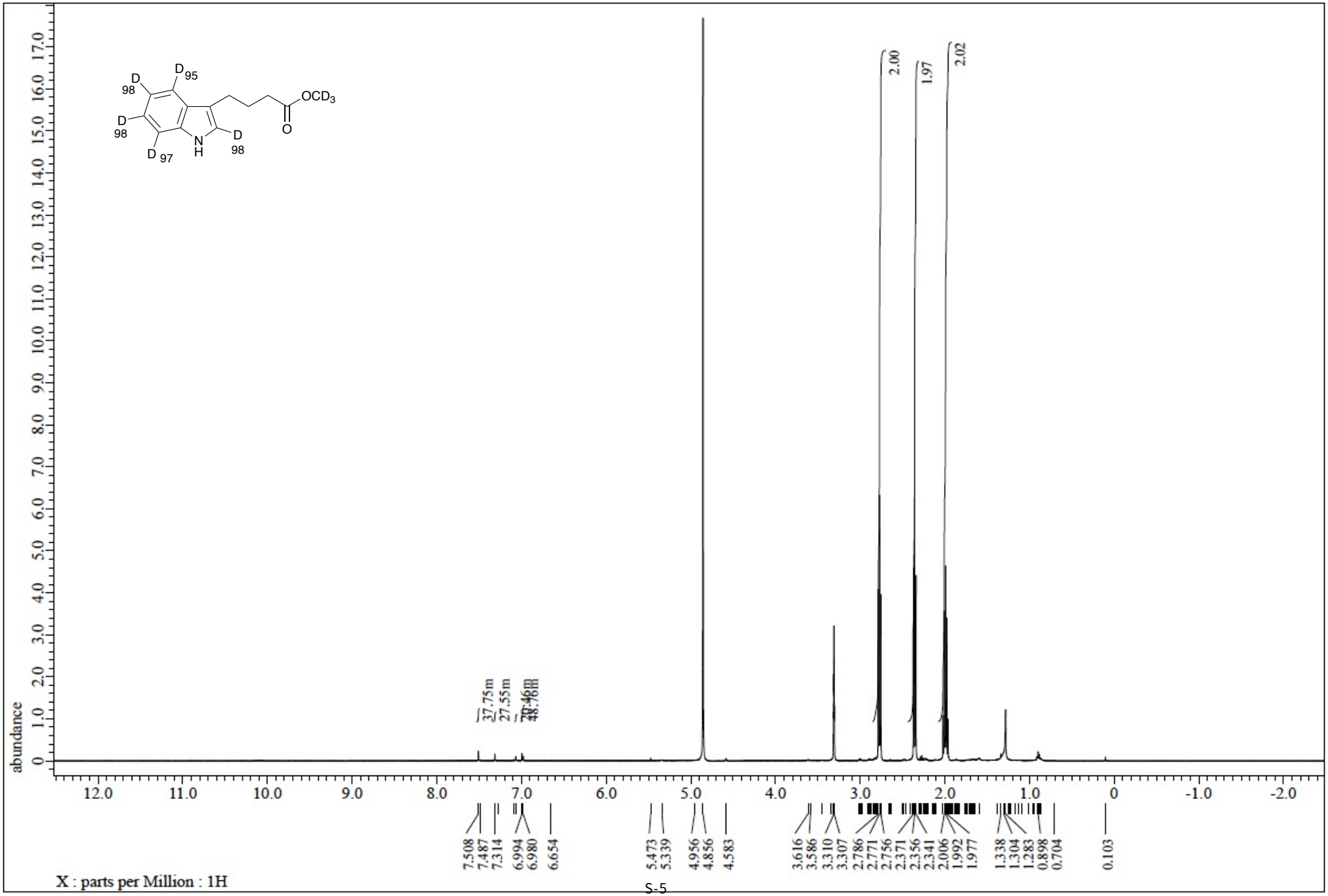


Figure S2. ^{1}H NMR (500 MHz) spectra of deuterated IAA CD_3 ester (**8**) in CD_3OD

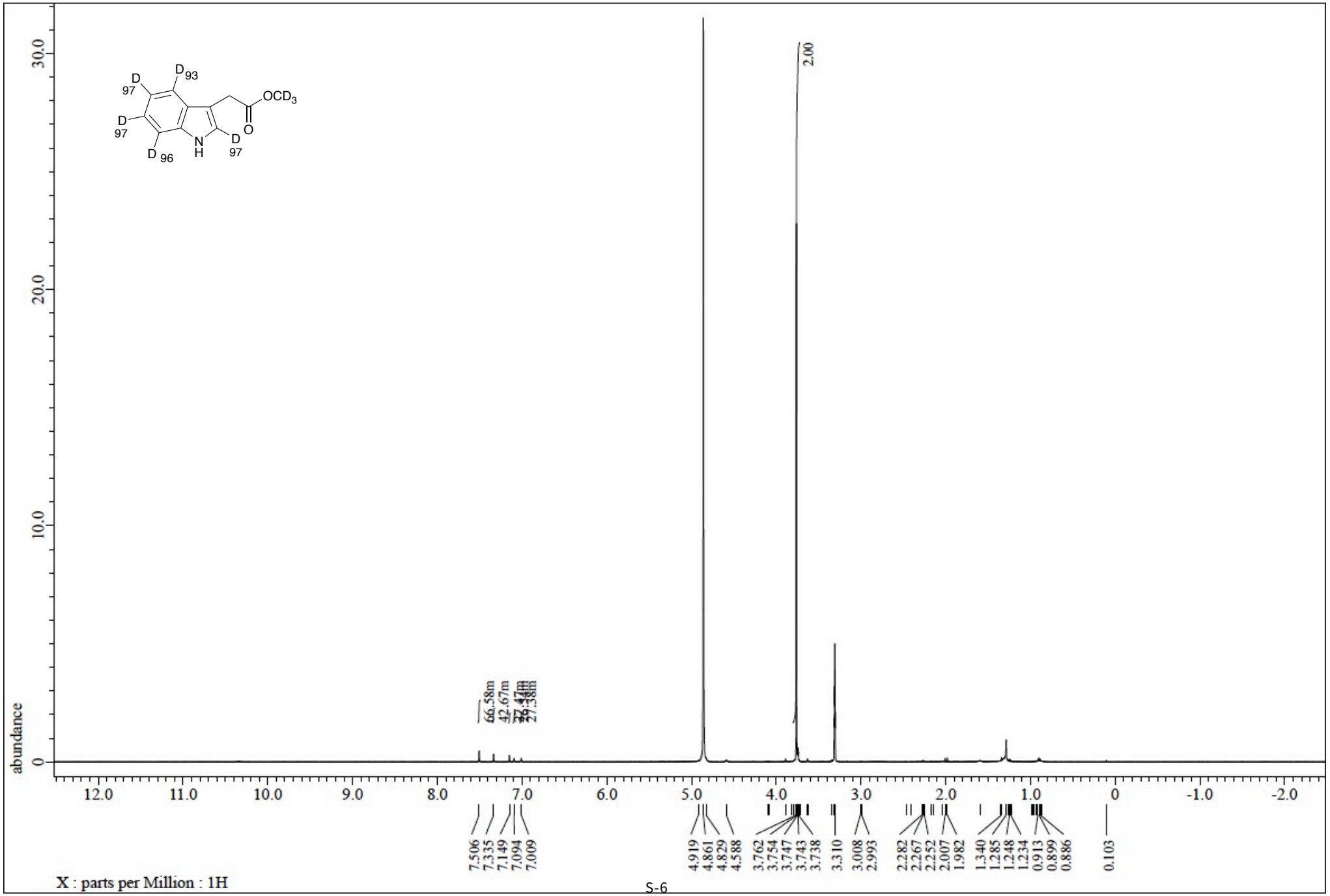


Figure S3. ^{1}H NMR (500 MHz) spectra of deuterated L-Trp-CD_3 ester (**9**) in CD_3OD

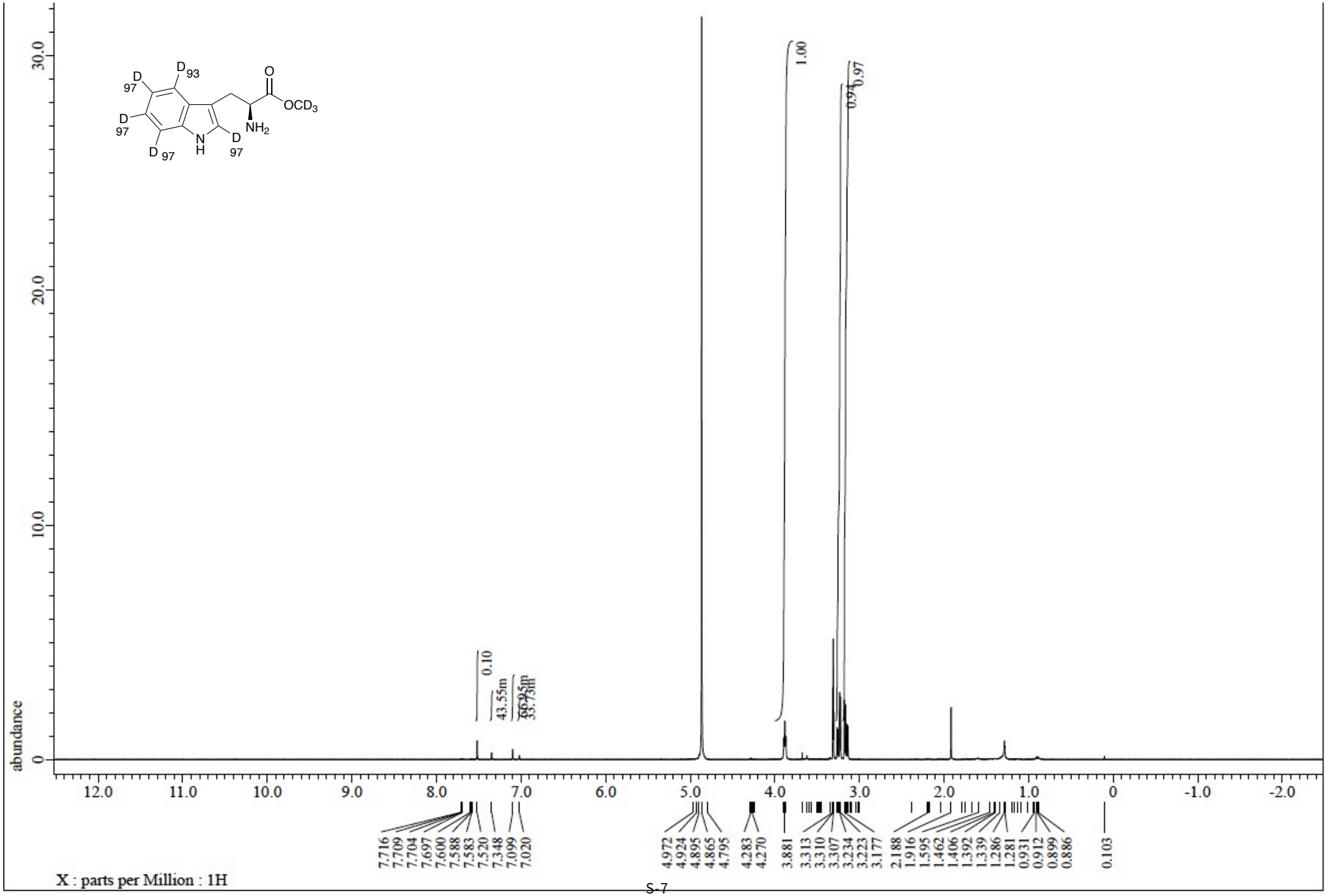


Figure S4. ^{1}H NMR (400 MHz) spectra of 3-(5-Chloroindoly)propanoic acid methyl ester (**10**) in $CDCl_3$

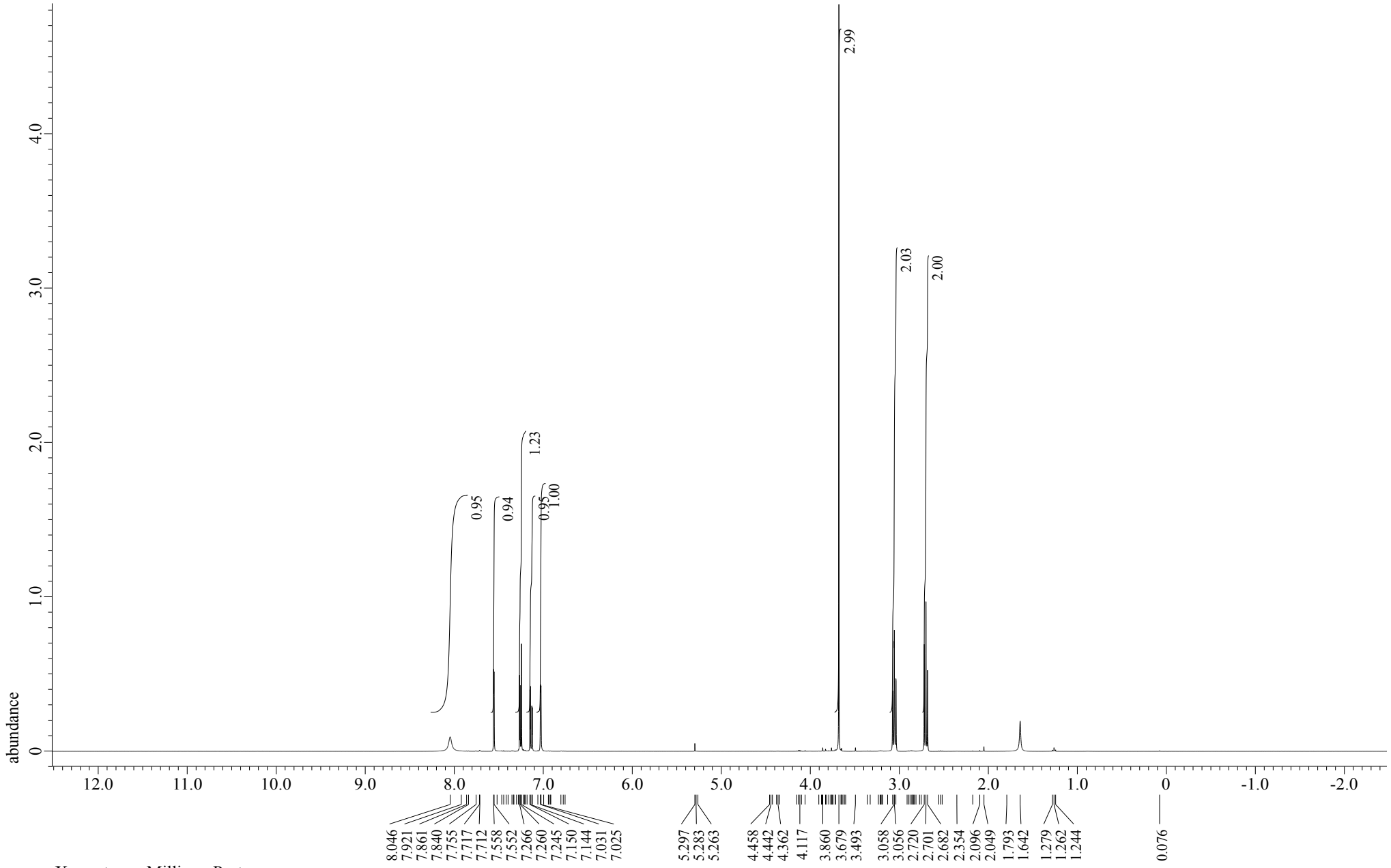


Figure S5. ^{1}H NMR (400 MHz) spectra of deuterated 3-(5-Chloroindoly)propanoic acid CD_3 ester (**11**) in CD_3OD

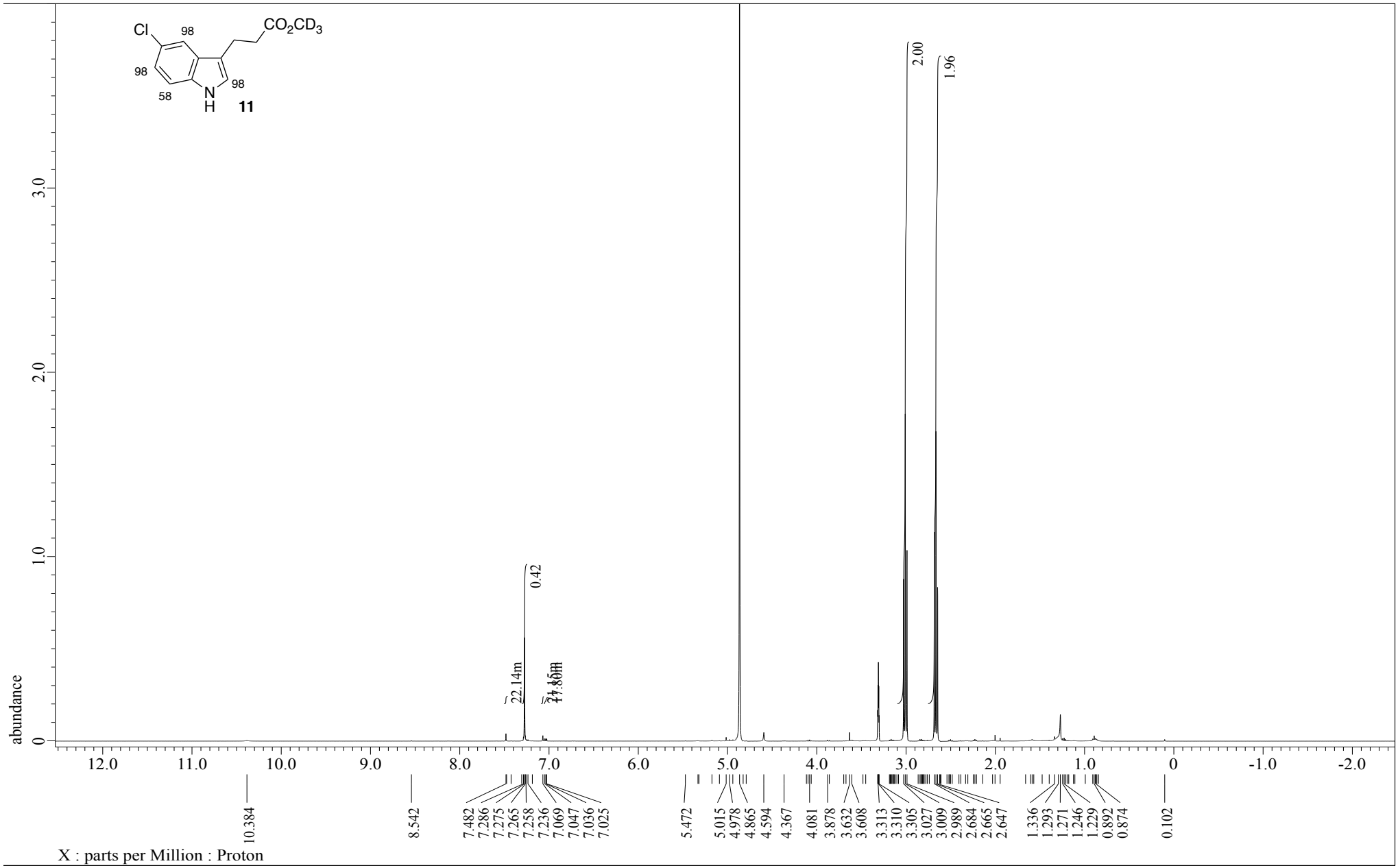


Figure S6. ^{1}H NMR (600 MHz) spectra of deuterated *N*-methyl-IBA CD_3 ester (**13**) in CD_3OD

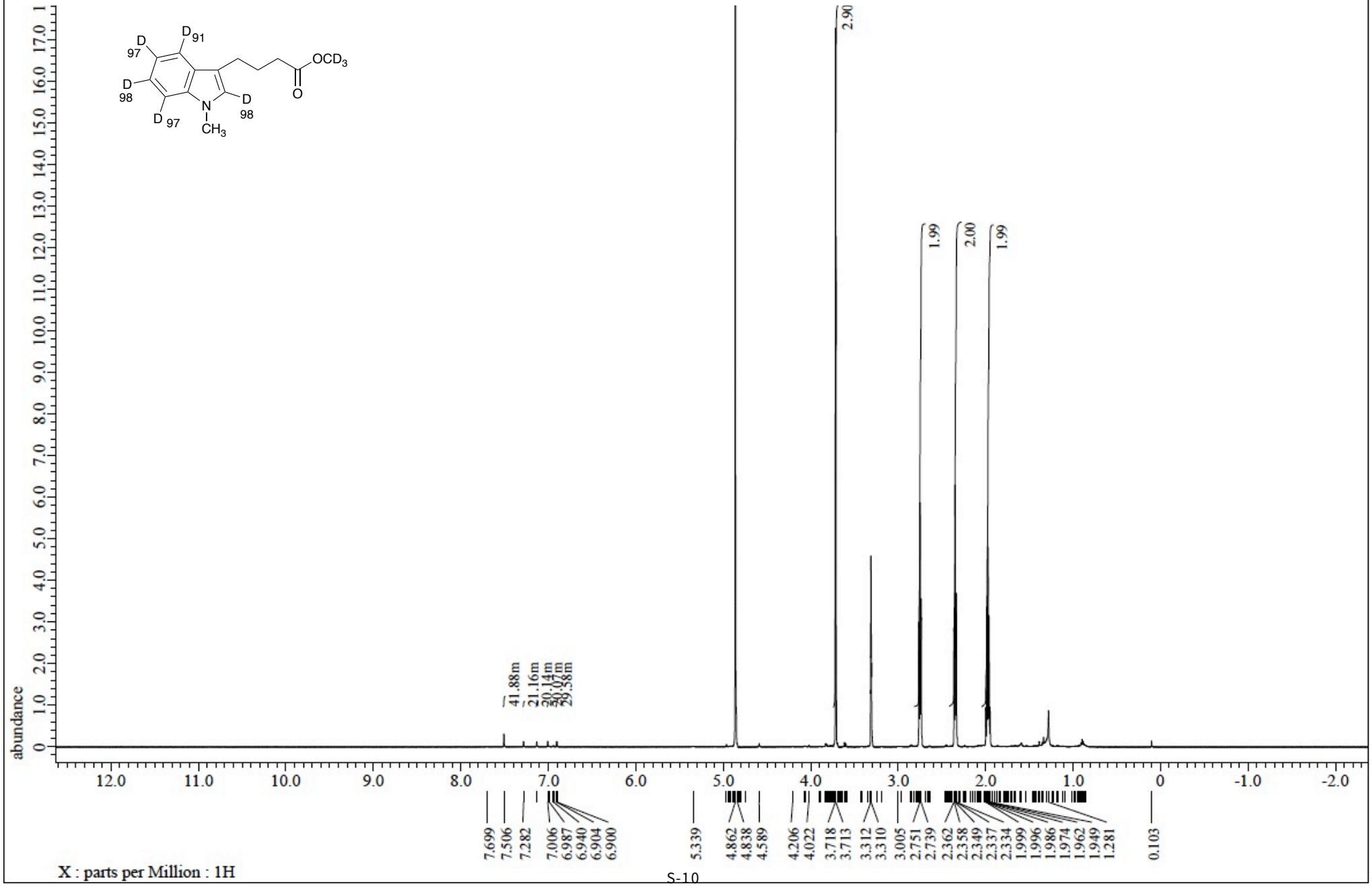


Figure S7. ^{1}H NMR (600 MHz) spectra of **15** in CD_3OD

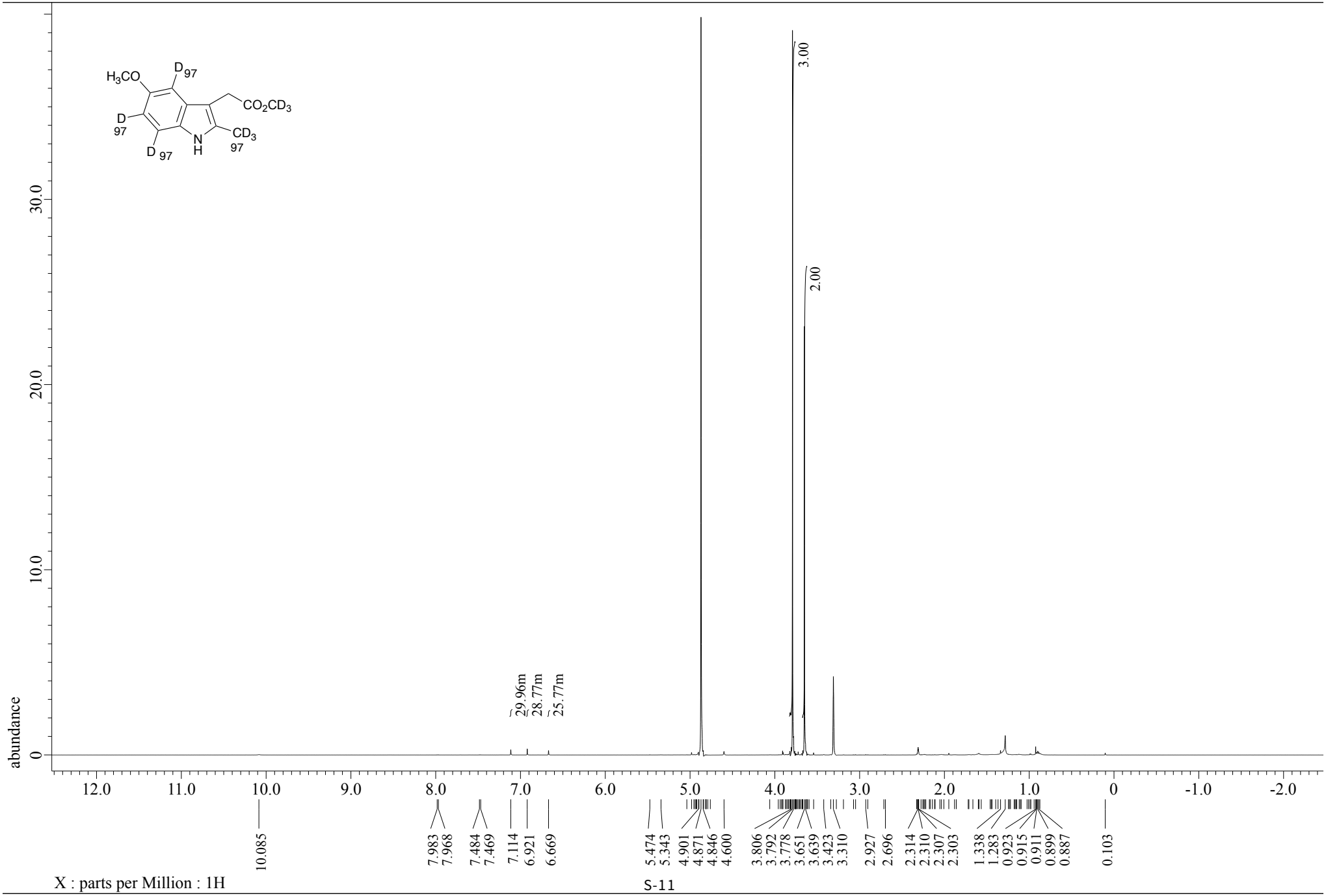


Figure S8. ^{1}H NMR (600 MHz) spectra of deuterated yohimbine (**17**) in CD_3OD

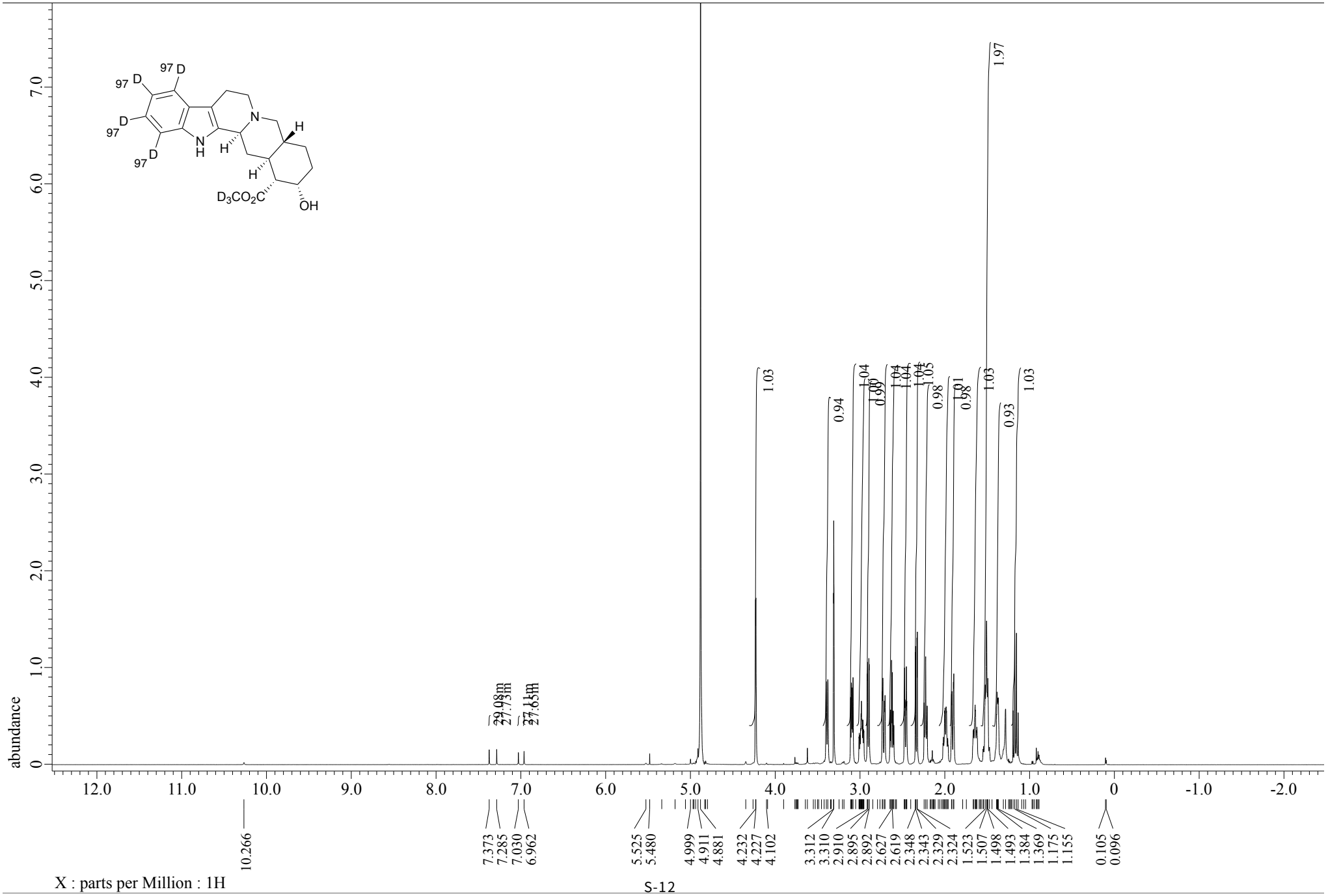


Figure S9. ^{1}H NMR (400 MHz) spectra of deuterated carbazole (**19**) in acetone-d6

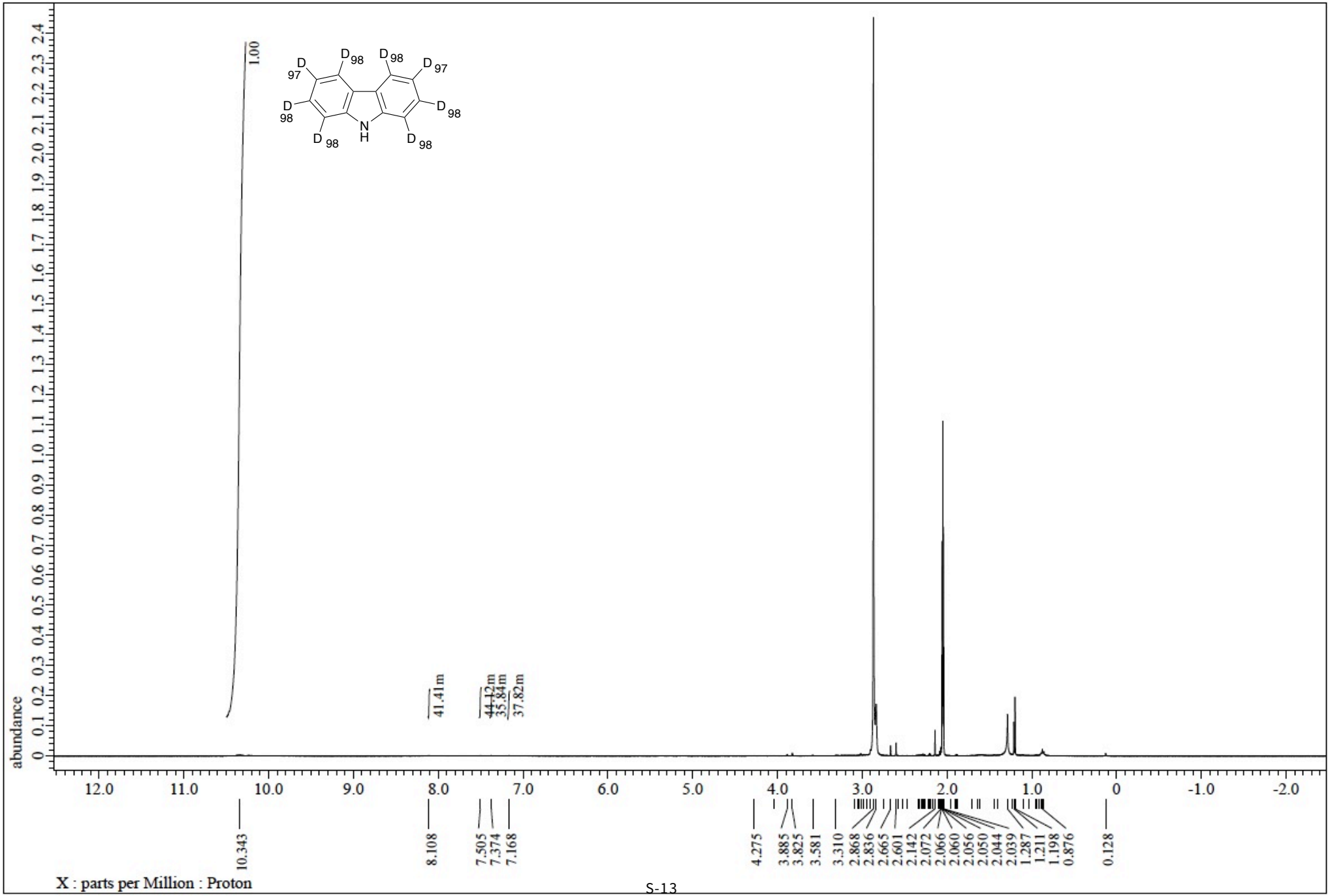


Figure S10. ^{1}H NMR (400 MHz) spectra of deuterated *N*-methylcarbazole (**30**) in acetone-d6

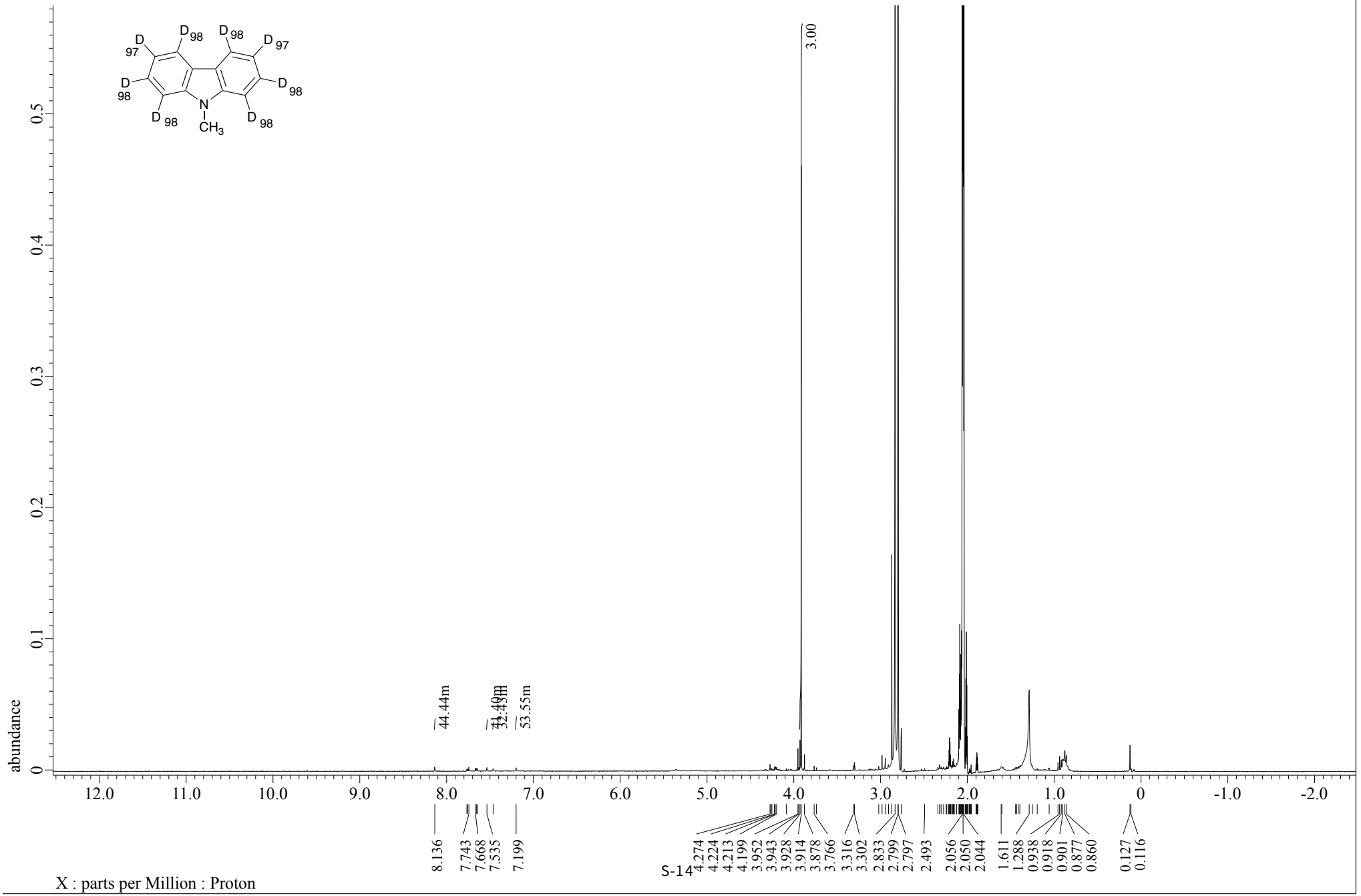


Figure S11. ^{1}H NMR (600 MHz) spectra of deuterated harmine (**21**) in CD_3OD

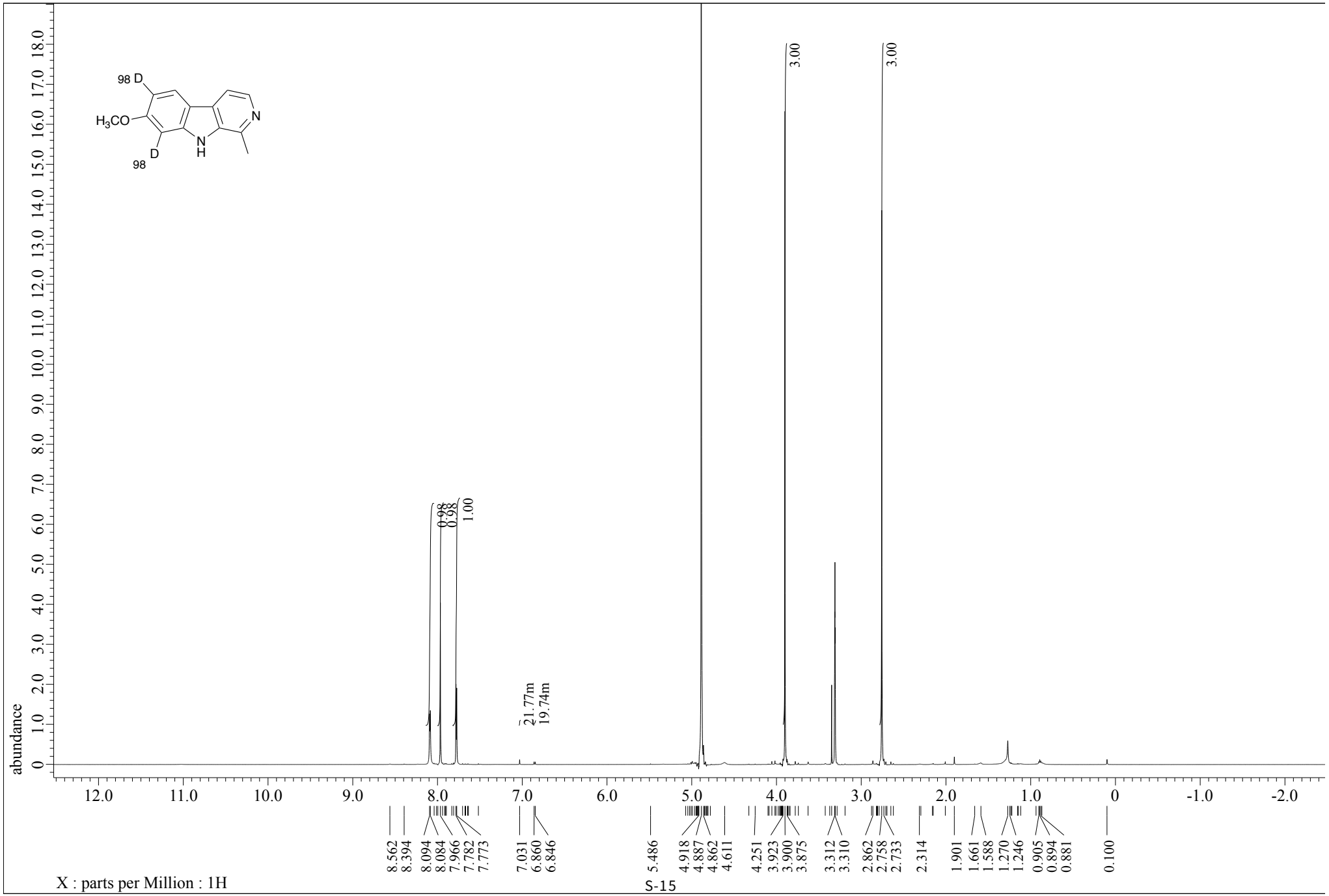


Figure S12. ^{1}H NMR (600 MHz) spectra of deuterated indole (**24**) in CD_3OD

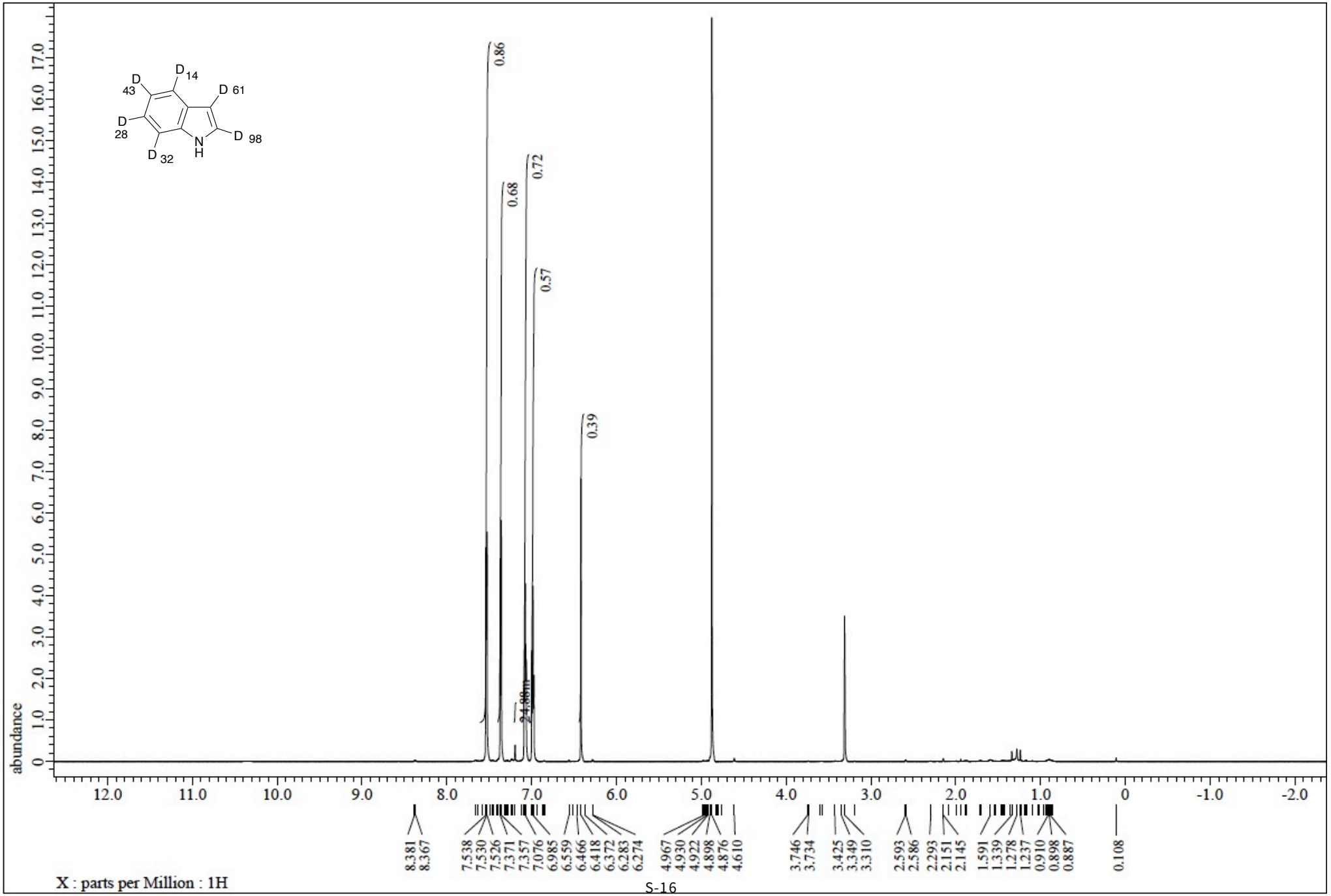


Figure S13. ^{1}H NMR (600 MHz) spectra of deuterated *N*-methylindole (**31**) in acetone-d6

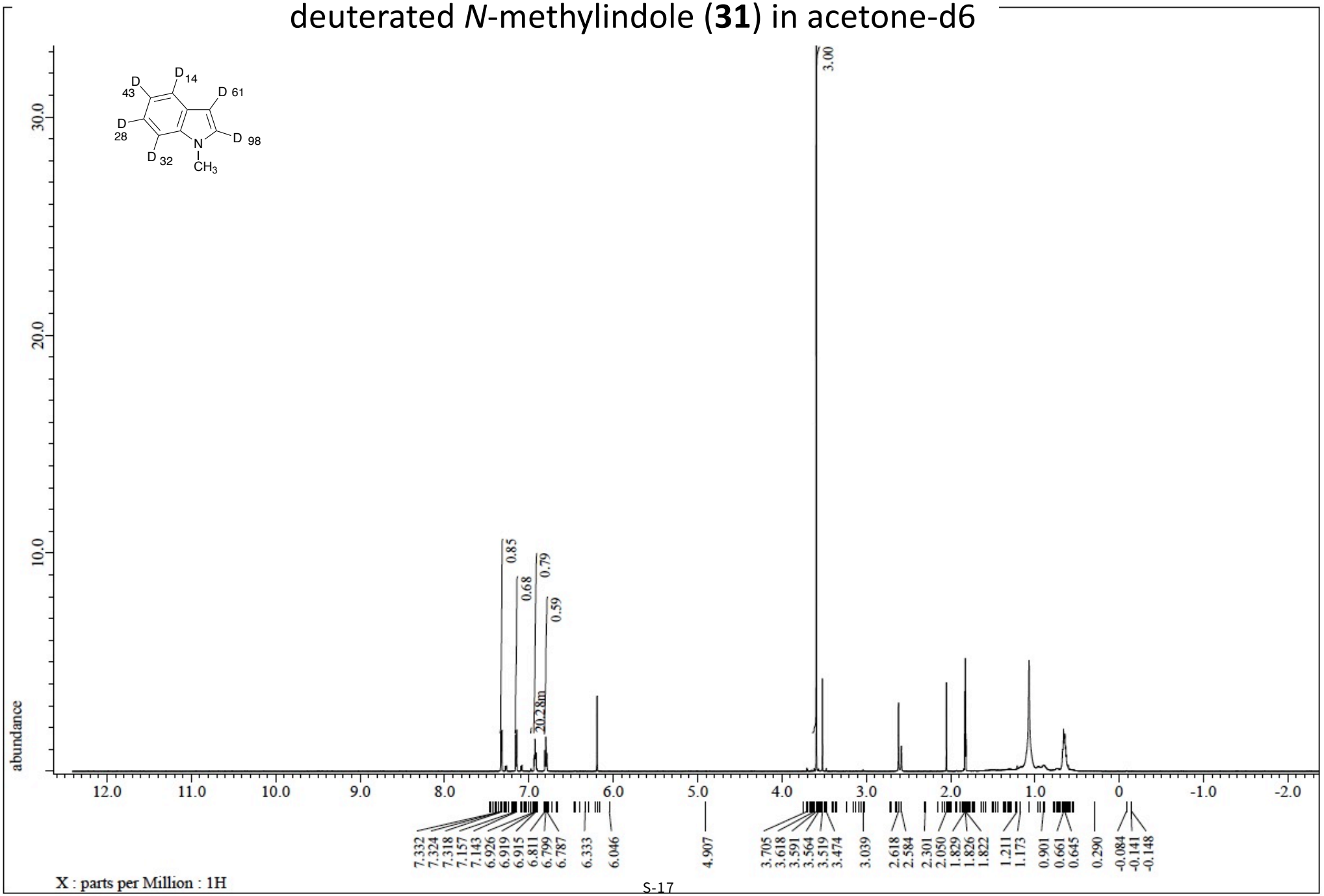


Figure S14. ^{1}H NMR (400 MHz) spectra of deuterated *N*-ethylindole (**25**) in acetone-d6

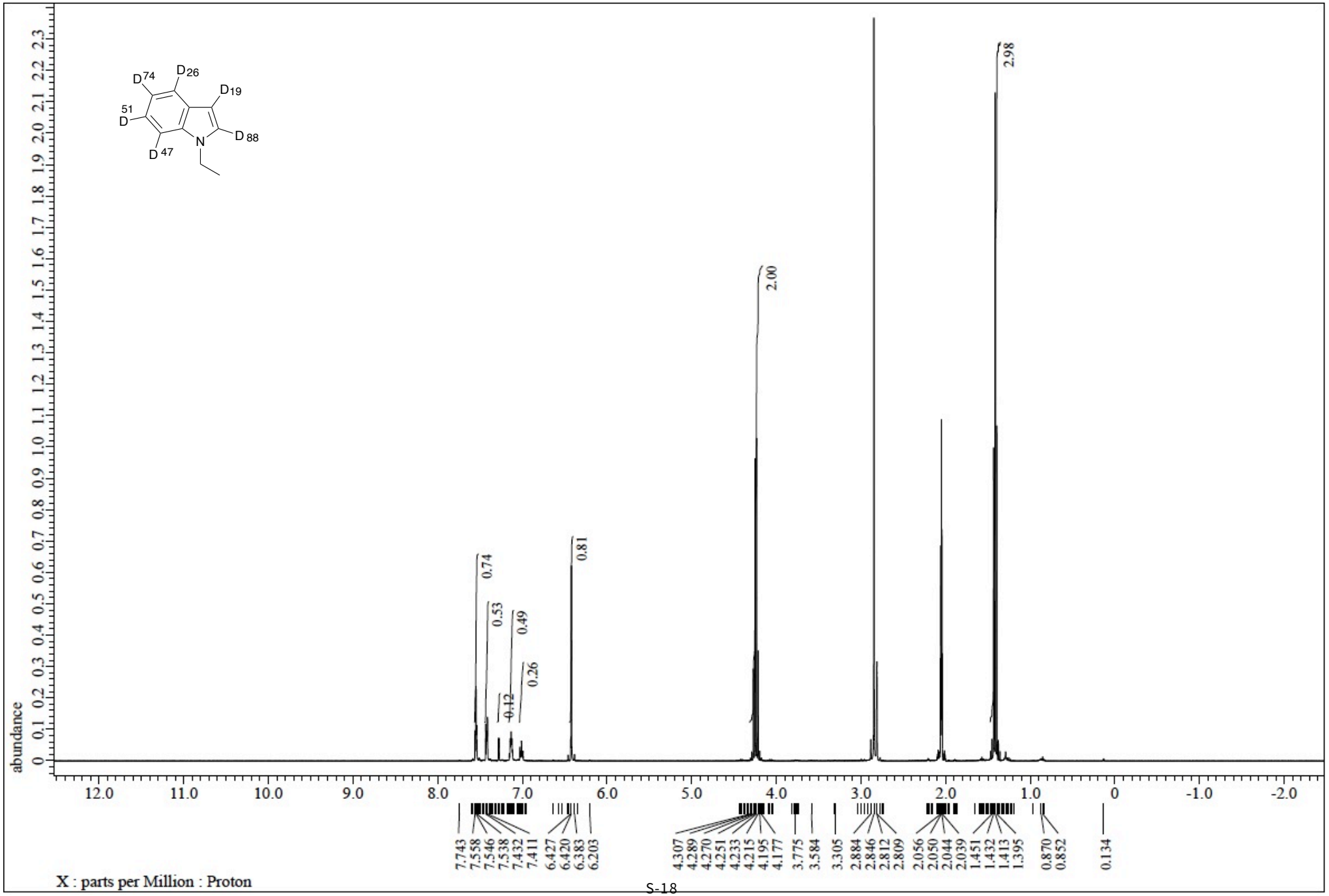


Figure S15. ^{1}H NMR (500 MHz) spectra of deuterated 2-methylindole (**26**) in CD_3OD

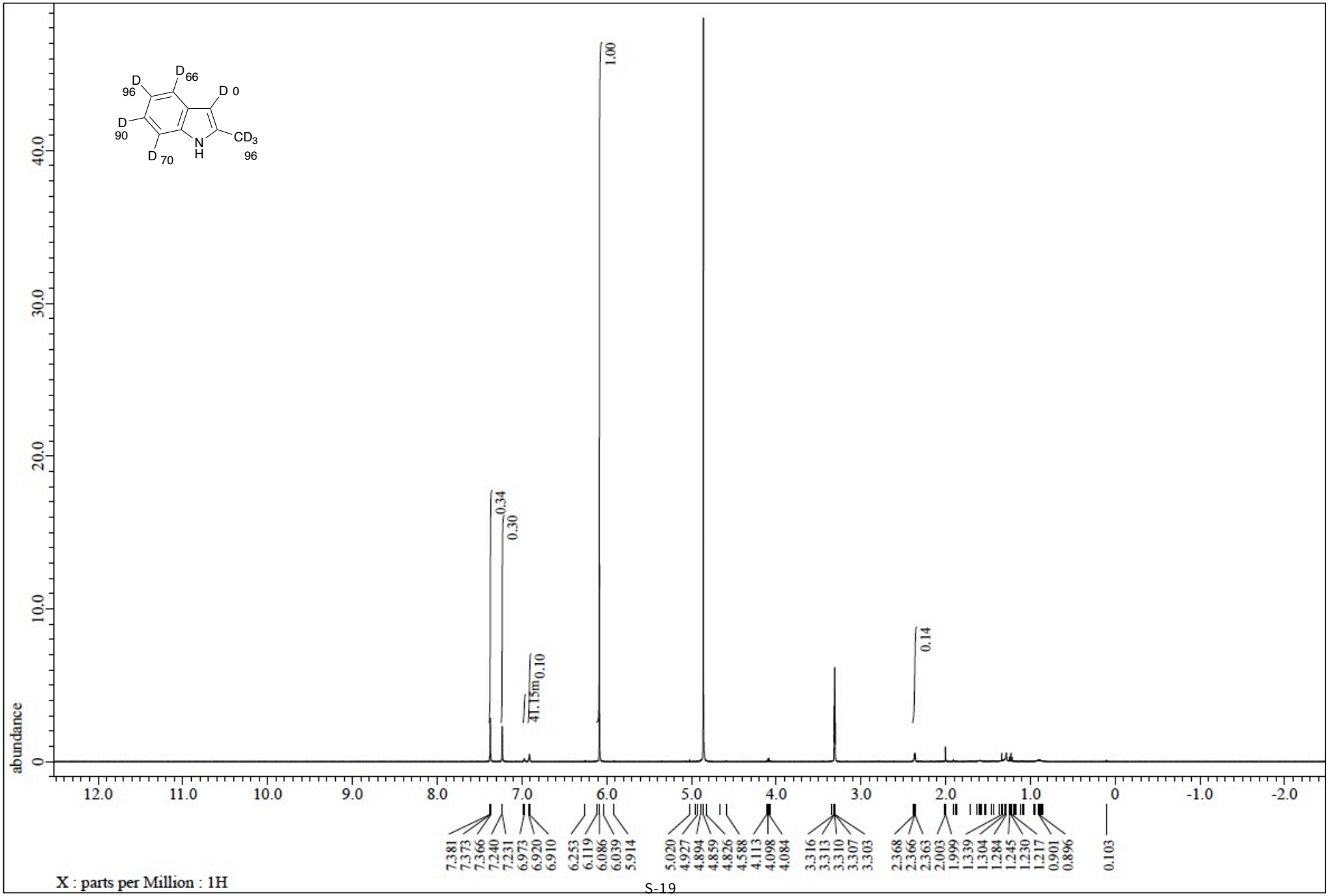


Figure S16. ^{1}H NMR (600 MHz) spectra of deuterated 4-methylindole (**27**) in CD_3OD

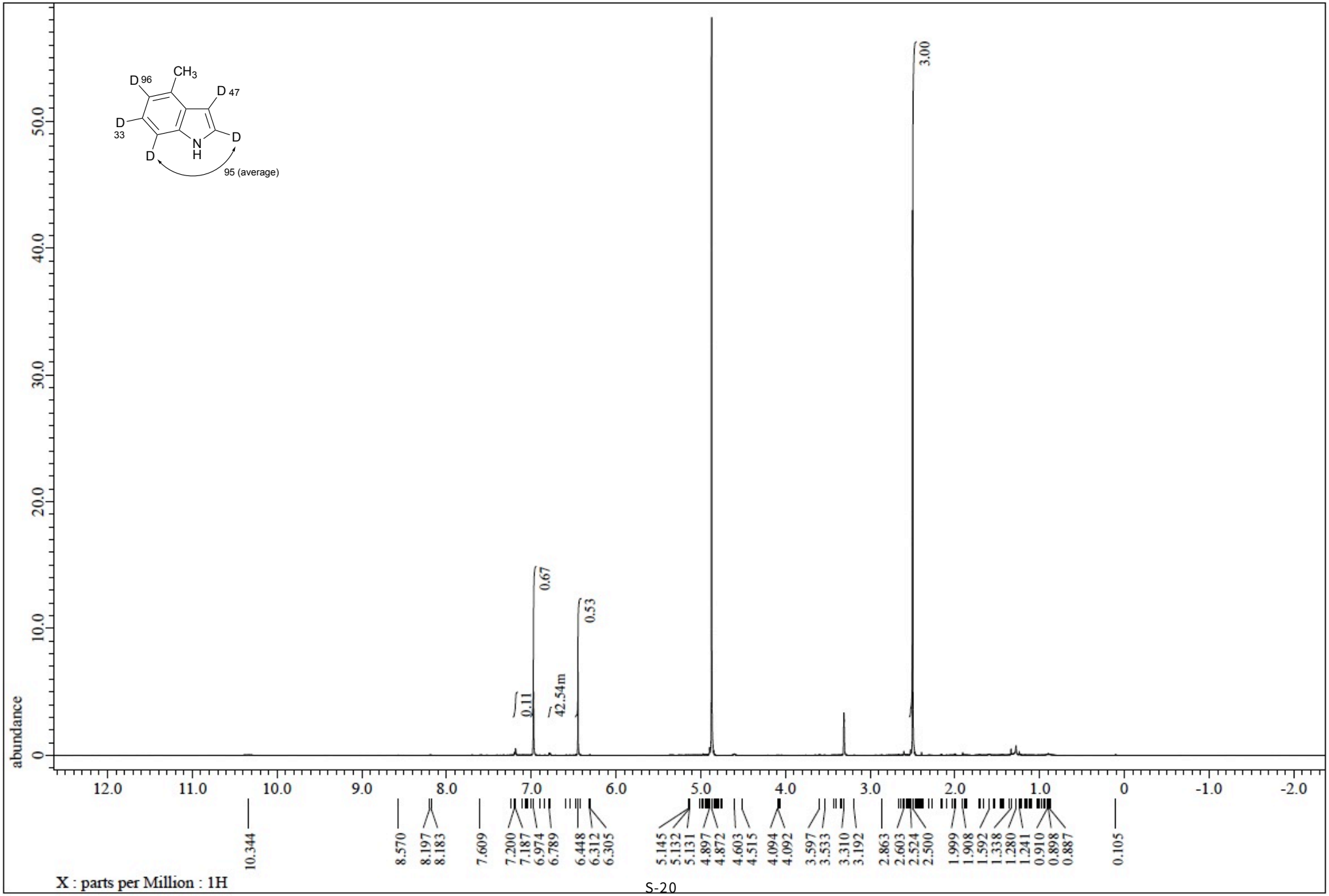


Figure S17. ^{1}H NMR (600 MHz) spectra of deuterated 5-methylindole (**28**) in CD_3OD

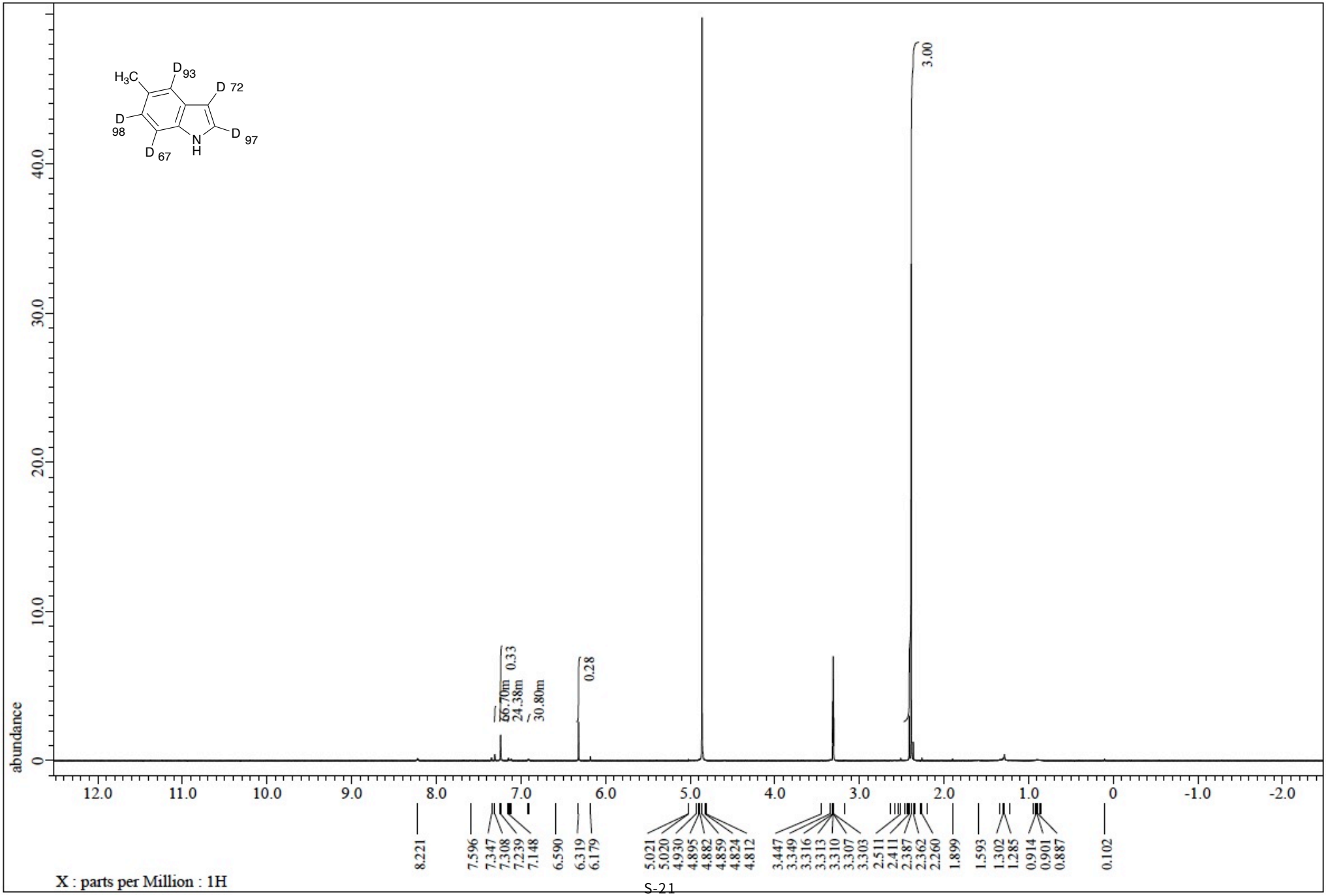


Figure S18. ^{1}H NMR (600 MHz) spectra of deuterated 7-ethylindole (**29**) in CD_3OD

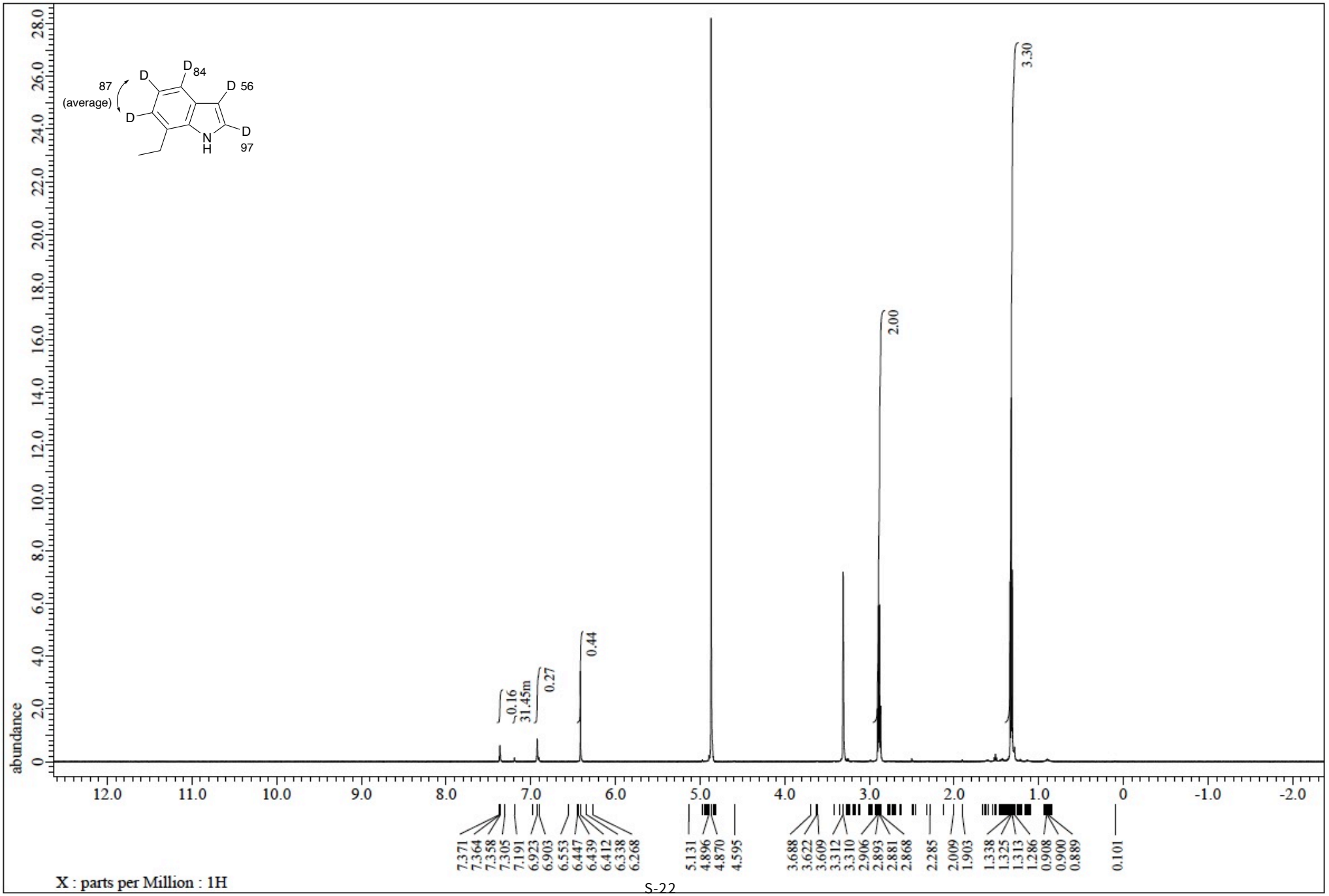


Figure S19. ^{1}H NMR (600 MHz) spectra of deuterated IBA (**4**) in CD_3OD

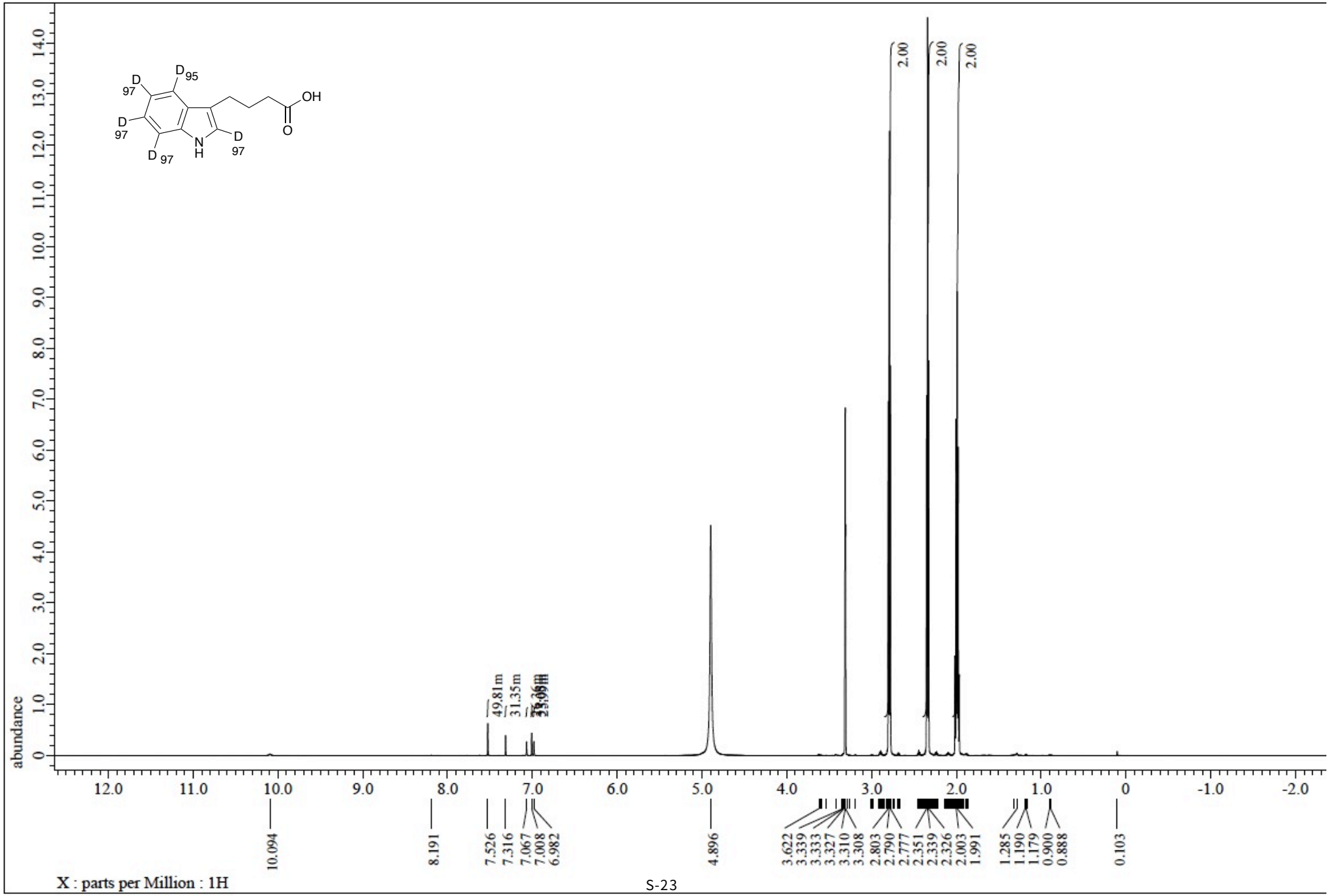


Figure S20. ^{1}H NMR (600 MHz) spectra of deuterated IAA (**3**) in CD_3OD

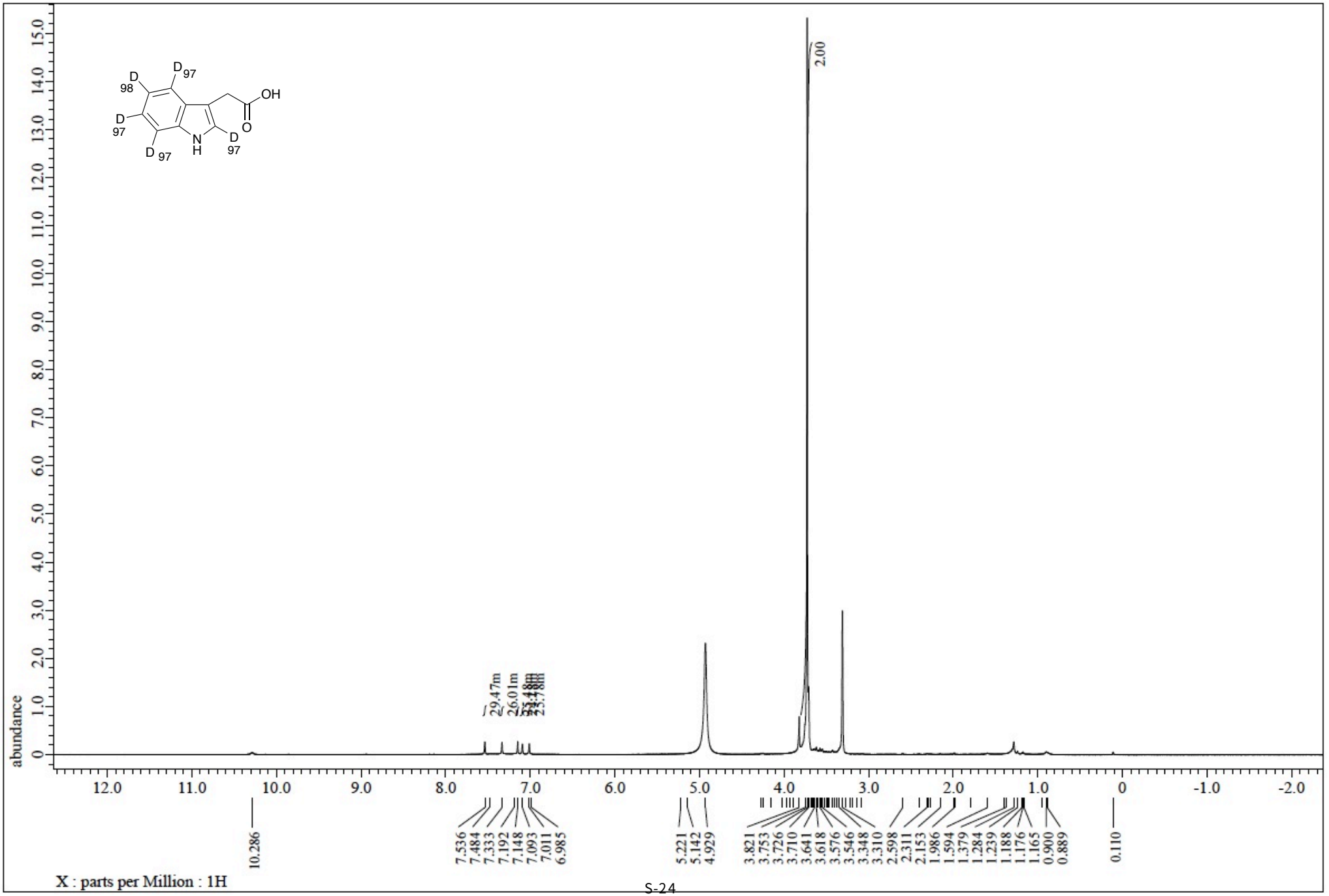


Figure S21. ^{13}C NMR (125 MHz) spectra of deuterated IBA CD_3 ester (**7**) in CD_3OD

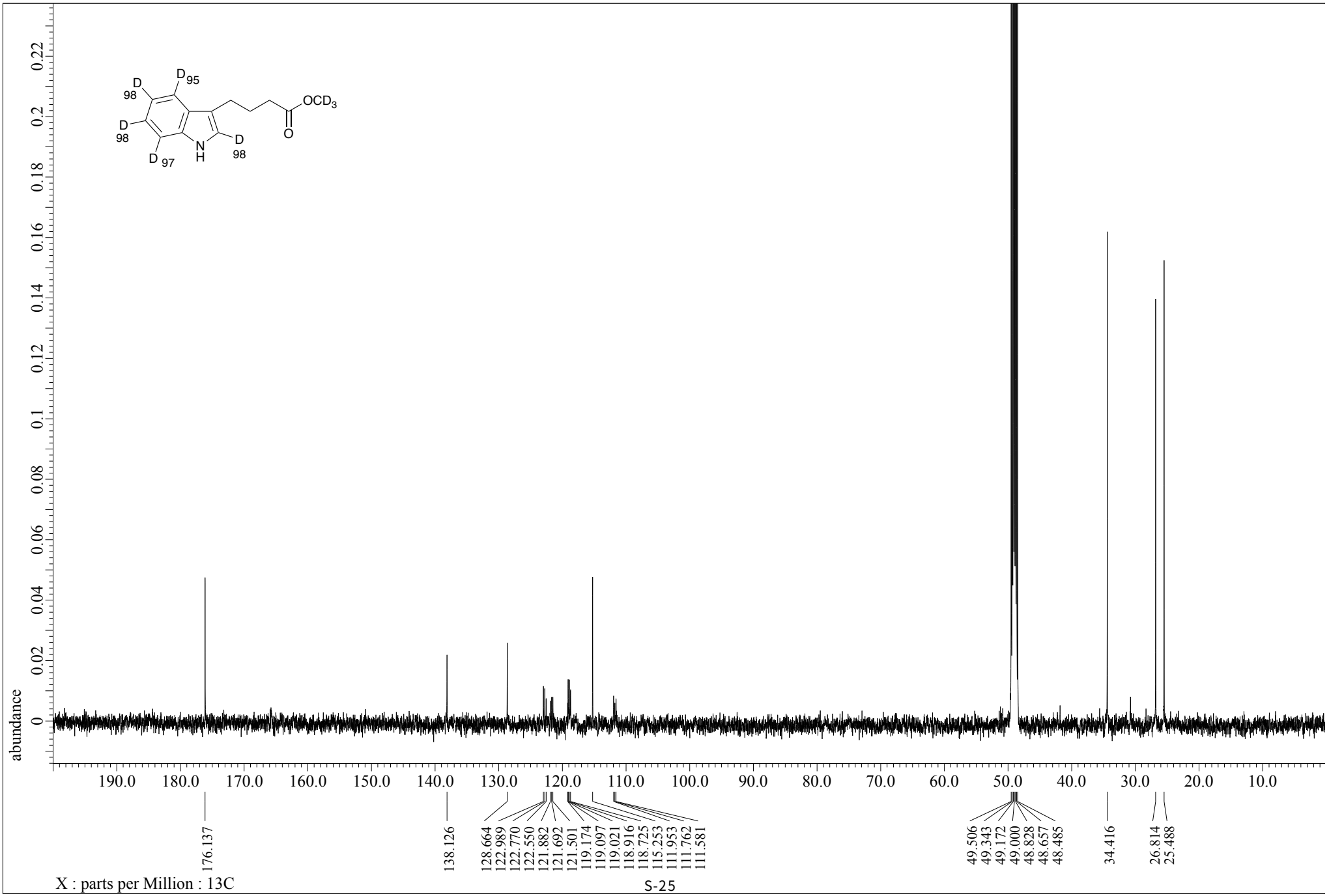


Figure S22. ^{13}C NMR (125 MHz) spectra of deuterated IAA CD_3 ester (**8**) in CD_3OD

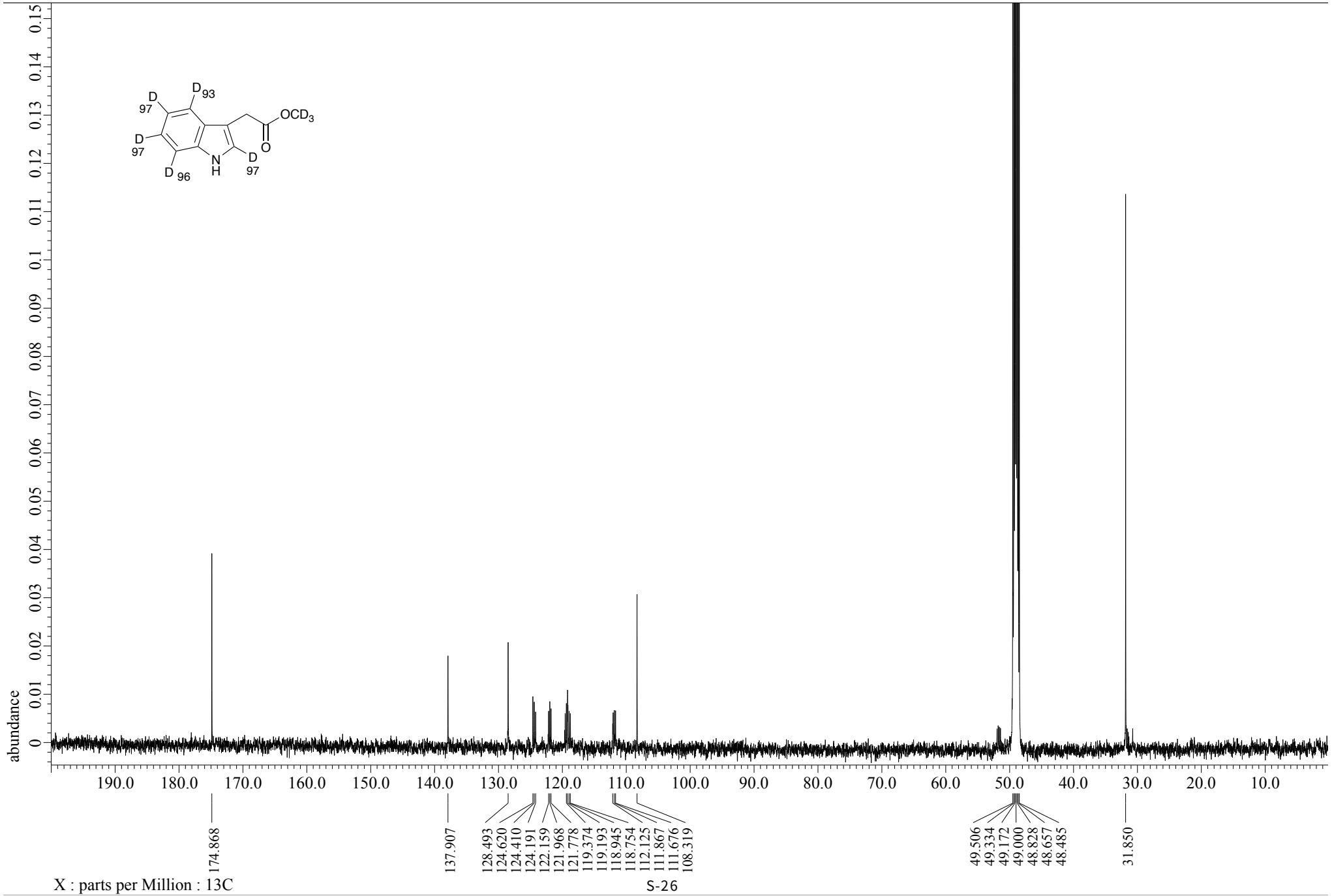


Figure S23. ^{13}C NMR (125 MHz) spectra of deuterated L-Trp-CD_3 ester (**9**) in CD_3OD

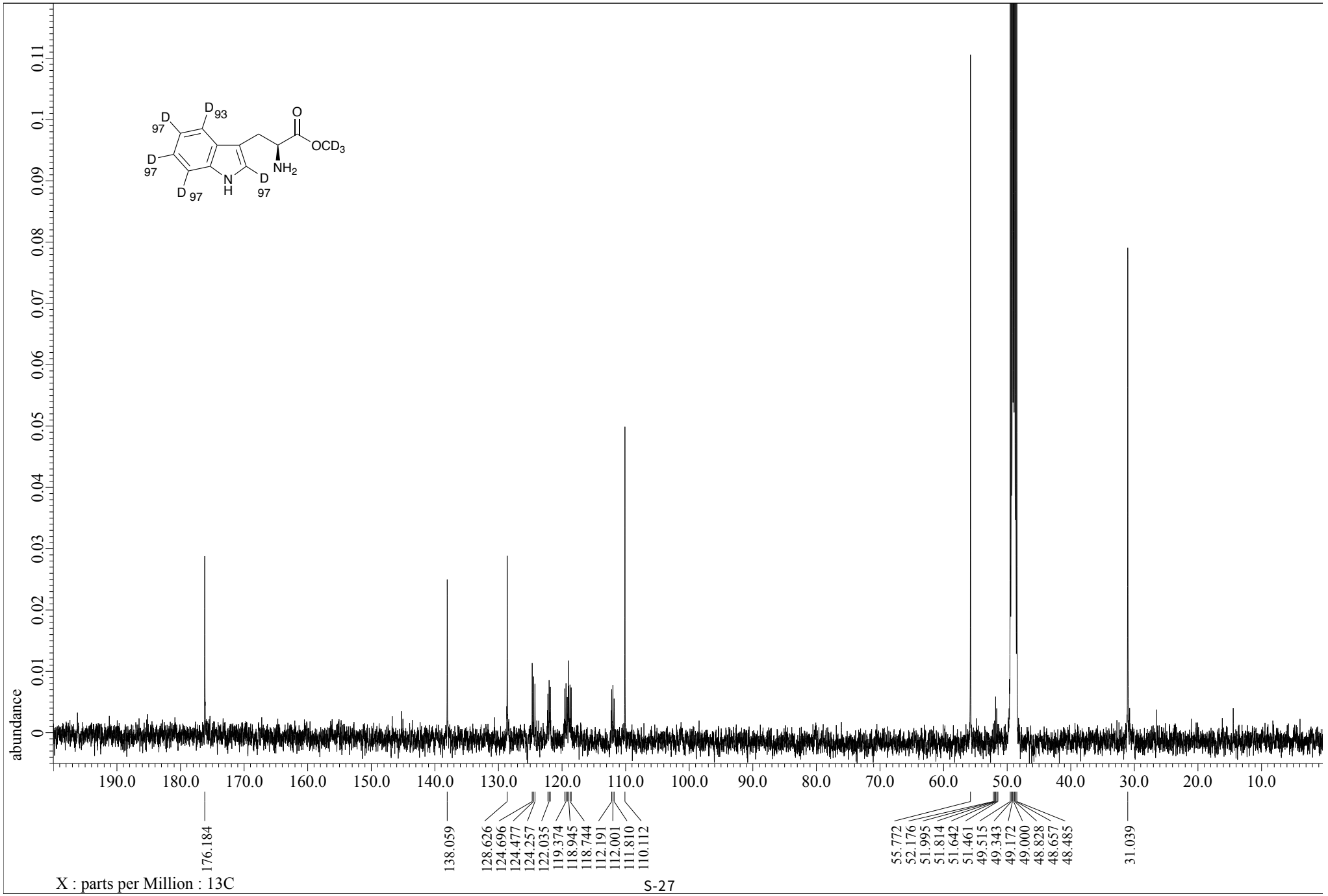


Figure S24. ^{13}C NMR (400 MHz) spectra of 3-(5-Chloroindol-3-y)propanoic acid methyl ester (**10**) in $CDCl_3$

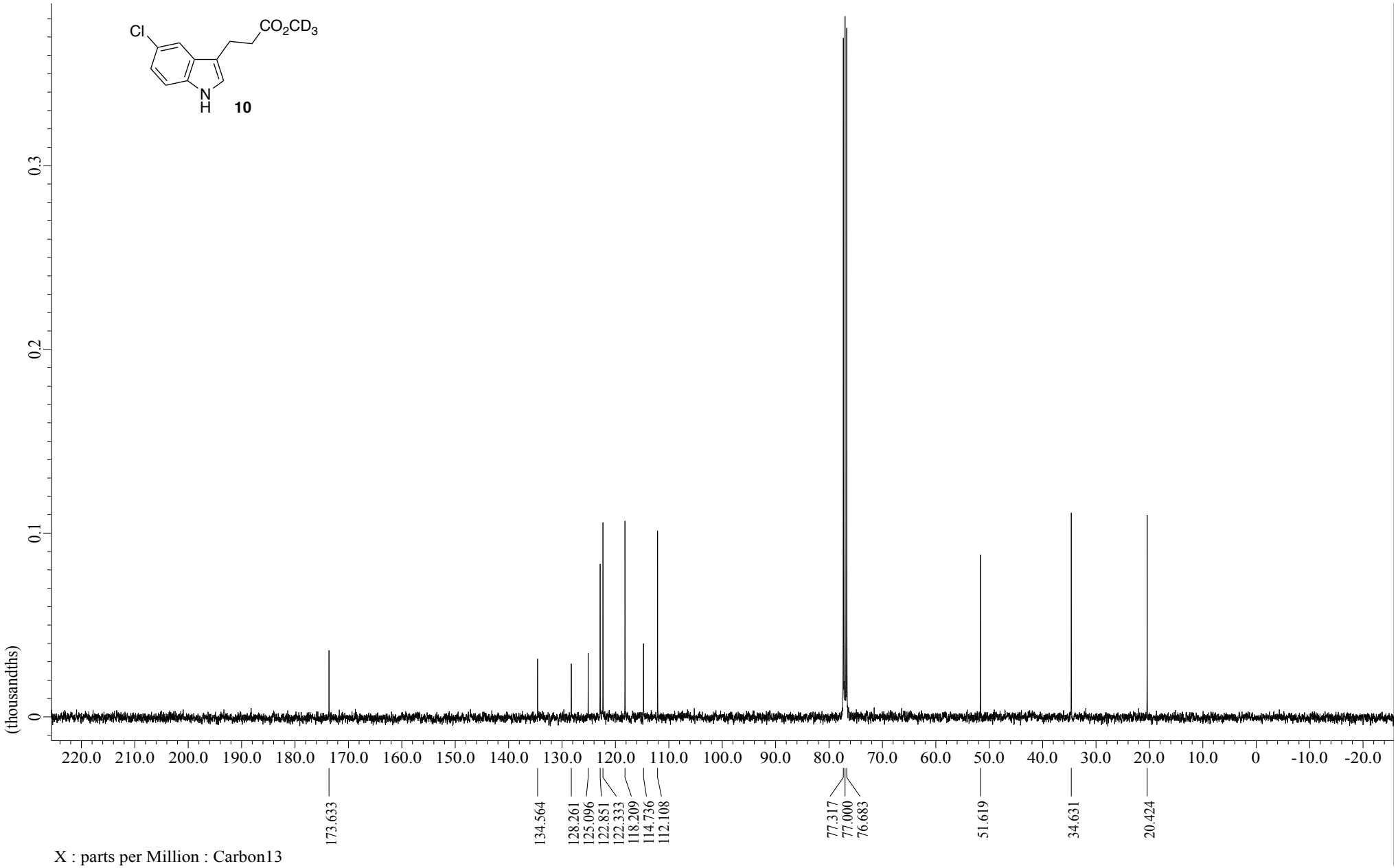


Figure S25. ^{13}C NMR (400 MHz) spectra of deuterated 3-(5-Chloroindol-3-yl)propanoic acid CD_3 ester (**11**) in CD_3OD

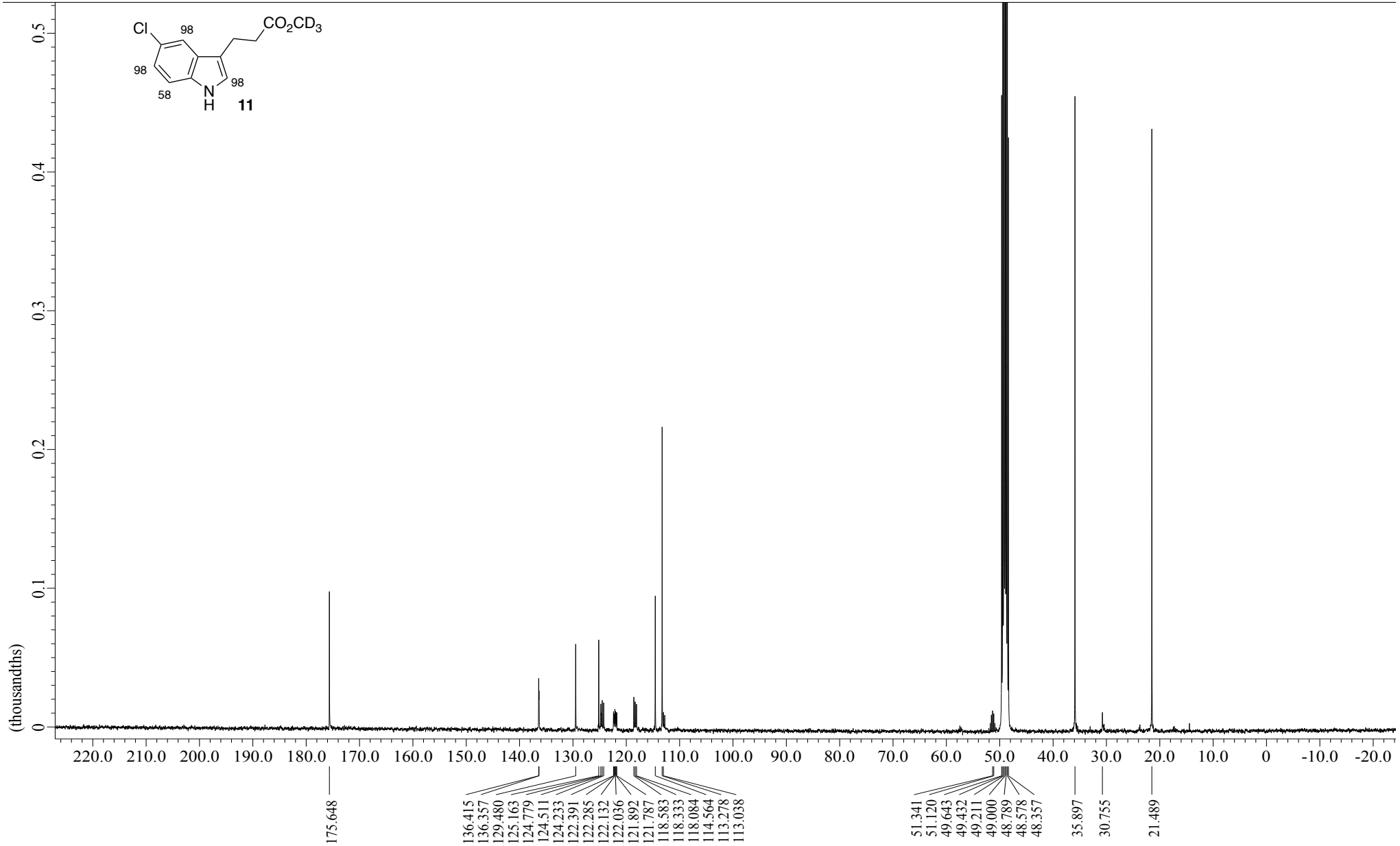


Figure S26. ^{13}C NMR (150 MHz) spectra of deuterated *N*-methyl-IBA CD_3 ester (**13**) in CD_3OD

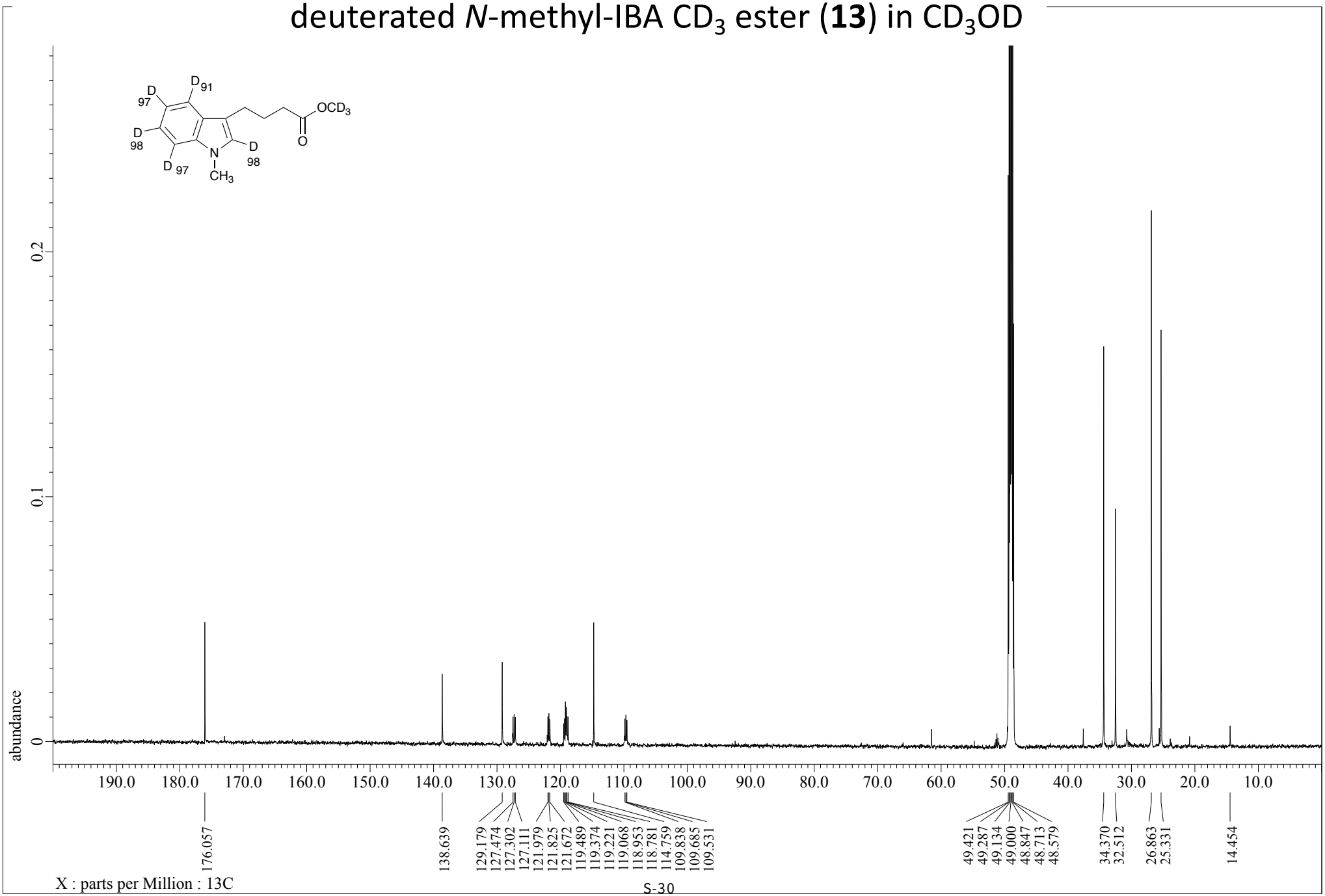


Figure S27. ^{13}C NMR (100 MHz) spectra of **15** in CD_3OD

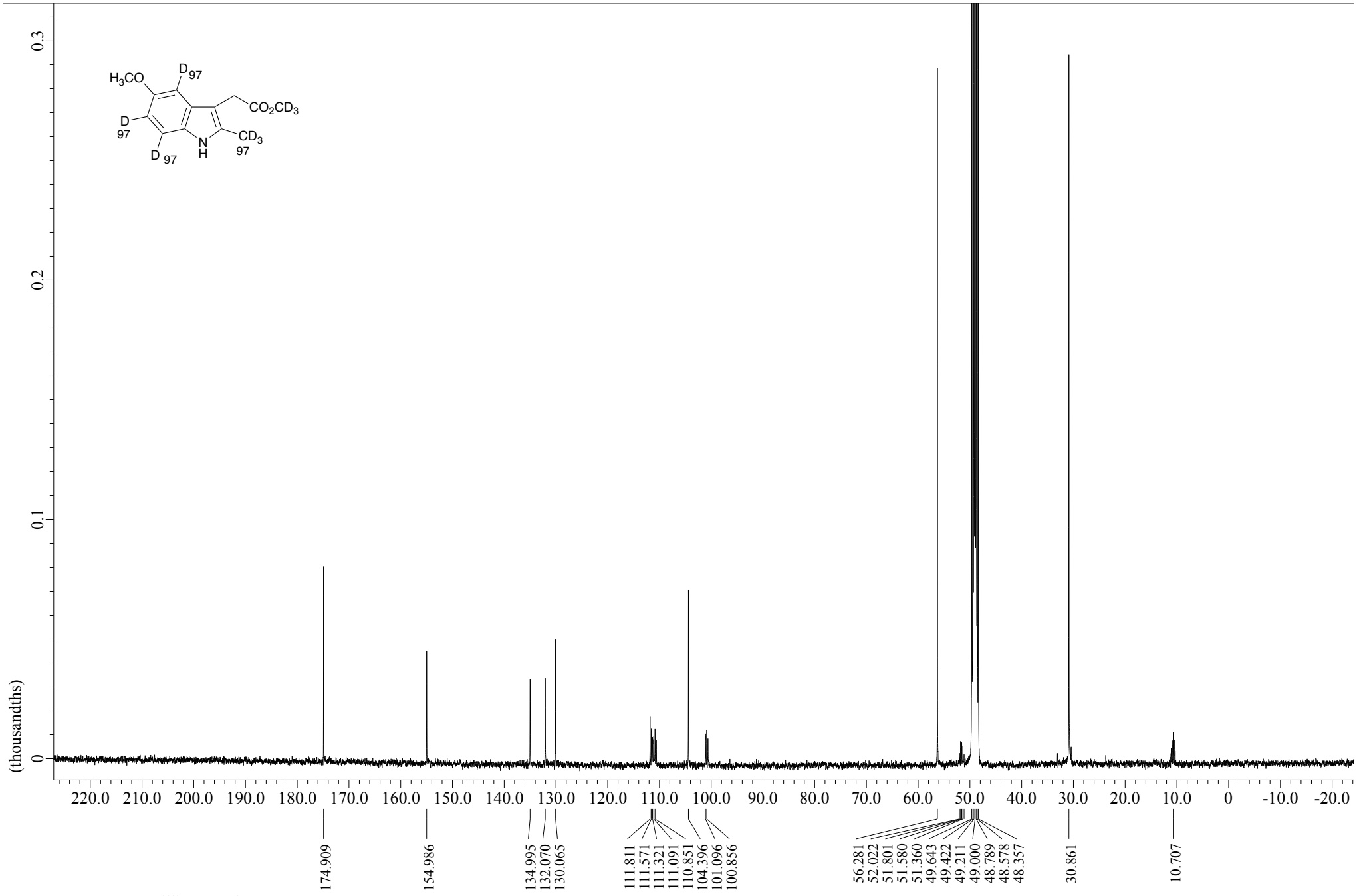


Figure S28. ^{13}C NMR (100 MHz) spectra of deuterated yohimbine (**17**) in CD_3OD

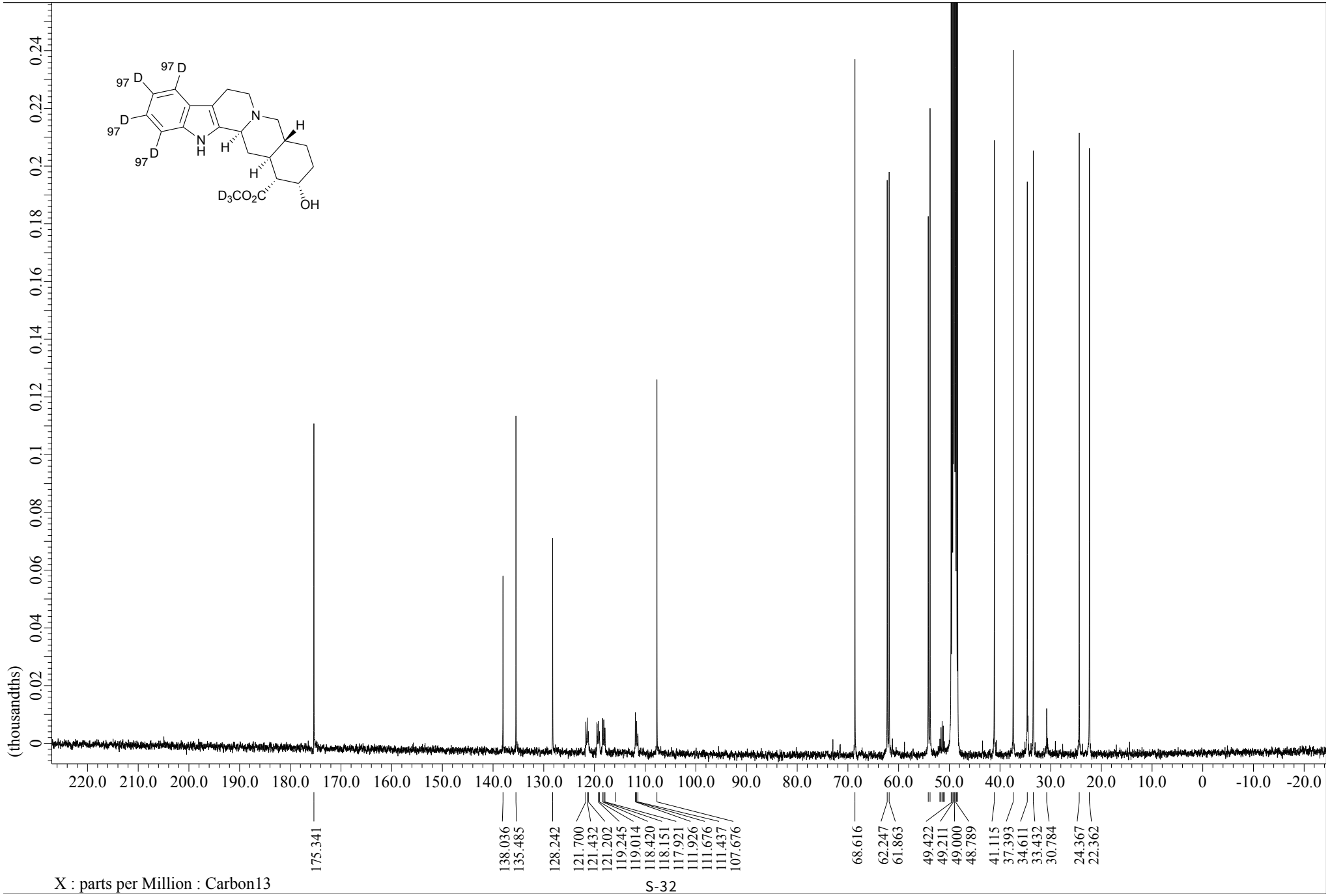


Figure S29. ^{13}C NMR (150 MHz) spectra of deuterated carbazole (**19**) in acetone-d6

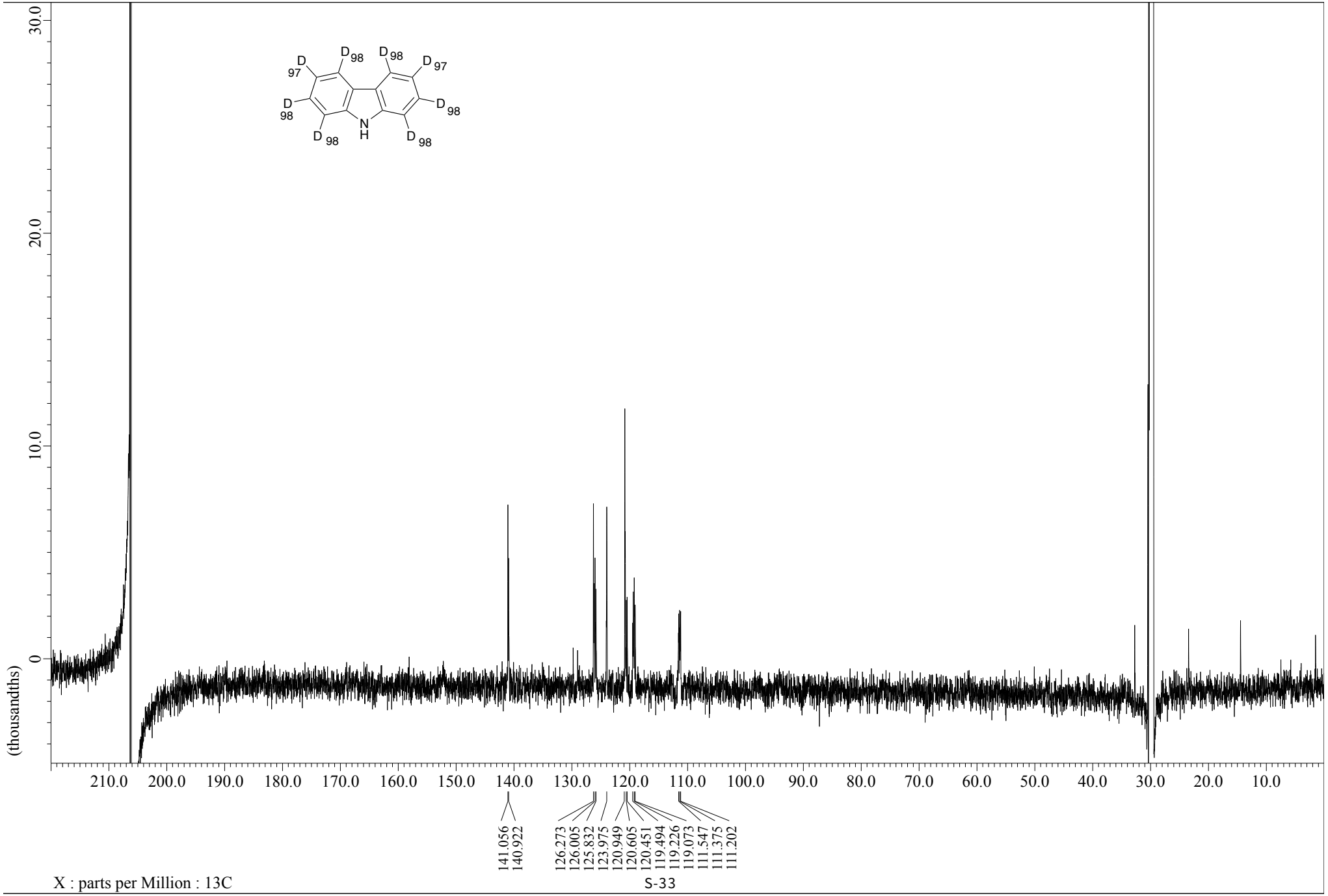


Figure S30. ^{13}C NMR (100 MHz) spectra of deuterated harmine (**21**) in CD_3OD

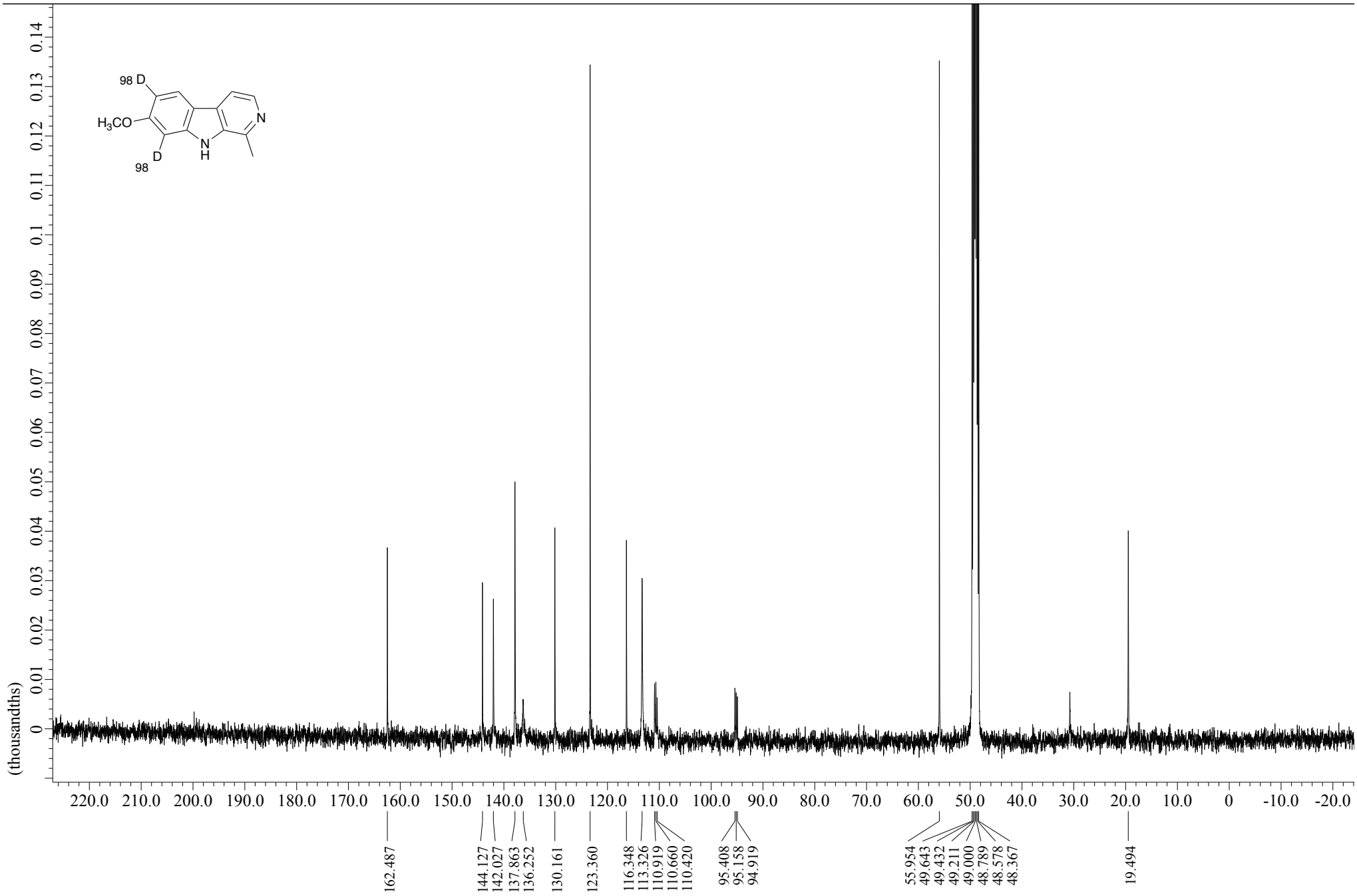


Figure S31. ^{13}C NMR (100 MHz) spectra of deuterated indole (**24**) in CD_3OD

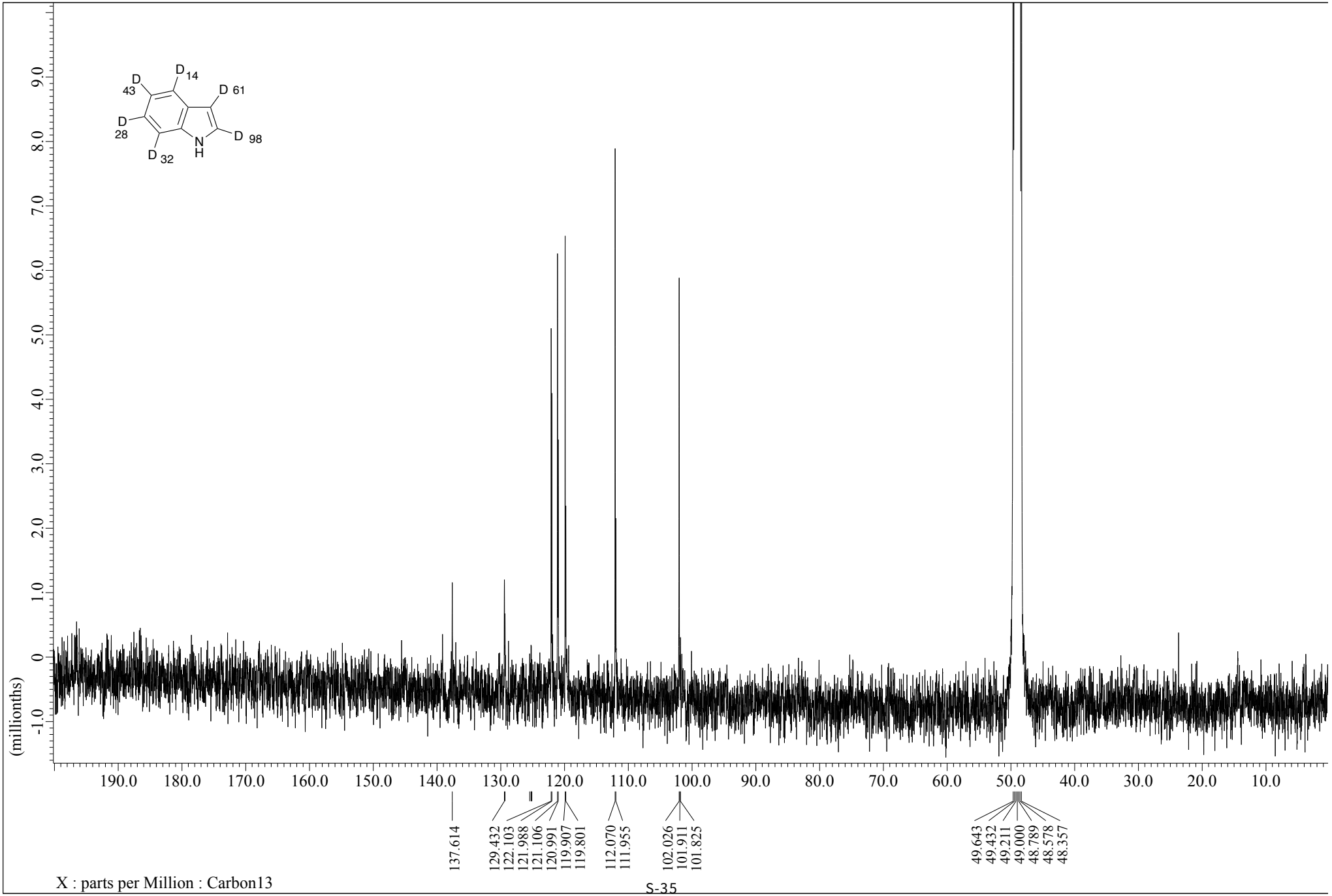


Figure S32. ^{13}C NMR (100 MHz) spectra of deuterated *N*-ethylindole (**25**) in $CDCl_3$

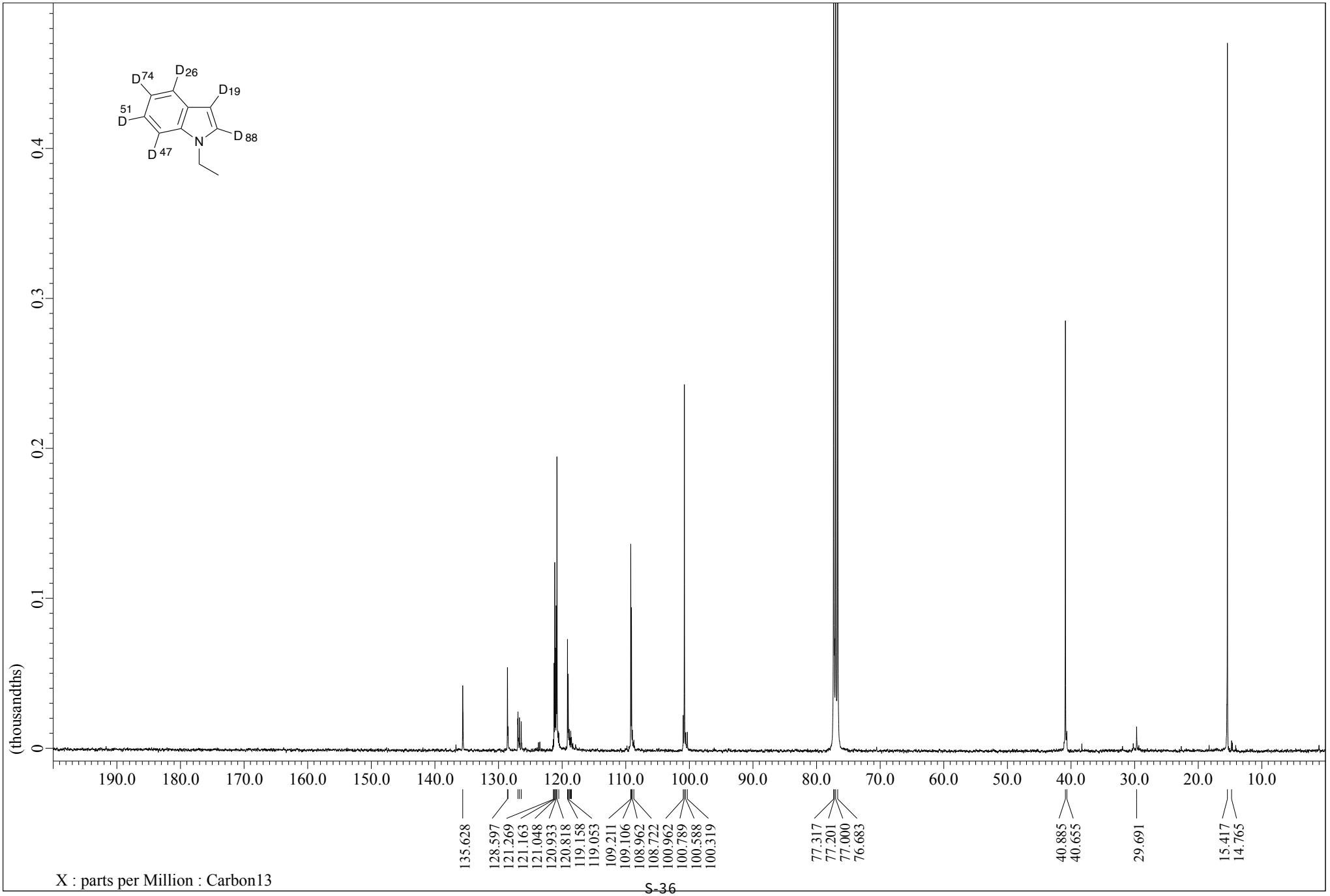


Figure S33. ^{13}C NMR (125 MHz) spectra of deuterated 2-methylindole (**26**) in CD_3OD

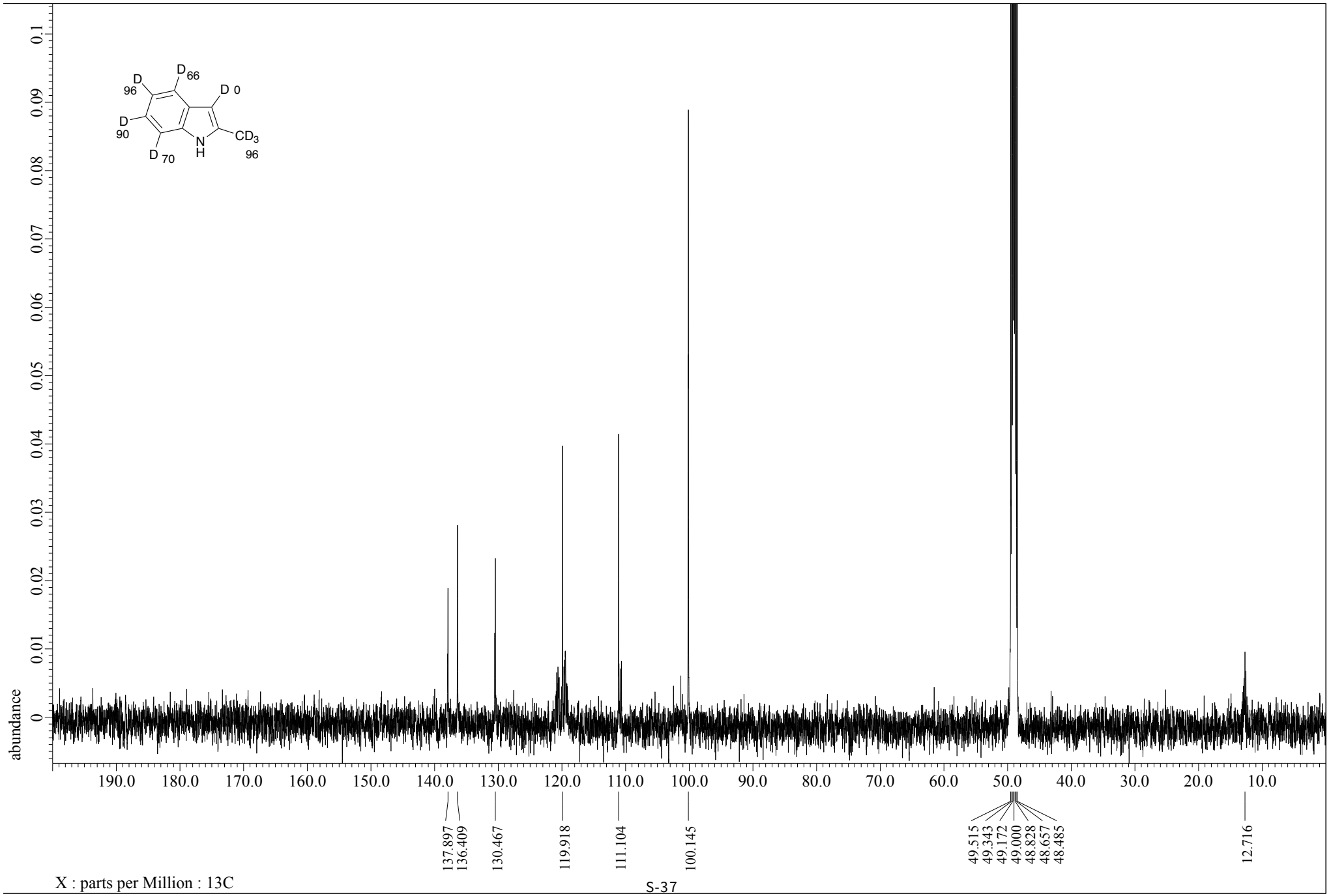


Figure S34. ^{13}C NMR (150 MHz) spectra of deuterated 4-methylindole (**27**) in CD_3OD

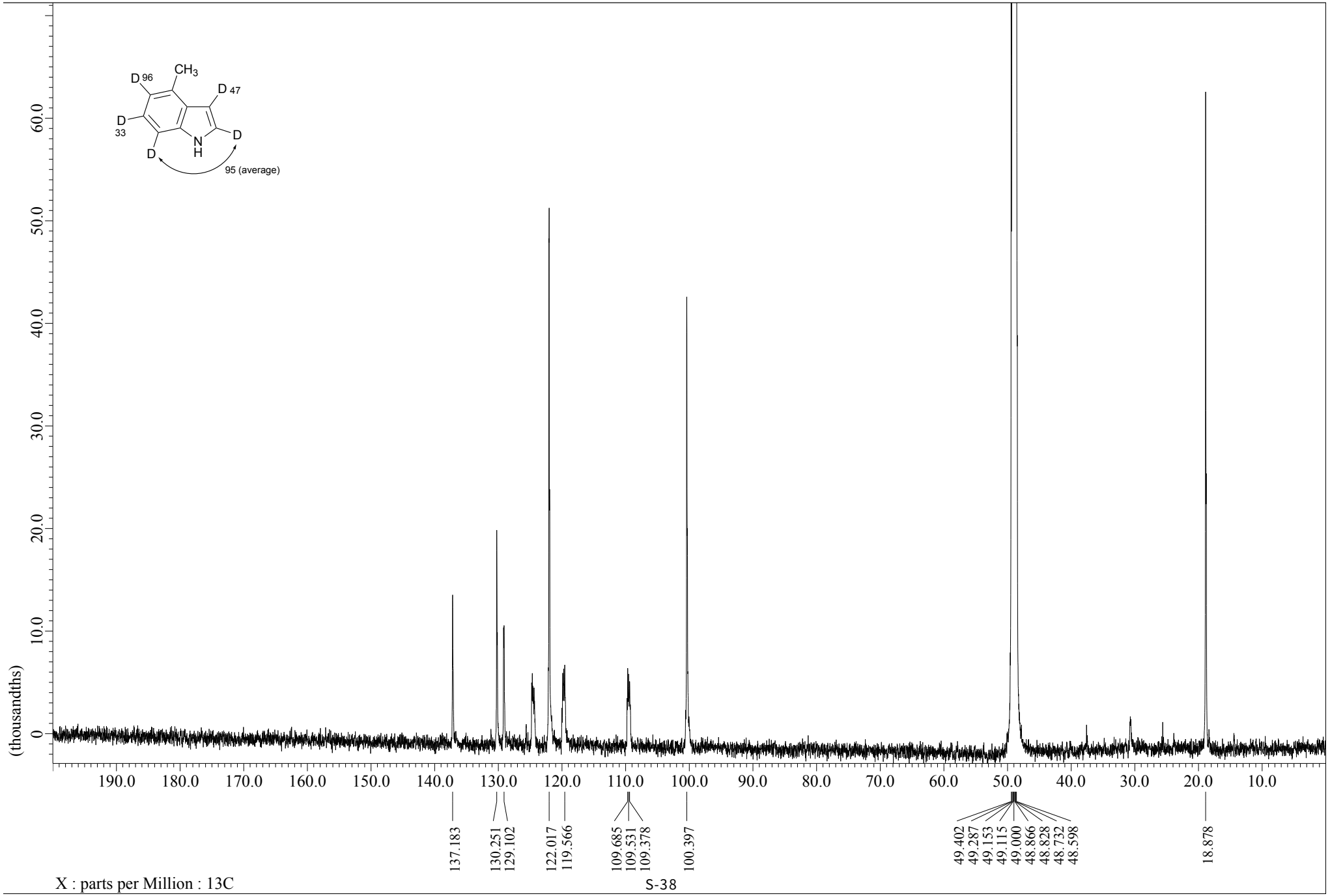


Figure S35. ^{13}C NMR (125 MHz) spectra of deuterated 5-methylindole (**28**) in CD_3OD

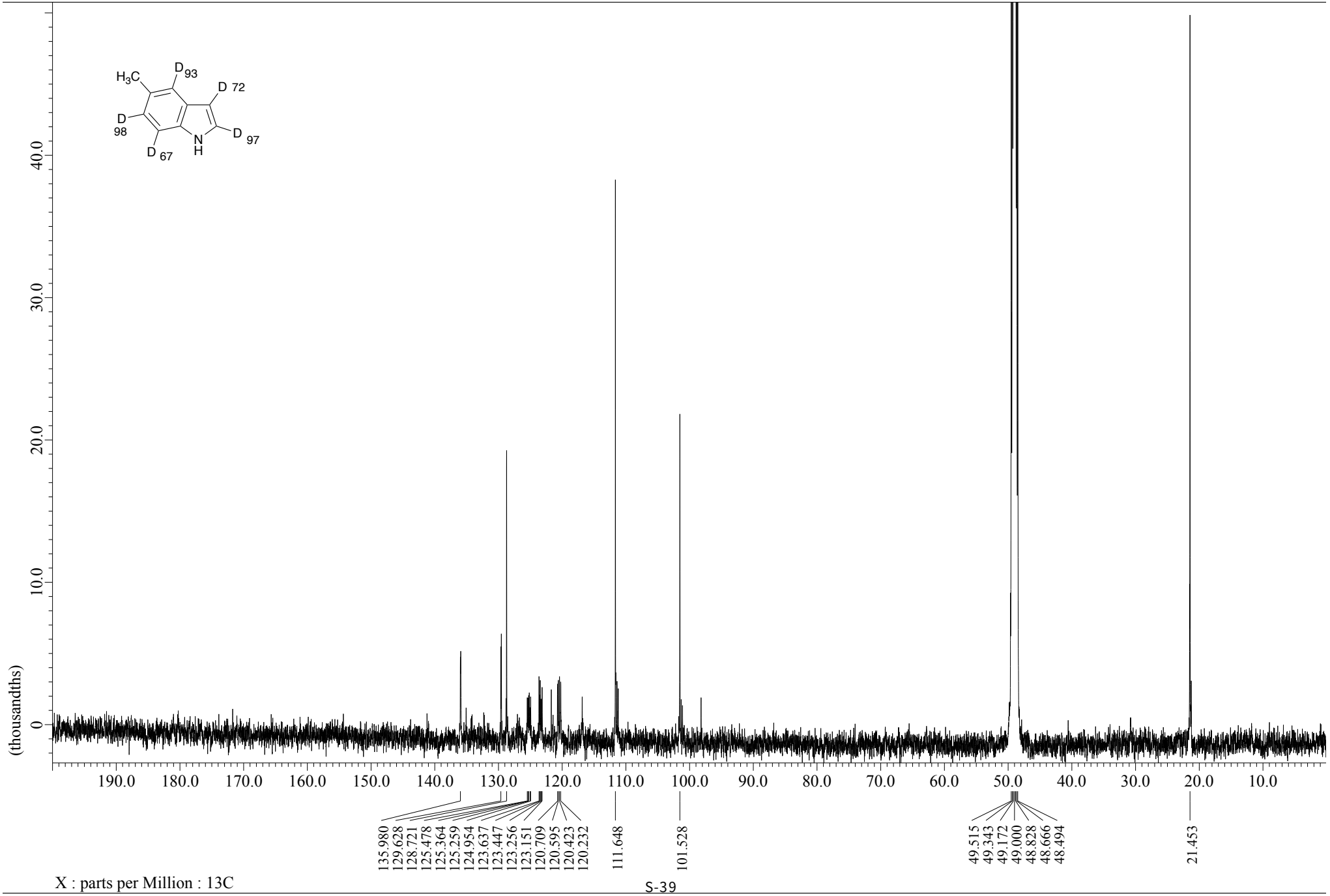


Figure S36. ^{13}C NMR (150 MHz) spectra of deuterated 7-ethylindole (**29**) in CD_3OD

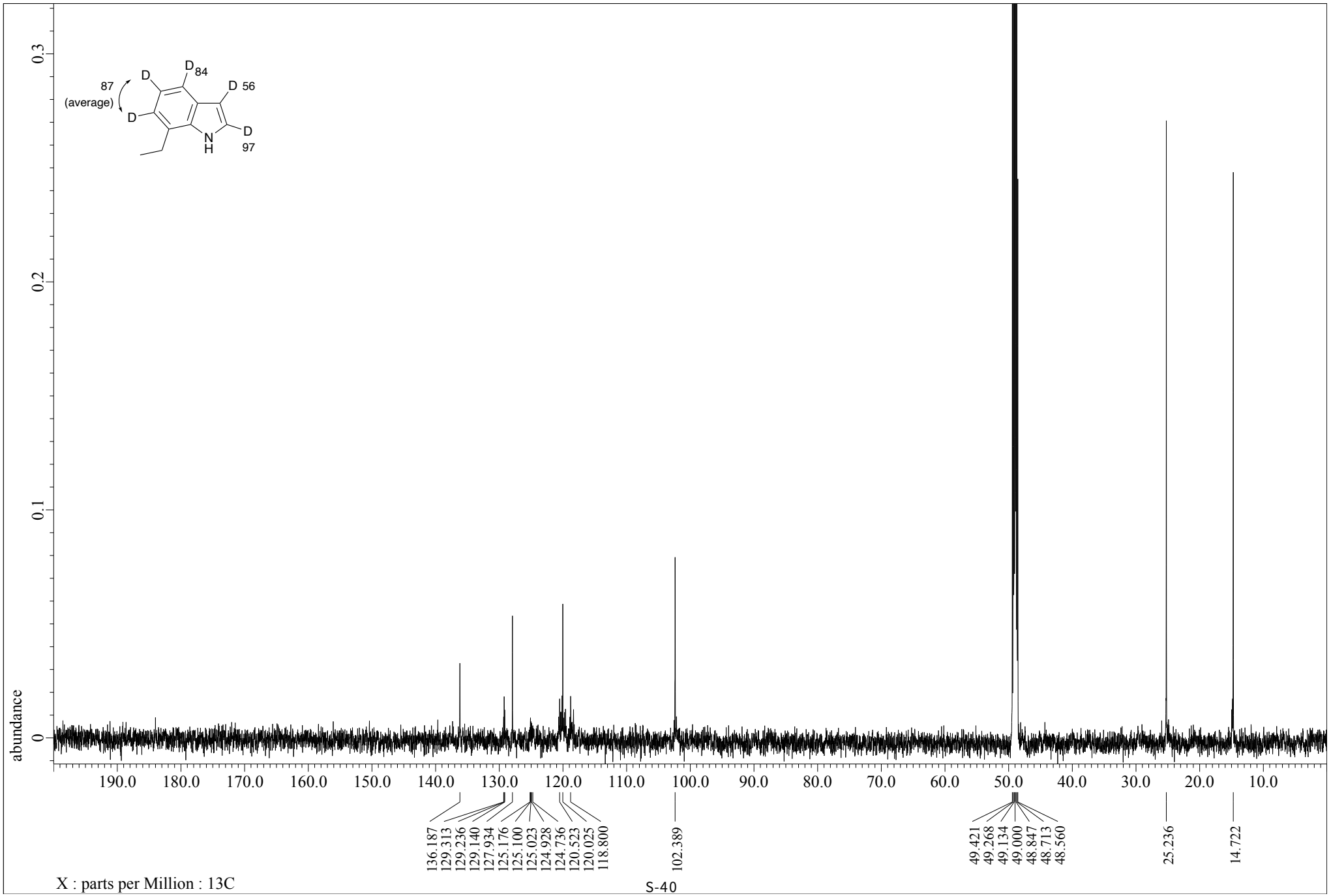


Figure S37. ^{13}C NMR (150 MHz) spectra of deuterated IBA (**4**) in CD_3OD

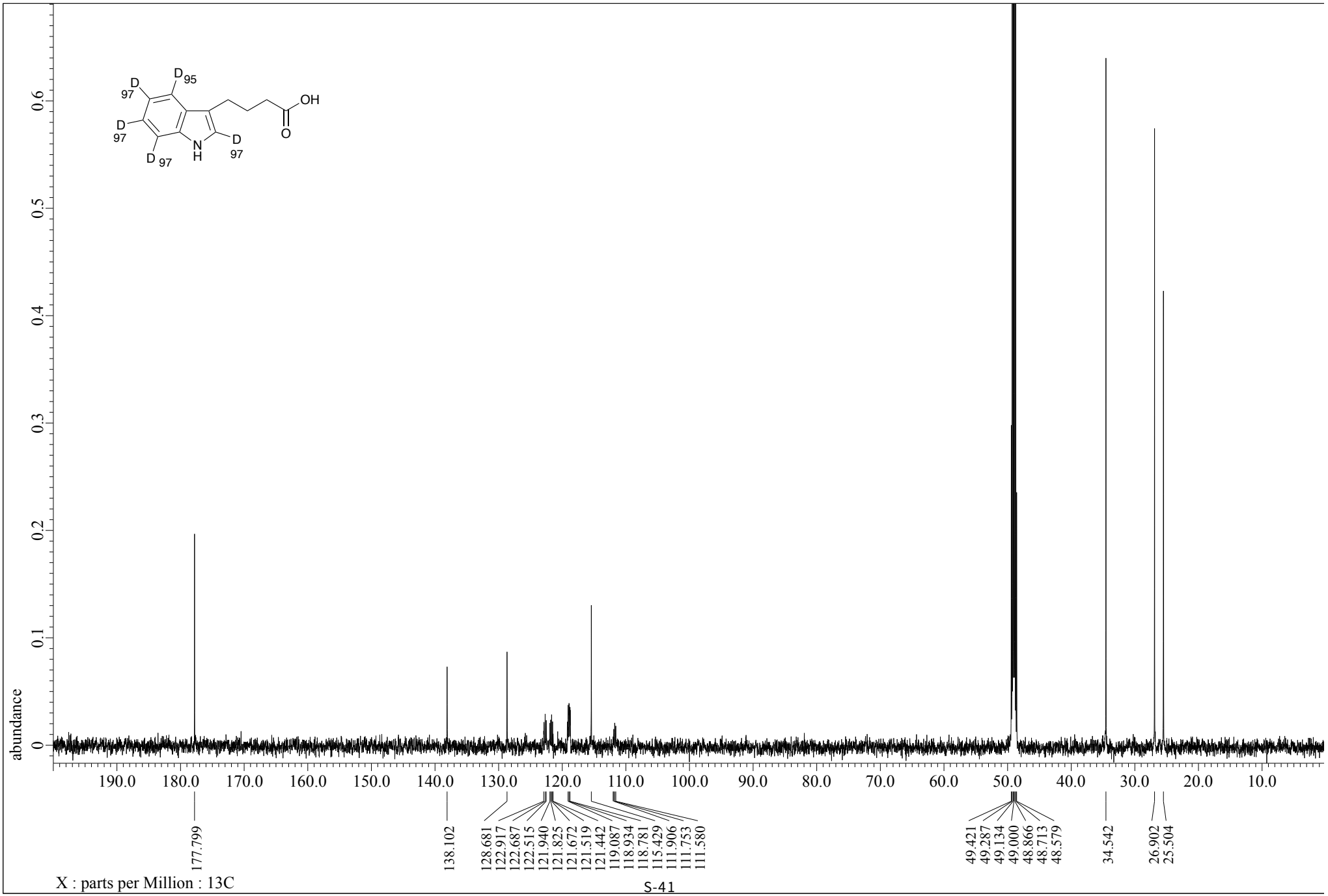


Figure S38. ^{13}C NMR (150 MHz) spectra of deuterated IAA (**3**) in CD_3OD

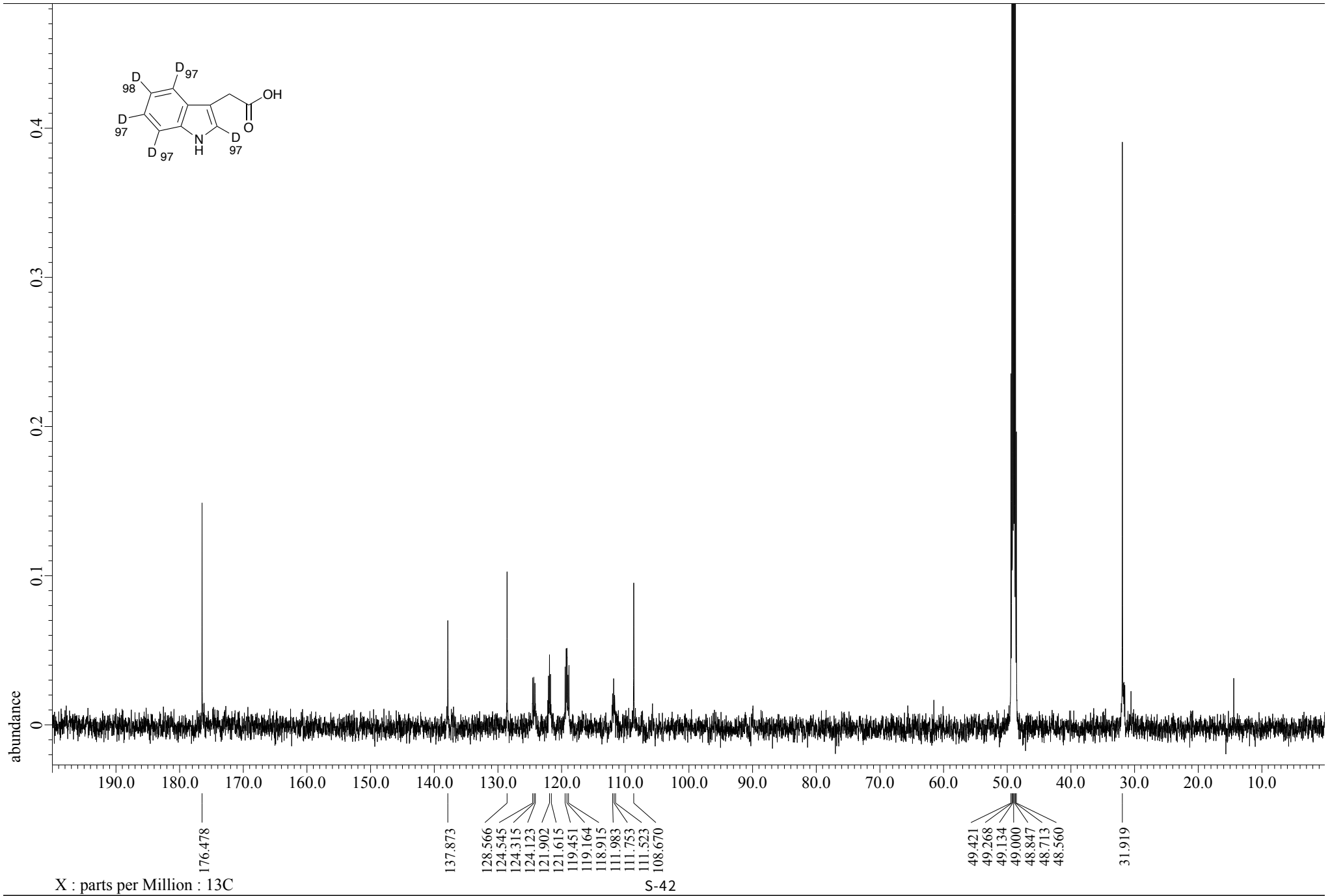
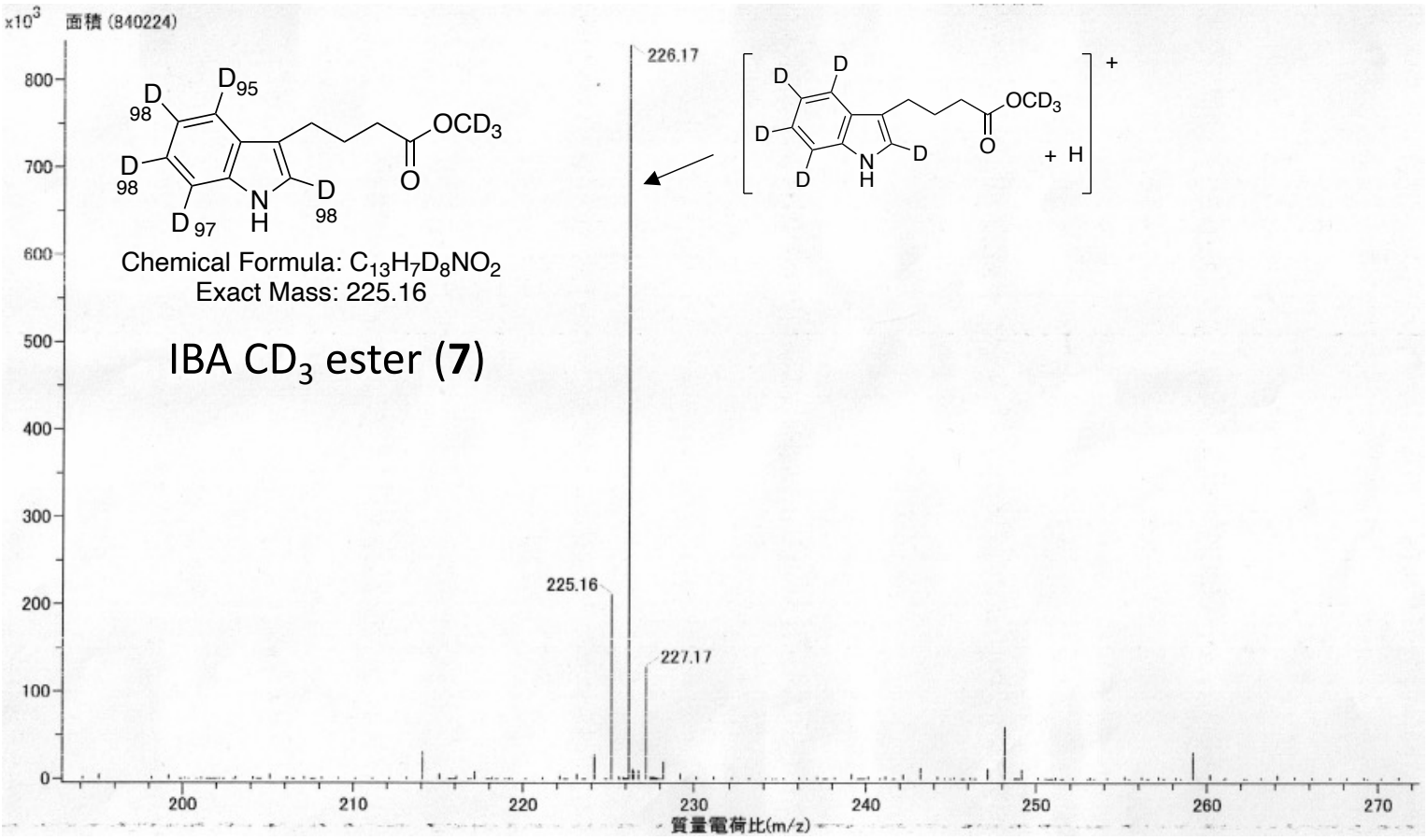


Figure S39. TOF-MS (ESI+) spectra of deuterated IBA CD_3 ester (**7**)



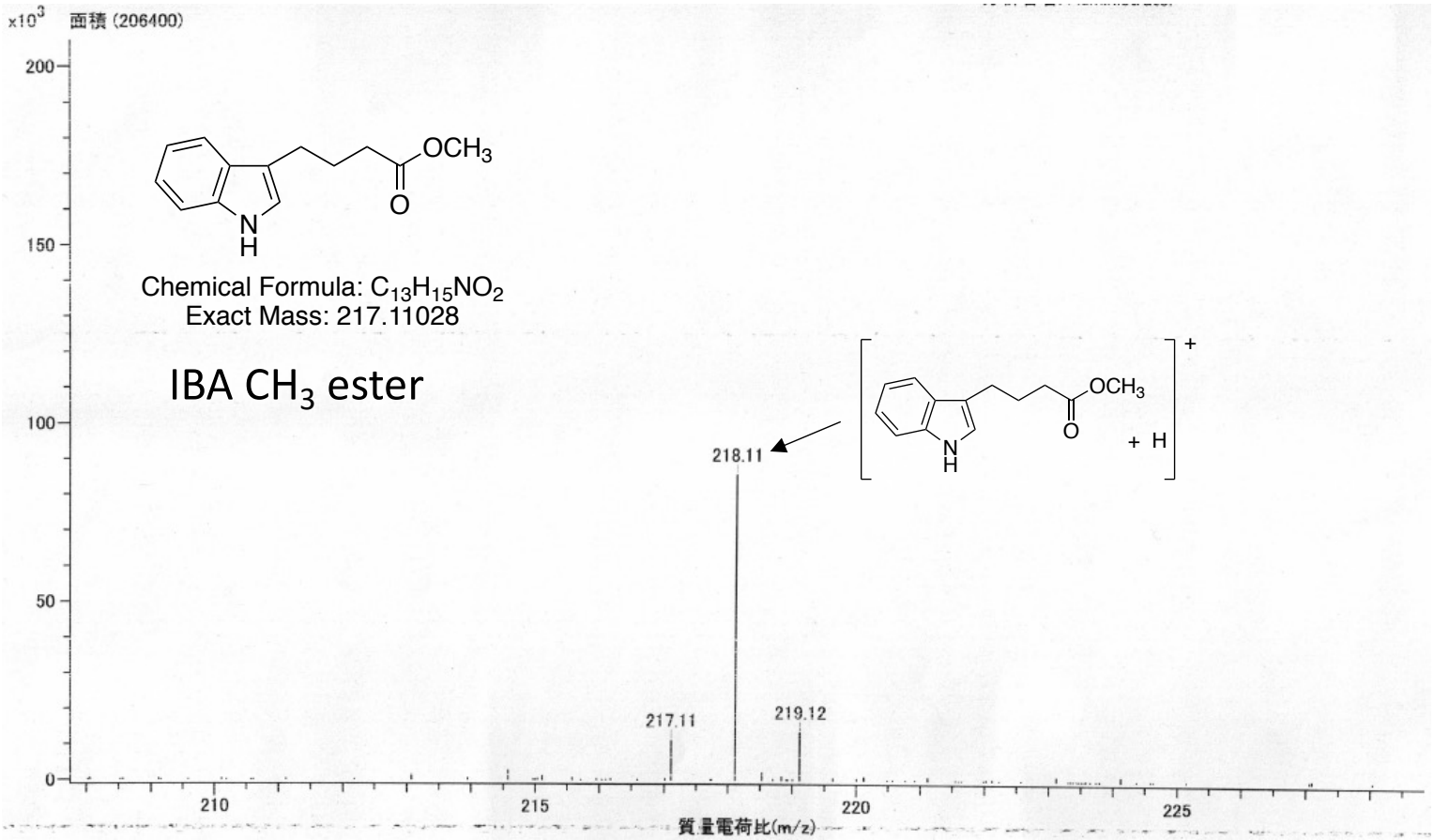


Figure S40. TOF-MS (ESI+) spectra of deuterated IBA CD_3 ester (**8**)

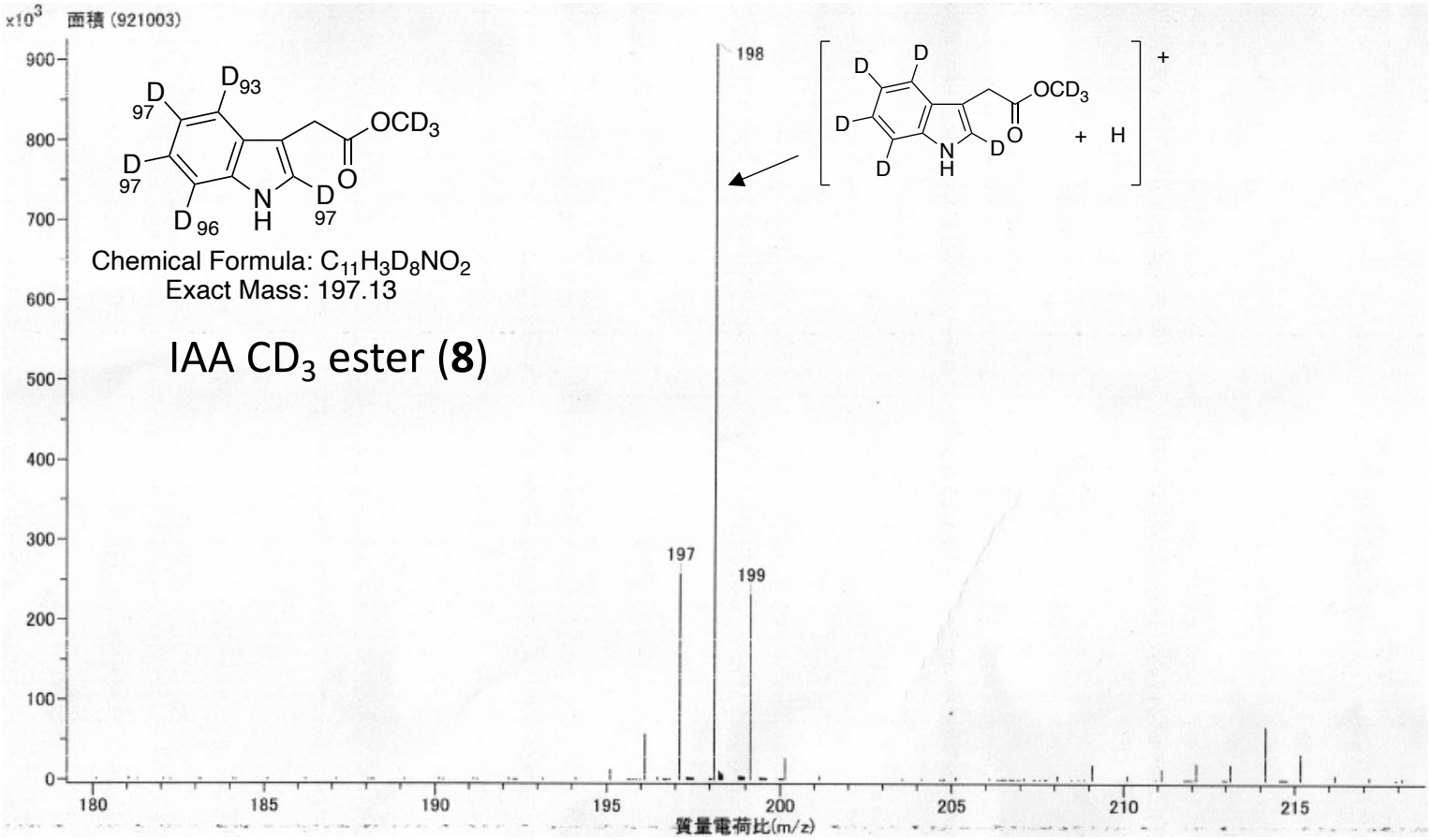


Figure S41. TOF-MS (ESI+) spectra of deuterated Trp CD_3 ester (**9**)

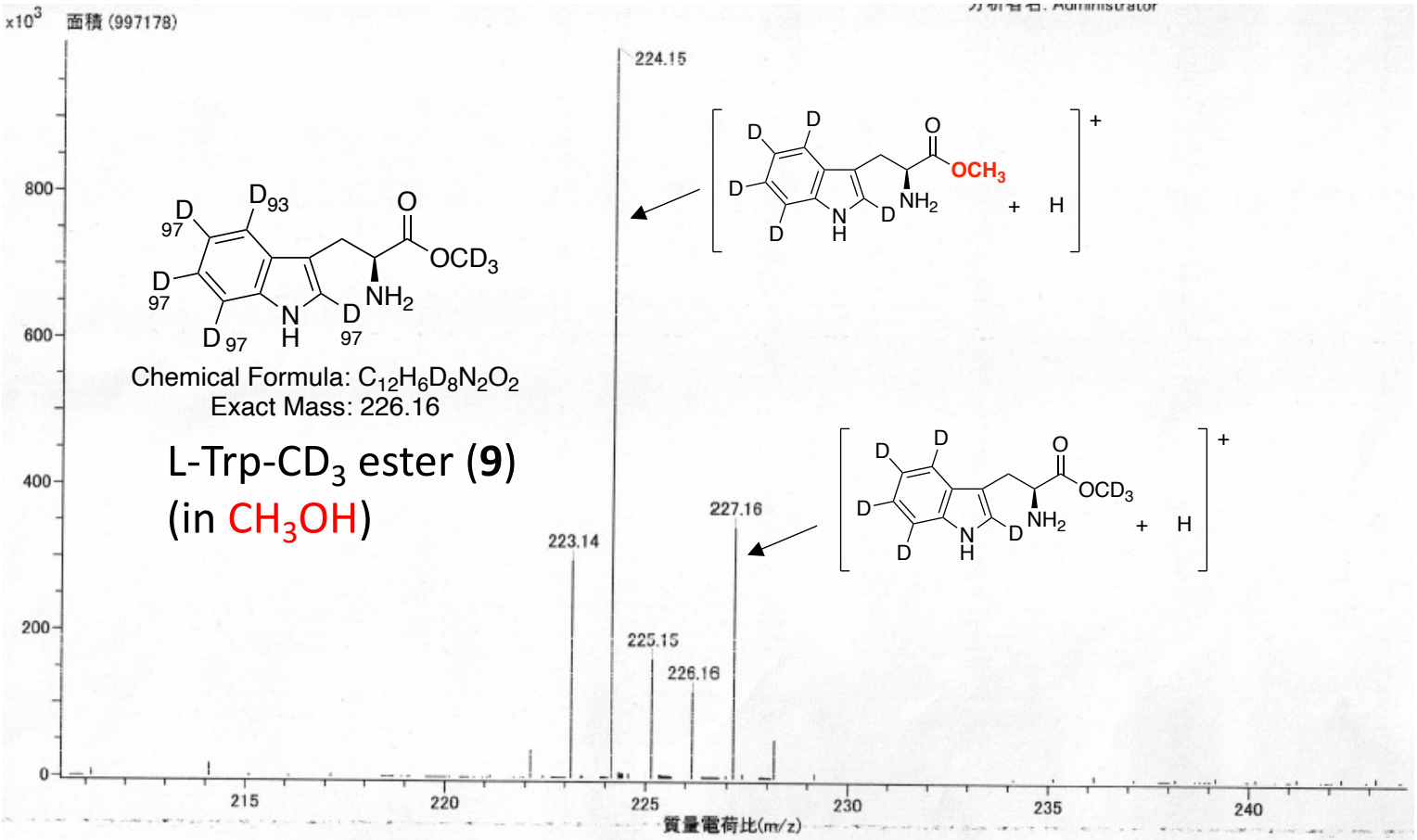
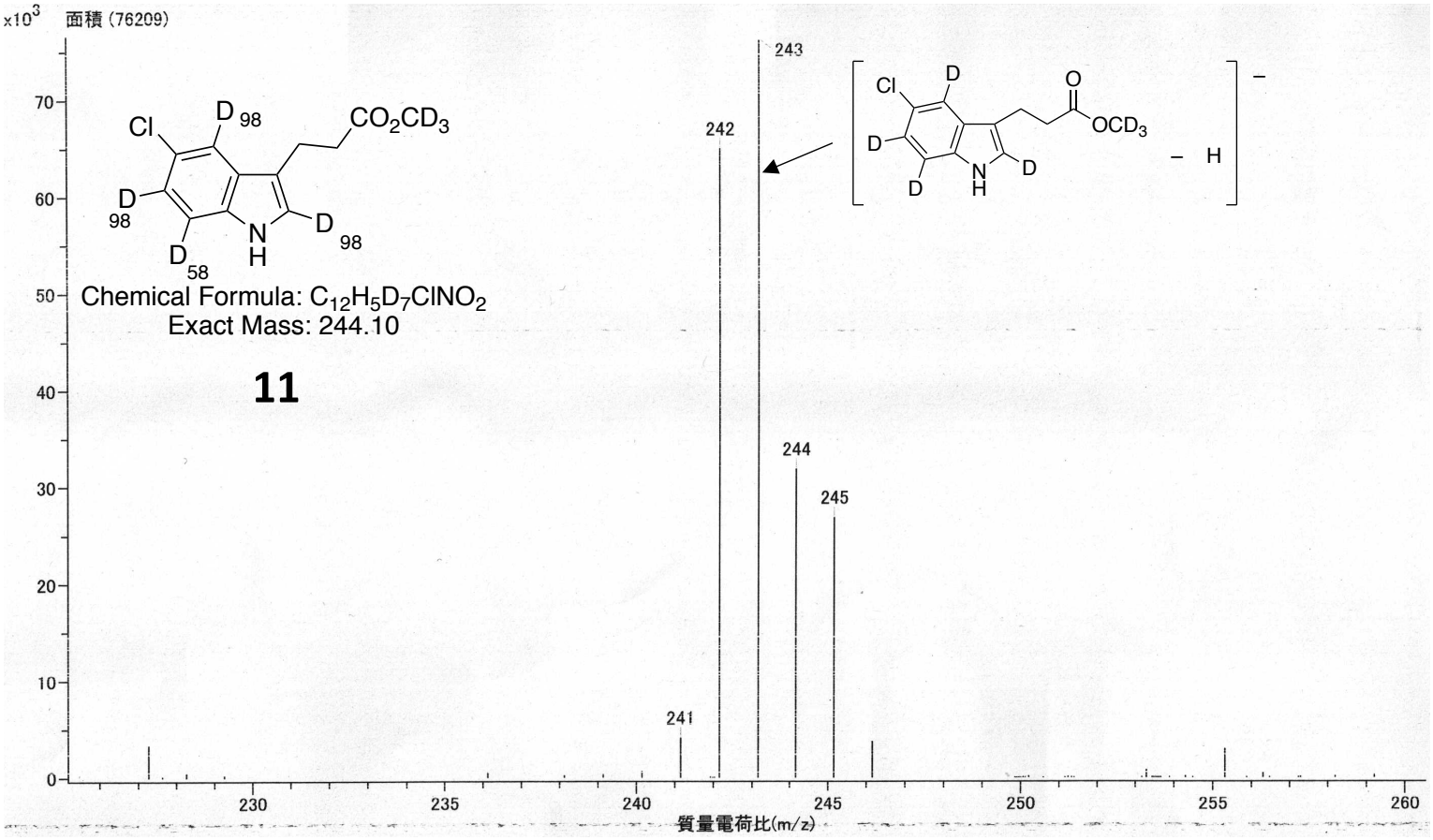


Figure S42. TOF-MS (ESI⁻) spectra of **11**



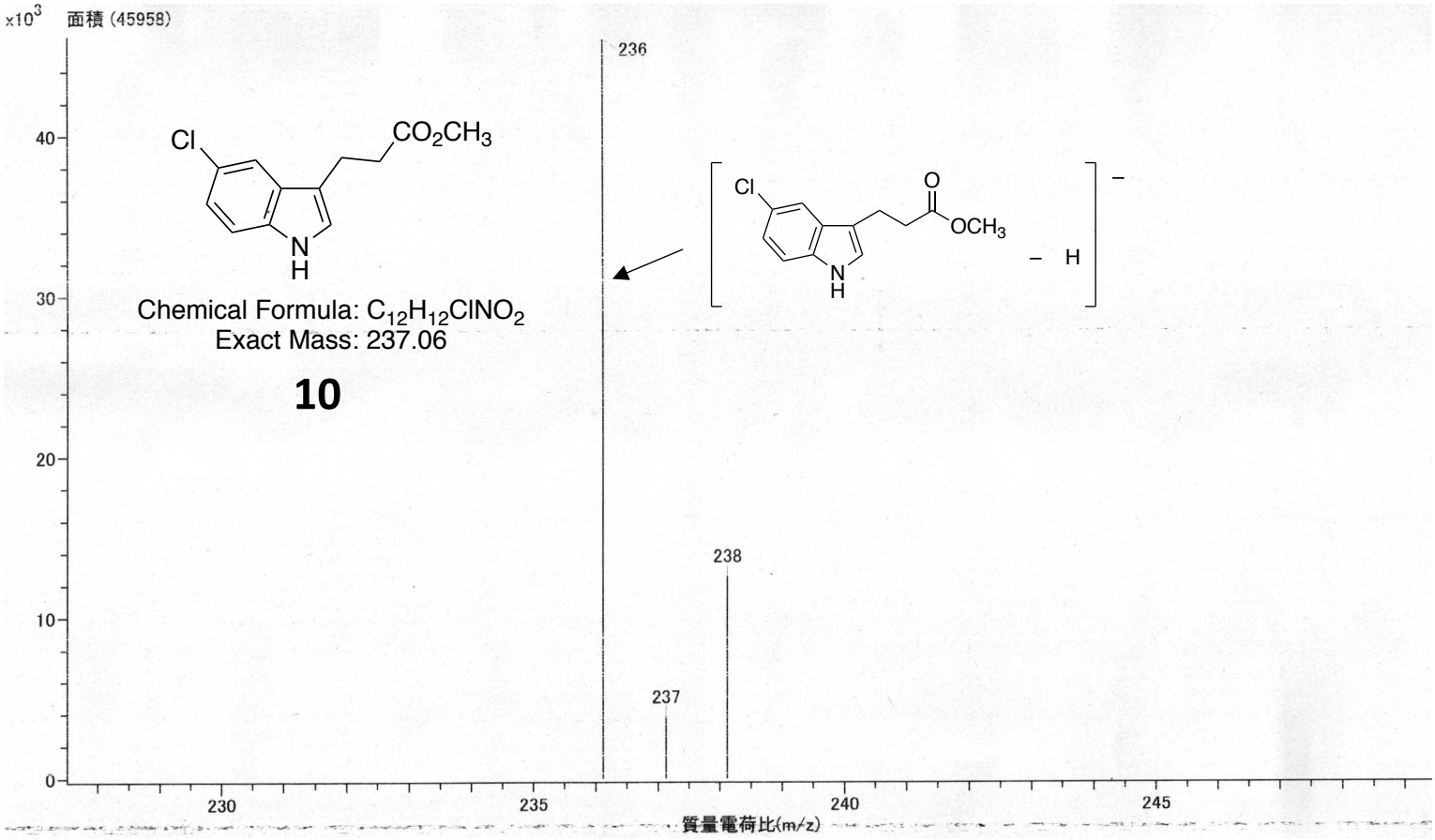
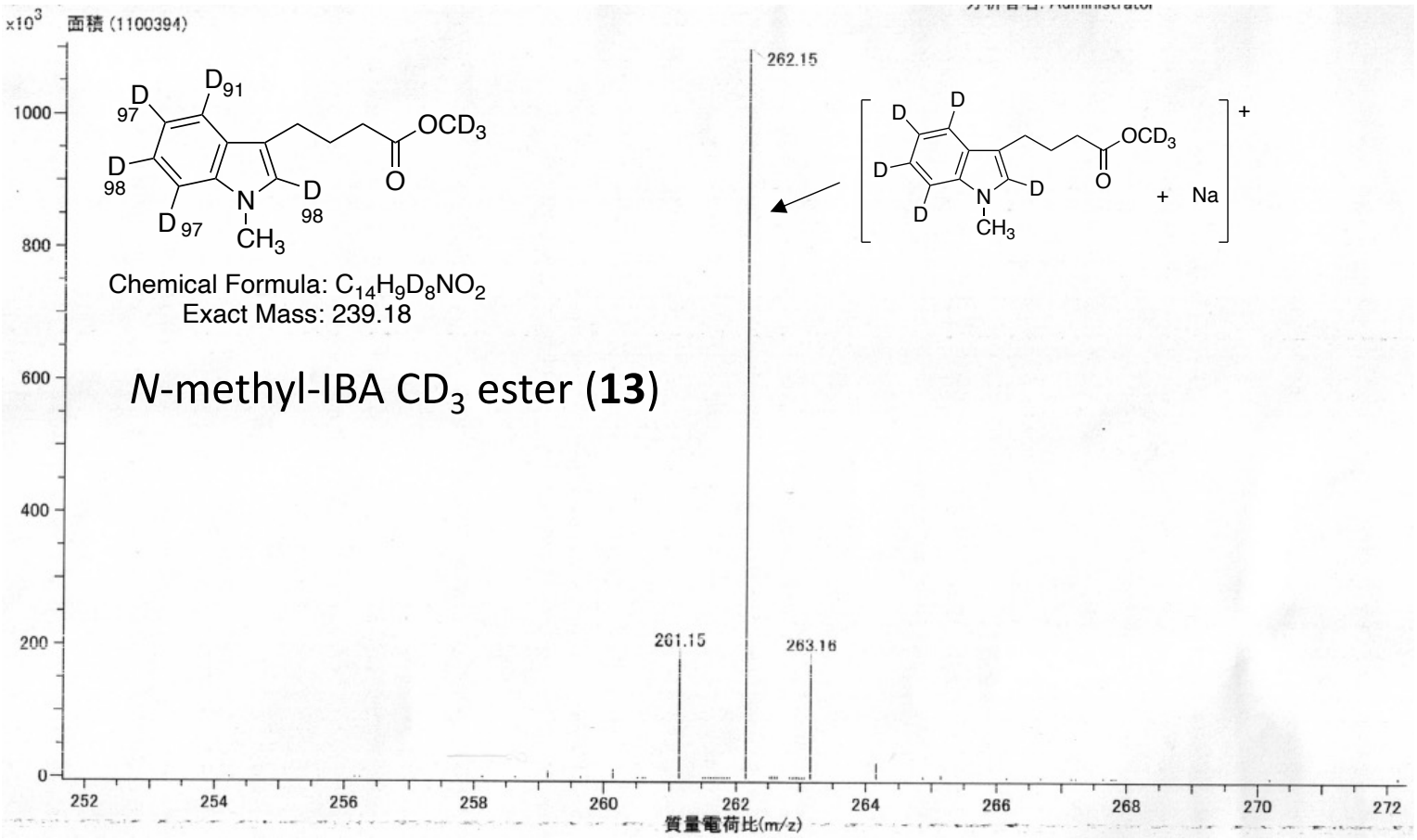


Figure S43. TOF-MS (ESI+) spectra of deuterated *N*-methyl-IBA CD_3 ester (**13**)



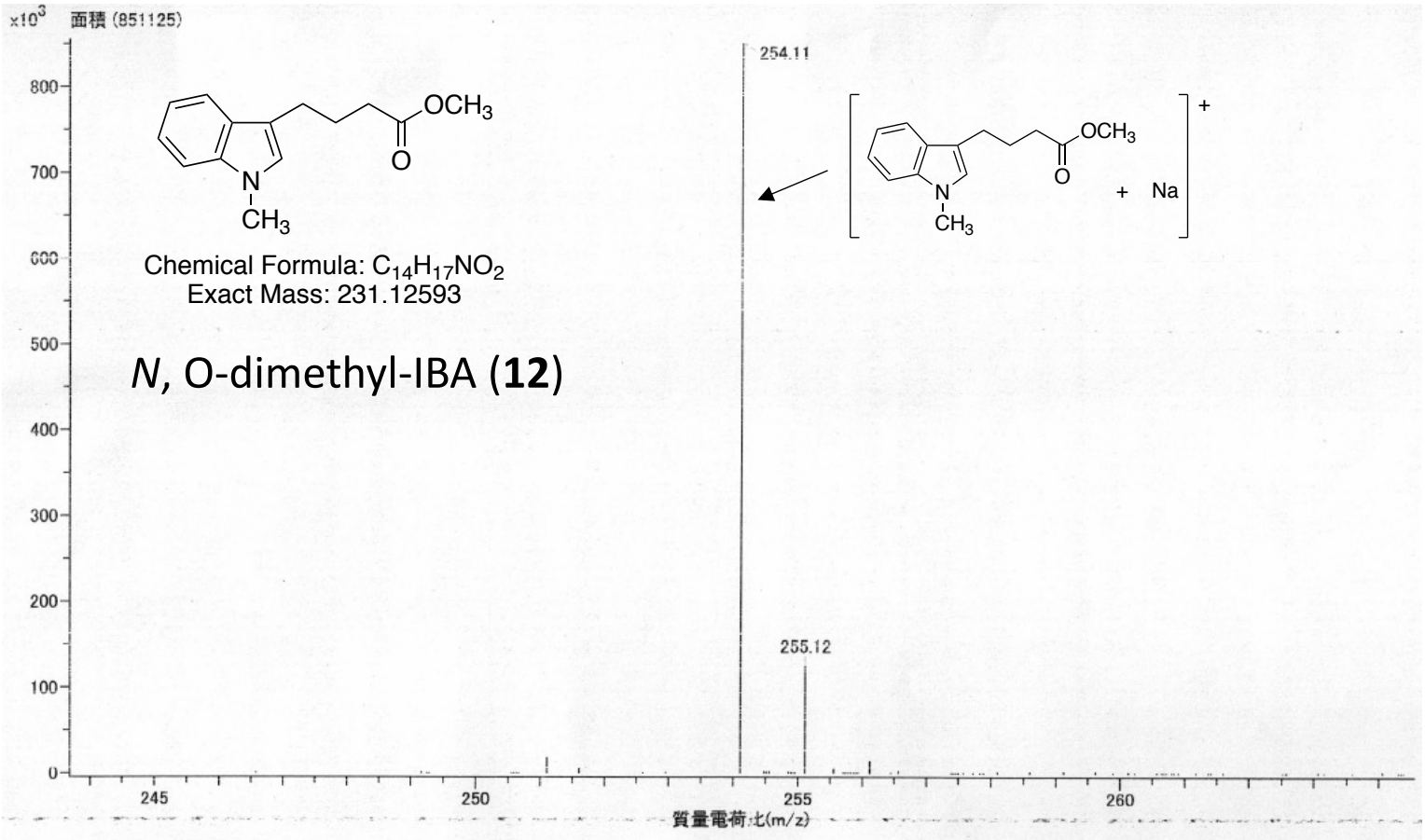


Figure S44. TOF-MS (ESI+) spectra of **15**

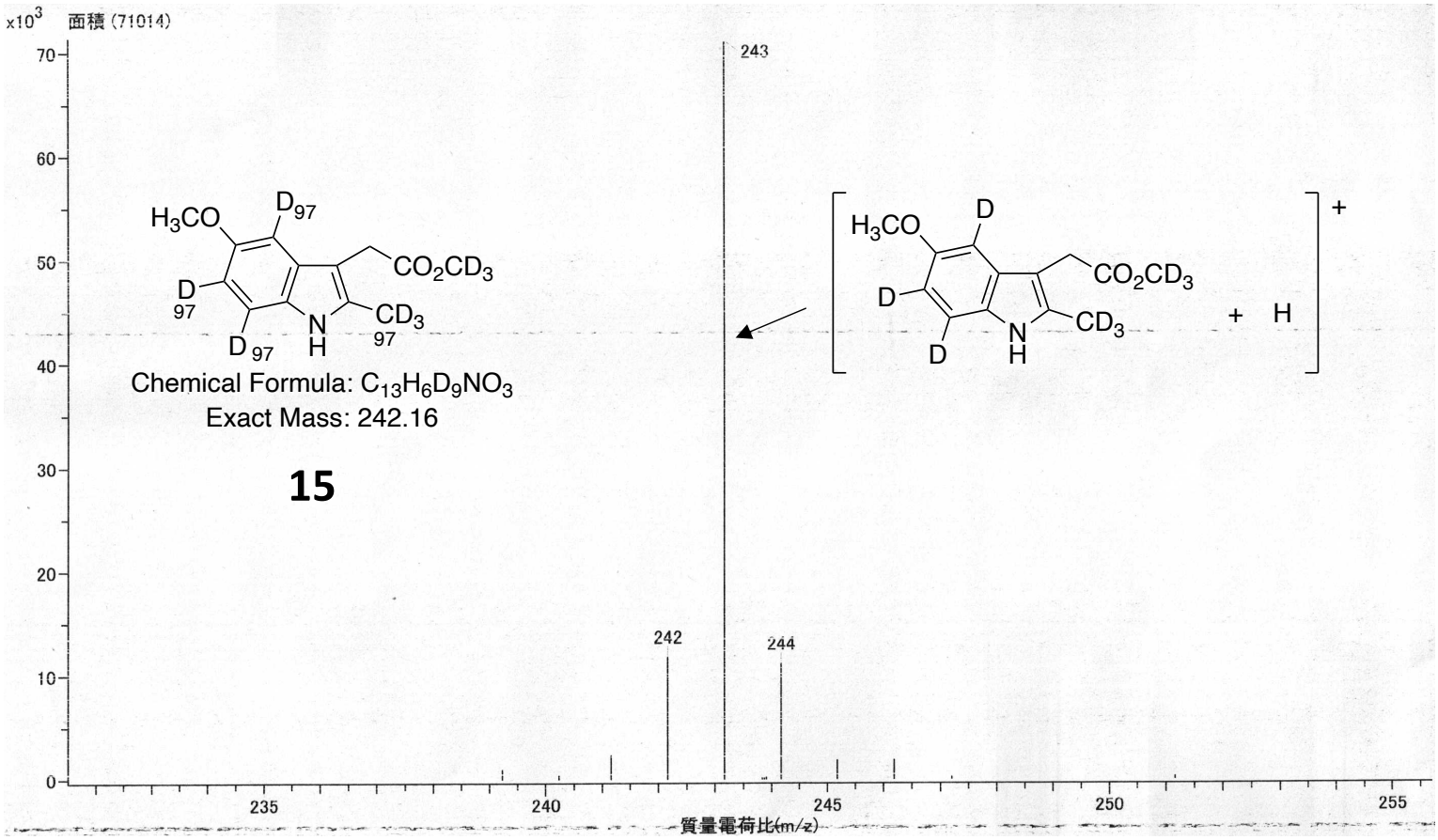


Figure S45. TOF-MS (ESI+) spectra of deuterated yohimbine (**17**)

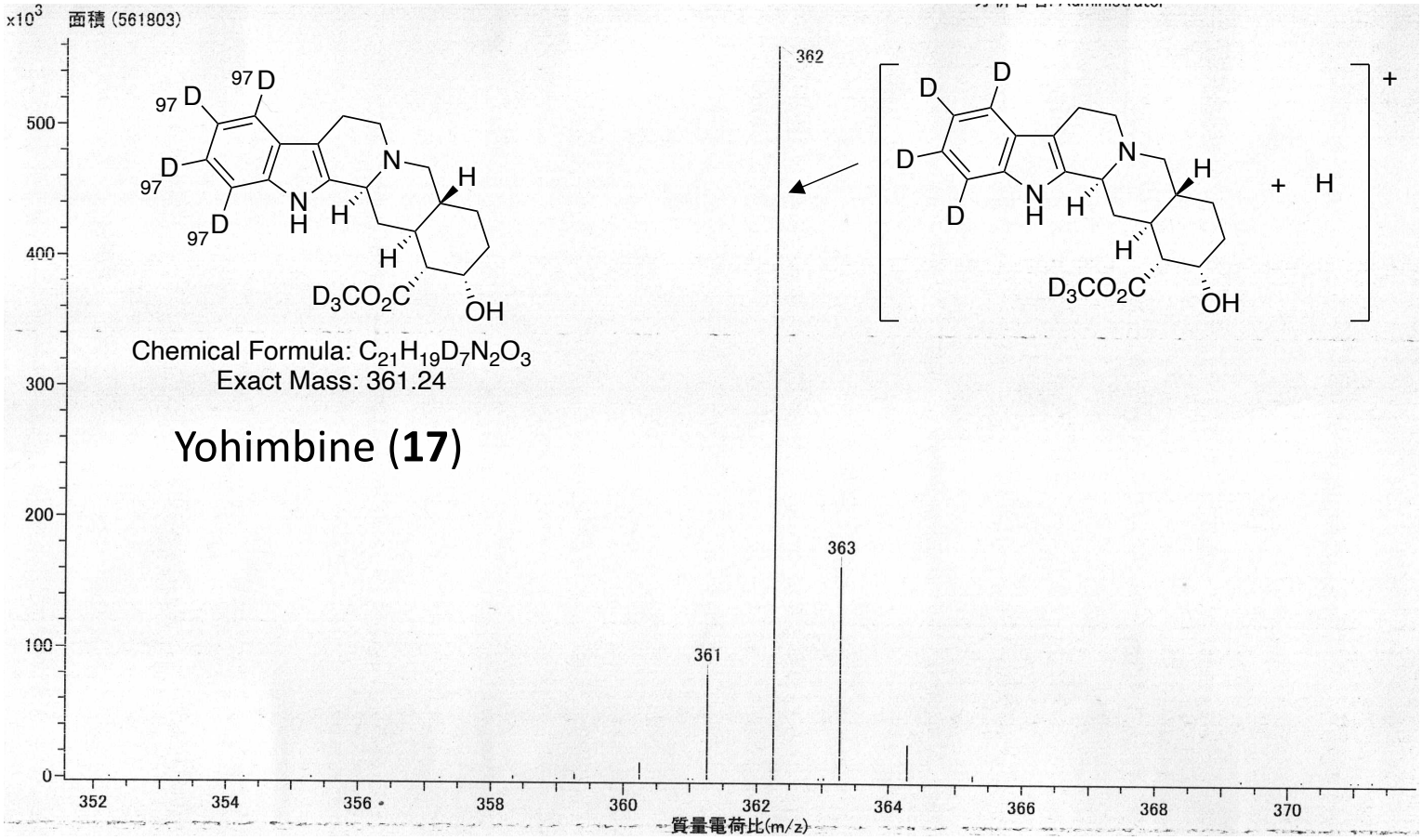
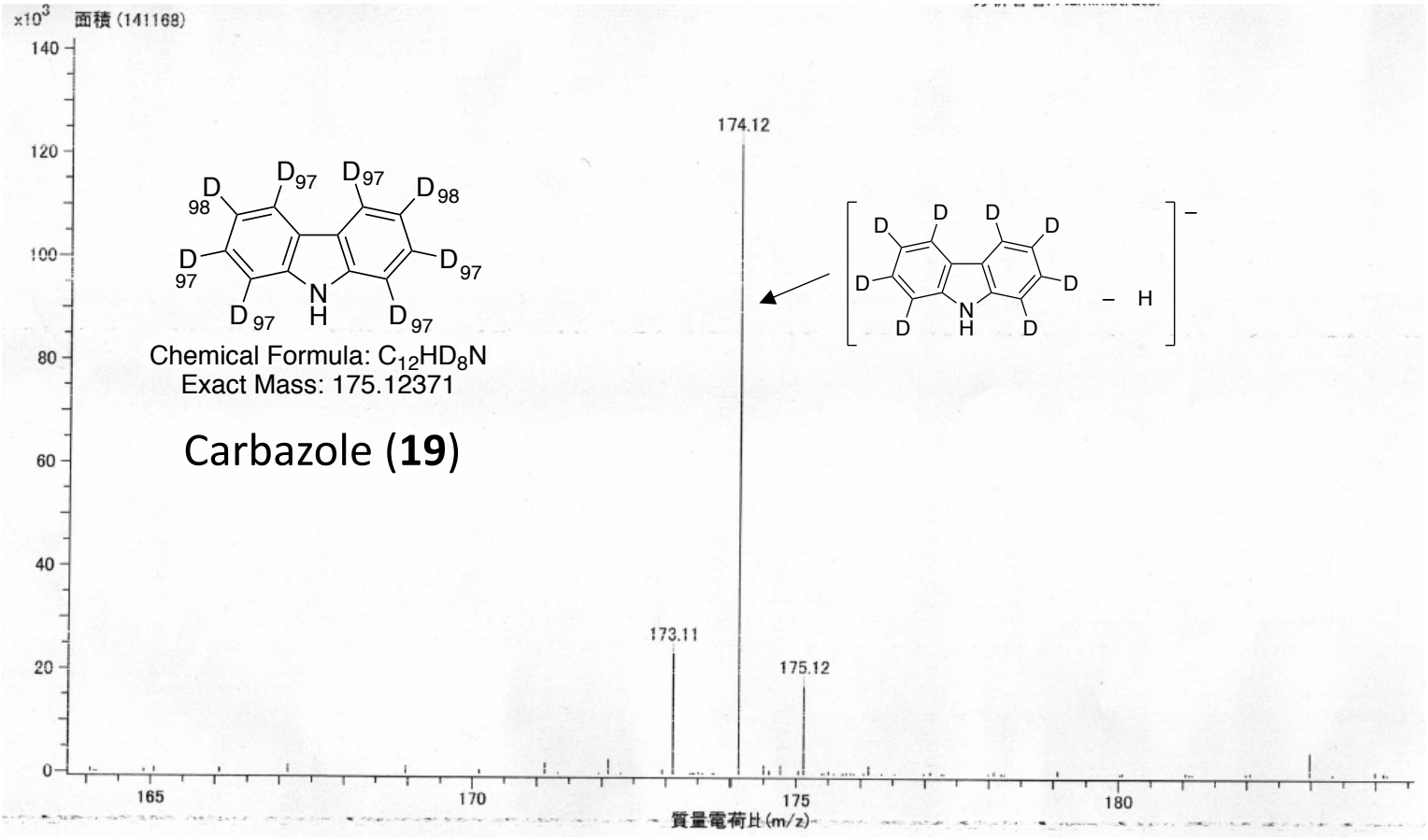


Figure S46. TOF-MS (ESI⁻) spectra of deuterated carbazole (**19**)



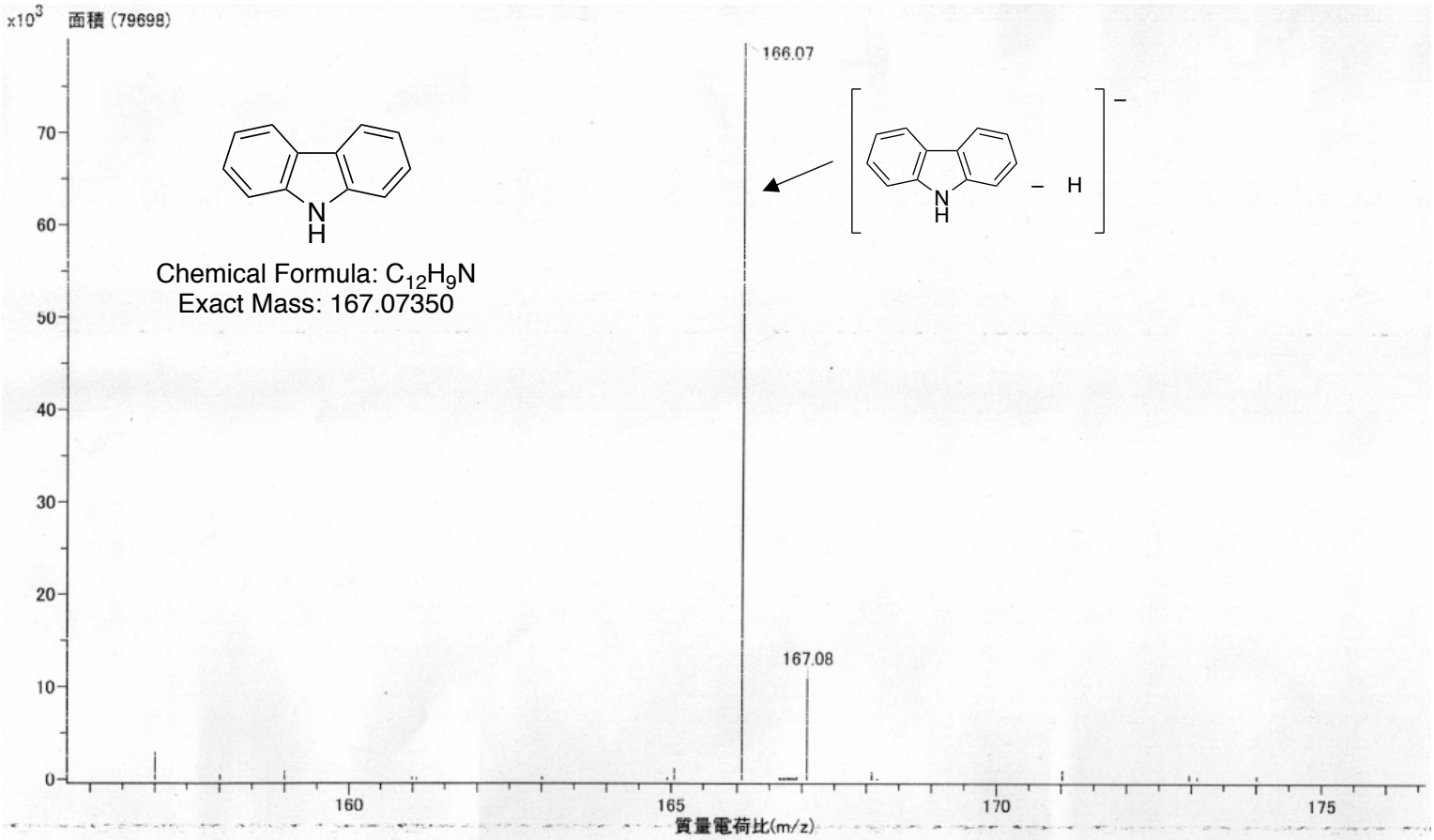


Figure S47. TOF-MS (ESI$^+$) spectra of deuterated harmine (**21**)

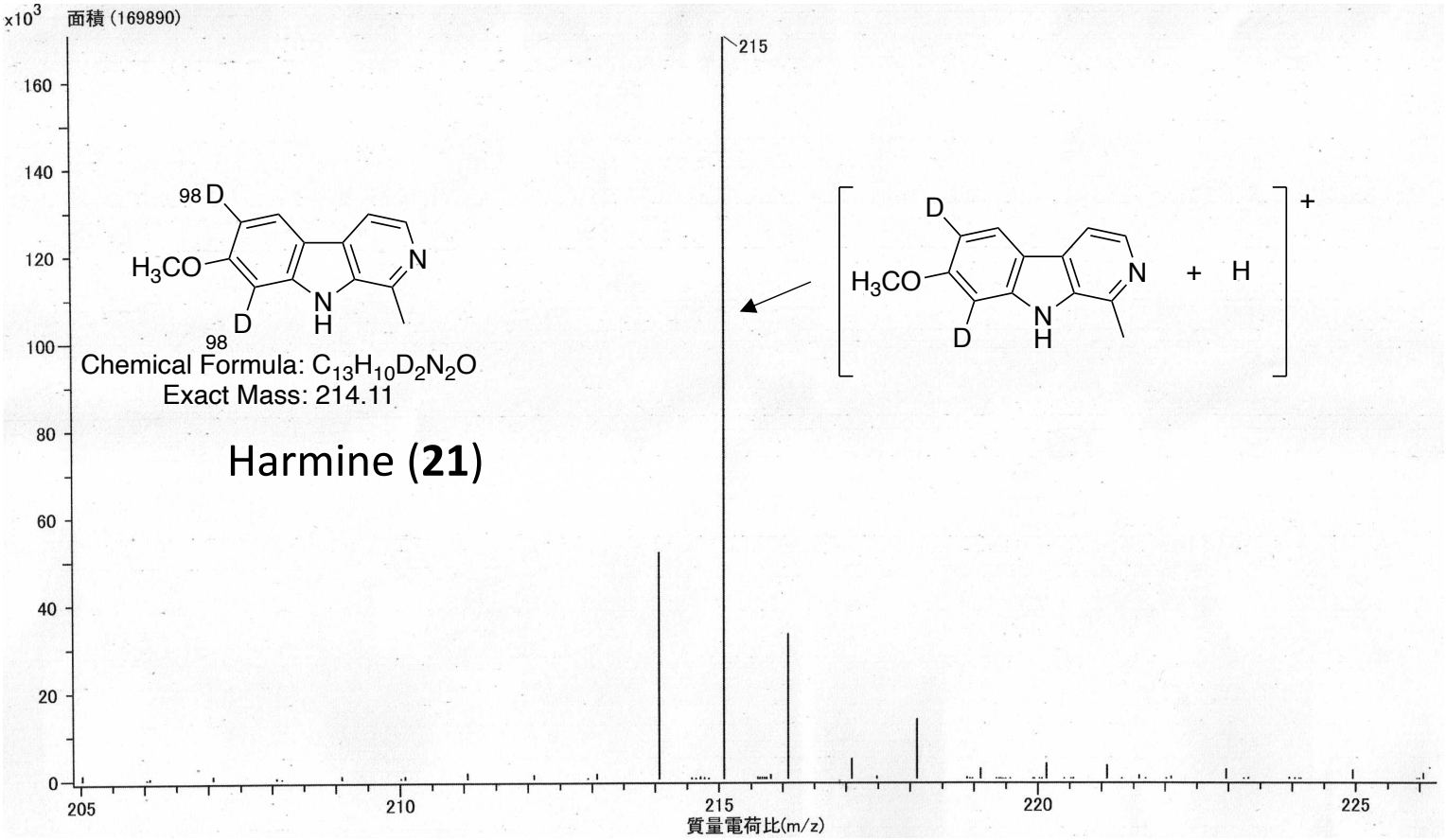
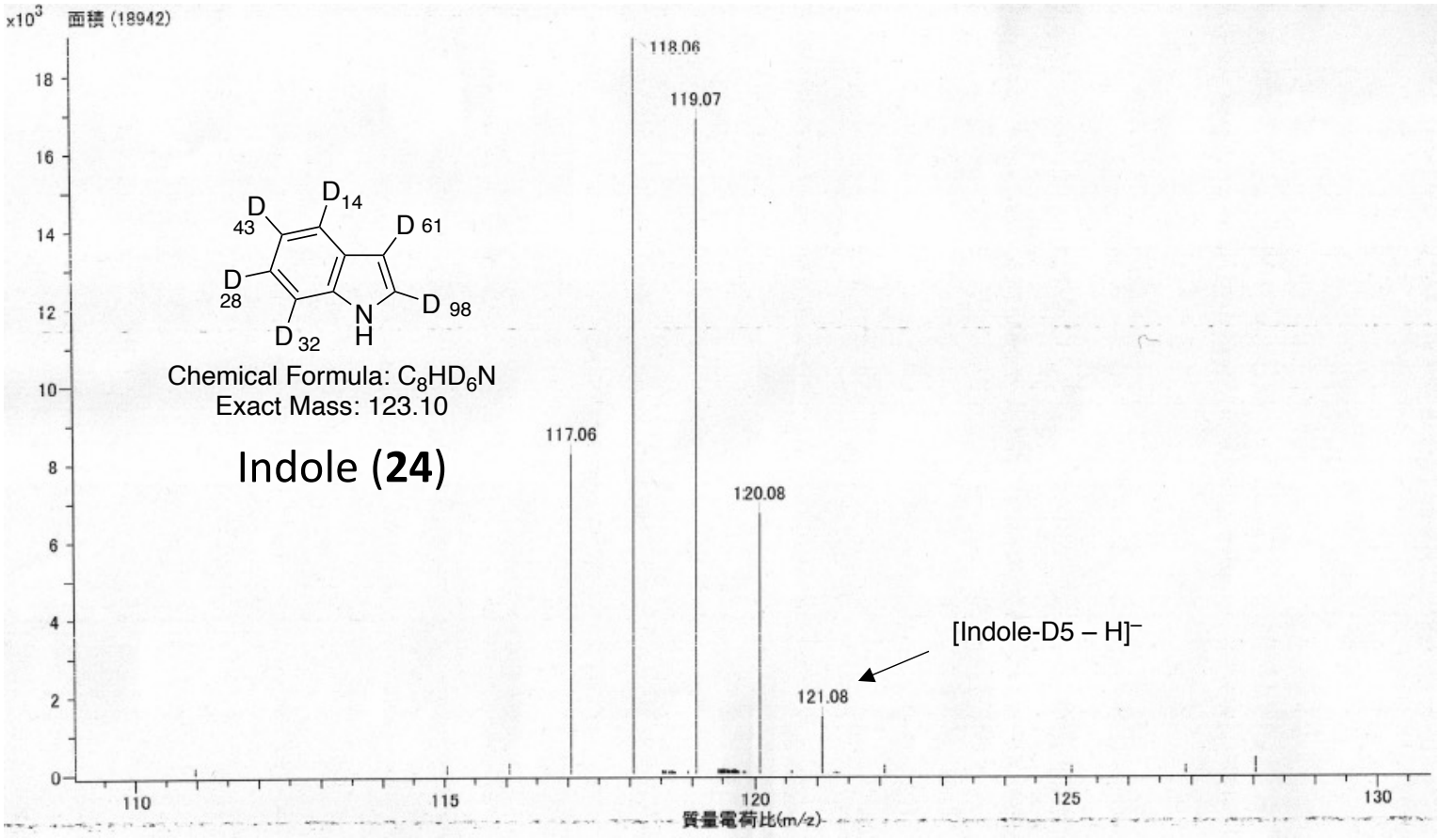


Figure S48. TOF-MS (ESI⁻) spectra of deuterated indole (**24**)



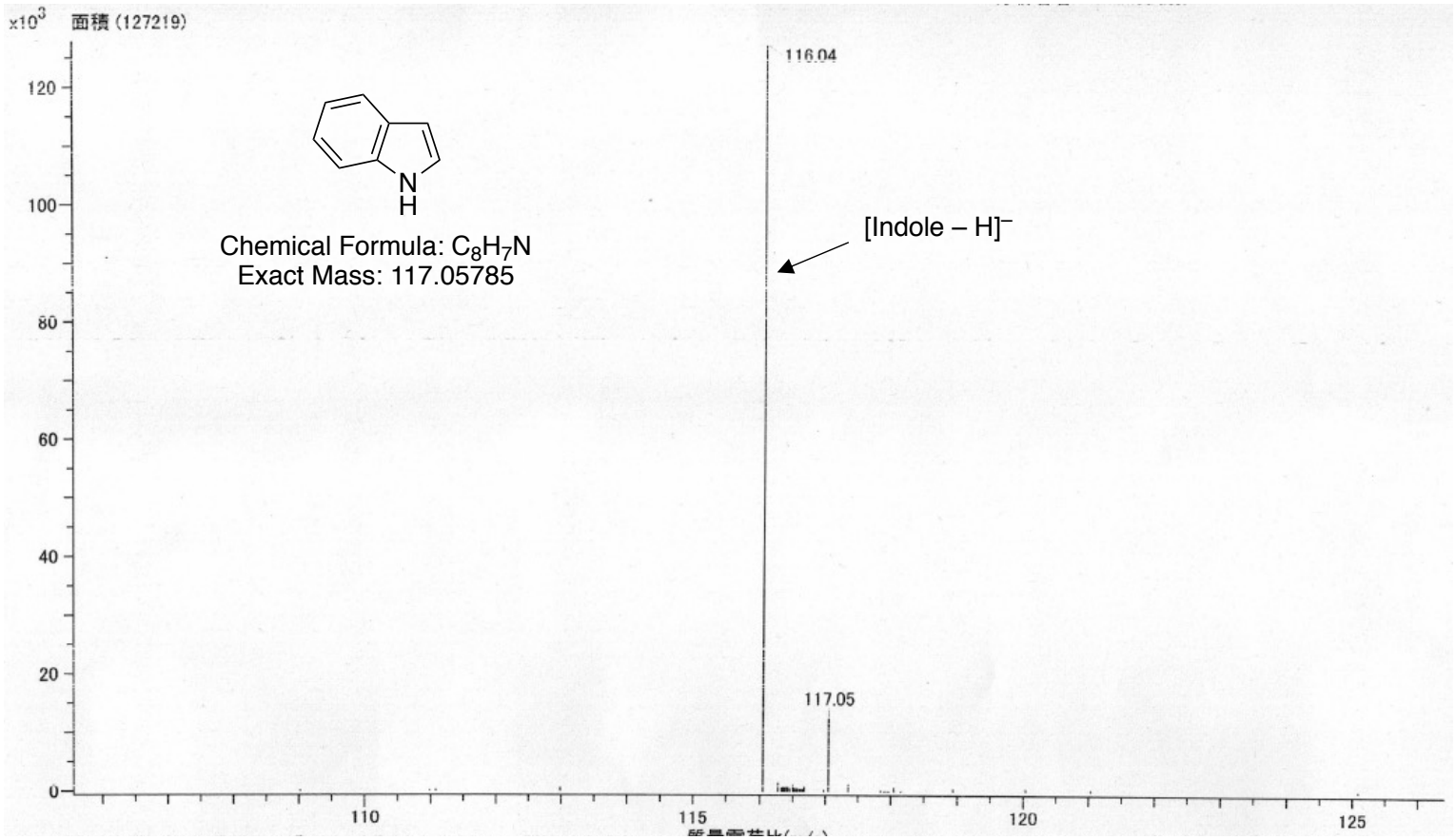
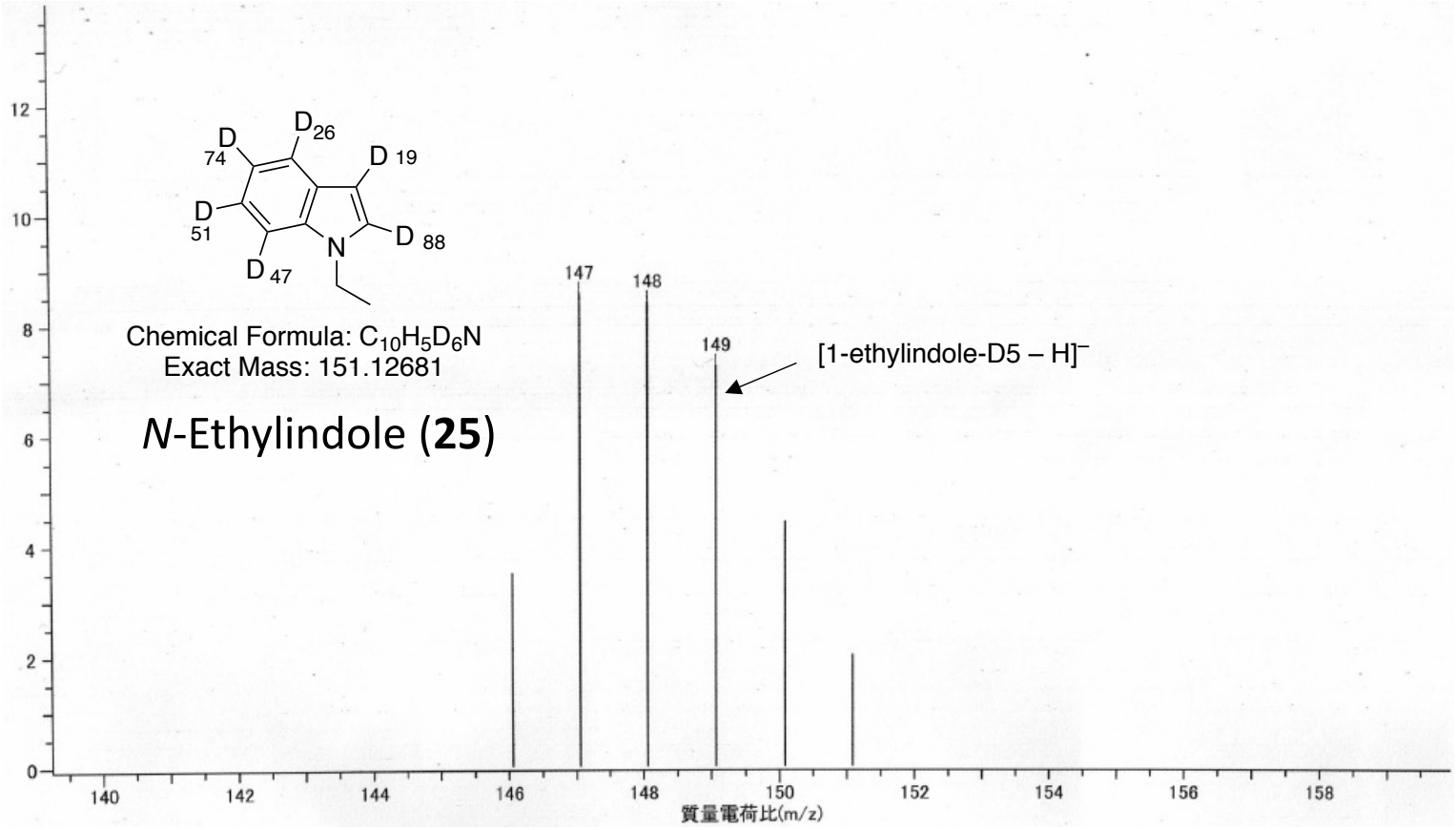


Figure S49. TOF-MS (ESI⁻) spectra of deuterated 1-ethylindole (**25**)



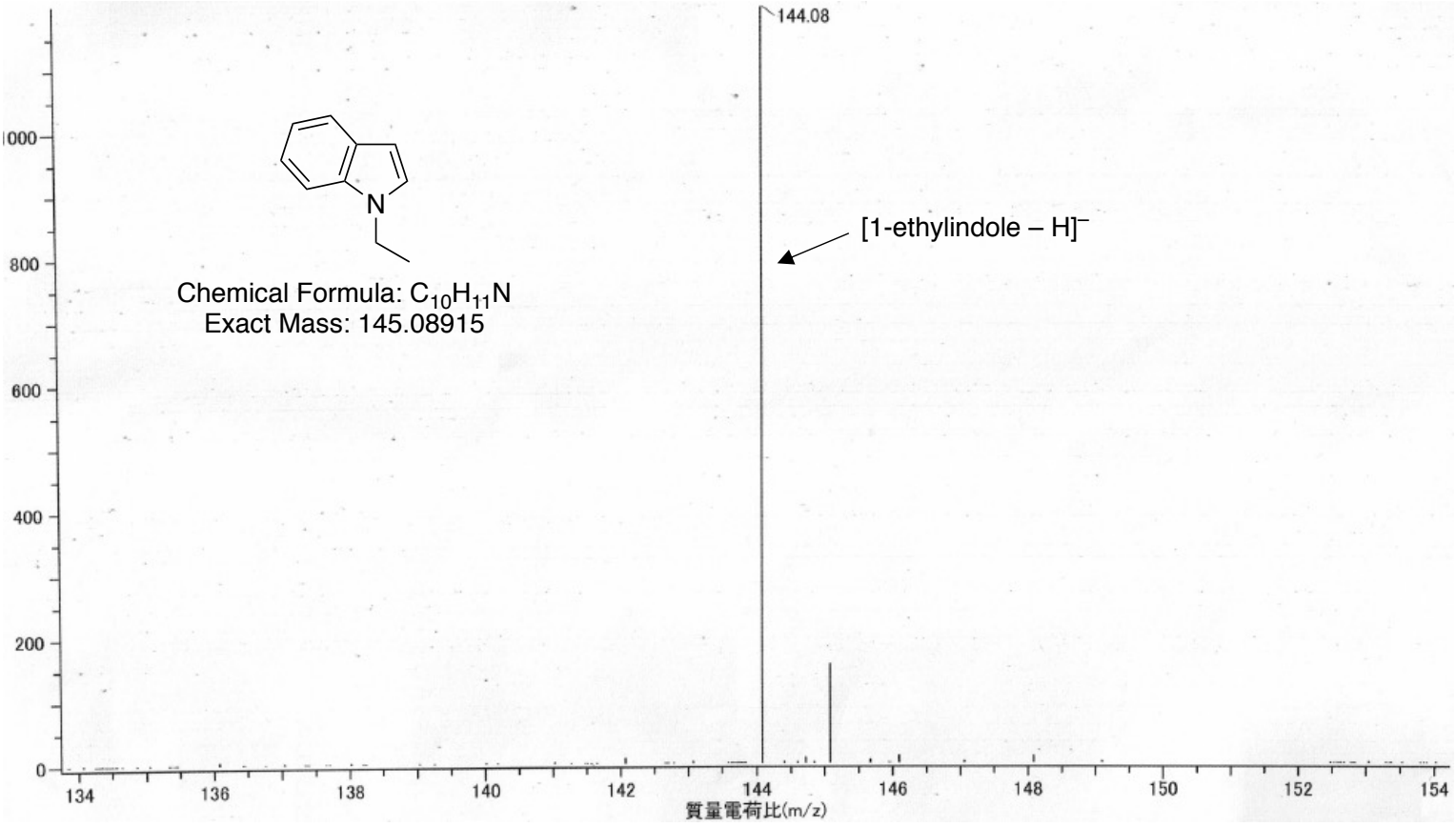
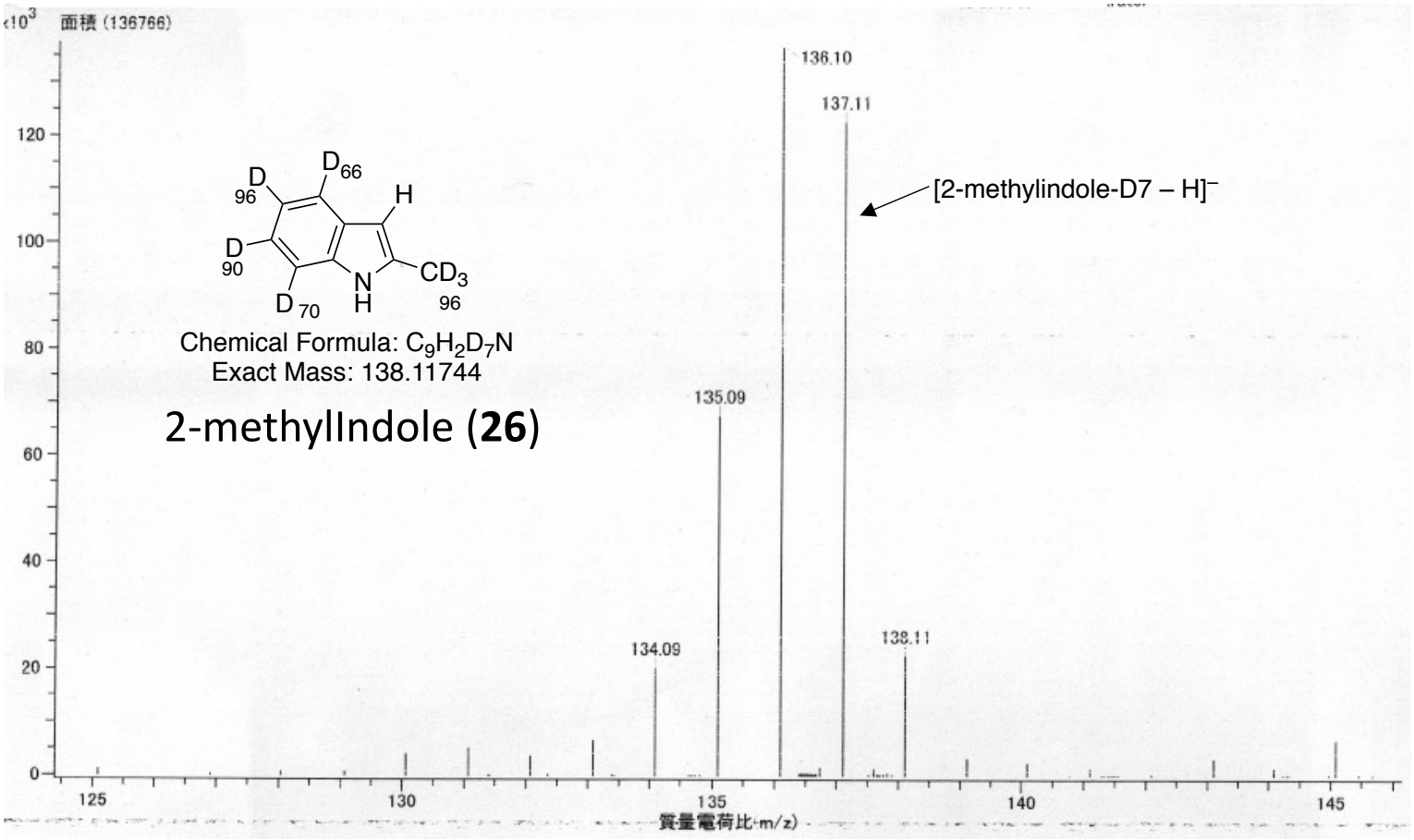


Figure S50. TOF-MS (ESI⁻) spectra of deuterated 2-methylindole (**26**)



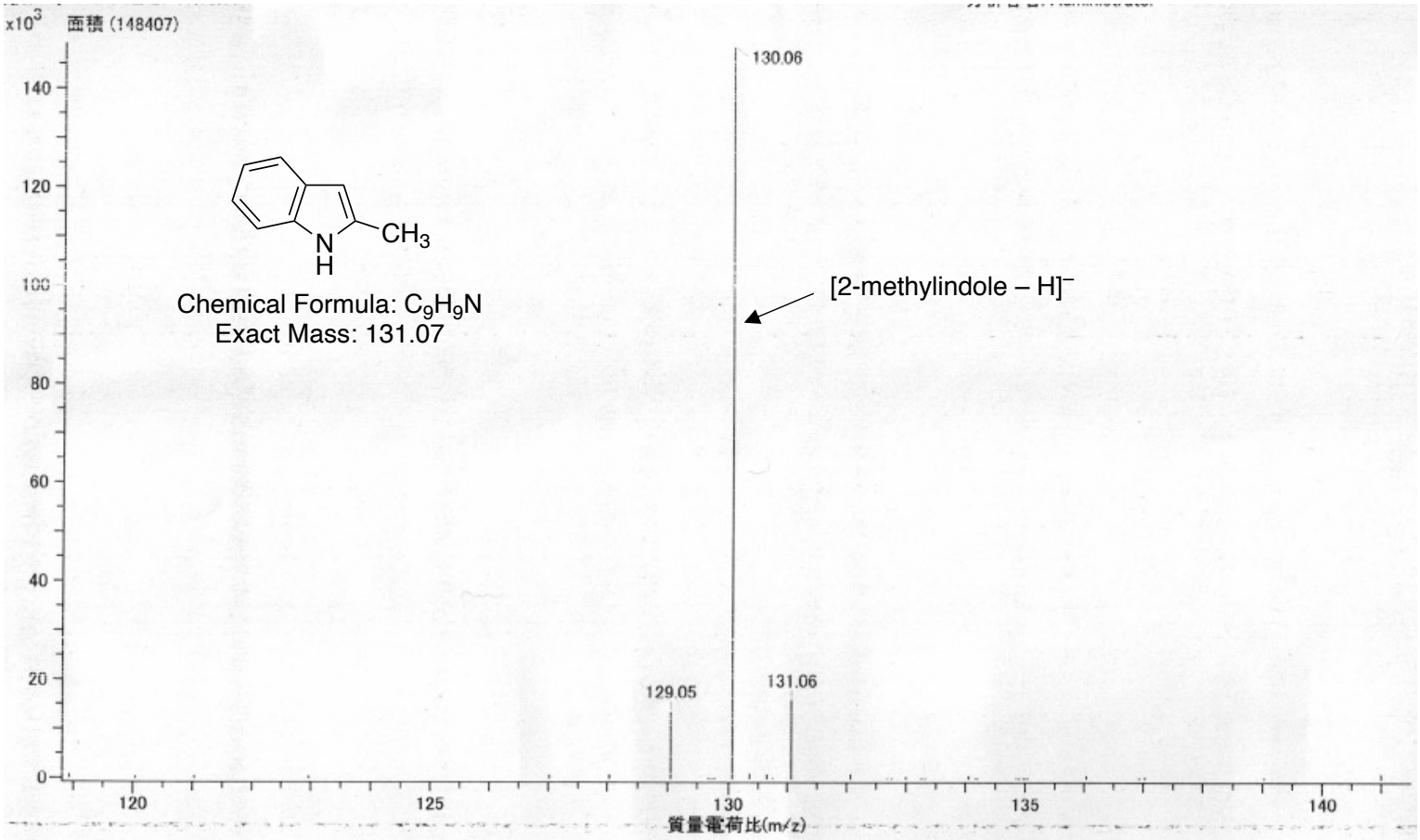
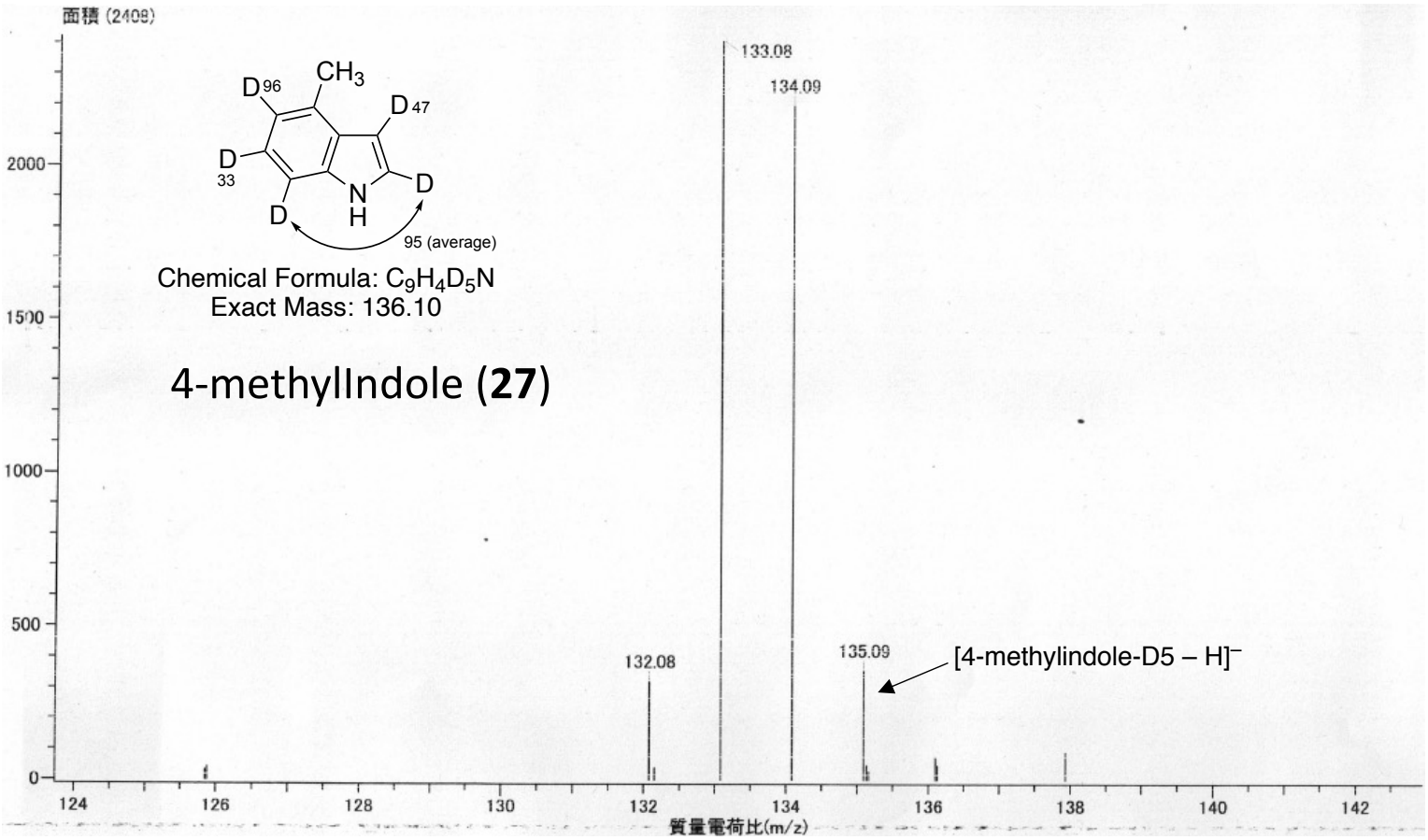


Figure S51. TOF-MS (ESI⁻) spectra of deuterated 4-methylindole (**27**)



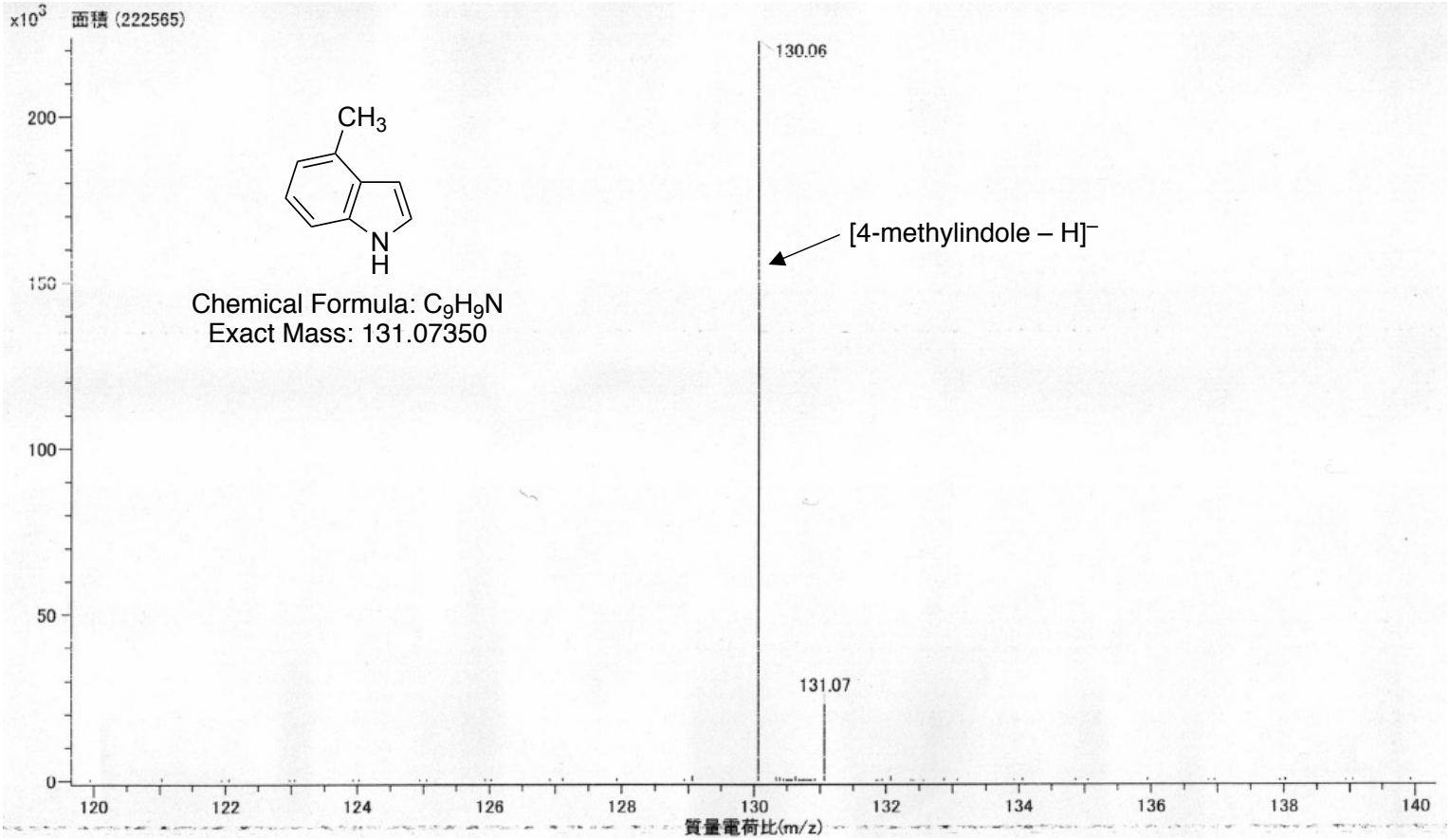
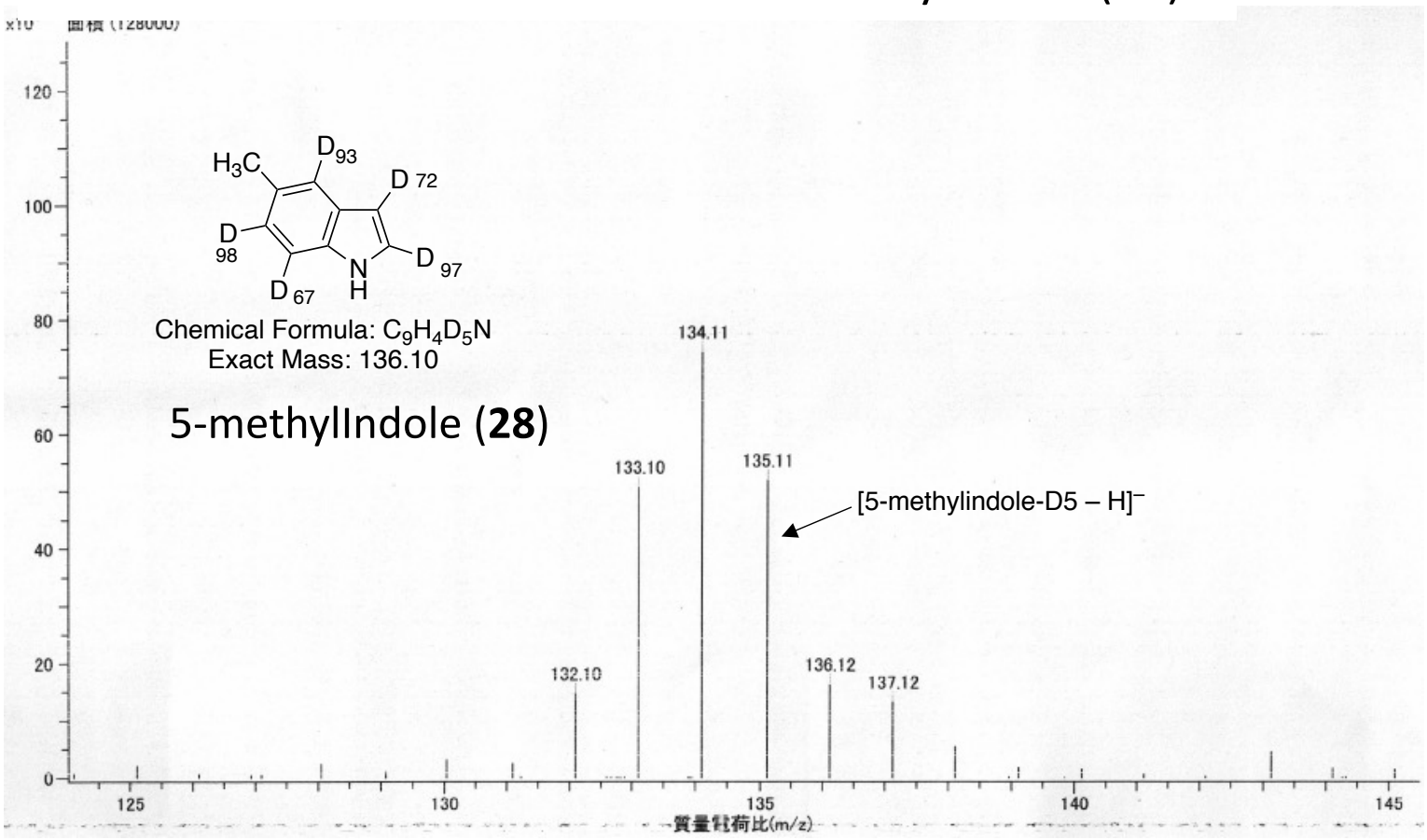


Figure S52. TOF-MS (ESI⁻) spectra of deuterated 5-methylindole (**28**)



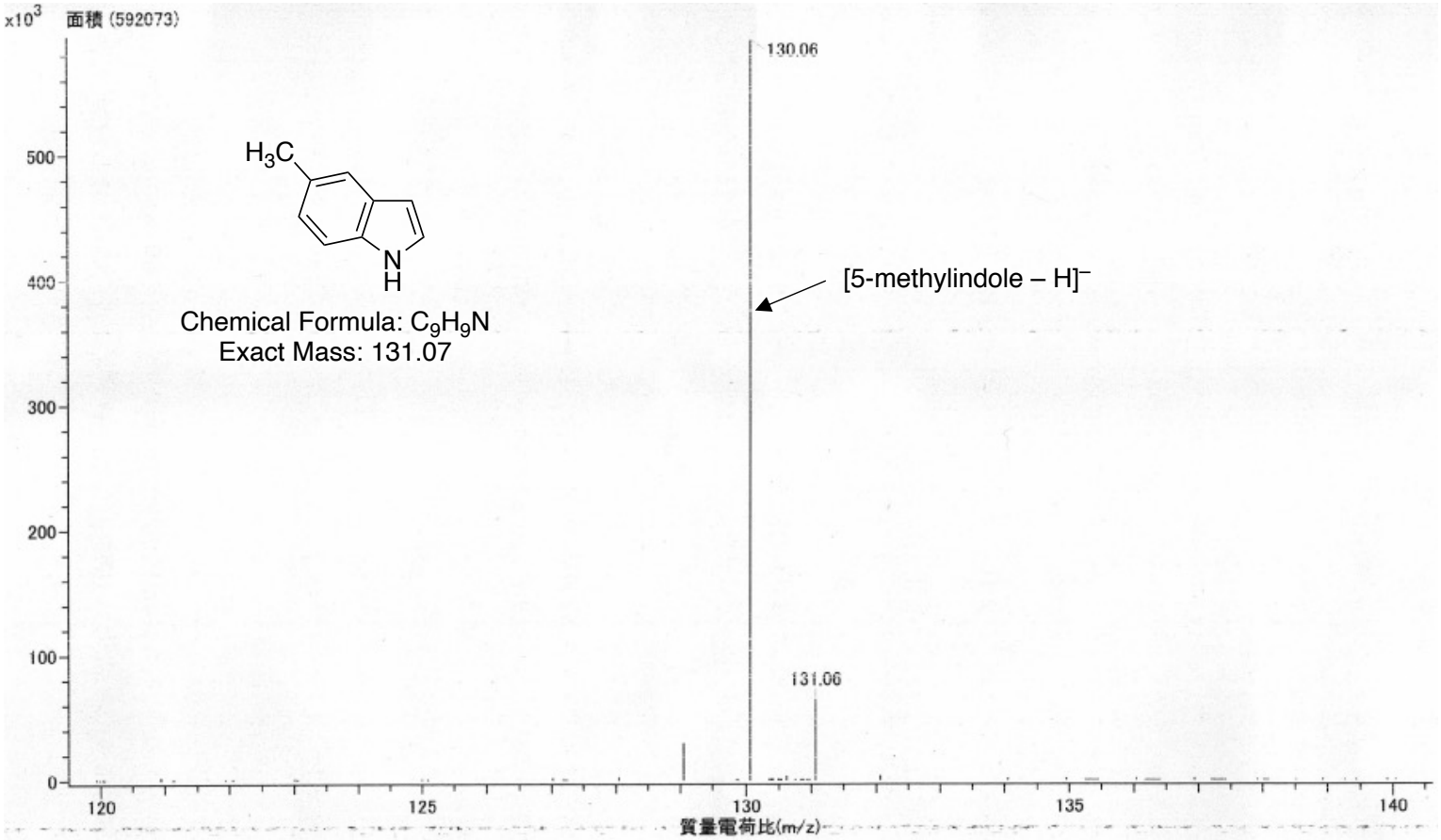
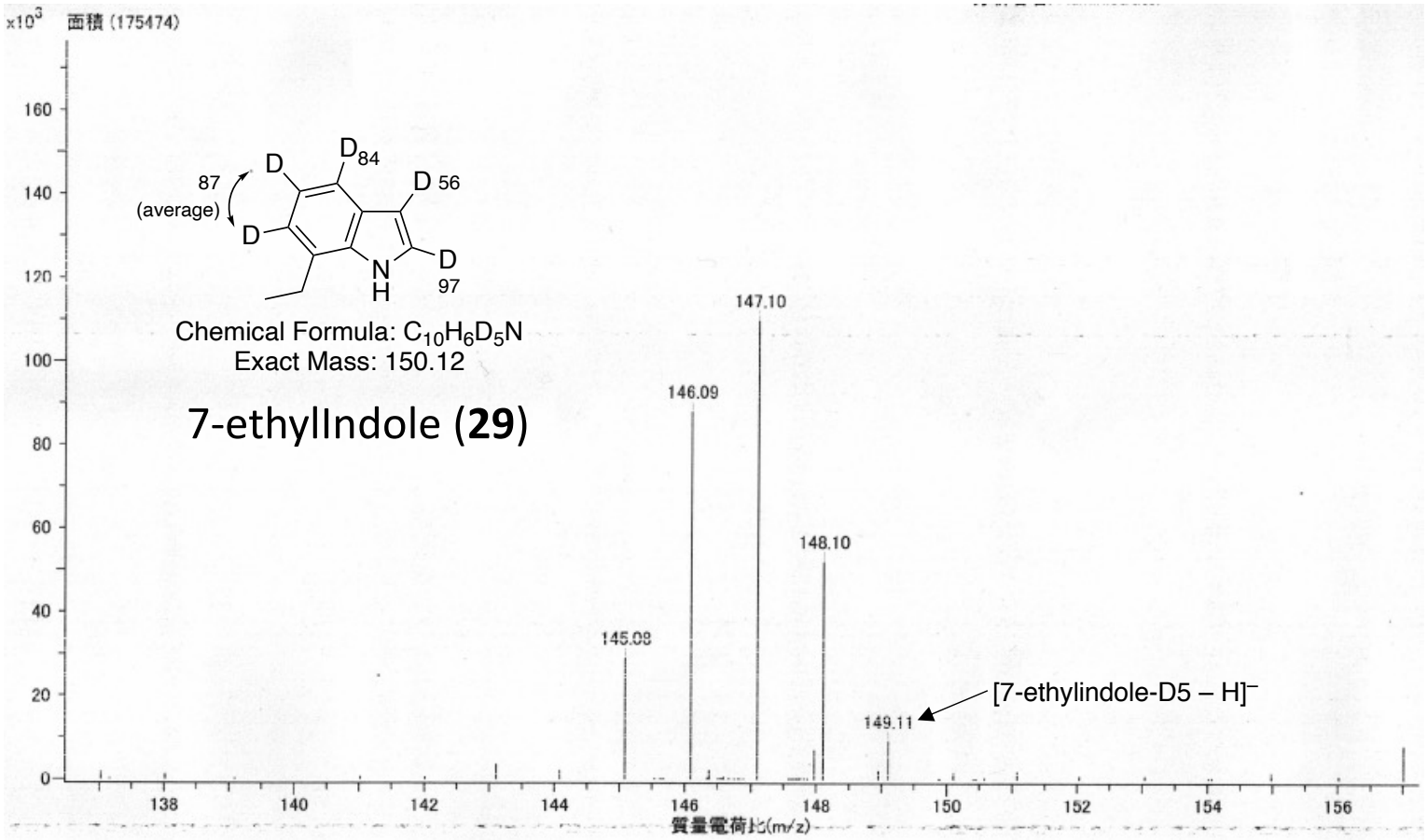


Figure S53. TOF-MS (ESI⁻) spectra of deuterated 7-ethylindole (**29**)



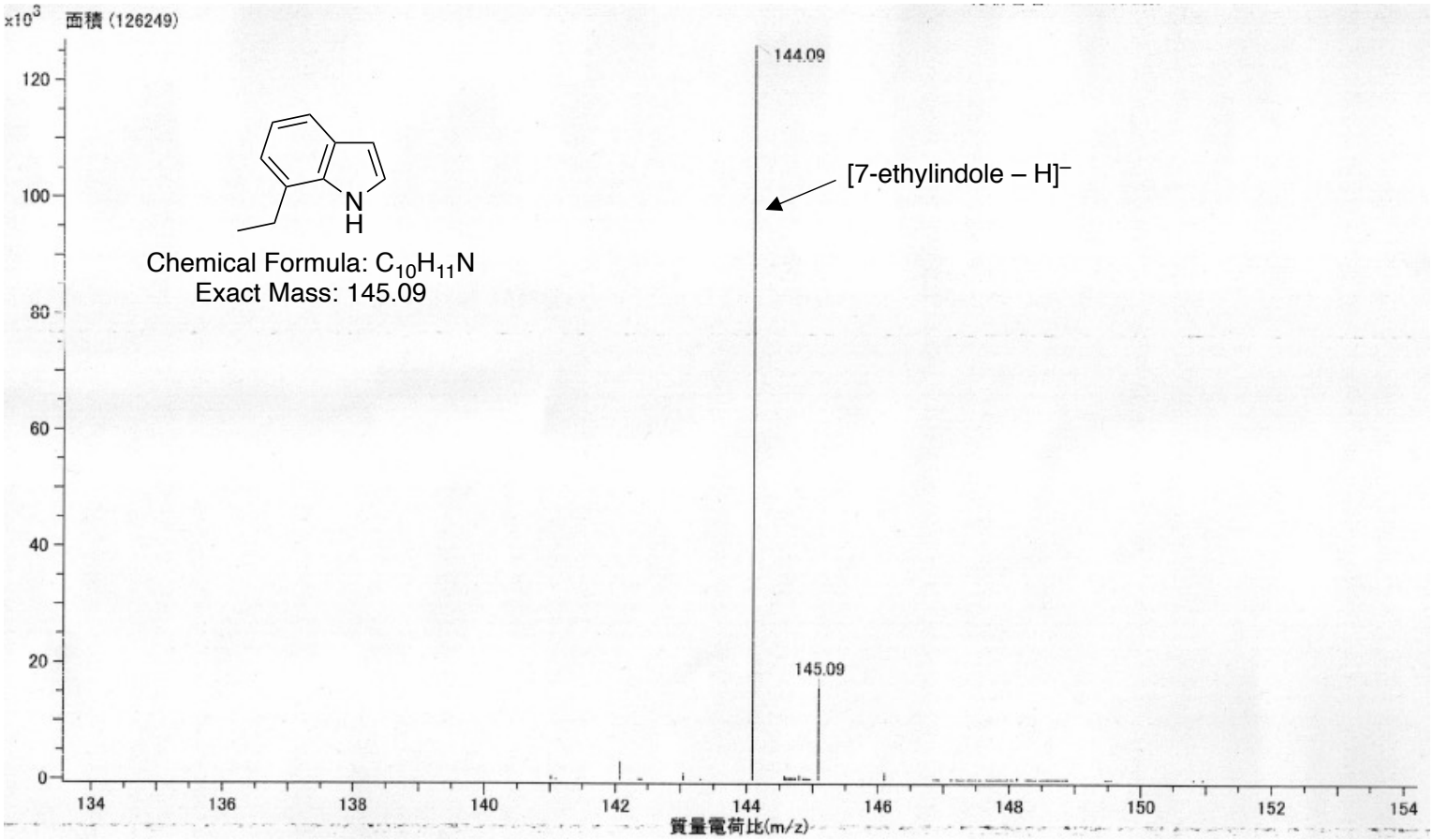
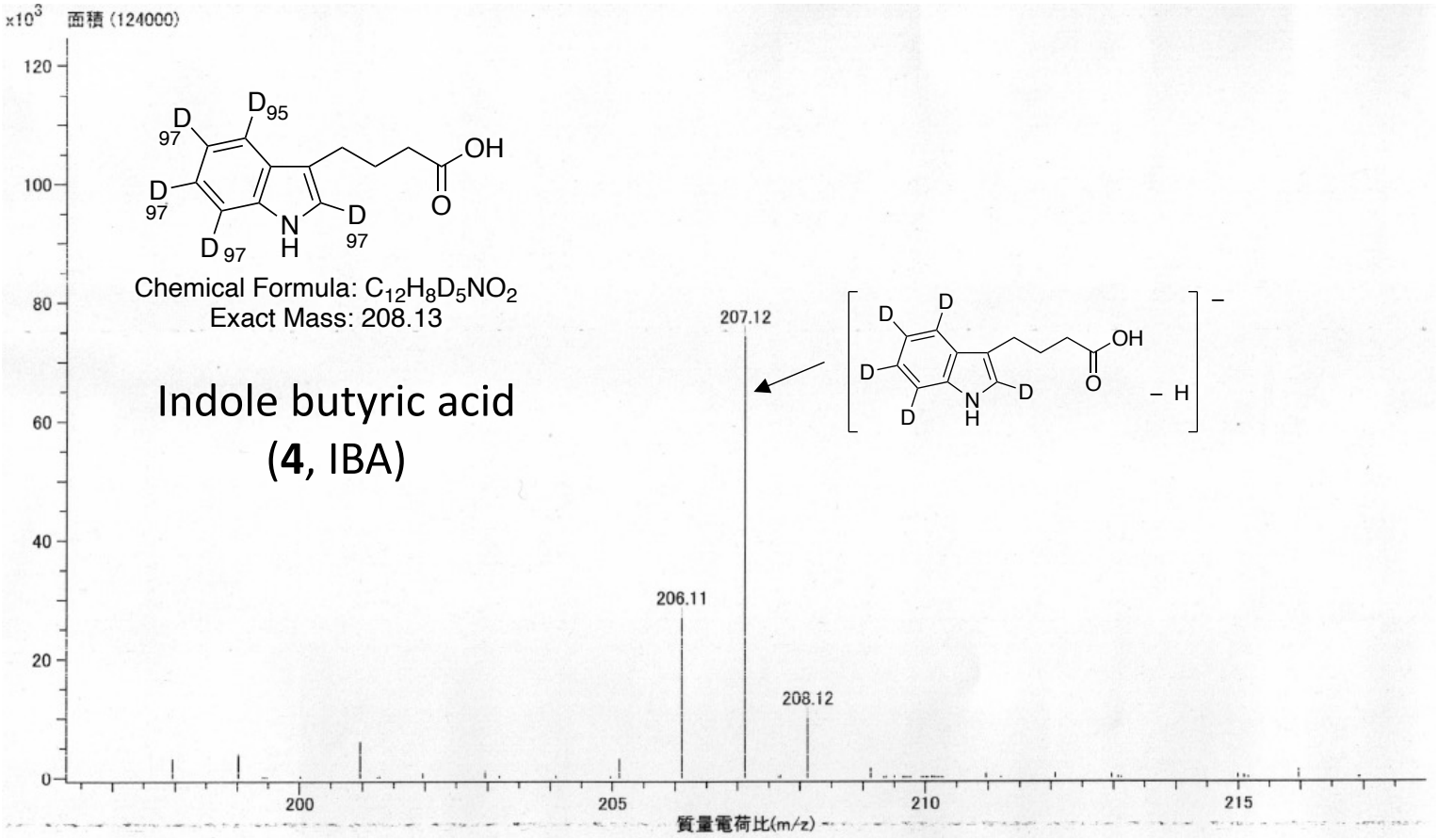


Figure S54. TOF-MS (ESI⁻) spectra of deuterated IBA (**4**)



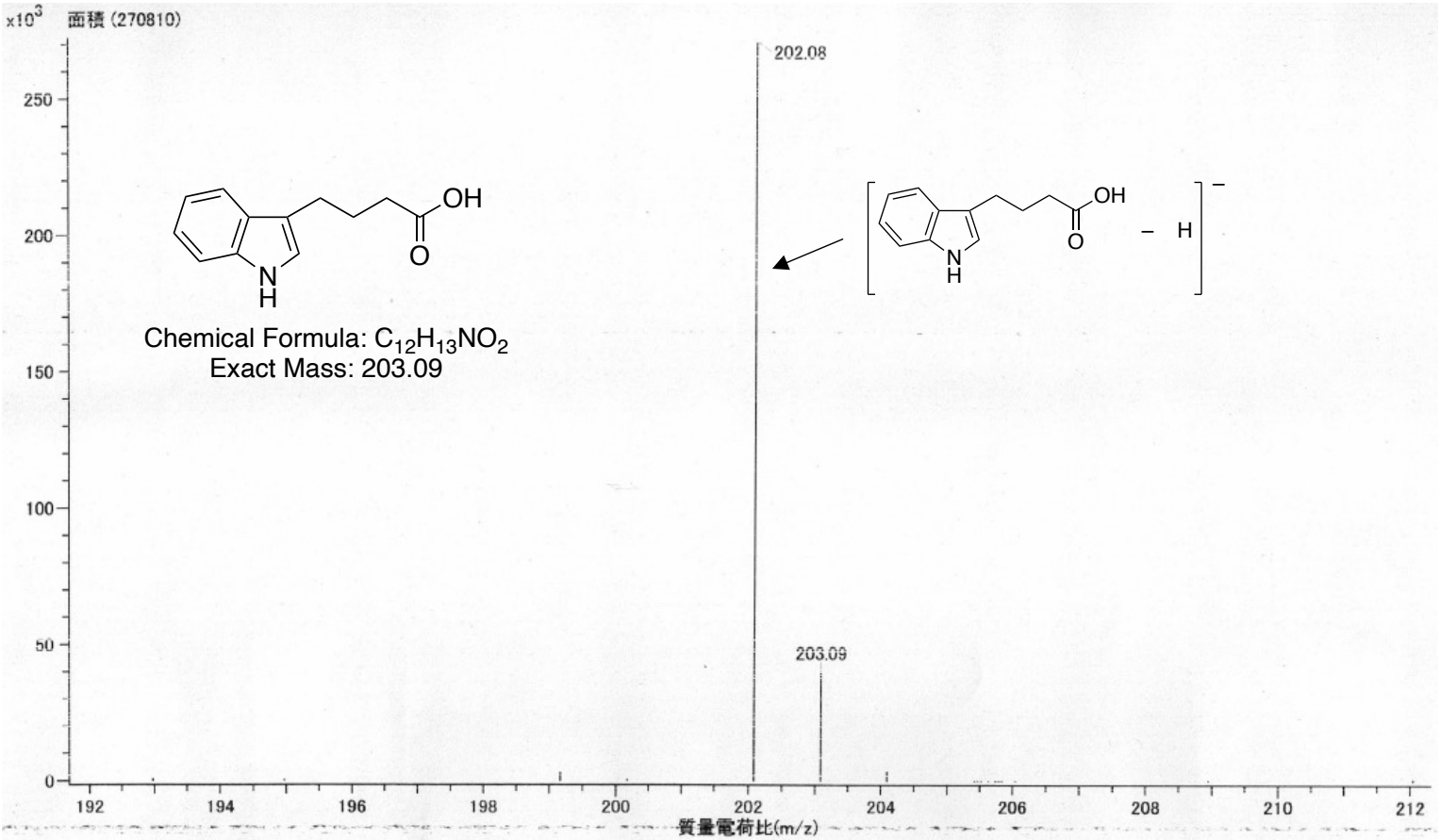


Figure S55. TOF-MS (ESI⁻) spectra of deuterated IAA (**3**)