“Fruiting Liquid” of Mushroom-Forming Fungi, A Novel Source of Bioactive Compounds : Fruiting-Body Inducer and HIF and Axl Inhibitors

Supporting Information

“Fruiting Liquid” of Mushroom-Forming Fungi; Novel Source of Bioactive Compounds –Fruiting-Body Inducer, and HIF- and Axl-Inhibitor–

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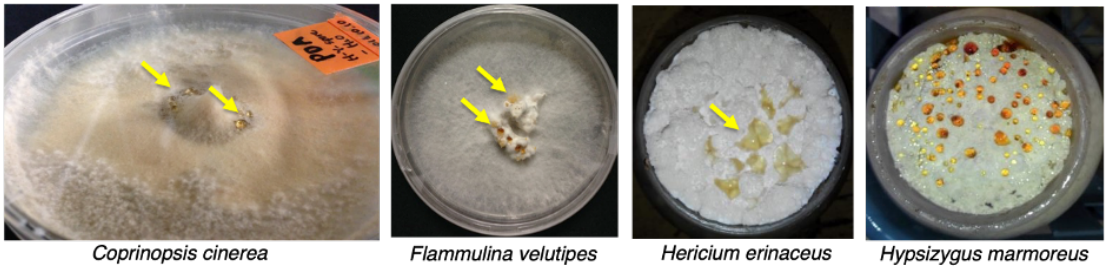


Figure S1. “Fruiting liquid” of mushroom-forming fungi.

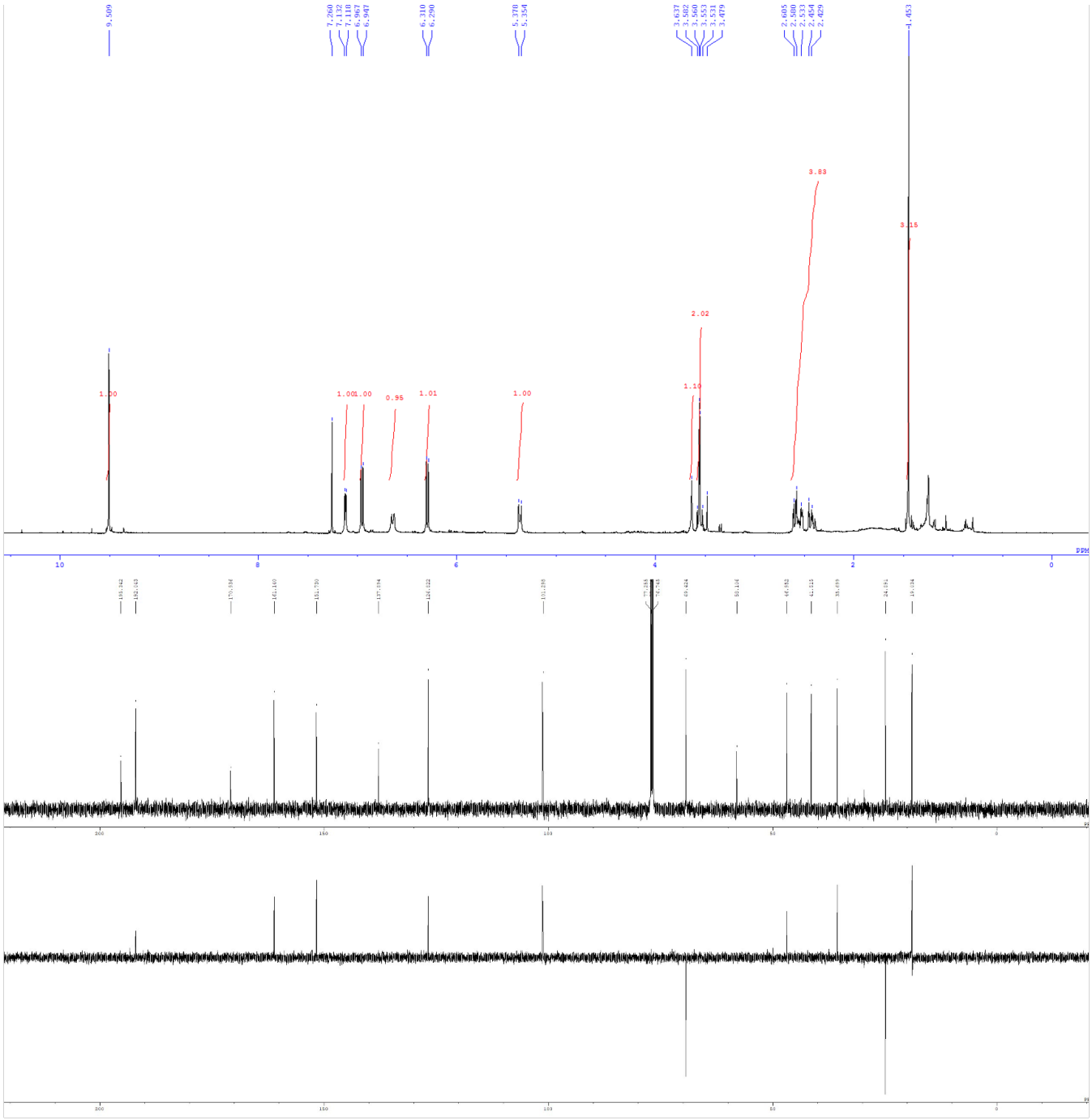


Figure S2. ^{1}H NMR,^{13}C NMR and DEPT spectra for compound **1** ($CDCl_3$).

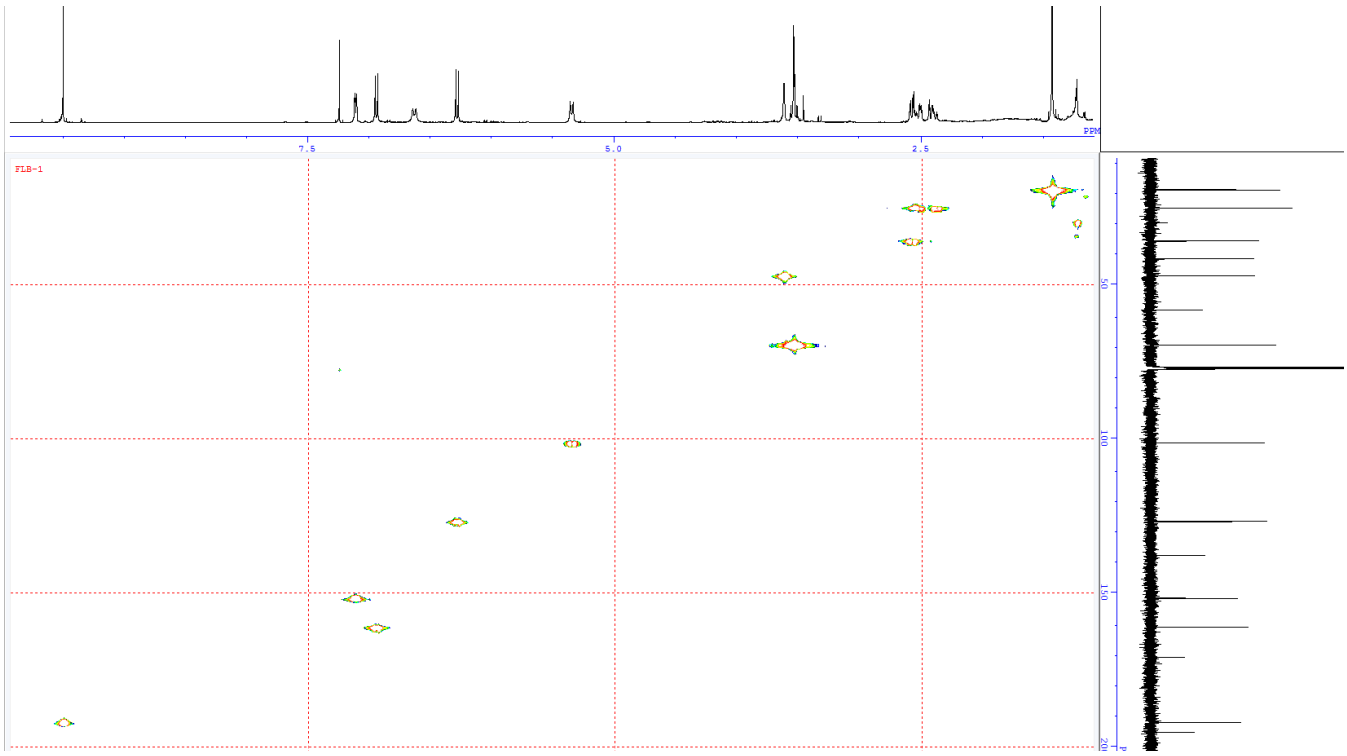


Figure S3. HMQC spectrum for compound **1** ($CDCl_3$).

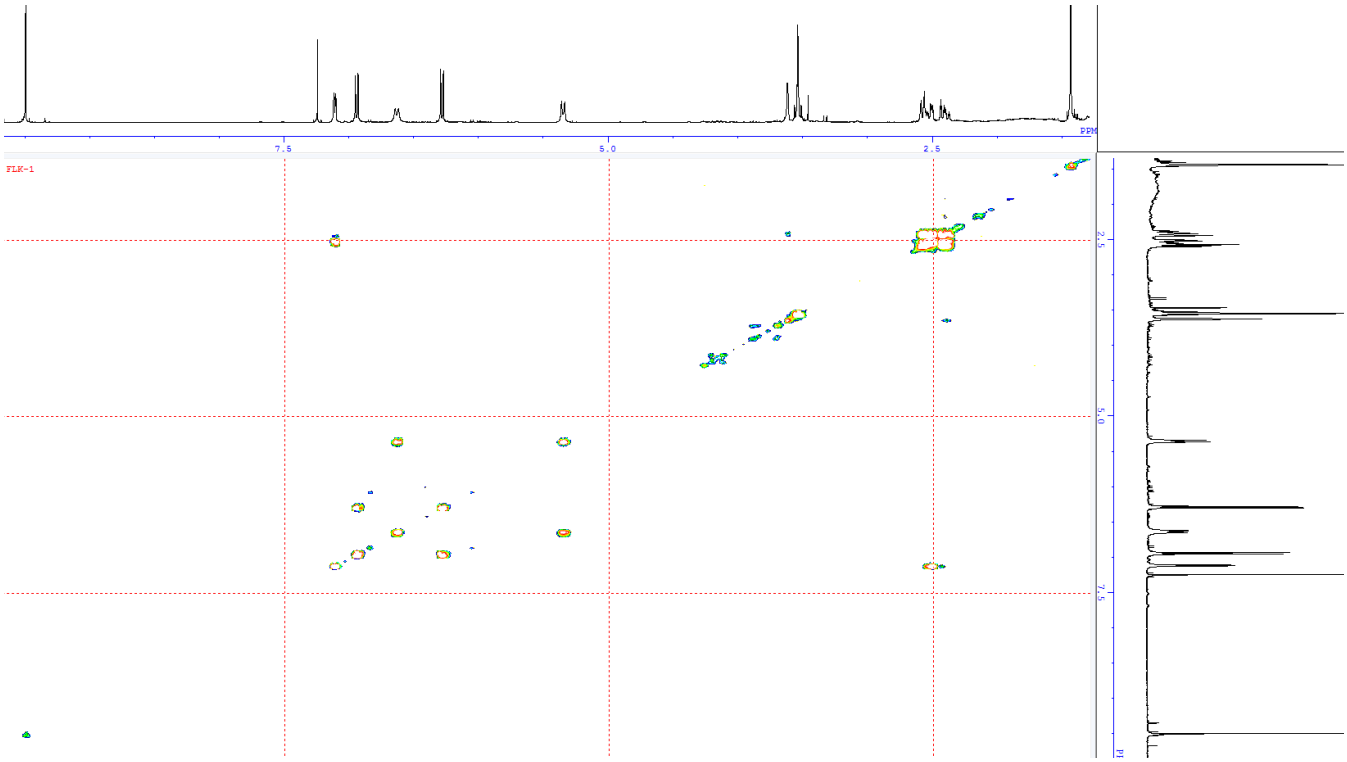


Figure S4. COSY spectrum for compound **1** ($CDCl_3$).

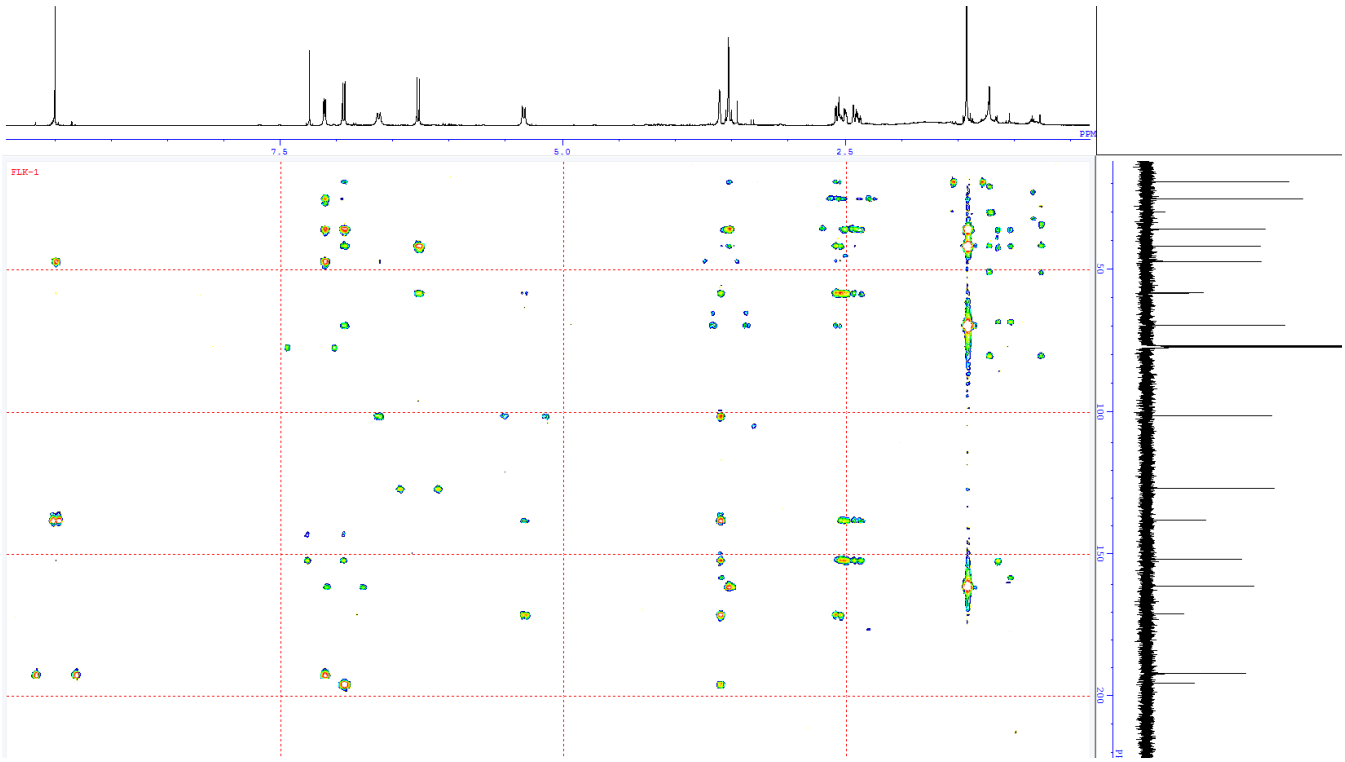


Figure S5. HMBC spectrum for compound **1** ($CDCl_3$).

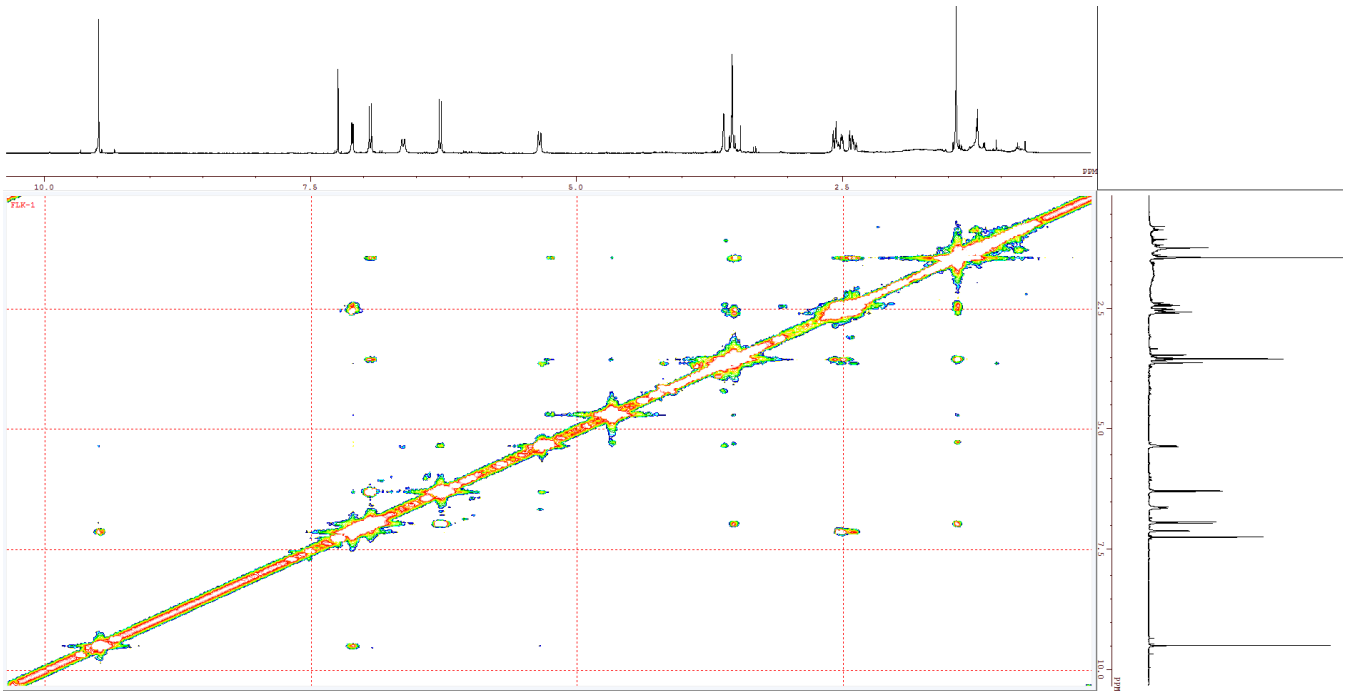
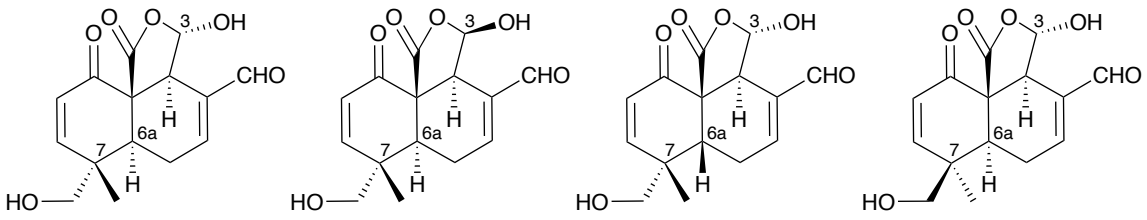
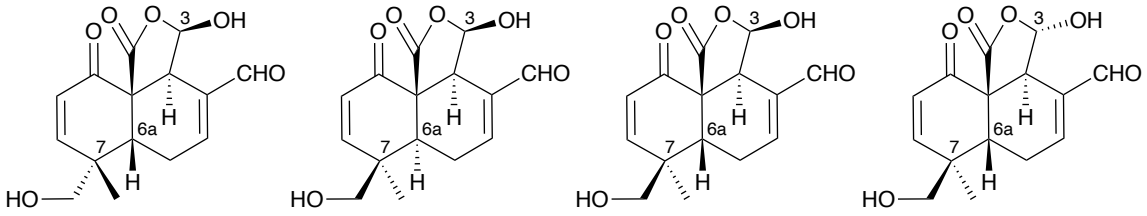


Figure S6. NOESY spectrum for compound **1** ($CDCl_3$).

Table S1. The ^{13}C and ^{1}H of **1** accordance.



expected | 3-isomer | 6a-isomer | 7-isomer



3,6a-isomer | 3,7-isomer | 3,6a,7-isomer | 6a,7-isomer

	^{13}C			^{1}H			$^{13}C+^{1}H$
	RMSD (ppm)	max absolute (ppm)	DP4	RMSD (ppm)	max absolute (ppm)	DP4	DP4
expected	**1.6**	**3.1**	**94.1%**	**0.15**	**0.28**	**100.0%**	**100.0%**
3-isomer	2.1	5.0	5.9%	0.40	1.23	0.0%	0.0%
6a-isomer	3.8	12.2	0.0%	0.29	0.58	0.0%	0.0%
7-isomer	3.8	9.2	0.0%	0.31	0.57	0.0%	0.0%
3,6a-isomer	3.1	6.8	0.0%	0.42	1.13	0.0%	0.0%
3,7-isomer	3.6	9.0	0.0%	0.55	1.50	0.0%	0.0%
3,6a,7-isomer	4.4	7.9	0.0%	0.41	0.93	0.0%	0.0%
6a,7-isomer	3.0	6.6	0.0%	0.32	0.76	0.0%	0.0%

RMSD: root mean square of deviation

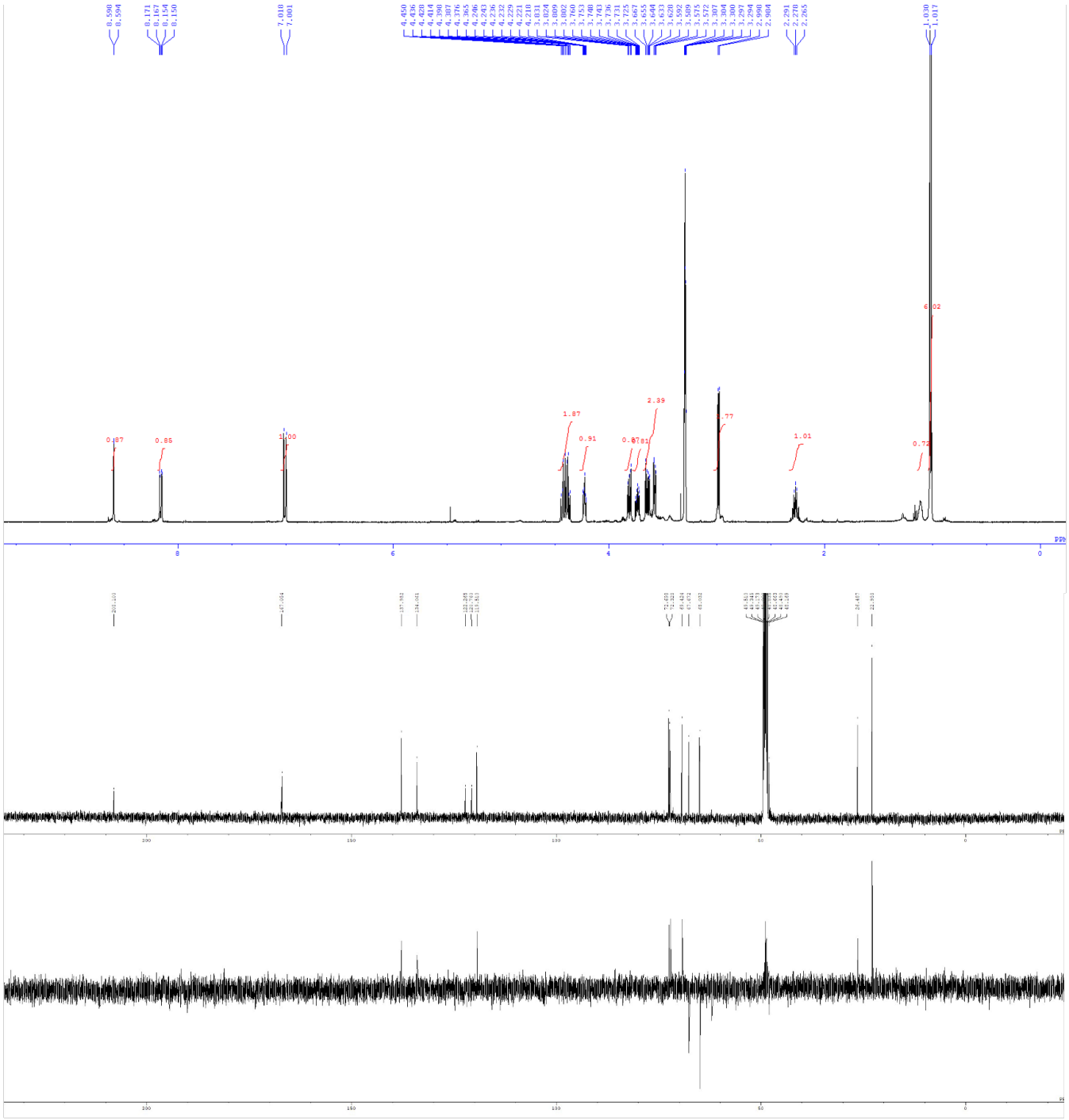


Figure S7. ^{1}H NMR,^{13}C NMR and DEPT spectra for compound **2** (CD_3OD).

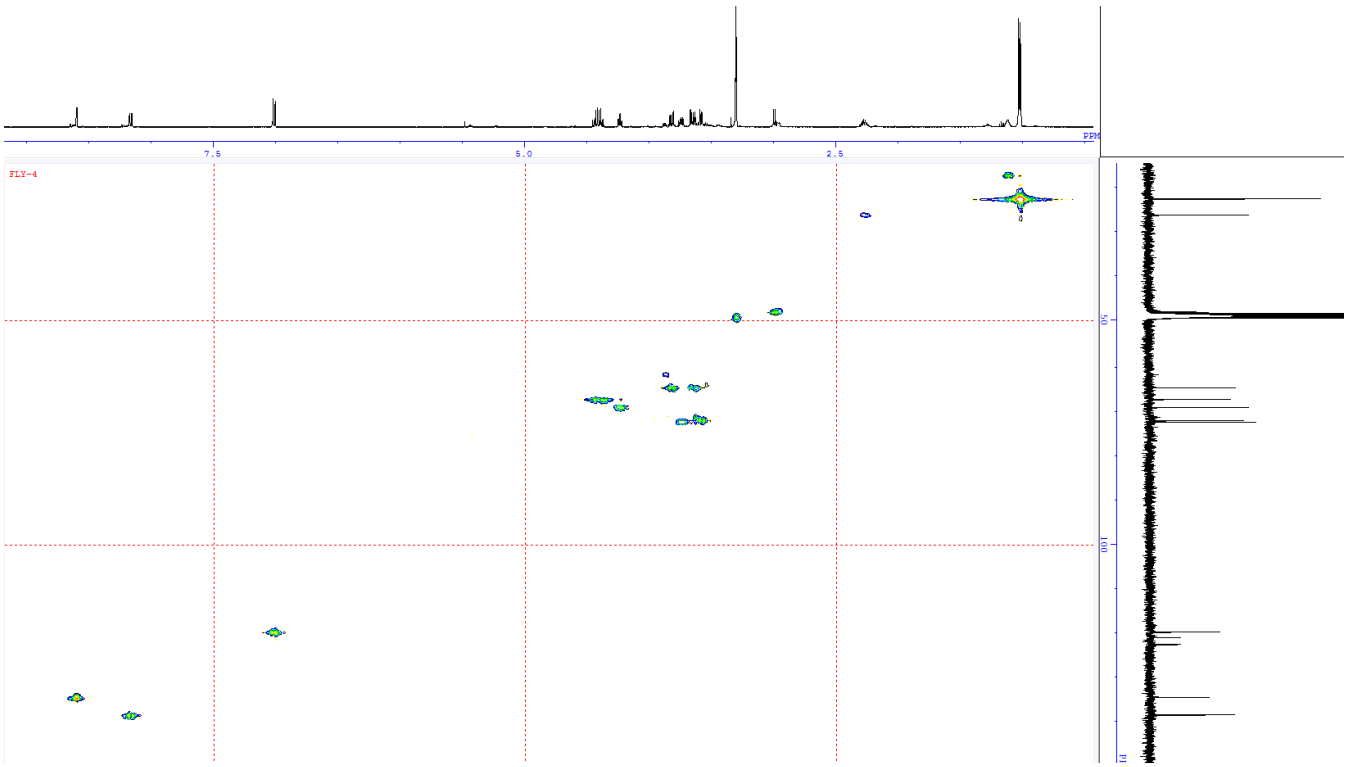


Figure S8. HMQC spectrum for compound **2** (CD_3OD).

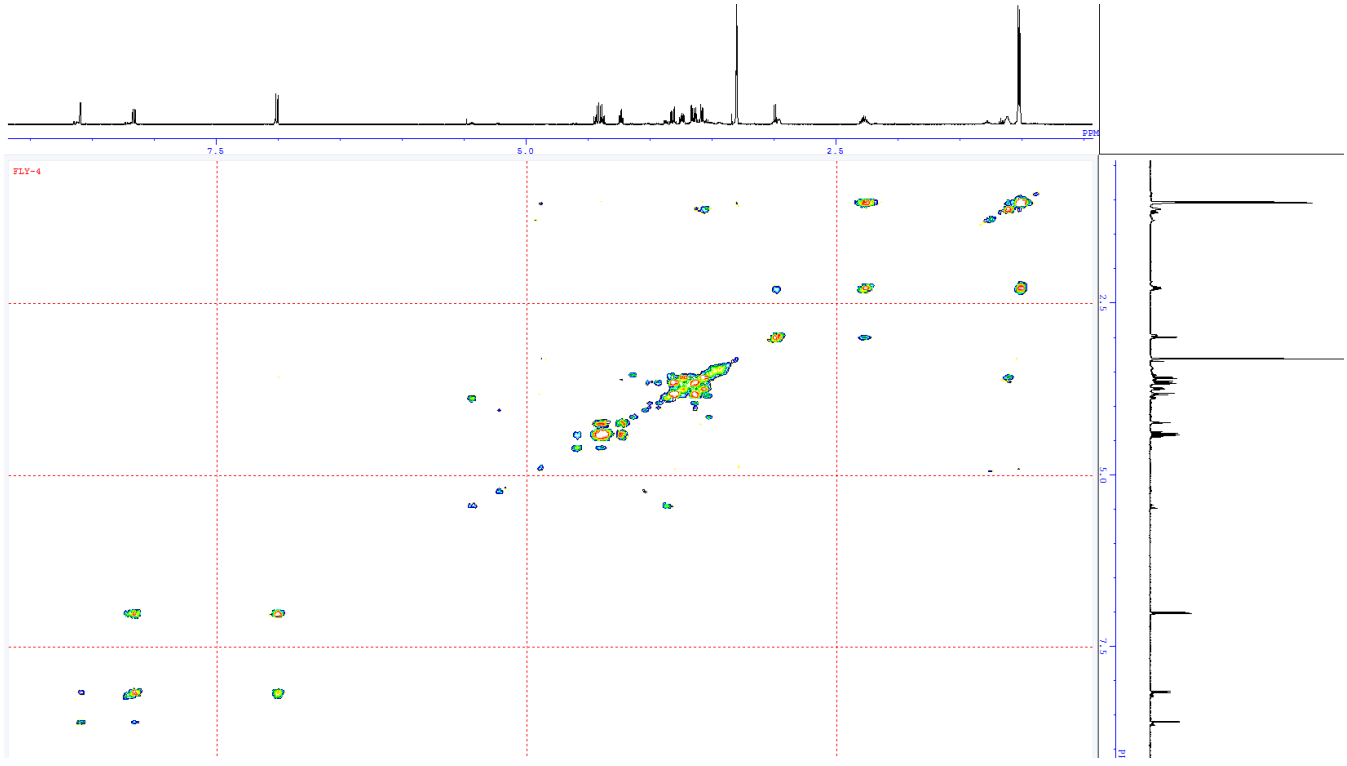


Figure S9. COSY spectrum for compound **2** (CD_3OD).

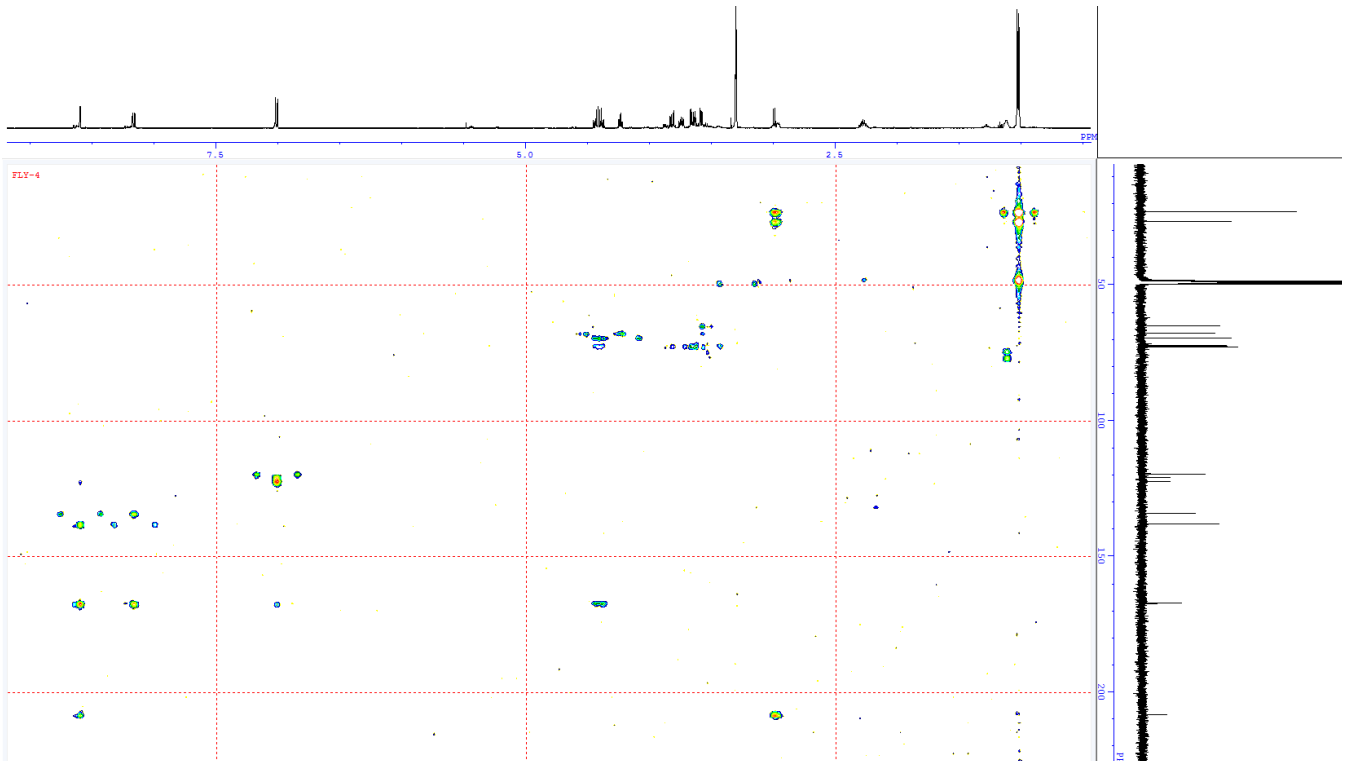


Figure S10. HMBC spectrum for compound **2** (CD_3OD).

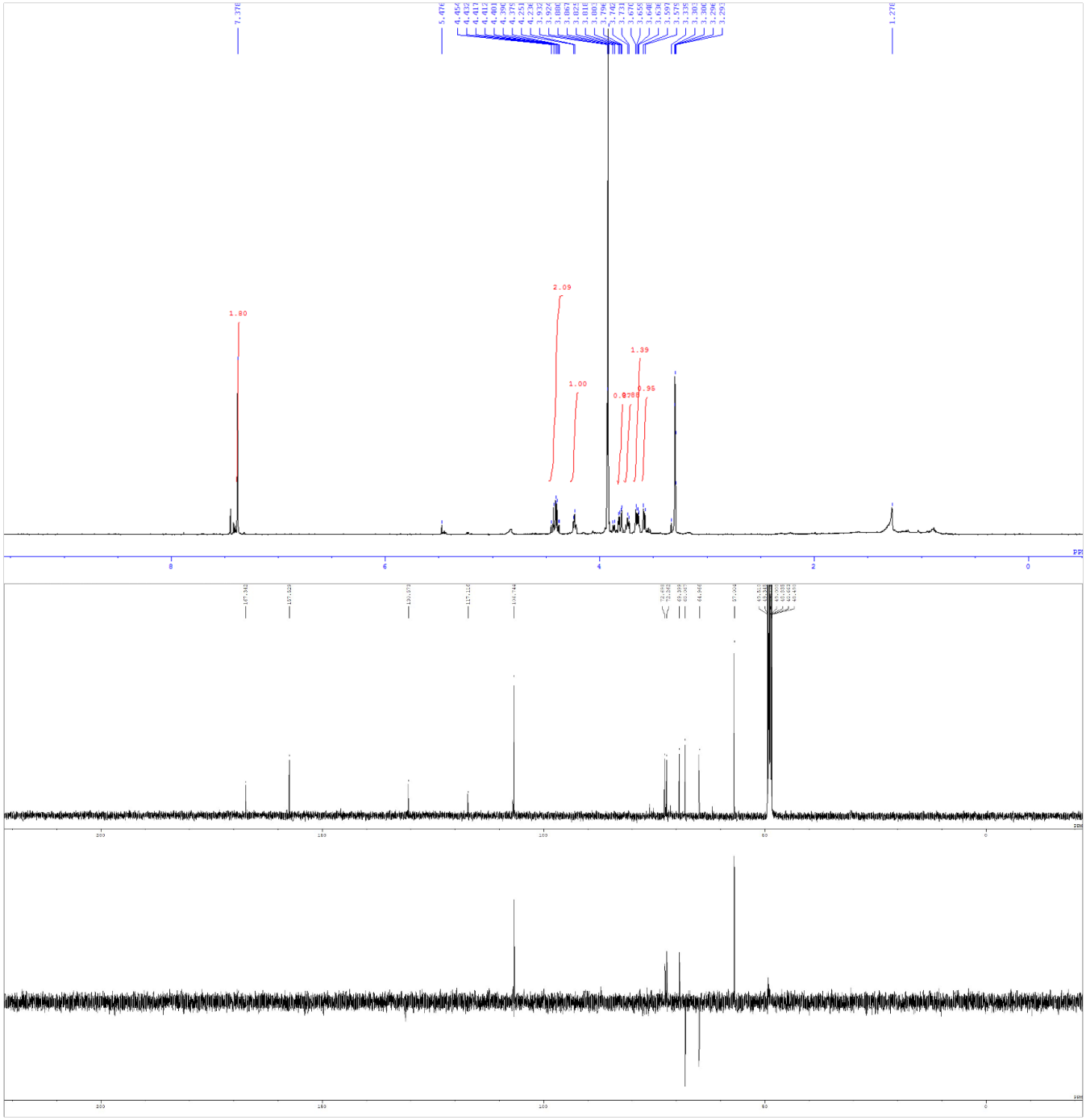


Figure S11. ^{1}H NMR,^{13}C NMR and DEPT spectra for compound **3** (CD_3OD).

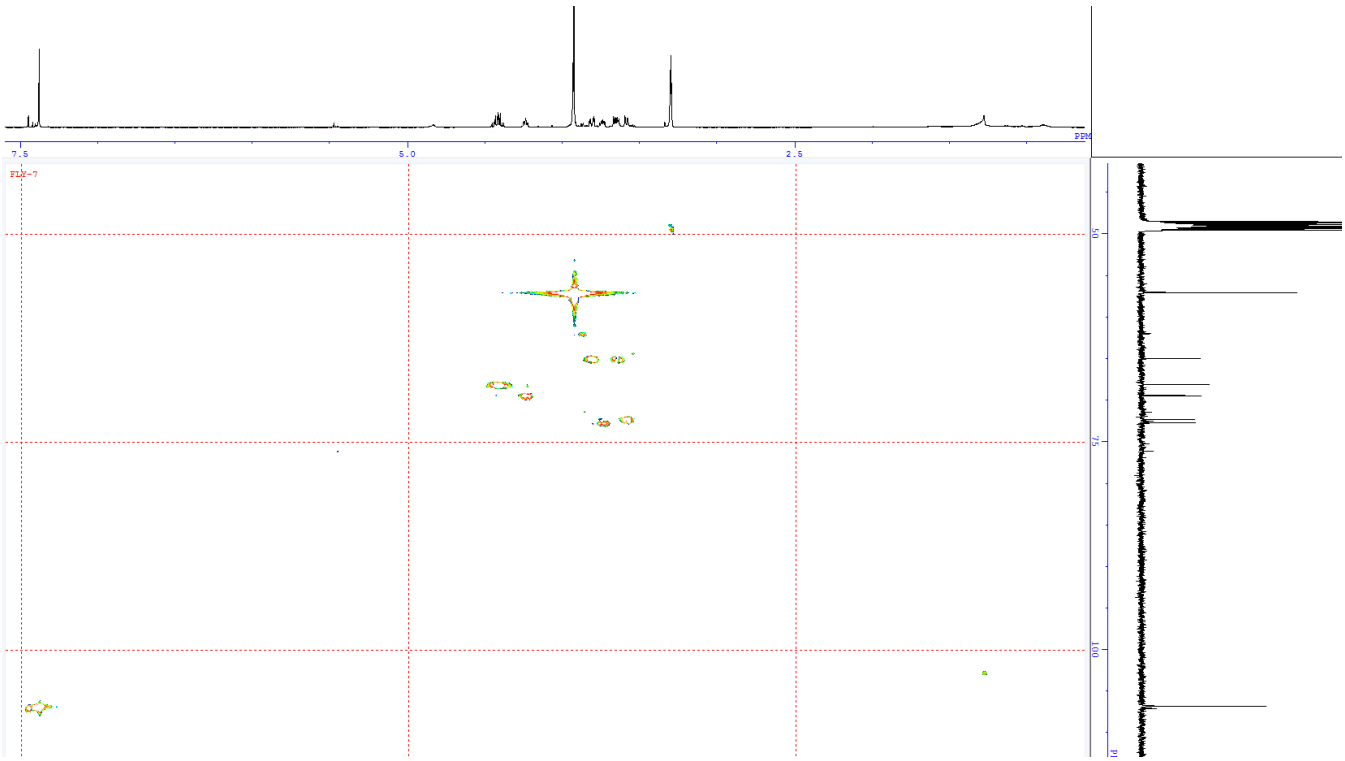


Figure S12. HMQC spectrum for compound **3** (CD_3OD).

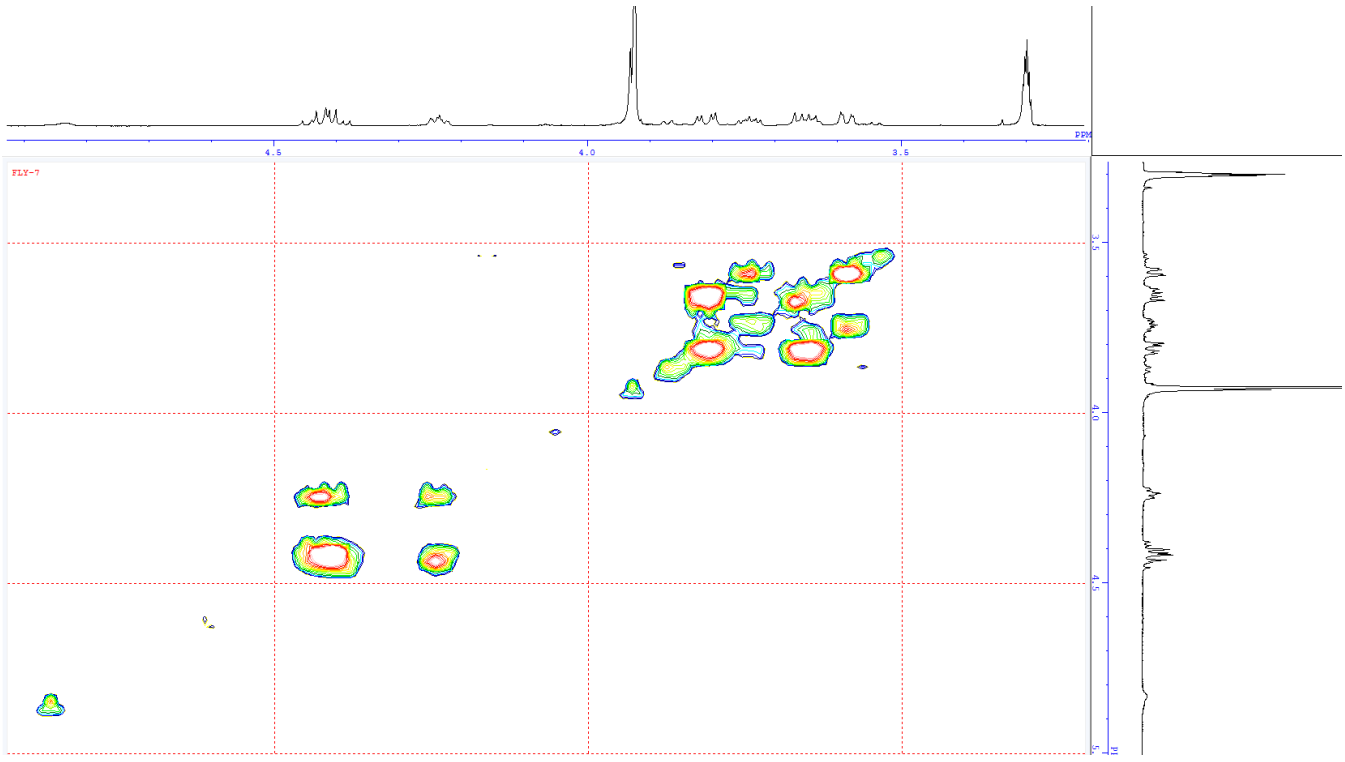


Figure S13. COSY spectrum for compound **3** (CD_3OD).

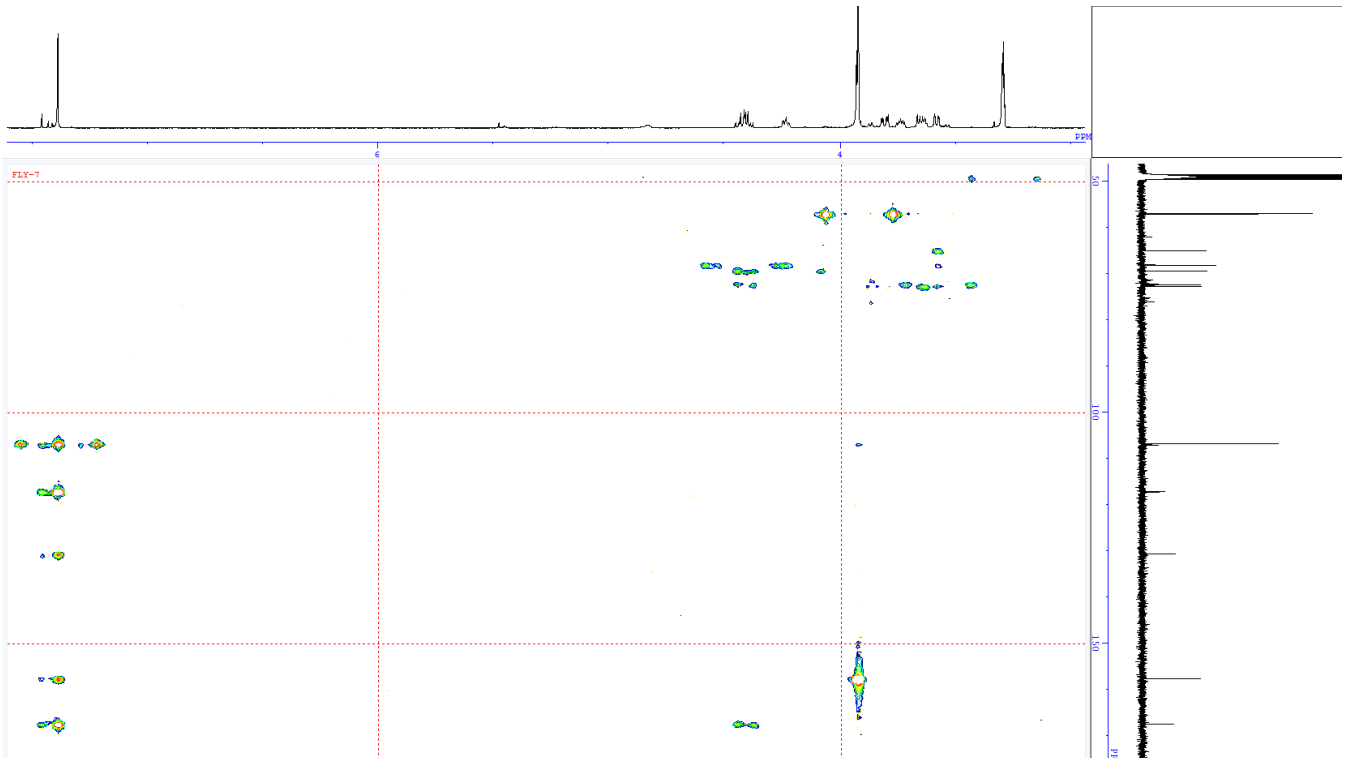


Figure S14. HMBC spectrum for compound **3** (CD_3OD).

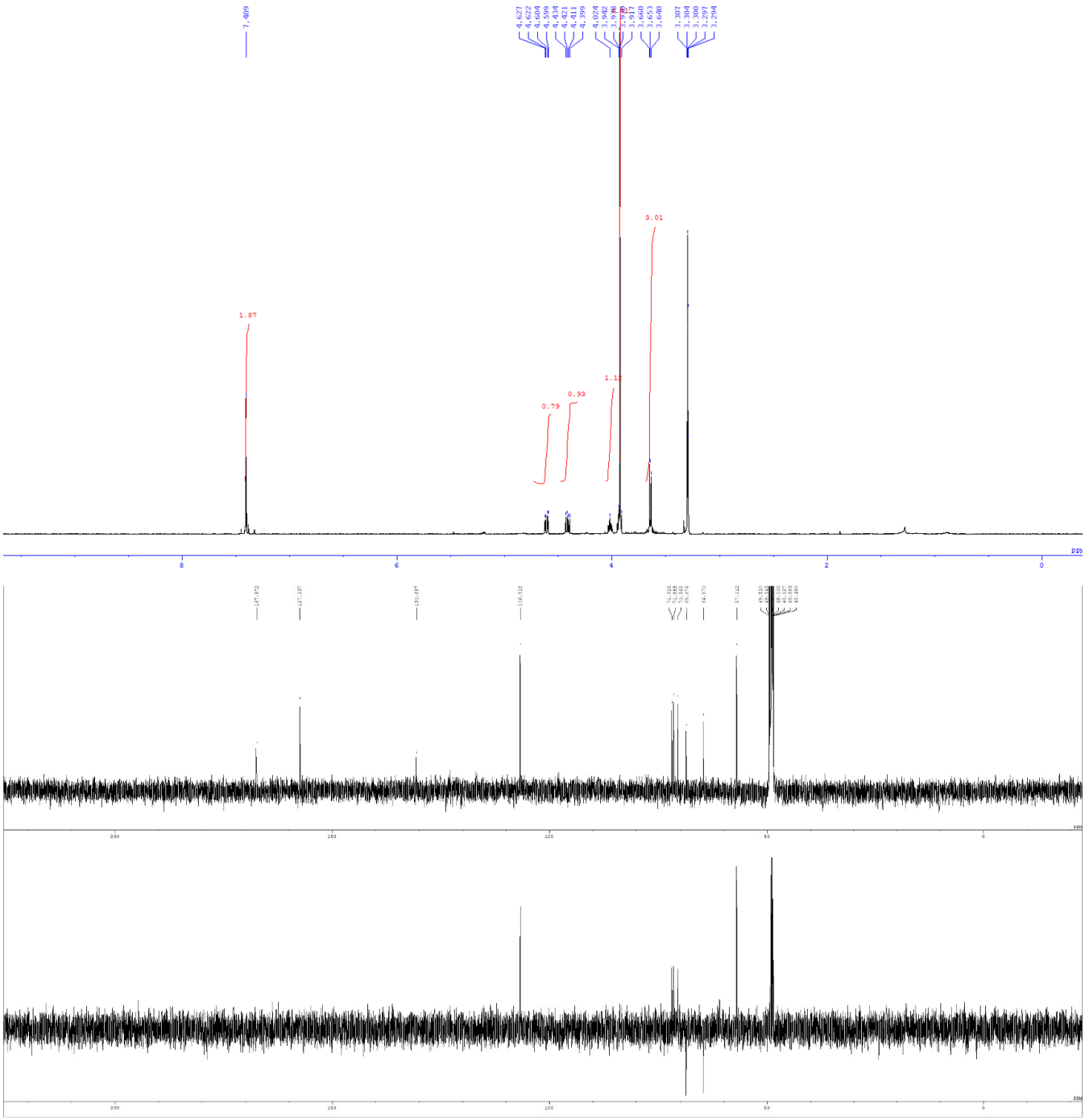


Figure S15. ^{1}H NMR,^{13}C NMR and DEPT spectra for compound **4** (CD_3OD).

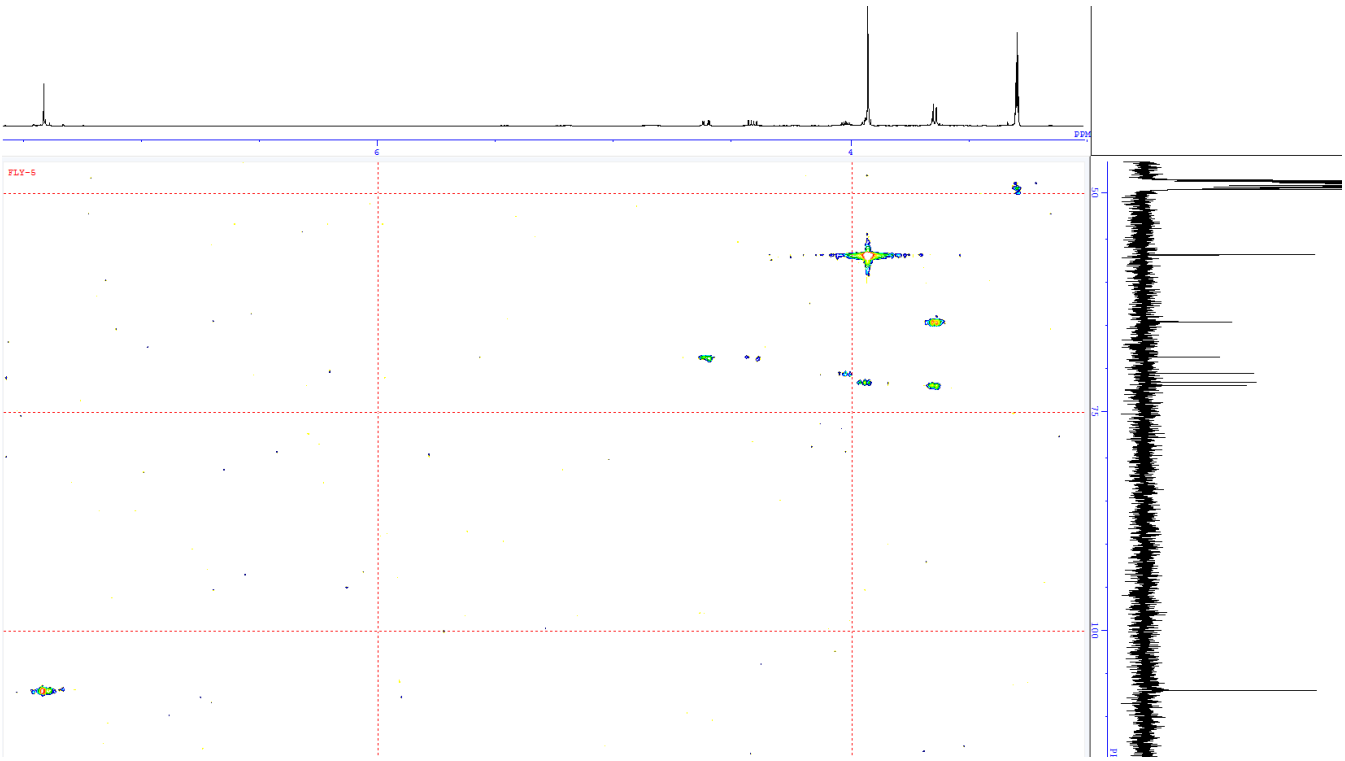


Figure S16. HMQC spectrum for compound **4** (CD_3OD).

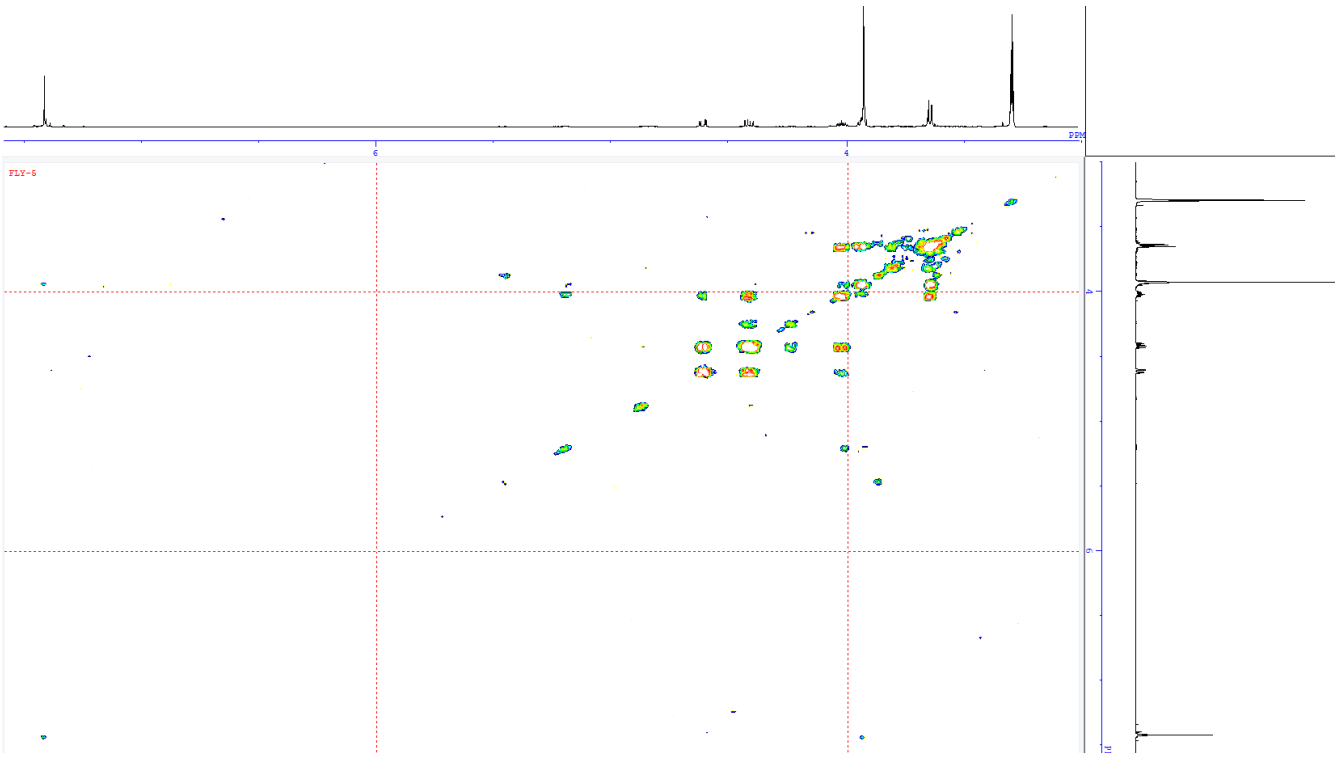


Figure S17. COSY spectrum for compound **4** (CD_3OD).

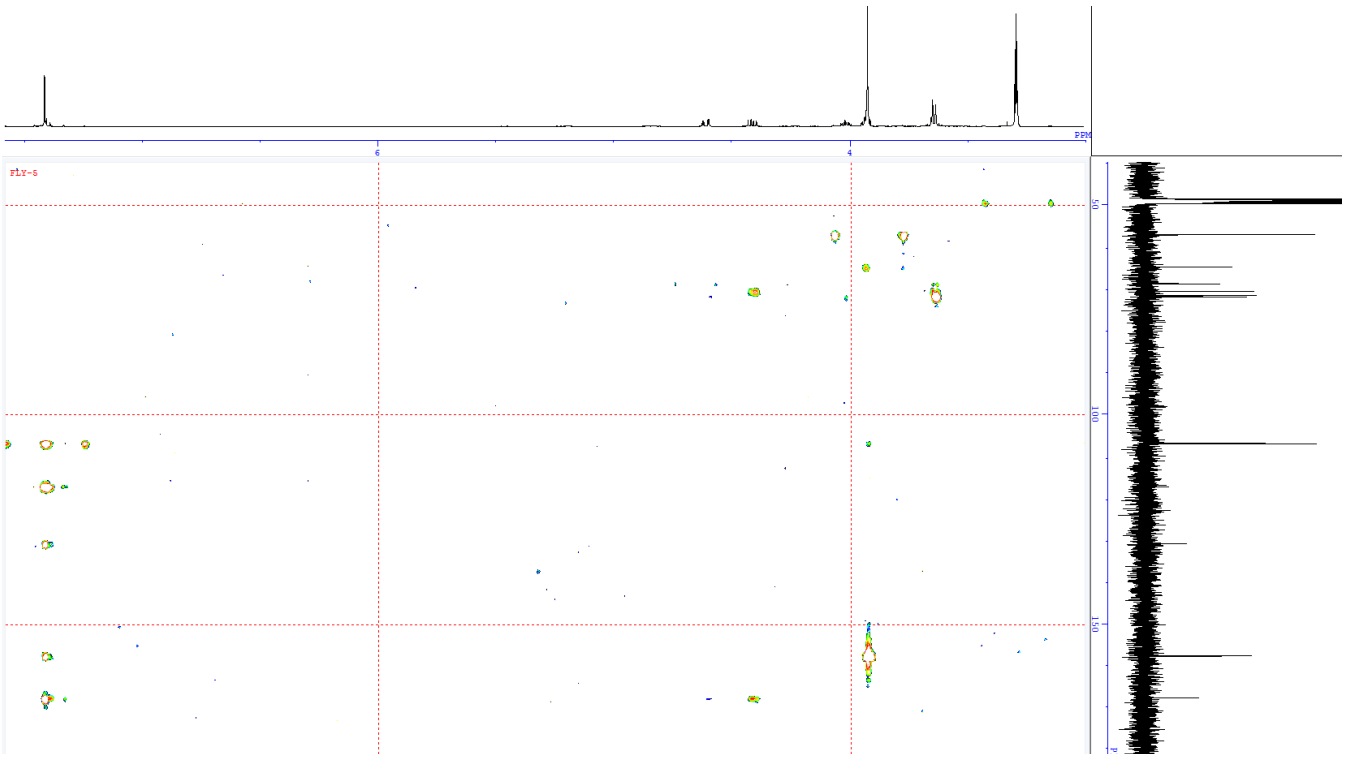


Figure S18. HMBC spectrum for compound **4** (CD_3OD).

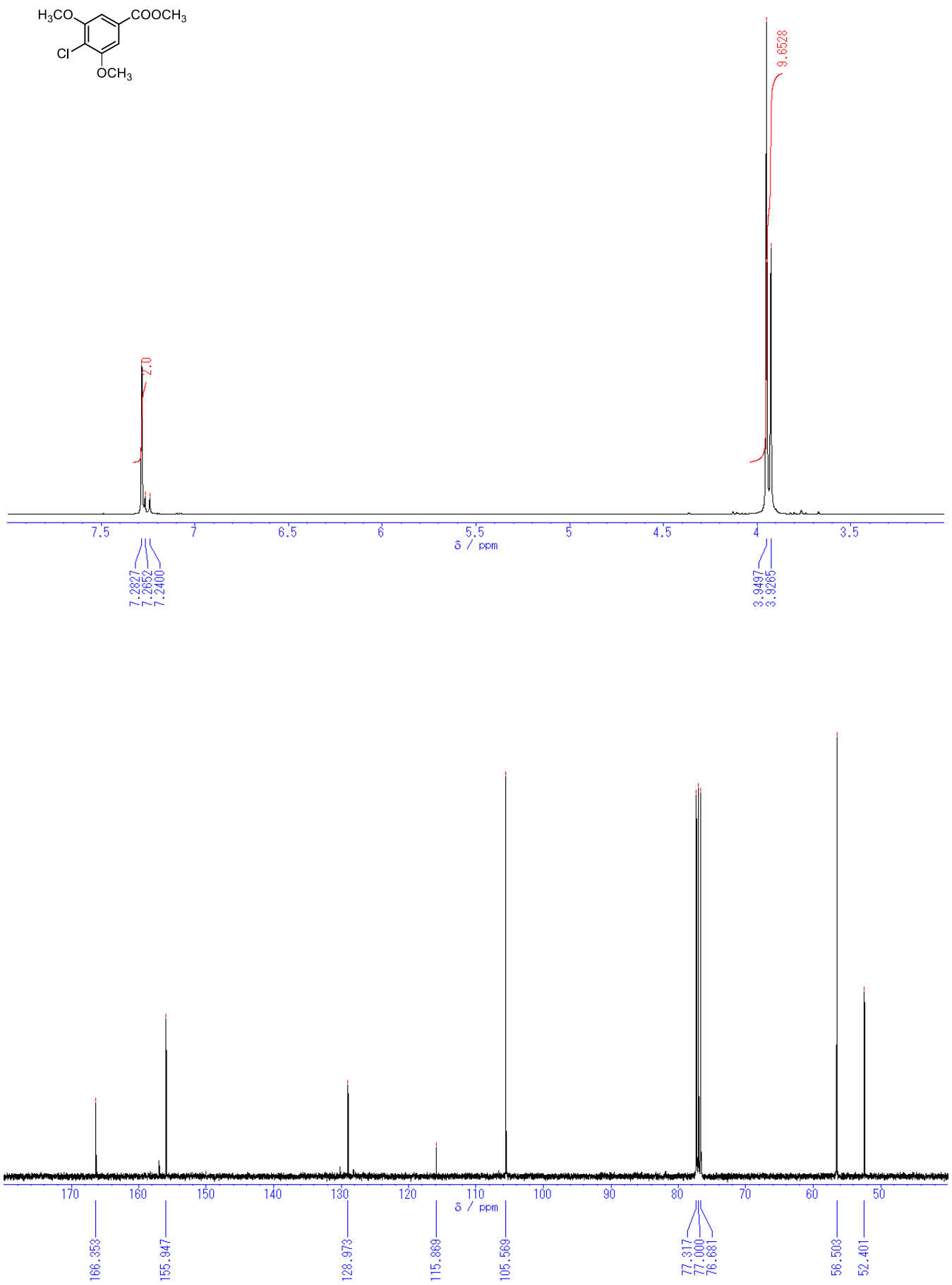


Figure S19. ^{1}H NMR and ^{13}C NMR spectra for compound **6** ($CDCl_3$).

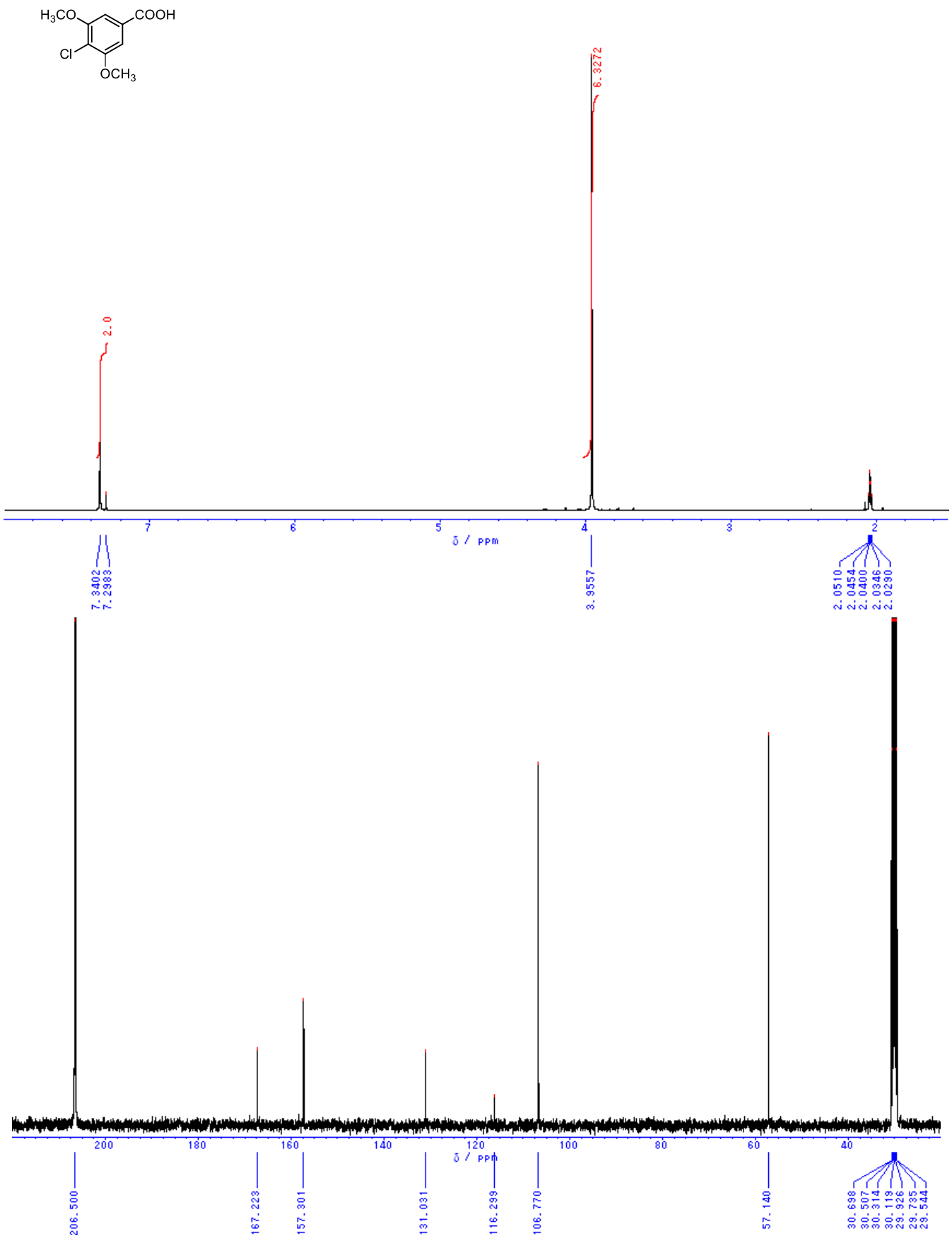


Figure S20. ^{1}H NMR and ^{13}C NMR spectra for compound **7** ($CDCl_3$).

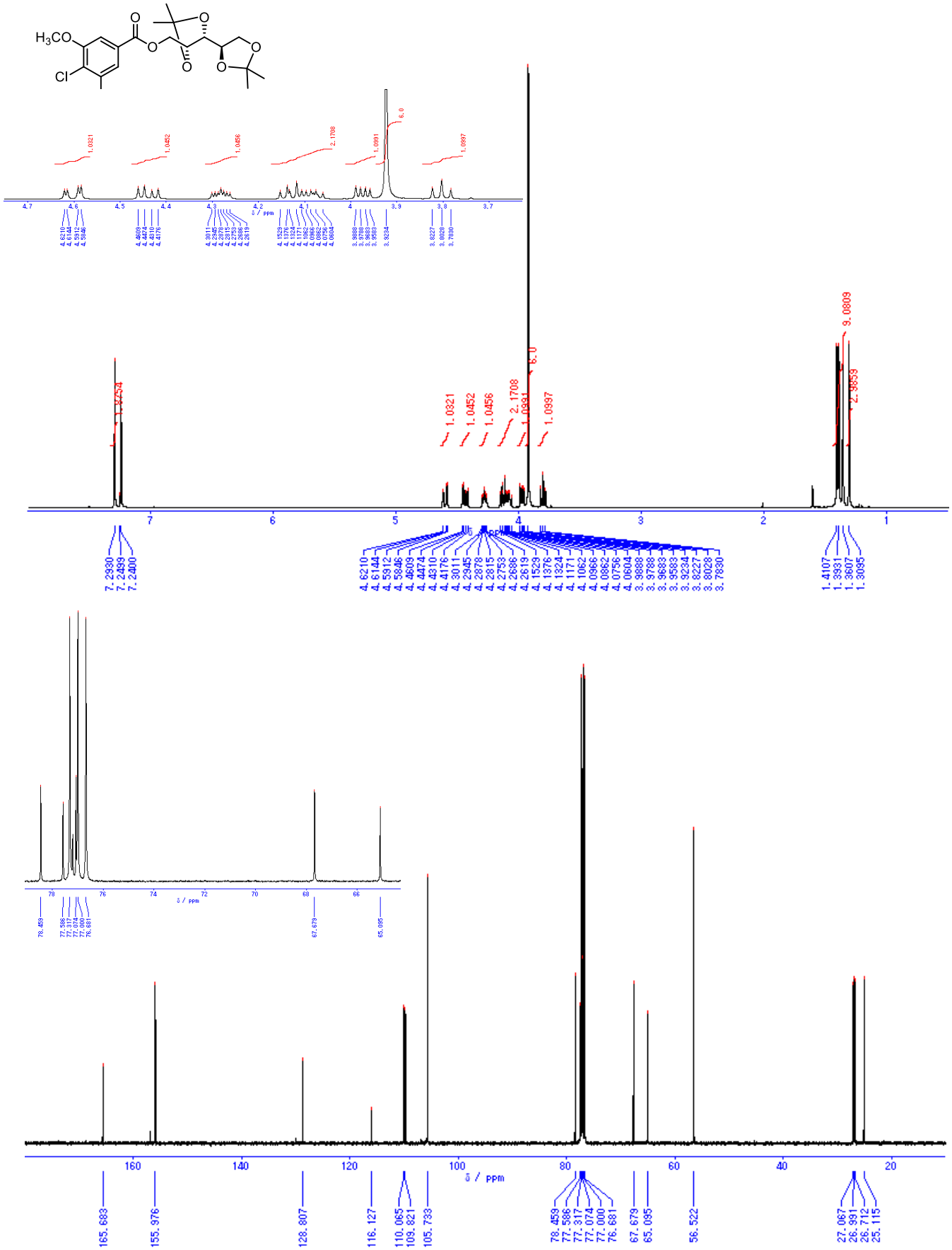


Figure S21. ^{1}H NMR and ^{13}C NMR spectra for compound **10** ($CDCl_3$).

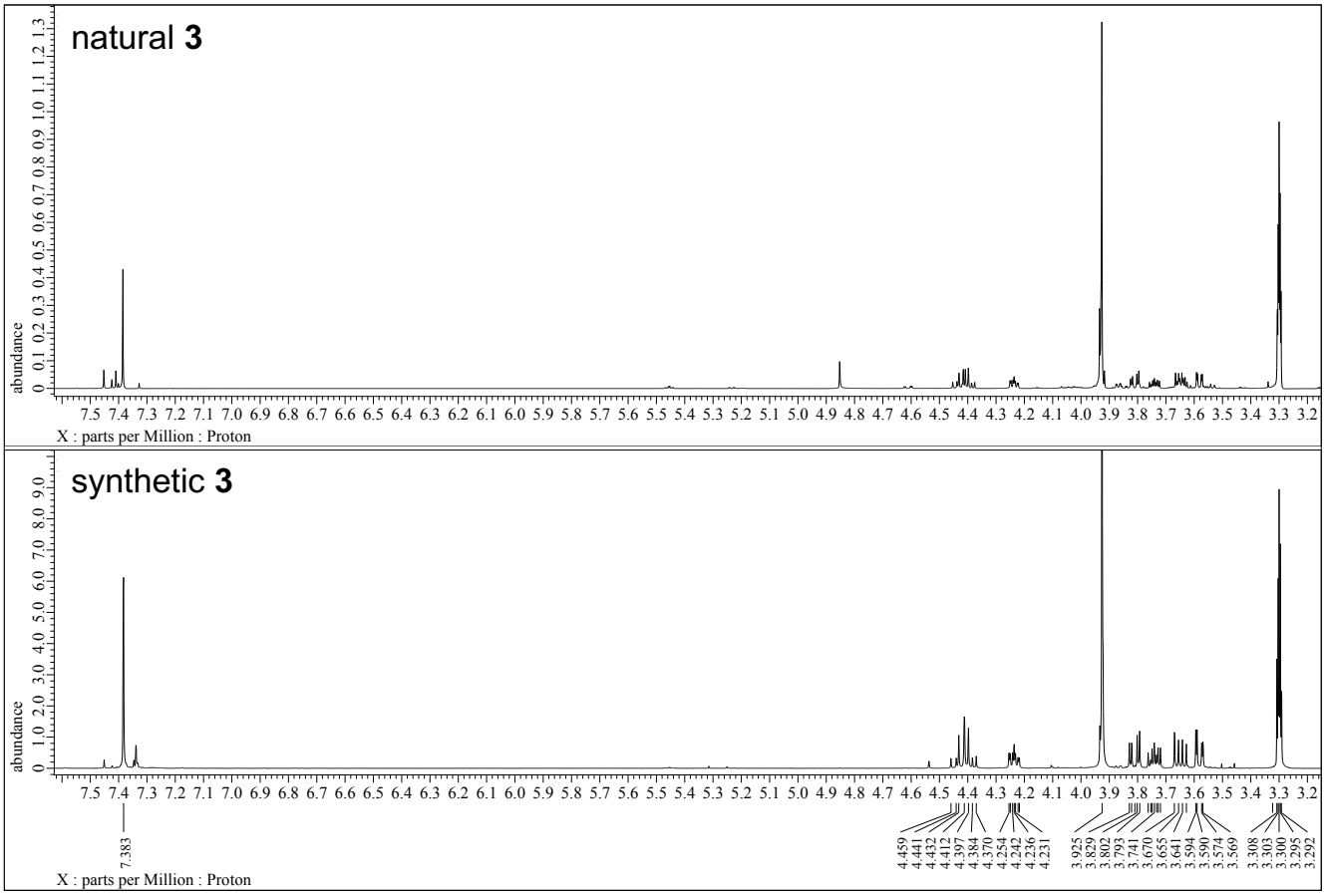


Figure S22. ^{1}H NMR spectra for natural **3** and synthetic **3** (CD_3OD).

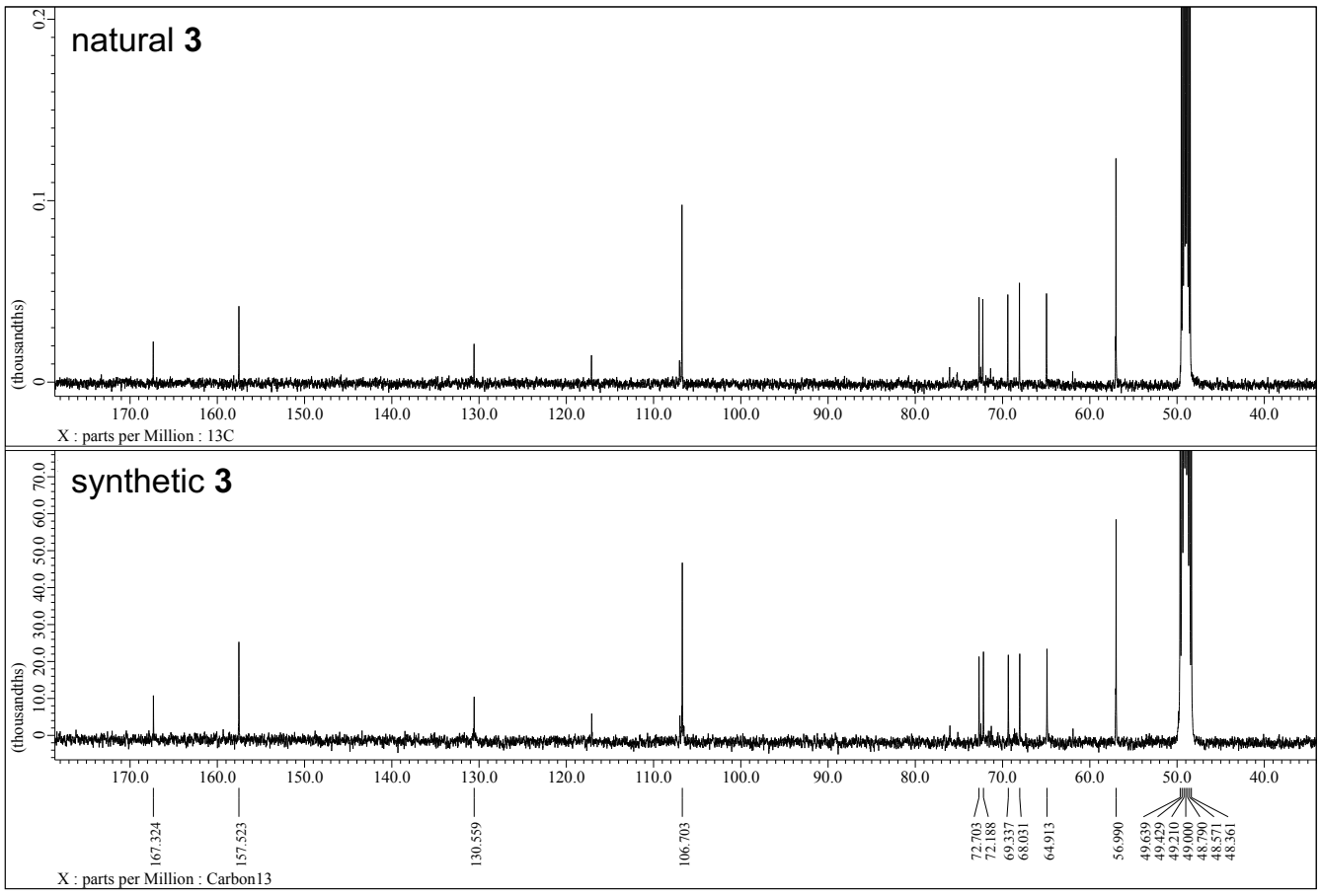
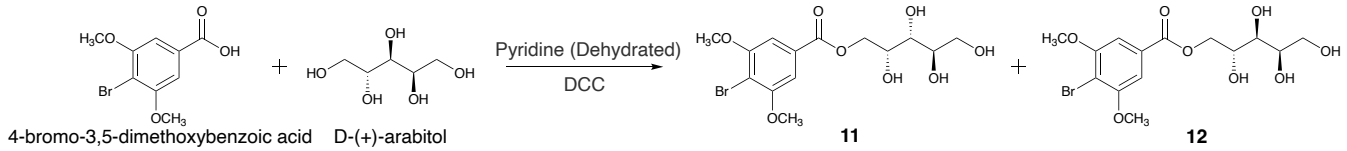


Figure S23. ^{13}C NMR spectra for natural **3** and synthetic **3** (CD_3OD).

Syntheses of 11 and 12



4-bromo-3,5-dimethoxybenzoic acid D-(+)-arabitol **11** **12**

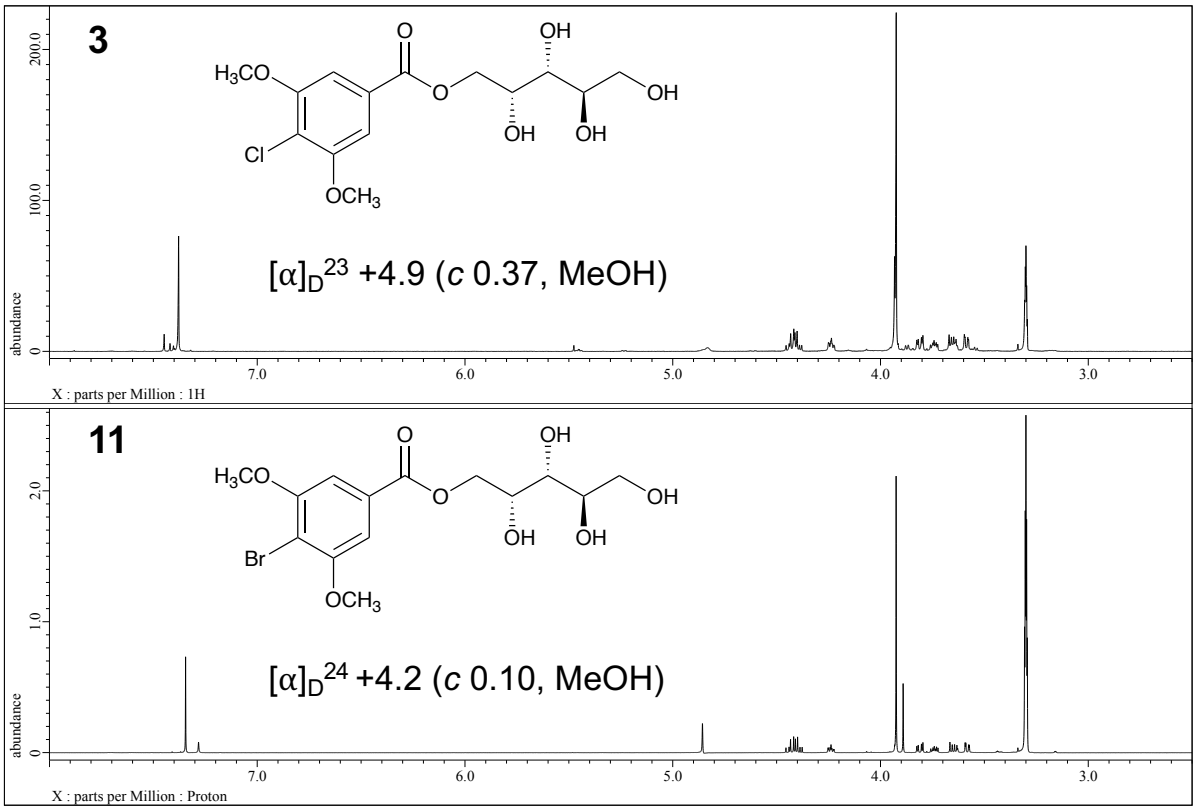


Figure S24. ^{1}H NMR spectra for compounds **3** and **11** (CD_3OD).

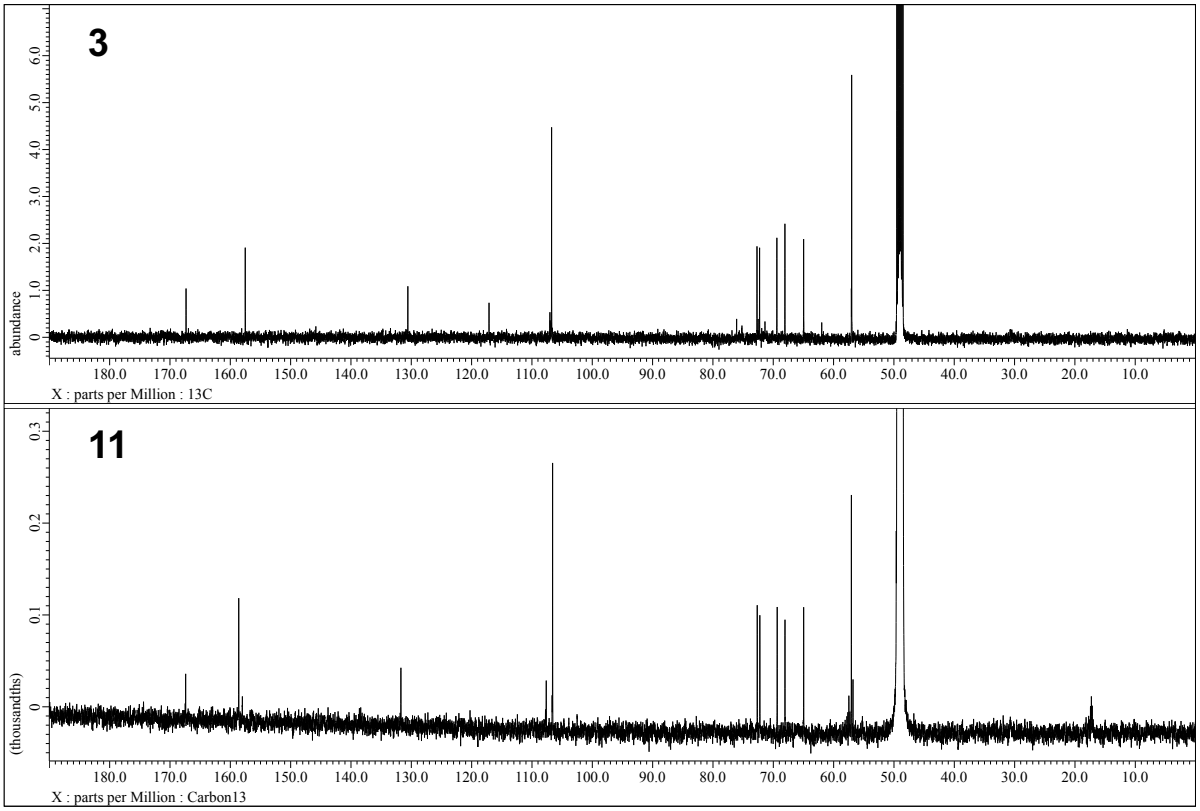


Figure S25. ^{13}C NMR spectra for compounds **3** and **11** (CD_3OD).

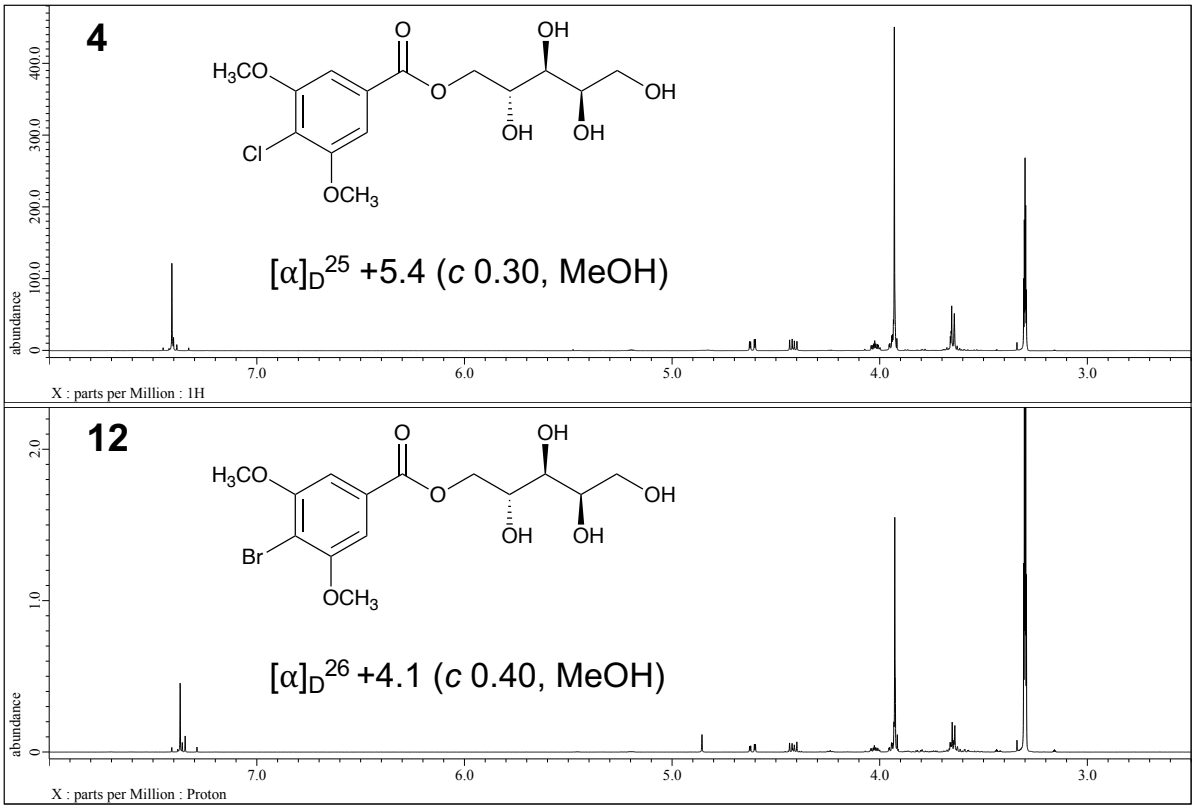


Figure S26. ^{1}H NMR spectra for compounds **4** and **12** (CD_3OD).

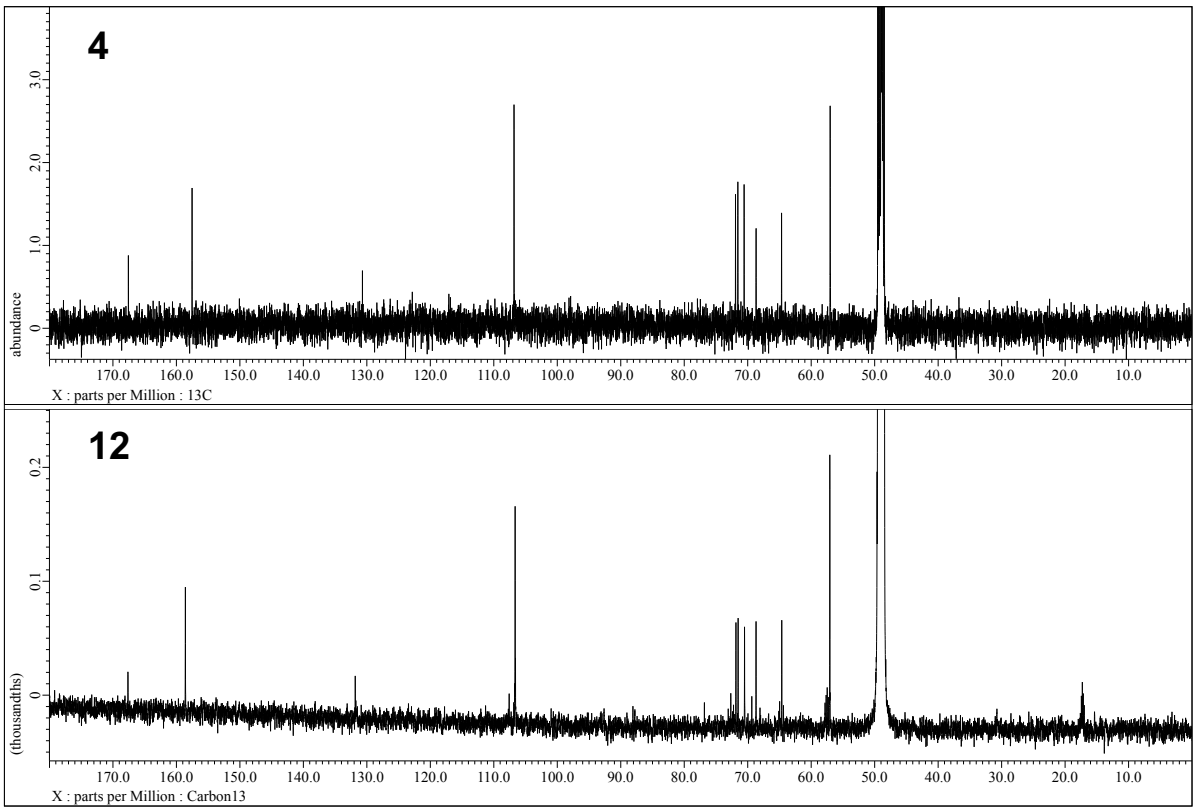


Figure S27. ^{13}C NMR spectra for compounds **4** and **12** (CD_3OD).

Table S2. Crystallographic data of **2** and **3**.

	2	**3**
Formula	$C_{17}H_{24}O_8$	$C_{14}H_{19}ClO_8$
Formula weight	356.36	350.74
Crystal system	monoclinic	triclinic
Space Group	*I*2	*P*1
a /Å	10.5226(5)	6.09830(10)
b /Å	5.7292(3)	9.27910(10)
c /Å	28.8051(13)	14.06900(10)
α /°	90	96.4020(10)
β /°	94.548(4)	91.0450(10)
γ /°	90	91.0990(10)
V /Å^3	1731.08(15)	790.842(17)
Z	4	2
D_x, g cm^{-3}	1.367	1.473
F(000)	760.0	368.0
μ /mm^{-1}	0.919	2.515
Temperature/°C	-100	-100
reflections collected	15769	68656
unique reflections	3371 (R_{int} = 0.0668)	6144 (R_{int} = 0.0442)
parameters refined	245	433
R_1 (*I*>2s(*I*))	0.0751	0.0269
ωR_2 (all data)	0.2155	0.0765
GOF	1.063	1.118

$R_1=\Sigma||F_o|-|F_c||/\Sigma|F_o|$. $wR_2=[\Sigma w(F_o^2-F_c^2)^2/\Sigma w(F_o^2)^2]^{1/2}$.

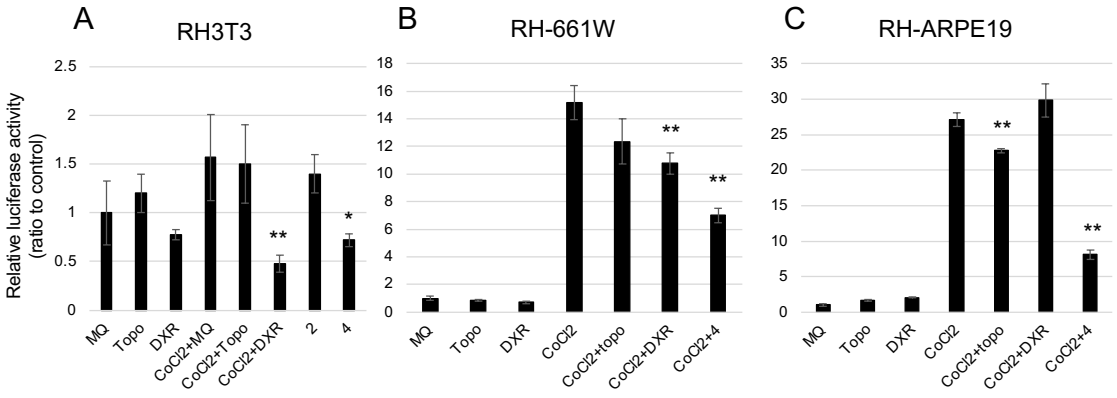


Figure S28. Effect of compounds **2** and **4** on HIF activation *in vitro*. (A) Administration of **2** and **4** suppressed HIF activation in 3T3 cells. (B) Administration of **4** suppressed $CoCl_2$-induced HIF activation in 661W cells. (C) Administration of **4** suppressed $CoCl_2$-induced HIF activation in ARPE19 cells. $^{**}p < 0.01$, $^{*}p < 0.05$ compared with $CoCl_2$ without topotecan (Topo) and doxorubicin (DXR), n = 3.

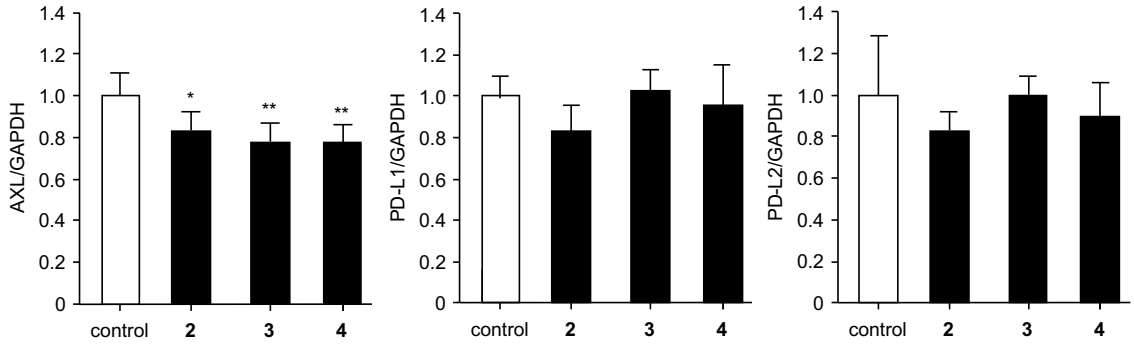


Figure S29. Effect of compounds **2** to **4** on expressions of Axl and immune checkpoints (PD-L1 and PD-L2) on lung cancer cell line A549 cells. Values indicate means with standard deviation from three independent triplicate experiments. Statistical analysis was performed using Fisher's test ($^{**}p < 0.01$, $^{*}p < 0.05$ vs control, n = 3).