

Construction of the Plukenetione-type Adamantane Core of Polycyclic Polyprenylated Acylphloroglucinols

Ryukichi Takagi, Yuta Inoue, and Katsuo Ohkata*

Department of Chemistry, Graduate School of Science, Hiroshima University, 1-3-1 Kagamiyama,
Higashi-Hiroshima 739-8526, Japan

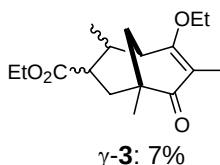
Table of Contents

General Methods.....	S2
Characterization Data of γ - 3 , 11 , 12 , and 14-16	S2-S4
NMR Spectra of 6 , 3 , γ - 3 , 7-9 , 11-17 , 2 , and 1	S5-S60
X-Ray Crystal Structure Determination.....	S61
ORTEP Drawings of 8 and 12	S62-S63

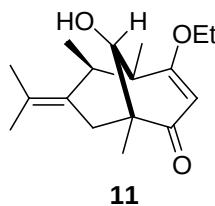
General Method

All reactions involving air- and moisture-sensitive reagents were carried out under N₂. CH₂Cl₂, toluene, dimethyl sulfoxide (DMSO) and N,N-dimethylformamide (DMF) were distilled over CaH₂ before use. Tetrahydrofuran (THF) and diethyl ether (Et₂O) were distilled after refluxing over Na-benzophenone before use. Silica gel F₂₅₄ TLC aluminum sheets were used for routine monitoring of reactions. Column chromatography was performed on silica gel (70-230 mesh, ASTM).

¹H and ¹³C NMR spectra were recorded at 500 and 125 MHz respectively. Internal references for ¹H NMR spectra were 0.0 ppm (Me₄Si) for CDCl₃, 3.30 ppm for CD₃OD, and 7.16 ppm for C₆D₆. Chemical shifts for ¹³C NMR spectra were referenced to CDCl₃ (77.0 ppm), CD₃OD (49.0 ppm), and C₆D₆ (128.0 ppm). MS were recorded under electron ionization (EI; 70eV).

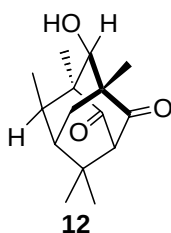


4-Ethoxy-7-ethoxycarbonyl-1,3,6-trimethylbicyclo[3.3.1]non-3-en-2-one (γ-3). a diastereomer of γ-3: ¹H NMR (500 MHz, CDCl₃) δ 4.26-4.19 (m, 1 H), 4.05-3.86 (m, 3 H), 2.84-2.82 (m, 1 H), 2.60-2.56 (m, 1 H), 2.45 (dt, *J* = 13.9, 2.1 Hz, 1 H), 2.25-2.18 (m, 2 H), 2.04 (ddd, *J* = 12.3, 3.4, 2.6 Hz, 1 H), 1.62 (dd, *J* = 12.3, 3.2 Hz, 1 H), 1.60 (s, 3 H), 1.47 (d, *J* = 7.6 Hz, 3 H), 1.45 (dd, *J* = 13.9, 6.8 Hz, 3 H), 1.31 (t, *J* = 7.0 Hz, 3 H), 1.18 (t, *J* = 7.2 Hz, 3 H); a diastereomer of γ-3: ¹H NMR (500 MHz, CDCl₃) δ 4.20-4.12 (m, 1 H), 4.11-4.00 (m, 2 H), 3.97-3.90 (m, 1 H), 2.86 (qd, *J* = 7.2, 0.8 Hz, 1 H), 2.62-2.59 (m, 1 H), 2.32 (d, *J* = 19.8 Hz, 1 H), 2.31 (bs, 1 H), 1.85 (dd, *J* = 12.8, 3.1 Hz, 1 H), 1.80 (dt, *J* = 12.8, 2.4 Hz, 1 H), 1.60-1.56 (m, 1 H), 1.55 (s, 3 H), 1.37 (t, *J* = 7.0 Hz, 3 H), 1.27 (d, *J* = 7.5 Hz, 3 H), 1.20 (t, *J* = 7.2 Hz, 3 H), 1.09 (s, 3 H); LR-EIMS *m/z* (%): 57 (100), 69 (45), 83 (55), 97 (37), 154 (55), 194 (43), 297 (27) [M⁺].

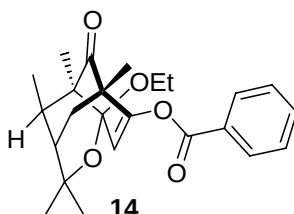


4-Ethoxy-9-hydroxy-7-(1'-methylethylidene)-1,5,6*exo*-trimethylbicyclo[3.3.1]non-3-en-2-one

(11). ^1H NMR (500 MHz, CD_3D) δ 3.91 (dq, $J = 10.1, 6.9$ Hz, 2 H), 3.79 (dq, $J = 10.1, 6.9$ Hz, 2 H), 2.61 (q, $J = 7.4$ Hz, 1 H), 2.25 (d, $J = 13.7$ Hz, 1 H), 2.14 (d, $J = 13.7$ Hz, 1 H), 1.52 (s, 6 H), 1.32 (t, $J = 6.9$ Hz, 3 H), 1.27 (s, 3 H), 1.17 (d, $J = 7.1$ Hz, 3 H), 1.11 (s, 3 H); LR-EIMS m/z (%): 77 (5), 83 (9), 107 (15), 121 (100), 205 (1), 232 (1), 233 (0.5) [$\text{M}^+ - \text{OEt}$].



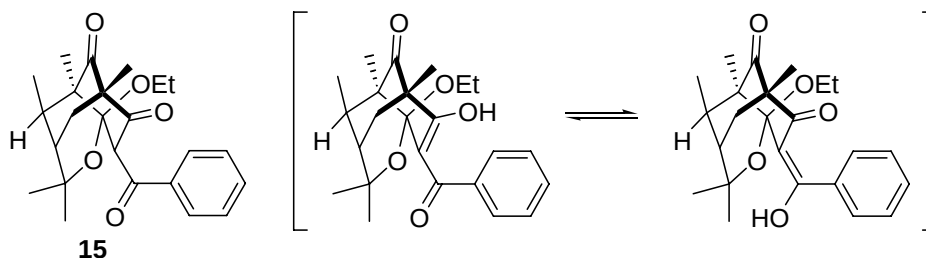
9-Hydroxy-1,5,6*exo*,10,10-pentamethyltricyclo[3.3.1.1^{3,7}]deca-2,4-dione (12). ^1H NMR (500 MHz, CD_3OD) δ 2.94 (bs, 1 H), 2.83 (d, $J = 1.5$ Hz, 1 H), 2.45 (dd, $J = 2.5, 13.9$ Hz, 1 H), 2.15 (qt, $J = 7.2, 1.0$ Hz, 1 H), 1.75 (dddt, $J = 13.9, 3.5, 1.3$ Hz, 1 H), 1.56-1.52 (m, 1 H), 1.34 (d, $J = 7.2$ Hz, 3 H), 1.11 (s, 3 H), 1.02 (s, 3 H), 1.00 (s, 6 H); ^{13}C NMR (125 MHz, CD_3OD) δ 210.3, 209.7, 79.4, 75.5, 54.8, 52.0, 48.5, 46.0, 40.1, 29.8, 26.5, 26.1, 18.6, 16.7, 16.4; LR-EIMS m/z (%): 69 (36), 83 (100), 108 (46), 121 (17), 136 (46), 149 (23), 177 (17), 192 (24), 248 (34), 250 (0.5) [M^+].



2-Benzoyloxy-4-ethoxy-1,5,6*exo*,10,10-pentamethyl-11-oxabicyclo[3.3.1.2^{7,4}]undec-2-en-9-one

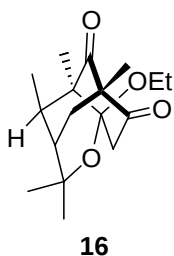
(14). ^1H NMR (500 MHz, CD_3OD) δ 8.02-7.98 (m, 2 H), 7.62-6.58 (m, 1 H), 7.49-7.44 (m, 2 H), 5.00 (s, 1 H), 3.83 (dq, $J = 9.6, 7.0$ Hz, 1 H), 3.67 (dq, $J = 9.6, 7.0$ Hz, 1 H), 2.63 (qt, $J = 7.2, 2.3$ Hz, 1 H), 2.20 (dt, $J = 13.8, 2.3$ Hz, 1 H), 1.78 (dd, $J = 13.8, 4.2$ Hz, 1 H), 1.71 (bs, 1 H), 1.42 (s, 3 H), 1.37 (s, 3 H), 1.30 (t, $J = 7.1$ Hz, 3 H), 1.16 (s, 3 H), 1.12 (s, 3 H), 0.97 (d, $J = 7.2$ Hz, 3 H); ^{13}C NMR (125 MHz, CD_3OD) δ 211.2, 165.8, 157.7, 134.5, 131.8, 130.6, 129.7, 107.6, 101.9, 78.4, 64.6, 53.4, 52.4, 47.2,

44.7, 36.8, 32.5, 26.9, 18.4, 18.0, 15.6, 14.5; LR-EIMS m/z (%): 77 (30), 105 (100), 122 (8), 136 (8), 149 (4), 177 (3), 192 (4), 221 (2), 248 (6), 312 (4), 398 (0.2) [M^+].



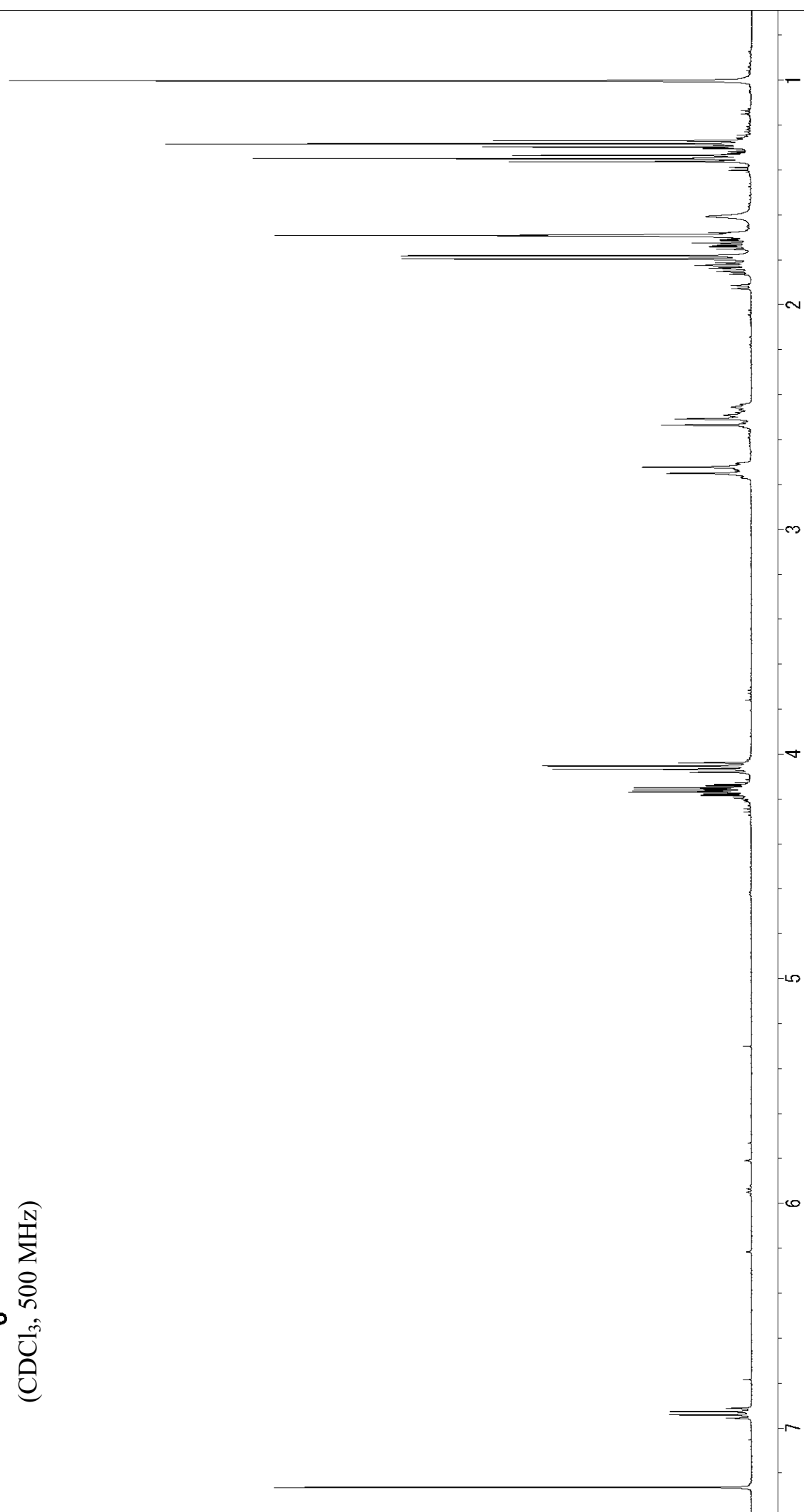
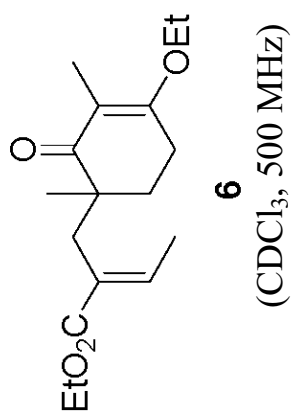
3-Benzoyl-4-ethoxy-1,5,6exo,10,10-pentamethyl-11-oxabicyclo[3.3.1.2^{7.4}]undeca-2,9-dione (15).

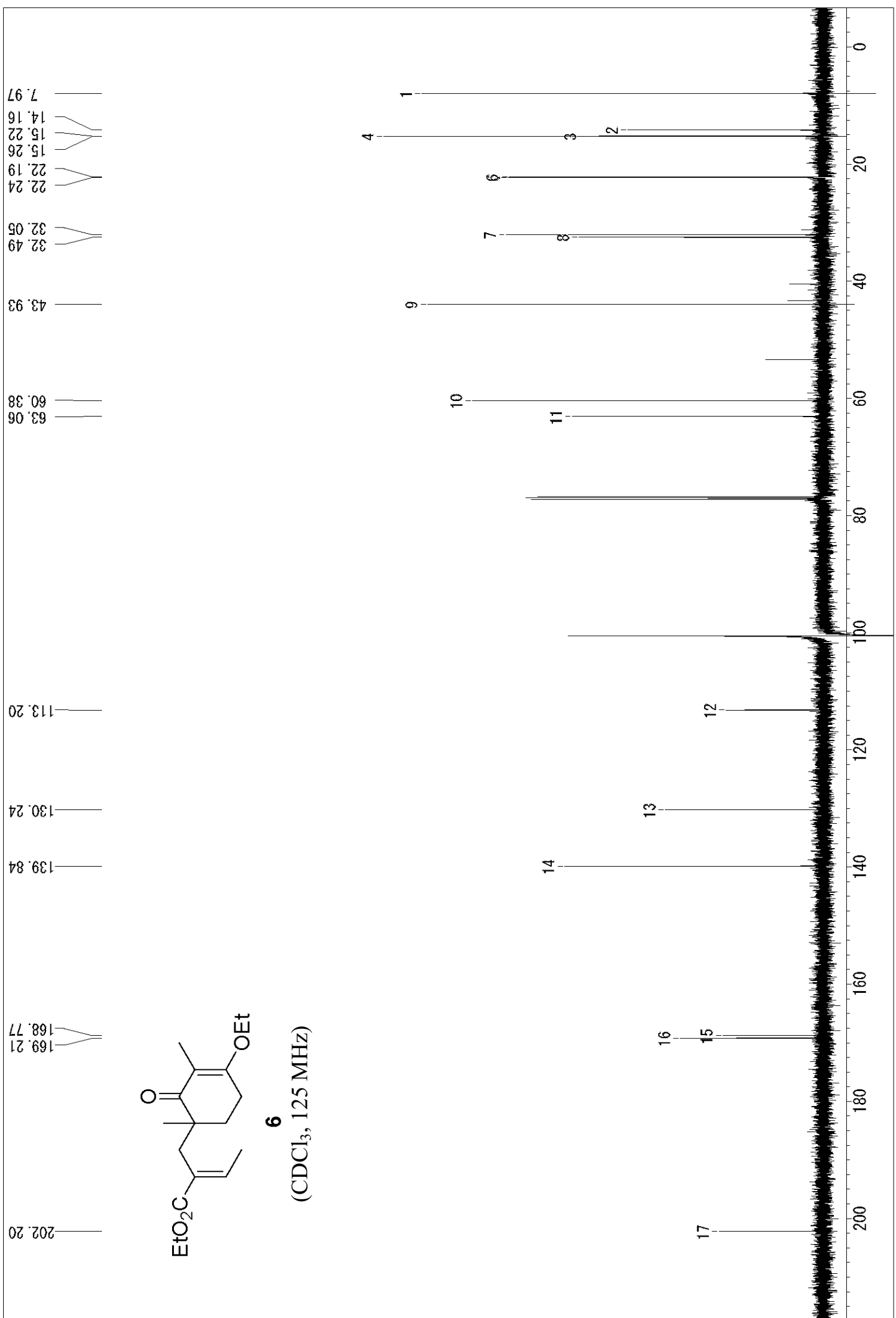
major isomer: ^1H NMR (500 MHz, CD_3OD) δ 8.08-8.03 (m, 2 H), 7.70-7.64 (m, 1 H), 7.56-7.49 (m, 2 H), 5.95 (s, 1 H), 3.75 (dq, $J = 9.3, 7.0$ Hz, 1 H), 3.56 (dq, $J = 9.3, 7.0$ Hz, 1 H), 2.71 (dt, $J = 14.8, 1.8$ Hz, 1 H), 2.42 (qt, $J = 7.3, 1.8$ Hz, 1 H), 1.92 (dd, $J = 14.8, 6.5$ Hz, 1 H), 1.68-1.65 (m, 1 H), 1.52 (s, 3 H), 1.32 (s, 3 H), 1.14 (t, $J = 7.0$ Hz, 3 H), 1.12 (s, 3 H), 1.09 (s, 3 H), 0.91 (d, $J = 7.4$ Hz, 3 H); detectable signals: ^{13}C NMR (125 MHz, CD_3OD) δ 211.3, 169.6, 165.9, 151.3, 135.3, 135.2, 131.1, 130.9, 130.4, 130.0, 128.9, 119.6, 77.0, 64.9, 59.5, 57.4, 54.8, 50.2, 44.9, 41.3, 38.8, 32.2, 30.8, 27.3, 17.2, 16.0, 14.9, 14.8; HR-EIMS m/z : calcd for $\text{C}_{24}\text{H}_{30}\text{O}_5$ [M^+] 398.2093, found 398.2099.

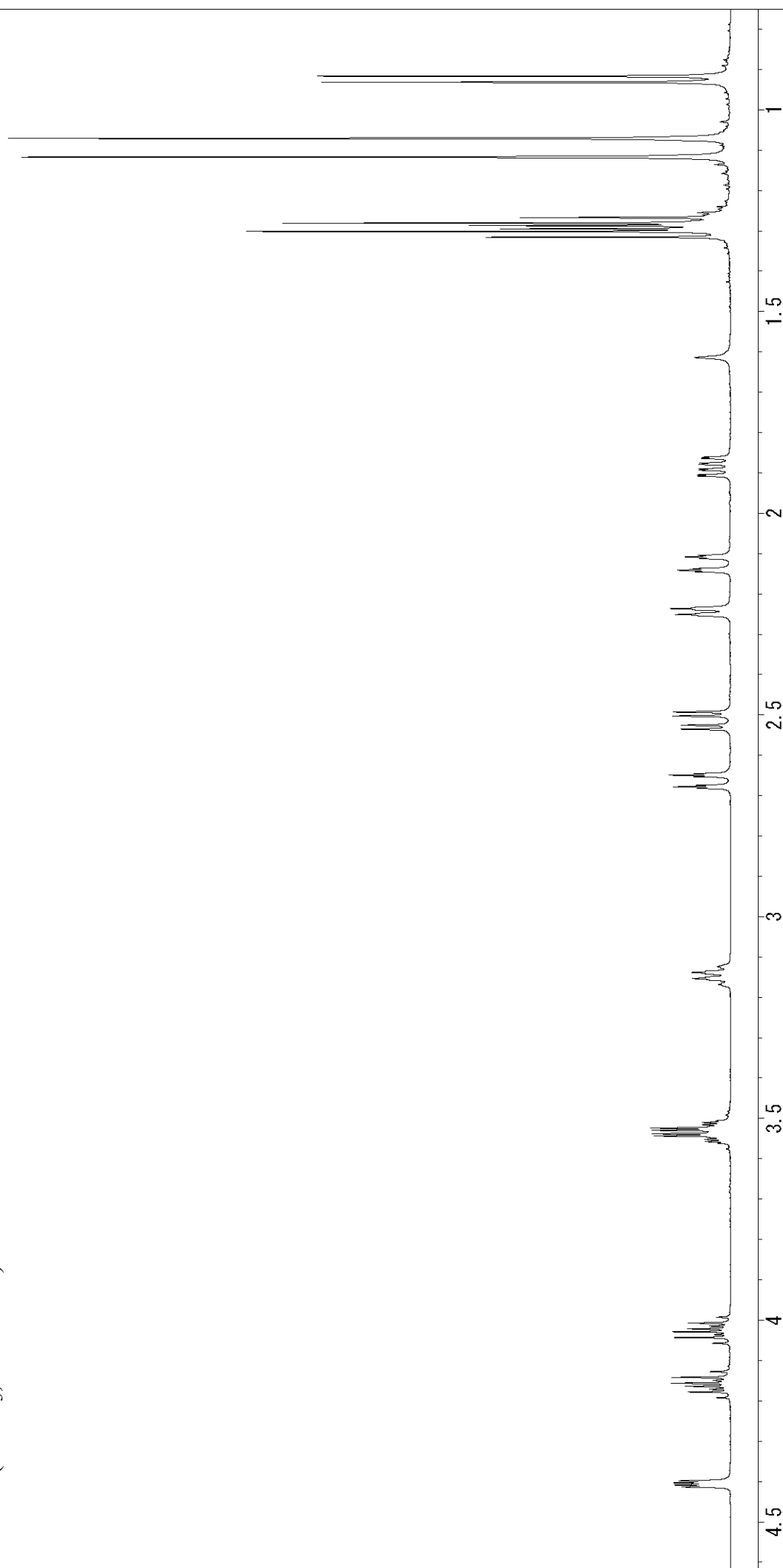
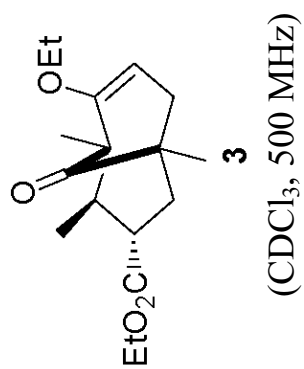


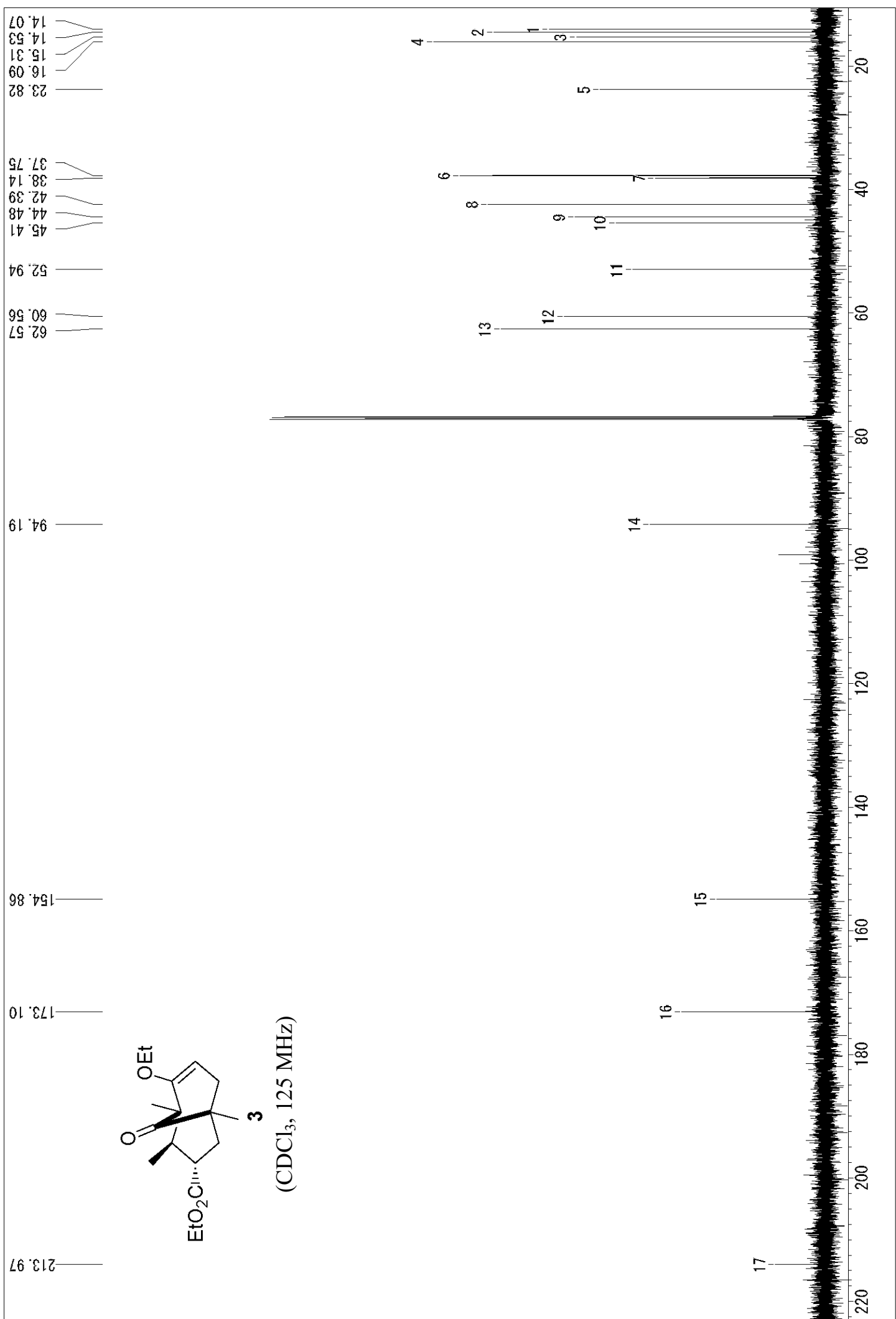
4-Ethoxy-1,5,6exo,10,10-pentamethyl-11-oxabicyclo[3.3.1.2^{7.4}]undeca-2,9-dione (16).

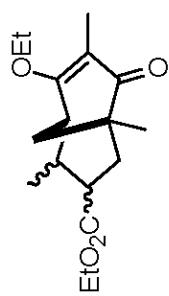
^1H NMR (500 MHz, CD_3OD) δ 3.73 (bq, $J = 9.3, 7.0$ Hz, 1 H), 3.55 (bq, $J = 9.3, 7.0$ Hz, 1 H), 2.78 (d, $J = 14.6$ Hz, 1 H), 2.77 (qt, $J = 7.2, 1.2$ Hz, 1 H), 2.31 (ddd, $J = 15.0, 2.0, 1.2$ Hz, 1 H), 2.24 (d, $J = 14.6$ Hz, 1 H), 1.86 (dd, $J = 15.0, 5.9$ Hz, 1 H), 1.55 (ddd, $J = 5.9, 2.0, 1.2$ Hz, 1 H), 1.39 (s, 3 H), 1.18 (s, 3 H), 1.16 (s, 3 H), 1.13 (t, $J = 7.0$ Hz, 3 H), 1.09 (s, 3 H), 0.87 (d, $J = 7.2$ Hz, 3 H); ^{13}C NMR (125 MHz, CD_3OD) δ 213.5, 207.4, 100.0, 76.4, 61.3, 58.7 (x2), 51.9, 44.5, 40.7, 38.5, 29.0, 28.1, 18.3, 15.7, 15.4, 15.1; LR-EIMS m/z (%): 69 (100), 83 (87), 153 (67), 182 (64), 219 (40), 248 (31), 276 (17), 294 (10) [M^+].





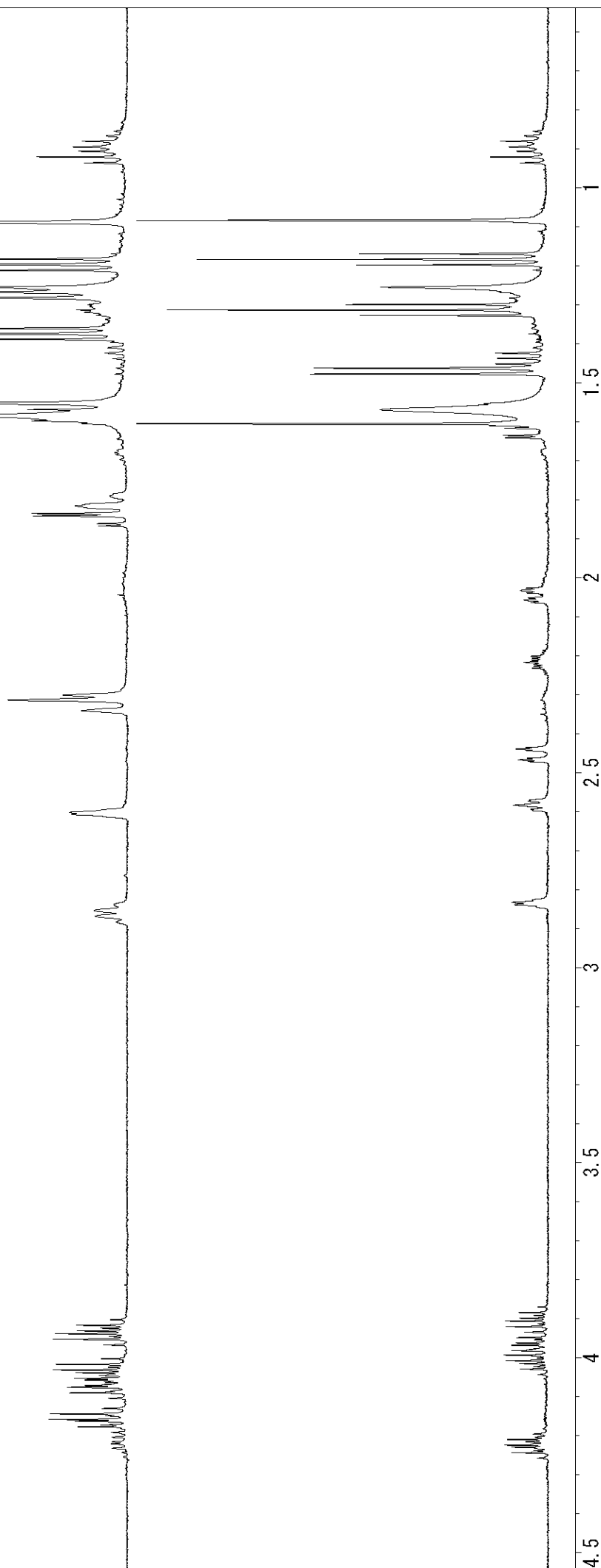


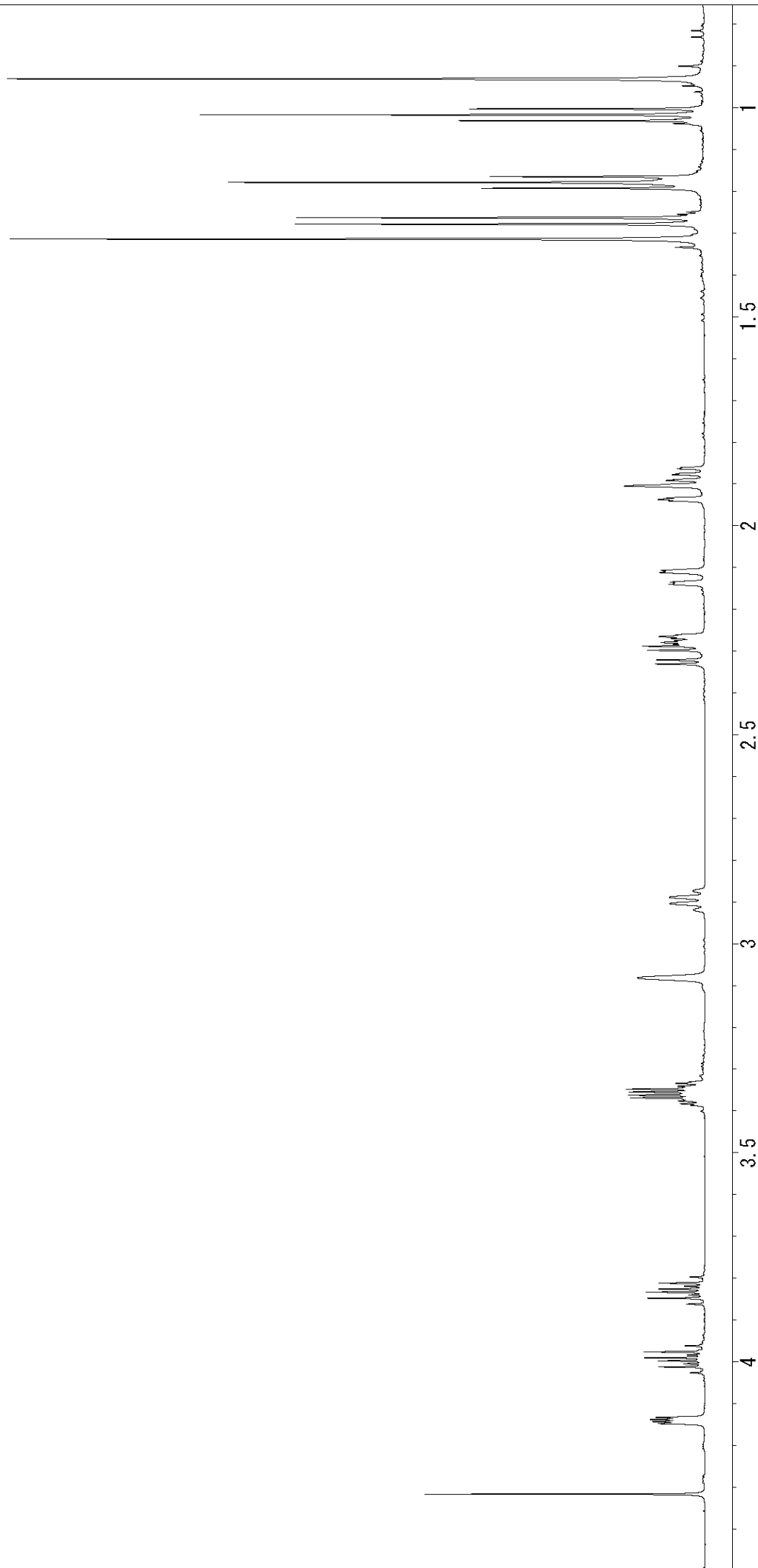


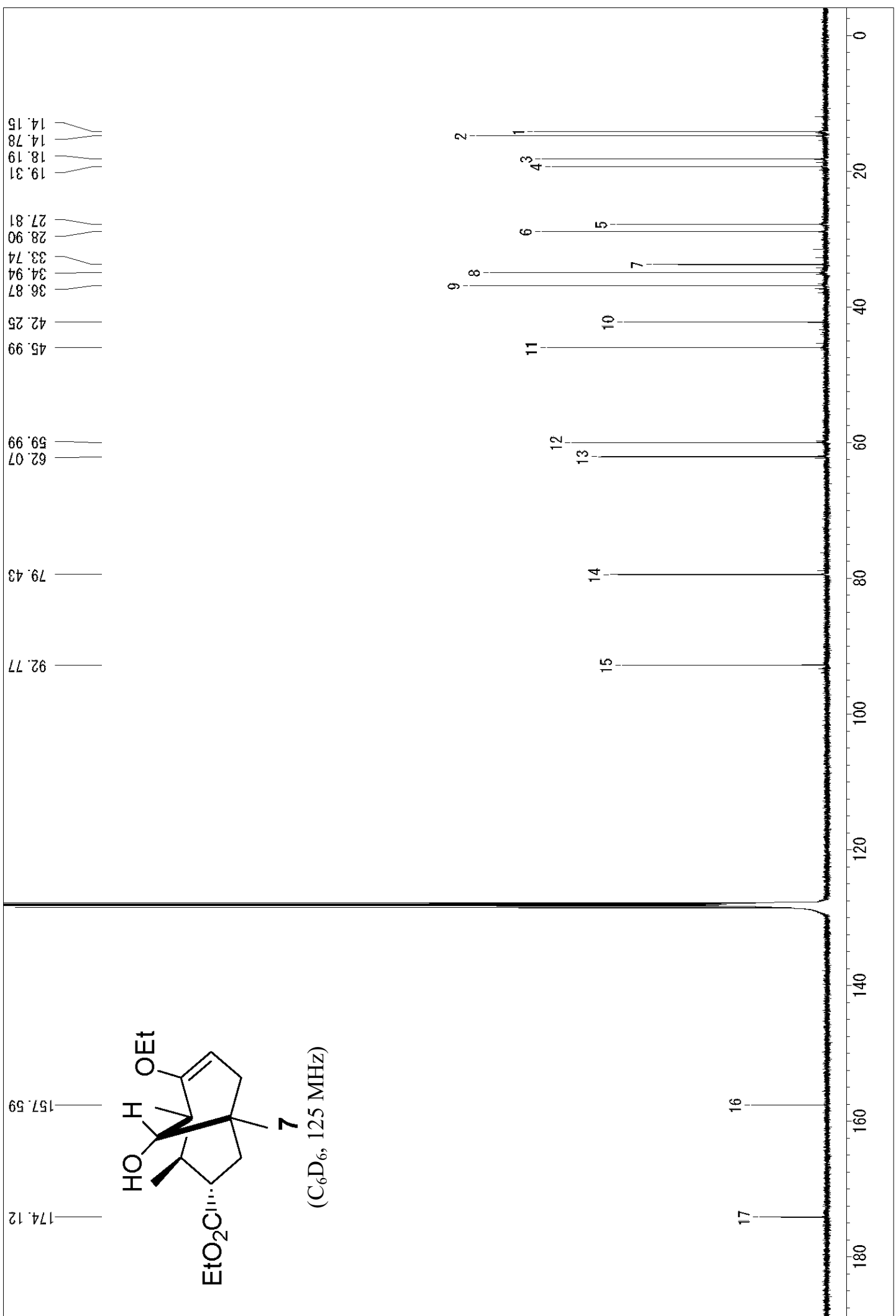


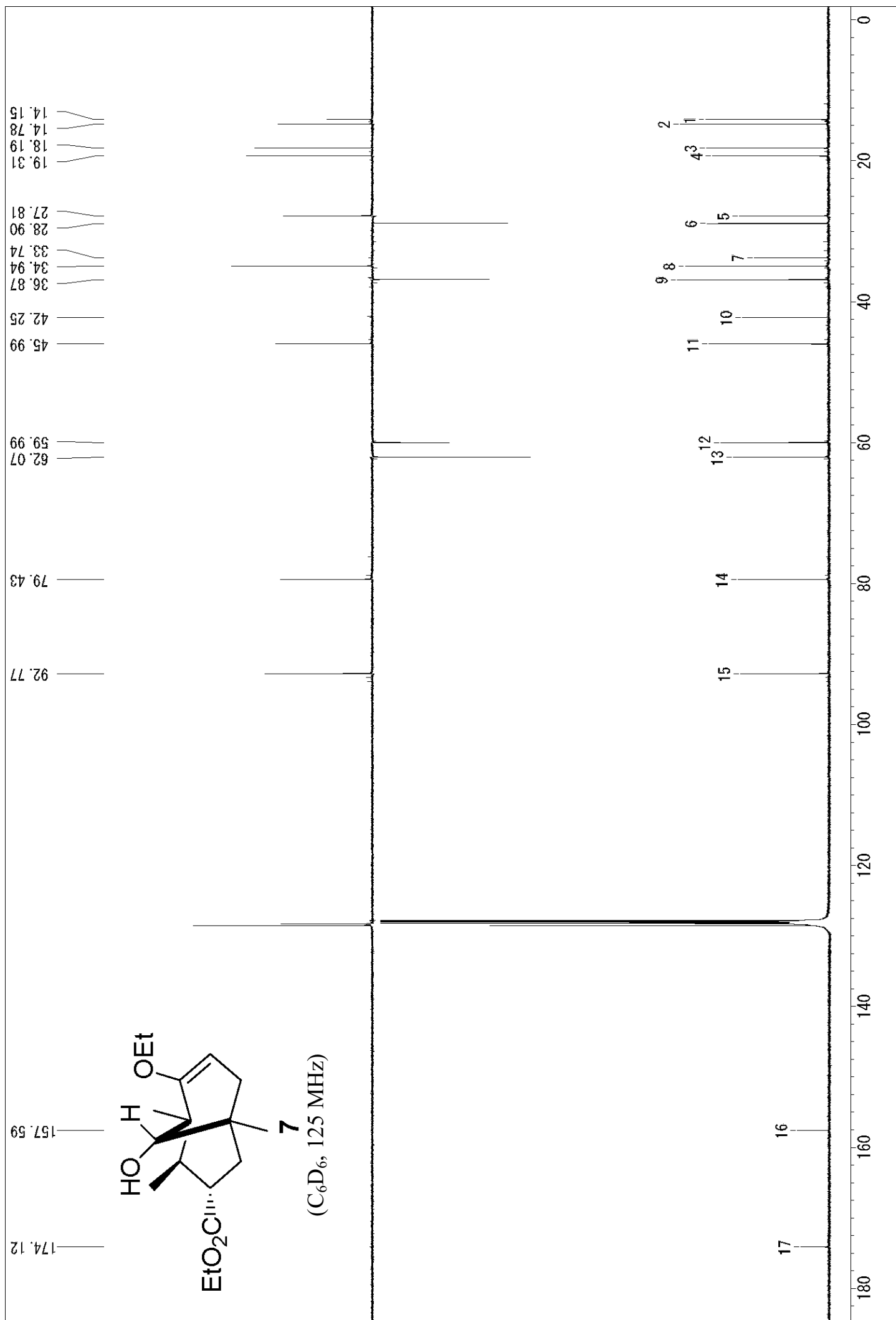
γ -3

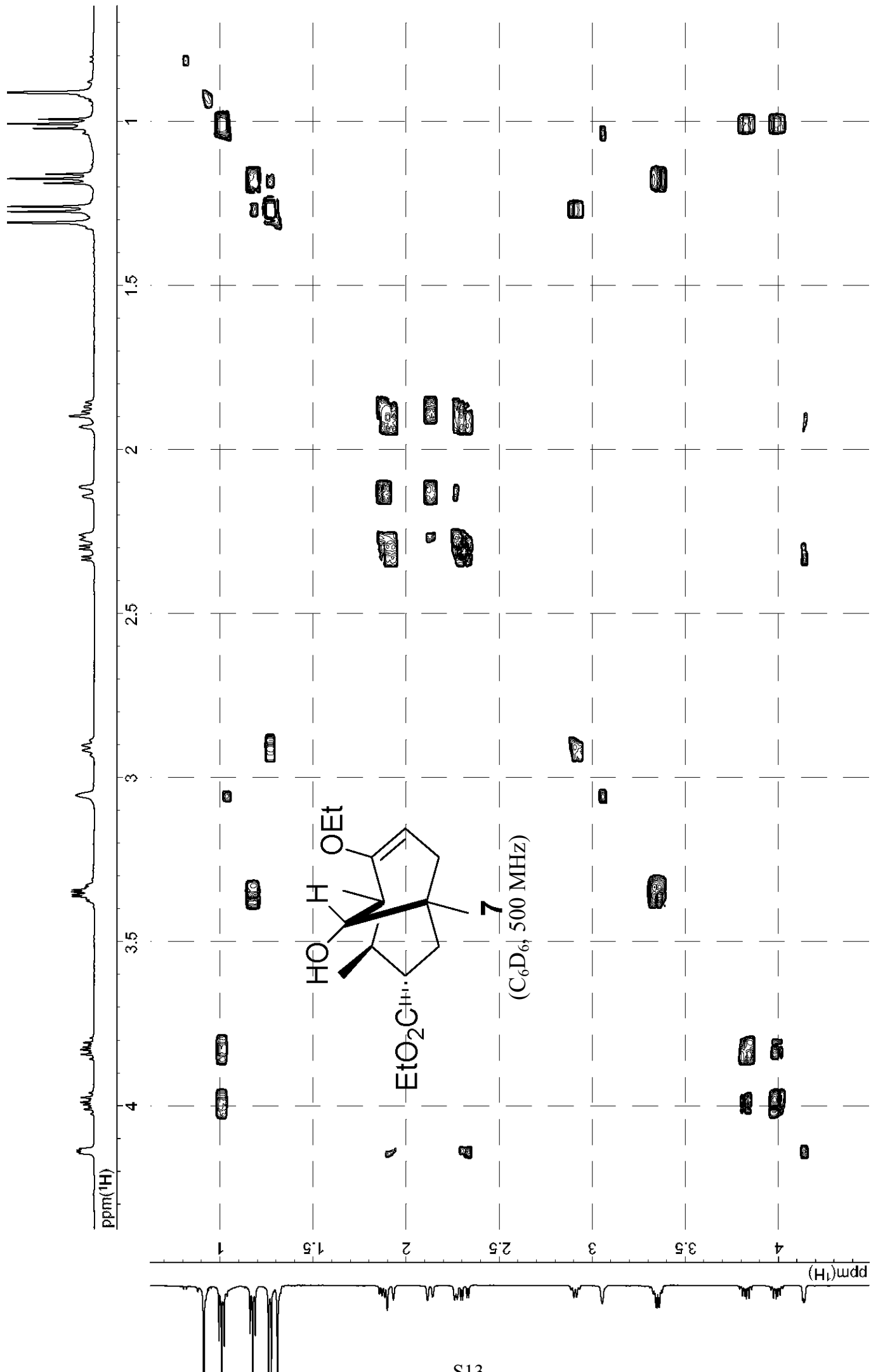
(CDCl₃, 500 MHz)

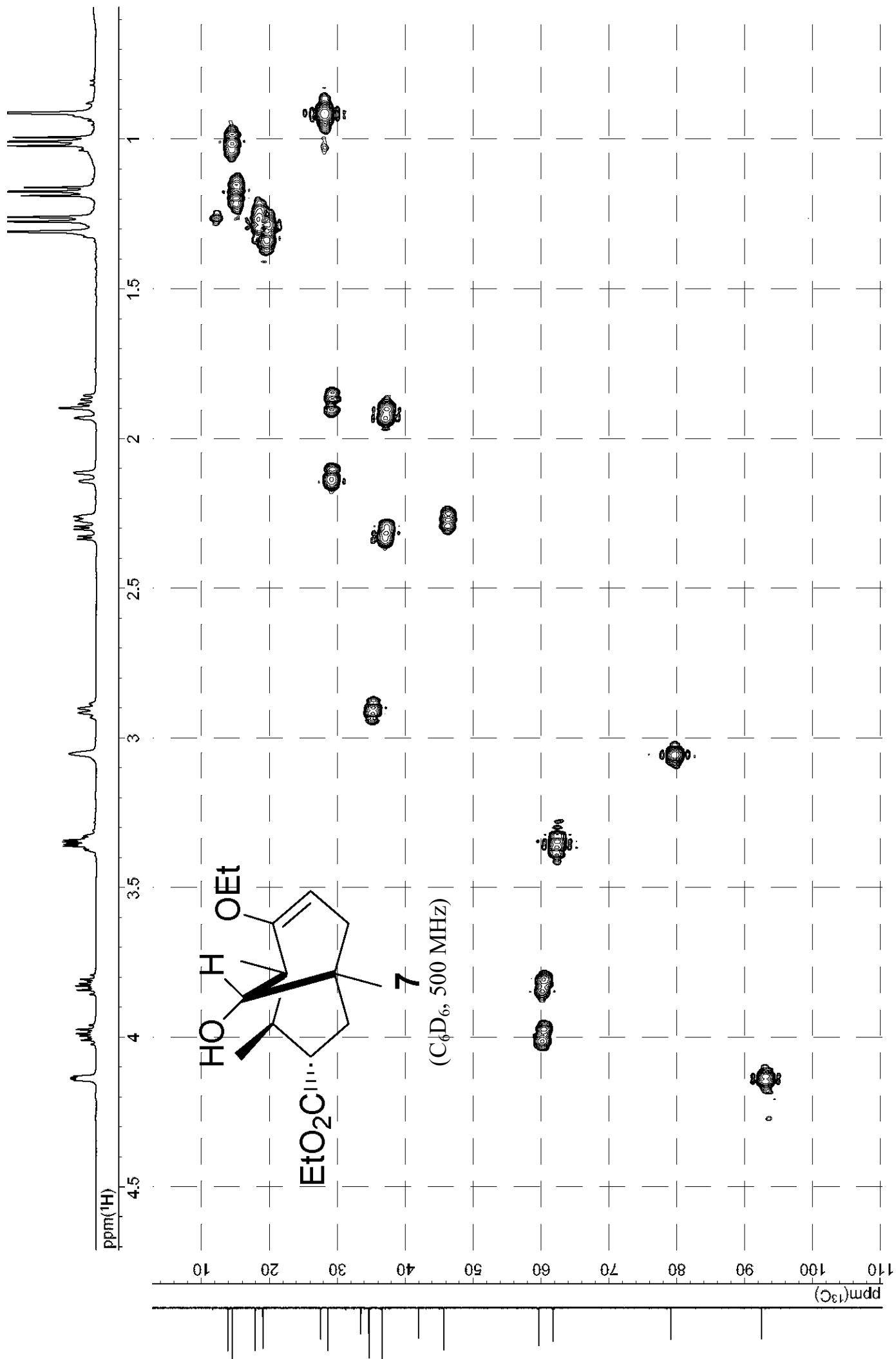


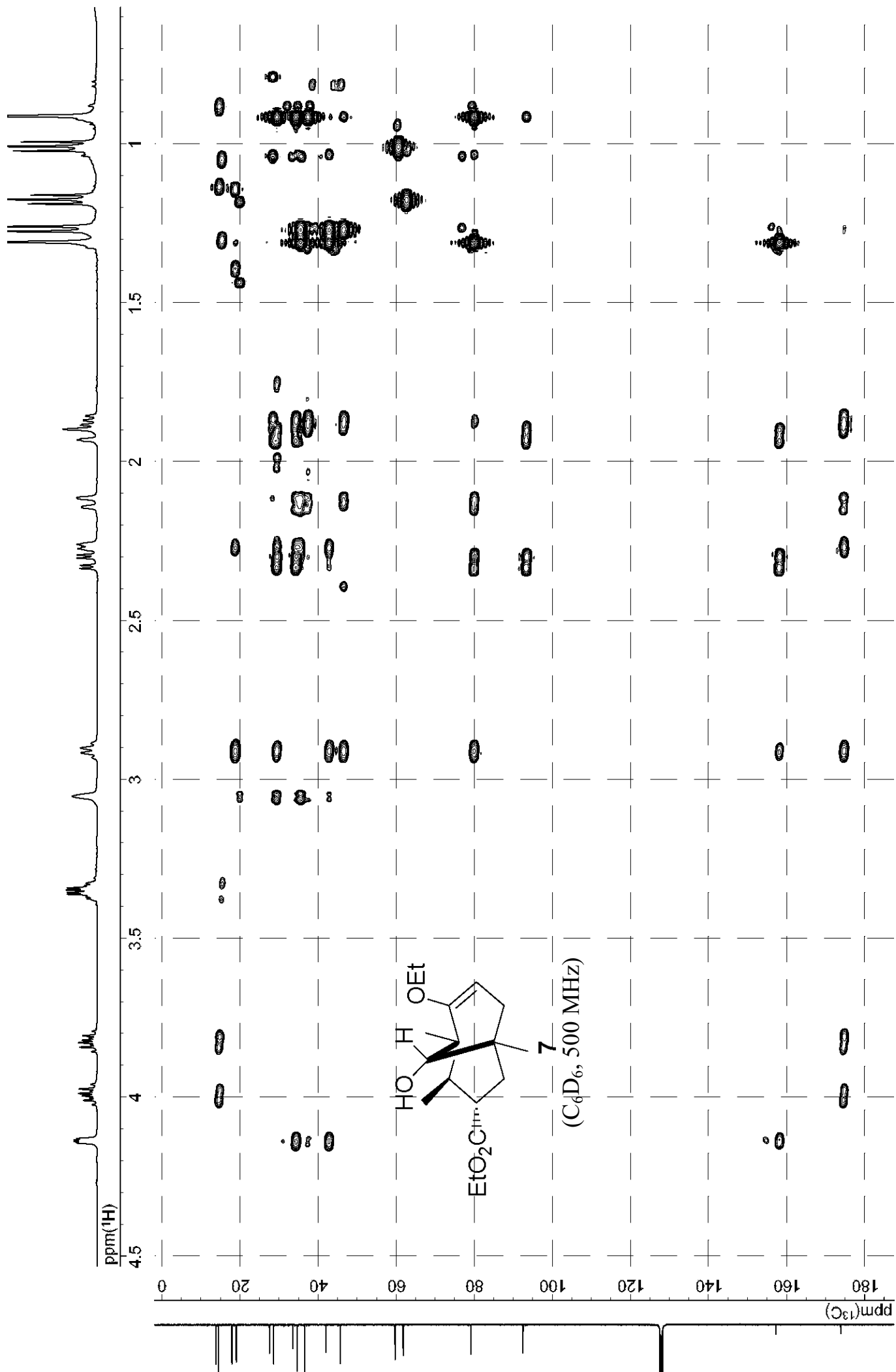


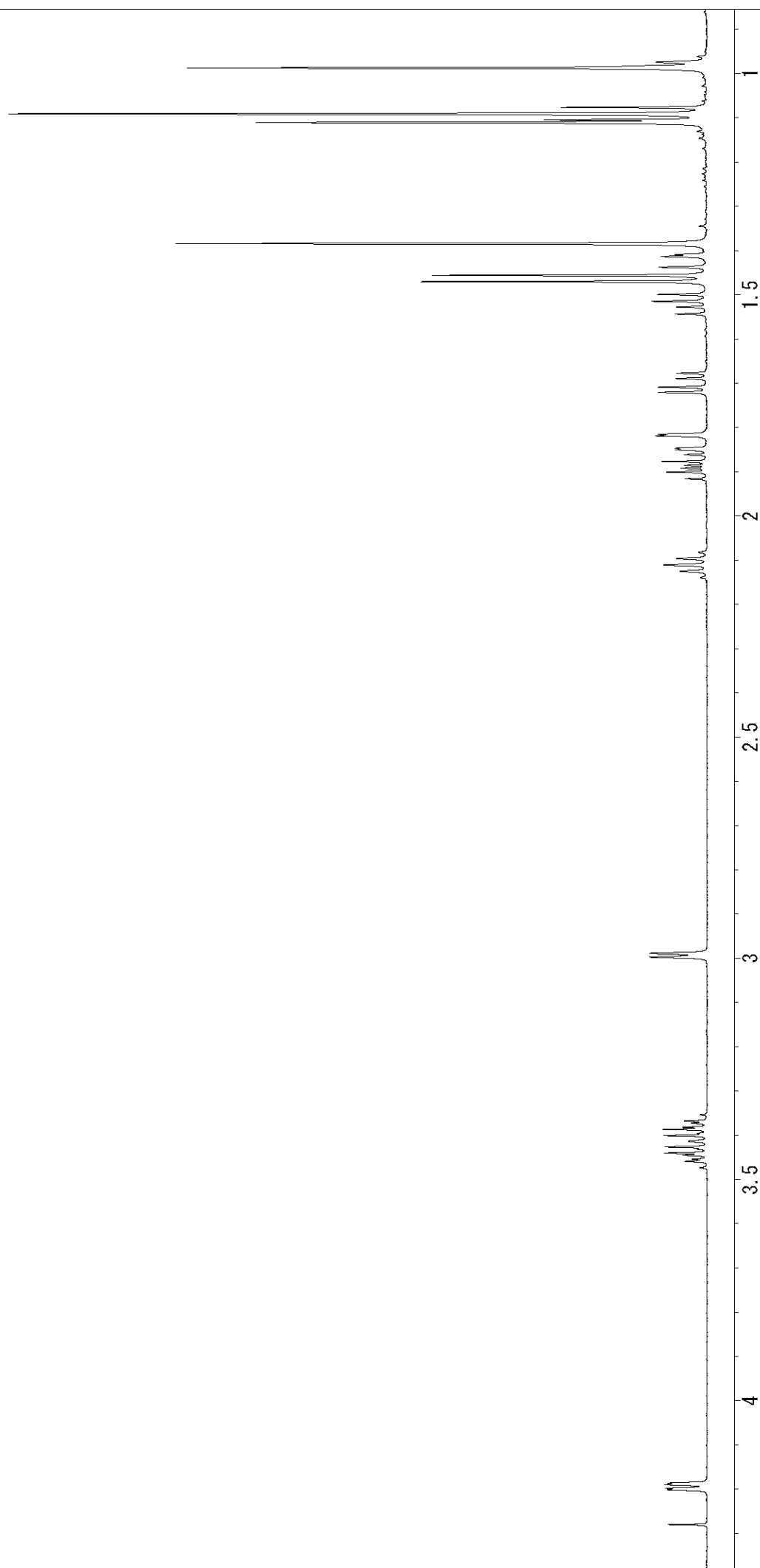
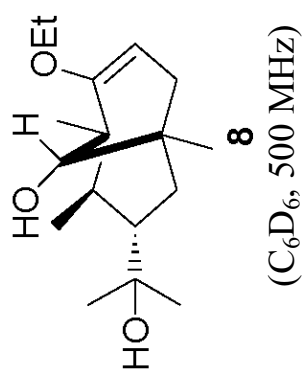


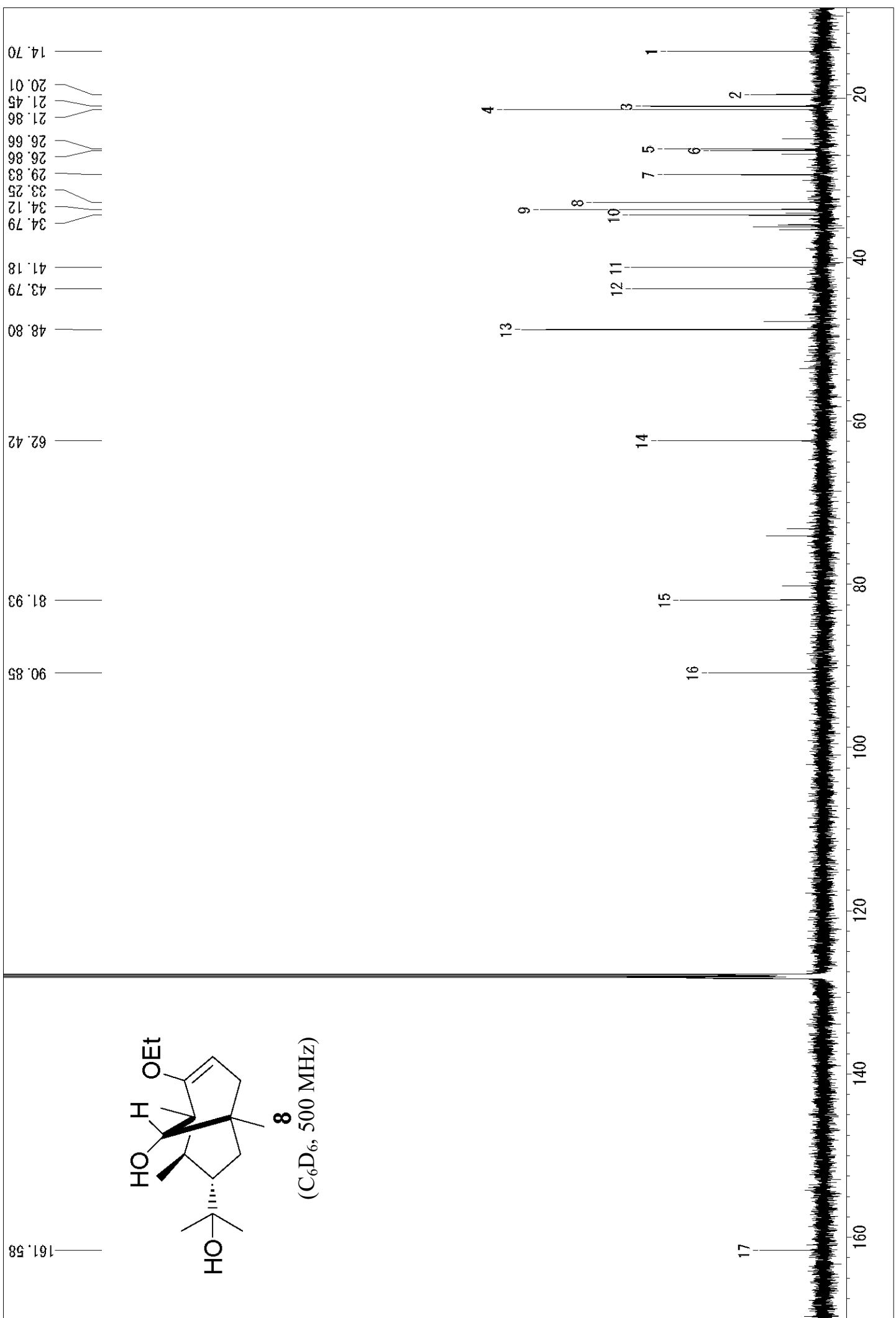


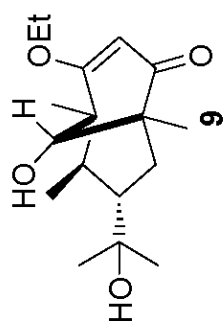




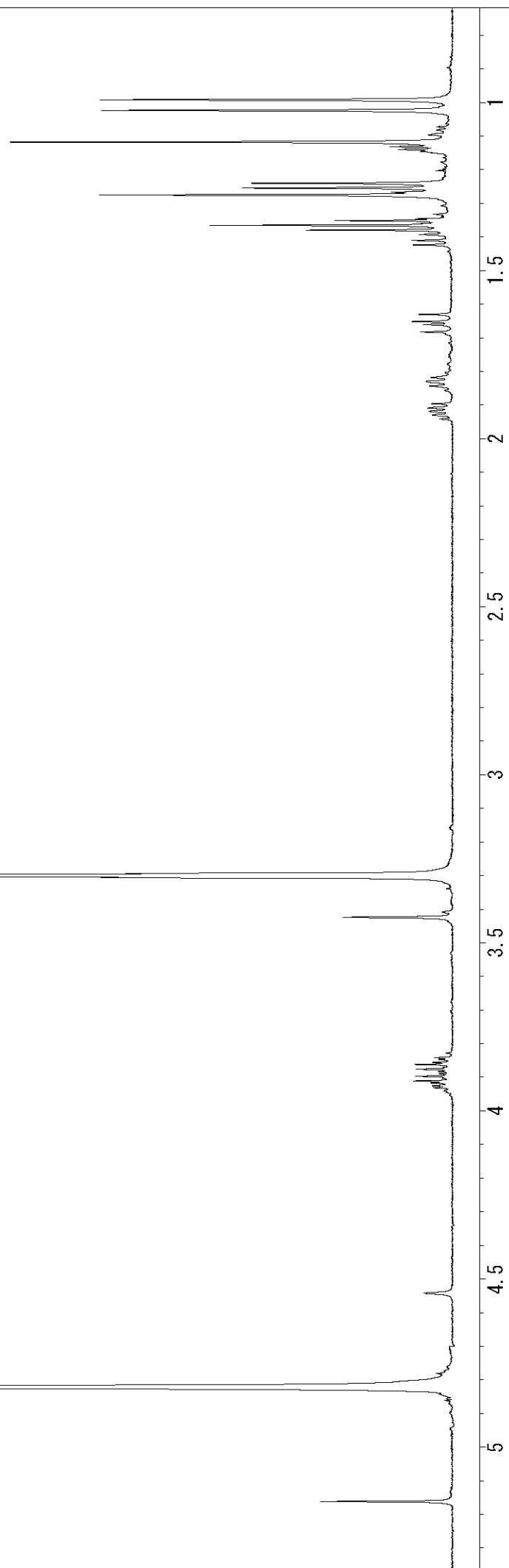


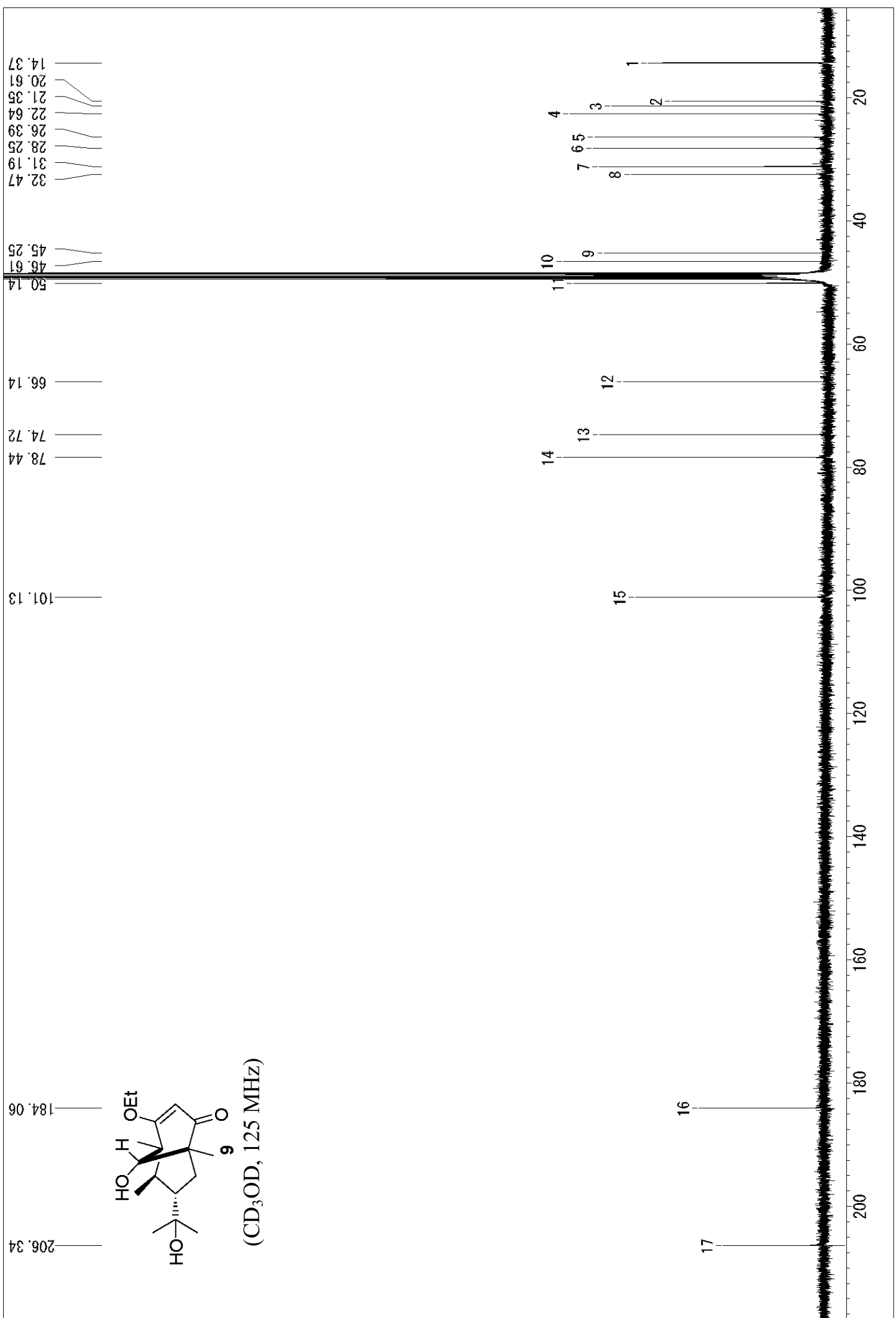




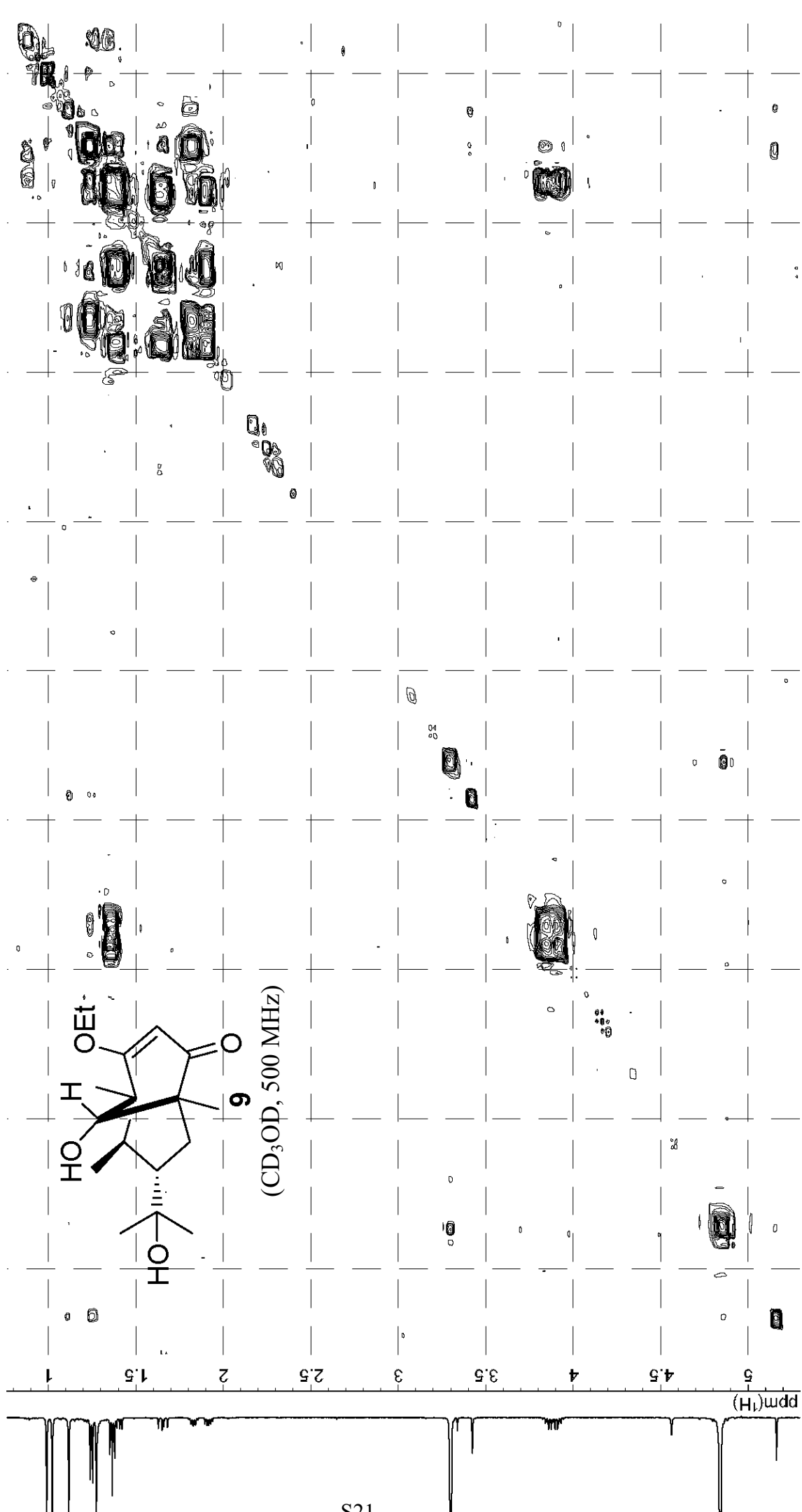


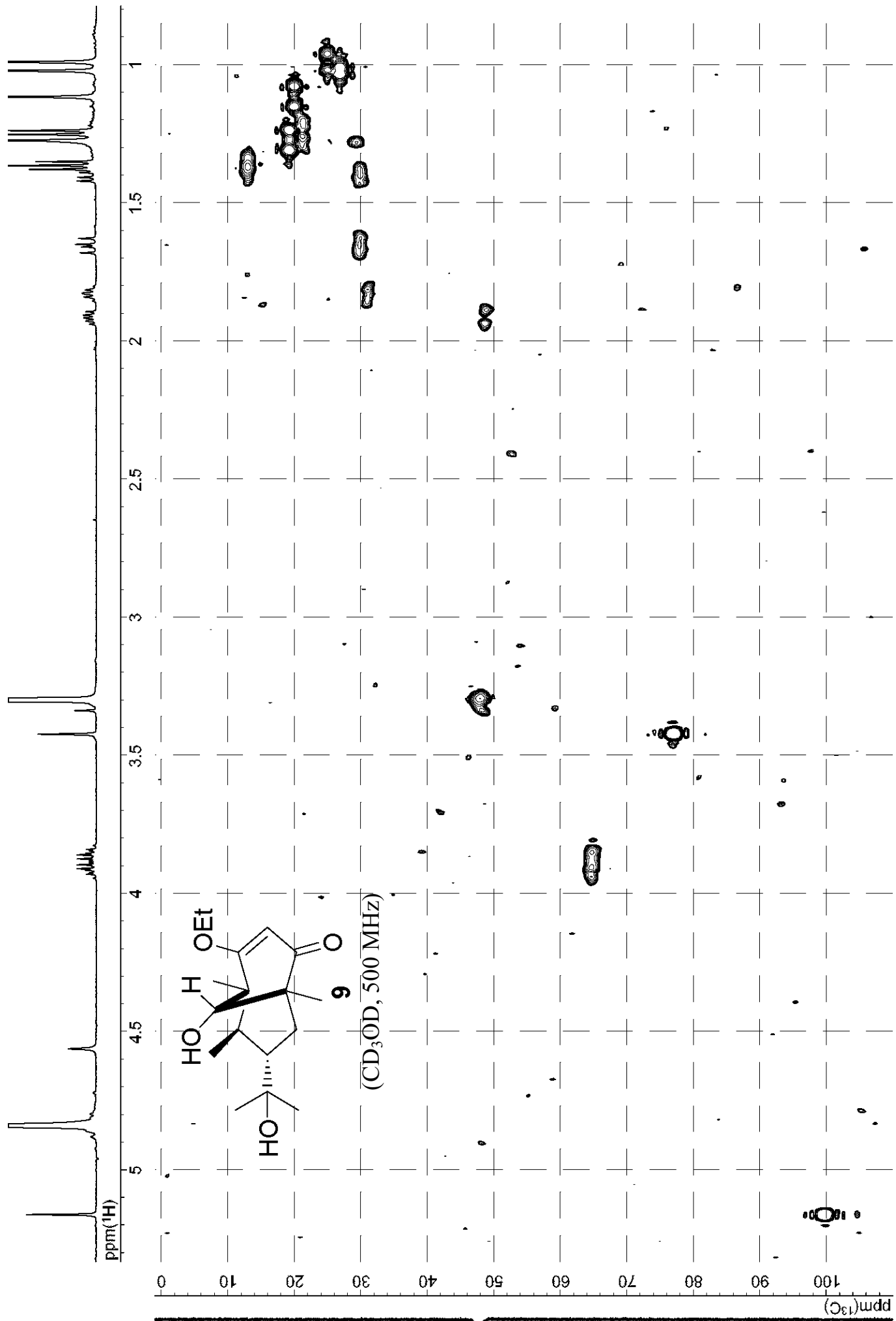
(CD₃OD, 500 MHz)

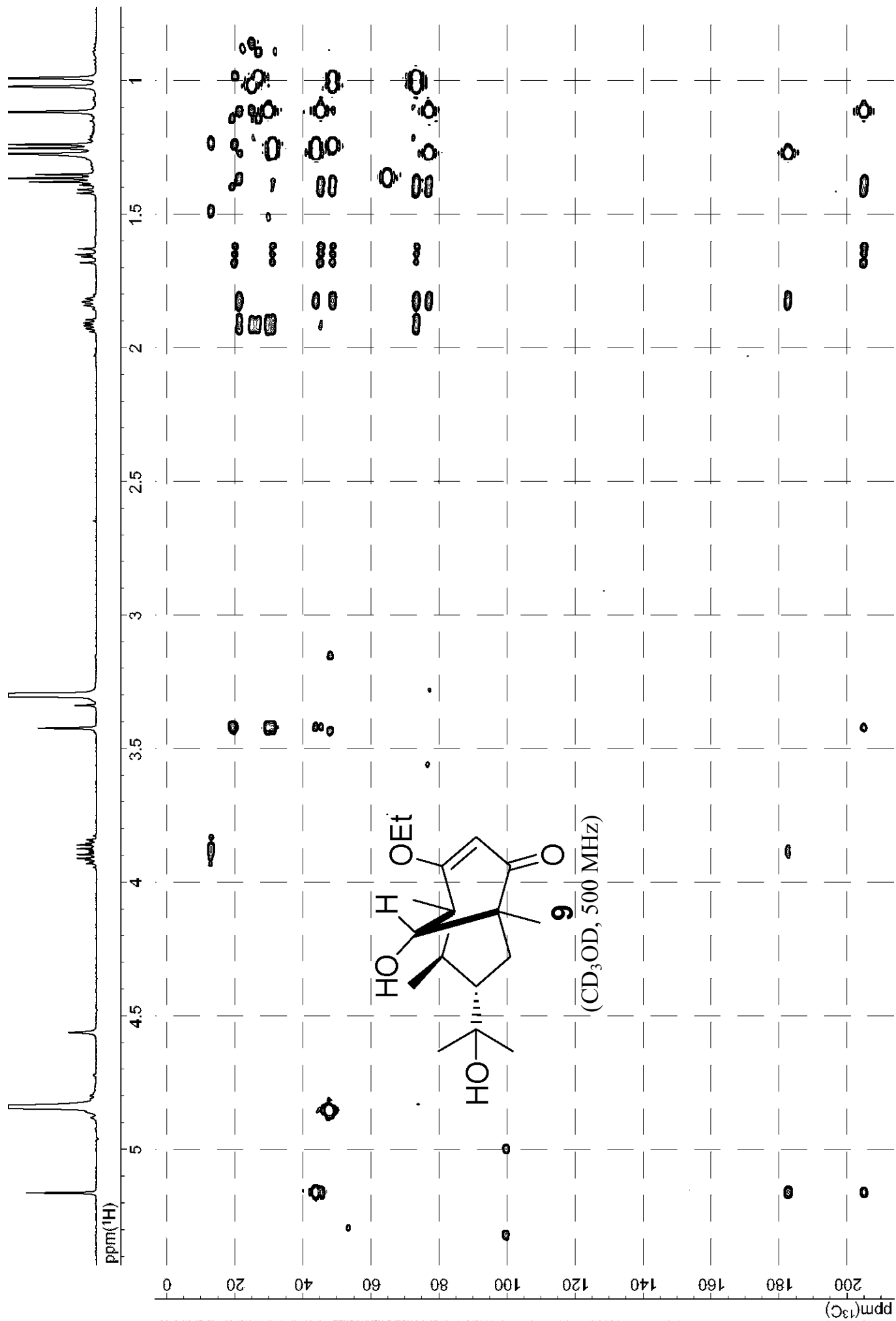


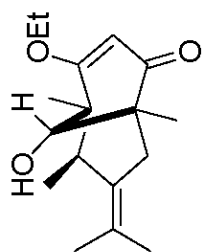












11

(CD₃OD, 500 MHz)

11

decomposed compound of THF by HCl

11+decomposed compound of THF

4

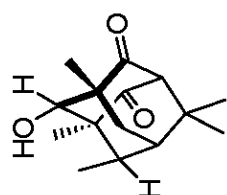
1.5

2

2.5

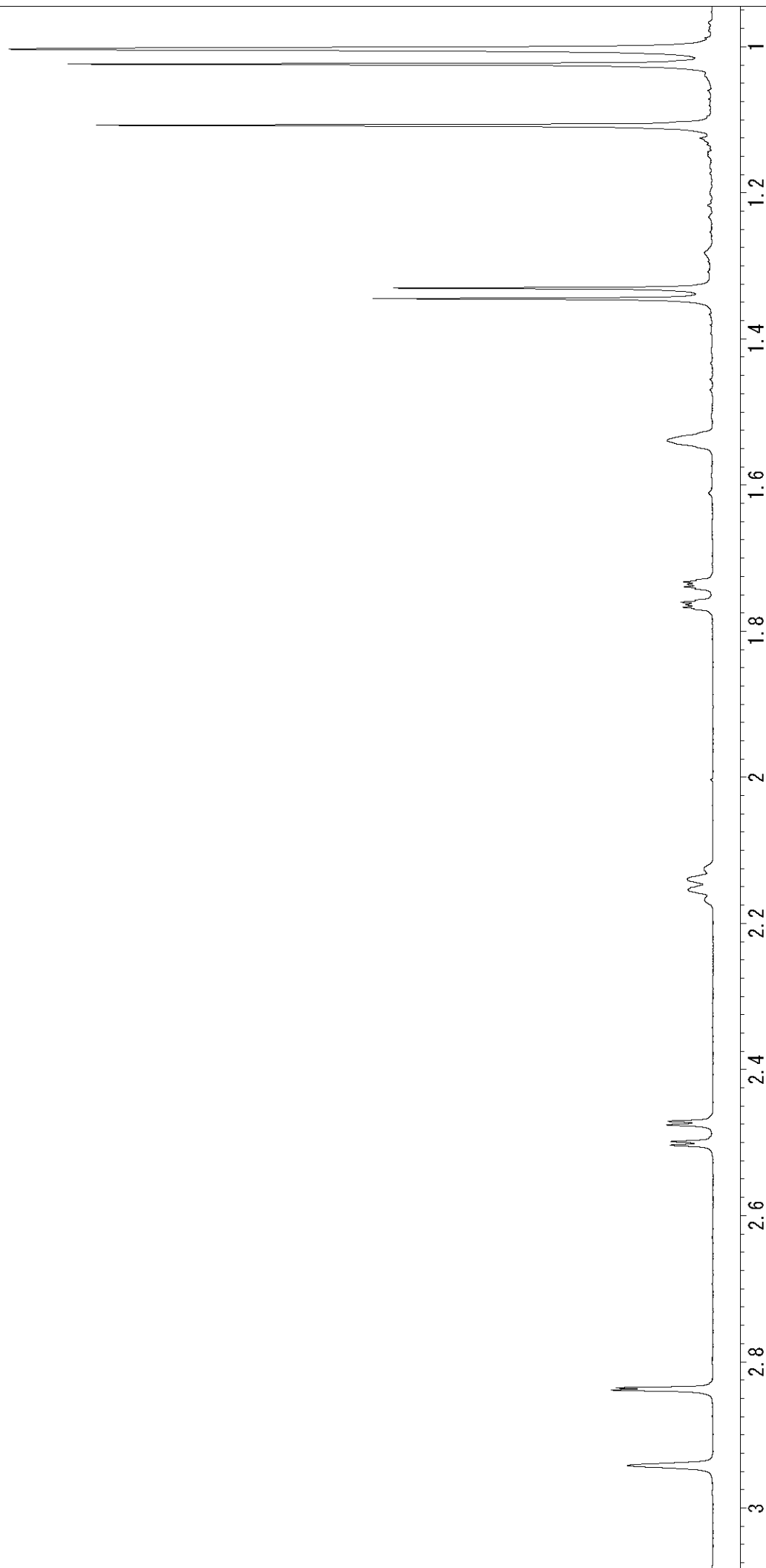
3

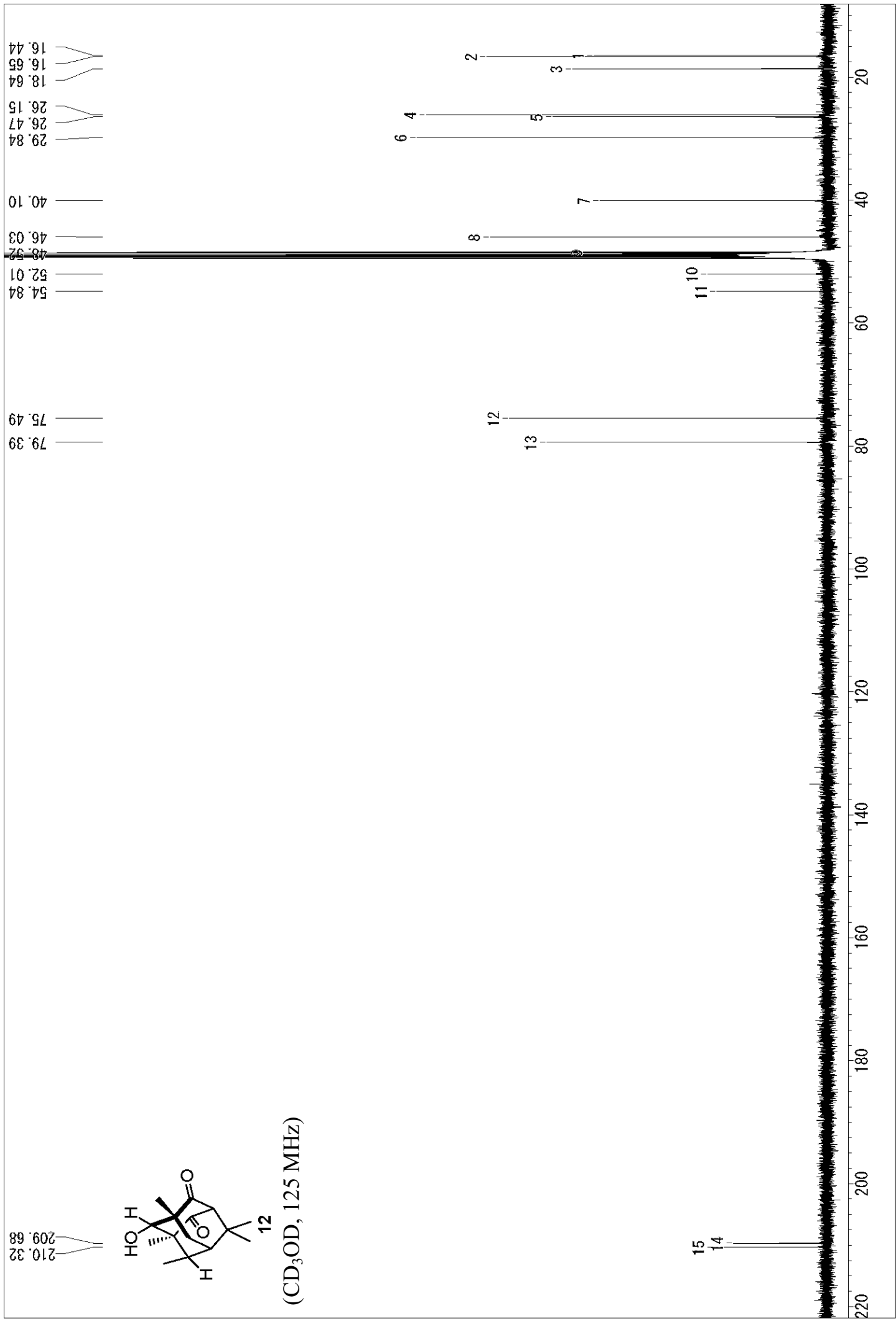
3.5

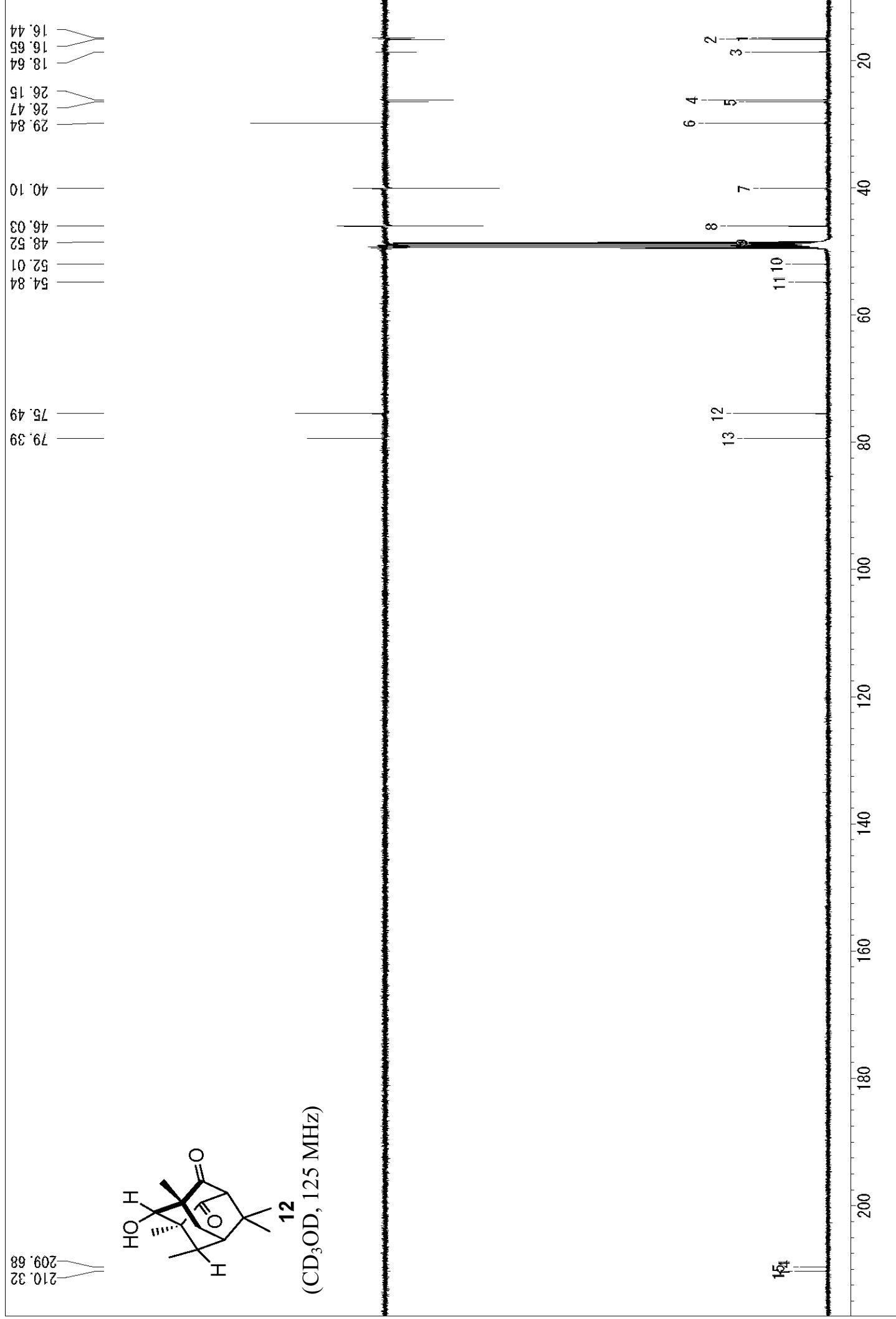


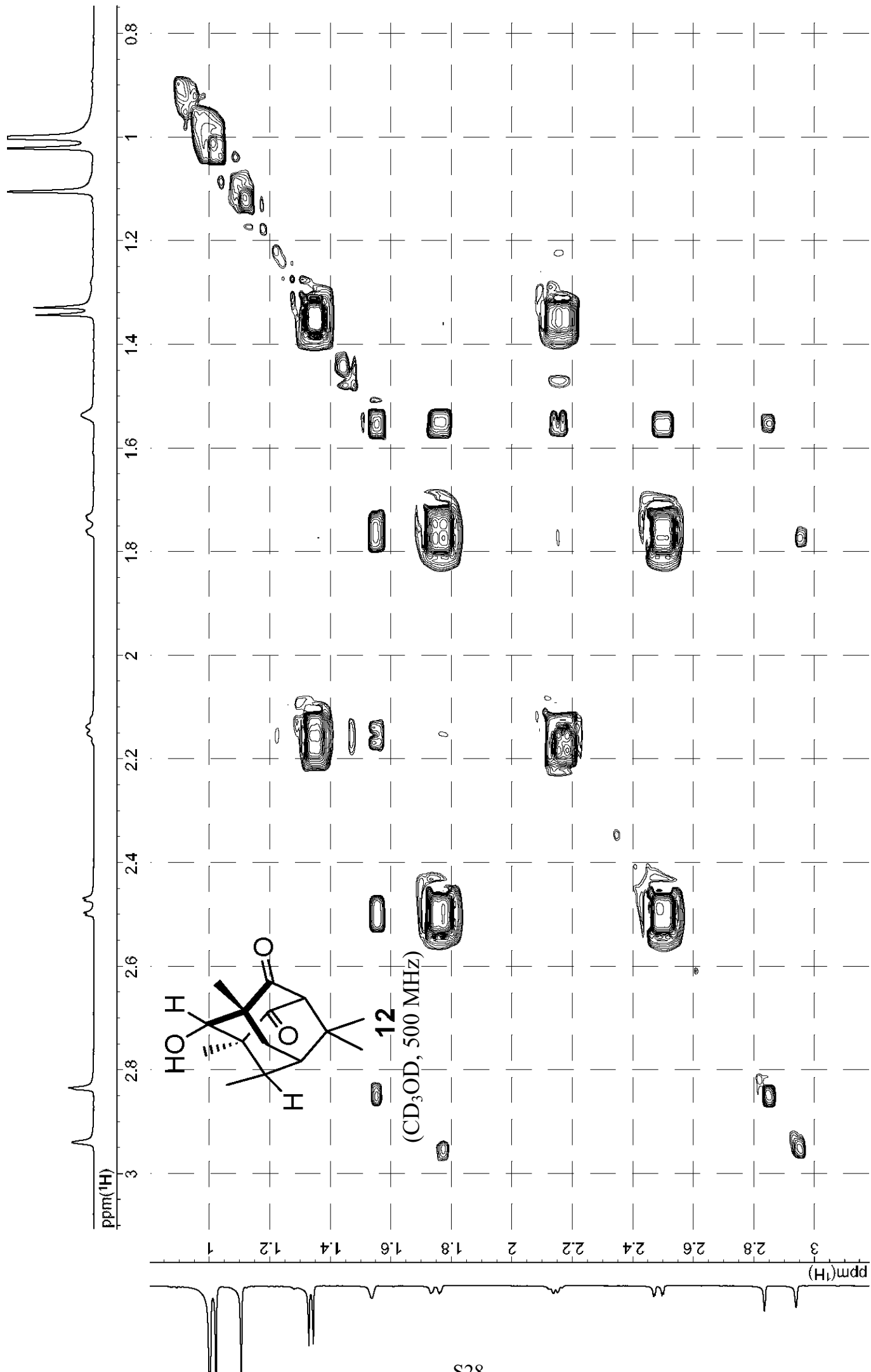
12

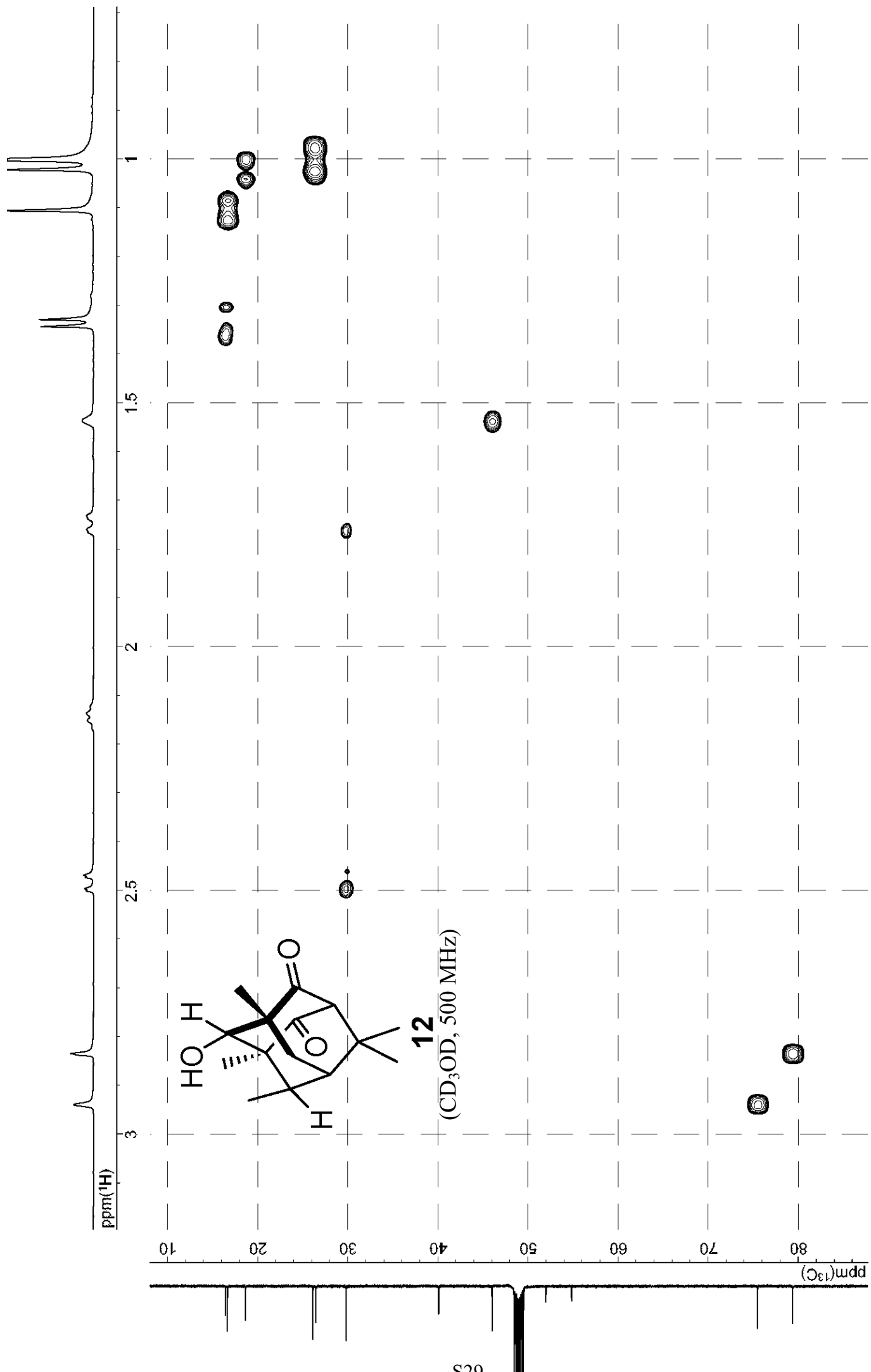
(CD₃OD, 500 MHz)

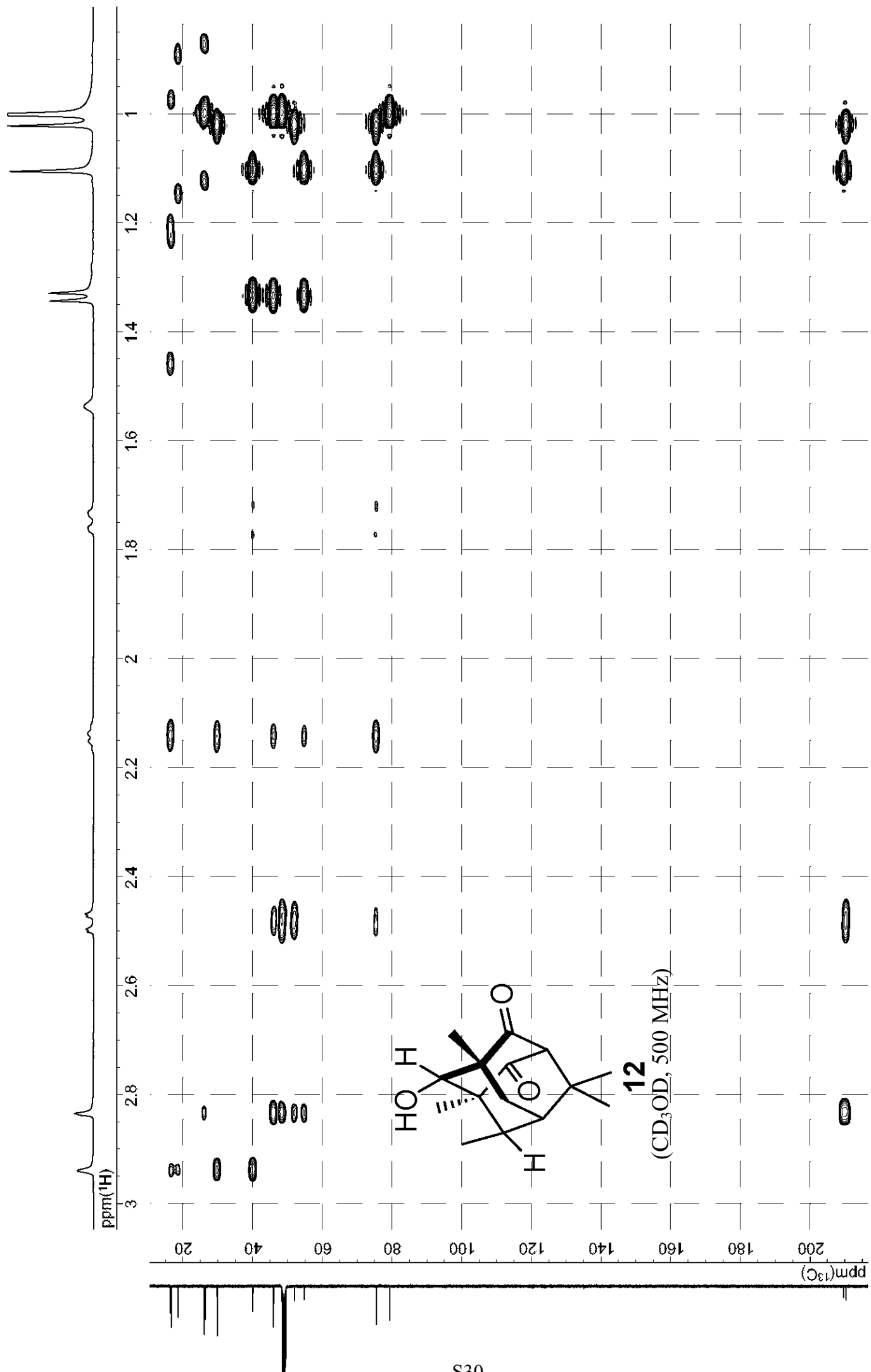


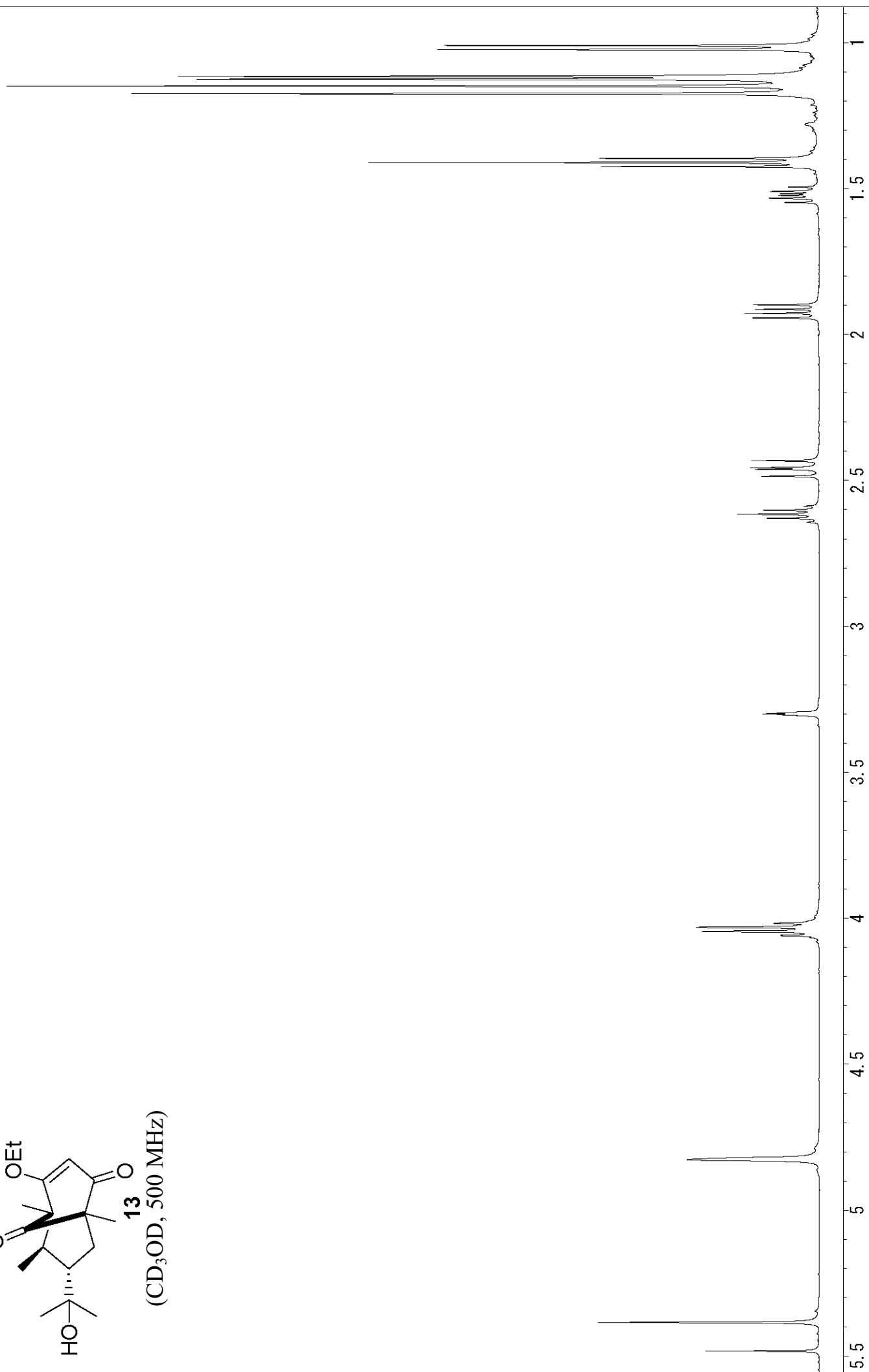
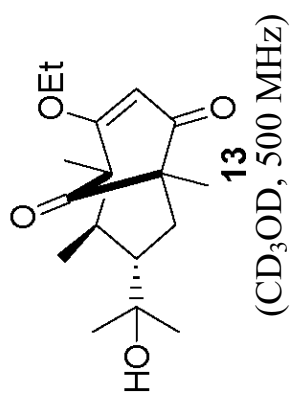


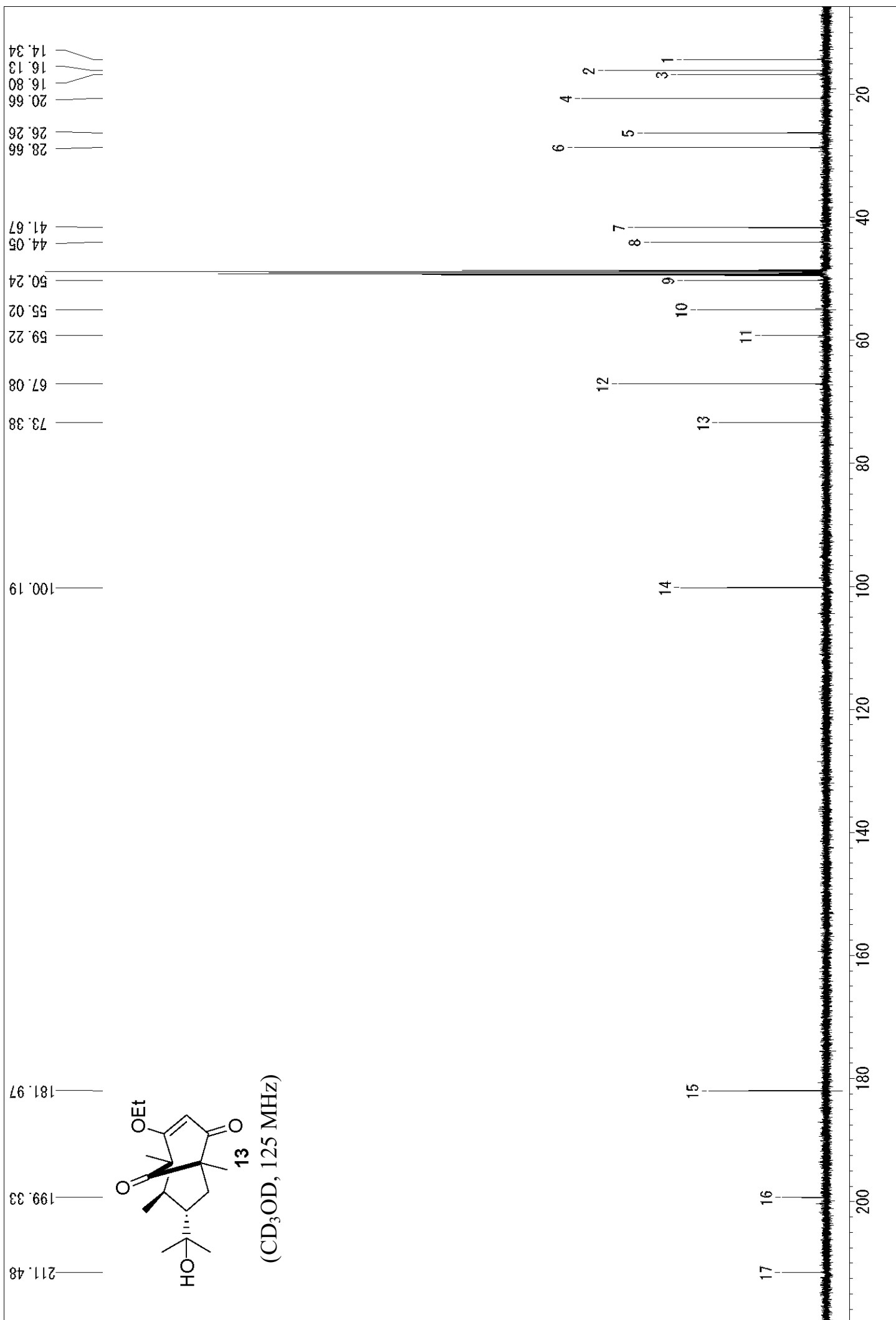




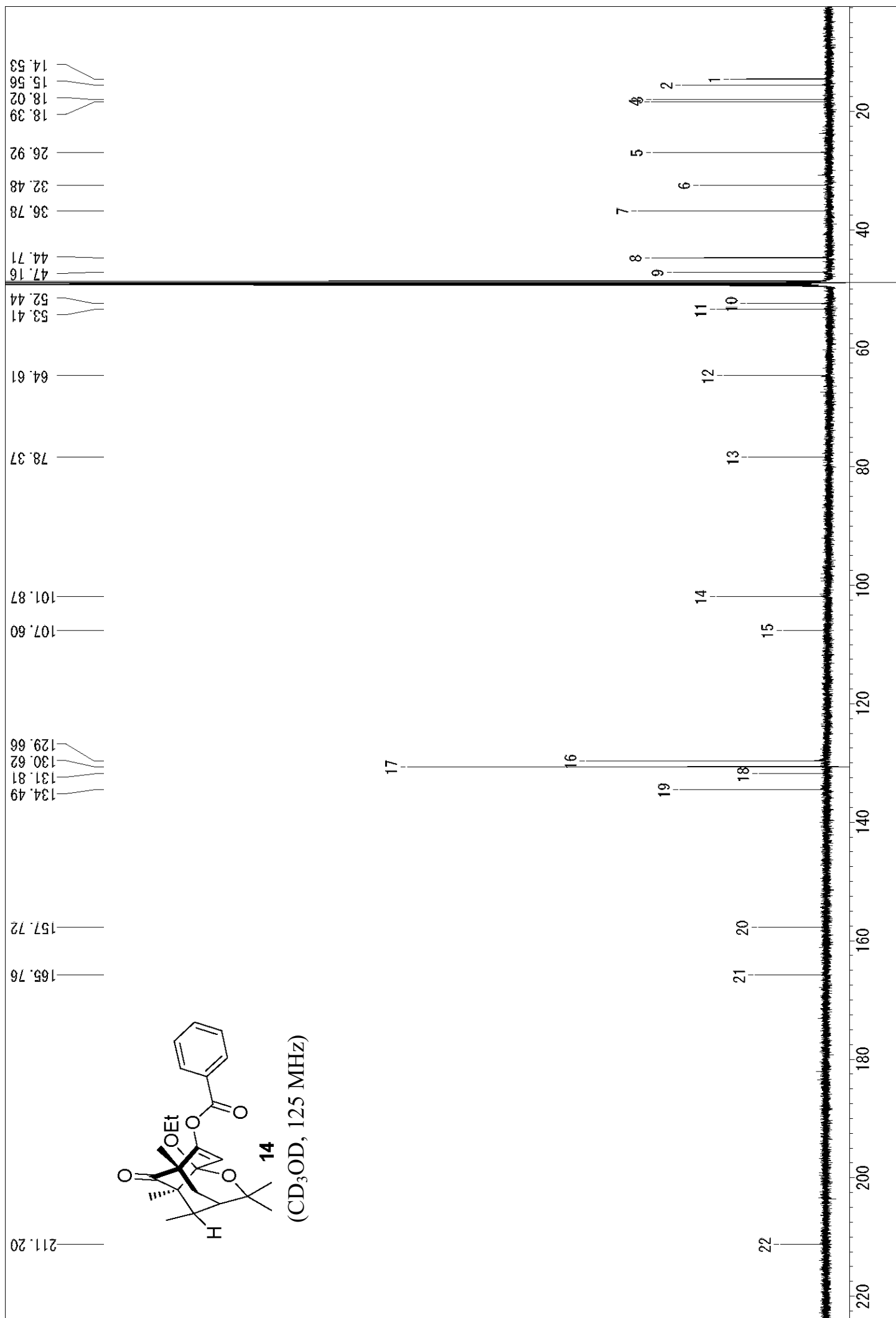


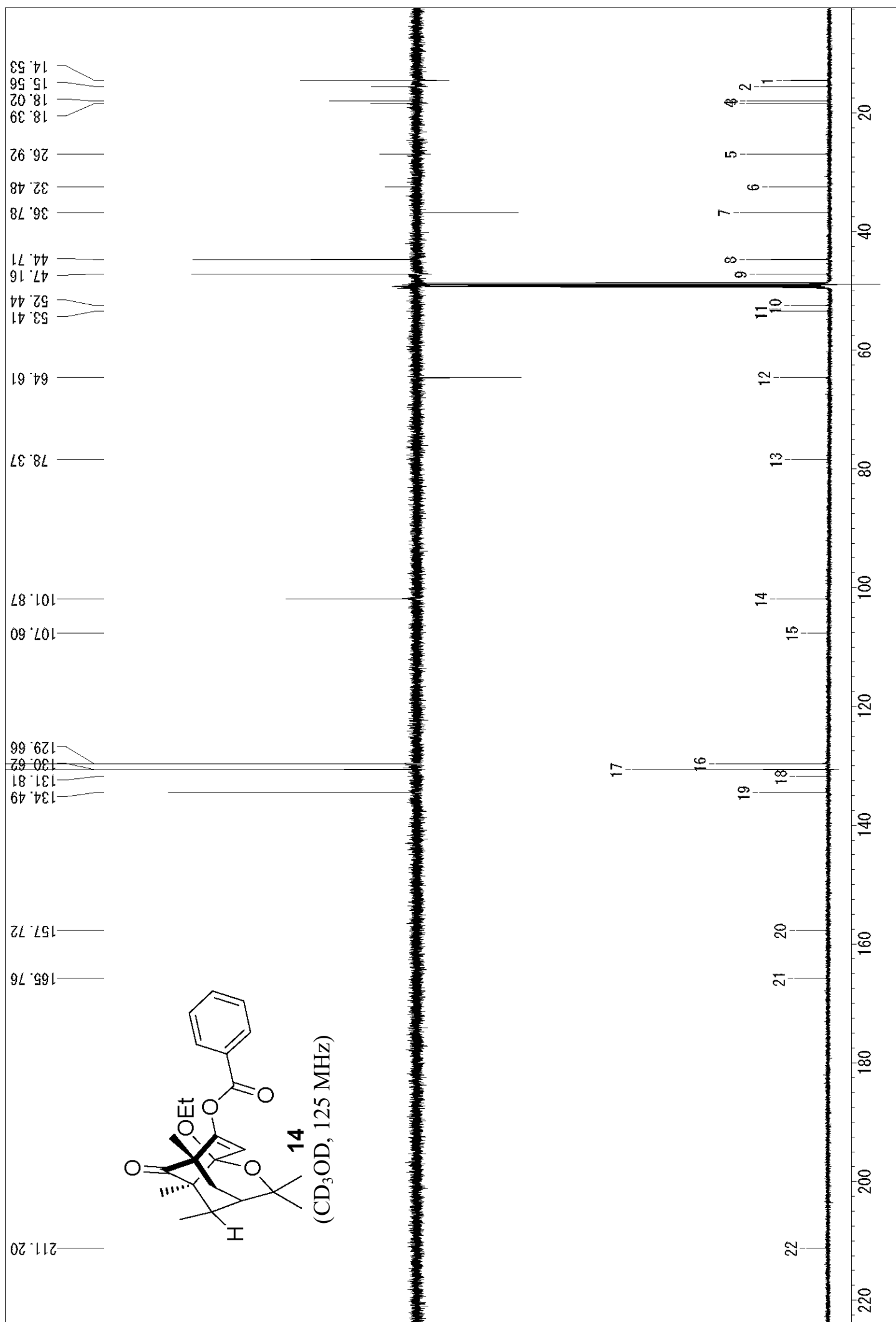


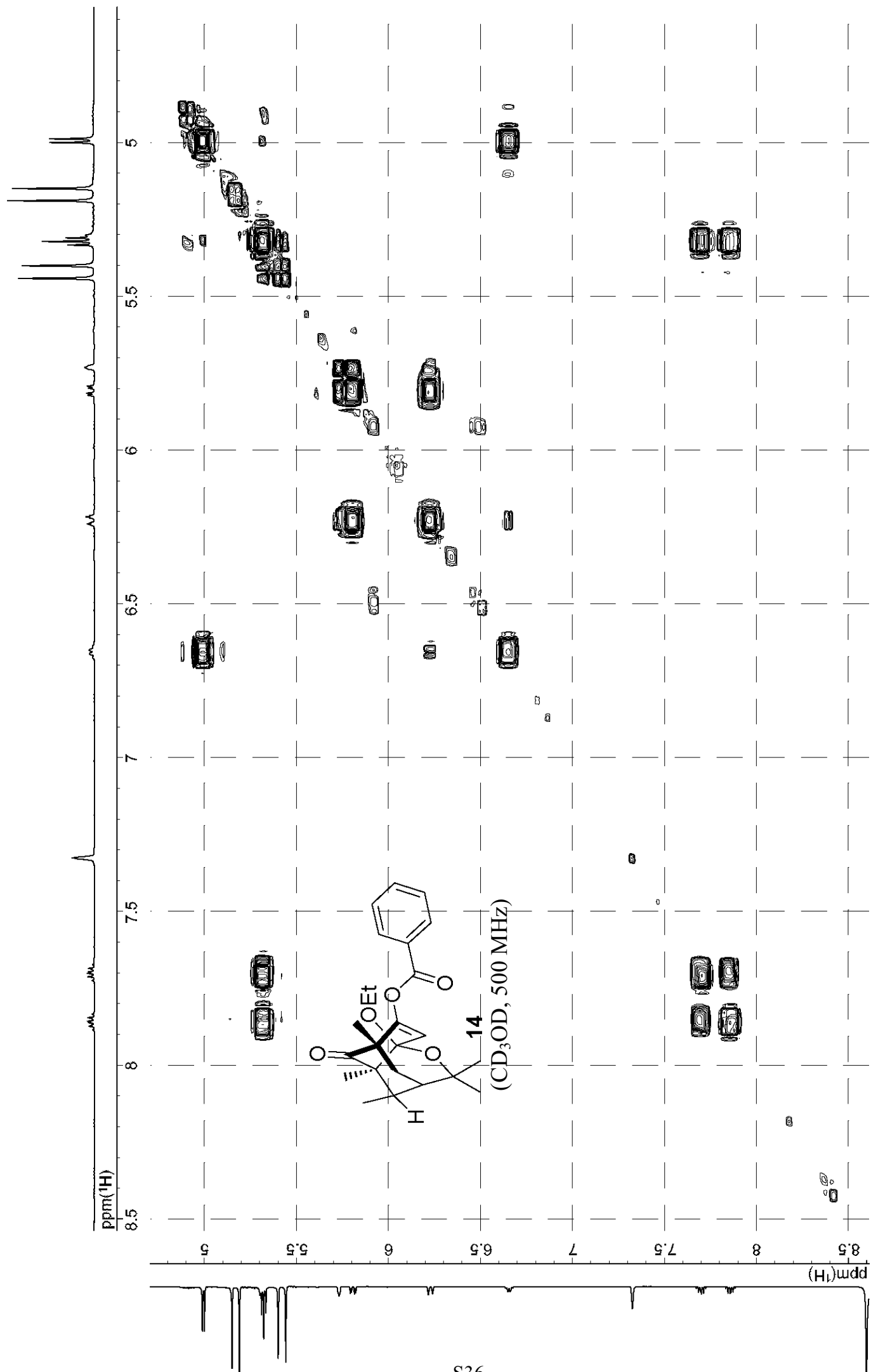


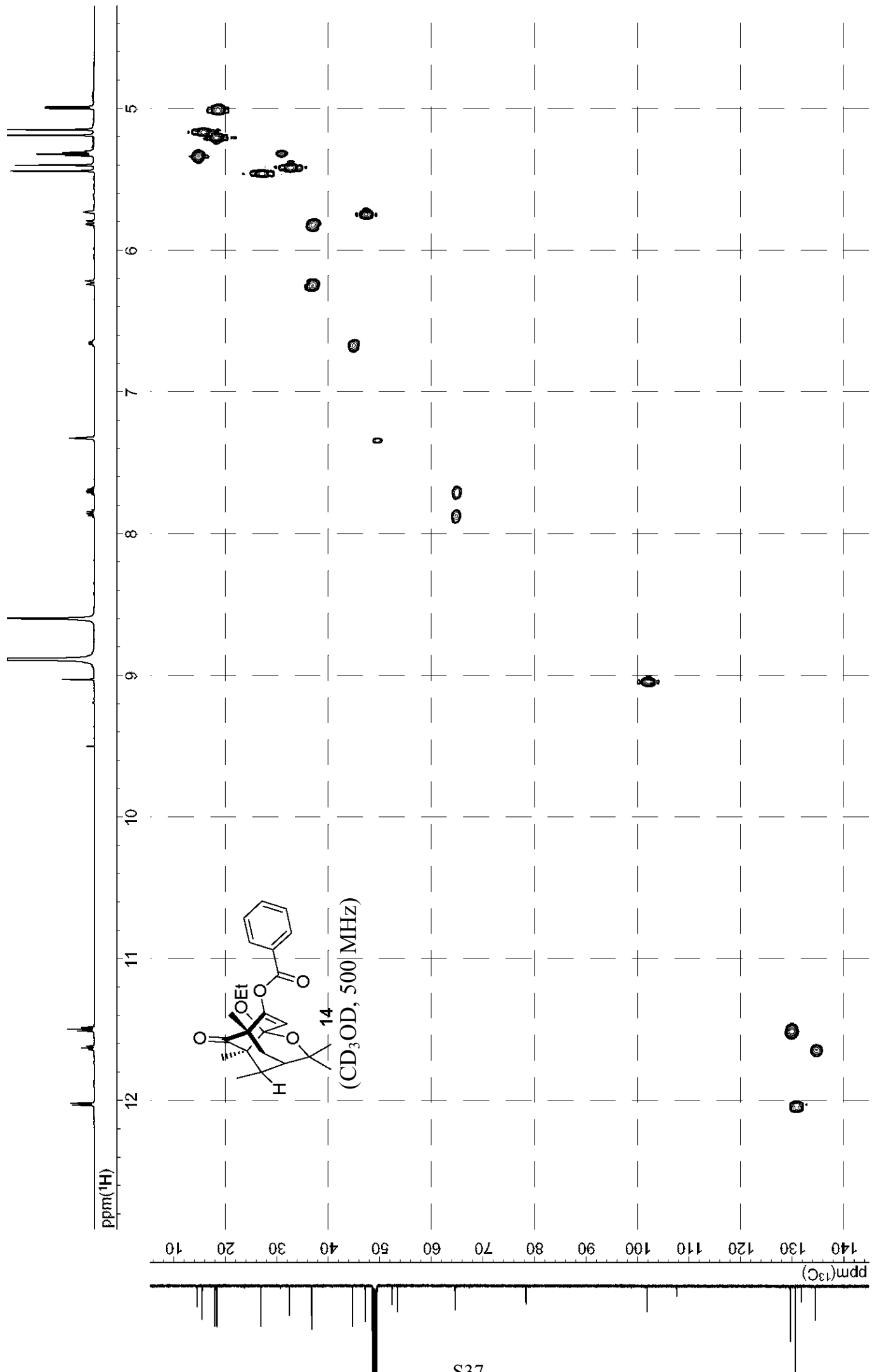


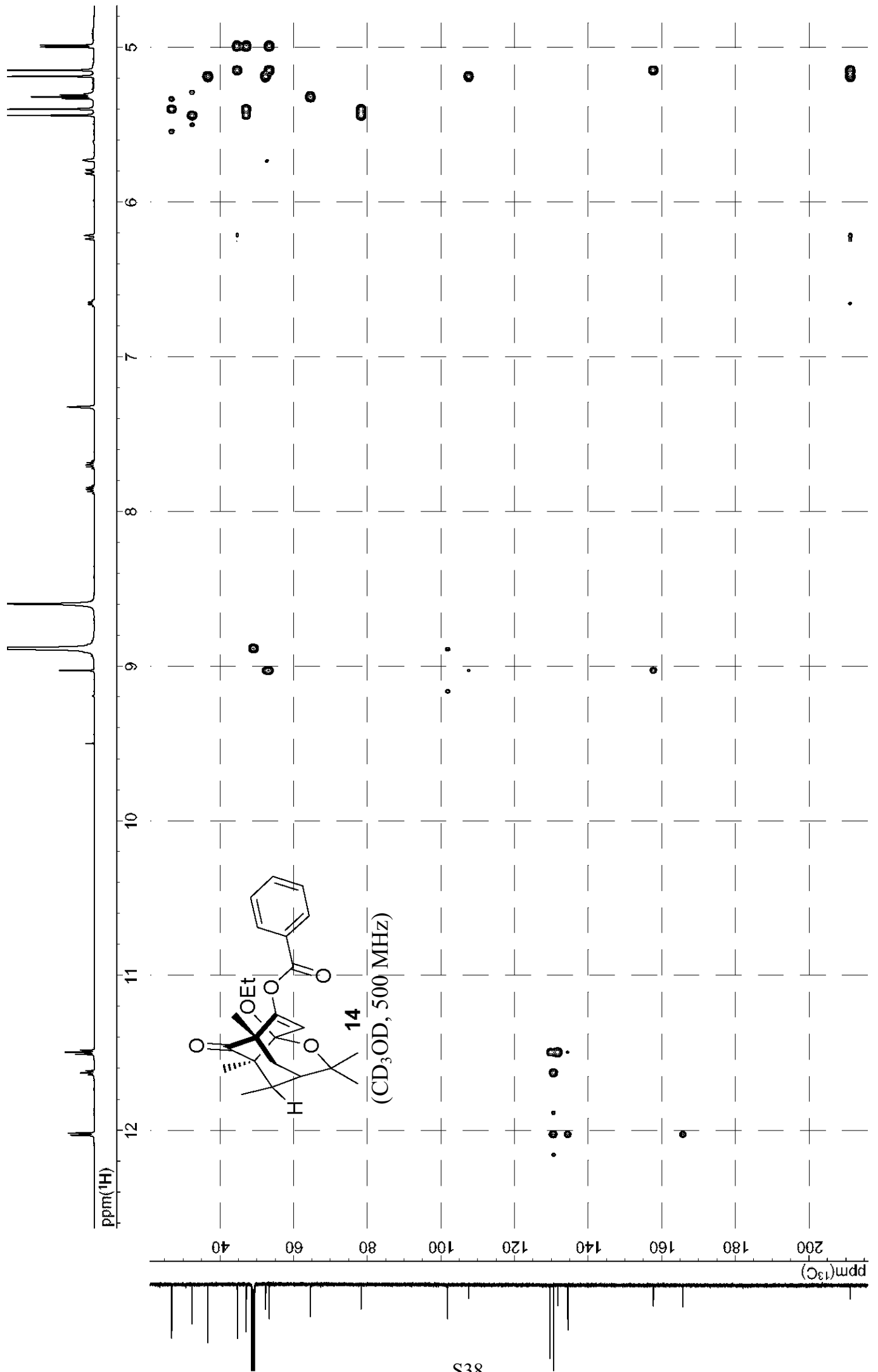


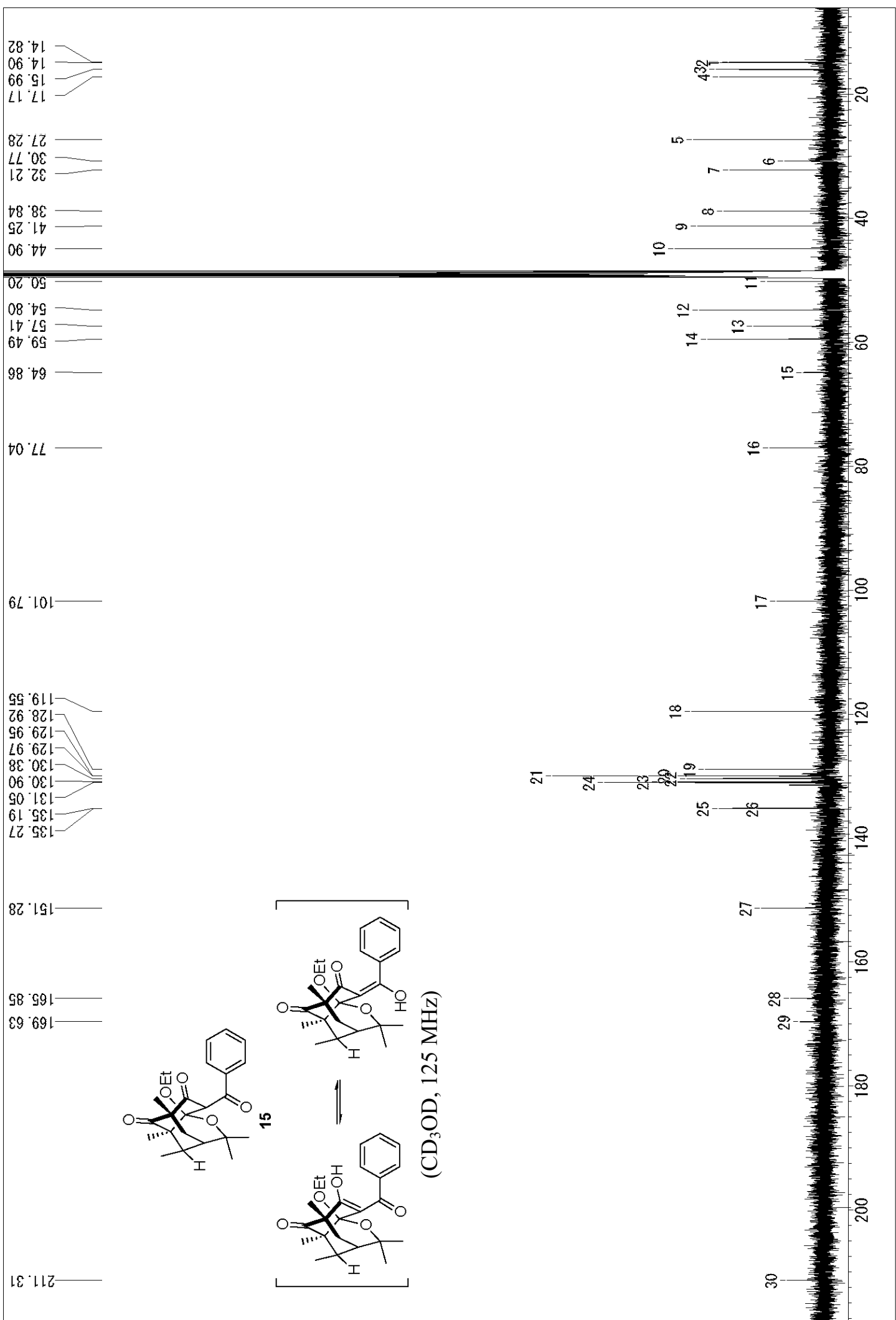


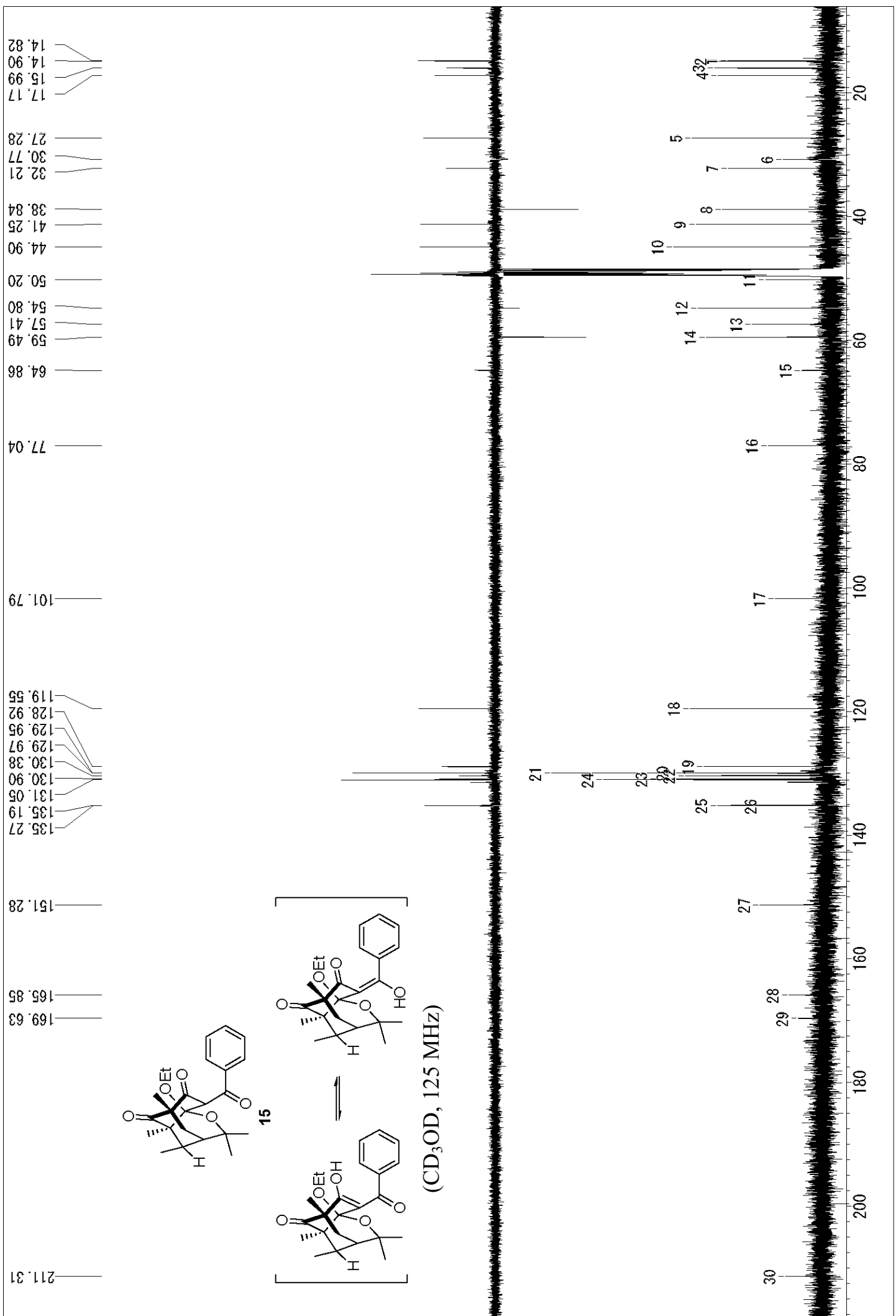


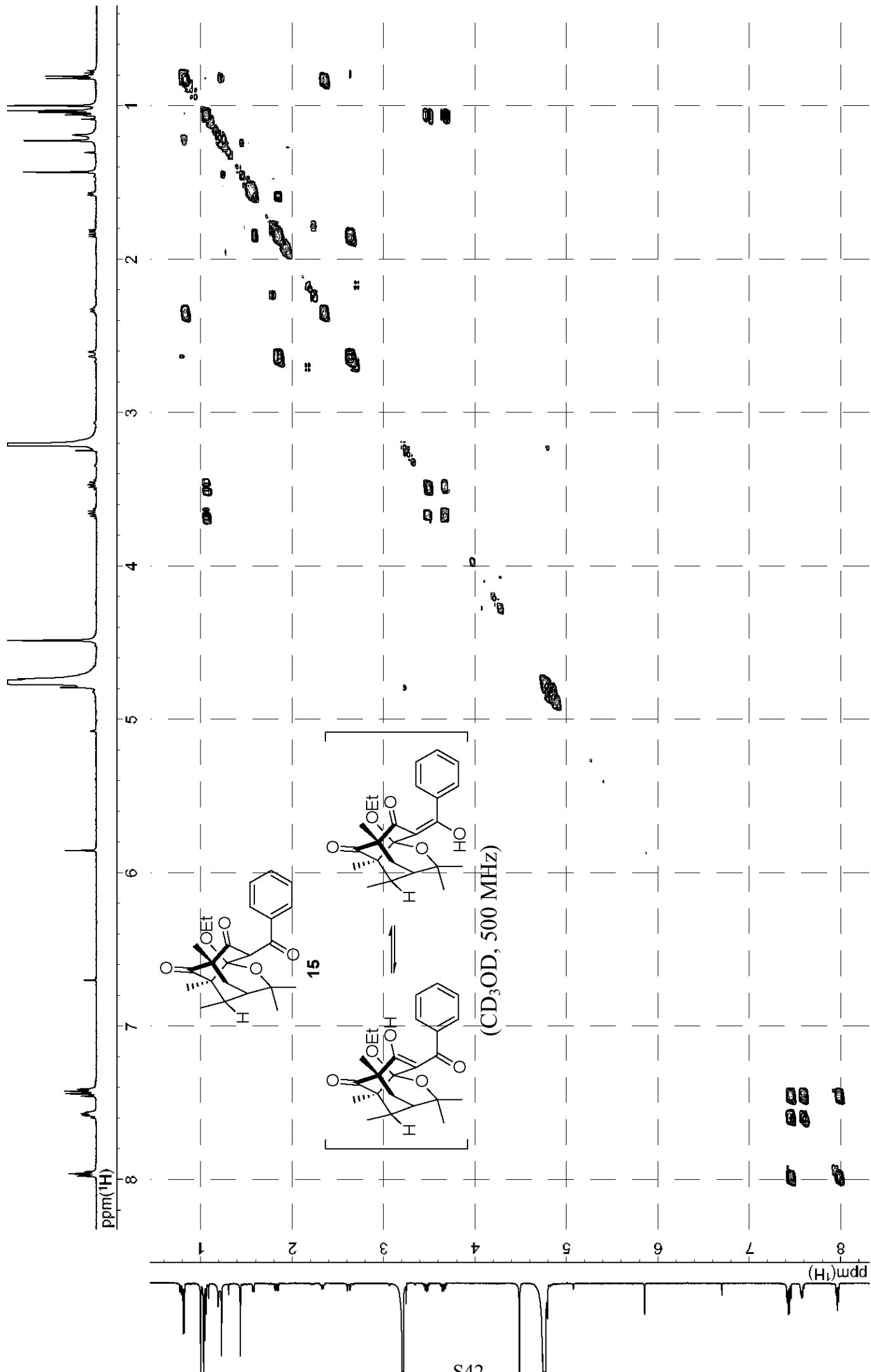


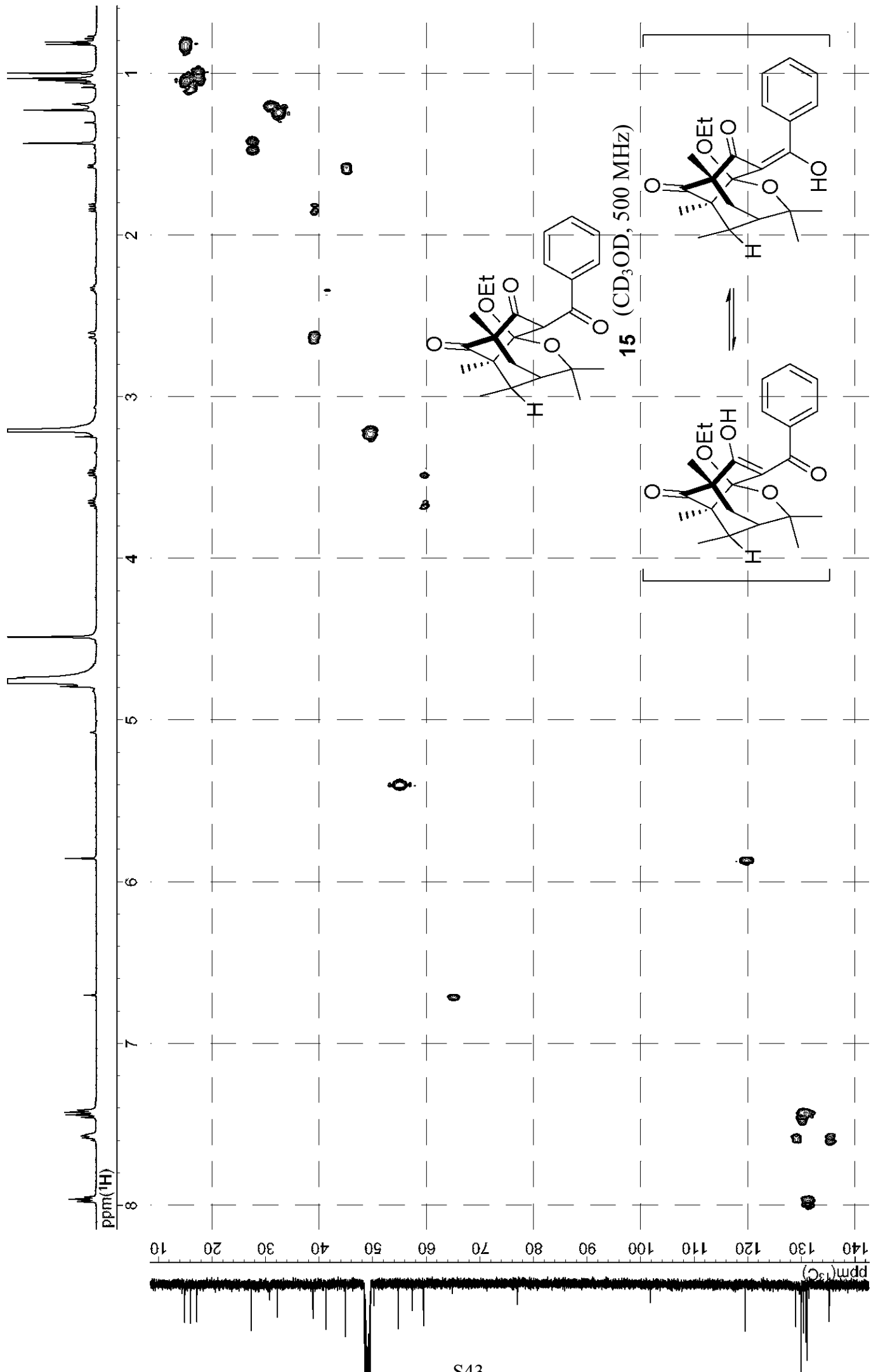


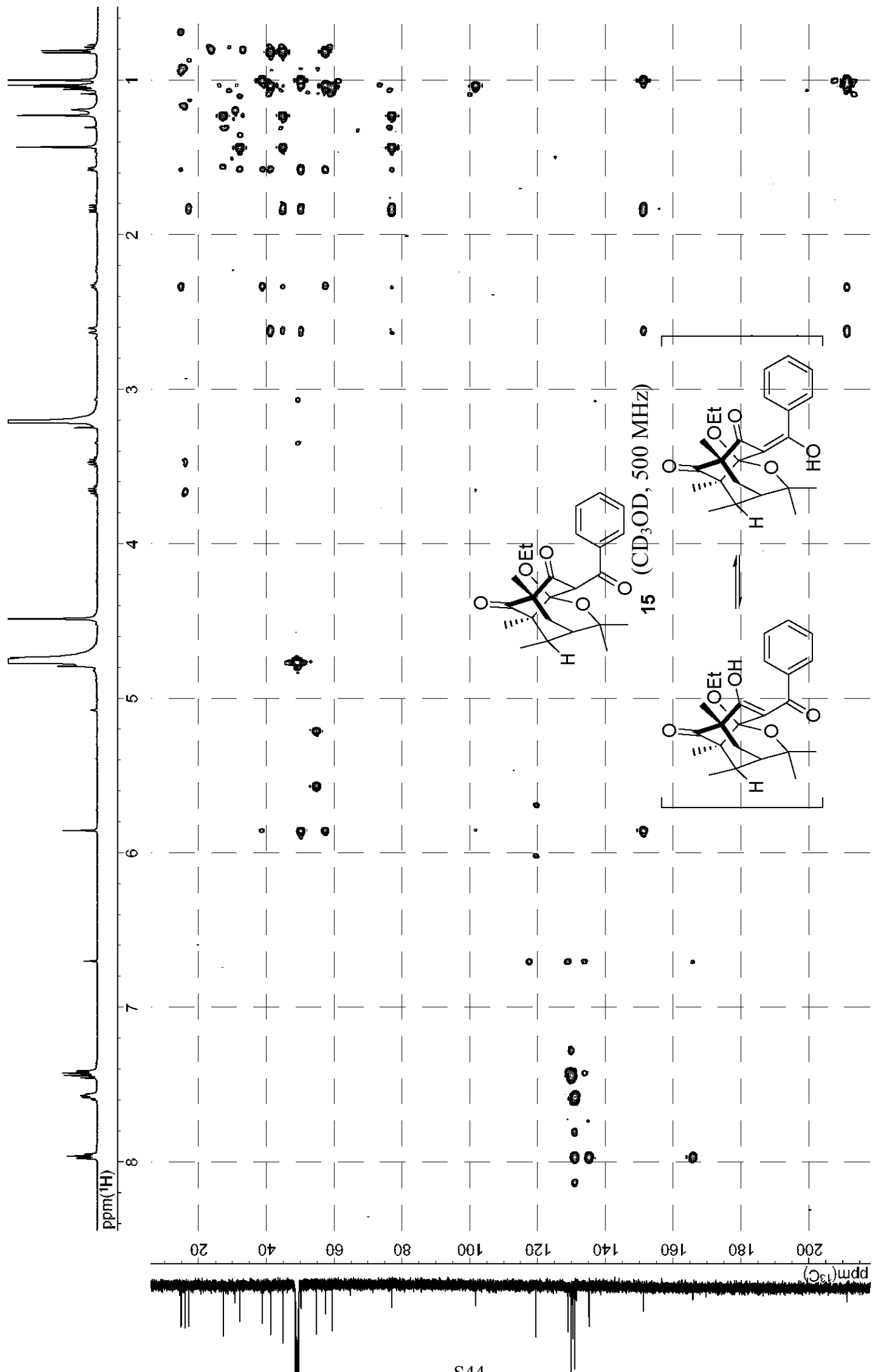


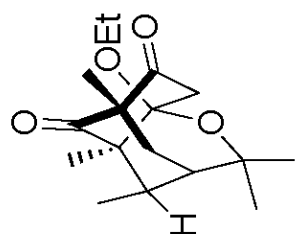




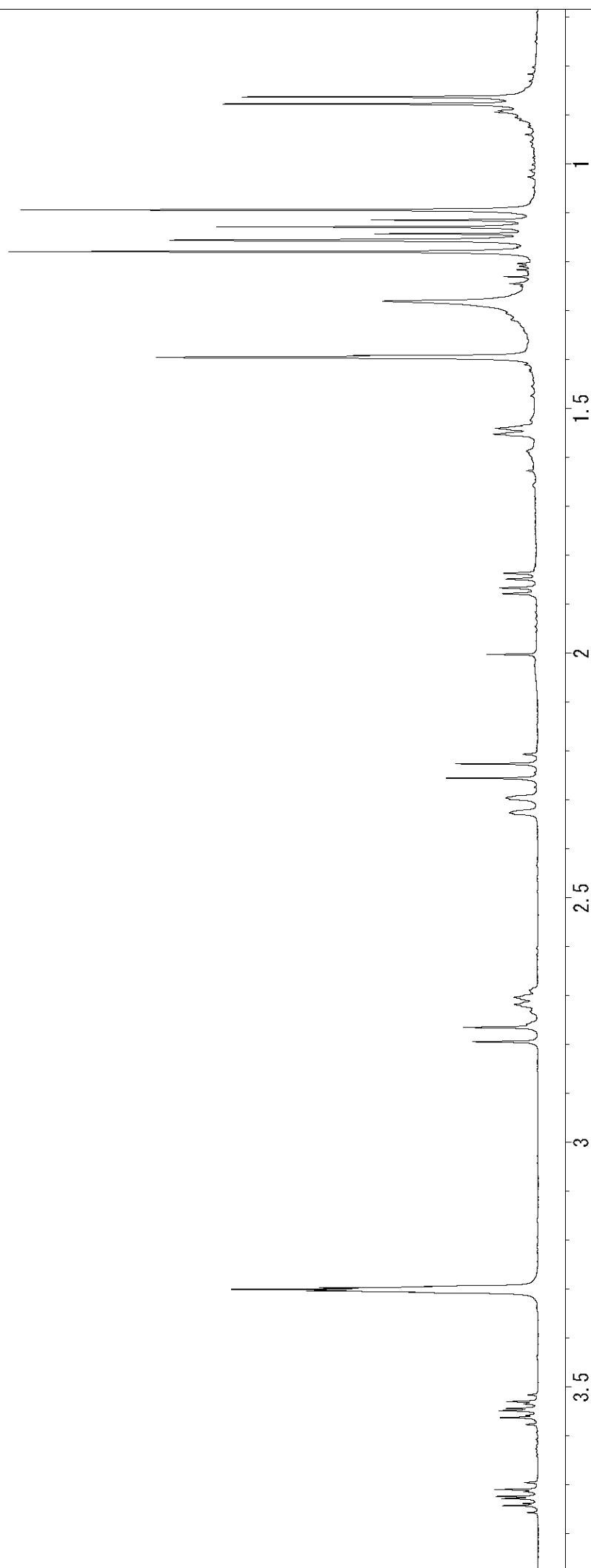


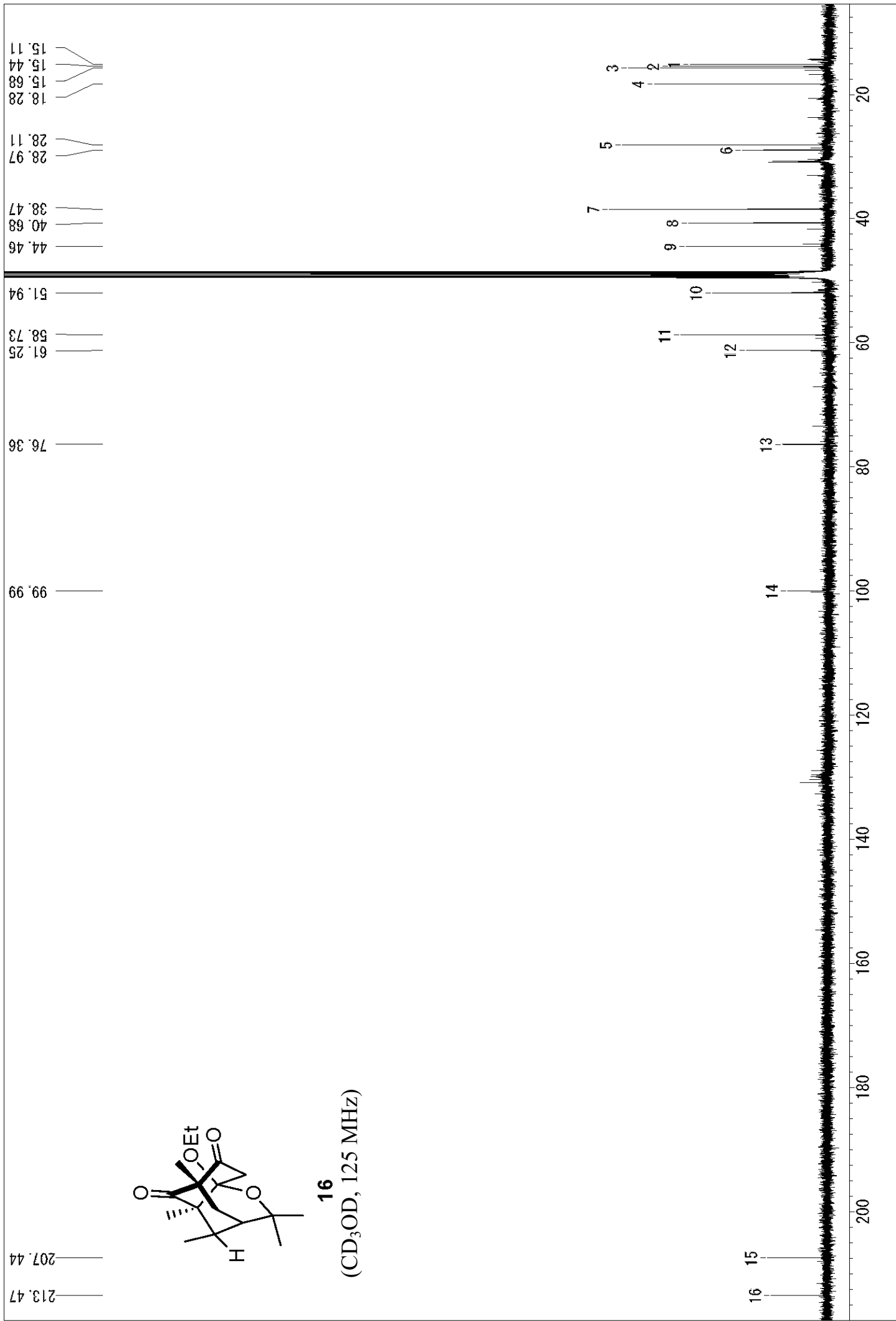


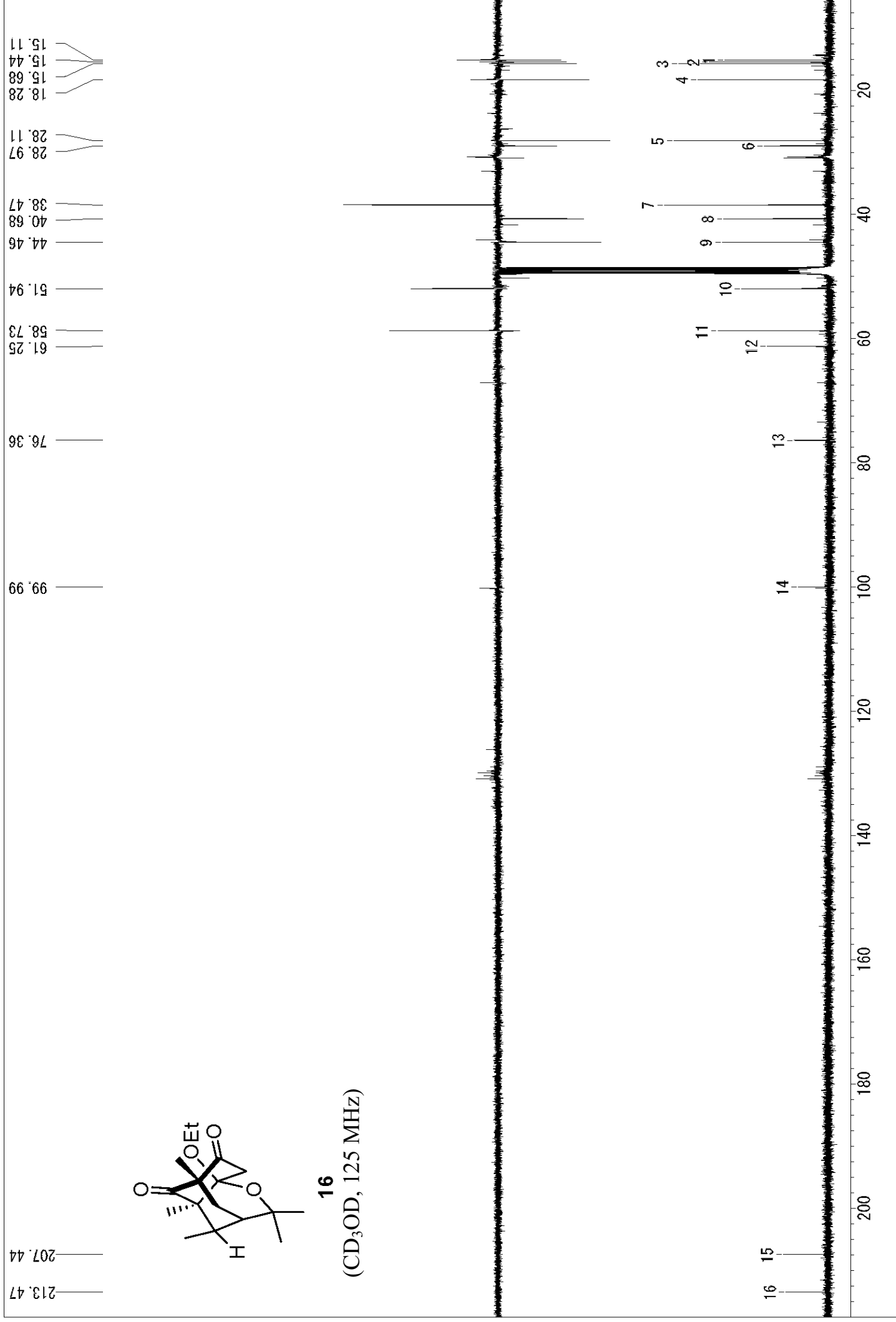


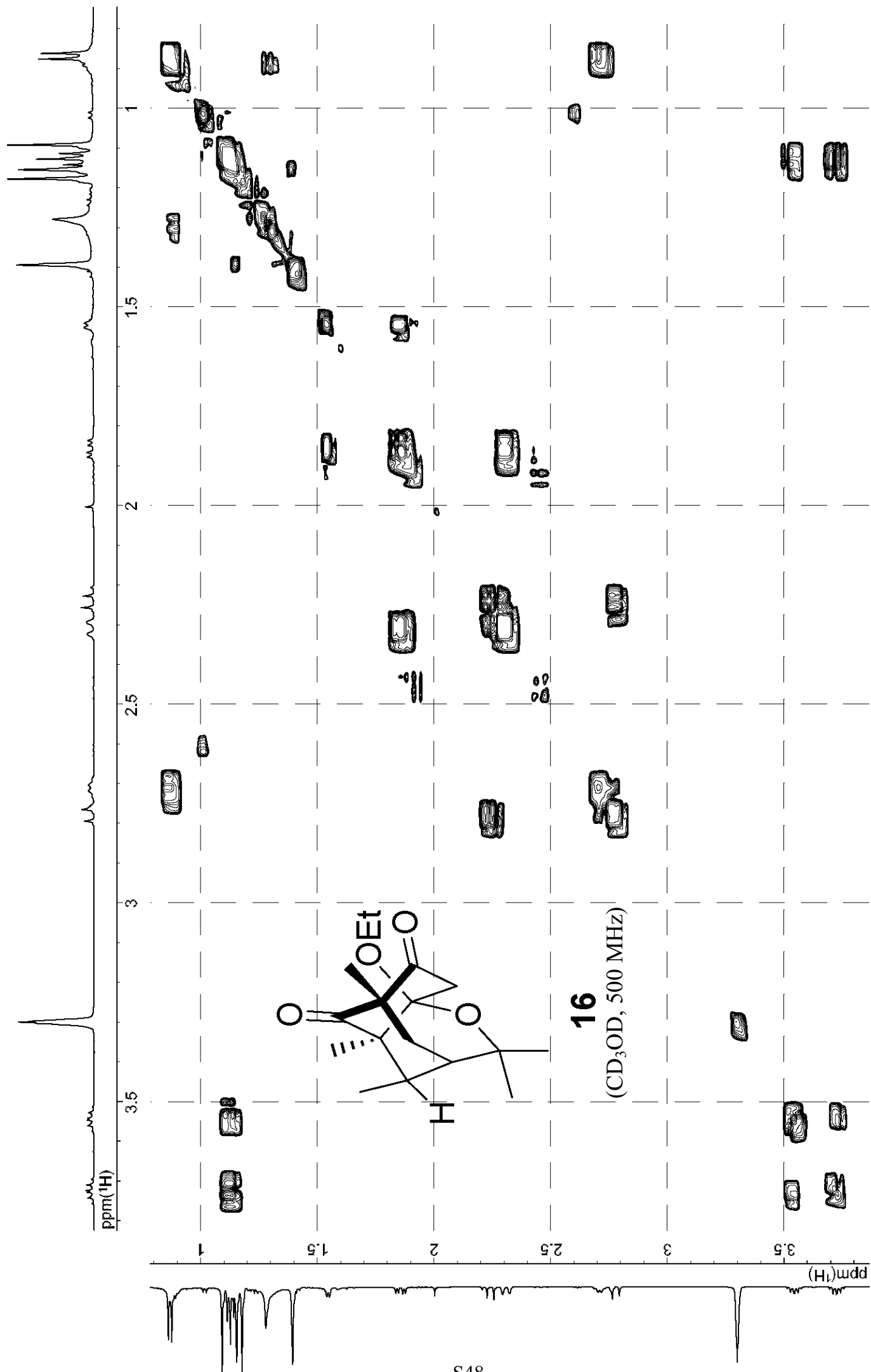


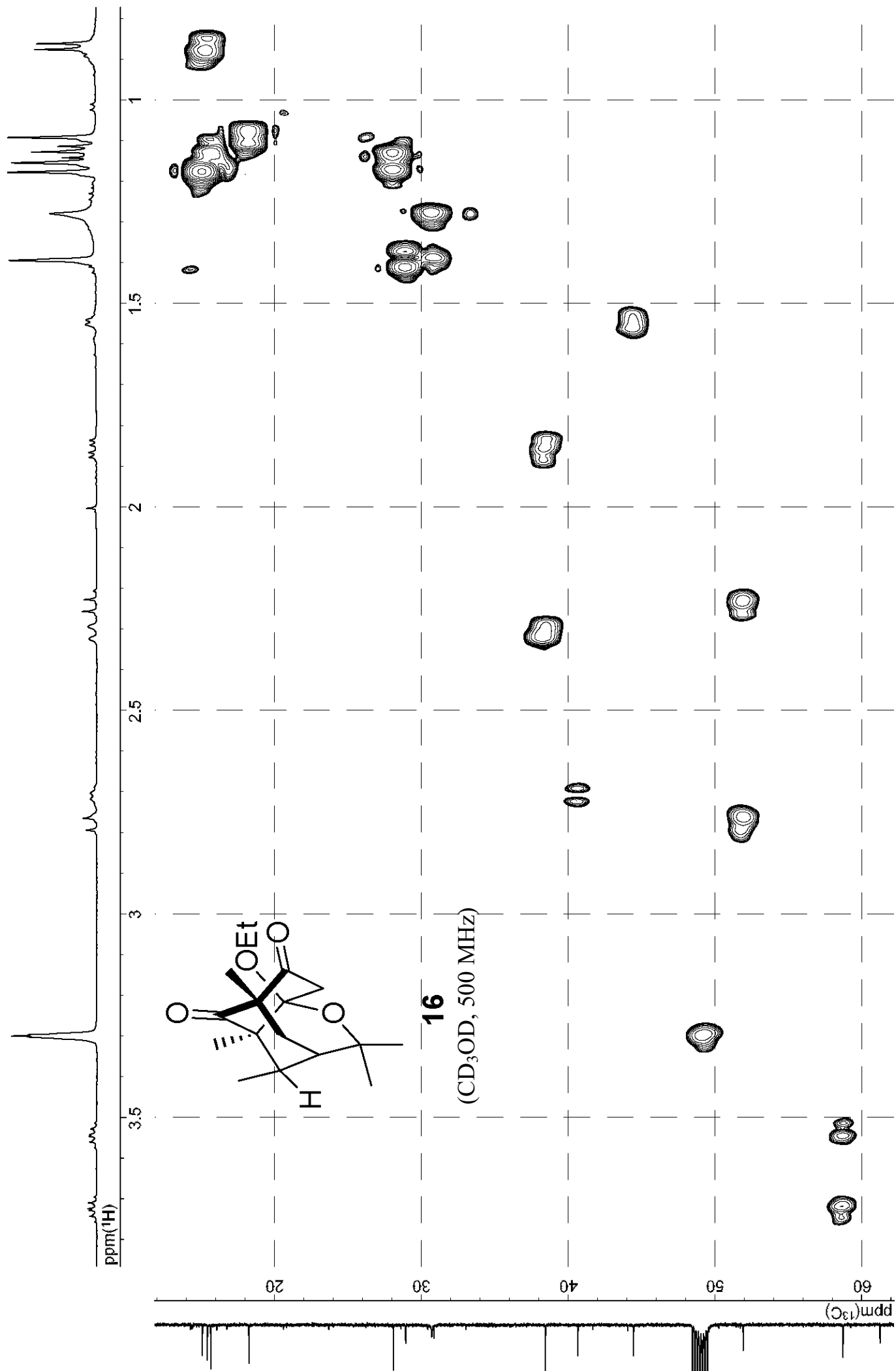
16
(CD₃OD, 500 MHz)

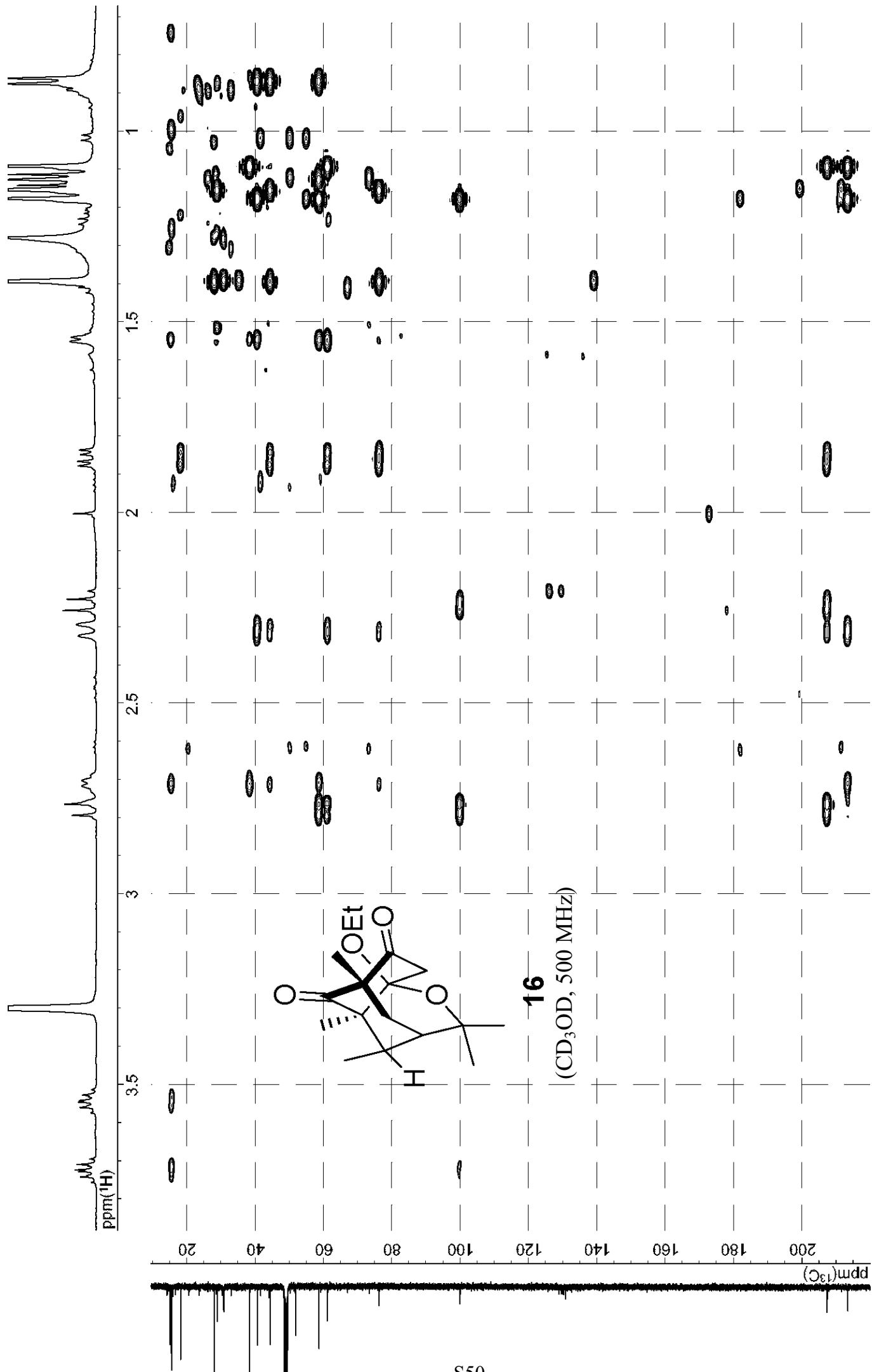


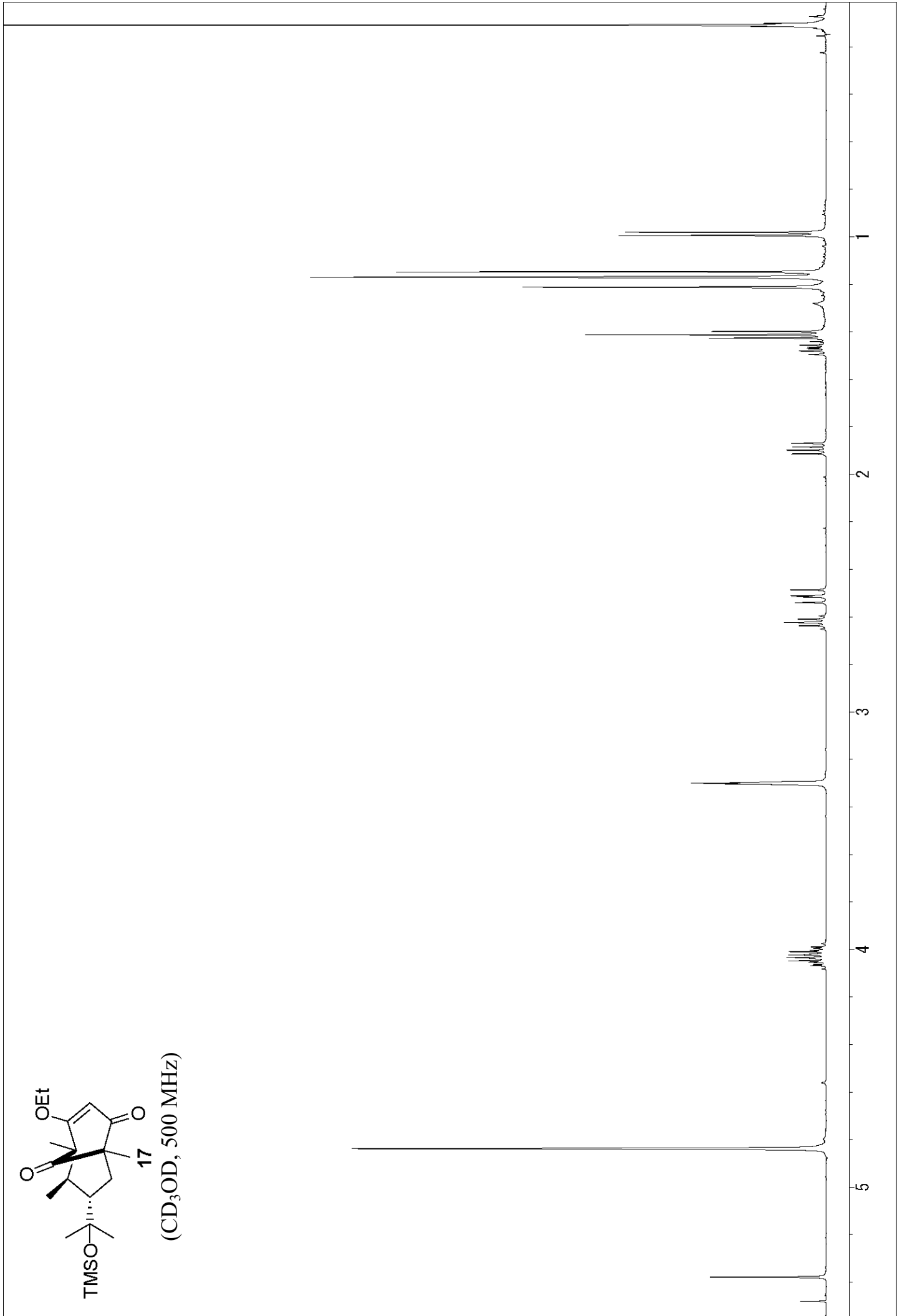


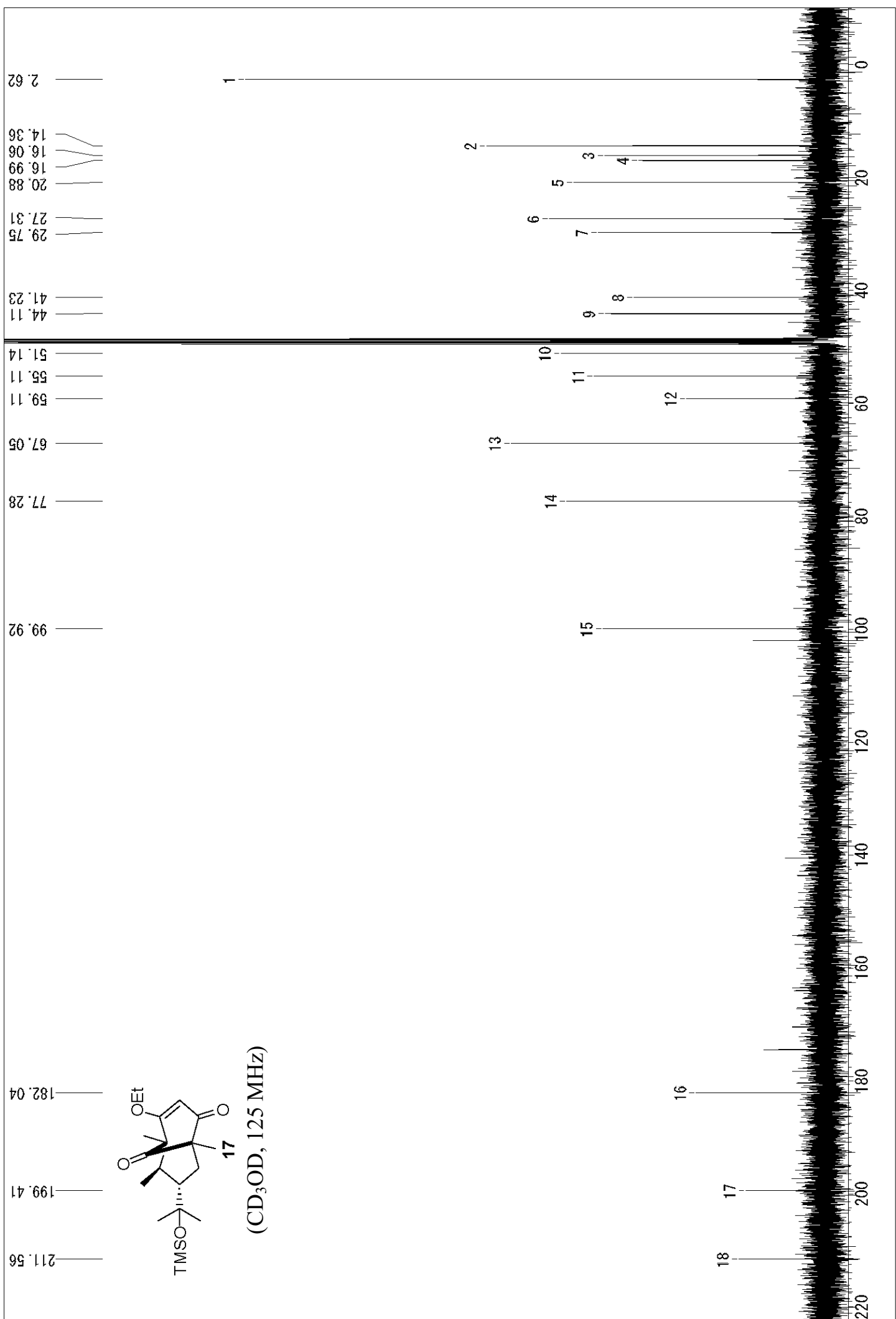


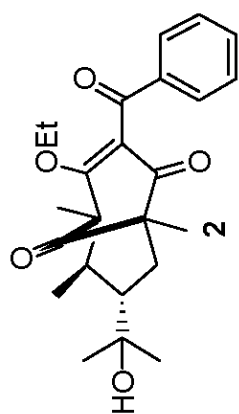




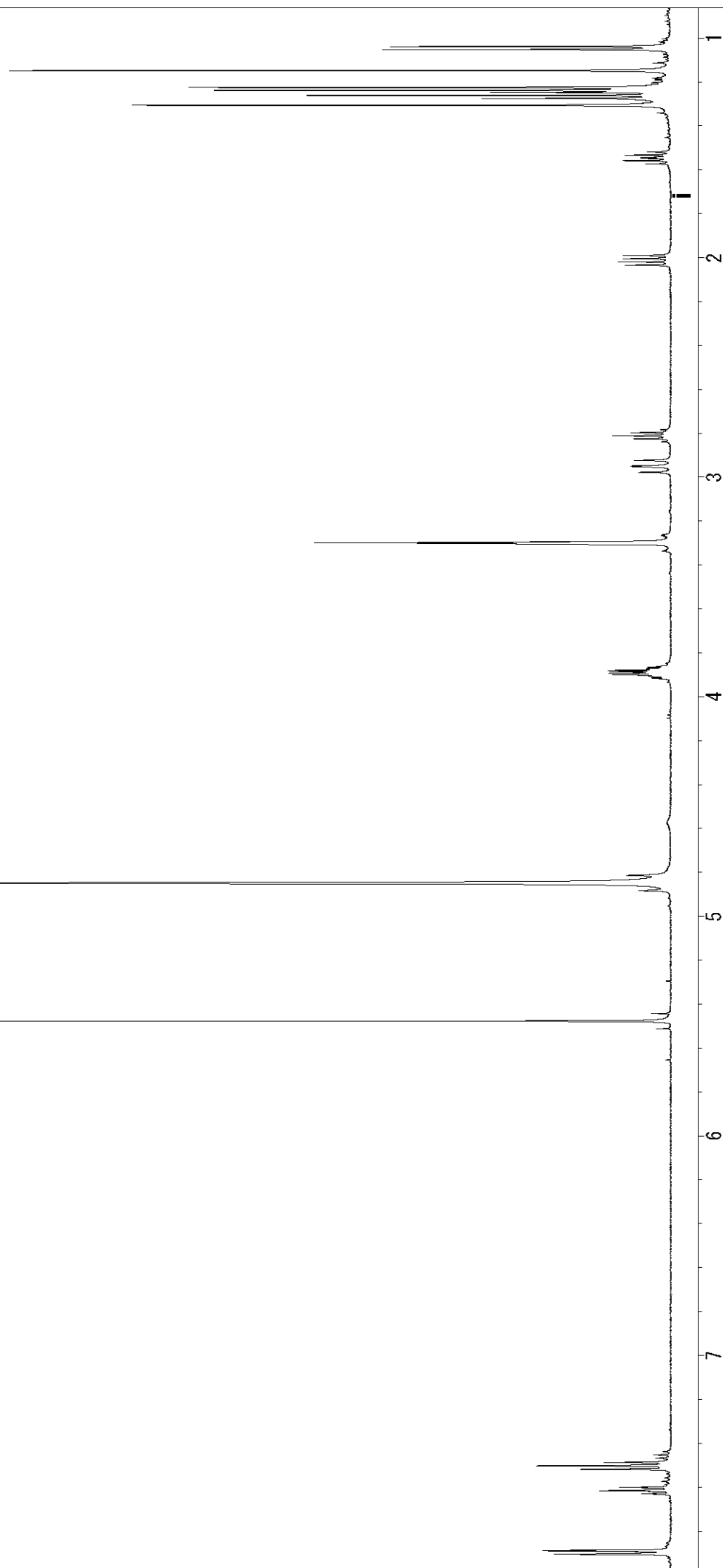


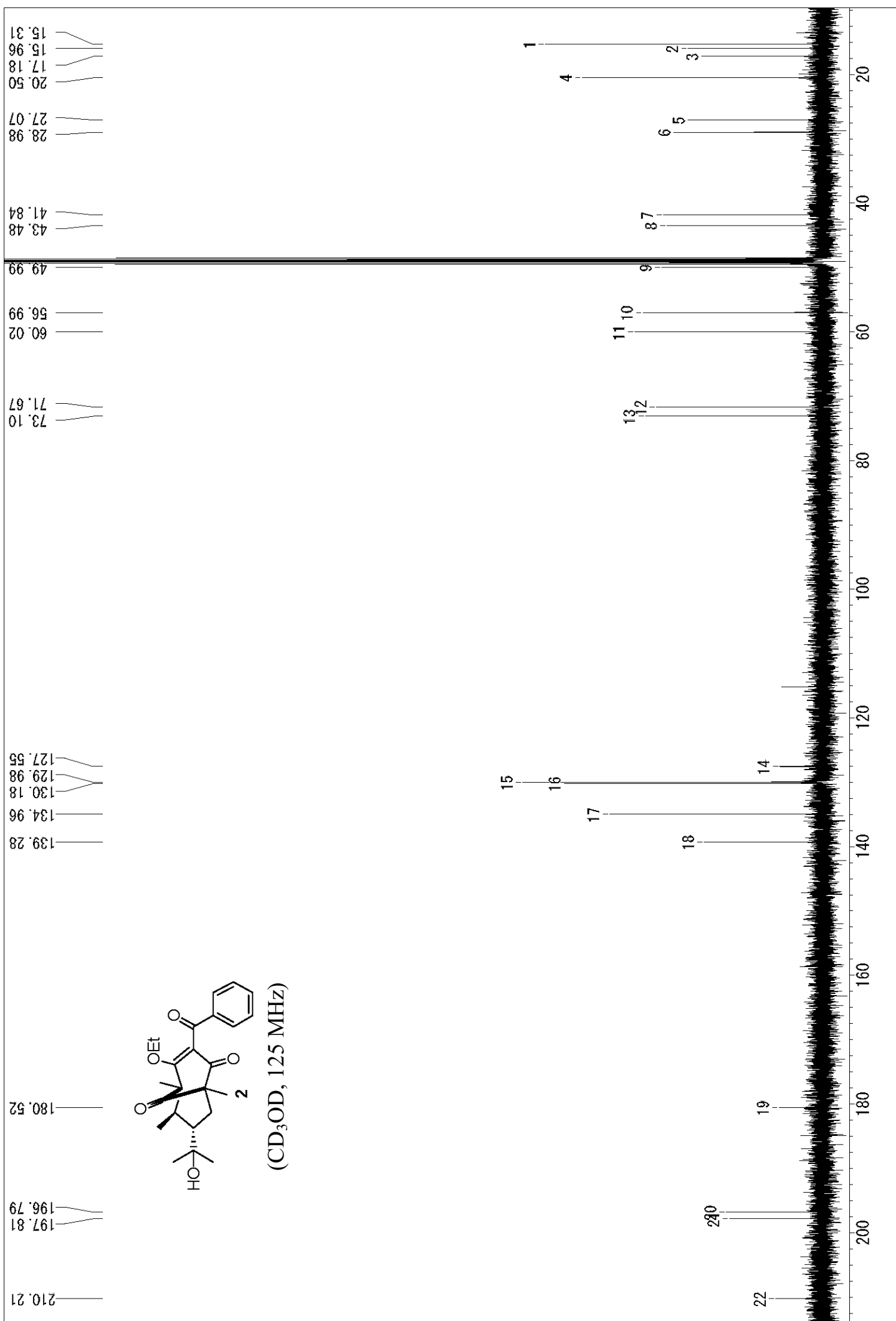


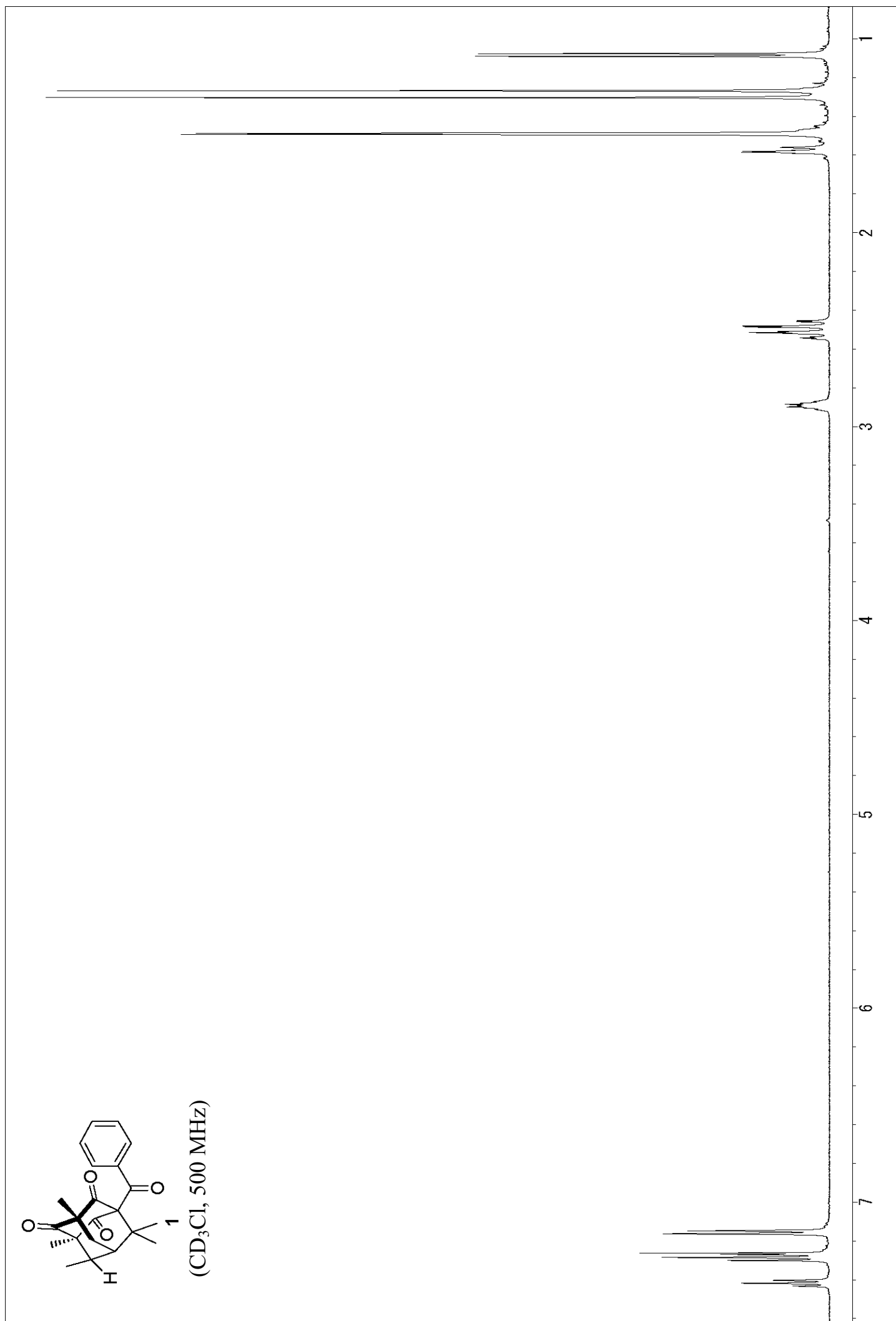


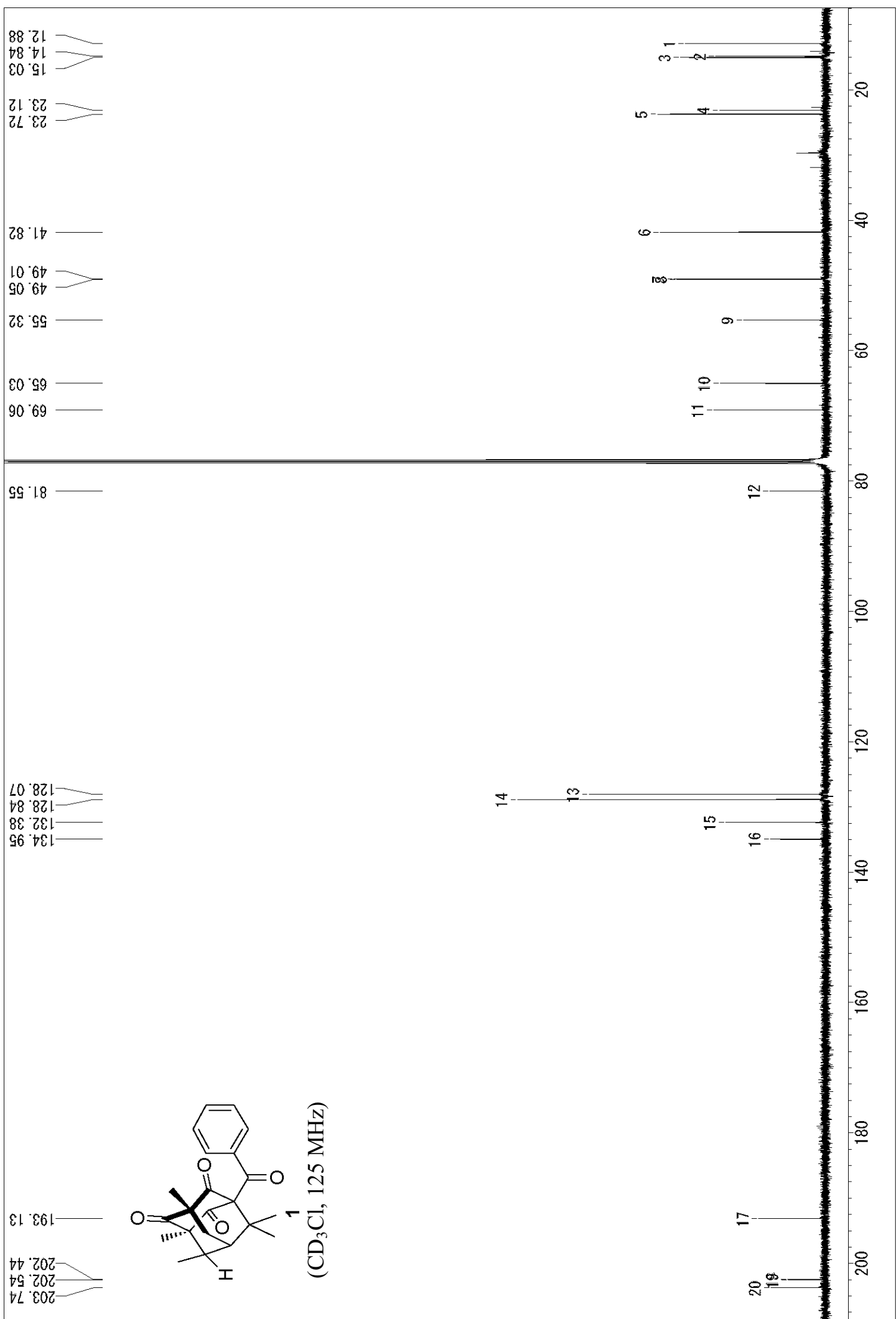


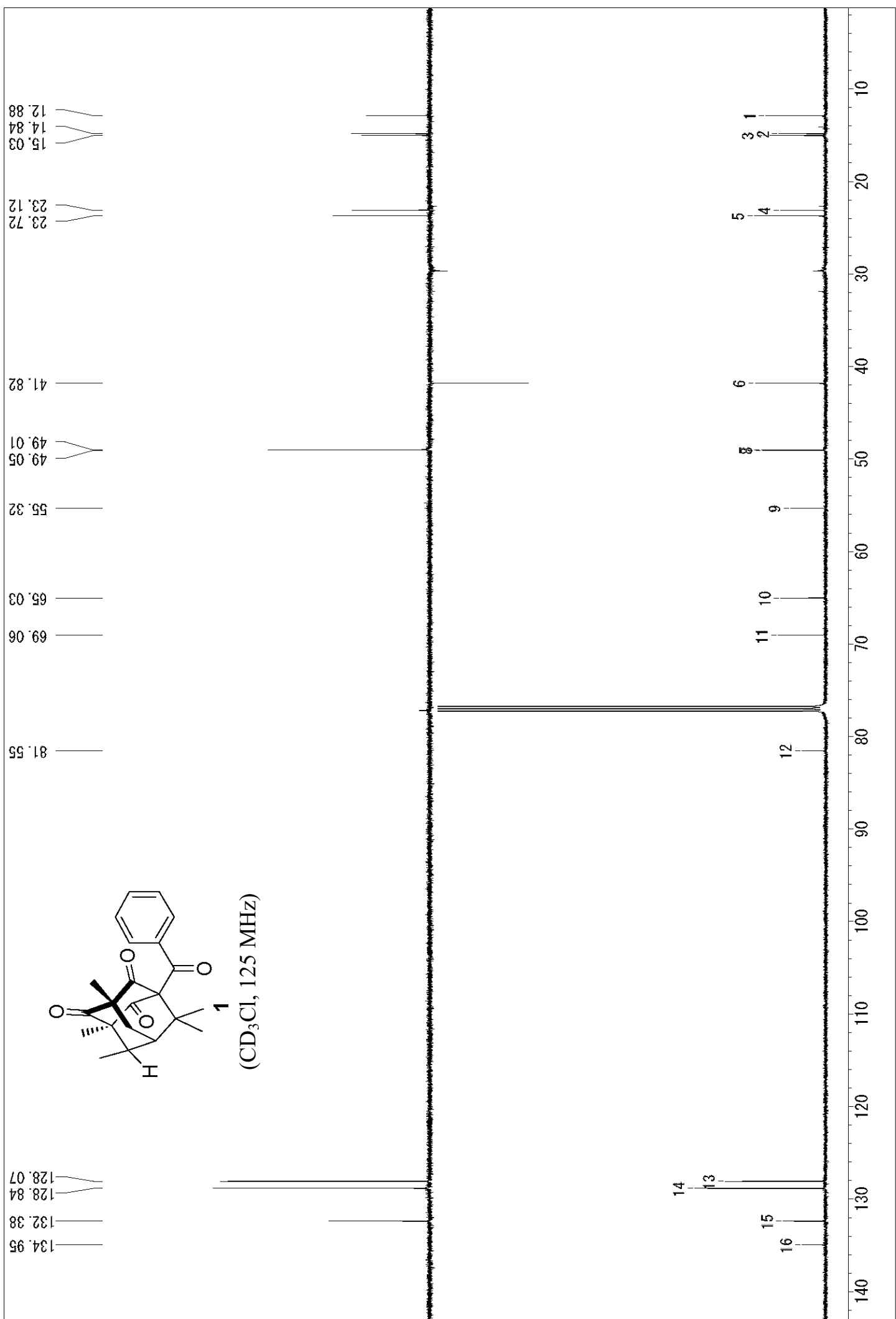
2
(CD₃OD, 500 MHz)



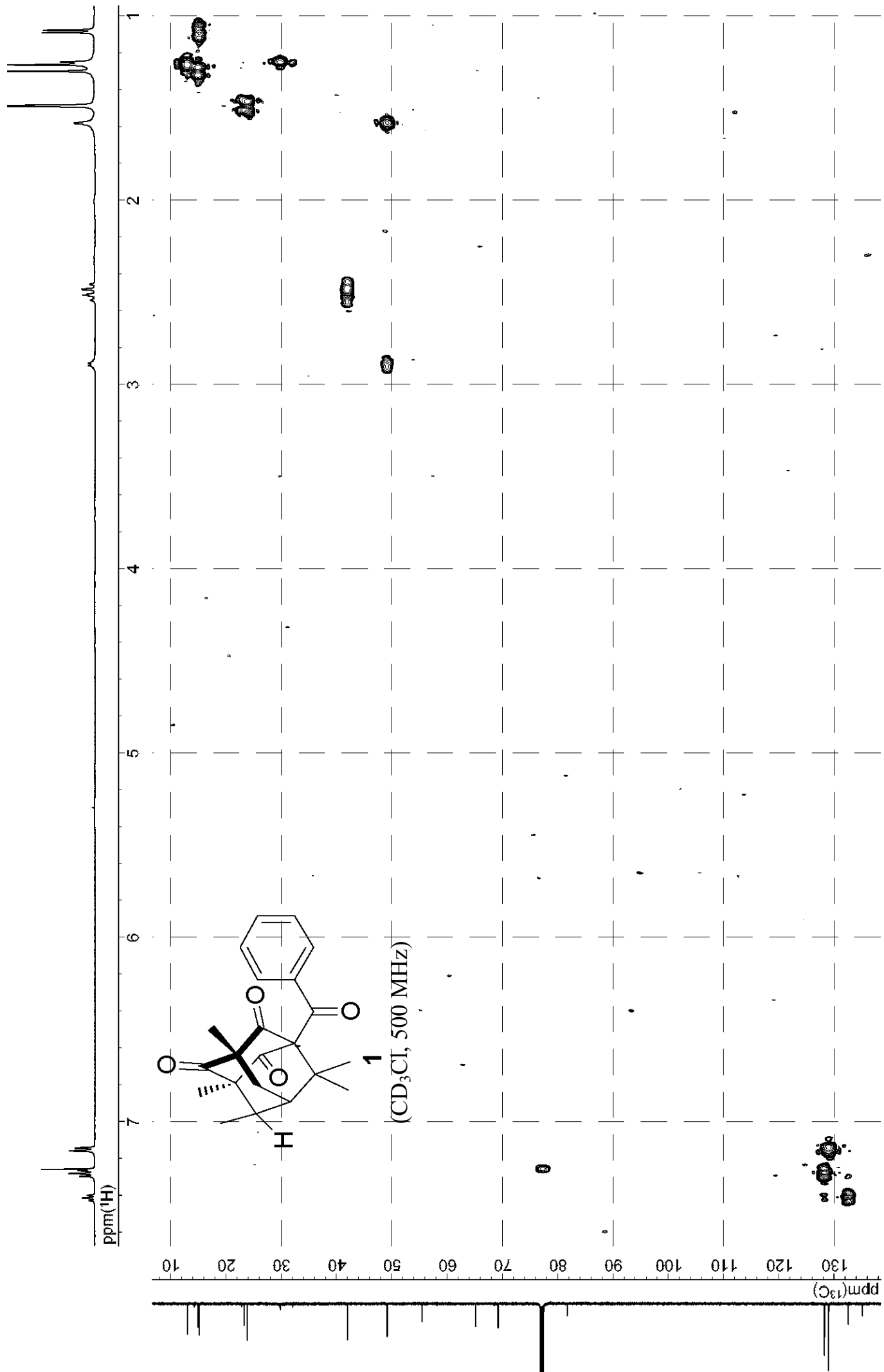


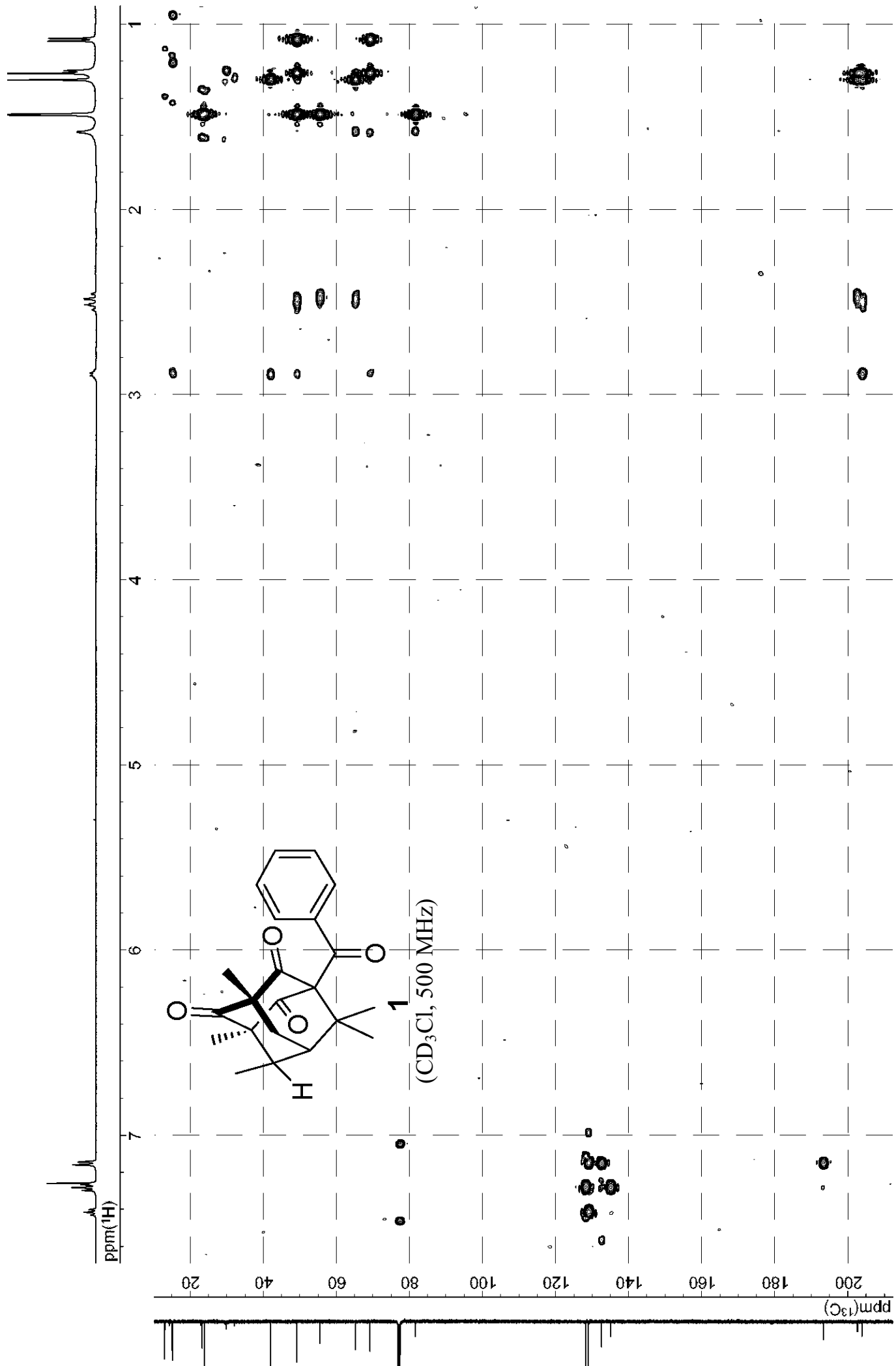










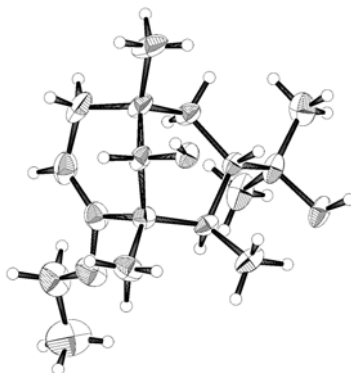


X-ray Crystal Structure Determination. A crystal suitable for X-ray structure determination was mounted on an imaging plate equipped with graphite-monochromated Mo-K α radiation ($\lambda=0.71073$ Å). Unit-cell parameters were determined by autoindexing several images in each data set separately with the DENZO program.¹ For each data set, rotation images were collected in 3° increments with a total rotation of 180° about ϕ (60 frames). Data were processed by using the SCALEPACK program.¹ The structures were solved by a direct method and refined by full-matrix least-squares methods with the TeXsan (Rigaku) program.² Crystallographic data for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Center; **8**: CCDC-693403; **12**: CCDC-693404.

REFERENCES:

- (1) *DENZO and SCALEPACK: Processing of X-ray Diffraction Data Collected in Oscillation Mode*; Z. Otwinowsky and W. Minor, *Methods Enzymol.*, 1997, 276. The program is available from Mac Science Co.
- (2) *TeXsan: Single-Crystal Analysis Software, version 1.9*, Molecular Structure Corporation, The Woodlands, Texas 77381, USA, 1998. The program is available from Mac Science Co.

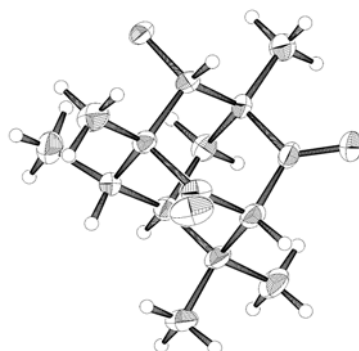
X-Ray Structure Report for **8**



ORTEP drawing of **8** showing the thermal ellipsoids
at the 30% probability level.

Crystal data: Crystal data: monoclinic system, space group C2/c (#15), $a = 27.9040(6)$ Å, $b = 8.0610(2)$ Å, $c = 15.3390(4)$ Å, $V = 3348.5(1)$ Å³, $Z = 8$, $\rho_{\text{calc}} = 1.120$ g cm⁻³, $F(000) = 1248$, $R = 0.133$ ($R_w = 0.324$) for 3571 reflections out of 4079 collected (181 parameters) with $I > 3(I)$. Goodness of fit = 1.43.

X-Ray Structure Report for 12



ORTEP drawing of **12** showing the thermal ellipsoids
at the 30% probability level.

Crystal data: Crystal data: triclinic system, space group $P\bar{1}$ (#2), $a = 8.3450(4)$ Å, $b = 13.1120(5)$ Å, $c = 14.2230(6)$ Å, $V = 1359.1(1)$ Å³, $Z = 4$, $\rho_{\text{calc}} = 1.223$ g cm⁻³, $F(000) = 544$, $R = 0.183$ ($R_w = 0.416$) for 5275 reflections out of 5569 collected (325 parameters) with $I > 3$ (I). Goodness of fit = 1.88.