

Electronic Supplementary Information

**Pyrimidinedione-mediated selective Histone Deacetylase Inhibitors
with Antitumor Activity in Colorectal Cancer HCT116 Cells.**

Yi-Min Liu,^a Hsueh-Yun Lee,^a Mei-Jung Lai,^b Shiow-Lin Pan,^c Hsiang-Ling Huang,^a Fei-Chiao Kuo,^a Mei-Chuan Chen,^{*d} and Jing-Ping Liou^{*a}

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HPLC purity determination:

The percentage purity of compounds were determined by an Agilent 1100 series HPLC system using C18 column.

Elution conditions: Mobile phase A-Acetonitrile; Mobile phase B-Water containing 0.1% formic acid + 10 mmol NH₄OAc. The flow-rate was 0.2 ml/min and the injection volume was 5 µl. The system operated at 25 °C. Peaks were detected at 210 nm.

Table 1. Elution condition

Time (min)	Mobile Phase A (ratio)	Mobile Phase B (ratio)
0	10	90
45	90	10
50	10	90
60	10	90

Table 2. Purity of synthetic compounds

C18 column: Agilent ZORBAX Eclipse XDB-C18 5µm. 4.6 mm × 150 mm column

Compounds	Retention time (min)	% Purity
6	15.00	95.32
7	23.57	99.61
8	18.63	99.71
9	26.66	99.49
10	19.94	98.85
11	19.62	98.13

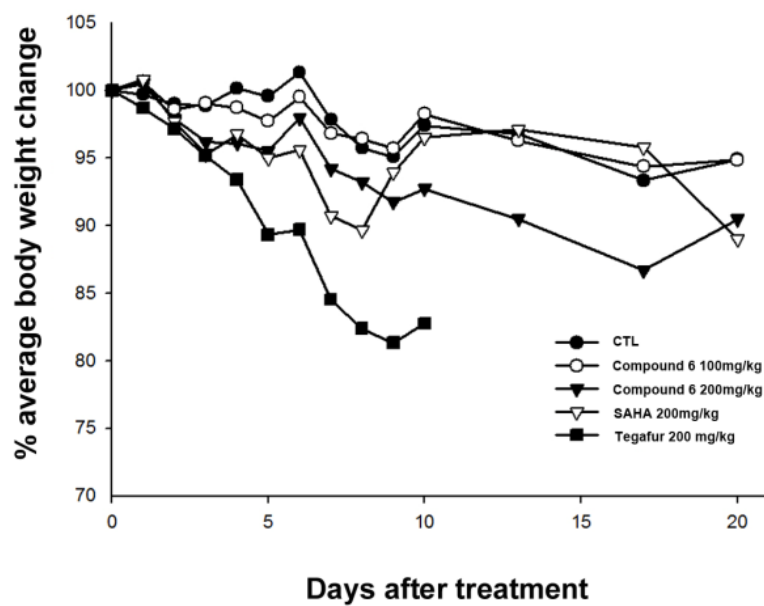


Figure S1. Mean change from baseline in weight in HCT116 xenograft model.

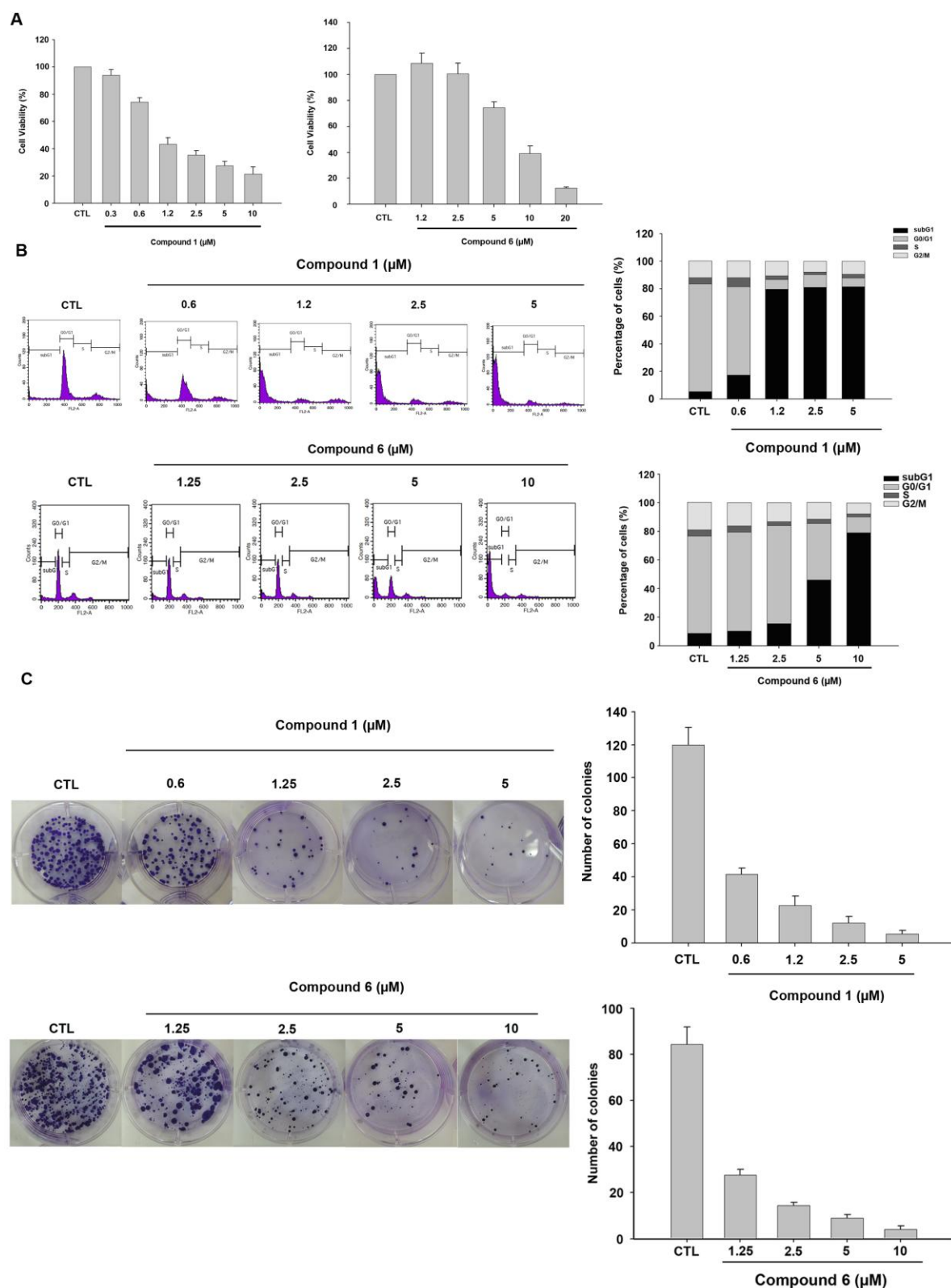
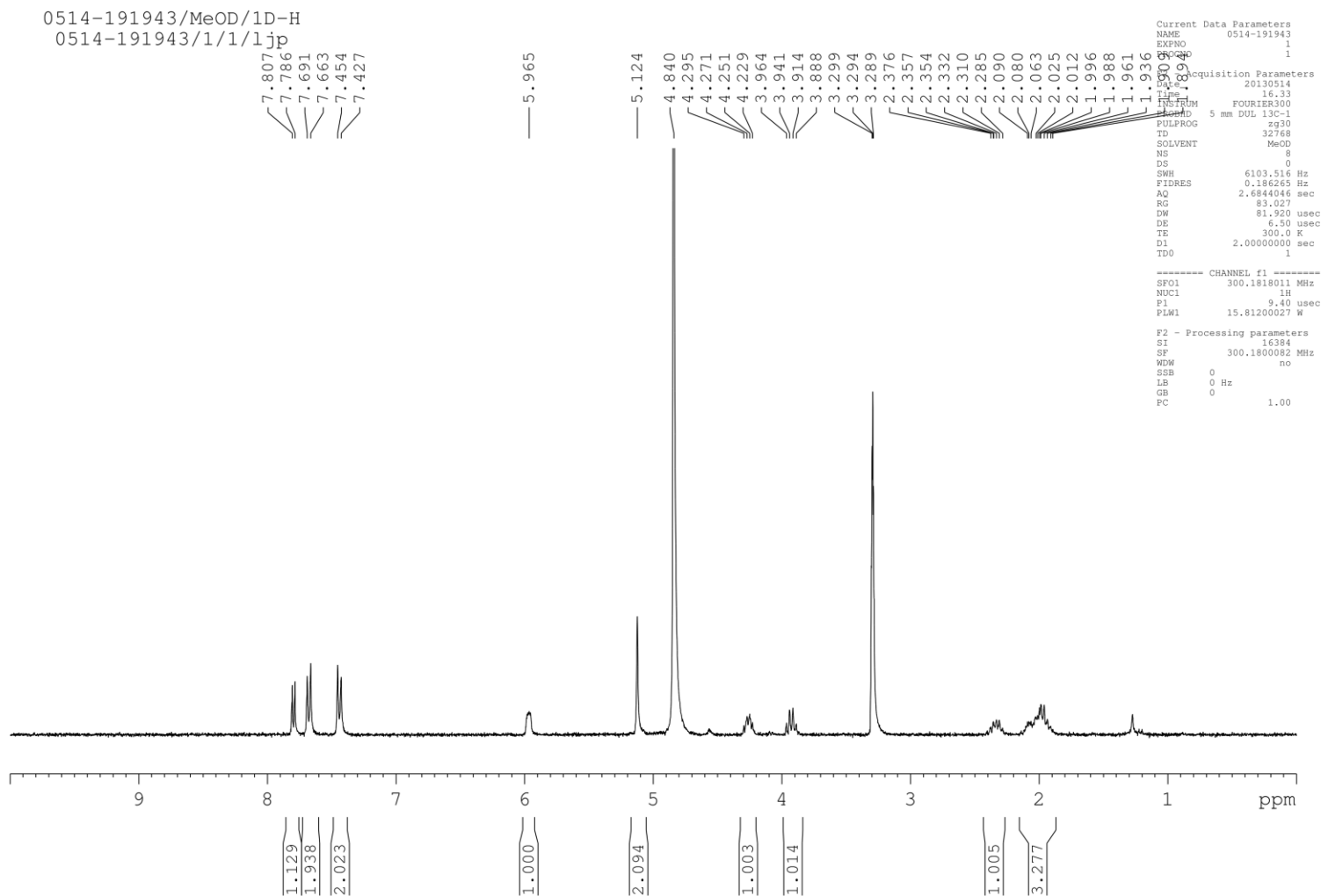
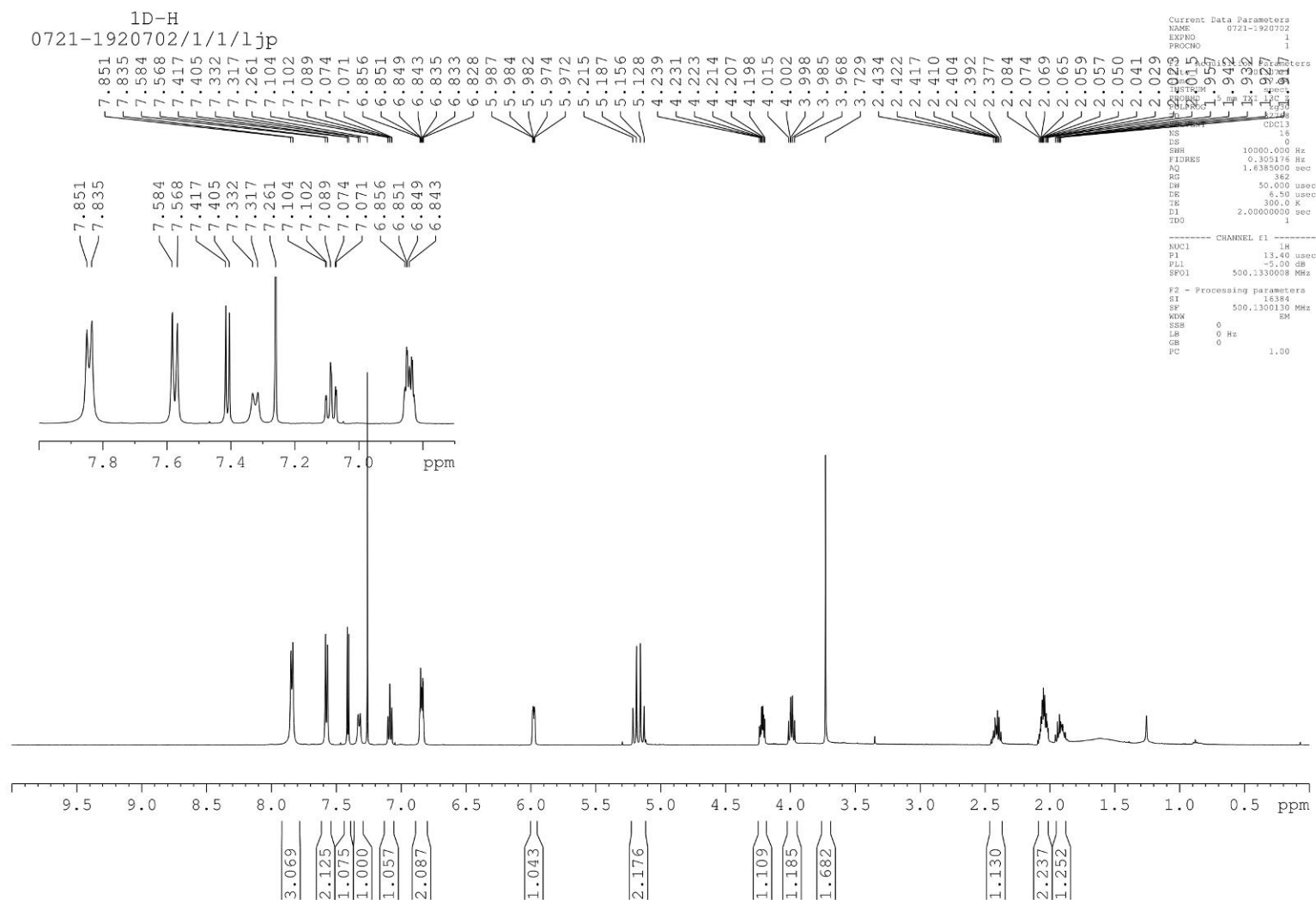


Figure. S2. The comparison of compound 1 and 6 in HCT116 cell models. Cells were treated with indicated concentrations of indicated drugs for 48 h in MTT assay (A) and Flow cytometric analysis (B). Clonogenic survival (C) was assessed as described in the Experimental section.

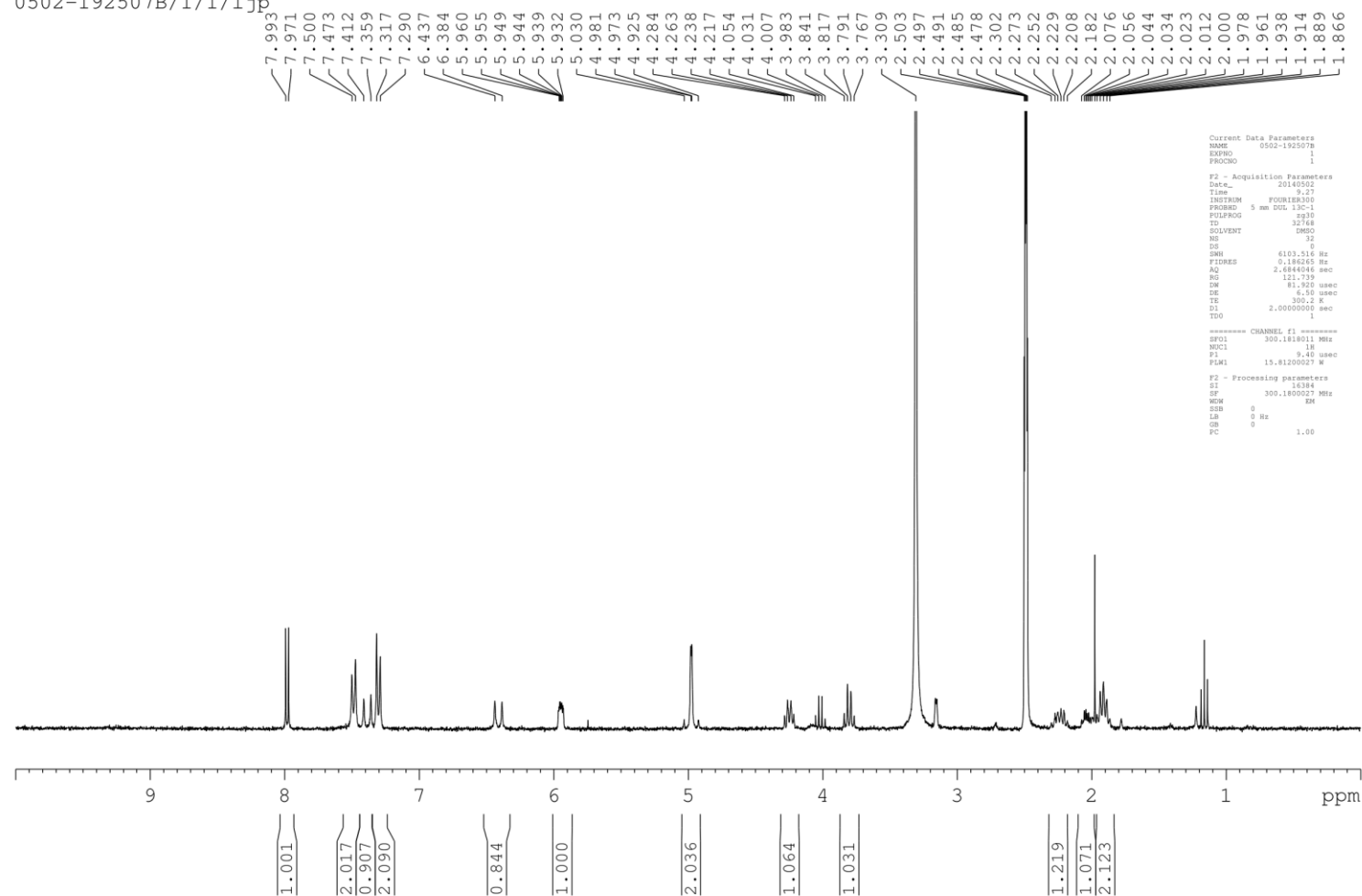
¹H Spectrum for compound 6

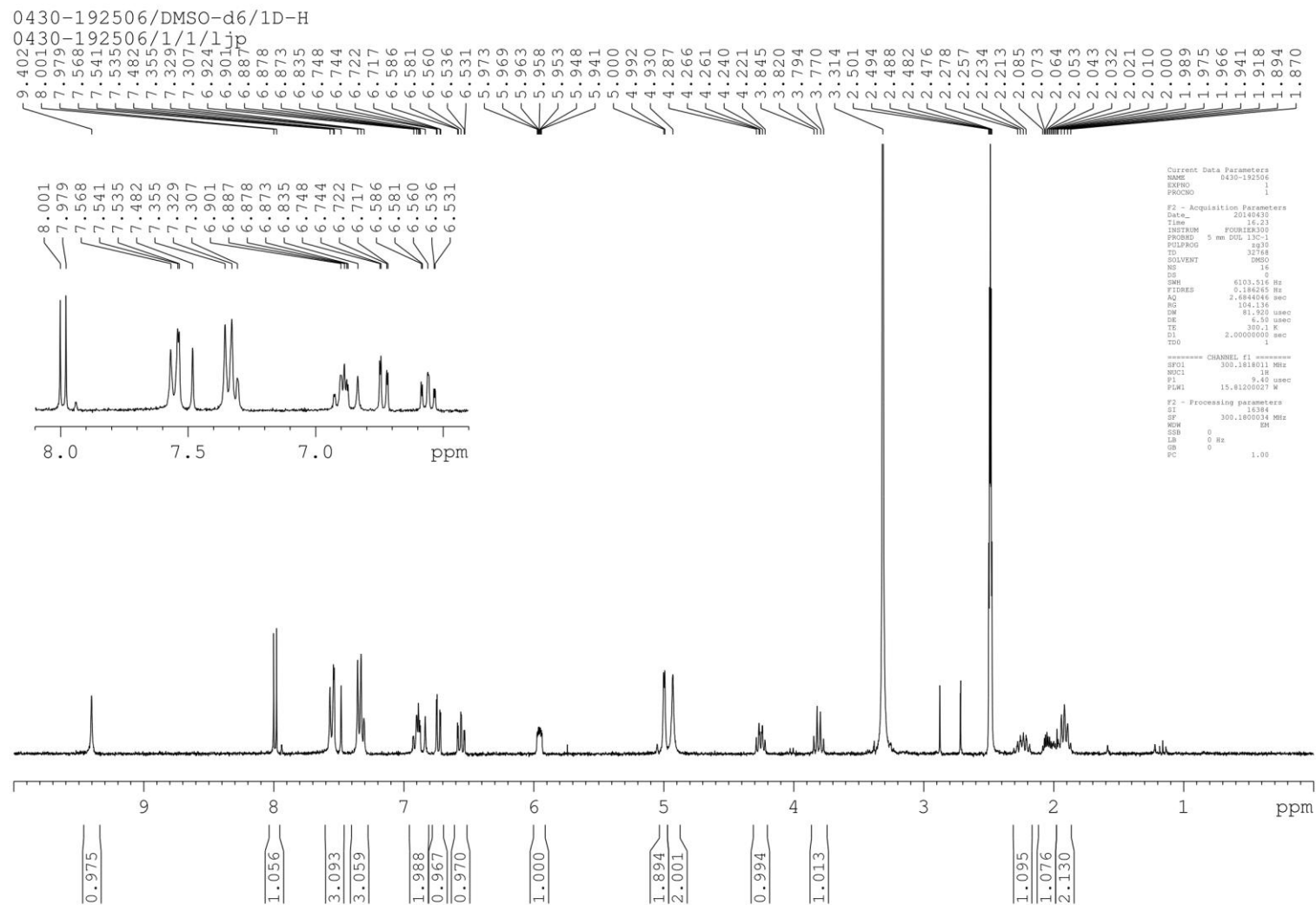
¹H Spectrum for compound 7

¹H Spectrum for compound 8

0502-192507B/DMSO-d6/1D-H

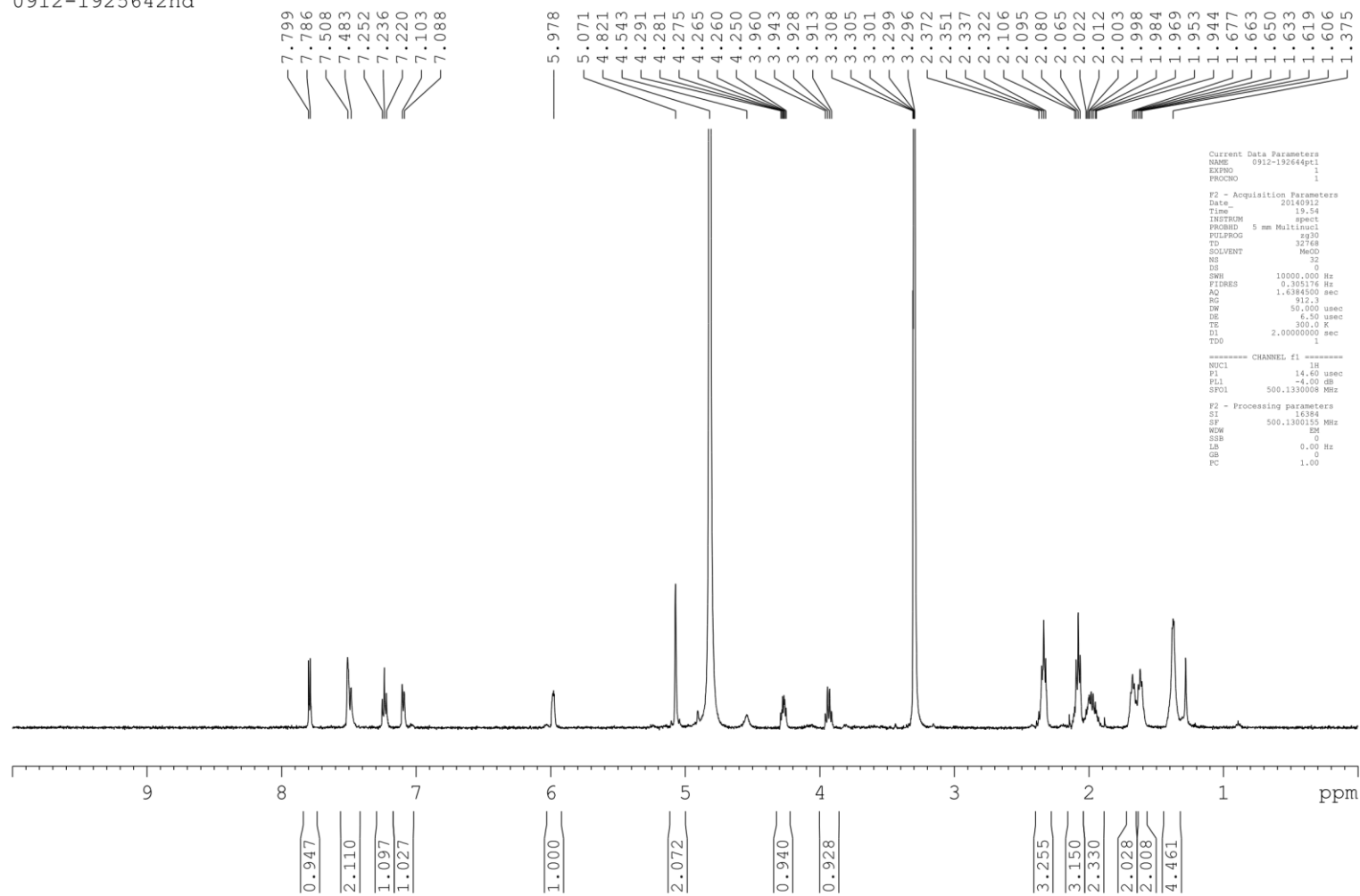
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¹H Spectrum for compound 9

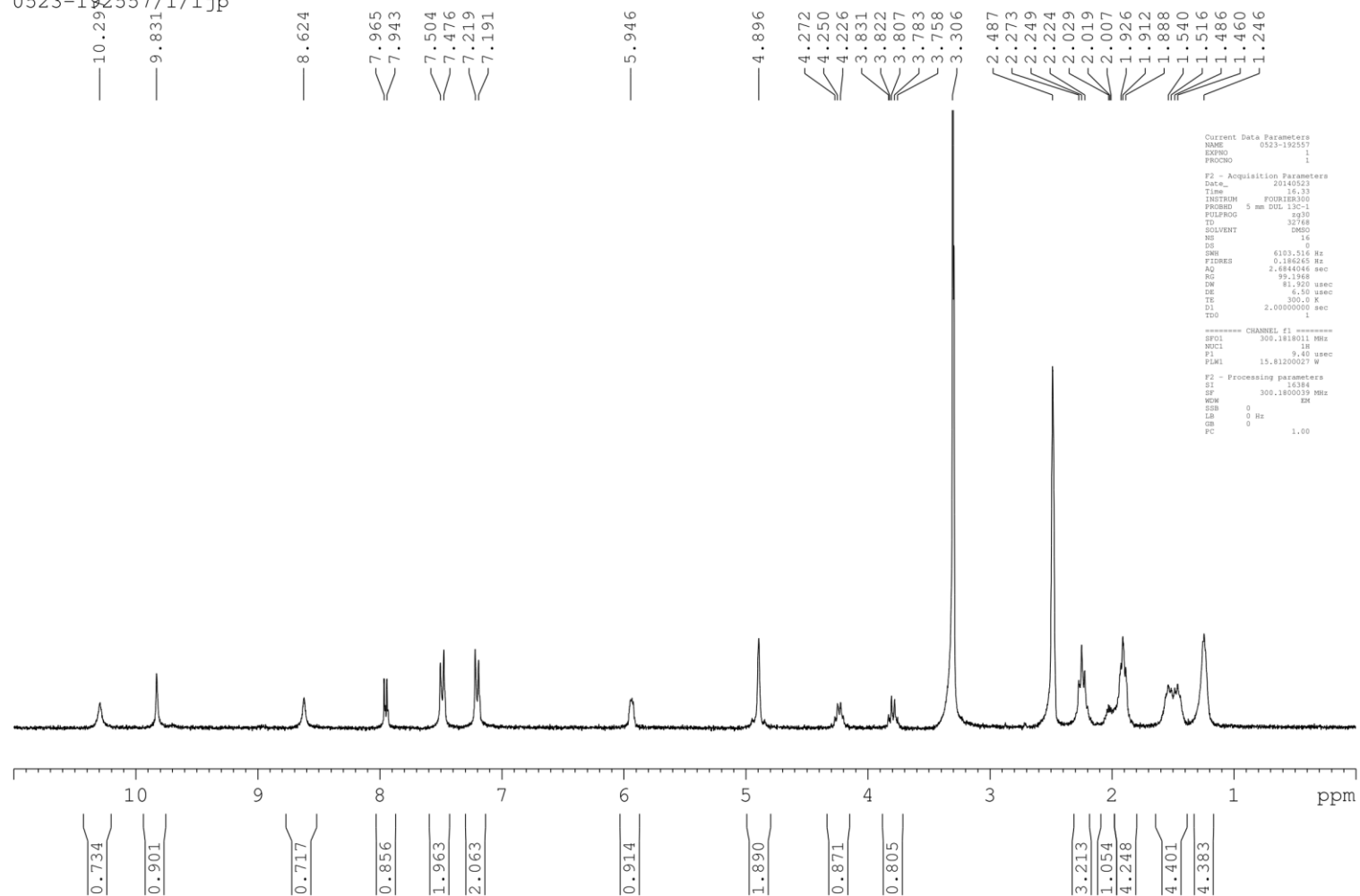
¹H Spectrum for compound 10

1D-H
0912-1925642nd

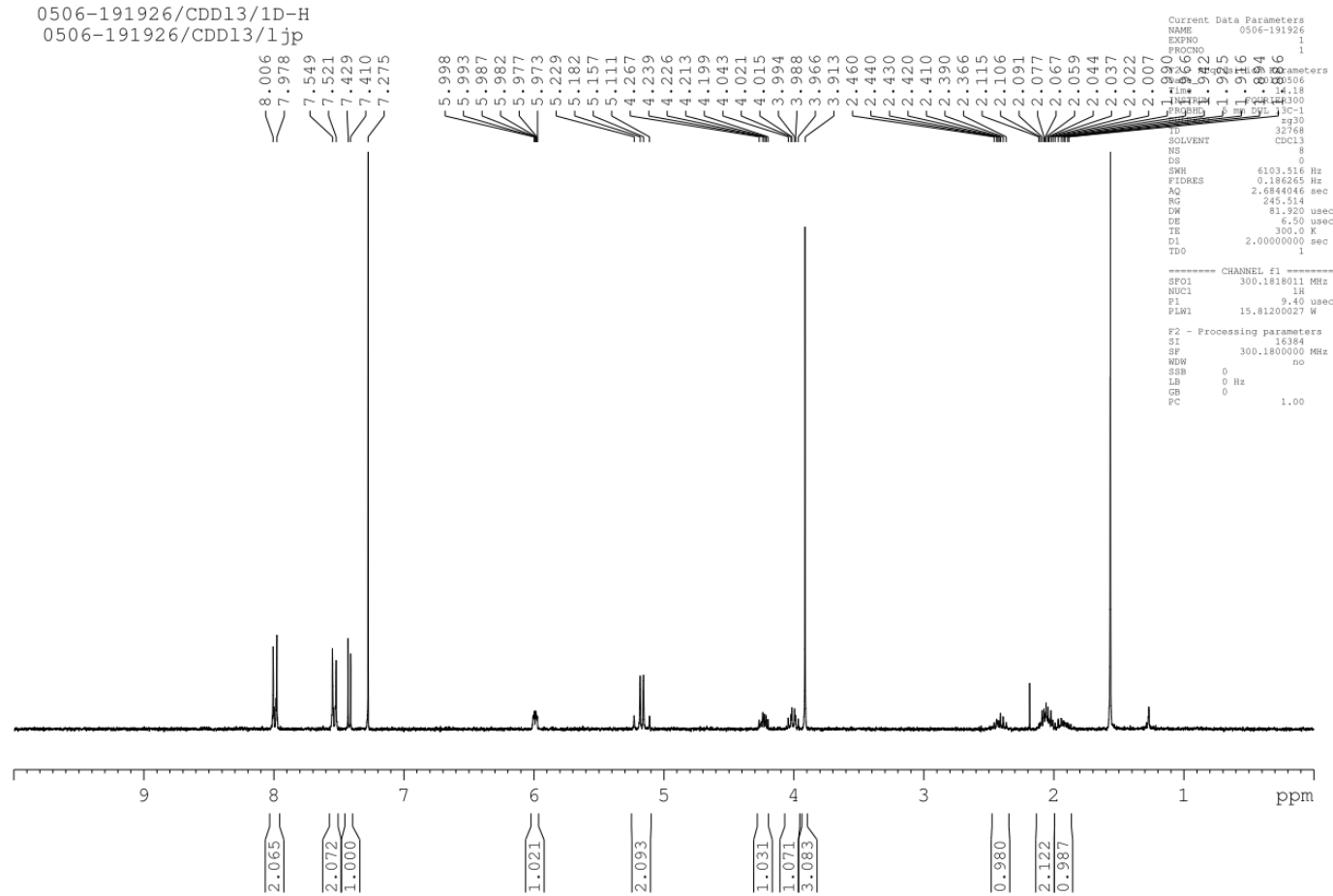


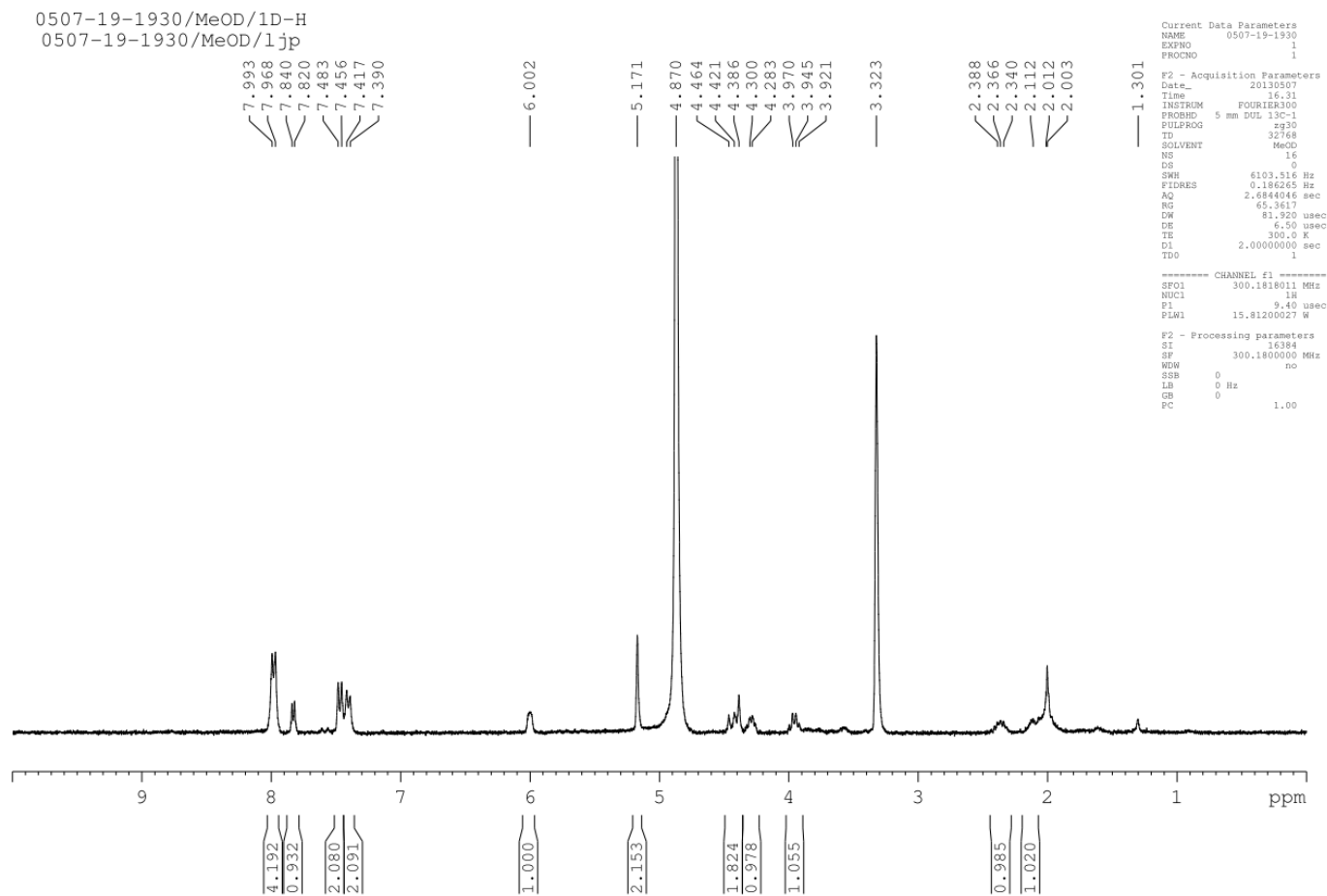
¹H Spectrum for compound 11

0523-192557/DMSO-d6/1D-H
0523-192557/1/1.jp

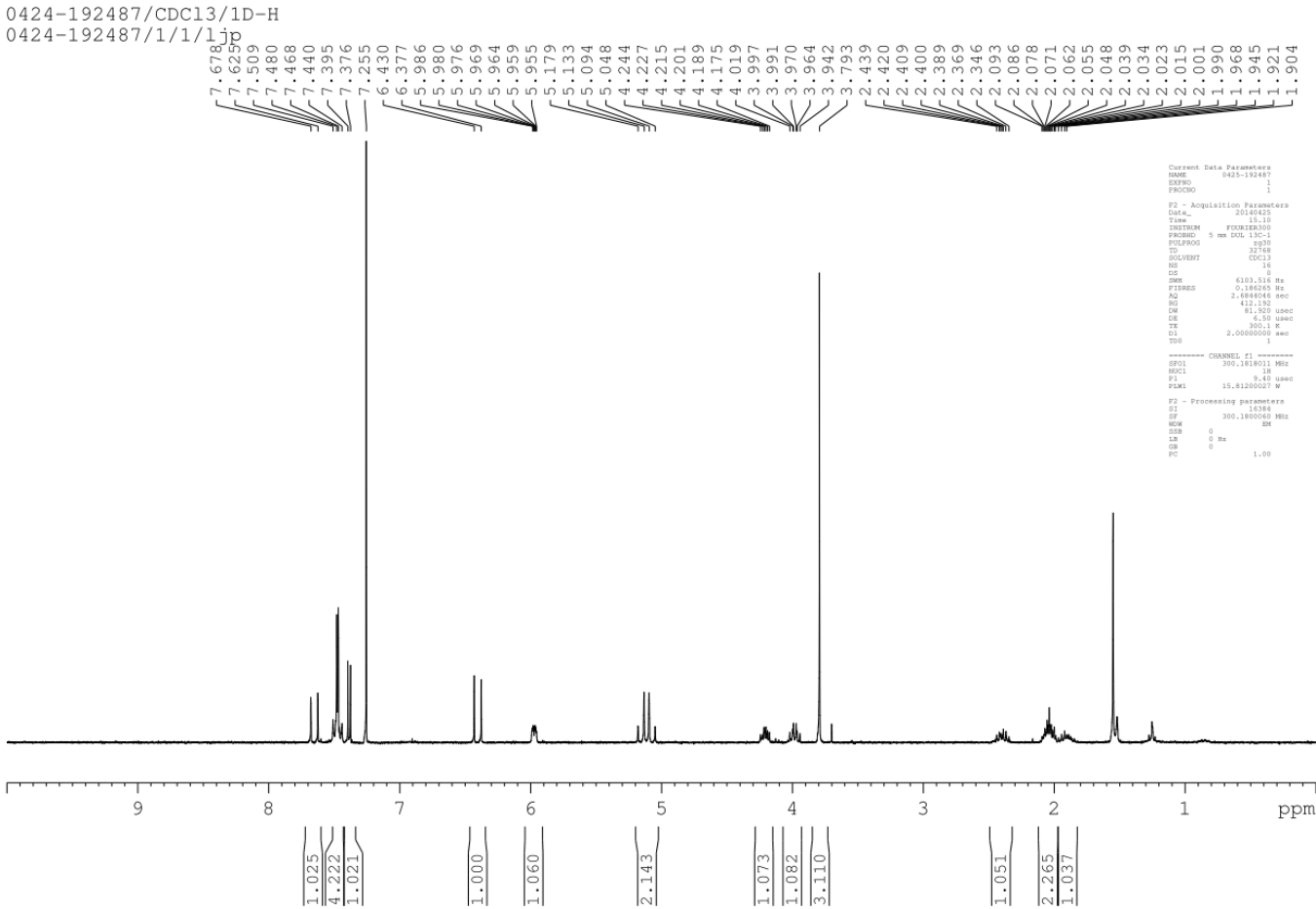


¹H Spectrum for compound 12



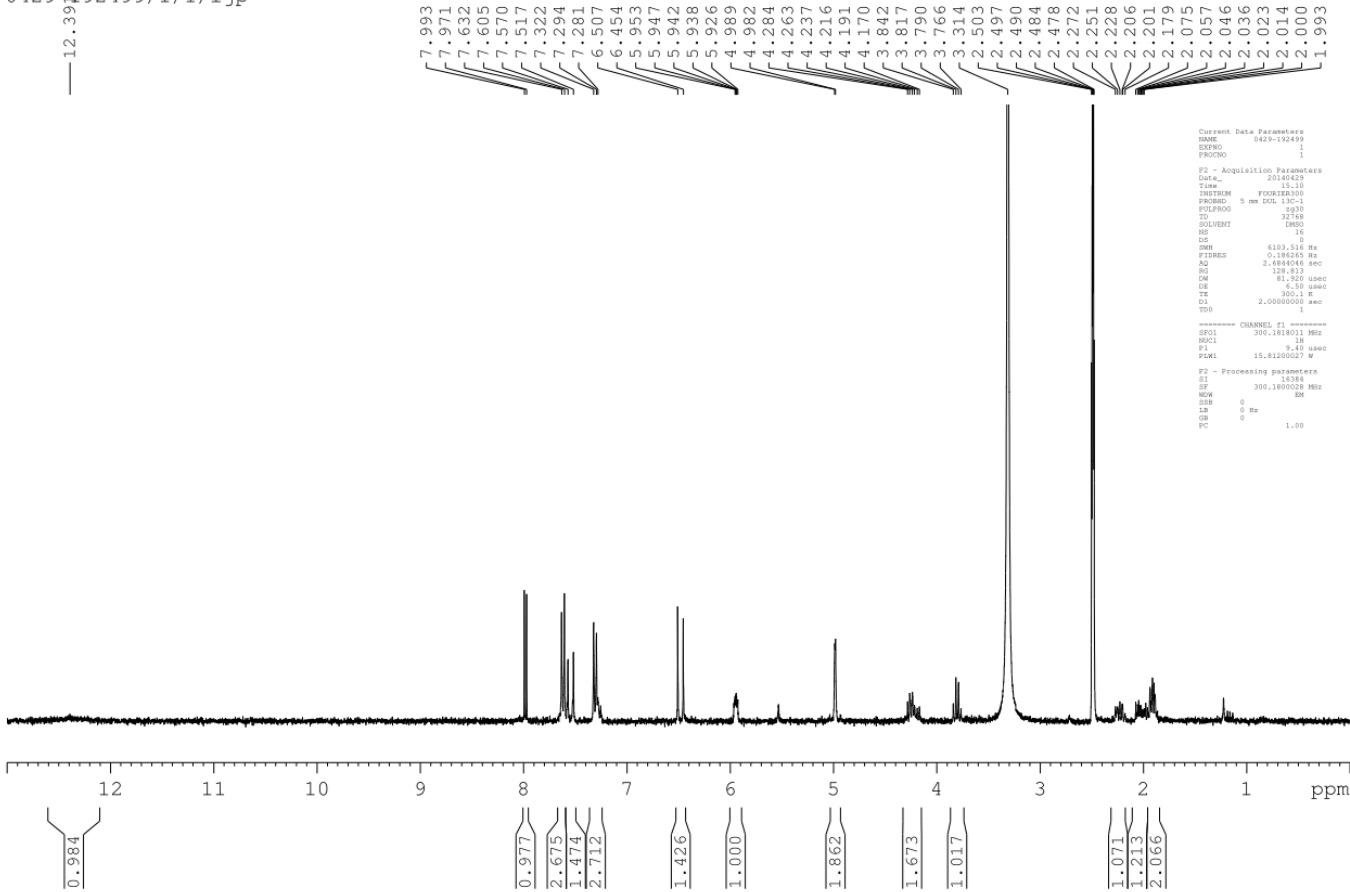
^1H Spectrum for compound 13

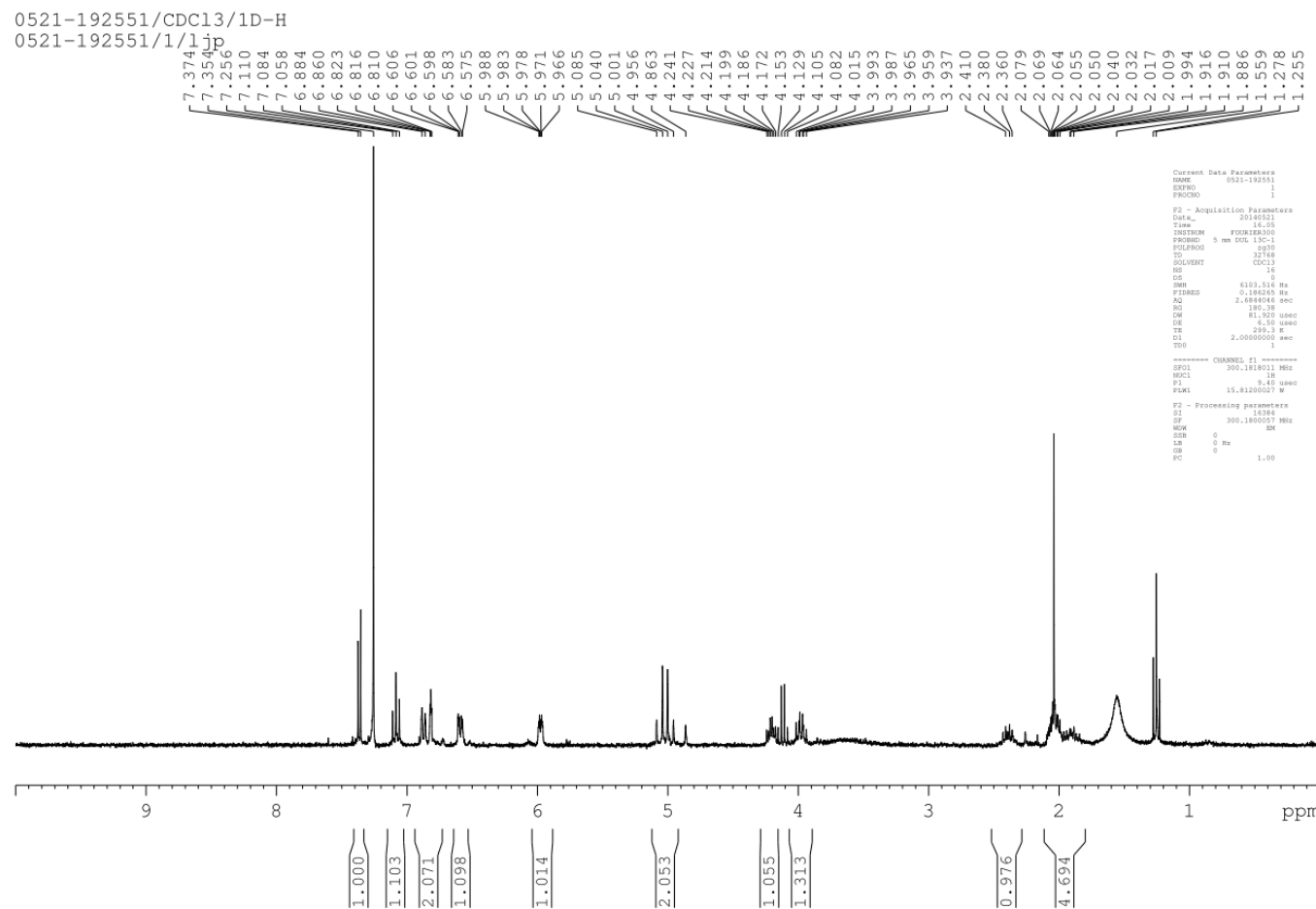
¹H Spectrum for compound 14



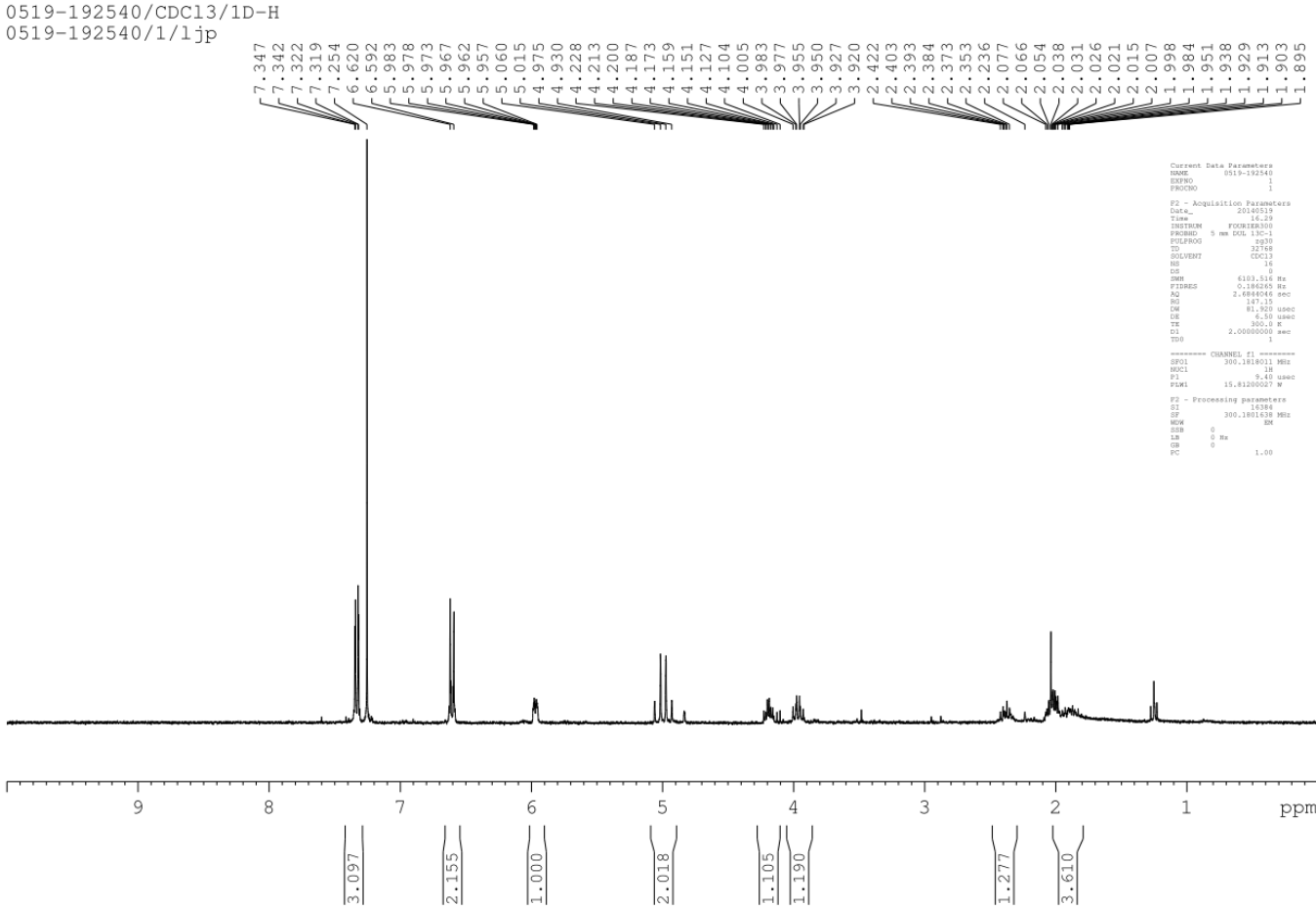
¹H Spectrum for compound 15

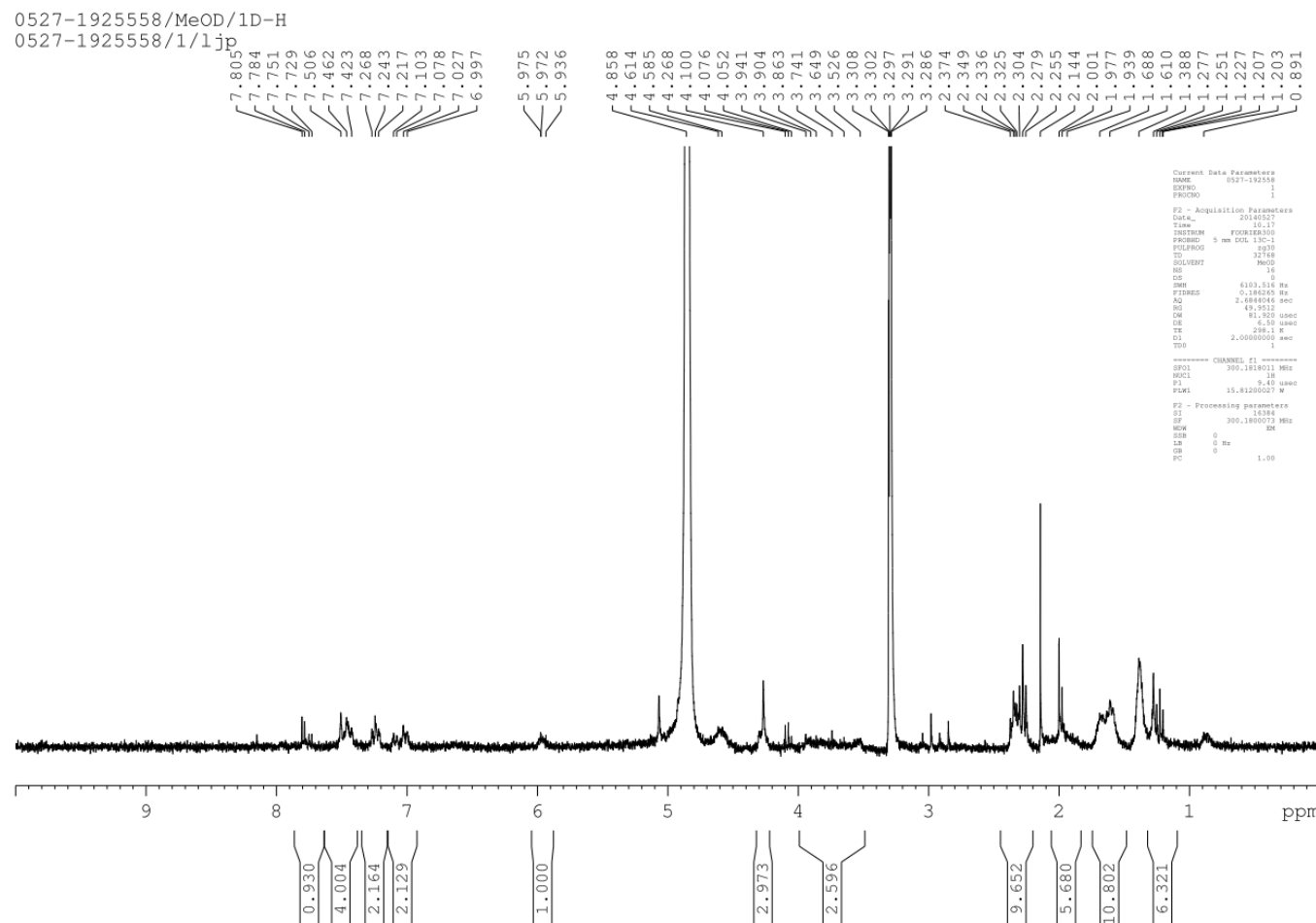
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0429-192499/1/1/1jp

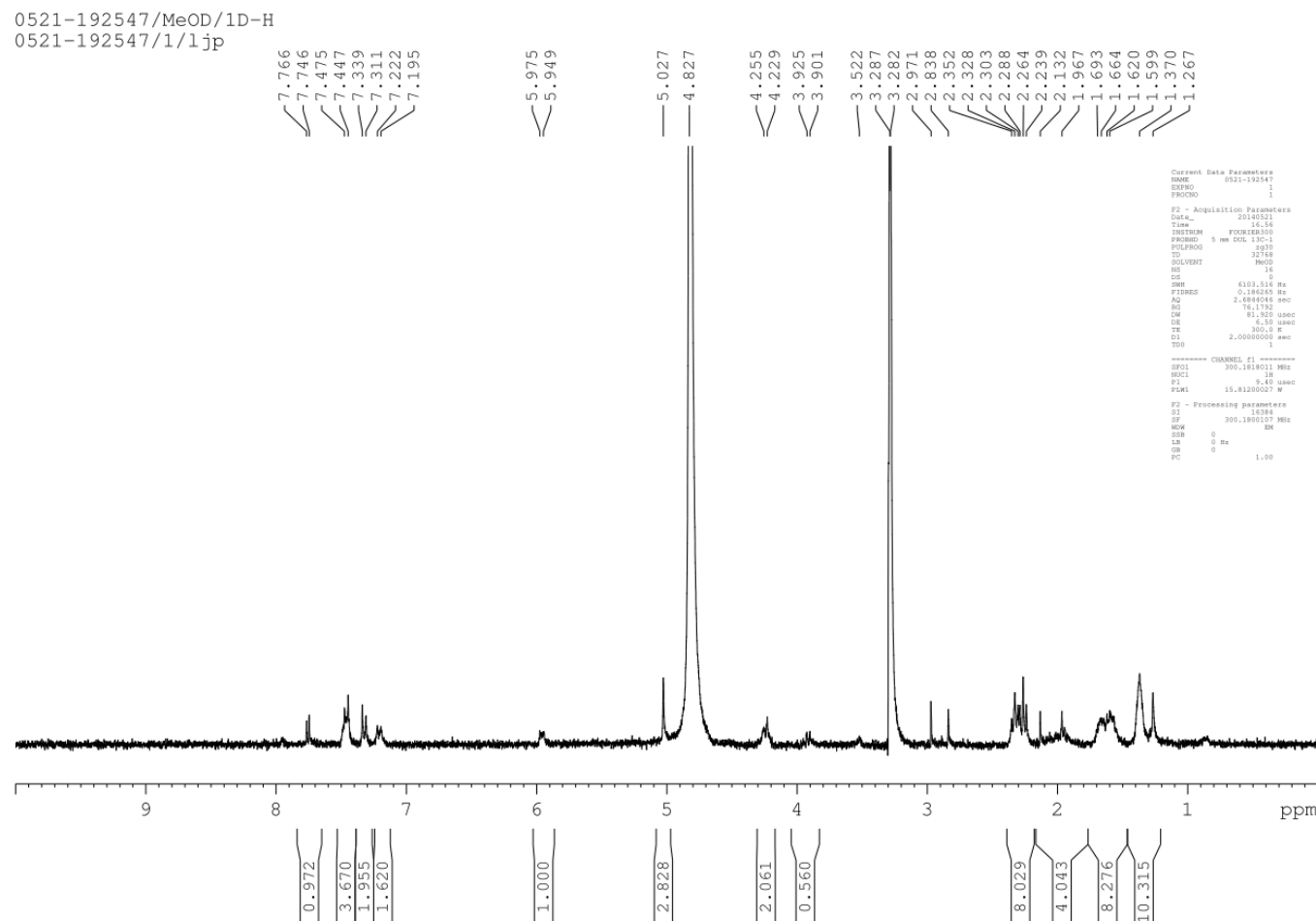


^1H Spectrum for compound 16a

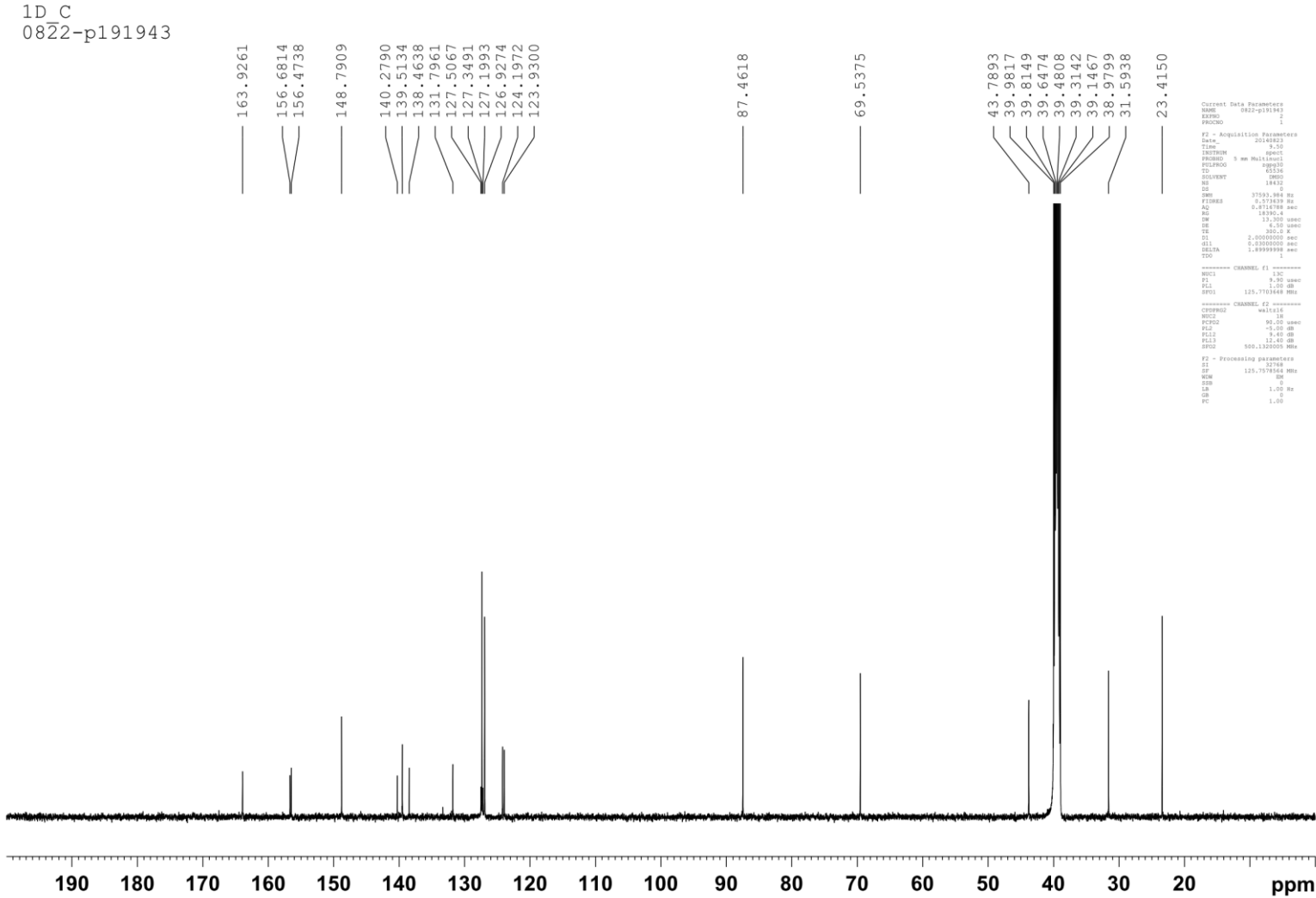
¹H Spectrum for compound 16b



¹H Spectrum for compound 17a

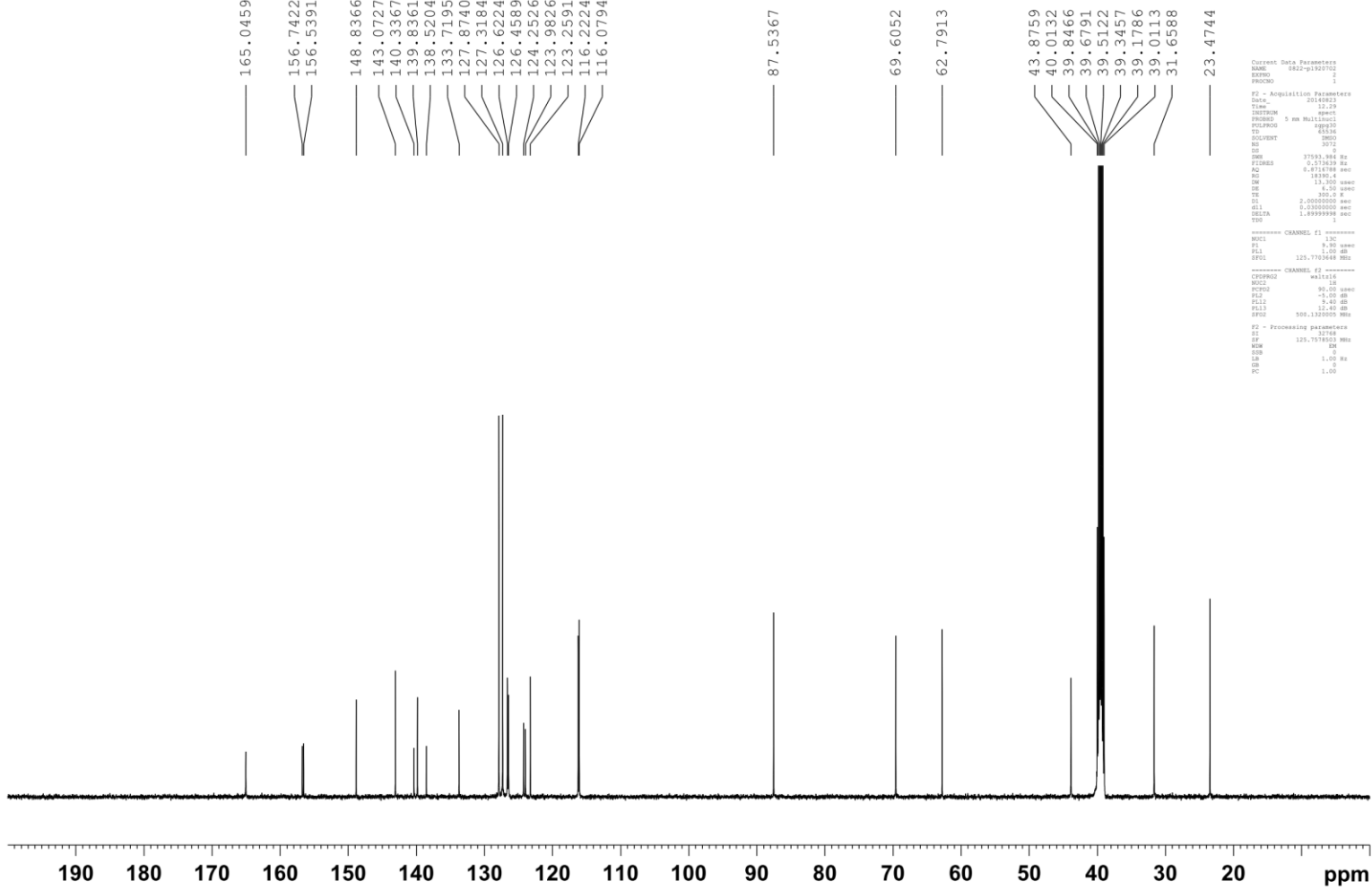
^1H Spectrum for compound 17b

¹³C Spectrum for compound 6



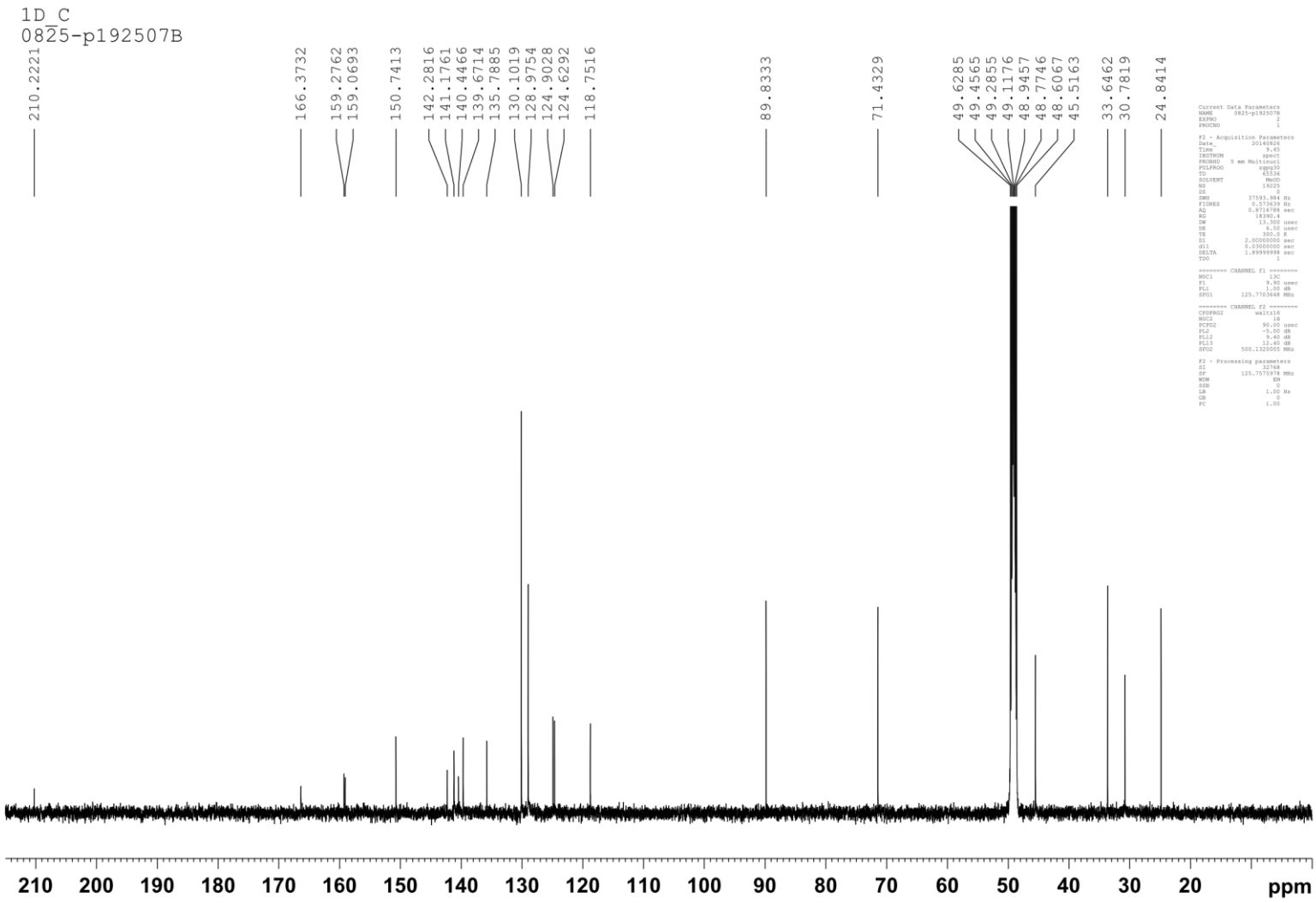
¹³C Spectrum for compound 7

1D_C
0822-p1920702



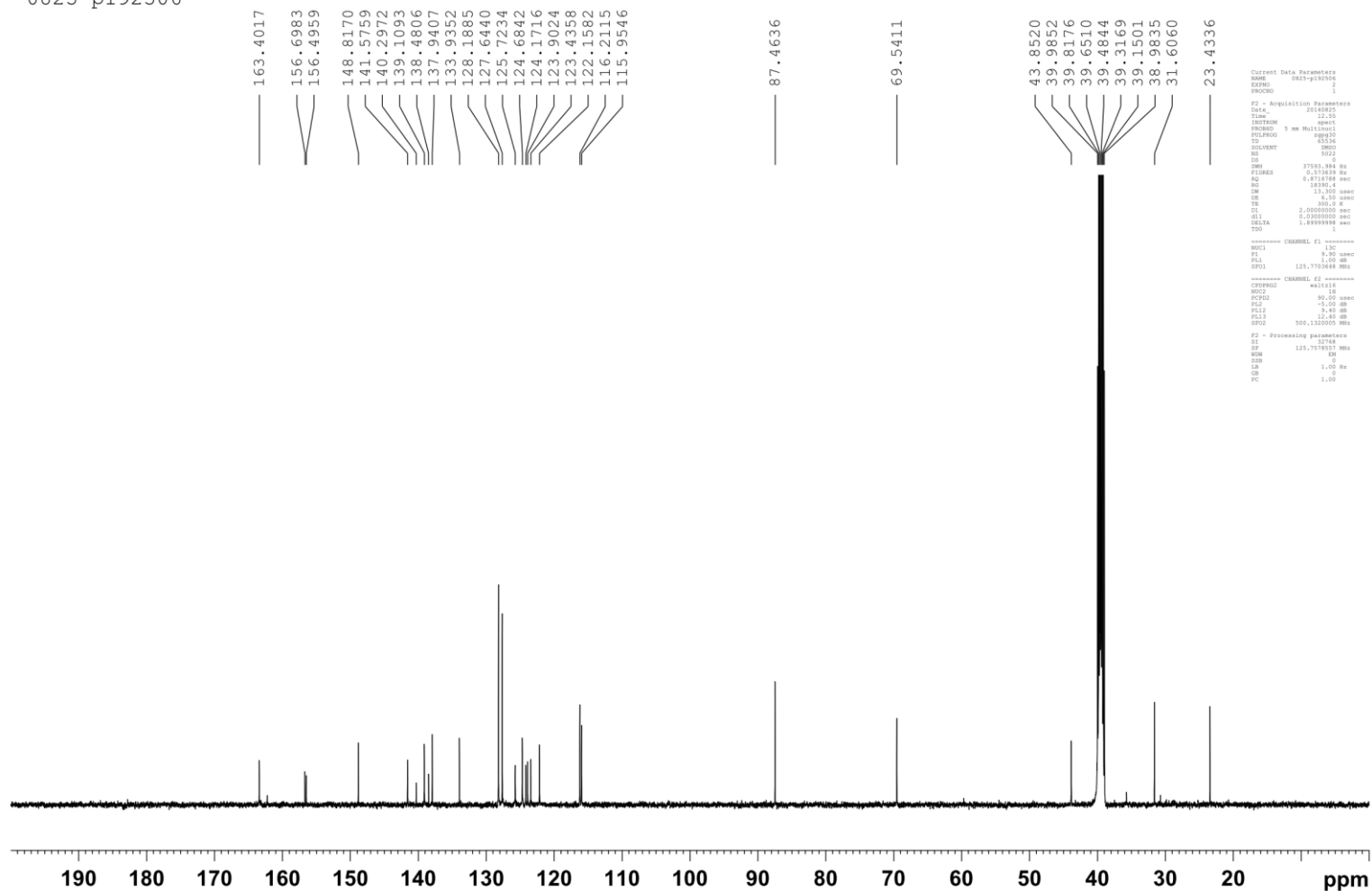
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FIDRES 0.571819 Hz
AQ 0.6716788 sec
RG 18387.4
DM 13.300 umsec
DE 6.50 umsec
TE 300.2 K
SI 2.00000000 sec
SFI 0.00000000 sec
DELTA 1.99999998 sec
TD 1
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NUC1 13C
P1 16.00 umsec
PL1 0.00 dB
SFO1 125.7703648 MHz
===== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
P2 9.00 umsec
PL2 0.00 dB
PL12 19.00 dB
PL13 19.00 dB
SFO2 500.1320050 MHz
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GB 0.00 Hz
PC 1.00

¹³C Spectrum for compound 8



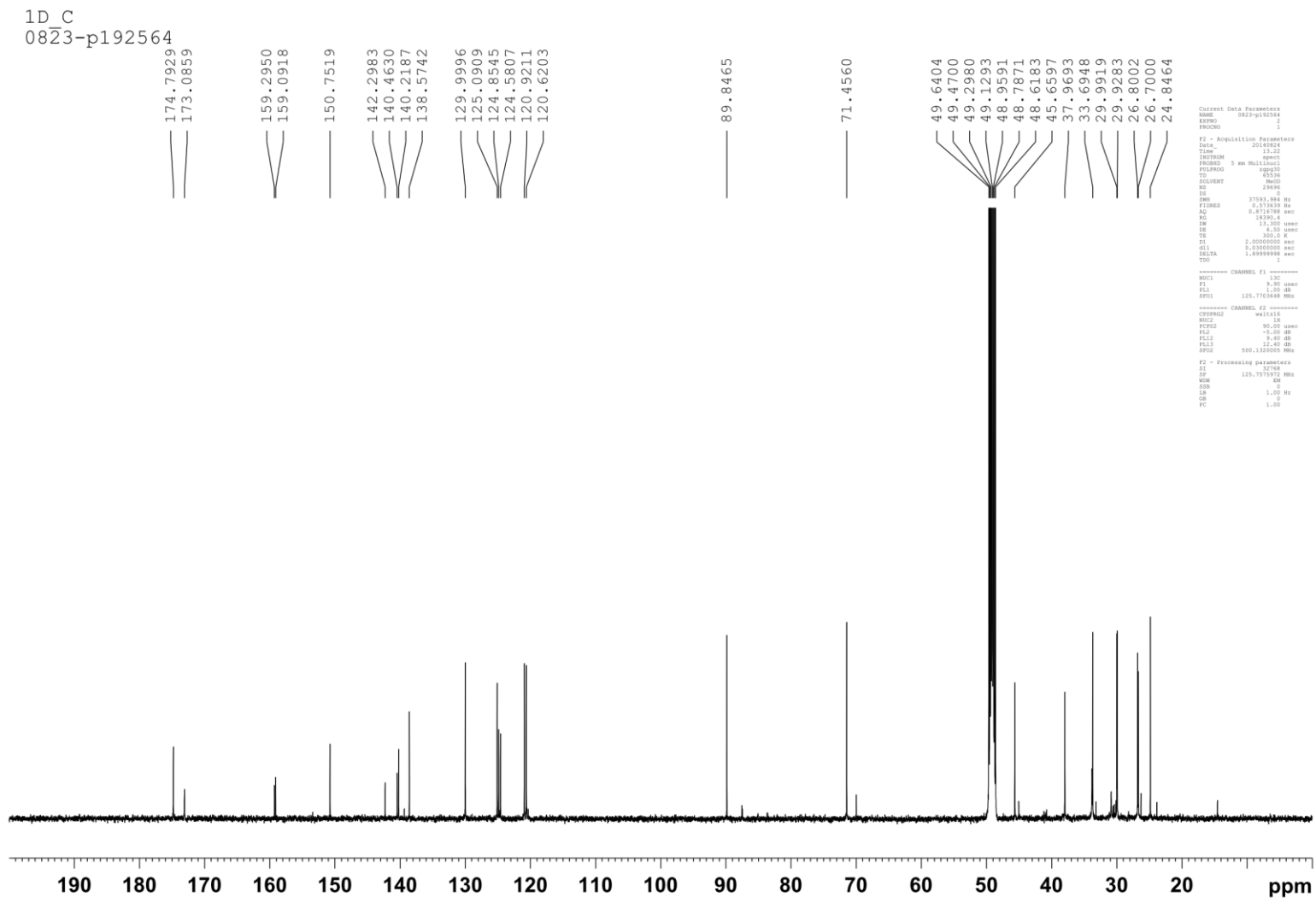
^{13}C Spectrum for compound 9

1D_C
0825-p192506

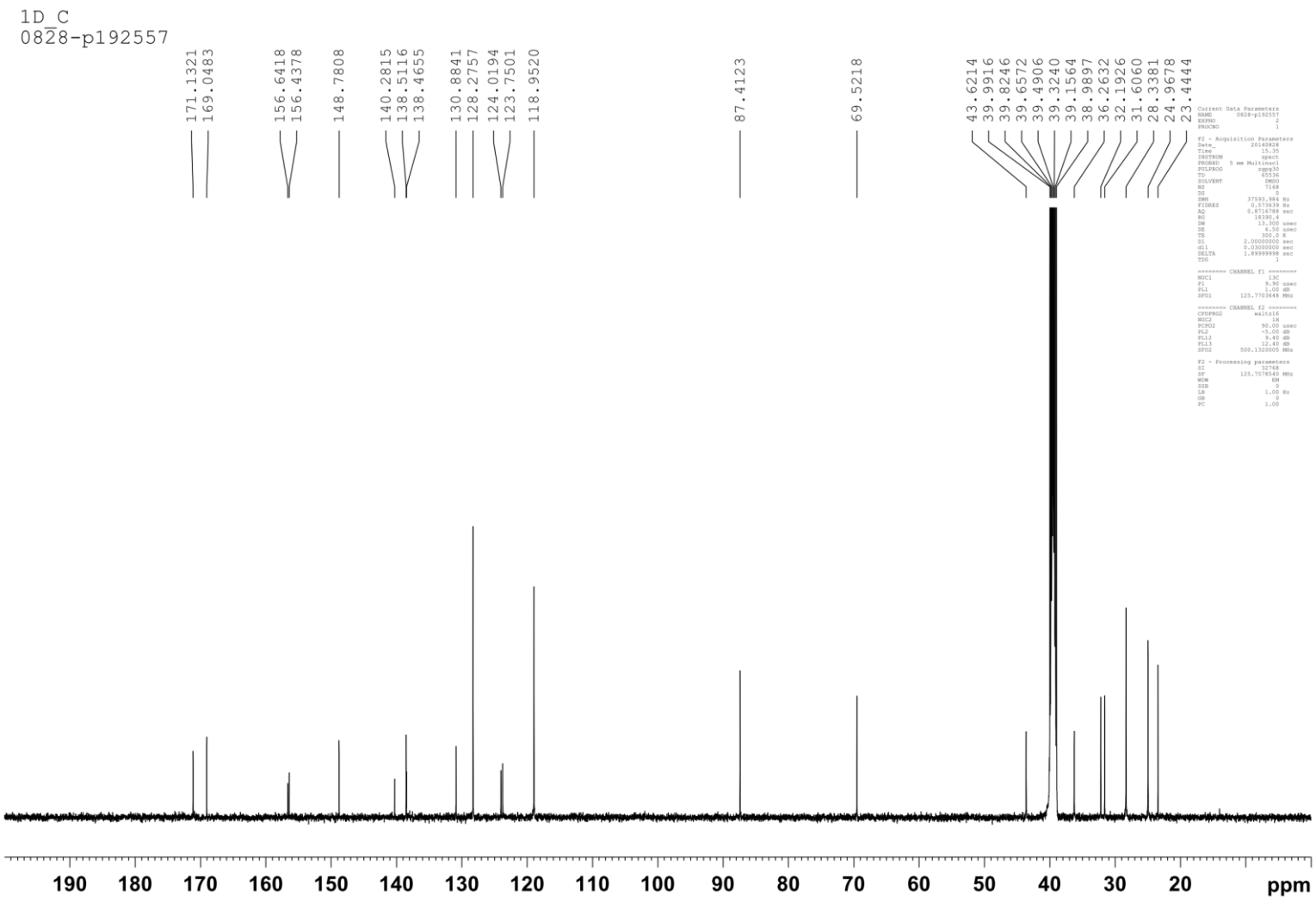


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NS 1022
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SWH 37501.884 Hz
FIDRES 0.1718339 Hz
AQ 0.1810198 sec
RG 18180.4
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UH 6.50 umol
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Q1 2.0000000 sec
Q11 0.0000000 sec
DELTA 1.8999999 sec
TD0 1
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SFO1 125.7603649 MHz
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NUC2 1H
PCPD2 90.00 umol
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PL12 9.40 dB
PL13 12.40 dB
SFO2 500.1320005 MHz
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GB 0
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¹³C Spectrum for compound 10



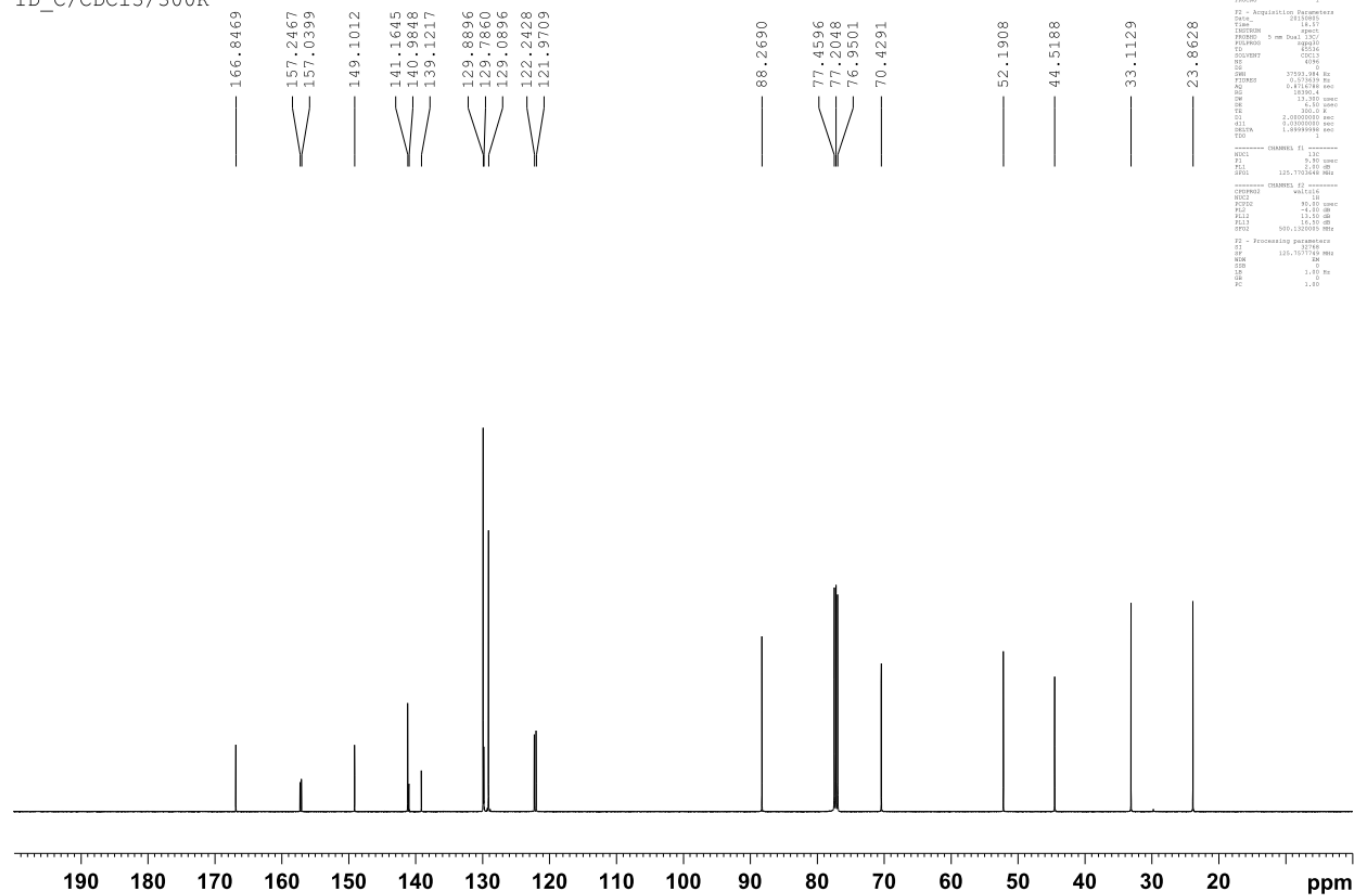
¹³C Spectrum for compound 11



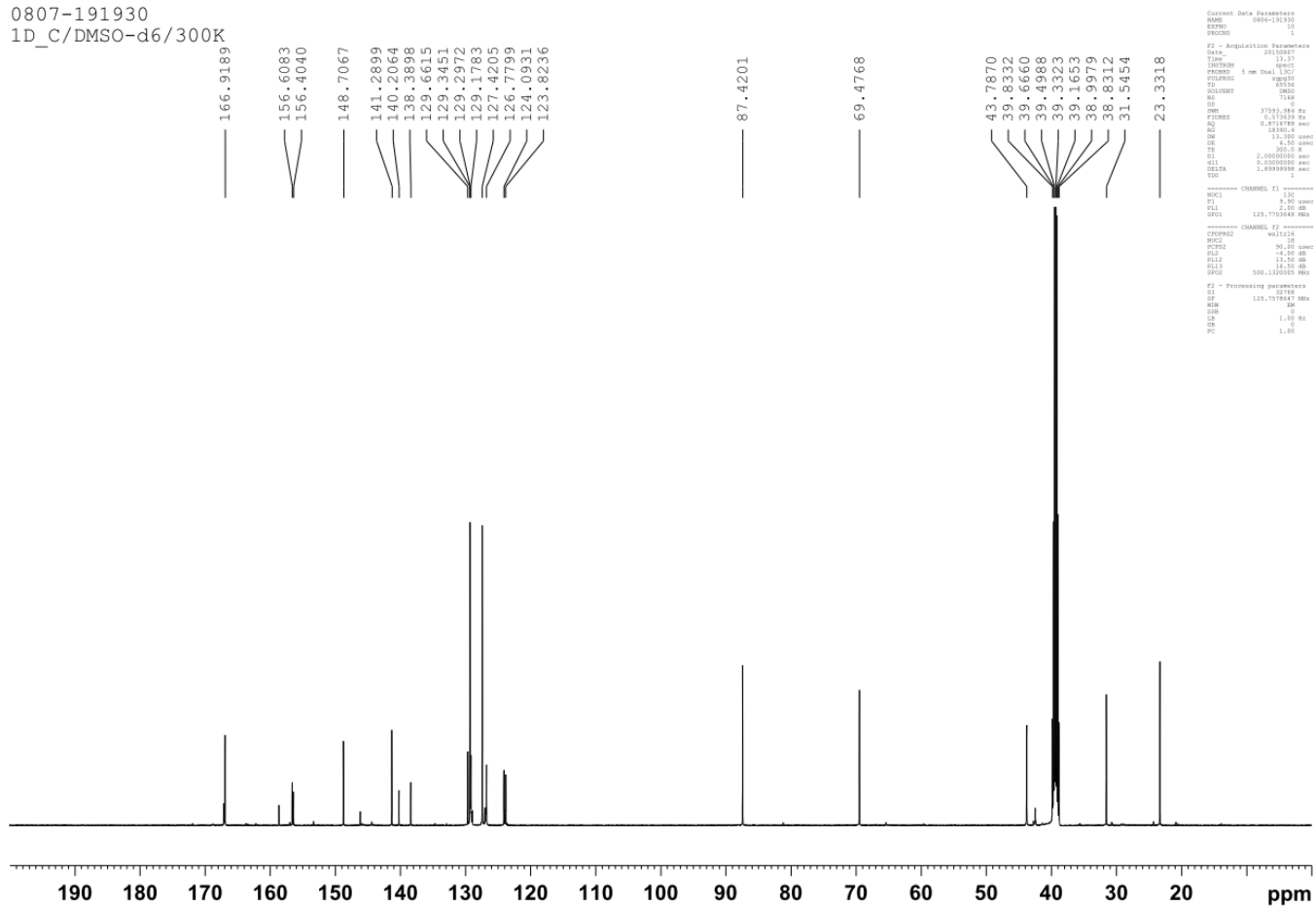
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SOLVENT DMSO
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DECCA 1.89999998 sec
TDS 3
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SFO1 125.760448 MHz
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CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 kHz
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PL12 0.40 dB
PL13 0.40 dB
PL14 0.40 dB
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^{13}C Spectrum for compound 12

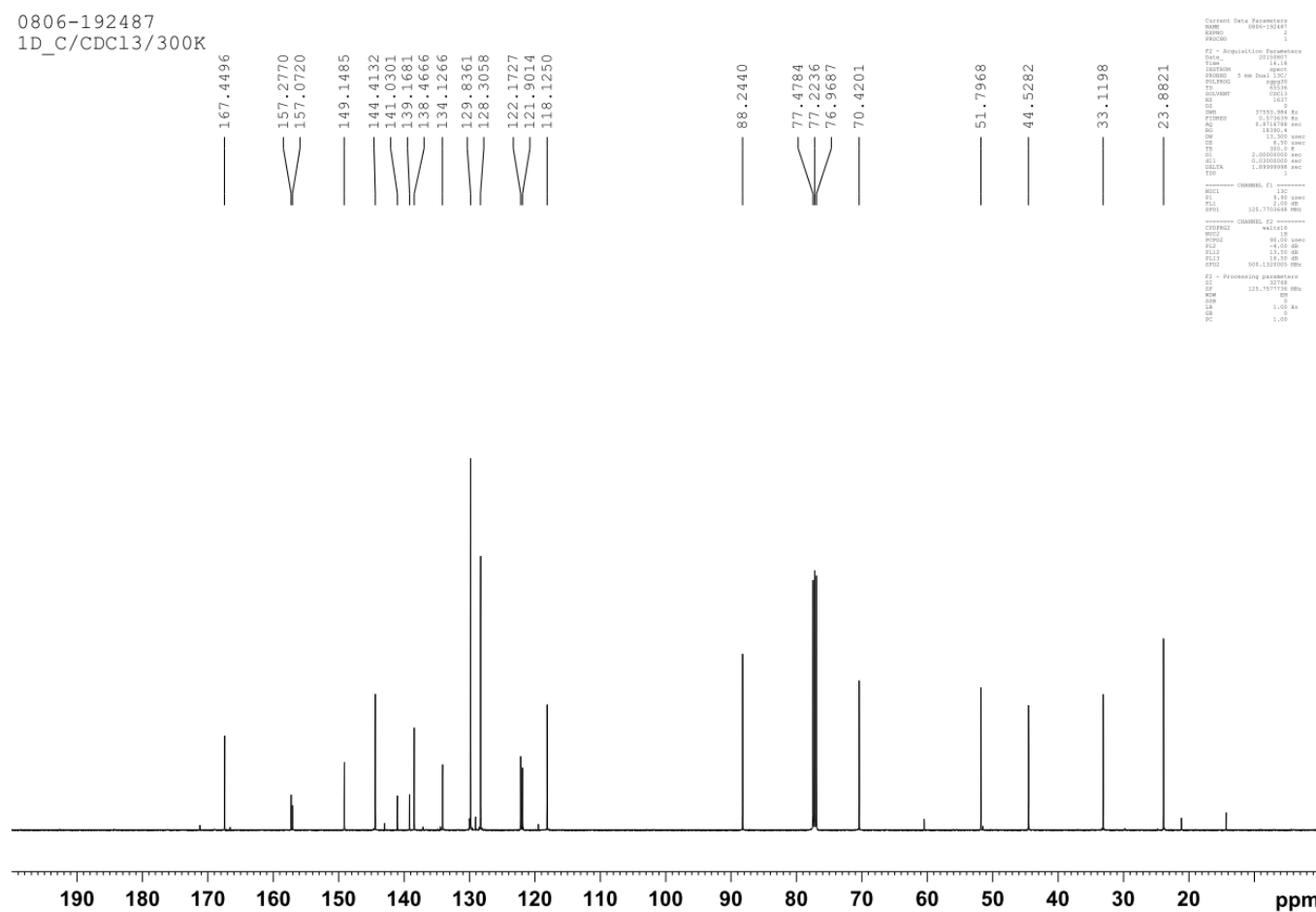
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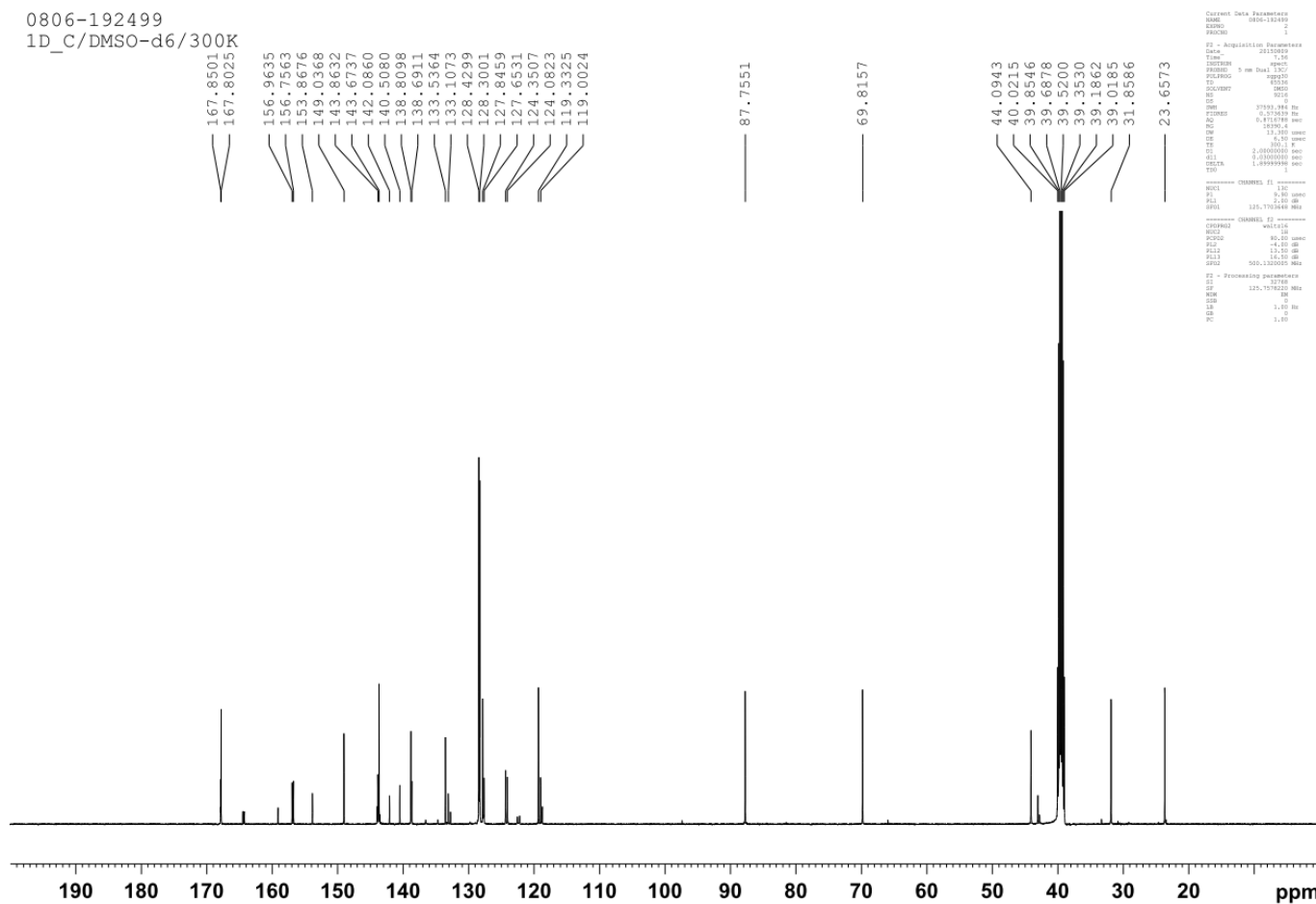


¹³C Spectrum for compound 13



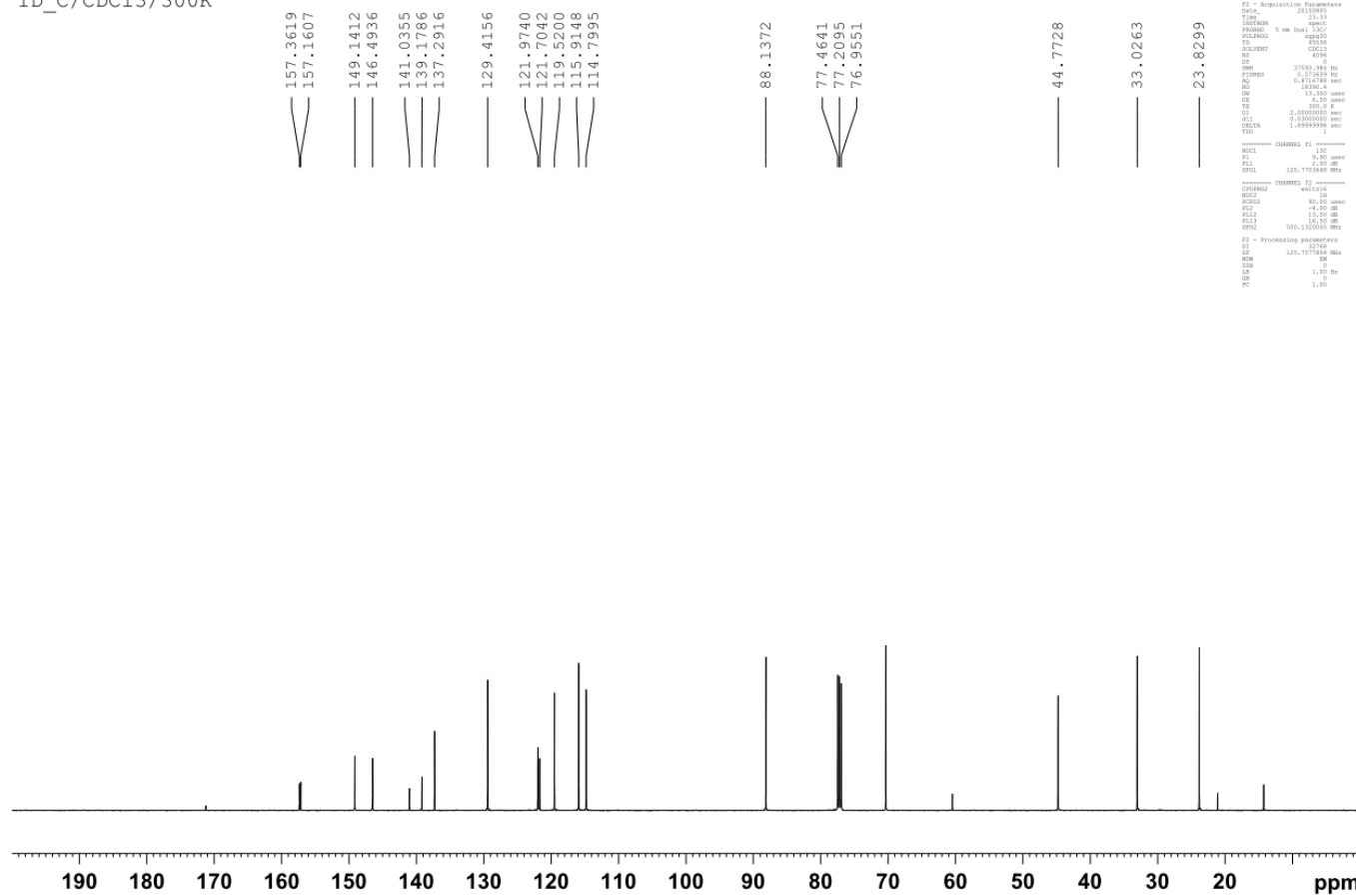
¹³C Spectrum for compound 14

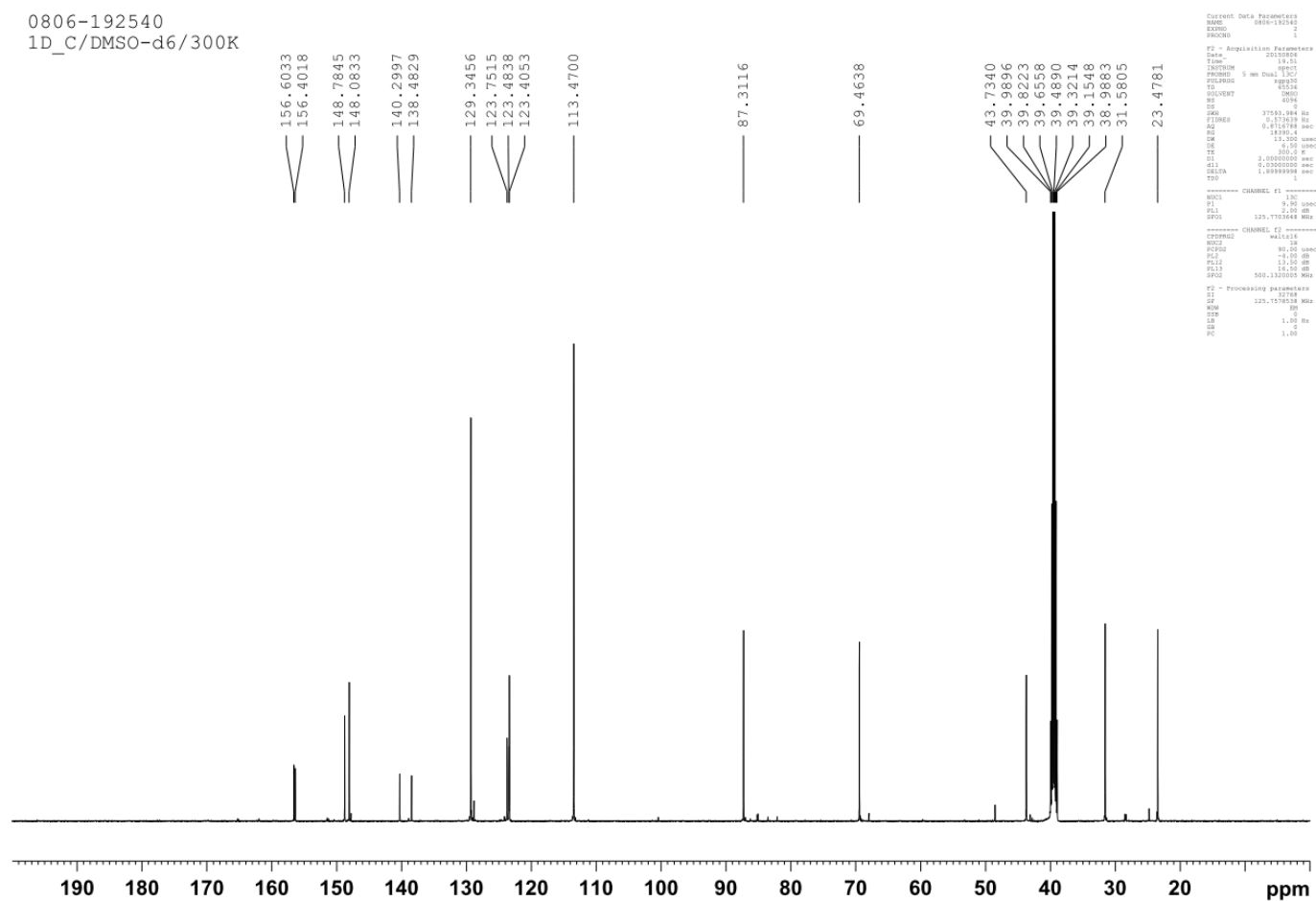


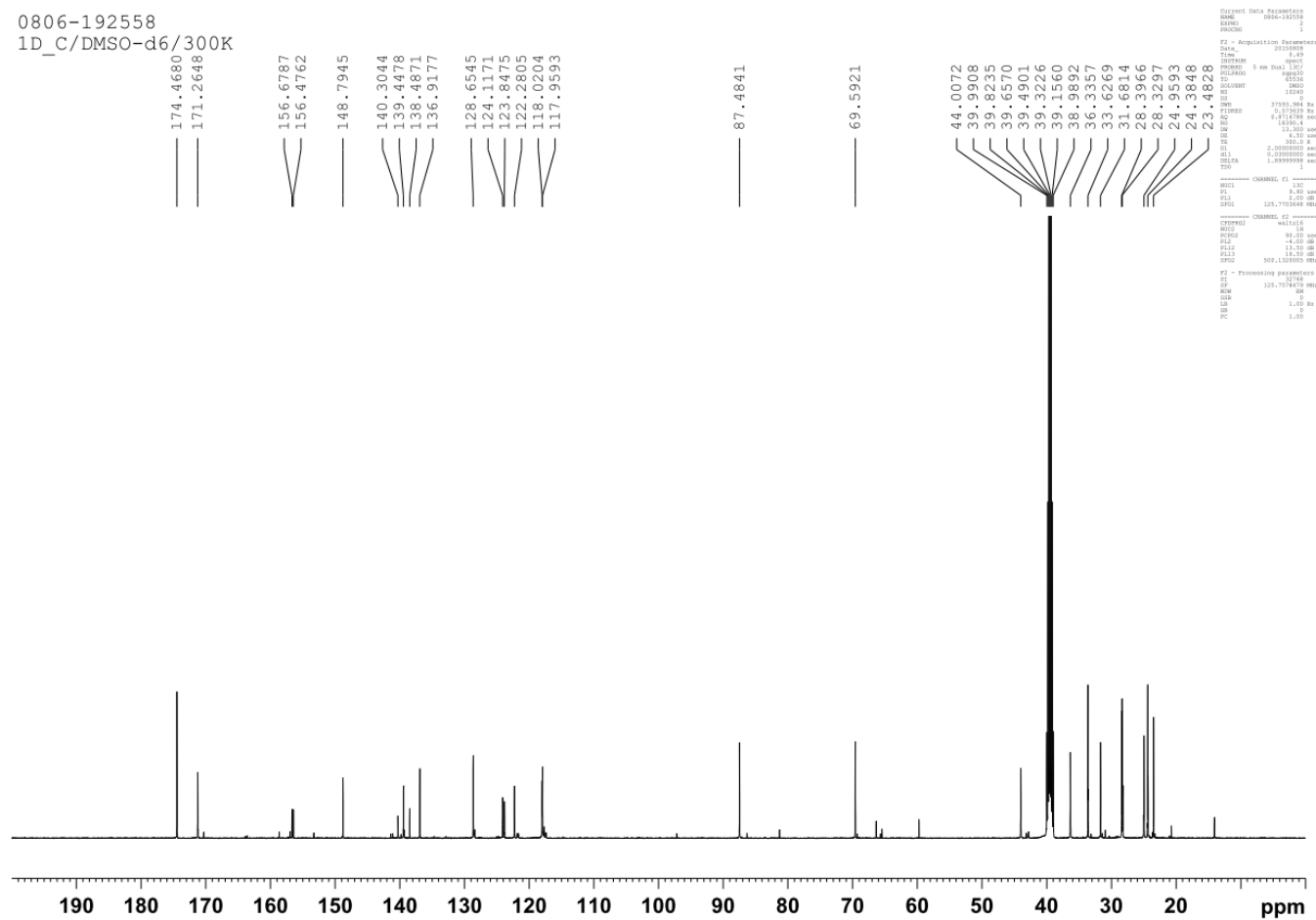
^{13}C Spectrum for compound 15

¹³C Spectrum for compound 16a

0804-192551
1D_C/CDC13/300K







^{13}C Spectrum for compound 17b