Synthesis of LSD1 Inhibitor–Pyrrole Imidazole Polyamide Conjugates for Region-Specific Alterations of Histone Modification

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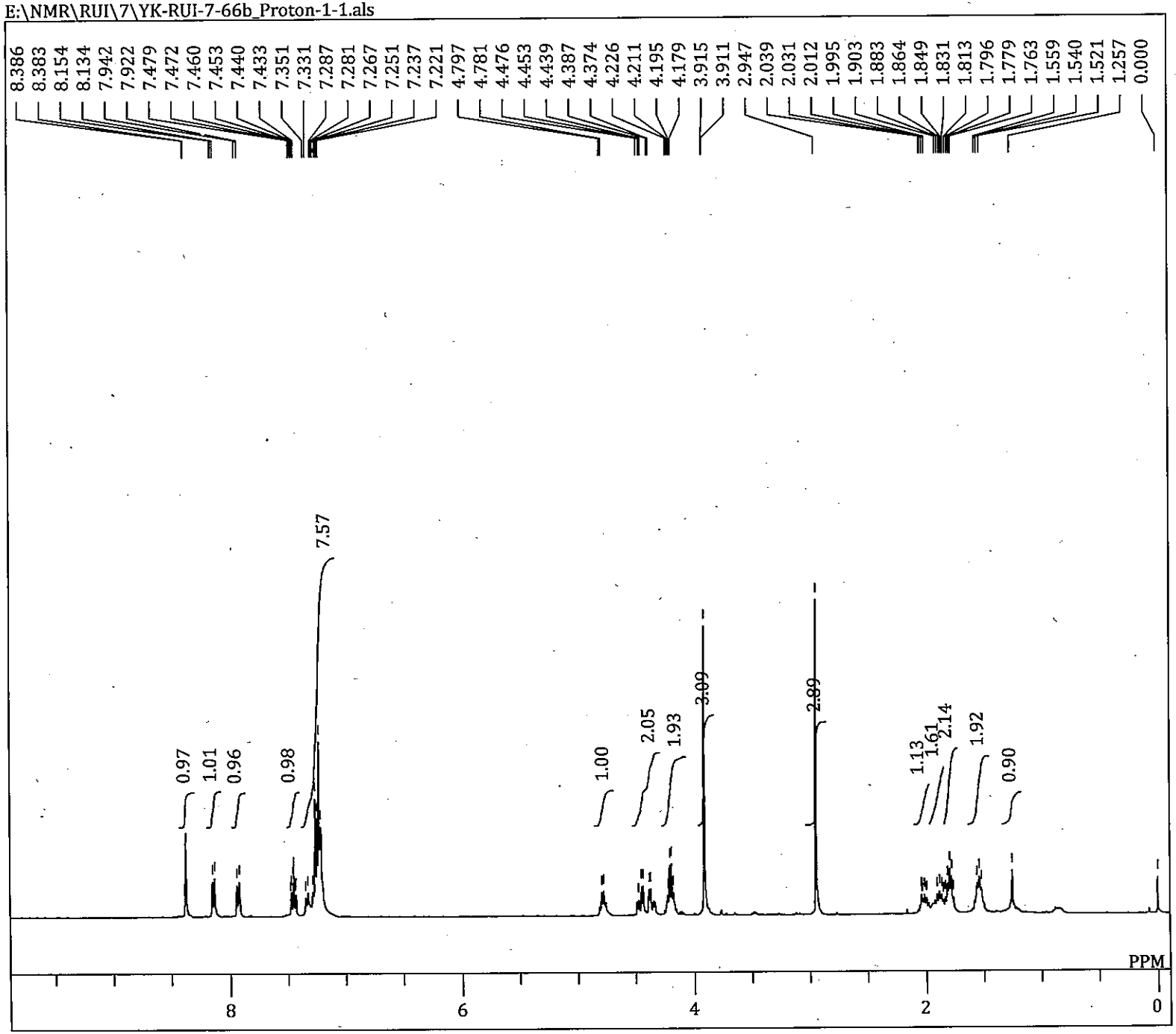
Supporting Information

single_pulse

E:\NMR\RUI\7\YK-RUI-7-66b_Proton-1-1.als



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OBFIN	7.29 Hz
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SCANS	8
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PD	5.0000 sec
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IRNUC	1H
CTEMP	24.7 c
SLVNT	CDCL3
EXREF	0.00 ppm
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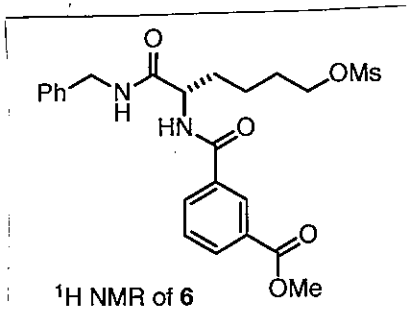
RGAIN	36



^{1}H NMR of **6**

single pulse decoupled gated NOE

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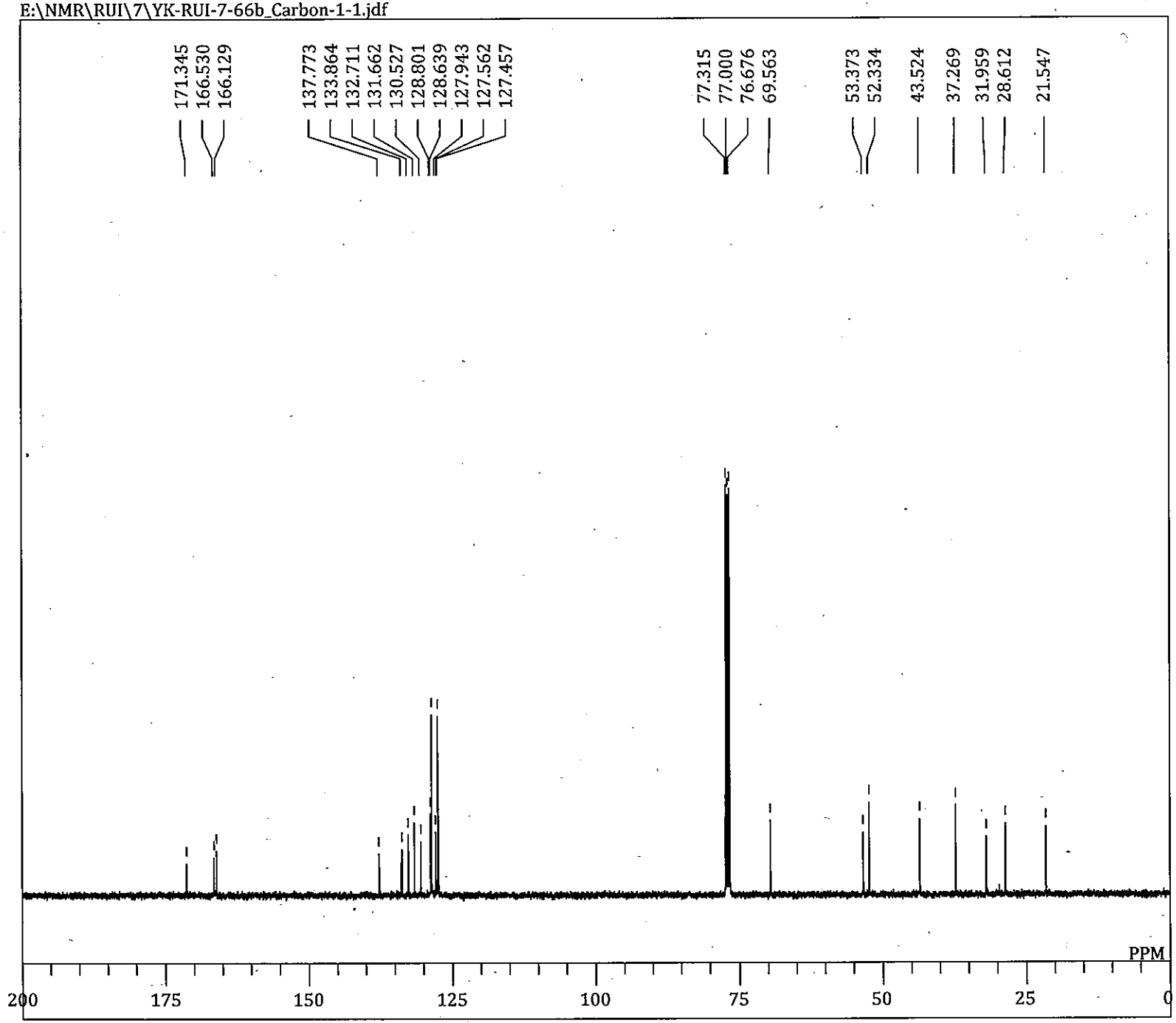

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PD	2.0000 sec
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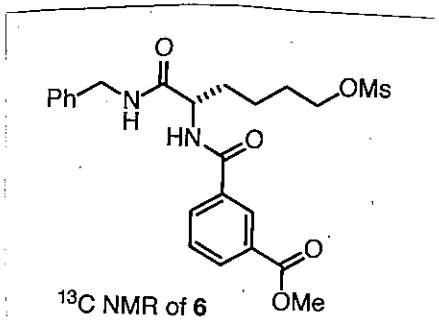
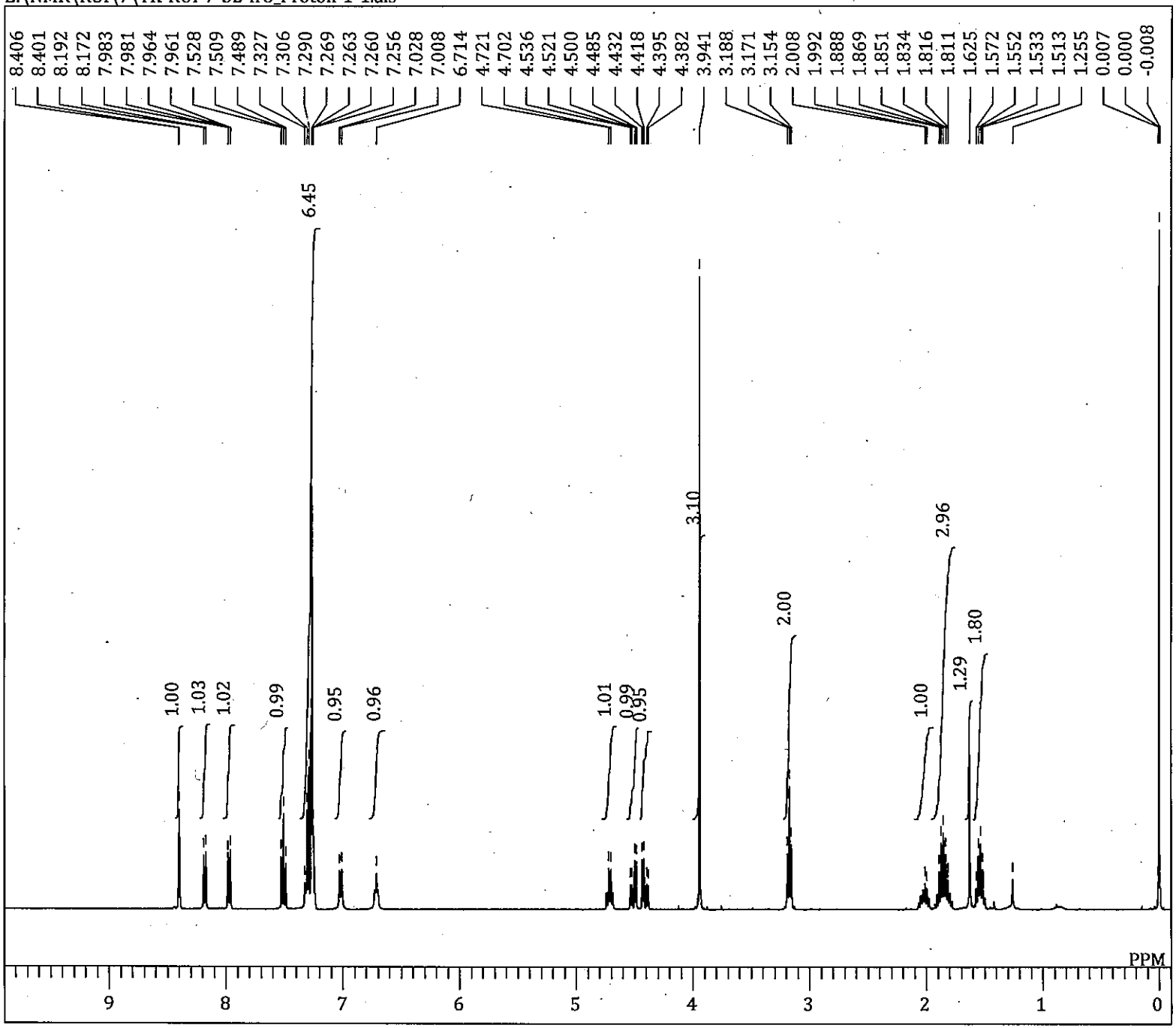
CTEMP	24.8 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	1.20 Hz
RGAIN	50



^{13}C NMR of **6**

single_pulse

E:\NMR\RUI\7\YK-RUI-7-52-fr8_Proton-1-1.als



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POINT	13107
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SCANS	8
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PD	5.0000 sec
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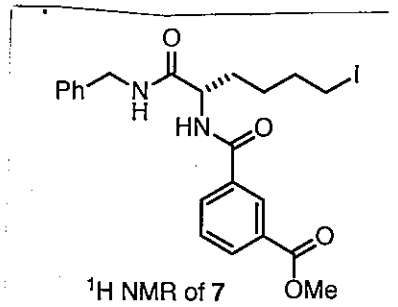
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	48



^{1}H NMR of **7**

single pulse decoupled gated NOE

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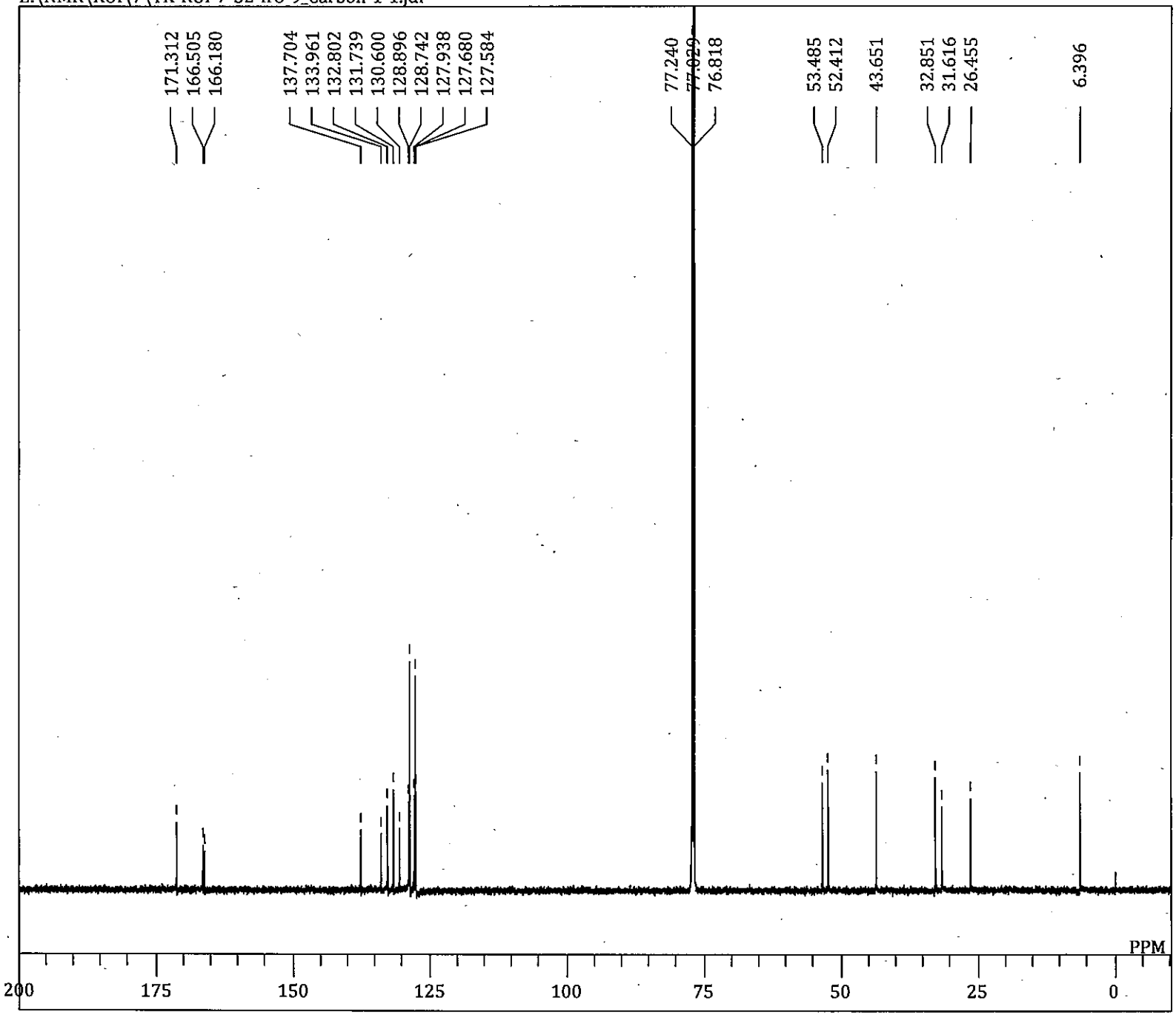

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OBFIN	1.74 Hz
POINT	32767
FREQU	47348.49 Hz
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ACQTM	0.6921 sec
PD	2.0000 sec
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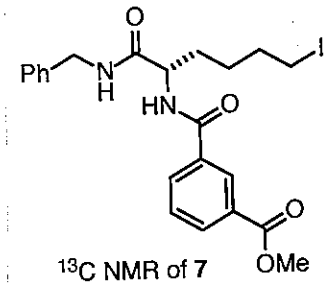
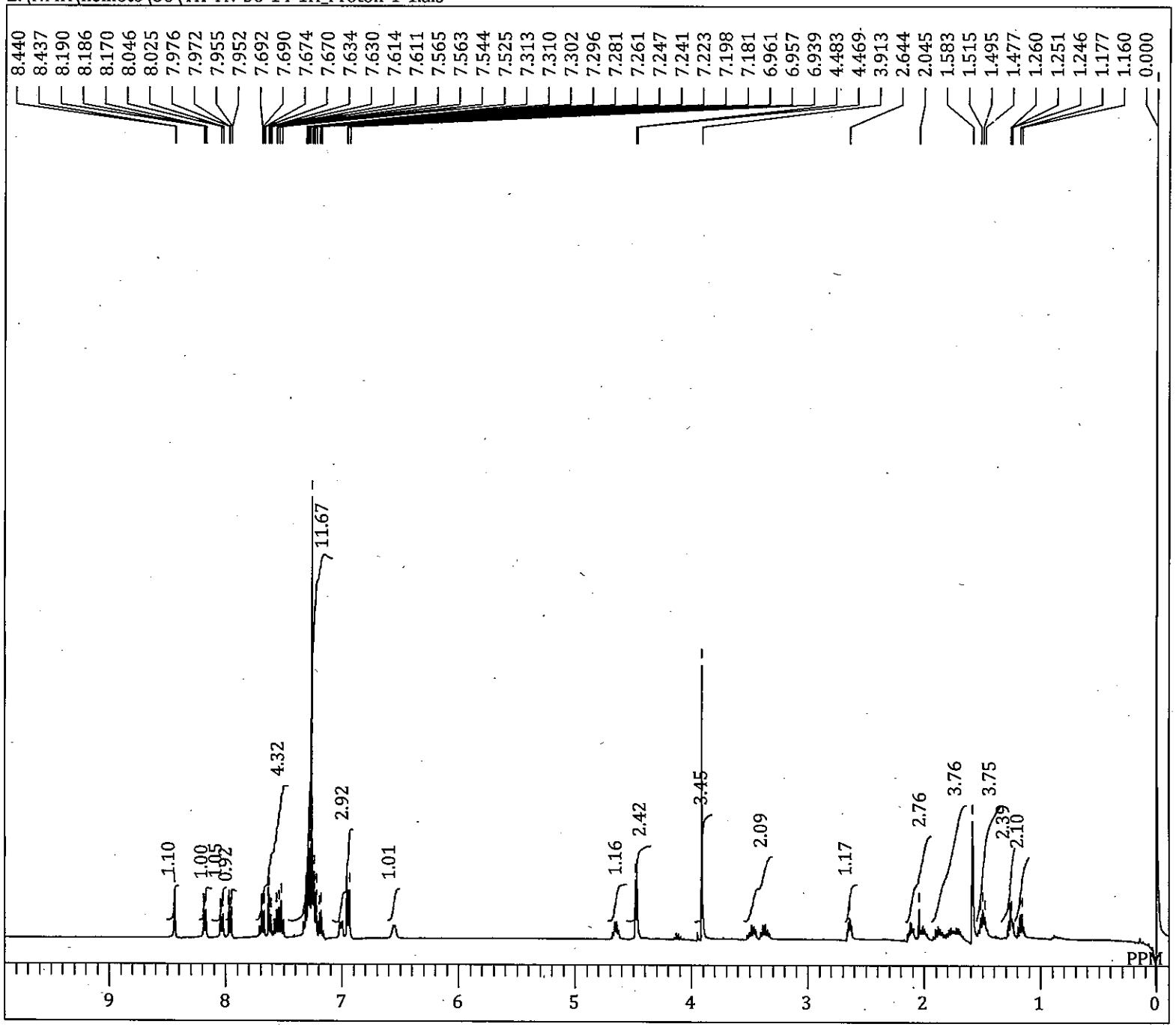
CTEMP	22.5 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	1.20 Hz
RGAIN	50



^{13}C NMR of **7**

single_pulse

E:\NMR\nemoto\36\YK-TN-36-14-1H_Proton-1-1.als



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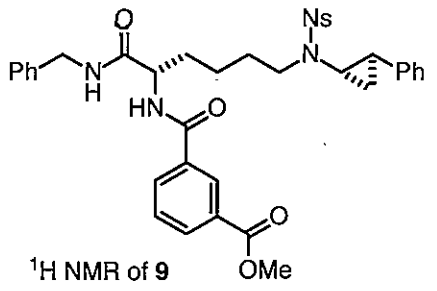
OBSET	4.19 KHz
OBFIN	7.29 Hz
POINT	13107
FREQU	5995.20 Hz
SCANS	8
ACQTM	2.1863 sec
PD	5.0000 sec
PW1	3.20 usec
IRNUC	1H
CTEMP	24.1 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	56



^{1}H NMR of **9**

single pulse decoupled gated NOE

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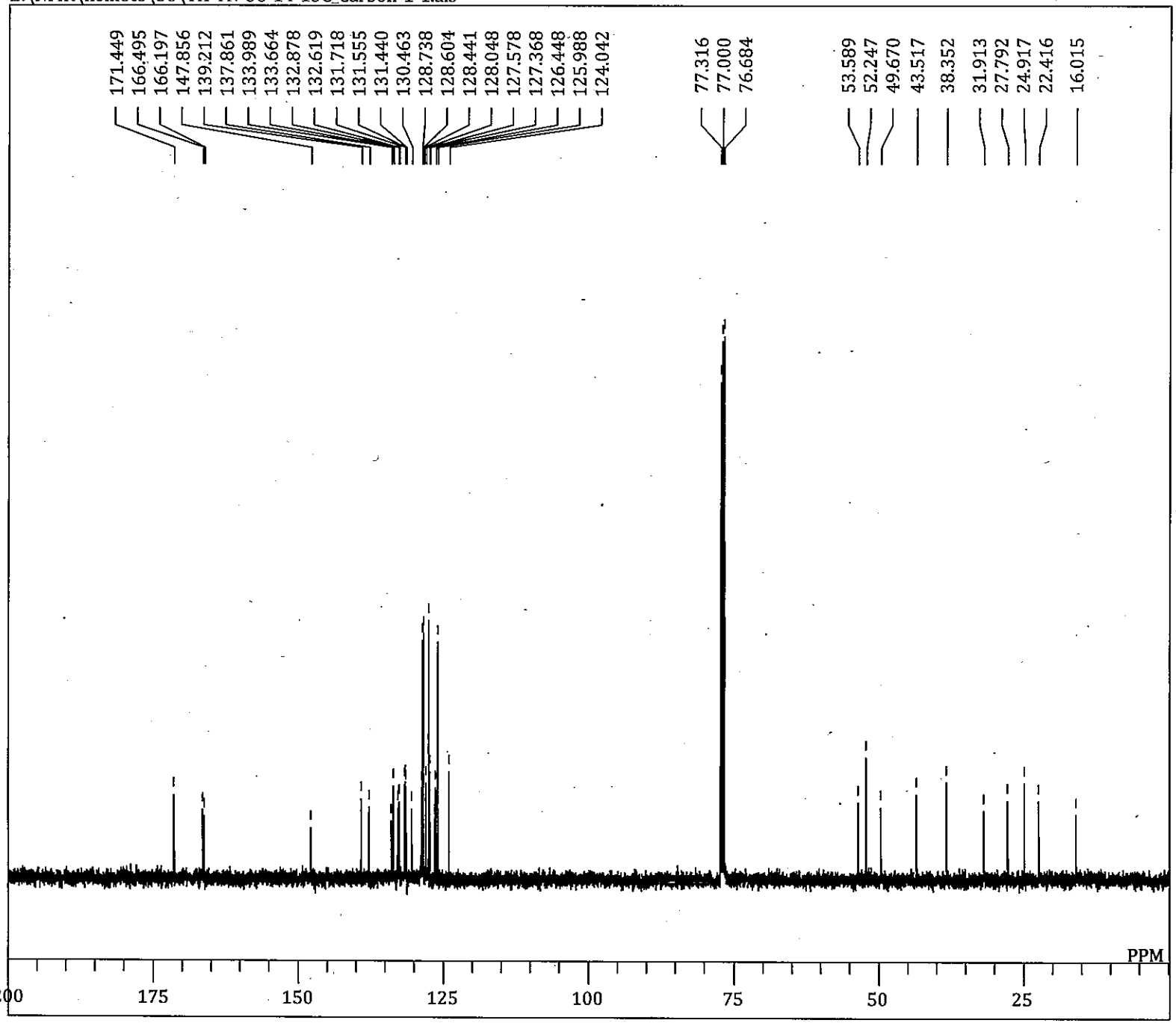

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EXMOD	carbon.jxp
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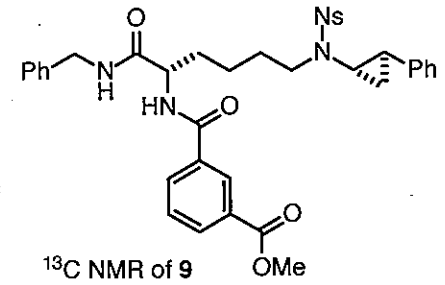
OBSET	5.35 KHz
OBFIN	5.86 Hz
POINT	26214
FREQU	25252.53 Hz
SCANS	128
ACQTM	1.0381 sec
PD	2.0000 sec
PW1	3.33 usec
IRNUC	1H
CTEMP	24.1 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	1.20 Hz
RGAIN	50



^{13}C NMR of **9**

single_pulse

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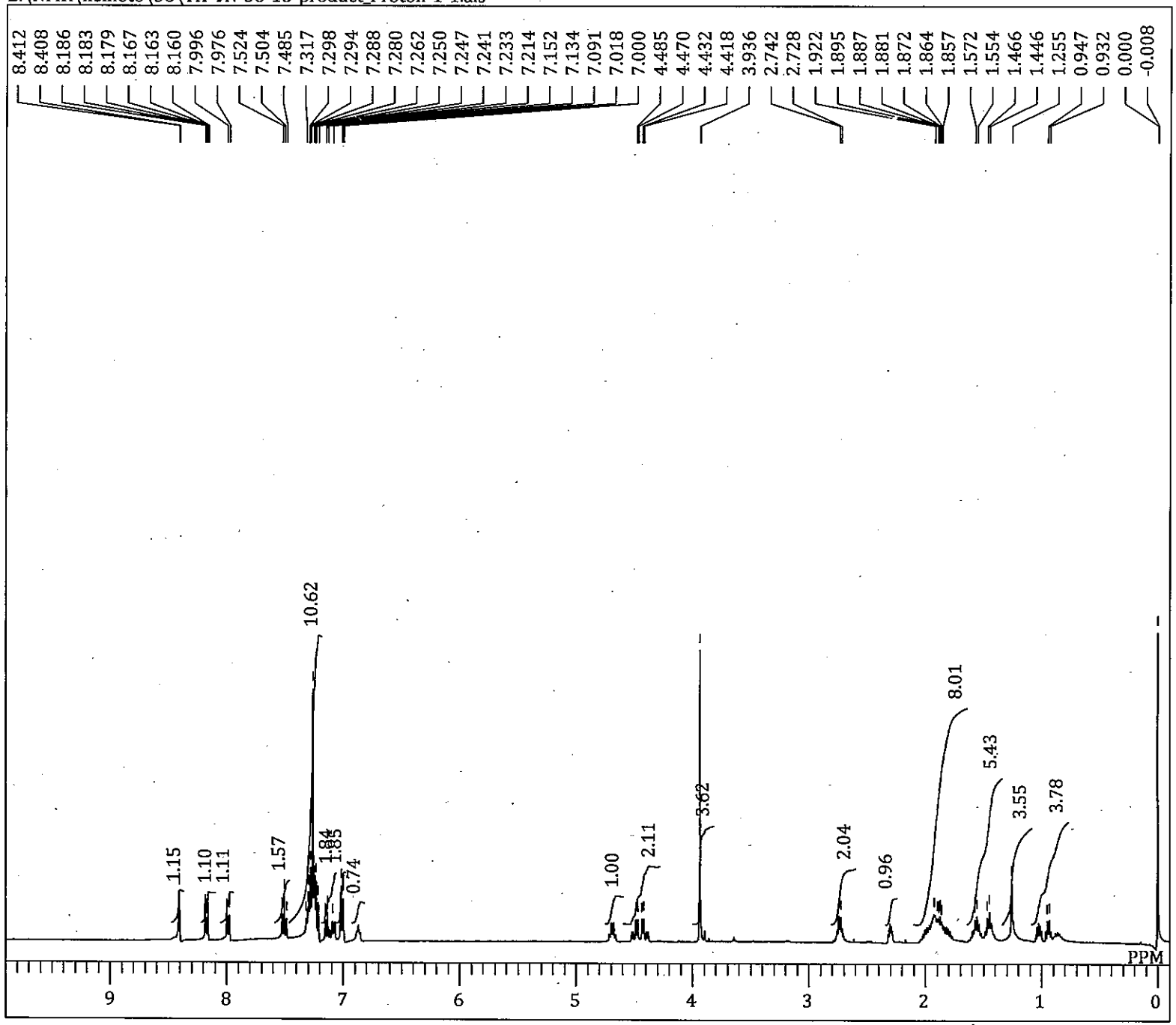

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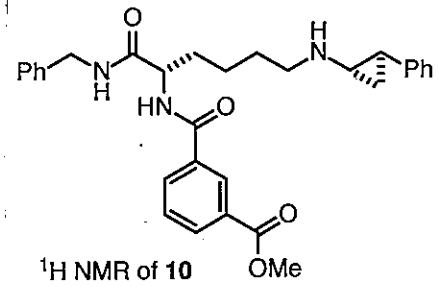
OBFIN	7.29 Hz
POINT	13107
FREQU	5995.20 Hz
SCANS	8
ACQTM	2.1863 sec
PD	5.0000 sec
PW1	3.20 usec
IRNUC	1H
CTEMP	24.6 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	56



^{1}H NMR of **10**

single pulse decoupled gated NOE

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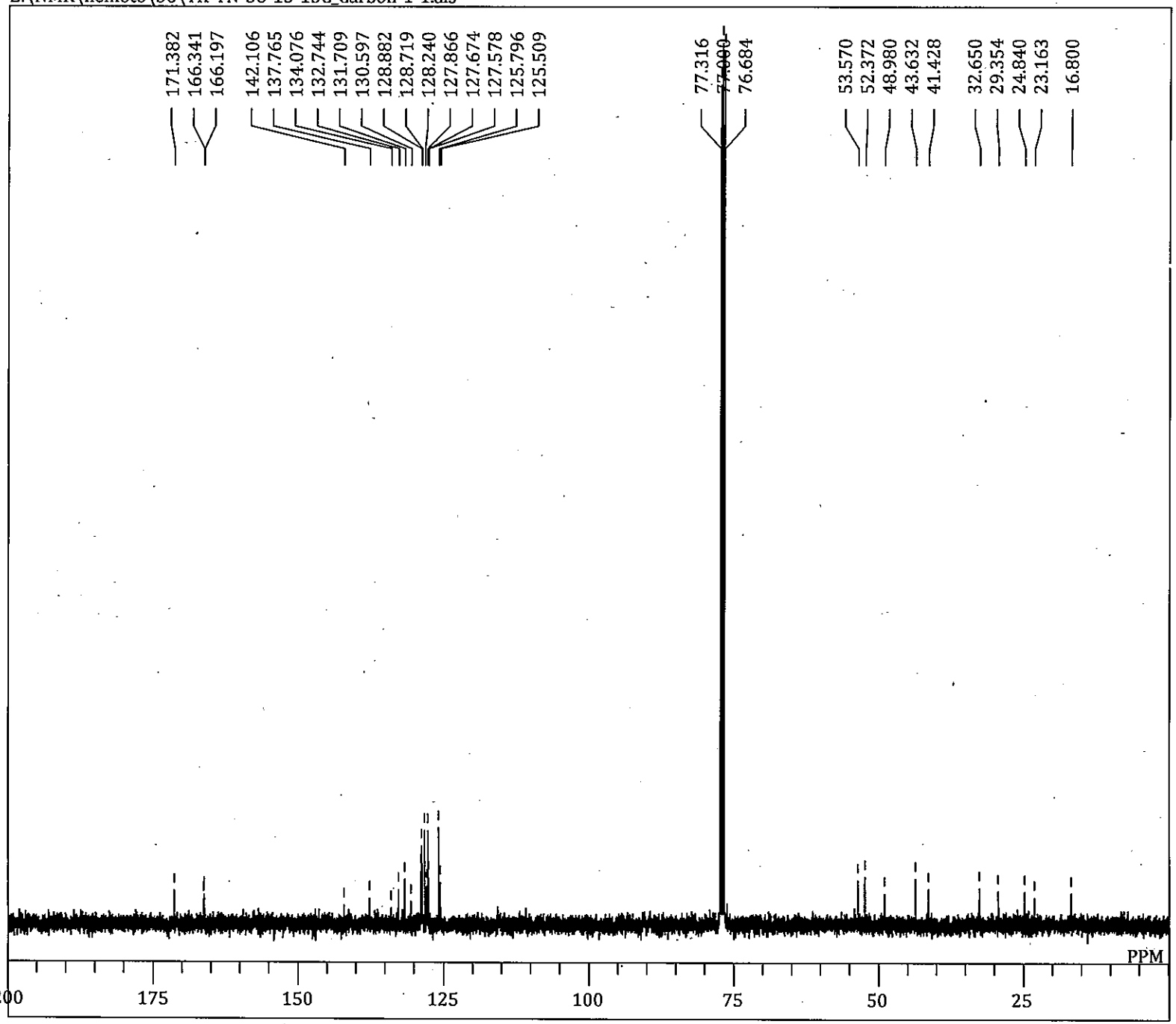

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EXMOD	carbon.jxp
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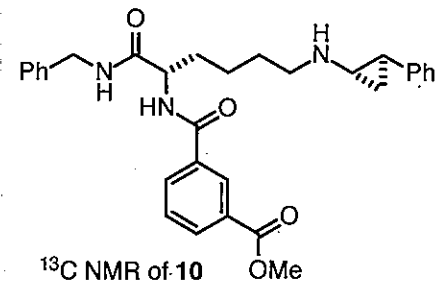
OBSET	5.35 KHz
OBFIN	5.86 Hz
POINT	26214
FREQU	25252.53 Hz
SCANS	256
ACQTM	1.0381 sec
PD	2.0000 sec
PW1	3.33 usec
IRNUC	1H
CTEMP	24.3 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	1.20 Hz
RGAIN	50



^{13}C NMR of **10**

single_pulse

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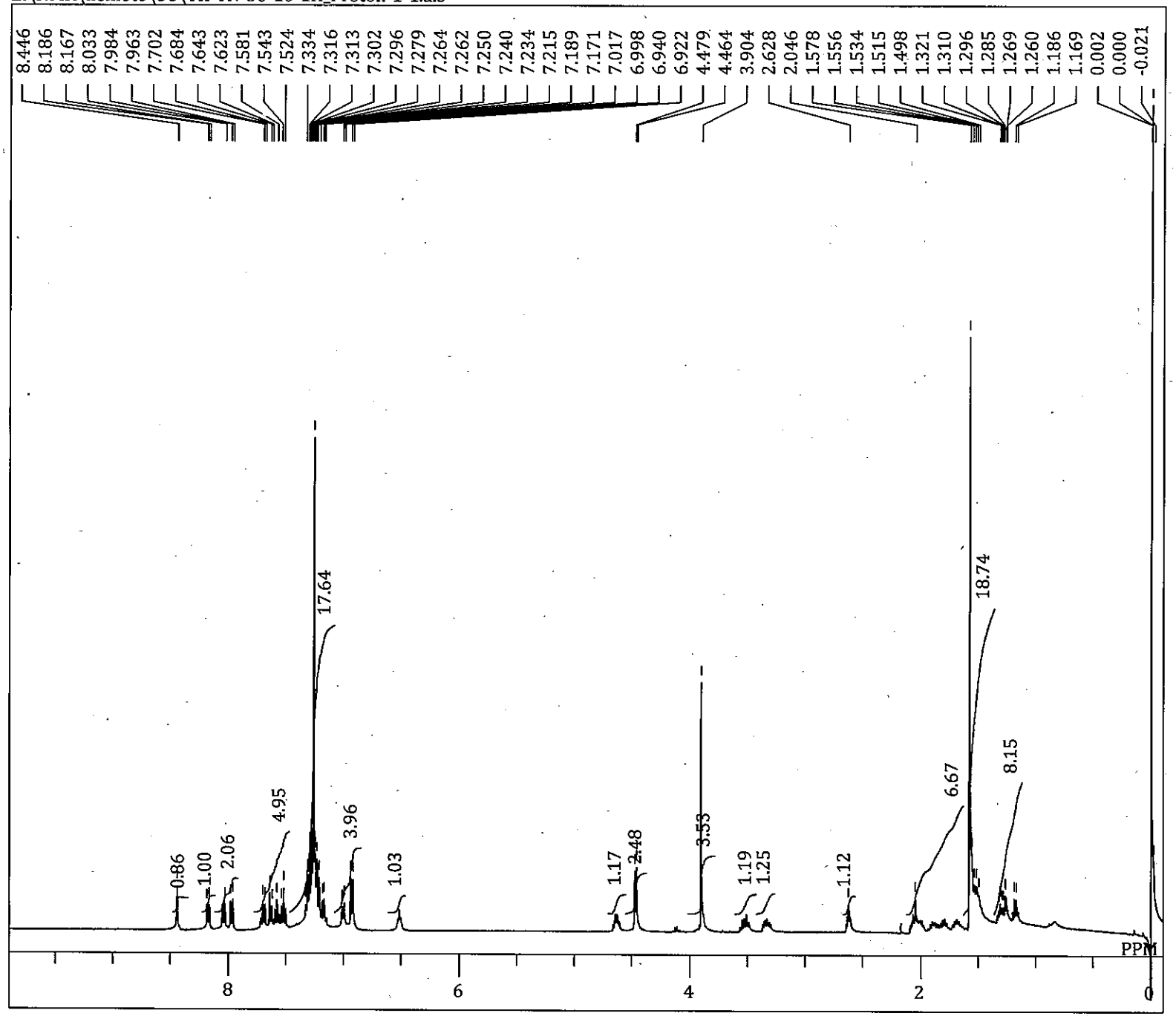

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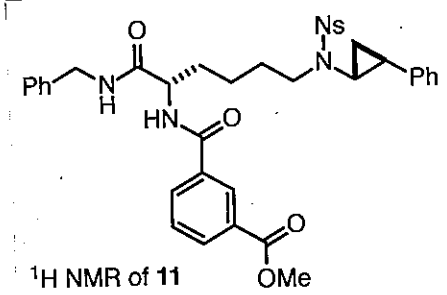
OBSET	4.19 KHz
OBFIN	7.29 Hz
POINT	13107
FREQU	5995.20 Hz
SCANS	16
ACQTM	2.1863 sec
PD	5.0000 sec
PW1	3.20 usec
IRNUC	1H
CTEMP	23.7 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	56



^{1}H NMR of **11**

single pulse decoupled gated NOE

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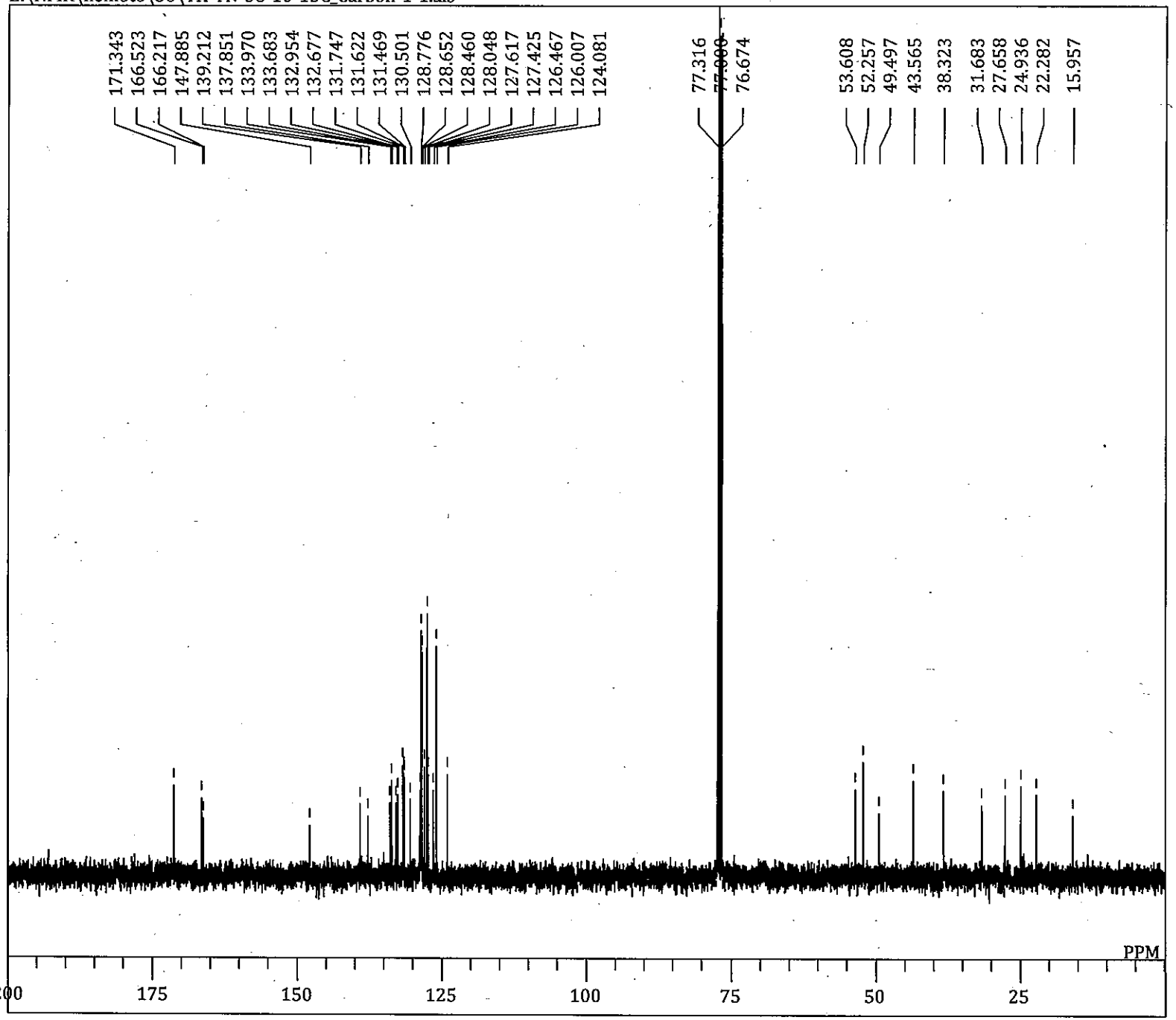

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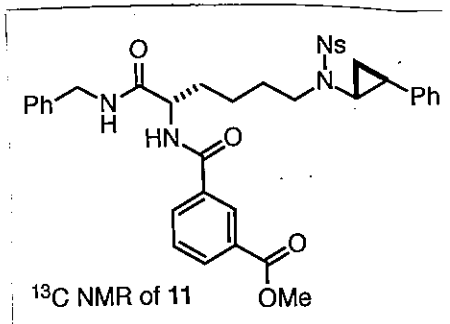
OBFIN	5.86 Hz
POINT	26214
FREQU	25252.53 Hz
SCANS	128
ACQTM	1.0381 sec
PD	2.0000 sec
PW1	3.33 usec
IRNUC	1H
CTEMP	23.8 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	1.20 Hz
RGAIN	50



^{13}C NMR of 11

11

single_pulse

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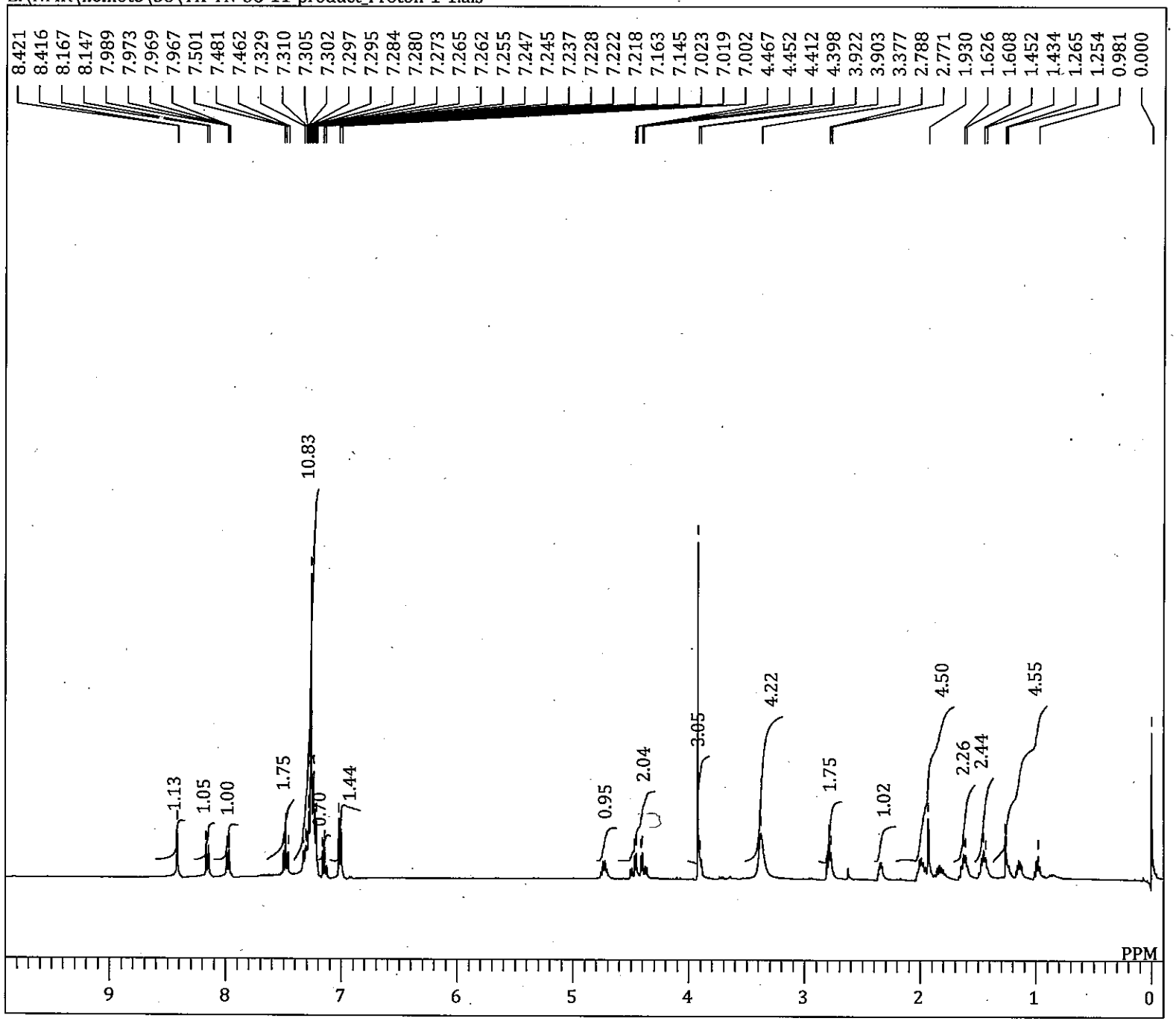

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OBFIN	7.29 Hz
POINT	13107
FREQU	5995.20 Hz
SCANS	8
ACQTM	2.1863 sec
PD	5.0000 sec
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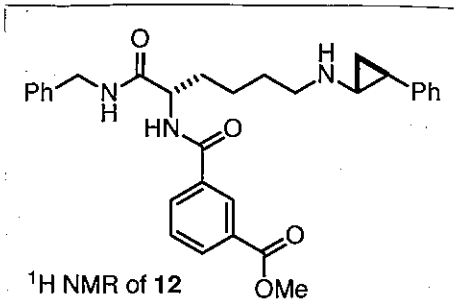
RGAIN	46



^{1}H NMR of **12**

single pulse decoupled gated NOE

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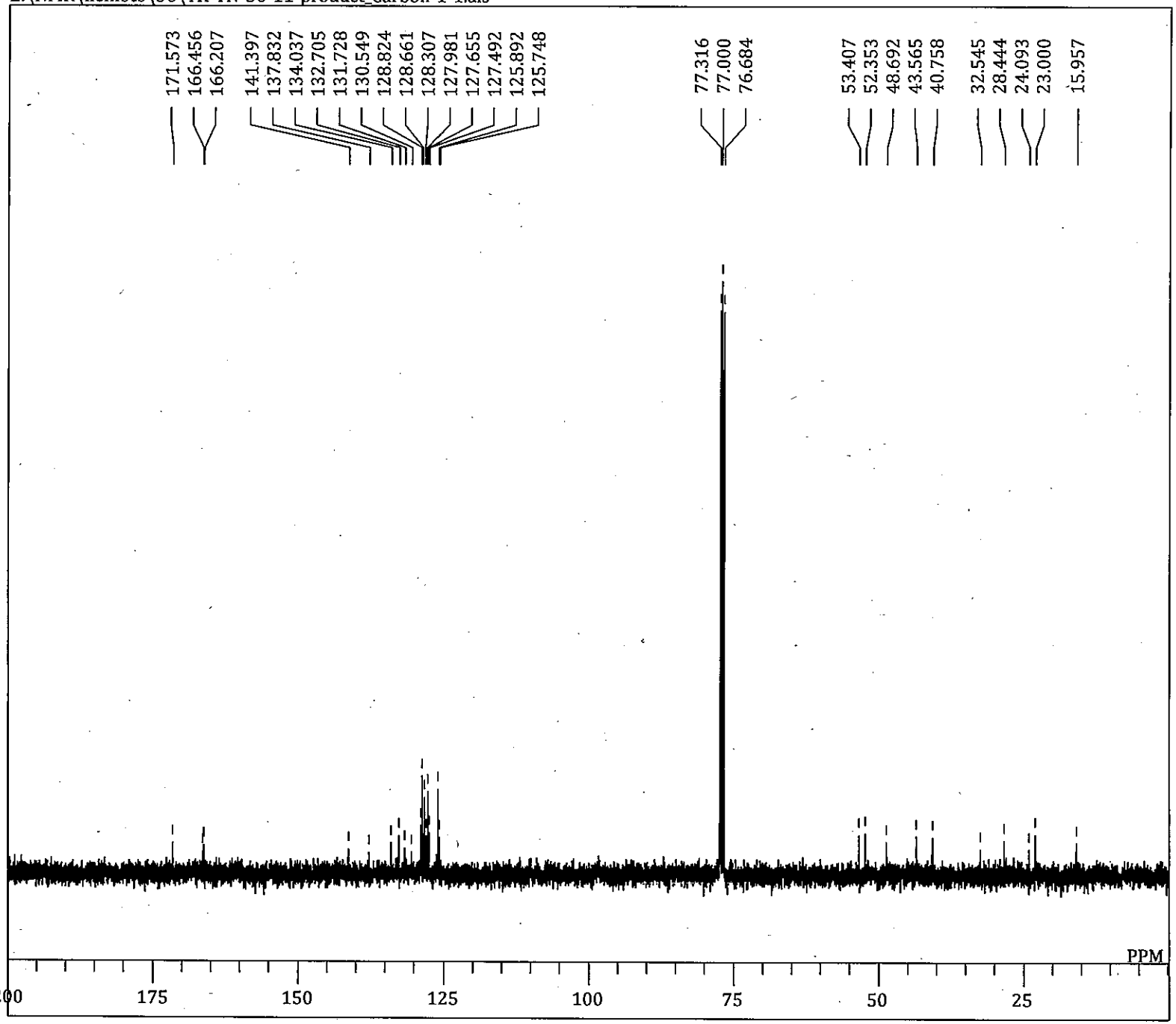

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OBSET	5.35 KHz
OBFIN	5.86 Hz
POINT	26214
FREQU	25252.53 Hz
SCANS	64
ACQTM	1.0381 sec
PD	2.0000 sec
PW1	3.33 usec
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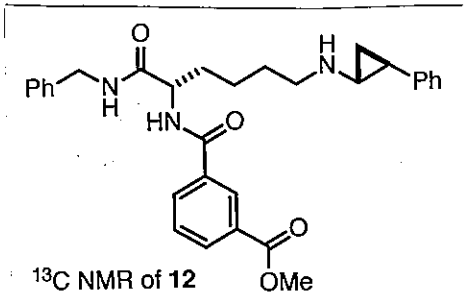
BF	1.20 Hz
RGAIN	50



^{13}C NMR of **12**

single_pulse

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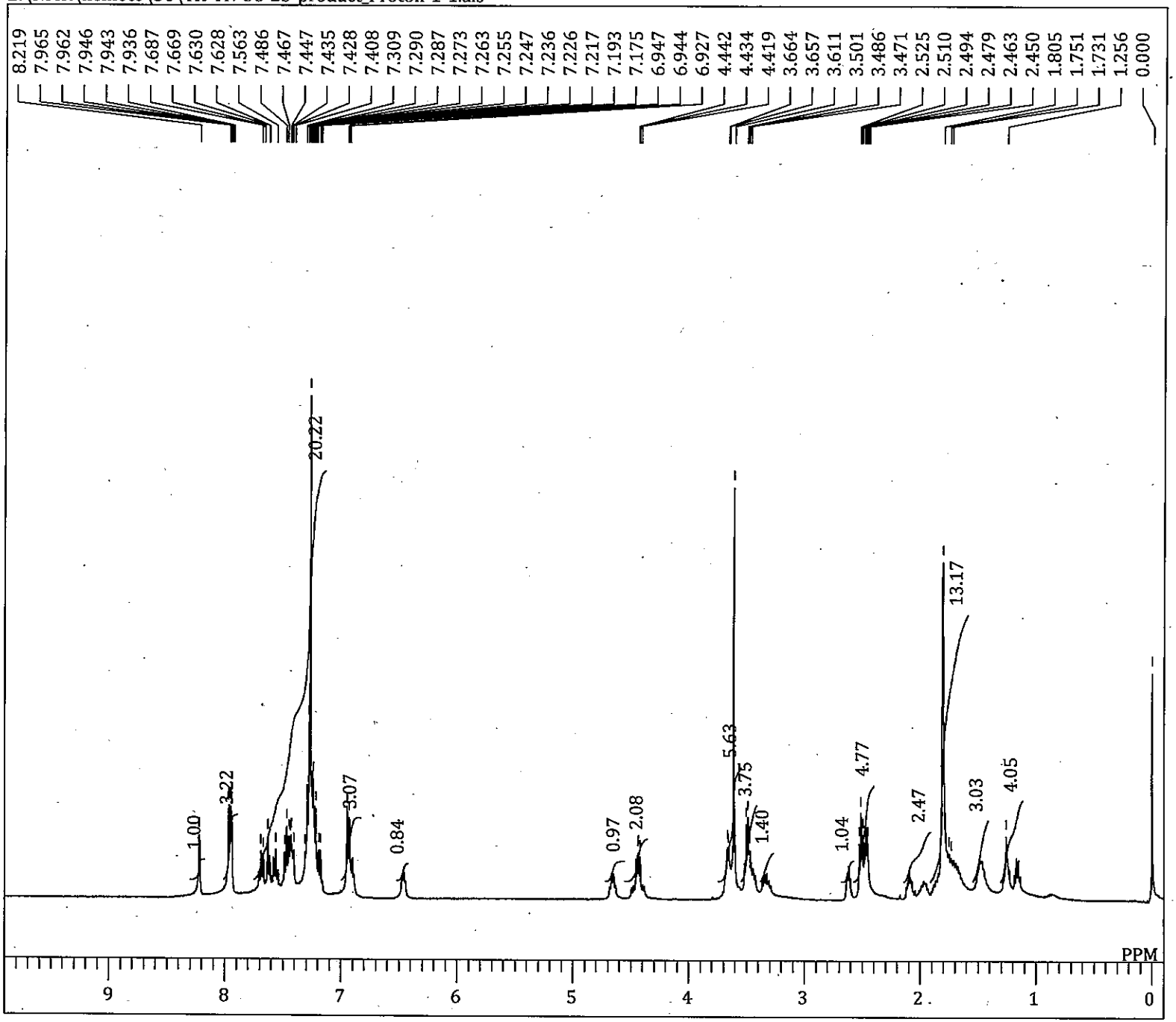

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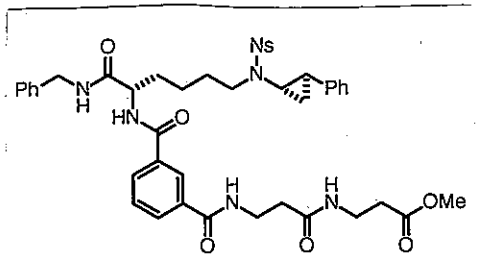
OBFIN	7.29 Hz
POINT	13107
FREQU	5995.20 Hz
SCANS	8
ACQTM	2.1863 sec
PD	5.0000 sec
PW1	3.20 usec
IRNUC	1H
CTEMP	23.6 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	56



^{1}H NMR of **14**

single pulse decoupled gated NOE

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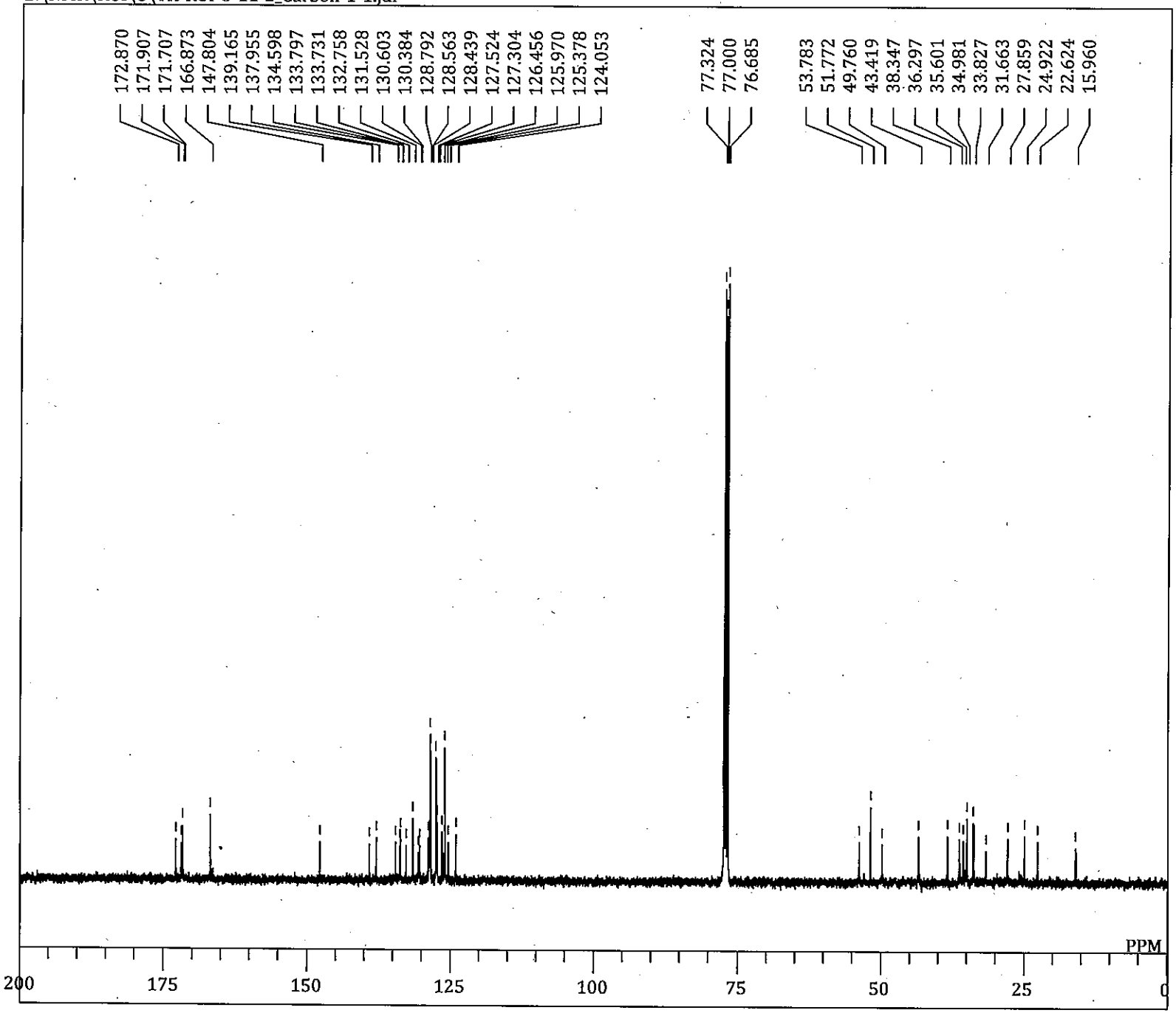

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EXMOD	carbon.jxp
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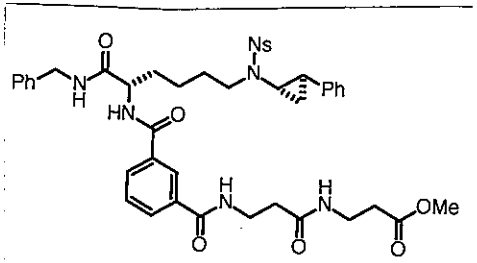
OBSET	5.35 KHz
OBFIN	5.86 Hz
POINT	32767
FREQU	31407.04 Hz
SCANS	626
ACQTM	1.0433 sec
PD	2.0000 sec
PW1	2.93 usec
IRNUC	1H
CTEMP	24.3 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	1.20 Hz
RGAIN	50



^{13}C NMR of **14**

single_pulse

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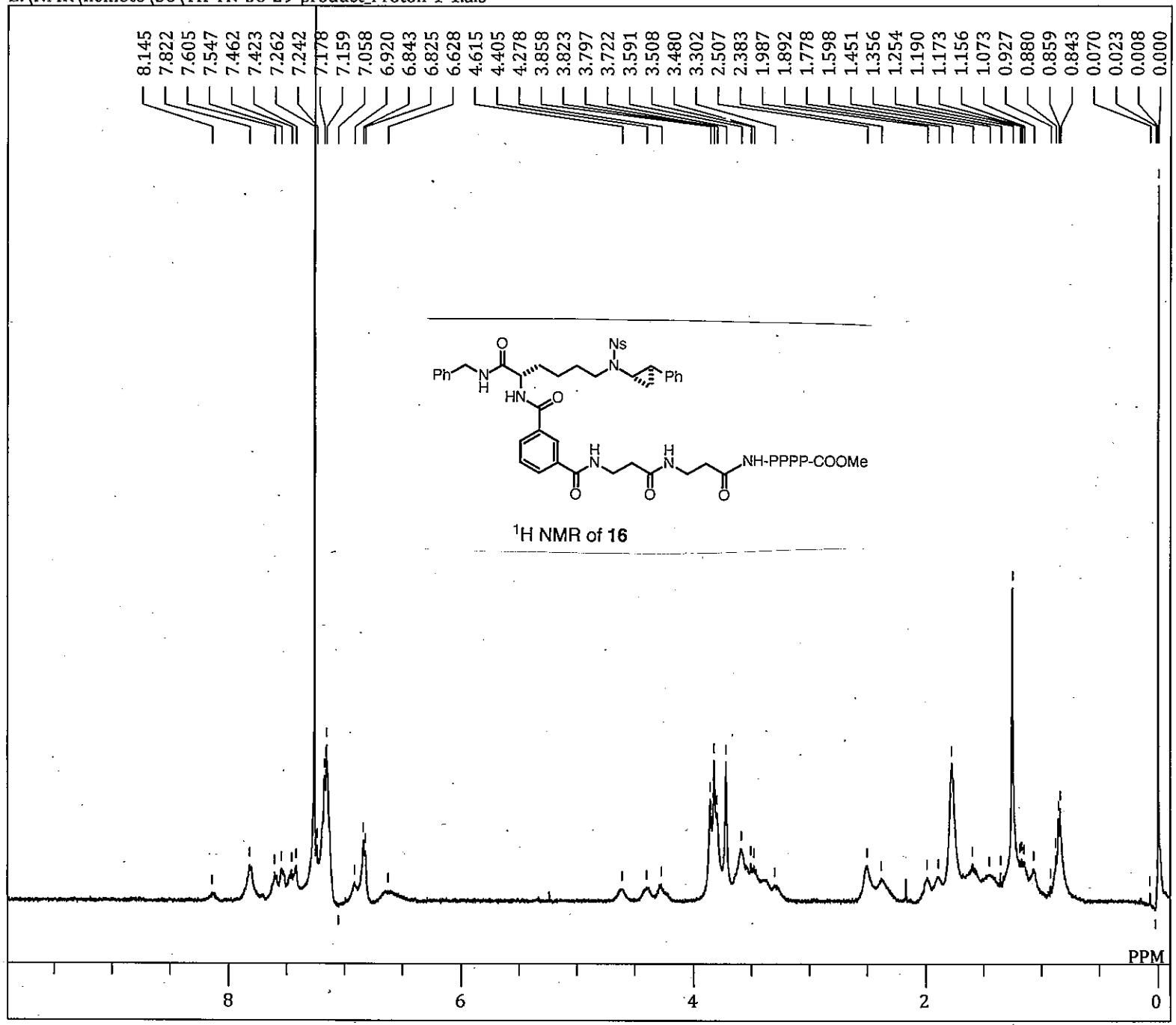

^{1}H NMR of **16**

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OBFIN	7.29 Hz
POINT	13107
FREQU	5995.20 Hz
SCANS	8
ACQTM	2.1863 sec
PD	5.0000 sec
PW1	3.20 usec
IRNUC	1H
CTEMP	24.2 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	66

single_pulse

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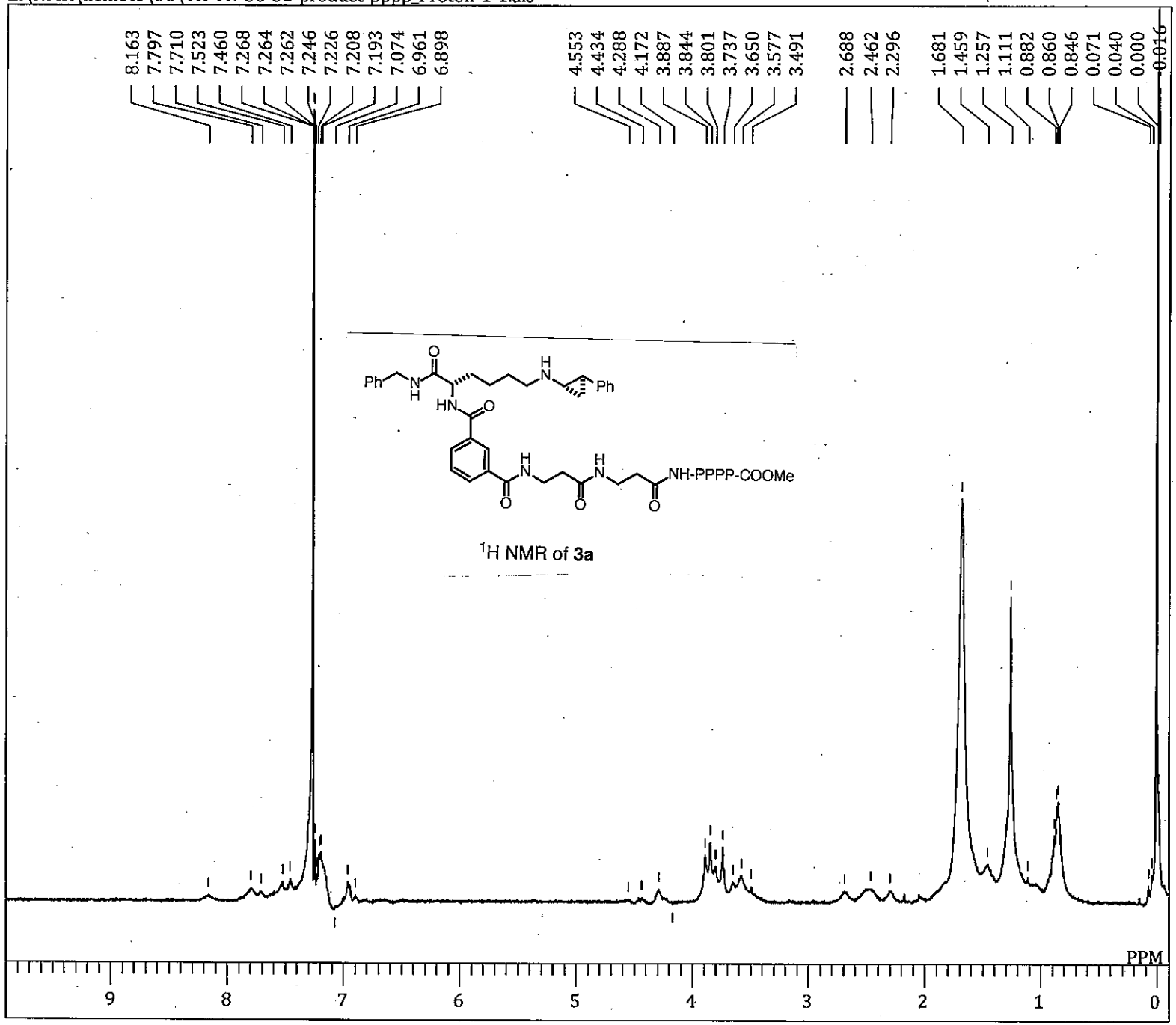

^{1}H NMR of **3a**

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DATIM	2018-09-04 14:38:24
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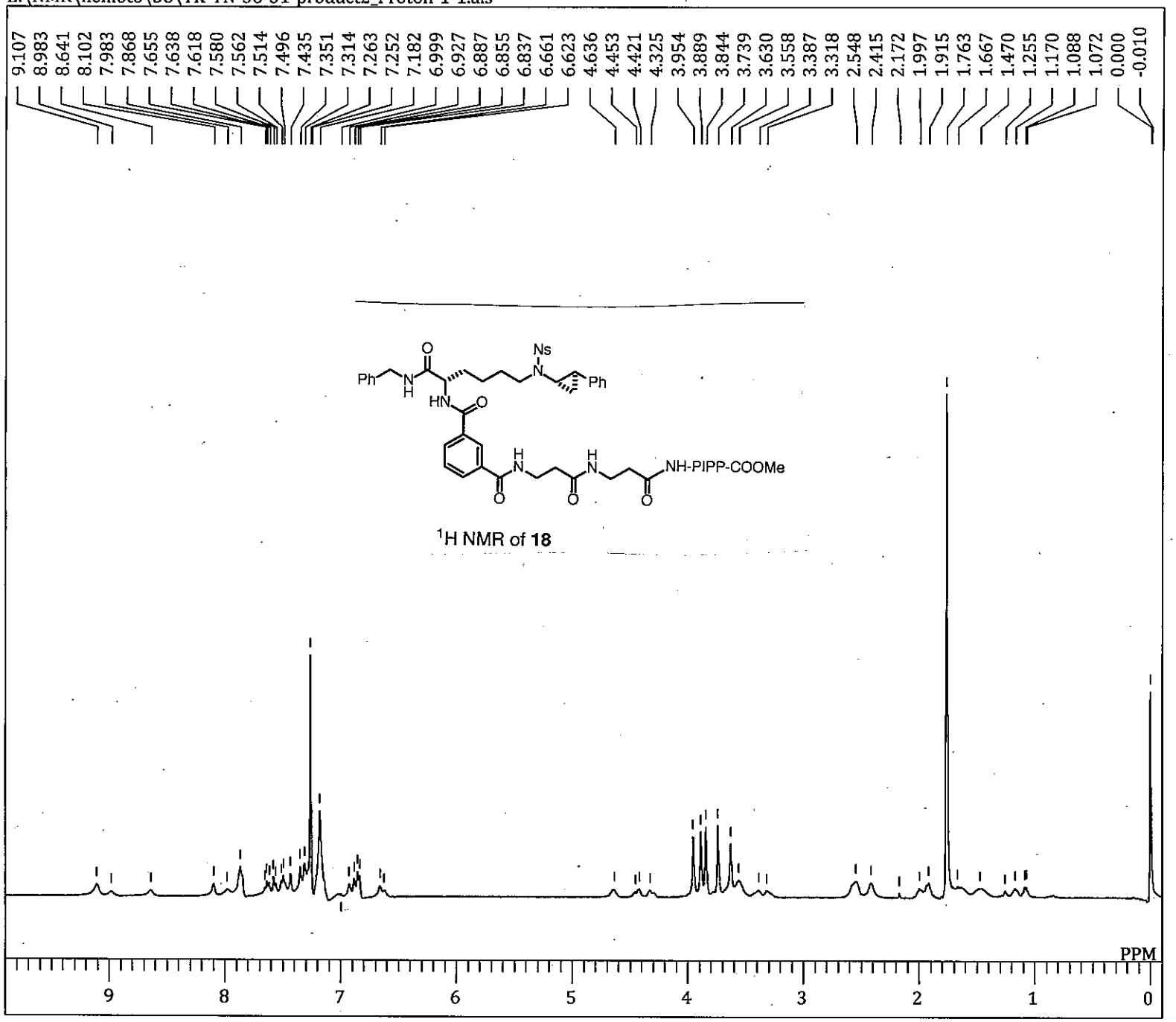
OBSET	4.19 KHz
OBFIN	7.29 Hz
POINT	13107
FREQU	5995.20 Hz
SCANS	16
ACQTM	2.1863 sec
PD	5.0000 sec
PW1	3.20 usec
IRNUC	1H
CTEMP	23.9 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	66

single_pulse

E:\NMR\nemoto\36\YK-TN-36-31-product2_Proton-1-1.als

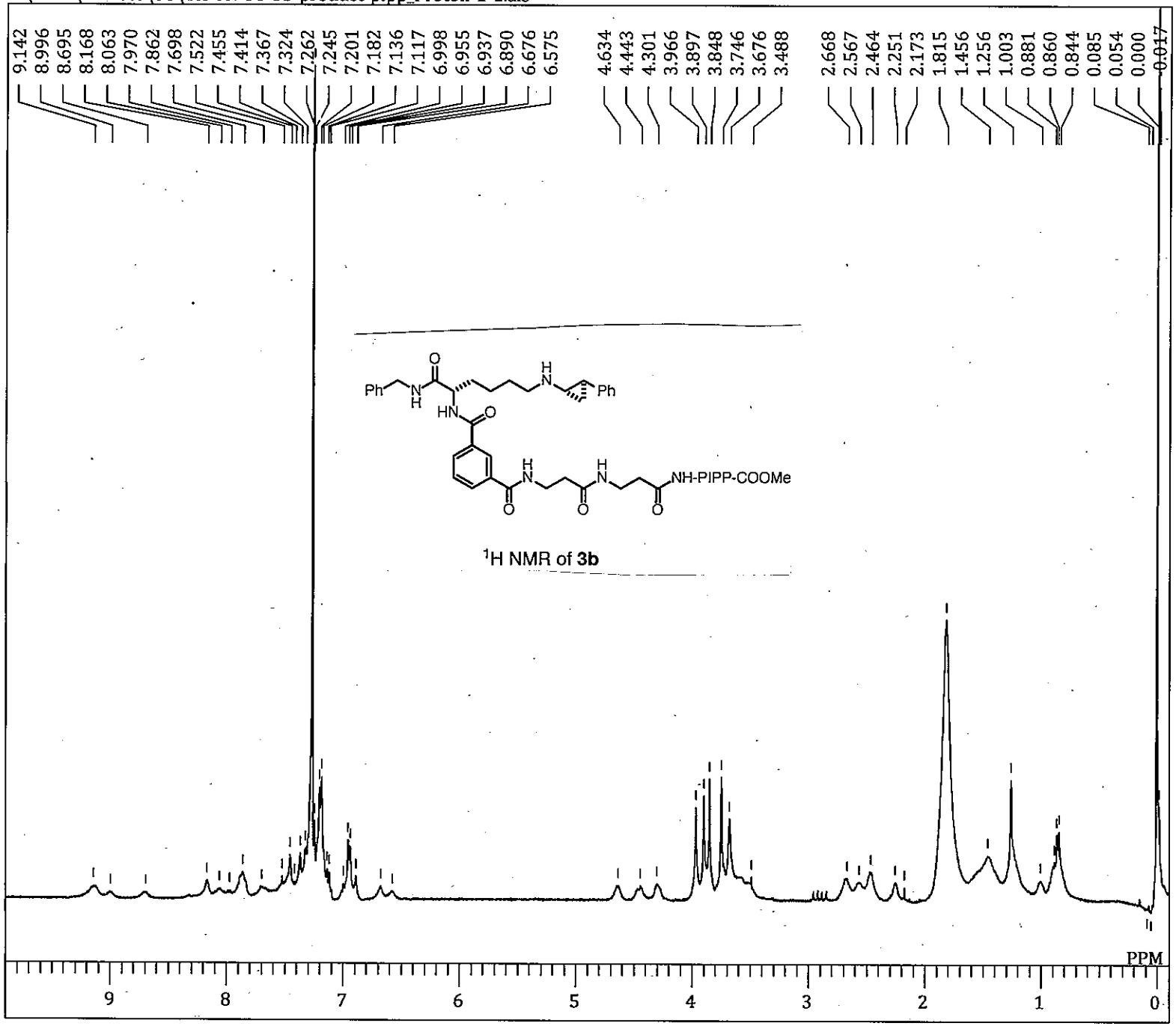


^{1}H NMR of **18**

DFILE	YK-TN-36-31-product2_Proton-1-1.al
COMNT	single_pulse
DATIM	2018-08-30 18:35:38
OBNUC	1H
EXMOD	proton.jxp
OBFRQ	399.78 MHz
OBSET	4.19 KHz
OBFIN	7.29 Hz
POINT	13107
FREQU	5995.20 Hz
SCANS	8
ACQTM	2.1863 sec
PD	5.0000 sec
PW1	3.20 usec
IRNUC	1H
CTEMP	24.2 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	56

single_pulse

E:\NMR\nemoto\36\YK-TN-36-33-product-pipp_Proton-1-1.als



^{1}H NMR of **3b**

DFILE	YK-TN-36-33-product-pipp_Proton-1
COMNT	single_pulse
DATIM	2018-09-04 14:43:32
OBNUC	1H
EXMOD	proton.jxp
OBFRQ	399.78 MHz
OBSET	4.19 KHz
OBFIN	7.29 Hz
POINT	13107
FREQU	5995.20 Hz
SCANS	16
ACQTM	2.1863 sec
PD	5.0000 sec
PW1	3.20 usec
IRNUC	1H
CTEMP	23.9 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	56

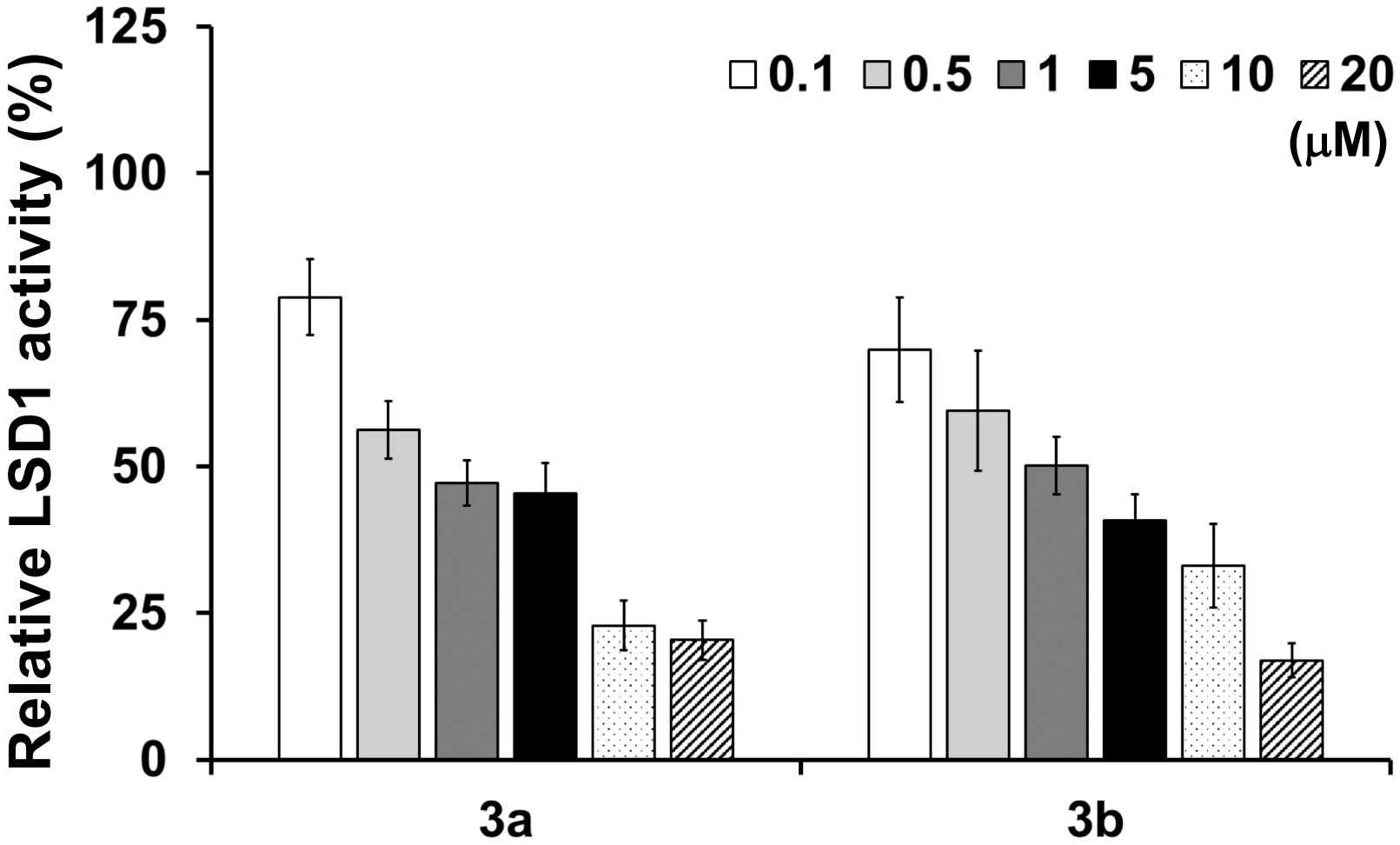


Figure 1S. Inhibition of LSD1 activity by conjugates **3a** and **3b** *in vitro*. LSD1 activities were assessed using an LSD1 fluorometric drug discovery kit. Relative LSD1 activities are shown as bars filled with white, light grey, grey, black, dots and slashed lines in presence 0.1, 0.5, 1, 5, 10 and 20 μM of the compounds, respectively. LSD1 activities were estimated by comparison with 1% DMSO control as 100%. Data represent the mean of three independent replicates ± SD.