

Supplementary Materials for

Two-step synthesis of solasodine pivalate from diosgenin pivalate

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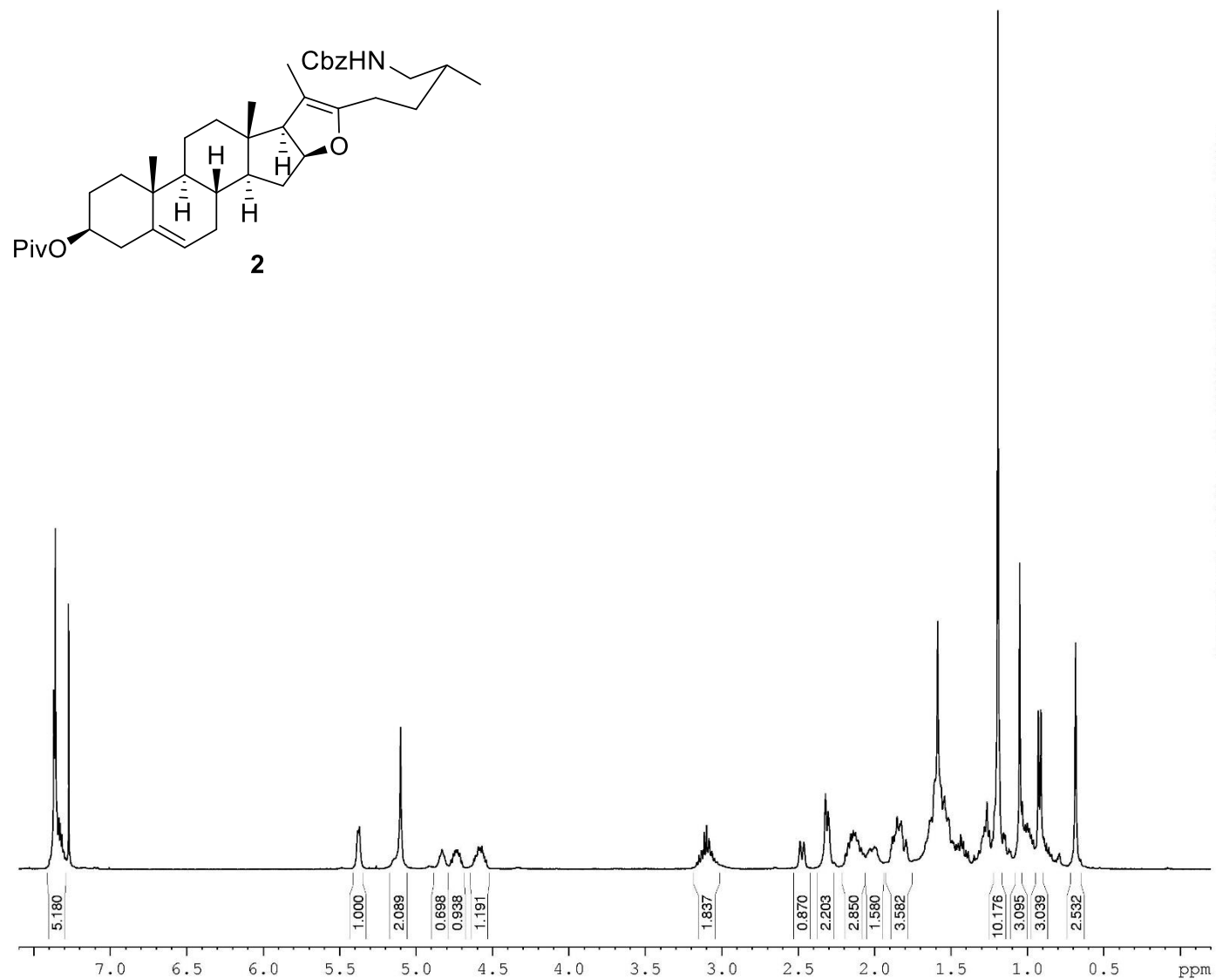
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Table S1. Comparison of prices and hazards of reagents used in three recent syntheses of solasodine.

Reference no. in manuscript	Number of steps	Total yield of product	Reagents (equiv, price*, hazards#)
This paper	2	45% (solasodine pivalate)	TMSOTf (2 equiv. 1.6 €/g, H226, H314) CbzNH₂ (2.2. equiv. 0.9 €/g, According to SDS#: Not a hazardous substance or mixture according to Regulation (EC) No. 1272/2008. Not a hazardous substance or mixture according to EC-directives 67/548/EEC or 1999/45/EC.) AcBr (4 – 22 equiv. 0.3 €/g, H314) BuOH (58.60 €/l, H226, H315, H318, H335, H336)
21	7	57% (solasodine)	TFAT (1.5 equiv. 42.6 €/g, H301, H314) Ac₂O (5 equiv. 0.016 €/g, H226, H302, H314, H330) Pyridine (10 equiv. 0.17 €/g, H225, H302+H312+H332, H315, H319)) TsCl (2 equiv. 0.068 €/g, H290, H315, H317, H318) NaN₃ (3 equiv. 0.195 €/g, H300+H310, H373, H410), TMSCl (2 equiv. 1.06 €/g, H225, H301+H331, H312, H315, H318) NaI (2 equiv. 2.36 €/g, H315, H319, H400)
22	3	50% (solasodine)	BF₃xOEt₂ (5 equiv. 0.22 €/g, H226, H302, H314, H330, H372) LiBr (8 equiv. 0.4 €/g, H302, H315, H317, H319), NaN₃ (2 equiv. 0.195 €/g, H300+H310, H373, H410), DMF (146 €/l, H226, H312+H332, H319, H360D), TMSCl (2.2 equiv. 1.06 €/g, H225, H301+H331, H312, H315, H318) NaI (2 equiv. 2.36 €/g, H315, H319, H400)
23	3	43% (solasodine)	BF₃xOEt₂ (4 equiv. 0.22 €/g, H226, H302, H314, H330, H372) p-TsNH₂ (4 equiv. 0.065 €/g, Not a hazardous substance or mixture according to Regulation (EC) No. 1272/2008.), Na (10 equiv. 1 €/g, H260, H314), naphthalene (100 equiv., 0.05 €/g, H228, H302, H351, H410), TMSCl (6.3 equiv. 1.06 €/g, H225, H301+H331, H312, H315, H318)

*Price from Sigma Aldrich catalogue (<https://www.sigmaaldrich.com/catalog/search>).

#SDS found on website: <https://www.sigmaaldrich.com/catalog/product/aldrich/b18200?lang=en®ion=GB>

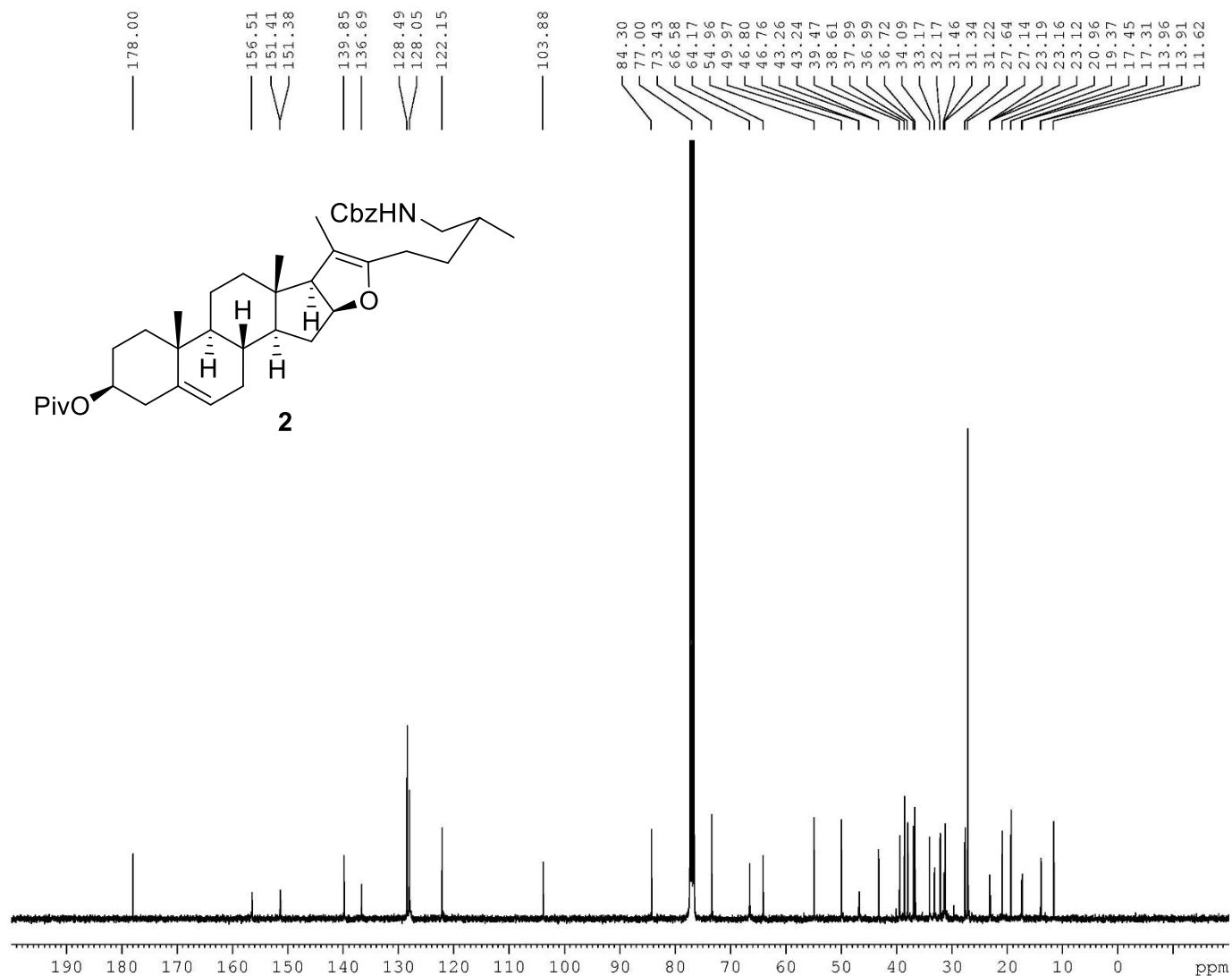


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 FIDRES 0.125483 Hz
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 RG 256
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 DE 8.00 us
 TE 298.7 K
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 TD0 1

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 PL1 -3.00 dB
 SFO1 400.1524711 MH

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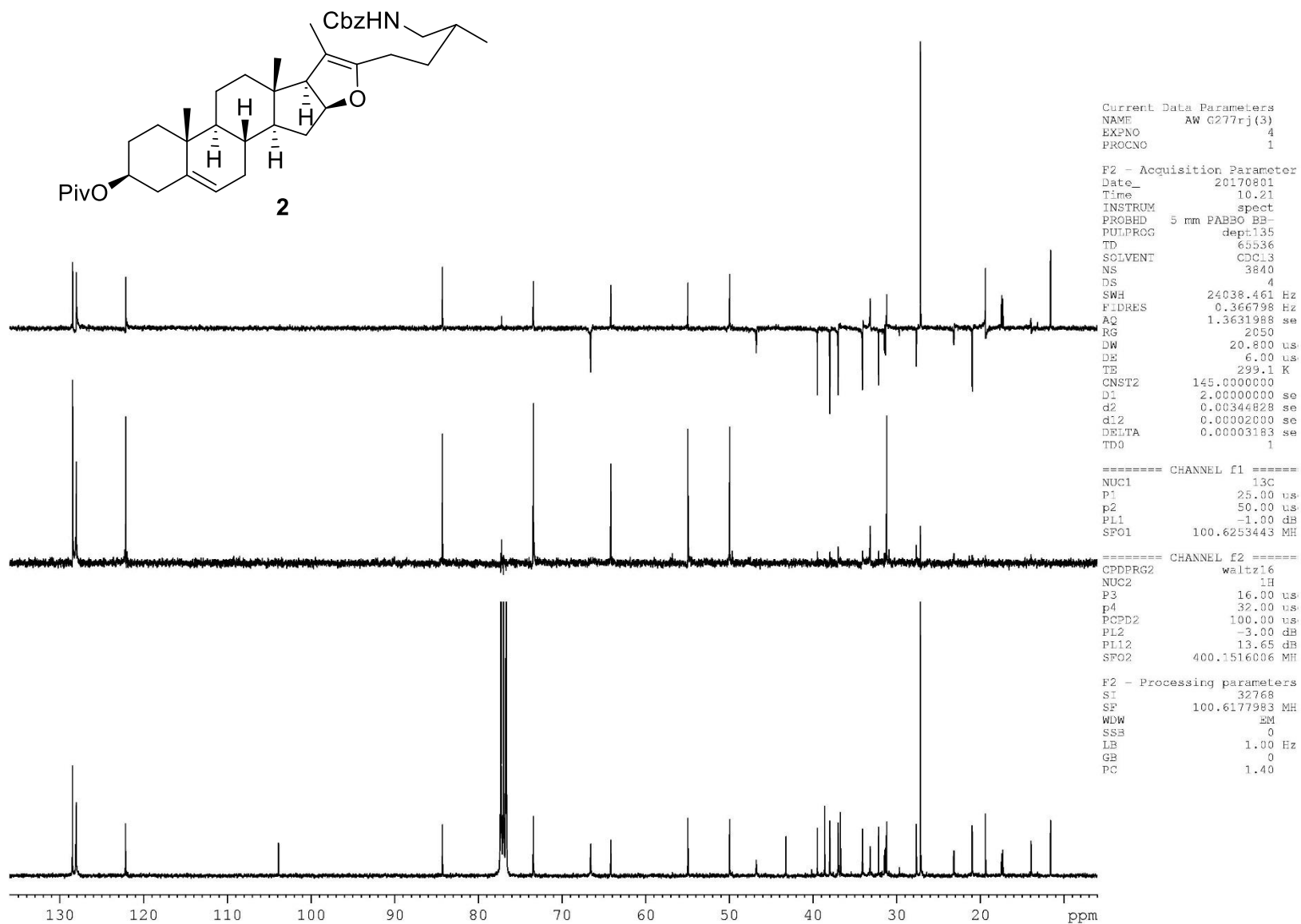
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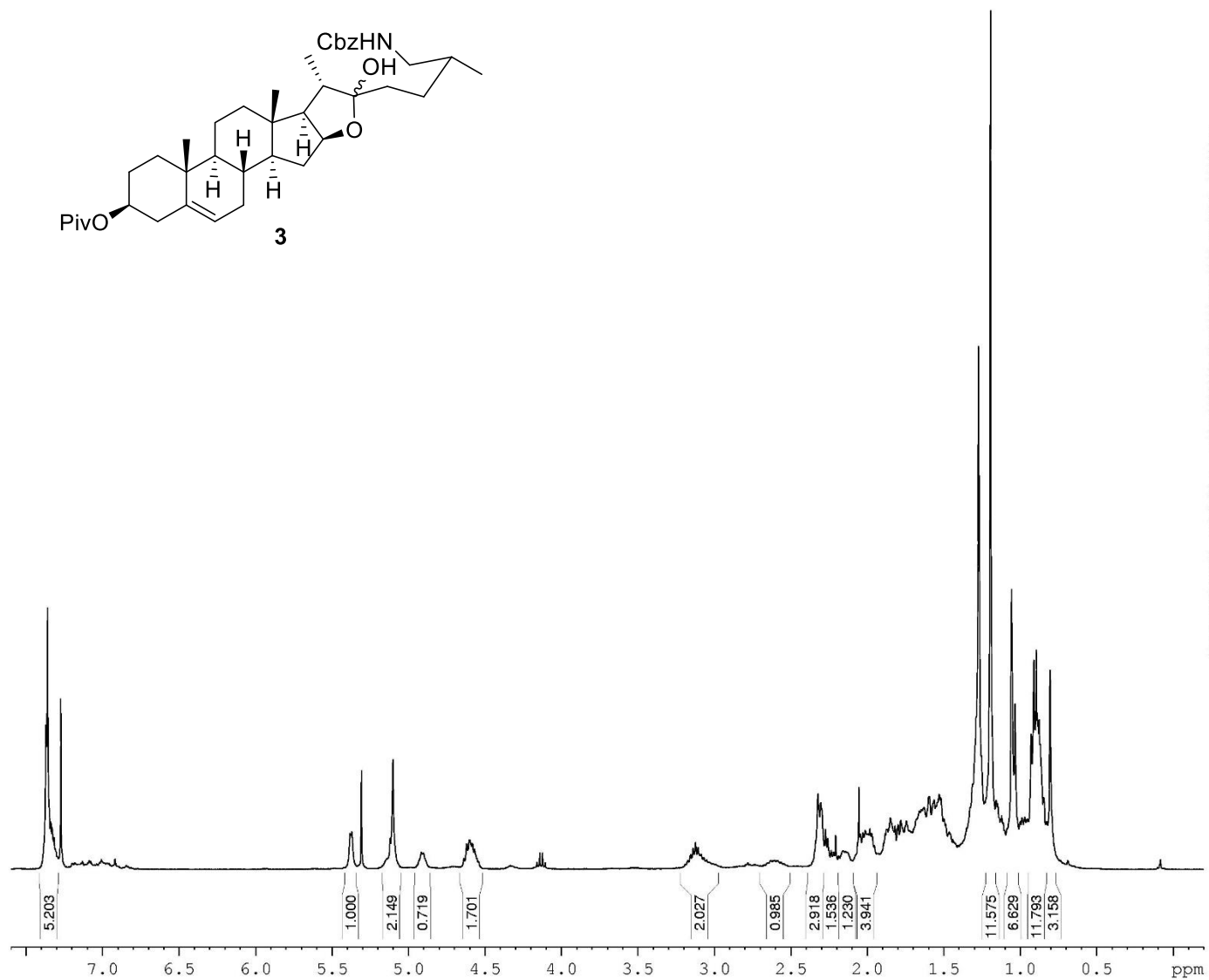
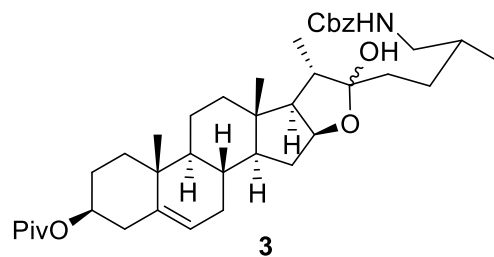
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 FIDRES 0.414641 Hz
 AQ 1.2059124 se
 RG 114
 DW 18.400 us
 DE 6.00 us
 TE 299.6 K
 D1 2.0000000 se
 d11 0.0300000 se
 DELTA 1.89999998 se
 TD0 1

===== CHANNEL f1 =====
 NUC1 13C
 P1 25.00 us
 PL1 -1.00 dB
 SFO1 100.6288660 MH

===== CHANNEL f2 =====
 CPDPRG2 waltz16
 NUC2 1H
 PCPD2 100.00 us
 PL2 -3.00 dB
 PL12 13.65 dB
 PL13 18.00 dB
 SFO2 400.1516006 MH

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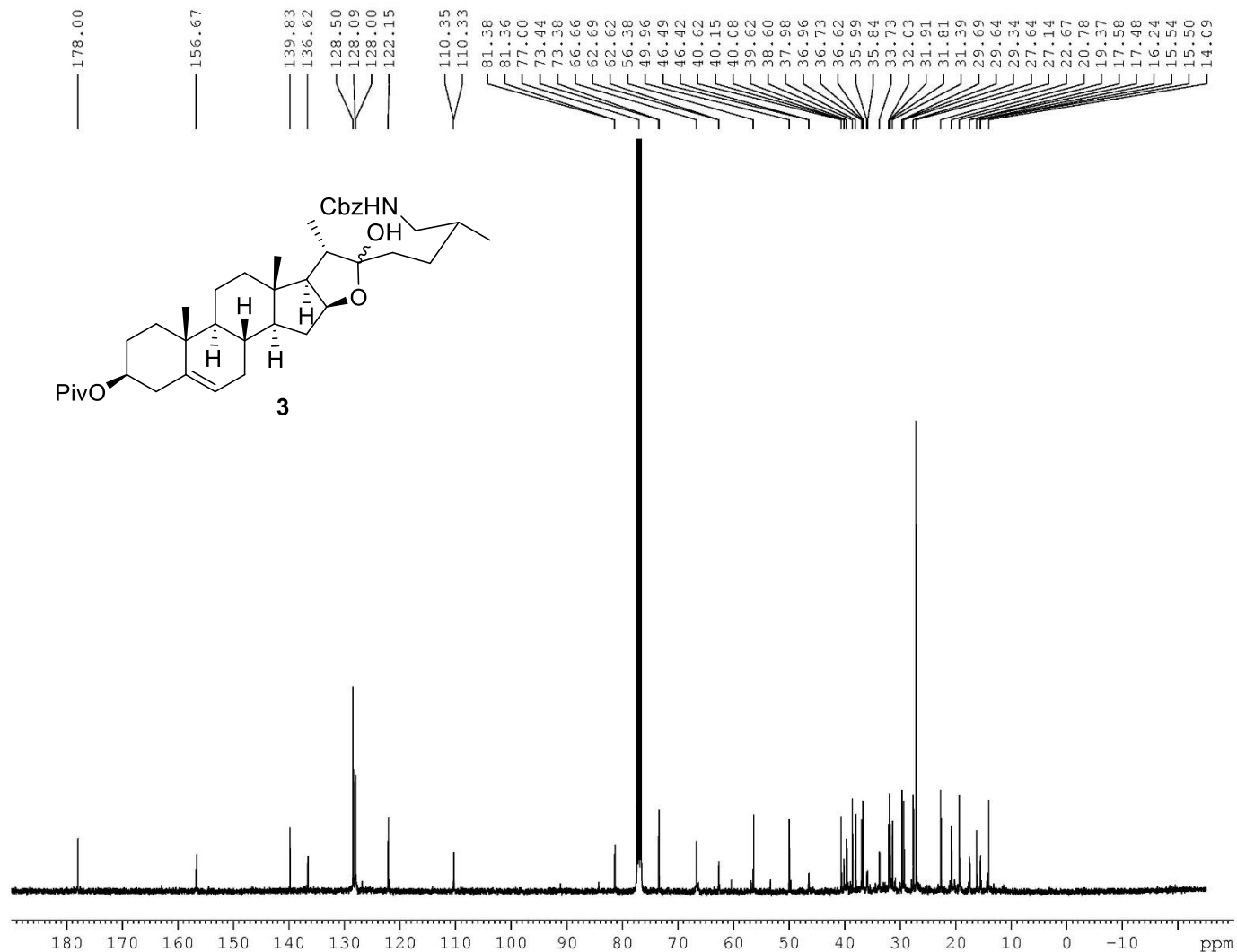


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 SOLVENT CDCl3
 NS 128
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 SWE 8223.685 Hz
 FIDRES 0.125483 Hz
 AQ 3.9846387 se
 RG 645
 DW 60.800 us
 DE 8.00 us
 TE 298.5 K
 D1 1.00000000 se
 TD0 1

===== CHANNEL f1 =====
 NUC1 1H
 P1 11.15 us
 PL1 -3.00 dB
 SFO1 400.1524711 MH

F2 - Processing parameters
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 SF 400.1500000 MH
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 SSB 0
 LB -0.20 Hz
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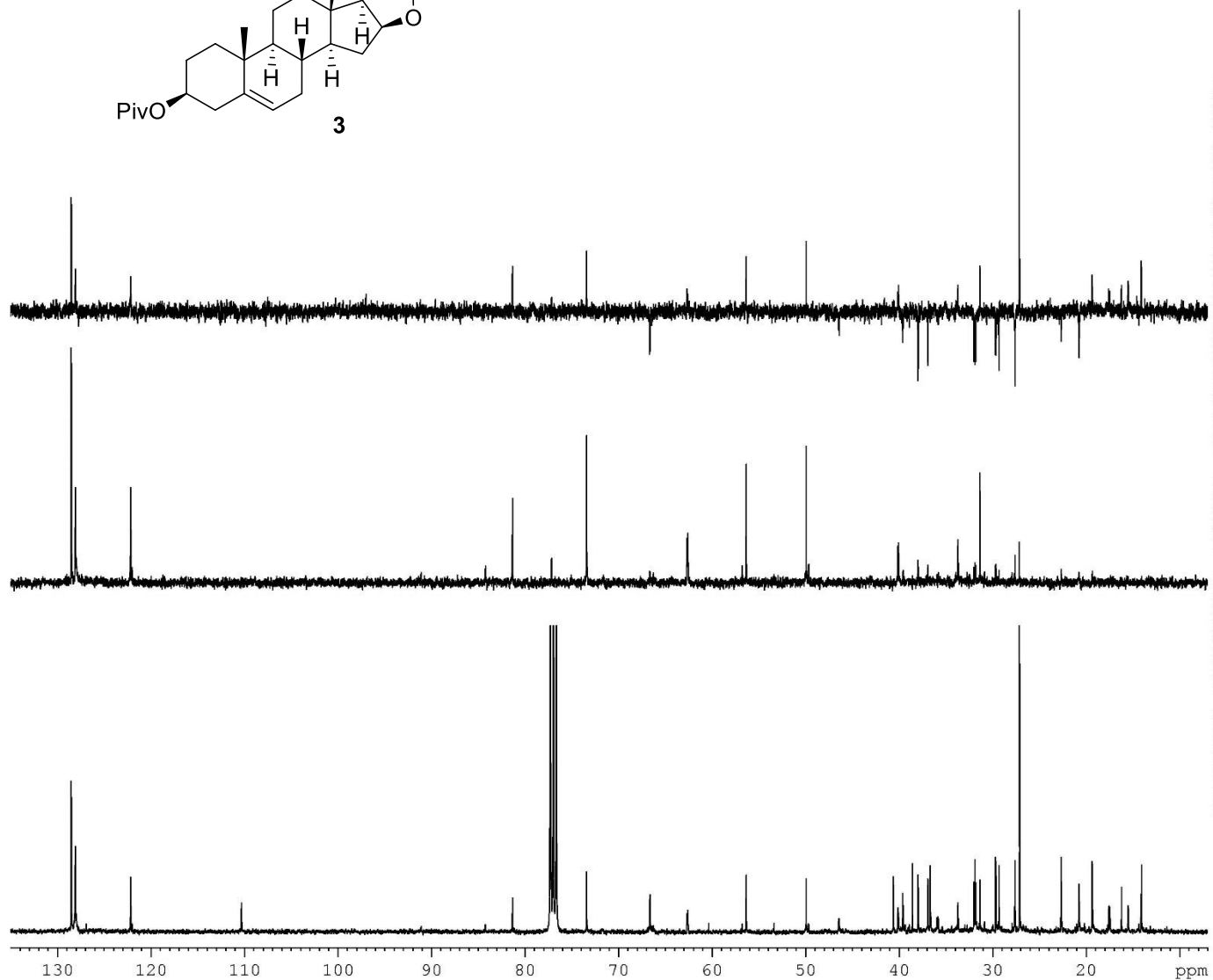
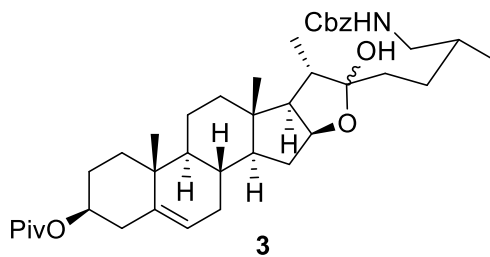
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TD 65536
SOLVENT CDCL3
NS 12800
DS 4
SWH 27173.912 Hz
FIDRES 0.414641 Hz
AQ 1.2059124 se
RG 161
DW 18.400 us
DE 6.00 us
TE 299.1 K
D1 2.0000000 se
d11 0.0300000 se
DELTA 1.89999998 se
TD0 1

===== CHANNEL f1 =====
NUC1 13C
P1 25.00 us
PL1 -1.00 dB
SFO1 100.6288660 MH

===== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 us
PL2 -3.00 dB
PL12 13.65 dB
PL13 18.00 dB
SFO2 400.1516006 MH

F2 - Processing parameters
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WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 0.20



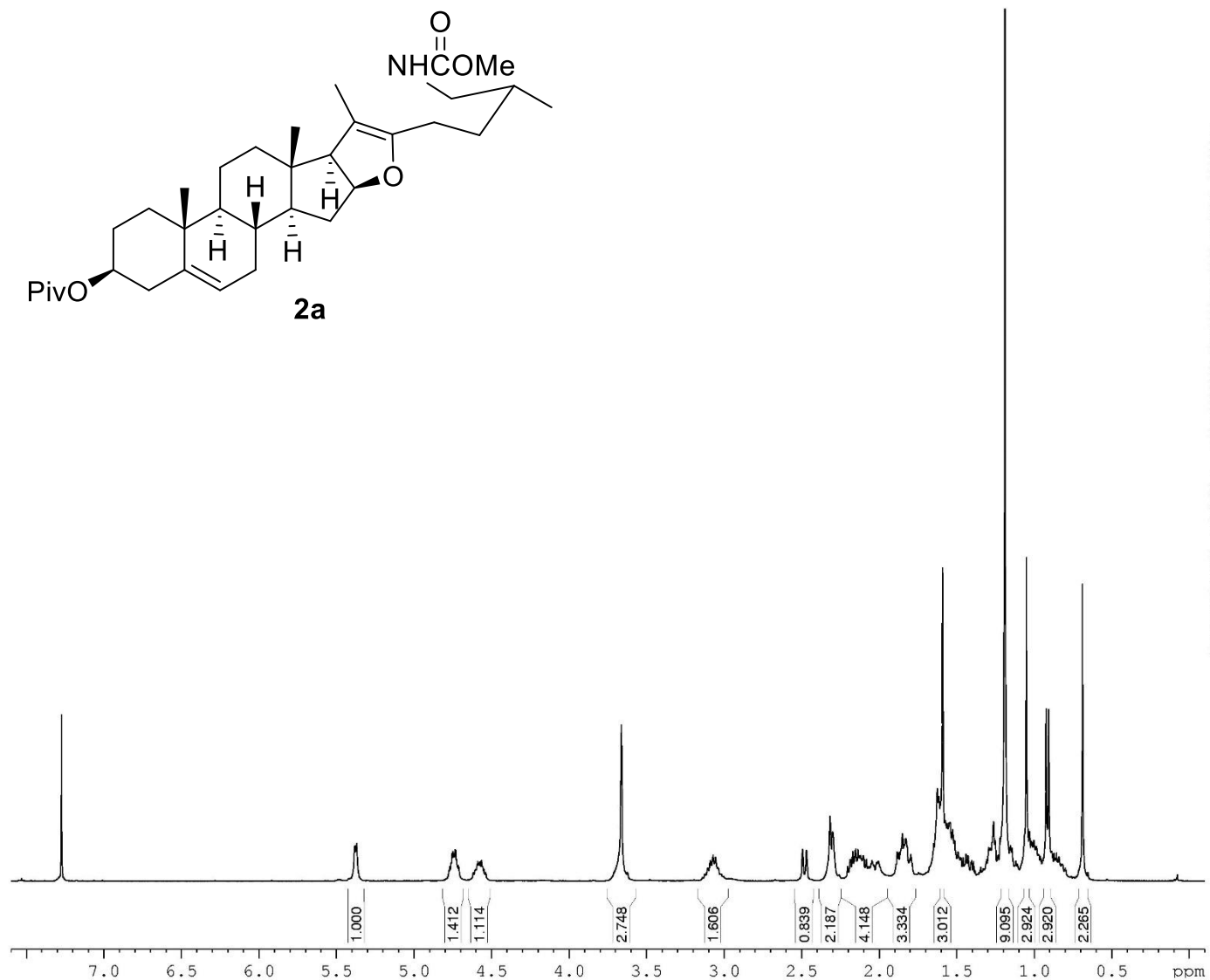
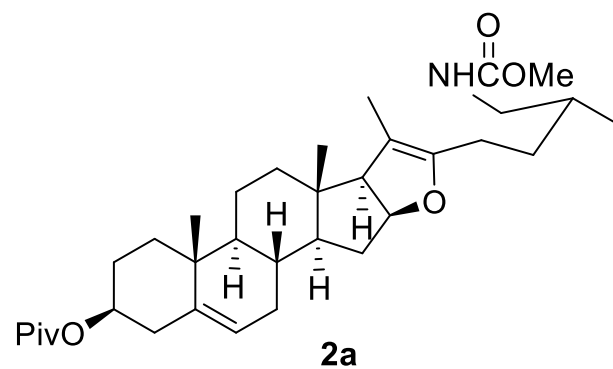
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TD 65536
SOLVENT CDCL3
NS 256
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631988 se
RG 2050
DW 20.800 us
DE 6.00 us
TE 299.1 K
CNST2 145.000000
D1 2.0000000 se
d2 0.00344828 se
d12 0.0000200 se
DELTA 0.00003183 se
TD0 1

===== CHANNEL f1 =====
NUC1 13C
P1 25.00 us
p2 50.00 us
PL1 -1.00 dB
SFO1 100.6248412 MH

===== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
P3 15.00 us
p4 30.00 us
PCPD2 100.00 us
PL2 -3.00 dB
PL12 13.65 dB
SFO2 400.1516006 MH

F2 - Processing parameters
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WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 0.20

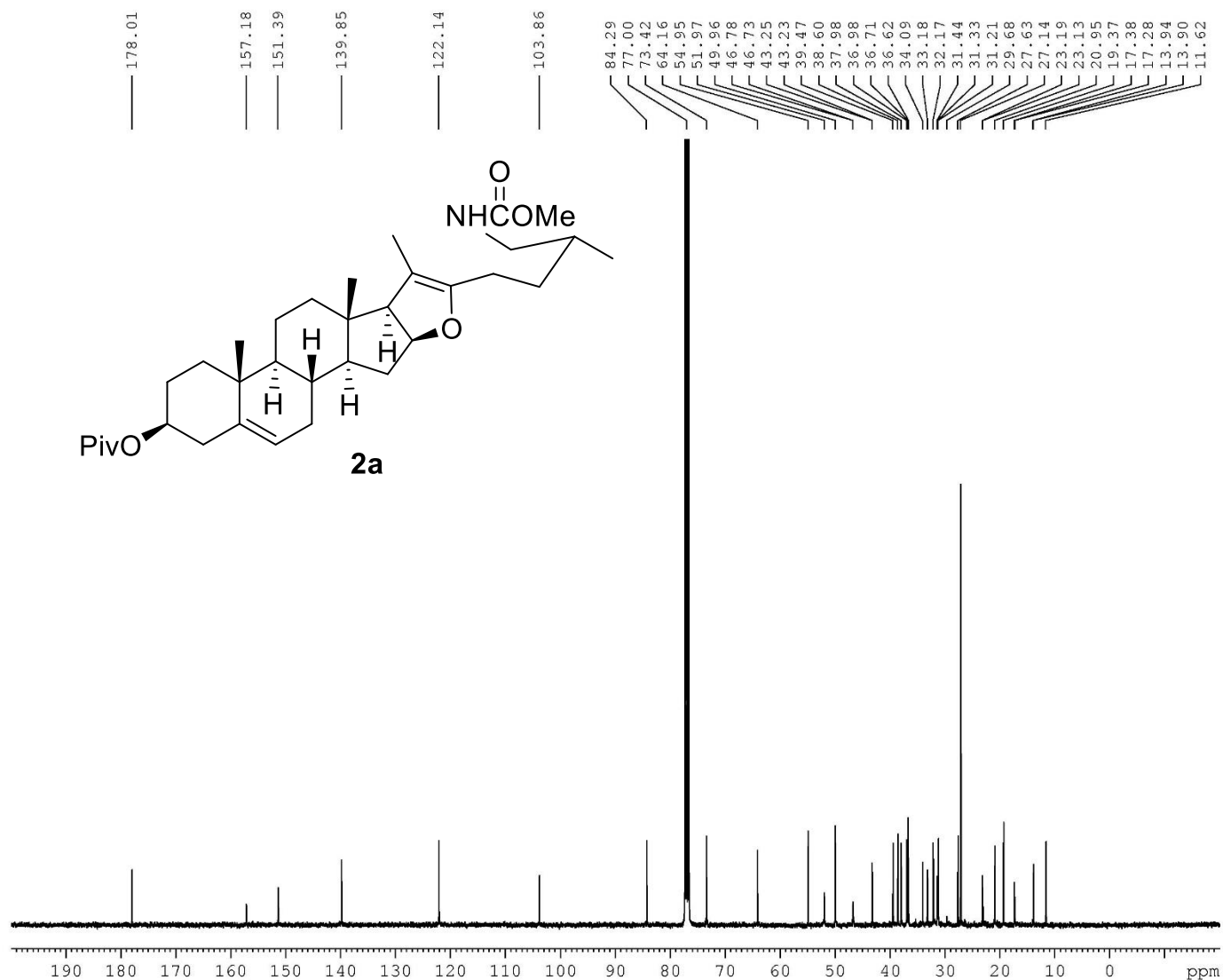


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 SOLVENT CDCl3
 NS 192
 DS 0
 SWE 8223.685 Hz
 FIDRES 0.125483 Hz
 AQ 3.9846387 se
 RG 228
 DW 60.800 us
 DE 8.00 us
 TE 297.9 K
 D1 1.00000000 se
 TD0 1

===== CHANNEL f1 =====
 NUC1 1H
 P1 11.15 us
 PL1 -3.00 dB
 SFO1 400.1524711 MH

F2 - Processing parameters
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 SF 400.1500000 MH
 WDW GM
 SSB 0
 LB -0.20 Hz
 GB 0.2
 PC 1.00



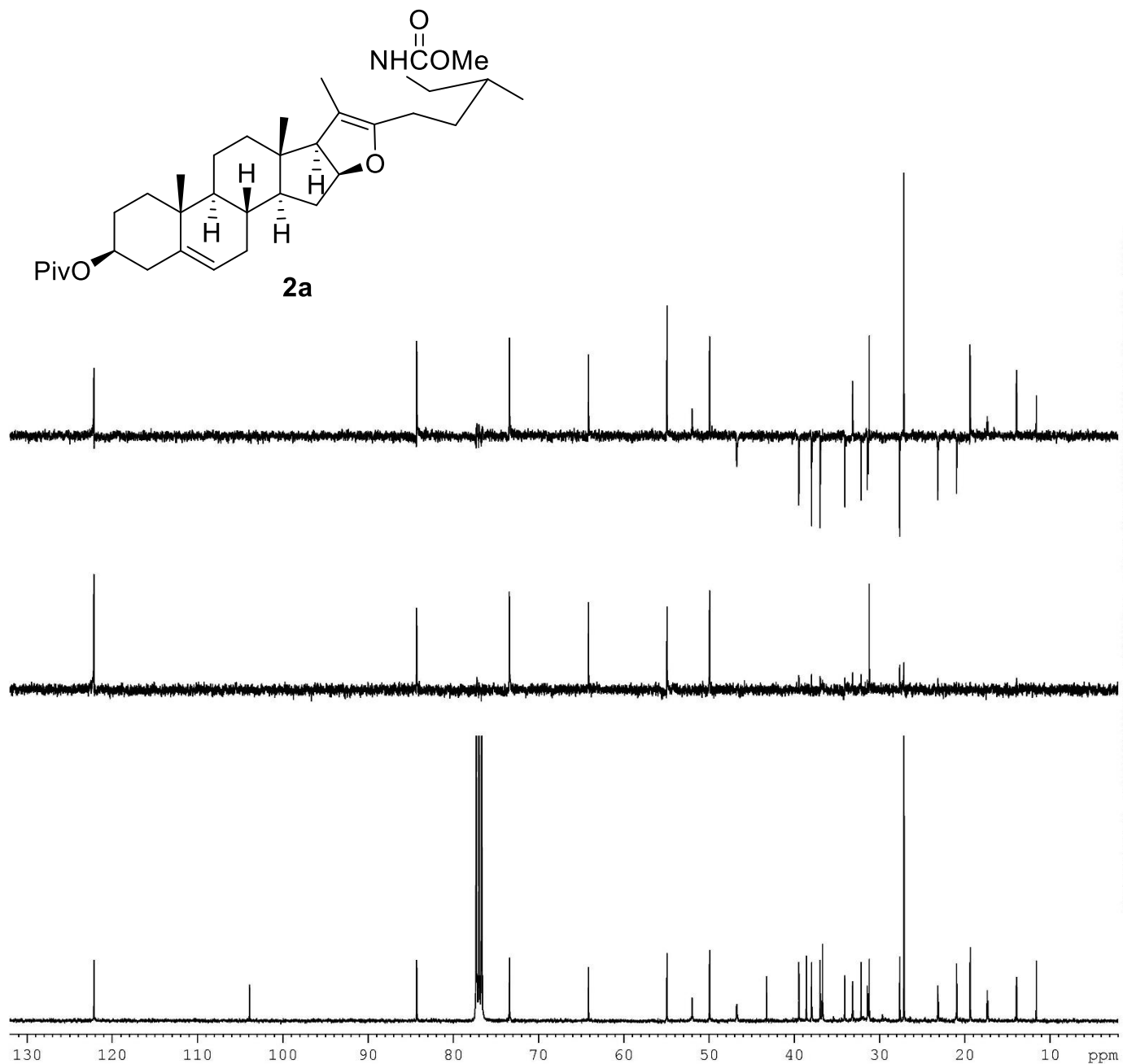
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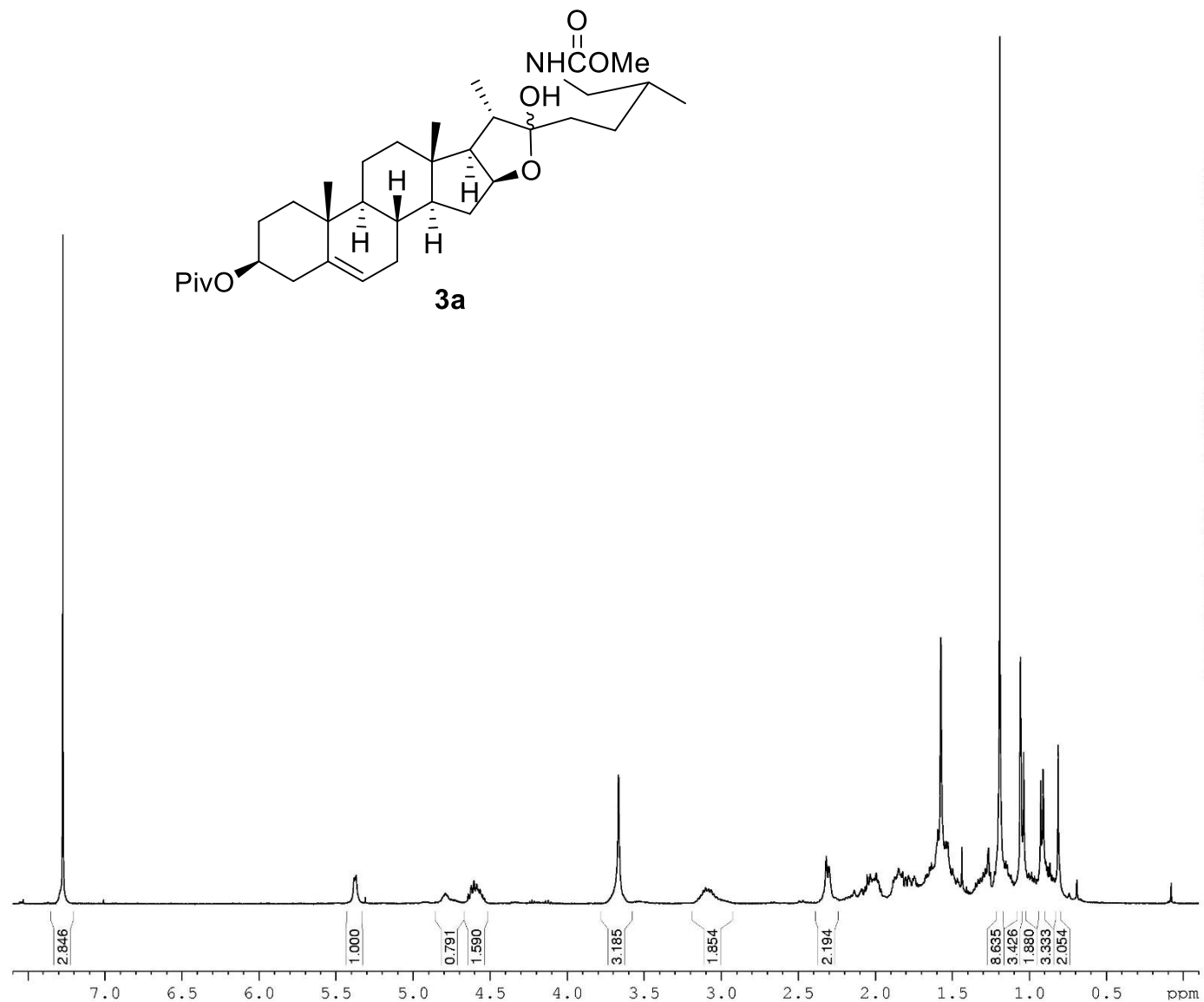
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 TD 65536
 SOLVENT CDCL3
 NS 11264
 DS 4
 SWH 27173.912 Hz
 FIDRES 0.414641 Hz
 AQ 1.2059124 se
 RG 36
 DW 18.400 us
 DE 6.00 us
 TE 298.5 K
 D1 2.0000000 se
 d11 0.0300000 se
 DELTA 1.89999998 se
 TD0 1

===== CHANNEL f1 =====
 NUC1 13C
 P1 30.00 us
 PL1 -1.00 dB
 SFO1 100.6288660 MH

===== CHANNEL f2 =====
 CPDPRG2 waltz16
 NUC2 1H
 PCPD2 100.00 us
 PL2 -3.00 dB
 PL12 13.65 dB
 PL13 18.00 dB
 SFO2 400.1516006 MH

F2 - Processing parameters
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 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 0.20



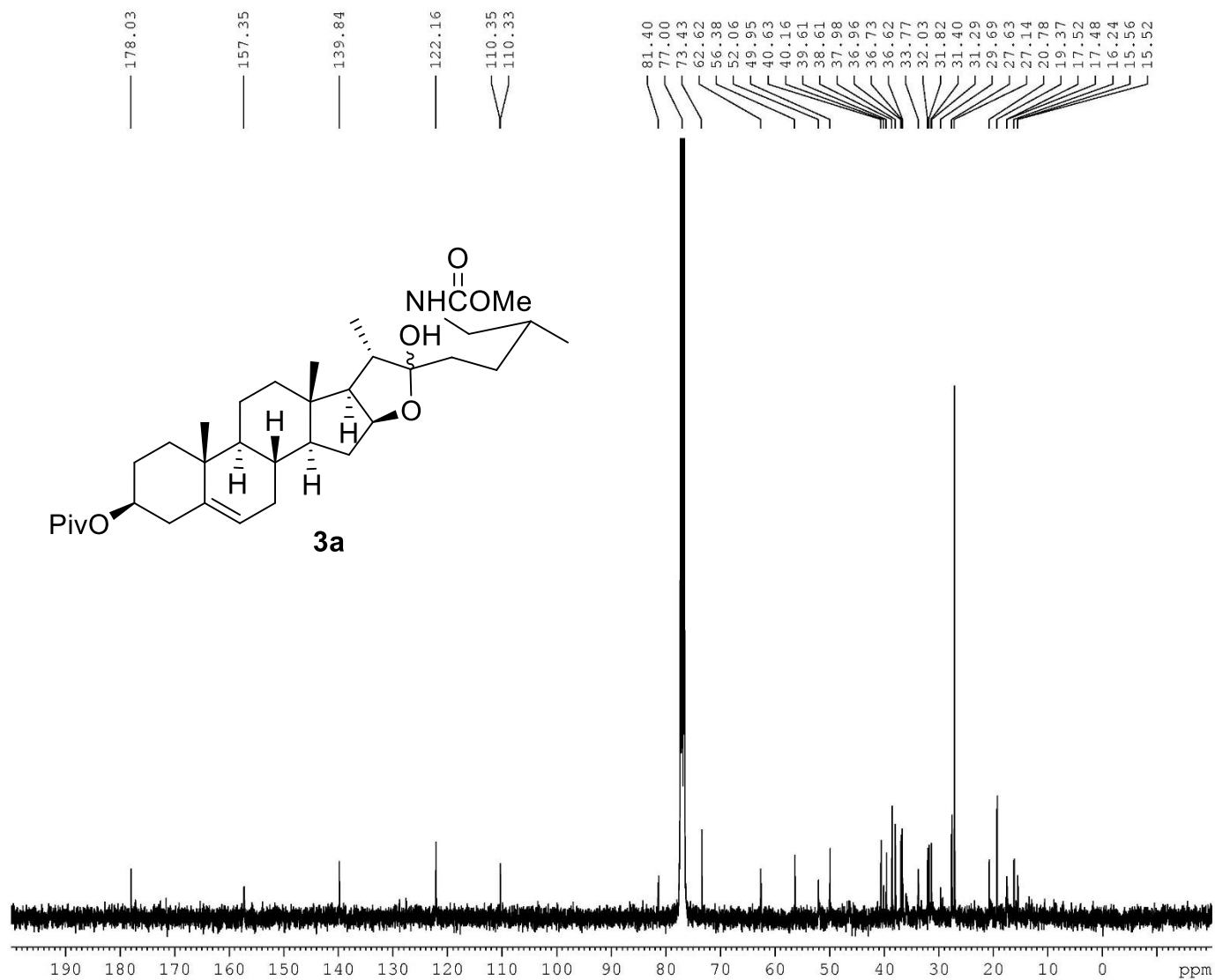


Current Data Parameters
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EXPNO 1
PROCNO 1

F2 - Acquisition Parameter
Date_ 20171013
Time 14.00
INSTRUM spect
PROBED 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 192
DS 0
SWE 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 se
RG 256
DW 60.800 us
DE 8.00 us
TE 298.0 K
D1 1.0000000 se
TD0 1

===== CHANNEL f1 =====
NUC1 1H
P1 25.00 us
PL1 -3.00 dB
SFO1 400.1524711 MH

F2 - Processing parameters
SI 32768
SF 400.150000 MH
WDW GM
SSB 0
LB -0.20 Hz
GB 0.2
PC 1.00



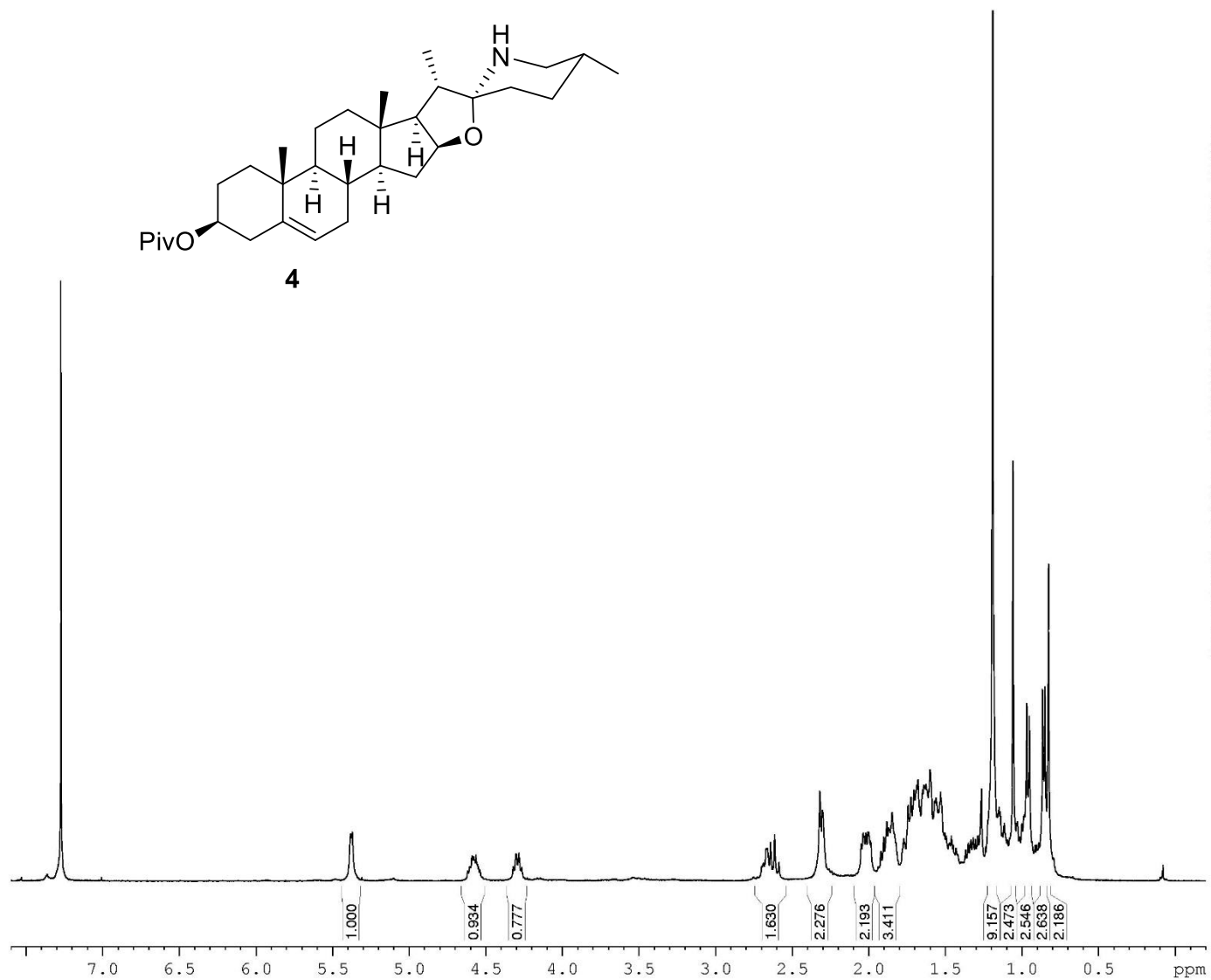
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EXPNO 2
PROCNO 1

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Time 3.23
INSTRUM spect
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PULPROG zgpg30
TD 65536
SOLVENT CDCL3
NS 16384
DS 4
SWH 27173.912 Hz
FIDRES 0.414641 Hz
AQ 1.2059124 se
RG 181
DW 18.400 us
DE 6.00 us
TE 298.6 K
D1 2.0000000 se
d11 0.0300000 se
DELTA 1.89999998 se
TD0 1

===== CHANNEL f1 =====
NUC1 13C
P1 30.00 us
PL1 -1.00 dB
SFO1 100.6288660 MH

===== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 us
PL2 -3.00 dB
PL12 13.65 dB
PL13 18.00 dB
SFO2 400.1516006 MH

F2 - Processing parameters
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WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 0.20

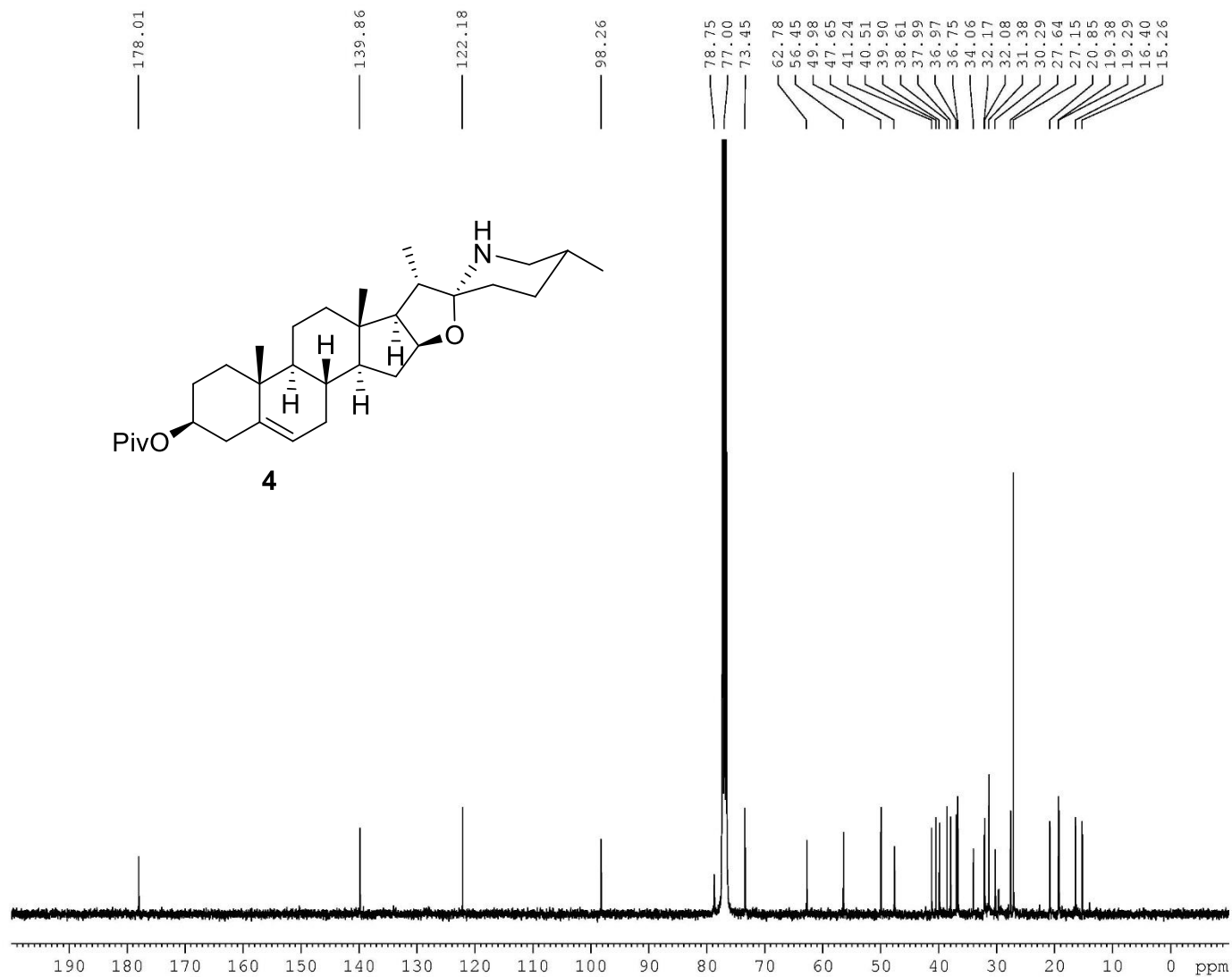


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 PULPROG zg30
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 SOLVENT CDCl3
 NS 192
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 SWH 8223.685 Hz
 FIDRES 0.125483 Hz
 AQ 3.9846387 se
 RG 228
 DW 60.800 us
 DE 8.00 us
 TE 297.5 K
 D1 1.00000000 se
 TD0 1

===== CHANNEL f1 =====
 NUC1 1H
 P1 25.00 us
 PL1 -3.00 dB
 SFO1 400.1524711 MH

F2 - Processing parameters
 SI 32768
 SF 400.1500000 MH
 WDW GM
 SSB 0
 LB -0.20 Hz
 GB 0.2
 PC 1.00



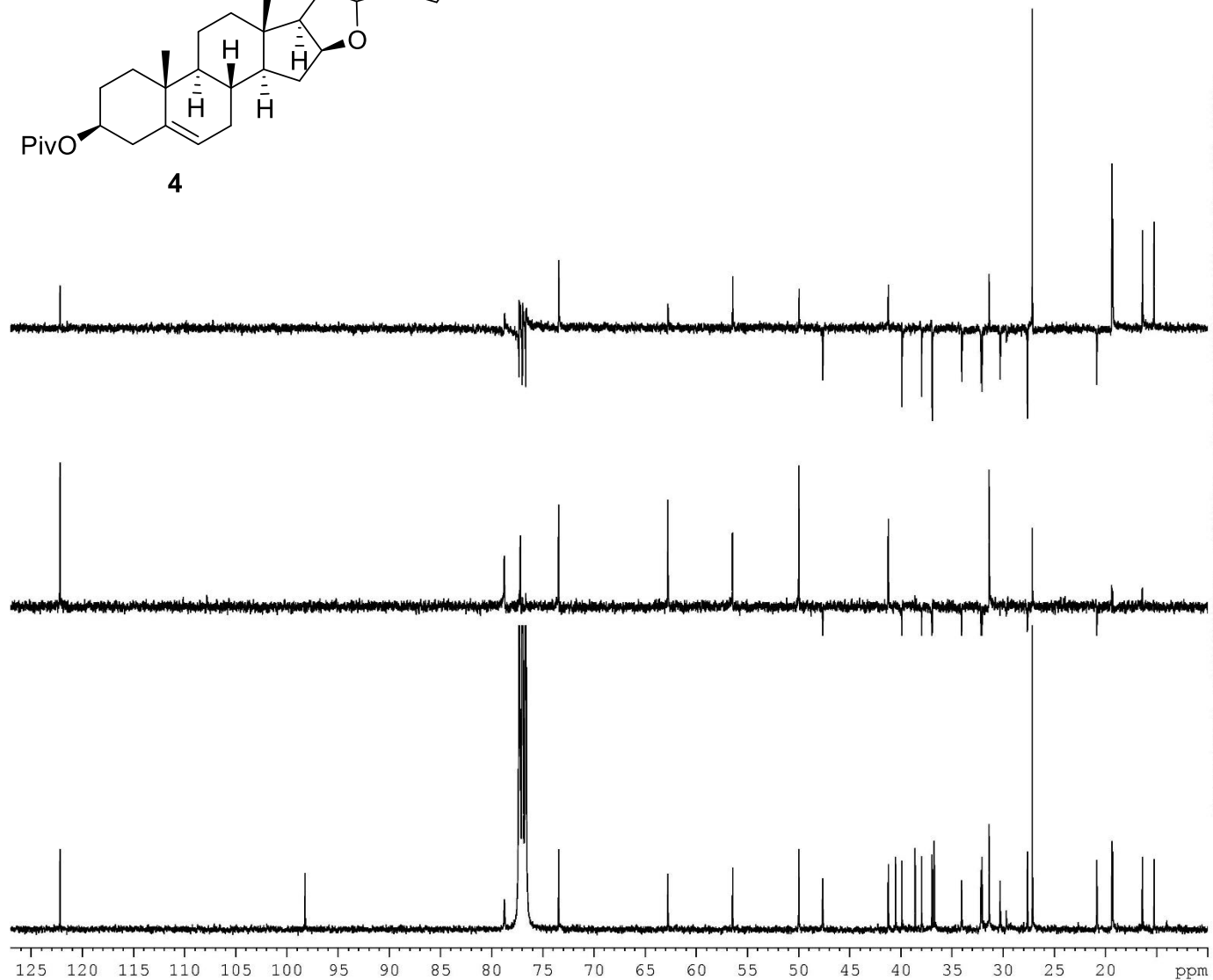
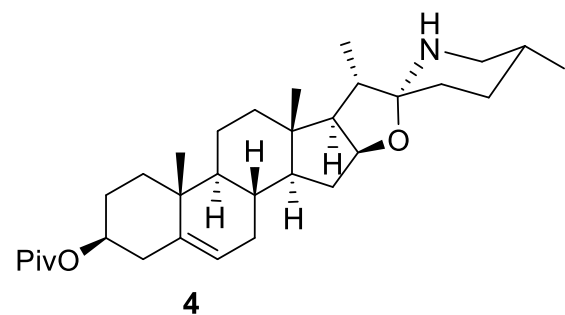
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 EXPNO 2
 PROCNO 1

F2 - Acquisition Parameter
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 Time 9.27
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 PULPROG zgpg30
 TD 65536
 SOLVENT CDCL3
 NS 40960
 DS 4
 SWH 27173.912 Hz
 FIDRES 0.414641 Hz
 AQ 1.2059124 se
 RG 114
 DW 18.400 us
 DE 6.00 us
 TE 298.7 K
 D1 2.0000000 se
 d11 0.0300000 se
 DELTA 1.89999998 se
 TD0 1

===== CHANNEL f1 =====
 NUC1 13C
 P1 25.00 us
 PL1 -1.00 dB
 SFO1 100.6288660 MH

===== CHANNEL f2 =====
 CPDPRG2 waltz16
 NUC2 1H
 PCPD2 100.00 us
 PL2 -3.00 dB
 PL12 13.65 dB
 PL13 18.00 dB
 SFO2 400.1516006 MH

F2 - Processing parameters
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 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 0.20



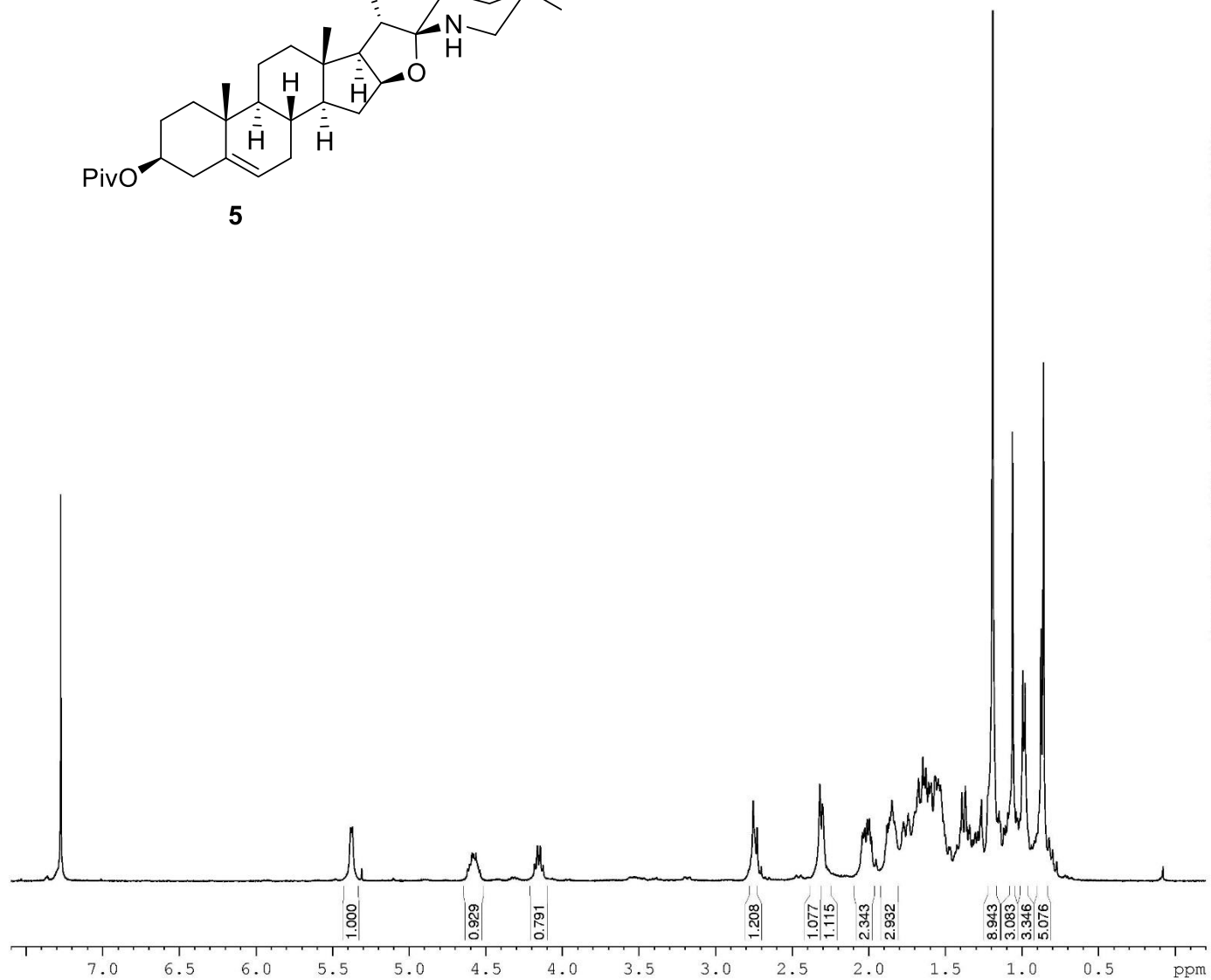
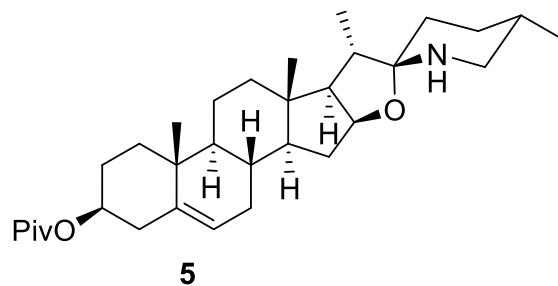
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EXPNO 4
PROCNO 1

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PULPROG dept135
TD 65536
SOLVENT CDCl3
NS 14400
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631988 se
RG 2050
DW 20.800 us
DE 6.00 us
TE 298.5 K
CNST2 145.000000
D1 2.0000000 se
d2 0.00344828 se
d12 0.00002000 se
DELTA 0.00003183 se
TD0 1

===== CHANNEL f1 =====
NUC1 13C
P1 25.00 us
p2 50.00 us
PL1 -1.00 dB
SFO1 100.6228289 MH

===== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
P3 18.00 us
p4 36.00 us
PCPD2 100.00 us
PL2 -3.00 dB
PL12 13.65 dB
SFO2 400.1516006 MH

F2 - Processing parameters
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GB 0
PC 0.20

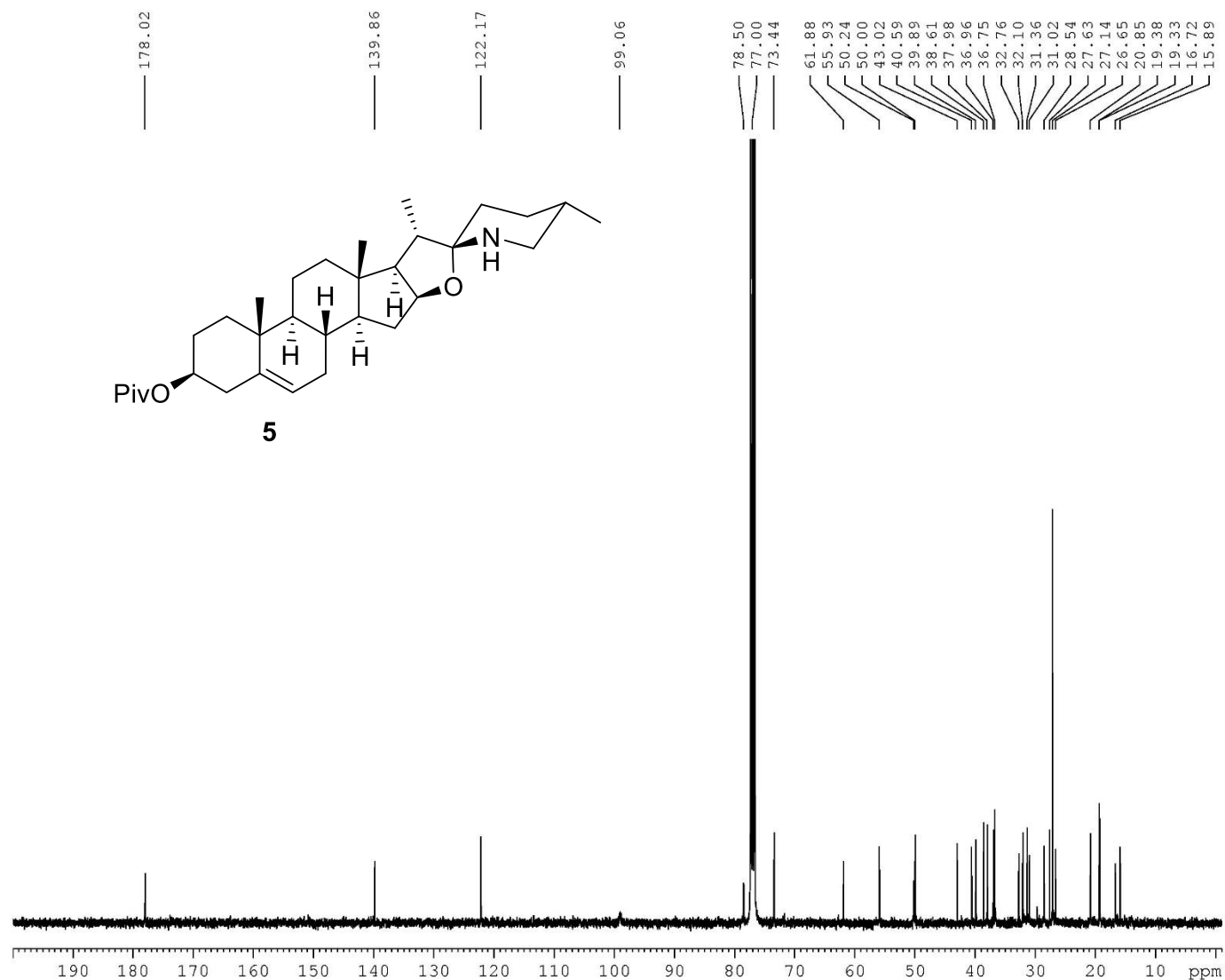


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 PULPROG zg30
 TD 65536
 SOLVENT CDCl3
 NS 192
 DS 0
 SWH 8223.685 Hz
 FIDRES 0.125483 Hz
 AQ 3.9846387 sec
 RG 287
 DW 60.800 use
 DE 8.00 use
 TE 298.4 K
 D1 1.0000000 sec
 TDO 1

----- CHANNEL f1 -----
 NUC1 1H
 P1 11.15 use
 PL1 -3.00 dB
 SFO1 400.1524711 MHz

F2 - Processing parameters
 SI 32768
 SF 400.1500000 MHz
 WDW GM
 SSB 0
 LB -0.20 Hz
 GB 0.2
 PC 1.00



Current Data Parameters
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 EXPNO 2
 PROCNO 1

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 PROBED 5 mm PABBO BB
 PULPROG zgpg30
 TD 65536
 SOLVENT CDC13
 NS 12800
 DS 4
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 FIDRES 0.414641 Hz
 AQ 1.2059124 sec
 RG 181
 DW 18.400 use
 DE 6.00 use
 TE 298.7 K
 D1 2.00000000 sec
 d11 0.03000000 sec
 DELTA 1.89999998 sec
 TDO 1

===== CHANNEL f1 =====
 NUC1 13C
 P1 25.00 use
 PL1 -1.00 dB
 SFO1 100.6288660 MHz

===== CHANNEL f2 =====
 CPDPRG2 waltz16
 NUC2 1H
 PCPD2 100.00 use
 PL2 -3.00 dB
 PL12 13.65 dB
 PL13 18.00 dB
 SFO2 400.1516006 MHz

F2 - Processing parameters
 SI 32768
 SF 100.6171981 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 0.20

