

Conformationally Constrained 5-Fluoro- and 5-Hydroxymethanopyrrolidines. Ring Puckered Mimics of *Gauche* and *anti*-3-Fluoro- and 3-Hydroxypyrrolidines.

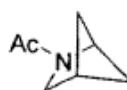
Supplemental Section

Page

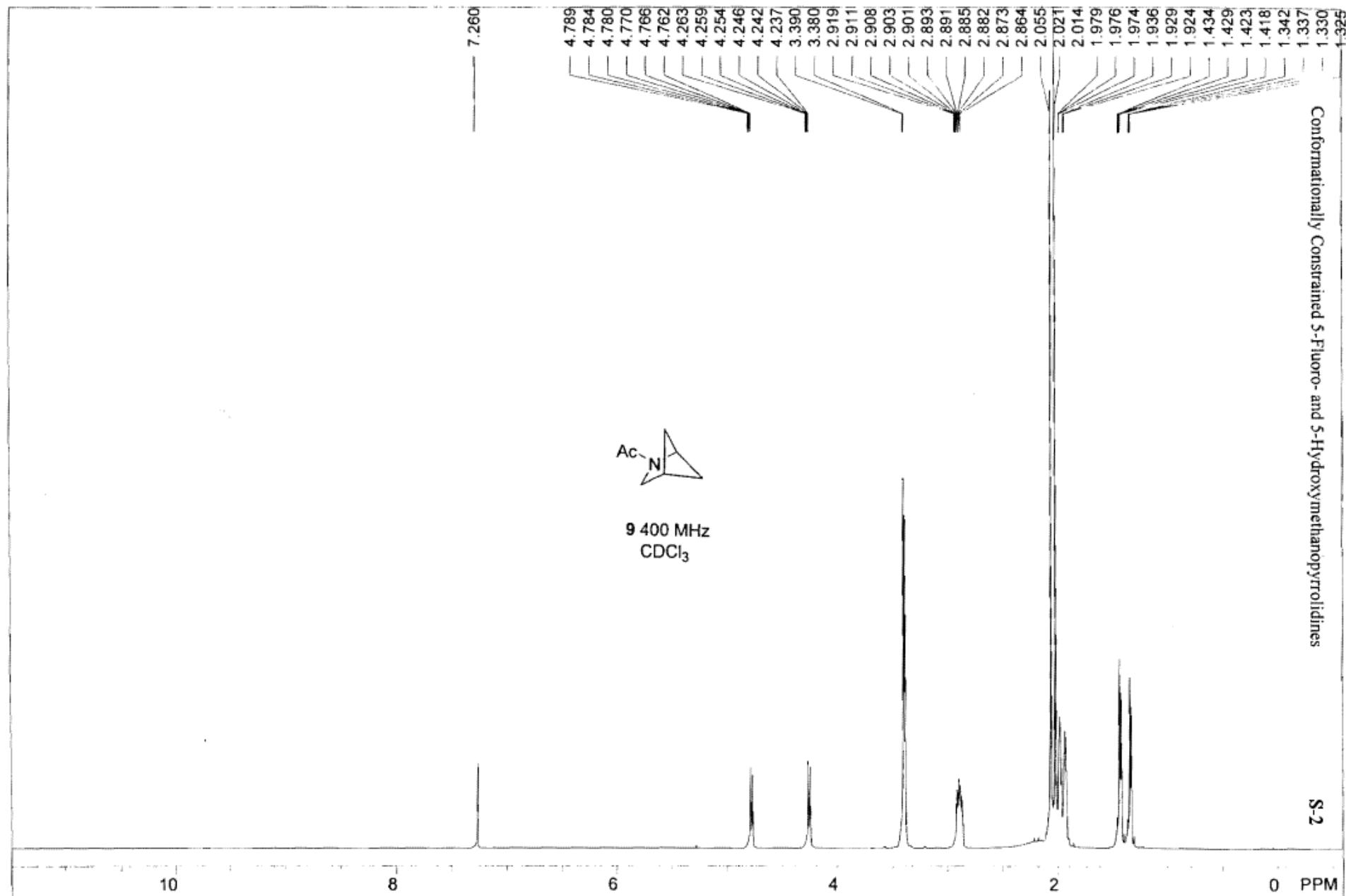
- | | |
|--------------|---|
| S-2 to S-26 | Spectra for <i>N</i> -Boc and <i>N</i> -Ac compounds 7, 10a-b, 11a-b, 12b, 13a-b . |
| S-27 to S-34 | Spectra for fluoride precursors 19-23 . |
| S-35 to S-49 | Spectra for <i>syn</i> -alcohol precursors 25-31 . |
| S-50 to S-55 | Spectra for <i>anti</i> -alcohol precursors 33-35 . |
| S-56 to S-60 | Spectra for benzoate 36 and acetate 37 . |

Conformationally Constrained 5-Fluoro- and 5-Hydroxymethanopyrrolidines

S-2



9 400 MHz
 CDCl_3



NAc[2.1.1], proton.atm,

F1: 400.191 F2: 1.000

EX:

SW1: 8278

PW: 9.8 usec

QF1: 2003.3

PD:

1.0 sec

NA: 16

LB:

0.1

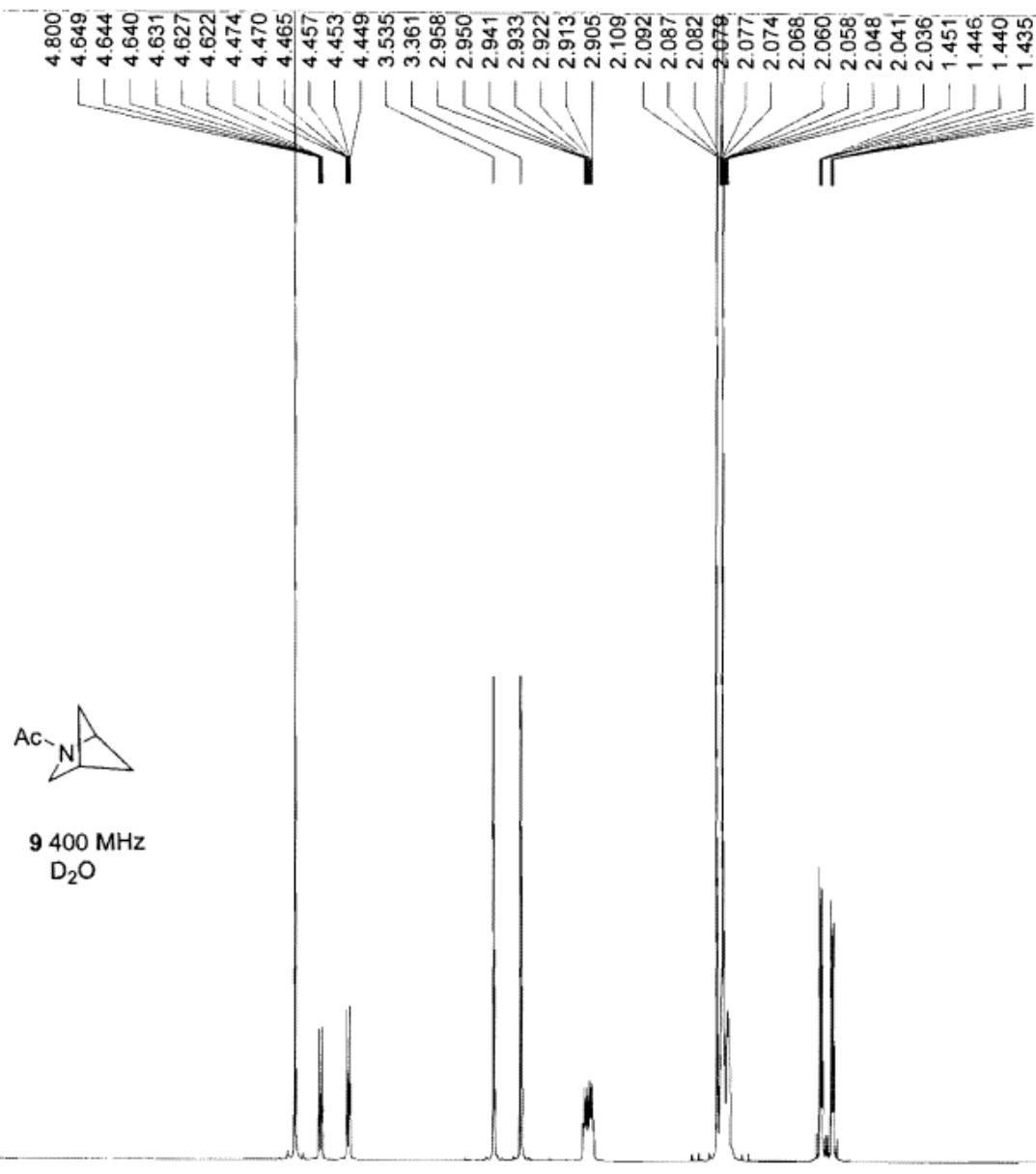
USER: temple -- DATE: Sep 7 20:37:38 2007 EDT (UT-4h) temp -

PTS1d: 32768

WinNuts - NAc[2.1.1]-(692).H1--CDCl3

Conformationally Constrained 5-Fluoro- and 5-Hydroxymethanopyrrolidines

S-3



10

8

6

4

2

0PPM

NAc[2.1.1], proton atm.

F1: 400.191 F2: 1.000

SW1: 8278

OF1: 2038.3

PTS1d: 32768

EX:

PW: 9.8 usec

PD: 1.0 sec

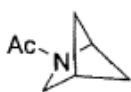
NA: 16

USER: temple -- DATE: Sep 11 12:29:02 2007 EDT (UT-4h) templ

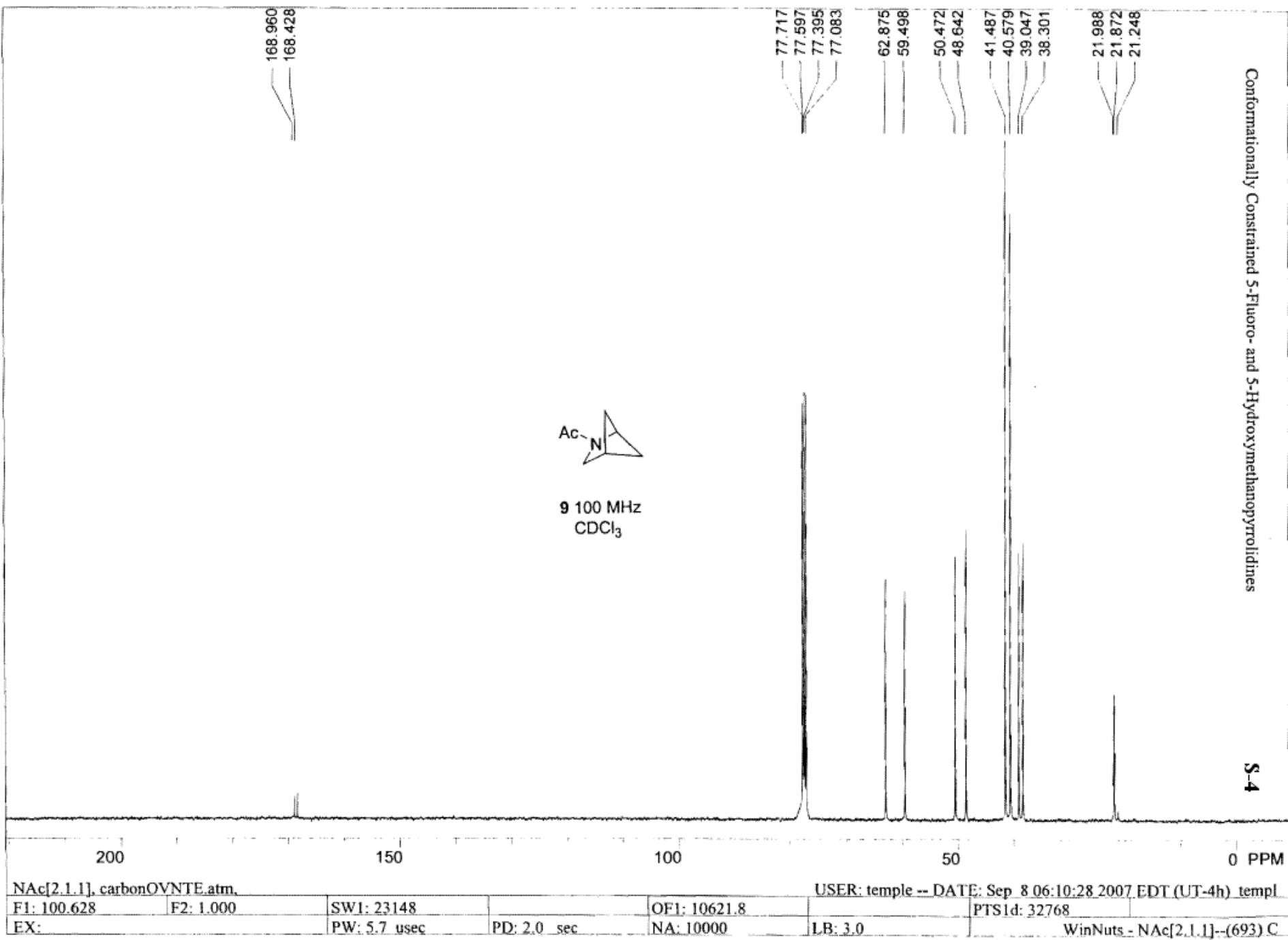
WinNuts - NAc[2.1.1]-(700) H1 {D2O}

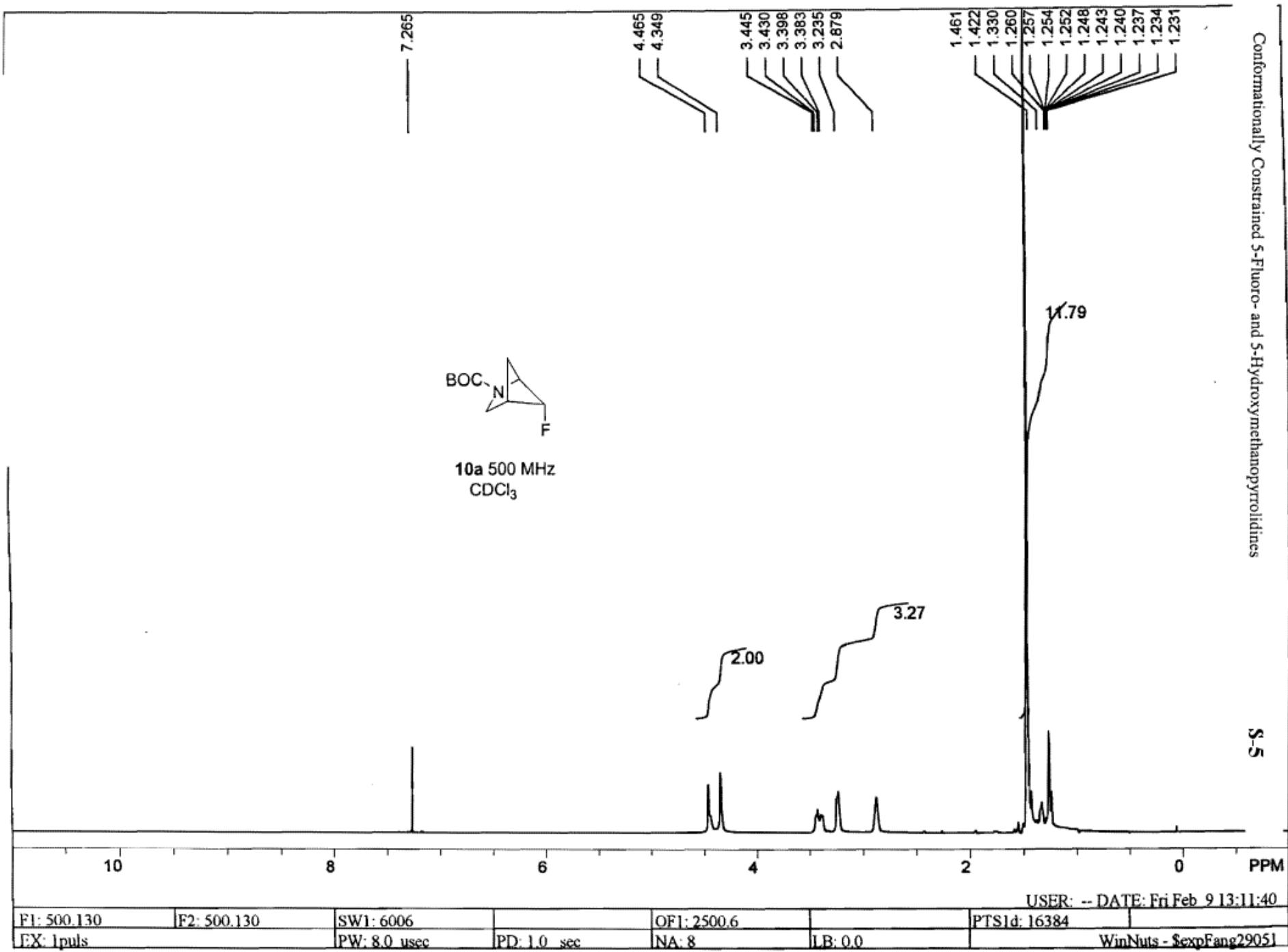
Conformationally Constrained 5-Fluoro- and 5-Hydroxymethanopyrrolidines

S-4



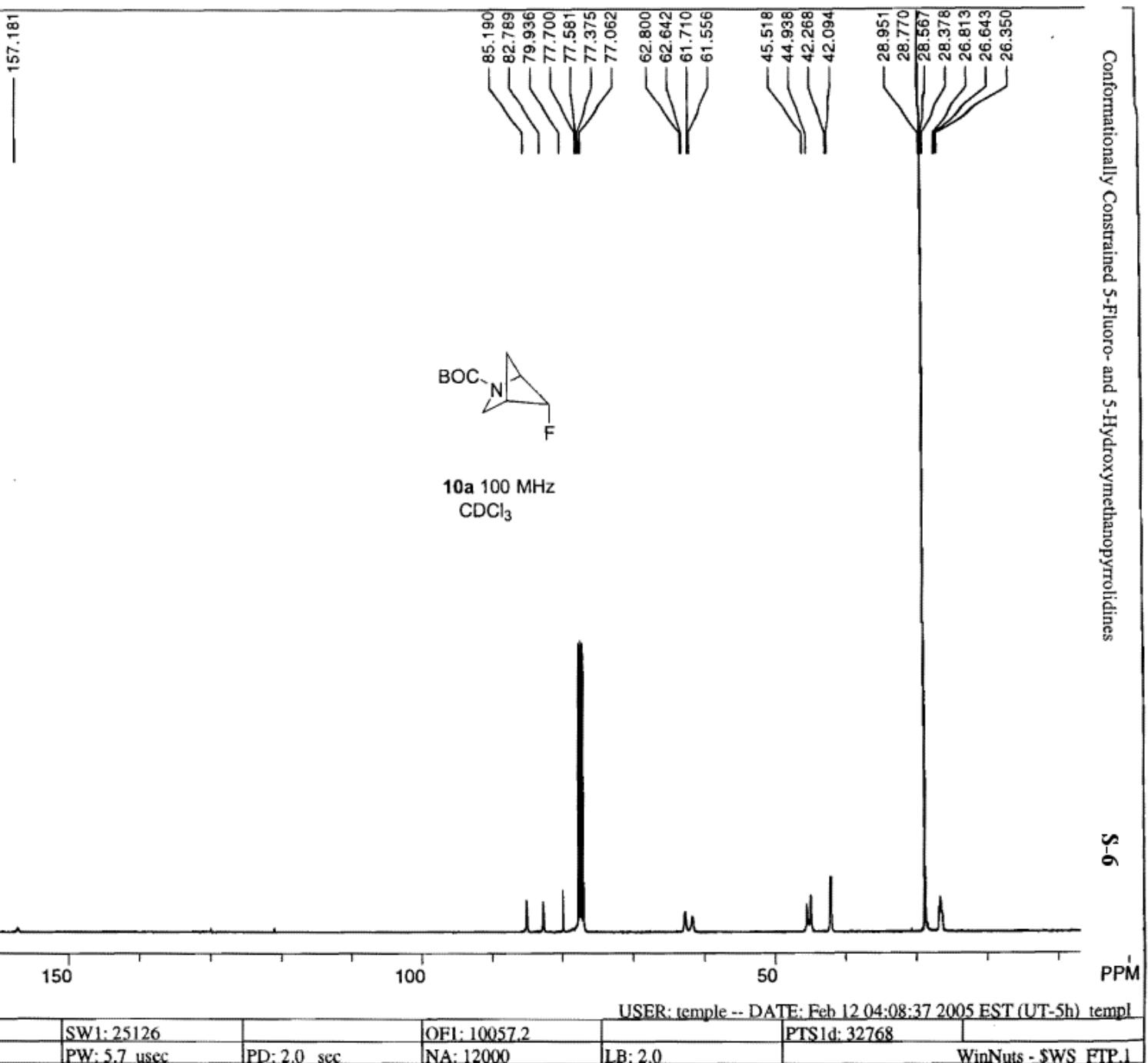
9 100 MHz
 CDCl_3

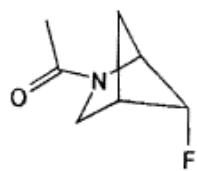




Conformationally Constrained 5-Fluoro- and 5-Hydroxymethanopyrrolidines

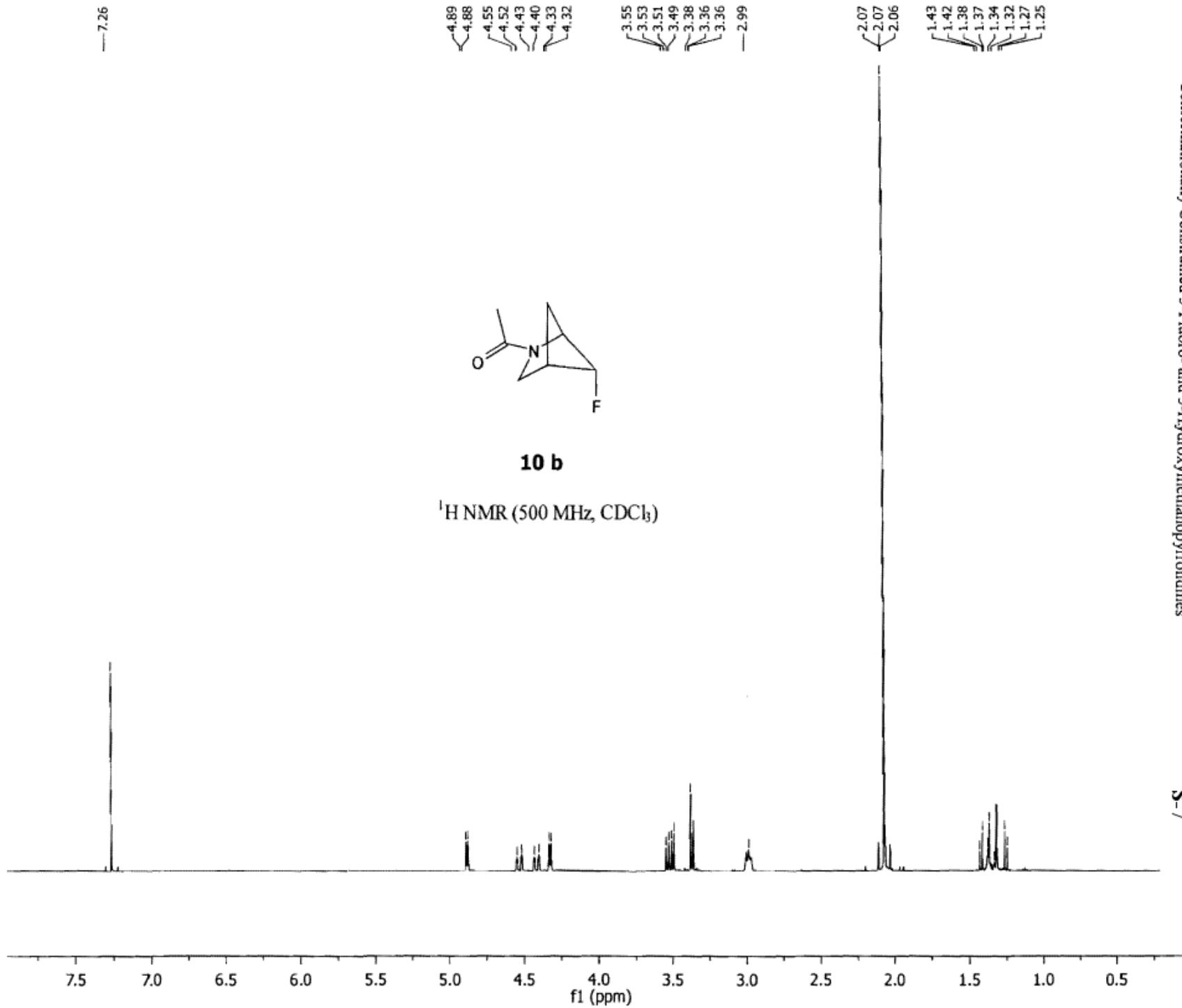
S-6

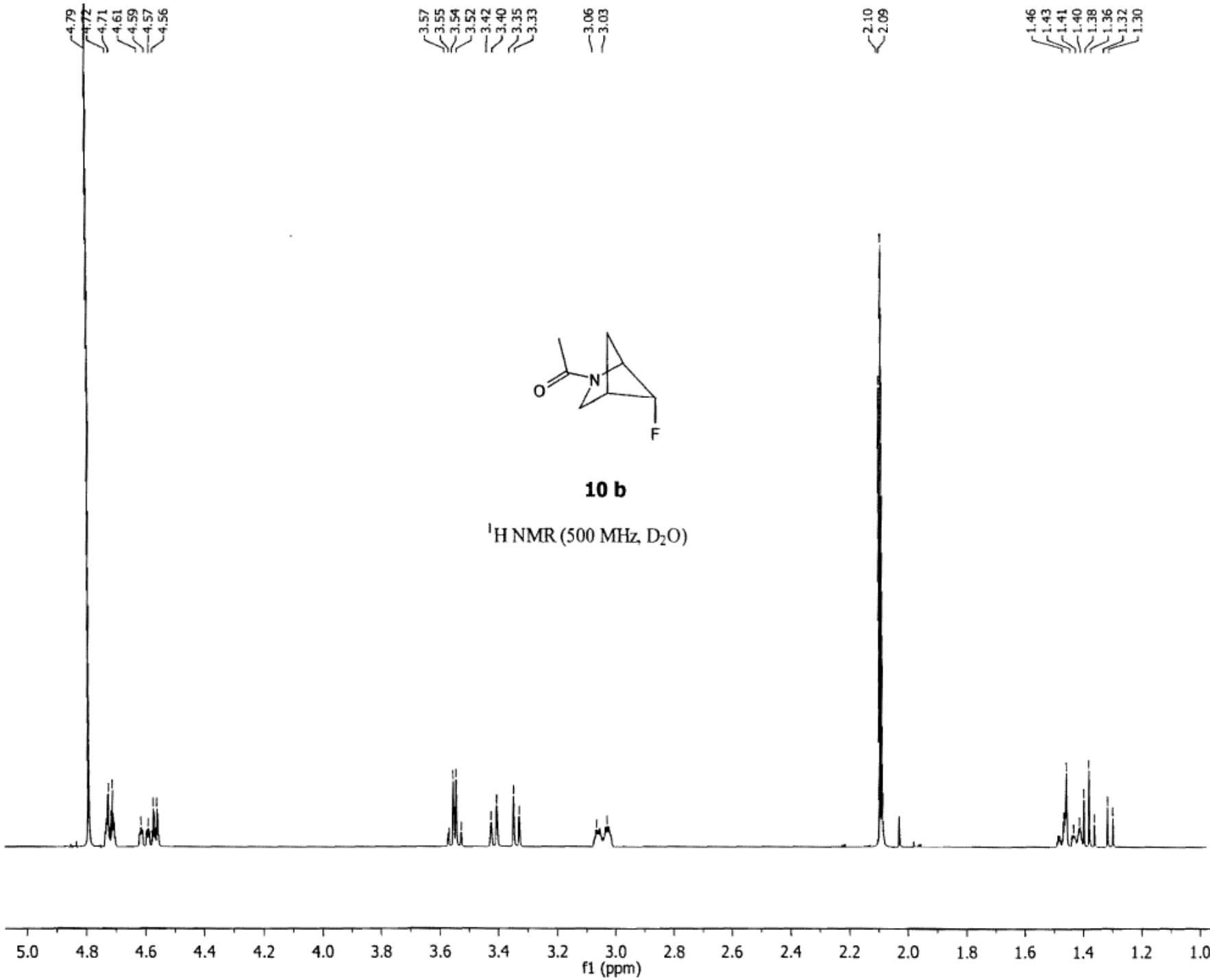


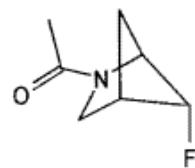


10 b

¹H NMR (500 MHz, CDCl₃)

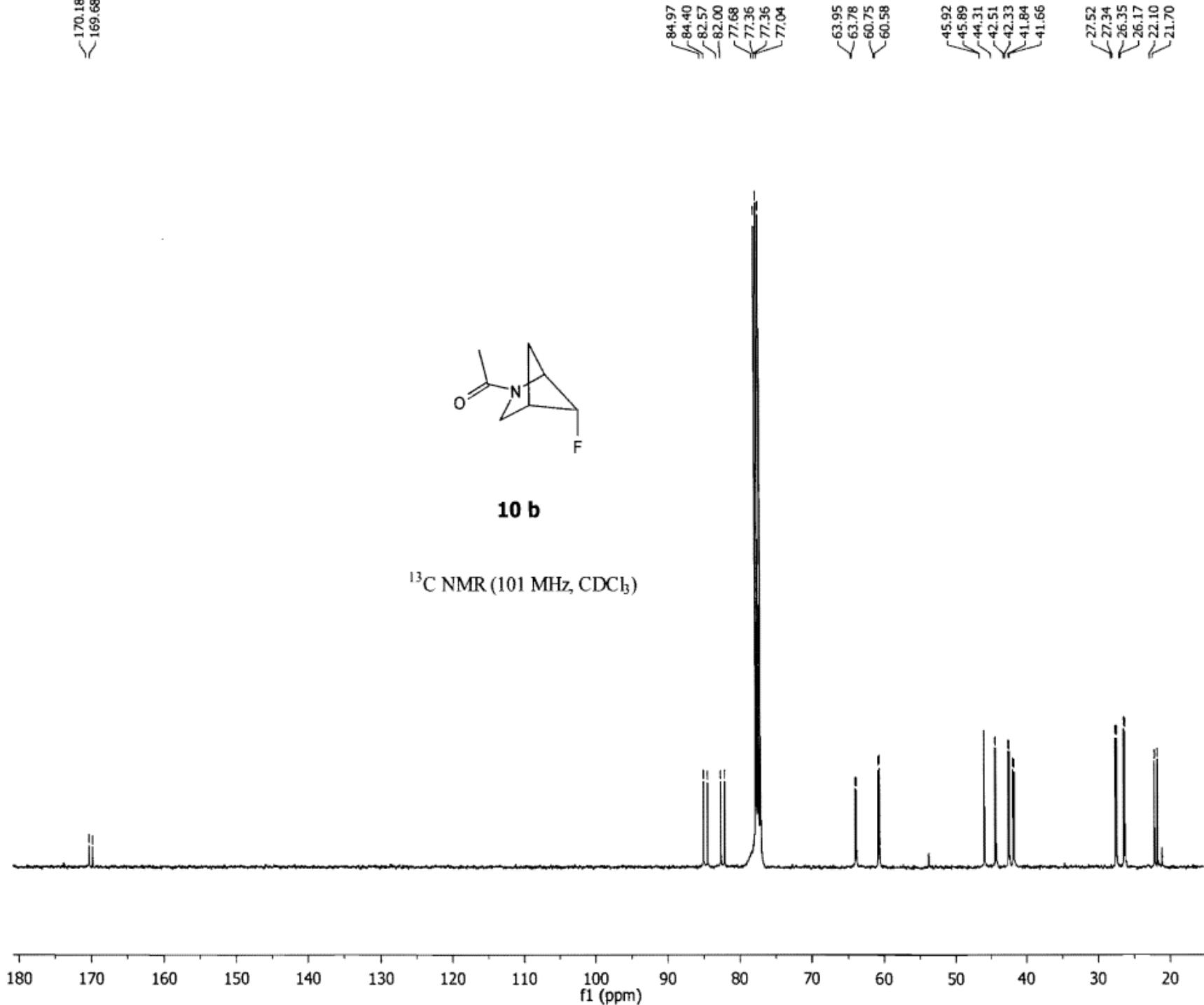


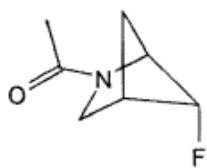




10 b

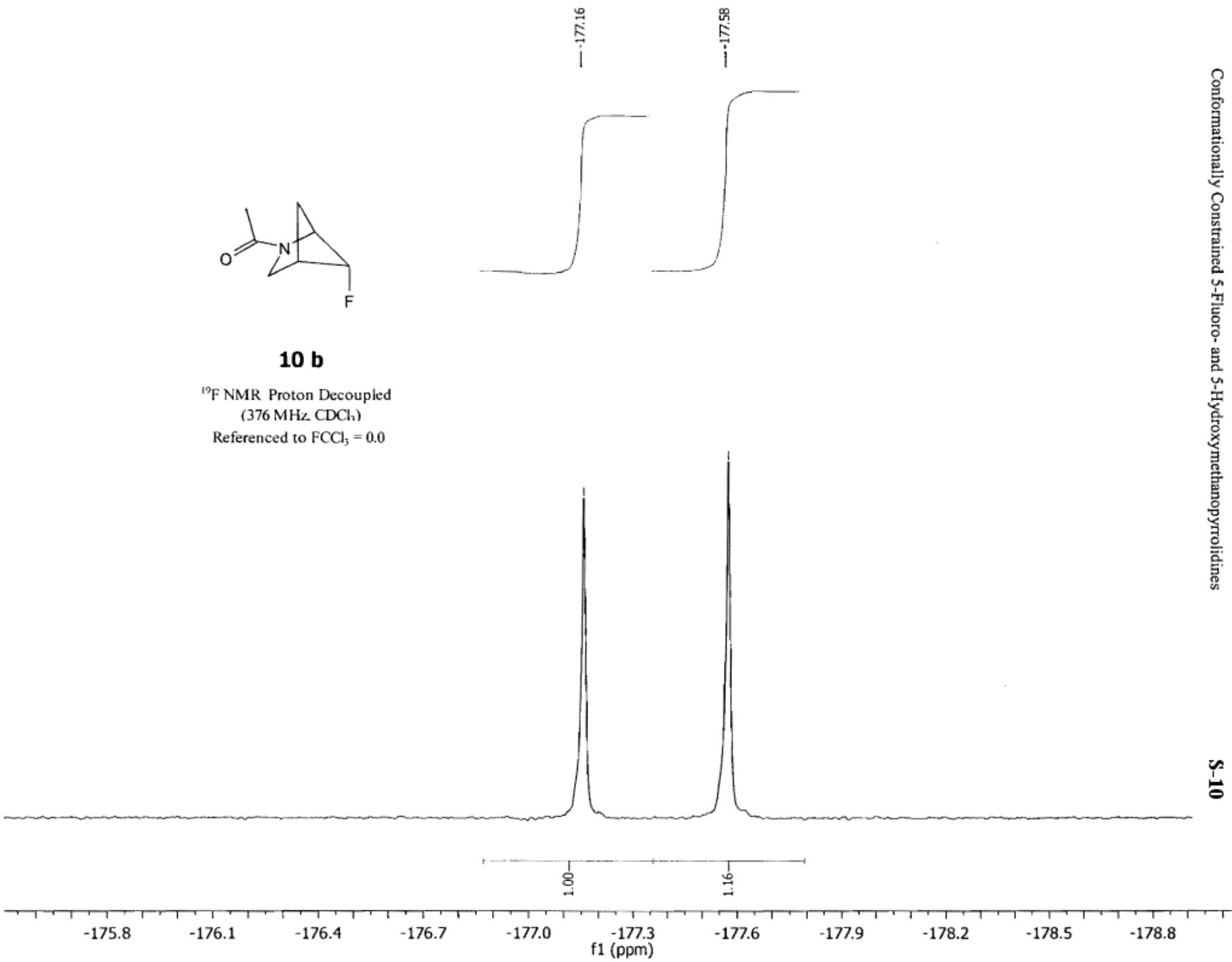
¹³C NMR (101 MHz, CDCl₃)

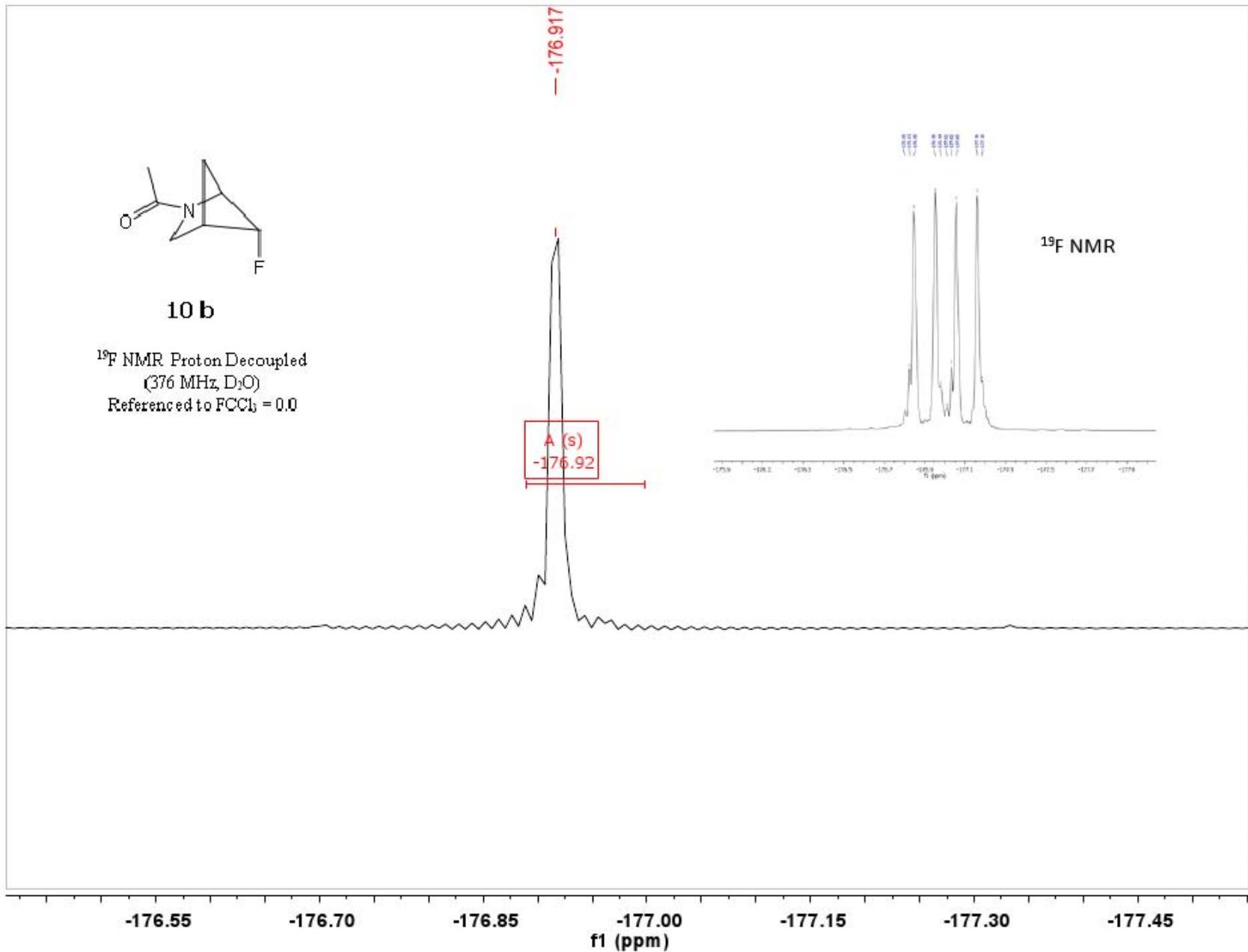




10 b

^{19}F NMR Proton Decoupled
(376 MHz, CDCl_3)
Referenced to $\text{FCCl}_3 = 0.0$





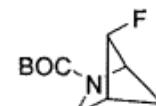
deepa/350_15Apr2004

expt s2pul

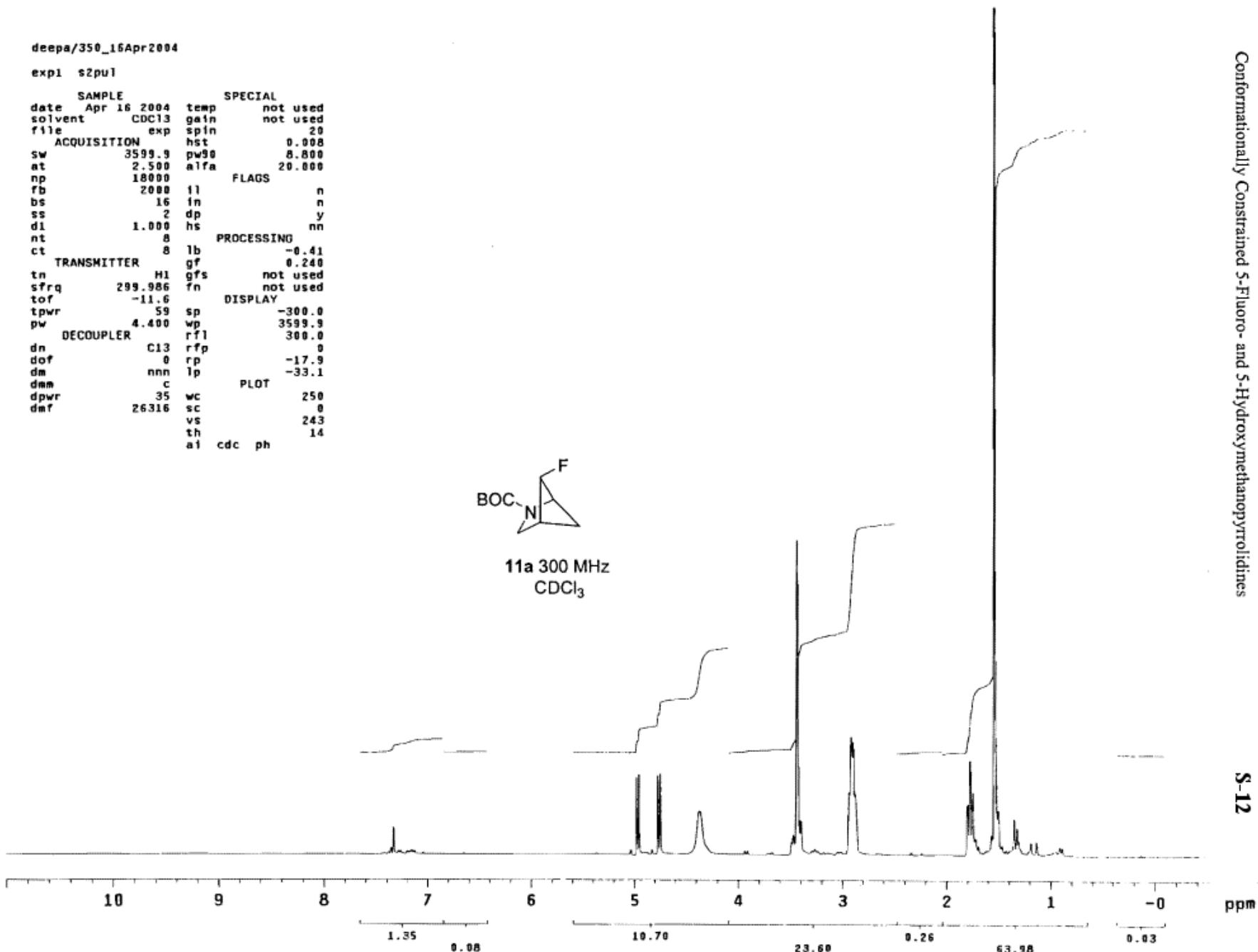
```

SAMPLE          SPECIAL
date Apr 16 2004 temp    not used
solvent   CDCl3 gain     not used
file      exp spin    20
          ACQUISITION hst      0.008
sw       3599.9 pw90     8.800
at        2.500 alfa    20.000
np       18000  FLAGS
fb        2000 11      n
bs         16  in      n
ss         2  dp      y
di       1.000 hs      nn
nt         8  PROCESSING
ct         8  1b      -0.41
          TRANSMITTER gf      0.240
tn        H1 gfs     not used
sfrq     299.986 fn     not used
tof      -11.6  DISPLAY
tpwr      59  sp      -300.0
pw       4.400 wp      3599.9
          DECOUPLER rfl     300.0
dn        C13 rfp     0
dof       0  rp      -17.9
dm       nnn lp      -33.1
dmm      c  PLOT
dpwr      35  wc      250
dmf     26316 sc      0
          vs      243
          th      14
          ai  cdc ph

```

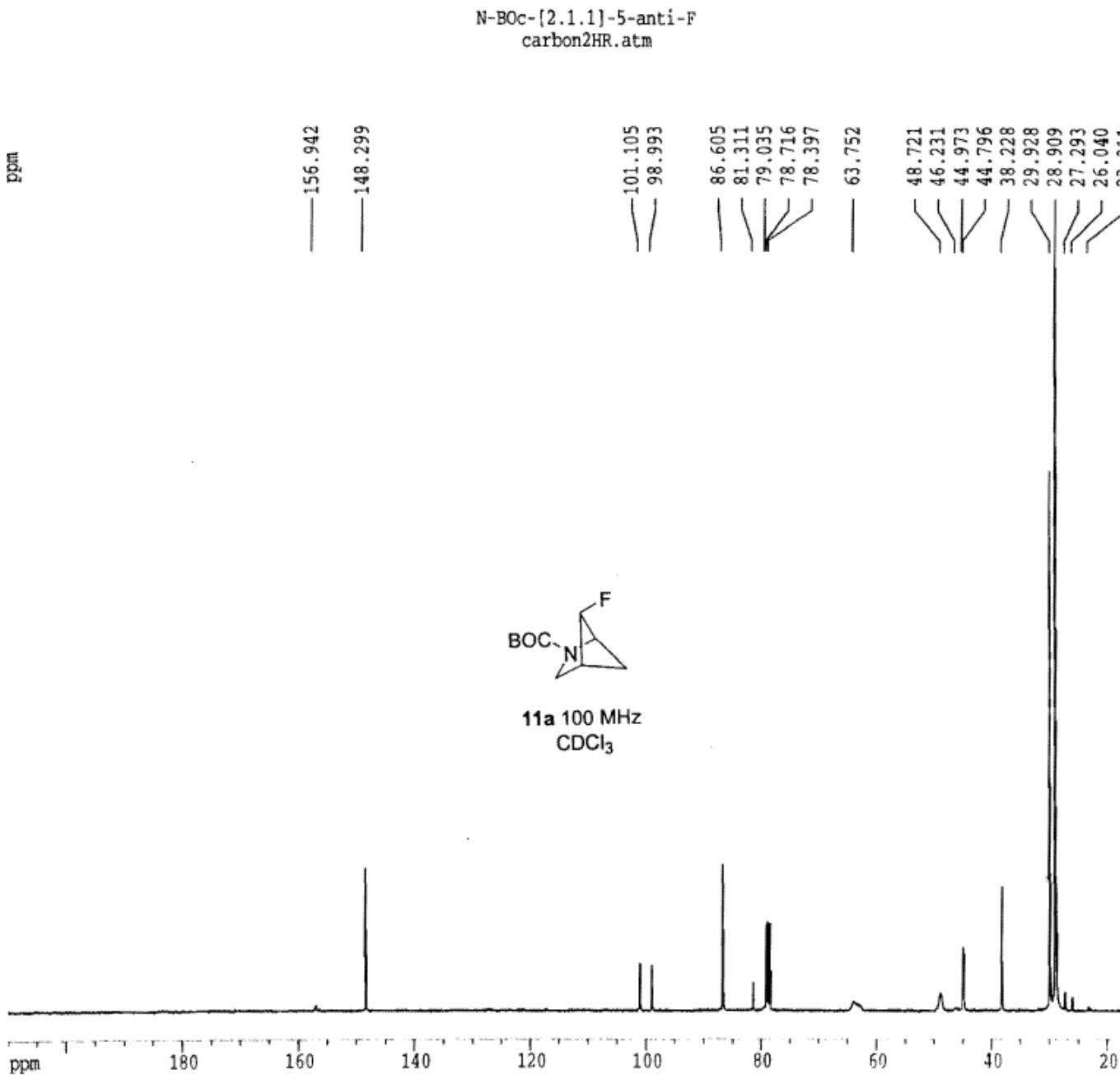


11a 300 MHz
CDCl₃



Conformationally Constrained 5-Fluoro- and 5-Hydroxymethanopyrrolidines

S-13



Current Data Parameters
 NAME deepa03
 EXPNO 40
 PROCHNO 1

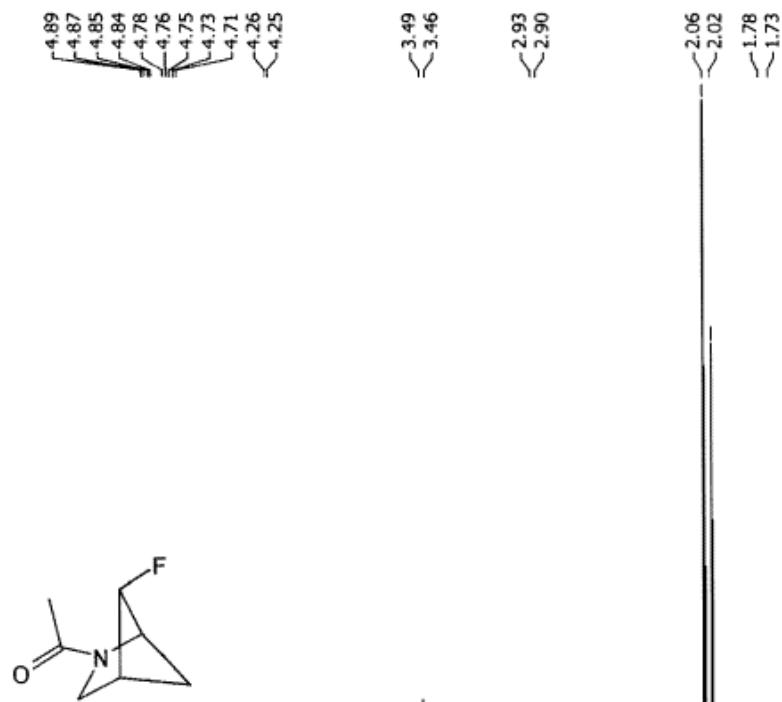
 F2 - Acquisition Parameters
 Date_ 20050110
 Time 10.40
 INSTRUM spect
 PROBHD 5 mm PABBO BB-
 PULPROG zgpp60
 TD 65536
 SOLVENT CDCl3
 NS 1042
 DS 2
 SWH 25125.629 Hz
 FIDRES 0.383387 Hz
 AQ 1.3042164 sec
 RG 18390.4
 DW 19.900 use
 DE 6.00 use
 TE 300.0 K
 D1 2.00000000 sec
 d11 0.03000000 sec
 d12 0.00002000 sec

===== CHANNEL f1 ======
 NUC1 13C
 P1 5.70 use
 PL1 2.00 dB
 SFO1 100.5951275 MHz

===== CHANNEL f2 ======
 CPDPRG2 waltz16
 NUC2 1H
 PCPD2 92.00 use
 PL2 0.00 dB
 PL12 11.00 dB
 PL13 120.00 dB
 SFO2 400.0216001 MHz

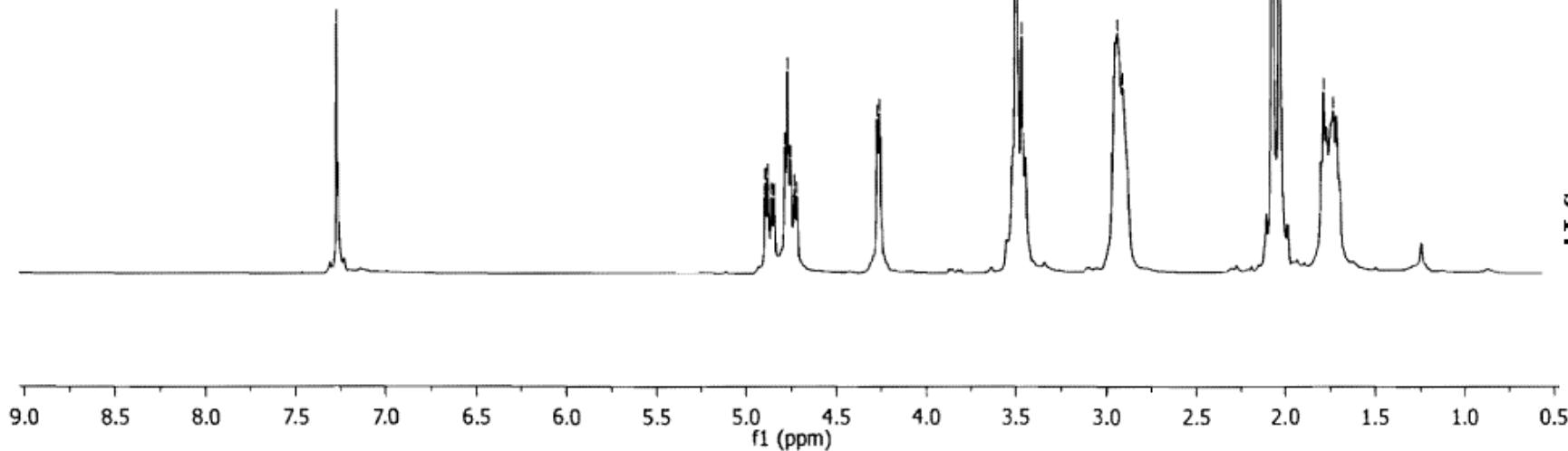
F2 - Processing parameters
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 SF 100.5349428 MHz
 DW EM
 SSB 0
 LB 3.00 Hz
 GB 0
 PC 1.40

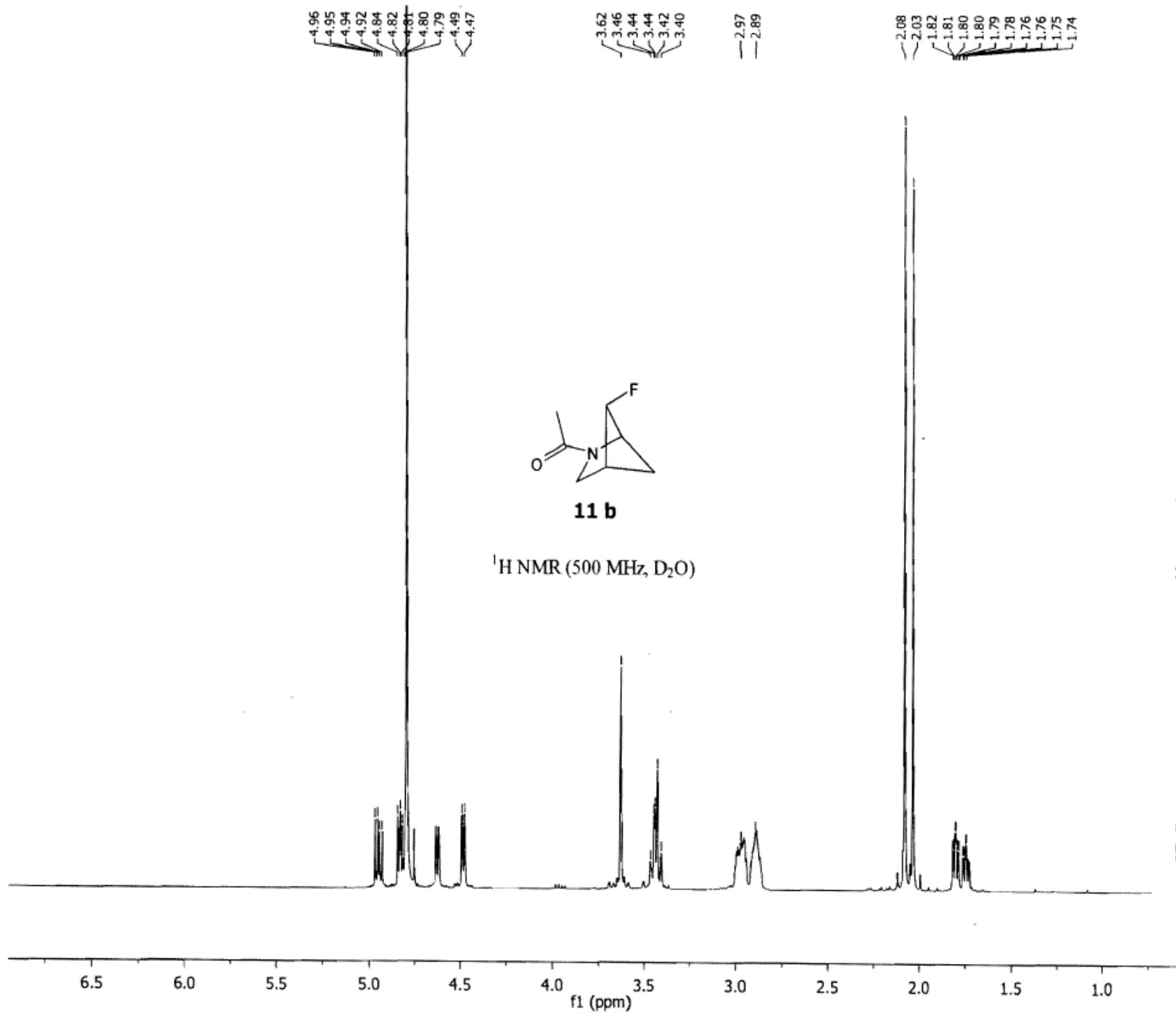
1D NMR plot parameters
 CX 22.00 cm
 F1P 210.000 ppm
 F1 21122.84 Hz
 F2P -10.000 ppm
 F2 -1005.85 Hz
 PPNCM 10.00000 ppm/cm
 HZCM 1005.84949 Hz/cm

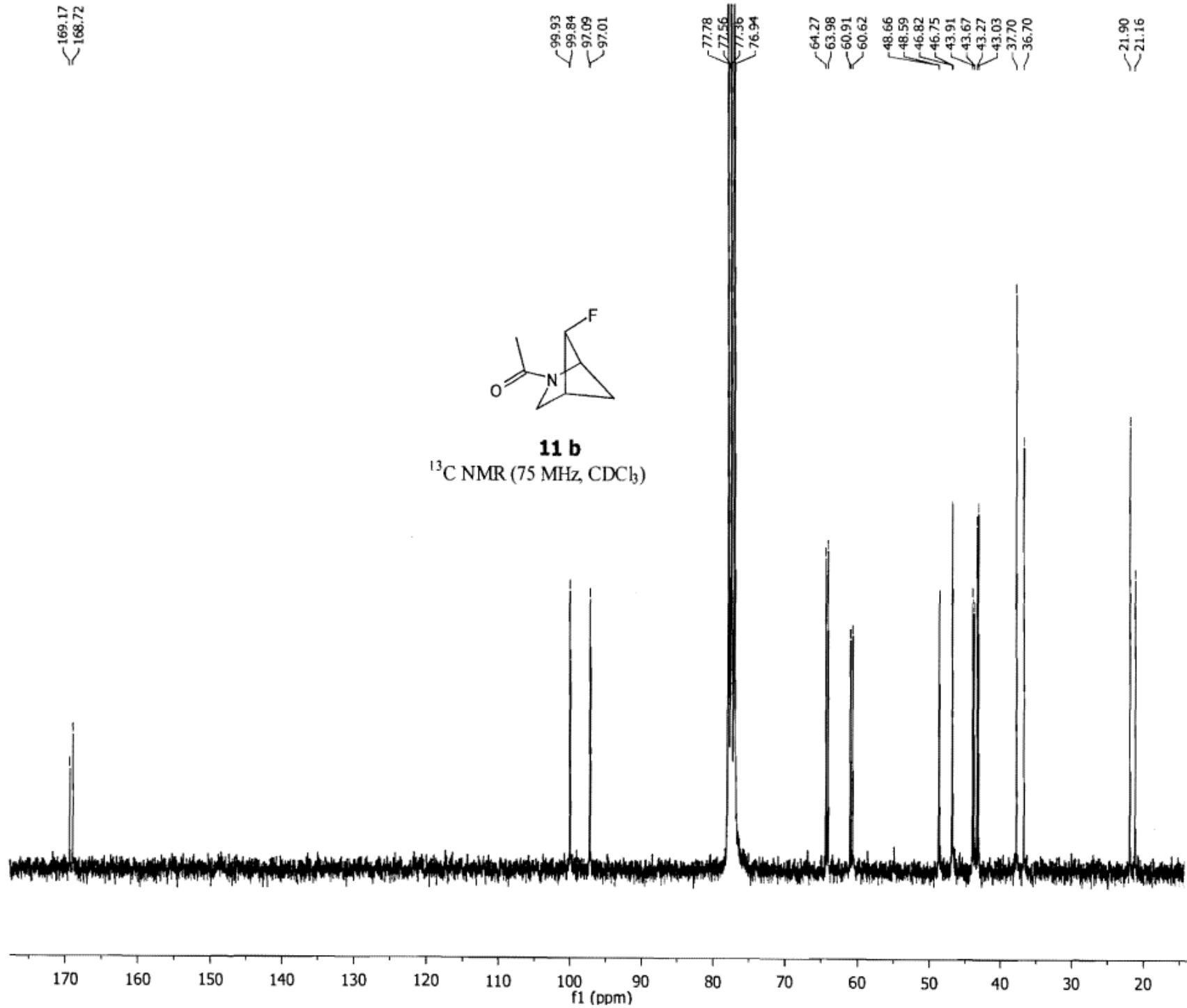


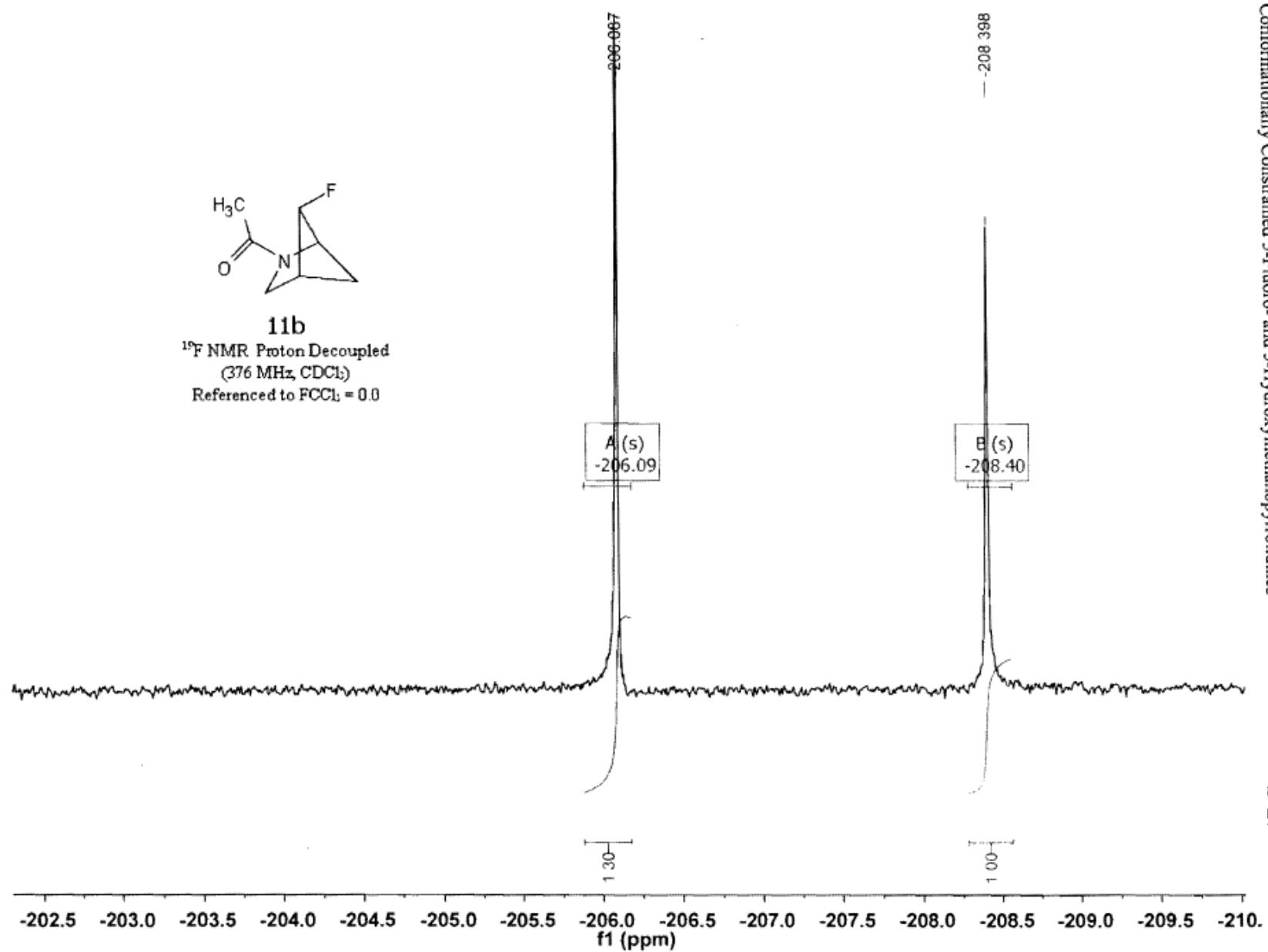
11 b

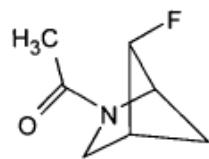
^1H NMR (500 MHz, CDCl_3)





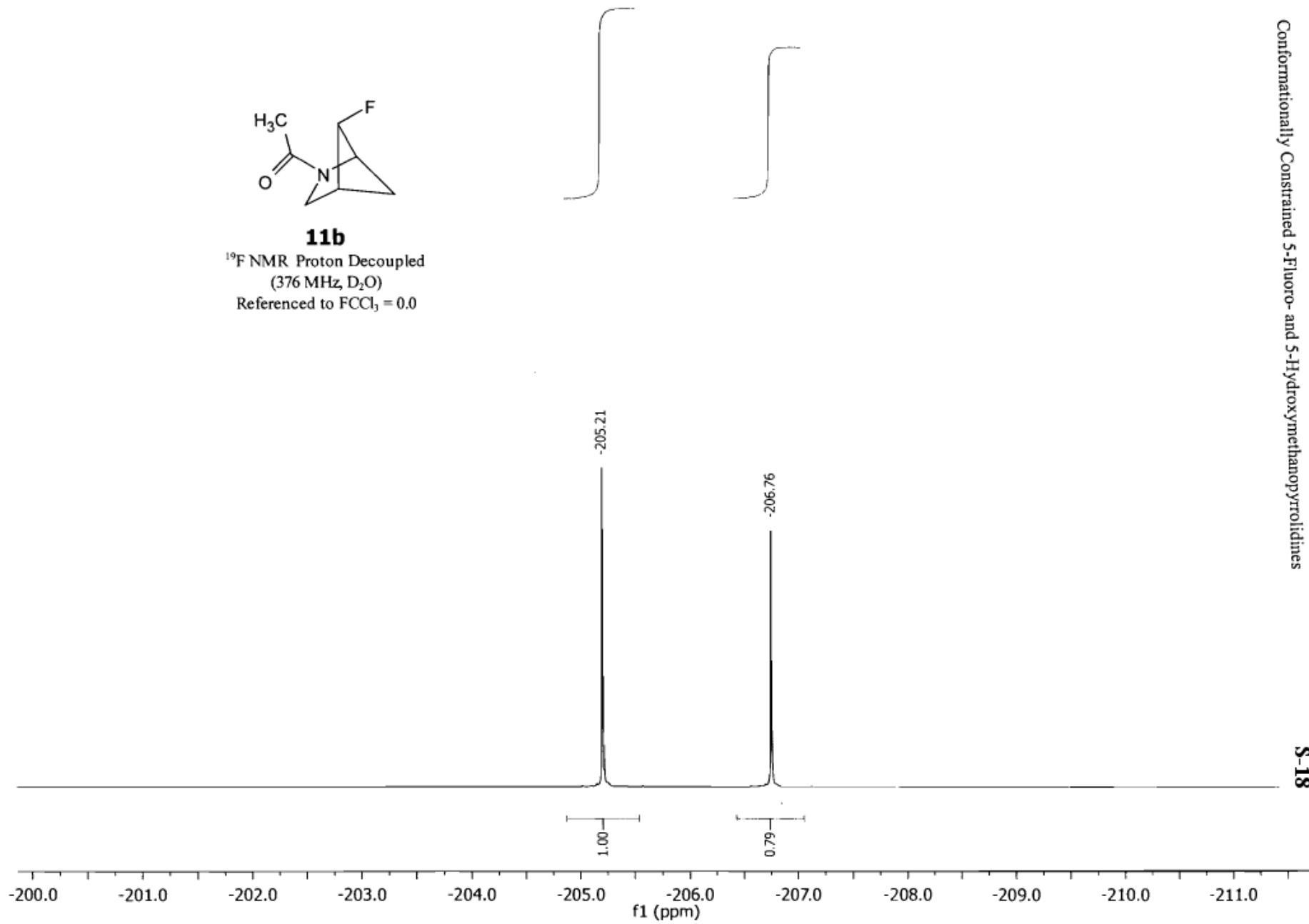






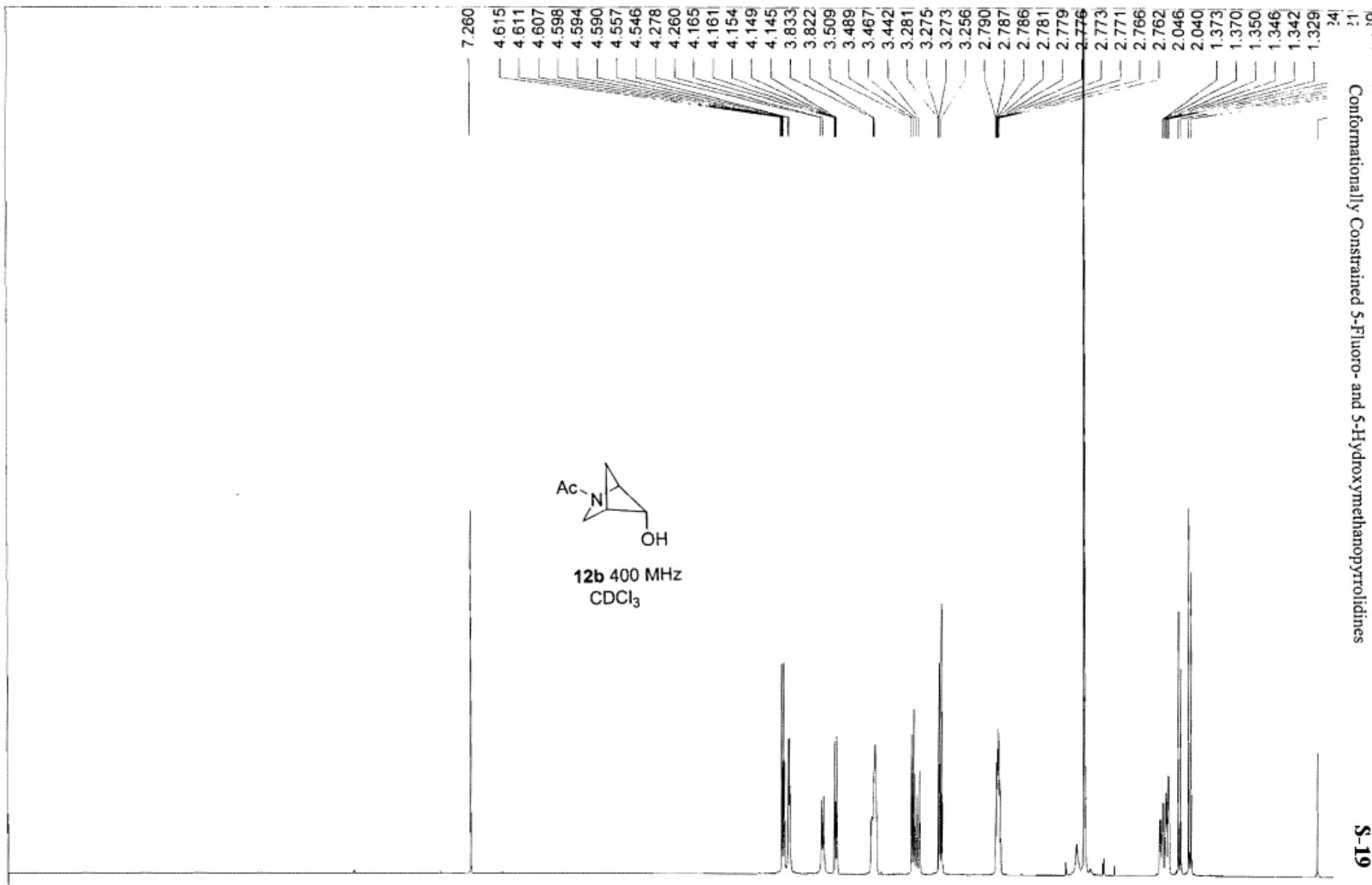
11b

^{19}F NMR Proton Decoupled
(376 MHz, D_2O)
Referenced to $\text{FCCl}_3 = 0.0$



Conformationally Constrained 5-Fluoro- and 5-Hydroxymethanopyrrolidines

S-19

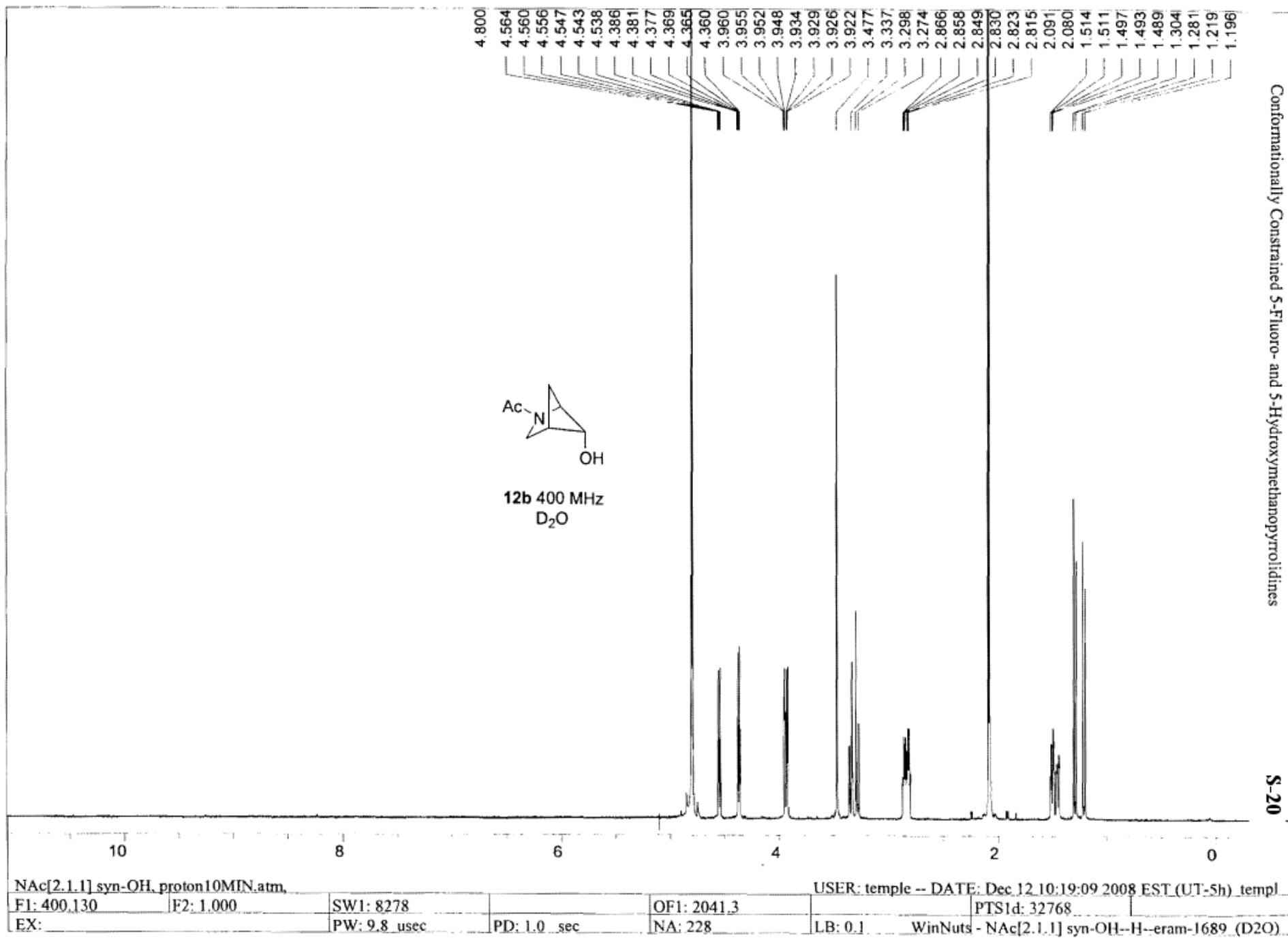


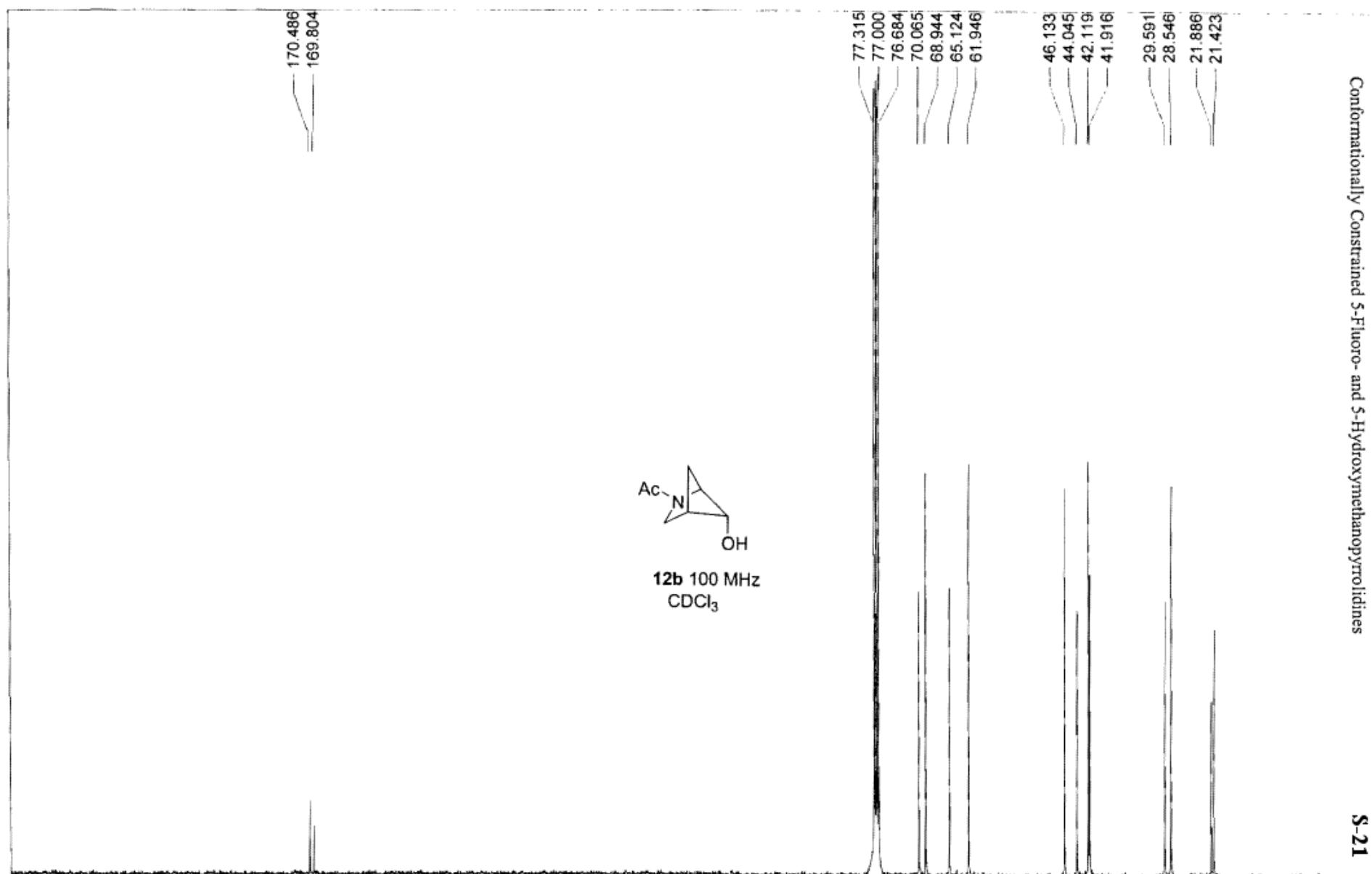
NAc[2.1.1]syn-OH, proton10MIN,atm,

F1: 400.130	F2: 1.000	SW1: 8278		OF1: 2004.2		PTS1d: 32768
EX:		PW: 9.8 usec		PD: 1.0 sec	NA: 128	LB: 0.1

USER: temple -- DATE: Nov 22 23:08:55 2008 EST (UT-5h) templ

WinNuts - NAc[2.1.1] syn-OH--H--eram-168J

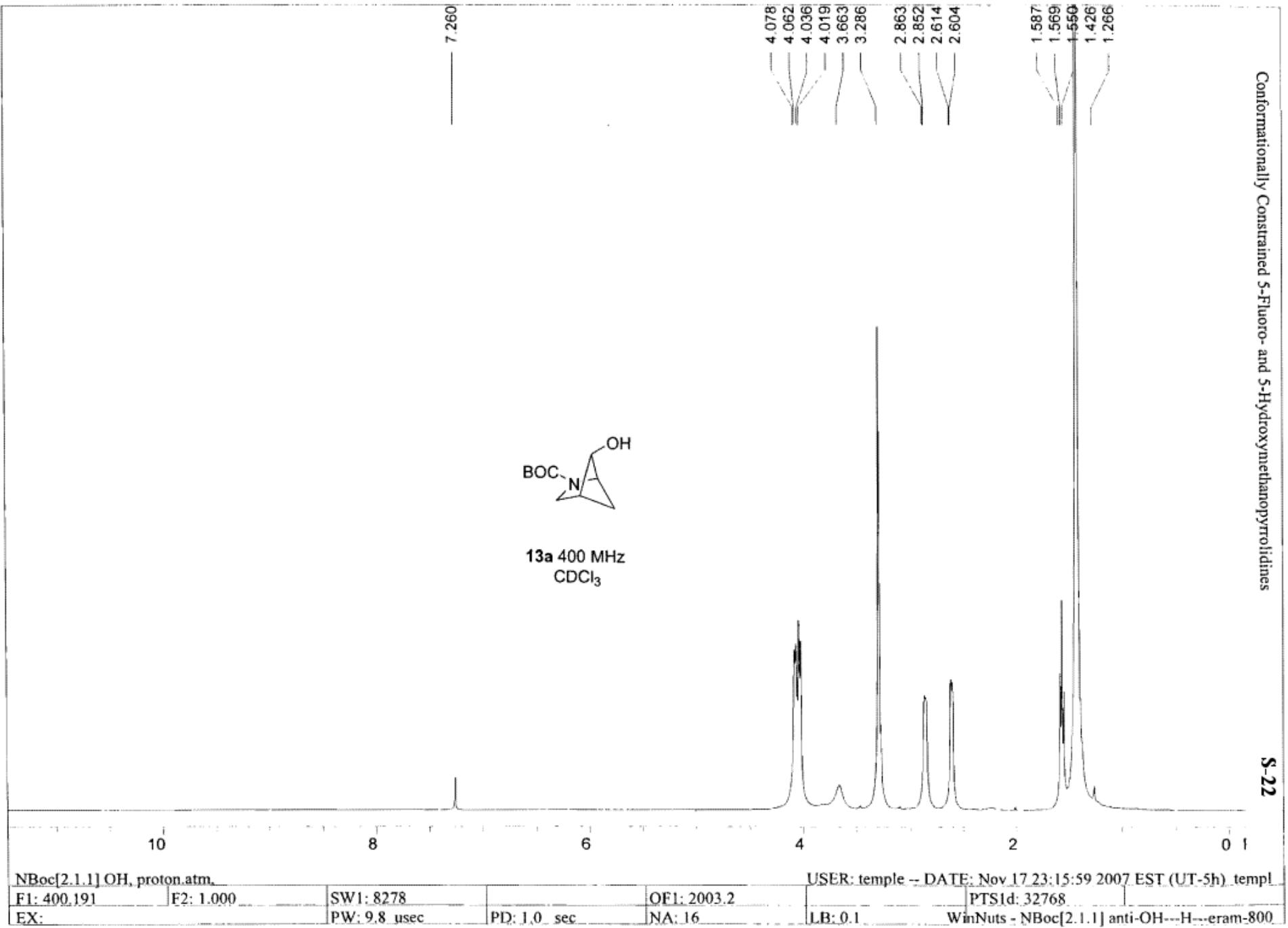




NAc[2.1.1] syn-OH, carbonOVNTE,all,

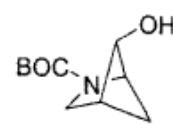
F1: 100.613	F2: 1.000	SW1: 25126	OF1: 10021.1	PTS1d: 32768
EX:		PW: 5.7 usec	PD: 2.0 sec	NA: 11000 LB: 3.0 WinNuts - NAc[2.1.1] syn-OH--C--eram-1682

USER: temple -- DATE: Nov 23 09:18:27 2008 EST (UT-5h) templ

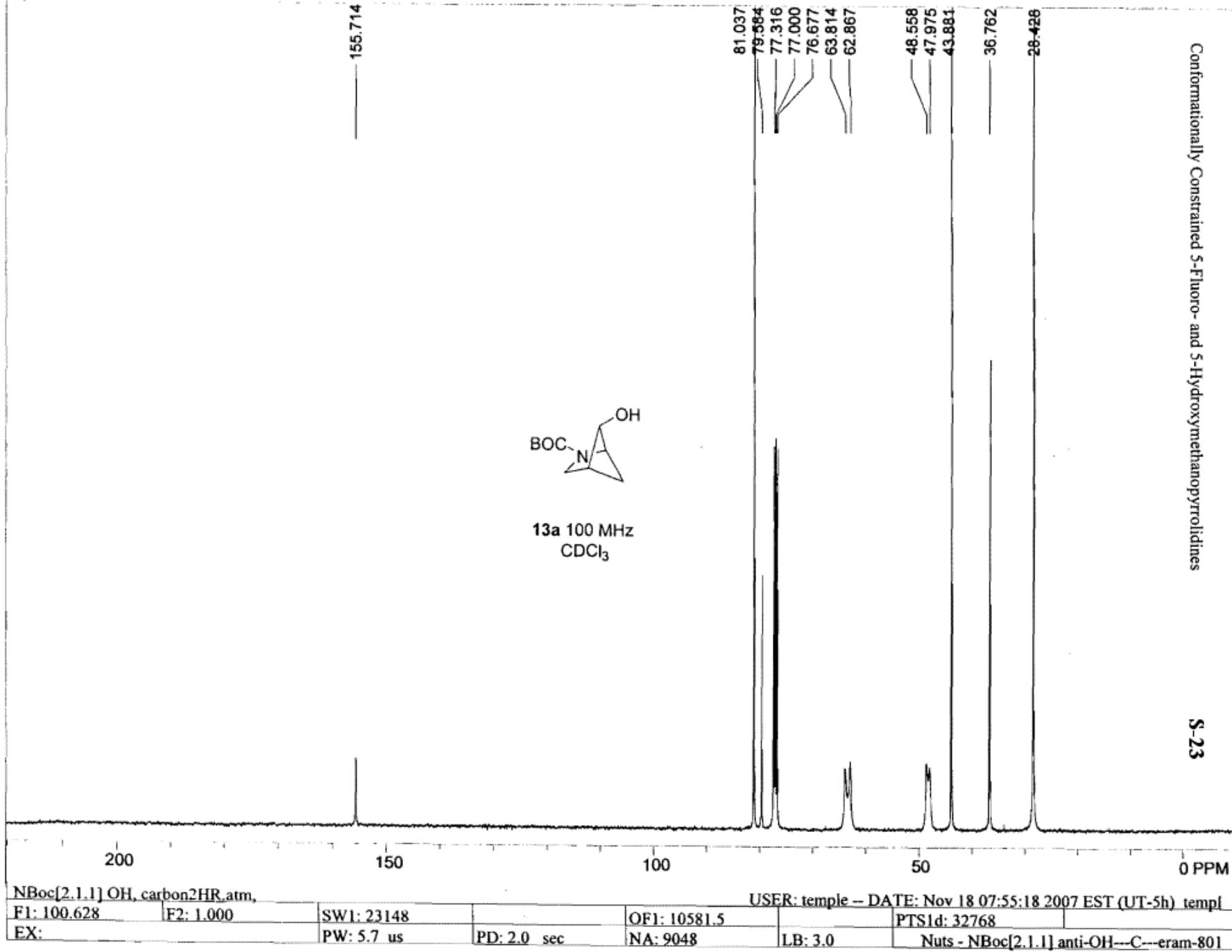


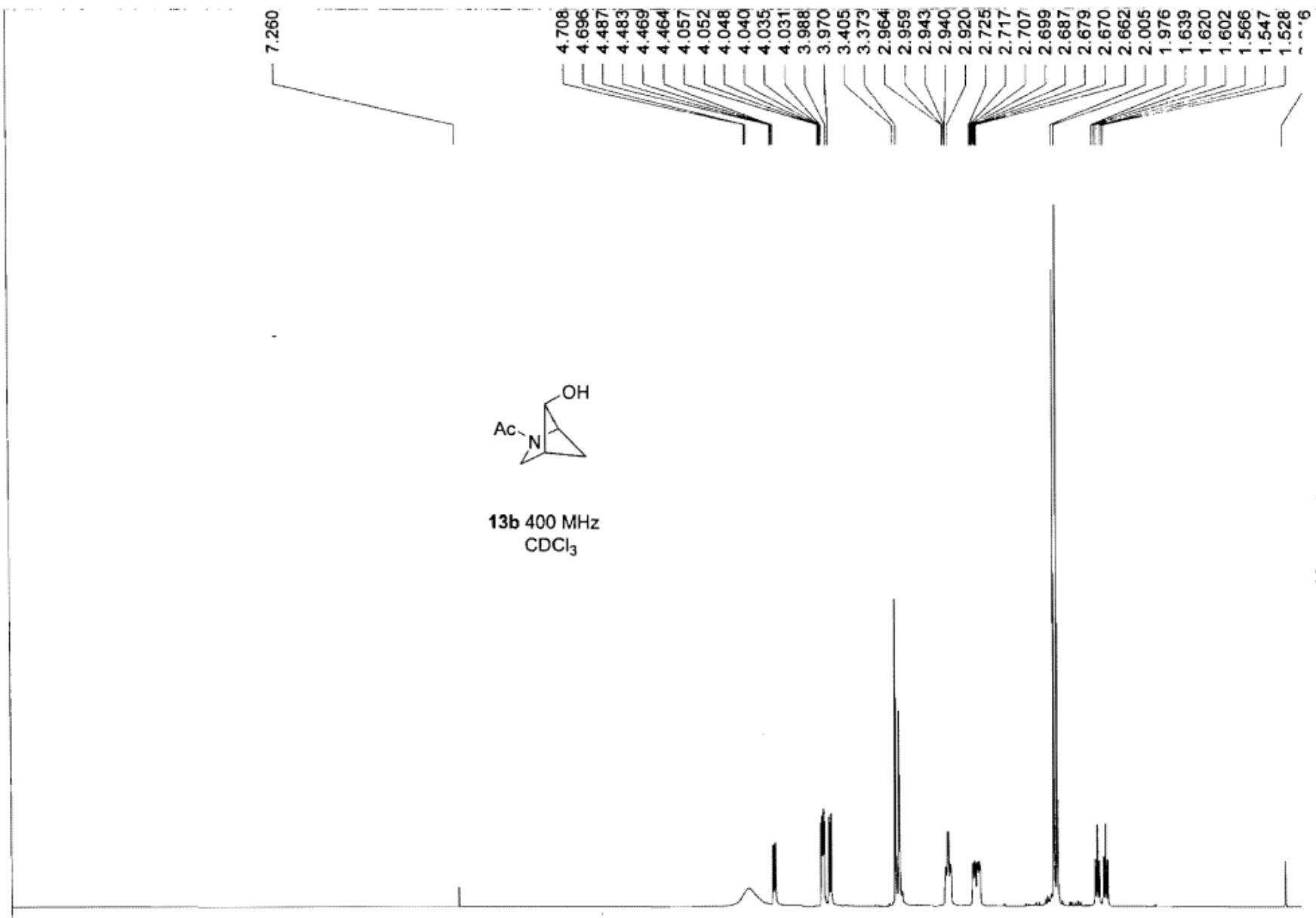
Conformationally Constrained 5-Fluoro- and 5-Hydroxymethanopyrrolidines

S-23



13a 100 MHz
 CDCl_3





NAc[2.1.1]OH, proton.atm,

F1: 400,130 F2: 1,000

11.

EX-

SW1: 8278

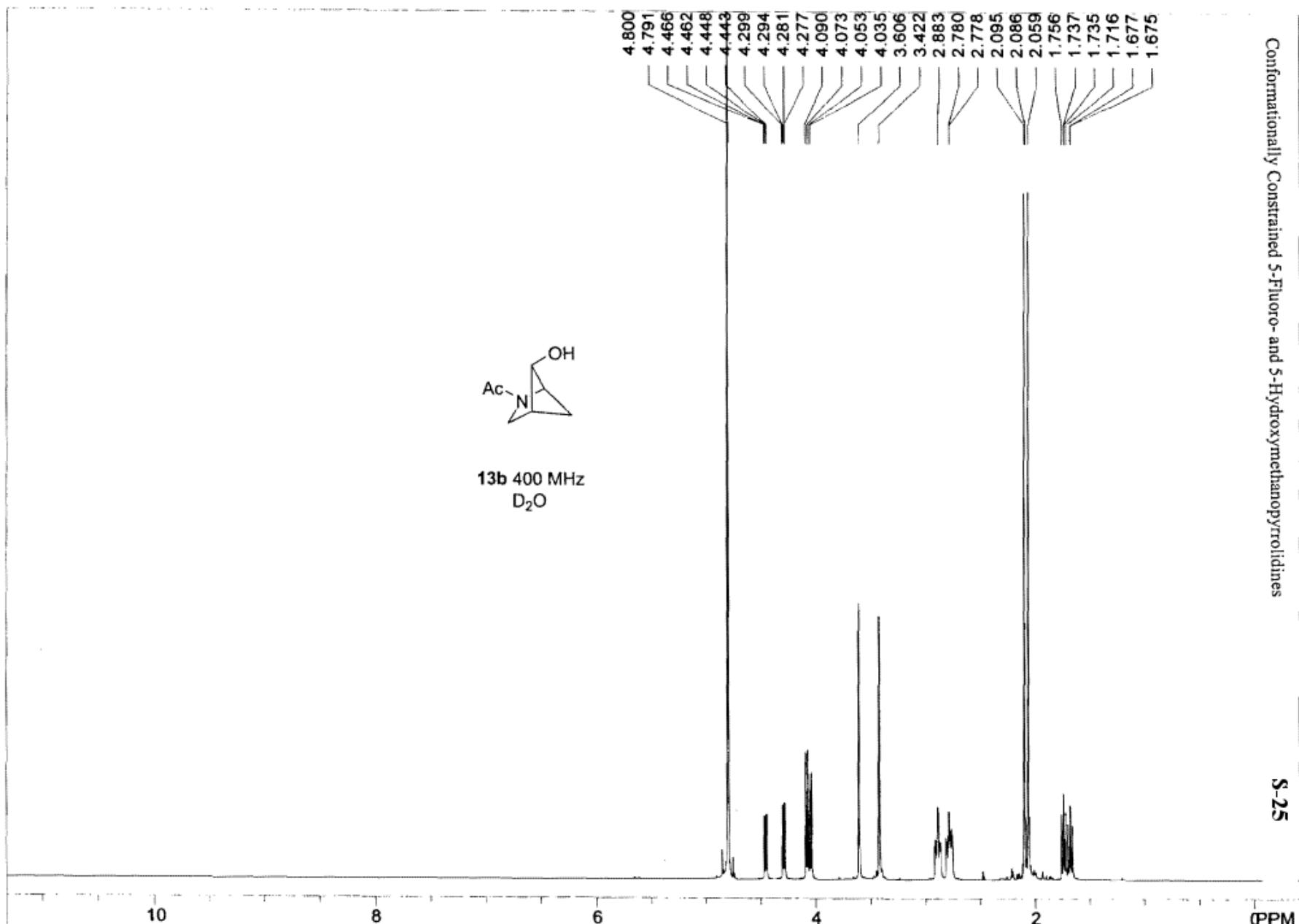
PW-9.8 us

OF1: 2004.2

NA-16

PTS1d: 32768

Nuts = NAc[2.1.1]



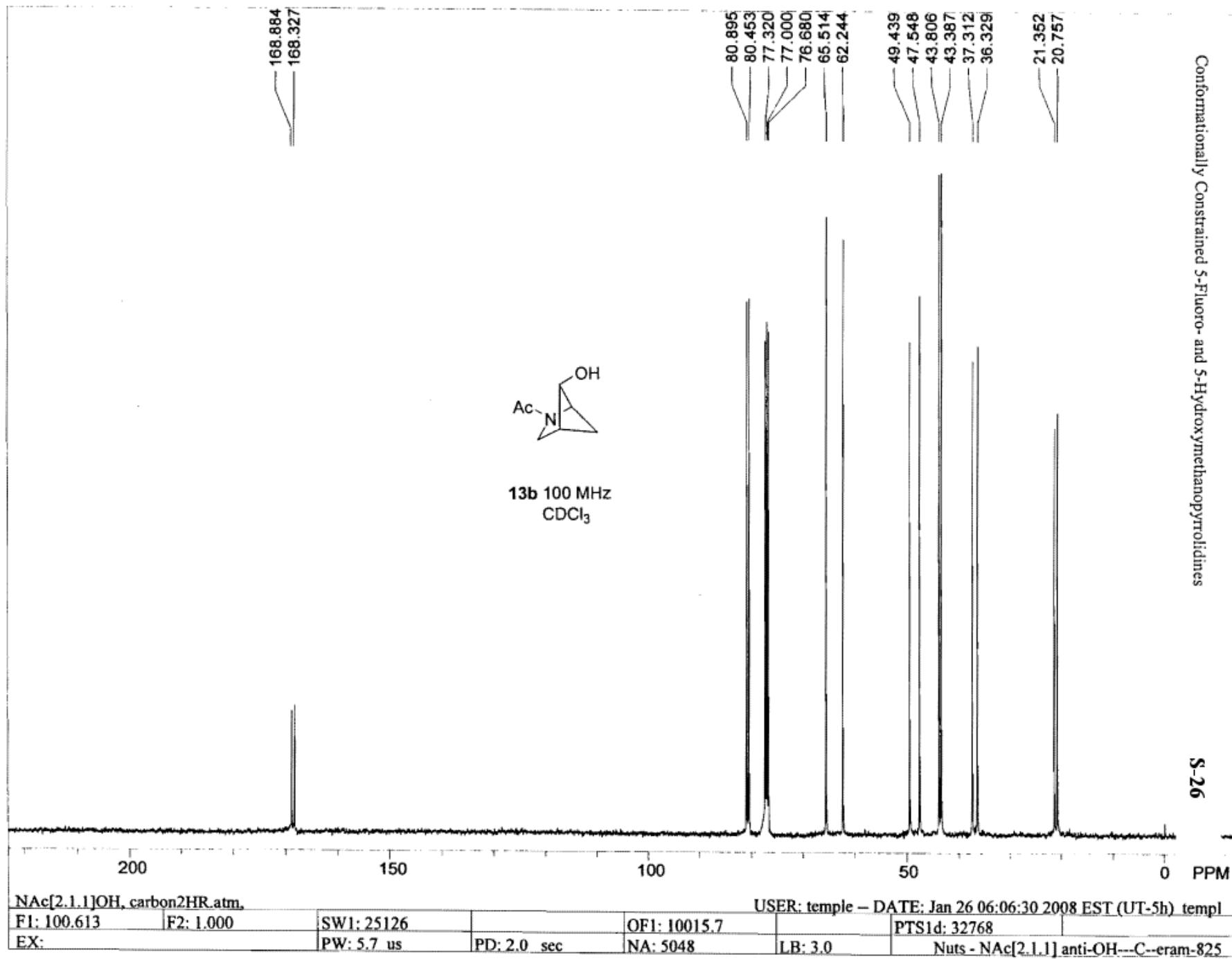
NAC[2.1.1] anti-OH, proton 10MIN.atm.

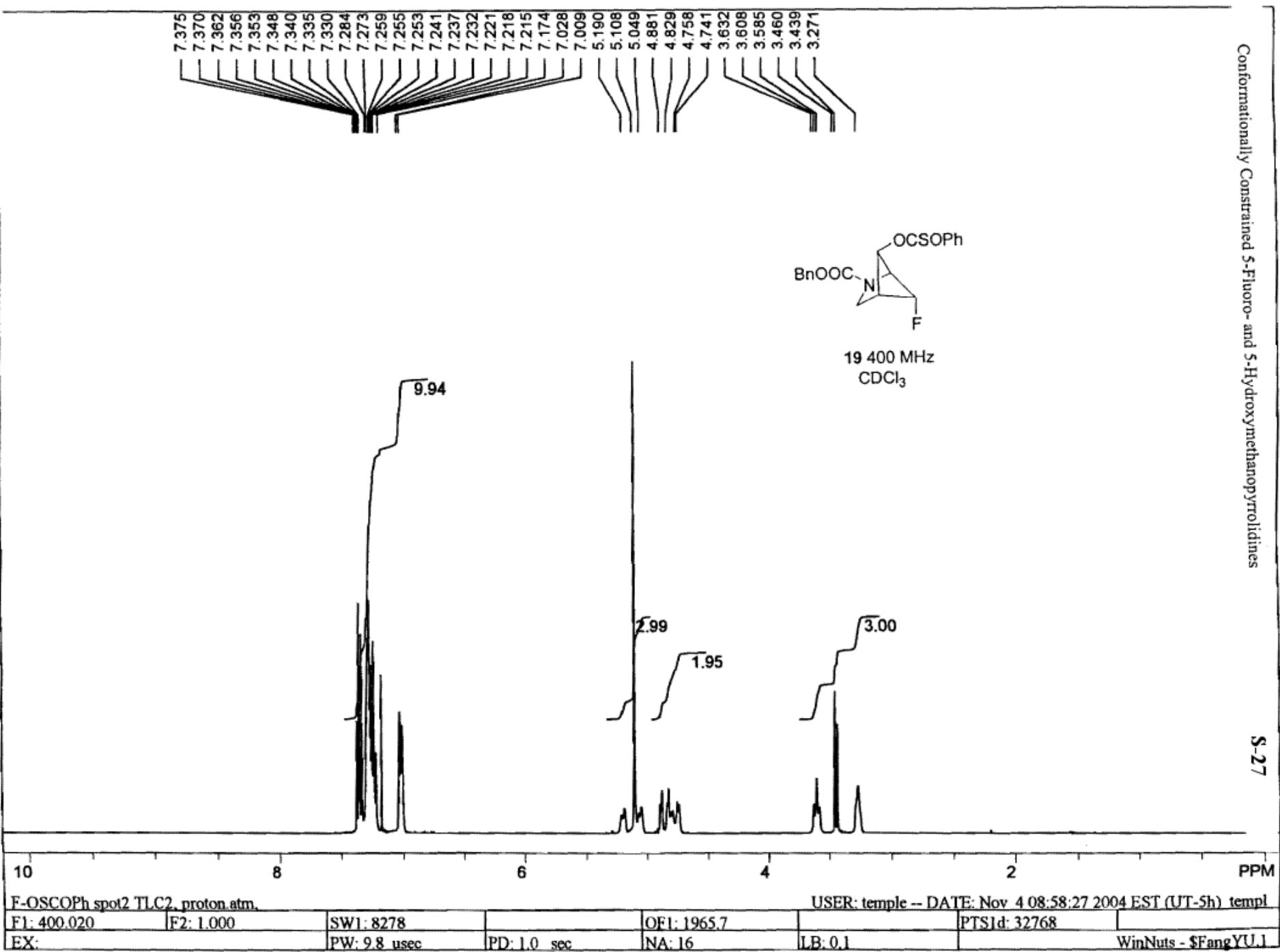
F1: 400.130	F2: 1.000	SW1: 8278		OF1: 2040.5		PTS1d: 32768
EX:		PW: 9.8 us	PD: 1.0 sec	NA: 228	LB: 0.1	Nuts - NAC[2.1.1] anti-OH---H-D2O--eram-1400

USER: temple -- DATE: Jul 16 16:00:11 2008 EDT (UT-4h) templ

Conformationally Constrained 5-Fluoro- and 5-Hydroxymethanopyrrolidines

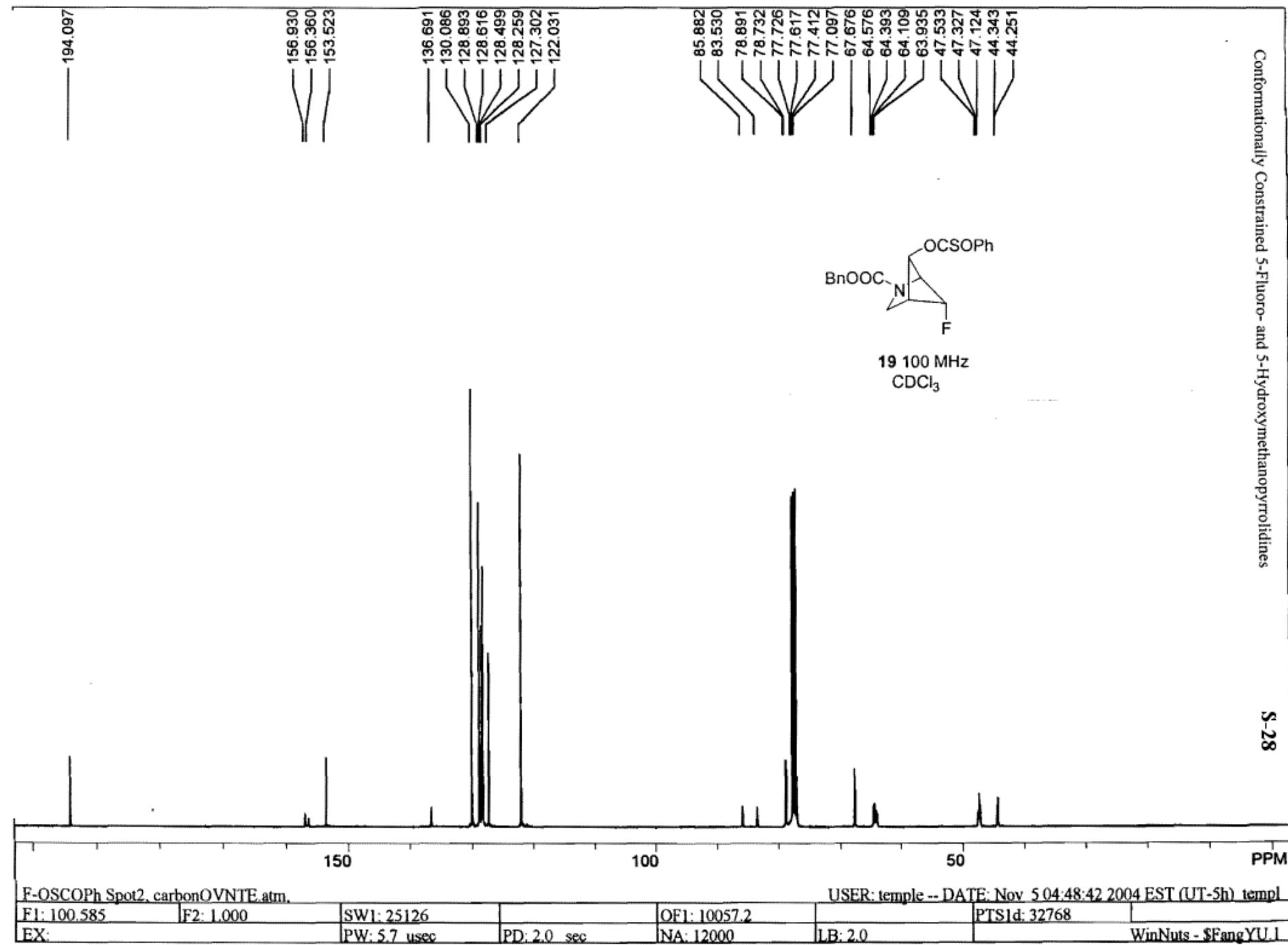
S-26





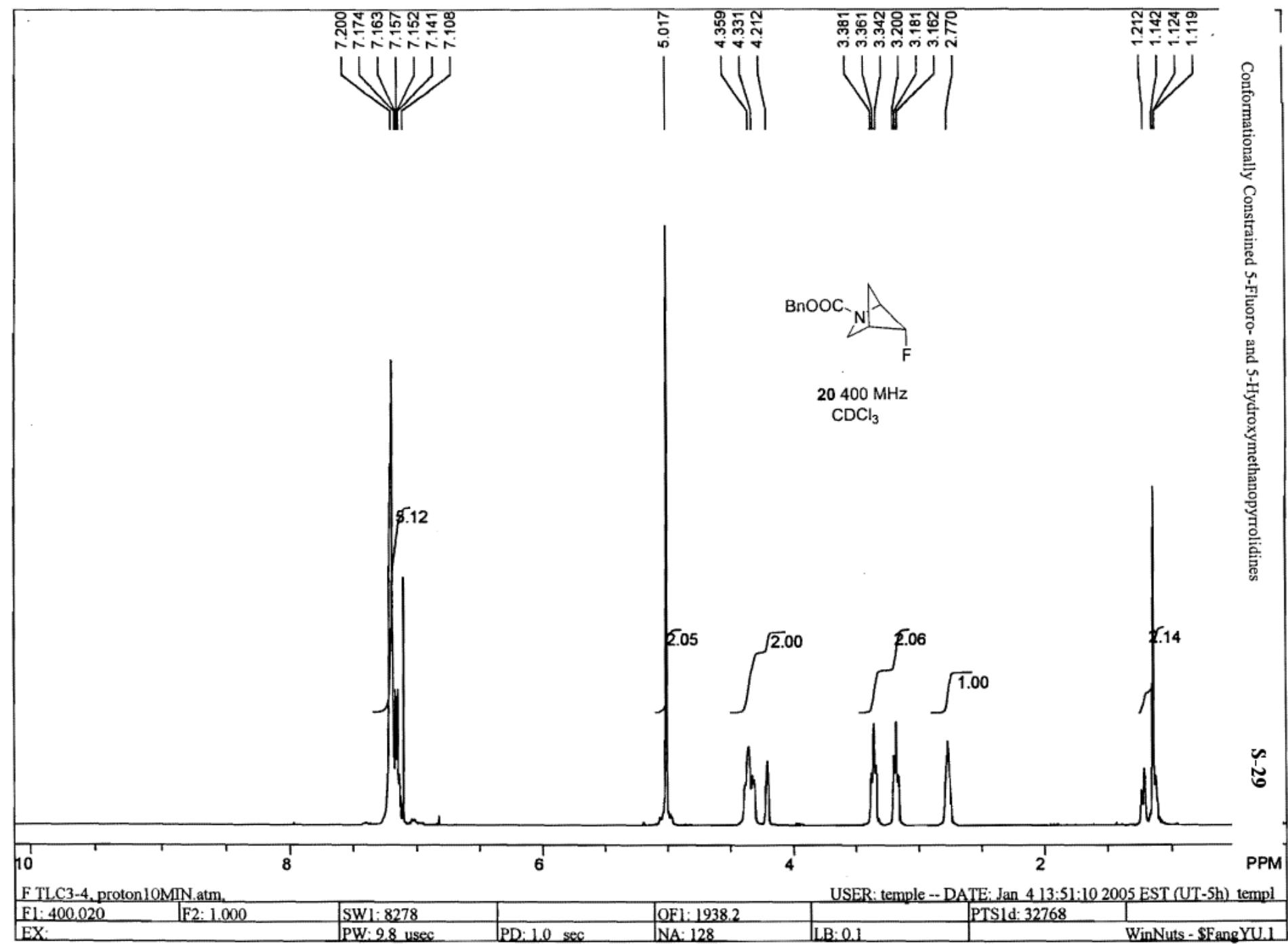
Conformationally Constrained 5-Fluoro- and 5-Hydroxymethanopyrrolidines

S-28



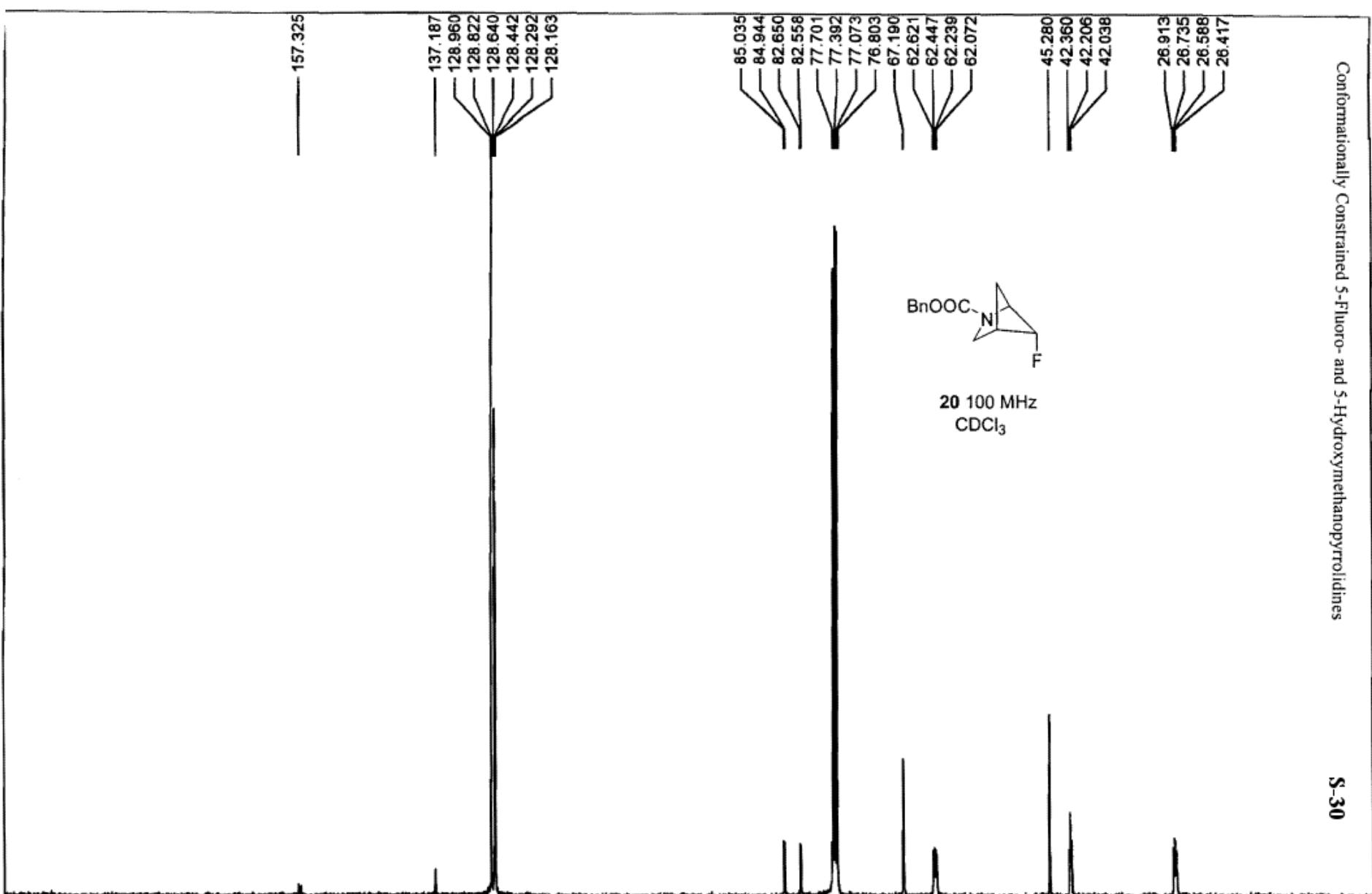
Conformationally Constrained 5-Fluoro- and 5-Hydroxymethanopyrrolidines

S-29



Conformationally Constrained 5-Fluoro- and 5-Hydroxymethanopyrrolidines

S-30



F TLC3-4, carbonOVNTE.atm.

F1: 100.585 F2: 1.000

SW1: 25126

OF1: 10057.2

PTS1d: 32768

EX:

PW: 5.7 usec

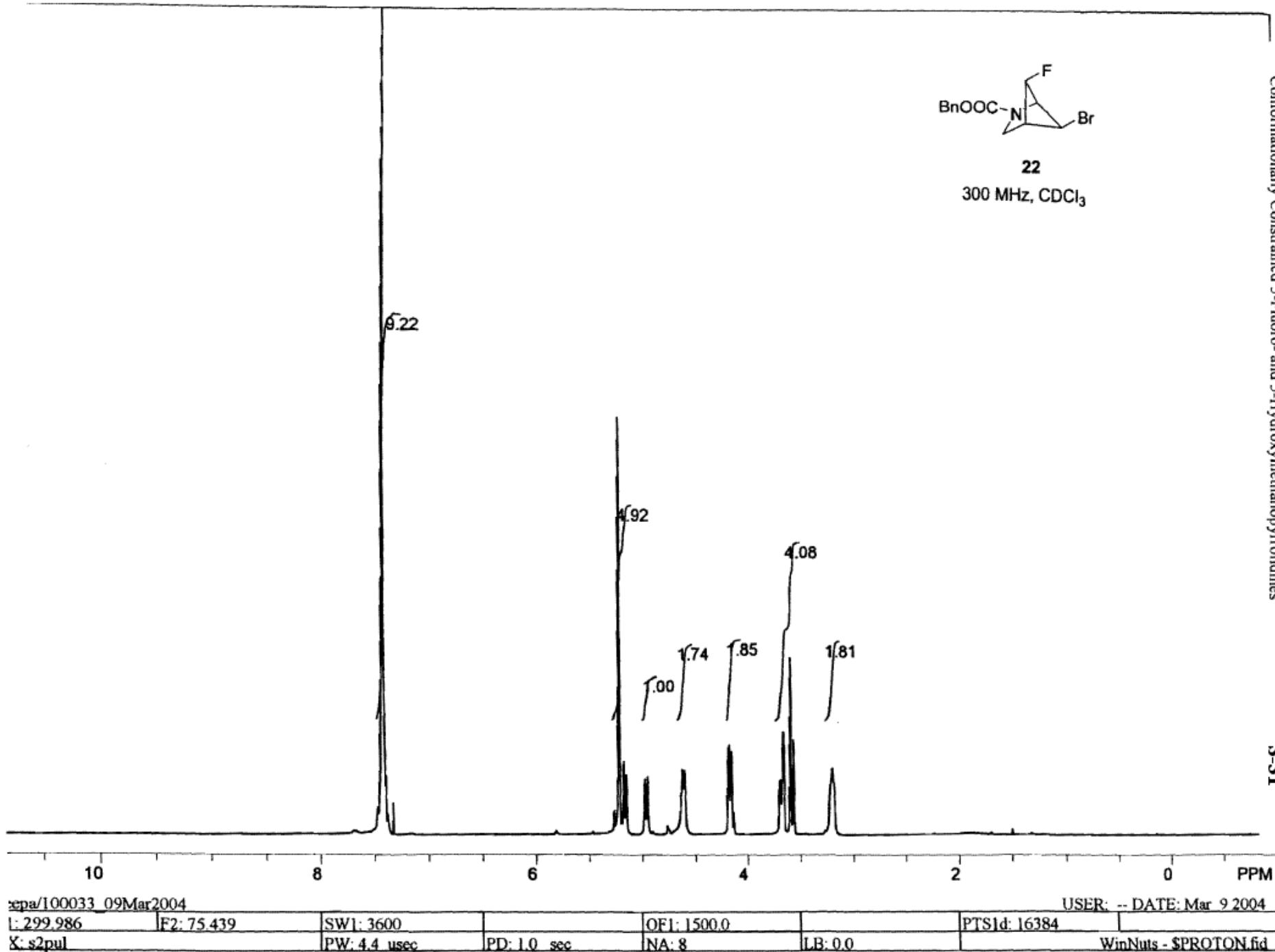
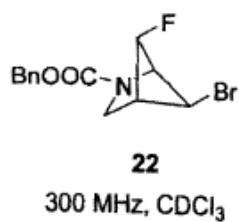
PD: 2.0 sec

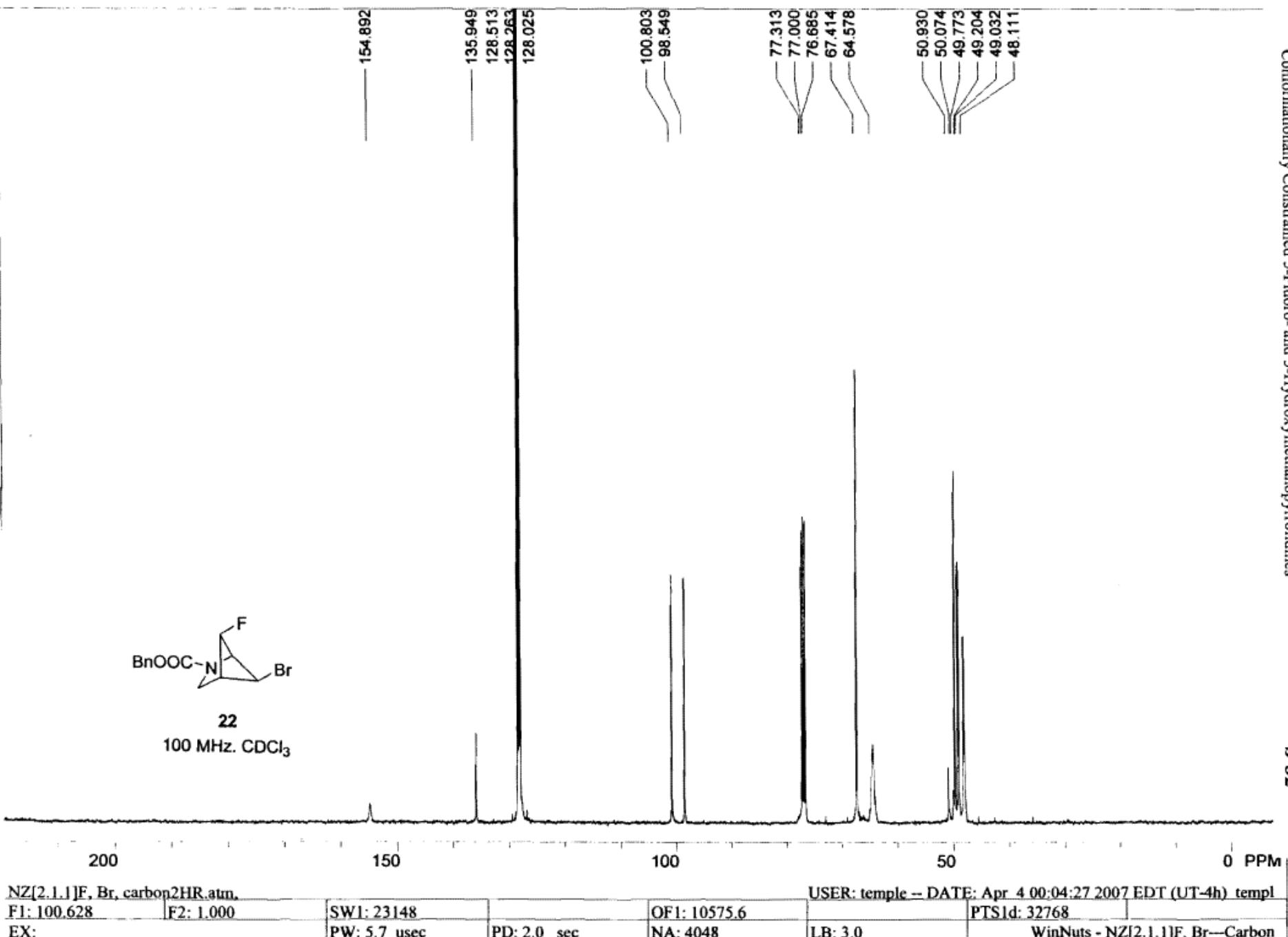
NA: 12000

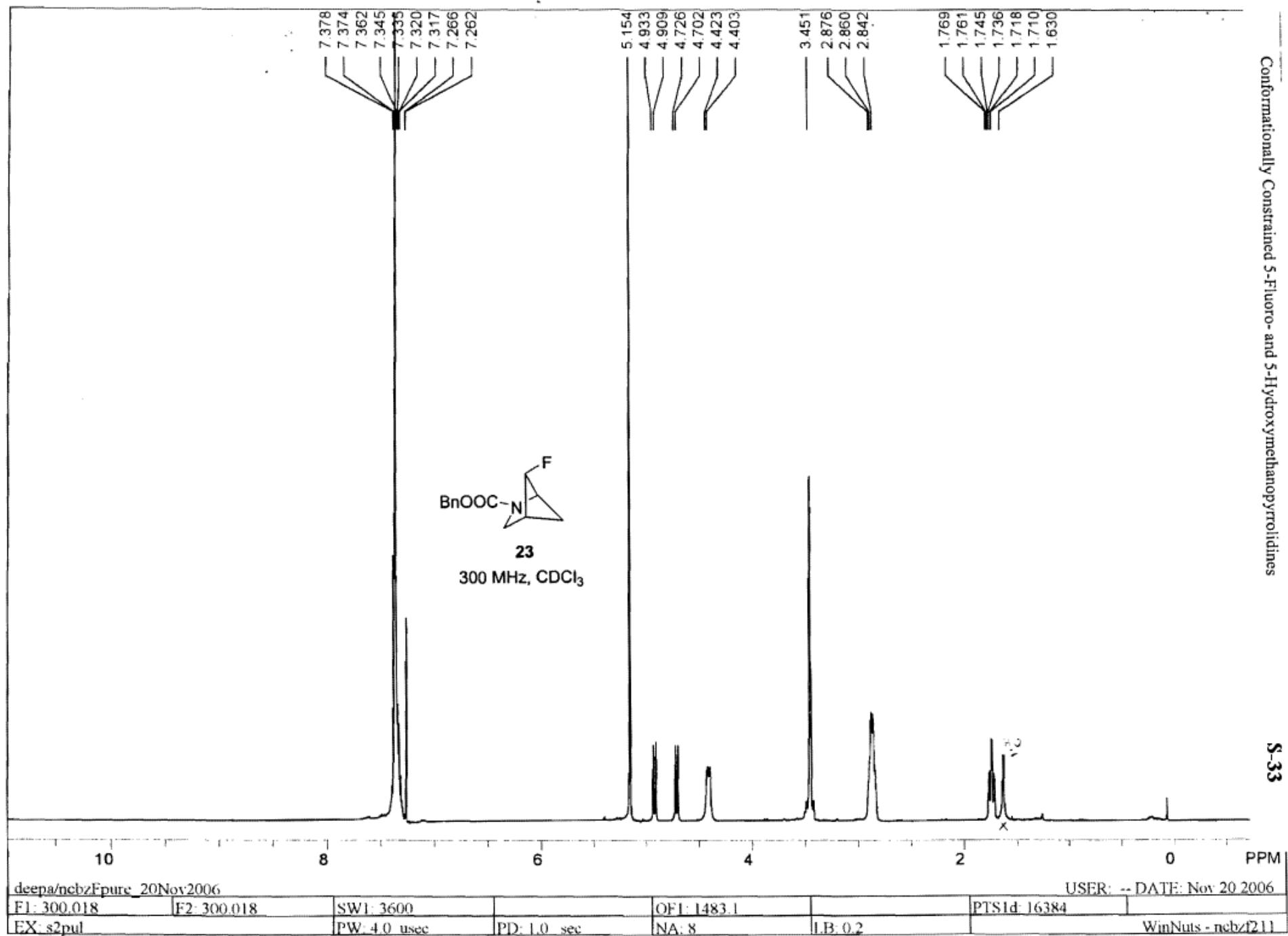
LB: 2.0

WinNuts - \$FangYU.J

USER: temple -- DATE: Jan 4 05:25:45 2005 EST (UT-5h) temple

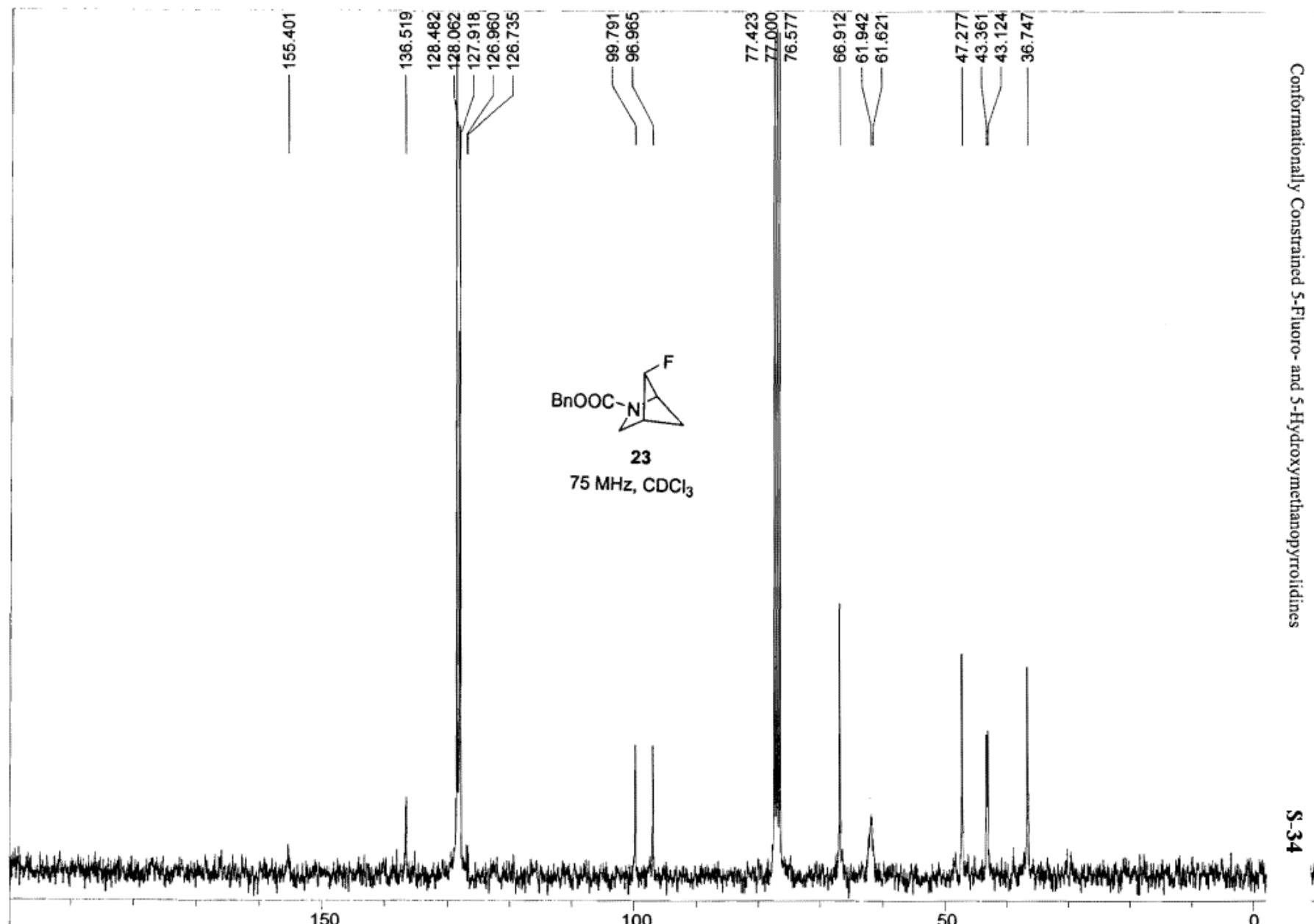






Conformationally Constrained 5-Fluoro- and 5-Hydroxymethanopyrrolidines

S-34



N-Benzylxy-2-azabicyclo-5-anti-fluoro-[2.1.1]-hexane

F1: 75.438

F2: 299.986

SW1: 15842

OF1: 7144.1

USER: -- DATE: Nov 20 2003

EX: s2pul

PW: 3.9 us

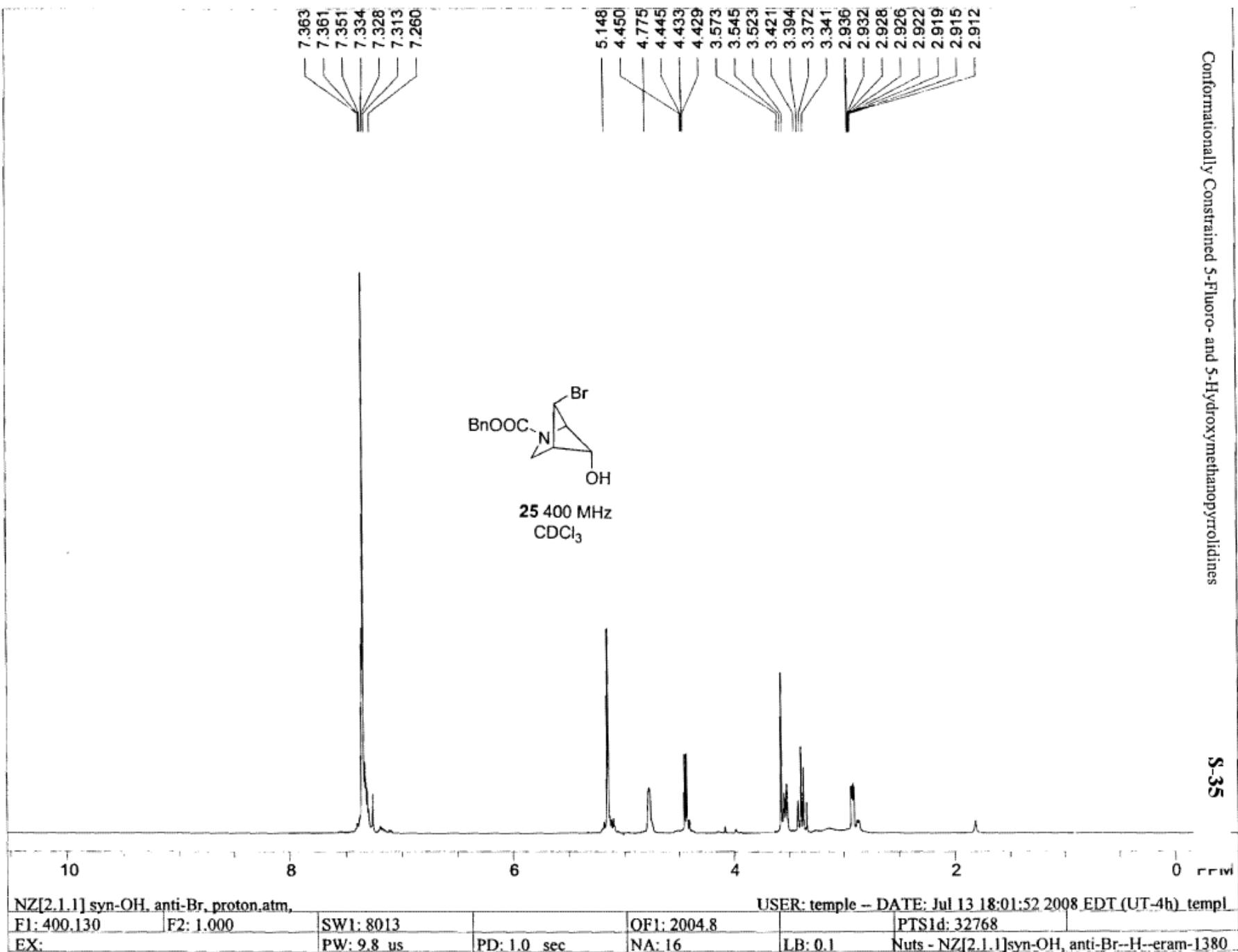
PD: 1.0 sec

NA: 896

LB: 3.6

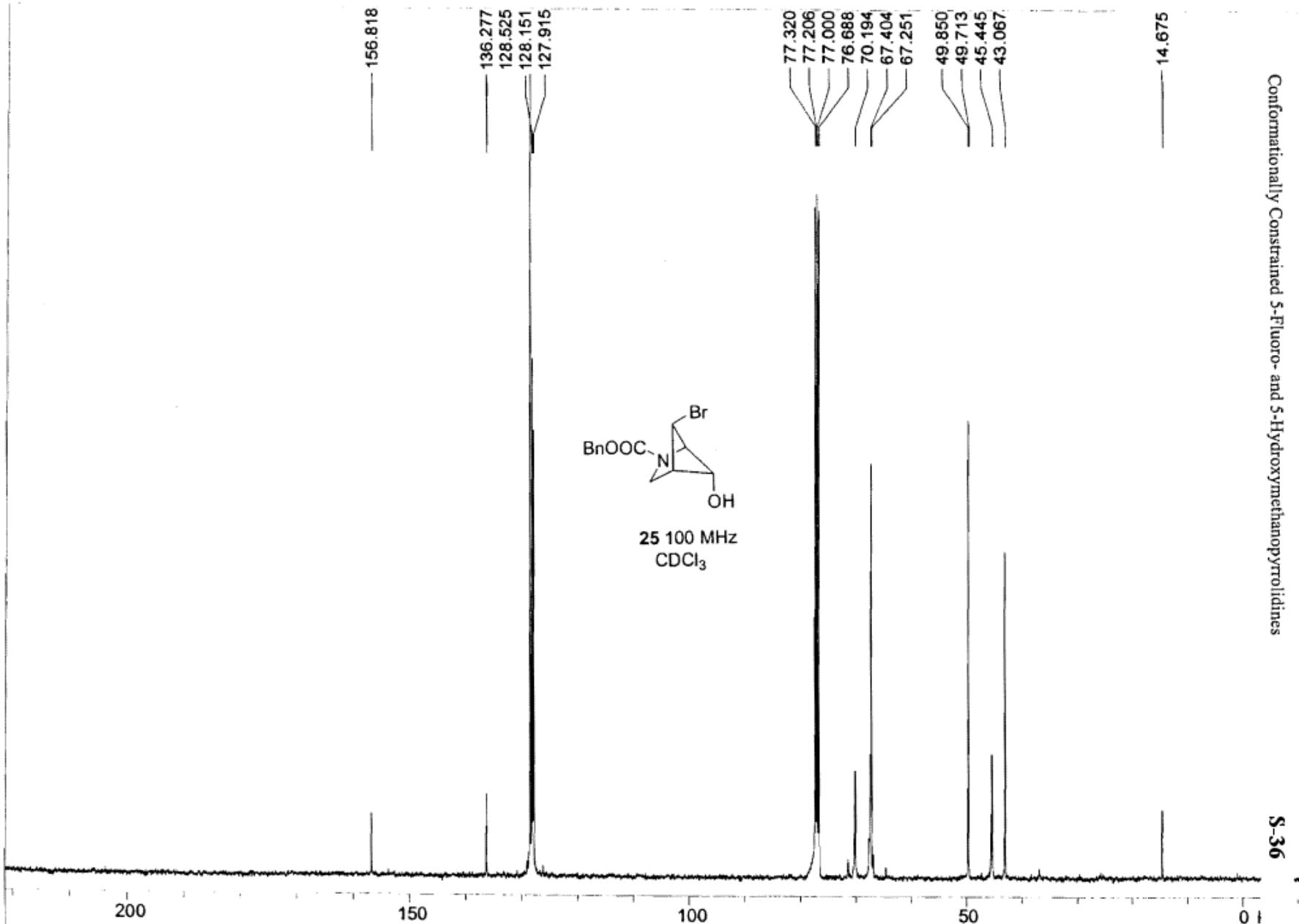
PTS1d: 28754 , 65536

Nuts - nutsproc



Conformationally Constrained 5-Fluoro- and 5-Hydroxymethanopyrrolidines

S-36



NZ[2.1.1]syn-OH, anti-Br, carbonOVNTE, atm,

F1: 100.613

F2: 1.000

SW1: 25126

OF1: 10019.6

PTS1d: 32768

EX:

PW: 5.7 us

PD: 2.0 sec

NA: 8000

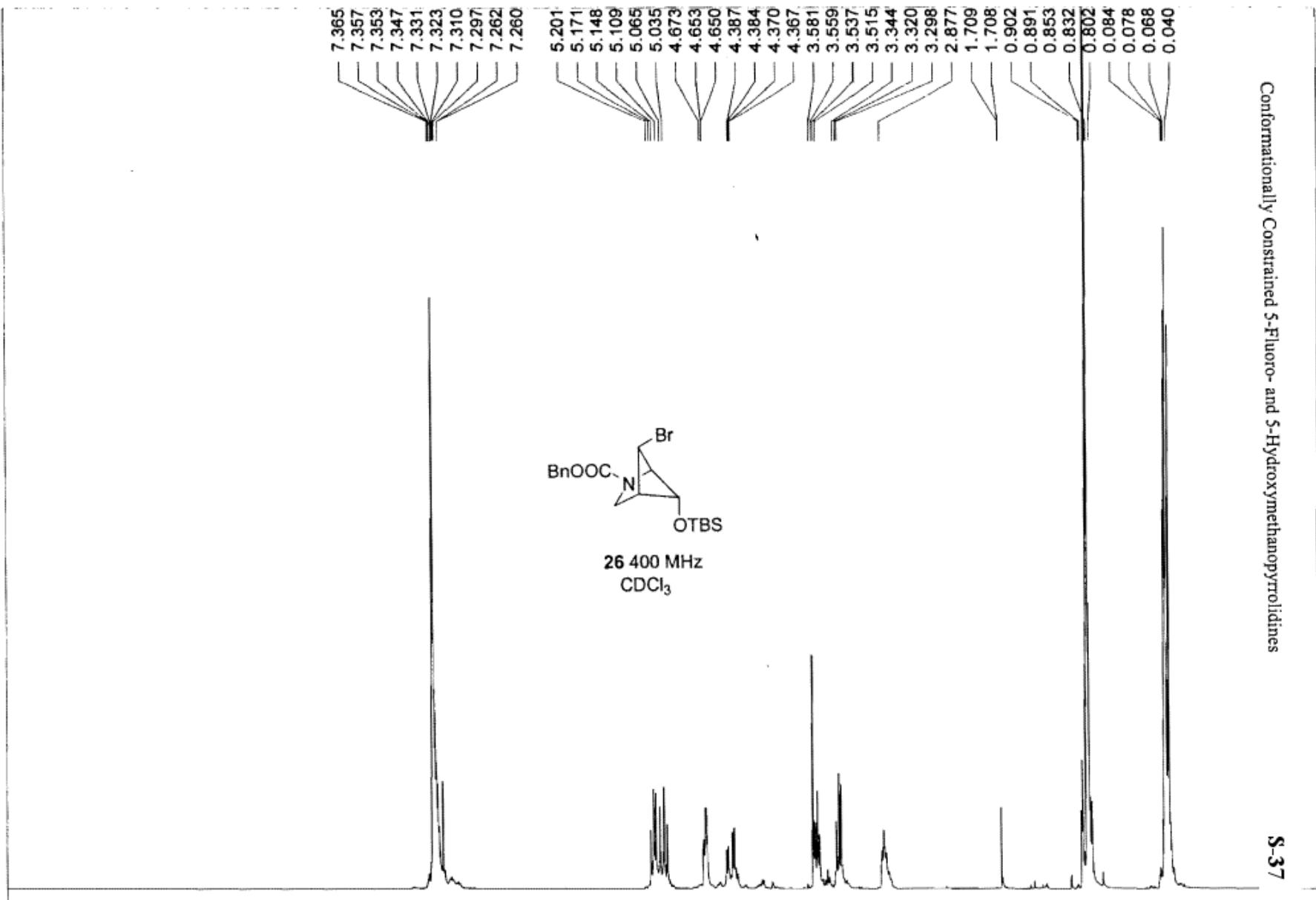
LB: 3.0

Nuts - NZ[2.1.1]syn-OH, anti-Br--C--eram-962

USER: temple -- DATE: Mar 4 06:42:08 2008 EST (UT-5h) templ

Conformationally Constrained 5-Fluoro- and 5-Hydroxymethanopyrrolidines

S-37



NZ[2.1.1]anti-Br, syn-OTBS, proton.atm.

F1: 400.130 F2: 1.000

SW1: 8013

USER: temple - DATE: Apr 16 23:24:29 2008 EDT (UT-4h) templ

EX:

PW: 9.8 us

PD: 1.0 sec

OF1: 2004.6

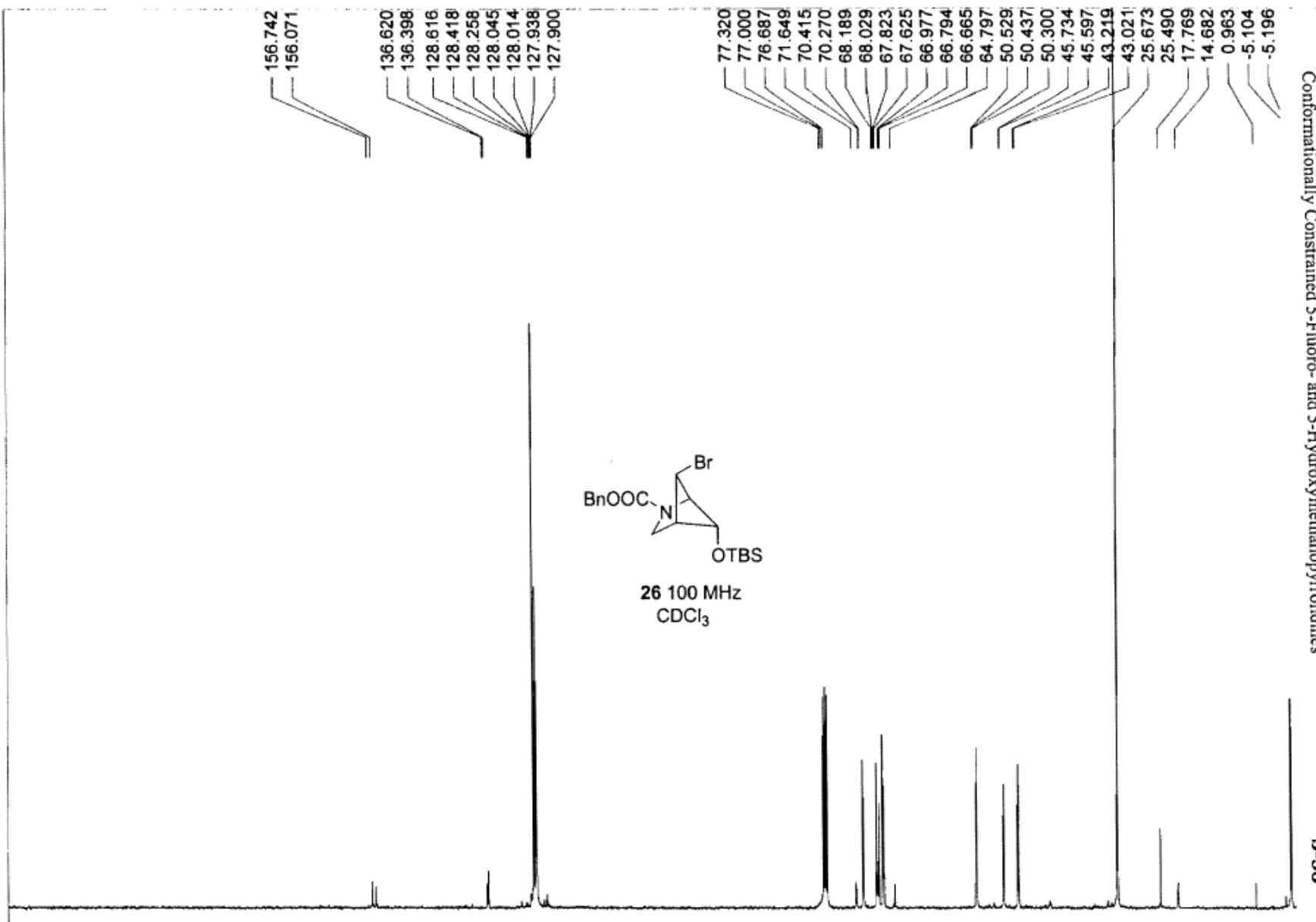
NA: 16

PTS1d: 32768

LB: 0.1 Nuts - NZ[2.1.1]syn-OTBS, anti-Br--H-eram-1072

Conformationally Constrained 5-Fluoro- and 5-Hydroxymethanopyrrolidines

S-38

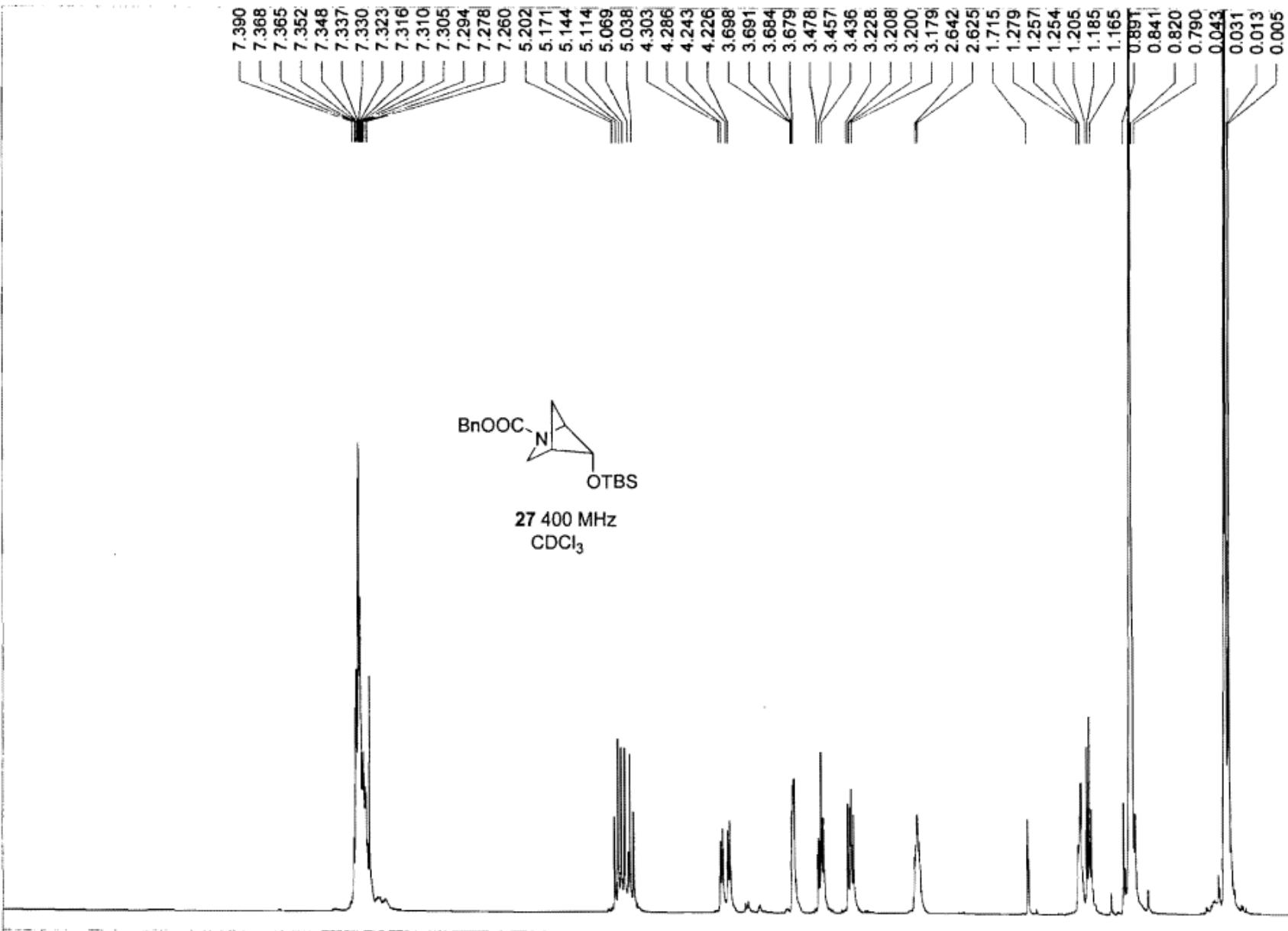


NCbz[2.1.1] syn-OTBS, anti-Br, carbon1HR_atm.

F1: 100.613	F2: 1.000	SW1: 25126	OF1: 10017.3	PTS1d: 32768
EX:		PW: 5.7 us	PD: 2.0 sec	NA: 3200 LB: 3.0 Nuts - NZ[2.1.1]syn-OTBS, anti-Br--C--eram-1320

Conformationally Constrained 5-Fluoro- and 5-Hydroxymethanopyrrolidines

۲۳۵



NZ[2,1,1]syn-OTBS, proton atm-

F1: 400,130 F2: 1,000

EX:

SW1-8013

PW: 98 us

PD: 1.0 sec

OEI-2004-0

NA: 16

USER: temple -- DATE: Apr 16 22:54:39 2008 EDT (UT-4h) temple

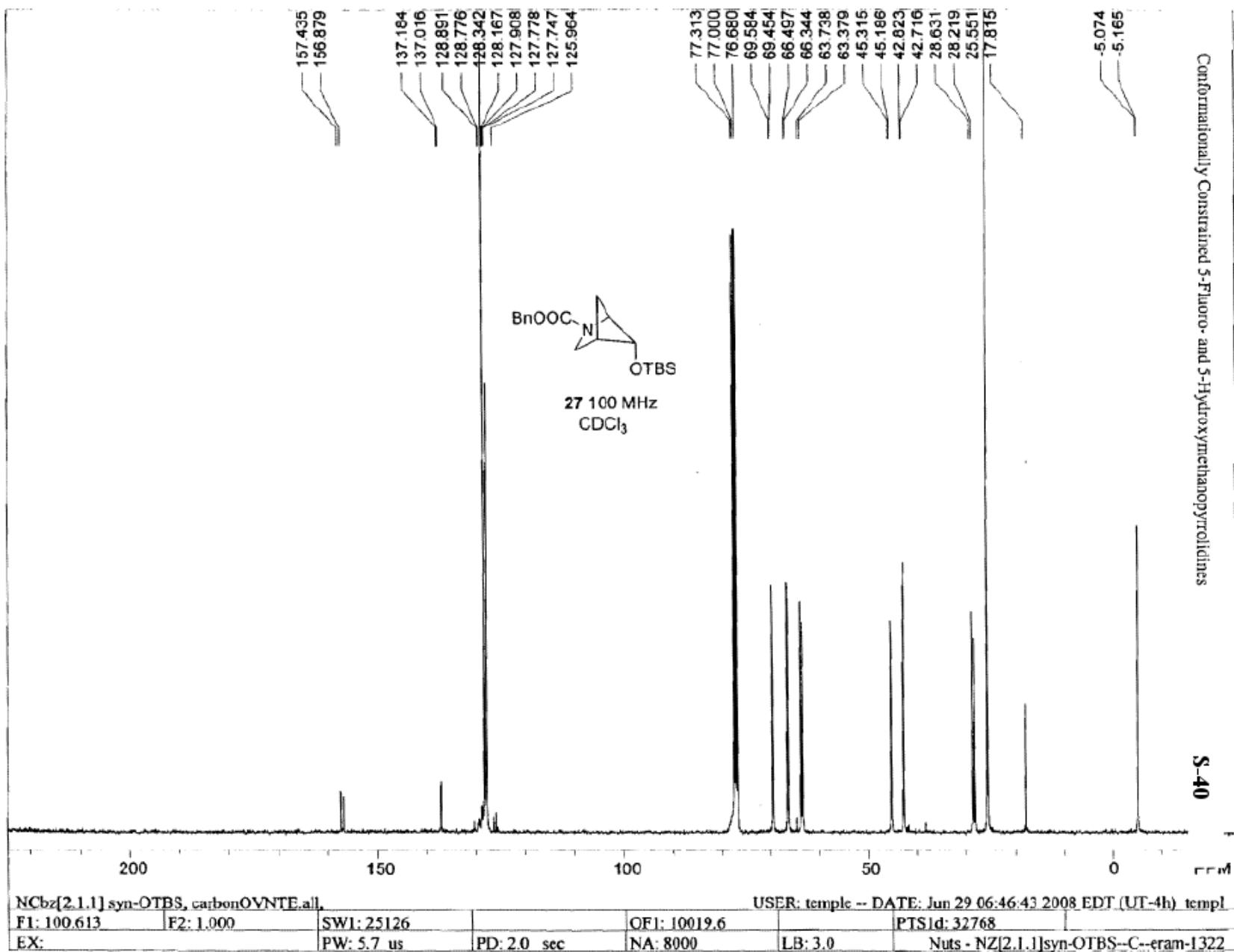
USER: temple - DATE: Apr 16 22

J.B.: 0.1

Nuts - NZ[2.1]syn-QTBS--H--eram-1071

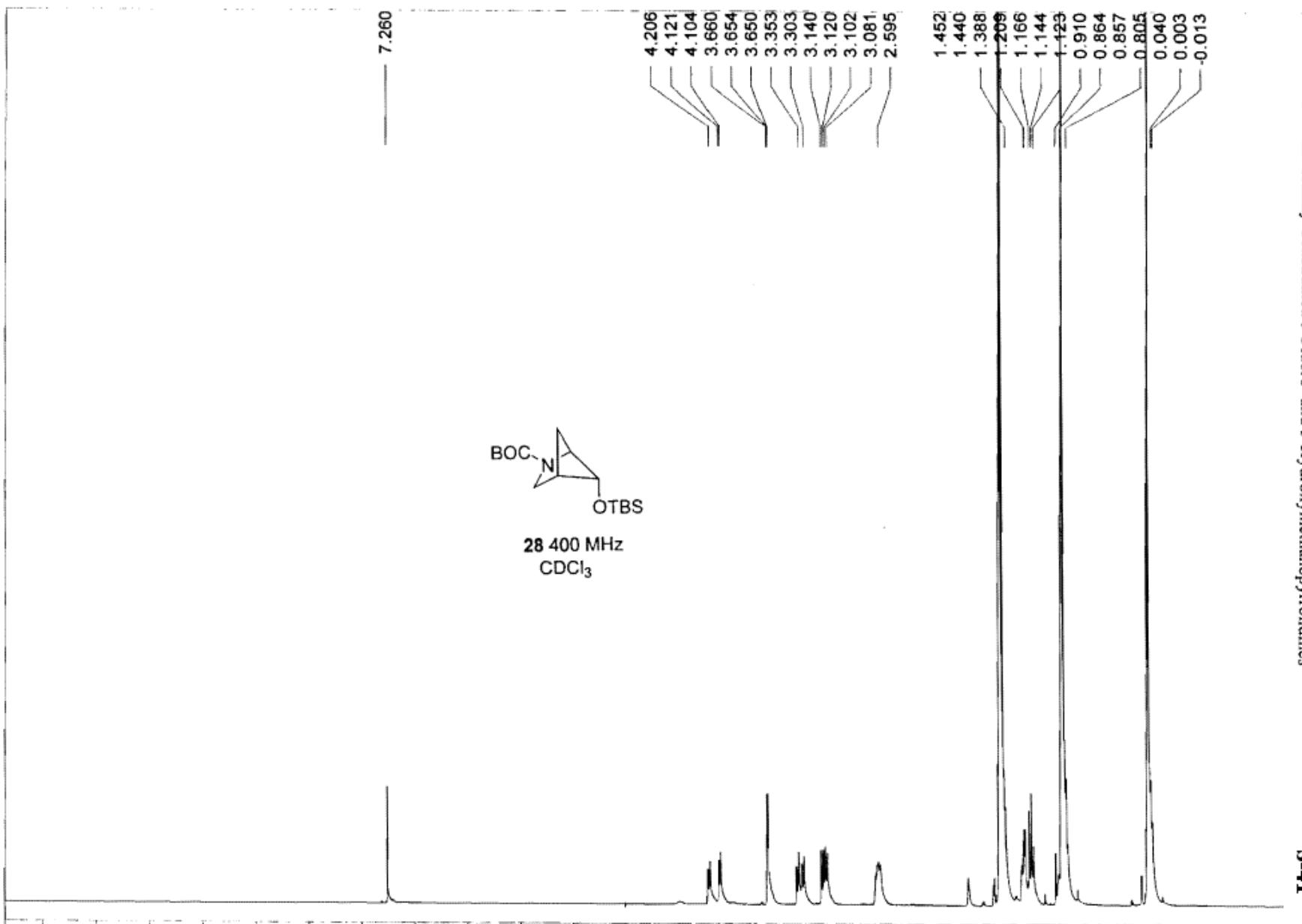
Conformationally Constrained 5-Fluoro- and 5-Hydroxymethanopyrrolidines

S-40



Conformationally Constrained 5-Fluoro- and 5-Hydroxymethanopyrrolidines

S-41



NBoc[2.1.1]syn-OTBS, proton.atm,

F1: 400.130 F2: 1.000

SW1: 8013 PW: 9.8 us

PD: 1.0 sec

EX:

USER: temple -- DATE: Apr 16 22:43:50 2008 EDT (UT-4h) templ

OF1: 2004.0

PTS1d: 32768

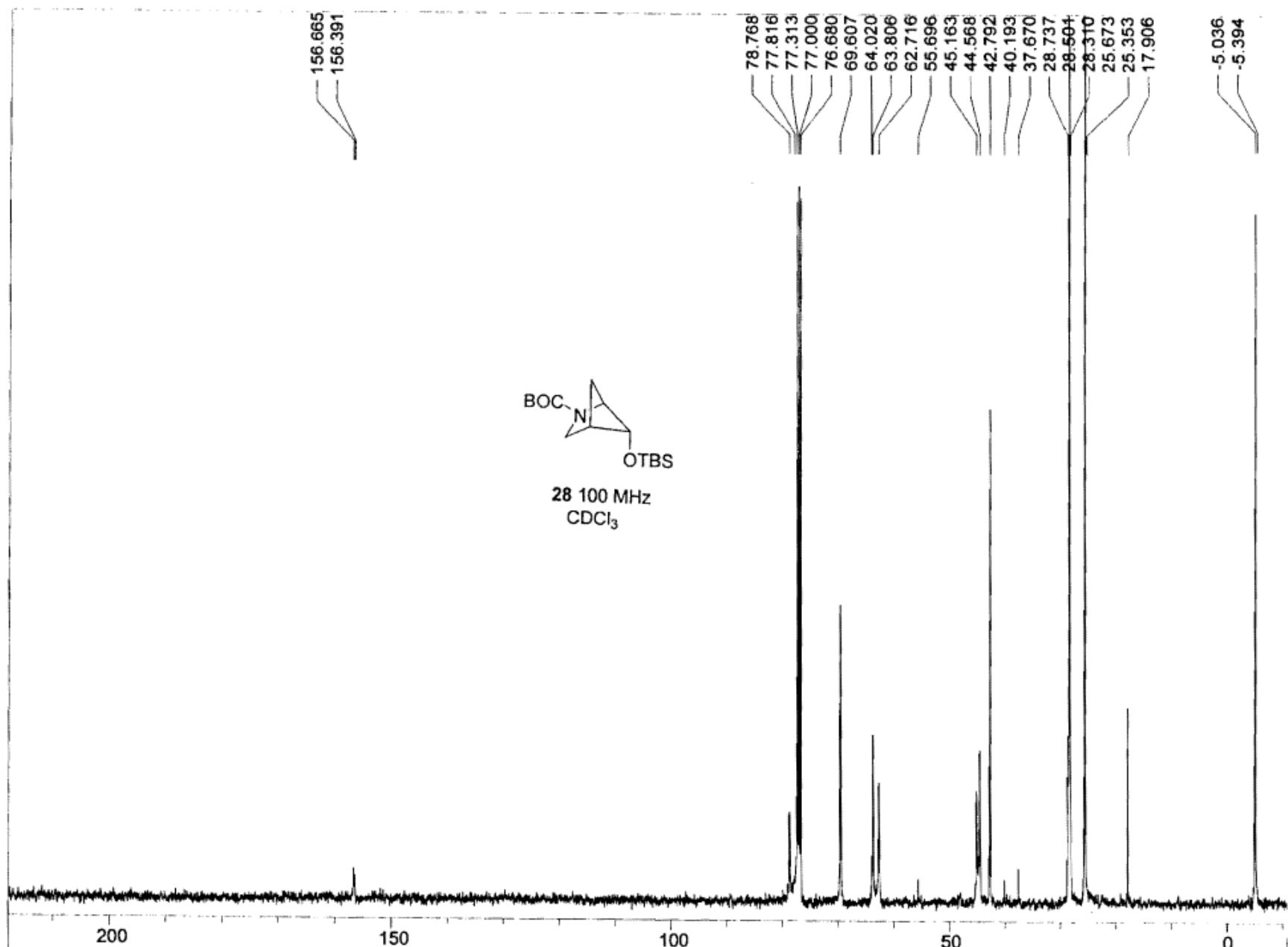
NA: 16

LB: 0.1

Nuts - NBoc[2.1.1] syn-OTBS--H--eram-1070

Conformationally Constrained 5-Fluoro- and 5-Hydroxymethanopyrrolidines

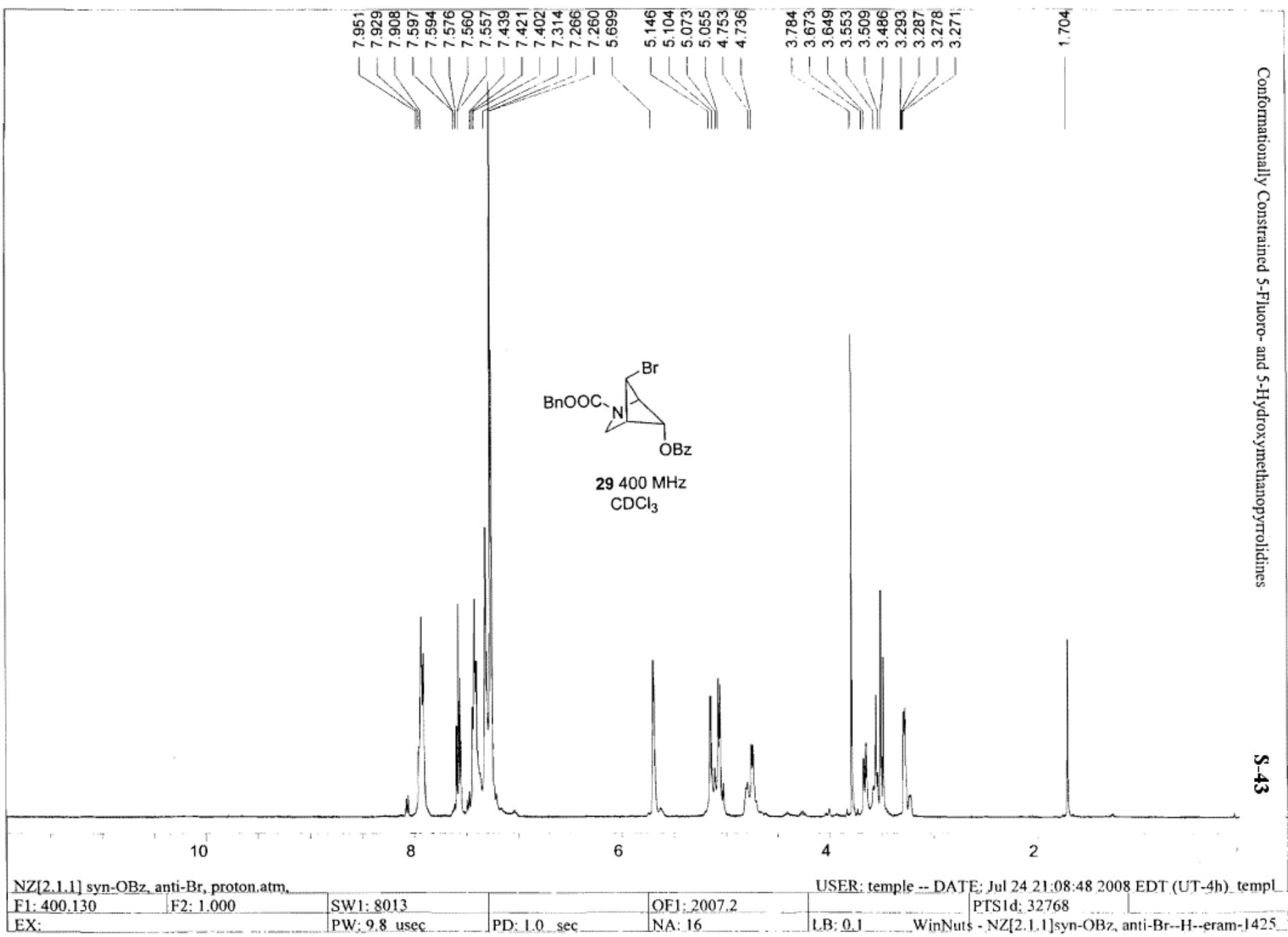
S-42

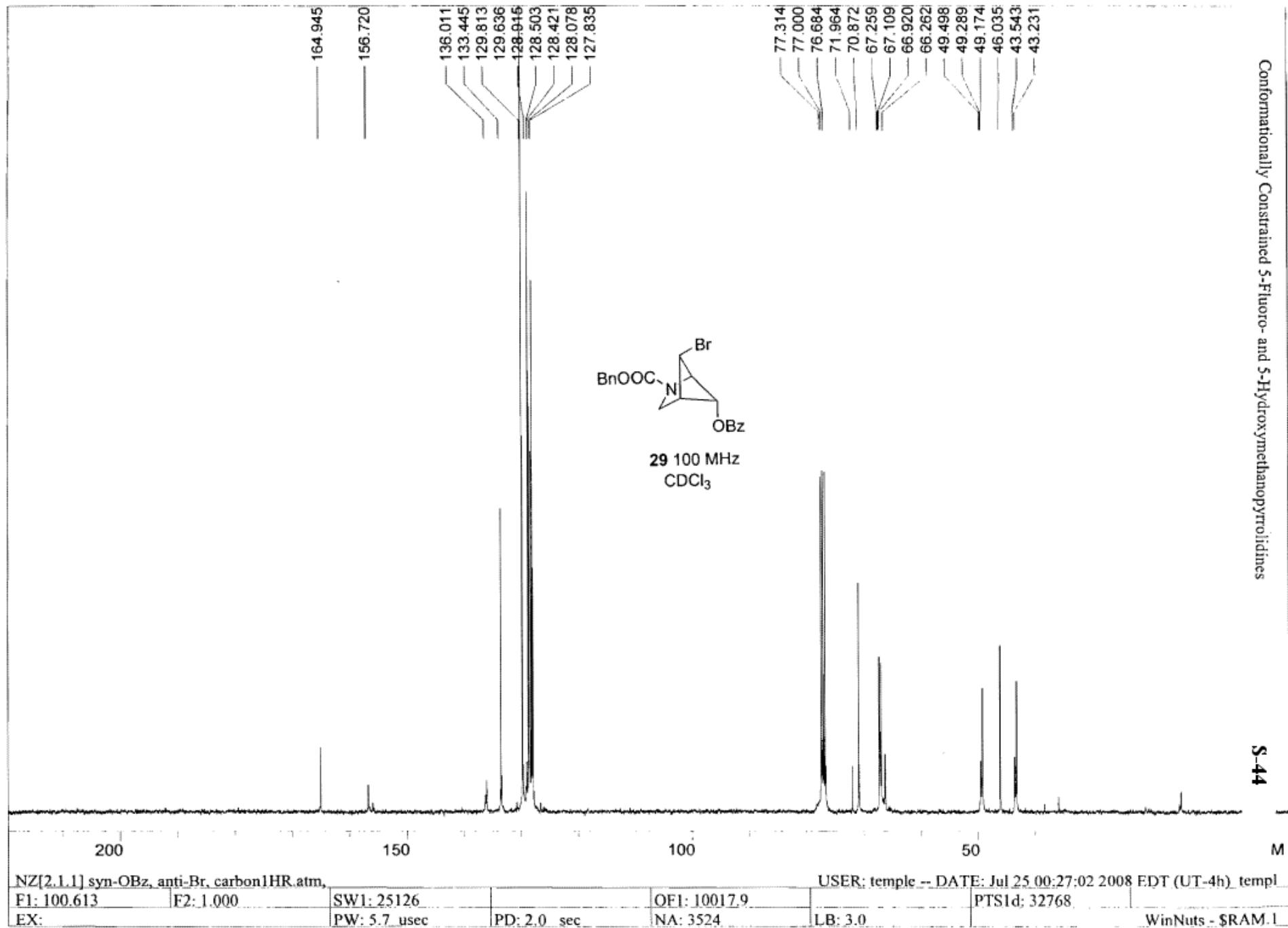


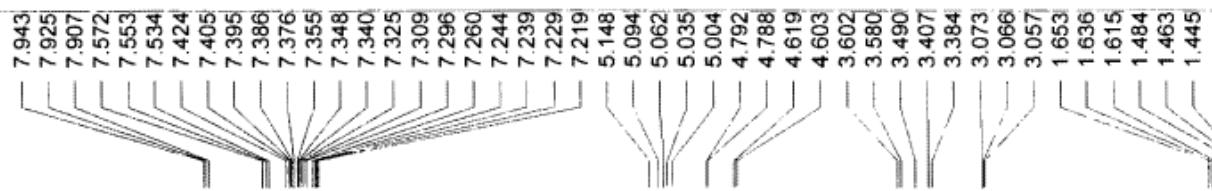
NBoc[2.1.1] syn-OTBS, carbon1HR.atm,

F1: 100.613	F2: 1.000	SW1: 25126		OF1: 10021.1		PTS1d: 32768
EX:		PW: 5.7 us	PD: 2.0 sec	NA: 2200	LB: 3.0	Nuts - NBoc[2.1.1] syn-OTBS--C--eram-1312

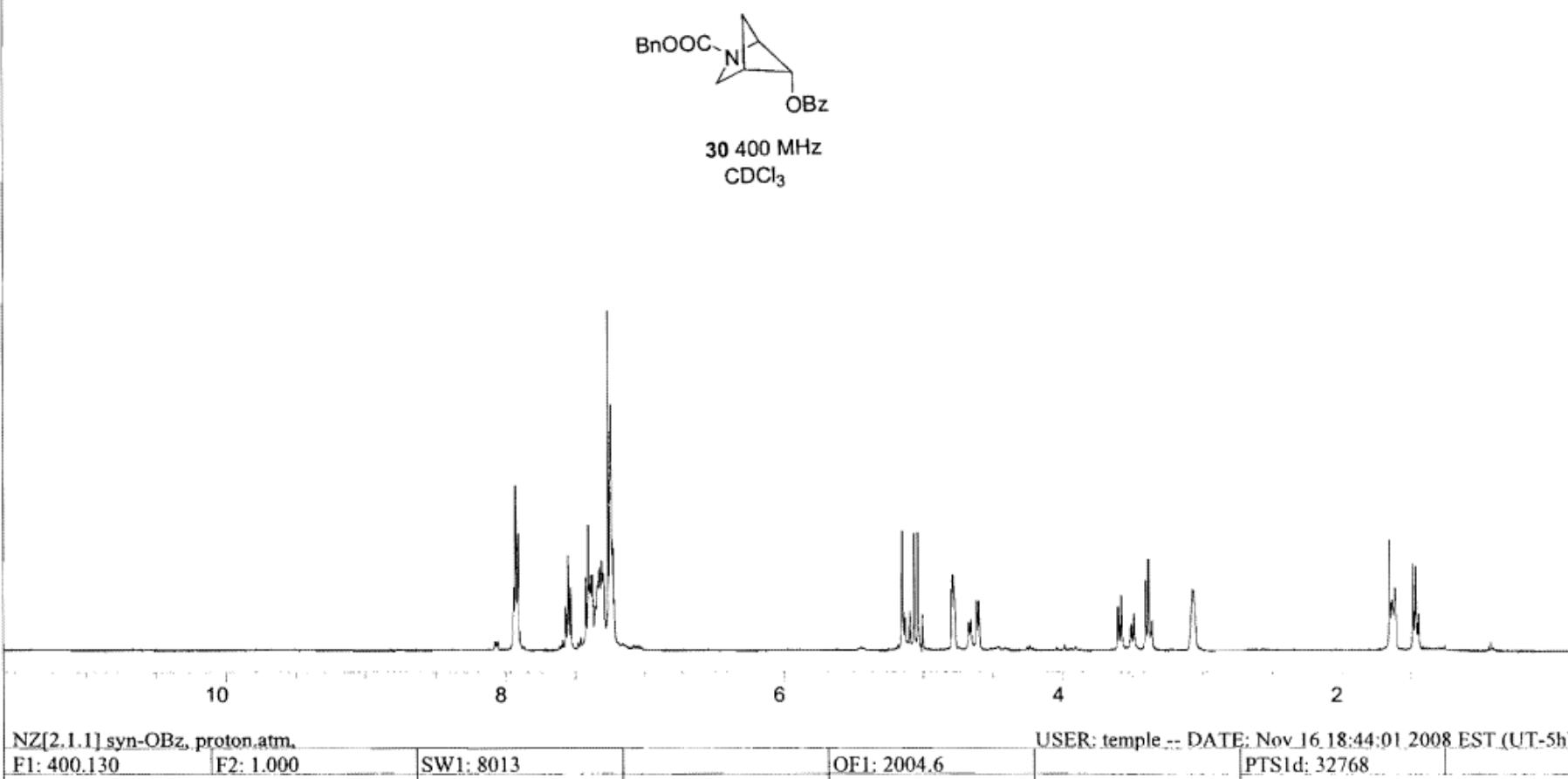
USER: temple - DATE: Jun 27 23:05:38 2008 EDT (UT-4h) templ







30 400 MHz
 CDCl_3



NZ[2,1,1]syn-OBz, proton, atm.

F1: 400.130 F2: 1.000

SW1: 8013 PW: 9.8 usec

PD: 1.0 sec

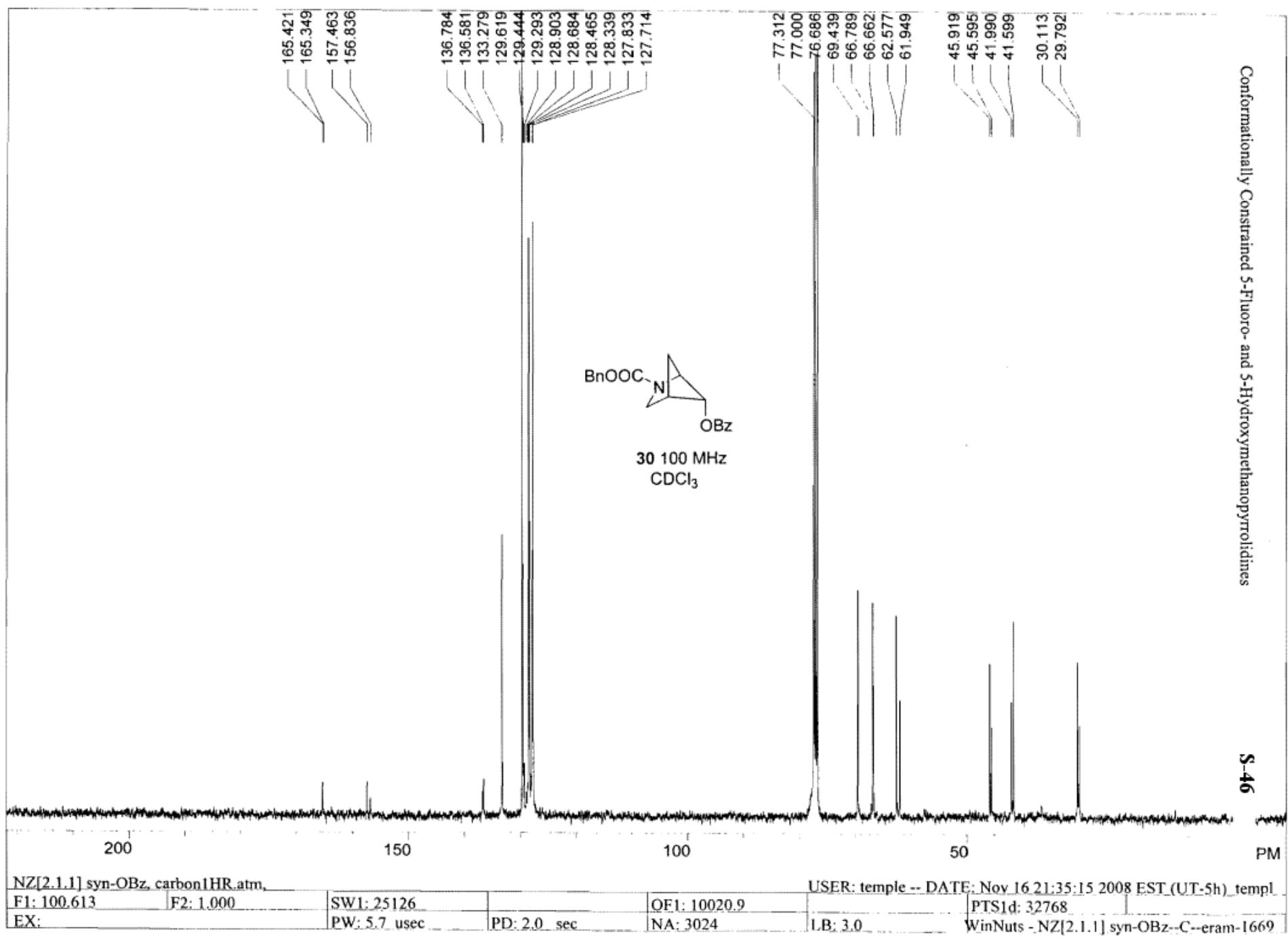
OF1: 2004.6 NA: 16

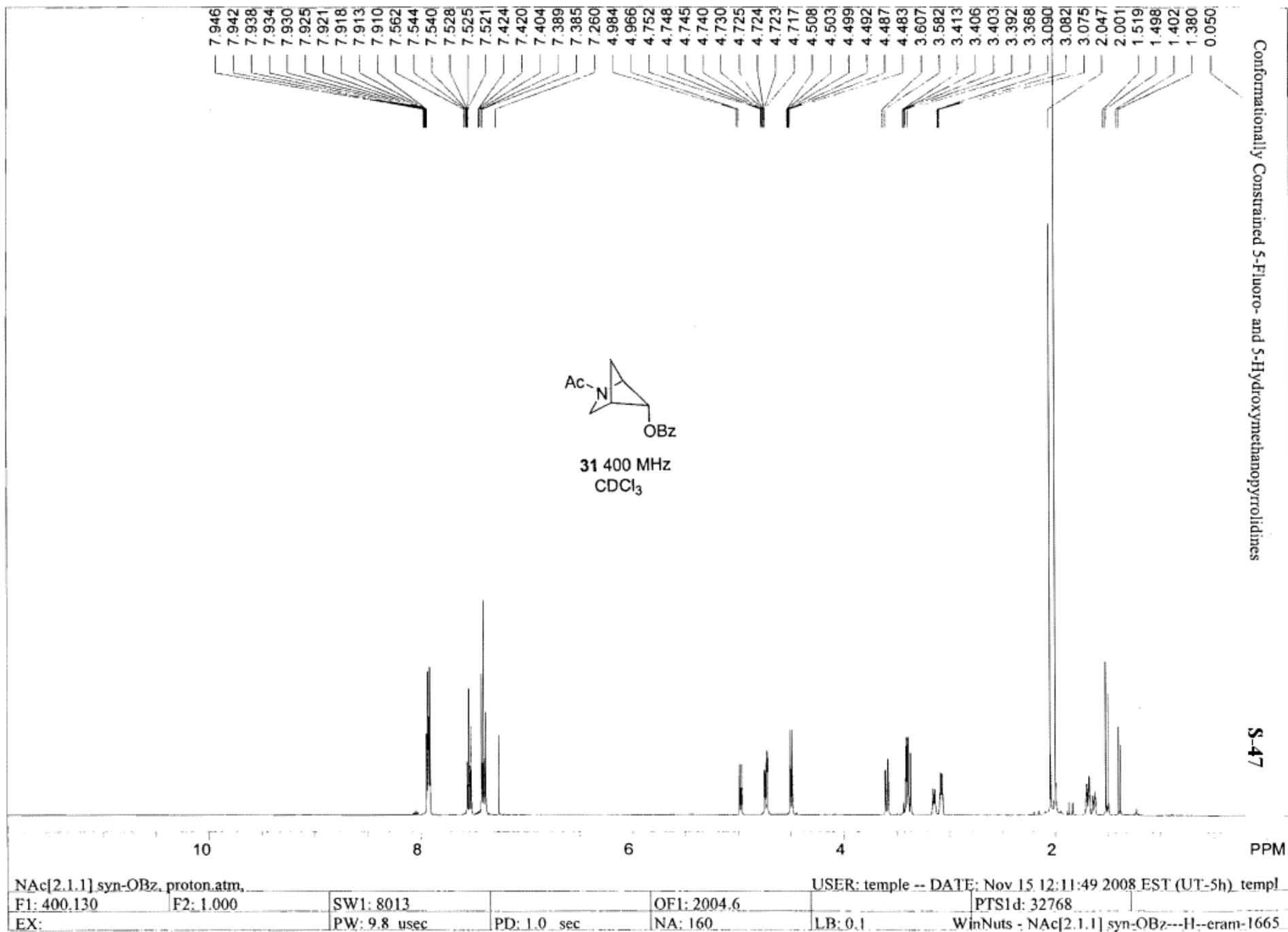
LB: 0.1

USER: temple -- DATE: Nov 16 18:44:01 2008 EST (UT-5h) templ

PTS1d: 32768

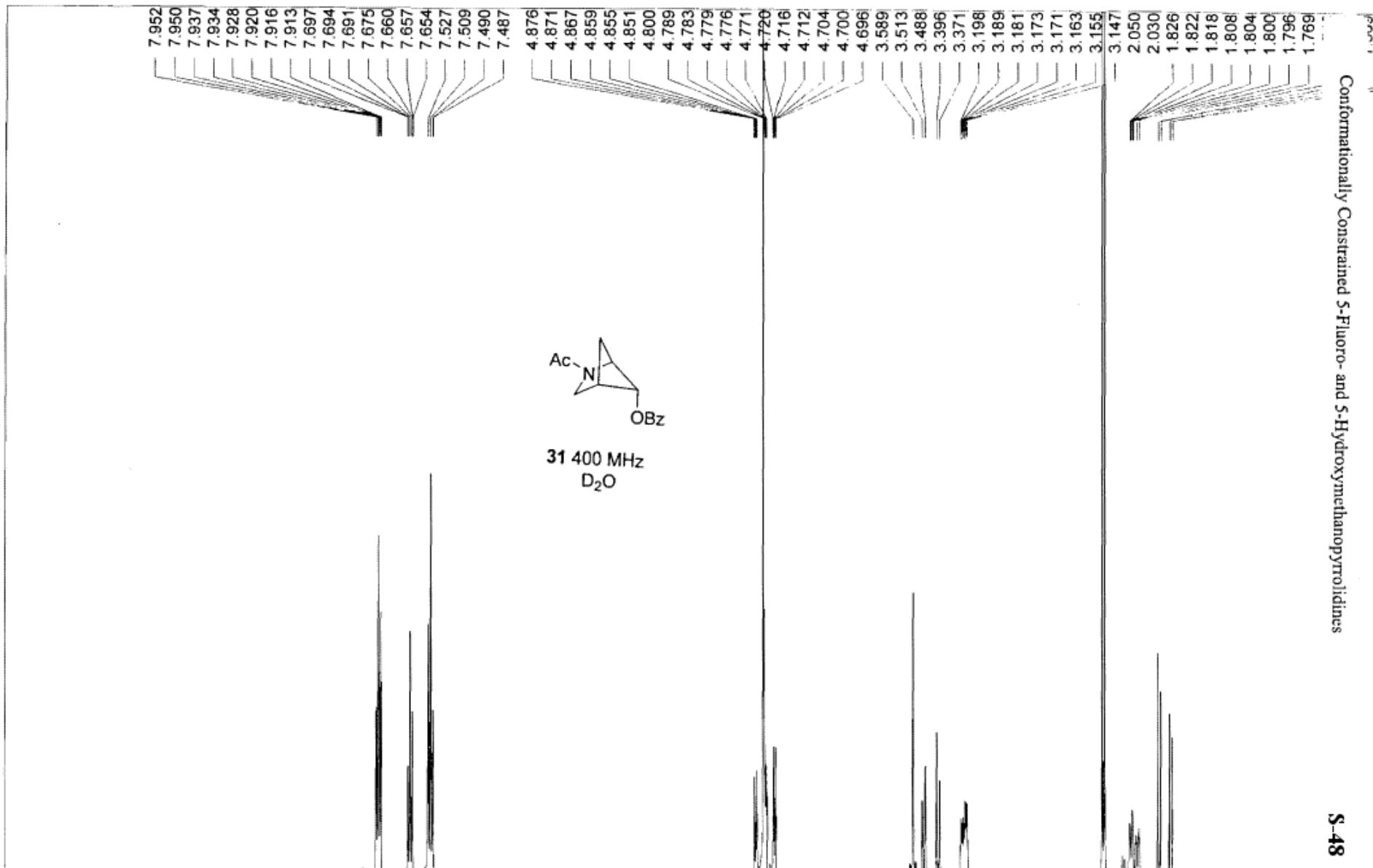
WinNuts - NZ[2,1,1]syn-OBz--H--eram-1668





Conformationally Constrained 5-Fluoro- and 5-Hydroxymethanopyrrolidines

S-48



NAc[2.1.1]syn-OBz, proton10MIN.atm,

F1: 400.130

F2: 1.000

SW1: 8278

EX:

PW: 9.8 usec

PD: 1.0 sec

NA: 428

OF1: 2041.5

LB: 0.1

WinNuts

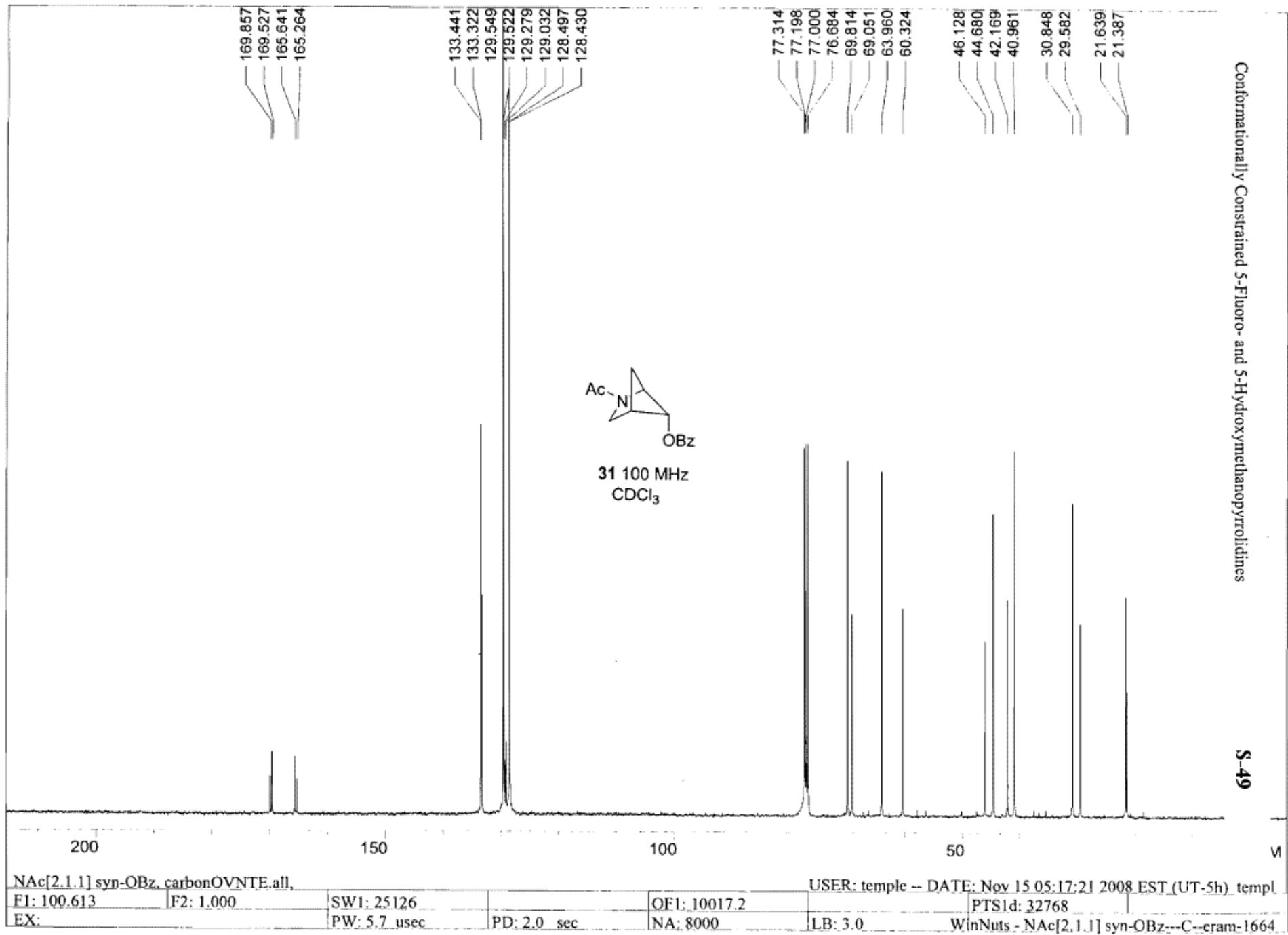
USER: temple -- DATE: Nov 22 22:17:52 2008 EST (UT-5h).templ

PTS1d: 32768

NAc[2.1.1]syn-OBz---H--eram-1680 (D2O)

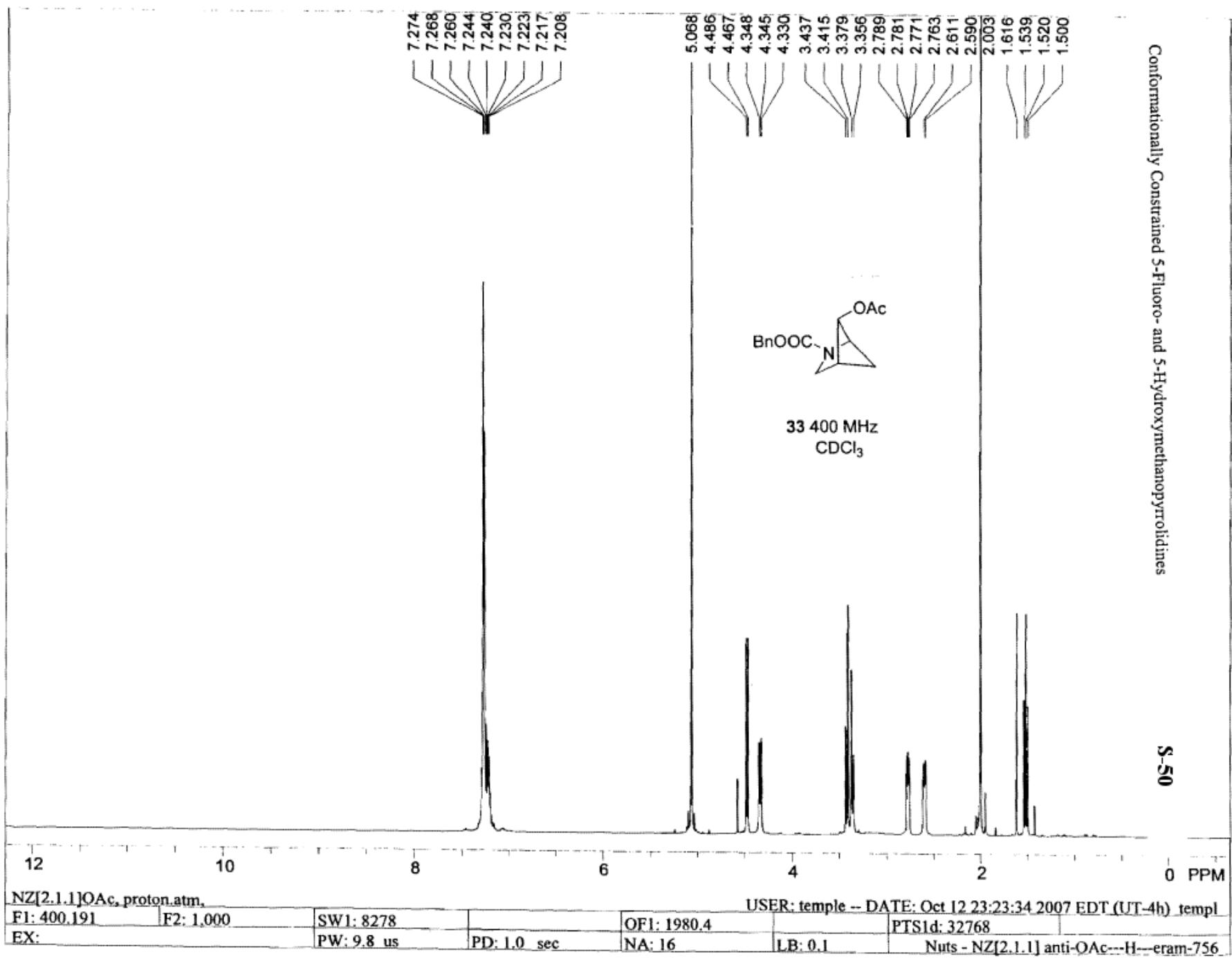
Conformationally Constrained 5-Fluoro- and 5-Hydroxymethanopyrrolidines

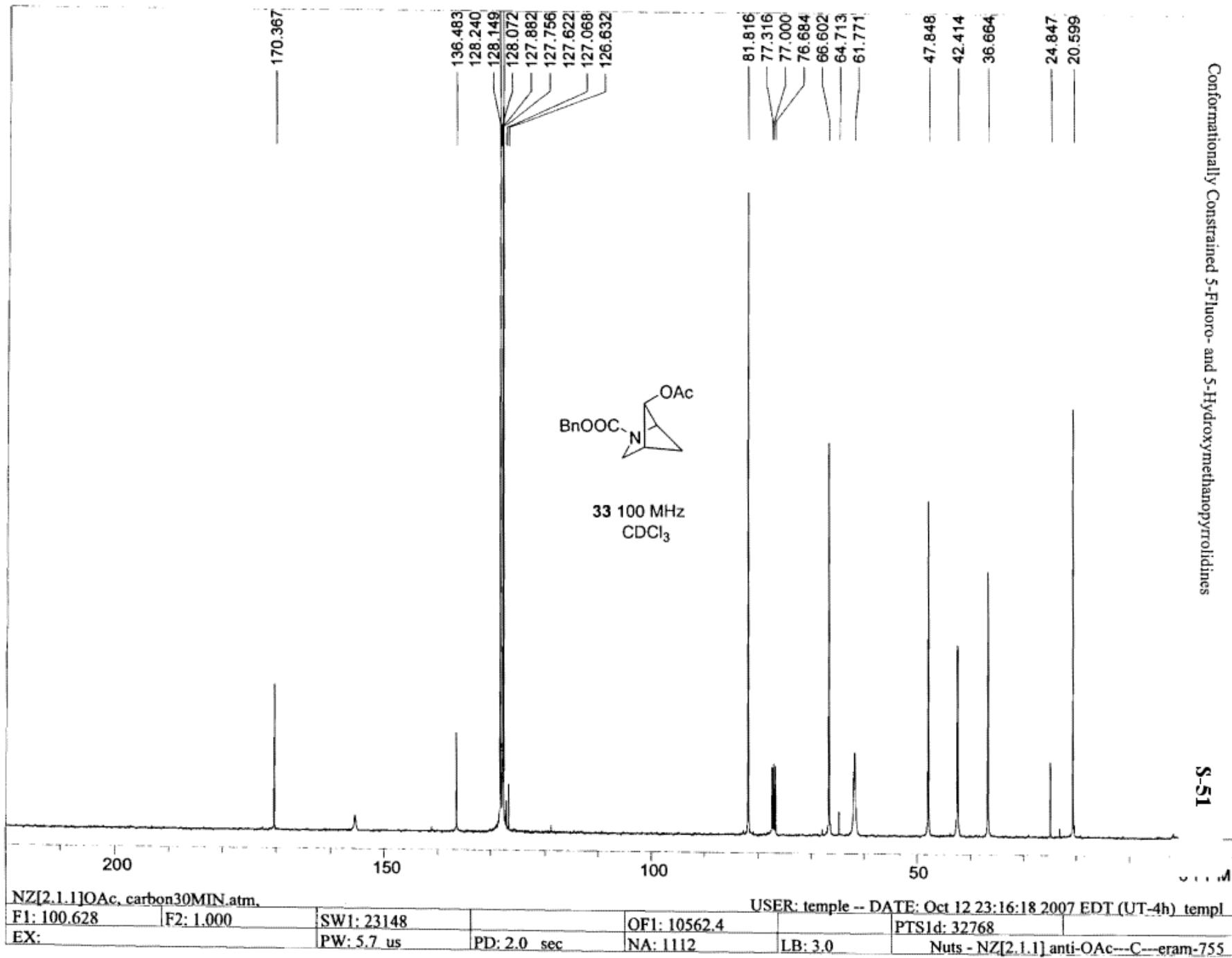
S-49



Conformationally Constrained 5-Fluoro- and 5-Hydroxymethanopyrrolidines

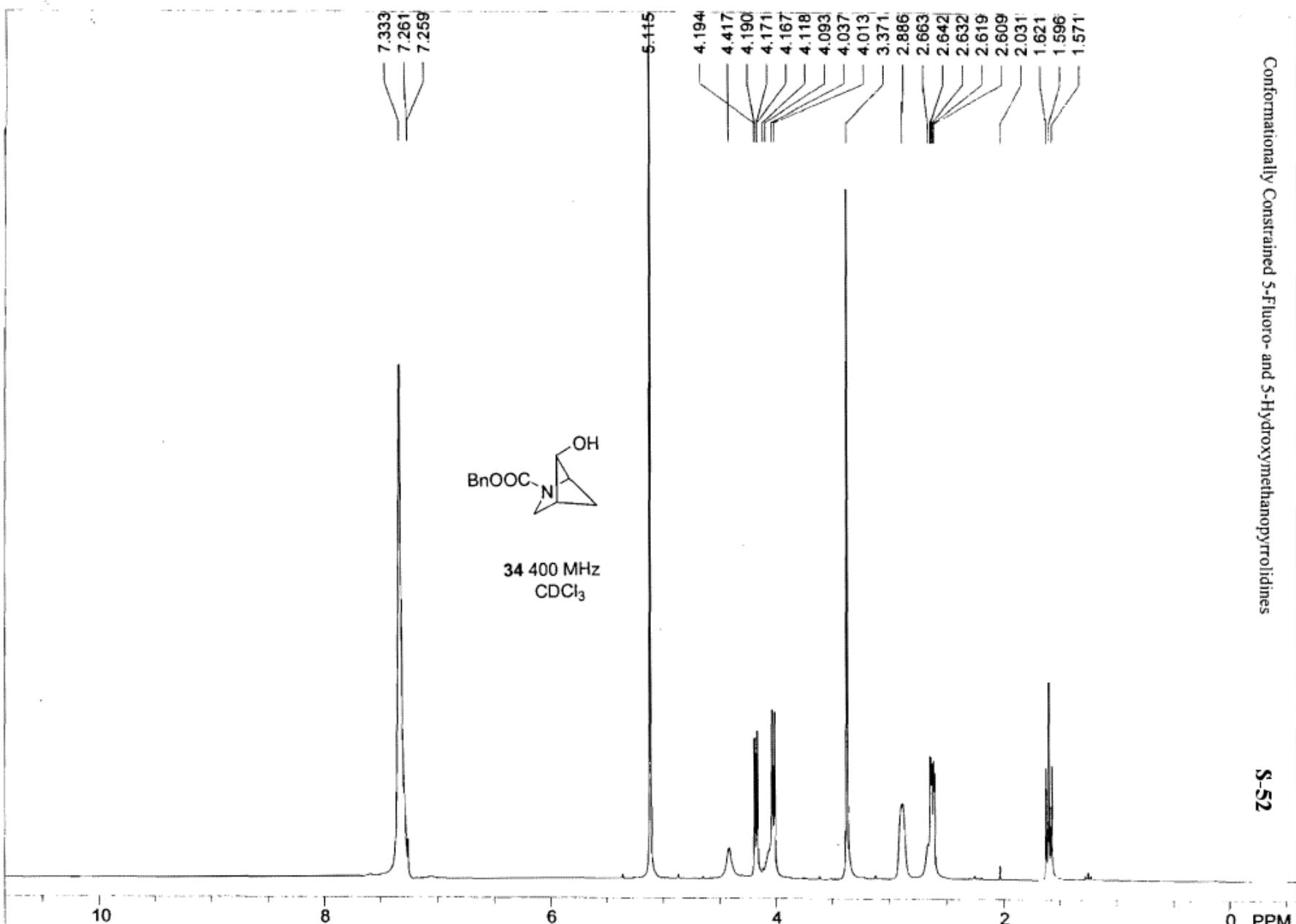
S-50





Conformationally Constrained 5-Fluoro- and 5-Hydroxymethanopyrrolidines

S-52

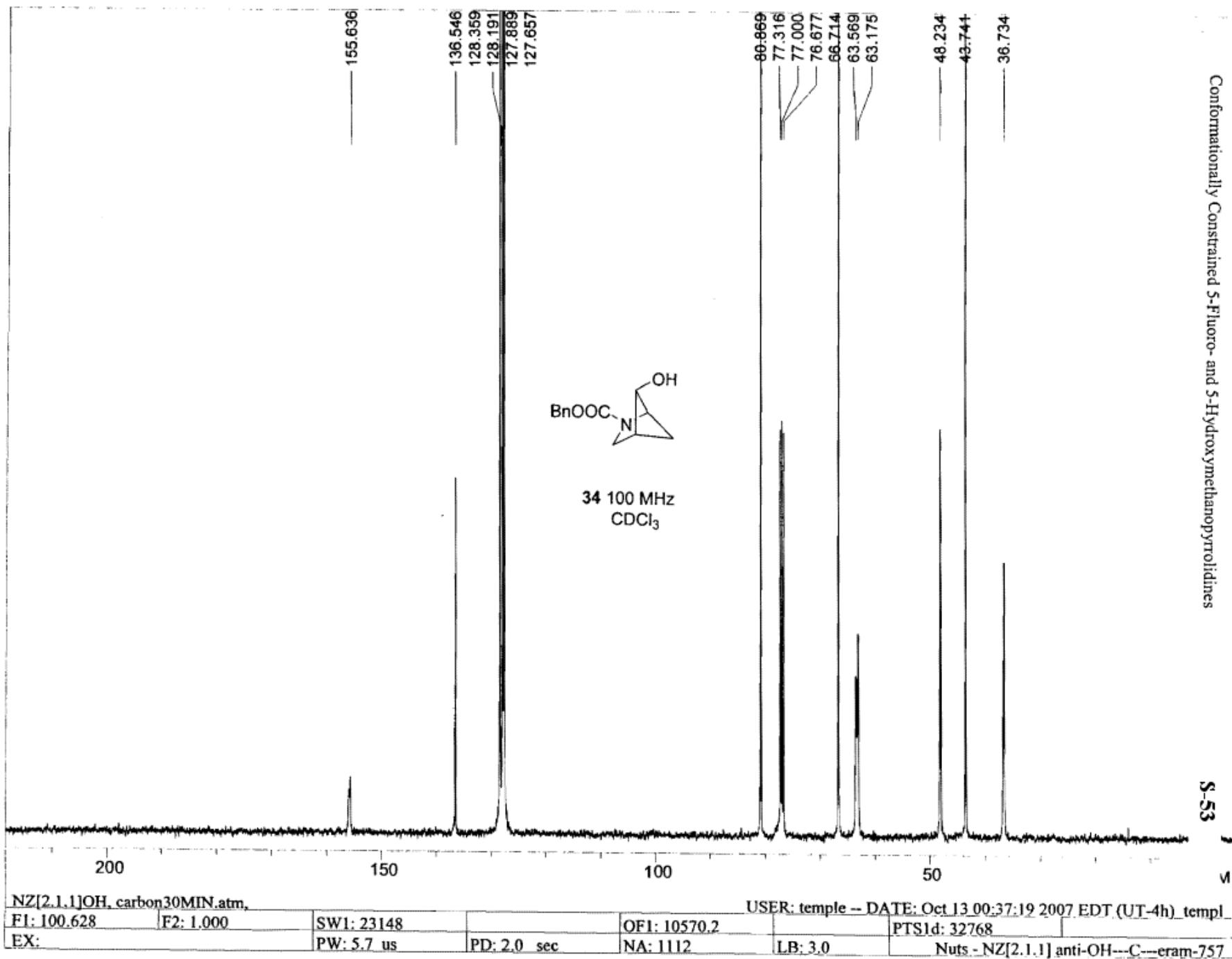


eram/12-53-2_13Oct2007

F1: 300.018	F2: 300.018	SW1: 4800		OF1: 1782.0		PTS1d: 16384	USER: -- DATE: Oct 13 2007
EX: s2pul		PW: 4.0 us	PD: 1.0 sec	NA: 8	LB: 64ats - NZ[2,1,1] anti-OH---H--eram-12-53-2 on 300 NMR		

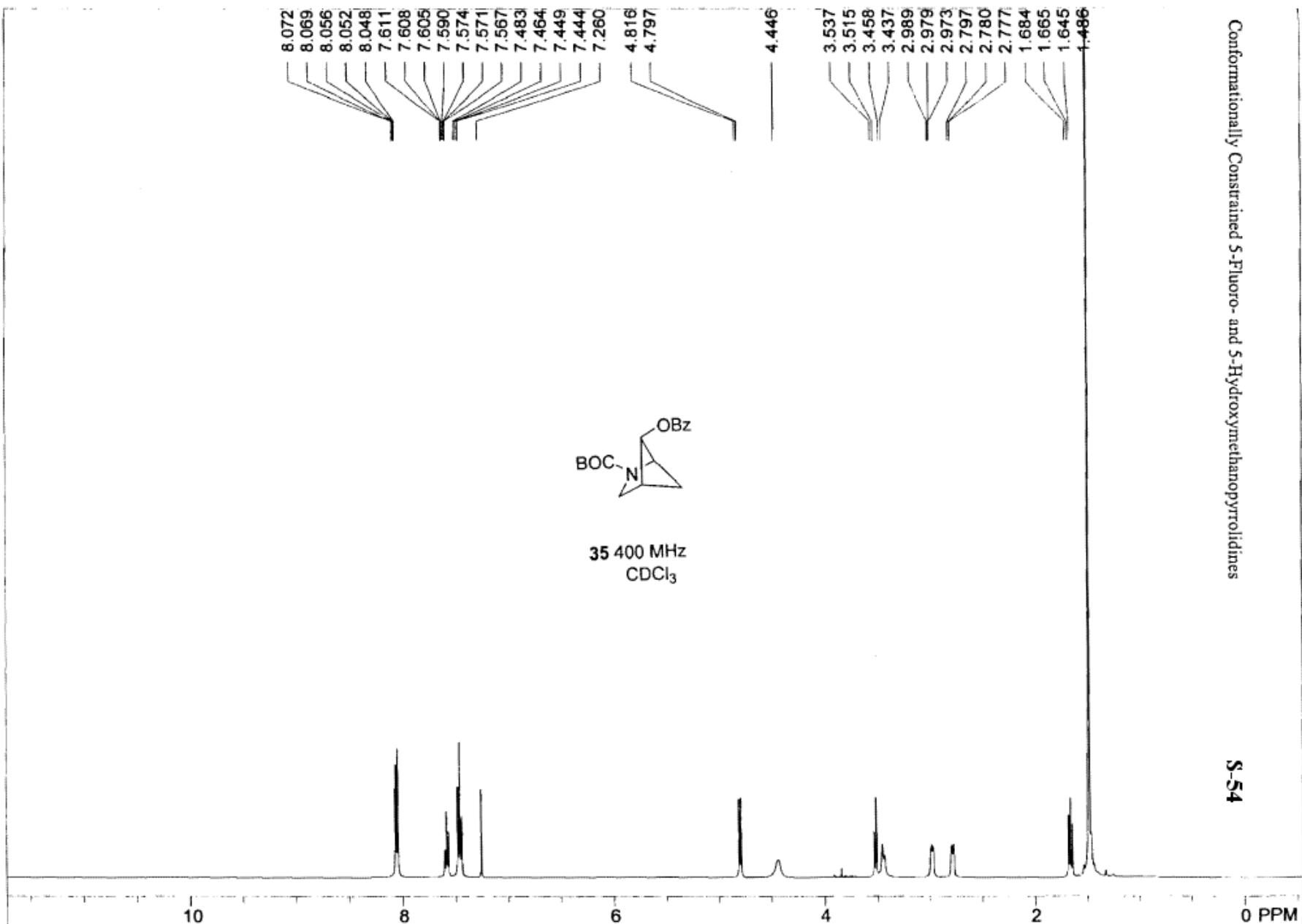
Conformationally Constrained 5-Fluoro- and 5-Hydroxymethanopyrrolidines

S-53

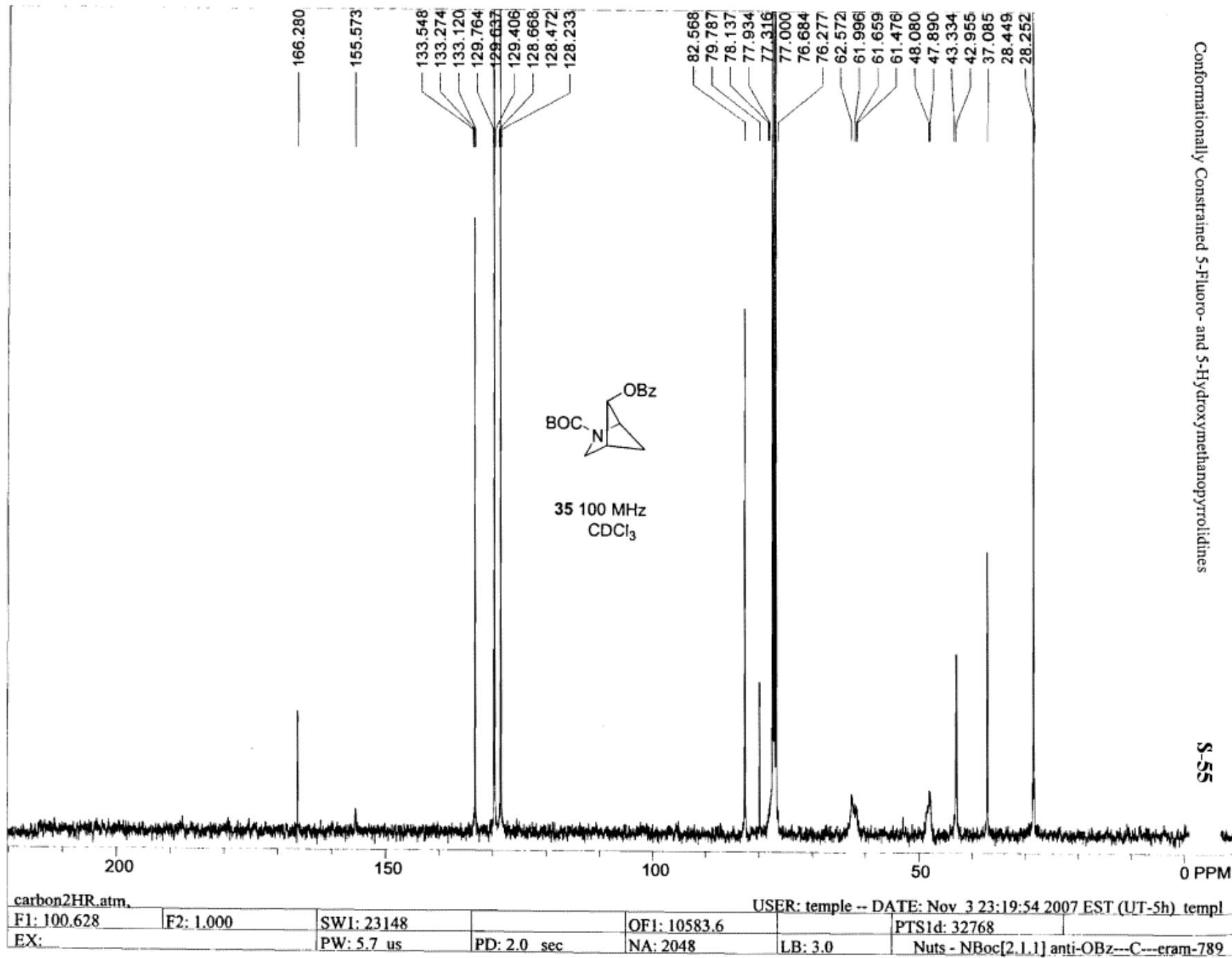


Conformationally Constrained 5-Fluoro- and 5-Hydroxymethanopyrrolidines

S-54

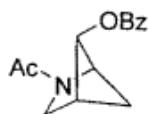
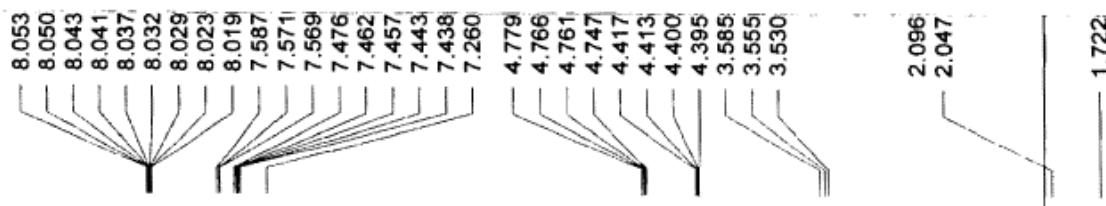


proton.atm.						USER: temple -- DATE: Nov 3 23:37:03 2007 EST (UT-5h) templ	
F1: 400.191	F2: 1.000	SW1: 8278		OF1: 2002.6		PTS1d: 32768	
EX:		PW: 9.8 us	PD: 1.0 sec	NA: 16	LB: 0.1	Nuts - NBoc[2,1,1]anti-OBz---H---eram-790	

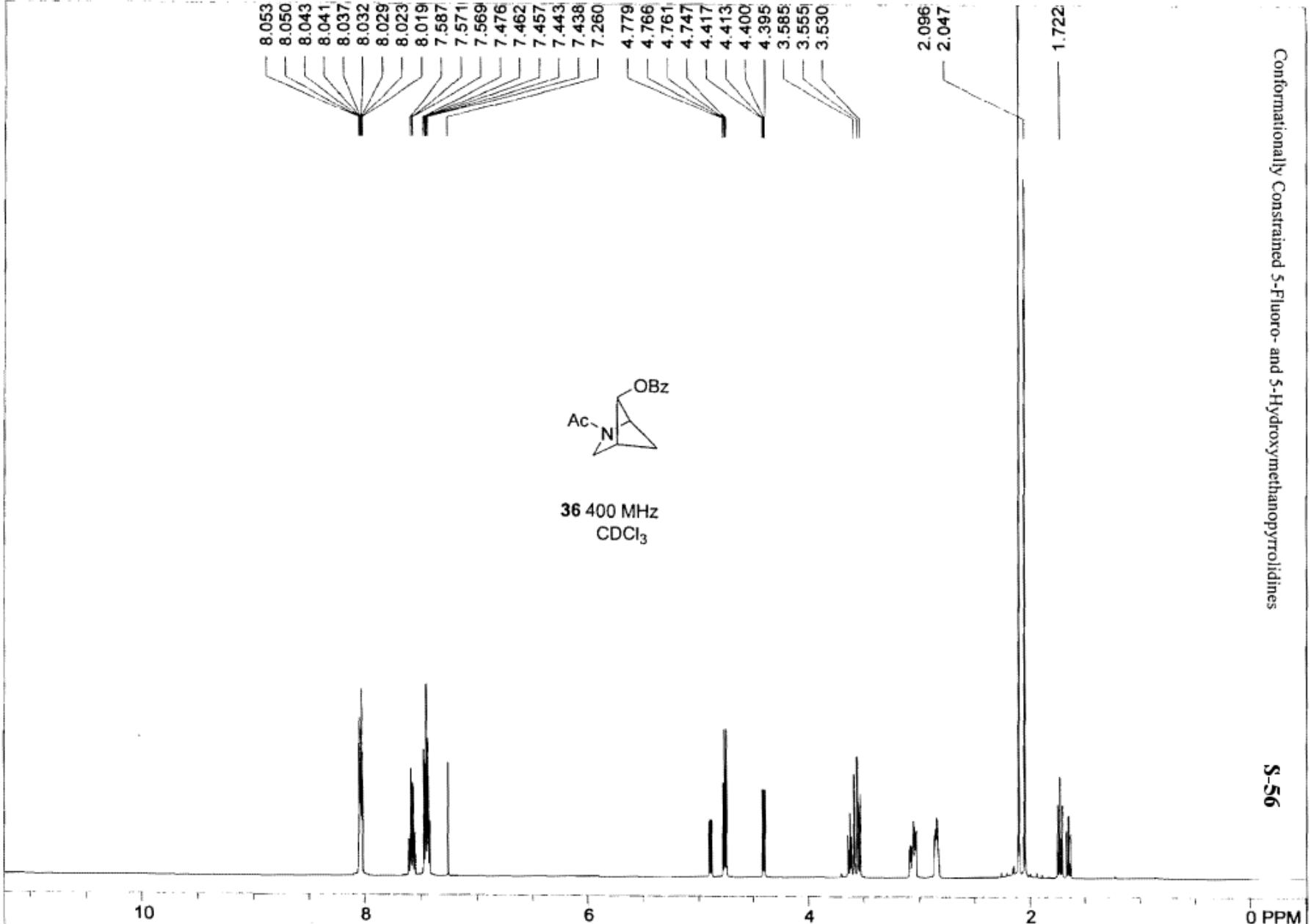


Conformationally Constrained 5-Fluoro- and 5-Hydroxymethanopyrrolidines

S-56



36 400 MHz
 CDCl_3



NAc[2.1.1]anti-OBz, proton.atm,

F1: 400.130

F2: 1.000

SW1: 8278

OF1: 2004.2

PTS1d: 32768

EX:

PW: 9.8 us

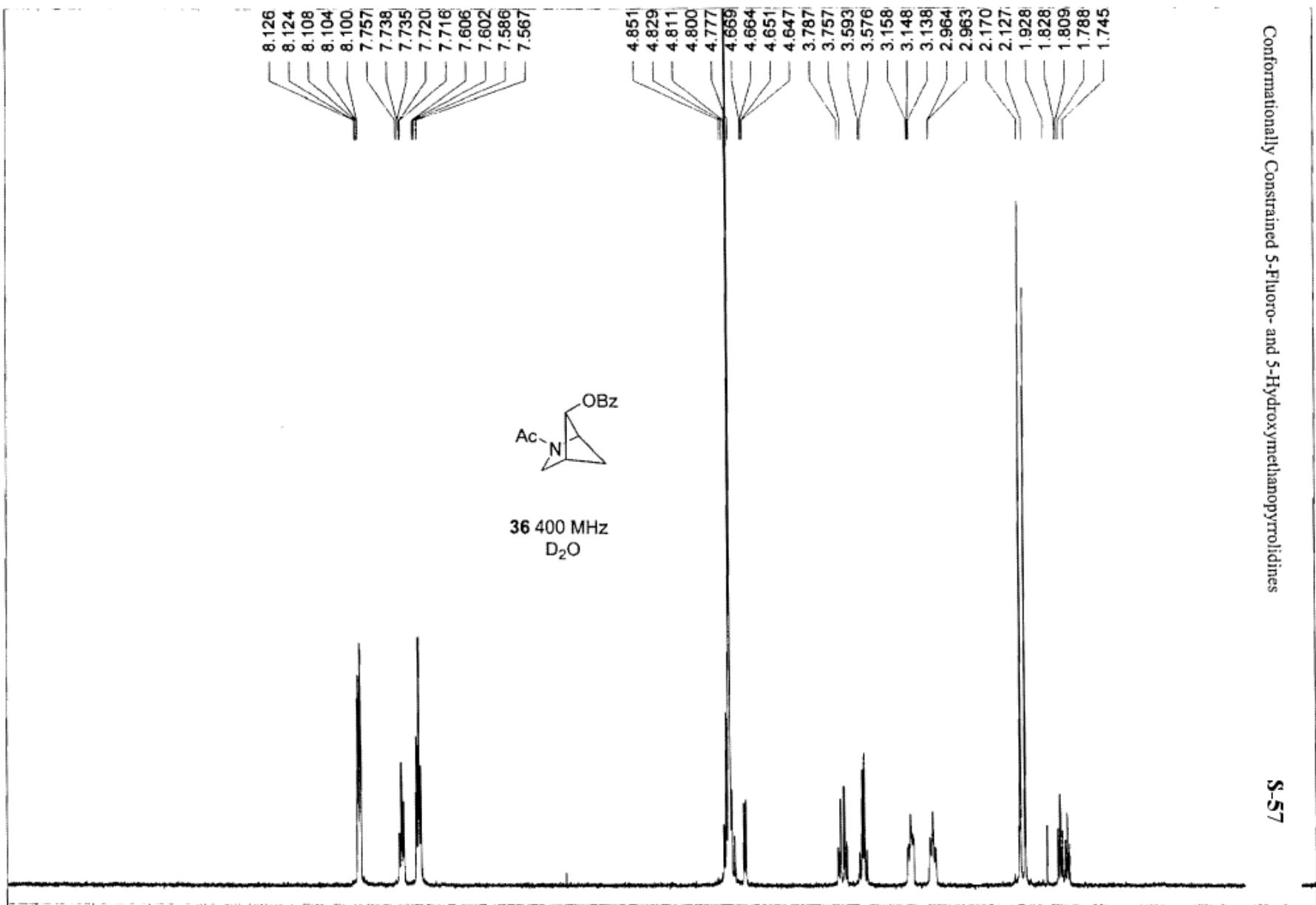
PD: 1.0 sec

NA: 16

LB: 0.1

Nuts - NAc[2.1.1] anti-OBz---H-- CDCl_3 --eram-851

USER: temple -- DATE: Feb 1 23:25:52 2008 EST (UT-5h) templ



NAC[2.1.1] anti-OBz, proton10MIN.atm,

F1: 400.130

F2: 1.000

SW1: 8278

OF1: 2040.7

PTS1d: 32768

EX:

PW: 9.8 us

PD: 1.0 sec

NA: 228

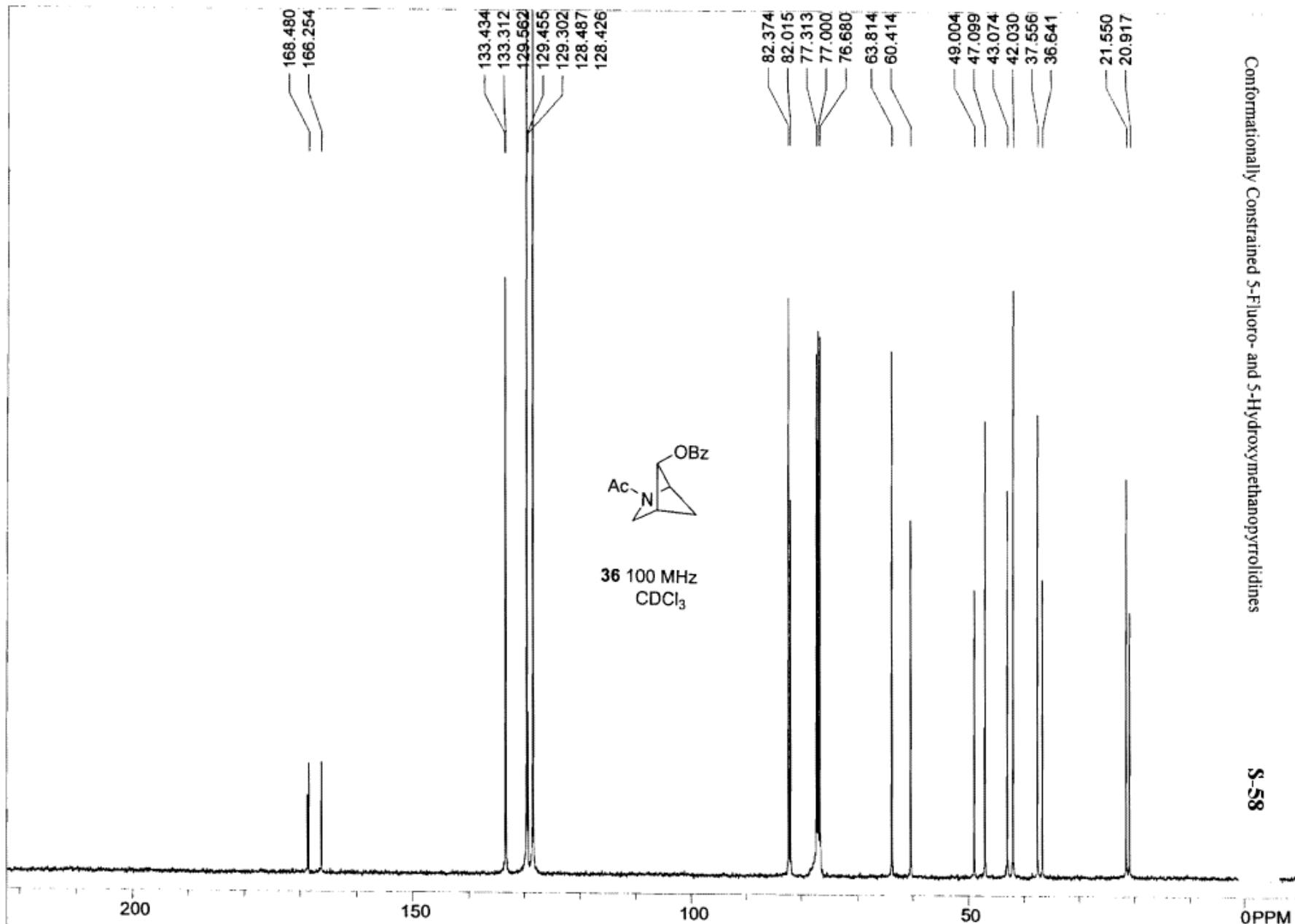
USER: temple -- DATE: Jul 16 20:12:15 2008 EDT (UT-4h) templ

LB: 0.1

Nuts - NAC[2.1.1] anti-OBz--H--D2O--eram1402

Conformationally Constrained 5-Fluoro- and 5-Hydroxymethanopyrrolidines

S-58



NAc[2.1.1]anti-OBz, carbon2HR.atm.

F1: 100.613 F2: 1.000

EX:

SW1: 25126

PW: 5.7 us

PD: 2.0 sec

OF1: 10015.0

NA: 7548

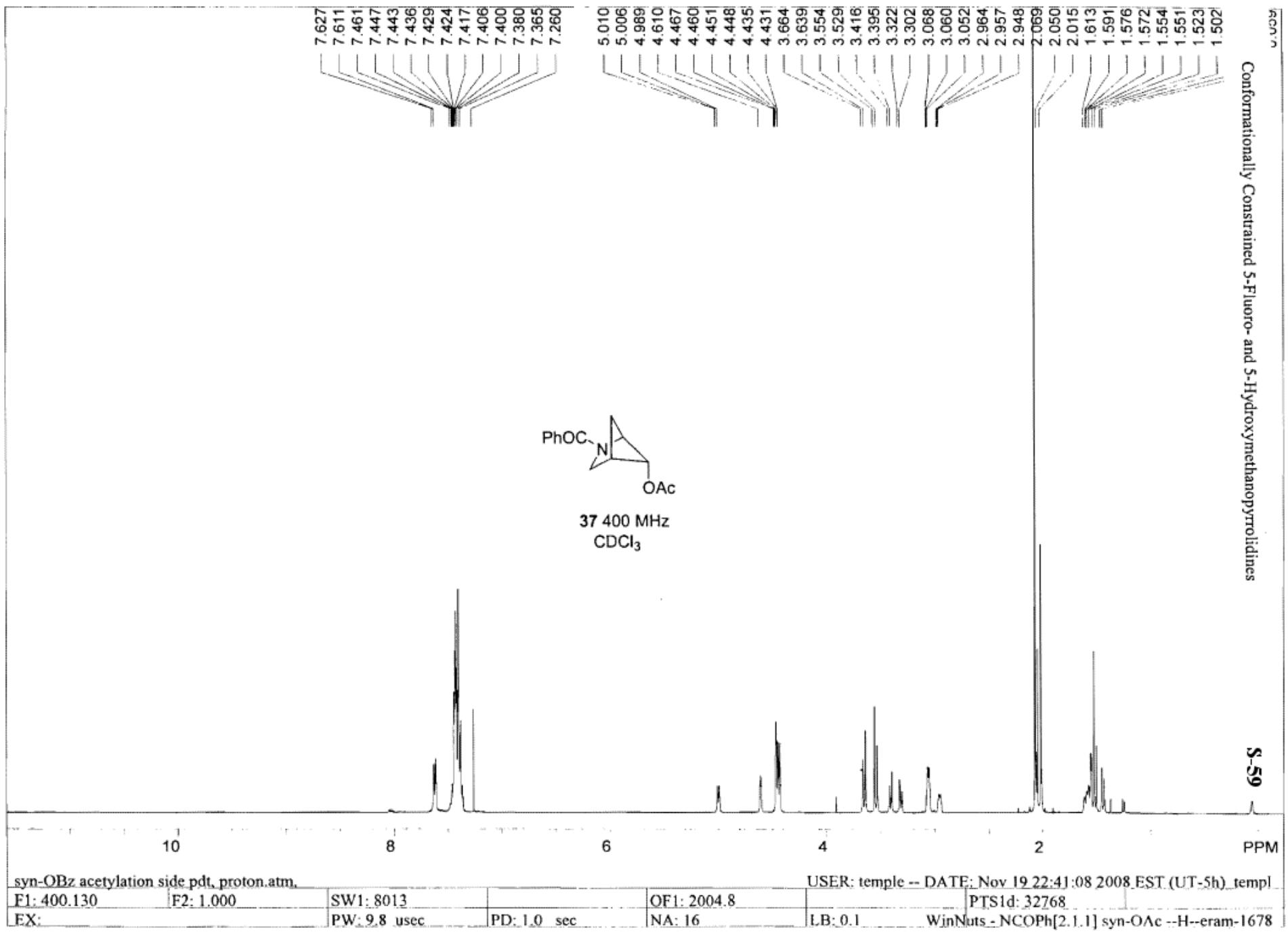
PTS1d: 32768

USER: temple - DATE: Feb 2 06:25:06 2008 EST (UT-5h) templ

LB: 3.0 Nuts - NAc[2.1.1] anti-OBz--C-- CDCl_3 --eram-852

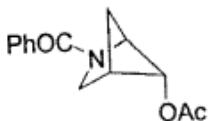
Conformationally Constrained 5-Fluoro- and 5-Hydroxymethanopyrrolidines

5

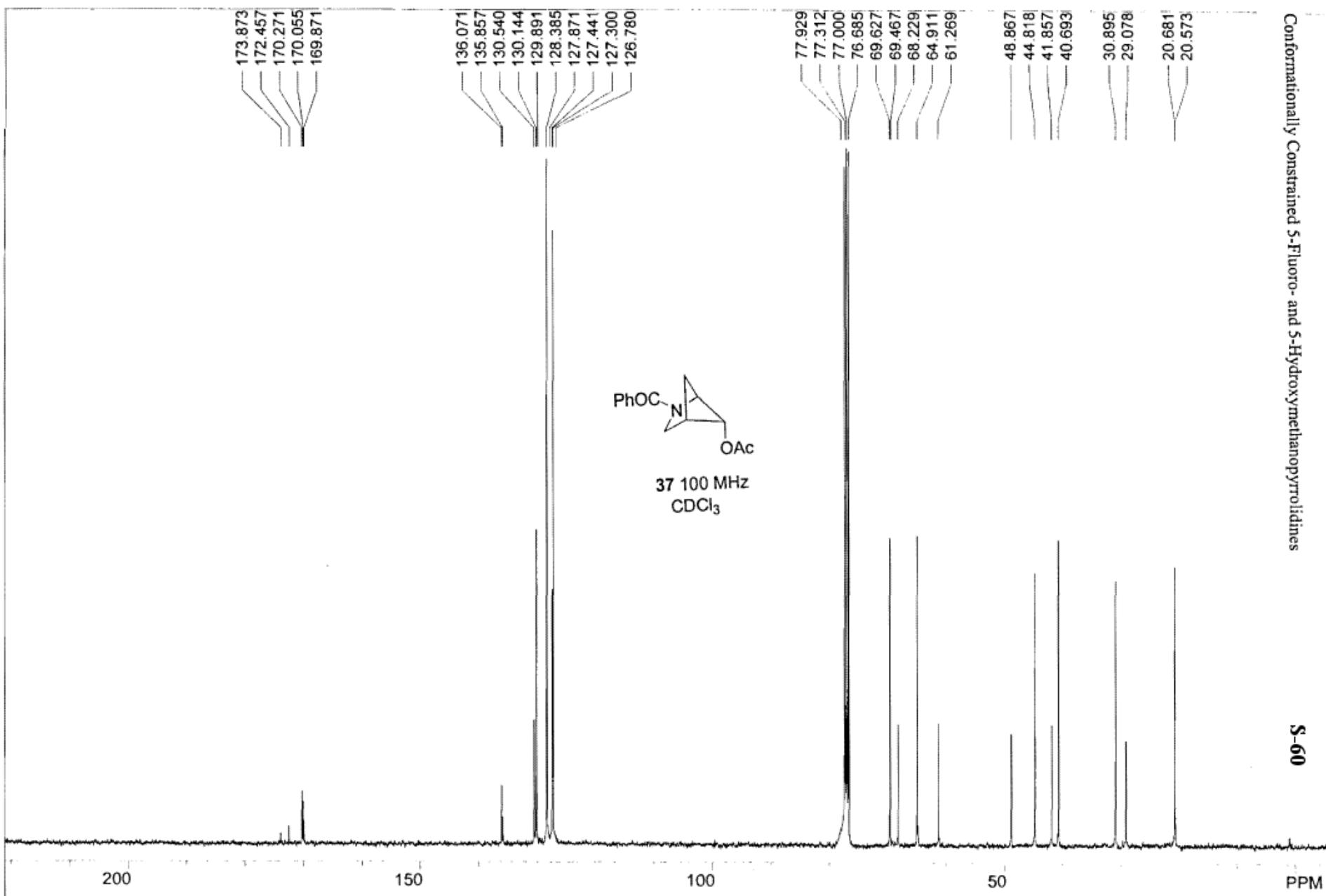


Conformationally Constrained 5-Fluoro- and 5-Hydroxymethanopyrrolidines

S-60



37 100 MHz
 CDCl_3



syn-OBz acetylation side pdt, carbonOVNTE all,

F1: 100.613

F2: 1.000

SW1: 25126

EX:

PW: 5.7 usec

OF1: 10020.2

NA: 8000

PD:

2.0 sec

USER: temple -- DATE: Nov 20 06:03:36 2008 EST (UT-5h) templ

PTSId: 32768

WinNuts - NCOPh[2.1.1] syn-OAc --C--eram-1679