

Supplementary Material

Synthesis of a Novel, anti-HIV Active Integrase Inhibitor

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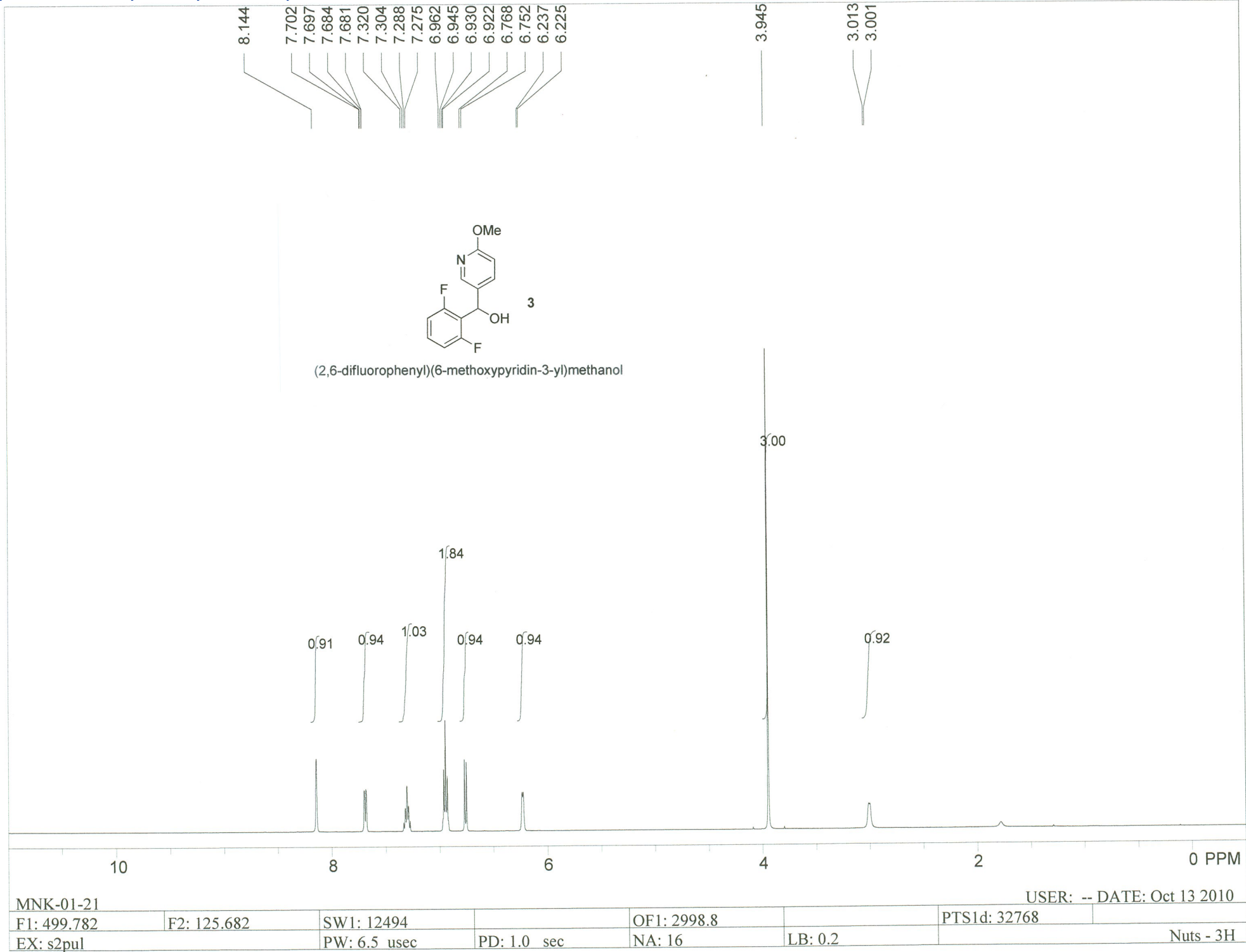
Contents

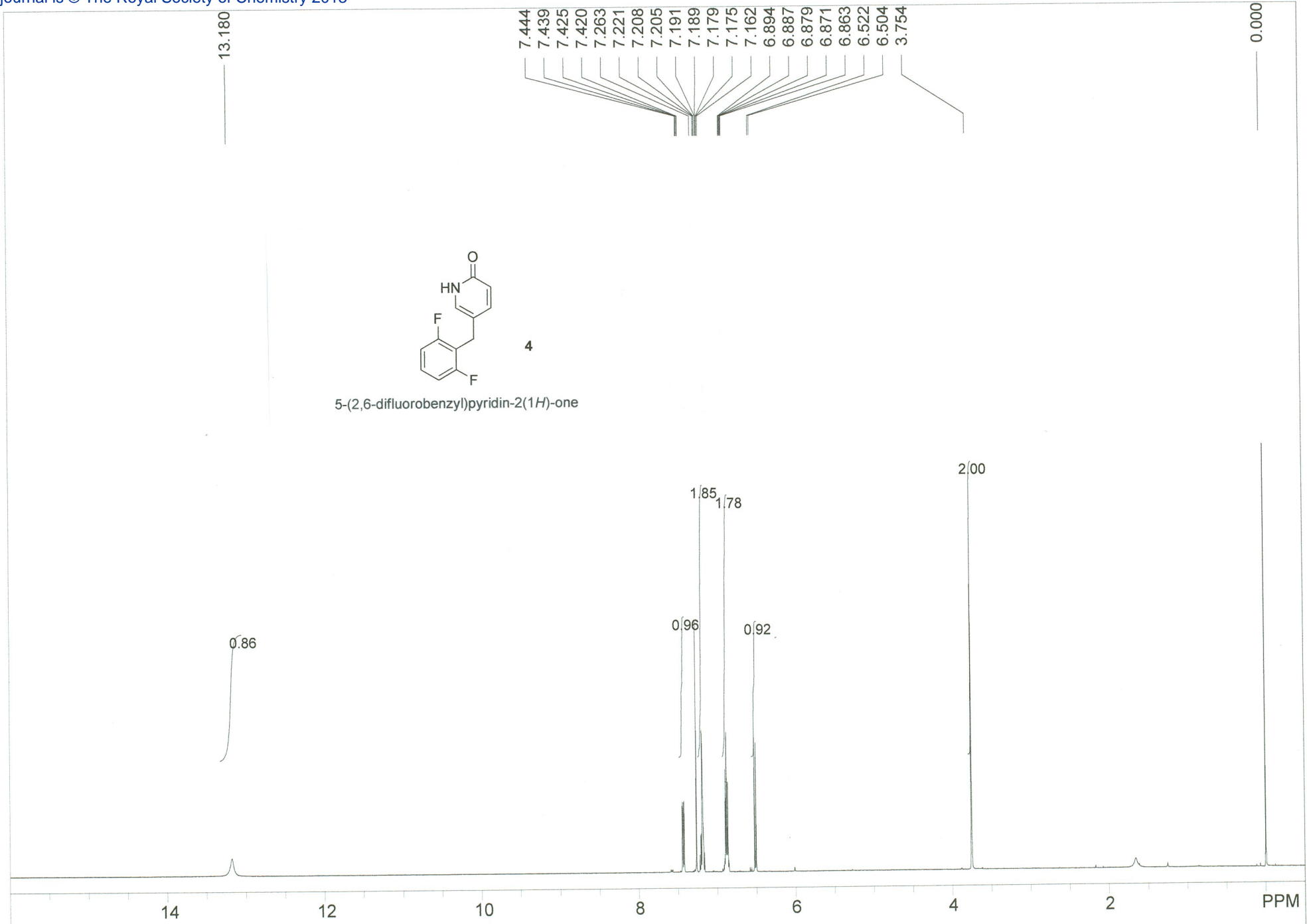
¹H and ¹³C NMR Spectra.....S2

¹H and ¹³C NMR Spectra of Intermediates **3** (in CDCl₃), **4** (in CDCl₃), **5a** (in CDCl₃),
5b (in CDCl₃), **6** (in CDCl₃), **7** (in CDCl₃), **8** (in CDCl₃ and DMSO-*d*6), **9** (in CDCl₃),
10 (DMSO-*d*6).

¹H and ¹³C NMR Spectra of Target Molecule **1** (in CDCl₃)

HPLC Chromatogram of Target Molecule **1** and Analysis Table for Purity.....S22





MNK-01-31B

F1: 499.782

F2: 125.682

SW1: 12494

PD: 1.0 sec

OF1: 2980.4

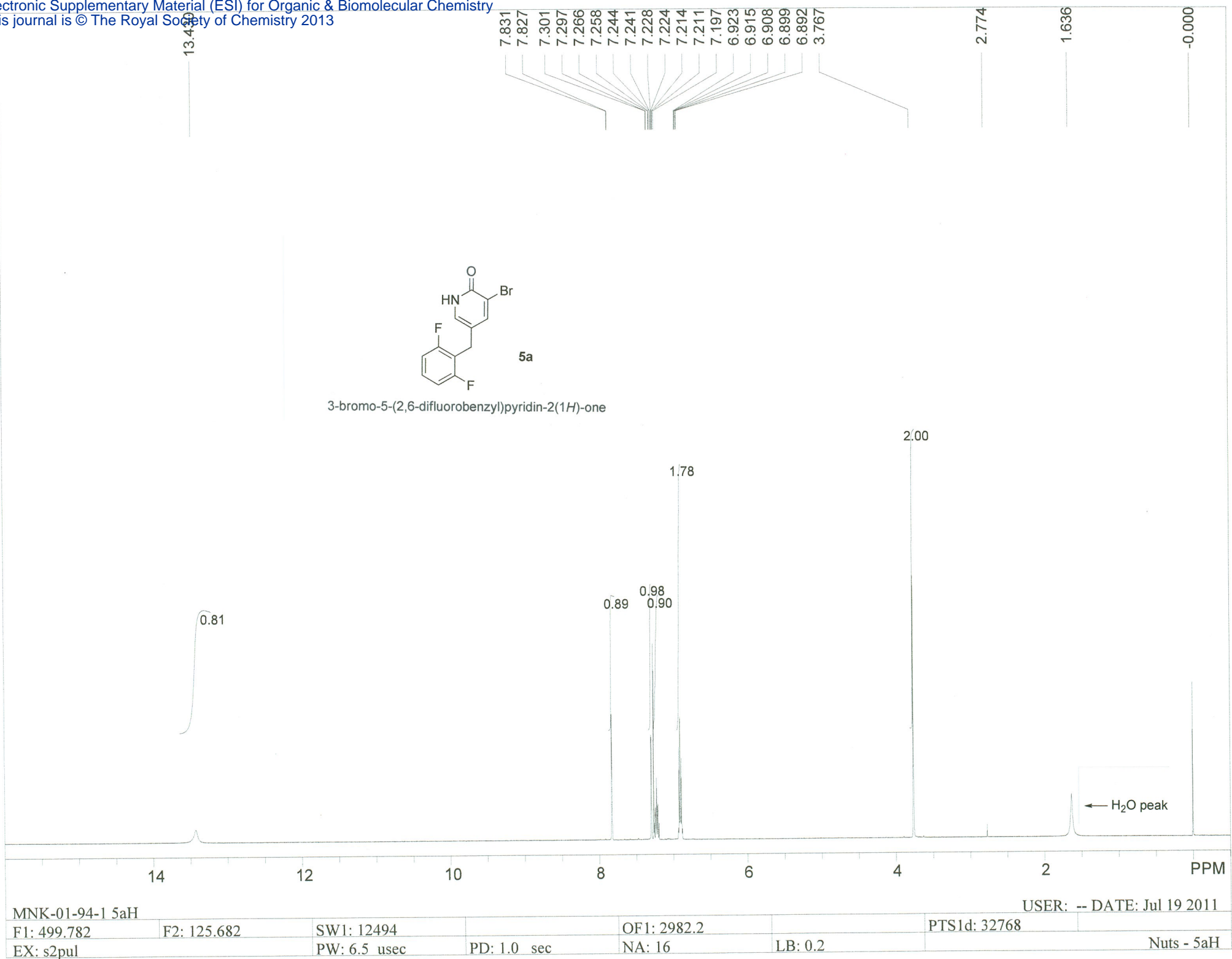
NA: 16

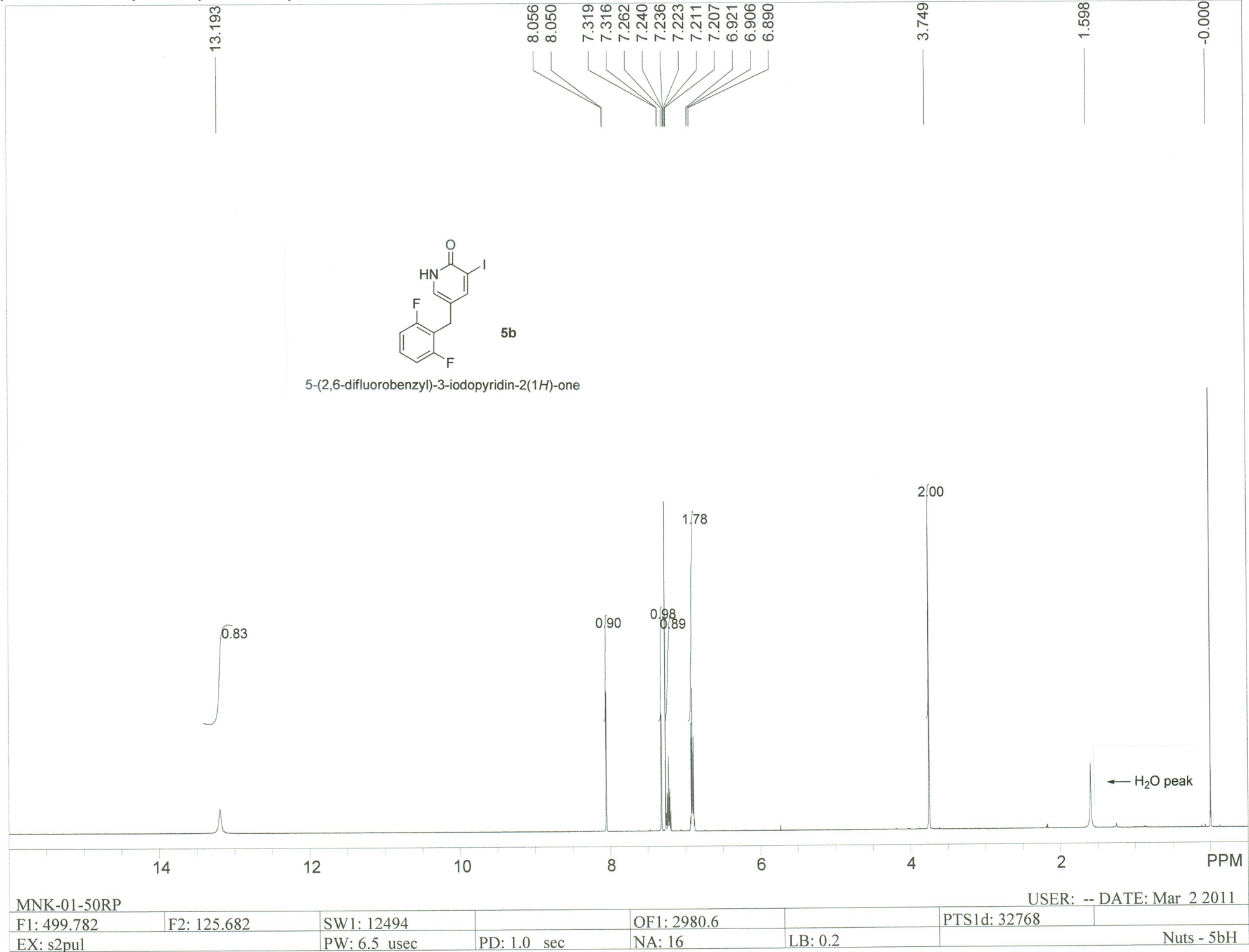
LB: 0.2

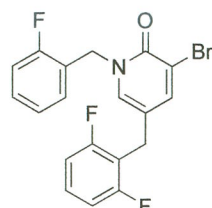
PTS1d: 32768

USER: -- DATE: Nov 19 2010

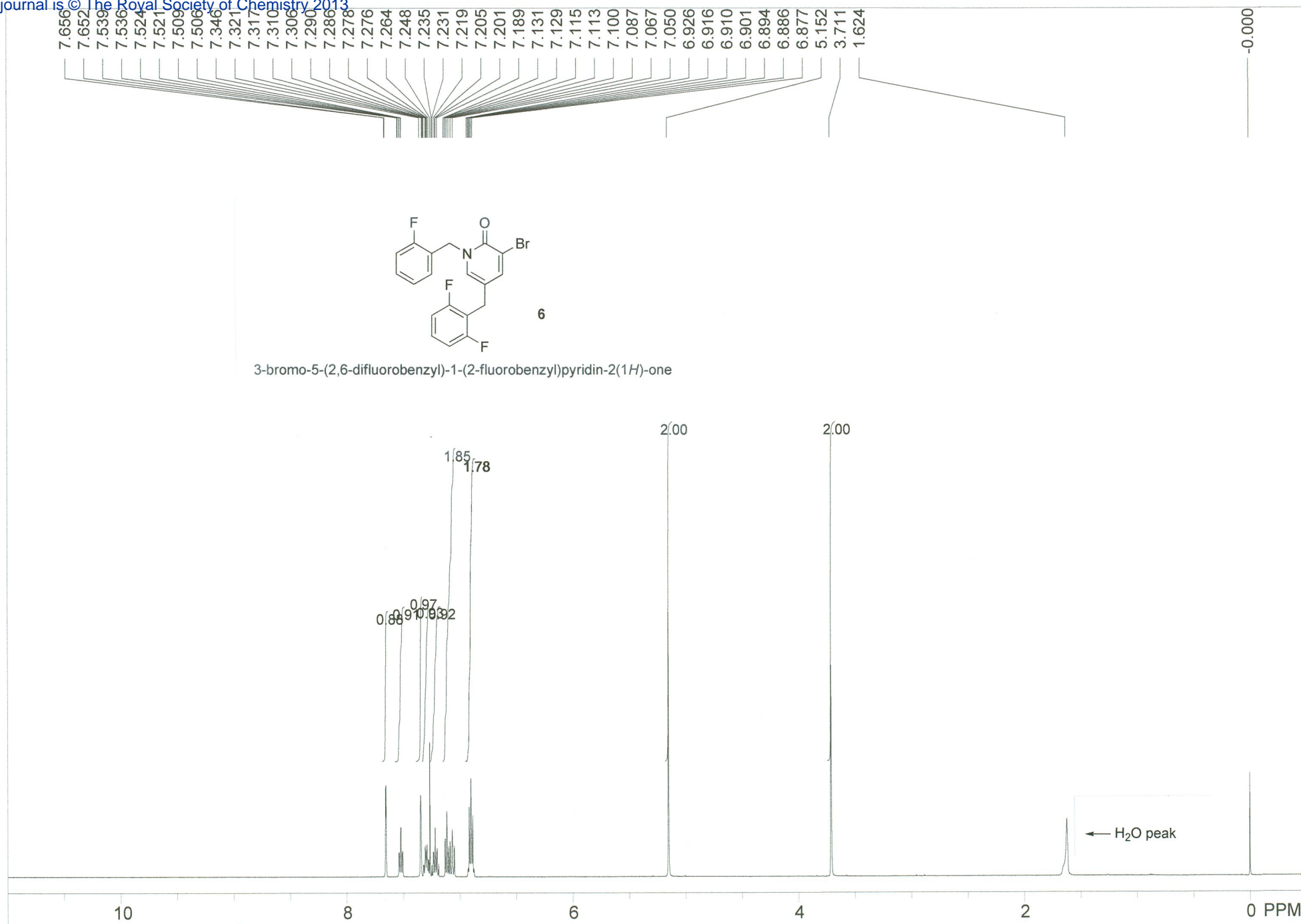
Nuts - 4H







3-bromo-5-(2,6-difluorobenzyl)-1-(2-fluorobenzyl)pyridin-2(1H)-one



MNK-01-95

USER: -- DATE: Jul 21 2011

F1: 499.782

F2: 125.682

SW1: 12494

OF1: 2981.4

PTS1d: 32768

EX: s2pul

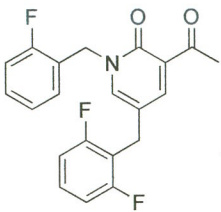
PW: 6.5 usec

PD: 1.0 sec

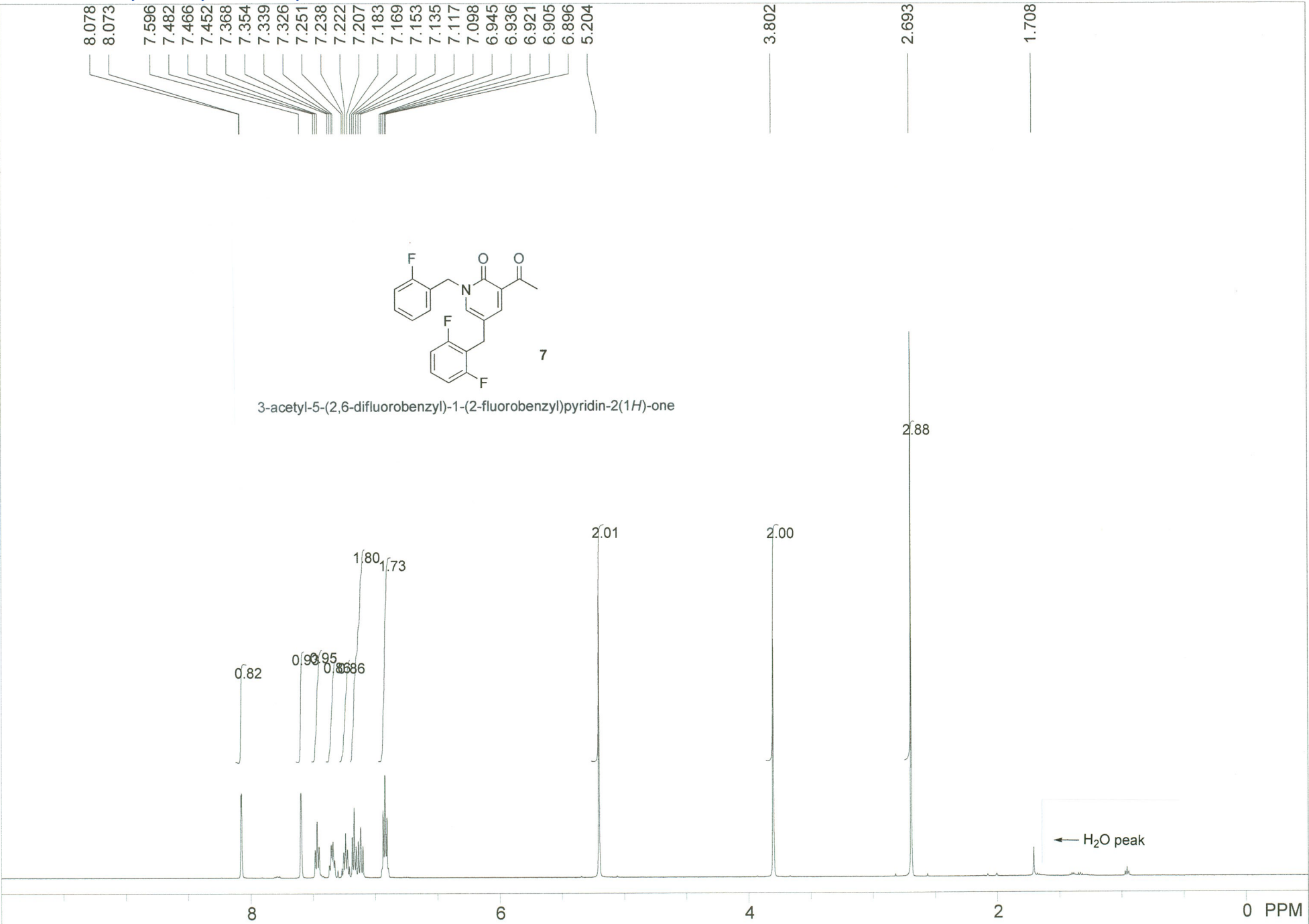
NA: 16

LB: 0.2

Nuts - 6H



3-acetyl-5-(2,6-difluorobenzyl)-1-(2-fluorobenzyl)pyridin-2(1*H*)-one



MAN_VI_22H

USER: -- DATE: Apr 8 2010

F1: 499.782

F2: 125.682

SW1: 7997

OF1: 2998.8

PTS1d: 16384

EX: s2pul

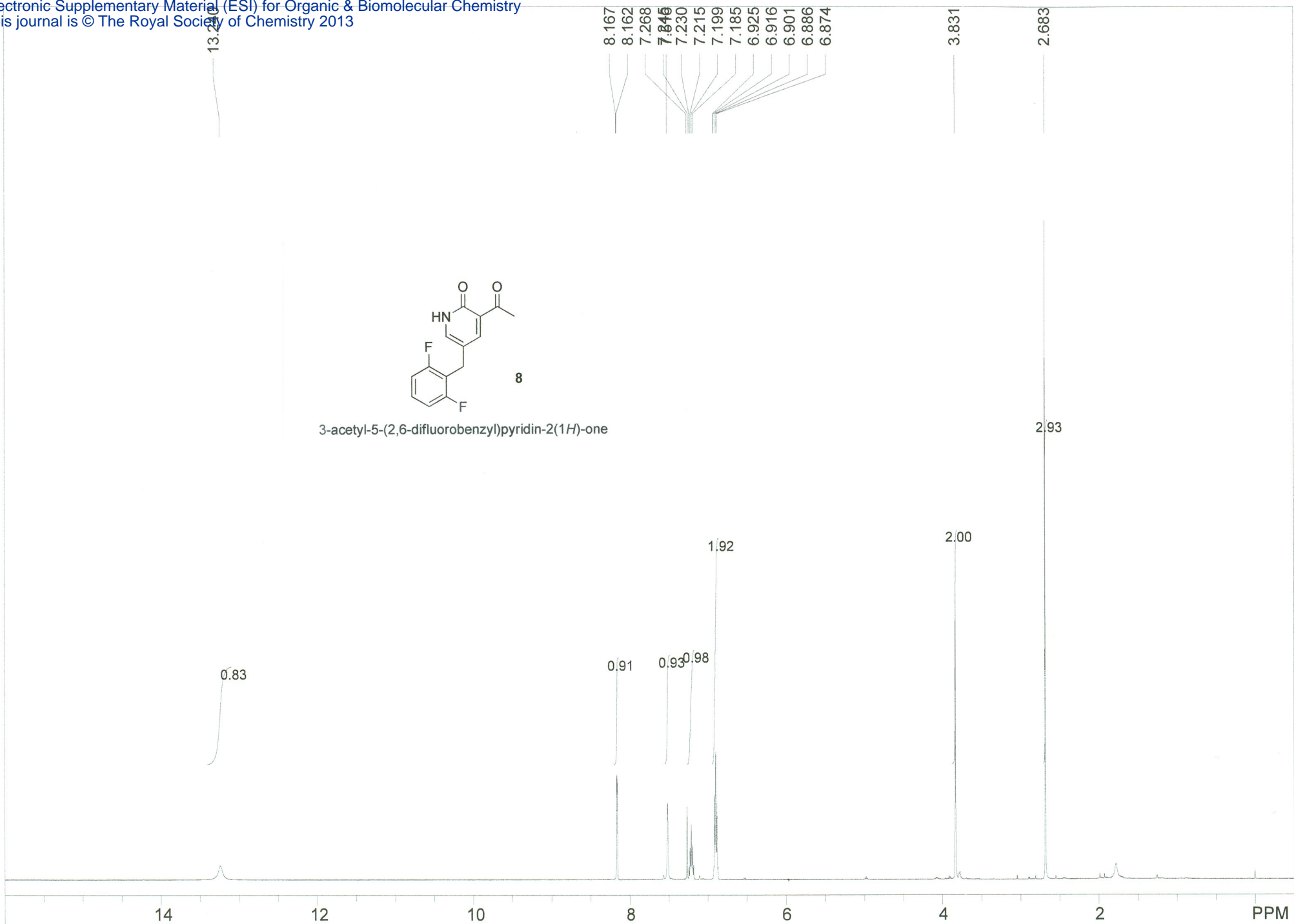
PW: 6.5 usec

PD: 1.0 sec

NA: 8

LB: 0.2

Nuts - 7malikH



MNK-01-133 8HCDCl₃

USER: -- DATE: Apr 4 2012

F1: 499.782

F2: 125.682

SW1: 12494

OF1: 2982.9

PTS1d: 32768

EX: s2pul

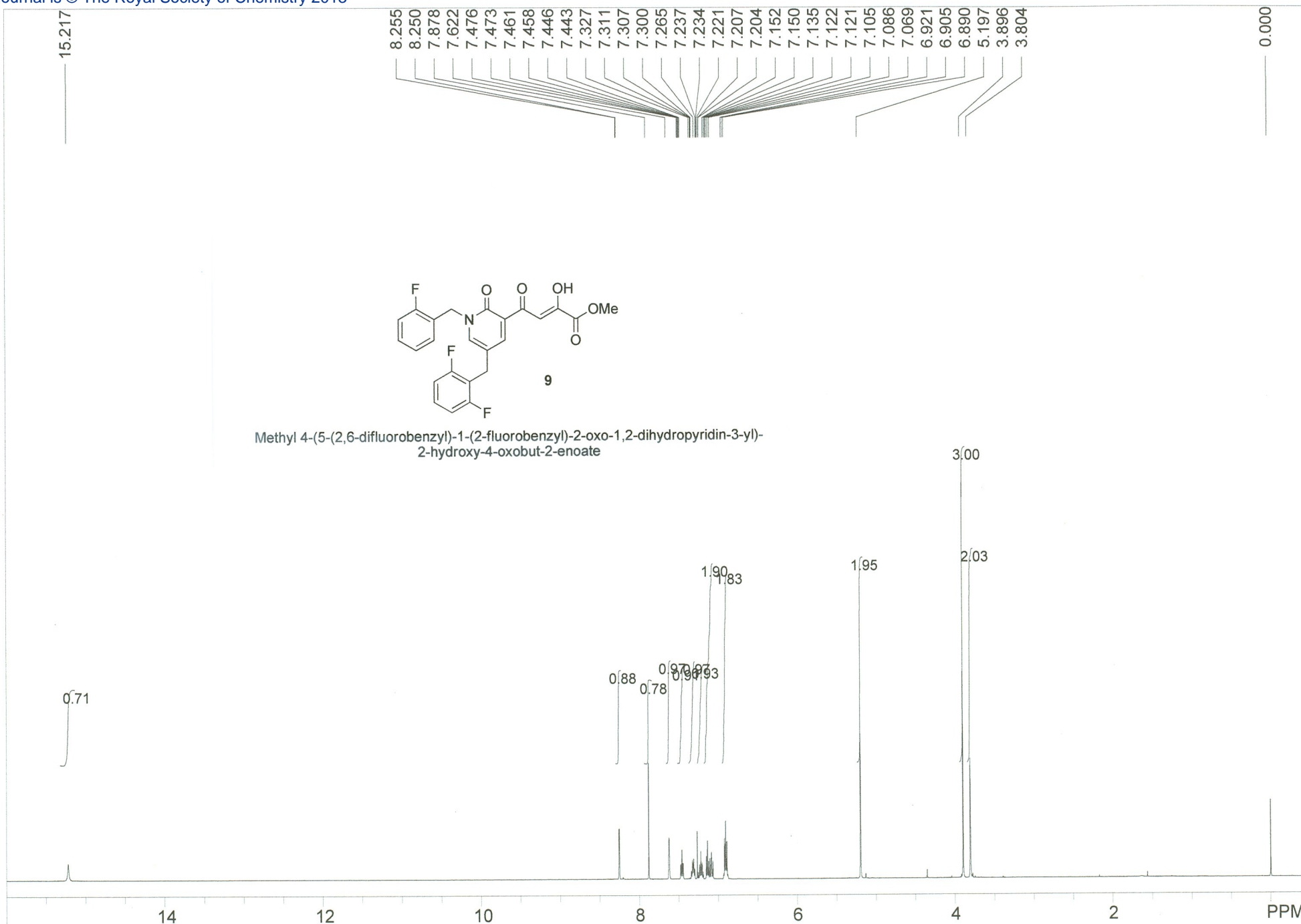
PW: 6.5 usec

PD: 1.0 sec

NA: 16

LB: 0.2

Nuts - 8HCDCl₃



MeStr 2F26diF

USER: -- DATE: Jan 24 2011

F1: 499.782

F2: 125.682

SW1: 12494

OF1: 2981.1

PTS1d: 32768

EX: s2pul

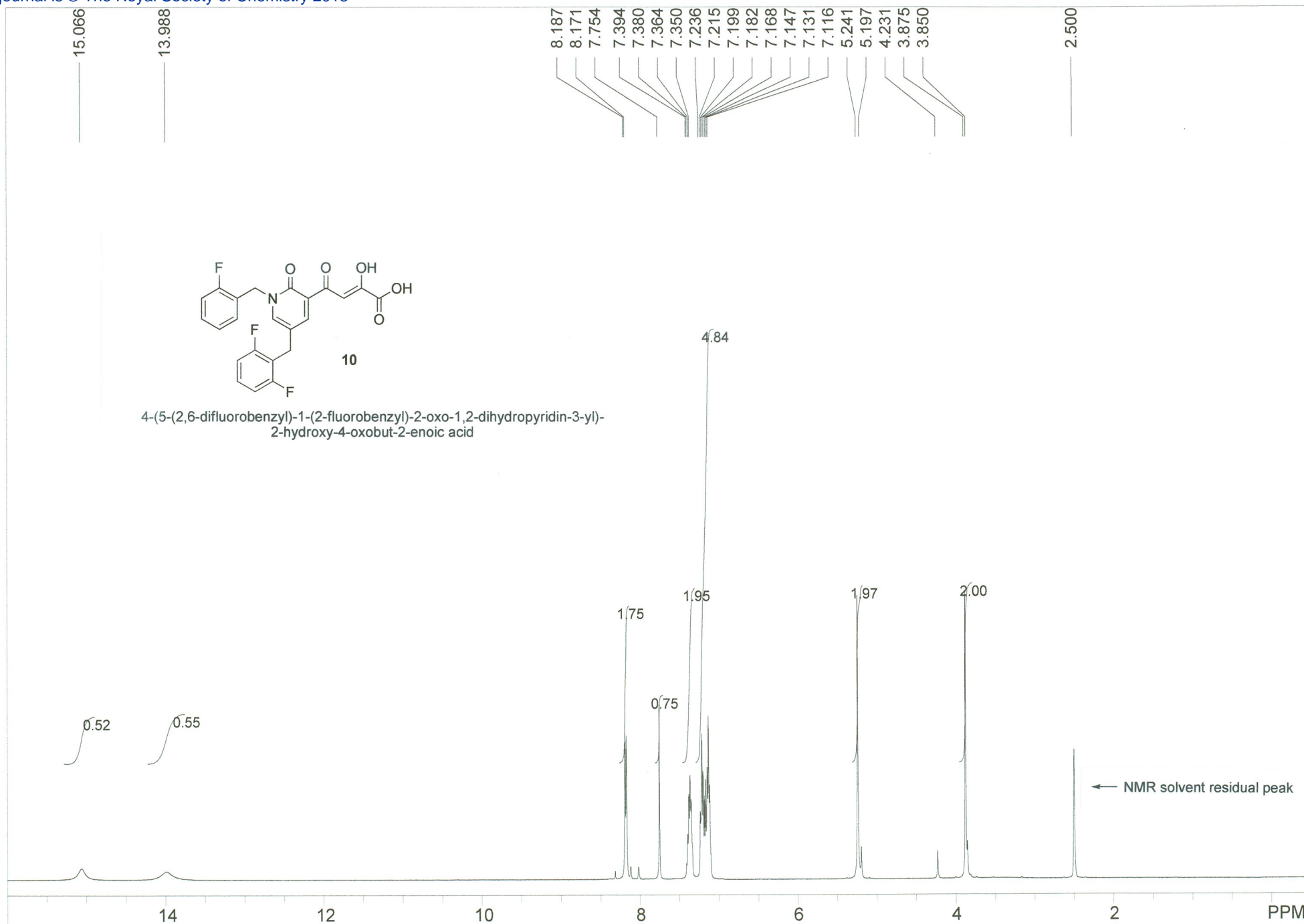
PW: 6.5 usec

PD: 1.0 sec

NA: 16

LB: 0.2

Nuts - 9H



MNK-01-40-wash2

USER: -- DATE: Jan 24 2011

F1: 499.785

F2: 125.682

SW1: 12494

OF1: 2984.9

PTS1d: 32768

EX: s2pul

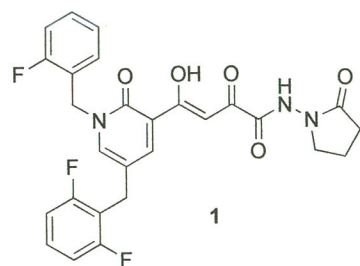
PW: 6.5 usec

PD: 1.0 sec

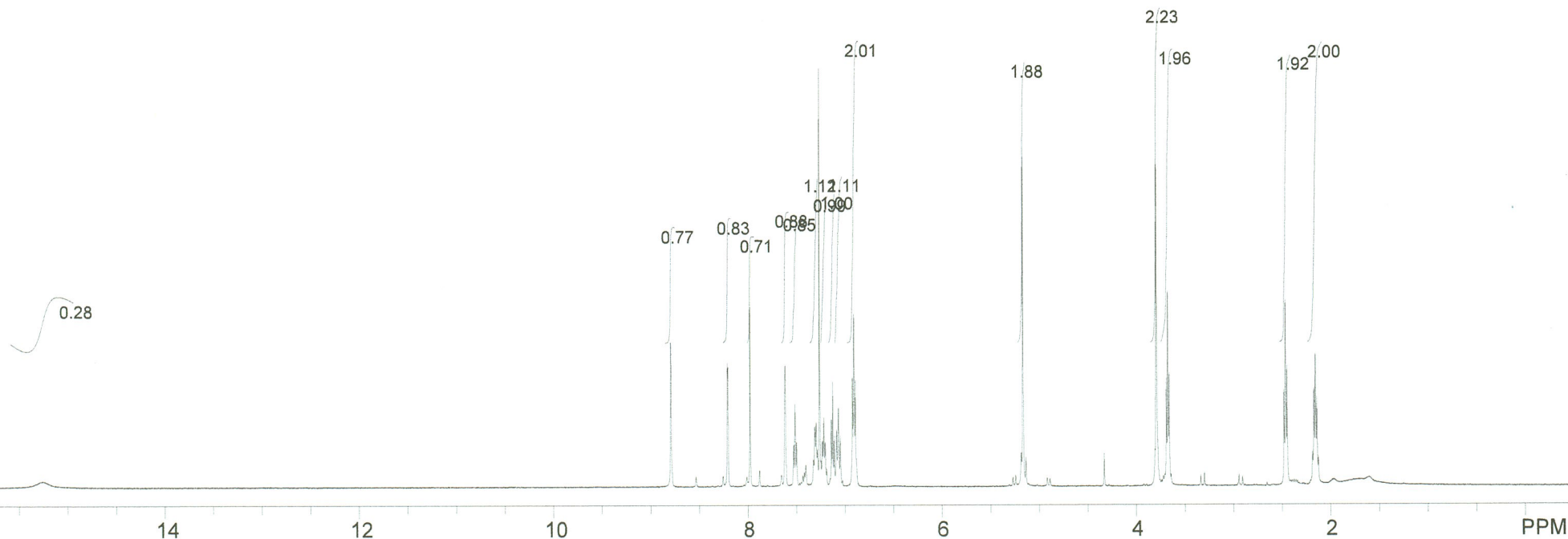
NA: 16

LB: 0.2

Nuts - 10H



1
4-(5-(2,6-difluorobenzyl)-1-(2-fluorobenzyl)-2-oxo-1,2-dihydropyridin-3-yl)-
4-hydroxy-2-oxo-N-(2-oxopyrrolidin-1-yl)but-3-enamide



196-amide

USER: -- DATE: May 4 2011

F1: 499.782

F2: 125.682

SW1: 12494

OF1: 2979.5

PTS1d: 32768

EX: s2pul

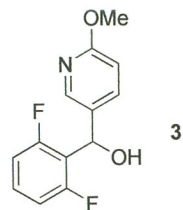
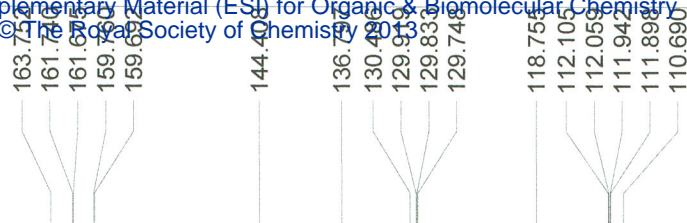
PW: 6.5 usec

PD: 1.0 sec

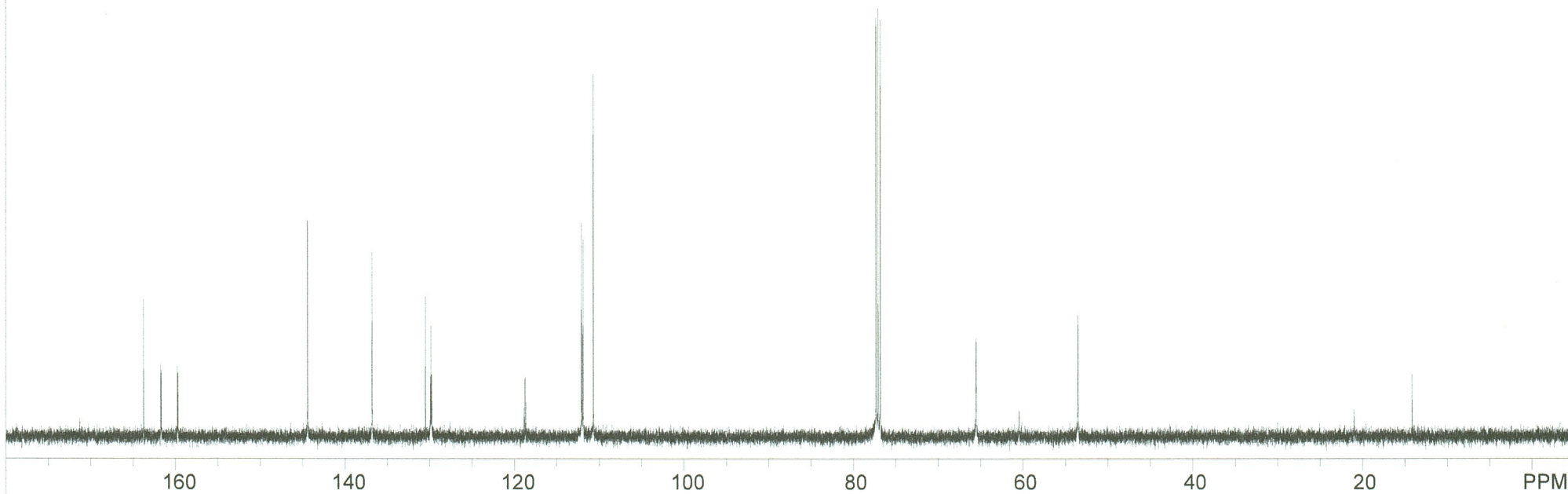
NA: 32

LB: 0.2

Nuts - 1H



(2,6-difluorophenyl)(6-methoxypyridin-3-yl)methanol



MAN_VI_14C3

USER: -- DATE: Mar 31 2010

F1: 125.683

F2: 499.782

SW1: 31422

OF1: 13823.6

PTS1d: 65536

EX: s2pul

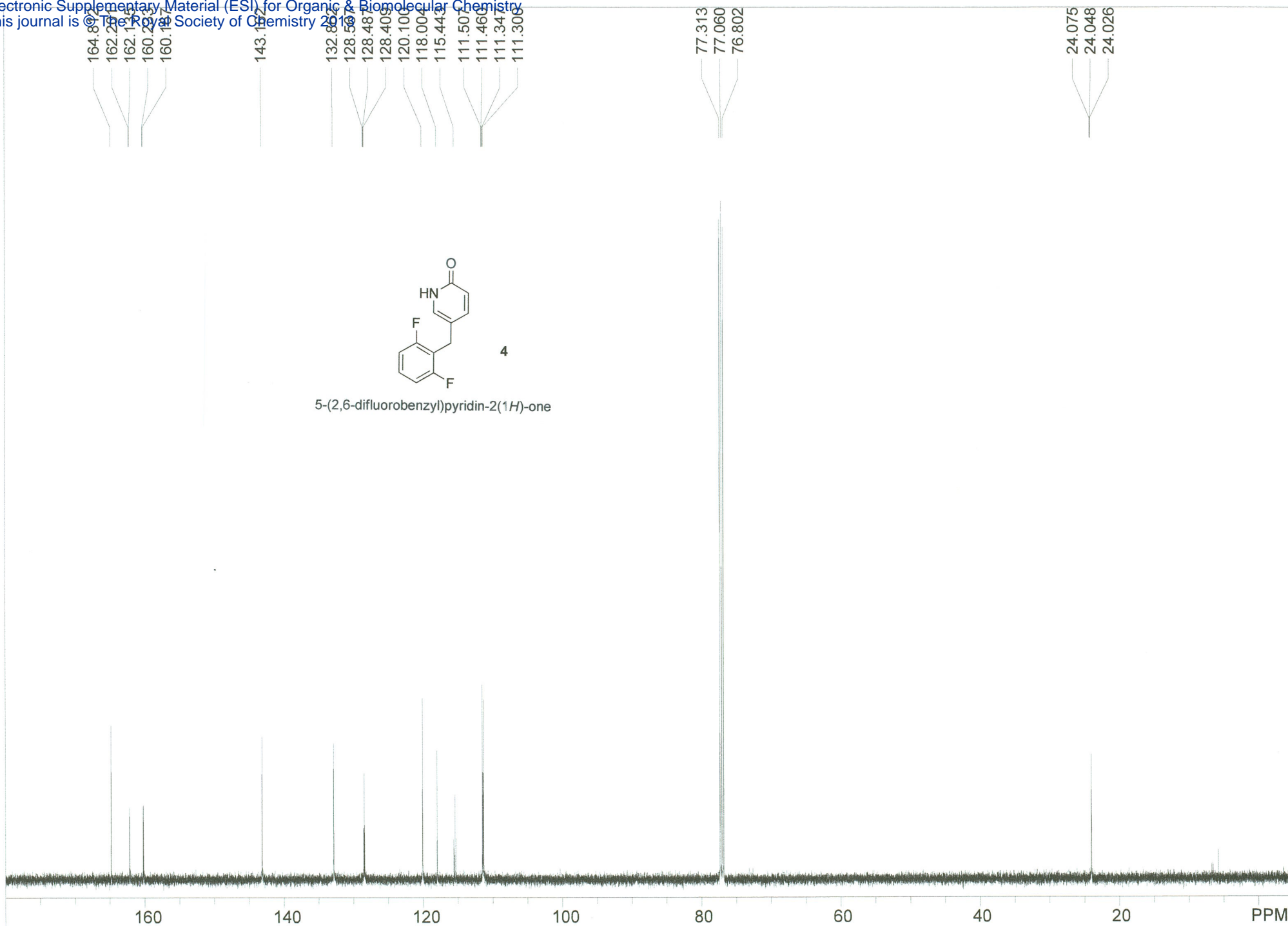
PW: 7.4 usec

PD: 2.0 sec

NA: 256

LB: 0.2

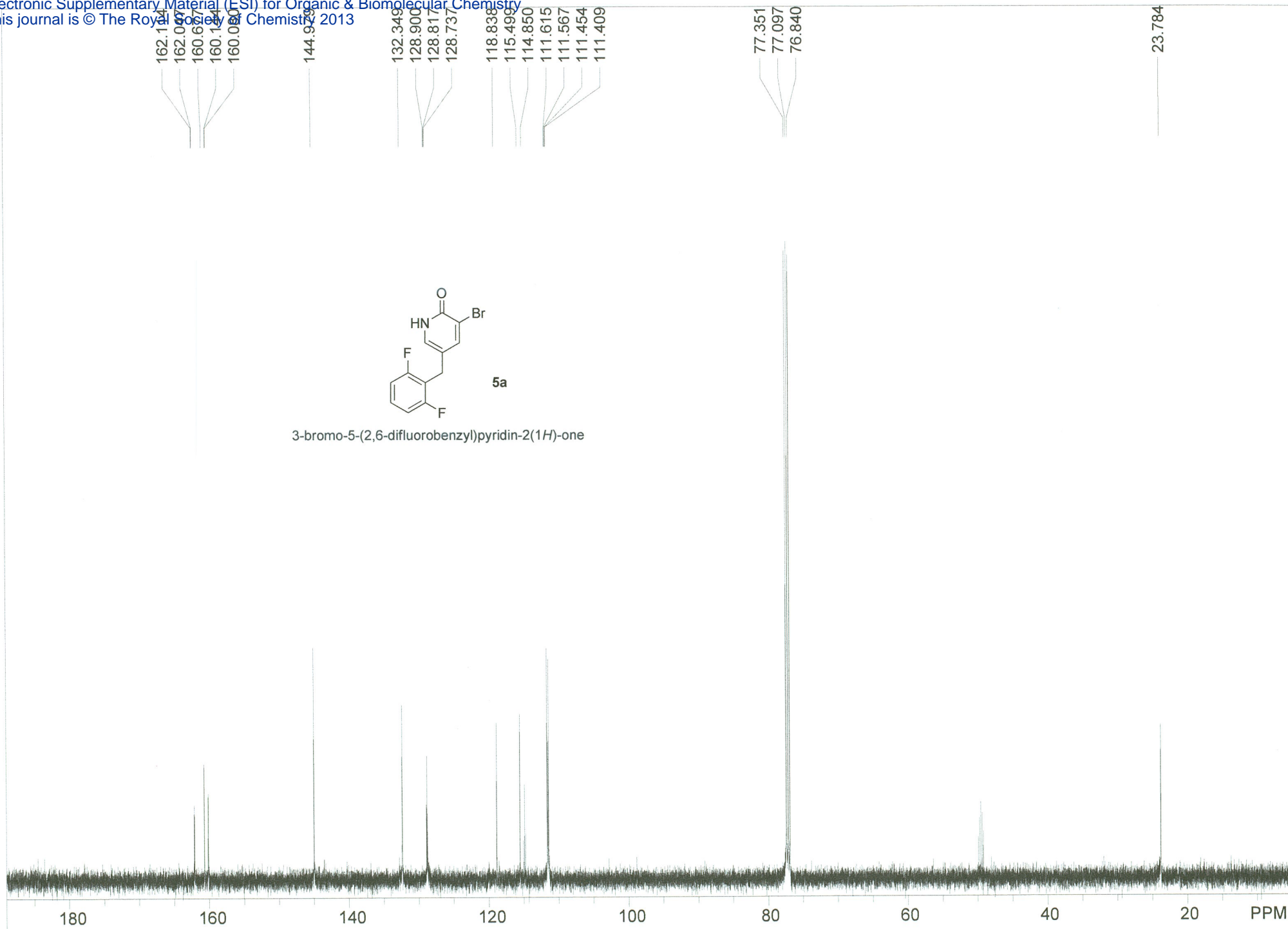
Nuts - \$CARBON_01.fid



MAN_VI_16C 4

USER: -- DATE: Apr 2 2010

F1: 125.683	F2: 499.782	SW1: 31422	OF1: 13823.6	PTS1d: 65536
EX: s2pul	PW: 7.4 usec	PD: 2.0 sec	NA: 256	LB: 0.2
Nuts - 4C				



MAN_VI_18C5aC

USER: -- DATE: Apr 5 2010

F1: 125.683

F2: 499.782

SW1: 31422

OF1: 13823.6

PTS1d: 65536

EX: s2pul

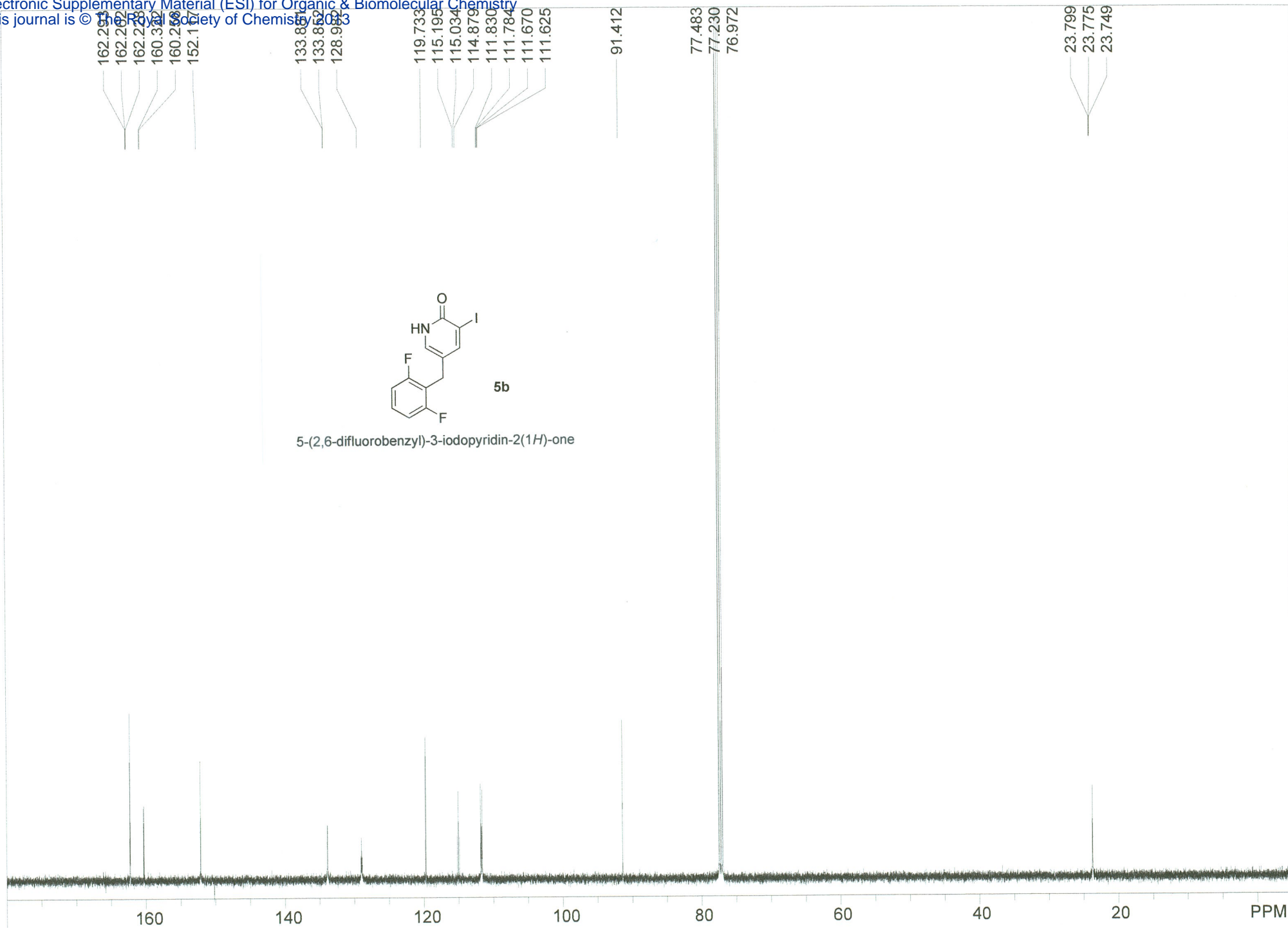
PW: 7.4 usec

PD: 2.0 sec

NA: 256

LB: 0.2

Nuts - \$CARBON_01.fid



5-(2,6-difluorobenzyl)-3-iodopyridin-2(1H)-one 5bC

USER: -- DATE: May 6 2011

F1: 125.683

F2: 499.782

SW1: 31422

OF1: 13843.6

PTS1d: 65536

EX: s2pul

PW: 7.4 usec

PD: 1.0 sec

NA: 1280

LB: 0.2

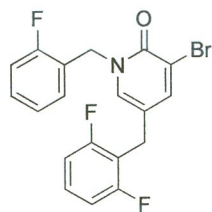
Nuts - 5bC

162.162
160.160
158.338
142.756
135.446
132.085
132.066
130.330
130.268
128.766
124.618
124.594
117.087
116.913
115.503
115.330
111.622
111.576
111.462
111.416

77.313
77.060
76.802

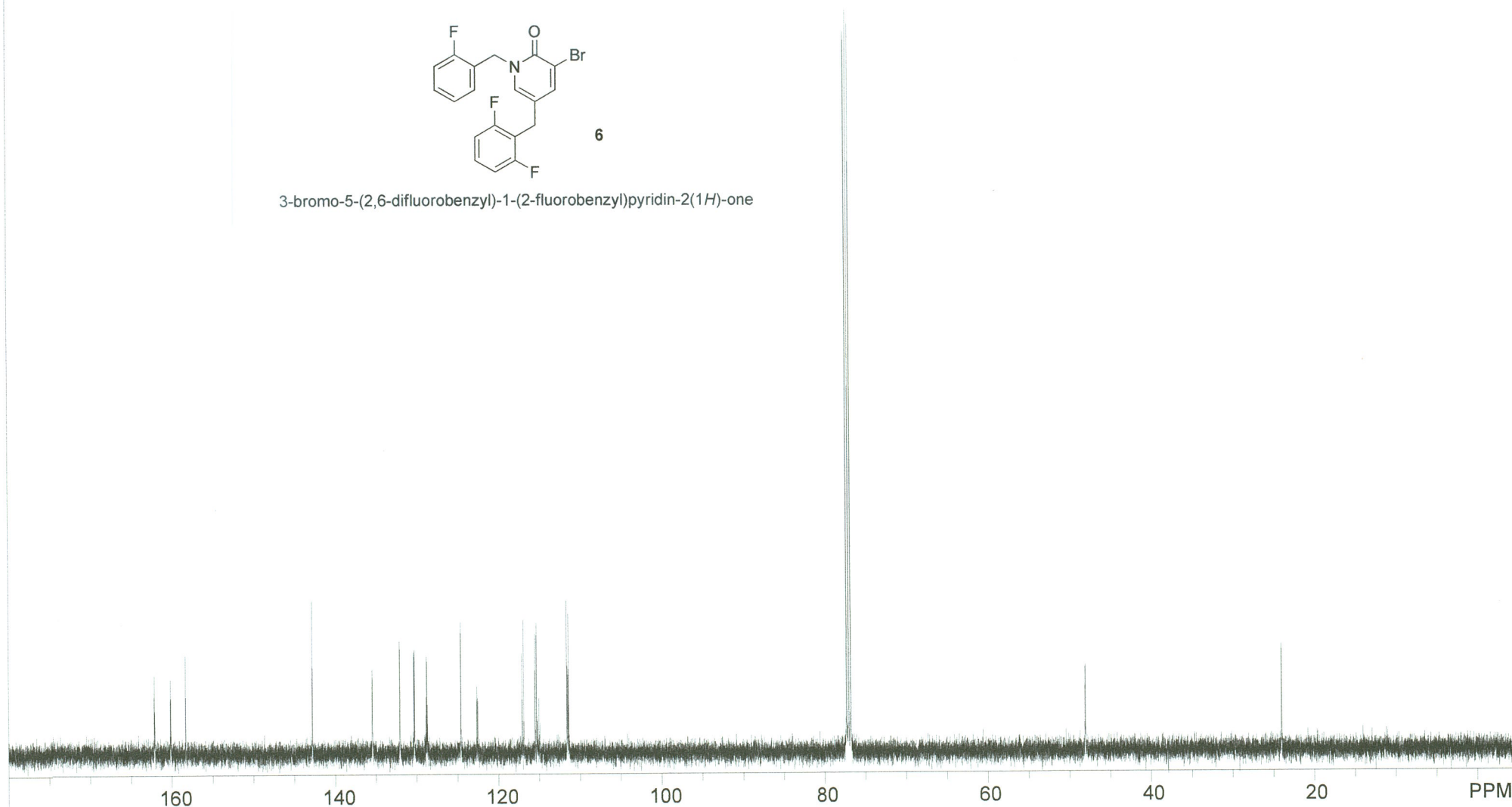
48.077
48.053

24.057
24.032



6

3-bromo-5-(2,6-difluorobenzyl)-1-(2-fluorobenzyl)pyridin-2(1H)-one



MAN_VI_20C 6C

USER: -- DATE: Apr 6 2010

F1: 125.683

F2: 499.782

SW1: 31422

OF1: 13823.6

PTS1d: 65536

EX: s2pul

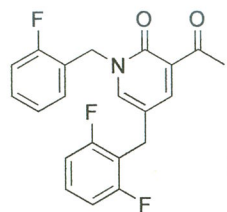
PW: 7.4 usec

PD: 2.0 sec

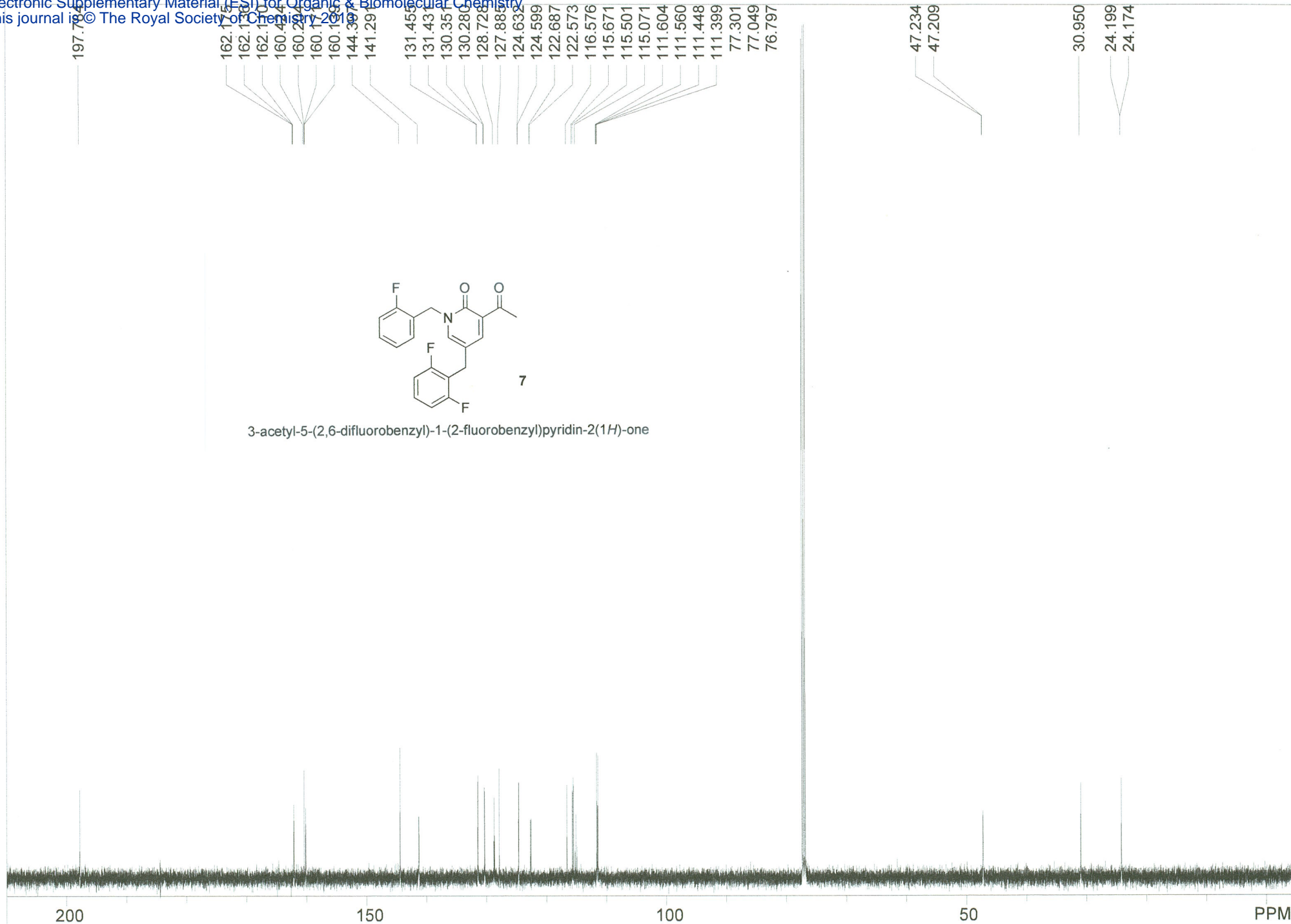
NA: 256

LB: 0.2

Nuts - \$CARBON_01.fid



3-acetyl-5-(2,6-difluorobenzyl)-1-(2-fluorobenzyl)pyridin-2(1*H*)-one



MAN_VI_22C 7C

USER: -- DATE: Apr 8 2010

F1: 125.683

F2: 499.782

SW1: 31422

OF1: 13823.6

PTS1d: 65536

EX: s2pul

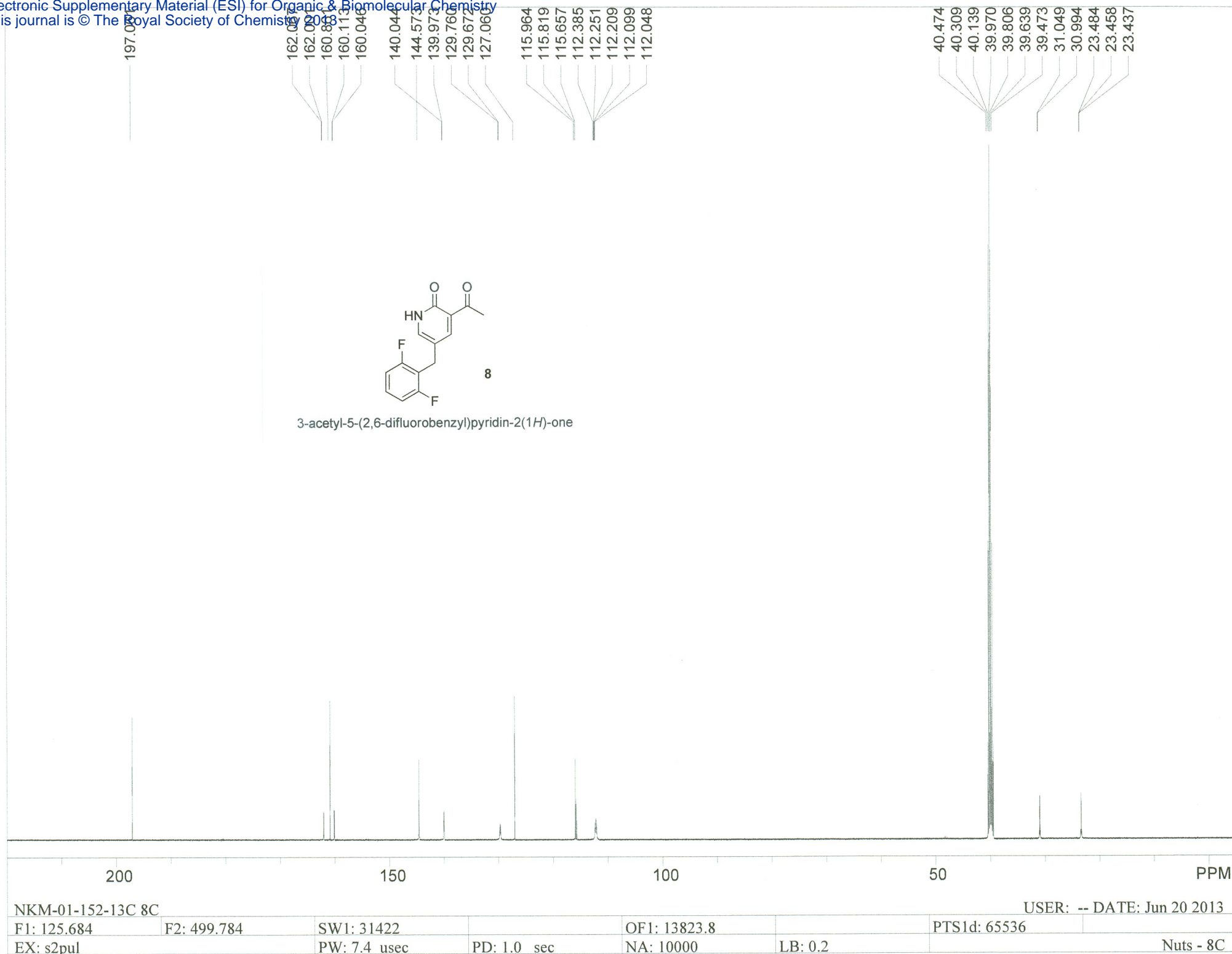
PW: 7.4 usec

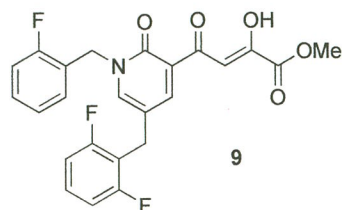
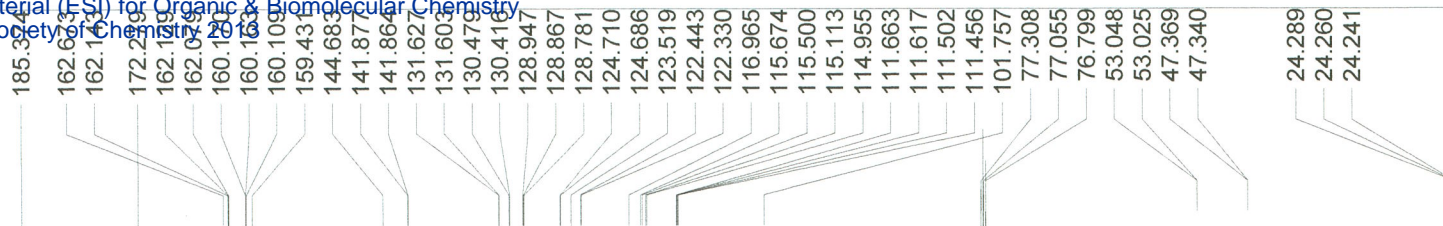
PD: 2.0 sec

NA: 256

LB: 0.2

Nuts - \$CARBON_01.fid





Methyl 4-(5-(2,6-difluorobenzyl)-1-(2-fluorobenzyl)-2-oxo-1,2-dihydropyridin-3-yl)-
2-hydroxy-4-oxobut-2-enoate

200 150 100 50 PPM

MAN_VI_24C 9C

USER: -- DATE: Apr 12 2010

F1: 125.683

F2: 499.782

SW1: 31422

OF1: 13823.6

PTS1d: 65536

EX: s2pul

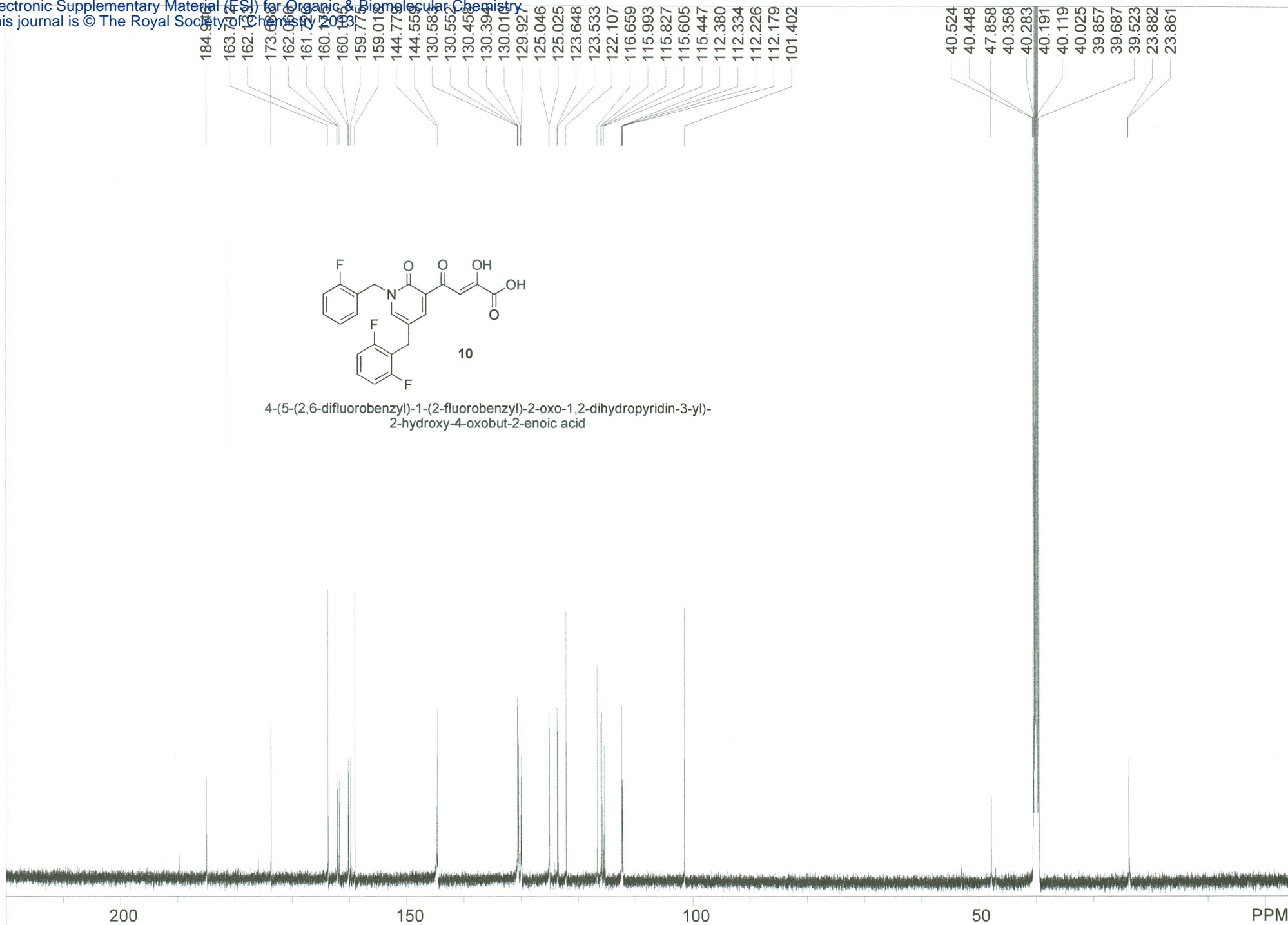
PW: 7.4 usec

PD: 2.0 sec

NA: 1000

LB: 0.2

Nuts - \$CARBON_01.fid



MAN_VI_26C 10C

USER: -- DATE: Apr 14 2010

F1: 125.684

F2: 499.784

SW1: 31422

OF1: 13823.8

PTS1d: 65536

EX: s2pul

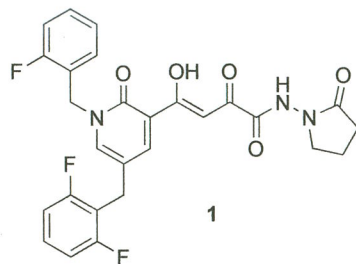
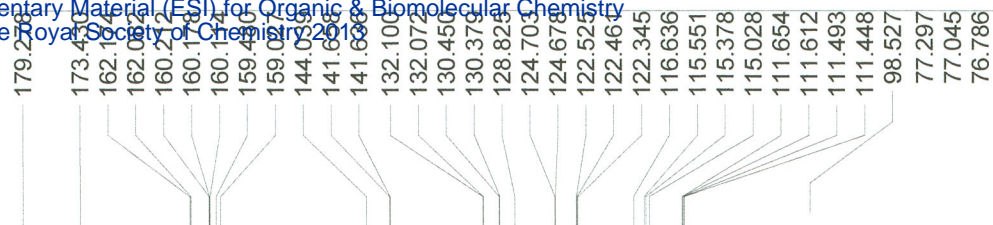
PW: 7.4 usec

PD: 2.0 sec

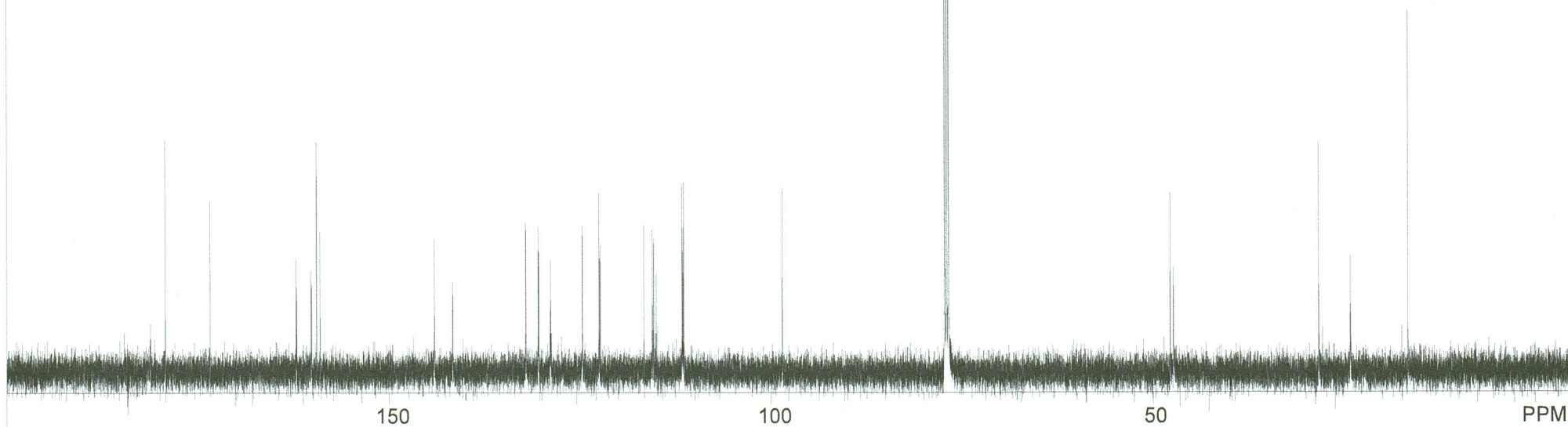
NA: 5000

LB: 0.2

Nuts - \$CARBON_01.fid



4-(5-(2,6-difluorobenzyl)-1-(2-fluorobenzyl)-2-oxo-1,2-dihydropyridin-3-yl)-
4-hydroxy-2-oxo-*N*-(2-oxopyrrolidin-1-yl)but-3-enamide



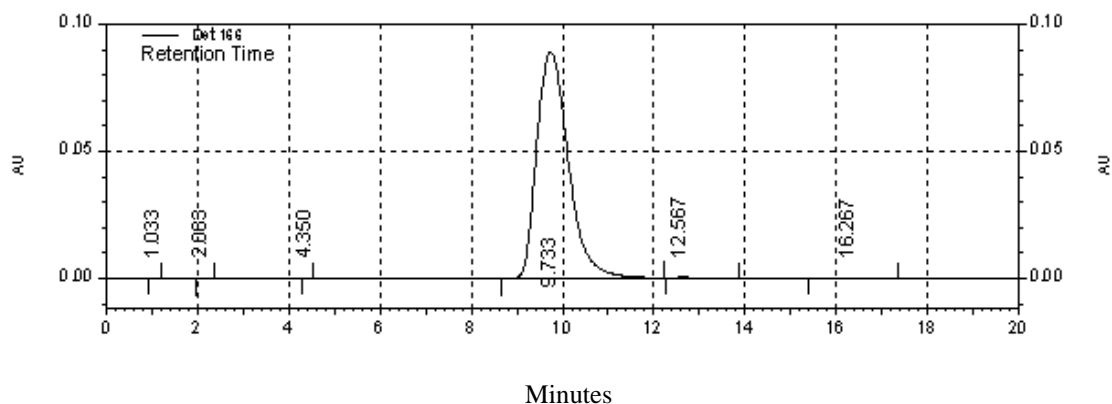
MAN_VI_30HC 1C

USER: -- DATE: Apr 19 2010

F1: 125.683	F2: 499.782	SW1: 31422	OF1: 13823.6	PTS1d: 65536
EX: s2pul	PW: 7.4 usec	PD: 2.0 sec	NA: 1200	LB: 0.2
Nuts - 1C				

HPLC Chromatogram of Target Molecule 1 and Analysis Table for Purity

Analysis was done by reversed-phase HPLC on an analytical Delta Pak C18 column with a mobile phase of (A) 10 mM potassium phosphate buffer (pH 6.5) and (B) acetonitrile: 0-2 min, 30 % B, 2- 8 min, 30-60 % B, 8- 18 min, 60 % B. The flow rate was 1.5 mL/min, with UV detection at 360 nm. The retention time for compound **1** was 9.73 min and the purity was 99.61 %.



Time	Area	Area %	Height	Height %
1.033	401	0.01	48	0.05
2.083	1363	0.03	121	0.13
4.350	275	0.01	31	0.03
9.733	4296146	99.61	89112	99.36
12.567	8878	0.21	252	0.28
16.267	5695	0.13	118	0.13