

Design, Synthesis, Docking, ADMET and Anticancer Evaluations of *N*-Alkyl Substituted Iodoquinazoline Derivatives as Dual VEGFR-2 and EGFR Inhibitors

Marwa Alsulaimany¹, Khaled El-Adl^{2,3,*}, Ahmed K. B. Aljohani⁴, Hussam Y. Alharbi⁵, Omar M. Alatawi⁶, Majed S. Aljohani⁵, Ahmed El-morsy⁷, Sara A. Almadani⁸, Abdulrahman A. Alsimaree⁹, Samir A. Salama¹⁰, Doaa E. Keshek^{11,12}, and Abeer A. Mohamed^{3,13}

¹College of Pharmacy, Department of Pharmacognosy & Pharmaceutical Chemistry, Taibah University, Medina, 42353, Saudi Arabia

²Pharmaceutical Medicinal Chemistry and Drug Design Department, Faculty of Pharmacy (Boys), Al-Azhar University, Nasr City 11884, Cairo, Egypt

³Chemistry Department, Faculty of Pharmacy, Heliopolis University for Sustainable Development, Cairo, Egypt

⁴Pharmacognosy and Pharmaceutical Chemistry Department, College of Pharmacy, Taibah University, Al-Madinah Al-Munawarah 41477, Saudi Arabia

⁵Department of Chemistry, Faculty of Science, Taibah University, Yanbu, Saudi Arabia

⁶Department of Chemistry, Faculty of Science, University of Tabuk, Tabuk, 47512, Saudi Arabia

⁷Pharmaceutical Chemistry Department, College of Pharmacy, The Islamic University, Najaf, Iraq

⁸Department of Pharmacology and Toxicology, College of Pharmacy, Taibah University, Medina 42353, Saudi Arabia

⁹Department of Basic Science (Chemistry), College of Science and Humanities, Shaqra University, Afif, Saudi Arabia

¹⁰ Division of Biochemistry, Department of Pharmacology, College of Pharmacy, Taif University, P.O. Box 11099, Taif 21944, Kingdom of Saudi Arabia.

¹¹Department of biology, Jumum College University, Umm Al-Qura University, P.O Box7388, Makkah 21955, Sudia Arabia

¹²Agriculture Genetic Engineering Research Institute (AGERI), Agriculture Research Centre, Giza, Egypt

¹³Egyptian Drug Authority (EDA) 51 Wezaret El-Zeraa St, Dokki, Giza, A. R. Egypt

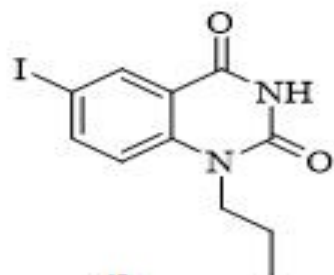
Corresponding Author:

Khaled El-Adl, eladlkhaled74@yahoo.com; eladlkhaled74@azhar.edu.eg; khaled.eladl@hu.edu.eg

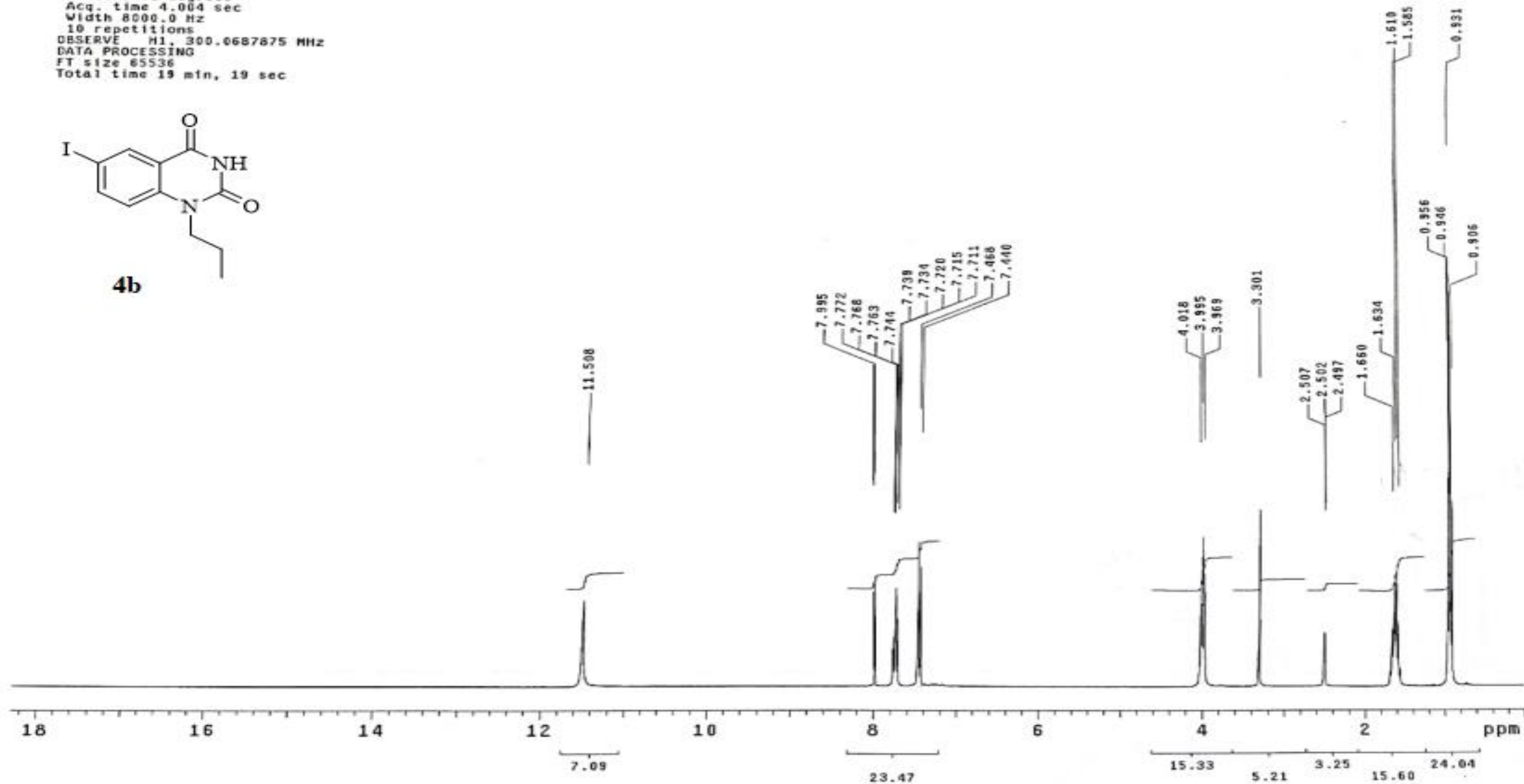
Pulse Sequence: s2pu1

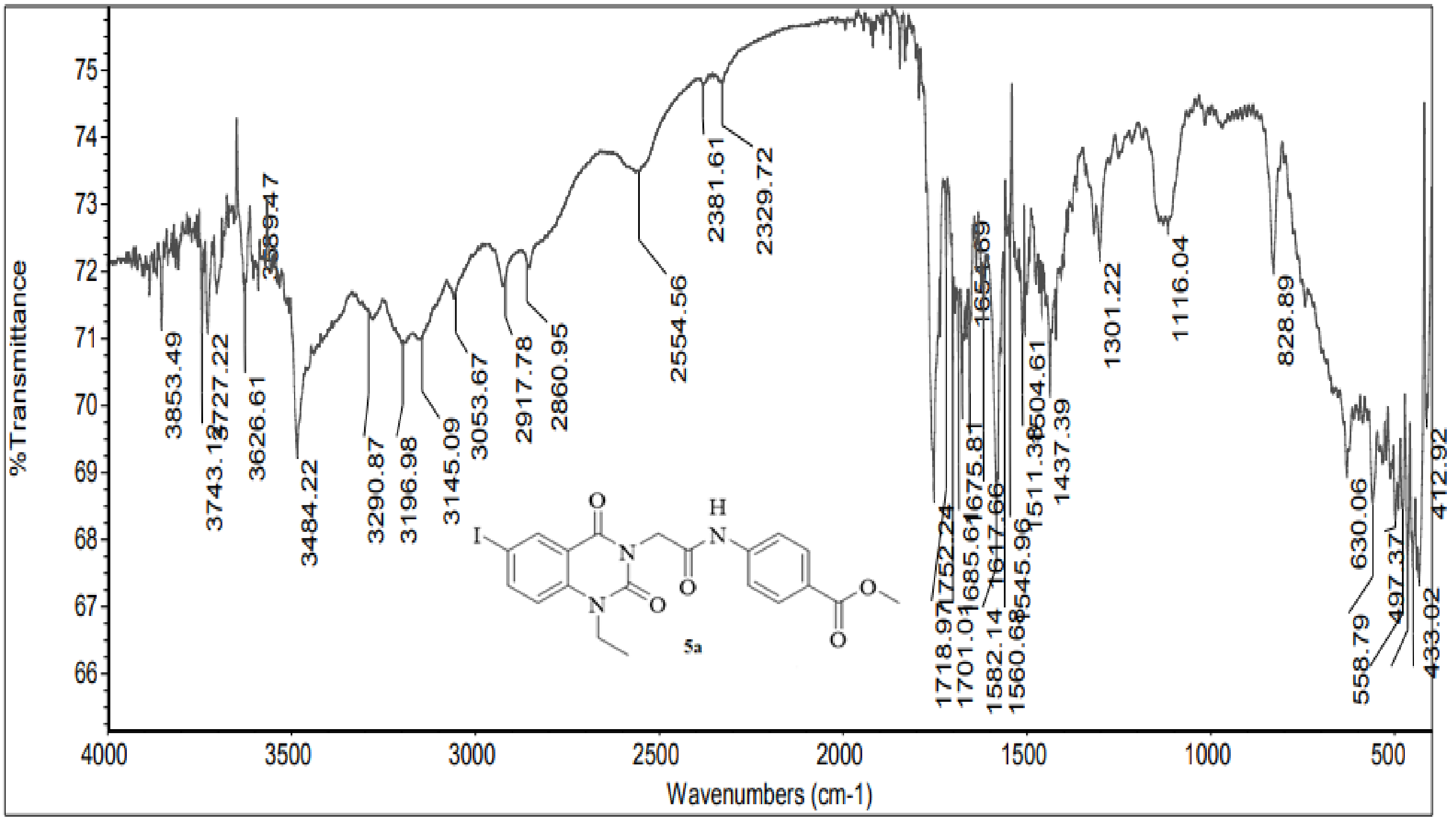
Solvent: DMSO
Temp. 30.0 C / 303.1 K
Mercury-30088 "NMR300"

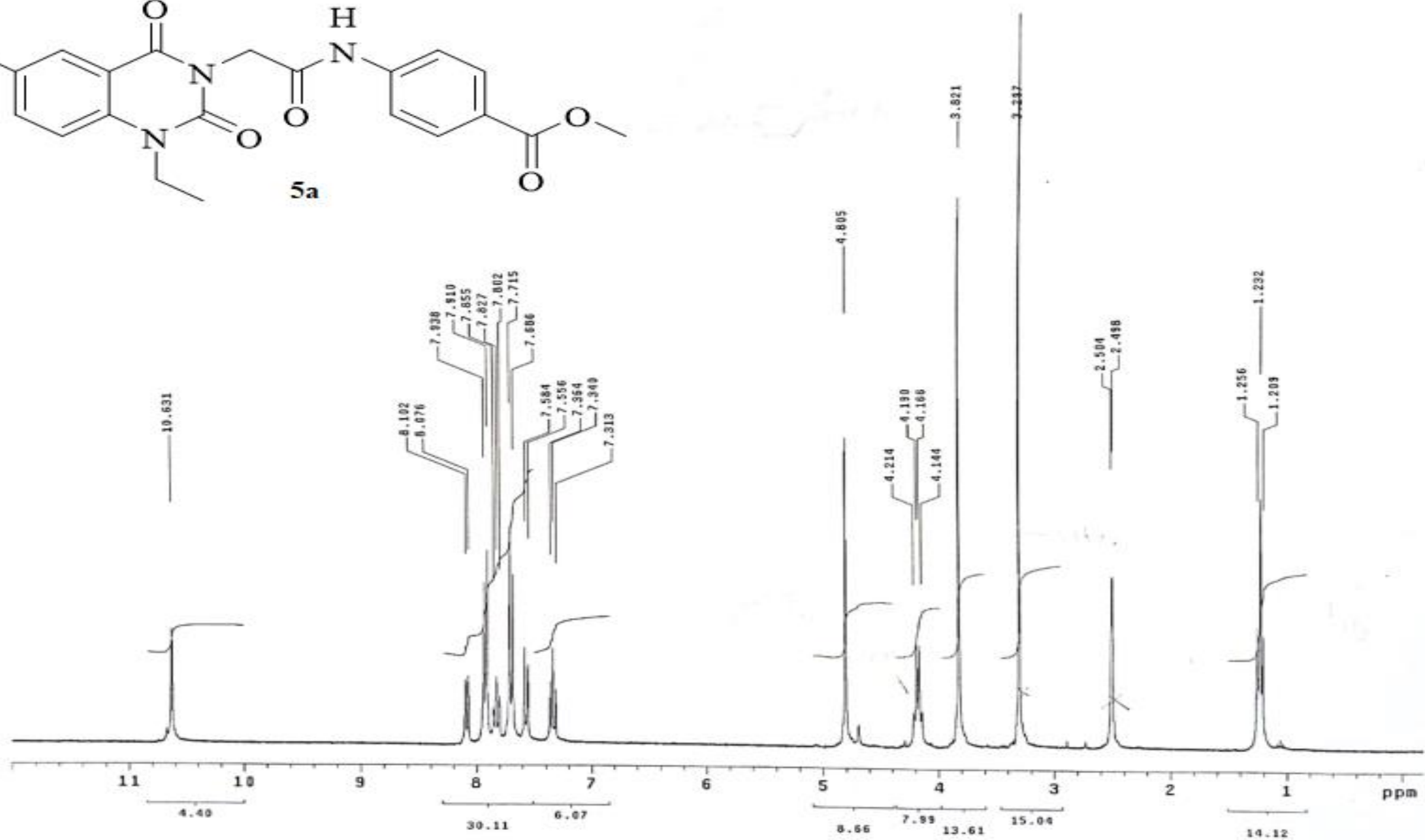
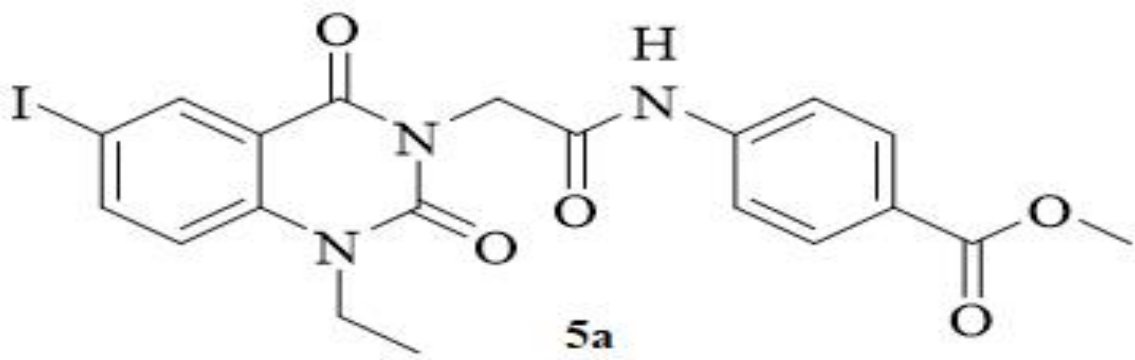
Relax. delay 1.000 sec
Pulse 74.1 degrees
Acq. time 4.004 sec
Width 8000.0 Hz
10 repetitions
OBSERVE H1, 300.0687875 MHz
DATA PROCESSING
FT size 65536
Total time 19 min, 19 sec



4b

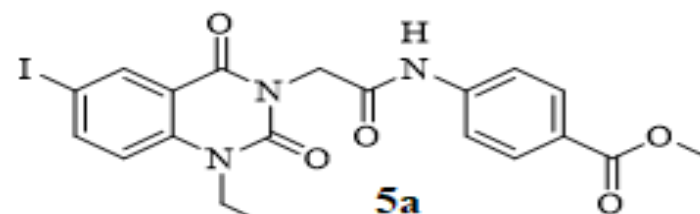








Current Data Parameters
NAME K-9
EXPNO 2
PROCNO 1

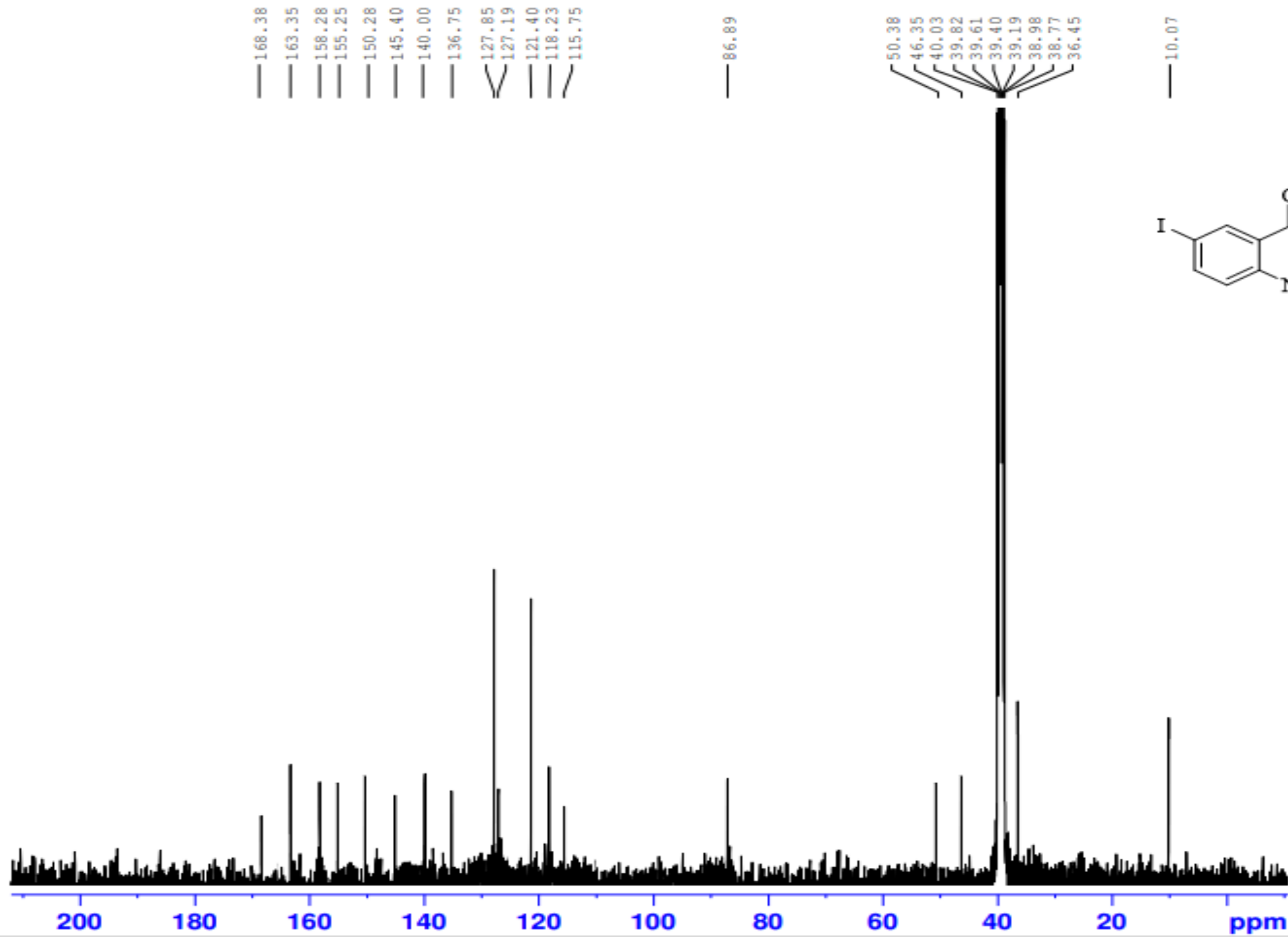


DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 205.37
DW 20.800 usec
DE 6.50 usec
TE 300.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

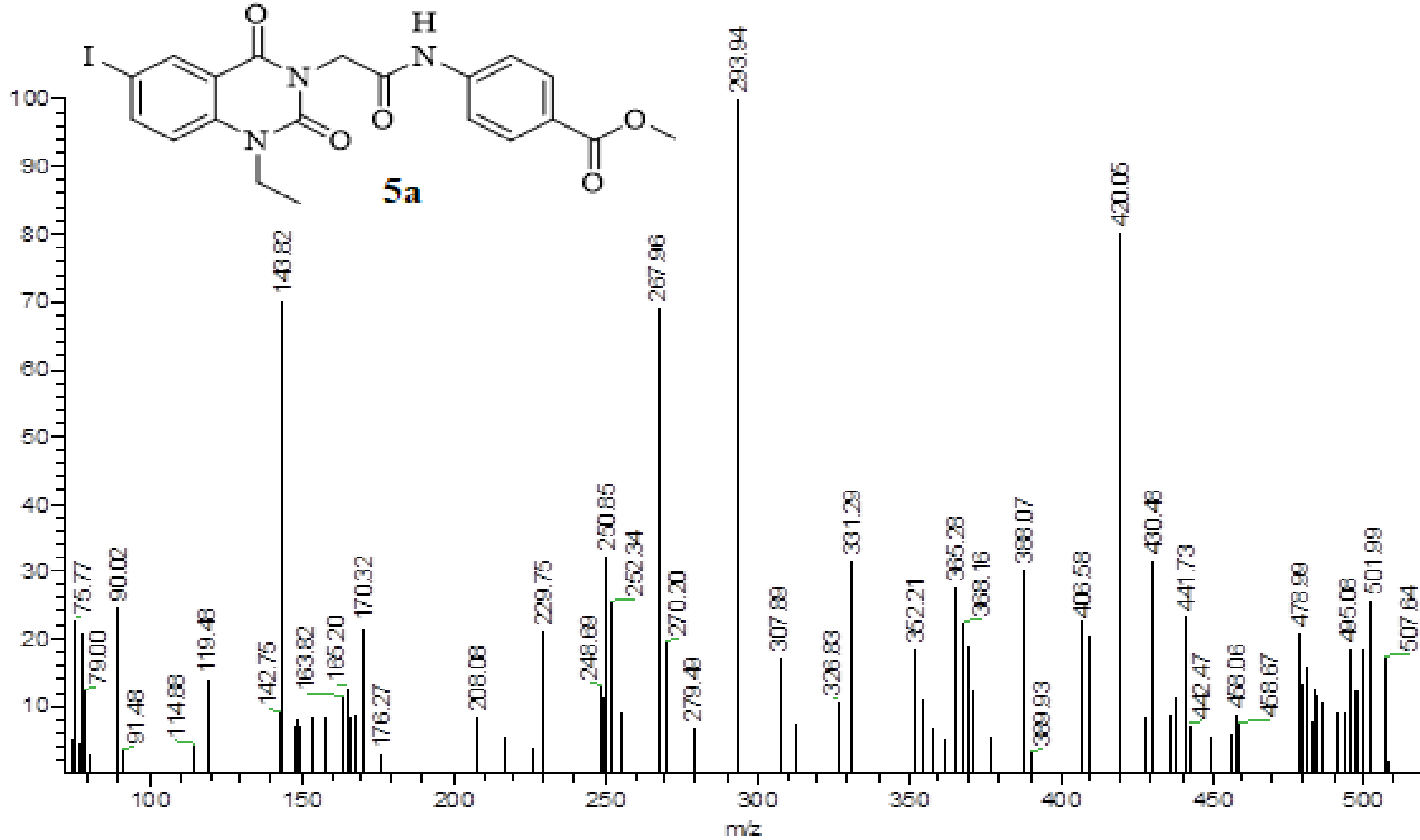
----- CHANNEL f1 -----
SFO1 100.6278588 MHz
NUC1 13C
P1 10.00 usec
PLW1 47.00000000 W

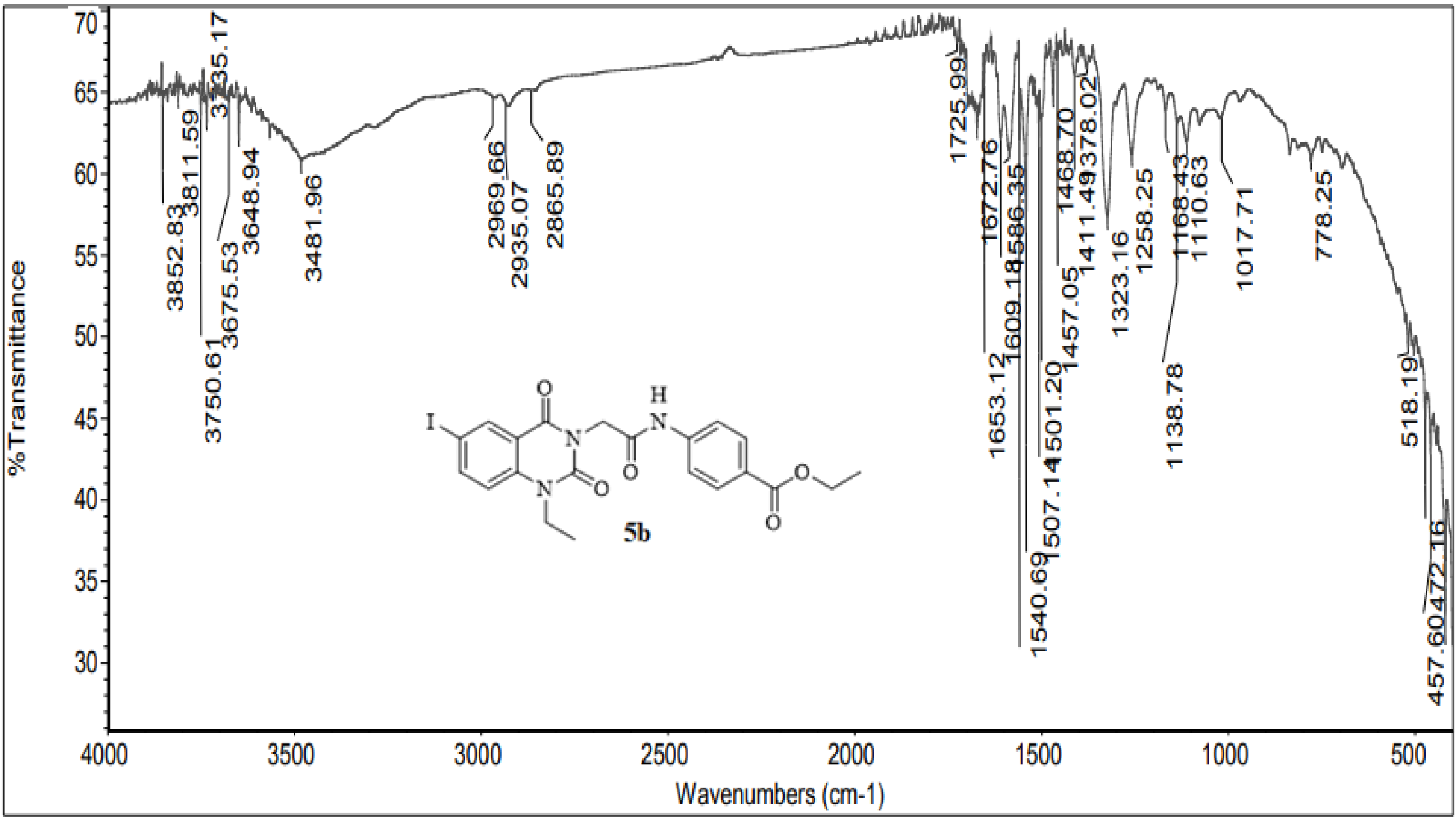
----- CHANNEL f2 -----
SFO2 400.1516006 MHz
NUC2 1H
PCPD2 waltz16
PCPD2 90.00 usec
PLW2 18.00000000 W
PLW12 0.34722000 W
PLW13 0.28125000 W

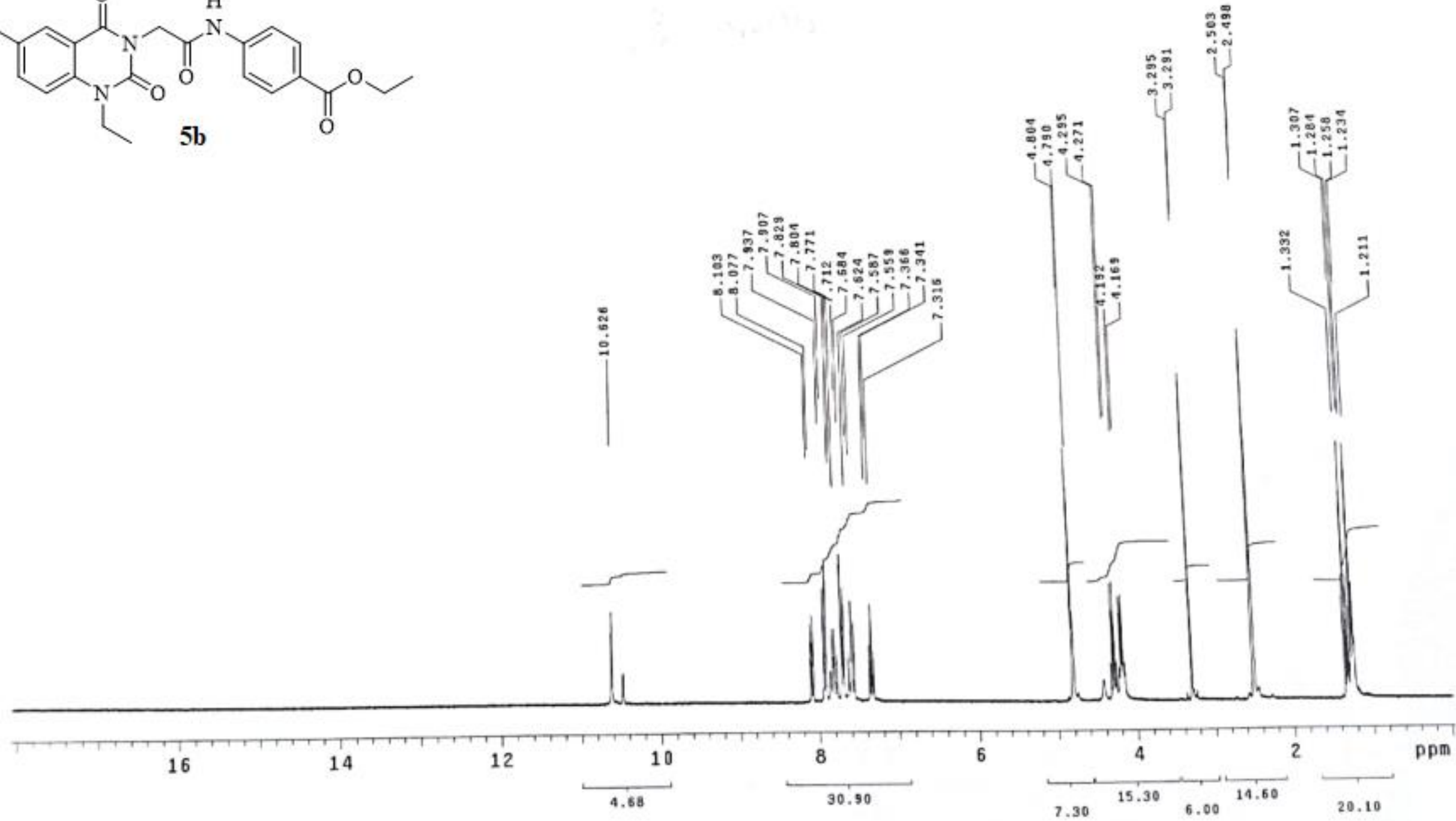
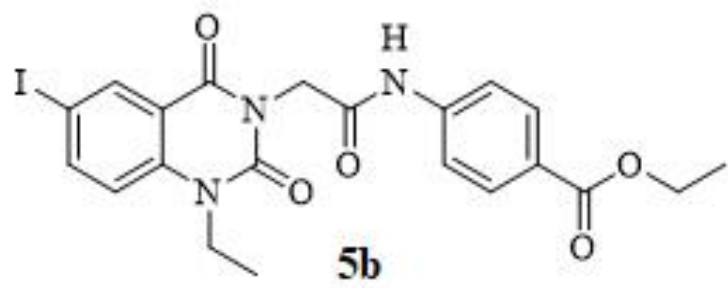
F2 - Processing parameters
SI 32768
SF 100.6177975 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40



Relative Abundance

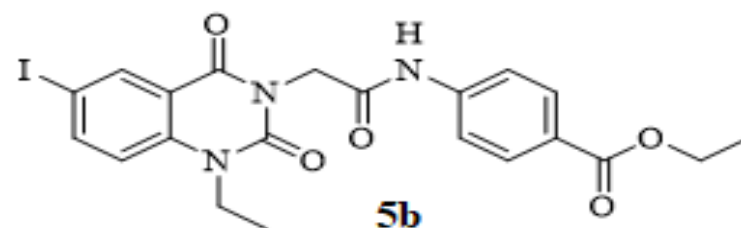








Current Data Parameters
NAME K-H
EXPNO 3
PROCNO 1

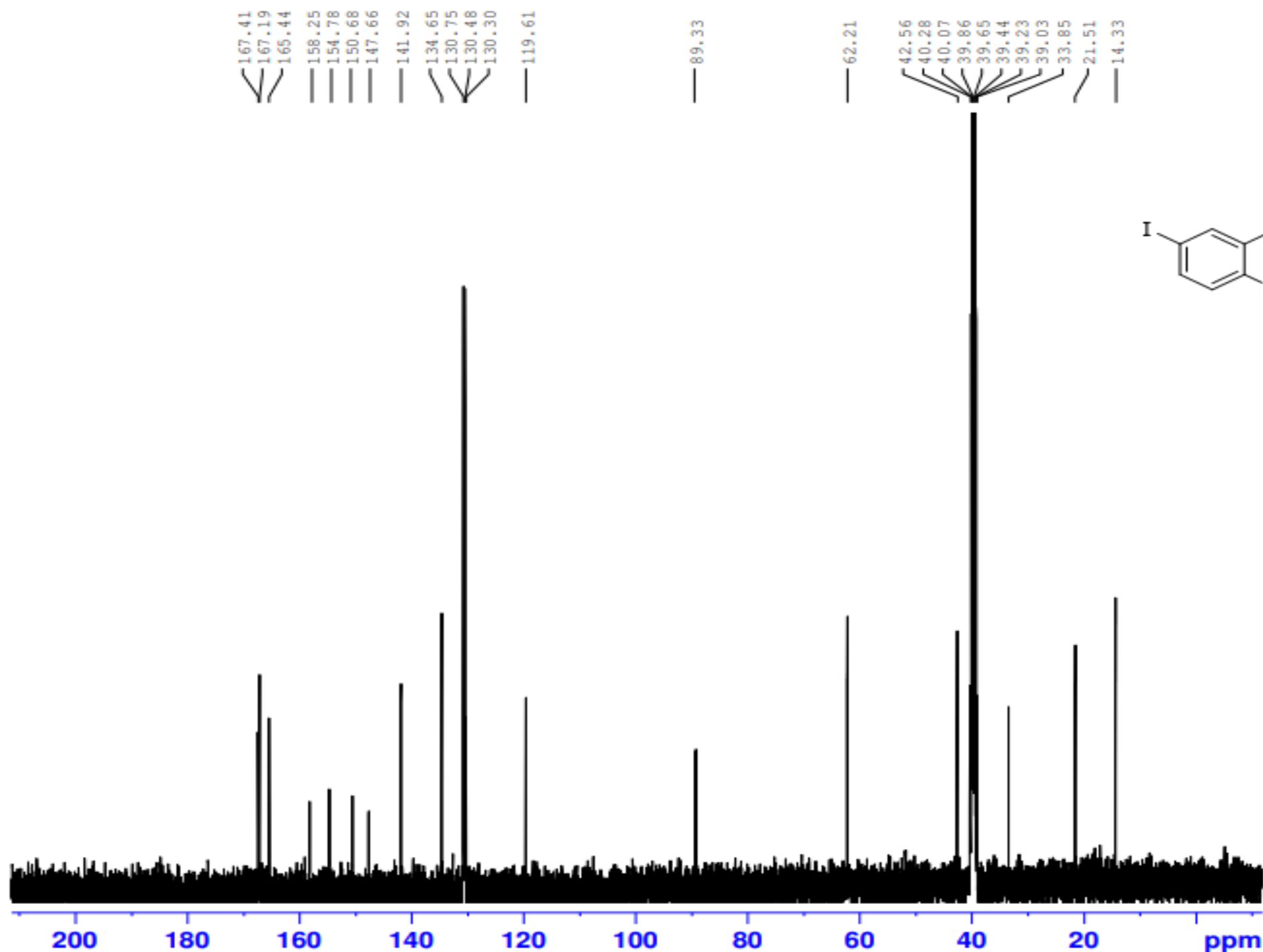


DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 205.37
DW 20.800 usec
DE 6.50 usec
TE 300.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

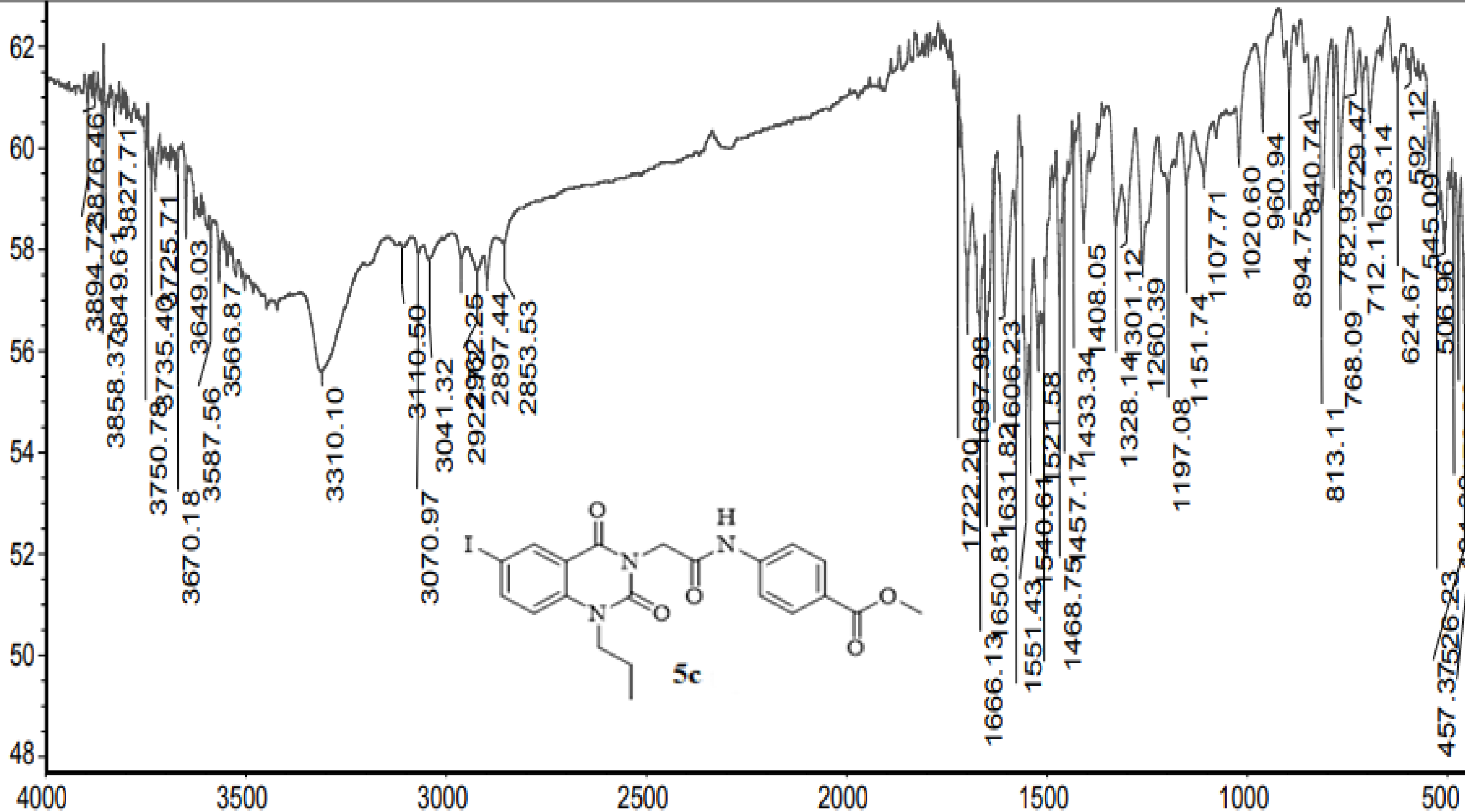
----- CHANNEL f1 -----
SFO1 100.6278588 MHz
NUC1 13C
P1 10.00 usec
PLW1 47.00000000 W

----- CHANNEL f2 -----
SFO2 400.1516006 MHz
NUC2 1H
CPDPRG[2] waltz16
PCPD2 90.00 usec
PLW2 18.00000000 W
PLW12 0.34722000 W
PLW13 0.28125000 W

F2 - Processing parameters
SI 32768
SF 100.6177975 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

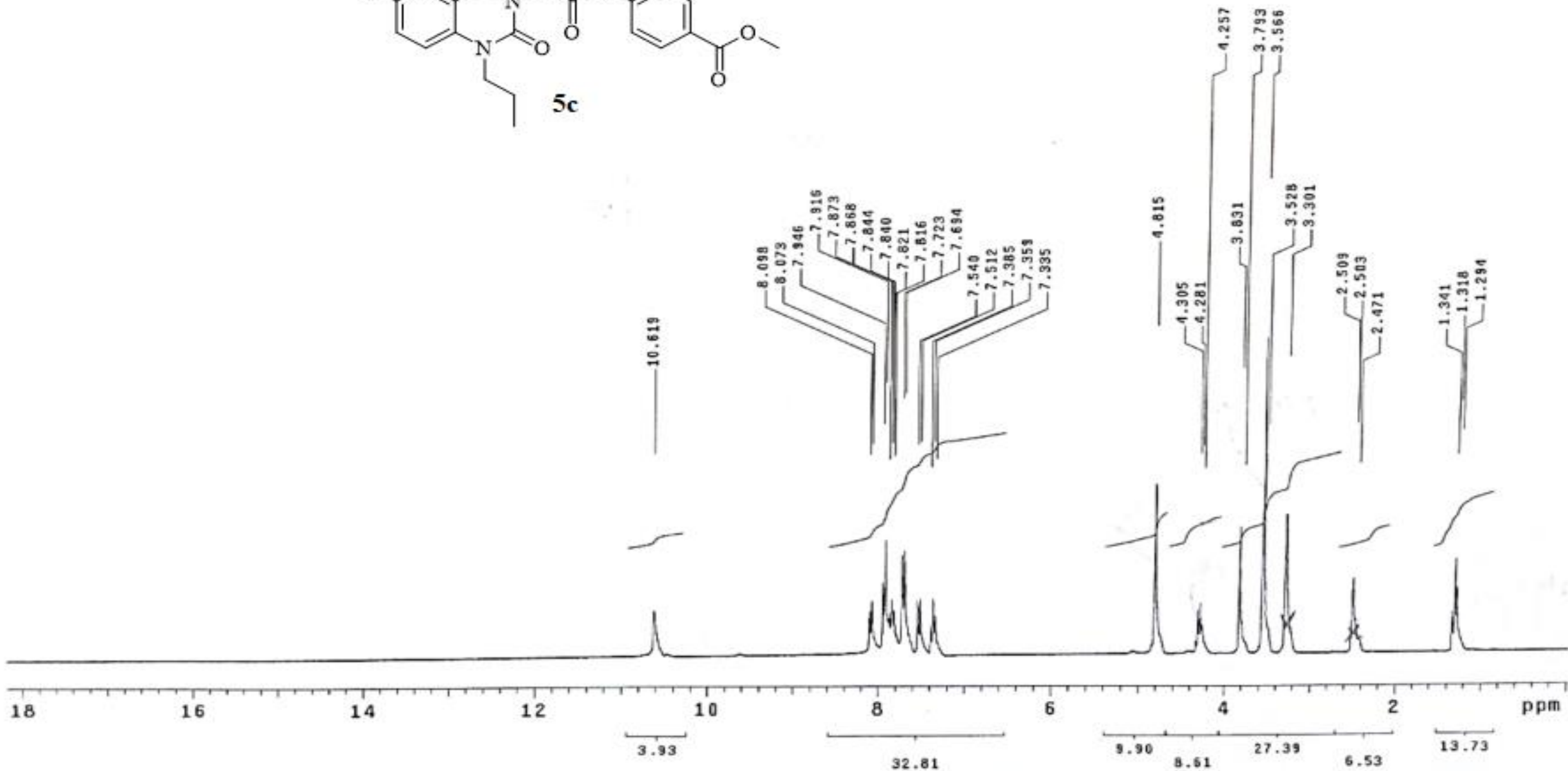
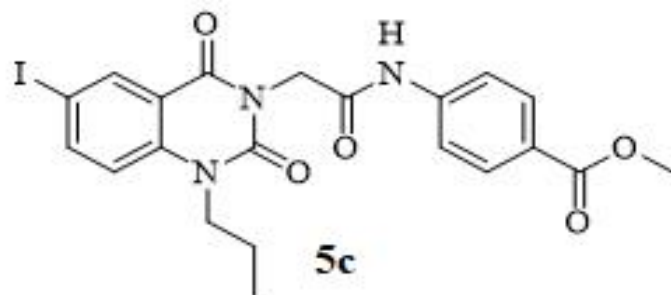


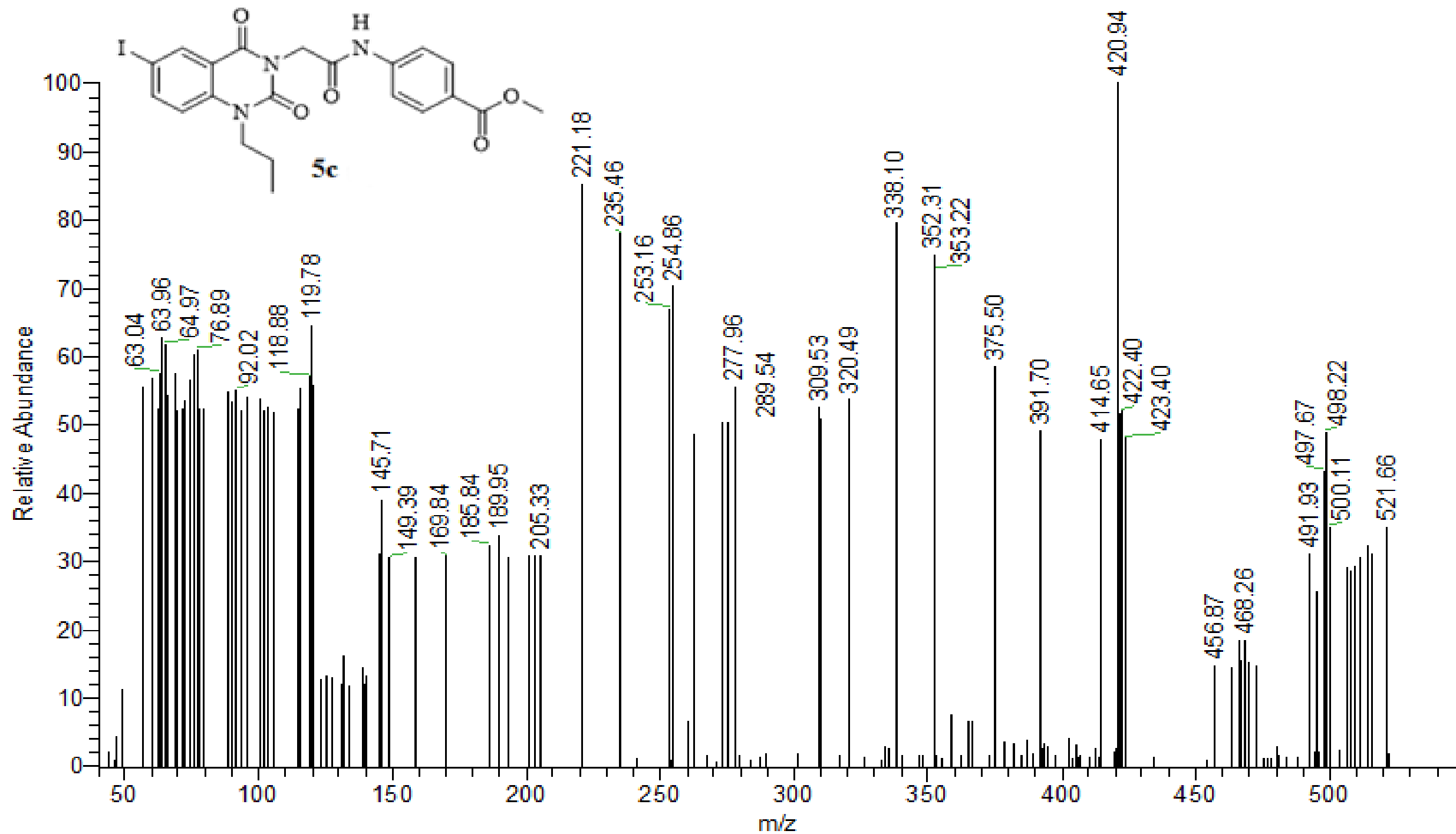
% Transmittance

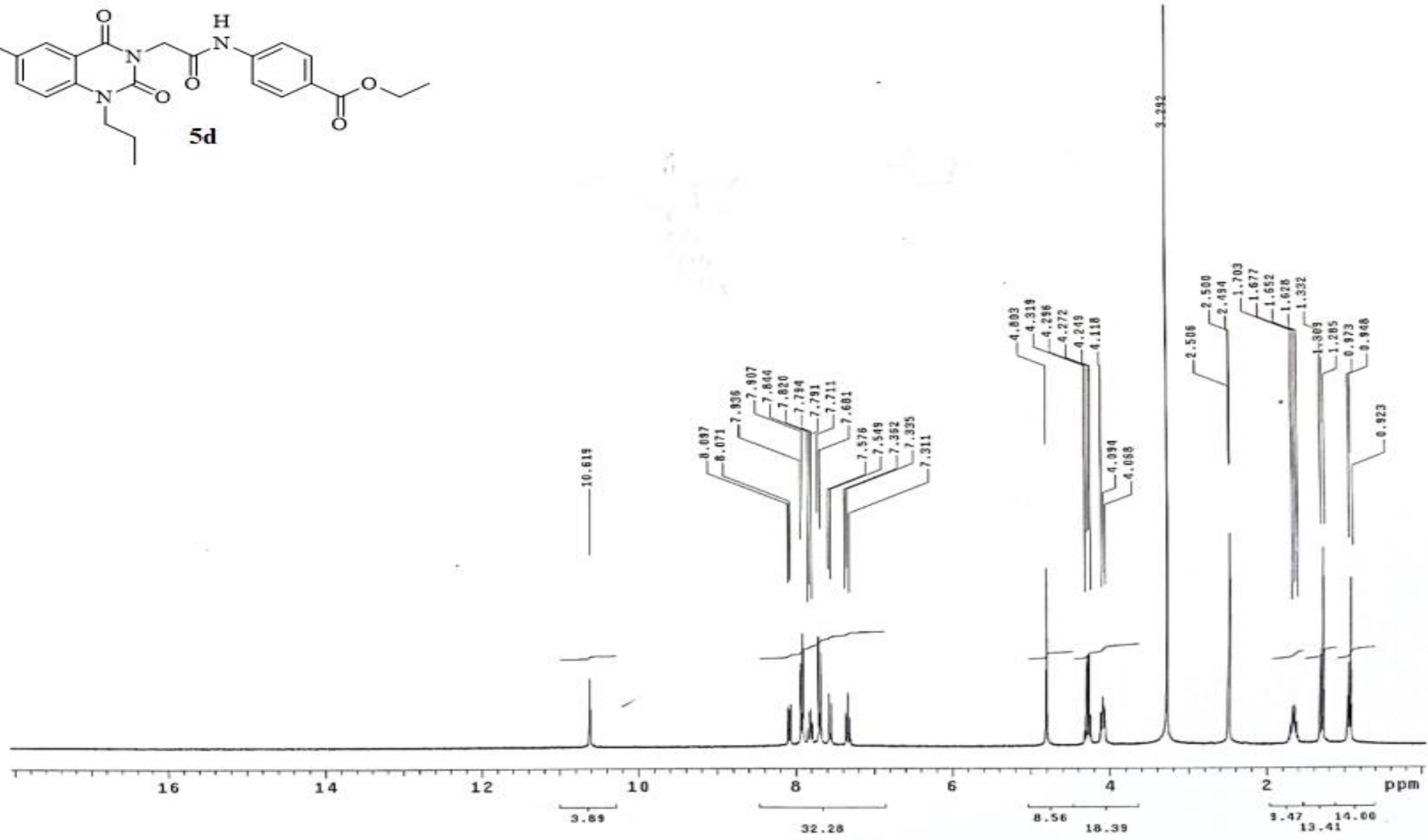
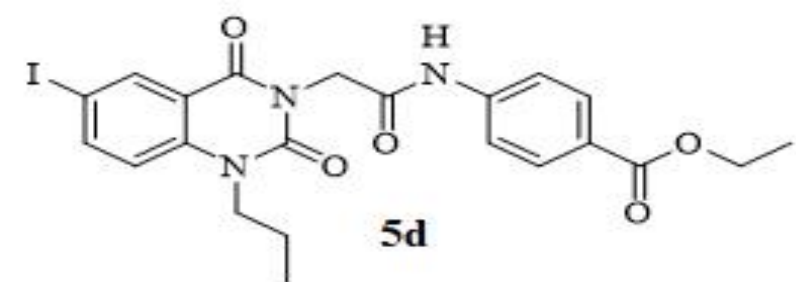


Wavenumbers (cm-1)

Acq. time 4.004 sec
Width 8000.0 Hz
14 repetitions
OBSERVE H1, 300.0687875 MHz
DATA PROCESSING
FT size 65536
Total time 19 min, 19 sec

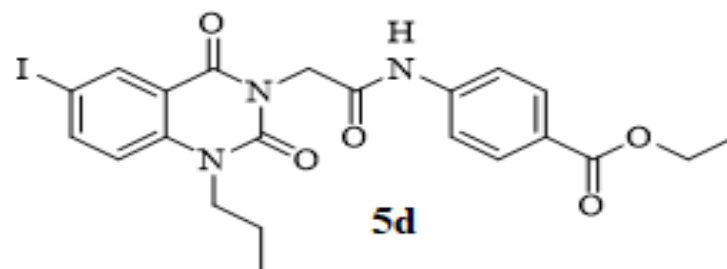








Current Data Parameters
NAME K-1
EXPNO 2
PROCNO 1

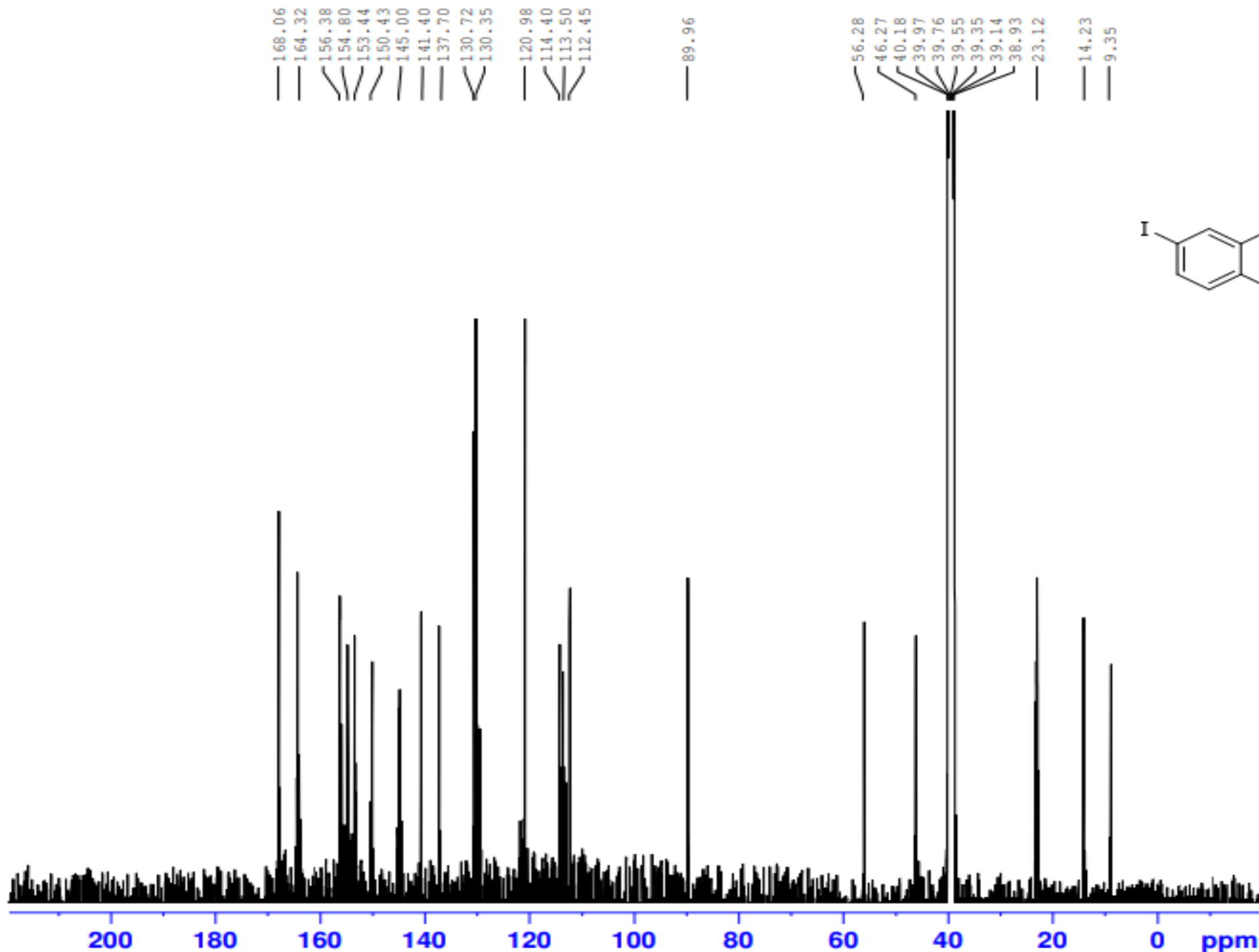


FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 205.37
DW 20.800 usec
DE 6.50 usec
TE 300.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

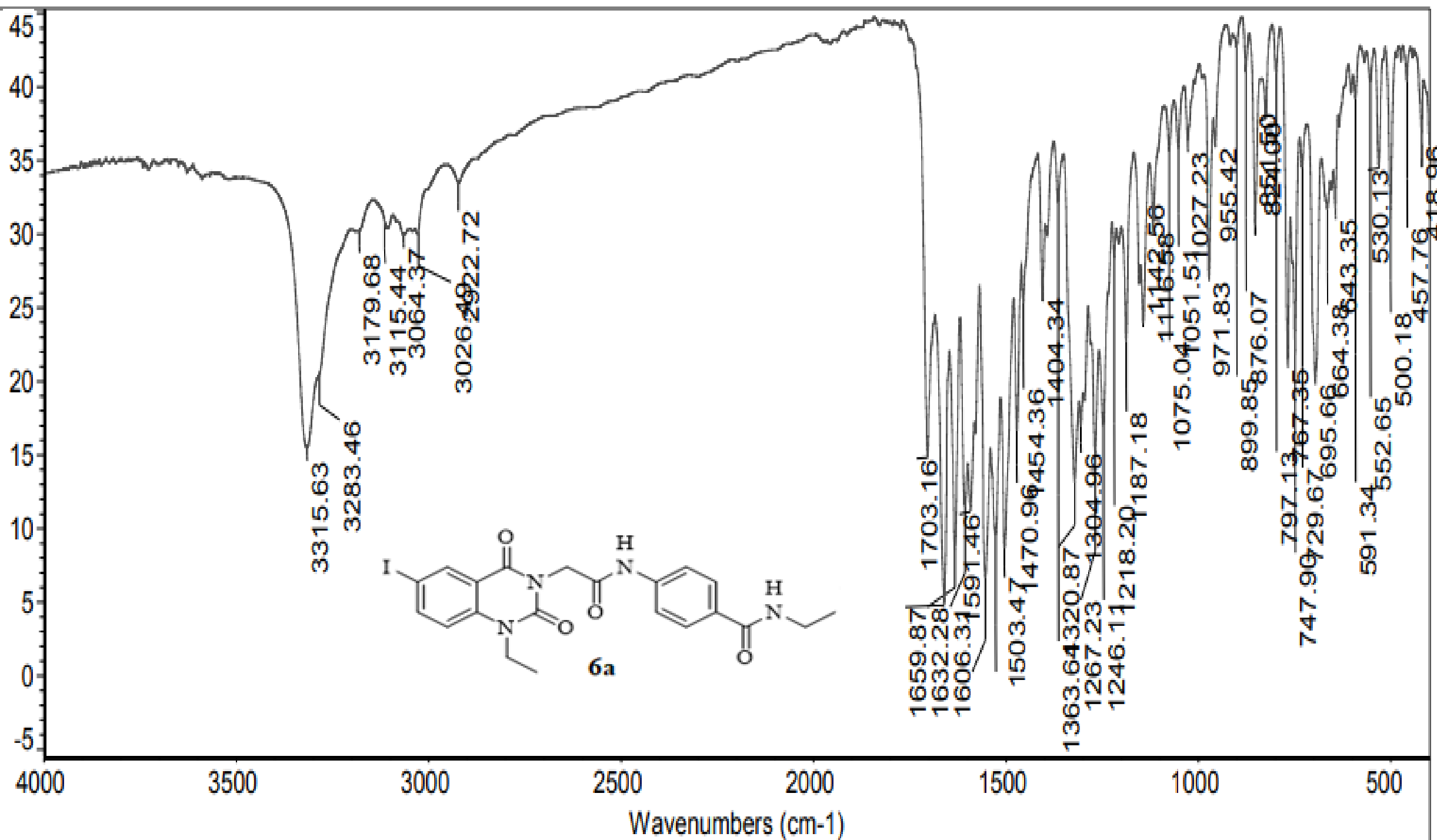
----- CHANNEL f1 -----
SFO1 100.6278588 MHz
NUC1 13C
P1 10.00 usec
PLW1 47.00000000 W

----- CHANNEL f2 -----
SFO2 400.1516006 MHz
NUC2 1H
CPDPRG[2] waltz16
PCPD2 90.00 usec
PLW2 18.00000000 W
PLW12 0.34722000 W
PLW13 0.28125000 W

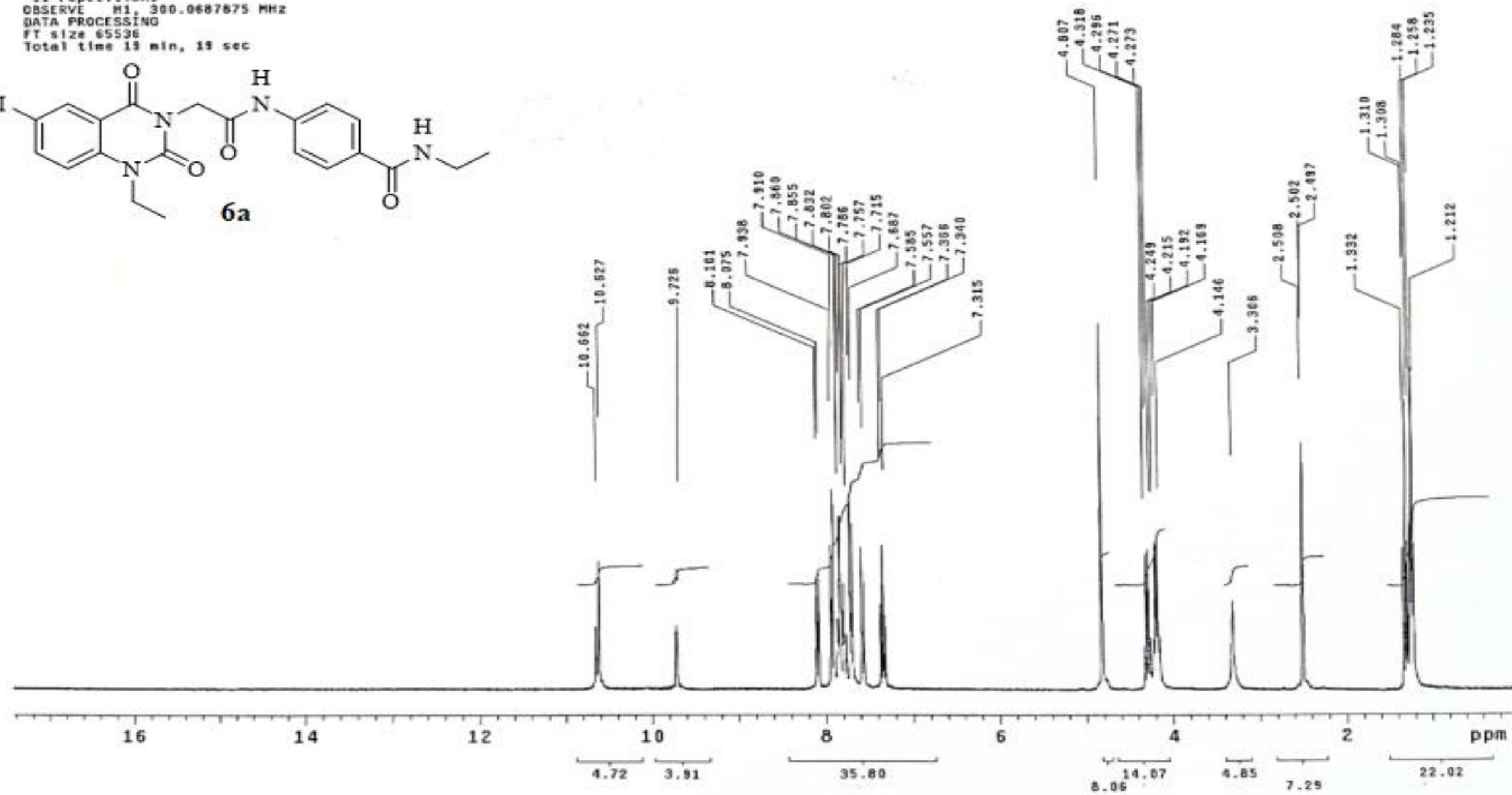
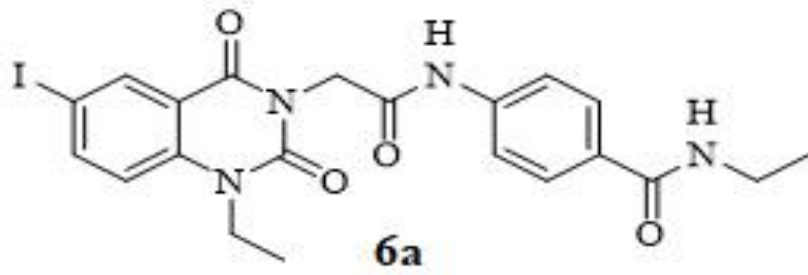
F2 - Processing parameters
SI 32768
SF 100.6177975 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40



% Transmittance

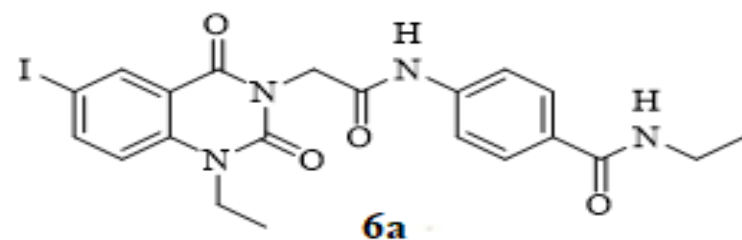


Relax. delay 1.000 sec
 Pulse 74.1 degrees
 Acq. time 4.064 sec
 Width 8000.0 Hz
 11 repetitions
 OBSERVE M1, 300.0687675 MHz
 DATA PROCESSING
 FT size 65536
 Total time 19 min, 19 sec





Current Data Parameters
NAME K-E
EXPNO 2
PROCNO 1

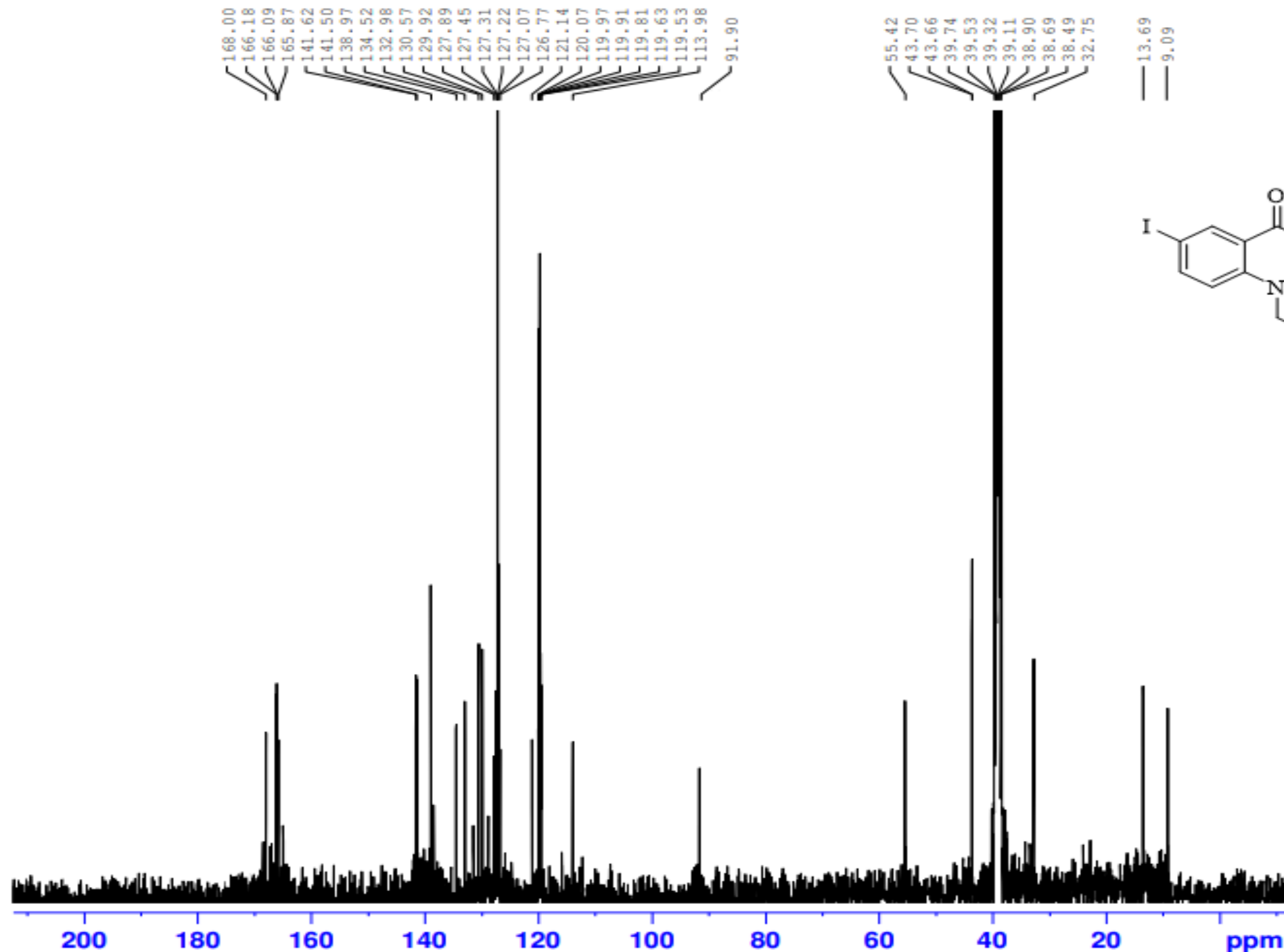


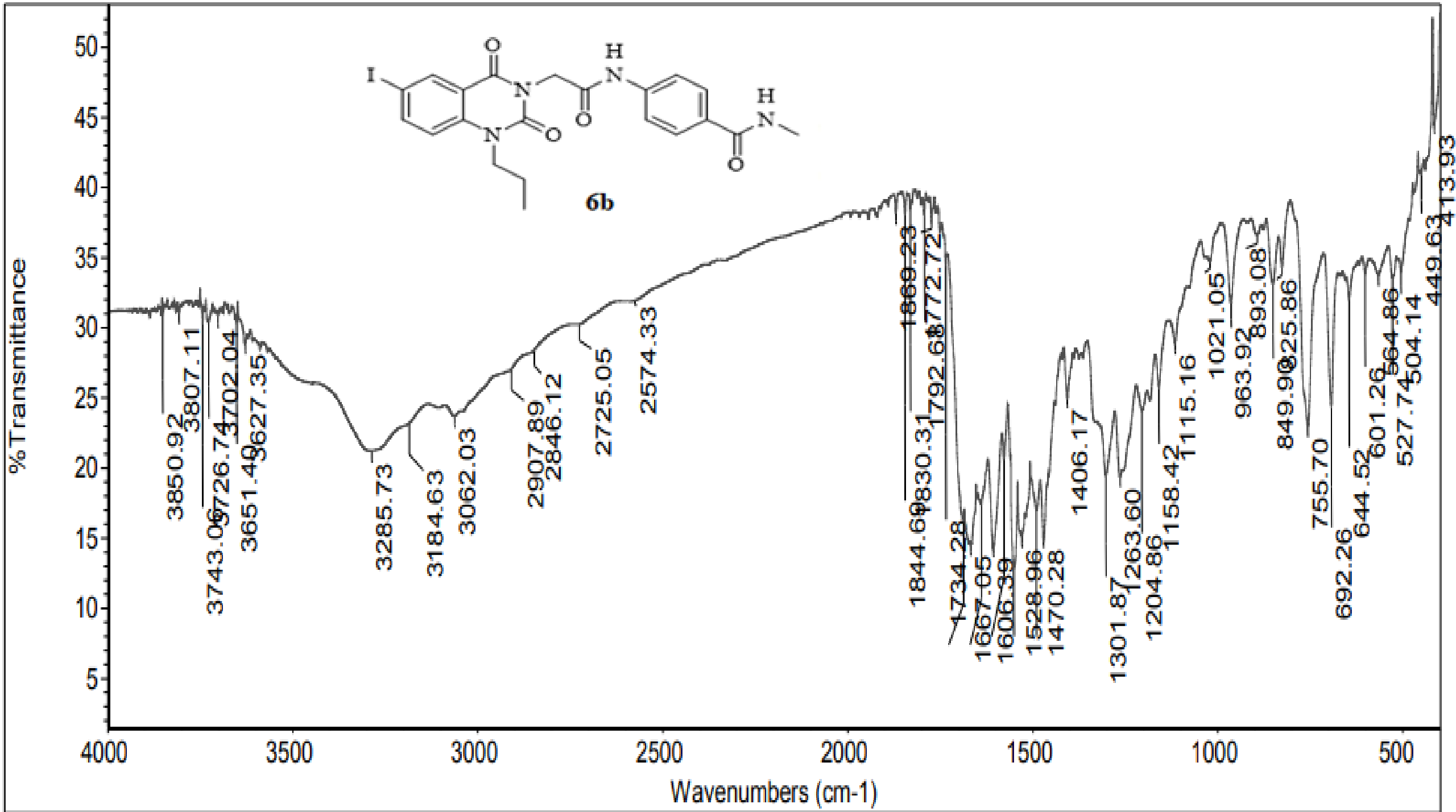
AQ 0.300750 sec
RG 1.3631488 sec
DW 205.37
DE 20.800 usec
TE 6.50 usec
D1 300.0 K
D11 2.00000000 sec
D11 0.03000000 sec
TD0 1

----- CHANNEL f1 -----
SFO1 100.6278588 MHz
NUC1 13C
P1 10.00 usec
PLW1 47.00000000 W

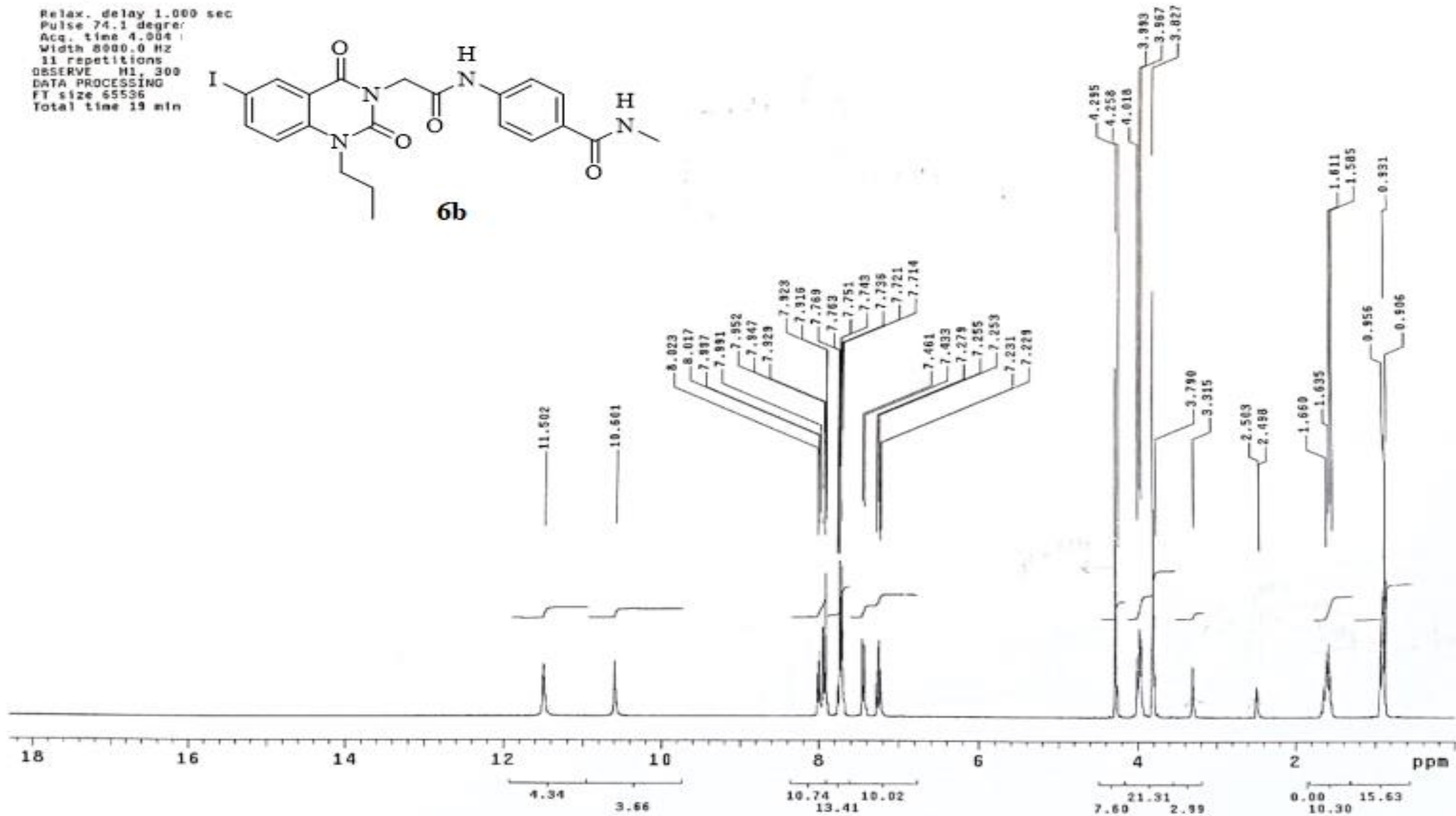
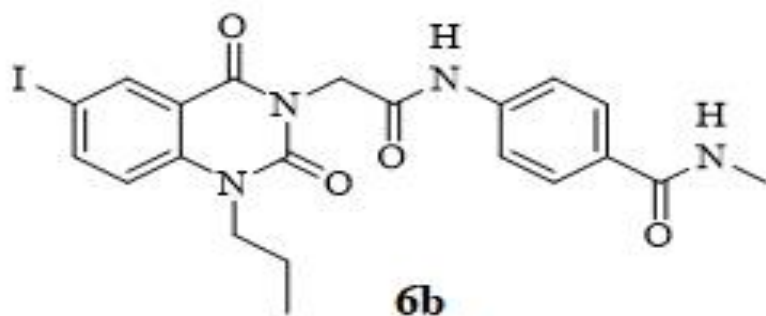
----- CHANNEL f2 -----
SFO2 400.1516006 MHz
NUC2 1H
CPDPRG[2] waltz16
PCPD2 90.00 usec
PLW2 18.00000000 W
PLW12 0.34722000 W
PLW13 0.28125000 W

F2 - Processing parameters
SI 32768
SF 100.6177975 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

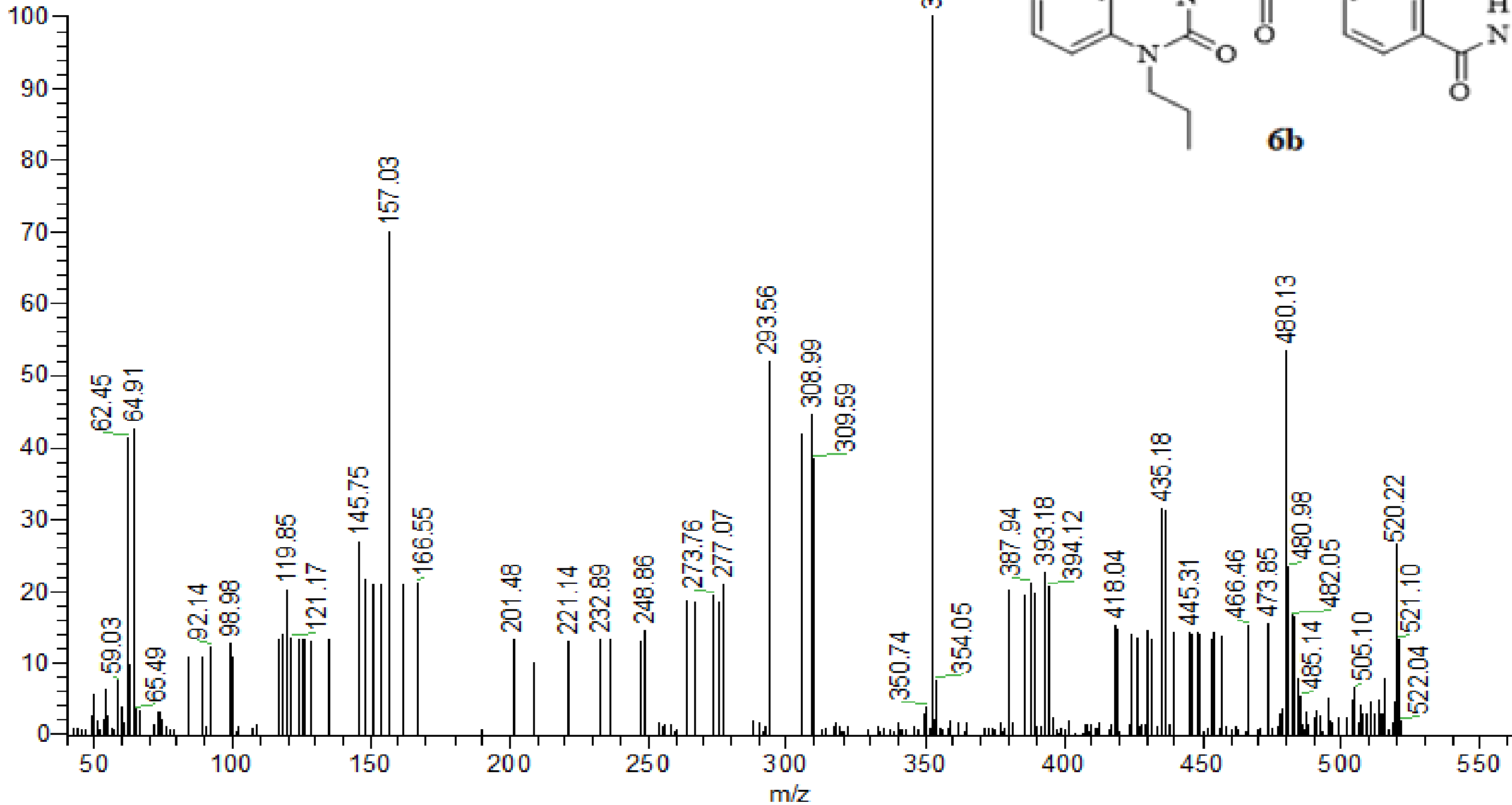


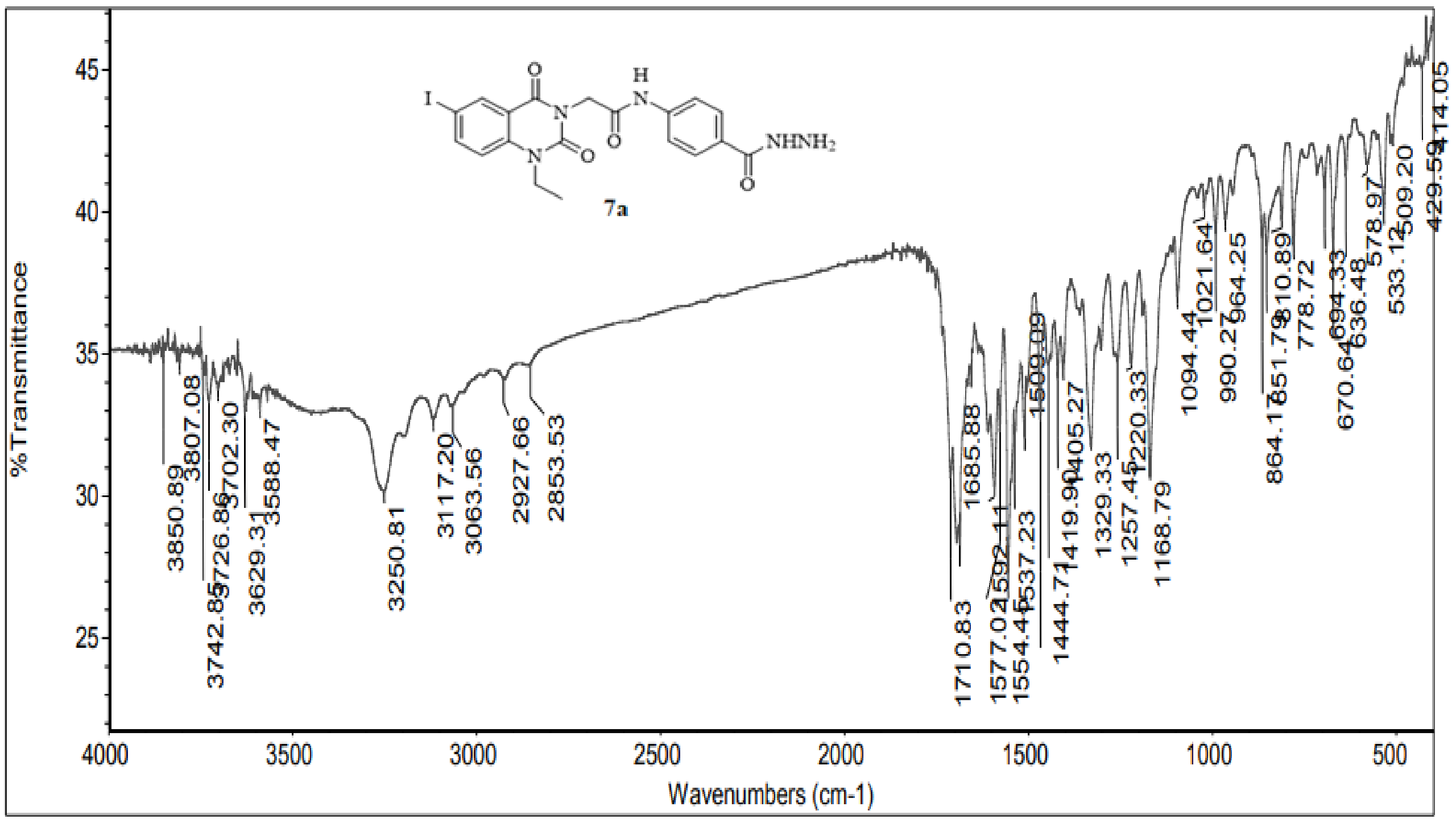


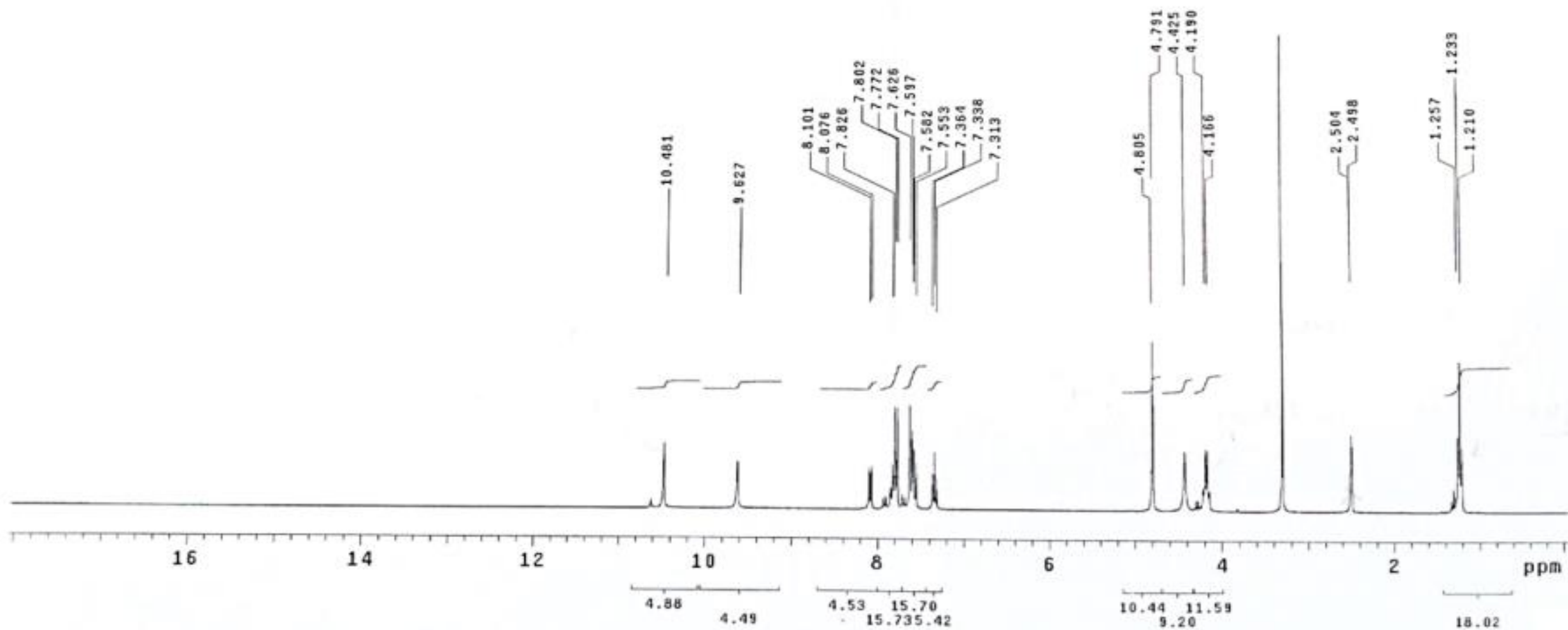
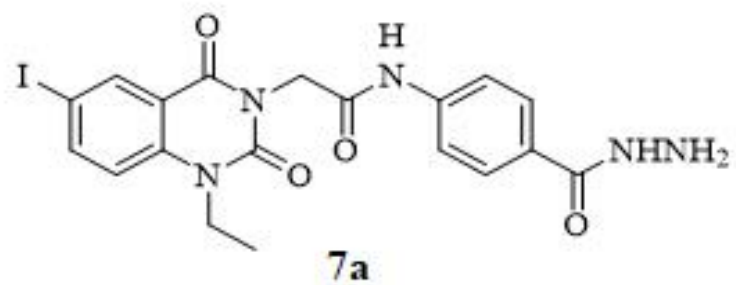
Relax. delay 1.000 sec
 Pulse 74.1 degree
 Acq. time 4.004
 Width 8000.0 Hz
 11 repetitions
 OBSERVE M1 300
 DATA PROCESSING
 FT size 65536
 Total time 19 min



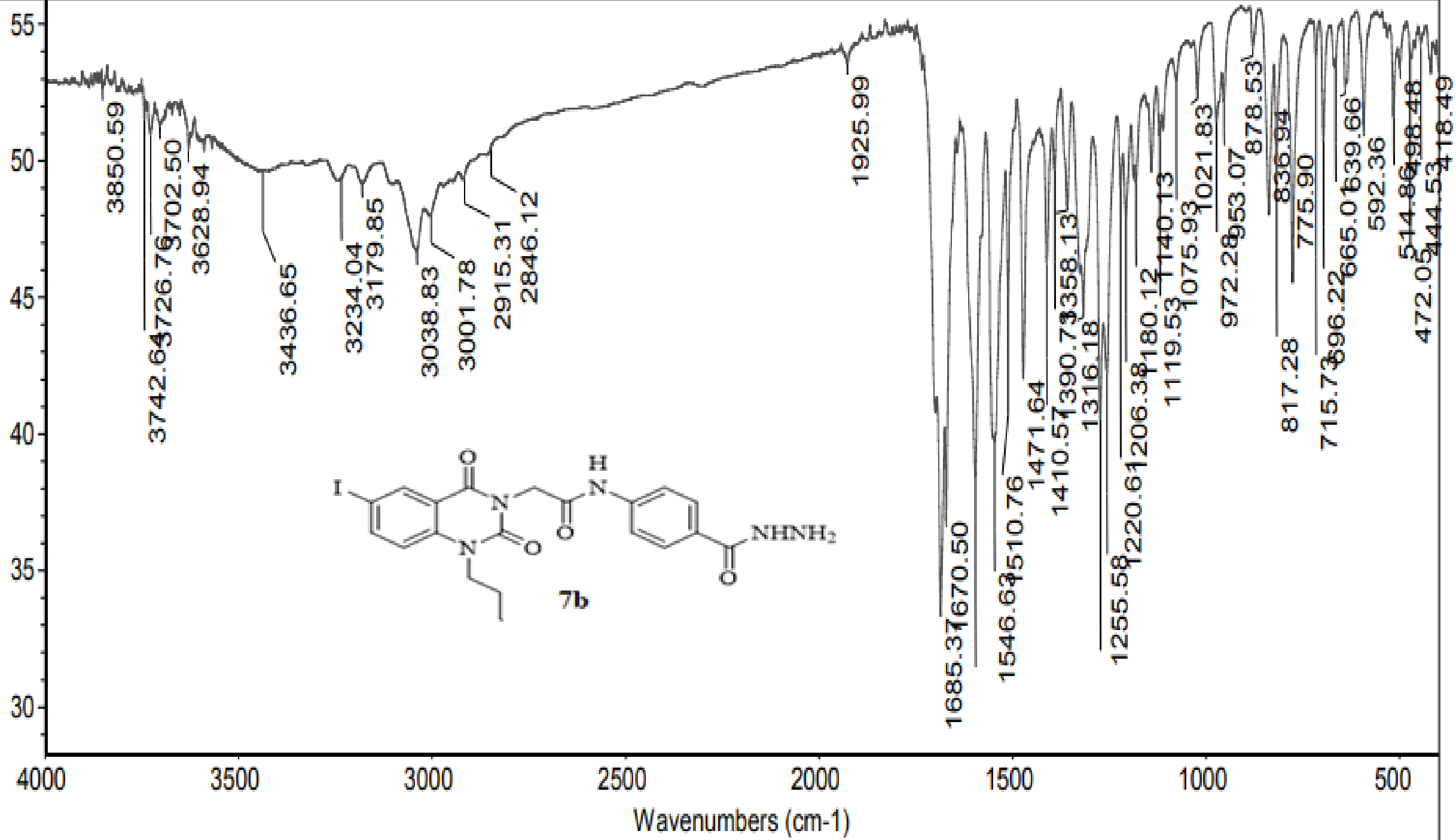
Relative Abundance



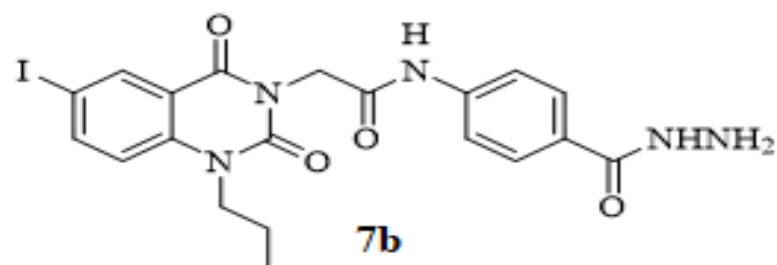




% Transmittance



Current Data Parameters
 NAME K-B
 EXPNO 2
 PROCNO 1

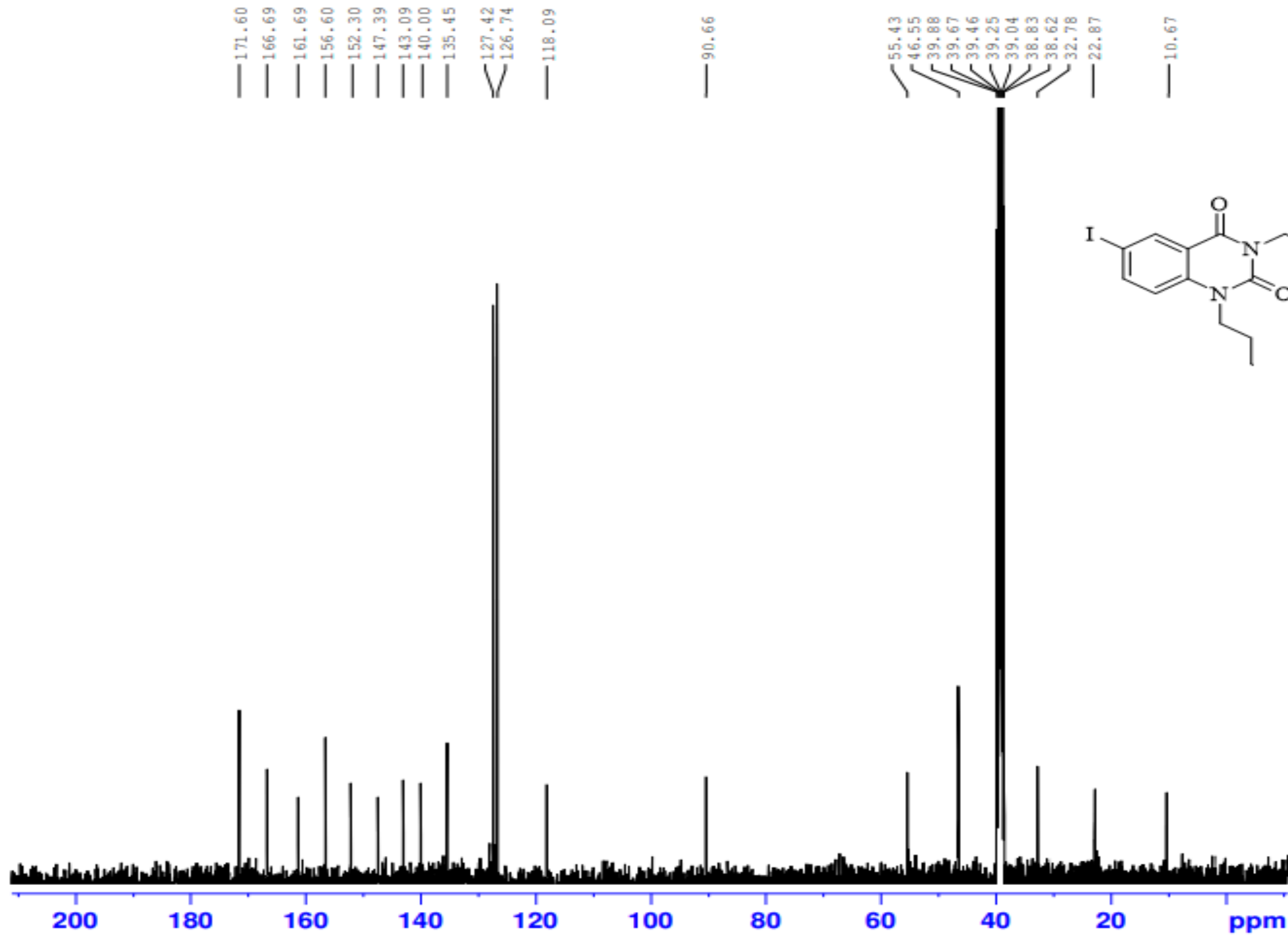


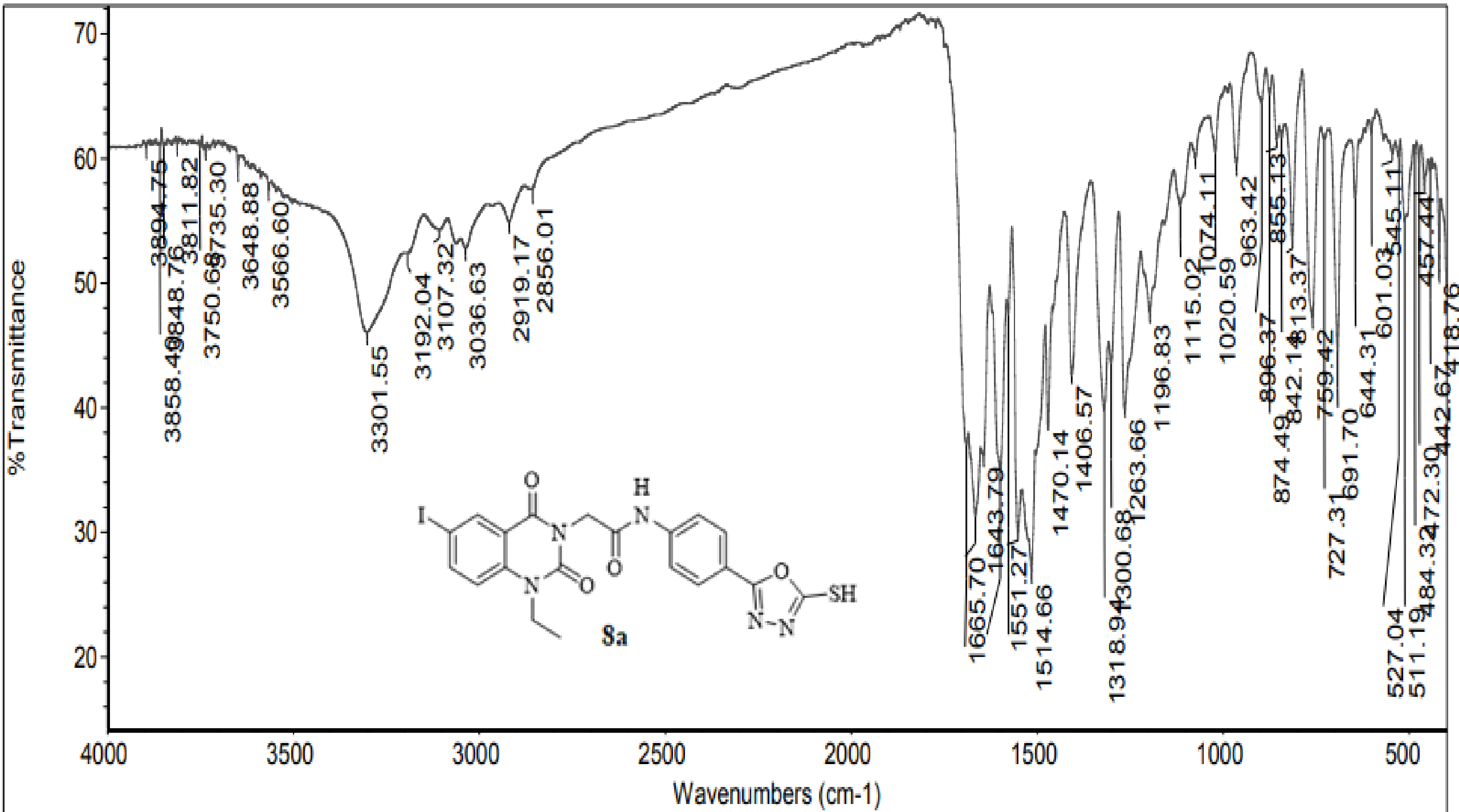
 AQ 1.3631488 sec
 RG 205.37
 DW 20.800 usec
 DE 6.50 usec
 TE 300.0 K
 D1 2.00000000 sec
 D11 0.03000000 sec
 TD0 1

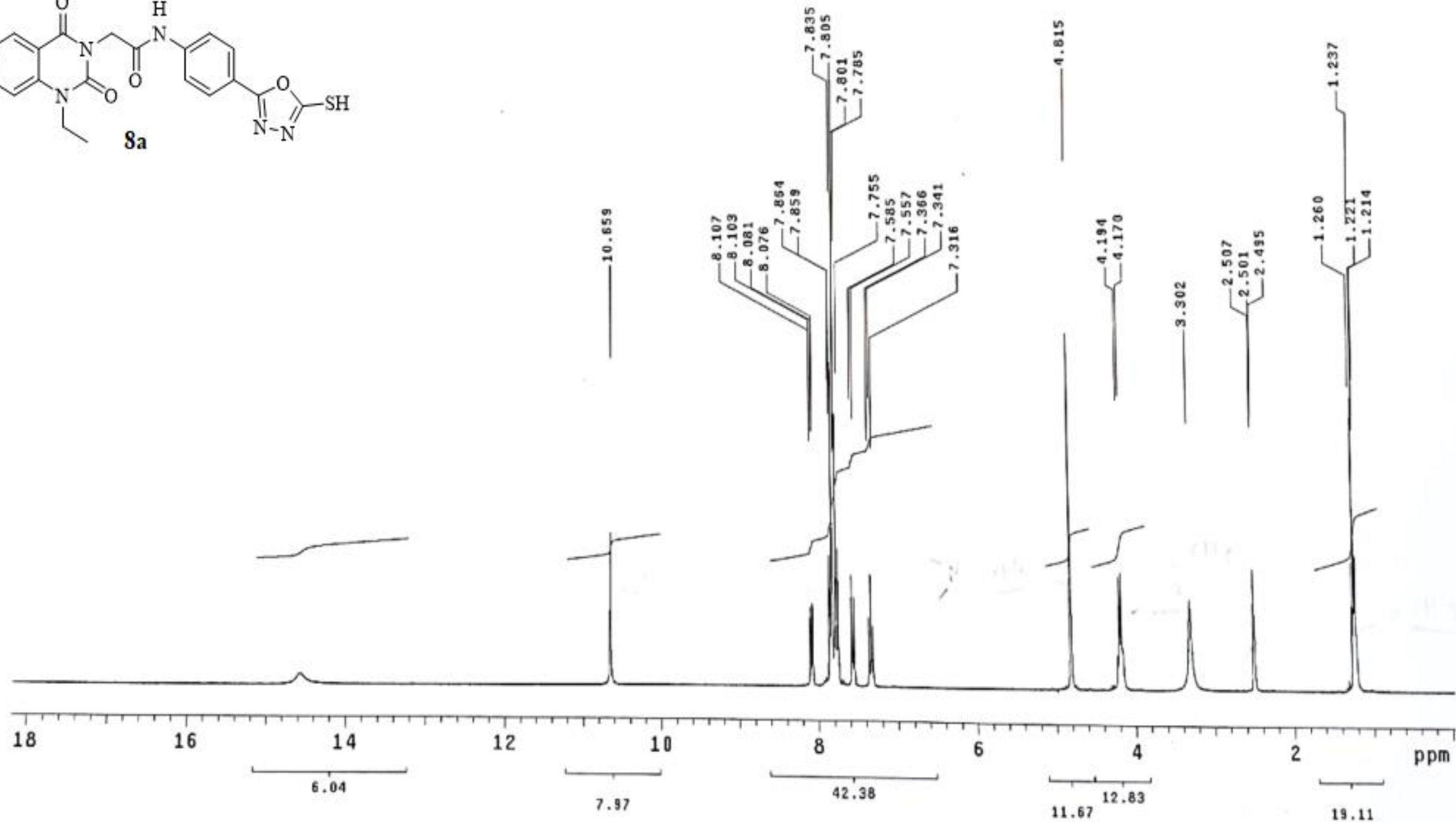
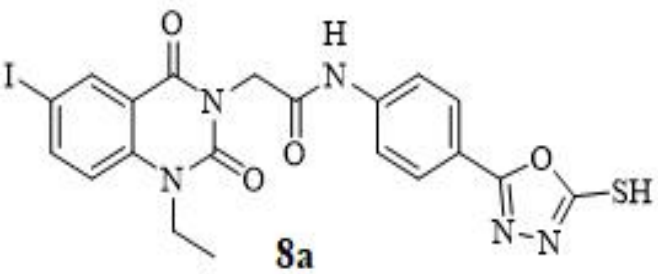
----- CHANNEL f1 -----
 SFO1 100.6278588 MHz
 NUC1 13C
 P1 10.00 usec
 PLW1 47.00000000 W

----- CHANNEL f2 -----
 SFO2 400.1516006 MHz
 NUC2 1H
 CPDPRG[2] waltz16
 PCPD2 90.00 usec
 PLW2 18.00000000 W
 PLW12 0.34722000 W
 PLW13 0.28125000 W

F2 - Processing parameters
 SI 32768
 SF 100.6177975 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

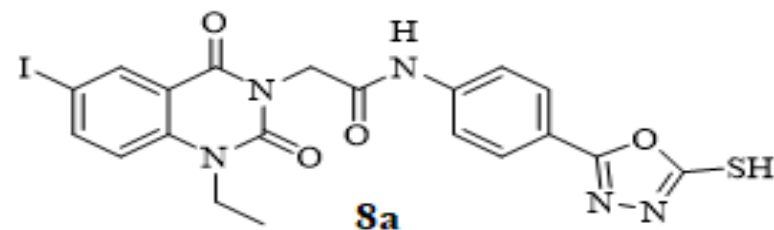








Current Data Parameters
NAME K-K
EXPNO 2
PROCNO 1

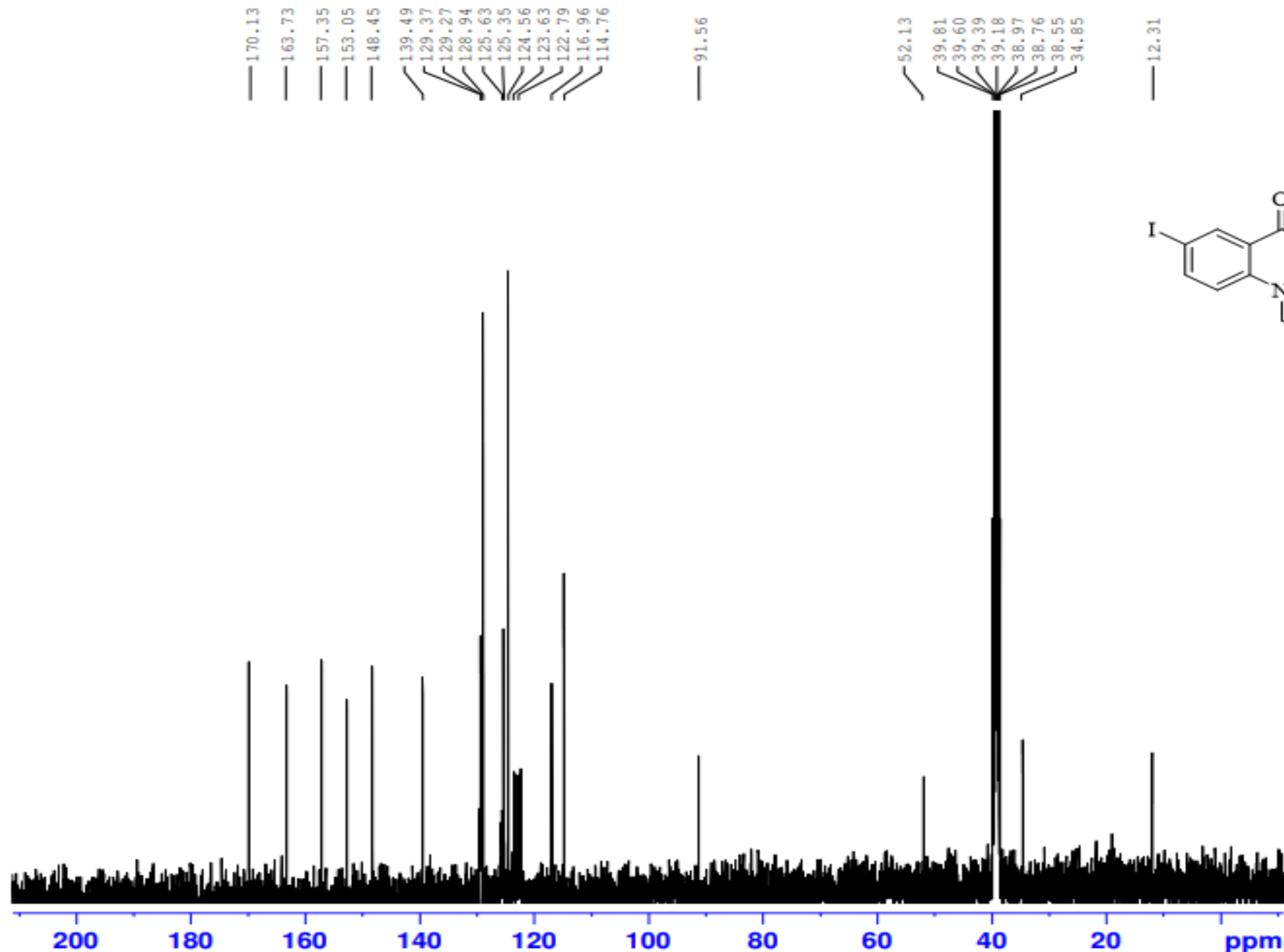


SWH 24038.461 MHz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 205.37
DW 20.800 usec
DE 6.50 usec
TE 300.0 K
D1 2.0000000 sec
D11 0.0300000 sec
TD0 1

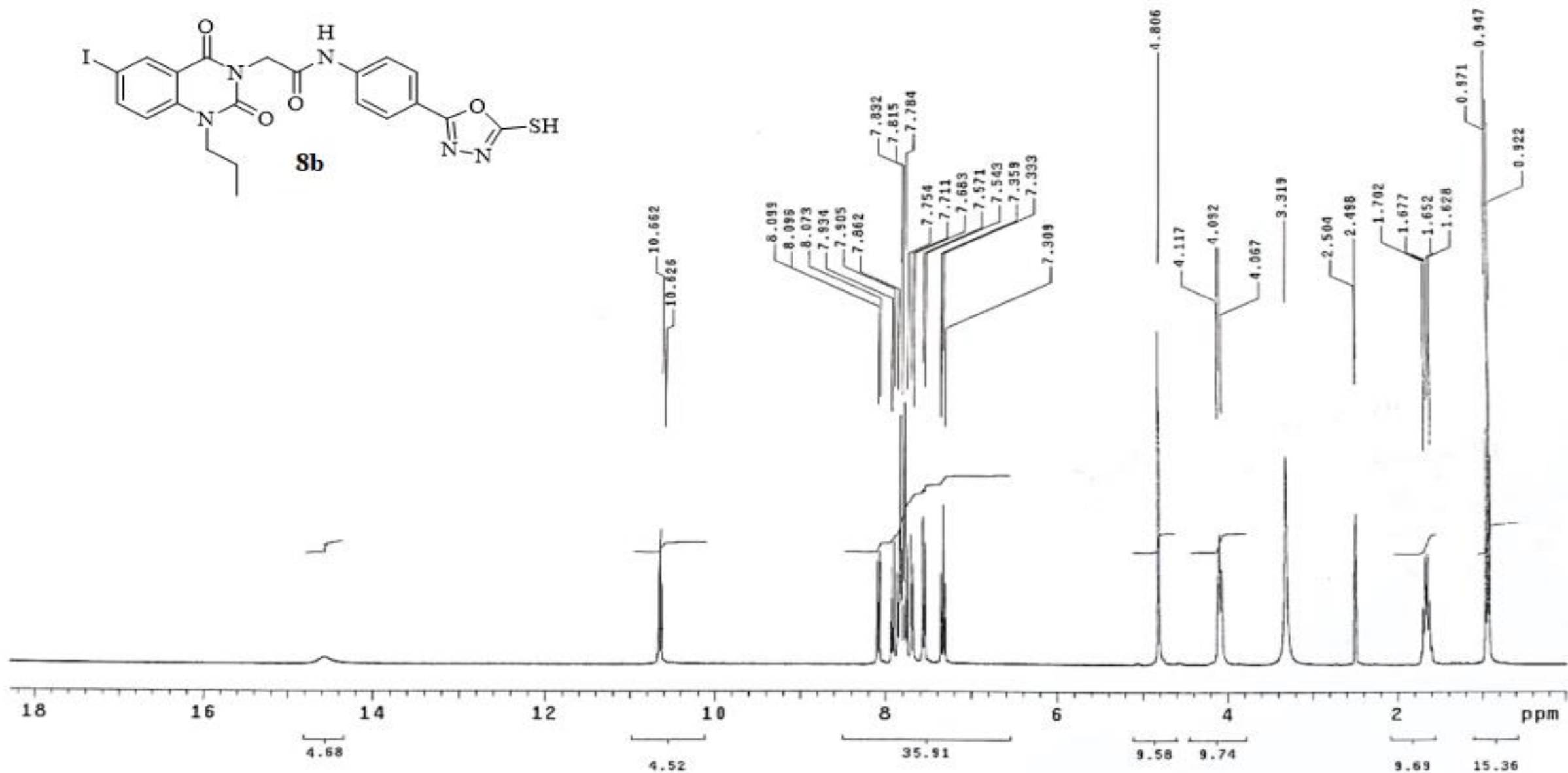
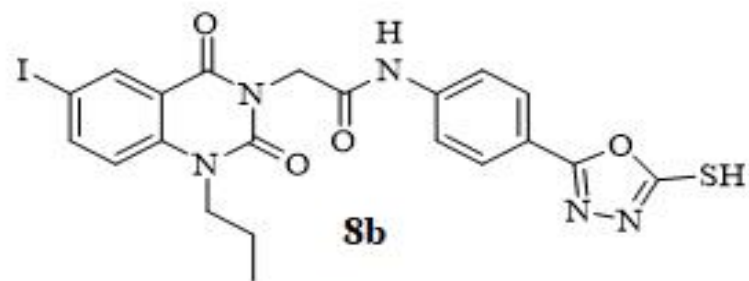
----- CHANNEL f1 -----
SFO1 100.6278588 MHz
NUC1 13C
P1 10.00 usec
PLW1 47.0000000 W

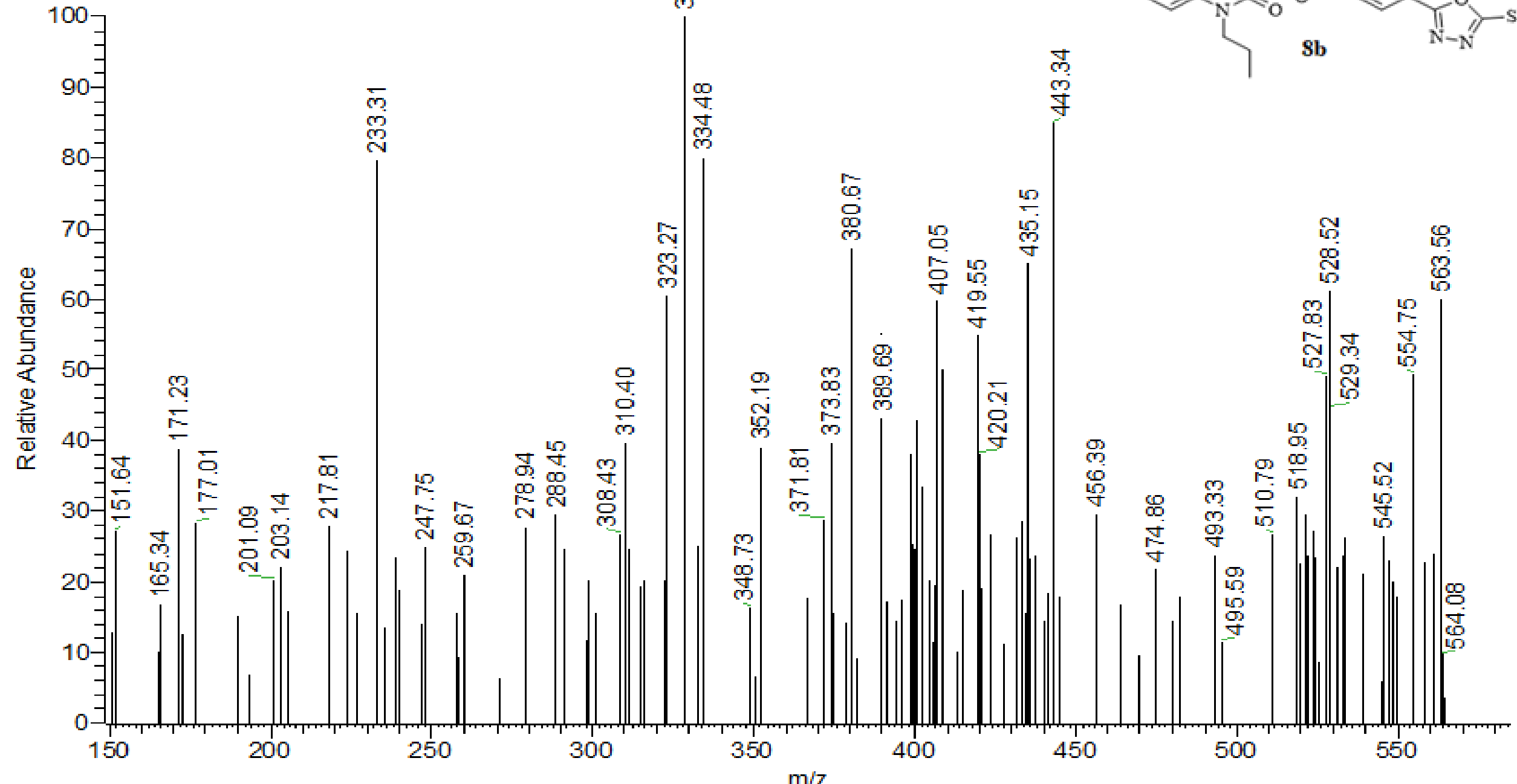
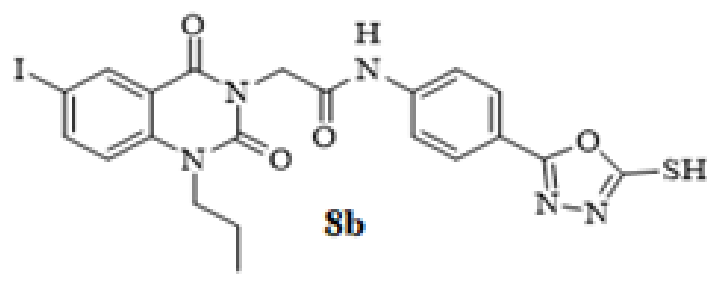
----- CHANNEL f2 -----
SFO2 400.1516006 MHz
NUC2 1H
CPDPRG[2] waltz16
PCPD2 90.00 usec
PLW2 18.0000000 W
PLW12 0.3472200 W
PLW13 0.2812500 W

F2 - Processing parameters
SI 32768
SF 100.6177975 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

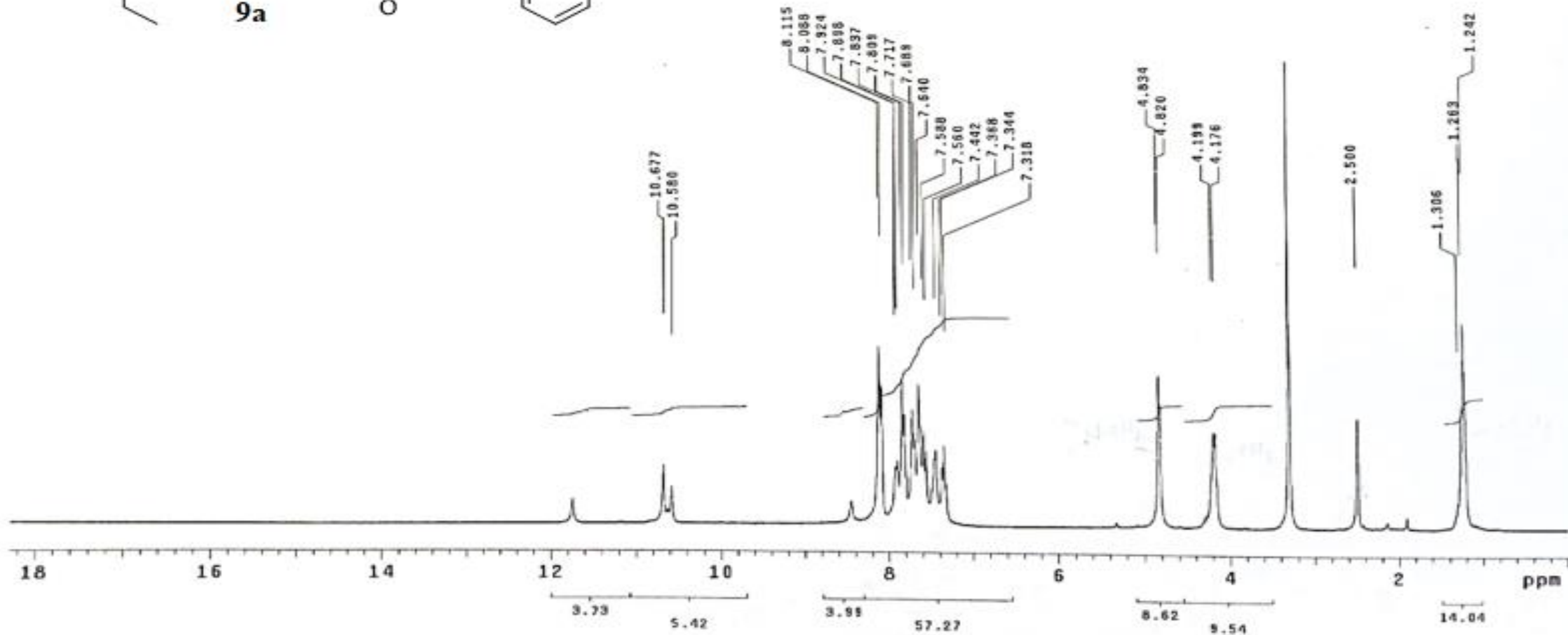
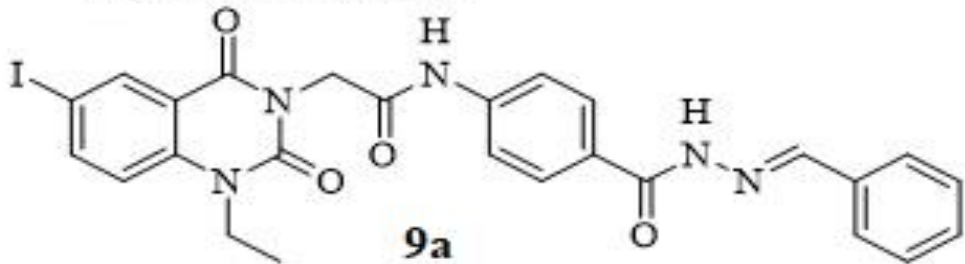


Relax. delay 1.000 sec
Pulse 74.1 degrees
Acq. time 4.904 sec
Width 8000.0 Hz
10 repetitions
OBSERVE H1, 300.9687875 MHz
DATA PROCESSING
FT size 65536
Total time 19 min, 19 sec



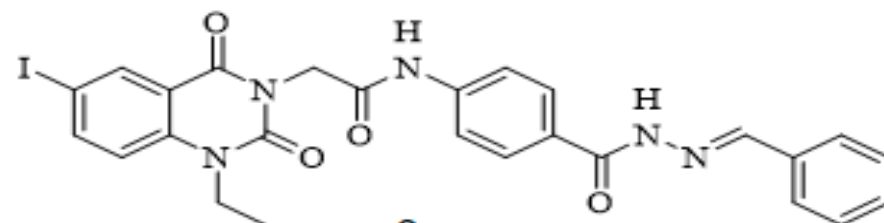


Relax. delay 1.000 sec
Pulse 74.1 degrees
Acq. time 4.004 sec
Width 8000.0 Hz
14 repetitions
OBSERVE H1, 300.0687875 MHz
DATA PROCESSING
FT size 65536
Total time 13 min. 13 sec





Current Data Parameters
NAME K-C
EXPNO 2
PROCNO 1



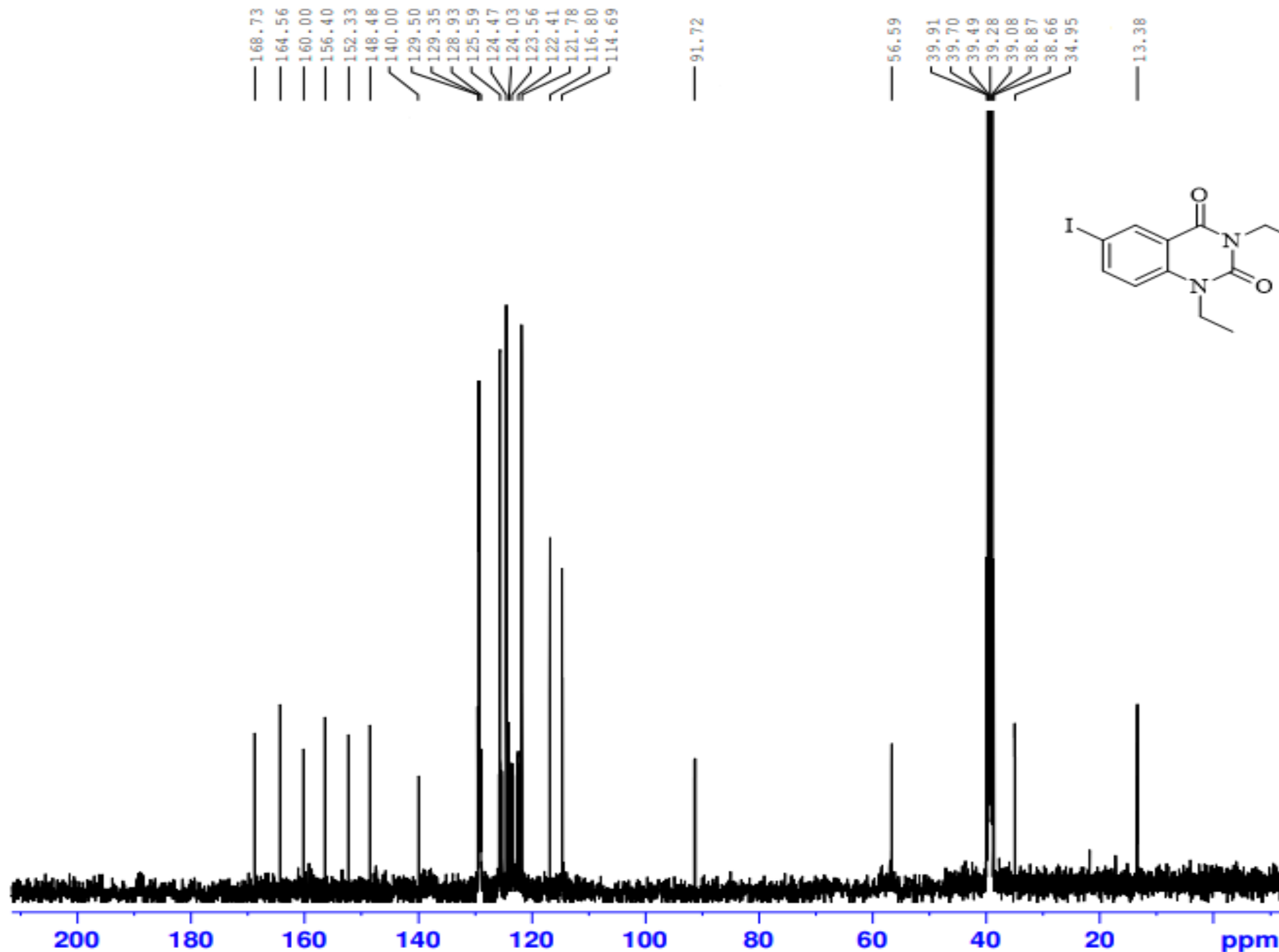
9a

FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 205.37
DW 20.800 usec
DE 6.50 usec
TE 300.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

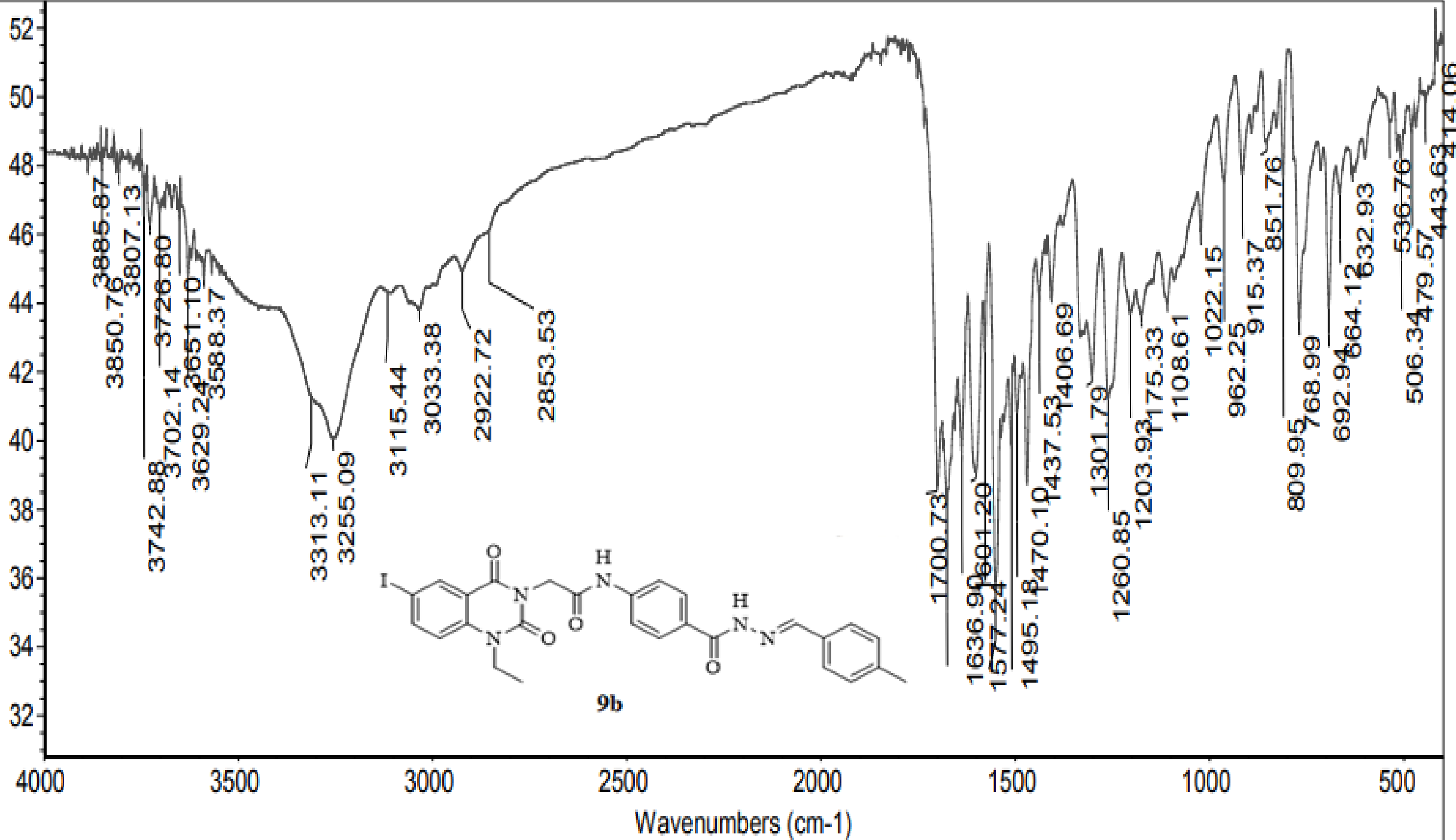
----- CHANNEL f1 -----
SFO1 100.6278588 MHz
NUC1 13C
P1 10.00 usec
PLW1 47.00000000 W

----- CHANNEL f2 -----
SFO2 400.1516006 MHz
NUC2 1H
CPDPRG[2] waltz16
PCPD2 90.00 usec
PLW2 18.00000000 W
PLW12 0.34722000 W
PLW13 0.28125000 W

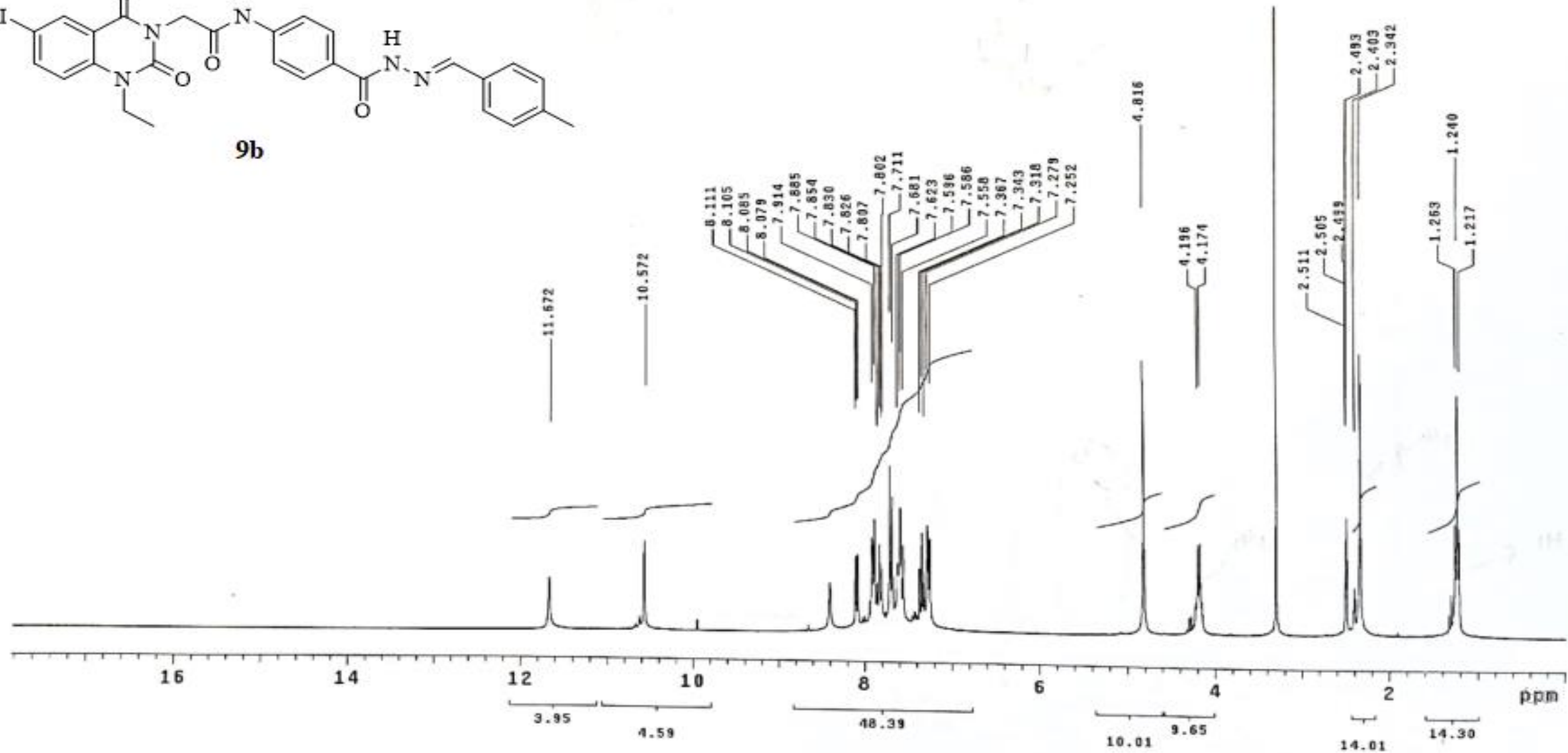
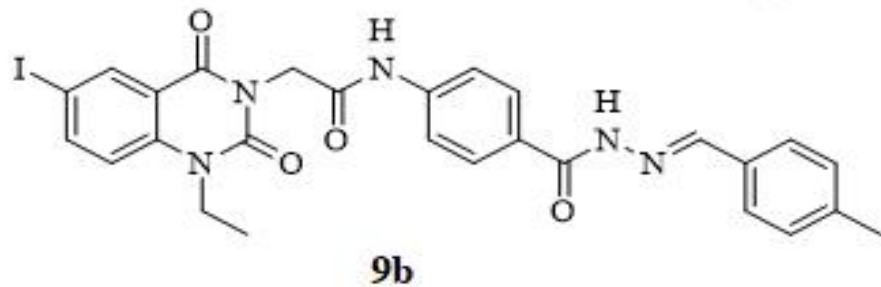
F2 - Processing parameters
SI 32768
SF 100.6177975 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40



% Transmittance



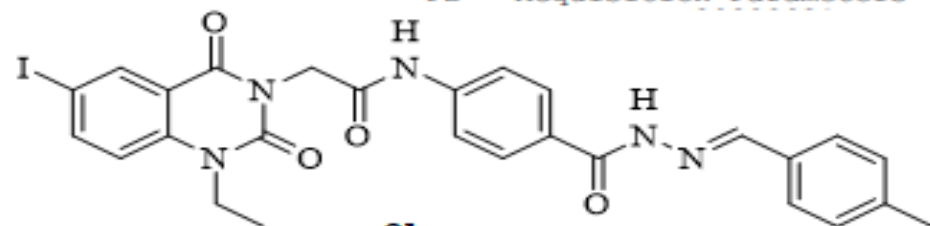
Relax. delay 1.000 sec
 Pulse 74.1 degrees
 Acq. time 4.004 sec
 Width 8000.0 Hz
 25 repetitions
 OBSERVE M1, 300.0687875 MHz
 DATA PROCESSING
 FT size 65536
 Total time 19 min, 19 sec





Current Data Parameters
NAME K-F
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters

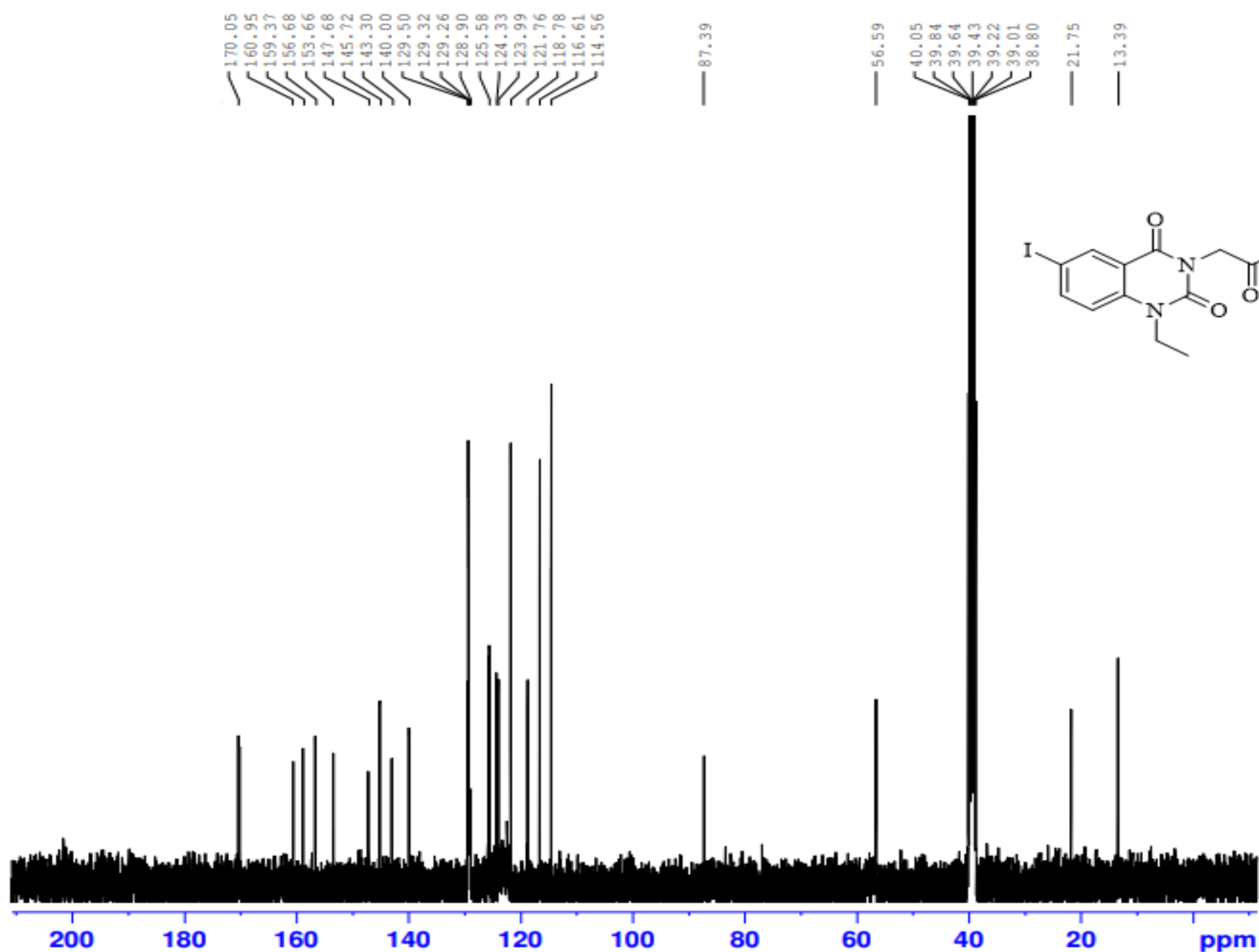


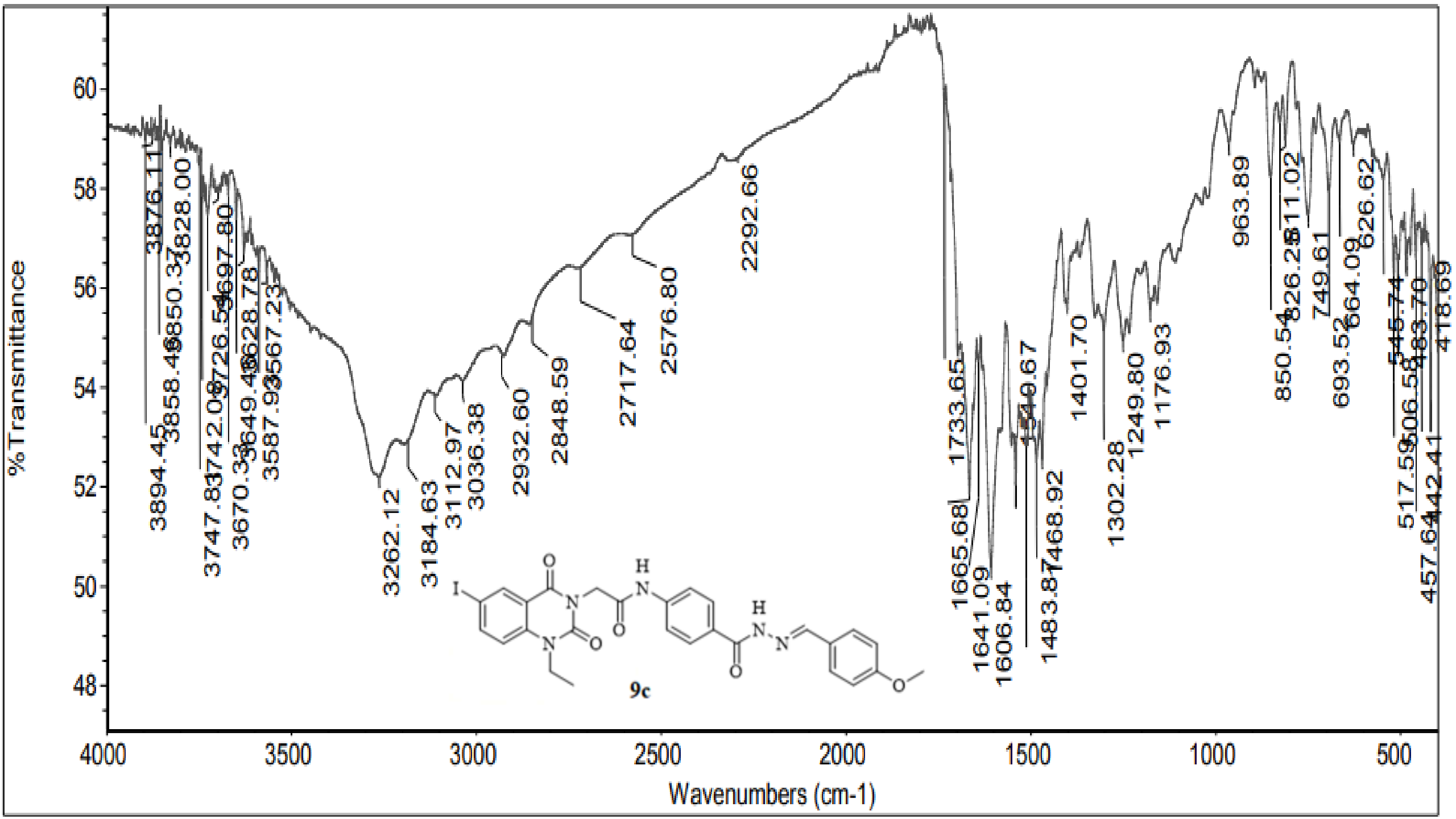
AQ 0.300750 sec
RG 1.3631488 sec
DW 205.37
DE 20.800 usec
TE 6.50 usec
D1 300.0 K
D11 2.00000000 sec
D11 0.03000000 sec
TD0 1

----- CHANNEL f1 -----
SFO1 100.6278588 MHz
NUC1 13C
P1 10.00 usec
PLW1 47.00000000 W

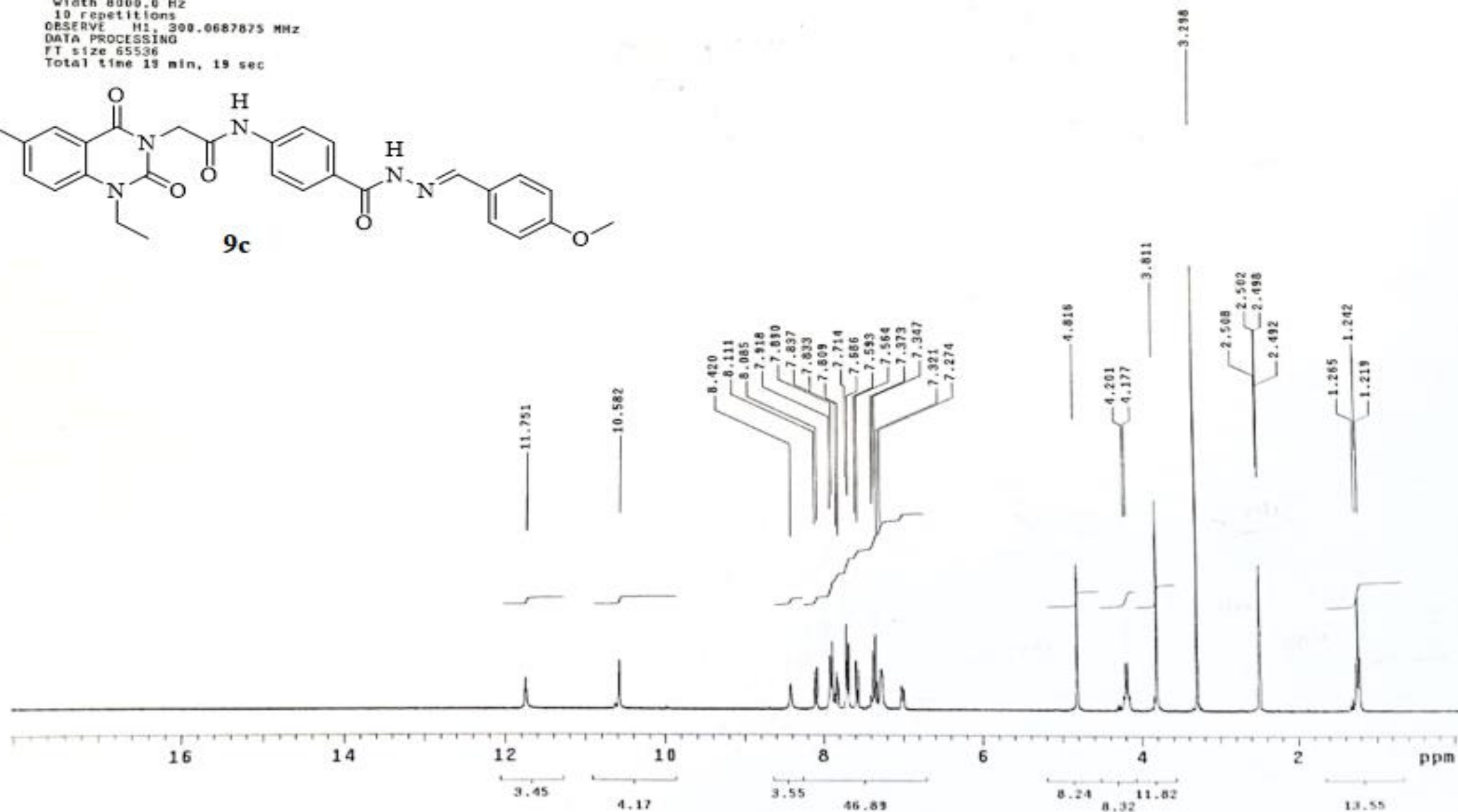
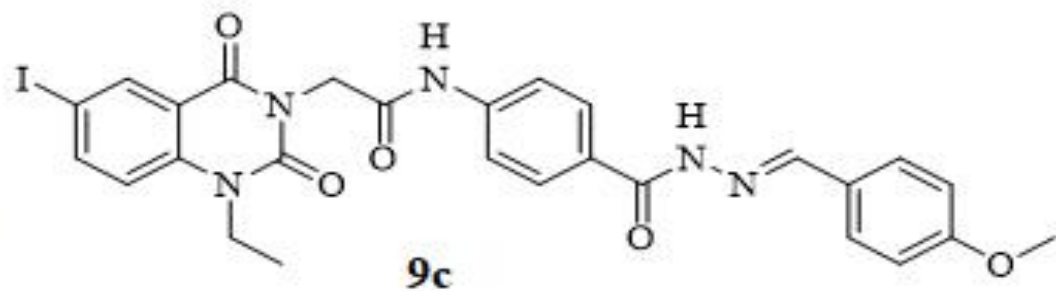
----- CHANNEL f2 -----
SFO2 400.1516006 MHz
NUC2 1H
CPDPRG[2] waltz16
PCPD2 90.00 usec
PLW2 18.00000000 W
PLW12 0.34722000 W
PLW13 0.28125000 W

F2 - Processing parameters
SI 32768
SF 100.6177975 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40



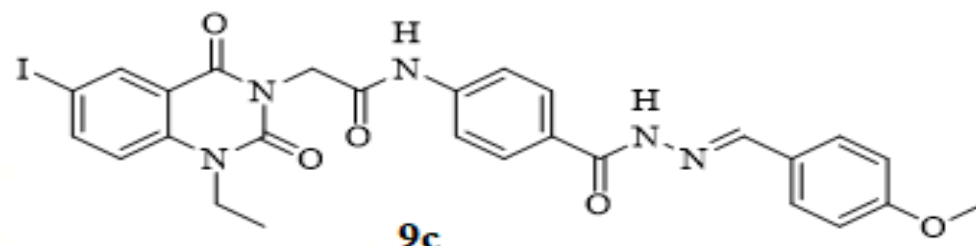


Relax. delay 1.000 sec
Pulse 74.1 degrees
Acq. time 4.004 sec
Width 8000.0 Hz
10 repetitions
OBSERVE H1, 300.0687875 MHz
DATA PROCESSING
FT size 65536
Total time 19 min, 19 sec





Current Data Parameters
NAME K-A
EXPNO 2
PROCNO 1

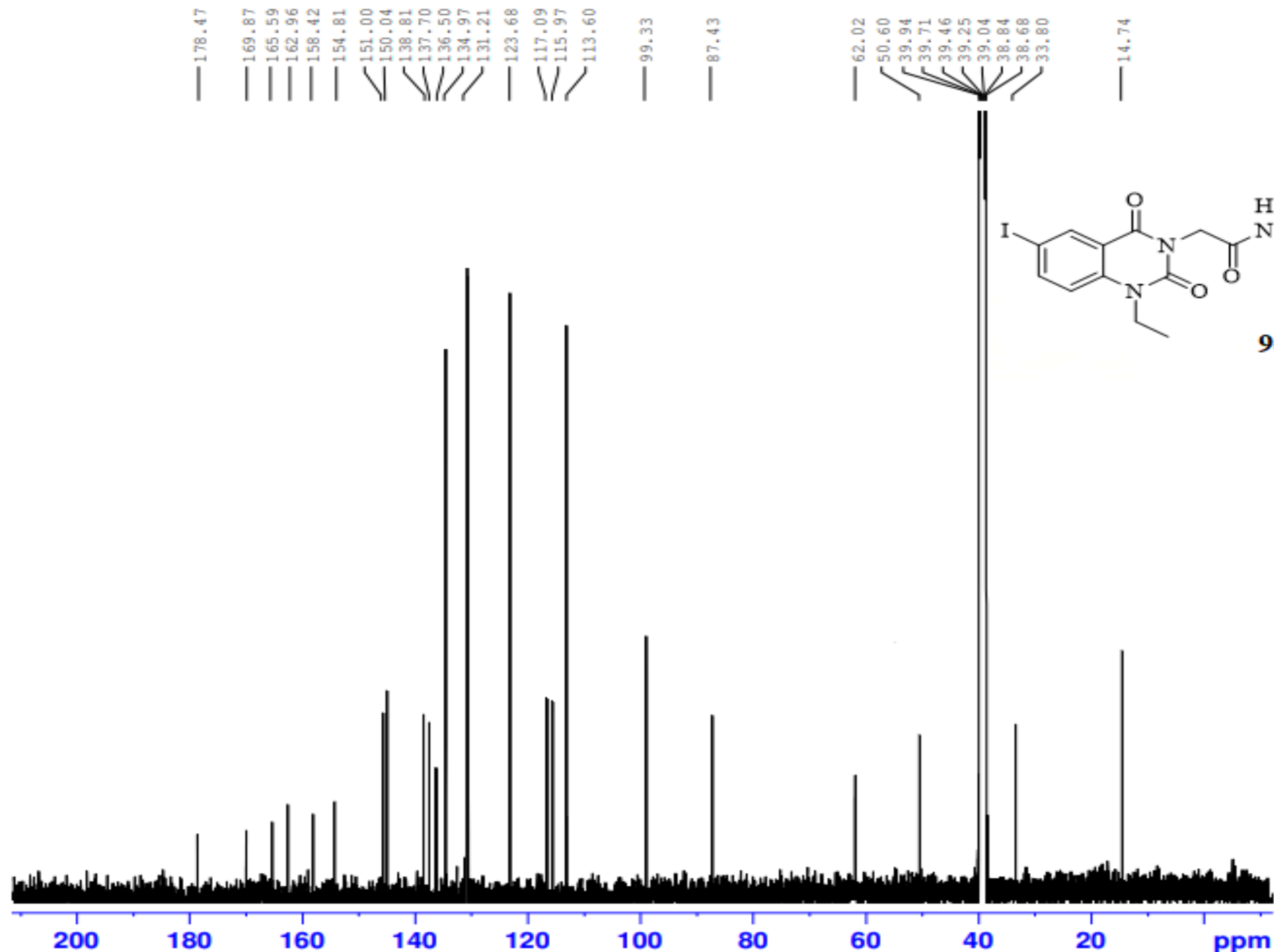


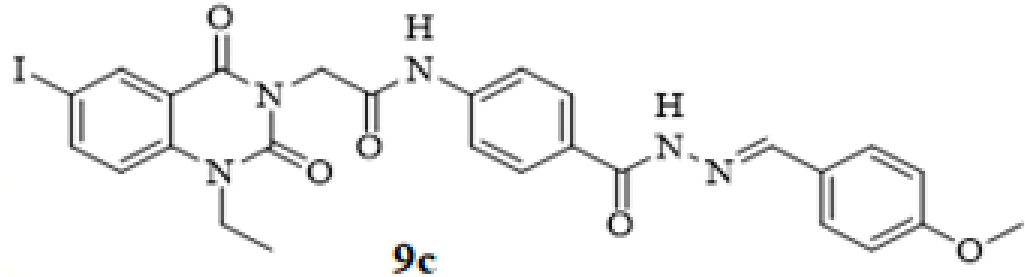
FIDRES 0.366798 HZ
AQ 1.3631488 sec
RG 205.37
DW 20.800 usec
DE 6.50 usec
TE 300.0 K
D1 2.0000000 sec
D11 0.0300000 sec
TD0 1

----- CHANNEL f1 -----
SFO1 100.6278588 MHz
NUC1 13C
P1 10.00 usec
PLW1 47.00000000 W

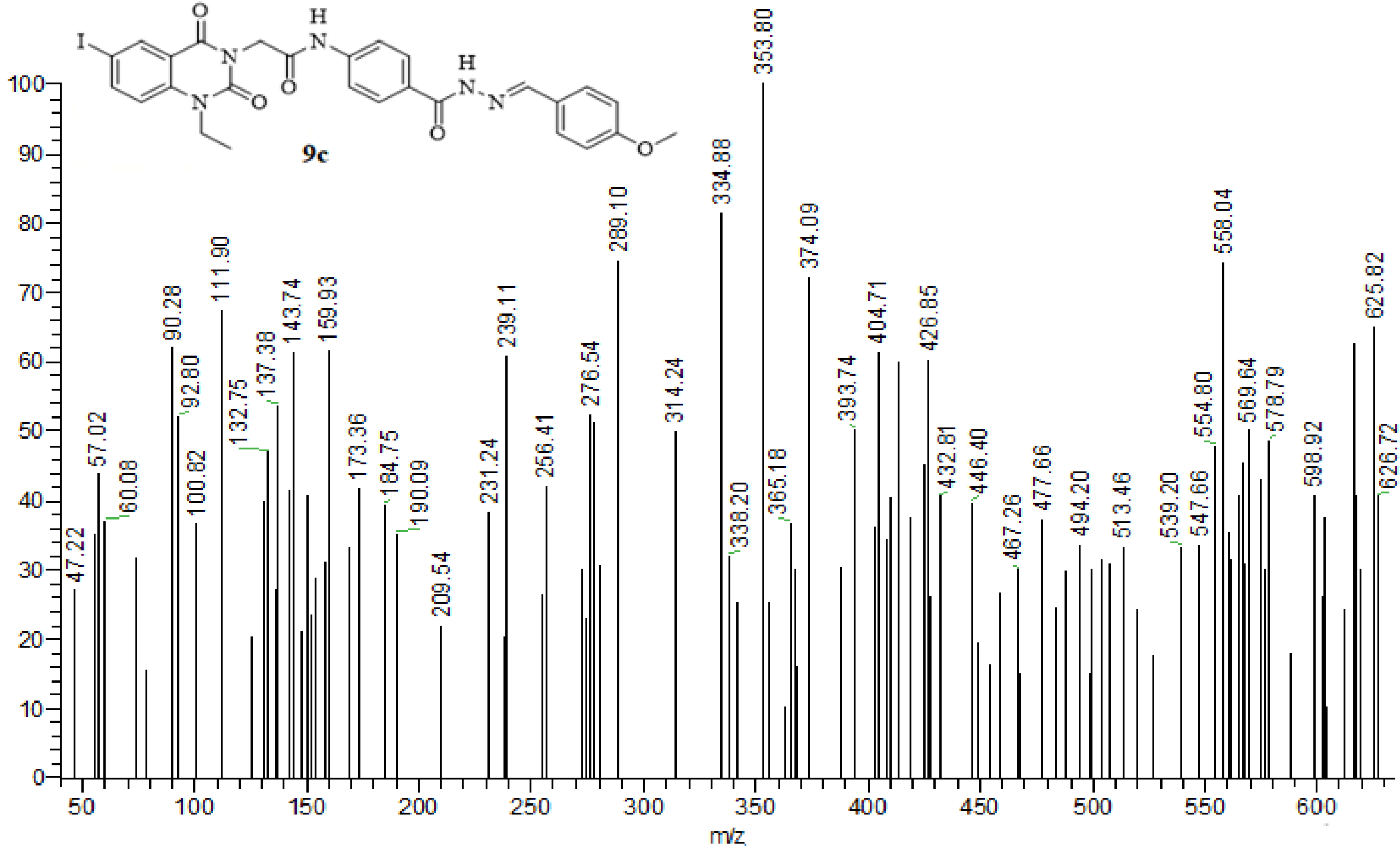
----- CHANNEL f2 -----
SFO2 400.1516006 MHz
NUC2 1H
CPDPRG[2] waltz16
PCPD2 90.00 usec
PLW2 18.00000000 W
PLW12 0.34722000 W
PLW13 0.28125000 W

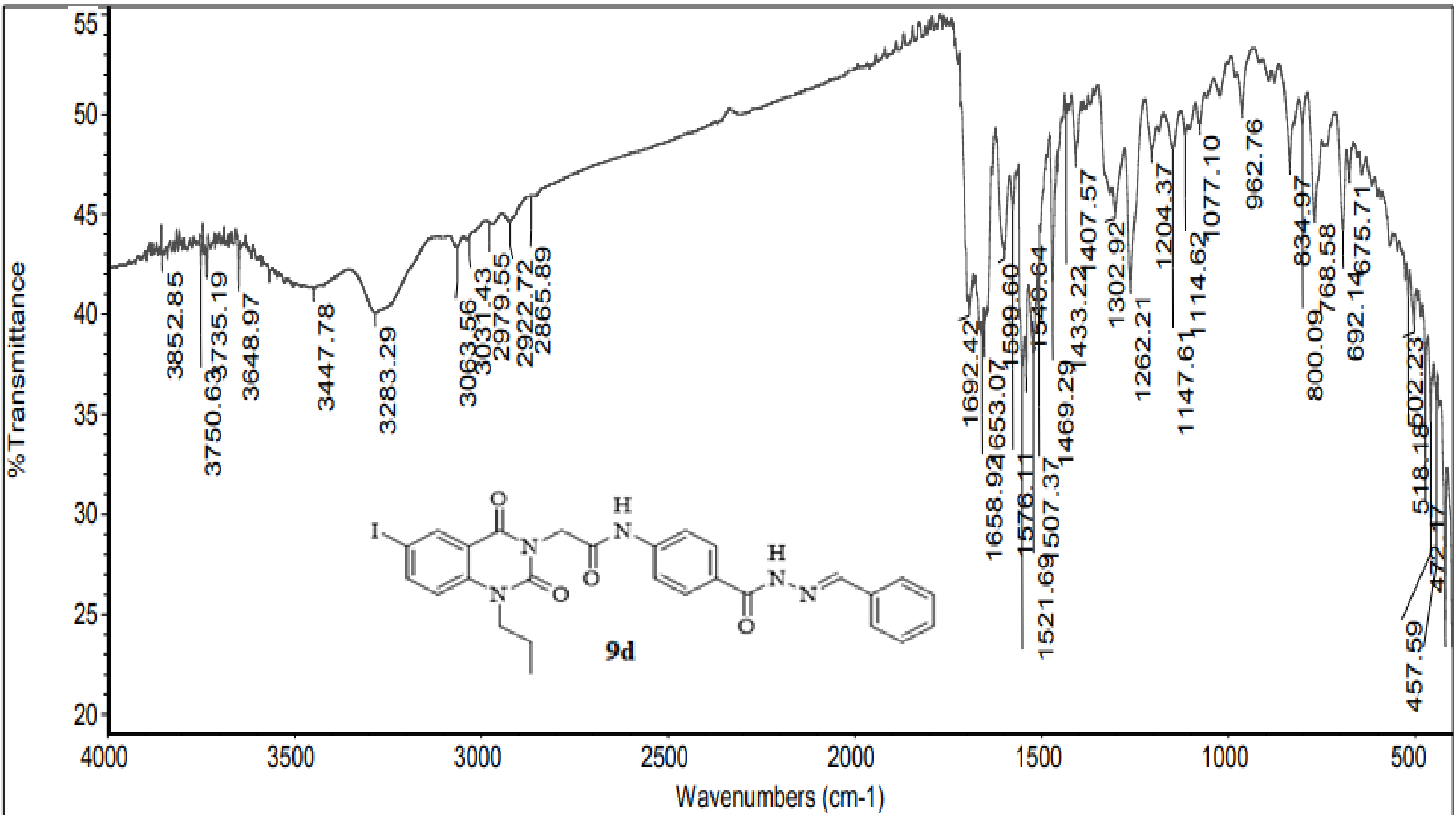
F2 - Processing parameters
SI 32768
SF 100.6177975 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40



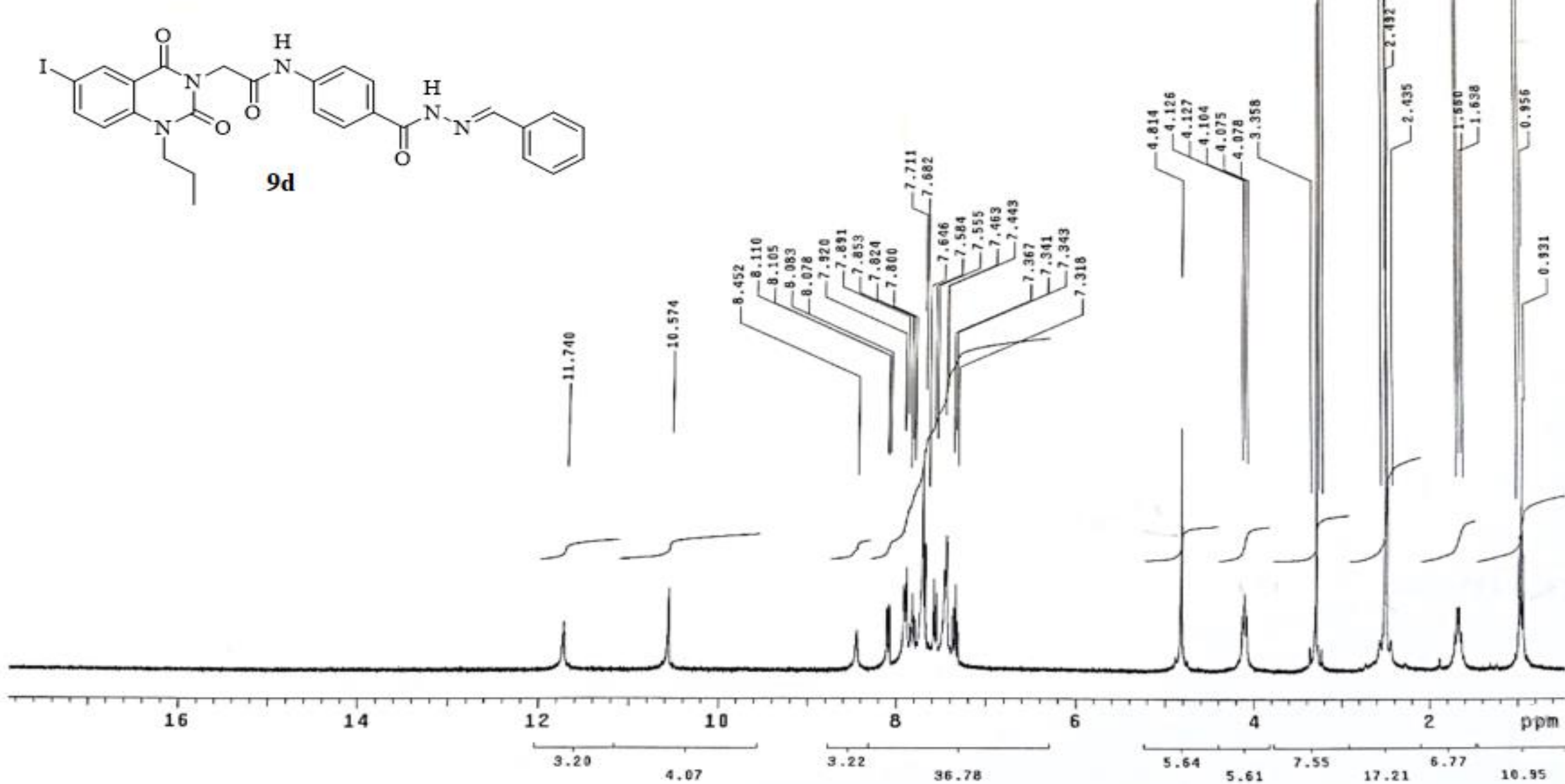
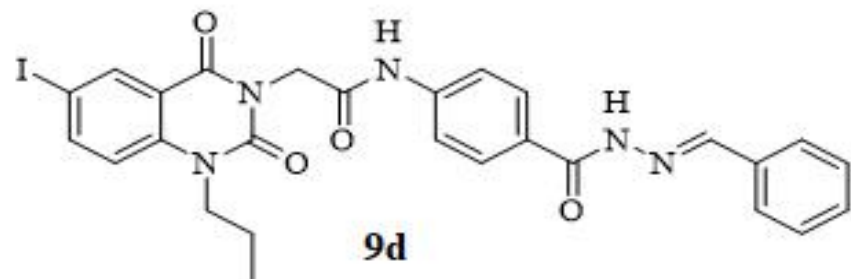


Relative Abundance

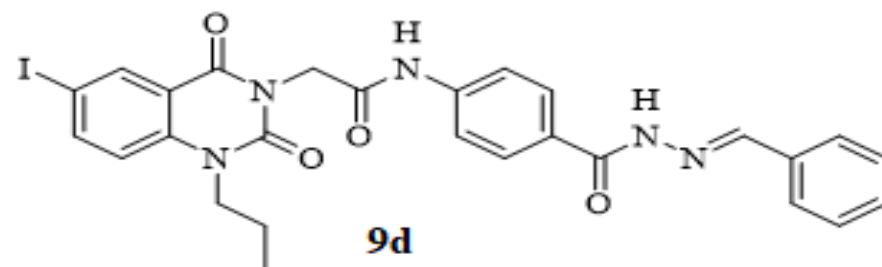




Relax. delay 1.000 sec
Pulse 74.1 degrees
Acq. time 4.004 sec
Width 8000.0 Hz
14 repetitions
OBSERVE H1, 300.0687875 MHz
DATA PROCESSING
FT size 65536
Total time 19 min, 19 sec



Current Data Parameters
 NAME K-2
 EXPNO 3
 PROCNO 1

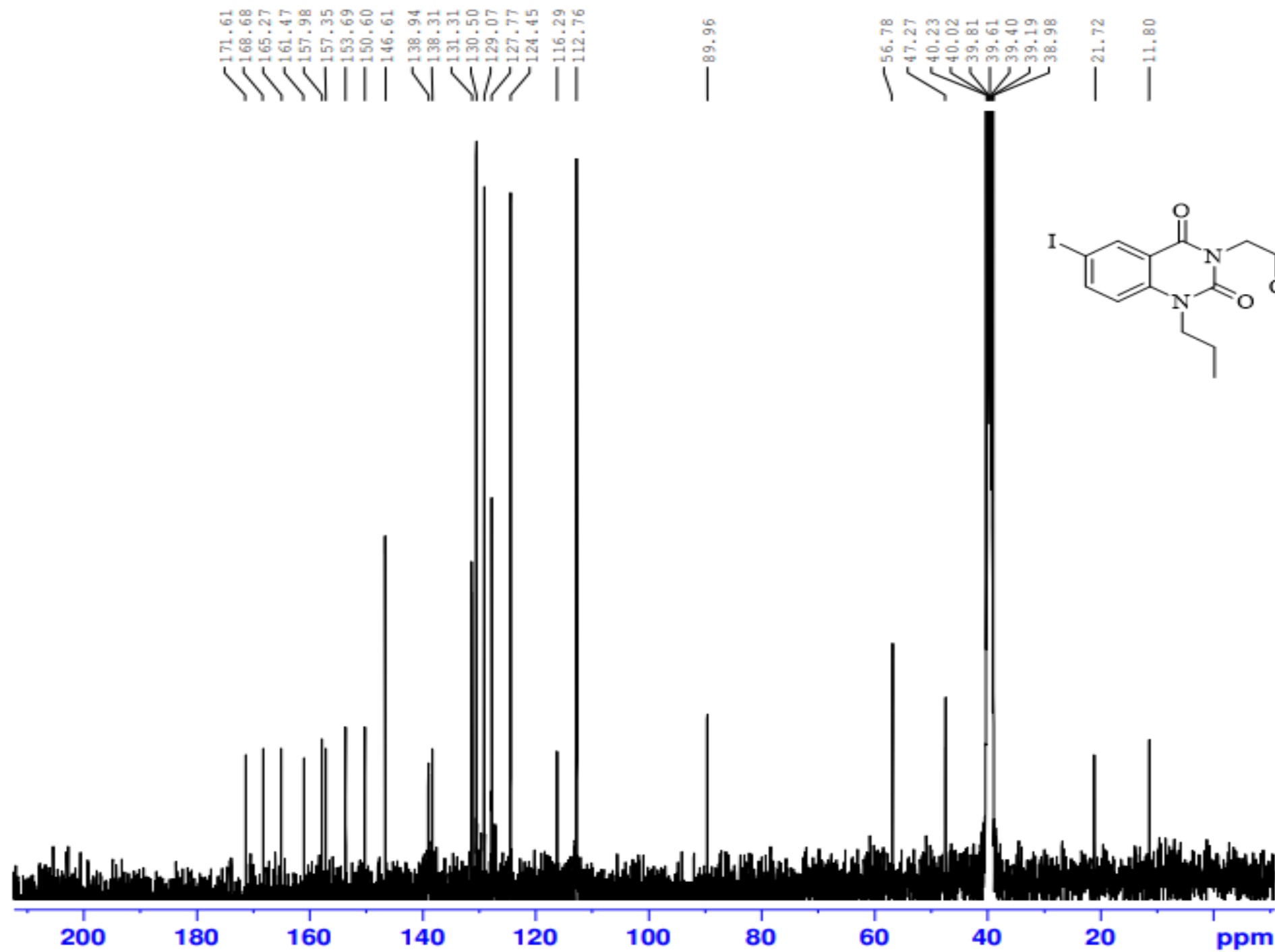


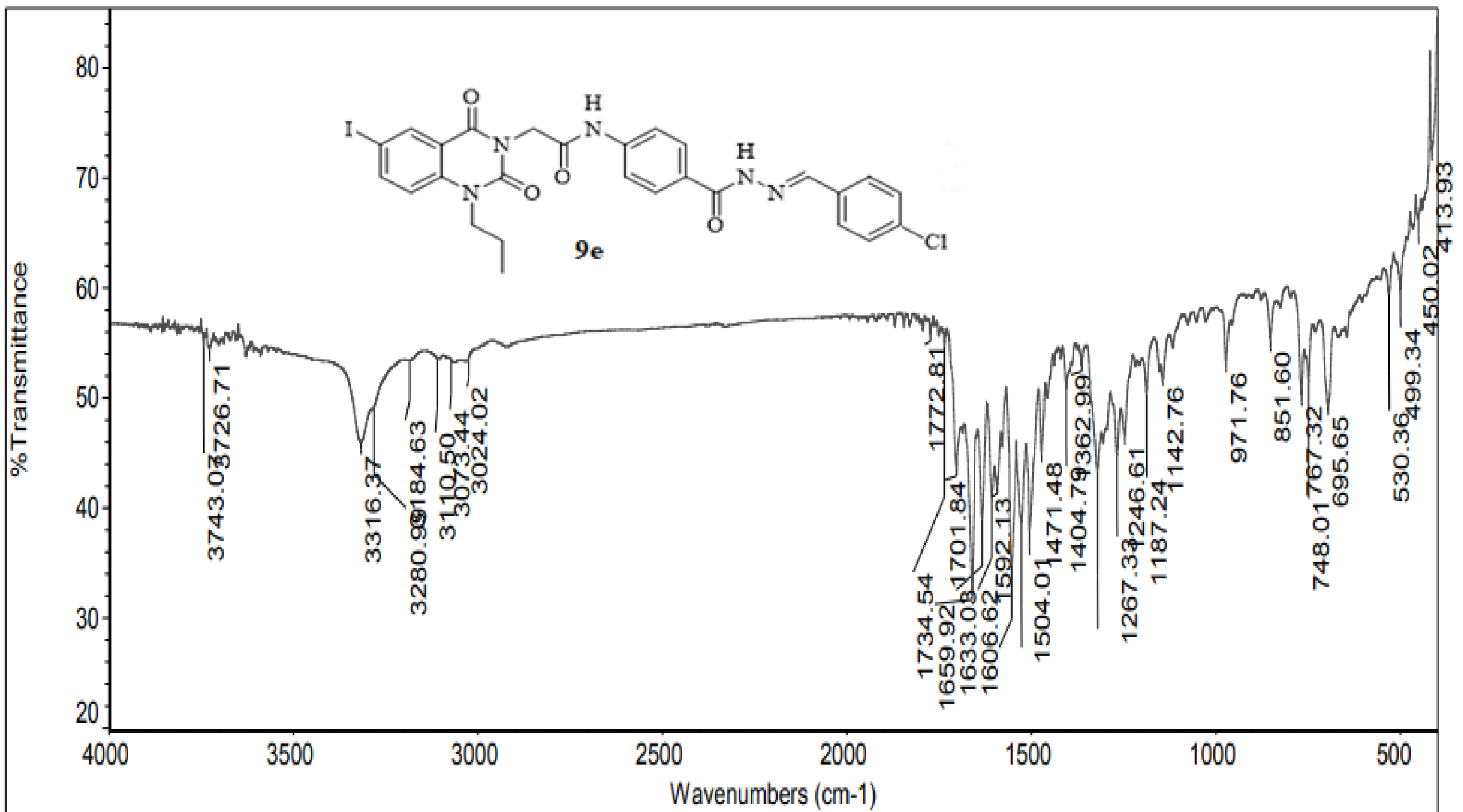
AQ 1.3631488 sec
 RG 205.37
 DW 20.800 usec
 DE 6.50 usec
 TE 300.0 K
 D1 2.00000000 sec
 D11 0.03000000 sec
 TD0 1

----- CHANNEL f1 -----
 SFO1 100.6278588 MHz
 NUC1 13C
 P1 10.00 usec
 PLW1 47.00000000 W

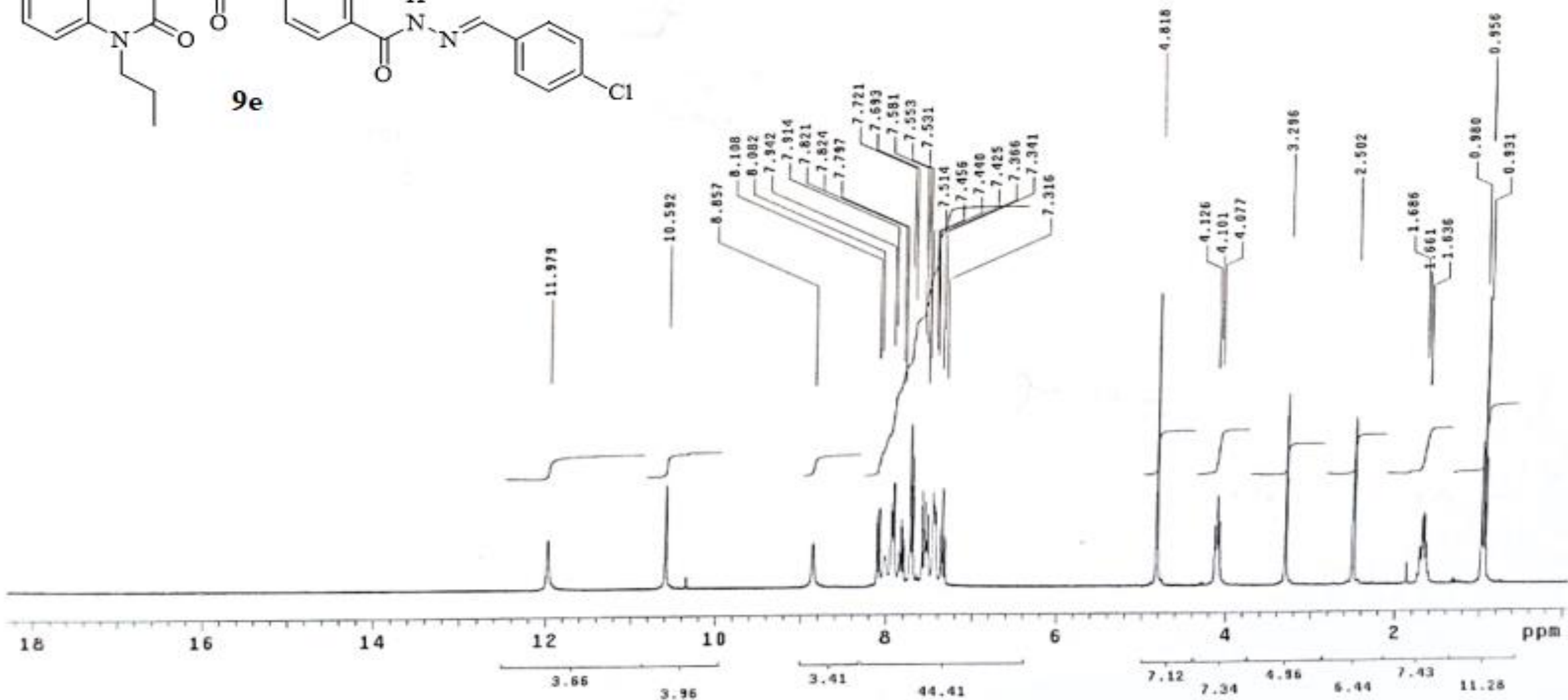
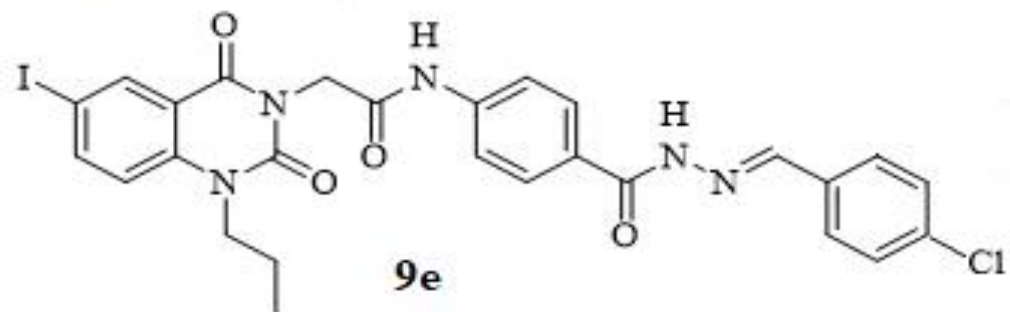
----- CHANNEL f2 -----
 SFO2 400.1516006 MHz
 NUC2 1H
 CPDPRG[2] waltz16
 PCPD2 90.00 usec
 PLW2 18.00000000 W
 PLW12 0.34722000 W
 PLW13 0.28125000 W

F2 - Processing parameters
 SI 32768
 SF 100.6177975 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40





Relax. delay 1.000 sec
 Pulse 74.1 degrees
 Acq. time 4.004 sec
 Width 8000.0 Hz
 22 repetitions
 OBSERVE M1, 300.0687875 MHz
 DATA PROCESSING
 FT size 65536
 Total time 19 min, 19 sec





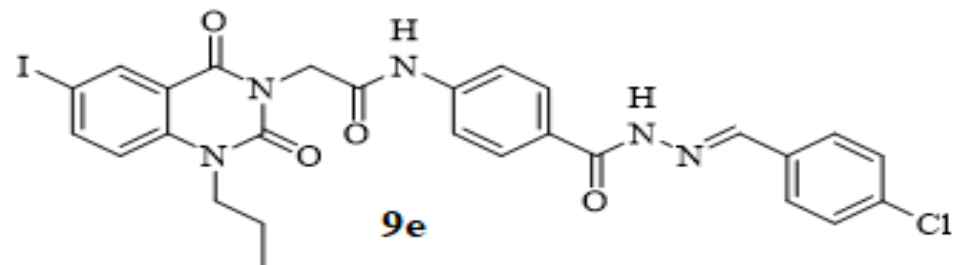
Current Data Parameters
NAME K-3
EXPNO 2
PROCNO 1

169.40
160.00
153.18
152.92
152.45
148.76
143.45
142.74
131.78
129.94
129.89
129.69
125.60
124.36
123.62
122.86
122.72
122.15
118.94
113.89
96.78

54.98
46.82
40.26
40.05
39.84
39.64
39.43
39.22
39.01

21.29

10.96



9e

AQ 1.3631488 sec
RG 205.37
DW 20.800 usec
DE 6.50 usec
TE 300.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

----- CHANNEL f1 -----
SFO1 100.6278588 MHz
NUC1 13C
P1 10.00 usec
PLW1 47.00000000 W

----- CHANNEL f2 -----
SFO2 400.1516006 MHz
NUC2 1H
CPDPRG[2] waltz16
PCPD2 90.00 usec
PLW2 18.00000000 W
PLW12 0.34722000 W
PLW13 0.28125000 W

F2 - Processing parameters
SI 32768
SF 100.6177975 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

