

Design, Synthesis, Molecular Docking, and Evaluation Antioxidant and Antimicrobial Activities for Novel 3-Phenylimidazolidin-4-One and 2-Aminothiazol-4-One Derivatives

Wesam S. Shehab ^{1,*}, Maged A. Aziz ^{1,†}, Nourhan Kh. R. Elhoseni ¹, Mohamed G. Assy ¹, Magda H. Abdellattif ², and Eman O. Hamed ¹

Docking study

A molecular docking study of the sixteen newly designed and synthesized 3-phenylimidazolidin-4-one and 2-aminothiazol-4-one compounds was performed using MOE 2019.0102 program. The newly synthesized compounds were drawn using ChemDraw, imported into the MOE program window, converted for their 3D forms, adjusted for the partial charges, and energy minimized as described earlier. The database was built containing the newly synthesized candidates (1–11) together with the co-crystallized ascorbic acid as a reference standard. A general docking process was performed using the site of the co-crystallized ascorbic acid inside cytochrome *c* peroxidase and streptococcus pneumoniae hyaluronate lyase enzyme as the docking site. Also, all the other docking parameters were adjusted as previously discussed in detail. Moreover, it is worth mentioning that a program validation process was performed at first before applying the docking process by redocking the co-crystallized ascorbic acid at its binding pocket of the cytochrome *c* peroxidase enzyme and streptococcus pneumoniae hyaluronate lyase enzyme. A valid performance was confirmed by obtaining a low RMSD value (<1).

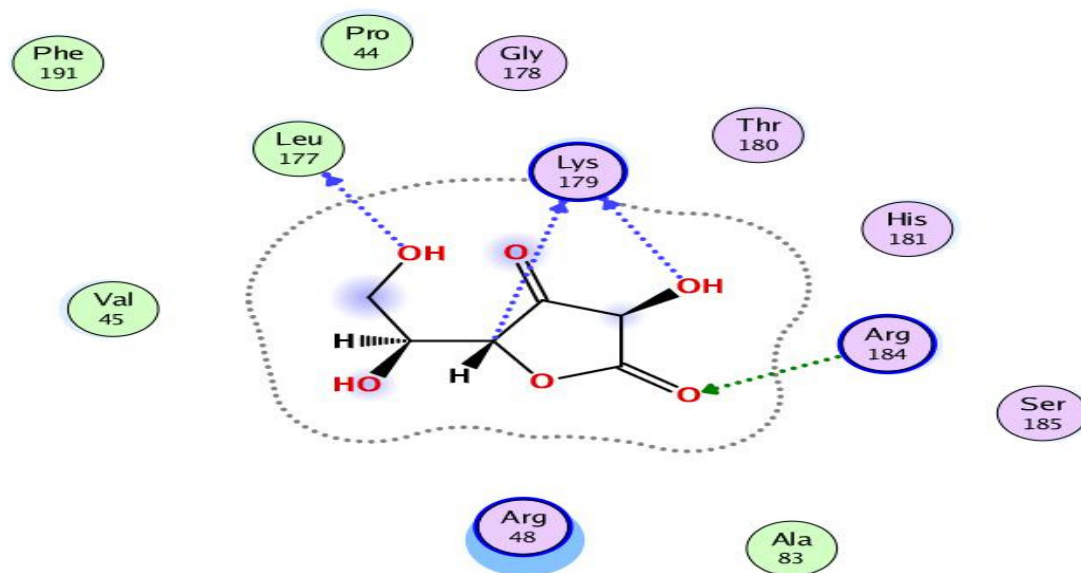


Figure S1. 2D interaction images of ascorbic acid with the active sites of 2X08.

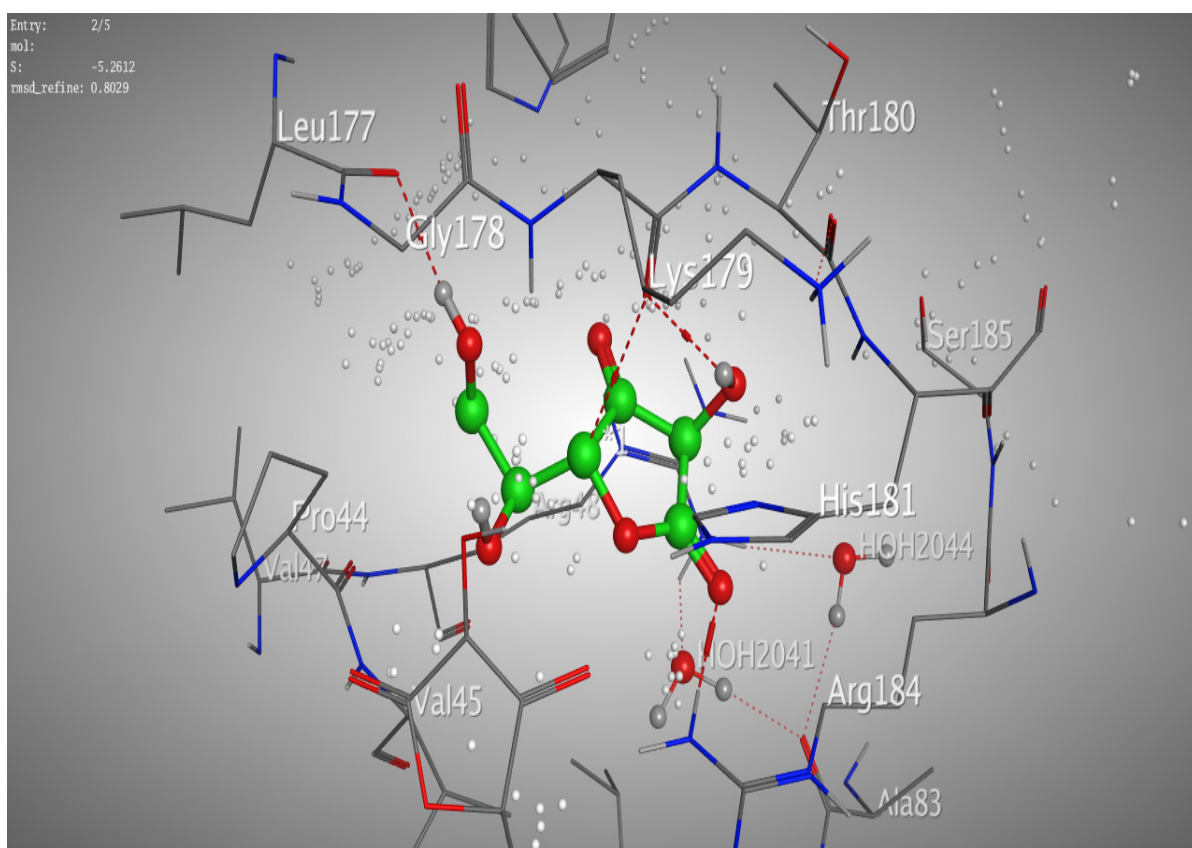


Figure S2. 3D interaction images of ascorbic acid with the active sites of 2X08.

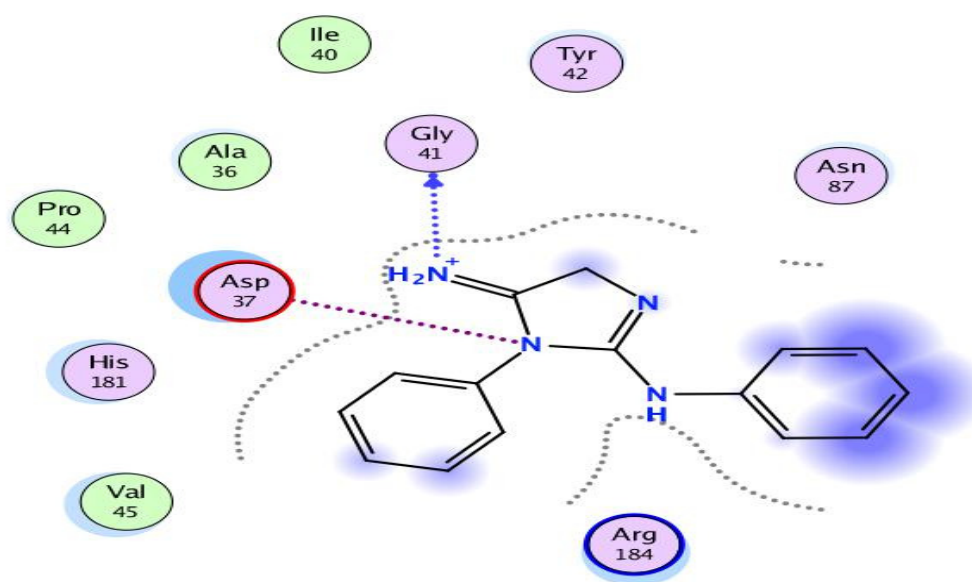


Figure S3. 2D interaction images of compound 2 with the active sites of 2X08.

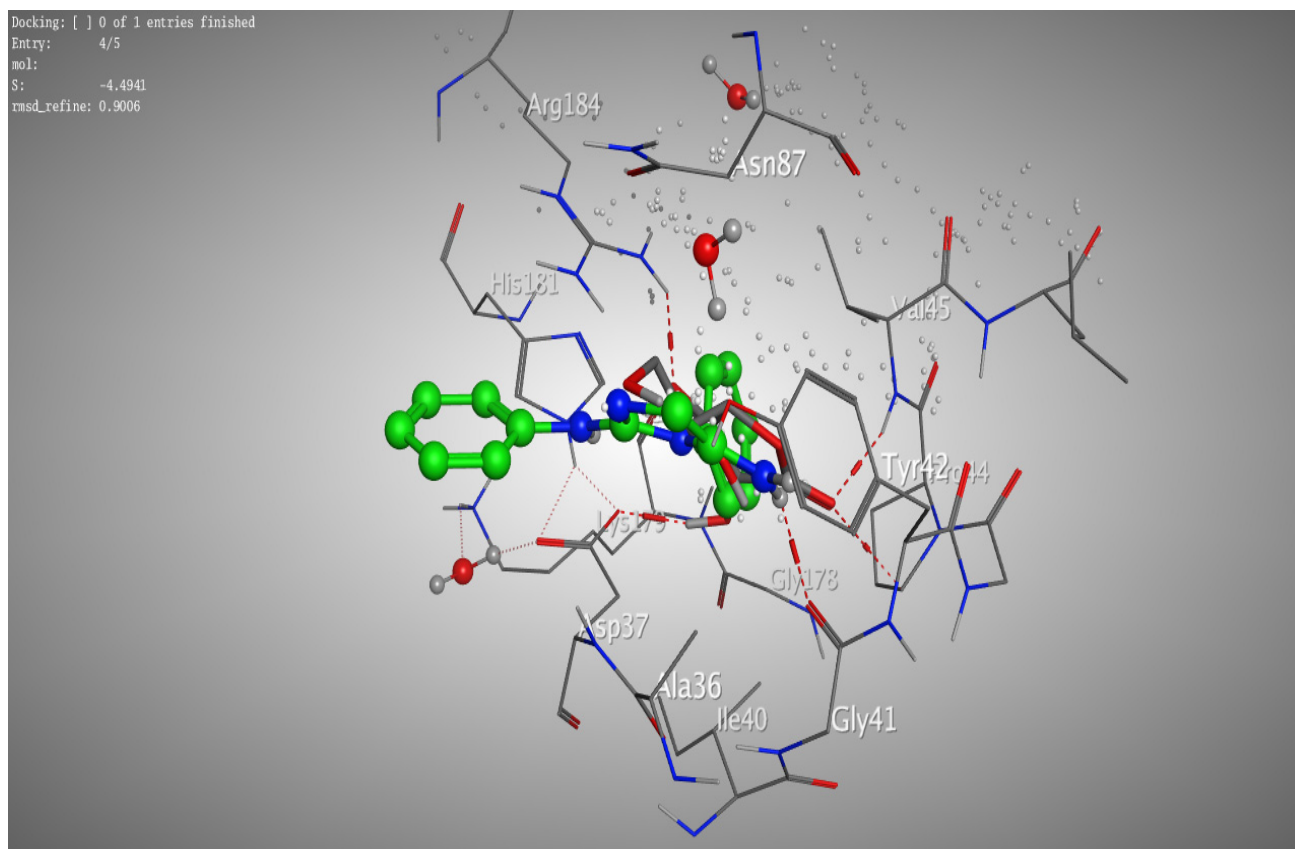


Figure S4. 3D interaction images of compound 2 with the active sites of 2X08.

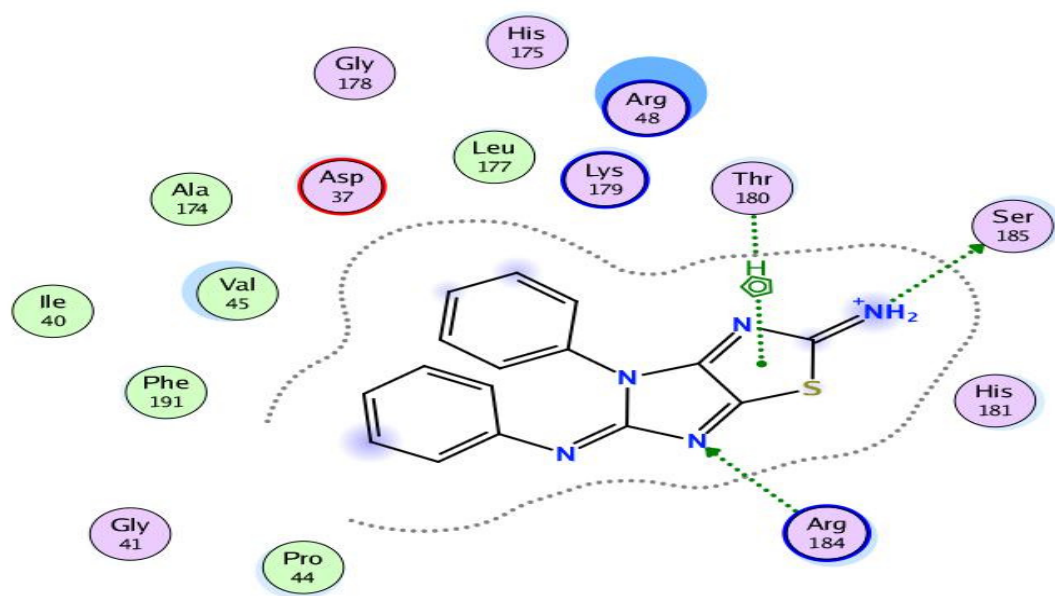


Figure S5. 2D interaction images of compound 3 with the active sites of 2X08.

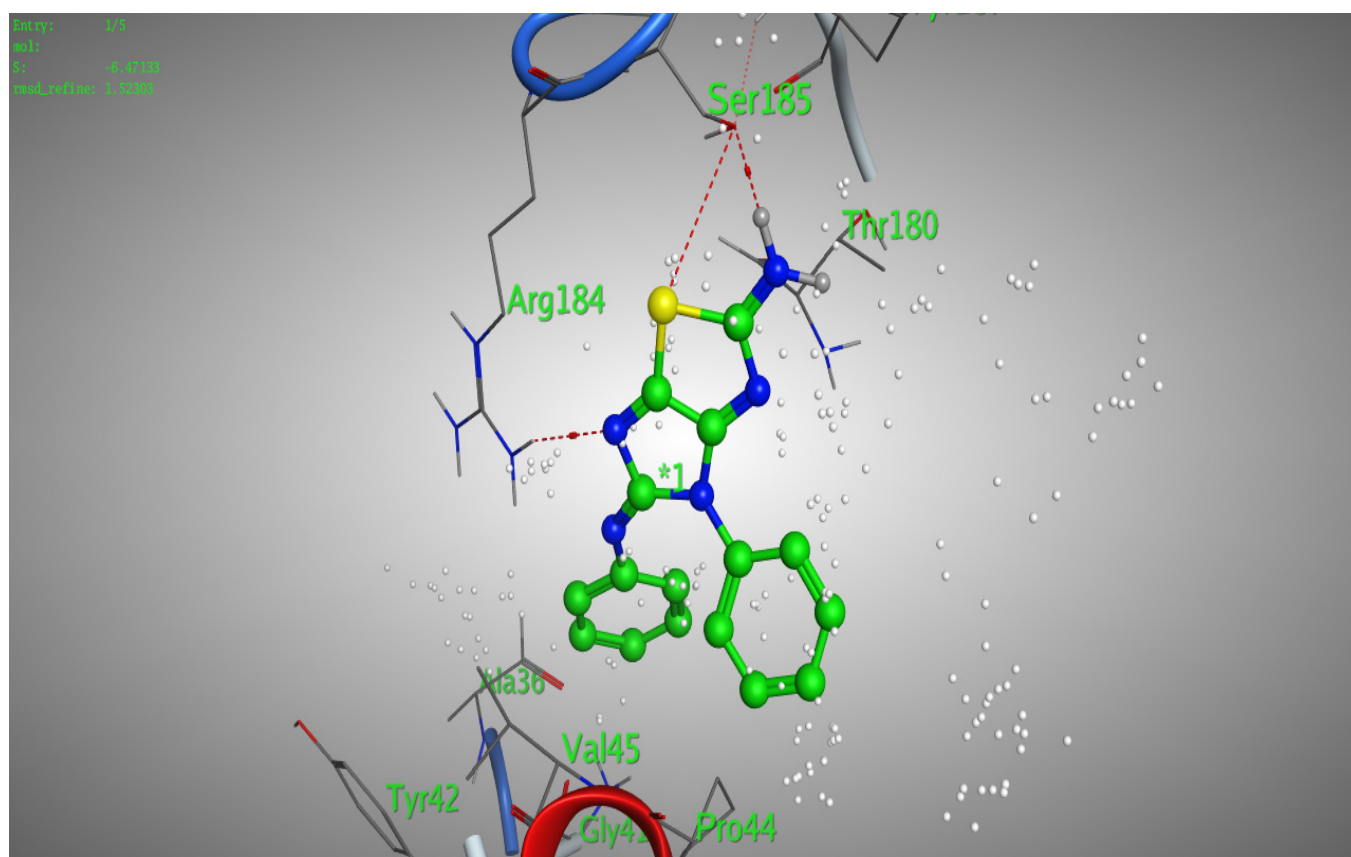


Figure S6. 3D interaction images of compound 3 with the active sites of 2X08.

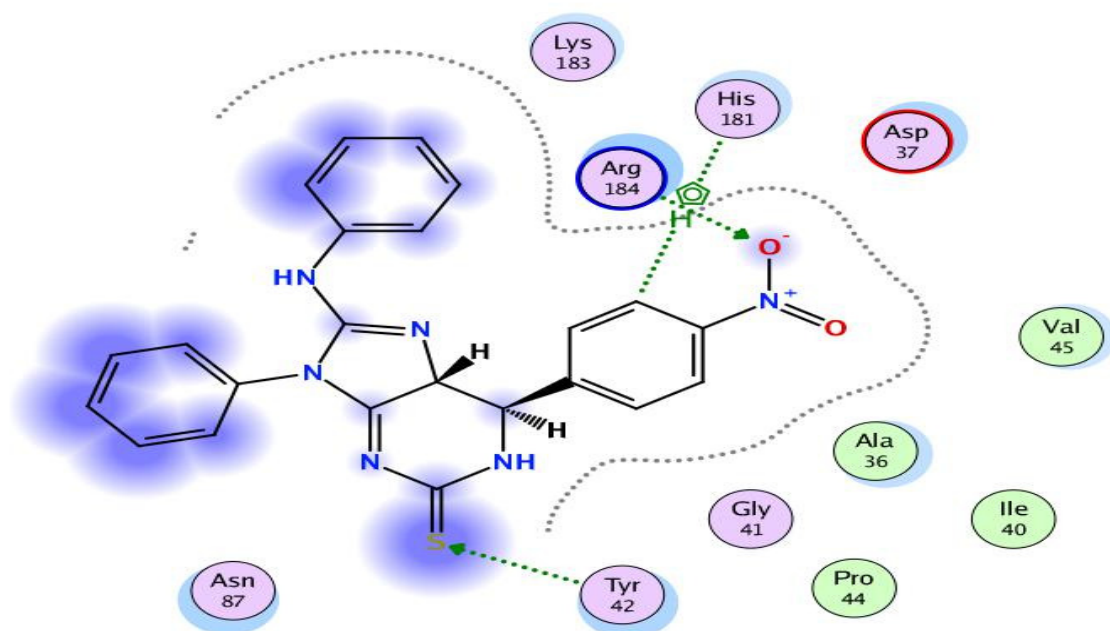


Figure S7. 2D interaction images of compound 5 with the active sites of 2X08.

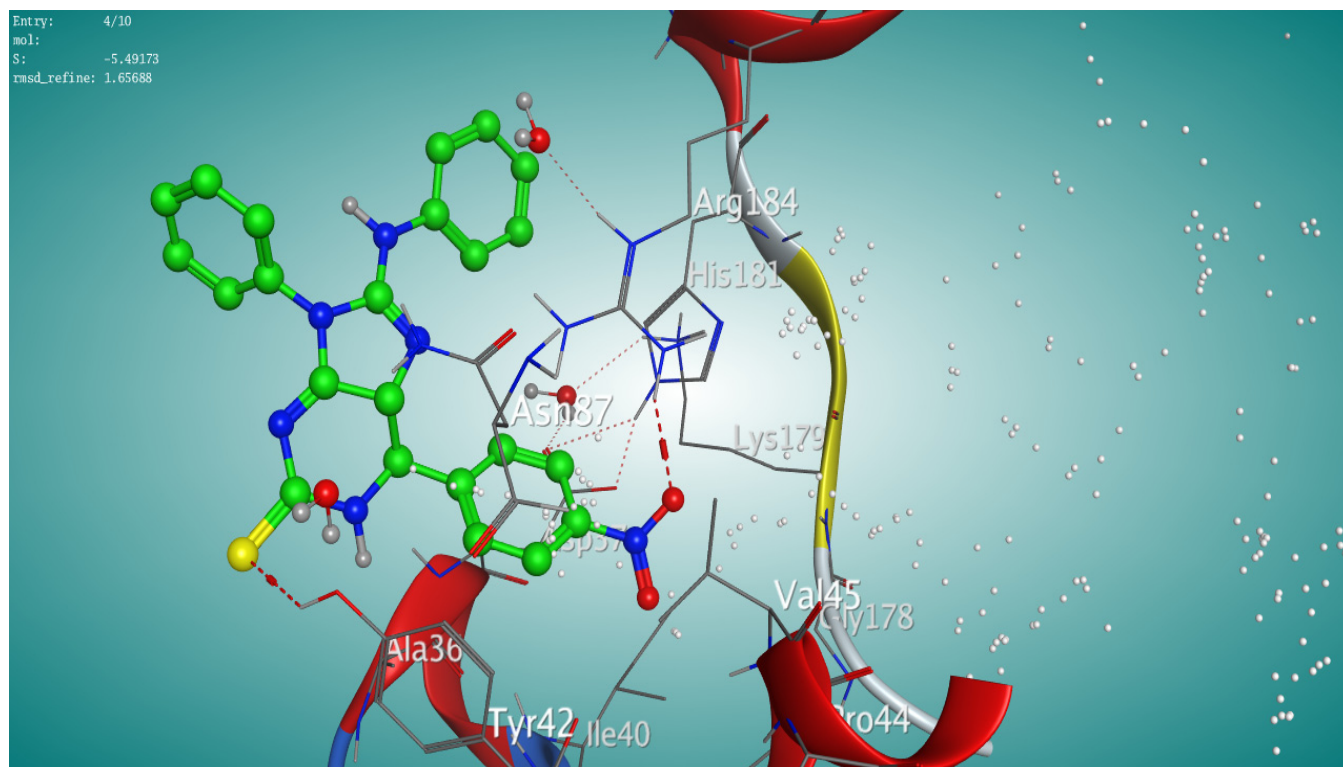


Figure S8. 3D interaction images of compound 5 with the active sites of 2X08.

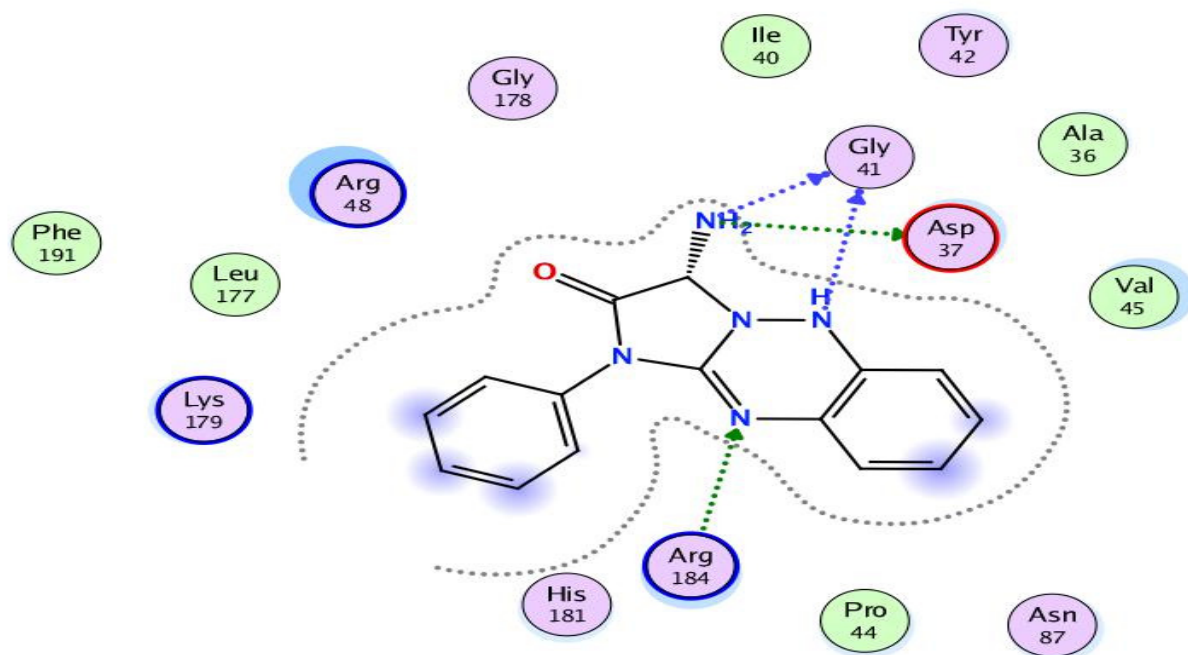


Figure S9. 2D interaction images of compound 6 with the active sites of 2X08.

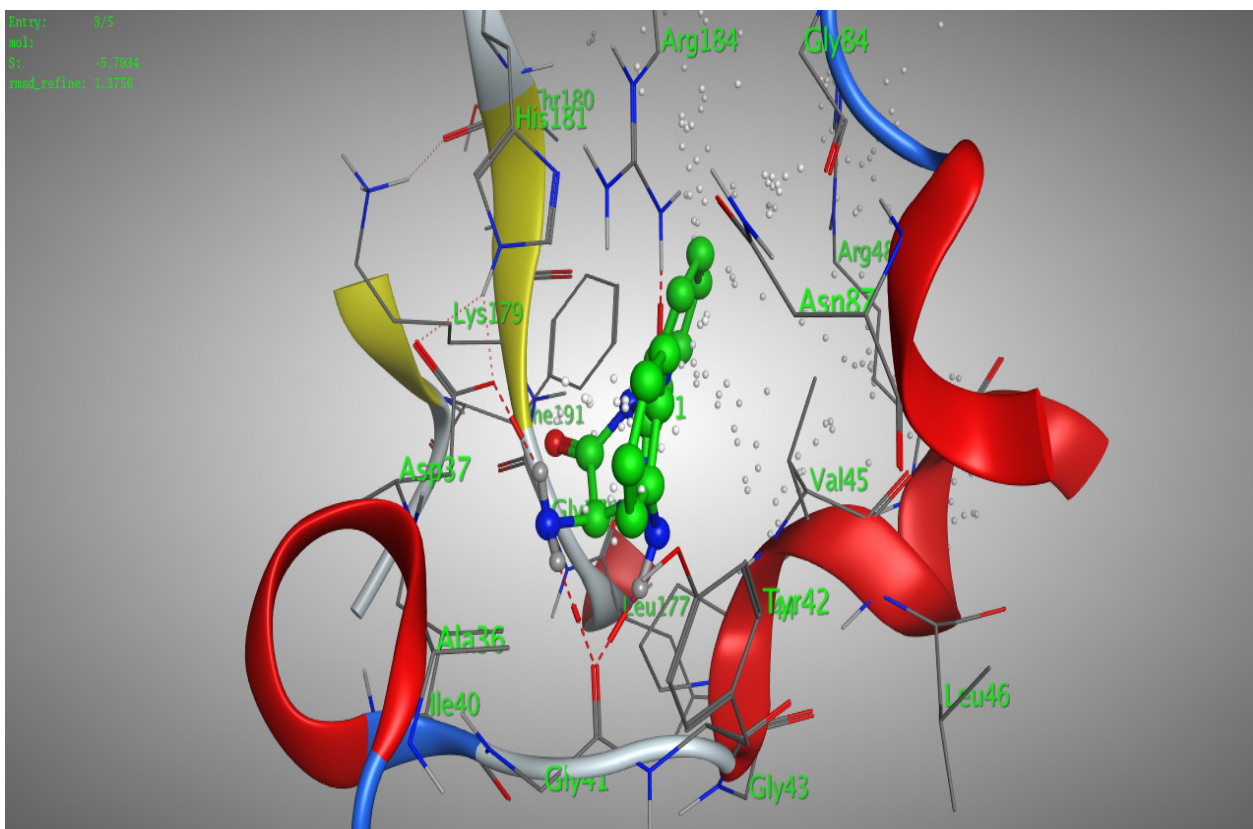


Figure S10. 3D interaction images of compound **6** with the active sites of 2X08.

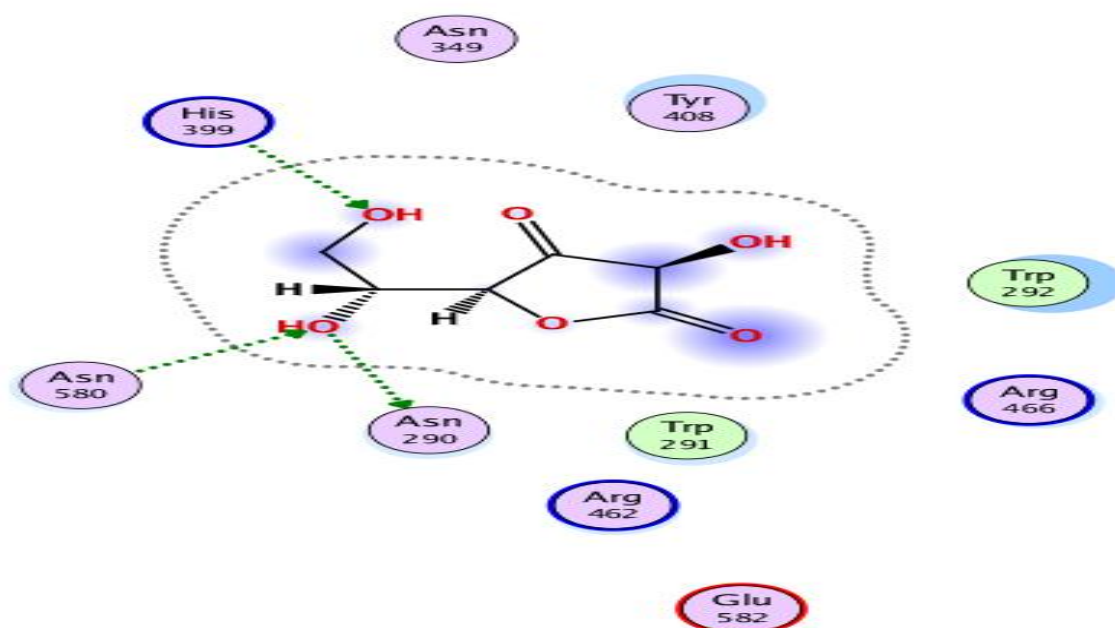


Figure S11. 2D interaction images of ascorbic acid with the active sites of 1F9G.

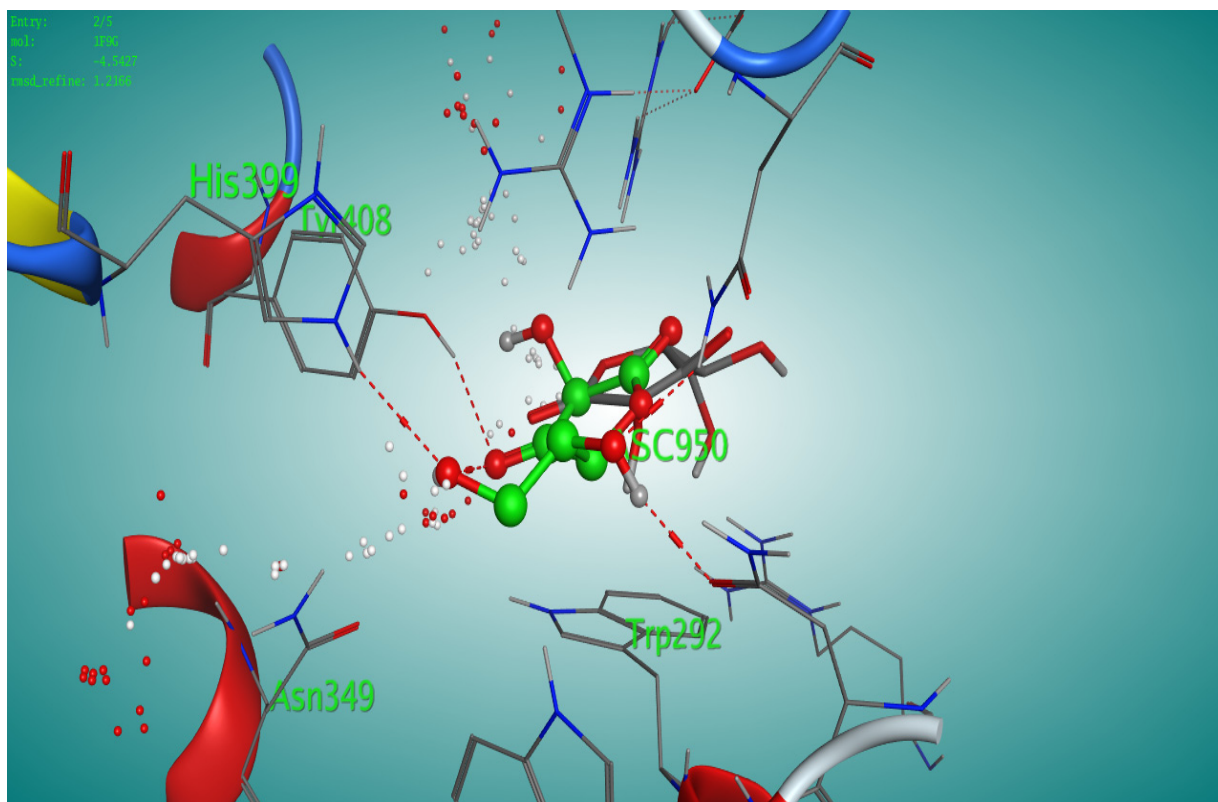


Figure S12. 3D interaction images of ascorbic acid with the active sites of 1F9G.

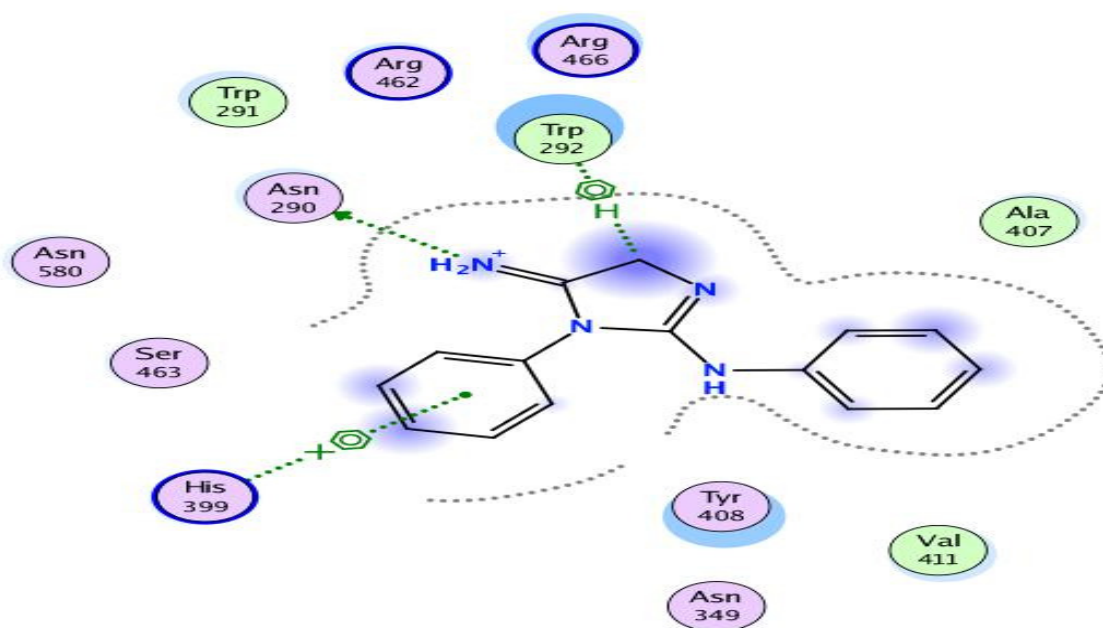


Figure S13. 2D interaction images of compound **2** with the active sites of 1F9G.

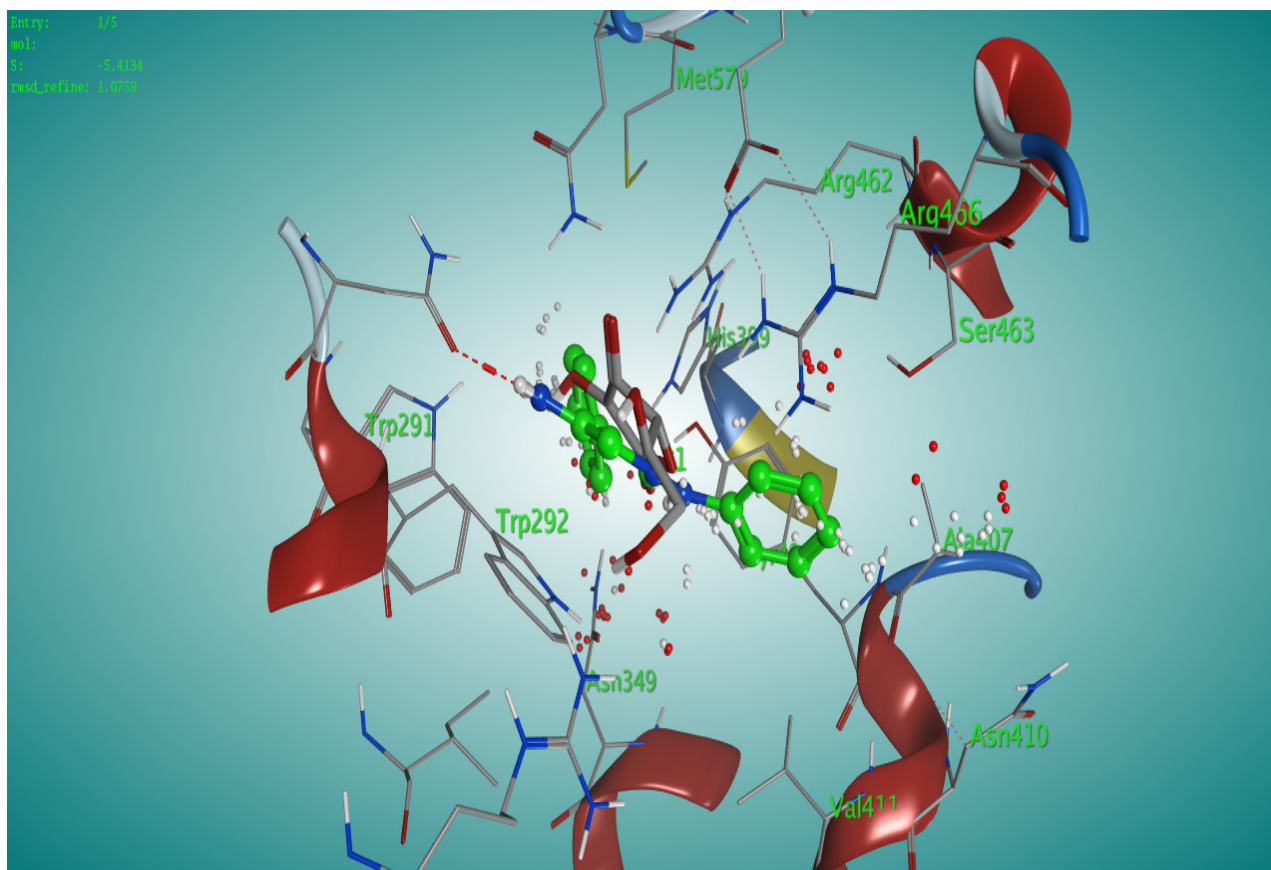


Figure S14. 3D interaction images of compound **2** with the active sites of 1F9G.

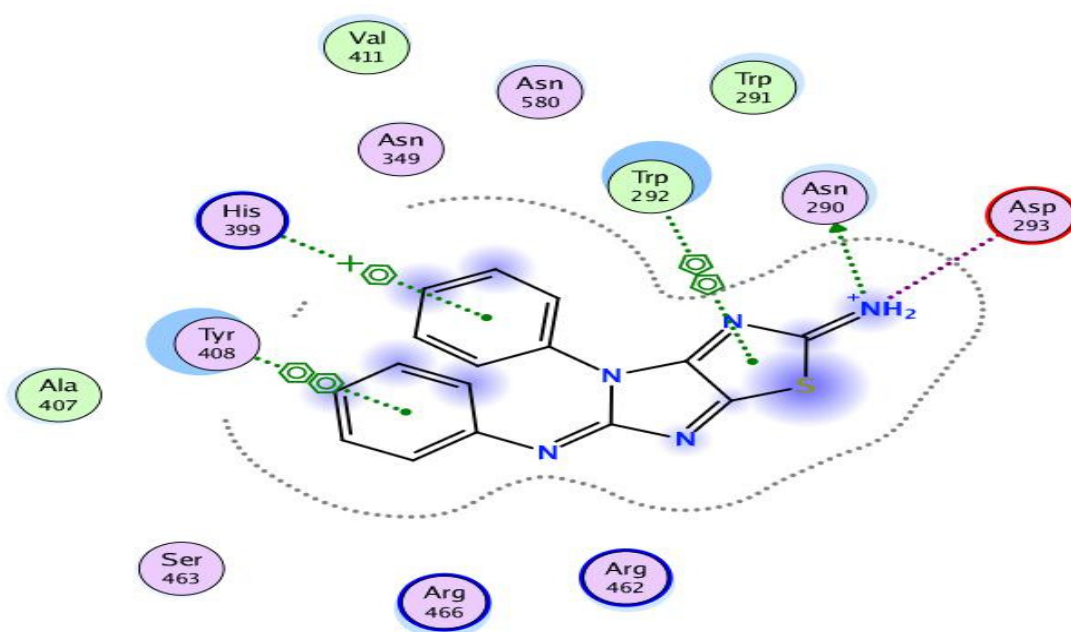


Figure S15. 2D interaction images of compound **3** with the active sites of 1F9G.

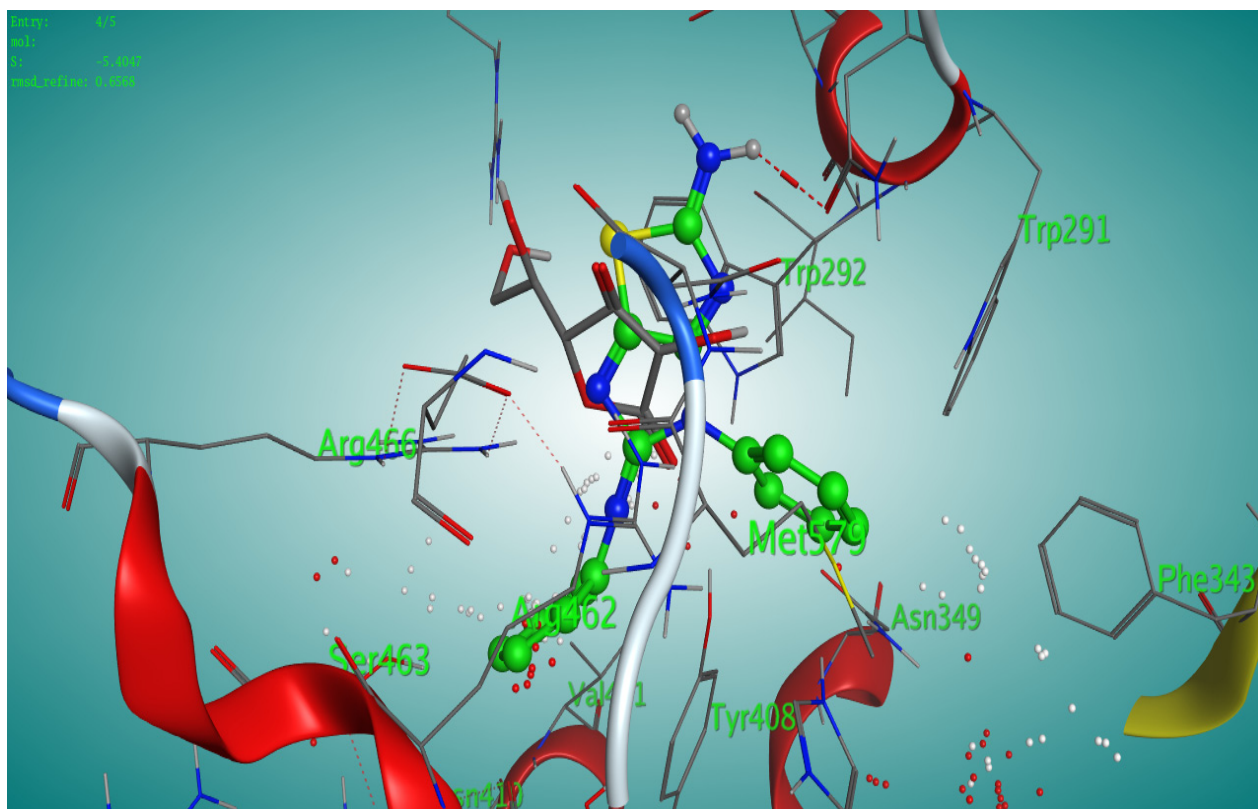


Figure S16. 3D interaction images of compound 3 with the active sites of 1F9G.

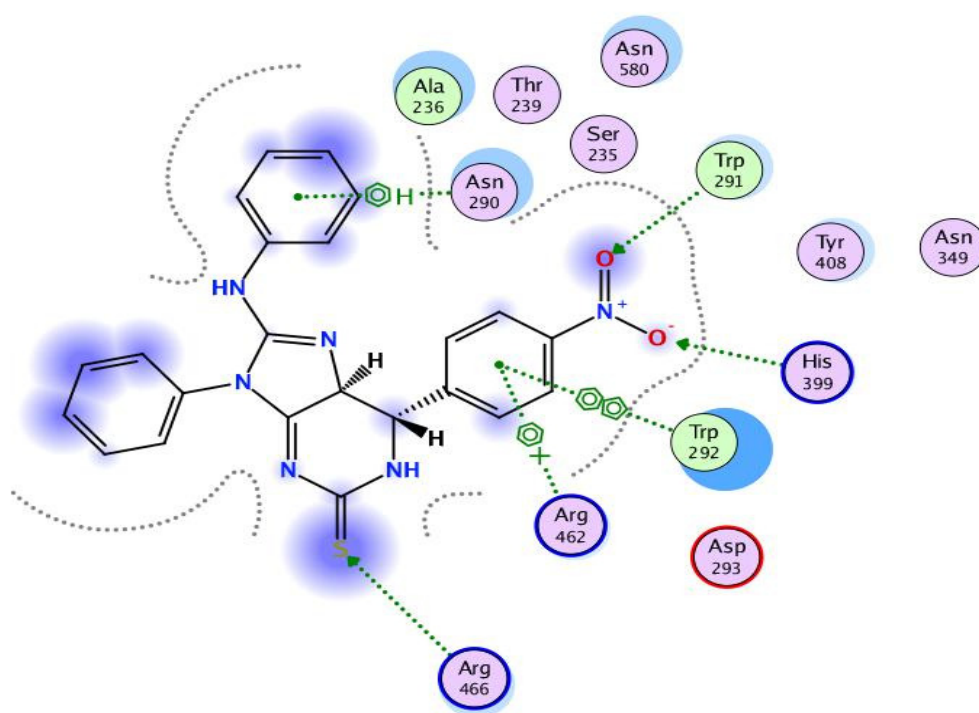


Figure S17. 2D interaction images of compound 5 with the active sites of 1F9G.

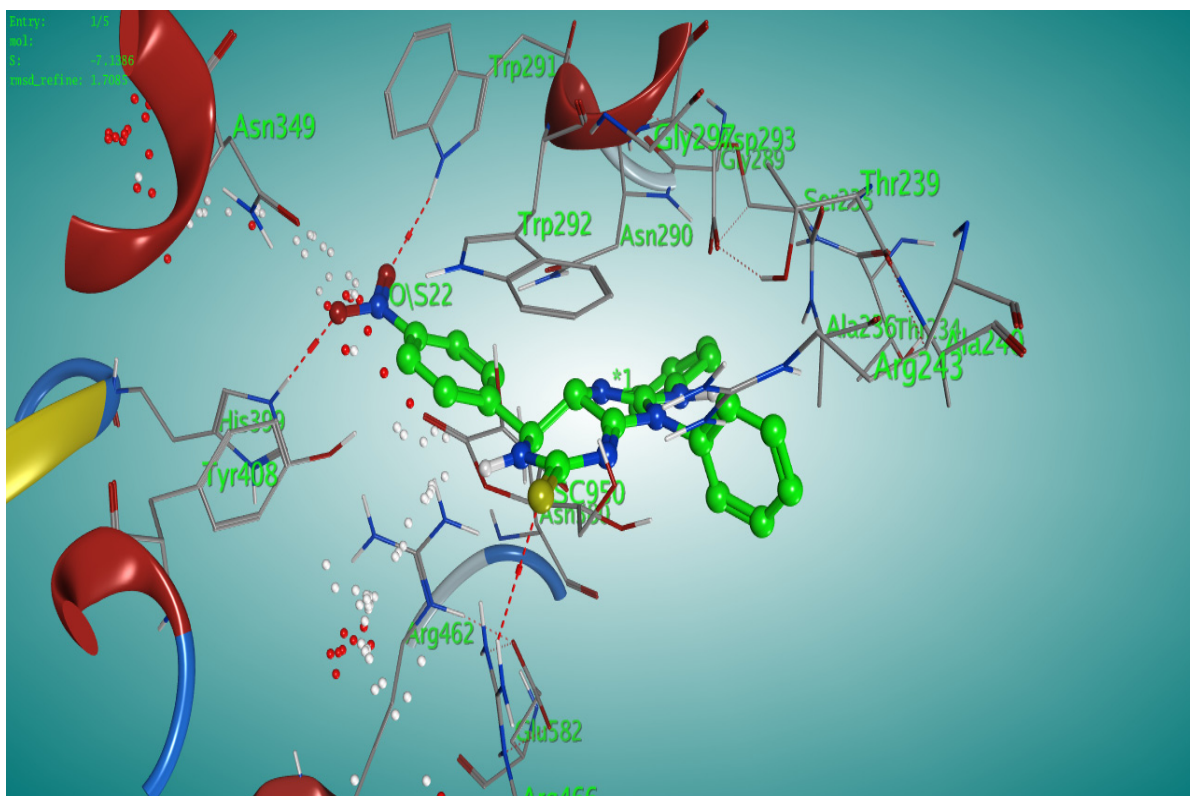


Figure S18. 3D interaction images of compound 5 with the active sites of 1F9G.

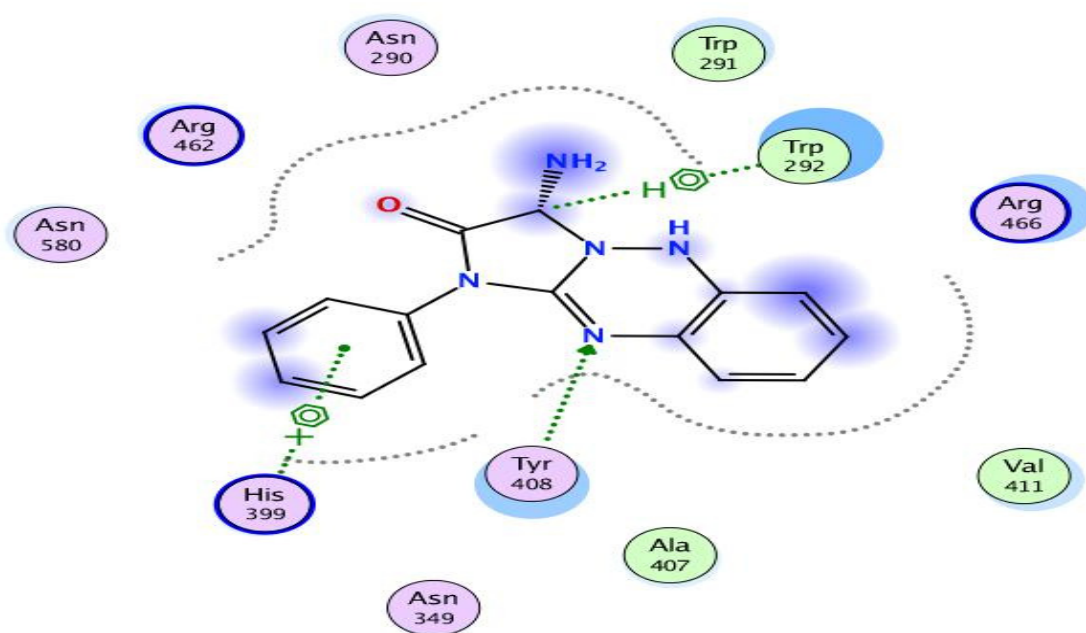


Figure S19. 2D interaction images of compound 6 with the active sites of 1F9G.

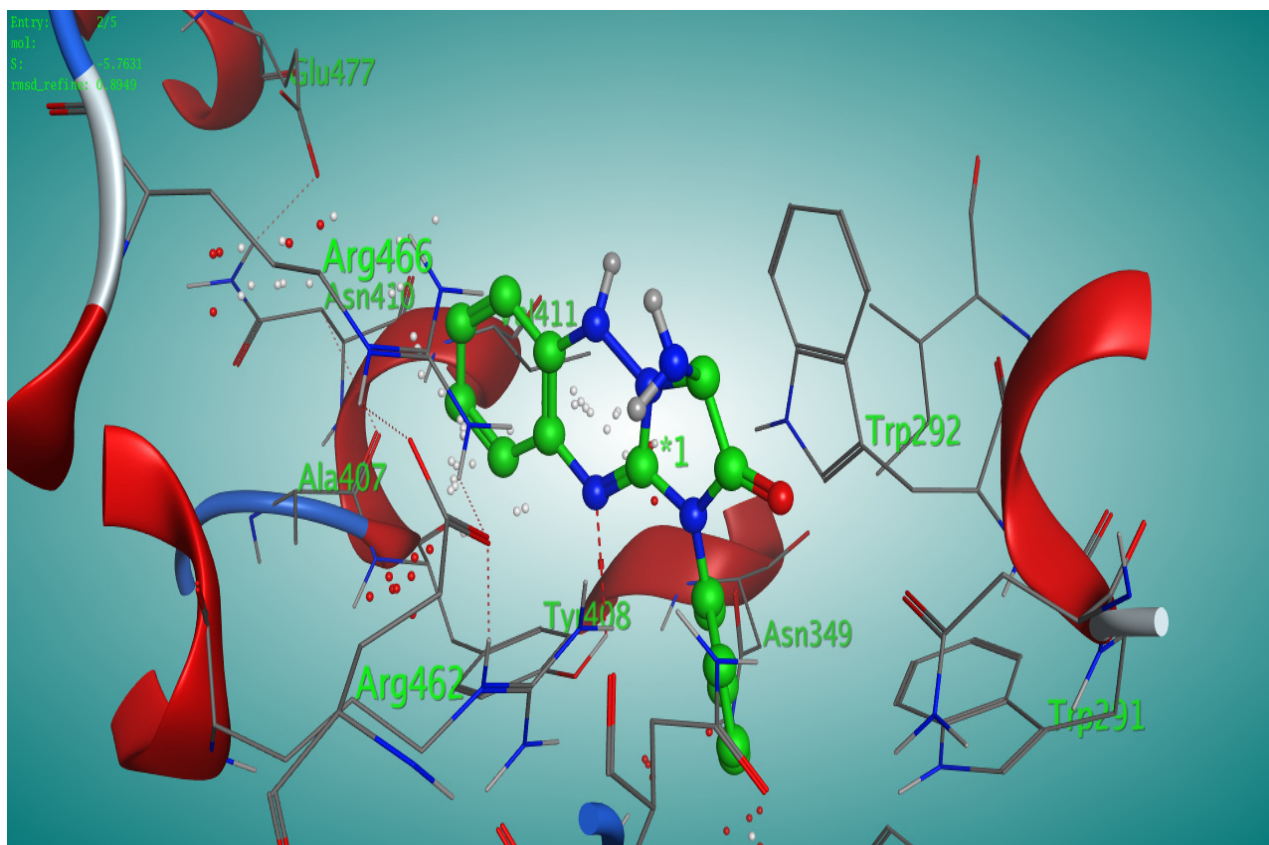


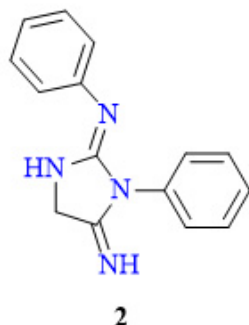
Figure S20. 3D interaction images of compound **6** with the active sites of 1F9G.

Chemistry

All chemicals were purchased from Sigma-Aldrich (Taufkirchen, Germany), and all solvents were purchased from El-Nasr Pharmaceutical Chemicals Company (analytical reagent grade, Egypt). All chemicals were used as supplied without further purification. The melting points were measured by a digital Electrothermal IA 9100 Series apparatus Cole-Parmer, Beacon Road, Stone, Staffordshire, ST15 OSA, UK) and were uncorrected. C, H, and N analyses were carried out on a PerkinElmer CHN 2400. IR spectra were recorded on FT-IR 460 PLUS (KBr disks) in the range from 4000 to 400 cm^{-1} . ^1H and ^{13}C -NMR spectra were recorded on a Bruker 400 MHz NMR Spectrometer using tetramethylsilane (TMS) as the internal standard, chemical shifts are expressed in δ (ppm), and DMSO- d_6 was used as the solvent. At the Regional Centre for Mycology & Biotechnology (RCMB) Al-Azhar University, Naser City, Cairo.



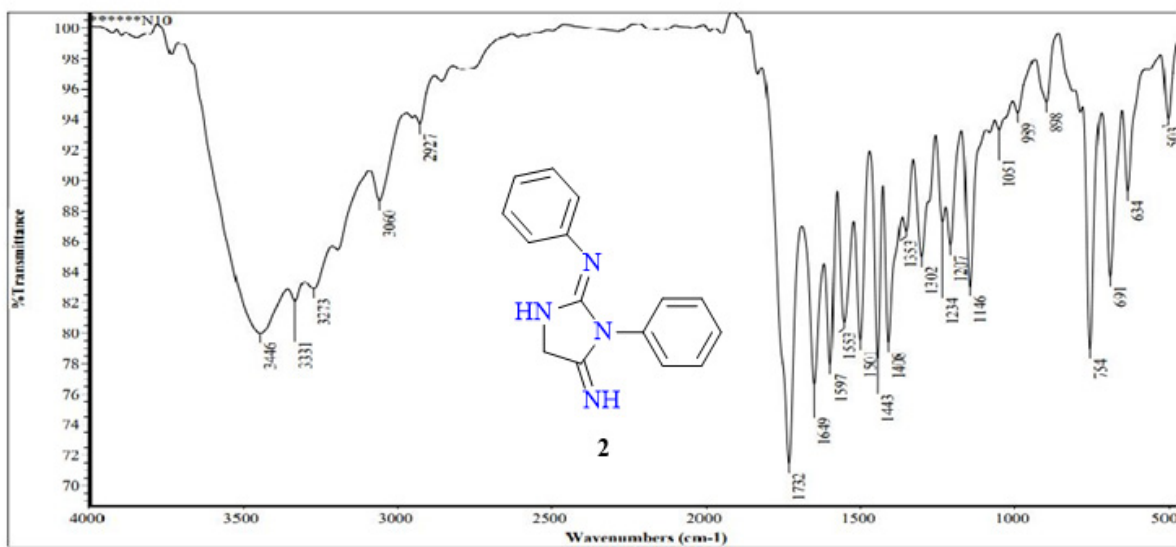
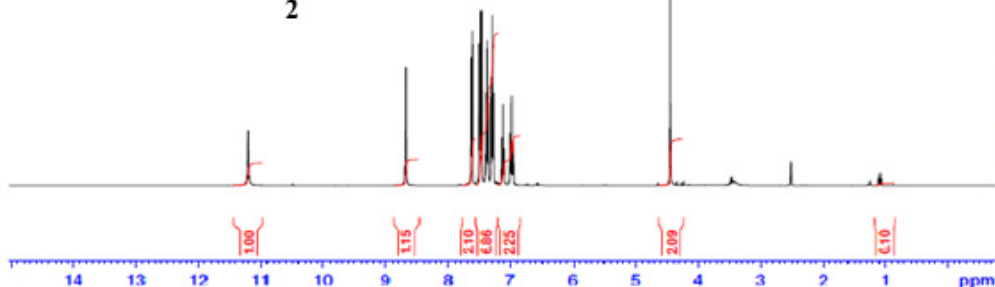
MOH (N10) -1



Current Data Parameters
 Date: 20180221
 Time: 12.57
 INSTRUM: spect
 PROBHD: 5 mm PABBO BBO
 PULPROG: zg30
 TD: 65536
 SOLVENT: DMSO
 NS: 64
 DS: 2
 SWH: 8012.820 Hz
 FIDRES: 0.122266 Hz
 AQ: 6.0884465 sec
 RG: 30.98
 EQ: 62.400 usec
 DE: 4.50 usec
 TE: 300.2 K
 D1: 1.00000000 sec
 TDO: 1

===== CHANNEL f1 =====
 ZFO1: 400.1724712 MHz
 NUC1: 1H
 P1: 10.00 usec
 PLM1: 14.50000000 W

F2 - Processing parameters
 SI: 65536
 SF: 400.1700000 MHz
 GCW: 32K
 LB: 0.30 Hz
 CB: 0
 PC: 1.00



*****N10

Number of sample scans: 32
 Number of background scans: 32
 Resolution: 4.000
 Sample gain: 2.0
 Optical velocity: 0.4747
 Aperture: 80.00

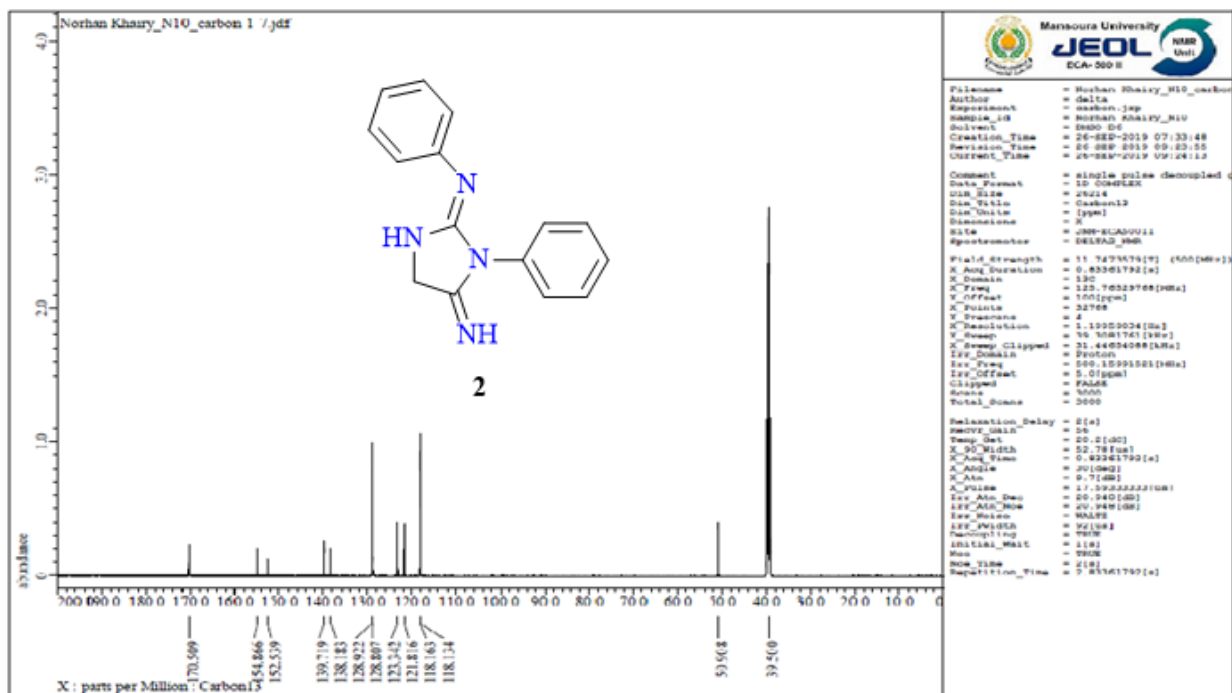


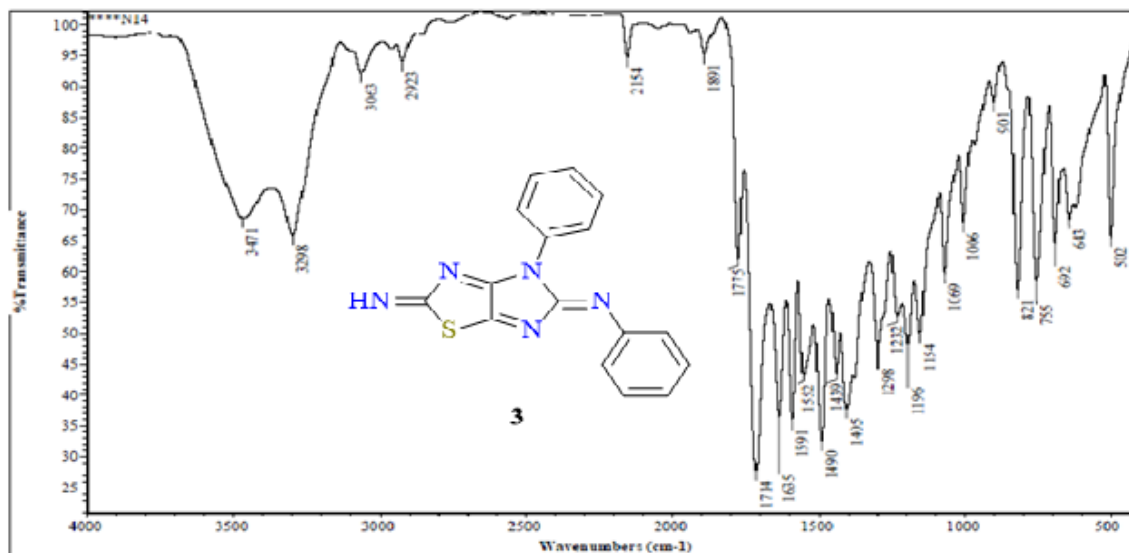
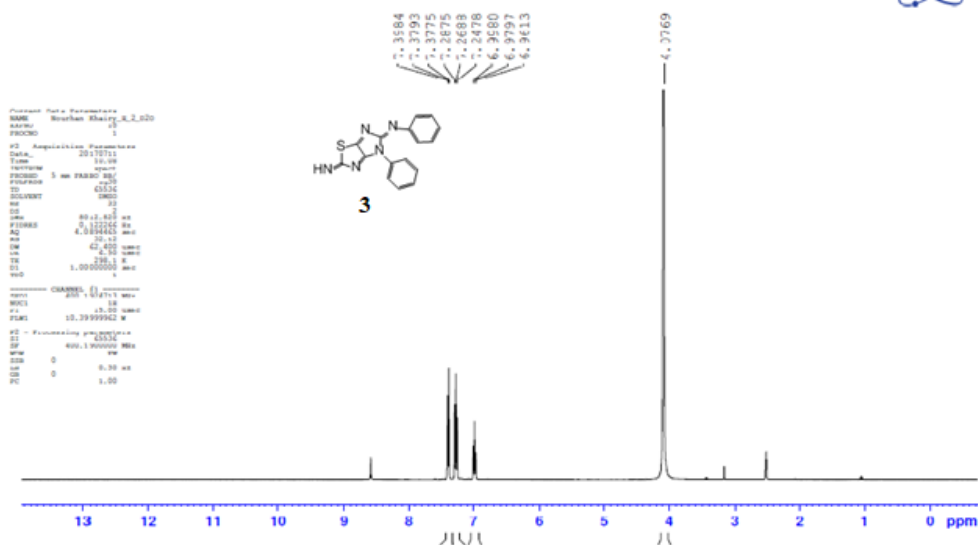
ThermoFisher
 SCIENTIFIC



Mansoura University
 Faculty of Science
 Spectral Analyses unit
 Chemistry Department
 ThermoFisher Nicolette IS10, US/
 Spectral range: 4000 - 400 cm-1

Sat Mar 10 08:58:46 2018 (GMT-08:00)





¹⁴N14

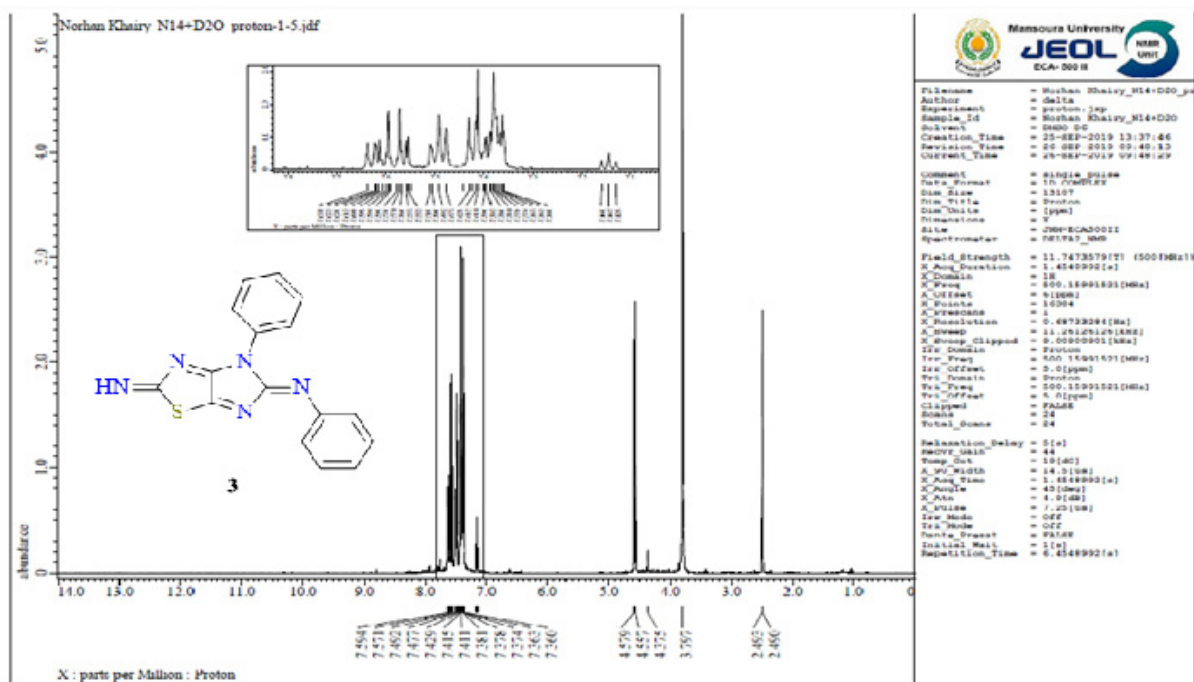
Number of sample scans: 32
Number of background scans: 32
Resolution: 4.000
Sample gain: 4.0
Optical velocity: 0.4747
Aperture: 80.00

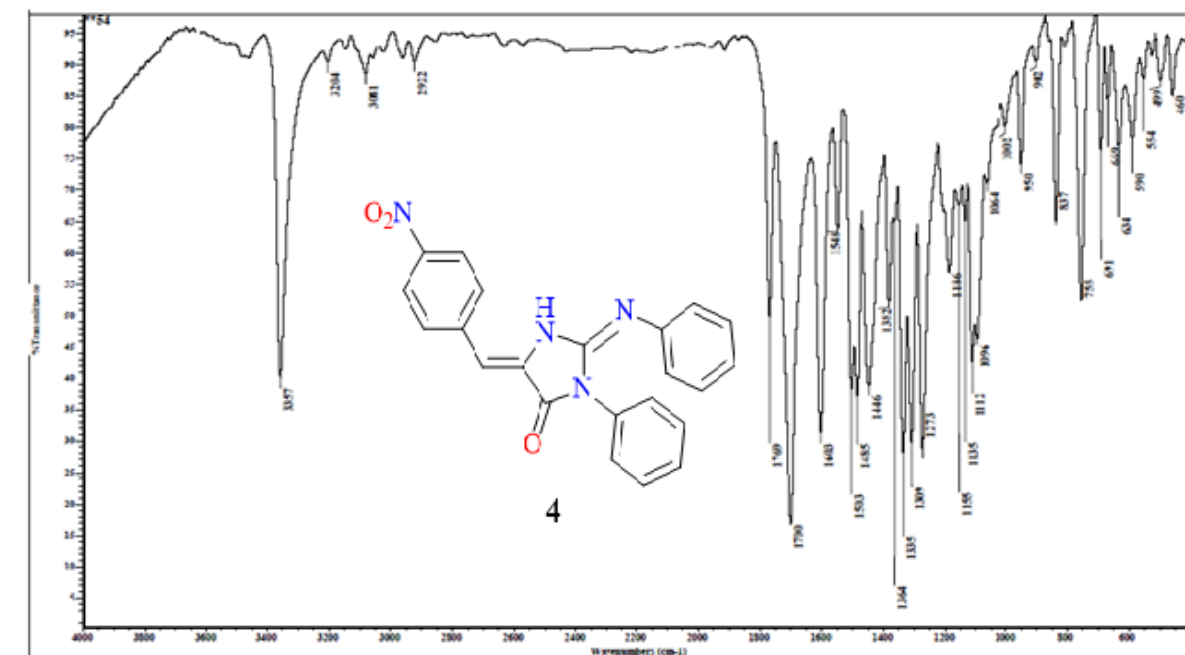


ThermoFisher
SCIENTIFIC

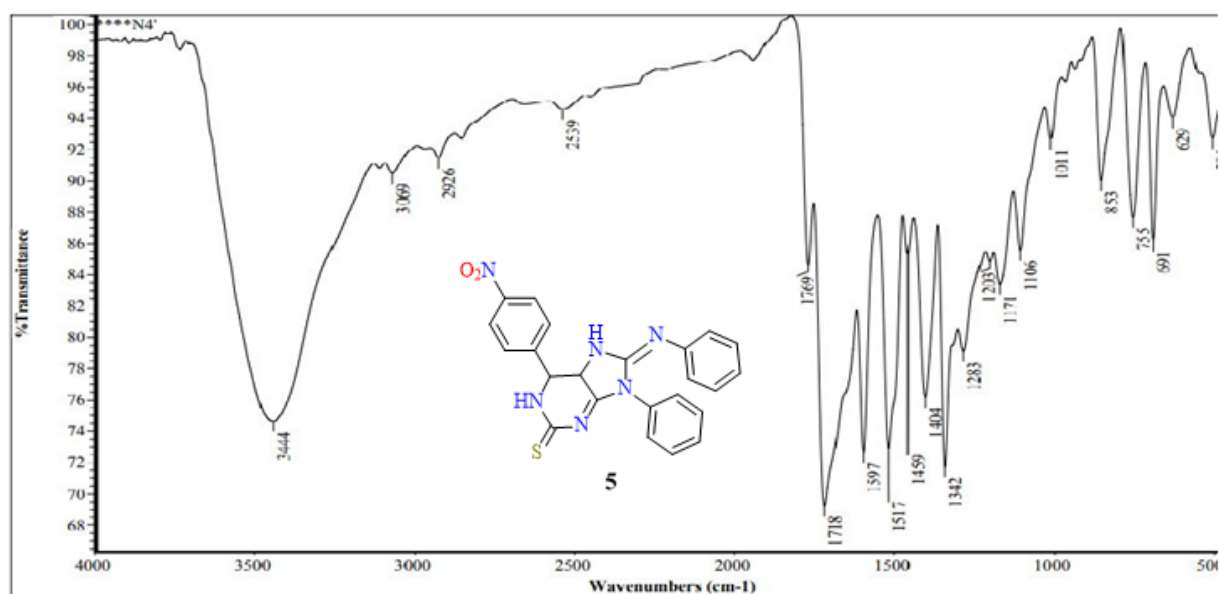
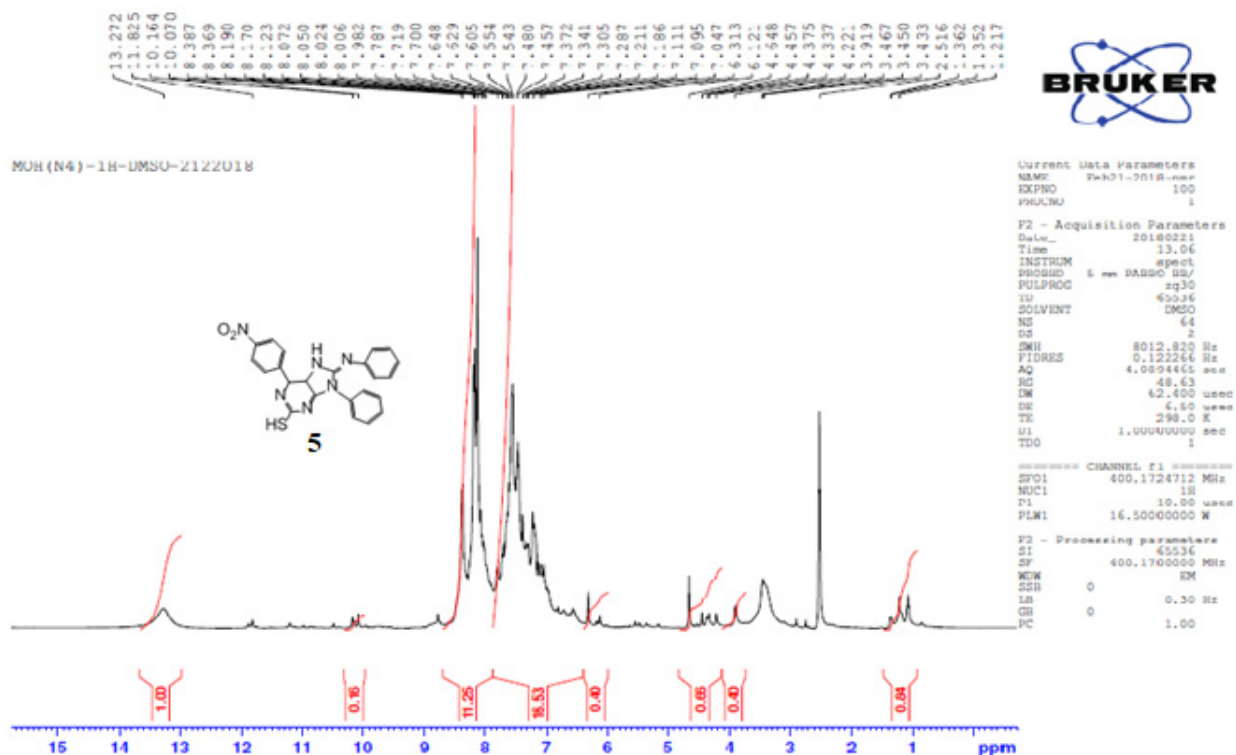


Mansoura University
Faculty of Science
Spectral Analyses unit
Chemistry Department
ThermoFisher Nicolette IS10, USA
Spectral range: 4000 - 400 cm⁻¹





*Mansoura University
Faculty of Science
Spectral Analysis Unit
unitofspectra@gmail.com*



***N4'

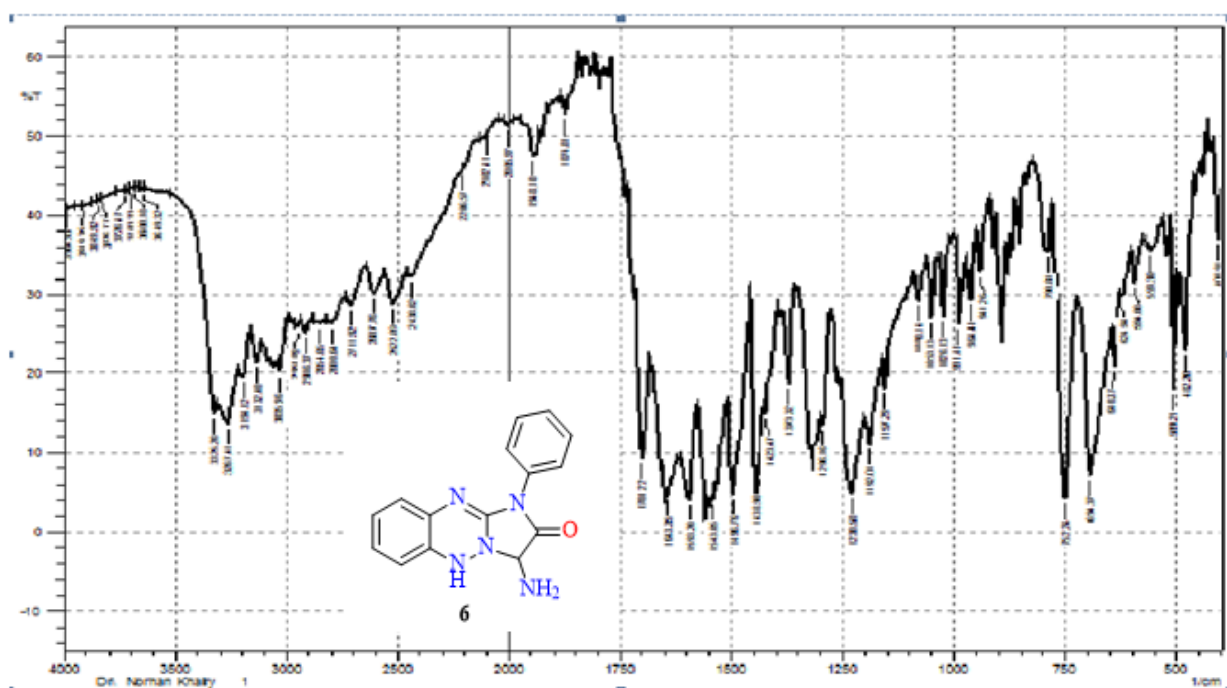
Number of sample scans: 32
Number of background scans: 32
Resolution: 4.000
Sample gain: 2.0
Optical velocity: 0.4747
Aperture: 80.00

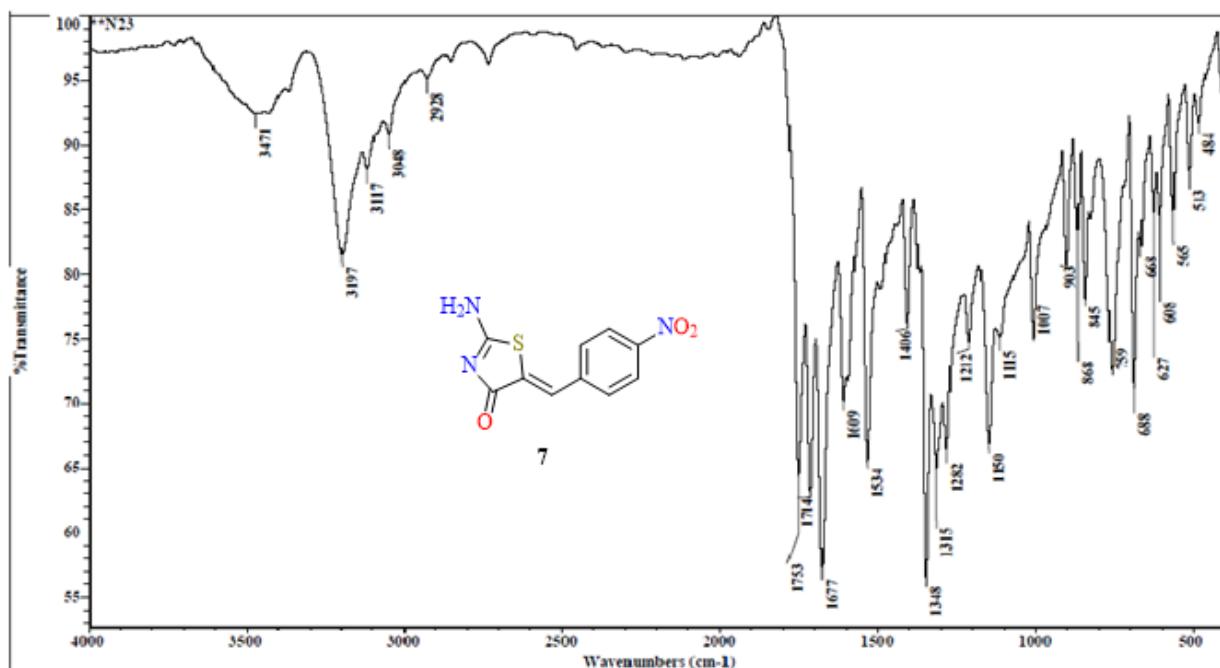
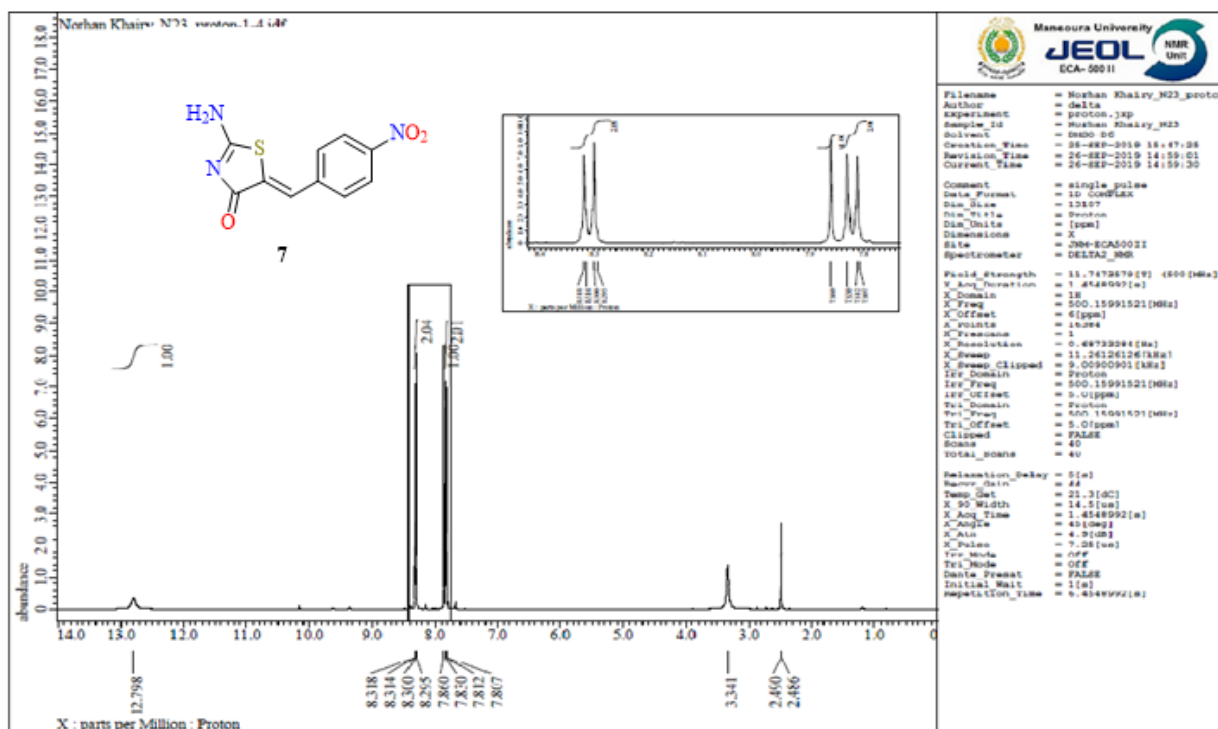


ThermoFisher
SCIENTIFIC



Mansoura University
Faculty of Science
Spectral Analyses unit
Chemistry Department
ThermoFisher Nicolette IS10, US.
Spectral range: 4000 - 400 cm-1

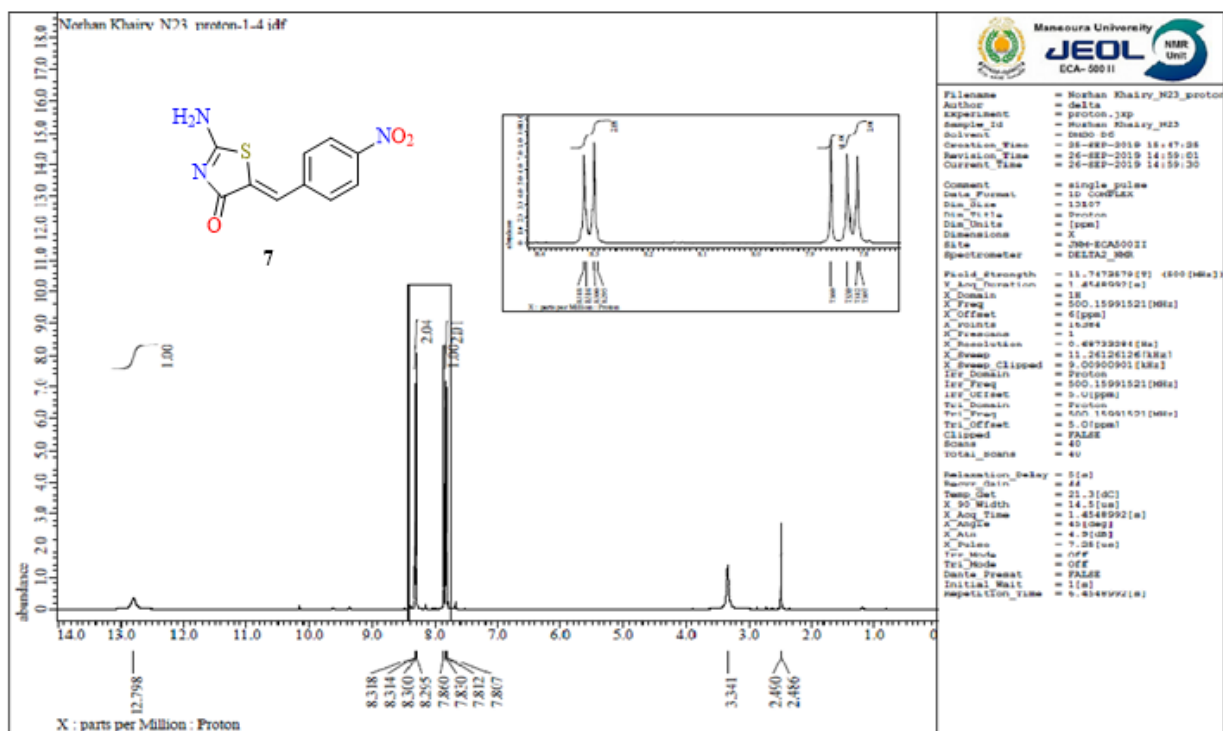


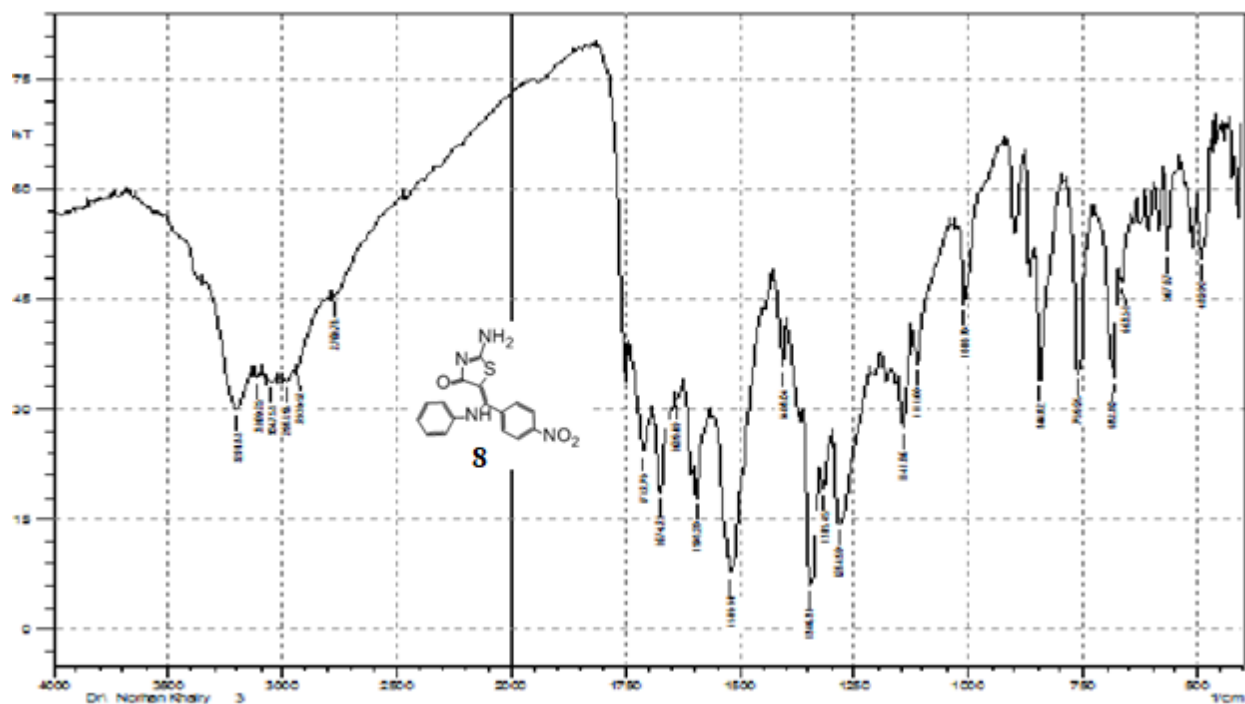


Number of sample scans: 32
 Number of background scans: 32
 Resolution: 4.000
 Sample gain: 2.0
 Optical velocity: 0.4747
 Aperture: 80.00

ThermoFisher
 SCIENTIFIC
 Thu Sep 12 09:37:07 2019 (GMT+02:00)

Mansoura University
 Faculty of Science
 Spectral Analysis Unit
 unitofspectra@gmail.com





Nourhan Khairy_H_3_D2O

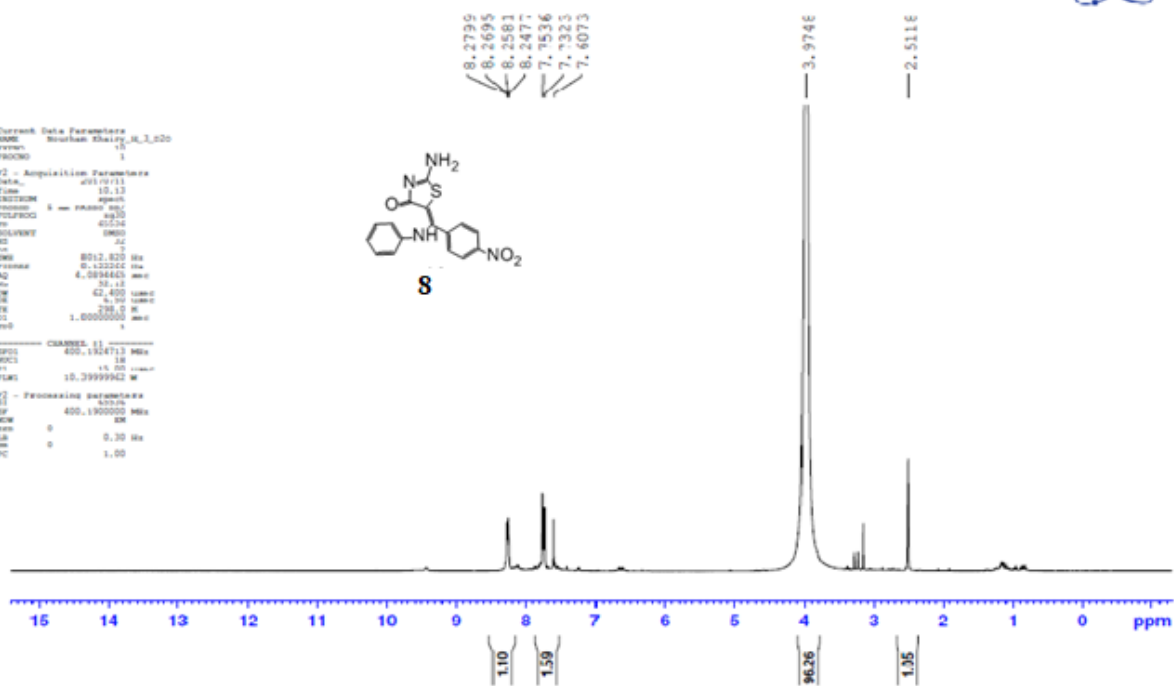
Microanalytical Unit - FOPCU - NMR laboratory
www.pharma.cu.edu.eg dr-mau.fopcu@pharma.cu.edu.eg



Current Data Parameters
NAME: Nourhan Khairy_H_3_D2O
PROCNO: 1
F2 - Acquisition Parameters
Date_: 20110111
Time: 10.13
INSTRUM: spect
PROBHD: 5 mm mmQNP 1H/1
PULPROG: zg30
PC: 612.14
SOLVENT: DMSO
NS: 25
DS: 4
AQ: 8012.820 Hz
RG: 6.122244 Hz
AD: 4.0894460 sec
SW: 30.10
FIDRES: 0.276 Hz
SF: 400.146013 MHz
WDW: EM
SSB: 0
LB: 1.0000000 Hz
GB: 0
PC: 1.00

===== CHANNEL f1 =====
NUC1: 13C
P1: 15.00 sec
PL1: 0.00 dB

F2 - Processing parameters
SI: 32768
SF: 400.1460000 MHz
WDW: EM
SSB: 0
LB: 0.30 Hz
GB: 0
PC: 1.00

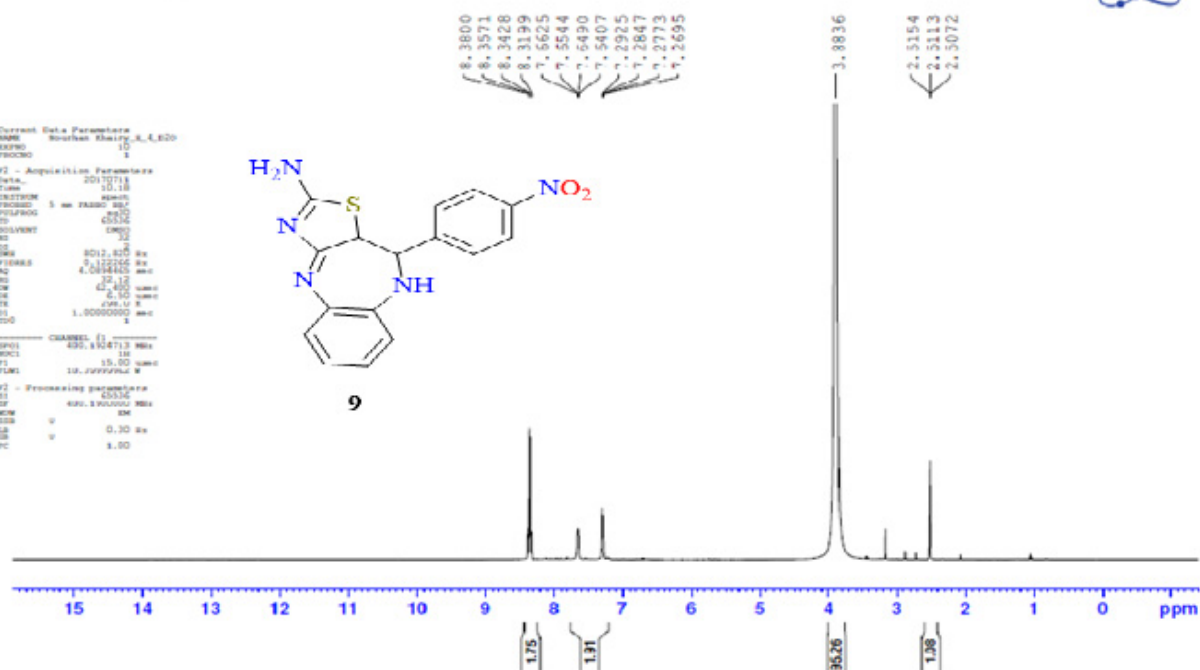
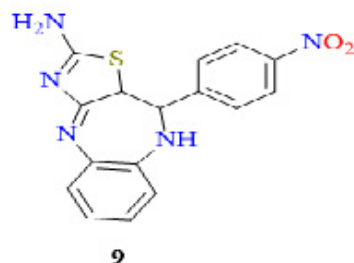


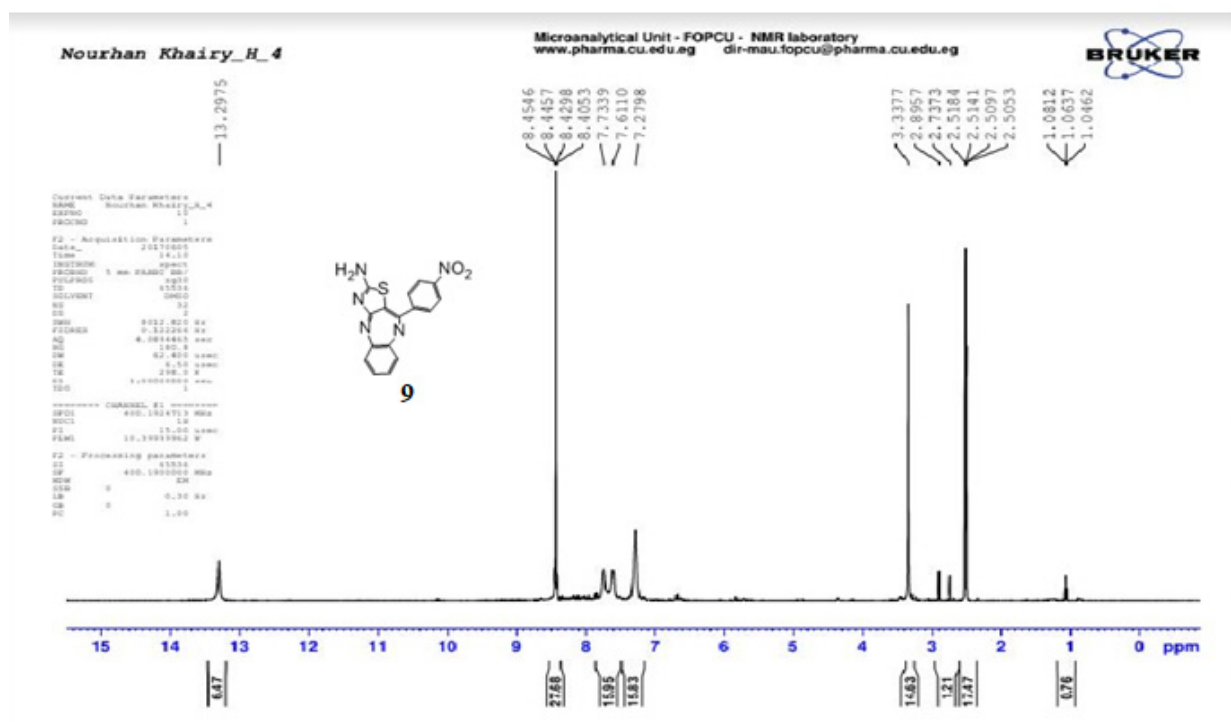
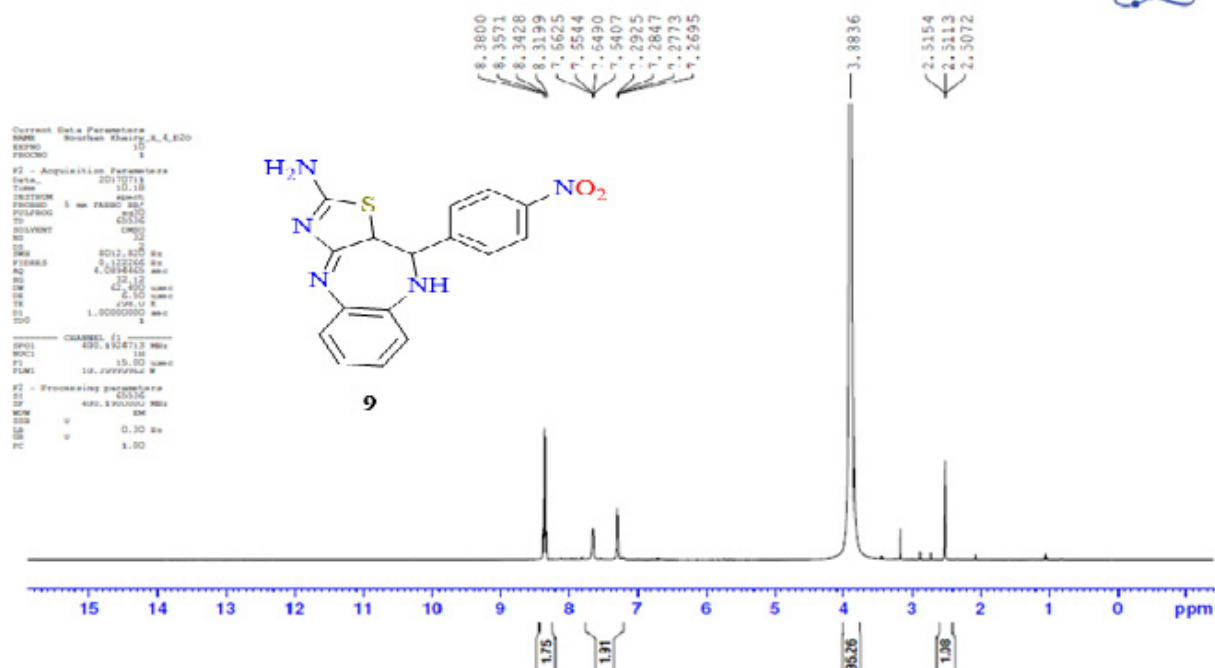
Current Data Parameters
NAME Nourhan Khairy_R_4_D2O
EXPNO 10
PROCNO 1

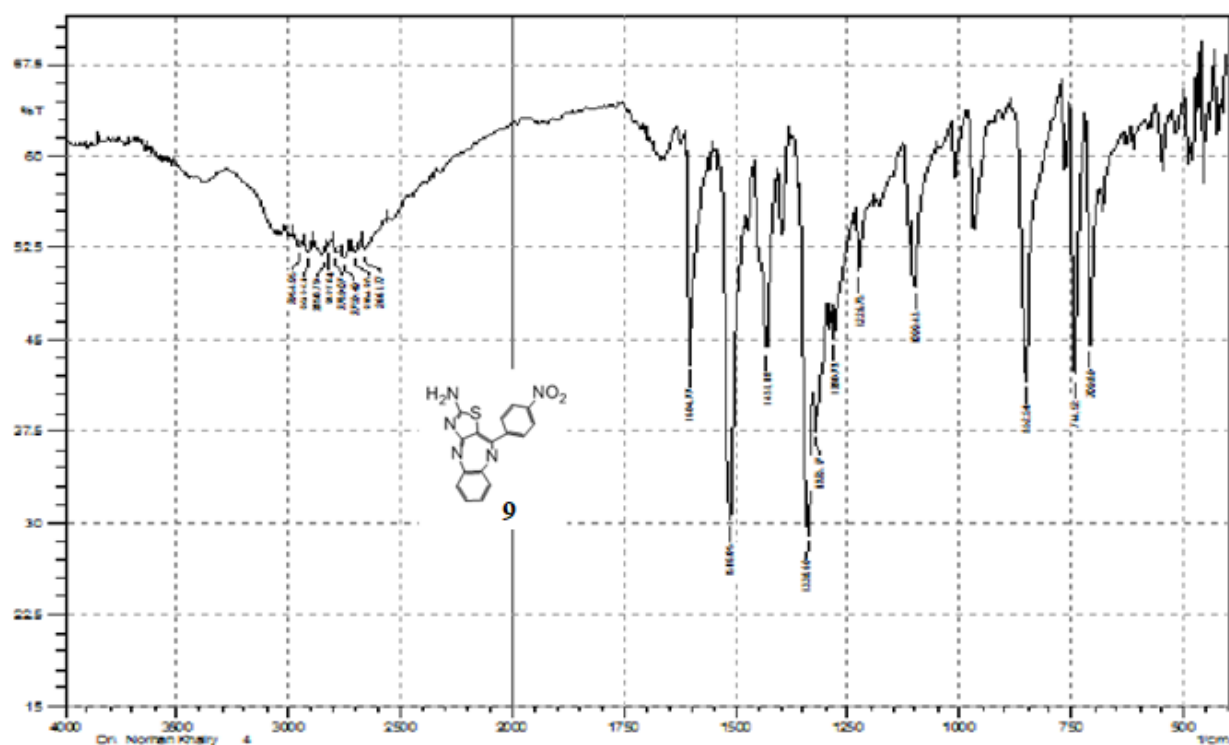
F2 - Acquisition Parameters
Date_ 20170718
Time 10:18
PULPROG zgpg30
PCLOCK 5.0000000
POLPROG zgpg30
RS 0.0000000
SOLVENT DMSO
NS 32
DS 2
SWH 8012.625 Hz
FIDRES 0.122246 Hz
AQ 6.089441 sec
RG 32.12
GB 0.0000000
DB 0.1000000
TS 0.0000000
SS 1.0000000 sec
TD 65536

===== CHANNEL f1 =====
NUC1 13C
P1 15.0000000
PL1 0.0000000

F2 - Processing parameters
SI 32768
SF 400.146000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

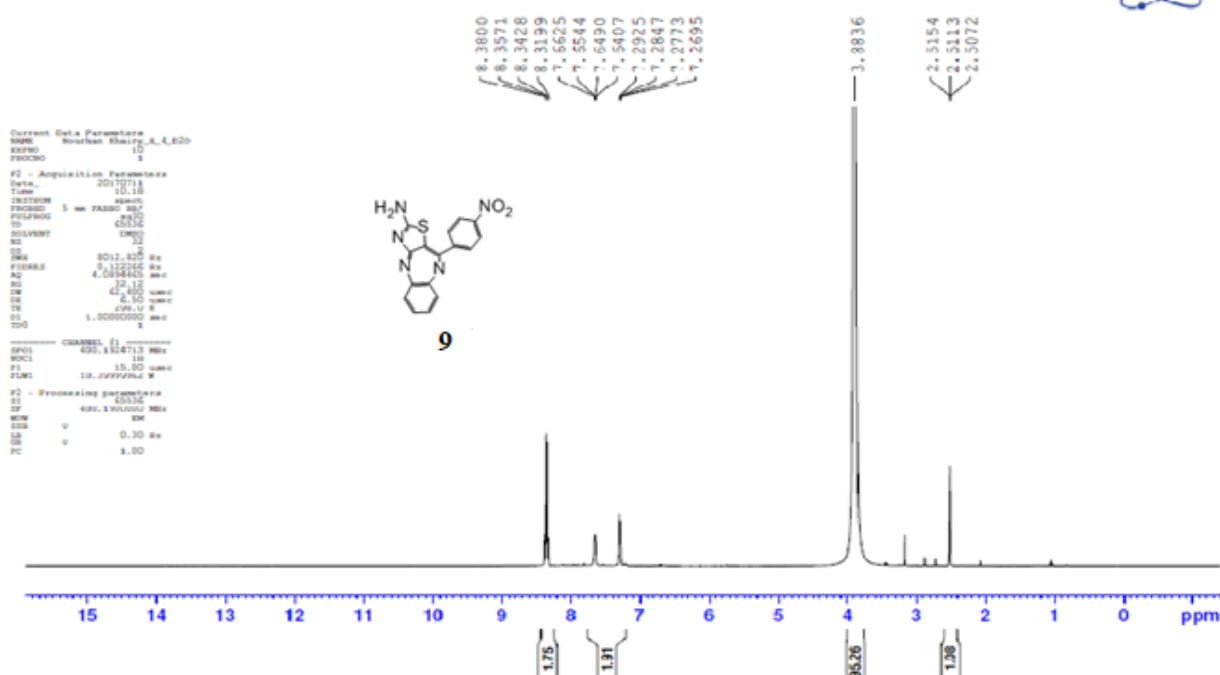


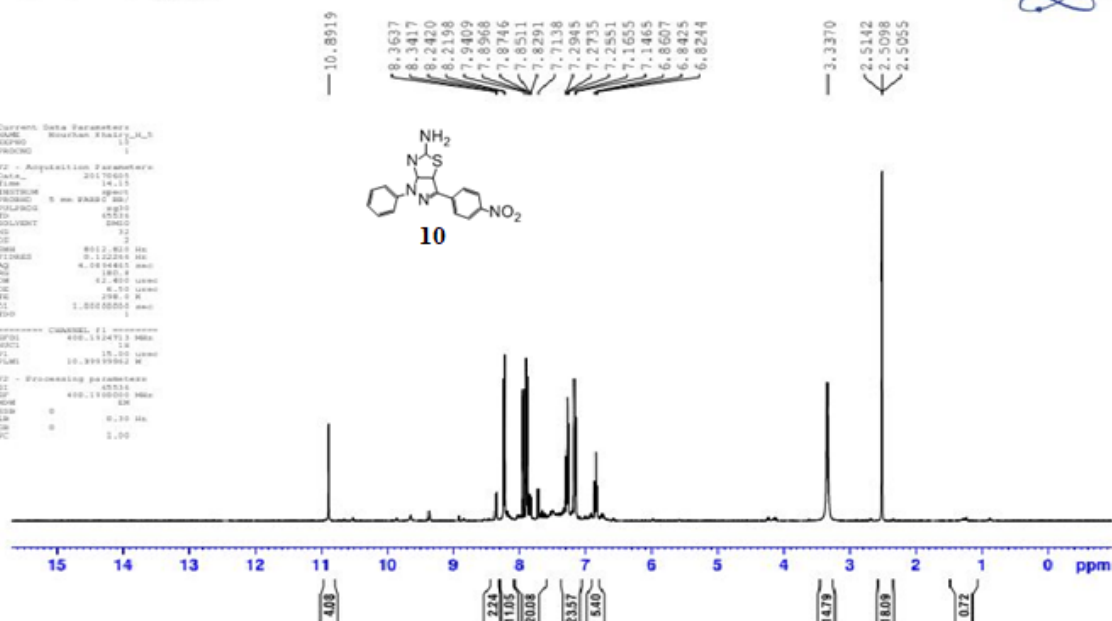
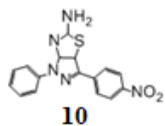




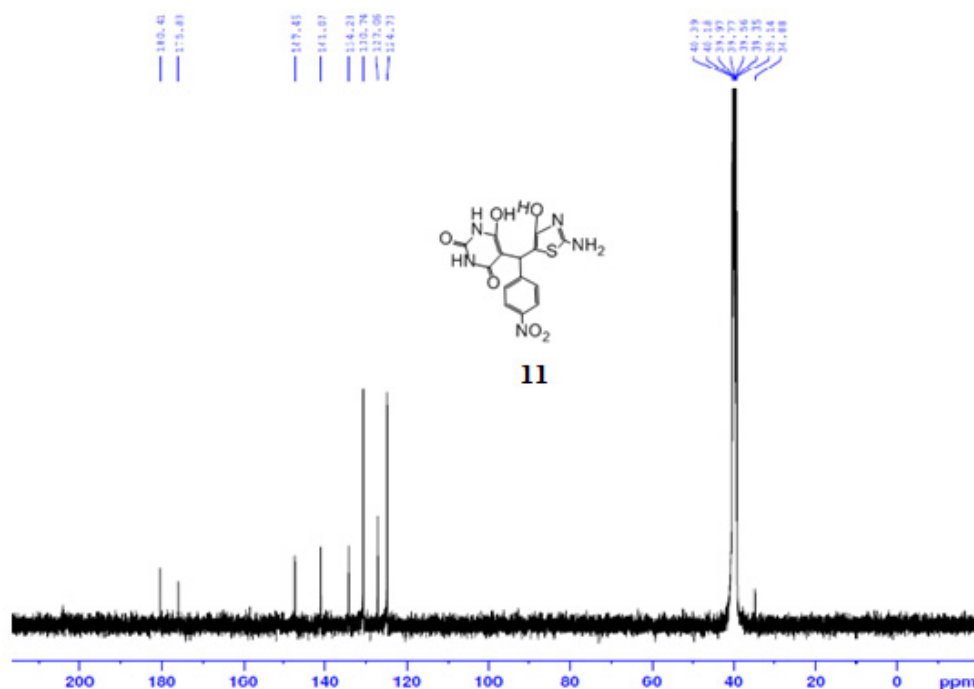
Nourhan Khairy_R_4_D2O

Microanalytical Unit - FOPCU - NMR laboratory
www.pharma.cu.edu.eg dir-mau.fopcu@pharma.cu.edu.eg



Current Data Parameters
NAME Nourhan Khairy_H_5
EXPNO 1F2 - Acquisition Parameters
Date_ 20170801
Time 14.15
INSTRUM spect
PROBHD 5 mm QNP400 80/
PULPROG zgpg30
TD 65536
SOLVENT dmso
NS 32
DS 2
SWH 8012.800 MHz
FIDRES 0.122244 MHz
AQ 4.0834613 sec
RG 180.4
CW 32.400 uVHz
DE 6.50 uVHz
TE 298.2 K
F1 100.625000 MHz
F2 400.146000 MHz===== CHANNEL f1 =====
NUC1 15N
P1 12.00 uVHz
PL1 0.00 dBF2 - Processing parameters
SI 32768
SF 400.146000 MHz
WDW EM
SSB 0
LB 0.10 Hz
GB 0
PC 0.00

N34-13C-DMSO-1582018



Current Data Parameters
NAME: Aug15 2018-nmr
EXPNO: 80
PROCNO: 1

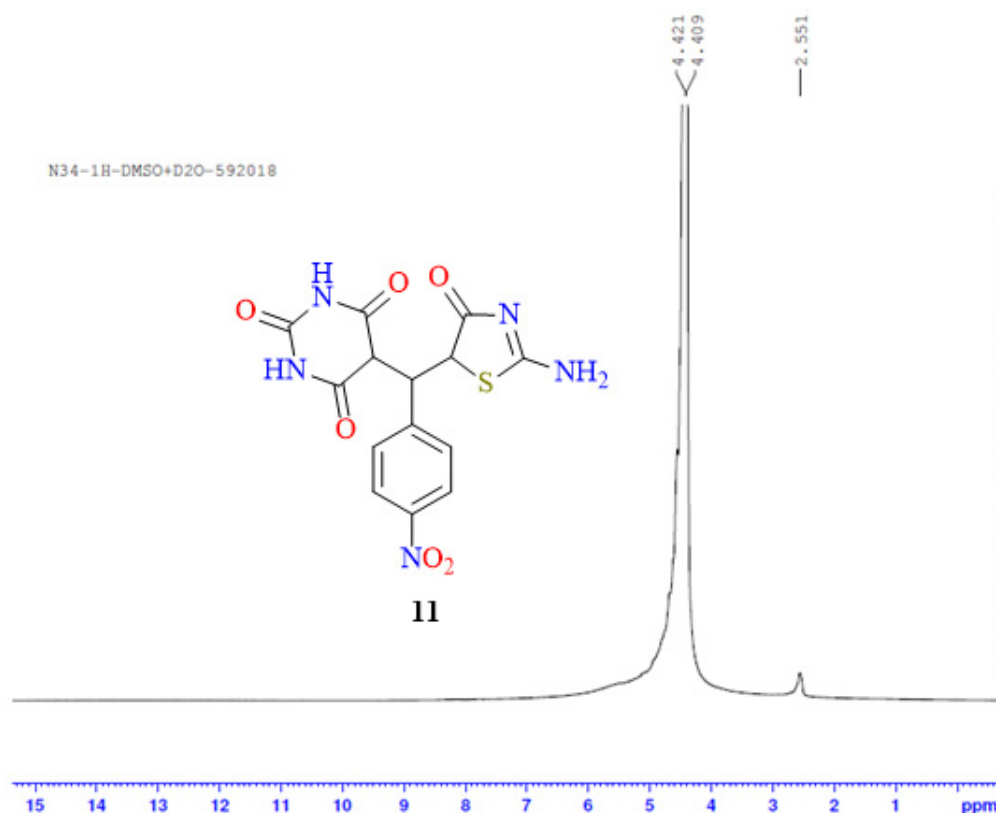
F2 - Acquisition Parameters
Date_: 20180815
Time: 14.59
INSTRUM: spect
PROBHD: 5 mm PASSEL 1H/13C
PULPROG: zgpg30
TD: 65536
SOLVENT: DMSO
NS: 1024
DS: 2
SWH: 24038.461 Hz
FIDRES: 0.366798 Hz
AQ: 1.3631488 sec
RG: 194.81
DW: 20.800 usec
DE: 6.50 usec
TE: 300.0 K
D1: 2.00000000 sec
D11: 0.03000000 sec
TD0: 1

===== CHANNEL f1 =====
SFO1: 100.628883 MHz
NUC1: 13C
P1: 10.00 usec
PLM1: 66.0000000 M

===== CHANNEL f2 =====
SFO2: 400.1716007 MHz
NUC2: 1H
PCPDPRG2: waltz16
PCPD2: 90.00 usec
PLM2: 16.50000000 M
PLM12: 0.20370001 M
PLM13: 0.16500001 M

F2 - Processing parameters
SI: 32768
SF: 100.6288270 MHz
WDW: EM
SSB: 0
LB: 1.00 Hz
GB: 0
PC: 1.40

N34-1H-DMSO+D2O-592018

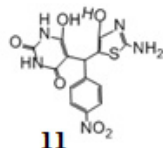


Current Data Parameters
NAME: Sep05-2018-nmr
EXPNO: 80
PROCNO: 1

F2 - Acquisition Parameters
Date_: 20180905
Time: 13.36
INSTRUM: spect
PROBHD: 5 mm PASSEL 1H/13C
PULPROG: zg30
TD: 65536
SOLVENT: DMSO
NS: 64
DS: 2
SWH: 8012.820 Hz
FIDRES: 0.122244 Hz
AQ: 4.0894465 sec
RG: 30.88
DW: 62.400 usec
DE: 6.50 usec
TE: 298.0 K
D1: 1.00000000 sec
TD0: 1

===== CHANNEL f1 =====
SFO1: 400.1724712 MHz
NUC1: 1H
P1: 10.00 usec
PLM1: 16.50000000 M

F2 - Processing parameters
SI: 65536
SF: 400.1700000 MHz
WDW: EM
SSB: 0
LB: 0.30 Hz
GB: 0
PC: 1.00



ThermoFisher
SCIENTIFIC

