Novel Spiro-pyrrolizidine-Oxindole and Spiropyrrolidine-Oxindoles: Green synthesis Under Classical, Ultrasonic, and Microwave Conditions and Molecular Docking Simulation for antitumor and type 2 diabetes

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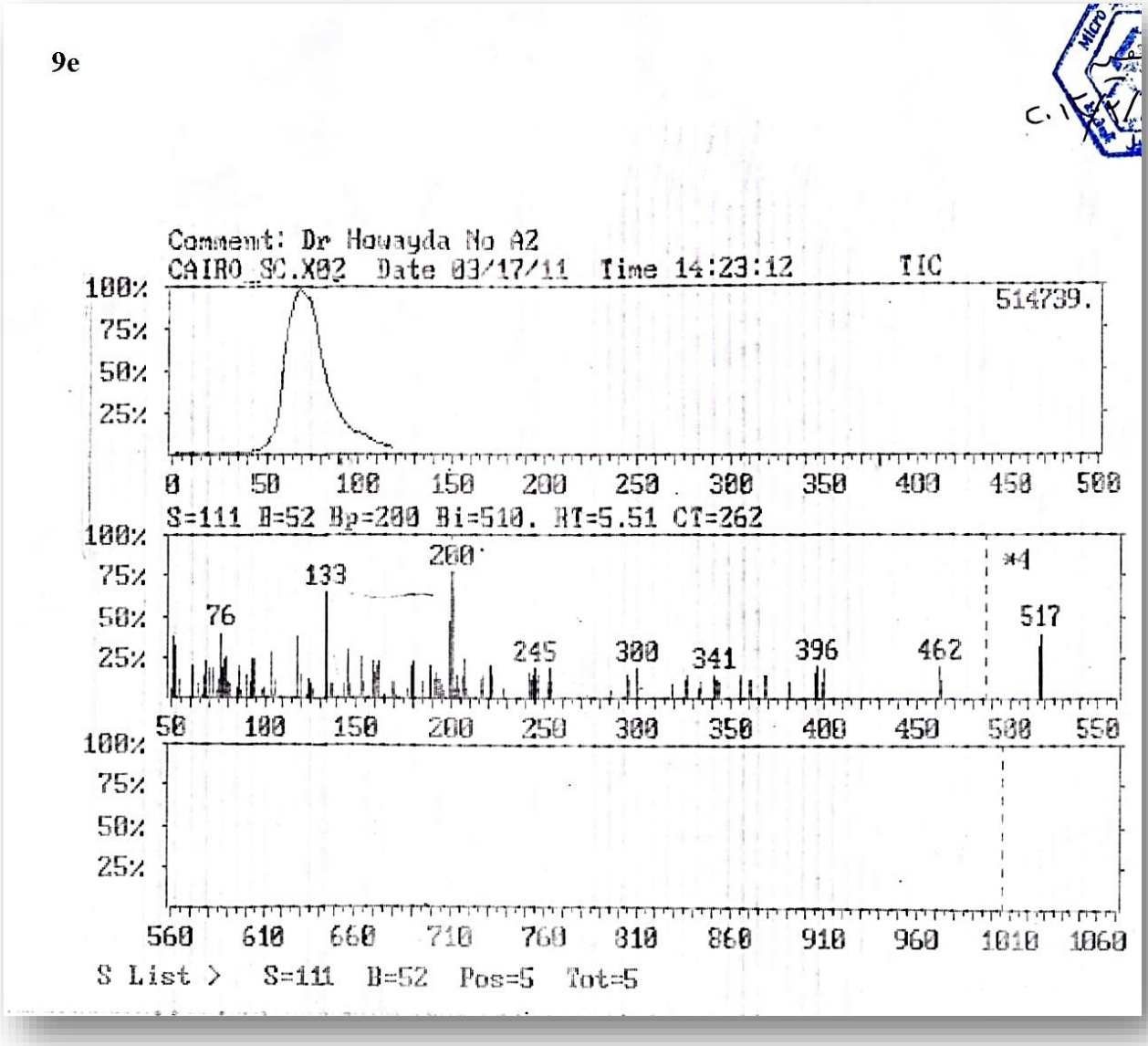
Experimental Section

Instrumentation

Melting points were measured with a Stuart melting point apparatus and are uncorrected. The IR spectra were recorded using an FTIR Bruker–vector 22 spectrophotometer as KBr pellets. The ^{1}H and ^{13}C NMR spectra were recorded in DMSO–d_6 as a solvent on Varian Gemini NMR spectrometer at 300 MHz and 75 MHz, respectively, using TMS as an internal standard. Chemical shifts are reported as δ values in ppm. Mass spectra were recorded with a Shimadzu GCMS–QP–1000 EX mass spectrometer in EI (70 eV) model. The elemental analyses were performed at the Microanalytical Centre, Cairo University. Ultrasound irradiation was performed in a BonderlinSonorex RK156. The reaction flask was located in the maximum energy area in the cleaner, where the surface of reactants (reaction vessel) is slightly lower than the level of the water, and addition or removal of water was used to control the temperature of the water bath. Microwave experiments were carried out using a CEM Discover Labmate™ microwave apparatus (300 W with ChemDriver™ Software). The experiments were performed in MW Discover CEM using both modes of operation (with and without simultaneous cooling). Chemicals are commercially available and were used without further purification.

Examples of spectra and biological data

9e



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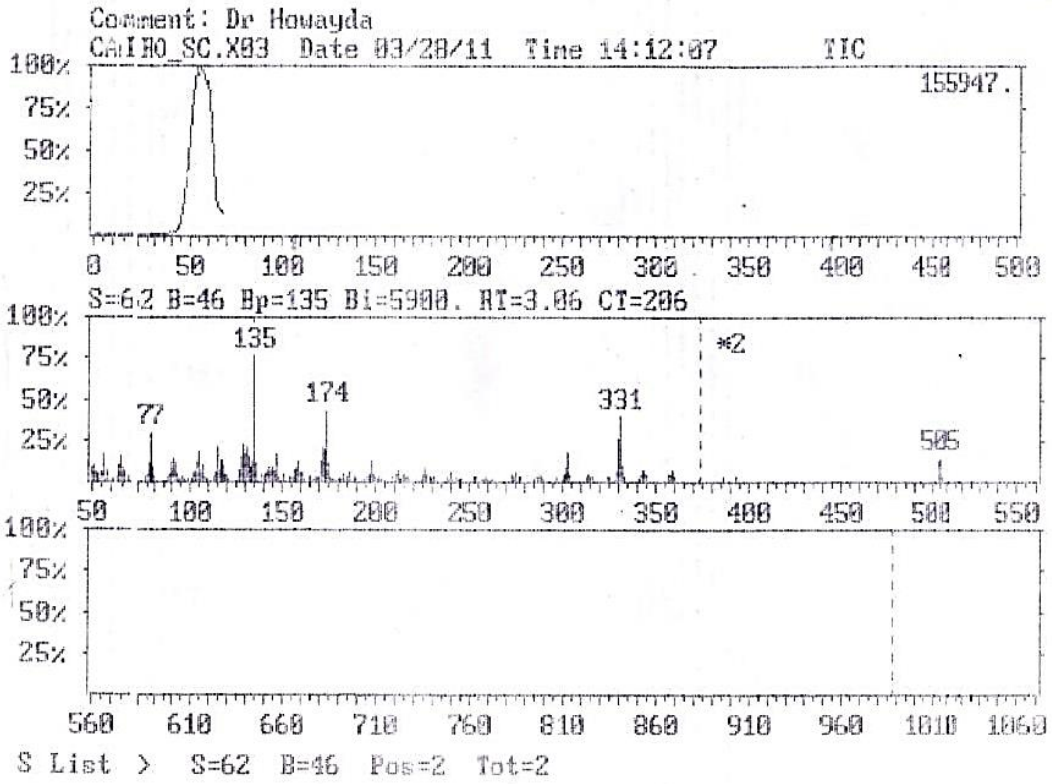
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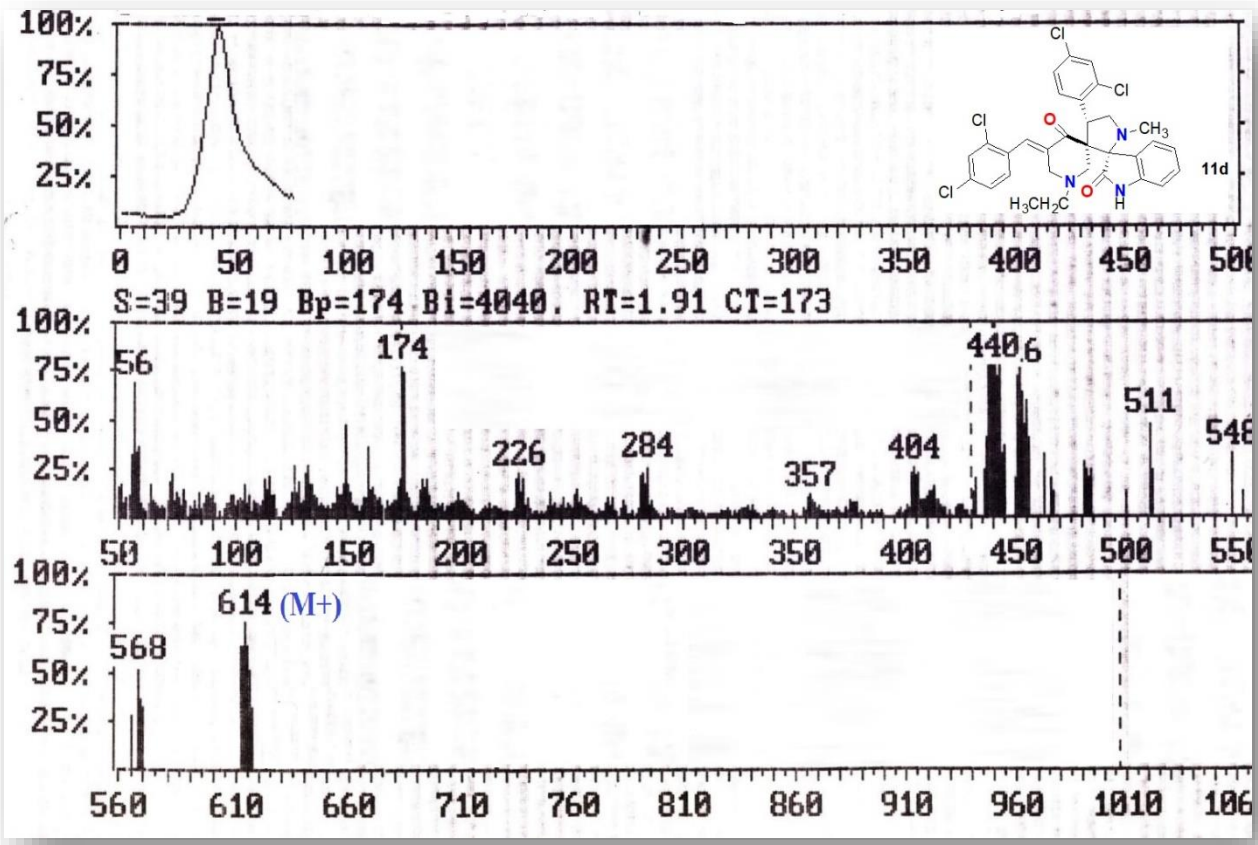
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357
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614 (M+)
568
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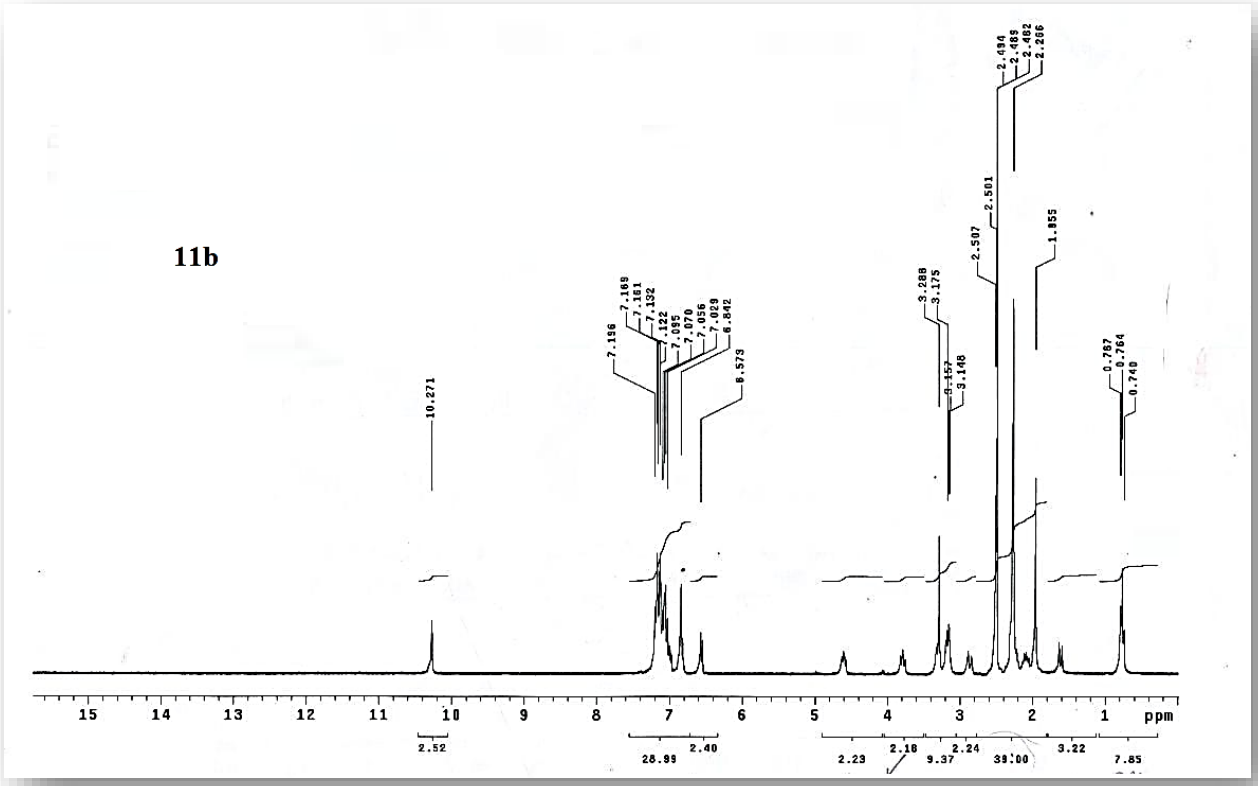
11d

11b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7.070
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7.029
6.842
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3.288
3.175
3.157
3.140
2.494
2.488
2.482
2.286
2.501
2.507
1.855
0.787
0.764
0.740
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 ppm
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2.40
2.23
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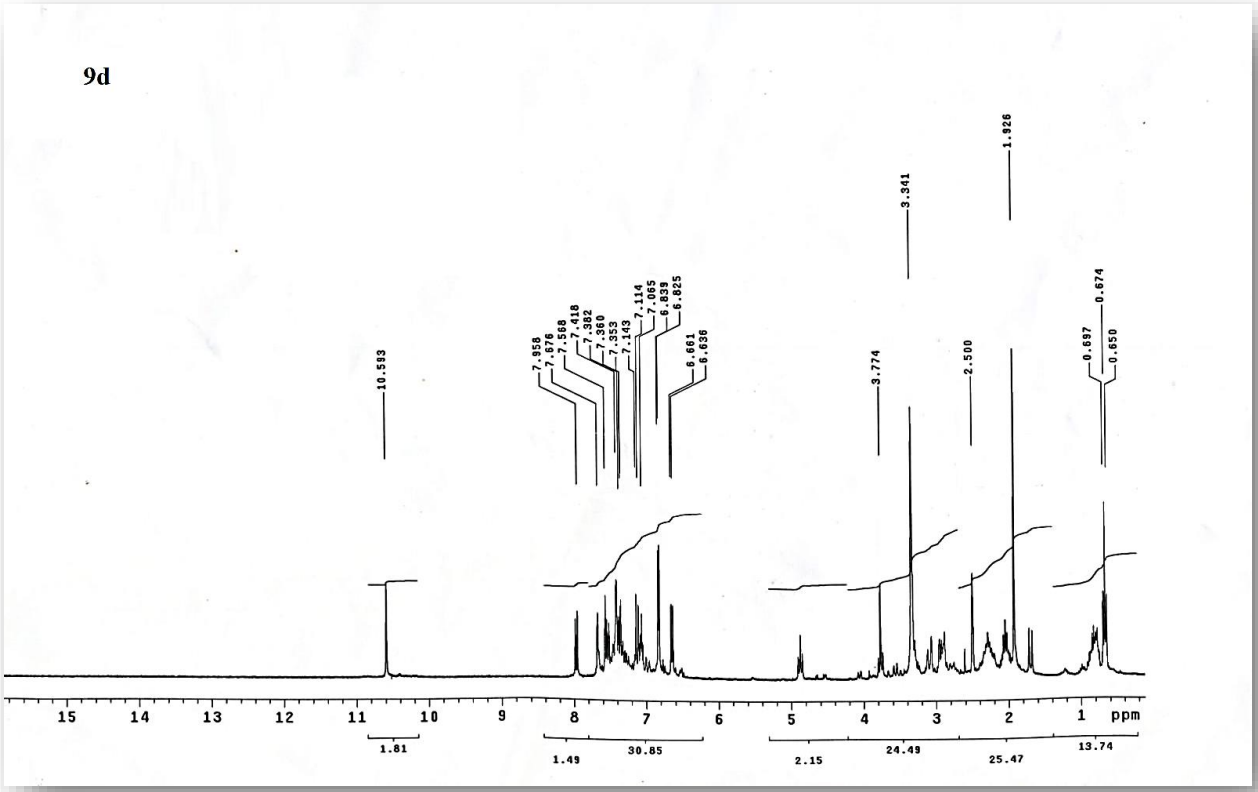
39.00
3.22
7.85

9d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6.661
6.638
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0.687
0.674
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25.47
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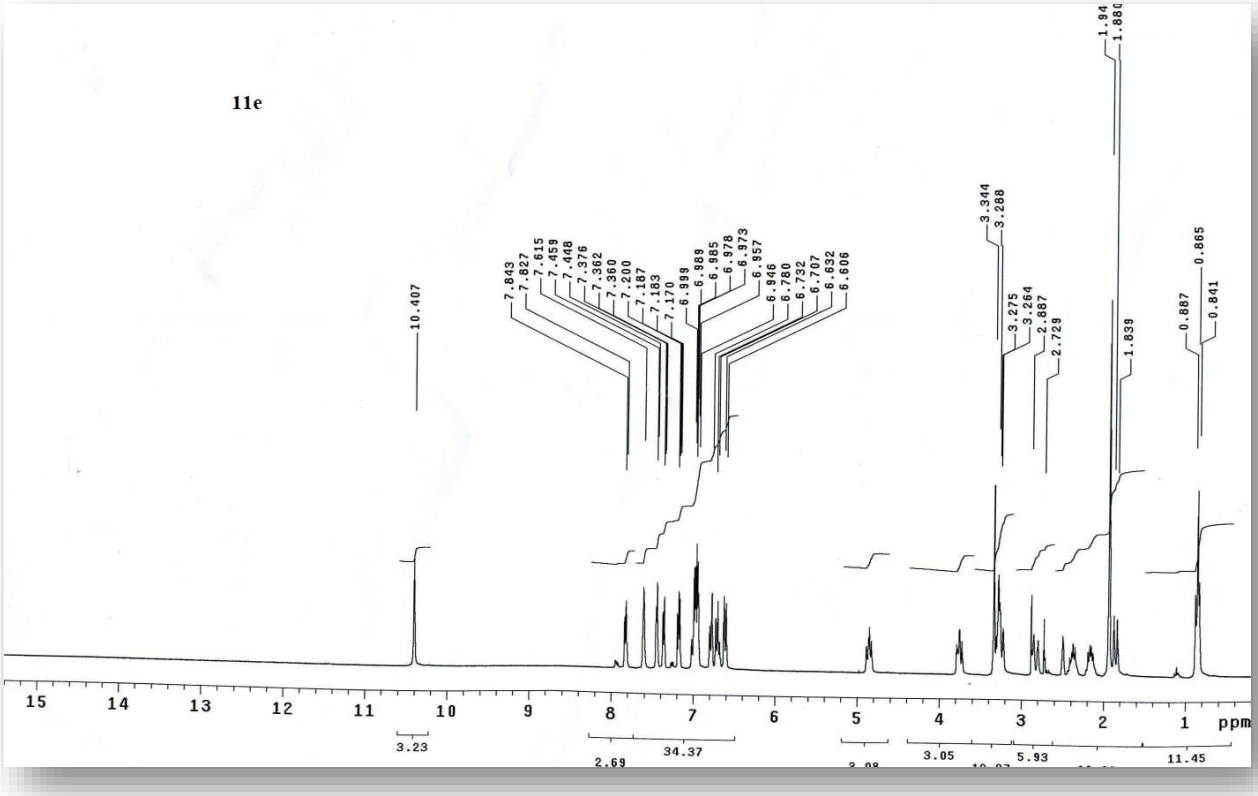
11e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6.978
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6.957
6.846
6.780
6.732
6.707
6.632
6.606
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3.288
3.275
3.264
2.887
2.729
1.839
1.84
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0.865
0.841
15
14
13
12
11
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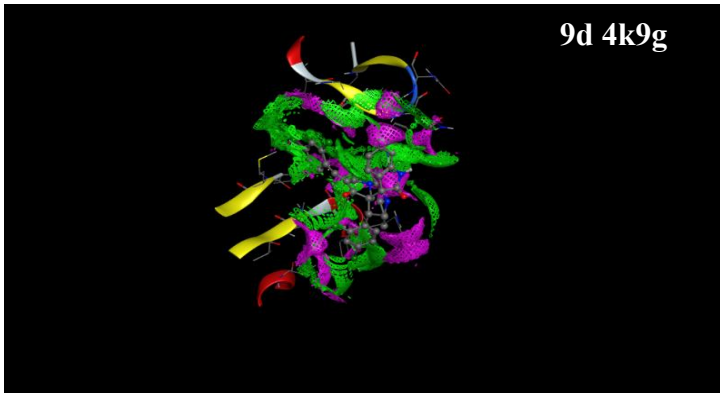
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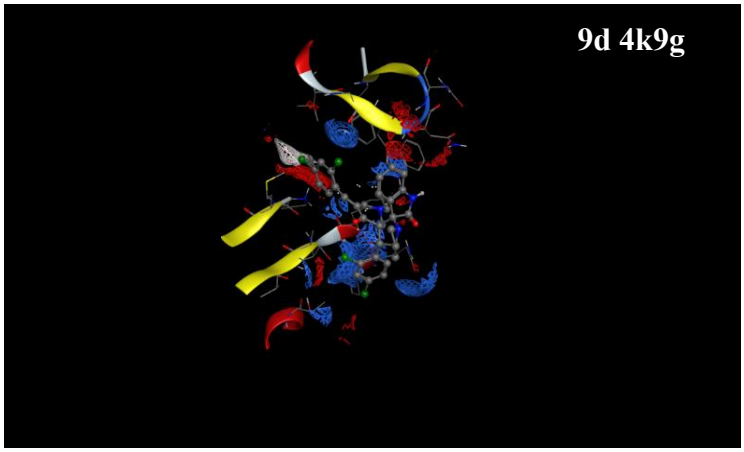
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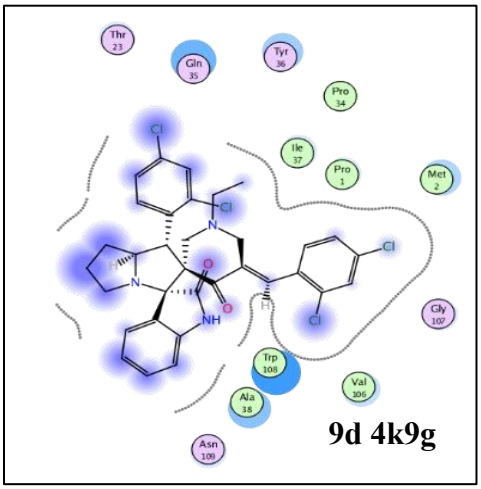
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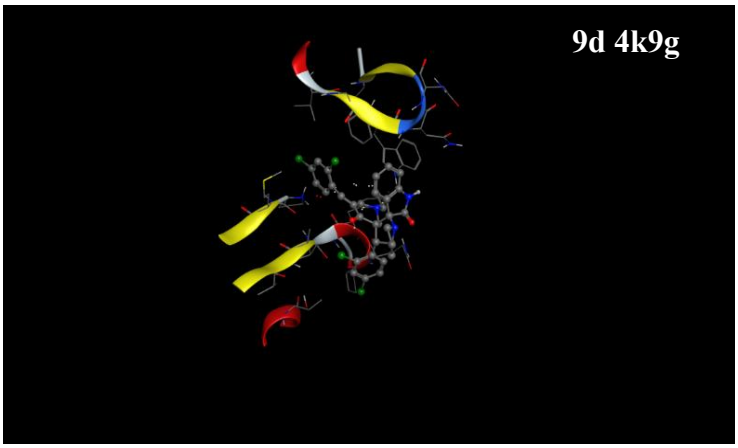
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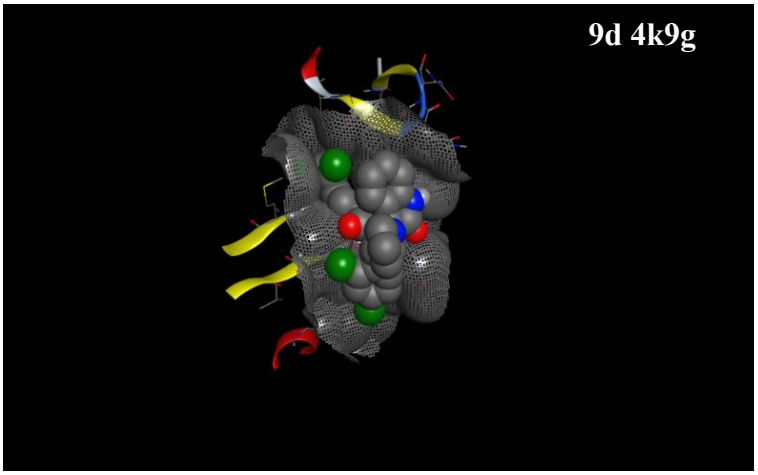
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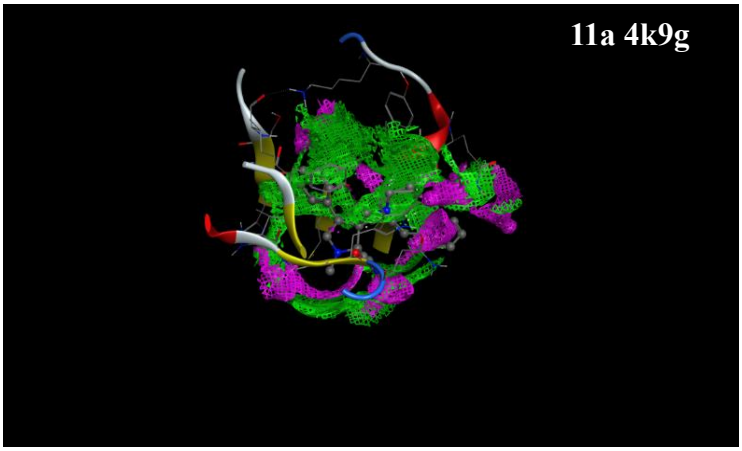
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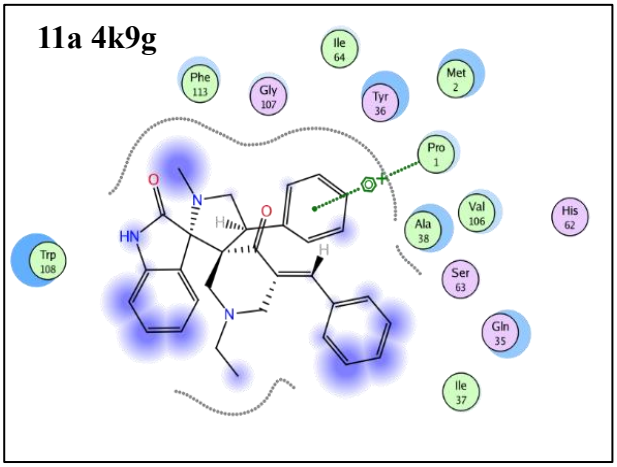
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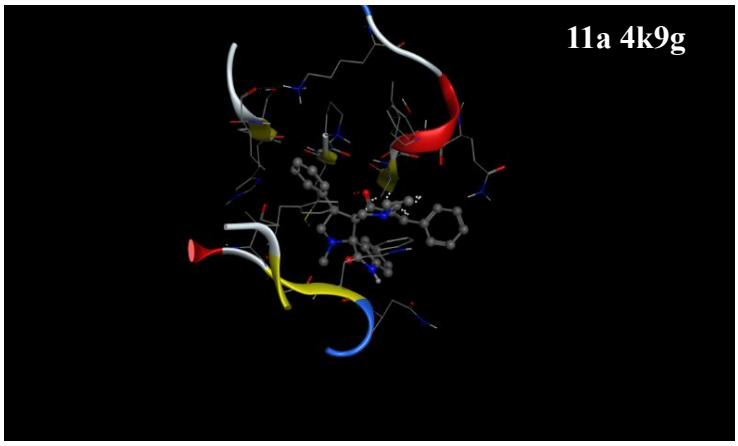
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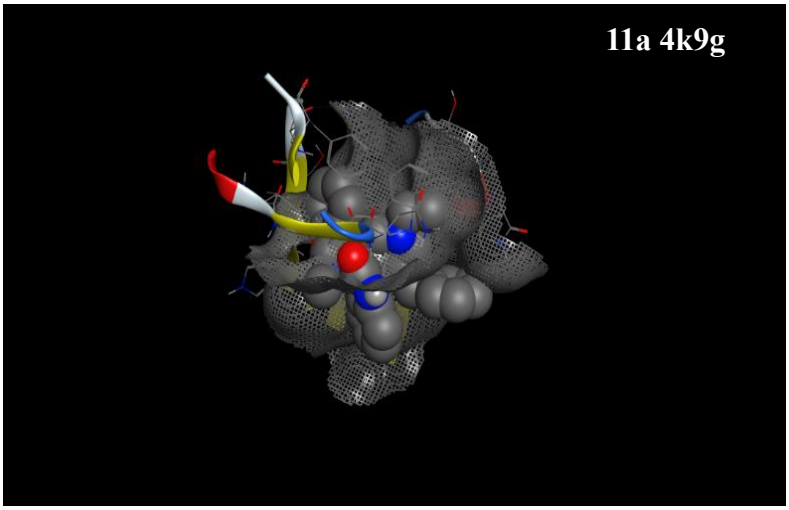
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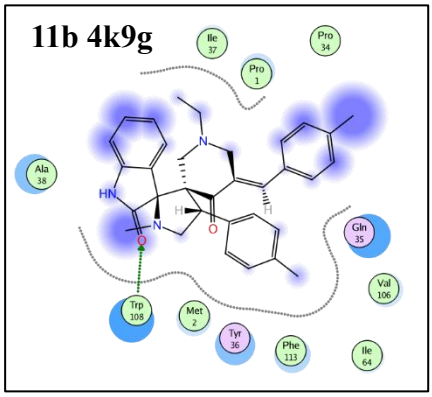
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Gln 35
Val 106
Trp 108
Met 2
Tyr 36
Phe 113
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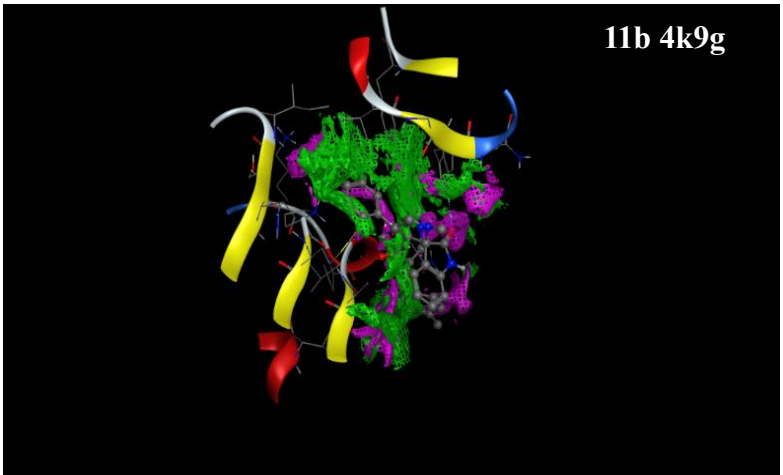
HN
N
O
H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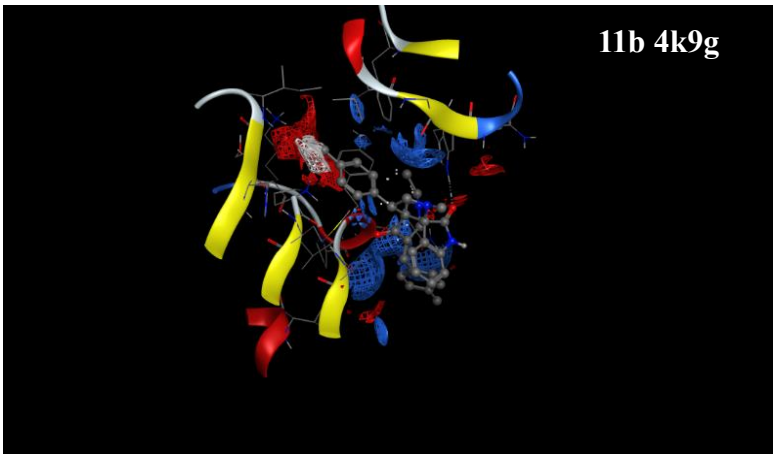
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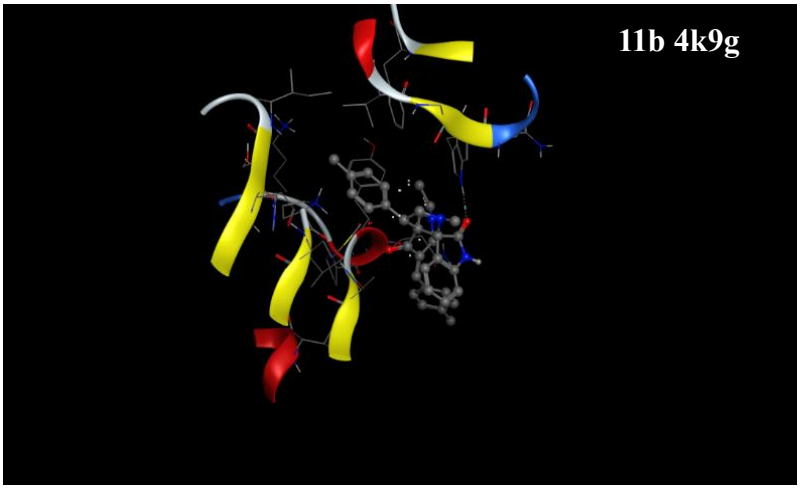
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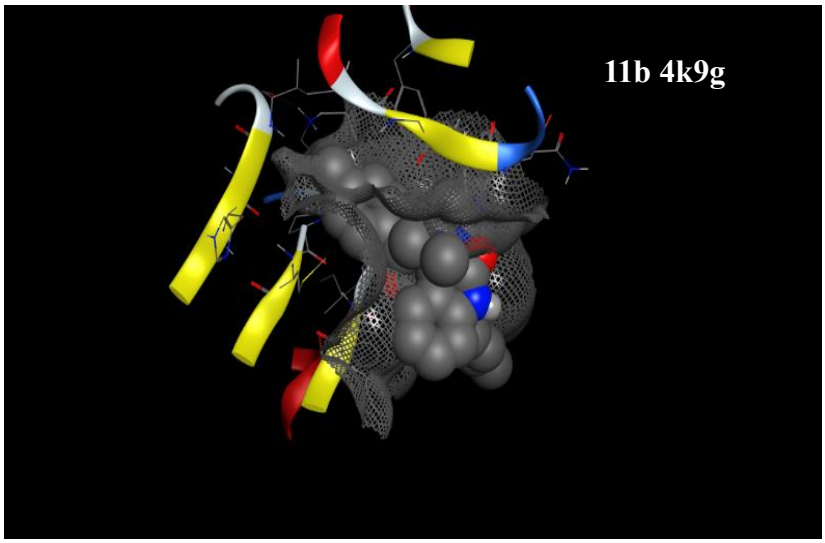
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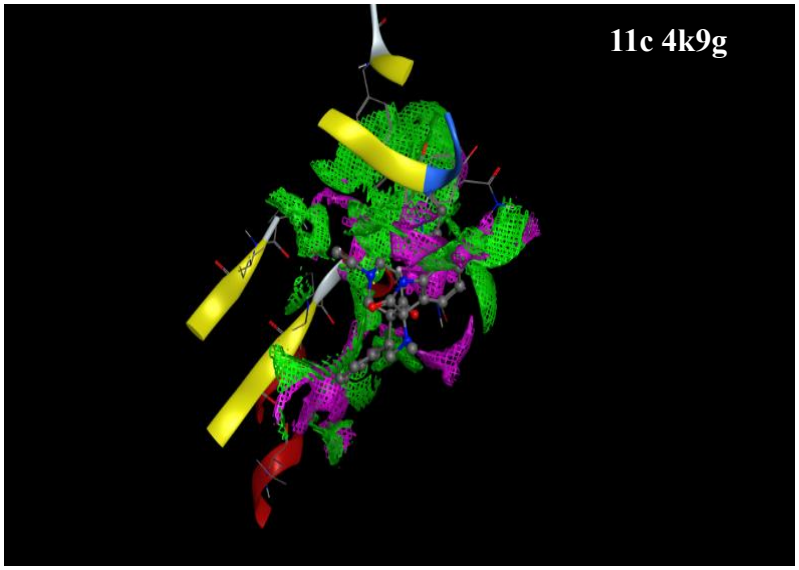
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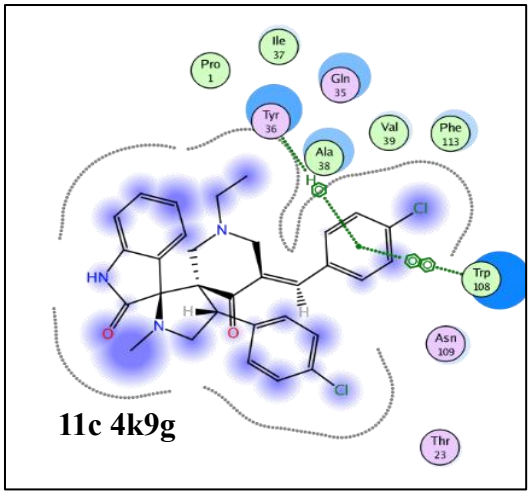
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Pro 1
Gln 35
Tyr 36
Val 39
Phe 113
Ala 38
Cl
HN
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Trp 108
H
O
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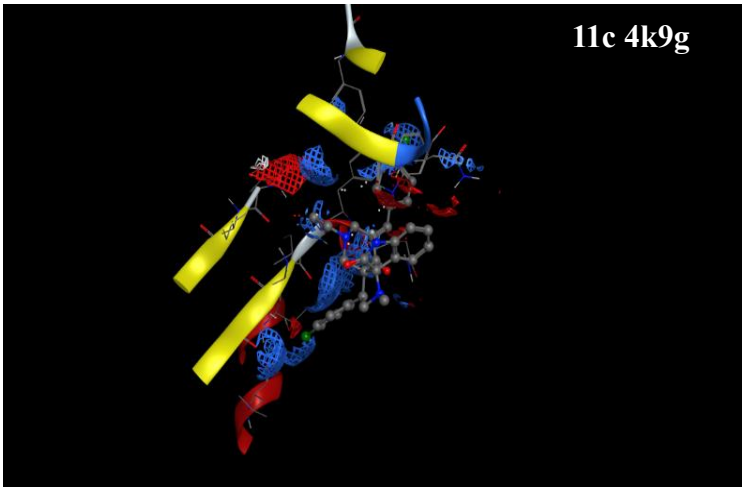
Cl
11c 4k9g
Thr 23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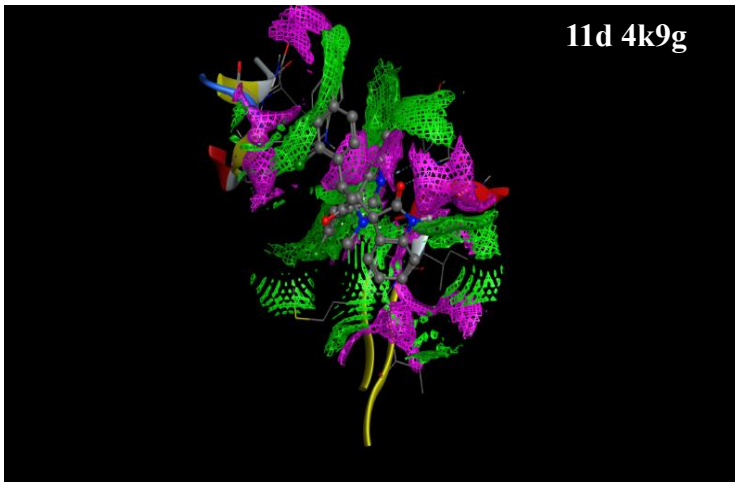
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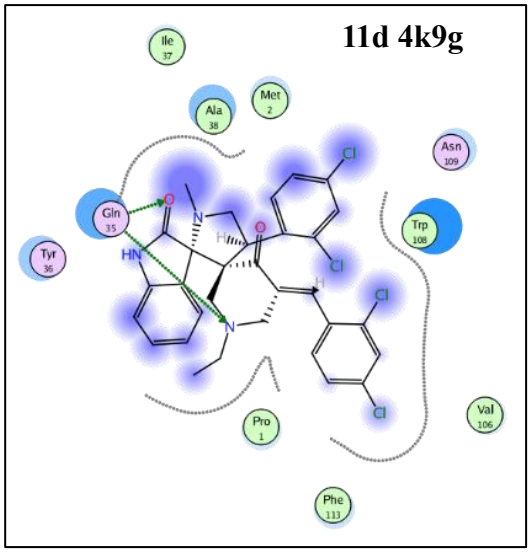
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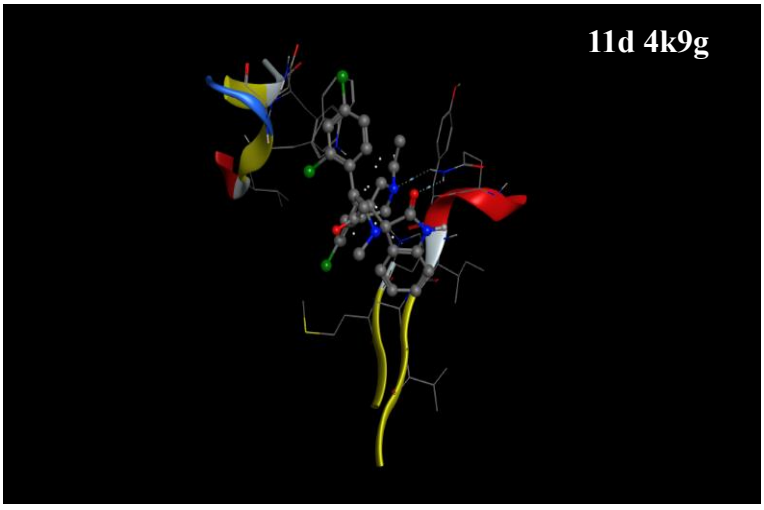
11d 4k9g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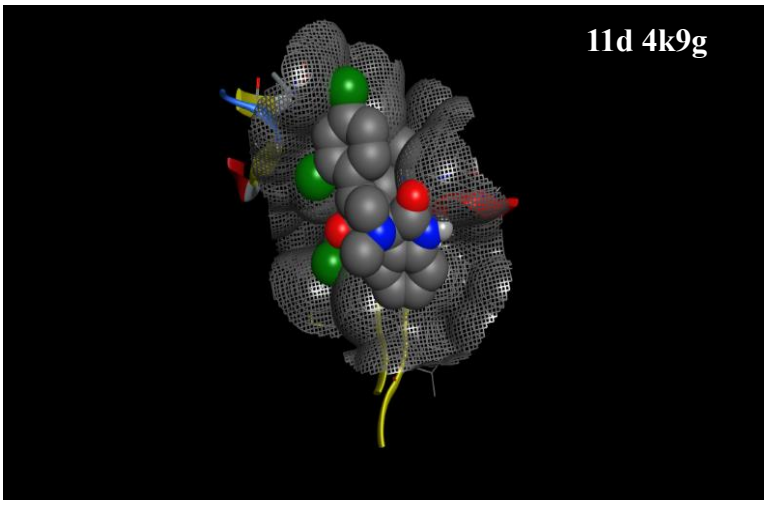
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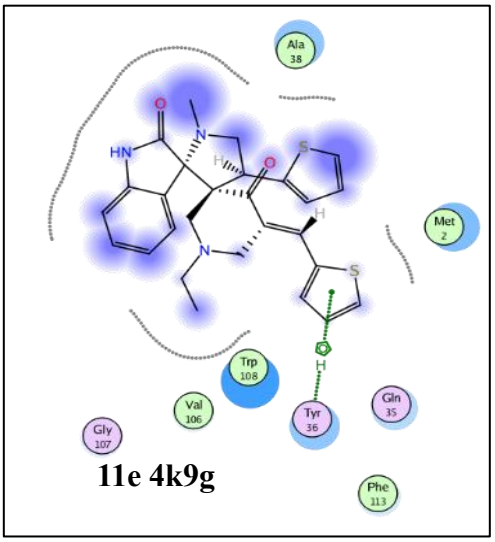

Ala 38
Met 2
Trp 108
Val 106
Tyr 36
Gln 35
Gly 107
Phe 113
11e 4k9g

Al-Azhar University

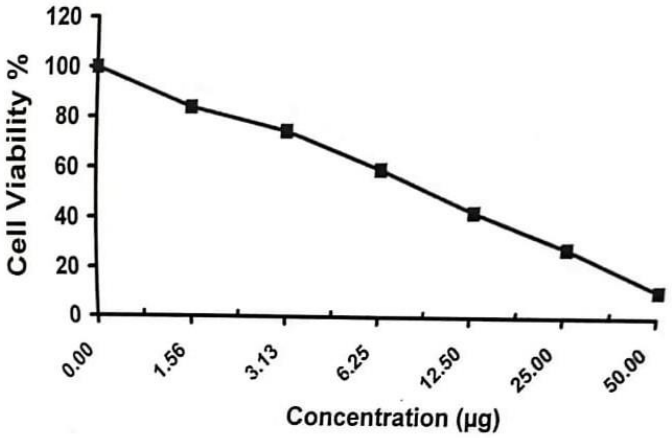
The Regional Center for Mycology & Biotechnology

Evaluation of cytotoxicity against HEPG2 cell line

Requester Data:

Name: Dr. Thoureya
Authority: Cairo University
Sample Code: (2)

HepG 2 2



Sample conc. (µg)	Viability %
50	10.97
25	28.13
12.5	42.56
6.25	59.28
3.125	74.16
1.56	83.72
0	100

Comment:

Inhibitory activity against Hepatocellular carcinoma cells was detected under these experimental conditions with IC_{50} = 9.7 µg.

Investigator (s)

Director

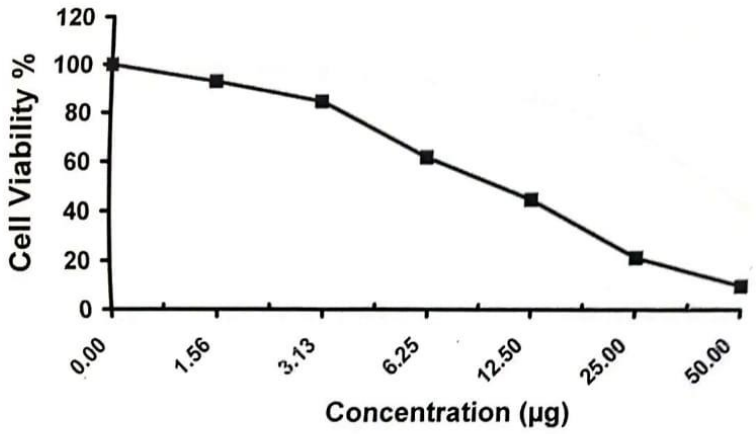
Al-Azhar University
The Regional Center for Mycology & Biotechnology

Evaluation of cytotoxicity against HEPG2 cell line

Requester Data:

Name: Dr. Thoureya
Authority: Cairo University
Sample Code: (5)

HepG 2 5



Sample conc. (µg)	Viability %
50	9.85
25	21.41
12.5	44.92
6.25	61.78
3.125	84.30
1.56	92.74
0	100

Comment:

Inhibitory activity against Hepatocellular carcinoma cells was detected under these experimental conditions with IC_{50} = 10.6 µg.

Investigator (s)

Director

Al-Azhar University

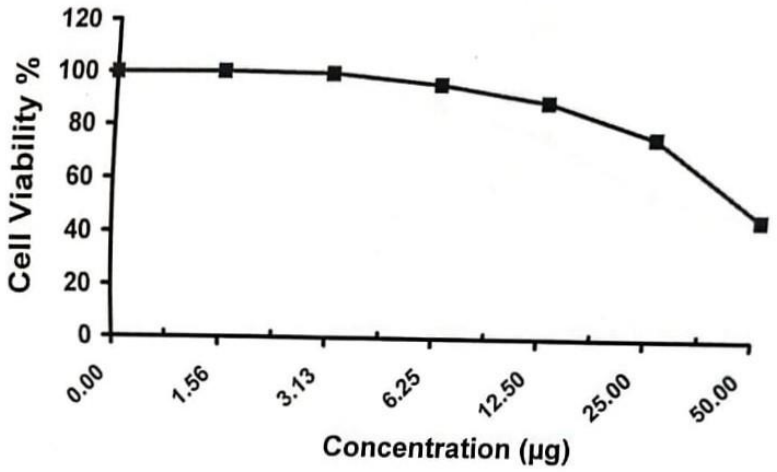
The Regional Center for Mycology & Biotechnology

Evaluation of cytotoxicity against HEPG2 cell line

Requester Data:

Name: Dr. Thoureya
Authority: Cairo University
Sample Code: (3)

HepG 2 3



Sample conc. (µg)	Viability %
50	45.42
25	75.33
12.5	88.56
6.25	95.12
3.125	99.08
1.56	100
0	100

Comment:

Inhibitory activity against Hepatocellular carcinoma cells was detected under these experimental conditions with IC_{50} = *46.2 µg.*

Investigator (s) **Director**

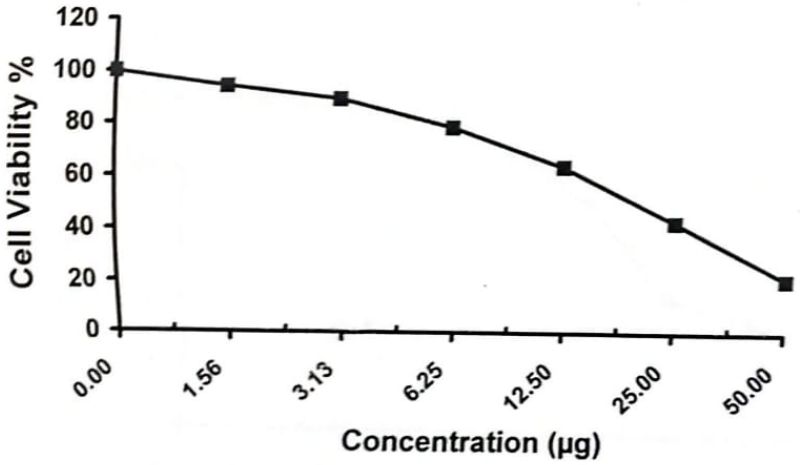
Al-Azhar University
The Regional Center for Mycology & Biotechnology

Evaluation of cytotoxicity against MCF-7 cell line

Requester Data:

Name: Dr. Thoureya
Authority: Cairo University
Sample Code: (8)

MCF-7 8



Sample conc. (µg)	Viability %
50	21.28
25	43.24
12.5	64.19
6.25	78.86
3.125	89.34
1.56	94.12
0	100

Comment:

Inhibitory activity against Breast carcinoma cells was detected under these experimental conditions with IC_{50} = 21.0 µg.

Investigator (s) **Director**

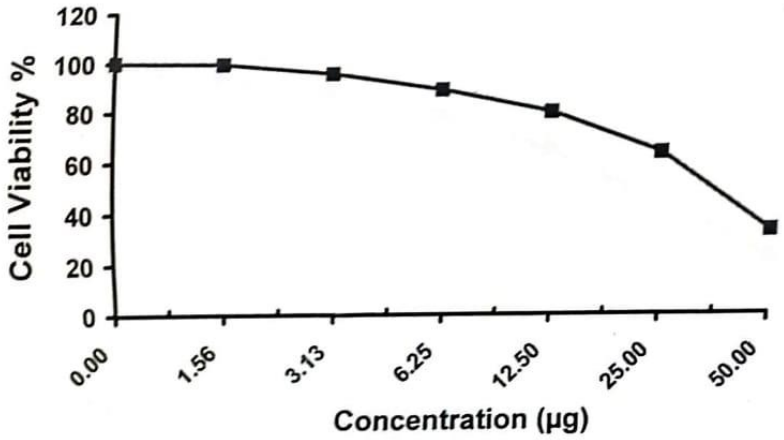
Al-Azhar University
The Regional Center for Mycology & Biotechnology

Evaluation of cytotoxicity against MCF-7 cell line

Requester Data:

Name: Dr. Thoureya
Authority: Cairo University
Sample Code: (7)

MCF-7 7



Sample conc. (µg)	Viability %
50	32.84
25	63.19
12.5	79.22
6.25	88.16
3.125	94.75
1.56	98.93
0	100

Comment:

Inhibitory activity against Breast carcinoma cells was detected under these experimental conditions with IC_{50} = 35.9 µg.

Investigator (s) **Director**

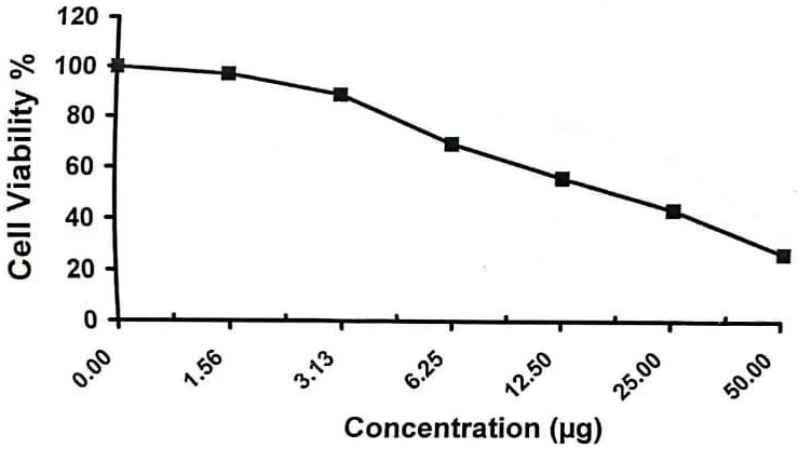
Al-Azhar University
The Regional Center for Mycology & Biotechnology

Evaluation of cytotoxicity against MCF-7 cell line

Requester Data:

Name: Dr. Thoureya
Authority: Cairo University
Sample Code: (4)

MCF-7 4



Sample conc. (µg)	Viability %
50	26.84
25	43.90
12.5	56.27
6.25	69.43
3.125	88.61
1.56	96.88
0	100

Comment:

Inhibitory activity against Breast carcinoma cells was detected under these experimental conditions with IC_{50} = *18.8 µg.*

Investigator (s) **Director**

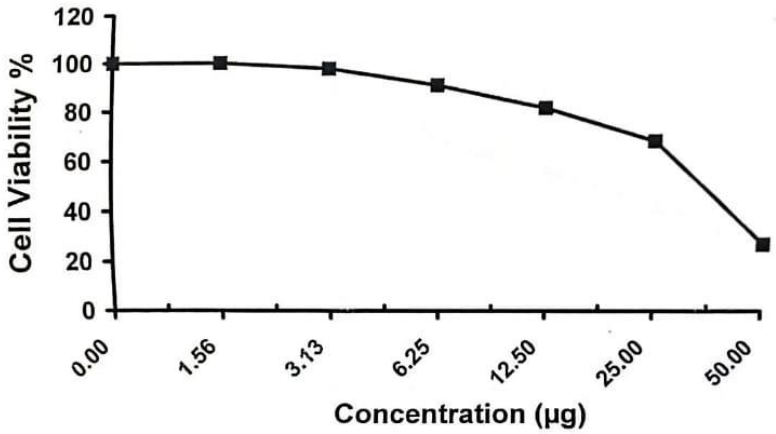
Al-Azhar University
The Regional Center for Mycology & Biotechnology

Evaluation of cytotoxicity against MCF-7 cell line

Requester Data:

Name: Dr. Thoureya
Authority: Cairo University
Sample Code: (3)

MCF-7 3



Sample conc. (µg)	Viability %
50	27.16
25	68.24
12.5	81.53
6.25	90.72
3.125	97.48
1.56	100
0	100

Comment:

Inhibitory activity against Breast carcinoma cells was detected under these experimental conditions with $IC_{50} = 36.1$ *µg.*

Investigator (s) **Director**

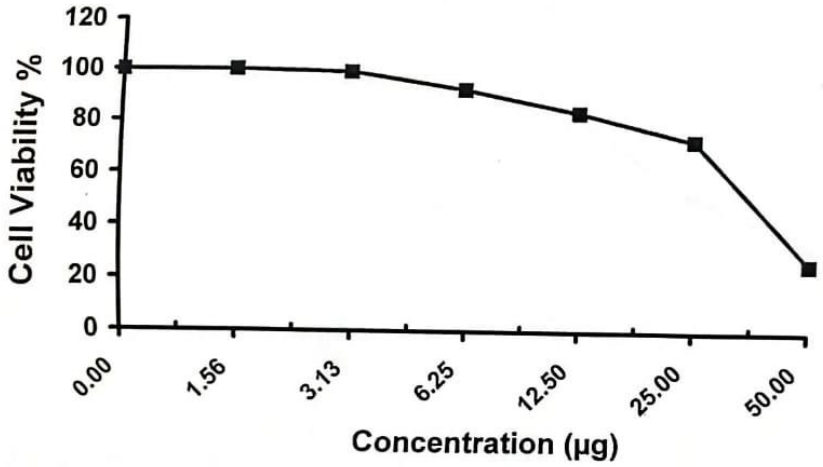
Al-Azhar University
The Regional Center for Mycology & Biotechnology

Evaluation of cytotoxicity against HEPG2 cell line

Requester Data:

Name: Dr. Thoureya
Authority: Cairo University
Sample Code: (7)

HepG 2 7



Sample conc. (µg)	Viability %
50	26.15
25	72.69
12.5	83.38
6.25	92.17
3.125	98.94
1.56	100
0	100

Comment:

Inhibitory activity against Hepatocellular carcinoma cells was detected under these experimental conditions with $IC_{50} = 37.2$ µg.

Investigator (s)

Director

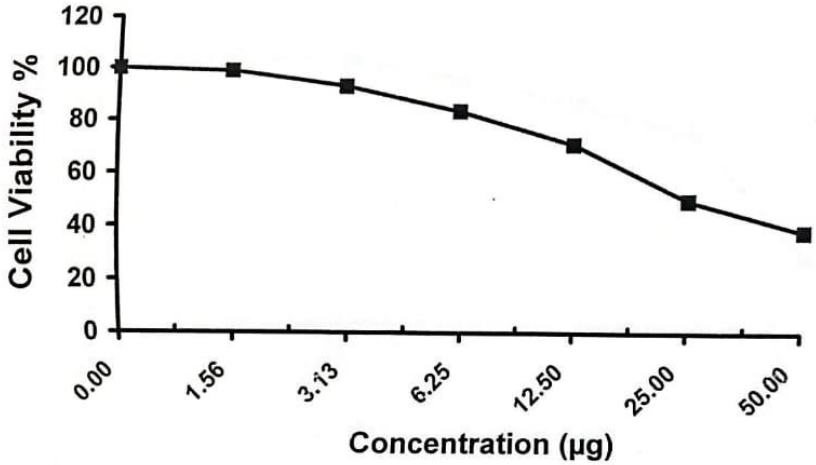
Al-Azhar University
The Regional Center for Mycology & Biotechnology

Evaluation of cytotoxicity against HEPG2 cell line

Requester Data:

Name: Dr. Thoureya
Authority: Cairo University
Sample Code: (4)

HepG 2 4



Sample conc. (µg)	Viability %
50	38.17
25	49.74
12.5	70.68
6.25	83.14
3.125	92.52
1.56	98.66
0	100

Comment:

Inhibitory activity against Hepatocellular carcinoma cells was detected under these experimental conditions with $IC_{50} = 24.8$ µg.

Investigator (s) **Director**

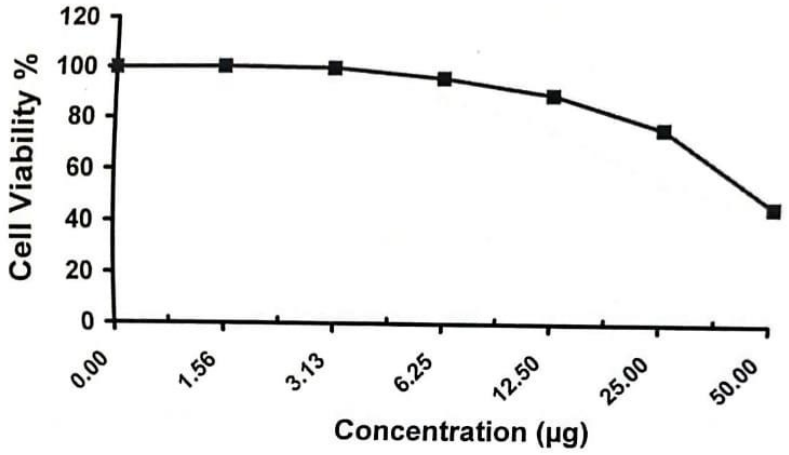
Al-Azhar University
The Regional Center for Mycology & Biotechnology

Evaluation of cytotoxicity against HEPG2 cell line

Requester Data:

Name: Dr. Thoureya
Authority: Cairo University
Sample Code: (3)

HepG 2 3



Sample conc. (µg)	Viability %
50	45.42
25	75.33
12.5	88.56
6.25	95.12
3.125	99.08
1.56	100
0	100

Comment:

Inhibitory activity against Hepatocellular carcinoma cells was detected under these experimental conditions with IC_{50} = 46.2 µg.

Investigator (s) **Director**

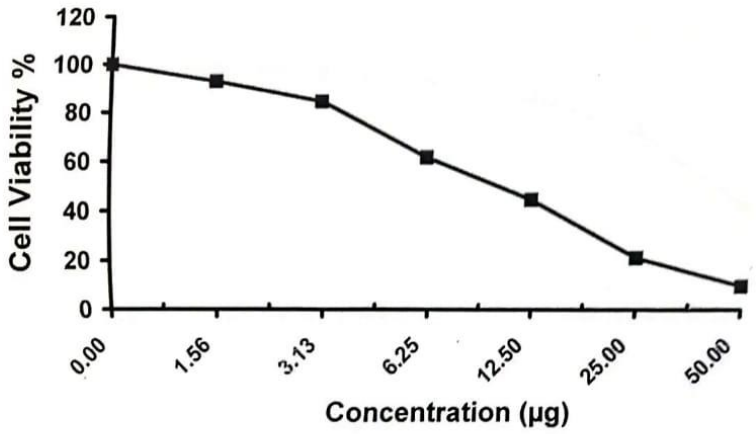
Al-Azhar University
The Regional Center for Mycology & Biotechnology

Evaluation of cytotoxicity against HEPG2 cell line

Requester Data:

Name: Dr. Thoureya
Authority: Cairo University
Sample Code: (5)

HepG 2 5



Sample conc. (µg)	Viability %
50	9.85
25	21.41
12.5	44.92
6.25	61.78
3.125	84.30
1.56	92.74
0	100

Comment:

Inhibitory activity against Hepatocellular carcinoma cells was detected under these experimental conditions with IC_{50} = 10.6 µg.

Investigator (s)

Director

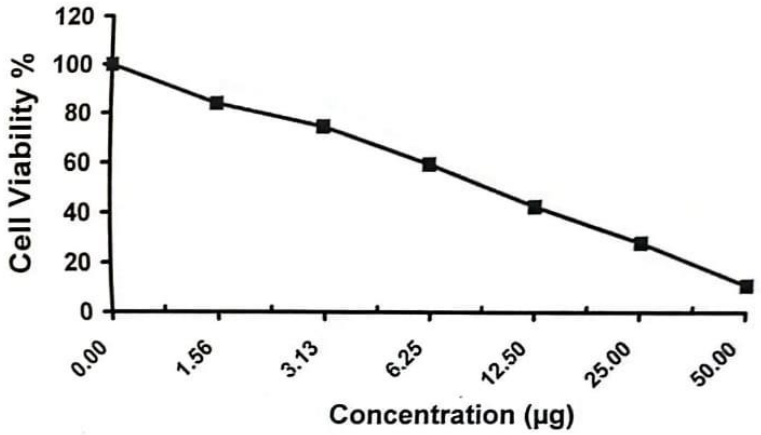
Al-Azhar University
The Regional Center for Mycology & Biotechnology

Evaluation of cytotoxicity against HEPG2 cell line

Requester Data:

Name: Dr. Thoureya
Authority: Cairo University
Sample Code: (2)

HepG 2 2



Sample conc. (µg)	Viability %
50	10.97
25	28.13
12.5	42.56
6.25	59.28
3.125	74.16
1.56	83.72
0	100

Comment:

Inhibitory activity against Hepatocellular carcinoma cells was detected under these experimental conditions with IC_{50} = 9.7 µg.

Investigator (s) **Director**

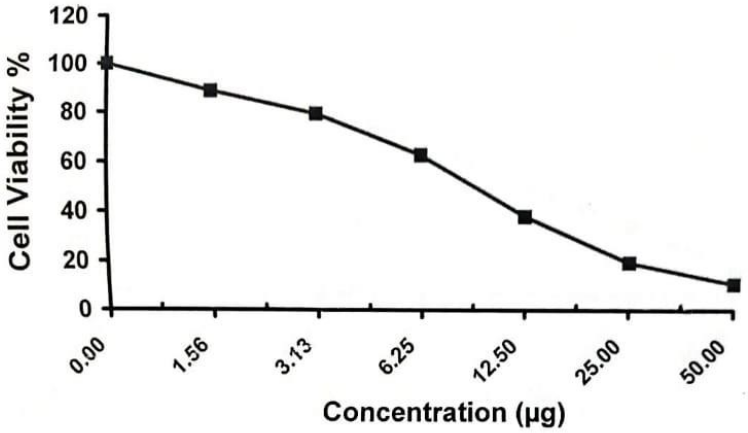
Al-Azhar University
The Regional Center for Mycology & Biotechnology

Evaluation of cytotoxicity against MCF-7 cell line

Requester Data:

Name: Dr. Thoureya
Authority: Cairo University
Sample Code: (2)

MCF-7 2



Sample conc. (µg)	Viability %
50	10.85
25	19.54
12.5	38.12
6.25	62.58
3.125	79.04
1.56	88.56
0	100

Comment:

Inhibitory activity against Breast carcinoma cells was detected under these experimental conditions with $IC_{50} = 9.5\ \mu g$.

Investigator (s)

Director