LAMPIRAN-LAMPIRAN

LAMPIRAN I

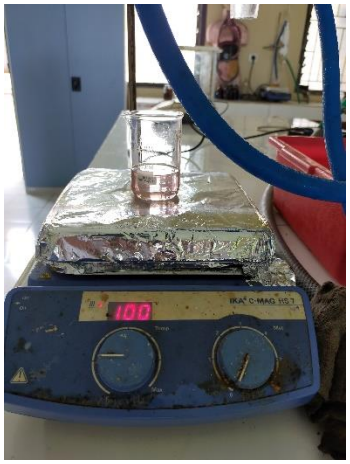
SINTESIS *BIS-(1-4-DECYLBENZOYL)-3-METHYLTHIOUREA) COBALT (III)*

Penimbangan *1,4-Decylbenzoyl-3-methylthiourea*

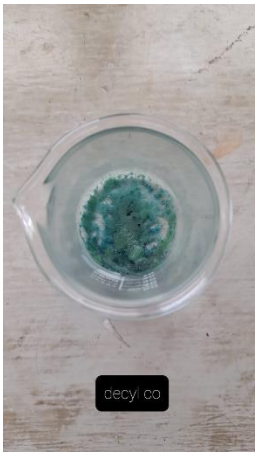
Penimbangan $Co(BF_4)_2.6H_2O$

Proses refluks selama 5 jam pada suhu 75^oC

Hasil refluks



Proses penguapan hasil refluks



Hasil sintesis

Perhitungan Stoikiometri

$2C_{19}H_{29}OSN_2 + Co(BF_4)_2.6H_2O \longrightarrow Co(C_{19}H_{29}OSN_2)_2 + 6H_2O$

m	0,250 mmol	0,125 mmol	-	-
b	0,125 mmol	0,125 mmol	0,125 mmol	0,125 mmol
s	0,125 mmol	-	0,125 mmol	0,125 mmol

$C_{19}H_{29}OSN_2$ = mmol x massa molar

= 0,250 x 333

= 83,25 mg

$Co(BF_4)_2.6H_2O$ = mmol x massa molar

= 0,125 x 340,63

= 42,57mg

$Co(C_{19}H_{29}OSN_2)_2$ = mmol x massa molar

= 0,125 x 725

= 90,625 mg

$C_{19}H_{29}OSN_2$ = mmol x massa molar

= 0,125 x 333

= 41,625 mg

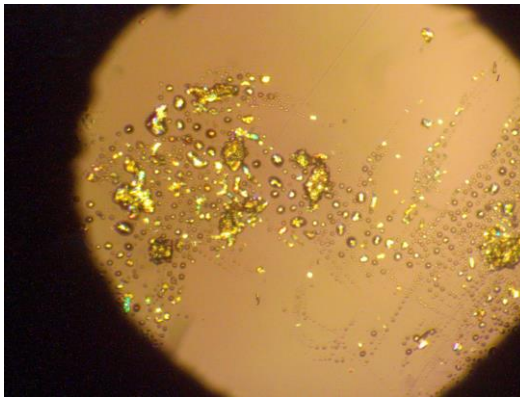
$$\%yield = \frac{Bobot\ Sintesis}{Bobot\ Teori} x100\%$$

$$= \frac{54{,}5\ mg}{90{,}625\ mg} x100\%$$

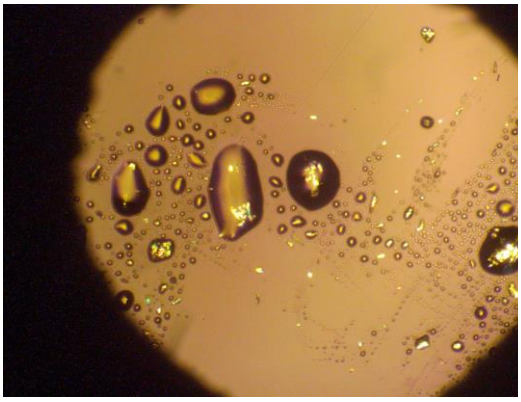
$$= 60{,}13\%$$

LAMPIRAN II

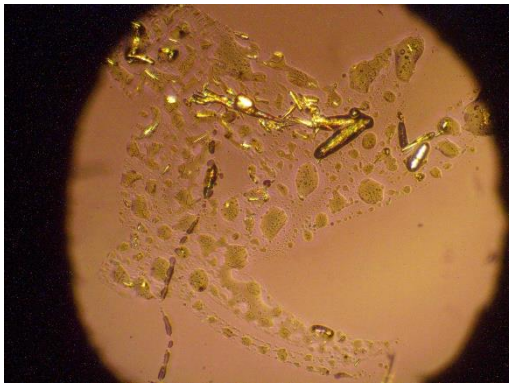
UJI KEMURNIAN



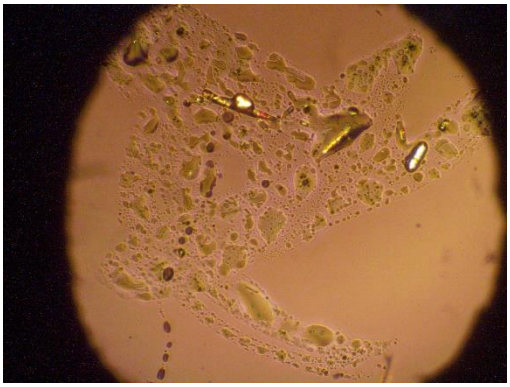
Senyawa *1,4-Decylbenzoyl-3-methylthiourea* sebelum melebur



Senyawa *1,4-Decylbenzoyl-3-methylthiourea* sesudah melebur



Senyawa kompleks *Bis-(1,4-Decylbenzoyl-3-methylthiourea) Cobalt (III)* sebelum melebur



Senyawa kompleks *Bis-(1,4-Decylbenzoyl-3-methylthiourea) Cobalt (III)* seudah melebur

LAMPIRAN III

SPEKTROFOTOMETRI UV-VIS

1. Perhitungan Nilai Absorptivitas Molar

Hukum Lambert-Beer:

$$A = Ɛ.b.C$$

Keterangan:

A = absorbansi

Ɛ = absorptivitas molar (L mol^{-1} cm^{-1})

b = jarak yang ditempuh (cm)

C = konsentrasi (mol L^{-1})

- Perhitungan Konsentrasi

  a. $Co(BF_4)_2.6H_2O$

  $$M = \frac{g}{Mr} \text{ x } \frac{1000}{mL}$$

  $$M = \frac{0,002}{340,63} \text{ x } \frac{1000}{10}$$

  $$M = \frac{2}{3406,3}$$

  $$M = 0,00058$$

  b. *Bis-(1-4-decylbenzoyl)-3-methylthiourea) Cobalt (III)*

  $$M = \frac{g}{Mr} \text{ x } \frac{1000}{mL}$$

  $$M = \frac{0,0021}{725} \text{ x } \frac{1000}{10}$$

  $$M = \frac{2,1}{7250}$$

  $$M = 0,00029$$

- Perhitungan Nilai Absorptivitas Molar

  a. $Co(BF_4)_2.6H_2O$

  $A = Ɛ.b.C$

  $0,133 = Ɛ.1.0,00058$

  $0,133 = Ɛ.0,00058$

  $$Ɛ = \frac{0,133}{0,00058}$$

  $Ɛ = 229,31$ L mol^{-1} cm^{-1}

b. *Bis-(1-4-decylbenzoyl)-3-methylthiourea) Cobalt (III)*

A = Ɛ.b.C

1,588 = Ɛ.1.0,00029

1,588 = Ɛ.0,00029

$$Ɛ = \frac{1,588}{0,00029}$$

$Ɛ = 5475,86$ L mol^{-1} cm^{-1}

c. Harga absorptivitas molar senyawa kompleks *Bis-(1-4-decylbenzoyl)-3-methylthiourea) Cobalt (III)* dan $Co(BF_4)_2.6H_2O$ ditunjukan pada tabel berikut ini:

Tabel 4.3 Data Spektrum Elektronik

No	Senyawa	Mr (g/mol)	λ_{max} (nm)	υ (cm^{-1})	A	ε (L mol^{-1} cm^{-1})
1	$Co(BF_4)_2.6H_2O$	340,63	326	3067,48	0,133	229,31
2	*Bis-(1,4-Decylbenzoyl)-3 methylthiourea) Cobalt (III)*	725	267	3745,31	1,588	5475,86

2. Perhitungan Energi Pembelahan Kompleks

Dengan mengetahui panjang gelombang maksimum spektra kompleks dapat dihitung besarnya energi transisi (10 Dq) dengan rumus:

$$\Delta_o = \frac{(hc\,No)}{\lambda}$$

Keterangan:

Δ_o = selisih energi orbitas d (J mol^{-1})

h = konstanta planck (6,626 x 10^{-34})

c = kecepatan cahaya (2,998 x 10^8 ms^{-1})

N_o = bilangan Avogadro (6,023 x 10^{23} mol^{-1})

λ = panjang gelombang yang diserap (nm)

a. $Co(BF_4)_2.6H_2O$

$$\Delta_o = \frac{(hc\,No)}{\lambda}$$

$$\Delta_o = \frac{(6,626x10^{-34}.2,998x10^{8}.6,023x10^{23})}{326}$$

$\Delta_o = \frac{(0,119645)}{326}$

Δ_o = 3,6701 x 10^{-4} J.mol^{-1}

10 Dq = 367,01 KJ.mol^{-1}

b. *Bis-(1,4-Decylbenzoyl)-3 methylthiourea) Cobalt (III)*

$\Delta_o = \frac{(hc\ No)}{\lambda}$

$\Delta_o = \frac{(6,626x10^{-34}.2,998x10^{8}.6,023x10^{23})}{267}$

$\Delta_o = \frac{(0,119645)}{267}$

Δ_o = 4,4811 x 10^{-4} J.mol^{-1}

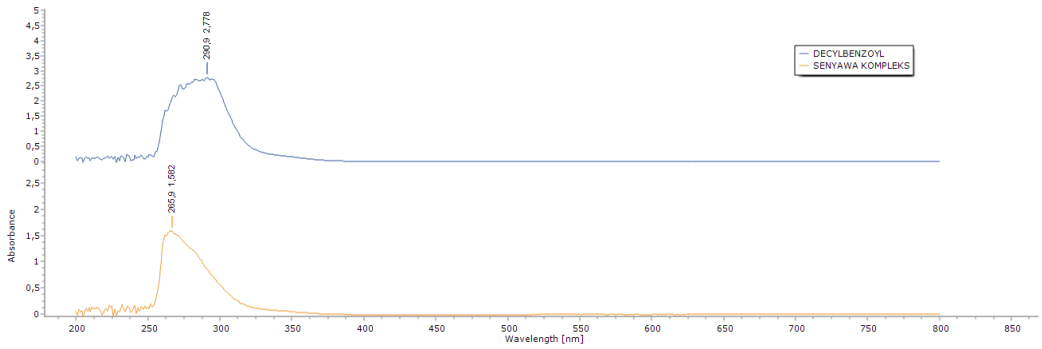
10 Dq = 448,11 KJ.mol^{-1}

Harga 10 Dq untuk senyawa kompleks *Bis-(1,4-Decylbenzoyl)-3 methylthiourea) Cobalt (III)* dan logam $Co(BF_4)_2.6H_2O$ adalah sebagai berikut:

Tabel 4.4 Harga 10 Dq $CO(BF_4)_2.6H_2O$ dan Kompleks *Bis-(1,4-Decylbenzoyl)-3 methylthiourea) Cobalt (III)*

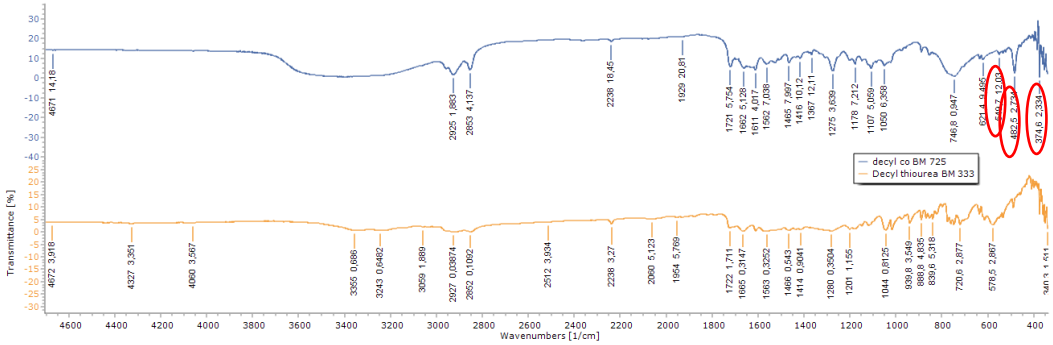
No	Senyawa	λ_{max} (nm)	10 Dq (KJ mol^{-1})
1	$Co(BF_4)_2.6H_2O$	326	467,01
2	*Bis-(1,4-Decylbenzoyl)-3 methylthiourea) Cobalt (III)*	267	448,11

3. Spektrum Senyawa *1,4-Decylbenzoyl-3-methylthiourea* dan Kompleks *Bis-(1,4-Decylbenzoyl)-3 methylthiourea) Cobalt (III)*



LAMPIRAN IV

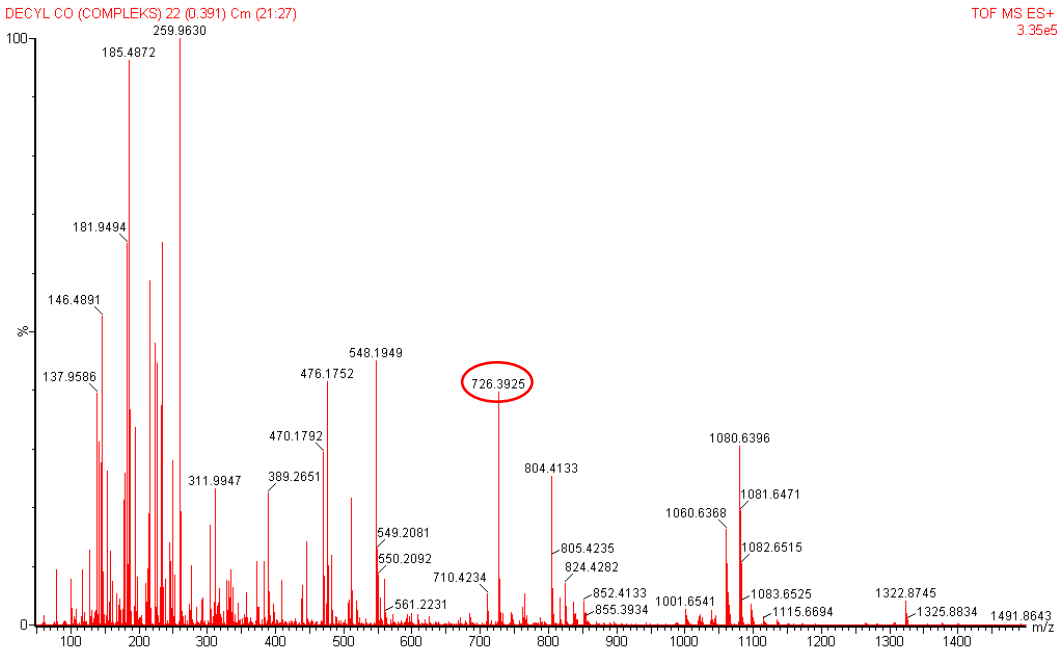
SPEKTROFOTOMETER INFRAMERAH



Spektrum Inframerah *Bis-(1-4-decylbenzoyl)-3-methylthiourea) Cobalt (III)* dan *1,4-Decylbenzoyl-3-methylthiourea*

LAMPIRAN V

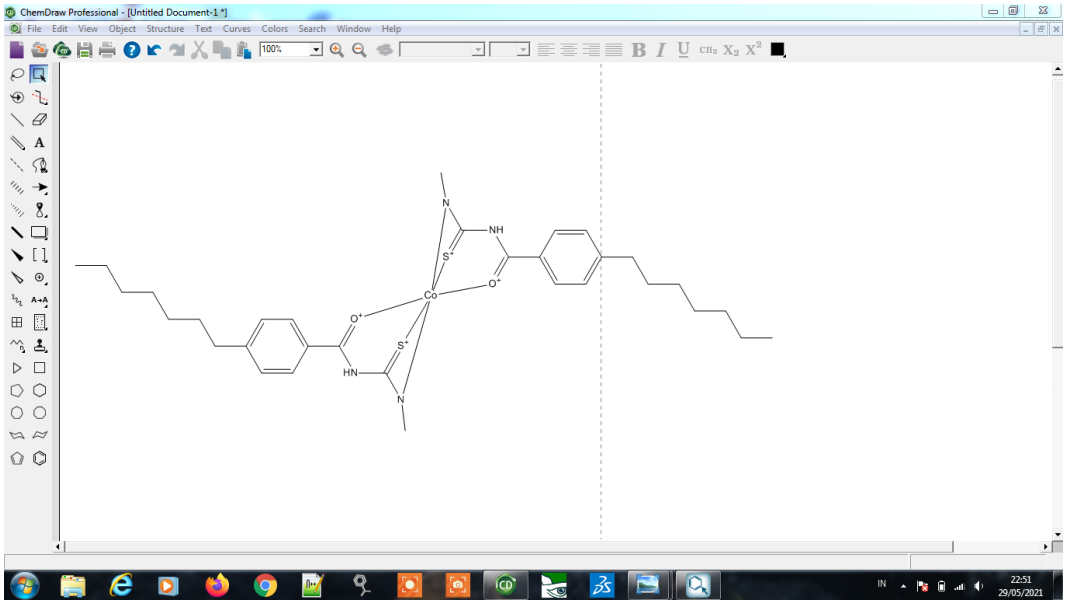
SPEKTROMETRI MASSA



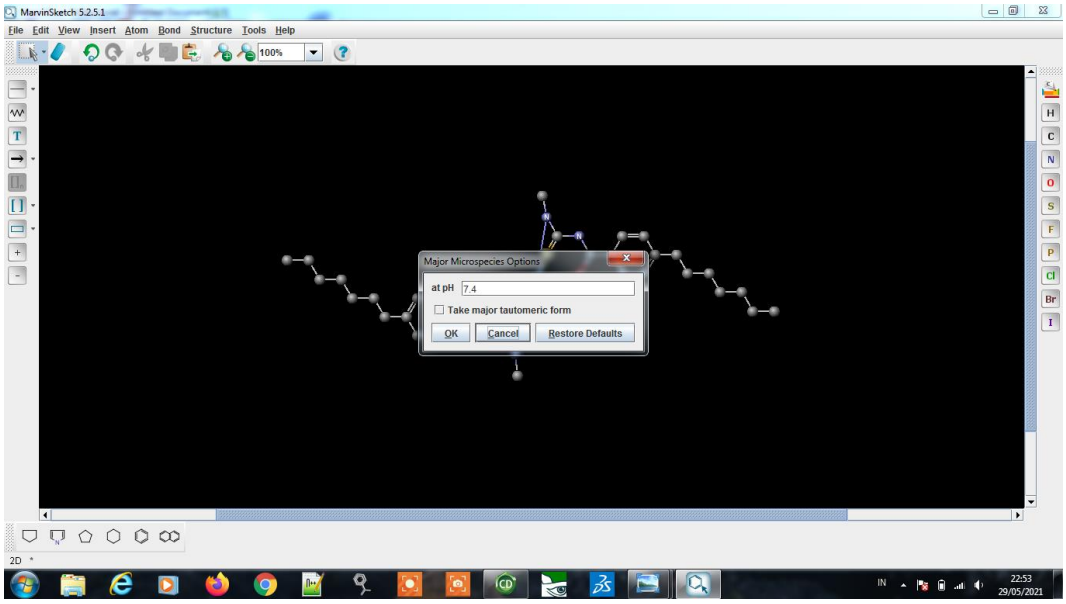
Hasil Analisis *Mass Spectrometry* Senyawa Kompleks *Bis-(1-4-decylbenzoyl)-3-methylthiourea) Cobalt (III)*

LAMPIRAN VI

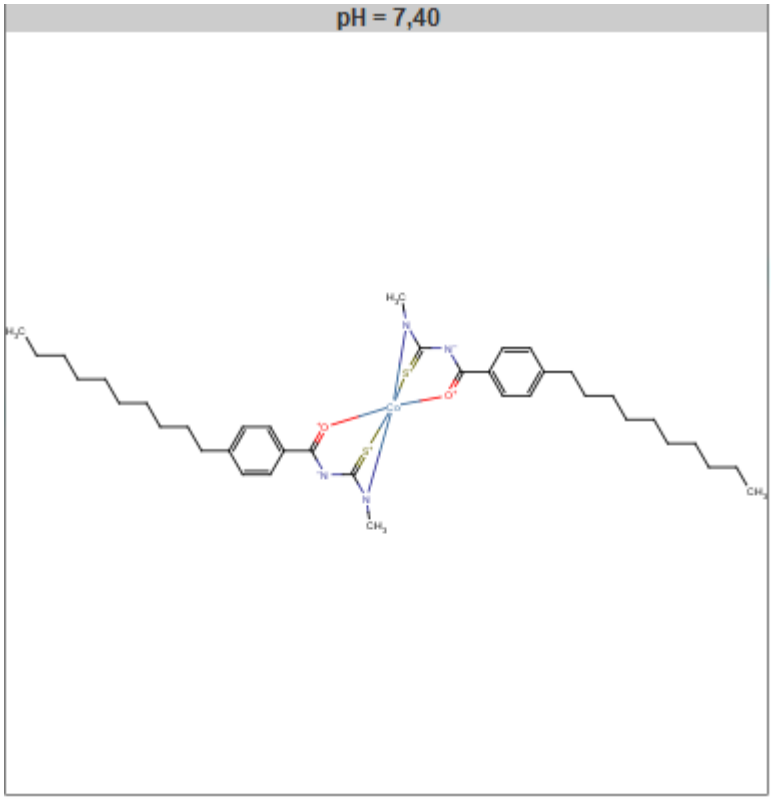
PREPARASI LIGAN



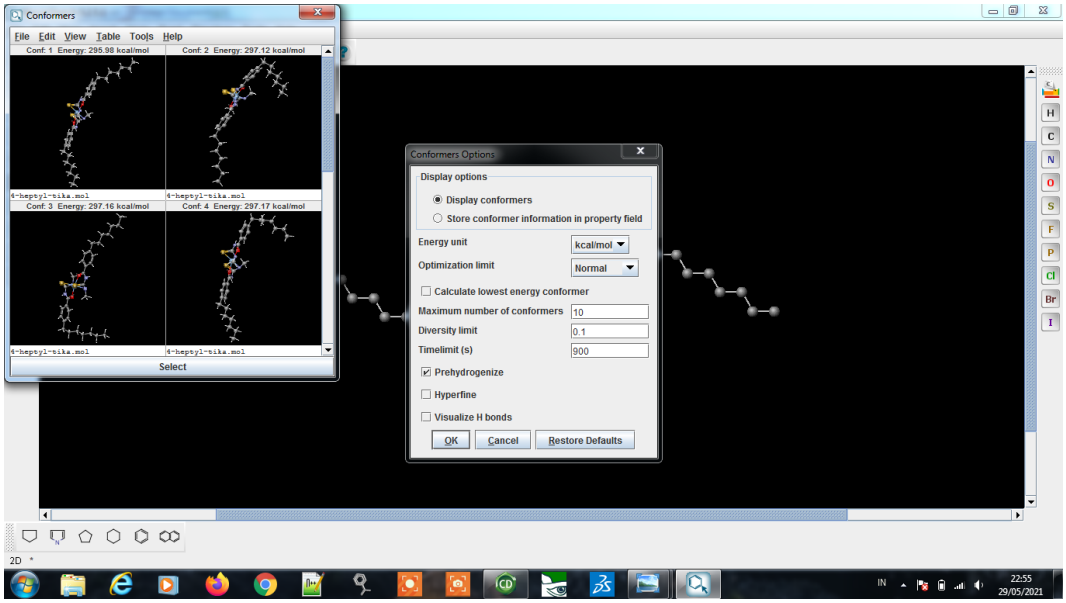
Pembuatan struktur ligan di *software ChemDraw Ultra 8.0*



Ligan diprotonasi di *software MarvinSketch 5.2.5.1*

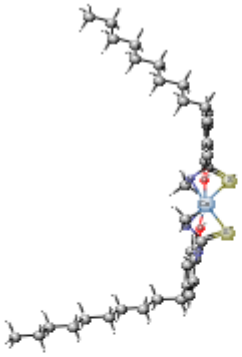


Ligan hasil protonasi

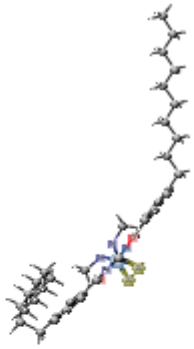


Ligan dikonformasi

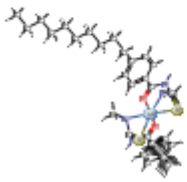
Conf: 1 Energy: 307.53 kcal/mol



Conf: 2 Energy: 308.36 kcal/mol

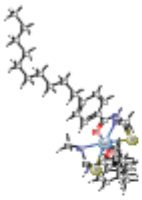


Conf: 3 Energy: 308.37 kcal/mol

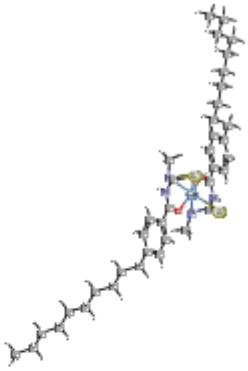


Conf: 4 Energy: 308.4 kcal/mol

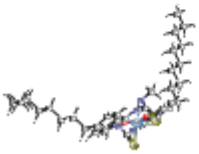
Conf: 5 Energy: 308.97 kcal/mol



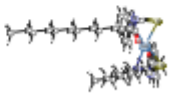
Conf: 6 Energy: 308.99 kcal/mol

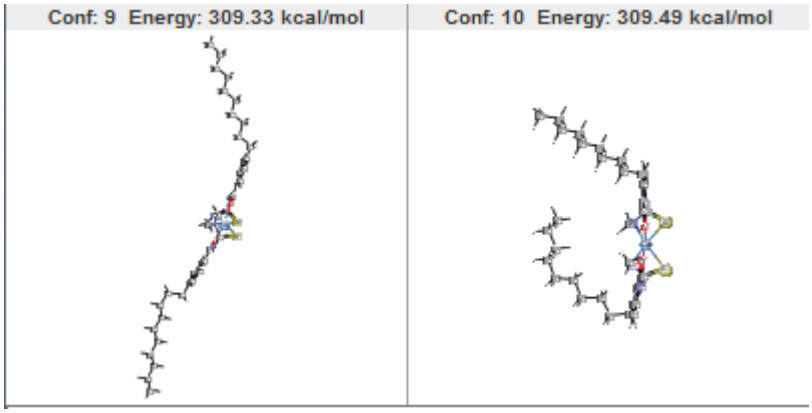


Conf: 7 Energy: 309.1 kcal/mol



Conf: 8 Energy: 309.15 kcal/mol



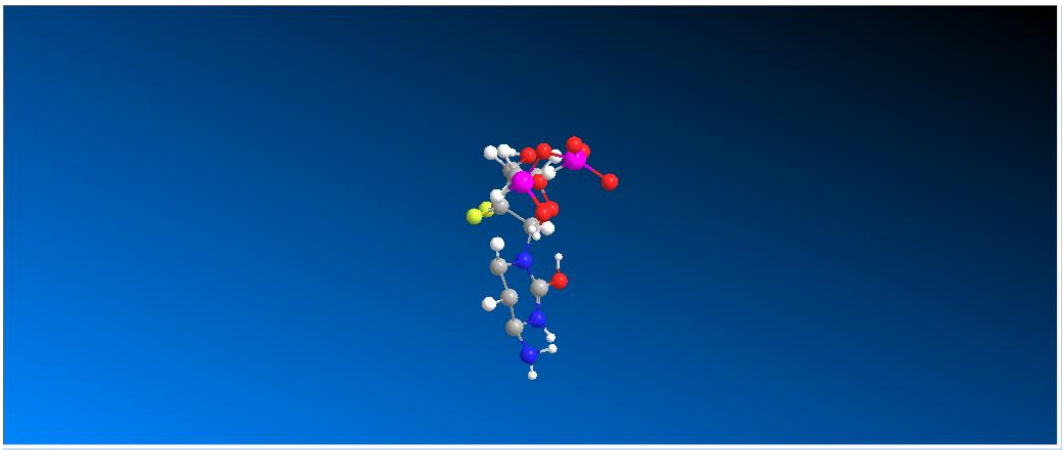


Ligan hasil konformasi

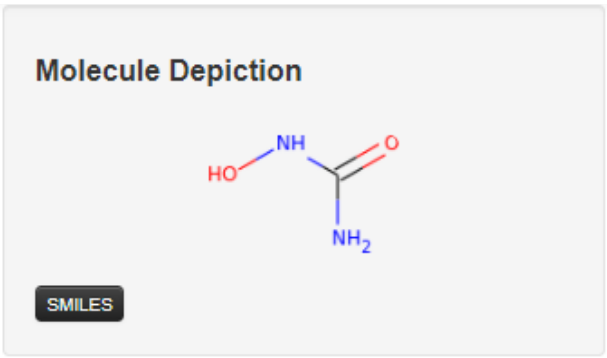
LAMPIRAN VII

DRUG SCAN

1. Ligan Alami



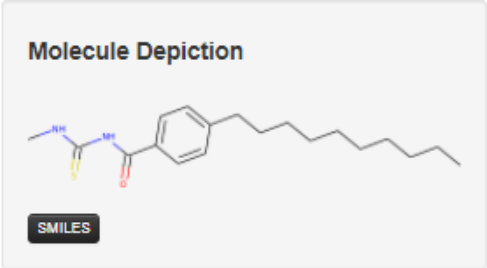
2. *Hydroxyurea*



Molecule properties:

Descriptor	Value
Molecular Weight	76.055
LogP	-0.9561
#Rotatable Bonds	0
#Acceptors	2
#Donors	3
Surface Area	28.539

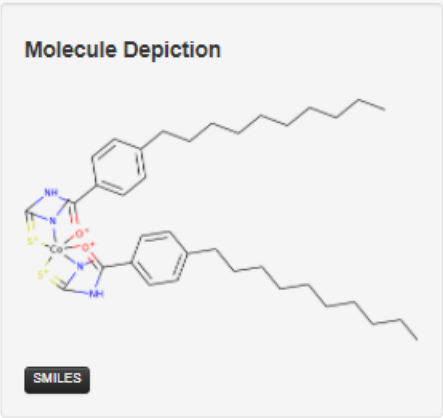
3. Senyawa *1-4-Decylbenzoyl)-3-methylthiourea*



Molecule properties:

Descriptor	Value
Molecular Weight	334.529
LogP	4.6039
#Rotatable Bonds	10
#Acceptors	2
#Donors	2
Surface Area	145.796

4. **Senyawa Kompleks *Bis-(1-4-Decylbenzoyl)-3-methylthiourea) Cobalt (III)***

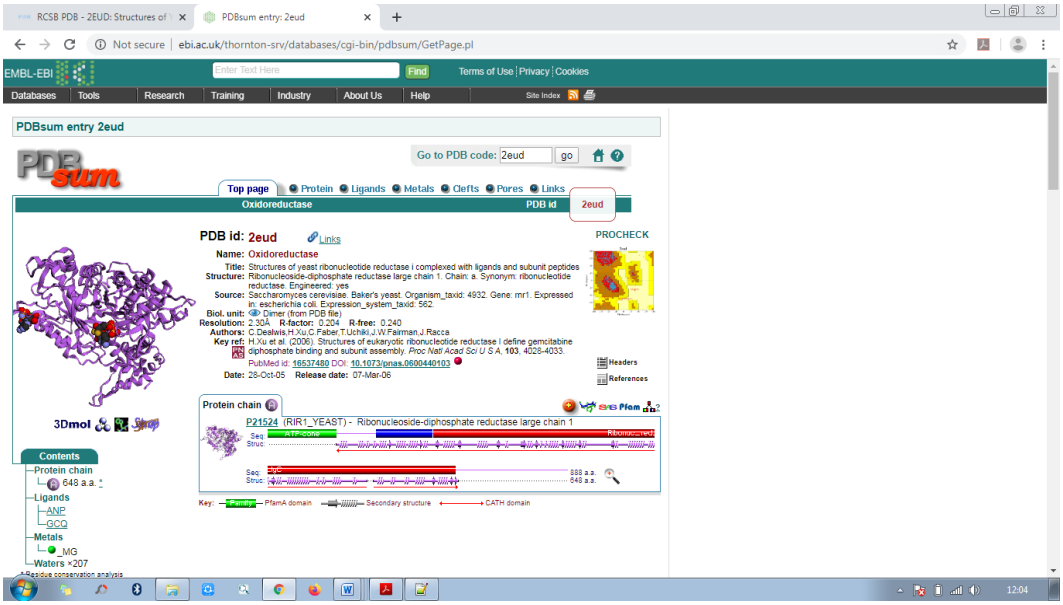


Molecule properties:

Descriptor	Value
Molecular Weight	725.975
LogP	8.2575
#Rotatable Bonds	20
#Acceptors	4
#Donors	2
Surface Area	289.115

LAMPIRAN VIII

ANALISIS RESEPTOR



Pengunduhan Ramachandran Plot PDB 2EUD melalui *website*

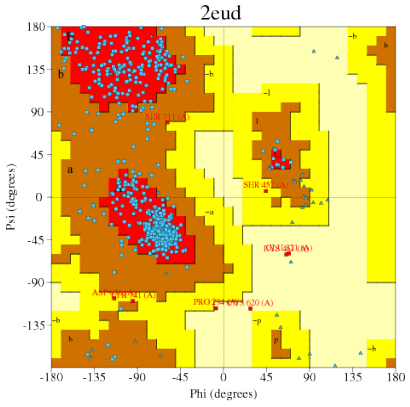
https://www.ebi.ac.uk/pdbsum/

PROCHECK statistics

1. Ramachandran Plot statistics

		No. of residues	%-tage
Most favoured regions	[A,B,L]	509	88.8%★
Additional allowed regions	[a,b,l,p]	57	9.9%
Generously allowed regions	[~a,~b,~l,~p]	4	0.7%
Disallowed regions	[XX]	3	0.5%★
Non-glycine and non-proline residues		573	100.0%
End-residues (excl. Gly and Pro)		4	
Glycine residues		42	
Proline residues		29	
Total number of residues		648	

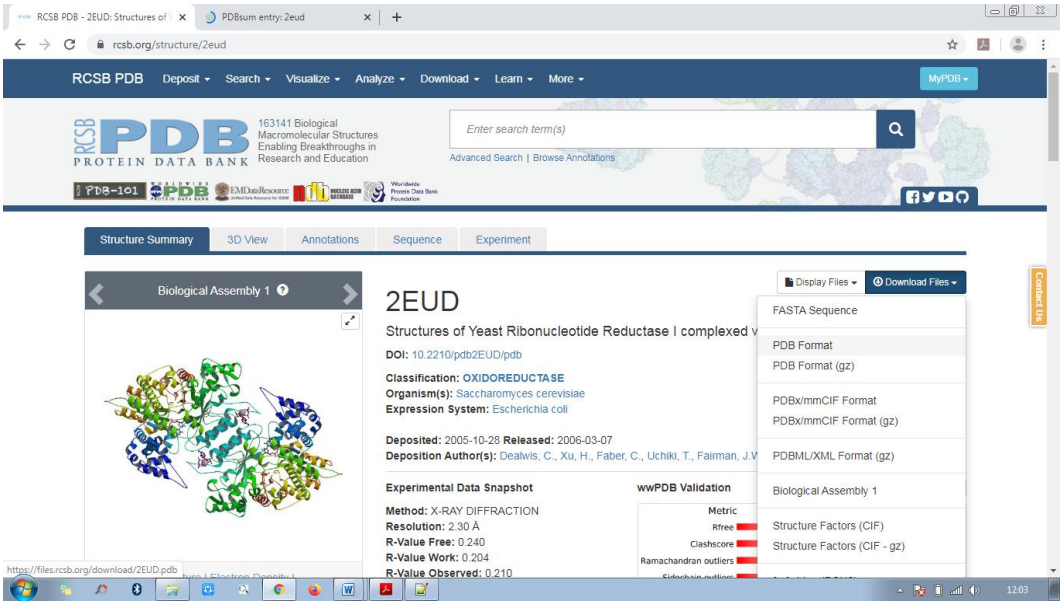
Based on an analysis of **118** structures of resolution of at least **2.0** Angstroms and *R*-factor no greater than **20.0** a good quality model would be expected to have over **90%** in the most favoured regions [A,B,L].



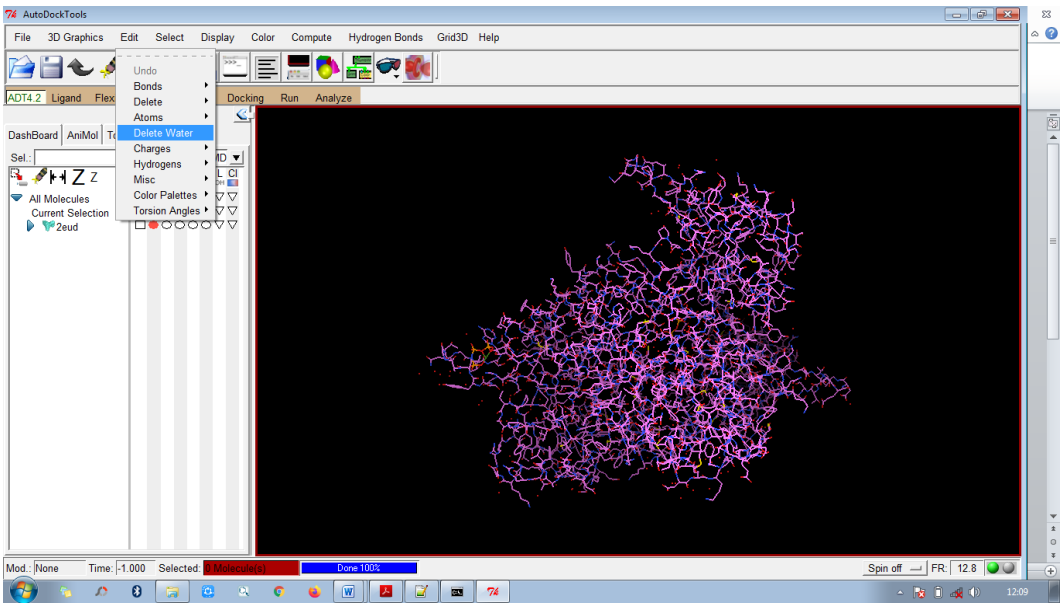
Ramachandran plot PDB 2EUD

LAMPIRAN IX

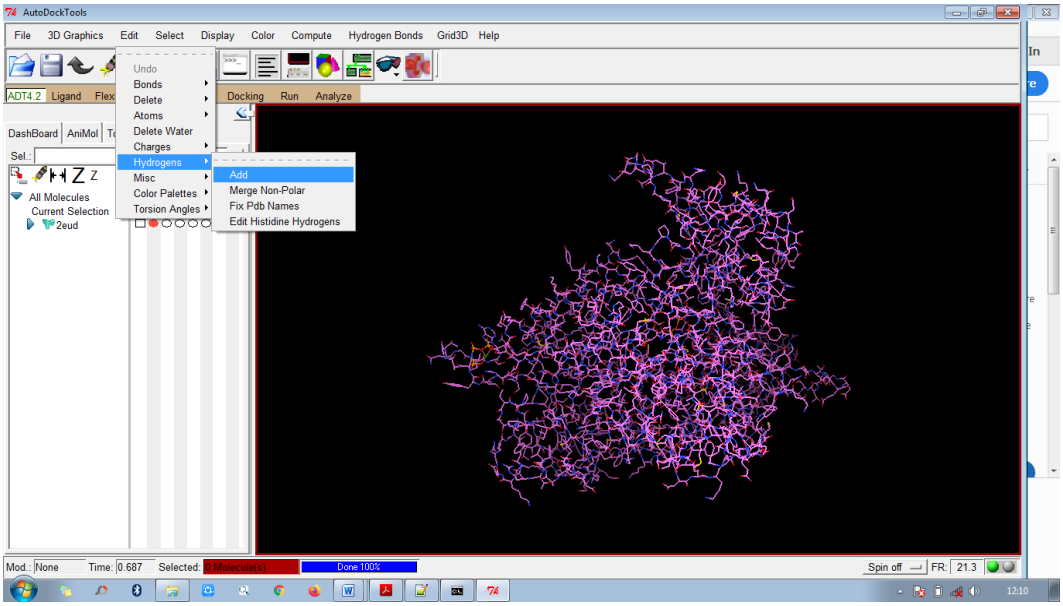
PREPARASI RESEPTOR



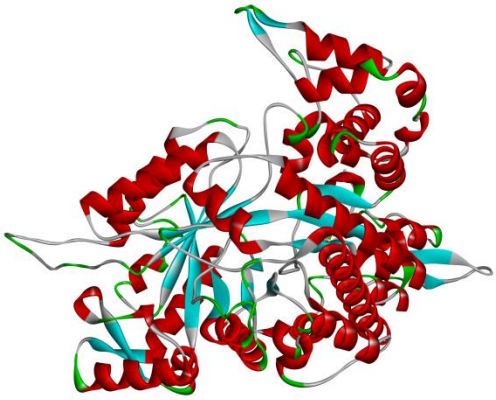
Pengunduhan reeptor 2EUD melalui *website* https://rscb.org/2eud



Proses penghilangan molekul air



Proses penambahan molekul hidrogen



Reseptor 2EUD dalam bentuk 3D dalam berbagai macam posisi

LAMPIRAN X

VALIDASI METODE *DOCKING*

RMSD TABLE

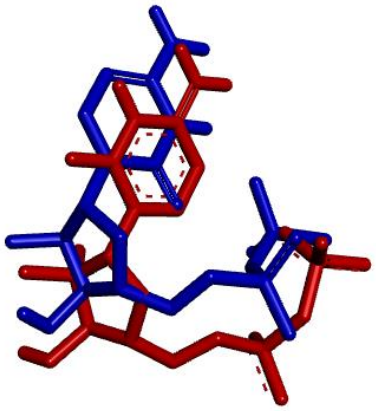
Rank	Sub-Rank	Run	Binding Energy	Cluster RMSD	Reference RMSD	Grep Pattern
1	1	75	-17.62	0.00	1.91	RANKING
1	2	23	-17.49	0.31	1.90	RANKING
1	3	35	-17.48	0.28	1.91	RANKING
1	4	52	-17.48	1.32	1.70	RANKING
1	5	49	-17.46	0.30	1.90	RANKING
1	6	61	-17.43	0.26	1.86	RANKING
1	7	46	-17.42	0.30	1.86	RANKING
1	8	70	-17.41	0.91	1.74	RANKING
1	9	95	-17.38	1.37	1.72	RANKING
1	10	20	-17.36	0.23	1.89	RANKING
1	11	83	-17.36	0.64	1.94	RANKING
1	12	50	-17.33	1.36	1.70	RANKING
1	13	2	-17.32	0.28	1.88	RANKING
1	14	72	-17.32	0.24	1.98	RANKING
1	15	8	-17.31	1.37	1.72	RANKING
1	16	30	-17.29	1.15	1.68	RANKING
1	17	53	-17.26	0.30	1.93	RANKING
1	18	22	-17.25	1.22	1.64	RANKING
1	19	45	-17.22	1.47	1.67	RANKING
1	20	91	-17.21	0.28	1.83	RANKING
1	21	19	-17.18	0.51	1.93	RANKING
1	22	54	-17.17	0.63	1.87	RANKING
1	23	87	-17.16	1.37	1.62	RANKING
1	24	33	-17.12	0.45	1.86	RANKING
1	25	76	-17.09	0.81	1.73	RANKING
1	26	63	-17.09	1.39	1.71	RANKING
1	27	7	-17.09	1.03	1.72	RANKING
1	28	89	-17.03	1.39	1.91	RANKING
1	29	51	-17.03	0.90	1.92	RANKING
1	30	41	-16.99	1.35	1.79	RANKING
1	31	62	-16.95	0.95	1.83	RANKING
1	32	31	-16.94	0.96	1.84	RANKING
1	33	80	-16.94	0.55	1.94	RANKING
1	34	78	-16.93	0.66	1.81	RANKING
1	35	55	-16.93	1.33	1.80	RANKING
1	36	69	-16.88	1.41	1.74	RANKING
1	37	93	-16.83	1.06	1.81	RANKING
1	38	84	-16.82	1.27	1.77	RANKING
1	39	34	-16.82	1.49	1.66	RANKING
1	40	67	-16.78	1.34	1.70	RANKING
1	41	28	-16.76	0.59	1.93	RANKING
1	42	65	-16.74	0.66	1.99	RANKING
1	43	66	-16.73	1.22	1.79	RANKING
1	44	79	-16.73	1.00	1.77	RANKING
1	45	12	-16.73	0.62	1.93	RANKING
1	46	90	-16.72	0.91	1.83	RANKING

1	47	86	-16.71	1.10	1.72	RANKING
1	48	42	-16.66	0.93	1.92	RANKING
1	49	94	-16.58	0.89	1.90	RANKING
1	50	59	-16.54	1.62	2.31	RANKING
1	51	15	-16.45	1.05	1.87	RANKING
1	52	44	-16.45	2.00	2.45	RANKING
1	53	26	-16.40	1.14	1.73	RANKING
1	54	13	-16.36	1.15	1.64	RANKING
1	55	16	-16.33	1.13	1.90	RANKING
1	56	68	-16.29	0.84	2.11	RANKING
1	57	43	-16.20	1.66	2.08	RANKING
1	58	18	-16.20	1.83	2.32	RANKING
1	59	14	-16.09	1.10	1.75	RANKING
1	60	29	-16.07	1.81	2.12	RANKING
1	61	38	-16.02	1.65	2.18	RANKING
1	62	92	-15.95	1.80	2.45	RANKING
1	63	96	-15.89	1.36	2.02	RANKING
1	64	37	-15.83	1.42	1.76	RANKING
1	65	9	-15.60	1.38	1.90	RANKING
1	66	99	-15.50	1.61	2.12	RANKING
1	67	40	-15.49	1.79	2.35	RANKING
1	68	1	-15.49	1.67	1.59	RANKING
1	69	71	-15.07	1.65	1.27	RANKING
2	1	17	-17.08	0.00	3.78	RANKING
2	2	74	-17.04	0.62	3.91	RANKING
2	3	25	-16.78	0.80	3.99	RANKING
2	4	27	-16.74	0.98	3.60	RANKING
2	5	60	-15.79	0.67	3.77	RANKING
3	1	32	-16.56	0.00	4.22	RANKING
3	2	98	-15.86	1.06	4.07	RANKING
4	1	73	-16.54	0.00	4.81	RANKING
4	2	11	-16.53	0.84	4.87	RANKING
4	3	48	-16.45	1.10	4.95	RANKING
4	4	24	-16.36	0.70	4.85	RANKING
4	5	3	-16.32	0.64	4.84	RANKING
4	6	82	-16.26	1.46	5.07	RANKING
4	7	6	-16.22	0.95	5.09	RANKING
4	8	100	-16.19	0.83	4.92	RANKING
4	9	57	-15.97	1.24	4.93	RANKING
4	10	4	-15.51	1.64	4.99	RANKING
4	11	56	-15.45	1.20	4.59	RANKING
4	12	39	-14.67	1.53	4.76	RANKING
5	1	58	-16.44	0.00	3.90	RANKING
5	2	5	-16.12	0.22	3.92	RANKING
6	1	88	-16.37	0.00	2.43	RANKING
6	2	10	-16.16	0.44	2.33	RANKING
6	3	21	-15.93	0.88	2.37	RANKING
7	1	77	-16.36	0.00	4.16	RANKING
7	2	47	-15.51	0.70	4.00	RANKING
8	1	97	-16.16	0.00	3.03	RANKING
9	1	36	-15.48	0.00	3.75	RANKING
10	1	81	-15.46	0.00	3.63	RANKING
11	1	85	-15.31	0.00	2.03	RANKING
12	1	64	-14.66	0.00	5.82	RANKING

Perolehan nilai *Binding affinity* dan RMSD (*Root Mean SquareDeviation*) Ligan Alami

```
Keeping original residue number (specified in the input PDBQ file) for outputting.

MODEL       75
USER    Run = 75
USER    Cluster Rank = 1
USER    Number of conformations in this cluster = 69
USER
USER    RMSD from reference structure       = 1.912 A
USER
USER    Estimated Free Energy of Binding    =  -17.62 kcal/mol  [=(1)+(2)+(3)-(4)]
USER    Estimated Inhibition Constant, Ki   =  121.78 fM (femtomolar)  [Temperature = 298.15 K]
USER
USER    (1) Final Intermolecular Energy     =  -19.71 kcal/mol
USER        vdW + Hbond + desolv Energy     =  -16.55 kcal/mol
USER        Electrostatic Energy            =   -3.15 kcal/mol
USER    (2) Final Total Internal Energy     =   -0.35 kcal/mol
USER    (3) Torsional Free Energy           =   +2.09 kcal/mol
USER    (4) Unbound System's Energy  [=(2)] =   -0.35 kcal/mol
```

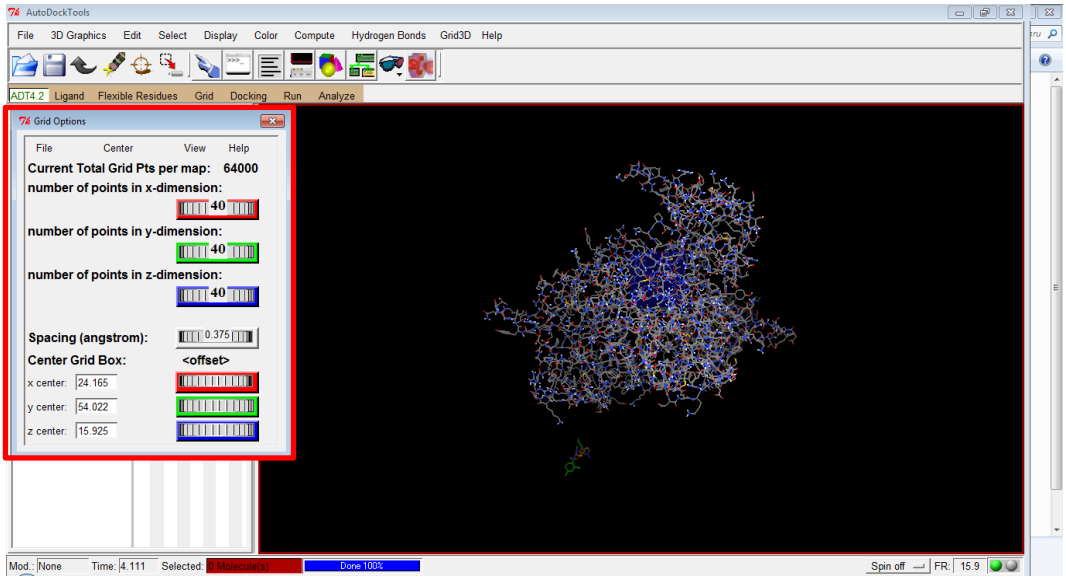
Perolehan nilai *Konstanta inhibition* (Ki) Ligan Alami

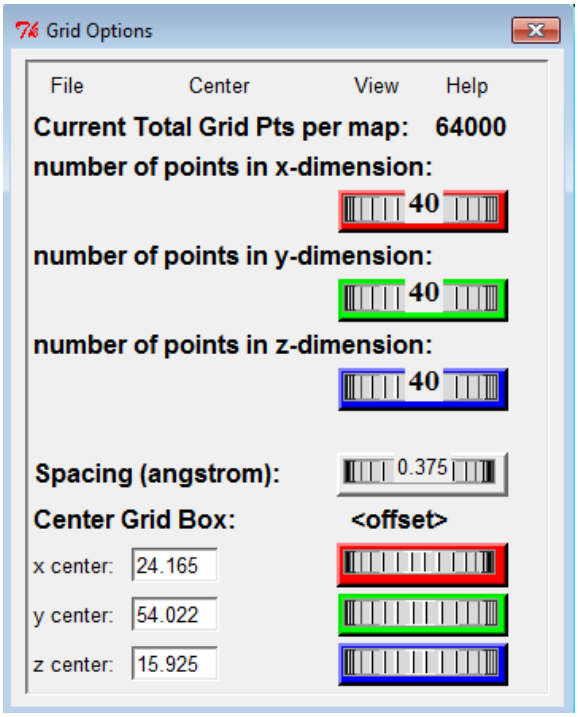


Ligan Alami (Merah), dan Ligan Hasil Docking (Biru)

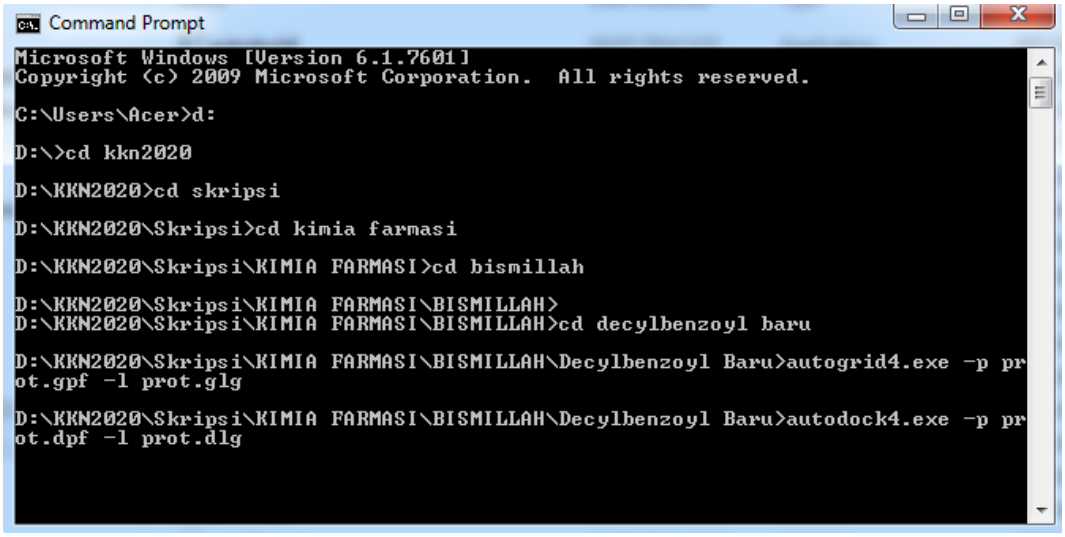
LAMPIRAN XI

DOCKING LIGAN UJI TERHADAP RESEPTOR TARGET





Pengaturan *grid box center* untuk proses *docking*



Proses *docking* melalui *Command Prompt*

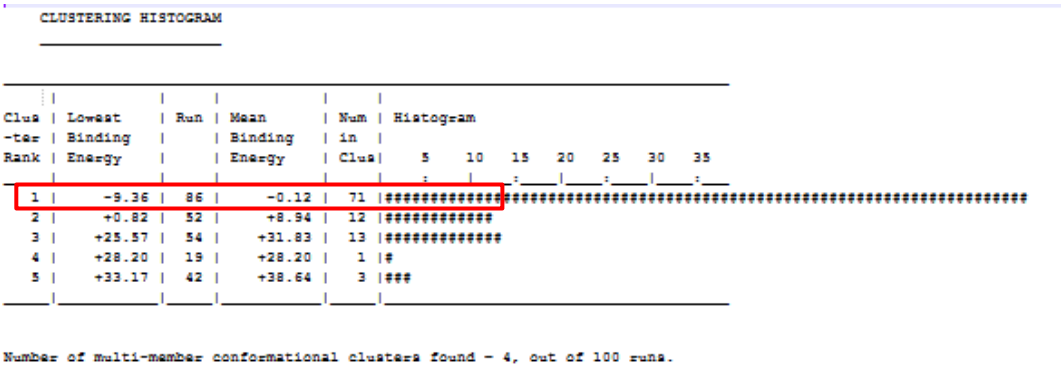
CLUSTERING HISTOGRAM

Clus-ter Rank	Lowest Binding Energy	Run	Mean Binding Energy	Num in Clus	Histogram 5 10 15 20 25 30 35
1	-11.36	90	-10.07	51	##
2	-10.42	20	-9.11	11	###########
3	-10.10	16	-9.10	8	########
4	-9.87	99	-9.11	6	######
5	-9.59	48	-8.52	11	###########
6	-9.53	69	-9.02	5	#####
7	-9.49	6	-9.46	4	####
8	-9.43	57	-9.00	2	##
9	-8.41	84	-8.04	2	##

Perolehan nilai *Binding affinity* senyawa *1,4-Decylbenzoyl-3-methylthiourea*

```
Keeping original residue number (specified in the input PDBQ file) for outputting.

MODEL        90
USER    Run = 90
USER    Cluster Rank = 1
USER    Number of conformations in this cluster = 51
USER
USER    RMSD from reference structure       = 55.419 A
USER
USER    Estimated Free Energy of Binding    =  -11.36 kcal/mol  [=(1)+(2)+(3)-(4)]
USER    Estimated Inhibition Constant, Ki   =    4.69 nM (nanomolar)  [Temperature = 298.15 K]
USER
USER    (1) Final Intermolecular Energy     =  -14.94 kcal/mol
USER        vdW + Hbond + desolv Energy     =  -14.95 kcal/mol
USER        Electrostatic Energy            =   +0.01 kcal/mol
USER    (2) Final Total Internal Energy     =   -1.54 kcal/mol
USER    (3) Torsional Free Energy           =   +3.58 kcal/mol
USER    (4) Unbound System's Energy  [=(2)] =   -1.54 kcal/mol
```

Perolehan nilai *Konstanta inhibition* (Ki) senyawa *1,4-Decylbenzoyl-3-methylthiourea*

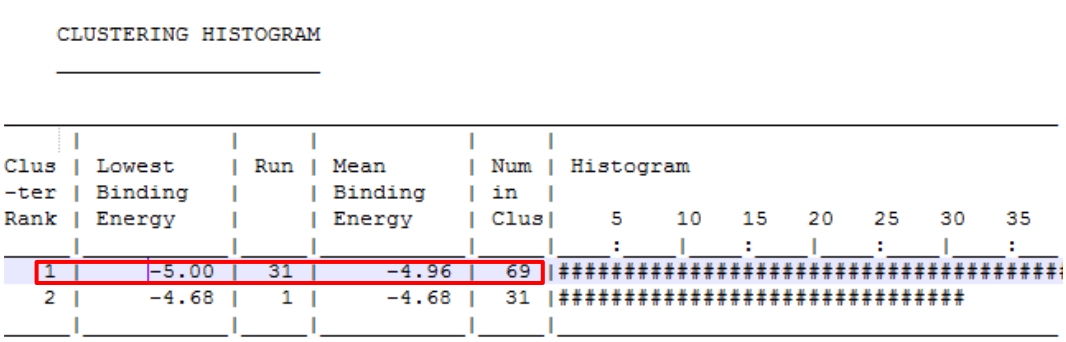


```
    CLUSTERING HISTOGRAM
    ____________________

_____|____________|_____|____________|_____|________________________________________
     |            |     |            |     |
Clus | Lowest     | Run | Mean       | Num | Histogram
-ter | Binding    |     | Binding    | in  |
Rank | Energy     |     | Energy     | Clus|    5    10   15   20   25   30   35
_____|____________|_____|____________|_____|____:____|____:____|____:____|____:___
   1 |     -9.36 |  86 |     -0.12 |  71 |##############################################################################
   2 |     +0.82 |  52 |     +8.94 |  12 |#############
   3 |    +25.57 |  54 |    +31.83 |  13 |##############
   4 |    +28.20 |  19 |    +28.20 |   1 |#
   5 |    +33.17 |  42 |    +38.64 |   3 |###
_____|____________|_____|____________|_____|________________________________________

Number of multi-member conformational clusters found = 4, out of 100 runs.
```

Perolehan nilai *Binding affinity* senyawa Kompleks *Bis-(1-4-decylbenzoyl)-3-methylthiourea) Cobalt (III)*

```
Keeping original residue number (specified in the input PDBQ file) for outputting.

MODEL       86
USER    Run = 86
USER    Cluster Rank = 1
USER    Number of conformations in this cluster = 71
USER
USER    RMSD from reference structure       = 48.298 A
USER
USER    Estimated Free Energy of Binding    =   -9.36 kcal/mol  [=(1)+(2)+(3)-(4)]
USER    Estimated Inhibition Constant, Ki   =  136.66 nM (nanomolar)  [Temperature = 298.15 K]
USER
USER    (1) Final Intermolecular Energy     =  -14.30 kcal/mol
USER        vdW + Hbond + desolv Energy     =  -14.24 kcal/mol
USER        Electrostatic Energy            =   -0.07 kcal/mol
USER    (2) Final Total Internal Energy     =   +1.98 kcal/mol
USER    (3) Torsional Free Energy           =   +4.94 kcal/mol
USER    (4) Unbound System's Energy  [=(2)] =   +1.98 kcal/mol
```

Perolehan nilai *Konstanta inhibition* (Ki) senyawa Kompleks *Bis-(1-4-decylbenzoyl)-3-methylthiourea) Cobalt (III)*



```
    CLUSTERING HISTOGRAM
    ____________________

_____|____________|_____|____________|_____|________________________________________
     |            |     |            |     |
Clus | Lowest     | Run | Mean       | Num | Histogram
-ter | Binding    |     | Binding    | in  |
Rank | Energy     |     | Energy     | Clus|    5    10   15   20   25   30   35
_____|____________|_____|____________|_____|____:____|____:____|____:____|____:___
   1 |     -5.00 |  31 |     -4.96 |  69 |#########################################
   2 |     -4.68 |   1 |     -4.68 |  31 |################################
_____|____________|_____|____________|_____|________________________________________
```

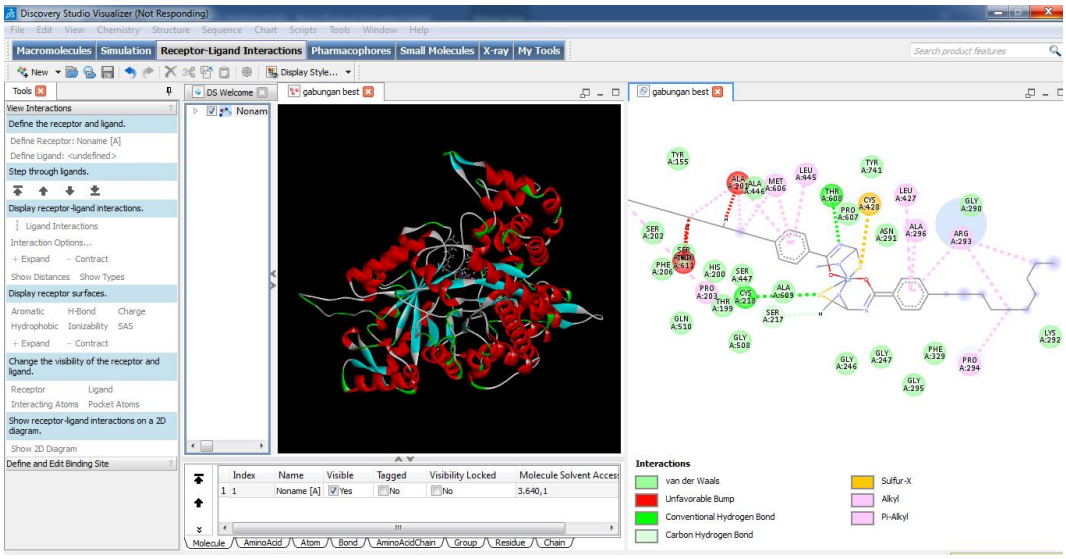
Perolehan nilai *Binding affinity* senyawa *Hydroxyurea*

```
Keeping original residue number (specified in the input PDBQ file) for outputting.

MODEL        31
USER    Run = 31
USER    Cluster Rank = 1
USER    Number of conformations in this cluster = 69
USER
USER    RMSD from reference structure       = 61.628 A
USER
USER    Estimated Free Energy of Binding    =   -5.00 kcal/mol  [=(1)+(2)+(3)-(4)]
USER    Estimated Inhibition Constant, Ki   =  215.61 uM (micromolar)  [Temperature = 298.15 K]
USER
USER    (1) Final Intermolecular Energy     =   -5.30 kcal/mol
USER        vdW + Hbond + desolv Energy     =   -5.27 kcal/mol
USER        Electrostatic Energy            =   -0.03 kcal/mol
USER    (2) Final Total Internal Energy     =   -0.66 kcal/mol
USER    (3) Torsional Free Energy           =   +0.30 kcal/mol
USER    (4) Unbound System's Energy  [=(2)] =   -0.66 kcal/mol
```

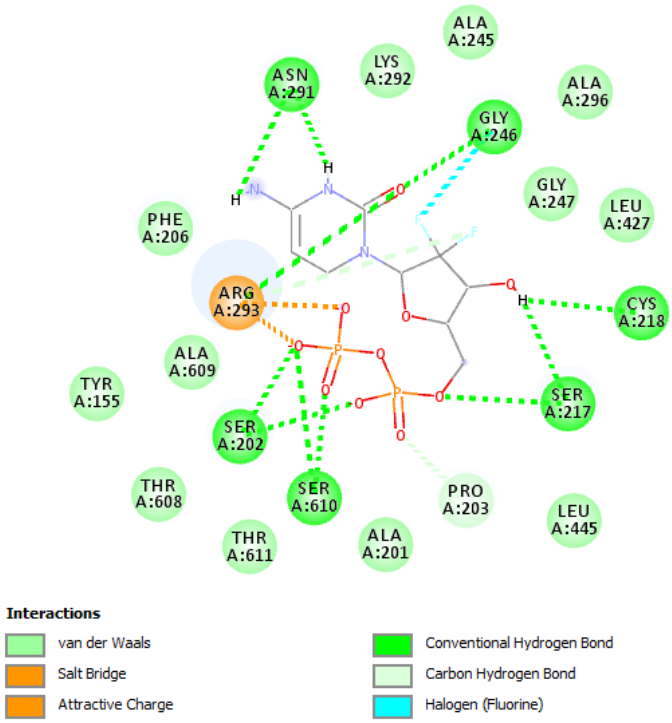
Perolehan nilai *Konstanta inhibition* (Ki) senyawa *Hydroxyurea*

LAMPIRAN XII

VISUALISASI HASIL *DOCKING*

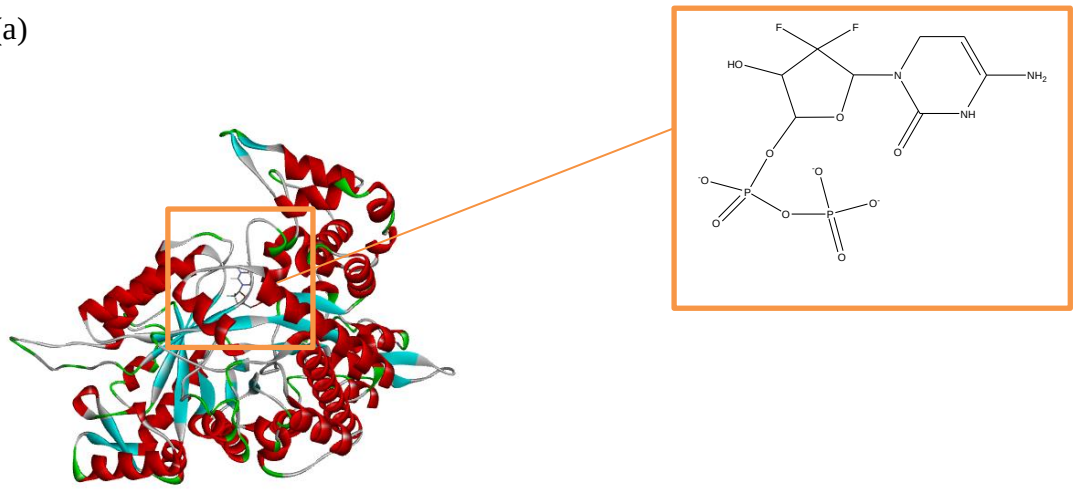


Visualisasi 2D dan 3D hasil *docking* senyawa kompleks menggunakan *discovery studio visualizer*

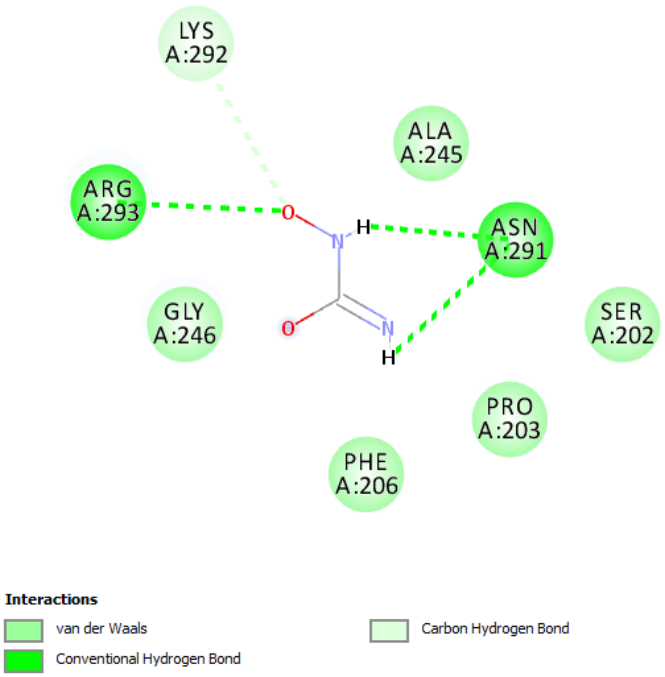


Hasil Visualisasi 2D Ligan Alami

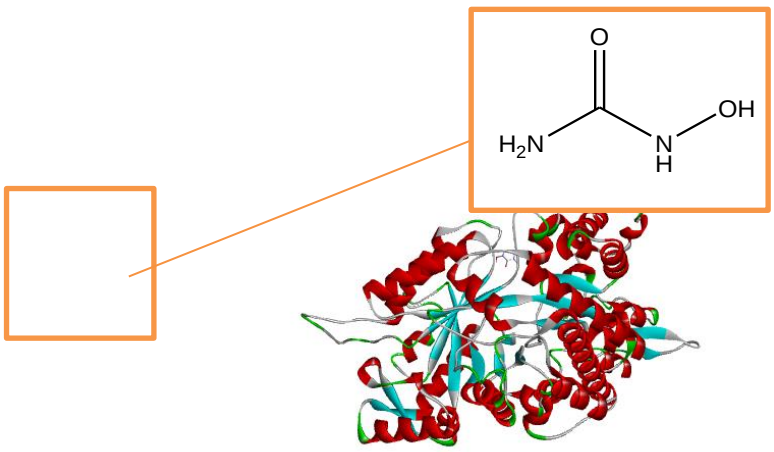
(a)



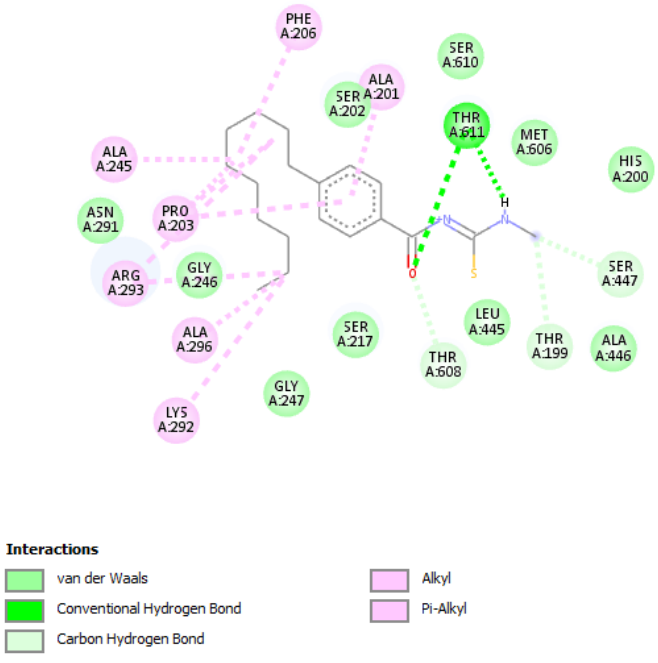
Hasil Visualisasi 3D Ligan Alami



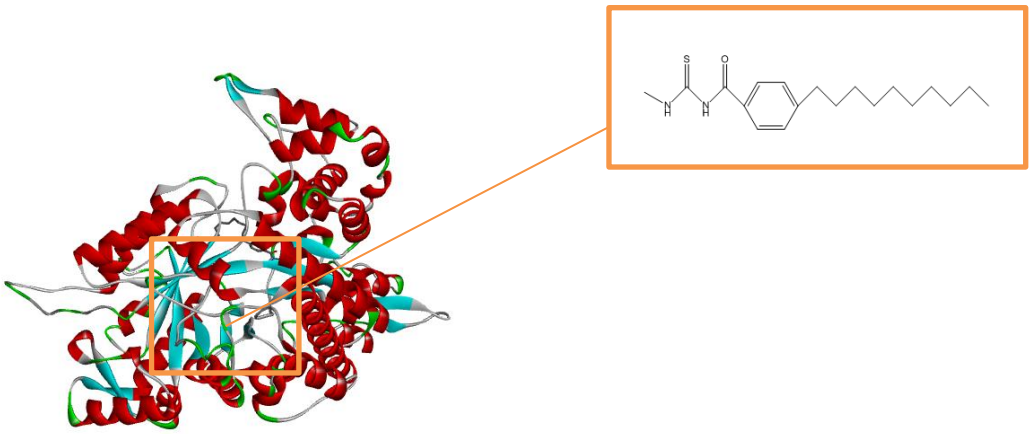
Hasil Visualisasi 2D *Hydroxyurea*



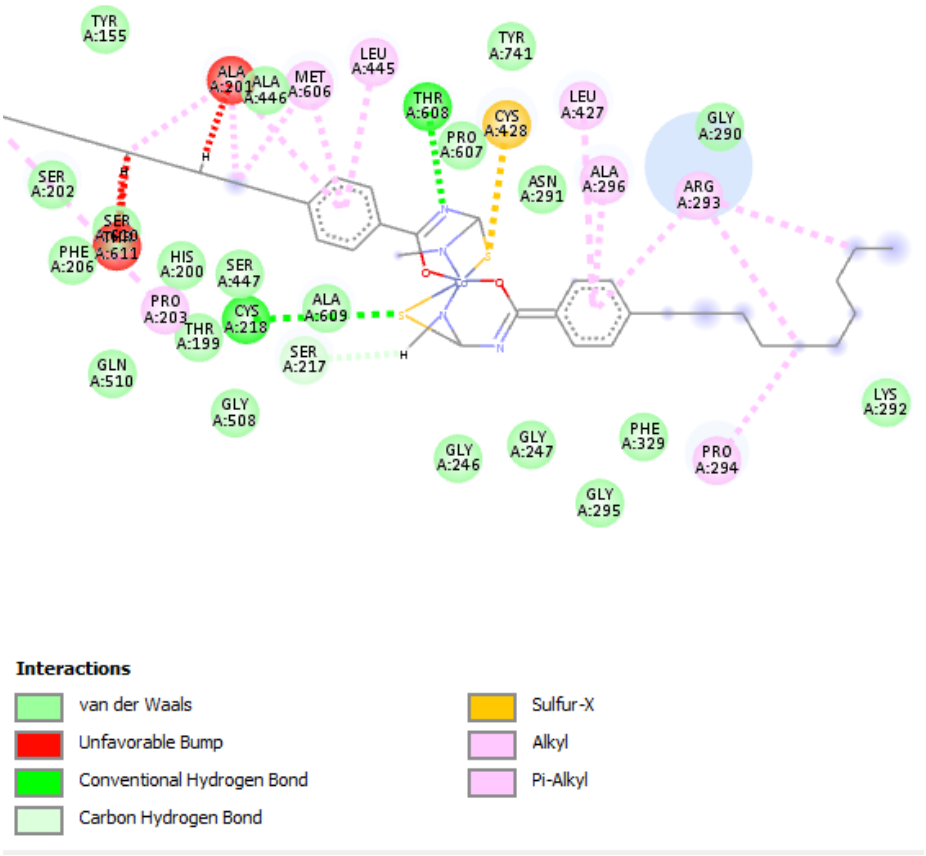
Hasil Visualisasi 3D *Hydroxyurea*



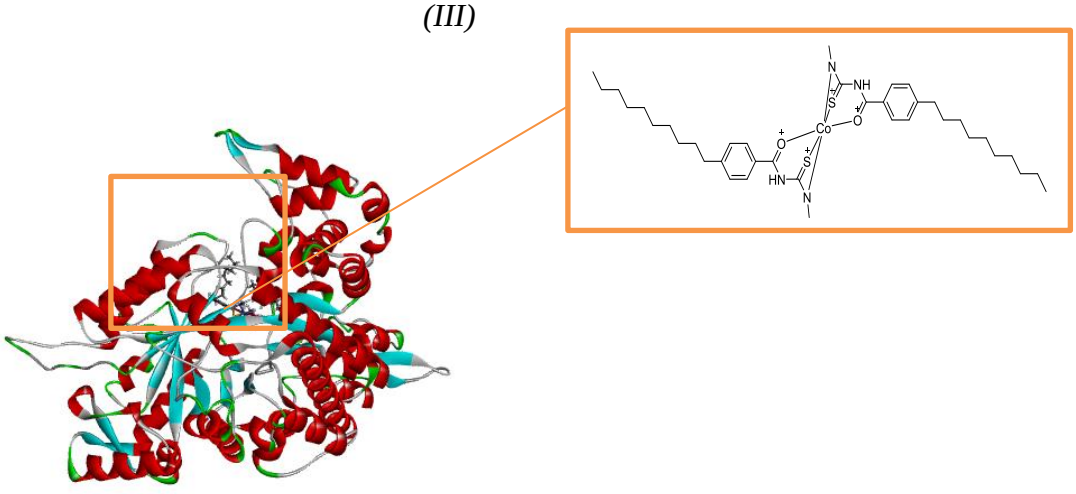
Hasil Visualisasi 2D Senyawa *1,4-Decylbenzoyl-3-methylthiourea*



Hasil Visualisasi 3D Senyawa *1,4-Decylbenzoyl-3-methylthiourea*



Hasil Visualisasi 2D Kompleks *Bis-(1-4-decylbenzoyl)-3-methylthiourea) Cobalt (III)*



Hasil Visualisasi 3D Kompleks *Bis-(1-4-decylbenzoyl)-3-methylthiourea) Cobalt (II*

LAMPIRAN XIII

PREDIKSI ADME DAN TOKSISITAS

1. *Hydroxyurea*

   a. preADMET

ADME

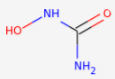
ID	Value
BBB	0.156784
Buffer_solubility_mg_L	1645.27
Caco2	2.3587
CYP_2C19_inhibition	Inhibitor
CYP_2C9_inhibition	Non
CYP_2D6_inhibition	Inhibitor
CYP_2D6_substrate	Weakly
CYP_3A4_inhibition	Non
CYP_3A4_substrate	Non
HIA	61.074276
MDCK	293.367
Pgp_inhibition	Non
Plasma_Protein_Binding	4.835029
Pure_water_solubility_mg_L	151115
Skin_Permeability	-3.88489
SKlogD_value	-1.570750
SKlogP_value	-1.570750
SKlogS_buffer	-1.664890
SKlogS_pure	0.298180

Toksisitas

ID	Value
algae_at	0.446487
Ames_test	mutagen
Carcino_Mouse	negative
Carcino_Rat	positive
daphnia_at	5.40892
hERG_inhibition	low_risk
medaka_at	28.0847
minnow_at	11.0734
TA100_10RLI	negative
TA100_NA	negative
TA1535_10RLI	positive
TA1535_NA	negative

   b. *pkCSM*

Molecule Depiction



SMILES

Molecule properties:

Descriptor	Value
Molecular Weight	76.055
LogP	-0.9561
#Rotatable Bonds	0
#Acceptors	2
#Donors	3
Surface Area	28.539

Property	Model Name	Predicted Value	Unit
Absorption	Water solubility	0.726	Numeric (log mol/L)
Absorption	Caco2 permeability	0.519	Numeric (log Papp in 10^{-8} cm/s)
Absorption	Intestinal absorption (human)	73.467	Numeric (% Absorbed)
Absorption	Skin Permeability	-4.294	Numeric (log Kp)
Absorption	P-glycoprotein substrate	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein I inhibitor	No	Categorical (Yes/No)
Absorption	P-glycoprotein II inhibitor	No	Categorical (Yes/No)
Distribution	VDss (human)	-0.448	Numeric (log L/kg)
Distribution	Fraction unbound (human)	0.852	Numeric (Fu)
Distribution	BBB permeability	-0.604	Numeric (log BB)
Distribution	CNS permeability	-3.139	Numeric (log PS)
Metabolism	CYP2D6 substrate	No	Categorical (Yes/No)
Metabolism	CYP3A4 substrate	No	Categorical (Yes/No)
Metabolism	CYP1A2 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2C19 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2C9 inhibitior	No	Categorical (Yes/No)

Metabolism	CYP2D6 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP3A4 inhibitior	No	Categorical (Yes/No)
Excretion	Total Clearance	0.655	Numeric (log ml/min/kg)
Excretion	Renal OCT2 substrate	No	Categorical (Yes/No)
Toxicity	AMES toxicity	No	Categorical (Yes/No)
Toxicity	Max. tolerated dose (human)	1.706	Numeric (log mg/kg/day)
Toxicity	hERG I inhibitor	No	Categorical (Yes/No)
Toxicity	hERG II inhibitor	No	Categorical (Yes/No)
Toxicity	Oral Rat Acute Toxicity (LD50)	2.369	Numeric (mol/kg)
Toxicity	Oral Rat Chronic Toxicity (LOAEL)	2.747	Numeric (log mg/kg_bw/day)
Toxicity	Hepatotoxicity	No	Categorical (Yes/No)
Toxicity	Skin Sensitisation	No	Categorical (Yes/No)
Toxicity	*T.Pyriformis* toxicity	-1.246	Numeric (log ug/L)
Toxicity	Minnow toxicity	3.736	Numeric (log mM)

2. *1,4-Decylbenzoyl-3-methylthiourea*
    a. preADMET

ADME

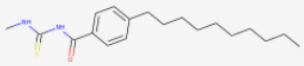
ID	Value
BBB	9.10756**
Buffer_solubility_mg_L	1.30698e-009**
Caco2	20.4488**
CYP_2C19_inhibition	Non
CYP_2C9_inhibition	Non
CYP_2D6_inhibition	Non
CYP_2D6_substrate	Weakly
CYP_3A4_inhibition	Inhibitor
CYP_3A4_substrate	Substrate
HIA	98.412437**
MDCK	0.0511585**
Pgp_inhibition	Inhibitor
Plasma_Protein_Binding	90.313805**
Pure_water_solubility_mg_L	21659.6**
Skin_Permeability	-4.15248**
SKlogD_value	5.438620**
SKlogP_value	5.438620**
SKlogS_buffer	-14.744640**
SKlogS_pure	-1.525260**

Toksisitas

ID	Value
algae_at	3.82325e-005**
Ames_test	mutagen
Carcino_Mouse	out of range
Carcino_Rat	out of range
daphnia_at	1.07869e-005**
hERG_inhibition	medium_risk
medaka_at	7.14948e-010**
minnow_at	3.21883e-009**
TA100_10RLI	negative
TA100_NA	negative
TA1535_10RLI	negative
TA1535_NA	positive

b. pkCSM

Molecule Depiction



SMILES

Molecule properties:

Descriptor	Value
Molecular Weight	334.529
LogP	4.6039
#Rotatable Bonds	10
#Acceptors	2
#Donors	2
Surface Area	145.796

Property	Model Name	Predicted Value	Unit
Absorption	Water solubility	-5.572	Numeric (log mol/L)
Absorption	Caco2 permeability	1.51	Numeric (log Papp in 10^{-6} cm/s)
Absorption	Intestinal absorption (human)	89.945	Numeric (% Absorbed)
Absorption	Skin Permeability	-2.74	Numeric (log Kp)
Absorption	P-glycoprotein substrate	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein I inhibitor	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein II inhibitor	No	Categorical (Yes/No)
Distribution	VDss (human)	0.379	Numeric (log L/kg)
Distribution	Fraction unbound (human)	0.012	Numeric (Fu)
Distribution	BBB permeability	-0.19	Numeric (log BB)
Distribution	CNS permeability	-0.946	Numeric (log PS)
Metabolism	CYP2D6 substrate	No	Categorical (Yes/No)
Metabolism	CYP3A4 substrate	Yes	Categorical (Yes/No)
Metabolism	CYP1A2 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2C19 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2C9 inhibitior	Yes	Categorical (Yes/No)
Metabolism	CYP2D6 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP3A4 inhibitior	Yes	Categorical (Yes/No)
Excretion	Total Clearance	-0.031	Numeric (log ml/min/kg)
Excretion	Renal OCT2 substrate	No	Categorical (Yes/No)
Toxicity	AMES toxicity	No	Categorical (Yes/No)
Toxicity	Max. tolerated dose (human)	-0.148	Numeric (log mg/kg/day)
Toxicity	hERG I inhibitor	No	Categorical (Yes/No)
Toxicity	hERG II inhibitor	Yes	Categorical (Yes/No)
Toxicity	Oral Rat Acute Toxicity (LD50)	3.029	Numeric (mol/kg)
Toxicity	Oral Rat Chronic Toxicity (LOAEL)	0.828	Numeric (log mg/kg_bw/day)
Toxicity	Hepatotoxicity	Yes	Categorical (Yes/No)
Toxicity	Skin Sensitisation	Yes	Categorical (Yes/No)
Toxicity	*T.Pyriformis* toxicity	1.941	Numeric (log ug/L)
Toxicity	Minnow toxicity	1.375	Numeric (log mM)

3. *Bis-(1-4-decylbenzoyl)-3-methylthiourea) Cobalt (III)*
   a. preADMET

ADME

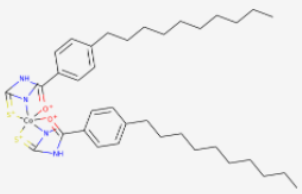
ID	Value
BBB	7.48782
Buffer_solubility_mg_L	2.6347
Caco2	45.3267
CYP_2C19_inhibition	Non
CYP_2C9_inhibition	Non
CYP_2D6_inhibition	Non
CYP_2D6_substrate	Non
CYP_3A4_inhibition	Non
CYP_3A4_substrate	Non
HIA	94.886836
MDCK	21.4449*
Pgp_inhibition	Inhibitor
Plasma_Protein_Binding	100.000000
Pure_water_solubility_mg_L	0.202461
Skin_Permeability	-1.04686
SKlogD_value	5.975280
SKlogP_value	5.975280
SKlogS_buffer	-5.103690
SKlogS_pure	-6.218080

Toksisitas

ID	Value
algae_at	0.00210918
Ames_test	mutagen
Carcino_Mouse	negative
Carcino_Rat	negative
daphnia_at	0.00307948
hERG_inhibition	medium_risk
medaka_at	2.25435e-005
minnow_at	1.61255e-005
TA100_10RLI	negative
TA100_NA	positive
TA1535_10RLI	negative
TA1535_NA	negative

b. *pkCSM*

Molecule Depiction



SMILES

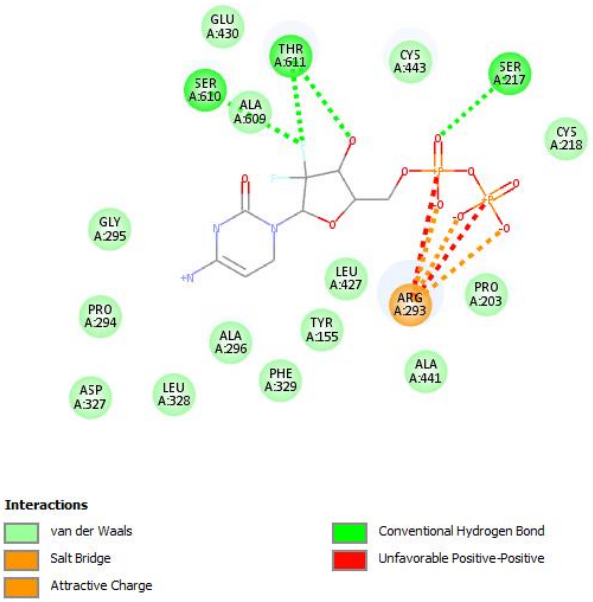
Molecule properties:

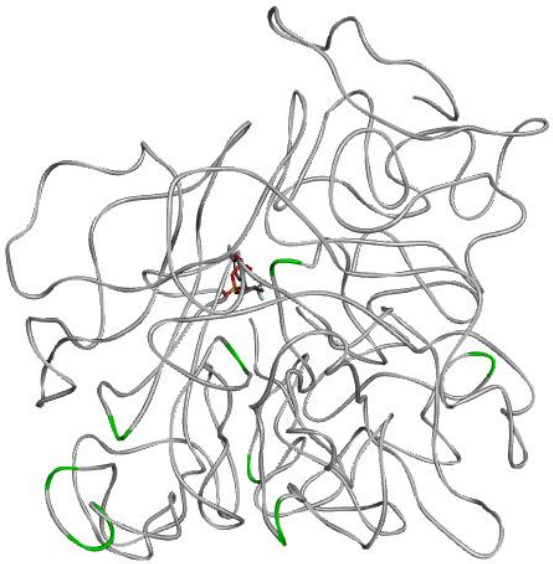
Descriptor	Value
Molecular Weight	725.975
LogP	8.2575
#Rotatable Bonds	20
#Acceptors	4
#Donors	2
Surface Area	289.115

Property	Model Name	Predicted Value	Unit
Absorption	Water solubility	-3.758	Numeric (log mol/L)
Absorption	Caco2 permeability	0.874	Numeric (log Papp in 10^{-6} cm/s)
Absorption	Intestinal absorption (human)	88.719	Numeric (% Absorbed)
Absorption	Skin Permeability	-2.736	Numeric (log Kp)
Absorption	P-glycoprotein substrate	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein I inhibitor	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein II inhibitor	Yes	Categorical (Yes/No)
Distribution	VDss (human)	0.187	Numeric (log L/kg)
Distribution	Fraction unbound (human)	0.144	Numeric (Fu)
Distribution	BBB permeability	-0.779	Numeric (log BB)
Distribution	CNS permeability	-2.488	Numeric (log PS)
Metabolism	CYP2D6 substrate	Yes	Categorical (Yes/No)
Metabolism	CYP3A4 substrate	Yes	Categorical (Yes/No)
Metabolism	CYP1A2 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2C19 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2C9 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP2D6 inhibitior	No	Categorical (Yes/No)
Metabolism	CYP3A4 inhibitior	No	Categorical (Yes/No)
Excretion	Total Clearance	0.353	Numeric (log ml/min/kg)
Excretion	Renal OCT2 substrate	No	Categorical (Yes/No)
Toxicity	AMES toxicity	No	Categorical (Yes/No)
Toxicity	Max. tolerated dose (human)	0.079	Numeric (log mg/kg/day)
Toxicity	hERG I inhibitor	No	Categorical (Yes/No)
Toxicity	hERG II inhibitor	Yes	Categorical (Yes/No)
Toxicity	Oral Rat Acute Toxicity (LD50)	3.069	Numeric (mol/kg)
Toxicity	Oral Rat Chronic Toxicity (LOAEL)	1.537	Numeric (log mg/kg_bw/day)
Toxicity	Hepatotoxicity	No	Categorical (Yes/No)
Toxicity	Skin Sensitisation	No	Categorical (Yes/No)
Toxicity	*T.Pyriformis* toxicity	0.285	Numeric (log ug/L)
Toxicity	Minnow toxicity	-0.993	Numeric (log mM)

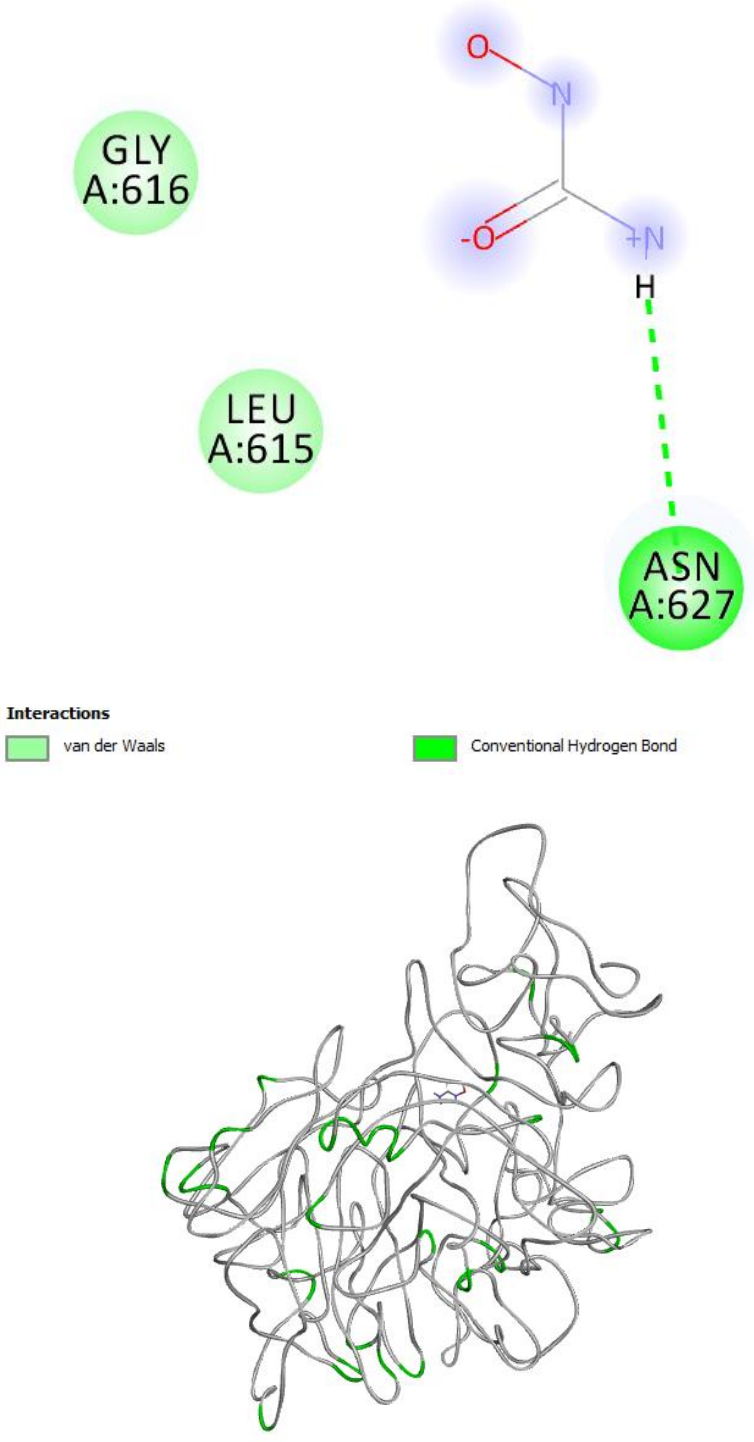
LAMPIRAN XIV

MOLECULAR DYNAMICS



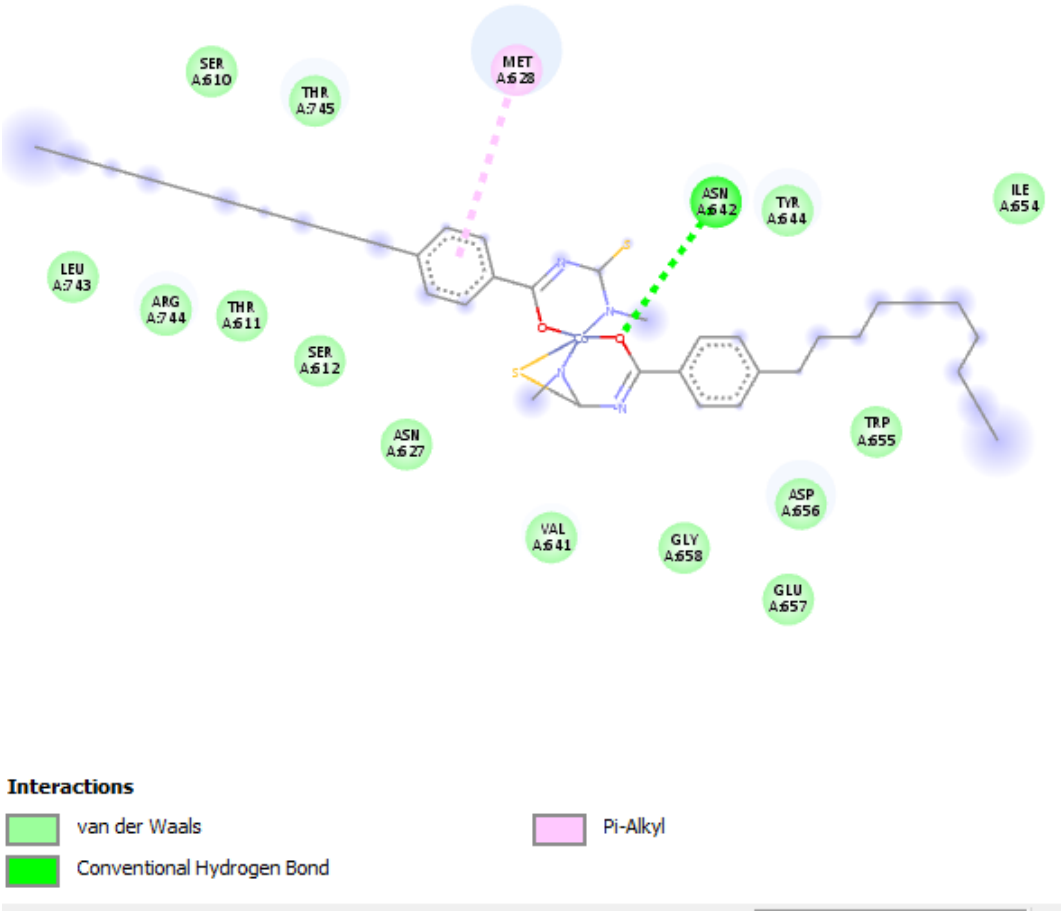


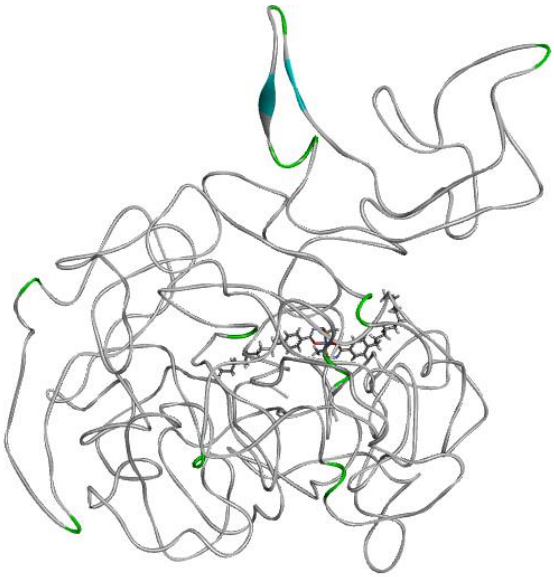
Hasil Visualisasi Molecular Dynamic 2D dan 3D Ligan Alami



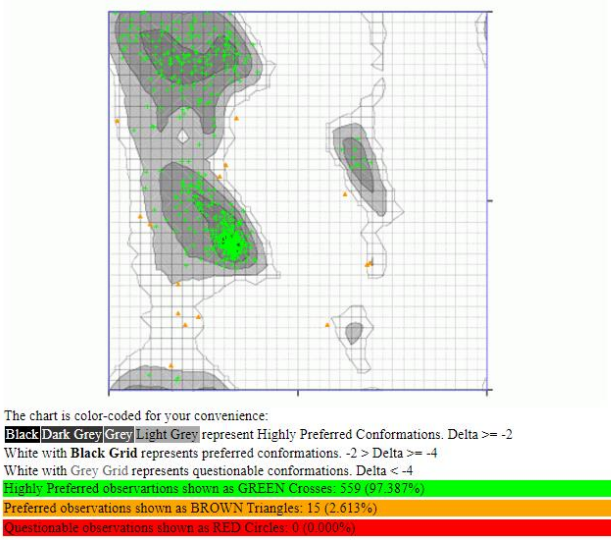
Hasil Visualisasi Molecular Dynamic 2D dan 3D *Hydroxyurea*

Hasil Visualisasi Molecular Dynamic 2D dan 3D Senyawa *1-4-decylbenzoyl-3-methylthiourea*

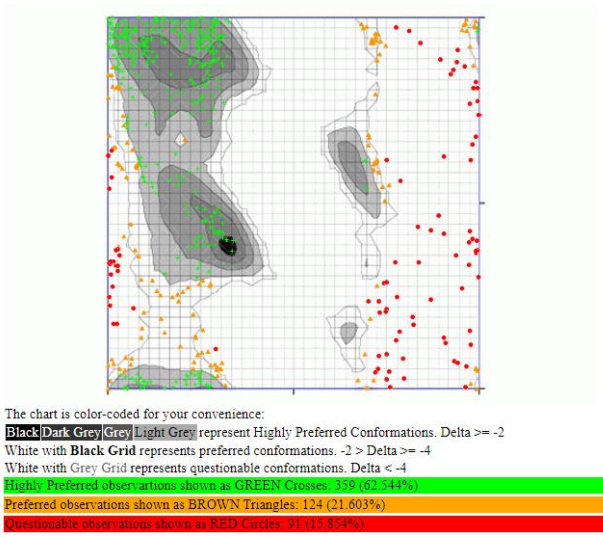




Hasil Visualisasi Molecular Dynamic 2D dan 3D Senyawa Kompleks *Bis-(1-4-decylbenzoyl)-3-methylthiourea) Cobalt (III)*



Plot Ramachandran Kompleks *Bis-(1-4-decylbenzoyl)-3-methylthiourea) Cobalt (III)* Sebelum Simulasi *Molecular Dynamics*



Plot Ramachandran Kompleks *Bis-(1-4-decylbenzoyl)-3-methylthiourea) Cobalt (III)* Setelah Simulasi *Molecular Dynamics*