Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.

Supporting Information

Ligand	*RMSd (Å)*
PHT	0.08 ± 0.02
MLI	0.66 ± 0.31
THI	1.46 ± 0.22
FES-1	0.25 ± 0.09
FES-2	0.48 ± 0.20
FAD	0.69 ± 0.14

Table SI 1. Mean RMSd values obtained obtained for each ligand from the 10 ns until the end of the MD simulation. The calulations of these RMSd values were conducted to help to verify if the adapted force field parameters for each did not lead to any aberrant behaviour. The small RMSd values obtained in addition to visual analysis of the behaviour of the each ligand during the simulations further strengthens our confidence on the adopted parameters. THI is the ligand that exhibited the highest mean value which can be attributed to the fact that it is located at the surface of the enzyme hence, its movement is not as constrained by the enzyme environment as much as for the other ligands. Nonetheless, all ligands maintained a coherent structure throughout all the simulations conducted in the present work.

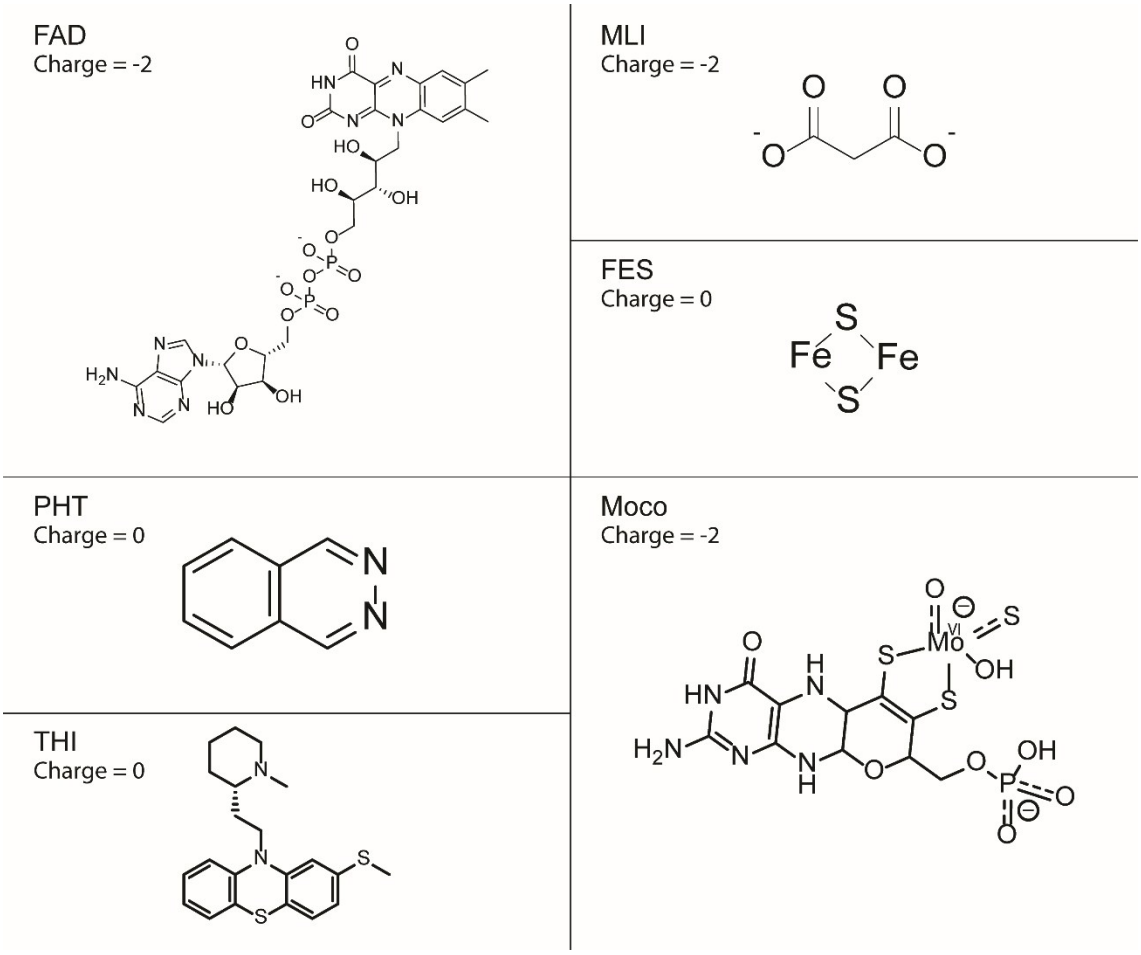

Figure SI 1. 2D representations of all ligands of the hAOX that are present in the x-ray structure with the pdb code: 4UHX whose impact on the structure of the enzyme hAOX was studied. The formal charge of each ligand is indicated in the figure. In the Moco representation, the negative charges are indicated between the oxygen and sulphur ligands of the Mo ion and between the two oxygen atoms of the phosphate group since, in the atomic point charges calculation, we observed that the negative charge is evenly distributed between those atoms and not concentrated in one in specific as it is usually represented. FAD = Flavine-Adenine Dinucleotide; PHT = Phthalazine; THI = Thioridazine; MLI = Malonate ion; FES = Iron-Sulphur cluster; Moco = Molybdenum cofactor.

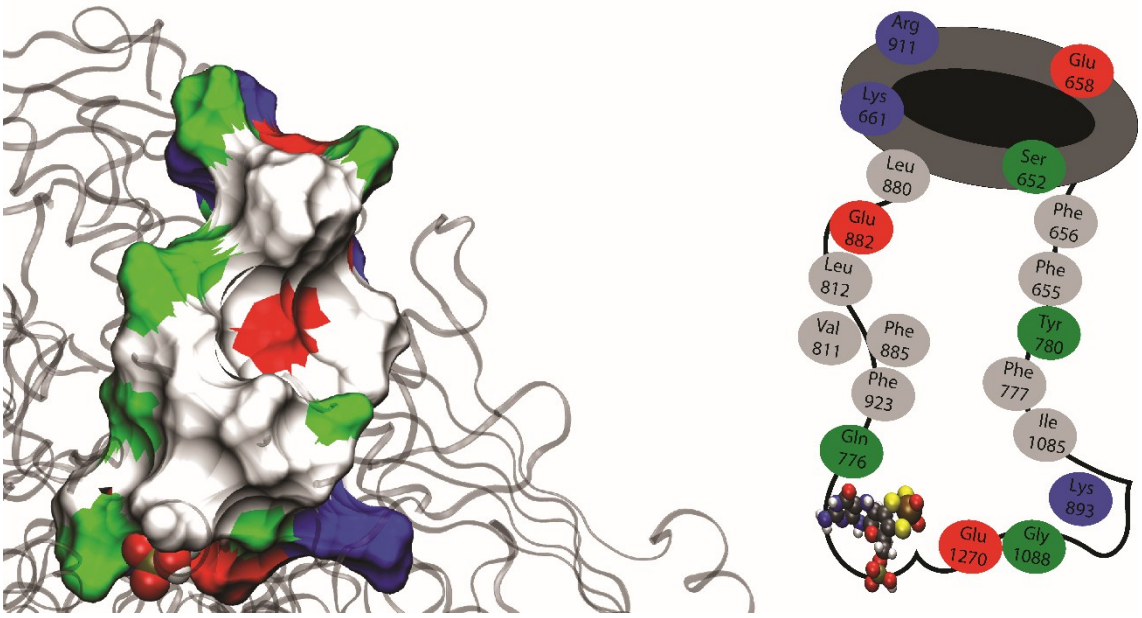

Figure SI 2. 3D representation of the catalytic tunnel of the hAOX and the main residues that compose its walls. The residues are coloured according to their type. Blue for positively charged, red for negatively charged, green for polar and gray for nonpolar residues. The Moco is also represented for easier interpretation of the image.

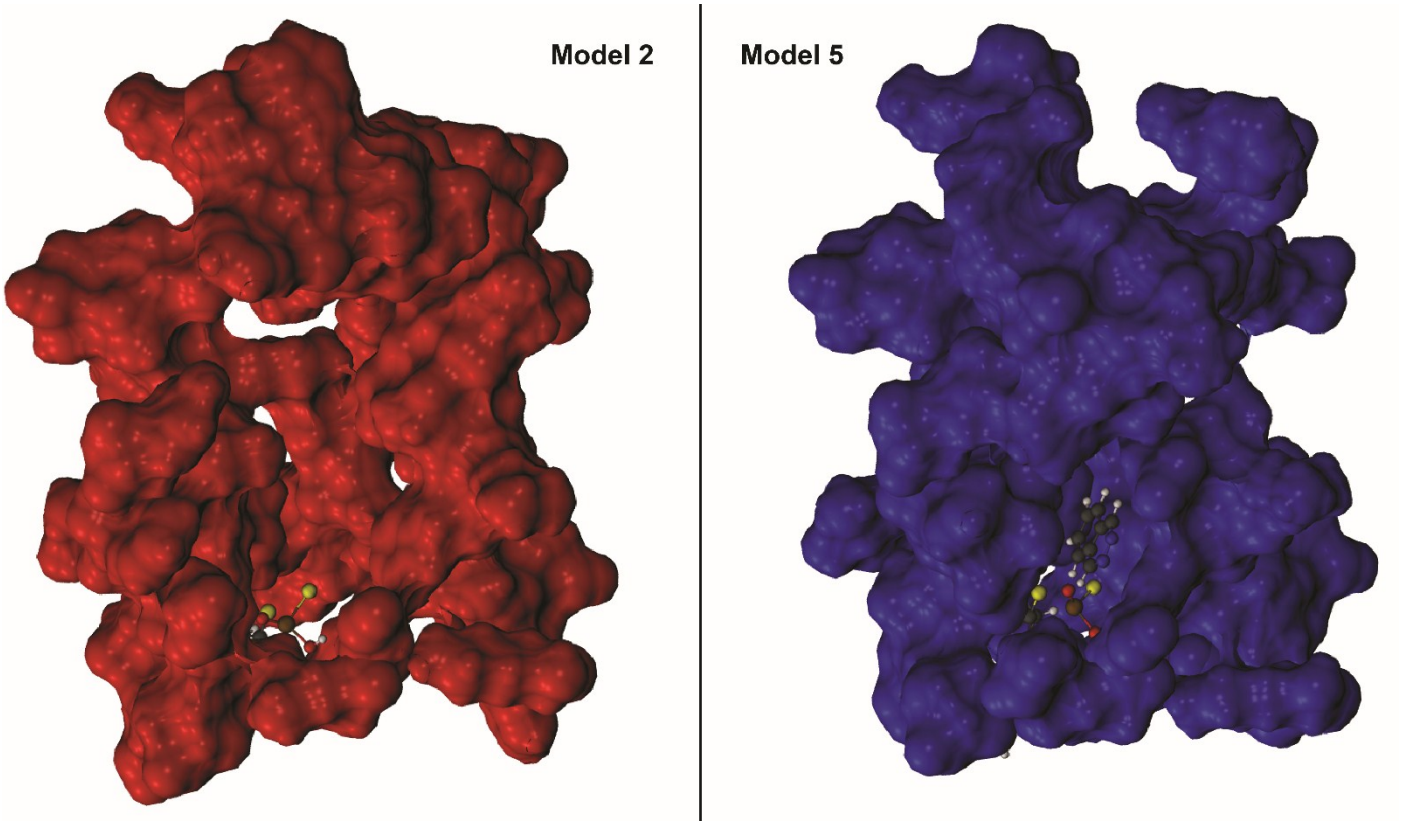

Figure SI 3. 3D representation of the portion of the enzyme delimiting the catalytic tunnel in model 2 and model 5. The structures correspond to an average structure of the 300 ns MD simulation. The selection of the residues and perspective of viewing is the same in both models. In this figure, it is possible to see that in model 5 the catalytic tunnel remained tight around the substrate while in model 2 (which differs from model 5 by having the ligands THI and MLI), the catalytic tunnel widened and let the substrate exit the enzyme. This happened in all the three replicates.

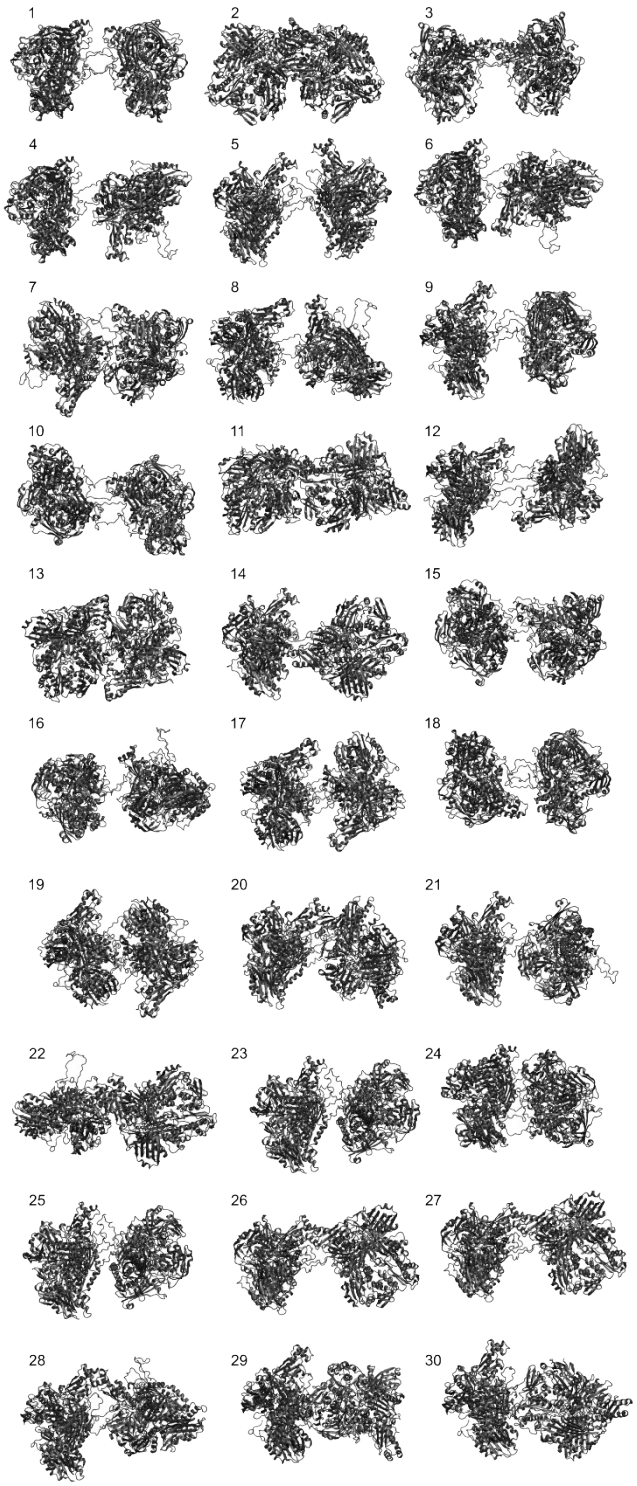

Figure SI 4. 3D representation of all the structures obtained from the protein-protein docking protocol. The model number 2 was the one considered the best one by visual analysis and docking score and was the model used for further analysis.

Force field parameters used to treat THI, MLI, FAD, PHT and the FES

The substrate (Phthalazine - PHT), the allosteric inhibitor (Thioridazine - THI), malonate ions (MLI) and the FAD were parameterized using the ANTECHAMBER module [13] of the AMBER12 package[14] and the GAFF force field. The parameters of the Fe_2S_2 clusters (FES) were taken from the literature[15].

THI.prep

```
    0    0    2

This is a remark line
molecule.res
THI   XYZ  0
CHANGE     OMIT DU   BEG
  0.0000
   1  DUMM  DU    M        999.000     999.0      -999.0           .00000
   2  DUMM  DU    M        999.000    -999.0       999.0           .00000
   3  DUMM  DU    M       -999.000     999.0       999.0           .00000
   4  CAC   c1    M        -35.546000    3.803000  -71.726000   -0.094609
   5  CAH   c1    S        -34.272000    4.100000  -71.245000   -0.281236
   6  CAR   c2    S        -33.614000    3.188000  -70.426000    0.316992
   7  NAW   na    B        -32.379000    3.458000  -69.953000   -0.353335
   8  CAN   c1    S        -31.382000    4.123000  -70.850000    0.146368
   9  CAL   c1    S        -31.723000    3.862000  -72.334000   -0.247957
  10  CAP   c2    S        -30.558000    3.026000  -72.837000    0.065870
  11  CAG   c1    S        -29.366000    3.861000  -73.206000   -0.134995
  12  CAE   c1    S        -28.167000    2.922000  -73.367000   -0.079140
  13  CAF   c1    S        -28.486000    1.637000  -74.199000   -0.019505
  14  CAM   c1    S        -29.876000    1.145000  -73.937000    0.042367
  15  NAV   n3    S        -30.875000    2.211000  -74.016000   -0.345922
  16  CAA   c1    E        -32.240000    1.645000  -74.024000   -0.131763
  17  CAS   c2    S        -32.087000    3.127000  -68.677000    0.167476
  18  CAO   c1    S        -31.347000    3.975000  -67.864000   -0.170354
  19  CAQ   c2    B        -31.064000    3.623000  -66.548000    0.179666
  20  CAJ   c1    S        -31.535000    2.427000  -66.027000   -0.208917
  21  CAK   c1    S        -32.274000    1.574000  -66.833000   -0.102895
  22  CAU   c2    E        -32.548000    1.930000  -68.149000   -0.029939
  23  SAX   ss    S        -30.155000    4.745000  -65.600000   -0.261729
  24  CAB   c1    E        -29.054000    3.845000  -64.560000   -0.161920
  25  CAD   c1    M        -36.163000    2.595000  -71.403000   -0.264083
  26  CAI   c1    M        -35.511000    1.681000  -70.590000   -0.031644
  27  CAT   c2    M        -34.244000    1.985000  -70.108000   -0.052117
  28  SAY   ss    M        -33.464000    0.889000  -69.141000   -0.159415


LOOP
  CAT  CAR
  NAV  CAP
  CAU  CAS
  SAY  CAU

IMPROPER
  CAH  CAT  CAR  NAW
  CAN  CAS  NAW  CAR
  CAG  CAL  CAP  NAV
  CAO  CAU  CAS  NAW
  CAO  CAJ  CAQ  SAX
  CAK  CAS  CAU  SAY
```

```
  CAI  CAR  CAT  SAY

DONE
STOP
```

THI.frcmod

```
MASS
c1 12.010         0.360
c2 12.010         0.360
na 14.010         0.530
n3 14.010         0.530
ss 32.060         2.900

BOND
c1-c1  986.20   1.181
c1-c2  625.00   1.307
c2-na  411.10   1.391
c2-c2  589.70   1.324
na-c1  452.00   1.362
c2-n3  486.30   1.340
c1-n3  409.80   1.392
c2-ss  280.00   1.736
ss-c1  325.40   1.679

ANGLE
c1-c1-c2   60.840     180.000
c1-c1-c1   64.410     180.000
c1-c2-na   72.756     113.050
c1-c2-c2   70.340     121.620
c2-na-c1   64.320     125.200
c2-na-c2   67.800     110.370
c2-c2-ss   79.470     122.860
na-c2-c2   69.830     121.380
na-c1-c1   61.230     176.750
c1-c2-c1   72.260     116.770
c1-c2-n3   72.822     117.620
c2-n3-c1   65.090     124.010
c1-c1-n3   59.770     180.000
c1-n3-c1   64.090     123.340
c2-c1-c2   58.200     180.000
c1-c2-ss   81.090     118.505
c2-ss-c1   40.637      98.930
c2-ss-c2   39.870      99.560

DIHE
ca-nb-nb-ca   1    0.000       180.000          2.000
c1-c1-c2-na   1    0.000       180.000          2.000
c1-c1-c2-c2   1    0.000       180.000          2.000
c1-c1-c1-c2   1    0.000       180.000          2.000
c1-c1-c1-c1   1    0.000       180.000          2.000
c1-c2-na-c1   1    0.625       180.000          2.000
c1-c2-na-c2   1    0.625       180.000          2.000
c1-c2-c2-c1   1    6.650       180.000          2.000
c1-c2-c2-ss   1    6.650       180.000          2.000
c2-na-c1-c1   1    0.000       180.000          2.000
c2-na-c2-c2   1    0.625       180.000          2.000
c2-c2-ss-c2   1    1.100       180.000          2.000
na-c2-c2-c1   1    6.650       180.000          2.000
```

```
na-c2-c2-ss   1    6.650       180.000           2.000
na-c1-c1-c2   1    0.000       180.000           2.000
na-c2-c1-c2   1    0.000       180.000           2.000
c1-na-c2-c2   1    0.625       180.000           2.000
c1-c1-c2-c1   1    0.000       180.000           2.000
c1-c1-c2-n3   1    0.000       180.000           2.000
c1-c2-n3-c1   1    0.300       180.000           2.000
c2-n3-c1-c1   1    0.000       180.000           2.000
c1-c1-c1-n3   1    0.000       180.000           2.000
c1-c1-n3-c1   1    0.000       180.000           2.000
c2-c1-c2-c1   1    0.000       180.000           2.000
c2-c1-c2-ss   1    0.000       180.000           2.000
c1-c2-ss-c1   1    1.100       180.000           2.000
c2-c1-c2-c2   1    0.000       180.000           2.000
c2-c1-c1-c2   1    0.000       180.000           2.000
c1-c1-c2-ss   1    0.000       180.000           2.000
c1-c2-ss-c2   1    1.100       180.000           2.000

IMPROPER
c1-c2-c2-na          1.1          180.0         2.0
c1-c2-na-c2          1.1          180.0         2.0
c1-c1-c2-n3          1.1          180.0         2.0
c1-c1-c2-ss          1.1          180.0         2.0
c1-c2-c2-ss          1.1          180.0         2.0

NONBON
  c1          1.9080  0.2100
  c2          1.9080  0.0860
  na          1.8240  0.1700
  n3          1.8240  0.1700
  ss          2.0000  0.2500
```

FAD.lib

```
!!index array str
 "FAD"
!entry.FAD.unit.atoms table  str name  str type  int typex  int resx  int flags
int seq  int elmnt  dbl chg
 "N1" "nc" 0 1 131072 1 -1 -0.757470
 "C10" "cd" 0 1 131072 2 -1 0.399640
 "C2" "c" 0 1 131072 3 -1 0.993610
 "O2" "o" 0 1 131072 4 -1 -0.670980
 "N3" "n" 0 1 131072 5 -1 -0.770530
 "H136" "hn" 0 1 131072 6 -1 0.376140
 "C4" "c" 0 1 131072 7 -1 0.712580
 "O4" "o" 0 1 131072 8 -1 -0.606550
 "C4X" "cd" 0 1 131072 9 -1 0.219190
 "N5" "ne" 0 1 131072 10 -1 -0.561450
 "C5X" "ca" 0 1 131072 11 -1 0.500380
 "C6" "ca" 0 1 131072 12 -1 -0.452920
 "H138" "ha" 0 1 131072 13 -1 0.208200
 "C7" "ca" 0 1 131072 14 -1 0.189550
 "C7M" "c3" 0 1 131072 15 -1 -0.357400
 "H140" "hc" 0 1 131072 16 -1 0.096350
 "H142" "hc" 0 1 131072 17 -1 0.096350
 "H144" "hc" 0 1 131072 18 -1 0.096350
 "C8" "ca" 0 1 131072 19 -1 0.090190
 "C8M" "c3" 0 1 131072 20 -1 -0.206390
```

"H146" "hc" 0 1 131072 21 -1 0.105850
"H148" "hc" 0 1 131072 22 -1 0.105850
"H150" "hc" 0 1 131072 23 -1 0.105850
"C9" "ca" 0 1 131072 24 -1 -0.296590
"H152" "ha" 0 1 131072 25 -1 0.213570
"C9A" "ca" 0 1 131072 26 -1 -0.098630
"N10" "nh" 0 1 131072 27 -1 -0.043610
"C1'" "c3" 0 1 131072 28 -1 0.113590
"H154" "h1" 0 1 131072 29 -1 0.033180
"H156" "h1" 0 1 131072 30 -1 0.033180
"C2'" "c3" 0 1 131072 31 -1 0.370170
"O2'" "oh" 0 1 131072 32 -1 -0.727170
"H160" "ho" 0 1 131072 33 -1 0.410650
"H158" "h1" 0 1 131072 34 -1 3.000000E-05
"C3'" "c3" 0 1 131072 35 -1 0.051170
"O3'" "oh" 0 1 131072 36 -1 -0.687680
"H164" "ho" 0 1 131072 37 -1 0.492840
"H162" "h1" 0 1 131072 38 -1 0.049990
"C4'" "c3" 0 1 131072 39 -1 0.363640
"O4'" "oh" 0 1 131072 40 -1 -0.741340
"H168" "ho" 0 1 131072 41 -1 0.391490
"H166" "h1" 0 1 131072 42 -1 0.075060
"C5'" "c3" 0 1 131072 43 -1 0.181830
"H170" "h1" 0 1 131072 44 -1 0.009420
"H172" "h1" 0 1 131072 45 -1 0.009420
"O5'" "os" 0 1 131072 46 -1 -0.556330
"P" "p5" 0 1 131072 47 -1 1.264660
"O2P" "o" 0 1 131072 48 -1 -0.803550
"O3P" "os" 0 1 131072 49 -1 -0.453190
"PA" "p5" 0 1 131072 50 -1 1.183400
"O1A" "o" 0 1 131072 51 -1 -0.780140
"O2A" "o" 0 1 131072 52 -1 -0.780140
"O5B" "os" 0 1 131072 53 -1 -0.536970
"C5B" "c3" 0 1 131072 54 -1 -0.014160
"C4B" "c3" 0 1 131072 55 -1 0.217620
"O4B" "os" 0 1 131072 56 -1 -0.539570
"C1B" "c3" 0 1 131072 57 -1 0.448600
"C2B" "c3" 0 1 131072 58 -1 0.274100
"C3B" "c3" 0 1 131072 59 -1 0.087940
"O3B" "oh" 0 1 131072 60 -1 -0.733380
"H120" "ho" 0 1 131072 61 -1 0.442610
"H118" "h1" 0 1 131072 62 -1 0.093580
"O2B" "oh" 0 1 131072 63 -1 -0.715350
"H124" "ho" 0 1 131072 64 -1 0.443370
"H122" "h1" 0 1 131072 65 -1 0.113290
"N9A" "na" 0 1 131072 66 -1 -0.281720
"C8A" "cc" 0 1 131072 67 -1 0.339830
"N7A" "nd" 0 1 131072 68 -1 -0.618880
"C5A" "ca" 0 1 131072 69 -1 -0.057760
"C6A" "ca" 0 1 131072 70 -1 0.766360
"N6A" "nh" 0 1 131072 71 -1 -0.930850
"H130" "hn" 0 1 131072 72 -1 0.392820
"H132" "hn" 0 1 131072 73 -1 0.392820
"N1A" "nb" 0 1 131072 74 -1 -0.846340
"C2A" "ca" 0 1 131072 75 -1 0.630870
"N3A" "nb" 0 1 131072 76 -1 -0.815180
"C4A" "ca" 0 1 131072 77 -1 0.554700
"H134" "h5" 0 1 131072 78 -1 0.028140
"H128" "h5" 0 1 131072 79 -1 0.162960
"H126" "h2" 0 1 131072 80 -1 0.045030
"H116" "h1" 0 1 131072 81 -1 0.028160

```
 "H112" "h1" 0 1 131072 82 -1 0.119840
 "H114" "h1" 0 1 131072 83 -1 0.119840
 "O1P" "o" 0 1 131072 84 -1 -0.803550
!entry.FAD.unit.atomspertinfo table  str pname  str ptype  int ptypex  int
pelmnt  dbl pchg
 "N1" "nc" 0 -1 0.0
 "C10" "cd" 0 -1 0.0
 "C2" "c" 0 -1 0.0
 "O2" "o" 0 -1 0.0
 "N3" "n" 0 -1 0.0
 "H136" "hn" 0 -1 0.0
 "C4" "c" 0 -1 0.0
 "O4" "o" 0 -1 0.0
 "C4X" "cd" 0 -1 0.0
 "N5" "ne" 0 -1 0.0
 "C5X" "ca" 0 -1 0.0
 "C6" "ca" 0 -1 0.0
 "H138" "ha" 0 -1 0.0
 "C7" "ca" 0 -1 0.0
 "C7M" "c3" 0 -1 0.0
 "H140" "hc" 0 -1 0.0
 "H142" "hc" 0 -1 0.0
 "H144" "hc" 0 -1 0.0
 "C8" "ca" 0 -1 0.0
 "C8M" "c3" 0 -1 0.0
 "H146" "hc" 0 -1 0.0
 "H148" "hc" 0 -1 0.0
 "H150" "hc" 0 -1 0.0
 "C9" "ca" 0 -1 0.0
 "H152" "ha" 0 -1 0.0
 "C9A" "ca" 0 -1 0.0
 "N10" "nh" 0 -1 0.0
 "C1'" "c3" 0 -1 0.0
 "H154" "h1" 0 -1 0.0
 "H156" "h1" 0 -1 0.0
 "C2'" "c3" 0 -1 0.0
 "O2'" "oh" 0 -1 0.0
 "H160" "ho" 0 -1 0.0
 "H158" "h1" 0 -1 0.0
 "C3'" "c3" 0 -1 0.0
 "O3'" "oh" 0 -1 0.0
 "H164" "ho" 0 -1 0.0
 "H162" "h1" 0 -1 0.0
 "C4'" "c3" 0 -1 0.0
 "O4'" "oh" 0 -1 0.0
 "H168" "ho" 0 -1 0.0
 "H166" "h1" 0 -1 0.0
 "C5'" "c3" 0 -1 0.0
 "H170" "h1" 0 -1 0.0
 "H172" "h1" 0 -1 0.0
 "O5'" "os" 0 -1 0.0
 "P" "p5" 0 -1 0.0
 "O2P" "o" 0 -1 0.0
 "O3P" "os" 0 -1 0.0
 "PA" "p5" 0 -1 0.0
 "O1A" "o" 0 -1 0.0
 "O2A" "o" 0 -1 0.0
 "O5B" "os" 0 -1 0.0
 "C5B" "c3" 0 -1 0.0
 "C4B" "c3" 0 -1 0.0
 "O4B" "os" 0 -1 0.0
```

```
 "C1B" "c3" 0 -1 0.0
 "C2B" "c3" 0 -1 0.0
 "C3B" "c3" 0 -1 0.0
 "O3B" "oh" 0 -1 0.0
 "H120" "ho" 0 -1 0.0
 "H118" "h1" 0 -1 0.0
 "O2B" "oh" 0 -1 0.0
 "H124" "ho" 0 -1 0.0
 "H122" "h1" 0 -1 0.0
 "N9A" "na" 0 -1 0.0
 "C8A" "cc" 0 -1 0.0
 "N7A" "nd" 0 -1 0.0
 "C5A" "ca" 0 -1 0.0
 "C6A" "ca" 0 -1 0.0
 "N6A" "nh" 0 -1 0.0
 "H130" "hn" 0 -1 0.0
 "H132" "hn" 0 -1 0.0
 "N1A" "nb" 0 -1 0.0
 "C2A" "ca" 0 -1 0.0
 "N3A" "nb" 0 -1 0.0
 "C4A" "ca" 0 -1 0.0
 "H134" "h5" 0 -1 0.0
 "H128" "h5" 0 -1 0.0
 "H126" "h2" 0 -1 0.0
 "H116" "h1" 0 -1 0.0
 "H112" "h1" 0 -1 0.0
 "H114" "h1" 0 -1 0.0
 "O1P" "o" 0 -1 0.0
!entry.FAD.unit.boundbox array dbl
 -1.000000
 0.0
 0.0
 0.0
 0.0
!entry.FAD.unit.childsequence single int
 2
!entry.FAD.unit.connect array int
 1
 84
!entry.FAD.unit.connectivity table  int atom1x  int atom2x  int flags
 1 2 1
 1 3 1
 2 9 1
 2 27 1
 3 4 1
 3 5 1
 5 6 1
 5 7 1
 7 8 1
 7 9 1
 9 10 1
 10 11 1
 11 12 1
 11 26 1
 12 13 1
 12 14 1
 14 15 1
 14 19 1
 15 16 1
 15 17 1
 15 18 1
```

19 20 1
19 24 1
20 21 1
20 22 1
20 23 1
24 25 1
24 26 1
26 27 1
27 28 1
28 29 1
28 30 1
28 31 1
31 32 1
31 34 1
31 35 1
32 33 1
35 36 1
35 38 1
35 39 1
36 37 1
39 40 1
39 42 1
39 43 1
40 41 1
43 44 1
43 45 1
43 46 1
46 47 1
47 48 1
47 49 1
47 84 1
49 50 1
50 51 1
50 52 1
50 53 1
53 54 1
54 55 1
54 82 1
54 83 1
55 56 1
55 81 1
55 59 1
56 57 1
57 58 1
57 66 1
57 80 1
58 59 1
58 63 1
58 65 1
59 60 1
59 62 1
60 61 1
63 64 1
66 67 1
66 77 1
67 68 1
67 79 1
68 69 1
69 70 1
69 77 1
70 71 1

```
 70 74 1
 71 72 1
 71 73 1
 74 75 1
 75 76 1
 75 78 1
 76 77 1
!entry.FAD.unit.hierarchy table  str abovetype  int abovex  str belowtype  int
belowx
 "U" 0 "R" 1
 "R" 1 "A" 1
 "R" 1 "A" 2
 "R" 1 "A" 3
 "R" 1 "A" 4
 "R" 1 "A" 5
 "R" 1 "A" 6
 "R" 1 "A" 7
 "R" 1 "A" 8
 "R" 1 "A" 9
 "R" 1 "A" 10
 "R" 1 "A" 11
 "R" 1 "A" 12
 "R" 1 "A" 13
 "R" 1 "A" 14
 "R" 1 "A" 15
 "R" 1 "A" 16
 "R" 1 "A" 17
 "R" 1 "A" 18
 "R" 1 "A" 19
 "R" 1 "A" 20
 "R" 1 "A" 21
 "R" 1 "A" 22
 "R" 1 "A" 23
 "R" 1 "A" 24
 "R" 1 "A" 25
 "R" 1 "A" 26
 "R" 1 "A" 27
 "R" 1 "A" 28
 "R" 1 "A" 29
 "R" 1 "A" 30
 "R" 1 "A" 31
 "R" 1 "A" 32
 "R" 1 "A" 33
 "R" 1 "A" 34
 "R" 1 "A" 35
 "R" 1 "A" 36
 "R" 1 "A" 37
 "R" 1 "A" 38
 "R" 1 "A" 39
 "R" 1 "A" 40
 "R" 1 "A" 41
 "R" 1 "A" 42
 "R" 1 "A" 43
 "R" 1 "A" 44
 "R" 1 "A" 45
 "R" 1 "A" 46
 "R" 1 "A" 47
 "R" 1 "A" 48
 "R" 1 "A" 49
 "R" 1 "A" 50
 "R" 1 "A" 51
```

```
 "R" 1 "A" 52
 "R" 1 "A" 53
 "R" 1 "A" 54
 "R" 1 "A" 55
 "R" 1 "A" 56
 "R" 1 "A" 57
 "R" 1 "A" 58
 "R" 1 "A" 59
 "R" 1 "A" 60
 "R" 1 "A" 61
 "R" 1 "A" 62
 "R" 1 "A" 63
 "R" 1 "A" 64
 "R" 1 "A" 65
 "R" 1 "A" 66
 "R" 1 "A" 67
 "R" 1 "A" 68
 "R" 1 "A" 69
 "R" 1 "A" 70
 "R" 1 "A" 71
 "R" 1 "A" 72
 "R" 1 "A" 73
 "R" 1 "A" 74
 "R" 1 "A" 75
 "R" 1 "A" 76
 "R" 1 "A" 77
 "R" 1 "A" 78
 "R" 1 "A" 79
 "R" 1 "A" 80
 "R" 1 "A" 81
 "R" 1 "A" 82
 "R" 1 "A" 83
 "R" 1 "A" 84
!entry.FAD.unit.name single str
 "FAD"
!entry.FAD.unit.positions table  dbl x  dbl y  dbl z
 -19.021000 2.395000 2.304000
 -17.892000 2.343000 1.578000
 -19.001000 2.723000 3.616000
 -20.079000 2.754000 4.238000
 -17.874000 3.016000 4.278000
 -17.933000 3.267000 5.316000
 -16.682000 3.004000 3.682000
 -15.648000 3.278000 4.315000
 -16.618000 2.657000 2.249000
 -15.452000 2.623000 1.583000
 -15.421000 2.302000 0.276000
 -14.199000 2.281000 -0.373000
 -13.287000 2.521000 0.173000
 -14.136000 1.955000 -1.715000
 -12.807000 1.932000 -2.414000
 -12.950000 1.656000 -3.459000
 -12.155000 1.203000 -1.933000
 -12.350000 2.920000 -2.359000
 -15.377000 1.628000 -2.456000
 -15.292000 1.275000 -3.914000
 -16.291000 1.065000 -4.296000
 -14.663000 0.394000 -4.039000
 -14.860000 2.110000 -4.466000
 -16.606000 1.648000 -1.809000
 -17.517000 1.407000 -2.357000
```

```
 -16.671000 1.976000 -0.464000
 -17.903000 2.015000 0.215000
 -19.170000 1.677000 -0.438000
 -19.013000 0.771000 -1.024000
 -19.907000 1.483000 0.342000
 -19.739000 2.735000 -1.362000
 -20.377000 3.746000 -0.584000
 -21.153000 3.317000 -0.021000
 -18.942000 3.186000 -1.954000
 -20.762000 2.078000 -2.280000
 -20.087000 1.441000 -3.362000
 -19.539000 2.155000 -3.902000
 -21.318000 1.361000 -1.675000
 -21.746000 3.079000 -2.867000
 -22.441000 3.741000 -1.813000
 -22.964000 3.034000 -1.239000
 -21.197000 3.814000 -3.455000
 -22.739000 2.369000 -3.774000
 -22.256000 1.504000 -4.229000
 -23.594000 2.040000 -3.184000
 -23.184000 3.249000 -4.794000
 -23.217000 2.814000 -6.336000
 -21.799000 2.667000 -6.814000
 -23.898000 1.361000 -6.353000
 -24.078000 0.561000 -7.730000
 -22.902000 -0.353000 -7.880000
 -24.407000 1.526000 -8.826000
 -25.375000 -0.349000 -7.467000
 -25.954000 -0.488000 -6.171000
 -27.140000 -1.447000 -6.209000
 -28.333000 -0.743000 -5.875000
 -29.236000 -0.693000 -6.978000
 -28.501000 -1.257000 -8.174000
 -27.352000 -2.033000 -7.590000
 -27.739000 -3.406000 -7.488000
 -26.985000 -3.947000 -6.997000
 -26.446000 -1.975000 -8.193000
 -29.340000 -2.130000 -8.922000
 -28.786000 -2.568000 -9.699000
 -28.177000 -0.469000 -8.854000
 -29.611000 0.714000 -7.231000
 -28.760000 1.697000 -7.553000
 -29.413000 2.871000 -7.713000
 -30.715000 2.645000 -7.493000
 -31.953000 3.455000 -7.499000
 -31.923000 4.777000 -7.784000
 -30.993000 5.255000 -8.010000
 -32.830000 5.345000 -7.783000
 -33.111000 2.829000 -7.213000
 -33.150000 1.518000 -6.932000
 -32.069000 0.726000 -6.908000
 -30.841000 1.220000 -7.174000
 -34.119000 1.070000 -6.710000
 -27.684000 1.568000 -7.670000
 -30.143000 -1.264000 -6.780000
 -26.923000 -2.246000 -5.500000
 -25.202000 -0.876000 -5.483000
 -26.294000 0.488000 -5.825000
 -24.136000 3.754000 -7.058000
!entry.FAD.unit.residueconnect table  int c1x  int c2x  int c3x  int c4x  int
c5x  int c6x
```

```
 1 84 0 0 0 0
!entry.FAD.unit.residues table  str name  int seq  int childseq  int startatomx
str restype  int imagingx
 "FAD" 1 85 1 "?" 0
!entry.FAD.unit.residuesPdbSequenceNumber array int
 0
!entry.FAD.unit.solventcap array dbl
 -1.000000
 0.0
 0.0
 0.0
 0.0
!entry.FAD.unit.velocities table  dbl x  dbl y  dbl z
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
```

```
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
```

FAD.frcmod

```
BOND
cd-ne  381.80   1.414

ANGLE
cd-cd-ne   69.300     121.150
cd-nh-ca   65.500     123.660
c -cd-ne   65.257     121.360
c -cd-ne   68.400     120.890
cd-ne-ca   66.700     118.670

DIHE
cd-cd-ne-ca   1    0.800       180.000           2.000
c -cd-ne-ca   1    0.800       180.000           2.000

IMPROPER
cd-nc-cd-nh         1.1          180.0         2.0
n -nc-c -o         10.5          180.0         2.0
c -c -n -hn         1.1          180.0         2.0
cd-n -c -o         10.5          180.0         2.0
```

```
c -cd-cd-ne         1.1          180.0         2.0
ca-ca-ca-ne         1.1          180.0         2.0
ca-ca-ca-ha         1.1          180.0         2.0
ca-ca-ca-nh         1.1          180.0         2.0
c3-ca-nh-cd         1.1          180.0         2.0
c3-ca-na-cc         1.1          180.0         2.0
h5-na-cc-nd         1.1          180.0         2.0
ca-ca-ca-nd         1.1          180.0         2.0
ca-nb-ca-nh         1.1          180.0         2.0
ca-hn-nh-hn         1.1          180.0         2.0
h5-nb-ca-nb         1.1          180.0         2.0
ca-na-ca-nb         1.1          180.0         2.0
```

MLI.prep

```
    0    0    2

This is a remark line
molecule.res
MLI   XYZ  0
CHANGE     OMIT DU   BEG
  0.0000
   1  DUMM  DU    M        999.000     999.0      -999.0           .00000
   2  DUMM  DU    M        999.000    -999.0       999.0           .00000
   3  DUMM  DU    M       -999.000     999.0       999.0           .00000
   4  C1    c1    M        -50.299000  -25.615000  -37.181000   -0.228110
   5  C3    c     B        -49.564000  -26.679000  -37.965000    0.928881
   6  O8    o     E        -49.095000  -27.654000  -37.342000   -0.888259
   7  O9    o     E        -49.444000  -26.543000  -39.200000   -0.888259
   8  C2    c     M        -49.410000  -24.416000  -36.938000    0.928881
   9  O7    o     E        -49.959000  -23.320000  -36.699000   -0.888259
  10  O6    o     M        -48.166000  -24.540000  -36.989000   -0.888259


LOOP

IMPROPER
   C1   O8   C3   O9
   C1   O7   C2   O6

DONE
STOP
```

MLI.frcmod

```
MASS
c1 12.010        0.360
c  12.010        0.616
o  16.000        0.434

BOND
c1-c   379.80   1.460
c -o   648.00   1.214

ANGLE
c1-c -o    69.920     122.340
c -c1-c    58.200     180.000
o -c -o    78.170     130.380
```

```
DIHE
c -c1-c -o    1    0.000       180.000           2.000

IMPROPER
c1-o -c -o          1.1          180.0         2.0
NONBON
  c1          1.9080  0.2100
  c           1.9080  0.0860
  o           1.6612  0.2100
```

PHT.lib

```
!!index array str
 "PHT"
!entry.PHT.unit.atoms table  str name  str type  int typex  int resx  int flags
int seq  int elmnt  dbl chg
 "C1" "ca" 0 1 131075 1 6 0.233278
 "N1" "nb" 0 1 131075 2 7 -0.322793
 "N2" "nb" 0 1 131075 3 7 -0.322793
 "C8" "ca" 0 1 131075 4 6 0.233278
 "H6" "h4" 0 1 131075 5 1 0.032126
 "H1" "h4" 0 1 131075 6 1 0.032126
 "C2" "ca" 0 1 131075 7 6 0.138014
 "C3" "ca" 0 1 131075 8 6 0.138014
 "C4" "ca" 0 1 131075 9 6 -0.333391
 "H2" "ha" 0 1 131075 10 1 0.176854
 "C5" "ca" 0 1 131075 11 6 -0.038360
 "H3" "ha" 0 1 131075 12 1 0.114270
 "C6" "ca" 0 1 131075 13 6 -0.038360
 "H4" "ha" 0 1 131075 14 1 0.114270
 "C7" "ca" 0 1 131075 15 6 -0.333391
 "H5" "ha" 0 1 131075 16 1 0.176854
!entry.PHT.unit.atomspertinfo table  str pname  str ptype  int ptypex  int
pelmnt  dbl pchg
 "C1" "ca" 0 -1 0.0
 "N1" "nb" 0 -1 0.0
 "N2" "nb" 0 -1 0.0
 "C8" "ca" 0 -1 0.0
 "H6" "h4" 0 -1 0.0
 "H1" "h4" 0 -1 0.0
 "C2" "ca" 0 -1 0.0
 "C3" "ca" 0 -1 0.0
 "C4" "ca" 0 -1 0.0
 "H2" "ha" 0 -1 0.0
 "C5" "ca" 0 -1 0.0
 "H3" "ha" 0 -1 0.0
 "C6" "ca" 0 -1 0.0
 "H4" "ha" 0 -1 0.0
 "C7" "ca" 0 -1 0.0
 "H5" "ha" 0 -1 0.0
!entry.PHT.unit.boundbox array dbl
 -1.000000
 0.0
 0.0
 0.0
 0.0
!entry.PHT.unit.childsequence single int
```

```
 2
!entry.PHT.unit.connect array int
 1
 15
!entry.PHT.unit.connectivity table  int atom1x  int atom2x  int flags
 1 2 1
 1 6 1
 1 7 1
 2 3 1
 3 4 1
 4 5 1
 4 8 1
 7 8 1
 7 15 1
 8 9 1
 9 10 1
 9 11 1
 11 12 1
 11 13 1
 13 14 1
 13 15 1
 15 16 1
!entry.PHT.unit.hierarchy table  str abovetype  int abovex  str belowtype  int
belowx
 "U" 0 "R" 1
 "R" 1 "A" 1
 "R" 1 "A" 2
 "R" 1 "A" 3
 "R" 1 "A" 4
 "R" 1 "A" 5
 "R" 1 "A" 6
 "R" 1 "A" 7
 "R" 1 "A" 8
 "R" 1 "A" 9
 "R" 1 "A" 10
 "R" 1 "A" 11
 "R" 1 "A" 12
 "R" 1 "A" 13
 "R" 1 "A" 14
 "R" 1 "A" 15
 "R" 1 "A" 16
!entry.PHT.unit.name single str
 "PHT"
!entry.PHT.unit.positions table  dbl x  dbl y  dbl z
 -1.294000 1.329000 0.0
 -2.439000 0.684000 0.0
 -2.439000 -0.684000 0.0
 -1.294000 -1.329000 0.0
 -1.369000 -2.416000 0.0
 -1.369000 2.416000 0.0
 -0.012000 0.709000 0.0
 -0.012000 -0.709000 0.0
 1.216000 -1.411000 0.0
 1.211000 -2.498000 0.0
 2.403000 -0.708000 0.0
 3.349000 -1.240000 0.0
 2.403000 0.708000 0.0
 3.350000 1.240000 0.0
 1.216000 1.411000 0.0
 1.211000 2.498000 0.0
```

```
!entry.PHT.unit.residueconnect table  int c1x  int c2x  int c3x  int c4x  int
c5x  int c6x
 1 15 0 0 0 0
!entry.PHT.unit.residues table  str name  int seq  int childseq  int startatomx
str restype  int imagingx
 "PHT" 1 17 1 "?" 0
!entry.PHT.unit.residuesPdbSequenceNumber array int
 0
!entry.PHT.unit.solventcap array dbl
 -1.000000
 0.0
 0.0
 0.0
 0.0
!entry.PHT.unit.velocities table  dbl x  dbl y  dbl z
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
```

PHT.frcmod

```
MASS

BOND

ANGLE

DIHE
ca-nb-nb-ca   1    3.000       180.000          -2.000
ca-nb-nb-ca   1    2.800         0.000           1.000

IMPROPER
ca-h4-ca-nb          1.1          180.0         2.0
ca-ca-ca-ca          1.1          180.0         2.0
ca-ca-ca-ha          1.1          180.0         2.0
```

FES.lib (see ref 15)

```
!!index array str
 "FES"
!entry.FES.unit.atoms table  str name  str type  int typex  int resx  int flags
int seq  int elmnt  dbl chg
 "FE1" "FE" 0 1 131075 1 26 0.0
 "FE2" "FE" 0 1 131075 2 26 0.0
 "S1" "S" 0 1 131075 3 16 0.0
```

```
 "S2" "S" 0 1 131075 4 16 0.0
!entry.FES.unit.atomspertinfo table  str pname  str ptype  int ptypex  int
pelmnt  dbl pchg
 "FE1" "FE" 0 -1 0.600400
 "FE2" "FE" 0 -1 -0.516400
 "S1" "S" 0 -1 -0.516400
 "S2" "S" 0 -1 0.600400
!entry.FES.unit.boundbox array dbl
 -1.000000
 0.0
 0.0
 0.0
 0.0
!entry.FES.unit.childsequence single int
 2
!entry.FES.unit.connect array int
 0
 0
!entry.FES.unit.connectivity table  int atom1x  int atom2x  int flags
 1 4 1
 1 3 1
 2 4 1
 2 3 1
!entry.FES.unit.hierarchy table  str abovetype  int abovex  str belowtype  int
belowx
 "U" 0 "R" 1
 "R" 1 "A" 1
 "R" 1 "A" 2
 "R" 1 "A" 3
 "R" 1 "A" 4
!entry.FES.unit.name single str
 "FES"
!entry.FES.unit.positions table  dbl x  dbl y  dbl z
 -46.072000 -17.691000 -47.369000
 -43.131000 -18.246000 -47.529000
 -44.468000 -16.853000 -48.658000
 -44.800000 -19.268000 -46.487000
!entry.FES.unit.residueconnect table  int c1x  int c2x  int c3x  int c4x  int
c5x  int c6x
 0 0 0 0 0 0
!entry.FES.unit.residues table  str name  int seq  int childseq  int startatomx
str restype  int imagingx
 "FES" 1 6 1 "?" 0
!entry.FES.unit.residuesPdbSequenceNumber array int
 0
!entry.FES.unit.solventcap array dbl
 -1.000000
 0.0
 0.0
 0.0
 0.0
!entry.FES.unit.velocities table  dbl x  dbl y  dbl z
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
 0.0 0.0 0.0
```

FES.frcmod (see ref 15)

```
# param FE

MASS
FE 55.0
S 32.06
SH 32.06

BOND
FE-S  93.4 2.17
FE-SH 82.6 2.23

ANGLE
FE-SH-CT 65.5 108.44
S-FE-S   17.3 102.84
HS-SH-FE 65.5 108.44
SH-FE-SH 65.5 108.44
SH-FE-S  17.3 102.84
FE-S-FE  17.3 77.200

DIHE
FE-S-FE-S  1 0.0 0.0  0.0
S-FE-SH-CT 1 0.0 0.0  0.0
HS-SH-FE-SH 1 0.0 0.0  0.0
HS-SH-FE-S 1 0.0 0.0  0.0
SH-FE-SH-CT 1 0.0 0.0  0.0
SH-FE-SH-HS 1 0.0 0.0  0.0
SH-FE-S-FE 1 0.0 0.0  0.0
CT-SH-FE-SH 1 0.0 0.0  0.0
HS-SH-FE-S 1 0.0 0.0  0.0

NONBOND
FE  2.65 0.045
S   2.0000  0.2500                                    #W. Cornell CH3SH and
CH3SCH3 FEP's
SH  2.0000  0.2500                                    #W. Cornell CH3SH and
CH3SCH3 FEP's
```

Table SI 2. Equilibrium values and force constants obtained for each bond and angle of the AOX model. Adapted from reference 12.

Bond	**l_0 / Å**	**K_l / kcal mol^{-1} Å^{-2}**
MO-OT	1.711	545.30
MO-SO	2.200	232.30
MO-OR	1.965	206.90
MO-S1	2.466	93.02
MO-S2	2.509	80.08
Angle	**θ_0 / deg**	**K_θ / kcal.mol^{-1}.rad^{-2}**
S1-MO-S2	78.70	289.40
S1-MO-SO	89.08	53.63
S1-MO-OT	100.12	35.23
S1-MO-OR	149.28	34.82
S2-MO-SO	141.45	16.12
S2-MO-OT	108.85	20.20
S2-MO-OR	76.32	125.50
OR-MO-SO	99.47	63.83
SO-MO-OT	109.24	67.92
OT-MO-OR	104.65	53.11
HR-OR-MO	117.06	21.07
C2-S2-MO	109.03	122.00
C2-S1-MO	108.50	119.80