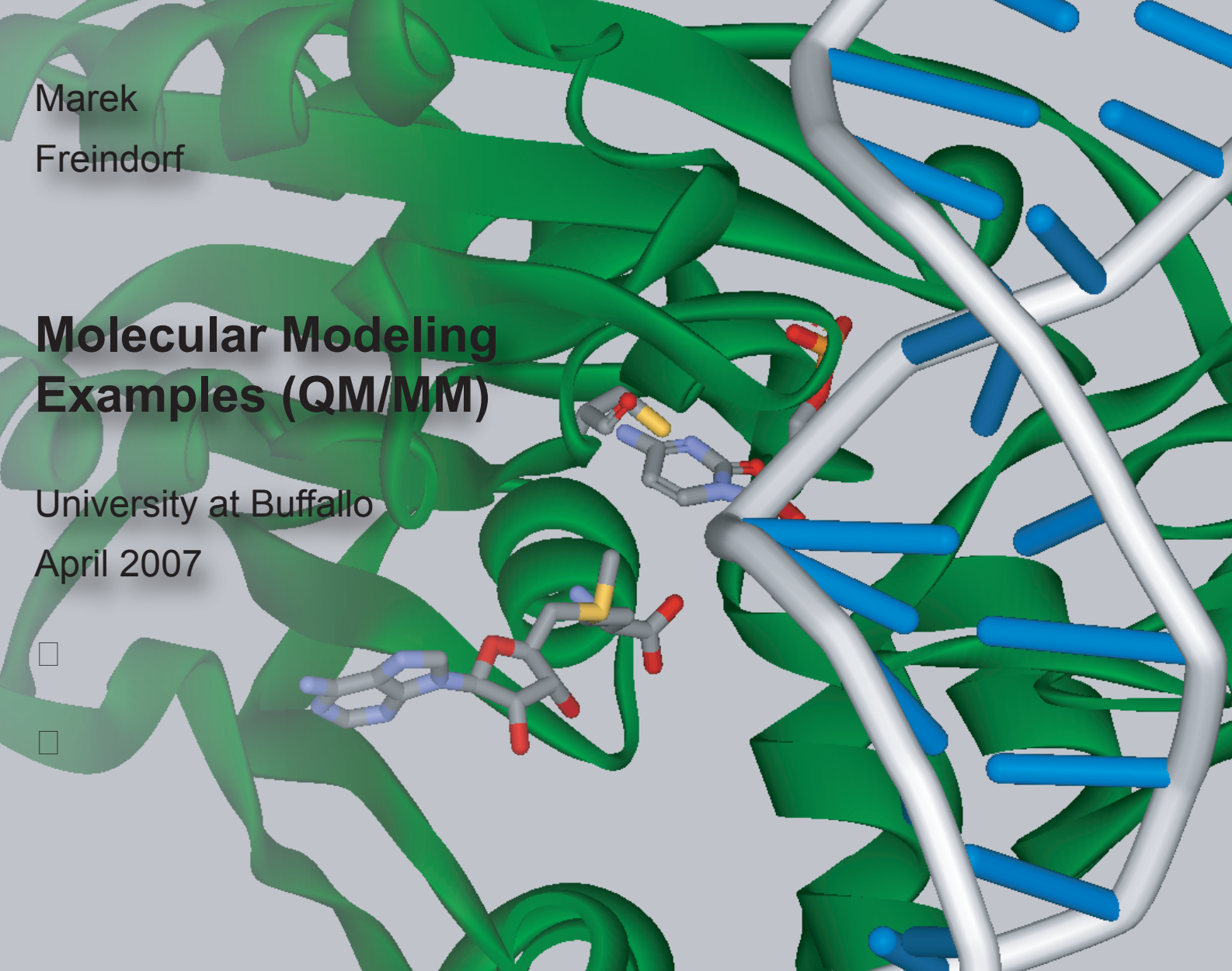
Marek
Freindorf

Molecular Modeling Examples (QM/MM)

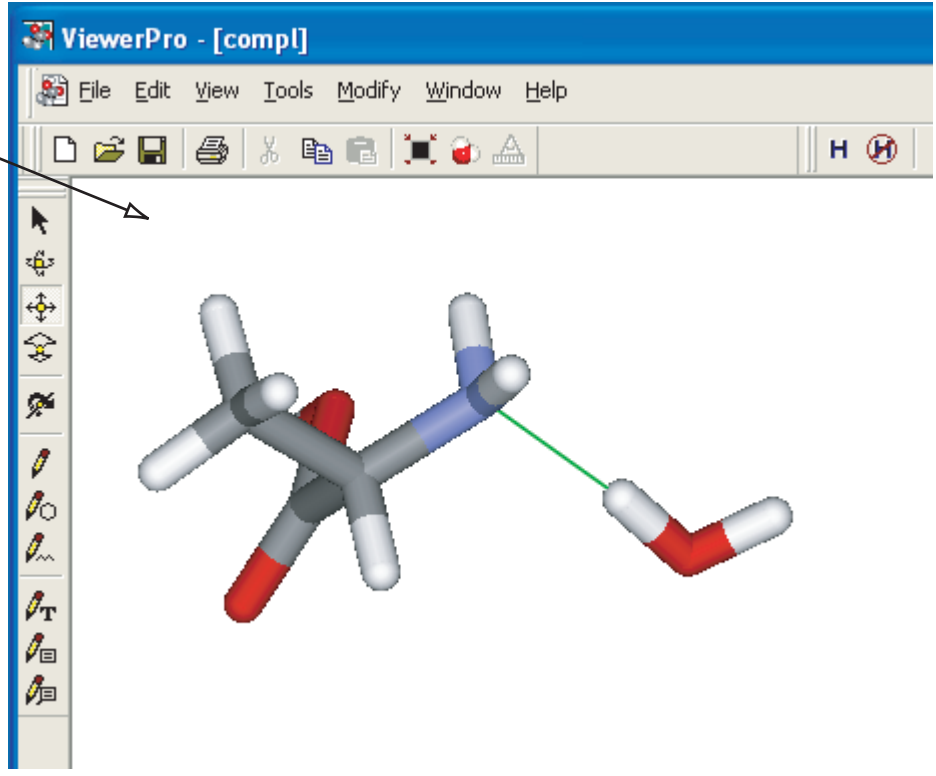
University at Buffallo

April 2007

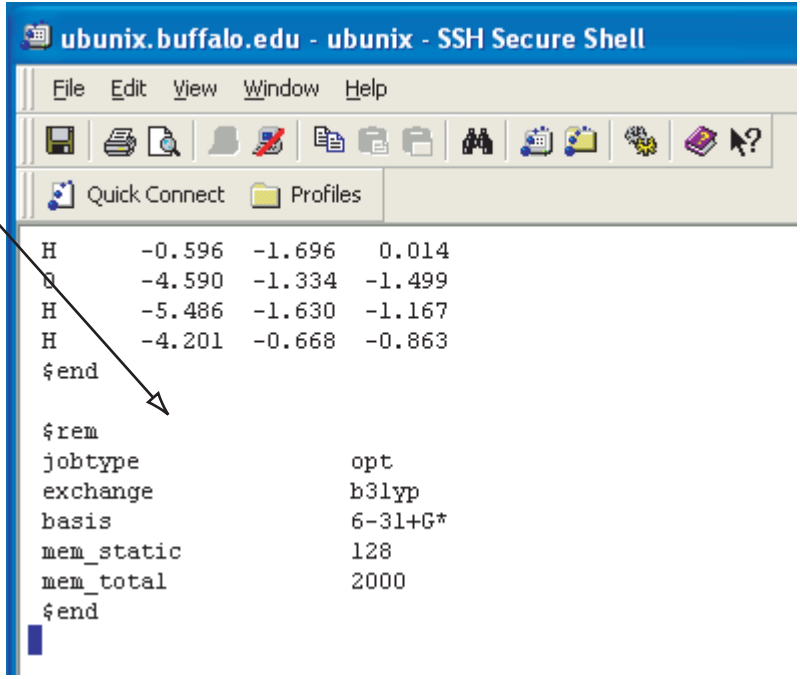


QM/MM calculations of alanine water dimer

Geometry optimization of the alanine water dimer

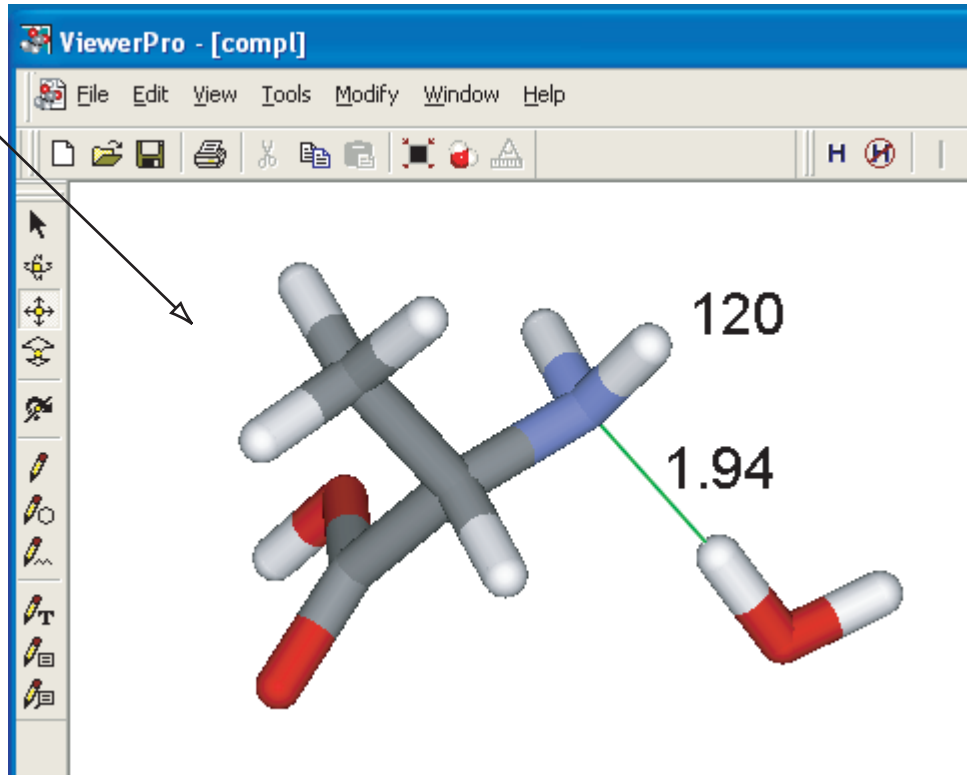


Technical details of the QM calculations



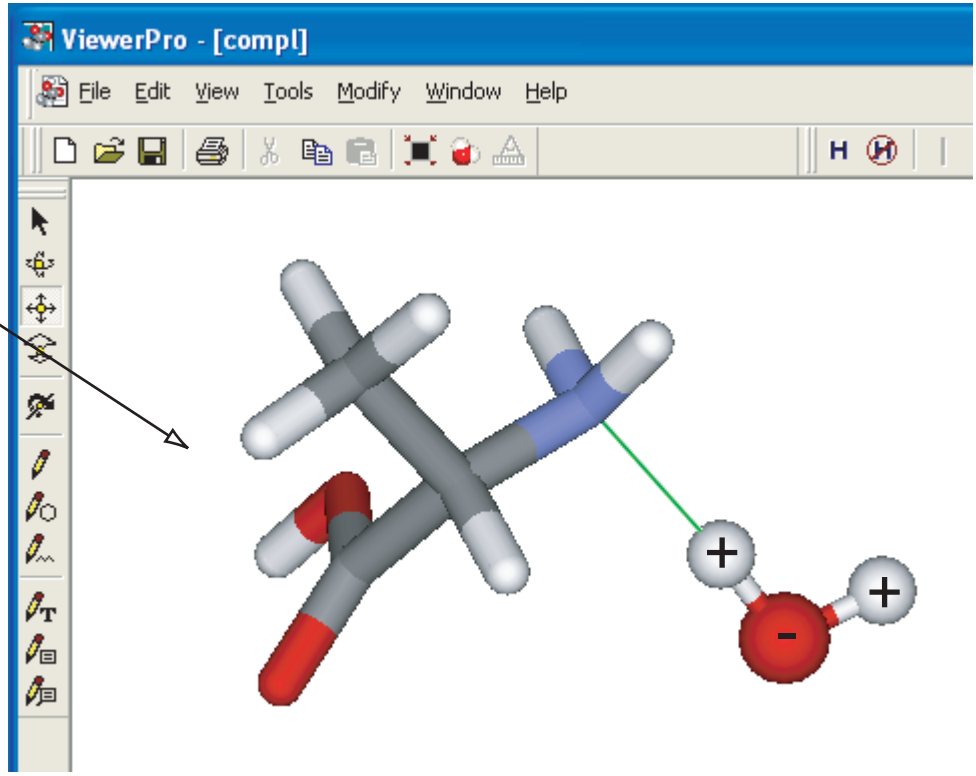
QM/MM calculations of alanine water dimer

Final structure after QM geometry optimization



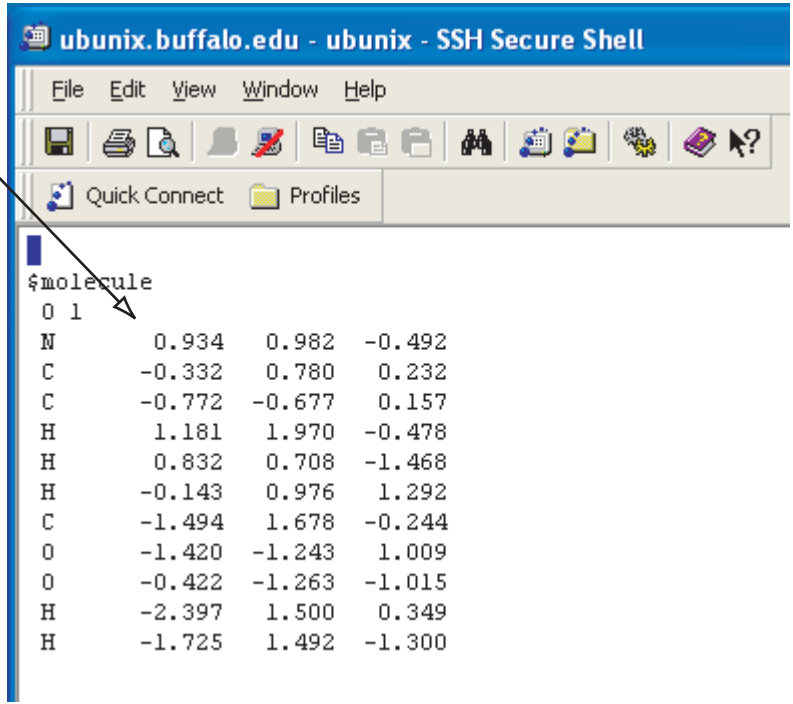
QM/MM calculations of alanine water dimer

Geometry optimization of alanine in the presence of the fixed MM atoms of water

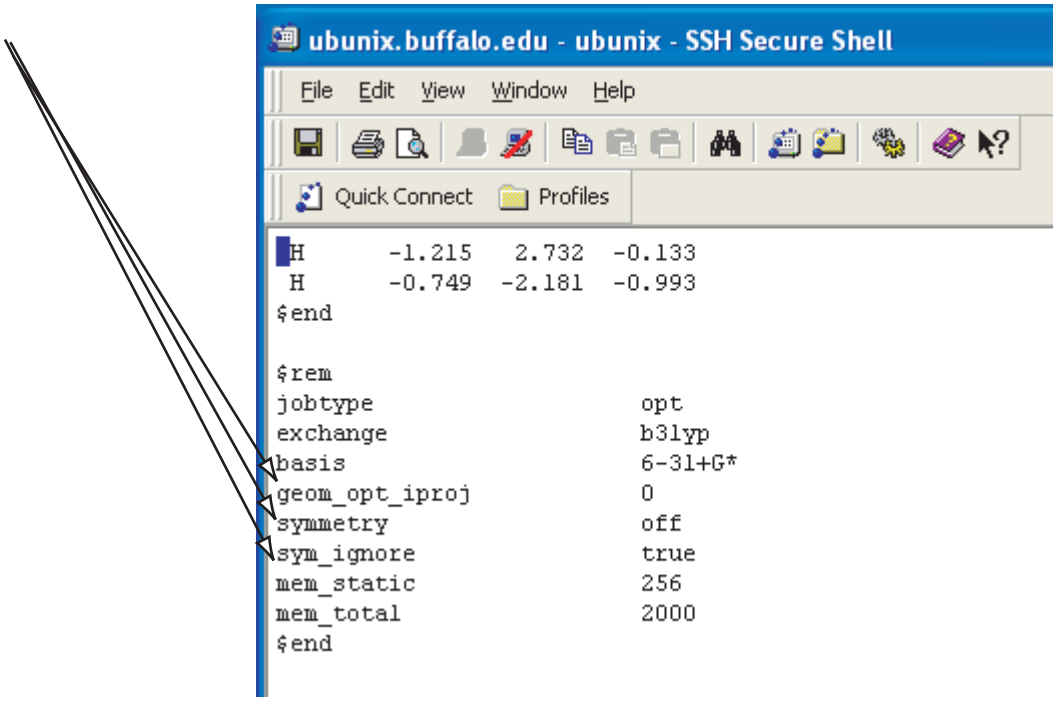


QM/MM calculations of alanine water dimer

Cartesian coordinates
of the alanine only



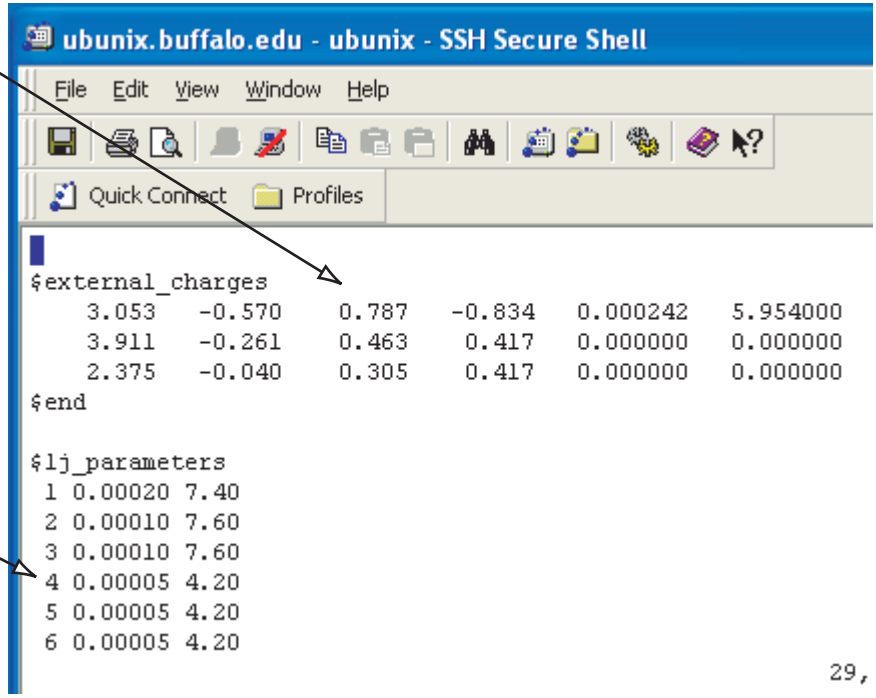
Additional commands
of the QM calculations



QM/MM calculations of alanine water dimer

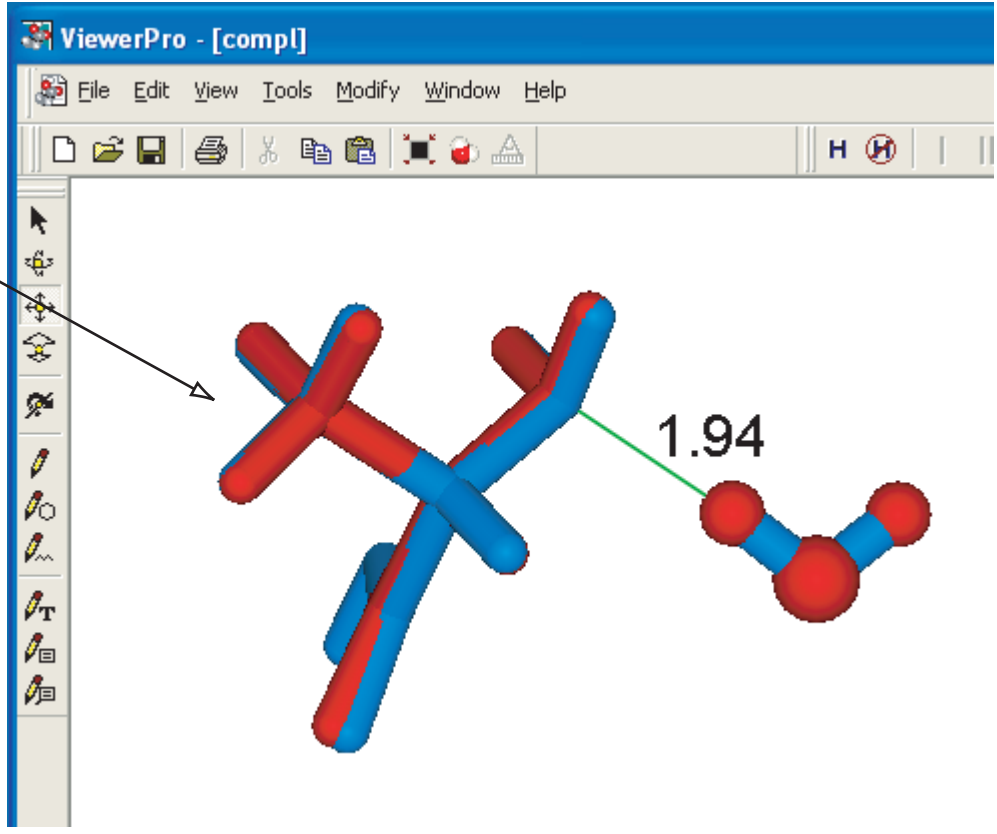
MM atoms are represented by point charges and vdW spheres

vdW spheres of the QM atoms

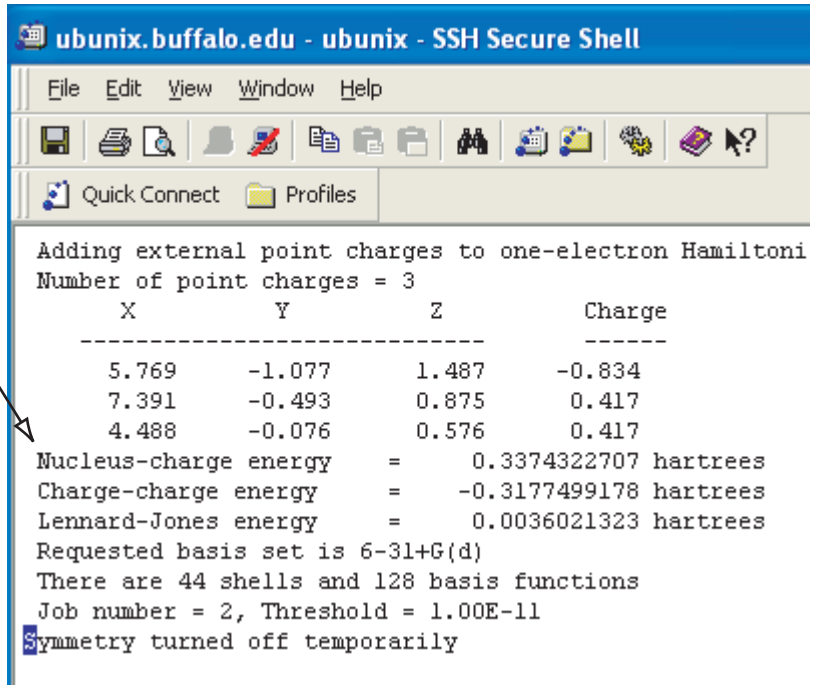


QM/MM calculations of alanine water dimer

Final QM/MM geometry (red) of alanine, compared with full QM geometry of the dimer (blue)

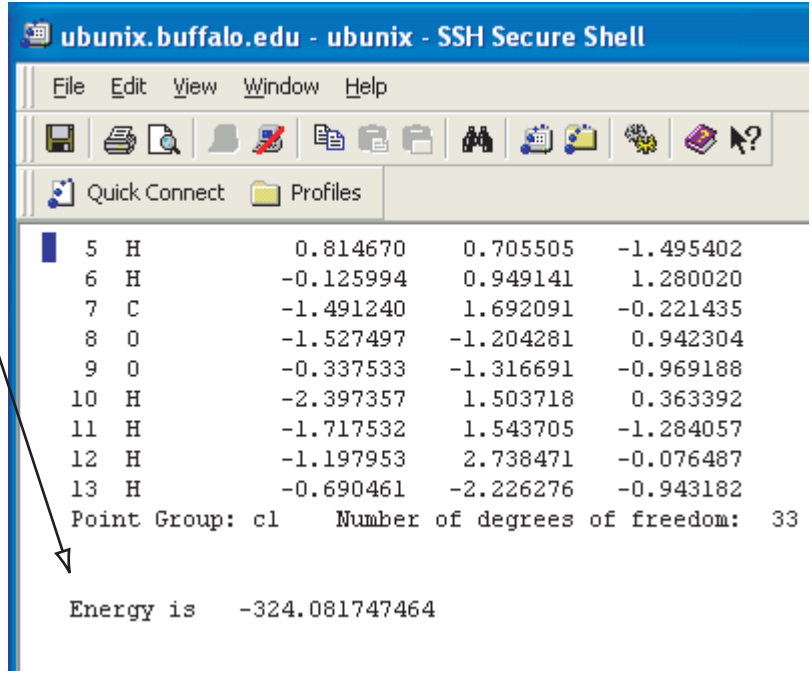


Energy components in the QM/MM calculations

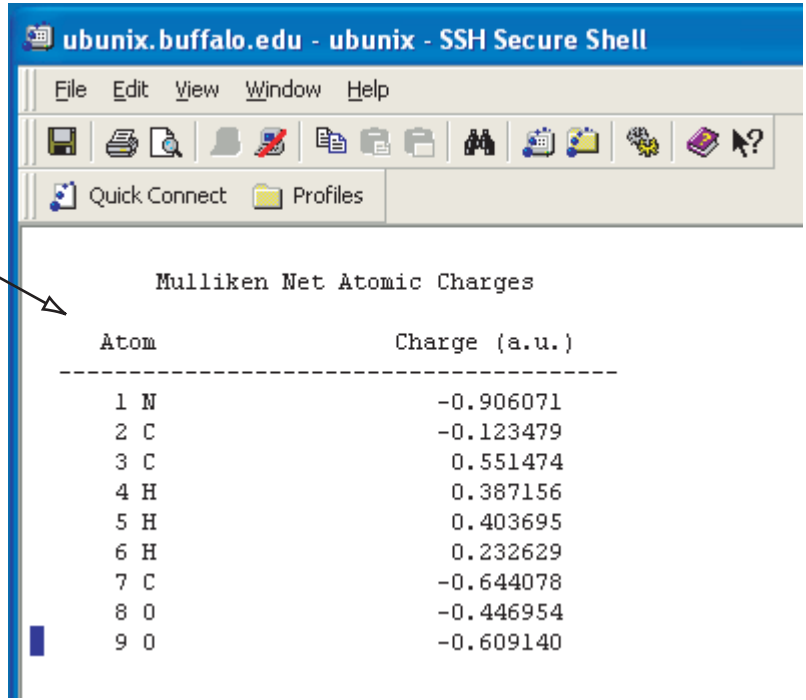


QM/MM calculations of alanine water dimer

Final total energy of QM alanine, calculated in the presence of MM

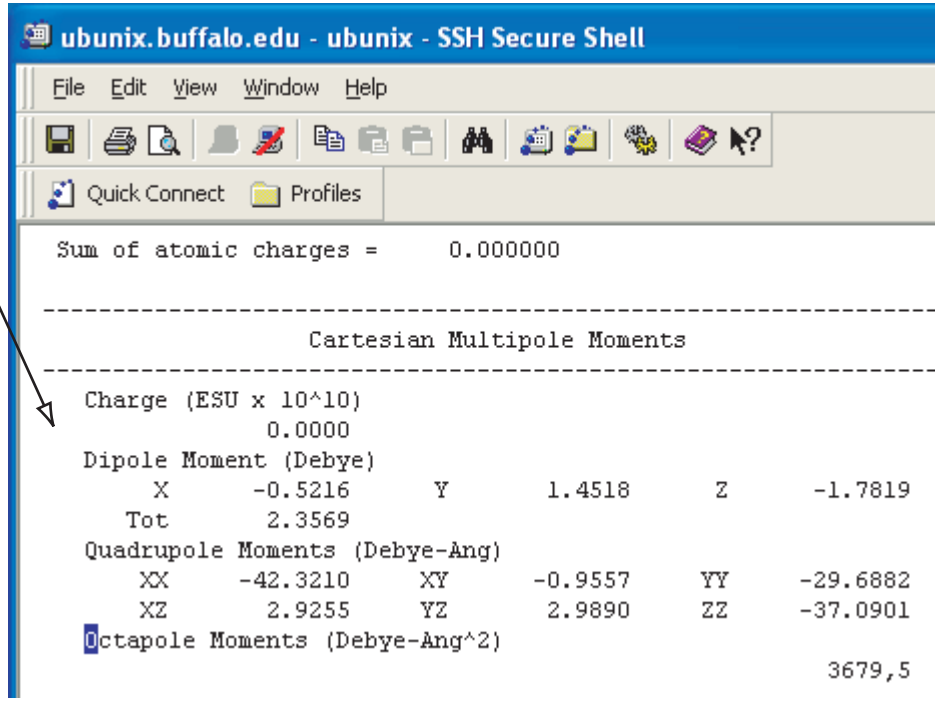


Atomic charges of QM alanine with the presence of MM water molecule



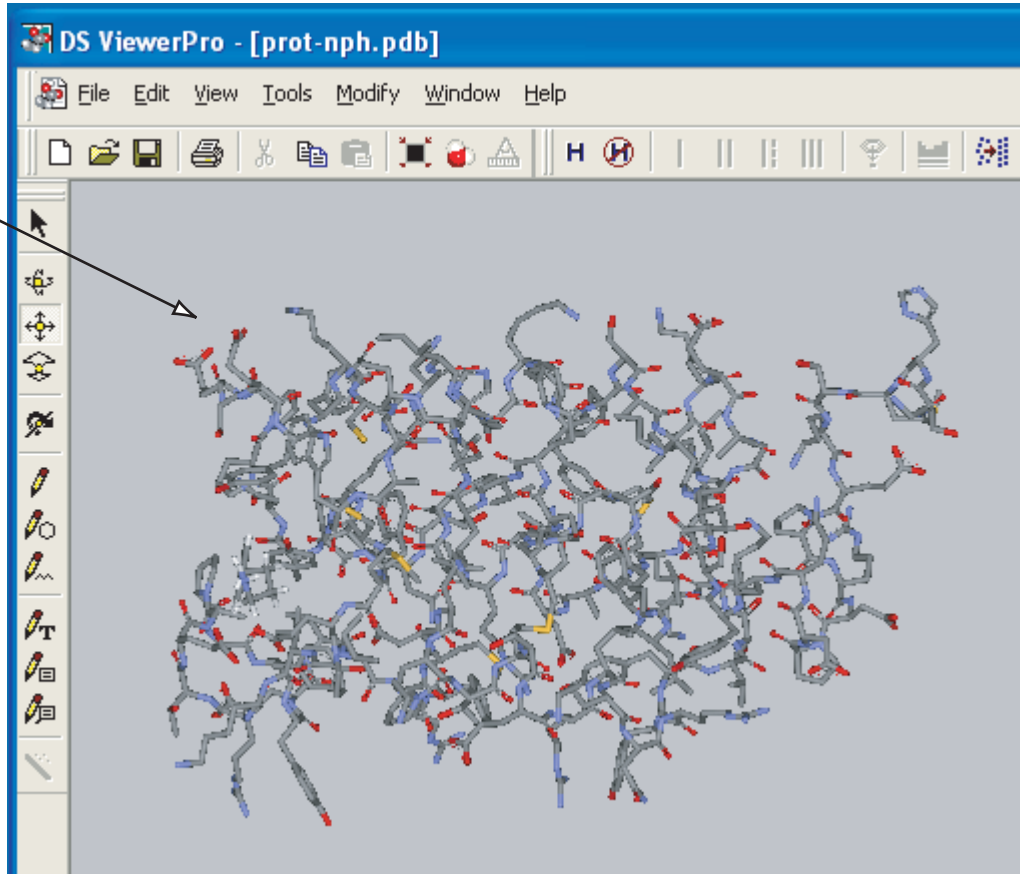
QM/MM calculations of alanine water dimer

Dipole moment of QM alanine with the presence of MM water molecule

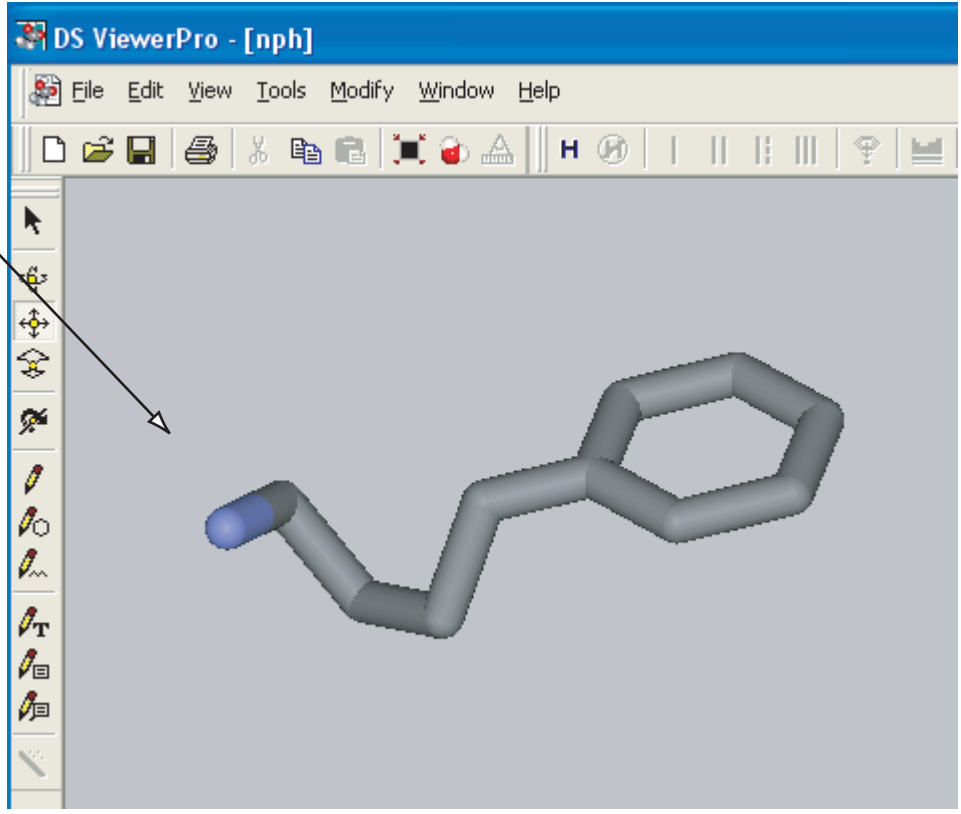


QM/MM calculations of active site of PCAF

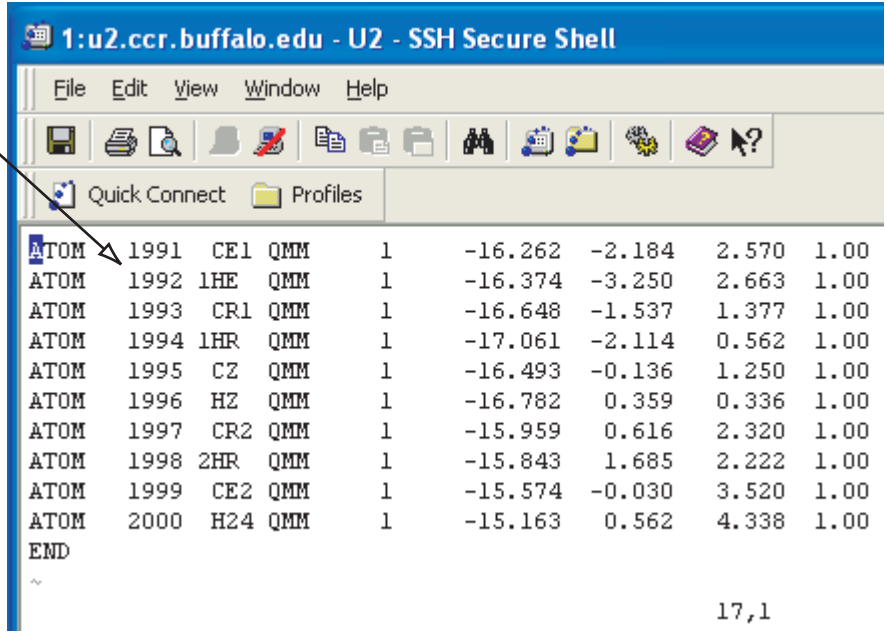
Experimental structure of the PCAF protein with a ligand



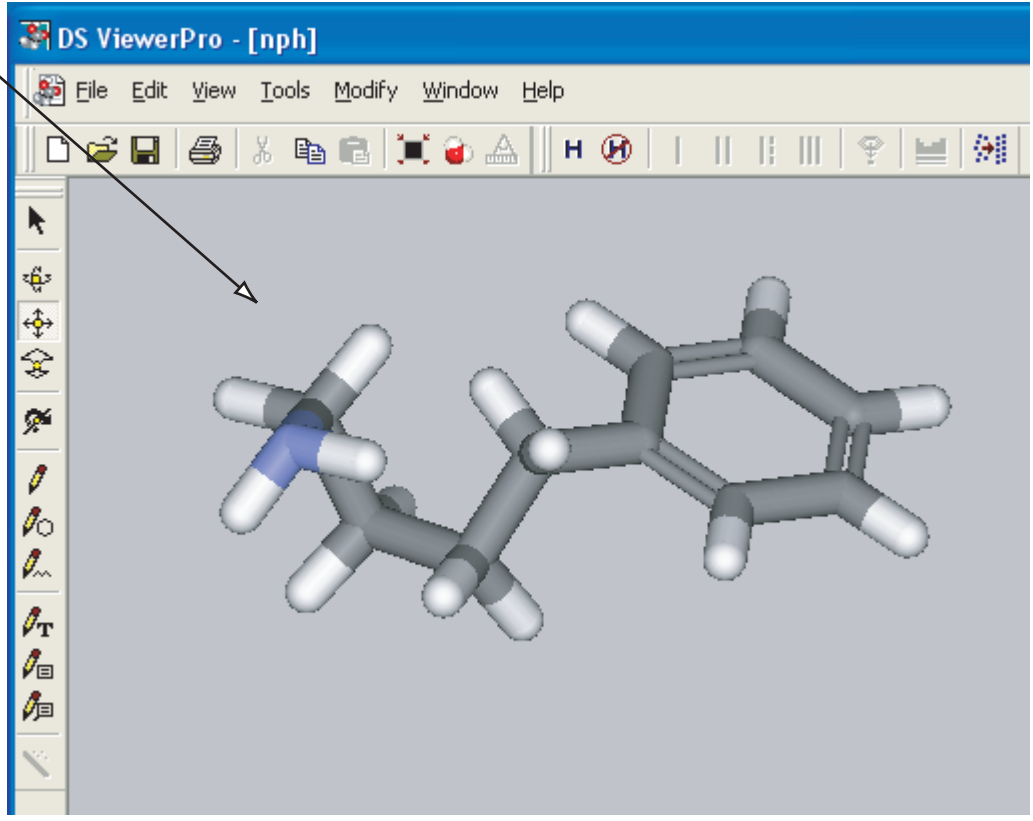
The ligand of the PCAF protein



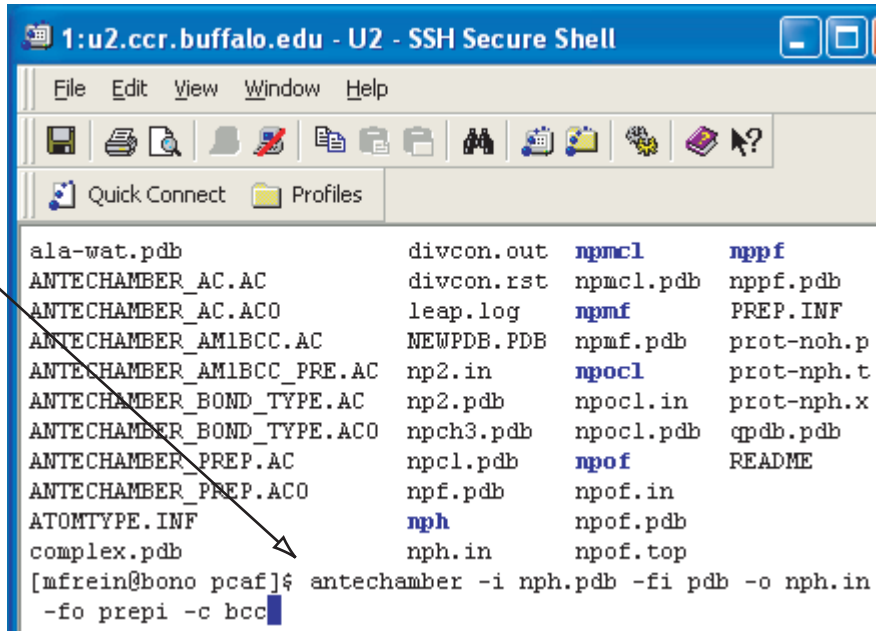
PDB file of the ligand, should have the residue name: QMM



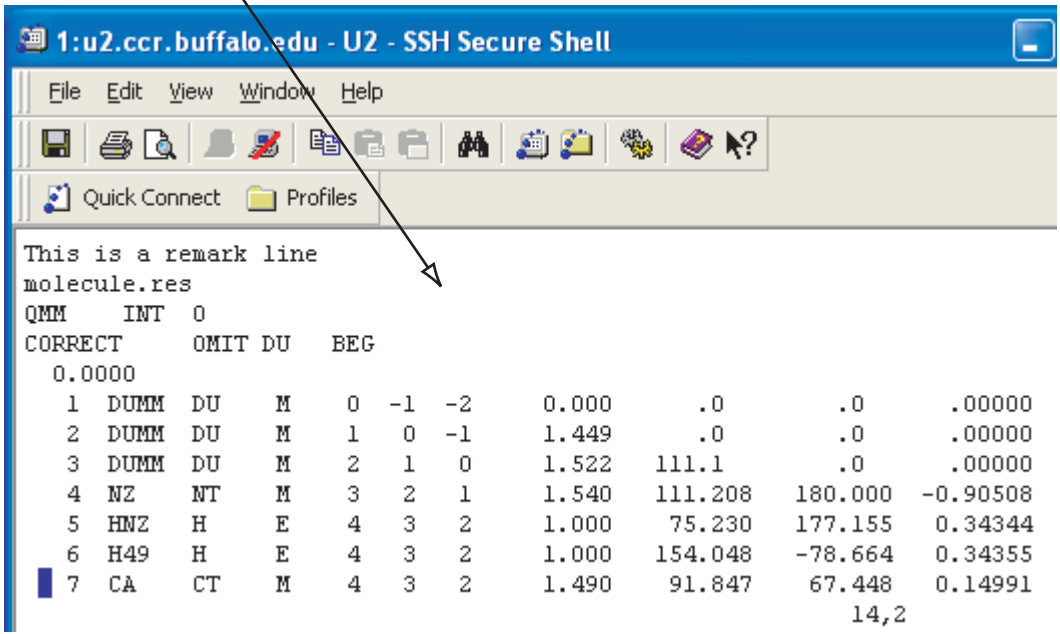
The ligand with hydrogen atoms



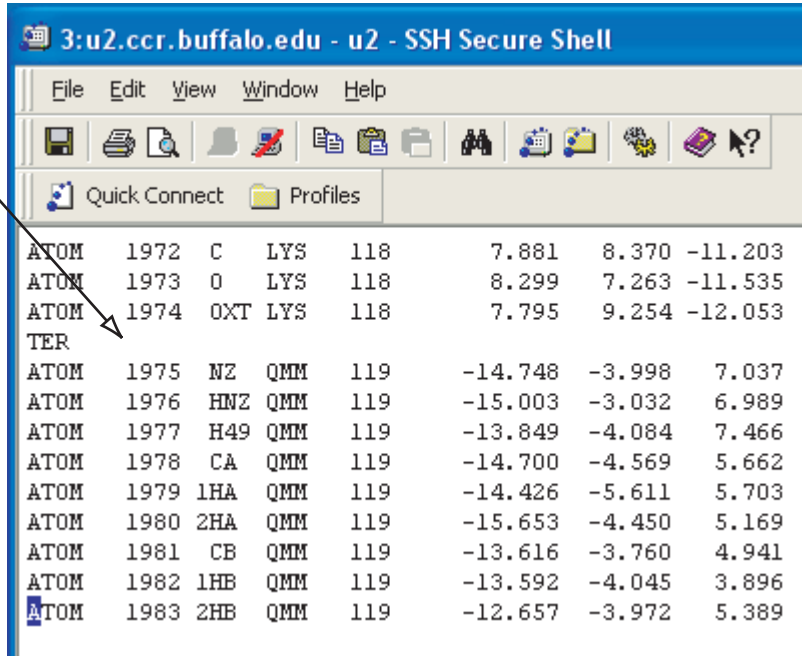
Antechamber program creating the preparations file of the ligand



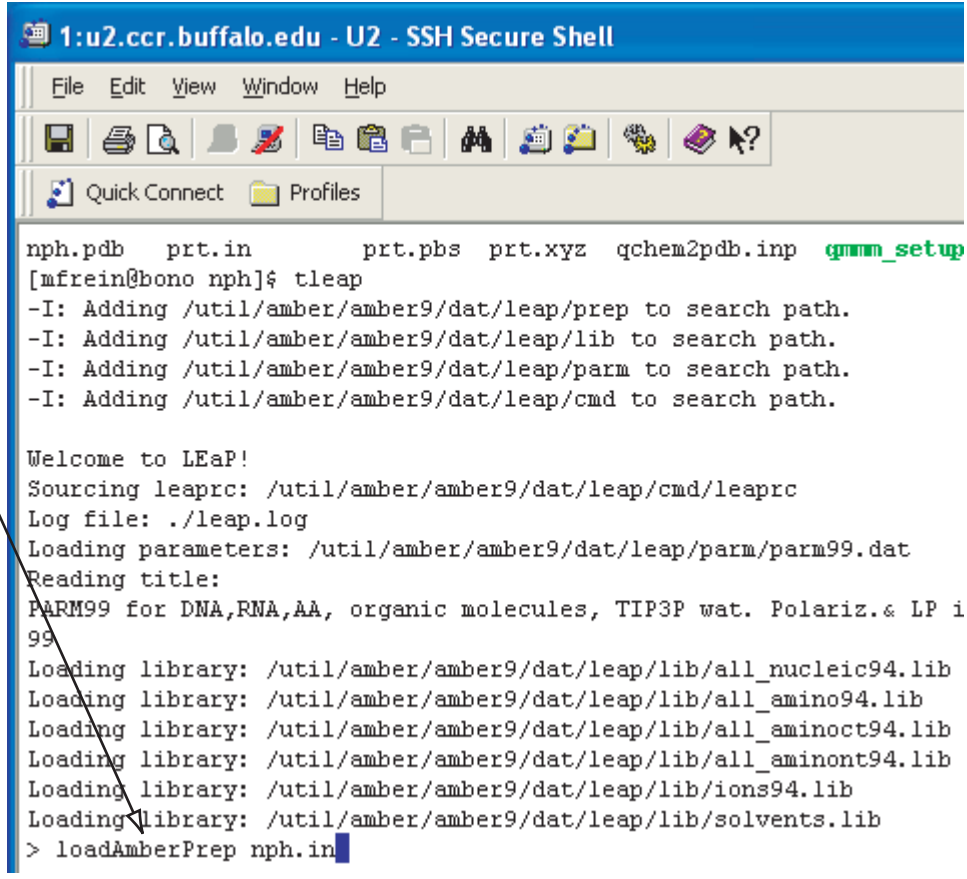
The preparation file, generated by the "antechamber" program



Merging the pdb structure of the ligand with the pdb structure of the protein

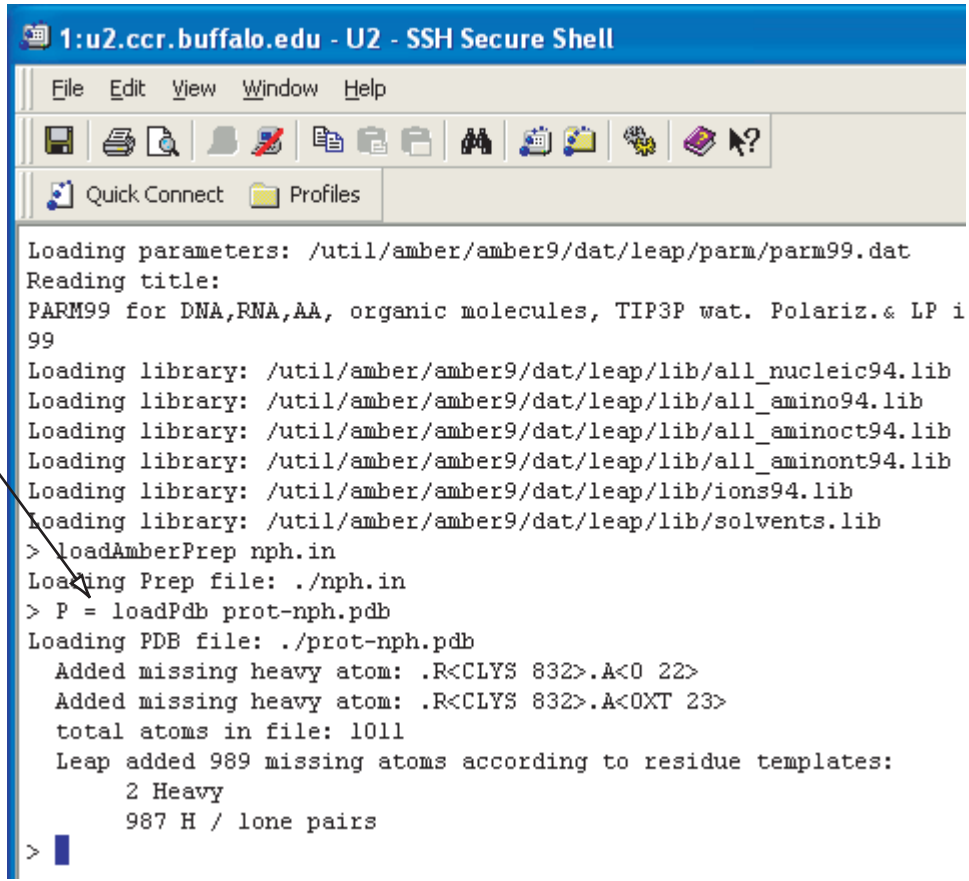


The "tleap" program reading the preparation file



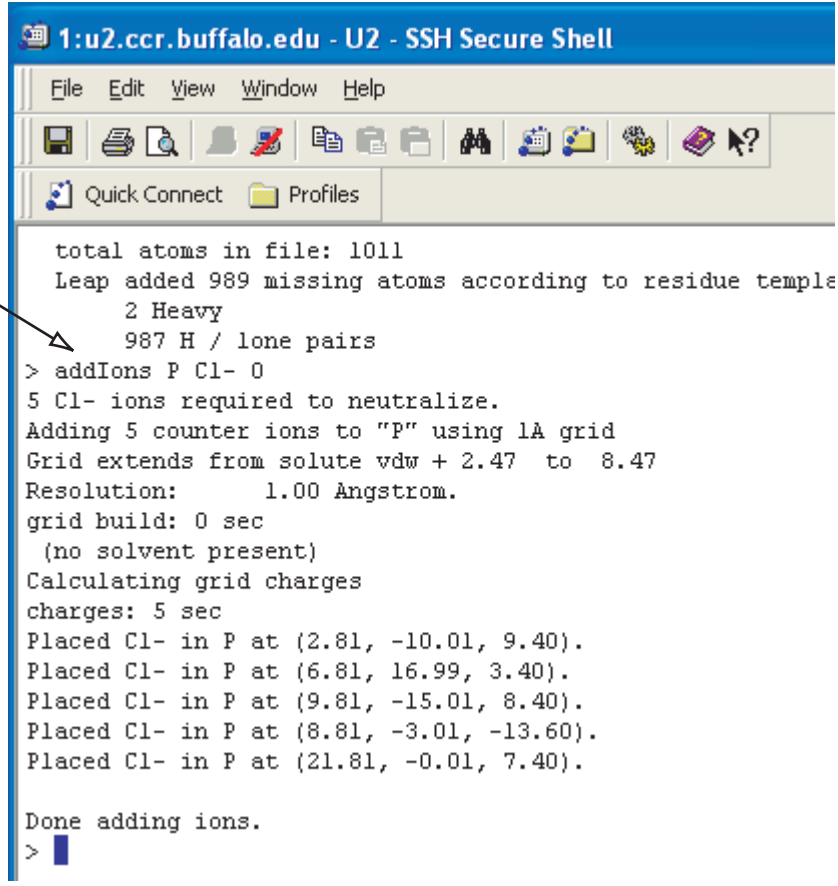
QM/MM calculations of active site of PCAF

The "tleap" program reading the PDB file of the protein and the ligand

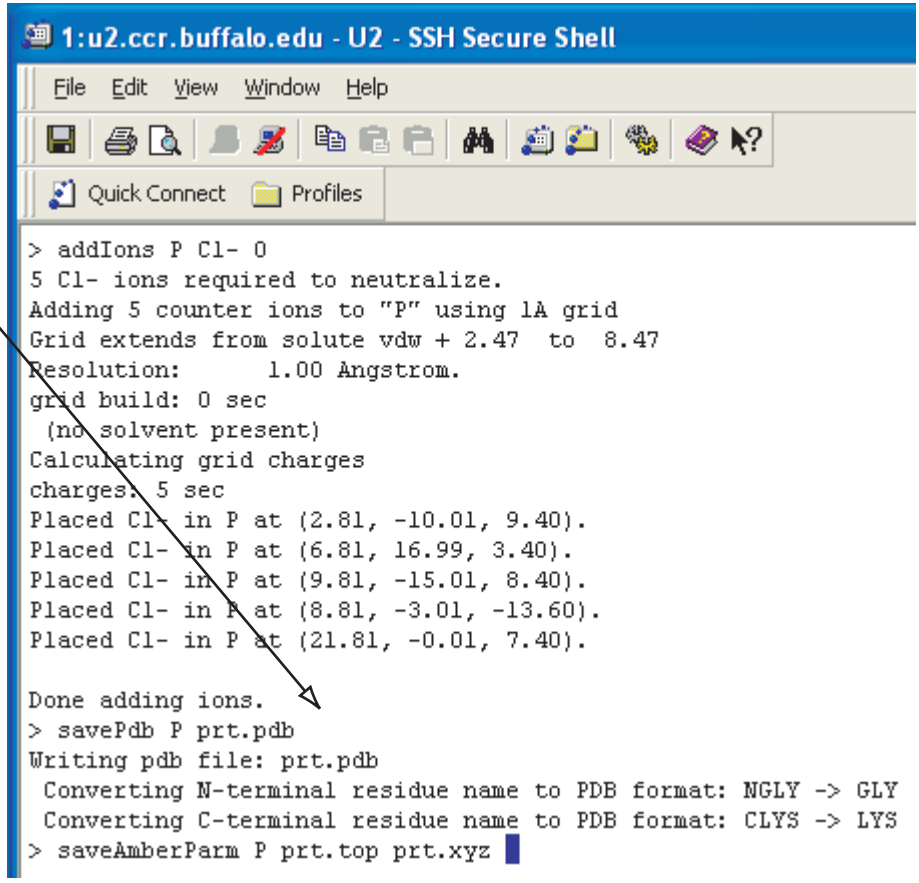


QM/MM calculations of active site of PCAF

The "tleap" program adding Chlorine anions for neutralization

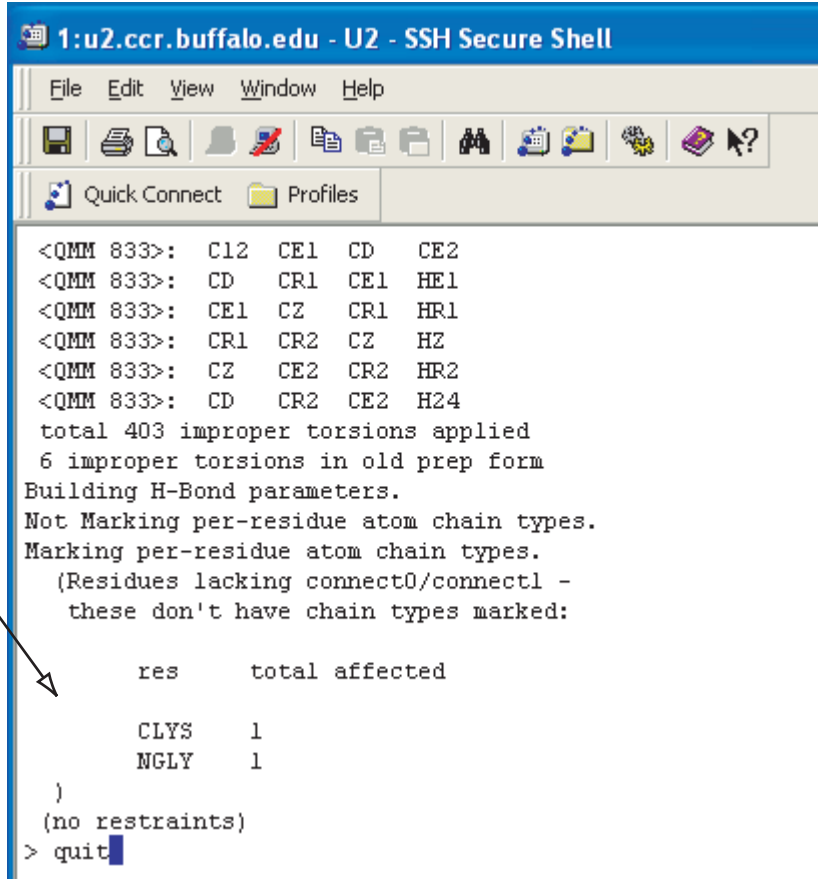


The "tleap" program saving the PDB file, the topology file and the coordinates file



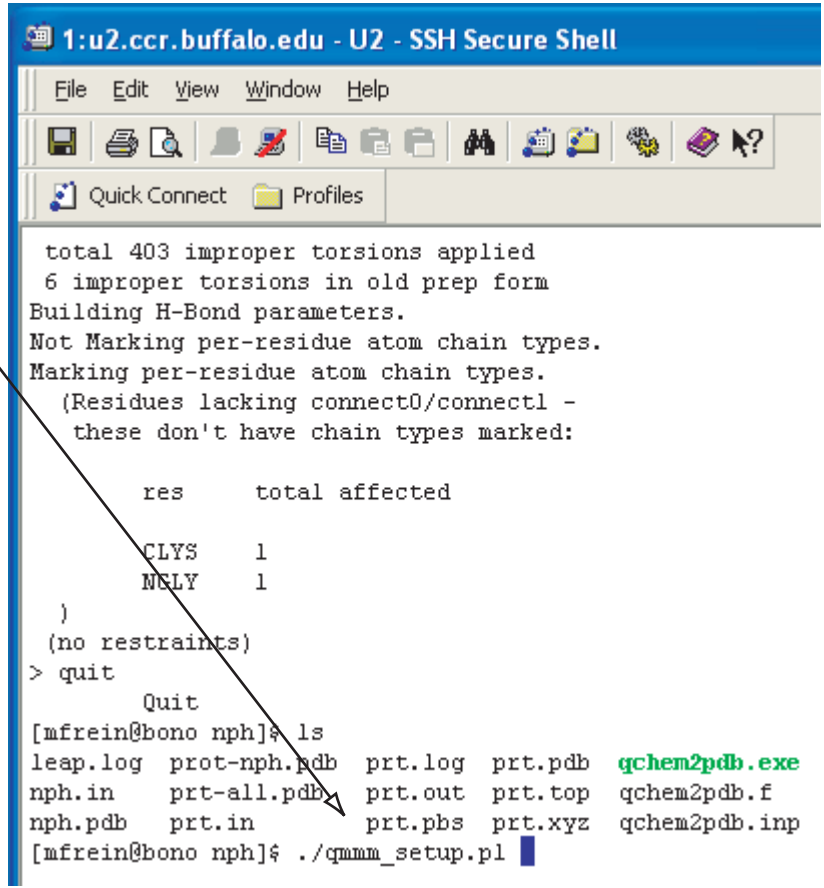
QM/MM calculations of active site of PCAF

Quiting the "tleap" program



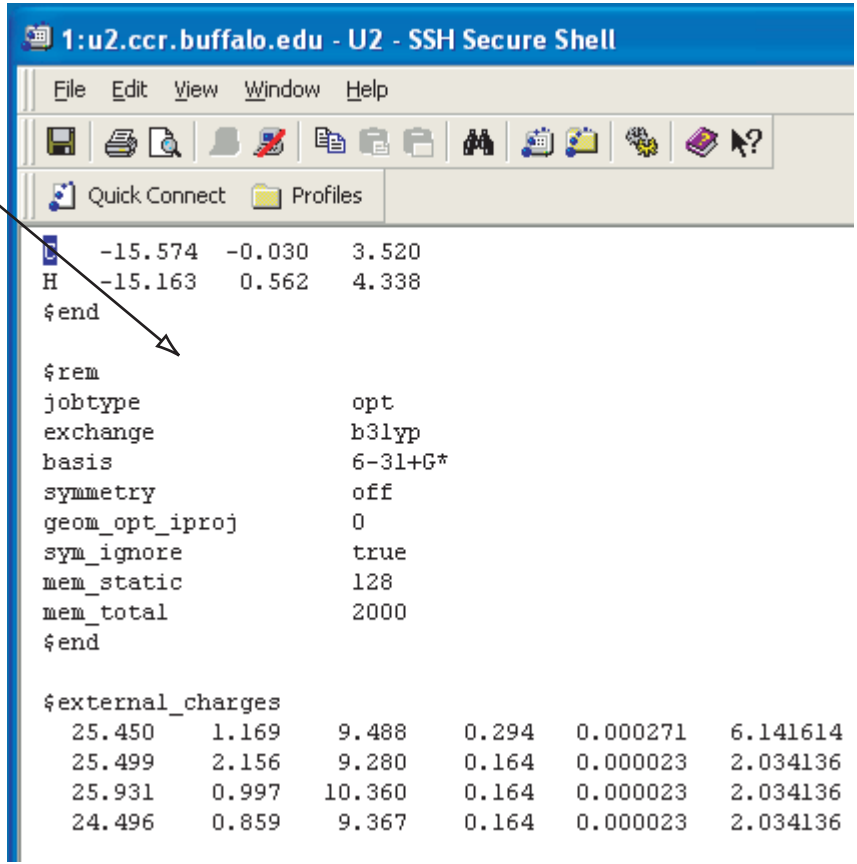
QM/MM calculations of active site of PCAF

Running the "perl" script generating the input file for the QM/MM calculations



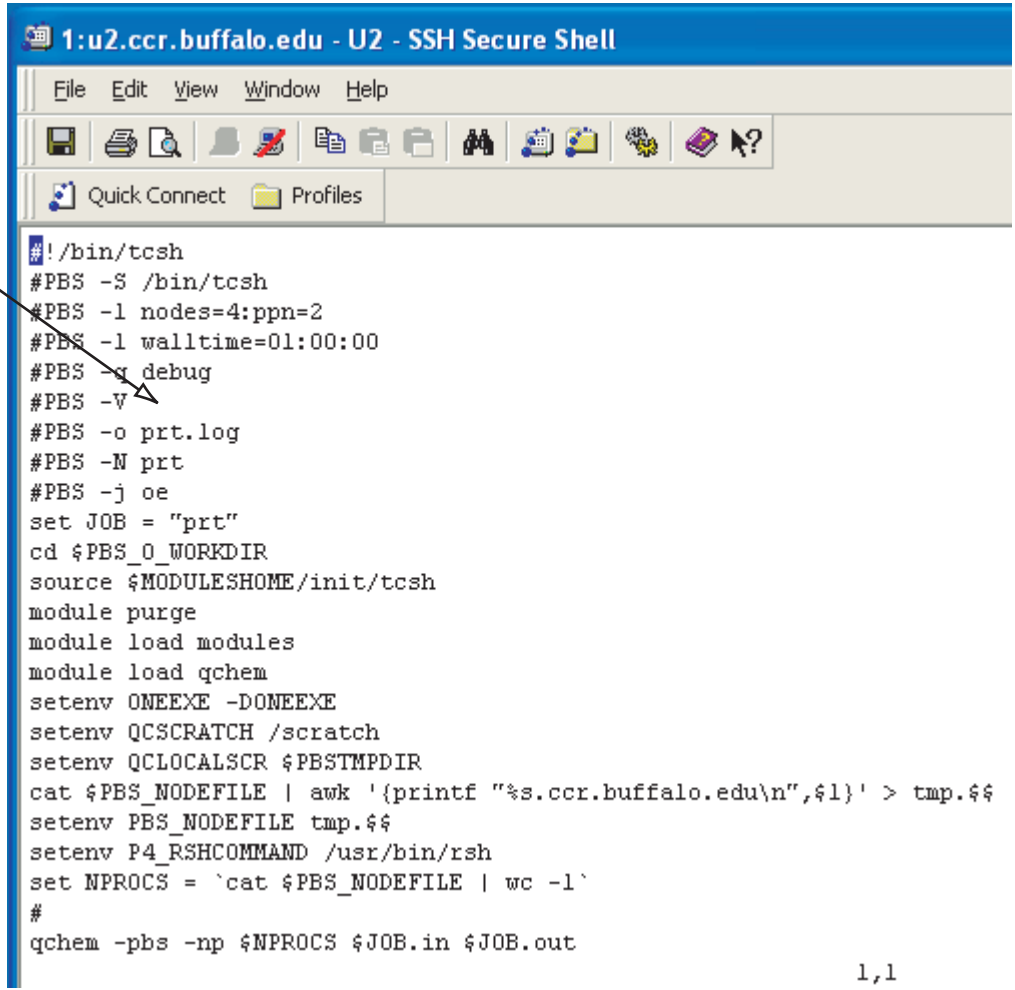
QM/MM calculations of active site of PCAF

The input file for the QM/MM calculations



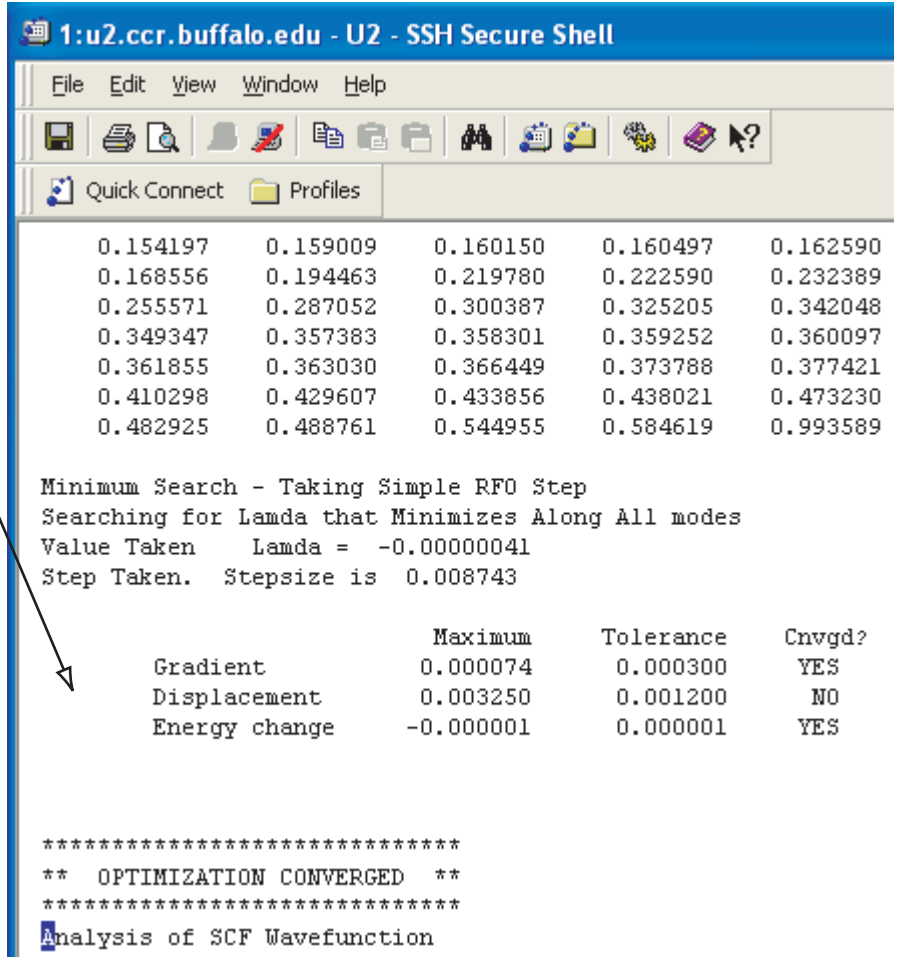
QM/MM calculations of active site of PCAF

The PBS script for the QM/MM calculations



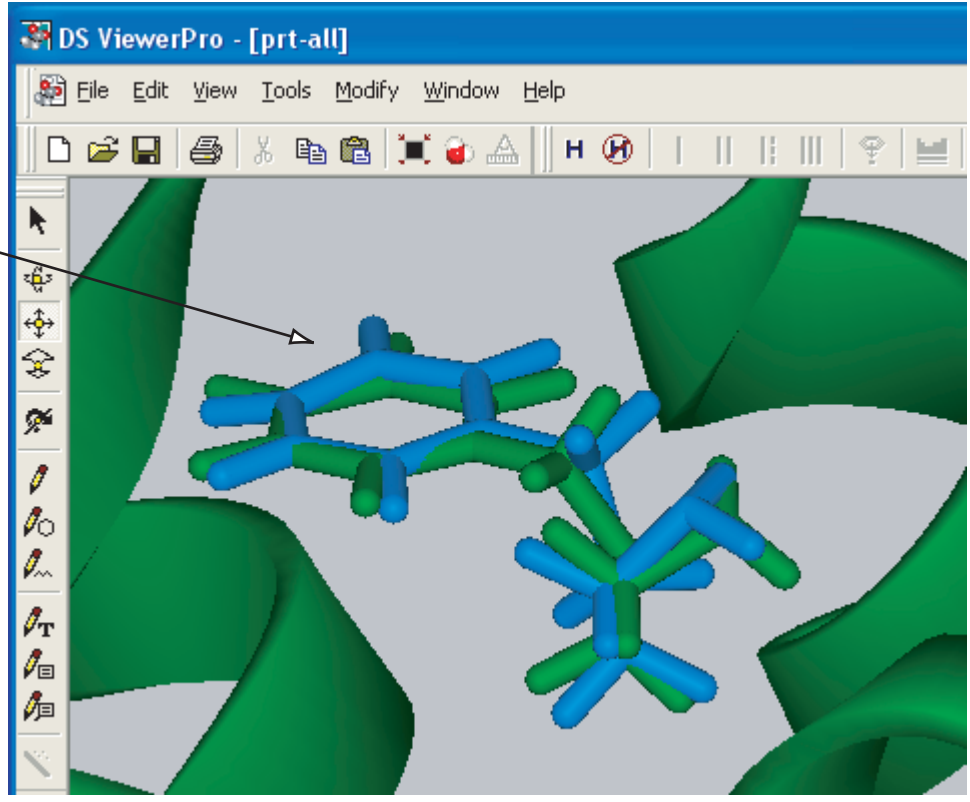
QM/MM calculations of active site of PCAF

Final results of the QM/MM calculations

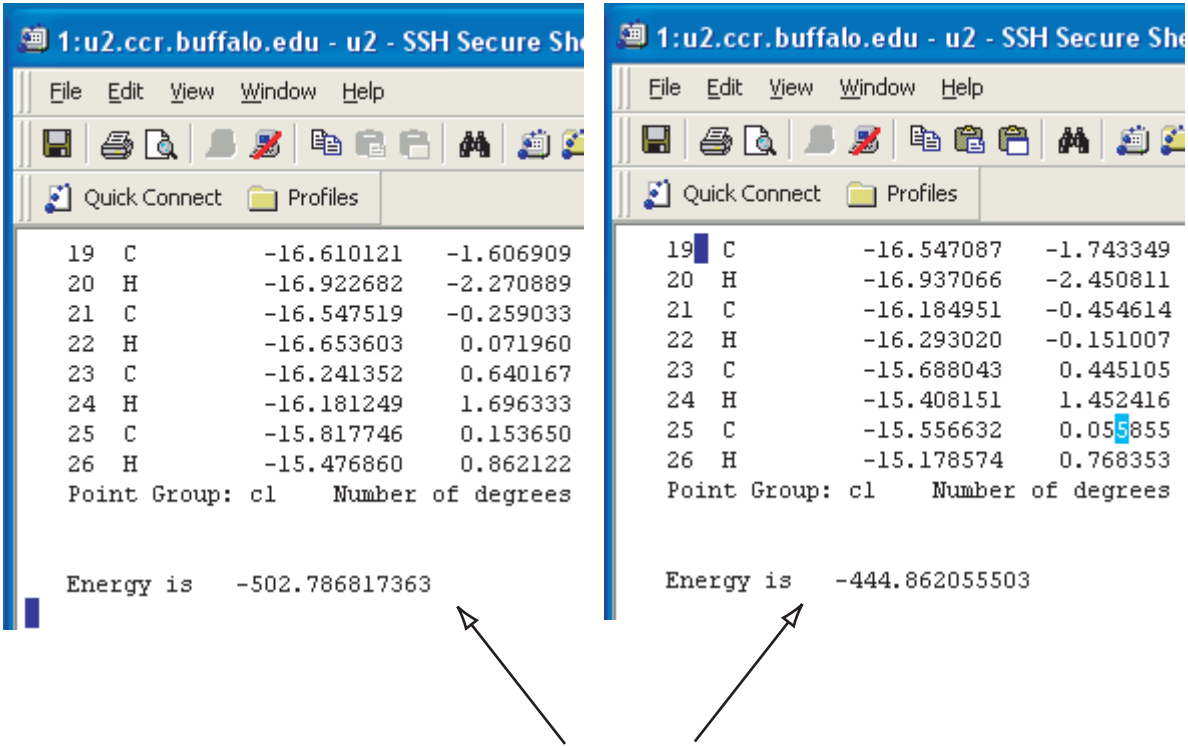


QM/MM calculations of active site of PCAF

The optimal calculated geometry of the ligand (blue) compared with the initial experimental geometry of the ligand (green)

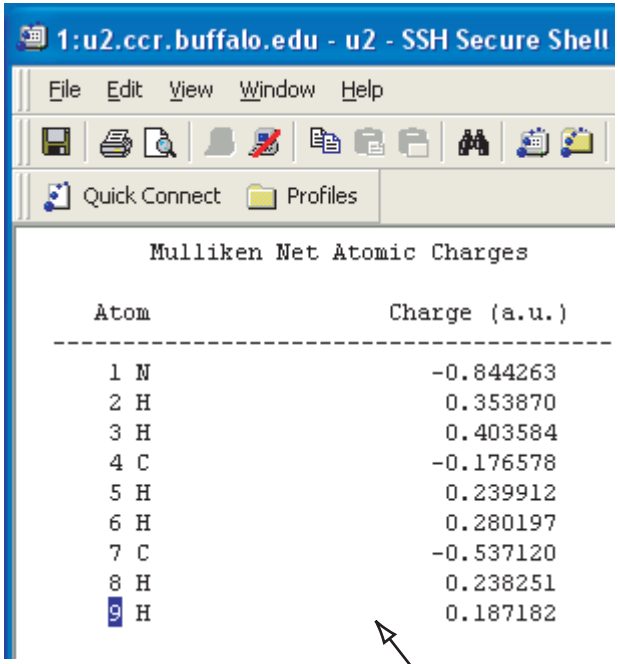


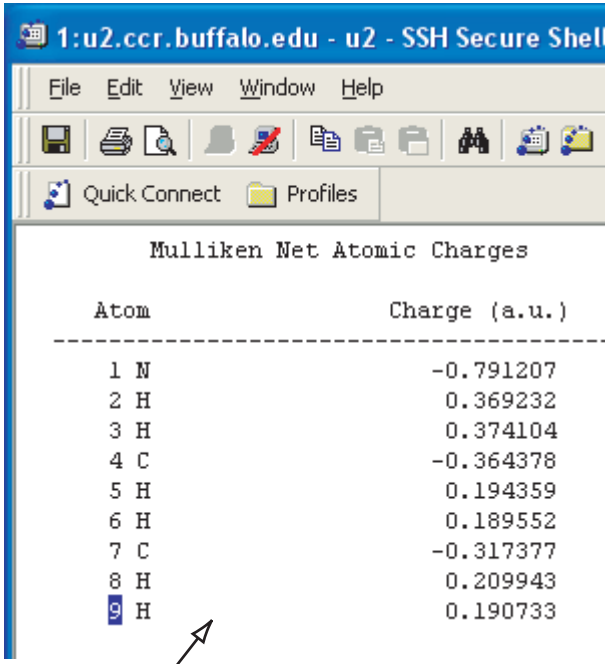
QM/MM calculations of active site of PCAF



Total energy of the ligand in the protein (left) and in the gas phase (right)

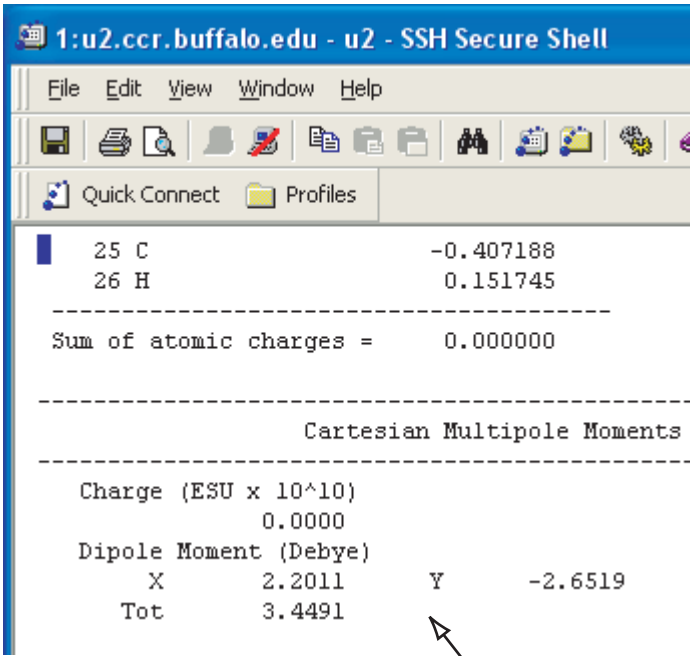
QM/MM calculations of active site of PCAF

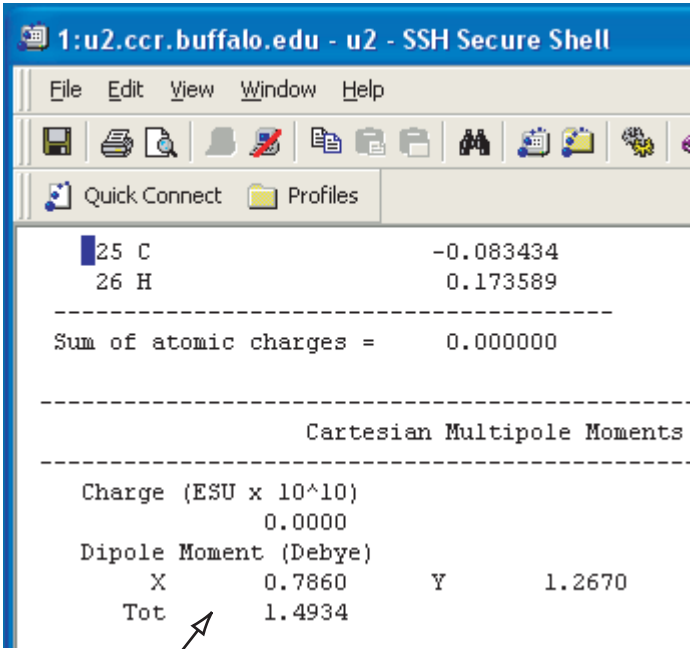




Atomic charges of the ligand in the protein (left) and in the gas phase (right)

QM/MM calculations of active site of PCAF

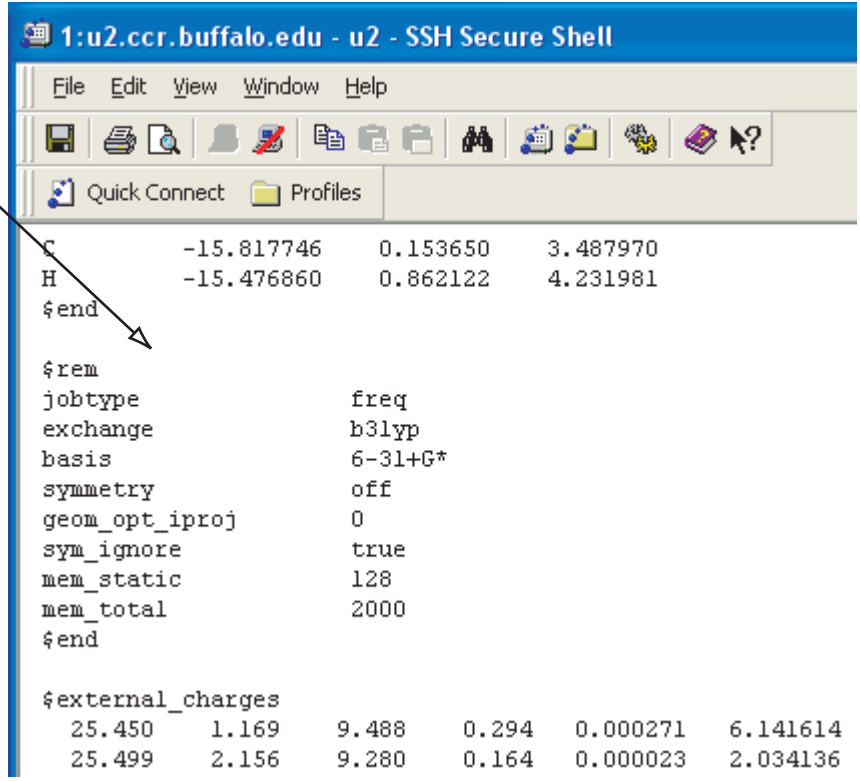




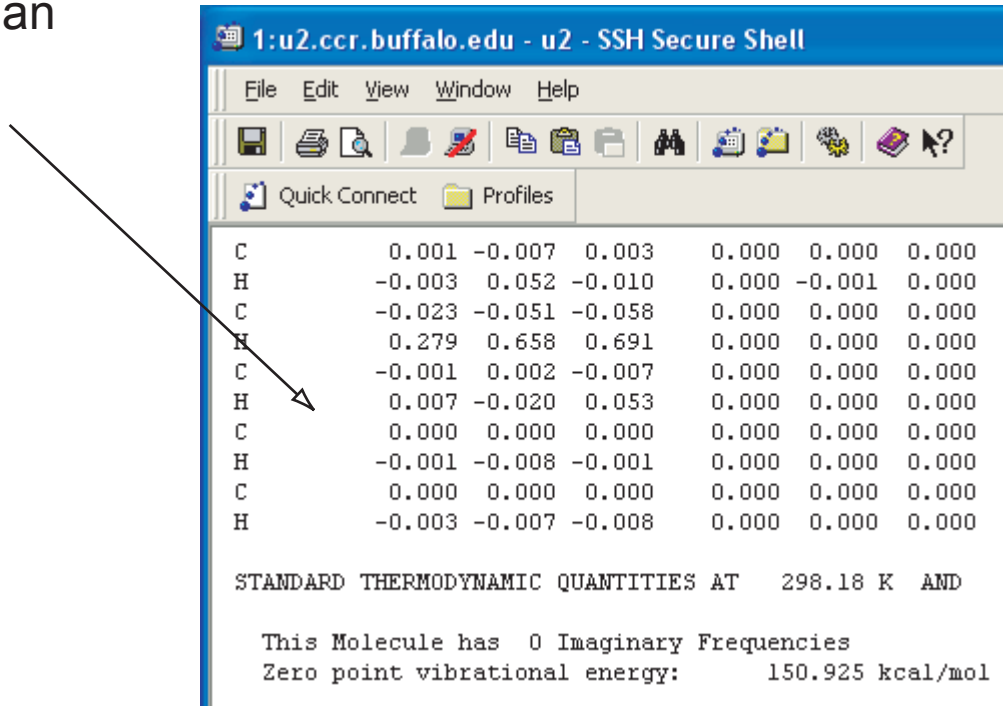
Dipole moment of the ligand in the protein (left) and in the gas phase (right)

QM/MM calculations of active site of PCAF

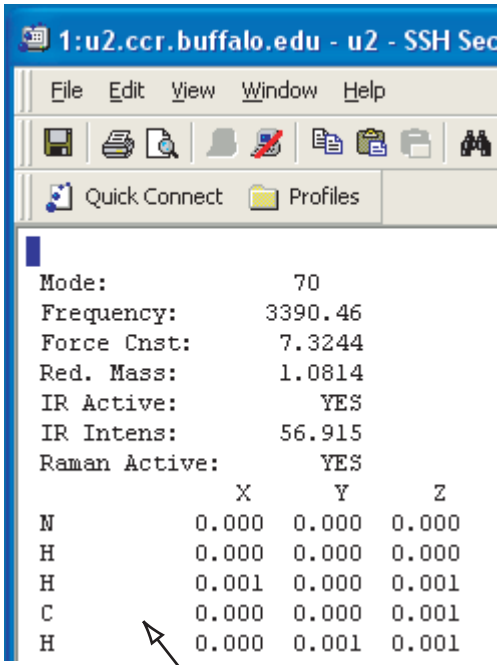
Molecular oscillation calculations of the ligand inside the protein

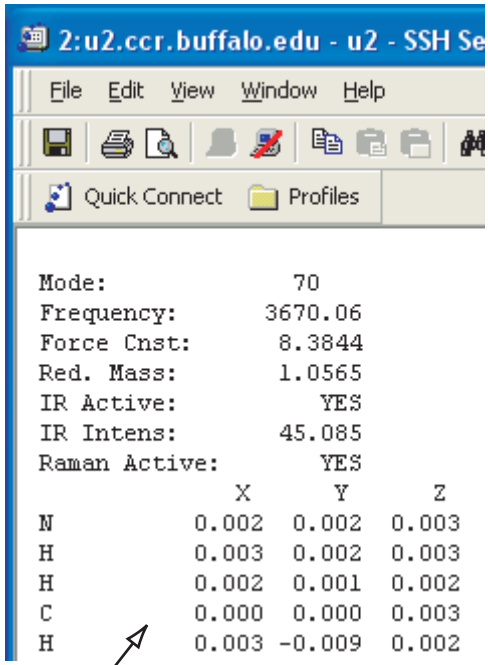


Final results of the oscillation hessian calculations



QM/MM calculations of active site of PCAF

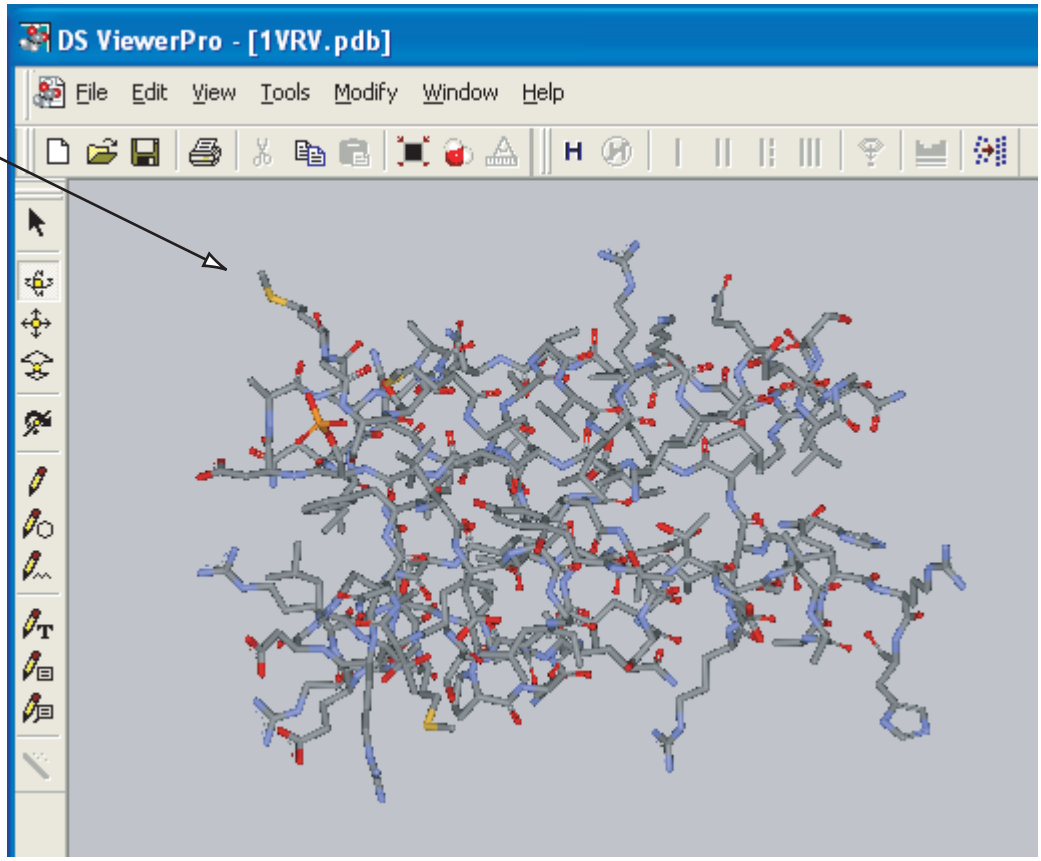




High frequency oscillations of the ligand in the protein (left) and in the gas phase (right)

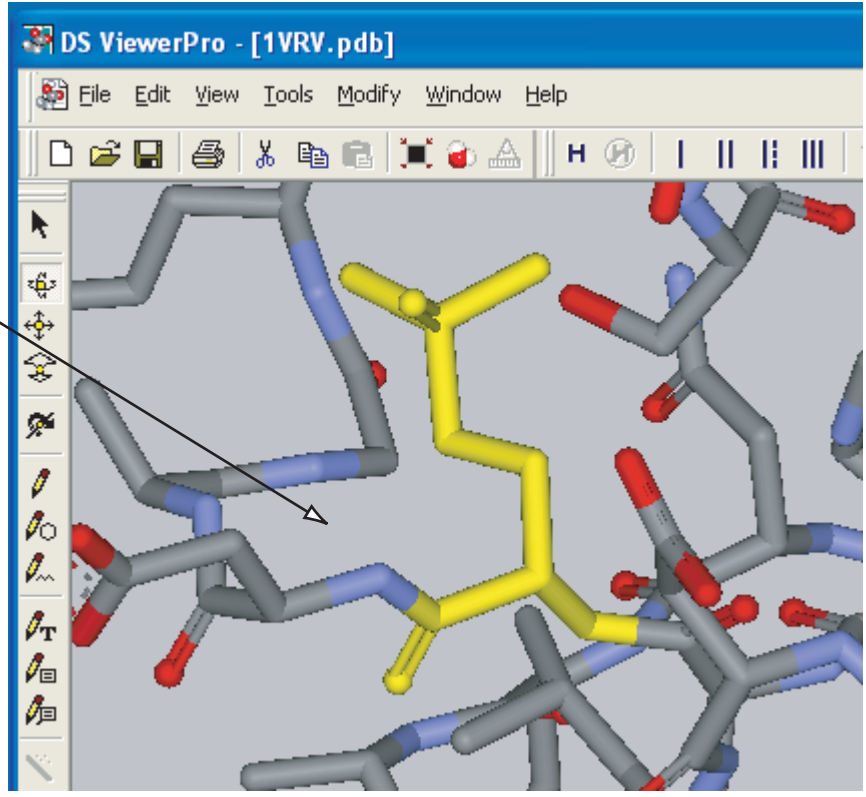
QM/MM calculations of active site of mannitol enzyme

Experimental structure of the mannitol enzyme



QM/MM calculations of active site of mannitol enzyme

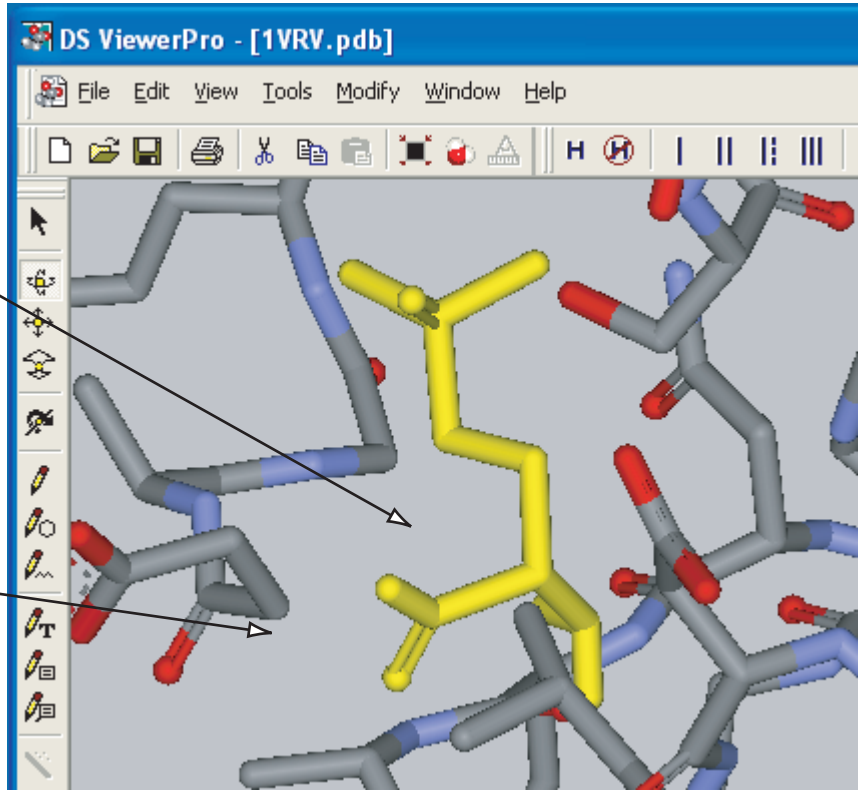
The active site of the enzyme, which is connected by two chemical bonds with the protein backbone



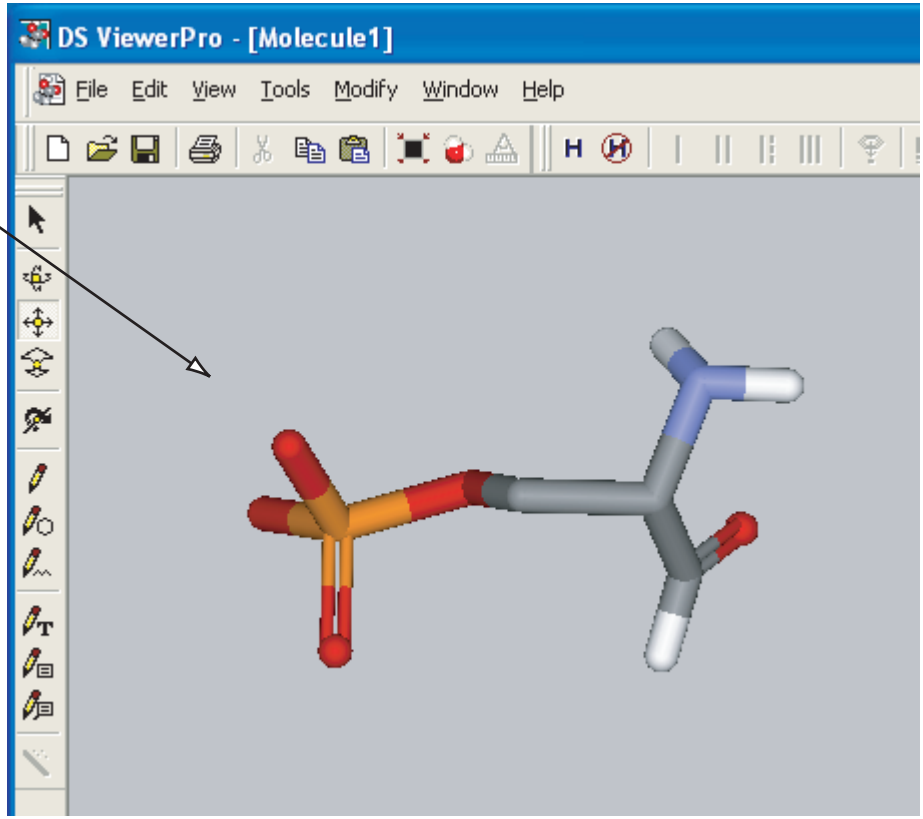
QM/MM calculations of active site of mannitol enzyme

Two chemical bonds have been cut, and free chemical valences of the active site have been filled out by hydrogens

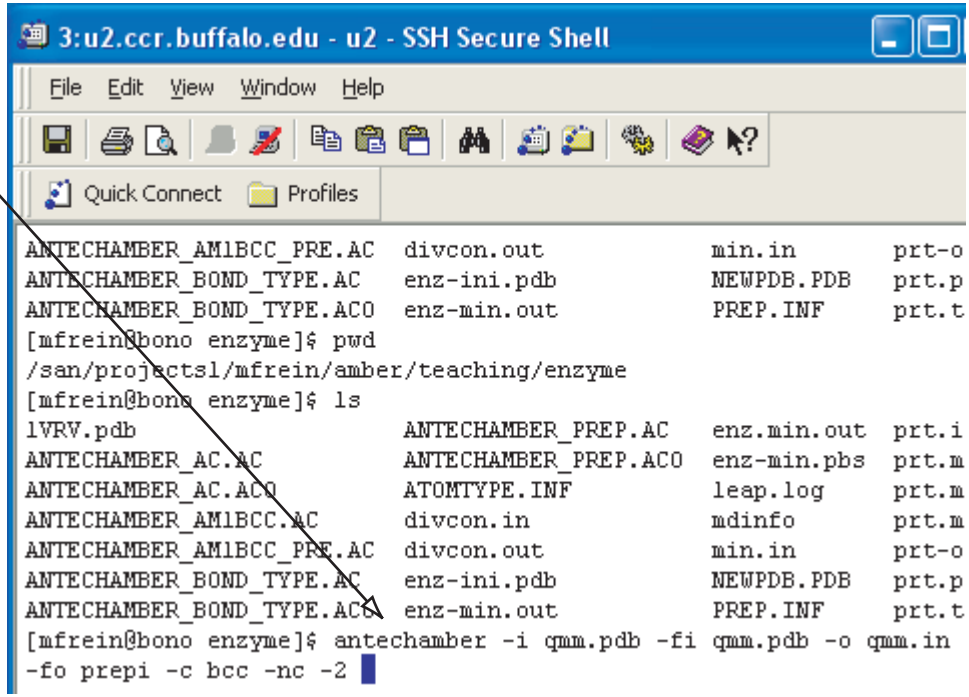
Heavy atoms from both sides of the backbone have been removed



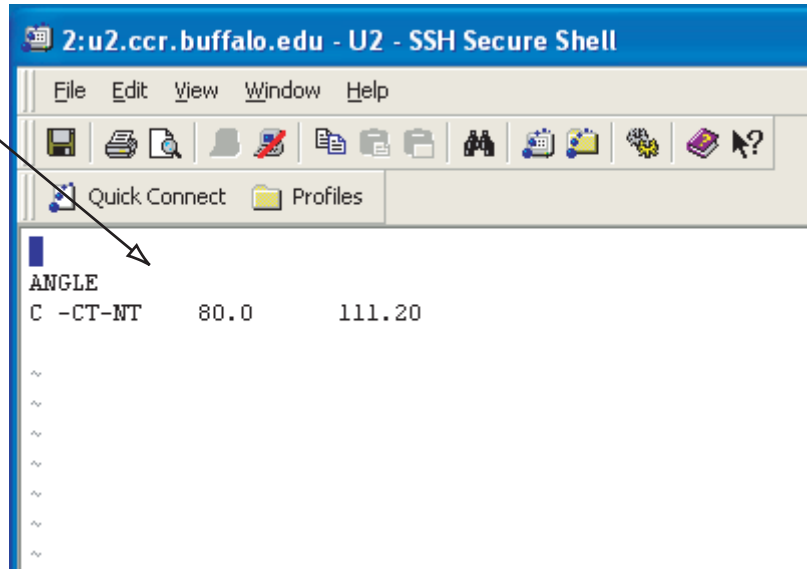
The active site of the enzyme has been temporary separated from the protein structure



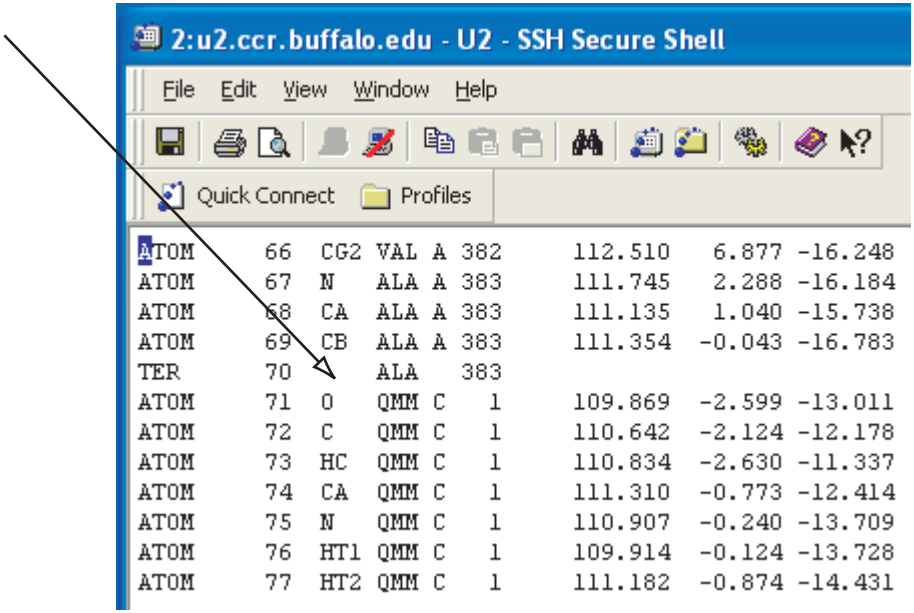
The "antechamber" program has been used to generate the preparation file of the active site



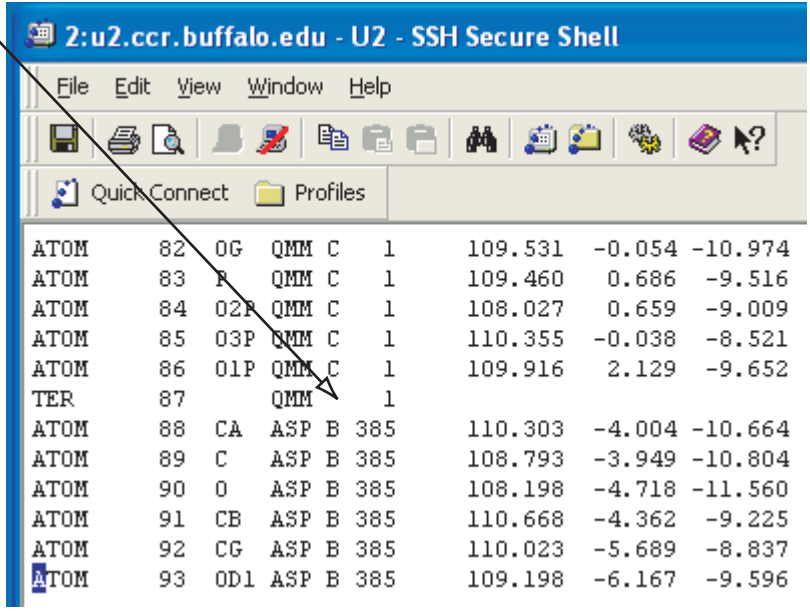
Missing parameters of the active site have been included in the parameter file



The new pdb structure of the active site has been merged with the protein structure

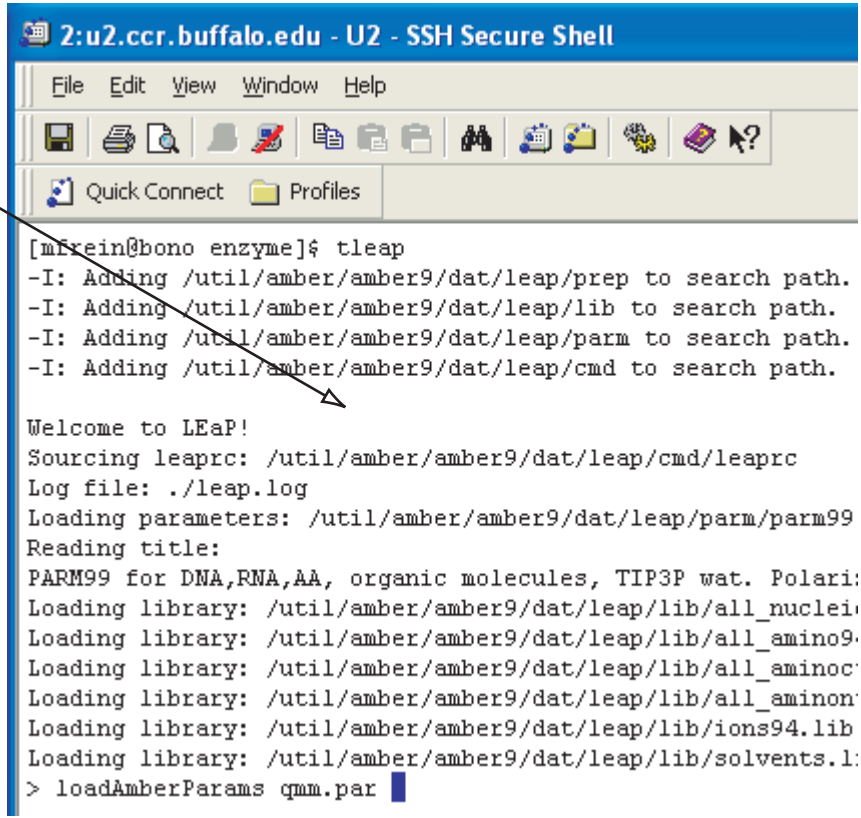


The main backbone of the protein has been divided into three chains

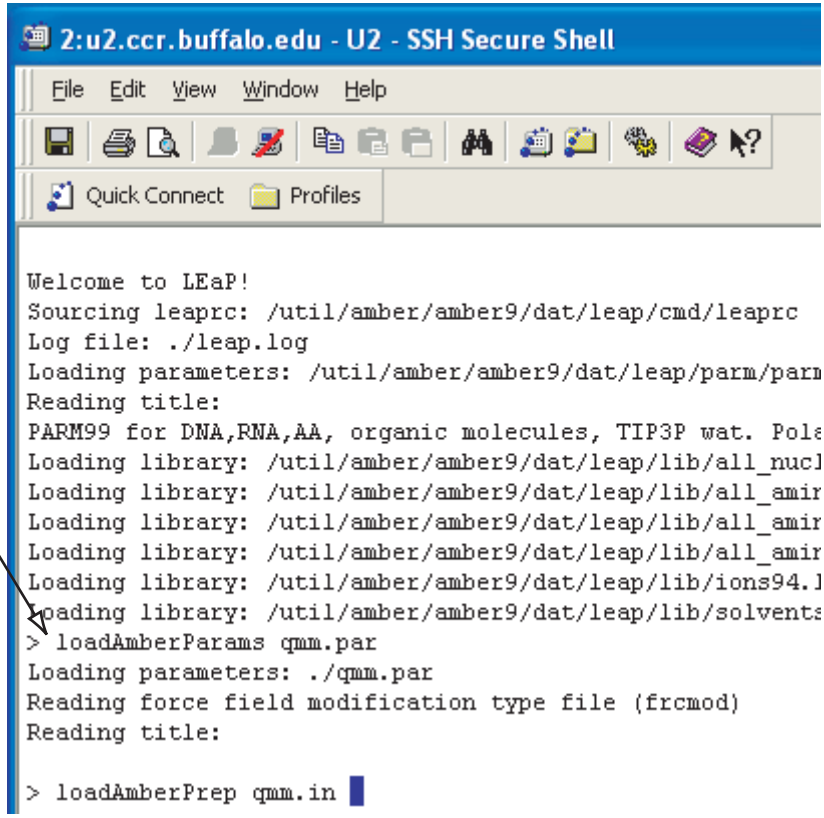


QM/MM calculations of active site of mannitol enzyme

The"tleap" program has been used to generate the topology and PDB file of the enzyme with the modified active site

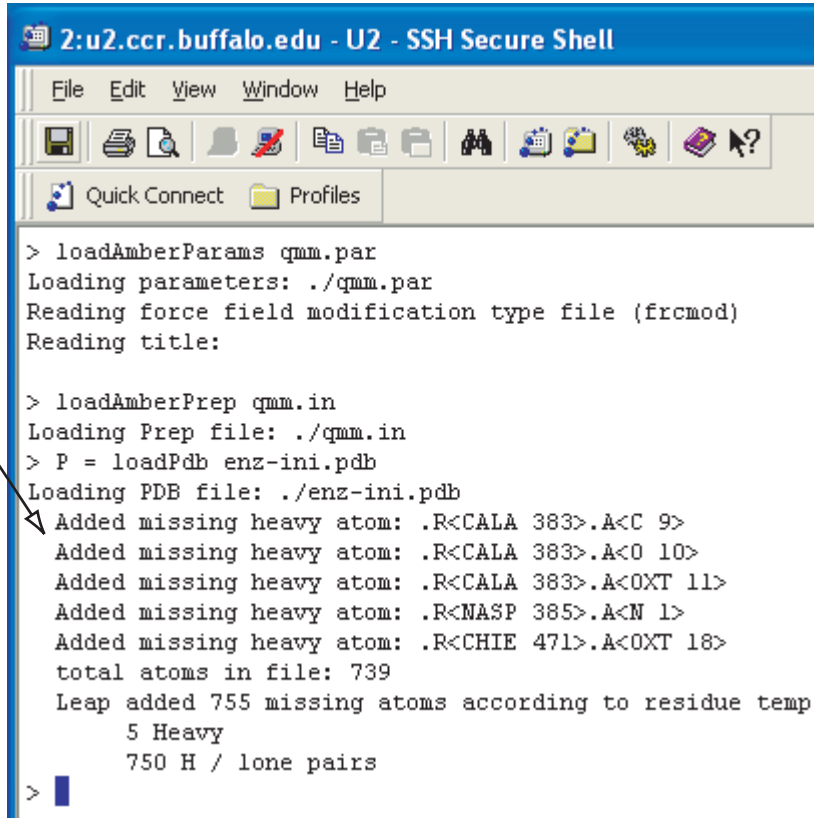


First the parameter and the preparation files of the active site have been loaded

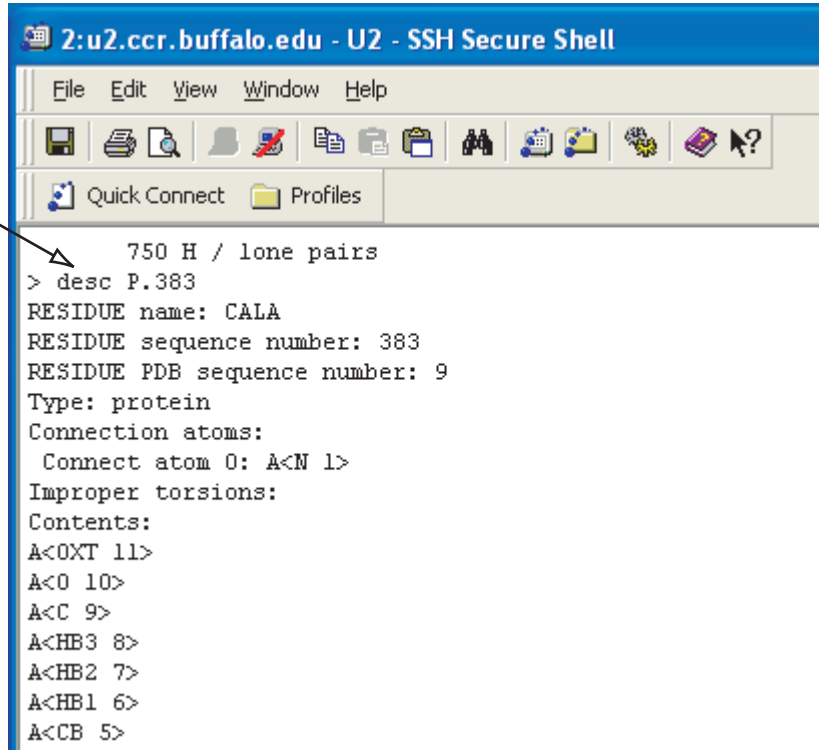


QM/MM calculations of active site of mannitol enzyme

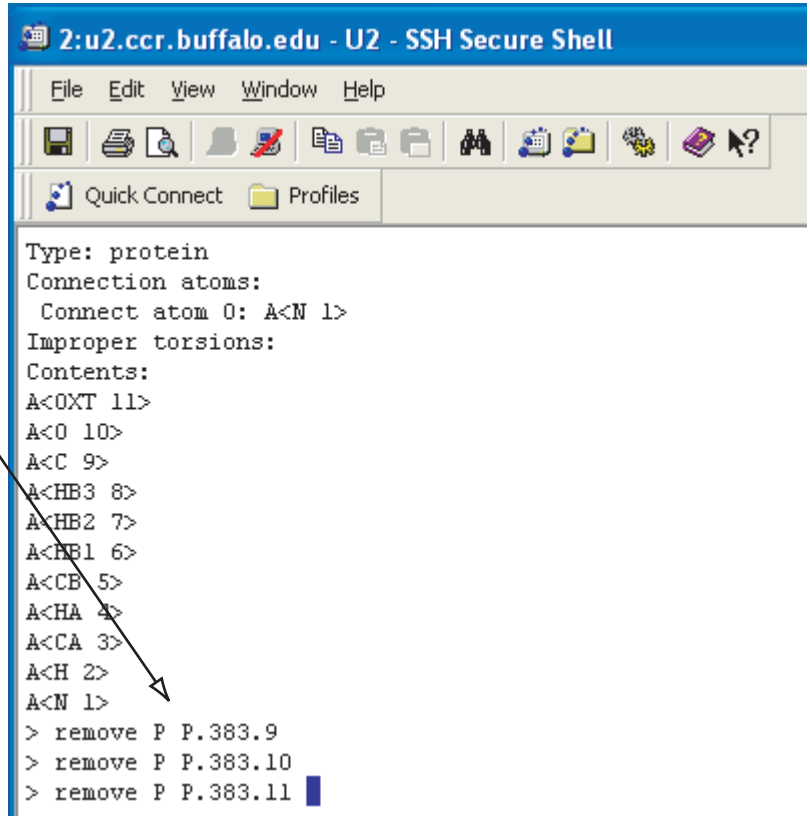
After loading the PDB file of the system, the program generated additional atoms



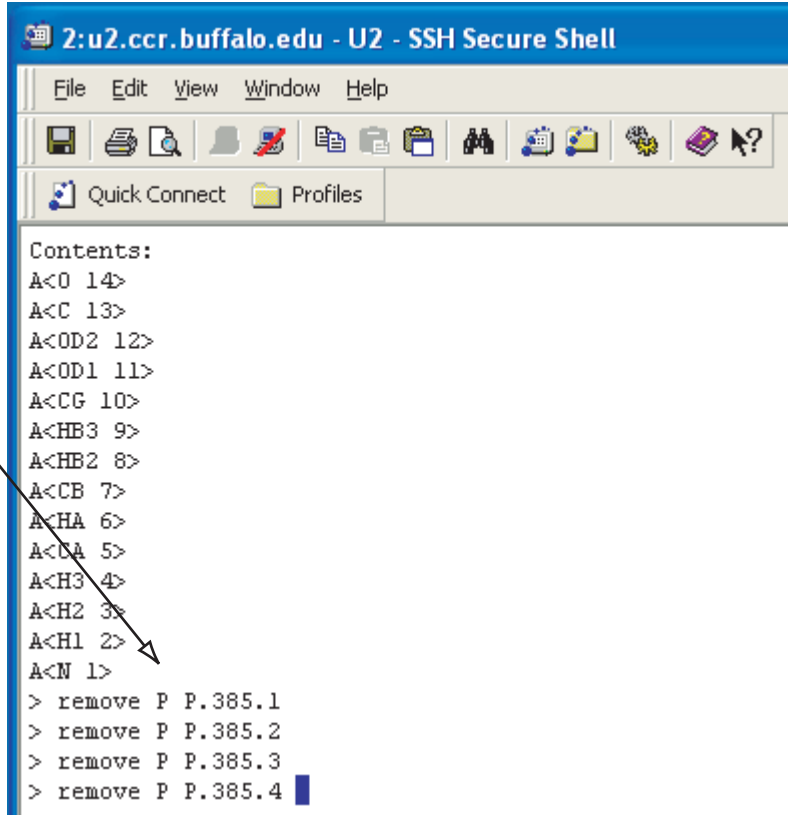
The "desc" command has been used for description of the ALA residue



The "remove" command has been used to delete atoms between the protein and the active site

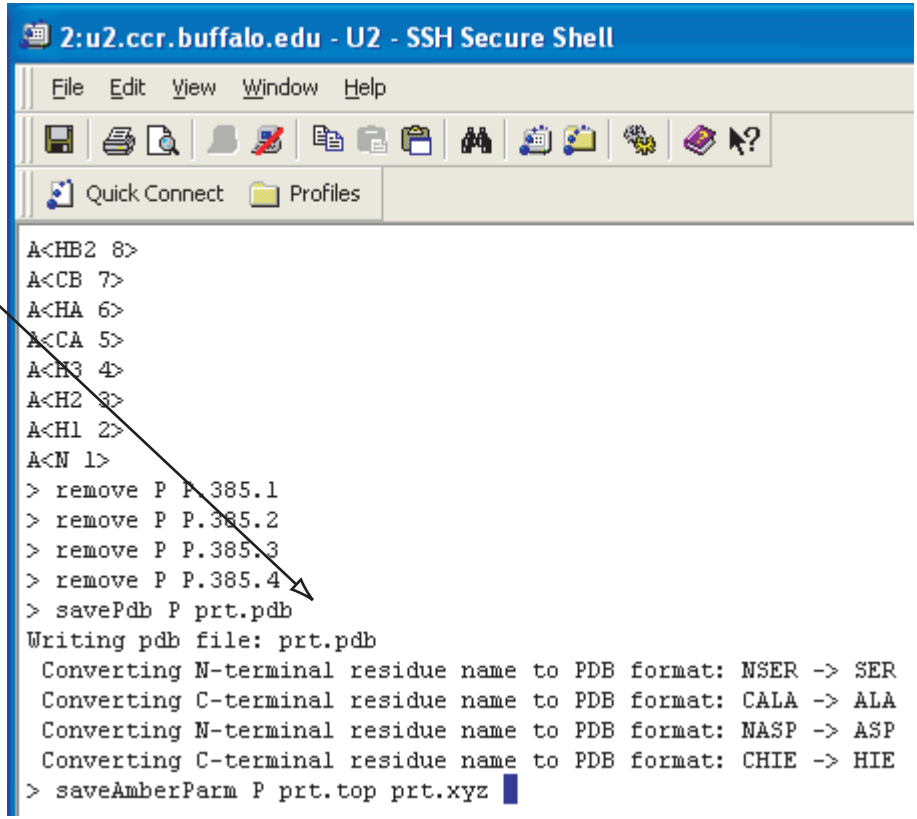


In the similar way, protein atoms from the other side of the active site have been removed

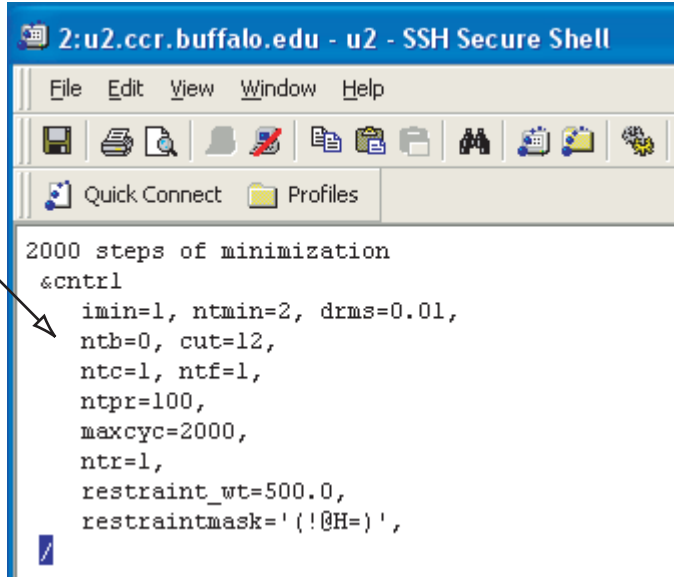


QM/MM calculations of active site of mannitol enzyme

The PDB file, the topology file and the coordinates file have been saved

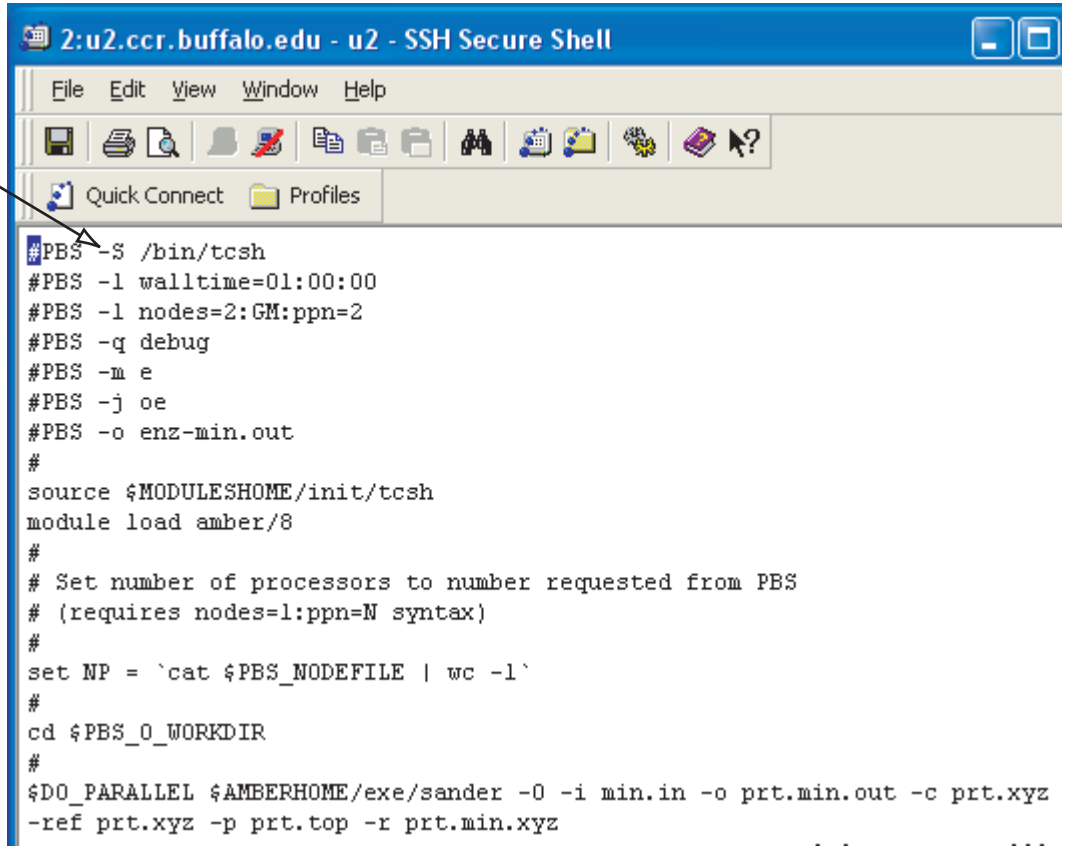


The input file for minimization of all hydrogens

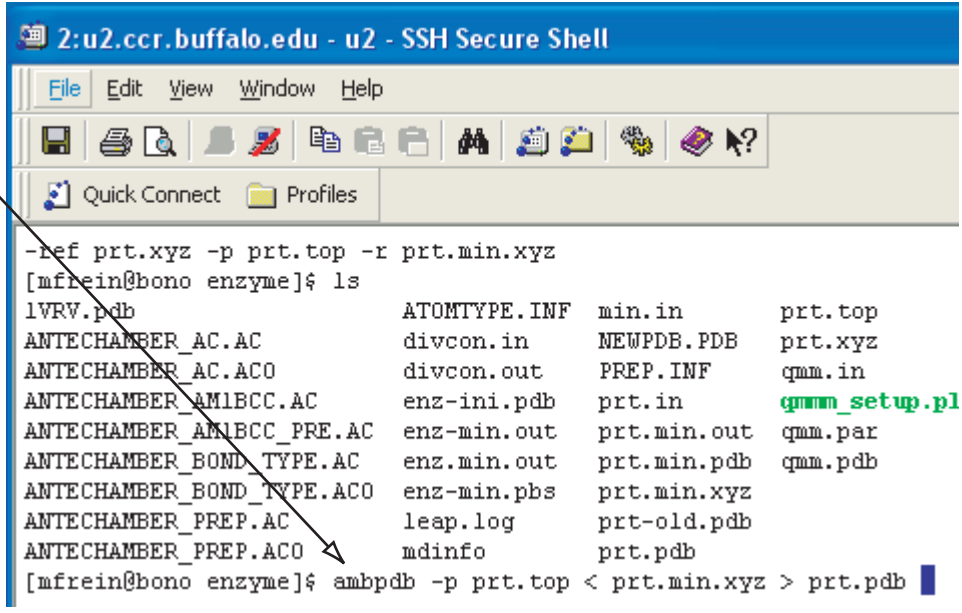


QM/MM calculations of active site of mannitol enzyme

The pbs script for minimization

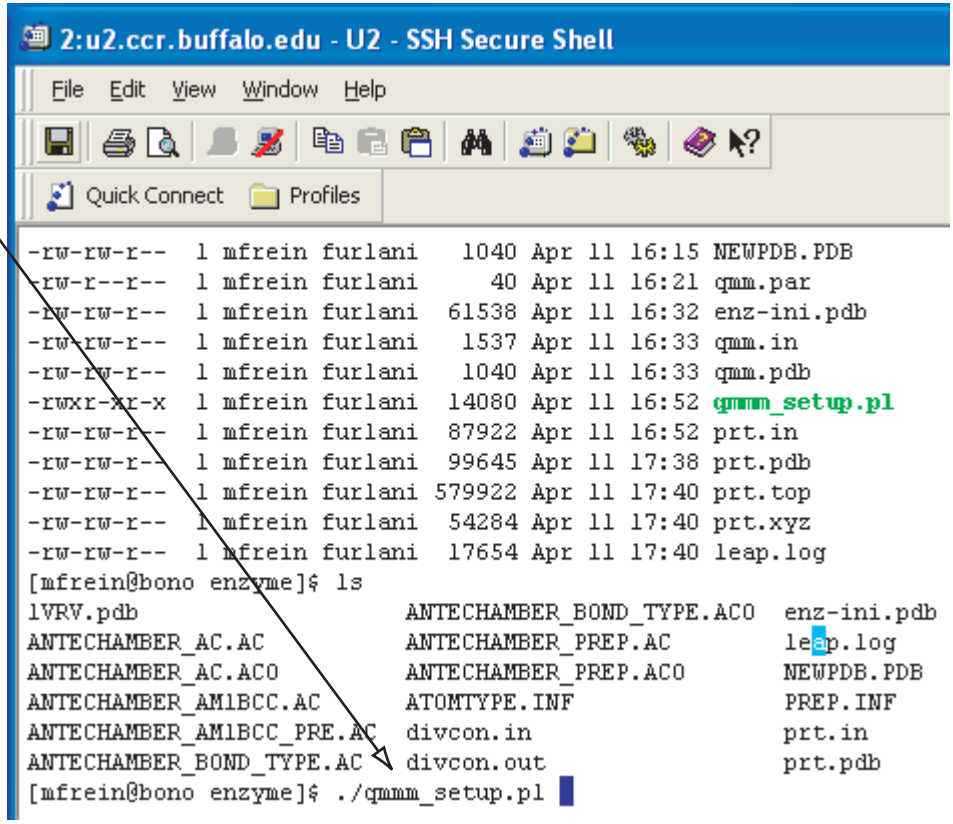


Generating the pdb file from the minimized protein coordinates



QM/MM calculations of active site of mannitol enzyme

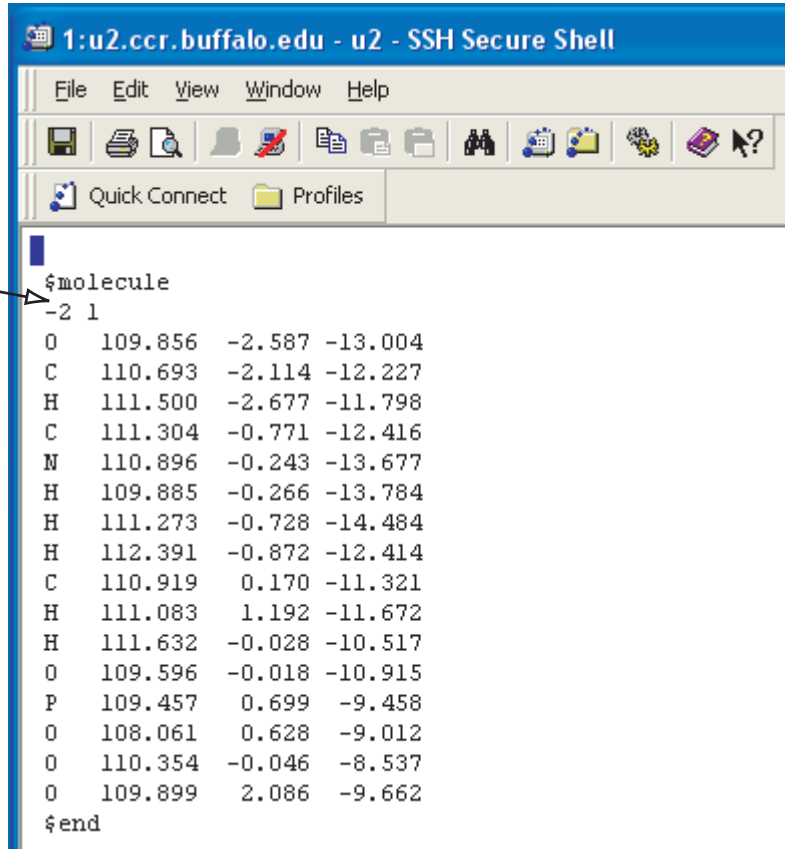
The "qmm_setup" perl script has been used to create the q-chem input file for the QM/MM calculations



QM/MM calculations of active site of mannitol enzyme

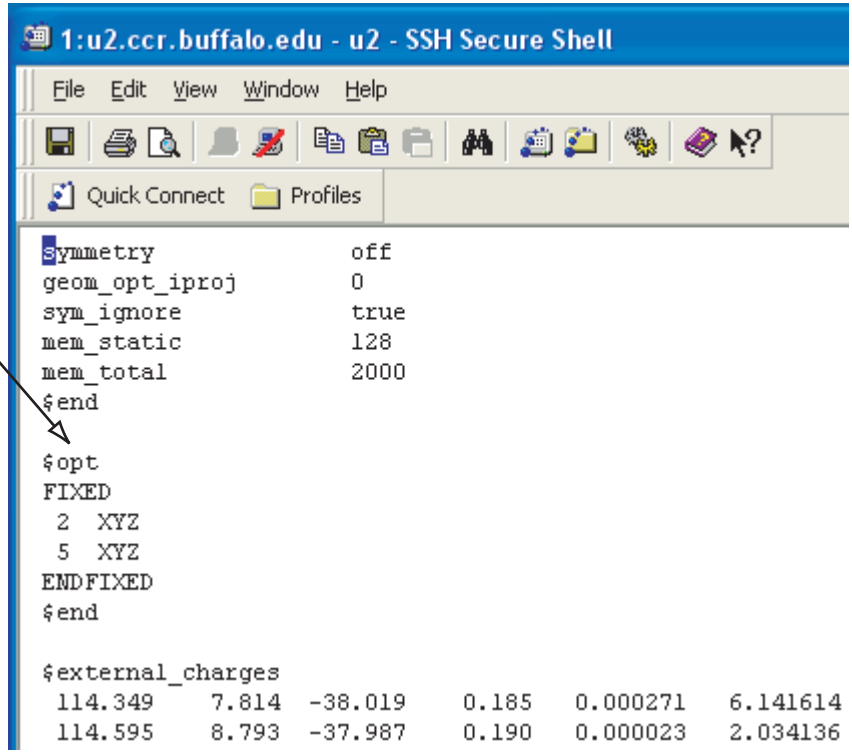
The q-chem input file for the QM/MM calculations

The charge of the molecule should be changed

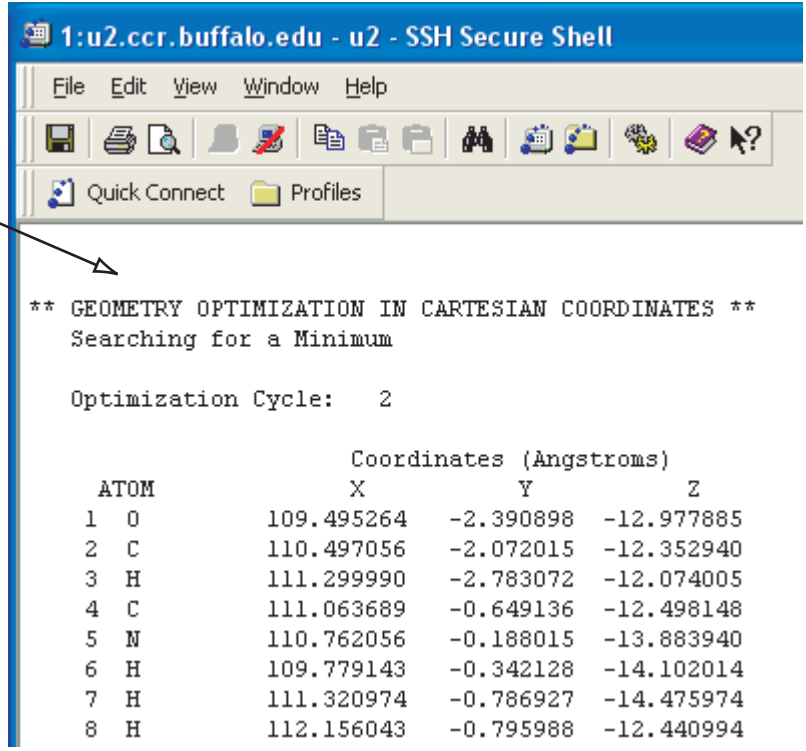


QM/MM calculations of active site of mannitol enzyme

The calculations with the fixed position of two atoms of the ligand

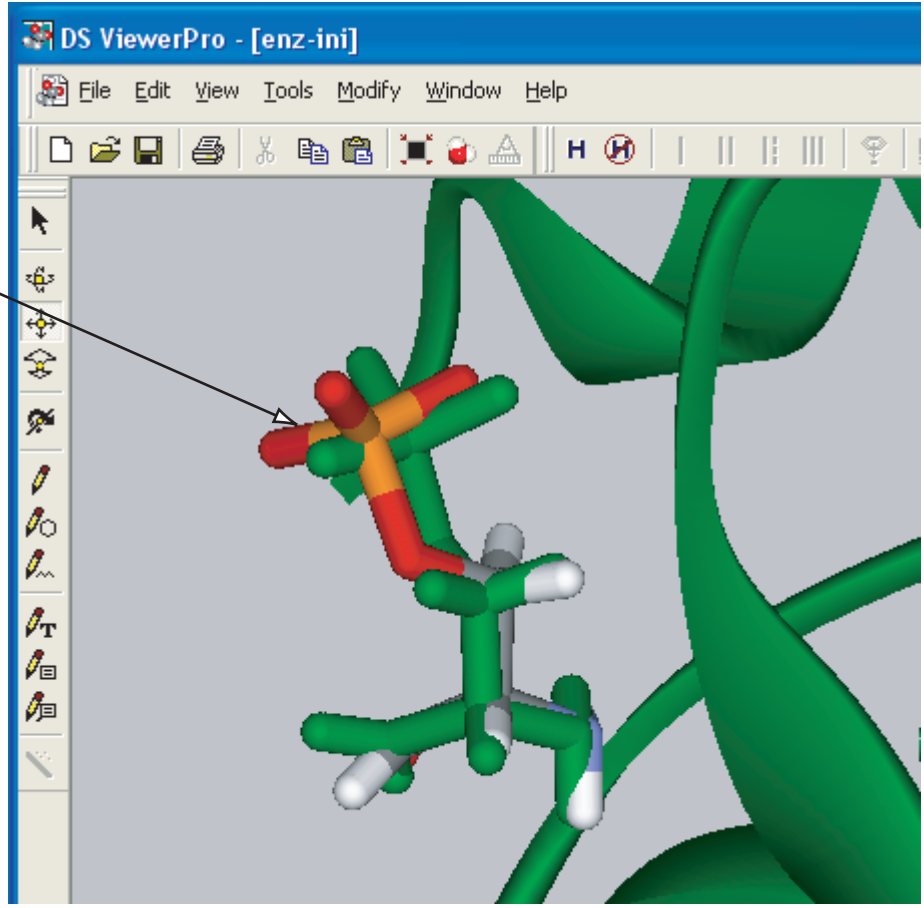


The geometry optimization in cartesian coordinates



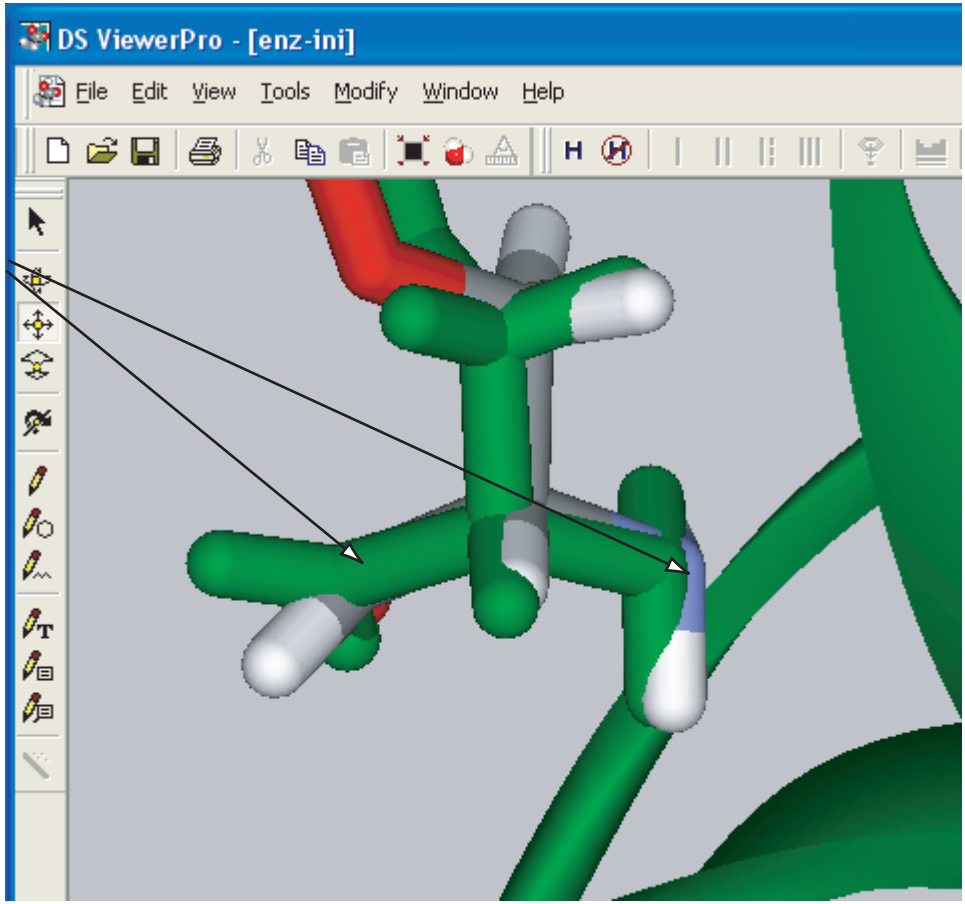
QM/MM calculations of active site of mannitol enzyme

The calculated optimal geometry and the initial experimental geometry (green) of the ligand in the protein



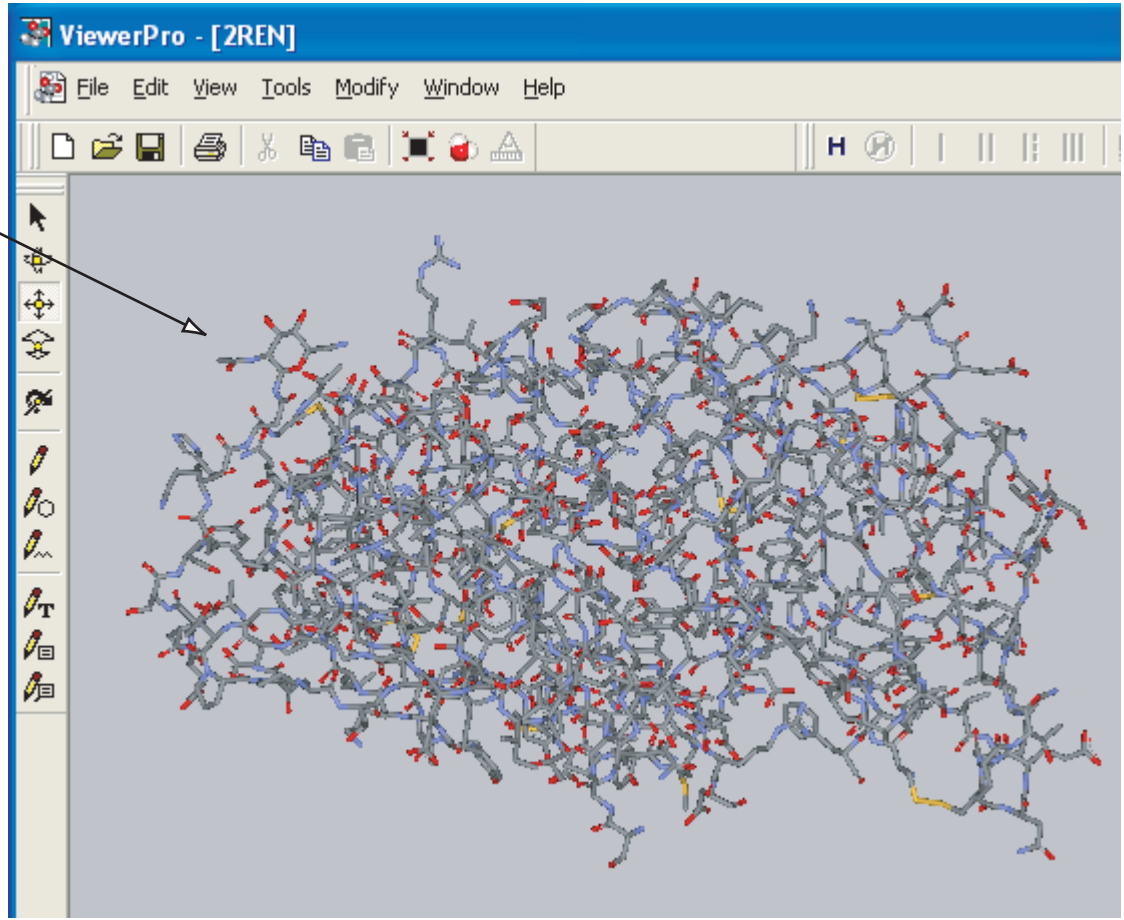
QM/MM calculations of active site of mannitol enzyme

The fixed atoms used in the caclulations

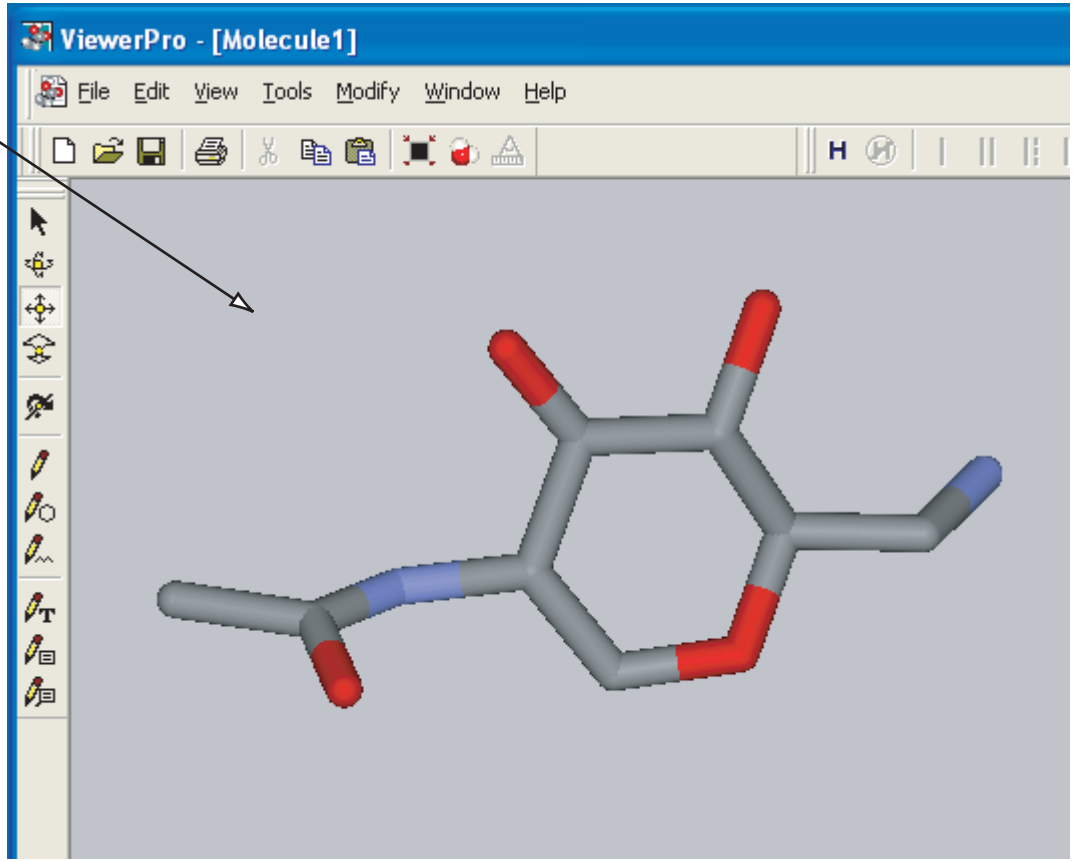


QM/MM calculations of chemical reaction in renin protein

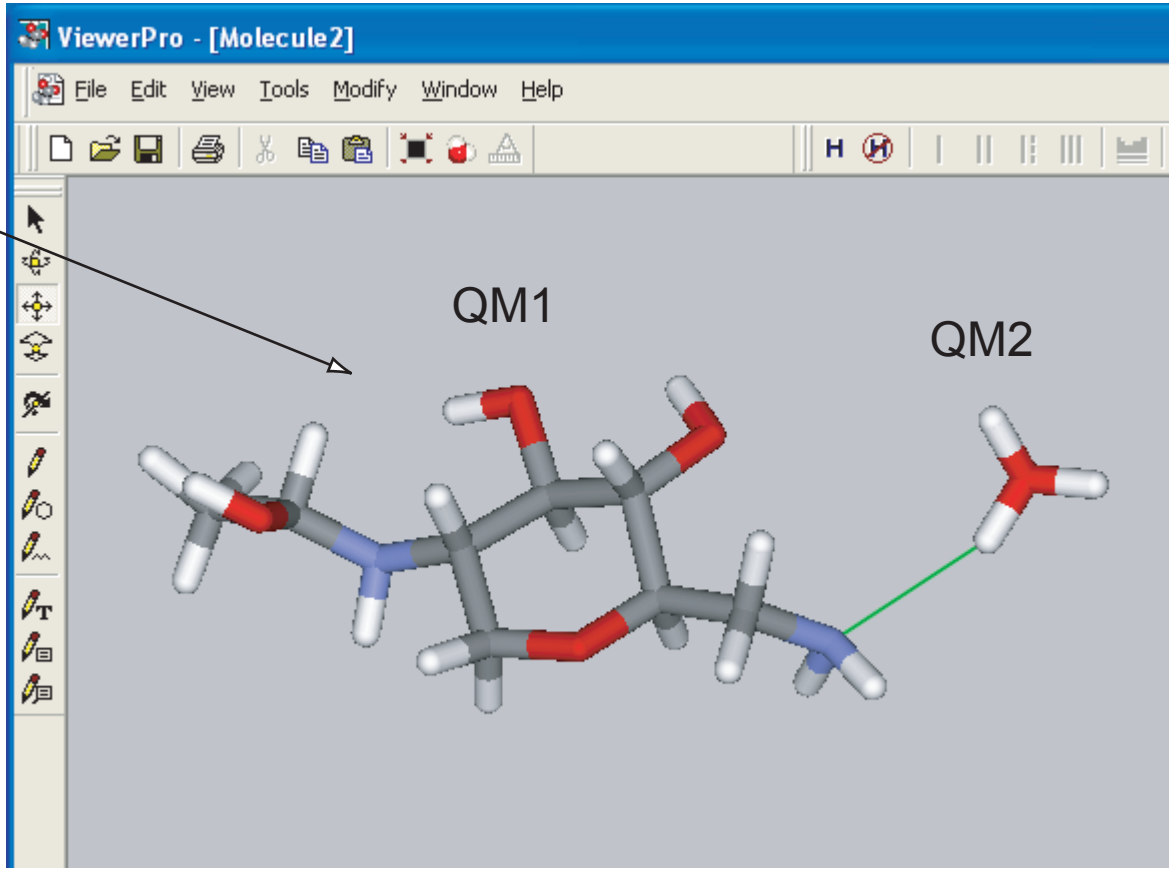
Experimental structure of the renin protein



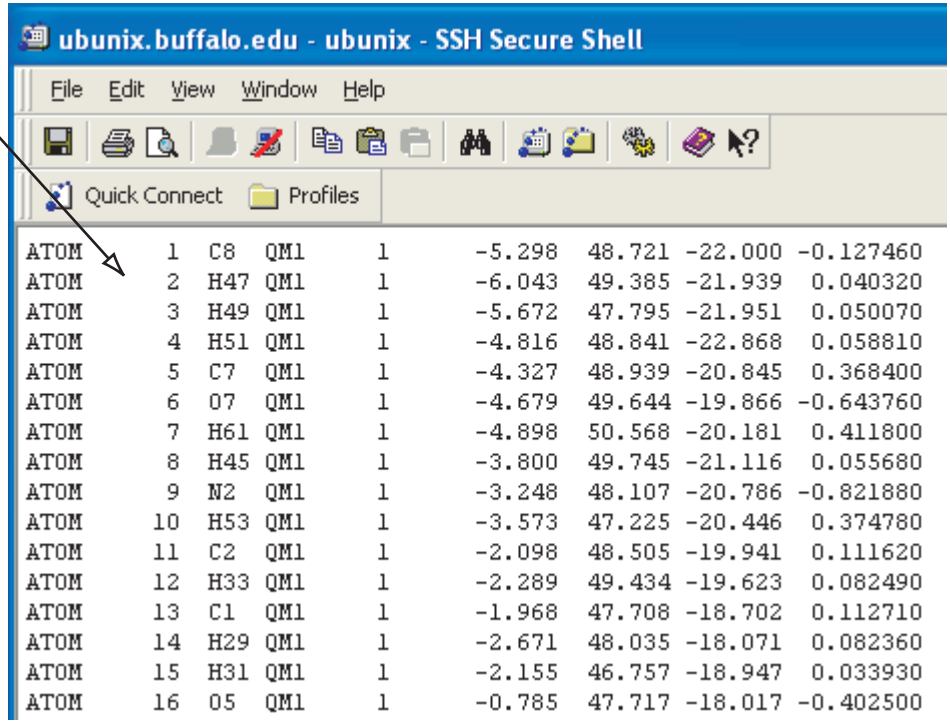
The active site of the renin protein



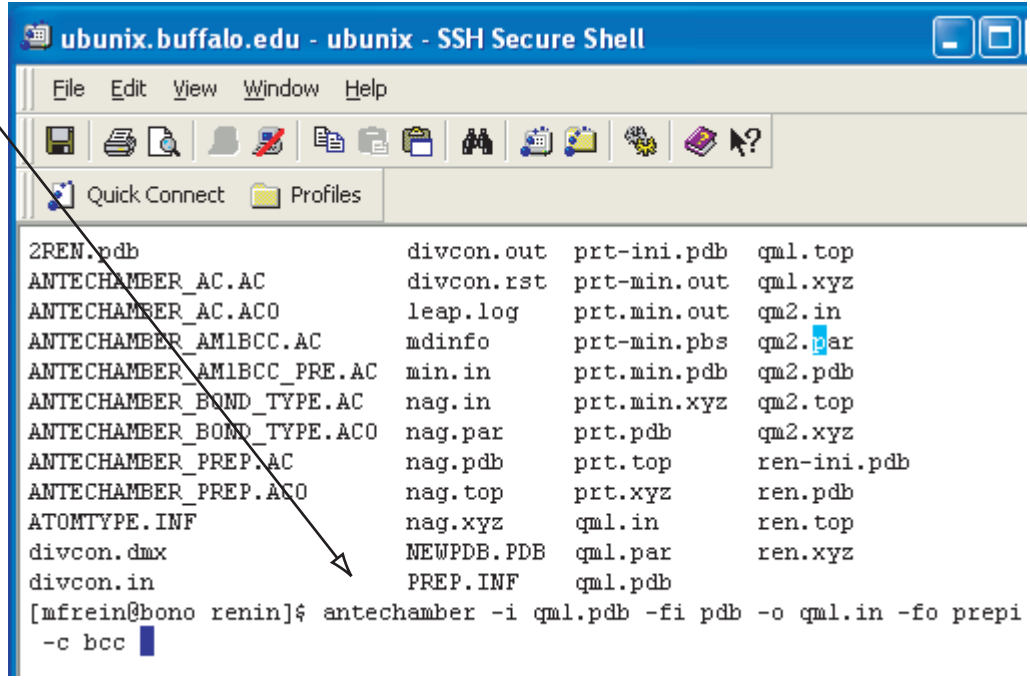
The protonation reaction of the renin ligand



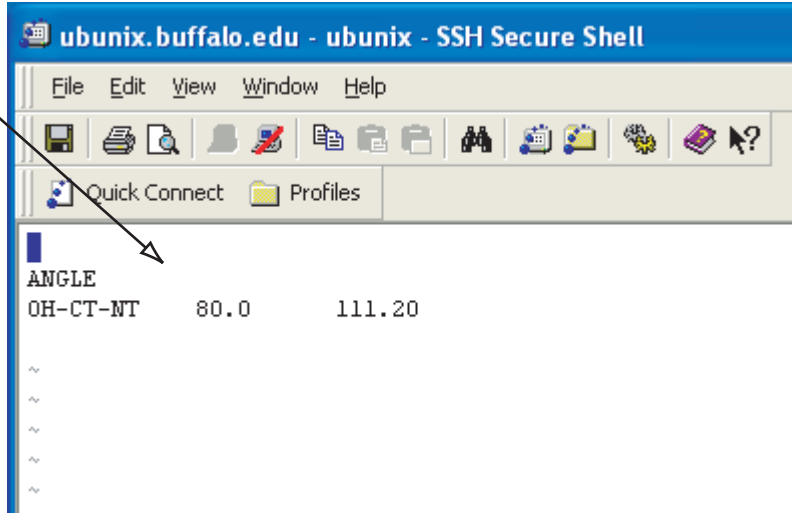
The pdb file of the renin ligand



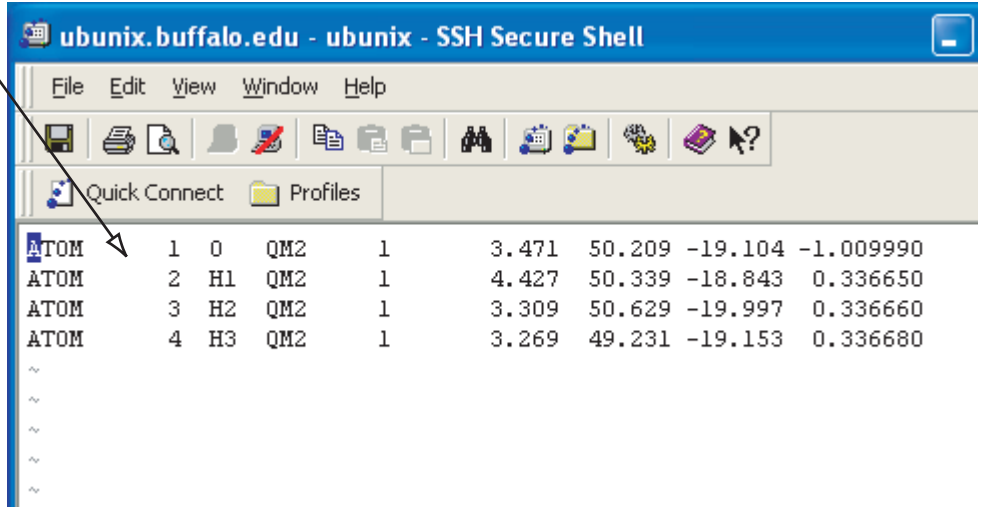
Generating the preparation file for the ligand



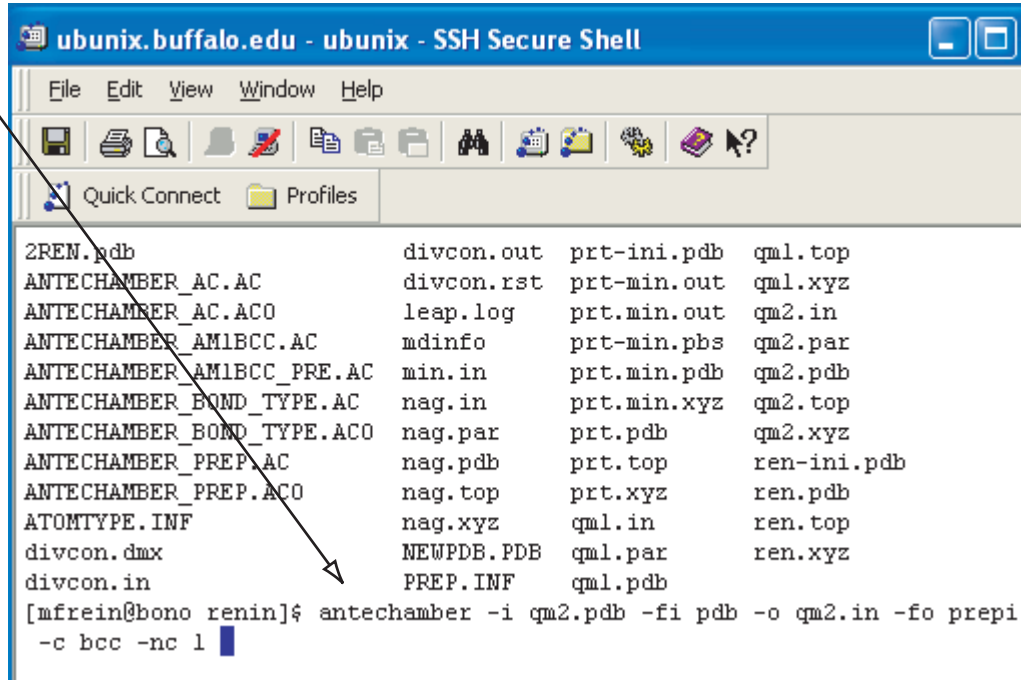
The parameter file of the ligand



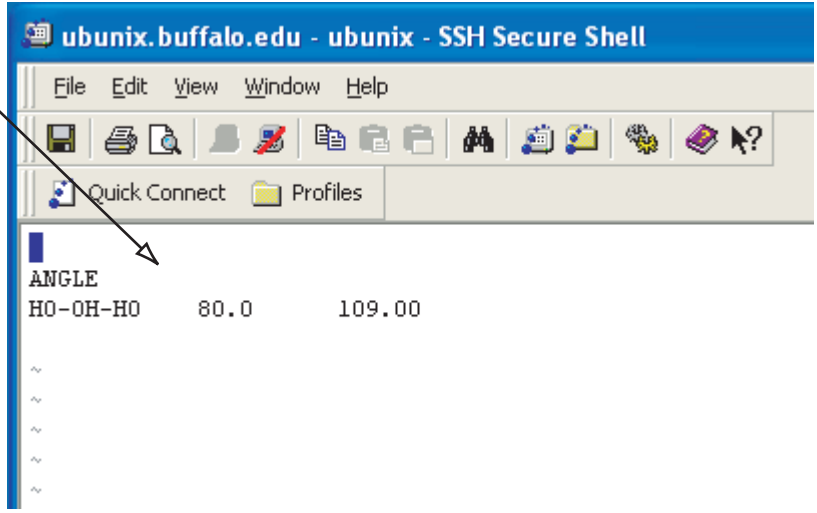
The pdb file of the substrat of the reaction



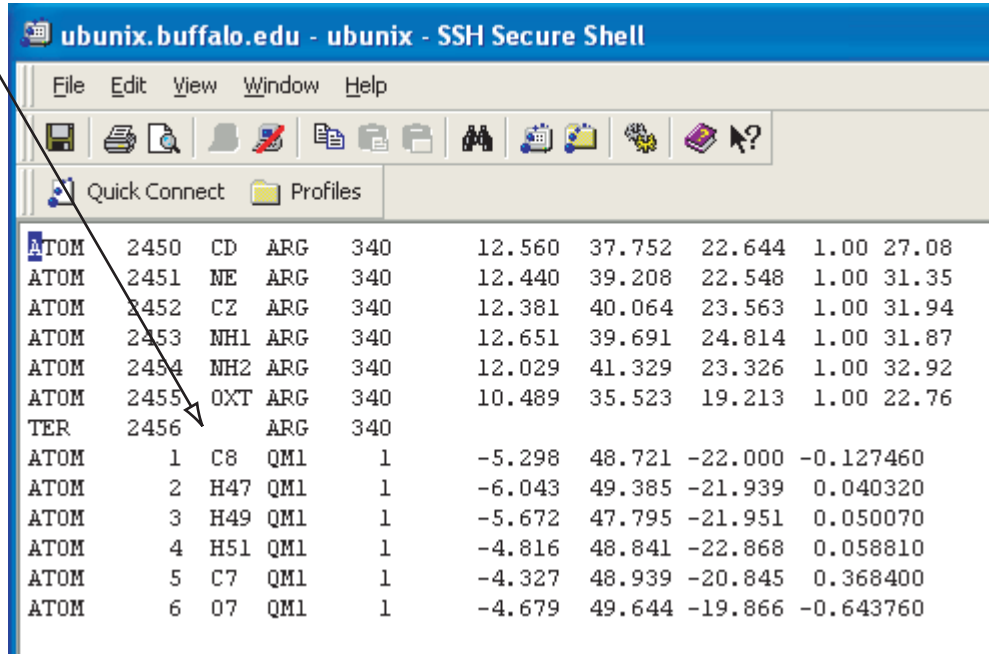
Generating the preparation file for the substrat



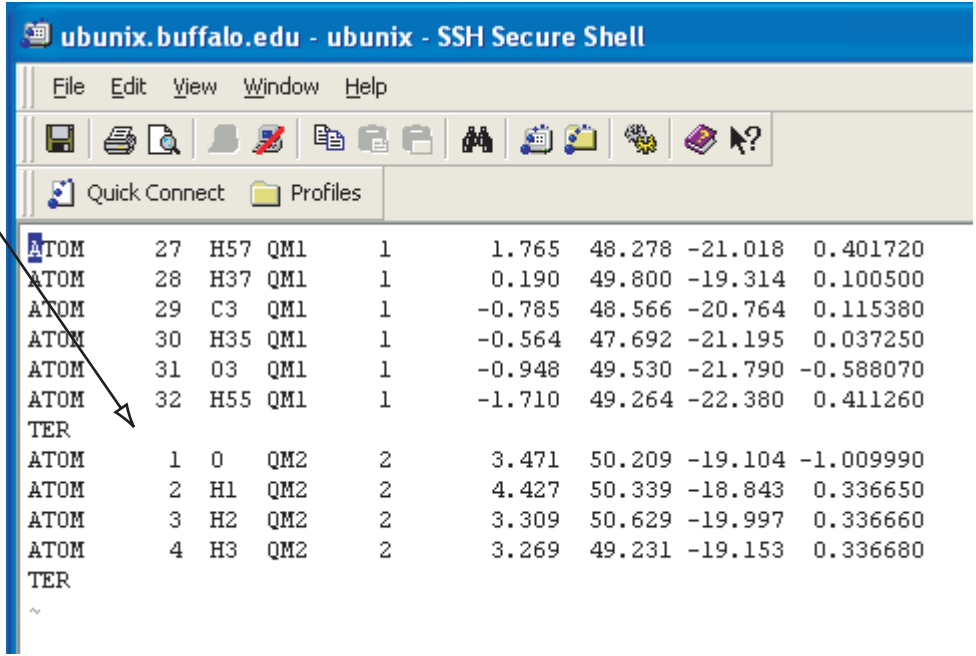
The parameter file
of the substrat



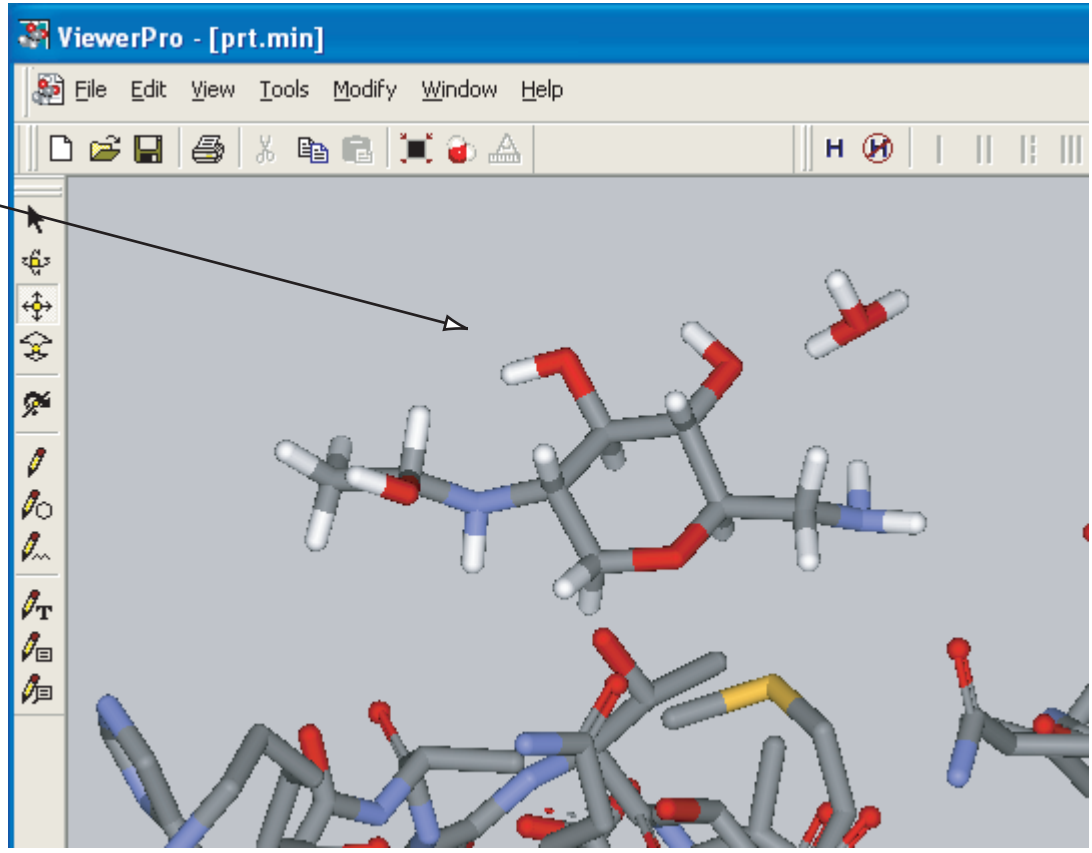
Merging the ligand pdb file with the protein structure



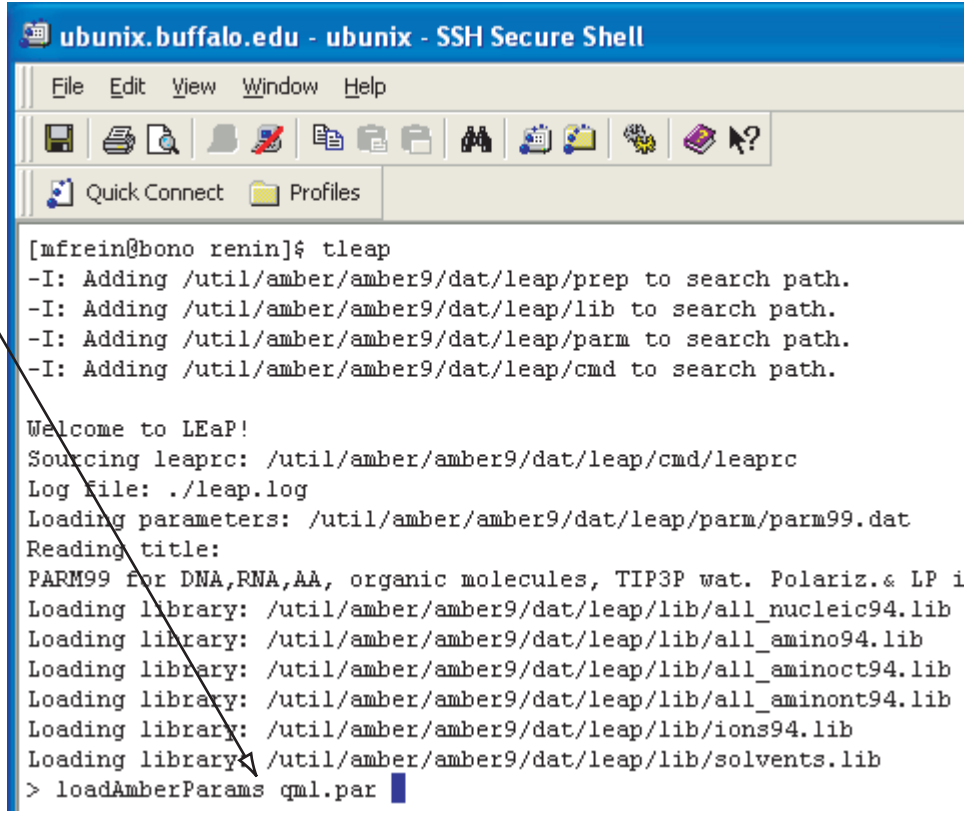
Merging the substrat pdb file with the protein structure



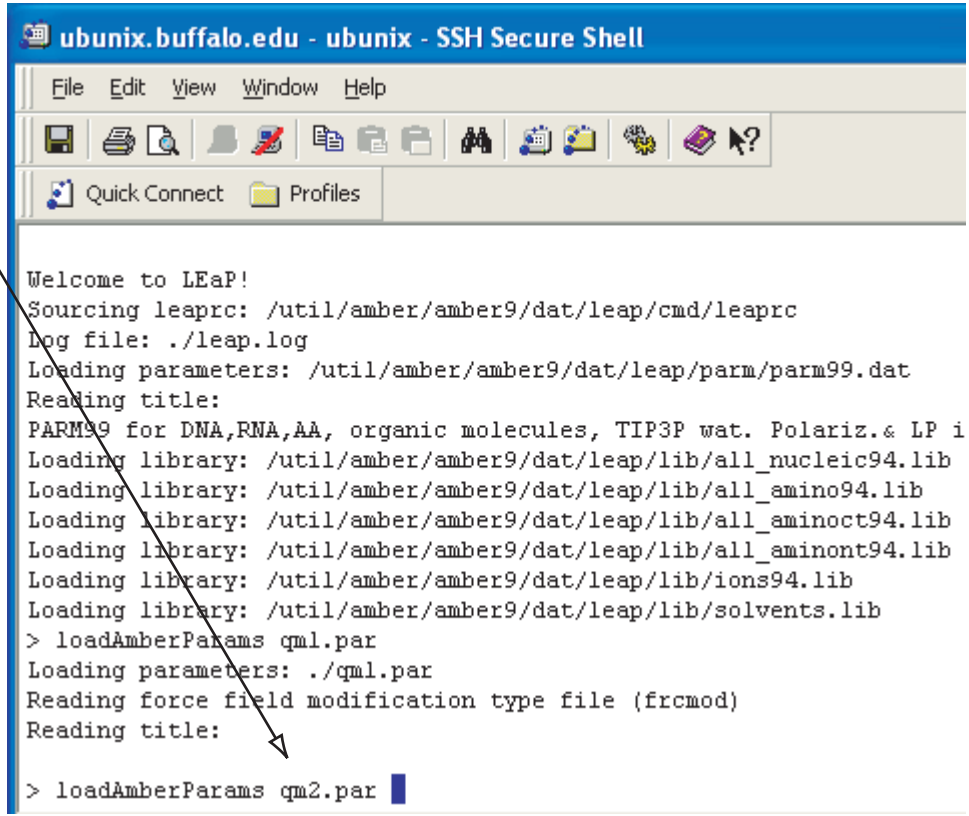
The initial pdb file of the protein with the ligand and the substrat



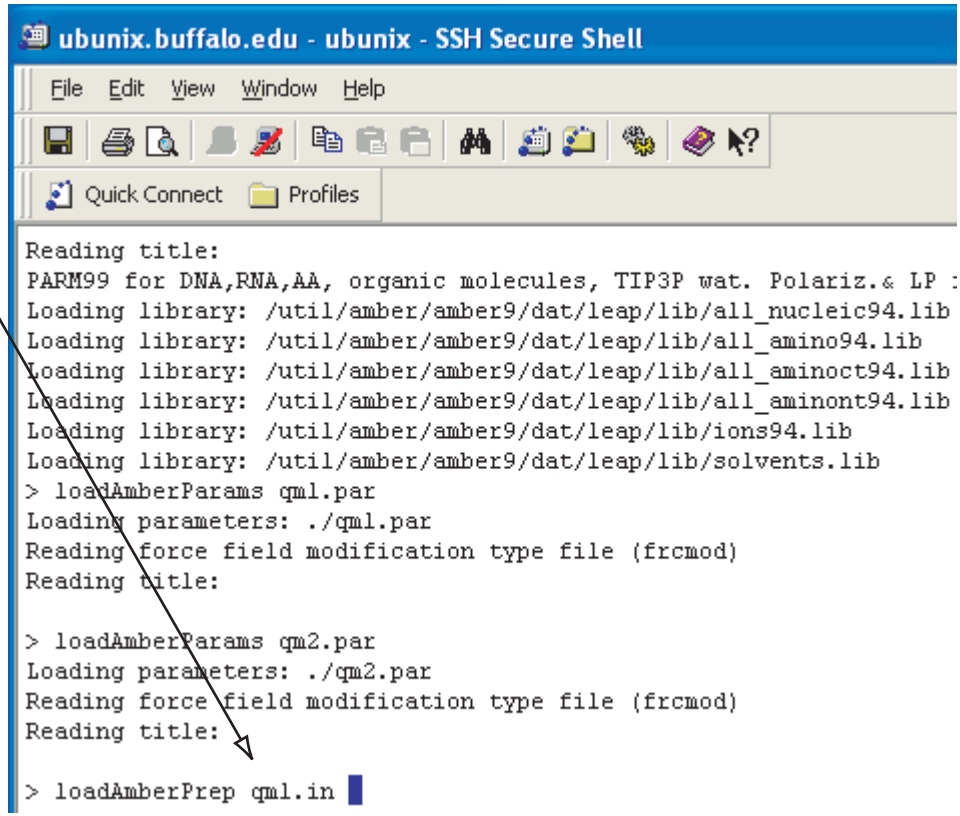
Loading the parameter file of the ligand in the "tleap" program



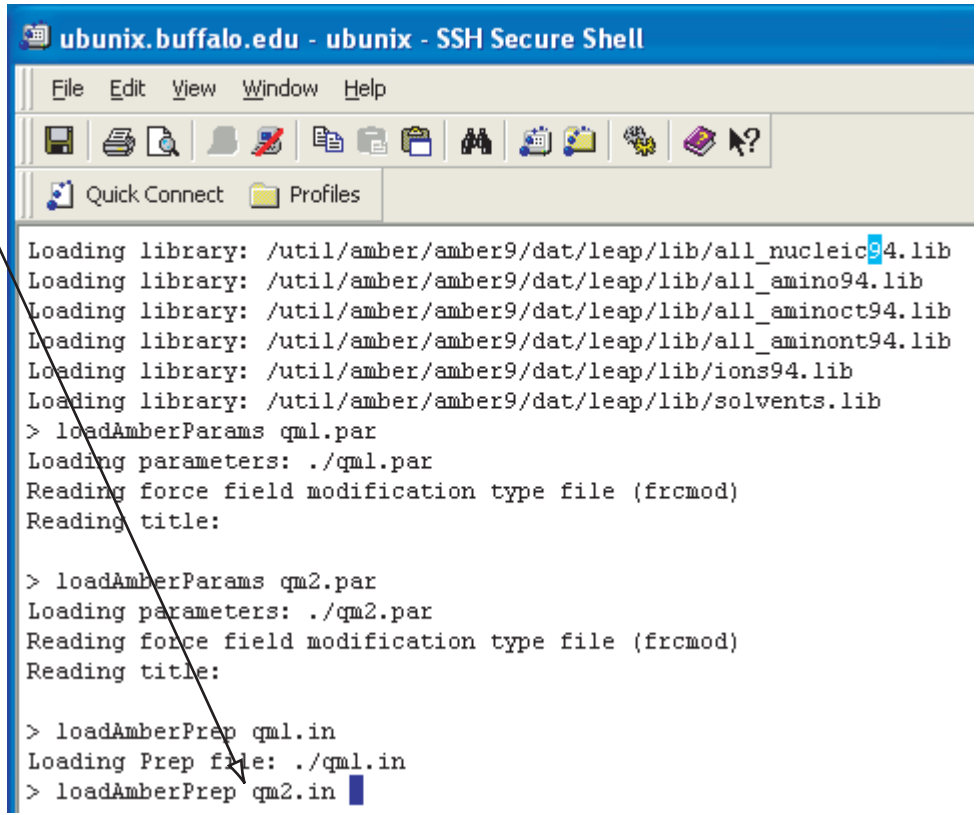
Loading the parameter file of the substrat in the "tleap" program



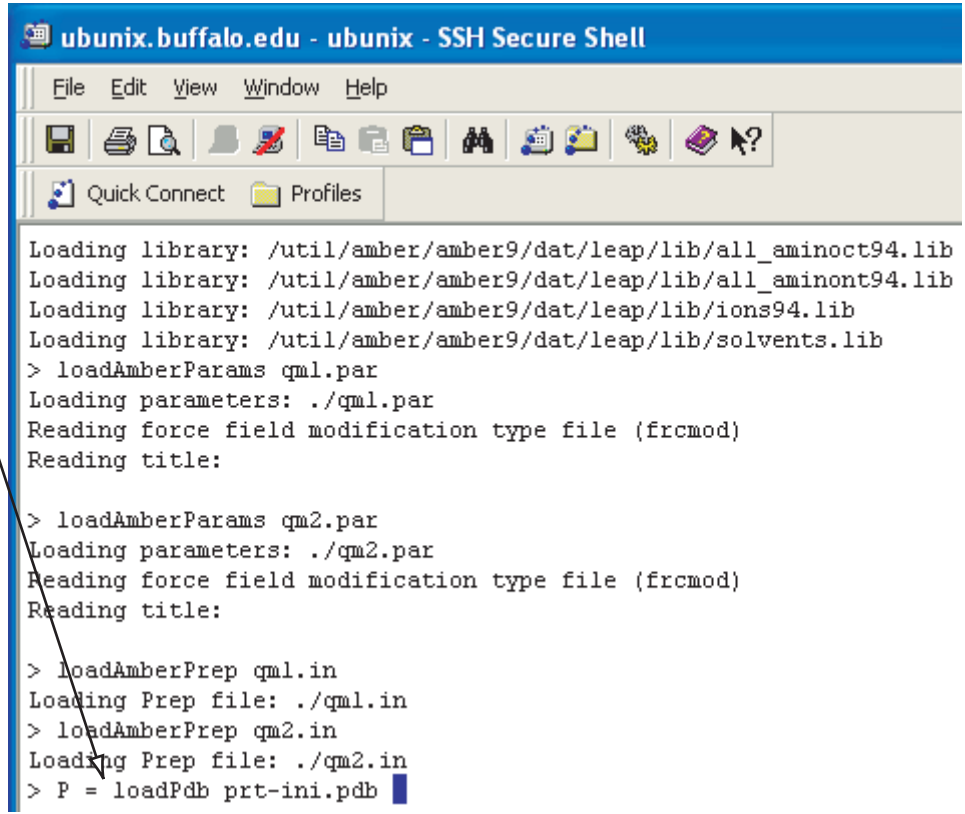
Loading the preparation file of the ligand in the "tleap" program



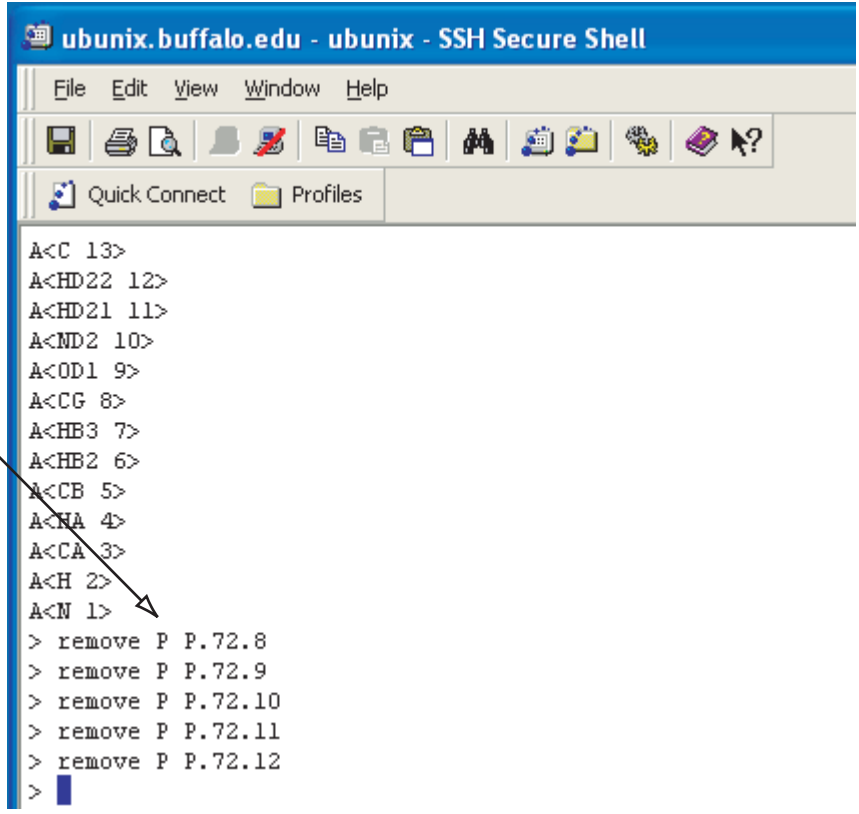
Loading the preparation file of the substrat in the "tleap" program



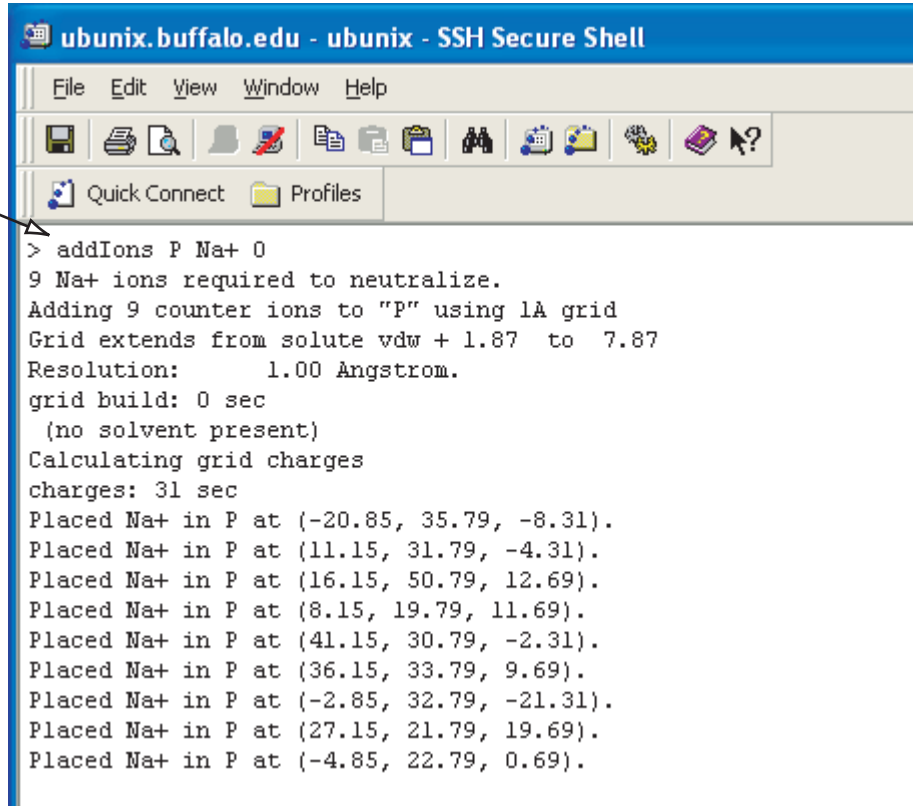
Loading the pdb file of the protein, the ligand and the substrat in the "tleap" program



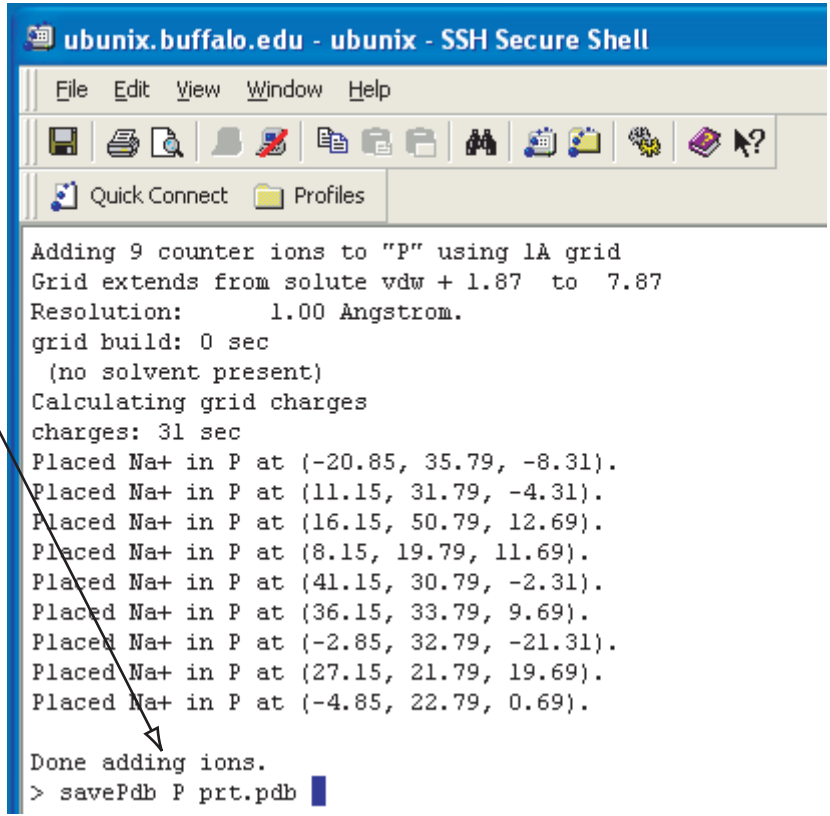
Removing atoms of the protein which are too close to the ligand



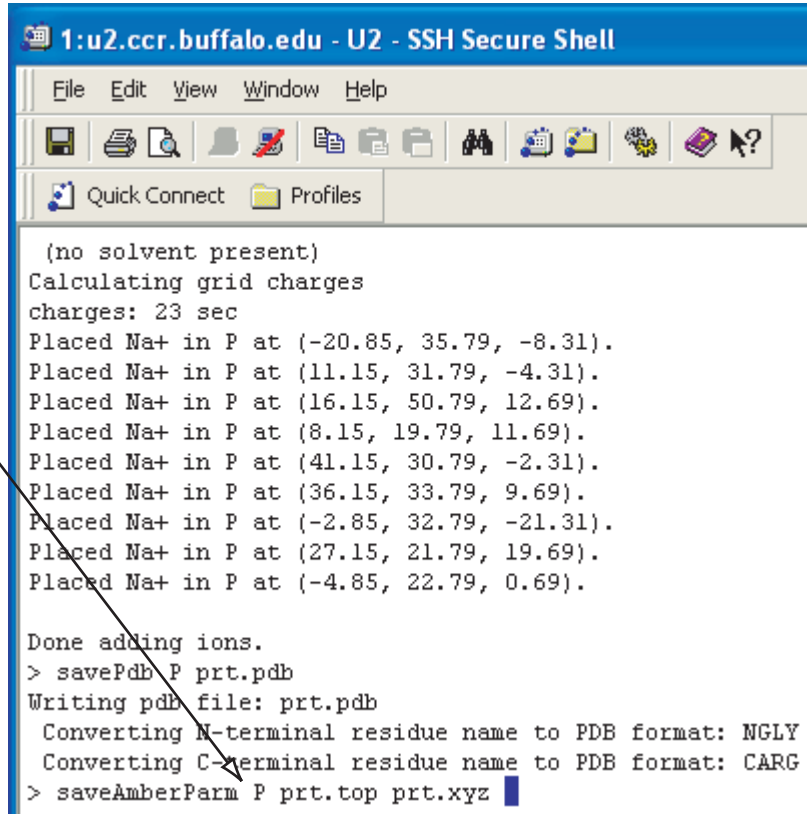
Adding sodium cations (Na+) to neutralize the protein system



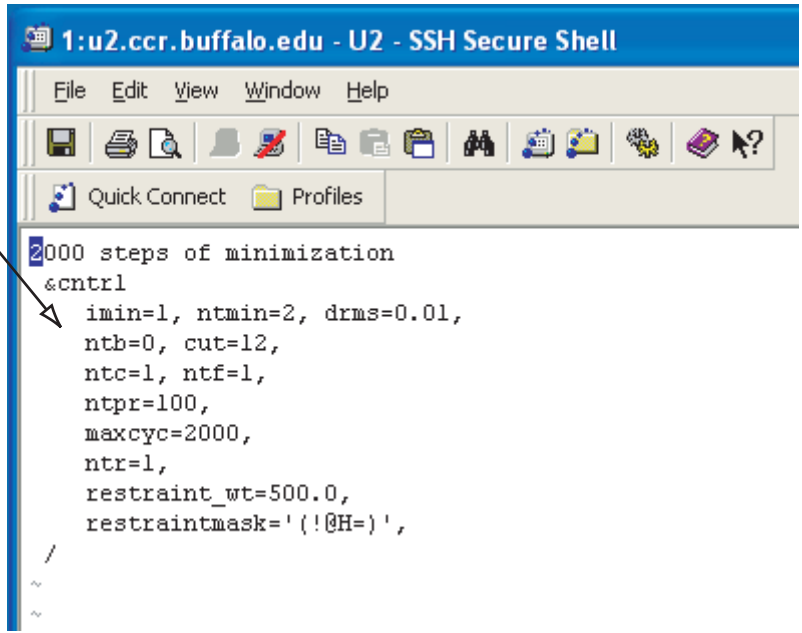
Saving the pdb file of the protein system



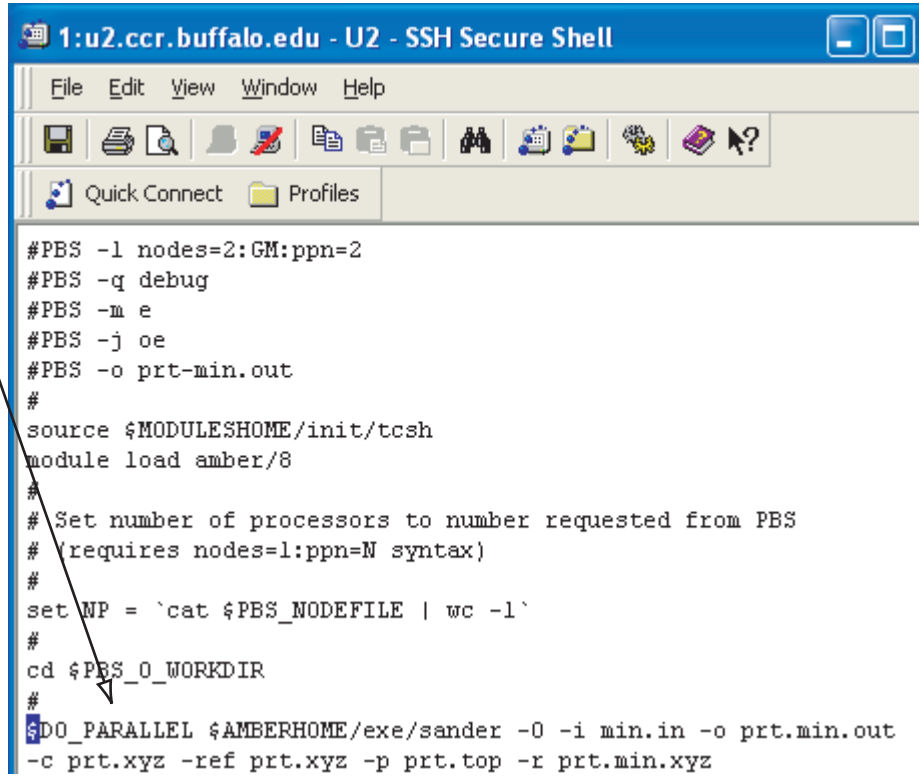
Saving the topology and the coordinates files



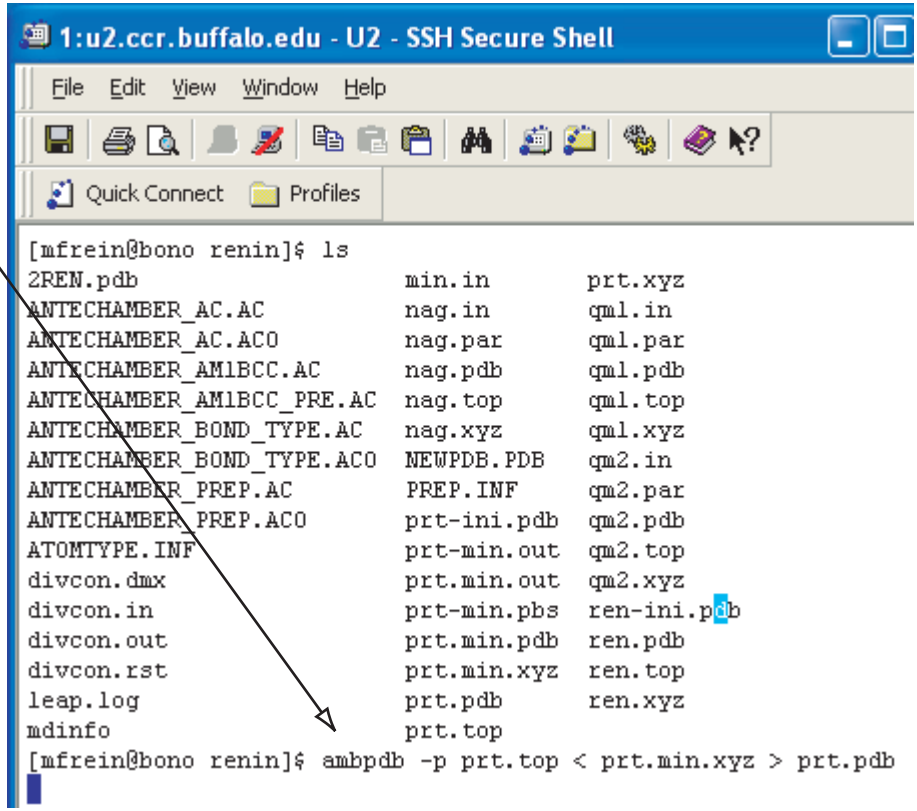
The input file for the minimization of the protein system



The pbs script for the minimization

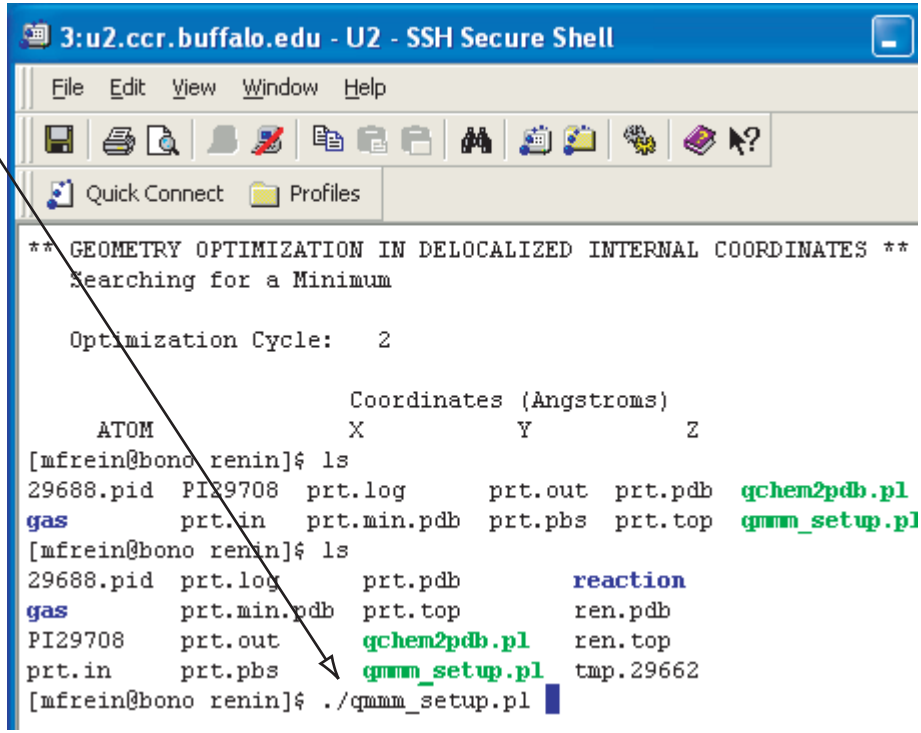


Generating the pdb file of the minimized protein structure

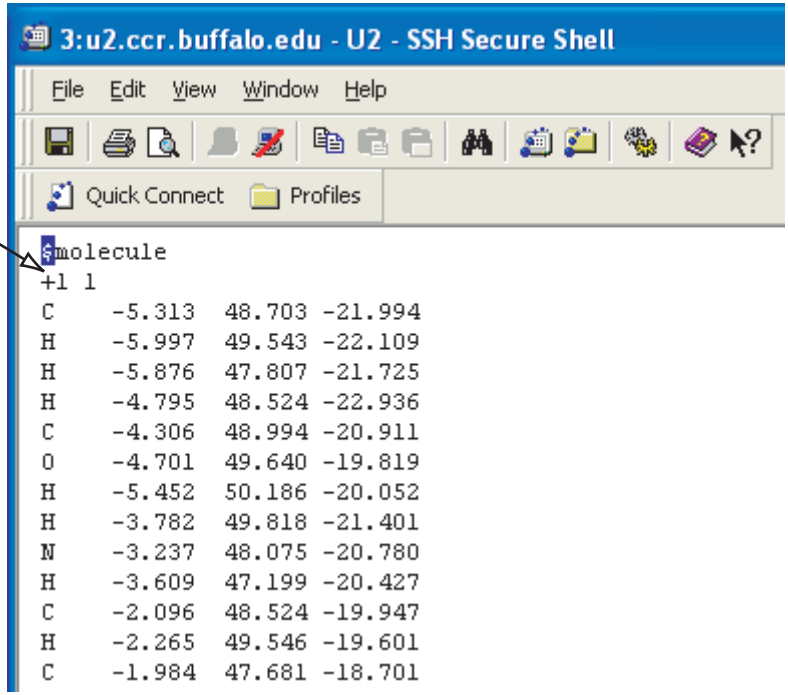


Creating the q-chem input file for the QM/MM calculations

The script assumes that the topology file has a name "prt.top", the pdb file has a name "prt.pdb", and the QM molecules have residue names with the "QM" keyword



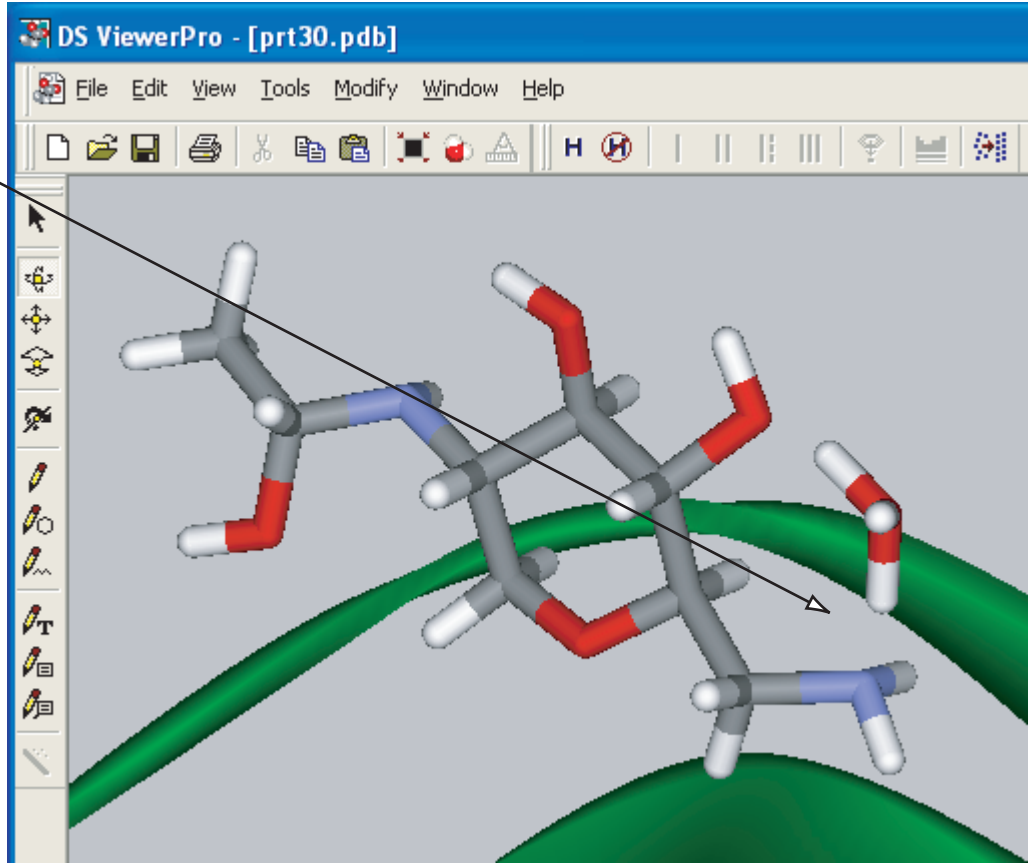
The input file of the q-chem program, the charge of the molecule is "+1"



QM/MM calculations of chemical reaction in renin protein

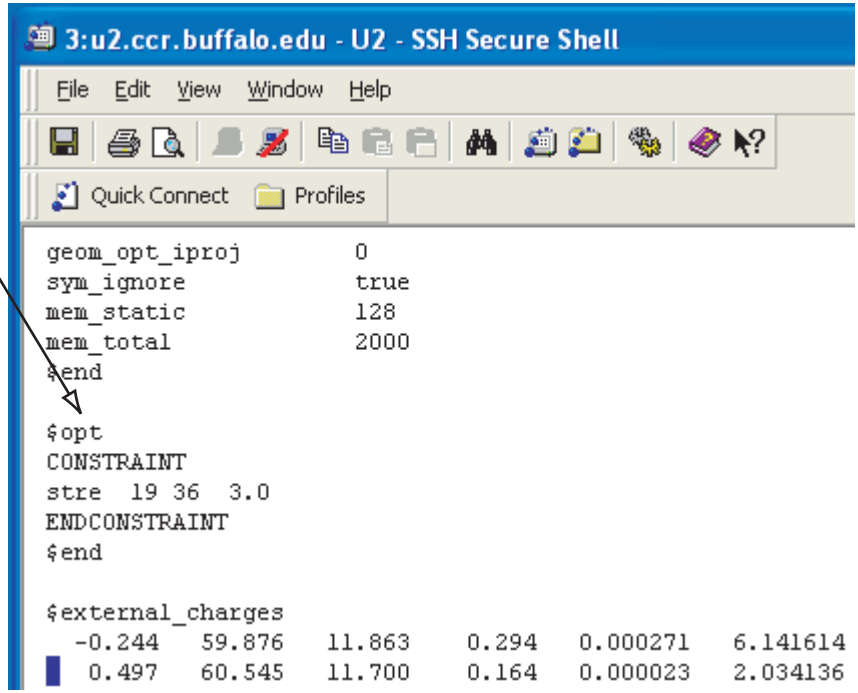
There are two reaction coordinates:

N-H distance
O-H distance



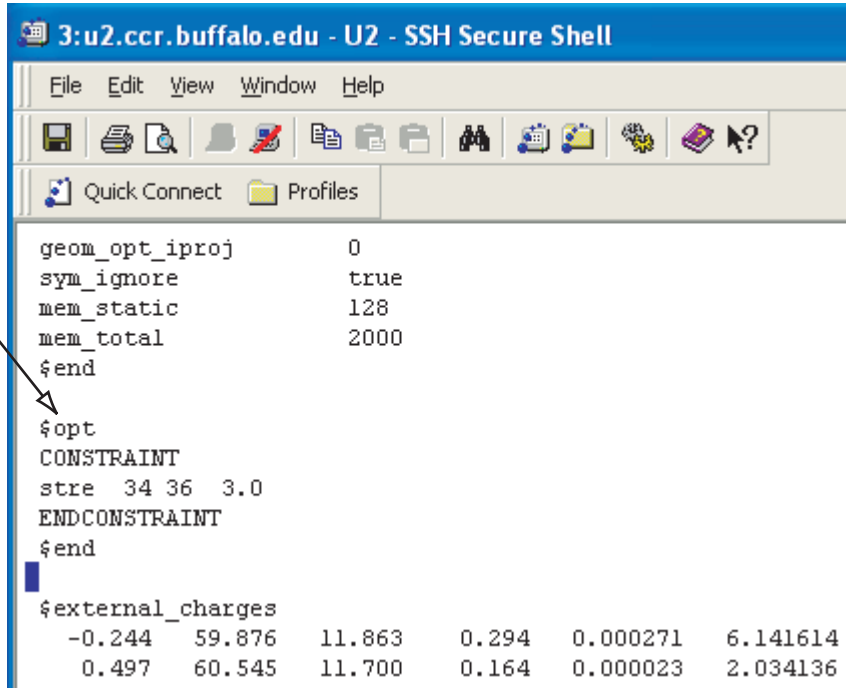
The calculations for the reactants valley

N-H distance constrained

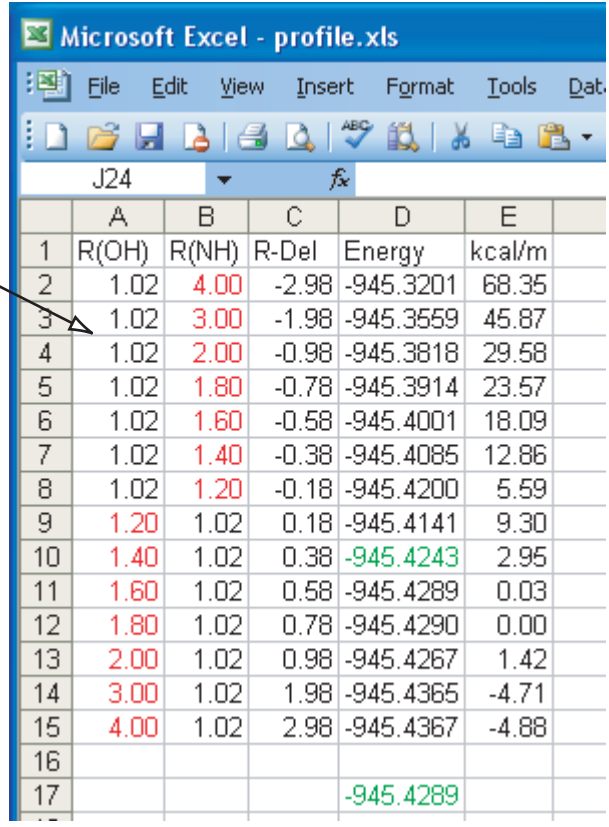


The calculations for the products valley

O-H distance constrained

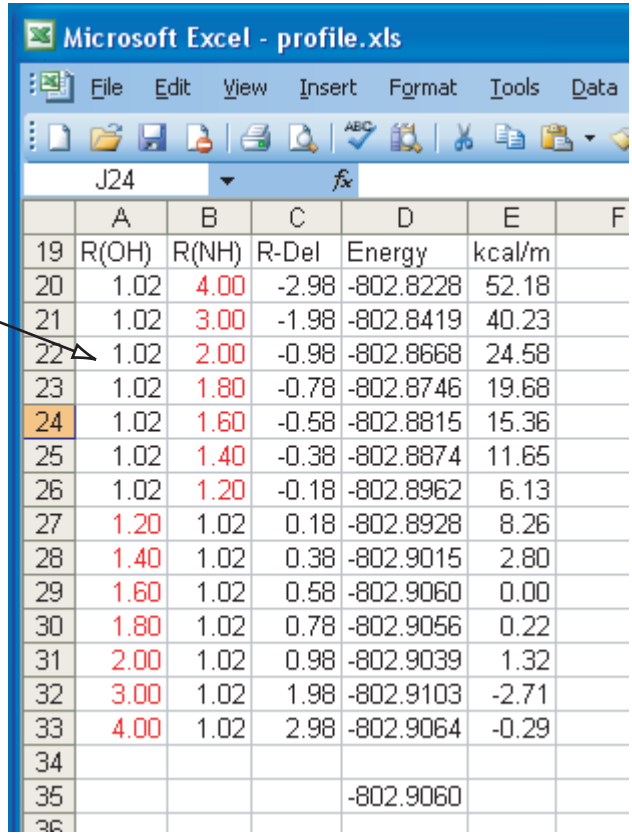


The energy of the QM systems as the function of the reaction coordinate in the protein



	A	B	C	D	E
1	R(OH)	R(NH)	R-Del	Energy	kcal/m
2	1.02	4.00	-2.98	-945.3201	68.35
3	1.02	3.00	-1.98	-945.3559	45.87
4	1.02	2.00	-0.98	-945.3818	29.58
5	1.02	1.80	-0.78	-945.3914	23.57
6	1.02	1.60	-0.58	-945.4001	18.09
7	1.02	1.40	-0.38	-945.4085	12.86
8	1.02	1.20	-0.18	-945.4200	5.59
9	1.20	1.02	0.18	-945.4141	9.30
10	1.40	1.02	0.38	-945.4243	2.95
11	1.60	1.02	0.58	-945.4289	0.03
12	1.80	1.02	0.78	-945.4290	0.00
13	2.00	1.02	0.98	-945.4267	1.42
14	3.00	1.02	1.98	-945.4365	-4.71
15	4.00	1.02	2.98	-945.4367	-4.88
16					
17				-945.4289	

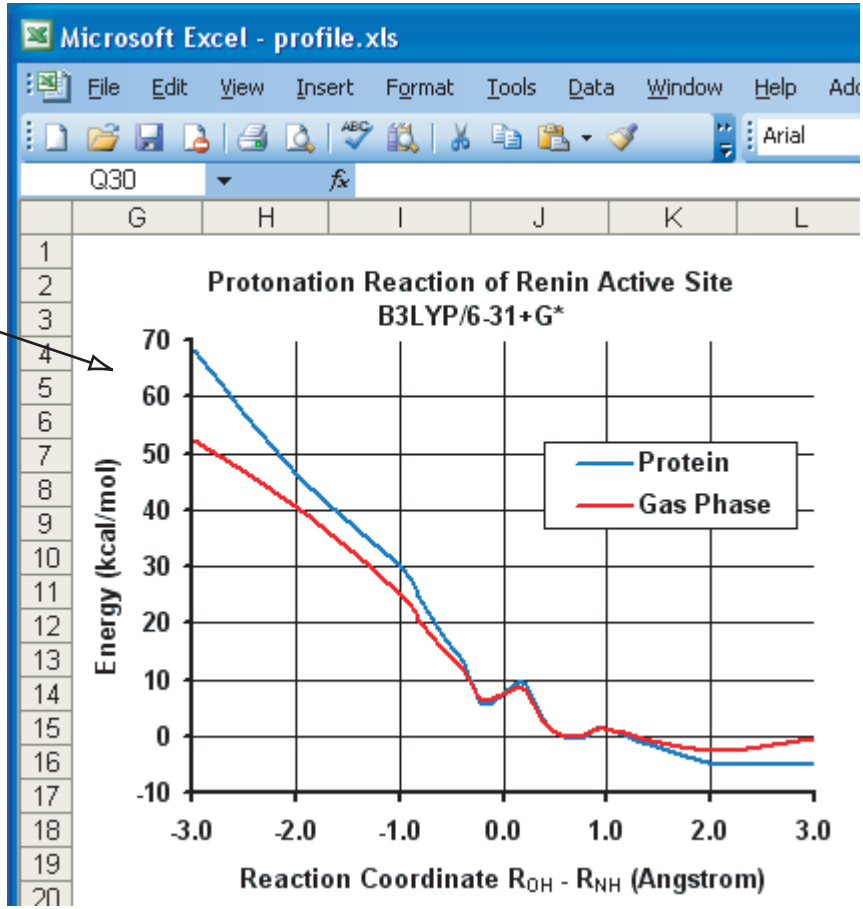
The energy of the QM systems as the function of the reaction coordinate in the gas phase



	A	B	C	D	E	F
19	R(OH)	R(NH)	R-Del	Energy	kcal/m	
20	1.02	4.00	-2.98	-802.8228	52.18	
21	1.02	3.00	-1.98	-802.8419	40.23	
22	1.02	2.00	-0.98	-802.8668	24.58	
23	1.02	1.80	-0.78	-802.8746	19.68	
24	1.02	1.60	-0.58	-802.8815	15.36	
25	1.02	1.40	-0.38	-802.8874	11.65	
26	1.02	1.20	-0.18	-802.8962	6.13	
27	1.20	1.02	0.18	-802.8928	8.26	
28	1.40	1.02	0.38	-802.9015	2.80	
29	1.60	1.02	0.58	-802.9060	0.00	
30	1.80	1.02	0.78	-802.9056	0.22	
31	2.00	1.02	0.98	-802.9039	1.32	
32	3.00	1.02	1.98	-802.9103	-2.71	
33	4.00	1.02	2.98	-802.9064	-0.29	
34						
35				-802.9060		

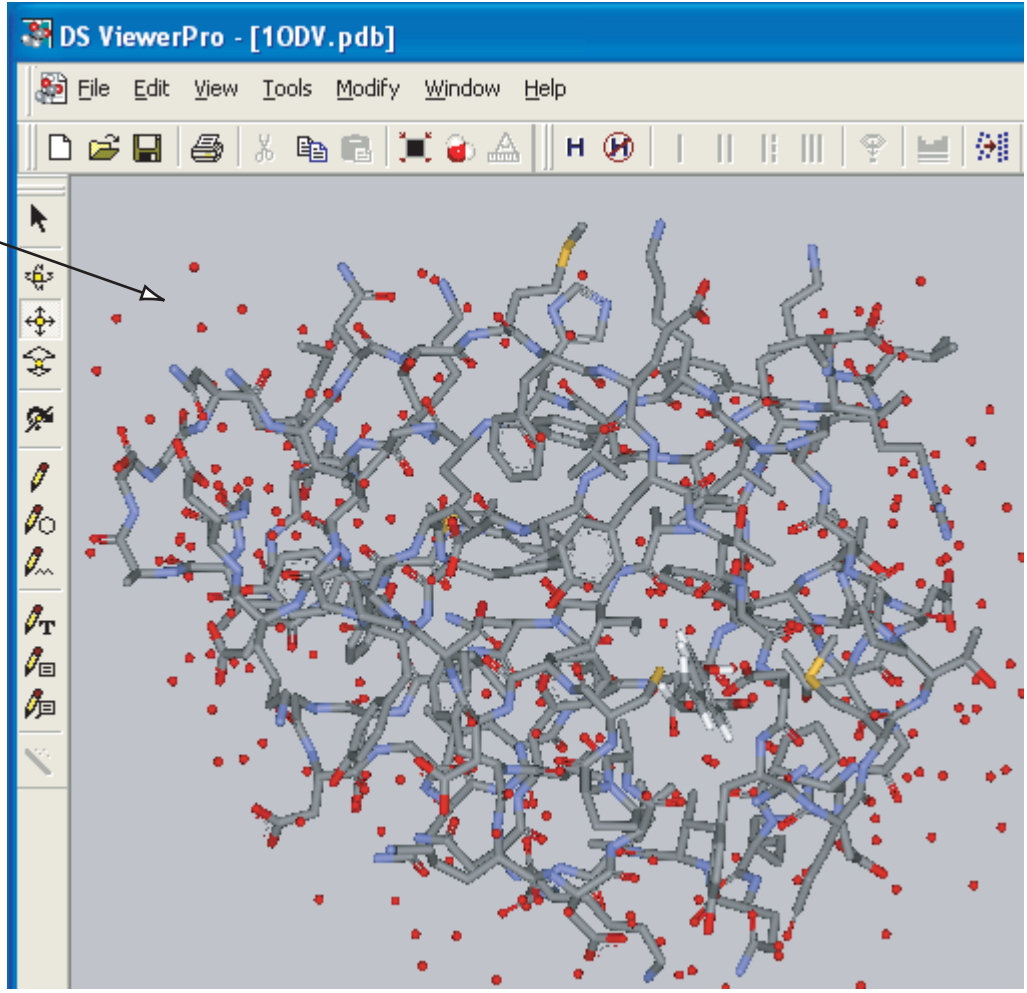
QM/MM calculations of chemical reaction in renin protein

The final results of the reaction profile calculations in the protein and in the gas phase

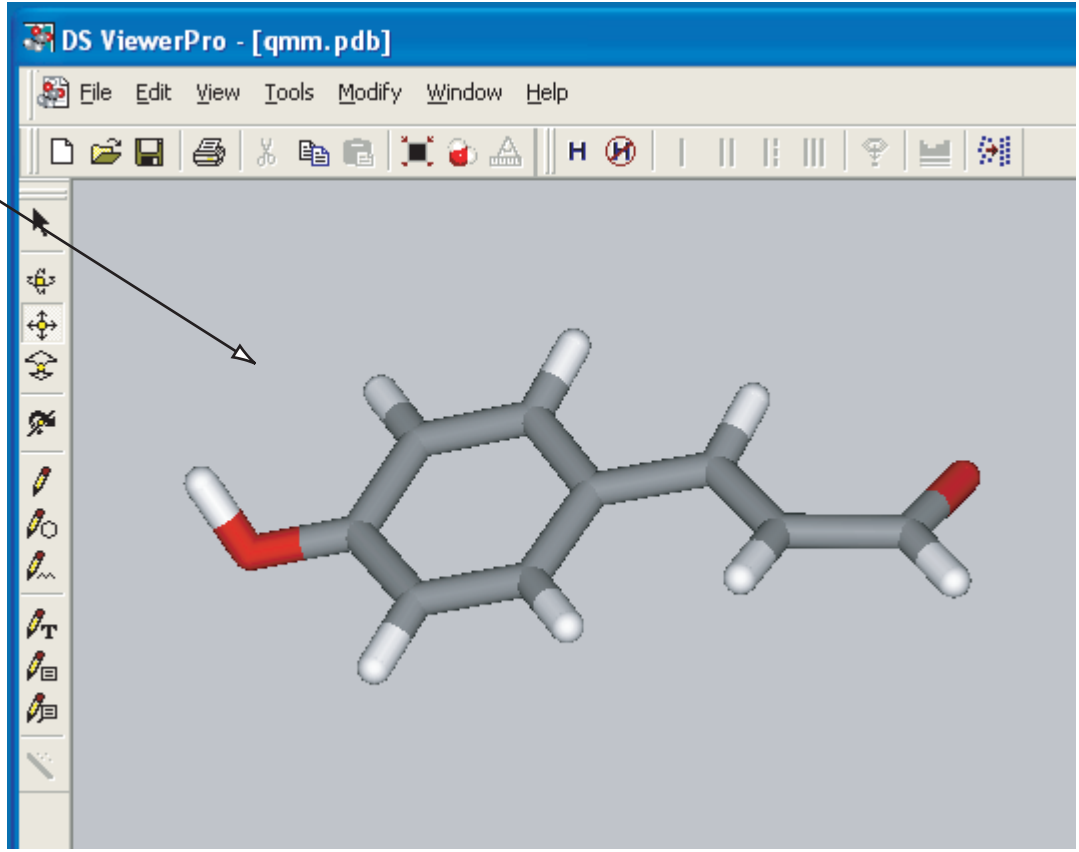


QM/MM electronic excitations in yellow protein

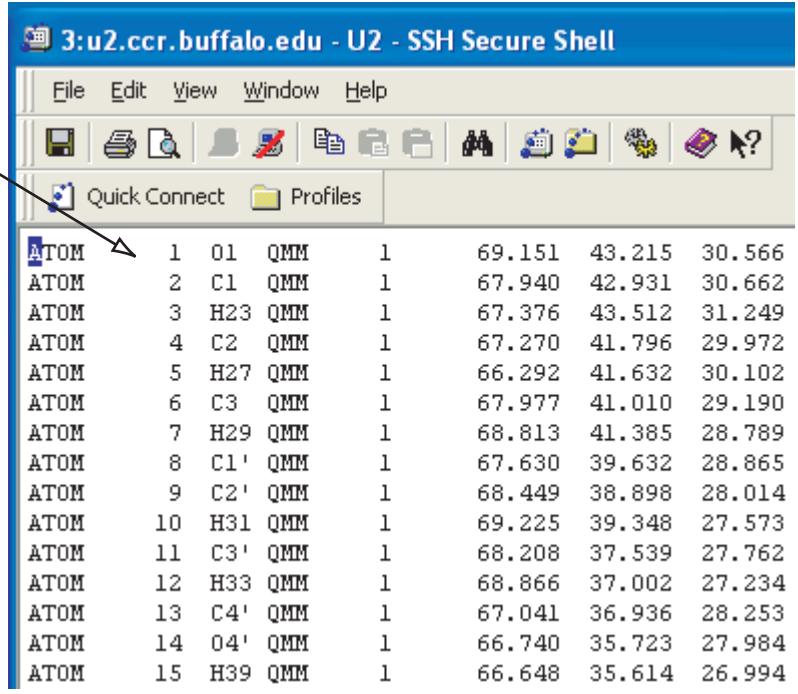
Experimental structure of the yellow protein



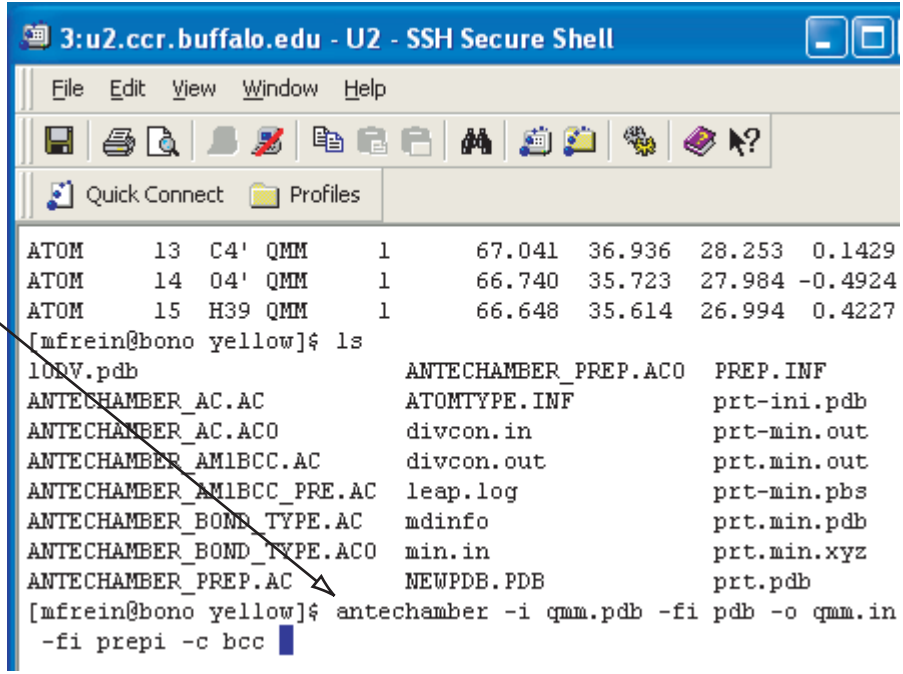
The active site of the yellow protein



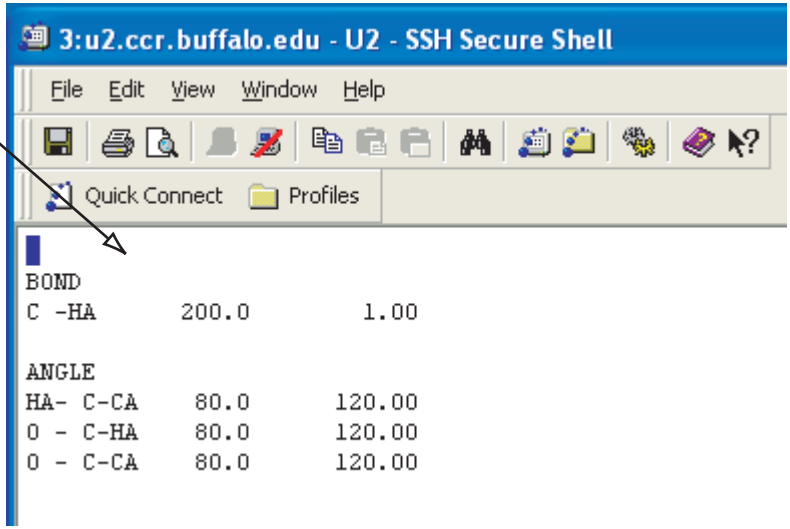
The pdb file of the ligand



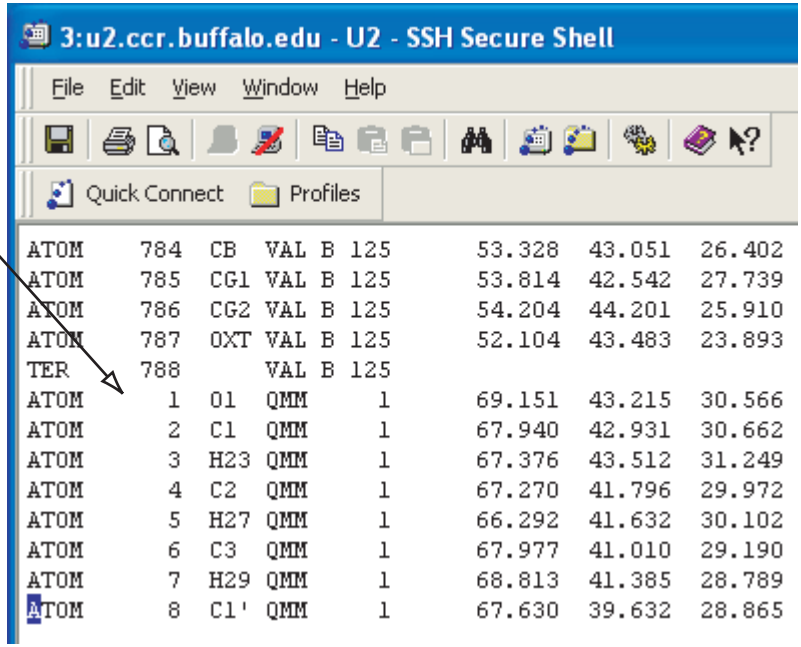
Creating the preparation file of the ligand, using the "antechmaber" program



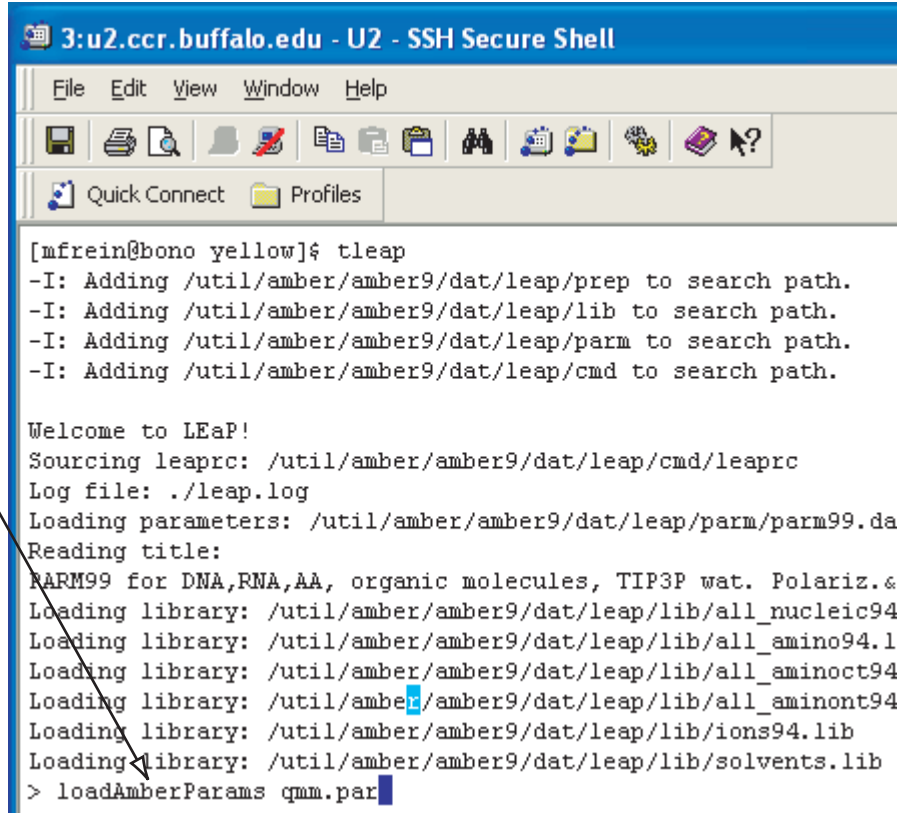
Creating the parameter file of the ligand



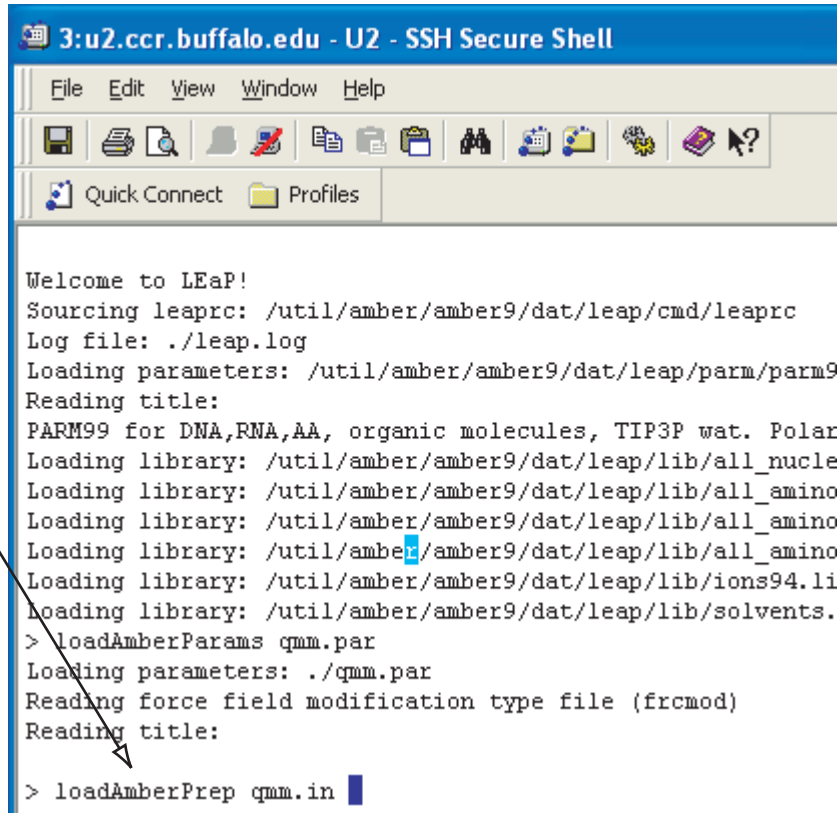
Merging the pdb structure of the ligand with the structure of the protein



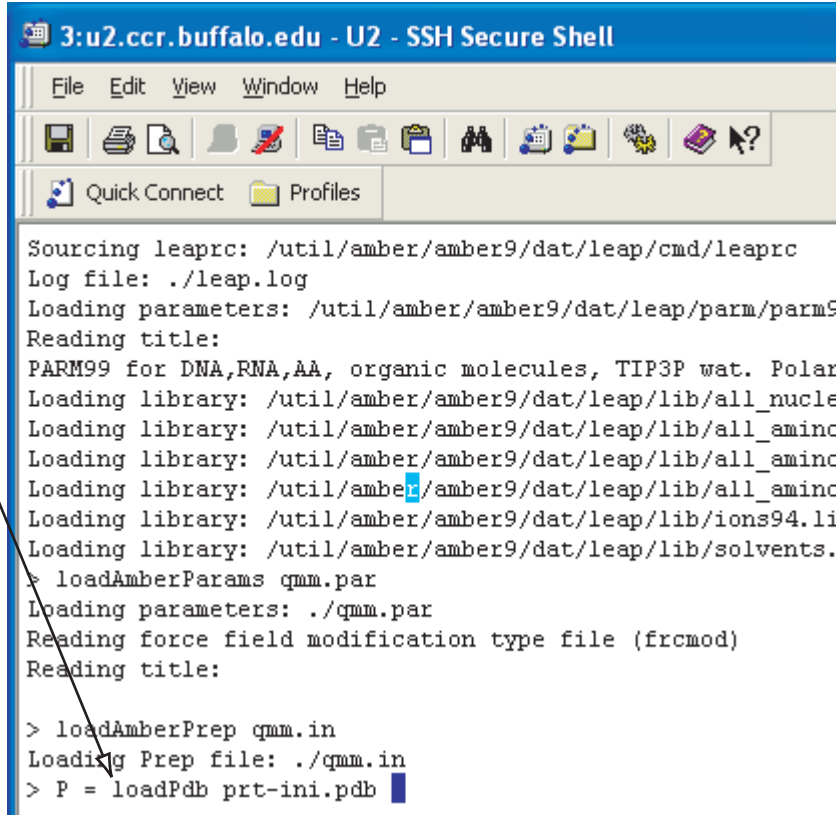
Running the "tleap" program, loading the parameter file of the ligand



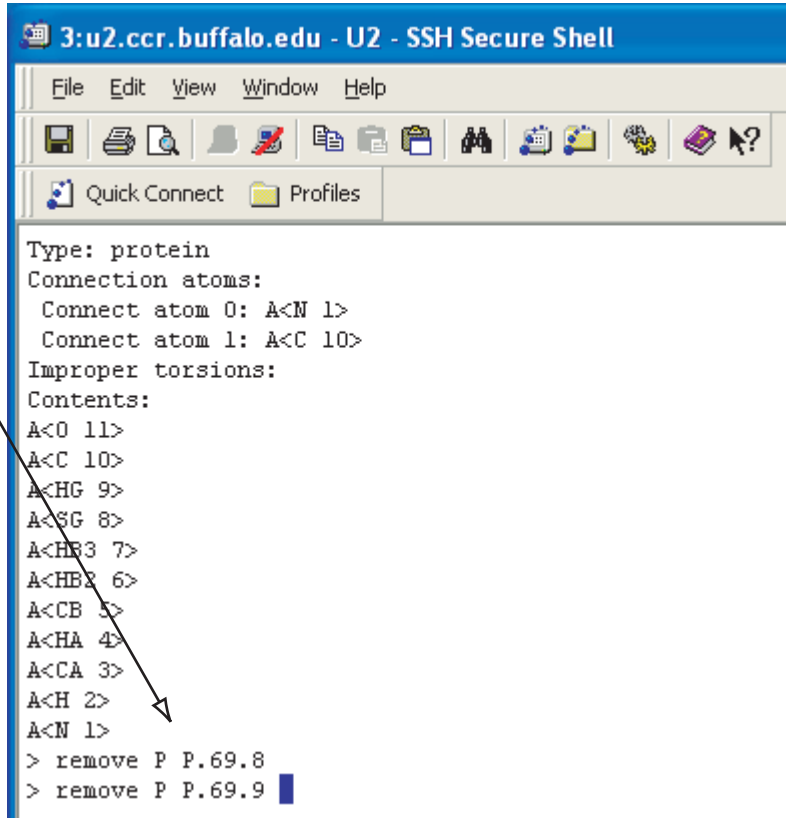
Loading the preparation file of the ligand



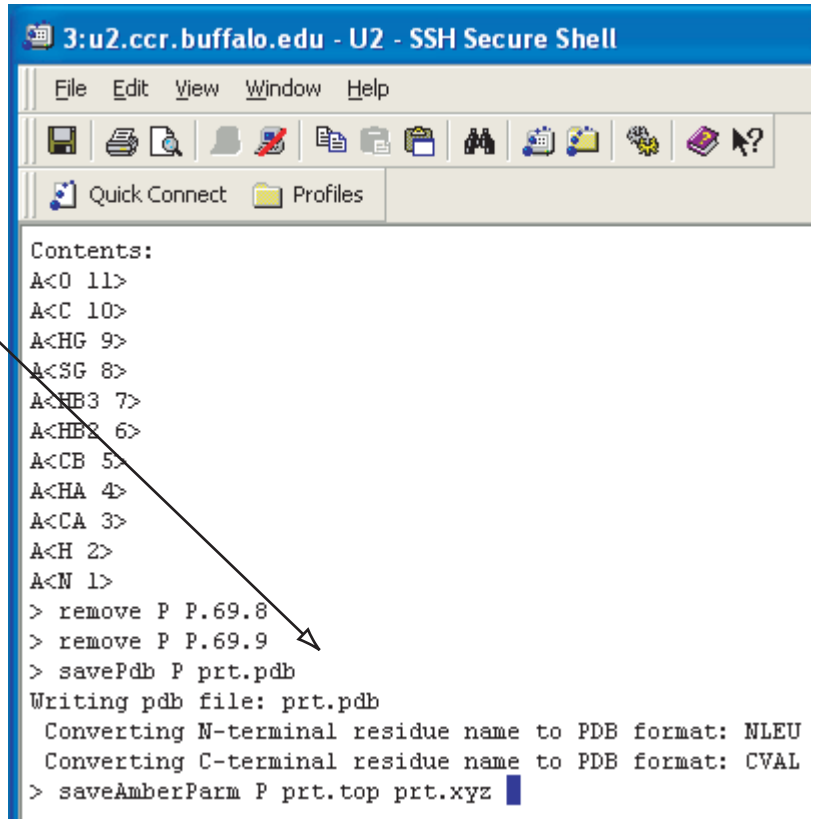
Loading the pdb file of the protein and the ligand



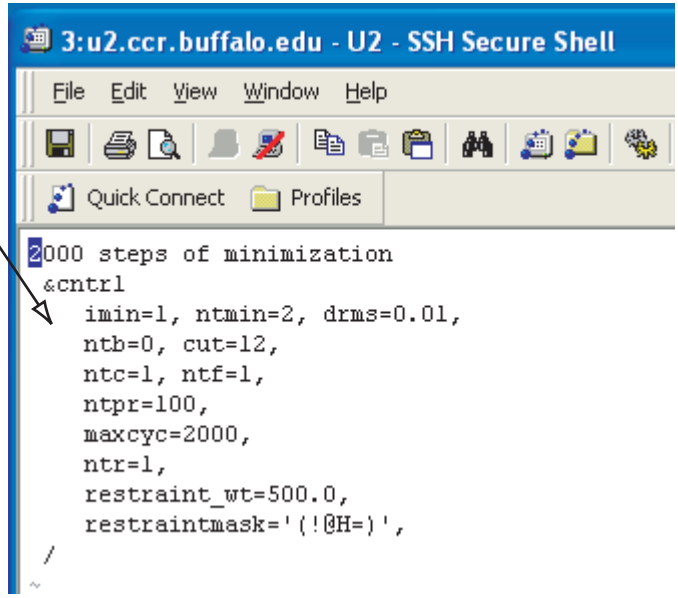
Removing protein atoms which are too close to the ligand



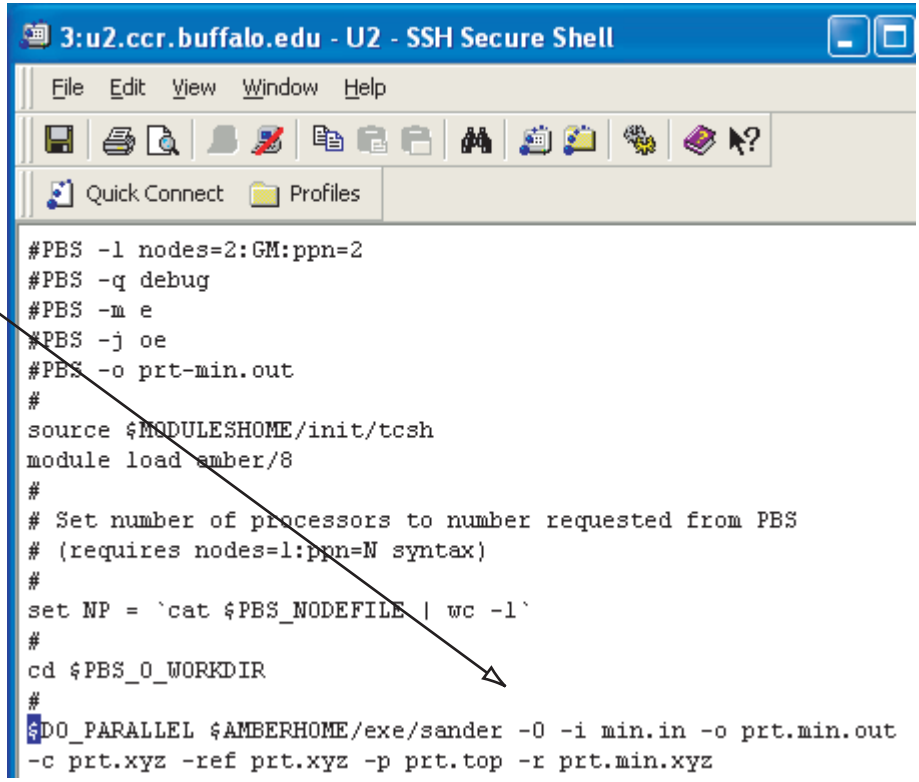
Saving the pdb, the topology and the coordinates files of the protein system



Creating the input file
for the minimization

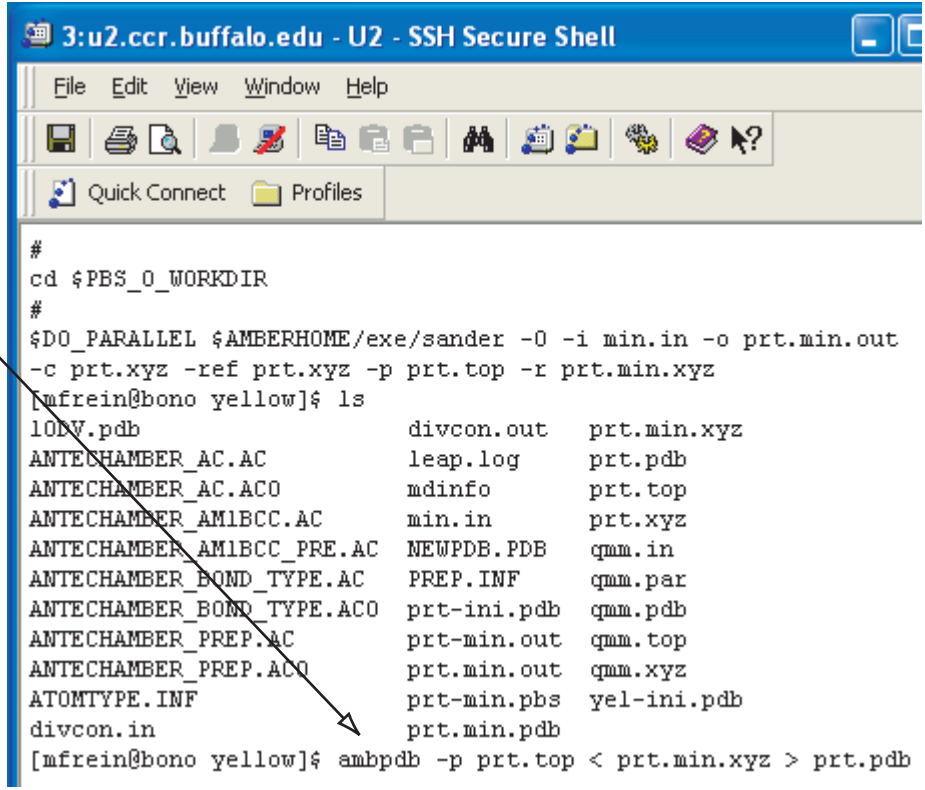


Creating the pbs script for the minimization



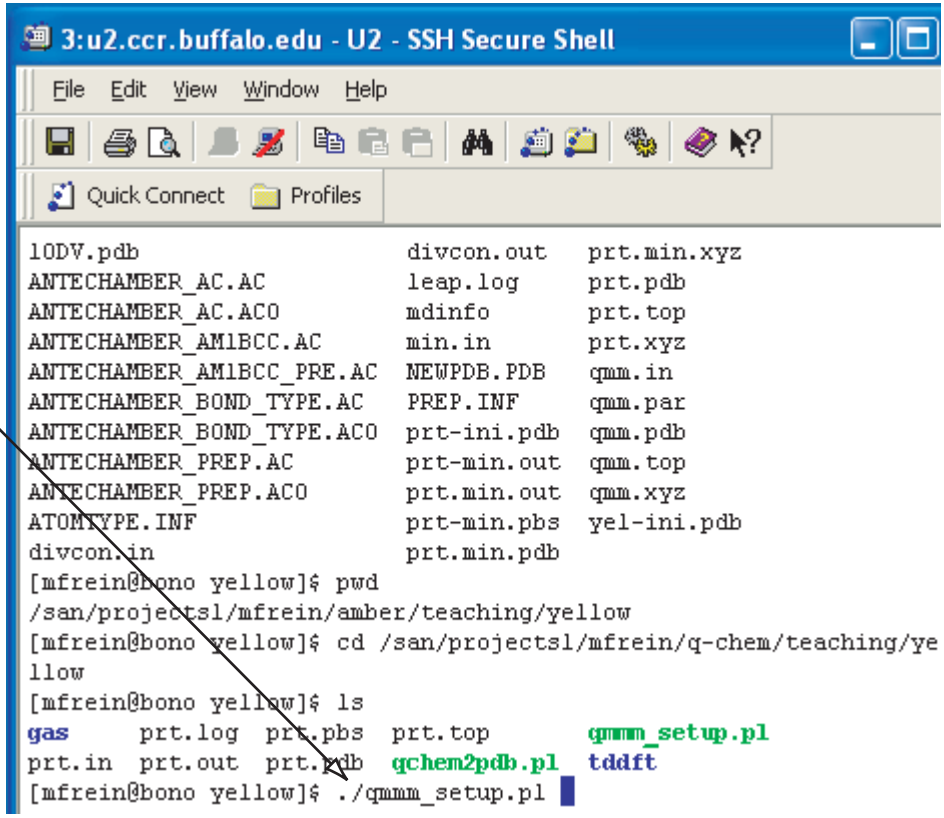
QM/MM electronic excitations in yellow protein

Converting the minimized coordinates into the pdb format



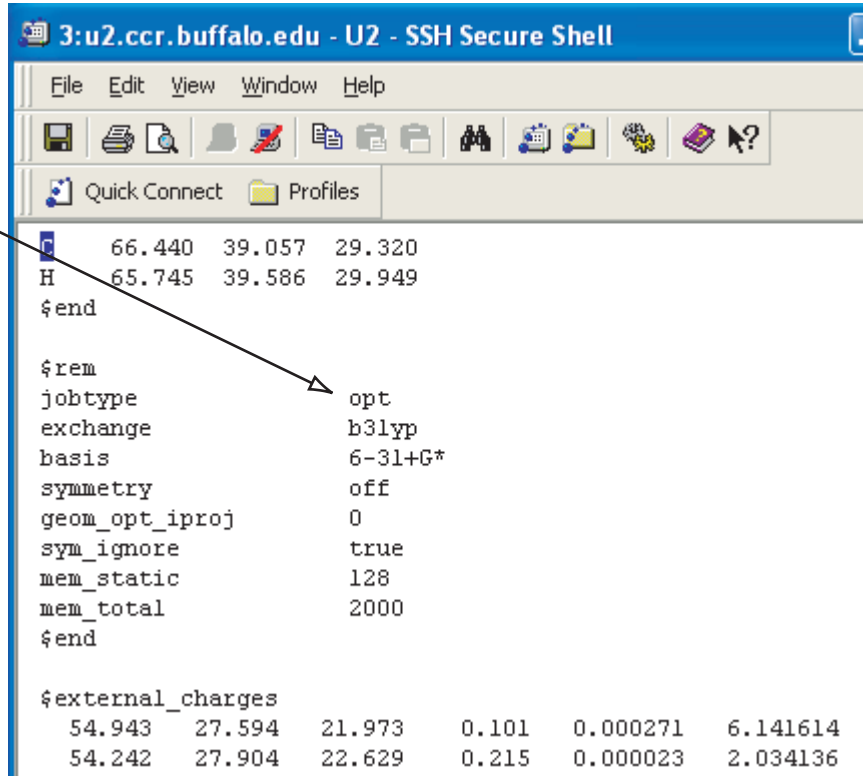
QM/MM electronic excitations in yellow protein

Generating the q-chem input file for the QM/MM calculations

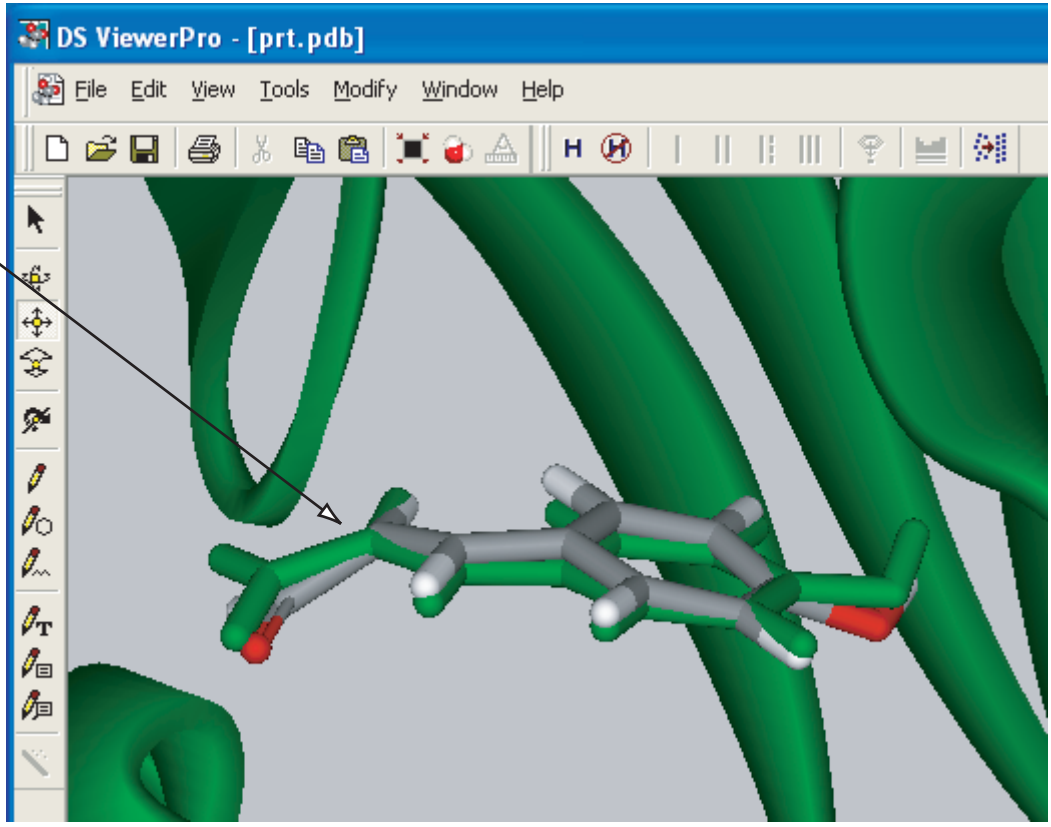


QM/MM electronic excitations in yellow protein

Geometry optimization of the ligand inside the protein

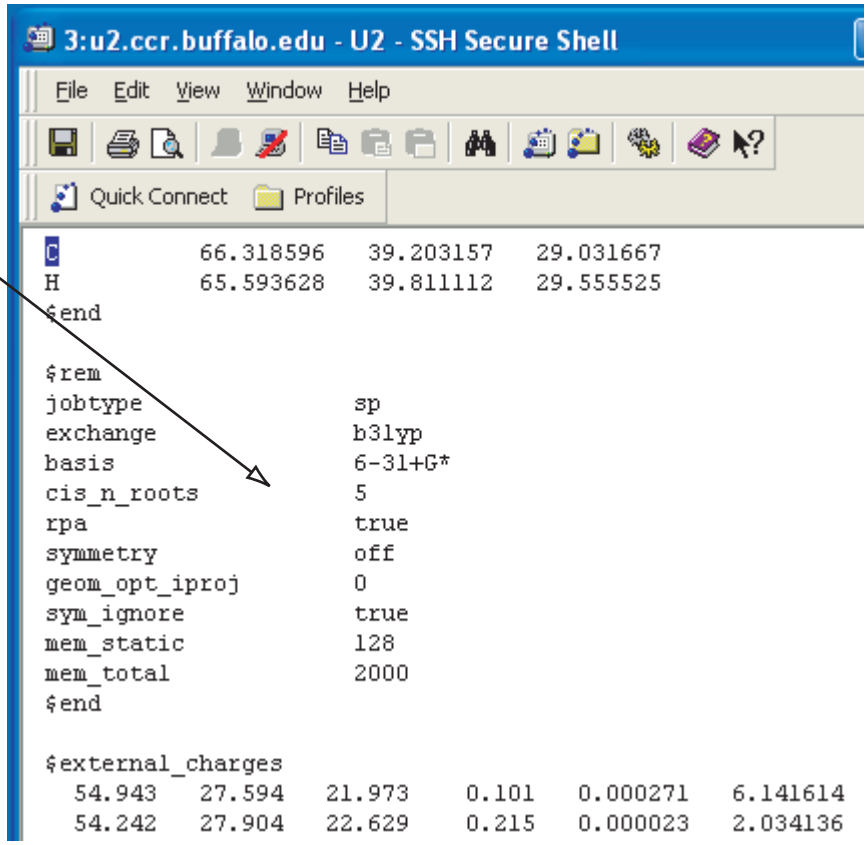


The calculated optimal geometry of the ligand inside the protein



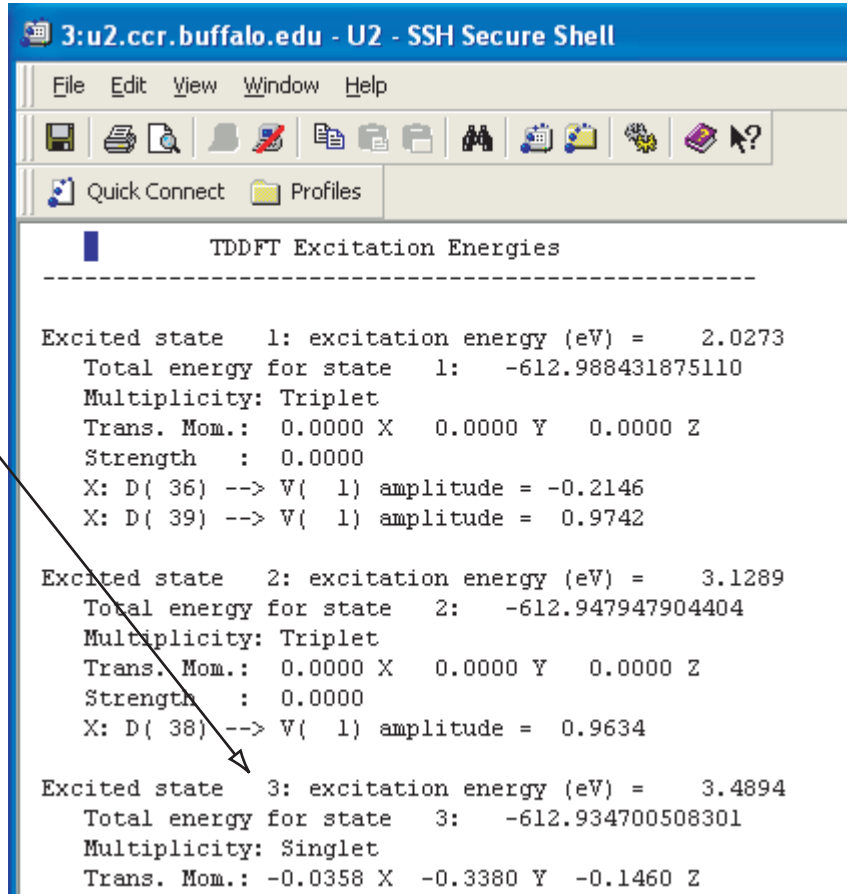
QM/MM electronic excitations in yellow protein

TDDFT calculations in the protein, based on the optimal geometry of the ligand in the protein



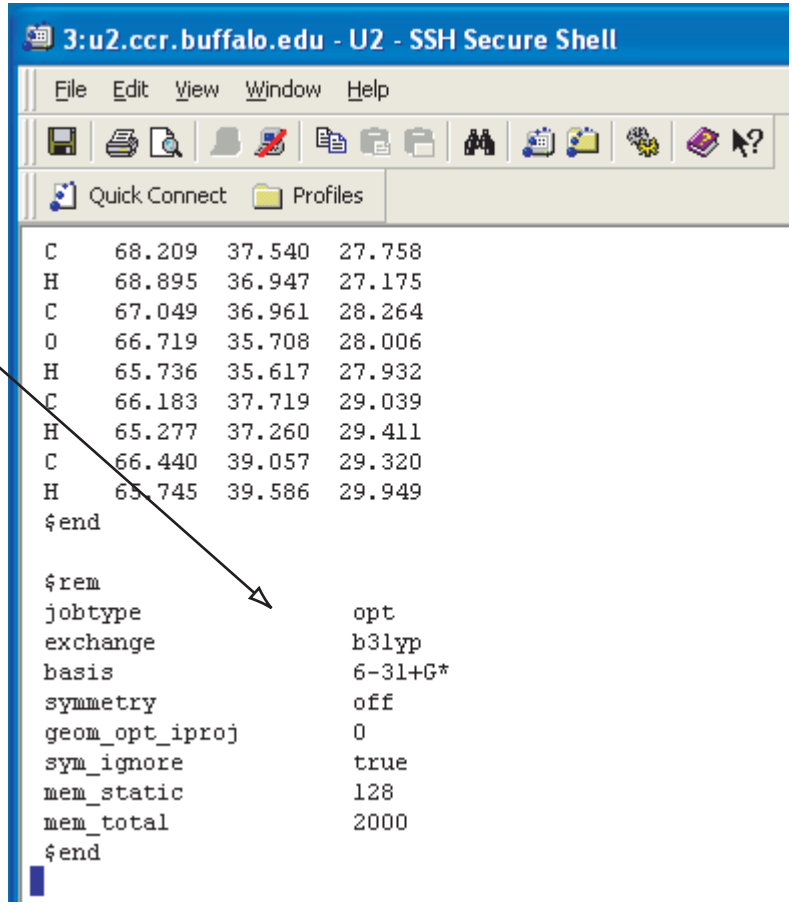
QM/MM electronic excitations in yellow protein

The excitation energy of the first excited singlet electronic state

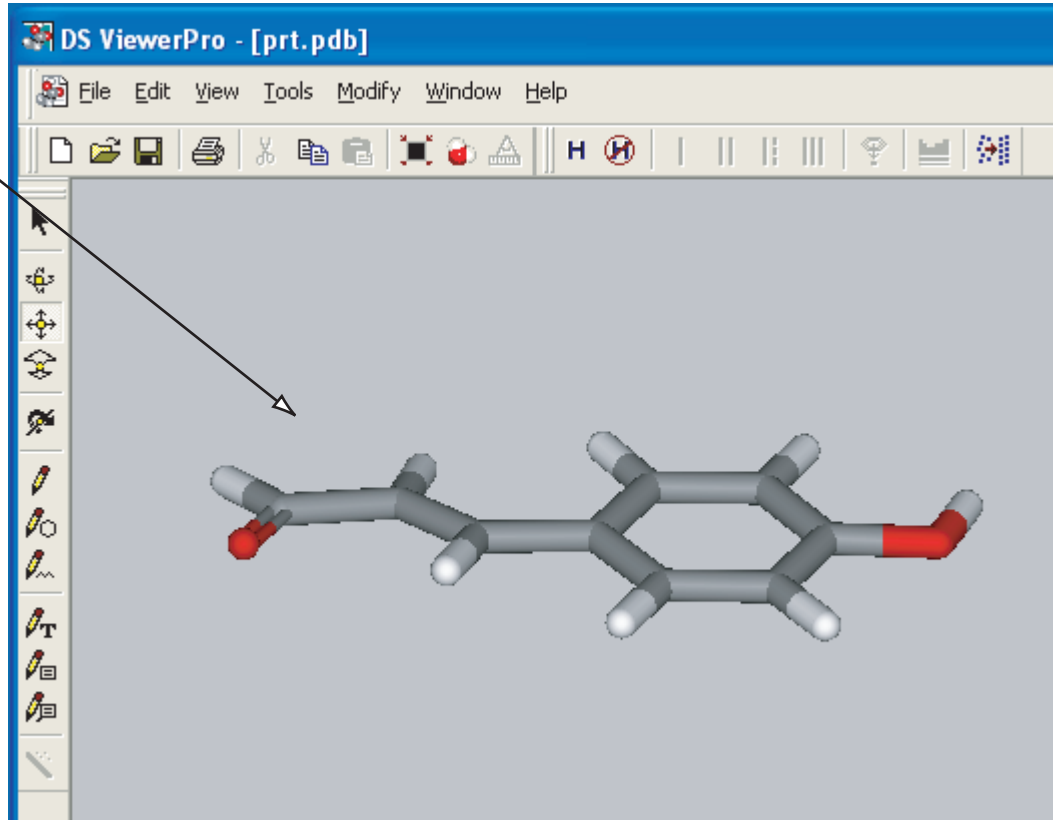


QM/MM electronic excitations in yellow protein

Geometry optimization of the ligand in the gas phase

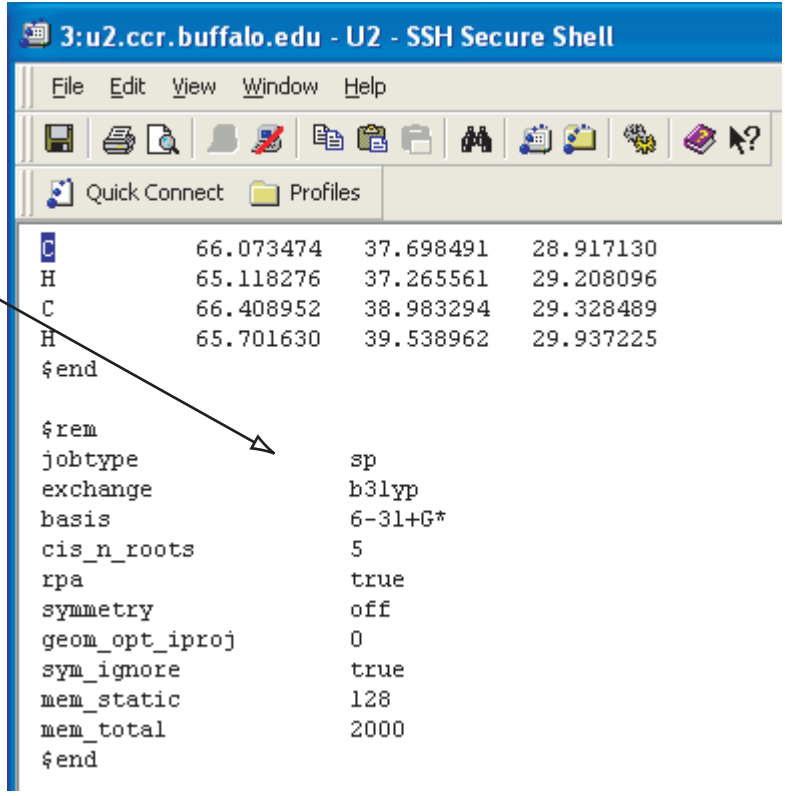


The calculated optimal geometry of the ligand in the gas phase



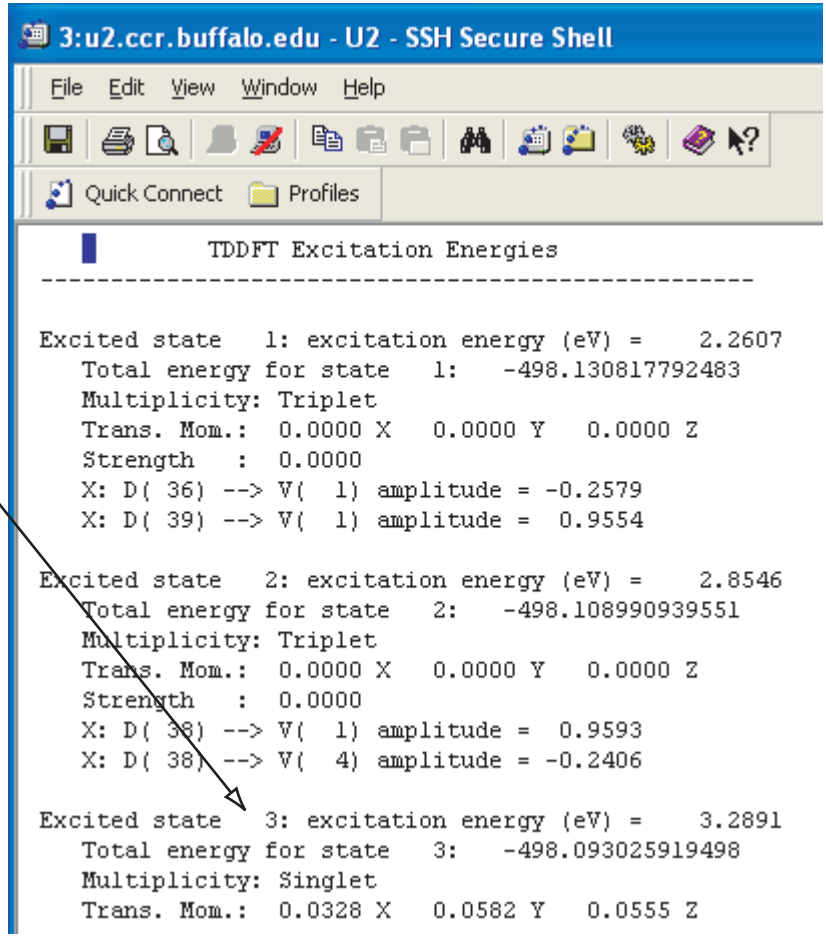
QM/MM electronic excitations in yellow protein

TDDFT calculations of the ligand in the gas phase, for the optimal geometry of the ligand in the gas phase



QM/MM electronic excitations in yellow protein

The excitation energy of the first excited singlet electronic state of the ligand



QM/MM electronic excitations in yellow proteins

The comparison the calculated excitation energies of the ligand with the experiemntal UV spectrum

$\Delta E(cal.) = -23$ nm

$\Delta E(exp.) = -14$ nm