Computational Calculations of pK_a Values of Imidazole in Cu(II) Complexes of Biological Relevance

Jorge Alí-Torres, Luis Rodríguez-Santiago, and Mariona Sodupe*

Departament de Química, Universitat Autònoma de Barcelona, Bellaterra 08193, Spain

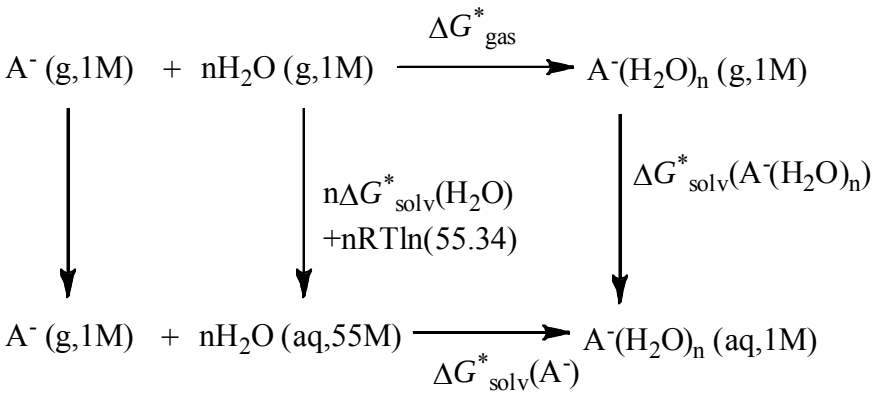
Table of contents

This journal is © the Owner Societies 2011

Determination of the value of n in the cluster-continuum model.

The number of water molecules (n) to include in the ion cluster in this method is determined using cycle S1:

Cycle S1



In this approach the solvation free energy of the ionic species $\Delta G^*_{solv}(A^-)$ is calculated using the following expression:

$$\Delta G^*_{solv}(A^-) = \Delta G^*_{gas} + \Delta G^*_{solv}(A^-(H_2O)_n) - n\Delta G^*_{solv}(H_2O) - nRTln(55.34) \qquad (S1)$$

The size of the ion cluster is determined "variationally" in the sense that corresponds to the value that provides the minimum of the free energy of solvation of the ion ($\Delta G^*_{solv}(A^-)$).

Table S1: Calculated energies at the B3LYP/6-311G++(d,p) level kcal mol^{-1}.

Compound	E_{gas}	G_{gas}	ΔG_{solv}
H_2O	-76.458531	-76.454890	-0.010242
$OH^-(H_2O)_3$	-305.318293	-305.271929	-0.085779
ImH_2^+	-226.654921	-226.596279	-0.104038
ImH	-226.282843	-226.238270	-0.014550
Im^-	-225.714073	-225.683046	-0.094341
$Im^- + H_2O$	-302.199965	-302.150176	-0.084259
$Im^- + 2(H_2O)$	-378.683852	-378.615368	-0.075947
$Im^- + 3(H_2O)$	-455.162424	-455.075706	-0.072353
$Cu^{2+}(HimH)_2$	-2360.680668	-2360.426909	-0.248901
$Cu^{2+}(HimH)(Him^-)$	-2360.361182	-2360.122867	-0.092374
$Cu^{2+}(HimH)(Him^-) + H_2O$	-2436.839096	-2436.579326	-0.084236
$Cu^{2+}(ImH)(H_2O)_3$	-2095.634181	-2095.528778	-0.308457
$Cu^{2+}Im^-(H_2O)_3$	-2095.381872	-2095.296902	-0.079280
cis-$Cu^{2+}(ImH)_2(H_2O)_2$	-2245.512142	-2245.361357	-0.278383
cis-$Cu^{2+}(ImH)Im^-(H_2O)_2$	-2245.208326	-2245.073372	-0.107024
cis-$Cu^{2+}(ImH)Im^-(H_2O)_2 + H_2O$	-2321.695130	-2321.535561	-0.100817
trans-$Cu^{2+}(ImH)_2(H_2O)_2$	-2245.514762	-2245.363502	-0.275741
trans-$Cu^{2+}(ImH)Im^-(H_2O)_2$	-2245.229258	-2245.100990	-0.068111
cis-$Cu^{2+}(ImH)_3(H_2O)$	-2395.382421	-2395.186700	-0.252197
cis-$Cu^{2+}(ImH)_2Im^-(H_2O)$	-2395.063604	-2394.882725	-0.095193
cis-$Cu^{2+}(ImH)_2Im^-(H_2O) + H_2O$	-2471.548353	-2471.342799	-0.090307
trans-$Cu^{2+}(ImH)_3(H_2O)$	-2395.382421	-2395.186700	-0.252197
trans-$Cu^{2+}(ImH)_2Im^-(H_2O)$	-2395.058891	-2394.878768	-0.101724
trans-$Cu^{2+}(ImH)_2Im^-(H_2O) + H_2O$	-2471.540590	-2471.337994	-0.089680

Table S2: Calculated energies at the MPWB1K/6-311G++(d,p) level kcal mol^{-1}.

Compound	E_{gas}	G_{gas}	ΔG_{solv}
H_2O	-76.416258	-76.412441	-0.010027
$OH^-(H_2O)_3$	-305.141119	-305.092334	-0.085956
ImH_2^+	-226.539705	-226.478253	-0.104374
ImH	-226.165845	-226.118664	-0.014913
Im^-	-225.593723	-225.560470	-0.095656
$Im^- + H_2O$	-302.036918	-301.984171	-0.085404
$Im^- + 2(H_2O)$	-378.478225	-378.406032	-0.076817
$Im^- + 3(H_2O)$	-454.914655	-454.821902	-0.069562
$Cu^{2+}(HimH)_2$	-2360.472859	-2360.209058	-0.251538
$Cu^{2+}(HimH)(Him^-)$	-2360.149239	-2359.900340	-0.099621
$Cu^{2+}(HimH)(Him^-) + H_2O$	-2436.587421	-2436.315877	-0.089866
$Cu^{2+}(ImH)(H_2O)_3$	-2095.577142	-2095.462534	-0.310457
$Cu^{2+}Im^-(H_2O)_3$	-2095.281938	-2095.182715	-0.130503
$Cu^{2+}Im^-(H_2O)_3 + H_2O$	-2171.732406	-2171.609753	-0.118119
cis-$Cu^{2+}(ImH)_2(H_2O)_2$	-2245.379337	-2245.219024	-0.282602
cis-$Cu^{2+}(ImH)Im^-(H_2O)_2$	-2245.071323	-2244.924712	-0.112290
cis-$Cu^{2+}(ImH)Im^-(H_2O)_2)+ H_2O$	-2321.518518	-2321.348551	-0.104595
trans-$Cu^{2+}(ImH)_2(H_2O)_2$	-2245.382459	-2245.223992	-0.277744
trans-$Cu^{2+}(ImH)Im^-(H_2O)_2$	-2245.071986	-2244.926062	-0.112892
trans-$Cu^{2+}(ImH)Im^-(H_2O)_2 + H_2O$	-2321.519617	-2321.349957	-0.103322
cis-$Cu^{2+}(ImH)_3(H_2O)$	-2395.175916	-2394.969682	-0.255903
cis-$Cu^{2+}(ImH)_2Im^-(H_2O)$	-2394.855048	-2394.661443	-0.098565
cis-$Cu^{2+}(ImH)_2Im^-(H_2O) + H_2O$	-2471.297209	-2471.081945	-0.091608
trans-$Cu^{2+}(ImH)_3(H_2O)$	-2395.175916	-2394.969682	-0.255903
trans-$Cu^{2+}(ImH)_2Im^-(H_2O)$	-2394.849308	-2394.656499	-0.103759
trans-$Cu^{2+}(ImH)_2Im^-(H_2O) + H_2O$	-2471.281641	-2471.067169	-0.101357

Table S3: Calculated single point CCSD(T)/6-311++G(d,p) energies in kcal mol^{-1}

Compound	**CCSD(T)//B3LYP**	**CCSD(T)//MPWB1K**
ImH_2^+	-226.067591	-226.065009
ImH	-225.694154	-225.691498
Im^-	-225.124442	-225.121749
$Cu^{2+}(ImH)(H_2O)_3$	--	-2093.295819
$Cu^{2+}Im^-(H_2O)_3$	--	-2093.002826
cis-$Cu^{2+}Im_2(H_2O)_2$	-2242.764969	-2242.759526
cis-$Cu^{2+}(ImH)Im^-(H_2O)_2$	-2242.457273	-2242.453460
trans-$Cu^{2+}Im_2(H_2O)_2$	--	-2242.761764
trans-$Cu^{2+}(ImH)Im^-(H_2O)_2$	--	-2242.452234

Table S4: Calculated energies at different levels with the 6-311++G(2df,2pd) basis set in kcal mol^{-1}.

	E_{gas}	G_{gas}	ΔG_{solv}
B3LYP			
ImH_2^+	-226.670301	-226.611659	-0.104038
ImH	-226.298050	-226.253477	-0.014550
Im^-	-225.727448	-225.696421	-0.094341
MPWB1K			
ImH_2^+	-226.556156	-226.494704	-0.104374
ImH	-226.181549	-226.134368	-0.014913
Im^-	-225.607356	-225.574103	-0.095656
CCSD(T)//B3LYP			
ImH_2^+	-226.199123		
ImH	-225.826160		
Im^-	-225.255496		
CCSD(T)//MPWB1K			
ImH_2^+	-226.197808		
ImH	-225.824650		
Im^-	-225.253801		

Table S5: Gibbs energy of solvation of the deprotonated complexes computed using cycle S1 in kcal mol^{-1}.

Compound	n = 0	n = 1	n = 2
B3LYP			
Im^-	-59.20	-58.50	-57.70
cis-$Cu^{2+}(ImH)Im^-(H_2O)_2$	-67.16	-65.79	
cis-$Cu^{2+}(ImH)Im_2^-(H_2O)$	-59.73	-57.87	
trans-$Cu^{2+}(ImH)_2Im^-(H_2O)$	-63.83	-56.95	
MPWB1K			
Im^-	-60.03	-58.61	-57.08
$Cu^{2+}Im^-(H_2O)_3$	-81.89	-81.23	
cis-$Cu^{2+}(ImH)Im^-(H_2O)_2$	-70.46	-70.74	
trans-$Cu^{2+}(ImH)Im^-(H_2O)_2$	-70.84	-69.97	
cis-$Cu^{2+}(ImH)_2Im^-(H_2O)$	-61.85	-62.72	
trans-$Cu^{2+}(ImH)_2Im^-(H_2O)$	-65.11	-60.44	

Table S6: pK_a values for $Cu^{2+}(ImH)_n(H_2O)_{4-n}$ complexes computed using cycle 4 and UAHF radii. All calculations were carried out using the 6-311++G(d,p) basis set.

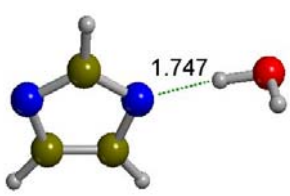
	n = 0		**n = 1**	
	B3LYP	**MPWB1K**	**B3LYP**	**MPWB1K**
$Cu^{2+}(ImH)(H_2O)_3$	--	5.6	--	4.9
cis-$Cu^{2+}(ImH)_2(H_2O)_2$	6.4	7.9	7.0	6.7
trans-$Cu^{2+}(ImH)_2(H_2O)_2$	--	7.1	--	6.8
$Cu^{2+}(ImH)_3(H_2O) \rightarrow$ *cis*-$Cu^{2+}(ImH)_2Im^-(H_2O) + H^+$	7.2	8.3	8.3	6.8
$Cu^{2+}(ImH)_3(H_2O) \rightarrow$ *trans*-$Cu^{2+}(ImH)_2Im^-(H_2O) + H^+$	6.3	8.5	10.8	11.3

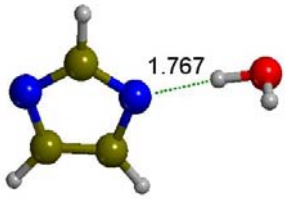
Table S7: Gas phase and solution acidities of ImH and $Cu^{2+}(ImH)_m(H_2O)_{4-m}$ complexes in kcal mol^{-1}. All calculations were carried out using the 6-311++G(d,p) basis set.

	Gas phase		**Solution**	
	B3LYP	**MPWB1K**	**B3LYP**	**MPWB1K**
ImH	342.1	344.0	28.0	29.3
$Cu^{2+}(ImH)(H_2O)_3$	--	169.3	--	18.2
cis-$Cu^{2+}(ImH)_2(H_2O)_2$	174.4	178.4	18.0	21.3
trans-$Cu^{2+}(ImH)_2(H_2O)_2$	--	180.7	--	20.1
$Cu^{2+}(ImH)_3(H_2O) \rightarrow$ *cis*-$Cu^{2+}(ImH)_2Im^{-}(H_2O) + H^{+}$	184.5	187.1	19.0	21.9
$Cu^{2+}(ImH)_3(H_2O) \rightarrow$ *trans*-$Cu^{2+}(ImH)_2Im^{-}(H_2O) + H^{+}$	187.0	190.2	17.4	21.7

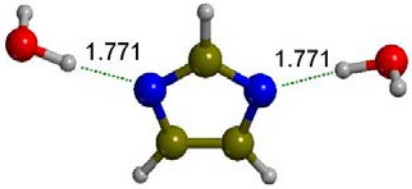
Figure S1. Optimized structures of deprotonated imidazole considering explicit solvent molecules. Distances are given in Å.

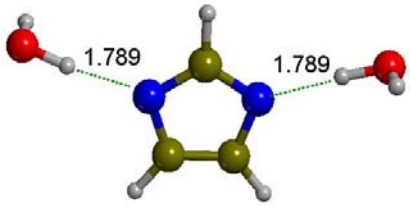
B3LYP **MPWB1K**



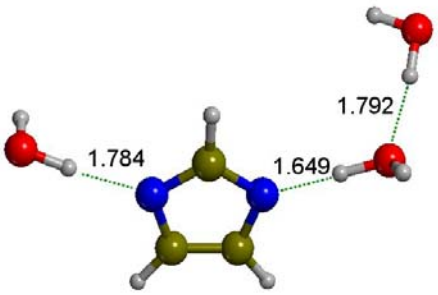


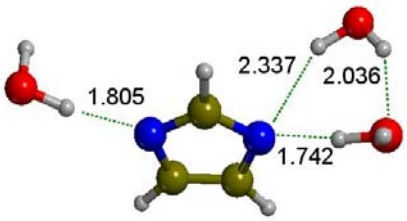
$Im^- + H_2O$





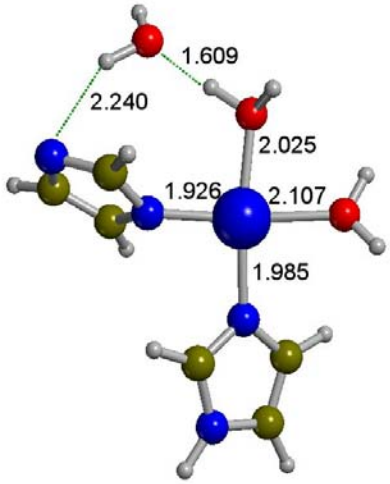
$Im^- + 2(H_2O)$



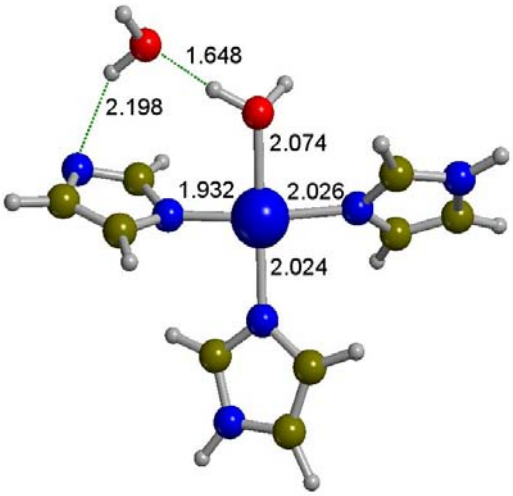


$Im^- + 3(H_2O)$

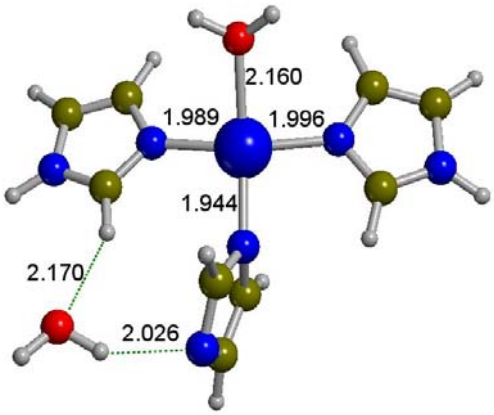
Figure S2. B3LYP optimized structures of deprotonated complexes considering one explicit solvent molecule. Distances are given in Å.



***cis*-$Cu^{2+}(ImH)Im^{-}(H_2O)_2 + H_2O$**

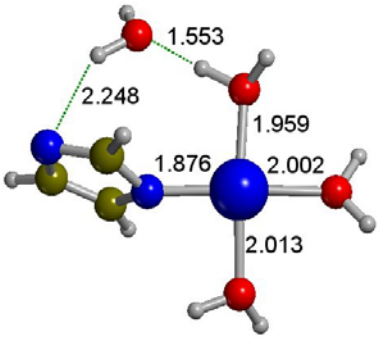


***cis*-$Cu^{2+}(ImH)_2Im^{-}(H_2O) + H_2O$**

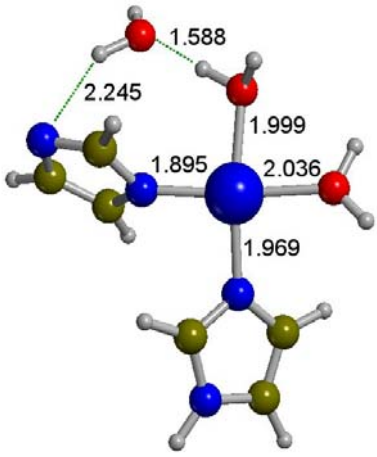


***trans*-$Cu^{2+}(ImH)_2Im^{-}(H_2O) + H_2O$**

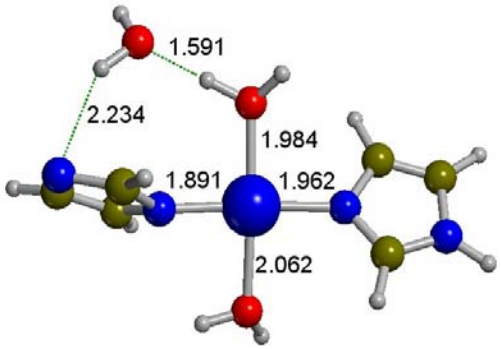
Figure S3. MPWB1K optimized structures of deprotonated complexes considering one explicit solvent molecule. Distances are given in Å.



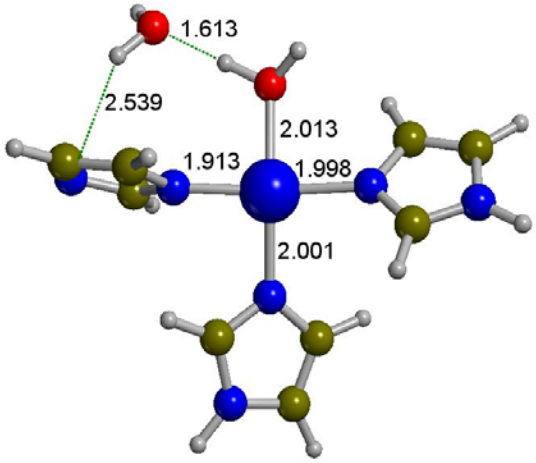
$Cu^{2+}Im^{-}(H_2O)_3 + H_2O$



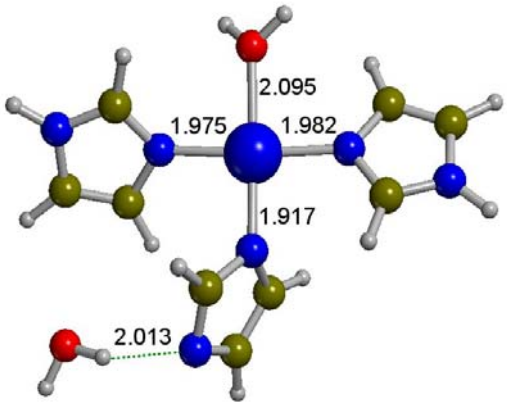
***cis*-$Cu^{2+}(ImH)Im^{-}(H_2O)_2 + H_2O$**



***trans*-$Cu^{2+}(ImH)Im^{-}(H_2O)_2 + H_2O$**



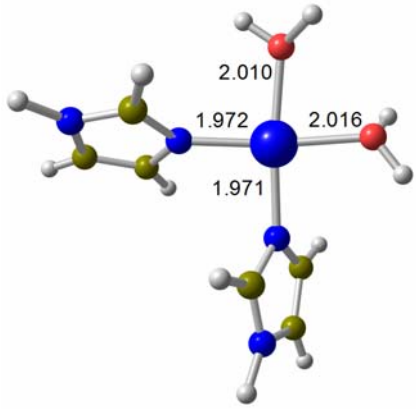
***cis*-$Cu^{2+}(ImH)_2Im^{-}(H_2O) + H_2O$**



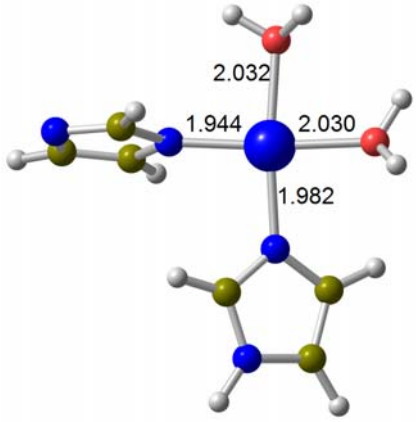
***trans*-$Cu^{2+}(ImH)_2Im^{-}(H_2O) + H_2O$**

Figure S4. B3LYP and MPWB1K solution optimized structures of protonated and deprotonated cis-$Cu^{2+}(ImH)_2(H_2O)_2$. Distances are given in Å.

B3LYP

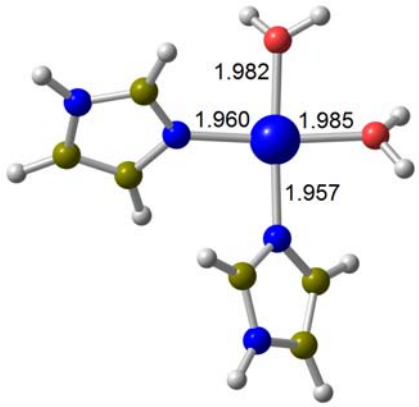


***cis*-$Cu^{2+}(ImH)_2(H_2O)_2$**

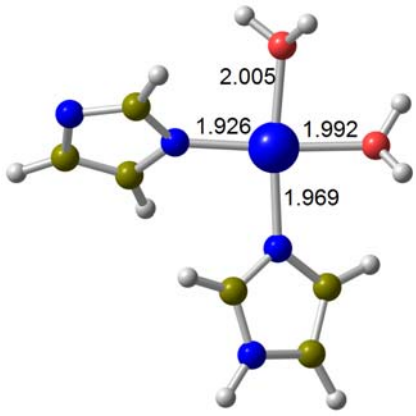


***cis*-$Cu^{2+}(ImH)Im^{-}(H_2O)_2$**

MPWB1K



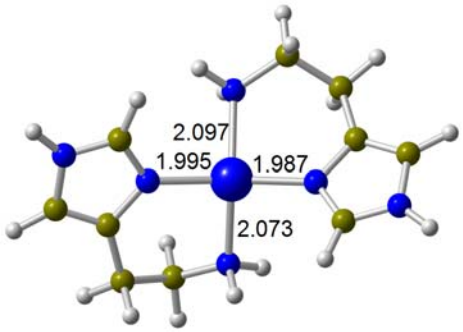
***cis*-$Cu^{2+}(ImH)_2(H_2O)_2$**



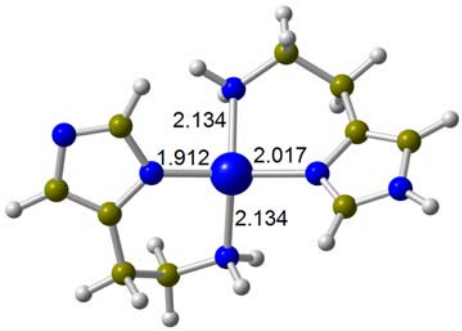
***cis*-$Cu^{2+}(ImH)Im^{-}(H_2O)_2$**

Figure S5. B3LYP and MPWB1K optimized structures of $Cu^{2+}(Him)_2$ and $Cu^{2+}(HimH)(Him^-)$ complexes Distances are given in Å.

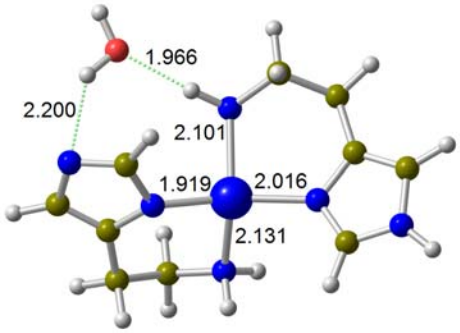
B3LYP



$Cu^{2+}(Him)_2$

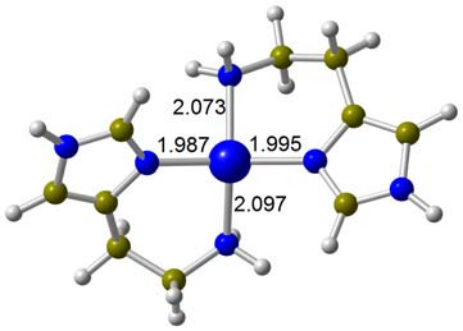


$Cu^{2+}(HimH)(Him^-)$

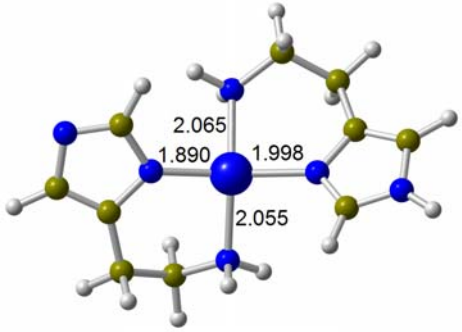


$Cu^{2+}(HimH)(Him^-) + H_2O$

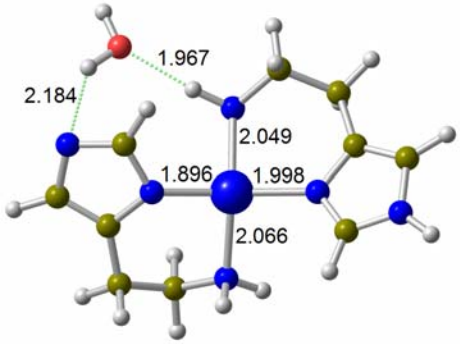
MPWB1K



$Cu^{2+}(Him)_2$



$Cu^{2+}(HimH)(Him^-)$



$Cu^{2+}(HimH)(Him^-) + H_2O$