Article

Supplementary Information - Determination of pK_a Values via *ab initio* Molecular Dynamics and its Application to Transition Metal Based Water Oxidation Catalysts

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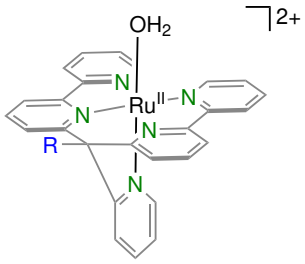
Version June 11, 2019 submitted to Inorganics

1. Ligand Structure



$[Ru(II)Py_5R(OH_2)]^{2+}$, where R = Me or OMe

Figure S 1. Lewis structure of $[Ru(II)Py_5R(H_2O)]^{2+}$, where R = Me or OMe.

2. Potentials of Mean Force

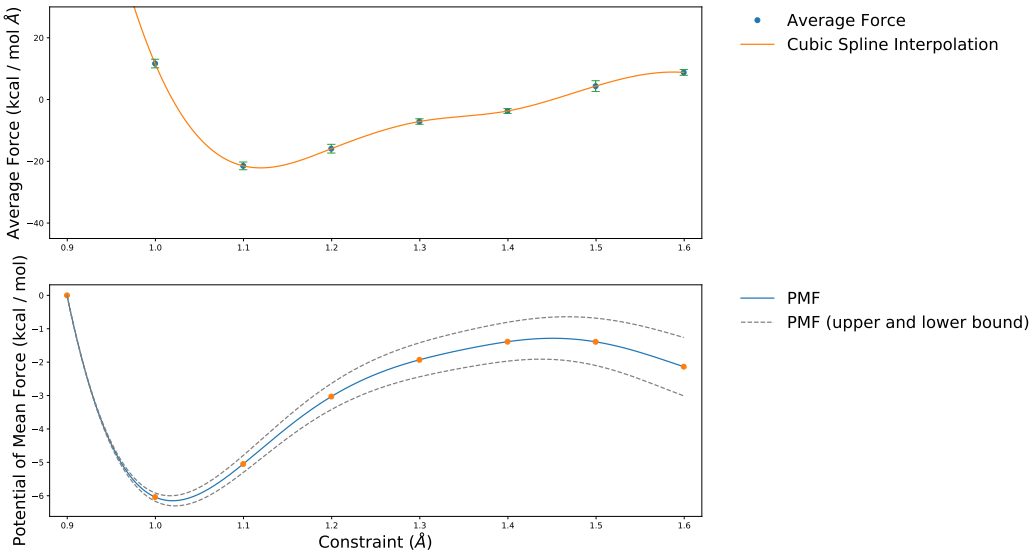


Figure S 2. Average force and PMF profile of HCOOH in a cubic box with a side length of 15.6406 Å.

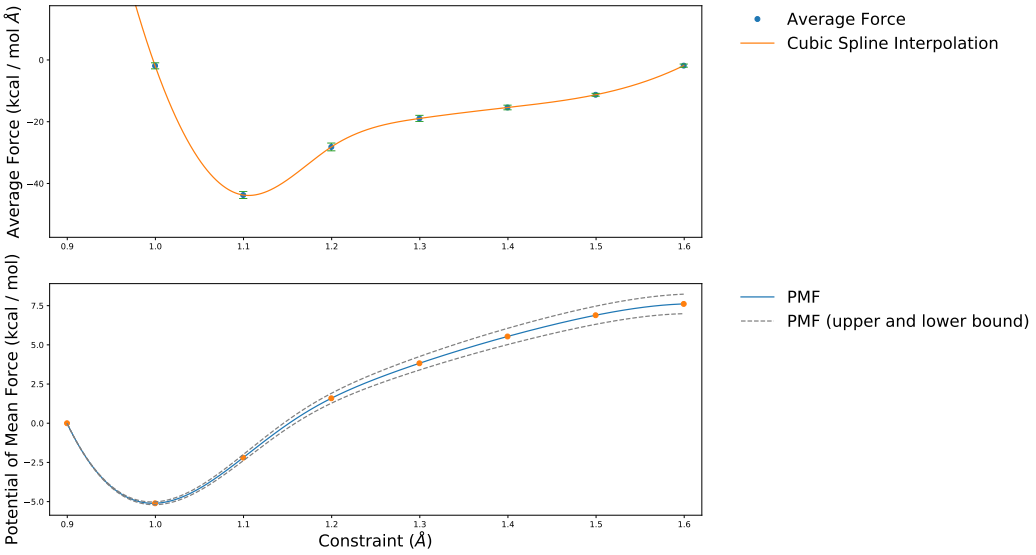


Figure S 3. Average force and PMF profile of PhOH in a cubic box with a side length of 15.6406 Å.

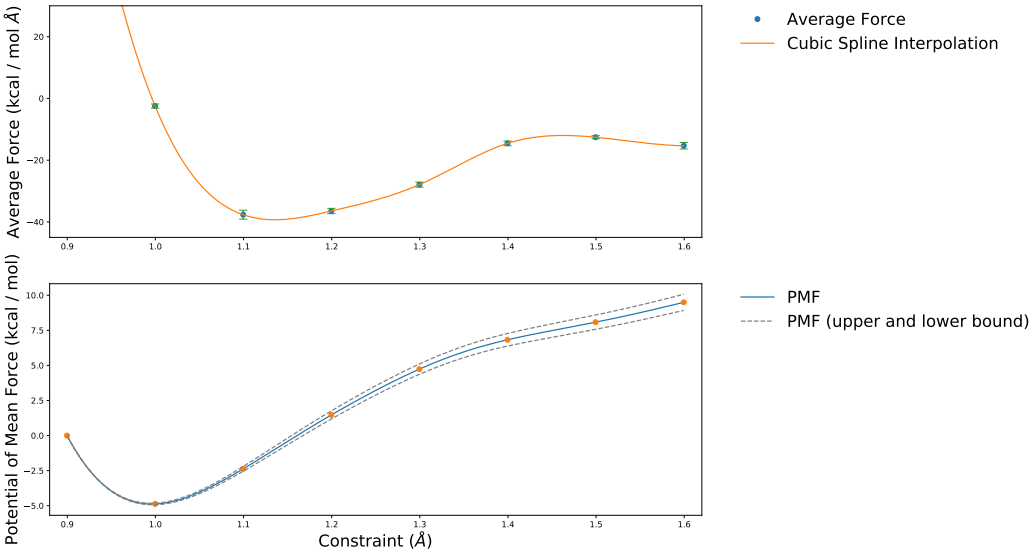


Figure S 4. Average force and PMF profile of $[Ru(II)Py_5Me(H_2O)]^{2+}$ in a cubic box with a side length of 15.6406 Å.

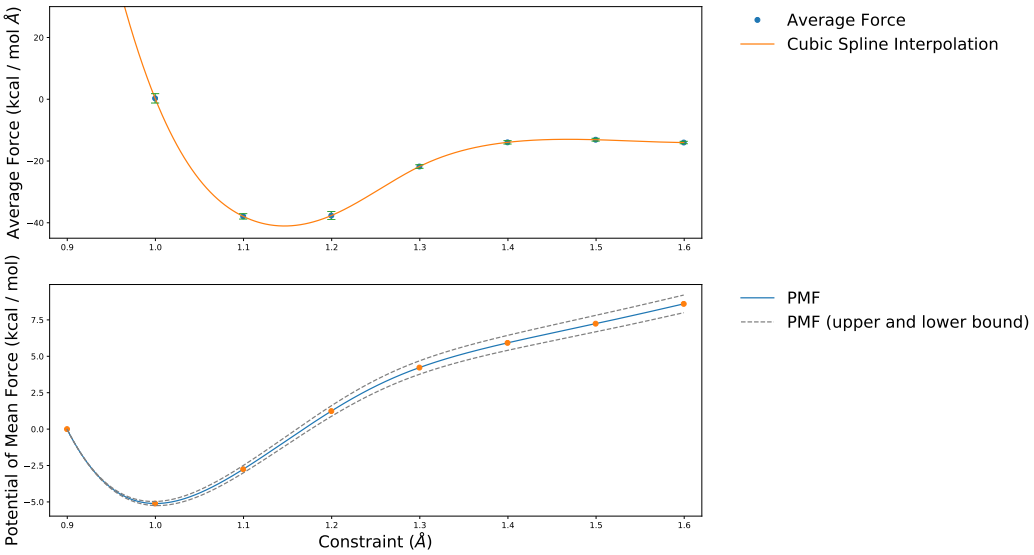


Figure S 5. Average force and PMF profile of $[Ru(II)Py_5OMe(H_2O)]^{2+}$ in a cubic box with a side length of 15.6406 Å.

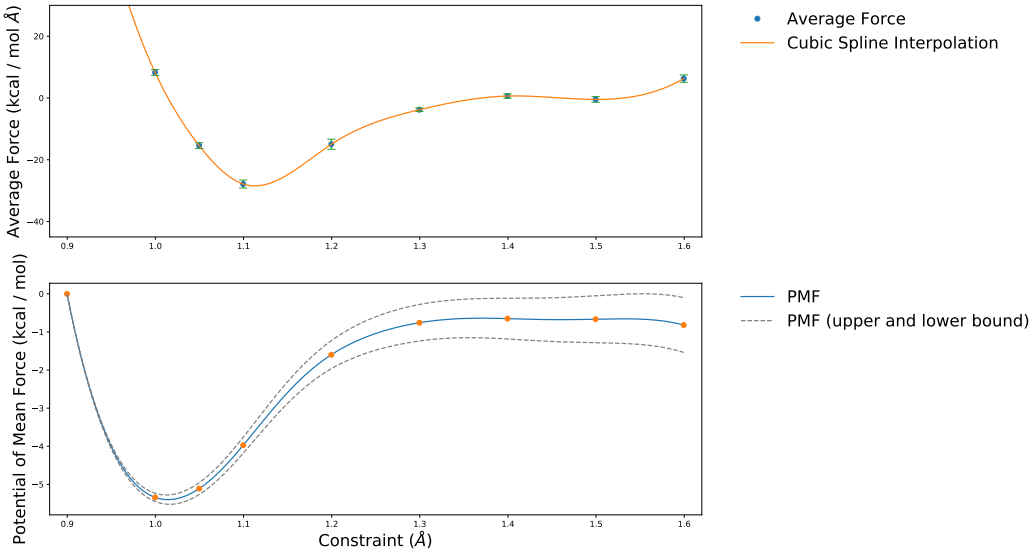


Figure S 6. Average force and PMF profile of $[Ru(III)Py_5OMe(H_2O)]^{3+}$ in a cubic box with a side length of 15.6406 Å.

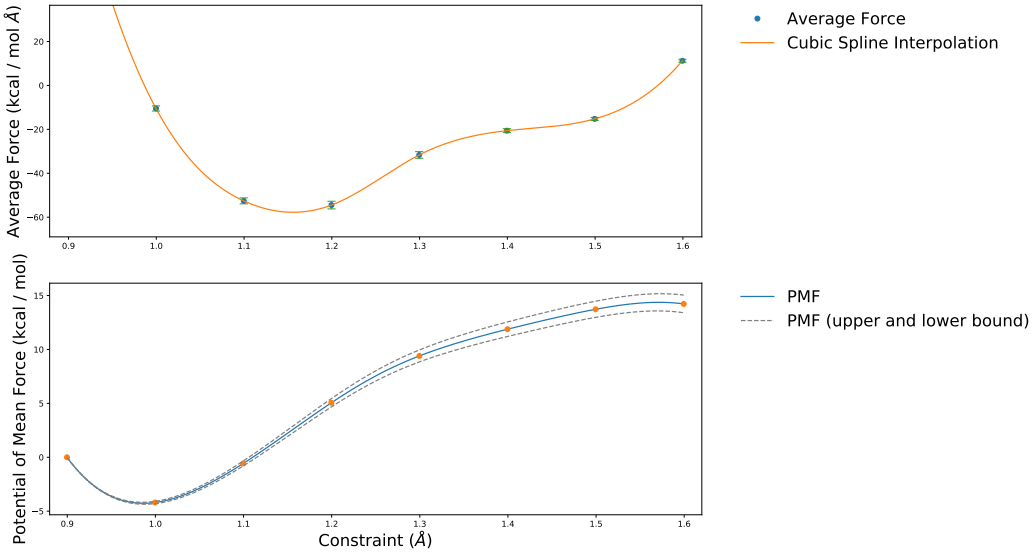


Figure S 7. Average force and PMF profile of water in a cubic box with a side length of 19.7340 Å.

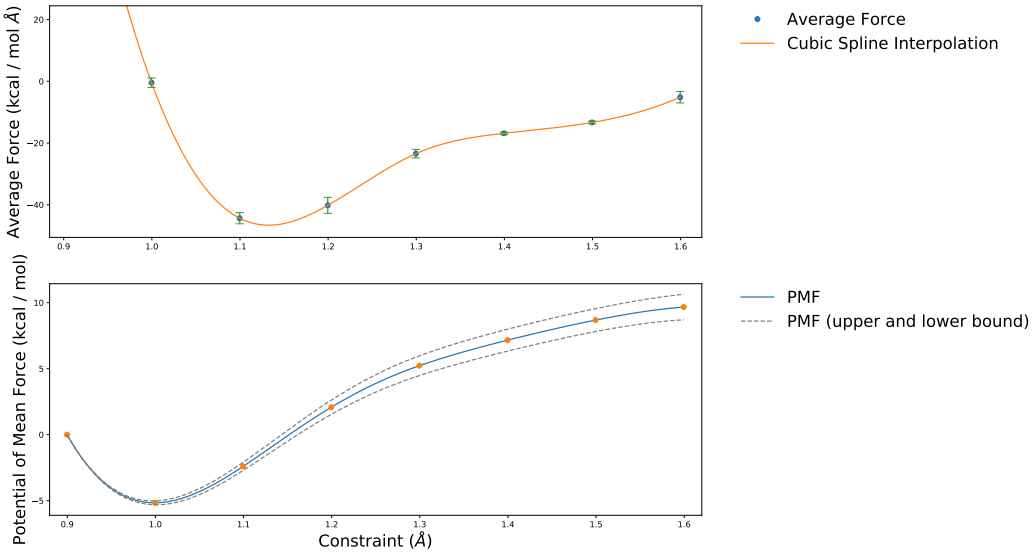


Figure S 8. Average force and PMF profile of $[Ru(II)Py_5OMe(H_2O)]^{2+}$ in a cubic box with a side length of 19.7340 Å.

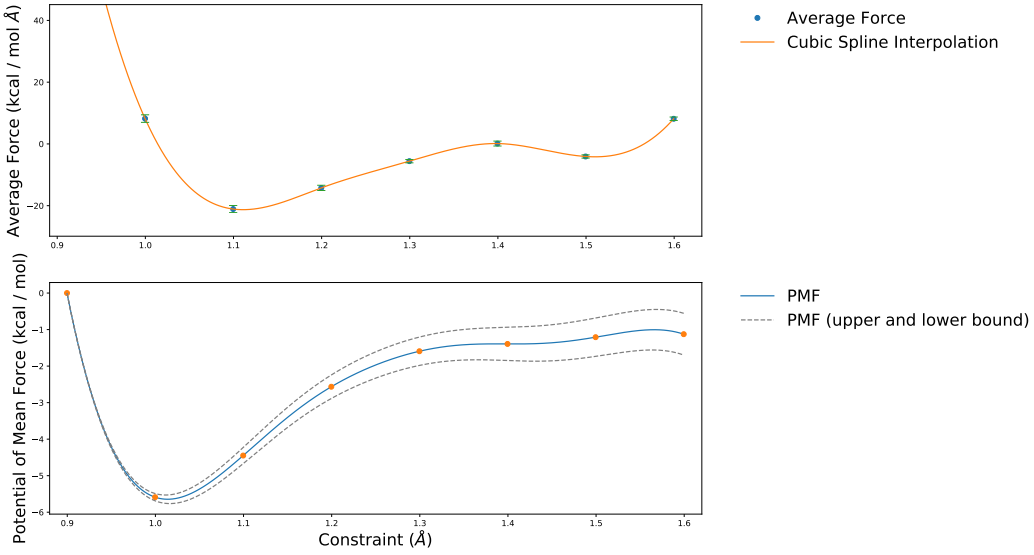


Figure S 9. Average force and PMF profile of $[Ru(III)Py_5OMe(H_2O)]^{3+}$ in a cubic box with a side length of 19.7340 Å.

3. Absolute and probabilistic pK_a

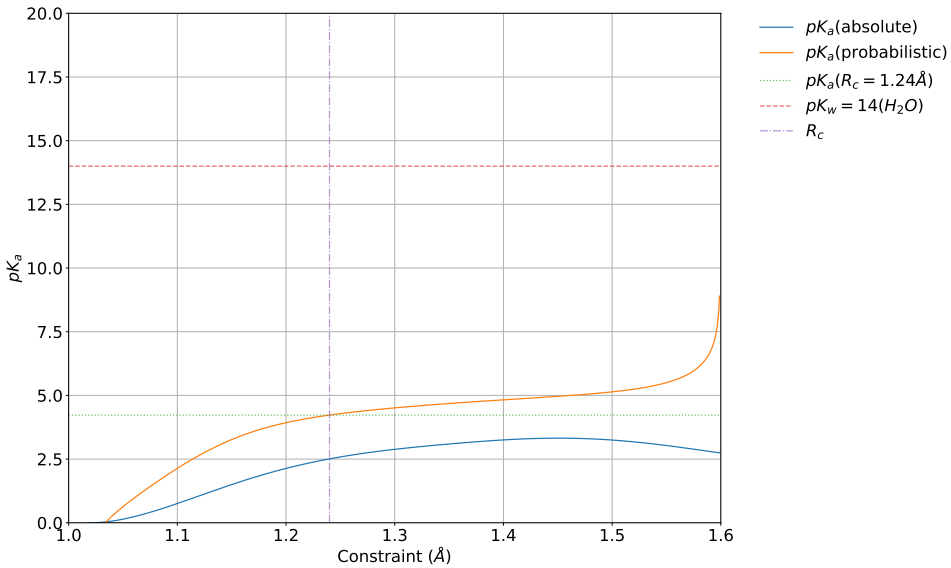


Figure S 10. Absolute and probabilistic pK_a calculated for HCOOH in a cubic box with a side length of 15.6406 Å.

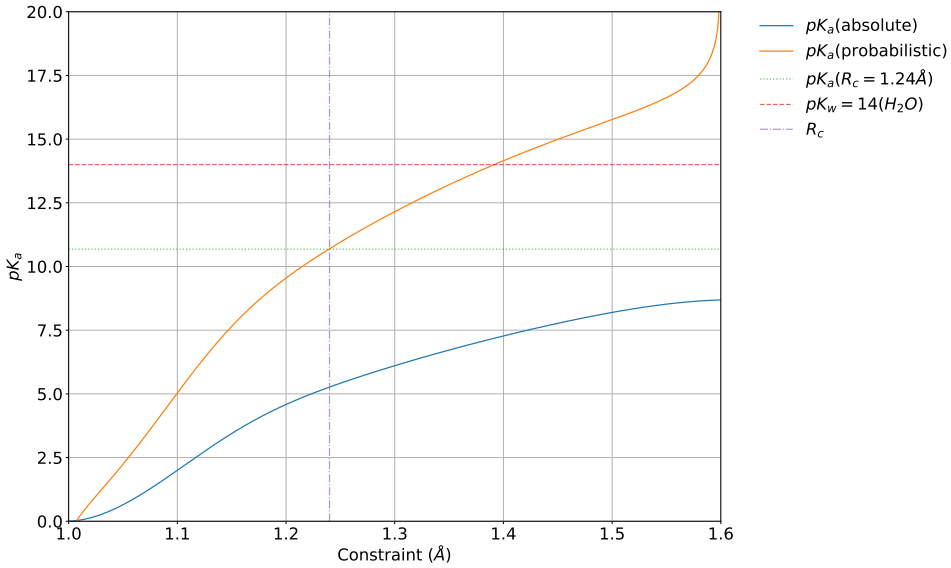


Figure S 11. Absolute and probabilistic pK_a calculated for PhOH in a cubic box with a side length of 15.6406 Å.

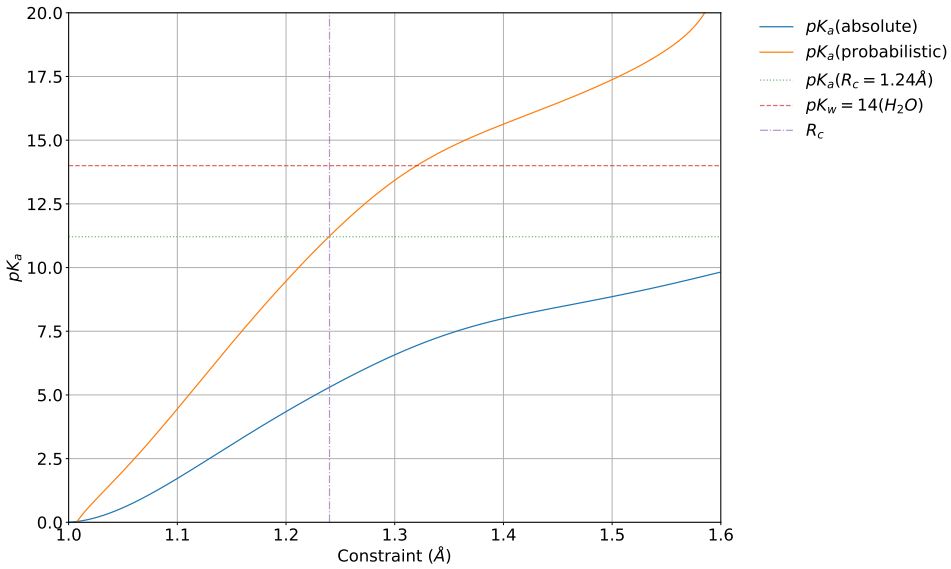


Figure S 12. Absolute and probabilistic pK_a calculated for $[Ru(II)Py_5Me(H_2O)]^{2+}$ in a cubic box with a side length of 15.6406 Å.

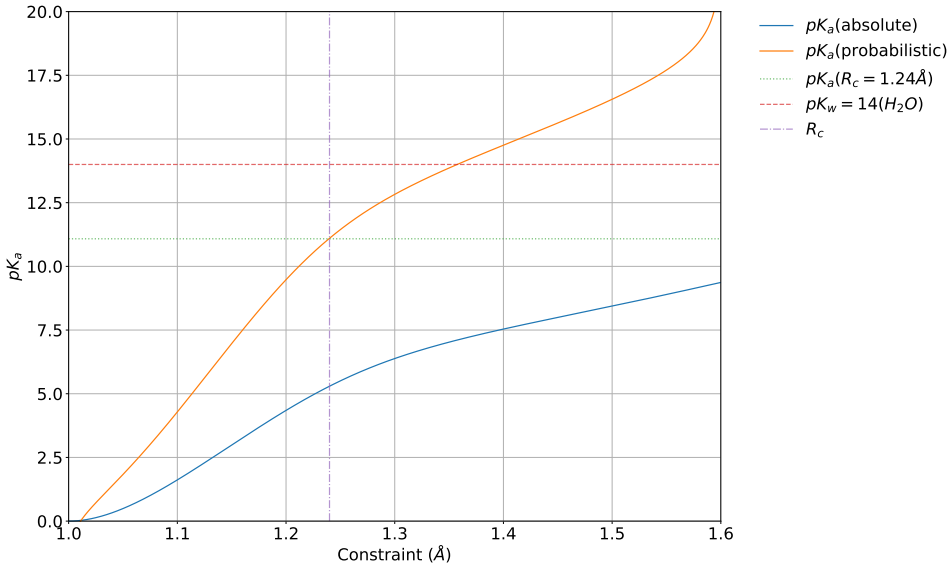


Figure S 13. Absolute and probabilistic pK_a calculated for $[Ru(II)Py_5OMe(H_2O)]^{2+}$ in a cubic box with a side length of 15.6406 Å.

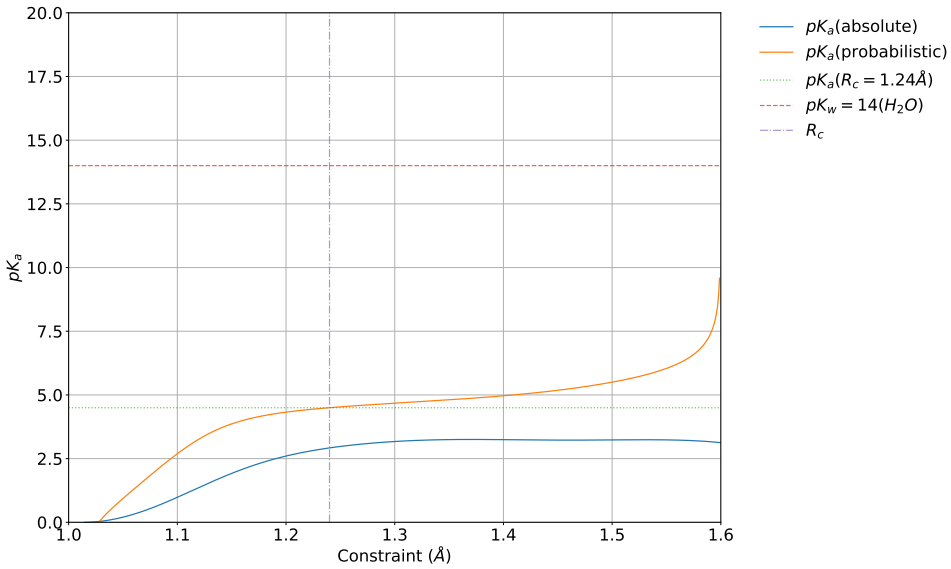


Figure S 14. Absolute and probabilistic pK_a calculated for [Ru(III)Py$_5$OMe(H$_2$O)]$^{3+}$ in a cubic box with a side length of 15.6406 Å.

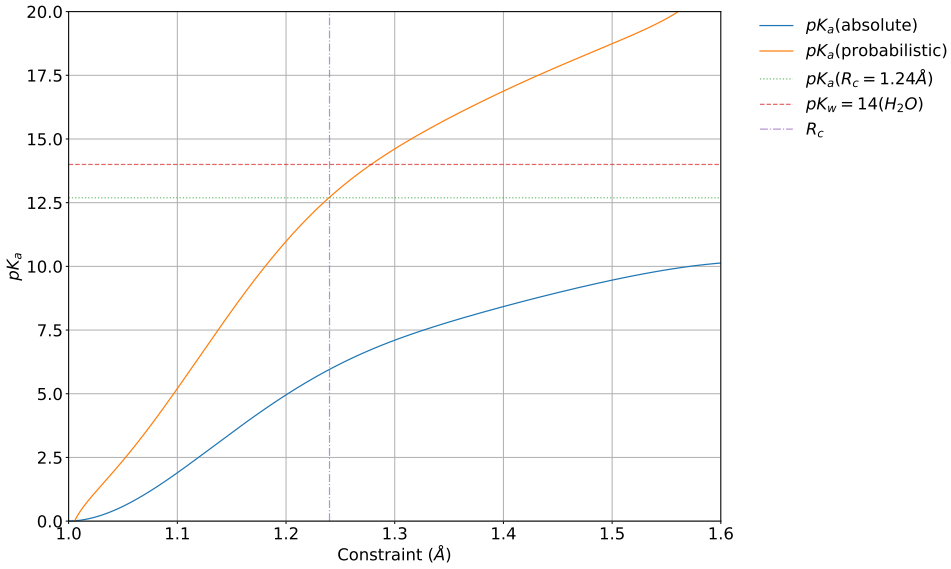


Figure S 15. Absolute and probabilistic pK_a calculated for [Ru(II)Py$_5$OMe(H$_2$O)]$^{2+}$ in a cubic box with a side length of 19.7340 Å.

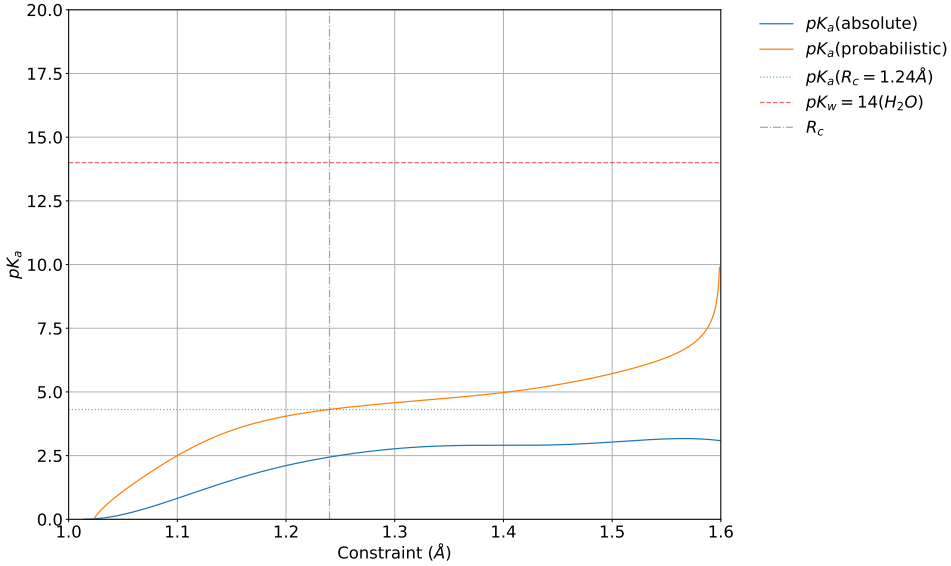


Figure S 16. Absolute and probabilistic pK_a calculated for [Ru(III)Py$_5$OMe(H$_2$O)]$^{3+}$ in a cubic box with a side length of 19.7340 Å.

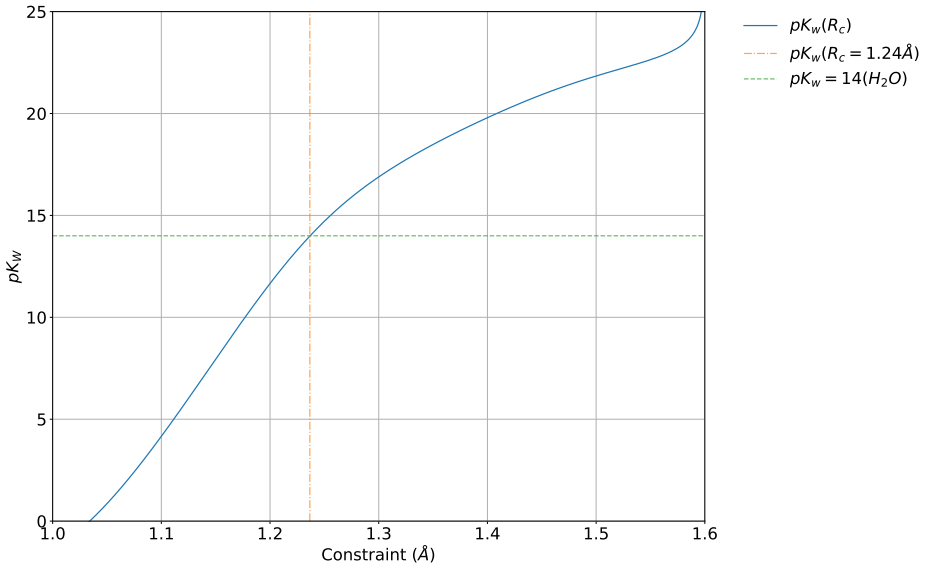


Figure S 17. Determination of R_c from the simulation of water, by fitting to the experimental value in box with a side length of 19.7340 Å.

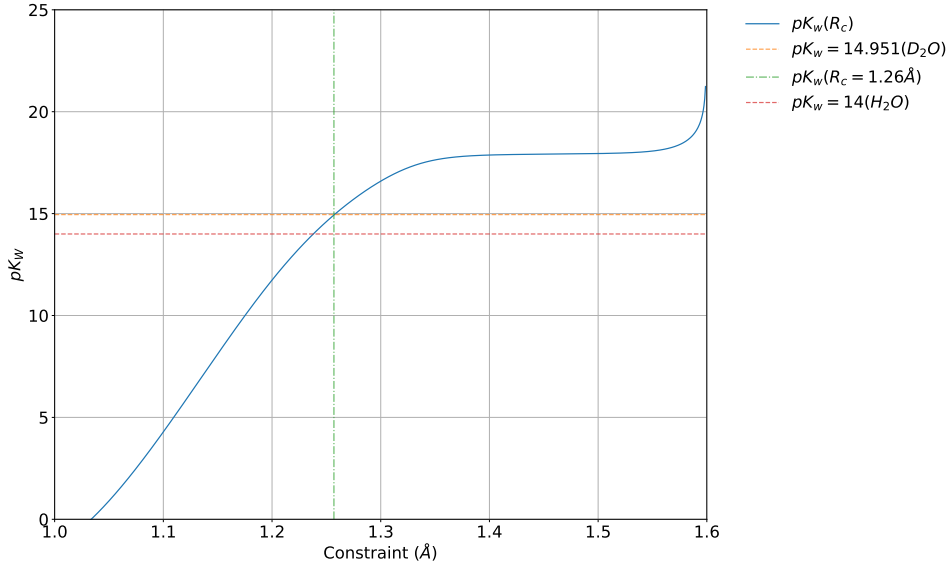


Figure S 18. Determination of R_c from the simulation of water, by fitting to the experimental value of D_2O in box with a side length of 15.6406 Å.

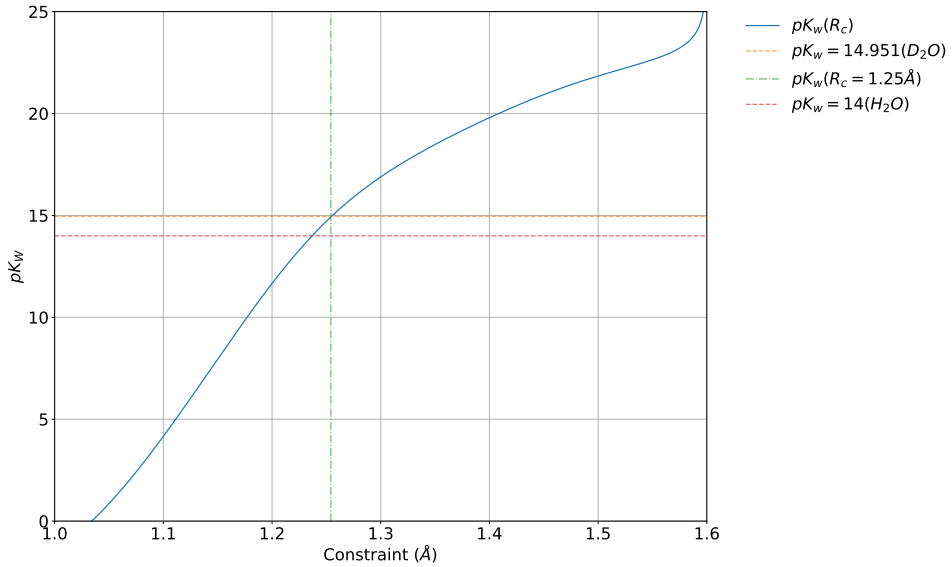


Figure S 19. Determination of R_c from the simulation of water, by fitting to the experimental value of D_2O in box with a side length of 19.7340 Å.

4. Probabilistic pK_a - dependence on R_c

Table S 1. All results presented here are calculated at 320 K, for a cubic box with a side length of 15.6406 Å, over a trajectory of about 20 ps (where the first 5 ps were not included in the evaluation). The pK_a values were calculated using the probabilistic method for different values of R_c. The '*' indicates the that R_c value determined was determined from clean water using the same settings.

Molecule	pK_a (exp.)	1.19 Å	1.22 Å	1.24* Å	1.28 Å	1.30 Å
H_2O	14.0	-	-	-	-	
HCOOH	3.8 [1]	3.8	4.1	4.2	4.4	4.5
PhOH	10.0 [1]	9.2	10.1	10.7	11.7	12.1
$[Ru(II)Py_5Me(H_2O)]^{2+}$	∼11[2]	9.0	10.4	11.2	12.8	13.4
$[Ru(II)Py_5OMe(H_2O)]^{2+}$	∼11[2]	9.0	10.3	11.1	12.3	12.8
$[Ru(III)Py_5OMe(H_2O)]^{3+}$	∼2.5[2]	4.3	4.4	4.5	4.6	4.7

Table S 2. All results presented here are calculated at 320 K, for a cubic box with a side length of 19.7340 Å, over a trajectory of about 20 ps (where the first 5 ps were not included in the evaluation). The pK_a values were calculated using the probabilistic method for different values of R_c. The '*' indicates the that R_c value determined was determined from clean water using the same settings.

Molecule	pK_a (exp.)	1.22 Å	1.24* Å	1.28 Å	1.30 Å
H_2O	14.0	-	-	-	-
$[Ru(II)Py_5OMe(H_2O)]^{2+}$	∼11[2]	11.9	12.7	14.0	14.6
$[Ru(III)Py_5OMe(H_2O)]^{3+}$	∼2.5[2]	4.2	4.3	4.5	4.6

5. Absolute pK_a - convergence

The value for the absolute pK_a converges quickly to a constant value, however there is no guarantee that the dissociated state (i.e. A−H = 1.6 Å) is always the same (reprotonation, proton hopping).

Table S 3. Absolute pK_a calculated at 320 K, for a cubic box with a side length of 15.6406 Å and a cutoff a cutoff R_c = 1.24 Å, increasing the equilibration time (ps) - total length of all trajectories is about 20 ps minus the equilibration time.

equilibration time	2.5 ps	5 ps	7.5 ps	10 ps	12.5 ps
HCOOH	2.7	2.7	2.7	2.3	1.9
PhOH	8.8	8.7	8.7	8.8	8.6
$[Ru(II)Py_5Me(H_2O)]^{2+}$	9.7	9.8	9.9	10.0	10.1
$[Ru(II)Py_5OMe(H_2O)]^{2+}$	9.4	9.4	9.4	9.4	9.6
$[Ru(III)Py_5OMe(H_2O)]^{3+}$	3.0	3.1	3.3	3.5	3.4

6. Probabilistic pK_a - convergence

The value for the probabilistic pK_a requires more steps to converge, in particular for the highly charged system.

Table S 4. probabilistic pK_a calculated at 320 K, for a cubic box with a side length of 15.6406 Å and a cutoff R_c = 1.24 Å, increasing the equilibration time (ps) - total length of all trajectories is about 20 ps minus the equilibration time.

equilibration time	2.5 ps	5 ps	7.5 ps	10 ps	12.5 ps
HCOOH	4.1	4.2	4.2	3.9	3.4
PhOH	11.0	10.7	10.6	10.7	10.5
$[Ru(II)Py_5Me(H_2O)]^{2+}$	11.0	11.2	11.5	11.7	11.6
$[Ru(II)Py_5OMe(H_2O)]^{2+}$	11.1	11.1	11.3	11.4	11.5
$[Ru(III)Py_5OMe(H_2O)]^{3+}$	4.4	4.5	4.8	5.1	4.7

7. Relative pK_a - convergence

Table S 5. Relative pK_a calculated at 320 K, for a cubic box with a side length of 15.6406 Å and a cutoff R_c = 1.24 Å, increasing the equilibration time (ps) - total length of all trajectories is about 20 ps minus the equilibration time.

equilibration time	2.5 ps	5 ps	7.5 ps	10 ps	12.5 ps
HCOOH	6.7	6.8	6.6	6.4	6.0
PhOH	12.6	12.6	12.6	12.8	12.5
$[Ru(II)Py_5Me(H_2O)]^{2+}$	13.5	13.7	13.8	13.9	14.0
$[Ru(II)Py_5OMe(H_2O)]^{2+}$	13.3	13.3	13.3	13.4	13.5
$[Ru(III)Py_5OMe(H_2O)]^{3+}$	6.9	7.1	7.3	7.5	7.4

8. Relative pK_a - reduced constraint

Table S 6. Relative pK_a calculated at 320 K, for a cubic box with a side length of 15.6406 Å and a cutoff R_c = 1.24 Å, where only constraints within 0.9 to 1.4 Å where considered for the water reference.

molecule	pK_a
HCOOH	5.8
PhOH	11.8
$[Ru(II)Py_5Me(H_2O)]^{2+}$	12.0
$[Ru(II)Py_5OMe(H_2O)]^{2+}$	12.3
$[Ru(III)Py_5OMe(H_2O)]^{3+}$	6.2

9. Implications of using D_2O

Absolute pK_a

If the pK_a values are considered to be pK_a^D values due to the use of molecular mass of deuterium, then the absolute pK_a values have to be corrected according to the linear relation discussed in the MS. Applying those conversion factors lowers all pK_a values and leads in most cases to a worse agreement with the experiment.

Table S 7. All results presented here are calculated at 320 K, for a cubic box with side length of 15.6406 Å, over a trajectory of about 20 ps (where the first 5 ps were not included in the evaluation). The pK_a^D obtained using the absolute method were converted to pK_a^H values according to Equation 10 [a], respectively Equation 13 [b] in the MS.

Molecule	pK_a (exp.)	pK_a^D	$pK_a^H[a]$	$pK_a^H[b]$
H_2O	14.0	-	-	-
HCOOH	3.8 [1]	2.7	2.3	2.6
PhOH	10.0 [1]	8.7	8.0	8.1
$[Ru(II)Py_5Me(H_2O)]^{2+}$	∼11 [2]	9.8	9.1	9.2
$[Ru(II)Py_5OMe(H_2O)]^{2+}$	∼11 [2]	9.3	8.6	8.7
$[Ru(III)Py_5OMe(H_2O)]^{3+}$	∼2.5 [2]	3.1	2.7	2.9

Table S 8. All results presented here are calculated at 320 K, for a cubic box with side length of 19.7340 Å, over a trajectory of about 20 ps (where the first 5 ps were not included in the evaluation). The pK_a^D obtained using the absolute method were converted to pK_a^H values according to Equation 10 [a], respectively Equation 13 [b] in the MS.

Molecule	pK_a (exp.)	pK_a^D	$pK_a^H[a]$	$pK_a^H[b]$
H_2O	14.0	-	-	-
$[Ru(II)Py_5OMe(H_2O)]^{2+}$	∼11 [2]	10.1	9.4	9.4
$[Ru(III)Py_5OMe(H_2O)]^{3+}$	∼2.5 [2]	3.1	2.7	2.9

Relative pK_a

As for the probabilistic pK_a values the pK_a of D_2O had to be considered for the calculation of the relative pK_a values. The comparison of pK_a^H values obtained by converting pK_a^D values with pK_a^H obtained by referencing to H_2O revealed an overall reduction of the pK_a values by more than 1 unit. As a consequence there is a better agreement for basic compounds.

Table S 9. All results presented here are calculated at 320 K, for a cubic box with side length of 15.6406 Å, over a trajectory of about 20 ps (where the first 5 ps were not included in the evaluation). All pK_a values were obtained using the relative method. The $pK_a^H[a]$ values were calculated relative to H_2O, while pK_a^D were calculated relative to D_2O. The latter were converted into pK_a^H values according to Equation 10 [a], respectively Equation 13 [b] in the MS.

Molecule	pK_a (exp.)	$pK_a^H[a]$	pK_a^D	$pK_a^H[b]$	$pK_a^H[c]$
H_2O	14.0	-	-	-	-
HCOOH	3.8 [1]	6.7	5.7	5.2	5.5
PhOH	10.0 [1]	12.5	11.5	10.8	10.8
$[Ru(II)Py_5Me(H_2O)]^{2+}$	∼11 [2]	13.7	12.7	11.9	11.9
$[Ru(II)Py_5OMe(H_2O)]^{2+}$	∼11 [2]	13.3	12.3	11.5	11.5
$[Ru(III)Py_5OMe(H_2O)]^{3+}$	∼2.5 [2]	7.1	6.1	5.6	5.8

Table S 10. All results presented here are calculated at 320 K, for a cubic box with side length of 19.7340 Å, over a trajectory of about 20 ps (where the first 5 ps were not included in the evaluation). All pK_a values were obtained using the relative method. The $pK_a^H[a]$ values were calculated relative to H_2O, while pK_a^D were calculated relative to D_2O. The latter were converted into pK_a^H values according to Equation 10 [a], respectively Equation 13 [b] in the MS.

Molecule	pK_a (exp.)	$pK_a^H[a]$	pK_a^D	$pK_a^H[b]$	$pK_a^H[c]$
H_2O	14.0	-	-	-	-
$[Ru(II)Py_5OMe(H_2O)]^{2+}$	∼11 [2]	11.5	10.6	9.9	9.9
$[Ru(III)Py_5OMe(H_2O)]^{3+}$	∼2.5 [2]	4.6	3.7	3.3	3.5

10. Overview simulation time

Table S 11. Number of simulation steps per model system / constraint for a cubic box with a side length of 15.6406 Å Each time step corresponds to 0.5 fs.

d(A – H)	H_2O	PhOH	HCOOH	Ru(II)Py_5Me	Ru(II)Py_5OMe	Ru(III)Py_5OMe
0.9Å	30529	38380	39245	39731	40735	43373
1.0Å	45516	37244	40913	38672	40224	43360
1.1Å	44861	40056	40233	48999	40268	37874
1.2Å	44386	33873	39109	53620	41574	43101
1.3Å	40309	36914	40913	54654	40162	43778
1.4Å	39632	32981	40205	39987	39384	42555
1.5Å	39871	37802	40188	40797	38697	41321
1.6Å	39340	39260	40112	40368	38732	42472

Table S 12. Number of simulation steps per model system / constraint for a cubic box with a side length of 19.7340 Å. Each time step corresponds to 0.5 fs.

d(A – H)	H_2O	Ru(II)Py_5OMe	Ru(III)Py_5OMe
0.9Å	33538	32542	33592
1.0Å	34498	31453	33905
1.1Å	28697	31082	28762
1.2Å	31662	31161	32810
1.3Å	29924	31933	33278
1.4Å	30428	31864	32835
1.5Å	30556	31575	32175
1.6Å	26253	30264	33664

11. References

1. A., B.E.; Nachod, F.C. *Determination of Organic Structures by Physical Methods*; Vol. 1, Academic Press., Inc., 1955.
2. Gil-Sepulcre, M.; Axelson, J.C.; Aguiló, J.; Solà-Hernández, L.; Francàs, L.; Poater, A.; Blancafort, L.; Benet-Buchholz, J.; Guirado, G.; Escriche, L.; Llobet, A.; Bofill, R.; Sala, X. Synthesis and Isomeric Analysis of Ru(II) Complexes Bearing Pentadentate Scaffolds. *Inorg. Chem.* **2016**, *55*, 11216–11229. doi:10.1021/acs.inorgchem.6b01755.