

SUPPLEMENTARY MATERIALS

Table S1. Detailed information on free energy profiles calculation setup. Atomic serial numbers in model structures: OH2^{WT1} – 12778, H2^{WT1} – 12780, U^{UO2} – 1483, SG^{Cys162} – 849 for stage I (hydrolysis); COO^{Glu190} – 1291, 1292, 1293, U^{UO2} – 1476, OH2^{WT2} – 1487 for stage II (association).

Stage	Reaction coordinate λ , Å	Spectrum of λ , Å	Number of trajectories computed	Harmonic force constant, kcal/mol	Trajectories lengths, ps
<i>I</i>	d(OH2 ^{WT1} , H2 ^{WT1}) + d(U ^{UO2} , SG ^{Cys162})	3.65 ... 6.25	21	60-80	4.5-6.0
<i>II</i>	d(U ^{UO2} , COO ^{Glu190}) – d(OH2 ^{WT2} , U ^{UO2})	-0.80 ... 2.60	32	60-80	5.0-8.0

Table S2. Bonding properties of uranyl complexes with different ligand compositions. N stands for a number of ligands of a particular type. For those formulas that have several structural representations, average values are presented.

Formula	$N(\text{CH}_3\text{S}^-)$	$N(\text{H}_2\text{O})$	$N(\text{OH}^-)$	Bond lengths			Mayer bond orders			IBSI			Charge trans. to UO ₂ (-e)		
				U-SCH ₃	U-H ₂ O	U-OH	U-SCH ₃	U-H ₂ O	U-OH	U-SCH ₃	U-H ₂ O	U-OH	SCH ₃	H ₂ O	OH
<i>s2w2</i>	2	2	0	2.67	2.48	x	0.85	0.27	x	0.26	0.21	x	0.63	0.16	x
<i>s2w1oh1</i>	2	1	1	2.73	2.56	2.18	0.79	0.25	0.56	0.23	0.18	0.42	0.55	0.14	0.37
<i>s2oh2</i>	2	0	2	2.82	x	2.22	0.65	x	0.44	0.2	x	0.38	0.47	x	0.34
<i>s3w1</i>	3	1	0	2.70	2.53	x	0.81	0.24	x	0.24	0.19	x	0.56	0.16	x
<i>s3oh1</i>	3	0	1	2.78	x	2.2	0.49	x	0.5	0.21	x	0.4	0.38	x	0.34
<i>s2w3</i>	2	3	0	2.71	2.59	x	0.87	0.25	x	0.24	0.17	x	0.62	0.19	x
<i>s2w2oh1</i>	2	2	1	2.75	2.64	2.22	0.66	0.25	0.60	0.19	0.15	0.37	0.5	0.18	0.4
<i>s2oh3</i>	2	0	3	3.06	x	2.29	0.44	x	0.51	0.13	x	0.35	0.25	x	0.34
<i>s3w2</i>	3	2	0	2.70	2.7	x	0.78	0.26	x	0.2	0.15	x	0.69	0.13	x
<i>s3oh2</i>	3	0	2	3.02	x	2.28	0.36	x	0.47	0.14	x	0.33	0.26	x	0.41

Table S3. Solute and solvent thermodynamic properties change upon transition from state I to state II.

Free energy component	Value, kcal/mol
$\Delta H_{\text{reac}}^{I \rightarrow II}$	2.8
$\Delta H_{\text{conf}}^{I \rightarrow II}$	4.4
$T\Delta S_{\text{conf}}^{I \rightarrow II}$	19.4
$\Delta H_{\text{solv}}^{I \rightarrow II}$	-4.1
$T\Delta S_{\text{solv}}^{I \rightarrow II}$	-15.7
$\Delta G_{\text{tot}}^{I \rightarrow II} = -0.6 \text{ kcal/mol}$	

Table S4. Solute and solvent thermodynamic properties change upon transition from state I to state III.

Free energy component	Value, kcal/mol
$\Delta H_{\text{reac}}^{I \rightarrow III}$	-8.9
$\Delta H_{\text{conf}}^{I \rightarrow III}$	1.8
$T\Delta S_{\text{conf}}^{I \rightarrow III}$	1.1
$T\Delta S_{\text{rot}}^{I \rightarrow III}$	0.4
$T\Delta S_{\text{trans}}^{I \rightarrow III}$	< 4.2
$\Delta H_{\text{solv}}^{I \rightarrow III}$	-2.1
$T\Delta S_{\text{solv}}^{I \rightarrow III}$	-7.5
$\Delta G_{\text{tot}}^{I \rightarrow III} \sim -7.4 \text{ kcal/mol}$	

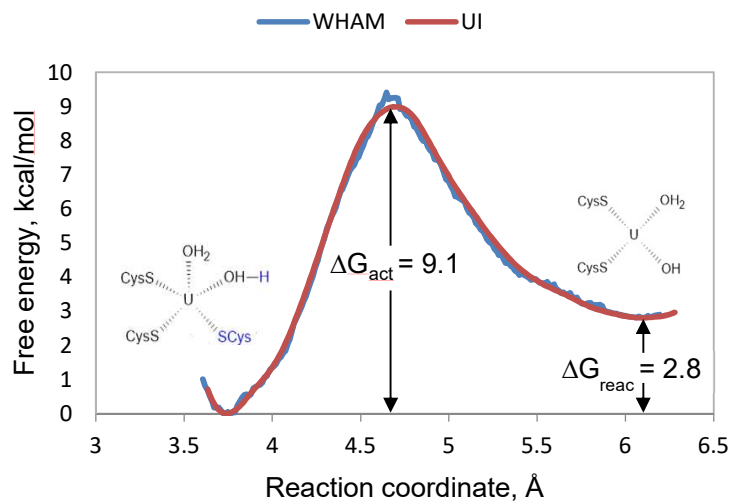


Figure S1. Internal hydrolysis reaction free energy profile derived from Umbrella sampling calculations. Color corresponds to US results analysis method. The reaction coordinate is $d(\text{OH2}^{\text{WT1}}, \text{H2}^{\text{WT1}}) + d(\text{U}^{\text{UO2}}, \text{SG}^{\text{Cys162}})$.

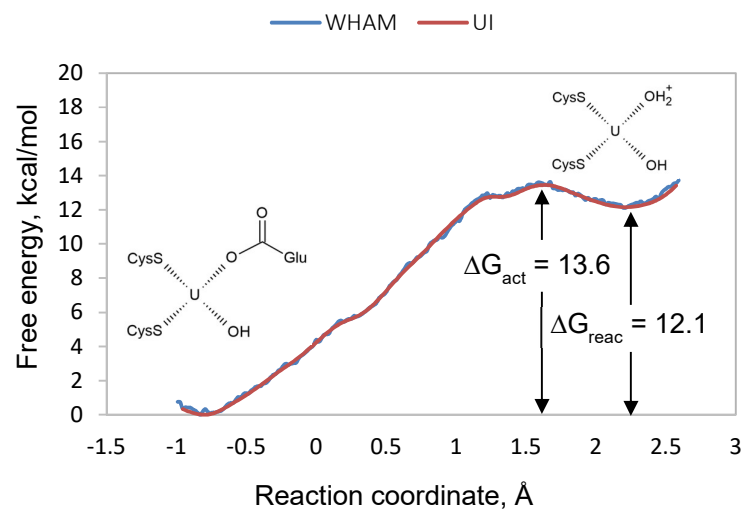


Figure S2. Association reaction free energy profile derived from Umbrella sampling calculations. Color corresponds to US results analysis method. The reaction coordinate is $d(\text{U}^{\text{UO2}}, \text{COO}^{\text{Glu190}}) - d(\text{OH2}^{\text{WT2}}, \text{U}^{\text{UO2}})$.