

PRO-OXIDANT ACTIVITY OF ALUMINUM THROUGH AL-SUPEROXIDE FORMATION.

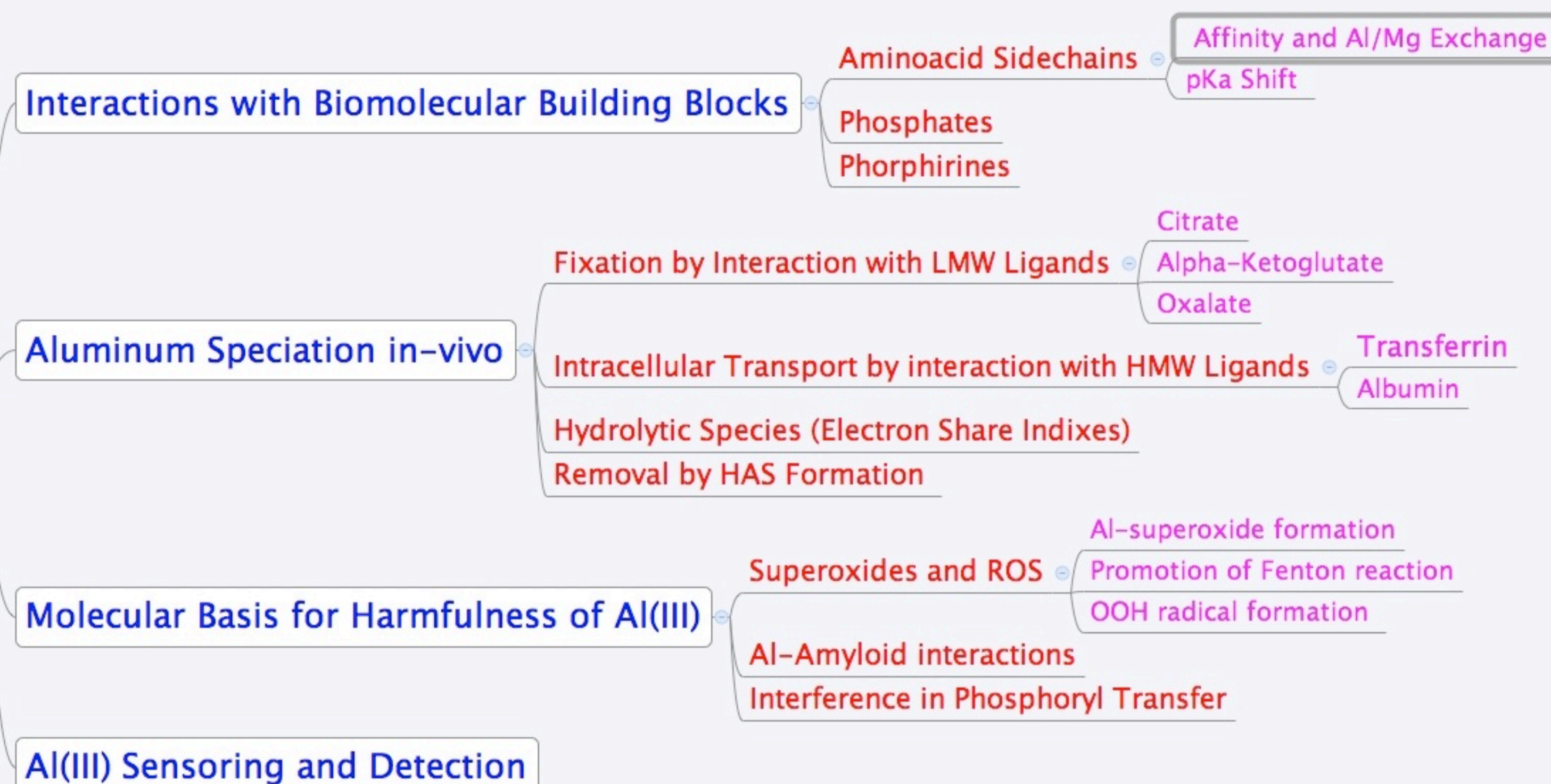
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Al(III) Biochemistry



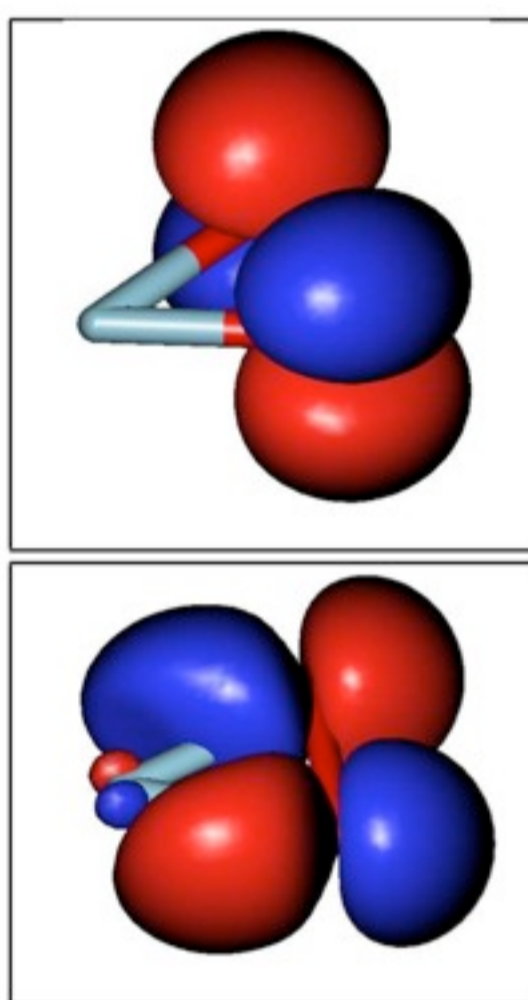
INTRODUCTION

- The existence of an Al-superoxide (O_2^-) complex has been hypothesized [1] as a key species in the pro-oxidant activity of Al [2], a non-redox metal.
- The possibility of Al-superoxide formation is investigated using a variety of theoretical methods, determining:
 - *ESR g-tensor values of the interaction of various biologically relevant metals with superoxide, an indicator that has demonstrated a good correlation with the pro-oxidant activity of a given metal[3-5]
 - *Thermodynamics of Al-superoxide formation in solution for various hydrolytic species
- We also analyze the possibility of the resultant al-superoxide complexes to promote Fenton reaction by reducing Fe(III) to Fe(II), a possible route for its pro-oxidant activity.

INTRINSIC AFFINITY OF AL(III) TO SUPEROXIDE

$\Delta\epsilon_{\pi_g}$, (estimated from g-tensor value, Vancoille et al Chem. Phys. Chem. 2007), IP of $M^{n+}O_2^-$ and EA of $M^{n+}O_2^-$ in eV, calculated at CASPT2.

M^{n+}	$\Delta\epsilon_{\pi_g}$ (eV)		IP (eV)	EA (eV)
	CASPT2	Exp.		
Na ⁺	0.35	0.34	7.3	4.9
K ⁺	0.31	—	6.8	4.1
Mg ²⁺	0.65	0.65	15.6	13.5
Ca ²⁺	0.56	0.58	13.9	11.0
Al ³⁺	1.11	—	25.5	25.1

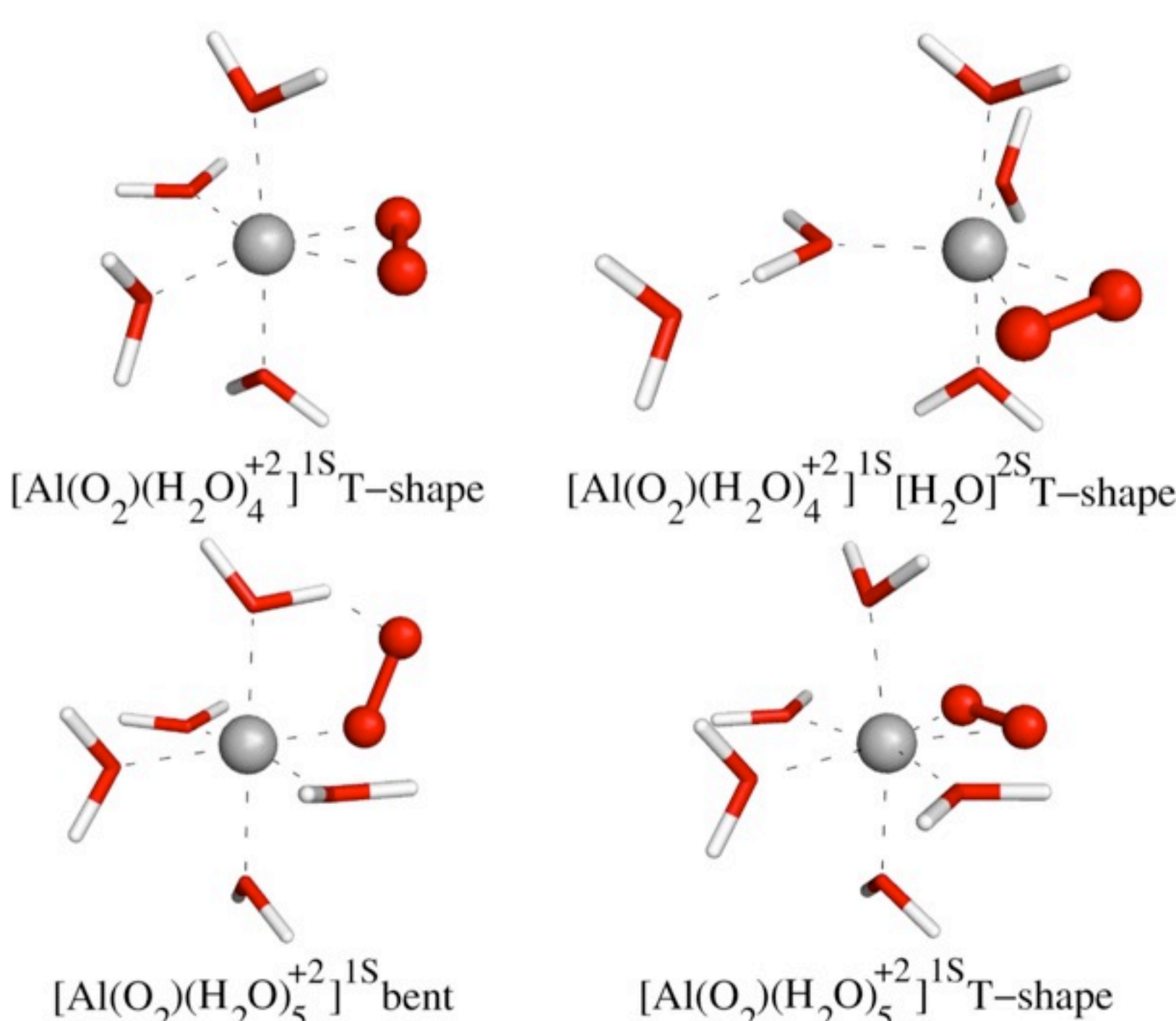


- Good agreement with experimental values.
- Charge is the dominating factor over volume.
- Al(III) shows a strong interaction as it corresponds to a +3 charge and small volume, similar to Sc³⁺ (1.0 eV).

MICROSOLVATED STRUCTURES

CASPT2 level of theory	$\Delta\epsilon_{\pi_g}$ (eV)	ΔE (kcal/mol)
T-[Al ³⁺ O ₂ ⁻](H ₂ O) ₄ ^{1S}	0.86	0.0
T-[Al ³⁺ O ₂ ⁻](H ₂ O) ₄ ^{1S} (H ₂ O) ₂ ^{2S}	0.80	0.0
Bent-[Al ³⁺ O ₂ ⁻](H ₂ O) ₅ ^{1S}	0.73	3.5
T-[Al ³⁺ O ₂ ⁻](H ₂ O) ₅ ^{1S}	0.62	7.9
T-[Mg ²⁺ O ₂ ⁻](H ₂ O) ₄ ^{1S}	0.42	0.0
Bent-[Mg ²⁺ O ₂ ⁻](H ₂ O) ₄ ^{1S} (H ₂ O) ₂ ^{2S}	0.37	0.0
T-[Mg ²⁺ O ₂ ⁻](H ₂ O) ₄ ^{1S} (H ₂ O) ₂ ^{2S}	0.42	7.0
Bent-[Mg ²⁺ O ₂ ⁻](H ₂ O) ₅ ^{1S}	0.42	8.9
T-[Mg ²⁺ O ₂ ⁻](H ₂ O) ₅ ^{1S}	0.32	12.1

- Microsolvation weakens Al(III)-superoxide interaction
- Still, Al intrinsic affinity for a superoxide is much higher than other biologically relevant metals such as Mg(II)



THERMODYNAMICS OF AL-SUPEROXIDE FORMATION

METHOD AND CALIBRATION

- Gas Phase: B3LYP, M06X and PBE0 // 6-311++G(3df,2p)
- Bulk Solvent:
 - * PCM HF/6-31G* UAHF
 - * SMD at B3LYP/6-311++G(3df,2p)

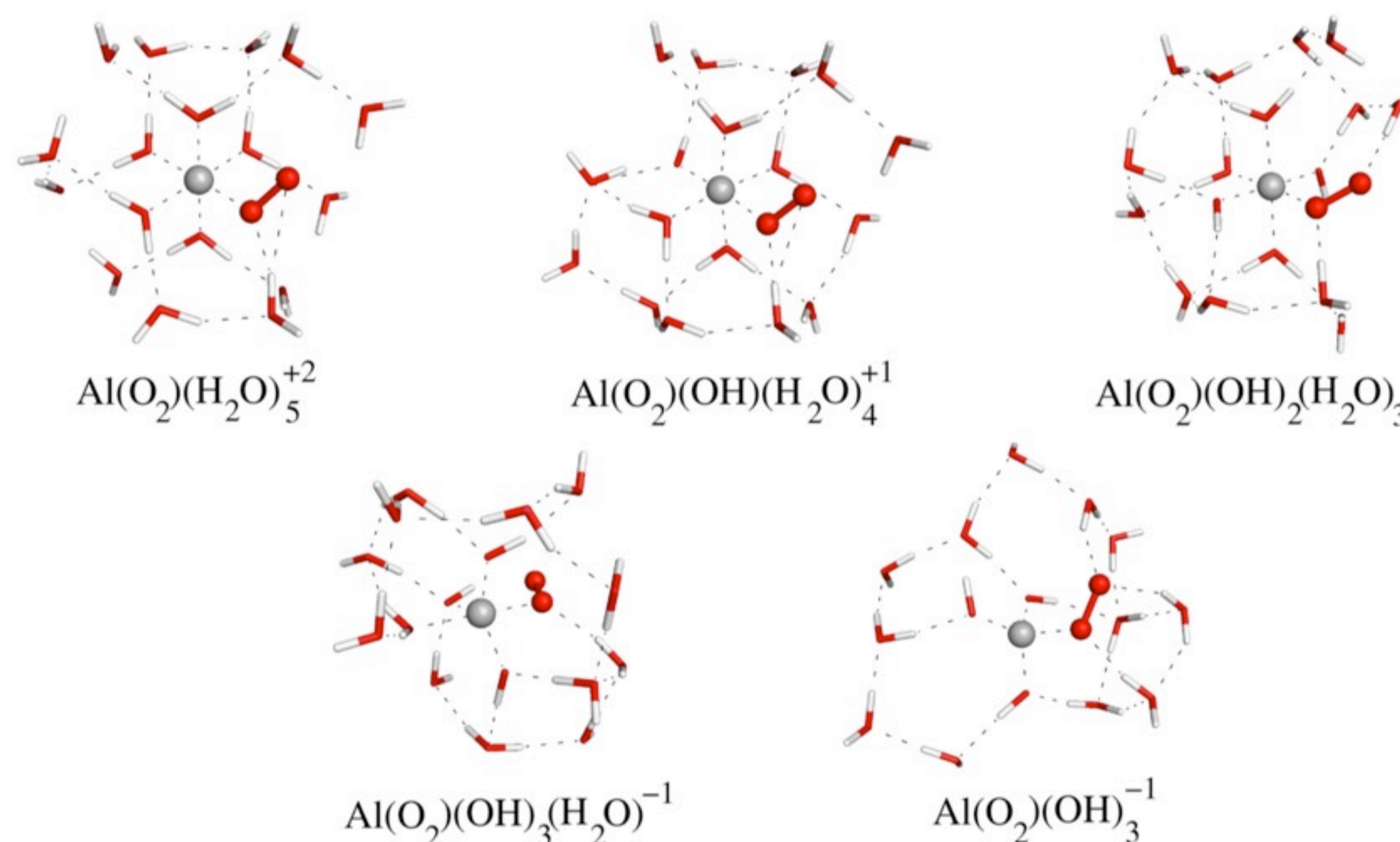
ΔG_{aq}^{exp} (298K)	ΔG_{aq}^{SMD}	$\Delta G_{aq}^{PCM/HF}$
-14.9 kcal/mol		
$OOH + OH^- \rightarrow O_2^- + H_2O$	-24.5	-6.5
$OOH(H_2O)_2 + OH^-(H_2O)_2 \rightarrow O_2^-(H_2O)_2 + H_2O(H_2O)_2$	-17.6	-12.6

PROMOTION OF FENTON REACTION

	ΔE				ΔG_g	ΔG_{aq}^{SMD}	ΔG_{aq}^{HF}
	B3LYP	PBE	M062X	CASPT2			
$Fe^{3+} + AlO_2^{2+} \rightarrow Fe^{2+} + AlO_2^{2+}$							
Bare ion	-135.7	-130.1	-125.7	-116.2	-136.6	100.4	37.4
First shell	-20.1	-18.8	-17.5	-14.6	-26.4	-2.9	16.6
Second shell ^a	-10.1	-7.5	0.0		-21.0	-9.9	4.4
$Fe^{3+} + Al(OH)O_2^+ \rightarrow Fe^{2+} + Al^{3+} + O_2$							
Bare ion	-51.0	-49.2	-45.5		-57.6	141.1	109.6
First shell	-60.2	-60.8	-61.9		-64.2	-31.9	-47.2
Second shell	-42.0	-41.3	-39.6		-39.1	-19.8	-7.4
$Fe^{3+} + Al(OH)_2O_2^+ \rightarrow Fe^{2+} + Al(OH)^{2+} + O_2$							
Bare ion	-277.7				-288.1	64.9	
First shell	-145.3				-149.0	-24.2	-14.8
Second shell	-101.4	-100.0	-97.5		-104.9	-19.2	-9.2

^a O₂ not bound to Al, but optimized

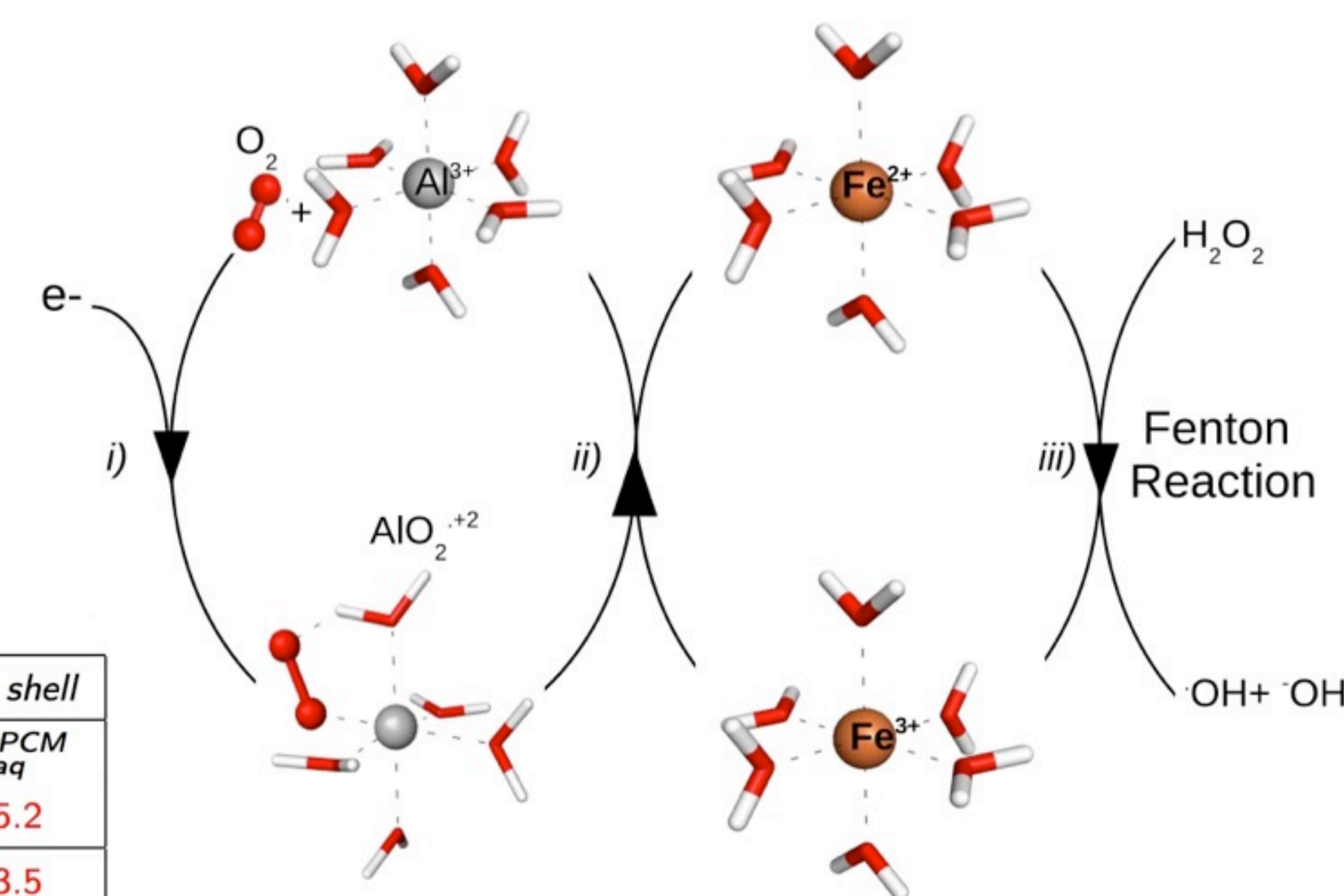
EXOTHERMIC FORMATION OF AL-SUPEROXIDE COMPOUNDS WITH WATER DISPLACEMENT FROM HYDROLYTIC SPECIES



- Substitution of a water molecule in an Aluminum hydrolytic species is exoergonic, whereas OH⁻ substitution is endoergonic.
- Main source of Al-superoxide formation is Al³⁺ and Al(OH)²⁺

B3LYP Reaction Free Energies, kcal/mol		1 st + 2 nd coord. shell	
		ΔG_{aq}^{SMD}	ΔG_{aq}^{PCM}
$Al(H_2O)_6^{+3} + O_2^- \rightarrow Al(O_2)(H_2O)_5^{+2} + H_2O$		-8.3	-15.2
$Al(OH)(H_2O)_5^{+2} + O_2^- \rightarrow Al(O_2)(OH)(H_2O)_4^{+1} + H_2O$		-8.7	-13.5
$Al(O_2)(H_2O)_5^{+2} + OH^- \rightarrow Al(O_2)(OH)(H_2O)_4^{+1} + H_2O$		13.5*	11.6*
$Al(OH)_2(H_2O)_4^{+1} + O_2^- \rightarrow Al(O_2)(OH)_2(H_2O)_3 + H_2O$		-1.7	-2.8
$Al(O_2)(OH)(H_2O)_4^{+1} + OH^- \rightarrow Al(O_2)(OH)_2(H_2O)_3 + H_2O$		11.8*	7.8*
$Al(OH)_3(H_2O)_2 + O_2^- \rightarrow Al(O_2)(OH)_3(H_2O) + H_2O$		-2.0	-1.8
$Al(O_2)(OH)_2(H_2O)_3 + OH^- \rightarrow Al(O_2)(OH)_3(H_2O) + H_2O$		12.3*	6.8*
$Al(OH)_4^{-1} + O_2^- \rightarrow Al(O_2)(OH)_3^{-1} + OH^-$		15.8	11.2

*only 1S



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