

**Can the Peroxosuccinate Complex in the Catalytic Cycle of
Taurine/ α -Ketoglutarate Dioxygenase (TauD) Act as an
Alternative Oxidant? A Density Functional Study.**

*Sam P. de Visser**

The Manchester Interdisciplinary Biocenter and the School of Chemical Engineering
and Analytical Science
The University of Manchester
131 Princess Street
Manchester M1 7DN
United Kingdom

Tel.: +44-161-3064882

FAX: +44-161-3064399

Email: sam.devisser@manchester.ac.uk

Methods.

We use commonly accepted procedures for our calculations,¹ which we will briefly summarize here. The calculations employ the UB3LYP hybrid density functional method^{2,3} in combination with a double- ζ quality (LACVP) basis set on iron which includes an Electron Core Potential (ECP) while all other atoms are described by a 6-31G basis set.⁴ All structures were fully optimized (without constraints) in the Jaguar 5.5 program package.⁵ A subsequent analytical frequency calculation in Gaussian-03 verified that the structures were local minima with real frequencies only or transition state structures with one imaginary frequency.⁶ To test the effect of the basis set on the relative energies, we ran single point calculations with a triple- ζ quality (LACV3P+*) basis set on iron and 6-311+G* basis set on the rest of the atoms.⁴ All energies reported in this work were taken from the single point LACV3P+* data with ZPE and environmental corrections at the LACVP level of theory.

The model studied was based upon the 1OS7 pdb of O'Brien et al⁷ and contained the immediate surrounding of the iron atom, whereby the histidine ligands were abbreviated by imidazole and the aspartate by acetic acid. In addition, we replaced α -ketoglutarate by α -ketopropionate in order to keep the overall charge of the model neutral. We added hydrogen atoms and molecular oxygen to the pdb and replaced taurine by propene. In previous work¹ we calculated propene activation by the oxoiron species of TauD enzymes and therefore we use the same substrate here for testing the second oxidant hypothesis of the peroxosuccinate complex. During the catalytic cycle calculations propene was inactive and virtually stayed in the same position. We studied the reaction profile on the triplet, quintet and septet spin states, which are identified as a superscript in the structure names. However, the triplet and septet spin states were much higher in energy than the quintet spin state.

The effect of the environment on the relative energies was tested with the self-consistent reaction field (SCRF) model as implemented in Jaguar 5.5 using dielectric constants (ϵ) of 5.7 with a probe radius of 2.72.

References:

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Table S1. Group spin densities, group charges, absolute and relative energies of UB3LYP/LACVP optimized geometries of critical points in the catalytic cycle of α -ketoglutarate dioxygenase as calculated with Jaguar 5.5.

(a) Spin Densities.

	E	ρ_{Fe}	ρ_{His99}	ρ_{His255}	ρ_{Asp101}	$\rho_{\alpha\text{KG}}$	ρ_{O1}	ρ_{O2}
⁵ 1	-1414.151774	3.86	0.06	0.06	0.17	0.13	0.03	-0.31
⁵ TS_A	-1414.145408	2.78	-0.03	0.02	0.21	-0.01	0.50	0.53
⁵ 2	-1414.162839	2.74	0.03	0.11	0.07	1.05	0.00	-
⁵ TS_B	-1414.151682	4.04	0.09	0.09	0.25	-0.25	-0.22	-
⁵ 3	-1414.228760	3.72	0.04	0.04	0.09	0.00 ^a	0.11 ^b	-
⁵ TS_C	-1414.204021	2.71	0.09	0.00	0.02	0.00 ^a	0.28 ^b	0.90
⁵ 4	-1414.239857	2.95	0.09	-0.01	0.05	0.00 ^a	0.14 ^c	0.78
⁵ TS_D	-1414.194894	3.75	0.03	0.03	0.08	0.00 ^a	0.12 ^{b,d}	
⁵ TS_E	-1414.184882	3.75	0.03	0.03	0.09	0.00 ^a	0.15 ^{b,e}	

a. $\rho(\text{CO}_2)$

b. $\rho(\text{CH}_3\text{COO}^-)$

c. $\rho(\text{Ac}^-)$

d. $\rho(\text{CH}_2) = 0.01$; $\rho(\text{CH}) = -0.02$; $\rho(\text{CH}_3) = 0.00$

e. $\rho(\text{CH}_3) = -0.04$; $\rho(\text{CH}) = 0.02$; $\rho(\text{CH}_2) = -0.03$

(b) Charges.

	ΔE	Q_{Fe}	Q_{His99}	Q_{His255}	Q_{Asp101}	$Q_{\alpha\text{KG}}$	Q_{O1}	Q_{O2}
⁵ 1	0.0	0.94	0.16	0.17	-0.52	-0.51	-0.19	-0.05
⁵ TS_A	4.0	0.83	0.24	0.20	-0.48	-0.45	-0.16	-0.18
⁵ 2	-6.9	0.87	0.21	0.17	-0.41	-0.84	-	-
⁵ TS_B	0.1	0.99	0.17	0.18	-0.47	-0.27	-0.60	-
⁵ 3	-48.3	0.80	0.14	0.13	-0.58	0.00 ^a	-0.49 ^b	-
⁵ TS_C	-32.8	0.79	0.18	0.20	-0.53	0.02 ^a	-0.34 ^b	-0.32
⁵ 4	-55.3	0.82	0.18	0.23	-0.50	0.02 ^a	-0.43 ^c	-0.32
⁵ TS_D	-27.1	0.77	0.14	0.13	-0.58	0.00 ^a	-0.59 ^{b,d}	
⁵ TS_E	-20.8	0.78	0.14	0.13	-0.58	0.00 ^a	-0.69 ^{b,e}	

a. $Q(\text{CO}_2)$

b. $Q(\text{CH}_3\text{COO}^-)$

c. $Q(\text{Ac}^-)$

d. $Q(\text{CH}_2) = 0.07$; $Q(\text{CH}) = 0.05$; $Q(\text{CH}_3) = 0.01$

e. $Q(\text{CH}_3) = 0.15$; $Q(\text{CH}) = 0.08$; $Q(\text{CH}_2) = -0.01$

Table S2. Group spin densities, group charges, absolute and relative energies of UB3LYP/LACV3P+* single points on UB3LYP/LACVP optimized geometries of critical points in the catalytic cycle of α -ketoglutarate dioxygenase as calculated with Jaguar 5.5.

(a) Spin Densities.

	E	ρ_{Fe}	ρ_{His99}	ρ_{His255}	ρ_{Asp101}	$\rho_{\alpha\text{KG}}$	ρ_{O1}	ρ_{O2}
⁵ 1	-1414.895087	3.99	0.04	0.05	0.14	0.10	0.01	-0.33
⁵ TS_A	-1414.880991	2.87	-0.04	0.01	0.18	-0.03	0.51	0.50
⁵ 2	-1414.905586	4.21	0.07	0.08	0.21	0.33	-0.39	-0.51
⁵ TS_B	-1414.898900	4.21	0.08	0.07	0.21	-0.42	0.06	-0.21
⁵ 3	-1414.988938	3.78	0.02	0.03	0.07	0.00 ^a	0.10 ^b	-
⁵ TS_C	-1414.961766	2.80	0.08	-0.02	0.01	0.01 ^a	0.27 ^c	0.85
⁵ 4	-1415.002833	3.08	0.08	-0.02	0.03	0.00 ^a	0.11 ^c	0.72
⁵ TS_D	-1414.949478	3.82	0.01	0.02	0.07	0.00 ^a	0.09 ^b	-
⁵ TS_E	-1414.937069	3.82	0.03	0.02	0.08	0.00 ^a	0.09 ^b	-

a. $\rho(\text{CO}_2)$

b. $\rho(\text{CH}_3\text{COO}^-)$

c. $\rho(\text{Ac}^-)$

d. $\rho(\text{CH}_2) = 0.01$; $\rho(\text{CH}) = -0.02$; $\rho(\text{CH}_3) = 0.00$

e. $\rho(\text{CH}_3) = -0.03$; $\rho(\text{CH}) = 0.02$; $\rho(\text{CH}_2) = -0.03$

(b) Charges.

	ΔE	Q_{Fe}	Q_{His99}	Q_{His255}	Q_{Asp101}	$Q_{\alpha\text{KG}}$	Q_{O1}	Q_{O2}
⁵ 1	0.0	0.55	0.16	0.24	-0.46	-0.41	-0.05	-0.04
⁵ TS_A	8.9	0.57	0.19	0.25	-0.44	-0.54	0.00	-0.03
⁵ 2	-6.6	0.67	0.16	0.25	-0.41	-0.57	-0.05	-0.05
⁵ TS_B	-2.4	0.73	0.16	0.23	-0.45	-0.58	-0.13	0.04
⁵ 3	-58.9	0.60	0.14	0.06	-0.51	-0.02 ^a	-0.24 ^b	-
⁵ TS_C	-41.8	0.48	0.29	0.20	-0.50	0.06 ^a	-0.32 ^c	-0.18
⁵ 4	-67.6	0.44	0.27	0.27	-0.45	0.05 ^a	-0.38 ^c	-0.16
⁵ TS_D	-34.1	0.72	0.17	0.13	-0.57	0.00	-0.37	-
⁵ TS_E	-26.3	0.68	0.18	0.09	-0.55	-0.02	-0.55	-

a. $Q(\text{CO}_2)$

b. $Q(\text{CH}_3\text{COO}^-)$

c. $Q(\text{Ac}^-)$

d. $Q(\text{CH}_2) = -0.05$; $Q(\text{CH}) = -0.01$; $Q(\text{CH}_3) = -0.02$

e. $Q(\text{CH}_3) = 0.14$; $Q(\text{CH}) = 0.06$; $Q(\text{CH}_2) = -0.03$

Table S3. Group spin densities, group charges, absolute and relative energies of dielectric constant single points ($\epsilon = 5.7$) on UB3LYP/LACVP optimized geometries of critical points in the catalytic cycle of α -ketoglutarate dioxygenase as calculated with Jaguar 5.5.

(a) Spin Densities.

	E	ρ_{Fe}	ρ_{His99}	ρ_{His255}	ρ_{Asp101}	$\rho_{\alpha\text{KG}}$	ρ_{O1}	ρ_{O2}
⁵ 1	-24.44	3.88	0.07	0.07	0.17	0.11	0.02	-0.32
⁵ TS_A	-23.79	2.78	-0.04	0.01	0.21	0.01	0.53	0.50
⁵ 2	-24.25	4.07	0.10	0.12	0.26	0.34	-0.39	-0.50
⁵ TS_B	-21.87	4.05	0.11	0.11	0.25	-0.39	0.07	-0.20
⁵ 3	-20.47	3.72	0.04	0.04	0.08	0.00 ^a	0.12 ^b	-
⁵ TS_C	-21.54	2.71	0.09	-0.01	0.02	0.00 ^a	0.30 ^c	0.89
⁵ 4	-22.16	2.95	0.10	-0.01	0.05	0.00 ^a	0.13 ^c	0.78
⁵ TS_D	-20.07	3.75	0.04	0.04	0.08	0.00 ^a	0.10 ^b	-
⁵ TS_E	-21.05	3.76	0.04	0.04	0.09	0.00 ^a	0.12 ^b	-

a. $\rho(\text{CO}_2)$

b. $\rho(\text{CH}_3\text{COO}^-)$

c. $\rho(\text{Ac}^-)$

d. $\rho(\text{CH}_2) = 0.01$; $\rho(\text{CH}) = -0.02$; $\rho(\text{CH}_3) = 0.00$

e. $\rho(\text{CH}_3) = -0.04$; $\rho(\text{CH}) = 0.02$; $\rho(\text{CH}_2) = -0.03$

(b) Charges.

	ΔE^f	Q_{Fe}	Q_{His99}	Q_{His255}	Q_{Asp101}	$Q_{\alpha\text{KG}}$	Q_{O1}	Q_{O2}
⁵ 1	0.0	0.93	0.19	0.20	-0.53	-0.51	-0.19	-0.09
⁵ TS_A	11.1	0.83	0.27	0.24	-0.49	-0.53	-0.20	-0.18
⁵ 2	-5.3	0.99	0.20	0.21	-0.47	-0.57	-0.22	-0.19
⁵ TS_B	0.6	0.99	0.20	0.21	-0.48	-0.33	-0.34	-0.25
⁵ 3	-54.8	0.80	0.16	0.15	-0.59	0.00 ^a	-0.50 ^b	-
⁵ TS_C	-38.2	0.78	0.21	0.23	-0.55	0.02 ^a	-0.33 ^c	-0.35
⁵ 4	-64.6	0.81	0.21	0.27	-0.51	0.02 ^a	-0.46 ^c	-0.35
⁵ TS_D	-29.8	0.76	0.16	0.15	-0.60	0.00 ^a	-0.60 ^b	-
⁵ TS_E	-25.9	0.77	0.16	0.15	-0.59	0.00 ^a	-0.71 ^b	-

a. $Q(\text{CO}_2)$

b. $Q(\text{CH}_3\text{COO}^-)$

c. $Q(\text{Ac}^-)$

d. $Q(\text{CH}_2) = 0.07$; $Q(\text{CH}) = 0.06$; $Q(\text{CH}_3) = 0.00$

e. $Q(\text{CH}_3) = 0.16$; $Q(\text{CH}) = 0.08$; $Q(\text{CH}_2) = -0.02$

f. Energy taken from LACV3P+* single points with ZPE and $E_{\epsilon=5.7}$ corrections at LACVP level of theory.

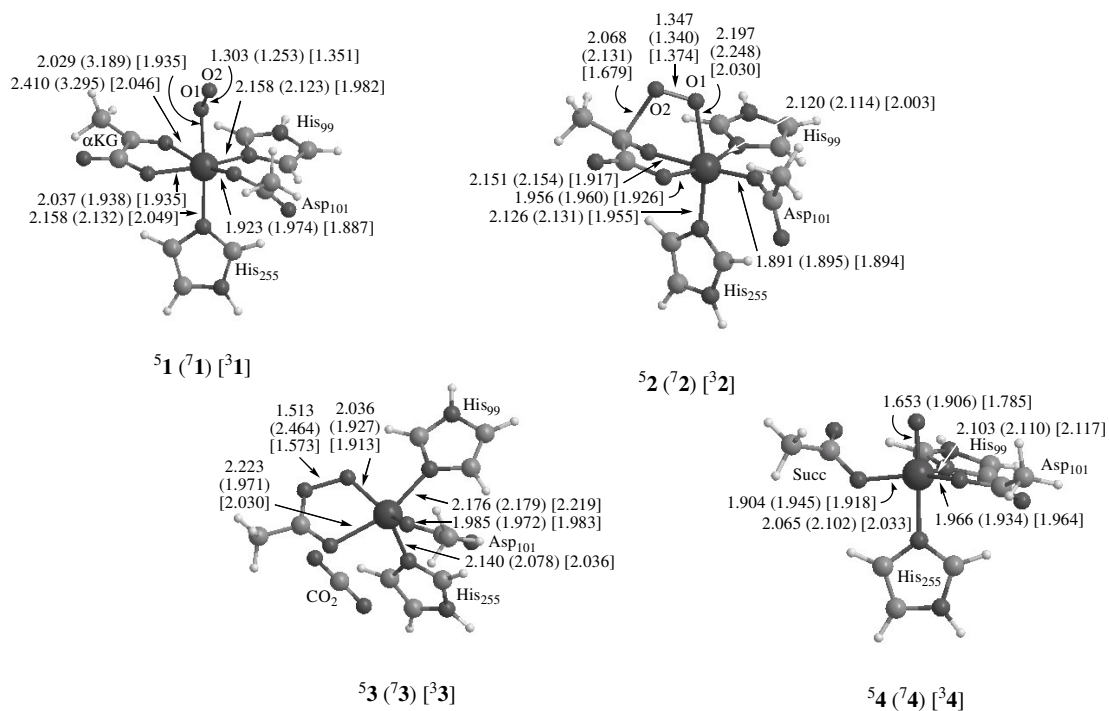


Figure S1. Optimized geometries in the quintet (septet) and [triplet] spin states of **1**, **2**, **3**, and **4** in Jaguar 5.5 as calculated with UB3LYP/LACVP. Bond lengths are in Angstroms.

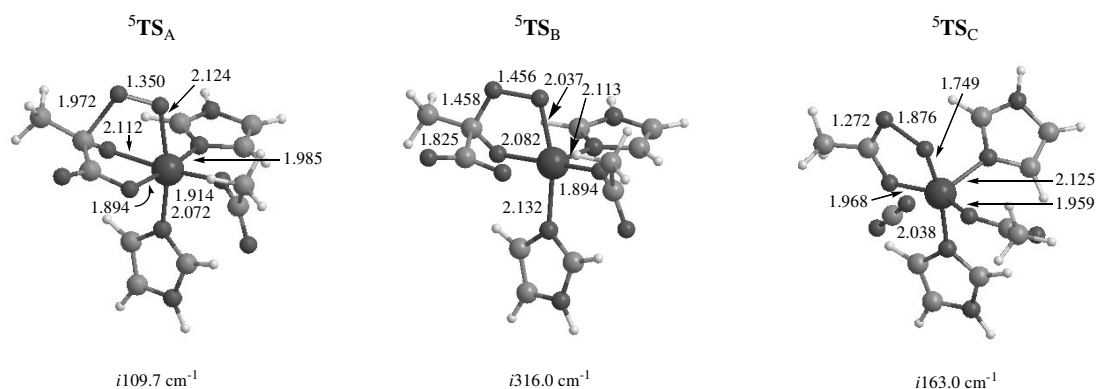


Figure S2. Optimized geometries of $5TS_A$, $5TS_B$ and $5TS_C$ in Jaguar 5.5 as calculated with UB3LYP/LACVP. Bond lengths are in Angstroms and the imaginary frequency of the transition state is in cm^{-1} .