

A Six-Coordinate High-Spin Fe^{IV}=O Species of Cucurbit[5]uril: A Highly Potent Catalyst for C-H Hydroxylation of Methane, If synthesised

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Abstract:

*DFT and ab initio DLPNO-CCSD(T) calculations predict a stable S = 2 six-coordinate Fe^{IV}=O species with cucurbit[5]uril (CB[5]) as a ligand ([CB[5])Fe^{IV}=O(H₂O)]²⁺(**1**). The aggressive reactivity pattern of **1** far exceeds even metalloenzymes such as sMMOs in activating inert substrates such as methane, setting a stage for new generation biomimic catalysts.*

Keywords: Iron(IV)-oxo, C–H activation, Cucurbit[5]uril, DFT, High-spin S = 2

High-valent metal-oxo species are well known for their biological and industrial role in various oxidation reactions, such as C–H activation of aromatic and aliphatic hydrocarbons.^[1] Among others, biomimic high-valent iron-oxo species gain attention in recent years due to their aggressive oxidising abilities. One way to enhance the reactivity of non-heme Fe^{IV}=O species is to stabilize a high-spin S = 2 as its ground state^[2] similar to that found in enzymes such as pterin-dependent hydroxylases and α -ketoglutarate (α -KG) dependent oxygenases, etc.^[3] Unlike the metalloenzymes, most of the biomimic models have an S = 1 ground state which enforces an obligatory spin-crossover during the reaction diminishing its reactivity substantially compared to that of enzymes.^[4] Stabilizing a six-coordinate high-spin S = 2 is thus a great challenge; though this feat has been achieved in other coordination numbers, these are often less reactive.^[5] The only well characterised high-spin S = 2 species is [(H₂O)₅Fe^{IV}=O]²⁺ Fenton reagent, whose reactivity surpasses synthetic non-heme models.^[5] Some tetradentate aminopyridine ligands are also reported to stabilize the high-spin ground state with solvent/H₂O occupying the sixth coordination sphere^[6], and these species are also very reactive.

While weakening the ligand via oxygen donor atoms is the best way to obtain high-spin Fe^{IV}=O species, the oxygen donor bound to Fe is much weaker, leading to faster decomposition.^[7] An alternative way to synthesize Fe^{IV}=O is to utilize rigid frameworks such as MOFs and generate in situ Fe^{IV}=O species for efficient catalytic transformations, and this has been recently attempted.^[8] In this work, we have taken an unconventional route of binding the Fe^{IV}=O species in a cage such as a cucurbit[5]uril (CB[5])^[9] which inherently possess oxygen donor atoms as desired, and are redox stable, unlike POMs.^[10] The CB[5] is a pumpkin-like macrocycle based on 5-glycoluril units having a constricted hydrophobic cavity and polar carbonyls at the rigid portals.^[9] Encouraged by the fact that it binds transition metal as well as lanthanide/actinide ions, as demonstrated for example with Co(II)^[11] and V^{IV}=O^[12] species lately, we have modelled using DFT (B3LYP-D3/TZVP) and *ab initio* methods (see computational details) [(CB[5])Fe^{IV}=O(H₂O)]²⁺(**1**) species to understand its electronic structure and reactivity

towards various substrates such as dihydroanthracene (DHA), methane, and ethane. Our calculations reveal a high-spin $S = 2$ ground state for **1** with an exceptionally small barrier for the activation of sp^3 C-H bonds, and this unveils a putative candidate with a catalytic potential far exceeding compound I of P450 or sMMOs.^{[13],[14]}

DFT calculations on **1** yield quintet $S = 2$ as the ground state with the $S = 1$ state 87.2 kJ/mol higher. Not only the high-spin state is stabilized here, but also the triplet state is significantly destabilized. To further verify the nature of the ground state, *ab initio* DLPNO-CCSD(T) calculations were performed, which also resulted in $S = 2$ as the ground state, with the triplet being 128.8 kJ/mol higher in energy. The $S = 2$ state has $(\delta_{xy})^1(\pi^*_{xz})^1(\pi^*_{yz})^1(\sigma^*_{x^2-y^2})^1(\sigma^*_z)^0$ configuration (see Figure S1 in ESI) with a strong π character between O- $p_{x/y}$ orbitals and Fe- d_{xz}/d_{yz} orbitals. The Fe–O bond distance is found to 1.600 Å, which is the shortest among any known Fe^{IV}=O moieties (1.62-1.70 Å) and is extremely close to Fe–O bond distance found for TauD and other non-heme Fe^{IV}=O enzymes (see Figure 1a and Table S1 in ESI)^[1c, 5] and for this reason the computed Fe–O stretching frequency of 946 cm^{-1} is also higher than reported values (799 to 862 cm^{-1}).^[1c, 15] The Fe–O bonds are found to be strongly covalent (NBO analysis, Figure S2 in ESI) with a WBI (Wiberg Bond Index) value of 1.543, suggesting Fe=O character. Further, a significant spin density ($\rho_O=0.608$) is detected at the ferryl oxygen atom similar to other high-spin Fe^{IV}=O species, and this could hold the key to its unprecedented reactivity computed.^[16] The spin-natural orbital (SNO) analysis reveals the presence of 4.27e on the iron centre, and this agrees with the formal Fe^{IV}=O species expected for **1** (see Figure S3 in ESI).

To understand the nature of the oxidation state further, we have computed the Mössbauer parameters of **1**, and the isomer shift (δ) value is estimated to be 0.432 mm/s with the quadrupole splitting parameter (ΔE_Q) of -0.207 mm/s which are very close to $S = 2$ [(H₂O)₅Fe^{IV}=O]²⁺ species.^[1c] The higher isomer shift for **1** indicates the presence of the weak equatorial oxygen coordination of CB[5] ligand. The *ab initio* CASSCF/NEVPT2 computed zero-field splitting (D) parameter of **1**^[17] is 4.55 cm^{-1} with $E/D = 0.208$ which is also in agreement with other high-spin $S = 2$ Fe^{IV}=O species.^[16, 18] The CASSCF calculations reveal that $S = 2$ state is strongly single-determinant with 94% of contribution arising from the ground state electronic configuration with excited quintet states lying very high in energy with the closest excited $S = 2$ state at ~200 kJ/mol higher, revealing a unique preference for single-state reactivity, even within quintet states.

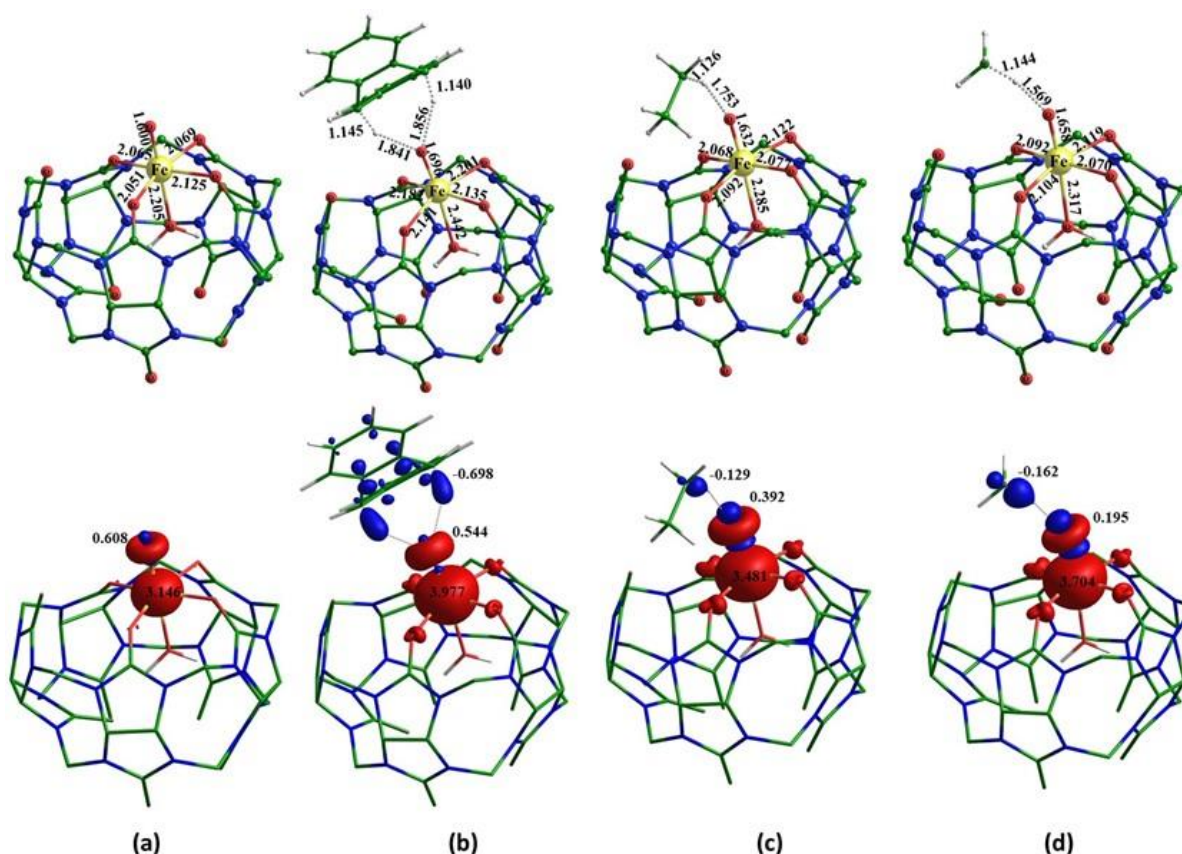


Figure 1. B3LYP-D3 optimised structure of the ground state of the (a) $[(\text{CB})\text{Fe}^{\text{IV}}(=\text{O})(\text{H}_2\text{O})]^{2+}$ (species **1**) and the transition states (b) **TS1_{DHA}**, (c) **TS1_{Et}**, (d) **TS1_{Me}** with corresponding spin density plots.

The formation energy of **1** from Fenton's reagent $[(\text{H}_2\text{O})_5\text{Fe}^{\text{IV}}=\text{O}]^{2+}$ and CB[5] ligand was computed to be extremely favourable (-71.8 kJ/mol, see ESI for details) and also from the regular iodosobenzene precursor $[(\text{CB}[5])\text{Fe}^{\text{II}}(\text{PhIO})(\text{H}_2\text{O})]^{2+}$ employed for the generation of $\text{Fe}^{\text{IV}}=\text{O}$ species. The dissociation of the axial water ligand is found to be endothermic by 13.4 kJ/mol. This suggests that the axial ligand is likely to be labile and could be replaced by other axial donor atoms. In an attempt to check the nature of various axial ligands on the stability of the high-spin state, we have varied the axial ligand in $-(\text{X})$ in $[(\text{CB}[5])\text{Fe}^{\text{IV}}=\text{O}(\text{X})]^{2+}$ ($\text{X} = -\text{SH}, -\text{Cl}, -\text{CN}, -\text{OH}$ and $-\text{N}_3$). In all cases, the $S = 2$ is found to be the ground state with the $S = 1$ found to lie 140.2 kJ/mol, 104.2 kJ/mol, 98.9 kJ/mol, 66.4 kJ/mol and 120.4 kJ/mol higher for $-\text{SH}, -\text{Cl}, -\text{CN}, -\text{OH}$ and $-\text{N}_3$ species, respectively.

To probe the reactivity of **1**, we have used 9,10-Dihydroanthracene (DHA), ethane (Et) and methane (Me) as substrates with increasing order of C-H bond dissociation energy (BDE) (DHA = 78 kcal/mol, C_2H_6 = 101 kcal/mol and CH_4 = 105 kcal/mol). For the DHA substrate, we have identified an asynchronous concerted transition state (**TS1_{DHA}**) leading to anthracene product (See Figure 1b). For methane (Me) and ethane (Et) substrates, a stepwise HAT mechanism via **TS1_{Me/Et}** leading to a radical intermediate (**Int1_{Me/Et}**) was detected (See Figure 1c and 1d). In the subsequent step, an oxygen-rebound is expected to take place. The ultrafast

radical clock experiments reported earlier reveal a short-lived radical intermediate which generally has a very low barrier for the rebound compared to the HAT step.^[19]

The C–H activation barrier of all three substrates is lower than the quintet and triplet state gap, and hence we report only the quintet transition state for all the species (Figure 2). We note that both hydrogen atoms are simultaneously abstracted by **1** through the transition state ⁵TS_{DHA} with a barrier height of only 2.2 kJ/mol, and this is rather unusual compared to the radical mechanism proposed for all the metal-oxo species reported so far.

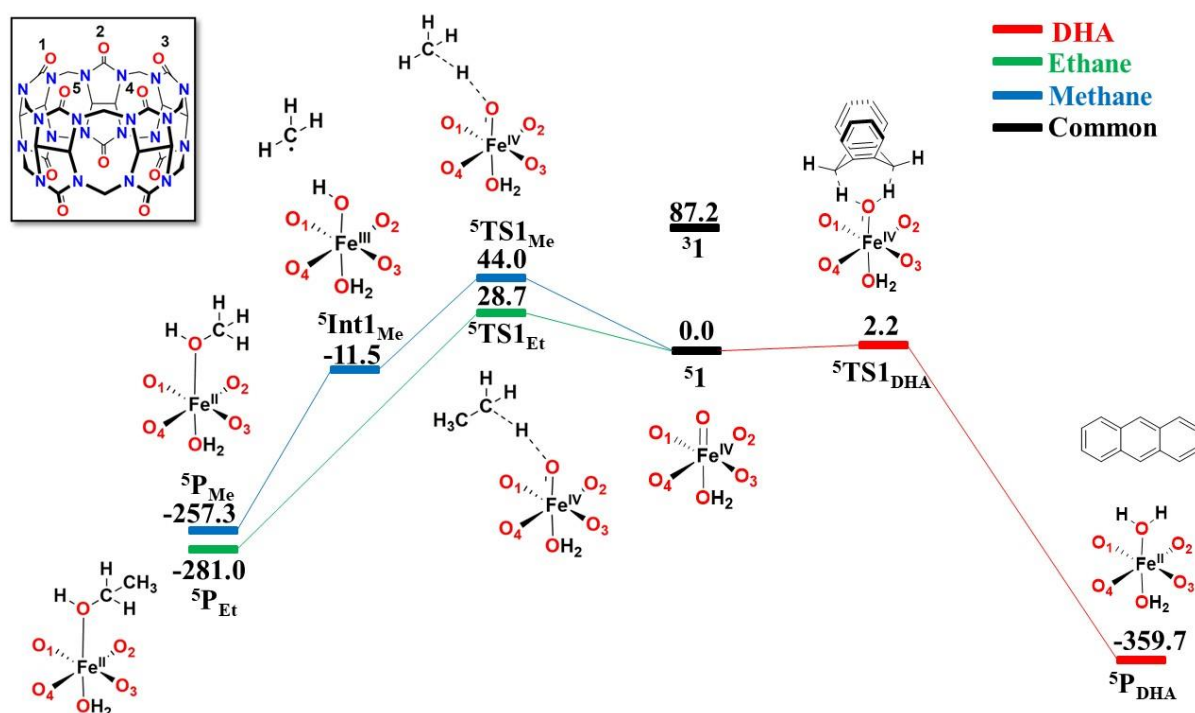


Figure 2. Computed potential energy surface (ΔG in kJ/mol) for C–H activation with DHA (red), Ethane (green), Methane (blue) by $[(\text{CB}5)\text{Fe}^{\text{IV}}=\text{O}(\text{H}_2\text{O})]^{2+}$ (**1**).

For Et and Me substrates, the barriers are estimated to be 28.7 kJ/mol (⁵TS_{1Et}) and 44.0 kJ/mol (⁵TS_{1Me}), respectively (see Figure 2). Further, our predicted barrier for the DHA/Et/Me substrates are the lowest among all the reported high-valent mono/dinuclear $\text{Fe}^{\text{IV/V}}\text{O}$ species, making species **1** the most potent catalyst for C–H bond activation (for CpD I of P450, the estimated barriers are 110.8 kJ/mol for methane, and 88.3 kJ/mol for ethane and dinuclear sMMO has a barrier of 81.6 kJ/mol for methane^[13], see Table S2 in ESI for comprehensive comparison)^{[14] [8a] [8b]}

To understand the origin of the very high reactivity observed, we analysed the structural parameters, frontier orbitals and performed deformation analysis. As the quintet state is the reactive species, transfer of α (spin-up) electron is expected to enhance the exchange-enhanced reactivity EER.^[4] The SNO analysis indicates a greater charge transfer (α -electron transfer) for the DHA, followed by ethane and methane, which is in the same order as the estimated barrier heights. At the transition state, the Fe–O bond length is found to be elongate by ~ 0.096 – 0.032

Å and C...H bonds are partially broken (>1.126 Å for all three substrates), and the O...H bonds are partially formed ($O...H < 1.856$ Å for all three substrates). In DHA, the Fe–O bond elongation at the transition state is larger compared to the other two substrates. A longer Fe–O bond and longer C...H bond facilitates a greater overlap between the donor and acceptor orbitals, stabilizing the transition state. This is evident from the deformation energy analysis performed wherein the transition state of the DHA has a tiny barrier due to extremely favourable orbital stabilization term (See Figure S4), albeit considerable deformation energy (+61.5 kJ/mol). This orbital stabilization is still present for Et, diminishing the net energy barrier. For Me substrate, the deformation energy is relatively small (13.2 kJ/mol) which offset the orbital stabilization term resulting in smaller barriers. The computed energy of donor orbital (EDO) and acceptor orbital (EAO) reveal the EDO-EAO gap of 1.5, 4.1 and 5.5 eV for DHA, Et and methane substrate, respectively. A smaller gap facilitates greater overlap and hence lower barrier height.

Various factors contribute to the overall aggressive reactivity observed for this species, and these are: (a) a high-spin state reactivity, enhances the EER and substantially reduces the barrier height. This is evident from the huge barrier height computed for the corresponding triplet state (101.8 kJ/mol at the $S = 1$ state compared to 44.0 kJ/mol for methane substrate) (b) a weak ligand field such as the one found for **1**, stabilize the empty $\sigma^*d_z^2$ orbital closer to the SOMOs and this facilitates a greater interaction with the substrate orbital reducing the EDO-EAO gap (c) the equatorial ligand found in **1** are weaker than even water found in the Fenton's reagent. This extremely weak equatorial ligand stabilizes the EAO by weakening the antibonding interaction and, at the same time, offer greater charge transfer to the low-lying EDO (d) as the equatorial ligand fields are extremely weak, this pushes the energy of the triplet state far apart and eliminating other possible pathways which could possibly lower the reactivity (e) the axial *trans* water molecule offer weak interaction, which also stabilize the EAO orbital by orbital interaction and lower the overall barrier height (f) the overall molecule has a net charge +2 which also offer stronger delocalization of EAO leading to lower barrier height. All these factors contribute to the aggressive catalytic ability of **1** observed here.

In conclusion, in silico design using DFT and *ab initio* method predicts a high-valent iron(IV)-oxo species strapped with CB[5] has a high-spin $S = 2$ ground state with a strongly destabilized triplet state, similar to the active site of many non-heme metalloenzymes. Reactivity of this species tested with DHA, methane, and ethane reveals aggressive oxidising capability with an extremely low barrier height that even the metalloenzymes can not match.

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Entry for the Table of Contents

TOC: High reactivity of $\text{Fe}^{\text{IV}}=\text{O}$ species generate using cucurbit[5]uril (CB[5]).

