Spin-forbidden reactivity of transition metal-oxo species: exploring the potential energy surfaces

Damiano Ricciarelli, a Leonardo Belpassibc, Jeremy N. Harveya, Paola Belanzoniabc*

^a Department of Chemistry, Biology and Biotechnology, University of Perugia, via Elce di Sotto 8, 06123 Perugia, Italy E-mail: paola.belanzoni@unipg.it

b CNR Institute of Chemical Science and Technologies "Giulio Natta" (CNR-SCITEC), via Elce di Sotto 8, 06123 Perugia, Italy

c Consortium for Computational Molecular and Materials Sciences (CMS)2, via Elce di Sotto 8, 06123 Perugia, Italy

d Department of Chemistry, KU Leuven, Celestijnenlaan 200F, B-3001 Leuven, Belgium E-mail: jeremy.harvey@kuleuven.be

Abstract

Spin-forbidden reactions are frequently encountered when transition metal-oxo species are involved, particularly in oxygen transfer reactivity. The computational study of such reactions is challenging, because reactants and products are located on different spin potential energy surfaces (PESs). One possible approach to describe these reactions is the so-called minimum energy crossing point (MECP) between the diabatic reactants and products PESs. Alternatively, inclusion of spinorbit coupling (SOC) effects allows to locate a saddle point on a single adiabatic PES (TS SOC). The TS SOC approach is rarely applied yet because of its high computational cost. Recently evidence for a TS SOC impact on significantly lowering the activation barrier in dioxygen addition to a carbene-gold(I)-hydride complex reaction (Chem. Sci. 2016, 7, 7034-7039) or even on predicting a qualitatively different reaction mechanism in mercury methylation by cobalt corrinoid (Angew. Chem. Int. Ed. 2016, 55, 11503-11506) has been put forward. Using MECP and TS SOC approaches we provide here a systematic analysis of three prototypical transition metal-oxo spinforbidden processes to investigate their implications on reactivity. Cycloaddition of ethylene to chromyl chloride ($CrO_2Cl_2 + C_2H_4$), iron oxide cation insertion into the hydrogen molecule (FeO₊ + H₂) and H-abstraction from toluene by a Mn(V)-oxo-porphyrin cation (MnOP(H₂O)+ + C₆H₅CH₃) are case studies. For all these processes we compare the MECP and TS SOC results which show that the spin-forbidden reactivity of transition metal-oxo species can be safely described by a MECP approach, at least for the first row transition metals investigated here, where the spin-orbit coupling is relatively weak. However, for the Mn-oxo reactivity, the MECP and TS SOC have been found to be crucial for a correct description of the reaction mechanism. In particular, the TS SOC approach allows to straightforwardly explore detailed features of the adiabatic potential energy surface which in principle could affect the overall reaction rate in cases where the involved diabatic PESs are tricky.

Introduction

Spin-forbidden processes involve a change in the total electronic spin state from reactants to products during the reaction event. These reactions are very common in the chemistry of first row transition-metal containing compounds,1 such as manganese or iron. Particularly, transition metal-oxo intermediates represent fundamental reactive species, which play an important role both in inorganic and bio-inorganic catalytic processes.2 They are especially relevant in biological transformations involving oxygen activation and transfer. High-valent iron-oxo porphyrin complexes with a strong oxidant character, for instance, have a key role in C-H hydroxylation in heme enzymes like cytochrome P4503 and synthetic manganese porphyrins are excellent C-H hydroxylation catalysts as well.4 Manganese-oxo species are also relevant to oxygen transfer reactions in biological systems like oxidation of water to molecular oxygen in photosystem II.5

The computational study of such reactions is challenging, because reactants and products are located on different spin potential energy surfaces (PESs). One possible approach to describe these reactions using the standard electronic structure theory Hamiltonian is to calculate the electronic states corresponding to such potential energy surfaces (defined as diabatic PESs), which are disconnected from each another, and to locate the regions in which the different PESs cross one another.6 More specifically, the basic idea is to find minima on the crossing hypersurfaces, i.e. the so called minimum energy crossing points or MECPs.7 The properties of these MECPs can be used to predict the rate with which the system can move from one surface to another around the MECP ("hopping" between two diabatic PESs of pure spin states).8 Such description is suitable when coupling (SOC) effects are small. This MECP approach has been applied with success to a number of spin-forbidden reactions, both in a qualitative way9 and more quantitatively.10 However, the MECP is not a stationary point and therefore the activation energy barrier of the reaction can be only estimated. An alternative approach consists of evolving smooth transition from one spin states to another along an adiabatic PES which is a mixture of the two different spin states, with a well-

defined transition state (TS SOC). This approach is more adequate when SOC effects are large, usually for very heavy atoms. The most accurate methods to include SOC in a calculation are those based on four-component Hamiltonian derived from the Dirac equation. However, since four-components approaches cannot be used in routine studies yet, due to the high computational cost, two-component electronic structure methods which include spin-orbit coupling and which are available in some electronic structure codes, have to be used.11

Since the MECP is not a stationary point, the computation of the activation barrier ΔG_{t} of a spinforbidden reaction would require to locate the TS on an adiabatic SOC PES (TS SOC). However, evaluating SOC effects typically requires expensive relativistic calculations. Hence such reports are not yet widely available. To our knowledge, only two papers on TS search including SOC were available from literature on the reaction of Ti+ with acetone12 and on the C-H activation in the reactions of Os+ with CH₃F, which was found to be facilitated by strong SOC.13 More recently, the TS SOC approach has been applied to a couple of spin-forbidden reactions, namely dioxygen addition into a carbene-gold(I)-hydride complex14 and mercury methylation by cobalt corrinoid,15 where it has been shown to be fundamental for a correct description of the reaction mechanism. In the gold chemistry investigation by some of us, MECP and TS SOC methodologies are found to qualitatively agree with the oxidation addition step representing the rate determining step (RDS) of the reaction, although quantitatively inclusion of SOC effects has a sizable impact on lowering the activation energy barrier (by about 3 kcal/mol).14 In the mercury chemistry study, inclusion of SOC effects predicts even a qualitatively different mechanism with respect to the MECP approach.15

Inspired by the relevance of transition metal-oxo species in living organisms and by the implications of the TS SOC approach on reactivity in the few cases for which it has only be tested so far, we decided to investigate whether the reactivity of such key transition metal-oxo species could be dramatically (or weakly) changed by the inclusion of spin-orbit coupling SOC effects. To this aim, we carried out mechanistic studies on three prototypical spin-forbidden processes involving transition metal-oxo compounds and we compare MECP and TS SOC results, pointing out the implications of SOC on reactivity. In this paper, for the first time the TS SOC approach is applied for a transition metal-oxo reactivity study. Specifically, we investigated: (I) cycloaddition of ethylene to chromyl chloride (CrO₂Cl₂ + C₂H₄), (II) iron oxide cation insertion into the hydrogen molecule (FeO₊ + H₂) and (III) H-abstraction from toluene by a Mn(V)-oxo-porphyrin cation (MnOP(H₂O)₊ + C₆H₅CH₃, P=porphyrin). For each of these spin-forbidden processes, we performed two-component density functional theory (DFT) calculations with the zero-order regular approximation (ZORA)₁₆ either including spin-orbit coupling (relativistic SOC) and not including SOC (relativistic scalar), namely by applying both the TS SOC and MECP approaches, respectively.

A schematic representation of the three studied prototypical reactions is shown in Scheme 1. Prototypical reaction (I) is representative of transition metal-oxo species used as oxidants in processes where oxygen is added to an olefin double bond,17 and prototypical reaction (II) is an important model for many similar inorganic and bio-inorganic oxidations occurring through dihydrogen activation yielding the inserted intermediate [HFeOH]+ which successively undergoes reductive elimination to form water.18 Prototypical reaction (III) represents a model for C-H bond hydroxylation by high valent metal-oxo porphyrin species in connection with enzymatic oxidation by heme enzymes for which the rebound mechanism involving H-abstraction from the substrate is widely accepted as the rate-determining step (RDS).19 For all the three reaction typologies some studies are available in the literature.20,21,22,23,24 A brief summary of the most relevant theoretical and experimental data on each reaction-type is given at the beginning of the corresponding section.



$$CH_3 \begin{bmatrix} OH_2 \end{bmatrix}$$
 $CH_2 \begin{bmatrix} OH_2 \end{bmatrix}$

Scheme 1: Schematic representation of prototypical reactions (I) $CrO_2Cl_2 + C_2H_4$ (top), (II) FeO₊ + H₂ (middle) and (III) MnOP(H₂O)₊ + C₆H₅CH₃ (bottom) studied in this work.

Computational details

All calculations to locate reactants, transition states, intermediates and products involved in the considered reaction processes were carried out with the ADF 2014.04 program package,25 employing a BP86 functional,26 Grimme3 BJ damping dispersion corrections (DFT-D3-BJ),27 a Slater-type TZ2P quality basis set and a ZORA Hamiltonian to include relativistic effects.16 We used both scalar and spin-orbit (SOC) ZORA Hamiltonians. The DFT + ZORA including spin-orbit coupling effects approach was employed within the unrestricted noncollinear approximation28 in order to locate transition states of the reactions on the lowest adiabatic PESs. The computation of the minimum energy crossing points (MECP) was carried out using a program developed by J.N. Harvey7_c) and interfaced with the ADF package, with the computational details described above. All calculations were performed in the gas phase.

The level of the DFT theory (BP86) used to describe the spin state energetics has been validated in a previous work of some of us₂₉ vs. highly accurate DMRG-CASPT2/CC calculations for the reactivity of the Mn(V)OP(H₂O)₊ system in substrate hydroxylation. The BP86 functional has been shown to overestimate the singlet-triplet energy gap for the Mn-oxo complex by only 1.9 kcal/mol, which is accurate for the modelling of the systems under study. Along the same lines, an investigation on the Mn(V)OP₊ system performed by Pierloot et al.₂₃ with correlated ab initio methods (CASPT2, RASPT2) has shown that in a density functional theory framework pure functionals have to be preferred over hybrid ones, since for the system in study the hybrid functionals are extremely dependent on the contribution of exact exchange and hence, inadequate for quantitative reaction mechanism studies.

Results and Discussion

Spin-forbidden reactivity by MECP and TS SOC approaches

Cycloaddition of ethylene to chromyl chloride - CrO2Cl2 + C2H4

The first prototypical process selected for our quantitative analysis on transition metal-oxo reactivity was theoretically investigated by Ziegler et al. using density functional theory.20 This is

the cycloaddition of ethylene to chromium-oxygen bonds in chromyl chloride, as schematically shown in Scheme 1.

Transition metal oxides are applied extensively as oxidants in processes where oxygen is added to an olefin double bond.¹⁷ In general, it was found that these oxidizers are gentler and remarkably more specific than the direct application of elemental oxygen. Mechanistic studies, on both experimental and theoretical side, carried out for molybdenum complexes, permanganate, ruthenium tetraoxide and osmium tetraoxide showed that the main products of the reaction with olefins are diols.³⁰ In the case of the reaction of chromyl chloride (CrO₂Cl₂) and olefins a complex mixture is produced rather than diols, where the main products are epoxides and cischlorohydrins.^{17c}) Ziegler et al.²⁰ demonstrated that, in the case of oxidation of olefins by CrO₂Cl₂, the [2+3] cycloaddition was favored over the [2+2] one, with the final evolution to epoxides and cis-chlorohydrins, arising from a subsequent arrangement of the [2+3] intermediate. Such a [2+3] ethylene addition path to a Cr=O bond was found to be exothermic with an enthalpy of -9.6 kcal/mol and an activation barrier of 15.8 kcal/mol. The reactants were studied on a singlet spin PES, since both CrO₂Cl₂ and ethylene have a singlet ground state, whilst the product was investigated on a triplet PES. The five-membered ring transition state TS was found on the singlet PES.

Based on the work of Ziegler et al.,²⁰ we have studied this spin-forbidden reaction where singlet ethylene adds to Cr=O bonds in singlet CrO₂Cl₂ via a [2+3] pathway leading to a triplet five membered ester product. Firstly, we have explored the reaction along the singlet (reactants spin state) and triplet (product spin state) potential energy surfaces by estimating the activation barrier at the minimum energy crossing point (MECP, at scalar relativistic level). A preliminary PES scan has been done by considering the two CrO₂Cl₂-ethylene O-CH₂ distances having the same magnitude and varying to the same extent as reaction coordinate. Constrained geometry optimizations have been performed for both the singlet and the triplet spin states by varying the above two distances from 2.2 to 1.3 Å. Results of the two PES scans are reported in Figure S1 in the SI. The final reaction profile is shown in Figure 1 (top).



Figure 1: Reaction profile for the [2+3] cycloaddition of ethylene to CrO₂Cl₂ at the scalar ZORA (top) and SOC ZORA (bottom) level of theory.

Our results show that a transition state is located on the singlet potential energy surface and it is responsible for the energy activation barrier of the reaction which amounts to 18.0 kcal/mol, with the reaction being exothermic by -12.3 kcal/mol.

These findings are in full agreement with those obtained by Ziegler et al. at a different level of theory.₂₀ The reaction path involves a spin crossover from the singlet PES to the triplet PES once the transition state has been past. This singlet/triplet crossover occurring after the transition state 1TS on the singlet potential energy surface is described by the MECP geometry which is very close to that of 1TS (Figure 1, top).

The corresponding reaction profile calculated by including SOC effects is also shown in Figure 1 (bottom). The SOC PES scan is also reported in Figure S1 in the SI. The energy stabilization of the transition state TS SOC is negligible (about 0.1 kcal/mol) and it could be considered within the error of the functional. The TS SOC geometry is very close to both the 1TS and MECP geometries. Inclusion of SOC effects for the TS search neither lowers the activation barrier nor changes the reaction path of this prototypical reaction.

Iron oxide cation insertion into the hydrogen molecule - FeO₊ + H₂

The second reaction we studied is the FeO₊ insertion into the hydrogen molecule. This process is part of the more general reaction $FeO_+ + H_2 \rightarrow Fe_+ + H_2O_{.31}$ It is known that the iron oxide cation FeO₊ is a remarkable oxidant, capable of transferring oxygen to very unreactive species such as dihydrogen or methane in the gas phase.

The entire reaction mechanism has been previously investigated by Harvey et al.21 and Mondal et al.22 and it was shown that this reaction is a prototype of "Two-State Reactivity".1 The iron oxide cation and the iron cation product both have a sextet ground state as well as H₂ co-reactant and H₂O co-product both are singlet species, therefore the sextet PES represents the ground states for both reactants and products. However, evidence for key transition states and intermediates along the path towards the products lying on a lower quartet potential energy surface has been provided in different experimental and theoretical investigations 1,21,22,32 Particularly, Harvey et al.21 have shown that the formation of an FeO₊ \cdot H₂ sextet reactant complex is followed by a spin-state change through a minimum energy crossing point MECP1 near the quartet FeO₊ \cdot H₂ reactant complex

minimum and subsequently the dihydrogen activation occurs through a four membered ring transition state and yields the inserted intermediate [HFeOH]+. Hence, the process studied is of spin-forbidden type since it involves a crossing from a sextet (reactants) to a quartet (product) spin state.

According to the picture provided by Mondal et al.22 a reasonable reaction coordinate to carry out our investigation is the angle formed by Fe, O and the closest H atom, defined as shown in Scheme 2.



Scheme 2: Reaction coordinate definition for the iron oxide cation insertion into the hydrogen molecule reaction.

A preliminary scan of the sextet (reactant ground state) and the quartet (product ground state) potential energy surfaces obtained by varying the chosen reaction coordinate from 180 to 0 degrees is reported in Figure S2 in the SI. The sextet PES shows a reactant complex geometry minimum, 6RC, from which the energy continuously increases without showing any reactivity behavior.

The quartet PES is somewhat more tricky. It shows two minimum energy structures (intermediates), one saddle point structure (transition state) and a crossing with the sextet PES occurring between the first saddle point and the second minimum energy structure before forming the final product [HFeOH]+. Along the quartet PES, a rotation of the H₂ molecule from a parallel to a perpendicular and back to a parallel position with respect to the [HFeO]+ plane is observed, suggesting possible different orientations of the FeO+ attack on the H₂ molecule.

The reaction profile, calculated at the scalar ZORA level of theory, is reported in Figure 2 (top). It actually shows two possible pathways to reach the final 4I₃ intermediate from the ₆RC reactant complex. They only differ for the orientation of the hydrogen molecule with respect to the [HFeO]₊ plane and they are characterized by two different MECPs (MECP1 and MECP2) and intermediate (4I₁ and 4I₂) structures. Note that 4I₁ is a local minimum and a rotation of H₂ out of the HFeO plane, accompanied with a H-H bond elongation, leads to a lower energy minimum, represented by 4I₂. In MECP1 the H₂ molecule lies on the overall molecular plane, while in MECP2 it is rotated by 90° with respect to such a plane.





Figure 2: Reaction profiles (path 1 and path 2) for the iron oxide cation FeO₊ insertion into the hydrogen molecule at the scalar ZORA (top) and SOC ZORA (bottom) level of theory.

A scan of the SOC potential energy surface for path 1 and path 2 is depicted in Figure S3 in the SI. The presence of the two 4I₁ and 4I₂ intermediates was also detected in the literature. In ref. 32 b) two quartet states, 4A' and 4A", with different energies were calculated for the excited encounter complex (H₂)FeO₊ and the transition state for the H-H activation was observed to be lower in the case of 4A". Analogously, in ref. 21 a) the 4A" transition state was also found lower, with the 4A' transition state being not much higher in energy and two different MECPs were found.

The general picture we get for the iron oxide insertion into the hydrogen molecule suggests that the spin crossover occurs before the transition state for the FeO₊ insertion into H₂ is reached. Particularly, for path 1 the spin crossover occurs at 7.2 kcal/mol above the 6RC (MECP1), with an activation energy barrier for the iron oxide insertion, having a transition state located on the quartet PES (4TS), of 4.4 kcal/mol. For path 2, the spin crossover takes place at 6.8 kcal/mol above the 6RC (MECP2), with an activation energy barrier of 9.4 kcal/mol for the iron oxide insertion. Notably, path 1 energy profile is always higher in energy than the path 2 one.

The corresponding reaction profiles obtained employing the TS SOC approach are shown in Figure 2 (bottom).

The energy stabilization arising by inclusion of SOC effects is significant only around the MECPs region and it is respectively 0.3 kcal/mol for socTS₁ and 0.9 kcal/mol for socTS₂. Note that geometries of socTS₁ and socTS₂ are very similar to those of the corresponding MECP1 and MECP2.

Our study suggests that, even for this second process, a MECP approach could be safely employed to get a sufficiently accurate quantitative description of the FeO₊ reactivity and that the benefit from the TS SOC approach is very low.

H-abstraction from toluene by a Mn(V)-oxo-porphyrin cation - MnOP(H2O)+ + C6H5CH3, P=porphyrin

In this section we present the third and last prototypical reaction considered for our analysis. We studied the abstraction of a hydrogen from toluene performed by a Mn(V)-oxo porphyrin complex

with an axial water ligand, MnOP(H₂O)₊, leading to a Mn(IV)-OH intermediate and a toluyl radical (see Scheme 1).

Generally for metalloporphyrin-catalyzed oxidation of substrates, the so-called Groves rebound mechanism is widely accepted.19d), 19e), 19f) It consists of three steps: 1) oxidation of the Mn(III)P (P=porphyrin) catalyst to Mn(V)OP oxo intermediate, 2) H atom abstraction from the substrate C-H bond, leading to an organic radical and a Mn(IV)OHP hydroxo intermediate, and 3) OH-rebound by OH transfer to the organic radical. The rate-determining step (RDS) is the H-abstraction step and the key intermediate is the Mn(V)OP oxo species.

Mn(V)OP compounds were first isolated and spectroscopically characterized by Groves and coworkers33 and successively Nam and co-workers34 and Newcomb and co-workers35 extended Groves pioneering work. Nam et al.34 showed experimentally that the singlet state of [MnO(tdcpp)]+ (tdcpp=tetra-(2,6-dichlorophenyl)-porphyrin) was not able to oxygenate alkanes and thus active species were predicted to be probably high spin. On the basis of Nam et al. findings,34 Eisenstein and co-workers24a) carried out DFT investigations on the Groves rebound mechanism for the oxidation of toluene catalyzed by a model of [MnO(tdcpp)]+ where it was shown that the singlet state of the oxo intermediate was not active, and that the reaction could easily take place on the lowest lying triplet and quintet surfaces with very low energy barriers.

A strong pH dependence of O-transfer reactivity for Mn(V)O TMP (TMP=tetramesitylporphirin) was experimentally found by Groves and co-workers₃₆ which was computationally investigated by Eisenstein and co-workers.^{24b}) These studies both rationalized the fact that, experimentally, these compounds are less reactive in basic than in acid conditions and provided a new perspective about Mn-oxo porphyrin reactivity based on the finding that the largest the low spin/high spin energy gap the less reactive the compound.

In a work by Pierloot et al.23 with correlated ab initio methods (CASPT2, RASPT2) the $Mn(V)OP_+$ singlet ground state was proven to lack the oxyl character and to be kinetically inert. As proposed by Jin and Groves,₃₆ Pierloot and co-workers₂₃ demonstrated that the release of oxygen from $Mn(V)OP_+$ should proceed via a thermally accessible reactive high spin state (triplet or quintet) which provides a sufficient oxyl character to the system for reacting.

Finally, the [MnOP(H₂O)]⁺ mechanism for substrate hydroxylation has been computationally studied in a very recent work by some of us.²⁹ MECP calculations on H-abstraction from toluene by [MnOP(H₂O)]⁺ have been performed, indicating a first crossover from a singlet spin state of the Mn-oxo porphyrin system to a low-lying triplet spin state, followed by the RDS which is a facile H-abstraction by the triplet complex from the toluene substrate. On the basis of our computational results and experimental kinetic data by Newcomb and co-workers³⁷, a stepwise model for the

reaction has been proposed, which consists of a first equilibrium between the singlet and the triplet Mn(V)OP complex and a second irreversible reaction of the latter with the organic substrate.29

In view of the above results,²⁹ it is interesting to investigate if the proposed reactivity pattern of $[Mn(V)OP(H_2O)]_+$ would be confirmed within a TS SOC approach. In the present work, the $Mn(V)OP(H_2O)_+ + C_6H_5CH_3$ reaction is explored in detail, both on the low spin (singlet) and on the high spin (triplet) potential energy surfaces, where the O-H distance between the hydrogen of the organic substrate methyl group and the catalyst oxo group was chosen as reaction coordinate. Constrained geometry optimizations were performed, starting from 2.2 Å up to 1.0 Å values of the reaction coordinate. The results of this PES scan are now reported in Figure S4 in the SI. On the singlet PES, starting from a well established minimum representing the singlet reactant complex 1RC, the energy increases constantly and neither a saddle point nor a minimum energy structure representing the products were found.

The triplet surface is somewhat more complicated. At the beginning of the reaction the triplet PES slightly varies within an energy range between -1.5 and -3.0 kcal/mol and, after a maximum is reached, it rapidly decreases. In this PES we can detect three stationary points, indicating the presence of a triplet reactant complex ₃RC, a triplet transition state ₃TS, and a triplet product ₃I.

From a preliminary look one could establish the spin-crossover from singlet to triplet to occur at a point placed before the transition state 3TS is reached. However, at the spin-crossover point the two spin states geometries are significantly different, as shown in Figure S5 in the SI. For instance, the Mn-OH₂ distance is larger in the singlet spin state than in the triplet (2.314 vs 2.278 Å respectively), whereas the Mn-O bond is larger in the triplet than in the singlet spin state (1.644 vs. 1.560 Å respectively). Interestingly, this finding suggests that the spin-crossing point detected through scans of the triplet and singlet PES cannot be an estimate of the MECP. To find a reasonable geometry and energy of the spin-crossover reaction point a MECP calculation needs to be performed.

The reaction profile calculated at the scalar ZORA level of theory has been reported in ref. 29 and it is now showed in Figure 3 (top) to compare with the TS SOC approach results (Figure 3, bottom). The singlet reactant complex 1RC is stabilized by -6.5 kcal/mol with respect to the separated reactants. The MECP is placed at the beginning of the reaction and it is thermally accessible by the system (only 3.7 kcal/mol are needed to access the triplet PES within the accuracy of the BP86 functional). Then the triplet reactant complex 3RC is formed and the substrate H atom is abstracted via a transition state located on the triplet PES (3TS) at only 0.5 kcal/mol above the triplet reactant complex 3RC.



Figure 3: Reaction profile for the H-abstraction from toluene by MnOP(H₂O)₊ at the scalar ZORA (top) and SOC ZORA (bottom) level of theory.

In ref. 29 these findings have been rationalized within a reactivity picture where the process occurs through a preliminary spin-crossover taking place on the MnOP(H₂O)₊ complex from singlet to triplet and a subsequent H-abstraction of the toluene hydrogen with a very low activation barrier of 0.5 kcal/mol, promoted by the oxyl character of the triplet Mn-oxo-porphyrin complex. The corresponding reaction profile obtained employing the TS SOC approach is also depicted in

Figure 3 (bottom).

This SOC profile suggests the presence of a transition state in the SOC PES with a geometrical structure intermediate between those of the MECP and of the 3RC. The socRC geometry as well as the socI1 one are nearly identical to the corresponding 1RC and 3RC (compare Figure 3, top and Figure 3, bottom). From a qualitative perspective, these SOC ZORA calculations indicate that also for this prototypical reaction the inclusion of spin-orbit coupling effects doesn't change the reactivity picture. From a quantitative point of view, the TS SOC is calculated at a slightly higher energy than the MECP (-1.7 vs. -2.8 kcal/mol, respectively), which is a surprising result since the TS SOC is expected at a lower energy than the MECP. However, we should point out here that convergence has been reached for TS SOC only using the collinear approximation, which has been coherently also used for calculating all the stationary points along the path. Since the collinear approach breaks rotational symmetry, in molecular calculations one may find different energies for different orientation of the molecule.28b) To test our results, we also optimized the socRC geometry with the noncollinear approximation and we found that both geometry and energy with respect to the isolated reactants remain unchanged. In addition, single point SOC calculations employing the noncollinear approximation on both the MECP and TS SOC geometry give the same energies obtained with the collinear approximation (i.e. -2.8 and -1.7 kcal/mol, respectively). Thus, the energy difference between MECP and TS SOC, which is well within the accuracy of the method employed (DFT BP86), can be genuinely ascribed to their different geometrical structures. In particular, the different substrate H - OMn and Mn-O moiety distances indicate that the MECP

should occur earlier than the TS SOC along the path. It has been noted that finding the MECP is not sufficient when looking at the reactivity of spin-forbidden reactions. The shape of the PES is of equal importance, as demonstrated in several studies.9 Thus, one possible scenario to rationalize the higher energy TS SOC with respect to MECP is schematically shown in Figure 4.



Figure 4: Spin state scenario for the H-abstraction from toluene by MnOP(H₂O)+.

The singlet-triplet energy surfaces cross before a saddle point on the triplet PES (TS SOC) occurs, followed by a local minimum (3RC) and a second saddle point (3TS) which represents the H-abstraction activation energy barrier. Then, the MECP occurs at a lower energy than TS SOC, which should be entirely located on the triplet PES. A transition state calculation in the triplet state confirm the TS SOC as a triplet state structure. To further substantiate this finding single point singlet and triplet spin calculations have been performed on the TS SOC geometry which show that the singlet lies at +1.3 kcal/mol and the triplet at -1.7 kcal/mol above the separated reactants, the latter value being identical to that obtained for the TS SOC.

The above results lead to the important conclusion that the MECP and TS SOC approaches are crucial for the description of the path from the MECP to 3RC, passing through the triplet state transition state TS SOC. Previous theoretical studies on C-H oxidation by Mn-oxo species by

Eisenstein and co-workers24a),b) were based on the assumption that the ground singlet state is unreactive for these species and only the thermally accessible triplet (or quintet) state has the oxyl character needed for reactivity. Then the reaction mechanism was studied along the triplet PES starting from 3RC, thus completely neglecting the transition state on the triplet PES leading to 3RC (TS SOC). On the basis of our results this assumption is certainly valid within the 1.3 kcal/mol difference between the TS SOC and 3RC energies. In principle, however, neglecting such a MECP-TS SOC-3RC path could be unsafe, particularly if the TS SOC energy is high, and it could severely affect the overall reaction rate. An additional interesting conclusion is that MECP structure can also be significantly different from the TS SOC structure, and thus it could not be a good approximation of TS SOC, as usually is expected to be. In this case study the TS SOC calculations, although not changing the qualitative reactivity picture, allow to prevent the pitfalls that one can encounter when crossing between two PESs occurs, since a complete description of the reaction along the whole path on the adiabatic PES is given.

Overall, the TS SOC calculations confirm what we have found previously, namely that a rapid conversion from the singlet to the triplet spin state of the system takes place and the reactivity path is entirely located on the triplet PES.29

As a general conclusion, based on the results for the three prototypical case studies, the spin-orbit coupling (SOC) effects appear to do not substantially change, nor qualitatively neither quantitatively, the spin-forbidden reactivity picture of transition metal-oxo species which can be safely described by a MECP approach, at least for the investigated first row transition metals Cr, Fe and Mn. However, the shape of the involved PESs, which plays an important role in the description of spin-forbidden reactions, can be explored in details by the TS SOC approach, which allows to straightforwardly locate all the possible intermediates and transition states on the adiabatic PES.

Conclusion

This work represents a pioneering study on the spin-forbidden transition metal-oxo species reactivity tackled by application of adiabatic transition states using spin-orbit coupled DFT (TS SOC) approach. The results of our TS SOC investigations on three prototypical spin-forbidden reactions: (I) CrO_2Cl_2 + ethylene, (II) FeO₊ + H₂ and (III) MnOP(H₂O)₊ + toluene are compared to those obtained by applying the more commonly used minimum energy crossing point (MECP)

between the diabatic potential energy surfaces (PESs) approach. The aim is to explore the qualitative and quantitative impact of MECP and TS SOC approaches on the reactivity picture of such key transition metal-oxo species. The merit of the TS SOC approach is that, allowing the reaction to occur on a single adiabatic PES, a transition state (TS SOC) as well as an activation free energy can be calculated, whereas the MECP is not a stationary point and the activation energy can be only estimated.

Our results suggest that the SOC effects are weak and that generally transition metal-oxo spinforbidden reactions could be safely described by the MECP approach rather than by employing the TS SOC one, at least for first row transition metals considered here (Cr, Fe and Mn). Most of the reactions (Cr, Fe) show no massive gain in insight from the TS SOC approach. The benefit in these case studies from the ZORA SOC approach is very low, with non-ZORA calculations together with the MECPs being reliable. Large ZORA SOC effects are expected with heavy metals and where the MECP forms the main barrier to reaction. This was the case for the dioxygen addition to a carbene-Au(I)-H complex₁₄ and Hg methylation by cobalt corrinoid₁₅ chemistry. However, in cases where these processes are tricky and a potential energy surface with several intermediate and transition state species is involved, as for the $MnOP(H_2O)_+$ + toluene process, exploration of their adiabatic SOC surface is a straightforward approach to find all the intermediates or transition states that could describe the overall reaction mechanism. Although inclusion of SOC doesn't change the specific MnOP(H2O)+ reactivity picture, the structurally different MECP and TS SOC species suggested that, after the singlet-triplet spin crossing occurs at the MECP, the reaction proceeds at the triplet spin surface, whose topological features can be accurately retrieved through the TS SOC which locates before the triplet state reactant complex 3RC. In the whole reaction mechanism, the MECP-TS SOC- 3RC step can be neglected, but in principle and in different transition metal-oxo cases it could seriously affect the reaction rate. Thus, when tricky PESs are involved, the TS SOC approach would allow a detailed description of the overall reaction path along the adiabatic PES, avoiding possible pitfalls. A drawback of the TS SOC approach is that it cannot afford routine mechanistic studies yet, due to the heavy computational effort and convergence problems for large molecular systems, such as in the case of MnOP(H₂O)+ + toluene reaction, where the calculation of a TS SOC in a noncollinear approximation was not successful. This result should spur the theoretical chemistry community to develop more efficient algorithms for enabling the TS SOC approach routine application to large dimension systems.

Acknowledgements

D.R., L.B. and P.B. gratefully acknowledge financial support from the Ministero dell'Istruzione, dell'Università e della Ricerca (MIUR) and the University of Perugia through the program "Dipartimenti di Eccellenza – 2018-2022" (grant AMIS).

Conflict of interest

The authors declare no conflict of interest.

Keywords:

Adiabatic transition states, density functional theory, minimum energy crossing point, spinforbidden reactions, transition metal-oxo reactivity, spin-orbit coupling

References

¹ D. Schröder, S. Shaik, H. Schwarz, *Acc. Chem. Res.* **2000**, *33*, 139-145.

² a) J.T. Groves, *J. Inorg. Biochem.* 2006, *100*, 434-447; b) E.I. Solomon, T.C. Brunold, M.I. Davis, J.N. Kemsley,
 S.-K. Lee, N. Lehnert, F. Neese, A.J. Skulan, Y.-S. Yang, J. Zhou, *Chem. Rev.* 2000, *100*, 235-350; c) M. Costas,
 M.P. Mehn, M.P. Jensen, L. Que, Jr., *Chem. Rev.* 2004, *104*, 939-986; d) C. Krebs, D. Galonić Fujimori, C.T.
 Walsh, J.M. Bollinger, *Acc. Chem. Res.* 2007, *40*, 484-492.

³ a) B. Meunier, S.P. de Visser, S. Shaik, *Chem. Rev.* **2004**, *104*, 3947-3980; b) S. Shaik, D. Kumar, S.P. de Visser, A. Altun, W. Thiel, *Chem. Rev.* **2005**, *105*, 2279-2328; c) R. Lonsdale, J.N. Harvey, A.J. Mulholland, *J. Chem. Theory Comput.* **2012**, *8*, 4637-4645; d) R. Lonsdale, K.T. Houghton, J. Zurek, C.M. Bathelt, N. Foloppe, M.J. de Groot, J.N. Harvey, A.J. Mulholland, *J. Am. Chem. Soc.* **2013**, *135*, 8001-8015.

⁴ a) T.G. Spiro, R.S. Czernuszewicz, X.Y. Li, *Coord. Chem. Rev.* **1990**, *100*, 541-571; b) D. Mansuy, *Coord. Chem. Rev.* **1993**, *125*, 129-141; c) *Metalloporphyrins in Catalytic Oxidations*, (Ed: R.A. Sheldon), Marcel Dekkers, Inc., **1994**.

⁵ V. K. Yachandra, K. Sauer, M. P. Klein, *Chem. Rev.* **1996**, *96*, 2927-2950.

⁶ J.N. Harvey, WIREs Comput. Mol. Sci. **2014**, *4*, 1-14.

⁷ a) N. Koga, K. Morokuma, *Chem. Phys. Lett.* **1985**, *119*, 371-374; b) M.J. Bearpark, M.A. Robb, H.B. Schlegel, *Chem. Phys. Lett.* **1994**, *223*, 269-274; c) J.N. Harvey, M. Aschi, H. Schwarz, W. Koch, *Theor. Chem. Acc.* **1998**, *99*, 95-99.

⁸ a) J. C. Lorquet, B. Leyh-Nihant, *J. Phys. Chem.* **1988**, *92*, 4778-4783; b) Q. Cui, K. Morokuma, J. M. Bowman, S. J. Klippenstein, *J. Chem. Phys.* **1999**, *110*, 9469-9482; c) J. N. Harvey, M. Aschi, *Phys. Chem. Chem. Phys.* **1999**, *1*, 5555 – 5563.

⁹ R. Poli, J. N. Harvey, *Chem. Soc. Rev.* **2003**, *32*, 1 – 8.

¹⁰ M. Besora, J.-L. Carreón-Macedo, A. J. Cowan, M. W. George, J. N. Harvey, P. Portius, K. L. Ronayne, X.-Z. Sun, M. Towrie, *J. Am. Chem. Soc.* **2009**, *131*, 3583 – 3592.

¹¹ a) G. te Velde, F. M. Bickelhaupt, E. J. Baerends, C. Fonseca Guerra, S. J. A. van Gisbergen, J. G. Snijders, T. Ziegler, *J. Comput. Chem.* **2001**, *22*, 931-967; b) E. van Lenthe, E. J. Baerends, J. G. Snijders, *J. Chem. Phys.* **1993**, *99*, 4597-4610.

¹² J. Kim, T.K. Kim, H. Ihee, *J. Phys. Chem. A* **2009**, *113*, 11382-11389.

¹³ J. Kim, K. Hong, H.K. Kim, Y.S. Lee, T.K. Kim, *J. Chem. Theory Comput.* **2013**, *9*, 1087-1092.

¹⁴ a) C.A. Gaggioli, L. Belpassi, F. Tarantelli, D. Zuccaccia, J.N. Harvey, P. Belanzoni, *Chem. Sci.* 2016, 7, 7034-7039; b) C.A. Gaggioli, L. Belpassi, F. Tarantelli, J.N. Harvey, P. Belanzoni, *Dalton Trans.* 2017, 46, 11679-11690; c) C.A. Gaggioli, L. Belpassi, F. Tarantelli, J.N. Harvey, P. Belanzoni, *Chem. Eur. J.* 2018, 24, 5006-5015.

¹⁵ T.B. Demissie, B.D. Garabato, K. Ruud, P.M. Kozlowski, *Angew. Chem. Int. Ed.* **2016**, *55*,11503-11506; *Angew. Chem.* **2016**, *128*,11675-11678.

¹⁶ a) E. van Lenthe, E. J. Baerends, J. G. Snijders, J. Chem. Phys. **1994**, 101, 9783-9792; b) E. van Lenthe,
A. Ehlers, E.J. Baerends, J. Chem. Phys. **1999**, 110, 8943-8953; c) E. van Lenthe, R. van Leeuwen, E. J.
Baerends, J.G. Snijders, Int. J. Quantum Chem. **1996**, 57, 281-293; d) E. van Lenthe, J.G. Snijders, E.J.
Baerends, J. Chem. Phys. **1996**, 105, 6505-6516.

¹⁷ a) Organic synthesis by oxidation with metal compounds, (Eds: W.J. Mijs, C.R.H.I. de Jonge), Plenum, New York, **1986**; b) R. Stewart in Oxidation in organic chemistry, Part A (Ed: K.B. Wiberg), Academic Press, New York, **1965**, pp. 1-68; c) K.B. Sharpless, A.Y. Teranishi, J.E. Bäckvall, J. Am. Chem. Soc. **1977**, 99, 3120-3128; d) D.G. Lee in Oxidation in organic chemistry, Part B (Ed: W. S. Trahanovsky), Academic Press, New York, **1973**.

¹⁸ a) S. Shaik, S. Coen, Y. Wang, H. Chen, D. Kumar, W. Thiel, *Chem. Rev*. **2010**, *110*, 949-1017; S.T. Kleespies,
 W.N. Oloo, A. Mukherjee, L. Que, Jr., *Inorg. Chem.* **2015**, *54*, 5053-5064; c) K. Ray, F.F. Pfaff, B. Wang, W.
 Nam, *J. Am. Chem. Soc.* **2014**, *136*, 13942-13958; d) K. Krebs, D.G. Fujimori, C.T. Walsh, M. Bollinger, Jr., *Acc. Chem. Res.* **2007**, *40*, 484-492; e) B.E.R. Snyder, P. Vanelderen, M.L. Bols, S. Hallaert, L.H. Böttger, L. Ungur, K.
 Pierloot, R.A. Schoonheydt, B.F. Sels, E.I. Solomon, *Nature* **2016**, *536*, 317-321.

¹⁹ a) L.-L. Wong, S.G. Bell in *Encyclopedia of Inorganic Chemistry*, 2nd edn, vol 4 (Ed: R.B. King), Wiley, New York, **2005**; b) C.L. Hill, B.C. Schardt, *J. Am. Chem. Soc.* **1980**, *102*, 6374-6375; c) B. Meunier, *Chem. Rev.* **1992**, *92*, 1411-1456; d) J.T. Groves, *J. Chem. Educ.* **1985**, *62*, 928-931; e) J.T. Groves, *J. Porphyrins Phthalocyanines* **2000**, *4*, 350-352; f) L.M. Slaughter, J.P. Collman, T.A. Eberspacher, J.I. Brauman, Inorg. Chem. **2004**, *43*, 5198-5204.

²⁰ M. Torrent, L. Deng, T. Ziegler, *Inorg. Chem.* **1998**, *37*, 1307-1314.

²¹ a) J. N. Harvey, D.P. Tew, Int. J. Mass Spect. **2013**, 354-355, 263-270; b) S. Essafi, D.P. Tew, J.N. Harvey, Angew. Chem. Int. Ed. **2017**, 56, 5790-5794.

²² B. Mondal, L. Roy, F. Neese, S. Ye, *Isr. J. Chem.* **2016**, *56*, 763-772.

²³ S.A. Venturinelli Jannuzzi, Q.M. Phung, A. Domingo, A.L. Barboza Formiga, K. Pierloot, *Inorg. Chem.* **2016**, *55*, 5168-5179.

²⁴ a) D. Balcells, C. Raynaud, R.H. Crabtree, O. Eisenstein, *Chem. Commun.* 2008, 744-746; b) D. Balcells, C. Raynaud, R.H. Crabtree, O. Eisenstein, *Inorg. Chem.* 2008, 47, 10090-10099; c) F. De Angelis, N. Jin, R. Car, J.T. Groves, *Inorg. Chem.* 2006, 45, 4268-4276.

²⁵ a) C. Fonseca Guerra, J.G. Snijders, G. te Velde, E.J. Baerends, *Theor. Chem. Acc.* **1998**, *99*, 391-403; b) ADF2014.04, SCM, Theoretical Chemistry, Vrije Universiteit, Amsterdam, The Netherlands, http://www.scm.com.

²⁶ a) A. D. Becke, *Phys. Rev. A* **1988**, *38*, 3098-3100; b) J. P. Perdew, Y. Wang, *Phys. Rev. B* **1986**, *33*, 8800-8802; *Phys. Rev. B* **1989**, *40*, 3399.

²⁷ S. Grimme, S. Ehrlich, L. Goerigk, J. Comput. Chem. 2011, 32, 1456-1465.

²⁸ a) H. Eschrig, V.D.P. Servedio, J. Comput. Chem. 1999, 20, 23-30; b) C. Van Wüllen, J. Comput. Chem.
2002, 23, 779-785; c) J. Anton, B. Fricke, E. Engel, Phys. Rev. A 2004, 69, 012505-1, 012505-10.

²⁹ D. Ricciarelli, Q.M. Phung, L. Belpassi, J.N. Harvey, P. Belanzoni, *Inorg. Chem.* **2019**, *58*, 7345-7356.

³⁰ a) H.O. House in *Modern synthetic reactions*, Benjamin, Menlo Park, CA, **1972**, pp. 257-291; b) D.M.
Walba, M.D. Wand, M.C. Wilkes, *J. Am. Chem. Soc.* **1979**, *101*, 4396-4397; c) J.E. Baldwin, M.J. Crossley, E.M.
Lehtonen, *J. Chem. Soc., Chem. Commun.* **1979**, 918-920; d) E. Klein, W. Rojahn, *Tetrahedron* **1965**, *21*, 2353-2358; e) M. Schröder, *Chem. Rev.* **1980**, *80*, 187-213; f) K.B. Sharpless, C.A. Chong, K.J. Oshima, *J. Org. Chem.* **1976**, *41*, 177-179;g) E. Herranz, K.B. Sharpless, *J. Org. Chem.* **1978**, *43*, 2544-2548; h) E. Herranz, S.A. Biller, K.B. Sharpless, *J. Am. Chem. Soc.* **1978**, *100*, 3596-3598; i) E. Herranz, K.B. Sharpless, *J. Org. Chem.* **1980**, *45*, 2710-2713.

³¹ A. Altun, J. Breidung, F. Neese, W. Thiel, J. Chem. Theory Comput. **2014**, 10, 3807-3820.

³² a) S. Shaik, D. Danovich, A. Fiedler, D. Schröder, H. Schwarz, *Helv. Chim. Acta* **1995**, *78*, 1393-1407; b) A. Fiedler, D. Schröder, S. Shaik, H. Schwarz, *J. Am. Chem. Soc.* **1994**, *116*, 10734-10741.

³³ J.T. Groves, J. Lee, S.S. Marla, J. Am. Chem. Soc. **1997**, 119, 6269-6273.

³⁴ W.J. Song, M.S. Seo, S. DeBeer George, T. Ohta, R. Song, M.-J. Kang, T. Tosha, T. Kitagawa, E.I. Solomon, W. Nam, *J. Am. Chem. Soc.* **2007**, *129*, 1268-1277.

³⁵ R. Zhang, M. Newcomb, J. Am. Chem. Soc. 2003, 125, 12418-12419.

³⁶ N. Jin, M. Ibrahim, T.G. Spiro, J.T. Groves, J. Am. Chem. Soc. **2007**, 129, 12416-12417.

³⁷ R. Zhang, J.H. Horner, M. Newcomb, *J. Am. Chem. Soc.* **2005**, *127*, 6573-6582.

Table of Contents

Spin-forbidden reactivity of first row transition metal-oxo species is computationally investigated through both the minimum energy crossing point (MECP) between the diabatic reactants and products PESs approach and the TS SOC approach which allows to explore a single adiabatic PES through inclusion of spinorbit coupling. Both approaches provide qualitatively and quantitatively similar reactivity pictures. The TS SOC straightforward exploration of a single adiabatic PES can avoid possible pitfalls when tricky diabatic PESs are involved.

