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Theory of Hydride-Proton Transfer (HPT) Carbonyl Reduction by $[Os^{III}(tpy)(Cl)(NH{=}CHCH_3)(NSAr)]$

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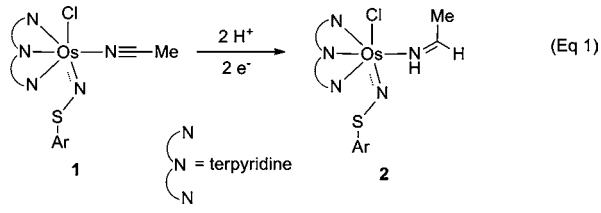
Abstract: Quantum mechanical analysis reveals that carbonyl reduction of aldehydes and ketones by the imine-based reductant *cis*-$[Os^{III}(tpy)(Cl)(NH{=}CHCH_3)(NSAr)]$ (**2**), which is accessible by reduction of the analogous nitrile, occurs by hydride-proton transfer (HPT) involving both the imine and sulfilimido ligands. In carbonyl reduction, water or alcohol is necessary to significantly lower the barrier for proton shuttling between ligands. The −N(H)SAr group activates the carbonyl group through hydrogen bonding while the $-NC(H)CH_3$ ligand delivers the hydride.

Polypyridyl Os^{VI} nitrido complexes display a remarkably versatile redox reactivity, including one-electron reduction with N−N bond coupling, N^- transfer, and N−O bond formation; S/Se-atom transfer; and addition reactions by phosphine, amine, and thiol nucleophiles.[1] Reaction of *cis*-$[Os^{VI}(tpy)(Cl)_2(N)]^+$ with the aromatic thiols C_6H_5SH, 4-MeC_6H_4SH, and 3,5-$Me_2C_6H_3SH$ in acetonitrile gives the corresponding adducts *cis*-$[Os^{IV}(tpy)(Cl)_2\{NS(H)Ar\}]^+$. In acetonitrile with added water, they undergo solvolysis and proton loss to yield spin-paired, d^4 *cis*-$[Os^{IV}(tpy)(Cl)(NCCH_3)(NSAr)]^+$.[2] In cyclic voltammograms of *cis*-$[Os^{IV}(tpy)(Cl)(NCCH_3)(NSAr)]^+$ (Ar = 3,5-$Me_2C_6H_3SH$) in 1:1 (V:V) H_2O/MeCN 1.0 M in NH_4PF_6 a reversible $Os^{IV/III}$ wave appears at 0.67 V vs SSCE (saturated sodium calomel electrode; 0.24 V vs NHE) followed by a reversible, pH-dependent, two-electron wave that gives the corresponding, neutral Os^{III}-imine, $[Os^{III}(tpy)(Cl)(NH{=}HCCH_3)(NSAr)]$, eq 1. The nitrile to imine interconversion is remarkable for its kinetic facility.[3] It is also remarkable that the ligand based couple undergoes reversible redox chemistry with organic aldehydes and ketones, a reactivity shared with the enzyme Liver Alcohol Dehydrogenase.[4] Here we report a quantum mechanical investigation that highlights this ligand redox chemistry, the mechanism of carbonyl reduction, and an important role for water or alcohol.



(Eq 1)

All B3LYP density functional theory (DFT) structures were optimized in the gas phase and verified as minima or first-order saddle points by calculation of the Hessian using Gaussian 03.[5a] All geometries reported are spin-unrestricted UB3LYP with the 6-31G(d,p)[LANL2DZ] basis set (small). (U)M06/LACVP** geometries were optimized in Jaguar 7.7.[5b] Electronic energies were evaluated with the 6-311++G(2d,p)/LANL2TZ(f) basis set (large).[6] For Os atoms the triple-ζ valence d exponents used were 1.183, 0.4492, and 0.1463. The polarizing f function exponent was set to 0.886.[7] Enthalpic and entropic gas-phase corrections were computed at 298 K and 1 atm. The free energy of solvation was estimated using the implicit CPCM model with the ukas radii model in acetonitrile.[8] ΔE values discussed below are $\Delta E_{large} + \Delta E_{ZPE(small)} + \Delta G_{solv(small)}$. ΔG values also include vibrational, rotational, and translational enthalpies and entropies. Computed redox potentials (adjusted to SCE with an absolute potential of 0.24 V versus NHE (4.36 V)) were evaluated by using standard gas-phase to solution-phase thermodynamic cycles of each species and $E = -\Delta G/nF$.

In accord with experiment, optimization of *cis*-$[Os^{IV}(tpy)(Cl)(NCCH_3)(NSC_6H_5)]^+$ gives a diamagnetic closed-shell B3LYP solution with $\langle S^2\rangle = 0.0$ due to the large singlet−triplet gap of 21.3 kcal/mol. The computed Os−N(sulfilimido) bond length of 1.91 Å is close to 1.90 Å reported experimentally, but the computed N−S bond length of 1.62 Å is too long (experiment =1.54 Å, see Supporting Information (SI)). Optimization of this complex with the M06 density functional gives a N−S bond length of 1.64 Å. The NSPh angle of 105° is close to the 107° measured experimentally. The computed $Os^{V/IV}$ and $Os^{IV/III}$ couples in MeCN are +1.3 and +0.3 V (versus SCE) and are in reasonable agreement with experimental values of +1.56 and +0.65 V (in 1:1 H_2O:MeCN; $I = 1.0$).[2] This indicates that B3LYP is suitable to describe the electronic structure of Os sulfilimido complexes. The one electron, formally $Os^{IV} + e^- \rightarrow Os^{III}$, reduction populates π^* (Os=NSPh) sulfilimido giving $[Os^{III}(tpy)(Cl)(NCCH_3)(NSPh)]$ (**1**). This π^* orbital is mainly centered on the ligand, and reduction increases Os−N from 1.91 to 1.96 Å and N−S from 1.62 to 1.65 Å. The highest energy singly occupied molecular orbital and excess spin density are mainly centered on the N and S atoms but is also delocalized onto the Os center and tpy ligand (Figure 1). Inspection of the α and β molecular orbitals shows that the correct d^5 Os^{III} electronic state is modeled for complex **1** (see SI). The double-quartet energy gap is 22.5 kcal/mol.

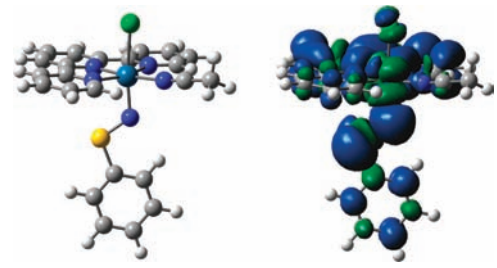


Figure 1. Structure of **1** (left) and UB3LYP spin density (right).

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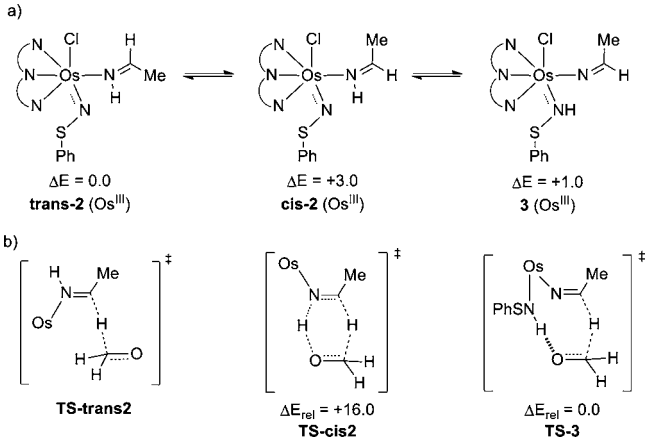
Further $2e^-/2H^+$ reduction of **1** occurs experimentally at $E_{1/2}$ = 0.29 V at pH 0.48 (for the 3,5-$Me_2C_6H_3S$-analog) to give **2**. This second reduction occurs at the nitrile ligand to give the corresponding imine, [Os^{III}(tpy)(Cl)(NH=$CHCH_3$)(NSC_6H_5)] (**2**). There is an isomerism associated with the imine, Scheme 1, with the **trans-2** isomer more stable than **cis-2** by 3.0 kcal/mol. The SOMO and spin density of **trans-2** and **cis-2** remain delocalized similar to the case for **1**. In an alternate tautomer, two electrons and one proton reside on the nitrile ligand with the second proton on NSPh, structure **3** in Scheme 1a. **3** is only 1.0 kcal/mol higher in energy than **trans-2**. In **3** the proton binds to the nitrogen lone pair in the Os−N−S plane. **Trans-2**, **cis-2**, and **3** have doublet-quartet energy gaps greater than 20 kcal/mol suggesting that redox reactions with aldehydes and ketones likely proceed on the doublet energy surface without spin crossover.

Scheme 1. (a) Possible Two Electron Reduction Products of *cis*-[Os^{III}(tpy)(Cl)($NCCH_3$)(NSPh)]$^+$; (b) Possible Transition States for CH_2O Reduction (Os = [Os^{III}(tpy)(Cl)] or [Os^{III}(tpy)(Cl)](NSPh))



Scheme 1b outlines the possible mechanisms/transition states (TSs) for formaldehyde reduction by **trans-2**, **cis-2**, and **3**. Despite solvent stabilization, a reaction pathway involving C−H bond hydride transfer from **trans-2** to formaldehyde results in charge separated products, CH_3O^- and [Os^{IV}(tpy)(Cl)($NHCCH_3$)(NSAr)]$^+$ (**TS-trans-2**) with a reaction energy of ∼60 kcal/mol. The *trans*-imine geometry precludes the NH proton from stabilizing the incipient alkoxide as it forms.

The *cis* geometry of the imine ligand in **cis-2** allows concerted hydride-proton transfer (HPT), net H_2 transfer to formaldehyde, to occur through **TS-cis2** (Figure 2). In this transition state N−H and C−H bonds are both elongated to 1.31 Å and add to the same face of the C=O bond. The forming O−H partial bond (1.18 Å) is more advanced than the forming C−H bond (1.38 Å), and the H−C−O addition occurs at an angle of 103°. Mulliken charges on the added hydrogens of +0.46 (OH) and +0.05 (CH) in the transition state support the concerted HPT label. Despite the relative simplicity of H_2 addition across the C=O bond from **cis-2**, reduction via **TS-cis2** has an activation energy of ∼35 kcal/mol and this pathway is inconsistent with observed rates; reduction of PhCHO by **2** occurs with $k = 1.0 \times 10^{-2}$ M^{-1} s^{-1}.[2] The barrier for PhCHO via a transition state similar to **TS-cis2** is ∼40 kcal/mol, which corresponds to an approximate rate of 10^{-17} M^{-1} s^{-1}.[9]

In a third pathway, the NH proton of **cis-2** (or **trans-2**) is initially transferred to NSPh to give **3** via **TS-23** (Figure 3). Direct proton migration has a barrier of 22 kcal/mol. When an explicit water molecule mediates proton shuttling, the activation energy is reduced to 15 kcal/mol (**TS-23water**). Methanol, the product of reduction, can also serve as a mediator for proton shuffling (**TS-23MeOH**) with a barrier of only 7 kcal/mol. This type of solvent mediated proton shuttling is akin to other examples reported for organometallic and biological processes.[10]

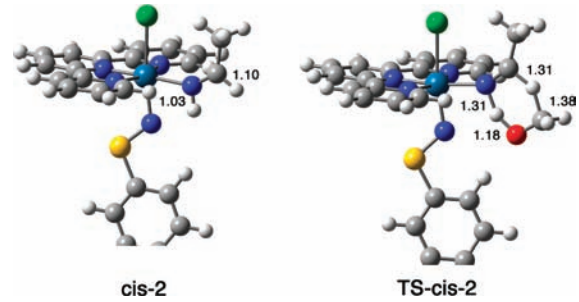


Figure 2. Ground state and transition state for **cis-2** reduction of CH_2O.

From **3**, hydride addition to formaldehyde via **TS-3** (Figure 4) has a 19 kcal/mol barrier, which is 16 kcal/mol lower than **TS-cis2**. Following the intrinsic reaction coordinate (IRC) from **TS-3** to products shows that it gives methoxide that is hydrogen bonded to the HNSPh ligand. After 13 steps of the IRC, the forming C−H bond has a length of 1.16 Å and is nearly formed while the methoxide O−H forming bond length is 1.62 Å. Subsequent deprotonation to give methanol regenerates Os^{III} nitrile complex **2** with a reaction energy of −10 kcal/mol and free energy of reaction of 2 kcal/mol. The predicted, nearly thermoneutral reaction energy indicates that, as reported experimentally, net H_2 addition to carbonyl groups is reversible.

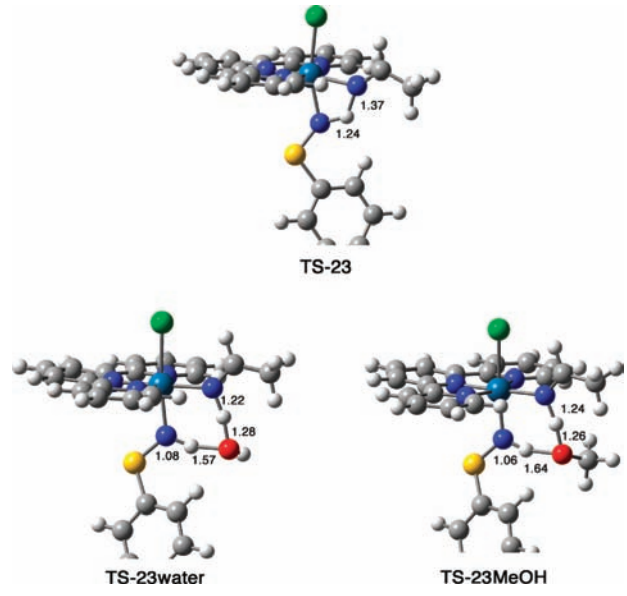


Figure 3. Proton shuttling transition states.

In **TS-3** the breaking C−H bond is stretched to 1.34 Å and the forming C−H bond length is 1.37 Å. There are three noteworthy features of **TS-3**: (1) the protonated sulfilimido ligand forms a hydrogen bond at 1.73 Å which polarizes the C=O bond. This hydrogen bond is advantageous because in this geometry the hydrogen bond interaction can form perpendicular to the carbonyl face where hydride addition occurs. In contrast, the proton and hydride add to the same carbonyl C=O bond face in **TS-cis2**. (2) The imine C−H bond hydride transfer is stimulated by the adjacent, deprotonated N atom. (3) This unique eight-membered geometry allows precise hydride addition at the optimal Bürgi−Dunitz (HCO) angle of 107°.

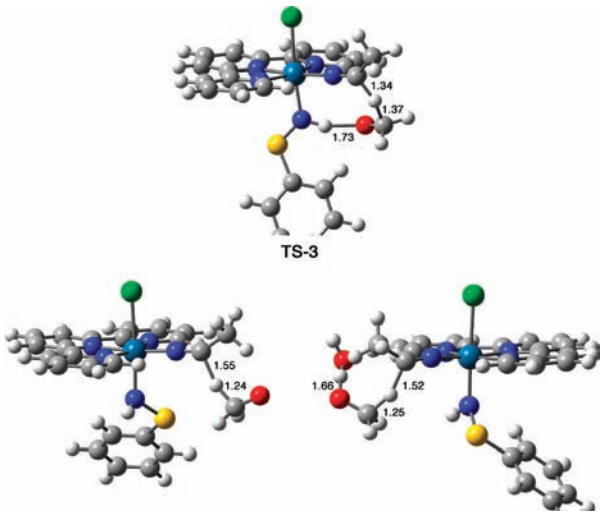


Figure 4. Formaldehyde reduction TSs.

To estimate the magnitude of the hydrogen bonding interaction in **TS-3**, the transition state was located without the HNSPh interaction with the carbonyl oxygen atom. The activation barrier for this process (**TS-3alt**) is 30 kcal/mol, pointing to significant stabilization (11 kcal/mol) by the protonated sulfilimido ligand. This result highlights the active role played by the protonated sulfilimido ligand in the reduction reaction. Alternatively, it is plausible that solvent water/hydronium or methanol (experimental pH of 1.8) serves as the hydrogen bond donor in the reduction reaction. The activation barrier for a water hydrogen bonding process (**TS-3water**, Figure 4) is 16 kcal/mol. This pathway is 3 kcal/mol lower than **TS-3** and competitive with intramolecular protonation. Similar to **TS-3**, water forms a hydrogen bonding interaction perpendicular to the carbonyl face accepting the C−H hydride. This result demonstrates that there is no special hydrogen bonding feature of the HNSPh group except its ability to obtain the optimal geometry in the transition state.

It is important to note that the carbonyl reduction mechanism described above does not directly involve the sulfilimido SOMO orbital of **3** which is orthogonal to the HN sulfilimido bond. Further, initial electron transfer to generate the $CH_2O^{-\bullet}$ radical and a cationic Os^{IV} **3** can also be ruled out based on an unfavorable thermodynamic potential for the former ($E^o = \sim 3$ V versus SCE).

In conclusion, the electronic structure and nitrile ligand redox chemistry of $[Os^{III}(tpy)(Cl)(NHCHCH_3)(NSAr)]$ provide a novel mechanism for carbonyl reduction involving hydride-proton transfer, HPT. This mechanism utilizes the reduced nitrile ligand, the sulfilimido ligand, and water or alcohol to achieve a low-energy pathway for H_2 addition. It is different than typical concerted transfer hydrogenation mechanisms, such as that described by Noyori,[11] but is related to multicomponent or bifunctional hydrogenation reactions.[12]

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Supporting Information Available: *XYZ* coordinates, absolute energies of transition structures, full ref 5a, and orbitals for structure **1**. This material is available free of charge via the Internet at http://pubs.acs.org.

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