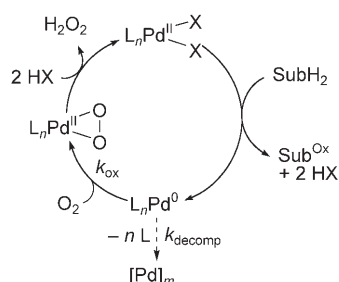


Reaction of Molecular Oxygen with an NHC-Coordinated Pd⁰ Complex: Computational Insights and Experimental Implications**

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Palladium-catalyzed aerobic oxidation reactions continue to emerge as versatile methods for the selective oxidation of organic molecules.^[1] These reactions are thought to proceed through a two-stage mechanism consisting of Pd^{II}-mediated oxidation of the substrate (SubH₂) followed by dioxygen-coupled oxidation of Pd⁰ (Scheme 1). One of the most significant challenges in this field is the tendency of Pd⁰ to

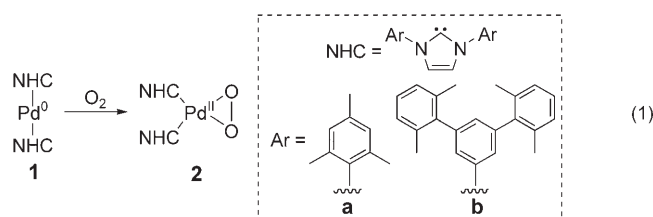


Scheme 1. Proposed catalytic cycle for Pd-catalyzed aerobic oxidation of organic substrates.

decompose through aggregation into inactive Pd metal. This problem can be addressed by increasing the rate of Pd⁰ oxygenation (k_{ox}) relative to the rate of catalyst decomposition (k_{decomp}).^[2] Recently, we have been investigating fundamental reactions between dioxygen and well-defined Pd⁰ complexes to probe the mechanism and understand factors that affect the rate of Pd⁰ oxygenation.^[3] We present herein a computational study of the reaction between O₂ and [(NHC)₂Pd⁰] (NHC = N-heterocyclic carbene). Prior computational studies of Pd⁰ oxygenation have been reported by us^[4] and others;^[5] however, the present system is the first to model an experimentally observed transformation.^[3b,6,7] Therefore,

the results can be compared to experimental data and be used to guide future studies. For example, the insights described herein have led to the demonstration of reversible O₂ binding at an NHC-coordinated Pd center. We also evaluate two mechanistic pathways that have been proposed for Pd⁰ oxygenation, the first involving sequential inner-sphere, one-electron-transfer steps and the second involving concerted two-electron oxidative addition of dioxygen to Pd⁰. The latter studies provide a foundation for the future interpretation of experimental ¹⁸O kinetic isotope effects.^[8]

The reaction of closed-shell [(NHC)₂Pd⁰] complexes with molecular oxygen is formally spin-forbidden but proceeds with remarkable facility. For example, [(IMes)₂Pd⁰] (**1a**) reacts nearly instantaneously with O₂ at −78°C in toluene solution to produce [(IMes)₂Pd^{II}(η²-O₂)] (**2a**) [Eq. (1)],^[3b] and



two different [(NHC)₂Pd⁰] complexes, **1a** and **1b**, have been shown to react rapidly with O₂ in the solid state to produce **2a** and **2b**.^[3b,6] The reactions in Equation (1) are ideal for computational investigation because of their simplicity relative to other Pd⁰ oxygenation reactions that involve dissociation or displacement of other ancillary ligands.^[3a,8a]

For the present study, we substituted the large *N*-aryl substituents of the NHC ligands with methyl groups (i.e., NHC = IMe). Calculations using the spin-unrestricted density functional theory (UDFT) were performed with the Gaussian03 computational package, and a number of different basis sets and functionals were evaluated by comparing the computed structures of [(IMe)₂Pd⁰] (**3**), [(IMe)₂Pd^{II}(η²-O₂)] (**4**), and triplet dioxygen with the corresponding experimental parameters for [(IMes)₂Pd] complexes and O₂ (see the Supporting Information).^[9] From these benchmark calculations, we selected the B3LYP hybrid density functional and a basis-set combination of the triple-ζ Stuttgart RSC 1997 ECP on Pd and the Pople-style all-electron 6-31 + G(d) basis set (Basis A) on all other atoms for geometry optimization calculations and normal-mode analyses. The larger triple-ζ 6-311 + + G(d,p) basis (Basis B) was employed for all non-Pd atoms for single-point energy corrections.^[9]

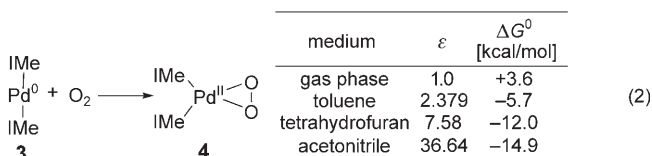
The thermodynamic driving force for oxygenation of [(IMe)₂Pd⁰] (**3**) was calculated in the gas phase and in several

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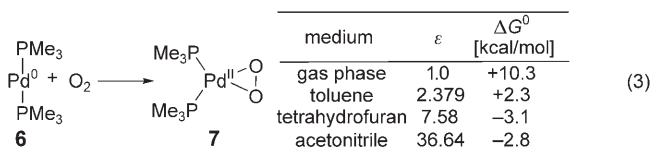
Supporting information (including computational details, all benchmarking results, and isotope-effect calculation details) for this article is available on the WWW under <http://www.angewandte.org> or from the author.

different solvents, the latter using the integral equation formalism-polarizable continuum model (IEF-PCM). The free energy of reaction is highly dependent on the dielectric constant of the medium [Eq. (2)]. The reaction is calculated



to be endergonic by 3.6 kcal mol^{−1} in the gas phase, but increasingly favorable in solvents with increasing polarity. This effect appears to reflect the significant dipole moment associated with complex **4** relative to the negligible dipole moments in **3** and O₂.

The near-thermoneutrality of the oxygenation reaction was unexpected on the basis of prior unsuccessful attempts to observe dissociation of O₂ from **2a** experimentally.^[3b] Only one Pd^{II}-peroxo complex, [(Ph₄Bu₂P)₂-Pd(O₂)] (**5**), is known to undergo simple dissociation of O₂.^[10] This complex differs from **2** solely by the presence of monodentate phosphine ligands rather than NHCs. Therefore, we evaluated the reaction of the model phosphine complex [(Me₃P)₂Pd⁰] (**6**) with O₂ by using DFT methods. As shown in Equation (3), O₂ coordination to **6** is considerably less favorable than reaction with the NHC-coordinated complex **3** [Eq. (2)]. This out-



come can be rationalized, in part, by recognizing the stronger σ -donor character of NHC ligands relative to phosphines,^[11] which should promote increased charge transfer into the O₂ fragment and tighter binding. Indeed, natural population analysis of the gas-phase-optimized complexes **4** and **7** reveal that the peroxo oxygen atoms of complex **4** possess a greater negative natural charge than those of the phosphine complex **7**, −0.471 and −0.416, respectively.

The computational results in Equation (2) prompted us to re-evaluate the reversibility of O₂ binding to [(IMes)₂Pd⁰] (**1a**). As described previously, sparging a toluene solution of **2a** with an inert gas (N₂) or repeated dissolution of **2a** in toluene followed by solvent evaporation fail to induce dissociation of O₂.^[3b] Nevertheless, heating a solid sample of **2a** under vacuum for one week at 80 °C resulted in a 31 % yield of the Pd⁰ complex **1a**. In contrast, phosphine complex **5**

releases O₂ much more readily under similar conditions. Nearly quantitative dissociation of O₂ from **5** is observed when a solid-state sample is heated under vacuum at 60 °C for only 8 h. Although various factors, including the influence of solid-state packing effects, prevent detailed interpretation of these results, the observations highlight the experimental relevance of the computational studies.

After investigating the thermodynamics of Pd⁰ oxygenation, we turned our attention to the reaction mechanism. Gas-phase calculations were performed initially, followed by re-optimization of each of the structures in toluene, THF, and CH₃CN by using the IEF-PCM (see the Supporting Information).^[12] The computed reaction coordinate in toluene, the experimental solvent, is shown in Figure 1. Dioxygen approaches the Pd center end-on and forms a Pd(η^1 -O₂)

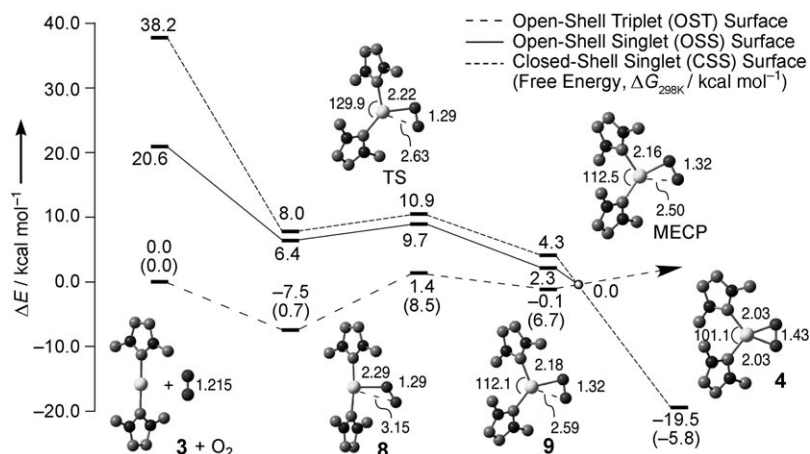


Figure 1. DFT-optimized energetic and geometric profile for the oxygenation of **3** in toluene.

adduct **8** in which the NHC ligands are in the *trans* configuration. Rate-limiting ligand isomerization into the *cis* configuration and crossover from the triplet to singlet electronic surface enables formation of the second Pd–O bond of the η^2 -peroxo product, **4**.

The initial O₂ adduct **8** possesses an open-shell-triplet (OST) electronic configuration. The corresponding configurations of open-shell and closed-shell singlets (OSS and CSS) are considerably less stable than the OST (by 13.9 and 15.5 kcal mol^{−1} on the total energy surfaces, respectively). Formation of this adduct involves charge transfer from a Pd⁰ lone pair into a singly occupied π^* orbital of dioxygen, creating a three-electron bonding interaction. The unpaired electron density is delocalized over the Pd center and both oxygen atoms, as revealed by the natural spin-density plots (Figure 2; the spin density at each oxygen atom is approximately spherical because both unpaired electrons of the same spin occupy perpendicular π^* orbitals on the O₂ fragment). The O–O bond length in **8** is 1.29 Å, intermediate between the bond lengths of dioxygen (1.21 Å) and superoxide (1.35 Å).

Isomerization of the NHC ligands from the *trans* to *cis* configuration proceeds through a transition state (TS), which subsequently collapses to intermediate **9**. The latter species

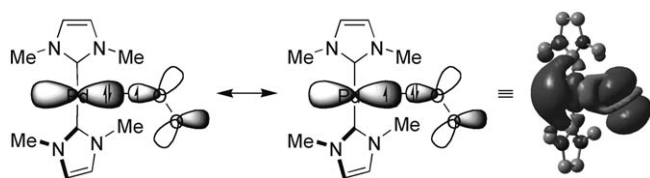


Figure 2. Localized Lewis-like resonance structures and the corresponding natural spin-density plot (darker shade: alpha spin orientation; lighter shade: beta spin orientation) for the OST ground-state configuration of the Pd^I-superoxide adduct **8**. Hydrogen atoms have been removed for clarity.

exhibits an O–O bond length of 1.32 Å and is best described as a Pd^I superoxide adduct with an OST electronic configuration. The ligand isomerization step to form **9** creates an open coordination site on the metal center adjacent to the Pd–O bond and induces redistribution of the electron density at Pd, resulting in significant unpaired electron density in the region of the newly created coordination site. Formation of the second Pd–O bond requires spin-crossover from the triplet to singlet electronic surface. Prior to this point, the OST state is more stable than the singlet electronic structures. The minimum-energy crossing point structure (MECP) was identified by using the method of Harvey et al.^[13] The optimized MECP exhibits a very similar geometry and distribution of electron spin density relative to **9**, and its energy is only slightly above that of **9** (Figure 1). Once surface crossing has occurred, formation of the second Pd–O bond leading to the Pd^{II}(η²-peroxo) complex **4** proceeds without a barrier in an energetically favorable process.

Natural population analysis, performed on the Pd and O atoms in each structure along the reaction coordinate, reveals a systematic progression of Pd→O charge transfer (Table 1).

Table 1: Charges obtained from natural population analyses at the geometries of complexes in Figure 1.

Charge	3 + O ₂	OST- 8	OST-TS	OST- 9	MECP	4
Pd	−0.351	0.133	0.275	0.344	0.348	0.545
O1 ^[a]	–	−0.266	−0.281	−0.300	−0.302	−0.519
O2	–	−0.279	−0.285	−0.341	−0.331	−0.519

[a] Oxygen atom 1 (O1) is defined as the oxygen atom nearest to the Pd center.

Despite the η¹-coordination mode of dioxygen in structures **8**, TS, **9**, and MECP, both oxygen atoms experience a similar buildup of negative charge, consistent with delocalization of the electron density within the O–O π* orbital (Figure 2). The charge on the oxygen atoms of the final η²-peroxo complex **4** is approximately twice that observed for the η¹-O₂ adducts (**8**, TS, **9**, and MECP). This observation supports the notion that the reaction of dioxygen with **3** to form **4** proceeds through sequential, one-electron-transfer steps rather than a concerted two-electron-transfer process. The stepwise-electron-transfer mechanism is possibly favored because delocalization of unpaired electron density onto the Pd center brings the singlet and triplet surfaces closer in energy by reducing exchange stabilization of the triplet state.^[4]

The DFT-derived mechanism in Figure 1 differs from conclusions reached in recent experimental studies. Roth and co-workers measured a series of oxygen-18 kinetic isotope effects (¹⁸O KIEs) for the oxygenation of late-transition-metal complexes, including the Pd⁰ complex, [Pd(PPh₃)₄].^[8] The ¹⁸O KIEs were compared with those of established benchmark reactions involving O₂, and it was also noted that the magnitudes of KIEs roughly correlate with the rate of the oxygenation reaction. Analysis of the data led the authors to conclude that oxygenation of late-transition-metal complexes proceeds through concerted transfer of two electrons to dioxygen as the O₂ unit approaches the metal center in a symmetrical, side-on manner.^[8]

To assess the viability of a concerted, oxidative addition mechanism by computational methods, it was necessary to impose the geometry constraint that the two Pd–O bond lengths must be identical along the reaction coordinate.^[14] This constraint ensures a side-on orientation of the O₂ unit with respect to the Pd center. The resulting reaction coordinate (Figure 3) suggests that an energetic maximum

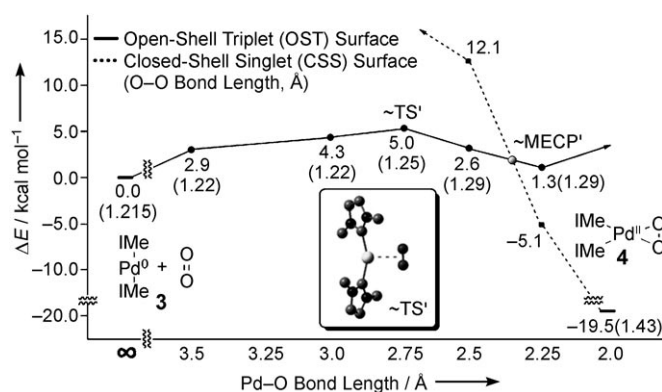


Figure 3. Energy profile for the oxygenation of **3** in which the interaction of O₂ with the Pd center is constrained to a symmetrical, side-on orientation.

occurs on the OST surface at Pd–O bond lengths of about 2.75 Å. This approximate transition state (TS') is primarily associated with *trans*–*cis* ligand isomerization as very little charge transfer has occurred to the O₂ fragment and the O–O bond length (1.25 Å) is only slightly elongated relative to that of dioxygen. The OST and CSS surfaces converge at a shorter Pd–O₂ distance (*r*_{Pd–O} ≈ 2.3 Å) in which the energy is lower than that of TS'. On the basis of the O–O bond lengths, electron transfer from Pd to dioxygen occurs very late in the reaction coordinate. The computational results summarized in Figures 1 and 3 indicate that the reaction between Pd⁰ and O₂ clearly favors initial formation of an η¹-O₂ adduct.^[15] Nevertheless, the concerted pathway in Figure 3 is only slightly energetically disfavored relative to the stepwise sequence: ΔΔ*E*_{TS–TS'}⁺ ≈ −3.6 kcal mol^{−1}.

The measurement of ¹⁸O KIEs can provide valuable insights into reactions involving dioxygen,^[16] however, understanding the mechanistic origin of the experimental results is nontrivial and subject to debate. Computational studies, such as those described herein, can play an important role in

assisting the interpretation of the data.^[17] We note, for example, that in the ¹⁸O KIE studies described above,^[8] it was argued that ¹⁸O KIEs = 1.02 were incompatible with an η^1 -superoxide transition state (e.g., TS in Figure 1). On the basis of the present DFT results, however, an ¹⁸O KIE of 1.026 was calculated for the reaction sequence depicted in Figure 1.^[18] The similarity of this value to those measured for the oxygenation of late transition metals (1.009–1.027) suggests that the stepwise mechanism in Figure 1 is consistent with the experimental data. We cannot calculate a precise KIE for the concerted pathway in Figure 3 because of the imposed constraints.^[19] Future experimental measurement of ¹⁸O KIEs for the oxygenation of **1a** will help to reconcile the divergent conclusions arising from experimental and computational studies.

The UDFT calculations described herein have provided experimentally relevant insights into the energetics and mechanism of the oxygenation of [(NHC)₂Pd⁰] complexes. The discovery that the reaction thermodynamics depend strongly on solvent polarity not only resulted in the detection of reversible oxygenation of [(IMes)₂Pd⁰], but also has important implications for catalytic reactions. Namely, the nonpolar solvents commonly used in catalysis potentially enhance the prospect of O₂ dissociation from a Pd^{II}-peroxo species and thereby contribute to catalyst decomposition. The calculated reaction pathway, involving stepwise formation of the Pd^{II}(η^2 -O₂) product through one-electron steps, provides an important starting point for understanding the origin of heavy-atom isotope effects in these and related reactions. The tandem implementation of computational and experimental studies will play a critical role in future developments in this area.

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