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The Origin of Exo-Selectivity in Methyl Cyanoformate Addition onto the C=C Bond of Norbornene in Pd-Catalyzed Cyanoesterification

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A computational investigation has been carried out to elucidate the origin of the exclusive exo-selectivity in the Pd-catalyzed cyanoesterification of strained cyclic olefins, such as norbornene and norbornadiene. A hybrid density functional was selected for the level of theory with triple-ζ quality basis set, which was proposed in an earlier study to provide experimentally sound ground state electronic structure description for palladium(II) and palladium(IV) complexes from multi-edge X-ray absorption spectroscopic measurements. Given that the product of oxidative addition can be isolated, we focused on the olefin coordination as the earliest possible origin of exo-selectivity. The calculated geometric structure for the trans-Pd(CN)(COOR)(PPh₃)₂ complex at the BHandHLYP/def2TZVP/PCM(toluene) level is in an excellent agreement with its experimental structure from crystallographic measurements. Upon dissociation of one of its phosphane ligands, the coordinatively unsaturated trans-isomer is only 17 kJ mol⁻¹ away from the isomerization transition state leading to the 14-electron cis-isomers that are 17 to 37 kJ mol⁻¹ lower in energy than the trans-isomer. Regardless of the starting complex for olefin coordination, the exo-isomer for the norbornene complex is at least 23 kJ mol⁻¹ lower than the corresponding endo-isomer. The origin of this considerable difference in Gibbs free energy can be attributed to the remarkably different steric and agostic hydrogen interactions between the methylene and the ethylene bridges of the norbornene and the adjacent cis-ligands at the Pd²⁺ center.

Introduction

The Pd-catalyzed cyanoesterification of norbornene (NBE) and norbornadiene (NBD) have been developed to provide a selective method for addition of cyano and ester groups onto C=C bonds through C–C bond cleavage. This double functionalization and specifically the installation of CN⁻ and COOMe⁻ functional groups have high utility value in organic chemical transformations. The cyanoesterification reaction studied here utilizes 10 mol% of tetrakis(triphenylphosphane)palladium(0) complex as the pre-catalyst. At 110 °C in toluene after 24 h, the reaction of Pd(PPh₃)₄ pre-catalyst with cyanoester reagent and NBE or NBE substrates provided the exo-product without observing even traces of the endo-isomer. The origin of this strong exo-selectivity has yet to be explored.

Beside the exo-selectivity, another remarkable feature of the proposed reaction mechanism (Scheme 1) of the Pd(PPh₃)₄ (1)-catalyzed cyanoesterification of NBE is the possibility to isolate the oxidative addition product alkoxy carbonylpalladium(II) complex (Pd⁹⁺(CN)(COOR)(PPh₃)₂, 2). The addition of alkyl cyanoformates (NC–COOR) to complex 1 can take place at room temperature or below 50 °C in toluene. The resulting trans isomer of 2 (2t²P, Scheme 2) can be isolated in 89-98% yields.

(Insert Schemes 1 and 2)

The cis-isomer of 2 (2c²P, Scheme 2) has yet to be successfully isolated. Quite a few of the derivatives of 2t²P with various alkyl substituents (R = Me, Pr, i-Pr, and t-Bu) have been structurally characterized by X-ray diffraction analyses. The isolation of 2t²P at lower temperatures than required for olefin activation is an important feature of the reaction; hence, the origin of the exclusive exo-selectivity cannot be related to the oxidative addition step taking place at ambient temperature even in the presence of olefin substrate. Furthermore, the use of
2t2P as a pre-catalyst, showed also a remarkable chemoselectivity. Experimentally, neither ethylene nor cyclopentene gave the desired double functionalized C-C bonds.\textsuperscript{1b} The exclusive chemoselectivity for strained cyclic olefins and the exclusive regioselectivity for \textit{exo} preference of the addition suggest two dominantly different reasons that govern product formation. The latter observation suggest that the initial substrate coordination to the 14-electron, allows for the calibration of density functional theory and the reasonable combination of density functional and basis set for the definition of basis set saturation limit with respect of metal-ligand bonding. The XAS results suggested that the most appropriate basis set saturation limit with respect of electronic structure. In order to explore the origin of \textit{exo}-selectivity, we carried out density functional theory-based potential energy surface studies for \textit{i}) the structure, stability with respect of a ligand dissociation, and isomerization of 2 and \textit{ii}) NBE olefin substrate coordination (3). The detailed study on the oxidative addition step, migratory insertion, and reduction elimination will be discussed in follow up publications. The structural insights gained into this remarkable reaction from completing the above two tasks warrant a detailed and focused theoretical treatment as presented here.

Computational Methods

The electronic structure calculations and consequent potential energy surface mapping were carried out using Gaussian09 Revision C.01.\textsuperscript{5} The level of theory was defined by the BHandHLYP hybrid functional\textsuperscript{6} and the def2-TZVP basis set\textsuperscript{7} for all atoms. The specific combination of density functionals and basis sets was selected for the given study on the basis of an earlier multi-edge X-ray absorption spectroscopic (XAS) study.\textsuperscript{3} The independent XAS investigation from the given study defined the experimental ground state electronic structure for low and high-valent chloropalladium complexes and bridging and terminal chloride ligands. The specific knowledge of the composition of the frontier orbitals from experiments allows for the calibration of density functional theory and the definition of basis set saturation limit with respect of metal-ligand bonding. The XAS results suggested that the most reasonable combination of density functional and basis set for Pd\textsuperscript{III} and Pd\textsuperscript{IV} complexes is a hybrid functional that contains at least 50\% Hartree-Fock exchange and triple-\(\zeta\) quality basis set. The latter can be considered as a good approximation of the basis-set saturation limit with respect of electronic structure. In this work, solvent effects of electrostatic origin were treated implicitly \textit{via} a polarizable continuum model (PCM, \(\varepsilon = 2.37\), solvent radius = 2.82 Å).\textsuperscript{9} The covalent nature of solvent effects was considered by using one or two explicit solvent molecules \textit{via} \(\eta^3\)-toluene coordination to unsaturated, 14-electron Pd\textsuperscript{III} complexes. Scheme 2 summarizes the schematic structures of the complex for 2tPT, 2tT-O, 2tT-OMe, 2tT, 2eNT, and 2eOT. Given that the toluene molecule may compete with olefin in coordination, the calculated thermochemical properties were corrected by the reaction quotient \((+RT \ln Q)\) due to the bulk toluene concentration (\(c = 9.36\) M). In addition, we have also corrected for the difference in the entropic contributions in condensed phase vs. gas phase as proposed by Whitesides (see Supporting Information for the implementation).\textsuperscript{10} In the given study the helicity of the PPh\textsubscript{3} ligands were not investigated given the expected small energetic contribution in comparison to the decisive difference among the \textit{exo}- vs. \textit{endo}-coordination modes of the olefin substrate.

Electronic structure analysis was carried out by means of Mulliken population analysis.\textsuperscript{11} The orbital compositions were determined by singly occupying an orbital of interest. The resulting atomic spin densities for an unpaired electron were used as the measure percent atomic contributions to a given orbital. Energy decomposition analysis was carried out by means of Kitaura-Morokuma-Ziegler-Rauk\textsuperscript{12} as implemented in Amsterdam Density Functional program\textsuperscript{13} from single point energy calculations on equilibrium structures at BHandHLYP/TZVP level with COSMO–RS\textsuperscript{14} based toluene implicit solvent environment. In order to obtain chemically meaningful values for the various contributions to fragment bonding energy, the complexes were broken down to Pd\textsuperscript{II}, CN\textsuperscript{−}, COOMe\textsuperscript{−} ionic fragments and phosphane, toluene, olefin ligands.

Results and Analysis

Geometric and Electronic Structures of trans-Pd(CN)(COOMe)(PPh\textsubscript{3})\textsubscript{2}

The comparison of the experimental crystal structure and the spectroscopically validated DFT optimized structures of complex 2t2P is shown in Fig. 1. The root mean square deviations of the [PdP\textsubscript{3}C\textsubscript{3}] moiety is 0.10 Å, while it only increases to 0.20 Å when the atoms shown in Fig. 1 are considered (Pd(CN)(COOC)(PC\textsubscript{3})\textsubscript{3}). With respect to internal coordinates, the root mean square deviations of the highlighted bond lengths and bond angles are 0.05 Å and 3.0º. The largest deviations between the calculated and the experimental internal coordinates were found for the C–N and C–O bonds of the CN\textsuperscript{−} and the COOMe\textsuperscript{−} ligands (0.09 and –0.14 Å, respectively); while all other bond length deviations are within 0.05 Å. All the calculated bond angles are within 3º of the experimental values, except the ester C–O–C angle. A closer look at the network of intermolecular interactions of the experimental structure defining the crystal packing forces (the Supporting Information, Fig. S1) provides an explanation for the considerable difference between these experimental and theoretical values. Both CN\textsuperscript{−} and COOMe\textsuperscript{−} ligands are involved in multiple aromatic C–H–O/N hydrogen bonds. These are expected to cause distortions in a crystal phase structure relative to the toluene solvated structures, as modeled here.

(Insert Fig. 1)
A detailed electronic structure analysis is warranted here given its implication toward ligand exchange, olefin coordination, and in general the importance of orbital and steric interactions in determining the relative stability of the complexes. Despite the formally straightforward electronic structure that is expected for a 16-electron, yet coordinatively saturated Pd\(^{III}\) complex with 4d\(^{8}\) electron configuration, 2t2P displays a remarkably rich electronic structure as manifested by the frontier unoccupied orbitals. The HOMO/LUMO gap is large (7.1 eV), but the LUMOs are close to each other in energy due to the numerous \(\sigma^*\) and \(\pi^*\) orbitals of the ligands as represented by the first 3 eV energy range containing 26 orbitals. The first 15 orbitals are shown in Fig. S2 along with an orbital energy diagram. As expected, the LUMO corresponds to the \(\sigma^*\) orbital between the Pd 4d\(_{\text{z}^2}\) and the combination of ligand orbitals. It is notable that the P lone pair has a non-negligible \(\pi\)-mixing with the 2p orbitals in the ipso-positions of the aromatic ring. The LUMO composition can be described with 15\% Pd, 3\% CN, 12\% COOMe, and 70\% PPh\(_3\) contributions. This reflects a highly covalent bonding with remarkably high P–Pd electron donation. The energetically higher lying LUMOs mainly localized on the aromatic rings of the phosphine ligands with varied contributions (up to 2\%) from occupied Pd 4d orbitals. These metal contributions can be considered as the measure of Pd–ligand back-donation. LUMO+12, which is still within 1.5 eV of the LUMO started to show the large lobes generally associated with Rydberg orbitals (5s and 5p). Unexpectedly, LUMO+13, which closes a block of LUMOs up to 1.4 eV in energy relative to the LUMO has similar \(\sigma^*\) interaction for C-P bond as shown in the isocontour plot of the LUMO. The orbital composition is 17\% Pd 4d\(_{\text{z}^2}\), 5\% CN, and 11\% COOMe, and again approximately 70\% PPh\(_3\) contributions, but the latter is dominantly aromatic \(\pi^*\). This is a remarkable electronic structural feature of this complex and shows how important the covalent interactions are in structure and stability of these Pd\(^{III}\) complexes.

In addition to the atomic composition and graphical illustrations of the unoccupied frontier orbitals, we also carried out energy decomposition analysis\(^{16}\) of the metal and ligand interactions according to the Kitaura-Morokuma-Ziegler-Rauk method.\(^{12}\) Starting from the distorted ligand fragments as in complex 2t2P, the total fragment bonding energy is 3820 kJ mol\(^{-1}\), which originates from –1414 kJ mol\(^{-1}\) steric (Electrostatic + Pauli repulsion), –2338 kJ mol\(^{-1}\) orbital relaxation energies, and –67 kJ mol\(^{-1}\) solvation energy. The presence of two negatively charged ligands, the polarizable phosphine ligands, as well as the composition of molecular orbitals described above well justifies the large magnitude of these bonding energy contributions. As expected from the covalent bonding picture from the molecular orbital analysis, the orbital interactions are dominating the bonding energy. When we consider the distortion energy of the ligands relative to their fully optimized, but solvated structures, the steric interactions drop to –194 kJ mol\(^{-1}\), but the orbital contribution further increases to 3263 kJ mol\(^{-1}\) with negligible solvation energy contribution (–10 kJ mol\(^{-1}\)), the total bonding energy remains practically similar in order of magnitude (3533 kJ mol\(^{-1}\)). This further emphasizes the importance of covalent bonding. Each ligand undergoes an 8–18 kJ mol\(^{-1}\) distortion upon coordinating to the Pd\(^{II}\), which originates from 143, 167, and 744 kJ mol\(^{-1}\) steric, but -142, -159, -718 orbital energy contributions for CN\(^-\), PPh\(_3\), and COOMe\(^-\), respectively. The large difference between the structure of the free and the coordinated alkoxycarbonyl ligand is notable, as upon binding the carboxylato C–O bond contracts by approximately 0.1 Å, while all the other O containing bonds remain the same within 0.02 Å. This structural change correlates with the change of the electronic structure of formally sp\(^3\) O by involving its out-of-plane lone pair with \(\pi\)-interactions with the Pd 4d orbitals (see LUMO and LUMO+13 in Fig. S2).

**Potential energy surface of ligand dissociation and isomerization from 2t2P**

In order to evaluate the reactivity of 2t2P, we carried out a detailed potential energy surface study with respect to formation of the 14-electron complex trans-Pd\(^{IV}\)(CN)(COOMe)(PPh\(_3\)), 2tP after the dissociation of a PPh\(_3\) ligand from 2t2P. We have evaluated several possible pathways for the isomerization of the CN\(^-\) and COOMe\(^-\) ligands from trans to cis position giving complexes 2cOP and 2cNP. The ‘OP’ and ‘NP’ suffixes indicate trans/relationship between the CN\(^-\) and the COOMe\(^-\) ligands, respectively, and the PPh\(_3\) ligand. The schematic molecular structures for all the intermediates considered in this study are summarized in Scheme 2. Either of the 14-electron cis-Pd\(^{IV}\)(CN)(COOMe)(PPh\(_3\)) complex can accept a PPh\(_3\) ligand to complete its coordination environment and form a complex cis-Pd\(^{IV}\)(CN)(COOMe)(PPh\(_3\))\(_2\), 2c2P. Given that we will be exploring the reactivity of the 14-electron complexes toward olefins, we have also considered explicit solvent molecules, since toluene can form \(\pi^2\)-complexes with 2tP, 2cOP, or 2cNP. Fig. 2 summarizes the relative Gibbs free energies of all the considered species toward the activation of 2t2P for the olefin coordination.

Starting from the most stable and experimentally isolable 2t2P complex, the initial PPh\(_3\) ligand dissociation requires activation energy of approximately 80 kJ mol\(^{-1}\). This is a reasonable energy for the ligand dissociation at elevated temperatures of 110 °C as can be judged from established experimental enthalpy change of 129 kJ mol\(^{-1}\) for reactions at temperatures ranging 85–119 °C.\(^{17}\) The covalent nature of the Pd-P bond has already been discussed in the previous electronic structure analysis section. It is remarkable that the 16-electron toluene complex 2t2PT is practically energetically degenerate to the 2tP complex and thus indicates that 2t2PT may be formed in solution. The dissociation of the second PPh\(_3\) ligand to give 2t is energetically prohibitive (+206 kJ mol\(^{-1}\)). The coordination of one (isomers 2tT-Q and 2tT-OMe) or two (2T2T) toluene solvent molecule although stabilizes the 12-electron complex
It is more relevant to consider the two transition states at 97±1 kJ mol\(^{-1}\) labeled \(c/t\) TS in Fig. 2. These transition states \(2c\text{NP}\_TS\) and \(2c\text{OP}\_TS\) correspond to the isomerization of \(2t\) to the cis-isomer with trans-CN/PPh\(_3\) ligands (2cNP) at 98 kJ mol\(^{-1}\) and the isomerization of 2cNP to the other cis-isomer with trans-COOMe/PPh\(_3\) (2cOP) at 96 kJ mol\(^{-1}\), respectively. For the sake of completeness, we have also located the transition state connecting 2\(t\) with 2cOP, but it was found to be much higher (188 kJ mol\(^{-1}\)) than any of the above two. This correlates well with the structural analysis above indicating that the COOMe\(^{-}\) undergoes large structural reorganizations upon coordination to the Pd\(^{II}\) center due to the possibility of multiple bonding interactions. Upon coordination of a PPh\(_3\) ligand to either 2cNP or 2cOP, the \(cis\)-Pd\(^{II}\)(CN)(COOMe)(PPh\(_3\)) complex (2c2P) is formed, which is approximately 30 kJ mol\(^{-1}\) higher in energy than the \(trans\) isomer 2t2P. It is worth noting that considering the explicit solvation, the both \(cis\)-isomers can coordinate toluene instead of the PPh\(_3\) ligand; however, their relative energies shown in Fig. 2 are much higher (110 and 131 kJ mol\(^{-1}\) for 2cNT and 2cOT, respectively) than the corresponding \(trans\)-isomer (85 kJ mol\(^{-1}\) for 2tPT). The large relative energy differences indicate that these complexes will not be competitive with olefin substrate coordination.

(Insert Fig. 2)

Fig. 3 compares the immediate coordination environment of the key intermediates from the potential energy surface in Fig. 2. Upon dissociation of a PPh\(_3\) ligand from 2t2P (Fig. 1B), the resulting 14-electron complex 2tP (Fig. 3A) undergoes a minor structural rearrangement with respect to Pd-ligand bond lengths, with the exception of the Pd-P bond, which contracts by 0.1 Å due to eliminating the \(trans\) influence of the phosphane ligands. Consequently, the removal of the bulky PPh\(_3\) ligand allows for larger angular distortion around the Pd centre as the remaining three ligands will take advantage of the vacant coordination site. The changes in bond angles are as large as 10º. The replacement of a PPh\(_3\) ligand with a toluene solvent molecule (Fig. 3B) slightly reverses the trend, but judging from the Pd-P distances in 2t2P, 2tP, and 2tPT the toluene is a much poorer donor than PPh\(_3\). The toluene coordinates in \(η^2\)-fashion at 2.50 Å distance between the Pd\(^{II}\) ion and the centroid of the coordinated C=C bond (indicated by a transparent blue sphere in Fig. 3B). The plane of the toluene ring is bent by approximately 20º relative to the perpendicular arrangement to the basal plane defined by [PdCCP].

(Insert Fig. 3)

The optimized structures of the 14-electron, \(cis\) isomers are shown in Figs. 3C and 3D with remarkable, but not unexpected differences in the inner coordination environment of the Pd\(^{II}\) ion. The COOMe\(^{-}\) ligand structure is comparable in both 2cNP and 2cOP; however, the Pd-P and Pd-CN distances differ greatly according to the \(trans\)-influence of the PPh\(_3\) and CN\(^{-}\) ligands. In 2cNP, the Pd-P distance is short (2.37 Å), while the Pd-CN distance is long (2.03 Å), relative to the 2cOP complex with the corresponding bond lengths of 2.46 Å and 1.95 Å, respectively. Furthermore, the P-Pd-CN bond angle (178º) is only a few degrees off from the ideal linear value in 2cNP; while the P-Pd-COOMe angle (167º) is similarly distorted as the NC–Pd-COOMe angle (170º) in 2cOP. The \(cis\)-isomer for the 16-electron complex 2c2P in Fig. 3E shows the competition of the ligands for the Pd\(^{II}\) central ion, with the longest Pd-P bond (2.50 Å) being \(trans\) to the COOMe\(^{-}\) ligand; while the other Pd-P bond (2.39 Å) \(trans\) to the CN\(^{-}\) ligand is comparable to that in 2t2P (2.38 Å). The steric bulk of the PPh\(_3\) ligands in 2c2P generates so much repulsion that the P-Pd-P bond angle opens up by 10º relative to the ideal perpendicular value. While the complex remains tetragonal, the result of this steric repulsion is the compression of the NC–Pd-COOMe bond angle by approximately 10º.

The molecular structures corresponding to the three possible isomerization transition states for the 14-electron complexes are summarized in Fig. 4. The displacement vectors corresponding to the normal modes with imaginary frequencies (\(trans\)-cisNP (119i cm\(^{-1}\)), cisOP-cisNP (101i cm\(^{-1}\)), \(trans\)-cisOP (256i cm\(^{-1}\)) are shown in Fig. S3. It is notable that by looking at the structural distortions relative to the 14-electron complexes one can anticipate the nature of the transition state. In Fig. 4A, the Pd-P and Pd-COOMe distances are remarkably short (2.26 and 1.94 Å, respectively), while the Pd-CN distance is quite long (2.17 Å). In addition, the P-Pd-CN and the MeOOC–Pd-CN bond angles are approximately the same within a few degrees. These all together indicate that the CN\(^{-}\) ligand is transitioning between positions corresponding to 2tP and 2cNP. In Fig. 4B, the PPh\(_3\) ligands becomes partially detached from the Pd\(^{II}\) ion, and forms symmetrical angles relative to the other two, stronger coordinating anionic ligands. The latter structural distortions correspond to a transition between 2cNP and 2cOP, as also indicated by the normal mode vectors in Fig. S3B. The third transition state has a weakened Pd-COOMe bond, which has the highest energetic penalty, as shown in Fig. 2. In Fig. 4C, the P-Pd-COOMe and the NC–Pd-COOMe angles become equally distorted around 138º, and the Pd-COOMe bond is record long among all the structures presented in Figs. 4 and 5. The transition state structures and their relative energies nicely illustrates the connectedness of the Pd–PPh\(_3\) and Pd-CN bonds, while the Pd-COOMe bond is very strong with even multiple bonding character, as presented by the electronic structure of 2t2P.

There is a notable inverted trend for the stability of \(cis\)- and \(trans\)-isomers for the 16- (2t2P versus 2c2P) and the 14-electron (2cNP/2cOP versus 2tP) complexes, which requires further analysis. Therefore, we have carried out detailed energy decomposition analysis for all the relevant intermediates presented in Fig. 2 and structurally analysed in Figs. 4 and 5. The different relative energies can be related to the relative importance of covalent interactions versus the steric repulsion. This initial hypothesis was generated on the basis of L-Pd-L
bond angles in 2c2P showing greater deviation from the ideal 90/180° tetragonal coordination environment than those in 2t2P.

(Insert Figs. 4 and 5)

The results of energy decomposition analysis are summarized in Table 1. Notably, the numbers in Table 1 for 2t2P are different than those used for the energy decomposition analysis above, because in Table 1 the penalty of fragment reorganization was already included as all numbers were defined relative to the relaxed, equilibrium geometries of every ligand and the $S = 1$ spin state of the isolated Pd$^{2+}$ ion. Table 1 nicely supports numerically the hypothesis generated on the basis of structural distortions. In going from 2t2P to 2c2P, the steric energy contributions go from negative to positive; respectively. Although the orbital stabilization increases in the same order (-88 kJ mol$^{-1}$ for 4 ligands); however it cannot make up for steric repulsion increase (+381 kJ mol$^{-1}$) and thus the total bonding energy will be less favourable for the cis-isomer by 24 kJ mol$^{-1}$. The steric energy differences between the 14-electron complexes 2t2P and 2cNP follow a similar trend (+270 kJ mol$^{-1}$) as for 2t2P to 2c2P; but now the ligands allowed to come in closer to the metal due to the lack of the bulky PPh$_3$ ligand, have better overlap, and thus contribute to a larger covalent orbital stabilization for 2cNP than for 2t2P (-95 kJ mol$^{-1}$ for 3 ligands). The reverse trend in the bonding energetically favours 2cNP versus 2t2P by 19 kJ mol$^{-1}$. The finer structural differences between the two 14-electron cis isomers are also elaborated by the energy decomposition analysis. Placing the bulkier COOMe$_2$ ligand trans to the PPh$_3$ ligand in 2cOP results in reduced steric repulsion (-139 kJ mol$^{-1}$), but the stronger trans influence of the COOMe$^-$ and the PPh$_3$ ligands also reduces the orbital stabilization (+143 kJ mol$^{-1}$) and overall contribute to weaker bonding for 2cOP versus 2cNP.

(Insert Table 1)

The larger orbital energy stabilization in 2c2P (-3612 kJ mol$^{-1}$) relative to 2t2P (-3263 kJ mol$^{-1}$) has electronic structural origins. Fig. S4 summarizes the relevant orbitals for the first 15 LUMOs in 2c2P similarly to Fig. S2 for 2c2t. A cursory comparison of the LUMOs and their orbital energy levels for 2c2P and 2t2P already reveals the much more pronounced mixing of metal and ligand fragment orbitals in the cis-isomer. This is directly responsible for the larger orbital stabilization, as shown in Table 1. Both the LUMO and LUMO+1 has approximately 9% Pd 4d,$x^2$,$y^2$ orbital contribution with a comparable COOMe$^-$ and only a few percent of CN$^-$ orbital contributions, while the rest is all coming from the PPh$_3$ ligands. LUMO+3, 4, 6, 8, and 10 have much larger Pd 4d orbital character and thus larger back-donation than in the trans-isomer. However, similarly to 2t2P, LUMO+13 shows the typical orbital lobes expected for a square planar Pd$^{II}$ complex with 18% Pd, 5% CN$^-$, 11% COOMe$^-$, and the rest is from PPh$_3$ ligand. It is then understandable why and how the interplay of steric and orbital interactions, the mixing of ligand/metal and ligand/ligand orbitals are important for the origin of exclusive trans-selectivity in the cyanoesterification reaction of norbornene.

Olefin Substrate (Norbornene) Coordination to give Complexes 3

The most striking feature of the potential energy surface of the olefin coordination to the various isomers of [Pd$^{II}$(CN)(COOMe)(PPh$_3$)$_3$] complexes. The unambiguous energetic separation of the exo- and endo-coordinated NBE complexes. The highest energy conformer of exo-3cOP was calculated to be 8 kJ mol$^{-1}$ lower in energy than the lowest energy conformer of endo-3tP-N. These computational results clearly predict a strong preference for exo-coordination of the olefin substrate, which then results in the experimentally observed exo-selectivity of the cyanoesterification reaction of NBE using Pd(PPh$_3$)$_3$ precatalyst. As presented above for the preference between cis and trans isomers for the 16- versus 14-electron complexes, upon the norbornene coordination the trans isomers become lower in energy for both exo- and endo-NBE coordination modes. For the exo-coordination mode, the most stable complex exo-3tP-O has comparable Gibbs free energy to the lowest 14-electron complex 2cNP. Using data shown in Fig. S5, which displays the enthalpy of an NBE coordination versus a reaction coordinate, we can estimate the binding energy of NBE relative to 2cNP to be -29, -17, -8, and +2 kJ mol$^{-1}$ for exo-3tP-O, exo-3tP-N, exo-3cNP, and exo-3cOP, respectively. The comparable relative binding enthalpy values are +9, +11, +13, and +31 kJ mol$^{-1}$ for endo-3tP-N, endo-3tP-O, endo-3cNP, and endo-3cOP, respectively. The relative binding free energies of the most stable exo-complexes, exo-3tP-N and exo-3tP-O to 2cNP are +37 and +37 kJ mol$^{-1}$, respectively.

(Insert Fig. 5)

The origin of large energetic difference between the endo- and exo-coordination of NBE was further investigated by comparing their molecular structures (Figs. 6 and 7) and energy decomposition of the metal-ligand bonding energies (Table 2). The major difference among the exo- and endo-coordination isomers of NBE complexes is the distance between the Pd$^{II}$ ion and the C=C bond. The shorter and thus stronger Pd$^{II}$-olefin $\pi$-bonds correspond exclusively to the exo-coordination. As a limited conformation analysis of the olefin orientation relative to the Pd-ligands, we considered two characteristic conformations, when the NBE methylene bridge in the exo- and the distal C=C bond in the endo-coordination are eclipsed with the CN$^-$ or COOMe$^-$ ligands in a cis-position to NBE. In all cases the pre-set conformation has remained with the exception of exo-3tP-O (Fig. 6A), where the olefin rotated to be parallel with the trans MeOOC–Pd–CN bonds and the proximal H atom of the methylene bridge formed an agostic H–bond with Pd via the doubly occupied 4d,$x^2$ orbital. This interaction leads to the...
most stable olefin complex with the shortest Pd--C=C bond distance of 2.33 Å. Formally, a 90° rotation along the Pd--C=C bond centroid axis will result in \textit{exo}-3\text{IP}-N (Fig. 6B), which now have a considerably elongated Pd--C=C bond centroid distance of 2.41 Å; however, with a much shorter methylene bridge H--C(CN) distance of 2.39 Å. As discussed above, the strong trans-influence of the COOMe ligand results in the longest and thus the weakest Pd-olefin π-bond in \textit{exo}\textit{-3cNP} (Fig. 6C). However, when the olefin is \textit{trans} to the CN− ligand, its distance to Pd drastically reduced as can be seen for \textit{exo}-3cOP (Fig. 6D). The structural differences of the various isomers are well paralleled by the energy differences in Fig. 5 (Gibbs free energy) and Fig. S5 (enthalpy).

(Insert Figs. 6 and 7)

The molecular structures of all the \textit{endo}-NBE complexes in Fig. 7, clearly indicate the unfavourable coordination of the olefin due to the steep angles between the plane of the C=C bond and the Pd\textsuperscript{II}--olefin bond centroid axis. The kinked coordination of NBE reduces the efficiency of the olefin→Pd electron donation in comparison to those in the \textit{exo}-isomers. The interaction between the H atoms at the distal C--C bond of NBE and the CN− or COOMe− ligands slightly contributes to the stability of the complexes, but not enough degree to affect the preference for the \textit{exo}-coordination. Interestingly, the shortest Pd--C=C bond centroid distance was found for the least stable complex (\textit{endo}-3cOP, Fig. 7D), which is a difference to the \textit{exo}-isomers. Strong trans-influence of the COOMe− ligand is also visible for \textit{endo}-3cNP (Fig. 7C) by elongating the Pd--C=C bond centroid distance to more than 2.8 Å. Given that the two distal H atoms of the NBE ligand in the \textit{trans} isomers can only form weak agostic interactions with the Pd\textsuperscript{II} ion; both eclipsed isomers were localized as stationary structures (\textit{endo}-3tP-N, O, Figs. 7A and B) with comparably short Pd--C=C bond centroid distance (2.61 and 2.59 Å, respectively). Their relative Gibbs free energy (Fig. 5) and enthalpy (Fig. S5) values are practically identical.

The energy decomposition analyses of overall complex formation (left side of Table 2) and the NBE dissociation energy (right side of Table 2) further elaborate the structural and energetic differences described above. Comparison of the orbital and steric contributions to the bonding energy for the complex formation suggests the importance of covalent orbital interactions, similarly to the complexes prior to the olefin coordination. With the exceptions of \textit{exo}-3tP-O and \textit{exo}-3tP-N, the steric and solvation contributions to the total binding energy can be neglected relative to the orbital relaxation energy between the separate free ligands and Pd\textsuperscript{II} ion and their corresponding complexes. The large negative steric contribution in the latter complexes indicates the lack of a steric repulsion for the \textit{exo}-coordination of NBE to the Pd\textsuperscript{II}(PPh\textsubscript{3})(CN)(COOMe) complexes with either the CN− or the COOMe− ligands being \textit{trans} to the PPh\textsubscript{3} ligand.

The comparison of the NBE dissociation energies relative to the free, relaxed NBE ligand and the corresponding 14-electron Pd\textsuperscript{II} complexes shows a notable trend. The strongest NBE binding is calculated for \textit{exo}-3cOP with 133 kJ mol\textsuperscript{-1} bonding energy when NBE is trans to the weakest donor ligand (CN−) and form C-H···O hydrogen bonding interactions at 2.34 Å with the π-bonds of the COOMe− ligand (Fig. 6D). Considering the bonding energy of all the ligands, the same complex will be the least stable (-3438 kJ mol\textsuperscript{-1} in Table 2). A similar set of interactions explains the exceptionally high bonding energy for \textit{endo}-3cOP as an anomaly among the \textit{endo}-isomers. The weakest NBE bonding in \textit{endo}-3cNP (41 kJ mol\textsuperscript{-1}) correlates well with the longest Pd--C=C bond centroid distance of 2.81 Å among all the studied NBE complexes (Fig. 7C).

Discussions

A detailed structural and energetic analyses of the initial olefin coordination step after the oxidative addition step revealed the origin of exclusive \textit{exo}-selectivity in the cyanoesterification reaction of norbornene catalysed by Pd(PPh\textsubscript{3})\textsubscript{2}. The given study was started from the last intermediates of the oxidative addition steps. The justification of the \textit{in media res} investigation of the molecular mechanism of the reaction is provided by the experimental observation that room-temperature reaction of the pre-catalyst and the cyanoformate substrate allows for the isolation of the oxidative addition product 2c2P. We evaluated computationally the possibility of formation of the 2c2P isomer by warming up the solution to overcome the barrier for isomerization reaction upon dissociation of a PPh\textsubscript{3} ligand. The potential energy surface mapping suggested that the key step in the isomerization is the dissociation of the PPh\textsubscript{3} ligand (ΔG = +81 kJ mol\textsuperscript{-1}), which can be aided by the coordination of the solvent toluene. From the coordinatively unsaturated, 14-electron complex 2tP, the isomerization transition state is only 17 kJ mol\textsuperscript{-1} higher, which allows this complex to convert into the most stable 14-electron \textit{cis}-isomer 2cNP (+44 kJ mol\textsuperscript{-1}). Through a 52 kJ mol\textsuperscript{-1} barrier, 2cNP can isomerize to the other \textit{cis}-isomer 2cOP, which is higher in energy by 20 kJ mol\textsuperscript{-1}. Due to the steric bulk of the coordinated PPh\textsubscript{3} ligand, none of the \textit{cis}-isomer showed a preference for solvent toluene coordination. However, the dissociated PPh\textsubscript{3} ligand can coordinate to 2cNP giving 2c2P coordinatively saturated complex, which is 31 kJ mol\textsuperscript{-1} higher energy than the preparatively accessible 2t2P, but it is 13 kJ mol\textsuperscript{-1} more stable than the lowest energy 14-electron complex, 2cNP.

Norbornene coordination and further activation toward the installation of the CN− and COOR′ groups over the C=C bond requires elevated temperatures, such as 110 °C. From the above analysis of the isomerization of 2t2P to 2c2P, we can assume that some non-negligible percentage of the coordinatively unsaturated complexes would be present at elevated reaction temperature relative to the oxidative addition step. From the potential energy surface map in Fig. 5, the 2cNP complex will likely be the dominant coordinatively unsaturated species,
which is activated toward the coordination of NBE to the Pd centre. Formation of the exo-2cNP complex is preferred by 17 kJ mol\(^{-1}\) over the endo-isomer. Relevancy to the main goal of the given study, there is a clear energetic preference for the exo-isomer when considering all the possible NBE complexes. An energy range formed by the possible exo-isomers does not even overlap with the energy range of the endo-isomers. The calculated differences in Gibbs free energy, as well as the enthalpy of the norbornene coordination clearly demonstrate the exclusive exo-selectivity of the norbornene cyanoesterification reaction.

The origin of exo-selectivity thus must lie in the nature of the NBE coordination to 14-electron Pd\(^{11}\)(CN)(COOMe)(PPh\(_3\)) complex. By comparing the NBE \(\pi\)-complex structures of both exo- and endo-coordination modes an apparent difference can be noted. In order to form a stable \(\pi\)-complex, the acceptor Pd 4d orbital needs to be perpendicular to the plane of the highest occupied \(\pi\)-orbital. This automatically maximizes the possibility for \(\pi\)-back-donation if the metal is electron-rich enough. For the endo-isomers this angle was calculated to be approximately 133\(^\circ\), while for the exo-isomers it is 11\(^\circ\) closer to the ideal 90\(^\circ\) value. These values were obtained by measuring the angle formed by the Pd, C=C bond centroid, and C–C=C–C plane centroid. The distortion of 11\(^\circ\) corresponds to approximately 17-30 kJ mol\(^{-1}\) stabilization with respect of Gibbs free energy.

The exo-face of the LUMO points toward a five-membered ring of NBE; while the endo-face toward the six-membered ring. The methylene bridge C and proximal H atoms in the exo-coordination mode are 2.24 and 2.56 Å away from the coordinated C=C bond centroid; respectively, while these distances are 2.56 and 2.82 Å away in the endo-coordination mode for the C and the H atoms of the ethylene bridge. These metric differences would indicate that there is “more” room available for the coordination in the endo-isomer; however, the governing factor for the olefin coordination is the orientation of the lobes of the \(\pi\)-LUMO. In the six-membered ring, the \(\pi\)-complex cannot approach the ideal 90\(^\circ\) for maximal Pd 4d, \(\pi\)-ligand orbital overlap, because the centroid of the ethylene bridge of NBE would collide with the cis ligand on the metal. Contrary, in the exo-isomer the methylene bridge has a smaller steric bulk in addition to the presence of C–H bonds that can form agostic H-bond with the metal or with the cis-ligand and thus allowing the Pd 4d, C=C centroid, C–C=C–C centroid angle to get considerably closer to the ideal 90\(^\circ\) than in the endo-isomer, thus for a more stable olefin \(\pi\)-complex.

Conclusions

The use of spectroscopically calibrated, hybrid density functional theory allowed us to provide key insights into the effect of different reaction conditions on the oxidative addition products and their isomerization. We have identified key transition states that connect the late steps of oxidative addition. These steps are also the starting point for olefin \(\pi\)-complex formation for the transfer of the cyano and ester groups from the Pd complex to the C=C bond. We have shown that even without the complete molecular description of the reaction mechanism of the Pd-catalysed cyanoesterification of norbornene, we can define the key structural factors that govern the exclusive exo-selectivity. The key recognition of the relative stability of exo- versus endo-isomers originates from the composition and structure of norbornene substrate itself. The smaller steric bulk of the bridging methylene group and the possibility for the C–H bond of the methylene bridge to form weak, but non-negligible H-bonding interaction provide a 17-30 kJ mol\(^{-1}\) preference for the exo-isomer. In the endo-isomer, the bulkier ethylene bridge of norbornene bends the olefin \(\pi\)-donor orbital away from the ideal perpendicular orientation by 11\(^\circ\) more relative to the exo-isomer. Furthermore, the cis-ligands of Pd to norbornene are between the two proximal C–H bonds, which practically eliminate the possibility for the formation of any stabilizing C–H···acceptor atom/group H–bonding interaction. Consequently the difference in the six- versus the fix-membered ring faces of NBE corresponding to the endo-versus exo-coordination, propagates through the reaction mechanism; however, the energetic preference of exo-isomer is large enough for the selectivity to manifest already at the initial substrate binding step. The entire mechanism of the cyanoesterification reaction will be a subject of our forthcoming investigations.

Acknowledgements

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Notes and references

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\(^{†}\) Electronic Supplementary Information (ESI) available: [Corrections of translational entropy from Ref 10, Figs. S1-S5 and Cartesian coordinates in XYZ format, and non-truncated molecular structures for all computational models. This material is available free of charge via the Internet at http://pubs.acs.org. Further supporting information with formatted Gaussian checkpoint files, molecular orbital contour maps, computational output files are provided at]
Scheme 1 Schematic reaction mechanism for norbornene cyanoesterification by palladium(0) catalyst as proposed in Ref. 1b.

Scheme 2 Schematic representation of intermediates considered in the given study.
Fig. 1 Comparison of experimental crystal structure (A, CCDB code: DAPRES) and BHandHLYP/def2TZVP/PCM(toluene) calculated structure (B) of 2t2P. Selected bond lengths and angles are given in Å and degrees. Aromatic H atoms were omitted for clarity and the structures were truncated to emphasize the coordination environment of the central palladium(II) ion.

Fig. 2 Corrected Gibbs free energy surface of activation of 2t2P toward olefin coordination with modification to the solution phase entropy, consideration of the thermodynamic driving force from bulk toluene solvent, for reaction temperature of 110 °C at the BHandHLYP/def2TZVP/PCM(toluene) level.
Fig. 3 Calculated molecular structures at the BHandHLYP/def2TZVP/PCM(toluene) level for complexes 2tP (A), 2tPT (B), 2cNP (C), 2cOP (D), and 2c2P (E). Selected bond lengths and angles are given in Å and degrees. Aromatic H atoms were omitted for clarity and the structures were truncated to emphasize the coordination environment of the central palladium(II) ion.

Fig. 4 Molecular structures of isomerization transition states at the BHandHLYP/def2TZVP/PCM(toluene) level for going between 2tP and 2cNP (A), between 2cNP and 2cOP (B), and between 2tP and 2cOP (C). Selected bond lengths and angles are given in Å and degrees. Aromatic H atoms were omitted for clarity and the structures were truncated to emphasize the coordination environment of the central palladium(II) ion. The displacement vectors indicating the change in atomic positions at a given transition state are shown in Fig. S3.

Fig. 5 Relative Gibbs free energy surface of norbornene complexes (3) of the 14-electron palladium(II) complexes (2) calculated at the BHandHLYP/def2TZVP/PCM(toluene) level. ‘N’, and ‘O’ suffixes refer to the position of the norbornene methylene bridge versus CN, and COOMe ligands.
Fig. 6 Molecular structures of \textit{exo}-coordination isomers of NBE to Pd^{II}(CN)(COO\text{Me})(PPh\textsubscript{3}) (2) (A: \textit{exo}-3tP-O, B: \textit{exo}-3tP-N, C: \textit{exo}-3cNP, A: \textit{exo}-3cOP) calculated at the BH\textit{a}ndHLYP/def2TZVP/PCM(toluene) level. Selected bond lengths and angles are given in Å and degrees. Aromatic H atoms were omitted for clarity and the structures were truncated to emphasize the coordination environment of the central palladium(II) ion.

Fig. 7 Molecular structures of \textit{endo}-coordination isomers of NBE to Pd^{II}(CN)(COO\text{Me})(PPh\textsubscript{3}) (2) (A: \textit{endo}-3tP-O, B: \textit{endo}-3tP-N, C: \textit{endo}-3cNP, A: \textit{endo}-3cOP) calculated at the BH\textit{a}ndHLYP/def2TZVP/PCM(toluene) level. Selected bond lengths and angles are given in Å and degrees. Aromatic H atoms were omitted for clarity and the structures were truncated to emphasize the coordination environment of the central palladium(II) ion.
Table 1  The results of Kitaura-Morokuma-Ziegler-Rauk energy decomposition analysis\textsuperscript{12,13} in kJ mol\textsuperscript{-1} for key 16- and 14-electron complexes related to the activation of the oxidative addition product Pd\textsuperscript{II}(CN)(COOMe)(PPh\textsubscript{3})\textsubscript{2} for olefin coordination (steric energy is the sum of electrostatic and Pauli repulsion terms, orbital energy is the sum of kinetic, Coulomb, and exchange/correlation terms using BHandHLYP functional, bonding is the sum of steric, orbital, and solvation energies).

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<th>Bonding</th>
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Table 2 The results of Kitaura-Morokuma-Ziegler-Rauk energy decomposition analysis\(^{12,13}\) in kJ mol\(^{-1}\) for the NBE complexes of Pd\(^{II}\)(CN)(COOMe)(PPh\(_3\)) (steric energy is the sum of electrostatic and Pauli repulsion terms, orbital energy is the sum of kinetic, Coulomb, and exchange/correlation terms using BHandHLYP functional, bonding is the sum of steric, orbital, and solvation energies).

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<thead>
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The origin of exclusive \textit{exo}-selectivity in the Pd-catalyzed cyanoesterification reaction of methyl cyanoformate is attributed from decisive energy gap between \textit{exo}- and \textit{endo}-coordination of norbornene to Pd$^{II}$ 14-electron, coordinatively unsaturated complex.