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Origins of Selective Formation of 5-Vinyl-2-methylene Furans from Oxyallyl/Diene (3+2) Cycloadditions with Pd(0) Catalysis

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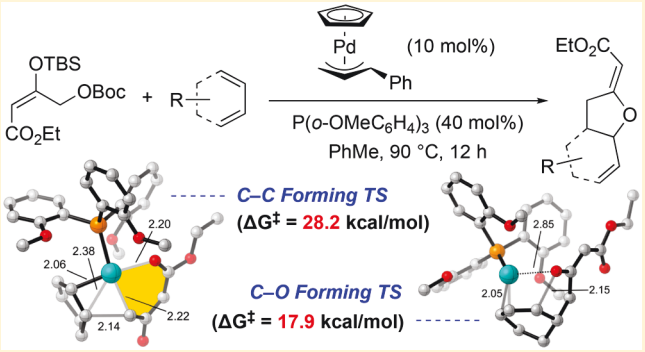
Supporting Information

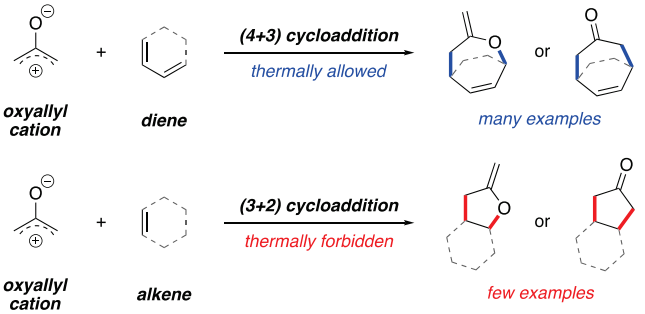
ABSTRACT: The (3+2) cycloadditions between electron-deficient Pd-oxyallyls and conjugated dienes have been investigated with density functional theory calculations. A stepwise mechanism with C−C bond formation occurring first is supported by computations. The key electron-withdrawing ester substituent on the Pd-oxyallyl species decreases the migratory insertion barrier by both lowering the LUMO energy and enabling a less-strained six-membered coordination mode. The lack of (3+2) reactivity with monoenes is attributed to higher migratory insertion barriers due to a lower-energy HOMO, as well as high C−O reductive elimination barriers, which become rate-determining. Conjugated dienes enable the formation of a highly electrophilic η^3 Pd-allyl species and greatly facilitates C−O formation.



INTRODUCTION

Cycloaddition reactions are invaluable synthetic tools to organic chemistry, as they enable the expedient and convergent construction of cyclic motifs.[1] Reactions of oxyallyl cations with dienes[2] are an attractive method to access challenging seven-membered rings through symmetry-allowed (4+3) cycloadditions (Scheme 1).[3] Due to the thermally forbidden nature of the uncatalyzed concerted (3+2) cycloaddition pathway, however, it has proven much more difficult to leverage the synthetic potential of oxyallyl cations for the construction of five-membered rings.[4] Prior to Trost's work,[5] only a limited number of stepwise (3+2) cycloadditions employing stoichiometric metal-based reagents were reported.[6−9]

Scheme 1. Different Cycloaddition Reactivity Modes of Oxyallyl Cations



In 2018, Trost et al. disclosed a successful catalytic (3+2) cycloaddition involving Pd-oxyallyl species to yield a diverse range of *cis*-fused methylene tetrahydrofurans (Scheme 2).[5] The (3+2) cycloaddition involving reaction of the oxyallyl moiety was observed when a Pd(0) source, CpPd(cinnamyl), was used as the precatalyst in conjunction with a monodentate triarylphosphine ligand, P(*o*-OMeC$_6$H$_4$)$_3$. A variety of cyclic and acyclic conjugated dienes served as effective (3+2) partners. This breakthrough in harnessing (3+2) cycloaddition reactivity of oxyallyls depended upon the employment of a Pd-oxyallyl bearing an electron-withdrawing ester (CO_2Et) substituent, as well as a conjugated diene as the coupling partner. When the electron-withdrawing ester was substituted with a phenyl ring or a hydrogen, no (3+2) cycloadduct was observed. Monoenes were also completely unreactive toward the (3+2) cycloaddition.

Our group's continued interest in oxyallyl cycloadditions[10] led us to investigate the factors that facilitate the unique (3+2) reactivity exhibited in Trost's practical and powerful transformation. Using density functional theory (DFT) calculations, we demonstrate how the combination of an electron-deficient Pd-oxyallyl and a conjugated diene enables the catalytic (3+2) cycloaddition mode.

COMPUTATIONAL METHODS

Density functional theory computations were performed in Gaussian 09.[11] Molecular geometries were optimized using the ωB97X-D functional,[12] which has been shown to give accurate geometries for transition metal complexes.[13] The LANL2DZ basis set (including effective core potential)[14] was used for Pd, and the 6-31G(d) basis set was used for all other atoms. Solvation effects were incorporated

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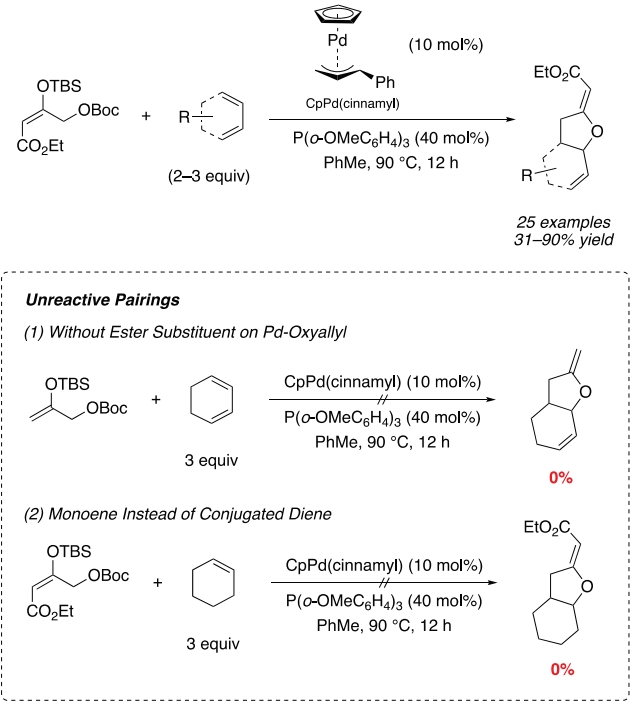
Scheme 2. Pd-Oxyallyl/Diene (3+2) Cycloaddition Reported by Trost et al.[9]



during geometry optimizations using the SMD[15] solvation model. Frequency calculations were performed at the same level of theory as for geometry optimization to characterize the stationary points as either minima (no imaginary frequencies) or first-order saddle points (one imaginary frequency) on the potential energy surface, as well as to obtain thermal Gibbs free energy corrections. Intrinsic reaction coordinate calculations were performed to ensure that the first-order saddle points found were true transition states (TS) connecting the reactants and the products. Single-point energies were calculated with the ωB97X-D functional, with the SDD[16] basis set for Pd and the 6-311++G(d,p) basis set for all other atoms. Molecular structure visualizations were obtained using CYLview.[17] Monte Carlo conformational searches were performed with the Merck molecular force field implemented in Spartan'16 to locate the low-energy conformations.

RESULTS AND DISCUSSION

Experimentally, the Pd-oxyallyl species is generated from bifunctional precursor **1** containing both a silyl enol ether and an allyl carbonate. Oxidative addition, followed by extrusion of CO_2 and alkoxide, furnishes **2**. Desilylation by the nucleophilic alkoxide anion leads to Pd-oxyallyl **3** (Figure 1a). The possible resting states of the purported Pd-oxyallyl species are shown in Figure 1b. The η^3-coordinated isomer **3a** is calculated to be the most stable resting state. However, the presence of the ester group enables alternative coordination modes, including **3b**, which lies only 2.8 kcal/mol above **3a** in energy. In both **3a** and **3b**, the *ortho* methoxy group on the phosphine ligand stabilizes the complex by coordinating to the Pd center (Figure 1c).

We explored the possible concerted and stepwise mechanisms for the (3+2) cycloaddition. A concerted (3+2) cycloaddition TS could not be located. For the rest of our investigation, we turned our attention to the stepwise pathways.

Stepwise Cycloaddition Mechanism. The stepwise pathway for the (3+2) cycloaddition between Pd-oxyallyl **3**

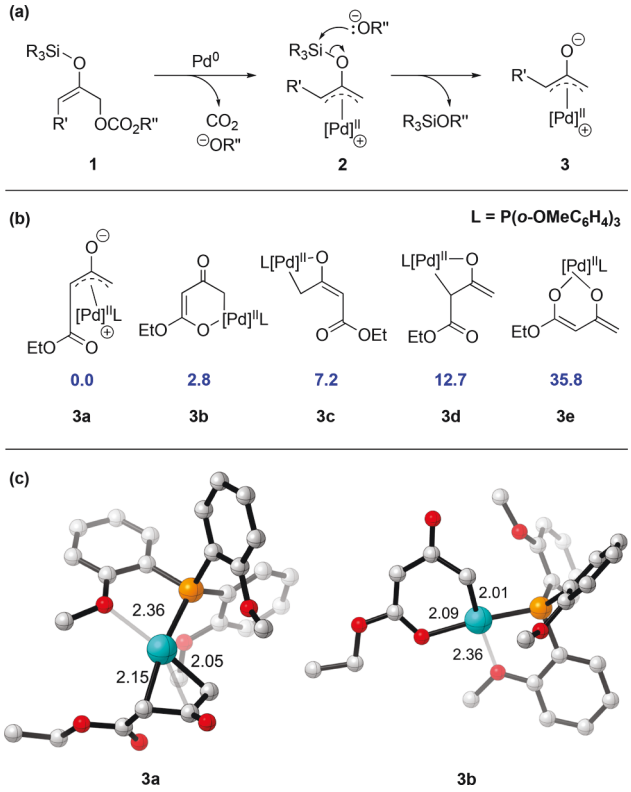


Figure 1. (a) Generation of Pd-oxyallyl species **3**. (b) Computed free energies (in kcal/mol) of the isomers of **3**. (c) Computed structures of Pd-oxyallyl isomers **3a** and **3b**. Hydrogen atoms are omitted for clarity. Interatomic distances are in angstroms.

and diene species proceeds in two stages. In the first stage, C−C bond formation occurs through a nucleophilic attack on Pd-oxyallyl **3** by the diene. The second stage, C−O bond formation, can take place either directly via C−O reductive elimination or though the nucleophilic attack of oxygen on a newly formed Pd-allyl moiety. The alternative pathway, a C−O bond formation followed by C−C reductive elimination, was ruled out because the C−O formation TS has a free energy barrier of 42.1 kcal/mol (see Figure S1 in the Supporting Information).

Role of the Ester Substituent on Pd-Oxyallyl. Trost et al. found that the electron-withdrawing ester substituent on Pd-oxyallyl **1** (R′ in Figure 1a) is instrumental in promoting the desired (3+2) reaction. Replacement of the ester R′ group with either phenyl or hydrogen resulted in 0% yield of the (3+2) adduct. To elucidate the role of the electron-withdrawing ester substituent, we calculated the transition states for the C−C bond formation step (migratory insertion of 1,3-cyclohexadiene into Pd−C of **3**) with different Pd-oxyallyl structures.

The calculated transition states for the C−C forming migratory insertion step are shown in Figure 2. **TS-2**, the migratory insertion TS for 1,3-cyclohexadiene with the unsubstituted Pd-oxyallyl **4**, has a very high free energy barrier of 39.5 kcal/mol. In the analogous **TS-3a**, where the ester-substituted Pd-oxyallyl **3c** reacts with 1,3-cyclohexadiene, the free energy barrier is reduced to 30.6 kcal/mol. The 8.9 kcal/mol difference in free energies of activation can be partly attributed to the electron-withdrawing effects of the ester, which lowers the energy of the Pd-oxyallyl LUMO from 0.98 eV in **5** to 0.86 eV in **3c** (Figure 2), leading to more favorable

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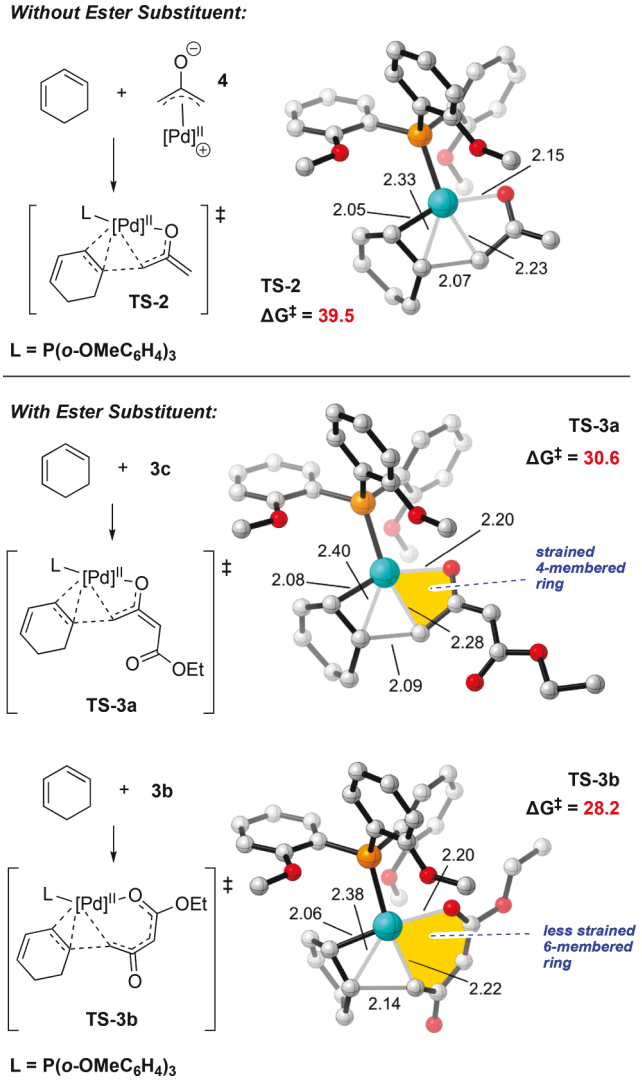

Figure 2. Computed transition state structures for the C−C forming migratory insertion of 1,3-cyclohexadiene into Pd-oxyallyl species with and without an electron-withdrawing ester. Hydrogen atoms are omitted for clarity. Interatomic distances are in angstroms, and energies are in kcal/mol. Activation free energies are calculated with respect to the isolated reactants 1,3-cyclohexadiene and **3a**.

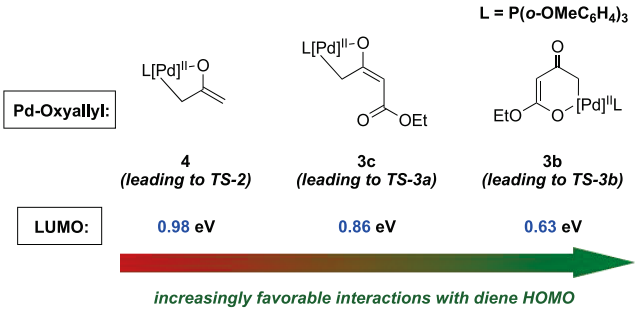

Figure 3. Calculated LUMO energies of Pd-oxyallyl species.

interactions with the diene HOMO. More importantly, the ester moiety also enables the migratory insertion to proceed through **TS-3b**, in which the Pd-oxyallyl species adopts a six-membered coordinating mode. **TS-3b** further lowers the C−C formation barrier by 2.4 kcal/mol compared to **TS-3a**. This decrease in barrier height is partly due to a less strained six-membered ring in the Pd-oxyallyl portion compared to the more strained four-membered ring in **TS-3a**. In addition, the LUMO of **3b**, the active Pd-oxyallyl species leading to **TS-3b**, is lower (0.63 eV) than the LUMO of **3c** (0.86 eV) due to its more extensive conjugation (Figure 3). The electron-withdrawing ester substituent serves two functions in promoting the migratory insertion step: (1) lowering the Pd-oxyallyl LUMO and (2) enabling a less-strained six-membered coordination mode in the TS.

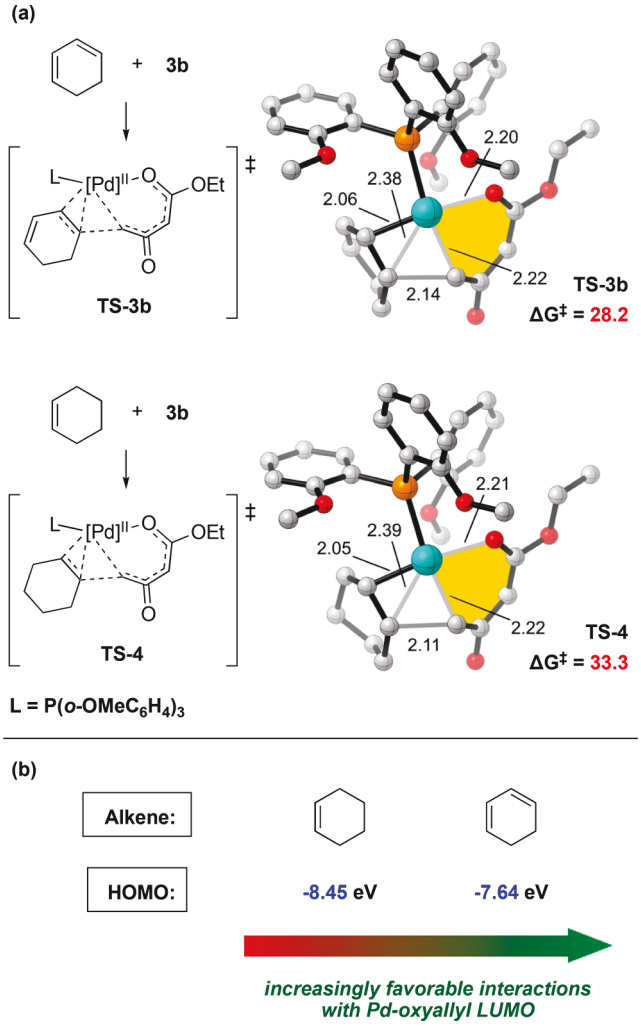

Figure 4. (a) Computed transition structures for the C−C forming migratory insertion of 1,3-cyclohexadiene and cyclohexene into Pd-oxyallyl **3b**. Hydrogen atoms are omitted for clarity. Interatomic distances are in angstroms, and energies are in kcal/mol. Activation free energies are calculated with respect to the isolated reactants (alkene and **3a**). (b) Calculated HOMO energies of alkenes.

Role of Conjugated Diene in (3+2) Reactivity. Another notable feature of the Pd-oxyallyl (3+2) cycloaddition is the necessity of having a conjugated diene as the 2π partner. Attempts to access five-membered rings through (3+2) cycloadditions of Pd-oxyallyls with unconjugated alkenes all proved unsuccessful.[18−21] To elucidate the origins of this striking difference in (3+2) reactivity between monoenes and dienes, we computationally compared the performances of cyclohexene and 1,3-cyclohexadiene in the stepwise reaction pathway.

The calculated C−C forming migratory insertion transition states for 1,3-cyclohexadiene and cyclohexene reacting with

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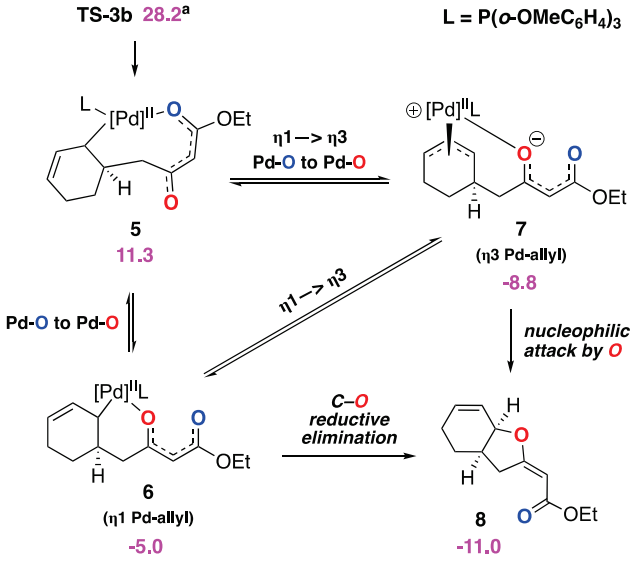
Scheme 3. Possible Mechanistic Pathways Leading to Fused Tetrahydrofuran Product



Pd-oxyallyl **3b** are shown in Figure 4. Similar to the case of 1,3-cyclohexadiene, a TS containing a less-strained six-membered ring (**TS-4**) is also found to be preferred for cyclohexene. However, the migratory insertion of cyclohexene proceeds with a barrier of 33.3 kcal/mol, 5.1 kcal/mol higher than that of 1,3-cyclohexadiene. This difference is largely due to the higher HOMO energy of the conjugated 1,3-cyclohexadiene (−7.64 eV) compared to cyclohexene (−8.45 eV), which enables stronger interactions with the Pd-oxyallyl LUMO,[22] as well as better stabilization of the partial positive charge in the TS.

In addition to lowering the C−C formation barrier, the conjugated diene promotes the C−O formation step via the formation of a highly electrophilic η^3 Pd-allyl species (Scheme 3). The migratory insertion TS, **TS-3b**, leads to intermediate **5**, which contains an eight-membered palladacycle. For the tetrahydrofuran C−O bond to form, **5** must undergo a Pd−O coordination mode change to η^1 Pd-allyl **6**. Two ways of C−O formation are possible: Pd-allyl **6** either undergoes C−O reductive elimination directly or experiences $\eta^1 \rightarrow \eta^3$ isomerization to **7**, calculated to be 3.8 kcal/mol more stable than **6**. Intramolecular nucleophilic attack on the η^3 Pd-allyl moiety by oxygen from **7** then leads to the tetrahydrofuran product **8**.

Our calculations (Figure 5) show that direct C−O reductive elimination from η^1 Pd-allyl **6** has a very high free energy barrier of 36.0 kcal/mol (**TS-5**). The magnitude of this barrier is similar to the 37.0 kcal/mol barrier predicted for the direct C−O reductive elimination in the reaction of the unconjugated cyclohexene (**TS-6**). However, the intramolecular nucleophilic attack (**TS-7a**) on η^3 Pd-allyl **7** is facile, with a barrier of only 17.9 kcal/mol.[23] Interestingly, the lowest-energy intramolecular nucleophilic attack TS (**TS-7a**) from **7** exhibits a partially inner-sphere geometry, with the nucleophilic oxygen mostly dissociated but still maintaining interaction with the Pd center (Pd···O distance 2.85 Å). A fully outer-sphere intramolecular nucleophilic attack TS (**TS-7b**), with the incoming oxygen completely dissociated from Pd and approaching the η^3 Pd-allyl moiety from the alternate π face, was calculated to be 0.9 kcal/mol higher in energy. Considering the relatively small magnitude of these barriers, both the partially inner-sphere and

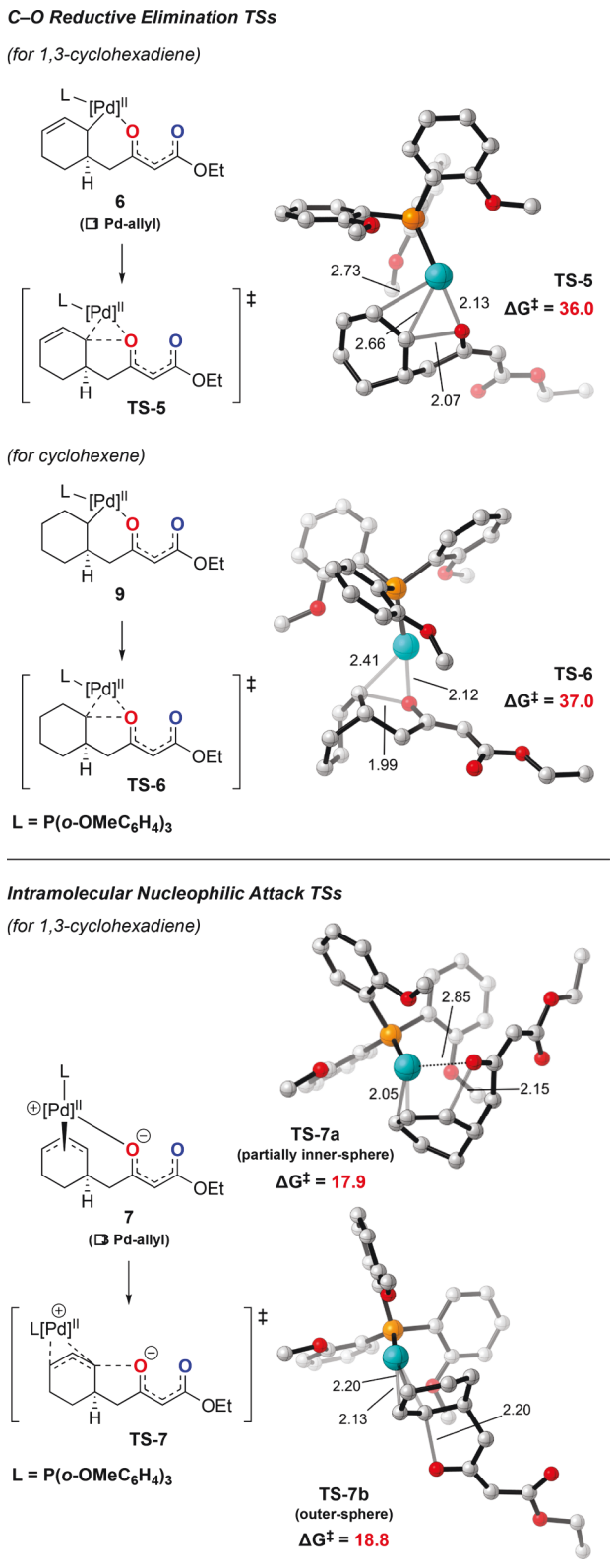


Figure 5. Computed transition state structures for the C−O forming mechanistic steps for the formal (3+2) cycloaddition of 1,3-cyclohexadiene and cyclohexene with Pd-oxyallyl **3**. Hydrogen atoms are omitted for clarity. Interatomic distances are in angstroms, and energies are in kcal/mol. Activation free energies are calculated with respect to the most stable resting states preceding the TSs (see Supporting Information).

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the outer-sphere nucleophilic attacks are likely operational in the C−O formation step, leading to the same *cis*-fused stereochemistry in the tetrahydrofuran product.

Overall, our results suggest that the observed lack of (3+2) reactivity when Pd-oxyallyls are paired with monoenes can be attributed primarily to two factors. First, monoenes are not sufficiently nucleophilic to effectively interact with the Pd-oxyallyl LUMO, resulting in high migratory insertion (C−C formation) barriers and less stabilization of the partial positive charge in the TS. Second, monoenes also have prohibitively high C−O formation barriers because they lack a conjugated π bond, which would enable the formation of a highly electrophilic η^3 Pd-allyl species that can be intramolecularly attacked with ease.

CONCLUSIONS

DFT calculations demonstrated why the combination of an electron-deficient Pd-oxyallyl and a conjugated diene permits access to the previously elusive (3+2) reactivity mode, enabling the expedient construction of fused tetrahydrofurans. Comparison with an unsubstituted system showed that the electron-withdrawing ester substituent on the Pd-oxyallyl is key to decreasing the barrier height of the C−C forming migratory insertion step. In addition to lowering the energy of the Pd-oxyallyl LUMO, the ester group also facilitates the migratory insertion by enabling a less-strained, six-membered coordination mode in the TS. The conjugated diene reaction partner promotes migratory insertion due to its higher-energy HOMO and drastically lowers the C−O formation barrier by enabling the formation of a highly electrophilic η^3 Pd-allyl species, which undergoes facile intramolecular nucleophilic attack to furnish the methylenetetrahydrofuran product.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.9b05762.

Energies and coordinates of computed structures (PDF)

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Notes

The authors declare no competing financial interest.

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REFERENCES

(1) Kobayashi, S.; Jørgensen, K. A., Eds. *Cycloaddition Reactions in Organic Synthesis*; Wiley, 2001.

(2) Mann, J. The Synthetic Utility of Oxyallyl Cations. *Tetrahedron* **1986**, *42*, 4611.

(3) For reviews, see: (a) Hoffman, H. M. R. The Cycloaddition of Allyl Cations to 1,3-Dienes: General Method for the Synthesis of Seven-Membered Carbocycles. New Synthetic Methods. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 1. (b) Noyori, R.; Hayakawa, Y. *Organic Reactions*; Paquette, L. A., Ed.; John Wiley & Sons, Inc: New York, 1983; Vol. *29*, p 163. (c) Rigby, J. H.; Pigge, F. C. *Organic Reactions*; Paquette, L. A., Ed.; John Wiley & Sons, Inc: New York, 1997; Vol. *51*, p 351. (d) Harmata, M. Asymmetric Catalytic [4 + 3] Cycloaddition Reactions. *Adv. Synth. Catal.* **2006**, *348*, 2297. (e) Harmata, M. The (4 + 3)-Cycloaddition Reaction: Heteroatom-Substituted Allylic Cations as Dienophiles. *Chem. Commun.* **2010**, *46*, 8904.

(4) (a) Li, H.; Wu, J. (3 + 2)-Cycloaddition Reactions of Oxyallyl Cations. *Synthesis* **2014**, *47*, 22. (b) DiPoto, M. C.; Hughes, R. P.; Wu, J. Dearomative Indole (3 + 2) Reactions with Azaoxyallyl Cations − New Method for the Synthesis of Pyrroloindolines. *J. Am. Chem. Soc.* **2015**, *137*, 14861. (c) DiPoto, M. C.; Wu, J. Synthesis of 2-Aminoimidazolones and Imidazolones by (3 + 2) Annulation of Azaoxyallyl Cations. *Org. Lett.* **2018**, *20*, 499.

(5) (a) Trost, B. M.; Huang, Z.; Murhade, G. M. Catalytic Palladium-Oxyallyl Cycloaddition. *Science* **2018**, *362*, 564. (b) Trost, B. M.; Huang, Z. Catalytic (3 + 2) Palladium-Aminoallyl Cycloaddition with Conjugated Dienes. *Angew. Chem., Int. Ed.* **2019**, *58*, 6396.

(6) Noyori, R.; Hayakawa, Y.; Funakura, M.; Takaya, H.; Murai, S.; Kobayashi, R.; Tsutsumi, S. Mechanistic Aspects of the Reaction of α,α'-Dibromo Ketones and Iron Carbonyl. Reductive Rearrangements of Dibromo Ketones. *J. Am. Chem. Soc.* **1972**, *94*, 7202.

(7) Hayakawa, Y.; Yokoyama, K.; Noyori, R. Iron Carbonyl Promoted Reaction of α,α'-Dibromo Ketones and Aromatic Olefins Leading to 3-Arylcyclopentanones. The [3 + 2] Cycloaddition Involving an Allylic Cation. *J. Am. Chem. Soc.* **1978**, *100*, 1791.

(8) Noyori, R. Organic Syntheses via the Polybromo Ketone-Iron Carbonyl Reaction. *Acc. Chem. Res.* **1979**, *12*, 61.

(9) Masuya, K.; Domon, K.; Tanino, K.; Kuwajima, I. Highly Regio- and Stereoselective [3 + 2] Cyclopentanone Annulation Using a 3-(Alkylthio)-2-siloxyallyl Cationic Species. *J. Am. Chem. Soc.* **1998**, *120*, 1724.

(10) For select recent computational studies, see: (a) He, C. Q.; Yu, P.; Lam, Y.-h.; Houk, K. N. Origins of Stereoselectivity in Chiral Aminoalcohol Catalysis of Oxyallyl Cation-Indole Reactions. *Org. Lett.* **2017**, *19*, 5685. (b) Krenske, E. H.; He, S.; Huang, J.; Du, Y.; Houk, K. N.; Hsung, R. P. Intramolecular Oxyallyl-Carbonyl (3 + 2) Cycloadditions. *J. Am. Chem. Soc.* **2013**, *135*, 5242. (c) Lohse, A. G.; Krenske, E. H.; Antoline, J. E.; Houk, K. N.; Hsung, R. P. Regioselectivities of (4 + 3) Cycloadditions between Furans and Oxazolidinone-Substituted Oxyallyls. *Org. Lett.* **2010**, *12*, 5506.

(11) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. *Gaussian 09*; Gaussian Inc.: Wallingford, CT, 2009.

(12) Chai, J. D.; Head-Gordon, M. Long-Range Corrected Hybrid Density Functionals with Damped Atom-Atom Dispersion Corrections. *Phys. Chem. Chem. Phys.* **2008**, *10*, 6615.

DOI: 10.1021/jacs.9b05762
J. Am. Chem. Soc. 2019, 141, 12382−12387

(13) Minekov, Y.; Singstad, Å.; Occhipinti, G.; Jensen, V. R. The Accuracy of DFT-Optimized Geometries of Functional Transition Metal Compounds: a Validation Study of Catalysts for Olefin Metathesis and Other Reactions in the Homogeneous Phase. *Dalton Trans.* **2012**, *41*, 5526.
(14) Hay, P. J.; Wadt, W. R. Ab initio Effective Core Potentials for Molecular Calculations. Potentials for K to Au Including the Outermost Core Orbitals. *J. Chem. Phys.* **1985**, *82*, 299.
(15) Marenich, A. V.; Cramer, C. J.; Truhlar, D. G. Universal Solvation Model Based on Solute Electron Density and on a Continuum Model of the Solvent Defined by the Bulk Dielectric Constant and Atomic Surface Tensions. *J. Phys. Chem. B* **2009**, *113*, 6378.
(16) (a) Haüssermann, U.; Dolg, M.; Stoll, H.; Preuss, H.; Schwerdtfeger, P.; Pitzer, R. M. Accuracy of Energy-Adjusted Quasirelativistic Ab initio Pseudopotentials. *Mol. Phys.* **1993**, *78*, 1211. (b) Küchle, W.; Dolg, M.; Stoll, H.; Preuss, H. Energy-Adjusted Pseudopotentials for the Actinides. Parameter Sets and Test Calculations for Thorium and Thorium Monoxide. *J. Chem. Phys.* **1994**, *100*, 7535.
(17) Legault, C. Y. *CYLview*, 1.0b; Université de Sherbrooke, 2009; http://www.cylview.org.
(18) Trost, B. M.; Schneider, S. On an (Oxatrimethylenemethane)-palladium(0) Complex. An Unusual Palladium(0)-Catalyzed Cyclopropanation. *J. Am. Chem. Soc.* **1989**, *111*, 4430.
(19) Trost, B. M.; Urabe, H. Regioselective Cyclopropanation via Unsymmetrical Oxatrimethylenemethane Palladium Intermediates. *Tetrahedron Lett.* **1990**, *31*, 615.
(20) Ohe, K.; Matsuda, H.; Ishihara, T.; Ogoshi, S.; Chatani, N.; Murai, S. Palladium-Catalyzed Reaction of 5-Methylene-1,3-dioxolan-2-ones. A New Access to and Reactivity of Oxatrimethylenemethane-Palladium. *J. Org. Chem.* **1993**, *58*, 1173.
(21) Ikeda, I.; Ohsuka, A.; Tani, K.; Hirao, T.; Kurosawa, H. One-Step Synthesis of Oxodimethylenemethane−Transition Metal Complexes and Palladium-Catalyzed Cycloaddition Reaction. *J. Org. Chem.* **1996**, *61*, 4971.
(22) Another more nucleophilic alkene, methyl vinyl ether, was calculated to have a HOMO energy of 8.06 eV, intermediate between that of cyclohexane and 1,3-cyclohexadiene. The migratory insertion TS of methyl vinyl ether reacting with **3b** was calculated to have a 30.9 kcal/mol barrier, also intermediate between that of cyclohexane and 1,3-cyclohexadiene. This result further illustrates the importance of alkene nucleophilicity on the migratory insertion step.
(23) A similar intramolecular nucleophilic attack TS that forms the (4+3) adduct was calculated to proceed with a barrier of 23.9 kcal/mol. See the Supporting Information for details.

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