J|A|C|S
ARTICLES

Pd(0) Mechanism of Palladium-Catalyzed Cyclopropanation of Alkenes by CH_2N_2: A DFT Study

Bernd F. Straub*

Contribution from the Department Chemie der Ludwig-Maximilians-Universität München,
Butenandtstrasse 5-13 (Haus F), D-81377 München, Germany

Received July 18, 2002

Abstract: Pathways for the reaction of ethene with diazomethane to cyclopropane and dinitrogen catalyzed by Pd(0) complexes have been investigated at the B3LYP level of theory. The computed Gibbs free activation energy of 71.7 kJ mol^{-1} for the most favorable catalytic cycle is by far lower than previously reported computed barriers for Pd(II)-catalyzed pathways of this reaction and is now in the range of experimental expectations. $\mathrm{Pd}(\eta^2\text{-}\mathrm{C_2H_4})_2$ is predicted to be the resting state of the catalyst and the product of a $\mathrm{Pd(OAc)_2}$ precatalyst reduction. The Pd(0) ethene complex is in equilibrium with $\mathrm{Pd}(\eta^2\text{-}\mathrm{C_2H_4})(\kappa C\text{-}\mathrm{CH_2N_2})$, from which N_2 is eliminated in the rate-determining step. The resulting carbene complex $(\eta^2\text{-}\mathrm{C_2H_4})\mathrm{Pd{=}CH_2}$ reacts without intrinsic barrier with CH_2N_2 to $\mathrm{Pd}(\eta^2\text{-}\mathrm{C_2H_4})_2$ and N_2 and with ethene to the palladacyclobutane $(\eta^2\text{-}\mathrm{C_2H_4})\mathrm{Pd^{II}}[\kappa C^1,\kappa C^3\text{-}(\mathrm{CH_2})_3]$. The N_2 elimination from $\mathrm{Pd}(\eta^2\text{-}\mathrm{C_2H_4})_2(\kappa C\text{-}\mathrm{CH_2N_2})$ to $(\eta^2\text{-}\mathrm{C_2H_4})_2\mathrm{Pd{=}CH_2}$ leads to an overall Gibbs free activation energy of 84.2 kJ mol^{-1}. The intramolecular rearrangement of $(\eta^2\text{-}\mathrm{C_2H_4})_2\text{-}\mathrm{Pd{=}CH_2}$ to the palladacyclobutane $(\eta^2\text{-}\mathrm{C_2H_4})\mathrm{Pd^{II}}[\kappa C^1,\kappa C^3\text{-}(\mathrm{CH_2})_3]$ and the subsequent reductive elimination of cyclopropane are facile. At the BP86 level of theory, Pd(0) preferentially coordinates three ligands. $\mathrm{Pd}(\eta^2\text{-}\mathrm{C_2H_4})_3$ is predicted to be the resting state, and the N_2 elimination from the model complex $\mathrm{Pd}(\eta^2\text{-}\mathrm{C_2H_4})_2(\kappa C\text{-}\mathrm{CH_2N_2})$ is the rate-determining transition state leading to an overall Gibbs free activation energy of 69.4 kJ mol^{-1}.

Introduction

The addition of a methylene unit across terminal, strained cyclic, or acyl substituted carbon−carbon double bonds by CH_2N_2/$\mathrm{Pd(OAc)_2}$ is of major importance for the synthesis of cyclopropane derivatives. The reaction typically proceeds at 0−5 °C with an excess of diazomethane and in the presence of about 1 mol % $\mathrm{Pd(OAc)_2}$ precatalyst.[1] Vigorous gas evolution and completion of the reaction within 10 min are in accord with the generation of highly reactive intermediates.[1c] It is thus no surprise that the identity of the active catalyst has remained elusive. However, experimental data based on alkene competition studies strongly support the occurrence of catalytically relevant palladium alkene intermediates.[2] Tomilov et al. explicitly proposed the reduction of Pd(II) by diazomethane and the π-complexation of Pd(0) by alkene substrates.[2b] In contrast to such Pd(0) mechanisms, only Pd(II) catalysts without alkene coordination have been investigated by DFT studies so far.[3] Therein, the predicted Gibbs free activation energies for the proposed catalytic cycles of 99.2 kJ mol^{-1} [Pd(II) carbene intermediate][3a] and at least 144.0 kJ mol^{-1} [phosphane Pd(II) carbenoids][3c] are too high to account for the observed reaction rate. We were interested in whether a computed Pd(0) cycle could better reproduce the experimental selectivities and reactivities.

The reduction of Pd(II) complexes by CH_2N_2 is well-documented. The McCrindle group observed precipitation of palladium metal from solutions of several phosphane or amine $\mathrm{PdCl_2}$ complexes after addition of an excess of diazomethane.[4] In the $\mathrm{Pd(OAc)_2}$-catalyzed cyclopropanation of enoyl sultams, the Hacksell group experienced that "larger concentrations of catalyst should be avoided since they often result in precipitation of Pd(0) and subsequent termination of the reaction".[5] However, the occurrence of Pd(0) species in the reaction mixture is no proof of their catalytic necessity. Nevertheless, a successful

---

* E-mail: Bernd.F.Straub@cup.uni-muenchen.de.

(1) (a) Paulissen, R.; Hubert, A. J.; Teyssié, P. *Tetrahedron Lett.* **1972**, *15*, 1465. (b) Kottwitz, J.; Vorbrüggen, H. *Synthesis* **1975**, 636. (c) Suda, M. *Synthesis* **1981**, 714. (d) Mende, U.; Radüchel, B.; Skuballa, W.; Vorbrüggen, H. *Tetrahedron Lett.* **1975**, *9*, 629. (e) Dzhemilev, U. M.; Dokichev, V. A.; Sultanov, S. Z.; Khusnutdinov, R. I.; Tomilov, Y. V.; Nefedov, O. M.; Tolstikov, G. A. *Izv. Akad. Nauk, Ser. Khim.* **1989**, *8*, 1861. (f) Doyle, M. P. *Chem. Rev.* **1986**, *86*, 919. (g) Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.* **1996**, *96*, 49. (h) Noels, A. F.; Demonceau, A. *Appl. Homogeneous Catal. Organomet. Compd.* **1996**, *2*, 733. (i) Tomilov, Y. V.; Dokitchev, V. A.; Dzhemilev, U. M.; Nefedov, O. M. *Usp. Khim.* **1993**, *62*, 847.

(2) (a) Anciaux, A. J.; Hubert, A. J.; Noels, A. F.; Petiniot, N.; Teyssié, P. *J. Org. Chem.* **1980**, *45*, 695. (b) Tomilov, Y. V.; Bordakov, V. G.; Dolgii, I. E.; Nefedov, O. M. *Izv. Akad. Nauk, Ser. Khim.* **1984**, *3*, 582. (c) Dzhemilev, U. M.; Dokichev, V. A.; Sultanov, S. Z.; Khursan, S. L.; Nefedov, O. M.; Tomilov, Y. V.; Kostitsyn, A. B. *Izv. Akad. Nauk, Ser. Khim.* **1992**, *10*, 2353.

(3) (a) Rodríguez-García, C.; Oliva, A.; Ortuño, R. M.; Branchadell, V. *J. Am. Chem. Soc.* **2001**, *123*, 6157. (b) Rodríguez-García, C.; Gonzáles-Blanco, O.; Oliva, A.; Ortuño, R. M.; Branchadell, V. *Eur. J. Inorg. Chem.* **2000**, *3*, 1073. (c) Bernardi, F.; Bottoni, A.; Miscione, G. P. *Organometallics* **2001**, *20*, 2751. (d) Bernardi, F.; Bottoni, A.; Miscione, G. P. *Organometallics* **2000**, *19*, 5529.

(4) McCrindle, R.; Arsenault, G. J.; Farwaha, R.; McAlees, A. J.; Sneddon, D. W. *J. Chem. Soc., Dalton Trans.* **1989**, 761.

(5) Vallgårda, J.; Appelberg, U.; Csöregh, I.; Hacksell, U. *J. Chem. Soc., Perkin Trans. 1* **1994**, 461. For $\mathrm{Pd(NCPh)_2Cl_2}$ precatalyst reduction, see Tomilov, Y. V.; Kostitsyn, A. B.; Shulishov, E. V.; Nefedov, O. M. *Synthesis* **1990**, *3*, 246.

10.1021/ja027762+ CCC: $22.00 © 2002 American Chemical Society

quantum-chemical computation of a Pd(0) catalytic cycle with a low activation barrier would strongly support the importance of Pd(0) complexes in the $Pd(OAc)_2$-catalyzed alkene cyclopropanation reaction. A more detailed knowledge about the catalytically active palladium species would be of high relevance for the design of chiral spectator ligands to achieve enantioselective cyclopropanation of α,β-unsaturated esters and ketones.[6]

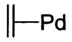
Computational Details

The B3LYP/LACV3P**++//B3LYP/LACV3P* level of theory[7] with fine grid density as implemented in the Jaguar 4.1 quantum chemistry program package[8] has been utilized throughout this study. For O, N, C, and H, the 6-311G* basis set of Pople and co-workers was used for geometry optimizations.[9] For palladium, a Hay−Wadt small effective core potential (ECP) replaces the 28 innermost core electrons.[10] For nickel, the ECP replaces the 10 innermost electrons.[10] The basis set on both palladium and nickel has triple ζ quality (contraction scheme for palladium {3211/2111/211} and for Ni {3211/2111/311}). Full geometry optimizations and numerical vibrational frequency calculations have been performed for all model compounds. Stationary points are characterized by exactly zero imaginary vibrations; transition structures are characterized by exactly one imaginary vibration. Visual inspection of imaginary vibrations was performed with the Molden program package.[11] Single-point energies were computed with the LACV3P**++ basis set, which is characterized by the 6-311G**++ basis set for main group elements[9,12] and by an additional diffuse d function for the transition metals (coefficient 0.052 for palladium and 0.065 for nickel). A SCF energy convergence threshold of 1×10^{-5} au was applied for single-point energy calculations. The Gibbs free energies G refer to 273.15 K and 1 atm and are based on unscaled molecular vibrations and ideal gas-phase conditions. Scans of the energy hypersurface were performed to ensure that no total electronic energy barrier is present in the reaction of ethene and diazomethane with model complex **23** and of diazomethane with model complex **26** (see Supporting Information). Additional calculations at the BP86/LACV3P**++//BP86/LACV3P* level were performed for ethene, diazomethane, and the palladium model complexes **2**, **3**, **22**, and **25** to obtain information about the functional dependency of the relative stabilities of the most important palladium species.[13]

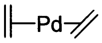
Results and Discussion

In this study, we attempt to find a viable pathway for the ethene cyclopropanation by diazomethane catalyzed by mononuclear Pd(0) complexes. Since the reduction of Pd(II) by CH_2N_2 is obvious from the literature[2b,4,5] and preliminary model calculations support a substantial driving force toward Pd(0) complexes in the reaction mixture,[14] we did not attempt to model a detailed Pd(II) reduction mechanism. Our main goal is the identification of the catalyst resting state, of the rate-determining transition state, and of all catalytic intermediates.

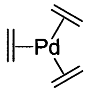
Catalyst Resting State. First, the comparison of the relative Gibbs free energies of Pd(0) ethene and diazomethane complexes and respective free ligands in isodesmic reactions will identify the most stable species—the catalyst resting state. From all palladium model complexes in this study, only the ethene complexes **1**−**3** have been observed experimentally.[15] At the B3LYP level of theory, diethene complex **2** has a lower relative Gibbs free energy than monoethene complex **1** and triethene complex **3**.[16] Thus, all Gibbs free energies will be normalized to that of complex **2**. However, the relative stability of trialkene Pd(0) species such as **3** will increase at lower temperatures or with strained cyclic or electron-withdrawing alkene ligands. Furthermore, the computed energy difference between the dialkene complex **2** and the trialkene complex **3** can be overcome by the functional dependency of the ligand coordination strength to palladium (vide infra).



1 G_{rel} = 61.0 kJ mol^{-1}

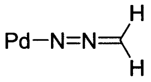


2 G_{rel} = 0.0 kJ mol^{-1}

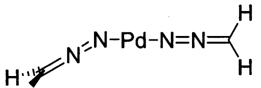


3 G_{rel} = 20.8 kJ mol^{-1}

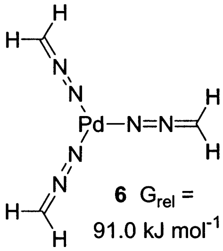
Diazomethane preferentially ligates palladium either by the terminal nitrogen (κN) or by the carbon atom (κC). The relative Gibbs free energies of the κN complexes **4**−**9** are too high to function as resting states of the catalytic cycle. Only negligible concentrations of these complexes should be present in solution.



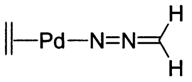
4 G_{rel} = 106.7 kJ mol^{-1}



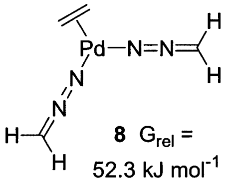
5 G_{rel} = 50.5 kJ mol^{-1}



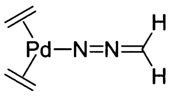
6 G_{rel} = 91.0 kJ mol^{-1}



7 G_{rel} = 21.0 kJ mol^{-1}



8 G_{rel} = 52.3 kJ mol^{-1}



9 G_{rel} = 29.6 kJ mol^{-1}

---

(6) Denmark, S. E.; Stavenger, R. A.; Faucher, A.-M.; Edwards, J. P. *J. Org. Chem.* **1997**, *62*, 3375.

(7) (a) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648. (b) Volko, S. H.; Wilk, L.; Nusair, M. *Can. J. Phys.* **1980**, *58*, 1200. (c) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785.

(8) Jaguar 4.1, release 59; Schrödinger, Inc.: Portland, OR, 2001.

(9) Krishnan, R.; Binkley, J. S.; Seeger, R.; Pople, J. A. *J. Chem. Phys.* **1980**, *72*, 650.

(10) Hay, P. J.; Wadt, W. R. *J. Chem. Phys.* **1985**, *82*, 299.

(11) Schaftenaar, G.; Noordik, J. H. *J. Comput.-Aided Mol. Des.* **2000**, *14*, 123.

(12) (a) Frisch, M. J.; Pople, J. A.; Binkley, J. S. *J. Chem. Phys.* **1984**, *80*, 3265. (b) Clark, T.; Chandrasekhar, J.; Spitznagel, G. W.; Schleyer, P. v. R. *J. Comput. Chem.* **1983**, *4*, 294.

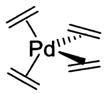
(13) (a) Becke, A. D. *Phys. Rev. A* **1988**, *38*, 3098. (b) Perdew, J. P.; Zunger, A. *Phys. Rev. B* **1981**, *23*, 5048. (c) Perdew, J. P. *Phys. Rev. B* **1986**, *33*, 8822.

(14) The reductive elimination of 1,2-diacetoxyethane from a proposed catalytic resting state complex *cis*-$Pd^{II}[\kappa C\text{-}CH_2O(\kappa O\text{-}MeC{=}O)]_2$ (ref 3a) in the presence of ethene to $Pd(\eta^2\text{-}C_2H_4)_2$ is computed to be exergonic by ΔG (273.15 K, 1 atm) = -82.6 kJ mol^{-1} in the gas phase.

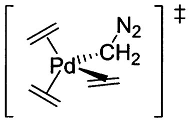
(15) (a) Green, M.; Howard, J. A. K.; Laguna, A.; Murray, M.; Spencer, J. L.; Stone, F. G. A. *Chem. Commun.* **1975**, 451. (b) Csaszar, P.; Goggin, P. L.; Mink, J.; Spencer, J. L. *J. Organomet. Chem.* **1989**, *379*, 337.

(16) For comparison, the dissociation of one ethene ligand from $Ni(\eta^2\text{-}C_2H_4)_3$ is computed to be endergonic by ΔG(273.15 K, 1 atm) = 5.6 kJ mol^{-1} (dissociation of two ethene ligands from $Ni(\eta^2\text{-}C_2H_4)_3$: ΔG (273.15 K, 1 atm) = 107.4 kJ mol^{-1}). The higher computed stability of the triethene nickel adduct as compared to its palladium analogue correlates with the higher experimental thermal stability of the nickel complex: Fischer, K.; Jonas, K.; Wilke, G. *Angew. Chem.* **1973**, *85*, 620; *Angew. Chem., Int. Ed. Engl.* **1973**, *12*, 565.

For Pd(0), coordination numbers of 2 and 3 are predicted to be favored over coordination numbers of 1 or 4. The palladium tetraethene model complex **10** is thermodynamically strongly disfavored. Indeed, a tetraalkene Pd(0) complex has only been reported with a chelating 5-vinyl-2-cyclohexenone derivative.[17]



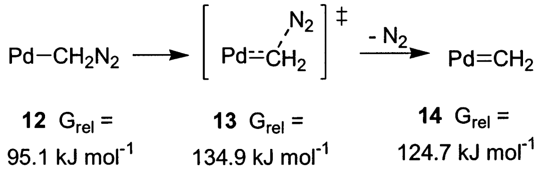
10 G_{rel} = 99.0 kJ mol^{-1}



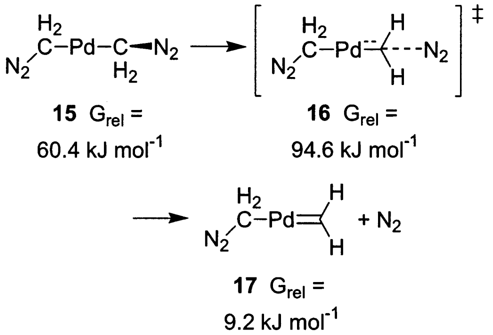
11 G_{rel} = 89.1 kJ mol^{-1}

Complex **11** with one *κC*-diazomethane ligand is a ligand exchange transition state.[18] Further *κC*-diazomethane complexes are depicted in Schemes 1−7. Although these complexes were all found to possess higher relative Gibbs free energies, the *κC*-diazomethane coordination mode is mandatory for a facile N_2 elimination and carbene complex formation.

Scheme 1



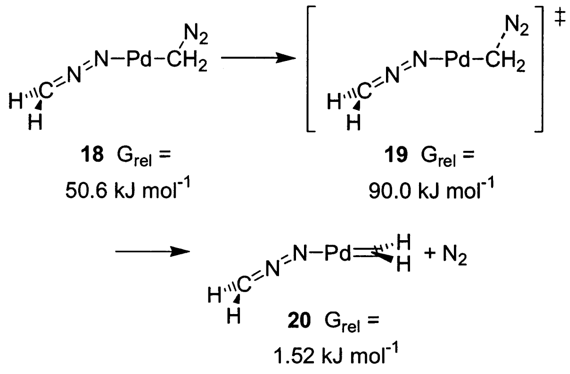
Scheme 2



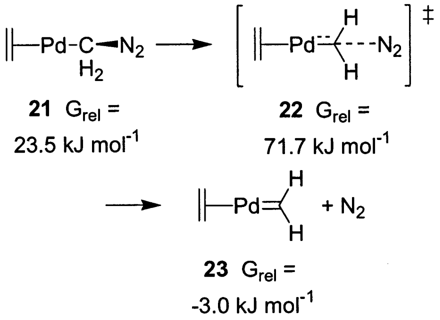
N_2 **Elimination.** Seven pathways were computed to identify the lowest-energy N_2 elimination transition state (Schemes 1−7). In Scheme 1, the N_2 loss of the simplest *κC*-diazoalkane complex **12** proceeds via transition structure **13** to the palladium carbene fragment **14**. A Gibbs free activation energy of 134.9 kJ mol^{-1} is obviously too high as compared to the expectations derived from the experimental cyclopropanation conditions.[1] Bisdiazomethane complex **15** eliminates N_2 via **16** with a Gibbs free activation energy of only 34.2 kJ mol^{-1} (Scheme 2). However, the overall barrier still amounts to 94.6 kJ mol^{-1} because of the high relative Gibbs free energy of **15** of 60.4 kJ mol^{-1}.

The N_2 elimination from the mixed *κC*,*κN*-bisdiazomethane complex (**18**) leads to a similar overall barrier of 90.0 kJ mol^{-1} (Scheme 3). The most favorable N_2 elimination pathway at the B3LYP level of theory is depicted in Scheme 4. Monoethene diazomethane complex **21** has a relative Gibbs free energy of 23.5 kJ mol^{-1} and loses N_2 via transition state **22** with an overall Gibbs free activation energy of 71.7 kJ mol^{-1}. Despite the N_2 formation, carbene complex **23** retains a surprisingly high relative Gibbs free energy, reflecting the weakness of the palladium−carbon double bond.

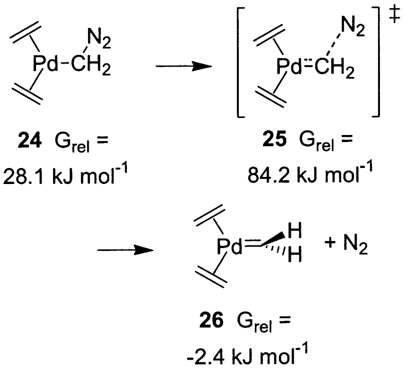
Scheme 3



Scheme 4



Scheme 5



The N_2 loss from the analogous diethene diazoalkane complex **24** via transition state **25** is computed to be 12.5 kJ mol^{-1} higher in Gibbs free activation energy than the monoethene pathway at the B3LYP level of theory (Scheme 5). This additional barrier is too small to identify monoethene transition state **22** with absolute certainty as the lowest-energy N_2 elimination transition state (see functional dependency vide infra). Additionally, electron-withdrawing alkene substituents will stabilize higher palladium coordination numbers[15a,17] and thus favor transition states analogous to **25**.

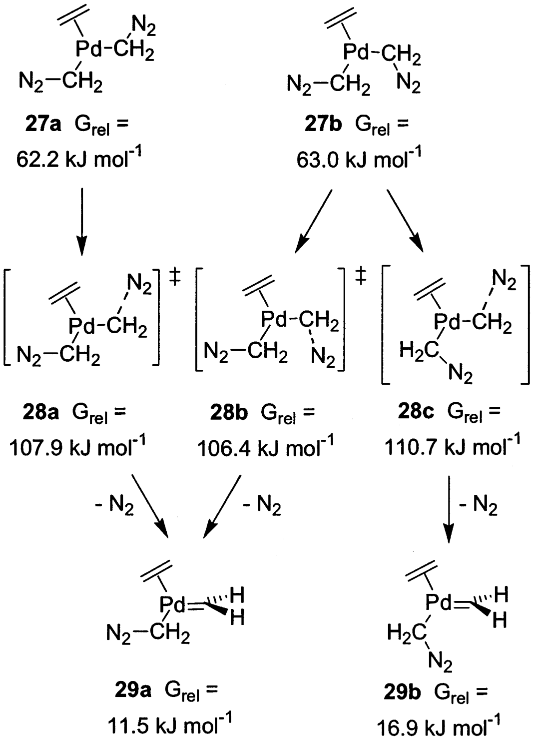
Pd(0) and Ni(0) dialkene complexes similar to **26** with stabilizing amine substituents at the carbene fragment have indeed been structurally characterized.[19] The N_2 elimination from other *κC*-diazomethane complexes is not competitive. The overall barriers of 106.4−110.7 kJ mol^{-1} for the formation of ethene *κC*-diazomethane carbene complexes **29a** and

---

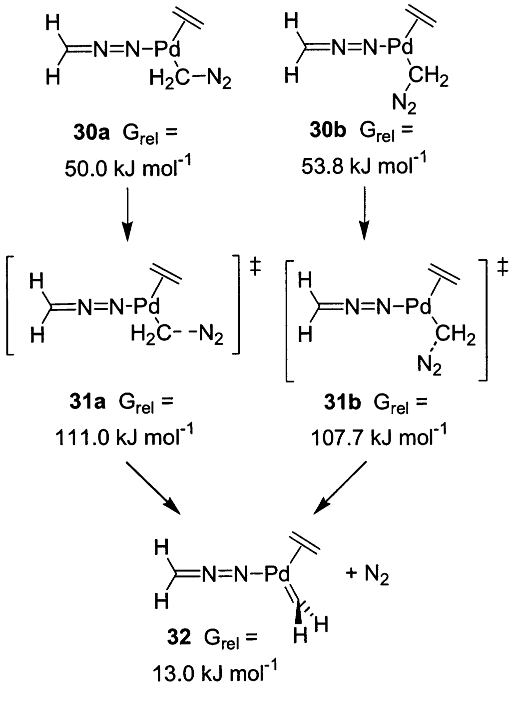
[17] Porth, S.; Bats, J. W.; Trauner, D.; Giester, G.; Mulzer, J. *Angew. Chem.* **1999**, *111*, 2159; *Angew. Chem., Int. Ed. Engl.* **1999**, *38*, 2015.

[18] Dissociative pathways characterized by palladium coordination numbers of 2 and 3 are favored for ethene diazomethane ligand exchange reactions both enthalpically and entropically.

Scheme 6

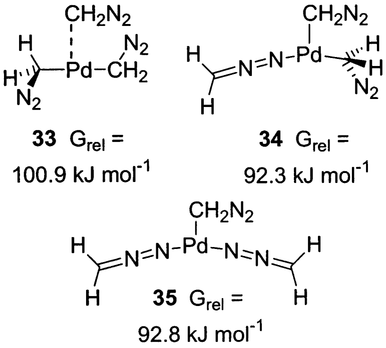


Scheme 7

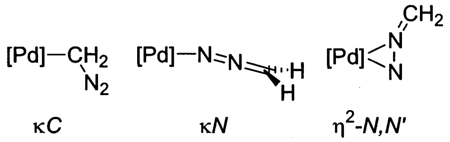


29b are too high to be relevant (Scheme 6). The same is true for the ethene *κN*-diazomethane carbene complex **30** (Scheme 7).

Other *κC*-diazomethane complexes with a palladium coordination number of 3 are imaginable. However, complexes such as **33**−**35** are predicted to possess relative Gibbs free energies (92.3−100.9 kJ mol^{-1}), which are already higher than the N_2 elimination transition states **22** or **25** (71.7 and 84.2 kJ mol^{-1}). The N_2 elimination transition states derived from **33**−**35** will thus be irrelevant.



Besides *κC*- and the *κN*-diazomethane ligation, the η^2-*N,N′*-diazomethane coordination mode has also been investigated. This coordination mode has been observed with several d^{10} transition metal fragments and electrophilic diazoalkanes.[20] Although equilibrium structures with the η^2-*N,N′*-diazomethane coordination mode exist, their relative Gibbs free energies are 14−42 kJ mol^{-1} higher than those of their *κN*-isomers (see Supporting Information). Since *κN,κC*-bisdiazomethane complexes possess high N_2 elimination barriers, the even more disfavored *κC*,η^2-*N,N′*-bisdiazomethane species should also be irrelevant for cyclopropanation catalysis.



Carbene Complex Reactivity. The alkene palladium carbene complexes **23** and **26** are predicted to be the most probable active species for ethene cyclopropanation. Therefore, their reactivity and selectivity will determine the further course of the reaction. The intramolecular rearrangement of ethene carbene complex **23** via **36** to the palladacyclobutane **37** is characterized by a barrier of 77.0 kJ mol^{-1} (Scheme 8). The coordination process of ethene to the palladium center in carbene complex **23** via the ethene adduct **38** and transition state **39** features a Gibbs free activation energy of 42.3 kJ mol^{-1}. Both pathways are irrelevant, however, since complex **23** can react with ethene without any total electronic activation energy via a [2+2] cycloaddition to the palladacyclobutane derivative **40**. For this ethene addition reaction, a Gibbs free activation energy will certainly exist because of entropic contributions. Since two molecules collapse to one, the activation entropy $\Delta S^{\ddagger}$ should be highly negative. However, it is not trivial to reliably quantify Gibbs free activation energies for such reactions by quantum-chemical methods.[21]

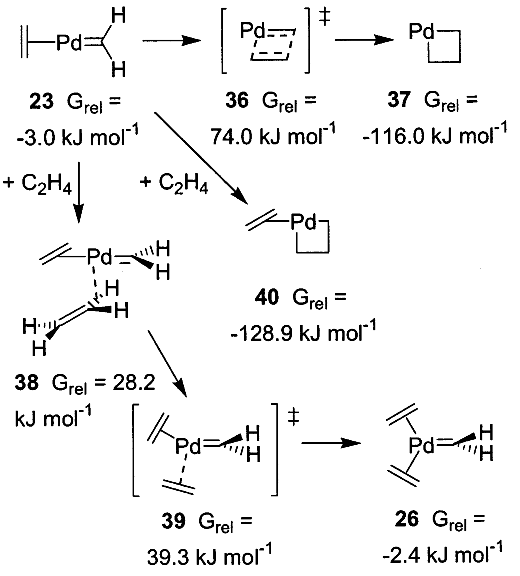
---

(19) (a) Gabor, B.; Krueger, C.; Marczinke, B.; Mynott, R.; Wilke, G. *Angew. Chem.* **1991**, *103*, 1711; *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1666. (b) Jackstell, R.; Andreu, M. G.; Frisch, A.; Selvakumar, K.; Zapf, A.; Klein, H.; Spannenberg, A.; Röttger, D.; Briel, O.; Karch, R.; Beller, M. *Angew. Chem., Int. Ed.* **2002**, *114*, 1028; *Angew. Chem., Int. Ed.* **2002**, *41*, 986.

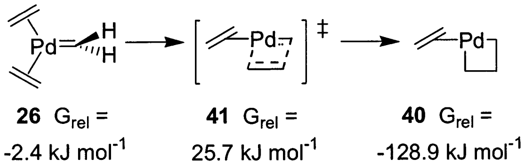
(20) (a) Otsuka, S.; Nakamura, A.; Koyama, T.; Tatsuno, Y. *J. Chem. Soc., Chem. Commun.* **1972**, 1105. (b) Otsuka, S.; Nakamura, A.; Koyama, T.; Tatsuno, Y. *Liebigs Ann. Chem.* **1975**, 626. (c) Nakamura, A.; Yoshida, T.; Cowie, M.; Otsuka, S.; Ibers, J. A. *J. Am. Chem. Soc.* **1977**, *99*, 2108. (d) Schramm, K. D.; Ibers, J. A. *Inorg. Chem.* **1980**, *19*, 2441. (e) Straub, B. F.; Hofmann, P. *Inorg. Chem. Commun.* **1998**, *1*, 350.

(21) (a) Houk, K. N.; Rondan, N. G.; Mareda, J. *J. Am. Chem. Soc.* **1984**, *106*, 4291. (b) Houk, K. N.; Rondan, N. G. *J. Am. Chem. Soc.* **1984**, *106*, 4293.

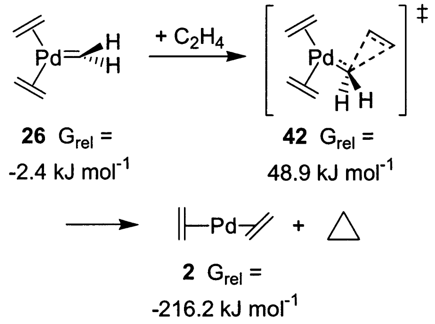
Scheme 8



Scheme 9



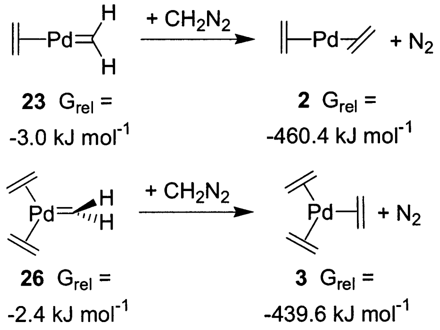
Scheme 10



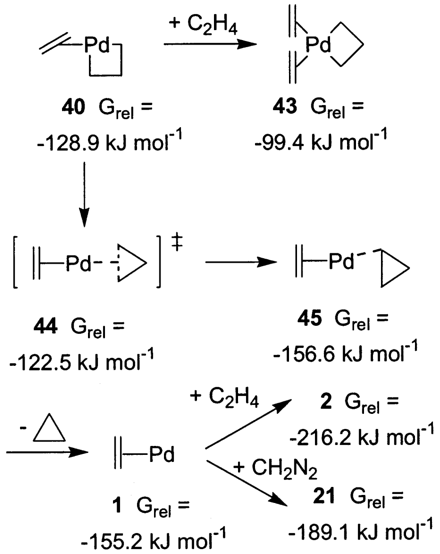
The second ethene ligand alters the reactivity of carbene complex **26** significantly as compared to monoethene complex **23**. A cis rearrangement via transition state **41** to the palladacyclobutane derivative **40** is a viable pathway associated with a Gibbs free activation energy of only 28.1 kJ mol^{-1} (Scheme 9). The role of pallada(II)cyclobutane derivatives in Pd(OAc)$_2$-catalyzed cyclopropanation is supported by the isolation and observed reactivity of this class of complexes. With a bidentate nitrogen ligand, a pallada(II)cyclobutane derivative has been structurally characterized.[22] Facile reductive elimination of cyclopropane derivatives is observed for such palladacycles.[22,23]

A potential alternative pathway is characterized by ethene attack on diethene carbene model complex **26** (Scheme 10). Cyclopropane and complex **2** are formed via transition state **42**. This step has a strong similarity to the alkene attack on d^{10}-ML$_3$-type copper(I) carbenes in copper-catalyzed cyclopropanation.[24] However, the intramolecular cis rearrangement via transition state **41** (Scheme 9) is clearly superior to the entropically disfavored intermolecular ethene attack on **26** (Scheme 10). Both carbene model complexes **23** and **26** react with diazomethane without any total electronic activation energy (Scheme 11). Such short-circuit reactions are presumably the origin of the necessity of an excess of diazomethane to achieve completion of the cyclopropanation reaction.

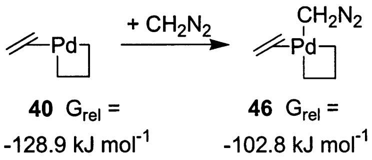
Scheme 11



Scheme 12



Scheme 13



Reductive Elimination. Palladacycle **40** is the only Pd(II) model species in the catalytic cycle. Although d^8-ML$_3$ complex **40** seems to be coordinatively unsaturated, ethene coordination and formation of diethene complex **43** are endergonic (Scheme 12). The reductive elimination of cyclopropane from Pd(II) complex **40** via transition state **44**, however, is extremely facile with a Gibbs free activation barrier of only 6.4 kJ mol^{-1}. After ligand exchange of the resulting cyclopropane adduct **45**, the catalyst resting state **2** is regenerated.

We also computed the *κC*-diazomethane complex **46** (Scheme 13). As for its ethene analogue, the relative Gibbs free energy of the *κC*-diazomethane complex **46** is higher than that of the

---

[22] Hoffmann, H. M. R.; Otte, A. R.; Wilde, A.; Menzer, S.; Williams, D. J. *Angew. Chem.* **1995**, *107*, 73; *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 100.

[23] Grigg, R.; Kordes, M. *Eur. J. Org. Chem.* **2001**, *4*, 707.

[24] (a) Straub, B. F.; Hofmann, P. *Angew. Chem.* **2001**, *113*, 1328; *Angew. Chem., Int. Ed.* **2001**, *40*, 1288. (b) Fraile, J. M.; García, J. I.; Martínez-Merino, V.; Mayoral, J. A.; Salvatella, L. *J. Am. Chem. Soc.* **2001**, *123*, 7616.

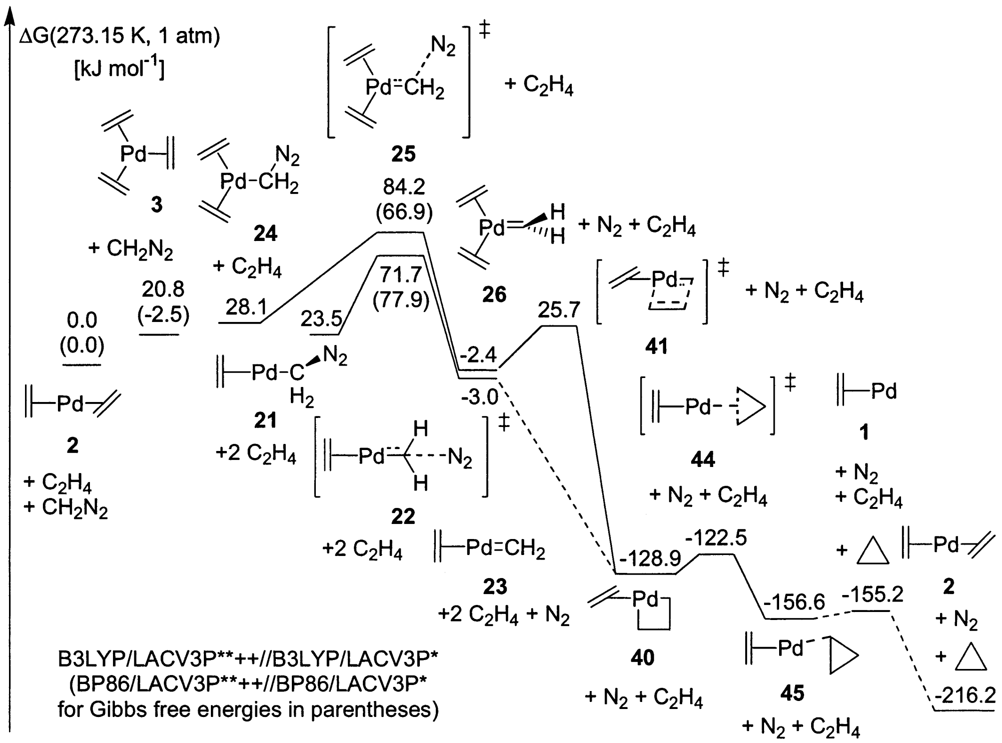
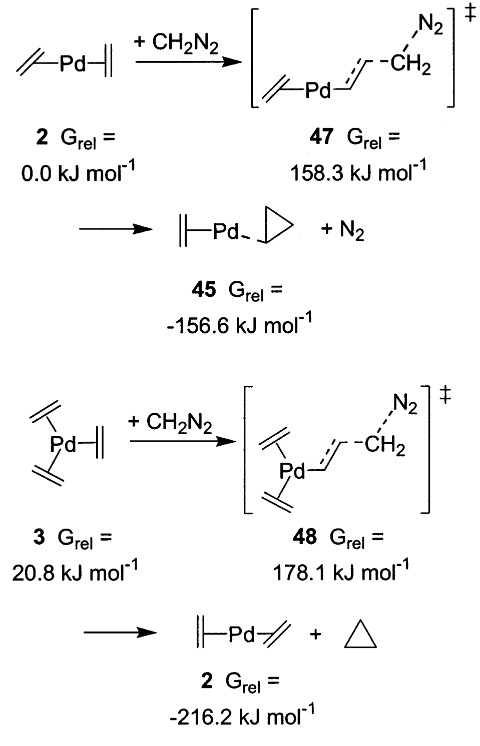


Figure 1. Profile of the computed relative Gibbs free energies for gas-phase model structures at 273.15 K and 1 atm. Intermolecular reactions with no total electronic activation energy are characterized by dashed lines.

reductive elimination transition state **44**. For alkene substituents, however, which stabilize palladacyclobutanes, diazomethane complexes such as **46** may well be the cause of the formation of cyclobutane and cyclopentane derivatives. Lukin and Zefirov observed such oligomethylenation products for phenyl allene and biscyclopropylidene.[25] They proposed the "cyclopalladation of the alkene with Pd:CH$_2$, affording a palladiacyclobutane intermediate which accumulates methylene units".[25a]

CH$_2$N$_2$ Attack on Coordinated Ethene. A referee suggested the direct reaction of diazomethane with an alkene ligand of a palladium complex as an alternative pathway. Thus, we computed the pathways for CH$_2$N$_2$ attack on Pd(η^2-C$_2$H$_4$)$_2$ **2** and Pd(η^2-C$_2$H$_4$)$_3$ **3** (Scheme 14). The computed Gibbs free activation energies of 158.3 and 178.1 kJ mol^{-1} for the model transition states **46** and **47**, however, are clearly too high to be compatible with the rate of the experimental cyclopropanation reaction.

Scheme 14

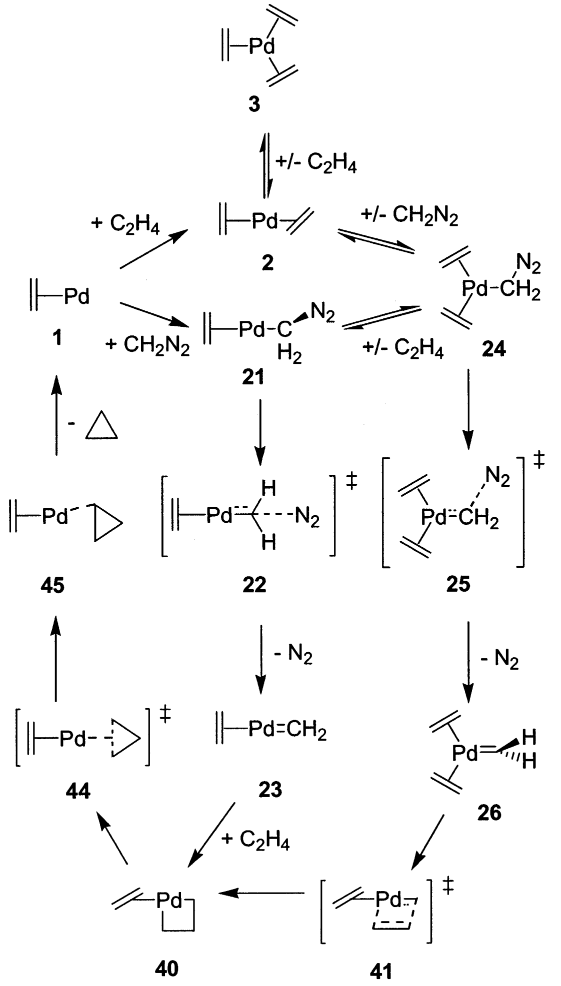


Relative Energy Dependence on the Functionals. We are well aware of artifacts due to inaccurate computational predictions of palladium ligand bond strengths. Computed relative energies of complexes with different palladium coordination numbers will inherently bear a large uncertainty. Since the alternative resting states Pd(η^2-C$_2$H$_4$)$_2$ (**2**) and Pd(η^2-C$_2$H$_4$)$_3$ (**3**) as well as the alternative rate-determining transition states Pd(η^2-C$_2$H$_4$)(κC-CH$_2$−N$_2$)‡ **22** and Pd(η^2-C$_2$H$_4$)$_2$(κC-CH$_2$−N$_2$)‡ **25** possess different palladium coordination numbers, this may well have an effect on the computed catalytic cycle. Thus, we recalculated ethene, diazomethane, and the model complexes **2**, **3**, **22**, and **25** at the BP86/LACV3P**++//BP86/LACV3P* level of theory. The model structures **3** (G_{rel} = −2.5 kJ mol^{-1}) and **25** (G_{rel} = 66.9 kJ mol^{-1}) with their coordination number 3 were significantly stabilized relative to the more unsaturated species **2** (normalized to G_{rel} = 0.0 kJ mol^{-1}) and **22** (G_{rel} = 77.9 kJ mol^{-1}) by the BP86 functionals (Figure 1). Obviously, the assignment of both the resting state and the rate-determining transition state are functional dependent. Despite the changes in the relative stabilities of the key model structures, the predicted Gibbs free energy barrier of 69.4 kJ mol^{-1} at the BP86

---

(25) (a) Lukin, K. A.; Zefirov, N. S. *Dokl. Akad. Nauk SSSR* **1989**, *305*, 631. (b) Lukin, K. A.; Zefirov, N. S. *Zh. Org. Khim.* **1989**, *25*, 92. (c) Lukin, K. A.; Kuznetsova, T. S.; Kozhushkov, S. I.; Piven, V. A.; Zefirov, N. S. *Zh. Org. Khim.* **1988**, *24*, 1644.

Scheme 15. Proposed Mechanistic Pathways for Pd(0)-Catalyzed Cyclopropanation of Ethene with CH_2N_2



level of theory deviates only slightly from the barrier of 71.7 kJ mol^{-1} computed with the B3LYP functionals.

Conclusion

In this DFT study, model calculations predict a catalytic cycle for ethene cyclopropanation by diazomethane/Pd(0) ethene complexes with an overall barrier of less than 72 kJ mol^{-1} (Figure 1). As a consequence, Pd(II) pathways appear to be improbable in $Pd(OAc)_2$-catalyzed alkene cyclopropanation. $Pd(OAc)_2$ is thus presumably not the catalyst but the precatalyst of the cyclopropanation reaction. The actual catalytic resting state is $Pd(\eta^2\text{-}C_2H_4)_n$ ($n = 2$ or 3), which undergoes reversible ligand exchange reactions (Scheme 15). The resulting $Pd(\eta^2\text{-}C_2H_4)_{n-1}(\kappa C\text{-}CH_2N_2)$ eliminates N_2 in the rate-determining step. The assumption of a change in the N_2 elimination mechanism because of the influence of alkene substituents offers an explanation for the high reactivity of alkenes with a strong coordinating ability to Pd(0) and for the inertness of internal alkenes in palladium-catalyzed cyclopropanation. Internal alkenes should have a tendency to yield monoalkene carbene complexes, which might well preferentially attack diazomethane substrates in a short-circuit reaction. Terminal, strained cyclic, and activated alkenes should form dialkene carbene complexes, which preferentially undergo an intramolecular rearrangement to palladacyclobutanes. This assumption is in accord with the cyclopropanation study of Anciaux et al.[2a] In 1980, they concluded from their alkene competition experiments that "a mechanism in which a palladium-coordinated carbene ... reacts with an olefin coordinated to the same metal in a fashion reminiscent of a 'cis rearrangement' (possibly via the formation of a metallacyclobutane) fits best the data at hand". In our study, the resulting monoethene palladacyclobutane intermediate is predicted to reductively eliminate cyclopropane easily, and subsequent ligand exchange completes the catalytic cycle.

The predicted role of Pd(0) in alkene cyclopropanation has obvious consequences for the design of spectator ligands for this reaction. An enantiopure chiral ancillary ligand will only be able to achieve nonzero enantioselectivities if it binds more strongly to Pd(0) than to the alkene substrate. Additionally, the ancillary ligand should react with the $Pd{=}CH_2$ fragment neither in the palladium coordination sphere nor intermolecularly. Thus, chiral phosphorus ligands and maleic esters of chiral alcohols are promising ligands for attempts to achieve enantioselective palladium-catalyzed alkene cyclopropanation by diazomethane.

Acknowledgment. This paper is dedicated to Prof. Robert G. Bergman in recognition of his 60th birthday. A Liebig habilitation fellowship and financial support of the Fonds der Chemischen Industrie and the Bundesministerium für Wissenschaft und Forschung as well as generous support from Prof. Herbert Mayr and the Chemistry Department of the Ludwig-Maximilians-Universität München are gratefully acknowledged.

Supporting Information Available: Molecular modeling coordinates and computed thermochemical data of energy minima, transition states, and hypersurface scans. This material is available free of charge via the Internet at http://pubs.acs.org.

JA027762+