Mechanistic Studies of the Cycloisomerization of Dimethyl Diallylmalonate Catalyzed by a Cationic Palladium Phenanthroline Complex

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Abstract: The mechanism of the cycloisomerization of dimethyl diallylmalonate (**1**) catalyzed by the cationic palladium phenanthroline complex $[(phen)Pd(Me)CNCH_3]^+[BAr_4]^-$ [Ar = 3,5-$C_6H_3(CF_3)_2$] (**2**) has been investigated. Heating a solution of **1** and **2** (5 mol %) in DCE at 40 °C led to zero-order decay of **1** to ∼80% conversion ($k_{obs} = (7.1 \pm 0.3) \times 10^{-7}$ M s^{-1}) with formation of a 27:2.2:1.0 mixture of 3,3-bis(carbomethoxy)-1,5-dimethylcyclopentene (**3**), 4,4-bis(carbomethoxy)-1,2-dimethylcyclopentene (**4**), and 1,1-bis(carbomethoxy)-4-methyl-3-methylenecyclopentane (**5**) and traces (∼3.5%) of ethyl-substituted carbocycles **6** of the chemical formula $C_{12}H_{18}O_4$. Cyclopentenes **3** and **4** were formed both kinetically (**3**:**4** = 30:1 at 40 °C) and via secondary isomerization of **5** (**3**:**4** = 1:2.5 at 40 °C); the kinetic pathway accounted for the 93% of cyclopentene formation at 40 °C. Carbocycles **6** were formed predominantly (≥90%) within the first two catalyst turnovers as byproducts of catalyst activation. Stoichiometric reaction of **1** and **2** at room temperature for 1.5 h led to the isolation of the palladium cyclopentyl chelate complex $[(phen)Pd\overline{CHCH(Me)CH(Et)CH_2C(COOMe)(COOMe)}]^+[BAr_4]^-$ (**7**) in 26% yield as a ∼2:1 mixture of isomers. The structure of *trans*,*trans*-**7** was determined by X-ray crystallography. Kinetic studies of the formation of **7** established the rate law: rate = k[**1**][**2**], where $k = (2.1 \pm 0.3) \times 10^{-2}$ M^{-1} s^{-1} ($\Delta G^{\ddagger}_{298K} = 19.7 \pm 0.1$ kcal mol^{-1}) at 25 °C. Thermolysis of **7** at 50 °C formed carbocycles **6** in 65% yield by GC analysis. ^1H and ^{13}C NMR analysis of an active catalyst system generated from **1** and a catalytic amount of **2** led to the identification of the cyclopentyl chelate complex $[(phen)Pd\overline{CHCH(Me)CH(Me)CH_2C(COOMe)(COOMe)}]^+[BAr_4]^-$ (**8**) as the catalyst resting state. Cycloisomerization of **1**-2,6-d_2 formed predominantly (∼90%) 3,3-bis(carbomethoxy)-5-deuterio-1-(deuteriomethyl)-5-methylcyclopentene (**3**-d_2); no significant (≤10%) kinetic isotope effect or intermolecular H/D exchange was observed. Cycloisomerization of **1**-3,3,5,5-d_4 formed a 1:2.6 mixture of 3,3-bis(carbomethoxy)-2,4,4-trideuterio-1,5-dimethylcyclopentene (**3**-d_3) and 3,3-bis(carbomethoxy)-2,4,4-trideuterio-5-(deuteriomethyl)-1-methylcyclo pentene (**3**-d_4); while no significant (≤10%) kinetic isotope effect was detected, extensive intermolecular H/D exchange was observed. These data are consistent with a mechanism involving hydrometalation of an olefin of **1**, intramolecular carbometalation, isomerization via reversible β-hydride elimination/addition, and turnover-limiting displacement of the cyclopentenes from palladium.

Introduction

Functionalized carbocycles and heterocycles are among the most common structural components of naturally occurring and biologically active molecules.[1]As a result, considerable effort has been directed toward the development of efficient annulation procedures, and in this area, transition metal-based approaches have been particularly effective.[2] Noteworthy are procedures for the cycloisomerization of enynes catalyzed by Ni,[3] Ru,[4] Ti,[5] and especially Pd[6] complexes. Palladium-catalyzed enyne cycloisomerization, and the closely related reductive cyclization of enynes,[7] have been utilized in the synthesis of a number of naturally occurring polycyclic compounds.[8] Dienes are typically less reactive toward transition metals than are enynes, and consequently, diene cycloisomerization remains less developed than does enyne cycloisomerization. Nevertheless, the cycloisomerization of dienes catalyzed by d^0-metallocene,[9] Ru(I),[10]

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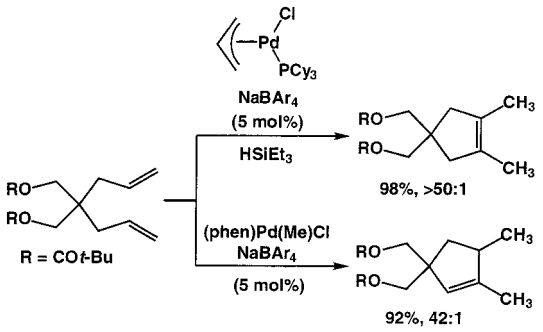
Scheme 1



Ni(II),[11,12] group IV alkoxide,[13] Pd(II),[11,14] Pt,[15] and Rh(III)[16] complexes has been reported.

Our contribution to the area of transition metal-catalyzed cycloisomerization has been the development of a pair of palladium-catalyzed diene cycloisomerization procedures. In one process, a 1:1 mixture of the π-allyl palladium complex (η^3-C_3H_5)Pd(Cl)PCy_3 and $NaBAr_4$ [Ar = 3,5-$C_6H_3(CF_3)_2$] in the presence of a stoichiometric amount of $HSiEt_3$ catalyzed the cycloisomerization of functionalized 1,6-dienes to form symmetric 1,2-dimethylcyclopentenes in good yield with high selectivity (Scheme 1, top reaction).[17,18] In a complementary procedure, a 1:1 mixture of the palladium phenanthroline complex (phen)Pd(Me)Cl [phen = 1,10-phenanthroline] and $NaBAr_4$ catalyzed the cycloisomerization of 1,6-dienes to form chiral 1,5-dimethylcyclopentenes in good yield with high selectivity (Scheme 1, bottom reaction).[19] In both cases, the active cationic palladium(II) catalyst was generated in situ via halide abstraction from the appropriate palladium chloride precatalyst with $NaBAr_4$.

In contrast to the many advances which have been made in the development and synthetic applications of transition metal-catalyzed cycloisomerization, little information regarding the mechanisms of these transformations has been forwarded. In fact, no detailed mechanistic study of any type of cycloisomerization has been reported and existing information has been gleaned primarily from several isotopic labeling studies[20] and from product analysis.[21] The lack of mechanistic information regarding transition metal-catalyzed cycloisomerization is unfortunate as an understanding of these mechanisms could facilitate the development of new and more selective cycloisomerization catalysts as well as the development of new transition metal-catalyzed procedures.

In response to the limited understanding of the mechanisms of transition metal-catalyzed cycloisomerization, we have previously investigated the mechanism of the silane-promoted cycloisomerization of dimethyl diallylmalonate (**1**) catalyzed by (η^3-C_3H_5)Pd(Cl)PCy_3/$NaBAr_4$. Unfortunately, the complexity of the system, due primarily to the excess silane which complicated both deuterium labeling and in situ ^{1}H NMR studies, precluded detailed mechanistic analysis.[18] In an effort to avoid these experimental difficulties and obtain detailed mechanistic information regarding a transition metal-catalyzed cycloisomerization process, we turned our attention to the palladium phenanthroline system which does not require silane for catalyst activation. In contrast to the (π-allyl)palladium-catalyzed process, palladium phenanthroline-catalyzed cycloisomerization has proven amenable to mechanistic study. Here we report an account of our study of the mechanism of the cycloisomerization of dimethyl diallylmalonate (**1**) catalyzed by the cationic palladium phenanthroline complex [(phen)Pd(Me)CH_3CN]$^+$[BAr_4]$^-$(**2**).

Results

Product Distribution. We have previously reported the cycloisomerization of dimethyl diallylmalonate (**1**) catalyzed by the cationic palladium phenanthroline complex [(phen)Pd(Me)$CNCH_3$]$^+$[BAr_4]$^-$ [Ar = 3,5-$C_6H_3(CF_3)_2$] (**2**) (5 mol %) at 40 °C to form a 27:2.2:1.0:1.5 mixture of the carbocycles 3,3-bis(carbomethoxy)-1,5-dimethylcyclopentene (**3**), 4,4-bis(carbomethoxy)-1,2-dimethylcyclopentene (**4**), 1,1-bis(carbomethoxy)-4-methyl-3-methylenecyclopentane (**5**), and the ethyl-substituted carbocycles **6** of the chemical formula $C_{12}H_{18}O_4$ in >98% combined yield (GC) (Scheme 2).[19] The ethyl-substituted carbocycles **6** were formed as a 9:2.5:1 mixture of isomers of which only 1-ethyl-2-methyl-4,4-bis(carbomethoxy)cyclopentane (20% of **6**) could be identified unambiguously by comparison with an authentic sample. On the basis of the isomeric composition of dimethyl-substituted carbocycles **3**−**5**, we assume the unidentified isomers of **6** are 3,3-bis(carbomethoxy)-1-methyl-5-ethylcyclopentene and 1,1-bis(carbomethoxy)-4-ethyl-3-methylenecyclopentane. The **3**:**4** selectivity of the cycloisomerization of **1** decreased with increasing temperature, and at 70 °C a 26:9:1.0:1.5 mixture of carbocycles **3**:**4**:**5**:**6** was formed.

To probe for carbocyclic intermediates in the cycloisomerization of **1**, a solution of **1** and a catalytic amount of **2** (5 mol

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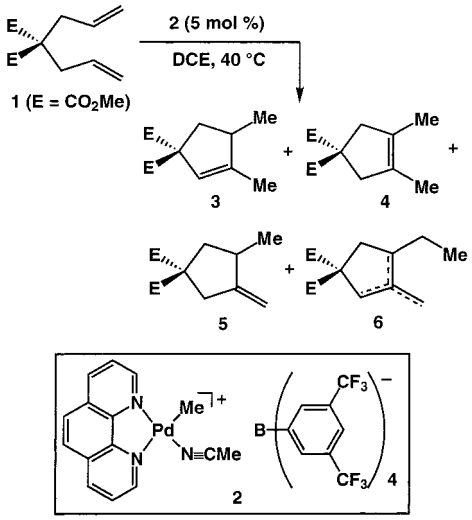
Scheme 2



%) in 1,2-dichloroethane (DCE) which contained CH_3CN (0.1 M) was heated at 40 °C and monitored periodically by GC analysis.[22] Disappearance of **1** obeyed zero-order kinetics to ~80% conversion with an observed rate constant of $k_{obs} = (7.1 \pm 0.3) \times 10^{-7}$ M s^{-1} and then decreased more slowly over the following 18 h (Figure 1).[23,24] The relative concentration of cyclopentene **3** increased steadily to approximately ~75% after 18 h and then increased slowly to a final value of 88%. In comparison, the relative concentration of **4** increased steadily throughout complete conversion of **1** to a final value of 7%, while the relative concentration of methylenecyclopentane **5**

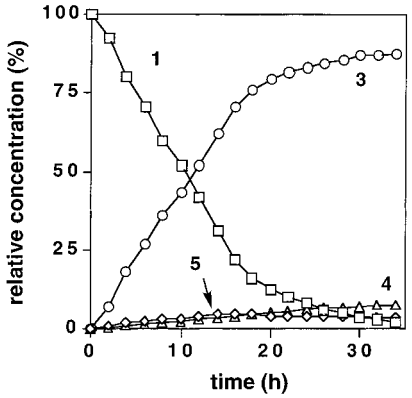


Figure 1. Concentration versus time plot for the conversion of **1** (49 mM) to **3**−**5** catalyzed by **2** (2.4 mM) in DCE at 40 °C where the relative concentrations of **1** and **3**−**5** refer to $[\mathbf{1}]_t/[\mathbf{1}]_0$, $[\mathbf{3}]_t/[\mathbf{1}]_0$, $[\mathbf{4}]_t/[\mathbf{1}]_0$, and $[\mathbf{5}]_t/[\mathbf{1}]_0$, respectively. Carbocycles **6** are omitted for clarity.

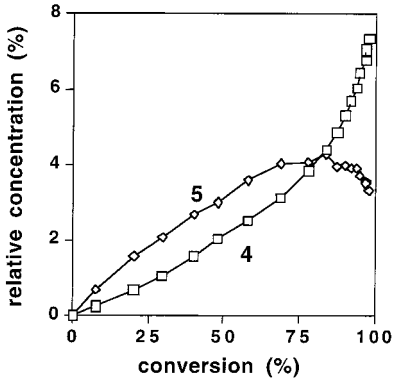


Figure 2. Plot of the relative concentrations of carbocycles **4** and **5** as a function of conversion in the cycloisomerization of **1** (49 mM) catalyzed by **2** (2.4 mM) at 40 °C in DCE where the relative concentrations of **4** and **5** refer to $[\mathbf{4}]_t/[\mathbf{1}]_0$ and $[\mathbf{5}]_t/[\mathbf{1}]_0$, respectively.

reached a maximum of ~4% after 14 h and then decreased slowly to ~3% after 34 h (Figure 1). Carbocycles **6** were formed predominantly (≥90%) within the first two catalyst turnovers and accounted for ~3.5% of the final reaction mixture (Figure S1).[23] The concentration versus time plot for the cycloisomerization of **1** at 70 °C displayed an appearance similar to the plot obtained at 40 °C with more prominent formation of **4** at the expense of **3** (Figure S2).[22−24]

Primary and Secondary Reaction Pathways. Calculations indicate that symmetric cyclopentene **4** is 4.0 kcal mol^{-1} more stable than chiral cyclopentene **3** and 7.4 kcal mol^{-1} more stable than methylenecyclopentane **5**,[25] suggesting the potential isomerization of both **5** and **3** under reaction conditions. Analysis of concentration versus conversion plots[26] was consistent with the partial isomerization of **5** under reaction conditions to form predominantly **4**.[26] Specifically, a plot of the relative concentration of **5** versus conversion displayed a negative deviation from linearity (Figure 2) and a plot of the relative concentration of **4** versus conversion displayed a positive deviation from linearity (Figure 2), while a plot of the relative concentration of **3** versus conversion was linear (Figure S3). To determine the relative rate and selectivity of the isomerization of **5** under reaction

(22) The rate of cycloisomerization of **1** catalyzed by **2** (5 mol %) in 1,2-dichloroethane (DCE) which contained CH_3CN (100 mM) was also determined at 25 °C ($k_{obs} = 2.2 \pm 0.1 \times 10^{-7}$ M s^{-1}) and 70 °C ($k_{obs} = 7.7 \pm 0.4 \times 10^{-6}$ M s^{-1}) (Figure S2). Acetonitrile was initially employed in these reactions in an effort to avoid catalyst decomposition and did not affect the outcome of these experiments as the reaction rate was independent of $[CH_3CN]$. For example, the observed rate constant for the cycloisomerization of **1** catalyzed by **2** in the presence of 2.4 mM acetonitrile at 70 °C was $k_{obs} = (6.8 \pm 0.5) \times 10^{-6}$ M s^{-1}. The amount of **6** formed in the catalyst activation step (which may serve as a marker of the amount of active catalyst) was invariant of changes in temperature or acetonitrile concentration and was proportional to catalyst loading. However, because the amount of **6** represents the sum of three separate isomers, each of which accounted for ~1% of the reaction mixture, the error in the determination of [**6**] may be substantial. Because of this, no effort was made to derive activation parameters or the second-order rate constant for the cycloisomerization of **1** catalyzed by **2**.

(23) The shape of the kinetic plots of catalytic reactions can often be misleading when catalyst activation is slow relative to turnover frequency.[23b] In the cycloisomerization of **1** catalyzed by **2** at low catalyst loading (≤5 mol %), conditions of rapid catalyst activation appear to be satisfied as carbocycles **6**, the byproducts of catalyst activation, were formed completely within the first ~10% consumption of **1**. However, at 20% catalyst loading, complete formation of **6** did not occur until ~40% of **1** had been consumed. In this case, the observed slope (which remained linear) represents a composite of the rate of catalyst activation and catalyst turnover (the linearity of these plots also points to the similar rates of catalyst activation/turnover frequency). As a result, catalyst dependence data is not reported although these data were consistent with the anticipated first-order dependence of the rate on [**2**]. (b) Rosner, T.; Pfaltz, A.; Blackmond, D. G. *J. Am. Chem. Soc.* **2001**, *123*, 4621.

(24) The rate of the cycloisomerization of **1** catalyzed by **2** decreased at high conversion (>80%), as indicated from the tailing of plots of [**1**] versus time (Figures 1 and S2). This decrease in reaction rate could potentially be caused by a number of factors including catalyst decomposition, product inhibition, or loss of saturation kinetics. To distinguish between these possibilities, the cycloisomerization of **1** catalyzed by **2** at 70 °C was monitored throughout complete conversion (>4 half-lives) and a second equivalent of **1** was added to the same reaction mixture. The initial rate for disappearance of the first and second equivalents of **1** differed by ≤10%. This observation suggests that the decrease in the rate of the cycloisomerization of **1** at high conversion results from neither catalyst decomposition nor product inhibition and points to a loss of saturation kinetics at low [**1**].

(25) (a) Calculations were performed by employing the MM2* force field within the Macromodel program.[25b] Relative energies of selected isomers were confirmed by DFT calculations using Jaguar 4.1.[25c] (b) Mohamadi, F.; Richards, N. G. J.; Guida, W. C.; Liskamp, R.; Lipton, M.; Canfield, C.; Chang, G.; Hendrickson, T.; Still, W. C. *J. Comput. Chem.* **1990**, *11*, 440. (c) Jaguar 4.1, Schrödinger, Inc., Portland, OR, 1991−2000.

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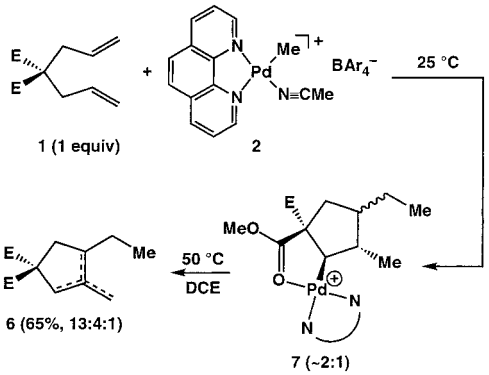
conditions, an equimolar solution of **5** and diethyl diallylmalonate (**1a**) was heated at 40 °C and monitored periodically by GC analysis. After 12 h, ~90% of **1a** and ~20% of **5** had undergone isomerization, the latter to form a 2.5:1 mixture of **4**:**3** (Figure S4).[27] At 70 °C, isomerization of **5** was ~3.5 times slower than the cycloisomerization of **1a** and formed a 2.8:1 mixture of **4**:**3** (Figure S5).

The linear plot of the relative concentration of **3** versus conversion (Figure S3) indicated that **3** was neither formed nor consumed to a significant degree via secondary isomerization. To further probe the stability of **3** under reaction conditions, a solution of **1a** (35 mM), **3** (12 mM), **4** (**3**:**4** = 56:1), and a catalytic amount of **2** (2.4 mM) was heated at 70 °C and monitored periodically by GC analysis. After 75 min, 95% of **1a** had been consumed with no detectable decrease in the concentration of **3** relative to internal standard (<2%) (Figure S6). However, isomerization of **3** after 75 min was revealed by a slight decrease in the **3**:**4** ratio from 56:1 to 45:1, which corresponds to a 0.5% decrease in the initial concentration of **3**.[28] Therefore, isomerization of **3** is ~190 times slower than the cycloisomerization of **1** under comparable conditions.[27] The corresponding experiment involving **1a** and **4** led to no detectable isomerization of **4** upon complete consumption of **1a**.

Secondary isomerization of **5** to form predominantly **4**, coupled with the stability of **3** under reaction conditions, led to a decrease of the **3**:**4** ratio and an increase of the **3**:**5** ratio with increasing consumption of **1**. For example, at 40 °C, the **3**:**4** ratio decreased from an initial value of 30:1 to a final value of 12:1, while the **3**:**5** ratio increased from an initial value of 10:1 to a final value of 25:1 (Figure S7). From these values and from the **3**:**4** selectivity for the isomerization of **5** (**3**:**4** = 1:2.5 at 40 °C), we estimate that the total contributions of the kinetic and isomerization pathways to the formation of carbocycles **3** and **4** in the cycloisomerization of **1** at 40 °C were 93% and 7%, respectively.[29] Due to the selectivity of the respective processes, ~98% of **3** and ~35% of **4** was formed via the kinetic pathway.[29]

The contribution of the secondary isomerization pathway to the formation of cyclopentenes **3** and **4** in the cycloisomerization of **1** increased with increasing temperature. At 70 °C, the **3**:**4** ratio decreased from an initial value of 6:1 to a final value of 3:1 and the **3**:**5** ratio increased from an initial value of 9:1 to a final value of 25:1 (Figures S8−S10). From these values and from the **3**:**4** selectivity for the isomerization of **5** (**3**:**4** = 1:2.8 at 70 °C), we estimate that the total contributions of the kinetic and isomerization pathways to the formation of carbocycles **3** and **4** in the cycloisomerization of **1** at 70 °C were 82% and 18%, respectively, with 94% of **3** and ~50% of **4** formed via the kinetic pathway.[29]

Scheme 3



Organopalladium Species Formed in the Conversion of 1 to 6. Carbocycles **6** were formed predominantly (≥90%) within the first two turnovers in the cycloisomerization of **1** and possessed an additional methylene group relative to carbocycles **3**−**5**. These observations indicated that carbocycles **6** were formed as byproducts of catalyst activation resulting from transfer of a methyl group from **2** to **1**. In an effort to probe the mechanism of catalyst activation, an equimolar solution of **1** and **2** (36 mM) in DCE-d_4 was monitored periodically by ^{1}H NMR spectroscopy at room temperature. No displacement of acetonitrile by **1** was observed, indicating that acetonitrile is a significantly better ligand toward (phen)Pd(Me)$^+$ than is **1**. Nevertheless, **2** disappeared over the course of 30 min to form the palladium cyclopentyl chelate complex

$$[(\text{phen})\text{PdCHCH(Me)CH(Et)CH}_2\text{C(COOMe)(COOMe)}]^+[\text{BAr}_4]^-$$

(**7**) as a 2:1 mixture of isomers which accounted for ≥95% of the palladium-containing products (Scheme 3). No formation of carbocycles **6** was observed throughout complete conversion of **2** to **7**.

In a preparative-scale reaction, an equimolar solution of **1** and **2** was stirred in ether for 1.5 h, diluted with hexane, concentrated, and cooled to −20 °C to give tan crystals of **7** in 26% yield as a ~2:1 mixture of isomers. Although the structure of **7** could not be determined by spectroscopy alone (see below), spectroscopic data established the presence of both free and chelated carbomethoxy groups. For example, the ^{1}H NMR spectrum of **7** displayed two pairs of singlets centered at δ 4.16 (~2:1) and δ 3.77 (~2:1), while the solid-state IR spectrum displayed two carbonyl stretches of roughly equal intensity at 1607 and 1720 cm^{-1}. Likewise, the ^{13}C NMR of the labeled derivative **7a**-($^{13}CO_2$Et)$_2$ [generated from a 1:1 mixture of **2** and **1a**-($^{13}CO_2$Et)$_2$] displayed a 1:1 ratio of carbonyl peaks at δ 191.1 and 171.2.

The solid-state structure of *trans,trans*-**7** was determined by X-ray crystallography (Figure 3, Tables 1 and 2). The palladium atom and the four Pd-bound atoms form a distorted square plane with two large (>97°) N−Pd−X (X = C, O) and two small (~81°) N−Pd−N and C−Pd−O angles. The Pd−N bond trans to the cyclopentyl group is significantly (~0.1 Å) longer than the Pd−N bond trans to the oxygen atom, presumably due to the greater trans effect of the alkyl group relative to the oxygen atom.[30] A trans arrangement exists between the exocyclic methyl and ethyl groups and also between the exocyclic methyl group and the (phen)Pd moiety of the cyclopentyl ring. The similar

(27) In a separate reaction, a 1: 1 mixture of **1** and **1a** and a catalytic amount of **2** were heated at 70 °C.; the rate at which dienes **1** and **1a** reacted differed by <5%.

(28) This calculation assumes that **3** isomerizes exclusively to **4** without decomposition.

(29) The equation used to determine the fraction of carbocycles **3** and **4** formed kinetically at 40 °C was the following: $0.92 = (0.97)x + (0.29)(1 - x)$, where 0.92 is the **3**/(**3** + **4**) fraction formed at complete conversion, 0.97 is the **3**/(**3** + **4**) fraction formed kinetically, 0.29 is the **3**/(**3** + **4**) fraction formed via isomerization of **5**, x is the fraction of cyclopentenes formed via the kinetic process, and $1 - x$ is the fraction of cyclopentenes formed via isomerization of **5**. Solving for x gives $x = 0.93$. Therefore, the fraction of **3** formed kinetically at 40 °C equals $\{0.97 \times 0.93\}/0.92 = 0.98$ and the fraction of **4** formed kinetically at 40 °C equals $\{0.93 \times 0.03\}/0.08 = 0.35$. Similar equations were employed to calculate the fraction of cyclopentenes **3** and **4** formed via the kinetic and thermodynamic pathways at 70 °C: $0.75 = (0.86)x + (0.25)(1 - x)$; solving for x gives $x = 0.82$. The fraction of **3** formed kinetically at 70 °C equals $\{0.86 \times 0.82\}/0.75 = 0.94$. The fraction of **4** formed kinetically at 70 °C equals $\{0.86 \times 0.14\}/0.25 = 0.48$. These analyses assume that the observed change in the **3**:**4** ratio with increasing conversion is due solely to secondary isomerization of **5**.

(30) Miessler, G. L.; Tarr, D. A. *Inorganic Chemistry*, 2nd ed.; Prentice Hall: Upper Saddler River, NJ, 1999; pp 406−409.

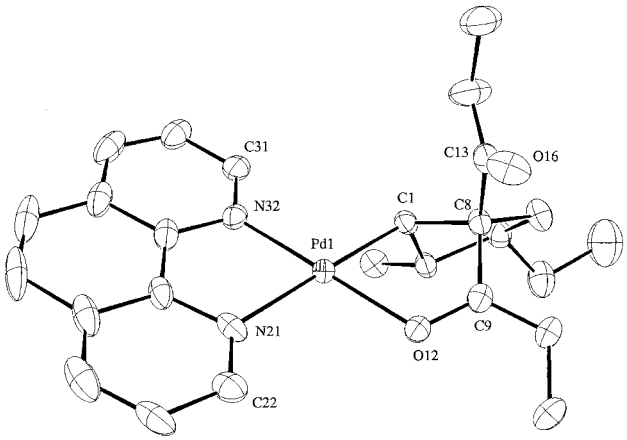


Figure 3. ORTEP diagram of *trans,trans*-**7**.

Table 1. Selected Bond Lengths (Å), Bond Angles (deg), and Torsion Angles (deg) for *trans,trans*-**7**

Pd1−N21	2.122(4)	Pd1−C1	2.022(5)
Pd1−N32	2.032(4)	C9−O12	1.241(6)
Pd1−O12	2.064(3)	C13−O16	1.206(7)
N21−Pd1−N32	81.27(18)	C1−Pd1−O12	81.10(15)
N32−Pd1−C1	99.94(18)	Pd1−O12−C9	112.5(3)
N21−Pd1−O12	97.69(16)	Pd1−C1−C8	107.7(3)
O12−Pd1−N21−C22	−2.7(4)	N21−Pd1−O12−C9	−167.4(6)
C1−Pd1−N32−C31	1.5(4)	N32−Pd1−C1−C8	150.5(6)

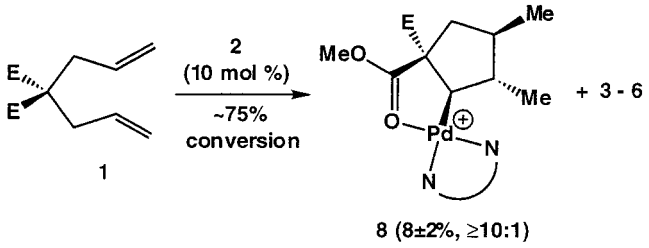
Table 2. X-ray Crystal Data and Collection and Refinement Parameters for *trans,trans*-**7**

empirical formula	$PdC_{56}H_{40}N_2O_4F_{24}$
fw	1378.05
cryst size, mm	0.3 × 0.25 × 0.10
cryst system	monoclinic
space group	$P2_1/n$
a, Å	13.6855(5)
b, Å	28.583(1)
c, Å	14.6784(5)
β, deg	105.671(1)
V, Å^3	5528.3(3)
Z	4
scan mode	w
2*θ* limits (deg)	$5.0 \le 2\theta \le 50.0$
D_c (g cm^{-3})	1.65
abs coeff (mm^{-1})	0.47
unique reflcns	9765
data with $I > 2.5\sigma(I)$	8759
F(000)	2754.56
R(*F*)	0.063
$R_w(F)$	0.089
GoF	3.6
no. of params	820
max Δ/σ	0.18
largest resid density (e/Å^3)	0.69

C═O bond distances of the chelated (1.24 Å) and free (1.21 Å) carbonyl groups indicated predominant *σ*-donation from the chelated oxygen atom to palladium.

The second isomer of **7** not characterized by X-ray crystallography is presumably *cis,trans*-**7**, which possesses a cis arrangement between the exocyclic methyl and ethyl groups and a trans arrangement between the exocyclic methyl group and the (phen)Pd moiety of the cyclopentyl ring.[31] Although we have no direct evidence which establishes *trans,trans*-**7** as the major isomer formed in the reaction of a stoichiometric mixture of **1** and **2** or which establishes *cis,trans*-**7** as the unidentified isomer formed in this transformation, related evidence supports these assignments (see below).

Scheme 4



In the presence of a 10-fold excess of **1** (0.12 M), disappearance of **2** at 25 °C obeyed first-order kinetics to >3 half-lives with a pseudo-first-order rate constant of $k_{obs} = (4.6 \pm 0.1) \times 10^{-3}$ s^{-1} (Figure S11). Pseudo-first-order rate constants for the formation of **7** were determined as a function of diene concentration from 0.07 to 0.41 M. A linear plot of observed rate constants versus [**1**] established the first-order dependence of the reaction rate on [**1**] and the second-order rate law: rate = k[**1**][**2**], where $k = (2.1 \pm 0.3) \times 10^{-2}$ M^{-1} s^{-1} ($\Delta G^{\ddagger}_{298K}$ = 19.7 ± 0.1 kcal mol^{-1}) (Figure S12). Extrapolation of this second-order rate constant to low diene concentration indicates that the reaction of **1** and **2** under catalytic conditions ([**1**]$_0$ = 49 mM, $k_{obs} \approx 1 \times 10^{-3}$ s^{-1}) is ≥10 times faster than the turnover frequency of the cycloisomerization of **1** catalyzed by **2** (TOF = 9.2×10^{-5} s^{-1} at 25 °C).

Thermolysis of a solution of **7** in DCE at 50 °C for 2 h formed carbocycles **6** as a 13:4:1 mixture of isomers in 65% yield by GC analysis (Scheme 3).[32] Kinetic analysis of the decomposition of **7** by ^{1}H NMR spectroscopy was precluded by excessive broadening of the carbomethoxy resonances of **7** during thermolysis. However, the predominant (≥90%) formation of carbocycles **6** within the first two catalyst turnovers in the cycloisomerization of **1** catalyzed by **2** indicates that decomposition of **7** under catalytic conditions occurs at a rate comparable to the catalyst turnover frequency. In addition, an isolated sample of **7** catalyzed the cycloisomerization of **1** with a rate not significantly (≤5%) different from the rate of the cycloisomerization of **1** catalyzed by **2** ($k_{obs} = (8.0 \pm 0.3) \times 10^{-6}$ s^{-1} at 70 °C).

Catalyst Resting State. A solution of **2** and excess **1** (10 equiv) in DCE-d_4 at 50 °C was monitored periodically by ^{1}H NMR spectroscopy until 75% of the diene had been consumed (~7 turnovers) and carbocycles **6** had been formed completely. In addition to resonances corresponding to diene **1** and carbocycles **3**−**6**, ^{1}H NMR analysis of the solution revealed the presence of the palladium cyclopentyl chelate complex [(phen)PdCHCH(Me)CH(Me)CH$_2$C(COOMe)(COOMe)]$^+$ [BAr$_4$]$^-$ (**8**), which accounted for 8 ± 2% of the reaction mixture by ^{1}H NMR analysis (Scheme 4). The structure of **8** was assigned by comparison of its spectroscopy to that of **7** and from reaction with silane (see below). For example, the ^{1}H NMR spectrum of **8** displayed a 1:1 ratio of carbomethoxy resonances at *δ* 4.16 and 3.77 and the ^{13}C NMR spectrum of

(31) An isomer in which the exocyclic methyl group and the (phen)Pd moiety of the cyclopentyl ring are cis is not a viable structure for **7** or **8** because such an isomer could be neither formed nor consumed via *β*-hydride addition/elimination.

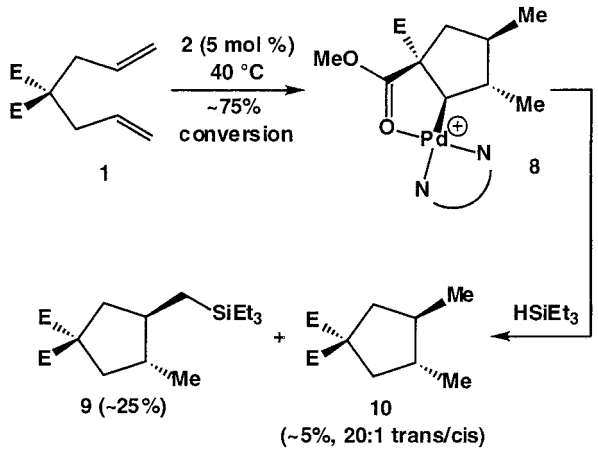
(32) The yield of carbocycles **6** formed in the thermolysis of **7** parallels the yield of carbocycles **6** (relative to catalyst loading) formed under reaction conditions. Note that the relative amount of the isomers of **6** formed under catalytic conditions and in the thermolysis of **7** differ only with respect to the minor isomer. For example, the 13:4:1 ratio of isomers of **6** formed under catalytic conditions corresponds to 73%, 21%, and 6% of the respective isomers while the 9:2.5:1 ratio of isomers formed in the thermolysis of **7** corresponds to 72%, 20% and 8% of the respective isomers.

8a-($^{13}CO_2Et)_2$ [generated from **2** and excess **1a**-($^{13}CO_2Et)_2$] displayed a 1:1 ratio of carbonyl resonances at δ 191.6 and 171.0. Both ^1H and ^{13}C NMR spectroscopy indicated that the isomeric purity of **8** formed under these conditions was ≥10:1, in contrast to the low isomeric purity of **7** (∼2:1).

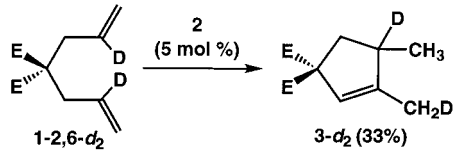
The formation of byproducts **6** in the first two catalyst turnovers indicated that the initially formed intermediate **7** decomposed at a rate comparable to the catalytic turnover frequency, as would be expected on the basis of the similar structures of **7** and **8**. However, to ensure that the resonances attributed to catalyst resting states **8** and **8a** in the experiments described in the preceding paragraph did not correspond to residual **7** and **7a**, respectively, two additional experiments were performed. In one experiment, a DCE-d_4 solution of **7a**-($^{13}CO_2$-Et) [generated in situ from reaction of **2** and **1a**-($^{13}CO_2Et$) (1.1 equiv), 25 °C, 12 h] was treated with excess **1** (10 equiv), heated at 40 °C, and monitored periodically by ^1H and ^{13}C NMR spectroscopy. When ∼60% of **1** had been consumed, resonances corresponding to the carbonyl carbon atoms of **7a**-($^{13}CO_2Et$) were not detected in the ^{13}C NMR spectrum while the carbomethoxy methyl protons of **8** were observed in the ^1H NMR spectrum. In a complementary experiment, a DCE-d_4 solution of **7** was treated with an excess of **1a**-($^{13}CO_2Et$) (10 equiv), heated at 40 °C, and monitored periodically by ^1H NMR spectroscopy. When ∼60% of **1a**-($^{13}CO_2Et$) had been consumed, resonances corresponding to the carbomethoxy groups of **7** were not observed in the ^1H NMR spectrum while peaks corresponding to the carbonyl carbon atoms of **8a**-($^{13}CO_2Et$) were observed in the ^{13}C NMR spectrum.

For neither **7** nor **8** was the stereochemistry of the major isomer determined through spectroscopic or crystallographic analysis.[31] However, cationic palladium alkyl phenanthroline complexes are known to react with triethylsilane to release the alkane and form the corresponding palladium silyl complex.[33] We therefore considered that silylative cleavage of the cyclopentyl group from **8** might facilitate stereochemical analysis of this complex.[34] To this end, a solution of **2** and excess **1** (20 equiv) in DCE-d_4 was heated at 40 °C and monitored periodically by ^1H NMR analysis. When ∼75% of **1** had reacted to form a mixture of carbocycles **3**−**6** and resting state **8** (∼5 h), the solution was treated with excess $HSiEt_3$ (Scheme 5). GC Analysis of the resulting dark solution 4 h after silane addition revealed complete consumption of **1** with formation of *trans*-1,1-bis(carbomethoxy)-3-((triethylsilyl)methyl)-4-methylcyclopentane (**9**) (∼25%), formed via cyclization/hydrosilylation of **1**.[35] In addition to **9**, 1,1-bis(carbomethoxy)-3,4-dimethylcyclopentane (**10**), generated from direct silylation of **8**, had formed in ∼5% yield as a 20:1 mixture of trans:cis isomers.[36,37] From this result, we conclude that, at 40 °C, oxapalladacycle **8** is formed as a 20:1 mixture of trans,trans and trans,cis isomers.[31]

Scheme 5



Scheme 6



The **3**:**4** selectivity of the cycloisomerization of **1** catalyzed by **2** increased with decreasing temperature. We considered that the *trans,trans*-**8**:*trans,cis*-**8** selectivity might also be temperature dependent and related to the **3**:**4** selectivity. To probe this possibility, a solution of **8** in DCE-d_4 was generated at 70 °C, cooled to room temperature, and treated with excess $HSiEt_3$. GC analysis of the resulting solution revealed formation of **10** as a 4.1:1 mixture of trans:cis isomers, significantly lower than the 20:1 trans:cis ratio formed at 40 °C. From this result, we conclude that, at 70 °C, cyclopentyl chelate complex **8** is formed as a 4.1:1 mixture of trans,trans and trans,cis isomers.[31] The predominant trans stereochemistry of the exocyclic methyl groups of **8** is not surprising as the cyclization/hydrosilylation of **1** and $HSiEt_3$ catalyzed by cationic palladium phenanthroline complexes forms **9** with high (>50:1) trans selectivity.[35]

Deuterium Labeling Studies. Several deuterium labeling experiments were performed to probe for H/D exchange and kinetic isotope effects in the cycloisomerization of **1** catalyzed by **2**. In one experiment, a solution of **1**-2,6-d_2 and a catalytic amount of **2** in DCE was stirred at room temperature for 1 week to form a 32:2:1 mixture of **3**-*d*, **4**-*d*, and **5**-*d* along with traces (∼3.5%) of **6**-*d*. GC/MS analysis of the crude reaction mixture revealed that **3**-*d* consisted predominantly (≥95%) of the d_2 isotopomer while **4**-*d* and **5**-*d* consisted of 60:40 and 37:63 mixtures of d_1:d_2 isotopomers, respectively (Table 3, entries 1−3).[38] Evaporation of solvent and chromatography led to the isolation of **3**-*d* in 33% yield with 97% isomeric purity (Scheme 6).

NMR analysis of **3**-*d* isolated from cycloisomerization of **1**-2,6-d_2 was consistent with predominant (≥90%) formation of 3,3-bis(carbomethoxy)-5-deuterio-1-(deuteriomethyl)-5-methylcyclopentene (**3**-d_2) contaminated with small amounts of C(5)−H and C(5)−CH_2D isotopomers (Scheme 6). For example, the ^{13}C NMR spectrum of **3**-*d* displayed a 1:1:1 triplet at δ 14.1 (J_{CD} = 19.5 Hz), assigned to the C(1) CH_2D group, an

(33) LaPointe, A. M.; Rix, F. C.; Brookhart, M. *J. Am. Chem. Soc*. **1997**, *119*, 906.

(34) In reaction of cationic palladium(II) alkyl complexes with silane, hindered palladium alkyl complexes often isomerize via β-hydride addition/elimination followed by silylation of the least hindered isomer.[33] However, isomerization of **8** prior to silylative cleavage would not change the trans/cis ratio of **10** provided that palladium does not dissociate during isomerization. Furthermore, related evidence suggests that silylation of **8** occurs without prior isomerization. Specifically, reaction of [(phen)PdCHCH(Me)CH(CH_2SiEt_3)CH_2C(COOMe)(COOMe)]$^+$[BAr_4]$^-$ with $DSiEt_3$ formed cyclopentene **9**-d_1 with ≥80% deuterium incorporation at the C(2) carbon atom: Perch, N. S.; Widenhoefer, R. A. Unpublished results.

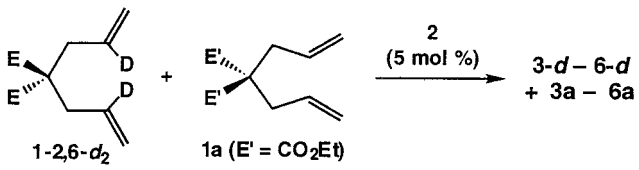
(35) Widenhoefer, R. A.; DeCarli, M. A. *J. Am. Chem. Soc*. **1998**, *120*, 3805.

(36) Compounds *trans*-**10** and *cis*-**10** were identified by GC/MS analysis and by co-injection with authentic samples.[37]

(37) Perch, N. S.; Kisanga, P.; Widenhoefer, R. A. *Organometallics* **2000**, *19*, 2541.

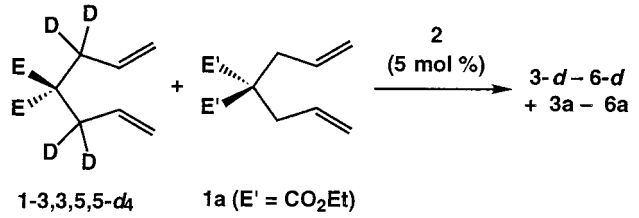
(38) Because cyclopentene **4**-*d* was formed both kinetically (∼40%) and via isomerization of **5** (∼60%), detailed analysis of the isotopic composition of **4**-*d* formed from **1**-2,6-d_2 or **1**-3,3,5,5-d_4 was precluded. The isotopic composition of **6**-*d* was not determined.

Table 3. Isotopomers Formed in the Cycloisomerization of **1**-2,6-d_2 and in the Cycloisomerization of a 1:1 Mixture of **1**-2,6-d_2 and **1a** Catalyzed by **2** in DCE



					isotopic composition			
entry	**1a**/(**1a** + **1**-d_2)	temp (°C)	conversion (%)	compd analyzed	d_0	d_1	d_2	d_3
1	0	25	100	**3**-*d*	–	3	95	2
2	0	25	100	**4**-*d*	–	60	40	
3	0	25	100	**5**-*d*	–	37	63	
4	50	70	80	recovered **1**-*d*	–	–	⩾98	–
5	50	70	80	recovered **1a**	96	4	–	–
6	50	70	80	**3**-*d*	–	–	≥98	–
7	50	70	80	**4**-*d*	–	57	43	–
8	50	70	80	**3a**	96	4	–	–
9	50	70	80	**4a**	94	6	–	–

Table 4. Isotopomers Formed in the Cycloisomerization of **1**-3,3,5,5-d_4 and in the Cycloisomerization of a 1:1 Mixture of **1**-3,3,5,5-d_4 and **1a** Catalyzed by **2** in DCE



					isotopic composition						
entry	**1a**/(**1a** + **1**-d_2)	temp (°C)	conversion (%)	compd analyzed	d_0	d_1	d_2	d_3	d_4	d_5	d_6
1	0	25	100	**3**-*d*	–	–	–	28	72	–	–
2	0	25	100	**4**-*d*	–	–	–	6	34	43	16
3	0	25	100	**5**-*d*	–	–	–	–	33	67	–
4	50	70	90	recovered **1**-*d*	–	–	–	–	⩾98	–	–
5	50	70	90	recovered **1a**	≥98	–	–	–	–	–	–
6	50	70	50	**3**-*d*	–	–	–	68	32	–	–
7	50	70	50	**4**-*d*	–	–	–	–	73	24	3
8	50	70	50	**5**-*d*	–	–	–	–	67	33	–
9	50	70	50	**3a**	64	36	–	–	–	–	–
10	50	70	50	**4a**	73	27	–	–	–	–	–

overlapping singlet and 1:1:1 triplet at δ 42 (J_{CD} = 19.8 Hz, isotopic shift = 354 ppb), assigned to the C(5)H and C(5)D carbon atoms, respectively, and an overlapping singlet and 1:1:1 triplet at δ 19 (J_{CD} = 19.4 Hz, isotope shift = 144 ppb), assigned to the C(5)CH_3 and C(5)CH_2D groups, respectively. Integration of the ^{1}H NMR spectrum indicated that C(5)H/C(5)CH_2D isotopomers constituted ≤10% of the isotopic mixture.

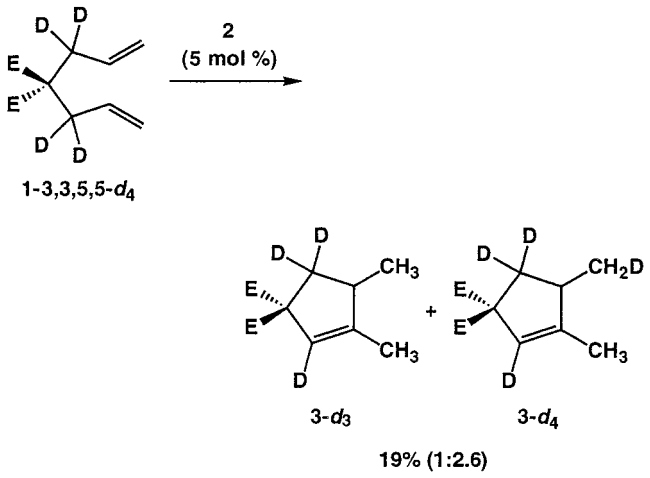
To probe for intermolecular H/D exchange in the cycloisomerization of **1**-2,6-d_2, an equimolar solution of **1**-2,6-d_2 and diethyl diallylmalonate (**1a**) and a catalytic amount of **2** in DCE was heated at 70 °C and monitored periodically by GC/MS analysis. The rate at which dienes **1a** and **1**-2,6-d_2 reacted differed by ≤10%.[27] Intermolecular deuterium transfer did not occur to a significant extent either prior to or during cycloisomerization. For example, at ~80% conversion no substantial (≤2%) loss of deuterium was detected in either unreacted diene **1**-2,6-d_2 or in cyclopentene **3**-d_2 (Table 3, entries 4 and 6). Similarly, no significant (≤4%) deuterium incorporation was detected in unreacted diene **1a** or in cyclopentene **3a** (Table 3, entries 5 and 8).

Several experiments were also performed with the tetradeuteride **1**-3,3,5,5-d_4. Cycloisomerization of **1**-3,3,5,5-d_4 catalyzed by **2** at room temperature formed an 18:1:2 mixture of **3**-*d*, **4**-*d*, and **5**-*d* along with traces (~3%) of **6**-*d*. GC/MS analysis of the crude reaction mixture revealed that **3**-*d* consisted of a 1:2.6 mixture of d_3:d_4 isotopomers, **4**-*d* consisted of a mixture of d_3–d_6 isotopomers, and **5**-*d* consisted of a 1:2 mixture of d_4:d_5 isotopomers (Table 4, entries 1–3).[38,39] Cyclopentene **3**-*d* was isolated from this mixture in 19% yield with 96% isomeric purity (Scheme 7).

NMR analysis of **3**-*d* isolated from cycloisomerization of **1**-3,3,5,5-d_4 was consistent with a ~1:2.6 mixture of 3,3-bis(carbomethoxy)-2,4,4-trideuterio-1,5-dimethylcyclopentene (**3**-d_3) and 3,3-bis(carbomethoxy)-2,4,4-trideuterio-5-(deuteriomethyl)-1-methylcyclopentene (**3**-d_4) (Scheme 7). For example, both ^{13}C and ^{1}H NMR spectra indicated complete (≥90%) deuteration

(39) GC/MS data indicated that the average number of deuterium atoms/molecule in carbocycles **3**–**5** formed in the cycloisomerization of **1**-3,3,5,5-d_4 was 3.86, which points to an external source of hydrogen atoms which exchange with a Pd–D intermediate in the conversion of **1**-3,3,5,5-d_4 to **3**–**5**. However, the source of the excess hydrogen atoms remains unknown as neither the substitution of DCE-d_4 for DCE nor the addition of D_2O (10 μL) to the reaction mixture increased the amount of deuterium in carbocycles **3**–**5**. Nevertheless, this exchange pathway does not affect the conclusions which are drawn from the experiments involving **1**-3,3,5,5-d_4.

Scheme 7



at the C(2) and C(4) carbon atoms, with no detectable (≤10%) deuterium incorporation at the C(5) carbon atom and the C(1) methyl group. A ~1:2.6 ratio of C(5) CH_3 and CH_2D groups was established both from an overlapping singlet and 1:1:1 triplet at δ 19 in the ^{13}C NMR spectrum and from an overlapping doublet and a 1:1:1 triplet of doublets at δ 1.04 ($J_{HD} = 2.0$ Hz, $J_{HH} = 7.0$ Hz, isotopic shift = 18 ppb) in the ^1H NMR spectrum.

To probe for intermolecular H/D exchange in the cycloisomerization of **1**-3,3,5,5-d_4, an equimolar solution of **1**-3,3,5,5-d_4 and diethyl diallylmalonate (**1a**) and a catalytic amount of **2** in DCE was heated at 50 °C and monitored periodically by GC/MS analysis. The rate at which dienes **1a** and **1**-3,3,5,5-d_4 reacted differed by ≤10%.[27] Intermolecular H/D exchange did not occur to a significant extent prior to cycloisomerization and at ~90% conversion, ≤2% H/D exchange was detected in unreacted dienes **1**-3,3,5,5-d_4 and **1a** (Table 4, entries 4 and 5). Conversely, intermolecular H/D exchange occurred to a significant degree during cycloisomerization as evidenced by the loss of deuterium from cyclopentene **3** and the incorporation of deuterium into cyclopentene **3a**. For example, at ~50% conversion, cyclopentene **3**-*d* had formed as a ~2:1 mixtures of d_3:d_4 isotopomers while **3a** had formed as a ~2:1 mixture of d_0:d_1 isotopomers (Table 4, entries 6−10).[39]

An experiment was also performed to probe for H/D exchange of methylenecyclopentane **5** under reaction conditions.[40] A 1:1 mixture of **1**-3,3,5,5-d_4 and **5a** and a catalytic amount of **2** was heated at 70 °C and monitored periodically by GC analysis. GCMS analysis after 75% consumption of **1**-3,3,5,5-d_4 (~15% consumption of **5a**) revealed no detectable (≤2%) deuterium incorporation into unreacted **5a**.

Discussion

Proposed Mechanism. The mechanism of the cycloisomerization of **1** catalyzed by **2** shown in Scheme 8 is consistent with all our experimental observations. β-Migratory insertion of the coordinated olefin into the Pd−H bond of **Ia** could form the palladium alkyl intermediate **II**. Coordination of the pendant olefin would form palladium alkyl olefin chelate complex **III,** which could undergo β-migratory insertion to form the palladium cyclopentylmethyl complex **IV**. β-Hydride elimination would form the palladium methylenecyclopentane complex **Va** (Scheme 8). Olefin rotation and reinsertion prior to dissociation would form the palladium cyclopentyl intermediate **VI**. From **VI**, β-elimination of a secondary or tertiary hydrogen atom would form palladium olefin complexes **Vb,c**, respectively, while β-elimination of a primary hydride would regenerate **Va**. Ligand exchange of complexes **V** with acetonitrile would then release carbocycles **3**−**5** with formation of the palladium acetonitrile adduct **Ib**. Reversible displacement of acetonitrile from **1b** with **1** would then regenerate palladium olefin intermediate **Ia**.

Catalyst Resting State and Turnover-Limiting Step. Transfer of the palladium-bound hydride to the more substituted olefinic carbon atom of intermediate **Vb** coupled with carbonyl chelation would form catalyst resting state **8**, the only palladium species observed under catalytic conditions (Scheme 8). The five-membered oxametallacycle generated via oxygen chelation presumably stabilizes complex **8** with respect to β-hydride elimination by filling the vacant coordination site required for elimination.[41] The proposed stability of **8** is supported by the isolation of the closely related cyclopentyl chelate complex **7**. Similarly, five- and six-membered palladium[42]and rhodium[43] oxametallacycles have been isolated from or observed in catalytic transformations involving the dimerization or polymerization of functionalized monomers such as methyl acrylate. Also noteworthy is that resting state **8** does not lie within the catalytic cycle for the cycloisomerization of **1** and presumably retards the rate of cycloisomerization by limiting the amount of palladium available for catalysis.

Identification of palladium cyclopentyl chelate complex **8** as the catalyst resting state designates the first irreversible step which consumes **8** as turnover-limiting. We can safely rule out consumption of **8** via irreversible β-hydride elimination to form **Vb** since **8** is formed via β-hydride addition to **Vb**. In addition, formation of cyclopentenes **3**−**5** from **8** requires fast interconversion of palladium olefin intermediates **V** relative to olefin displacement.[44] Facile interconversion of intermediates **Va** and **VI** prior to olefin displacement from **Va** was independently established from the formation of **5**-d_2 in the cycloisomerization of **1**-2,6-d_2 (see below). Facile β-hydride addition/elimination is also in accord with both the absence of a significant kinetic deuterium isotope effect in the cycloisomerization of **1**-2,6-d_2 or **1**-3,3,5,5-d_4,[45−48] and with the established reactivity of cationic palladium(II) alkyl complexes.[33,42]

(40) Of the carbocycles **3**−**5**, only methylenecyclopentane **5** has the potential to undergo H/D exchange via an addition/elimination mechanism without isomerization.

(41) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1987; p 386.

(42) (a) Johnson, L. K.; Mecking, S.; Brookhart, M. *J. Am. Chem. Soc.* **1996**, *118*, 267. (b) Rix, F. C.; Brookhart, M.; White, P. S. *J. Am. Chem. Soc.* **1996**, *118*, 4746. (c) Mecking, S.; Johnson, L. K.; Wang, L.; Brookhart, M. *J. Am. Chem. Soc*. **1998**, *120*, 888. (d) DiRenzo, G.; White, P. S.; Brookhart, M. *J. Am. Chem. Soc*. **1996**, *118*, 6225.

(43) Hauptman, E.; Sabo-Etienne, S.; White, P. S.; Brookhart, M.; Garner, J. M.; Fagan, P. J.; Calabrese, J. *J. Am. Chem. Soc*. **1994**, *116*, 8038.

(44) This group of interconverting intermediates may also include **IV**.

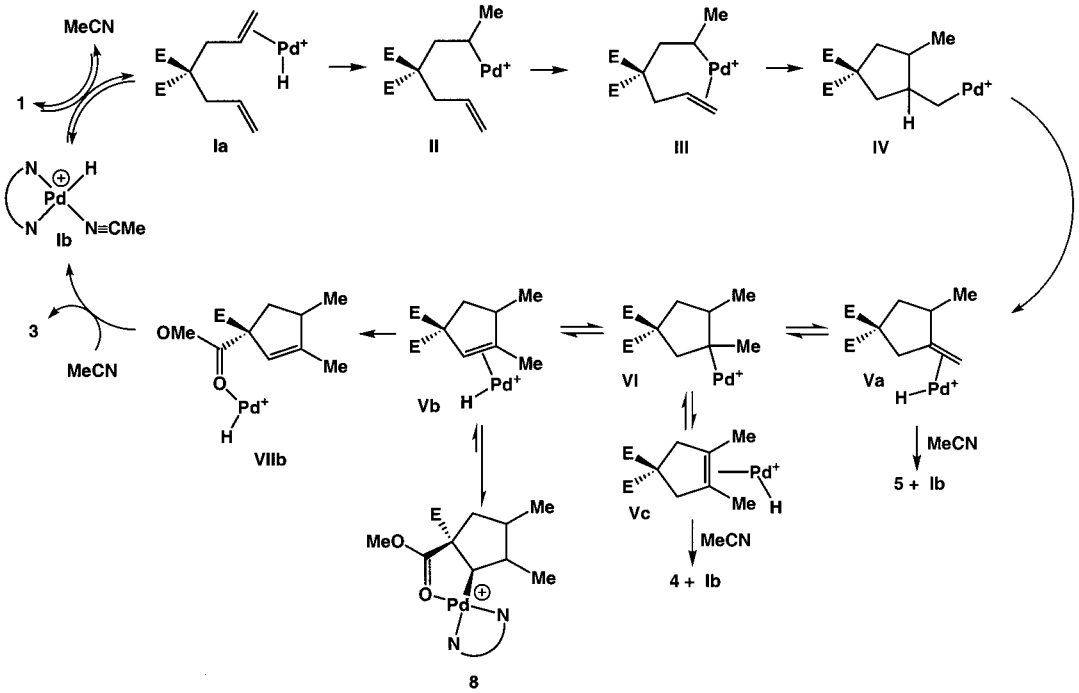
(45) In stoichiometric studies involving the β-hydride elimination of alkyl or alkoxy groups, rate-limiting C−H bond scission leads to a kinetic isotope effect of $k_H/k_D = 2.5-3$,[46] while rapid and reversible C−H bond scission followed by rate-limiting dissociation of the unsaturated fragment leads to a negligible kinetic isotope effect ($k_H/k_D \approx 1$).[47]

(46) (a) Blum, O.; Milstein, D. *J. Am. Chem. Soc.* **1995**, *117*, 4582. (b) Alibrandi, G.; Scolaro, L. M.; Minniti, D.; Romeo, R. *Inorg Chem*. **1990**, *29*, 3467. (c) Brainard, R. L.; Whitesides, G. M. *Organometallics* **1985**, *4*, 1550. (d) Romeo, R.; Alibrandi, G.; Scolaro, L. M. *Inorg Chem*. **1993**, *32*, 4688. (e) Evans, J.; Schwartz, J.; Urquhart, P. W. *J. Organomet. Chem*. **1974**, *81*, C37. (f) Ikariya, T.; Yamamoto, A. *J. Organomet. Chem.* **1976**, *120*, 257.

(47) (a) Bryndza, H. E.; Calabrese, J. C.; Marsi, M.; Roe, D. C.; Tam, W.; Bercaw, J. E. *J. Am. Chem. Soc*. **1986**, *108*, 4805. (b) Alibrandi, G.; Cusumano, M.; Minniti, D.; Scolaro, L. M.; Romeo, R. *Inorg Chem*. **1989**, *28*, 342.

(48) The measured kinetic isotope effects represent the sum of values for olefin displacement and for the conversion of **8** to **V**.

Scheme 8



The failure of cyclopentene **3** to isomerize to a significant extent under reaction conditions established the irreversible displacement of **3** from palladium olefin complex **Vb**. Because tetrasubstituted olefins coordinate even more poorly to transition metals than do trisubstituted olefins,[49] displacement of **4** from **Vc** must also be irreversible. Although methylenecyclopentane **5** isomerized under reaction conditions, this process was slow relative to the catalytic turnover frequency and represented a minor reaction pathway. These observations together establish turnover-limiting olefin displacement from palladium olefin complexes **V**. However, the mechanism of olefin displacement from intermediates **V** is not straightforward. For example, a mechanism initiated by olefin dissociation appears unlikely given the propensity of square planar palladium(II) complexes to undergo associative ligand exchange.[50] Conversely, direct associative displacement of the coordinated olefin from **Vb** with **1** or acetonitrile is inconsistent with the zero-order dependence of the rate of cycloisomerization on both [**1**] and [CH_3CN].[22−24]

To account for the zero-order dependence of both [**1**] and [CH_3CN] in the cycloisomerization of **1**, we invoke turnover-limiting, intramolecular displacement of the coordinated olefin from intermediate **Vb** with a pendant carbonyl group to form the palladium σ-carbonyl intermediate **VIIb**, which is then trapped with acetonitrile to form **Ib** (Scheme 8).[51,52] Although reaction of **VIIb** with either acetonitrile or **1** is consistent with our experimental data, initial reaction with acetonitrile appears likely as acetonitrile is both a better ligand for Pd^+ than is **1** and was present in higher concentrations than was **1**. The requisite palladium olefin intermediate **Ia** could then form reversibly via associative displacement of acetonitrile from **Ib** with **1** (Scheme 8).[53] Intramolecular displacement of a coordinated olefin with a pendant carbonyl group has previously been observed in cationic palladium diimine complexes.[54]

The failure of CH_3CN to react directly with palladium olefin complexes **V** yet react rapidly with palladium carbonyl complexes **VII** is presumably a steric phenomenon. The C═C bond of the coordinated carbocyclic olefin should be oriented perpendicular to the coordination plane[55] and therefore hinder attack of an incoming ligand at the palladium dz^2 orbital.[50] Conversely, this mode of olefin coordination should orient the carbonyl oxygen atom in close proximity to the palladium dz^2 orbital, facilitating intramolecular olefin displacement. The dz^2 orbital of the resulting palladium ester complex **VII** should be much more sterically accessible than in **V**, facilitating rapid reaction with external ligand. Analogous behavior was observed in the ligand substitution reactions of the nickel diimine complexes $[(N{-}N)Ni(Me)(L)]^+[BAr_4]^-$ [N−N = Ar′N═C(Me)C(Me)═NAr′; Ar′ = 2,6-$C_6H_3Me_2$; L = OEt_2 (**11a**), H_2O (**11b**), $H_2C{=}CH_2$ (**11c**)].[56] Although water rapidly and quantitatively displaced ether from **11a** to form **11b**, ethylene reacted much faster with the aquo adduct **11b** than with the less stable ether adduct **11a**. This unusual behavior was presumably the result

(49) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1987; p 149.

(50) (a) Howell, J. A. S.; Burkinshaw, P. M. *Chem. Rev.* **1983**, *83*, 557. (b) Darensbourg, D. J. *Adv. Organomet. Chem.* **1982**, *21*, 113. (c) Cross, R. J. *Chem. Soc. Rev.* **1985**, *14*, 197. (d) Zhong, H. A.; Widenhoefer, R. A. *Inorg. Chem.* **1997**, *36*, 2610. (e) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1987; Chapter 4. (f) Atwood, J. D. *Inorganic and Organometallic Reaction Mechanisms*; Brooks/Cole: Monterey, CA, 1985; Chapter 4. (g) Langford, C. H.; Gray, H. B. *Ligand Substitution Processes*; W. A. Benjamin: New York, 1965.

(51) At low [CH_3CN], **1** presumably reacts directly with **VIIb** to form **Ia,** and because the rate of cycloisomerization did not decrease at low [CH_3CN], reaction of **VIIb** with either acetonitrile or **1** must be fast relative to the conversion of **Vb** to **VIIb**. Turnover-limiting associative olefin displacement by solvent followed by rapid reaction with CH_3CN or **1** is also consistent with the zero-order dependence of the rate on [**1**] and [CH_3CN]. However, it appears that intermolecular attack of solvent on **Vb** would be favored relative to attack of acetonitrile or **1**.

(52) Presumably, intermediates **Va**,**c** decompose in a similar manner as the **3**:**4**:**5** ratio formed in the cycloisomerization of **1** was not significantly affected by either [**1**] or [CH_3CN].

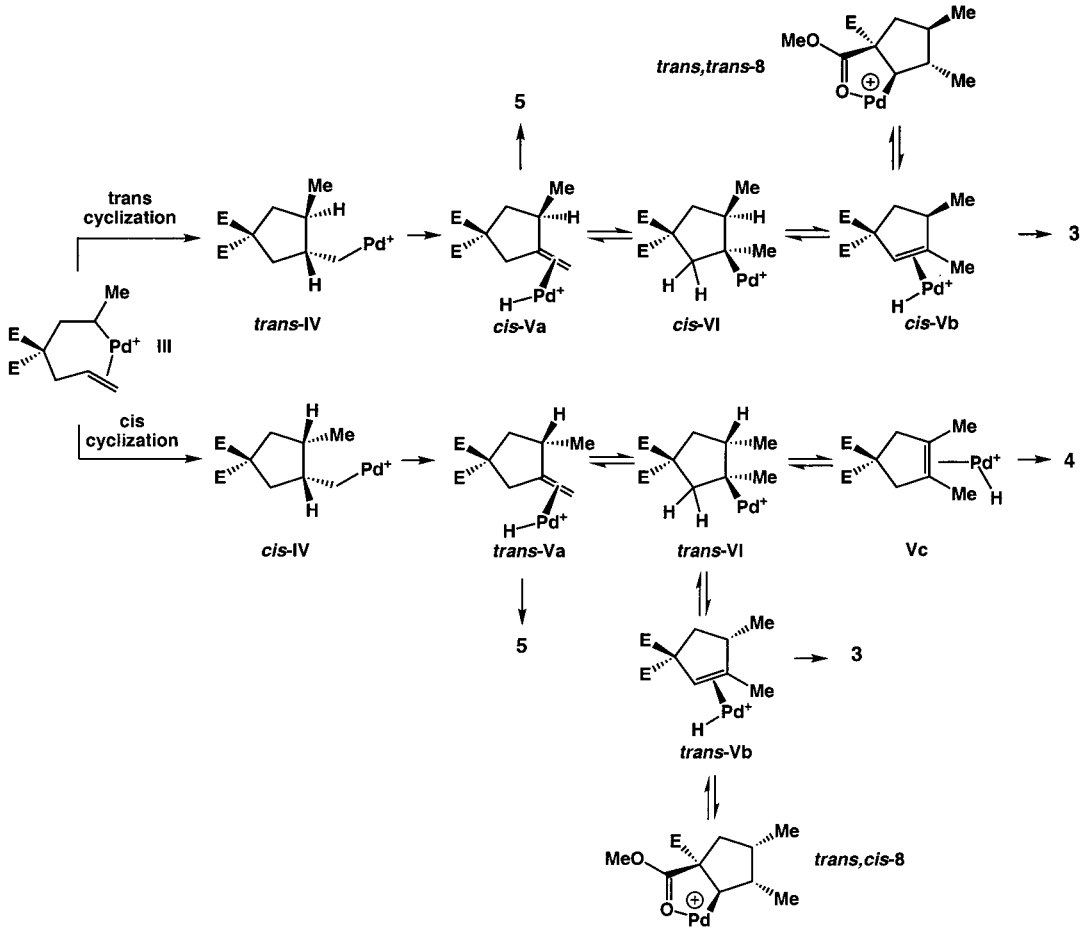
(53) The unfavorable displacement of CH_3CN with **1** may be responsible for the observed decrease of the rate of cycloisomerization at high conversion.

(54) Mecking, S.; Johnson, L, K.; Wang, L.; Brookhart, M. *J. Am. Chem. Soc*. **1998**, *120*, 888.

(55) Tempel, D. J.; Johnson, L. K.; Huff, R. L.; White, P. S.; Brookhart, M. *J. Am. Chem. Soc.* **2000**, *122*, 6686.

(56) Svejda, S. A.; Johnson, L, K.; Brookhart, M. *J. Am. Chem. Soc.* **1999**, *121*, 10634.

Scheme 9



of unfavorable steric interaction between ethylene and the ether ligand in the transition state for the conversion of **11a** to **11c**.[56]

Product Selectivity. In the cycloisomerization of **1**, cyclopentenes **3** and **4** were formed both kinetically and via secondary isomerization of **5**. The high kinetic **3**:**4** selectivity (30:1 at 40 °C) can be traced to the high trans selectivity of carbometalation (**III** → *trans*-**IV**, Scheme 9). Initial trans carbocyclization can lead to the formation of carbocycles **3** and **5** but not **4**, while cis-carbocyclization can lead to the formation of carbocycles **3**−**5** (Scheme 9). For example, β-hydride elimination from *trans*-**IV** would form exclusively *cis*-**Va**, which could undergo olefin rotation and reinsertion to form the palladium cyclopentyl intermediate *cis*-**VI**.[54] The palladium atom of *cis*-**VI** has or can adopt a syn relationship with the primary and secondary β-hydrogen atoms but not with the tertiary hydrogen atom (Scheme 9). Therefore, β-hydride elimination from *cis*-**VI** could form palladium olefin intermediates *cis*-**Va** or *cis*-**Vb** but not **Vc**. Olefin displacement from complexes *cis*-**Vb** and *cis*-**Va** would then form carbocycles **3** and **5**, respectively, to the exclusion of **4**. The facile rearrangement of *cis*-**Vb** prior to olefin displacement would form resting state *trans,trans*-**8** to the exclusion of *trans,cis*-**8**. Note that although the *trans*-**IV**:*cis*-**IV** ratio could not be measured directly, this value was mirrored by the *trans,trans*-**8**:*trans,cis*-**8** ratio due to the non-dissociative nature of the conversion of **IV** to **8** (Scheme 9).

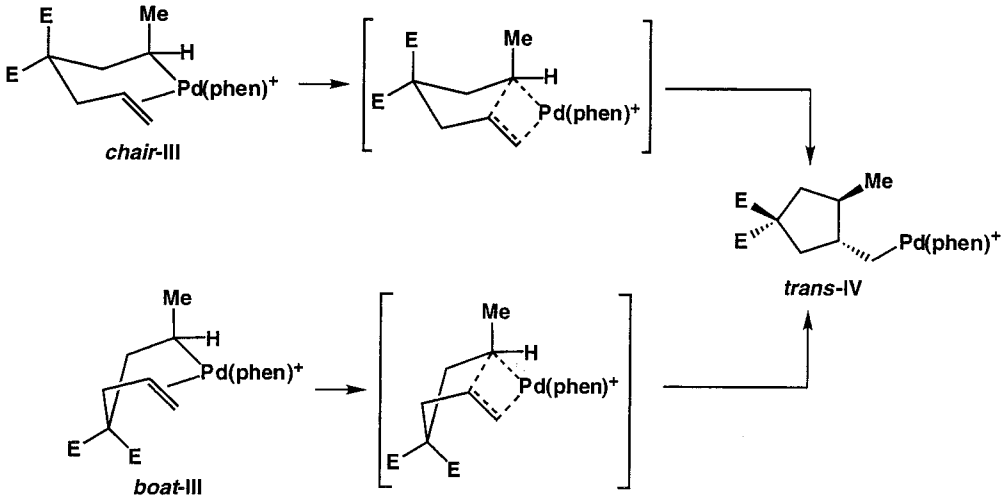
Initial cis-cyclization of **III** would lead to sequential formation of *cis*-**IV**, *trans*-**Va**, and *trans*-**VI** (Scheme 9). The palladium atom of *trans*-**VI** has or can adopt a syn relationship with a primary, secondary, or tertiary β-hydrogen atom and therefore, β-hydride elimination could regenerate *trans*-**Va** or form either *trans*-**Vb** or **Vc**. Olefin displacement from these complexes would then form carbocycles **3**−**5**. The facile rearrangement of *trans*-**Vb** prior to olefin displacement would form resting state *trans,cis*-**8** to the exclusion of *trans,trans*-**8**. Because the kinetic **3**:**4** selectivity of the cycloisomerization of **1** (30:1 at 40 °C, 6:1 at 70 °C) was higher than the trans-selectivity of carbocyclization (20:1 at 40 °C, 4:1 at 70 °C), *trans*-**VI** must serve as a source of both **3** and **4**; if *trans*-**VI** formed **4** to the exclusion of **3**, the kinetic **3**:**4** selectivity would equal the trans:cis selectivity of carbocyclization. From the values noted above, we calculate that *trans*-**VI** leads ultimately to the formation of a ∼1:2 mixture of **3**:**4**.[58]

The diastereoselectivity of carbocyclization protocols employing 1,6- and 1,7-dienes and related substrates has typically been rationalized by maximizing the number of pseudoequatorial substituents in a chair-like transition state for ring closure.[59] In this context, the high trans-selectivity for carbocyclization of **III** appears somewhat unusual as the transition state which would convert the chair-like palladium alkyl olefin intermediate **III** (*chair*-**III**) to palladium cyclopentylmethyl intermediate *trans*-**IV** requires a pseudoaxial α-methyl substituent (Scheme 10).[60] Such an intermediate and transition state appear particularly unfavorable due to the 1,3-diaxial interaction with a carbo-

(57) The stereochemical designators for intermediates **IV**−**VI** refer to the relationship between the palladium atom and the exocyclic methyl group.

(58) The equation used to determine the **3**:**4** ratio formed from *trans*-**VI** was the following: $30 = \{(20) + (1)(x)\}/(1)(1 - x)$, where 30 is the kinetic **3**:**4** ratio, 20 and 1 are the relative amounts of *cis*-**VI** and *trans*-**VI**, respectively, x is the fraction of *trans*-**VI** which forms **3**, and $1 - x$ is the fraction of *trans*-**VI** which forms **4**. Solving for x gives 0.33. This analysis assumes *cis*-**VI** forms exclusively **3** and *trans*-**VI** forms exclusively **3** and **4**. Because **5** is formed as a minor product in this transformation (∼4%), error introduced due to the formation of **5** should be minimal.

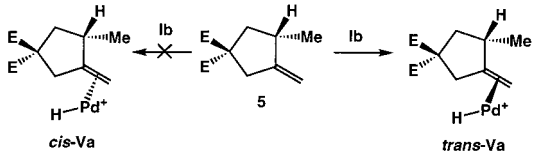
Scheme 10



methoxy group. In addition, because β-alkyl elimination has been observed only in the case of electrophilic d^0-metallocene complexes[61] and in strained cyclobutylmethyl complexes,[62] it is unlikely that the trans-selectivity of carbocyclization is established thermodynamically. Rather, we propose a boatlike conformation for both the alkyl olefin chelate complex **III** (*boat*-**III**) and the corresponding transition state for insertion. These boatlike conformations would presumably avoid the unfavorable 1,3-diaxial interactions present in the chairlike conformations. A boatlike conformation for the alkyl olefin chelate complex **III** is supported by DFT calculations of the analogous palladium diimine complex {(NH═CHCH═NH)Pd[η^1,η^2-CH(CH_2Me)-$CH_2C(Me)_2CH_2CH═CH_2$]}$^+$.[63]

The high trans selectivity of carbocyclization (**III** → *trans*-**IV**) accounts for the high kinetic **3**:**4** selectivity in the cycloisomerization of **1** but does not account for the high kinetic **3**:**5** selectivity (10:1 at 40 °C) as both *trans*-**IV** and *cis*-**IV** can lead to the formation of **5**. Rather, the **3**:**5** selectivity is presumably controlled by the relative rates of intramolecular olefin displacement from palladium olefin complexes **Vb** and **Va**, respectively. The rate of olefin displacement should depend on both the coordinating ability of the carbocyclic olefin and on the accessibility of the carbonyl oxygen atom to the palladium dz^2 orbital in complexes **V**. Although the second criterion is difficult to evaluate, consideration of olefin coordination ability alone, which should decrease in the order **5** (disubstituted) > **3** (trisubstituted) > **4** (tetrasubstituted),[49] accounts for the high kinetic **3**:**5** selectivity in the cycloisomerization of **1**. Consideration of olefin coordination ability also accounts for the preferential formation of **4** relative to **3** (**3**:**4** ≈1:2) from intermediate *trans*-**VI**.

Scheme 11



Isomerization of **5** in the presence of **1a** led to the formation of a 2.5:1 mixture of **4** and **3** at 40 °C (**4**:**3** = 2.8:1 at 70 °C). The close similarity of this ratio to the calculated ratio of **3**:**4** (∼1:2) formed from intermediate *trans*-**VI** suggests that reaction of **Ib** with free **5** forms predominantly *trans*-**Va** (as opposed to *cis*-**Va**) (Scheme 11). The selective formation of *trans*-**Va** from reaction of **Ib** and **5** is consistent with attack of **Ib** from the face opposite the proximal methyl group of **5**, as would be predicted on the basis of steric considerations.

Catalyst Activation. Conversion of the palladium methyl precatalyst **2** to the active palladium hydride catalyst **I** could occur by a series of transformations analogous to those depicted in Scheme 8, initiated by β-migratory insertion of an olefin of **1** into the Pd−Me bond of **2**. This hypothesis is supported by the close structural similarity between the byproducts of catalyst activation (**6**) and the products of catalysis (**3**−**5**) and also by the similar structures of the palladium cyclopentyl chelate complexes formed during catalyst activation (**7**) and during catalysis (**8**). The predominant (≥90%) formation of carbocycles **6** within the first two catalyst turnovers in the cycloisomerization of **1** catalyzed by **2** was consistent with the comparable rates of catalyst activation and turnover frequency. This conclusion is not surprising given the similar structures of complex **7** and resting state **8**.

Reversible β-Hydride Addition/Elimination. Formation of carbocycles **3**−**5** from resting state **8** requires facile interconversion of palladium olefin intermediates **V** via reversible β-hydride addition/elimination. Reversible conversion of intermediates **Va** and **VI** was independently established by the formation of significant amounts (63%) of the **5**-d_2 isotopomer in the cycloisomerization of **1**-2,6-d_2. For example, cyclization of intermediate **II**-d_2 and subsequent β-deuteride elimination from **IV**-d_2 would form palladium cyclopentyl intermediate **Va**-d_2

(59) (a) Molander, G. A.; Hoberg, J. O. *J. Am. Chem. Soc.* **1992**, *114*, 3123. (b) Molander, G. A.; Nichols, P. J. *J. Am. Chem. Soc.* **1995**, *117*, 4415. (c) Molander, G. A.; Nichols, P. J.; Noll, B. C. *J. Org. Chem.* **1998**, *63*, 2292. (d) Molander, G. A.; Retsch, W. H. *J. Org. Chem.* **1998**, *63*, 5507. (e) Berk, S. C.; Grossman, R. B.; Buchwald, S. L. *J. Am. Chem. Soc.* **1994**, *116*, 8593. (f) Lund, E. C.; Livinghouse, T. *J. Org. Chem.* **1989**, *54*, 4487. (g) Pagenkopf, B. L.; Lund, E. C.; Livinghouse, T. *Tetrahedron* **1995**, *51*, 4421. (h) Magnus, P.; Becker, D. P. *J. Am. Chem. Soc.* **1987**, *109*, 7495. (i) Negishi, E.-i.; Jensen, M. D.; Kondakov, D, Y.; Wang, S. *J. Am. Chem. Soc.* **1994**, *116*, 8404.

(60) Selective trans-carbocyclization (≥50:1) has also been observed in the closely related cyclization/hydrosilylation of dienes catalyzed by **2**.[35]

(61) (a) Watson, P. L.; Parshall, G. W. *Acc. Chem. Res.* **1985**, *18*, 51. (b) Horton, A. D. *Organometallics* **1996**, *15*, 2675.

(62) (a) Flood, T. C.; Statler, J. A. *Organometallics* **1984**, *3*, 1795. (b) Flood, T. C.; Bitler, S. P. *J. Am. Chem. Soc.* **1984**, *106*, 6076. (c) Ermer, S. P. Struck, G. E.; Bitler, S. P.; Richards, R.; Bau, R.; Flood, T. C. *Organometallics* **1993**, *12*, 2634. (d) Bunel, E.; Burger, B. J.; Bercaw, J. E. *J. Am. Chem. Soc.* **1988**, *110*, 976. (e) Pinke, P. A.; Miller, R. G. *J. Am. Chem. Soc.* **1974**, *96*, 4221. (f) Yang, X.; Jia, L.; Marks, T. J. *J. Am. Chem. Soc.* **1993**, *115*, 3392.

(63) These calculations indicated that the axial boat conformation was 3.1 kcal mol^{-1} more stable than was the axial chair conformation: Landis, C. R.; Feldgus, S. Unpublished results.

Scheme 12

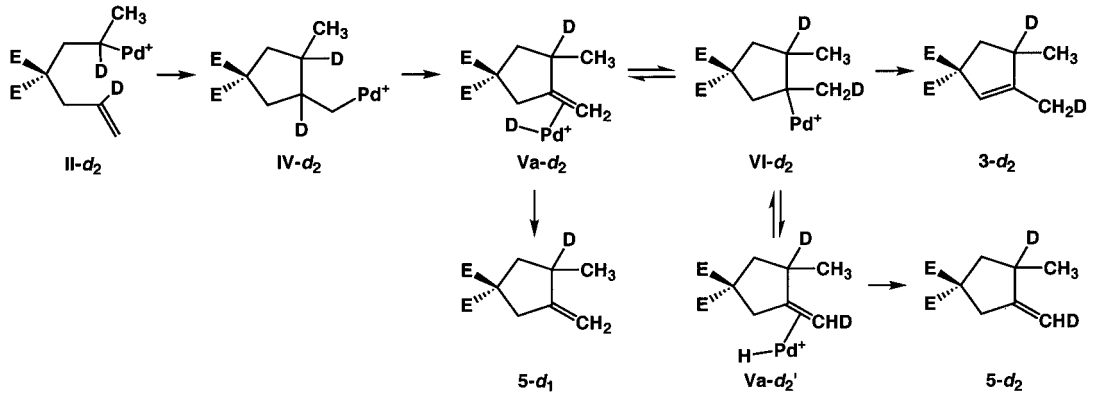
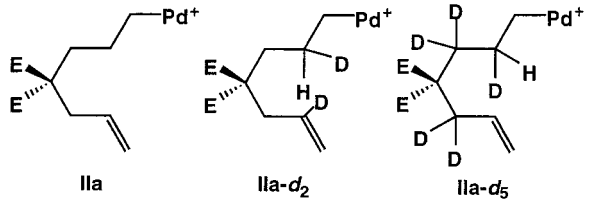


Chart 1



(Scheme 12). Because intermediate **Va**-d_2 possesses a palladium-bound deuterium atom, olefin displacement from **Va**-d_2 would form exclusively **5**-d_1. Alternatively, β-deuteride addition to **Va**-d_2 could form palladium cyclopentyl intermediate **VI**-d_2. β-Elimination of the primary deuterium atom from **VI**-d_2 would regenerate **Va**-d_2 while β-elimination of the primary hydrogen atom from **VI**-d_2 would form palladium olefin intermediate **Va**-d_2', which possesses a Pd−H group. Olefin displacement from **Va**-d_2' would then form **5**-d_2 (Scheme 12).[64]

Both 1,2- and 2,1-β-migratory insertion of α-olefins into the Pd−X (X = H, C, and Si) bonds of cationic palladium(II) alkyl complexes have been documented.[33,42,65] However, 1,2-insertion of **1a** to form the palladium primary alkyl intermediate **IIa** was not a significant process in the cycloisomerization of **1** (Chart 1). For example, reversible formation of **IIa**-d_2 and **IIa**-d_5 in the cycloisomerization of **1**-2,6-d_2 and **1**-3,3,5,5-d_4, respectively, would lead to the accumulation of both hydrogen and deuterium at the C(5) position of cyclopentene **3**-*d* formed in these reactions. Rather, ^{1}H NMR analysis of **3**-*d* isolated from the cycloisomerization of **1**-2,6-d_2 indicated ≤10% proton accumulation at the C(5) carbon atom while ^{1}H and ^{13}C NMR analysis of **3**-*d* isolated from the cycloisomerization of **1**-3,3,5,5-d_4 revealed no detectable deuterium accumulation at the C(5) position. In addition, the failure to observe intermolecular H/D scrambling of the unreacted dienes in the cocycloisomerization of **1a** and either **1**-2,6-d_2 or **1**-3,3,5,5-d_4 precludes reversible formation of **IIa**-*d* or **IIa**-d_5, respectively, coupled with olefin displacement from **Ia**-*d* (Chart 1).[66]

Intermolecular H/D Transfer. Mechanisms initiated by either hydrometalation (Scheme 8) or reductive cyclization have been postulated for the cycloisomerization of enynes and dienes.[1−20] A distinguishing feature between these mechanisms is that intermolecular H/D transfer is required in the former pathway but not in the latter.[67] Therefore, the substantial intermolecular H/D exchange which accompanied the cycloisomerization of **1**-3,3,5,5-d_4 is consistent with the proposed hydrometalation/carbometalation mechanism.[64] In accord with our proposed mechanism, formation of each molecule of **3**-*d* in the cycloisomerization of **1**-3,3,5,5-d_4 should also form a molecule of **Ib**-*d*, while formation of each molecule of **4**-*d* and **5**-*d* should generate a molecule of **Ib**, assuming no intramolecular scrambling (Scheme 13). Attack of **Ib** on **1**-3,3,5,5-d_4 would lead to the formation of **3**-d_3 (Scheme 13, X = H) while attack of **Ib**-*d* on **1**-3,3,5,5-d_4 would lead to the formation of **3**-d_4 (Scheme 13, X = D). In accord with this analysis, the 14:86 mixture of **3**-*d*:**4**-*d* + **5**-*d* formed in the cycloisomerization of **1**-3,3,5,5-d_4 was in fair agreement with the 28:72 ratio of **3**-d_3:**3**-d_4 isotopomers formed in this transformation (Table 4, entry 1).[39]

Intermolecular H/D was also evident in the cycloisomerization of a 1:1 mixture of **1**-3,3,5,5-d_4 and **1a**. In this case, a molecule of **Ib**-*d* should form with each molecule of **3**-*d*, while a molecule of **Ib** should form with each molecule of **3a**, **4a**, **5a**, **4**-*d*, and **5**-*d*, assuming no intramolecular scrambling. Attack of **Ib** on **1a** or **1**-3,3,5,5-d_4 would lead to the formation of **3a** or **3**-d_3, respectively, while attack of **Ib**-*d* on **1a** or **1**-3,3,5,5-d_4 would lead to the formation of **3a**-d_1 or **3**-d_4, respectively. In accord with this analysis, the 57:43 mixture of **3**-*d*:**4**-*d* + **5**-*d* + **3a** + **4a** + **5a** formed in the cycloisomerization of a 1:1 mixture of **1**-3,3,5,5-d_4 and **1a** was in good agreement with the ∼65:35 ratios of **3**-d_3:**3**-d_4 and **3a**:**3a**-d_1 isotopomers formed in this transformation (Table 4, entries 6 and 9).[39]

Conclusions

The mechanism shown in Scheme 8 is consistent with all our observations regarding the cycloisomerization of dimethyl diallylmalonate (**1**) catalyzed by **2** to form carbocycles **3**−**5**. The key steps in this mechanism include the β-migratory insertion of a coordinated olefin into the Pd−H bond of **Ia**, carbometalation of the resulting palladium alkyl olefin chelate complex **III** to form the palladium cyclopentylmethyl intermediate **IV**, isomerization of **IV** via rapid and reversible β-hydride

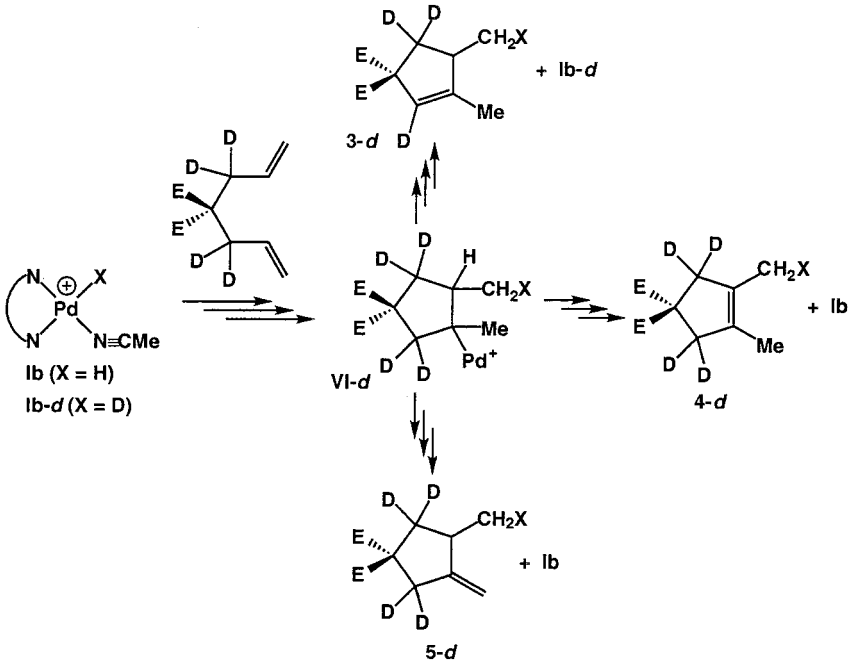
(64) Intermolecular deuterium transfer was not a significant process in the cycloisomerization of **1**-2,6-d_2 because formation of the major carbocyclic product (**3**-d_2) occurred with release of the Pd−H species **Ia**.

(65) Ittel, S. D.; Johnson, L, K.; Brookhart, M. *Chem. Rev.* **2000**, *100*, 1169.

(66) No experimental evidence implicating the reversible formation of a palladium 4-pentenyl intermediate, formed via elimination of the secondary β-hydride of **II** followed by olefin rotation and reinsertion, was obtained. Reversible formation of a palladium 4-pentenyl intermediate in the cycloisomerization of **1**-3,3,5,5-d_4 would presumably have led to the accumulation of hydrogen atoms at the C(4) carbon of **3**-*d*, which was not observed.

(67) Several additional experimental observations rule out reductive cyclization as a possible mechanism for the cycloisomerization of **1** catalyzed by **2**. For example, a reductive cyclization mechanism does not readily account for the formation of carbocycles **6** as byproducts of catalyst activation, nor is it consistent with the intermediacy of palladium cyclopentyl chelate complexes **7** and **8** in the conversion of **1** to **6** and **1** to **3**−**5**, respectively.

Scheme 13



addition/elimination to form a mixture of palladium olefin complexes **V**, and termination by displacement of the coordinated olefins of **V** with acetonitrile to form carbocycles **3**−**5** and palladium acetonitrile adduct **Ib**. Carbocycles **6** were presumably formed by a similar set of transformations initiated by β-migratory insertion of a coordinated olefin of **1** into the Pd−Me bond of precatalyst **2**.

Cyclopentenes **3** and **4** were formed both kinetically and via secondary isomerization of **5**. The kinetic pathway formed predominantly **3** (**3**:**4** = 30:1 at 40 °C) while secondary isomerization of **5** formed predominantly **4** (**3**:**4** = 1:2.5 at 40 °C); the kinetic pathway accounted for the majority (93% at 40 °C) of cyclopentene formation. Due to the selectivity of the respective pathways, the chiral cyclopentene **3** was formed nearly exclusively via the kinetic pathway, while the achiral cyclopentene **4** was formed to a significant extent via both pathways. The presence of these competing pathways led to a decrease in the **3**:**4** ratio and an increase in the **3**:**5** ratio with increasing consumption of **1**.

The cycloisomerization of **1** displayed high kinetic selectivity for the chiral cyclopentene **3** relative to the achiral cyclopentene **4** and the methylenecyclopentane **5**. The high kinetic **3**:**4** selectivity stemmed from the high trans selectivity of carbocyclization (**III** → *trans*-**IV**). Specifically, β-hydride elimination from *trans*-**IV** would form *cis*-**Va**, which would undergo β-hydride addition to form exclusively *cis*-**VI** (Scheme 9). Because the palladium atom of *cis*-**VI** had access to the primary and secondary but not the tertiary β-hydrogen atoms, β-hydride elimination from *cis*-**VI** would form palladium olefin intermediates *cis*-**Va** and *cis*-**Vb** to the exclusion of **Vc**. Olefin displacement from *cis*-**Va** and *cis*-**Vb** would then form carbocycles **5** and **3** without formation of **4**.

The selective kinetic formation of **3** relative to **5** required both facile β-hydride addition/elimination relative to olefin displacement and preferential displacement of **3** relative to **5** from palladium olefin intermediates **V**. Because β-hydride elimination from *trans*-**IV** formed exclusively *cis*-**Va**, olefin displacement prior to β-hydride addition would lead to the formation of **5** as the exclusive kinetic product of cycloisomerization, which was not observed (Scheme 8). Rather, facile β-hydride addition/elimination prior to displacement of **5** from *cis*-**Va** generated a rapidly interconverting mixture of *cis*-**Va** and *cis*-**Vb**. Because the disubstituted olefin **5** coordinates more strongly to palladium than does the trisubstituted olefin **3**, cyclopentene **3** is displaced more readily than is methylenecyclopentane **5**, leading to preferential formation of **3**.

Facile transfer of the palladium-bound hydride to the more substituted olefinic carbon atom of **Vb** coupled with carbonyl coordination formed the cyclopentyl chelate complex **8**, the only palladium species detected during catalysis (Scheme 8). However, **8** did not lie along the reaction pathway for the conversion of **1** to carbocycles **3**−**5**. Because of this, and because formation of **8** was both kinetically and thermodynamically favorable, **8** served to remove palladium from the catalytic cycle and retard the rate of cycloisomerization. Resting state **8** was consumed by turnover-limiting, intramolecular displacement of the coordinated olefins of **V** by a pendant carbonyl group to generate the palladium ester complexes **VII**. Complexes **VII** were subsequently trapped with acetonitrile to release the carbocyclic olefins **3**−**5** and form the palladium acetonitrile adduct **Ib** (Scheme 8).

Experimental Section

General Methods. All reactions were performed under an atmosphere of nitrogen by employing standard Schlenk techniques. NMR spectra were recorded on a Varian spectrometer operating at 400 MHz for ^{1}H and 100 MHz for ^{13}C at room temperature unless otherwise noted. IR spectra were obtained on a Bomen MB-100 FT IR spectrometer. Routine gas chromatography was performed on a Hewlett-Packard 5890 gas chromatograph equipped with a 25 m poly(dimethylsiloxane) capillary column. Flash chromatography was performed employing 200−400 mesh silica gel (EM). Elemental analyses were performed by Complete Analysis Laboratories (Parsippany, NJ). CH_2Cl_2 and 1,2-dichloroethane (DCE) were distilled from CaH_2 under nitrogen. CD_2Cl_2 and DCE-d_4 (Cambridge Isotope Labs) were distilled from CaH_2 under nitrogen, degassed, and stored in an inert-atmosphere glovebox. Benzene, acetonitrile, hexanes, and diethyl ether (Aldrich, anhydrous) were used as received.

Catalyst **2** was synthesized according to a published procedure and stored in a desiccator prior to use.[68] Dimethyl diallylmalonate and diethyl diallylmalonate (Lancaster) were used as received. $(^{13}COEt)_2$-Diethyl diallylmalonate was synthesized from reaction of 1,3-$^{13}C_2$-diethyl malonate (Aldrich), allyl bromide, and NaH in THF. Labeled dienes **1**-2,6-d_2 and **1**-3,3,5,5-d_4 were previously prepared in our laboratory.[18] The rates of the cycloisomerization of **1** catalyzed by **2** at 40 and 70 °C were performed in duplicate, and error limits for the corresponding rate constants refer to the deviation between the two runs. Error limits for the remaining rate constants refer to the standard deviation of the corresponding kinetic plot.

Cycloisomerization of 1 Catalyzed by 2. Diene **1** (105 mg, 0.49 mmol) was added via syringe to a solution of **2** (29 mg, 0.024 mmol), naphthalene (15 mg, 0.12 mmol), and CH_3CN (39 mg, 0.96 mmol) in DCE (10 mL), and the resulting solution was stirred at 40 ± 1 °C. Aliquots (100 μL) were removed via syringe at 60 min intervals, filtered through a small plug of silica gel, and analyzed by capillary GC. The concentrations of **1** and **3**−**6** were determined from the area of the respective peaks relative to naphthalene in the GC spectrum. A plot of [**1**] versus time was linear to ∼80% conversion with an observed rate constant of $k_{obs} = (7.1 \pm 0.3) \times 10^{-7}$ M s^{-1} (Figure 1). The concentration versus time plot for the cycloisomerization of **1** catalyzed by **2** at 70 °C was performed analogously (Figure S2) with an observed rate constant of $k_{obs} = (7.7 \pm 0.4) \times 10^{-6}$ M s^{-1}. At both 40 and 70 °C, multiple runs produced observed rate constants which differed by ≤7%.

Cycloisomerization of 1-2,6-d_2. A solution of **1**-2,6-d_2 (105 mg, 0.49 mmol) and **2** (29 mg, 0.025 mmol) in DCE (10 mL) was stirred at room temperature for 1 week to form a mixture of carbocycles **3**-*d*−**6**-*d*. The isotopic composition of carbocycles **3**-*d*−**5**-*d* was determined by GC/MS analysis of the crude reaction mixture (Table 3, entries 1−3). The crude reaction mixture was concentrated under vacuum and chromatographed (SiO_2; 24:1 hexanes−ether) to give **3**-d_2 (35 mg, 33%) with 97% isomeric purity and 95% isotopic purity. NMR and MS analysis were consistent with predominant (≥90%) formation of 3,3-bis(carbomethoxy)-5-deuterio-1-(deuteriomethyl)-5-methylcyclopentene (**3**-d_2). ^{1}H NMR (CD_2Cl_2): δ 5.39 (br s, 1 H), 3.69 (s, 3 H), 3.76 (s, 3 H), 2.71 (d, J = 14 Hz, 1 H), 1.90 (d, J = 14 Hz, 1 H), 1.70 [q, $J_{HD} = J_{HH}$ = 2.0 Hz, 2 H, −C(5)CH_2D], 1.03 (s, 3 H). ^{13}C{^{1}H} NMR (CD_2Cl_2): δ 172.4, 172.0, 150.2, 122.1, 65.8, 65.0, 52.6, 42.0 [s, −C(5)H], 41.7 [(t, J_{CD} = 19.8 Hz, −C(5)D], 40.6, 18.8 [s, −C(5)-CH_3], 18.6 [(t, J_{CD} = 19.4 Hz, C(5)−CH_2D], 14.1 [t, J_{CD} = 19.5 Hz, C(1)−CH_2D].

Cycloisomerization of a 1:1 Mixture of 1-2,6-d_2 and 1a. A solution of **1**-2,6-d_2 (105 mg, 0.49 mmol), **1a** (100 mg, 0.41 mmol), naphthalene (15 mg, 0.12 mmol), CH_3CN (39 mg, 0.96 mmol), and **2** (58.4 mg, 0.048 mmol) in DCE (10 mL) was heated at 70 °C and analyzed periodically by GC analysis. The relative concentrations of dienes **1**-2,6-d_2 and **1a** were determined from the area of the respective peaks relative to naphthalene in the GC spectrum. After 40 min, 60% of **1**-d_2 and 65% of **1a** had reacted. GC/MS Analysis after 70 min (∼80% conversion) provided the isotopic composition of unreacted dienes **1** and **1a** and carbocycles **3**-*d*−**5**-*d* and **3a**−**5a** (Table 3, entries 4−9). Cycloisomerization of a 1:1 mixture of **1**-3,3,5,5-d_4 and **1a** at 70 °C was performed analogously. After 30 min, 53% of **1**-3,3,5,5-d_4 and 49% of **1a** had reacted. GC/MS analysis at this time provided the isotopic composition of carbocycles **3**-*d*−**5**-*d* and **2a**−**5a** (Table 3, entries 6−10). GC/MS analysis after 80 min (∼90% conversion) provided the isotopic composition of dienes **1**-3,3,5,5-d_4 and **1a** (Table 4, entries 4 and 5).

Cycloisomerization of 1-3,3,5,5-d_4. A solution of **1**-3,3,5,5-d_4 (105 mg, 0.49 mmol) and **2** (29 mg, 0.024 mmol) in DCE (10 mL) was stirred at room temperature for 1 week to form a mixture of carbocycles **3**-*d*−**6**-*d*. The isotopic composition of carbocycles **3**-*d*−**5**-*d* was determined by GC/MS analysis of the crude reaction mixture (Table 4, entries 1−3). The crude reaction mixture was concentrated under vacuum and chromatographed (SiO_2; 24:1 hexanes−ether) to give **3**-*d* (20 mg, 19%) with 97% isomeric purity as a ∼2.6:1 mixture of 3,3-bis(carbomethoxy)-2,4,4-trideuterio-1,5-dimethylcyclopentene (**3**-d_3) and 3,3-bis(carbomethoxy)-2,4,4-trideuterio-5-(deuteriomethyl)-1-methylcyclopentene (**3**-d_4) as determined by NMR and MS analysis. ^{1}H NMR (CD_2Cl_2): δ 3.67 (s, 3 H), 3.65 (s, 3 H), 2.68 (t, J = 7 Hz, 1 H), 1.69 (s, 3 H), {1.04 [d, J_{HH} = 7.0 Hz, −C(5)CH_3], 1.02 [td, J_{HD} = 1.8 Hz, J_{HH} = 7.0 Hz, −C(5)CH_2D], ∼1:2.5, 3 H}. ^{13}C{^{1}H} NMR (CD_2Cl_2): δ 172.5, 172.0, 150.2, 122 (m), 52.6, 41.8, 40.5 (br), 18.9 [s, −C(5)CH_3], 18.6 [(t, J_{CD} = 19.1 Hz, −C(5)CH_2D], 14.4.

Stability of 3 under Reaction Conditions. DCE (10 mL), **1a** (16 mg, 0.065 mmol), and **3** (13 mg, 0.059 mmol), which contained traces of **4** (**3**:**4** = 56:1), were added sequentially to a mixture of **2** (16 mg, 0.013 mmol), naphthalene (4 mg, 0.03 mmol), and acetonitrile (25 μL, 0.5 mmol) at 25 °C. The solution was heated at 70 °C and monitored periodically by GC analysis. After 75 min, **1a** had been completely consumed and 0.5% of **3** had isomerized to **4**, as evidenced by the decrease in the **3**:**4** ratio from 56:1 to 45:1 as determined by GC analysis.

Stability of 5 under Reaction Conditions. Diene **1a** (100 mg, 0.41 mmol), **5** (105 mg, 0.5 mmol), and DCE (10 mL) were added sequentially to a mixture of **2** (55.5 mg, 0.05 mmol), naphthalene (15 mg, 0.12 mmol), and acetonitrile (50 μL, 0.96 mmol) at 25 °C. The resulting solution was heated at 40 °C and analyzed periodically by GC. After 12 h, 87% of **1a** and 20% of **5** had reacted to form a 2.5:1 mixture of **4**:**3** along with carbocycles resulting from cycloisomerization of **1a** (Figure S4). The stability of **5** under reaction conditions at 70 °C was determined analogously (Figure S5).

Isomerization of 5 in the Presence of 1-3,3,5,5-d_4. DCE (10 mL), **1**-3,3,5,5-d_4 (40 mg, 0.19 mmol), and **5a** (13 mg, 0.059 mmol) were added sequentially to a mixture of **2** (15 mg, 0.012 mmol), naphthalene (4 mg, 0.03 mmol), and acetonitrile (50 μL, 0.96 mmol) at 25 °C. The solution was heated at 70 °C and monitored periodically by GC analysis. Aliquots were removed at 10, 25, 50, and 70% consumption of **1**-3,3,5,5-d_4. GC/MS analysis of the aliquot removed after 70% conversion revealed no detectable deuterium incorporation into unreacted **5a**.

[(phen)PdCHCH(Me)CH(Et)CH$_2$C(COOMe)(COOMe)]$^+$ [BAr$_4$]$^-$ (7). A solution of dimethyl diallylmalonate (**1**) (18 mg, 0.08 mmol) and [(phen)Pd(Me)NCCH$_3$]$^+$[BAr$_4$]$^-$ (**2**) (89.5 mg, 0.07 mmol) in ether (25 mL) was stirred at room temperature for 1.5 h to form a yellow solution. Hexane (25 mL) was added, and the solution was cooled to 0 °C, concentrated to 20 mL under vacuum, and cooled to −20 °C for 4 days to give **7** (28 mg, 26%) as tan crystals. ^{1}H NMR (CD_2Cl_2): δ 8.93 (dd, J = 1.4, 4.8 Hz, 1 H), 8.85 (dd, J = 1.5, 5.0 Hz, 1 H), 8.63 (dt, J = 1.4, 9.3 Hz, 2 H), 8.07, 8.03 (ABq, J = 8.4 Hz, 2 H), 7.91 (m, 2 H), 7.71 (s, 8 H), 7.54 (s, 4 H), [4.17 (s), 4.16 (s), ∼2:1, 3 H], [3.78 (s), 3.77 (s), ∼2:1, 3 H], 2.81 (dd, J = 7.8, 13.6 Hz, 1 H), 2.50 (dd, J = 3.6, 10.4 Hz, 1 H), 1.72 (m, 3 H), [1.21 (d, J = 6.3 Hz), 1.07 (d, J = 6.3 Hz), ∼2:1, 3 H], [0.94 (t, J = 7.4 Hz), 0.88 (t, J = 6.9 Hz), ∼2:1, 3 H]; three cyclopentyl ring protons obscured. IR (KBr, cm^{-1}): 1720, 1607 (C=O). Anal. Calcd (found) for $PdC_{56}H_{40}N_2O_4BF_{24}$: C, 49.24 (48.84); H, 2.90 (2.69); N, 2.02 (2.08).

A single crystal of *trans*,*trans*-**7** obtained from the above preparation was analyzed by X-ray crystallography. Diffraction data were obtained with graphite-monochromated Mo Kα radiation (λ = 0.710 73 Å) on a Brüker SMART diffractometer using the ω scan mode (Tables 1, 2, and S1−S6; Figures 3 and S13). Of the 45 563 reflections, 8759 independent, observed reflections ($I > 2.5\sigma(I)$) were obtained with maximum *h*, *k*, *l* values of 15, 33, and 17, respectively. An absorption correction was applied (DASABS). The structure was refined by full matrix, least squares on F; H atoms were fixed, and all other atoms were refined anisotropically (Table 2).

[(phen)PdCHCH(Me)CH(Et)CH$_2$C(^{13}COOEt)(^{13}COOEt)]$^+$ [BAr$_4$]$^-$ [7a-(^{13}CO$_2$Et)$_2$]. Reaction of $(^{13}CO_2Et)_2$-dimethyl diallylmalonate [**1a**-$(^{13}CO_2Et)_2$] (8.1 mg, 0.03 mmol) and **2** (37 mg, 0.03 mmol) in CD_2Cl_2 at room temperature for 1 h led to complete consumption of **2** with formation of **7a**-$(^{13}CO_2Et)_2$ as the exclusive product as determined by ^{1}H NMR spectroscopy and was analyzed by ^{13}C NMR spectroscopy without isolation. ^{13}C{^{1}H} NMR (CD_2Cl_2): δ 191.1, 171.2.

(68) Brookhart, M.; Rix, F. C.; DeSimone, J. M. *J. Am. Chem. Soc.* **1992**, *114*, 5894.

Kinetics of the Formation of 7. An NMR tube containing **1** (18 mg, 0.08 mmol, 0.12 M), **2** (10 mg, 0.008 mmol, 0.015 M), and trimethylphenylsilane (0.13 mg, 0.001 mmol) in CD_2Cl_2 (0.57 mL) was monitored periodically by ^{1}H NMR spectroscopy at 25 °C. The concentration of **2** was determined by integrating the Pd−CH_3 resonance of **2** (δ 1.32) relative to the $SiMe_3$ resonance of trimethylphenylsilane (δ 0.0). The pseudo-first-order rate constant for the disappearance of **2** was determined from a plot of ln $[\mathbf{2}]_t/[\mathbf{2}]_0$ versus time where $k_{obs} = (4.6 \pm 0.1) \times 10^{-3}$ s^{-1} (Figure S11). Pseudo-first-order rate constants for the reaction of **1** and **2** were determined analogously at [**1**] = 0.072, 0.28, and 0.41 M. The second-order rate constant for the reaction of **1** and **2** to form **7** at 25 °C ($k = (2.1 \pm 0.3) \times 10^{-2}$ M^{-1} s^{-1}) was determined from a plot of pseudo-first-order rate constants versus [**1**] (Figure S12).

Thermolysis of 7. A solution of **7** (10 mg, 0.057 mmol), naphthalene (1.0 mg), and **1a** (10 μL, 0.04 mmol) in DCE (5 mL) was heated at 50 °C for 2 h to form a dark solution. The concentration of carbocycles **6** were determined from the area of the respective peaks in the GC spectrum relative to the peak of naphthalene. The GC response factor of carbocycles **6** relative to naphthalene was estimated from the GC response factor of **5** relative to naphthalene.

[(phen)PdCHCH(Me)CH(Me)CH$_2$C(COOMe)(COOMe)]$^+$ [BAr$_4$]$^-$ (8). A solution of **2** (10 mg, 0.008 mmol) and excess **1** (18 mg, 0.08 mmol) in DCE-d_4 at 50 °C was monitored periodically by ^{1}H NMR analysis. When 75% of **1** had been consumed, **8** constituted 8 ± 2% of the reaction mixture and was analyzed by ^{1}H NMR spectroscopy without isolation. ^{1}H NMR (DCE-d_4): δ 4.16 and 3.77.

[(phen)PdCHCH(Me)CH(Me)CH$_2$C(^{13}COOEt)(^{13}COOEt)]$^+$ [BAr$_4$]$^-$ [8a-(^{13}CO$_2$Et)$_2$]. Reaction of ($^{13}CO_2Et)_2$-diethyl diallylmalonate [**1a**-($^{13}CO_2Et)_2$] (10 mg, 0.04 mmol) and **2** (5 mg, 0.004 mmol) in CD_2Cl_2 at 50 °C was monitored periodically by ^{1}H NMR analysis. When 73% of **1a** had been consumed, **8a**-($^{13}CO_2Et)_2$ constituted ~10% of the reaction mixture and was analyzed by ^{13}C NMR spectroscopy without isolation. ^{13}C{^{1}H} NMR (DCE-d_4): δ 191.6 and 171.0.

Reaction of 8 with HSiEt$_3$. A solution of **2** (10 mg, 8.3×10^{-3} mmol), **1** (34 μL, 0.17 mmol), and phenyltrimethylsilane (~3 mg, 0.02 mmol) in DCE-d_4 (0.60 mL) was heated at 40 °C and monitored periodically by ^{1}H NMR spectroscopy. The extent of reaction was determined by integrating the allylic methylene resonances of **1** (δ 2.68) relative to the trimethylsilyl resonance of phenyltrimethylsilane (δ 0.0). After 5 h (~75% conversion), $HSiEt_3$ (5 μL, 0.31 mmol) was added via syringe, and the solution was stirred at 40 °C for an additional 4 h to form a dark solution containing carbocycles **3**−**6**, **9**, and **10**. The concentrations of carbocycles **9** and **10** were determined from the area of the peaks for **9** and **10** relative to the total area of the peaks for carbocycles **3**−**6**, **9**, and **10**. The GC response factor for silylated cyclopentane **9** relative to cyclopentene **3** was determined from a standard solution of **3** and **9**. The identity and diastereomeric purity of **10** were established by GC analysis and by co-injection of an authentic sample.[37]

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Supporting Information Available: Kinetic plots and tables of crystallographic data for *trans,trans*-**7**. This material is available free of charge via the Internet at http://pubs.acs.org.

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