Development, Synthetic Scope, and Mechanistic Studies of the Palladium-Catalyzed Cycloisomerization of Functionalized 1,6-Dienes in the Presence of Silane

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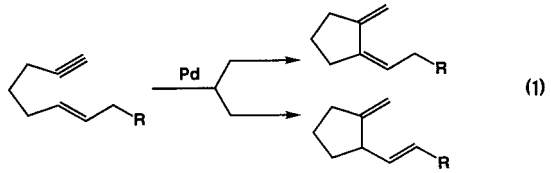
Received May 18, 2000

Abstract: A 1:1 mixture of the π-allyl palladium complex (η^3-C_3H_5)Pd(Cl)PCy_3 (**1a**) and NaB[3,5-C_6H_3-$(CF_3)_2$]$_4$ in the presence of $HSiEt_3$ catalyzed the cycloisomerization of diethyl diallylmalonate (**2b**) to form 4,4-dicarbomethoxy-1,2-dimethylcyclopentane (**3b**) in 98% yield with 98% isomeric purity. The procedure tolerated a range of functionality including esters, ketones, sulfones, protected alcohols, and substitution at the allylic and terminal olefinic carbon atoms. Cycloisomerization of **2b** obeyed zero-order kinetics to >3 half-lives with initial formation of 1,1-dicarboethoxy-4-methyl-3-methylenecyclopentane (**4b**), followed by secondary isomerization to **3b**. Deuterium labeling studies revealed that the conversion of **2b** to **4b** was accompanied by significant H/D exchange, consistent with an addition/elimination pathway coupled with facile H/D exchange of the Pd−H(D) intermediates with free silane.

Introduction

The transition metal-catalyzed cycloisomerization of enynes is an effective method for the synthesis of functionalized cyclopentane derivatives.[1,2] The most highly developed enyne cycloisomerization procedures use palladium (II) salts in conjunction with phosphine or bidentate nitrogen ligands as catalysts to form either dialkylidene cyclopentanes or alkenyl alkylidene cyclopentanes (eq 1).[2,3] Other transition metal complexes that have been used as enyne cycloisomerization catalysts include ruthenium complexes such as RuClH(CO)-$(PPh_3)_3$[4] and CpRu(COD)Cl,[5] polymer-bound nickel complexes,[6] and low-valent titanocene complexes.[7] Related transformations include the cycloisomerization/rearrangement of 1,6- or 1,7-enynes to form alkenylcycloalkenes catalyzed by the dimeric ruthenium complex $[RuCl_2(CO)_3]_2$ (eq 2),[8] and the Rh(I)-catalyzed cycloisomerization of dienynes[9] or vinylcyclopropyl alkynes[10] to form more complex polycyclic products.



The development of diene cycloisomerization has lagged behind enyne cycloisomerization because most enyne cycloisomerization catalysts display little reactivity toward dienes. However, neutral scandocene[11] and cationic zirconocene[12] complexes catalyze the cycloisomerization of unfunctionalized dienes (eq 3), although the synthetic utility of these procedures is limited by the high oxophilicity and excessive air and moisture sensitivity of the catalysts. Similarly, early attempts to catalyze diene cycloisomerization with Pd or Rh salts required forcing conditions in an acidic medium.[13] However, selective diene cycloisomerization under mild conditions has been demonstrated recently. For example, Ru(I),[14] Ni(II),[15,16] or Ti(II)[17] complexes

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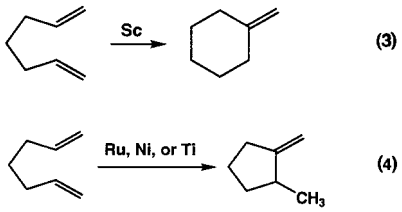
10.1021/ja001730+ CCC: $19.00
Published on Web 09/27/2000

catalyze the selective cycloisomerization of 1,6-dienes to form methylenecyclopentanes in good yield (eq 4). In contrast, a general and selective catalyst for the isomerization of 1,6-dienes to cyclopentenes has not been identified.[18,19] Here we report the development, synthetic scope, and mechanistic studies of a palladium-catalyzed, silane-promoted procedure for the selective conversion of 1,6-dienes to 1,2-disubstituted cyclopentenes under mild conditions.[20]



Results

Identification of an Active Catalyst System. We recently reported several related procedures for the cyclization/hydrosilylation of functionalized dienes catalyzed by cationic palladium phenanthroline[21] and pyridine-oxazoline complexes.[22] These complexes were initially targeted as diene cyclization/hydrosilylation catalysts because of their high activity as catalysts for olefin dimerization,[23] ethylene/CO copolymerization,[24] and olefin hydrosilylation.[25] Likewise, the cationic π-allyl palladium complex $[(\eta^3\text{-}C_3H_5)Pd(OEt_2)PCy_3]^+ [BAr_4]^-$ [Ar = 3,5-C_6H_3-$(CF_3)_2$] (**1**) catalyzes the dimerization of methyl acrylate,[26] and was therefore considered as a potential cyclization/hydrosilylation catalyst. However, complex **1** failed to catalyze diene cyclization/hydrosilylation and instead catalyzed the highly selective cycloisomerization of 1,6-dienes to 1,2-dimethylcyclopentenes. For example, treatment of dimethyl diallylmalonate (**2a**), with an excess of triethylsilane (1.5 equiv) and a catalytic amount of **1** [generated in situ from a 1:1 mixture of $(\eta^3\text{-}C_3H_5)$-Pd(Me)PCy_3 and $HBAr_4{\cdot}OEt_2$][26] (5 mol %) formed an initially colorless solution which darkened rapidly after 15 min at room temperature. Evaporation of solvent and chromatography of the residue gave 4,4-dicarbomethoxy-1,2-dimethylcyclopentene (**3a**) as the exclusive product in 89% yield as a 49:1 mixture of isomers (Scheme 1).

Scheme 1

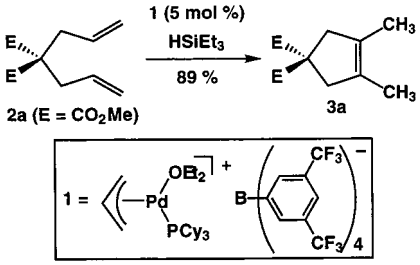
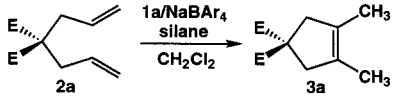


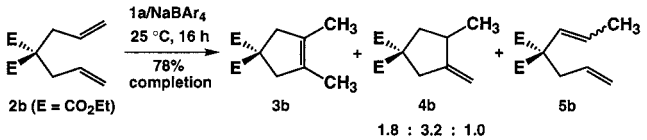
Table 1. Cycloisomerization of **2a** in the Presence of Silane (1.5 equiv) and a Catalytic 1:1 Mixture of **1a** and $NaBAr_4$ (5 mol %) at 25 °C in CH_2Cl_2 as a Function of Silane



entry	silane	time	yield (%)[a]	isomer ratio[b]
1	$HSiEt_3$	20 min	86	48:1
2	$HSiMe_2Ph$	20 min	74	22:1
3	$HSiMe_2Et$	10 min	95	52:1
4	$HSiMe_2t$-Bu	12 h	92	14:1

[a] Yield refers to isolated material of >95% purity. [b] Determined by capillary GC.

Scheme 2



Cationic palladium phenanthroline and pyridine-oxazoline catalysts used in diene cyclization/hydrosilylation were generated in situ either from protonation of dimethyl precatalysts (N−N)$PdMe_2$ with $HBAr_4{\cdot}OEt_2$ or by halide abstraction from methyl chloride precatalysts (N−N)Pd(Cl)Me with $NaBAr_4$.[21,22] In general, the latter method produced cleaner reaction mixtures and also benefited from the enhanced thermal stability and greater availability of the precatalysts. In a similar manner, halide abstraction from the palladium chloride complex $(\eta^3\text{-}C_3H_5)$-Pd(Cl)PCy_3 (**1a**) with $NaBAr_4$ generated an active diene cycloisomerization catalyst.[27] For example, reaction of **2a** with $HSiEt_3$ and a catalytic mixture of **1a** and $NaBAr_4$ for 20 min at room temperature led to complete consumption of the starting material and isolation of **3a** in 86% yield as 48:1 mixture of isomers (Table 1, entry 1).

Although not consumed in the reaction, silane was crucial for efficient and selective palladium-catalyzed diene cycloisomerization. For example, treatment of diethyl diallylmalonate (**2b**) with a catalytic mixture of **1a** and $NaBAr_4$ in the absence of $HSiEt_3$ led to 78% completion after 16 h at room temperature to form a 1.8:3.2:1.0 mixture of **3b**, 1,1-dicarboethoxy-3-methyl-4-methylenecyclopentane (**4b**), and 4,4-dicarboethoxy-1,5-heptadiene (**5b**), which together accounted for >90% of the products (Scheme 2). Products **4b** and **5b** were identified by gas chromatography-mass spectrometry (GCMS) and comparison to authentic samples. Use of substoichiometric amounts of $HSiEt_3$ led to inefficient and unselective cycloisomerization. Dimethylphenylsilane and dimethylethylsilane also served as

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(18) Rajanbabu has reported 74% selectivity (91% yield) for the conversion of **2a** to **3a** catalyzed by a 1:2:2 mixture of $[(\eta^3\text{-}C_3H_5)PdCl]_2$, AgOTf, and $P(4\text{-}C_6H_4OMe)_3$.[15]

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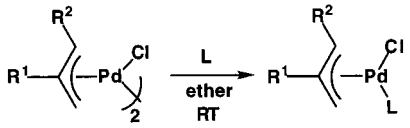
(27) The catalyst generated from $(\eta^3\text{-}C_3H_5)Pd(Me)PCy_3$ and $HBAr_4{\cdot}OEt_2$ must differ slightly from that generated from **1a** and $NaBAr_4$, because no ether is present in $NaBAr_4$ used in the latter protocol. In this latter case, the vacant coordination site on palladium presumably is occupied by some other weakly coordinated ligand such as solvent, water, or silane.

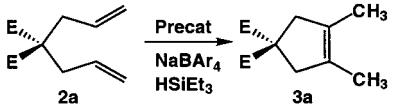
Table 2. Synthesis of π-Allyl Palladium Chloride Precatalysts **1a**−**1o**



R^1	R^2	L	precatalyst	yield (%)
H	H	$P(Cy)_3$	**1a**	86[a]
Ph	H		**1b**	79
Me	H		**1c**	70
H	Me		**1d**	70
H	H	$P(cyclopentyl)_3$	**1e**	72
		$P(i\text{-}Pr)_3$	**1f**	88
		$P(n\text{-}Bu)_3$	**1g**	84[a]
		PPh_3	**1h**	90[b]
		$P(o\text{-}tolyl)_3$	**1i**	83
		$P(OPh)_3$	**1j**	95
		$P(Oi\text{-}Pr)_3$	**1k**	81
		$P(t\text{-}Bu)_3$	**1l**	78
		pyridine	**1m**	85
		$P(t\text{-}Bu)_2(2\text{-}C_6H_4Ph)$	**1n**	78
		$P(Cy)_2(2\text{-}C_6H_4Ph)$	**1o**	88

[a] Previously reported in ref 26. [b] Previously reported in ref 48.

Table 3. Palladium-Catalyzed (5 mol %) Cycloisomerization of **2a** in the Presence of $HSiEt_3$ (1.2−1.5 equiv) at 25 °C in CH_2Cl_2 as a Function of Palladium Precatalyst



entry	precatalyst	time	yield (%)[a]	isomer ratio[b]
1	**1b**	20 min	94	26:1
2	**1c**	15 min	91	44:1
3	**1d**	50 min	95	31:1
4	**1e**	10 min	98	>50:1
5	**1f**	10 min	88	>50:1
6	**1g**	1 h	74	2.6:1
7	**1h**	12 h	86	0.5:1
8	**1i**	30 min	91	2.1:1
9	**1j**	12 h	87	0.6:1
10	**1k**	1.5 h	86	1.1:1
11	**1l**	12 h	NR	−
12	**1m**	12 h	NR	−
13	**1n**	12 h	NR	−
14	**1o**	12 h	NR	−

[a] Yield refers to isolated material of >95% purity. [b] Determined by capillary GC, refers to the ratio of **3a** to the sum of all other isomers.

effective promoters for the cycloisomerization of **2a** (Table 1, entries 2 and 3), whereas dimethyl-*tert*-butylsilane led to a dramatic drop in reaction rate although yield and selectivity remained high (Table 1, entry 4).

Effect of Precatalyst Structure on Cycloisomerization. The efficiency and selectivity of transition metal-catalyzed processes can be strongly affected by the nature of the ancillary ligands on the metal complex. Because of this, the efficiency of palladium-catalyzed cycloisomerization was probed as a function of the ligands on the π-allyl palladium precatalyst. The requisite π-allyl palladium complexes **1a** − **1o** were prepared by reaction of the π-allyl palladium chloride dimer with the appropriate ligand in ether at room temperature (Table 2). Concentration of solvent followed by filtration gave the desired complexes as off-white or pale yellow solids,[28] and new complexes were characterized by spectroscopy and elemental analysis. ^{1}H NMR of all new phosphine-substituted complexes displayed five resonances corresponding to the unique protons of the static π-allyl ligand. In contrast, the ^{1}H NMR spectra of the phosphite-substituted complexes **1j** and **1k** displayed a quintet at δ 5.0 (J = 10.2 Hz) corresponding to the central allylic hydrogen atom and a broad resonance between δ 4.5 and 2.0 corresponding to the four time-averaged terminal allylic protons. A process involving $\pi-\sigma-\pi$ interconversion of the allyl ligand coupled with rotation about the C−C single bond of the σ-allyl intermediate is sufficient to exchange all four terminal allylic protons.[29]

The rate, yield, and selectivity of cycloisomerization was relatively insensitive to substitution on the palladium-bound allyl group. For example, complexes that possessed an internal phenyl (**1b**) or methyl group (**1c**) or a terminal methyl group (**1d**) on the allyl ligand all served as effective precatalysts for the cycloisomerization of **2a** to form **3a** in >90% yield with >95% isomeric purity (Table 3, entries 1−3). GCMS analysis of the crude reaction mixtures of the cycloisomerization of **2a** using catalysts **1a**−**1d** revealed no detectable formation of byproducts other than small amounts of hexaethyldisiloxane. For example, neither allyl triethylsilane nor any higher molecular weight organosilanes were detected in the isomerization of **2a** in the presence of $HSiEt_3$ catalyzed by **1a**/$NaBAr_4$ (10 mol %). Similarly, neither α-methylstyrene nor any hydrogenation, hydrosilylation, or dimerization products of α-methylstyrene were detected in the reaction of **2a** with $HSiEt_3$ catalyzed by **1b**/$NaBAr_4$ (10 mol %).

In contrast to the relative insensitivity of cycloisomerization with respect to the allyl ligand, the rate, yield, and selectivity of palladium-catalyzed cycloisomerization was highly sensitive to the nature of the phosphine ligand. Specifically, only complexes that possessed a tri(secondary alkyl) phosphine such as **1a** [L = PCy_3], **1e** [L = $P(cyclopentyl)_3$], and **1f** [L = $P(i\text{-}Pr)_3$] catalyzed the selective conversion of **2a** to **3a** (Table 3, entries 4 and 5). In contrast, use of palladium precatalysts that possessed a $P(n\text{-}Bu)_3$ (**1g**), triarylphosphine (**1h**, **1i**), or phosphite (**1j**, **1k**) ligand led to a precipitous drop in selectivity for **3a** although yields remained high (Table 3, entries 6−10). Palladium complexes that possessed a $P(t\text{-}Bu)_3$ (**1l**), pyridine (**1m**), or $P(2\text{-}C_6H_4Ph)R_2$ [R = *t*-Bu (**1n**), Cy (**1o**)] ligand failed to catalyze the cycloisomerization of **2a** (Table 3, entries 11−14).

Scope of Cycloisomerization. A range of functionalized 1,6-dienes underwent cycloisomerization in the presence of $HSiEt_3$ (1.2 equiv) and a catalytic 1:1 mixture of $NaBAr_4$ and either **1a** or **1e** (5 mol %) to form 1,2-disubstituted cyclopentenes in good yield with high selectivity (Table 4). For example, dienes which possessed homoallylic ester, ketone, acetoxy, or pivaloyl groups (**2b**−**2d**, and **7**−**13**) underwent palladium-catalyzed cycloisomerization within 20 min at room temperature to form the corresponding 1,2-disubstituted cyclopentenes **3b**−**3d**, and **14**−**20** in >70% yield with high selectivity (Table 4, entries 1−13). The sulfonyl-substituted dienes **21** and **22** also cyclized to form 1,2-disubstituted cyclopentenes **23** and **24**, albeit with somewhat diminished selectivity (Table 4, entries 14 and 15). Dienes that possessed only one homoallylic substituent did not undergo efficient cycloisomerization, presumably because of the absence of a kinetic Thorpe−Ingold effect.[30] In addition, dienes that did not possess at least one homoallylic oxygenated group

(28) Complex **1g** was isolated as a viscous, pale yellow oil and was >95% pure as determined by NMR spectroscopy, but had been previously reported as a white solid.[26] This difference presumably stems from the isomeric purity of the $P(n\text{-}Bu)_3$ used in the respective syntheses of **1g**.

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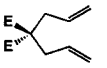
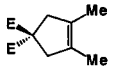
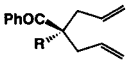
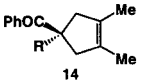
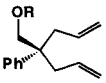
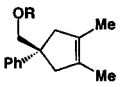
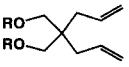
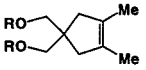
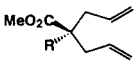
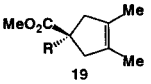
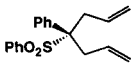
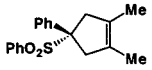
Table 4. Cycloisomerization of 4,4-Disubstituted 1,6-Dienes Catalyzed by a 1:1 Mixture of $NaBAr_4$ and **1a** or **1e** (5 mol %) in the Presence of $HSiEt_3$ (1.2−1.5 equiv) at 25 °C

entry	diene	conditions[a]	carbocycle	yield (%)[b]	isomeric ratio[c]
					
1	2b (E = CO_2Et)	A	3b	98	50:1
2	2c (E = CO_2Bn)	A	3c	82	50:1
3	2d (E = CO_2t-Bu)	B	3d	71	44:1
					
4	7 (R = Ph)	B	14	95	48:1
					
5	8 (R = COMe)	A	15	85	36:1
6	9 (R = CO*t*-Bu)	A	16	89	35:1
7		B		95	24:1
					
8	10 (R = COMe)	A	17	99	52:1
9		B		96	48:1
10	11 (R = CO*t*-Bu)	A	18	89	60:1
11		B		88	48:1
					
12	12 (R = Ph)	A	19	79	19:1
13	13 (R = COMe)	A	20	89	50:1
14	21 (R = SO_2Me)	B	23	86	9.8:1
					
15	22	B	24	76	7.6:1

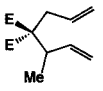
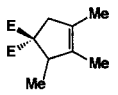
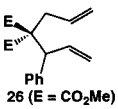
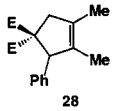
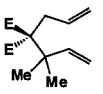
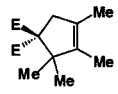
[a] A = **1a**/$NaBAr_4$ in CH_2Cl_2; B = **1e**/$NaBAr_4$ in 1,2-dichloroethane. [b] Yield refers to isolated material of >95% purity. [c] Determined by capillary GC.

failed to undergo efficient cycloisomerization, as observed in palladium-catalyzed diene cyclization/hydrosilylation.[21,22]

Palladium-catalyzed diene cycloisomerization also tolerated allylic substitution. For example, dienes which possessed an allylic methyl (**25a**, **25b**) or phenyl (**26**) group isomerized to form the corresponding cyclopentenes (**27**−**28**) in good yield and with good selectivity (Table 5, entries 1−3). Isomerization of dienes **25** and **26** led to no detectable formation of the isomeric cyclopentenes in which the double bond occupied the α,β-position relative to the quaternary carbon atom, even though these carbocycles would also possess a tetrasubstituted olefin. Dienes which possessed disubstitution at an allylic carbon atom such as the gem-dimethyl-substituted **29** also underwent efficient palladium-catalyzed cycloisomerization forming cyclopentene **30** in 82% yield (Table 5, entry 4).

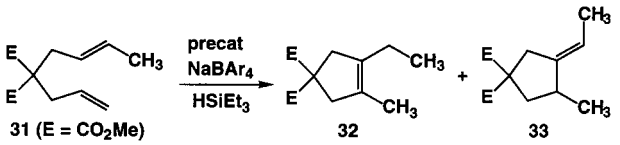
Under the conditions described above, palladium-catalyzed cycloisomerization of dienes which possessed an internal olefin gave poor selectivity. For example, treatment of 4,4-dicarbomethoxy-1,6-octadiene (**31**) with a 1:1 mixture of **1a** and $NaBAr_4$ in the presence of $HSiEt_3$ (1.5 equiv) led to the formation of a 3:1 mixture of the expected cyclopentene **32** and 1,1-dicarbomethoxy-3-ethylidene-4-methylcyclopentane (**33**) in 84% combined yield (Table 6, entry 1). Use of precatalysts **1e**

Table 5. Cycloisomerization of Allylic-Substituted 1,6-Dienes Catalyzed by a 1:1 Mixture of $NaBAr_4$ and **1a** or **1e** (5 mol %) in the Presence of $HSiEt_3$ (1.2−1.5 equiv) at 25 °C

entry	diene	conditions[a]	carbocycle	yield (%)[b]	isomeric ratio[c]
					
1	25a (E = CO_2Me)	A	27a	82	52:1
2	25b (E = CO_2Et)	B	27b	83	49:1
3	 26 (E = CO_2Me)	A	 28	71	39:1
4	 29 (E = CO_2Me)	A	 30	82	23:1

[a] A = **1a**/$NaBAr_4$ in CH_2Cl_2; B = **1e**/$NaBAr_4$ in 1,2-dichloroethane. [b] Yield refers to isolated material of >95% purity. [c] Determined by capillary GC.

Table 6. Palladium-Catalyzed (5 mol %) Cycloisomerization of **31** in the Presence of $HSiEt_3$ in CH_2Cl_2 as a Function of Precatalyst, Temperature, and [$HSiEt_3$]



entry	precatalyst	temp (°C)	time	[$HSiEt_3$] (M)	yield (%)[a]	32:33[b]
1	**1a**	25	20 min	0.075	84	3:1
2	**1e**	25	20 min	0.075	86	1:1
3	**1f**	25	20 min	0.075	84	1:1
4	**1a**	25	12 h	0.075	88	1:1
5	**1a**	70[c]	5 min	0.075	89	1:1
6	**1a**	25	12 h	0.20	77	6:1
7	**1a**	25	12 h	0.40	83	31:1

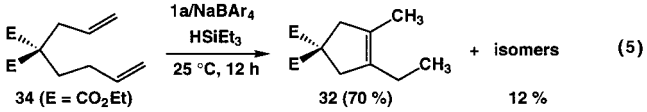
[a] Yield refers to isolated material of >95% purity. [b] Determined by capillary GC. [c] Solvent = 1,2-dichloroethane.

or **1f**, or increasing the reaction time or temperature did not lead to a significant increase in the selectivity for cyclopentene **32** (Table 6, entries 2−5). In contrast, the selectivity for cyclopentene **32** increased with increasing silane concentration (Table 6, entries 6 and 7). For example, in the presence of an 8-fold excess of silane, isomerization of **31** at room temperature overnight led to the isolation of **32** in 83% yield with >96% selectivity (Table 6, entry 7).

In contrast to the highly selective cycloisomerization of 1,6-dienes to form cyclopentenes, palladium-catalyzed cycloisomerization of 1,7-dienes did not lead to the selective formation of cyclohexenes. For example, reaction of 4,4-dicarboethoxy-1,7-octadiene (**34**) with triethylsilane and a 1:1 mixture of **1a**/$NaBAr_4$ at room temperature overnight led to the isolation of an 82:7:6:1 mixture of cyclopentene **32** and three unidentified isomers in 82% combined yield (eq 5). Repeated chromatography of the mixture led to the isolation of pure **32** in 46% yield, which was identical with the sample of **32** isolated from cycloisomerization of diene **31**.[31] The predominant formation of **32** from **34** presumably results from initial isomerization to **31** followed by cyclization (see below).

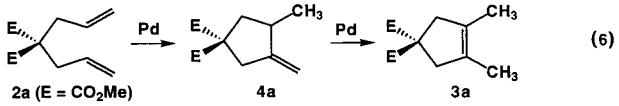
(30) (a) DeTar, D. F.; Luthra, N. P. *J. Am. Chem. Soc.* **1980**, *102*, 4505. (b) Kirby, A. J. *Adv. Phys. Org. Chem.* **1980**, *17*, 208. (c) Eliel, E. L. *Stereochemistry of Carbon Compounds*; McGraw-Hill: New York, 1962; p 106.

(31) Other substrates that failed to undergo effective palladium-catalyzed cycloisomerization include terminally disubstituted and internally substituted 1,6-dienes, and 1,6-enynes and diynes.



(5)

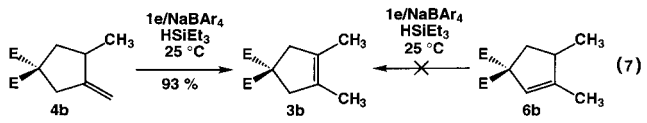
Intermediates in the Conversion of 2 to 3. Transition metal-catalyzed cycloisomerization of a 1,6-diene typically forms the corresponding methylenecyclopentane as the primary product.[11−19] Furthermore, the cycloisomerization of diene **31** in the presence of 1.5 equiv of silane produced considerable amounts of ethylenecyclopentane **33** (Table 6, entries 1−5). Therefore, it appeared likely that methylene cyclopentanes were general intermediates in the palladium-catalyzed cycloisomerization of 1,6-dienes. In accord with this hypothesis, GC analysis of the cyclization of **2a** in the presence of $HSiEt_3$ (1.2 equiv) and **1a**/$NaBAr_4$ (5 mol %) at room temperature after 10 min revealed that 84% of **2a** had been consumed with the formation of a 19:1 mixture of **4a**:**3a** (eq 6). After 20 min, **2a** had been completely consumed with the exclusive (>98%) formation of **3a**.



(6)

To gain more detailed information concerning the formation and consumption of intermediates in the conversion of **2** to **3**, the reaction of **2b** (0.05 M), $HSiEt_3$ (0.095 M), and a 1:1 mixture of **1a** and $NaBAr_4$ (2.5 mM) at 0 °C was monitored periodically by GC. A plot of [**2b**] versus time was linear to >3 half-lives with a zero-order rate constant of $k = 8.1 \times 10^{-5}$ s^{-1} ($t_{1/2}$ = 103 min) (Figure S1).[32] After 150 min, 72% of **2b** had reacted without formation of detectable quantities of **3b**. Rather, the products consisted of a 12:1 mixture of **4b** and **5b**, which accounted for >97% of the products. The relative concentration of **4b** reached a maximum of 80% after 225 min, and then decreased rapidly to <3% after 255 min with the concomitant formation of cyclopentene **3b** (Figure 1). A plot of [**4b**] versus time from 225 to 255 min (Figure S2) provided a lower limit for the rate of disappearance of **4b** of $k \geq 5 \times 10^{-4}$ s^{-1} ($t_{1/2} \leq$ 17 min), which is ≥ 6 times faster than the initial disappearance of **2b**. In comparison, the relative concentration of intermediate **5b** rose to a maximum of ∼4% after ∼100 min, remained relatively constant until approximately 240 min, and then disappeared during the next 20 min (Figure 1).

The isomerization of methylenecyclopentane **4b** to cyclopentene **3b** under reaction conditions occurred at a significant rate only after the concentration of **2b** had decreased to approximately 10% (≤ 5 mM) of its original concentration, which suggests that the isomerization of **4b** was inhibited by excess **2b**. In accord with this hypothesis, treatment of an authentic sample of **4b** with triethylsilane (1.2 equiv) and a catalytic mixture of **1e**/$NaBAr_4$ at room temperature in the absence of **2b** led to immediate darkening of the solution and complete isomerization within 1 min with the isolation of **3b** in 93% yield as a 60:1 mixture of isomers (eq 7). This



(7)

isomerization of **4b** to **3b** is ∼10 times faster than conversion of **2b** to **3b** under comparable conditions (Table 3, entry 4),

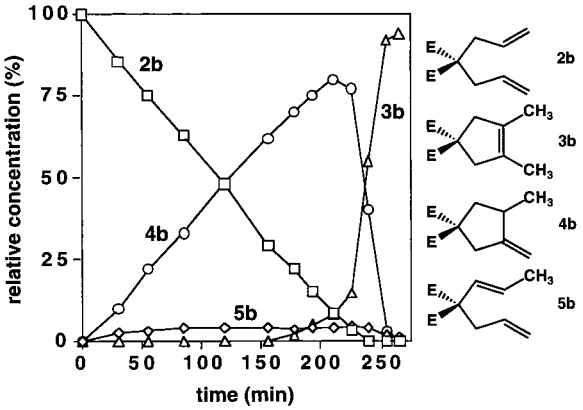


Figure 1. Concentration versus time plot for the conversion of **2b** (0.05 M) to **3b**, **4b**, and **5b** in the presence of $HSiEt_3$ (0.075 M) and a catalytic mixture of **1a**/$NaBAr_4$ (2.5 mM) in CH_2Cl_2 at 0 °C.

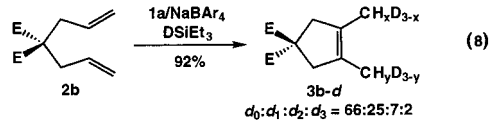
consistent with the relative rates of the isomerization of **2b** to **4b** and **4b** to **3b** under reaction conditions.

In contrast to methylenecyclopentane **4b**, the isomeric cyclopentene 3,3-dicarbomethoxy-1,5-dimethylcyclopentene (**6b**) was neither observed in the conversion of **2b** to **3b**, nor did an authentic sample of **6b** isomerize to **3b** under reaction conditions (eq 7). In addition, both the conversion of **2b** to **3b** and **4b** to **3b** were accompanied by rapid darkening of the reaction mixture upon consumption of **4b**. The resulting dark solutions were catalytically inactive and addition of either **2b** or **4b** to these dark solutions led to no detectable formation of **3b**.

Deuterium Scrambling in the Conversion of 2 to 3. Our attempts to probe the mechanism of diene cycloisomerization by spectroscopic analysis of catalytic mixtures proved largely unsuccessful, partly because of the large excess of silane (relative to catalyst) required for efficient cycloisomerization, which obscured key resonances. Therefore, we turned to deuterium-labeling studies to gain information on the mechanism of palladium-catalyzed cycloisomerization. In one experiment, reaction of **2b** (0.5 M), $DSiEt_3$ (0.95 M), and a 1:1 mixture of **1a**/$NaBAr_4$ (2.5 mM) at 0 °C was monitored periodically by GC. Little change was observed in the concentration of **2b** early in the reaction, and then after ∼30 min the rate of reaction increased and followed zero-order decay to ∼90% conversion (Figure S3). The zero-order rate constant ($k = 8.8 \times 10^{-5}$ s^{-1}, $t_{1/2}$ = 95 min) obtained from the linear portion of the slope was not significantly (<10%) different from the rate obtained in the presence of $HSiEt_3$.

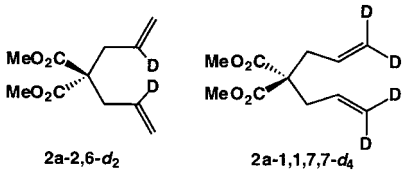
A preparative scale isomerization of **2b** in the presence of $DSiEt_3$ and **1a**/$NaBAr_4$ led to the isolation of carbocycle **3b**-*d* in 92% yield (eq 8). Analysis of **3b**-*d* by ^{13}C and ^{2}H NMR spectroscopy was consistent with deuterium incorporation exclusively into the exocyclic methyl groups with the formation of multiple isotopomers. For example, the ^{13}C NMR spectrum displayed a singlet at δ 13.5 and a 1:1:1 triplet at δ 13.2 (J = 19 Hz, isotopic shift = 270 ppb), corresponding to exocyclic CH_3 and CH_2D groups, along with several resonances upfield of the 1:1:1 triplet. Similarly, the ^{2}H NMR spectrum of **3b**-*d* displayed a ∼1:3:2 ratio of resonances at δ ∼1.64, 1.61, and 1.58 (isotopic shift ≈ 30 ppb). Mass spectral analysis of **3b**-*d* established a 66:25:7:2 ratio of d_0, d_1, d_2, and d_3 isotopomers with an average of 0.45 deuterium atoms per molecule (eq 8).

(32) Additional silane had little effect on the reaction rate. For example, a 4-fold increase in silane concentration ([$HSiEt_3$] = 0.38 M) in the isomerization of **2** at 0 °C led to <15% increase in the reaction rate ($k = 9.2 \times 10^{-5}$ s^{-1}).



(8)

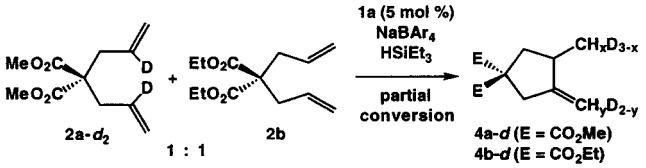
Several additional labeling experiments were performed with use of deuterated dienes and $HSiEt_3$. For example, cycloisomerization of 4,4-dicarbomethoxy-2,6-dideuterio-1,6-heptadiene (**2a**-2,6-d_2) in the presence of $HSiEt_3$ led to isolation of 4,4-dicarbomethoxy-1,2-dimethylcyclopentene (**3a**-*d*) in 92% yield as a 23:38:28:11 mixture of d_0-d_3 isotopomers (1.28 D/molecule). Similarly, palladium-catalyzed isomerization of 4,4-dicarbomethoxy-1,1,7,7-tetradeutero-1,6-heptadiene (**2a**-1,1,7,7-d_4) in the presence of $HSiEt_3$ led to the isolation of **3a**-*d* in 82% yield as a 3:17:27:30:15:2 mixture of d_1-d_6 isotopomers (3.25 D/molecule).



Deuterium Scrambling in the Conversion of 2 to 4. The H/D exchange detected in the conversion of **2** to **3** represented the cumulative scrambling that had occurred in all the steps leading up to the formation of **3**. Therefore, H/D exchange was studied in each step independently. In one experiment, cyclization of a 1:1 mixture of **2a**-2,6-d_2 and **2b** in the presence of $HSiEt_3$ (1.2 equiv) and **1a**/$NaBAr_4$ (5 mol %) at 0 °C was monitored periodically by GCMS analysis (Table 7). After 13% conversion (30 min), unreacted dienes **2a**-2,6-d_2 and **2b** and carbocycle **4b** had undergone ~15% H/D exchange, consisting of 83% **2a**-d_2, 86% **2b**-d_0, and 91% **4b**-d_0, respectively (Table 7). In contrast, carbocycle **4a** had lost a considerable amount of deuterium and consisted predominantly (84%) of the **4a**-d_1 isotopomer (Table 7). GCMS analysis of the reaction at 70% conversion revealed considerable isotopic scrambling of all species in the reaction mixture (Table 7).

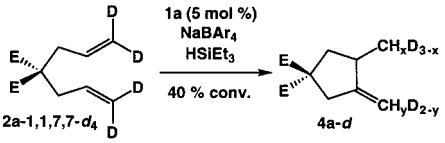
In a second experiment, GCMS analysis of the isomerization of the tetradeuteride **2a**-1,1,7,7-d_4 in the presence of $HSiEt_3$ (1.2 equiv) and **1a**/$NaBAr_4$ (5 mol %) at 40% conversion revealed

Table 7. Isotopic Composition of **2a**, **2b**, **4a**, and **4b** Formed in the Partial Conversion of a 1:1 Mixture of **2a**-2,6-d_2 and **2b** to **4a** and **4b** in the Presence of $HSiEt_3$ (1.2 equiv) and a 1:1 Mixture of **1a** and $NaBAr_4$ (5 mol %) in CH_2Cl_2 at 0 °C



compound	conversion (%)	deuterium per molecule	isotopic composition d_0	d_1	d_2	d_3
recovered **2a**	13	1.87	0	15	83	2
4a	13	1.14	2	82	16	0
recovered **2b**	13	0.16	86	11	3	0
4b	13	0.11	91	7	2	0
recovered **2a**	70	1.47	10	38	41	9
4a	70	0.98	20	64	14	2
recovered **2b**	70	1.11	27	44	26	4
4b	70	0.41	64	29	6	1

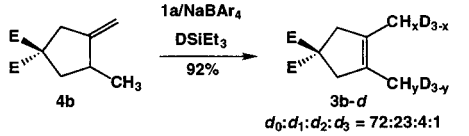
Scheme 3



compound	D/molecule	isotopic composition d_1	d_2	d_3	d_4	d_5	d_6
recovered 2a	3.25	4	15	35	38	6	2
4a-*d*	3.32	2	6	46	22	16	2

significant H/D exchange in both the unreacted diene and in the methylenecyclopentane **4a**-*d* (Scheme 3).

Deuterium Scrambling in the Conversion of 4 to 3. The isomerization of methylenecyclopentane **4** to cyclopentene **3** was also accompanied by isotopic scrambling. For example, treatment of **4b** with $DSiEt_3$ (1.2 equiv) and **1a**/$NaBAr_4$ (5 mol %) at room temperature for 10 min led to the isolation of **3b** as a 72:23:4:1 mixture of d_0-d_3 isotopomers which contained an average of 0.34 deuterium atoms per molecule of **3b** (eq 9). A second experiment established that all H/D exchange occurred prior to formation of **3**. Specifically, a 1:1 mixture of diene **2b** and cyclopentene **3a** were reacted with $DSiEt_3$ (1.2 equiv) and a 1:1 mixture of **1a**/$NaBAr_4$ (5 mol %) for 20 min at room temperature to form a 1:1 mixture of **3a** and **3b**. GCMS analysis of the reaction mixture after 40 min (approximately twice the time required for complete conversion of **2b** to **3b**) revealed no significant (<2%) deuterium incorporation into recovered **3a**.



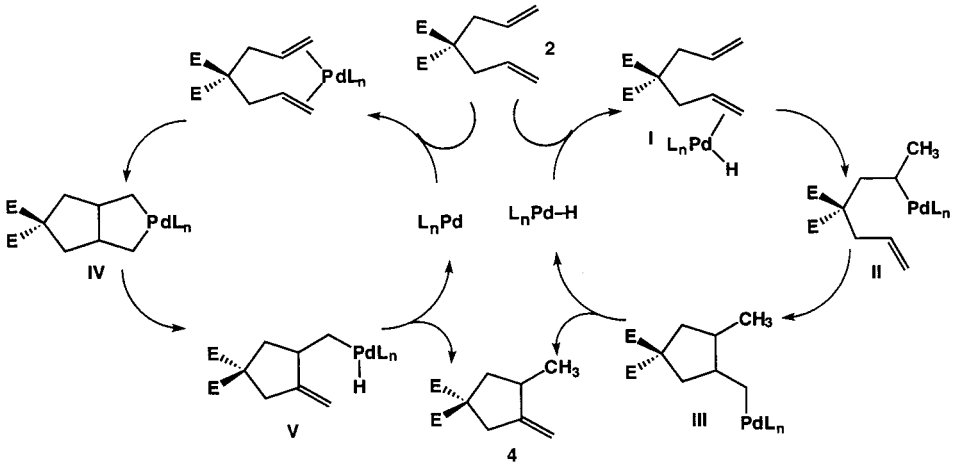
(9)

Discussion

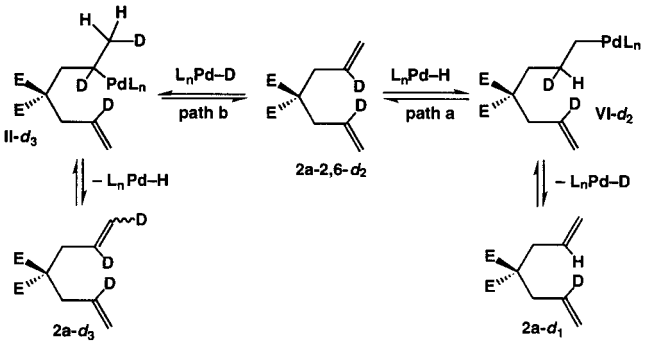
Possible Mechanisms for the Conversion of 2 to 4. Mechanisms involving both intramolecular carbometalation and reductive cyclization have been postulated for the cycloisomerization of enynes and dienes.[1-19] These two mechanisms were also considered in the conversion of **2** to **4**. For example, coordination of an olefin of **2** to a palladium hydride species (L_nPd-H) would generate palladium hydride olefin intermediate **I**, which could undergo β-migratory insertion to form palladium alkyl olefin intermediate **II** (Scheme 4, right cycle). Coordination and insertion of the pendant olefin into the Pd−C bond would generate palladium cyclopentylmethyl intermediate **III**, which could undergo β-hydride elimination to form **4** and regenerate the palladium hydride species. In the second mechanism, coordination of diene **2** to a palladium complex (L_nPd) followed by reductive cyclization would form the palladacyclopentene intermediate **IV** (Scheme 4, left cycle). β-Hydride elimination from **IV** would form the palladium alkyl hydride complex **V**, which could undergo reductive elimination to form **4**.

The considerable H/D exchange observed in the cyclization of **2** to **4** is consistent with the intermediacy of palladium hydride complexes that undergo facile H/D exchange with free silane. Because both the carbometalation and oxidative cyclization mechanisms invoke palladium-hydride intermediates, this observation does not distinguish between the two pathways. However, the isotopic composition of the dienes recovered from reaction of **2a**-2,6-d_2/**2b** with $HSiEt_3$ is not in accord with H/D exchange via the oxidative cyclization mechanism. For example,

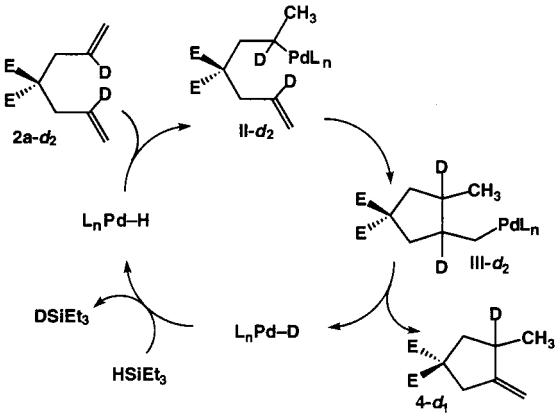
Scheme 4



Scheme 5



Scheme 6



even if all the steps in the oxidative cyclization mechanism preceding reductive elimination were reversible,[33] and H/D exchange of intermediate **V** with silane were fast, only the two internal olefinic H/D atoms of the diene would undergo exchange (Scheme 4). Therefore, the recovery of significant amounts of **2a**-d_3 (9%) and **2b**-d_3 (4%) from the reaction of **2a**-2,6-d_2/**2b** with $HSiEt_3$ at 70% conversion (Table 7) and the significant scrambling of the terminal olefinic deuterium atoms of **2a**-1,1,7,7-d_4 recovered from the reaction with $HSiEt_3$ (Scheme 3) are not in accord with H/D exchange via the oxidative cyclization mechanism.[34]

The isotopic composition of the dienes recovered from reaction of **2a**-2,6-d_2/**2b** or **2a**-1,1,7,7-d_4 with $HSiEt_3$ is consistent with exchange via an addition/elimination pathway. For example, reversible 1,2-hydrometalation of **2a**-2,6-d_2 via the palladium (primary alkyl) intermediate **VI**-d_2 would lead to H/D exchange of the internal olefinic positions with formation of **2a**-d_1 and L_nPd-D (Scheme 5, path a). Reversible 2,1-deuteriometalation of **2a**-2,6-d_2 with L_nPd-D released in the transformation above could lead to formation of **2a**-d_3 via palladium (secondary alkyl) intermediate **II**-d_3 (Scheme 5, path b).[35] An analogous series of insertion/elimination reactions would also exchange the olefinic H/D atoms of diene **2a**-1,1,7,7-d_4. Unfortunately, the addition/elimination process that leads to exchange of the olefinic H/D atoms of **2** is not necessarily related to the process that converts **2** to **4**, as the two events could occur in separate reaction manifolds.[36] Nevertheless, these experiments support the carbometalation pathway by providing evidence for palladium alkyl complex **II**, a key intermediate in the carbometalation mechanism.

An H/D exchange process that is clearly tied to the cycloisomerization of **2** to **4** is the significant loss of deuterium in the conversion of **2a**-2,6-d_2 to **4a** in the presence of $HSiEt_3$ early in the reaction (Table 7). The carbometalation mechanism accounts for this behavior provided that H/D exchange between palladium deuteride intermediates and silane early in the reaction is fast and essentially complete. For example, successive hydrometalation and carbometalation of **2a**-2,6-d_2 would form palladium alkyl intermediate **III**-d_2, which could undergo β-deuteride elimination to form **4a**-d_1 and L_nPd-D (Scheme 6). The palladium-deuteride intermediate could then undergo H/D

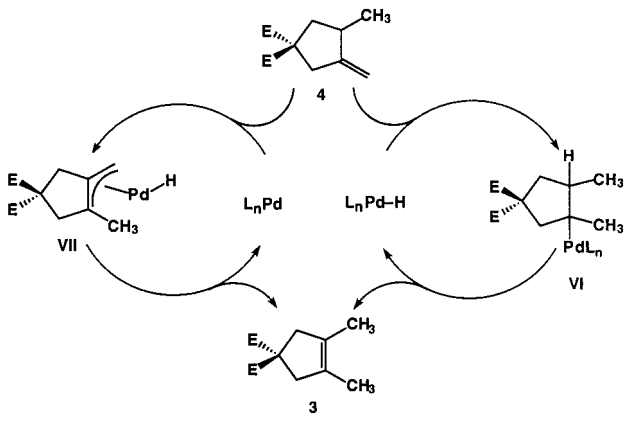
(33) Grubbs, R. H.; Miyashita, A. *J. Organomet. Chem*. **1978**, *161*, 371. (b) Grubbs, R. H.; Miyashita, A. *J. Am. Chem. Soc*. **1978**, *100*, 1301. (c) Grubbs, R. H.; Miyashita, A.; Liu, M.; Burk, P. *J. Am. Chem. Soc*. **1978**, *100*, 2418. (d) McLain, S. J.; Wood, C. D.; Schrock, R. R. *J. Am. Chem. Soc*. **1979**, *101*, 4558. (e) Knight, K. S.; Wang, D.; Waymouth, R. M.; Ziller, J. *J. Am. Chem. Soc*. **1994**, *116*, 1845. (f) Taber, D. F.; Louey, J. P.; Lim, J. A. *Tetrahedron Lett*. **1993**, *34*, 2243.

(34) For the observed scrambling to result from the reductive cyclization mechanism, a reversible ring contraction of palladium alkyl hydride intermediate **V** involving a palladacyclobutane intermediate would be required. For examples of ring contraction from metallacyclopentanes see: (a) Yang, G. K.; Bergman, R. G. *Organometallics* **1985**, *4*, 129. (b) Smith, G.; Milan, S. J.; Schrock, R. R. *J. Organomet. Chem*. **1980**, *202*, 269. (c) Schrock, R. R.; McLain, S.; Sanch, J. *Pure Appl. Chem*. **1980**, *52*, 729 (d) McLain, S. J.; Sancho, J.; Schrock, R. R. *J. Am. Chem. Soc*. **1980**, *102*, 5610.

(35) Both 1,2- and 2,1- insertion of α-olefins into the Pd−C bonds of cationic palladium(II) alkyl complexes have been documented with the regioselectivity determined by the steric and electronic nature of the olefin: Ittel, S. D.; Johnson, L, K.; Brookhart, M. *Chem. Rev*. **2000**, *100*, 1169.

(36) For example, the palladium alkyl hydride intermediate **V** or a palladium-hydride impurity could be responsible for the observed H/D exchange. For such an example see: Thorn, M. G.; Hill, J. E.; Waratuke, S. A.; Johnson, E. S.; Fanwick, P. E.; Rothwell, I. P. *J. Am. Chem. Soc*. **1997**, *119*, 8630.

Scheme 7



exchange with free silane to regenerate L_nPd-H, which would then attack a second molecule of **2a**-2,6-d_2 (Scheme 6).[37,38] The overall process would result in the loss of one deuterium atom per **2a**-2,6-d_2 → **4a**-d_1 cycle. However, the likely conditions of incomplete H/D exchange of the Pd-D intermediate with $HSiEt_3$ or exchange of the olefinic H/D atoms of the diene prior to cyclization would result in the loss of <1 deuterium atom in the conversion of **2a**-2,6-d_2 to **4a**, as was observed experimentally (Table 7).

Possible Mechanisms for the Conversion of 4 to 3. Olefin isomerization catalyzed by soluble transition metal complexes has been studied extensively,[39] and mechanisms involving addition/elimination[40] or 1,3-hydrogen migration have been established.[41] In a similar manner, the isomerization of **4** to **3** could occur via initial hydrometalation of the exocyclic methylene group of **4** to the palladium cyclopentyl intermediate **VI** followed by β-elimination of the tertiary hydride to form **3** (Scheme 7). Alternatively, oxidative addition of tertiary allylic hydrogen of **4** could form the palladium π-allyl hydride intermediate **VII** followed by reductive elimination to form **3** and regenerate L_nPd (Scheme 7). Either of these pathways could account for the scrambling observed in the conversion of **4b** to **3b** in the presence of $DSiEt_3$. However, because H/D exchange in the conversion of **2** to **4** occurred via an addition/elimination pathway, it is also likely that an addition/elimination pathway is responsible for H/D exchange and isomerization of **4** to **3**.

Kinetics and Role of Silane. The zero-order disappearance of **2b** under reaction conditions is consistent with the formation of a catalyst−substrate adduct which undergoes turnover-limiting unimolecular reaction to form product **4b** (saturation kinetics). This kinetic behavior also appears consistent with the failure of methylenecyclopentane **4b** to isomerize to **3b** in the presence of significant concentrations (≥5 mM) of **2b**. Specifically, a monosubstituted olefin of diene **2b** should coordinate more strongly with palladium than does the 1,1-disubstituted olefin of **4b**.[42] Therefore, when the concentration of **2b** is sufficiently high (≥5 mM), the bulk of the catalyst is tied up as a catalyst−substrate adduct and unavailable for the isomerization of **4b** to **3b**. Possible candidates for the catalytic resting state in the carbometalation pathway are the palladium alkyl olefin intermediates **II** or **III**, either of which could be further stabilized by coordination of a pendant carbonyl group (Scheme 4).[35]

The dramatic increase in the rate of diene cycloisomerization upon addition of silane points to activation of the precatalyst by silane, perhaps by hydride donation to palladium. For example, the induction period observed in the cyclization of **2b** in the presence of $DSiEt_3$ is consistent with H(D)−Si bond cleavage during catalyst activation, and deuterium-labeling experiments established the intermediacy of Pd−H(D) complexes. In addition, organosilanes, including triethylsilane, have been employed as hydride donors in the palladium-catalyzed reductive cyclization of enynes and diynes.[43] However, if palladium hydride complexes are formed by hydride donation from silane, the mechanism of this transfer remains unclear. For example, the direct reaction of a silane with a cationic palladium π-allyl complex to form a palladium-hydride complex seems unlikely.[44,45] Furthermore, no direct or indirect evidence for the formation of palladium hydride complexes was obtained from spectroscopic analysis of mixtures of **1a**/$NaBAr_4$, $HSiEt_3$, and **2a**, or from product analysis of the crude reaction mixtures.

Several experimental observations suggest that excess silane also serves to stabilize the active palladium catalyst, which facilitates the secondary isomerization of alkylidene cyclopentane to cyclopentene. For example, poor selectivity in the cycloisomerization of **2** was observed when <1 equiv of silane (relative to diene) was used. Similarly, the selectivity for the formation of cyclopentene **32** from the cycloisomerization of **31** increased with increasing silane concentration, but not with increasing reaction time or temperature (Table 6). Triethylsilane has been shown to bind to the cationic palladium (II) fragment $[(phen)Pd(SiEt_3)]^+$ and is readily displaced by an olefin.[25] In a similar manner, excess silane could perhaps stabilize the palladium-hydride catalyst responsible for secondary isomerization by serving as a weakly bonded ligand.

Conclusions

A 1:1 mixture of (η^3-C_3H_5)Pd(Cl)PR_3 [R = Cy (**1a**), cyclopentyl (**1e**), or *i*-Pr (**1f**)] and $NaB[3,5\text{-}C_6H_3(CF_3)_2]_4$ in the presence of a stoichiometric amount of $HSiEt_3$ catalyzed the cycloisomerization of functionalized 1,6-dienes to form 1,2-disubstituted cyclopentenes in good yield with high selectivity. Effective cycloisomerization required both a tri(secondary alkyl)

(37) Under the reaction conditions, L_nPd-H would also be produced from the concurrent cyclization of **2b**.

(38) The loss of deuterium in the conversion of **2a**-2, 6-d_2 to **4a** can also be accounted for by the reductive cyclization mechanism. For example, β-deuteride elimination from palladacyclopentane **IV**-d_2 would form the palladium deuteride **V**-d_2. H/D exchange of the deuteride ligand of **V**-d_2 with free silane could generate **V**-d_1, and subsequent reductive elimination would form **4**-d_1.

(39) Parshall, G. W.; Ittel, S. D. *Homogeneous Catalysis*, 2nd ed.; John Wiley & Sons: New York, 1992; pp 10−23.

(40) Orchin, M. *Adv. Catal*. **1966**, *16*, 1. (b) Andrieux, J.; Barton, D. H. R.; Patin, J. *J. Chem. Soc., Perkin Trans. 1* **1977**, 359. (c) Tolman, C. A. *J. Am. Chem. Soc*. **1972**, *94*, 2994. (d) Tolman, C. A.; McKinney, R. J.; Seidel, W. C.; Druliner, J. D.; Stevens, W. R. *Adv. Catal.* **1985**, *33*, 1. (e) Bingham, D.; Webster, D. E.; Wells, P. B. *J. Chem. Soc., Dalton Trans.* **1974**, 1514. (f) Bingham, D.; Webster, D. E.; Wells, P. B. *J. Chem. Soc., Dalton Trans.* **1974**, 1519. (f) Cramer, R. *J. Am. Chem. Soc*. **1966**, *88*, 2272. (g) Cramer, R. *Acc. Chem. Res*. **1968**, *1*, 186.

(41) (a) Bingham, D.; Hudson, B.; Webster, D. E.; Wells, P. B. *J. Chem. Soc., Dalton Trans.* **1974**, 1521. (b) Tuner, M.; Jouanne, J. V.; Brauer, H.-D.; Kelm, H. *J. Mol. Catal*. **1979**, *5*, 425. (c) Tuner, M.; Jouanne, J. V.; Brauer, H.-D.; Kelm, H. *J. Mol. Catal*. **1979**, *5*, 433. (d) Tuner, M.; Jouanne, J. V.; Brauer, H.-D.; Kelm, H. *J. Mol. Catal*. **1979**, *5*, 447.

(42) Hegedus, L. S. *Transition Metals in the Synthesis of Complex Organic Molecules*; University Science Books: Mill Valley, CA, 1994; p 50.

(43) (a) Trost, B. M.; Rise, F. *J. Am. Chem. Soc*. **1987**, *109*, 3161. (b) Trost, B. M.; Lee, D. C. *J. Am. Chem. Soc*. **1988**, *110*, 7255.

(44) A palladium-hydride complex could be generated through metathesis of the H−Si bond of the silane with the Pd−C σ-bond of the allyl ligand or by oxidative addition of the silane H−Si bond. However, metathesis of a silane with an electrophilic late-transition metal alkyl complex typically forms a M-Si complex,[25,45] whereas it seems unlikely that a palladium (IV) alkyl hydride complex would be stable with respect to C−H reductive elimination.

(45) (a) Burger, P.; Bergman, R. G. *J. Am. Chem. Soc*. **1993**, *115*, 10462. (b) Brookhart, M.; Grant, B. E. *J. Am. Chem. Soc*. **1993**, *115*, 2151. (c) Marciniec, B.; Pietraszuk, C. *Organometallics* **1997**, *16*, 4320.

phosphine ligand on the palladium precatalyst and a stoichiometric amount of silane. The procedure tolerated a range of functionality including esters, ketones, sulfones, and protected alcohols. However, dienes which possessed only one homoallylic substituent or did not possess at least one homoallylic oxygenated group failed to undergo efficient cycloisomerization. Cycloisomerization also tolerated substitution at the allylic and terminal olefinic position of the diene, although a 6-fold excess of silane was required for good selectivity in the latter case.

Palladium-catalyzed cycloisomerization of diethyl diallylmalonate (**2b**) obeyed zero-order kinetics to >3 half-lives with initial formation of 1,1-dicarboethoxy-4-methyl-3-methylenecyclopentane (**4b**) along with traces (≤4%) of 4,4-dicarboethoxy-1,5-heptadiene (**5b**). The zero-order disappearance of **2b** was indicative of the rapid formation of a substrate−catalyst adduct which underwent turnover-limiting intramolecular rearrangement to form **4b**. The relative concentration of **4b** increased to ∼80% of the reaction mixture and then underwent secondary isomerization ≥6 times faster than the initial disappearance of **2b** to form 4,4-dicarbomethoxy-1,2-dimethylcyclopentene (**3b**). The unusual accumulation/consumption behavior of **4b** appeared to result from both the saturation kinetics and the greater coordinating ability of **2b** relative to **4b**. Specifically, in the presence of significant concentration of **2b** (≥5 mM), rapid and quantitative formation of the catalyst−substrate adduct rendered the active catalyst unavailable for isomerization of **4b** to **3b**.

Deuterium-labeling experiments involving **2b** with $DSiEt_3$ or deuterated dienes **2a**-2,6-d_2 or **2a**-1,1,7,7-d_2 with $HSiEt_3$ revealed that conversion of **2** to **4** led to considerable exchange of the olefinic H/D atoms of recovered diene **2** as well as the exocyclic H/D atoms of carbocycle **4**. These data were consistent with H/D exchange via an addition/elimination pathway coupled with rapid H/D exchange of the Pd−H(D) intermediates with free silane. Although H/D exchange did not necessarily occur within the same reaction manifold as the conversion of **2** to **4**, these experiments provided support for the palladium alkyl complex **II**, a key intermediate in the carbometalation pathway. Furthermore, the carbometalation mechanism was consistent with all of our observations concerning isotopic exchange in the conversion of **2** to **4** and **4** to **3**.

Silane served dual roles in the palladium-catalyzed cycloisomerization of 1,6-dienes. First, silane activated the π-allyl palladium precatalyst, perhaps via hydride donation, to generate an active species which catalyzed the cycloisomerization of the diene to the alkylidene cyclopentane. Second, silane stabilized the active palladium hydride catalyst which facilitated the secondary isomerization of the alkylidene cyclopentane to the cyclopentene.

Experimental Section

General Methods. All reactions were performed under an atmosphere of nitrogen using standard Schlenk techniques. NMR were obtained at 300 MHz for ^{1}H and 75 MHz for ^{13}C in $CDCl_3$ unless otherwise noted. 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 E+R Microanalytical Laboratories (Parsippany, NJ). Methylene chloride and 1,2-dichloroethane (DCE) were distilled from CaH_2 under nitrogen. Dimethyl and diethyl diallylmalonate (Lancaster) and silanes (Aldrich) were used as received. Deuterated dienes **2a**-2,6-d_2, **2a**-1,1,7,7-d_4, and **2a**-3,3,5,5-d_4 were synthesized by standard procedures (see Supporting Information) and were >95% isotopically pure as determined by NMR and GC analysis. Palladium π-allyl chloride complexes including the known complexes (η^3-C_3H_5)Pd(Me)-PCy_3,[46] **1a**,[47] **1g**,[48] and **1h**,[48] were prepared by a modified literature procedure (see Supporting Information).[26,46,47] $NaBAr_4$ and $HBAr_4{\cdot}OEt_2$ [Ar = 3,5-$C_6H_3(CF_3)_2$]$_4$ were prepared using known procedures.[48] Authentic samples of methylenecyclopentanes **4a**, **4b**, and **33** were synthesized by the method of Urabe et al.[49]

Cyclopentenes. 4,4-Dicarbomethoxy-1,2-dimethylcyclopentene (3a). Dimethyl diallylmalonate (**2a**) (100 mg, 0.47 mmol) and $HSiEt_3$ (80 mg, 0.70 mmol) were added sequentially via syringe to a solution of **1a** (10 mg, 0.022 mmol) and $NaBAr_4$ (24 mg, 0.024 mmol) in CH_2Cl_2 (8 mL) at 0 °C. The resulting yellow solution was stirred at room temperature for 20 min to form a dark brown solution. Solvent and silane were evaporated under vacuum, and the oily residue was chromatographed (hexane:EtOAc, 12:1) to give **3a** (89 mg, 89%) as a colorless oil. ^{1}H NMR: δ 3.69 (s, 6 H), 2.92 (s, 4 H), 1.56 (s, 6 H). ^{13}C{^{1}H} NMR: δ 172.9, 127.9, 57.0, 45.8, 13.1. IR (neat, cm^{-1}): 1731 (C=O). Anal. Calcd (found) for $C_{11}H_{16}O_4$: H, 7.60 (7.33); C, 62.26 (61.99).

The procedure given for the synthesis of **3a** was applied to the synthesis of all cyclopentenes found in Table 4 unless otherwise stated.

1,2-Dimethyl-4-phenyl-4-benzyloxycyclopentene (14). ^{1}H NMR: δ 7.60−7.09 (m, 10 H), 3.30 (d, J = 15.2 Hz, 2 H), 2.70 (d, J = 15.2 Hz, 2 H), 1.60 (s, 6 H). ^{13}C{^{1}H} NMR: δ 201.9, 146.7, 136.2, 132.0, 130.3, 129.1, 128.4, 128.2, 126.5, 125.6, 60.4, 49.9, 13.7. IR (neat, cm^{-1}): 1669 (C=O). Anal. Calcd (found) for $C_{20}H_{20}O$: H, 7.30 (7.32); C, 86.91 (86.62).

4-Acetoxymethyl-1,2-dimethyl-4-phenylcyclopentene (15). ^{1}H NMR: δ 7.26 (m, 5 H), 4.10 (m, 2 H), 2.72 (d, J = 14.9 Hz, 2 H), 7.25 (d, J = 14.6 Hz, 2 H), 1.94 (s, 3 H), 1.62 (s, 6 H). ^{13}C{^{1}H} NMR: δ 170.5, 146.4, 128.4, 127.4, 126.2, 125.3, 71.0, 47.2, 47.1, 20.2, 13.1. IR (neat, cm^{-1}): 1748 (C=O). Anal. Calcd (found) for $C_{16}H_{20}O_2$: H, 8.25 (8.12); C, 78.65 (78.43).

4-Trimethylacetoxymethyl-1,2-dimethyl-4-phenylcyclopentene (16). ^{1}H NMR: δ 7.25 (m, 5 H), 4.04 (s, 2 H), 2.74 (d, J = 14.8 Hz, 2 H), 2.55 (d, J = 14.6 Hz, 2 H), 1.62 (s, 6 H), 1.07 (s, 9 H). ^{13}C{^{1}H} NMR: δ 178.7, 147.4, 129.3, 128.2, 127.2, 126.1, 72.3, 48.2, 48.1, 39.1, 27.3, 14.0. IR (neat, cm^{-1}): 1729 (C=O). Anal. Calcd (found) for $C_{19}H_{26}O_2$: H, 9.15 (8.91); C, 79.68 (79.42).

4,4-Bis(acetoxymethyl)-1,2-dimethylcyclopentene (17). ^{1}H NMR: δ 3.99 (s, 2 H), 2.15 (s, 2 H), 2.04 (s, 3 H), 1.55 (s, 3 H). ^{13}C{^{1}H} NMR: δ 170.5, 127.9, 66.7, 43.7, 42.0, 20.2, 12.9. IR (neat, cm^{-1}): 1741 (C=O). Anal. Calcd (found) for $C_{13}H_{20}O_4$: H, 8.39 (8.67); C, 64.98 (64.96).

4,4-Bis(trimethylacetoxymethyl)-1,2-dimethylcyclopentene (18). ^{1}H NMR: δ 3.97 (s, 4 H), 2.17 (s, 4 H), 1.55 (s, 4 H), 1.17 (s, 18 H). ^{13}C{^{1}H} NMR: δ 178.5, 128.8, 67.7, 44.9, 43.3, 39.1, 27.4, 13.8. IR (neat, cm^{-1}): 1730 (C=O). Anal. Calcd (found) for $C_{19}H_{32}O_4$: H, 9.95 (9.84); C, 70.32 (70.35).

4-Carbomethoxy-1,2-dimethyl-4-phenylcyclopentene (19). ^{1}H NMR: δ 7.27 (m, 5 H), 3.62 (s, 3 H), 3.28 (dd, J = 0.7, 14.3 Hz, 2 H), 2.70 (dd, J = 0.8, 15.3 Hz, 2 H), 1.63 (s, 6 H). ^{13}C{^{1}H} NMR: δ 177.1, 155.6, 129.4, 128.5, 126.8, 126.6, 56.7, 52.6, 48.4, 13.9. IR (neat, cm^{-1}): 1730 (C=O). Anal. Calcd (found) for $C_{15}H_{18}O_2$: H, 7.88 (8.09); C, 78.22 (78.07).

4-Acetyl-4-carbomethoxy-1,2-dimethylcyclopentene (20). ^{1}H NMR: δ 3.62 (s, 3 H), 2.83 (m, 4 H), 2.13 (s, 3 H), 1.56 (s, 6 H). ^{13}C{^{1}H} NMR: δ 202.4, 173.1, 127.3, 62.9, 51.9, 43.6, 25.1, 12.6. IR (neat, cm^{-1}): 1738 (C=O). Anal. Calcd (found) for $C_{11}H_{16}O_3$: H, 8.22 (8.00); C, 67.32 (67.34).

4-Carbomethoxy-4-methylsulfonyl-1,2-dimethylcyclopentene (23). 10:1 Mixture of diastereomers. ^{1}H NMR: δ 3.81 (s, 3 H), 3.08 (s, 4 H), 3.00 (s, 3 H), 1.56 (s, 6 H). ^{13}C{^{1}H} NMR: δ 170.3, 128.3, 74.5, 53.9, 43.1, 38.0, 13.5. IR (neat, cm^{-1}): 1748 (C=O), 1306, 1121 (S=O). Anal. Calcd (found) for $C_{10}H_{16}O_4S$: H, 6.94 (7.00); C, 51.71 (51.16).

1,2-Dimethyl-4-phenyl-4-phenylsulfonylcyclopentene (24). ^{1}H NMR: δ 7.26−7.54 (aromatic region, 10 H), 3.22 (ABq, J = 16.4 Hz,

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4 H), 1.40 (s, 6 H). $^{13}C\{^1H\}$ NMR: δ 137.5, 136.7, 133.4, 130.4, 129.9, 2129.3, 128.5, 128.4, 128.0, 75.8, 46.4, 13.3. IR (neat, cm^{-1}): 1295, 1137, (S═O). HRMS Calcd (found) for $C_{19}H_{20}O_2S$ (M^+): 312.1184 (312.1186).

4,4-Dicarboethoxy-1,2,3-trimethylcyclopentene (27b). ^1H NMR: δ 4.18 (m, 4 H), 3.32 (q, J = 3.9 Hz, 1 H), 3.19 (d, J = 16.6 Hz, 1 H), 2.51 (d, J = 16.8 Hz, 1 H), 1.56 (s, 6 H), 1.22 (t, J = 7.1 Hz, 3 H), 1.21 (t, J = 7.1 Hz, 1 H), 0.91 (d, J = 7.1 Hz, 3 H). $^{13}C\{^1H\}$ NMR: δ 172.8, 171.0, 133.4, 127.1, 62.6, 61.3, 61.2, 48.9, 44.1, 14.3, 14.2, 13.7, 12.0. IR (neat, cm^{-1}): 1720 (C═O). Anal. Calcd (found) for $C_{14}H_{22}O_4$: H, 8.72 (8.93); C, 66.12 (66.31).

4,4-Dicarbomethoxy-1,2-dimethyl-3-phenylcyclopentene (28). ^1H NMR: δ 7.25 (m, 3 H), 7.10 (d, J = 6.8 Hz, 2 H), 4.56 (s, 1 H), 3.72 (s, 3 H), 3.28 (d, J = 16.8 Hz, 1 H), 3.09 (s, 3 H), 2.62 (d, J = 17.0 Hz, 1 H), 1.72 (s, 3 H), 1.44 (s, 3 H). $^{13}C\{^1H\}$ NMR: δ 173.2, 170.3, 139.2, 132.0, 130.2, 129.4, 128.2, 127.3, 64.1, 61.8, 53.1, 44.9, 13.8, 12.8. IR (neat, cm^{-1}): 1737 (C═O). HRMS (EI) Calcd (found) for $C_{17}H_{19}O_4$ ($M - H^+$): 287.1283 (287.1288).

4,4-Dicarbomethoxy-1,2,3,3-tetramethylcyclopentene (30). ^1H NMR: δ 3.67 (s, 6 H), 2.72 (s, 2 H), 1.59 (s, 3 H), 1.49 (s, 3 H), 1.05 (s, 6 H). $^{13}C\{^1H\}$ NMR: δ 171.9, 136.1, 126.3, 66.4, 52.2, 52.0, 43.1, 22.4, 14.0, 9.8. IR (neat, cm^{-1}): 1733 (C═O). Anal. Calcd (found) for $C_{13}H_{20}O_4$: H, 8.39 (8.46); C, 64.98 (64.93).

4,4-Dicarbomethoxy-1-ethyl-2-methylcyclopentene (32) and 1,1-Dicarbomethoxy-3-ethylidene-4-methylcyclopentane (33). A solution of diene **31** (100 mg, 0.47 mmol), $HSiEt_3$ (80 mg, 0.70 mmol), **1a** (10 mg, 0.022 mmol), and $NaBAr_4$ (24 mg, 0.024 mmol) in CH_2Cl_2 (8 mL) was stirred at 0 °C for 10 min to form a dark brown solution. Evaporation of solvent and chromatography (hexane:EtOAc, 12:1) gave a 3:1 mixture of **32** and **33** (84 mg, 84%) as a colorless oil. Carbocycle **33** was identified by comparison of the spectroscopy with that of an authentic sample. In a separate reaction, a solution of diene **31** (100 mg, 0.47 mmol), $HSiEt_3$ (440 mg, 3.8 mmol), **1a** (10 mg, 0.022 mmol), and $NaBAr_4$ (24 mg, 0.024 mmol) in CH_2Cl_2 (8 mL) was stirred at room temperature for 12 h to form a dark brown solution. Evaporation of solvent and chromatography (hexane:EtOAc, 12:1) gave **32** (84 mg, 84%) as a colorless oil as a 33:1 mixture of **32**:**33**. Anal. Calcd (found) for $C_{12}H_{18}O_4$: H, 8.02 (7.88); C, 63.70 (63.57).

For 32. ^1H NMR: δ 3.69 (s, 6 H), 2.92 (overlapping region, 4 H), 2.00 (q, J = 1 Hz, 2 H), 1.56 (s, 3 H), 0.92 (t, J = 7.6 Hz, 3 H). $^{13}C\{^1H\}$ NMR: δ 173.2, 134.1, 127.5, 57.4, 52.9, 46.1, 43.4, 21.2, 13.3, 12.6. IR (neat, cm^{-1}): 1737 (C═O).

For 33. ^1H NMR: δ 5.16 (q, J = 4.4 Hz, 1 H), 3.68 (s, 6 H), 2.95 (d, J = 17.2 Hz, 1 H), 2.80 (qd, J = 2.0, 17.6 Hz, 1 H), 2.46 (m, 2 H), 1.65 (m, 1 H), 1.55 (m, 3 H), 1.01 (d, J = 6 Hz, 3 H). $^{13}C\{^1H\}$ NMR: δ 172.7, 144.0, 115.3, 58.4, 52.8, 42.6, 37.3, 18.1, 14.6. IR (neat, cm^{-1}): 1734 (C═O).

Detection of Intermediates in the Isomerization of 2b. A solution of **2b** (100 mg, 0.47 mmol), $HSiEt_3$ (110 mg, 0.94 mmol), **1a** (10 mg, 0.022 mmol), $NaBAr_4$ (24 mg, 0.024 mmol), and naphthalene (21 mg) in CH_2Cl_2 (10 mL) was stirred at 0 °C and monitored periodically by GC analysis. Relative concentrations of **2b**, **3b**, **4b**, and **5b** were determined from the area of the respective peaks relative to the naphthalene peak in the GC. Intermediates **4b** and **5b** were identified by comparison to authentic samples. A plot of [**2b**] versus time was linear to >3 half-lives from which a zero-order rate constant of $k = 8.1 \times 10^{-5}$ s^{-1} was obtained (Figure S1).

Isomerization of a 1:1 Mixture of 2a-2,6-d_2 and 2b. A solution of **2a**-2,6-d_2 (50 mg, 0.47 mmol), **2b** (50 mg, 0.47 mmol), $HSiEt_3$ (80 mg, 0.70 mmol), **1a** (10 mg, 0.022 mmol), and $NaBAr_4$ (24 mg, 0.024 mmol), and naphthalene (21 mg) in CH_2Cl_2 (10 mL) was stirred at 0 °C and analyzed periodically by GC. Relative concentrations of **2a**-2,6-d_2 and **2b** were determined from the area of the respective peaks relative to the naphthalene peak in the GC. Deuterium incorporation was determined from GCMS of the respective aliquots.

Acknowledgment is made to the National Institutes of Health (GM59830-01) and the donors of the Petroleum Research Fund (33131-G1), administered by the American Chemical Society for support of this research. R.W. thanks the Camille and Henry Dreyfus Foundation and DuPont for young faculty awards and the Alfred P. Sloan Foundation for a Research Fellowship. We thank Nicholas Perch for performing some initial experiments.

Supporting Information Available: Experimental procedures, spectroscopic, and analytical data for relevant compounds (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

JA001730+