Cycloisomerization of Functionalized 1,5- and 1,6-Dienes Catalyzed by Cationic Palladium Phenanthroline Complexes

Philip Kisanga, Laurel A. Goj, and Ross A. Widenhoefer*

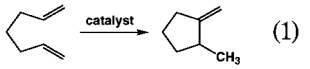
P. M. Gross Chemical Laboratory, Duke University, Durham, North Carolina 27708-0346

rwidenho@chem.duke.edu

Received November 9, 2000

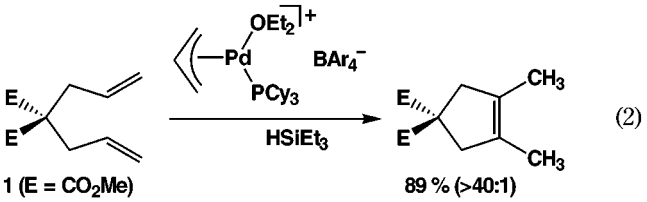
Introduction

Although diene cycloisomerization remains less developed than enyne cycloisomerization,[1] Sc(III),[2] Ru(I),[3] Ni(II),[4] Pd(II),[4] and Ti(II)[5] complexes catalyze the selective conversion of 1,6-dienes to methylenecyclopentanes (eq 1). Similarly, the cationic π-allyl palladium complex



(1)

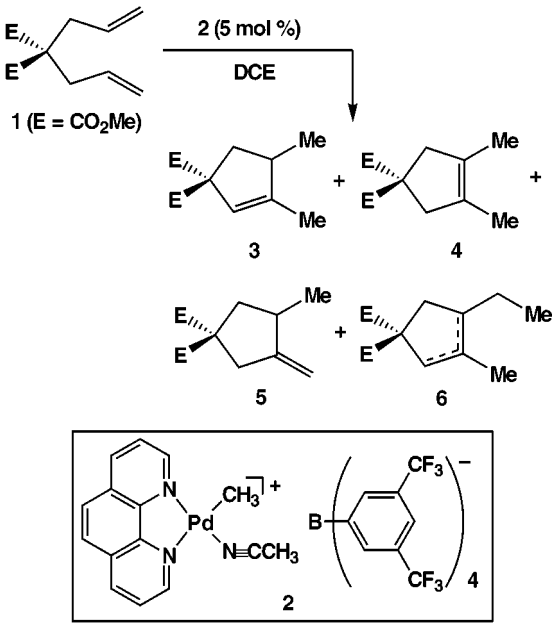
$[(\eta^3\text{-}C_3H_5)Pd(OEt_2)PCy_3]^+ [BAr_4]^-$ [Ar = 3,5-$C_6H_3(CF_3)_2$] catalyzes the selective conversion of 1,6-dienes to 1,2-dimethylcyclopentenes in the presence of $HSiEt_3$ (eq 2).[6]



(2)

In contrast, the selective conversion of 1,6-dienes to 1,5-dimethylcyclopentenes remains rare,[7] and the selective cycloisomerization of 1,5-dienes to form cyclopentenes has been achieved only in the case of the nickel-catalyzed cycloisomerization of 1,5-cyclooctadiene.[4b] Because cationic palladium phenanthroline,[8,9] bisoxazoline,[9,10] and pyridine−oxazoline[9,11] complexes catalyze the cyclization/hydrosilylation of functionalized dienes, we considered that these complexes might also serve as effective diene cycloisomerization catalysts. Here we report that cationic palladium phenanthroline complexes catalyze the selective cycloisomerization of 1,5- and 1,6-dienes to form 1-methylcyclopentenes and 1,5-dimethylcyclopentenes, respectively.

Scheme 1



Results and Discussion

When a solution of dimethyl diallylmalonate (**1**), the cationic palladium phenanthroline complex [(phen)Pd(Me)$CNCH_3$]$^+$ $[BAr_4]^-$ [Ar = 3,5-$C_6H_3(CF_3)_2$] (**2**), and naphthalene as an internal standard in 1,2-dichloroethane (DCE) was heated at 70 °C, diene **1** disappeared over 3 h with formation of a 26:9:1 mixture of the isomeric carbocycles 3,3-dicarbomethoxy-1,5-dimethylcyclopentene (**3**), 4,4-dicarbomethoxy-1,2-dimethylcyclopentene (**4**), and 1,1-dicarbomethoxy-4-methyl-3-methylenecyclopentane (**5**) along with traces (∼4%) of the ethyl-substituted cyclopentenes (**6**, 3.4:1 mixture of isomers) as determined by GC analysis. Carbocycles **3**−**6** together accounted for >99% of the reaction mixture (Scheme 1).[12] The selectivity for cyclopentene **3** increased with decreasing temperature, and at 40 °C, isomerization of **1** formed a 27:2.2:1.0:1.5 mixture of carbocycles **3**, **4**, **5**, and **6** in 99% combined GC yield.

An active cycloisomerization catalyst was also generated in situ from a 1:1 mixture of (phen)Pd(Me)Cl (**2a**) and $NaBAr_4$.[13] For example, reaction of **1** and a catalytic 1:1 mixture of **2a** and $NaBAr_4$ at 0 °C for 14 h led to

(1) Trost, B. M.; Krische, M. J. *Synlett* **1998**, 1.
(2) Piers, W. E.; Shapiro, P. J.; Bunel, E. E.; Bercaw, J. E. *Synlett* **1990**, 74.
(3) Yamamoto, Y.; Ohkoshi, N.; Kameda, M.; Itoh, K. *J. Org. Chem.* **1999**, *64*, 2178.
(4) (a) Radetich, B.; RajanBabu, T. V. *J. Am. Chem. Soc.* **1998**, *120*, 8007. (b) Bogdanovic, B. *Adv. Organomet. Chem.* **1979**, *17*, 105.
(5) (a) Okamoto, S.; Livinghouse, T. *J. Am. Chem. Soc.* **2000**, *122*, 1223. (b) Lehmkuhl, H.; Tsien, Y. L. *Chem. Ber.* **1983**, *116*, 2437.
(6) Widenhoefer, R. A.; Perch, N. S. *Org. Lett.* **1999**, *1*, 1103.
(7) Existing procedures typically suffer from forcing conditions and/or lack of generality: (a) Grigg, R.; Mitchell, T. R. B.; Ramasubbu, A. *J. Chem. Soc., Chem. Commun.* **1980**, 27. (b) Grigg, R.; Malone, J. F.; Mitchell, T. R. B.; Ramasubbu, A.; Scott, R. M. *J. Chem. Soc., Perkin Trans. 1* **1984**, 1745. (c) Grigg, R.; Mitchell, T. R. B.; Ramasubbu, A. *J. Chem. Soc., Chem. Commun.* **1979**, 669. (d) Heumann, A.; Moukhliss, M. *Synlett* **1998**, 1211. (e) Schmitz, E.; Heuck, U.; Habisch, D. *J. Prakt. Chem.* **1976**, *318*, 471. (f) Schmitz, E.; Urban, R.; Heuck, U.; Zimmerman, G.; Grundemann, E. *J. Prakt. Chem.* **1976**, *318*, 185.
(8) (a) Widenhoefer, R. A.; DeCarli, M. A. *J. Am. Chem. Soc.* **1998**, *120*, 3805. (b) Stengone, C. N.; Widenhoefer, R. A. *Tetrahedron Lett.* **1999**, *40*, 1451. (c) Widenhoefer, R. A.; Stengone, C. N. *J. Org. Chem.* **1999**, *64*, 8681. (d) Widenhoefer, R. A.; Vadehra, A. *Tetrahedron Lett.* **1999**, *40*, 8499.
(9) Pei, T.; Widenhoefer, R. A.*Org. Lett.* **2000**, *2*, 1469.
(10) Perch, N. S.; Kisanga, P.; Widenhoefer, R. A. *Organometallics* **2000**, *19*, 2541.
(11) (a) Perch, N. S.; Widenhoefer, R. A. *J. Am. Chem. Soc.* **1999**, *121*, 6960. (b) Perch, N. S.; Pei, T.; Widenhoefer, R. A. *J. Org. Chem.* **2000**, 65, 3836. (c) Pei, T.; Widenhoefer, R. A. *Tetrahedron Lett.* **2000**, *41*, 7597.
(12) Carbocycles **6** were characterized by GCMS analysis and comparison to an authentic sample of 1-ethyl-2-methyl-4,4-dicarbomethoxycyclopentene.

10.1021/jo001596b CCC: $20.00
Published on Web 12/28/2000

Table 1. Cycloisomerization of 1,5- and 1,6-Dienes Catalyzed by a 1:1 Mixture of 2a and $NaBAr_4$ (4 mol %) in DCE at 0 °C for 14 h (entries 1−4) or at 70 °C for 3 h (entries 5−8)

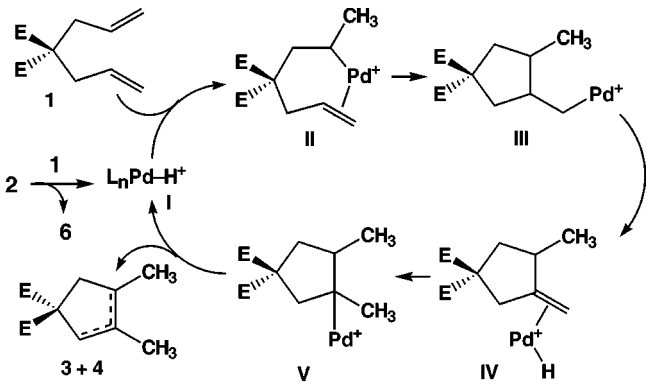
entry	diene	carbocycle	isomeric purity (%) crude[a]	isomeric purity (%) isolated[b]	yield (%)[c]
1	1 (E = CO_2Me)	3	90	98	71
2	7 (E = CO_2Bn)	8	75	96	49
3	9 (R = Pv)	11	98	98	87
4	10 (R = Ac)	12	98	98	90
5	13 (R = Ac)	14	96	96	92
6	15 (R = Pv)	16	98	98	73
7	17 (E = CO_2Et)	19	88	92	62
8	18 (R = Ac)	20	83	95	56

[a] Refers to the ratio of the major isomer to the sum of the minor isomers as determined by GC analysis of the crude reaction mixture. [b] Refers to isolated material of >95% purity. [c] Refers to the ratio of the major isomer to the sum of the minor isomers as determined by GC analysis after column chromatography.

formation of carbocycles **3**−**5** with 90% selectivity for **3** along with a trace (~3%) of **6** (Table 1, entry 1). Evaporation of solvent and chromatography of the residue on silica gel led to the isolation of **3** in 71% yield with 98% isomeric purity. The selectivity of diene cycloisomerization was dependent on the nature of the homoallylic groups of the diene. For example, cycloisomerization of the dicarbobenzyloxy-substituted diene **7** occurred with only 75% selectivity for the chiral cyclopentene **8**, which was isolated in 49% yield with 96% isomeric purity (Table 1, entry 2). In comparison, cycloisomerization of the bis(acetoxymethyl)- or bis(trimethylacetoxy)-substituted dienes **9** and **10** occurred with >97% selectivity for chiral cyclopentenes **11** and **12**, respectively, which were isolated in >85% yield (Table 1, entries 3, 4).

Mixtures of palladium phenanthroline complex **2a** and $NaBAr_4$ also catalyzed the selective cycloisomerization of 1,5-dienes to form 1-methylcyclopentenes, although more forcing conditions were required than those employed in the cyclization of 1,6-dienes (Table 1, entries 5−8). For example, when a DCE solution of 3,3-bis(acetoxymethyl)-1,5-hexadiene (**13**) and a catalytic 1:1 mixture of **2a** and $NaBAr_4$ (5 mol %) was heated at 70 °C, diene **13** underwent complete cycloisomerization within 3 h with ≥95% selectivity for 3,3-bis(acetoxymethyl)-1-methylcyclopentene (**14**), which was isolated in 92% yield (Table 1, entry 5). Similarly, the bis(trimethylacetoxymethyl)-substituted 1,5-diene **15** isomerized under these conditions to form cyclopentene **16** in 73% yield with 98% isomeric purity. The dicarbomethoxy-substituted diene **17** and monocarbomethoxy-substituted diene **18** also underwent cycloisomerization with >80% selectivity for cyclopentenes **19** and **20**, respectively (Table 1, entries 7, 8).

Scheme 2



We propose a mechanism for cycloisomerization of **1** catalyzed by **2** initiated by hydrometalation of an olefin of **1** with the cationic palladium hydride complex (phen)-$Pd(L)H^+$ (L = CH_3CN, solvent) (**I**) to form palladium alkyl olefin intermediate **II** (Scheme 2). Intramolecular carbometalation of **II** followed by β-hydride elimination from palladium cyclopentylmethyl complex **III** would form the palladium methylenecyclopentane complex **IV**. β-Elimination of a secondary or tertiary hydrogen atom of **V** would form cyclopentenes **3** or **4**, respectively, with regeneration of **I** (Scheme 2). Initial formation of **I** by a similar series of transformations initiated by β-migratory insertion of an olefin of **1** into the Pd−Me bond of **2** is supported by the formation of cyclopentenes **6** (Scheme 2).

In summary, cationic palladium phenanthroline complexes catalyze the cycloisomerization of functionalized 1,5- and 1,6-dienes to form cyclopentenes which possess a trisubstituted olefin in good yield and with good selectivity.

Experimental Section

General Methods. All reactions were performed under an atmosphere of nitrogen employing standard Schlenk techniques. NMR were obtained on a Varian spectrometer operating at 400 MHz for ^1H and 100 MHz for ^{13}C in $CDCl_3$ 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) eluting with mixtures of hexane and ether. 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. Dimethyl diallylmalonate (Lancaster) was used as received. 3,3-Dicarboethoxy-1,5-hexadiene,[14] **2**,[15] **2a**,[16] and $NaBAr_4$[17] were synthesized according to published procedures. Methyl allylphenylacetate[18] was synthesized in 93% yield from reaction of phenyl acetate, allyl bromide, and LDA in THF at 0 °C.

(13) Halide abstraction generates the requisite cationic palladium complex: (a) Rix, F. C.; Brookhart, M.; White, P. S. *J. Am. Chem. Soc.* **1996**, *118*, 4746. (b) Brookhart, M.; Wagner, M. I. *J. Am. Chem. Soc.* **1996**, *118*, 7219.

(14) Bunce, R. A.; Burns, S. E. *Org. Prep. Proced. Int.* **1999**, *31*, 99.

(15) De Delice, V.; Albano, B. G.; Castellari, C.; Cucciolito, M. E.; De Renzi, A. *J. Organomet. Chem.* **1991**, *403*, 269.

(16) Rix, F. C.; Brookhart, M.; White, P. S. *J. Am. Chem. Soc.* **1996**, *118*, 4746.

(17) Brookhart, M.; Grant, B.; Volpe, A. F. *Organometallics* **1992**, *11*, 3920.

(18) Edgar, M. T. Pettit, G. R.; Smith, T. H. *J. Org. Chem.* **1978**, *43*, 4115.

General Procedure for Cycloisomerization. 1,2-Dichloroethane (DCE) (10 mL) and diene (0.5 mmol) were added sequentially to a mixture of **2a** (7 mg, 0.025 mmol) and $NaBAr_4$ (23 mg, 0.025 mmol) at 0 °C and then stirred at the temperature and time specified in Table 1. Solvent was evaporated under vacuum, and the residue was chromatographed (ether−hexane = 2 → 30%) to give the carbocycle as a colorless oil in ≥95% chemical purity; isomeric purity of the carbocycles both prior to, and following, chromatography is given in Table 1.

3,3-Dicarbomethoxy-1,5-dimethylcyclopentene (3). ^{1}H NMR: δ 5.39 (s, 1 H), 3.69 (s, 3 H), 3.67 (s, 3 H), 2.63−2.77 (m, 2 H), 1.92, 1.88 (ABq, J = 5.6 1 H), 1.69 (t, J = 1.6 Hz, 3 H), 1.02 (d, J = 7.2 Hz, 3 H). ^{13}C{^{1}H} NMR: δ 172.7, 172.2, 150.4, 122.1, 65.1, 52.8, 42.1, 40.8, 19.1, 14.8. IR (neat, cm^{-1}): 1735 (C═O). HRMS calculated (found) for $C_{11}H_{16}O_4$ (M^+): 212.1049 (212.1039). Anal. Calcd (found) for $C_{11}H_{16}O_4$: H, 7.60 (7.88); C, 62.25 (62.02).

3,3-Dicarbobenzyloxy-1,5-dimethylcyclopentene (8). ^{1}H NMR: δ 7.21−7.31 (m 10 H), 5.46 (s, 1 H), 5.10 (m, 4 H), 2.63−2.81 (m, 2 H), 1.94 (ddd, J = 1.2, 4.8, 7.2 Hz, 1 H), 1.71 (s, 3 H), 1.03 (d, J = 6.8 Hz, 3 H). ^{13}C{^{1}H} NMR: δ 171.9, 171.4, 150.7, 135.8, 128.7, 128.3, 128.1, 128.0, 122.0, 67.1, 65.4, 42.2, 40.7, 19.2, 14.8. (neat, cm^{-1}): 1730 (C═O). HRMS calculated (found) for $C_{23}H_{24}O_4$ (M^+): 364.1674 (364.1663). Anal. Calcd (found) for $C_{23}H_{24}O_4$: H, 6.64 (6.62); C, 75.80 (75.75).

3,3-Bis(trimethylacetoxymethyl)-1,5-dimethylcyclopentene (11). ^{1}H NMR: δ 5.11 (s, 1 H), 3.95 (m, 4 H), 2.63 (m, 1 H), 2.04 (d, J = 8.4 Hz, 1 H), 1.64 (s, 3 H), 1.27 (s, 18 H), 1.16 (dd, J = 0.8, 3.6 Hz, 3 H). ^{13}C{^{1}H} NMR: δ 178.6, 148.3, 125.2, 68.2, 67.1, 51.7, 41.7, 39.5, 39.1, 27.4, 20.1, 14.9. IR (neat, cm^{-1}): 1731 (C═O). HRMS calculated (found) for $C_{19}H_{32}O_4$ (M^+): 324.2301 (324.2289). Anal. Calcd (found) for $C_{19}H_{32}O_4$: H, 9.94 (9.92); C, 70.33 (70.26).

3,3-Bis(acetoxymethyl)-1,5-dimethylcyclopentene (12). ^{1}H NMR: δ 5.09 (s, 1 H), 3.92 (m, 4 H), 2.59 (m, 1 H), 2.00 (s, 3 H), 1.99 (s, 3 H), 1.62 (t, J = 1.6 Hz, 3 H), 1.23 (dd, J = 6.8 Hz, 1 H), 0.99 (d, J = 7.2 Hz, 3 H). ^{13}C{^{1}H} NMR: δ 171.2, 148.3, 124.9, 68.3, 67.3, 51.2, 41.7. 39.4, 21.0, 20.0, 14.8. IR (neat, cm^{-1}): 1742 (C═O). HRMS calculated (found) for $C_{13}H_{20}O_4$ (M^+): 240.1362 (240.1354).

3,3-Bis(acetoxymethyl)-1-methylcyclopentene (14). ^{1}H NMR: δ 5.45 (s, 1 H), 4.02 (s, 4 H), 2.19 (m, 2 H), 2.00 (s, 6 H), 1.78 (t, J = 7.6 Hz, 2 H), 1.62 (m, 3 H). ^{13}C{^{1}H} NMR: δ 171.2, 140.1, 129.0, 66.7, 53.0, 31.3, 29.5, 21.1, 13.8. IR (neat cm^{-1}): 1742 (C═O). HRMS calculated (found) for $C_{12}H_{18}O_4$ (M^+): 226.1205 (226.1205). Anal. Calcd (found) for $C_{12}H_{18}O_4$: H, 8.02 (8.12); C, 63.70 (63.76).

3,3-Bis(trimethylacetoxymethyl)-1-methylcyclopentene (16). ^{1}H NMR: δ 5.44 (s, 1 H), 4.04, 3.96 (ABq, J = 11.2 Hz, 4 H), 2.22 (m, 1 H), 1.79 (dd, J = 6.7, 8.0 Hz, 1 H), 1.65, 1.64 (ABq, J = 2.4 Hz, 3 H), 1.14 (s, 18 H). ^{13}C{^{1}H} NMR: δ 178.5, 140.2, 128.8, 66.4, 53.4, 39.1, 31.3, 29.5, 27.3, 13.9. IR (neat, cm^{-1}): 1731 (C═O). HRMS calculated (found) for $C_{18}H_{30}O_4$ (M^+): 310.2144 (310.2141).

3,3-Dicarboethoxy-1-methylcyclopentene (19). ^{1}H NMR: δ 5.61 (s, 1 H), 4.15 (q, J = 7.2 Hz, 4 H), 2.46 (dt, J = 0.8, 6.8 Hz, 2 H), 2.32 (m, 2 H), 1.82 (q, J = 2.0 Hz, 3 H), 1.22 (t, J = 7.2 Hz, 6 H). ^{13}C{^{1}H} NMR: δ 171.4, 137.6, 131.8, 68.2, 61.3, 34.2, 30.5, 14.7, 14.3. IR (neat, cm^{-1}): 1730 (C═O). HRMS calculated (found) for $C_{12}H_{18}O_4$ (M^+): 226.1205 (226.1213).

3-Acetoxymethyl-1-methyl-3-phenylcyclopentene (20). ^{1}H NMR: δ 7.12−7.32 (5 H), 5.63 (d, J = 1.6 Hz, 1 H), 4.49, 4.44 (ABq, J = 11.2 Hz, 2 H), 2.33 (m, 2 H), 2.21 (m, 1 H), 2.01−2.06 (m, 4 H), 1.53, 1.52 (ABq, J = 2.0 Hz, 3 H). ^{13}C{^{1}H} NMR: δ 171.6, 144.9, 142.8, 128.6, 126.6, 126.4, 67.9, 57.7, 38.4, 30.3, 21.3, 14.0. IR (neat, cm^{-1}): 1741 (C═O). HRMS calculated (found) for $C_{15}H_{18}O_2$ (M^+): 230.1307 (230.1312). Anal. Calcd (found) for $C_{15}H_{18}O_2$: H, 7.88 (7.91); C, 78.23 (78.06).

Acknowledgment is made to the National Institutes of Health (GM59830-01) for support of this research. R.W. thanks the Camille and Henry Dreyfus Foundation and DuPont for new faculty awards and the Alfred P. Sloan Foundation for a research fellowship.

JO001596B