This study is being extended to other metal ions and other free atoms. Preliminary experiments indicate that chromium carbonyl and tungsten carbonyl ions behave similarly to iron carbonyl ions toward hydrogen and nitrogen atoms.

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Catalytic Palladium-Mediated Tetraene Carbocyclizations: The Cycloisomerizations of Acyclic Tetraenes to Cyclized Trienes

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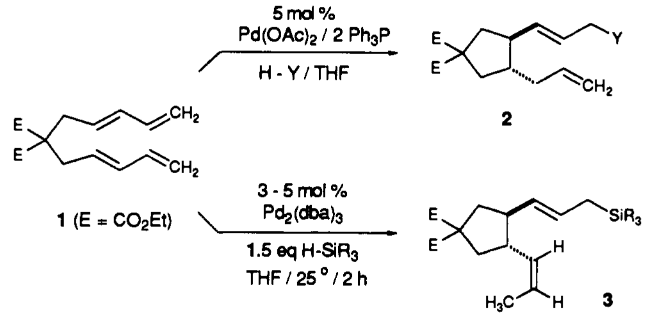
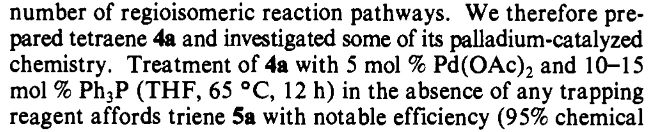
Among the more important new catalytic strategies for the construction of common organic ring systems are the transition-metal-mediated carbocyclizations[1] of substrates containing two or more elements of unsaturation. For example, catalytic transition-metal-mediated cycloisomerization reactions are under development which effect intramolecular cyclizations via formal cycloaddition,[2–6] hydrovinylation,[7–9] and ene[10–14] reaction pathways. We recently initiated a study of the catalytic transition-metal-mediated carbocyclizations of certain tetraene substrates containing within their structures two 1,3-diene subunits. Such substrates are appealing as synthetic intermediates in that they are readily accessible,[15] are reasonably robust,[16] and leave functionality in the cyclized product that is useful for further synthetic transformation. To date, we have reported two novel palladium-catalyzed tetraene cyclizations. One bond construction involves the cyclization of simple symmetric tetraenes (e.g., **1**) with incorporation of a "protic" H–Y trapping reagent (e.g., H–Y = HOR, HNR_2, HS(O)Ar, RCH_2NO_2, $H_2C(CO_2R)_2$) to afford products with the general structure **2**.[19,20] The second mode of cyclization leads to compounds of general structure **3** and is observed when "nonprotic" trapping reagents (e.g., hydrosilanes, tin hydrides, disilanes) are employed.[21] Both cyclization modes follow directly from what is known for the palladium-catalyzed dimerization of 1,3-butadiene and are in effect intramolecular variants of butadiene telomerization reactions.[22]



An issue critical to the synthetic utility of palladium-catalyzed tetraene cyclizations is whether efficient control elements can be found to direct the regioselective cyclization of unsymmetrical tetraene substrates, since substrates in which the two 1,3-diene subunits are differently substituted can potentially react via a number of regioisomeric reaction pathways. We therefore prepared tetraene **4a** and investigated some of its palladium-catalyzed chemistry. Treatment of **4a** with 5 mol % $Pd(OAc)_2$ and 10–15 mol % Ph_3P (THF, 65 °C, 12 h) in the absence of any trapping reagent affords triene **5a** with notable efficiency (95% chemical yield) and selectivity (>95% isomeric purity). Triene **5a** is the net result of palladium-catalyzed carbocyclization followed by apparent intramolecular transfer of an allylic hydrogen.[23] The overall transformation of an acyclic tetraene to a cyclized triene defines a new palladium-mediated reaction mode of tetraenes.[24,25]



Carbocyclization of **4a** affords predominantly the trans relative stereochemistry between substituents on the newly formed cyclopentane ring (vide infra) and predominantly the *E* geometry for the newly formed diene side chain. In a similar fashion, tetraene **4b** readily undergoes palladium-catalyzed cycloisomerization in refluxing THF to afford triene **5b** (93% yield, >93% isomeric purity). Of particular note in this latter example is the predominant *E,E* geometry of the newly formed 1,4-disubstituted 1,3-diene subunit within the upper side chain.

In contrast to **4a** and **4b**, alcohol **6** reacts only slowly (>24 h) in refluxing THF. We find that a variety of other solvents are suitable for these palladium-catalyzed cyclizations (e.g., 2-propanol, acetonitrile, toluene) and that it is often beneficial to add 5–10 equiv of triethylamine as a cocatalyst.[26] Palladium-catalyzed reaction of **6** proceeds more readily in acetonitrile/Et_3N (11 h) to afford a 1.6:1 mixture of **7a**:**7b** (66% yield). Confirmation of the trans relative stereochemistry of the side chains and

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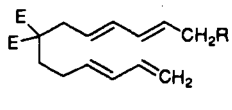
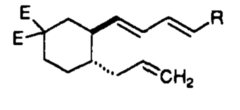
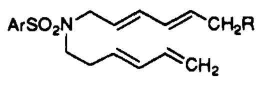
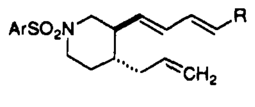
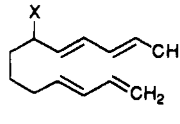
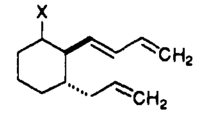
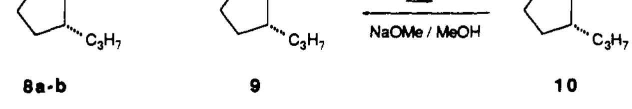
Table I. Six Membered Ring Forming Palladium-Catalyzed Carbocyclizations of Simple Tetraene Substrates[a]

Substrate	Product	Yield
		
11a (R = H; E = CO$_2$Et)	**12a** (R = H; E = CO$_2$Et)	90%
11b (R = C$_2$H$_5$; E = CO$_2$Et)	**12b** (R = C$_2$H$_5$; E = CO$_2$Et)	84%
		
13a (R = H; Ar = p-MeC$_6$H$_4$)	**14a** (R = H; Ar = p-MeC$_6$H$_4$)	72%
13b (R = C$_2$H$_5$; Ar = p-MeC$_6$H$_4$)	**14b** (R = C$_2$H$_5$; Ar = p-MeC$_6$H$_4$)	86%
		
15 (X = OTBDMS)	**16a/b** (X = OTBDMS)	62%
17 (X = OH)	**18a/b** (X = OH)	76%

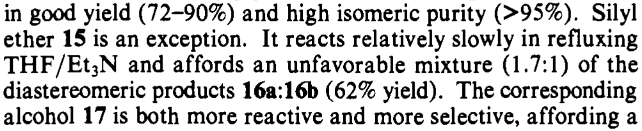
[a] All reactions are carried out with approximately 1 mmol of substrate, 0.05 mmol of Pd(OAc)$_2$, 0.10–0.15 mmol of Ph$_3$P, and 5 mmol of triethylamine in 10 mL of refluxing THF unless otherwise noted. The reaction progress is monitored by TLC.

assignment of the hydroxyl stereochemistry for **7a,b** is made on the following basis. Hydrogenation of a mixture of **7a** and **7b** (1 atm of H$_2$/EtOH/5% Rh on Al$_2$O$_3$/24 h) gives the corresponding mixture of **8a** and **8b**. PCC oxidation affords predominantly cyclopentanone **9** (>95% trans). Base-catalyzed equilibration of **9** with its less favorable cis isomer **10** confirms the trans assignment of **7a,b** and, by analogy, **5a,b**. Reduction of **9** (Li(*sec*-Bu)$_3$BH/THF/−78 °C) re-forms **8b**, enabling assignment of the stereochemistry shown in **7b** to the minor isomer formed in the palladium-catalyzed cyclization of **6**.



6

7a (X^1 = OH, X^2 = H)
b (X^1 = H, X^2 = OH)



8a-b **9** **10**

The results of several six membered ring forming cyclizations are summarized in Table I. Simple functionalized cyclohexanes (**12a,b**) and *N*-sulfonylpiperidines (**14a,b**) are generally formed in good yield (72–90%) and high isomeric purity (>95%). Silyl ether **15** is an exception. It reacts relatively slowly in refluxing THF/Et$_3$N and affords an unfavorable mixture (1.7:1) of the diastereomeric products **16a**:**16b** (62% yield). The corresponding alcohol **17** is both more reactive and more selective, affording a 5:1 ratio of diastereomeric alcohols **18a,b** (76%), with the all-equatorial isomer **18a** predominating.

In summary, the palladium-catalyzed reaction of tetraene substrates provides a promising new cyclization strategy in the case of substrates in which one of the 1,3-diene subunits is appropriately 1,4-disubstituted. Cyclization proceeds with high diastereoselectivity, and the cyclized product contains functionality that should prove useful for further synthetic transformations.

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Supplementary Material Available: An experimental procedure for the palladium-catalyzed tetraene cyclization and characterization data for compounds **5a,b**, **7a,b**, **12a,b**, **14a,b**, and **18a,b** (8 pages). Ordering information is given on any current masthead page.

Generation and Chemical Trapping of a Bis(ethano) Derivative of Tricyclo[3.3.0.0^{3,7}]oct-1(5)-ene: The Consummate Member of a Series of Pyramidalized Alkenes

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Tricyclo[3.3.0.0^{3,7}]oct-1(5)-ene (**1**) is the consummate member of the homologous series[1] of pyramidalized olefins,[2] which one of our groups has been studying. The hydrogenation energy of **1** is calculated to be greater than that of the unbridged alkene, bicyclo[3.3.0]oct-1(5)-ene, by fully 70.6 kcal/mol,[3,4] and to exceed even those of cubene[3-5] and homocub-4(5)-ene[4,6] by, respectively, 11.9 and 5.1 kcal/mol. The very high olefin strain energy[3,7] (70.6 kcal/mol) computed for **1** is due largely to the weakness of the highly pyramidalized "π" bond in this olefin, which is calculated to have a dissociation energy of only 13.3 kcal/mol.[8] This bond dissociation energy (BDE) is 52.9 kcal/mol less than the calculated π BDE of bicyclo[3.3.0]oct-1(5)-ene, 9.7 kcal/mol less than the "π" BDE of cubene, and 4.6 kcal/mol less than that of homocub-4(5)-ene.[8,10] The calculated energy difference between the

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(9) Energies of doublet and triplet states were calculated at the ROHF/6-31G*//UHF/3-21G level.

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