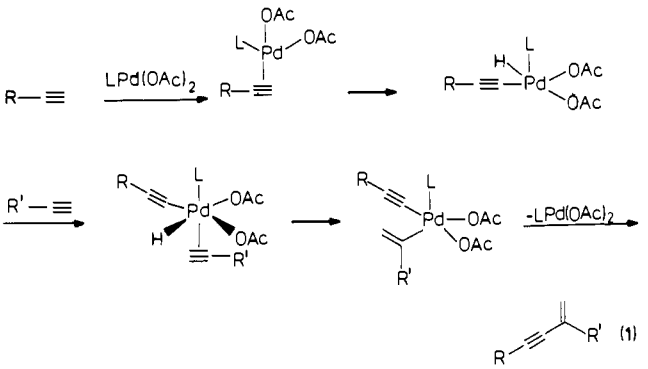
ipated that using a highly sterically crowded ligand should suppress bidentate coordination as in **5** (R = H) and favor monodentate coordination as in **4** (R = H). In fact, use of the novel phosphine tris(2,6-dimethoxyphenyl)phosphine (**6**)[7,8] provides the corresponding enyne **3** (R = H) in 71% isolated yield. With this latter system, we explored the generality of this enyne synthesis as summarized in Table I. Invoking the monodentate complex **4** suggests that the additional double bond is not required. Entries 3–5 verify this supposition. Entries 1, 4, and 5 demonstrate the compatibility of ester and hydroxyl groups.

Extending this approach to a cross-coupling reaction would greatly expand the scope of the process. Incorporating an equivalent amount of an electron-deficient internal acetylene in the reaction of a terminal acetylene with 2 mol % of palladium acetate and 2 mol % of **6** leads only to the cross-coupling products as single geometric isomers (entries 6–11). Assignment of the *E* configuration rests on the low-field shift of the hydrogens of the methyl group which arises by deshielding by the cis-situated electron-withdrawing group (see Table I, footnote *d*). In all cases, only a single regioisomer arising from head-to-tail coupling is observed.

In a typical experiment, 1.2 equiv of ethyl butynoate and 1.0 equiv of dimethyl propargylmalonate were added to a solution of 2 mol % of palladium acetate and 2 mol % of **6** in benzene (0.4 M concentration of reactants). After 15 h at room temperature, the reaction was evaporated in vacuo and directly chromatographed on silica gel, eluting with 30% ether in hexane to give 87.3% of ethyl 7,7-bis(carbomethoxy)-3-methyl-2(*E*)-hepten-4-ynoate (**7**).[9]

Equation 1 illustrates a possible mechanistic interpretation. The



insertion of low-valent metals into C–H bonds of terminal acetylenes has been invoked in the formation of vinylidene metal complexes.[10–12] The addition of palladium hydride across the terminal acetylene followed by reductive elimination then follows established reactivity patterns.[13] This scheme invokes Pd(+4) intermediates.[10] An alternative pathway invoking insertion into the acetylenic C–H bond by a Pd(0) complex leading to Pd(+2) intermediates may also be envisioned. To test this latter pathway, dimethyl propargylmalonate was subjected to $(dba)_3Pd_2 \cdot CHCl_3$ in the presence of **6**. While dimerization did occur, it was extremely slow compared to the above conditions and gave only a 65% conversion after 27.5 h. Addition of allyl acetate to the palladium(0) complex and **6** does increase the rate such that 94% conversion occurs in 23.5 h. Since the latter experiment presumably generates a Pd(+2) species in situ, the Pd(+2)–Pd(+4) cycle appears more likely at the moment.

Acknowledgment. We thank the National Science Foundation for their generous support of our programs.

(7) (a) Wada, M.; Higashizaki, S. *J. Chem. Soc., Chem. Commun.* **1984**, 482. (b) Horner, L.; Simons, G. *Phosphorus Sulfur* **1983**, *14*, 189. (c) Mp 156–158 °C (lit.[7b] mp 155 °C).

(8) While we have attributed the effect of the 2,6-dimethoxy substitution of the phosphine to steric factors, we also take note of the enhanced basicity of this ligand which may also be important. See ref 7a.

(9) **7**: ^{1}H NMR (270 MHz, $CDCl_3$) δ 5.95 (1 H, q, J = 1.2 Hz), 4.13 (2 H, q, J = 7.1 Hz), 3.75 (6 H, s), 3.59 (1 H, t, J = 7.7 Hz), 2.92 (2 H, d, J = 7.7 Hz), 2.20 (3 H, d, J = 1.4 Hz), 1.24 (3 H, t, J = 7.1 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.1 (2), 165.9, 137.4, 124.1, 90.0, 84.6, 59.8, 52.8 (2), 50.8, 19.8, 19.5, 14.2; IR (neat) 2220, 1750, 1735, 1710, 1615. Anal. Calcd for $C_{14}H_{18}O_6$: C, 59.57; H, 6.43. Found: C, 59.70; H, 6.50.

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(12) For a review, see: Bruce, M. I.; Swincer, A. G. *Adv. Organomet. Chem.* **1983**, *22*, 59.

(13) Addition of the C–Pd bond across the acetylene followed by reductive elimination to form the C–H bond in a second step (i.e., inverting the order of the two bond-forming steps) may also be envisioned. The first step would correspond to a Heck-type addition which has been shown to occur preferentially to an acetylene in the presence of an olefin with the regiochemistry required. See: Trost, B. M.; Burgess, K. *J. Chem. Soc., Chem. Commun.* **1985**, 1084.

A Novel Palladium-Catalyzed Reductive Cyclization

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The well-documented electrophilic properties of (π-allyl)palladium complexes have proven valuable in synthesis.[1] Inverting their electronic properties would create a whole new avenue for developing synthetic methodology whereby relatively unreactive substrates such as allylic acetates,[1] sulfones,[2] amines,[3] nitro compounds,[4] etc. may be transferred into nucleophilic building blocks.[5–8] We wish to record a novel chemoselective reductive cyclization catalyzed by palladium according to eq 1.

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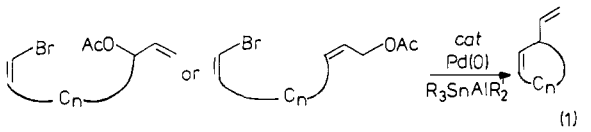
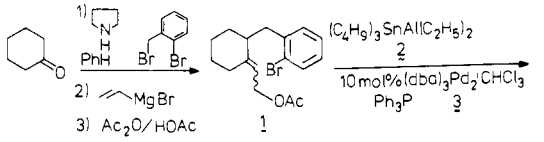
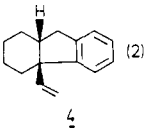


(1)

To explore the cyclization, we prepared the substrate **1** very readily from cyclohexanone as outlined in eq 2. Treatment of





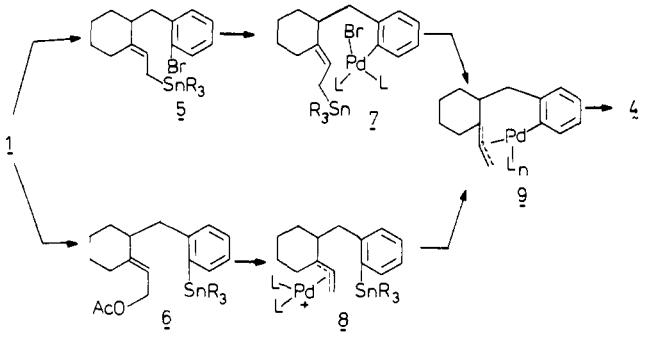
(2)

4

1 with 1 equiv of (tri-*n*-butylstannyl)diethylalane (**2**),[5a,b] 10 mol % of the Pd(0) catalyst, and 4–6 equiv of Ph_3P per Pd in THF, initially at room temperature, then at 60 °C, and finally at 100 °C, gave the desired cyclization product **4** in 60% yield. Spectroscopic and chromatographic analysis indicates it is homogeneous. Spin decoupling shows the large coupling constants to the bridgehead hydrogen (δ 2.30) are due to coupling with the benzylic protons and not the cyclohexyl protons—a fact suggestive of a cis ring fusion. Table I reveals the generality of the reaction.

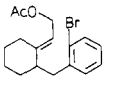
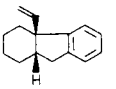
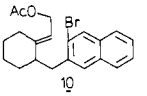
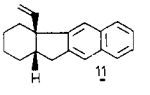
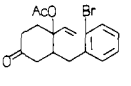
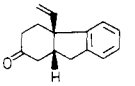
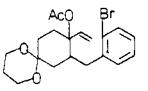
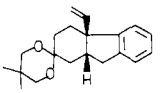
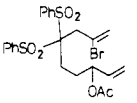
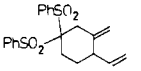
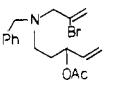
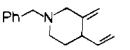
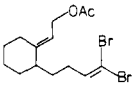
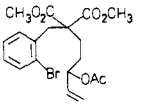
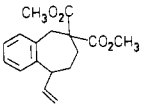
Aryl and vinyl bromides, substrates that participate well in metal-catalyzed cross-coupling reactions,[9] participate smoothly in this reductive cyclization. Either regioisomer of the allyl acetate may be employed (cf. entries 1 and 2 to entries 3 and 4). Five- (entries 1–4), six- (entries 5–7), and seven-membered (entry 8) rings as well as heterocyclic rings (entry 6) can be constructed. The chemoselectivity is excellent. Ketones, esters, sulfones, ketals, and amines all are compatible. The vinylidene dibromide (entry 7) is quite interesting since the product retains a vinyl bromide; yet no apparent complications arise.

The mechanism of this reductive coupling may be envisioned to involve formation of an organostannane such as **5**[5] or **6**,[10] Cross coupling of allylstannanes with aryl bromides as well as arylstannanes with allyl acetates are known[9] and presumed to proceed through **7** or **8** to **9**, either as a π- or σ-complex. Regioselective



reductive elimination favors the five-membered ring even though it involves creation of a quaternary center. Formation of a metallocycle such as **9** accounts for the bias for formation of the cis ring juncture. The normally faster rate of oxidative addition of Pd(0) to an allyl acetate[5] compared to an aryl or vinyl bromide[9,11] leads us to favor the pathway through **5** and **7**.[12]

Table I. Palladium-Catalyzed Reductive Cyclization[a]

entry	allyl acetate	cyclization product[b]	isolated yield
1			60%
2			76%
3			63%
4			72%
5			62%
6			75%
7			50%
8			52%

[a] For a typical procedure see text. [b] All new compounds have been fully characterized by spectroscopic analysis and elemental composition has been established either by combustion analysis and/or high-resolution mass spectroscopy.

A typical procedure follows. In a medium-pressure bottle equipped with a plastic screw cap was placed 13.4 mg (0.013 mmol) of **3** and 30.1 mg (0.11 mmol) of triphenylphosphine in 2 mL of dry THF. A solution of 78 mg (0.20 mmol) of **10** (Table I, entry 2) in 1 mL of THF and of 1 equiv of the tin–aluminum reagent **2** in 2 mL of THF was added. After it was stirred 30 min at 60 °C, the reaction was kept 20 h at 105 °C. Direct chromatographic purification gave 76% of tetracycle **11**: ^{1}H NMR ($CDCl_3$) δ 8.20–8.10 (m, 1 H), 7.85–7.75 (m, 1 H), 7.65, (d, J = 8 Hz, 1 H), 7.50–7.30 (m, 3 H), 6.25 (dd, J = 16, 12 Hz, 1 H), 5.29 (dd, J = 11.1 Hz, 1 H), 5.22 (dd, J = 16, 1 Hz, 1 H), 3.00 (m, 2 H), 2.55–2.30 (m, 2 H), 1.80–1.45 (m, 7 H). Calcd for $C_{19}H_{20}$: C, 90.88; H, 8.12; NW, 248.1565. Found: C, 90.57; H, 7.90; MW, 248.1555.

Acknowledgment. We thank the National Science Foundation for their generous support of our program and the Schweizerischen Nationalfond for a postdoctoral fellowship.

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(11) There is an example of a faster oxidative addition to a vinyl bromide compared to an allyl acetate in a cross-coupling reaction. See: Nwokogu, G. C. *J. Org. Chem.* **1985**, *50*, 3900.

(12) It is also possible to invoke the intermediacy of (σ-allyl)palladium complexes corresponding to **8** and/or **9**. The lack of any detailed mechanistic information refrains us from making more refined proposals, but we do not rule out the possibility of such species. They are not required to explain the observations.