in Scheme II which require *that cyclization to the aldehyde occurs in preference to cyclization to the alkene irrespective of ring size.* As observed in our recent work,[9] aldehyde transposition frequently occurs quantitatively if a more stable radical can be formed thereby. The rearrangement VII → VIII is therefore understandable in view of the stability of the allylic radical.[10,11]

The absence of an *aldehydo* methyl cyclopentane implies that path c is kinetically preferred to path d. This follows because the retrocyclization, X → VI, is not in keeping with the ample literature precedents.[2,3,5]

Furthermore, since the competing sites in VI for radical attack are both neopentyl, do the results imply that an aldehyde may be less susceptible to steric hindrance in radical attack than an alkene?

Answers to questions such as the foregoing and a full exposition of the kinetic implications of the case histories in Chart I must await further study. However, for the present it seems beyond question that radical cyclization of a 5-formyl-*n*-pentyl radical to give a cyclohexanol seems to be preferred to cyclization of a 5-hexenyl radical. Further examination of this surprising departure from conventional wisdom is under way and will be reported in due course.

Acknowledgment. We are deeply indebted to our colleague, Professor Ned Porter, for his sustained interest and several helpful discussions.

Metal-Mediated Approach to Enynes

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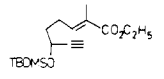
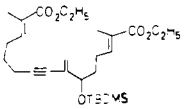
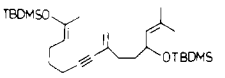
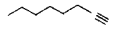
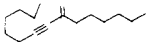
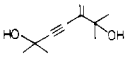
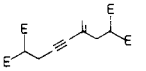
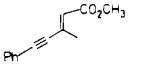
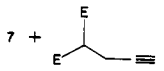
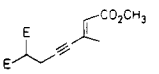
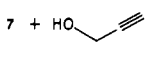
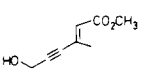
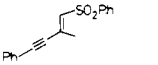
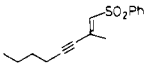
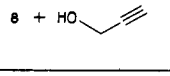
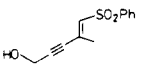
The presence of enynes in natural products and their utility as building blocks for further structural elaboration stimulate the interest in seeking simple synthetic routes to them. One of the more attractive is the coupling of terminal acetylenes with vinyl halides or triflates.[1] The direct coupling of two acetylenes, while highly attractive since economy of mass is optimized (i.e., the product corresponds to the exact sum of the two reactants) has failed to be synthetically useful[2-4] due to lack of control and the preference for trimerization. We wish to report that the homocoupling and cross-coupling of acetylenes can be achieved in high yield by using a palladium template.

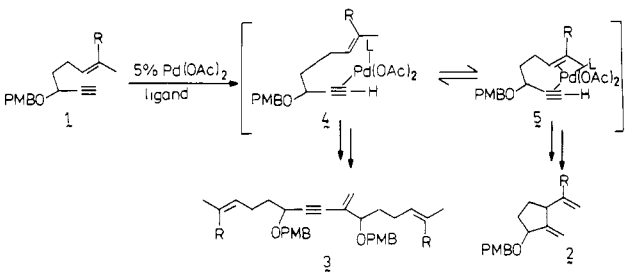
During the course of our studies of the enyne cyclization[5] of **1** (R = CH_3) using Ph_3P and $Pd(OAc)_2$, we noted that in competition with the anticipated cyclization to cyclopentane **2** (R = CH_3), we obtained a dimeric product whose spectral data identified it as enyne **3** (R = CH_3).[6] Anticipating that formation of the cyclopentane required bidentate coordination as illustrated in **5** (R = CH_3), the unexpected formation of the dimer may arise from the steric hindrance associated with a trisubstituted double bond serving as a ligand. By favoring the monodentate coordination as in **4** (R = CH_3), insertion in the acetylene hydrogen may compete with cyclization and ultimately produce the enyne **3** (R = CH_3). This explanation suggests that increasing the steric bulk of the ligand should disfavor formation of **5** (R = CH_3) and thus disfavor formation of the cyclization product **2** (R = CH_3). By use of tri-*o*-tolylphosphine in lieu of triphenylphosphine, the isolated yield of enyne jumps from between 9% and 22% to 66.5%.

In seeking to generalize this useful coupling with substrates possessing less substituted olefins such as **1** (R = H), we antic-

Table I. Additional Homo- and Codimerization of Acetylenes[a]

entry	acetylene(s)	time, h	enyne[e]	yield
1[b]		16		83%
2		14		89%
3		64		63%
4[c]		24		64%
5		19		81%
6[d]	$CH_3C{\equiv}CCO_2CH_3$ (**7**) + $PhC{\equiv}CH$	0.5		92%
7[d]		15		87%
8[d]		7		67%
9[d]	$CH_3C{\equiv}CSO_2Ph$ (**8**) + $PhC{\equiv}CH$	2		91%
10[d]	**8** + $nC_4H_9C{\equiv}CH$	24		54%
11[d]		18		50%

[a] All reactions were done at room temperature either in PhH or PhH-d_6 using 2-5 mol % palladium acetate and 2-5 mol % phosphine **6** unless stated otherwise. [b] In this case, tri-*o*-tolylphosphine was employed. [c] The dimeric product has a mp 77-78 °C (lit.[2a] mp 77.5-79°). In addition, we obtained 21% of a trimeric product. [d] CH_3 group and vinyl H shifts at δ 2.38 and 6.14 (entry 6), δ 2.20 and 5.95 (entry 7), δ 2.29 and 6.06 (entry 8), δ 2.38 and 6.63 (entry 9), δ 2.22 and 6.43 (entry 10), and δ 2.23 and 6.50 (entry 11). [e] See ref 6.



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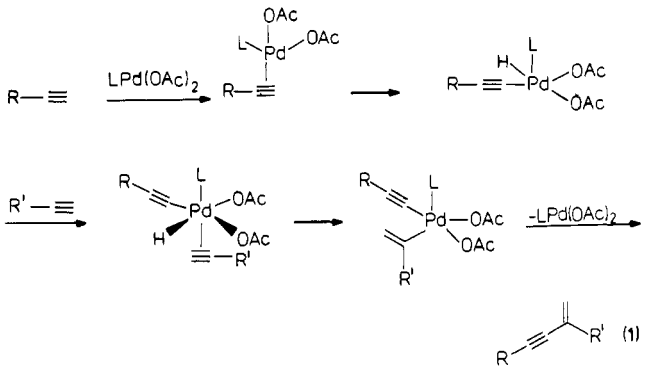
ipated that using a highly sterically crowded ligand should suppress bidentate coordination as in **5** (R = H) and favor monodentate coordination as in **4** (R = H). In fact, use of the novel phosphine tris(2,6-dimethoxyphenyl)phosphine (**6**)[7,8] provides the corresponding enyne **3** (R = H) in 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



(1)

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.

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(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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(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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