white solid, which was dissolved in 40 mL of dry acetonitrile to which was added 210 μL (1.51 mmol) of dry triethylamine. After the mixture was stirred for 5 min, 208 mg (1.01 mmol) of dicyclohexylcarbodiimide was added, and the reaction was stirred at 65 °C for 5 h. The reaction was cooled to room temperature and the solvent was removed in vacuo. Chromatography of the residue on 30 g of silica gel (elution with ether–hexane, 1:1) afforded 205 mg (84%) of β-lactam **16** as a viscous oil: R_f 0.28 (Et_2O); IR ($CHCl_3$) 3400, 3055, 2990, 2920, 2880, 2845, 1747, 1650, 1585, 1490, 1485, 1455, 1450, 1425, 1390, 1375, 1360, 1325, 1260, 1235, 1185, 1165, 1140, 1110, 1090, 1060, 1025, 1005, 995, 970, 950, 905, 855, 820, 695 cm^{-1}; NMR (220 MHz, $CDCl_3$) δ 7.70–7.20 (m, 15 H), 5.95 (br s, 1 H), 4.55 (AB q, 2 H, J = 12.5 Hz, $\Delta\nu_{AB}$ = 27.3 Hz), 3.86 (quintet, 1 H, J = 6.0 Hz), 3.73 (m, 3 H), 2.85 (dd, 1 H, J = 2.0, 7.0 Hz), 2.00–1.68 (m, 2 H), 1.27 (d, 3 H, J = 6.0 Hz), 1.03 (s, 9 H); high-resolution MS, calcd for $C_{30}H_{37}NO_3Si$, 487.2543; found, 487.2551.

Acknowledgment. This investigation was supported by a Public Health Service Research Grant (CA 28865) from the National Cancer Institute. The 360-MHz NMR instrument (Nicolet) used in the above studies were purchased in part through funds provided by the National Science Foundation (Grant CHE-81-05004). We are grateful to S. Bongers and D. Zabrowski for experimental assistance during the early stages of this work. We thank Dr. D. G. Melillo for providing us with details for the transformation of **17** (R = H) into **2**.

Registry No. (±)-**1**, 65750-57-4; (±)-**2**, 77171-46-1; **3**, 91994-21-7; **4**, 91994-22-8; **5**, 92076-89-6; **6**, 91994-23-9; **7**, 91994-24-0; **8**, 91994-25-1; **9**, 91994-26-2; **10**, 91994-27-3; **11**, 91994-29-5; **12**, 91994-30-8; **13**, 91994-31-9; **14**, 92076-90-9; **15**, 91994-32-0; **16**, 91994-33-1; **17** (R = H), 78501-85-6; **17** (R = CH_2Ph), 91994-34-2; p-$NO_2C_6H_4CH_2OC(O)CH_2CO_2H$, 77359-11-6; 1,1-dimethylethyl [2*R*-[2α,3β(*R**)]]-2-[2-[[(1,1-dimethylethyl)diphenylsilyl]oxy]ethyl]-6-oxo-3-[1-(phenylmethoxy)ethyl]-1-piperidinecarboxylate, 91994-28-4; 1,1-dimethylethyl [2*R*-[2α,3β(*R**),5α]]-2-[2-[[(1,1-dimethylethyl)diphenylsilyl]oxy]-ethyl]-6-oxo-5-(phenylthio)-3-[1-(phenylmethoxy)ethyl]-1-piperidinecarboxylate, 92009-74-0; 1,1-dimethylethyl [2*R*-[2α,3β(*R**),5β]]-2-[2-[[(1,1-dimethylethyl)diphenylsilyl]oxy]ethyl]-6-oxo-5-(phenylthio)-3-[1-(phenylmethoxy)ethyl]-1-piperidinecarboxylate, 92009-80-8; 1,1-dimethylethyl 2-[2-[[(1,1-dimethylethyl)diphenylsilyl]oxy]ethyl]-6-oxo-5-(phenylsulfinyl)-3-[1-(phenylmethoxy)ethyl]-1-piperidinecarboxylate, 92009-81-9.

Palladium-Catalyzed Cross-Coupling of Vinyl Iodides with Organostannanes: Synthesis of Unsymmetrical Divinyl Ketones

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Abstract: The palladium-catalyzed cross-coupling reaction of vinyl iodides with trimethyl- or tributylvinylstannanes in the presence of carbon monoxide gives unsymmetrical divinyl ketones in good yields. The reaction conditions are neutral and mild enough (40–50 °C, 15–50 psig carbon monoxide) that other functional groups in either coupling partner can be brought unaltered into the coupled product. The *E* geometry in both partners is retained in the coupling product, and the *Z* geometry in the vinyltin reagent is maintained during the coupling reaction, but the coupled product undergoes slow *Z* to *E* isomerization under the usual reaction conditions. Isomerization of the divinyl ketone in the reaction medium is slowed in the dark. The reaction rate is especially sensitive to substituents on the vinyltin reagent, probably as a result of steric hindrance in the transmetalation step of the catalytic cycle. The sequence of reactions, including conversion of a cycloalkanone to a cycloakenyl iodide, the carbonylative coupling of the iodide to yield a cycloalkenyl vinyl ketone, and the acid–catalyzed cyclization of the divinyl ketone, presents a method of annelation of the parent ketone to a bicyclo[*n*.3.0] system.

Divinyl ketones, especially unsymmetrical divinyl ketones, are important intermediates in the synthesis of a wide variety of organic compounds. Not only are they Michael acceptors[1] for different nucleophiles, including organocopper reagents,[2] but they also undergo the Nazarov reaction[3] to provide, in some cases, an efficient route to cyclopentenones. This cyclization offers, therefore, an annelation procedure for five-membered rings and construction of the bicyclo[*n*.3.0] skeleton.

A number of methods of synthesis of divinyl ketones are available. Aldol-type condensations generally are efficient only in the synthesis of symmetrical divinyl ketones.[4] Unsymmetrical divinyl ketones are most often synthesized by the reaction of α,β-unsaturated acids or acid halides with various olefinic reagents. The direct acylation of alkenes with α,β-unsaturated acids in the presence of polyphosphoric acid or with acid halides in the presence of a aluminum chloride usually leads to mixtures of products and does not give particularly high yields of the divinyl ketone.[5] The reaction of α,β-unsaturated acid chlorides with vinylsilanes in the presence of Lewis acids is a cleaner reaction which gives moderate to excellent yields,[6] but the reaction does not work well with acryloyl chloride because of the accompanying polymerization.[6a,b] In certain examples, mixtures (double bond isomers) of α,β-unsaturated ketones are obtained, requiring a second isomerization reaction.[6b] The reaction of a vinyl mercurial with an α,β-unsaturated acid chloride in the presence of aluminum chloride gives an excellent yield of the unsymmetrical divinyl ketone, although under the reaction conditions, rearrangements are observed in some systems.[7] A similar reaction of acid chlorides with vinyl zirconium reagents takes place, although this procedure has not been adapted

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to divinyl ketone synthesis. One of the more successful acylation reactions, those with divinylcuprates, gives uniformly high yields of the unsymmetrical divinyl ketones.[9]

The palladium-catalyzed coupling reaction of acid chlorides with organotin reagents gives excellent yields of unsymmetrical ketones under mild conditions.[10] Although the reaction occurs with acryloyl or cinnamoyl chlorides[10a,e] and tetramethyltin, as well as with various saturated aliphatic or aromatic acid chlorides and vinyltin reagents,[10a-d,f] the combination of the two, α,β-unsaturated acid chloride and vinyltin reagent, has not yet been reported for the synthesis of unsymmetrical divinyl ketones.

An attractive method of introducing the carbonyl function into a divinyl ketone is by the reaction of carbon monoxide with various vinyl reagents. There are a number of stoichiometric reactions of transition-metal complexes[11] that generate ketones from carbon monoxide and organic reagents. Vinylmercuric chlorides react with carbon monoxide under mild conditions with rhodium catalysis to give high yields of divinyl ketones.[12] This reaction is limited, however, to the synthesis of symmetrical divinyl ketones.

A number of transition-metal catalyzed coupling reactions of organic halides with organometallic reagents in the presence of carbon monoxide have been shown to give ketones. Nickel catalyzes the carbonylative coupling of bromobenzene with phenylmagnesium bromide to yield benzophenone.[13] Nickel- or palladium-catalyzed coupling reactions of organic halides with organotin reagents in the presence of carbon monoxide have been reported more recently.[14] In most of these reactions, however, relatively high reaction temperatures (120 °C) and carbon monoxide pressures (20–30 atm) were utilized.[14a,b]

We have shown that the palladium-catalyzed cross-coupling of allyl halides with aryl- and vinyltin reagents in the presence of carbon monoxide (1–3 atm) gives high yields of the unsymmetrical allyl vinyl or allyl aryl ketones.[15] The mild reaction conditions allowed the coupling to be carried out with allyl halide and organotin partners containing functional groups that tend to be somewhat reaction sensitive (e.g., aldehyde, alcohol, ester, etc.). This suggested that the coupling reaction of vinyl halides with vinyltin reagents in the presence of carbon monoxide would lead to an efficient unsymmetrical divinyl ketone synthesis. The introduction of the carbonyl function from the carbon monoxide instead of from the acid chloride should allow the introduction of functional groups into the divinyl ketone that ordinarily could not be brought unprotected into the coupling reaction.

Results and Discussion

The palladium-catalyzed reaction of vinyl iodides with vinyltin reagents in the presence of carbon monoxide gives good yields of the divinyl ketones (eq 1, Table I). A number of features of this

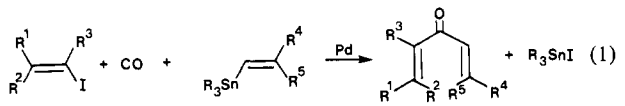
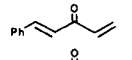
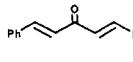
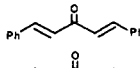
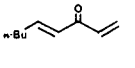
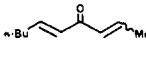
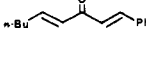
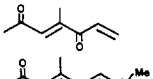
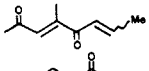
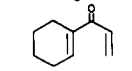
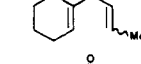
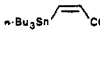
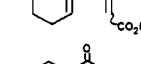
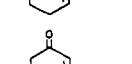
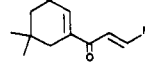
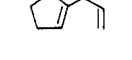


Table I. Carbonylative Cross-Coupling of Vinyl Iodides with Organostannanes

Example	Vinyl Iodide	Tin Reagent	Time (h)	Product	% Yield[b]
1			13		65 (63)
2			22		46[d]
3			12		75
4			66		70
5			12[e]		70 (75)
6			5[e]		65
7			48		62
8			44		70
9			23		40
10			18		65
11			2		50
12			55		58
13			24		93
14			24		83
15			80		45
16			48		40
17			12		71
18			18		70 (90)
19			6		86 (90)
20			24		63
21			8		60
22			10		40 (65)
23			7		54
24			8[f]		74
25			5[f]		65

[a] All reactions were run under 50 psig of carbon monoxide at 45–50 °C, unless otherwise noted. [b] Isolated yields. Yields in parentheses were determined by ^{1}H NMR. *Z*:*E* isomer ratios with reaction times for the various entries are as follows: entry 7, 48 h, *E* only; 24 h, 2.5. Entry 12, 0.9. Entry 14, 24 h, 0.7. Entry 15, 25 h, 1.6. Entry 17, 24 h, 0.12; 12 h, 1.2. Entry 20, 24 h, 0.3; 18 h, 0.4. Entry 20, 12 h, 1.2. [c] The vinyltin reagents had the following *Z*/*E* ratios: $Bu_3SnCH{=}CH{-}CH_3$, 6; $Me_3SnCH{=}CH{-}Me$, 2. [d] When this reaction was run in the dark, the *Z*/*E* ratio of the propenyl double bond was 0.2. [e] Run at 35–40 °C. [f] Run at 65 °C.

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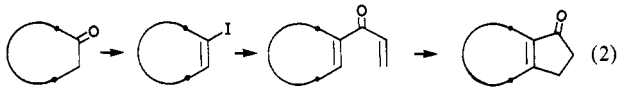
reaction make it especially synthetically attractive. The reaction takes place under neutral, mild reaction conditions, 45–50 °C, and low carbon monoxide pressures, 15–50 psig. The reaction is highly catalytic, requiring only 1–2 mol % of palladium(II) catalyst. Both benzylchlorobis(triphenylphosphine)palladium(II) and dichlorobis(triphenylphosphine)palladium(II) are equally effective, each being reduced in situ by the tin reagent via transmetalation, reductive elimination sequences to yield the active palladium(0) catalyst.[10d] This organic halide–organotin type of coupling reaction is known to endure a variety of functional groups on both coupling partners.[10,15] Although the broad range of functionality which the partners could bear was not probed in this vinyl iodide–vinyltin carbonylative coupling reaction, ester and ketone (methyl and cyclic) as well as the vinyl ketone product can be present.

Because the cycloalkenyl iodides were prepared from the cyclic ketones by the reaction of the corresponding hydrazone with iodine,[16] this coupling procedure allows the overall annelation of a cycloalkanone by a sequence (eq 2) which concludes with a


(2)

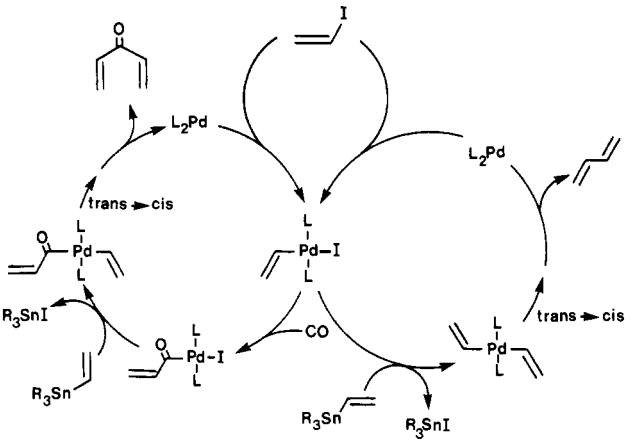
Nazarov cyclization,[3] thereby affording entry into functionalized bicyclo[*n*.3.0] ring systems. The vinyl iodides also will enter into the carbonylative cross-coupling reaction with phenyl and acetylenic tin reagents, giving moderate yields of phenyl vinyl and acetylenic vinyl ketones, respectively. Exclusive transfer of the single vinyl, phenyl, or acetylenic group takes place, with the three alkyl groups, methyl or butyl, remaining on tin. Thus, the one group on tin is utilized selectively provided the other groups are alkyl.[10d] Both the trimethylvinyl- and tributylvinylstannanes can be used in this reaction, and in several of the reactions a comparison between the two reagents can be made. The trimethyltin reagents have the advantage that the workup of the reaction mixture is simple since the trimethyltin iodide can be removed by a water wash. Tributyltin iodide, resulting from the use of tributylvinyltin reagents, is much more difficult to remove from the reaction mixture, and its separation usually requires conversion to the insoluble tributyltin fluoride by exhaustive treatment with aqueous potassium fluoride solutions.[10a,17] In addition, the reaction times required for the trimethyltin reagents generally are shorter than those necessary for the tributyltin analogues (entries 5 vs. 6 and 18 vs. 19). The yields of a given divinyl ketone are essentially the same, however, whether the trimethyl- or tributyltin reagents are used, provided the reaction times are sufficient.

The carbonylative cross-coupling reaction may be carried out under 50 psig of carbon monoxide without competition from a direct coupling of the vinyl iodide and vinyltin partners. With the use of 15 psig of carbon monoxide, transmetalation of the vinyltin reagent to the vinylpalladium(II) complex and subsequent reductive elimination compete with carbon monoxide insertion (Scheme I).

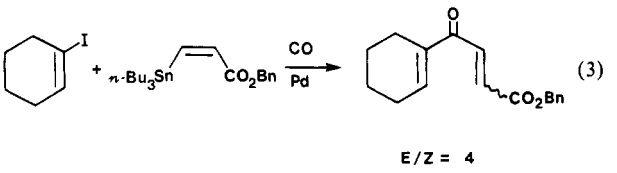
For example, in the reaction of (*E*)-β-iodostyrene with (*E*)-β-styryltributylstannane under 1 atm of carbon monoxide, a 1:1 mixture of carbonylated and directly coupled products was obtained. By contrast, the coupling of (*E*)-1-iodohexene with tributylvinylstannane under 1 atm of carbon monoxide gave exclusively the carbonylated product, in moderate yield. Whether the directly coupled product or the product of carbonylative coupling is obtained evidently depends on the competitive rates of carbon monoxide insertion and transmetalation, as dictated by the vinyl group σ-bonded to palladium, the vinylstannane, and the carbon monoxide pressure.

The *E* geometry of the double bonds in both the vinyl iodide and vinyltin partners is maintained in the coupled product. Although the *Z* geometry of the double bond in the vinyltin partner

Scheme I

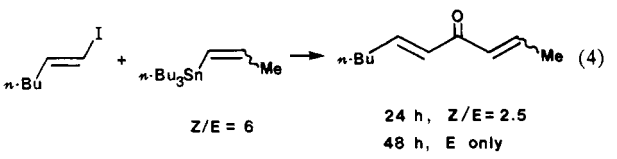


was retained through the coupling sequence, partial isomerization of the coupled product was observed under the reaction conditions. The reaction of cyclohexenyl iodide, for example, with benzyl (*Z*)-3-(tributylstannyl)propenoate for 80 h resulted in a coupled product having an *E*/*Z* ratio of 4. Recovered unreacted tin reagent remained unisomerized (eq 3). Comparison of coupling exper-


(3)

E/Z = 4

iments with benzyl (*E*)-3-(tributylstannyl)propenoate clearly showed that the *E* isomer reacted much faster than the *Z* isomer. It is possible, therefore, that the predominant reaction sequence is isomerization of the tin reagent, *Z* to *E*, followed by a rapid coupling reaction of the *E* isomer, such that the *E* isomer would not be detected in the unreacted reagent. Under simulated reaction conditions, without any vinyl iodide present, no isomerization of the vinyltin reagent was observed. Thus, the loss of stereochemistry occurred either in the transmetalation step and/or in the coupled product. The coupling reaction of (*E*)-1-iodohexene with 1-(tributylstannyl)propene, which was predominately the *Z* isomer, gave a product in which the *Z*/*E* isomer ratio of the double bond derived from the propenyltin reagent depended on the reaction time, larger amounts of *E* isomer being obtained at longer reaction times (Table I, footnote *b*; eq 4). Again, recovered, unreacted


(4)

Z/E = 6 24 h, Z/E = 2.5 48 h, E only

tin reagent maintained the initial *Z*/*E* ratio. Thus, the loss in geometry seems to occur at the product stage. The loss of geometry in the product could be accounted for, in part, by a photoisomerization reaction, since a reaction which gave only the *E* isomer after 48 h in the light gave 20% *Z* isomer under the same conditions, in the dark.

In none of the carbonylative cross-coupling reactions were byproducts detected. Further addition of the vinyltin reagent to the divinyl ketone product does not take place, and homocoupling products from either partner, as a result of carbonylative coupling, were not observed. The moderate yields in certain reactions (entries 9, 11, 19, and 16 in Table I) can be attributed to decomposition of the products under the reaction conditions. Removal of the catalyst by flash chromatography on alumina immediately following the completion of the reaction helped to prevent further decomposition during workup. Additionally, loss of product can be reduced by avoiding prolonged chromatography.

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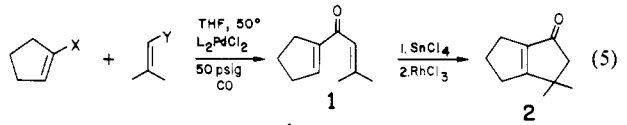
Yields in the coupling reactions are sensitive to steric hindrance, particularly on the vinyltin partner. Vinyltin reacts faster than any of the other linear vinyltin reagents, and *E* isomers react faster than *Z* isomers (vide supra). The reaction of cyclopentenyl iodide with 2-methyl-1-(tributylstannyl)propene under the standard reaction conditions gave no detectable amount of divinyl ketone **1** (eq 5, X = I, Y = $SnBu_3$). However, when the iodo and tin



(5)

1

2

X	Y	% Yield **1**
I	$SnBu_3$	0
$SnBu_3$	I	40
$SnBu_3$	COCl	85

groups (X = $SnBu_3$, Y = I) are interchanged, the carbonylative cross-coupling reaction gave a 40% yield of **1**. Since (*Z*)-1-(tributylstannyl)propene will undergo the carbonylative coupling reaction with cyclopentenyl iodide, whereas 2-methyl-1-(tributylstannyl)propene will not, the difference in reactivities probably is a reflection of the ease with which the transmetalation reaction occurs, but not the result of differences in the CO insertion step. Further, the difference cannot be attributed to a difference in the reductive elimination step (vide infra).

Divinyl ketone **1** also was prepared by the reaction of 1-(tributylstannyl)cyclopentene with 3,3-dimethylacryloyl chloride in 85% yield. The ketone was cyclized to 3,3-dimethyl-4,5,6-trihydro-2*H*-pentalen-1-one (**2**) with stannic chloride.[5] This pentalenone is a key intermediate in a synthesis of modhephene.[5c]

Experimental Section

The following instrumentation was utilized: ^1H NMR, Varian EM 360, JEOL FX 100, IBM WP 270, Nicolet NT 360; IR, Beckman 4250 or Acculab 3; ^{13}C NMR, JEOL FX 100, IBM WP 270. Tetrahydrofuran (THF) was distilled from sodium–benzophenone under a nitrogen atmosphere. All NMR spectra were obtained in $CDCl_3$ and are reported in δ relative to tetramethylsilane. High-resolution mass spectral (HRMS) data for new compounds were obtained from the Midwest Center for Mass Spectrometry at the University of Nebraska. Elemental analyses of new compounds were performed by Micro-Tech Laboratories, Inc., and Atlantic Microlab.

Tin Reagents. The following tin reagents were prepared according to literature methods: tributylvinylstannane,[18] 1-(tributylstannyl)propene (*Z*:*E* = 6),[19] benzyl (*Z*)- and (*E*)-3-(tributylstannyl)propenoate,[10e] phenyltributylstannane,[20] (*E*)-β-(tributylstannyl)styrene,[21] (*E*)-1-(tributylstannyl)hexene,[21] trimethylvinylstannane,[19] 2-methyl-1-(tributylstannyl)propene,[22] 1-(tributylstannyl)cyclopentene.[18]

1-(Tributylstannyl)pentyne. This compound was prepared by analogy to a literature method[23] in 84% yield: bp 118–120 °C (1 mmHg); IR (neat) 2100 (C≡C) cm^{-1}; ^1H NMR δ 0.50–1.70 (m, 32 H), 2.20 (t, 2H, *J* = 7 Hz); ^{13}C NMR δ 11.0, 13.4, 13.7, 22.2, 22.6, 27.0, 29.0, 81.2, 111.6; HRMS calcd for $C_{13}H_{25}Sn$ (M − 57) 301.0976, found 301.0977.

Vinyl Iodides. The following vinyl iodides were synthesized by literature procedures: (*E*)-β-iodostyrene,[24] (*E*)-1-iodo-1-hexene,[24] 1-iodocyclopentene,[25] 1-iodocyclohexene,[25] 1-iodocycloheptene,[26] 1-iodocyclooctene,[27] 5,5-dimethyl-3-iodocyclohex-2-enone,[28] and 2-methyl-3-iodocyclopent-2-enone.[28] The 1-iodo-2-methylpropene[29] was prepared by treatment of 2-methyl-1-(tributylstannyl)propene with iodine.[30]

4-Iodo-3-penten-2-one. To 800 mL of acetonitrile and 14.4 g (0.055 mol) of triphenylphosphine at 0 °C was added dropwise a 250-mL acetonitrile solution containing 14.0 g (0.055 mol) of iodine. After the addition of the iodine was complete, 5.5 g (0.05 mol) of dry triethylamine and 5.0 g (0.05 mol) of acetylacetone were added successively in single portions. The mixture was stirred for 5 days at ambient temperature. The solvent was then removed under reduced pressure, and the crude product was extracted with pentane several times. The pentane washes were combined, and the solvent was removed under reduced pressure. The product was a mixture of *E* and *Z* isomers which were separated by medium pressure liquid chromatography on silica gel eluting with hexanes/ethyl acetate (20/1, v/v). *E* isomer: ^1H NMR δ 2.17 (s, 3H), 2.96 (d, 3 H, *J* = 1.5 Hz), 7.03 (br s, 1 H); ^{13}C NMR δ 30.94, 31.28, 120.21, 138.14, 194.99; IR (neat) 1690 (C=O) and 1580 (C=C) cm^{-1}. Anal. Calcd for C_5H_7IO: C, 28.66; H, 3.44. Found: C, 28.57; H, 3.52. *Z* isomer: IR (neat) 1690 (C=O) and 1580 (C=C) cm^{-1}; ^1H NMR δ 2.26 (s, 3 H), 2.74 (d, 3 H, *J* = 1.5 Hz), 6.71 (br s, 1 H); ^{13}C NMR δ 31.34, 36.48, 109.17, 131.14, 195.00.

General Procedure for Palladium-Catalyzed Carbonylative Cross-Coupling Reactions of Vinyl Iodides and Organostannanes. Under a nitrogen atmosphere a Fischer–Porter pressure tube (3 oz obtained from Lab-Crest Scientific Division) containing a pressure gauge was charged with a magnetic stirring bar, 0.10 mmol (2.0 mol %) of palladium(II) catalyst, either benzylchorobis(triphenylphosphine)palladium(II)[31] or dichlorobis(triphenylphosphine)palladium(II),[32] 5 mL of freshly distilled and degassed (Na/benzophenone) tetrahydrofuran (THF), 5.0 mmol of vinyl iodide, and 5.2 mmol of vinylstannane, in that order. The Fischer–Porter tube was assembled, and the vessel was pressurized to 50 psig with carbon monoxide and then released. This was repeated two more times. The 50 psig of carbon monoxide in each cycle was maintained for ca. 1 min with rapid stirring of the solution. This process usually produced a color change in the solution from light yellow to orange. The tube was placed in an oil bath for the appropriate time and designated temperature (see Table I for exact times and reaction temperatures). The progress of the reactions was monitored by carbon monoxide uptake; typically a 5.0-mmol reaction reduced the carbon monoxide pressure 12 psig in the tube. The coupled products were isolated by different methods depending on whether tributyl- or trimethylvinylstannanes had been used in the reaction.

A. Tributylvinylstannanes. The THF was removed in vacuo from the reaction mixture, and the crude product was chromotographed (flash column 2 × 10 cm) on alumina with 100 mL of hexanes/ethyl acetate (9/1, v/v). The solvent was removed, leaving an oil which was redissolved in 100 mL of ether and partitioned between 100 mL of 50% saturated aqueous potassium fluoride by vigorous stirring for 2 h. The precipitated fluorotributylstannane was removed by filtration through a glass wool plug, and the organic layer was separated and dried (Na_2SO_4 or $MgSO_4$). Removal of the ether followed by medium-pressure chromatography on silica gel (Woelm 32–63) with hexanes/ethyl acetate (see below for each compound) gave pure samples of the divinyl ketones.

B. Trimethylvinylstannanes. The workup procedure was identical with that described above except that only a simple water extraction of the trimethyliodostannane was required, thus replacing treatment with potassium fluoride.

The NMR yields reported were measured following the first flash column chromatography on alumina. A known weight of 1,2-dichloroethane was added to the reaction mixture, and the integration ratio of 1,2-dichloroethane peak to the vinyl proton resonances of the divinyl ketone product was measured.

Coupling Products. The following compounds were isolated according to the general procedure (using reaction times and temperatures listed in Table I) and were identified by comparison of their spectroscopic and physical data to those previously reported: (*E*,*E*)-1,5-diphenyl-1,4-pentadien-3-one,[33] (*E*)-1-phenyl-1,4-pentadien-3-one,[34] (*E*,*E*)-1-phenyl-1,4-hexadien-3-one,[35] 1-(cyclopenten-1-yl)-2-propen-1-one,[36] (*E*)-1-(cyclopenten-1-yl)-2-buten-1-one,[37] 1-(cyclohexen-1-yl)-2-propen-1-one,[38] 1-(cyclohexen-1-yl)-2-buten-1-one,[38] 1-(cyclohexen-1-yl)-1-phenylmethanone,[39] and 1-(cyclohepten-1-yl)-2-propen-1-one.[40]

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1,4-Nonadien-3-one (Entry 5). Final purification utilized medium-pressure chromatography with hexanes/ethyl acetate (19/1, v/v). IR (neat) 1660 (C=O) and 1625 (C=C) cm^{-1}; ^1H NMR (270 MHz) δ 0.92 (t, 3 H, J = 7.1 Hz), 1.34–1.62 (m, 4 H), 2.26 (psuedo q, 2 H, J = 7.0 Hz), 5.81 (dd, 1 H, J = 10.6, 1.3 Hz), 6.28 (dd, 1 H, J = 17.3, 1.3 Hz), 6.36 (dt, 1 H, J = 15.7, 1.3 Hz), 6.61 (dd, 1 H, J = 17.4, 10.5 Hz), 6.95 (dt, 1 H, J = 15.7, 7.0 Hz); ^{13}C NMR δ 13.8, 22.2, 30.2, 32.3, 127.9, 134.6, 148.7, 189.3; HRMS calcd for $C_9H_{14}O$ 138.1041, found 138.1044.

2,5-Decadien-4-one (Entry 7). After 48 h of reaction only the *E,E* isomer was isolated by chromatography on silica gel with hexanes/ethyl acetate (12/1, v/v). *E,E* isomer: IR (neat) 1665 (C=O), 1635 (C=C) cm^{-1}; ^1H NMR (60 MHz) δ 0.85–1.85 (m, 7 H), 1.92 (dd, 3 H, J = 6.5, 1.5 Hz), 2.00–2.20 (m, 2 H), 6.00–6.40 (md, 2 H, J = 16.0 Hz), 6.5–7.1 (m, 2 H); ^{13}C NMR δ 13.3, 17.7, 21.8, 29.8, 31.8, 127.9, 129.6, 141.8, 146.8, 190.0; HRMS calcd for $C_{10}H_{16}O$ 152.1197, found 152.1194.

When the reaction was stopped at 24 h, the *Z,E* isomer/*E,E* isomer ratio was 1/3, respectively. The isomers were separated by chromatography on silica gel, eluting with hexanes/ethyl acetate (19/1, v/v). The *Z,E* isomer was eluted first. *Z,E* isomer: ^1H NMR (60 MHz) δ 0.85–1.60 (m, 7 H), 2.10 (d, 3 H, J = 5.2, 1.5 Hz), 2.00–2.20 (m, 2 H), 6.06–6.42 (m, 2 H), 6.43–7.10 (m, 2 H); ^{13}C NMR δ 13.7, 17.6, 25.6, 27.9, 28.2, 32.4, 128.4, 130.1, 142.7, 147.9, 189.2.

(*E,E*)-1-Phenyl-1,4-nonadien-3-one (Entry 9). Purification was carried out by utilizing chromatography on silica gel with hexanes/ethyl acetate (19/1, v/v) to afford pure product: IR (neat) 1655 (C=O) and 1625 (C=C) cm^{-1}; ^1H NMR (100 MHz) δ 0.80–1.57 (m, 7 H), 2.18–2.32 (m, 2 H), 6.42 (dd, 1 H, J = 15.6, 1.5 Hz), 6.51–7.72 (m, 8 H); ^{13}C NMR δ 13.9, 22.4, 30.3, 32.5, 124.6, 128.1, 128.7, 129.1, 130.1, 134.6, 142.7, 148.2, 189.9. Anal. Calcd for $C_{15}H_{14}O$: C, 83.12; H, 8.46. Found: C, 83.35; H, 8.40.

(*E*)-4-Methyl-3,6-heptadiene-2,5-dione (Entry 11). Final purification of this product was achieved by chromatography on silica gel with hexanes/ethyl acetate (19/1, v/v). IR (neat) 1685, 1665 (C=O), 1605 (C=C) cm^{-1}; ^1H NMR (100 MHz) δ 2.20 (d, 3 H, J = 10.3, 1.8 Hz), 6.31 (dd, 1 H, J = 19.0, 1.9 Hz), 6.76 (br s, 1 H), 6.84 (dd, 1 H, J = 18.9, 10.4 Hz); ^{13}C NMR δ 13.8, 31.8, 130.4, 130.8, 131.6, 147.3, 193.3, 198.8; HRMS calcd for $C_8H_8O_2$ 138.0684, found 138.0680.

4-Methyl-3,6-octadiene-2,5-dione (Entry 12). Carbonylative coupling of (*E*)-4-iodo-3-penten-2-one with 1-(tributylstannyl)propene (4/1 mixture of *E/Z*, respectively) produced a 47:53 mixture of *E,Z* and *E,E* isomers. The isomers were separated by chromatography on silica gel with hexanes/ethyl acetate (19/1, v/v). The *E,Z* isomer elutes first off the column. (*E,Z*)-4-Methyl-3,6-octadiene-2,5-dione: IR (neat) 1685, 1655 (C=O), and 1605 (C=C) cm^{-1}; ^1H NMR (100 MHz) δ 2.09 (dd, 3 H, J = 5.4, 1.7 Hz), 2.20 (d, 3 H, J = 1.5 Hz), 2.32 (s, 3 H), 6.32–6.55 (s and dd overlapping, 2 H), 6.77 (br s, 1 H); ^{13}C NMR δ 13.8, 16.3, 32.1, 124.6, 130.5, 144.6, 149.0, 194.3, 199.4. (*E,E*)-4-Methyl-3,6-octadiene-2,5-dione: IR (neat) 1685, 1655 (C=O), and 1605 (C=C) cm^{-1}; ^1H NMR (100 MHz) δ 1.96 (dd, 3 H, J = 6.6, 1.2 Hz), 2.21 (d, 3 H, J = 1.5 Hz), 2.32 (s, 3 H), 6.51 (dq, 1 H, J = 15.4, 1.5 Hz), 6.70 (q, 1 H, J = 1.5 Hz), 6.98 (dq, 1 H, J = 15.4, 6.6 Hz); ^{13}C NMR δ 14.4, 18.5, 31.9, 127.1, 129.7, 145.8, 148.6, 193.3, 199.0; HRMS calcd for $C_9H_{12}O_2$ 152.0837, found 152.0835.

1-(Cyclohexen-1-yl)-2-buten-1-one (Entry 14).[38] Chromtography on silica gel with hexanes/ether (15/1, v/v) was used to separate the *E/Z* (ratio 1.4) isomers formed in the reaction. The isomers were unambiguously identified by using the vinyl proton coupling constants (*E*, J = 15.2 Hz; *Z*, J = 11.7 Hz).

Benzyl 1-(Cyclohexen-1-yl)-1-oxo-2-propene-3-carboxylate (Entry 15). Final purification was performed by chromatography on silica gel with hexanes/ethyl acetate (19/1, v/v). The *E* isomer eluted first in the chromatography. *Z* isomer: IR ($CDCl_3$) 1721, 1660 (C=O), and 1625 (C=C) cm^{-1}; ^1H NMR (100 MHz) δ 1.36–1.80 (m, 4 H), 1.95–2.3 (m, 4 H), 5.10 (s, 2 H), 6.10 (d, 1 H, J = 12.0 Hz), 6.71 (d, 1 H, J = 12.0 Hz), 6.78 (m, 1 H), 7.31 (s, 5 H); ^{13}C NMR δ 21.6, 22.4, 26.2, 66.8, 124.4, 128.3, 128.4, 135.2, 139.2, 142.3, 143.9, 164.4, 194.8; HRMS calcd for $C_{17}H_{18}O_3$ 270.1256, found 270.1247.

E isomer: IR ($CDCl_3$) 1720, 1660 (C=O), and 1625 (C=C) cm^{-1}; ^1H NMR (100 MHz) δ 1.40–1.75 (m, 4 H), 2.00–2.42 (m, 4 H), 5.20 (s, 2 H), 6.65 (d, 1 H, J = 16.2 Hz), 6.95 (m, 1 H), 7.29 (s, 5 H), 7.63 (d, 1 H, J = 16.2 Hz); ^{13}C NMR δ 21.2, 21.5, 22.9, 26.2, 66.6, 127.9, 128.2, 129.7, 135.2, 136.3, 139.5, 143.2, 165.1, 189.1.

(*E*)-1-(5,5-Dimethyl-1-oxo-cyclohex-2-en-3-yl)-2-buten-1-one (Entry 17). Final purification was chromatography on silica gel with hexanes/ethyl acetate (19/1, v/v). IR ($CDCl_3$) 1670 (C=O) and 1622 (C=C) cm^{-1}; ^1H NMR (100 MHz) δ 1.11 (s, 6 H), 1.99 (d, 3 H, J = 6.2 Hz), 2.35 (s, 2 H), 2.50 (d, 2 H, J = 1.6 Hz), 6.41–7.45 (m, 3 H); ^{13}C NMR δ 18.4, 28.0, 33.2, 38.1, 51.3, 126.5, 129.7, 145.9, 153.4, 191.7, 200.5; HRMS calcd for $C_{12}H_{17}O_2$ 192.1150, found 192.1141.

(*Z*)-1-(Cyclopenten-1-yl)-2-buten-1-one (Entry 20). Purification of the reaction mixture by chromatography on silica gel with hexanes/ether (15/1, v/v) gave products corresponding to the *Z* and *E* isomers,[37] in that order and in a ratio of 1:2.6, respectively. *Z* isomer: IR ($CDCl_3$) 1655 (C=O) and 1612 (C=C) cm^{-1}; ^1H NMR (360 MHz) δ 1.88–1.97 (dd overlapping a m, 5 H, J = 7.2, 1.8 Hz), 2.54–2.60 (m, 4 H), 6.19 (dq, 1 H, J = 11.6, 7.2 Hz), 6.55 (dq, J = 11.6, 1.8 Hz), 6.64 (m, 1 H); ^{13}C NMR δ 17.3, 22.1, 30.3, 33.4, 126.9, 140.2, 142.0, 145.3, 186.2; HRMS calcd for $C_9H_{12}O$ 136.0888, found 136.0887.

(*E*)-3-Phenyl-1-(cyclopenten-1-yl)-2-propen-1-one (Entry 21). Purification was carried out on silica gel with hexanes/ethyl acetate (19/1, v/v). IR ($CDCl_3$) 1650 (C=O) and 1599 (C=C) cm^{-1}; ^1H NMR δ 1.80–2.30 (m, 2 H), 2.40–2.99 (m, 4 H), 6.9 (m, 1 H), 7.2–7.9 (m, 7 H); ^{13}C NMR δ 22.6, 31.0, 34.0, 122.3, 127.9, 128.5, 129.7, 134.7, 141.6, 143.3, 146.4, 187.3; HRMS calcd for $C_{14}H_{14}O$ 198.1045, found 198.1036.

Benzyl (*E*)-1-(Cyclopenten-1-yl)-1-oxo-2-propene-3-carboxylate (Entry 22). Chromatography on silica gel with hexanes/ethyl acetate (9/1, v/v) yielded pure product: IR ($CDCl_3$) 1723, 1661 (C=O) and 1622 (C=C) cm^{-1}; ^1H NMR δ 1.94 (m, 2 H), 2.39 (t, 4 H, J = 7.3 Hz), 5.21 (s, 2 H), 6.75 (d, 1 H, J = 15.8 Hz), 6.87 (br s, 1 H), 7.33 (s, 5 H), 7.64 (d, 1 H, J = 15.5 Hz); ^{13}C NMR δ 22.5, 30.6, 34.2, 66.6, 127.9, 128.0, 128.2, 129.6, 135.3, 136.9, 145.9, 165.0, 186.0. Anal. Calcd for $C_{16}H_{16}O_3$: C, 74.98; H, 6.29. Found: C, 74.81; H, 6.33.

1-(Cyclopenten-1-yl)-2-hexyn-1-one (Entry 23). Chromatography was carried out on silica gel with hexanes/ethyl acetate (19/1, v/v). IR ($CDCl_3$) 2229 (C≡C) and 1614 (C=O) cm^{-1}; ^1H NMR δ 0.73–2.96 (m, 13 H), 7.13 (br s, 1 H); ^{13}C NMR δ 13.3, 20.7, 21.2, 23.0, 29.5, 33.6, 79.5, 92.5, 146.8, 149.1, 175.3; HRMS calcd for $CH_{14}O$ 23.0, 162.1045, found 162.1039.

1-(Cycloocten-1-yl)-2-propen-1-one (Entry 24). This compound was purified by chromatography on silica gel with hexanes/ethyl acetate (50/1). IR ($CDCl_3$) 1665 (C=O) and 1620 (C=C); ^1H NMR (CCl_4) δ 6.97 (dd, 1 H, J = 17, 10 Hz), 6.86 (t, 1 H, J = 8 Hz), 6.14 (dd, 1 H, J = 17, 2 Hz), 5.62 (dd, 1 H, J = 10, 2 Hz), 2.83–1.98 (m, 4 H), 1.98–1.17 (m, 8 H); ^{13}C NMR δ 23.9, 26.0, 26.4, 27.4, 28.9, 29.1, 127.1, 132.0, 142.8, 143.4, 191.3. Anal. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.82. Found: C, 80.41; H, 9.81.

Coupling Reactions under 15 psig of Carbon Monoxide. The general procedure described above was used except that the reaction was pressurized with 15 psig of carbon monoxide. (*E*)-β-Iodostyrene reacted with (*E*)-β-(tributylstannyl)styrene over a period of 25 h at 50 °C. The carbonylated and direct coupled products, (*E,E*)-1,5-diphenyl-1,4-pentadien-3-one[33] and (*E*)-1,4-diphenyl-1,3-butadiene,[41] respectively, were separated and each isolated in 15% yield. Similarly, (*E*)-1-iodohexene reacted with tributylvinylstannane for 25 h at 50 °C; however, only (*E*)-1,4-nonadien-3-one was isolated in 56% yield.

Coupling of 3,3-Dimethylacryloyl Chloride with 1-(Tributylstannyl)-cyclopentene. A Fischer–Porter tube was charged with a magnetic stirring bar, 190 mg (2 mol %) of dichlorobis(triphenylphosphine)palladium(II), 10 mL of THF, 1.70 g (14.3 mmol) of 3,3-dimethylacryloyl chloride, and 5.5 g (15.4 mmol) of 1-(tributylstannyl)cyclopentene, in that order, under an atmosphere of nitrogen. The vessel was capped, purged with carbon monoxide, and then filled to 50 psig with carbon monoxide. The vessel was placed in an oil bath at 50 °C and stirred for 16 h. The reaction workup was as reported in the general procedure above. Final purification using medium-pressure chromatography on silica gel with gradient elution (hexanes to hexanes/ethyl acetate, 19/1, v/v) afforded 2.10 g (85%) of pure **1**.[5c]

Cyclization of 1 with Stannic Chloride. To 20 mL of dichloromethane was added 0.75 g (4.3 mmol) of **1** and 3.37 g (12.9 mmol, 1.51 mL) of stannic chloride. The mixture was heated at 40 °C for 19 h, cooled to ambient tempeature, and then poured onto ice water. The mixture was extracted with ether (3 × 50 mL); the organic washes were combined, washed with 5% aqueous hydrochloric acid (100 mL), and then brine, and finally dried over $MgSO_4$. The ether was removed in vacuo, and the resulting yellow oil was dissolved in absolute ethanol and treated with 30 mg of rhodium(III) chloride hydrate at 60 °C for 48 h. The ethanol was removed in vacuo and the crude product purified by medium-pressure chromatography on silica gel with hexanes/ethyl acetate (9/1, v/v) to give pure **2**[5c] (0.47 g, 62%).

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Registry No. 1, 41414-30-6; **2**, 72233-31-9; (*E*)-PhCH=CHI, 42599-24-6; (*E*)-*n*-BuCH=CHI, 16644-98-7; (*E*)-CH_3COCH=$C(CH_3)$I, 91897-71-1; (*Z*)-CH_3COCH=$C(CH_3)$I, 91897-72-2; $(CH_3)_2$C=CHI, 20687-01-8; $(CH_3)_2$C=CHCOCl, 3350-78-5; *n*-Bu_3SnCH=CH_2, 7486-35-3; (*E*)-*n*-Bu_3SnCH=CHMe, 66680-85-1; (*Z*)-*n*-Bu_3SnCH=CHMe, 66680-84-0; (*E*)-Me_3SnCH=CHMe, 4964-07-2; (*Z*)-Me_3SnCH=CHMe, 4964-06-1; (*E*)-*n*-Bu_3SnCH=CHPh, 66680-88-4; Me_3SnCH=CH_2, 754-06-3; (*E*)-Me_3SnCH=CHPh, 7422-28-8; (*Z*)-*n*-Bu_3SnCH=$CHCO_2Bn$, 86633-18-3; *n*-Bu_3SnPh, 960-16-7; (*E*)-*n*-Bu_3SnCH=$CHCO_2Bn$, 86633-19-4; *n*-Bu_3SnC≡C-*n*-Pr, 86633-17-2; *n*-Bu_3SnCH=$C(CH_3)_2$, 66680-86-2; (*E*)-PhCH=CHCOCH=CH_2, 73291-51-7; (*E*,*E*)-PhCH=CHCOCH=CHMe, 91897-73-3; (*Z*,*E*)-PhCH=CHCOCH=CHMe, 91897-74-4; (*E*,*E*)-PhCH=CHCOCH=CHPh, 35225-79-7; (*E*)-*n*-BuCH=CHCOCH=CH_2, 84118-55-8; (*E*,*E*)-*n*-BuCH=CHCOCH=CHMe, 91897-75-5; (*Z*,*E*)-*n*-BuCH=CHCOCH=CHMe, 91897-76-6; (*E*,*E*)-*n*-BuCH=CHCOCH=CHPh, 91897-77-7; (*E*)-CH_3COCH=$C(CH_3)$COCH=CH_2, 91928-33-5; (*E*,*E*)-CH_3COCH=$C(CH_3)$COCH=CHMe, 91897-78-8; (*Z*,*E*)-CH_3COCH=$C(CH_3)$COCH=CHMe, 91897-79-9; $CH_3COCH_2COCH_3$, 123-54-6; CO, 630-08-0; PhCH=CHCH=CHPh, 886-65-7; 1-iodocyclohexene, 17497-53-9; 5,5-dimethyl-3-iodo-2-cyclohexenone, 56671-85-3; 1-(tributylstannyl)cyclopentene, 91897-90-4; 1-iodocyclopentene, 17497-52-8; 1-iodocyclooctene, 17497-54-0; 1-iodocycloheptene, 49565-03-9; 1-(cyclohexen-1-yl)-2-propen-1-one, 62672-77-9; (*E*)-1-(cyclohexen-1-yl)-2-buten-1-one, 91897-80-2; (*Z*)-1-(cyclohexen-1-yl)-2-buten-1-one, 91897-81-3; benzyl (*E*)-1-(cyclohexen-1-yl)-1-oxo-2-propene-3-carboxylate, 91897-82-4; benzyl (*Z*)-1-(cyclohexen-1-yl)-1-oxo-2-propene-3-carboxylate, 91897-83-5; 1-benzoylcyclohexene, 17040-65-2; (*E*)-1-(5,5-dimethyl-1-oxo-cyclohex-2-en-3-yl)-2-buten-1-one, 91897-84-6; 1-(cyclopenten-1-yl)-2-propen-1-one, 62672-81-5; (*E*)-1-(cyclopenten-1-yl)-2-buten-1-one, 15450-55-2; (*Z*)-1-(cyclopenten-1-yl)-2-buten-1-one, 15450-56-3; (*E*)-3-phenyl-1-(cyclopenten-1-yl)-2-propen-1-one, 91897-85-7; benzyl (*E*)-1-(cyclopenten-1-yl)-1-oxo-2-propen-3-carboxylate, 91897-86-8; 1-(cyclopenten-1-yl)-2-hexyn-1-one, 91897-87-9; 1-(cycloocten-1-yl)-2-propen-1-one, 91897-88-0; 1-(cyclohepten-1-yl)-2-propen-1-one, 91897-89-1.

Communications to the Editor

Titanium-Mediated Synthesis of *E*,*E*-Exocyclic Dienes. Application to the Preparation of Polycyclic Compounds

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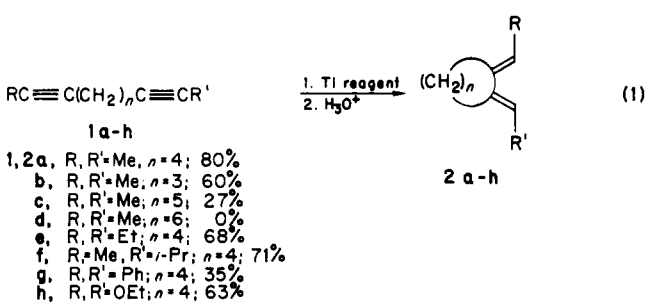
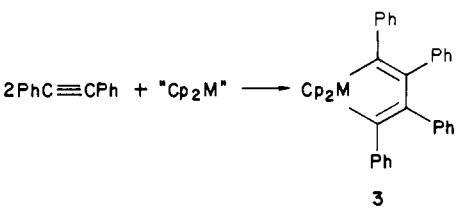
We wish to report a versatile, stereoselective cyclization of diynes **1**[1] to *E*,*E*-exocyclic dienes (**2**). It was anticipated that



(1)

an efficient synthesis of **2** would allow the rapid, stereocontrolled preparation of substituted polycyclic molecules via subsequent Diels–Alder reactions.[2] This expectation has been borne out.

There have been several reports[3,4] of the intermolecular cyclization of diphenylacetylene at low-valent metal centers (eq 2).



(2)

3

Accordingly, we screened the known cyclopentadienyl and pentamethylcyclopentadienyl chlorides of the group 4A and 5A metals in the presence of reducing agents for the intramolecular cyclization (eq 1) of **1a**.[1] In general, the reactions afforded predominantly oligomers of **1a**, resulting from intermolecular C–C bond formation. However, a system consisting of dicyclopentadienyltitanium dichloride, methyldiphenylphosphine, and sodium amalgam (molar ratio 1:1:2) at −20 °C proved uniquely effective for eq 1. Upon hydrolysis, the desired (*E*,*E*)-diethylidenecyclohexane **2a** was obtained in 80% yield.[5] A metallacyclic intermediate analogous to **3** was not isolated, but its existence was suggested by deuterolysis experiments using 20% D_2SO_4/D_2O. Under these conditions, the product **2a** was found to be 91% dideuterated in the vinyl position.

This titanium-mediated cyclization could also be applied to the synthesis of five- and seven-membered rings as illustrated by the

(1) Of the starting materials in this study, compounds **1a–d** were commercially available from Farchan Labs. The others were prepared by standard (acetylide displacement) procedures: Brandsma, L. "Preparative Acetylenic Chemistry"; Elsevier: New York, 1971.

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(4) Another related reaction is the cobalt-catalyzed cyclotrimerization reaction (Vollhardt, K. P. C. *Acc. Chem. Res.* **1977**, *10*, 1–8) for which cobaltacyclopentadiene intermediates are proposed. To our knowledge, this procedure has not been successfully applied to the synthesis of exocyclic dienes. See also: Chiusoli, G. P.; Costa, M.; Masarat, E. *J. Organomet. Chem.* **1983**, *255*, C35–C38.

(5) In a typical procedure 450 g (97.9 mmol) of 0.5% Na amalgam was added rapidly dropwise to a suspension of dicyclopentadienyltitanium dichloride (9.3 g, 37.3 mmol) and methyldiphenylphosphine (9.0 g, 45.0 mmol) in THF (400 mL) at −50 °C. The temperature of this stirred mixture under N_2 was allowed to rise to −20 to −25 °C where it was maintained 15 min. Thereupon 2,8-decadiyne (3.9 g, 29.1 mmol) in THF (100 mL) was added dropwise and the temperature was kept at −20 to −25 °C for another 3 h. The solution was quenched with 200 mL of 20% H_2SO_4 and extracted with ether (2 × 250 mL). After distillation of solvent and flash chromatography to remove remaining phosphine, the product was distilled (15 torr, 67–69 °C) to afford **2a** (3.16 g, 23.2 mmol, 80%). Anal. Calcd for $C_{10}H_{16}$: C, 88.16; H, 11.84. Found: C, 88.03; H, 11.92. ^1H NMR (C_6D_6) δ 1.59 (d, J = 7 Hz, 6 H), 1.59 (m, 4 H), 2.10 (m, 4 H), 5.38 (q, J = 7 Hz, 2 H).

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