Pd-Catalyzed Cycloisomerization to 1,2-Dialkylidenecycloalkanes. 1

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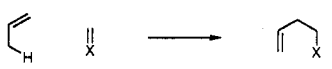
Abstract: Enhancing synthetic efficiency requires the development of synthetic reactions that, to the extent possible, are simple additions wherein everything else is required only in catalytic amounts. The Alder ene reaction constitutes a classical reaction that meets this requirement that has much unrealized potential. A transition-metal-catalyzed version helps to increase that potential by permitting this reaction to proceed under mild conditions. A significant benefit of transition metal catalysis is the feasibility of diverting the reaction along pathways not feasible under thermal conditions. The synthesis of 1,3-dienes rather than 1,4-dienes is a very important diversion because of the utility of 1,3-dienes as reaction partners in the Diels–Alder reaction, another highly atom economical process. A catalyst derived from palladium acetate cycloisomerizes 1,6- and 1,7-enynes to dialkylidenecyclopentanes and -cyclohexanes. 1,3-Diene formation is favored over the Alder ene process by both steric and electronic effects. The reaction is highly chemoselective—tolerating a wide diversity of functionality including hydroxyl groups, ketones, esters, alkynyl and enol ethers, alkynyl and vinyl silanes, and enones. Many of the substrates are available by palladium-catalyzed alkylation reactions—highlighting the effectiveness of palladium catalyzed methodology in organic synthesis. The atom-economical nature of these reactions combined with the Diels–Alder reaction permit butadiene and dimethyl propargylmalonate to be molded into a polyhydro-*as*-indacene. The mechanism of this reaction may involve a tautomerization of an enyne–Pd(+2) complex to a pallada(+4)cyclopentene intermediate as a key step.

The Alder ene reaction (eq 1, X = carbon) has a great deal of promise yet to be realized in complex synthesis.[1] Like its

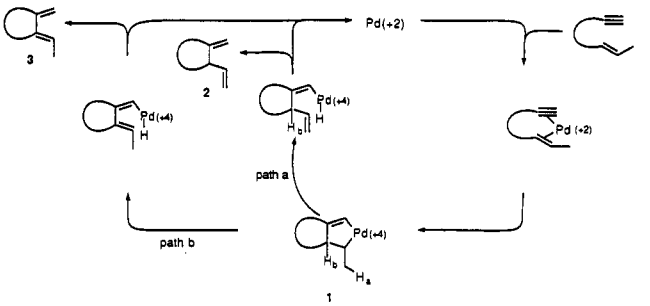


(1)

electronic relative, the Diels–Alder reaction, this simple addition typifies the kind of synthetic reaction that maximizes atom economy. Unlike the Diels–Alder reaction, selectivity issues have restricted its applicability. The limitations stem, in part, from the high temperatures required and low chemoselectivity of the thermal process. The oxaene reaction (eq 1, X = O) has drawn more attention because of the ease with which it can be catalyzed by Lewis acids, thereby lowering the requisite temperatures of reaction and enhancing the chemoselectivity.[2] An additional benefit of Lewis acid catalysis has been the feasibility of catalytic asymmetric induction.[3] Catalysis for the Alder ene reaction could bring similar benefits.[1] Indeed, recent efforts in these laboratories have revealed the feasibility of using transition-metal complexes to catalyze both the inter-[4] and intramolecular[5] versions—the latter being cycloisomerizations.[6]

A major additional benefit of a transition-metal-catalyzed process is the feasibility of diverting the reaction to new pathways not feasible in the thermal reaction. Consider one of the mechanistic rationales of the palladium catalyzed cycloisomerization of enynes (Scheme 1, path a). Assuming a palladacyclopentene intermediate (eg., **1**), the Alder ene product derives

Scheme 1. Path for the Pd(+2)-Catalyzed Cycloisomerization of Enynes



from preferential β-elimination of the C–H_a bond to generate the 1,4-diene product **2**. This rationale suggests that a 1,3-diene product **3** may be possible if β-elimination of the C–H_b bond would dominate. While the geometry of the palladacycle **1** may favor path a, path b need not be impossible.[7] The general importance of 1,3-dienes in cycloadditions makes path b of prime interest. The mechanism of the Alder ene reaction precludes formation of such a product in a thermal process. Dialkylidenecycloalkenes are normally particularly difficult 1,3-dienes

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(2) Snider, B. B. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Heathcock, C. H., Eds.; Pergamon Press: Oxford, U.K., 1991; pp 527–561.

(3) Mikami, K.; Shimizu, M. *Chem. Rev.* **1992**, *92*, 1021. Oppolzer, W. C. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 876.

(4) Trost, B. M.; Indolese, A. *J. Am. Chem. Soc.* **1993**, *115*, 4361.

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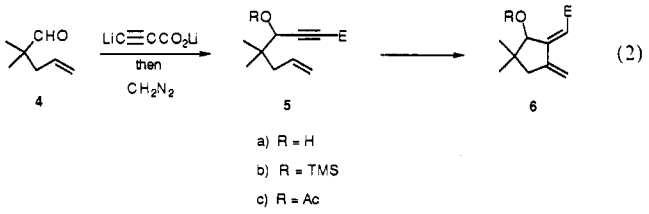
to generate because of the thermodynamic instability of an exocyclic double bond.[8] Thus, simple elimination processes fail unless there are not other regioisomeric products possible. Even so, the harshness of the elimination conditions frequently decomposes the desired product. In this and the accompanying paper, we record a simple cycloisomerization of acyclic enynes to such 1,3-dialkylidenecycloalkanes and its scope and limitations. One of the major applications of this methodology is the utility of the products in subsequent Diels–Alder reactions. Incorporating the dienophile into the substrate then permits this protocol to become a polycyclization by simple cycloisomerization.[9]

Initial Studies

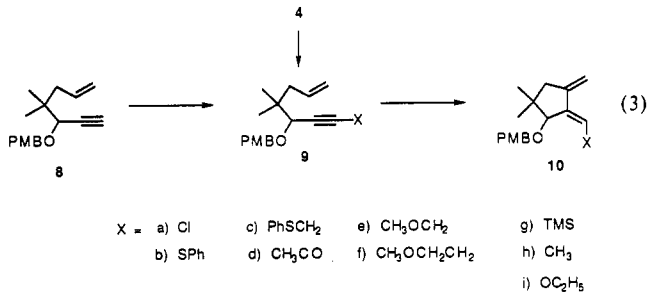
To explore the feasibility of the process, we examined the reactivity of the enyne **5** available from the well-known aldehyde **4**[10] as outlined in eq 2. Subjecting the hydroxy enyne **5a** to 5 mol



(2)

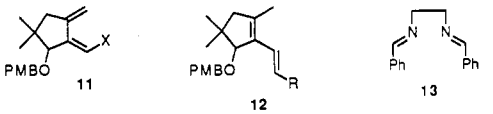
% palladium acetate in C_6D_6 at room temperature gave a 50% yield of the hydroxy diene **6a**, whose structure is easily verified by ^1H NMR spectroscopy (see Experimental Section). The instability of this product led us to investigate whether this factor was responsible for the modest yield. Cyclization of the corresponding silyl ether **5b** proceeded more slowly—requiring 60 °C rather than room temperature—but the yield increased to 70%. The acetate **5c** cyclized with 5 mol % $(Ph_3P)_2Pd(OAc)_2$ (**7**)[11] to give the diene **6c** in 57% yield at reflux in C_6D_6.

To probe the effect of substitution on the acetylene, we used the enyne **8** as the template in which the lithio species was quenched with *N*-chlorosuccinimide (NCS)[12] (to give **9a**, 33%), phenylbenzenethiosulfonate[13] (to give **9b**, 65%), chloromethyl phenyl sulfide (to give **9c**, 20%), acetic anhydride–boron trifluoride etherate[14] (to give **9d**, 43%), chloromethyl methyl ether (to give **9e**, 92%), ethylene oxide followed by methyl iodide (to give **9f**, 42%), trimethylchlorosilane (to give **9g**, 78%), and methyl iodide (to give **9h**, 86%). The ethoxyacetylene **9i** was prepared by adding lithium ethoxyacetylide to **4** followed by *p*-methoxybenzylation (48% yield).



(3)

Not surprisingly, neither the chloro- nor (phenylthio)acetylides **9a** and **9b** gave any cycloadducts regardless of reaction conditions. Somewhat more surprisingly, the (phenylthio)methyl derivative **9c** also failed. In many cases, thioethers are compatible with homogeneous catalysts. Whether the presence of the thio substituent at the propargylic position was specifically responsible for the failure has not yet been established. The acetyl derivative **9d** behaved similarly to the ester **5** but gave the product **10d** in only 40% yield. The methoxymethyl derivative **9e** cycloisomerizes to diene **10e**, but the yield depends upon the quality of the catalyst. Utilizing the crystallized complex bis(tri-*o*-tolylphosphine)-palladium acetate[11] gave a 77% yield; on the other hand, less pure catalyst not only gave lower yields but also formed an isomeric mixture of the *E* (i.e., **10e**) and *Z* (i.e., **11e**) isomers. The *Z* diene **11** is characterized by the vinyl proton adjacent to X being at



higher field than in the *E* diene (δ 5.77 vs 6.16) and the CH_2 adjacent to O being at lower field than in the isomer (δ 4.21 vs 4.06)—consistent with the expected deshielding effect of the adjacent double bond. Considering that MM2 calculations indicated a 4.9 kcal/mol lower energy for the *E* isomer, this equilibration is most surprising. The alkyl- and silyl-substituted acetylenes (**9e–h**) generally reacted more slowly—requiring higher temperatures and/or longer reaction times. Under these conditions, further reaction of the initial products led to isomerization and/or lower yields (due to decomposition). Using nonligated palladium acetate did speed up the reactions but led to more isomerization and/or decomposition. For example, the methoxyethyl and methyl substrates **9f** and **9h** cyclized to a mixture of three isomers: **10**, **11** (X = $CH_3OCH_2CH_2$; X = CH_3), and **12** (R = CH_3OCH_2; R = H) (from **9**, X = $CH_3OCH_2CH_2$, 74%, 2:1:1) (from **9**, X = CH_3, 81%, 3.5:1:1). The trimethylsilyl analogue **9g** cycloisomerized under similar conditions to a 3:1 mixture of **10g** and **11g** in 55% yield.

Convinced that the source of the problems with these latter substrates rested on the reactivity of the catalyst, we turned to the question of ligand design as a way to fine-tune reactivity. The ligand must impart sufficient kinetic reactivity to allow these more sluggish substrates to react but inhibit further reactions of our products. In conjuction with a project directed toward the total synthesis of the picrotoxane family, we encountered a similar problem.[15] Our solution proved to be the use of *N*,*N*-bis-(benzylidene)ethylenediamine (BBEDA, **13**) as ligand. The acceptor–donor properties of this ligand appear to represent a reasonable compromise in adjusting the reactivity of the palladium acetate. It had dramatic effects on these cyclizations. For example, cyclization of **9f** now gave almost pure diene **10f** in virtually quantitative yield using 5% BBEDA and 5% palladium acetate as catalyst. Similar results were obtained in the cyclizations of **9g** (to **10g**, 89% yield) and **9h** (to **10h**, 88% yield). The sensitivity of the ethoxyacetylene substrate and its cycloisomer

(8) For a few representative illustrations, see: Bailey, W. J.; Sorenson, W. J. *J. Am. Chem. Soc.* **1954**, *76*, 5421. Blomquist, A. T.; Verdol, J. A. *J. Am. Chem. Soc.* **1956**, *78*, 109. Bartlett, P. D.; Wingrove, A. S.; Ouyang, R. *J. Am. Chem. Soc.* **1968**, *90*, 6067. Van Straten, J. W.; Van Norden, J. J.; Schark, T. A. M.; Franke, G. T.; De Wolf, W. H.; Bickelhaupt, F. *Recl. Trav. Chim. Pays-Bas* **1978**, *97*, 105. Scharf, H. D.; Plum, H.; Fleishhauer, J.; Joerg, S. W. *Chem. Ber.* **1979**, *112*, 862, 883, 890. Trost, B. M.; Shimizu, M. *J. Am. Chem. Soc.* **1982**, *104*, 4299. Ardecky, R. J.; Dominguez, D.; Cava, M. P. *J. Org. Chem.* **1982**, *47*, 409. Block, E.; Aslam, M.; Eswarakrishnan, V.; Wall, A. *J. Am. Chem. Soc.* **1983**, *105*, 6165. Baran, J.; Klein, H.; Schade, C.; Will, E.; Koschinsky, R.; Bäuml, E.; Mayr, H. *Tetrahedron* **1988**, *44*, 2181. Baran, J.; Mayr, H. *Tetrahedron* **1989**, *45*, 3347. Barko, A.; Benetti, S.; Casolari, A.; Manfredini, S.; Pollini, G. P.; Polo, E.; Zanirato, V. *Tetrahedron* **1989**, *45*, 3935. Sustmann, R. *Chem. Ber.* **1989**, *122*, 1551.

(9) For preliminary reports of portions of this work, see: Trost, B. M.; Lautens, M. *J. Am. Chem. Soc.* **1985**, *107*, 1781. Trost, B. M.; Hipskind, P. A.; Chung, J. Y. L.; Chan, C. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 1502.

(10) Salomon, R. G.; Ghosh, S. *Org. Synth.* **1984**, *62*, 125. Magnus, P. D.; Nobbs, M. S. *Synth. Commun.* **1980**, 273.

(11) For preparation of phosphine complexes of palladium, see: Stephenson, T. A.; Morehouse, S. M.; Powell, A. R.; Heffer, J. P.; Wilkinson, G. *J. Chem. Soc.* **1965**, 3622. For "crystallized" complex, a mixture of 1 equiv of palladium acetate and 3 equiv of tri-*o*-tolylphosphine in benzene was warmed until homogeneous. An equal volume of hexane was added, and the mixture was allowed to crystallize in a refrigerator.

(12) Cf. Murray, R. E. *Synth. Commun.* **1980**, *10*, 345.

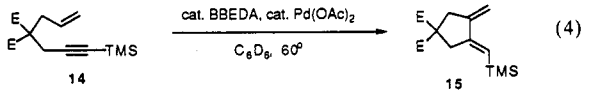
(13) Trost, B. M.; Massiot, G. S. *J. Am. Chem. Soc.* **1977**, *99*, 4405.

(14) Brown, H. C.; Racherla, U. S.; Singh, S. M. *Tetrahedron Lett.* **1984**, *25*, 2411.

(15) Trost, B. M.; Jebaratnam, D. J. *Tetrahedron Lett.* **1987**, *28*, 1611.

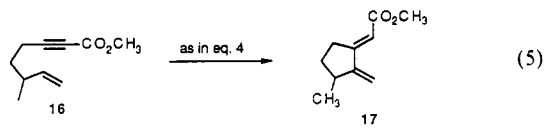
only led to decomposition with all catalysts except that derived from the employment of BBEDA where the cycloisomer **10i** was isolated in 32% yield.

The effects of substituents on the tether were briefly examined. The order of reactivity in the above cases suggests that electron-withdrawing groups by both resonance and inductive effects enhance the rate of these reactions. In order to ascertain the role, if any, of the propargylic alkoxy substituent which was present simply from the point of view of synthetic convenience in cases where the other terminal alkyne substituent did not possess an electron withdrawing group, we examined the silylacetylene **14** (eq 4). Using BBEDA as ligand, cycloisomerization occurred



(4)

smoothly at 60 °C to give diene **15** as a single geometric isomer in 85% yield. The presence of the geminal alkyl substituents also stems from ease of availability of substrates. While such groups may faciliate cyclization due to the Thorpe–Ingold effect, they are not required. Cyclization of the enyne **16** (eq 5) proceeded with facility equal to that of many of the others recorded above to give diene **17** in 83% yield, also as a single geometric isomer using BBEDA as ligand.



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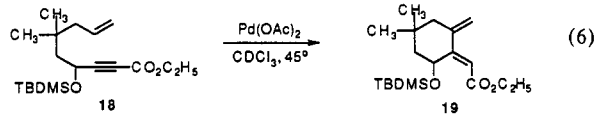
We have concentrated our efforts on formation of five-membered rings. Nevertheless, we did examine one case for formation of a six-membered ring (eq 6). This reaction proved

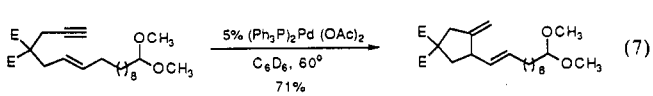


(6)

more sensitive to exact reaction conditions. The use of ligands inhibited reaction; thus, palladium acetate under ligandless conditions proved to be the superior catalyst. Solvent also had an effect. The normally employed solvents like benzene and 1,2-dichloroethane (DCE) gave lower yields of cycloisomer **19** (~30%). Cyclization of **18** proceeded best with 5% $Pd(OAc)_2$ in $CDCl_3$ at 45 °C whereby a 60% yield of the diene **19** arose after 7 h. The purity of the substrate also had a rate effect. Chromatographed **18** required 18 h at 55 °C to give a 57% yield of diene **19**; whereas, distilled **18** gave the best result, as stated above.

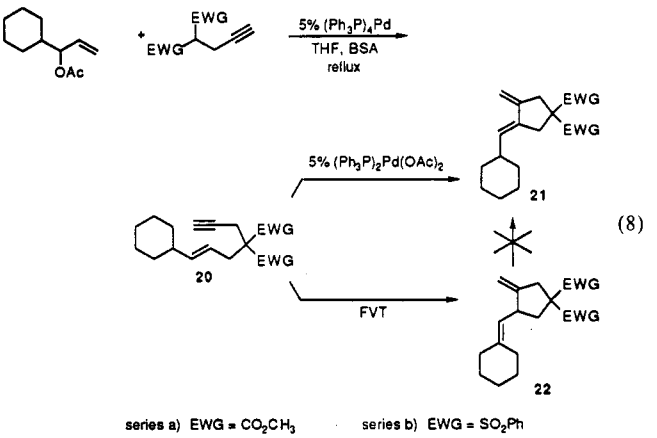
Allylic Substitutent Effects on Regioselectivity

In all of the above cases, the absence of an allylic substituent bearing hydrogen that could lead to a normal ene type product (eq 1) dictates that only 1,3-dienes can form. The utility of the reaction increases if this structural feature is not a requirement for successful synthesis of the 1,3-diene. Steric factors influence regioselectivity. Whereas an allylic methylene group led smoothly to the Alder ene type product (eq 7),[5] branching at the allylic



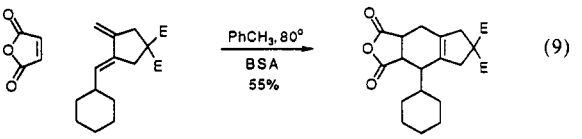
(7)

position completely changed the regioselectivity. For example, an allylic methylene group led smoothly to the Alder ene type product (eq 7),[5] but branching at the allylic position completely changed the regioselectivity. The cyclohexyl substrate **20a**, readily available by Pd(0)-catalyzed alkylation (**20a**, 71% yield) (eq 8),



(8)

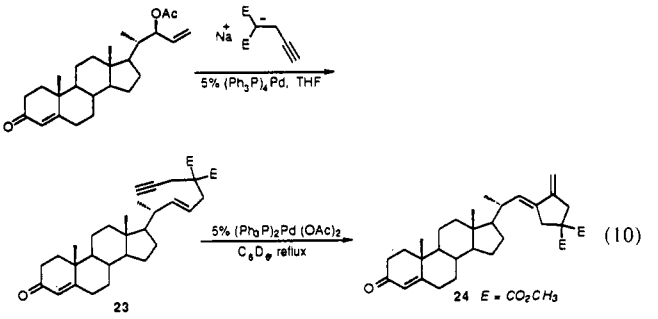
was smoothly cycloisomerized to give a diene in 64% yield (THF, 66°). That the diene was not the Alder ene type product **22a** was first demonstrated by its nonidentity with the compound prepared by flash vacuum thermolysis. The UV spectrum suggested the 1,3-diene **21** (λ_{MAX} 255 nm ϵ 5800), which was verified by its smooth participation in a Diels–Alder reaction (eq 9). Further-



(9)

more, the 1,3-diene **21a** did not arise by isomerization of the Alder ene product **22a**, which was demonstrated by an unsuccessful attempt to convert the latter to the former under the palladium-catalyzed reaction conditions. Replacing the methoxycarbonyl groups by the bulkier phenylsulfonyl groups led to a rate enhancement. Enyne **20b** cyclized at ambient temperature in C_6D_6 to give diene **21b** in 72% yield.

The regioselectivity may derive from the strain associated with placing a double bond exocyclic to a six-membered ring, as present in the Alder ene type product **22**. To explore this possibility as well as the chemoselectivity, the steroidal enyne **23**, also prepared

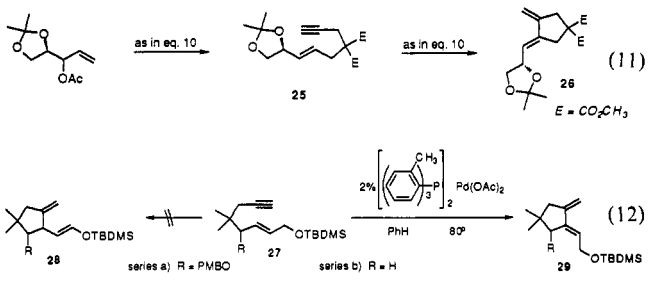


(10)

by Pd(0)-catalyzed alkylation (62% yield), was examined. Cycloisomerization with 5% $(Ph_3P)_2Pd(OAc)_2$ in benzene at reflux gave a single diene (80% yield) whose spectroscopic properties clearly indicated it was the 1,3-diene **24**. Particularly diagnostic was the presence of the side-chain methyl group (δ 1.00) as a doublet (J = 7 Hz) in the ^1H NMR spectrum.

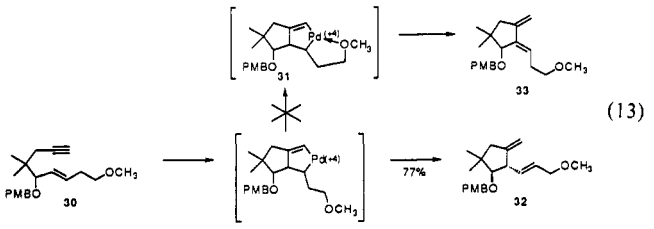
Heteroatom branching led to a similar result. Thus, cycloisomerization of enyne **25**, prepared by the "standard" method (55% yield), gave the 1,3-diene **26** as the sole product (eq 11). ^1H NMR spectroscopy (see Experimental Section) unambiguously defined the structure.

There also appears to be an electronic effect operating in the latter case. Thus, the "unbranched" substrate **27a** might have been expected to yield the Alder ene type product **28a**; instead,



its cycloisomerization produced only 1,3-diene **29a** in 80% yield. That the (*p*-methoxybenzyl)oxy group did not play a role in affecting the regioselectivity was indicated by the cyclization of **27b** under identical conditions, which gave only 1,3-diene **29b** in 92% yield (eq 12).

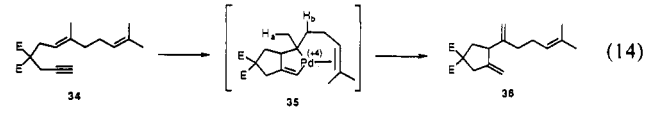
What is the source of the regioselectivity in these latter cyclizations? Could the potential coordinating properties of oxygen to palladium influence the regioselectivity? The use of the TBDMS group should minimize such a role for the oxygen substituent. Examination of enyne **30** further probes this point, since (1) the methyl ether should coordinate more strongly than a silyl ether and (2) coordination via a five-membered ring (e.g. **31**) should be better than that for the four-membered ring required



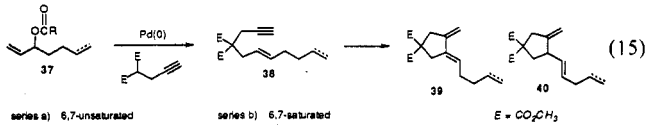
in the case of enynes **25** and **27**. The fact that the Alder ene product **32** rather than the 1,3-diene **33** was formed suggests that oxygen coordination is not the regiochemical determining factor in the cycloisomerization of eqs 11 and 12. Thus the source of the oxygen effect appears to be electronic in nature.

Remote Binding

The notion that coordination as depicted in **31** could influence regioselectivity derived from our studies of the cycloisomerization of the geranyl-derived substrate **34**, which cyclized exclusively to the triene **36** (eq 14).[5,16] The critical role that the remote



double bond played in controlling the regioselectivity led us to suggest that coordination of this double bond as depicted in **35** could geometrically preclude β-hydrogen elimination of the C–H_b bond, therefore directing elimination toward C–H_a. While an oxygen substituent apparently does not play such a role, we were intrigued as to whether a double bond might. By analogy to the case of **34**, the cycloisomerization of **38a** was compared with that of its saturated derivative **38b** to examine the feasibility of remote



binding as a regiochemical control element. Both substrates were readily accessible by Pd(0)-catalyzed allylic alkylation from allyl

(16) Trost, B. M.; Lautens, M. *Tetrahedron Lett.* **1985**, *26*, 4887.

Table 1. Regioselectivity of Cycloisomerization of Enynes **38a** and **b**

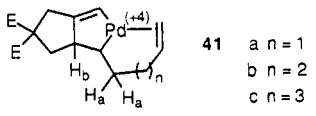
entry	substrate	catalyst	ratio **39/40**	yield
1	**38a**	$Pd(OAc)_2$	15:1	77%
2	**38a**	$[(o\text{-}CH_3C_6H_4)_3P]_2Pd(OAc)_2$	2.7:1	87%
3	**38a**	$(Ph_3P)_2Pd(OAc)_2$	1:2.1	73%
4	**38a**	BBEDA–$Pd(OAc)_2$	6.9:1	70%
5	**38b**	$Pd(OAc)_2$	only **40**	39%
6	**38b**	$[(o\text{-}CH_3C_6H_4)_3P]_2Pd(OAc)_2$	1:2.6	74%
7	**38b**	$(Ph_3P)_2Pd(OAc)_2$	1:2.9	78%

Table 2. Regioselectivity of the Cycloisomerization of Dienynes **42a** and **b**

		ratio **43/44** (% yield)	
entry	catalyst	from **42a**	from **42b**
1	$Pd(OAc)_2$	21:1 (76%)	1.1:1 (75%)
2	$[(o\text{-}CH_3C_6H_4)_3P]_2Pd(OAc)_2$	>20:1 (N.D.)[a]	1:1.6 (74%)
3	$(Ph_3P)_2Pd(OAc)_2$	2.7:1 (N.D.)	1:4.6 (81%)
4	$3Ph_3P$, $2Pd(OAc)_2$	1:2.3 (24%)	

[a] N.D. = not determined.

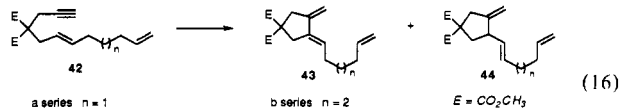
esters **37a** and **b** (see Experimental Section). The results are summarized in Table 1. The important role played by the remote double bond is clearly established by comparing entries 1 and 5 whereby excellent selectivity for formation of the 1,3-diene **39** occurred in the presence of the remote olefin (i.e., **38a**) and excellent selectivity for formation of the 1,4-diene **40** occurred in its absence (i.e., **38b**). An intermediate such as **41** accom-



modates these observations whereby remote binding geometrically precludes β-hydrogen elimination of the C–H_a bond. While the geometry for insertion into the C–H_b bond is not ideal, a fact which explains the normal preferential formation of the Alder ene type products, its lower bond strength due to its allylic nature compensates for the geometrical impediment.

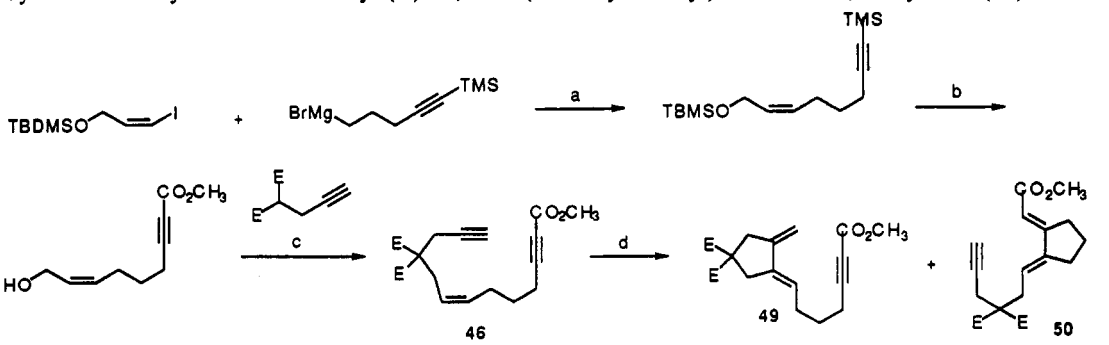
To the extent that an external ligand may compete with the double bond for coordination, this effect should be diminished. This trend is observed. Adding *o*-tolylphosphine decreased the selectivity for 1,3-diene formation (entry 2), and the stronger binder triphenylphosphine (entry 3) reversed the selectivity, i.e., favored formation of the 1,4-diene. In the latter case, the results were very comparable to those of the saturated analogue **38b** (cf. entries 3 and 7). BBEDA proved a poorer competitor for the olefin coordination than the phosphines. This observation is in accord with the normally better coordinating properties of phosphines compared to imines toward palladium.

Moving the remote double bond one more carbon away would lead to an internally coordinated structure such as **41b**, which should be as favorable or perhaps more favorable than **41a** because of the larger ring size. Equation 16 and Table 2 summarize the



results. The observations strongly support the notion that coordination with a three-carbon spacer is stronger than that with a two-carbon spacer. In the absence of an external ligand, the intrinsic regioselectivity was higher (**42a**, entry 1). It took a higher ratio of external ligand to phosphine of a stronger coordinating phosphine to compete effectively with the internal coordination (**42a**, entries 2–4). Extending the tether by an additional carbon as in **42b** requires an internal coordination via

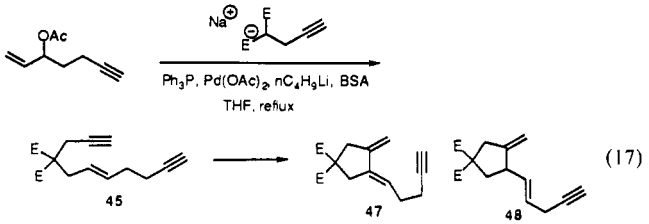
Scheme 2. Synthesis and Cyclization of Methyl (*Z*)-10,10-bis(methoxycarbonyl)tridec-7-en-2,12-diynoate (46)[a]



[a] Conditions: (a) $ZnCl_2$, $(Ph_3P)_4Pd$, THF, rt, 83%. (b) (i) K_2CO_3, CH_3OH, rt; (ii) *n*-C_4H_9Li, THF, −78 °C, $ClCO_2CH_3$; (iii) H_2O, HOAc, rt; 48% overall. (c) (i) PBr_3, C_5H_5, hexane–ether, 0 °C; (ii) NaH, dimethyl propargylmalonate, THF, rt; 95% overall. (d) See text.

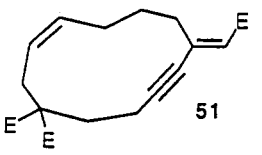
41c which virtually abolishes this effect (eq 16 and Table 2, **42b**, entries 1–3).

Since an acetylene should coordinate with palladium more strongly than an olefin, we explored substrates **45** and **46**. The former was prepared by straightforward Pd(0)-catalyzed allylic alkylation (eq 17), and the latter, by the route outlined in Scheme 2. The ratio of the 1,3-diene **47** to the 1,4-diene **48** increased to 26:1 compared to the analogous substrate bearing an olefin as a remote binding site (eq 15, 15:1) using palladium acetate as catalyst.

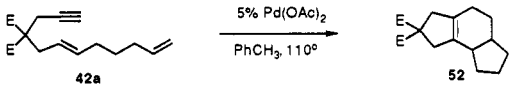


(17)

Enediyne **46** examines the issue of chemoselectivity as well as explores the role of the remote binding group. Cyclization with palladium acetate in the presence or absence of BBEDA in DCE gave only 1,3-dienes but as a mixture of the two possibilities **49** and **50** (2.5:1 to 1:1 in the absence and presence of ligand, respectively). Thus, while a Thorpe–Ingold effect favors **49**, the electronic effect favoring **50** sufficiently competes to lead to both products being formed. In the absence of ligand, a 9% yield of a macrocyclic isomer **51** was also detected—a type of reactivity that we have previously optimized by use of strong donor phosphine ligands on palladium.[17]



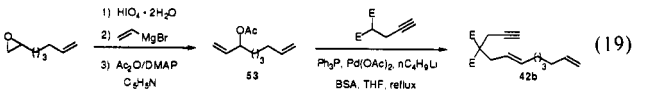
The excellent regioselectivity for formation of 1,3-dienes in substrates bearing an olefin or an acetylene separated from the enyne by a two- or three-carbon spacer led us to consider a one-pot tandem double cycloisomerization of the dienyne **42a** involving the palladium-catalyzed enyne cyclization followed by a thermal Diels–Alder reaction. Heating a toluene solution of **42a** containing 5% palladium acetate generated the tricycle **52** in 72% yield (eq 18). Following the reaction by gas chromatography revealed the enyne cyclization was complete in only 30 min under these conditions.



(18)

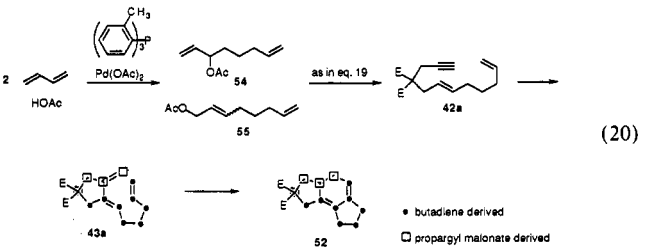
Discussion

This *catalytic* cycloisomerization of enynes to 1,3-dienes constitutes a simple and highly efficient method for the construction of 1,2-dialkylidenecyclopentanes and -cyclohexanes. Furthermore, construction of many of the substrates also takes advantage of palladium-catalyzed methodology.[18] For example, the enyne **42b** was prepared as outlined in eq 19[19] (also cf. eqs 8, 10, and 11) as a 4:1 *E*/*Z* ratio which was used in the subsequent cyclizations.



(19)

The synthesis of **42a** and ultimately the tricycle **52** proves most interesting from a strategic point of view (eq 20). Palladium-



(20)

catalyzed addition of butadiene and acetic acid generated a 1:3 ratio of regioisomeric allylic acetates **54** and **55**.[20] Since the regioselectivity of the subsequent allylic alkylation is independent of the regioisomeric nature of the starting material, this mixture was directly employed in a second palladium-catalyzed alkylation to give dienyne **42a** in 70% yield as a 6.3:1 *trans*/*cis* ratio. Palladium-catalyzed cycloisomerization generated triene **43a** or, if performed at higher temperature, the tricycle **52**. The tricycle was then derived from the equivalent of simple addition of butadiene and dimethyl propargylmalonate by three consecutive palladium-catalyzed reactions with acetic acid being recyclable. Thus, these palladium-catalyzed processes create synthetic strategy with extremely high atom economy.

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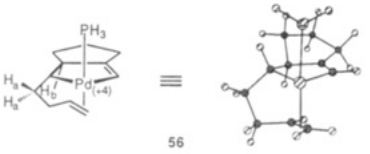
(19) For oxidative cleavage of an epoxide, see: Nagarkatti, J. P.; Ashley, K. R. *Tetrahedron Lett.* **1973**, 4599.

(20) Rose, D.; Lepper, H. *J. Organomet. Chem.* **1973**, *49*, 473.

The mechanism of this reaction as outlined in Scheme 1 must be considered speculative at the present time. Support derives from an analogous pathway with tetracarbomethoxycyclopentadiene,[22] but a hydridopalladium acetate pathway also exists.[21] Whether the reactions catalyzed by palladium acetate follow one or the other of these pathways or as yet an undefined one cannot be stated with any degree of confidence. On the other hand, there are clear differences between a hydridopalladium acetate pathway and that using palladium acetate.[23] For this reason, we currently favor the pathway depicted in Scheme 1.[24] The fact that there is increasing evidence for the involvement of the +4 valence state in the organic chemistry of palladium lends further credence to this proposal.[25]

In examining the palladacyclopentene **1**, we see that the weakest β-C–H bond is that of H_b, which would have led to the expectation that the products should be the 1,3-dienes. The normal preference for the Alder ene type product (Scheme 1, path a) must then derive from the poor overlap of this C–H_b bond and the C–Pd in the palladacyclopentene. On the other hand, if we increase the steric congestion around H_a or make the carbon to which H_a is attached electron deficient by adding an electronegative substituent, we tilt the reaction in favor of the 1,3-diene product (Scheme 1, path b).

The third factor that favors 1,3-diene formation is geometrical. Since the β-hydrogen elimination is known to favor a dihedral angle as close to zero as possible,[26] geometrically inhibiting such an orientation directs the regioselectivity away from that hydrogen. The presence of an additional C–C unsaturation two or three atoms away from the olefin creates a pseudocycle which forces the dihedral angles between C–Pd and C–H_a to be >90°, as depicted in **56**. Removing the geometric flexibility for this angle

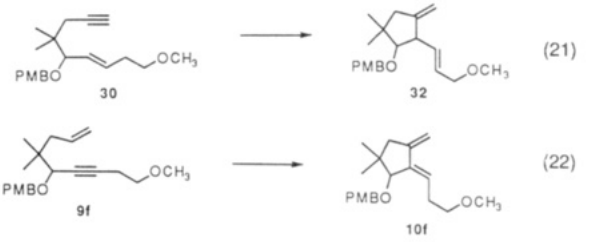


56

to approach 0° easily for C–H_a makes this geometric factor equivalent for insertion into either C–H_a or C–H_b and then allows the lower bond strength of C–H_b to dominate as a contributor to the transition state energy for the β-hydrogen elimination.

By proper choice of substrate, either type of product may be obtained, as illustrated in eqs 21[5] and 22. Enyne **30** follows the "normal" Alder ene type pathway (eq 21). Simply interconverting the olefin and acetylene as in **9f** then provides access to the 1,3-diene product **10f** (eq 22).

The importance of these difficultly obtainable dienes has led to the generation of other methods for their construction.[8,27] The



recently disclosed reductive cyclizations of diynes provides useful alternatives. Two methods have been developed: (1) a palladium-*catalyzed* reductive cyclization using *stoichiometric* amounts of an acid and a silane[28] and (2) a *stoichiometric* reduction with low-valent titanium or zirconium followed by *stoichiometric* protonation.[29,30] An important difference between these two strategies is the difference in atom economy. The current method is a simple isomerization with anything else being used only catalytically, which is *not* the case for either of the above processes. On the other hand, there will be cases where one method succeeds and the others fail.

The formation of polycycles mediated by cobalt also provides a powerful method for cycloisomerization involving direct capture of a presumed cobaltacyclopentadiene.[31] This method does not provide access to the dienes but requires the presence of an additional unsaturation, either external or internal. While the products are at a different oxidation level than that achieved by cyclization to a diene followed by Diels–Alder reactions, the structural motif generated will be similar.

All of these variations have their individual strengths and weaknesses. They share a potential simplicity of folding readily available acyclic structures into ring systems, and thus all should find utility in organic synthesis.

Experimental Section

General Techniques. Reactions were generally run under a positive pressure of dry nitrogen in glassware which was flame-dried under a stream of dry nitrogen. Anhydrous solvents or reaction mixtures were distilled before use: benzene, dichloromethane, 1,2-dichloroethane, diisopropylamine, hexane, and methyl chloroformate from calcium hydride; dimethylformamide from barium hydroxide; ether, tetrahydrofuran (THF), and toluene from sodium benzophenone ketyl; pyridine and triethylamine from potassium hydroxide; chlorotrimethylsilane from tri-*n*-butylamine or calcium hydride. Palladium acetate was used as provided from Aldrich Chemical Company. Flash chromatography following the method of Still[32] employed E. Merck silica gel (Kieselgel 60, 200–400 mesh). Analytical thin-layer chromatography was performed with 0.2 mm coated commercial silica gel plates (E. Merck, DC-Plastikfolien, Kieselgel 60 F_{254}). Melting points were obtained on a Thomas–Hoover apparatus in open capillary tubes and are uncorrected. Boiling points are also uncorrected. Kugelrohr distillation was performed on a Buchi GKR-50 glass tube oven.

Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on a Bruker WP-200 (200 MHz), Bruker WP-270 (270 MHz), Bruker AM-500 (500 MHz), Nichole NT-300 (300 MHz), or Varian XL-400 (400 MHz). Chemical shifts are reported in δ units, parts per million (ppm) downfield from tetramethylsilane, or ppm relative to the singlet at 7.24 ppm for chloroform-d_1. Splitting patterns are designated as follows: s, singlet; d, doublet; t, triplet; q, quartet; p, pentet; m, multiplet; br, broad. Coupling constants are reported in hertz (Hz). Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a Varian Gemini 300 (75 MHz), Varian XL-400 (100 MHz), or Bruker AM-500 (125 MHz) spectrometer and are reported in ppm relative to the center line of a triplet at 77.00 ppm for chloroform-d_1. Routine ^{13}C NMR

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(23) See following paper in this issue.

(24) For a leading reference regarding metallacycles, see ref 5.

(25) For an overview, see: Canty, A. J. *Acc. Chem. Res.* **1992**, *25*, 83. Also see: Uson, R.; Fornies, J.; Navarro, R. *J. Organomet. Chem.* **1975**, *96*, 307. Ito, T.; Tsuchiya, H.; Yamamoto, A. *Bull Chem. Soc. Jpn.* **1977**, *50*, 1319. Gillie, A.; Stille, J. K. *J. Am. Chem. Soc.* **1980**, *102*, 4933. Loar, M. K.; Stille, J. K. *J. Am. Chem. Soc.* **1981**, *103*, 4174. Morawsky, A.; Stille, J. K. *J. Am. Chem. Soc.* **1981**, *103*, 4182. Kurosawa, H.; Emoto, M.; Urabe, A. *Chem. Commun.* **1984**, 968. Diversi, P.; Fasce, D.; Santini, R. *J. Organomet. Chem.* **1984**, *269*, 285. Sebald, A.; Strader, C.; Wrackmeyer, B.; Bensch, W. *J. Organomet. Chem.* **1986**, *311*, 233. For a theoretical treatment, see: Low, J. J.; Goddard, W. A., III. *J. Am. Chem. Soc.* **1986**, *108*, 6115.

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(27) Also see: Trost, B. M.; Shimizu, M. *J. Am. Chem. Soc.* **1982**, *104*, 4299 and references therein.

(28) Trost, B. M.; Lee, D. C. *J. Am. Chem. Soc.* **1988**, *110*, 7255.

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(32) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

spectra were fully decoupled by broad-band decoupling. The degree of substitution at carbon was determined by ERNST techniques on the Bruker AM-500 or the attached proton test (APT) on the Varian FX-400.

Infrared (IR) spectra were recorded in 0.1 mm path length sodium chloride cavity cells on a Nicolet 205 FT-IR or Perkin-Elmer 1420. High resolution mass spectra (MS) were recorded on an AE1-MS902, Kratos MS25, Kratos MS80, or Kratos MS9 spectrometer at an ionizing current of 98 mA and an ionizing voltage of 70 eV, unless otherwise noted, and are reported as *m/e* (relative intensity). Low-resolution mass spectra were recorded on a Hewlett Packard gas chromatograph/mass spectrometer, using a Hewlett Packard 5890A gas chromatograph with a 25 m × 0.25 mm i.d. SE-30 column and a Hewlett Packard 5970 series mass selective detector with an ionizing voltage of 70 eV. The detection range was restricted to M ± 5 units and is reported as *m/e* (relative intensity). Microanalyses were performed by Sprang Microanalytical Laboratories, Eagle Harbor, MI, or Robertson Laboratory Inc., Madison, NJ.

Analytical gas chromatography (GC) was performed on a Varian Model 3700 gas chromatograph using an ALLTECH 25 m × 0.25 mm i.d. SE-30 column, with flame ionization detection. Three temperature programs were used: (method A) T_i = 50 °C, T_f = 250 °C, rate = 10 °C/min; (method B) T_i = 100 °C, T_f = 250 °C, rate = 10 °C/min; (method C) T_i = 150 °C, T_f = 250 °C, rate = 10 °C/min holding T_f for 10 min. Analytical GC was also performed using a stainless steel 10% OV-101 on Chromosorb WHP 80/100, 10 ft × 0.085 in. i.d. column, using the temperature program of method D: T_i = 50 °C, T_f = 250 °C, rate = 10 °C/min. Preparative GC was performed on a Varian Model 3700 gas chromatograph using a stainless steel 10% OV-101 on Chromosorb WHP 80/100, 10 ft × 0.210 in. i.d. column. The separations were performed isothermally with thermal conductivity detection.

Preparation of Methyl 5,5-Dimethyl-4-hydroxyoct-7-en-2-ynoate (5a). *n*-Butyllithium (1.3 mL, 2.0 mmol) was added dropwise to a solution of propiolic acid (0.061 mL, 1.0 mmol) in THF (5 mL) at −78 °C followed, after 30 min at −78 °C, by 2,2-dimethyl-4-pentenal (112 mg, 1.0 mmol). The resulting solution was stirred for 30 min at −78 °C and then warmed to room temperature and stirred a further 1.5 h. The reaction was poured into ether-saturated aqueous sodium carbonate, and the aqueous phase was then acidified to pH 1 with concentrated hydrochloric acid. Extraction of the aqueous phase with ether (3×) was followed by drying the solvent over magnesium sulfate. Evaporation of the solvent *in vacuo* yielded a yellow oil which was dissolved in ether (5 mL). An etheral solution of diazomethane was added to the former solution until the evolution of bubbles ceased, at which time a few drops of acetic acid were added. The solvent was then removed *in vacuo* and the resultant oil purified by flash chromatography (2:1 hexane/ether) to yield the title compound as a clear oil, 118 mg (67%). IR ($CDCl_3$): 3602, 3080, 2978, 1713, 1437, 1258, 1028 cm^{-1}. ^{1}H NMR (270 MHz, C_6D_6): δ 5.71 (dq, *J* = 16, 9.6 Hz, 1H), 5.09 (d, *J* = 16 Hz, 1H), 5.08 (d, *J* = 9.6 Hz, 1H), 3.94 (d, *J* = 4.5 Hz, 1H), 3.32 (s, 3H), 2.20 (bd, *J* = 9.6 Hz, 1H), 2.08 (bd, *J* = 9.6 Hz, 1H), 1.71 (d, *J* = 4.5 Hz, 1H), 0.99 (s, 3H), 0.96 (s, 3H). Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.33; H, 8.22. Found: C, 67.25; H, 8.25.

Preparation of Methyl 5,5-Dimethyl-4-(trimethylsiloxy)oct-7-en-2-ynoate (5b). A mixture of the hydroxy ene **5a** (50 mg, 0.26 mmol) and *N,O*-bis(trimethylsilyl)acetamide (BSA) (0.188 mL, 3 equiv) in THF (1 mL) was heated at reflux for 6 h. After evaporation of the solvent *in vacuo*, the oil was purified by flash chromatography (hexane), yielding the title compound as a clear oil, 66 mg (96%). IR ($CDCl_3$): 3074, 2960, 2229, 1709, 1639, 1432, 1260, 1094, 1059, 855, 840 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ 5.77 (m, 1H), 4.09 (s, 1H), 3.75 (s, 3H), 2.08 (m, 2H), 0.92 (s, 3H), 0.90 (s, 3H), 0.24 (s, 9H). HRMS: calcd for $C_8H_{13}SiO_3$($M^+ - C_6H_{11}$) 185.1743, found 185.1531.

Preparation of Methyl 4-Acetoxy-5,5-dimethyloct-7-en-2-ynoate (5c). Alcohol **5a** (50 mg, 0.24 mmol), pyridine (0.040 mL, 0.4 mmol), and DMAP (3 mg, 0.02 mmol) were added to 2 mL of methylene chloride. After cooling the solution to 0 °C, acetic anhydride (0.05 mL, 0.52 mmol) was added dropwise and the resulting solution stirred for 2 h. Workup of the reaction involved pouring the crude mixture into a separatory funnel containing ether-saturated aqueous copper sulfate. The organic phase was washed with saturated sodium chloride and the solvent dried over magnesium sulfate. Evaporation of the solvent *in vacuo* followed by flash chromatography (5:1 hexane/ether) yielded the title compound as a clear oil, 47 mg (52%). IR ($CDCl_3$): 3080, 2979, 2938, 2221, 1740, 1713, 1641, 1436, 1371, 1260, 1227, 1021 cm^{-1}. ^{1}H NMR (200 MHz, C_6D_6): δ 5.66 (ddt, *J* = 16, 10, 7.5 Hz, 1H), 5.45 (s, 1H), 5.04 (d, *J* = 10 Hz, 1H), 5.00 (d, *J* = 16 Hz, 1H), 3.27 (s, 3H), 2.10 (d, *J* = 7.5 Hz, 2H), 1.62 (s, 3H), 1.00 (s, 3H), 0.98 (s, 3H). HRMS: calcd for $C_{13}H_{18}O_4$ (M^+) 238.1200, found 238.1185.

Preparation of (*E*)-2-(Carbomethoxymethylidene)-4,4-dimethyl-3-hydroxy-1-methylenecyclopentane (6a). A mixture of enyne **5a** (12 mg, 0.07 mmol) and palladium acetate (0.9 mg, 5 mol %) in benzene-d_6 (0.450 mL) was stirred at room temperature for 6 h. Flash chromatography (2:1 hexane/ether) through a short plug of silica gel provided the title compound as an unstable clear oil, 6 mg (50%). IR ($CDCl_3$): 3480, 2959, 1691, 1649, 1620, 1439, 1350, 1208, 1044, 1019 cm^{-1}. ^{1}H NMR (270 MHz, $CDCl_3$): δ 6.22 (d, *J* = 1.5 Hz, 1H), 5.63 (br s, 1H), 5.11 (br s, 1H), 4.89 (d, *J* = 1.5, 1H), 4.49 (br s, 1H), 3.74 (s, 3H), 2.39 (d, *J* = 12.8 Hz, 1H), 2.17 (d, *J* = 12.8 Hz, 1H), 1.03 (s, 3H), 0.98 (s, 3H). MS: 178 (0.7), 177 (10.2), 163 (26.0), 153 (13.5), 149 (29.8), 135 (40.7), 121 (14.7), 93 (40.3), 55 (95.1), 43 (100.0). HRMS: calcd for $C_{11}H_{16}O_3$ ($M^+ - H_2O$) 178.1014, found 178.1007.

Preparation of (*E*)-2-(carbomethoxymethylidene)-4,4-dimethyl-1-methylene-3-(trimethylsiloxy)cyclopentane (6b). A mixture of the siloxy enyne **5b** (20 mg, 0.07 mmol) and palladium acetate (0.8 mg, 5 mol %) in benzene-d_6 (0.450 mL) was heated at 70 °C for 5 h. The crude oil was passed through a plug of Florisil (15:1 hexane/ether) to yield the title compound as a clear oil, 14 mg (70%). IR ($CDCl_3$): 2960, 1711, 1655, 1620, 1436, 1359, 1340, 1250, 1204, 1175, 1090, 877, 841 cm^{-1}. ^{1}H NMR (270 MHz, $CDCl_3$): δ 6.13 (s, 1H), 5.62 (s, 1H), 5.11 (s, 1H), 4.90 (s, 1H), 3.72 (s, 3H), 2.50 (d, *J* = 14 Hz, 1H), 2.00 (d, *J* = 14 Hz, 1H), 1.04 (s, 3H), 0.75 (s, 3H), 0.09 (s, 9H). HRMS: calcd for $C_{12}H_{17}Cl_2$ ($M^+ - CH_3$–CH_3OH) 221.2113, found: 221.2176.

Preparation of 3-Acetoxy-(*E*)-2-[(*E*)-carbomethoxymethylidene]-4,4-dimethyl-1-methylenecyclopentane (6c). A solution of **5c** (21 mg, 0.09 mmol) and bis(triphenylphosphine)palladium acetate (3.4 mg, 5 mol %) in benzene-d_6 (0.450 mL) was heated at 70 °C for 4.5 h. The crude reaction mixture was added to a flash chromatography column and the diene **6c** eluted (7:2 hexane/ether) as a clear oil, 12 mg (57%). ^{1}H NMR (200 MHz, $CDCl_3$): δ 6.28 (s, 1H), 5.94 (s, 1H), 5.68 (t, *J* = 1.5, 1H), 5.16 (s, 1H), 3.70 (s, 3H), 0.92 (s, 3H). HRMS calcd for $C_{13}H_{18}O_4$ (M^+) 238.1200, found: 238.1205.

4,4-Dimethyl-3-((*p*-methoxybenzyl)oxy)-6-hepten-1-yne (8). A solution of aldehyde **4** (5.00 g, 44.6 mmol) in 10 mL of THF was added to a −78 °C solution of lithium (trimethylsilyl)acetylide generated from *n*-butyllithium (44.6 mL of 1.5 M solution in hexane, 67 mmol) and (trimethylsilyl)acetylene (6.56 g, 67 mmol) in 10 mL of THF. After 3 h at room temperature, the reaction was quenched with saturated ammonium chloride and the reaction mixture extracted with ether. After concentration of the ethereal extracts, the residue was stirred in 30 mL of 10% methanolic potassium hydroxide at room temperature overnight. Evaporation of solvent followed by standard aqueous extractive workup gave a yellow oil which was distilled at 75–7 °C at 12.5 mmHg to give 5.09 g (83% yield) of 4,4-dimethyl-6-hepten-1-yn-3-ol. IR (neat): 3410, 3295, 3060, 2100, 1635, 1030 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ 5.82 (m, 1H), 5.09 (dm, *J* = 3.8 Hz, 1H), 5.02 (s, 1H), 4.06 (db, *J* = 2.0 Hz, 1H), 2.45 (d, *J* = 2.0 Hz, 1H), 2.13 (m, 2H), 1.89 (s, 1H), 0.96 (s, 6H).

A solution of this alcohol (2.6 g, 19 mmol) in 15 mL of THF was added to a suspension of KH (35 wt % in oil, 2.38 g, 20.7 mmol, washed free of oil with hexane) in 5 mL of THF at 0 °C. After 5 min, a solution of *p*-methoxybenzyl bromide (PMB-Br; 4.54 g, 22.6 mmol) in 20 mL of THF was added. After 3 h at room temperature, and quenching with ammonium chloride, standard extractive workup and purification by flash chromatography on silica gel (gradient elution using from 3% to 5% ether/hexane) gave 3.63 g (82% yield) of **8**, R_f 0.37 (5% ether/hexane). IR (neat): 3285, 3060, 2950, 2010, 1610, 1510, 1245, 1065, 1030 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.28 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 5.75 (m, 1H), 5.02 (dd, *J* = 12, 1 Hz, 1H), 5.00 (dd, *J* = 15, 1 Hz, 1H), 4.78 (d, *J* = 11.5 Hz, 1H), 4.39 (d, *J* = 11.5 Hz, 1H), 3.80 (s, 3H), 3.72 (d, *J* = 2.1 Hz, 1H), 2.45 (d, *J* = 2.1 Hz, 1H), 2.14 (m, 2H), 0.98 (s, 3H), 0.96 (s, 3H). HRMS calcd for $C_{17}H_{22}O_2$ 258.1618, found 258.1616.

6,6-Dimethyl-5-((*p*-methoxybenzyl)oxy)-8-nonen-3-yn-2-one (9d). A solution of *n*-butyllithium (0.84 mL of 1.5 M solution, 1.26 mmol) was added to alkyne **8** (308.5 mg, 1.196 mmol) in 10 mL of THF at −78 °C. After 1.5 h, boron trifluoride etherate (170 mg, 1.196 mmol) was added and the mixture stirred for another 40 min. A solution of acetic anhydride (0.17 mL, 1.79 mmol) in 3 mL of THF was precooled to −78 °C and then added to the mixture in one portion. After another hour of stirring, the mixture was quenched with 2 N aqueous NaOH solution at −78 °C. Normal ethereal extractive workup followed by flash chromatography (ether/hexane) gave the starting material (**8**) (134.2 mg, 43.5% recovery,

R_f 0.36) followed by the title compound (156 mg, 43.5%, R_f 0.11 with SiO_2). IR (neat): 3060, 2950, 2190, 1675, 1610, 1510, 1240, 1215 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.27 (d, J = 8.7 Hz, 2H), 6.88 (d, J = 8.7 Hz, 2H), 5.72 (m, 1H), 5.06 (s, 1H), 4.98 (dm, J = 4.3 Hz, 1H), 4.73 (d, J = 11.5 Hz, 1H), 4.38 (d, J = 11.5 Hz, 1H), 3.87 (s, 1H), 3.81 (s, 3H), 2.38 (s, 3H), 2.13 (m, 2H), 0.99 (s, 3H), 0.96 (s, 3H). HRMS calcd for $C_{19}H_{24}O_3$ 300.1719, found: 300.1726.

5,5-Dimethyl-1-methoxy-4-((*p*-methoxybenzyl)oxy)-7-octen-2-yne (9e). Freshly distilled methoxymethyl chloride (113 mg, 1.4 mmol) was added to a solution of lithiated acetylene **8** prepared as described above from *n*-butyllithium (0.9 mL of 1.5 M solution, 1.28 mmol) and **8** (301 mg, 1.17 mmol) in 20 mL of THF. After 3 h at room temperature, quenching with saturated aqueous ammonium chloride solution, extracting with ether, drying over $MgSO_4$, and evaporation of solvent, the resultant yellow liquid was flash chromatographed (15% ether/hexane) to give the title compound [0.3241 g, 92%, R_f 0.07 (5% ether/hexane)]. IR (neat): 3060, 2945, 2920, 2855, 2820, 1605, 1505, 1240, 1110, 1090 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.28 (d, J = 8.5 Hz, 2H), 6.87 (d, J = 8.5 Hz, 2H), 5.75 (m, 1H), 5.04 (d, J = 1.1 Hz, 1H), 4.97 (m, 1H), 4.75 (d, J = 11.5 Hz, 1H), 4.37 (d, J = 11.5 Hz, 1H), 4.20 (t, J = 1.6 Hz, 2H), 3.81 (s, 3H), 3.78 (t, J = 1.6 Hz, 1H), 3.42 (s, 3H), 2.14 (m, 2H), 0.98 (s, 3H), 0.95 (s, 3H). HRMS calcd for $C_{19}H_{26}O_3$ 302.1875, found: 302.1882.

6,6-Dimethyl-1-methoxy-5-((*p*-methoxybenzyl)oxy)-8-nonen-3-yne (9f). To a solution of lithiated **8** prepared from alkyne **8** (251 mg, 0.973 mmol) and *n*-butyllithium (0.72 mL of 1.5 M solution, 1.07 mmol) in 10 mL of hexane at −78 °C as above was added *N,N,N',N'*-tetramethylethylenediamine (TMEDA) (0.15 mL, 0.973 mmol) followed by a large excess of ethylene oxide in ether (2 mL). The mixture was stirred at −78 °C to room temperature overnight, the reactionwas quenched with saturated NH_4Cl solution, and the reaction mixture was extracted with ether and flash chromatographed (60% ether/hexane) to give 6,6-dimethyl-1-hydroxy-5-((*p*-methoxybenzyl)oxy)-8-nonen-3-yne (123.2 mg, 41.9%, R_f 0.23 using 60% ether/hexane). IR (neat): 3360, 3060, 2950, 1610, 1510, 1240, 1060, 1030 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.25 (d, J = 8.7 Hz, 2H), 6.85 (d, J = 8.7 Hz, 2H), 5.75 (m, 1H), 5.01 (s, 1H), 4.96 (m, 1H), 4.71 (d, J = 11.5 Hz, 1H), 4.36 (d, J = 11.5 Hz, 1H), 3.79 (s, 3H), 3.72 (t, J = 6.4 Hz, 2H), 3.69 (d, J = 1.7 Hz, 1H), 2.52 (dt, J = 6.3, 1.9 Hz, 2H), 2.21 (m, 2H), 0.94 (s, 3H), 0.92 (s, 3H).

A solution of the above alcohol (123.3 mg, 0.408 mmol) in 3 mL of THF was added to a slurry of KH (35% w/w in oil dispersion, 56 mg, 0.49 mmol, washed with hexane) in 2 mL of THF at 0 °C and stirred for 5 min. Methyl iodide (0.051 mL, 0.82 mmol) was added. After 2 h, the mixture was quenched with saturated NH_4Cl solution, extracted with ether, and flash chromatographed (15% ether/hexane) to give the title compound (R_f 0.23 using 15% ether/hexane) in quantitative yield. IR (neat): 3060, 2950, 2920, 2860, 1610, 1510, 1240, 1110, 1060 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.27 (d, J = 8.4 Hz, 2H), 6.85 (d, J = 8.4 Hz, 2H), 5.75 (m, 1H), 5.02 (m, 1H), 4.96 (m, 1H), 4.73 (d, J = 11.5 Hz, 1H), 4.37 (d, J = 11.5 Hz, 1H), 3.80 (s, 3H), 3.70 (t, J = 3.0 Hz, 1H), 3.53 (t, J = 7.1 Hz, 2H), 3.38 (s, 3H), 2.54 (dt, J = 7.1, 2.0 Hz, 2H), 2.12 (m, 2H), 0.95 (s, 3H), 0.92 (s, 3H). HRMS calcd for $C_{20}H_{28}O_3$ 316.2031, found 316.2030.

4,4-Dimethyl-3-((*p*-methoxybenzyl)oxy)-1-(trimethylsilyl)-6-hepten-1-yne (9g). To a solution of lithiated **8** generated from the corresponding alkyne (209 mg, 0.81 mmol) and *n*-butyllithium (0.7 mL of a 1.5 M solution, 1.05 mmol) at −78 °C was added TMSCl (0.27 mL, 2.11 mmol) in 5 mL of THF. After being stirred at room temperature for 2 h, the mixture was quenched with saturated aqueous ammonium chloride and worked-up as above to give, after column chromatography (3% ether/hexane), the title compound, 209 mg (78%, R_f 0.5 with 10% ether/hexane). IR (neat): 3060, 2950, 2160, 1610, 1510, 1245, 1168, 1065, 1035, 840, 755 cm^{-1}. ^{1}H NMR (270 MHz, $CDCl_3$): δ 7.26 (d, J = 8.7 Hz, 2H), 6.85 (d, J = 8.7 Hz, 2H), 5.73 (ddt, J = 17.8, 9.3, 7.5 Hz, 1H), 5.00 (m, 1H), 4.95 (m, 1H), 4.72 (d, J = 11.5 Hz, 1H), 4.36 (d, J = 11.5 Hz, 1H), 3.79 (s, 9H), 3.68 (s, 1H), 2.11 (bd, J = 7.5 Hz, 2H), 0.95 (s, 3H), 0.92 (s, 3H), 0.18 (s, 9H). HRMS calcd for $C_{20}H_{30}SiO_2$ 330.2015, found: 330.2007.

5,5-Dimethyl-4-((*p*-methoxybenzyl)oxy)-7-octen-2-yne (9h). Methyl iodide (193 mg, 1.36 mmol) was added to lithiated **8** generated from alkyne and *n*-butyllithium (0.83 mL of 1.5 M solution, 1.24 mmol) in 5 mL of THF at −78 °C. After being stirred for 2 h at −78 °C to room temperature, the mixture was quenched with saturated aqueous ammonium chloride and worked-up as before to give, after column chromatography (5% ether/hexane), the title product 281.6 mg (86%, R_f 0.32 with 10% ether/hexane). IR (neat) 3060, 2950, 2920, 1610, 1510, 1460, 1297, 1240, 1168, 1060, 1030, 910, 820 cm^{-1}. ^{1}H NMR (270 MHz, $CDCl_3$): δ 7.26 (d, J = 8.8 Hz, 2H), 6.85 (d, J = 8.8 Hz, 2H), 5.74 (ddt, J = 17.8, 9.2, 7.5 Hz, 1H), 5.01 (m, 1H), 4.96 (m, 1H), 4.73 (d, J = 11.5 Hz, 1H), 4.35 (d, J = 11.5 Hz, 1H), 3.79 (s, 3H), 3.66 (q, J = 2.1 Hz, 1H), 2.10 (dd, J = 7.5, 1.4 Hz, 2H), 1.89 (d, J = 2.1 Hz, 3H), 0.94 (s, 3H), 0.91 (s, 3H). HRMS calcd for $C_{18}H_{24}O_2$ 272.1776, found: 272.1774.

4,4-Dimethyl-1-ethoxy-3-((*p*-methoxybenzyl)oxy)-6-hepten-1-yne (9i). To a solution of lithium ethoxyacetylide (generated from 0.6 g, 8.6 mmol of ethoxyacetylene and 5.7 mL, 8.6 mmol of 1.5 M *n*-butyllithium) in 10 mL of THF at −78 °C was added aldehyde **4** (0.8 g, 7.14 mmol) in 5 mL of THF. After 1.5 h, the reaction was quenched with saturated aqueous sodium chloride solution and the reaction mixture was worked-up as before to give, after column chromatography (10% then 20% ether/hexane) the title compound (1.07 g, 82.3%, R_f 0.20 with 20% ether/hexane). IR (neat): 3430, 3070, 2060, 2260, 1640, 1235, 1000 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ 5.86 (m, 1H), 5.10 (m, 1H), 5.03 (s, 1H), 4.10 (q, J = 7.1 Hz, 3H), 2.12 (m, 2H), 1.65 (d, J = 4.9 Hz, 1H), 1.38 (t, J = 7.1 Hz, 3H), 0.95 (s, 3H), 0.94 (s, 3H).

A solution of the above alcohol (400 mg, 2.2 mmol) in 5 mL of THF was added to a slurry of KH (35% w/w in oil, 0.276 g, 2.42 mmol washed with hexane) in 2 mL of THF at 0 °C. After a few minutes, PMB-Br (0.486 g, 2.42 mmol) in 3 mL of THF was added. After 4.5 h at room temperature, the reaction was quenched with saturated aqueous ammonium chloride and the reaction mixture was worked-up as before to give, after flash chromatography (gradient from 3% to 5% ether/hexane), the title compound (381.2 mg, 57.4%). IR (neat): 3070, 2960, 2937, 2905, 2260, 1640, 1615, 1588, 1513, 1247 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.27 (d, J = 8.6 Hz, 2H), 6.94 (d, J = 8.6 Hz, 2H), 5.78 (m, 1H), 4.99 (d, J = 15 Hz, 1H), 4.98 (d, J = 12 Hz, 1H), 4.72 (d, J = 11.6 Hz, 1H), 4.35 (d, J = 11.6 Hz, 1H), 4.11 (q, J = 7.1 Hz, 2H), 3.80 (s, 3H), 3.75 (s, 1H), 2.12 (m, 2H), 1.40 (t, J = 7.1 Hz, 3H), 0.95 (s, 3H), 0.93 (s, 3H). HRMS calcd for $C_{19}H_{26}O_3$ 302.1873, found 302.1877.

Pd(II) Reaction of 9d. Formation of Diene 10d. A mixture of ketone **9d** (26.3 mg, 0.087 mmol), $Pd(OAc)_2$ (2 mg, 0.008 mmol), and BBEDA (2.1 mg, 0.008 mmol) in CD_2Cl_2 (0.5 mL) was heated at 45 °C in an NMR tube. After 23.5 h, reaction was completed. The mixture was diluted with hexane to transfer, evaporated *in vacuo*, and directly chromatographed (eluting with 20% ether/hexane) to give **10d** as as ca. 10:1 *trans/cis* ratio (17.5 mg, 67%, R_f 0.38 with 40% ether/hexane). This product was very unstable and polymerizes very readily even at room temperature. IR (neat): 2945, 2860, 2830, 1680, 1595, 1508, 1245, 1170, 1155, 1030 cm^{-1}. ^{1}H NMR (270 MHz, $CDCl_3$): δ 7.23 (d, J = 8.7 Hz, 2H), 6.83 (d, J = 8.7 Hz, 2H), 6.67 (s, 1H), 5.69 (m, 1H), 5.12 (s, 1H), 4.73 (s, 1H), 4.53 (d, J = 11.2 Hz, 1H), 4.46 (d, J = 11.2 Hz, 1H), 3.78 (s, 3H), 2.29 (s, 3H), 2.55 (d, J = 15.6 Hz, 1H), 2.04 (d, J = 15.6 Hz, 1H), 1.16 (s, 3H), 0.81 (s, 3H). HRMS calcd for $C_{19}H_{24}O_3$ 300.1725, found 300.1721.

Pd(II) Reaction of 9e. Formation of diene 10e. A mixture of enyne **9e** (140.7 mg, 0.466 mmol) and $[(o\text{-}CH_3C_6H_4)_3P]_2Pd(OAc)_2$ (19.4 mg, 0.023 mmol) in 5 mL of benzene was heated at 60 °C for 50 min. The cooled mixture was poured onto a silica gel column and eluted with 5% ether/hexane to give diene **10e** (108.28 mg, 77%, R_f 0.27 with 20% ether/hexane). IR (neat): 3075, 2957, 1617, 1515, 1250, 1085, 1037, 825 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.25 (d, J = 8.7 Hz, 2H), 6.87 (d, J = 8.7 Hz, 2H), 6.16 (t, J = 6.8 Hz, 1H), 5.38 (s, 1H), 4.88 (s, 1H), 4.47 (d, J = 11.5 Hz, 1H), 4.36 (d, J = 11.5 Hz, 1H), 4.06 (t, J = 6.8 Hz, 2H), 3.90 (s, 1H), 3.80 (s, 3H), 3.32 (s, 3H), 2.52 (d, J = 15.5 Hz, 1H), 2.07 (d, J = 15.5 Hz, 1H), 1.16 (s, 3H), 0.88 (s, 3H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 159.07, 146.80, 142.92, 131.20, 128.78 (2C), 121.97, 113.76 (2C), 104.87, 85.38, 70.22, 70.12, 57.99, 55.23, 44.81, 40.58, 26.65, 22.16. HRMS calcd for $C_{19}H_{26}O_3$ 302.1882, found 302.1883.

NMR data of **11e** were discernible by NMR difference from reactions run with crystallized versus precipitated catalyst. ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.23 (d, J = 8.5 Hz, 2H), 6.83 (d, J = 8.5 Hz, 2H), 5.77 (t, J = 5.4 Hz, 1H), 5.10 (s, 1H), 4.92 (s, 1H), 4.57 (d, J = 11.7 Hz, 1H), 4.38 (d, J = 11.7 Hz, 1H), 4.21 (m, 2H), 3.74 (s, 3H), 3.60 (s, 1H), 3.34 (s, 3H), 2.48 (d, J = 14 Hz, 1H), 2.11 (d, J = 14 Hz, 1H), 0.97 (s, 3H), 0.91 (s, 3H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 159.07, 145.13, 141.32, 131.17, 128.99 (2C), 126.46, 113.72 (2C), 112.09, 90.18, 70.87, 70.09, 58.16, 55.20, 46.14, 40.18, 26.62, 21.44.

Pd(II) Reaction of 9f. Formation of diene 10f. A mixture of enyne **9f** (57.9 mg, 0.183 mmol), $Pd(OAc)_2$ (4.3 mg, 0.018 mmol), and BBEDA (4.5 mg, 0.018 mmol) in C_6D_6 (0.6 mL) was heated at 60 °C in an NMR tube. After 14.75 h, ^{1}H NMR showed completion of the reaction. The mixture was directly poured onto a silica gel column and eluted with 10%

and then 25% ether/hexane to give diene **10f** (>11:1 *trans/cis*) (53.6 mg, 93%, R_f 0.32 with 40% ether/hexane). IR (neat): 3060, 2940, 2860, 1610, 1510, 1243, 1110, 1075, 1030, 867, 820 cm^{-1}. ^{1}H NMR (270 MHz, $CDCl_3$): δ 7.20 (d, J = 8.5 Hz, 2H), 6.81 (d, J = 8.5 Hz, 2H), 6.03 (t, J = 7.9 Hz, 1H), 5.24 (s, 1H), 4.74 (s, 1H), 4.45 (d, J = 11.3 Hz, 1H), 4.34 (d, J = 11.3 Hz, 1H), 3.84 (s, 1H), 3.75 (s, 3H), 3.38 (td, J = 6.8, 1.17 Hz, 2H), 3.29 (s, 3H), 2.43 (dt, J = 8.9, 7.0 Hz, 2H), 2.48 (d, J = 15.5 Hz, 1H), 2.01 (d, J = 15.5 Hz, 1H), 1.12 (s, 3H), 0.81 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.81, 147.34, 142.01, 131.32, 128.69 (2C), 122.27, 113.58 (2C), 103.35, 85.19, 72.18, 70.10, 58.55, 55.20, 44.98, 40.39, 30.31, 26.63, 22.3. Anal. Calcd for $C_{20}H_{28}O_3$: C, 75.91; H, 8.92; MW, 316.2038. Found: C, 75.87; H, 8.87; MW, 316.2034.

NMR data of **11f** were discernible by difference between the 2:1 mixture from $Pd(OAc)_2$ alone and the above. ^{1}H NMR (270 MHz, $CDCl_3$): δ 7.25 (d, J = 8.5 Hz, 2H), 6.85 (d, J = 8.5 Hz, 2H), 5.62 (t, J = 6.6 Hz, 1H), 5.21 (s, 1H), 5.07 (s, 1H), 4.56 (d, J = 11.8 Hz, 1H), 4.40 (d, J = 11.8 Hz, 1H), 3.78 (s, 3H), 3.57 (s, 1H), 3.48 (t, J = 6.8 Hz, 2H), 3.35 (s, 3H), 2.60 (q, J = 6.3 Hz, 2H), 2.4–2.6 (other d overlapping with signals from *Z*-isomer, 1H), 2.11 (d, J = 15.8 Hz, 1H), 0.99 (s, 3H), 0.91 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.87, 145.49, 140.55, 131.29, 129.01 (2C), 125.67, 113.60 (2C), 111.00, 90.68, 72.07, 70.57, 58.54, 55.23, 46.62, 39.87, 29.44, 26.76, 21.52.

Pd (II) Reaction of 9g. Preparation of diene 10g. Following the above protocol, enyne **9g** (30.1 mg, 0.091 mmol), $Pd(OAc)_2$ (3.1 mg, 0.014 mmol), and BBEDA (3.3 mg, 0.014 mmol) in 0.5 mL of C_6D_6 at 60 °C gave after 14 h (note: silica gel column pretreated with 1% triethylamine in hexane, eluting with 5% ether/hexane) the diene **10g** (26.7 mg, 89%, R_f 0.49 with 10% ether/hexane). IR (neat): 3060, 2840, 1610, 1510, 1460, 1298, 1240, 1167, 1080, 1032, 855, 840, 830 cm^{-1}. ^{1}H NMR (270 MHz, $CDCl_3$): δ 7.22 (d, J = 8.7 Hz, 2H), 6.83 (d, J = 8. Hz, 2H), 6.15 (s, 1H), 5.38 (t, J = 2.2 Hz, 1H), 4.85 (s, 1H), 4.48 (d, J = 10.9 Hz, 1H), 4.41 (d, J = 10.9 Hz, 1H), 3.85 (s, 1H), 3.78 (s, 3H), 2.49 (dt, J = 15.9, 2.5 Hz, 1H), 2.06 (d, J = 15.9 Hz, 1H), 1.13 (s, 3H), 0.90 (s, 3H), 0.13 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.76, 155.78, 148.43, 131.36, 128.62 (2C), 123.96, 113.53 (2C), 105.44, 88.11, 69.90, 55.24, 44.15, 40.08, 26.79, 22.18, 0.53 (3C). Anal. Calcd for $C_{20}H_{30}SiO_2$: C, 72.67; H, 9.15. Found: C, 72.73; H, 9.27.

^{1}H NMR (270 MHz, $CDCl_3$) of *Z*-isomer **11g** discernible from the 3:1 *E/Z* mixture obtained from using $Pd(OAc)_2$ only: δ 7.28 (d, J = 8.7 Hz, 2H), 6.87 (d, J = 8.7 Hz, 2H), 5.62 (d, J = 1.5 Hz, 1H), 5.35 (s, 1H), 4.99 (s, 1H), 4.63 (d, J = 11.7 Hz, 1H), 4.48 (d, J = 11.7 Hz, 1H), 3.79 (s, 3H), 3.68 (d, J = 1.7 Hz, 1H), 2.31 (dt, J = 15.7, 2.1 Hz, 1H), 2.14 (dt, J = 15.7, 2.4 Hz, 1H), 0.97 (s, 3H), 0.90 (s, 3H), 0.16 (s, 9H).

Pd(II) Reaction of 9h. Preparation of Diene 10h. Following the above protocol, enyne **9h** (34.2 mg, 0.126 mmol), $Pd(OAc)_2$ (4.2 mg, 0.02 mmol), and BBEDA (4.5 mg, 0.02 mmol) in C_6D_6 (0.5 mL) gave after 22.5 h the diene **10h**, which was purified by flash chromatography (26.9 mg, 79%, R_f 0.38 with 10% ether/hexane). IR (neat): 3060, 2940, 2860, 1610, 1505, 1462, 1295, 1240, 1168, 1072, 1030, 865, 820 cm^{-1}. ^{1}H NMR (270 MHz, $CDCl_3$): δ 7.23 (d, J = 8.7 Hz, 2H), 6.84 (d, J = 8.7 Hz, 2H), 6.16 (q, J = 7.2 Hz, 1H), 5.23 (s, 1H), 4.75 (s, 1H), 4.48 (d, J = 11.4 Hz, 1H), 4.37 (d, J = 11.4 Hz, 1H), 3.90 (s, 1H), 3.78 (s, 3H), 2.53 (d, J = 15.5 Hz, 1H), 2.03 (d, J = 15.5 Hz, 1H), 1.80 (d, J = 7.2 Hz, 3H), 1.16 (s, 3H), 0.82 (s, 3H). HRMS calcd for $C_{18}H_{24}O_2$ 272.1776, found 272.1785.

^{1}H NMR (270 MHz, $CDCl_3$) of **11h** discernible from the 74% *E* and 22% *Z* mixture of the geometrical isomers from the $Pd(OAc)_2$ reation: δ 7.2 (d, J = 8.8 Hz, 2H), 6.8 (d, J = 8.8 Hz, 2H), 5.70 (q, J = 7.3 Hz, 1H), 5.18 (s, 1H), 5.03 (s, 1H), 4.51 (d, J = 11.3 Hz, 1H), 4.36 (d, J = 11.3 Hz, 1H), 3.73 (s, 3H), 3.51 (s, 1H), 2.38 (d, J = 15.5 Hz, 1H), 2.06 (d, J = 15.5, 1H), 1.84 (d, J = 7.3 Hz, 3H), 0.93 (s, 3H), 0.86 (s, 3H).

Pd(II) Reaction of 9i. Following the above protocol, enyne **9i** (33.9 mg, 0.11 mmol), $Pd(OAc)_2$ (2.7 mg, 0.011 mmol), and BBEDA (2.9 mg, 0.011 mmol) in 0.5 mL of C_6D_6 gave after 1 h and flash chromatography (5% ether/hexane containing 1% triethylamine) **10i** (10.8 mg, 32%, R_f 0.24 with 10% ether/hexane). ^{1}H NMR (270 MHz, $CDCl_3$): δ 7.27 (d, J = 8.7 Hz, 2H), 6.85 (d, J = 8.7 Hz, 2H), 6.27 (s, 1H), 5.04 (s, 1H), 4.61 (s, 1H), 4.53 (d, J = 11.8 Hz, 1H), 4.40 (d, J = 11.8 Hz, 1H), 4.01 (s, 1H), 3.92 (q, J = 7.1 Hz, 2H), 3.80 (s, 3H), 2.52 (d, J = 15.4 Hz, 1H), 2.00 (d, J = 15.4 Hz, 1H), 1.31 (t, J = 7.1 Hz, 3H), 1.11 (s, 3H), 0.83 (s, 3H). The sensitivity of this compound toward hydrolysis led to its characterization as the hydrolysis product 2-formyl-3-((*p*-methoxybenzyl)oxy)-1,4,4-trimethyl-1-cyclopentene. IR (neat): 2940, 2900, 2745, 2715, 1665, 1610, 1505, 1240, 1075, 1050, 1030, 830, 810 cm^{-1}. ^{1}H NMR (270 MHz, $CDCl_3$): δ 10.03 (s, 1H), 7.29 (d, J = 8.7 Hz, 2H), 6.85 (d, J = 8.7 Hz, 2H), 4.62 (d, J = 10.7 Hz, 1H), 4.57 (d, J = 10.7 Hz, 1H), 4.21 (s, 1H), 3.79 (s, 3H), 2.14 (s, 3H), 2.66 (d, J = 18.4 Hz, 1H), 2.11 (d, J = 18.4 Hz, 1H), 1.18 (s, 3H), 0.98 (s, 3H). HRMS calcd for $C_{17}H_{22}O_3$ 274.1569, found: 274.1568.

Pd(II) Reaction of 14. Preparation of Diene 15. Following the above procedure, enyne **14** (43.8 mg, 0.155 mmol), $Pd(OAc)_2$ (5.2 mg, 0.023 mmol), and BBEDA (5.5 mg, 0.023 mmol) in 0.6 mL of C_6D_6 gave, after 13.5 h and flash chromatography (20% ether/hexane), the diene **15** (37 mg, 85%, R_f 0.42 with 40% ether/hexane). IR (neat): 3060, 2940, 1733, 1430, 1255, 1240, 1225, 1195, 1065, 855, 840 cm^{-1}. ^{1}H NMR (270 MHz, $CDCl_3$): δ 5.98 (t, J = 2.2 Hz, 1H), 5.37 (t, J = 2.2 Hz, 1H), 4.91 (t, J = 1.7 Hz, 1H), 3.71 (s, 6H), 3.01 (m, 4H), 0.12 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.39 (2C), 151.62, 145.51, 119.35, 105.38, 57.55, 52.63 (2C), 40.78, 40.28, –0.72 (2C). Anal. Calcd for $C_{14}H_{22}SiO_4$: C, 59.54; H, 7.85; MW, 282.1287. Found: C, 59.35; H, 7.81; MW, 282.1289.

Pd(II) Reaction of Enyne 16. Preparation of Diene 17. Following the above protocol, enyne **16** (310 mg, 1.87 mmol), $Pd(OAc)_2$ (21.5 mg, 0.096 mmol), and BBEDA (23.3 mg, 0.099 mmol) in 3.7 mL of benzene at 45–50 °C gave, after 1 h and flash chromatography (5% ethyl acetate in pentane), the diene **17** (257.2 mg, 83%, R_f 0.29 with 5% ethyl acetate in hexane). IR ($CHCl_3$): 3018, 2962, 1719, 1652, 1623, 1439, 1358, 1250, 1196, 1177 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ 6.13 (t, J = 2.5 Hz, 1H), 5.58 (d, J = 2.7 Hz, 1H), 4.99 (d, J = 2.5 Hz, 1H), 3.70 (s, 3H), 3.12 (ddt, J = 19.0, 8.0, 2.6 Hz, 1H), 2.46–2.73 (m, 2H), 1.92–2.07 (m, 1H), 1.18–1.30 (m, 1H), 1.11 (d, J = 6.6 Hz, 3H). HRMS calcd for $C_{10}H_{14}O_2$ (M^+) 166.0994, found 166.0998.

Pd(II) Reaction of Enyne 18. Preparation of Diene 19. The 1,7-enyne **18** (distilled at 190 °C oven temperature at <1 mmHg before use, 68.4 mg, 0.202 mmol) and $Pd(OAc)_2$ (3.1 mg, 0.014 mmol) dissolved in $CDCl_3$ (0.41 mL) in an NMR tube were heated at 45 °C. After 7.25 h, the solvent was removed *in vacuo* (cool water bath) and the residue was chromatographed on silica gel (elution with neat hexane to 3% ethyl acetate in hexane) to give **19** as a colorless oil, 41.1 mg (60% yield), R_f 0.29 with 1% ethyl acetate in hexane. IR (neat): 3070, 2947, 2850, 1718, 1641, 1470, 1386, 1370, 1332, 1254, 1194, 1157, 1066, 1035, 1004, 917, 840, 793 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ 5.71–5.75 (m with sharp singlet at 5.74, 2H), 5.03 (t, J = 1.8 Hz, 1H), 4.82 (t, J = 1.9 Hz, 1H), 4.14 (qd, J = 7.2, 1.2 Hz, 2H), 2.23 (dd, J = 13.4, 1.8 Hz, 1H), 2.02 (d, J = 13.4 Hz, 1H), 1.69 (m, 1H), 1.51 (dd, J = 14.5, 3.5 Hz, 1H), 1.26 (t, J = 7.2 Hz, 3H), 1.11 (s, 3H), 0.88 (s, 3H), 0.81 (s, 9H), 0.03 (s, 3H), –0.06 (s, 3H). HRMS calcd for $C_{19}H_{34}O_3Si$ (M^+) 338.2277, found 338.2276.

Preparation of 1-Acetoxy-1-cyclohexyl-2-propene. Cyclohexanecarboxaldehyde (1.1 g, 10 mmol) was added dropwise to vinylmagnesium bromide (15 mL of a 1 M solution in THF, 15 mmol) at –78 °C. After 15 min, acetic anhydride (1.5 mL, 17 mmol) was added and the mixture stirred at room temperature for 1.5 h. The reaction mixture was poured into ether and 10% aqueous hydrochloric acid. The organic phase was washed with 10% aqueous potassium hydroxide, water, and saturated aqueous sodium chloride. Drying of the organic phase with magnesium sulfate was followed by evaporation of volatiles at reduced pressure and bulb-to-bulb distillation (60% at 0.05 mmHg) to yield the title compound, 1.05 g (58%), as a clear oil. IR ($CDCl_3$): 2939, 2860, 1730, 1452, 1373, 1251 cm^{-1}. ^{1}H NMR (270 MHz, $CDCl_3$): δ 5.78 (ddd, J = 16.9, 6.8, 6.8 Hz, 1H), 5.19 (d, J = 6.8 Hz, 1H), 5.05 (t, J = 6.8 Hz, 1H), 2.09 (s, 3H), 1.72 (m, 6H), 1.55 (m, 1H), 1.20–0.90 (m, 4H). Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.45; H, 9.98. Found: C, 72.05; H, 10.41.

Preparation of (*E*)-1-Cyclohexyl-4,4-dicarbomethoxyhept-1-ene-6-yne (20a). Dimethyl propargylmalonate (204 mg, 1.2 mmol) was added to a rapidly stirred suspension of sodium hydride (46 mg, 1.15 mol) in THF (0.500 mL). To this solution was added the above allylic acetate (150 mg, 0.82 mmol), triphenylphosphine (7 mg, 3 mol %), and a solution of tetrakis(triphenylphosphine)palladium(0) (30 mg, 3 mol %) in THF (0.500 mL). The mixture was heated at reflux for 8 h. The crude reaction mixture was added to a flash column and the title compound eluted (10:1 hexane/ether), providing an oil which slowly crystallized, 170 mg (71%), mp 36–37 °C. IR ($CDCl_3$): 3305, 2928, 2850, 1738, 1452, 1441, 1210 cm^{-1}. ^{1}H NMR (270 MHz, $CDCl_3$): δ 5.45 (dd, J = 15, 6.8 Hz, 1H), 5.11 (dt, J = 15, 7.4 Hz, 1H), 3.69 (s, 6H), 2.72 (d, J = 2.7 Hz, 2H), 2.65 (d, J = 7.5 Hz, 2H), 1.95 (t, J = 2.7 Hz, 1H), 1.85 (m, 1H), 1.60 (m, 4H), 1.20-0.90 (m, 6H). HRMS calcd for $C_{17}H_{24}O_4$ (M^+) 292.1668, found 292.1677.

Preparation of (*E*)-1-(Cyclohexylmethylidene)-2-methylene-4,4-dicarbomethoxycyclopentane (21a). The yellow solution resulting from addition of palladium acetate (2 mg, 0.008 mmol) and triphenylphosphine

(5 mg, 0.016 mmol) to enyne **20** (25 mg, 0.086 mmol) in 0.75 mL of THF was heated at reflux for 4 h. Purification consisted of eluting through a flash chromatography column (10:1 hexane/ether) to give a clear oil, 16 mg (64% yield). IR ($CDCl_3$): 2939, 2859, 1733, 1455, 1441, 1255 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): δ 5.80 (dt, J = 6.9, 2.5 Hz, 1H), 5.22 (s, 1H), 4.79 (s, 1H), 3.72 (s, 6H), 2.98 (t, J = 2.5 Hz, 4H), 2.10 (m, 1H), 1.70–1.00 (m, 10H). UV (95% EtOH) λ_{max} = 255 nm, ϵ = 5800. HRMS calcd for $C_{17}H_{24}O_4$ (M^+) 292.1668, found 292.1667.

Preparation of 6,6-Dicarbomethoxy-4α-cyclohexyl-1,3-dioxo-1,3aβ,4,5,6,7,8,8aβ-octahydroindeno[5,6-c]furan (Diels–Alder Adduct of 21a). A mixture of the diene **21** (25 mg, 0.087 mmol), maleic anhydride (11.5 mg, 0.117 mmol), and BSA (0.010 mL) in toluene (0.750 mL) was heated at 80 °C for 4 h. The toluene was removed *in vacuo*, and the resulting oil was purified by flash chromatography (1:1 hexane/ether), yielding a white solid, 18 mg (55%), mp 124-125.5 °C. IR ($CDCl_3$): 2935, 2859, 1850, 1780, 1736, 1439, 1265 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): δ 3.75 (s, 3H), 3.73 (s, 3H), 3.55 (dd, J = 11.4, 5.7 Hz, 1H), 3.45 (dt, J = 8.9, 2.4 Hz, 1H), 3.19 (d, J = 6.4 Hz, 1H), 3.05 (d, J = 6.4 Hz, 1H), 3.04 (AB, J = 17.7 Hz, 2H), 2.65 (d, J = 17.5, 1H), 2.30 (m, 1H), 2.20 (m, 1H), 2.00–1.65 (m, 6H), 1.50–0.80 (m, 5H). HRMS calcd for $C_{21}H_{26}O_7$ (M^+) 390.1671, found 390.1679.

Preparation of 4,4-Dicarbomethoxy-1-methylene-2-(cyclopentylmethylidene)cyclohexane (22). The enyne **20** (30 mg, 0.10 mmol) was passed through a hot zone at 575 °C and 0.05 mmHg using a flash vacuum thermolysis apparatus. The oil, collected using a dry-ice trap, was purified by flash chromatography (10:1 hexane/ether), yielding a clear colorless oil, 21 mg (70%). IR ($CDCl_3$): 2962, 2940, 2860, 1734, 1445, 1281 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): δ 4.89 (s, 1H), 4.85 (s, 1H), 4.75 (s, 1H), 3.74 (s, 3H), 3.69 (s, 3H), 3.38 (m, 1H), 3.00 (AB, J = 16.8 Hz, 2H), 2.52 (dd, J = 13.5, 6.7 Hz, 1H), 2.10 (m, 4H), 1.86 (t, J = 13.5 Hz, 1H), 1.50 (m, 6H). HRMS calcd for $C_{27}H_{24}O_4$ (M^+) 292.16688, found 292.1664.

Preparation of (*E*)-4,4-Bis(phenylsulfonyl)-7-cyclohexylhept-6-en-1-yne (20b). To a solution of 4,4-bis(phenylsulfonyl)-3-butyne (108 mg, 0.30 mmol) in THF (0.500 mL) was added sodium hydride (11 mg, 0.28 mmol) in one poroom temperatureion followed by BSA (0.010 mL), 1-acetoxy-1-cyclohexyl-2-propene (45 mg, 0.25 mmol), triphenylphosphine (93 mg, 0.012 mmol), and a solution of tetrakis(triphenylphosphine)-palladium(0) (14 mg, 0.012 mmol) in THF (0.500 mL). After being heated at reflux for 3.5 h, the crude reaction mixture was added to a flash chromatography column and the title compound eluted (1:1 hexane/ether) as an oil (90 mg, 72%) which crystallized (mp 162–164 °C). IR ($CDCl_3$): 3310, 3065, 2926, 2852, 1731, 1582, 1447, 1330, 1310, 1143, 1074, 968 cm^{-1}. ^1H NMR (200 MHz, C_6D_6): δ 8.22 (d, J = 7, 1 Hz, 4H), 7.1–6.9 (m, 6H), 5.90 (dt, J = 15, 6 Hz, 1H), 5.57 (dd, J = 7, 15 Hz, 1H), 3.29 (m, 4H), 1.92 (m, 1H), 1.80–1.00 (m, 11H). Anal. Calcd for $C_{25}H_{28}O_4S_2$: C, 65.76; H, 6.18. Found: C, 65.84; H, 6.48.

Preparation of (*E*)-1-(Cyclohexylmethylidene)-2-methylene-4,4-bis-(phenylsulfonyl)cyclopentane (21b). A mixture of enyne **20b** (18 mg, 0.042 mmol) and bis(triphenylphosphine)palladium acetate (1.6 mg, 0.002 mmol) in 0.4 mL of C_6D_6 was stirred at room temperature for 20 h. Addition to a flash chromatography column and elution (2:1 hexane/ether) provided the title compound as a viscous oil (13 mg, 72%). IR ($CDCl_3$): 3037, 2928, 2855, 1448, 1328, 1310, 1143, 1076 cm^{-1}. ^1H NMR (270 MHz, C_6D_6): δ 8.12 (dd, J = 6.4, 1 Hz, 2H), 7.26 (s, 4H), 7.00 (m, 4H), 5.66 (dt, J = 2.0, 9.6 Hz, 1H), 5.12 (t, J = 1.5 Hz, 1H), 4.50 (br s, 1H), 3.71 (d, J = 9.6, 2.0 Hz, 1H), 5.12 (t, J = 1.5 Hz, 1H), 4.50 (br s, 1H), 3.71 (d, J = 2.0 Hz, 2H), 3.49 (t, J = 1.5 Hz, 2H), 1.90 (m, 1H), 1.70–0.90 (m, 10H). Anal. Calcd for $C_{25}H_{28}O_4S_2$: C, 65.76; H, 6.18. Found: C, 66.16; H, 6.29.

Preparation of 4,4-Dicarbomethoxy 7(*R*),8-Diol Acetonide (25). BSA (0.020 mL), 3-acetoxypent-1-ene-4(*R*),5-diol acetonide (85 mg, 0.425 mmol), and triphenylphosphine (7 mg, 5 mol %) followed by a solution of tetrakis(triphenylphosphine)palladium(0) (20 mg, 5 mol %) in THF (0.750 mL) were added to dimethyl sodiopropargylmalonate prepared by adding the malonate (110 mg, 0.65 mmol) to a slurry of sodium hydride (27 mg, 0.62 mmol) in THF (0.75 mL). The resulting yellow solution was heated at reflux for 11 h and the crude reaction mixture added to a flash chromatography column and eluted (5:1 hexane/ether) to yield a clear oil, 72 mg (55%). IR ($CDCl_3$): 3307, 2994, 2960, 2980, 1738, 1440, 1210, 1059 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): δ 5.61 (m, 2H), 4.45 (q, J = 6.75 Hz, 1H), 4.08 (t, J = 6.75 Hz, 1H), 3.76 (s, 6H), 3.55 (t, J = 6.75 Hz, 1H), 2.80 (m, 4H), 2.05 (t, J = 1.5 Hz, 1H), 1.42 (s, 3H), 1.38 (s, 3H). Anal. Calcd for $C_{18}H_{22}O_6$: C, 61.92; H, 7.14; MW, 295.1176. Found: C, 61.92; H, 7.09; MW, 295.1184.

Pd(II) Reaction of Enyne 25. Preparation of Diene 26. A mixture of enyne **25** (14 mg, 0.045 mmol), bis(triphenylphosphine)palladium acetate (2 mg, 0.002 mmol), and triphenylphosphine (0.6 mg, 0.002 mmol) in C_6D_6 was heated at 66 °C for 1.75 h. Direct addition of the mixture to a flash chromatography column and elution (5:1 hexane/ether) gave a clear oil (10 mg, 71% yield) identified as the title compound. IR ($CDCl_3$): 2985, 2955, 1731, 1434, 1250, 1203, 1051 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): δ 5.82 (dt, J = 1.5, 6.8 Hz, 1H), 5.38 (s, 1H), 4.97 (s, 1H), 4.74 (q, J = 6.8 Hz, 1H), 4.12 (t, J = 6.8 Hz, 1H), 3.74 (s, 6H), 3.60 (t, J = 6.8 Hz, 1H), 3.10 (s, 2H), 3.04 (d, J = 9 Hz, 2H), 1.46 (s, 3H), 1.40 (s, 3H). HRMS calcd for $C_{16}H_{22}O_6$ (M^+) 310.1410, found: 310.1419.

Pd(II) Reaction of Enyne 27a. Preparation of Diene 29a. A solution of enyne **27a**[33] (2.59 g, 6.43 mmol) and bis(tri-o-tolylphosphine) palladium acetate (107 mg, 0.129 mmol) in 26 mL of benzene was heated at 80 °C for 1 h. Upon concentration *in vacuo*, the residue was flash chromatographed (4% ethyl acetate in hexane) to give 2.08 g (80% yield) of diene **29a** as a colorless oil. IR (neat): 2850, 1655, 1615, 1585, 1515, 830 cm^{-1}. ^1H NMR (200 MHz, C_6D_6): δ 7.27 (d, J = 8.8 Hz, 2H), 6.8 (d, J = 8.8 Hz, 2H), 6.33 (bt, J = 6.6 Hz, 1H), 5.43 (bs, 1H), 4.87 (bs, 1H), 4.52 (d, J = 11.5 Hz, 1H), 4.34 (dd, J = 5.5, 2.7 Hz, 2H), 4.28 (d, J = 2.7 Hz, 1H), 3.89 (s, 1H), 3.30 (s, 3H), 2.63 (bd, J = 15.3 Hz, 1H), 2.00 (bd, J = 15.3 Hz, 1H), 1.22 (s, 3H), 0.97 (s, 9H), 0.85 (s, 3H), 0.07 (s, 6H). ^{13}C NMR (15.0 MHz, $CDCl_3$): δ 158.8, 146.7, 140.2, 131.0, 128.6, 125.2, 113.6, 104.3, 85.2, 70.1, 61.4, 55.2, 44.9, 40.6, 26.8, 26.1, 25.7, 22.3, 18.4, –5.0. HRMS calcd for $C_{24}H_{38}O_3Si$ 402.2591, found 402.2579.

Pd(II) Reaction of Enyne 27b. Following the above protocol, enyne **27b** (1.83 g, 6.86 mmol) and bis(tri-*o*-tolylphosphine)palladium acetate (171 mg, 0.206 mmol) gave after 30 min at 70 °C and flash chromatography (3% ethyl acetate in hexane) 1.679 g (92% yield) of diene **29**. ^1H NMR (270 MHz, $CDCl_3$): δ 6.14 (m, 1H), 5.37 (bs, 1H), 4.83 (bs, 1H), 4.26 (d, J = 6.4 Hz, 1H), 2.07 (s, 2H), 2.03 (s, 2H), 0.99 (s, 9H), 0.92 (s, 6H), 0.11 (s, 6H). ^{13}C NMR (15 MHz, $CDCl_3$): δ 148.7, 140.2, 120.2, 103.1, 61.8, 48.7, 45.0, 36.5, 28.0, 26.2, 18.6, –4.8. HRMS calcd for $C_{16}H_{30}OSi$ 266.3200, found 266.3188.

Preparation of 3-Acetoxy-1,6-heptadiene (37a). Following the procedure for 3-hydroxy-1,8-nonadiene (*vide infra*), a mixture of 1,2-epoxy-5-hexene (4.91 g, 5.60 mL, 50.0 mmol) and periodic acid dihydrate (17.09 g, 75.0 mmol) in ether (100 mL) at reflux for 2 h followed by addition of vinylmagnesium bromide (55 mL of a 0.5 M solution in THF, 27.5 mmol) afforded, after workup and flash chromatography (2:1 hexane/ether), 1.75 g (31% yield) of 3-hydroxy-1,6-heptadiene. IR ($CDCl_3$): 3590, 1640 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 5.80 (m, 2H), 5.40–4.88 (m, 4H), 4.15 (br m, 1H), 2.11 (br q, J = 7.2 Hz, 2H), 1.64 (m, 3H).

Acetylation of the above was performed by standard methods using 3-hydroxy-1,6-heptadiene (1.62 g, 14.4 mmol), acetic anhydride (2.94 g, 2.72 mL, 28.8 mmol), pyridine (2.85 g, 2.91 mL, 36 mmol), and DMAP (0.17 g, 1.44 mmol) in methylene chloride (60 mL) at 0 °C for 1 h to afford, after workup and Kugelrohr distillation (80 °C/0.1 mm Hg), 1.45 (65% yield) of the title compound. IR ($CDCl_3$): 3060, 1724, 1638 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 5.77 (m, 2H), 5.10 (m, 5H), 2.10 (m, 2H), 2.07 (s, 3H), 1.75 (m, 2H). HRMS calcd for $C_9H_{14}O_2$ (M^+) 154.0994, found 154.1000.

Preparation of 8,8-Dicarbomethoxy-1,5-undecadien-10-yne (38a). The title compound was prepared analogously to compound **42b** (*vide infra*) using sodium hydride (50% dispersion in oil, 587 mg, 12.2 mmol), methyl 2-carbomethoxy-4-pentynoate (2.41 mmol), allyl acetate **37a** (1.45 g, 9.4 mmol), palladium acetate (41 mg, 0.18 mmol), triphenylphosphine (316 mg, 1.20 mmol), and *n*-butyllithium (0.54 mL of a 1.55 M solution in hexane, 0.36 mmol) in THF (20 mL) at 60 °C for 12 h to afford, after workup and flash chromatography (5:1 hexane/ether), 1.72 g (69% yield) of **38a** as a 4.8:1 *trans/cis* mixture of isomers by gas chromatography (retention time: *trans*, 12.1 min; *cis*, 12.3 min). IR ($CDCl_3$): 3295, 1735, 1638 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 5.65 (m, 2H), 5.24 (dt, J = 15.1, 7.8 Hz, 1H), 5.03 (m, 2H), 3.72 (s, 6H), 2.76 (d, J = 2.7 Hz, 2H), 2.73 (d, J = 7.8 Hz, 2H), 2.09 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.75 (2C), 137.62, 134.95, 123.10, 114.50, 71.17, 56.80 52.25 (2C), 35.05, 33.20, 31.64, 22.33. Anal. Calcd for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63; MW, 292.1675. Found: C, 67.99; H, 7.61; MW, 292.1683.

Pd(II) Reaction of Enyne 38a. Preparation of Diene 39a. Palladium acetate (7.0 mg, 0.031 mmol) and enyne **38a** (272 mg, 1.02 mmol) in benzene were heated at 60 °C for 2 h to afford, after flash chromatography (5:1 hexane/ether), 217 mg (82% yield) of trienes **39a** and **40a** as a 15.3:1

(33) Trost, B. M.; Chung, J. Y. L. *J. Am. Chem. Soc.* **1985**, *107*, 4586.

mixture by gas chromatography (retention time: **39a**, 12.8 min; **40a**, 12.4 min). IR ($CDCl_3$): 1732, 1540, 1434 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 6.0–5.7 (m, 2H), 5.27 (bs, 1H), 5.08 (d, J = 17 Hz, 1H), 4.99 (d, J = 10 Hz, 1H), 4.80 (bs, 1H), 3.75 (s, 6H), 2.75 (b, 4H), 2.20 (b, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.75 (2C), 145.06, 138.05, 136.85, 121.52, 114.86, 102.92, 62.73, 41.50, 37.79, 33.24, 29.01. HRMS calcd for $C_{15}H_{20}O_4$ 264.1362, found 264.1367.

A 1:2.1 mixture of **39a** and **40a** (20 mg, 0.075 mmol) prepared in 77% yield using bis(triphenylphosphine)palladium acetate as catalyst was allowed to stand with maleic anhydride (14.8 mg, 0.15 mmol) in 0.1 mL of benzene at room temperature for 12 h to afford, after flash chromatography (1:2 hexane/ether), 5.1 mg (60% yield based on the recovery of **40a**) of the Diels–Alder adduct and 11.2 mg (81% recovery) of 1,4-diene **40a**.

Diels–Alder Adduct. IR ($CDCl_3$): 1845, 1778, 1730, 1640 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 5.78 (ddt, J = 17.1, 10, 6.5 Hz, 1H), 5.06 (dq, J = 17.1, 1.7 Hz, 1H), 5.02 (dm, J = 10.3 Hz, 1H), 3.74 (s, 6H), 3.43 (td, J = 8.8, 3.3 Hz, 1H), 3.36 (dd, J = 9.6, 6.3 Hz, 1H), 3.04 (m, 4H), 2.64 (bd, J = 17.3 Hz, 1H), 2.59 (bd, J = 6.3 Hz, 1H), 2.37 (bdd, J = 17.3, 8.8 Hz, 1H), 2.17 (m, 2H), 1.87 (dq, J = 13.6, 6.5 Hz, 1H), 1.64 (dq, J = 13.6, 65 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.85, 172.08, 171.84, 171.23, 137.23, 136.12, 132.30, 115.72, 58.25, 52.94, 43.93, 43.49, 42.22, 40.19, 34.90, 31.63, 28.61, 23.47. HRMS calcd for $C_{19}H_{22}O_7$ (M^+) 362.1365, found 362.1365.

1,4-Diene **40a**. IR ($CDCl_3$): 1725, 1655, 1638, 1431 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 5.78 (ddt, J = 17.7, 10.1, 6.3 Hz, 1H), 5.51 (td, J = 15.3, 6.3 Hz, 1H), 5.28 (dd, J = 15.3, 7.9 Hz, 1H), 5.00 (m, 3H), 4.81 (bd, J = 2.0 Hz, 1H), 3.73 (s, 6H), 3.10 (bd, J = 17.1 Hz, 2H), 2.95 (dq, J = 17.1, 2.2 Hz, 1H), 2.78 (td, J = 6.3, 1.3 Hz, 2H), 2.55 (ddd, J = 17.1, 7.6, 2.2 Hz, 1H), 1.98 (dd, J = 13.0, 11.1 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 172.8, 171.99, 150.95, 136.91, 131.90, 129.80, 115.08, 107.80, 58.47, 52.77, 52.70, 46.60, 40.73, 40.30, 36.51.

Preparation of 4,4-DiCarbomethoxy-6-undecen-1-yne (38b). To a solution of *n*-butyllithium (12.5 mL of a 1.57 M solution in hexane, 19.6 mmol) in THF (36 mL) at –78 °C was added acrolein (1.00 g, 1.19 mL, 17.8 mmol) slowly. After 15 min, methyl chloroformate (2.52 g, 2.1 mL, 26.7 mmol) was added and the reaction mixture was warmed to 0 °C then to room temperature and stirred for 12 h. The reaction mixture was poured into ether, washed with water (2×) and saturated aqueous sodium chloride, and dried over anhydrous magnesium sulfate. The solvent was removed *in vacuo* to afford 2.57 g (84% yield) of crude methyl 1-hepten-3-ylcarbonate. IR ($CDCl_3$): 1750, 1440, 1268 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 5.78 (ddd, J = 17.2, 10.1, 7.2 Hz, 1H), 5.29 (d, J = 17.2 Hz, 1H), 5.19 (d, J = 10.2 Hz, 1H), 5.02 (q, J = 7.2 Hz, 1H), 3.75 (s, 3H), 1.57 (m, 2H), 1.31 (m, 2H), 0.87 (m, 3H).

To the above carbonate (344 mg, 2.0 mmol) and methyl 2-carbomethoxy-4-pentynoate (340 mg, 2.0 mmol) in THF (4 mL) at room temperature was added tetrakis(triphenylphosphine)palladium [prepared *in situ* from tris(dibenzylideneacetone)dipalladium–chloroform (52 mg, 0.05 mmol) and triphenylphosphine (79 mg, 0.30 mmol)] in THF (2 mL). After 12 h at 60 °C, the solvent was removed *in vacuo*, and the crude material was flash chromatographed (5:1 hexane/ether). A few of the fractions containing the desired product also contained dibenzylideneacetone. These fractions were collected, and 2-thioethanol was added. This solution was stirred at room temperature for 12 h, the solvent was removed *in vacuo*, and the crude material was filtered through silica gel eluting with 5:1 hexane/ether to give a total yield of 268 mg (50% yield) of the title compound as a 7.5:1 mixture of *trans/cis* isomers. IR ($CDCl_3$): 3300, 2120, 1735, 1440 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 5.60 (dt, J = 13.1, 6.8 Hz, 1H), 5.19 (dt, J = 13.1, 6.7 Hz, 1H), 3.73 (s, 6H), 2.78 (m, 4H), 2.04 (m, 3H), 1.29 (m, 4H), 0.89 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.76, 170.70, 136.81, 123.05, 79.43, 71.74, 57.64, 53.19, 53.10, 35.84, 32.73, 31.97, 23.09, 22.59, 14.35. HRMS calcd for $C_{15}H_{22}O_4$ ($M^+ - OCH_3$) 235.1335, found 235.1337.

Pd (II) Reaction of Enyne 38b. Preparation of Diene 40b. Palladium acetate (4 mg, 0.018 mmol) and enyne **38b** (100 mg, 0.37 mmol) in 1,2-dichloroethane (3.7 mL) were heated at 60 °C for 12 h to afford, after flash chromatography (5:1 hexane/ether), 39 mg (39% yield) of diene **40b**. IR ($CDCl_3$): 3040, 1730, 1661, 1439 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 5.45 (dt, J = 15.2, 6.8 Hz, 1H), 5.32 (dd, J = 15.2, 8.2 Hz, 1H), 4.92 (d, J = 2.1 Hz, 1H), 4.77 (d, J = 2.1 Hz, 1H), 3.72 (s, 3H), 3.70 (s, 3H), 3.07 (m, 3H), 2.89 (dq, J = 18.7, 2.3 Hz, 1H), 2.52 (dd, J = 13.4, 7.1 Hz, 1H), 1.96 (m, 3H), 1.36 (sextet, J = 7.3 Hz, 2H), 0.87 (t, J = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.28, 172.10, 155.22, 132.49, 130.68, 107.65, 58.36, 52.78 (2C), 46.74, 40.79, 40.18, 34.51, 22.55, 13.58. HRMS calcd for $C_{15}H_{22}O_4$ (M^+) 266.1519, found: 266.1510.

Preparation of 9,9-Dicarbomethoxy-1,6-dodecadien-11-yne (42a). The title compound was prepared analogously to **42b** using a mixture of allyl acetates[20] **54** and **55** (1.43 g, 8.5 mmol), sodium hydride (50% dispersion in oil, 556 mg, 116 mmol), methyl 2-carbomethoxy-4-pentynoate (2.28 g, 13.4 mmol), palladium acetate (100 mg, 0.44 mmol), triphenylphosphine (690 mg, 2.64 mmol), and *n*-butyllithium (0.57 mL of a 1.55 M solution in hexane) in THF (20 mL) at 60 °C for 3 h to afford, after workup and flash chromatography (5:1 hexane/ether), 1.70 g (70% yield) of **42a** as a 6.3:1 *trans/cis* mixture of isomers by gas chromatography (retention time: *trans*, 13.1 min; *cis*, 13.3 min). IR ($CDCl_3$): 3300, 2258, 1731, 1635, 1434 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 5.78 (ddt, J = 17.0, 10.2, 6.7 Hz, 1H), 5.58 (dt, J = 15.2, 6.8 Hz, 1H), 5.22 (dt, J = 15.2, 7.2 Hz, 1H), 5.00 (dq, J = 17.0, 1.7 Hz, 1H), 4.94 (dq, J = 10.2, 1.7 Hz, 1H), 3.73 (s, 6H), 2.78 (d, J = 2.4 Hz, 2H), 2.74 (d, J = 6.8 Hz, 2H), 2.01 (m, 5H), 1.43 (p, J = 7.5 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.21 (2C), 138.57, 135.85, 123.11, 114.53, 78.98, 71.26, 57.20, 52.61 (2 C), 35.42, 33.10, 31.95, 28.59, 22.69. Anal. Calcd for $C_{16}H_{22}O_4$: C, 69.04; H, 7.97. Found: C, 69.06; H, 8.08.

Pd(II) Reaction of Enyne 42a. Palladium acetate (8 mg, 0.036 mmol) and enyne **42a** (278 mg, 1.00 mmoL) in benzene (10 mL) were heated at 60 °C for 23 h to afford, after flash chromatography (5:1 hexane/ether), 211 mg (76% yield) of product as a 21:1 **43a**/**44a** mixture by gas chromatography (retention time: **43a**, 14.2 min; **44a**, 13.8 min). ^1H NMR (200 MHz, $CDCl_3$): δ 6.00–5.70 (m, 1H), 5.25 (bs, 1H), 5.05 (d, J = 16.5 Hz, 1H), 4.95 (d, J = 10 Hz, 1H), 4.80 (bs, 1H), 3.74 (s, 6H), 2.75 (m, 4H), 2.10 (m, 4H), 1.50 (m, 2H).

The above mixture (170 mg, 0.61 mmol) was reacted with maleic anhydride (105 mL, 1.08 mmol) in benzene (0.7 mL) at 0 °C to room temperature over 2 h to afford, after flash chromatography (1:2 hexane/ether), 104 mg (76% yield) of the Diels–Alder adduct and 5 mg (65% recovery) of **44a**.

Diels–Alder adduct. IR ($CDCl_3$): 1846, 1780, 1730, 1639, 1431, 1262 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): δ 5.78 (ddt, J = 17.7, 10.6, 7.8 Hz, 1H), 5.01 (dq, J = 17.1, 1.5 Hz, 1H), 4.94 (dd, J = 10.6, 1.5 Hz, 1H), 3.73 (s, 6H), 3.45 (td, J = 9.6, 3.4 Hz, 1H), 3.36 (dd, J = 9.6, 6.0 Hz, 1H), 3.04 (bd, J = 9.7 Hz, 4H), 2.63 (m, 2H), 2.37 (dd, J = 15.4, 7.8 Hz, 1H), 2.09 (m, 2H), 1.73 (m, 1H), 1.49 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.97, 172.11, 171.88, 171.30, 127.91, 126.11, 132.00, 124.99, 58.15, 52.95, 52.92, 44.10, 43.43, 42.38, 40.02, 35.58, 33.48, 29.02, 27.03, 23.25. HRMS calcd for $C_{20}H_{24}O_7$ (M^+) 376.1522, found 376.1522.

Triene **44**. IR ($CDCl_3$): 3063, 1730, 1434 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 5.78 (m, 1H), 5.46 (dt, J = 12.8, 7.0 Hz, 1H), 5.21 (dd, J = 12.8, 8.1 Hz, 1H), 4.99 (dd, J = 17.0, 1.9 Hz, 1H), 4.94 (dd, J = 11.8, 1.9 Hz, 1H), 4.92 (s, 1H), 4.77 (s, 1H), 3.08 (bs, 1H), 3.05 (bd_{ab}, J = 17.0 Hz, 1H), 2.90 ($d_{ab}q$, J = 17.0, 2.3 Hz, 1H), 2.51 (dd, J = 13.0, 8.1, 1.5 Hz, 1H), 2.11 (m, 4H), 1.94 (dd, J = 13.0, 11.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.13 (2C), 151.09, 138.25, 131.79, 131.09, 114.73, 107.82, 58.38, 52.83, 52.77, 46.70, 40.75, 40.21, 33.69, 31.83. HRMS calcd for $C_{16}H_{22}O_4$ (M^+) 278.1519, found 278.1505.

Preparation of 3-Acetoxy-1,8-nonadiene. To a solution of periodic acid dihydrate (27.58 g, 0.120 mmol) in 100 mL of ether at room temperature was added dropwise 1,2-epoxy-7-octene[20] (12.62 g, 15.08 mL, 0.100 mol). After the reaction mixture was heated at reflux for 5.5 h and filtered (washing the solid several times with ether), the resulting filtrate was washed with water (3 × 25 mL) and saturated aqueous sodium chloride (25 mL), dried over anhydrous magnesium sulfate, and concentrated. The crude aldehyde was added dropwise to a stirred solution of vinylmagnesium bromide (300 mL of a 0.5 M solution in THF, 150 mmol) at 0 °C. After 3 h at room temperature, the reaction was quenched with saturated aqueous ammonium chloride (75 mL). The organic phase was decanted, and the aqueous phase was washed with ether (3 × 75 mL). The combined organic phases were washed with saturated aqueous sodium chloride (50 mL) and dried over anhydrous magnesium sulfate. Concentration *in vacuo* and flash chromatography of the crude material (1:2 hexane/ether) afforded 5.55 g (40% yield from epoxide) of 3-hydroxy-1,8-nonadiene. IR ($CDCl_3$): 3580, 1630 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 5.98 (ddd, J = 17.6, 10.2, 7.2 Hz, 1H), 5.77 (tdd, J = 17.6, 10.2, 7.2 Hz, 1H), 5.22 (dt, J = 17.6, 1.3 Hz, 1H), 5.11 (dt, J = 10.2, 1.3 Hz, 1H), 4.98 (m, 2H), 4.11 (br p, J = 4.0 Hz, 1H), 2.08 (br d, J = 8.0 Hz, 2H), 1.37 (m, 7H).

To a solution of acetic anhydride (8.17 g, 7.55 mL, 80 mmol), pyridine (7.91 g, 8.10 mL, 100 mmol), and DMAP (0.488 g, 4 mmol) in 80 mL of methylene chloride at room temperature was added 3-hydroxy-1,8-

nonadiene (5.55 g, 40 mmol) dropwise. After 2 h at room temperature, the solution was diluted with 30 mL of ether, washed with saturated aqueous copper(II) sulfate (2 × 40 mL) and saturated aqueous sodium chloride (1 × 40 mL), and dried over anhydrous magnesium sulfate. Concentration and flash chromatography of the crude material (2:1 hexane/ether) afforded 6.45 g (88% yield) of the title compound. IR ($CDCl_3$): 1725, 1630 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 5.81 (m, 2H), 5.34 (m, 3H), 5.00 (m, 2H), 2.25 (s, 3H), 2.08 (m, 2H), 1.64 (br m, 2H), 1.35 (br m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.25, 138.64, 136.53, 116.54, 114.44, 74.73, 34.01, 33.56, 28.60, 24.50, 21.24. HRMS calcd for $C_{11}H_{18}O$ (M^+) 182.1307, found 182.1301.

Preparation of 10,10-Dicarbomethoxy-1,7-tridecadien-12-yne (42b). Methyl 2-carbomethoxy-4-pentynoate (281 mg, 1.65 mmol) was added dropwise to a suspension of sodium hydride (60% oil dispersion, 57 mg, 1.43 mmol, washed with THF) in 2 mL of dry THF at 0 °C. After 15 min at 50 °C, allylic acetate **37a** (200 mg, 1.10 mmol) was added at room temperature. The carbanion solution was added to tetrakis(triphenylphosphine)palladium [generated in situ from palladium acetate (12 mg, 0.055 mmol), triphenylphosphine (87 mg, 0.33 mmol), and *n*-butyllithium (0.075 mL of a 1.47 M solution in hexane, 0.11 mmol)] in THF (0.64 mL) at room temperature. After 20 h at 60 °C, the reaction mixture was cooled to room temperature, diluted with ether (1 mL), washed with water (1 × 1 mL), and dried over anhydrous magnesium sulfate. The solvent was removed *in vacuo*, and the crude material was purified by flash chromatography (5:1 hexane/ether) to afford 302 mg (95% yield) of the title compound as a 4:1 *trans/cis* mixture. IR ($CDCl_3$): 3250, 2245, 1735, 1065 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 5.80 (ddt, J = 17.0, 10.2, 6.7 Hz, 1H), 5.55 (dt, J = 15.1, 6.8 Hz, 1H), 5.20 (dt, J = 15.1, 7.5 Hz, 1H), 4.98 (m, 2H), 3.75 (s, 6H), 2.78 (d, J = 2.6 Hz, 2H), 2.73 (d, J = 7.5 Hz, 2H), 2.02 (m, 5H), 1.48 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.18, 170.13, 138.77, 136.00, 122.87, 114.25, 78.93, 71.27, 57.16, 52.54 (2C), 35.38, 33.51, 32.35, 28.75, 28.28, 22.65. Anal. Calcd for $C_{17}H_{24}O_4$: C, 69.84; H, 8.27; MW, 292.1675. Found: C, 69.93; H, 8.25; MW, 292.1683.

Preparation of (*Z*)-1-Iodo-3-(*tert*-butyldimethylsiloxy)-1-propene. Following the standard procedure,[34] imidazole (85.1 g, 1.25 mol), *tert*-butylchlorodimethylsilane (90.4 g, 600 mmol), and propargyl alcohol (28.0 g, 29.0 mL, 500 mmol) in DMF (60 mL) gave, after distillation (55–60 °C/10 mmHg, lit.[34] 37–39 °C/4.0 mmHg), 82.43 g (97% yield) of 3-(*tert*-butyldimethylsiloxy)-1-propyne. IR ($CDCl_3$): 3295, 2110, 1255, 1080 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 4.29 (d, J = 2.3 Hz, 2H), 2.37 (t, J = 2.3 Hz, 1H), 0.89 (s, 9H), 0.10 (s, 6H).

To a solution of the above silyl ether (10.00 g, 59 mmol) in THF at −78 °C was added *n*-butyllithium (48.6 mL of a 1.33 M solution in hexane, 64.6 mmol). After 1 h at −78 °C, a solution of iodine (17.14 g, 67.5 mmol) in 25 mL of THF at room temperature was added to the cold solution and the mixture was warmed to room temperature to give a dark-brown solution. After addition of ether, the organic phase was washed with saturated aqueous sodium thiosulfate (3×) and saturated aqueous sodium chloride, dried over anhydrous magnesium sulfate, and filtered, and the solvent was removed *in vacuo* to give 19.95 g of crude 1-iodo-3-(*tert*-butyldimethylsiloxy)-1-propyne. IR ($CDCl_3$): 2205, 1255, 1080 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 4.46 (s, 2H), 0.09 (s, 9H), 0.11 (s, 6H).

Following standard procedures,[35] dicyclohexylborane prepared from a borane–dimethyl sulfide complex (4.93 g, 6.15 mL, 65 mmol) and cyclohexene (11.75 g, 14.5 mmol, 143 mmol) reacted with crude alkynyl iodide (59 mmol) followed by protonation with 20 mL of glacial acetic acid to give, after Kugelrohr distillation (110–120 °C/0.50 mmHg), 6.71 g (38% yield) of (*Z*)-1-iodo-3-(*tert*-butyldimethylsiloxy)-1-propene. IR ($CDCl_3$): 1615, 1465, 1260, 1095 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 6.41 (dt, J = 17.0, 5.3 Hz, 1H), 6.22 (dt, J = 17.0, 1.8 Hz, 1H), 4.24 (dd, J = 5.3, 1.8 Hz, 2H), 0.90 (s, 9H), 0.09 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.24, 80.09, 66.83, 25.86, 18.25, −5.18. Anal. Calcd for $C_9H_{19}IOSi$: C, 38.22; H, 6.42. Found: C, 37.88; H, 6.65.

Preparation of *cis*-1-(*tert*-Butyldimethylsiloxy)-8-(trimethylsilyl)-2-octen-7-yne. Chlorotrimethylsilane (16.15 g, 18.9 mL, 148.7 mmol) was added dropwise to lithiated 4-pentyn-1-ol prepared from the alcohol (5.00 g, 59.5 mmol) and *n*-butyllithium (98.3 mL of a 1.33 M solution, 130.8 mmol) in THF at −78 °C. The reaction mixture was warmed to room temperature to give a clear homogenous solution. To this solution was added aqueous 3 N HCl (160 mL). After 4 h at room temperature, the organic phase was washed with saturated aqueous sodium bicarbonate (2×) and saturated aqueous sodium chloride and dried over anhydrous magnesium sulfate. The solvent was removed *in vacuo* to give the crude alcohol. IR ($CDCl_3$): 3600, 2165, 1247 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 3.75 (m, 2H), 2.34 (t, J = 7.5 Hz, 2H), 1.77 (p, J = 7.5 Hz, 2H), 1.61 (bs, 1H), 0.13 (s, 9H).

The above crude alcohol was added to a mixture of triphenylphosphine (17.17 g, 65.45 mmol) and bromine (10.46 g, 65.45 mmol) in methylene chloride (120 mL) at 0 °C. After 3 h at room temperature, hexane was added, and the organic phase was washed with saturated aqueous sodium bicarbonate and saturated aqueous sodium chloride, dried over anhydrous magnesium sulfate, and filtered. The solvent was removed *in vacuo*, and the crude product was distilled (78–85 °C/13 mmHg) to give 10.39 g (80% yield) of 1-bromo-5-(trimethylsilyl)-4-pentyne. IR ($CDCl_3$): 2175, 1439, 1256 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 3.49 (t, J = 7.5 Hz, 2H), 2.39 (t, J = 7.5 Hz, 2H), 2.02 (p, J = 7.5 Hz, 2H), 0.13 (s, 9H).

To a nonstirring mixture of magnesium turnings (289 mg, 11.87 mmol) in enough THF to barely cover the turnings to which was added one crystal of iodine was added a few drops of the above bromide.[36] The reaction mixture was warmed slightly (30–35 °C) until the mixture began to effervesce. The remainder of the bromide in 10 mL of THF was added dropwise to a stirred solution of the above mixture at a rate to maintain a gentle reflux. After an additional hour at 50 °C, this Grignard reagent was transferred via cannula into a suspension of anhydrous zinc(II) chloride (12.87 g, 13.69 mmol) in ether (10 mL) at 0 °C which came to room temperature over 1 h to give a thick white suspension. To this rapidly stirred mixture was added (*Z*)-iodo-3-(*tert*-butyldimethylsiloxy)-1-propene (2.72 g, 9.13 mmol) and tetrakis(triphenylphosphine)palladium [prepared from dichlorobis(triphenylphosphine)palladium (322 mg, 0.46 mmol), triphenylphosphine (360 mg, 1.37 mmol), and diisobutylaluminum hydride (0.91 mL of a 1.0 M solution in hexane)] in THF (2 mL). The reaction mixture was stirred at room temperature for 24 h; an ether/water mixture was then added. Aqueous 3 N HCl was added to the aqueous phase to make it homogenous. The aqueous phase was extracted with ether (3×), the combined organic phases were dried over anhydrous magnesium sulfate and filtered, and the solvent was removed *in vacuo*. The crude product was flash chromatographed (5:1 hexane/ether) to give 2.35 g (83% yield) of the title compound. IR ($CDCl)_3$: 3150, 2168, 1460, 1250, 1075 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 5.54 (dtt, J = 10.9, 6.1 Hz, 1H), 5.38 (dtt, J = 10.9, 7.3, 1.3 Hz, 1H), 4.22 (d, J = 5.4 Hz, 2H), 2.20 (t, J = 7.2 Hz, 2H), 2.12 (q, J = 7.4 Hz, 2H), 1.55 (p, J = 7.2 Hz, 2H), 0.88 (s, 9H), 0.13 (s, 9H), 0.05 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 130.62, 129.55, 107.05, 84.71, 59.40, 28.36, 26.53, 25.95, 19.28, 18.34, 0.14 (3C), −5.09 (2C). HRMS calcd for $C_{17}H_{34}OSi$ (M^+) 310.2149, found 310.2163.

Preparation of Methyl *cis*-9-Hydroxy-7-nonen-2-ynoate. To a solution of the above silyl ether in methanol (10 mL) at 0 °C was added potassium carbonate (0.86 g, 6.24 mmol). The reaction mixture was warmed to room temperature and stirred for 8 h. An ether/water mixture was added, and the organic phase was washed with water and saturated aqueous sodium chloride, dried over anhydrous magnesium sulfate, and filtered to give 1.25 g (92% yield) of crude *cis*-1-(*tert*-butyldimethylsiloxy)-2-octen-7-yne. IR ($CDCl)_3$: 3305, 1208 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 5.54 (dtt, J = 10.9, 6.1, 1.5 Hz, 1H), 5.38 (dtt, J = 10.9, 7.3, 1.3 Hz, 1H), 4.22 (dd, J = 5.8, 1.2 Hz, 2H), 2.17 (td, J = 7.3, 2.5 Hz, 2H), 2.15 (t, J = 7.3 Hz, 2H), 1.93 (t, J = 2.5 Hz, 1H), 1.57 (p, J = 7.3 Hz, 2H), 0.88 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 130.73, 129.46, 84.22, 68.46, 59.39, 28.22, 26.46, 25.98 (3C), 18.39, 17.84, −5.10 (2C).

To a solution of the above alkyne in THF at −78 °C was added *n*-butyllithium (4.46 mL of a 1.40 M solution in hexane, 6.2 mmol). After 45 min at −78 °C, methyl chloroformate (786 mg, 0.64 mL, 8.3 mmol) was added slowly and the reaction mixture was warmed to room temperature. Ether was added, the solution was filtered, and the solvent was removed *in vacuo* to give 1.51 g (98% yield) of crude methyl *cis*-9-(*tert*-butyldimethylsiloxy)-7-nonen-2-ynoate. IR ($CDCl_3$): 3120, 1710, 1415 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 5.54 (dtt, J = 10.9, 6.1, 1.5 Hz, 1H), 5.38 (dtt, J = 10.9, 7.3, 1.3 Hz, 1H), 4.22 (dd, J = 5.4, 1.6 Hz, 2H), 3.76 (s, 3H), 2.34 (t, J = 7.2 Hz, 2H), 2.16 (q, J = 7.5 Hz, 2H), 1.65 (p, J = 7.2 Hz, 2H), 0.90 (s, 9H), 0.07 (s, 6H).

A solution of the above ynoate (1.51 g, 5.09 mmol) in THF (4 mL), water (4 mL), and glacial acetic acid (12 mL) was stirred at room

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temperature for 2 h. Ether and water were added, and the acidic solution was neutralized by adding solid sodium carbonate. The organic phase was washed with saturated aqueous sodium bicarbonate (3×) and saturated aqueous sodium chloride, dried over anhydrous magnesium sulfate, and filtered. The crude product was flash chromatographed (2:1 ethyl acetate:/hexane) to give 412 mg (48% overall yield) of the title compound. IR ($CDCl_3$): 3600, 2240, 1710, 1440, 1260 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 5.68 (dtt, J = 10.9, 6.1, 1.5 Hz, 1H), 5.48 (dtt, J = 10.9, 7.3, 1.3 Hz, 1H), 4.22 (dd, J = 5.4, 1.6 Hz, 2H), 3.76 (s, 3H), 2.36 (t, J = 7.2 Hz, 2H), 2.21 (q, J = 7.5 Hz, 2H), 1.67 (p, J = 7.2 Hz, 2H), 1.58 (bs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.17, 130.77, 130.07, 89.14, 73.21, 58.43, 52.60, 26.99, 26.17, 17.88. HRMS calcd for $C_{10}H_{14}O_3$ (M^+ – OH) 165.0916, found 165.0912.

Preparation of Methyl *cis*-10,10-Dicarbomethoxy-7-tridecen-2,12-diynoate (46). To a solution of the above allyl alcohol (400 mg, 2.19 mmol) in hexane/ether (1:1, 10 mL) and pyridine (11 μL) at 0 °C was added phophorus tribromide (683 mg, 0.24 mL, 2.52 mmol). The reaction mixture was stirred at 0 °C for 10 min and then poured into a saturated aqueous sodium bicarbonate/ice mixture. The aqueous phase was extracted with hexane (2×), the combined organic phases were dried over anhydrous magnesium sulfate and filtered, and the solvent was removed *in vacuo*. The crude bromide was filtered through a pad of silica gel, eluting with ethyl acetate/hexane (2:1) to give 530 mg (99% yield) of methyl *cis*-9-bromo-7-nonen-2-ynoate. IR ($CDCl_3$): 2240, 1710, 1433, 1258 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 5.78 (dtt, J = 10.9, 6.1, 1.5 Hz, 1H), 5.52 (dtt, J = 10.9, 7.3, 1.3 Hz, 1H), 3.98 (dd, J = 5.4, 1.6 Hz, 2H), 3.76 (s, 3H), 2.36 (t, J = 7.2 Hz, 2H), 2.21 (q, J = 7.5 Hz, 2H), 1.67 (p, J = 7.2 Hz, 2H).

To THF-washed sodium hydride (53 mg of a 60% dispersion in oil, 1.32 mmol) suspended in THF (4 mL) at room temperature was added methyl 2-carbomethoxy-4-pentynoate (225 mg, 1.32 mmol). The reaction mixture was stirred at room temperature until hydrogen evolution ceased (about 10 min). To this solution was added the above bromide (270 mg, 1.10 mmol). After 4.5 h at room temperature, an ether/water mixture was added. The aqueous phase was extracted with ether (3×), the combined organic phases were dried over anhydrous magnesium sulfate and filtered, and the solvent was removed *in vacuo*. The crude product was flash chromatographed (3:1 hexane/ether) to give 350 mg (95% yield) of the title compound. IR ($CDCl_3$): 3390, 2230, 1735, 1438 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 5.51 (dtt, J = 10.9, 7.8, 1.5 Hz, 1H), 5.17 (dtt, J = 10.9, 7.8, 1.5 Hz, 1H), 3.73 (s, 6H), 3.72 (s, 3H), 2.81 (d, J = 7.8 Hz, 2H), 2.75 (d, J = 2.7 Hz, 1H), 2.32 (t, J = 7.3 Hz, 2H), 2.19 (q, J = 7.3 Hz, 2H), 2.03 (t, J = 2.7 Hz, 1H), 1.62 (p, J = 7.5 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.71 (2C), 154.14, 133.11, 123.46, 89.23, 78.86, 73.08, 71.51, 56.76, 52.78 (2C), 52.51, 29.87, 27.32, 26.38, 22.56, 18.19. Anal. Calcd for $C_{18}H_{22}O_6$: C, 59.53; H, 7.87. Found: C, 59.96; H, 7.96.

Pd(II) Reaction of Enediyne 46. A solution of palladium acetate (1.7 mg, 0.007 mmol) and enyne **46** (50 mg, 0.15 mmol) in 1,2-dichloroethane was stirred at 60 °C for 6 h. After being cooled to room temperature, the solvent was removed *in vacuo*, and the crude product was flash chromatographed (3:1 hexane/ether) to give 4.3 mg (9% yield) of methyl (2*Z*)-[*cis*-5,5-dicarbomethoxy-7-cycloundecen-2-yn-1-ylidene]acetate (**51**) as a white solid (mp 66–69 °C, unrecrystallized) and 23 mg (47% yield) of a 2.5:1 mixture of methyl (2*E*)-[2-(3,3-dicarbomethoxy-5-hexyn-1-ylidene)cyclopent-1-ylidene]acetate (**50**) and methyl (7*E*)-7-(3,3-dicarbomethoxy-5-methylidenecyclopent-1-ylidene)-2-heptynoate (**49**). Compounds **49** and **50** were isolated by MPLC (200–400 mesh Kieselgel silica gel, 10 psig, 2 mL/min, 5:1 cyclohexane/ethyl acetate).

49. IR ($CDCl_3$): 2230, 1735 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 5.44 (t, J = 6.8 Hz, 1H), 5.19 (s, 1H), 5.15 (s, 1H), 3.72 (s, 3H), 3.70 (s, 6H), 3.14 (s, 2H), 2.98 (s, 2H), 2.35 (m, 4H), 1.70 (p, J = 6.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.76 (2C), 154.22, 143.91, 136.07, 125.93, 111.07, 89.28, 57.42, 52.84 (2C), 52.60, 42.90, 42.66, 29.71, 27.46, 18.38. HRMS calcd for $C_{18}H_{22}O_6$ (M^+) 334.1417, found 343.1404.

50. IR ($CDCl_3$): 1735, 1715 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 6.16 (s, 1H), 5.53 (t, J = 7.0 Hz, 1H), 3.76 (s, 6H), 3.73 (s, 3H), 3.11 (d, J = 7.0 Hz, 2H), 2.96 (td, J = 7.5, 2.6 Hz, 2H), 2.86 (d, J = 2.7 Hz, 2H), 2.37 (td, J = 7.5, 1.9 Hz, 2H), 2.03 (t, J = 2.7 Hz, 1H), 1.71 (p, J = 7.5 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.44 (2C), 159.55, 144.55, 122.03, 114.35, 78.47, 71.76, 56.87, 52.84, 52.73, 50.94, 35.59, 33.69, 31.61, 23.25, 22.89. HRMS calcd for $C_{18}H_{22}O_6$ (M^+) 334.1417, found 334.1407.

51. IR ($CDCl_3$): 2210, 1730, 1710, 1616, 1604, 1425 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 6.02 (s, 1H), 5.61 (dt, J = 10.7, 7.8 Hz, 1H), 5.25 (dt, J = 10.7, 7.8 Hz, 1H), 3.77 (s, 6H), 3.69 (s, 3H), 2.98 (s, 2H), 2.82 (bs, 2H), 2.19 (bs, 2H), 1.76 (bs, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.71 (2C), 166.39, 143.24, 134.74, 122.79, 121.75, 95.10, 84.76, 56.11, 53.06 (2C), 51.19, 31.57, 30.80, 27.01, 25.98, 24.04. HRMS calcd for $C_{18}H_{22}O_6$ (M^+) 334.1417, found 334.1417.

Preparation of Tricycle 52. A solution of dienyne **42a** (278 mg, 1.00 mmol) and palladium acetate (11 mg, 0.05 mmol) in 10 mL of toluene was heated at 110 °C for 72 h to afford, after flash chromatography (5:1 hexane/ether), 199 mg (72% yield) of **52** as a 2:1 diastereomeric mixture. IR ($CDCl_3$): 1730, 1635, 1435 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): (mixture of isomers) δ 3.73 (s, 6H), 2.91 (m, 4H), 2.29 (br d, J = 9.0 Hz, 0.5H), 2.08 (m, 2H), 1.87 (m, 1H), 1.66 (m, 6H), 1.15 (p, J = 11.8 Hz, 0.5H). ^{13}C NMR (125 MHz, $CDCl_3$): (major isomer) δ 172.90 (2C), 134.23, 130.86, 57.68, 52.56, 45.17, 43.98, 42.70, 39.67, 37.36, 30.13, 27.21, 26.28, 24.25, 22.40; (minor isomer) δ 172.90 (2C), 134.78, 131.35, 58.10, 52.66, 44.68, 43.68, 41.84, 29.66, 37.36, 29.49, 27.46, 26.62, 23.46. HRMS calcd for $C_{16}H_{22}O_4$ (M^+) 278.1518, found 278.1521.

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