# Pd-Catalyzed Cycloisomerization to 1,2-Dialkylidenecycloalkanes. 2. Alternative Catalyst System

**Barry M. Trost,* Donna L. Romero, and Frode Rise**

*Contribution from the Departments of Chemistry, Stanford University, Stanford, California 94035-5080, and University of Wisconsin, Madison, Wisconsin 53706*

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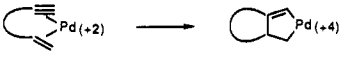
**Abstract:** The mechanisms by which palladium complexes may catalyze the cycloisomerization of 1,6- and 1,7-enynes to dialkylidenecycloalkanes were probed by exploring a catalyst system different than a ligated palladium acetate which previously has proven to be successful. Although carboxylic acids showed no discernible interaction with palladium(0) complexes, this combination proved to be a powerful catalyst system to effect this cycloisomerization. The fact that the two catalyst systems do not have the same reactivity profile suggests this new catalyst system may operate by a different mechanism. Evidence supporting a pathway invoking formation of a hydridopalladium acetate followed by hydropalladation as initiation is presented. Steric and electronic effects direct the regioselectivity of the termination step to form either 1,3- or 1,4-diene products. The 1,3-diene products participate exceedingly well in Diels–Alder reactions, both inter- and intramolecularly. The presence of an oxygen substituent at the position allylic to the diene served as both a regiochemical control element for the palladium-catalyzed cycloisomerization and a diastereochemical control element for the Diels–Alder reaction. The net result of these two steps, the first of which is a catalyzed isomerization and the second an addition, is a highly efficient approach to complex polycycles in terms of both selectivity and atom economy.

The cycloisomerization of enynes to dialkylidene cycloalkanes by palladium acetate complexes followed by cycloaddition of the resultant products with dienophiles for further structural elaboration potentially constitutes a powerful and versatile highly atom economical approach for construction of complex molecules. An understanding of the mechanism of the palladium-catalyzed cycloisomerization reaction becomes important in order to enhance its selectivity and scope. Our initial rationalization focused on the question of a valence tautomerization between an enyne–Pd(+2) and pallada(+4)cyclopentene species (eq 1).[1] However,



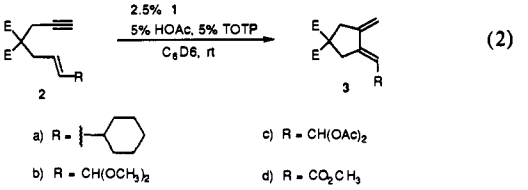

(1)

even though we begin with palladium acetate, we cannot rule out its *in situ* reduction to a Pd(0) species (*inter alia* via Wacker oxidation[2] of an olefin) and acetic acid. The formation of such entities may be envisioned to lead to catalysis for the cycloisomerization, as illustrated in Scheme 1. The key product-determining event is the regioselectivity of the elimination, which should favor insertion into C–$H_a$, leading to the 1,3-diene because of its allylic nature (i.e., lower bond strength). Formation of the Alder ene type product would arise because of lower steric hindrance around $H_b$ compared to $H_a$ and/or geometrical restrictions imposed upon the dihedral angle between C–$H_a$ and C–Pd by internal coordination of the olefin. Most of the observations reported in the preceding paper would be in accord with such a mechanism (*vide infra*).

Although no precedent existed for the oxidative addition of acetic acid to Pd(0), stronger acids including trifluoroacetic acid have been observed to undergo such reactions.[3] On the other hand, simply mixing $(dba)_3Pd_2{\cdot}CHCl_3$ (**1**) (dba = dibenzylideneacetone) with acetic acid and various ligands led to no discernible changes in the NMR spectrum. While this result is not encouraging, it does not rule out the establishment of an equilibrium that lies on the side of Pd(0) and acetic acid. Thus, we embarked upon a study to determine whether these reactants could constitute a catalytic system for cycloisomerization. In this paper, we record our successful realization of this proposal and its potential, coupled with the Diels–Alder reaction,[4] to construct polycycles with high diastereoselectivity by simple addition processes from acyclic substrates.[5]

## Cycloisomerization of Enynes

In order to test the feasibility of this mechanistic hypothesis, the enyne **2a**[1] was exposed to 2.5 mol % **1**, 5 mol % acetic acid, and 5 mol % tri-*o*-tolylphosphine (TOTP) in $C_6D_6$ at room temperature (eq 2). Following the reaction by NMR spectroscopy




(2)

revealed the smooth replacement of the signals for **2a** by those for **3a**, which was isolated in 95% yield, a marked improvement

* Address correspondence to this author at Stanford University.

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(1) Trost, B. M.; Tanoury, G. J.; Lautens, M.; Chan, C.; MacPherson, D. T. *J. Am. Chem. Soc.*, preceding paper in this issue and references therein.

(2) Tsuji, J. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Ley, S. V., Eds.: Pergamon Press: Oxford, U.K., 1991; Vol. 7, Chapter 3.4, pp 444–468.

(3) Werner, H.; Bertleff, W. *Chem. Ber.* **1983**, *116*, 823. Also see: Zudin, V. N.; Chinakov, V. D.; Nekipelov, V. M.; Likholobov, V. A.; Yermakov, Y. I. *J. Organomet. Chem.* **1985**, *289*, 425.

(4) For some examples of the synthesis of dialkylidenecyclopentanes and their use in Diels–Alder reactions, see: Sustmann, R.; Daute, P.; Sauer, R.; Sommer, A.; Trahanovsky, W. S. *Chem. Ber.* **1989**, *122*, 1551. Barco, A.; Benetti, S.; Casolari, A.; Manfredini, S.; Pollini, G. P.; Polo, E.; Zanirato, V. *Tetrahedron* **1989**, *45*, 3935. Baran, J.; Mayr, H. *Tetrahedron* **1989**, *45*, 3347. Baran, J.; Klein, H.; Schade, C.; Will, E.; Koschinsky, R.; Bäuml, E.; Mayr, H. *Tetrahedron* **1988**, *44*, 2181. Fagan, P. J.; Nugent, W. A. *J. Am. Chem. Soc.* **1988**, *110*, 2310. Nugent, W. A.; Thorn, D. L.; Harlow, R. L. *J. Am. Chem. Soc.* **1987**, *109*, 2788. Negishi, E.; Cederbaum, F. E.; Takashi, T. *Tetrahedron Lett.* **1986**, *27*, 2829. Kozikowski, A. P.; Jung, S. H. *Tetrahedron Lett.* **1986**, *27*, 3227. Nugent, W. A.; Calabrese, J. C. *J. Am. Chem. Soc.* **1984**, *106*, 6422. Block, E.; Aslam, M. J. *J. Am. Chem. Soc.* **1983**, *105*, 6165.

(5) For preliminary reports of portions of this work, see: Trost, B. M.; Lee, D. C.; Rise, F. *Tetrahedron Lett.* **1989**, *30*, 651. Trost, B. M.; Lee, D. C. *J. Org. Chem.* **1989**, *54*, 2271.

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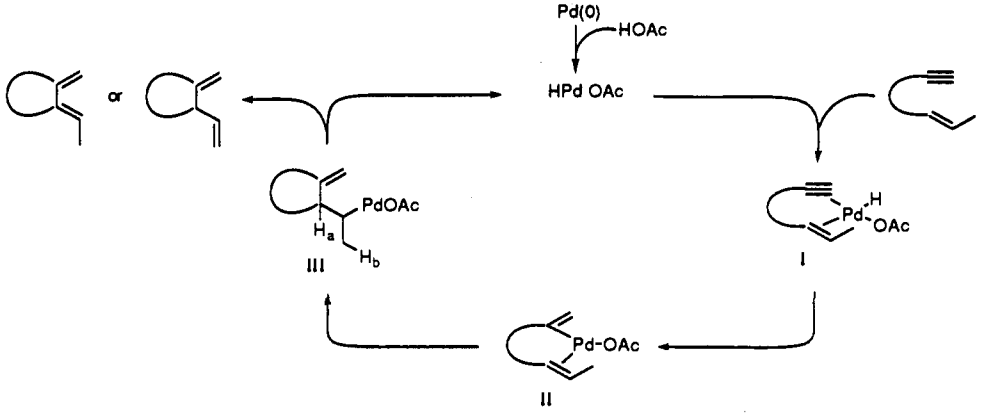
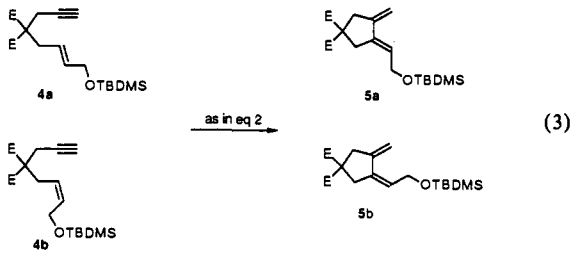
**Scheme 1.** Hydridopalladium Acetate Mechanism for Enyne Cycloisomerization




from the 64% yield using the palladium acetate catalyst which required 60 °C. In spite of the employment of an acid, albeit a weak one like acetic acid, the acid-sensitive allylic dimethyl acetal **2b** exhibited no complications leading to the diene **3b** in 86% yield under the above conditions.

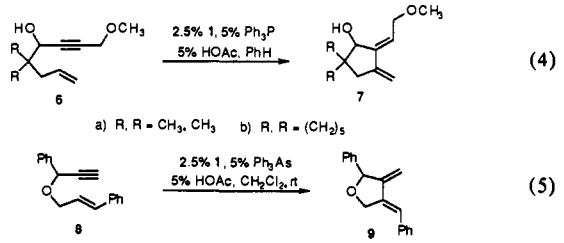
The use of a phosphine and Pd(0) immediately raised the specter of poorer chemoselectivity with respect to allylic acetates as substrates. We therefore examined the reaction of the *gem* diacetate **2c** under both Pd(+2) and Pd(0) catalysis. Allowing a room temperature solution of enyne **2c** to stir with 6 mol % palladium acetate and 6 mol % TOTP gave a 66% yield of the diene **3c**. Using the Pd(0) conditions of eq 2 gave the same product in 75% yield. Not only was the allylic acetate compatible but a somewhat higher yield was also obtained under Pd(0) conditions.

The regioselectivity observed with the acetal **2b** favoring 1,3- over 1,4-diene formation arises from both steric (i.e., branching) and electronic (i.e., electronegative oxygen substituent) effects. Thus, we explored the silyl ether **4**, which was available to us from the Pd(0) alkylation of butadiene monoepoxide as a 2.8:1 *E*/*Z* ratio.[6] It rapidly (10 min) cycloisomerizes to a 3.2:1 ratio of *E* (**5a**) and *Z* (**5b**) dienes, as determined by VPC and NMR analyses, in 93% yield (eq 3), compared to a 52% yield using the palladium acetate catalyst system.




(3)

A sensitive acrylate unit as in the substrate **2d** generated an even more sensitive dienoate **3d** in excellent yield, 82% (eq 2). A free alcohol does not jeopardize the reaction, as shown by the successful use of propargyl alcohols **6a** and **b** (eq 4). Both cyclize in excellent yields (76–78%). On the other hand, the allylic



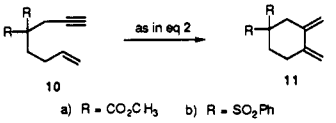

(4)




(5)

propargylic ether **8** produced only a 20% yield of the very sensitive dialkylidenetetrahydrofuran **9** under the conditions indicated in eq 5. By comparison, $(Ph_3As)_2Pd(OAc)_2$ ($CH_2Cl_2$, room temperature) catalyzed this cycloisomerization in 96% yield.[7]

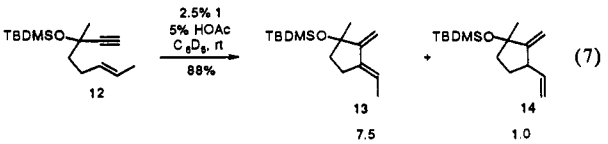
While the work focused on five-membered ring formation, six-membered rings also can be formed. Both the diester and disulfone substrates **10a** and **b** cyclized to the 1,2-dimethylenecyclohexanes **11a** and **b** in 76% and 62% yields, respectively (eq 6). We chose




(6)

the latter example to explore the effect of the nature of the acid on the efficacy of the cyclization. Using standard conditions of 2.5% **1** and 5% $Ph_3P$ in PhH at room temperature, carboxylic acids of different acidity (formic and trifluoroacetic acid) and of different steric demands (mandelic acid) as well as a dibasic acid (camphoric acid) all gave 60–63% yields, virtually identical to that using acetic acid. On the other hand, sulfonic acids (pyridinium *p*-toluenesulfonate (PPTS) camphorsulfonic acid) failed, as did *p*-nitrophenol. It would appear that not acidity but the ability of the anion to coordinate to palladium is the determining factor.

The factors that determine the regioselectivity of this process are not straightforward. Not only are the nature of the substituents at the allylic site leading to Alder ene products important but the substitution pattern of the tether linking the acetylene and olefin also may be important. For example, the substrate bearing geminal propargylic substituents **12** gave mainly the 1,3-diene **13** rather than the expected Alder ene product **14** (eq 7). This reaction was performed in the absence of any phosphine—a fact that suggests ligands may not be required for these transformations.




(7)

## Cycloisomerization–Cycloaddition

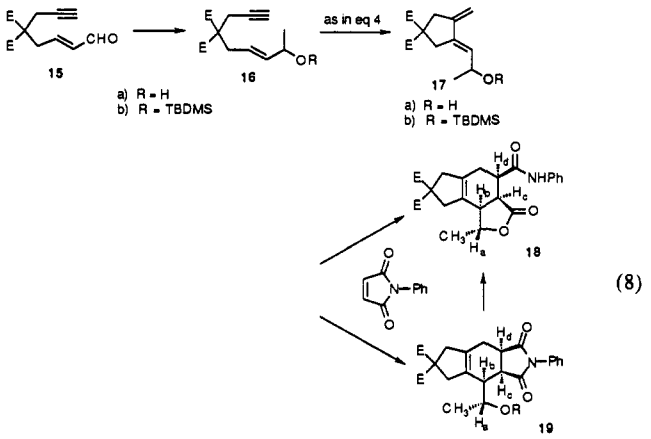
A key aspect of these cycloisomerizations is that the resultant product is a 1,3-diene rather than a 1,4-diene, as results from a normal Alder ene type process—the former being the normal partners in Diels–Alder reactions. Our results indicate that a hydroxyl group at the allylic position serves as a regiochemical control element. Indications that this substituent may serve as a diastereochemical control element in Diels–Alder reactions

(6) Trost, B. M.; Molander, G. A. *J. Am. Chem. Soc.* **1981**, *103*, 5969.

(7) Trost, B. M.; Edstrom, E. D.; Carter-Petillo, M. B. *J. Org. Chem.* **1989**, *54*, 4489.

began to appear at the initiation of this work.[8,9] We, therefore, undertook an investigation of the sequential cycloisomerization–cycloaddition as a highly atom economical and diastereoselective construction of polycycles.

We initiated our studies wherein the cycloaddition would be performed intermolecularly. The enyne **16** was available from the alcohol precursor of **4a** and **b** (eq 3) whose oxidation with pyridinium chlorochromate (PCC) was accompanied by olefin isomerization to the (*E*)-enal **15** followed by addition of

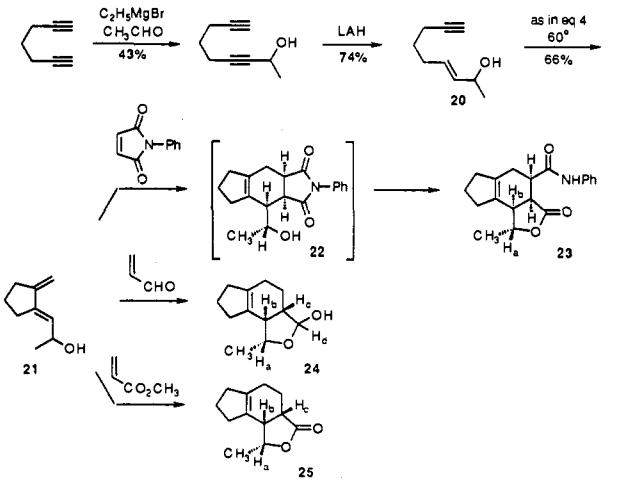



(8)

methylmagnesium bromide. Using **1** and acetic acid with triphenylphosphine (TPP) as ligand at room temperature gave an 81% yield of the diene **17a**. Diels–Alder cycloaddition with *N*-phenylmaleimide occurred at room temperature simply upon mixing in benzene to give cycloadducts in 85% yield. Spectroscopic analysis allowed the assignment of structure **18** to the major cycloadduct. Both infrared and $^{13}C$ analysis indicated the absence of an imide and the presence of the lactone. The stereochemistry derived from an analysis of the coupling constants of $H_a$–$H_d$ and the chemistry. The spontaneous formation of the lactone under the cycloaddition conditions suggests a *cis* relationship of the hydroxyethyl and imide units in the initial cycloadduct **19a**. This assignment is supported by the vicinal coupling constants $J_{bc}$ = 7 Hz and $J_{cd}$ = 3 Hz, which suggest a half-chair cyclohexene conformation wherein $H_c$ is pseudoequatorial and $H_d$ pseudoaxial. Molecular modeling indicates dihedral angles of 36° for $H_b$–$H_c$ and 60° for $H_c$–$H_d$, consistent with the experimental data. The fact that $H_a$ appeared as a quartet ($\delta$ 4.65, $J$ = 6.6 Hz) demonstrated that $J_{ab} \sim 0$ Hz, indicative of a ~90° dihedral angle with $H_b$, which occurs when these two are *trans*, as depicted (calculated 96°). Close models (*vide infra*) suggest that a *cis* relationship of these two protons would give a coupling constant of approximately 6 Hz.

Performing this same Diels–Alder reaction with the *tert*-butyldimethylsilyl ether **17b** (PhH, room temperature) available in 80% yield by cycloisomerizing **16b** gave an 8:1 diastereomeric mixture of cycloadducts in 75% yield. The major diastereomer **19** revealed a coupling pattern for $H_a$–$H_d$ consistent with the stereochemistry depicted. That the stereochemistry corresponds to that obtained with the free alcohol was proven by smooth conversion of **19b** to **18** under desilylation conditions (HCl, HOAc, THF, $H_2O$).

To examine the role of tether substituents, the completely unsubstituted enyne **20**, available from 1,6-heptadiyne as outlined in eq 9, was cycloisomerized to diene **21** using the same conditions




(9)

as previously but at 60° rather than room temperature. Thus, the normal Thorpe–Ingold effect that leads to acceleration of cyclizations is observed in this metal-catalyzed reaction, since the removal of the *gem* diester groups causes a rate deceleration. The Diels–Alder reaction of diene **21** and *N*-phenylmaleimide proceeded under the same conditions as that of **17** to give only the lactone **23** with the intermediate imide **22** not being observed. Once again, the appearance of $H_a$ ($\delta$ 4.62) as only a quartet ($J$ = 6.5 Hz) indicated that $J_{ab} \sim 0$, consistent with the stereochemistry depicted.

Acrolein reacted similarly at room temperature to give a 73% yield of a 6:1 diastereomeric mixture epimeric at the hydroxyl group. The absence of any carbonyl group and the presence of the hydroxyl group reveal the adduct exists exclusively in the lactol form. This fact combined with the normal endo preference leads to the assignment of the *cis*-lactol. This adduct shows $H_a$ ($\delta$ 3.88) as a dq, $J$ = 8.0, 6.2 Hz. Molecular modeling indicates that the dihedral angle for $H_a$–$H_b$ is 90° if they are *trans* and 43° if they are *cis*. The observed 8.0-Hz coupling therefore demands the latter assignment. The 3-Hz coupling for $J_{cd}$ in the major diastereomer suggests these hydrogens are *trans*, since molecular modeling indicates a dihedral angle of 133° for *trans* and nearly 0° for *cis*. Thus, the large $J_{ab}$ in complete contrast to that of the lactone **23** supports the stereochemistry depicted in **24**, indicating a change in facial selectivity. The formation of a single regioisomer is to be noted.

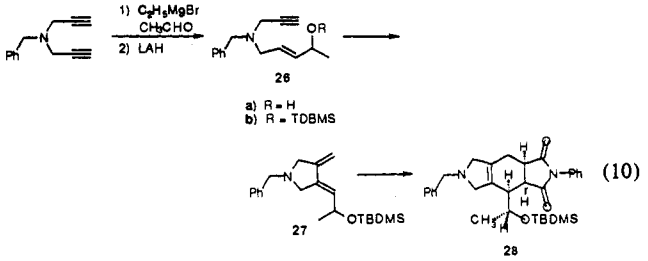
A similar high regioselectivity was observed in the cycloaddition of methyl acrylate with diene **21** wherein a *single* cycloadduct formed in benzene at 60 °C in 81% yield. The absence of any hydroxyl bands at 3500–3600 $cm^{-1}$ and the presence of a lactone band at 1760 $cm^{-1}$ rather than an ester showed lactonization accompanied cycloaddition—consistent with a *cis* relationship of the hydroxyethyl and methoxycarbonyl groups in the initial cycloadduct—as predicted on the basis of the *endo* addition rule. The appearance of $H_a$ in the $^1H$ NMR spectrum as a qd, $J$ = 6.4, 4.8 Hz, combined with molecular modeling which shows a dihedral angle for $H_a$–$H_b$ of 96° when *trans* and 32° when *cis* supports the stereochemistry depicted in **25**. The fact that adduct **23** shows

(8) Gree, R.; Kessabi, J.; Mossel, P.; Martelli, J.; Carrie, R. *Tetrahedron Lett.* **1984**, *25*, 3697. Franck, R. W.; Argade, S.; Subramanian, C. S.; Frechet, D. M. *Tetrahedron Lett.* **1985**, 3187. Schlessinger, R. H.; Wong, J. W.; Poss, M. A.; Springer, J. P. *J. Org. Chem.* **1985**, *50*, 3951. Sternbach, D.; Rossana, D. M.; Onan, K. D. *Tetrahedron Lett.* **1985**, *26*, 591. Jones, R. C. F.; Tunnicliffe, J. H. *Tetrahedron* **1985**, *50*, 3421. Marshall, J. A.; Andra, J. E.; Grote, J. *J. Org. Chem.* **1986**, *51*, 1155. McDougal, P. G.; Rico, J. G.; Van Derveer, D. *J. Org. Chem.* **1986**, *51*, 4491. For more recent references, see: Tripathy, R.; Franck, R. W.; Onan, K. D. *J. Am. Chem. Soc.* **1988**, *110*, 3257. Fisher, M. J.; Hehre, W. J.; Kahn, S. D.; Overman, L. E. *J. Am. Chem. Soc.* **1988**, *110*, 4625. Herezegh, P.; Zsely, M.; Szilagyi, L.; Bognar, R. *Tetrahedron Lett.* **1988**, *29*, 481. Macaulay, J. B.; Fallis, A. G. *J. Am. Chem. Soc.* **1988**, *110*, 4074. Reitz, A. B.; Jordan, A. D., Jr.; Maryanoff, B. E. *J. Org. Chem.* **1987**, *52*, 4800. Marshall, J. A.; Shearer, B. G.; Crooks, S. L. *J. Org. Chem.* **1987**, *52*, 1236.

(9) For effects on intramolecular reactions, see: Roush, W. R. *J. Am. Chem. Soc.* **1980**, *102*, 1390. Roush, W. R.; Hall, S. E. *J. Am. Chem. Soc.* **1981**, *103*, 5200. Funk, R. L.; Zeller, W. E. *J. Org. Chem.* **1982**, *47*, 180. Huaina, M.; Uei, M. *J. Am. Chem. Soc.* **1982**, *104*, 4251. Roush, W. R.; Hall, S. E. *J. Org. Chem. Soc.* **1982**, *47*, 4611. Boeckman, R. K.; Barta, T. E. *J. Org. Chem.* **1985**, *50*, 3421. Roush, W. R.; Kageyama, M.; Riva, R.; Brown, B. B.; Warmus, J. S.; Moriarty, K. J. *J. Org. Chem.* **1991**, *56*, 1192.

no coupling between $H_a$ and $H_b$ where the dihedral angle is calculated to be 97° lends strong support for these stereochemical assignments. Once again, the extraordinary level of regioselectivity is to be noted.

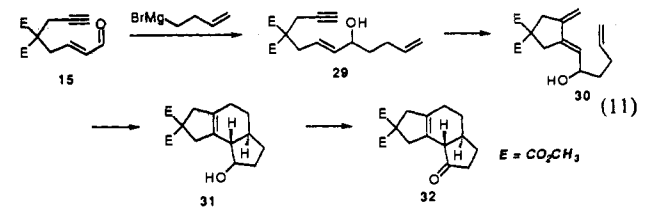
The lack of requirement for *gem*-alkyl substitution on the tether led us to test the feasibility of a substrate bearing a basic nitrogen as illustrated in eq 10. Cycloisomerization attempts with the



(10)

free alcohol **26a** proved fruitless in this case—in contrast to the case of the non-nitrogen-bearing substrates. Thus, attention focused on the silyl ether **26b**. At first, the presence of the basic nitrogen might be thought to be incompatible with the Pd(0)—acetic acid catalyst system which led initially to employment of our palladium acetate catalyst. Nevertheless, the catalyst derived from palladium acetate and triphenylphosphine cycloisomerized **26b** to the diene **27** in only 38% in benzene at 60 °C. On the other hand, our Pd(0) catalyst system as in eq 4 cycloisomerized **26b** in 52% yield at room temperature using excess acetic acid. *In situ* protonation of the basic nitrogen under these latter conditions may inhibit its deactivation of the catalyst and account for the normal reactivity. Diels–Alder reaction with *N*-phenylmaleimide proceeded at room temperature to give a single cycloadduct. Analogy to the earlier reactions leads us to assign structure **28** (eq 10).

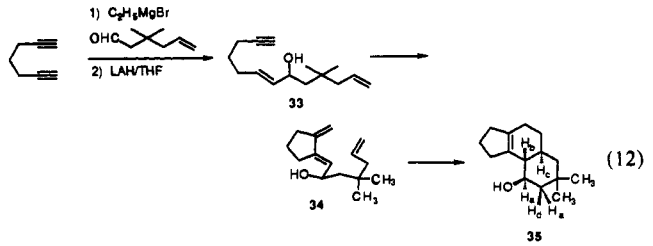
Incorporating the dienophile into the enyne substrate should act synergistically with the hydroxyl group to direct the palladium-catalyzed cycloisomerization to the 1,3-mode. Addition of 3-butenylmagnesium bromide to aldehyde **15** (64% yield) rather than methylmagnesium bromide as in eq 8 generated the dienyne **29** (eq 11). Exposure of **29** to the standard Pd(0) catalyst effected



(11)

smooth cycloisomerization to the triene **30** at room temperature in 80% yield. The subsequent thermal cycloisomerization (the intramolecular Diels–Alder reaction) required 172 °C in toluene containing *N,O*-bis(trimethylsilyl)acetamide (BSA) and 2,6-di-*tert*-butyl-4-methyl phenol (BHT) in a sealed tube. Since BSA silylates the alcohol, the product obtained in 84% yield was worked-up with fluoride ion to liberate the alcohol **31** (64% yield) as a 5.2:1 mixture. The mixture likely results from epimers at the hydroxyl-bearing carbon, since the Moffatt–Swern oxidation generated a single ketone **32**. While we cannot rule out that isomerization of the ketone might occur under the oxidation conditions, the absence of any detectable isomers makes that less likely. The *E* ring junction stereochemistry derives from analogy to other cycloadditions producing [6.5] ring fusions.[10,11]

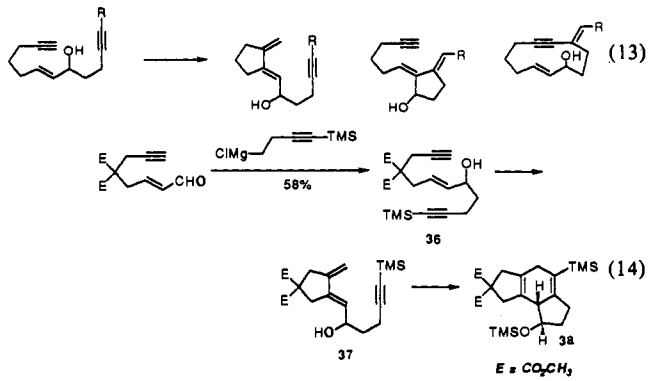
Ring-size variation involves simply adjustment of the tether length. The importance of the [6.6.5] polycycle led us to explore a simple route using this strategy as outlined in eq 12. Once again, 1,6-heptadiyne serves as a convenient starting material, since the propargyl alcohol derived from addition of the mono-



(12)

magnesium salt to an aldehyde which was obtained in 53% yield underwent chemoselective reduction[12] to the allyl alcohol **33** (81% yield). Cycloisomerization with our standard catalyst proceeded at 60 °C without complications to the triene **34** (72% yield) in contrast to a 41% yield using triphenylphosphine and palladium acetate as catalyst. Intramolecular Diels–Alder reaction was best performed in the presence of BSA and BHT and gave a 74% yield of a single product which was desilylated (silylation occurred under the reaction conditions due to the use of BSA) to a diastereomerically pure alcohol. Decoupling experiments reveal $J_{ab}$ = 10.0 Hz, $J_{ad}$ = 10.0 Hz, and $J_{ac}$ = 4.6 Hz. Unfortunately, $J_{bc}$ could not be determined. These couplings reveal a conformationally rigid cyclohexane ring which corresponds to a *trans* [6.6] but not a *cis* [6.6] ring junction in which both $H_a$ and $H_b$ are axial, as is accommodated by structure **35**. The *trans* ring fusion for similar intramolecular Diels–Alder reactions also has ample analogy.[10]

Replacing the alkene as a dienophile by an acetylene raises the serious question of chemoselectivity in the palladium-catalyzed cycloisomerization, since at least three pathways can be anticipated and have been observed (eq 13).[1] Since reactivity of the acetylene



(13) (14)

initiator appears dependent upon the acetylenic substituents, choice of an appropriate R may permit chemoselectivity. For practical purposes and synthetic versatility we chose R = TMS, which led to the synthesis of enediyne **36**, as outlined in eq 14. Palladium-catalyzed cycloisomerization proceeded at ambient temperature in 83% yield to a single product whose proton NMR spectrum clearly reveal it to be dienyne **37**. Thus, excellent chemoselectivity was obtained. The second thermal cycloisomerization under conditions similar to those of the other related reactions in the presence of BSA and BHT gave a 6:1 diastereomeric mixture of silyl ethers **38** for which the stereochemistry of the major diastereomer is suggested by analogy.

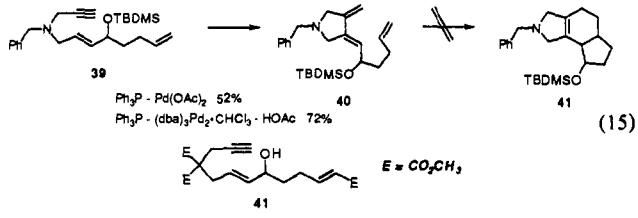
A few limitations were observed. For example, the dienyne **39** underwent smooth palladium-catalyzed cycloisomerization to

(10) Sustmann, R.; Sauer, J. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 779. Taber, D. F. *Intramolecular Diels–Alder Reactions and Alder ene Reactions*; Springer-Verlag: New York, 1984. Ciganek, E. *Org. React.* **1984**, *32*, 1. Fallis, A. G. *Can. J. Chem.* **1984**, *62*, 183. Craig, D. *Chem. Soc. Rev.* **1987**, *16*, 187. Roush, W. R. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Paquette, L. A., Eds.; Pergamon Press: Oxford, U.K., Vol. 5, Chapter 4.4, pp 513–550.

(11) Also see: Ichihara, A.; Kimura, R.; Yamada, S.; Sakamura, S. *J. Am. Chem. Soc.* **1980**, *102*, 6353 and ref 4.

(12) Denmark, S. E.; Jones, T. K. *J. Org. Chem.* **1982**, *47*, 4595.

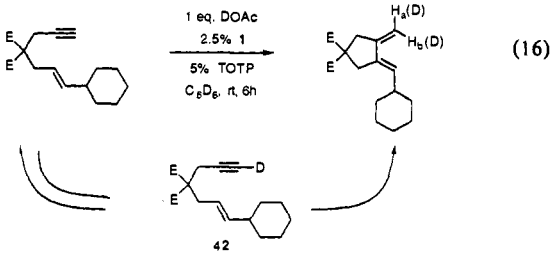
diene **40** with both catalyst systems; however, the Pd(0)–HOAc combination gave a somewhat higher yield (eq 15). The sensitivity




of the diene **40** and/or the Diels–Alder adduct **41** precluded successful thermal [4 + 2] cycloisomerization under the harsh conditions required with such substrates bearing unactivated dienophiles. On the other hand, the acrylate substrates **41** failed to undergo cycloisomerization under our standard catalyst conditions. Our experience in related cases suggests that such limitations frequently can be overcome by modification of the catalyst—one of the major advantages of transition-metal-catalyzed reactions—but this prospect has not been pursued in this case.

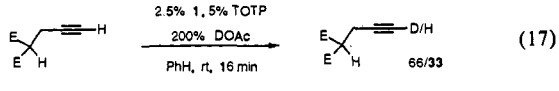
## Discussion

The employment of palladium(0), acetic acid, and a ligand is an excellent general catalyst for cycloisomerization of 1,6- and 1,7-enynes to dialkylidenecyclopentanes and -cyclohexanes. The mechanistic speculation presented in Scheme 1 gains some support from a deuterium-labeling experiment in which 1 equiv of DOAc was employed (eq 16). Mass spectral analysis reveals the product



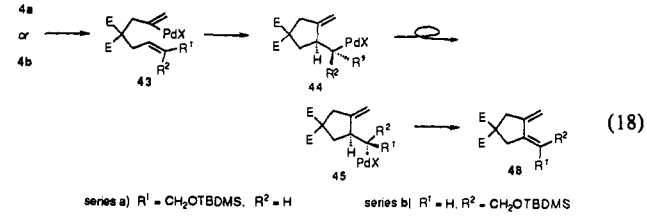

consists of 54% $d_0$, 39% $d_1$, and 7% $d_2$. $^1$H NMR analysis indicates 13% D in place of H for $H_a$ and 32% for $H_b$, in good agreement with the mass spectral analysis of total deuterium content. The reaction sequence requires generation of 1 equiv of HOAc for each equivalent of product. Thus, at 50% conversion, the acetic acid pool will consist of a 50:50 mixture of labeled and unlabeled acetic acid. Since oxidative addition of Pd(0) to the acetic acid must be fast and reversible on the basis of our early NMR observations, the hydropalladation step will determine the amount of deuterium incorporation. Since any isotope effect would be anticipated to favor proton over deuteron incorporation, obtainment of $\ll$100% $d_1$-containing product is expected.

However, *a priori*, the observed labeling pattern is not expected, since incorporation of only one deuterium exclusively in lieu of $H_b$ is predicted. While replacement of $H_b$ by D is the major labeled product, as predicted, significant quantities of D replacement of $H_a$ and dideuterated product must be accounted for. The explanation resides in competitive exchange of the acetylenic hydrogen of the starting material to give **42**. Hydropalladation of the latter would give $d_1$ product with $H_a$ replaced, and deuteriopalladation would give $d_2$ product. That such exchange can occur reasonably rapidly is clearly indicated by the observed exchange with a substrate that cannot undergo further reaction, dimethyl propargylmalonate (eq 17). After only 16 min, an

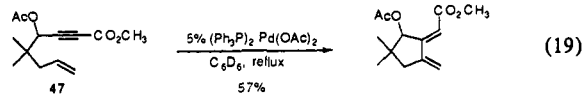



equilibrium seemed to be reached with 200% DOAc in which 66% of the acetylenic hydrogen had exchanged. While the results of eq 16 demand that cyclization be somewhat faster than exchange, it is obvious that such exchange must be occurring. Thus, the initiation step involving hydridopalladium acetate is strongly supported.

The dependence of olefin geometry of the product on that of the starting material (eq 3) supports the proposed involvement of carbopalladation (**II** → **III**, see Scheme 1) and $\beta$-hydrogen elimination (III → products) for the cyclization and termination steps. Thus, the proposed vinylpalladium intermediate **43a** from **4a** would produce **44a** via a *cis–syn* addition and **46a** from **45** by a *cis–syn* $\beta$-elimination. The geometrical isomer **4b** would provide complementary results. The observations (eq 3) support these conclusions.



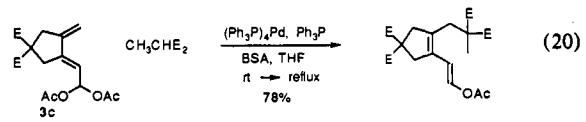

How does the mechanism of this cycloisomerization compare to that of the one catalyzed by palladium acetate? It is tempting to propose that the two catalysts involve the same process, since reduction of palladium acetate to a palladium(0) species and acetic acid under the reaction conditions by a Wacker type reaction can be envisioned. However, the reaction profiles are *not* identical. In many instances, the efficacy of the two catalysts differ markedly with the current conditions being favored in some cases and palladium acetate in others. For example, enyne **47** cyclo-




isomerizes under the palladium acetate conditions but not under the conditions reported herein. On the other hand, cyclization of the simple 1,7-enynes **10a** and **b** fail with the palladium acetate catalyst. Thus, it appears that two different mechanisms may indeed be operating, a Pd(+2)–Pd(+4) cycle with palladium acetate and a hydridopalladium acetate mechanism in the present case. A cautionary note must be interjected. While the comparison cases involve conditions and apparent ligands that are the same in both cases, the reaction conditions cannot be precisely controlled. Since we are dealing with a catalytic process in which small amounts of an agent may have profound effects, the observed differences may derive from slight variation in reaction parameters that are uncontrollable.

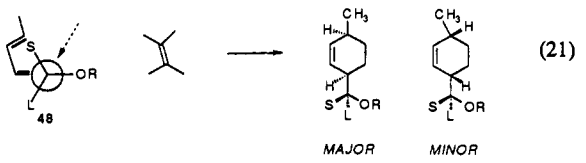
The effects of substituents on regioselectivity are identical for the two catalytic systems. Thus, both steric and electronic effects promote formation of the versatile 1,3-dienes rather than 1,4-dienes. The alkylpalladium intermediate III of Scheme 1 would have no geometric barrier to overcome for $\beta$-elimination of $H_a$, which involves the weaker C–H bond, unless the palladium would coordinate with the olefin. The fact that 1,4-diene formation is frequently observed as the exclusive pathway suggests that such coordination may indeed occur. On the other hand, this catalyst system shows a lower intrinsic preference for the Alder ene type product. For example, ether substituents as in **12** (eq 7) may influence the regioselectivity in favor of 1,3-diene formation. In this case, the presence of the *gem* substitution at the propargylic position places significant steric hindrance at the allylic position of intermediate III of Scheme 1 which will diminish the ability of the olefin to coordinate to the palladium and thereby direct the regioselectivity.

The excellent chemoselectivity is noteworthy. The compatibility of free alcohols, silyl ethers, esters, amines, and very acid labile groups like acetals has been explicitly demonstrated. The compatibility of the allylic *gem* diacetate as in **2c** is particularly astounding given that either the starting material **2c** or its product **3c** could have undergone ionization with a phosphine-coordinated palladium(0) catalyst, as is present in these reactions.[13] That the product is a substrate for Pd(0)-catalyzed allylic alkylations has been demonstrated and illustrates a utility of this particular cyclization (eq 20).




(20)

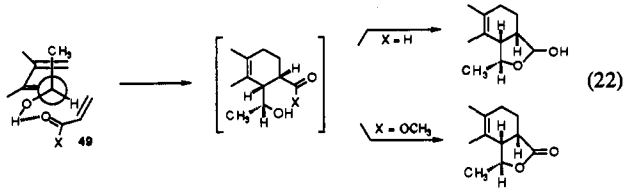
The major obvious synthetic utility of the products of these reactions is a second addition reaction—the Diels–Alder reaction. These dialkylidenecycloalkanes, being rigidly cisoid dienes, are superb reaction partners for this process. A significant issue is diastereoselectivity. In this regard, the substrates bearing an allylic oxygen substituent are most interesting, since it can play a dual role—a regiochemical control element for the palladium-catalyzed cycloisomerization and a diastereochemical control element for the Diels–Alder reaction. Previous work suggested that the presence of an oxygen substituent at a position allylic to the diene may influence the diastereofacial selectivity, as illustrated in eq 21.[8,9,14] The degree of facial selectivity is a




(21)

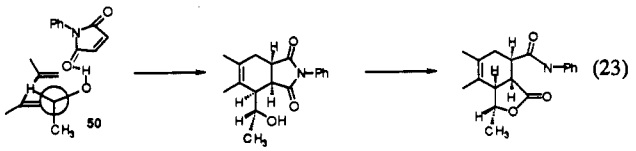
function of (1) the substituents on the diene, (2) the substituents on the dienophile, and (3) the nature of the oxygen. Our results are in accord with this model except that our diastereoselectivity is considerably enhanced. For example, the diene **48**, S = H, L = $CH_3$, R = H, produced a 5:1 diastereomeric mixture with *N*-phenylmaleimide compared to a 10:1 ratio in one of our cases (eq 8) and exclusive formation of a single diastereomer in another (eq 9).

Remarkably, a quite different result pertains when an unsymmetrical acyclic dienophile is employed. A possible explanation derives from the role the hydroxyl group may play in stabilizing the *endo* transition state. Assuming the dienophile prefers the *cis–syn* conformation as the more reactive one as depicted in **49**,[15] the hydroxyl group must adopt a *syn* relationship with respect




(22)

to the diene rather than the *anti* relationship depicted in **48** (eq 21). In this conformation, the delivery of the dienophile to the least hindered face *anti* to the methyl group rather than hydrogen involves the face of the diene that is diastereotopic to that observed with *N*-phenylmaleimide. This explanation also addresses another concern—why are these reactions so highly regioselective? While "*ortho*" selectivity for 1-substituted dienes is normally expected, observation of only one regioisomer in thermal reactions is not.[16] The difference between *N*-phenylmaleimide and acrolein or methyl acrylate may stem from two effects. Firstly, the intrinsic higher reactivity of *N*-phenylmaleimide may make it less prone to catalysis especially by such a weak acid. Secondly, its enforced *anti* conformation means that, to the extent any such catalysis would play a role, the hydroxyl group would be able to adopt the *anti* relationship, as depicted in **50**, and still serve as an internal




(23)

"acid catalyst". The stereochemical bias of this catalysis reinforces the intrinsic bias in the absence of such an effect. Indeed, there is a somewhat enhanced diastereoselectivity for the free alcohol compared to the silyl ether in spite of the larger size and enhanced inductive effect of a siloxy group.

The discovery of an effective catalytic method to generate dialkylidenecycloalkanes from acyclic enynes enhances our ability to construct polycycles in a highly atom economical approach by its pairing with the Diels–Alder reaction. Some structural parameters that favor 1,3- over 1,4-diene formation in the palladium catalyzed cycloisomerization have been established—notably a steric effect and an electronic effect. It would also appear likely that further expansion of the scope may evolve by understanding the conformational effects of tether substituents. The observations of the effect of the allylic oxygen substituent on *both* the palladium-catalyzed cycloisomerization and the Diels–Alder reaction whereby polycycles are sculpted from acyclic precursors with high stereochemical control by a sequence of simple isomerizations and/or additions portend well for further exploitation of these principles for enhanced efficiency in the construction of complex molecular arrays.

## Experimental Section

**Preparation of 4,4-Bis(methoxycarbonyl)-2-methylene-1-(cyclohexylmethylidene)cyclopentane (3a).** Acetic acid (0.3 μL, $4.8 \times 10^{-3}$ mmol) was added to a solution of complex **1** (2.5 mg, $2.4 \times 10^{-1}$ mmol), TOTP (1.5 mg, $4.8 \times 10^{-3}$ mmol) and enyne **2a**[1] (27.8 mg, $9.54 \times 10^{-2}$ mmol) in 0.5 mL of $C_6D_6$. After being stirred for 4 h at room temperature, the mixture was applied to a flash chromatography column and eluted with 1:9 ether/hexane to give 26.6 mg (95%) of the title compound identical to an authentic sample.[1]

**Preparation of Methyl 2-(Methoxycarbonyl)-2-propargyl-6-hydroxy-4-hexenoate.** Butadiene monoepoxide (1.31 g, 18.7 mmol) in 10 mL of THF was added over a period of 1 h to a solution of complex **1** (96.9 mg, $9.36 \times 10^{-1}$ mmol), TPP (196.5 mg, 0.749 mmol), and dimethyl propargylmalonate (3.19 g, 18.73 mmol) in 100 mL of THF. After the reaction mixture was stirred for 24 h at room temperature and evaporated *in vacuo*, flash chromatographic purification (1:1 hexane/ether) gave the title compound as a 3:1 ratio of geometric isomers, 2.66 g (93%) as a colorless oil. IR (neat): 3500–3350, 3300, 2960, 1750 $cm^{-1}$. $^1H$ NMR (200 MHz, $C_6D_6$): δ 5.6 (m, 2H), 3.31 (s) and 3.29 (s) (total 6H), 3.04 (m, 4H), 2.99 (d, $J$ = 2.7 Hz) and 2.93 (d, $J$ = 2.7 Hz) (total 2H), 1.75 (t, $J$ = 2.7 Hz) and 1.71 (t, $J$ = 2.7 Hz) (total 1H). MS (EI 30 eV): 239 ($M - 1^+$, 0.24), 223 (14), 209 (4), 201 (3), 183 (12), 181 (9), 180 (9), 171 (23), 170 (55), 169 (17), 163 (54), 162 (43), 151 (24), 149 (34), 139 (26), 121 (33), 110 (46).

**Preparation of Methyl 2-(Methoxycarbonyl)-2-propargyl-6,6-dimethoxy-4-hexenoate (2b).** The above alcohol (100 mg, 0.417 mmol) was added to PCC (35 mg, 0.625 mmol) in 1.5 mL of dichloromethane at 0 °C.

(13) Trost, B. M.; Vercauteren, J. *Tetrahedron Lett.* **1985**, *26*, 131.

(14) For theoretical treatments, see: Houk, K. N.; Paddon-Row, M. N.; Rordan, N. G.; Wu, Y. D.; Brown, F. K.; Spellmeyer, D. C.; Meta, J. T.; Li, Y.; Loucharich, R. J. *Science* **1985**, *231*, 1108. Kahn, S. D.; Hehre, W. S. *J. Am. Chem. Soc.* **1987**, *109*, 663.

(15) Birney, D. M.; Houk, K. N. *J. Am. Chem. Soc.* **1990**, *112*, 4127. Also see: Loncharich, R. J.; Brown, F. K.; Houk, K. N. *J. Org. Chem.* **1989**, *54*, 1129.

(16) For some recent reviews, see: Pindur, U.; Lutz, G.; Otto, C. *Chem. Rev.* **1993**, *93*, 741. Oppolzer, W. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Paquette, L. A., Eds.; Pergamon Press: Oxford, U.K., Vol. 5, Chapter 4.1, pp 315–399. Fringuelli, F.; Taticchi, A. *Dienes in the Diels–Alder Reaction*; Wiley-Interscience: New York, 1990.

**Table 1.** Experimental Details for Cycloisomerizations

| entry | enyne mg, mmol | 1 mg, $10^{-3}$ mmol | ligand[a] mg, mmol | HOAc μL, $10^{-3}$ mmol | solvent[b] mL | time[c] h | diene mg, % yield | chromatographic solvent[e] |
|---|---|---|---|---|---|---|---|---|
| | **2d** | | TPP | | | | **3d** | |
| 1 | 25.0, 0.093 | 2.4, 2.3 | 1.2, $4.6 \times 10^{-3}$ | 0.3, 4.6 | 1 | 18 | 20.5, 82 | 15% ether in pentane |
| | **4** | | TOTP | | | | 3.2:1 **5a/5b** | |
| 2 | 100.0, 0.282 | 7.3, 706 | 4.3, $1.4 \times 10^{-2}$ | 0.8, 1.4 | 2 | 10 | 93.1, 93 | 10% ether in pentane |
| | **6a** | | TPP | | | | **7a** | |
| 3 | 25.0, 0.137 | 3.5, 3.4 | 1.8, $6.8 \times 10^{-3}$ | 0.4, 6.8 | 1 | 48 | 19.4, 78 | 15% ether in hexane |
| | **6b** | | TPP | | | | **7b** | |
| 4 | 25.0, 0.113 | 2.9, 2.8 | 1.5, $5.6 \times 10^{-3}$ | 0.32, 5.6 | 1 | 24 | 19.0, 76 | 15% ether in pentane |
| | **10a** | | TOTP | | | | **11a** | 10–25% ether |
| 5 | 100, 0.446 | 11.5, 11 | 6.8, $22 \times 10^{-3}$ | 1.3, 22 | 5 | 6 | 76, 76% | in hexane gradient |
| | **10b** | | TOTP | | | | **11b** | 25% $C_2H_5OAc$ |
| 6 | 50, 0.13 | 3.3, 3.2 | 2.0, $6.4 \times 10^{-3}$ | 0.42, 6.4 | 2 | 5 | 31, 62% | in hexane |
| | **12** | | | | | | 7.5:1 **13/14** | |
| 7 | 148, 0.588 | 15.2, 14.7 | | 1.7, 29 | 1.5 | 19 | 130.5, 88 | 5% ether in hexane |
| | **16a** | | TPP | | | | **17a** | |
| 8 | 25, 0.098 | 2.5, 2.5 | 1.3, $4.9 \times 10^{-3}$ | 0.31, 4.9 | 1 | 48 | 20, 81 | 40% ether in hexane |
| | **16b** | | TPP | | | | **17b** | |
| 9 | 50, 0.136 | 3.5, 3.4 | 1.8, $6.8 \times 10^{-3}$ | 0.42, 6.8 | 1 | 20 | 40, 80 | 7% ether in hexane |
| | **20** | | TPP | | | | **21** | |
| 10 | 20, 0.14 | 4.5, 4.5 | 4.7, $18 \times 10^{-3}$ | 0.5, 9 | 1 | 18, 3[d] | 13.2, 66 | 10% ether in hexane |
| | **29** | | TPP | | | | **30** | |
| 11 | 50, 0.17 | 4.4, 4.2 | 2.2, $8.5 \times 10^{-3}$ | 0.5, 9 | 1 | 20 | 40, 80 | 20% ether in hexane |
| | **33** | | TPP | | | | **34** | |
| 12 | 25, 0.114 | 2.9, 2.9 | 3.0, $11 \times 10^{-3}$ | 0.17, 2.9 | 1 | 0.25, 1.5[d] | 18, 72 | 5% ether in pentane |
| | **36** | | TPP | | | | **37** | 7% $C_2H_5OAc$ |
| 13 | 26, 0.068 | 1.7, 1.7 | 0.9, $3.4 \times 10^{-3}$ | 0.2, 3.4 | 1 | 18 | 21, 83 | in hexane |

[a] TPP = triphenylphosphine; TOTP = tri-*o*-tolylphosphine. [b] Solvent is either benzene or benzene-$d_6$. [c] All reactions performed at room temperature unless otherwise noted. [d] First time is at room temperature and second time is at 60 °C. [e] Purification by flash chromatography.

After being stirred for 2 h, the reaction mixture was diluted with 5 mL of ether and filtered through a plug of silica gel and Celite. After concentration *in vacuo*, the crude aldehyde **15** was added to a solution of PPTS (0.04 mmol, 0.01 g) in 4 mL of anhydrous methanol. After being stirred for 1 h at room temperature, the reaction mixture was poured into 20 mL of saturated aqueous sodium bicarbonate and extracted with ether (2 × 20 mL). The organic layers were combined, washed with brine (30 mL), dried over anhydrous potassium carbonate, and concentrated *in vacuo*. Purification by flash column chromatography (20% ether/hexane) provided 89.2 mg (74%) of the title compound. IR ($CDCl_3$): 3300, 2950, 2830, 1735, 1440, 1210, 1070, 1050, 980 $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$): δ 5.57 (m, 2H), 4.63 (d, $J$ = 4 Hz, 1H), 3.69 (s, 6H), 3.22 (s, 6H), 2.78 (d, $J$ = 5.5 Hz, 2H), 2.75 (d, $J$ = 2.5 Hz, 2H), 1.98 (t, $J$ = 2.5 Hz, 1H). $^{13}C$ NMR (50.1 MHz, $CDCl_3$): δ 169.8, 132.0, 127.9, 102.3, 78.5, 71.6, 56.8, 52.6, 52.4, 34.9, 22.8. HRMS calcd for $C_{14}H_{20}O_6$ 284.1260, found 284.1248.

**Preparation of 4,4-Bis(methoxycarbonyl)-2-methylene-1-(2′,2′-dimethoxyethylidene)cyclopentane (3b).** Enyne **2b** (21.0 mg, 0.088 mmol) and acetic acid (2.5 mg, 0.0044 mmol) were added to a solution of complex **1** (2.3 mg, $2.2 \times 10^{-3}$ mmol) and TPP (1.1 mg, $4.4 \times 10^{-3}$ mmol) in 1 mL of $C_6D_6$. After 24 h at room temperature and concentration *in vacuo*, the product was purified by flash column chromatography (7% ether in hexane) to provide 18.0 mg (86% yield) of the title compound. IR ($CDCl_3$): 3000, 2960, 2840, 1735, 1440, 1280, 1250, 1210, 1055, 970 $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$): δ 6.05 (dt, $J$ = 3, 6 Hz, 1H), 5.30 (t, $J$ = 2.5 Hz, 1H), 5.06 (d, $J$ = 6 Hz, 1H), 4.81 (br s, 1H), 3.36–3.10 (m, 4H), 3.09 (s, 3H), 3.11 (s, 3H). $^{13}C$ NMR (50.1 MHz, $CDCl_3$): δ 171.4, 144.4, 140.9, 118.0, 106.0, 101.1, 57.8, 52.7, 52.6, 52.3, 40.7, 37.9. HRMS calcd for $C_{14}H_{20}O_6$ 284.1260, found 284.1228.

**Preparation of Methyl 2-(Methoxycarbonyl-2-propargyl-6,6-diacetoxy-4-hexenoate (2c).** γ-Bromocrotonaldehyde diacetate[17] (3.41 g, 13.57 mmol) in 10 mL of THF was added to a solution of dimethyl sodiopropargylmalonate, made from sodium hydride (0.261 g, 10.8 mmol) and dimethyl propargylmalonate (1.85 g, 10.8 mmol), in 50 mL of THF at −60 °C under nitrogen. The resulting mixture was stirred at −15 to −20 °C for 12 h. Precipitated salt was removed by filtration and the solvent evaporated—cold *in vacuo*. The resulting slurry was subjected to flash chromatography (4:1 hexane/ether) to give 2.32 g (70% yield) of an oil that solidifies in the refrigerator, mp 20–30 °C. IR (neat): 3280, 1775, 1740, 1440, 1377 $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$): δ 7.40 (d, $J$ = 6.1 Hz, 1H), 6.01 (m, 1H), 5.75 (dd, $J$ = 15.5, 6.2 Hz, 1H), 3.30 (s, 6H), 2.99 (dd, $J$ = 7.5, 0.9 Hz, 2H), 2.93 (d, $J$ = 2.7 Hz, 2H), 1.73 (t, $J$ = 2.7 Hz, 1H), 1.59 (s, 6H). HRMS calcd for $C_{14}H_{17}O_6$ ($M^+$ − OAc) 281.1024, found 281.0980.

**Preparation of Diene 3c.** Following the protocol for the preparation of **3a**, enyne **2c** (100 mg, 0.294 mmol), complex **1** (7.6 mg, $7.35 \times 10^{-3}$ mmol), TOTP (4.5 mg, $1.47 \times 10^{-2}$ mmol), and acetic acid (0.84 μL, $1.47 \times 10^{-2}$ mmol) in 4 mL of benzene at room temperature gave 75.1 mg (75% yield) of diene **3c** after flash chromatography (ether/hexane gradient from 1:9 to 1:3). IR (neat): 1760, 1745, 1465, 1380 $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$): δ 7.72 (d, $J$ = 8.3 Hz, 1H), 6.01 (dt, $J$ = 8.4, 2.4 Hz, 1H), 5.30 (bs, 1H), 4.81 (bs, 1H), 3.50 (d, $J$ = 2.4 Hz, 2H), 3.30 (s, 6H), 3.03 (bs, 2H), 1.61 (s, 6H). HRMS calcd for $C_{16}H_{20}O_8$ ($M^+$) 340.1150, found 340.1158.

**Cycloisomerizations.** The protocols for the preparation of **3a–c** were followed for the majority of the remaining cycloisomerizations. The details for each run are summarized in Table 1. Characterization data for the products follow.

**3d.** IR (neat): 3000, 2950, 2840, 1730, 1653, 1437, 1350 $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$): δ 6.20 (t, $J$ = 2.5 Hz, 1H), 5.27 (t, $J$ = 2.5 Hz, 1H), 4.80 (t, $J$ = 1 Hz, 1H), 3.91 (d, $J$ = 2.5 Hz, 2H), 3.39 (s, 3H), 3.20 (s, 6H), 3.02 (t, $J$ = 2.5 Hz, 2H). HRMS calcd for $C_{13}H_{16}O_6$ 268.0947, found 268.0945.

**5a.** IR ($CDCl_3$): 1760 $cm^{-1}$. $^1H$ NMR (270 MHz, $CDCl_3$): δ 5.91 (m, 1H), 5.30 (s, 1H), 4.88 (s, 1H), 4.23 (d, $J$ = 6.3 Hz, 2H), 3.69 (s, 6H), 2.97 (m, 4H), 0.87 (s, 9), 0.04 (s, 6H). $^{13}C$ NMR (125 MHz, $CDCl_3$): δ 172.6, 144.7, 136.2, 121.5, 104.5, 61.4, 57.7, 52.8, 41.0, 37.6, 25.9, −5.2. HRMS calcd for $C_{18}H_{30}O_5Si$ 354.1862, found 354.1868.

**7a.** IR ($CDCl_3$): 3600, 3450, 2950, 1470, 1085 $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$): δ 6.20 (td, $J$ = 6, 3 Hz, 1H), 5.30 (t, $J$ = 2.5 Hz, 1H), 4.82 (bs, 1H), 4.25–4.00 (m, 3H), 3.36 (s, 3H), 2.70 (bs, 1H), 2.40 (dt, $J$ = 15.5, 2.5 Hz, 1H), 2.06 (d, $J$ = 15.5 Hz, 1H), 1.01 (s, 3H), 0.82 (s, 3H). $^{13}C$ NMR (50.1 MHz, $CDCl_3$): δ 147.5, 146.2, 119.3, 104.6, 79.5, 69.2, 57.9, 44.7, 39.6, 25.9, 20.8. HRMS calcd for $C_{11}H_{18}O_2$ 181.1228, found 181.1230.

**7b.** IR ($CDCl_3$): 3600, 3450, 2920, 2855, 1455, 1382, 1100, 1020 $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$): δ 6.07 (t, $J$ = 7.5 Hz, 1H), 5.37 (bs, 1H), 4.82 (bs, 1H), 4.27 (br s, 1H), 4.05 (dd, $J$ = 13, 6 Hz, 1H), 3.78 (dd, $J$ = 13, 7.5 Hz, 1H), 3.00 (s, 3H), 2.50 (dt, $J$ = 16, 2.5 Hz, 1H), 2.49 (s, 1H), 2.09 (bd, $J$ = 16 Hz, 1H), 1.80–1.00 (m, 10H). HRMS calcd for $C_{14}H_{22}O_2$ 222.1620, found 222.1623.

**11a.** IR (neat): 1754, 1600 $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$): δ 5.06 (b, 1H), 4.98 (b, 1H), 4.80 (b, 1H), 4.70 (b, 1H), 3.73 (s, 6H), 2.78 (s, 2H), 2.33 (m, 2H), 2.16 (m, 2H). $^{13}C$ NMR (50 MHz, $CDCl_3$): δ 171.28, 146.38, 144.03, 111.31, 108.98, 55.59, 52.57, 39.42, 31.15, 30.83. HRMS calcd for $C_{12}H_{16}O_4$ 224.1049, found 224.1051.

(17) Schmid, H.; Grob, E. *Helv. Chim. Acta* **1949**, *32*, 77. Spath, E.; Schmid, H. *Chem. Ber.* **1940**, *73*, 243.

**11b.** IR ($CDCl_3$): 3050, 2940, 1440, 1320, 1140, 1070, 670 $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$): $\delta$ 8.07 (d, $J$ = 8 Hz, 4H), 7.62 (m, 6H), 5.29 (s, 1H), 5.17 (s, 1H), 4.78 (b, 2H), 3.09 (b, 2H), 2.60 (m, 2H), 2.43 (m, 2H). HRMS calcd for $C_{14}H_{14}SO_2$ (M – $SO_2Ph$) 247.0793, found 247.0791.

**13.** IR (neat): 3065, 3005, 2840, 2915, 2850, 1655, 1622, 1465, 1455, 1245, 1170, 1120, 830, 765 $cm^{-1}$. $^1H$ NMR (270 MHz, $CDCl_3$): $\delta$ 5.96 (q, $J$ = 7.5 Hz, 1H), 5.11 (bs, 1H), 4.65 (bs, 1H), 2.5–2.3 (m, 1H), 2.3–2.1 (m, 1H), 1.91 (d, $J$ = 7.5 Hz, 3H), 1.85–1.75 (m, 2H), 1.40 (s, 3H), 0.86 (s, 9H), 0.11 (s, 3H), 0.06 (s, 3H). HRMS calcd for $C_{15}H_{28}SiO$ 252.1909, found 252.1910.

**17a.** IR ($CDCl_3$): 3600, 2950, 2920, 1730, 1435, 1272, 1250, 1205, 1160, 1070 $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$): $\delta$ 5.87 (dt, $J$ = 9, 2.5 Hz, 1H), 5.35 (t, $J$ = 2.5 Hz, 1H), 4.90 (bs, 1H), 4.52 (m, 1H), 3.71 (s, 6H), 3.20–2.40 (m, 4H), 1.60 (br, 1H), 1.26 (d, $J$ = 6 Hz, 3H). HRMS calcd for $C_{13}H_{18}O_5$ 254.1154, found 254.1129.

**17b.** IR ($CDCl_3$): 2960, 2940, 2870, 1739, 1442, 1260, 1210, 1170, 1085, 840 $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$): $\delta$ 5.80 (dt, $J$ = 8, 1 Hz, 1H), 5.29 (s, 1H), 4.85 (s, 1H), 4.40 (m, 1H), 3.70 (s, 3H), 3.69 (s, 3H), 3.10–2.90 (m, 4H), 1.19 (d, $J$ = 6.5 Hz, 3H), 0.82 (s, 9H), 0.01 (s, 3H), 0.00 (s, 3H). HRMS calcd for $C_{19}H_{32}O_5Si$ 368.2016, found 368.2026.

**21.** IR ($CDCl_3$): 3600, 2980, 2870, 1430, 1370, 1250, 1040, 860 $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$): $\delta$ 5.80 (dt, $J$ = 9, 2.5 Hz, 1H), 5.29 (s, 1H), 4.85 (s, 1H), 4.55 (m, 1H), 2.60–2.20 (m, 4H), 1.80–1.55 (m, 2H), 1.50 (s, 1H), 1.26 (d, $J$ = 6.2 Hz, 3H). HRMS calcd for $C_9H_{14}O$ 138.1045, found 138.1047.

**30.** IR ($CDCl_3$): 3660, 2950, 1730, 1437, 1250, 1200 $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$): $\delta$ 5.80 (m, 2H), 5.35 (t, $J$ = 1 Hz, 1H), 5.10–4.90 (m, 3H), 4.33 (m, 1H), 3.72 (s, 6H), 3.00 (m, 4H), 2.10 (m, 2H), 1.80–1.60 (m, 2H), 1.61 (d, $J$ = 3 Hz, 1H). HRMS calcd for $C_{16}H_{22}O_5$ 294.1467, found 294.1457.

**34.** IR ($CDCl_3$): 3595, 3060, 2950, 1630, 1470 $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$): $\delta$ 5.95–5.70 (m, 2H), 5.27 (bs, 1H), 5.01 (d, $J$ = 10 Hz, 1H), 4.98 (d, $J$ = 16 Hz, 1H), 4.85 (bs, 1H), 4.49 (m, 1H), 2.60–2.30 (m, 4H), 2.01 (d, $J$ = 8 Hz, 2H), 1.80–1.60 (m, 2H), 1.60 (dd, $J$ = 14, 7.5 Hz, 1H), 1.39 (dd, $J$ = 14, 5 Hz, 1H), 1.30–1.20 (bs, 1H), 0.93 (s, 3H), 0.92 (s, 3H). HRMS calcd for $C_{15}H_{24}O$ 220.1827, found 220.1823.

**37.** IR ($CDCl_3$): 3600, 2950, 2162, 1729, 1435, 1249, 1201, 840 $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$): $\delta$ 5.79 (dt, $J$ = 9, 1.5 Hz, 1H), 5.32 (bs, 1H), 4.90 (bs, 1H), 4.50 (q, $J$ = 6 Hz, 1H), 3.70 (s, 6H), 3.10–2.95 (m, 4H), 2.30 (td, $J$ = 7.5, 5 Hz, 2H), 1.80 (dd, $J$ = 6, 13 Hz, 1H), 1.69 (m, 2H), 0.12 (s, 9H). $^{13}C$ NMR (50.1 MHz, $CDCl_3$): $\delta$ 171.5, 171.4, 144.5, 138.2, 123.4, 106.7, 105.2, 85.2, 69.1, 57.7, 52.8, 40.9, 37.7, 35.6, 16.2, 0.0. HRMS calcd for $C_{19}H_{28}O_5Si$ 364.1706, found 364.1702.

**Preparation of Enynes 4a and b.** Methyl 2-(methoxycarbonyl)-2-propargyl-6-hydroxy-4-hexenoate (4.17 g, 17.4 mmol), DMAP (3.18 g, 26.0 mmol), and *tert*-butyldimethylsilyl chloride (3.27 g, 21.7 mmol) were added in this order to 100 mL of dichloromethane at 0 °C and stirred at this temperature for 30 min before being allowed to reach room temperature. The solution was washed with copper sulfate and sodium chloride before drying ($MgSO_4$) and evaporation. Purification by flash chromatography (1:1 ether/hexane) followed by Kugelrohr distillation (150 °C at 0.1 mmHg) gave 5.238 g (85% yield) of an oil which solidifies around room temperature (mp ca. 25 °C) which is a 3:1 $E/Z$ olefin mixture. IR (neat): 3300, 1765 $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$): $\delta$ 5.62 (m, 2H), 5.40 (m, 1H), 5.17 (m, 1H), 4.21 (d) and 4.06 (d) (total 2H), 3.69 (s) and 3.68 (s) (total 6H), 2.73 (m, 4H), 1.98 (t, 1H), 0.84 (s, 9H), 0.017 (s, 6H). $^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta$ 169.9, 134.8, 134.6, 122.8, 122.4, 78.7, 78.6, 71.4, 63.1, 59.5, 56.8, 56.6, 52.6, 52.5, 34.7, 30.1, 25.7, 25.5, 22.5, –5.31, –5.4. HRMS calcd for $C_{18}H_{30}O_5Si$ 354.1862, found 354.1860.

**Preparation of 1-(1′-Hydroxy-4′-methoxy-2′-butynyl)-1-(3′-propenyl)-cyclohexane (6b).** *n*-Butyllithium (1.44 mL, 2.16 mmol, 1.5 M in hexane) was added to methyl propargyl ether (150 mg, 2.16 mmol) in 4 mL of THF at –78 °C. After the mixture was stirred for 10 min, 1-(3′-propenyl)-1-cyclohexanecarboxaldehyde (0.30 g, 1.97 mmol) was added all at once. The reaction mixture was slowly warmed to 0 °C over 15 min. It was diluted with 20 mL of ether, washed with water (25 mL) and brine (25 mL), dried over anhydrous magnesium sulfate, and concentrated *in vacuo*. Flash column chromatography (15% ether/pentane) provided 230 mg (53% yield) of the title compound. $^1H$ NMR (200 MHz, $CDCl_3$): $\delta$ 5.97–5.70 (m, 1H), 5.15–4.95 (m, 2H), 4.22 (br s, 1H), 4.12 (d, $J$ = 1 Hz, 3H), 3.35 (s, 3H), 2.38 (dd, $J$ = 14.5, 8.5 Hz, 1H), 2.20 (dd, $J$ = 14.5, 7.5 Hz, 1H), 2.14 (bs, 1H), 1.60–1.30 (m, 10H). $^{13}C$ NMR (50.1 MHz, $CDCl_3$): $\delta$ 135.2, 117.4, 86.1, 82.3, 68.6, 59.9, 57.4, 40.9, 37.1, 31.2, 30.0, 26.0, 21.4, 21.2. HRMS calcd for $C_{14}H_{22}O_2$ 222.1620, found 222.1618.

**Preparation of 4,4-Bis(methoxycarbonyl)-8-hydroxy-6(*E*)-nonen-1-yne (16a).** Methylmagnesium bromide (0.27 mL, 0.798 mmol, 3.0 M in ether) was added to a –78 °C solution of aldehyde **15** (0.19 g, 0.798 mmol) in 2 mL of THF. The reaction was warmed to –40 °C over 30 min and to 0 °C over 1 h. Then it was poured into 10 mL of saturated aqueous ammonium chloride and extracted with ether. The combined organic layers were washed with brine, dried over anhydrous magnesium sulfate, and concentrated *in vacuo*, and the resultant product was purified by flash column chromatography (40% ether/hexane) to give 170 mg (85% yield) of the title alcohol. IR ($CHCl_3$): 3600, 3300, 3010, 2950, 1732, 1437, 1290, 1220, 975 $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$): $\delta$ 5.67 (dd, $J$ = 15, 6 Hz, 1H), 5.42 (dt, $J$ = 15, 7.5 Hz, 1H), 4.21 (t, $J$ = 6 Hz, 1H), 3.72 (s, 6H), 2.80–2.69 (m, 4H), 1.96 (t, $J$ = 2.5 Hz, 1H), 1.60 (bs, 1H), 1.21 (d, $J$ = 6 Hz, 3H). $^{13}C$ NMR (50.1 MHz, $CDCl_3$): $\delta$ 170.0, 139.8, 122.5, 78.5, 71.5, 67.9, 52.6, 34.7, 23.1, 22.5. HRMS calcd for $C_{12}H_{15}O_5$ (M – $CH_3$) 239.0919, found 239.0924.

**Preparation of 4,4-Bis(methoxycarbonyl)-8-(*tert*-butyldimethylsiloxy)-6(*E*)-nonen-1-yne (16b).** Standard silylation of alcohol **16a** (98 mg, 0.38 mmol) with *tert*-butyldimethylsilyl triflate (150 mg, 0.58 mmol) and 2,6-lutidine (82 mg, 0.77 mmol) in 2 mL of dichloromethane gave, after 30 min at 0 °C, standard workup, and flash chromatography (5% ether in pentane), 140 mg (97% yield) of silyl ether **16b**. IR ($CDCl_3$): 3307, 2960, 2940, 2865, 1730, 1469, 1445, 1299, 1260, 1220, 1155, 1080, 840 $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$): $\delta$ 5.60 (dd, $J$ = 15, 5.3 Hz, 1H), 5.34 (dtd, $J$ = 7.5, 15, 1.3 Hz, 1H), 4.20 (m, 1H), 3.72 (s, 6H), 2.70–2.60 (m, 4H), 1.99 (t, $J$ = 2.6 Hz, 1H), 1.14 (d, $J$ = 6.4 Hz, 3H), 0.83 (s, 9H), 0.02 (s, 3H), 0.01 (s, 3H). HRMS calcd for $C_{19}H_{31}O_5Si$ (M – H): 367.1941, found 367.1955.

**Preparation of Diels–Alder Adduct 18.** 1,3-Diene **17a** (0.035 g, 0.139 mmol) and *N*-phenylmaleimide (0.024 g, 0.139 mmol) in 1 mL of benzene at room temperature were stirred for 48 h. The reaction mixture was concentrated *in vacuo* and submitted to flash column chromatography (25% ethyl acetate in hexane) to afford 50 mg (85% yield) of the adduct as a 10:1 ratio of diastereomers. IR ($CDCl_3$): 3290, 2950, 1732, 1673, 1600, 1541, 1499, 1440, 1267, 1200, 175 $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$): $\delta$ 9.69 (bs, 1H), 7.59 (t, $J$ = 7.5 Hz, 2H), 7.32 (t, $J$ = 7.5 Hz, 2H), 7.10 (t, $J$ = 7.5 Hz, 1H), 4.65 (q, $J$ = 6.6 Hz, 1H), 3.77 (s, 3H), 3.75 (s, 3H), 3.60 (dd, $J$ = 7, 3 Hz, 1H), 3.13 (bd, $J$ = 16 Hz, 1H), 3.03 (bs, 2H), 2.90–2.86 (m, 3H), 2.41 (bs, 2H), 1.45 (d, $J$ = 6.6 Hz, 3H). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 178.1, 172.1, 171.9, 170.8, 138.3, 135.9, 129.7, 129.0, 124.4, 120.3, 78.5, 58.2, 53.2, 44.3, 43.8, 43.4, 40.8, 39.8, 25.9, 20.0. HRMS calcd for $C_{23}H_{25}NO_7$ 427.1631, found 427.1622.

**Preparation of Diels–Alder Adduct 19.** Following the above procedure, diene **17b** (62 mg, 0.169 mmol) and *N*-phenylmaleimide (29 mg, 0.169 mmol) gave 68 mg (75% yield) of adduct as an 8:1 mixture of diastereomers. IR ($CDCl_3$): 2950, 2925, 2855, 1730, 1710, 1499, 1382, 1260, 1195, 832 $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$): $\delta$ 7.6–7.19 (m, 5H), 4.49 (m, 1H), 3.69 (s, 3H), 3.59 (s, 3H), 3.55 (dd, $J$ = 9.5, 6.0 Hz, 1H), 3.27 (td, $J$ = 9.5, 3.0 Hz, 1H), 3.20–3.00 (m, 4H), 2.70–2.30 (m, 3H), 1.12 (d, $J$ = 5.5 Hz, 3H), 0.87 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H). $^{13}C$ NMR (50.1 MHz, $CDCl_3$): $\delta$ 179.0, 176.9, 172.4, 172.0, 133.9, 133.6, 132.0, 129.0, 128.4, 126.5, 67.4, 58.5, 52.8, 45.1, 43.4, 43.0, 41.9, 39.9, 25.9, 24.9, 23.2, 18.0, –4.5, –4.7. HRMS calcd for $C_{29}H_{39}NO_7Si$ 541.2496, found 541.2496.

**Conversion of Adduct 19 into 18.** A solution of silyl ether **19** (15 mg, 0.028 mmol) in 0.03 mL of acetic acid, 0.01 mL of THF, and 0.01 mL of water was stirred for 18 h at room temperature. After 20 $\mu$L of concentrated aqueous hydrochloric acid was added and the mixture was stirred for 30 min at room temperature, the reaction was poured into water and extracted with ether to give, after chromatography (30% ethyl acetate in hexane), 11.1 mg (93% yield) of **18**, identical with the previously prepared compound.

**Preparation of 2-Hydroxy-3(*E*)-nonen-8-yne (20).** Ethylmagnesium bromide (7.95 mL, 21.7 mmol, 2.73 M in THF) was added to a 0 °C solution of 1,6-heptadiyne (2.0 g, 21.7 mmol) in 40 mL of THF. After 1 h, acetaldehyde (0.95 g, 21.7 mmol) was rapidly added. The reaction was stirred a further 15 min at 0 °C and poured into 60 mL of water. The product was extracted with ether, and the organic layers were washed with water and brine, dried over anhydrous magnesium sulfate, and concentrated *in vacuo*. The resulting crude oil was purified by flash chromatography (20% ether in pentane) to provide 1.27 g (43% yield) of 2-hydroxy-3,8-nonadiyne. IR ($CDCl_3$): 3600, 3305, 2940, 2013, 1457, 1439, 1380, 1260, 1050, 1080, 635 $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$):

δ 4.50 (m, 1H), 2.40–2.20 (qd, J = 7, 2 Hz, 4H), 1.97 (t, J = 2.5 Hz, 1H), 1.80–1.60 (m, 3H), 1.41 (d, J = 7.5 Hz, 3H). HRMS calcd for $C_9H_{11}O$ ($M^+$ – H) 135.0810, found 135.0809.

2-Hydroxy-3,8-nonadiyne (1.10 g, 8.08 mmol) was added to LAH (0.92 g, 24.2 mmol) in 16 mL of THF at 0 °C. The reaction mixture was warmed to room temperature over 15 min and stirred for 18 h. It was cooled to 0 °C and quenched by the dropwise addition of 0.94 mL of water, 0.94 mL of 10% aqueous sodium bicarbonate, and 2.7 mL of water. Anhydrous magnesium sulfate (~1 g) was added to the white slurry generated, and the reaction mixture was diluted with ether and filtered through a pad of Celite. After concentration *in vacuo*, flash chromatography (15% ether in pentane) afforded 830 mg (74% yield) of the 1,6 enyne **20**. IR ($CDCl_3$): 3600, 3300, 2980, 2940, 2120, 1457, 1440, 1380, 1257, 1050, 975 $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$): δ 5.68–5.47 (m, 2H), 4.26 (m, 1H), 2.25–2.02 (m, 4H), 1.93 (t, J = 2.6 Hz, 1H), 1.70–1.30 (m, 3H), 1.23 (d, J = 6.2 Hz, 3H). $^{13}C$ NMR (50.1 MHz, $CDCl_3$): δ 135.2, 129.3, 84.1, 68.6, 68.4, 30.9, 27.8, 23.4, 17.7. HRMS calcd for $C_9H_{13}O$ ($M^+$ – H) 137.0966, found 137.0966.

**Diels–Alder Reactions of Diene 21. With *N*-phenylmalelmide.** A solution of diene **21** (13.2 mg, 0.0956 mmol) and *N*-phenylmaleimide (16 mg, 0.096 mmol) in 2 mL of benzene was stirred for 48 h at room temperature. Concentration *in vacuo* and flash chromatography (15% ethyl acetate in hexane) gave 29.4 mg (99% yield) of adduct **23** as a 10:1 diastereomeric mixture. IR ($CDCl_3$): 3300–3250, 2920, 2842, 1740, 1670, 1600, 1550, 1495, 1442, 1323, 1187 $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$): δ 9.77 (bs, 1H), 7.57 (m, 2H), 7.30 (m, 2H), 7.07 (t, J = 7 Hz, 1H), 4.62 (q, J = 6.5 Hz, 1H), 3.56 (dd, J = 6.5, 3 Hz, 1H), 2.00–2.70 (m, 2H), 2.60–2.10 (m, 6H), 2.00–1.80 (m, 2H), 1.43 (d, J = 6.5 Hz, 3H). $^{13}C$ NMR (50.1 MHz, $CDCl_3$): δ 178.4, 171.3, 138.8, 138.3, 131.8, 128.9, 124.1, 120.1, 78.7, 44.9, 43.9, 40.1, 36.2, 32.8, 26.6, 22.1, 19.8. HRMS calcd for $C_{19}H_{21}NO_3$ 311.1521, found 311.1529.

**With Acrolein.** A solution of diene **21** (29 mg, 0.215 mmol) and acrolein (17 mg, 0.30 mmol) was stirred for 24 h at room temperature. An additional portion of acrolein (17 mg, 0.30 mmol) was added and the resultant mixture stirred for an additional 24 h at room temperature. Concentration *in vacuo* and flash chromatography (10% ether in pentane) gave 30 mg (73% yield) of adduct **24**. IR ($CDCl_3$): 3590, 2920, 2840, 1450, 1375, 1240, 1080, 1008, 978 $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$): δ 5.16 (d, J = 3 Hz, 1H), 3.88 (dq, J = 8, 6.2 Hz, 1H), 2.87 (d, J = 3 Hz, 1H), 2.60–2.40 (bt, J = 6 Hz, 1H), 2.40–2.20 (m, 4H), 2.05–1.65 (m, 6H), 1.40–1.30 (m, 1H), 1.38 (d, J = 6.2 Hz, 3H). $^{13}C$ NMR (50.1 MHz, $CDCl_3$): δ 135.7, 132.2, 102.8, 81.2, 46.6, 44.9, 35.6, 34.9, 24.6, 23.6, 23.2, 21.9. HRMS calcd for $C_{12}H_{18}O_2$ 194.1307, found 194.1307.

**With Methyl Acrylate.** A solution of diene **21** (32 mg, 0.23 mmol) and methyl acrylate (22 mg, 0.253 mmol) in 1 mL of benzene was stirred for 24 h at room temperature. An additional 9 mg (0.104 mmol) of methyl acrylate was added and the mixture heated at 60 °C for 24 h. Concentration *in vacuo* and flash chromatography (5% ether in hexane) gave 35.6 mg (81% yield) of adduct **25**. IR ($CDCl_3$): 2950, 2920, 2840, 1760, 1445, 1382, 1360, 1200, 1165, 955 $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$): δ 4.35 (qd, J = 6.4, 4.4 Hz, 1H), 2.87 (m, 1H), 2.60 (m, 1H), 2.50–1.70 (m, 10H), 1.40 (d, J = 6.5 Hz, 3H). $^{13}C$ NMR (50.1 MHz, $CDCl_3$): δ 178.5, 138.5, 130.6, 79.1, 43.4, 38.8, 36.1, 33.8, 22.9, 21.8, 21.4, 20.8. HRMS calcd for $C_{12}H_{16}O_2$ 192.1150, found 192.1139.

**Preparation of *N*-Benzyl-*N*-propargyl-4-(*tert*-butyldimethylsiloxy)-2(*E*)-pentenamine (26b).** A solution of benzylamine (17.9 g, 0.17 mmol) and progargyl bromide (8.24 mL, 55.8 mmol, 80% in toluene) in 120 mL of ether was stirred for 48 h at room temperature. The reaction was poured into aqueous saturated sodium bicarbonate and extracted with 1:1 dichloromethane/ether. The organic layers were combined, washed with water (75 mL) and brine (150 mL), dried over anhydrous magnesium sulfate, and concentrated *in vacuo*. Purification by flash chromatography (10% ether in pentane) provided 4.05 g (39% yield) of benzyldipropargylamine. IR ($CDCl_3$): 3300, 3010, 2920, 2820, 1645, 1495, 1452, 1110 $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$): δ 7.50–7.20 (m, 5H), 3.68 (s, 2H), 3.41 (d, J = 3 Hz, 4H), 2.23 (t, J = 3 Hz, 1H). HRMS calcd for $C_{13}H_{13}N$ 183.1048, found 183.1047.

Ethylmagnesium bromide (2.0 mL, 5.46 mmol, 2.73 M in THF) was added to a 0 °C stirred solution of *N*-benzyl-*N*,*N*-dipropargylamine (1.00 g, 5.46 mmol) in 10 mL of THF. After 1 h at 0 °C, acetaldehyde (240 mg, 5.46 mmol) was added all at once. After 10 min, the reaction was poured into water and extracted with ether. The combined organic layers were washed with water and brine, dried over anhydrous magnesium sulfate, and concentrated *in vacuo*. Flash column chromatographic purification (15% ether in pentane) provided 350 mg of the desired alcohol (28% yield) and 500 mg of recovered starting material (56% yield of desired material based on recovered starting material). IR ($CDCl_3$): 3600, 3300, 2980, 2920, 1170 $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$): δ 7.40–7.20 (m, 5H), 4.57 (m, 1H), 3.66 (s, 2H), 3.40 (d, J = 2.6 Hz, 2H), 3.38 (d, J = 1.8 Hz, 2H), 2.25 (t, J = 2.6 Hz, 1H), 1.75 (s, 1H), 1.44 (d, J = 6.6 Hz, 3H). HRMS calcd for $C_{15}H_{17}NO$ 227.1313, found 226.1316.

*N*-Benzyl-*N*-propargyl-4-hydroxy-2-pentynamine (350 mg, 1.54 mmol) in 1 mL of THF was added via cannula to a suspension of LAH (180 mg, 4.62 mmol) in 3 mL of THF at room temperature. After 20 h at room temperature, the reaction mixture was cooled to 0 °C and the reaction quenched by the slow addition of water (0.18 mL), 10% aqueous sodium hydroxide (0.18 mL), and water (0.54 mL). Anhydrous magnesium sulfate (~0.5 g) was added, and the resulting slurry was diluted with ether (15 mL) and filtered through a pad of Celite. After concentration *in vacuo*, flash column chromatography (25% ether in pentane) afforded 274 mg (86% yield) of the enyne **26a**. IR ($CDCl_3$): 3600, 3300, 2970, 2922, 2820, 1450, 1372, 1255, 975 $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$): δ 7.41–7.20 (m, 5H), 5.90–5.60 (m, 2H), 4.35 (m, 1H), 3.65 (s, 2H), 3.33 (d, J = 2.2 Hz, 2H), 3.18 (d, J = 5.3 Hz, 2H), 2.27 (t, J = 2.2 Hz, 1H), 1.60–1.50 (m, 1H), 1.29 (d, J = 6.2 Hz, 3H). HRMS calcd for $C_{15}H_{19}NO$ 229.1467, found 229.1466.

*tert*-Butyldimethylsilyl chloride (0.20 g, 1.32 mmol) was added to a mixture of alcohol **26a** (0.27 g, 1.20 mmol) and imidazole (0.18 g, 2.64 mmol) in methylene chloride (2.5 mL) at 0 °C. After 30 min, the reaction was poured into saturated aqueous sodium bicarbonate and extracted with ether. The combined organic layers were washed with brine, dried over anhydrous magnesium sulfate, and concentrated *in vacuo*. Purification by flash column chromatography (5% ether in pentane afforded 310 mg (76% yield) of the title enyne **26b**. IR ($CDCl_3$): 3300, 2950, 2920, 2860, 1470, 1360, 1250, 900, 725 $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$): δ 7.40–7.20 (m, 5H), 5.80–5.60 (m, 2H), 4.25 (m, 1H), 3.60 (s, 2H), 3.27 (d, J = 2.2 Hz, 2H), 3.12 (d, J = 5.7 Hz, 2H), 2.21 (t, J = 2.2 Hz, 1H), 1.18 (d, J = 6.4 Hz, 3H), 0.87 (s, 9H), 0.04 (s, 6H). $^{13}C$ NMR (50.1 MHz, $CDCl_3$): δ 138.6, 129.1, 128.2, 127.0, 125.4, 78.6, 73.1, 68.9, 57.1, 55.2, 41.3, 25.9, 24.6, 18.3, –4.6, –4.7. HRMS calcd for $C_{21}H_{33}NOSi$ 343.2331, found 343.2333.

***N*-Benzyl-3-methylene-4-(2-(*tert*-butyldimethylsiloxy)-1(*E*)-propylidene)-pyrrolidine (27).** Complex **1** (1.8 mg, 0.0018 mmol) was added to a solution of triphenylphosphine (0.96 mg, 0.0037 mmol) in 1 mL of $C_6D_6$. After 2 min at room temperature, the above enyne **26b** (25 mg, 0.073 mmol) and acetic acid (4.6 mg, 0.077 mmol) were added. The reaction was allowed to stand for 24 h at room temperature, at which point 5 mL of saturated aqueous potassium carbonate solution was added. After 20 min, the product was extracted with ether. The organic layers were washed with brine, dried over anhydrous magnesium sulfate, and concentrated *in vacuo*. The crude oil was purified by flash chromatography (5% ether in pentane) to provide 13 mg (52% yield) of the title 1,3-diene **27**. IR ($CDCl_3$): 2950, 2930, 2860, 1660, 1620, 1450, 1240, 1255, 1080, 835 $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$): δ 7.40–7.20 (m, 5H), 5.79 (dt, J = 9, 1 Hz, 1H), 5.27 (t, J = 1 Hz, 1H), 4.81 (s, 1H), 4.35 (dq, J = 9, 7 Hz, 1H), 3.64 (d, J = 4.5 Hz, 2H), 3.40–3.20 (m, 4H), 1.19 (d, J = 7 Hz, 3H), 0.86 (s, 9H), 0.02 (s, 3H), 0.00 (s, 3H). $^{13}C$ NMR (50.1 MHz, $CDCl_3$): δ 145.1, 138.6, 134.6, 128.8, 128.3, 127.1, 124.7, 101.9, 67.3, 60.6, 59.6, 56.6, 25.9, 24.2, 18.2, –4.4, –4.7. HRMS calcd for $C_{21}H_{33}NOSi$ 343.2331, found 343.2324.

**Preparation of Diels–Alder Adduct 28.** A solution of diene **27** (37.5 mg, 0.109 mmol) and *N*-phenylmaleimide (19 mg, 0.109 mmol) in 0.5 mL of benzene was stirred for 48 h at room temperature. Concentration *in vacuo* and flash chromatography (25% ethyl acetate in hexane) gave 46 mg (84% yield) of adduct **28**. IR ($CDCl_3$): 2950, 2920, 2850, 2797, 1770, 1705, 1500, 1500, 1450, 1380, 1250, 1195, 1115, 1092, 1000, 830 $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$): δ 7.45–7.10 (m, 10H), 4.39 (quintet, J = 6.2 Hz, 1H), 3.74 (s, 2H), 3.60–3.40 (m, 4H), 3.33–3.22 (m, 2H), 2.75–2.65 (t, J = 7 Hz, 1H), 2.60 (dd, J = 18, 3 Hz, 1H), 2.45 (dd, J = 18, 9.5 Hz, 1H), 1.02 (d, J = 6.2 Hz, 3H), 0.82 (s, 9H), 0.03 (s, 3H), 0.02 (s, 3H). $^{13}C$ NMR (50.1 MHz, $CDCl_3$): δ 178.9, 176.9, 139.4, 133.9, 133.7, 132.1, 129.1, 128.6, 128.5, 128.3, 127.0, 126.5, 67.4, 62.1, 62.0, 60.4, 44.0, 41.6, 39.8, 25.9, 23.2, 22.6, 18.0, –4.5, –4.7. HRMS calcd for $C_{31}H_{40}N_2O_3Si$ 516.2808, found 516.2765.

**Preparation of 9,9-Dicarbomethoxy-1(*E*),6(*E*)-dodecadien-11-yn-5-ol (29).** 4-Bromo-1-butene (27 mg, 0.19 mmol) was added to a mixture of magnesium metal (0.07 g, 2.74 mmol) and a crystal of iodine in 4 mL of ether at room temperature. The reaction was heated to reflux with a heat gun for 2 min. Once the reaction had initiated (as evidenced by the disappearance of the orange iodine color), the remaining bromide (280 mg, 2.07 mmol) was added dropwise. After the addition was

complete, the reaction was stirred for a further 30 min at room temperature. The Grignard reagent prepared above was transferred via cannula to a −78 °C solution of aldehyde **15** (380 mg, 1.60 mmol) in 2.0 mL of THF. The reaction was stirred for 15 min at −78 °C and then warmed to 0 °C over 20 min. It was poured into 20 mL of water and diluted with 50 mL of ether. The organic layer was washed with saturated aqueous ammonium chloride, water, and brine and dried over anhydrous magnesium sulfate. After concentration *in vacuo*, the crude material was purified by flash chromatography (25% ethyl acetate in hexane) to provide 300 mg (64% yield) of the title compound **29**. IR ($CDCl_3$): 3600, 3300, 2950, 1732, 1437, 1290, 1210, 978 $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$): δ 5.80 (ddt, $J$ = 17, 10, 6 Hz, 1H), 5.62 (dd, $J$ = 15, 6 Hz, 1H), 5.46 (dt, $J$ = 15, 8 Hz, 1H), 5.03 (d, $J$ = 17 Hz, 1H), 4.95 (d, $J$ = 10 Hz, 1H), 3.72 (s, 6H), 2.80–2.70 (m, 4H), 2.10 (m, 2H), 2.01 (t, $J$ = 2.6 Hz, 1H), 1.65–1.50 (m, 2H), 1.46 (d, $J$ = 4.4 Hz, 1H). $^{13}C$ NMR (50.1 MHz, $CDCl_3$): δ 169.8, 138.4, 138.0, 123.6, 114.5, 78.5, 71.4, 56.9, 52.5, 36.1, 34.8, 29.3, 22.6. HRMS calcd for $C_{16}H_{20}O_4$ ($M^+ - H_2O$) 276.1360, found 276.1322.

**Intramolecular Diels–Alder Reaction of 30.** A solution of triene **30** (39 mg, 0.13 mmol), BSA (79 mg, 0.39 mmol), and BHT (2.7 mg, 0.013 mmol) in 1.0 mL of toluene was heated at 172 °C in a screw-cap pressure ampule for 3 days. The reaction was filtered through a pipet of silica gel and concentrated *in vacuo*. Flash chromatography (5% ether in hexane) afforded 40 mg of the silylated Diels–Alder adduct (84% yield). This crude product was dissolved in 1 mL of THF to which was added 0.26 mL (0.26 mmol, 1 M in THF) of tetra-*n*-butylammonium fluoroborate (TBAF) at 0 °C. After 15 min at 0 °C and 3 h at room temperature, the reaction was poured into 10 mL of water and extracted with ether. The organic layer was washed with brine, dried over anhydrous magnesium sulfate, and concentrated *in vacuo*. Flash chromatography (25% ethyl acetate in pentane) afforded 9.1 mg (23% yield) of one isomer of the desired Diels–Alder adduct and 16.0 mg (41% yield) of a 3:1 ratio of the above isomer and a diastereomer (overall a 5.2:1 ratio of isomers). IR ($CDCl_3$): 3600, 2960, 2935, 1730, 1440, 1270, 1201, 1072, 1080 $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$): δ 4.05 (m, 1H), 3.70 (s, 6H), 3.12–2.85 (m, 4H), 2.40–2.15 (m, 2H), 1.85–1.78 (m, 4H), 1.60–1.20 (m, 4H). $^{13}C$ NMR (125 MHz, $CDCl_3$): δ 172.9, 172.8, 132.7, 131.7, 77.4, 76.9, 57.8, 52.8, 48.6, 43.9, 42.4, 35.5, 34.0, 27.2, 26.2, 22.9. HRMS calcd for $C_{16}H_{22}O_5$ 294.1467, found 294.1468.

**Preparation of 1-Oxo-7,7-bis(methoxycarbonyl)-2,3,3a(*S**),4,5,6,8,-8b(*S**)-octahydrocyclopenta[*e*]indene (32).** Oxalyl chloride (11.3 mg, 0.09 mmol) was added to a −78 °C stirred solution of alcohol **31** (11 mg, 0.037 mmol) and DMSO (21.0 mg, 0.164 mmol) in 0.1 mL of dichloromethane. After 15 min at −78 °C, triethylamine (0.038 g, 0.374 mmol) was rapidly added and the reaction mixture was allowed to warm to room temperature over 20 min. It was diluted with 5 mL of ether and poured into 10 mL of saturated aqueous sodium bicarbonate. The organic layer was separated, washed with brine, dried over anhydrous sodium sulfate, and concentrated *in vacuo*. The product was purified by flash chromatography (15% ether in pentane) to afford 9.0 mg (83% yield) of ketone **32**. IR ($CDCl_3$): 2960, 2940, 1730, 1440, 1275, 1170 $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$): δ 3.72 (s, 6H), 3.60–2.80 (m, 4H), 2.80–2.60 (m, 1H), 2.60–2.40 (m, 1H), 2.30–2.15 (m, 2H), 2.00–1.65 (m, 6H). HRMS calcd for $C_{16}H_{20}O_5$ 292.1311, found 292.1316.

**Preparation of 4,4-Dimethyl-6-hydroxy-1(*E*),7(*E*)-tridecadien-12-yne (33).** Ethylmagnesium bromide (3.81 mL, 10.4 mmol, 2.73 M in THF) was added to 1,6-heptadiyne (1.0 g, 10.41 mmol) in 20 mL of THF at 0 °C. The reaction was stirred for 50 min at 0 °C (a precipitate formed), at which point 3,3-dimethyl-5-hexen-1-al (2.05 g, 10.41 mmol, 64% solution in *p*-cymene) in 10 mL of THF was added via cannula. The reaction mixture was stirred for 15 min at 0 °C, diluted with 70 mL of ether, and poured into 10% aqueous hydrochloric acid. The organic layer was washed with water and brine, dried over anhydrous magnesium sulfate, and concentrated *in vacuo*. Purification by flash chromatography (7% ethyl acetate in hexane) afforded 1.21 g (53% yield) of 4,4-dimethyl-6-hydroxy-1-tridecen-7,12-diyne. IR ($CDCl_3$): 3600, 3300, 2950, 1470, 1370, 1000 $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$): δ 4.96–4.69 (ddt, $J$ = 17.5, 1, 7.5 Hz, 1H), 5.02 (d, $J$ = 11 Hz, 1H), 4.97 (d, $J$ = 17.5 Hz, 1H), 4.42 (m, 1H), 2.40–2.20 (m, 4H), 2.01 (d, $J$ = 7.5 Hz, 1H), 1.96 (t, $J$ = 3 Hz, 1H), 1.80–1.50 (m, 5H), 0.97 (s, 6H). $^{13}C$ NMR (50.1 MHz, $CDCl_3$): δ 135.5, 116.9, 84.0, 83.4, 68.8, 60.7, 50.4, 47.2, 32.8, 27.5, 25.9, 18.1, 17.8, 17.6, −4.1, −4.7. HRMS calcd for $C_{21}H_{35}OSi$ ($M^+$ − 1) 331.2457, found 331.2469.

The above diyne (1.21 g, 5.55 mmol) in 2 mL of THF was added dropwise to a slurry of LAH (0.70 g, 18.4 mmol) in 8 mL of THF at 0 °C. The reaction mixture was warmed to room temperature over 15 min and stirred for 18 h. The reaction mixture was cooled to 0 °C, and the reaction was quenched by the dropwise addition of water (0.70 mL), 10% aqueous sodium hydroxide, and water (2.1 mL). The resulting slurry was filtered through a plug of Celite and concentrated *in vacuo*. Purification by flash chromatography (5% ether in pentane) afforded 0.98 g (81% yield) of the title compound. IR ($CDCl_3$): 3600, 3302, 3090, 2960, 2880, 1640, 1470, 1440, 1390, 1370, 1000, 970 $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$): δ 5.95–5.70 (ddt, $J$ = 16.5, 11, 8 Hz, 1H), 5.65–5.40 (m, 2H), 5.02 (bd, $J$ = 11 Hz, 1H), 4.98 (bd, $J$ = 16.5 Hz, 1H), 4.22 (q, $J$ = 6.5 Hz, 1H), 2.25–2.10 (m, 4H), 2.02 (d, $J$ = 8 Hz, 2H), 1.98 (t, $J$ = 3 Hz, 1H), 1.60–1.40 (m, 4H), 1.40 (br, 1H), 0.91 (s, 3H), 0.89 (s, 3H). $^{13}C$ NMR (50.1 MHz, $CDCl_3$): δ 135.7, 135.5, 129.3, 116.9, 84.1, 70.3, 68.5, 48.7, 47.2, 32.9, 30.9, 27.8, 27.6, 17.8. HRMS calcd for $C_{15}H_{22}$ ($M^+ - H_2O$) 202.1721, found 202.1728.

**Cycloisomerization of Triene 34.** A solution of 1,3-diene **34** (17.5 mg, 0.08 mmol), BSA (49 mg, 0.24 mmol), and BHT (1.8 mg, 0.008 mmol) in 2 mL of toluene was heated at 180 °C in a screw-cap pressure ampule for 6 h. After concentration *in vacuo*, the reaction was submitted to flash chromatography (pentane) to provide 17.3 mg (74% yield) of the silylated intramolecular Diels–Alder adduct. $^1H$ NMR (200 MHz, $CDCl_3$): δ 3.59 (td, $J$ = 10.5, 4.5 Hz, 1H), 2.50–2.30 (m, 2H), 2.20–1.00 (m, 14H), 0.89 (s, 6H), 0.05 (s, 9H).

The silyl ether (0.17 mg, 0.059 mmol) in 1 mL of THF at 0 °C was treated with TBAF (0.12 mL, 1 M in THF, 0.12 mmol). After 20 min, the reaction mixture was diluted with ether and poured into water. The organic layer was washed with brine, dried over anhydrous magnesium sulfate, and concentrated *in vacuo*. Flash chromatography (7% ether in hexane) provided 11 mg (85% yield) of the Diels–Alder product **35**. IR ($CDCl_3$): 3600, 2950, 2910, 2860, 1602, 1470, 1010 $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$): δ 3.55 (td, $J$ = 10, 4.6 Hz, 1H), 2.69–2.40 (m, 2H), 2.30–1.90 (m, 3H), 1.83 (q, $J$ = 7.3 Hz, 2H), 1.72 (ddd, $J$ = 13, 4.6, 2.4 Hz, 1H), 1.65–1.00 (m, 9H), 0.95 (s, 3H), 0.93 (s, 3H). $^{13}C$ NMR (125 MHz, $CDCl_3$): δ 136.5, 135.1, 70.9, 50.6, 49.8, 46.0, 35.7, 35.4, 32.9, 32.1, 30.7, 26.6, 25.9, 22.4. HRMS calcd for $C_{15}H_{24}O$ 220.1827, found 220.1827.

**Preparation of 9,9-Dicarbomethoxy-5-hydroxy-1-(trimethylsilyl)dodec-6(*E*)-en-1,11-diyne (36).** (4-(Trimethylsilyl)-3-butynyl)magnesium chloride (9.33 mL, 0.42 mmol, 0.045 M in THF) was added to a −78 °C solution of enal **15** (100 mg, 0.42 mmol) in 1 mL of THF. After 15 min, the reaction mixture was warmed to −40 °C over 30 min then to 0 °C over an additional 30 min. It was poured into 10 mL of water and extracted with ether. The organic layers were combined, washed with water and brine, dried over anhydrous magnesium sulfate, and concentrated *in vacuo*. Purification by flash chromatography (15% ether in hexane) afforded 88 mg (58% yield) of the desired alcohol **36**. IR ($CDCl_3$): 3600, 3520, 3302, 2955, 2175, 1730, 1440, 1250, 850 $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$): δ 5.60 (dd, $J$ = 15, 6 Hz), 5.51 (dt, $J$ = 15, 7 Hz, 1H), 4.18 (m, 1H), 3.72 (s, 6H), 2.80–2.70 (m, 4H), 2.28 (td, $J$ = 7.5, 3.3 Hz, 2H), 2.00 (t, $J$ = 2.6 Hz, 1H), 1.79 (bs, 1H), 1.65 (q, $J$ = 7.5 Hz, 2H), 0.12 (s, 9H). HRMS calcd for $C_{17}H_{25}O_3Si$ ($M^+ - CO_2CH_3$) 305.1573, found 305.1560.

**Intramolecular Diels–Alder Reaction of 37.** A solution prepared by adding diene **37** (20 mg, 0.055 mmol) to BSA (34 mg, 0.165 mmol) and BHT (1.8 mg, 0.0055 mmol) in 1.0 mL of toluene was heated in a screw cap pressure ampule at 140 °C for 18 h and at 180 °C for 8 h. The reaction mixture was concentrated *in vacuo* and purified by flash chromatography (pentane) to afford 12 mg (52% yield) of the cycloadduct. IR ($CDCl_3$): 2950, 1740, 1425, 1250, 805 $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$): δ 3.80–3.62 (m, 1H), 3.38 (s, 3H), 3.30 (s, 3H), 3.25–3.20 (m, 1H), 2.80–2.10 (m, 5H), 1.90–1.20 (m, 5H), 0.11 (s, 9H), 0.10 (s, 9H). HRMS calcd for $C_{16}H_{19}O_2Si$ ($M^+ - C_5H_{18}O_3Si$) 271.1154, found 271.1163.

**Preparation of *N*-Benzyl-*N*-propargyl-*N*-(4-(*tert*-butyldimethylsiloxy)-2(*E*),7-octadienyl)amine (39).** Oxallyl chloride (2.02 g, 10.92 mmol) was added to a −78 °C, stirred slurry of 4-penten-1-ol (0.78 g, 9.1 mmol) and DMSO (1.56 g, 20.0 mmol) in 20 mL of THF. After being stirred for 5 min at −78 °C, the reaction mixture was warmed to −35 °C for 15 min. Then triethylamine (4.6 g, 45.5 mmol) was added at −35 °C, and the reaction mixture was allowed to warm to room temperature.

Ethylmagnesium bromide (3.33 mL, 9.1 mmol, 2.73 M in THF) was added dropwise to *N*-benzyl-*N*,*N*-dipropargylamine (1.67 g, 9.1 mmol) in 20 mL of THF at 0 °C. After this solution was stirred for 1 h, the reaction mixture formed above was added via a cannula. The reaction mixture was warmed to room temperature, stirred for 15 min, and then poured into 100 mL of water and extracted with ether. The combined organic layers were washed with water and brine, dried over anhydrous magnesium sulfate, and concentrated *in vacuo*. Purification by flash

chromatography (20% ethyl acetate in hexane) afforded 240 mg (10% yield) of *N*-benzyl-*N*-propargyl-*N*-(4-hydroxy-7-octen-2-ynyl)amine. IR ($CDCl_3$): 3550, 3400, 3300, 3080, 3010, 2910, 2810, 1640, 1492, 1450, 1360, 1325, 1120, 1000, 640 $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$): $\delta$ 7.40–7.20 (m, 5H), 5.82 (ddt, $J$ = 18, 10, 6 Hz, 1H), 5.05 (d, $J$ = 18 Hz, 1H), 4.96 (d, $J$ = 10 Hz, 1H), 4.40 (m, 1H), 3.65 (s, 2H), 3.41 (d, $J$ = 2 Hz, 2H), 3.39 (d, $J$ = 3 Hz, 2H), 2.21 (t, $J$ = 2 Hz, 1H), 2.20 (m, 2H), 1.80 (m, 2H), 1.75 (d, $J$ = 5.5 Hz, 1H). HRMS calcd for $C_{18}H_{22}NO$ ($M^+$ – H) 268.1701, found 268.1697.

The above diyne (240 mg, 0.89 mmol) was added to a slurry of LAH (100 mg, 2.67 mmol) in 2 mL of THF at 0 °C. The reaction mixture was warmed to room temperature and stirred for 20 h. At 0 °C, the reaction was quenched by the slow addition of 0.13 mL of water, 0.13 mL of 10% sodium hydroxide solution, and 0.39 mL of water. Anhydrous magnesium sulfate (~0.5 g) was added, and the resulting mixture was filtered through a pad of Celite and concentrated *in vacuo*. The crude oil obtained was dissolved in 3 mL of dichloromethane and cooled to 0 °C. Imidazole (0.15 g, 2.2 mmol) followed by *tert*-butyldimethylsilyl chloride (0.145 g, 0.98 mmol) was added. After 1 h at 0 °C and 1 h at room temperature, the reaction mixture was poured into 10 mL of saturated aqueous sodium bicarbonate and extracted with ether. The combined organic layers were washed with brine, dried over anhydrous magnesium sulfate, and concentrated *in vacuo*. Flash chromatographic purification (5% ether in hexane) provided 220 mg (64% yield) of the enyne **39**. IR ($CDCl_3$): 3301, 3010, 2950, 2860, 1460, 1355, 1250, 1070, 840 $cm^{-1}$ $^1H$ NMR (200 MHz, $CDCl_3$): $\delta$ 7.35–7.25 (m, 5H) 5.80 (ddt, $J$ = 18, 11, 6.5 Hz, 1H), 5.75–5.68 (m, 2H), 4.95 (bd, $J$ = 18 Hz, 1H), 4.90 (bd, $J$ = 11 Hz, 1H), 4.10 (q, $J$ = 6 Hz, 1H), 3.60 (s, 2H), 3.26 (d, $J$ = 2.2 Hz, 2H), 3.13 (d, $J$ = 5.5 Hz, 2H), 2.21 (t, $J$ = 2.2 Hz, 1H), 2.05 (m, 2H), 1.60–1.50 (m, 2H), 0.87 (s, 9H), 0.02 (s, 3H), 0.0 (s, 3H). $^{13}C$ NMR (50.1 MHz, $CDCl_3$): $\delta$ 138.7, 137.3, 129.1, 128.2, 127.1, 126.8, 114.4, 78.6, 73.1, 72.6, 57.2, 55.3, 41.4, 37.6, 29.4, 25.9, 18.2, –4.2, –4.7. HRMS calcd for $C_{24}H_{36}NOSi$ ($M^+$ – H) 382.2566, found 382.2563.

**Preparation of Diene 40.** Following the protocol for the preparation of diene **3b**, a solution of enyne **39** (25 mg, 0.065 mmol), complex **1** (1.7 mg, 0.0017 mmol), TPP (0.85 mg, 0.0032 mmol), and acetic acid (3.9 mg, 0.068 mmol) in 1.0 mL of $C_6D_6$ was stirred for 2 days at room temperature. After being diluted with 10 mL of ether, the reaction mixture was washed with saturated aqueous sodium bicarbonate (10 mL) and brine (10 mL), dried over anhydrous magnesium sulfate, and concentrated *in vacuo*. Purification by flash chromatrography (2% ether in hexane) afforded 18.0 mg (72% yield) of diene **40**. IR ($CDCl_3$): 3080, 2920, 2870, 1475, 1250, 1070, 840 $cm^{-1}$. $^1H$ NMR (200 MHz, $CDCl_3$): $\delta$ 7.40–7.20 (m, 4H), 5.85–5.65 (m, 2H), 5.28 (t, $J$ = 1 Hz, 1H), 5.98 (bd, $J$ = 17.5 Hz, 1H), 9.92 (bd, $J$ = 10 Hz, 1H), 4.83 (bs, 1H), 4.15 (m, 3H), 4.20–4.10 (q, $J$ = 8 Hz, 1H), 3.68 (d, $J$ = 14 Hz, 1H), 3.60 (d, $J$ = 14 Hz, 1H), 3.40–3.10 (m, 4H), 2.10–1.98 (m, 2 H), 1.70–1.40 (m, 2H), 0.93 (s, 9H), 0.01 (s, 3H), –0.02 (s, 3H). $^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta$ 138.5, 128.7, 128.3, 127.1, 123.4, 114.4, 102.2, 70.5, 60.5, 59.5, 56.8, 37.2, 29.4, 25.9, 18.2, –4.2, –4.8. HRMS calcd for $C_{24}H_{37}NOSi$ 383.2644, found 383.2643.

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