Palladium-Catalyzed Cyclizations of Polyenynes. A Palladium Zipper

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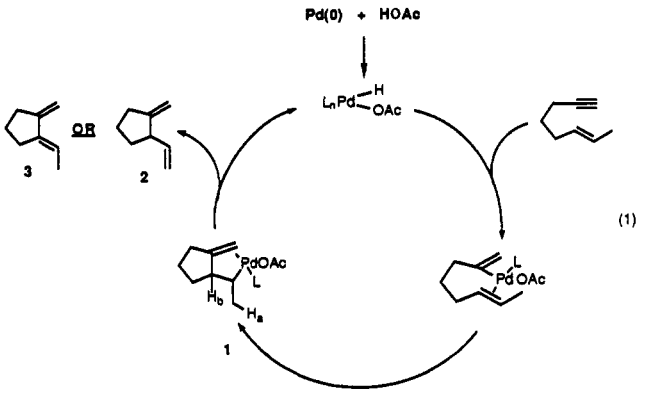
Abstract: The cycloisomerization of polyenynes with a catalyst derived from Pd(0), acetic acid, and a ligand to polycycles depends upon the juxtaposition of unsaturation. The process involves the stages of initiation (by addition of Pd–H to an acetylene), propagation (by intramolecular carbopalladation), and termination (by β-hydrogen elimination). With 2-homopropargylated 1,5- and 1,6-dienes, monocyclizations via 5-exo and 6-endo modes dominate with the ratio dependent upon ligand. The 5-exo mode is favored by tri-*o*-tolylphosphine, whereas triphenylstibine favors the 6-endo mode. On the other hand, a 3-homoallyl-3-homopropargylcyclopentene undergoes smooth bicyclization even when triphenylphosphine is used as ligand. Combining Pd(0)-catalyzed allylic alkylation to make the substrates with Pd(0)-catalyzed cycloisomerization simplifies triquinane and azatriquinane synthesis. A 2-allyl-2-homopropargyl-1-methylenecycloalkane array cycloisomerizes to [4.3.3]propellanes and [3.3.3]propellanes. Methallyl alcohol serves as a basic building block to construct acyclic substrates for construction of spirocycles. Both terminal and internal acetylenes serve as suitable initiators provided the proper ligand is employed. With a terminal acetylene as initiator, triphenylphosphine proves satisfactory, but an internal acetylene requires triphenylstibine. High diastereoselectivity may accompany formation of the spirocycle. Increasing the number of double bonds increases the number of rings formed. Substrates bearing 3, 4, 5, 6, and 7 double bonds generate polyspiranes consisting of 3, 4, 5, 6, and 7 rings. The regio- and diastereoselectivity may be understood on the basis of a conformational analysis of the reactive intermediate. This atom economical approach for construction of polycycles can be considered as the equivalent of a palladium zipper in which the π orbitals are the teeth and the palladium complex is the tab. Closing the zipper stitches the π bonds into σ bonds with creation of the polycycles.

The most atom economical reactions involve simple additions which, when performed intramolecularly, are cycloisomerizations. A classical example is the Diels–Alder reaction, whose immense utility and importance underscore the importance of these concepts. The related Alder ene reaction[1] has had much more limited applicability because of problems of chemoselectivity, high temperature, and restricted range of substrates. The evolution of a catalyst for this process might extend its scope. More importantly, processes not available in a thermal reaction may become feasible. In our evolution of a catalytic cycloisomerization of an enyne, as outlined in eq 1,[2] using a catalyst prepared by reacting a Pd(0) complex with acetic acid,[3] we proposed the σ complex **1** as an intermediate which undergoes β-hydrogen elimination of H_a to yield the Alder ene product **2**. A useful diversion from the Alder ene product is the prospect of a β-hydrogen elimination of H_b to give the synthetically valuable 1,3-dienes **3**, a pathway not possible by a thermal process.[2-4] This process is related to cyclizations that involve the Heck reaction[5]



(1)

but differs significantly in that a vinyl halide or pseudohalide is not required.

The above rationale raises the question of intercepting **1** as a mechanistic probe and a synthetic opportunity for additional structural elaboration. We have shown the ability to effect a reductive cyclization in which we invoke interception of **1** by a silicon hydride.[6] A very attractive prospect would be the interception of **1** by a remote unsaturation to create additional rings. In this paper, we explore the prospects for such a cycloisomerization, which is composed of three stages: initiation by addition of Pd–H to an acetylene, propagation by intramolecular carbopalladation, and termination by β-hydrogen elimination.[7] Contemporaneous to our studies, there have been excellent studies of polycyclizations involving the Heck reaction,[8-10]

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(1) For reviews, see: Hoffmann, H. M. R. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 557. Oppolzer, W.; Snieckus, V. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 476. Snider, B. B. *Acc. Chem. Res.* **1980**, *13*, 426. Taber, D. F. *Intramolecular Diels-Alder and Alder Ene Reactions*; Springer-Verlag: Berlin, 1984. Snider, B. B. In *Comprehensive Organic Synthesis*, Trost, B. M., Fleming, I., Paquette, L. A., Eds.; Pergamon Press: London, 1991; Vol. 5, pp 1–28.

(2) (a) Trost, B. M.; Lautens, M. Chan, C.; Jebaratnam, D. J.; Mueller, T. *J. Am. Chem. Soc.* **1991**, *113*, 636 and earlier references cited therein. (b) For overviews, see: Trost, B. M. *Acc. Chem. Res.* **1990**, *23*, 34. Trost, B. M. In *Studies in Natural Products Chemistry. Stereoselective Synthesis (Part E)*; Atta-ru-Rahman, Ed.; Elsevier: Amsterdam, 1991; pp 277–282.

(3) Trost, B. M.; Lee, D. C.; Rise, F. *Tetrahedron Lett.* **1989**, *30*, 651.

(4) Trost, B. M.; Lee, D. C. *J. Org. Chem.* **1989**, *54*, 2271. For synthetic applications, see: Trost, B. M.; Chung, J. Y. L. *J. Am. Chem. Soc.* **1985**, *107*, 4586. Trost, B. M.; Hipskind, P. A.; Chung, J. Y. L.; Chan, C. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 1502. Trost, B. M.; Hipskind, P. A. *Tetrahedron Lett.* **1992**, *33*, 4541.

(5) Heck. R. F. *Org. React.* (*N.Y.*) **1982**, *27*, 345. Heck, R. F. In *Comprehensive Organic Synthesis*, Trost, B. M., Fleming, I., Semmelhack, M. F., Eds.; Pergamon Press: London, 1991; Vol. 4, Chapter 4.3.

(6) Trost, B. M.; Rise, F. *J. Am. Chem. Soc.* **1987**, *109*, 3161. Trost, B. M.; Braslau, R. L. *Tetrahedron Lett.* **1988**, *29*, 1231. For a synthetic application, see: Trost, B. M.; Edstrom, E. D. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 520. Trost, B. M.; Kondo, Y. *Tetrahedron Lett.* **1991**, *32*, 1613.

(7) For a preliminary report of a portion of this work, see: Trost, B. M.; Shi, Y. *J. Am. Chem. Soc.* **1991**, *113*, 701.

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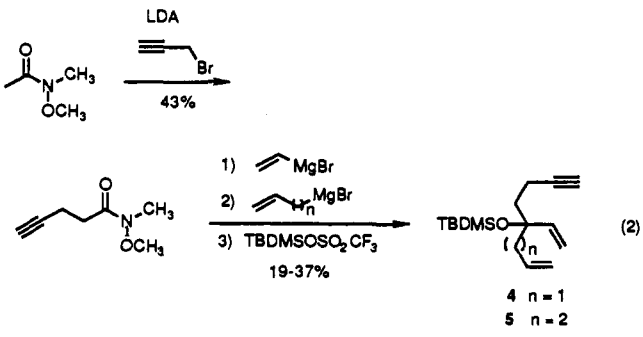
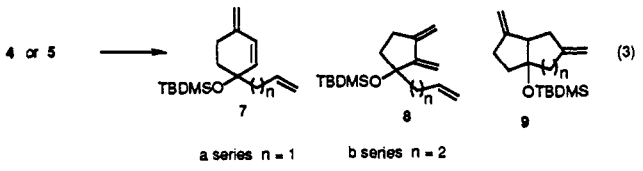
which differ in terms of the initiation, a feature which can be quite important because of the sensitivity of the system to reaction conditions.

Initial Studies: Exo vs Endo Mode of Cycloisomerization. The polyenynes **4** and **5**, prepared as in eq 2, became our first substrates.



(2)

Using our standard conditions of $(dba)_3Pd_2{\cdot}CHCl_3$ (**6**) and acetic acid in the presence of a phosphine- like triphenylphosphine (TPP) or *N,N'*-bis(benzylidene)ethylenediamine (BBEDA) as ligands in benzene even at room temperature led predominantly to the six-membered-ring product **7** rather than the five-membered ring **8** or the bicycle **9** (eq 3). For substrate **4**, the ratios of **7a:8a:9a**



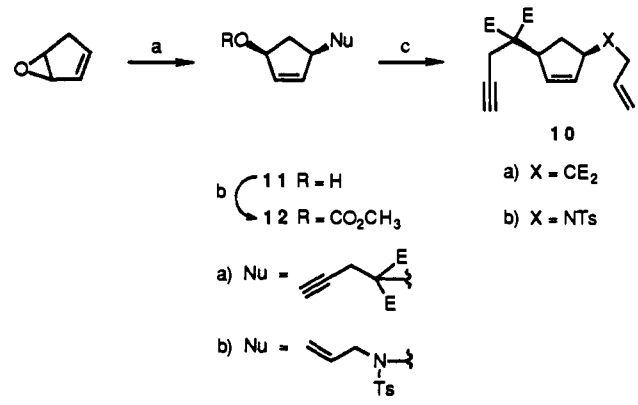
(3)

were 2.8:1.2:1.0 and 17.9:1.0:2.9, respectively, with TPP and BBEDA as ligands. Selectivity for formation of the cyclohexene **7a** could be optimized using triphenylstibene (TPS) as the ligand, which gave a 77% isolated yield of a 250:1.0:28 ratio of **7a:8a:9a**, as determined by gas chromatographic analysis. Switching to tri-*o*-tolylphosphine (TOTP) as ligand led to smooth reaction to produce predominantly the cyclopentane product in 74% isolated yield and a 1.0:24.5:5.8 ratio of **7a:8a:9a**. Using *o*-anisic acid instead of acetic acid with TOTP as ligand further increased the cyclopentane product (**7a:8a:9a**, 1.0:80:9.0, 42% yield). Significant yields of the bicycle **9** form upon (1) increasing acetic acid concentration and adding lithium acetate with TPP as ligand (7.2:1.0:4.7), (2) using 2-(diphenylphosphino)benzoic acid as ligand (74.0:1.0:33.0), or (3) increasing acid strength using TOTP as ligand (CCl_3CO_2H, 1.0:0.0:6.1; CF_3CO_2H, 1.4:0.0:1.0) (ratio of **7a:8a:9a**). The remarkable sensitivity of the product composition to reaction conditions provides an opportunity to tune the nature of the cyclization.

Analysis of the NMR spectrum for **7a**, **8a**, and **9a** provides easy differentiation. For **7a**, the two doublets at δ 6.10 and 5.72 (J = 9.8 Hz) in the ^{1}H NMR spectrum corresponded to the two endocyclic olefinic protons of the six-membered ring; a signal at δ 5.86 (ddd, J = 17.1, 10.3, 7.5 Hz) was assigned to the internal vinyl proton of the monosubstituted olefin; the multiplets at δ 5.03 were attributed to the methylene unit of the monosubstituted olefin; the exocyclic methylene unit was indicated by a multiplet at δ 4.86. In the ^{13}C NMR spectrum, six olefinic carbons resonated at δ 142.42, 135.17, 134.45, 130.28, 117.27, and 112.36, which indicated the existence of one monosubstituted olefin, one exocyclic olefin, and one 1,2-disubstituted olefin. For **8a**, a multiplet at δ 5.87 confirmed the existence of the internal vinyl proton of the monosubstituted olefin. The methylene unit of the monosubstituted olefin and two exocyclic methylene units appeared at δ 5.44 (bs, 1H), 5.39 (bs, 1H), 5.02 (m, 3H), and 4.89 (bs, 1H). In the ^{13}C NMR spectrum, six olefinic carbons resonated at δ 153.38, 146.55, 134.89, 117.05, and 105.22 (the high intensity of this peak indicated the overlap of the two exocyclic olefinic carbons), which suggested the presence of one monosubstituted olefin and two exocyclic olefins. For **9a**, the two exocyclic methylene units resonated as two multiplets at δ 4.88 and 4.78. In the ^{13}C NMR spectrum, signals at δ 155.57, 150.90, 106.50, and 106.38 confirmed the existence of two exocyclic olefins.

Increasing the chain length of one of the olefinic arms as in **5** gives a substrate where similar trends are observed but with somewhat different responses to variables. For example, TPS, which is the preferred ligand for the 6-endo product **7a** above, leads largely to recovered starting material with **5**. Best yields of **8b** are obtained using dppf (63%, 87% brsm)[11] or TOTP (65%) in the presence of acetic acid using **6** as the palladium source in benzene at room temperature. A 70% yield of the 6-endo product **7** arises by simply switching to trimesitylphosphite. In contrast to the above case, no significant amounts of the bicyclic product form under any conditions.

Scheme I. Synthesis of *Z*-3,5-Disubstituted Cyclopentenes[a]



[a] (a) For **11a**, dimethyl propargylmalonate, 2.5 mol % **6**, 10 mol % dppe, THF, 0 °C to room temperature, 55%; for **11b**, *N*-allyl-*p*-toluenesulfonamide, 2 mol % **6**, 8 mol % dppe, BSA, THF, 0 °C to room temperature, 60%. (b) $ClCO_2CH_3$, C_5H_5N, DMAP, CH_2Cl_2, 0 °C, 69% for **12a**, 62% for **12b**. (c) For **10a**, dimethyl sodioallylmalonate, 4 mol % $(Ph_3P)_4Pd$, 8% Ph_3P, THF, reflux, 53%; for **10b**, dimethyl sodiopropargylmalonate, 6 mol % $(Ph_3P)_4Pd$, 12 mol % Ph_3P, THF, reflux, 91%.

Triquinane Skeleton

Inhibition of β-hydrogen elimination should promote polycyclization. The cyclopentene substrate **10** meets this requirement since a cis carbametalation generates a σ-palladium species lacking any cis β-hydrogens and is easily synthesized using Pd(0)-catalyzed alkylations as outlined in Scheme I. Choice of ligand for the Pd-catalyzed reactions of the cyclopentadiene monoepoxide[12] proved important, with dppe being preferred.[13] The cis stereochemistry of the dialkylated products **10a** and **10b** derives from the significant differences in chemical shifts for the cyclopentyl methylene protons (**10a** δ 2.15, dt, J = 12.8, 7.8 Hz

(8) Gaudin, J. M. *Tetrahedron Lett.* **1991**, *32*, 6113. Grigg, R.; Coulter, T. *Tetrahedron Lett.* **1991**, *32*, 1359. Owczarczyk, Z.; Lamaty, F.; Vawter, E. J.; Negishi, E. *J. Am. Chem. Soc.* **1992**, *114*, 10091.

(9) Grigg, R.; Stevenson, P.; Worakun, T. *Chem. Commun.* **1984**, 1073. Grigg, R.; Worakun, T. *Tetrahedron* **1988**, *44*, 2033. Grigg, R.; Sridharan, V.; Stevenson, P.; Worakun, T. *Chem. Commun.* **1986**, 1697. Burns, B.; Grigg, R.; Ratananukul, P.; Sridharan, V.; Stevenson, P.; Worakun, T. *Tetrahedron Lett.* **1988**, *29*, 4329.

(10) Abelman, M. M.; Overman, L. E. *J. Am. Chem. Soc.* **1988**, *110*, 2328. Carpenter, N. E.; Kucera, D. J.; Overman, L. E. *J. Org. Chem.* **1989**, *54*, 5864. In this latter paper, it is reported that addition of more ligand decreased the amount of 6-endo product, an observation in accord with this interpretation. For a recent synthetic application, see: Overman, L. E.; Ricca, D. J.; Tran, V. D. *J. Am. Chem. Soc.* **1993**, *115*, 2042.

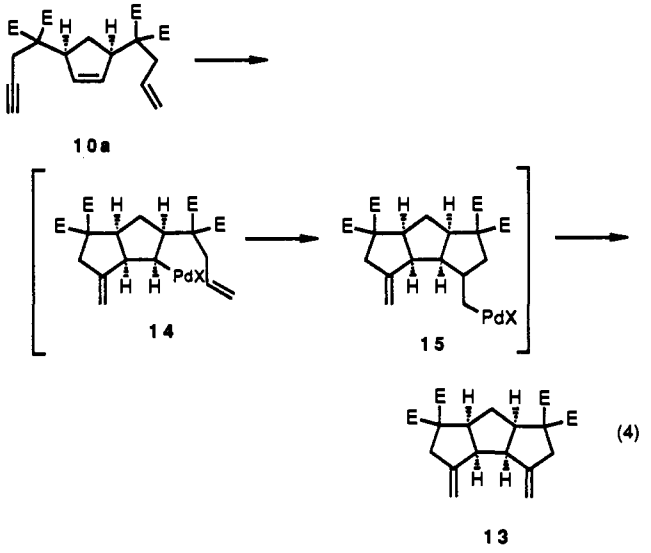
(11) BRSM = based upon recovered starting material.

(12) Trost, B. M.; Molander, G. A. *J. Am. Chem. Soc.* **1981**, *103*, 5969. Trost, B. M.; Kuo, G. H.; Benneche, T. *J. Am. Chem. Soc.* **1988**, *110*, 621. Trost, B. M.; Li, L.; Guile, S. D *J. Am. Chem. Soc.* **1992**, *114*, 8745.

(13) Trost, B. M.; Runge, T. A.; Jungheim, L. N. *J. Am. Chem. Soc.* **1980**, *108*, 2840.

and δ 1.36, td, J = 12.8, 10.0 Hz; **10b** δ 2.30 dt, J = 13.3, 7.8 Hz and δ 1.44, dt, J = 13.3, 9.2 Hz) and ample precedent for Pd catalyzed reactions to proceed with net retention of configuration.[14]

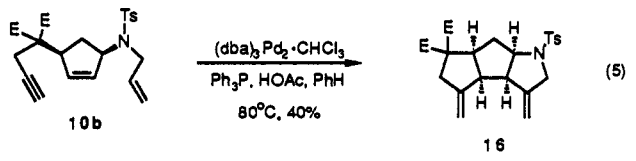
Heating a benzene solution of dienyne **10a** with 2.5 mol % **6**, 10 mol % TPP, and 10 mol % acetic acid at 53 °C gives a 43% yield of the fully symmetric triquinane **13** (eq 4). The yield



(4)

increases to 57% upon raising the temperature to 105 °C by switching to toluene as solvent. The shortened reaction time at the higher temperature decreases the amount of product decomposition. The structure of the product as **13** is readily apparent because of its high symmetry revealed in both the ^{1}H and ^{13}C NMR spectra. The ^{13}C spectrum shows only 11 signals; the ^{1}H NMR spectrum shows two broad singlets at δ 5.06 and 4.89 for both sets of exo methylene hydrogens and two singlets at δ 3.70 and 3.69 for both sets of methyl esters. Both the cis,anti,cis and cis,syn,cis triquinanes are possible structures. Mechanistic considerations which suggest intermediates **14** and **15** combined with the cis stereochemistry of the starting material lead us to favor the latter as depicted in **13**, on the basis of the facts that carbapalladations are known to be cis and σ-organopalladium intermediates do not interconvert rapidly.[5, 14a-c]

Reaction of substrate **10b** explores the effect of a heteroatom (eq 5). NMR spectroscopy indicates that the anticipated



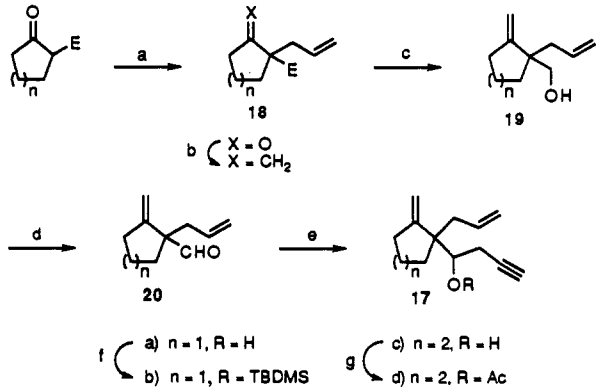
(5)

cycloisomerization product **16** forms. The ^{13}C NMR spectrum shows 21 different types of carbons with the appropriate chemical shifts for the two esters (δ 171.89, 170.07) and the two exocyclic methylene groups (δ 143.6, 143.5, 111.7, 109.0). The latter functional groups are confirmed by the absorptions at δ 5.00, 4.94, 4.91, and 4.86 in the ^{1}H NMR spectrum. The protons on the two isolated methylene groups appear as AB patterns at δ 3.94 and 3.76 (J = 14.7 Hz) (α to N) and δ 3.34 and 2.66 (J = 16.1 Hz) (α to malonate unit).

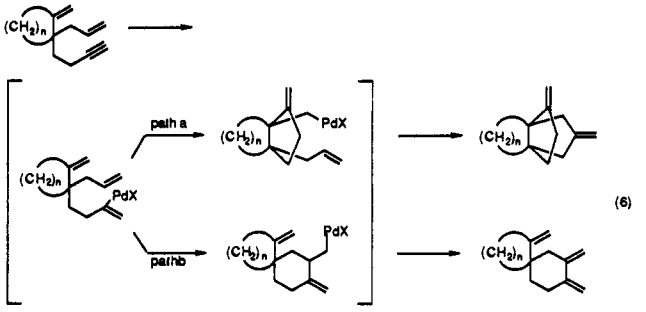
Propellanes

Changing the juxtaposition of the functional groups changes the nature of the ring system. Constructing a 2-allyl-2-homopropargyl-1-methylenecycloalkane provides an opportunity to construct propellanes (eq 6). The key becomes the initial

Scheme II. Synthesis of 2-Allyl-2-homopropargyl-1-methylenecycloalkanes[a]



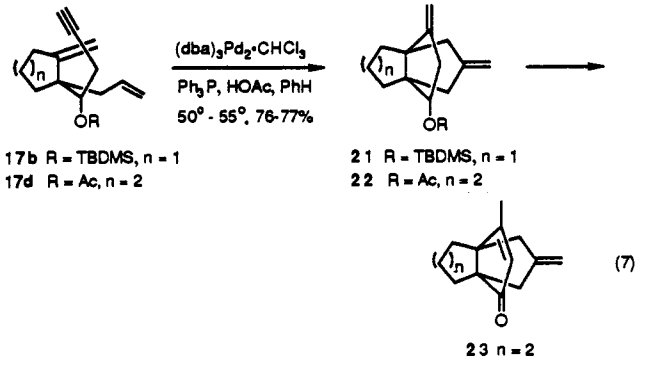
[a] (a) NaH, CH_2=$CHCH_2Br$, THF, room temperature, 90–98%. (b) CH_2I_2, Zn, $TiCl_4$, THF, 17%, or Ph_3PCH_3Br, $NaCH_2S(O)CH_3$, DMSO, room temperature, 61%. (c) LAH, THF, 0 °C. (d) ClCOCOCl, DMSO, $(C_2H_5)_3N$, CH_2Cl_2, –78 °C. (e) Zn, CH≡CCH_2Br, THF. (f) $TBDMSOSO_2CF_3$, 2,6-lutidine, CH_2Cl_2, 0 °C, 22% overall from **18**, n = 1. (g) Ac_2O, C_5H_5N, 0 °C, 35% overall from **18**, n = 2.



(6)

chemoselectivity for intramolecular carbapalladation to form a five-membered ring (eq 6, path a) rather than a six-membered ring (eq 6, path b). Scheme II summarizes the syntheses of the two substrates **17b** and **17d**.

Heating dienyne **17b** under our standard conditions results in smooth conversion of the starting material to a single product (eq 7). The disappearance of both the acetylene and monosubstituted

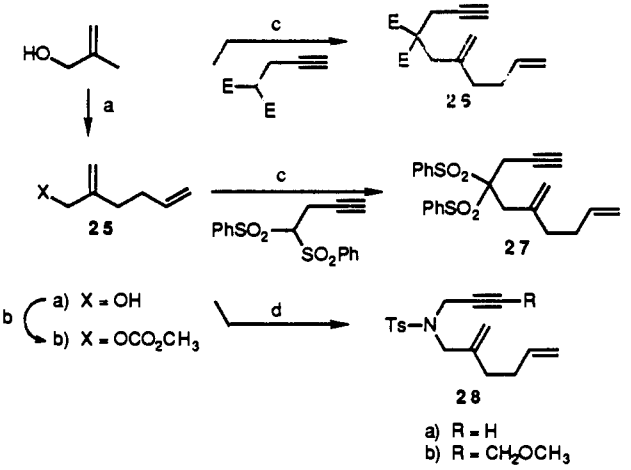


(7)

olefins and appearance of two exocyclic methylene groups [δ 4.66–4.82 and 156.9 (156.5), 152.1 (152.7), 105.6 (105.5), 104.7 (104.3); note that **17b** and **21** are mixtures of diastereomers, accounting for the doubling of the signals] confirm that the desired cyclization to the [3.3.3]propellane **21** occurred. Treating the homologue **17d** under similar conditions produces a product accompanied by a very similar set of spectral changes, supporting formation of the [4.3.3]propellane **22** (eq 7). To demonstrate that the doubling of peaks indeed arises from the mixture of

(14) For some reviews, see: (a) Trost, B. M. *Tetrahedron* **1977**, *33*, 2615. Trost, B. M. *Acc. Chem. Res.* **1980**, *13*, 385. (b) Tsuji, J. *Organic Synthesis with Palladium Compounds*; Springer-Verlag: Berlin, 1980. (c) Trost, B. M.; Verhoeven, T. R. *Compr. Organomet. Chem.* **1982**, *8*, 799. Tsuji, J. *Tetrahedron* **1986**, *42*, 4361. (d) Trost, B. M. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 1173.

Scheme III. Synthesis of Spirane Dienyne Precursors[a]

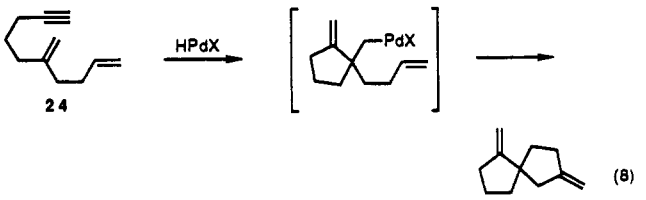


[a] (a) n-C_4H_9Li, TMEDA, CH_2=$CHCH_2Br$, THF. (b) CH_3OCOCl, C_5H_5N, 50% overall. (c) $(dba)_3Pd_2$·$CHCl_3$, Ph_3P, THF, 40–50 °C, 62–83%. (d) (i) $(dba)_3Pd_2$·$CHCl_3$, $TsNH_2$, BSA, THF, room temperature, 79%; (ii) NaH, THF, RC≡CCH_2Br, 65 °C, 67–82%.

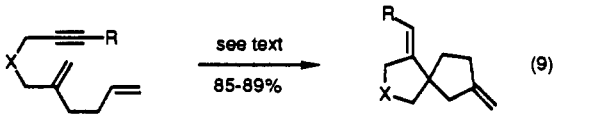
diastereomers present, the acetate **22** is hydrolyzed (K_2CO_3, CH_3OH, room temperature), oxidized (PCC, CH_2Cl_2, room temperature) and isomerized by olefin migration (DBU, $CHCl_3$, room temperature) to generate the [4.3.3]propellenone **23** as a single isomer. The conjugated enone is revealed by IR (1689 cm^{-1}), ^1H NMR (δ 5.90, 1H, bs; 2.02, 3H, d, J = 1.2 Hz), and ^{13}C NMR (δ 213.3, 181.9, 130.7) spectra.

Spiranes

The ring system created becomes a spirane if a 1,1-dialkylated olefin such as **24** is employed (eq 8). Scheme III summarizes the synthesis of the initial set of dienynes. Using the methallyl alcohol dianion previously exploited in this laboratory,[15] the pivotal intermediate **25** (Scheme III) is readily available.



Simply exposing dienyne **26** or **27** to 2.5% $(dba)_3Pd_2$·$CHCl_3$, TPP, and acetic acid in benzene even at room temperature leads to smooth consumption of starting material (eq 9). Following

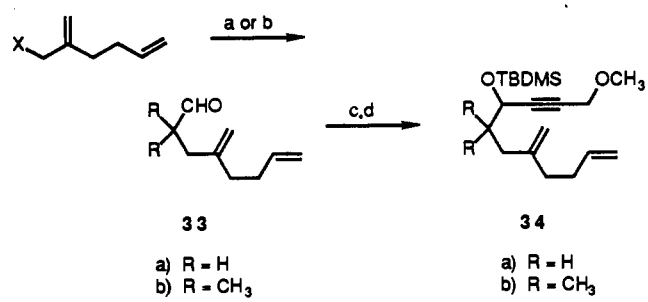


29 X = $C(CO_2CH_3)_2$, R = H
30 X = $C(SO_2Ph)_2$, R = H
31 X = NTs, R = H
32 X = NTs, R = CH_2OCH_3

the reaction by gas chromatography revealed a significant increase in cleanliness by switching the ligand to TOTP. Once again ^1H and ^{13}C NMR spectroscopy revealed the replacement of all the unsaturations of the starting materials (except for the phenyl groups of the sulfones in **27**) by two exocyclic methylene groups (e.g., for **29** ^1H NMR δ 4.86 m; ^{13}C NMR δ 155.2, 151.08, 106.1, 105.1; for **30** ^1H NMR δ 4.89, 4.86, 4.64, 4.62; ^{13}C NMR δ 1.52.6, 150.4, 106.8, 105.6), consistent with formation of the

(15) Trost, B. M.; Chan, D. M. T.; Nanninga, T. N. *Org. Synth.* **1984**, *62*, 58.

Scheme IV. Diastereoselectivity of Spirane Formation[a]



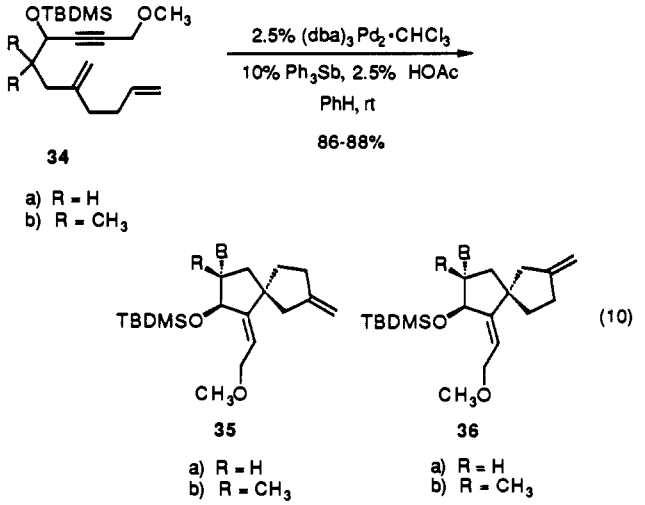
[a] (a) X = OH, C_2H_5OCH=CH_2, $Hg(OAc)_2$, 180–190 °C, 41%. (b) X = Br, LDA, $(CH_3)_2CHCH$=NC_6H_{11}, THF, –78 to –10 °C, 77%. (c) n-C_4H_9Li, HC≡CCH_2OCH_3, THF, 0 °C, 83–92%. (d) TBDMSOSO$_2CF_3$, 2,6-lutidine, CH_2Cl_2, 0 °C, 86–95%.

cycloisomers **29** and **30**. To test the importance of the gem-alkyl effect and simultaneously the prospect for the synthesis of heterospiranes, we examined the nitrogen analogue **28a**. Using the conditions as outlined for **29** and **30** gives quite comparable results, producing the cycloisomer **31** at room temperature in 89% yield.

Converting the terminal acetylene to an internal acetylene significantly retards the reaction. Dienyne **28b** does not react satisfactorily at room temperature but requires 60 °C. Both TPP and TOTP prove less satisfactory as ligands compared to TPS. With these modifications, cycloisomerization of **28b** occurs readily to produce azaspirane **32** in 86% yield as a single geometric isomer, which is assigned as depicted on the basis of mechanistic considerations.

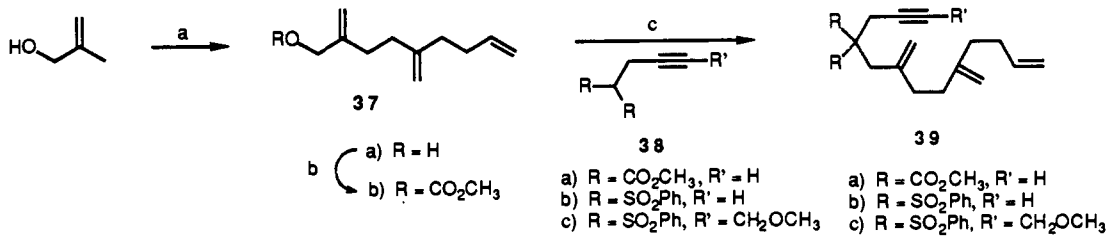
The requirement for TPS as ligand appears general for the internal acetylene initiators. To examine the diastereoselectivity of this process, we chose to examine the related internal acetylenic substrates **34a** and **34b**, which are prepared as outlined in Scheme IV.

Even though the initiator is a disubstituted acetylene, cycloisomerizations of both **34a** and **34b** proceed at room temperature in the presence of TPS as ligand (eq 10). The successful



cycloisomerization of **34a** clearly demonstrates the lack of a requirement for gem-alkyl substitution in the tethers in all carbon substrates. That gem-alkyl substitution does have a rate effect is apparent in the 3-fold difference in reaction time between substrates **34a** and **34b**, the latter reacting the faster. The gem-alkyl groups also have a marked effect on diastereoselectivity. Whereas the substrate possessing the simple tether **34a** provides a 1.4:1.0 ratio of the two diastereomeric products **35a**:**36a**, this ratio improves dramatically to 10:1 of **35b**:**36b** with the substrate bearing the *gem*-dimethyl groups **34b**.

Scheme V. Synthesis of Dispirane Substrates[a]

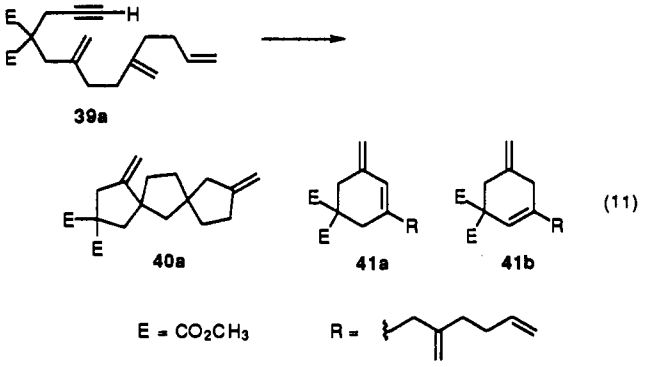


[a] (a) n-C_4H_9Li, TMEDA, ether, −78 °C, **25** X = Br, 84%. (b) CH_3OCOCl, C_5H_5N, CH_2Cl_2, 0 °C, 85%. (c) 2.5% $(dba)_3Pd_2{\cdot}CHCl_3$, 20% TPP, **38**, THF, 45–50 °C, 95–99%.

Polyspiranes

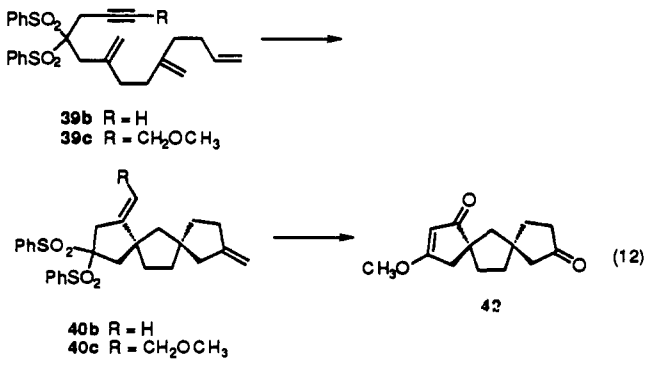
The fact that each carbametalation produces a new C–Pd bond which ultimately is destroyed by β-hydrogen elimination suggests the possibility that the cyclization process may continue if additional unsaturation is present. Scheme V outlines the synthesis of the substrates for tricyclization which were chosen to test the effect of steric bulk of the tether substituents and the role of an internal vs terminal acetylenic initiator.

The malonate substrate **39a** cycloisomerizes to a mixture of spiranes (**40a**) and six-membered ring products **41a** and **41b** (eq 11). In agreement with our initial cyclization studies, phosphine



(11)

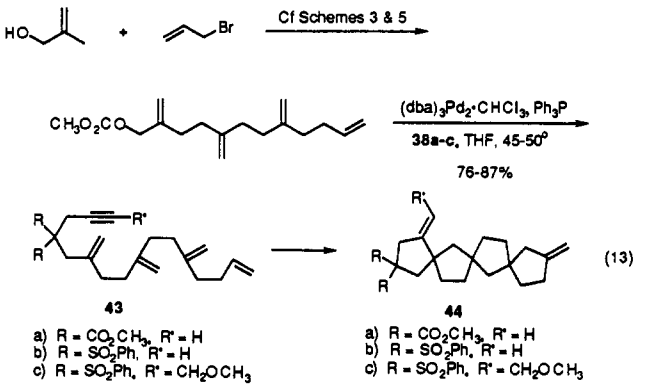
ligands favor 5-exo cyclization to form spiranes and stibine favors 6-endo cyclization to the methylenecyclohexenes **41a** and **41b**. In contrast to this result, only polyspirane formation is observed upon cycloisomerizing the bis-sulfone substrates **39b** and **39c**.



(12)

Both cyclizations proceed at room temperature, with the latter requiring about twice the reaction time. Following the general trends previously established, TOTP proves efficacious as the ligand for the cyclization of the terminal acetylenic substrate **39b** and TPS is the preferred ligand for the cyclization of the disubstituted acetylenic substrate **39c**. NMR spectroscopy indicates a surprisingly high diastereoselectivity of 7:1, in which the tentatively assigned major diastereomer is depicted in **40b**. The synthetic utility of the sulfone groups and further characterization of the dispiranes are provided by ozonolysis in methanol in the presence of triethylamine whereby the β-methoxy enone **42** is directly obtained as a 7:1 mixture of diastereomers. Both **40b** and **40c** produce the same enone, but the diastereomeric ratio is somewhat lower in the latter case (4:1).

The method of synthesis as outlined in Schemes III and V allows easy iteration of the sequence to create homologous substrates. Equation 13 illustrates the construction of the trispirane substrates **43a-c**, which ultimately derive from three molecules of methallyl alcohol, allyl bromide, and the malonate or bis-sulfone **38a-c**.

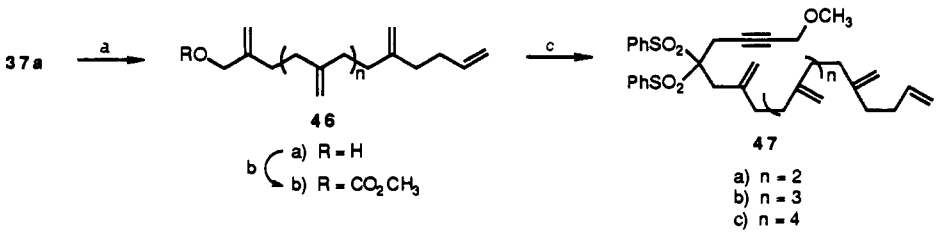


(13)

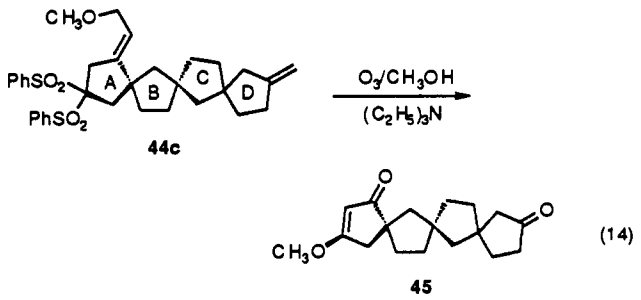
Increasing the number of unsaturations does affect the reactivity of the substrates. The malonate **43a** parallels the behavior of malonate **39a** in that it reacts to form a mixture of the trispiranes **44a** (mixture of diastereomers) and the cyclohexenes analogous to **41a** and **41b**. Cyclization of the corresponding bis-sulfone **43b** becomes significantly slower as well. While NMR spectroscopy indicates that the major product is likely the trispirane **44b** (two exocyclic methylene groups δ 4.87, 4.84, 4.61, and 4.56), a significant number of additional products likely resulting from 6-endo cyclization and/or dimerizations involving the terminal acetylene make the reaction unattractive. On the other hand, the substrate bearing the internal acetylenic initiator **43c** cyclizes very smoothly and cleanly in the presence of TPS as ligand at 40 °C to give the trispirane **44c** in 84% yield. The ^{1}H NMR spectrum is surprisingly simple, especially considering that there are four possible diastereomers. Absorptions appear at δ 5.26 (m, 1H) and 4.82 (m, 2H) for the olefinic protons, at δ 3.80 (d, J = 6.3 Hz, 2H) and 3.32 (s, 3H) for the methoxymethyl protons, at δ 3.31 for the allylic methylene protons adjacent to the sulfone units, at δ 2.70 for the nonallylic methylene protons adjacent to the sulfone, at δ 2.2–2.3 for the other four allylic methylene protons, and at δ 1.5–1.8 for the remaining protons. The ^{13}C NMR spectrum shows partial doubling of the absorptions for the olefinic carbons at δ 152.71 (152.67), 149.82 (149.60), 116.61, and 105.56 (105.47), suggesting that two of the four possible diastereomers dominate.

Confirmation of this interpretation derives from the oxidative cleavage which forms enone **45** (eq 14). The ^{13}C NMR spectrum exhibits four lines at δ 58.78, 58.59, 58.39, and 58.18 in the approximate ratio of 1.1:4.0:4.6:1.0 for the methoxy carbon, again supporting formation of two major diastereomers. Since for-

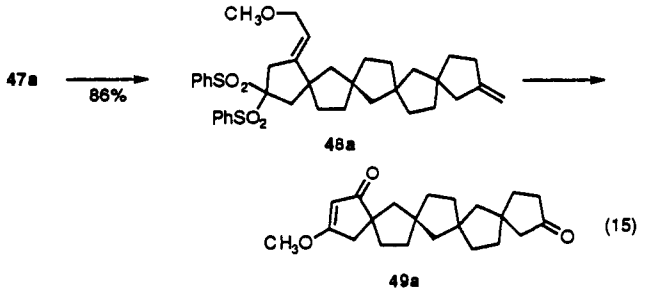
Scheme VI. Iterative Synthesis of Polyenynes



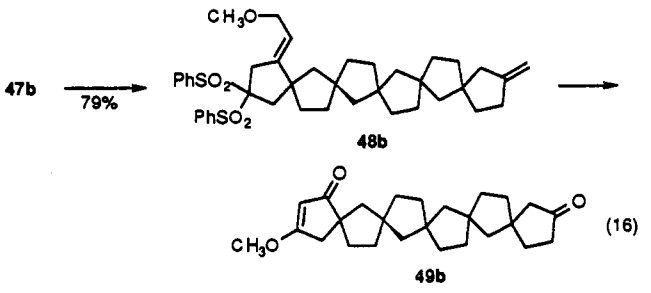
[a] (a) (i) Ph_3P, CCl_4 reflux, 70–81%; (ii) *n*-C_4H_9Li, TMEDA, $HOCH_2C(CH_3)=CH_2$, THF, −78 °C to room temperature, 60–78%. (b) CH_3OCOCl, C_5H_5N, DMAP, CH_2Cl_2, room temperature, 86–93%. (c) 2.5% $(dba)_3Pd_2{\cdot}CHCl_3$, 20% TPP, THF, 50 °C, 72–92%.



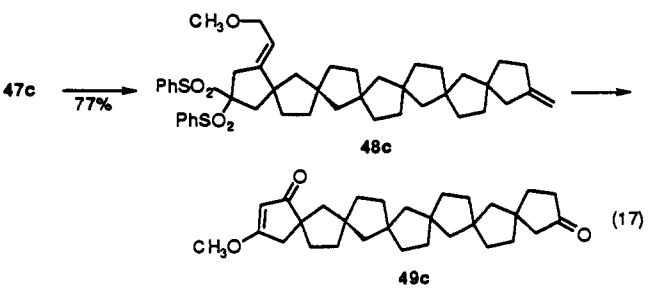
(14)



(15)



(16)



(17)

mation of the dispirane **40c** shows about a 4:1 selectivity, the major stereochemistry for the spiro fusions for rings A, B, and C of **44c** are presumably the same in both **40c** and **44c**, with the spiro fusion between rings C and D being stereorandom.

How many rings can be formed in one step by this palladium-catalyzed cycloisomerization? Repetition of the alkylation sequence as shown in step a in Scheme VI permits ready assembly of a series of homologous alkylating agents **46b**, for $n = 2$ twice, $n = 3$ three times, and $n = 4$ four times.

Pd(0)-catalyzed alkylation of each of these generates the pentaenyne **47a**, hexaenyne **47b**, and heptaenyne **47c** in excellent overall yields. Using what has now become our standard conditions for a substrate bearing a disubstituted acetylenic initiator [2.5% $(dba)_3Pd_2{\cdot}CHCl_3$, 10% Ph_3Sb, HOAc, PhH, 50–65 °C], the cyclization of each substrate is followed by ^1H NMR spectroscopy using C_6D_6 as solvent. The steady replacement of the signals attributable to the vinyl protons of the starting materials by the same signal pattern discussed for **44c** indicates that cyclization occurs completely to form the tetraspirane **48a** (86%), pentaspirane **48b** (79%), and heptacyclic **48c** (77%). Further confirmation for the penta-, hexa-, and heptacyclic nature of these products derives from ozonolysis to the enones **49a**, **49b**, and **49c**, respectively.

In spite of the fact that there are 8, 16, and 32 possible diastereomers for the respective cyclization products, the NMR spectra are deceptively simple. For example, the ^{13}C spectrum of **49a** displays only three lines at δ 102.94, 102.89, and 102.79 in a ratio of 3.6:2.3:1 for the olefinic carbon α to the carbonyl group, indicating only three out of eight isomers being detectable. Examining the methoxy region is more fruitful for the hexacycle **49b**, in which only four peaks at δ 58.70, 58.52, 58.35, and 58.19 in the ratio of 1.1:4.3:4.4:1.0 are observable, revealing only four out of 16 stereoisomers, two of which predominate. The region for the olefinic carbon α to the carbonyl group of **49c** displays only two signals at δ 102.93 and 102.82 in a ratio of 3:1, revealing only two out of 32 isomers. Because most of the stereogenic centers are remote from the functionality, it is impossible to ascertain exactly how many isomers are present and what they are.

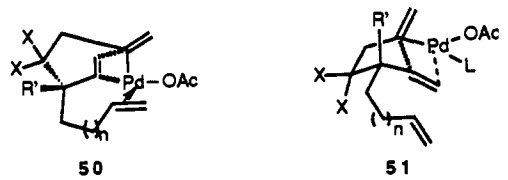
Discussion

The palladium-catalyzed cycloisomerizations using a catalyst derived by mixing a Pd(0) complex, a phosphine or stibine ligand, and a carboxylic acid involves three stages: (1) initiation, (2) propagation, and (3) termination (see Scheme VII). The initiation requires an acetylene, either monosubstituted or disubstituted. The absolute requirement of an acetylenic initiator means that the proposed hydridopalladium carboxylate intermediate has a very high chemoselectivity for attack on the triple bond even in the presence of overwhelming statistical odds favoring double-bond addition because of the number of double bonds present such as in **47c**. Furthermore, addition to the triple bond must dominate over insertion into the acetylenic hydrogen. In fact, as the reactions slow, this latter process becomes problematical. Thus, formation of the dispirane occurs smoothly with a terminal acetylenic initiator, but problems arise with larger substrates. On the other hand, the internal acetylenic initiator succeeds, even effecting an astounding heptacyclization! The choice of ligand proves critical. The internal acetylenic initiator requires a poorer donor and better acceptor ligand than a phosphine, a balance reached with TPS.[16]

Regioselectivity of the hydropalladation and subsequent carbapalladation steps is essential.[8-10,17,18] Bidentate coordination as depicted in eq 1 may be required. Failure to effect satisfactory

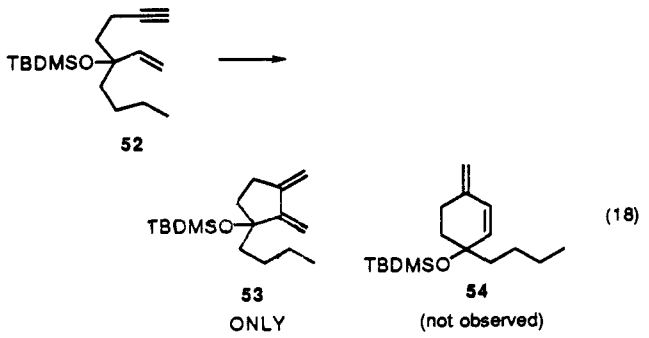
(16) Compare study of ligand effects in cross-coupling: Farina, V.; Krishnan, B. *J. Am. Chem. Soc.* **1991**, *113*, 9585.

bicyclization of **4** or **5** may, in part, derive from coordination of the additional site of unsaturation, thereby favoring a 6-endo mode **50** rather than the 5-exo mode **51**. In support of this



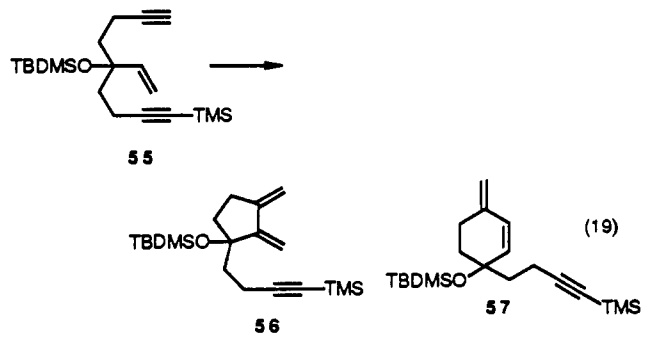
50 **51**

hypothesis, the monosaturated analogue of **5**, i.e., **52**, cyclizes solely to the five-membered-ring product **53** with none of the isomeric cyclohexene **54** (eq 18). In contrast to this result, the



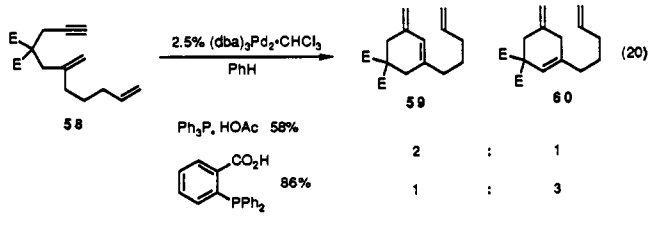
52 **53** ONLY **54** (not observed) (18)

diacetylenic substrate **55**, which possesses the more strongly coordinating acetylenic linkage as a remote binding substituent, cyclizes preferentially (ratio of **56**:**57** 1:16) to the methylenecyclohexene **57** (eq 19) in the presence of the more weakly coordinating TPS as ligand but to the dimethylenecyclopentane **56** only in the presence of a phosphine ligand.[10b]



55 **56** **57** (19)

Increasing the distance to the remote binding site which may facilitate internal coordination may also divert the reaction to the 6-endo mode. Thus, cycloisomerziation of dienyne **58** only produces the methylenecyclohexenes **59** and **60**. A very subtle



58 **59** **60** (20)

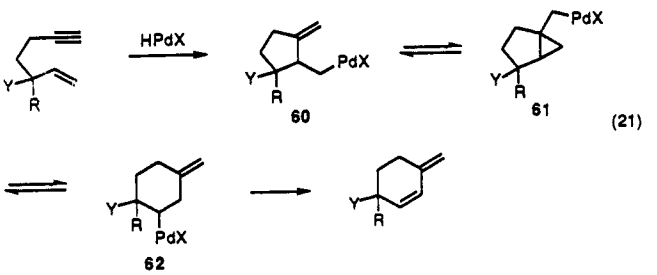
effect of conformation on this regioselectivity is observed in polycyclizations in switching from the diester as in **39a** and **43a** to the corresponding bis-sulfones as in **39b** and **43b** whereby the

(17) For an analogous effect in a Rh-catalyzed reaction, see: Grigg, R.; Stevenson, P.; Worakun, T. *Tetrahedron* **1988**, *44*, 4967.

(18) Also see: Trost, B. M.; Burgess, K. *Chem. Commun.* **1985**, 1084. Negishi, E.-I.; Tour, J. M. *Tetrahedron Lett.* **1986**, *27*, 4869. Trost, B. M.; Dumas, J. *Tetrahedron Lett.* **1993**, *34*, 19.

sterically more demanding sulfones favor the 5-exo mode.[17] The $A_{1,3}$ type steric strain between X and the palladium-substituted olefinic methylene group in **50** may account for this observation.

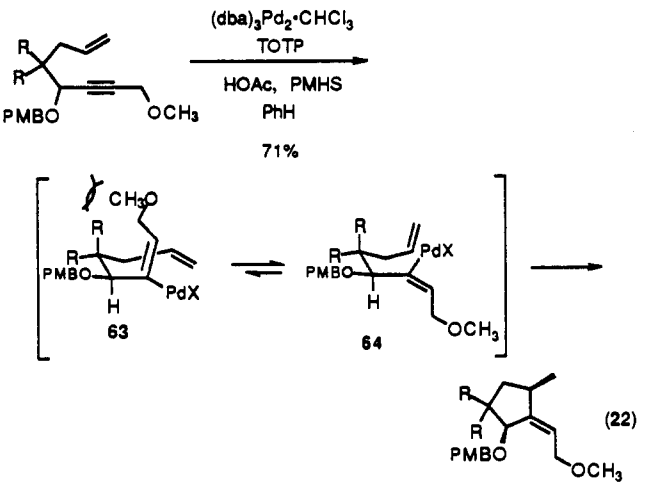
An alternative mechanism for formation of the six-membered-ring product involves homoallyl cyclopropylcarbinyl homoallyl rearrangement (**60** to **61** to **62**) as in eq 21. Such a mechanism



60 **61** **62** (21)

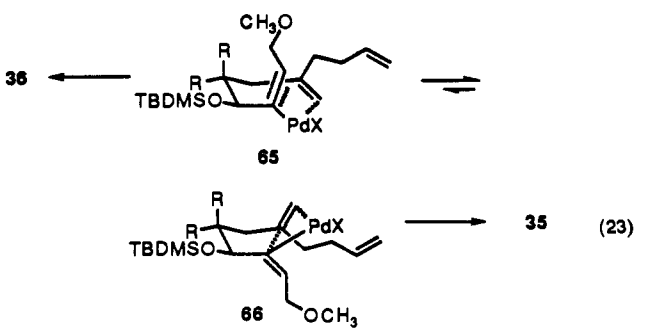
has been invoked in related cyclizations initiated by reactions of vinyl halides and Pd(0).[8] A drawback to this proposal is the requirement that cyclopropane formation from **60** must be faster than or at least competitive with β-hydrogen elimination.[19,20] The substituent effects are also more difficult to rationalize. Nevertheless, this option must be considered to be viable especially in light of recent observations.

The diastereoselectivity of the cyclization depicted in eq 10 derives from consideration of the reductive cyclization previously observed (eq 22), which is understood on the basis of the strong



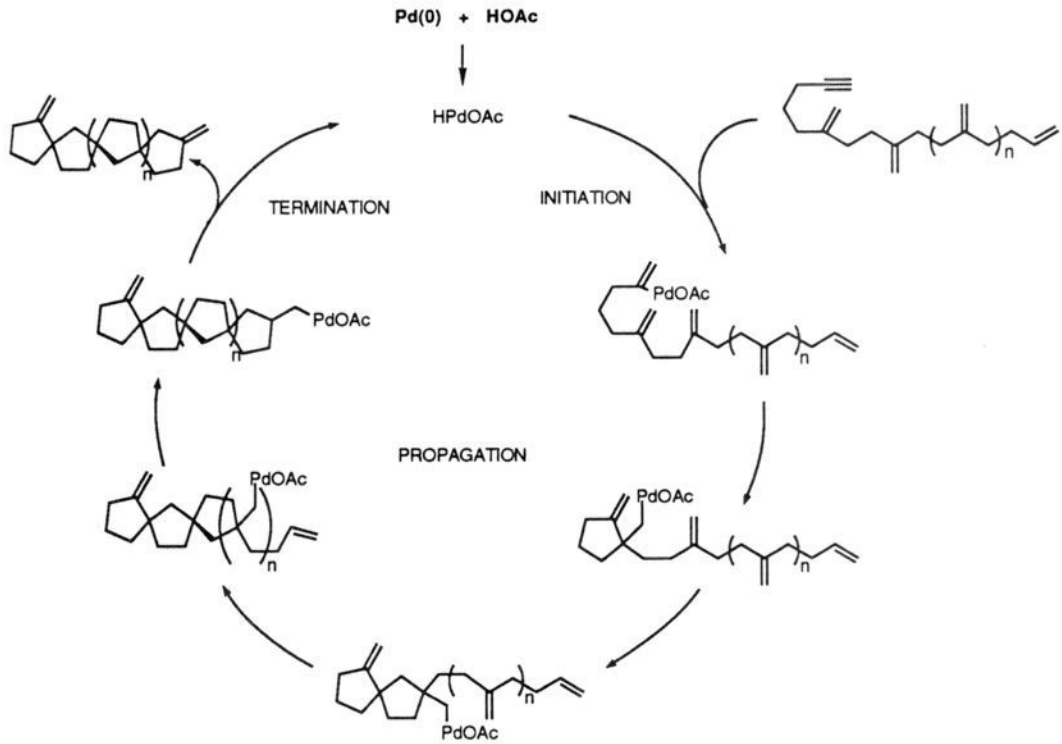
63 **64** (22)

destabilization of conformer **63** when R ≠ H.[21] Using this analogy, the relative energies of the two conformers **65** and **66** become similar when R = H, producing a nearly equimolar mixture of the diastereomeric spiranes (eq 23). When R = CH_3, the strong destabilization of conformer **65** leads to preferential reaction via conformer **66** to give the preference for diastereomer **35**.

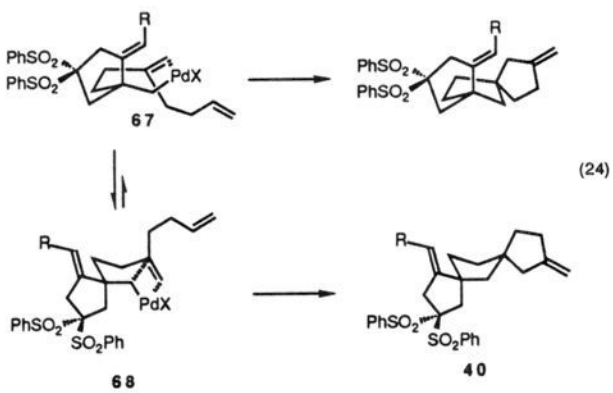


65 **66** **35** (23)

Scheme VII. Cycloisomerization of Spiranes



Analysis of the two reacting conformers **67** and **68** for the dispirane formation of eq 12 (see eq 24) suggests that the selectivity



(24)

derives from thrusting the exocyclic alkylidene group in **67** over the face of the newly forming five-membered ring, thereby favoring the sterically more accessible conformation **68**. This model also accommodates the observed small decrease in diastereoselectivity when R = CH_2OCH_3 since enhanced nonbonded interactions between this substituent and the forming ring are somewhat larger in **68** than in **67**. Once we move beyond the dispirane stage, the source of the diastereoselectivity disappears with respect to both the model and the experiment. Thus, the tetracycle **44c** exists as a mixture of four diastereomers in a 1.1:4.0:4.6:1.0 ratio, which is consistent with a ~4:1 diastereoselectivity for formation of the dispiro compound and the final spiro center being formed stereorandomly.

As a result, all higher spiranes **48a-c** are undoubtedly mixtures of *predominantly* 4, 8, and 16 diastereomers (assuming that the initial spirocyclization occurs with the same diastereoselectivity as above). Depending upon the stereochemistry, these polyspiranes may have quite different molecular shapes ranging from rigid rods to molecular bowls, as depicted in Figure 1. Prospects for controlling stereochemistry remain a goal for future endeavors. At this juncture, the ease of building up the requisite acyclic substrates from methallyl alcohol by repeated iteration of the same two-step sequence makes this approach to polyspiranes very simple. The limit in number of spiranes has not been reached. The facts that the yield of polycyclization is virtually independent of the number of rings being formed and that following the reaction by NMR spectroscopy permits the observation that the signals for the starting material are smoothly replaced by the product without the buildup of any detectable intermediates or production of significant byproducts suggest that much larger polyspiranes or "molecular ropes" may be formed.

This process may be likened to a zipper. Viewing the π orbitals as the teeth and the palladium catalyst as the tab, pulling the palladium across the π bonds converts them into σ bonds with accompanying ring formation (closing the zipper). The ultimate shape of the polycycle depends upon the juxtaposition of

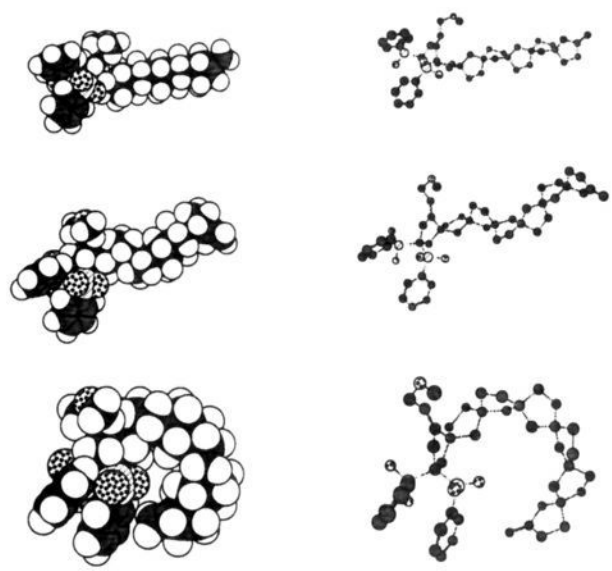
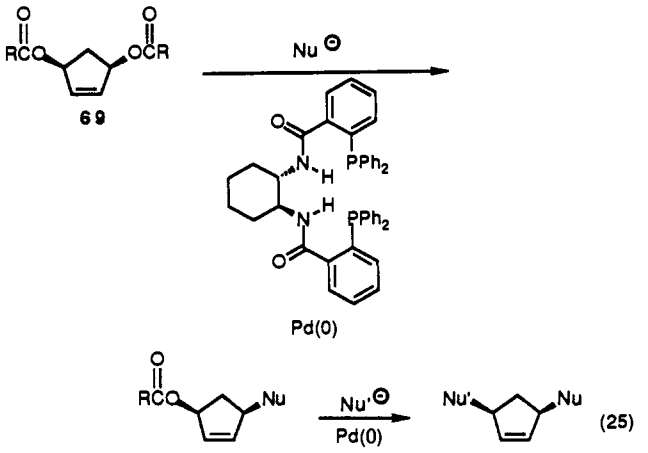


Figure 1. Computed molecular models of three possible diastereomers of heptacyclic spirane **48c**.

unsaturation, with three architectures being illustrated so far: fused polycycles, propellanes, and spiranes. The production of fused polycycles by this method benefits from the ease of access of the cyclization substrates by Pd(0)-catalyzed alkylations. A slight variation from that depicted in Scheme I, as depicted in eq 25, in which the 3,5-dicarboxylate **69** is employed as a surrogate for cyclopentadiene monoepoxide, converts this triquinane and azatriquinane synthesis into an asymmetric one.[22]



(25)

It is to be noted that, in each case, the product is a simple isomer of the starting material. Cycloisomerizations constitute a highly atom economical approach for ring construction. Related studies revolve around the employment of an oxidative addition of a Pd(0) complex with vinyl halides and pseudohalides in initiating cyclization and polycyclizations.[8-10,17-19,23] To the extent that the halide or pseudohalide coordinates to the metal, such interaction may have a significant effect on the selectivity.[24] However, parallels between our observations and these Heck type cyclizations do exist, further supporting the mechanistic proposals presented herein. Intrinsically, this latter strategy is less atom economical than the cycloisomerizations described above. To the extent that the vinyl halides are prepared from the corresponding acetylenes, this strategy also becomes somewhat less efficient. On the other hand, the restriction of acetylenes with respect to incorporation into cyclic initiators makes the Heck cyclization applicable to some cases inaccessible by cycloisomerization.[10] Thus, both methods should find important utility in synthetic chemistry.

Experimental Section

Reactions were generally run under a positive pressure of dry nitrogen. Anhydrous solvents or reaction mixtures were transferred by oven-dried syringe or cannula. Solvents were generally distilled before use: acetonitrile, benzene, dichloromethane, dichloroethane, diisopropylamine, dimethylformamide, lutidine, pyridine, and triethylamine from calcium hydride; ether and tetrahydrofuran (THF) from sodium benzophenone ketyl; dimethyl sulfoxide was dried using freshly activated 3A molecular sieves. All reactions were run under a blanket of nitrogen.

Flash chromatography following the method of Still[25] 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-Plaskitkfolien, Kieselgel 60 F_{254}).

Proton nuclear magnetic resonance spectra were measured at 200, 300, or 400 MHz on a Varian Gemini 200, Gemini 300, or Varian XL-400 instrument, respectively as indicated. Chemical shifts are reported in parts per million (ppm) downfield from tetramethylsilane and determined relative to the proton signal of the solvent ($CDCl_3$, 7.26 ppm). NMR data are reported in the following form: chemical shift (multiplicity, coupling constant(s) in hertz, number of hydrogens). Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; p, pentet; m, multiplet; b, broad. ^{13}C NMR spectra were fully decoupled, and chemical shifts are reported in parts per million (ppm) downfield from tetramethylsilane and determined relative to the carbon signals of the solvent ($CDCl_3$, 7.0 ppm).

Infrared spectra were recorded in 0.1 mm path length sodium chloride cavity cells on a Perkin-Elmer 1420 ratio-recording infrared spectrophotometer using polystyrene as a reference (1601 cm^{-1}) or on a Nicolet 205 FT-IR spectrometer and are reported in wavenumbers (cm^{-1}).

Melting points were determined using a Thomas-Hoover oil bath apparatus in open capillary tubes and are uncorrected. Boiling points are also uncorrected.

Analytical gas chromatography was performed on a Varian 3700 gas chromatograph using a 25 m × 0.25 mm poly(dimethylsiloxane) column from Alltech.

Microanalyses were performed by Robertson Laboratory, Inc., Madison, NJ. High-resolution mass spectra were performed by the mass spectrometry facility of the University of California at San Francisco.

Preparation of *N*-Methoxy-*N*-methyl-4-pentynamide. To a −78 °C solution of lithium diisopropylamide prepared from diisopropylamine (6.98 mL, 49.8 mmol) and *n*-butyllithium (32.3 mL, 47.7 mmol in hexane) in 25 mL of THF was added dropwise 4.28 g (41.52 mmol) of *N*-methoxy-*N*-methylacetamide[26] in 5 mL of THF. After being stirred at −78 °C for 1 h, the mixture was added to a solution of propargyl bromide (3.77 mL, 49.9 mmol) in HMPA (14.5 mL) and THF (10 mL) at −78 °C. After being stirred at −78 °C for 5 h, the mixture was warmed to room temperature during 30 min, and stirred at room temperature for 3 h. The mixture was then quenched with 5% aqueous sodium bisulfate solution and concentrated. The residue was extracted with ether (3 × 40 mL). The combined ether layers were washed with brine, dried ($MgSO_4$), filtered, concentrated, and flash chromatographed (hexane:ether = 1:1.5) to afford the title compound (2.44 g, 42.5%). ^1H NMR (400 MHz, $CDCl_3$): δ 3.70 (s, 3H), 3.19 (s, 3H), 2.69 (m, 2H), 2.52 (m, 2H), 1.97 (t, J = 2.7 Hz, 1H). Calcd for $C_7H_{11}NO_2$ (M^+): 141.0790. Found: 141.0803.

Preparation of 4-(*tert*-Butyldimethylsiloxy)-4-vinyl-1-octen-7-yne (4). To a solution of the above Weinreb amide[26] (5 g, 35.5 mmol) in THF (50 mL) was added vinylmagnesium bromide (0.97 M in THF) (73.2 mL, 71.0 mmol) at −78 °C. After being stirred at 0 °C for 1 h (GC showed no starting material present, and one major product was formed), the mixture was poured into ether–5% aqueous sodium bisulfate solution at 0 °C and extracted with ether (3 × 50 mL). The combined ether layers were washed with brine, dried ($MgSO_4$), and filtered. The solvent was removed by distillation to give the crude ketone for the next reaction.

To a solution of the above ketone in THF (50 mL) was added an excess of allylmagnesium bromide dropwise at −78 °C. After being stirred at 0 °C for 1 h (GC showed no starting material present, and one major product was formed), the mixture was poured into ether–saturated aqueous ammonium chloride at 0 °C and extracted with ether. The combined ether layers were washed with brine, dried ($MgSO_4$), filtered, and concentrated to give the crude alcohol for the next reaction.

To a solution of the above alcohol and 2,6-lutidine (8.2 mL, 70.1 mmol) in dichloromethane (35 mL) was added TBDMSOTf[27] (12.1 mL, 52.6 mmol) slowly at 0 °C. After being stirred at room temperature for 30 min (GC showed no starting material present), the mixture was diluted with dichloromethane and washed with saturated aqueous sodium bicarbonate solution and brine, respectively, dried (K_2CO_3), filtered, concentrated, and flash chromatographed (hexane) to give compound **4** as a colorless liquid (3.5 g, 37% overall three steps). IR ($CDCl_3$): 3314, 2134, 1636, 1252 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 5.72–5.84 (m, 2H), 5.02–5.22 (m, 4H), 2.34 (d, J = 7.0 Hz, 2H), 2.20 (m, 2H), 1.92 (t, J = 2.6 Hz, 1H), 1.81 (t, J = 8.3 Hz, 2H), 0.88 (s, 9H), 0.11 (s, 3H), 0.09 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.51, 133.90, 117.79, 113.81, 84.98, 76.91, 67.81, 45.47, 38.83, 26.17, 25.97, 18.53, 13.00, −1.96, −2.02. Calcd for $C_{15}H_{25}OSi$ ($M^+ - CH_3$): 249.1676. Found: 249.1680.

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Preparation of 3-Allyl-3-(*tert*-butyldimethylsiloxy)-6-methylenecyclohexene (7a). Substrate **4** (0.060 g, 0.23 mmol) followed by acetic acid (13.2 μL, 0.23 mmol) was added to a solution of $Pd_2(dba)_3$·$CHCl_3$[28] (0.006 g, 0.0058 mmol) and triphenylstibine (0.008 g, 0.023 mmol) in 2.0 mL of benzene. After being stirred at room temperature for 6 h, the mixture was concentrated and flash chromatographed (hexane) to give **7** (0.030 g, 50%) plus a mixture of isomers (0.016 g) (combined yield 77%). IR ($CDCl_3$): 3086, 3026, 2964, 2944, 2906, 2866, 1636, 1596, 1252, 1090, 1066, 1006, 836 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 6.10 (d, J = 9.8 Hz, 1H), 5.86 (ddd, J = 17.1, 10.3, 7.5 Hz, 1H), 5.70 (d, J = 9.8 Hz, 1H), 5.03 (m, 2H), 4.86 (m, 2H), 2.48 (m, 1H), 2.30 (m, 3H), 1.70 (m, 2H), 0.86 (s, 9H), 0.07 (s, 3H), 0.02 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.42, 135.17, 134.45, 130.28, 117.27, 112.36, 72.08, 47.41, 35.73, 26.90, 25.80, 18.25, –2.06, –2.42. Calcd for $C_{13}H_{23}OSi$ ($M^+ - C_3H_5$): 223.1519. Found: 223.1518.

Preparation of 1-Allyl-1-(*tert*-butyldimethylsiloxy)-2,3-bis(methylene)cyclopentane (8a). Run A. Substrate **4** (0.200 g, 0.76 mmol) followed by acetic acid (44.0 μL, 0.768 mmol) was added to $Pd_2(dba)_3$·$CHCl_3$ (0.020 g, 0.0193 mmol) and tri-*o*-tolylphosphine (0.023 g, 0.0757 mmol) in 5 mL of benzene. The mixture was stirred at room temperature for 8 h, concentrated, and flash chromatographed (hexane) to give a mixture of isomers (**7a**:**8a**:**9a** = 1.0:24.5:5.8) (0.147 g, 74%).

Run B. Substrate **4** (0.100 g, 0.38 mmol) followed by *o*-anisic acid (0.005 76 g, 0.038 mmol) was added to $Pd_2(dba)_3$·$CHCl_3$ (0.010 g, 0.0097 mmol) and tri-*o*-tolylphosphine (0.0115 g, 0.038 mmol) in 3 mL of benzene. The mixture was stirred at room temperature for 44 h, concentrated, and flash chromatographed (hexane) to give **8a** (0.026 g, 26%) plus a mixture of isomers (0.016 g) (combined yield 42%). ^1H NMR (400 MHz, $CDCl_3$): δ 5.87 (m, 1H), 5.44 (s, 1H), 5.39 (t, J = 2.3 Hz, 1H), 5.02 (m, 3H), 4.89 (bs, 1H), 2.46 (m, 1H), 2.38 (dd, J = 14.0, 6.5 Hz, 1H), 2.28 (m, 2H), 1.76 (m, 2H), 0.86 (s, 9H), 0.04 (s, 3H), 002 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.38, 146.55, 134.89, 117.05, 105.22, 82.73, 45.01, 36.96, 29.32, 25.83, 18.28, –2.42, –2.73. Calcd for $C_{16}H_{28}OSi$ (M^+): 264.1910. Found: 264.1907.

Preparation of 5-(*tert*-Butyldimethylsiloxy)-5-vinyl-1-nonen-8-yne (5). To a solution of the Weinreb amide (0.52 g, 3.69 mmol) in THF (10 mL) was added an excess of 3-butenylmagnesium bromide at 0 °C.[29] After reaction and workup as for the preparation of **4**, the solvent was removed by distillation to give the crude ketone for the next reaction.

To a solution of the above ketone in THF (10 mL) was added an excess of vinylmagnesium bromide at 0 °C. After reaction and workup as before, the combined ether layers were concentrated to give the crude alcohol for the next reaction.

To a solution of the above alcohol and 2,6-lutidine (0.85 mL, 7.38 mmol) in dichloromethane (4 mL) was added TBDMSOTf (1.25 mL, 5.53 mmol) slowly at 0 °C. After reaction and workup as before, flash chromatography (hexane) gave **5** (0.197 g, 19% overall three steps). IR ($CDCl_3$): 3291, 2111, 1639, 1255, 1044, 832 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 5.79 (ddd, J = 17.2, 10.4 , 6.8 Hz, 1H), 5.73 (dd, J = 17.2, 10.8 Hz, 1H), 5.20 (dd, J = 17.2, 1.2 Hz, 1H), 5.11 (dd, J = 10.8 , 1.2 Hz, 1H), 5.00 (dd, J = 17.2, 1.2 Hz, 1H), 4.94 (dd, J = 10.8, 1.2 Hz, 1H), 2.20 (m, 2H), 2.05 (m, 2H), 1.92 (t, J = 2.5 Hz, 1H), 1.82 (m, 2H), 1.62 (m, 2H), 0.90 (s, 9H), 0.10 (s, 3H), 0.09 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.50, 138.62, 114.30, 113.92, 84.90, 67,86, 39.69, 39.26, 28.24, 25.99, 18.57, 13.19, –2.10. Calcd for $C_{16}H_{27}OSi$ ($M^+ - CH_3$): 263.1832. Found: 263,1827.

Preparation of 3-(3′-Butenyl)-3-(*tert*-butyldimethylsiloxy)-6-methylenecyclohexene (7b). Substrate **5** (0.0632 g, 0.23 mmol) followed by acetic acid (13.2 μL, 0.23 mmol) was added to $Pd_2(dba)_3$·$CHCl_3$ (0.0060 g, 0.0058 mmol) and trimesityl phosphite (0.009 96 g, 0.023 mmol) in 2 mL of benzene. The mixture was stirred at room temperature for 48 h, concentrated, and flash chromatographed (hexane) to give compound **7b** (0.038 g, 60%). IR ($CDCl_3$): 1637, 1595, 1252, 1103, 1067, 1008, 840 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 6.09 (d, J = 10.0 Hz, 1H), 5.83 (ddd, J = 16.8, 10.0, 6.4 Hz, 1H), 5.69 (d, J = 10.0 Hz, 1H), 5.00 (bd, J = 16.8 Hz, 1H), 4.93 (bd, J = 10.0 Hz, 1H), 4.86 (bs, 1H), 4.85 (bs, 1H), 2.50 (m, 1H), 2.32 (m, 1H), 2.15 (m, 2H), 1.78 (m, 1H), 1.64 (m, 2H), 1.56 (m, 1H), 0.86 (s, 9H), 0.07 (s, 3H), 0.02 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.49, 139.27, 135.67, 129.95, 114.02, 112.17, 72.27, 42.01, 35.76, 27.99, 27.08, 25.81, 18.25, –2.09, –2.36. Calcd for $C_{17}H_{30}OSi$ (M^+): 278.2067. Found: 278.2071.

Preparation of 1-Butenyl-1-(*tert*-butyldimethylsiloxy)-2,3-bis(methylene)cyclopentane (8b). Substrate **5** (0.0385 g, 0.138 mmol) followed by acetic acid (1.6 μL, 0.0276 mmol) was added to $Pd_2(dba)_3$·$CHCl_3$ (0.003 58 g, 0.003 46 mmol) and tri-*o*-tolylphosphine (0.006 29 g, 0.0207 mmol) in 1.0 mL of benzene. The mixture was stirred at room temperature for 48 h, concentrated, and flash chromatographed (hexane) to give **8** as a colorless oil (0.0195 g, 51%). IR ($CDCl_3$): 1640, 1472, 1256, 1194, 1105 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 5.84 (m, 1H), 5.43 (s, 1H), 5.40 (t, J = 2.1 Hz, 1H), 5.03 (s, 1H), 5.00 (d, J = 17.3 Hz, 1H), 4.93 (d, J = 10.2 Hz, 1H), 4.88 (s, 1H), 2.45 (m, 1H), 2.30 (m, 1H), 2.15 (m, 2H), 1.60–1.87 (M, 3H), 1.54 (m, 1H), 0.87 (s, 9H), 0.03 (s, 3H), 0.02 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 153.69, 146.81, 139.50, 114.07, 105.32, 82.85, 38.98, 37.56, 29.13, 28.13, 25.68, 18.10, –2.75, –3.10. Calcd for $C_{17}H_{30}OSi$ (M^+): 278.2066. Found: 278.2051.

Preparation of *cis*-4-[1′,1′-Bis(methoxycarbonyl)-3′-butynyl]-2-cyclopenten-1-ol (11a). Epoxycyclopentene (0.500 g, 6.1 mmol) was added slowly at 0 °C over 2 h to a solution of $Pd_2(dba)_3$·$CHCl_3$ (0.158 g, 0.153 mmol) and dppe (0.243 g, 0.610 mmol) in THF (8 mL) containing dimethyl propargylmalonate[2a] (1.24 g, 7.32 mmol). After being stirred at 0 °C for 3 h and room temperature overnight, the mixture was concentrated and flash chromatographed (hexane:ether = 1:1.5) to give **11** as an oil (0.840 g, 54.5%). IR ($CDCl_3$): 3560, 3310, 2258, 1726, 1435, 1285, 1230, 1190, 1050 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 6.01 (m, 1H), 5.87 (m, 1H), 4.76 (m, 1H), 3.76 (s, 3H), 3.73 (s, 3H), 3.49 (m, 1H), 2.87 (d, J = 2.7 Hz, 2H), 2.55 (ddd, J = 14.1, 7.9, 8.6 Hz, 1H), 2.04 (t, J = 2.7 Hz, 1H), 1.80 (bs, 1H), 1.60 (ddd, J = 14.4, 5.6, 4.1 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.50, 170.45, 135.53, 134.29, 78.99, 76.08, 71.75, 60.00, 52.57, 52.44, 47.40, 35.40, 23.26. Calcd for $C_{13}H_{16}O_5$ (M^+): 252.0998. Found: 252.1010.

Preparation of *cis*-3-[1′,1′-Bis(methoxycarbonyl)-3′-butynyl]-5-[(methoxycarbonyl)oxy]cyclopentene (12a). To a solution of alcohol **11a** (0.810 g, 3.2 mmol), DMAP (0.02 g), and pyridine (1.30 mL, 16.0 mmol) in dichloromethane (5 mL) was added methyl chloroformate (1.23 mL, 16.0 mmol) at 0 °C. After being stirred at 0 °C for 10 min and at room temperature overnight, the mixture was diluted with dichloromethane, washed with water and brine, dried ($MgSO_4$), filtered, concentrated, and flash chromatographed (hexane:ether = 3:1) to give the carbonate **12a** (0.682 g, 69%). IR ($CDCl_3$): 3311, 1735, 1440, 1341, 1265, 1230, 1200, 1058, 1040 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 6.19 (m, 1H), 5.88 (m, 1H), 5.52 (m, 1H), 3.76 (s, 3H), 3.72 (s, 3H), 3.60 (m, 1H), 2.84 (d, J = 2.6 Hz, 2H), 2.62 (dt, J = 14.7, 8.2 Hz, 1H), 2.02 (t, J = 2.6 Hz, 1H), 1.72 (ddd, J = 14.7, 5.7, 4.2 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.06, 169.86, 155.66, 137.76, 130.52, 82.09, 78.73, 71.84, 59.81, 54.46, 52.63, 52.15, 46.62, 31.83, 23.03. Calcd for $C_{14}H_{14}O_6$ ($M^+ - CH_3OH$): 278.0790. Found: 278.0793.

Preparation of *cis*-3-[1′,1′-Bis(methoxycarbonyl)-3′-butenyl]-5-[1′,1′-bis(methoxycarbonyl)-3′-butynyl]cyclopentene (10a). To a suspension of sodium hydride (0.0144 g, 0.60 mmol) in THF (0.5 mL) was added dimethyl allylmalonate (0.103 g, 0.60 mmol). In a separate flask, a solution of carbonate **12a** (0.200 g, 0.650 mmol) in THF (0.5 mL) was added to $Pd(PPh_3)_4$ (0.0289 g, 0.025 mmol) and triphenylphosphine (0.0131 g, 0.050 mmol) in THF (1.0 mL), followed by a clear solution of the anion from the first flask. The combined mixture was stirred and heated at reflux for 1.5 h. The mixture was concentrated and flash chromatographed (hexane:ether = 2.5:1 to 2:1 to 1:1) to afford compound **10a** (0.130 g, 53%). IR ($CDCl_3$): 3311, 2259, 1730, 1638, 1435, 1290, 1260, 1225, 1141 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 5.85 (m, 2H), 5.69 (m, 1H), 5.10 (m, 2H), 3.75 (s, 3H), 3.71 (s, 3H), 3.70 (s, 3H), 3.67 (s, 3H), 3.60 (m, 1H), 3.35 (m, 1H), 2.80 (d, J = 2.6 Hz, 2H), 2.62 (m, 2H), 2.15 (dt, J = 12.8, 7.8 Hz, 1H), 2.00 (t, J = 2.6 Hz, 1H), 1.36 (dt, J = 12.8, 10.0 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.31, 170.82, 170.43, 169.98, 133.07, 132.76, 132.30, 119.11, 78.98, 71.39, 60.64, 59.49, 52.49, 52.24, 52.05, 51.84, 47.47, 47.24, 37.40, 27.12, 22.76. Calcd for $C_{20}H_{23}O_7$ ($M^+ - CH_3O$): 375.1444. Found: 375.1427. Anal. Calcd for $C_{21}H_{26}O_8$: C, 62.06; H, 6.45. Found: C, 62.20; H, 6.43.

Preparation of 5,5,9,9-Tetrakis(methoxycarbonyl)-3,11-bis(methylene)-tricyclo[6.3.0.0^{2,6}]undecane (13). Acetic acid (1.7 μL, 0.030 mmol) followed by substrate **10a** (0.012 g, 0.03 mmol) was added to $Pd_2(dba)_3$·$CHCl_3$ (0.000 78 g, 0.000 754 mmol) and triphenylphosphine (0.000 79 g, 0.003 02 mmol) in toluene (1.0 mL). The reaction mixture was stirred at 105 °C for 4 h, cooled, concentrated, and flash chromatographed (hexane:ether = 2:1) to give compound **13** (0.0070 g, 57%). IR ($CDCl_3$): 1730, 1456, 1432, 1271, 1233, 1219 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 5.06 (bs, 2H), 4.89 (bs, 2H), 3.70 (s, 6H), 3.69 (s, 6H), 3.41 (m, 2H), 3.24 (m, 2H), 3.03 (bd, J = 16.0 Hz, 2H), 2.63 (d, J = 16.0 Hz, 2H), 1.58 (dt, J = 12.4, 7.2 Hz, 1H), 0.96 (dt, J = 12.4, 12 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.74, 170.19, 146.04, 112.36, 60.98,

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(29) The order of addition of the two Grignard reagents is critical.

52.78, 52.48, 51.11, 50.23, 39.74, 30.63. Calcd for $C_{21}H_{26}O_8$: 406.1628. Found: 406.1617.

Preparation of *cis*-4-[(*p*-Tolylsulfonyl)-1′-aza-1′,3′-butenyl]-2-cyclopenten-1-ol (11b). A solution of allyl ethyl carbonate (0.78 g, 6.0 mmol) in THF (1.0 mL) was added to a room temperature mixture of *p*-toluenesulfonamide (1.54 g, 9.0 mmol), $Pd_2(dba)_3$ (0.110 g, 0.12 mmol), and triphenylphosphine (0.253 g, 0.96 mmol) in THF (5 mL) treated with BSA (*O,N*-bis(trimethylsilyl)acetamide) (2.44 g, 12.0 mmol). The reaction mixture was stirred at room temperature overnight, concentrated, and flash chromatographed (hexane:ether = 4:1 to 2:1) to give *N*-allyl-*p*-toluenesulfonamide (0.95 g, 75%). IR ($CDCl_3$): 3383, 3288, 2927, 1673, 1648, 1599, 1333, 1162, 1095, 1064 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.75 (d, J = 8.2 Hz, 2H), 7.31 (d, J = 8.2 Hz, 2H), 5.71 (m, 1H), 5.16 (dd, J = 17.2, 1.3, 1H), 5.10 (dd, J = 10.2, 1.2 Hz, 1H), 4.40 (m, 1H), 3.59 (t, J = 6.1 Hz, 2H), 2.43 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.68, 137.09, 133.13, 129.86, 127.27, 117.74, 45.57, 21.26.

The monoepoxide of cyclopentadiene (0.489 g, 5.96 mmol) was added very slowly at 0 °C to a mixture of *N*-allyl-*p*-toluenesulfonamide (0.84 g, 3.98 mmol), $Pd_2(dba)_3$ (0.0729 g, 0.0796 mmol), and dppe (0.1267 g, 0.318 mmol) in THF (4 mL) treated with BSA(1.21 g, 5.96 mmol). The mixture was stirred at room temperature for 24 h and concentrated to give a residue, which was dissolved in ether. The ether solution was washed with aqueous hydrochloric acid solution (5%), saturated aqueous sodium bicarbonate solution, and brine, respectively, dried ($MgSO_4$), filtered, concentrated, and chromatographed (hexane:ether = 1:3) to give compound **11b** as an oil (0.70 g, 60%). IR ($CDCl_3$): 3610, 1600, 1336, 1159, 1092 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.71 (d, J = 8.1 Hz, 1H), 7.29 (d, J = 8.1 Hz, 1H), 5.92 (m, 1H), 5.58 (m, 1H), 5.60 (m, 1H), 5.22 (dd, J = 17.2, 1.4 Hz, 1H), 5.13 (dd, J = 10.2, 1.4 Hz, 1H), 4.85 (m, 1H), 4.64 (m, 1H), 3.73 (m, 2H), 2.55 (m, 1H), 2.43 (s, 3H), 1.90 (bs, 1H), 1.43 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.56, 137.74, 137.16, 136.14, 133.32, 129.86, 127.40, 117.34, 74.64, 62.16, 46.59, 38.23, 21.29. Calcd for $C_{15}H_{26}NO_3S$ (M^+): 293.1086. Found: 293.1069.

Preparation of *cis*-3-[(*p*-Tolylsulfonyl-1′-aza-1′,3′-butenyl]-5-[(methoxycarbonyl)oxy]cyclopentene (12b). To a mixture of alcohol **11b** (0.43 g, 1.47 mmol), DMAP (0.01 g), and pyridine (0.36 mL, 4.41 mmol) in dichloromethane (2.5 mL) was added methyl chloroformate (0.34 mL, 4.41 mmol) at 0 °C. After being stirred at room temperature overnight, the mixture was diluted with dichloromethane, washed with water, saturated aqueous $CuSO_4$ solution, and brine, dried ($MgSO_4$), filtered, concentrated, and flash chromatographed (hexane:ether = 1:2) to give carbonate **12b** (0.32 g, 62%). IR ($CDCl_3$): 1745, 1599, 1444, 1341, 1271, 1161, 1092 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.71 (d, J = 8.2 Hz, 1H), 7.30 (d, J = 8.1 Hz, 1H), 5.95 (m, 1H), 5.84 (m, 1H), 5.76 (m, 1H), 5.37 (m, 1H), 5.20 (dd, J = 17.1, 1.3 Hz, 1H), 5.20 (dd, J = 10.3, 1.3 Hz, 1H), 5.00 (m, 1H), 3.75 (s, 3H), 3.71 (dd, J = 16.6, 5.6 Hz, 1H), 3.56 (dd, J = 16.6, 5.8 Hz, 1H), 2.59 (dt, J = 15.1, 8.2 Hz, 1H), 2.43 (s, 3H), 1.49 (dt, J = 15.1, 4.4 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.37, 143.68, 137.46, 136.58, 135.91, 132.74, 129.95, 127.37, 117.46, 80.34, 61.56, 54.65, 45.62, 34.28, 21.29. Calcd for $C_{10}H_{14}NO_3$-(M^+ – Ts): 196.0974. Found: 196.0982.

Preparation of *cis*-3-[(*p*-Tolylsulfonyl)-1′-aza-1′,3′-butenyl]-5-[1′,1′-bis(methoxycarbonyl)-3′-butynyl]cyclopentene (10b). To a suspension of sodium hydride (pentane-washed) (60%, 0.0776 g, 1.94 mmol) in THF (1 mL) was added dimethyl propargylmalonate (0.330 g, 1.94 mmol). The mixture was stirred at room temperature for 20 min.

A solution of carbonate **12b** (0.278 g, 0.79 mmol) in THF (1.5 mL) followed by a clear solution of the anion from the first flask was added to a separate flask charged with $Pd(Ph_3P)_4$ (0.005 65 g, 0.0485 mmol) and triphenylphosphine (0.002 54 g, 0.097 mmol) in 0.5 mL of THF at room temperature. The reaction mixture was heated at reflux for 1 h, cooled, concentrated, and flash chromatographed (hexane:ether = 4:3) to give compound **10b** as an oil (0.320 g, 91%). IR ($CDCl_3$): 3305, 2250, 1732, 1599, 1439, 1340 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.70 (d, J = 8.2 Hz, 2H), 7.30 (d, J = 8.2 Hz, 2H), 5.98 (m, 1H), 5.81 (m, 1H), 5.35 (m, 1H), 5.20 (dd, J = 17.1, 1.3 Hz, 1H), 5.11 (dd, J = 10.2, 1.3 Hz, 1H), 5.01 (m, 1H), 3.74 (s, 3H), 3.67 (s, 3H), 3.62 (m, 2H), 3.44 (m, 1H), 2.80 (dd, J = 17.3, 2.6 Hz, 1H), 2.77 (dd, J = 17.3, 2.6 Hz, 1H), 2.43 (s, 3H), 2.30 (dt, J = 13.3, 7.8 Hz, 1H), 2.00 (t, J = 2.6 Hz, 1H), 1.44 (dt, J = 13.3, 9.2 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.11, 169.87, 143.38, 138.09, 136.09, 135.48, 131.60, 128.77, 127.44, 117.06, 78.66, 71.68, 63.20, 59.30, 52.49, 52.26, 46.28, 45.76, 30.66, 22.96, 21.17. Calcd for $C_{16}H_{20}NO_4$(M^+ – 1): 290.1393. Found: 290.1396.

Preparation of 9,9-Bis(methoxycarbonyl)-3,11-bis(methylene)-5-(*p*-tolylsulfonyl)-5-azatricyclo[6.3.0.0^{2,6}]undecane (16). Acetic acid (1.6 μL, 0.0278 mmol) followed by substrate **10b** (0.062 g, 0.139 mmol) was added at room temperature to a mixture of $Pd_2(dba)_3$·$CHCl_3$ (0.0036 g, 0.0035 mmol) and triphenylphosphine (0.003 64 g, 0.0139 mmol) in benzene (3 mL). The reaction mixture was heated at 80 °C for 14 h, cooled, concentrated, and flash chromatographed (hexane:ether = 2:1 to 1:2) to give **16** (0.025 g, 40%). IR ($CDCl_3$): 1733, 1436, 1347, 1163, 1094 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.67 (d, J = 7.9 Hz, 2H), 5.00 (bs, 1H), 4.94 (bs, 1H), 4.90 (bs, 1H), 4.86 (bs, 1H), 3.94 (bd, J = 14.7 Hz, 1H), 3.88 (m, 1H), 3.76 (bd, J = 14.7 Hz, 1H), 3.74 (s, 3H), 3.69 (s, 3H), 3.35 (m, 1H), 3.34 (bd, J = 16.1 Hz, 1H), 3.21 (m, 2H), 2.66 (bd, J = 16.1 Hz, 1H), 2.42 (s, 3H), 2.00 (ddd, J = 15.0, 9.8, 7.0 Hz, 1H), 1.92 (ddd, J = 15.0, 8.3, 4.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.89, 170.07, 146.46, 143.61, 143.52, 133.62, 129.63, 127.81, 111.72, 108.99, 66.71, 62.31, 54.69, 54.57, 52.78, 52.57, 50.85, 50.42, 40.01, 34.82, 21.53. Calcd for $C_{23}H_{27}NO_6S$: 445.1560. Found: 445.1556.

Preparation of 1-Allyl-1-(methoxycarbonyl)-2-methylenecyclopentane (18, *n* = 1, X = CH$_2$). To a slurry of sodium hydride (pentane-washed) (2.0 g, 83 mmol) in THF (120 mL) was added methyl 2-oxocyclopentanecarboxylate (11.24 g, 79.0 mmol) at a rate to maintain a controlled evolution of hydrogen at 0 °C. When gas evolution was complete, allyl bromide (8.21 mL, 94.9 mmol) was added at 0 °C. Having been stirred at room temperature overnight, the mixture was quenched with water, extracted with ether, washed with brine, dried ($MgSO_4$), filtered, and concentrated to give the 2-allyl-2-(methoxycarbonyl)cyclopentanone (12.95 g, 90%).

Diiodomethane (5.40 mL, 67.48 mmol) was added at 25 °C to a stirred suspension of zinc (activated by washing with 5% aqueous HCl) in THF (150 mL) under nitrogen.[30] After 45 min, a solution of titanium(IV) chloride in dichloromethane (13.50 mL, 13.50 mmol) was added at 0 °C, and the resulting dark brown mixture was stirred at 25 °C for 30 min. A solution of 2-allyl-2-(methoxycarbonyl)cyclopentanone (2.46 g, 13.50 mmol) in THF (5 mL) was added dropwise at 25 °C. The mixture was stirred at room temperature for 1.5 h, then filtered through celite. The filtrate was washed with 1 N HCl, water, saturated aqueous sodium bicarbonate, and brine, dried ($MgSO_4$), filtered, concentrated, and flash chromatographed (5% ether/hexane) to give the title product (0.41 g, 17%). IR ($CDCl_3$): 2259, 1719, 1640, 1433, 1231, 1211, 1159 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 5.70 (m, 1H), 5.05 (m, 4H), 3.67 (s, 3H), 2.68 (dd, J = 13.9, 7.0 Hz, 1H), 2.40 (m, 2H), 2.26 (m, 2H), 1.77 (m, 1H), 1.68 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.54, 154.63, 134.78, 117.76, 107.65, 55.88, 52.06, 42.92, 34.68, 33.88, 23.92. Calcd for $C_{11}H_{16}O_2$ (M^+): 180.1150. Found: 180.1142.

Preparation of 1-Allyl-1-[1′-(*tert*-butyldimethylsiloxy)-3′-butynyl]-2-methylenecyclopentane (17b). A solution of LAH in THF (3.05 mL, 3.05 mmol) was added at 0 °C to the above ester (0.55 g, 3.05 mmol) dissolved in THF (10 mL). After being stirred at 0 °C for 30 min, the mixture was quenched with water (3 mL) and 2 N sodium hydroxide (4 mL) and filtered. The filtrate was diluted with ether. The layers were separated. The organic layer was washed with brine, dried ($MgSO_4$), filtered, and concentrated to give crude alcohol **19** (n = 1), which was directly used in the next reaction. The spectral analysis was based on a sample purified by flash chromatography. IR ($CDCl_3$): 3620, 3562, 3075, 2960, 2879, 1638, 1433, 1039 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 5.77 (m, 1H), 5.06 (m, 3H), 4.80 (s, 1H), 3.45 (dd, J =11.0, 6.7 Hz, 1H), 3.35 (dd, J =11.0, 5.6 Hz 1H), 2.38 (m, 2H), 2.22 (m, 2H), 1.62 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.75, 135.46, 117.45, 106.08, 67.86, 50.29, 40.94, 34.24, 33.69, 22.58. Calcd for $C_{10}H_{16}O$: 152.1201. Found: 152.1196.

The above alcohol in dichloromethane (2 mL) was added to a solution of oxalyl chloride (0.31 mL, 3.4 mmol) in dichloromethane (8 mL) at –50 to –60 °C to which DMSO (0.52 mL, 0.73 mmol) was added.[31] After 15 min, triethylamine (1.07 mL, 15.3 mmol) was added. The reaction mixture was stirred for 5 min at –50 to –60 °C and then allowed to warm to room temperature. Water was added. The mixture was extracted with dichloromethane. The organic layer was washed with brine, dried ($MgSO_4$), filtered, and concentrated to give crude aldehyde **20** (n = 1). The spectral analysis was based on a purified sample. IR ($CDCl_3$): 3078, 2961, 2720, 1716, 1640, 1430, 995 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 9.30 (s, 1H), 5.67 (m, 1H), 5.21 (t, J = 1.9 Hz, 1H), 5.07 (m, 2H),

(30) Cf.: Hibino, J.-I.; Okazoe, T.; Takai, K.; Nozaki, H. *Tetrahedron Lett.* **1985**, *26*, 5579.

(31) Cf.: Mancuso, A. J.; Huang, S.-L.; Swern, D. *J. Org. Chem.* **1978**, *43*, 2480.

4.88 (t, J = 2.2 Hz, 1H), 2.50 (dd, J = 14.0, 7.4 Hz, 1H), 2.40 (m, 2H), 2.31 (dd, J = 14.0, 7.0 Hz, 1H), 2.17 (m, 1H), 1.69 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 200.91, 152.07, 133.95, 110.29, 109.79, 60.73, 39.22, 33.94, 31.22, 23.49. Calcd for $C_{10}H_{14}O$ (M^+): 150.1045. Found: 150.1038.

A mixture of propargyl bromide (0.49 mL, 5.39 mmol) and the above aldehyde in THF (3 mL) was added dropwise to zinc (0.286 g, 4.38 mmol) with ice-bath cooling.[32] After being stirred at room temperature for 1 h, the mixture was poured into water, acidified by 20% aqueous acetic acid solution, and then extracted with ether. The organic layer was washed with saturated sodium bicarbonate and brine, dried ($MgSO_4$), filtered, and concentrated to give a crude alcohol.

To a solution of the above alcohol and 2,6-lutidine (0.69 mL, 6.10 mmol) in dichloromethane was added TBDMSOTf (1.05 mL, 4.67 mmol) slowly at 0 °C. The mixture was stirred at room temperature for 30 min and then diluted with dichloromethane. The organic layer was washed with water, saturated aqueous sodium bicarbonate, and brine, dried ($MgSO_4$), filtered, concentrated, and flash chromatographed (hexane) to give the title compound (0.20 g, 21.6% overall four steps). IR ($CDCl_3$): 3310, 3073, 2955, 2930, 2882, 2858, 2112, 1646, 1637, 1460, 1251, 1085, 835 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.75 (m, 1H), 4.97–5.09 (m, 3H), 4.85 (m, 0.3H), 4.70 (m, 0.7H), 3.76 (m, 1H), 2.47–2.57 (m, 1H), 2.13–2.40 (m, 5H), 1.90–2.00 (m, 2H), 1.47–1.58 (m, 3H), 0.93 (s, 6.3H), 0.89 (s, 2.7H), 0.20 (s, 2.1H), 0.14 (s, 0.9H), 0.12 (s, 2.1H), 0.06 (s, 0.9H). ^{13}H NMR (75 MHz, $CDCl_3$): δ 156.77, 156.23, 135.99, 117.20, 117.02, 106.97, 106.52, 84.01, 83.59, 78.25, 77.17, 70.20, 69.99, 53.93, 53.82, 43.48, 41.79, 35.76, 35.50, 32.33, 31.55, 25.96, 25.89, 23.89, 23.25, 23.09, 18.15, 18.08, –3.58, –4.34, –4.78, –4.95. Calcd for $C_{18}H_{29}OSi$ ($M^+ - CH_3$): 289.1988. Found: 289.2001.

Preparation of 2-(*tert*-Butyldimethylsiloxy)-4,7-bis(methylene)tricyclo-[3.3.3.0^{1,5}]undecane (21). Acetic acid (2.1 μL, 0.0325 mmol) followed by substrate **17b** (0.022 g, 0.075 mmol) was added to $Pd_2(dba)_3$·$CHCl_3$ (0.001 95 g, 0.000 19 mmol) and triphenylphosphine (0.001 97 g, 0.0075 mmol) in 2.0 mL of benzene. The reaction mixture was stirred at 55 °C under nitrogen for 1.5 h, cooled, concentrated, and chromatographed (hexane) to afford propellane **21** (0.017 g, 77%). IR ($CDCl_3$): 1659, 1465, 1260, 1140, 840 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.66–4.82 (m, 4H), 3.67 (m, 1H), 1.50–2.46 (m, 2H), 0.88, 0.87 (s, 9H), 0.04, 0.03 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.90, 156.51, 152.74, 152.08, 105.64, 105.46, 104.65, 104.31, 77.56, 77.21, 63.92, 63.53, 62.71, 62.28, 48.66, 46.50, 46.37, 42.86, 42.24, 42.10, 40.82, 39.57, 39.05, 34.21, 26.20, 25.78, 25.47, 18.04, –4.48, –4.84. Calcd for $C_{15}H_{23}OSi$ ($M^+ - {}^tC_4H_9$): 247.1518. Found: 247.1530.

Preparation of 1-Allyl-1-(1′-acetoxy-3′-butynyl)-2-methylenecyclohexane (17d). To a slurry of sodium hydride (60%, 3.36 g, 84 mmol) (washed with pentane) in THF (180 mL) was added ethyl 2-oxocyclohexanecarboxylate (13.6 g, 80 mmol) at a rate to maintain a controlled evolution of hydrogen at 0 °C. When gas evolution was complete, allyl bromide (8.3 mL, 96.0 mmol) was added. After being stirred at room temperature overnight, the mixture was quenched with water, extracted with ether, washed with brine, dried ($MgSO_4$), filtered, and concentrated to give 2-allyl-2-(ethoxycarbonyl)cyclohexanone (16.4 g, 97.6%).

A solution of methyltriphenylphosphonium iodide (8.08 g, 20 mmol) in DMSO (15 mL) was added to an ice cold solution of dimsyl sodium prepared by heating sodium hydride (60%, 0.8 g, 20 mmol) (washed with pentane) in dry DMSO (20 mL) at 75–80 °C for 1 h.[33] The above compound (4.2 g, 20 mmol) was added to the resulting dark red solution of the ylide at 0 °C. After being stirred at room temperature for 24 h, the mixture was quenched with water, extracted with ether, washed with water (2×) and brine, dried ($MgSO_4$), filtered, concentrated, and flash chromatographed (hexane:ether = 8:1) to give **18** (n = 2, X = CH_2) (2.5 g, 60.6%). IR ($CDCl_3$): 1719, 1641, 1445, 1210 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.76 (m, 1H), 5.05 (m, 2H), 4.90 (s, 1H), 4.80 (s, 1H), 4.14 (m, 2H), 2.64 (dd, J = 13.8, 6.8 Hz, 1H), 2.20–2.40 (m, 3H), 2.03 (td, J = 12.2, 3.9 Hz, 1H),1.70 (m, 1H), 1.61 (m, 2H), 1.37 (m, 1H), 1.25 (t, J = 7.1 Hz, 3H), 1.23 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 174.70, 150.32, 134.16, 117.84, 108.54, 60.37, 52.56, 41.08, 34.96, 34.86, 27.92, 22.77, 14.02. Calcd for $C_{13}H_{20}O_2$ (M^+): 208.1463. Found: 208.1480.

To a solution of the above compound (2.13 g, 10.3 mmol) in THF (20 mL) was added a solution of LAH in THF (10.3 mL, 10.3 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 30 min. Water (9 mL) followed by sodium hydroxide (2 N, 12 mL) was added. The mixture was stirred for 10 min and then filtered through Celite. The cake was washed with ether. The filtrate was diluted with ether. The layers were separated. The organic layer was washed with brine, dried ($MgSO_4$), filtered, and concentrated to give crude alcohol **19** (n = 2) (1.72 g) IR ($CDCl_3$): 3622, 3566, 1634, 1448, 1033, 992 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.80 (m, 1H), 5.08 (m, 2H), 4.93 (bs, 1H), 4.71 (bs, 1H), 3.65 (dd, J = 11.0, 5.5 Hz, 1H), 3.51 (dd, J = 11.0, 7.1 Hz, 1H), 2.45 (dd, J = 14.1, 7.1 Hz, 1H), 2.20 (m, 3H), 1.55 (m, 6H), 1.26 (dd, J = 7.1, 5.5 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 151.13, 135.12, 117.31, 109.29, 66.28, 44.19, 38.61, 33.45, 33.27, 27.56, 21.58. Calcd for $C_{11}H_{16}$ ($M^+ - H_2O$): 148.1252. Found: 148.1235.

A solution of the above alcohol (1.66 g, 10 mmol) in dichloromethane (10 mL) was added to a solution of oxalyl chloride (1.0 mL, 11 mmol) in dichloromethane (25 mL) at –50 to –60 °C to which DMSO (1.7 mL, 22 mmol) was added. After 15 min, triethylamine (7.0 mL, 50 mmol) was added. The mixture was stirred for 5 min and then allowed to warm to room temperature. Workup as for **20** (n = 1) gave aldehyde **20** (n = 2) (1.2 g, 74% overall two steps). IR ($CDCl_3$): 2728, 2710, 1719, 1638, 1446 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.39 (s, 1H), 5.70 (m, 1H), 5.00 (m, 3H), 4.74 (s, 1H), 2.51 (dd, J = 14.2, 7.1 Hz, 1H), 2.36 (dd, J = 14.2, 7.4 Hz, 1H), 2.28 (m, 1H), 2.00 (m, 2H), 1.60 (m, 3H), 1.50 (m, 1H), 1.35 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 203.99, 147.43, 133.45, 118.17, 111.07, 55.50, 37.25, 34.03, 30.86, 27.02, 21.69. Calcd for $C_{11}H_{16}O$ (M^+): 164.1202. Found: 164.1201.

A mixture of propargyl bromide (0.94 mL, 10.0 mmol) and aldehyde **20** (n = 2) (1.06 g, 6.46 mmol) in THF (6 mL) was added dropwise to zinc (activated by washing with 5% hydrochloric acid) (0.55 g, 8.4 mmol) at 0 °C. After being stirred at 0 °C for 1 h, workup as before for **17a** gave an alcohol **17c** with a diastereoisomeric ratio of 1.8:1.

Acetic anhydride (3.05 mL, 32.3 mmol) was added dropwise to a solution of the above alcohol in pyridine (15 mL) at 0 °C. After being stirred at room temperature overnight, the mixture was diluted with ether, washed with water, saturated aqueous $CuSO_4$ solution, and brine, dried ($MgSO_4$), filtered, concentrated, and flash chromatographed (5% ether in hexane) to give **17d** (0.75 g, 47% overall two steps). IR ($CDCl_3$): 3316, 1731, 1632, 1450, 1371, 1239 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.87 (m, 1H), 5.60 (dd, J = 9.0, 4.0 Hz, 0.7H), 5.50 (dd, J = 9.1, 3.4 Hz, 0.3H), 4.92–5.09 (m, 3H), 4.78 (s, 0.7H), 4.64 (s, 0.3 H), 2.40 (m, 4H), 2.22 (m, 2H), 2.13 (s, 2.1H), 2.06 (s, 0.9H), 1.96 (t, J = 2.7 Hz, 0.3H), 1.93 (t, J = 2.7 Hz, 0.7H), 1.27–1.80 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.67, 149.60, 148.85, 135.27, 134.85, 117.32, 117.05, 111.50, 111.22, 81.09, 80.96, 73.20, 71.72, 69.76, 69.68, 45.98, 45.94, 37.16, 36.42, 33.67, 33.26, 32.11, 32.00, 27.30, 26.85, 21.41, 21.06, 20.66, 20.58, 19.83, 19.62. Calcd for $C_{14}H_{18}$ (M^+ – HOAc): 186.1409. Found: 186.1421.

Preparation of 7-Acetoxy-9,11-bis(methylene)tricyclo[4.3.3.0^{1,6}]dodecane (22). Acetic acid (3.4 μL, 0.06 mmol) followed by substrate **17d** (0.0738 g, 0.3 mmol) was added at room temperature to a mixture of Pd_2-$(dba)_3$·$CHCl_3$ (0.0078 g, 0.0075 mmol) and triphenylphosphine (0.007 86 g, 0.030 mmol) in benzene (5.0 mL). After stirring at 50 °C for 3 h, the mixture was cooled, concentrated, and flash chromatographed (5% ether in hexane) to give propellane **22** (0.056 g, 76%). IR ($CDCl_3$): 3076, 2936, 2860, 1725, 1652, 1250 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.21 (dd, J = 8.3, 6.2 Hz, 0.7 H), 5.01 (t, J = 6.7 Hz, 0.3H), 4.88 (m, 4H), 3.08 (m, 1H), 2.05 (s, 0.9H), 2.03 (s, 2.1H), 1.23–2.58 (m, 16H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.47, 156.44, 153.21, 150.89, 149.83, 108.23, 106.61, 106.22, 105.62, 79.05, 76.05, 54.18, 53.98, 53.27, 53.19, 47.50, 42.45, 40.67, 40.05, 36.33, 36.04, 32.49, 30.95, 28.95, 25.75, 21.72, 21.27, 21.14, 20.79. Calcd for $C_{14}H_{18}$ (M^+ – HOAc): 186.1429. Found: 186.1392.

Preparation of 9-Methyl-11-methylenetricyclo[4.3.3.0^{1,6}]dodec-8-en-7-one (23). An excess of solid potassium carbonate was added to a solution of acetate **22** (0.050 g, 0.2 mmol) in methanol (2 mL). After being stirred at room temperature for 3 h, the mixture was filtered through cotton and the filtrate concentrated. The residue was dissolved in dichloromethane (2 mL) and some magnesium sulfate added. To the resultant suspension was added PCC (0.131 g, 0.6 mmol) in small portions. The mixture was stirred at room temperature for 2 h and filtered through a silica gel plug, and the filtrate was concentrated. The residue was dissolved in chloroform (1 mL) and one drop of DBU added. The reaction mixture was stirred at room temperature for 3 h, concentrated, and flash chromatographed (hexane:ether = 2.5:1 to 1:1) to give enone **23** (0.016 g, 36.6% overall three steps). IR ($CDCl_3$): 2941, 2860, 1689, 1619 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.90 (bs, 1H), 4.73 (bs, 2H), 2.46 (d, J = 15.6 Hz, 1H), 2.35 (bs, 2H), 2.24 (d, J = 15.6 Hz, 1H), 2.02 (d,

(32) Cf.: Friedrich, L. E.; deVera, N.; Hamilton, M. *Synth. Commun.* **1980**, *10*, 637.

(33) Cf.: Greenwald, R.; Chaykovsky, M.; Corey, E. J. *J. Org. Chem.* **1963**, *28*, 1128.

J = 1.2 Hz, 3H), 2.00 (m, 1H), 1.92 (m, 1H), 1.68 (m, 2H), 1.49 (m, 2H), 1.26 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 213.29, 181.94, 147.93, 130.05, 107.73, 57.34, 56.68, 43.28, 42.41, 29.65, 28.86, 18.36, 18.04, 14.53. Calcd for $C_{14}H_{18}O$ (M^+): 202.1358. Found: 202.1360.

Preparation of 2-Methylene-5-hexen-1-ol (25a). Methallyl alcohol (33.66 mL, 400.0 mmol) was added to a −78 °C stirred solution of TMEDA (120.7 mL, 800 mmol) and *n*-butyllithium (80.0 mL, 800.0 mmol) in dry ether (600 mL) mixed at 0 °C. The mixture was stirred and allowed to warm slowly to room temperature over 24 h. The resulting yellow suspension was cooled to −78 °C, and allyl bromide (25.4 mL, 300.0 mmol) in ether (50 mL) was added dropwise. After the mixture was stirred at −78 °C for 2 h, the cooling bath was removed. After being stirred for an additional 5 h, the mixture was quenched with saturated aqueous ammonium chloride solution. The aqueous layer was extracted with ether (3 × 50 mL). The combined ether layers were washed with water (200 mL), saturated aqueous $CuSO_4$ solution (3 × 150 mL), and brine (150 mL), respectively, dried ($MgSO_4$), filtered, concentrated, and distilled at 95–100 °C/20–25 mmHg to give alcohol **25a** as a colorless liquid (26.1 g, 78%). IR ($CDCl_3$): 3611, 3081, 2980, 1641, 1216, 1050, 1017 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.81 (m, 1H), 5.03 (dd, J = 17.3, 1.6 Hz, 1H), 5.05 (bs, 1 H), 4.97 (d, J = 10.5 Hz, 1H), 4.89 (bs, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 148.48, 138.29, 114.87, 109.67, 65.69, 31.95, 31.66. Calcd for $C_7H_{11}O$ (M^+ − 1): 111.0810. Found: 111.0814.

Preparation of 7,7-Bis(methoxycarbonyl)-5-methylene-1-decen-9-yne (26). To a solution of crude alcohol **25a** (3.73 g, maximum 33.3 mmol) (prepared from 48.9 mmol of methallyl alcohol), DMAP (0.02 g), and pyridine (13.50 mL, 166.5 mmol) in dichloromethane (40 mL) was added methyl chloroformate (12.90 mL, 166.5 mmol) slowly at 0 °C. After being stirred at 0 °C for 10 min and room temperature for 2 h, the mixture was diluted with dichloromethane, washed with water, saturated aqueous $CuSO_4$ solution, and brine, dried ($MgSO_4$), filtered, and concentrated. The residue was distilled (Kugelrohr, 110–120 °C at 4–5 mmHg) to give carbonate **25b** as a colorless liquid (2.60 g, 50% overall two steps). IR ($CDCl_3$): 1750, 1655, 1640, 1446, 1340,1270 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.81 (m, 1H), 4.94–5.10 (m, 4H), 4.58 (s, 2H), 3.79 (s, 3H), 2.21 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.93, 142.89, 137.93, 115.15, 113.40, 70.25, 54.70, 32.05, 31.41.

A solution of carbonate **25b** (0.312 g, 1.84 mmol) and dimethyl propargylmalonate (0.408 g, 2.4 mmol) in THF (1 mL) was added to a mixture of $Pd_2(dba)_3$·$CHCl_3$ (0.051 75 g, 0.05 mmol) and triphenylphosphine(0.105 g, 0.40 mmol) in dry THF (1 mL). The mixture was stirred at 40 °C overnight, concentrated, and flash chromatographed (hexane:ether = 6:1) to afford compound **26** as a colorless oil (0.400 g, 83%). IR ($CDCl_3$): 3315, 3080, 2960, 1739, 1640, 1440, 1295, 1210 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.77 (ddt, J = 17.0, 10.3, 6.6 Hz, 1H), 4.95 (m, 4H), 3.74 (s, 6H), 2.85 (s, 2H), 2.83 (d, J = 2.6 Hz, 2H), 2.18 (m, 2H), 2.04 (t, J = 2.6 Hz, 1H), 1.98 (m, 2H). ^{13} C NMR (75 MHz, $CDCl_3$): δ 170.80, 143.38, 138.14, 115.50 114.88, 79.09, 71.73, 56.54, 52.63, 37.22, 35.57, 31.88, 22.41. Calcd for $C_{14}H_{17}O_3$ (M^+ − CH_3O): 233.1178. Found: 233.1181.

Preparation of 3,3-Bis(methoxycarbonyl)-1,7-bis(methylene)spiro[4.4]-nonane (29). A solution of malonate **26** (0.132 g, 0.50 mmol) in benzene (1 mL) followed by acetic acid (2.9 μL, 0.05 mmol) was added to Pd_2-$(dba)_3$·$CHCl_3$ (0.012 94 g, 0.0125 mmol) and tri-*o*-tolylphosphine (0.030 44 g, 0.100 mmol) in 1 mL of benzene. The reaction mixture was stirred at room temperature overnight, concentrated, and flash chromatographed (hexane:ether = 10:1) to give spirane **29** as a colorless oil (0.112 g, 85%). IR ($CDCl_3$) 1730, 1650, 1440, 1260, 1176 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.86 (m, 4H), 3.73 (s, 3H), 3.72 (s, 3H), 3.10 (d, J = 16.5 Hz, 1H), 3.02 (d, J = 16.5 Hz, 1H), 238 (m, 6H), 1.70 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.41, 172.35, 155.20, 151.08, 106.06, 105.11, 57.67, 52.75, 52.27, 47.05, 46.05, 41.32, 39.63, 31.09. Calcd for $C_{15}H_{20}O_4$: 264.1362. Found: 264.1350. Anal. Calcd for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63, Found: C, 68.27; H, 7.75.

Preparation 7,7-Bis(phenylsulfonyl)-5-methylene-1-decen-9-yne (27). A solution of 4,4-bis(benzenesulfonyl)-1-butyne (0.390 g, 1.17 mmol) and carbonate **25b** (0.217 g, 1.27 mmol) in THF (1.5 mL) was added to a mixture of $Pd_2(dba)_3$·$CHCl_3$ (0.0234 g, 0.023 mmol) and triphenylphosphine(0.0474 g, 0.18 mmol) in THF (0.5 mL) at room temperature. The reaction mixture was stirred at 55 °C overnight, cooled, concentrated, and flash chromatographed (hexane:ether = 1.5:1) to give bis-sulfone **27** (0.31 g, 62%). IR ($CDCl_3$): 3309, 3074, 2926, 2258, 1637, 1582, 1448, 1332, 1310,1145,1085 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (dd, J = 7.3, 1.3 Hz, 4H), 7.70 (m, 2H), 7.56 (m, 4H), 5.8 (ddt, J = 17.0, 10.3, 6.7 Hz, 1H), 5.28 (s, 1H), 5.11 (d, J = 1.1 Hz, 1H), 5.02 (dd, J = 17.0, 1.8 Hz, 1H), 4.96 (dd, J = 10.3, 1.8 Hz, 1H), 3.40 (d, J = 2.8 Hz, 2H), 3.12 (s, 2H), 2.34 (m, 2H), 2.22 (m, 2H), 2.00 (t, J = 2.8 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 141.47, 138.24, 135.00, 131.93, 128.69, 117.95, 114.90, 90.67, 75.13, 36.22, 34.97, 32.23, 21.98. Anal. Calcd for $C_{23}H_{24}O_4S_2$: C, 64.46, H, 5.64. Found: C, 64.26, H, 5.26.

Preparation of 3,3-Bis(phenylsulfonyl)-1,7-bis(methylene)spiro[4.4]-nonane (30). To a solution of $Pd_2(dba)_3$·$CHCl_3$ (0.002 24 g, 0.0022 mmol), tri-*o*-tolylphosphine (0.0026 g, 0.0086 mmol), and bis-sulfone **27** (0.037 g, 0.086 mmol) in a NMR tube was added benzene-d_6 (0.8 mL) followed by acetic acid (4.95 μL, 0.086 mmol). The reaction was monitored by NMR spectroscopy. After standing for 16 h, the mixture was concentrated and flash chromatographed (hexane:ether = 2:1) to give compound **30** (0.033 g, 89%). IR ($CDCl_3$): 1658, 1583, 1450, 1429, 1325, 1310, 1145, 1075 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04 (m, 4H), 7.71 (m, 2H), 7.60 (m, 4H), 4.89 (bs, 1H), 4.86 (d, J = 1.2 Hz, 1H), 4.64 (t, J = 2.0 Hz, 1H), 4.62 (t, J = 1.7 Hz, 1H), 3.38 (dt, J = 17.5, 2.0 Hz, 1H), 3.20 (dt, J = 17.5, 1.7 Hz, 1H), 2.70 (s, 2H), 2.23–2.44 (m, 4H), 1.75 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 152.58, 150.44, 137.13, 136.89, 134.72, 131.55, 131.52, 128.89, 106.82, 105.64, 91.25, 53.03, 46.51, 42.79, 39.61, 39.33, 30.73. Calcd for $C_{17}H_{19}O_2S$ (M^+ − $PhSO_2$): 287.1107. Found: 287.1079.

Preparation of 2-[(*p*-Toluenesulfonamido)methyl]-1,5-hexadiene. Carbonate **25b** (0.364 g, 2.00 mmol) in THF (0.5 mL) was added at 0 °C to a mixture of *p*-toluenesulfonamide (0.514 g, 3.00 mmol), $Pd_2(dba)_3$ (0.0458 g, 0.0500 mmol), and triphenylphosphine (0.105 g, 0.400 mmol) in THF (2 mL) which was treated with BSA (0.814 g, 4.00 mmol). After being stirred at 0 °C for 30 min and room temperature for 3 h, the mixture was concentrated and flashed chromatographed (hexane:ether = 4:1 to 1:1) to give the title compound (0.42 g, 79%). IR ($CDCl_3$): 3382, 3283, 3080, 2981, 2930, 2859, 2258, 1636, 1596, 1490, 1436, 1402, 1350, 1156, 1090, 1055 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (d, J = 8.2 Hz, 2H), 7.32 (d, J = 8.2 Hz, 2H), 5.73 (ddt, J = 17.0, 10.3, 6.7 Hz, 1H), 4.98 (m, 2H), 4.92 (s, 1H), 4.86 (s, 1H), 4.42 (t, J = 6.2 Hz, 1H), 3.50 (d, J = 6.2 Hz, 2H), 2.44 (s, 3H), 2.12 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.03, 143.64, 137.89, 137.12, 129.84, 127.28, 115.06, 112.57, 47.76, 32.59, 31.34, 21.25. Calcd for $C_{13}H_{16}NO_2$ (M^+ − CH_3): 250.0902. Found: 250.0913.

Preparation of Methylene-7-(*p*-tolylsulfonyl)-7-aza-5,1-decen-9-yne (28a). After allowing a suspension of NaH (0.0543 g, 1.36 mmol) in THF (1 mL) and a solution of the above amide(0.300 g, 1.13 mmol) in THF (2 mL) to stir at room temperature for 30 min (the anion was not very soluble), propargyl bromide (0.40 mL, 4.52 mmol) was added. After heating at 65 °C for 4 h, the mixture was quenched with saturated aqueous ammonium chloride solution, concentrated, extracted with dichloromethane, washed with brine, dried ($MgSO_4$), filtered, concentrated, and flash chromatographed (hexane:ether = 4:1) to give **28a** (0.23g, 67%). IR ($CDCl_3$): 3308, 3075, 2980, 2920, 2254, 1645, 1638, 1598, 1346, 1329, 1309, 1159, 1081 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (d, J = 8.2 Hz, 2H), 7.30 (d, J = 8.2 Hz, 2H), 5.80 (ddt, J = 17.0, 10.3, 6.7 Hz, 1H), 4.96–5.09 (m, 4H), 4.05 (d, J = 2.4 Hz, 2H), 3.76 (s, 2H), 2.43 (s, 3H), 2.25 (m, 2H), 2.17 (m, 2H), 1.95 (t, J = 2.4 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.74, 142.50, 138.10, 136.18, 129.59, 128.00, 115.25, 115.07, 76.30, 73.76, 51.00, 35.31, 32.02, 21.30. Calcd for $C_{17}H_{21}NO_2S$: 303.1294. Found: 303.1303. Anal. Calcd for $C_{17}H_{21}NO_2S$: C, 67.30, H, 6.98, N, 4.62. Found: C, 67.39; H, 7.17; N, 4.44.

Preparation of 1,7-Bis(methylene)-3-(*p*-tolylsulfonyl)-3-azaspiro[4.4]-nonane (31). Acetic acid (2.2 μL, 0.038 mmol) followed by amide **28a** (0.0115 g, 0.038 mmol) was added to $Pd_2(dba)_3$·$CHCl_3$ (0.001 g, 0.000 97 mmol) and tri-*o*-tolylphosphine (0.003 45 g, 0.013 mmol) in 1.0 mL of benzene. The reaction mixture was stirred at room temperature for 10 h, concentrated, and chromatographed (hexane:ether = 4:1) to afford spirane **31** (0.0102 g, 88.7%). IR ($CDCl_3$): 3080, 2952, 2851, 1665, 1600, 1348, 1165, 1098 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (d, J = 8.1 Hz, 2H), 7.33 (d, J = 8.1 Hz, 2H), 4.96 (m, 4H), 3.91 (d, J = 14.0 Hz, 1H), 3.83 (d, J = 14.0 Hz, 1H), 3.09 (d, J = 9.2 Hz, 1H), 3.05 (d, J = 9.2 Hz, 1H), 2.45 (m, 1H), 2.44 (s, 3H), 2.30 (m, 1H), 2.29 (bs, 2H), 1.71 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.68, 149.65, 143.61, 132.62, 129.65, 127.80, 107.04, 104.92, 58.64, 52.72, 52.39, 44.01, 36.76, 30.87, 21.53. Calcd for $C_{17}H_{21}NO_2S$: 303.1294. Found: 303.1291.

Preparation of 11-Methoxy-7-(*p*-tolylsulfonyl)-7-aza-1-undecen-9-yne (28b). To a solution of 1,4-butynediol (176 g, 2.05 mmol) in THF (550 mL) was added dihydropyran (33.67 mL, 0.37 mmol), followed by PPTS (1 g, 0.003 98 mmol). Having been stirred at room temperature for 3 days, the mixture was diluted with ether, washed with water (4×) and

brine, dried ($MgSO_4$), filtered, and concentrated to give a mixture of mono- and diprotected products with a ratio of about 6:1 (46.7 g).

To a suspension of sodium hydride (60%, 12.8 g, 0.32 mmol) (washed with pentane) in THF (300 mL) was added slowly a solution of the above alcohol (46 g, 0.27 mmol) in THF (150 mL). The reaction mixture was stirred for 1 h at 0 °C. Methyl iodide (33.6 mL, 0.54 mmol) was added at 0 °C. The reaction mixture was stirred at room temperature for 2 h. Water was added carefully. The mixture was extracted with ether. The organic phase was washed with water and brine, dried ($MgSO_4$), filtered, and concentrated to give a residue, which was fractionally distilled (75–78 °C / 0.07–0.1 mmHg) to give 1-methoxy-4-(tetrahydropyranyloxy)-2-butyne (32 g, 47% overall two steps).

A solution of the above compound(15 g, 0.0815 mmol) in dichloromethane (20 mL) was added dropwise to a solution of triphenylphosphine bromine complex prepared from triphenylphosphine (22.42 g, 0.0856 mmol) and bromine (4.28 mL, 0.08313 mmol) at 0 °C in dichloromethane (150 mL).[34] After being stirred at 0 °C for 1.5 h, the mixture was poured into water, extracted with hexane, washed with saturated aqueous sodium bicarbonate solution and brine, dried ($MgSO_4$), filtered, and concentrated to give a residue, which was filtered through a silica gel plug, eluting with hexane. The filtrate was concentrated and distilled (80–90 °C / 50–60 mmHg) to give 1-bromo-4-methoxy-2-butyne(9.5 g, 71.5%). IR ($CDCl_3$): 1450, 1377, 1359, 1211, 1189, 1141 1096 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 4.15 (t, J = 1.9 Hz, 2H), 3.95 (t, J = 1.9 Hz, 2H), 3.38 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 82.71, 81.43, 59.77, 57.62, 13.87.

To a suspension of sodium hydride (60%, 0.134 g, 3.35 mmol) in THF (2 mL) was added a solution of2-(*p*-toluenesulfonamidomethyl)-1,5-hexadiene (0.74 g, 3.35 mmol) in THF (3 mL) dropwise at room temperature. After 30 min, a solution of 1-bromo-4-methoxy-2-butyne (0.683 g, 4.19 mmol) in THF (1 mL) was added. The reaction mixture was stirred at 60 °C for 4 h, quenched with saturated aqueous ammonium chloride solution, and extracted with dichloromethane. The combined layers were washed with brine, dried ($MgSO_4$), filtered, concentrated, and flash chromatographed (hexane:ether = 2.5:1) to give compound **28b** (0.794 g, 82%). IR ($CDCl_3$): 1638, 1596, 1345, 1158, 1090 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.74 (d, J = 8.1 Hz, 2H), 7.30 (d, J = 8.1 Hz, 2H), 5.80 (m, 1H), 4.97–5.08 (m, 4H), 4.08 (t, J = 1.8 Hz, 2H), 3.79 (t, J = 1.8 Hz, 2H), 3.74 (s, 2H), 3.17 (s, 3H), 2.42 (s, 3H), 2.25 (m, 2H), 2.16 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.60, 142.81, 138.12, 136.60, 129.57, 128.05, 115.05, 81.59, 79.15, 59.47, 57.21, 51.33, 35.74, 32.18, 31.38, 30.78, 21.21. Calcd for $C_{19}H_{25}NO_3S$: 347.1557. Found: 347.1530.

Preparation of 1-(Methoxyethylidene)-7-methylene-3-(*p*-tolylsulfonyl)-3-azaspiro[4.4]nonane (32). A solution of amide **28b** (0.043 g, 0.124 mmol) in benzene-d_6 (0.8 mL) followed by acetic acid (7.1 μL, 0.124 mmol) was added to $Pd_2(dba)_3{\cdot}CHCl_3$ (0.0032 g, 0.003 mmol) and triphenylstibine (0.0044 g, 0.0124 mmol). The reaction was monitored by NMR spectroscopy. After heating at 60 °C for 4.5 h, the mixture was cooled, concentrated, and flash chromatographed (hexane:ether = 4:1 to 2:1) to give azaspirane **32** (0.037 g, 86%). IR ($CDCl_3$): 1600, 1342, 1160, 1090 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.70 (d, J = 8.2 Hz, 2H), 7.33 (d, J = 8.2 Hz, 2H), 5.39 (m, 1H), 4.86 (t, J = 2.4 Hz, 2H), 3.88 (m, 2H), 3.80 (d, J = 6.4 Hz, 2H), 3.28 (s, 3H), 3.06 (d, J = 9.0 Hz, 1H), 3.01 (d, J = 9.0 Hz, 1H), 2.44 (s, 3H), 2.43 (m, 1H), 2.30 (m, 3H), 1.71 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 149.78, 145.17, 143.87, 133.39, 129.85, 127.99, 117.12, 107.21, 69.49, 58.35, 58.03, 52.82, 49.79, 44.21, 36.95, 30.75, 21.24. Calcd for $C_{19}H_{25}NO_3S$: 347.1555. Found: 347.1567.

Preparation of 4-Methylene-7-octenal (33a). Alcohol **25a** (5.0 g, 44.6 mmol) was dissolved in ethyl vinyl ether (400 mL) containing mercuric acetate (11.47 g, 36.0 mmol). After being refluxed for 30 h, the mixture was cooled, washed with 10% potassium hydroxide (3×) and brine, dried (K_2CO_3), filtered, and concentrated to give a crude vinyl ether, which was heated at 180–190 °C for 3 h. The mixture was flash chromatographed (hexane:ether = 10:1) to give aldehyde **33a** (2.5 g, 41%). IR ($CDCl_3$): 2734, 1721, 1682, 1642 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 9.78 (t, J = 1.7 Hz, 1H), 5.81 (m, 2H), 5.03 (dd, J = 1.71, 1.7 Hz, 1H), 4.97 (dd, J = 10.4, 0.8 Hz, 1H), 4.80 (bs, 1H), 4.74 (bs, 1H), 2.59 (m, 2H), 2.36 (m, 2H), 2.20 (m, 2H), 2.14 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 202.54, 147.22, 138.25, 114.89, 110.03, 41.64, 35.39, 31.68, 27.90. Calcd for $C_9H_{14}O$: 138.1045. Found: 138.1051.

Preparation of 8-(*tert*-Butyldimethylsiloxy)-11-methoxy-5-methylene-1-undecen-9-yne (34a). A solution of aldehyde **33a** (0.50 g, 3.62 mmol) in THF (2 mL) was added dropwise at 0 °C to a solution of methyl propargyl ether (0.76 g, 10.9 mmol) and *n*-butylmagnesium chloride (5.0 mL, 10.0 mmol). The reaction mixture was stirred at room temperature for 8 h, then quenched with saturated aqueous ammonium chloride solution, and extracted with ether (3×). The combined layers were washed with brine, dried (Na_2SO_4), filtered, concentrated, and flash chromatographed (hexane:ether = 2:1) to give an alcohol (0.696 g, 92%). IR ($CDCl_3$): 3608, 1642, 1094 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 5.82 (m, 1H), 5.00 (m, 2H), 4.79 (bs, 1H), 4.78 (bs, 1H), 4.45 (m, 1H), 4.14 (d, J = 1.7 Hz, 2H), 3.39 (s, 3H), 2.20 (m, 4H), 2.12 (m, 2H), 1.86 (m, 2H), 1.81 (d, J = 5.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.99, 138.28, 114.60, 109.73, 87.32, 80.79, 62.10, 59.86, 57.61, 35.64, 35.34, 31.89, 31.45.

To a solution of the above alcohol (0.463 g, 2.232 mmol) and 2,6-lutidine (0.51 mL, 4.46 mmol) in dichloromethane (2 mL) was added TBDMSOTf (0.76 mL, 3.35 mmol) at 0 °C. After being stirred at room temperature for 30 min, the mixture was diluted with dichloromethane, washed with water and brine, dried ($MgSO_4$), filtered, concentrated, and flash chromatographed (3.5% ether in hexane) to give compound **34a** (0.621 g, 86%). IR ($CDCl_3$): 1640, 1254, 1096 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 5.82 (m, 1H), 5.03 (dd, J = 17.2, 1.7 Hz, 2H), 4.96 (d, J = 10.1 Hz, 2H), 4.76 (s, 2H), 4.42 (t, J = 6.4 Hz, 1H), 4.13 (t, J = 1.5 Hz, 2H), 3.38 (s, 3H), 2.08–2.24 (m, 6H), 1.81 (m, 2H), 0.91 (s, 9H), 0.14 (s, 3H), 0.11 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 148.58, 138.60, 114.66, 109.49, 88.10, 79.88, 62.48, 59.85, 57.35, 36.63, 35.33, 31.78, 31.32, 25.58, 17.98, –4.80, –5.34. Calcd for $C_{15}H_{25}O_2Si$ ($M^+ - C_4H_9$): 265.1625. Found: 265.1597. Anal. Calcd for $C_{19}H_{34}O_2Si$: C, 70.75; H, 10.62. Found: C, 70.47; H, 10.27.

Preparation of 2-(*tert*-Butyldimethylsiloxy)-1-(methoxyethylidene)-7-methylenespiro[4.4]nonane (35a and 36a). Acetic acid (2.2 μL, 0 038 mmol) followed by dienyne **34a** (0.0488 g, 0.152 mmol) was added to the purple solution formed by adding $Pd_2(dba)_3CHCl_3$ (0.004 g, 0.003 86 mmol) to triphenylstibine (0.0054 g, 0.0153 mmol) in 1.0 mL of benzene. The reaction mixture was stirred at room temperature for 72 h, concentrated, and flash chromatographed (6% ether in hexane) to give spiranes **35a** and **36a** (0.042 g, 86%). ^1H NMR (400 MHz, $CDCl_3$): δ 5.45 (m, 1H), 4.85 (m, 2H), 4.73 (m, 1H), 4.10 (m, 1H), 3.334 (s, 1.5H), 3.332 (s, 1.5H), 2.19–2.51 (m, 4H), 1.35–1.90 (m, 6H), 0.89 (s, 5.2 H), 0.88 (s, 3.8H), 0.11 (s, 3H), 0.09 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 154.39, 154.23, 152.27, 120.02, 119.90, 105.87, 105.70, 73.24, 73.01, 69.96, 57.85, 51.91, 48.42, 46.76, 40.21, 39.21, 35.64, 35.48, 33.82, 31.07, 30.89, 25.61, 17.69, –4.18, –5.01. Calcd for $C_{15}H_{25}O_2Si$ ($M^+ - {}^tC_4H_9$): 265.1624. Found: 265.1597.

Preparation of 8-(*tert*-Butyldimethylsiloxy)-11-methoxy-7,7-dimethyl-5-methylene-1-undec-9-yne (34b). To a stirred cooled (0 °C) solution of alcohol **25a** (21.95 g, 196 mmol) and pyridine (1.5 mL) in ether (170 mL) was added over 0.5 h a solution of phosphorus tribromide (9.3 mL, 98 mmol) in ether (50 mL). The mixture was stirred at 0 °C for 1 h and, while still cool, was poured slowly into saturated aqueous sodium bicarbonate solution at 0 °C, allowing for frothing. The mixture was extracted with ether. The combined ether layers were washed with saturated aqueous sodium bicarbonate solution and brine, dried ($MgSO_4$), filtered, and concentrated. The residue was filtered through a silica gel plug, eluting with pentane, and the pentane was removed to give rather pure bromide(19.0 g, 55%). IR ($CDCl_3$): 1641, 1439, 1211 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 5.81 (m, 1H), 5.19 (bs, 1H), 5.03 (m, 2H), 4.98 (bs, 1H), 3.97 (s, 2H), 2.20–2.37 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 145.04, 137.87, 115.42, 115.23, 36.58, 32.39, 31.33.

The cyclohexylimine of isobutyraldehyde[35] (1.92 g, 12.57 mmol) in THF (2 mL) was added dropwise at 0 °C to LDA prepared from diisopropylamine (1.76 mL, 12.57 mmol) and *n*-butyllithium (7.86 mL, 12.57 mmol) dropwise in THF (20 mL). The mixture was stirred for 3 h and then cooled to–78 °C. A solution of 2-(bromomethyl)-1,5-hexadiene (2.0 g, 11.43 mmol) in THF (2 mL) was added dropwise. The mixture was stirred for 7 h. At this point, the bath temperature reached –10 °C. Hydrochloric acid (4 N, 15 mL) was added dropwise. The mixture was stirred at room temperature for 12 h, and neutralized by addition of solid sodium bicarbonate and water (40 mL). The mixture was extracted with ether (3 × 50 mL), washed with brine (50 mL), dried ($MgSO_4$), filtered, concentrated, and flash chromatographed (hexane:ether = 20:1) to give aldehyde **33b** as a light yellow liquid (1.46 g, 77%). IR ($CDCl_3$): 2712, 1724, 1641, 1468 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 9.54 (s, 1H), 5.78 (ddt, J = 16.7, 10.2, 6.4 Hz, 1H), 5.00 (m, 2H), 4.87 (d, J = 1.4 Hz, 1H), 4.73 (s, 1H), 2.25 (s, 2H), 2.17 (m, 2H), 1.99 (m, 2H), 1.06

(34) Cf.: Sonnet, P. E. *Synth. Commun.* **1976**, *6*, 21.

(35) DeJeso, B.; Pommier, J.-C. *J. Organomet. Chem.* **1976**, *122*, 123.

(s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 206.52, 145.00, 138.21, 114.92, 114.01, 46.09, 43.75, 36.28, 31.81, 21.61.

A solution of aldehyde **33b** (0.516 g, 3.11 mmol) in THF (2 mL) was added dropwise at 0 °C to a solution of lithiated methyl propargyl ether prepared from the ether (0.545 g, 7.78 mmol) and *n*-butyllithium (4.47 mL, 7.15 mmol) in THF (10 mL). After the reaction mixture was stirred at 0 °C for 1.5 h, the cooling bath was removed, and stirring was continued for an additional 5 h. The mixture was quenched with saturated aqueous ammonium chloride solution, extracted with ether (3 × 20 mL), washed with brine (30 mL), dried ($MgSO_4$), filtered, concentrated, and flash chromatographed (hexane:ether = 2:1) to give an alcohol as a colorless liquid (0.61 g, 83%). IR ($CDCl_3$): 3612, 3078, 2933, 1639, 1449, 1187 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.81 (m, 1H), 5.02 (dd, *J* = 17.7, 1.9 Hz, 1H), 4.95 (d, *J* = 10.2 Hz, 1H), 4.92 (d, *J* = 1.3 Hz, 1H), 4.84 (s, 1H), 4.17 (m, 1H), 4.16 (s, 2H), 3.29 (s, 3H), 2.18 (m, 6H), 1.81 (d, *J* = 6.1 Hz, 1H), 1.00 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 146.63, 138.61, 114.69, 114.13, 86.18, 82.09, 70.35, 59.82, 57.49, 43.51, 39.21, 37.28, 32.33, 23.20, 22.95. Calcd for $C_{14}H_{21}O_2$ ($M^+ - CH_3$): 221.1542. Found: 221.1539.

To a solution of the above alcohol (0.349 g, 1.48 mmol) and 2,6-lutidine (0.34 mL, 2.96 mmol) in dichloromethane (1.5 mL) was added TBDMSOTf (0.5 mL, 2.22 mmol) at 0 °C. After being stirred at room temperature for 40 min, the mixture was diluted with dichloromethane, washed with water and brine, dried ($MgSO_4$), filtered, concentrated, and flash chromatographed (5% ether in hexane) to give dienyne **34b** (0.49 g, 94.6%). IR ($CDCl_3$): 1638, 1467, 1383, 1362 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.81 (m, 1H), 5.02 (dd, *J* = 17.7, 1.9 Hz, 1H), 4.94 (d, *J* = 10.1 Hz, 1H), 4.88 (bs, 1H), 4.77 (bs, 1H), 4.15 (d, *J* = 1.6 Hz, 2H), 4.08 (bs, 1H), 3.38 (s, 3H), 2.15 (m, 6H), 0.94 (s, 6H), 0.91 (s, 9H), 0.14 (s, 3H), 0.09 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 146.87, 138.80, 114.54, 113.58, 87.06, 81.57, 71.36, 59.91, 57.30, 43.23, 39.83, 37.54, 32.44, 25.64, 23.08, 22.96, 18.01, –4.58, –5.46. Calcd for $C_{17}H_{29}O_2Si$ ($M^+ - {}^tC_4H_9$): 293.1937. Found: 293.1929.

Preparation of 2-(*tert*-Butyldimethylsiloxy)-1-(methoxyethylidene)-3,3-dimethyl-7-methyl-enespiro[4.4]nonane (35b). Acetic acid (1.7 μL, 0.030 mmol) followed by substrate **34b** (0.0525 g, 0.15 mmol). was added to a purple solution generated from $Pd_2(dba)_3$·$CHCl_3$ (0.0039 g, 0.003 75 mmol) and triphenylstibine (0.0053 g, 0.015 mmol) in 1.0 mL of benzene. The reaction mixture was stirred at room temperature for 24 h, concentrated, and flash chromatographed (5% ether in hexane) to give **35b** (0.046 g, 88%). IR ($CDCl_3$): 1656 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.45 (t, *J* = 6.7 Hz, 1H), 4.82 (m, 2H), 4.06 (m, 3H), 3.32 (s, 3H), 2.27–2.48 (m, 4H), 1.91 (m, 1H), 1.69 (d, *J* = 12.5 Hz, 1H), 1.60 (m, 1H), 1.36 (d, *J* = 12.5 Hz, 1H), 1.00 (s, 3H), 0.89 (s, 9H), 0.82 (s, 3H), 0.09 (s, 3H), 0.02 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.98, 152.53, 119.31, 105.39, 80.41, 70.40, 57.75, 52.92, 50.86, 50.77, 41.93, 40.47, 30.95, 26.37, 25.73, 23.32, 18.12, –4.58, –4.80. Calcd for $C_{20}H_{35}O_2Si$ ($M^+ - CH_3$): 335.2407. Found: 335.2414.

Preparation of 2,5-Bis(methylene)-8-nonen-1-ol (37a). 2-(Bromomethyl)-1,5-hexadiene (18.8 g, 107.0 mmol) in ether (50 mL) was added dropwise at –78 °C to methallyl alcohol (15.1 mL, 179.0 mmol) which was metalated as previously described by *n*-butyllithium (35.8 mL, 358.0 mmol) complexed with TMEDA (54.0 mL, 358.0 mmol) in dry ether (300 mL) at 0 °C. The mixture was stirred at –78 °C for 3 h and room temperature for 4.5 h. After quenching with saturated aqueous NH_4Cl solution (150 mL), the organic layer was washed with water (100 mL), saturated aqueous $CuSO_4$ solution (2 × 100 mL), water (100 mL), and brine (100 mL) respectively, dried ($MgSO_4$), filtered, concentrated, and flash chromatographed (hexane:ether = 4:1) to give alcohol **37a** (15.0 g, 84.4%). IR ($CDCl_3$): 3614, 3080, 2980, 2936, 2860, 2250, 1642, 1450, 1051, 1012 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.83 (ddt, *J* = 17.0 10.4, 6.6 Hz, 1H), 5.05 (bs, 1H), 5.00 (m, 2H), 4.91 (bs, 1H), 4.77 (bs, 2H), 4.70 (bs, 2H), 2.2 (m, 6H), 2.15 (m, 2H), 1.39 (bs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.68, 148.50, 138.36, 114.56, 109.50, 109.39, 65.95, 35.34, 34.21, 31.94, 31.09. Calcd for $C_{11}H_{18}O$ (M^+): 166.1358. Found: 166.1351.

Preparation of Methyl 2,5-Bis(methylene)-8-nonenyl Carbonate (37b). To a solution of alcohol **37a** (1.08 g, 6.51 mmol), DMAP (0.01 g), and pyridine (1.58 mL, 19.53 mmol) in dichloromethane (10 mL) was added methyl chloroformate (1.50 mL, 19.53 mmol) slowly at 0 °C. After being stirred at 0 °C for 10 min and at room temperature for 1 h, the mixture was diluted with dichloromethane (50 mL), washed with water (2 × 50 mL) and brine (50 mL), dried ($MgSO_4$), filtered, concentrated, and flash chromatographed (hexane:ether = 10:1) to give carbonate **37b** as a colorless liquid (1.24g, 85%). IR ($CDCl_3$): 1750, 1640, 1448, 1272 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.82 (ddt, *J* = 17.0, 10.3, 6.7 Hz, 1H), 5.09 (s, 1H), 5.03 (dd, *J* = 17.0 Hz, 1.7 Hz, 1H), 4.99 (s, 1H), 4.96 (dd, *J* = 10.3, 1.7 Hz, 1H), 4.76 (s, 2H), 4.59 (s, 2H), 3.80 (s, 3H), 2.21 (m, 6H), 2.11 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.94, 148.39, 143.26, 138.54, 114.71, 113.25, 169.73, 70.28, 54.71, 35.15, 33.79, 31.77, 30.99. Calcd for $C_{11}H_{17}$ ($M^+ - OCOCH_3$): 149.1331. Found: 149.1317. Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.82; H, 9.24.

Preparation of 10,10-Bis(methoxycarbonyl)-5,8-bis(methylene)-1-tridecen-12-yne (39a). A solution of carbonate **37b** (0.672 g, 3.0 mmol) and dimethyl propargylmalonate (0.612 g, 3.60 mmol) in THF (1.0 mL) was added at room temperature to a mixture of $Pd_2(dba)_3$·$CHCl_3$ (0.0687 g, 0.075 mmol) and triphenylphosphine(0.1572 g, 0.60 mmol) in dry THF (2.0 mL). The mixture was stirred at 45 °C for 16 h, cooled, concentrated, and flash chromatographed (hexane:ether = 10:1) to afford the title compound(0.94 g, 98.5%). IR ($CDCl_3$): 3316, 1736, 1640, 1440, 1298, 1210 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.82 (ddt, *J* = 17.0, 10.3, 6.7 Hz, 1H), 5.04 (dd, *J* = 17.0, 1.8 Hz, 1H), 4.98 (dd, *J* = 10.3, 1.8 Hz, 1H), 4.95 (bs, 1H), 4.89 (bs, 1H), 4.73 (bs, 1H), 4.72 (bs, 1H), 3.74 (s, 6H), 2.86 (s, 2H), 2.84 (d, *J* = 2.7 Hz, 2H), 2.01–2.22 (m, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.83, 148.67, 143.85, 138.58, 115.36, 114.69, 109.47, 79.15, 71.78, 56.59, 52.67, 37.24, 35.28, 34.67, 31.81, 22.45. Calcd for $C_{18}H_{23}O_3$ ($M^+ - CH_3O$): 287.1648. Found: 287.1630. Anal. Calcd for $C_{19}H_{26}O_4$: C, 71.67; H, 8.23. Found: C, 71.44; H, 8.33.

Preparation of 10,10-Bis(phenylsulfonyl)-5,8-bis(methylene)-1-tridecen-12-yne (39b). A solution of 3,3-bis(phenylsulfonyl)-1-butyne (0.1645 g, 0.49 mmol) and carbonate **37b** (0.1207 g, 0.54 mmol) in THF (1.5 mL) was added at room temperature to a mixture of $Pd_2(dba)_3$·$CHCl_3$ (0.0101 g, 0.0098 mmol) and triphenylphosphine(0.0205 g, 0.078 mmol) in THF (0.5 mL). The reaction mixture was stirred at 50 °C overnight, cooled, concentrated, and flash chromatographed (hexane:ether = 2:1) to give sulfone **39b** (0.224 g, 95%). IR ($CDCl_3$): 3308, 2258, 1639, 1449, 1332, 1310, 1149, 1075 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (dd, *J* = 8.6 Hz, 1.2 Hz, 4H), 7.70 (m, 2H), 7.56 (m, 4H), 5.82 (ddt, *J* = 17.0, 10.3, 6.7 Hz, 1H), 5.28 (bs, 1H), 5.11 (bs, 1H), 5.03 (dd, *J* = 17.0, 1.8 Hz, 1H), 4.96 (d, *J* = 10.3 Hz, 1H), 4.74 (bs, 2H), 3.40 (d, *J* = 2.7 Hz, 2H), 3.14 (s, 2H), 2.39 (m, 2H), 2.19 (m, 4H), 2.10 (m, 2H), 2.00 (t, *J* = 2.7 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 148.67, 141.90, 138.68, 137.78, 134.87, 131.95, 128.69, 117.75, 114.62, 109.70, 90.70, 77.15, 75.13, 35.30, 35.10, 34.75, 31.86, 22.01. Calcd for $C_{21}H_{25}O_3S$ ($M - PhSO_2$): 341.1577. Found: 341.1568. Anal. Calcd for $C_{27}H_{30}O_4S_2$: C, 67.19; H, 6.26; S, 13.28. Found: C, 67.45; H, 6.43; S, 13.45.

Preparation 3,3-Bis(phenylsulfonyl)-1,9-bis(methylene)dispiro[4.1.4.2]-tridecane (40b). A solution of substrate **39b** (0.032 g, 0.0664 mmol) in benzene-d_6 (1.0 mL) followed by acetic acid (3.8 μL, 0.0664 mmol) was added to $Pd_2(dba)_3$·$CHCl_3$ (0.001 72 g, 0.001 66 mmol) and tri-*o*-tolylphosphine (0.004 04 g, 0.0133 mmol). The reaction was monitored by NMR spectroscopy. After 8.5 h, the mixture was concentrated and flash chromatographed (hexane:ether = 2:1 to 1:1) to give dispirane **40b** as an oil (0.026 g, 81%). IR ($CDCl_3$): 1657, 1582, 1328, 1369, 1145, 1076 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03 (m, 4H), 7.71 (m, 2H), 7.60 (m, 4H), 4.85 (m, 2H), 4.60 (m, 2H), 3.25 (m, 2H), 2.78 (m, 2H), 2.37 (m, 2H), 2.23 (m, 2H), 1.52–1.82 (m, 8H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 154.69, 152.11, 137.24, 137.00, 134.70, 131.58, 131.54, 131.45, 128.89, 128.63, 106.01, 104.74, 91.43, 53.64, 52.29, 49.92, 47.70, 45.58, 40.94, 39.80, 39.70, 37.84, 31.10. Calcd for $C_{21}H_{24}O_2S$ ($M^+ - PhSO_2H$): 340.1497. Found: 340.1484. Anal. Calcd for $C_{27}H_{30}O_4S_2$: C, 67.19; H, 6.26; S, 13.28. Found: C, 67.51; H, 6.55; S, 13.52.

Ozonolysis of Dispirane 40b. Ozone was bubbled through a solution of **40b** in methanol (2 mL) at –78 °C until a blue color persisted. The solution was purged of excess ozone by bubbling nitrogen through it, and the ozonide was reduced by addition of dimethyl sulfide (1 mL). The mixture was warmed to room temperature. Triethylamine (0.5 mL) was added, and the mixture was stirred at room temperature for 3.5 h, concentrated, and flash chromatographed (ether) to give enone **42** (0.005 g, 79%). IR ($CDCl_3$): 1737, 1685, 1599, 1457, 1429, 1355, 1241, 1162 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.26 (s, 1H), 3.83 (s, 3H), 2.59 (m, 2H), 1.50–2.30 (m, 12H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 219.64, 209.79, 188.88, 102.77, 58.49, 54.69, 52.25, 49.55, 48.15, 45.87, 38.60, 37.82, 37.74, 35.52. Calcd for $C_{14}H_{18}O_3$ (M^+): 234.1256. Found: 234.1245.

Preparation of 1-Methoxy-5,5-bis(phenylsulfonyl)-2-pentyne (38c). Oxone,[36] 49.5% $KHSO_5$ (42.6 g, 69.4 mmol), was added portionwise to

(36) Cf.: Trost, B. M.; Curran, D. P. *Tetrahedron Lett.* **1981**, 1287.

1-methoxy-5,5-bis(phenylthio)-2-pentyne[37] (2.18 g, 6.94 mmol, prepared by alkylation of bis(phenylthio)methane with 1-bromo-4-methoxy-2-butyne) dissolved in methanol (60 mL) and water (60 mL) at 0 °C. The resulting suspension was stirred at room temperature for 24 h, diluted with water (100 mL), and extracted with ether (4 × 60 mL). The combined layers were washed with water (2 × 50 mL) and brine (50 mL), dried ($MgSO_4$), filtered, concentrated, and recrystallized (ethanol) to give the title compound as white needles (1.64 g, 63%), mp 99.5–100.5 °C. IR ($CDCl_3$): 1449, 1345, 1328, 1314, 1158, 1095, 1080 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.01 (dd, J = 8.4, 1.1 Hz, 4H), 7.71 (m, 2H), 7.60 (m, 4H), 4.58 (t, J = 6.1 Hz, 1H), 3.84 (d, J = 2.0 Hz, 2H), 3.28 (s, 3H), 3.19 (dt, J = 6.1, 2.0 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.01, 135.05, 130.02, 129.33, 82.01, 80.00, 79.39, 59.63, 57.57, 16.73. Calcd for $C_{18}H_{18}O_5S_2$ (M^+): 378.0596. Found: 378.0609. Anal. Calcd for $C_{18}H_{18}O_5S_2$: C, 57.13; H, 4.79. Found: C, 57.06; H, 4.41.

Preparation of 10,10-Bis(phenylsulfonyl)-14-methoxy-5,8-bis(methylene)-1-tetradecen-12-yne (39c). A solution of the above sulfone **38c** (0.15 g, 0.40 mmol) and carbonate **37b** (0.0933 g, 0.42 mmol) in THF (1.0 mL) was added at room temperature to a mixture of $Pd_2(dba)_3$·$CHCl_3$ (0.0083 g, 0.008 mmol) and triphenylphosphine (0.068 g, 0.064 mmol) in THF (0.5 mL). The reaction mixture was stirred at 50 °C overnight, cooled, concentrated, and flash chromatographed (hexane:ether = 1:1) to give **39c** (0.205 g, 97.4%). IR ($CDCl_3$): 1640, 1449, 1331, 1310, 1145, 1095, 1086 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.04 (dd, J = 7.3, 1.3 Hz, 4H), 7.70 (m, 2H), 7.50 (m, 4H), 5.81 (m, 1H), 5.25 (s, 1H), 5.10 (d, J = 1.0 Hz, 1H), 5.02 (dd, J = 17.1, 1.8 Hz, 1H), 4.95 (d, J = 10.1 Hz, 1H), 4.74 (bs, 2H), 3.82 (t, J = 2.0 Hz, 2H), 3.46 (t, J = 2.0 Hz, 2H), 3.24 (s, 3H), 3.10 (s, 2H), 2.40 (m, 2H), 2.18 (m, 4H), 2.10 (m, 2H). ^{13}C NMR (300 MHz, $CDCl_3$): δ 148.67, 141.94, 138.66, 137.97, 134.77, 131.88, 128.68, 117.71, 114.63, 109.64, 90.67, 82.71, 79.72, 59.82, 57.52, 35.29, 34.69, 31.84, 22.34. Calcd for $C_{23}H_{28}O_3S$ (M^+ – $PhSO_2H$): 384.1759. Found: 384.1770. Anal. Calcd for $C_{29}H_{34}O_5S_2$: C, 66.13; H, 6.51; S, 12.17. Found: C, 66.18; H, 6.66; S, 12.00.

Preparation of 3,3-Bis(phenylsulfonyl)-1-(methoxyethylidene)-9-methylenedispiro[4.1.4.2]tridecane (40c). A solution of bis-sulfone **39c** (0.036 g, 0.068 mmol) in benzene-d_6 (1.0 mL) followed by acetic acid (3.9 μL, 0.068 mmol) was added to $Pd_2(dba)_3$·$CHCl_3$ (0.001 77 g, 0.0017 mmol) and triphenylstibine (0.0024 g, 0.0068 mmol). The reaction was monitored by NMR spectroscopy. After standing at room temperature for 15 h, the reaction mixture was concentrated and flash chromatographed (hexane:ether = 1:1) to give dispirane **40c** (0.032 g, 88.9%). IR ($CDCl_3$): 1650, 1582, 1445, 1328, 1310, 1145, 1078 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.04 (m, 4H), 7.72 (m, 2H), 7.60 (m, 4H), 5.28 (m, 1H), 4.83 (m, 2H), 3.80 (d, J = 6.6 Hz, 2H), 3.32 (s, 3H), 3.31 (m, 2H), 2.71 (bs, 2H), 2.30 (m, 2H), 2.21 (bs, 2H), 1.72 (m, 4H), 1.50–1.65 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 152.10, 151.81, 149.50, 149.28, 137.05, 136.81, 134.76, 131.54, 128.93, 116.80, 106.01, 105.80, 92.13, 69.92, 58.02, 54.55, 54.43, 52.86, 49.81, 49.71, 47.73, 47.53, 45.16, 45.06, 41.57, 41.43, 40.06, 39.76, 37.94, 37.78, 35.43, 31.28, 31.05. Calcd for $C_{23}H_{18}O_3S$ (M^+ – $PhSO_2H$): 384.1759. Found: 384.1746. Anal. Calcd for $C_{29}H_{34}O_5S_2$: C, 66.13; H, 6.51; S, 12.17. Found: C, 66.20; H, 6.71; S, 11.90.

Ozonolysis of Dispirane 40c. Ozone was bubbled through a solution of **40c** (0.016 g, 0.0304 mmol) in methanol (2 mL) at –78 °C as previously described. Elimination and workup as before followed by flash chromatography (ether) gave enone **42** (0.006 g, 84%) identical to that obtained previously.

Preparation of Methyl 2,5,8-Tris(methylene)-11-dodecenyl Carbonate (46b, n = 1). To a solution of alcohol **37a** (12.0 g, 72.29 mmol) in carbon tetrachloride (80 mL) was added triphenylphosphine (24.62 g, 93.98 mmol).[38] The mixture was refluxed for 1 h and then cooled to room temperature. Hexane (150 mL) was added, and stirring was continued for an additional 5 min. The precipitate of triphenylphosphine oxide was filtered and washed with hexane (50 mL). The filtrate was concentrated and flash chromatographed (hexane) to give the chloride as a colorless liquid (10.5 g, 78.7%). IR ($CDCl_3$): 3081, 2935, 1643, 1445, 1258 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 5.81 (m, 1H), 5.14 (s, 1H), 5.03 (dd, J = 17.3 Hz, 1.7 Hz, 1H), 4.98 (s, 1H), 4.96 (d, J = 10.0 Hz, 1H), 4.76 (s, 2H), 4.06 (s, 2H), 2.33 (m, 2H), 2.18 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 148.37, 145.13, 138.54, 114.75, 114.68, 109.80, 48.25, 31.16, 33.71, 31.79, 30.98.

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The above chloride (10.0 g, 54.2 mmol) in ether (20 mL) was added dropwise at –78 °C to metalated methallyl alcohol which was prepared as previously described from alcohol (9.12 mL, 108.4 mmol), n-butyllithium (21.68 mL, 216.8 mmol), and TMEDA (32.72 mL, 216.8 mmol) in ether (250 mL) at 0 °C. The mixture was slowly warmed to room temperature overnight and quenched with saturated aqueous ammonium chloride solution. Workup as before followed by flash chromatography (hexane:ether = 4:1) gave the alcohol as a yellow oil (10.9 g, 91%). IR ($CDCl_3$): 3620, 3080, 2935, 1644, 1451 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 5.84 (m, 1H), 5.05 (s, 1H), 5.00 (m, 2H), 4.90 (s, 1H), 4.76 (bs, 4H), 4.10 (bs, 2H), 2.20 (m, 12H), 1.35 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 149.19, 149.05, 148.99, 138.65, 114.66, 109.65, 109.36, 65.93, 35.29, 34.19, 31.84, 31.04.

To a solution of this alcohol (0.62 g, 2.82 mmol), DMAP (10 g), and pyridine (0.68 mL, 8.46 mmol) in dichloromethane (6 mL) was added slowly methyl chloroformate (0.65 mL, 8.46 mmol) at 0 °C. After being stirred at 0 °C for 10 min and room temperature for 4 h, the mixture was diluted with dichloromethane (50 mL), washed with water (2 × 50 mL) and brine, (50 mL), dried ($MgSO_4$), filtered, concentrated, and flash chromatographed (hexane:ether = 10:1) to give carbonate **46b** (n = 1) as a colorless oil (0.64 g, 82%). IR ($CDCl_3$): 1748, 1644, 1444, 1275 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 5.82 (m, 1H), 5.09 (s, 1H), 5.00 (m, 3H), 4.75 (bs, 4H), 4.60 (s, 2H), 3.79 (s, 3H), 2.18 (m, 12H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.94, 149.00, 148.80, 143.26, 138.64, 114.66, 113.28, 109.56, 109.34, 70.28, 54.72, 35.26, 34.17, 34.12, 33.84, 31.82, 31.03. Anal. Calcd for $C_{17}H_{26}O_3$: C, 73.35; H, 9.41. Found: C, 73.69; H, 9.34.

Preparation of 13,13-Bis(phenylsulfonyl)-17-methoxy-5,8,11-tris(methylene)-1-heptadecen-15-yne (43c). A solution of **38c** (0.231 g, 0.67 mmol) and carbonate **46b** (n = 1) (0.170 g, 0.61 mmol) in THF (1.7 mL) was added at room temperature to a mixture of $Pd_2(dba)_3$·$CHCl_3$ (0.0158 g, 0.0153 mmol) and triphenylphosphine (0.032 g, 0.122 mmol) in THF (0.8 mL). The reaction mixture was stirred at 50 °C overnight, cooled, concentrated, and flash chromatographed (hexane:ether = 1:1) to give **43c** (0.27 g, 76%). IR ($CDCl_3$): 1639, 1445, 1331 1310, 1143, 1090, 1074 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.05 (dd, J = 7.3, 1.2 Hz, 4H), 7.70 (m, 2H), 7.56 (m, 4H), 5.82 (m, 1H), 5.25 (bs, 1H), 5.10 (bs, 1H), 5.03 (dd, J = 17.2, 1.9 Hz, 1H), 4.95 (dd, J = 10.1, 1.9 Hz, 1H), 4.74 (bs, 4H), 3.82 (t, J = 2.0 Hz, 2H), 3.46 (t, J = 2.0 Hz, 2H), 3.24 (s, 3H), 3.10 (s, 2H), 2.40 (m, 2H), 2.10–2.21 (m, 10H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 149.10, 141.96, 138.69, 137.98, 134.77, 131.88, 128.92, 128.69, 117.71, 114.59, 109.46, 109.36, 90.66, 82.71, 79.73, 59.82, 57.52, 35.36, 35.27, 34.71, 34.33, 31.88, 22.35. Calcd for $C_{27}H_{34}O_3S$ (M^+ – $PhSO_2H$): 438.2229. Found: 438.2252. Anal. Calcd for $C_{33}H_{40}O_5S_2$: C, 68.24; H, 6.94. Found: C, 68.30; H, 6.88.

Preparation of 3,3-Bis(phenylsulfonyl)-1-(methoxyethylidene)-11-methylenetrispiro[4.1.1.4.2.2]heptadecane (44c). A solution of substrate **43c** (0.032 g, 0.055 mmol) in benzene-d_6 (0.9 mL) followed by acetic acid (3.2 μL, 0.050 mmol) was added to $Pd_2(dba)_3$·$CHCl_3$ (0.001 43 g, 0.001 38 mmol) and triphenylstibine (0.001 94 g, 0.0055 mmol). The reaction was monitored by NMR spectroscopy. After standing at 41–43 °C for 38 h, the reaction mixture was concentrated and flash chromatographed (hexane:ether = 1:1) to give trispirane **44c** (0.027 g, 84%). IR ($CDCl_3$): 1448, 1329, 1310, 1145, 1078 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.05 (m, 4H), 7.72 (m, 2H), 7.60 (m, 4H), 5.26 (m, 1H), 4.82 (m, 2H), 3.80 (d, J = 6.3 Hz, 2H), 3.32 (s, 3H), 3.31 (m, 2H), 2.70 (m, 2H), 2.30 (m, 2H), 2.20 (m, 2H), 1.50–1.81 (m, 14H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 152.71, 152.67, 149.82, 149.60, 137.09, 136.96, 136.93, 134.73, 131.55, 128.91, 116.61, 105.56, 105.47, 92.23, 69.94, 58.01, 55.78, 54.41, 53.58, 50.24, 50.18, 50.15, 50.11, 48.13, 48.06, 45.22, 41.69, 40.75, 40.67, 40.46, 40.38, 37.85, 35.51, 31.31, 31.26. Calcd for $C_{27}H_{34}O_3S$ (M^+ – $PhSO_2H$): 438.2229. Found: 438.2220. Anal. Calcd for $C_{33}H_{40}O_5S_2$: C, 68.24; H, 6.94. Found: C, 68.57; H, 6.57.

Ozonolysis of Trispirane 44c. Ozone was bubbled through a solution of **44c** (0.043 g, 0.074 mmol) in dichloromethane (2 mL) and methanol (4 mL) at –78 °C until a blue color persisted. Reaction, workup, and elimination with 1.0 mL of triethylamine as previously described gave after flash chromatography (ether) enone **45** (0.010 g, 47%). IR ($CDCl_3$): 2942, 2860, 1736, 1684, 1599, 1355, 1241, 1169 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 5.52 (s, 1H), 3.83 (s, 3H), 2.51–2.70 (m, 2H), 2.00–2.30 (m, 6H), 1.50–1.97 (m, 12H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 219.70, 219.63, 209.90, 188.50, 102.95, 102.85, 102.66, 102.58, 58.78, 58.59, 58.39, 58.18, 54.98, 53.38, 53.27, 53.13, 53.05, 52.99, 52.91, 52.45, 52.25, 51.88, 51.80, 51.72, 51.59, 51.56, 51.53, 51.43, 51.29, 47.46, 46.37, 46.23, 46.08, 41.49, 41.39, 41.28, 41.18, 41.10, 41.04, 39.85, 39.67,

39.57, 38.36, 38.26, 38.15, 37.98, 37.93, 37.85, 37.78, 37.12, 37.00, 36.83. Calcd for $C_{18}H_{24}O_3$ (M^+): 288.1725. Found: 288.1711.

Preparation of Methyl 2,5,8,11-Tetrakis(methylene)-14-pentadecenyl Carbonate (46b) (n = 2). To a solution of alcohol **46a** (n = 1) (10.0 g, 45.45 mmol) in carbon tetrachloride (50 mL) was added triphenylphosphine (4.29 g, 54.45 mmol). The mixture was heated at reflux for 1.5 h and then cooled to room temperature. Hexane (150 mL) was added, and stirring was continued for an additional 5 min. The precipitate of triphenylphosphine oxide was filtered and washed with hexane (50 mL). The filtrate was concentrated and flash chromatographed (hexane) to give the chloride as a colorless oil (8.50 g, 78%). IR ($CDCl_3$): 3081, 2934, 1644, 1445 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 5.81 (m, 1H), 5.14 (s, 1H), 5.03 (dd, J = 17.2 1.6 Hz, 1H), 4.98 (s, 1H), 4.96 (d, J = 10.0 Hz, 1H), 4.78 (s, 2H), 4.76 (s, 2H), 4.06 (s, 2H), 2.33 (m, 2H), 2.18 (m, 10H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 149.01, 148.79, 145.17, 138.64, 114.68, 109.66, 109.40, 48.23, 35.28, 34.23, 34.15, 33.79, 31.85, 31.06.

The above chloride (8.20 g, 34.38 mmol) in ether (10 mL) was added dropwise at −78 °C to lithiated methallyl alcohol which was prepared from the alcohol (5.79 mL, 68.76 mmol) by metalation with n-butyllithium (13.75 mL, 137.5 mmol) and TMEDA (20.75 mL, 137.52 mmol) in ether (150 mL) at 0 °C. The mixture was slowly warmed to room temperature overnight and then quenched with saturated aqueous ammonium chloride solution. The normal workup followed by flash chromatography (hexane:ether = 4:1) gave alcohol **46a** (n = 2) as a colorless oil (7.20 g, 76%). IR ($CDCl_3$): 3611, 3080, 2933, 1644, 1450 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 5.84 (m, 1H), 5.05 (s, 1H), 5.00 (m, 2H), 4.90 (s, 1H), 4.75 (bs, 6H), 4.09 (d, J = 6.0 Hz, 2H), 2.20 (m, 6H), 1.35 (t, J = 6.0 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 149.47, 149.20, 149.12, 148.98, 138.67, 114.67, 109.66, 109.39, 109.32, 109.18, 65.95, 35.29, 34.24, 34.15, 31.84, 31.02.

To a solution of alcohol **46a** (n = 2)(0.86 g, 3.14 mmol), DMAP (0.01 g), and pyridine (0.76 mL, 9.42 mmol) in dichloromethane (8 mL) was added slowly methyl chloroformate (0.72 mL, 9.42 mmol) at 0 °C. After stirring at 0 °C for 10 min and at room temperature for 4 h, the mixture was diluted with dichloromethane (50 mL), washed with water (2 × 50 mL) and brine (50 mL), dried ($MgSO_4$), filtered, concentrated, and flash chromatographed (hexane:ether = 10:1) to give carbonate **46b** (n = 2) as a colorless oil (0.97 g, 93%). IR ($CDCl_3$): 1747, 1644, 1444, 1275 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 5.82 (m, 1H), 5.09 (s, 1H), 5.00 (m, 3H), 4.75 (bs, 6H), 4.60 (s, 2H), 3.79 (s, 3H), 2.18 (m, 16H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.94, 149.40, 149.09, 148.80, 143.26, 138.65, 114.65, 113.27, 109.57, 109.31, 109.17, 70.27, 54.72, 35.27, 34.23, 34.17, 33.83, 31.84, 31.03. Calcd for $C_{21}H_{32}O_3$ (M^+): 332.2353. Found: 332.2366. Anal. Calcd for $C_{21}H_{32}O_3$: C, 75.86; H, 9.70. Found: C, 75.94; H, 9.58.

Preparation of 16,16-Bis(phenylsulfonyl)-20-methoxy-5,8,11,14-tetrakis(methylene)-1-icosen-18-yne (47a). A solution of bis-sulfone **38c** (0.185 g, 0.49 mmol) and carbonate **46b** (n = 2)(0.148 g, 0.45 mmol) in THF (1.5 mL) was added at room temperature to a mixture of $Pd_2(dba)_3{\cdot}CHCl_3$ (0.011 64 g, 0.0113 mmol) and triphenylphosphine(0.0257 g, 0.098 mmol) in THF (0.5 mL). The reaction mixture was stirred at 50 °C for 17 h, cooled, concentrated, and flash chromatographed (hexane: ether = 2:1 to 1:1) to give compound **47a** (0.205 g, 72%). IR ($CDCl_3$): 1638, 1445, 1331, 1310, 1145, 1090 1075 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.04 (dd, J = 8.6, 1.2 Hz, 4H), 7.70 (m, 2H), 7.58 (m, 4H), 5.83 (m, 1H), 5.25 (bs, 1H), 5.11 (s, 1H), 5.03 (dd, J = 17.1, 1.8 Hz, 1H), 4.96 (dd, J = 10.1, 1.9 Hz, 1H), 4.75 (m, 6H), 3.82 (t, J = 2.0 Hz, 2H), 3.46 (t, J = 2.0 Hz, 2H), 3.24 (s, 3H), 3.10 (s, 2H), 2.42 (m, 2H), 2.18 (m, 14H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 149.55, 149.16, 149.11, 141.98, 138.68, 137.99, 134.77, 131.89, 128.68, 117.71, 114.61, 109.47, 109.34, 109.18, 90.67, 82.72, 79.74, 59.82, 57.52, 35.38, 35.28, 34.72, 34.39, 31.89, 22.36. Calcd for $C_{37}H_{46}O_5S_2$: 634.2787. Found: 634.2739. Anal. Calcd for $C_{37}H_{46}O_5S_2$: C, 70.00; H, 7.30. Found: C, 69.70; H, 7.28.

Preparation of 3,3-Bis(phenylsulfonyl)-1-(methoxyethylidene)-13-methylenetetraspiro[4.1.1.1.4.2.2.2]henicosane (48a). A solution of substrate **47a** (0.035 g, 0.055 mmol) in benzene-d_6 (1.0 mL) followed by acetic acid (3.2 μL, 0.05 mmol) was added to $Pd_2(dba)_3{\cdot}CHCl_3$ (0.001 43 g, 0.001 38 mmol), and triphenylstibine (0.001 94 g, 0.0055 mmol). The reaction was monitored by NMR spectroscopy. After standing at 53–55 °C for 24 h, the reaction mixture was cooled, concentrated, and flash chromatographed (hexane:ether = 2:1 to 1:1) to give tetraspirane **48a** (0.030 g, 85.7%). IR ($CDCl_3$): 1448, 1329, 1310, 1145, 1079 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.03 (m, 4H), 7.72 (m, 2H), 7.60 (m, 4H), 5.25 (m, 1H), 4.82 (m, 2H), 3.80 (d, J = 6.4 Hz, 2H), 3.32 (s, 3H), 3.31 (m, 2H), 2.70 (m, 2H), 2.32 (m, 2H), 2.20 (m, 2H), 1.50–1.80 (m, 20H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 153.01, 149.65, 137.13, 136.98, 134.72, 131.55, 128.91, 116.57, 105.29, 92.25, 69.95, 58.00, 56.31, 56.22, 56.14, 56.01, 55.91, 54.41, 53.80, 53.75, 50.59, 49.99, 49.85, 48.06, 45.45, 45.32, 41.82, 41.75, 41.01 , 40.94, 40.84, 40.73, 40.62, 40.49, 40.41, 40.34, 38.10, 38.05, 35.56, 35.48, 31.39, 31.33. Calcd for $C_{31}H_{42}O_3S$ (M^+ − $PhSO_2H$): 492.2698. Found: 492.2679. Anal. Calcd for $C_{37}H_{46}O_5S_2$: C, 70.00; H, 7.30. Found: C, 70.33; H, 7.11.

Ozonolysis of Tetraspirane 48a. Ozone was bubbled through a solution of **48a** (0.053 g, 0.166 mmol) in dichloromethane (2 mL) and methanol (4 mL) at −78 °C as previously described. Workup and elimination as before followed by flash chromatography (ether) gave **49a** (0.010 g, 35%). IR ($CDCl_3$): 2941, 2858, 1735, 1683, 1598, 1355 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 5.24 (s, 1H), 3.82 (s, 3H), 2.50–2.70 (m, 2H), 2.13 –2.30 (m, 4H), 2.05 (m, 2H), 1.90 (m, 2H), 1.50–1.82 (m, 16H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 220.40, 220.32, 210.65, 210.60, 188.98, 188.90, 102.94, 102.89, 102.79, 58.37, 55.58, 55.50, 55.44, 55.35, 54.98, 54.76, 54.59, 54.54, 54.36, 54.01, 53.93, 53.83, 53.71, 53.17, 53.12, 58.06, 52.98, 51.97, 51.82, 51.74, 51.22, 51.13, 50.99, 50.91, 50.58, 50.55, 49.90, 49.86, 47.05, 46.97, 46.93, 46.26, 46.20, 41.33, 41.16, 40.95. Calcd for $C_{22}H_{30}O_3$ (M^+): 342.2195. Found: 342.2195.

Preparation of Methyl 2,5,8,11,14-Pentakis(methylene)-17-pentadecenyl Carbonate (46b) (n = 3). To a solution of alcohol **46a** (n = 2) (5.80 g, 21.17 mmol) in carbon tetrachloride (25 mL) was added triphenylphosphine (6.66 g, 25.40 mmol). After reaction and workup as previously described, flash chromatography (hexane) gave the chloride as a light yellow oil (5.00 g, 81%). IR ($CDCl_3$): 3081, 2934, 1644, 1446, 1258 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 5.81 (m, 1H), 5.14 (s, 1H), 5.03 (dd, J = 17.2, 1.7 Hz, 1H), 4.98 (s, 1H), 4.96 (d, J = 10.0 Hz, 1H), 4.78 (s, 2H), 4.76 (s, 4H), 4.06 (s, 2H), 2.33 (m, 2H), 2.18 (m, 14H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 149.42, 149.10, 148.79, 145.13, 138.67, 114.67, 109.67, 109.33, 109.23, 48.25, 35.29, 34.25, 34.18, 33.76, 31.85, 31.03.

The above chloride (4.80 g, 16.41 mmol) in ether (20 mL) was added dropwise at −78 °C to lithiated methallyl alcohol generated from the latter (2.76 mL, 32.80 mmol) with n-butyllithium (6.56 mL, 65.6 mmol) and TMEDA (9.90 mL, 65.6 mmol) in ether (150 mL) at 0 °C. After reaction and workup as previously described, flash chromatography (hexane:ether = 4:1) gave alcohol **46b** (n = 3) as a colorless oil (4.20 g, 78%). IR ($CDCl_3$): 3612, 2935, 1644, 1450, 1439 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 5.81 (m, 1H), 5.05 (bs, 1H), 5.00 (m, 2H), 4.90 (bs, 1H), 4.76 (bs, 8H), 4.09 (d, J = 5.9 Hz, 2H), 2.20 (m, 21H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 149.52, 149.46, 149.18, 149.12, 148.96, 138.66, 114.66, 109.64, 109.38, 109.30, 109.19, 109.14, 65.93, 35.28, 34.29, 34.25, 34.15, 31.84, 31.01.

To a solution of alcohol **46a** (n = 3) (1.00 g, 3.044 mmol), DMAP (0.10 g), and pyridine (0.74 mL, 9.15 mmol) in dichloromethane (10 mL) was added slowly methyl chloroformate (0.71 mL, 9.15 mmol) at 0 °C. After reaction and workup as previously described, flash chromatography (hexane:ether = 20:1) gave carbonate **46b** (n = 3)as a colorless oil (1.01 g, 85.8%). IR ($CDCl_3$): 1748, 1644, 1444, 1274 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 5.82 (m, 1H), 5.10 (s, 1H), 5.00 (m, 3H), 4.76 (s, 8H), 4.60 (s, 2H), 3.80 (s, 3H), 2.18 (m, 20H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.94, 149.50, 149.41, 149.10, 148.79, 143.26, 138.66, 114.65, 113.28, 109.57, 109.30, 109.19, 109.14, 70.27, 54.72, 35.28, 34.27, 34.23, 34.17, 33.83, 31.83, 31.02. Anal. Calcd for $C_{25}H_{38}O_3$: C, 77.68; H, 9.91. Found: C, 77.89; H, 10.11.

Preparation of 19,19-Bis(phenylsulfonyl)-23-methoxy-5,8,11,14,17-pentakis(methylene)-1-tricosen-21-yne (47b). A solution of **38c** (n = 3) (0.303 g, 0.80 mmol) and carbonate **46b** (0.294 g, 0.762 mmol) in THF (2.0 mL) at room temperature was added to a mixture of $Pd_2(dba)_3{\cdot}CHCl_3$ (0.019 72 g, 0.019 05 mmol) and triphenylphosphine (0.039 82 g, 0.152 mmol) in THF (1.0 mL). The reaction mixture was stirred at 50 °C overnight, cooled, concentrated, and flash chromatographed (hexane: ether = 1.5:1) to give substrate **47b** as a light brown oil (0.48 g, 91.6%). IR ($CDCl_3$): 1643, 1448, 1336, 1312, 1148, 1078 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 8.04 (dd, J = 8.6, 1.4 Hz, 4H), 7.70 (m, 2H), 7.58 (m, 4H), 5.83 (m, 1H), 5.25 (bs, 1H), 5.11 (bs, 1H), 5.03 (dd, J = 17.1, 1.8 Hz, 1H), 4.96 (d, J = 10.1, 1.9 Hz, 1H), 4.75 (m, 8H), 3.82 (t, J = 1.8 Hz, 2H), 3.46 (t, J = 1.8 Hz, 2H), 3.24 (s, 3H), 3.10 (s, 2H), 2.42 (m, 2H), 2.18 (m, 18H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 147.47, 149.07, 149.00, 141.81, 138.63, 137.69, 134.83, 131.80, 128.69, 117.69, 114.63, 109.39, 109.28, 109.10, 90.33, 82.60, 79.63, 59.74, 57.51, 25.25, 35.11, 34.54, 34.21, 31.81, 22.26. Calcd for $C_{35}H_{46}O_2S$ (M^+ − $PhSO_2H$): 546.3168. Found: 546.3176.

Preparation of 3,3-Bis(phenylsulfonyl)-1-(methoxyethylidene)-15-methylenepentaspiro[4.1.1.1.1.4.2.2.2.2]pentacosane (48b). A solution of substrate **47b** (0.0495 g, 0.0719 mmol) in benzene-d_6 (1.0 mL) followed by acetic acid (4.1 μL, 0.0719 mmol) at room temperature was added to $Pd_2(dba)_3{\cdot}CHCl_3$ (0.001 86 g, 0.001 80 mmol), and triphenylstibine (0.002 54 g, 0.007 19 mmol). After standing at 60–65 °C for 12 h, the reaction mixture was cooled, concentrated, and flash chromatographed (hexane:ether = 15:1) to give pentaspirane **48b** as a colorless oil (0.039 g, 78.8%). IR ($CDCl_3$): 1602, 1585, 1448, 1329, 1311, 1148, 1079 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.03 (m, 4H), 7.72 (m, 2H), 7.60 (m, 4H), 5.25 (m, 1H), 4.82 (m, 2H), 3.79 (d, J = 6.4 Hz, 2H), 3.32 (s, 3H), 3.31 (m, 2H), 2.70 (m, 2H), 2.32 (m, 2H), 2.20 (m, 2H), 1.50–1.80 (m, 26H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 153.22, 153.16, 149.56, 136.78, 136.61, 134.80, 131.50, 128.92, 116.39, 105.25, 91.87, 69.89, 58.06, 56.37, 56.19, 55.90, 55.76, 54.26, 53.60, 53.52, 53.48, 50.33, 50.25, 50.16, 49.86, 49.76, 48.05, 45.28, 45.15, 41.70, 41.65, 41.12, 41.01, 40.82, 40.68, 40.58, 40.31, 38.00, 37.91, 35.41, 35.34, 31.35. Calcd for $C_{35}H_{46}O_2S$ (M^+ – $PhSO_2H$): 546.3168. Found: 546.3150. Anal. Calcd for $C_{41}H_{52}O_5S_2$: C, 71.48; H, 7.61; S, 9.31. Found: C, 71.70; H, 7.89; S, 9.01.

Ozonolysis of Pentaspirane 48b. Ozone was bubbled through a solution of **48b** (0.062 g, 0.090 mmol) in dichloromethane (2 mL) and methanol (4 mL) at –78 °C as previously described. Reaction, elimination, and workup as before followed by flash chromatography (ether) gave enone **49b** (0.012 g, 34%). IR ($CDCl_3$): 1734, 1683, 1598, 1355 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 5.24 (s, 1H), 3.82 (s, 3H), 2.50–2.68 (m, 2H), 1.84–2.28 (m, 8H), 1.48–1.80 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 220.06, 210.29, 188.64, 188.56, 136.76, 102.95, 102.83, 102.70, 102.57, 102.51, 58.70, 58.52, 58.35, 58.19, 56.34, 56.28, 56.21, 56.06, 56.02, 55.85, 55.73, 55.60, 55.52, 55.10, 54.99, 54.82, 54.72, 54.62, 54.13, 54.00, 53.94, 53.82, 53.34, 53.20, 53.07, 53.02, 52.22, 52.15, 52.01, 51.95, 51.89, 51.22, 51.05, 50.98, 50.47, 50.41, 50.26, 50.22, 47.17, 47.11, 47.08, 46.45, 46.39, 46.31, 46.19, 41.60, 41.54, 41.41, 41.33, 41.03, 40.84, 40.70, 40.58, 40.22, 40.15, 40.08, 39.99, 38.47, 38.38, 38.29, 38.19, 38.05, 37.97, 37.92, 37.04. Calcd for $C_{26}H_{36}O_3$ (M^+): 396.2664. Found: 396.2654.

Preparation of 2,5,8,11,14,17-Hexakis(methylene)-20-henicosenyl Carbonate (46b) (n = 4). To a solution of alcohol **46a** (n = 3) (2.86 g, 8.72 mmol) in carbon tetrachloride (10 mL) was added triphenylphosphine (2.74 g, 10.46 mmol). Reaction and workup as previously described followed by flash chromatography (hexane) gave the chloride as a colorless oil (2.10 g, 70%). IR ($CDCl_3$): 1644, 1446, 1258 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 5.81 (m, 1H), 5.14 (s, 1H), 5.03 (dd, J = 17.2, 1.3 Hz, 1H), 4.98 (s, 1H), 4.97 (d, J = 10.0 Hz, 1H), 4.78 (s, 2H), 4.76 (s, 6H), 4.06 (s, 2H), 2.33 (m, 2H), 2.18 (m, 18H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 149.52, 149.43, 149.13, 148.78, 145.14, 138.67, 114.67, 109.67, 109.31, 109.25, 109.16, 48.26, 35.29, 34.25, 34.18, 33.76, 31.85, 31.03.

The above chloride (1.90 g, 5.48 mmol) in ether (5 mL) was added dropwise at –78 °C to lithiated methallyl alcohol generated from the latter (0.92 mL, 10.96 mmol), n-butyllithium (2.20 mL, 22.0 mmol), and TMEDA (3.31 mL, 21.92 mmol) in ether (20 mL) at 0 °C. After reaction and workup as previously described, flash chromatography (hexane:ether = 4:1) gave alcohol **46a** (n = 4) as a colorless oil (1.25 g, 60%). IR ($CDCl_3$): 3620, 1644, 1450 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 5.84 (m, 1H), 5.05 (s, 1H), 5.00 (m, 2H), 4.90 (s, 1H), 4.76 (bs, 10H), 4.10 (d, J = 6.2 Hz, 2H), 2.20 (m, 24H), 1.37 (t, J = 6.2 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 149.51, 149.45, 149.17, 149.12, 148.96, 138.65, 114.66, 109.64, 109.39, 109.31, 109.16, 65.93, 35.28, 34.28, 34.24, 34.14, 31.83, 31.00.

To a solution of alcohol **46a** (n = 4) (1.10 g, 2.88 mmol), DMAP (0.01 g), and pyridine (0.70 mL, 8.64 mmol) in dichloromethane (10 mL) was added slowly methyl chloroformate (0.67 mL, 8.64 mmol) at 0 °C. Usual reaction and workup followed by flash chromatography (hexane:ether = 20:1) gave carbonate **46b** (n = 4) as a colorless oil (1.13 g, 89.2%). IR ($CDCl_3$): 1748, 1644, 1444 1275 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 5.82 (m, 1H), 5.10 (s, 1H), 5.00 (m, 3H), 4.76 (s, 10H), 4.60 (s, 2H), 3.80 (s, 3H), 2.18 (m, 24H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.94, 149.50, 149.40, 149.10, 148.79, 143.26, 138.66, 114.66, 113.28, 109.58, 109.30, 109.15, 70.27, 54.72, 35.28, 34.28, 34.24, 34.17, 33.84, 31.84, 31.02. Anal. Calcd for $C_{29}H_{44}O_3$: C, 79.04; H, 10.06. Found: C, 79.14; H, 10.31.

Preparation of 22,22-Bis(phenylsulfonyl)-26-methoxy-5,8,11,14,17,-20-hexakis(methylene)-1-hexacosen-24-yne (47c). A solution of **38c** (0.303 g, 0.80 mmol) and carbonate **46b** (n = 4) (0.335 g, 0.762 mmol) in THF (2.0 mL) was added at room temperature to a mixture of $Pd_2(dba)_3{\cdot}CHCl_3$ (0.0192 g, 0.019 05 mmol) and triphenylphosphine (0.0398 g, 0.152 mmol) in THF (1.0 mL). The reaction mixture was stirred at 50 °C overnight, cooled, concentrated, and flash chromatographed (hexane:ether = 1.5:1) to give substrate **47c** as a brown oil (0.50 g, 88.4%). IR ($CDCl_3$): 1043, 1448, 1336, 1312, 1148, 1098, 1078 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 8.05 (d, J = 8.0 Hz, 4H), 7.70 (m, 2H), 7.57 (m, 2H), 5.83 (m, 1H), 5.25 (bs, 1H), 5.11 (bs, 1H), 5.04 (dd, J = 17.3, 1.3 Hz, 1H), 4.96 (dd, J = 10.2, 0.9 Hz, 1H), 4.75 (bs, 10H), 3.82 (bs, 2H), 3.45 (bs, 2H), 3.24 (s, 3H), 3.10 (s, 2H), 2.44 (m, 2H), 2.18 (m, 22H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 149.48, 149.07, 148.99, 141.80, 138.63, 137.69, 134.83, 131.80, 128.69, 117.69, 114.64, 109.39, 109.29, 109.11, 90.33, 82.60, 79.63, 59.73, 57.51, 35.25, 35.10, 34.54, 34.21, 31.81, 22.26. Calcd for $C_{39}H_{52}O_3S$ (M^+ – $PhSO_2H$): 600.3637. Found: 600.3638.

Preparation of 3,3-Bis(phenylsulfonyl)-1-(methoxyethylidene)-17-methylenehexaspiro[4.1.1.1.1.1.4.2.2.2.2.2]nonacosane (48c). A solution of substrate **47c** (0.0582 g, 0.0784 mmol) in benzene-d_6 (1.0 mL) followed by acetic acid (4.5 μL, 0.0784 mmol) was added at room temperature to $Pd_2(dba)_3{\cdot}CHCl_3$ (0.002 03 g, 0.001 96 mmol), and triphenylstibine (0.002 77 g, 0.007 84 mmol). After standing at 60–65 °C for 12 h, the reaction mixture was cooled, concentrated, and flash chromatographed (hexane:ether = 1:1) to give hexaspirane **48c** as a colorless oil (0.0445 g, 77%). IR ($CDCl_3$): 1602, 1585, 1448, 1329, 1311, 1148, 1079 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.03 (m, 4H), 7.72 (m, 2H), 7.60 (m, 4H), 5.25 (m, 1H), 3.79 (m, 2H), 3.79 (d, J = 6.5 Hz, 2H), 3.32 (s, 3H), 3.31 (m, 2H), 2.70 (m, 2H), 2.32 (m, 2H), 2.20 (m, 2H), 1.50–1.80 (m, 32H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 153.26, 153.22, 149.59, 136.79, 136.62, 134.80, 131.50, 128.92, 116.38, 105.20, 91.88, 69.89, 58.06, 56.50, 56.39, 56.30, 56.21, 56.14, 55.92, 55.82, 55.77, 54.26, 53.54, 50.23, 49.95, 49.86, 49.79, 49.58, 48.05, 45.27, 45.14, 41.80, 41.72, 41.64, 41.18, 41.11, 41.06, 40.92, 40.83, 40.77, 40.64, 40.56, 40.32, 38.01, 37.95, 35.42, 35.35, 31.36, 31.29. Anal. Calcd for $C_{45}H_{58}O_5S_2$: C, 72.74; H, 7.87; S, 8.03. Found: C, 72.60; H, 7.80; S, 8.38.

Ozonolysis of Hexaspirane 48c. Ozone was bubbled through a solution of **48c** (0.059 g, 0.0795 mmol) in dichloromethane (2 mL) and methanol (4 mL) as described previously. Workup and elimination followed by flash chromatography (ether) gave enone **49c** (0.024 g, 67%). IR ($CDCl_3$): 1734, 1683, 1598, 1355 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 5.24 (s, 1H), 3.81 (s, 3H), 2.50–2.70 (m, 2H), 2.16–2.29 (m, 4H), 2.05 (m, 2H), 1.90 (m, 2H), 1.45–1.80 (m, 28H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 220.60, 210.82, 189.07, 189.01, 188.95, 102.93, 102.81, 58.35, 56.46, 56.37, 56.26, 56.16, 56.10, 55.99, 55.86, 55.76, 55.65, 55.04, 54.83, 54.77, 53.90, 53.13, 52.15, 52.02, 51.95, 51.14, 50.96, 50.89, 50.35, 50.23, 50.17, 50.00, 49.92, 49.62, 47.06, 46.97, 46.36, 46.29, 46.23, 41.52, 41.46, 41.34, 41.06, 40.93, 40.87, 40.78, 40.67, 40.62, 40.37, 40.26, 40.13, 40.01, 39.96, 39.87, 38.45, 38.34, 38.28, 38.22, 38.06, 37.91, 37.84, 36.92. Calcd for $C_{30}H_{42}O_3$ (M^+): 450.3134 Found: 450.3148.

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Supplementary Material Available: Copies of the spectra of the polyspiranes **40a-c**, **44c**, and **48a-c** (7 pages). Ordering information is given on any current masthead page.