Cyclooctane or Cyclohexane Annulations Based on Intramolecular Additions of Allylsilanes to Conjugated Dienones†,[1]

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The scope and limitations of alkenyl dienone cyclizations for the formation of fused cyclooctane or cyclohexane systems are described.

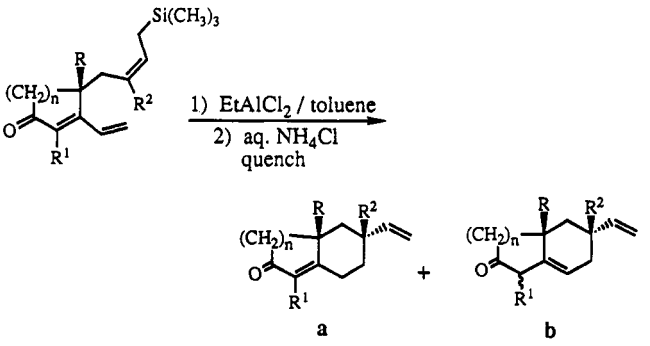
For several years we have studied the inter- and intramolecular Michael reaction of allylsilanes.[2] In a future article we discuss the scope of intramolecular additions of allylsilanes to simple cycloalkenones.[3] Scheme I illustrates that with a 4-butenyl dienone,[4] such as **1**, there are five possible modes of cyclization. Under Lewis acid catalysis allylsilanes react with simple cycloalkenones at the γ-position[5] via an S_E2' mechanism[6] and add in 1,6-fashion to conjugated dienones.[7] This was confirmed when treatment of trienone **1** with ethylaluminum dichloride produced the 6,6-fused bicyclic enone **2** in 77% yield.[8] Based on mechanistic and kinetic arguments,[9] we expected that treatment of **1** with fluoride ion would also give octalone **2**. Remarkably, the major product of this reaction was fused cyclooctane **3**, along with the 1,2-adduct **6**. Excited by the catalyst-controlled regioselectivity and the potential utility of these new annulation procedures, we extended our study to a series of substituted 3-vinylcycloalkenones.[11a] We also established the mechanism of the fluoride ion promoted reactions.[11b] The results of both studies are the focus of this paper. For clarity, our findings have been organized by the catalyst employed, the size of the annulated ring, and the type of ring closure.[4]

Cyclohexane Annulations

A. Lewis Acid Promoted 4-Alkenyl Dienone Cyclizations. We have found Lewis acid catalyzed additions of 4-butenyl dienones a useful means for annulating cyclohexane rings. Table I lists five such cyclizations that produce fused cyclohexanes in good yield on reaction scales ranging from 500 mg to 10 g of substrate. More significantly, side products resulting from protodesilylation were not observed and in each case only a single diastereomer was obtained. These annulations are run in toluene at 0 °C or at room temperature, using a 50% excess of Lewis acid, although a rapid reaction rate requires 2 equiv of catalyst. Quenching the reaction mixture with saturated aqueous ammonium chloride gives both the conjugated and unconjugated bicyclic enones (as shown), whereas workup with mild aqueous hydrochloride acid affords only the conjugated enones in comparable yield. Finally, quaternary centers can be created by cyclizing the appropriately functionalized trisubstituted allylsilane precursor.[12,13]

Examination of the reactions illustrated in Scheme II reveals the extent of substitution on the vinyl group tolerated in these cyclizations. γ-Substituted conjugated dienones readily cyclize (cf. **17** → **18**), while γ,δ-substituted dienones such as **19** produce either 1,2-adducts with ethylaluminum dichloride as catalyst (cf. **20**) or tricyclic products resulting from 1,6-addition if titanium tetrachloride is used (cf. **21**). To our disappointment, δ,δ-disubstituted dienones, such as **22**, fail to react with mild Lewis acids and give only 1,2-adducts (cf. **23**) upon

Table I



substr	n	R	R¹	R²	yields	
					a	b
7	1	H	H	H	8a (48%)	8b (0%)
9	1	CH_3	H	H	10a (44%)	10b (23%)
11	2	H	H	H	12a (47%)	12b (23%)
1	2	CH_3	H	H	2 (77%)	2b (0%)
13	2	CH_3	CH_3	H	14a (80%)	14b (0%)
15	2	CH_3	H	CH_3	16a (20%)	16b (43%)

† Dedicated to Professor Paul A. Grieco on the occasion of his receipt of The 1991 ACS Award for Creative Work in Synthetic Organic Chemistry.

(1) Taken in part from the Ph.D. Dissertation of Kenneth Hull, The University of Georgia, 1989.

(2) For recent surveys of allylsilane chemistry, see: (a) Fleming, I.; Dunogues, J.; Smithers, R. *Org. React.* **1989**, *37*, 57-575. (b) Majetich, G. "Allylsilanes in Organic Synthesis" in *Organic Synthesis, Theory and Applications*, Hudlicky, T., Ed.; Jai Press, Inc.: Greenwich, CT, 1989; pp 173-240.

(3) Majetich, G.; Defauw, J.; Hull, K. Manuscript in preparation.

(4) We have developed several annulation methods to produce six-, seven-, and eight-membered rings based on the intramolecular addition of an allylsilane to a 3-vinylcycloalkenone. For convenience, we use the following conventions to describe these various cyclizations: (1) the suffix dienone describes the 3-vinylcycloalkenone unit; (2) a locant for the allylsilane appendage is stated; (3) the nature of the allylsilane side chain is defined either as an isoalkenyl or *n*-alkenyl substituent; and (4) geometric isomers or substitutions are ignored.

isoalkenyl *n*-alkenyl

(5) For a discussion of the β-effect, see: (a) Hudrlick, P. F. *New Applications of Organometallic Reagents in Organic Synthesis*; Seyferth, D., Ed.; Elsevier: Amsterdam, 1976; p 127. (b) Colvin, E. W. *Chem. Soc. Rev.* **1978**, *7*, 15.

(6) For examples of S_E2' mechanisms, see: Sleezer, B.; Winstein, R.; Young, J. *J. Am. Chem. Soc.* **1963**, *85*, 1980.

(7) For a review of intramolecular additions of allylsilanes to dienones, see: Majetich, G.; Hull, K.; Lowery, D.; Ringold, C.; Defauw, J. "Intramolecular Additions of Allylsilanes to Dienones" in *Selectivities in Lewis Acid-Promoted Reactions*; Schinzer, D., Ed.; Kluwer Academic Publishers Group: Dordrecht, Holland; 1989.

(8) (a) All structures drawn here represent racemates, with only one enantiomer shown. (b) The spectroscopic data obtained for all new compounnds were fully consistent with the assigned structures. (c) Reaction conditions have not been optimized. (d) All yields are isolated yields.

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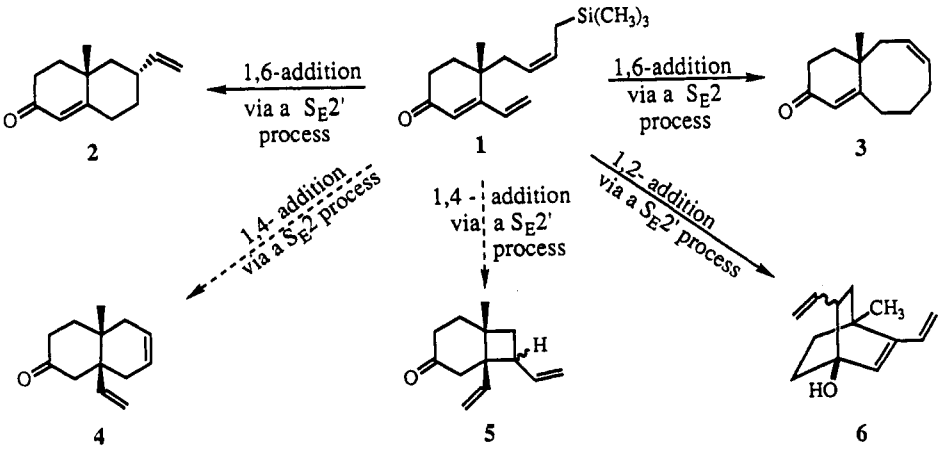
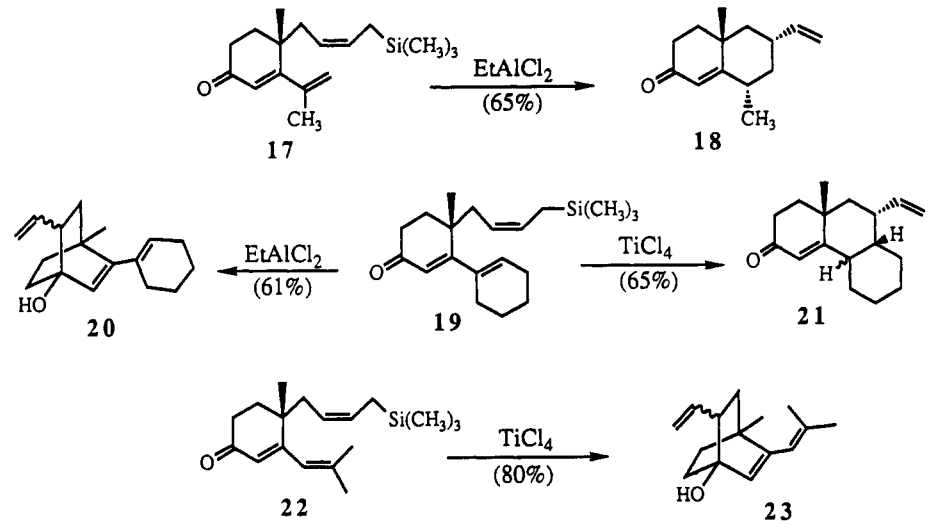
Scheme I



Scheme II

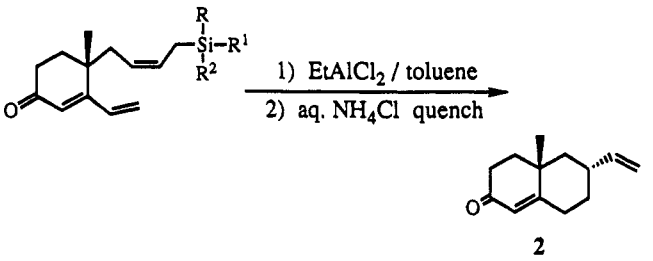


treatment with strong Lewis acids, such as $TiCl_4$.

We were curious to see whether changing the nature of the silicon ligands would modify the regioselectivity of these cyclizations (Table II). Thus trienones **24** and **25** were prepared and treated with ethylaluminum dichloride, using optimal conditions. In each case enone **2** was the only product, although its isolation was complicated by the presence of phenylsilanol byproducts.

Our mechanistic analysis for these annulations is shown in Scheme III. Addition of the first equivalent of ethylaluminum dichloride to trienone **1** undoubtedly forms an equilibrium mixture of 1:1 complexes in which the Lewis acids adds to either of the carbonyl's lone pairs (cf. i and ii).[14] Although either 1:1 complex can exist in either a transoid or cisoid diene conformation, 1,6-addition can only occur via the transoid conformer. In simple acyclic 1,3-dienones, the planar transoid conformation is more stable than the cisoid form.[15] In the case of complex i steric repulsion between the C(3) vinyl group and the various ligands of the Lewis acid force the vinyl moiety to favor the transoid conformation. Nucleophilic attack—in 1,6-fashion—by the allylsilane double-bond electrons produces

Table II



substr	R	R^1	R^2	yield
1	CH_3	CH_3	CH_3	(77%)
24	CH_3	CH_3	C_6H_5	(65%)
25	C_6H_5	C_6H_5	C_6H_5	(60%)

(9) Work by Illuminati and co-workers[10] has established that the formation of three-, five-, six-, and seven-membered rings is favored over the formation of four-, eight-, nine-, and ten-membered rings. The rate of formation of a six-membered ring is favored over that of an eight-membered ring by more than a factor of 10^4.

(10) (a) Galli, C.; Illuminati, G.; Mandolini, L.; Tamborra, P. *J. Am. Chem. Soc.* **1977**, *99*, 2591. (b) Illuminati, G.; Mandolini, L.; Masci, B. *J. Am. Chem. Soc.* **1975**, *97*, 4960.

(11) For a preliminary account of this study, see: (a) Majetich, G.; Hull, K.; Desmond, R. *Tetrahedron Lett.* **1985**, *26*, 2751. For a preliminary account of our mechanistic study, see: (b) Majetich, G.; Hull, K. *Tetrahedron Lett.* **1988**, *29*, 2773.

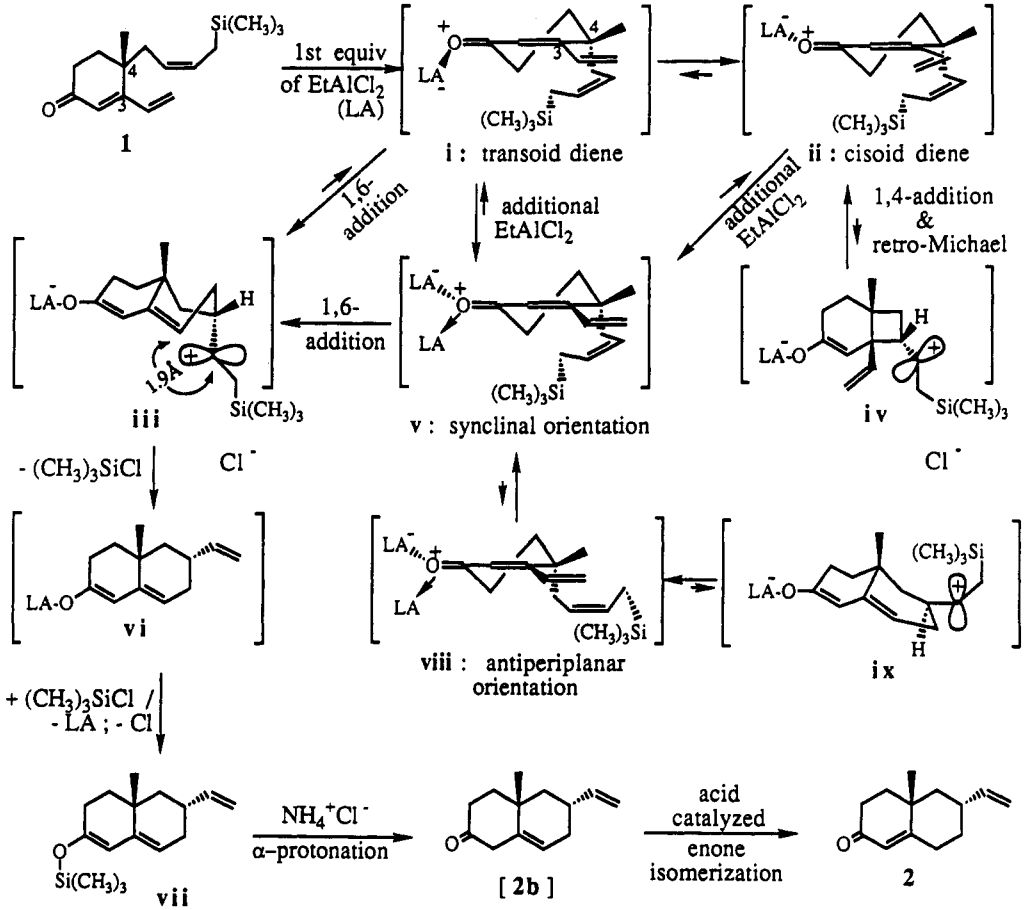
(12) Trisubstituted allylsilane **15** was prepared from (*Z*)-3-ethoxy-6-methyl-6-(2-methyl-4-(trimethylsilyl)-2-butenyl)-2-cyclohexen-1-one (**59**) by reaction with vinyllithium followed by mild acid hydrolysis. The preparation of enone **59** is described in a manuscript in preparation.

(13) Note that 1,3-axial interactions between the two β-face methyls cause unconjugated enone **16b** to be the major product of this reaction.

(14) We have assumed that the dominant conformation for intermediates i, ii, and v has the C(4) allylsilane-containing substituent oriented axially due to A-strain. See: Johnson, F. *Chem. Rev.* **1968**, *68*, 375.

(15) Aten, C. F.; Hedberg, L.; Hedber, K. *J. Am. Chem. Soc.* **1968**, *90*, 2463.

Scheme III



zwitterion iii, containing a silicon-stabilized carbonium ion. Loss of the trimethylsilyl group generates the vinyl group (cf. vi) and chlorotrimethylsilane, which can trap the aluminum enolate (vi) as a silyl dienol ether (cf. vii), thus regenerating the catalyst. Hydrolysis of vii upon workup with aqueous acid initially provides β,γ-unconjugated enone **2b**, which can rearrange to provide enone **2**.

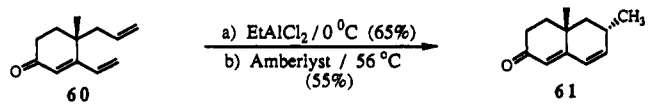
The situation is different with complex ii, in which nonbonded interactions between the C(3) and C(4) substituents destabilize the transoid conformation of the diene moiety, so that the cisoid orientation prevails. In this orientation both 1,2- and 1,6-addition are geometrically precluded; hence, intermediate ii can react only in 1,4-fashion. However, the strain energy associated with bicyclic 6,4-fused intermediate iv favors retro-Michael addition rather than desilylation. Thus in contrast with i, complex ii does not react. Alternatively, further addition of excess ethylaluminum dichloride to either of the 1:1 complexes leads to the formation of 2:1 complex v.[16] Here the cisoid conformation of the diene moiety is destabilized because of steric factors, causing the transoid orientation to prevail. Cyclization of complex v generates carbonium ion iii and therefore enone 2 via intermediates vi, vii, and 2b as described above.

This analysis satisfactorily accounts for the following observations: (1) only cyclohexane-containing products are obtained;[17] (2) these cyclizations are insensitive to the size of the cycloalkenone ring; (3) omission of the acid hydrolysis, or incomplete hydrolysis, results in the isolation of silyl dienol ethers; (4) the nature of the silicon ligands has no effect on the regioselectivity of the reaction; and (5) although these reactions proceed using a stoichiometric quantity of catalyst, they benefit from the use of excess Lewis acid. Moreover, the presence of substituents at the δ and/or γ positions does not impede cyclization provided these substituents do not cause steric repulsion with the equatorially oriented C(4) methyl group. In the case of δ,δ-disubstituted trienone **22**, steric congestion inhibits both 1,4- and 1,6-addition, hence 1,2-addition predominates.

As presented thus far, this mechanism does not account for the stereospecificity observed. Additions of allylsilanes to carbonyl compounds are commonly described in terms of either a synclinal (syn) or antiperiplanar (anti) orientation of the olefinic components prior to carbon–carbon bond formation.[18-21] Accordingly, 1,6-conjugate addition

(16) Support for our assumption that a 2:1 complex may be involved can be found in the intramolecular cyclizations of alkenes with simple enones by Snider and co-workers [Snider, B. B.; Rodini, D. J.; van Straten J. J. *Am. Chem. Soc.* **1980**, *102*, 5872]. Their study demonstrates that β-substituted enones required the formation of an enone-$[EtAlCl_2]_2$ complex before reaction occurred while β,β-disubstituted enones such as mesityl oxide or 3-methyl-2-cyclohexen-1-one failed to react independent of the amount of catalyst used.

(17) Intramolecular ene–dienone cyclizations are useful for the annulation of cyclohexane rings. For example, trienone **60** forms decalin **61** with either Lewis acid or Amberlyst catalysis. See: Majetich, G.; Khetani, V. *Tetrahedron Lett.* **1990**, *31*, 2243.



60 61

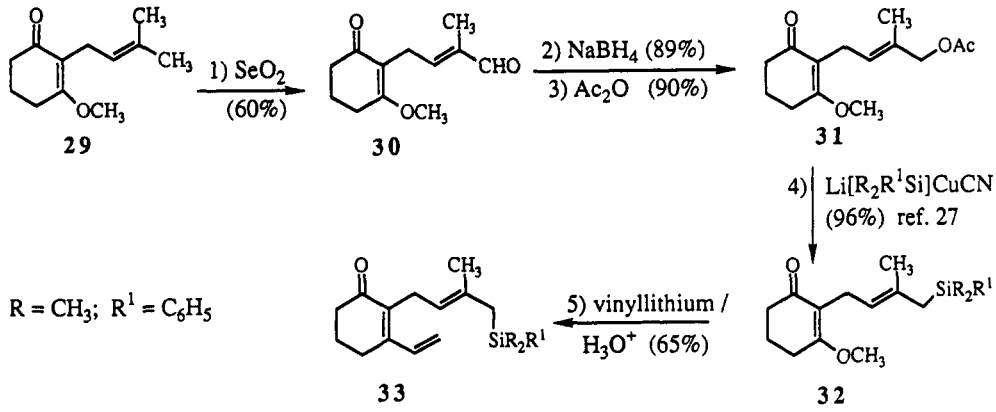
(18) Sarkar and Anderson were the first to study the stereochemical outcome of intramolecular allylsilane cyclizations.[19] Five years latter, Denmark and Weber[20] examined cyclizations wherein the dispositions of the reactive centers were well defined.

(19) Sarkar, T. K.; Andersen, N. H. *Tetrahedron Lett.* **1978**, 3513.

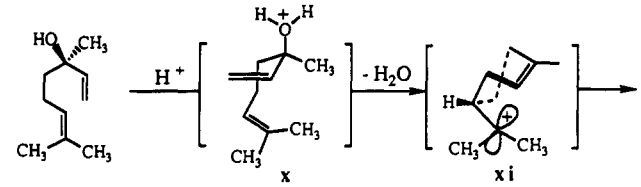
(20) Denmark, S.; Weber, W. *Helv. Chim. Acta* **1983**, *66*, 1655.

(21) Yamamoto, Y.; Sasaki, N. "The Stereochemistry of the Sakurai Reaction" in *The Chemistry of Organosilicon Compounds: Part 1*; Rappaport, S. P., Ed.; John Wiley & Sons: New York, 1989.

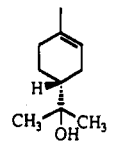
Scheme IV



of the allylsilane to the activated dienone unit, via a synclinal orientation of the allylsilane and dienone (cf. v), produces cationic intermediate iii, whereas reaction of the 2:1 complex via an antiperiplanar orientation gives zwitterion ix. Although both cations benefit from the ability of the silicon atom to stabilize β-carbonium ions, intermediate iii is further stabilized by "through space" π-overlap between the carbonium ion and the Lewis acid enolate while this additional stabilization is geometrically precluded in cationic intermediate ix. Such through-space stabilization was proposed by Arigoni in his stereochemical study of the olefinic cyclization of linalool (26) to terpineol (27),[22] wherein the attacking double bond adopts an orientation in which the π-system stabilizes the developing allylic carbonium ion through the intermediacy of cation xi despite steric considerations (eq 1).[23]



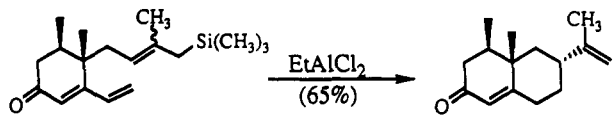
linalool (26)



(1)

terpineol (27)

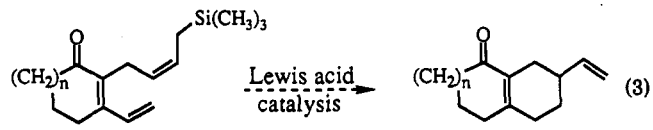
The synthetic utility of 4-alkenyl dienone cyclizations was first demonstrated in the synthesis of the eudesmane sesquiterpene nootkatone (28, eq 2), a flavor component of grapefruit (*Citrus paradisi* Macfayden).[24] Other synthetic applications are forthcoming.



E : Z = 2 : 1 (±)-Nootkatone (28)

(2)

B. Lewis Acid Promoted 2-Alkenyl Dienone Cyclizations. Scrutiny of molecular models suggested that placement of a butenyl allylsilane side chain at the α position of a conjugated dienone unit would permit the annulation of a new cyclohexane ring and provide a means of controlling the resulting ring fusion stereochemistry (i.e., xii → xiii, eq 3). With this goal in mind we set out to prepare a 2-alkenyl dienone.



(3)

xii xiii

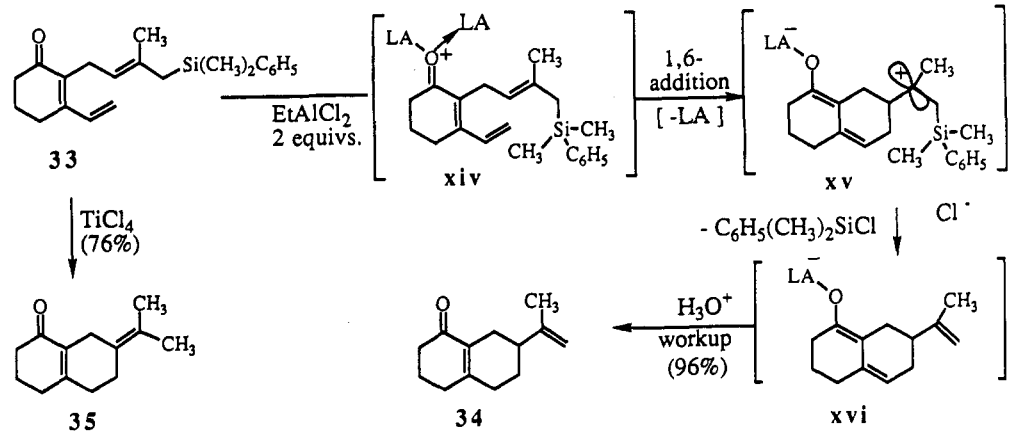
Introduction of an allylsilane appendage onto the C(2) position of a 3-vinylcycloalkenone proved laborious to achieve via conventional procedures (Scheme IV).[25] Alkylation of cyclohexane-1,3-dione with prenyl iodide,[26] followed by treatment with ethereal diazomethane, afforded enone **29** in 80% yield. Reaction of **29** with selenium dioxide produced a 60% yield of enal **30** along with some 2-(3-methyl-2-butenyl)-3-methoxyphenol, due to aromatization of the cyclohexenone system. Selective reduction of the aldehyde moiety using sodium borohydride and acetylation furnished allylic acetate **31**. We have found Fleming's procedure[27] for preparing allylsilanes extremely effective and versatile.[28] Treatment of acetate **31** with the silylcuprate derived from phenyldimethylchlorosilane formed phenyldimethylallylsilane **32** in good yield. Conversion of enone **32** to dienone **33** was achieved as shown.

Exposure of substrate **33** to ethylaluminum dichloride results in a high yield of hexahydronaphthalenone **34** (Scheme V),[29] while the use of $TiCl_4$ not only promotes annulation but also causes isomerization to **35**. A mechanistic analysis similar to that presented earlier can be envisioned for this annulation except that dienone–$[EtAlCl_2]_2$ complex xiv can react only via the less-favored cis diene conformation.

We have recently developed a practical preparation of 2-alkenyl dienones using Gilman reagents[30] derived from

(22) Godtfredsen, S.; Obrechit, J. P.; Arigoni, D. *Chimia* **1977**, *31*, 62.
(23) A manuscript discussing the diastereoselectivity of intramolecular additions of allylsilanes to conjugated dienones is in preparation.
(24) Majetich, G.; Behnke, M.; Hull, K. *J. Org. Chem.* **1985**, *50*, 3615.
(25) The alkylation of cyclohexane-1,3-dione with (*Z*)-4-(trimethylsilyl)-2-butenyl iodide is not feasible since this electrophile is prone to diene formation. For an example of the preparation of quinodimethanes using this strategy, see: Djuric, S.; Sarkar, T.; Magnus, P. *J. Am. Chem. Soc.* **1980**, *102*, 6686.
(26) Stetter, H.; Dierichs, W. *Chem Ber.* **1952**, *85*, 1061.
(27) Ager, D. J.; Fleming, I.; Patel, S. K. *J. Chem. Soc., Perkin Trans I* **1981**, 2520.
(28) For a recent review of allylsilane syntheses, see: Sarkar, T. K. "Methods for the Synthesis of Allylsilanes", *Synthesis* **1990**, 969, 1101.
(29) Wolinsky and co-workers have prepared decalone **34** in their synthesis of β-selinene. See: Moore, L.; Gooding, D.; Wolinsky, J. *J. Org. Chem.* **1983**, *43*, 3750.

Scheme V



Scheme VI

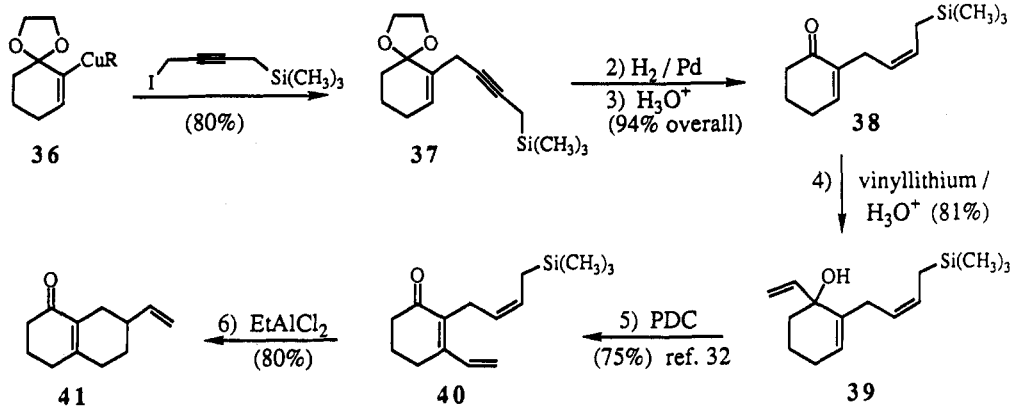
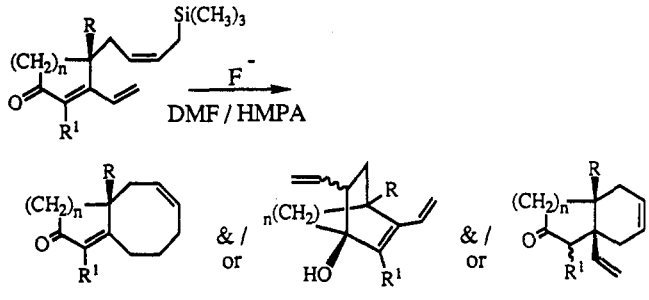


Table III



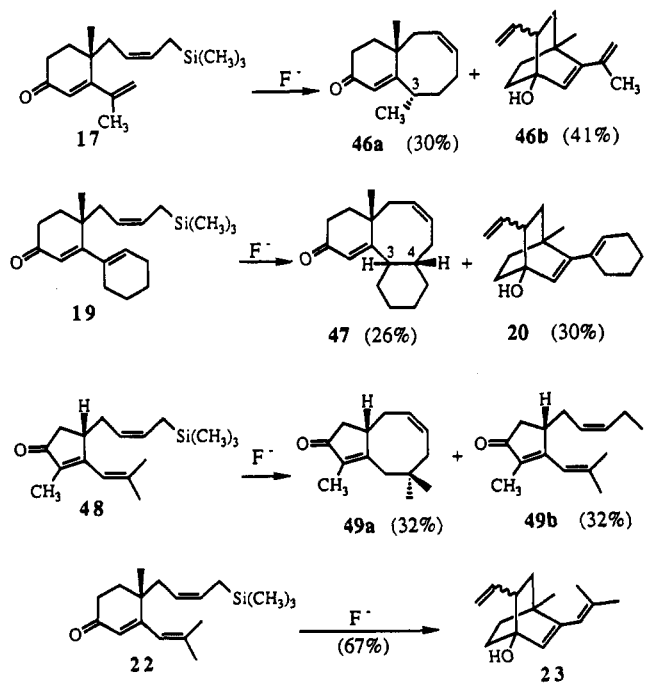
substr	n	R	R¹	yields		
7	1	H	H	**42a** (30%)	**42b** (0%)	**42c** (18%)
9	1	CH_3	H	**43a** (33%)	**43b** (0%)	**43c** (23%)
11	2	H	H	**44a** (0%)	**44b** (32%)	**44c** (30%)
1	2	CH_3	H	**3** (40%)	**6** (30%)	**4** (0%)
13	2	CH_3	CH_3	**45a** (65%)	**45b** (24%)	**45c** (0%)

2-lithio-2-cycloalken-1-one ethylene ketals (cf. **36** → **37**, Scheme VI).[31] With use of this procedure enone **41** was prepared in six steps and 37% overall yield from ketal **36**.

Eight-Membered Ring Annulations

Fluoride Ion Promoted 4-Alkenyl Dienone Cyclizations. The novelty of producing fused cyclooctanes by

Scheme VII



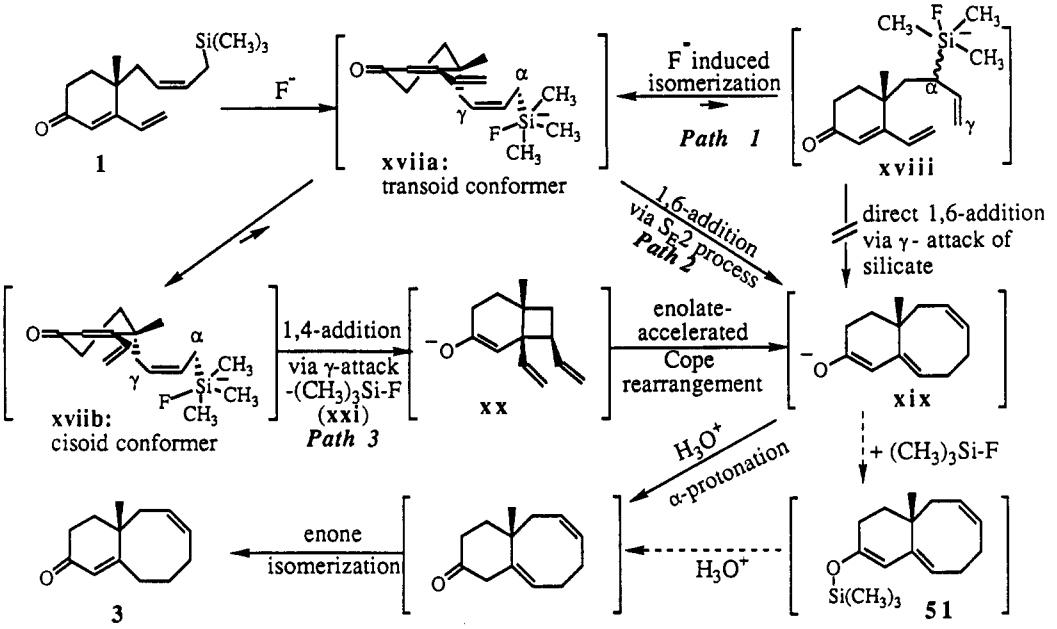
treating 4-butenyl dienones with fluoride ion led us to investigate these reactions further. The substrates that we prepared to establish the scope and limitations of the Lewis acid initiated cyclizations were also studied by using fluoride ion catalysis (Table III). In general, the fluoride ion catalyzed additions favored the formation of the eight-membered ring products, albeit in modest yields. The cyclohexadienone series also produced 1,2-adducts (i.e., **44b**, **6**, and **45b**), unlike the cyclopentadienone series,

(30) Majetich, G.; Leigh, A. J.; Condon, S. *Tetrahedron Lett.* **1991**, *32*, 605.

(31) (a) Guaciaro, M. A.; Wovkulich, P. M.; Smith, A. B., III. *Tetrahedron Lett.* **1978**, 4661. (b) Smith, A. B., III; Branca, S. J.; Pilla, N. N.; Guaciaro, M. A. *J. Org. Chem.* **1982**, *47*, 1855.

(32) Majetich, G.; Condon, S.; Hull, K.; Ahmad, S. *Tetrahedron Lett.* **1989**, *30*, 1033.

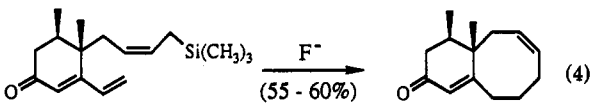
Scheme VIII



which afforded side products resulting from 1,4-addition by the primary center of the allylic nucleophile (i.e., **42c** and **43c**). Although these cyclizations could be carried out by using tetrahydrofuran as the solvent, the yields of cyclooctane-containing products were better in DMF (with 3 equiv of HMPA added) and the reaction times were shorter (<1 h). More importantly, these cyclizations occur with ease at either 0 °C or room temperature.

Scheme VII contains four cyclizations of substrates with substituted dienones. Only trienone **22** failed to form a cyclooctane product. This was unexpected since analogous trienone **48** affords 5,8-fused enone **49a**, a potential precapnelladiene precursor,[33] in 32% yield. Finally it is noteworthy that cyclooctanes **46a** and **47** are single diastereomers and that reaction of **48** also produced trienone **49b** as a result of protodesilylation.

The cyclizations shown in Table III and Scheme VII were carried out by using 0.1–1.0-g of precursor. Nevertheless, this annulation can be scaled up. For example, substrate **50** was routinely cyclized in 2-g batches in yields over 55% (eq 4) and once 7 g was cyclized in 51% yield.[34,35]

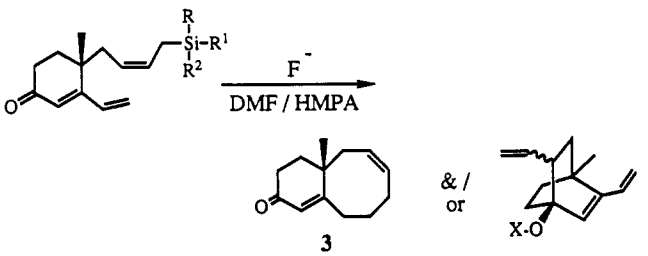


(4)

50

Unlike the Lewis acid catalyzed 4-butenyl dienone cyclizations, the fluoride ion promoted cyclizations show a profound ligand effect (Table IV). The best yield of cyclooctane **3** was obtained when trimethylallylsilane **1** was

Table IV



substr	R	R^1	R^2	yields
1	CH_3	CH_3	CH_3	(40%) X = H (**6**); (30%)
24	CH_3	CH_3	C_6H_5	(38%) X = $SiRR^1R^2$ (**6a**); (23%)
25	C_6H_5	C_6H_5	C_6H_5	(16%) X = $SiRR^1R^2$ (**6b**); (35%)

cyclized, whereas incorporation of three phenyl ligands led to the preferred formation of the silyl ether of the 1,2-adduct.

Three possible mechanisms, illustrated in Scheme VIII, account for the above results. Because allylsilanes are intrinsically nonnucleophilic, the first step in each explanation involves formation of an ambident pentacoordinate silicate anion.[36-39] The merits of each mechanism will be

(33) For recent precapnelladiene syntheses, see: (a) Paquette, L. A.; Andrews, D. R.; Springer, J. P. *J. Org. Chem.* **1983**, *48*, 1147. (b) Kinney, W. A.; Coghlan, M. J.; Paquette, L. A. *J. Am. Chem. Soc.* **1984**, *106*, 6868. (c) Kinney, W. A.; Coghlan, M. J.; Paquette, L. A. *Ibid.* **1985**, *107*, 7352. (d) Mehta, G.; Murthy, A. N. *J. Org. Chem.* **1987**, *57*, 2875.

(34) The utility of this cyclooctane annulation has been featured in a synthesis of neolemnane. See: Majetich, G.; Lowery, D.; Khetani, V.; Song, J.-S.; Hull, K.; Ringold, C. "Intramolecular Additions of Allylsilanes to Conjugated Dienones. Direct Stereoselective Syntheses of (±)-Neolemnanyl Acetate and (±)-Neolemnane," *J. Org. Chem.*, following article in this issue.

(35) Removal of the DMF on larger than 1-g-scale reactions was accomplished by distillation, instead of aqueous workup, prior to column chromatography.

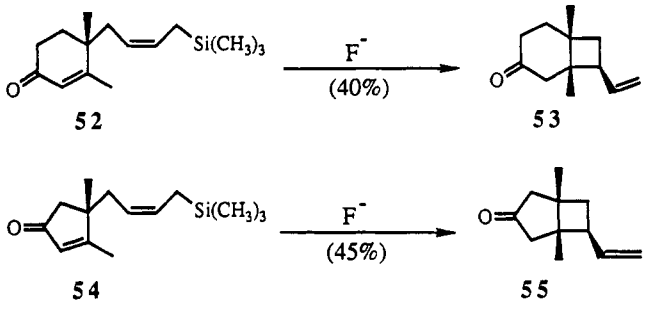
(36) For a comprehensive review discussing hypervalent silicon species as intermediates in the reaction of organosilicon compounds, see: (a) Corriu, R. J. P.; Cuerin, C.; Moreau, J. J. E. "Stereochemistry at Silicon" in *Topics in Stereochemistry*; Eliel, E. L., Wilen, S. H., Allinger, N. L., Eds.; Wiley-Interscience: New York, 1984; Vol XV, pp 43–198. For other examples of penta- or hexacoordinate siliconates, see: (b) Holmes, R. R.; Day, R. O.; Harland, J. J.; Holmes, J. M. *Organometallics* **1984**, *3*, 347. (c) Somberg, D. J.; Frebs, R. *Inorg. Chem.* **1984**, *23*, 1378. (d) Voronkow, M. G.; Deriglazov, N. M.; Brodskaya, E. I.; Kalistratova, E. E.; Gubanova, L. I. *J. Fluorine Chem.* **1982**, *19*, 299.

(37) When we first proposed that addition of fluoride ion to an allylsilane forms a nonbasic silicate nucleophile which can react at either end of the π-system,[38] this conjecture was disputed. Nevertheless, pentacoordinate silicon intermediates have recently been identified as the reactive intermediate in several allylsilane reactions.[39]

(38) (a) Majetich, G.; Casares, A.; Chapman, D.; Behnke, M. *J. Org. Chem.* **1986**, *51*, 1745. (b) Majetich, G.; Desmond, R. W., Jr.; Soria, J. J. *Ibid.* **1986**, *51*, 1753.

(39) For evidence of pentacoordinate silicate intermediates in fluoride ion catalyzed allylation using trimethylallylsilane, see: (a) Pernez, S.; Hamelin, J. *Tetrahedron Lett.* **1989**, *30*, 4081. (b) Kira, M.; Kobayashi, M.; Sakurai, H. *Tetrahedron Lett.* **1987**, *28*, 4081. (c) Hosomi, A.; Kohra, S.; Ogata, K.; Yanagi, T.; Tominaga, Y. *J. Org. Chem.* **1990**, *55*, 2415.

Scheme IX



evaluated by using the cyclization of 1 to 3.

Path 1. The first mechanistic pathway invokes the isomerization of silicate xviia (or xviib) to xviii followed by 1,6-addition of this nucleophile to the dienone unit via an S_E2' mechanism.[40,41] Note that this cyclization mode directly forms 1,5-cyclooctadiene xix, which isomerizes to enone 3 upon workup. In contrast to most allylmetal reagents, allylsilanes are not prone to rapid allylic rearrangement. Although conceptually appealing, the possibility that the initially formed silicate anion isomerizes to xviii under fluoride ion catalysis prior to carbon–carbon bond formation can be discounted. The fluoride ion induced cyclization of 1 occurs with ease at room temperature. Although the equilibration of substituted allylsilanes is known, the conditions required are relatively vigorous [catalytic tetra-*n*-butylammonium fluoride, THF, 100 °C, sealed tube, 24 h], and the more substituted olefin is formed.[42] These considerations obviate an isomerization of the silicate anions.

Path 2. An alternative mechanism requires that direct 1,6-conjugate addition occurs at the silicon-containing terminus of silicate xvii via an S_E2 process. Although ketones **42c** and **43c** (Table III) are clearly the result of 1,4-addition at the silicon-containing terminus, we were hesitant to conclude that it also explains cyclooctane formation since steric factors dictate that the dienone unit adopts a cisoid orientation (cf. xviib), which prevents 1,6-addition.

Path 3. The third mechanism features a novel tandem 1,4-Michael addition/Cope rearrangement. Since the more stable cisoid conformer precludes 1,6-addition, silicate xviib would react in a 1,4-fashion via an S_E2' process to form a 1,2-divinylcyclobutane (cf. xx). While the formation of cyclobutanes via intramolecular Michael condensation of stabilized nucleophiles is subject to retrograde Michael condensation and is unknown, fluoride ion promoted Michael additions are irreversible and can be used to produce fused cyclobutanes (cf. **52** or **54**, Scheme IX).

Given that divinylcyclobutane xx is a plausible reaction intermediate, the next step in this sequence is a [3,3]-sigmatropic rearrangement. While *cis*-1,2-divinylcyclobutane, the parent system, undergoes Cope rearrangement at 120 °C,[43] our cyclizations take place at ambient temperatures.[44] Based on the pioneering work of Evans and others,[45] we felt that the presence of an anionic charge proximate to the 1,5-hexadienyl unit would exhibit a profound rate enhancement on the Cope rearrangement, thus allowing the rearrangement to proceed even at room temperature. α-Protonation of cyclooctadiene xix affords enone xxiii; rearrangement to enone 3 completes this mechanism.

In order to differentiate between the direct 1,6-addition and the tandem Michael/Cope mechanism, we sought to trap enolate xx in situ and thereby establish its existence as a reaction intermediate. The ideal trapping agent was discovered in the course of preparing an authentic sample of ketone 4 (Scheme X). In 1974, Grieco and Miyashita reported the use of an aryl selenide as a protecting group for α-methylene lactones.[46] We felt that this concept would also be applicable to conjugated dienones. Indeed, 1,6-conjugate addition of sodium phenyl selenide anion to trienone 1 gave enone **56** in 90% yield. Our finding that β-substituted 4-butenyl dienones give vinylcyclobutanes under fluoride ion catalysis (cf. **52** or **54**) led us to expect that reaction of enone **56** with fluoride ion would achieve the desired cyclobutane annulation (i.e., **57**), followed by oxidative elimination of the phenyl selenide to furnish ketone 4. To our surprise, reaction of enone **56** with a stoichiometric quantity of fluoride ion gave ketone 4 in 40% yield having a cis orientation of the C(3) and C(8) vinyl groups based on 2D NMR experiments; the balance of the reaction material was either unreacted starting material or fused cyclooctene **3**. On the other hand, treatment of **56** with a catalytic amount of fluoride ion (<20%) gave only trienone 1 and required lengthy reaction times to produce trace amounts of **3**.[47] These results support the following sequence of events: (1) the fluoride ion first acts as a base and causes enolate-initiated elimination of the selenide anion to form 1; (2) the hydrogen fluoride, formed in the foregoing elimination, is consumed by the selenide anion to produce benzeneselenol and regenerate the catalyst; (3) addition of fluoride ion to the allylsilane generates silicate xviib, followed by formation of enolate xx; (4) with a proton source present in the reaction medium (the benzeneselenol) enolate xx is quenched to form ketone 4; and (5) the selenide anion is too weak a base to cause enolate formation—and subsequent Cope rearrangement—thus ensuring the isolation of 4. The use of a catalytic amount of fluoride ion merely retards silicate xvii formation, thereby slowing down the various reaction rates.

The fate of the trimethylfluorosilane (xxi), produced upon formation of enolate xx, has not been rigorously established. On a few occasions, workup of a fluoride ion catalyzed reaction furnished silyl dienol ether **51** derived by silylating dienolate xix. This observation, however, was not reproducible. Presumably fluorotrimethylsilane, which boils at 16 °C, escapes from the reaction mixture and therefore forces the reaction to completion, requiring that a stoichiometric quantity of fluoride ion be used.

With ketone 4 in hand, we were set to test the viability of the enolate-promoted Cope rearrangement. In control

(40) From a mechanistic viewpoint, substitution of an allylsilane *under nucleophilic conditions* is more appropriately considered an addition–elimination reaction, with the terms S_E2 and S_E2' aptly representing the elimination process.

(41) Kumada and Fleming have established that an S_E2' mechanism is involved in the electrophilic reactions of allylsilanes: (a) Hayashi, T.; Kabeta, K.; Hamachi, I.; Kumada, M. *Tetrahedron Lett.* **1983**, *24*, 2865. (b) Fleming, I.; Terrett, N. K. *Ibid.* **1983**, *24*, 4153.

(42) Hosomi, A.; Endo, M.; Sakurai, H. *Chem. Lett.* **1976**, 941.

(43) *trans*-1,2-Divinylcyclobutane requires temperatures greater than 180 °C before Cope rearrangement takes place. See: (a) Vogel, E. *Ann. Chem.* **1958**, *615*, 1. (b) Hammond, G. S.; DeBoer, C. D. *J. Am. Chem. Soc.* **1964**, *86*, 899.

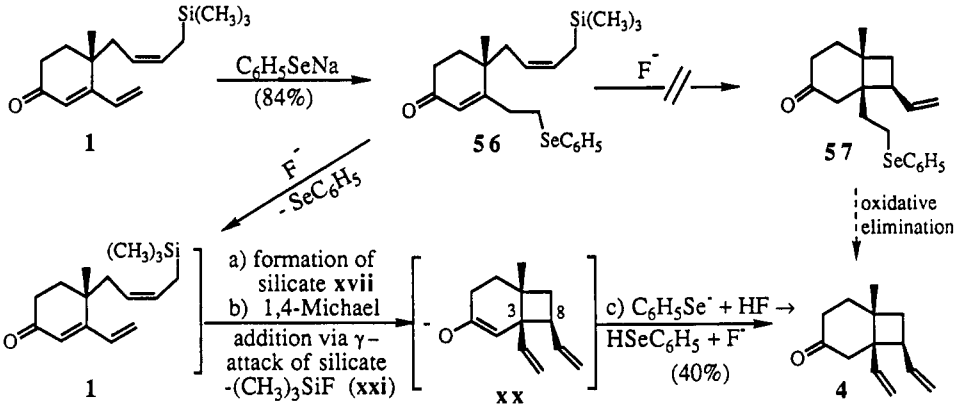
(44) Wender and co-workers have recently exploited the rearrangement of *cis*-divinylcyclobutanes for cyclooctane formation. See: Wender, P. A.; Correia, R. D. *J. Am. Chem. Soc.* **1987**, *109*, 2523.

(45) For examples of carbanion-accelerated Cope rearrangements, see: (a) Evans, D.; Golob, A. M. *J. Am. Chem. Soc.* **1985**, *107*, 5573. For examples of carbanion-accelerated Claisen rearrangements, see: (b) Denmark, S. E.; Harmata, M. A. *J. Am. Chem. Soc.* **1982**, *104*, 4972. (c) Denmark, S. E.; Harmata, M. A. *J. Org. Chem.* **1983**, *48*, 3370. (d) Carpenter, B. K. *Tetrahedron* **1978**, *34*, 1877.

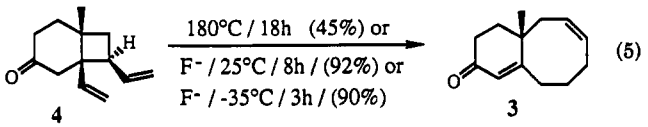
(46) Grieco, P. A.; Miyashita, M. *Tetrahedron Lett.* **1974**, 1869.

(47) Workup of this reaction after a 1-h period afforded a 72% yield of 1.

Scheme X



experiments, thermolysis of 4 required unexpectedly long reaction times and vigorous temperatures (eq 5). Moreover, these conditions resulted in a 45% yield of 3. In dramatic contrast, treatment of 2 with 1 equiv of fluoride ion in DMF at room temperature gave a nearly quantitative yield of enone 3.[48] Further investigation showed that this reaction occurs even at −35 °C in comparable yield.[49]



(5)

While the facile rearrangement of ketone 4, coupled with its in situ trapping, establishes the mechanism of this novel cyclooctane annulation, two points concerning this study remain to be addressed. First, the antiperiplanar (less congested) disposition of the reactive centers leads to the observed cis relationship of the vinyl groups in ketone 4 and by inference in enolate xx.[50] And second, efforts to prepare the more reactive *E* isomer of allylsilane 1 were plagued by protodesilylation.

Knowing the cyclooctane annulation mechanism allows us to understand the anomalous results found in Tables III and IV and Scheme VII. For example, alkyl groups at either the γ or (*E*)-δ position of the dienone unit do not destabilize the cisoid conformation necessary for intramolecular Michael addition (cf. xviib), whereas a (*Z*)-δ methyl group does and leads to 1,2-addition (cf. 48 or 22). Cyclopentenone 48 undergoes cyclization, in contrast to cyclohexenone 22, because cyclopentenones are more reactive toward conjugate addition than are cyclohexenones.[51] A common characteristic of all the cyclizations that gave products derived from an S_E2 process is the use of reactive cyclopentenone or unsubstituted cyclohexenone Michael acceptors.[52] Introduction of alkyl substituents at the β position of the conjugated dienone decreases the electrophilicity of the Michael acceptor and increases the steric congestion of the S_E2 transition state. Since γ-attack of the silicate is less sterically demanding, reaction occurs via an S_E2' pathway. Finally, models indicate that 4-butenyl dienones with silyl units consisting of phenyl ligands (cf. 24 or 25) suffer from increased steric congestion so that the intermediate leading to cyclooctane formation would predominate (cf. xviib). The propensity of substrates 24 and 25 to give mostly 1,2-adducts may reflect the relative stability of the silicate species—with the triphenylsilyl moiety being the most stable silicate anion—which results in the preferred production of the 1,2-adduct rather than the cyclooctane, the kinetic product.

Fluoride Ion Promoted 2-Alkenyl Dienone Cyclizations. Exposure of substrates 33 and 40 to fluoride ion caused a reaction; however, no identifiable products were isolated.

Conclusions

Three new, preparatively useful ring annulations have been investigated. In addition, the mechanism of each process has been established. The use of this methodology is presently in its infancy. However, in light of its remarkable versatility, this chemistry will undoubtedly be of considerable utility for the formation of fused cyclohexane or cyclooctane systems.

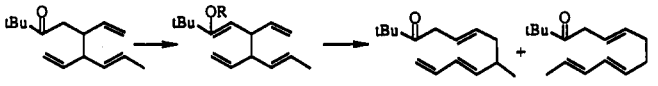
Experimental Section

General. Microanalysis was performed by Atlantic Microlab, Inc., Atlanta, GA. Anhydrous tetrahydrofuran (THF) and diethyl ether were prepared by reflux with, and distillation from, sodium/benzophenone under a nitrogen atmosphere in a recycling still. Anhydrous dimethylformamide (DMF) and hexamethylphosphoramide (HMPA) were prepared by reflux over and distillation from calcium hydride under a dry nitrogen atmosphere and stored over 4A molecular sieves. Anhydrous toluene and diisopropylamine were prepared by reflux over and distillation from calcium hydride and stored over sodium metal and potassium hydroxide pellets, respectively.

All reactions were run under an inert atmosphere of nitrogen and monitored by TLC analysis until the starting material was

(48) Fluoride ion in DMF is highly basic and was chosen only because of convenience. Other bases, such as NaH or LDA, also promoted this rearrangement.

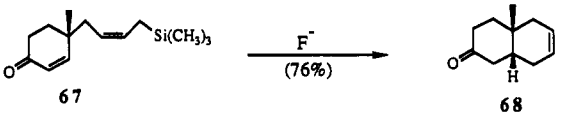
(49) Enolate-accelerated Cope rearrangements were first reported by Wender. The potassium enolate (64a) derived from ketone 63 undergoes Cope rearrangement at room temperature in 1 h to produce trienes 65 and 66, whereas silyl enol ether 64b had to be heated at 65 °C for 4 h to promote rearrangement. See: (a) Wender, P. A.; Sieburth, S. M. *Tetrahedron Lett.* **1981**, 2471. (b) Wender, P. A.; Holt, D. A.; Sieburth, S. M. *J. Am. Chem. Soc.* **1983**, *105*, 3348. (c) Wender, P. A.; Ternansky, R. J.; Sieburth, S. M. *Ibid.* **1985**, 4319.



(50) Majetich, G.; Defauw, J.; Hull, K.; Shawe, T. *Tetrahedron Lett.* **1985**, *26*, 4711.

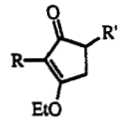
(51) House, H. O.; Huber, L. E.; Umen, M. *J. Am. Chem. Soc.* **1972**, *94*, 8471.

(52) For an account of the geometrical limitations of allylsilane cyclizations, see: Majetich, G.; Hull, K.; Defauw, J.; Shawe, T. *Tetrahedron Lett.* **1985**, *26*, 2755.

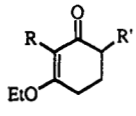


completely consumed. Unless otherwise indicated, all ethereal workups consisted of the following procedure: The reaction mixture was quenched at rt with saturated aq ammonium chloride. The organic solvent was removed under reduced pressure on a rotary evaporator and the residue was taken up in ether, washed with brine, and dried over anhydrous magnesium sulfate. Filtration, followed by concentration at reduced pressure on a rotary evaporator and at 1 Torr to constant weight, afforded a crude residue, which was purified by flash chromatography using NM silica gel 60 (230–400 mesh ASTM) and distilled reagent grade solvents. Spectral data is reported in the accepted formats. Unless otherwise indicated, all NMR spectra were obtained with $CDCl_3$ as solvent. Unless stated otherwise, all compounds were isolated as oils.

Preparation of the Substrates. The precursors listed in Tables I–IV as well as Schemes II and VII were prepared from known cycloalkenones A–F by using the Stork/Danheiser protocol.[53] The following three-step sequence of alkylation with 4-(trimethylsilyl)-2-butynyl iodide (**70**),[34] hydrogenation, and Grignard addition used to prepare trienone **7** is typical. For brevity, subsequent experimentals in this section will present only the quantities of reagents used, the amount(s) of isolated product(s), and relevant spectral data. The preparation of substrates **50**,[34] **52**, and **54** will be described elsewhere.[3]



R = H; R' = H (A)
R = H; R' = CH_3 (B)
R = CH_3; R' = CH_3 (E)



R = H; R' = H (C)
R = H; R' = CH_3 (D)
R = CH_3; R' = CH_3 (E)

(*Z*)-4-[4-(Trimethylsilyl)-2-butenyl]-3-vinyl-2-cyclopenten-1-one (7). To a solution of LDA, prepared from 0.66 mL (4.8 mmol) of diisopropylamine in 8 mL of THF and 1.75 mL (4.37 mmol) of *n*-butyllithium (2.5 M in hexanes), at −78 °C was added a solution of 0.50 g (4.0 mmol) of 3-ethoxy-2-cyclopenten-1-one (A) in 5 mL of THF containing 0.70 mL (4.0 mmol) of HMPA over a 30-min period. After an additional 20 min at −78 °C, iodide **70** (1.10 g, 4.37 mmol) was added and the reaction mixture was allowed to warm slowly to rt over a 12-h period. Standard ethereal workup provided 1.5 g of an oily residue. Purification on silica gel (elution with H:E, 1:1) afforded 0.57 g (58%) of 3-ethoxy-5-[4-(trimethylsilyl)-2-butynyl]-2-cyclopenten-1-one (**71**), which was homogeneous by TLC analysis (H:E, 1:2, R_f(A) = 0.20, R_f(**71**) = 0.45): ^{1}H NMR (90 MHz) δ 0.00 (s, 9 H), 1.34 (t, 2 H, *J* = 2 Hz), 1.37 (t, 3 H, *J* = 7 Hz), 2.35–2.58 (m, 4 H), 2.71 (dd, 1 H, *J* = 8 Hz, 18 Hz), 3.99 (q, 2 H, *J* = 7 Hz), 5.22 (s, 1 H); ^{13}C NMR 206.3 (s), 189.2 (s), 104.1 (d), 78.9 (s), 74.7 (s), 67.5 (s), 44.0 (d), 34.1 (t), 20.5 (t), 14.1 (q), 6.9 (t), −2.2 (q) ppm; IR (film) 2220, 1695 cm^{-1}.

Enone **71** (1.00 g, 4.00 mmol) was dissolved in 70 mL of pyridine/methanol (1:3, v/v) and 200 mg of 5% palladium on barium sulfate was added. The mixture was placed under hydrogen at atmospheric pressure and stirred for 2 h at rt. The mixture was diluted with ether and the catalyst was removed by filtration. The filtrate was concentrated in vacuo to yield 1.45 g of crude product, which was directly chromatographed on silica gel (elution with H:E, 4:1) to give 0.95 g (94%) of (*Z*)-3-ethoxy-5-[4-(trimethylsilyl)-2-butenyl]-2-cyclopenten-1-one (**72**), which was homogeneous by TLC analysis (H:E, 1:2, R_f(**71**) = 0.35, R_f(**72**) = 0.40): ^{1}H NMR (90 MHz) δ −0.10 (s, 9 H), 1.32 (t, 3 H, *J* = 7 Hz), 1.40 (d, 2 H, *J* = 8 Hz), 1.98–2.53 (m, 3 H), 2.23 (dd, 1 H, *J* = 2 Hz, 17 Hz), 2.36–2.49 (m, 2 H), 2.62 (dd, 1 H, *J* = 7 Hz, 17 Hz), 5.07–5.16 (m, 1 H), 5.17 (s, 1 H), 5.36–5.48 (m, 1 H); ^{13}C NMR 207.6 (s), 188.9 (s), 127.9 (d), 123.2 (d), 103.8 (d), 67.4 (t), 44.9 (d), 34.1 (t), 28.3 (t), 18.5 (t), 14.0 (q), −1.9 (q) ppm; IR (film) 1690, 1640, 1600 cm^{-1}; mass spectrum, *m*/*z* 252 (M$^+$).

A solution of 680 mg (2.70 mmol) of dienone **72** in 15 mL of THF at 0 °C was treated dropwise with 3.60 mL (5.40 mmol) of vinyllithium (2.1 M in THF) over a 5-min period. The reaction mixture was stirred for 1 h with slow warming to rt. Standard ethereal workup provided 427 mg (68%) of conjugated dienone **7**, which was homogeneous by TLC analysis (H:E, 1:2, R_f(**72**) = 0.40, R_f(**7**) = 0.70): ^{1}H NMR (90 MHz) δ −0.04 (s, 9 H), 1.39 (d, 2 H, *J* = 9 Hz), 1.95–2.12 (m, 2 H), 2.17 (dd, 1 H, *J* = 1 Hz, 20 Hz), 2.42–2.55 (m, 2 H), 2.52 (dd, 1 H, *J* = 7 Hz, 20 Hz), 5.06–5.17 (m, 1 H), 5.42–5.55 (m, 1 H), 5.54 (d, 1 H, *J* = 11 Hz), 5.75 (d, 1 H, *J* = 17 Hz), 6.04 (s, 1 H), 6.64 (dd, 1 H, *J* = 11 Hz, 17 Hz); ^{13}C NMR 208.7 (s), 175.0 (s), 131.5 (d), 130.7 (d), 128.6 (d), 122.9 (t), 122.7 (d), 41.6 (t), 39.6 (d). 31.3 (t), 18.8 (t), −1.8 (q) ppm; IR (film) 1715, 1690, 1630 cm^{-1}; mass spectrum *m*/*z* 234 (M$^+$).

(*Z*)-4-Methyl-4-[4-(trimethylsilyl)-2-butenyl]-3-vinyl-2-cyclopenten-1-one (9). 3-Ethoxy-5-methyl-2-cyclopenten-1-one (B) (1.25 g, 8.93 mmol) was alkylated with iodide **70** (2.50 g, 9.82 mmol) to provide 1.36 g (58%) of 3-ethoxy-5-methyl-5-[4-(trimethylsilyl)-2-butynyl]-2-cyclopenten-1-one (**73**), which was homogeneous by TLC analysis (H:E, 1:2, R_f(B) = 0.30, R_f(**73**) = 0.50): ^{1}H NMR (90 MHz) δ 0.00 (s, 9 H), 1.15 (s, 3 H), 1.34 (t, 2 H, *J* = 2 Hz), 1.37 (t, 3 H, *J* = 7 Hz), 2.23–2.28 (m, 2 H), 2.54 (AB q, 2 H, $\Delta\nu_{AB}$ = 123 Hz, *J* = 20 Hz), 3.99 (q, 2 H, *J* = 7 Hz), 5.14 (s, 1 H); ^{13}C NMR 209.1 (s), 187.8 (s), 102.4 (d), 79.1 (s), 74.8 (s), 67.4 (t), 47.0 (s), 41.7 (t), 27.8 (t), 23.4 (q), 14.1 (q), 6.9 (t), −2.2 (q) ppm; IR (film) 2220, 1680 cm^{-1}.

Hydrogenation of alkyne **73** (2.0 g, 7.6 mmol) gave 1.90 g (93%) of (*Z*)-3-ethoxy-5-methyl-5-[4-(trimethylsilyl)-2-butenyl]-2-cyclopenten-1-one (**74**), which was homogeneous by TLC analysis (H:E, 1:2, R_f(**73**) = 0.50, R_f(**74**) = 0.55): ^{1}H NMR (90 MHz) δ −0.08 (s, 9 H), 1.08 (s, 3 H), 1.32 (t, 3 H, *J* = 8 Hz), 1.37 (d, 2 H, *J* = 6 Hz), 2.11 (d, 2 H, *J* = 8 Hz), 2.36 (AB q, 2 H, $\Delta\nu_{AB}$ = 76 Hz, *J* = 19 Hz), 3.96 (q, 2 H, *J* = 8 Hz), 5.03–5.13 (m, 1 H), 5.12 (s, 1 H), 5.39–5.51 (m, 1 H); ^{13}C NMR 210.0 (s), 188.0 (s), 128.5 (d), 123.1 (d), 113.3 (d), 67.2 (t), 47.0 (s), 41.9 (t), 34.2 (t), 23.9 (q), 18.4 (t), 14.1 (q), −2.1 (q); IR (film) 1695, 1600 cm^{-1}; mass spectrum, *m*/*z* 266 (M$^+$).

Addition of 1.60 mL (2.44 mmol) of vinyllithium (2.1 M in THF) to 500 mg (1.88 mmol) of dienone **74** using the described experimental procedure, followed by aq acid hydrolysis, yielded 348 mg (75%) of conjugated dienone **9**, which was homogeneous by TLC analysis (H:E, 1:2, R_f(**74**) = 0.55, R_f(**9**) = 0.75): ^{1}H NMR (90 MHz) δ 0.10 (s, 9 H), 1.39 (s, 3 H), 1.54 (d, 2 H, *J* = 8 Hz), 2.38 (AB q, 2 H, $\Delta\nu_{AB}$ = 71 Hz, *J* = 20 Hz), 2.40 (d, 2 H, *J* = 9 Hz), 5.08–5.20 (m, 1 H), 5.56–5.78 (m, 1 H), 5.70 (d, 1 H, *J* = 11 Hz), 5.98 (d, 1 H, *J* = 18 Hz), 6.25 (s, 1 H), 6.57 (dd, 1 H, *J* = 11 Hz, 18 Hz); ^{13}C NMR 207.8 (s), 179.3 (s), 129.2 (d), 129.1 (d), 127.4 (d), 123.8 (t), 121.5 (d), 48.7 (t), 45.5 (s), 35.8 (t), 26.1 (q), 18.8 (t), −1.8 (q) ppm; IR (film) 1700, 1595, 1565 cm^{-1}; mass spectrum, *m*/*z* 248 (M$^+$).

(*Z*)-4-[4-(Trimethylsilyl)-2-butenyl]-3-vinyl-2-cyclohexen-1-one (11). 3-Ethoxy-2-cyclohexen-1-one (C) (1.10 g, 7.86 mmol) was alkylated with iodide **70** (2.18 g, 7.86 mmol) to afford 1.64 g (79%) of 3-ethoxy-6-[4-(trimethylsilyl)-2-butynyl]-2-cyclohexen-1-one (**75**), which was homogeneous by TLC analysis (H:E, 1:1, R_f(C) = 0.18, R_f(**75**) = 0.45): ^{1}H NMR (90 MHz) δ 0.00 (s, 9 H), 1.29 (t, 3 H, J = 7 Hz), 1.35 (t, 2 H, *J* = 2 Hz), 1.70–1.88 (m, 1 H), 2.16–2.25 (m, 3 H), 2.37–2.43 (m, 2 H), 2.62–2.69 (m, 1 H), 3.82 (q, 2 H, *J* = 7 Hz), 5.25 (s, 1 H); ^{13}C NMR 199.3 (s), 177.1 (s), 102.1 (d), 78.8 (s), 76.3 (s), 64.1 (t), 44.8 (d), 28.4 (t), 26.0 (t), 19.6 (t), 14.0 (q), 6.9 (t), −2.2 (q) ppm; IR (film) 2200, 1660, 1610 cm^{-1}.

Hydrogenation of alkyne **75** (1.57 g, 5.95 mmol) gave 1.40 g (90%) of (*Z*)-3-ethoxy-6-[4-(trimethylsilyl)-2-butenyl]-2-cyclohexen-1-one (**76**), which was homogeneous by TLC analysis (H:E, 1:1, R_f(**75**) = 0.45, R_f(**76**) = 0.50): ^{1}H NMR (90 MHz) δ −0.07 (s, 9 H), 1.29 (t, 3 H, *J* = 7 Hz), 1.40 (dd, 2 H, *J* = 5 Hz, 8 Hz), 1.59–1.72 (m, 1 H), 1.96–2.22 (m, 3 H), 2.34 (t, 2 H, *J* = 5 Hz), 2.44–2.57 (m, 1 H), 3.82 (q, 2 H, *J* = 7 Hz), 5.14–5.26 (m, 1 H), 5.24 (s, 1 H), 5.37–5.49 (m, 1 H); ^{13}C NMR 200.9 (s), 176.8 (s), 127.4 (d), 124.6 (d), 102.2 (d), 64.1 (t), 45.3 (d), 28.2 (t), 26.8 (t), 25.9 (t), 18.5 (t), 14.0 (q), −1.9 (q) ppm; IR (film) 1660, 1610 cm^{-1}; mass spectrum, *m*/*z* 266 (M$^+$).

Addition of 3.58 mL (7.52 mmol) of vinyllithium (2.1 M in THF) to 1.00 g (3.76 mmol) of dienone **76** using the described experimental procedure, followed by aq acid hydrolysis, yielded 800 mg (86%) of conjugated dienone **11**, which was homogeneous by TLC analysis (H:E, 1:1, R_f(**76**) = 0.50, R_f(**11**) = 0.80): ^{1}H NMR (90 MHz) δ −0.10 (s, 9 H), 1.38 (dd, 2 H, *J* = 8 Hz, 9 Hz), 1.82–2.08 (m, 2 H), 2.17 (t, 2 H, *J* = 7 Hz), 2.20–2.67 (m, 3 H), 5.17–5.27

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(m, 1 H), 5.38–5.52 (m, 1 H), 5.42 (d, 1 H, J = 11 Hz), 5.64 (d, 1 H, J = 17 Hz), 5.83 (s, 1 H), 6.33 (dd, 1 H, J = 11 Hz, 17 Hz); ^{13}C NMR 199.7 (s), 160.5 (s), 136.7 (d), 127.8 (d), 127.2 (d), 124.5 (d), 120.6 (t), 33.6 (t), 33.0 (t), 28.8 (t), 25.0 (t), 18.6 (t), –2.0 (q) ppm; IR (film) 1665, 1620 cm^{-1}; mass spectrum, m/z 248 (M$^+$). Anal. Calcd for $C_{15}H_{24}OSi$: C, 72.52; H, 9.74. Found: C, 72.73; H, 10.08.

(Z)-4-Methyl-4-[4-(trimethylsilyl)-2-butenyl]-3-vinyl-2-cyclohexen-1-one (1). 3-Ethoxy-6-methyl-2-cyclohexen-1-one (D) (2.91 g, 18.9 mmol) was alkylated with iodide **70** (5.24 g, 20.8 mmol) to give 4.08 g (78%) of 3-ethoxy-6-methyl-6-[4-(trimethylsilyl)-2-butynyl]-2-cyclohexen-1-one (**77**), which was homogeneous by TLC analysis (H:E, 1:1 R_f(D) = 0.25, R_f(**77**) = 0.50): ^{1}H NMR (90 MHz, CCl_4) δ 0.00 (s, 9 H), 1.05 (s, 3 H), 1.27 (t, 3 H, J = 7 Hz), 1.29 (t, 2 H, J = 2 Hz), 1.40–2.08 (m, 2 H), 2.18 (t, 2 H, J = 2 Hz), 2.28 (t, 2 H, J = 8 Hz), 3.77 (q, 2 H, J = 7 Hz), 4.95 (s, 1 H); IR (film) 2200, 1655, 1615 cm^{-1}.

Hydrogenation of alkyne **77** (1.20 g, 4.31 mmol) gave 1.10 g (90%) of (*Z*)-3-ethoxy-6-methyl-6-[4-(trimethylsilyl)-2-butenyl]-2-cyclohexen-1-one (**78**), which was homogeneous by TLC analysis (H:E, 1:1, R_f(**77**) = 0.50, R_f(**78**) = 0.55): ^{1}H NMR (90 MHz) δ 0.00 (s, 9 H), 1.07 (s, 3 H), 1.36 (t, 3 H, J = 7 Hz), 1.48 (d, 2 H, J = 8 Hz), 1.68–1.77 (m, 1 H), 1.90–2.02 (m, 1 H), 2.23 (t, 2 H, J = 8 Hz), 2.41 (t, 2 H, J = 7 Hz), 3.90 (q, 2 H, J = 8 Hz), 5.18–5.30 (m, 1 H), 5.27 (s, 1 H), 5.46–5.58 (m, 1 H); ^{13}C NMR 203.9 (s), 175.7 (s), 128.1 (d), 122.3 (d), 101.3 (d), 63.9 (t), 43.5 (s), 34.0 (t), 31.6 (t), 26.0 (t), 22.0 (q), 18.5 (t), 14.0 (q), –1.9 (q) ppm; IR (film) 1640, 1610 cm^{-1}; mass spectrum, m/z 218 (M$^+$).

Addition of 5.10 mL (10.7 mmol) of vinyllithium (2.1 M in THF) to 1.50 g (5.36 mmol) of dienone **78** using the described experimental procedure, followed by aq acid hydrolysis, yielded 1.04 g (74%) of conjugated dienone **1**, which was homogeneous by TLC analysis (H:E, 1:1, R_f(**78**) = 0.55, R_f(**1**) = 0.85): ^{1}H NMR (90 MHz) δ –0.02 (s, 9 H), 1.18 (s, 3 H), 1.43 (d, 2 H, J = 8 Hz), 1.58–1.75 (m, 1 H), 1.95–2.10 (m, 1 H), 2.18 (d, 1 H, J = 8 Hz), 2.21 (d, 1 H, J = 8 Hz), 2.41 (t, 2 H, J = 6 Hz), 5.08–5.22 (m, 1 H), 5.33 (dd, 1 H, J = 2 Hz, 11 Hz), 5.46 (m, 1 H), 5.66 (dd, 1 H, J = 2 Hz, 16 Hz), 6.08 (s, 1 H), 6.44 (dd, 1 H, J = 11 Hz, 16 Hz); ^{13}C NMR 199.0 (s), 165.8 (s), 134.2 (d), 128.9 (d), 123.7 (d), 121.8 (d), 120.1 (t), 38.0 (s), 36.3 (t), 34.1 (t), 33.8 (t), 24.6 (q), 18.8 (t), –1.8 (q) ppm; IR (film) 1670, 1595 cm^{-1}; mass spectrum, m/z 263 (M$^+$).

(Z)-2,4-Dimethyl-4-[4-(trimethylsilyl)-2-butenyl]-3-vinyl-2-cyclohexen-1-one (13). 3-Ethoxy-2,6-dimethyl-2-cyclohexen-1-one (E) (1.20 g, 7.14 mmol) was alkylated with iodide **70** (2.00 g, 7.86 mmol) to afford 1.25 g (60%) of 3-ethoxy-6,2-dimethyl-6-[4-(trimethylsilyl)-2-butynyl]-2-cyclohexen-1-one (**79**), which was homogeneous by TLC analysis (H:E, 1:1, R_f(E) = 0.35, R_f(**79**) = 0.55): ^{1}H NMR (90 MHz, CCl_4) δ 0.18 (s, 9 H), 1.04 (s, 3 H), 1.32 (t, 3 H, J = 7 Hz), 1.36 (t, 2 H, J = 2 Hz), 1.50–2.20 (m, 2 H), 1.68 (s, 3 H), 2.24 (t, 2 H, J = 2 Hz), 2.49 (t, 2 H, J = 8 Hz), 3.98 (q, 2 H, J = 7 Hz); IR (film) 2190, 1660, 1620 cm^{-1}.

Hydrogenation of alkyne **79** (1.25 g, 4.28 mmol) gave 1.15 g (91%) of (*Z*)-3-ethoxy-2,6-dimethyl-6-[4-(trimethylsilyl)-2-butenyl]-2-cyclohexen-1-one (**80**), which was homogeneous by TLC analysis (H:E, 1:1, R_f(**79**) = 0.55, R_f(**80**) = 0.60): ^{1}H NMR (90 MHz) δ –0.10 (s, 9 H), 0.97 (s, 3 H), 1.26 (t, 3 H, J = 7 Hz), 3.96 (q, 2 H, J = 7 Hz), 5.13 (br q, 1 H, J = 7 Hz), 5.41 (br q, 1 H, J = 7 Hz); ^{13}C NMR 202.9 (s), 169.2 (s), 127.8 (d), 122.5 (d), 112.9 (s), 62.9 (t), 42.6 (s), 34.1 (t), 31.1 (t), 22.1 (t), 22.0 (q), 18.3 (t), 15.1 (q), 7.7 (q), –2.0 ppm; IR (film) 1650, 1620 cm^{-1}; mass spectrum, m/z 294 (M$^+$).

Addition of 2.40 mL (3.40 mmol) of vinyllithium (2.1 M in THF) to 500 mg (1.70 mmol) of dienone **80** using the described experimental procedure, followed by mild acid hydrolysis, yielded 397 mg (85%) of conjugated dienone **13**, which was homogeneous by TLC analysis (H:E, 1:1, R_f(**80**) = 0.60, R_f(**13**) = 0.84): ^{1}H NMR (90 MHz) δ –0.05 (s, 9 H), 1.12 (s, 3 H), 1.41 (d, 2 H, J = 9 Hz), 1.55–1.67 (m, 1 H), 1.78 (s, 3 H), 1.95–2.07 (m, 1 H), 2.13 (dd, 2 H, J = 8 Hz, 18 Hz), 2.43 (t, 2 H, J = 6 Hz), 5.14 (dd, 1 H, J = 2 Hz, 18 Hz), 5.10–5.18 (m, 1 H), 5.45 (dd, 1 H, J = 2 Hz, 11 Hz), 5.42–5.53 (m, 1 H), 6.28 (dd, 1 H, J = 11 Hz, 18 Hz); ^{13}C NMR 199.6 (s), 160.9 (s), 134.0 (d), 131.0 (s), 128.4 (d), 122.3 (d), 120.9 (t), 38.7 (s), 36.7 (t), 34.1 (t), 33.3 (t), 24.8 (q), 18.8 (t), 13.4 (q), –1.8 (q) ppm; IR (film) 1660, 1640, 1625, 1600 cm^{-1}; mass spectrum m/z 276 (M$^+$). Anal. Calcd for $C_{17}H_{28}OSi$: C, 73.85; H, 10.21. Found: C, 74.05; H, 10.35.

4-Methyl-4-[2-methyl-4-(trimethylsilyl)-2-butenyl]-3-vinyl-2-cyclohexen-1-one (15). The preparation of 3-ethoxy-6-methyl-6-[2-methyl-4-(trimethylsilyl)-2-butenyl]-2-cyclohexen-1-one (**59**) as a 1:1 mixture of *E* to *Z* allylsilanes is described elsewhere.[12]

Addition of 0.34 mL (0.33 mmol) of vinyllithium (1 M in THF) to 90 mg (0.30 mmol) of enone **59** using the described experimental procedure, followed by mild acid hydrolysis, yielded 65 mg (77%) of conjugated dienone **15**, which was homogeneous by TLC analysis (H:E, 1:1, R_f(**59**) = 0.60, R_f(**15**) = 0.84): ^{1}H NMR (90 MHz) δ 0.00 (s, 9 H), 1.13 (s, 1.5 H), 1.8 (s, 1.5 H), 1.55 (s, 1.5 H), 1.65 (s, 1.5 H), 1.1–2.5 (m, 14 H), 5.1–5.3 (m, 2 H), 5.40 (t, 0.5 H, J = 2 Hz), 5.68 (t, 0.5 H, J = 2 Hz), 5.90 (s, 1 H), 6.2–6.5 (m, 1 H). This data represents a 1:1 mixture of *E*:*Z* allylsilanes.

(Z)-4-Methyl-3-(1-methyl-1-ethenyl)-4-[4-(trimethylsilyl)-2-butenyl]-2-cyclohexen-1-one (17). *tert*-Butyllithium (3.90 mL, 6.214 mmol, 1.6 M in pentane) was added dropwise over a 10-min period to a solution of 0.28 mL of 2-bromo-1-propene (376 mg, 3.11 mmol) in 10 mL of dry ether at –78 °C. The reaction mixture was allowed to warm to 0 °C over a 2-h period and the resulting mixture was cooled to –55 °C. A solution of enone **78** (300 mg, 1.07 mmol) in 3 mL of dry ether was added dropwise to the cold alkenyllithium solution. The resulting mixture was allowed to warm to 10 °C over a 3-h period and was quenched with saturated NH_4Cl. Standard ethereal workup furnished a crude alcohol, which was used directly in the next reaction.

The crude alcohol was dissolved in 15 mL of THF at rt and treated with 20 drops of 10% HCl. The reaction mixture was stirred for 30 min and then concentrated in vacuo. Standard ethereal workup provided 400 mg of a crude oily residue. The crude oil was chromatographed on silica gel (elution with H:E, 10:1) to provide 239 mg (81%) of conjugated dienone **17**, which was homogeneous by TLC analysis (H:E, 1.5:1, R_f(**78**) = 0.50, R_f(**17**) = 0.85): ^{1}H NMR (90 MHz) δ –0.07 (s, 9 H), 1.19 (s, 3 H), 1.61–1.72 (m, 1 H), 1.90 (s, 3 H), 1.88–2.03 (m, 1 H), 2.21 (d, 2 H, J = 7 Hz), 2.38 (t, 2 H, J = 7 Hz), 4.83 (s, 1 H), 4.97 (s, 1 H), 5.13–5.23 (m, 1 H), 5.42–5.53 (m, 1 H), 5.75 (s, 1 H); ^{13}C NMR 198.8 (s), 171.9 (s), 144.0 (s), 128.5 (d), 126.4 (d), 122.1 (d), 115.3 (t), 38.5 (s), 35.9 (t), 35.1 (t), 34.0 (t), 24.6 (q), 24.3 (q), 18.7 (t), –1.8 (q) ppm; IR (film) 1680, 1640 cm^{-1}; mass spectrum, m/z 276 (M$^+$).

(Z)-3-(1-Cyclohexenyl)-4-methyl-4-[4-(trimethylsilyl)-2-butenyl]-2-cyclohexen-1-one (19). *tert*-Butyllithium (4.26 mL, 7.25 mmol, 1.7 M in pentane) was added dropwise over a 10-min period to a solution of 1-bromo-1-cyclohexene (584 mg, 3.63 mmol) in 10 mL of dry ether at –78 °C. The reaction mixture was allowed to warm to 0 °C over a 2-h period and then cooled to –70 °C. A solution of enone **78** (350 mg, 1.250 mmol) dissolved in 3 mL of dry ether was added dropwise to the cold alkenyllithium solution. The resulting mixture was allowed to warm to 10 °C over a 3-h period. Standard ethereal workup furnished a crude alcohol, which was used directly in the next reaction.

The crude alcohol was dissolved in 20 mL of THF at rt and treated with 25 drops of 10% HCl. The reaction mixture was stirred for 30 min and then concentrated in vacuo. Standard ethereal workup gave 425 mg of a crude oily residue. The crude oil was chromatographed on silica gel (elution H:E, 10:1) to provide 220 mg (74%) of conjugated dienone **19**, which was homogeneous by TLC analysis (H:E, 2:1, R_f(**78**) = 0.47, R_f(**19**) = 0.75): ^{1}H NMR (90 MHz) δ –0.03 (s, 9 H), 1.17 (s, 3 H), 1.43 (d, 2 H, J = 10 Hz), 1.50–1.82 (m, 5 H), 1.85–2.30 (m, 5 H), 2.23 (d, 2 H, J = 8 Hz), 2.40 (t, 2 H, J = 7 Hz), 5.16–5.27 (m, 1 H), 5.44–5.58 (m, 1 H), 5.60 (br t, 1 H, J = 6 Hz), 5.73 (s, 1 H); ^{13}C NMR 200.6 (s), 173.5 (s), 137.7 (s), 128.3 (d), 126.4 (d), 126.1 (d), 122.3 (d), 38.7 (s), 36.2 (t), 35.4 (t), 34.0 (t), 29.7 (t), 25.1 (t), 24.7 (q), 22.6 (t), 21.6 (t), 18.7 (t), –1.8 (q) ppm; IR (film) 1680, 1660 cm^{-1}; mass spectrum, m/z 317 (M$^+$).

(Z)-4-Methyl-3-(2-methyl-1-propenyl)-4-[4-(trimethylsilyl)-2-butenyl]-2-cyclohexen-1-one (22). *tert*-Butyllithium (3.65 mL, 6.21 mmol, 1.7 M in pentane) was added dropwise over a 10-min period to a solution of 1-bromo-2-methyl-1-propene (420 mg, 3.11 mmol) in 10 mL of dry ether at –78 °C. The reaction mixture was allowed to warm to 0 °C over a 2-h period and then cooled to –30 °C. A solution of enone **78** (300 mg, 1.07 mmol) in 3 mL of dry ether was added dropwise to the cold alkenyllithium solution. The resulting mixture was allowed to warm to 20 °C

over a 4-h period. Standard ethereal workup furnished a crude alcohol, which was used directly in the next reaction.

The crude alcohol was dissolved in 20 mL of THF at rt and treated with 20 drops of 10% HCl. The reaction mixture was stirred for 30 min and then concentrated in vacuo. Standard ethereal workup, followed by chromatography (elution H:E, 10:1), provided 245 mg (79%) of conjugated dienone **22**, which was homogeneous by TLC analysis (H:E, 2:1, R_f(**78**) = 0.47, R_f(**22**) = 0.73: ^{1}H NMR (90 MHz) δ 0.00 (s, 9 H), 1.13 (s, 3 H), 1.42 (d, 2 H, J = 8 Hz), 1.60–2.78 (m, 1 H), 1.77 (s, 3 H), 2.84 (s, 3 H), 1.97–2.13 (m, 1 H), 2.22 (dd, 2 H, J = 9 Hz, 15 Hz), 2.43 (t, 2 H, J = 6 Hz), 5.08–5.19 (m, 1 H), 5.43–5.56 (m, 1 H), 5.76 (s, 1 H), 5.84 (s, 1 H); ^{13}C NMR 199.7 (s), 166.2 (s), 140.7 (s), 128.5 (d), 127.3 (d), 122.5 (d), 122.3 (d), 38.8 (s), 36.6 (t), 34.1 (t), 33.6 (t), 27.0 (q), 24.7 (q), 20.1 (q), 18.8 (t), -1.7 (q) ppm; IR (film) 1670, 1620, 1600 cm^{-1}; mass spectrum, m/z 290 (M^+). Anal. Calcd for $C_{17}H_{28}SiO$: C, 73.85; H, 10.21. Found: C, 74.17; H, 10.35.

Dimethylphenylpropargylsilane (79). To a stirred solution of magnesium powder (6.0 g, 0.5 mol), 10 mg of iodine (catalyst), and 400 mL of dry ether was added dropwise 18.86 mL of neat propargyl bromide (0.5 mol) over a 1-h period. The reaction flask was cooled periodically with an ice bath in order to maintain a controlled reflux. The mixture was stirred 30 min at rt, followed by cooling to -10 °C. To the cooled Grignard reagent was added 42.68 g of dimethylphenylsilyl chloride (0.5 mol) over a 2-min period. The resulting mixture was allowed to warm to rt (~3 h) and was quenched with saturated NH_4Cl. The ether layer was separated, dried over magnesium sulfate, and filtered. The ether was removed from the reaction mixture by distillation at atmospheric pressure through a 4-f silver jacketed Vigreaux column to yield 32.3 g (86%) of pure **79** (bp 75–80 °C at 1 mmHg): ^{1}H NMR (90 MHz, CCl_4) δ 0.20 (s, 6 H), 1.70 (br s, 2 H), 1.85 (t, 1 H, J = 3 Hz), 7.10–7.50 (m, 5 H). Anal. Calcd for $C_{11}H_{14}Si$: C, 75.82; H, 8.10. Found: C, 76.00; H, 8.31.

4-(Dimethylphenylsilyl)-2-butyn-1-ol (80). *n*-Butyllithium (20.2 mL, 50.5 mmol, 2.5 M in hexane) was added dropwise over a 40-min period to a solution of propargylsilane **79** (8.0 g, 46.0 mmol) in 100 mL of dry THF at -50 °C. The mixture was stirred for 20 min at -44 °C. To the cooled solution was added 4.14 g of paraformaldehyde (46.0 mmol), and the resulting mixture was allowed to slowly warm to rt while being stirred overnight. The reaction mixture was then refluxed at 66 °C for 1 h, followed by cooling to rt and quenching. Standard ethereal workup, followed by distillation (bp 115–120 °C at 1.0 mmHg), gave 4.48 g (48%) of silane **80**, which was homogeneous by TLC analysis (H:E, 2:1, R_f(**79**) = 0.95, R_f(**80**) = 0.45): ^{1}H NMR (90 MHz) δ 0.15 (s, 3 H), 0.25 (s, 3 H), 1.0 (br s, 1 H), 1.51 (t, 2 H, J = 2 Hz), 3.87 (t, 2 H, J = 2 Hz), 6.90–7.30 (m, 5 H).

4-(Dimethylphenylsilyl)-2-butynyl Iodide (81). To a solution of 4.45 g (21.9 mmol) of alcohol **80** in 50 mL of dry THF and 3.4 mL (2.44 g, 24.1 mmol) of TEA at 0 °C was added dropwise 1.9 mL (2.77 g, 24.1 mmol) of methanesulfonyl chloride over a 5-min period; a thick precipitate formed. The mixture was stirred for 2 h with gradual warming to rt. Filtration followed by careful evaporation of the solvent in vacuo afforded the crude mesylate, which was used directly in the next reaction without further purification.

The crude mesylate (ca. 22 mmol) was diluted with freshly distilled acetone (50 mL) and cooled to 0 °C. Anhyd NaI (4.94 g, ca. 33 mmol) was added, resulting in the formation of a thick yellow precipitate. The mixture was stirred for 2 h at 0 °C and then warmed to rt. The reaction mixture was filtered and the filtrate was concentrated in vacuo to afford 9.50 g of crude iodide, which was purified on silica gel (elution with petroleum ether) to give 4.97 g (72%) of iodide **81**, which was homogeneous by TLC analysis (hexanes, R_f(**80**) = 0.03, R_f(**81**) = 0.50): ^{1}H NMR (90 MHz) δ 0.18 (s, 3 H), 0.29 (s, 3 H), 1.54 (t, 2 H, J = 2 Hz), 3.60 (t, 2 H, J = 2 Hz), 7.00–7.31 (m, 5 H).

(*Z*)-4-Methyl-4-[4-(dimethylphenylsilyl)-2-butenyl]-3-vinyl-2-cyclohexen-1-one (24). Cyclohexenone D (1.11 g, 7.23 mmol) was alkylated with iodide **81** (2.5 g, 7.96 mmol) to afford 1.77 g (72%) of 3-ethoxy-6-methyl-6-[4-(dimethylphenylsilyl)-2-butynyl]-2-cyclohexen-1-one (**82**), which was homogeneous by TLC analysis (H:E, 1:1 R_f(D) = 0.50, R_f(**82**) = 0.60): ^{1}H NMR (90 MHz, CCl_4) δ 0.20 (s, 6 H), 0.90 (s, 3 H), 1.20 (t, 3 H, J = 7 Hz), 1.50 (t, 2 H, J = 2 Hz), 1.40–2.40 (m, 6 H), 3.80 (q, 2 H, J = 7 Hz), 4.95 (s, 1 H), 7.00–7.30 (m, 5 H).

Hydrogenation of alkyne **82** (1.7 g, 5.0 mmol) gave 1.54 g (99%) of (*Z*)-3-ethoxy-6-[4-(dimethylphenylsilyl)-2-butenyl]-2-cyclohexen-1-one (**83**), which was homogeneous by TLC analysis (H:E, 1:1, R_f(**82**) = 0.45, R_f(**83**) = 0.50): ^{1}H NMR (90 MHz) δ 0.20 (s, 6 H), 1.00 (s, 3 H), 1.31 (t, 3 H, J = 7 Hz), 1.15–2.40 (m, 8 H), 3.82 (q, 2 H, J = 7 Hz), 4.95–5.35 (m, 3 H), 5.00 (s, 1 H), 7.00–7.40 (m, 5 H).

Addition of 3.8 mL (8.77 mmol) of vinyllithium (2.3 M in THF) to 1.5 g (4.38 mmol) of dienone **83** using the described experimental procedure, followed by mild acid hydrolysis, yielded 1.04 mg (73%) of conjugated dienone **24**, which was homogeneous by TLC analysis (H:E, 1:1, R_f(**83**) = 0.60, R_f(**24**) = 0.80): ^{1}H NMR (90 MHz) δ 0.30 (s, 6 H), 1.15 (s, 3 H), 1.67 (d, 2 H, J = 9 Hz), 1.40–2.40 (m, 8 H), 5.11–5.72 (m, 4 H), 5.85 (s, 1 H), 6.05–6.30 (m, 1 H), 7.00–7.40 (m, 5 H).

4-(Triphenylsilyl)-2-butynyl Iodide (86). The Grignard reaction of 1.63 g of magnesium powder (67.2 mmol), 8.0 g of propargyl bromide (67.2 mmol), and 19.8 g of triphenylchlorosilane (67.2 mmol) produced 13.66 g (64%) of triphenylpropargylsilane (**84**), following chromatography (hexane elution, R_f(**84**) = 0.45): ^{1}H NMR (90 MHz, CCl_4) δ 1.70 (d, 2 H, J = 3 Hz), 2.20 (t, 1 H, J = 3 Hz), 7.05–7.60 (m, 15 H). Anal. Calcd for $C_{21}H_{18}Si$: C, 84.53; H, 6.09. Found: C, 84.73; H, 6.07.

A Brandsma reaction was carried out with 13.6 g of propargylsilane **84** (45.5 mmol) and 4.51 g of paraformaldehyde (50.1 mmol). Standard ethereal workup afforded 11.5 g of a crude alcohol, which was purified on silica gel (elution with H:E, 2:1, R_f(**84**) = 0.95, R_f(**85**) = 0.35) to give 8.67 g (58%) of 4-(triphenylsilyl)-2-butyn-1-ol (**85**): ^{1}H NMR (90 MHz, CCl_4) δ 1.00 (br s, 1 H), 2.24 (t, 2 H, J = 2 Hz), 3.85 (br s, 2 H), 7.00–7.50 (m, 15 H).

Alcohol **85** (8.5 g, 28.48 mmol) was converted to iodide **86** in 67% yield, using 3.59 g of methanesulfonyl chloride (31.3 mmol), 3.17 g of TEA (31.32 mmol), and the procedure described in the preparation of iodide **81**. Purification of **86** was achieved by chromatography (elution with H:E, 9:1, R_f(**85**) = 0.05, R_f(**86**) = 0.81): ^{1}H NMR (90 MHz) δ 2.12 (t, 2 H, J = 2 Hz), 3.35 (t, 2 H), J = 2 Hz), 7.00–7.50 (m, 15 H).

(*Z*)-4-Methyl-4-[4-(triphenylsilyl)-2-butenyl]-3-vinyl-2-cyclohexen-1-one (25). 3-Ethoxy-6-methyl-2-cyclohexen-1-one (D) (1.37 g, 8.90 mmol) was alkylated with iodide **86** (4.0 g, 9.79 mmol) to afford 3.2 g (82%) of 3-ethoxy-6-methyl-6-[4-(triphenylsilyl)-2-butynyl]-2-cyclohexen-1-one (**87**), which was homogeneous by TLC analysis (H:E, 1:1, R_f(C) = 0.48, R_f(**75**) = 0.57): ^{1}H NMR (90 MHz) δ 0.85 (s, 3 H), 1.4 (t, 3 H, J = 7.0 Hz), 1.00–2.40 (m, 8 H), 3.80 (q, 2 H, J = 7.0 Hz), 4.90 (s, 1 H), 6.90–7.25 (m, 15 H).

Hydrogenation of alkyne **87** (3.2 g, 7.34 mmol) gave 2.76 g (93%) of (*Z*)-3-ethoxy-5-methyl-5-[4-(triphenylsilyl)-2-butenyl]-2-cyclopenten-1-one (**88**), which was homogeneous by TLC analysis (H:E, 1:1, R_f(**87**) = 0.57, R_f(**88**) = 0.59): ^{1}H NMR (90 MHz) δ 1.00 (s, 3 H), 1.4 (t, 3 H, J = 7.0 Hz), 1.00–2.40 (m, 8 H), 3.90 (q, 2 H, J = 7.0 Hz), 4.80–5.08 (m, 1 H), 5.08–5.32 (m, 1 H), 6.80–7.30 (m, 15 H).

Addition of 3.4 mL (7.79 mmol) of vinyllithium (2.3 M in THF) to 1.7 g (3.89 mmol) of dienone **88** using the described experimental procedure, followed by aq acid hydrolysis, yielded 348 mg (75%) of conjugated dienone **25**, which was homogeneous by TLC analysis (H:E, 1:2 R_f(**88**) = 0.42, R_f(**25**) = 0.57): ^{1}H NMR (90 MHz) δ 1.10 (s, 3 H), 1.50–1.70 (m, 2 H), 1.90–2.10 (m, 2 H), 2.20–2.55 (m, 4 H), 5.2 (m, 1 H), 5.30 (dd, 1 H, J = 10.0 Hz, 1.5 Hz), 5.5 (m, 1 H), 5.60 (dd, 1 H, J = 17.0 Hz, 1.5 Hz), 6.0 (s, 1 H), 6.20 (dd, 1 H, J = 17.0 Hz, 10.0 Hz), 7.20–7.60 (m, 15 H).

2-(3-Methyl-2-butenyl)-3-methoxy-2-cyclohexen-1-one (29). A solution of 2.4 g (13.3 mmol) of 2-(3-methyl-2-butenyl)-cyclohexane-1,3-dione[27] was treated with an ethereal (100 mL) solution of diazomethane, prepared from 2.74 g of nitrosomethylurea (26.6 mmol), and stirred at rt for 10 min. Excess diazomethane was consumed by the careful dropwise addition of glacial acetic acid. The ethereal phase was washed with brine, dried over anhyd $MgSO_4$, filtered, and concentrated. Chromatography of the residue on silica gel (elution with H:E, 1:1) provided 2.11 g (82%) of enone **29**, which was homogeneous by TLC analysis (H:E, 1:1 R_f(dione) = 0.35, R_f(**29**) = 0.52): ^{1}H NMR (270 MHz) δ 1.60 (s, 3 H), 1.68 (s, 3 H), 1.96 (pent, 2 H, J = 6.0 Hz), 2.32 (t, 2 H, J = 6.0 Hz),

2.55 (t, 2 H, J = 6.0 Hz), 2.92 (d, 2 H, J = 7.0 Hz), 3.80 (s, 3 H), 5.00 (br t, 1 H, J = 7.0 Hz). Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 73.95; H, 9.20.

(*E*)-2-Methyl-4-[2-(3-methoxy-1-oxo-2-cyclohexenyl)]-2-buten-1-al (30). To a solution of 56 mg of selenium dioxide (0.51 mmol) in 5 mL of dry CH_2Cl_2 at rt was added 0.22 mL of *tert*-butyl hydroperoxide (90%). The reaction mixture was stirred for 25 min and 194 mg of diene **45** dissolved in 5 mL of dry CH_2Cl_2 was added dropwise. After 1 h the reaction mixture became slightly yellow in color. The reaction mixture was allowed to stir for 15 h. Standard ethereal workup, followed by chromatography (elution with ether), afforded 125 mg (60%) of aldehyde **44**, which was homogeneous by TLC analysis (ether, R_f(**45**) = 0.64, R_f(**47**) = 0.40): ^{1}H NMR (90 MHz, CCl_4) δ 1.8 (s, 3 H), 2.05 (pent, 2 H, J = 6.0 Hz), 2.40 (t, 2 H, J = 6.0 Hz), 2.63 (t, 2 H, J = 6.0 Hz), 3.30 (d, 2 H, J = 6.0 Hz), 3.85 (s, 3 H), 6.30 (br s., 1 H, J = 7.0 Hz), 9.25 (s, 1 H).

2-(3-Methyl-4-acetoxy-2-butenyl)-3-methoxy-2-cyclohexen-1-one (31). To a solution of 74 mg (0.35 mmol) of aldehyde **30** in 3 mL of absolute ethanol at 0 °C was added 14 mg (0.37 mmol) of sodium borohydride. The reaction mixture was stirred for 20 min and was then quenched with the addition of 3 drops of water. Standard ethereal workup provided an oil, which was purified by chromatography on silica gel (elution with ether) to afford 66 mg (89%) of an allylic alcohol, which was used immediately in the next reaction without further purification [ether, R_f(**30**) = 0.40, R_f(alcohol) = 0.30]: ^{1}H NMR (90 MHz) δ 1.8 (s, 3 H), 2.10 (pent, 2 H, J = 6.0 Hz), 2.40 (t, 2 H, J = 6.0 Hz), 2.60 (t, 2 H, J = 6.0 Hz), 3.05 (d, 2 H, J = 7.0 Hz), 3.80 (s, 3 H), 3.90 (br s, 2 H), 5.25 (br t, 1 H, J = 7.0 Hz).

To a solution of the above crude alcohol (66 mg, 0.31 mmol) in 2 mL of pyridine were added 2 mL of acetic anhydride and 5.0 mg of DMAP. The resulting mixture was allowed to stir at rt for 90 min. Standard ethereal workup yielded a crude yellow oil, which was purified via column chromatography (elution with ether) to yield 71.3 mg (90%) of acetate **31**, which was was homogeneous by TLC analysis (ether, R_f(alcohol) = 0.30, R_f(**20**) = 0.60): ^{1}H NMR (90 MHz) δ 1.75 (s, 3 H), 1.95 (m, 2 H), 2.00 (s, 3 H), 2.32 (t, 2 H, J = 6.0 Hz), 2.55 (t, 2 H, J = 6.0 Hz), 3.00 (d, 2 H, J = 7.0 Hz), 3.75 (s, 3 H), 4.35 (s, 2 H), 5.32 (br t, 1 H, J = 7.0 Hz).

2-[3-Methyl-4-(dimethylphenylsilyl)-2-butenyl]-3-methoxy-2-cyclohexen-1-one (32). Dimethylphenylchlorosilane (513 mg, 3.0 mmol), lithium metal (105 mg, 15.0 mmol), and dry THF (5 mL) were stirred, under nitrogen, for 17 h. The resulting red solution was added to copper(I) iodide (189 mg, 2.1 mmol) in 1 mL of THF at 0 °C. The mixture was stirred at 0 °C for 90 min and then cooled to −50 °C. A solution of 126 mg (0.5 mmol) of acetate **31** dissolved in 5 mL of dry THF was added. The resulting mixture was stirred at −60 °C for a 12-h period, warmed to −10 °C, and then poured into 30 mL of a saturated solution of NH_4Cl and Na_2CO_3 (1:1 mixture). Standard ethereal workup afforded 650 mg of an oily residue, which was purified via column chromatography (elution with ether) to yield 157 mg (96%) of allylsilane **32**, which was homogeneous by TLC analysis (H:E, 1:4, R_f(**31**) = 0.30, R_f(**32**) = 0.50): ^{1}H NMR (90 MHz) δ 0.03 (s, 6 H), 1.65 (s, 3 H), 1.70 (s, 2 H), 2.00 (pent, 2 H, J = 6.0 Hz), 2.35 (t, 2 H, J = 6.0 Hz), 2.50 (p, 2 H, J = 6.0 Hz), 3.00 (d, 2 H, J = 7.0 Hz), 3.70 (s, 3 H), 4.90 (br t, 1 H, J = 7.0 Hz), 7.10–7.50 (m, 5 H).

2-[3-Methyl-4-(dimethylphenylsilyl)-2-butenyl]-3-vinyl-2-cyclohexen-1-one (33). Addition of 0.26 mL (6.1 mmol) of vinyllithium (2.3 M in THF) to 100 mg (0.30 mmol) of enone **32** using the described experimental procedure, followed by aq acid hydrolysis, yielded 64 mg (65%) of conjugated dienone **33**, which was homogeneous by TLC analysis (H:E, 1:1, R_f(**32**) = 0.18, R_f(**33**) = 0.64): ^{1}H NMR (270 MHz) δ 0.30 (s, 6 H), 1.60 (s, 3 H), 1.70 (s, 2 H), 2.00 (pent, 2 H, J = 6.0 Hz), 2.45 (t, 2 H, J = 6.0 Hz), 2.52 (t, 2 H, J = 6.0 Hz), 3.12 (d, 2 H, J = 7.0 Hz), 4.72 (br t, 1 H, J = 7.0 Hz), 5.45 (d, 1 H, J = 10.0 Hz), 5.65 (d, 1 H, J = 17.0 Hz), 6.90 (dd, 1 H, J = 17.0 Hz, 10.0 Hz), 7.10–7.60 (m, 5 H).

6-[4-(Trimethylsilyl)-2-butynyl]-1,4-dioxaspiro[4.5]dec-6-ene (37). A solution of (phenylthio)copper(I) was prepared in the following manner: A round-bottom flask was charged with 3.65 mL of 2.5 M *n*-butyllithium (9.13 mmol) in hexanes. The solvent was removed under vacuum and 10 mL of anhyd ether was added. The solution was cooled to 0 °C and 0.94 mL of thiophenol (9.13 mmol) was added dropwise.

A second round-bottom flask was charged with 1.74 g of copper(I) iodide (9.13 mmol) and 20 mL of ether. To this mixture was added the solution of (phenylthio)lithium prepared earlier. The heterogeneous mixture of (phenylthio)copper(I) was cooled to −78 °C. In a third round-bottom flask was placed 4.4 mL of 2.5 M *n*-butyllithium (10.9 mmol) in hexanes. The solvent was removed under vacuum and 15 mL of diethyl ether was added. The solution was cooled to −78 °C and 2 g of 2-bromo-2-cyclopenten-1-one ethylene ketal (9.13 mmol) in 10 mL of diethyl ether was added. The solution was stirred for a 1-h period.

To the mixture of (phenylthio)copper(I) was added the solution of 2-lithio-2-cyclopenten-1-one ethylene ketal, the reaction mixture was stirred for 1 h at −78 °C, and iodide **70** (2.3 g, 2.45 mmol) in 10 mL of ether was added dropwise. The resulting mixture was slowly warmed to −35 °C. Standard ethereal workup, followed by chromatography (hexanes/diethyl ether, 4:1), provided 1.00 g (80% yield) of ketal **37**, which was homogeneous by TLC analysis (H:E, 5:1, R_f(ketal) = 0.48, R_f(**37**) = 0.54): ^{1}H NMR (300 MHz) δ 0.10 (s, 9 H), 1.49 (t, 2 H, J = 2.63 Hz), 1.55–1.83 (m, 4 H), 2.00–2.12 (m, 2 H), 2.88–3.18 (m, 2 H), 3.98 (s, 4 H), 6.13–6.23 (m, 1 H); ^{13}C NMR (300 MHz) 133.8, 129.3, 80.6, 75.2, 65.7, 65.0, 33.8, 25.1, 20.6, 19.2, 7.0, −2.0 ppm.

2-[4-(Trimethylsilyl)-2-butynyl]-2-cyclohexen-1-one (38). Hydrogenation of alkyne **37** (400 mg, 1.51 mmol) gave 370 mg (92%) of a cis allylsilane, which was homogeneous by TLC analysis (H:E, 1:2, R_f(**37**) = 0.50, R_f(allylsilane) = 0.55): ^{1}H NMR (300 MHz) δ 0.00 (s, 9 H), 1.47 (d, 2 H, J = 8.4 Hz), 1.64–1.84 (m, 4 H), 1.92–2.12 (m, 2 H), 2.74 (br d, 2 H, J = 7.0 Hz), 3.90 (s, 4 H), 5.25–5.45 (m, 1 H), 5.40–5.55 (m, 1 H), 5.60–5.82 (m, 1 H); ^{13}C NMR (300 MHz) 128.7, 126.4, 125.1, 107.6, 65.8, 65.0, 33.9, 26.4, 25.1, 20.7, 18.0, −1.7 ppm.

The above ketal (300 mg, 1.12 mmol) was dissolved in 10 mL of THF and 10 drops of 1 N aq sulfuric acid was added. The resulting mixture was stirred until TLC analysis revealed complete consumption of the starting material (approximately 5 min). Standard ethereal workup, followed by chromatography (H:E, 3:1), provided 240 mg (96% yield) of enone **38**, which was homogeneous by TLC analysis (H:E, 3:1, R_f(ketal) = 0.54, R_f(**38**) = 0.42): ^{1}H NMR (300 MHz) δ 0.00 (s, 9 H), 1.48 (d, 2 H, J = 8.5 Hz), 1.89–2.12 (m, 2 H), 2.28–2.38 (m, 2 H), 2.40–2.46 (m, 2 H), 2.89 (br d, 2 H, J = 7.3 Hz), 5.21–5.31 (m, 1 H), 5.48–5.10 (m, 1 H), 6.65–6.75 (m, 1 H); ^{13}C NMR (300 MHz) 199.4, 144.9, 138.5, 127.5, 123.7, 38.5, 26.3, 26.0, 23.0, 18.3, −1.7 ppm.

2-[4-(Trimethylsilyl)-2-butynyl]-3-vinyl-2-cyclohexen-1-one (40). Addition of 1.0 mL (0.99 mmol) of vinyllithium (1.0 M in THF) to 110 mg (0.495 mmol) of enone **38** using the described experimental procedure yielded 100 mg (80%) of tertiary alcohol **39**, which was homogeneous by TLC analysis (H:E, 1:1, R_f(**38**) = 0.50, R_f(**39**) = 0.45): ^{1}H NMR (300 MHz) δ 0.00 (s, 9 H), 1.48–1.55 (m, 2 H), 1.70–1.75 (m, 4 H), 2.00–2.06 (m, 2 H), 2.52–2.64 (m, 1 H), 2.75–2.88 (m, 1 H), 5.16 (dd, 1 H, J = 10.6 Hz, 1.5 Hz), 5.28 (dd, 1 H, J = 17.4 Hz, 1.5 Hz), 5.28–5.36 (m, 1 H), 5.46–5.55 (m, 1 H), 5.59–5.63 (m, 1 H), 5.89 (dd, 1 H, J = 17.4 Hz, 10.6 Hz); ^{13}C NMR (300 MHz) 143.5, 126.9, 125.7, 125.6, 113.0, 112.9, 74.0, 37.9, 28.8, 25.5, 18.9, 18.3, −1.7 ppm; mass spectrum, m/z 248 (M^+).

To a solution of 542 mg of pyridinium dichromate (1.44 mmol), 0.5 g of Celite, and 15 mL of anhyd CH_2Cl_2 was added a solution of 90 mg of **39** (0.36 mmol) in 5 mL of CH_2Cl_2. The reaction mixture was stirred for 12 h at rt. Standard ethereal workup, followed by chromatography (H:E, 3:1), provided 70 mg (78% yield) of dienone **40**, which was homogeneous by TLC analysis (H:E, 3:1, R_f(**39**) = 0.45, R_f(**40**) = 0.42): ^{1}H NMR (250 MHz) δ 0.03 (s, 9 H), 1.60–1.63 (m, 2 H), 1.99 (pent, 2 H, J = 6.0 Hz), 2.45 (t, 2 H, J = 6.0 Hz), 2.51 (t, 2 H, J = 6.0 Hz), 3.15 (t, 2 H, J = 6.0 Hz), 5.03–5.11 (m, 2 H), 5.34–5.43 (m, 1 H), 5.47 (dd, 1 H, J = 11.0 Hz, 0.8 Hz), 5.66 (dd, 1 H, J = 17.4 Hz, 0.8 Hz), 6.90 (dd, 1 H, J = 17.4 Hz, 11.0 Hz); ^{13}C NMR (300 MHz) 199.3, 149.6, 135.0, 126.0, 125.1, 120.2, 99.7, 38.0, 25.5, 22.6, 21.9, 18.5, −1.7 ppm.

(*Z*)-2-Methyl-3-(2-methyl-1-propenyl)-4-[4-(trimethylsilyl)-2-butenyl]-2-cyclopenten-1-one (48). 3-Ethoxy-2,5-dimethyl-2-cyclopenten-1-one (F) (1.50 g, 10.7 mmol) was alkylated with iodide **70** (2.70 g, 10.71 mmol) to give 1.92 g (68%) of 3-ethoxy-2-methyl-5-[4-(trimethylsilyl)-2-butynyl]-2-cyclopenten-

1-one (89), which was homogeneous by TLC analysis (H:E, 1:1, R_f(F) = 0.10, R_f(89) = 0.40): ^{1}H NMR (90 MHz) δ −0.01 (s, 9 H), 1.32 (t, 2 H, J = 2 Hz), 1.35 (t, 3 H, J = 7 Hz), 1.56 (s, 3 H), 2.29–2.58 (m, 4 H), 2.69–2.82 (m, 1 H), 4.19 (q, 2 H, J = 7 Hz); ^{13}C NMR 205.6 (s), 183.2 (s), 115.4 (s), 78.7 (s), 74.9 (s), 65.1 (t), 43.5 (d), 30.9 (t), 20.7 (t), 15.2 (q), 6.8 (t), 6.0 (q), −2.3 (q) ppm; IR (film) 2200, 1690, 1630 cm^{-1}.

Hydrogenation of alkyne 89 (1.92 g, 7.27 mmol) gave 1.80 g (93%) of (*Z*)-3-ethoxy-2-methyl-5-[4-(trimethylsilyl)-2-butenyl]-2-cyclopenten-1-one (90), which was homogeneous by TLC analysis (H:E, 1:1, R_f(89) = 0.40, R_f(90) = 0.43): ^{1}H NMR (90 MHz) δ −0.12 (s, 9 H), 1.28 (t, 3 H, J = 7 Hz), 1.38 (d, 2 H, J = 9 Hz), 1.52 (s, 3 H), 1.93–2.07 (m, 1 H), 2.18 (dt, 1 H, J = 2 Hz, 18 Hz), 2.33–2.48 (m, 2 H), 2.65 (dd, 1 H, J = 7 Hz, 18 Hz), 4.11 (q, 2 H, J = 7 Hz), 5.03–5.16 (m, 1 H), 5.33–5.46 (m, 1 H); ^{13}C NMR 206.9 (s), 183.0 (s), 127.9 (d), 123.5 (d), 115.1 (s), 65.0 (t), 44.4 (d), 30.9 (t), 28.7 (t), 18.6 (t), 15.2 (q), 5.9 (q), −1.9 ppm; IR (film) 1690, 1630 cm^{-1}.

tert-Butyllithium (19.2 mL, 33 mmol, 1.7 M in pentane) was added dropwise over a 25-min period to a solution of 1-bromo-2-methyl-1-propene (2.20 g, 16.3 mmol) in 20 mL of dry ether at −78 °C. The reaction mixture was allowed to warm to 0 °C over a 2-h period and then cooled to −30 °C. A solution of dienone 90 (1.50 g, 5.64 mmol) dissolved in 6 mL of dry ether was added dropwise to the cold alkenyllithium solution. The resulting mixture was allowed to warm to 20 °C over a 5-h period. Standard ethereal workup furnished a crude alcohol, which was used directly in the next reaction.

The crude alcohol was dissolved in 50 mL of THF at rt and treated with 50 drops of 10% HCl. The reaction mixture was stirred for 30 min and then concentrated in vacuo. Standard ethereal workup, followed by chromatography (elution H:E, 10:1), gave 1.16 g (74%) of conjugated dienone 48, which was homogeneous by TLC analysis (H:E, 1:1, R_f(90) = 0.43, R_f(48) = 0.85): ^{1}H NMR (90 MHz) δ −0.10 (s, 9 H), 1.39 (d, 2 H, J = 9 Hz), 1.62 (s, 3 H), 1.66 (s, 3 H), 1.85–1.97 (m, 1 H), 1.88 (s, 3 H), 2.08 (dd, 1 H, J = 2 Hz, 19 Hz), 2.28–2.42 (m, 1 H), 2.47 (dd, 1 H, J = 7 Hz, 19 Hz), 2.89 (br s, 1 H), 5.03–5.14 (m, 1 H), 5.38–5.52 (m, 1 H), 5.85 (s, 1 H); ^{13}C NMR 209.3 (s), 170.7 (s), 141.0 (s), 136.8 (s), 128.1 (d), 123.4 (d), 119.9 (d), 41.5 (d), 40.0 (t), 30.8 (t), 26.6 (q), 20.8 (q), 18.7 (t), 9.5 (q), −1.8 (q) ppm; IR (film) 1700, 1660, 1645, 1630 cm^{-1}; mass spectrum, m/z 276 (M$^+$).

Lewis Acid Catalyzed Annulations. General Procedure. Most of these reactions were carried out on 50–150 mg of substrate; scaling-up of the reaction (up to 1.0 g of substrate) had little effect (±5%) upon the overall yield. All reactions were run under an inert atmosphere of nitrogen at a concentration of ca. 0.3 M at 0 °C. For brevity, only the quantity of substrates used and the amount(s) of isolated product(s) are provided for each reaction. The following experimental procedure is typical for the $EtAlCl_2$ reaction.

Cyclization of 7. To a solution of 150 mg (0.64 mmol) of 7 in 1 mL of dry toluene cooled to 0 °C was added dropwise 0.88 mL (1.27 mmol, 1.45 M in toluene) of $EtAlCl_2$ over a 3-min period. The reaction mixture was stirred for 1.5 h at 0 °C. Standard ethereal workup gave an oily residue. Purification on silica gel (elution with H:E, 6:1) provided 54 mg (48%) of (3a*R**,5*S**)-3,3a,4,5,6,7-hexahydro-5-vinyl-2*H*-inden-2-one (8a), which was homogeneous by TLC analysis (H:E, 1:2, R_f(7) = 0.70, R_f(8a) = 0.60): ^{1}H NMR (90 MHz) δ 0.92–1.34 (m, 2 H), 1.92–2.08 (m, 2 H), 2.12–2.37 (m, 3 H), 2.57 (dd, 1 H, J = 7 Hz, 19 Hz), 2.66–2.86 (m, 2 H), 4.92 (dd, 1 H, J = 1 Hz, 11 Hz), 4.97 (dd, 1 H, J = 1 Hz, 19 Hz), 5.63–5.77 (m, 1 H), 5.80 (s, 1 H); ^{13}C NMR 208.9 (s), 183.6 (s), 141.8 (d), 126.9 (d), 113.2 (t), 42.2 (t), 41.1 (d), 40.4 (d), 40.2 (t), 32.4 (t), 30.1 (t) ppm; IR (film) 1700, 1640, 1625 cm^{-1}; mass spectrum, m/z 162 (M$^+$).

Cyclization of 9. Cyclization of 150 mg (0.605 mmol) of 9 with 0.90 mmol of $EtAlCl_2$ yielded 25.2 mg (23%) of (3a*R**,5*S**)-1,3,3a,4,5,6-hexahydro-3a-methyl-5-vinyl-2*H*-inden-2-one (10b), which was homogeneous by TLC analysis (H:E, 1:1,R_f(9) = 0.81, R_f(10b) = 0.93): ^{1}H NMR (90 MHz) δ 1.00–2.36 (m, 9 H), 1.20 (s, 3 H), 4.85–5.00 (m, 1 H), 5.05–5.12 (m, 1 H), 5.23 (br t, 1 H, J = 6.0 Hz), 5.65 (dd, 1 H, J = 16 Hz, 10 Hz).

Continued elution yielded 47 mg (44%) of (3a*R**,5*S**)-3,3a,4,5,6,7-hexahydro-3a-methyl-5-vinyl-2*H*-inden-2-one (10a), which was homogeneous by TLC analysis (H:E, 1:1, R_f(10a) = 0.56): ^{1}H NMR (250 MHz) δ 1.24 (s, 3 H), 1.12–1.34 (m, 2 H), 1.90–2.04 (m, 2 H), 2.23 (AB q, 2 H, $\Delta\nu_{AB}$ = 19 Hz, J = 20 Hz), 2.40–2.50 (m, 2 H), 2.63–2.70 (m, 1 H), 4.92 (d, 1 H, J = 11 Hz), 4.98 (d, 1 H, J = 18 Hz), 5.60–5.70 (m, 1 H), 5.75 (s, 1 H); ^{13}C NMR 208.0 (s), 187.4 (s), 142.0 (d), 126.3 (d), 113.3 (t), 52.1 (t), 46.1 (t), 43.1 (s), 37.0 (d), 33.3 (t), 27.2 (t), 24.8 (q) ppm; IR (film) 1705, 1620 cm^{-1}; mass spectrum, m/z 176 (M$^+$). Anal. Calcd for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 82.03; H, 9.27.

Cyclization of 11. Cyclization of 100 mg (0.40 mmol) of 11 with 0.80 mmol of $EtAlCl_2$ yielded 16 mg (23%) of (4a*R**,6*S**)-3,4,4a,5,6,7-hexahydro-6-ethenyl-2(1*H*)-naphthalenone (12b), which was homogeneous by TLC analysis (H:E, 1:1, R_f(11) = 0.81, R_f(12b) = 0.73): ^{1}H NMR (90 MHz) δ 1.00–2.45 (m, 12 H), 4.87–4.98 (m, 1 H), 5.00–5.06 (m, 1 H), 5.27 (br t, 1 H, J = 6.0 Hz), 5.62–5.70 (m, 1 H).

Continued elution yielded 48 mg (68%) of (4a*R**,6*S**)-4,4a,5,6,7,8-hexahydro-6-ethenyl-2(3*H*)-naphthalenone (12a), which was homogeneous by TLC analysis (H:E, 1:1, R_f(12a) = 0.51): ^{1}H NMR (90 MHz) δ 0.96–1.38 (m, 3 H), 1.50–2.00 (m, 4 H), 2.00–2.50 (m, 5 H), 4.92 (dd, 1 H, J = 2 Hz, 12 Hz), 4.98 (dd, 1 H, J = 2 Hz, 18 Hz), 5.63–5.79 (m, 1 H), 5.80 (s, 1 H); ^{13}C NMR 200.0 (s), 166.1 (s), 142.2 (d), 124.4 (d), 113.0 (t), 40.6 (d), 39.8 (t), 37.1 (d), 36.5 (t), 34.8 (t), 32.2 (t), 29.1 (t) ppm; IR (film) 1670, 1640, 1620 cm^{-1}; mass spectrum, m/z 176 (M$^+$).

Cyclization of 1. Cyclization of 100 mg (0.38 mmol) of 1 with 0.76 mmol of $EtAlCl_2$ yielded 56 mg (77%) of (4a*R**,6*S**)-4,4a,5,6,7,8-hexahydro-6-ethenyl-4a-methyl-2(3*H*)-naphthalenone (2), which was homogeneous by TLC analysis (H:E, 1:1, R_f(1) = 0.85, R_f(2) = 0.70): ^{1}H NMR (90 MHz) δ 1.10–1.36 (m, 2 H), 1.23 (s, 3 H), 1.63–1.96 (m, 4 H), 2.22–2.54 (m, 5 H), 4.91 (dd, 1 H, J = 2 Hz, 12 Hz), 4.98 (dd, 1 H, J = 2 Hz, 18 Hz), 5.62–5.75 (m, 1 H), 5.71 (s, 1 H); ^{13}C NMR 199.6 (s), 169.4 (s), 142.5 (d), 124.2 (d), 113.0 (t), 47.3 (t), 37.9 (t), 36.8 (d), 36.0 (s), 33.8 (t), 32.5 (t), 32.3 (t), 22.6 (q) ppm; IR (film) 1660, 1630, 1615 cm^{-1}; mass spectrum, m/z 190 (M$^+$).

Cyclization of 13. Cyclization of 130 mg (0.471 mmol) of 13 with 0.94 mmol of $EtAlCl_2$ yielded 78 mg (80%) of (4a*R**,6*S**)-4,4a,5,6,7,8-hexahydro-1,4a-dimethyl-6-ethenyl-2-(3*H*)-naphthalenone (14a), which was homogeneous by TLC analysis (H:E, 1:1, R_f(13) = 0.85, R_f(14a) = 0.70): ^{1}H NMR (90 MHz) δ 1.09–1.26 (m, 2 H), 1.21 (s, 3 H), 1.58–1.96 (m, 4 H), 1.73 (s, 3 H), 2.04–2.22 (m, 1 H), 2.32–2.57 (m, 3 H), 2.68–2.79 (m, 1 H), 4.91 (dd, 1 H, J = 2 Hz, 10 Hz), 4.98 (dd, 1 H, J = 2 Hz, 17 Hz), 5.62–5.76 (m, 1 H); ^{13}C NMR 199.0 (s), 161.7 (s), 142.8 (d), 128.6 (s), 112.9 (t), 47.9 (t), 37.6 (t), 36.5 (d), 36.3 (s), 33.7 (t), 32.4 (t), 27.3 (t), 23.0 (q), 10.9 (q) ppm; IR (film) 1640, 1620 cm^{-1}; mass spectrum, m/z 204 (M$^+$).

Cyclization of 15. Cyclization of 65 mg (0.23 mmol) of 15 with 0.30 mmol of $EtAlCl_2$ yielded 21 mg (43%) of (4a*R**,6*S**)-3,4,4a,5,6,7-hexahydro-4a,6-dimethyl-6-ethenyl-2(1*H*)-naphthalenone (16b), which was homogeneous by TLC analysis (H:E, 1:1, R_f(15) = 0.72, R_f(16b) = 0.72): ^{1}H NMR (60 MHz) δ 1.00–3.33 (m, 16 H), 1.10 (s, 3 H), 1.20 (s, 3 H), 4.7–4.9 (m, 1 H), 5.00–5.10 (m, 1 H), 5.15 (br t, 1 H, J = 6 Hz), 5.6–5.8 (m, 1 H).

Continued elution yielded 10 mg (20%) of (4a*R**,6*S**)-4,4a,5,6,7,8-hexahydro-4a,6-dimethyl-6-ethenyl-2(3*H*)-naphthalenone (16a), which was homogeneous by TLC analysis (H:E, 1:1, R_f(16a) = 0.52): ^{1}H NMR (60 MHz) δ 1.00 (s, 3 H), 1.00–2.60 (m, 16 H), 1.23 (s, 3 H), 4.70–4.90 (m, 1 H), 5.00–5.10 (m, 1 H), 5.80 (s, 1 H), 5.60–5.80 (m, 1 H).

Cyclization of 17. Cyclization of 100 mg (0.36 mmol) of 17 with 0.72 mmol of $EtAlCl_2$ yielded 45 mg (61%) of (4a*R**,6*S**)-4,4a,5,6,7,8-hexahydro-4a,8-dimethyl-6-ethenyl-2-(3*H*)-naphthalenone (18), which was homogeneous by TLC analysis (H:E, 1:1, R_f(17) = 0.90, R_f(18) = 0.75): ^{1}H NMR (90 MHz, CCl_4) δ 0.98–1.20 (m, 6 H), 1.30–1.95 (m, 5 H), 4.78–4.98 (m, 2 H), 5.20–5.68 (m, 2 H); IR (film) 1670, 1615 cm^{-1}.

Cyclization of 19. Cyclization of 150 mg (0.47 mmol) of 19 with 0.71 mmol of $EtAlCl_2$ yielded 70.6 mg (61%) of 4-methyl-3-(1-cyclohexenyl)-6-ethenylbicyclo[2.2.2]oct-2-en-1-ol (20), which was homogeneous by TLC analysis (H:E, 1:1, R_f(19) = 0.93, R_f(20) = 0.83): ^{1}H NMR (90 MHz, CCl_4) δ 1.05 (s, 3 H), 1.10–2.29 (m, 16 H), 4.89–5.20 (m, 2 H), 5.00 (s, 1 H), 5.40–5.60 (m, 1 H), 5.65 (s, 1 H); IR (film) 3600–3200 cm^{-1}; mass spectrum, m/z 244 (M$^+$).

Cyclization of 19 with $TiCl_4$. Cyclization of 220 mg (0.69 mmol) of 19 with 1.38 mmol of $TiCl_4$ yielded 110 mg (65%) of

the tricyclic enone **21**, which was homogeneous by TLC analysis (H:E, 1:1, R_f(**19**) = 0.93, R_f(**21**) = 0.83): ^{1}H NMR (90 MHz) δ 0.78–1.20 (m, 2 H), 1.22 (s, 3 H), 1.28–1.50 (m, 6 H), 1.62–2.07 (m, 5 H), 2.25–2.68 (m, 4 H), 4.93 (d, 1 H, J = 18 Hz), 4.97 (d, 1 H, J = 8 Hz), 5.67–5.80 (m, 1 H), 5.87 (s, 1 H); ^{13}C NMR 199.0, 171.5, 141.8, 125.6, 114.0, 43.5, 39.8, 39.0, 38.5, 38.0, 36.6, 33.0, 27.1, 26.5, 24.0, 22.1, 21.2 ppm; IR (film) 1670, 1655, 1620 cm^{-1}; mass spectrum, m/z 244 (M$^+$).

Cyclization of 22 with $TiCl_4$. Cyclization of 200 mg (0.69 mmol) of **22** with 1.38 mmol of $TiCl_4$ yielded 120 mg (80%) of (1*R**,4*R**)-4-methyl-3-(2-methyl-1-propenyl)-6-ethenylbicyclo-[2.2.2]oct-2-en-1-ol (**23**), which was homogeneous by TLC analysis (H:E, 2:1, R_f(**22**) = 0.73; R_f(**23**) = 0.65): ^{1}H NMR (90 MHz, CCl_4) δ 1.10 (s, 3 H), 1.15–2.30 (m, 7 H), 1.78 (br s, 6 H), 4.50–5.05 (m, 2 H), 5.10 (s, 1 H), 5.25–5.87 (m, 1 H), 5.83 (s, 1 H); ^{13}C NMR 141.7, 135.1, 131.7, 120.7, 117.1, 99.7, 73.7, 50.6, 42.1, 36.3, 34.2, 33.9, 26.5, 23.1, 19.5 ppm; IR (film) 3450–3100 cm^{-1}; mass spectrum, m/z 218 (M$^+$). These data represent a mixture of diastereomers.

Cyclization of 24. Cyclization of 100 mg (0.34 mmol) of dimethylphenylallylsilane **24** with 0.68 mmol of $EtAlCl_2$ yielded 42 mg (65%) of **2**, which was identical with that previously characterized.

Cyclization of 25. Cyclization of 100 mg (0.24 mmol) of triphenylallylsilane **25** with 0.48 mmol of $EtAlCl_2$ yielded 27.2 mg (60%) of **2**, which was identical with that previously characterized.

Cyclization of 33. Cyclization of 750 mg (2.31 mmol) of **33** with 4.63 mmol of $EtAlCl_2$ yielded 421 mg (96%) of 3,4,5,6,7,8-hexahydro-7-(2-propenyl)-1(2*H*)-naphthalenone (**34**), which was homogeneous by TLC analysis (H:E, 1:1, R_f(**33**) = 0.77, R_f(**34**) = 0.55): ^{1}H NMR (90 MHz) δ 1.75 (s, 3 H), 1.20–2.70 (m, 13 H), 4.70 (s, 1 H), 4.75 (s, 1 H); mass spectrum, m/z 190 (M$^+$).

Cyclization of 33 with $TiCl_4$. Cyclization of 220 mg (0.69 mmol) of **33** with $TiCl_4$ yielded 110 mg (76%) of 3,4,5,6,7,8-hexahydro-7-(1-methylethenylidene)-1(2*H*)-naphthalenone (**35**), which was homogeneous by TLC analysis (H:E, 1:1, R_f(**33**) = 0.75, R_f(**35**) = 0.40): ^{1}H NMR (90 MNz) δ 1.60 (s, 3 H), 1.70 (s, 3 H), 1.20–2.70 (m, 12 H); mass spectrum, m/z 190 (M$^+$).

Cyclization of 40. Cyclization of 30 mg (0.12 mmol) of **40** with $TiCl_4$ yielded 17.1 mg (80%) of 3,4,5,6,7,8-hexahydro-7-(2-ethenyl)-1(2*H*)-naphthalenone (**41**), which was homogeneous by TLC analysis (H:E, 1:1, R_f(**40**) = 0.86, R_f(**41**) = 0.48): ^{1}H NMR (90 MHz) δ 1.31–1.42 (m, 1 H), 1.81–2.03 (m, 4 H), 2.19–2.31 (m, 4 H), 2.37–2.58 (m, 4 H), 4.99 (td, 1 H, J = 10.5 Hz, 1.4 Hz), 5.05 (td, 1 H, J = 17.2 Hz, 1.5 Hz), 5.85 (ddd, 1 H, J = 17.2 Hz, 10.5 Hz, 6.3 Hz); mass spectrum, m/z 176 (M$^+$). Anal. Calcd for $C_{12}H_{16}O$: C, 81.76; H, 9.16. Found: C, 82.13; H, 9.31.

Fluoride Ion Catalyzed Annulations. General Procedure. All reactions were carried out on 100–240 mg of substrate at a concentration of ca. 0.3 M; scaling-up of the reaction (up to 1.0 g of substrate) had little effect (±5%) upon the overall yield. All reactions were run with TBAF (Alfa) and were under an inert atmosphere of nitrogen. Activated 4-Å molecular sieves were stored in an oven at 135 °C. Stock solutions of TBAF/DMF typically contained 10–30 mg of TBAF per 3 mL of solution. Unless otherwise indicated, 3 equiv of HMPA was used for each equivalent of substrate.

After addition of substrate via syringe pump was complete, the resulting mixture was stirred at rt for 3–14 h to ensure complete reaction and then diluted with water (10 mL). Standard ethereal workup gave an oily residue, which was directly purified by flash chromatography.

For brevity, only the quantity of cyclization precursor used and the amount(s) of product(s) isolated are provided for each cyclization. Chromatographic and spectral properties of the cyclization product(s) are then listed. The following experimental procedure is typical.

Cyclization of 7. A reaction vessel containing 4-Å molecular sieves was flame-dried under vacuum (5 min) and placed under nitrogen. A solution of 35 mg (0.13 mmol) of anhyd TBAF in 3 mL of DMF was added to the flask and stirred for 20 min, followed by addition of 0.54 mL (3.0 mmol) of HMPA. A solution of 150 mg (0.64 mmol) of **7** in 2.0 mL of DMF was added dropwise via syringe pump at rt over a 2-h period. The resulting mixture was stirred for an additional 12 h. Standard ethereal workup afforded 112 mg of a crude oily residue. Purification on silica gel (elution H:E, 10:1) provided 18 mg (18%) of *cis*-3a,4,7,7a-tetrahydro-3a-ethenyl-2-indanone (**42c**), which was homogeneous by TLC analysis (H:E, 1:1, R_f(**7**) = 0.65, R_f(**42c**) = 0.72): ^{1}H NMR (90 MHz) δ 1.00–1.20 (m, 1 H), 1.80–2.18 (m, 4 H), 2.18–2.26 (m, 2 H), 2.32 (AB q, 2 H, J = 17 Hz, $\Delta\nu_{AB}$ = 45 Hz), 5.01 (dd, 1 H, J = 2 Hz, 17 Hz), 5.13 (dd, 1 H, J = 2 Hz, 12 Hz), 5.69 (d, 2 H, J = 3 Hz), 6.00 (dd, 1 H, J = 12 Hz, 17 Hz); IR (film) 1745, 1640 cm^{-1}; mass spectrum, m/z 162 (M$^+$).

Further elution provided 32 mg (30%) of 1,2,4,5,9,9a-hexahydro-6*H*-cyclopentacycloocten-2-one (**42a**), which was homogeneous by TLC analysis (H:E, 1:1, R_f(**42a**) = 0.50): ^{1}H NMR (90 MHz) δ 1.10–1.25 (m, 2 H), 1.30–2.90 (m, 9 H), 5.42–5.60 (m, 2 H), 5.67 (s, 1 H); IR (film) 1690, 1610 cm^{-1}; mass spectrum, m/z 162 (M$^+$).

Cyclization of 9. Cyclization of 150 mg (0.605 mmol) of **9** yielded 24 mg (23%) of *cis*-3a,4,7,7a-tetrahydro-3a-ethenyl-7a-methyl-2-indanone (**43c**), which was homogeneous by TLC analysis (H:E, 1:1, R_f(**9**) = 0.70, R_f(**43c**) = 0.75): ^{1}H NMR (250 MHz) δ 1.01 (s, 3 H), 1.84–2.23 (m, 4 H), 2.17 (AB q, 2 H, J = 18 Hz, $\Delta\nu_{AB}$ = 40.6 Hz), 2.32 (AB q, 2 H, J = 18 Hz, $\Delta\nu_{AB}$ = 88 Hz), 4.98 (dd, 1 H, J = 1 Hz, 18 Hz), 5.10 (dd, 1 H, J = 1 Hz, 11 Hz), 5.65 (d, 2 H, J = 2 Hz), 5.96 (dd, 1 H, J = 11, Hz, 18 Hz); ^{13}C NMR 210.7, 141.2, 124.7, 124.2, 113.7, 50.6, 47.7, 45.0, 38.9, 34.3, 33.6, 23.5 ppm; IR (film) 1740, 1660, 1635 cm^{-1}; mass spectrum, m/z 176 (M$^+$).

Further elution provided 35 mg (33%) of 1,2,4,5,9,9a-hexahydro-9a-methyl-6*H*-cyclopentacycloocten-2-one (**43a**), which was homogeneous by TLC analysis (H:E, 1:1, R_f(**43a**) = 0.55): ^{1}H NMR (250 MHz) δ 1.22 (s, 3 H), 1.42–1.54 (m, 1 H), 1.85–1.97 (m, 1 H), 2.04–2.64 (m, 6 H), 2.27 (AB q, 2 H, J = 18 Hz, $\Delta\nu_{AB}$ = 45 Hz), 5.57–5.73 (m, 2 H), 5.82 (s, 1 H); ^{13}C NMR 208.4 (s), 190.3 (s), 132.7 (d), 130.7 (d), 127.3 (d), 49.3 (s), 48.3 (t), 35.4 (t), 29.2 (t), 28.3 (t), 26.7 (t), 26.4 (q) ppm; IR (film) 1680, 1660, 1610 cm^{-1}; mass spectrum, m/z 176 (M$^+$).

Cyclization of 11. Cyclization of 100 mg (0.40 mmol) of **11** provided 22.2 mg (30%) of 3,6-diethenylbicyclo[2.2.2]oct-2-en-1-ol (**44b**), which was homogeneous by TLC analysis (H:E, 1:1, R_f(**11**) = 0.81, R_f(**44b**) = 0.66): ^{1}H NMR (90 MHz, CCl_4) δ 1.15–2.32 (m, 8 H), 2.78 (br s, 1 H), 4.76–5.18 (m, 4 H), 5.40–6.31 (m, 2 H), 6.00 (s, 1 H); IR (film) 3600–3200 cm^{-1}; mass spectrum, m/z 176 (M$^+$).

Further elution yielded 23.7 mg (32%) of *cis*-3,4,4a,5,8,8a-hexahydro-8a-ethenyl-2(1*H*)-naphthalenone (**44c**), which was homogeneous by TLC analysis (H:E, 1:1, R_f(**44c**) = 0.36): ^{1}H NMR (90 MHz, CCl_4) δ 1.00–2.5 (m, 11 H), 4.65–5.10 (m, 3 H), 5.30–5.70 (m, 1 H).

Cyclization of 1. Cyclization of 100 mg (0.38 mmol) of **1** yielded 21 mg (30%) of 3,6-diethenyl-4-methylbicyclo[2.2.2]-oct-2-en-1-ol (**6**), which was homogeneous by TLC analysis (H:E, 1:1 R_f(**1**) = 0.85, R_f(**6**) = 0.78): ^{1}H NMR (90 MHz, CCl_4) δ 0.80–2.35 (m, 8 H), 1.12 (s, 3 H), 4.80–6.30 (m, 6 H), 5.32 (br s, 1 H); IR (film) 3550–3200 cm^{-1}.

Further elution provided 30 mg (40%) of 4,4a,5,8,9,10-hexahydro-4a-methyl-2(3*H*)-benzocyclooctenone (**3**), which was homogeneous by TLC analysis (H:E, 1:1, R_f(**3**) = 0.70): ^{1}H NMR (90 MHz) δ 1.15 (s, 3 H), 1.22–1.40 (m, 1 H), 1.58–1.67 (m, 1 H), 1.78–1.96 (m, 2 H), 2.03–2.54 (m, 8 H), 5.57–5.73 (m, 2 H), 5.79 (s, 1 H); ^{13}C NMR 199.3 (s), 173.5 (s), 132.0 (d), 128.6 (d), 128.3 (d), 42.7 (s), 36.6 (t), 34.2 (t), 34.0 (t), 32.6 (t), 29.9 (t), 26.6 (t), 24.8 (q) ppm; IR (film) 1660, 1605 cm^{-1}; mass spectrum, m/z 190 (M$^+$).

Cyclization of 13. Cyclization of 150 mg (0.54 mmol) of **13** yielded 20 mg (24%) of 3,6-diethenyl-2,4-dimethylbicyclo-[2.2.2]oct-2-en-1-ol (**45b**), which was homogeneous by TLC analysis (H:E, 1:1, R_f(**13**) = 0.88, R_f(**45b**) = 0.80): ^{1}H NMR (90 MHz, CCl_4) δ 1.10 (s, 3 H), 1.15–1.90 (m, 5 H), 1.92 (s, 3 H), 2.00–2.40 (m, 2 H), 4.80–5.18 (m, 4 H), 5.50–6.25 (m, 2 H) ppm; IR (film) 3550–3150 cm^{-1}.

Further elution provided 72 mg (65%) of 4,4a,5,8,9,10-hexahydro-2,4a-dimethyl-2(3*H*)-benzocycloocteneone (**45a**), which was homogeneous by TLC analysis (H:E, 1:1, R_f(**45a**) = 0.75): ^{1}H NMR (90 MHz) δ 1.14 (s, 3 H), 1.35–1.55 (m, 1 H), 1.57–1.67 (m, 1 H), 1.68 (s, 3 H), 1.76–1.89 (m, 2 H), 2.02–2.20 (m, 4 H), 2.30–2.65 (m, 4 H), 5.58–5.77 (m, 2 H); ^{13}C NMR 199.9 (s), 165.1 (s), 132.6 (s), 132.2 (d), 128.7 (d), 43.0 (s), 37.9 (t), 33.9 (t), 33.5 (t), 30.9 (t), 27.3 (t), 27.1 (t), 24.7 (q), 11.3 (q) ppm; IR (film) 1660, 1605 cm^{-1}; mass spectrum, m/z 204 (M$^+$).

Cyclization of 17. Cyclization of 120 mg (0.435 mmol) of **17** yielded 37 mg (41%) of 4-methyl-3-(2-propenyl)-6-ethenylbicyclo[2.2.2]oct-2-en-1-ol (**46b**), which was homogeneous by TLC analysis (H:E, 1:1, R_f(17) = 0.85, R_f(**46b**) = 0.80): ^{1}H NMR (90 MHz, CCl_4) δ 1.08 (s, 3 H), 1.23–1.45 (m, 5 H), 1.72 (s, 3 H), 1.80–2.28 (m, 2 H), 4.50–5.05 (m, 2 H), 5.10 (br s, 2 H), 5.20–5.85 (m, 1 H), 5.82 (s, 1 H); IR (film) 3450–3150 cm^{-1}; mass spectrum, m/z 204 (M^+).

Further elution provided 27 mg (30%) of (4a*R**,10*S**)-4,4a,5,8,9,10-hexahydro-4a,10-dimethyl-2(3*H*)-benzocyclooctenone (**46a**), which was homogeneous by TLC analysis (H:E, 1:1, R_f(**46a**) = 0.65): ^{1}H NMR (90 MHz) δ 0.99 (d, 3 H, J = 7 Hz), 1.13 (s, 3 H), 1.07–1.33 (m, 2 H), 1.55–1.64 (m, 2 H), 1.78–1.84 (m, 1 H), 1.91–2.05 (m, 2 H), 2.16–2.28 (m, 1 H), 2.30–2.50 (m, 3 H), 5.61–5.68 (m, 2 H), 5.85 (s, 1 H); ^{13}C NMR 199.7 (s), 178.2 (s), 131.9 (d), 127.9 (d), 125.0 (d), 41.8 (s), 37.0 (d), 36.6 (t), 36.1 (t), 34.6 (t), 34.0 (t), 25.9 (t), 24.0 (q), 23.1 (q) ppm; IR (film) 1670, 1640, 1615 cm^{-1}; mass spectrum, m/z 204 (M^+). Note: the relative stereochemistry of the secondary methyl group remains to be established.[54]

Cyclization of 19. Cyclization of 200 mg (0.633 mmol) of **19** yielded 45.4 mg (30%) of the 1,2-adduct **20**, which was identical with that produced in the $EtAlCl_2$-induced reaction of **19**.

Further elution provided 39 mg (26%) of the tricyclic enone **47**, which was homogeneous by TLC analysis (H:E, 1:1, R_f(**47**) = 0.72): ^{1}H NMR (90 MHz, CCl_4) δ 1.00 (s, 3 H), 1.10–2.20 (m, 18 H), 5.05–5.16 (m, 1 H), 5.25–5.37 (m, 1 H), 5.70 (s, 1 H); IR (film) 1665, 1630, 1600 cm^{-1}; mass spectrum, m/z 244 (M^+). Note: the relative stereochemistry for the B,C-ring junction of tricycle **47** remains to be established.[55]

Cyclization of 48. Cyclization of 150 mg (0.543 mmol) of **48** provided 35 mg (32%) of (*Z*)-4-(2-butenyl)-2-methyl-3-(2-methyl-1-propenyl)-2-cyclopenten-1-one (**49b**), which was homogeneous by TLC analysis (H:E, 1:1, R_f(**48**) = 0.85, R_f(**49b**) = 0.80): ^{1}H NMR (90 MHz) δ 1.56 (d, 3 H, J = 8 Hz), 1.61 (s, 3 H), 1.64 (s, 3 H), 1.89 (s, 3 H), 1.84–2.24 (m, 2 H), 2.34–2.53 (m, 2 H), 2.85–2.97 (m, 1 H), 5.14–5.27 (m, 1 H), 5.40–5.53 (m, 1 H), 5.84 (s, 1 H); ^{13}C NMR 209.2 (s), 170.5 (s), 141.1 (s), 136.8 (s), 126.7 (d), 126.1 (d), 119.9 (d), 41.3 (d), 39.9 (t), 30.6 (t), 26.6 (q), 20.8 (q), 12.9 (q), 9.5 (q) ppm; IR (film) 1695, 1665, 1650, 1635 cm^{-1}; mass spectrum, m/z 204 (M^+).

Continued elution provided 35 mg (32%) of 1,2,4,5,9,9a-hexahydro-1,8,8-trimethyl-6*H*-cyclopentacycloocten-2-one (**49a**), which was homogeneous by TLC analysis (H:E, 1:1, R_f(**49a**) = 0.65): ^{1}H NMR (90 MHz) δ 0.66 (s, 3 H), 1.04 (s, 3 H), 1.17–1.28 (m, 2 H), 1.66 (s, 3 H), 1.86–2.63 (m, 7 H), 4.96–5.12 (m, 2 H); ^{13}C NMR 209.0, 174.6, 138.7, 135.0, 116.1, 50.7, 49.7, 41.1, 39.9, 36.5, 30.2, 19.7, 7.5 ppm; IR (film) 1690, 1650, 1610 cm^{-1}; mass spectrum, m/z 204 (M^+).

Cyclization of 22. Cyclization of 200 mg (0.69 mmol) of **22** yielded 100.5 mg (67%) of the 1,2-adduct **23**, which was identical with that produced in the $TiCl_4$-induced cyclization of **22**.

Cyclization of 24. Cyclization of 250 mg (0.73 mmol) of dimethylphenylallylsilane **24** yielded 48 mg (23%) of the silylated 1,2-adduct **6a**, which was homogeneous by TLC analysis (H:E, 1:1, R_f(**24**) = 0.84, R_f(**6a**) = 0.79): ^{1}H NMR (90 MHz) δ 0.20 (s, 6 H), 1.05 (s, 3 H), 1.80–2.30 (m, 7 H), 4.70–6.20 (m, 7 H), 7.05–7.30 (m, 5 H).

Continued elution furnished 50 mg (38%) of cyclooctane **3**.

Cyclization of 25. Cyclization of 300 mg (0.71 mmol) of triphenylallylsilane **25** yielded 105 mg (35%) of the silylated 1,2-adduct **6b**, which was homogeneous by TLC analysis (H:E, 3:1, R_f(**25**) = 0.78, R_f(**6b**) = 0.77): ^{1}H NMR (90 MHz) δ 1.00 (s, 3 H), 1.05–2.10 (m, 7 H), 4.80–6.20 (m, 7 H), 7.10–7.65 (m, 15 H).

Continued elution furnished 21.5 mg (16%) of cyclooctane **3**.

Mechanism Study. (*Z*)-4-Methyl-3-[2-(phenylseleno)-1-ethanyl]-4-[4-(trimethylsilyl)-2-butenyl]-2-cyclohexen-1-one (56). To a solution of diphenyl diselenide (476 mg, 1.52 mmol) in 10 mL of absolute ethanol at rt was added 24 mg (0.71 mmol) of sodium borohydride. The reaction mixture was stirred for 15 min followed by dropwise addition of 400 mg (1.52 mmol) of **1** in 5 mL of absolute ethanol over a 5-min period. The resulting mixture was stirred for 4 h and then quenched. Standard ethereal workup provided 610 mg of a crude oily residue. Purification on silica gel (elution with H:E, 2:1) provided 543 mg of phenyl selenide **56** (86%), which was homogeneous by TLC analysis (H:E, 1:1 R_f(**1**) = 0.85, R_f(**56**) = 0.75): ^{1}H NMR (250 MHz) δ –0.02 (s, 9 H), 1.08 (s, 3 H), 1.39 (d, 2 H, J = 10 Hz), 1.58–1.69 (m, 1 H), 1.90–2.04 (m, 1 H), 2.10 (t, 2 H, J = 9 Hz), 2.38 (t, 2 H, J = 8 Hz), 2.55 (t, 2 H, J = 10 Hz), 2.97 (t, 2 H, J = 10 Hz), 5.03–5.15 (m, 1 H), 5.40–5.53 (m, 1 H), 5.82 (s, 1 H), 7.18–7.22 (m, 3 H), 7.42–7.48 (m, 2 H); ^{13}C NMR 199.0 (s), 170.1 (s), 132.7 (d) [represents two carbon atoms], 129.5 (s), 129.1 (d) [represents two carbon atoms], 128.9 (d), 127.1 (d), 125.7 (d), 121.6 (d), 39.0 (s), 35.8 (t), 34.1 (t), 34.0 (t), 32.5 (t), 24.6 (t), 24.2 (q), 18.7 (t), –1.03 (q) ppm; IR (film) 1670, 1640, 1615 cm^{-1}; mass spectrum, m/z 263 (M – 156).

Cyclization of 56 Using Stoichiometric Fluoride Ion. To a solution of 160 mg (0.51 mmol) of anhyd TBAF in 3 mL of DMF was added 0.30 mL (1.52 mmol) of HMPA, followed by the dropwise addition (via syringe pump at rt over a 2-h period) of a solution of 190 mg (0.50 mmol) of selenide **56** in 2.5 mL of DMF. The resulting mixture was stirred an additional 2 h. Standard ethereal workup, followed by chromatography (elution with H:E, 10:1), provided 35.2 mg (34%) of (1*R**,6*S**,8*R**)-1,8-diethenyl-6-methylbicyclo[4.2.0]octan-3-one (**4**), which was homogeneous by TLC analysis (H:E, 2:1, R_f(**56**) = 0.75, R_f(**4**) = 0.80): ^{1}H NMR (250 MHz) δ 1.08 (s, 3 H), 1.78–2.22 (m, 4 H), 2.38–2.70 (m, 3 H), 4.85–5.14 (m, 4 H), 5.73–5.88 (m, 1 H), 6.14 (dd, 1 H, J = 10 Hz, 18 Hz); ^{13}C NMR 213.5 (s), 139.1 (d), 138.5 (d), 114.7 (t), 113.0 (t), 48.2 (s), 45.7 (t), 43.6 (d), 37.0 (s), 36.4 (t), 34.1 (t), 34.0 (t), 25.5 (q) ppm; IR (film) 3100, 2950, 2880, 1710, 1640, 1460, 1420, 1390, 1330, 1260, 1380, 1330, 1000, 920 cm^{-1}; mass spectrum, m/z 190 (M^+).

Further elution provided 26.5 mg (20%) of trienone **1** and 18 mg (20%) of cyclooctane **3**.

Cyclization of 56 Using Catalytic Fluoride Ion. Cyclization of 140 mg (0.338 mmol) of selenide **56** using 35 mg of TBAF (0.13 mmol) and the above reaction conditions for 12 h afforded 63 mg (52%) of trienone **1**, 6 mg (10%) of **4**, and 10.8 mg of alcohol **6** (18%). In another experiment, workup of the reaction mixture after a 1-h period afforded a 72% yield of trienone, along with unreacted selenide **56**.

Thermal Rearrangement of Diene 4. Thirty milligrams of **4** was dissolved in 1 mL of xylene and sealed in a 2-mL high-pressure Pyrex ampule. The ampule was kept at a temperature of 180 °C in an oil bath for 18 h. The reaction mixture was concentrated in vacuo and directly chromatographed on silica gel (elution H:E, 6:1) to yield 13.5 mg (45%) of bicyclic enone **3**.

Base-Promoted Rearrangement of 4 (at 25 °C). A reaction vessel containing 4-Å molecular sieves was flame-dried under vacuum (5 min) and placed under nitrogen. A solution of 10 mg of anhyd TBAF in 2 mL of DMF was added to the flask and the solution was stirred for 20 min, followed by addition of 0.09 mL (0.47 mmol) of HMPA. A solution of 30 mg (0.158 mmol) of ketone **4** in 1.0 mL of DMF was added dropwise via syringe pump at rt over a 10-min period. The resulting mixture was stirred overnight (an additional 8 h). Standard ethereal workup, followed by chromatography (elution with H:E, 6:1), provided 28 mg (92%) of enone **3**.

Base-Promoted Rearrangement of 4 (–35 °C). A solution of 10 mg of anhyd TBAF in 2 mL of DMF was stirred for 20 min, followed by addition of 90 μL (0.47 mmol) of HMPA. The reaction vessel was cooled to –35 °C and a solution of 30 mg (0.16 mmol) of ketone **4** in 1.0 mL of DMF was added dropwise via syringe pump over a 10-min period. The mixture was stirred for 3 h at –35 °C. The reaction mixture was quenched at –35 °C by addition of water (10 mL). Standard ethereal workup yielded 35 mg of a crude oil. Purification on silica gel (elution with H:E, 6:1) provided 27 mg (90%) of enone **3**.

Acknowledgment. Support from the National Insti-

(54) Although the relative stereochemistry of the C(3) methyl group present in **46a** remains to be established, the configuration at the C(3) chiral center is governed by thermodynamic factors during the acid-catalyzed enone isomerization.

(55) The relative stereochemistry at the B,C-ring junction of tricycle **47** also remains to be determined. The stereochemistry shown is based on the following considerations: (1) the C(3) chiral center is controlled by thermodynamic factors during the acid-catalyzed enone isomerization and (2) models of the enolate-Cope precursor for enone **47** indicate that the C(4) methine is on the β face of the molecule.

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Abbreviations. Aqueous (aq), hexanes:ether (H:E), tetrabutylammonium fluoride (TBAF), and triethylamine (TEA).

Supplementary Material Available: Spectra for compounds prepared in this study (82 pages). Ordering information is given on any current masthead page.

Intramolecular Additions of Allylsilanes to Conjugated Dienones. A Direct Stereoselective Synthesis of (±)-14-Deoxyisoamijiol†,[1]

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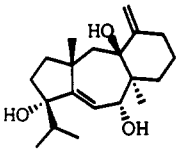
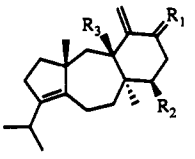
A 16-step synthesis of (±)-14-deoxyisoamijiol is reported featuring an intramolecular addition of an allylsilane to a conjugated dienone to construct stereospecifically the dolastane skeleton.

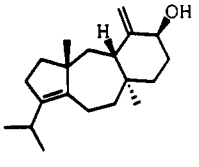
Dolatriol (1) was isolated in 1976 from extracts of the digestive gland of the poisonous Indian Ocean sea hare *Dolabella auricularia*.[3] Further work, however, established that this unusual diterpene was actually produced by the brown algae genus *Dictyota* and only concentrated by *Dolabella* through its diet. Today over 20 related natural products have been isolated and shown to have a 5-7-6 linearly fused tricyclic framework. Typical examples are amijiol (**2a**), isoamijiol (**2b**) and 14-deoxyamijiol (**2c**).[4] Many of the dolastane diterpenes exhibit promising biological activity. For example, 14-deoxyisoamijiol (**3**) has antimicrobial activity against *Mucor mucedo* and *Staphylococcus aureus*.[5]



Dolatriol (1)



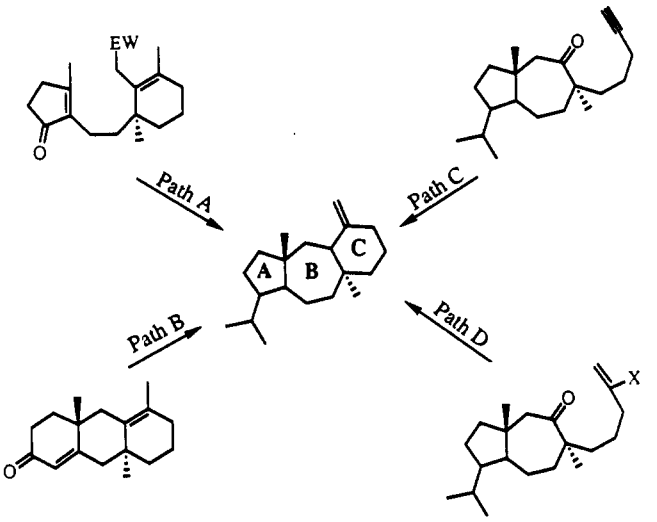
2 a) amijiol
R_1=H_2, R_2=R_3=OH
b) isoamijiol
R_1=β-OH, α-H, R_2=H, R_3=OH
c) 14-deoxyamijiol
R_1=H_2, R_2=OH, R_3=H



14-Deoxyisoamijiol (3)

Several approaches have been devised for the synthesis of the dolastane framework (Scheme I). One of the first strategies, devised by Paquette and co-workers, involved an intramolecular Michael addition to form the central

Scheme I



cycloheptane ring last in an "A + C → ABC" approach (path A).[6] When this strategy proved unsuccessful, Paquette performed a ring expansion–ring contraction of a functionalized hydroanthracene precursor to generate the 5-7-6 tricyclic nucleus (path B).[7] Three alternative strategies for the construction of the dolastane framework

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†Dedicated to Professor Paul A. Grieco on the occasion of his receipt of the 1991 ACS Award for Creative Work in Synthetic Organic Chemistry.

(1) Taken in part from the Ph.D. Dissertation of Clay Ringold, *The University of Georgia*, 1989. This work was presented at the 198th National Meeting of the American Chemical Society in Miami Beach, FL, Sept 1989 [Abstract ORGN #86].

(2) (a) Author to whom correspondence regarding the synthesis of **3** should be addressed. (b) Author to whom correspondence regarding the 2D NMR techniques employed to establish the structures of **7** and **42** should be addressed. (c) Author to whom correspondence regarding the X-ray crystallographic study of enone **37** should be addressed.

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