Intramolecular Additions of Allylsilanes to Conjugated Dienones. The Synthesis of Three Perforanes†[1]

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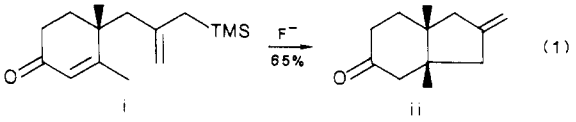
Intramolecular addition of allylsilanes to 3-vinylcycloalkenones provides a powerful means of constructing functionalized 5–5, 5–7, 6–5, and 6–7 bicyclic ring systems. Our results reveal a divergence in reactivity, dependent on reaction catalyst and substrate structure, which can be explained in terms of conformational and stereoelectronic effects. The synthesis of three perforanes is also presented.

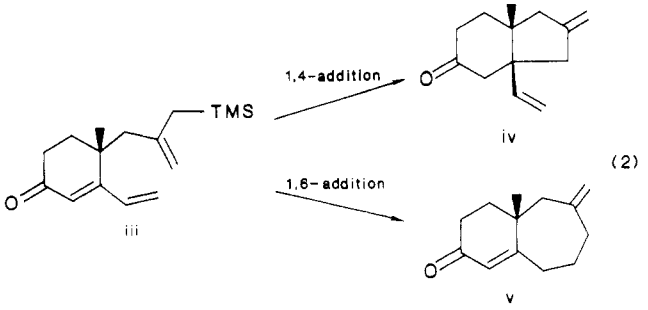
Synthetic methods with novel regioselectivities enhance our ability to prepare complex natural products. Although many ring annulation procedures have been developed, few are general enough for the formation of both cyclopentane[3] and cycloheptane rings.[4]

Our contributions to this area have focused on the addition of nonstabilized nucleophiles to internal electrophiles to produce functionalized polycyclic systems.[5] We have used the intramolecular addition of allylsilanes to cycloalkenones to efficiently construct five-membered rings.[5b,d,f] The cyclization of i is an example of this annulation approach[6] (eq 1).



(1)

In principle, compound iii has three electrophilic sites. In addition to the possibility of 1,2-addition, iii might react with the allylsilane moiety in either 1,4- or 1,6-fashion to annulate a cyclopentane or cycloheptane ring, respectively (cf. iv and v). At the outset of our investigations, the



(2)

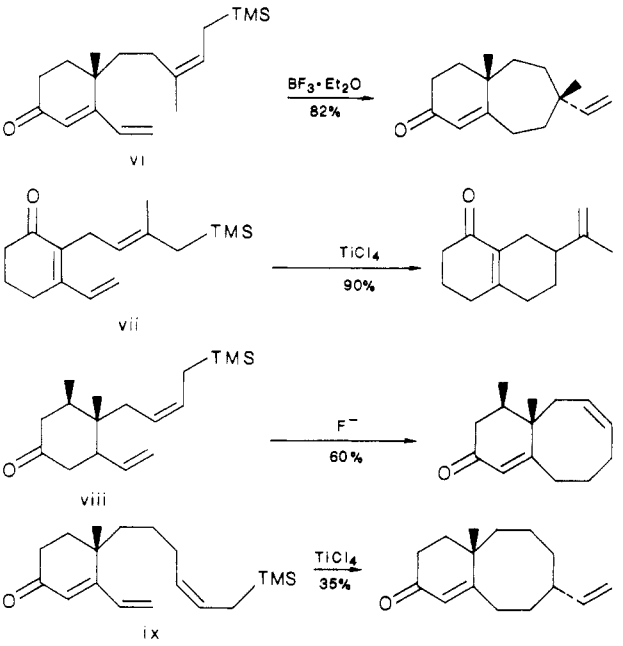
intramolecular addition of an internal nucleophile to a conjugated dienone was unknown.[7] We previously reported that this new annulation strategy produces not only the common ring sizes but more importantly polycyclic systems possessing the less-accessible seven- and eight-membered rings. Additional examples are illustrated in Scheme I.[8]

We conclude that the addition of allylsilanes to conjugated dienones is a significant and versatile method for application to a wide range of structures. Here we describe in full our systematic investigation of substrate iii analogues, which we term 4-isobutenyl dienones,[9] for the creation of 5–5, 6–5, 5–7, and 6–7 bicyclic ring systems. The application of this methodology to the stereoselective synthesis of three marine sesquiterpenes having 6,7-carbocyclic skeletons is also reported.

Results and Discussion

1,6-Nucleophilic additions to polyethylenic Michael acceptors are subject to steric and stereoelectronic effects. In intermolecular reactions which might undergo either

Scheme I



† Dedicated to Professor Walter Gensler (1917–1987).

(1) Reported in part in a preliminary communication: Majetich, G.; Defauw, J.; Desmond, R. *Tetrahedron Lett.* **1985**, *26*, 2751. This work was presented in part at the 35th SERM at Raleigh, NC, in October 1984, and at the 189th National Meeting of the American Chemical Society in Miami Beach, April 1985; Abstracts ORGN 219 and 220.

(2) The synthesis of perforenone has been communicated: Majetich, G.; Ringold, C. *Heterocycles* **1987**, *25*, 271. The perforane syntheses discussed in this manuscript were taken in part from the MS thesis of Clay Ringold, University of Georgia, 1986.

(3) For two comprehensive reviews on cyclopentane annulations, see: (a) Paquette, L. A. *Top. Curr. Chem.* **1984**, *119*, 1. (b) Ramaiah, M. *Synthesis* **1984**, 529.

(4) Long-standing interest in cycloheptane-containing natural products has generated numerous ways to prepare this medium-size ring. **Alkylation approaches**: (a) Grieco, P. A.; Majetich, G.; Ohfune, Y. *J. Am. Chem. Soc.* **1982**, *104*, 4226. (b) House, H. O.; Phillips, W. V.; Sayer, T. S. B.; Yau, C. C. *J. Org. Chem.* **1978**, *43*, 700. House, H. O.; Sayer, T. S. B.; Yau, C. C. *Ibid.* **1978**, *43*, 2153. **Cationic rearrangements**: (c) Lansbury, P. T.; Serelio, A. E. *Tetrahedron Lett.* **1978**, 1909. **Divinyl cyclopropane rearrangements**: (d) Wender, P. A.; Filosa, M. P. *J. Org. Chem.* **1976**, *41*, 3490. (e) Marino, J. P.; Kaneko, T. *Ibid.* **1974**, *39*, 3175. **3 + 4 Cycloaddition reactions**: (f) Hoffmann, H. M. R. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 1. (g) Noyori, R. *Acc. Chem. Res.* **1979**, *12*, 61. (h) Hosomi, A.; Otaka, K.; Sakurai, H. *Tetrahedron Lett.* **1986**, *27*, 2881.

(5) (a) Majetich, G.; Casares, A. M.; Chapman, D.; Behnke, M. *Tetrahedron Lett.* **1983**, *24*, 1909. (b) Majetich, G.; Desmond, R.; Casares, A. M. *Ibid.* **1983**, *24*, 1913. (c) Majetich, G.; Hull, K.; Desmond, R. *Ibid.* **1985**, *26*, 2751. (d) Majetich, G.; Hull, K.; Defauw, J.; Shawe, T. *Ibid.* **1985**, *26*, 2755. (e) Majetich, G.; Behnke, M.; Hull, K. *J. Org. Chem.* **1985**, *50*, 3615. (f) Maetich, G.; Defauw, J.; Hull, K.; Shawe, T. *Tetrahedron Lett.* **1985**, *26*, 4711. (g) Majetich, G.; Casares, A.; Chapman, D.; Behnke, M. *J. Org. Chem.* **1986**, *51*, 1745. (h) Majetich, G.; Desmond, R.; Soria, J., *Ibid.* **1986**, *51*, 1753.

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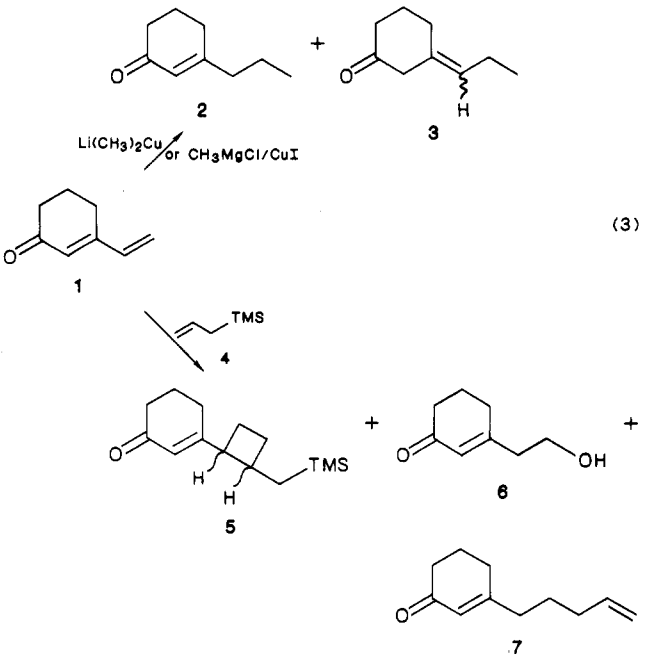
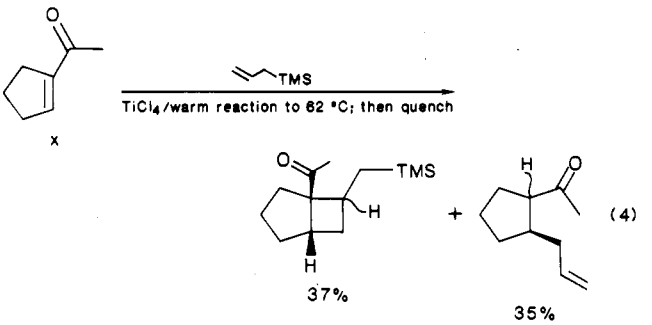
1,4- or 1,6-conjugate addition, early work by Munch-Peterson and co-workers showed that the copper-catalyzed addition of a Grignard reagent occurs at the terminal carbon atom of the conjugated system.[10] Marshall et al. have reported that 1,4-conjugate addition of organocuprate reagents is favored when the competing electrophilic centers are in roughly equivalent steric environments.[11] On the basis of these precedents, we were confident that allylsilanes would react in a 1,6-fashion with polyethylenic electrophiles. We observed, however, that the intermolecular condensation of trimethylallylsilane with conjugated dienoates and dienonitriles under fluoride catalysis exclusively affords 1,4-adducts.[5a,g] This observation was our impetus to examine how conjugated dienones react with allylsilanes using different catalysts.

As expected from Marshall's and Munch-Peterson's precedent, 3-vinyl-2-cyclohexen-1-one (1) gave only 1,6-adducts 2 and 3 when treated with either lithium dimethylcuprate or methylmagnesium chloride and copper iodide (eq 3). To our surprise, treatment of 1 with trimethylallylsilane (4) and titanium tetrachloride at −78 °C, followed by addition of water to the cold (−78 °C) reaction mixture, gave predominantly enone silane 5; enones 6 and 7 were also isolated as minor products. Ethylaluminum dichloride or boron trifluoride etherate did not promote reaction. Warming the reaction mixture to room temperature prior to hydrolysis led to only product 5. The formation of silane 5 is consistent with a reaction pathway in which the silicon-stabilized cationic intermediate, resulting from 1,6-addition by the allylsilane, undergoes intramolecular alkylation to form a cyclobutane ring. This analysis complements House's observation[12] that significant quantities of a cyclobutyl silane xi are produced when 4 reacts with an enone and $TiCl_4$ at elevated temperatures



(3)

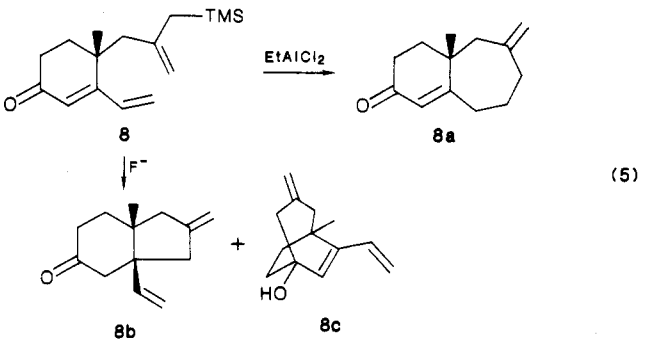
(eq 4).[13] It was unusual that enone 6, the result of 1,6-addition of water, was stable to silica gel chromatography but prone to regenerate 1 via retro-Michael addition. Note that ketone 7 is also a 1,6-adduct.



(4)

This aptitude of allylsilanes to react in a 1,6-fashion with conjugated dienones led us to prepare trienone 8, a substrate which can undergo intramolecular addition to result in cycloheptane formation.

The chemistry of trienone 8 proved intriguing. Treatment of 8 with Lewis acid catalysts gave the 6–7 fused bicyclic enone 8a in 55% yield, uncontaminated by other products. In contrast, treatment of 8 with fluoride ion produced hydrindanone 8b in 45% yield, accompanied by 5% of bicyclic alcohol 8c.



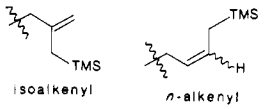
(5)

(6) For related work in this area, see: (a) Wilson, S. R.; Price, M. F. *J. Am. Chem. Soc.* **1982**, *104*, 1124. (b) Schinzer, D. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 108. (c) Schinzer, D.; Solyom, S.; Bechker, M. *Tetrahedron Lett.* **1985**, *26*, 1831. (d) Schinzer, D.; Steffen, J.; Solyom, S. *J. Chem. Soc., Chem. Commun.* **1986**, 829. (e) Tokoroyama, T.; Tsukamoto, M.; Ito, H. *Tetrahedron Lett.* **1984**, *25*, 5067.

(7) We reported the intramolecular 1,6-addition of allylsilanes for the annulation of cyclohexane, cycloheptane, and cyclooctane rings at the First Symposium on the Latest Trends in Organic Synthesis in Blacksburg, VA, May 1984. A cyclohexane annulation via the 1,6-conjugate addition of a lactone enolate to a 3-vinylcyclohexenone derivative was also presented there. For the use of this method, see: Kraft, M. E.; Kennedy, R. M.; Holton, R. A. *Tetrahedron Lett.* **1986**, *27*, 2087.

(8) Unpublished results of K. Hull, A. M. Casares, and R. D. Lowery.

(9) Each of the cyclizations in Scheme I is an intramolecular addition of an allylsilane moiety to a 3-vinylcycloalkenone. This description is far too general, yet formally derived names are impractical. In order to clarify this situation, we use the following convention: (1) the suffix "dienone" describes the 3-vinylcyclohexenone unit; (2) a locant for the allylsilane appendage is stated; and (3) the nature of the allylsilane side chain is defined either as an isoalkenyl or *n*-alkenyl substituent; geometric isomers or substitution are ignored (see eq 27). On the basis of these



(27)

principles, substrates vi, vii, viii, ix, and iii are described as a 4-*n*-pentenyl dienone, 2-*n*-butenyl dienone, a 4-*n*-butenyl dienone, a 4-*n*-hexenyl dienone, and a 4-isobutenyl dienone, respectively. The cyclizations in Scheme I will be the subject of future reports.

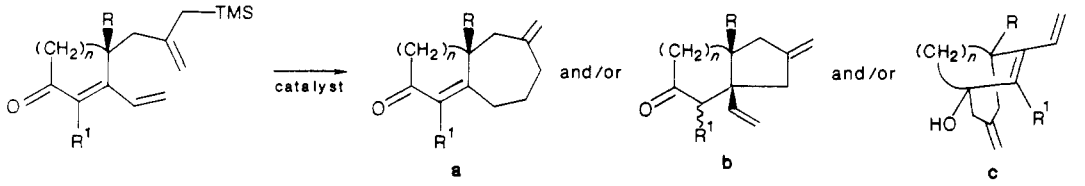
(10) (a) Munch-Peterson, J. *Bull. Soc. Chim. Fr.* **1966**, 471. (b) Bretting, C.; Munch-Peterson, J.; Jorgensen, P. M.; Refin, S. *Acta Chem. Scand.* **1960**, *14*, 151. (c) Munch-Peterson, J.; Bretting, C.; Jorgenson, P. M.; Refin, S.; Andersen, I. G. K. *Ibid.* **1961**, *15*, 277. (d) Jacobsen, S.; Jart, A.; Kindt-Larsen, T.; Andersen, I. G. K.; Munch-Peterson, J. *Ibid.* **1963**, *17*, 2423.

(11) Marshall, J. A.; Ruben, R. A.; Hirsch, L. K.; Phillippe, M. *Tetrahedron Lett.* **1971**, 3795.

(12) House, H. O.; Gaa, P. C.; VanDerveer, D. *J. Org. Chem.* **1983**, *48*, 1661.

(13) For similar observations, see: (a) Pardo, R.; Zahra, J. P.; Santelli, M. *Tetrahedron Lett.* **1979**, 4557. (b) Hosomi, A.; Kobayashi, H.; Sakurai, H. *Ibid.* **1980**, *21*, 955.

Table I



substrate					yield, %		
	N	R	R^1	catalyst	a	b	c
9	2	H	H	F^-	20	11	0
				$EtAlCl_2$	49	0	0
8	2	CH_3	H	F^-	0	45	5
				$EtAlCl_2$	60	0	0
10	2	H	CH_3	F^-	72	0	0
				$EtAlCl_2$	70	0	0
11	2	CH_3	CH_3	F^-	0	71	26
				$EtAlCl_2$	90	0	0
12	1	H	H	F^-	4	2	0
				$EtAlCl_2$	46	0	0
13	1	CH_3	H	F^-	0	29	43
				$EtAlCl_2$	70	0	0
14	1	H	CH_3	F^-	23	0	24
				$EtAlCl_2$	66	0	0
15	1	CH_3	CH_3	F^-	0	0	96
				$EtAlCl_2$	57	0	0

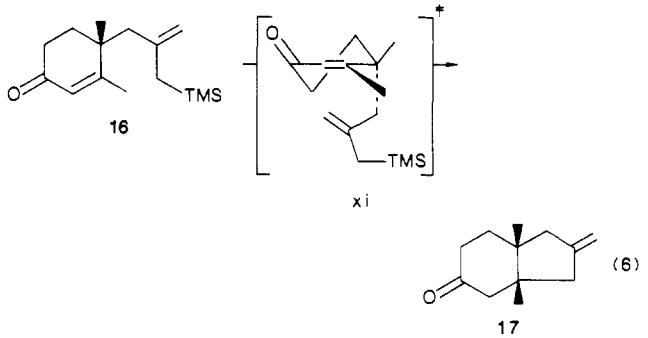
These results promoted us to study a series of substituted 3-vinylcyclohexenones and the analogous cyclopentenones to establish the scope and limitations of the process and the role of the catalyst (Table I).[14] Although these cyclizations were not optimized, we can draw two interesting conclusions from these data: (1) exposure of substrates **8–15** to Lewis acid catalysis gave only cycloheptane products in good yields, and (2) no side products resulting from protodesilylation were observed using either fluoride ion or Lewis acid catalysis. For clarity's sake, we will consider the fluoride-initiated cyclizations first, independent of the Lewis acid promoted reactions.

In a series of papers, Baldwin and co-workers have developed a set of empirical rules for predicting the likelihood of various ring closures.[15] Unfortunately, these qualitative rules cannot be used to decide which of two favored processes will predominate. The fluoride ion catalyzed reactions present such a dilemma.[16]

Recently we proposed three postulates for fluoride ion induced additions of allylsilanes to cycloalkenones: (1) Product formation is under kinetic control and is not reversible.[17] (2) Treatment of an allylsilane with fluoride ion results in formation of a nonbasic pentacoordinate organosilicon nucleophile.[18] (3) Michael addition predominates if the hypervalent silicate intermediate can readily adopt a spatial orientation favorable for conjugate addition, via either terminus of the allylsilane moiety;[19] otherwise 1,2-addition or protodesilylation predominates.

A comparison of the data obtained from the fluoride-induced cyclizations reported in Table I reveals three substrate dependencies which these postulates explain.

First, a correlation exists between the nature of the γ-substituent of the cycloalkenone and the reaction's regioselectivity. For example, entries 8 and 11, where R is a methyl substituent, generate hydrindanones **8a** and **11a** via 1,4-addition whereas entries **9** and **10**, where R is hydrogen, produce 6–7 fused bicyclic enones via 1,6-addition. This generalization is less pronounced in the set of cyclopentenones examined. Our explanation for this correlation is based on conformational arguments (eq 6).



Johnson and co-workers predicted that the dominant conformation for C(3),C(4)-dialkyl-substituted cyclo-

(14) The experimental procedures used for the preparation of the substrates presented in Table I are described in the Experimental Section.

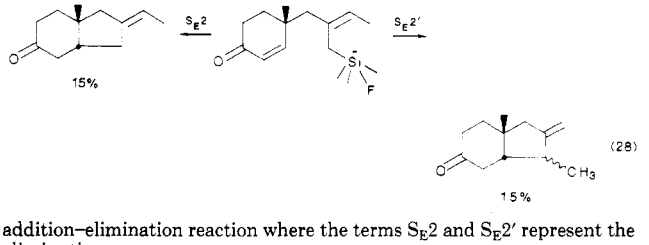
(15) (a) Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 734. (b) Baldwin, J. E.; Cutting, J.; DuPont, W.; Kruse, L.; Silberman, L.; Thomas, R. C. *Ibid.* **1976**, 736. (c) Baldwin, J. E.; Thomas, R. C.; Kruse, L.; Silberman, L. *J. Org. Chem.* **1977**, *42*, 3846.

(16) By use of Baldwin's nomenclature, reaction of trienone **8** in a 1,4-fashion is termed a 5-exo-trig cyclization, whereas 1,6-addition is a 7-endo-trig cyclization; both ring closures are favored processes.

(17) We have demonstrated that under fluoride ion catalysis the reaction products are formed under kinetic control, as all attempts to interconvert these products by either oxy-Cope (i.e., **8c** → **8b**) or enolate-Cope (**8b** → **8a**) pathways failed.

(18) For recent examples of pentacoordinate silicon, see: (a) Tandura, S. N.; Voronkov, M. G.; Alkseev, N. V. *Top. Curr. Chem.* **1986**, *131*, 99. (b) Damrauer, R.; Danahey, S. E. *Organometallics* **1986**, *5*, 1490. (c) Stevenson, W. H., III; Wilson, S.; Martin, J. C.; Farnham, W. B. *J. Am. Chem. Soc.* **1985**, *107*, 6340. (d) Stevenson, W. H., III; Martin, J. C. *Ibid.* **1985**, *107*, 6352.

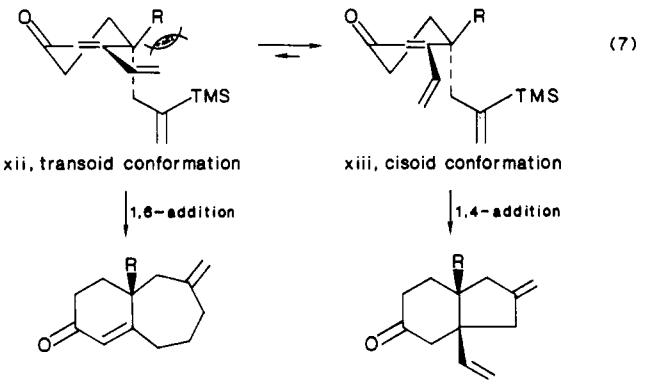
(19) On the basis of the example shown in eq 28, we presume that the silicate anion formed under fluoride catalysis reacts at both ends of the allylsilane. This overall process is more appropriately considered an



addition–elimination reaction where the terms S_E2 and S_E2' represent the elimination process.

hexenones, such as **16**, is the one with the C(4) substituent axially oriented due to A-strain, cf. xi.[20] This conformational preference dictates that Michael addition of the pentacoordinate allylic nucleophile generates a cis ring fusion.

The allylsilane side chain in dienone **8** would also favor a conformation with an axial orientation (eq 7). In addition, the diene moiety of **8** can exist in either a cisoid or a transoid conformation. In simple acyclic 1,3-dienes, the planar transoid conformation is more stable than the cisoid form.[21] Examination of a Drieding model of the transoid conformer of **8** suggests that nonbonded steric interactions between the equatorial C(4) methyl substituent and the C(3) vinyl group would force the dienone to prefer a cisoid conformation (cf. xii and xiii). This orientation clearly precludes 1,6-nucleophilic attack by the silicate species; thus, 1,4-addition takes place. In contrast, when C(4) is also substituted with a small group, such as hydrogen, the more stable transoid diene conformer would be expected to predominate. Steric factors encourage the reactive centers to assume a disposition leading to 1,6-conjugate addition.



(7)

The second substrate dependence noted was that cycloalkenone ring size affected the distribution of reaction products. In the cyclization of cyclopentenones **12**, **14**, and **15**, the major products were bridged bicyclic alcohols **12c**, **14c**, and **15c**, respectively. This is surprising since 2-cyclopenten-1-one is known to be more reactive toward conjugate addition than the analogous six- or seven-membered enones in intermolecular reactions.[22] By contrast, 1,2-addition did not predominate in any of the cyclohexenone cyclizations studied.

Finally, cyclization of the simplest cases, **9** and **12**, proved troublesome due to low yields and polymerization.

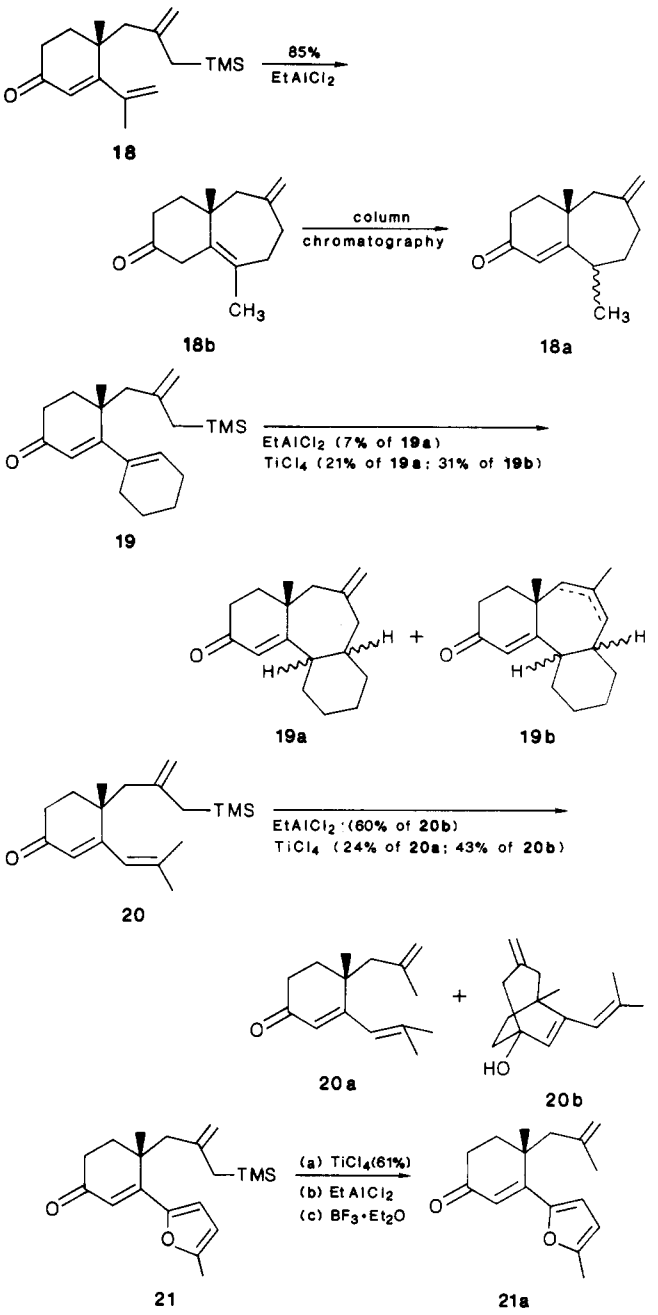
Examination of the Lewis acid catalyzed reactions illustrated in Table I and Scheme II reveals the extent of substitution on the vinyl group tolerated in these cyclizations. Note that exposure of furan **21** to several Lewis acids under a wide variety of conditions failed to promote cyclization; rather, protodesilylation occurred. Presumably the loss of aromaticity makes this cyclization thermodynamically disfavored. To date substrate **21** is the only 4-isobutenyl dienone[9] studied which has not cyclized.

Three aspects of these cyclizations show its general utility. First, this method is efficient and independent of reaction scale.[23] For example, we have cyclized 5 g of **10** in 90% isolated yield. Second, exposure of **18** to ethylaluminum dichloride produces **18b**, an unconjugated enone. This product isomerized upon chromatography or exposure to mild acid to afford **18a**. Finally, a versatile new strategy for the preparation of tricyclic compounds is illustrated by the cyclization of **19**. Unfortunately strong Lewis acids, which are required to initiate cyclization, also promote isomerization of the exocyclic olefin.

Use of a catalytic quantity of ethylaluminum dichloride (0.1 equiv) required longer reaction times and elevated temperatures to effect complete conversion. Under these conditions, significant protodesilylation was observed. Although a stoichiometric quantity of $EtAlCl_2$ proved effective, the reaction rate increased when a 50% excess of catalyst was used.

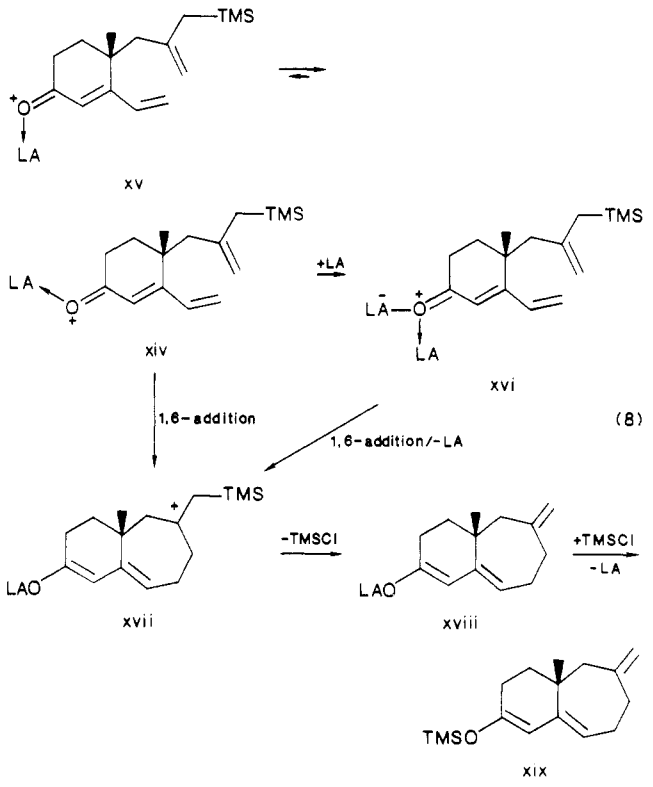
Our mechanistic analysis for cycloheptane formation under Lewis acid catalysis is shown in eq 8. It is reasonable to assume that addition of ethylaluminum dichloride to trienone **8** forms a 1:1 complex in which the Lewis acid is trans to the diene moiety (cf. xiv and xv).[24] Although this

Scheme II



(20) Johnson, F. *Chem. Rev.* **1968**, *68*, 375.
(21) Aten, C. F.; Hedberg, L.; Hedber, K. *J. Am. Chem. Soc.* **1968**, *90*, 2463.
(22) This reactivity parallels the order of the half-wave potential of their respective electrolytic reductions: House, H. O.; Huber, L. E.; Umen, M. J. *J. Am. Chem. Soc.* **1972**, *94*, 8471.
(23) To date, large-scale cyclizations have been conducted on only two examples, compounds **10** and **28**.

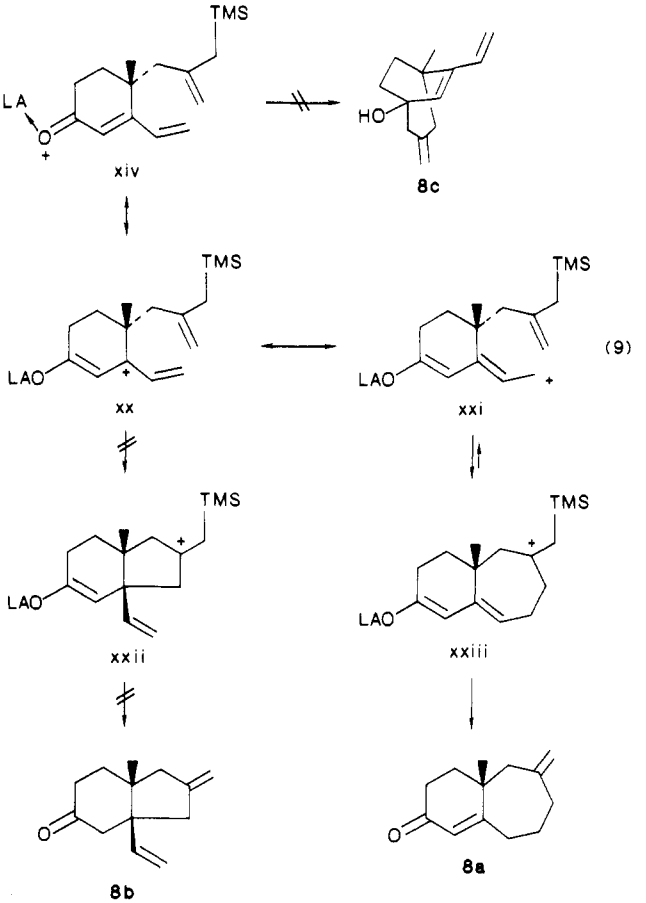
complex can exist in either a transoid or cisoid diene conformation, 1,6-addition can only occur via the transoid conformer.



Alternatively, further addition of ethylaluminum dichloride to the initial 1:1 complex leads to the formation of a 2:1 complex (xvi). Nonbonded interactions between the C(3) vinyl group and the various ligands of this complex would clearly destabilize the cisoid conformation of the diene moiety, so that the transoid orientation would prevail. Moreover, steric repulsion between the Lewis acid and the axially oriented allylsilane appendage also disfavors 1,2- or 1,4-addition. Both complexes generate cationic intermediate xvii containing a silicon-stabilized carbonium ion upon Michael addition.[25,26] Loss of the trimethylsilyl group generates an exocyclic olefin. Desilylation of xvii also generates chlorotrimethylsilane which traps the aluminum enolate as a silyl dienol ether, cf. xix, and regenerates the catalyst. Hydrolysis of xix upon workup with mild aqueous acid provides enone **8a**.[27]

This mechanism satisfactorily accounts for the following observations: (1) only cycloheptane-containing products are obtained; (2) these cyclizations are insensitive to the size of the cycloalkenone ring; (3) silyl enol ethers are isolated if acid hydrolysis is omitted from the reaction workup; and (4) although these reactions are catalytic in nature, they benefit from the use of excess catalyst. Support for the 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.[28] 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-methylcyclohexenone failed to react independent of the amount of catalyst used.

Earlier we noted that Baldwin's rules could not be used to differentiate between two favorable processes. Baldwin's principles, however, do offer an alternative explanation for why only 1,6-addition is observed under electrophilic conditions (eq 9).



Simple resonance theory predicts that Lewis acid activation of the carbonyl would result in the localization of the positive charge at three carbons of the dienone moiety represented by the resonance contributors xiv, xx, and xxi. Note that nucleophilic addition of the allylsilane to resonance structure xx produces cationic intermediate structure xxii, the result of cyclopentane annulation, while addition to resonance structure xxi leads to cycloheptane annulation, i.e., cationic intermediate xxiii. Both cations xxii and xxiii benefit from the ability of the silicon atom to stabilize β-carbonium ions. However, formation of cationic intermediate xxiii corresponds to a favored 7-endo-trig cyclization on the basis of Baldwin's rules,[15] whereas xxii results from a 5-endo-trig ring closure. This latter process is known to be disfavored; hence, cationic

(24) The complexation of Lewis acids have been examined with several carbonyl compounds. (a) **Enones**: Torri, J.; Azzaro, M. *Bull. Soc. Chim. Fr.* **1978**, 283. Fratiello, A.; Stover, C. S. *J. Org. Chem.* **1975**, *40*, 1244. (b) **Ketones**: Hartman, J. S.; Stilbs, P.; Forsen, S. *Tetrahedron Lett.* **1975**, 3497. (c) **Aldehydes**: Reetz, M. T.; Hullmann, M.; Massa, W.; Berger, S.; Rademacher, P.; Heymanns, P. *J. Am. Chem. Soc.* **1986**, *108*, 2405. Denmark, S. E.; Weber, E. J. *J. Am. Chem. Soc.* **1984**, *106*, 7970. Denmark, S. E.; Henke, B. R.; Weber, E. *J. Am. Chem. Soc.* **1987**, *109*, 2512. See also: Nelson, D. J. *J. Org. Chem.* **1986**, *51*, 3185 and references cited therein.

(25) Unlike the fluoride ion process, which can react at either end of the allylsilane moiety,[5h] the Lewis acid catalyzed processes react exclusively at the γ-position due to the well-established β-effect.

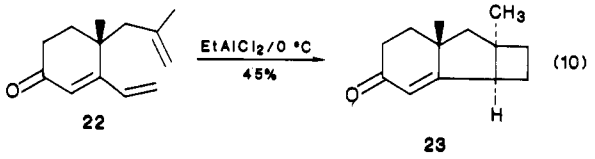
(26) For reviews discussing the β-effect, see: (a) Hudrlik, P. F. *New Applications of Organometallic Reagents in Organic Synthesis*; Seyferth, D., Ed.; Elsevier: Amsterdam, 1976; p 127. (b) Colvin, E. W., *Chem. Soc. Rev.* **1978**, *7*, 15. (c) Fleming, I. *Comprehensive Organic Chemistry*; Barton, D.; Ollis, W. D., Eds.; Pergamon: Oxford, 1979, Vol. 3, p 541. (d) Fleming, I. *Chem. Soc. Rev.* **1981**, *10*, 83.

(27) Omission of the acid hydrolysis, or incomplete hydrolysis, led to the isolation of the silyl dienol ether. This contrasts with our earlier observation that enol ether formation was not observed in the cyclization of simple cycloalkenones.[5h]

(28) Snider, B. B.; Rodini, D. J.; van Straten, J. *J. Am. Chem. Soc.* **1980**, *102*, 5872.

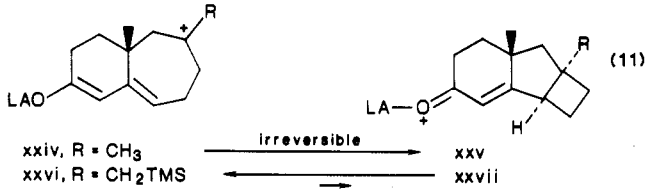
intermediate xxiii predominates.

The generality of these cyclizations caused us to question the necessity of using an allylsilane to achieve cycloheptane annulation. We therefore prepared trienone **22**, which lacks a trimethylsilyl moiety. To our amazement, treatment of **22** with ethylaluminum dichloride at 0 °C gave enone **23** in 45% yield. Obviously enone **23** results from



(10)

a ring closure which first forms a cycloheptane ring with a nonstabilized tertiary carbonium ion (cf. xxiv, eq 11); this intermediate then undergoes irreversible intramolecular alkylation.[29,30]

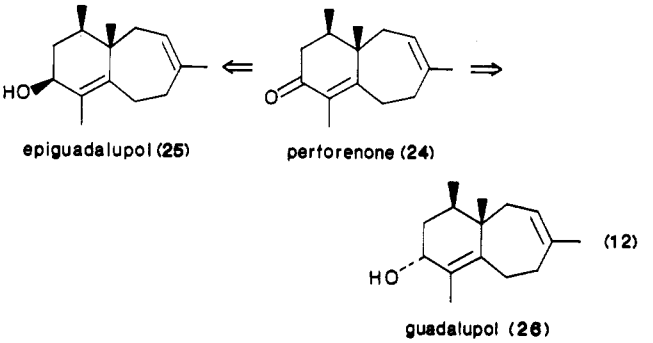


(11)

In contrast, we believe that the allylsilane cycloheptane annulations are thermodynamically controlled processes. The mechanistic pathways for the cyclization of trienones **8** and **22** both proceed via the intermediacy of reactive tertiary carbonium ions (eq 11). In theory, cationic intermediate xxvi is also capable of forming a cyclobutane tricycle (xxvii). However, unlike cation xxiv, carbocation xxvi benefits from silicon's known ability to stabilize cations β to it.[26] Moreover, ring strain favors the reversion of xxvii to intermediate xxvi. Desilylation of this more stable cation (xxvi) generates the exocyclic olefin.

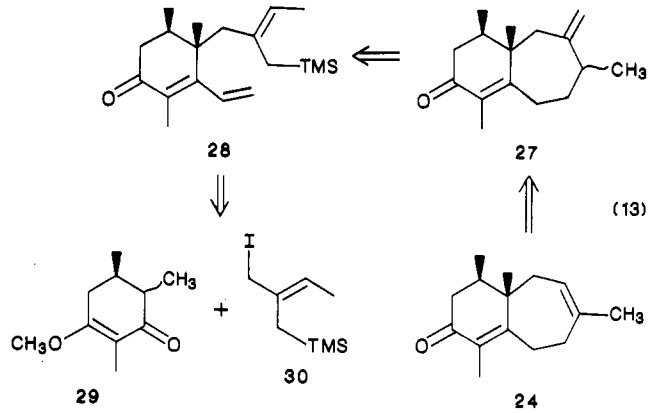
The above model studies provide a basis for predicting the products of 4-isobutenyl dienone cyclizations using different catalysts. We are currently investigating the possible extension of our fluoride ion catalyzed method to the synthesis of angularly fused triquinanes. We have exploited the efficient construction of functionalized 6,7-skeletal systems in the syntheses of *epi*-widdrol and three perforanes. The former synthesis will be described elsewhere,[8b] while the latter is discussed below.

Stereospecific Syntheses of Three Perforanes. The structural diversity of *Laurencia* metabolites has provided many challenges for organic chemists and made the genus *Laurencia* the most studied algae.[31] The following short, simple synthesis of perforenone (**24**), a metabolite isolated from marine alga *Laurencia perforata* by Gonzalez et al.,[32] illustrates the utility of our cycloheptane annulation procedure. Furthermore, perforenone serves as a common intermediate for the synthesis of two related sesquiterpenoids (eq 12).



(12)

We were confident that Lewis acid treatment of **28** would generate 6,7-bicyclic enone **27**, bearing a C(8) methyl group as shown in eq 13. Removal of the superfluous methylene carbon atom and introduction of the requisitite *tri*substituted double bond of perforenone were assumed to be straightforward. Accordingly, we desired a stereospecific synthesis of trienone **28**.



(13)

In our synthesis of nootkatone[5e] we showed that the cis-C(4),C(5)-dimethyl relationship found in trienone **28** could be established by successive alkylations using Stork and Danheiser[33] methodology; the relative configuration at carbons 5 and 6 was determined by the order of alkylation.[34] Assuming that this strategy could also be used to synthesize trienone **28** simplified our retrosynthetic analysis to the synthesis of enol ether **29** and iodo allylsilane **30**.[35]

The present synthesis of perforenone began with 5-methyldihydroresorcinol (**31**), prepared by the procedure of Crossly and Renouf (eq 14).[37] Reaction of this 1,3-dione with 4 N sodium hydroxide and methyl iodide furnished 2,5-dimethyl-1,3-cyclohexanedione (**32**) in good yield.[38] Treatment of **32** with ethereal diazomethane produced enol ether **33** in 85% yield. Alkylation of the lithium enolate of **33**, prepared by using kinetic control conditions,[33] with

(29) For a related internal acid-catalyzed alkylation, see: Stork, G.; Grieco, P. A. *J. Am. Chem. Soc.* **1969**, *91*, 4207.

(30) Snider and co-workers have reported the Lewis acid promoted formation of cyclobutane adducts in the conjugate addition of alkenes to acyclic α,β-unsaturated ketones or aldehydes. However, they note that "cyclobutanes were not observed with cyclic enones".[28]

(31) (a) Scheuer, P. J. *Chemistry of Marine Nature Products*; Academic: New York, 1973. (b) Scheuer, P. J. *Marine Natural Products—Chemical and Biological Perspectives*; Erickson, K., Ed.; Academic: New York, 1983; Vol. 5.

(32) **Isolation and first synthesis of perforenone**: (a) Gonzalez, A. B.; Agiuar, J. M.; Martin, J. D.; Norte, M. *Tetrahedron Lett.* **1975**, 2499. (b) Gonzales, A. B.; Darius, J.; Martin, J. D.; Melian, M. A. *Ibid.* **1978**, 481. **Isolation of guadalupol and epiguadalupol**: (c) Howard, B. M.; Fenical, W. Phytochemistry **1979**, *18*, 1224. (d) Gonzalez, A. G.; Darius, J.; Martin, J. D.; Rodriguez, M. L. *Ibid.* **1976**, *205*.

(33) Stork, G.; Danheiser, R. L. *J. Org. Chem.* **1973**, *38*, 1775.

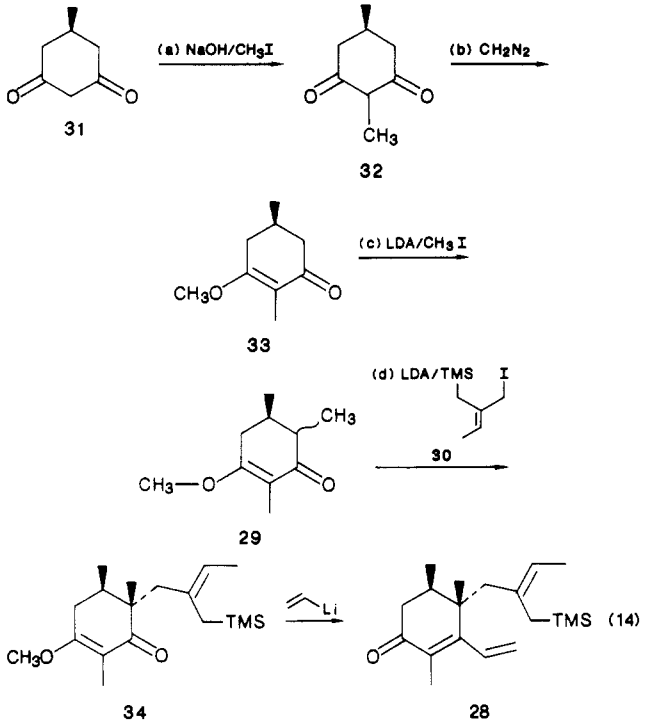
(34) Heathcock and Clark have reported a synthesis of nootkatone using the identical strategy for controlling the stereochemistry of the vicinal methyl groups, see: Heathcock, C. H.; Graham, S. L.; Pirrung, M. C.; Plavac, F.; White, C. T. In *The Total Synthesis of Natural Products*; Apsimon, J., Ed.; Wiley-Interscience: New York, 1983; Vol. V, p 184.

(35) (*E*)-2-[(Trimethylsilyl)methyl]buten-1-ol was prepared in 47% overall yield from tiglyl alcohol by using conditions developed by Trost and co-workers.[36] This material was converted into allylic iodide **30** by using routine procedures and is described in full in the Experimental Section.

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

(37) Crossly, A. W.; Renouf, N. *J. Chem. Soc.* **1915**, 602.

(38) Leed, A. R.; Boettger, S. D.; Ganem, B. *J. Org. Chem.* **1980**, *45*, 1098.

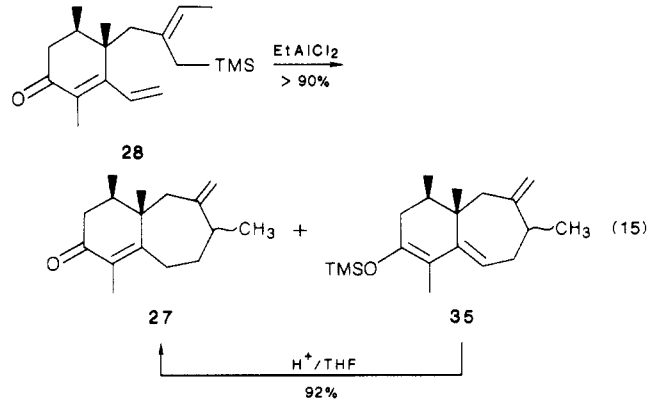


31 32 33 29 34 28

methyl iodide gave 1:1 mixture of the C(6) isomers of **29** in 64% yield.

The next synthetic step was the stereoselective coupling of enol ether **29** and allylic iodide **30**. Reaction of the kinetic enolate of either diastereomer of **29** with silylated iodide **30** provided the same 6:1 mixture of diastereomers of which **34** is the major isomer and was presumed to possess the desired cis relationship between the vicinal methyl groups at C(5) and C(6).

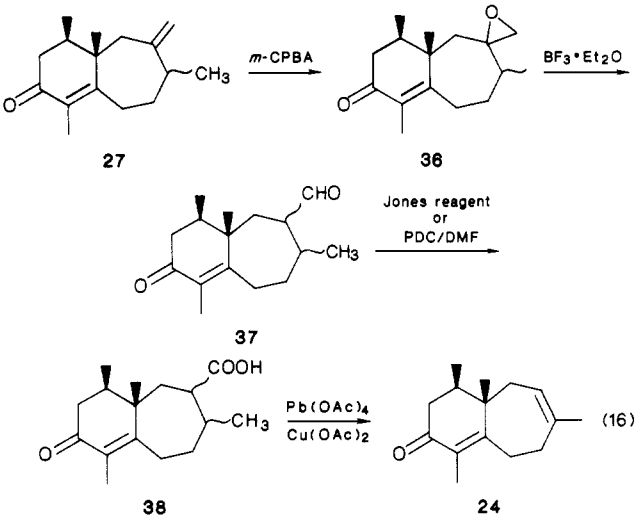
Treatment of **34** with vinyllithium in THF, followed by mild acid hydrolysis, gave trienone **28** in 70% overall yield. In preparative runs of up to a 3-g scale, reaction of **28** with ethylaluminum dichloride at 0 °C routinely gave 90% yields of bicyclic enone **27** as a 2:1 mixture of C(8) epimers (eq 15).[39] Occasionally, triene silyl enol ether **35** was



28 27 35

isolated from the reaction mixture as a minor product [<5%] due to incomplete hydrolysis. This material was readily converted to **27** in 92% yield upon treatment with mild acid.

The assumption that the exocyclic double bond of **27** could readily be converted into a *tri*substituted endocyclic double bond proved to be incorrect. Our initial strategy for achieving this transformation is outlined in eq 16. We



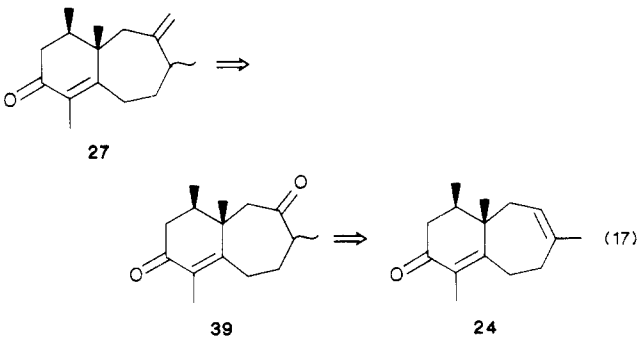
27 36 37 38 24

believed that selective epoxidation of the exocyclic double bond would permit the removal of the extra carbon atom present to yield perforenone via the following three-step sequence: (1) Lewis acid rearrangement of an epoxide into an aldehyde; (2) oxidation of the aldehyde to an acid; and (3) oxidative decarboxylation of the acid.

Treatment of enone **27** with MCPBA in methylene chloride resulted in a diastereomeric mixture of epoxides **36** in good yield. There was some concern that the Lewis acid catalyzed epoxide rearrangement might be plagued by competing rearrangements. Indeed, the nature of the catalyst proved influential. No reaction occurred with either magnesium bromide etherate[40a,b] or trimethylaluminum.[40c] Fortunately, only aldehyde **37** was obtained with boron trifluoride etherate; however, prolonged reaction times led to decomposition.[40d] This difficulty was avoided by monitoring the reaction via NMR analysis. Unfortunately, oxidation of **37** to **38** occurred in low yield with either Jones reagent or PDC.[41]

Since a small amount of **38** was available, its oxidative decarboxylation was attempted using Kochi's method.[42] Thermolysis of acid **38** with cupric acetate and lead tetraacetate in benzene provided a complex mixture of products, including only a trace amount of perforenone. This conclusion was based on TLC comparison of the reaction mixture with an authentic sample of perforenone. These discouraging results forced us to discontinue this route.

A second strategy for the synthesis of perforenone from dienone **27** is outlined in eq 17. Oxidative cleavage of the



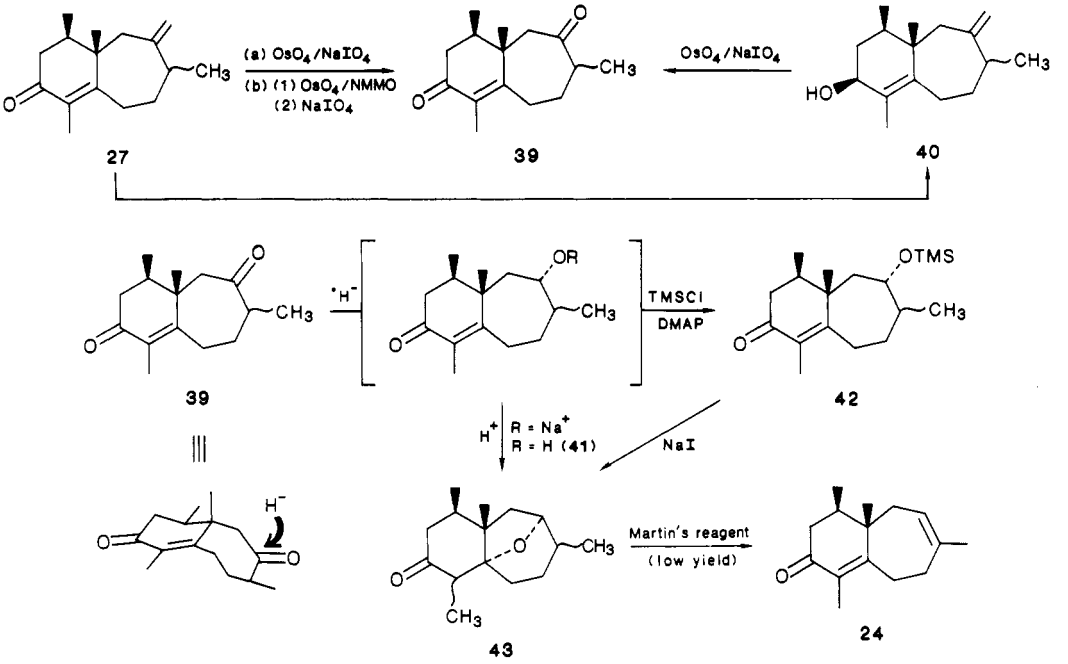
27 39 24

(39) Conducting this reaction at −78 °C resulted in a 3:1 mixture of C(8) epimers. Our rationalization for this diastereoselectivity is discussed in a future article: Majetich, G.; Hull, K.; Lowery, D., manuscript in preparation.

(40) (a) House, H. O. *J. Am. Chem. Soc.* **1955**, *77*, 5083. (b) Naqvi, S. M.; Horwitz, J. P.; Filler, R. *Ibid.* **1957**, *79*, 6283. (c) Kuran, W.; Synkiewicz, P. A.; Serzyko, J. *J. Organomet. Chem.* **1974**, *73*, 187. (d) Blackett, B. N.; Coxon, J. M.; Hartshorn, M. P.; Richards, K. E. *Tetrahedron* **1969**, *25*, 4999 and references cited therein.

(41) Corey, E. J.; Schmidt, G. *Tetrahedron Lett.* **1979**, 399.

(42) (a) Kochi, J. *J. Am. Chem. Soc.* **1965**, *87*, 3609. (b) Kochi, J. K.; Bacha, J. D.; Bethea, T. W., III. *Ibid.* **1967**, *89*, 6538.



exocyclic double bond bicyclic dienone **27** would produce diketone **39**. We believed that selective reduction of the cycloheptane carbonyl would generate an alcohol which would yield perforenone upon dehydration.

In the course of these investigations, four ways were examined to oxidatively cleave the exocyclic double bond. Ozonolysis of **39** gave a complex mixture of products. The next procedure studied was developed by Lemieux and Johnson[43] (eq 7). This catalytic procedure has received extensive application in synthesis for cleaving simple olefins and enones.[44] Oxidation of dienone **27** using this procedure should occur exclusively at the exocyclic double bond to generate enedione **39**. We reasoned that osmium tetraoxide, which is quite susceptible to steric effects, would form a π-complex with the more accessible and electron-rich exocyclic double bond, while steric hindrance would retard oxidation of the enone moiety. In our hands, treatment of **27** with a catalytic amount of osmium tetraoxide and 2 equiv of sodium metaperiodate in aqueous dioxane gave low yields of diketone **39**, presumably due to overoxidation although no trione was isolated.

We then converted the cyclohexenone moiety into an allylic alcohol prior to oxidative cleavage of the C(7) double bond. To our surprise, reaction of dienol **40** with the Lemieux/Johnson procedure produced enedione **39**. Osmium tetraoxide is known to affect allylic oxidations of hindered double bonds.[45] Hindsight suggests that steric factors retard the cycloaddition of OsO_4 to the tetrasubstituted cyclohexene double bond; thus hydride abstraction of the allylic alcohol methine by the OsO_4 predominates. The low yields of diketone **39** obtained by using the Lemieux/Johnson method are presumably the result of its decomposition under the reaction conditions rather than overoxidation.

The final method examined for the cleavage of the exocyclic double bond of **27** was developed by the Upjohn Company.[46] Dienone **27** was treated with a catalytic amount of osmium tetraoxide and a stoichiometric amount of the oxidant *N*-methylmorpholine *N*-oxide in aqueous acetone to generate only the vicinal diol. This diol was isolated and immediately treated with 1 equiv of $NaIO_4$ in aqueous dioxane to provide enedione **39** in 83% yield.

With diketone **39** in hand, we expected that the subsequent transformation to perforenone would proceed directly. We anticipated that the cycloheptane carbonyl would be selectively reduced with sodium borohydride.[47] Furthermore, MM2 calculations on **39** showed that the conformation shown in eq 9 represents the minimum energy conformation.[48] This prediction suggests that hydride addition would occur exclusively from the β-face of the molecule, giving an α-alcohol.

Although this conjecture proved correct, **41** underwent an intramolecular Michael addition to produce the tetrahydrofuran derivative **43** in 89% yield.

We speculated that the Michael addition occurred after workup; trapping alcohol **41** as a silyl ether would therefore preclude the formation of tetrahydrofuran **43**. This strategy was attractive since silyl ethers can be directly converted to the corresponding alkyl iodides,[49] which in our case could provide perforenone via dehydrohalogenation. With this strategy in mind, dienone **39** was reduced with $NaBH_4$ in ethanol at −25 °C, and the reaction mixture was treated in situ with 4-(dimethylamino)pyridine and excess chlorotrimethylsilane. Purification of the reaction mixture, however, furnished silyl ether **42** and tetrahydrofuran **43** in only 25% and 27% yields, respectively. Furthermore, iodide displacement of silyl ether **42** led only to isolation of **43**; presumably, cleavage of the labile trimethylsilyl ether predominated over displacement due to steric considerations.

Because we could not avoid the formation of tetrahydrofuran **43**, we attempted to convert it directly into

(43) Pappo, R.; Allen, D. S.; Lemieux, R. U.; Johnson, W. S. *J. Org. Chem.* **1956**, *218* 178.

(44) For examples of osmium tetraoxide cleavage of conjugated double bonds, see: Danishefsky, S.; Schuda, P. F.; Kitahara, T.; Etheredge, S. J. *J. Am. Chem. Soc.* **1977**, *99*, 6066 and references cited therein.

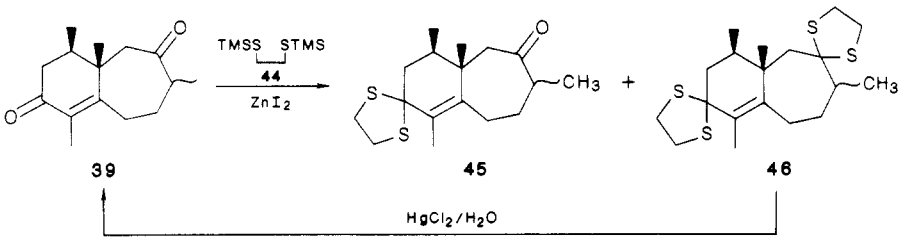
(45) Catalytic osmylations are known to fail with highly substituted double bonds, see: Akashi, K.; Palermo; R. E.; Sharpless, K. B. *J. Org. Chem.* **1978**, *43*, 2063. For an example of allylic oxidation during an OsO_4 hydroxylation, see: Corbett, R. E.; Lauren, D. R.; Weaver, R. T. *J. Chem. Soc., Perkin Trans. 1* **1979**, 1774.

(46) VanRheenen, V.; Kelly, R. C.; Cham, D. Y. *Tetrahedron Lett.* **1976**, 1973.

(47) Cocher, J. D.; Halsall, T. G. *J. Chem. Soc.* **1957**, 3441.

(48) Appreciation is extended to Dr. Philip Bowen for conducting the MM2 studies.

(49) Olah, G. A.; Narang, S. C.; Balaram, Gupta, B. G.; Malhotra, R. *J. Org. Chem.* **1979**, *44*, 1247.



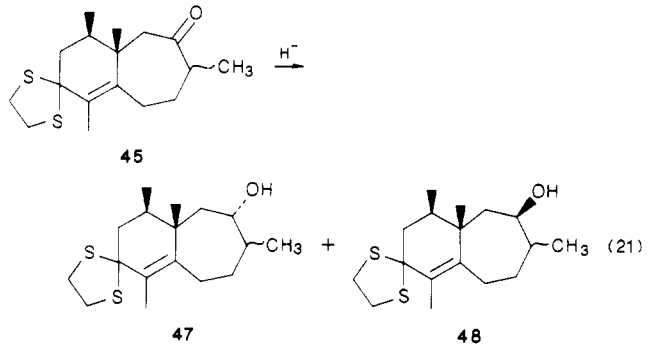
39 45 46 (20)

perforenone (see eq 19). However, treatment of **43** with Martin's sulfurane dehydrating reagent[50] at room temperature produced a trace amount of perforenone based on TLC comparison with authentic material; the remainder of the reaction mixture was unreacted **43**. Warming the reaction mixture led to a complex mixture of products from which perforenone was isolated in only 5% yield.

At this point, it was evident that in order to manipulate the cycloheptane carbonyl it would be necessary to selectively protect the cyclohexenone carbonyl of enedione **39**. This transformation was accomplished in 53% yield with Evans' reagent,[51] (1,2-ethylenedithio)bis(trimethylsilane) (**44**) and zinc iodide (see eq 20); bis(dithioketal) **46** was also isolated (15% yield), as well as unreacted **39** (30% yield). Deprotection of **46** using standard conditions afforded dienone **39**, which was recyclable.

Reduction of the C(7) carbonyl using $NaBH_4$ gave only 36% of two isomeric alcohols, consisting of a 2:1 mixture of the C(8) diastereomers, in a 5:1 ratio. We assumed that the major isomer was the result of β-attack (cf. **47**) on the basis of the reduction of enedione **39** using $NaBH_4$.

A variety of reducing agents and reaction conditions, listed in eq 21, were then examined to optimize this reduction. Although the reduction of **45** with $LiAlH_4$ or



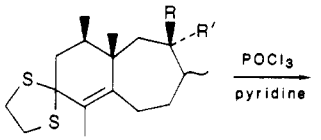
45 47 48 (21)

	ratio of 47:48	isolated yield
$NaBH_4$	5:1	36%
LAH	5:1	72%
$LiAl(O+)_3H$	5:1	94%
DIBAL-H	only **47**	64%

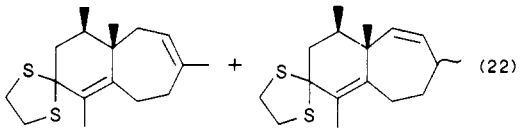
lithium tri-*tert*-butoxyaluminohydride resulted in excellent yields of alcohols **47** and **48**, the stereoselectivity was the same as that observed with $NaBH_4$. In contrast, treatment of **45** with DIBAL-H at −78 °C furnished only alcohol **47** in 64% yield.

At this point, all that remained for conversion of **47** and **48** to perforenone was the dehydration of the alcohol to generate the *tri*substituted double bond, followed by deprotection of the thioketal.

Dehydration of **47** was achieved in 95% yield by using an excess of freshly distilled phosphorus oxychloride in refluxing pyridine (eq 22),[23] while dehydration of **48** under the same reaction conditions led to a 1:1 mixture of **49** and isomeric diene **50**.

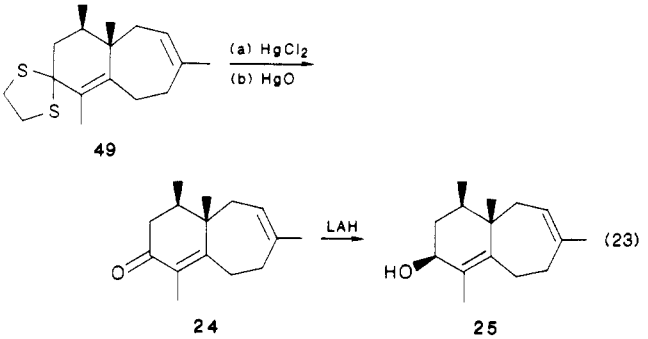


47, R = H, R' = OH
48, R = OH, R' = H



49 95% 40% **50** 0% 29% (22)

Hydrolysis of dithioketal **49** was achieved by the addition of **49** to a stirred suspension of mercuric chloride in aqueous acetonitrile,[52a] then refluxing for 5 h to give crystalline perforenone (mp 76–77 °C) in 47% yield, which matched the spectral and chromatographic properties of natural material (eq 23). The yield in the hydrolysis of **49** was later improved to 90% by using mercuric oxide and boron trifluoride etherate in aqueous THF.[52b]



49 **24** **25** (23)

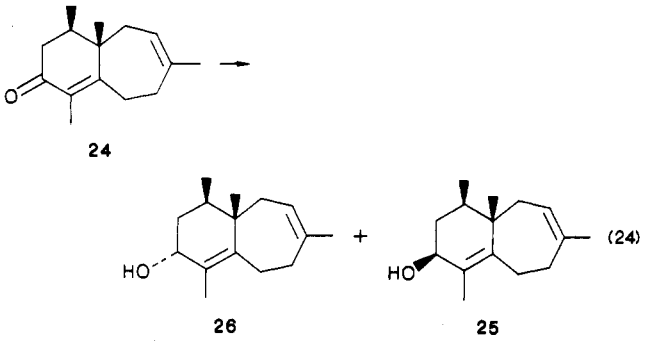
With perforenone in hand, we focused our attention on the preparation of epiguadalupol (**25**) and guadalupol (**26**).

We expected the reduction of perforenone with $LiAlH_4$ to stereospecifically provide epiguadalupol on the basis of Henbest's[53a] and Dauben's[53b] observations that rigid cyclic α,β-unsaturated ketones afford the thermodynamically more stable equatorial alcohol upon reduction. Indeed, treatment of **24** with $LiAlH_4$ in a solution of THF at −15 °C provided only epiguadalupol (**25**) in 95% yield. Our synthetic material had spectal properties identical with those reported by Howard and Fenical for natural **25**.[32c]

We next attempted the stereospecific synthesis of guadalupol (**26**) from perforenone; recall that guadalupol has

(50) Arhart, R. J.; Martin, J. C. *J. Am. Chem. Soc.* **1972**, *94*, 5003.
(51) Evans, D. A.; Truesdale, L. K.; Grimm, K. G.; Nesbitt, S. L. *J. Am. Chem. Soc.* **1977**, *99*, 5009.
(52) For dithioketal hydrolysis using mercuric chloride, see: (a) Corey, E. J.; Erickson, B. W. *J. Org. Chem.* **1971**, *36*, 3553. For achieving this deprotection using mercuric oxide, see: (b) Vedejs, E.; Fuchs, P. L. *Ibid.* **1971**, *36*, 366.
(53) (a) Henbest, H. B.; McEntee, J. *J. Chem. Soc.* **1961**, 4478. (b) Dauben, W. G.; Ashcraft, A. C. *J. Am. Chem. Soc.* **1963**, *85*, 3673.

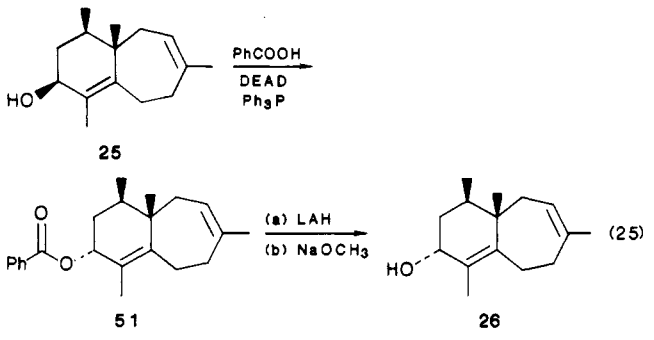
an axial allylic hydroxyl. During the past decade, there has been considerable effort to develop stereoselective reducing agents which produce the less thermodynamically stable axial alcohols. To date, several bulky reducing reagents have proven useful to achieve this transformation.[54] Unfortunately, as shown in eq 24, reduction of perforenone with DIBAL-H, L-Selectride (Aldrich), and lithium tri-*tert*-butoxyaluminohydride all generated mixtures of **25** and **26**. Regrettably, the more thermodynamically stable equatorial allylic alcohol **25** generally predominated. This lack of stereoselectivity is consistent with Dauben's general observation that reduction of bicyclic enones with bulky trialkylborohydrides is nonselective.[55,56]



ratio of 26:25

DIBAL-H	1:4
$LiAl(O+)_3H$	1:10
L-Selectride	1:1

We achieved a selective synthesis of guadalupol by inverting the stereochemistry of the C(3) hydroxyl of epiguadalupol using Mitsunobu methodology.[57] Since this inversion process is very susceptible to steric hindrance,[58] we were not surprised that treatment of **25** with triphenylphosphine, diethyl diazodicarboxylate, and benzoic acid in THF required several hours at room temperature to furnish benzoate **51** (eq 25) in good yield. Reduction of **51** with $LiAlH_4$ produced **26** in 66% yield, with spectra identical with those reported in the literature. Removal of the benzoyl group via reduction, however, proved troublesome in that the benzyl alcohol also produced by the reduction had nearly the same chromatographic properties as guadalupol. This problem was readily avoided by transesterification of **51** using sodium methoxide to furnish guadalupol in 61% yield.



Conclusion

In summary, we have shown how catalysts moderate the regioselectivity of intramolecular allylsilane additions to 3-vinylcycloalkenones. In all but one case, Lewis acid catalysis formed seven-membered rings in good yields, whereas fluoride-induced processes proved highly substrate dependent. These observations have been rationalized in terms of conformational and stereoelectronic effects.

This study establishes a straightforward synthesis of three perforanes and, moreover, represents a fundamentally new strategy for the preparation of bicyclic systems containing seven-membered rings. The synthetic utility of fluoride ion catalyzed processes will be demonstrated elsewhere. Many of the principles disclosed in this work can be applied to natural product synthesis.

Experimental Section

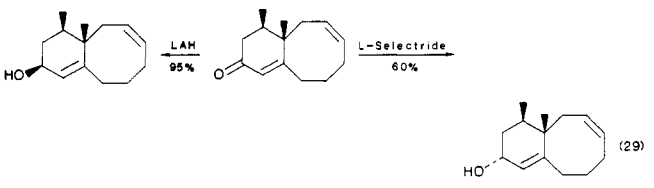
All melting points were determined on a Thomas-Hoover oil immersion capillary melting point apparatus and are uncorrected. Routine ^1H NMR spectra were recorded at 90 MHz on a Varian EM 390 spectrometer. Chemical shifts are reported in ppm on the δ scale relative to tetramethylsilane as 0.00 ppm. The data reported as integer numbers are accurate to within ±10% of the integer. ^1H NMR data are presented as follows: chemical shift (multiplicity, number of protons, coupling constants in hertz). Fourier transform NMR spectra were determined in $CDCl_3$ on a JEOL FX 90Q 90 (^1H)/22.5 MHz (^{13}C) instrument or a JEOL FX 270 MHz instrument with an ^2H internal lock. Infrared (IR) spectra were recorded as thin films between polished sodium chloride plates on a Perkin-Elmer 197 grating infrared spectrometer. All absorption bands are reported in wave numbers (cm^{-1}), which were calibrated against the 1601-cm^{-1} absorption band of polystyrene. Low-resolution mass spectra were recorded on a Finnigan 4023 chromatograph–mass spectrometer by a direct probe and are expressed in m/z units. Microanalysis was performed by Atlantic Microlab, Inc., Atlanta, GA.

Anhydrous tetrahydrofuran (THF) and diethyl ether were prepared by refluxing with and distillation from sodium/benzophenone under a nitrogen atmosphere in a recycling still. Anhydrous dimethylformamide (DMF) and hexamethylphosphoramide (HMPA) were prepared by refluxing over and distillation from calcium hydride under a dry nitrogen atmosphere and stored over 4A molecular sieves. Anhydrous toluene and diisopropylamine were prepared by refluxing 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 completely consumed. Unless otherwise indicated, all ethereal workups consisted of the following procedure: The reaction mixture was quenched at room temperature with saturated aqueous 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 0.1 Torr to constant weight, afforded a crude residue, which was purified by flash chromatography using MN silica gel 60 (230–400 mesh ASTM) and distilled reagent grade solvents.

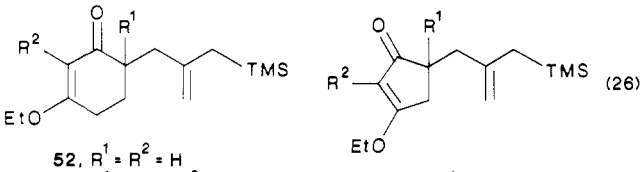
I. Preparation of Substrates. General Procedures. The precursors listed in Table I were prepared using the procedure of Stork and Danheiser[34] by the addition of vinyllithium to the appropriately substituted 3-ethoxy-2-cyclohexen-1-one (or 3-ethoxy-2-cyclopenten-1-one) derivative. Requisite ketones **52–59**

(54) Krishnamurthy, S.; Brown, H. C. *J. Am. Chem. Soc.* **1976**, *98*, 3383 and references cited therein.
(55) Dauben, W. G.; Ashmore, J. W. *Tetrahedron Lett.* **1978**, 4487.
(56) In contrast, we have observed the following unpublished results in preparing a key intermediate in a neolemnane synthesis (eq 29).



(57) For a review, see: (a) Mitsunobu, O. *Synthesis* **1981**, 1. For the experimental procedure we employed, see: (b) Grynkiewicz, G.; Burzynska, H. *Tetrahedron* **1976**, *32*, 2109.
(58) Bose, A. K.; Lae, B.; Hoffman, W. A.; Manhos, M. S. *Tetrahedron Lett.* **1973**, 1619.

were prepared as previously described.[5h] In general, 1.3 equiv of vinyllithium (1 M in THF) was added at 0 °C to 1 equiv of the required 3-ethoxy-2-cycloalkenone; acid hydrolysis was achieved by using a catalytic quantity (4–7 drops) of an aqueous 10% hydrochloric acid solution in reagent grade THF. A typical experimental procedure follows.



52, $R^1 = R^2 = H$
53, $R^1 = CH_3$, $R^2 = H$
54, $R^1 = H$, $R^2 = CH_3$
55, $R^1 = R^2 = CH_3$

56, $R^1 = R^2 = H$
57, $R^1 = CH_3$, $R^2 = H$
58, $R^1 = H$, $R^2 = CH_3$
59, $R^1 = R^2 = CH_3$

4-[2-[(Trimethylsilyl)methyl]allyl]-3-vinyl-2-cyclohexen-1-one (9). A solution of 0.50 g (1.9 mmol) of 3-ethoxy-6-[2-[(trimethylsilyl)methyl]allyl]-2-cyclohexen-1-one (**53**) in 8 mL of dry THF at 0 °C was treated dropwise with 2.44 mL (2.4 mmol) of vinyllithium (1 M in THF) over a 30-min period. The reaction mixture was then allowed to warm to room temperature and stirred at room temperature for 2 h. Standard ethereal workup provided 538 mg of crude residue, which was used directly in the next reaction.

The crude alcohol was dissolved in 20 mL of THF, and 5 drops of 10% hydrochloric acid was added. After being stirred at room temperature for 4 h, the mixture was concentrated to a residue, diluted with 50 mL of ethyl acetate, washed with brine, dried over anhydrous magnesium sulfate, and filtered. Following removal of the solvent, the crude dienone was chromatographed on silica gel (elution with hexanes/ether, 5:1) to provide 393 mg (84%) of dienone **9**, which was homogeneous by TLC analysis (hexanes/ether, 1:1; R_f(**53**) 0.39, R_f(**9**) 0.68): ^{1}H NMR ($CDCl_3$) δ 0.00 (s, 9 H), 1.48 (s, 2 H), 1.6–2.55 (m, 6 H), 2.6–2.9 (m, 1 H), 4.55 (br s, 2 H), 5.2–5.65 (m, 2 H), 5.75 (s, 1 H), 6.25 (dd, 1 H, J = 15, 11 Hz); IR (film) 3080, 3040, 2950, 1670, 1630, 1580, 1450, 1420, 1380, 1350, 1250, 1200, 1160, 995, 935, 925, 850 cm^{-1}; mass spectrum, m/z 248 (M^+). Anal. Calcd for $C_{15}H_{24}OSi$: C, 72.52; H, 9.73. Found: C, 72.87; H, 10.10.

4-Methyl-4-[2-[(trimethylsilyl)methyl]allyl]-3-vinyl-2-cyclohexen-1-one (8). Addition of 2.54 mL of vinyllithium (2.5 mmol) to 0.547 g (1.9 mmol) of 3-ethoxy-6-methyl-6-[2-[(trimethylsilyl)methyl]allyl]-2-cyclohexen-1-one (**52**) using the described experimental procedure afforded 445 mg of **8** (87%), which was homogeneous by TLC analysis (hexanes/ether, 1:1; R_f(**52**) 0.32, R_f(**8**) 0.75): ^{1}H NMR ($CDCl_3$) δ 0.00 (s, 9 H), 1.15 (s, 3 H), 1.50 (s, 2 H), 1.55–2.5 (m, 6 H), 4.55 (br s, 1 H), 4.60 (br s, 1 H), 5.15–5.7 (m, 2 H), 6.0 (s, 1 H), 6.34 (dd, 1 H, J = 15, 10 Hz); IR (film) 3080, 2970, 1670, 1620, 1590, 1460, 1420, 1330, 1250, 1160, 980, 850 cm^{-1}; mass spectrum, m/z 262 (M^+).

2-Methyl-4-[2-[(trimethylsilyl)methyl]allyl]-3-vinyl-2-cyclohexen-1-one (10). Addition of 1.65 mL of vinyllithium (1.6 mmol) to 0.340 g (1.3 mmol) of 3-ethoxy-2-methyl-6-[2-[(trimethylsilyl)methyl]allyl]-2-cyclohexen-1-one (**54**) using the described experimental procedure provided 213 mg (64%) of dienone **10**, which was homogeneous by TLC analysis (hexanes/ether, 1:1; R_f(**54**) 0.71, R_f(**10**) 0.84): ^{1}H NMR ($CDCl_3$) δ 0.00 (s, 9 H), 1.45 (s, 2 H), 1.80 (s, 3 H), 1.75–2.65 (m, 9 H), 2.65–3.0 (m, 1 H), 4.55 (br s, 2 H), 5.3–5.65 (m, 2 H), 6.67 (dd, 1 H, J = 17, 10 Hz); IR (film) 3070, 2950, 1650, 1625, 1570, 1440, 1240, 1190, 990, 850 cm^{-1}.

2,4-Dimethyl-4-[2-[(trimethylsilyl)methyl]allyl]-3-vinyl-2-cyclohexen-1-one (11). Addition of 2.69 mmol of vinyllithium (2.7 mmol) to 0.584 g (2.1 mmol) of 3-methoxy-2,6-dimethyl-6-[2-[(trimethylsilylmethyl]allyl]-2-cyclohexen-1-one (**55**) using the described experimental procedure provided 450 mg (78%) of dienone **11**, which was homogeneous by TLC analysis (hexanes/ether, 2:1; R_f(**55**) 0.58, Rf(11) 0.86): ^{1}H NMR ($CDCl_3$) δ 0.00 (s, 9 H), 1.15 (s, 3 H), 1.48 (s, 2 H), 1.8 (s, 3 H), 1.4–2.65 (m, 12 H), 4.55 (br s, 1 H), 4.60 (br s, 1 H), 4.95–5.55 (m, 2 H), 6.28 (dd, 1 H, J = 18, 12 Hz); IR (film) 3080, 2950, 1670, 1630, 1460, 1420, 1340, 1300, 1250, 940, 850 cm^{-1}; mass spectrum, m/z 276 (M^+).

4-[2-[(Trimethylsilyl)methyl]allyl]-3-vinyl-2-cyclopenten-1-one (12). Addition of 1.48 mL of vinyllithium (1.5 mmol) to 0.271 g (1.1 mmol) of 3-ethoxy-5-[2-[(trimethylsilyl)methyl]allyl]-2-cyclopenten-1-one (**56**) using the described experimental procedure provided 117 mg (44%) of dienone **12**, which was homogeneous by TLC analysis (hexanes/ether, 1:1; R_f(**56**) 0.39, R_f(**12**) 0.71): ^{1}H NMR ($CDCl_3$) δ 0.00 (s, 9 H), 1.45 (s, 2 H), 1.4–2.75 (m, 4 H), 3.0–3.3 (m, 1 H), 4.50 (br s, 2 H), 5.3–5.7 (m, 2 H), 5.90 (br s, 1 H), 6.48 (dd, 1 H, J = 17, 10 Hz); IR (film) 3080, 2960, 2930, 1700, 1630, 1470, 1410, 1250, 1180, 1000, 860 cm^{-1}.

4-Methyl-4-[2-[(trimethylsilyl)methyl]allyl]-3-vinyl-2-cyclopenten-1-one (13). Addition of 1.29 mL of vinyllithium (1.3 mmol) to 0.250 g (0.99 mmol) of 3-ethoxy-5-methyl-5-[2-[(trimethylsilyl)methyl]allyl]-2-cyclopenten-1-one (**57**) using the described experimental procedure provided 160 mg (64%) of dienone **13**, which was homogeneous by TLC analysis (hexanes/ether, 1:1; R_f(**57**) 0.40, R_f(**13**) 0.65): ^{1}H NMR ($CDCl_3$) δ 0.00 (s, 9 H), 1.25 (s, 3 H), 1.38 (s, 2 H), 2.20 (s, 2 H), 2.35 (AB q, 2 H, $\Delta\nu_{AB}$ = 28 Hz, J = 17 Hz), 4.45 (br s, 1 H), 4.55 (br s, 1 H), 5.3–5.9 (m, 2 H), 6.00 (br s, 1 H), 6.37 (dd, 1 H, J = 12, 11 Hz); IR (film) 3080, 2960, 2940, 1700, 1630, 1600, 1420, 1250, 1000, 850 cm^{-1}.

2-Methyl-4-[(trimethylsilyl)methyl]allyl]-3-vinyl-2-cyclopenten-1-one (14). Addition of 1.16 mL (1.1 mmol) of vinyllithium to 230 mg (0.86 mmol) of 3-ethoxy-2-methyl-5-[2-[(trimethylsilyl)methyl]allyl]-2-cyclopenten-1-one (**58**) using the described experimental procedure afforded 155 mg (72%) of dienone **14**, which was homogeneous by TLC analysis (hexanes/ether, 1:1; R_f(**58**) 0.68, R_f(**14**) 0.82): ^{1}H NMR ($CDCl_3$) δ 0.00 (s, 9 H), 1.40 (s, 2 H), 1.68 (s, 3 H), 1.3–2.7 (m, 9 H), 2.8–3.3 (m, 1 H), 4.3–4.5 (m, 2 H), 5.2–5.55 (m, 2 H), 6.52 (dd, 1 H, J = 18, 10 Hz); IR (film) 3080, 2970, 2930, 1705, 1640, 1600, 1420, 1385, 1370, 1250, 1200, 995, 850 cm^{-1}; mass spectrum, m/z 248 (M^+). Anal. Calcd for $C_{15}H_{24}OSi$: C, 72.52; H, 9.73. Found: C, 72.45; H, 9.99.

2,4-Dimethyl-4-[2-[(trimethylsilyl)methyl]allyl]-3-vinyl-2-cyclopenten-1-one (15). Addition of 5.57 mL (5.57 mmol) of vinyllithium (5.5 mmol) to 1.14 g (4.3 mmol) of 3-ethoxy-2,5-dimethyl-5-[2-[(trimethylsilyl)methyl]allyl]-2-cyclopenten-1-one (**59**) using the described experimental procedure afforded 0.746 g (70%) of dienone **15**, which was homogeneous by TLC analysis (hexanes/ether, 2:1; R_f(**59**) 0.50, R_f(**15**) 0.87): ^{1}H NMR (CCl_4) δ 0.00 (s, 9 H), 1.25 (s, 3 H), 1.40 (s, 2 H), 1.70 (s, 3 H), 2.20 (br s, 2 H), 2.25 (AB q, 2 H, $\Delta\nu_{AB}$ = 36 Hz, J = 18 Hz), 4.35 (br s, 1 H), 4.45 (br s, 1 H), 5.3–5.6 (m, 2 H), 6.35 (dd, 1 H, J = 16, 10 Hz); ^{13}C NMR ($CDCl_3$) 208, 170, 143, 136, 129, 123, 111, 48, 47, 46, 27.8, 27.2, 9, –1 ppm; IR (film) 3070, 2950, 2920, 1690, 1620, 1580, 1250, 1150, 1070, 995, 930, 850 cm^{-1}; mass spectrum, m/z 262 (M^+).

4-Methyl-4-[2-[(trimethylsilyl)methyl]allyl]-3-[2-propenyl]-2-cyclohexen-1-one (18). *tert*-Butyllithium (1.26 mL, 2.14 mmol, 1.7 M in pentane) was added dropwise over a 15-min period to a solution of 2-bromopropene (95 μL, 1.07 mmol) in 1 mL of dry ether at –65 °C. The reaction mixture was warmed to 0 °C. A solution of enone **53** (100 mg, 0.36 mmol) dissolved in 1 mL of ether was added dropwise to the cold solution of propenyllithium. The resulting mixture was stirred at –65 °C for 1 h and then gradually warmed to room temperature. The reaction was quenched with saturated ammonium chloride. Standard ethereal workup furnished 97 mg of an oily residue, which was purified on silica gel (elution with hexanes/ether, 10:1) to furnish 51 mg (51%) of trienone **18**, which was homogeneous by TLC analysis (hexanes/ether, 4:1; R_f(**53**) 0.51, R_f(**18**) 0.58): ^{1}H NMR ($CDCl_3$) δ 0.00 (s, 9 H), 1.23 (s, 3 H), 1.55 (br s, 2 H), 1.65–2.3 (m, 7 H), 1.94 (br s, 3 H), 2.23 (br s, 2 H), 2.35–2.5 (m, 2 H), 4.59 (br s, 1 H), 4.71 (br s, 1 H), 4.85 (br s, 1 H), 5.01 (br s, 1 H), 5.78 (s, 1 H): ^{13}C NMR ($CDCl_3$) 199.7 (s), 172.3 (s), 144.0 (s), 142.9 (s), 126.0 (d), 115.5 (t), 112.0 (t), 44.6 (t), 38.6 (s), 34.6 (t), 34.0 (t), 29.2 (t), 25.0 (q), 24.5 (q), –1.5 (q) ppm; IR (film) 2950–2800, 1660, 1615, 1445, 1405, 1360, 1320, 1240, 860 cm^{-1}; mass spectrum, m/z 276 (M^+).

4-Methyl-4-[2-[(trimethylsilyl)methyl]allyl]-3-cyclohexenyl-2-cyclohexen-1-one (19). A stirred solution of 345 mg (2.14 mmol) of cyclohexenyl bromide[59] in 2 mL of ether was cooled to –65 °C and combined within 30 min with 4.2 mmol of *tert*-

(59) Stevens, C. L.; Valicenti, J. A. *J. Am. Chem. Soc.* **1965**, *87*, 838.

butyllithium in pentane (1.7 M). The temperature of the reaction was kept at −65 °C for 1 h and then raised slowly to 0 °C (a 2-h period). Ketone **53** (200 mg, 0.71 mmol) in 1 mL of ether was added and the stirring continued for 30 min at −65 °C and 1 h at 0 °C. The reaction mixture was quenched with saturated ammonium chloride. Standard ethereal workup provided 210 mg of crude residue, which was purified on silica gel (hexenes/ether, 6:1) to provide 148 mg (66%) of **19**, which was homogeneous by TLC analysis (hexanes/ether, 3:1; R_f(**53**) 0.36; R_f(**19**) 0.54): ($CDCl_3$) 0.00 (s, 9 H), 0.91 (s, 3 H), 1.0–2.8 (m, 16 H), 4.58 (br s, 1 H), 4.68 (br s, 1 H), 5.72 (s, 1 H), 5.8 (br s, 1 H); ^{13}C NMR ($CDCl_3$) 200.1 (s), 173.6 (s), 143.2 (s), 137.8 (s), 126.6 (d), 125.9 (d), 111.4 (t), 45.7, 45.0, 42.1, 38.9, 34.9, 34.1, 30.3, 29.2, 29.1, 25.2, 22.6, 21.6, −1.4 (q) ppm; IR (film) 3070, 3020, 2950–2800, 1665, 1595, 1460, 1444, 1420, 1335, 1250, 1230, 1155, 850 cm^{-1}; mass spectrum, m/z 316 (M^+).

4-Methyl-4-[2-[(trimethylsilyl)methyl]allyl]-3-[1-(2-methylpropenyl)]-2-cyclohexen-1-one (20). *tert*-Butyllithium (1.26 mL, 2.14 mmol, 1.7 M in pentane) was added dropwise over a 15-min period to a solution of 1-bromo-2-methylpropene (110 μL, 1.07 mmol) in 1 mL of dry ether at −65 °C. The reaction mixture was warmed to 0 °C over a 1-h period and then cooled to −65 °C. A solution of enone **53** (100 mg, 0.36 mmol) dissolved in 1 mL of ether was added dropwise to the cold alkenyllithium solution. The resulting mixture was stirred at −65 °C for 1 h and then gradually warmed to room temperature. The reaction was quenched with saturated ammonium chloride. Standard ethereal workup furnished 80 mg of an oily residue, which was purified on silica gel (elution with hexanes/ether, 6:1) to furnish 59 mg (57%) of trienone **20**, which was homogeneous by TLC analysis (hexanes/ether, 4:1; R_f(**53**) 0.57, R_f(**20**) 0.70): ^1H NMR ($CDCl_3$) 0.00 (s, 9 H), 1.12 (s, 3 H), 1.50 (s, 2 H), 1.65–2.3 (m, 10 H), 1.7 (s, 3 H), 1.85 (s, 3 H), 2.35–2.5 (m, 2 H), 4.58 (br s, 1 H), 4.66 (br s, 1 H), 5.75 (s, 1 H), 5.86 (br s, 1 H); ^{13}C NMR ($CDCl_3$) 199.4 (s), 166.2 (s), 143.1 (s), 140.7 (s), 126.7 (d), 122.6 (d), 111.3 (t), 45.8 (t), 38.7 (s), 34.0 (t), 33.3 (t), 28.7 (t), 27.0 (q), 26.0 (q), 20.0 (q), −1.5 (q) ppm; IR (film) 3000–2850, 1680, 1635, 1600, 1450, 1420, 1380, 1330, 1250, 860 cm^{-1}; mass spectrum, m/z 290 (M^+).

4-Methyl-3-(5-methyl-2-furyl)-4-[2-[(trimethylsilyl)-methyl]allyl]-2-cyclohexen-1-one (21). *tert*-Butyllithium (1.03 mL, 1.4 mmol, 1.35 *M* in pentane) was added dropwise over a 15-min period to a solution of 0.17 mL of 2-methylfuran (140 mg, 1.71 mmol) in 1 mL of dry THF at −78 °C. The reaction mixture was warmed to −58 °C over a 2-h period, stirred at −58 °C for 45 min, and then cooled to −65 °C. A solution of enone **53** (300 mg, 1.07 mmol) dissolved in 3 mL of THF was added dropwise to the cold alkenyllithium solution. The resulting mixture was stirred at −65 °C for 8 h. The reaction was quenched with saturated ammonium chloride. Standard ethereal workup furnished 250 mg of an oily residue, which was purified on silica gel (elution with hexanes/ether, 20:1) to furnish 127 mg (38%) of **21**, which was homogeneous by TLC analysis (hexanes/ether, 4:1; R_f(**53**) 0.27, R_f(**21**) 0.33): ^1H NMR ($CDCl_3$) δ 0.00 (s, 9 H), 1.38 (s, 3 H), 1.48 (br s, 2 H), 1.2–2.0 (m, 7 H), 2.2–2.7 (m, 4 H), 4.5–4.7 (m, 2 H), 6.0 (d, 1 H, J = 3 Hz), 6.25 (s, 1 H), 6.60 (d, 1 H, J = 3 Hz); IR (film) 3070, 2960, 1665, 1630, 1615, 1565, 1515, 1460, 1420, 1365, 1335, 1250, 1200, 1160, 1030, 850 cm^{-1}; mass spectrum, m/z 316 (M^+).

4-Methyl-4-[2-methylallyl]-3-vinyl-2-cyclohexen-1-one (22). To a solution of lithium diisopropylamide, prepared from 0.87 mL (6.2 mmol) of diisopropylamine in 2 mL of freshly distilled THF and 2.4 mL of *n*-butyllithium (6.0 mmol, 2.5 M in hexane) at −78 °C, was added a solution of 0.8 g of 3-ethoxy-6-methyl-2-cyclohexen-1-one (5.2 mmol) in 2 mL of THF containing 900 mg (5.2 mmol) of HMPA over a 30-min period (via syringe pump). After an additional 2 h at −78 °C, 1.1 g (6.2 mmol) of methallyl iodide was added. The reaction was stirred at −78 °C for 1 h and then allowed to gradually warm to room temperature over 3 h. Standard etheral workup afforded an oily residue (1.6 g), which was purified on silica gel (hexanes/ether, 3:1) to provide 1.02 g (95%) of 3-ethoxy-6-methyl-6-(2-methylallyl)-2-cyclohexen-1-one which was homogeneous by TLC analysis (hexanes/ether, 1:1; R_f(sm) 0.30, R_f(adduct) 0.60): ^1H NMR ($CDCl_3$) δ 1.3 (s, 3 H), 1.47 (t, 3 H, J = 6 Hz), 1.75 (br s, 3 H), 1.65–2.4 (m, 7 H), 2.5–2.8 (m, 2 H), 4.00 (q, 2 H, J = 6 Hz), 4.75 (br s, 1 H), 4.95 (br s, 1 H), 5.35 (s, 1 H).

Addition of 2 mL of vinyllithium (4.58 mmol, 1 M in THF) to 353 mg (1.7 mmol) of the above enone using the described general procedure afforded 214 mg of trienone **22** (66%), which was homogeneous by TLC analysis (hexenes/ether, 1:1; R_f(ketone) 0.40, R_f(**22**) 0.69): ^1H NMR ($CDCl_3$) δ 1.13 (s, 3 H), 1.67 (s, 3 H), 1.55–1.75 (m, 5 H), 1.9–2.5 (m, 4 H), 4.66 (br s, 1 H), 4.82 (br s, 1 H), 5.30 (d, 1 H, J = 11 Hz), 5.63 (d, 1 H, J = 16 Hz), 6.03 (s, 1 H), 6.43 (dd, 1 H, J = 16, 11 Hz); ^{13}C NMR ($CDCl_3$) 199.1 (s), 165.6 (s), 141.5 (s), 134.2 (d), 123.1 (d), 119.8 (t), 115.1 (t), 46.0 (t), 37.6 (s), 33.9 (t), 33.6 (t), 25.7 (q), 24.4 (q) ppm; IR (film) 3080, 3050–2850, 1670, 1595, 1460, 1420, 1385, 1340, 990, 900 cm^{-1}; mass spectrum, m/z 190 (M^+).

II. Intermolecular Reactions of 3-Vinyl-2-cyclohexen-1-one. 3-*n*-Propyl-2-cyclohexen-1-one (2) and 3-Propylidenecyclohexan-1-one (3). These adducts were prepared via the following procedures.

(a) Lithium Dimethylcopper. To a stirred slurry of cuprous iodide (0.78 g, 4.1 mmol) in 10 mL of anhydrous ether at 0 °C was added by syringe 5.9 mL of 1.4 M (8.2 mmol) ethereal methyllithium. The resulting solution of lithium dimethylcopper was stirred at 0 °C for 5 min, and then a solution of 250 mg of 3-vinyl-2-cyclohexen-1-one (**1**)[60] in 10 mL of anhydrous ether was added dropwise over a 20-min period. Stirring was continued for an additional 2 h at 0 °C, and then the reaction mixture was quenched with saturated aqueous ammonium chloride. Standard etheral workup provided 251 mg of an oily residue [95%] whose NMR data indicated that it consisted of *E* and *Z* isomers of **3** [(CCl_4) δ 0.98 (t, 3 H, J = 6 Hz), 1.5–2.5 (m, 10 H), 2.9 (br s, 1 H), 3.0 (br s, 1 H), 5.1 (t, 0.5 H, J = 6 Hz), 5.2 (t, 0.5 H, J = 6 Hz)]. Purification by chromatography on silica gel (elution with hexanes/ether, 3:1) to afford 115 mg (39%) of **3**, which was homogenous by TLC analysis [hexanes/ether, 1:1; R_f(**1**) 0.45, R_f(**3**) 0.64]: ^1H NMR ($CDCl_3$) δ 1.00 (t, 3 H, J = 6 Hz), 1.55–2.7 (m, 8 H), 2.9–3.1 (br s, 2 H), 5.17 (t, 1 H, J = 6 Hz).

Continued elution gave 90 mg (32%) pure **2** [R_f(**2**) 0.25]: ^1H NMR ($CDCl_3$) δ 0.95 (t, 3 H, J = 6 Hz), 1.1–2.5 (m, 10 H), 5.85 (br s, 1 H); ^{13}C NMR ($CDCl_3$) 199.8 (s), 166.4 (s), 125.4 (d), 39.8 (t), 37.7 (t), 29.4 (t), 22.5 (t), 19.9 (t), 13.5 (q) ppm.

(b) The Copper-Catalyzed Grignard Addition. To 100 mg (0.52 mmol) of cuprous iodide in 5 mL of ether at 0 °C was added dropwise 0.7 mL of methylmagnesium bromide (2.26 mmol, 3.2 M solution in diethyl ether, Aldrich). After completion of Grignard addition, a solution of 250 mg of **1** (2.0 mmol) dissolved in 5 mL of ether was added dropwise. The reaction mixture was stirred at 0 °C for 1 h and quenched with saturated ammonium chloride. Standard ethereal workup provided 93 mg (34%) of **3** and 122 mg of **2** (43%), which were identical with those previously prepared.

$TiCl_4$-Catalyzed Reactions of 3-Vinyl-2-cyclohexen-1-one (1) and Allyltrimethylsilane (4). To 600 mg of **1** (4.92 mmol) dissolved in 2 mL of dry CH_2Cl_2 under nitrogen at −78 °C was added 940 μL of $TiCl_4$ (4.92 mmol) dropwise over a 5-min period. The resulting solution was allowed to stir at −78 °C for 5 min whereupon 940 μL (5.7 mmol) of freshly distilled **4** was added dropwise. After 1 min the reaction mixture became heterogeneous and TLC analysis indicated that all **1** had been consumed. The resulting blackish solution was quenched at −78 °C with 2 mL of water and allowed to gradually warm to room temperature over a 3-h period. The resulting mixture was extracted with three portions of methylene chloride (30 mL/portion). The combined organic extracts were washed with saturated sodium bicarbonate, brine, dried over anhydrous magnesium sulfate, filtered, and concentrated. The resulting crude residue (810 mg) was purified via chromatography on silica gel (elution with hexanes/ether, 4:1) to afford 58 mg (5%) of 3-[2-[(trimethylsilyl)methyl]cyclobutyl]-2-cyclohexen-1-one (**5**), which was homogeneous by TLC analysis (hexanes/ether, 1:1; R_f(**1**) 0.50; R_f(**5**) 0.64): ^1H NMR ($CDCl_3$) δ −0.05 (s, 9 H), 1.0–2.1 (m, 9 H), 2.2–2.45 (m, 4 H), 2.5–2.65 (m, 1 H), 5.8 (br s, 1 H); ^{13}C NMR ($CDCl_3$) 200.1 (s), 170.0 (s), 169.5 (s), 123.8 (d), 123.6 (d), 49.4 (d), 47.9 (d), 37.4 (t), 33.9 (t), 32.9, 32.0, 31.2, 28.5, 28.4, 26.6, 26.1, 25.1 (d), 22.9 (t), −3 (q) ppm; mass spectrum, m/z 236 (M^+). This data represents a 1:2 ratio of diastereomers based on quantitative ^{13}C experiments.

(60) Crisan, C.; Normant, H. *Bull. Soc. Chim. Fr.* **1957** 1451.

Continued elution (hexanes/ether, 4:1) provided 56 mg (7%) of enone 7, which was homogeneous by TLC analysis (hexanes/ether, 1:1; R_f(1) 0.50; R_f(7) 0.32): ^{1}H NMR ($CDCl_3$) δ 1.1–2.5 (m, 14 H), 5.5 (d, 1 H, J = 8 Hz), 5.72 (d, 1 H, J = 15 Hz), 6.05 (s, 1 H), 6.55 (dd, 1 H, J = 15, 8 Hz).

Further elution (hexanes/ether, 2:1) provided 270 mg [40%, R_f 0.19; hexenes/ether, 1:1] of a compound which was presumed to have the structure of enone **6** based on the following NMR data: ^{1}H NMR ($CDCl_3$) δ 2.0–2.1 (m, 2 H), 2.3–2.45 (m, 5 H), 2.69 (t, 2 H, J = 6 Hz), 3.68 (t, 2 H, J = 6 Hz), 5.93 (br s, 1 H); ^{13}C NMR ($CDCl_3$) 199.1 (s), 160.9 (s), 127.4 (d), 41.0 (t), 40.3 (t), 37.2 (t), 29.3 (t), 22.5 (t) ppm. Moreover, this compound decomposed over time to regenerate dienone **1**.

In 1983 House and co-workers showed that the product distribution of the $TiCl_4$ prompted addition of allyltrimethylsilane to enones was greatly influenced by the temperature at which hydrolysis was carried as well as time. In light of their results, we repeated the reaction described above except in this case the reaction mixture was warmed to room temperature before aqueous quench. Using these conditions silane **5** was obtained in 20% yield and an unidentified nonpolar component; enones **6** and **7** were not detected. In a subsequent experiment, the prehydrolysis reaction mixture, prepared as described above, was added to refluxing methylene chloride and the resulting mixture refluxed for a 30-min period. Addition of water and standard ethereal workup led to the isolation of enone **5** in ca. 15% yield with a higher proportion of nonpolar byproduct. Additional hydrolytic conditions were not examined.

III. Fluoride Ion Induced Cyclizations. General Procedure for Fluoride-Induced Cyclizations. All cyclizations were carried out on 50–200 mg of substrate. All reactions were run under an inert atmosphere with a substrate concentration of ca. 0.3 M. Activated 4A molecular sieves were stored in an oven at 130 °C. Stock solutions of anhydrous TBAF/DMF typically contained 10–30 mg of TBAF per 3 mL.[5g] In all cases, 3 equiv of HMPA was used for each equivalent of substrate.

After addition of the substrate via syringe pump was complete, the resulting mixture was stirred at room temperature for 3–12 h to ensure complete reaction and then diluted with water (20 mL). This mixture was extracted with ether (3 × 40 mL), and the combined ether extracts were washed with brine (20 mL) and dried over anhydrous magnesium sulfate. Filtration and evaporation of the solvent afforded an oily residue, which was directly purified via flash chromatography. The following experimental procedure is typical.

Cyclization of 9. A reaction vessel containing 4A molecular sieves was flame-dried under vacuum (5 min) and placed under nitrogen. A solution of 40 mg of anhydrous TBAF in 3 mL DMF was added to the flask and stirred 20 min, followed by 0.433 g (2.4 mmol) of HMPA. A solution of 200 mg (0.80 mmol) of dienone **9** in 2 mL of DMF was added dropwise via syringe pump at room temperature over a 2-h period, and the resulting mixture was then stirred an additional 13 h. The solution was diluted with 10 mL of water and extracted with three 25-mL portions of ether. The combined ethereal extracts were washed with 15 mL of brine and dried over anhydrous magnesium sulfate. Filtration followed by evaporation of the solvent afforded 87 mg of a crude residue. Purification on silica gel (elution with hexanes/ether, 12:1) gave 16 mg (11%) of the 1,4-adduct [3aR*,7aS*]-tetrahydro-2-methylene-3a-vinyl-5(4H)-indanone (**9b**), which was homogeneous by TLC analysis (hexanes/ether, 1:1; R_f(**9**) 0.65, R_f(**9b**) 0.73): ^{1}H NMR ($CDCl_3$) δ 1.4–2.8 (m, 11 H), 4.75–5.1 (m, 4 H), 5.72 (dd, 1 H, J = 15, 7 Hz); IR (film) 3090, 2970, 2940, 2980, 1720, 1620, 1455, 1380, 1300, 1235, 1000, 930, 890 cm^{-1}; mass spectrum, m/z 176 (M$^+$). Anal. Calcd for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 81.64; H, 9.15.

The 1,6-adduct 3,4,4a,5,6,7,8,9-octahydro-6-methylene-2H-benzocyclohepten-2-one (**9a**) (28 mg, 20%) was also isolated (R_f 0.38): ^{1}H NMR ($CDCl_3$) δ 1.4–2.8 (m, 13 H), 4.75 (br s, 1 H), 4.85 (br s, 1 H), 5.88 (br s, 1 H); IR (film) 3070, 2940, 2870, 1670, 1610, 1450, 1380, 1325, 1260, 1200, 900, 840 cm^{-1}; mass spectrum, m/z 176 (M$^+$). Anal. Calcd for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 81.47; H, 9.00.

Spectral Properties of the Products. For brevity, only the quantity of substrate used and the amount(s) of product(s) isolated are provided for each cyclization. Chromatographic, spectral, and analytical properties of the cyclization products are then listed.

Cyclization of 8. The cyclization of 200 mg (0.76 mmol) of **8** produced 65 mg (45%) of the 1,4-adduct [2aR*,7aS*]-tetrahydro-7a-methyl-2-methylene-3a-vinyl-5(4H)-indanone (**8b**), which was homogeneous on TLC analysis (hexanes/ether, 1:1; R_f(**2**) 0.71, R_f(**8b**) 0.80): ^{1}H NMR ($CDCl_3$) δ 1.10 (s, 3 H), 1.6–2.85 (m, 10 H), 4.8–5.2 (m, 4 H), 5.85 (dd, 1 H, J = 16, 12 Hz); IR (film) 3080, 2920, 1720, 1630, 1450, 1380, 1245, 1195, 1140, 1010, 920, 880 cm^{-1}. Anal. Calcd for $C_{13}H_{18}O$: C, 82.05; H, 9.53. Found: C, 81.97; H, 9.57.

The 1,2-adduct [1R*,4R*]-5-methyl-3-methylene-6-vinyl-bicyclo[3.2.2]non-6-en-1-ol (**8c**) (7 mg, 5%) was also isolated (R_f 0.48): ^{1}H NMR ($CDCl_3$) δ 1.15 (s, 3 H), 1.0–2.6 (m, 12 H), 4.75 (br s, 2 H), 4.8–5.45 (m, 2 H), 6.10 (br s, 1 H), 6.30 (dd, 1 H, J = 17, 10 Hz); IR (film) 3600–3150, 3080, 2960, 2940, 1640, 1460, 1380, 1340, 1070, 900 cm^{-1}; mass spectrum, m/z 190 (M$^+$).

Cyclization of 10. The cyclization of 49 mg (0.18 mmol) of **10** produced 26 mg (72%) of the 1,6-adduct 3,4,4a,5,6,7,8,9-octahydro-1-methyl-6-methylene-2H-benzocyclohepten-2-one (**10a**), which was homogeneous by TLC analysis (hexanes/ether, 2:1; R_f(**3**) 0.71, R_f(**10a**) 0.42): ^{1}H NMR ($CDCl_3$) δ 1.35–2.80 (m, 16 H), 1.70 (s, 3 H), 4.55 (br s, 1 H), 4.68 (br s, 1 H); IR (film) 3090, 2940, 2870, 1670, 1620, 1450, 1380, 1360, 1340, 1300, 1100, 900 cm^{-1}; mass spectrum, m/z 190 (M$^+$). Anal. Calcd for $C_{13}H_{18}O$: C, 82.05; H, 9.53. Found: C, 81.91; H, 9.57.

Cyclization of 11. The cyclization of 115 mg (0.42 mmol) of **11** produced 60 mg (71%) of the 1,4-adduct [3aR*,7aS*]-tetrahydro-4,7a-dimethyl-2-methylene-3a-vinyl-5(4H)-indanone (**11b**), which was homogeneous by TLC analysis (hexanes/ether, 2:1; R_f(**11**) 0.72, R_f(**11b**) 0.61): ^{1}H NMR ($CDCl_3$) δ 0.80–1.0 (m, 3 H), 1.20 (s, 3 H), 1.65–2.8 (m, 9 H), 4.75–5.9 (m, 5 H); IR (film) 3080, 2970, 2950, 2880, 1715, 1660, 1460, 1380, 1340, 1255, 1180, 1100, 1020, 920, 880 cm^{-1}; mass spectrum, m/z 204 (M$^+$).

The 1,2-adduct [1R*,4R*]-5,7-dimethyl-3-methylene-6-vinylbicyclo[3.2.2]non-6-en-1-ol (**11c**) (22 mg, 26%) was also isolated (R_f 0.31): ^{1}H NMR ($CDCl_3$) δ 1.00 (s, 3 H), 1.2–2.6 (m, 12 H), 1.9 (s, 3 H), 4.7 (br s, 2 H), 4.75–5.3 (m, 2 H), 6.10 (dd, 1 H, J = 15, 10, 2 Hz); IR (film) 3750–3100, 3080, 2950, 1640, 1450, 1380, 1340, 1200, 1060, 1020, 970, 920, 900 cm^{-1}; mass spectrum, m/z 204 (M$^+$).

Cyclization of 12. The cyclization of 100 mg (0.43 mmol) of **12** produced 8 mg (2%) of the 1,4-adduct [3aR*,6aS*]-hexahydro-5-methylene-6-vinyl-2(1H)-pentalenone (**12b**), which was homogeneous by TLC analysis (hexanes/ether, 1:1; R_f(**12**) 0.64, Rf(**12b**) 0.81): ^{1}H NMR ($CDCl_3$) δ 1.7–2.8 (m, 9 H), 4.8–5.2 (m, 4 H), 5.85 (dd, 1 H, J = 15, 12 Hz).

The 1,6-adduct 4,5,6,7,8,8a-hexahydro-7-methylene-2(1H)azulenone (**12a**) (11 mg, 4%) was also isolated (R_f 0.42): ^{1}H NMR ($CDCl_3$) δ 1.4–3.1 (m, 11 H), 4.8 (br s, 2 H), 5.82 (br s, 1 H); IR (film) 3080, 2960, 2870, 1710, 1620, 1460, 900 cm^{-1}; mass spectrum, m/z 162 (M$^+$). Anal. Calcd for $C_{11}H_{14}O$: C, 81.48; H, 8.64. Found: C, 81.40; H, 8.71.

Cyclization of 13. The cyclization of 98 mg (0.39 mmol) of **13** produced 20 mg (29%) of the 1,4-adduct *cis*-hexahydro-3a-methyl-5-methylene-6-vinyl-2(1H)-pentalenone (**13b**), which was homogeneous by TLC analysis (hexanes/ether, 4:1; R_f(**13**) 0.37, R_f(**13b**) 0.69): ^{1}H NMR ($CDCl_3$) δ 1.00 (s, 3 H), 2.1–2.75 (m, 8 H), 4.75–5.15 (m, 4 H), 5.80 (dd, 1 H, J = 18, 9 Hz); IR (film) 3080, 2950, 2870, 1740, 1620, 1460, 1410, 1260, 1180, 1000, 920, 890 cm^{-1}; mass spectrum, m/z 176 (M$^+$).

The 1,2-adduct [1R*,5R*]-5-methylene-6-vinylbicyclo[3.2.1]-oct-6-en-1-ol (**13c**) (30 mg, 43%) was also isolated (Rf 0.25): ^{1}H NMR ($CDCl_3$) δ 1.00 (s, 3 H), 1.1–2.5 (m, 7 H), 4.5 (br s, 2 H), 4.6–5.25 (m, 2 H), 5.4 (br s, 1 H), 5.85 (dd, 1 H, J = 15, 10 Hz); IR (film) 3800–3050, 3080, 2950, 1620, 1460, 1380, 1330, 1300, 1080, 980, 990 cm^{-1}. Anal. Calcd for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 81.72; H, 8.98.

Cyclization of 14. The cyclization of 115 mg (0.46 mmol) of **14** provided 20 mg (23%) of the 1,6-adduct 4,5,6,7,8,8a-hexahydro-8a-methyl-7-methylene-2(1H)-azulenone (**14a**), which was homogeneous by TLC analysis (hexanes/ether, 2:1; R_f(**14**) 0.63, R_f(**14a**) 0.46): ^{1}H NMR ($CDCl_3$) δ 1.6–3.0 (m, 14 H), 1.75 (s, 3 H), 4.75 (br s, 2 H); IR (film) 3080, 2930, 2970, 1715, 1640, 1450, 1410, 1385, 1320, 1070, 900 cm^{-1}; mass spectrum, m/z 176 (M$^+$). Anal. Calcd for $C_{12}H_{16}O$: C, 81.77; H, 9.14. Found: C, 81.68; H, 9.19.

The 1,2-adduct [1*R**,5*R**]-7-methyl-3-methylene-6-vinylbicyclo[3.2.1]oct-6-en-1-ol (**14c**) (20 mg, 24%) was also isolated (R_f 0.37): ^{1}H NMR ($CDCl_3$) δ 1.1–1.3 (m, 2 H), 1.4–3.0 (m, 8 H), 4.4–5.15 (m, 4 H), 6.35 (dd, 1 H, J = 15, 12 Hz); ^{13}C NMR ($CDCl_3$) 208 (s), 177 (s), 148 (s), 135 (s), 113 (t), 43 (d), 42 (t), 38 (t), 30 (t), 29 (t), 25 (t), 8 (q) ppm; IR (film) 3750–3100, 3070, 2950, 1680, 1640, 1440, 1310, 1200, 1140, 1060, 900 cm^{-1}; mass spectrum, m/z 176 (M^+). Anal. Calcd for $C_{12}H_{16}O$: C, 81.77; H, 9.14. Found: C, 81.57; H, 9.18.

Cyclization of 15. The cyclization of 150 mg (0.60 mmol) of **15** afforded 102 mg (96%) of the 1,2-adduct [1*R**,5*R**]-5,7-dimethyl-3-methylene-6-vinylbicyclo-[3.2.1]oct-6-en-1-ol (**15c**), which was homogeneous by TLC analysis (hexanes/ether, 1.5:1; R_f(**15**) 0.55, R_f(**15c**) 0.25): ^{1}H NMR (CCl_4) δ 0.8–1.0 (m, 2 H), 1.30 (s, 3 H), 1.65 (s, 3 H), 1.4–2.3 (m, 9 H), 2.05 (br s, 2 H), 2.25 (br s, 2 H), 4.55 (br s, 2 H), 4.8–5.2 (m, 2 H), 6.15 (dd, 1 H, J = 15, 10 Hz); IR (film) 3800–3100, 3080, 2940, 2870, 1640, 1450, 1380, 1330, 1300, 1110, 1050, 995, 900 cm^{-1}; mass spectrum, m/z 190 (M^+). Anal. Calcd for $C_{13}H_{18}O$: C, 82.05; H, 9.53. Found: C, 81.94; H, 9.56.

IV. Ethylaluminum Dichloride Catalyzed Cyclizations. General Procedures. These reactions were carried out in toluene at 0 °C using equimolar quantities of substrate and ethylaluminum dichloride; cyclizations were routinely performed on 40–200 mg of substrate. A typical example follows.

Cyclization of 9. To 0.135 g (0.54 mmol) of dienone **9** in 4 mL of dry toluene at 0 °C was added dropwise 0.37 mL of a 1.4 M solution of ethylaluminum dichloride in toluene (Alfa). The reaction mixture was stirred at 0 °C for 2 h. The reaction mixture was diluted with reagent grade ether, washed with brine, dried over anhydrous magnesium sulfate, filtered, and concentrated. The crude residue was chromatographed (elution with hexanes/ether, 6:1) to provide 50 mg (49%) of the 1,6-adduct **9a**, which was identical with that previously characterized.

Spectral Properties of the Products. For brevity, only the quantity of substrate used and the amount(s) of product(s) isolated are provided for each reaction. Chromatographic, spectral, and analytical properties of the cyclization products are then listed.

Cyclization of 8. The cyclization of 250 mg (0.95 mmol) of **8** produced 108 mg (60%) of the 1,6-adduct 3,4,4a,5,6,7,8,9-octahydro-4a-methyl-6-methylene-2*H*-benzocyclohepten-2-one (**8a**), which was homogeneous by TLC analysis (hexanes/ether, 1:2; R_f(**8**) 0.74, R_f(**8a**) 0.51): ^{1}H NMR ($CDCl_3$) δ 1.20 (s, 3 H), 1.4–2.8 (m, 12 H), 4.65 (br s, 1 H), 4.85 (br s, 1 H), 5.72 (br s, 1 H); IR (film) 3080, 2930, 2860, 1670, 1610, 1450, 1380, 1330, 1250, 1220, 1190, 1060, 900 cm^{-1}; mass spectrum, m/z 190 (M^+). Anal. Calcd for $C_{13}H_{18}O$: C, 82.05; H, 9.53. Found: C, 82.14; H, 9.58.

Cyclization of 10. The cyclization of 41 mg (0.15 mmol) of **10** afforded 21 mg (70%) of the 1,6-adduct **10a**, which was identical with that previously characterized.

Cyclization of 11. The cyclization of 100 mg (0.36 mmol) of **11** gave 68 mg (90%) of the 1,6-adduct 3,4,4a,5,6,7,8,9-octahydro-1,4a-dimethyl-6-methylene-2*H*-benzocyclohepten-2-one (**11a**), which was homogeneous by TLC analysis (hexanes/ether, 2:1; R_f(**11**) 0.69, R_f(**11a**) 0.48): ^{1}H NMR (CCl_4) δ 1.25 (s, 3 H), 1.72 (s, 3 H), 1.4–2.8 (m, 15 H), 4.65 (br s, 1 H), 4.85 (br s, 1 H); IR (film) 3070, 2950, 1660, 1610, 1460, 1380, 1010, 900 cm^{-1}.

Cyclization of 12. The cyclization of 60 mg (0.26 mmol) of **12** produced 19 mg (46%) of the 1,6-adduct **12a**, which was identical with that previously characterized.

Cyclization of 13. The cyclization of 145 mg (0.62 mmol) of **13** afforded 72 mg (70%) of the 1,6-adduct 4,5,6,7,8,8a-hexahydro-8a-methyl-7-methylene-2(1*H*)-azulenone (**13a**), which was homogeneous by TLC analysis (hexanes/ether, 1:1; R_f(**13**) 0.76, R_f(**13a**) 0.56): ^{1}H NMR ($CDCl_3$) δ 1.20 (s, 3 H), 1.3–2.9 (m, 10 H), 4.65 (br s, 1 H), 4.72 (br s, 1 H), 5.65 (br s, 1 H); ^{13}C NMR ($CDCl_3$) 208, 189, 145, 129, 114, 51, 46, 45, 37, 29, 28, 27 ppm; IR (film) 3080, 2950, 2860, 1720, 1620, 1450, 1410, 1380, 1340, 1280, 1240, 1200, 1050, 900 cm^{-1}; mass spectrum, m/z 176 (M^+). Anal. Calcd for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 81.62; H, 8.96.

Cyclization of 14. The cyclization of 90 mg (0.39 mmol) of **14** gave 42 mg (66%) of the 1,6-adduct **14a**, which was identical with the previously characterized.

Cyclization of 15. The cyclization of 40 mg (0.16 mmol) of **15** provided 16 mg (57%) of the 1,6-adduct 4,5,6,7,8,8a-hexahydro-3,8a-dimethyl-7-methylene-2(1*H*)azulenone (**15a**), which was homogeneous by TLC analysis (hexanes/ether, 1:1; R_f(**15**) 0.58, R_f(**15a**) 0.37): ^{1}H NMR ($CDCl_3$) δ 1.15 (s, 3 H), 1.55 (s, 3 H), 1.3–2.9 (m, 13 H), 4.60 (br s, 1 H), 4.65 (br s, 1 H); IR (film) 3080, 2930, 2870, 1690, 1640, 1450, 1410, 1380, 1330, 1305, 1240, 1200, 1160, 1060, 1000, 900 cm^{-1}. Anal. Calcd for $C_{13}H_{18}O$: C, 82.05; H, 9.53. Found: C, 81.92; H, 9.57.

Cyclization of 18. The cyclization of 100 mg (0.22 mmol) of **18** produced 92 mg (85%) of the 1,6-adduct having a nonconjugated enone moiety, i.e., [4a*R**]-2,3,4,4a,5,6,7,8-octahydro-4a,9-dimethyl-6-methylene-3-oxo-1*H*-benzocycloheptene (**18b**), which was homogeneous by TLC analysis (hexanes/ether, 1:1; R_f(**18**) 0.88, R_f(**18b**) 0.77): ^{1}H NMR ($CDCl_3$) δ 1.10 (s, 3 H), 1.3–2.6 (m, 13 H), 2.95–3.15 (m, 2 H), 4.55 (br s, 1 H), 4.65 (br s, 1 H).

Purification via chromatography on silica gel (elution with hexanes/ether, 10:1) provided 65 mg (60%) of [4a*R**]-2,3,4,4a,5,6,7,8-octahydro-4a,9-dimethyl-6-methylene-3-oxo-1*H*-benzocycloheptene (**18a**), which was homogeneous by TLC analysis (R_f(**18a**) 0.44; hexanes/ether, 1:1): ^{1}H NMR ($CDCl_3$) δ 1.1 (d, 1.5 H, J = 3 Hz), 1.22 (s, 3 H), 1.26 (d, 1.5 H, J = 3 Hz), 1.4–2.8 (m, 11 H), 4.62 (br s, 0.5 H), 4.70 (br s, 0.5 H), 4.82 (br s, 1 H), 5.80 (s, 0.5 H), 5.85 (s, 0.5 H); IR (film) 3060, 3010–2850, 1660, 1610, 1460, 1420, 1375, 1330, 1275, 1245, 1220, 900 cm^{-1}; mass spectrum, m/z 204 (M^+). These data represent a mixture of the C(9) methyl isomers.

Cyclization of 19. The cyclization of 148 mg (0.47 mmol) of **19** at room temperature for 30 min produced 8 mg (7%) of 3,4,4a,5,6,7,7a,8,9,10,11,11a-dodecahydro-4a-methyl-6-methylene-2*H*-dibenzo[*a*,*c*]cyclohepten-2-one (**19a**), which was homogeneous by TLC analysis (hexanes/ether, 2:1; R_f(**19**) 0.61, R_f(**19a**) 0.35): ^{1}H NMR ($CDCl_3$) δ 1.2 (s, 3 H), 1.0–2.7 (m, 20 H), 2.7–2.95 (m, 1 H), 4.77 (br s, 2 H), 6.1 (s, 1 H); IR (film) 3050, 3000–2800, 1650, 1620, 1440, 1325, 1270, 1250, 1220, 1020, 880 cm^{-1}; mass spectrum, m/z 244 (M^+). Unreacted **19** (117 mg, 78%) was also isolated.

Cyclization of 19 with Titanium Tetrachloride. The cyclization of 100 mg (0.24 mmol) of **19** produced 21 mg (21%) of **19a**, which was identical with that characterized above.

Continued elution gave 26 mg (31%) of **19b**, which was homogeneous by TLC analysis (hexanes/ether, 1:1; R_f(**19**) 0.47, R_f(**19b**) 0.40): ^{1}H NMR ($CDCl_3$) δ 1.15 (s, 3 H), 0.8–2.7 (m, 22 H), 1.71 (s, 3 H), 4.7–5.0 (m, 1 H), 5.8 (s, 1 H); IR (film) 3000–2800, 1680, 1640, 1470, 1430, 1350, 1230, 1020, 905, 865 cm^{-1}.

Cyclization of 20. The cyclization of 143 mg (0.49 mmol) of **20** produced 65 mg (60%) of the 1,2-adduct **20b**, which was homogeneous by TLC analysis (hexanes/ether, 2:1, R_f(**20**) 0.50, R_f(**20b**) 0.25): ^{1}H NMR ($CDCl_3$) δ 1.00 (s, 3 H), 0.8–2.6 (m, 18 H), 4.6–4.8 (m, 2 H), 5.65 (br s, 1 H), 5.75 (s, 1 H); ^{13}C NMR ($CDCl_3$) 145.4 (s), 143.3 (s), 135.1 (d), 134.7 (s), 122.4 (d), 114.7 (t), 49.0 (t), 47.7 (t), 37.3 (s), 35.5 (t), 32.4 (t), 27.6 (q), 26.3 (q), 19.3 (q) ppm; IR (film) 3600–3100, 3060, 3000–2800, 1640, 1470, 1450, 1385, 1345, 1200, 1070, 900 cm^{-1}.

Cyclization of 20 with Titanium Tetrachloride. The cyclization of 65 mg (0.22 mmol) of **20** at −78 °C produced 12 mg (24%) of the protodesilylation product **20a**, which was homogeneous by TLC analysis (hexanes/ether; R_f(**20**) 0.47, R_f(**20a**) 0.38): ^{1}H NMR ($CDCl_3$) δ 1.16 (s, 3 H), 1.75 (s, 3 H), 1.79 (s, 3 H), 1.88 (s, 3 H), 1.5–2.6 (m, 15 H), 4.72 (br s, 1 H), 4.90 (br s, 1 H), 5.89 (s, 1 H), 5.90 (br s, 1 H); IR (film) 3060, 3010, 3000–2800, 1670, 1590, 1460, 1440, 1420, 1380, 1330, 1260, 1220, 1180, 1020, 890 cm^{-1}; mass spectrum, m/z 218 (M^+).

Continued elution (hexanes/ether, 3:1) provide 21 mg (43%) of **20b**, which was identical with that previously characterized.

Cyclization of 21. To 100 mg (0.32 mmol) of **21** in 1 mL of dry toluene at 0 °C was added dropwise 54 μL of boron trifluoride etherate (0.44 mmol). The reaction mixture was stirred at 0 °C for 2 h and then diluted with 10 mL of reagent grade ether. Standard ethereal workup provide 91 mg of crude residue, which was purified by chromatography (elution with hexanes/ether, 3:1) to provide 46 mg (61%) of the protodesilylation product **21a**, which was homogeneous by TLC analysis (hexanes/ether, 2:1; R_f(**21a**) 0.48): ^{1}H NMR (CCl_4) δ 1.2–1.8 (m, 10 H), 1.3 (s, 3 H), 1.7 (s, 3 H), 2.2–2.5 (m, 5 H), 4.57 (br s, 1 H), 4.7 (br s, 1 H), 5.80 (d, 1 H, J = 3 Hz), 6.00 (s, 1 H), 6.4 (d, 1 H, J = 3 Hz).

Cyclization of 22. To 100 mg (0.52 mmol) of trienone **22** in 1.5 mL of dry toluene at 0 °C was added dropwise 435 μL of a 1.4 M solution of ethylaluminum dichloride in toluene (Alfa). The

reaction mixture was stirred at 0 °C for 20 min and then diluted with 30 mL of reagent grade ether. The organic phase was washed with brine, dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo. The crude residue was chromatographed (elution with hexanes/ether, 7:1) to provide 45 mg (45%) of enone **23** [2a*R**,6a*R**,7a*R**]-1,2,2a,5,6,6a,7,7a-octahydro-6a,7a-dimethyl-4*H*-cyclobut[*a*]inden-4-one, which was homogeneous by TLC analysis (hexanes/ether, 1:1; R_f(**22**) 0.63, R_f(**23**) 0.45): ^{1}H NMR ($CDCl_3$) δ 1.19 (s, 3 H), 1.55 (s, 3 H), 08–2.65 (m, 16 H), 2.8–2.9 (m, 1 H), 5.63 (s, 1 H); ^{13}C NMR ($CDCl_3$) 199.8 (s), 181.2 (s), 120.8 (d), 56.2 (t), 50.3 (d), 44.5 (s), 43.6 (s), 39.5 (t), 33.5 (t), 31.5 (t), 28.6 (q), 24.7 (q), 20.4 (t) ppm; IR (film) 3050–2800, 1670, 1455, 1420, 1380, 1340, 1320, 1210, 1010, 960, 860 cm^{-1}; mass spectrum, m/z 190 (M^+).

V. Perforane Syntheses. 2,5-Dimethylcyclohexane-1,3-dione (32). To a solution of 10.0 g (79.4 mmol) of 5-methylcyclohexane-1,3-dione (**31**), prepared according to the procedure of Crossley and Renorf,[37] in 25.8 mL of warm (55 °C) 4 N NaOH (0.10 mol) was added 9.9 mL of methyl iodide (0.16 mol). The reaction mixture was refluxed for 20 h and then cooled to 0 °C. Filtration of the cold reaction mixture afforded 6.45 g (58%) of crystalline **32**. The filtrate was acidified to pH 5 with 1 N HCl, and filtration provided an additional 0.75 g (14%; or 7.2 g total, 72%) of **32**, which was homogenous by TLC analysis (ether; R_f(**31**) 0.46, R_f(**32**) 0.64): mp 170–172 °C [lit. mp 170–172 °C[26]]; ^{1}H NMR (DMSO-d_6) δ 0.95 (d, 3 H, J = 2 Hz), 1.55 (s, 3 H), 1.8–2.55 (m, 5 H); IR (KBr) 3700–3200, 2960, 2930, 2630, 1640, 1580, 1245, 1090 cm^{-1}.

[5*R]-3-Methoxy-2,5-dimethyl-2-cyclohexen-1-one (33).** A solution of 8.78 g (62.7 mmol) of diketone **32** in 200 mL of ether was treated with an ethereal (500 mL) solution of diazomethane, prepared from 27.2 g of nitrosomethylurea (0.27 mol), and stirred at room temperature for 2 h. Excess diazomethane was consumed by the dropwise addition of glacial acetic acid. The ethereal phase was washed with brine, dried over anhydrous magnesium sulfate, filtered, and concentrated. Chromatography of the residue on silica gel (elution with ether) provided 9.30 g (96%) of **33**, which was homogeneous by TLC analysis (ether; R_f(**32**) 0.51, R_f(**33**) 0.62): ^{1}H NMR (CCl_4) δ 1.00 (d, 3 H, J = 4 Hz), 1.5 (s, 3 H), 1.55–2.5 (m, 5 H), 3.70 (s, 3 H); IR (KBr) 3500–3100, 2950, 1740, 1700–1540, 1380, 1240, 1110, 1000, 960, 895, 875, 840 cm^{-1}. Anal. Calcd for $C_9H_{14}O_2$: C, 70.09; H, 9.15. Found: C, 69.70; H, 9.55.

[5*R,6*S**]-3-Methoxy-2,5,6-trimethyl-2-cyclohexen-1-one (29).** To a solution of lithium diisopropylamide, prepared from 3.04 g (30.1 mmol) of diisopropylamine in 8.4 mL of THF and 11.2 mL of *n*-butyllithium (2.7 M in hexanes, 30.1 mmol) at −78 °C, was added a solution of 3.86 g of ketone **33** (25.1 mmol) in 4 mL of THF containing 4.4 mL (25.1 mmol) of HMPA over a 30-min period (via syringe pump). After an additional 30 min at −78 °C, 1.9 mL (4.27 g, 30.1 mmol) of methyl iodide was added. The reaction mixture was stirred at −78 °C for 1 h and then allowed to warm gradually to room temperature overnight (14 h). Standard ethereal workup provided 3.1 g of crude residue, which was purified on silica gel (elution with hexanes/ether, 1:1) to afford 1.27 g (30%) of a crystalline product which was homogeneous on TLC analysis (ether; R_f(**33**) 0.68, R_f(**29**) 0.74): mp 55–57 °C; ^{1}H NMR (CCl_4) δ 1.05–1.15 (m, 6 H), 1.5–1.6 (br s, 3 H), 1.3–2.8 (m, 7 H), 3.70 (s, 3 H); ^{13}C NMR ($CDCl_3$) 199.0, 168.2, 111.8, 53.4, 44.9, 33.0, 31.1, 18.6, 11.7, 6.2 ppm; IR (film) 2950, 1620, 1450, 1380, 1320, 1280, 1235, 1160, 1120, 1100, 980, 850 cm^{-1}; mass spectrum, m/z 168 (M^+).

Continued elution afforded 1.44 g (34%) of an oil [R_f 0.68] which was the C(6) epimer of **29**: ^{1}H NMR (CCl_4) δ 0.9–1.1 (m, 6 H), 1.5–1.6 (br s, 3 H), 1.8–2.7 (m, 5 H), 3.70 (s, 3 H); IR (film) 2950, 1640–1600, 1460, 1380, 1240, 1110, 1000, 970, 940, 900, 880 cm^{-1}. Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.35; H, 9.58. Found: C, 70.96; H, 9.97.

Preparation of (*E*)-2-[(Trimethylsilyl)methyl]-2-buten-1-yl Iodide (30). The procedure of Trost and co-workers was used to bis-silylate the dianion of tiglic alcohol.[36]

A 1-L three-necked flask fitted with a mechanical stirrer and rubber septa was charged with 49.4 mL of *n*-butyllithium (9.5 *M* in hexanes, 0.5 mole) and evacuated until all of the solvent was removed. To the resulting oil was added 220 mL of dry ether and 70.8 mL (0.5 mol) of tetramethylethylenediamine [TMEDA] at 0 °C. Tiglic alcohol (14.94 g, 0.17 mol) was then added dropwise (via syringe) over 30 min at 0 °C. The resulting mixture was stirred for 30 min and 217 mL of THF was added. The mixture was stirred at room temperature for 48 h during which time an orange-colored gum had formed. The reaction vessel was cooled to −45 °C, and freshly distilled chlorotrimethylsilane (99.2 mL, 0.8 mol) was added (via cannula) as rapidly as the very vigorous reaction permitted [ca. 5 min; during this period the solution turned clear, then cloudy white]. The resulting mixture was stirred at −45 °C for 10 min and then stirred for 20 min at room temperature. Saturated aqueous $NaHCO_3$ (750 mL) was cautiously added until bubbling subsided. The resultant mixture was extracted with ether until the ethereal phase was colorless. The combined ethereal extracts were washed with saturated copper sulfate (2–3 L), brine, and dried over anhydrous magnesium sulfate. After concentration via atmospheric distillation, the residue was distilled [180–205 °C at 760 Torr] to provide 27.0 g (72%) of (*Z*)-1-[(trimethylsilyl)oxy]-2-[(trimethylsilyl)methyl]-2-butene which was homogeneous on TLC analysis (hexanes/ether, 4:1; R_f 0.93): ^{1}H NMR (CCl_4) δ 0.00 (br s, 18 H), 1.52 (d, 3 H, J = 6 Hz), 1.35–1.70 (m, 5 H), 4.80 (br s, 2 H), 5.25 (q, 1 H, J = 6 Hz).

A solution of 27.0 g of the above silyl ether in 69 mL of distilled THF and 39 mL of 1 N aqueous sulfuric acid was stirred vigorously for 30 min at room temperature. Solid anhydrous potassium carbonate was added carefully until bubbling subsided. The layers were separated, and the aqueous layer was extracted twice with 100 mL of ether. The combined organic phases were dried over anhydrous magnesium sulfate and concentrated at atmospheric pressure. The resulting residue was distilled [4 Torr] to give a forerun of tiglic alcohol (1.57 g, 45–75 °C) and 14.1 g (93%) of the hydrolysis product (*Z*)-2-[(trimethylsilyl)methyl]-but-2-en-1-ol (75–85 °C), which was homogeneous on TLC analysis (hexanes/ether, 4:1; R_f(silyl ether) 0.93, R_f(alcohol) 0.50): ^{1}H NMR (CCl_4) δ 0.00 (s, 9 H), 1.3–1.6 (m, 5 H), 2.0 (br s, 1 H), 3.70 (br s, 2 H), 5.20 (q, 1 H, J = 6 Hz).

To a solution of 10.29 g (65.2 mmol) of the above alcohol in 165 mL of anhydrous THF and 10 mL of triethylamine (72 mmol) at 0 °C was added dropwise 8.96 g (78.2 mmol) of methanesulfonyl chloride over a 20-min period; a thick precipitate formed. The mixture was stirred for 4 h at 0 °C. Filtration followed by careful evaporation of the solvent in vacuo afforded the crude mesylate. This material was used directly in the next step without characterization.

The crude mesylate (ca. 66 mmol) was diluted with freshly distilled acetone (300 mL) and cooled to 0 °C. Anhydrous sodium iodide (14.66 g, ca. 98 mmol) was added, resulting in the formation of a thick yellow precipitate. The mixture was stirred at 0 °C for 2 h. Filtration followed by careful evaporation of the solvent in vacuo gave 18.1 g of crude iodide, which was purified on silica gel (elution with hexanes) to give 14.40 g (82% over two steps) of iodide **30**, which was homogeneous by TLC analysis (hexanes/ether, 1:1; R_f(**30**) 0.91): ^{1}H NMR ($CDCl_3$) δ 0.00 (s, 9 H), 1.4–1.7 (m, 5 H), 3.85 (br s, 2 H), 5.55 (q, 1 H, J = 7 Hz); IR (film) 2950–2850, 1640, 1420, 1380, 1350, 1250, 1160, 1065, 980, 840, 770, 695, 620 cm^{-1}.

[5*R,6*S**]-3-Methoxy-2,5,6-trimethyl-6-[2-[(trimethylsilyl)methyl]-2-butenyl]-2-cyclohexen-1-one (34).** To a solution of lithium diisopropylamide, prepared from 4.01 mL (10.8 mmol) of *n*-butyllithium (2.7 *M* in hexanes), followed by removal of the hexanes, and 1.51 mL (10.8 mmol) of diisopropylamine in 5 mL of THF at −78 °C was added a solution of 1.51 g (9 mmol) of ketone **29** in 6 mL of THF containing 1.57 mL of HMPA over a 90-min period (via syringe pump). After an additional 30 min at −78 °C, 2.66 g (9.9 mmol) of iodide **30** was added. The reaction was stirred at −78 °C for 30 min and then allowed to warm gradually to room temperature overnight (12 h). Standard ethereal workup provided 2.56 g of crude residue, which was purified on silica gel (hexanes/ether, 10:1) to afford 1.86 g (72%) of crystalline and alkylated material **34** [mp 79–81 °C], which was homogeneous by TLC analysis (hexanes/ether, 1:1; R_f(**29**) 0.47, R_f(**34**) 0.71): ^{1}H NMR (CCl_4) δ 0.00 (s, 9 H), 0.70 (s, 3 H), 0.68–1.0 (m, 6 H), 1.1–2.9 (m, 13 H), 1.50 (br s, 3 H), 3.68 (s, 3 H), 4.86 (q, 1 H, J = 6 Hz); ^{13}C NMR ($CDCl_3$) 203.1 (s), 168.1 (s), 134.7 (s), 119 (d), 113 (s), 54.6 (q), 46.8 (s), 45.5 (t), 34.4, 29.9, 21.1, 19.1, 15.9, 14.1, 8.0 (s), −0.6 (q) ppm; IR (film) 2960, 1630, 1460, 1380, 1360, 1320, 1240, 1120, 1000, 860 cm^{-1}; mass spectrum, m/z 308 (M^+). Anal. Calcd

for $C_{18}H_{32}O_2Si$: C, 70.07; H, 10.45. Found: C, 70.11; H, 10.27.

Continued elution provided 311 mg (12%) of the isomeric C(6) alkylated material (hexenes/ether, 1:1; R_f 0.73).

[4*R,5*S**]-2,4,5-Trimethyl-4-[2-[(trimethylsilyl)-methyl]-2-butenyl]-3-vinyl-2-cyclohexen-1-one (28).** A solution of 1.72 g (5.6 mmol) of **34** in 60 mL of THF at 0 °C was treated dropwise with 7.28 mL of vinyllithium (1 M, 7.3 mmol) over a 30-min period. The reaction mixture was then allowed to warm to room temperature and stirred for 90 min. Standard ethereal workup provided 2.0 g of crude residue, which was used directly in the next reaction.

The crude alcohol was dissolved in 140 mL of THF, and 20 drops of 10% HCl was added. After being stirred at room temperature for 1 h, the reaction was concentrated to a residue, diluted with 100 mL ether, washed with brine, dried over anhydrous magnesium sulfate, and then filtered. Following removal of the solvent, the crude dienone was chromatographed on silica gel (elution with hexanes/ether, 3:1) to provide 1.19 g (70%) of dienone **28**, which was homogeneous by TLC analysis (hexanes/ether, 3:1; R_f(**34**) 0.54, R_f(**28**) 0.70): ^{1}H NMR (CCl_4) δ 0.00 (s, 9 H), 1.0–1.15 (m, 6 H), 1.2–2.7 (m, 20 H), 1.8 (s, 3 H), 4.9–5.5 (m, 3 H), 6.20 (dd, 1 H, J = 18, 10 Hz); ^{13}C NMR ($CDCl_3$) 199 (s), 161 (s), 135 (d), 134 (s), 130.5 (s), 121 (t), 119 (d), 46, 42.6, 34, 28, 23, 22, 16.6, 14.6, 13.6, –0.5 (q) ppm; IR (film) 3100, 3000–2900, 1660, 1600, 1420, 1385, 1360, 1250, 1160, 1110, 1015, 1005, 940, 850 cm^{-1}; mass spectrum, m/z 304 (M$^+$). Anal. Calcd for $C_{19}H_{32}OSi$: C, 74.93; H, 10.59. Found: C, 74.68; H, 10.81.

[4*R,4a*S**]-3,4,4a,5,6,7,8,9-Octahydro-1,4,4a,7-tetramethyl-6-methylene-2*H*-benzocyclohepten-2-one (27).** To 374 mg (1.2 mmol) of trienone **28** in 13 mL of dry toluene at 0 °C was added dropwise 1.27 mL of a 1.45 M solution of ethylaluminum dichloride in toluene (Alfa). The reaction mixture was stirred at 0 °C for 20 min. The reaction mixture was diluted with 100 mL of wet ether, washed with brine, dried over anhydrous magnesium sulfate, filtered, and concentrated. The crude residue was chromatographed (elution with hexanes/ether, 4:1) to provide 0.27 g (95%) of enone **27**, which was homogeneous by TLC analysis (hexanes/ether, 3:1; R_f(**28**) 0.70, R_f(**27**) 0.53, 0.48): ^{1}H NMR (CCl_4) δ 0.83–1.15 (m, 11 H), 1.67 (br s, 3 H), 1.4–1.75 (m, 4 H), 1.85–2.6 (m, 7 H), 4.3–4.8 (m, 2 H): ^{13}C NMR ($CDCl_3$) 199 (s), 167 (s), 149 (s), 131 (s), 113 (t), 111 (t), 43.5, 42, 41.9, 41.3, 38.4, 37.7, 37.3, 36.4, 33.8, 32.7, 32.5, 28.7 (s), 25, 20, 19.6, 19.2 (d), 15.8 (d), 10.7 (d) ppm; IR (film) 3090, 3000–2900, 1660, 1615, 1460, 1440, 1380, 1350, 1280, 1200, 1165, 1120, 1060, 1020, 900, 865, 850, 780 cm^{-1}; mass spectrum, m/z 232 (M$^+$). Anal. Calcd for $C_{16}H_{24}O$: C, 82.70; H, 10.41. Found: C, 82.81; H, 10.17. These data represent a mixture of C(8) diastereomers.

Silylated trienone (1*R**,9a*S**)-[(2,6,7,8,9,9a-hexahydro-1,4,7,9a-tetramethyl-8-methylene-1*H*-benzocycloheptene-3-yl)-oxy]trimethylsilane (**35**) was often isolated in low yield (R_f 0.49; hexanes/ether, 3:1): ^{1}H NMR (CCl_4) δ 0.15 (s, 9 H), 0.75–1.05 (m, 9 H), 1.1–1.5 (m, 4 H), 1.55 (br s, 3 H), 1.7–2.55 (m, 4 H), 4.6–4.75 (m, 2 H), 5.35 (t, 1 H, J = 6 Hz); IR (film) 2950–2830, 1705, 1640, 1445, 1300, 1245, 1200, 1100, 950, 920, 740 cm^{-1}.

This material was hydrolyzed to provide bicyclic ketone **27** via the following procedure: To a solution of 203 mg (0.67 mmol) of silyl enol ether **35** in 15 mL of reagent grade THF was added 10 mL of 10% aqueous HCl. The solution was stirred 1 h at room temperature and was then quenched by the addition of 3 g of potassium carbonate. The reaction mixture was diluted with 30 mL of ether, washed with 10 mL of brine, dried over anhydrous magnesium sulfate, filtered, and concentrated. The crude residue was chromatographed on silica gel (elution with hexanes/ether, 3:1) to afford 142 mg (92%) of dienone **27** (hexanes/ether, 3:1; R_f(**35**) 0.49, R_f(**27**) 0.42), which was identical with that characterized above.

[4*R,4a*S**]-3,4,4a,5,8,9-Hexahydro-1,4,4a,7-tetramethylspiro[6*H*-benzocycloheptene-6,2′-oxiran]-2(7*H*)-one (36).** To a solution of 113 mg (0.48 mmol) of dienone **27** in 5 mL of dry methylene chloride was added 0.3 g (1.4 mmol) of 85% *m*-chloroperbenzoic acid [MCPBA] in four equal portions over a 1-h period at room temperature. The reaction mixture was stirred 60 min and was then diluted with 100 mL of ether. The ethereal phase was washed with cold brine and cold 10% NaOH and dried over anhydrous magnesium sulfate. Filtration and concentration of the ethereal phase furnished an oily residue. Purification by chromatography on silica gel (hexanes/ether, 4:1) afforded 35 mg (30%) of an epoxide which was homogeneous on TLC analysis (hexanes/ether, 3:1; R_f(**27**) 0.70, R_f(**36**) 0.42): ^{1}H NMR (CCl_4) δ 0.68 (d, 3 H), 0.90–1.0 (m, 6 H), 1.0–1.6 (m, 2 H), 1.67 (s, 3 H), 1.70–2.35 (m, 8 H), 2.4–2.65 (m, 2 H); IR (film) 2950–2540, 1710, 1650, 1620, 1440, 1380, 1200, 1095, 1000, 970, 760 cm^{-1}; mass spectrum, m/z 248 (M$^+$).

Continued elution afforded 35 mg (28%) of an isomeric epoxide which was homogeneous by TLC analysis (hexanes/ether, 3:1; R_f 0.34): ^{1}H NMR (CCl_4) δ 0.80–1.0 (m, 6 H), 1.0–1.6 (m, 7 H), 1.70 (s, 3 H), 1.75–2.65 (m, 8 H); IR (film) 2990–2940, 1710, 1650, 1620, 1450, 1380, 1320, 1200, 1095, 1020, 1000, 970, 910, 850, 760 cm^{-1}.

[4*R,4a*S**]-3,4,4a,5,6,7,8,9-Octahydro-1,4,4a,7-tetramethyl-2-oxo-2*H*-benzocycloheptene-6-carboxylic Acid (38).** A solution of 16.3 mg (0.06 mmol) of epoxide **36** in 600 μL of C_6D_6 was placed in a standard 5-mm NMR tube, and 4 μL of freshly distilled boron trifluoride etherate was added. The capped NMR tube was shaken and placed into the spectrometer. After 2–4 min, NMR analysis indicated that the rearrangement was complete [^{1}H NMR (C_6D_6) δ 0.8–1.2 (m, 9 H), 0.9 (s, 3 H), 1.2–2.3 (m, 16 H), 9.6 (br s, 0.2 H), 9.8 (br s, 0.8 H)]. The reaction mixture was diluted with 10 mL of reagent grade ether, dried over anhydrous magnesium sulfate, and concentrated. This material was used directly in the next step without purification or further characterization.

Further oxidation of [4*R**,4a*S*]-3,4,4a,5,6,7,8,9-octahydro-1,4,4a,7-tetramethyl-2-oxo-2*H*-benzocycloheptene-6-carboxaldehyde (**37**) was carried out via the following procedures.

(a) The crude aldehyde [15 mg] was diluted with 1 mL of reagent grade acetone, and 2 drops of standard Jones reagent was added at room temperature. After 20 min the reaction mixture was diluted with ether, washed with brine, and dried over anhydrous magnesium sulfate. Filtration and concentration gave 12 mg of a crude residue. Purification on silica gel gave 2 mg (12%) of acid **38**, which was homogeneous by TLC analysis (hexanes/ether, 1:1; R_f(**37**) 0.50; R_f(**38**) 0.10): ^{1}H NMR (DMSO-d_6) δ 0.8–2.4 (m, 22 H), 1.8 (br s, 3 H).

(b) The crude aldehyde [15 mg, 0.06 mmol] was diluted with 2 mL of freshly distilled DMF, and 60 mg of pyridinium dichromate (1.60 mmol) was added. The reaction mixture was stirred for 4 h at room temperature and then diluted with 20 mL of water. Standard ethereal workup provided 7 mg of crude residue, which was purified via chromatography on silica gel (elution with hexanes/ether, 1:1) to afford 3 mg of acid **38** (18%).

Attempted Preparation of (±)-Perforenone (24) via Oxidative Decarboxylation.[42] Cupric acetate (1 mg), lead tetraacetate (4 mg, 97%), and 4 mg of acid **38** were added to 1 mL of dry benzene in a thick-walled pressure tube [capacity 10 mL]. Argon was bubbled into the reaction mixture for a 5-min period to purge the system. The reaction vessel was sealed and immersed in an oil bath maintained at 81 °C for 4 h. TLC comparison of the reaction mixture with authentic perforenone revealed the presence of a small amount of perforenone in addition to three other products. No further characterization or purification of the crude residue was attempted.

[4*R,4a*S**]-3,4,4a,5,6,7,8,9-Octahydro-1,4,4a,7-tetramethyl-2*H*-benzocycloheptene-2,6-dione (39) via the Lemieux–Johnson Procedure.**[43] To a solution of 149 mg (0.64 mmol) of dienone **27** in 3.6 mL of freshly distilled *p*-dioxane and 1.3 mL of distilled water was added 10 mg (0.04 mmol) of osmium tetraoxide. The reaction mixture was stirred for 15 min, and 303 mg (1.4 mmol) of freshly ground sodium periodate was added in four equal portions over a 30-min period at room temperature. After the mixture was stirred for 30 min, standard ethereal workup provided 141 mg of a crude oil. Purification by chromatography on silica gel (elution with hexanes/ether, 3:1) gave 62 mg (41%) of enedione **39**, which was homogeneous by TLC analysis (hexanes/ether, 1:2; R_f(**27**) 0.77, R_f(**39**) 0.52): ^{1}H NMR (CCl_4) δ 0.85–1.15 (m, 12 H), 1.67 (s, 1.9 H), 1.74 (s, 1.1 H), 2.1–2.75 (m, 7 H): ^{13}C NMR ($CDCl_3$) 211 (s), 198 (s), 164 (s), 132 (s), 48, 44, 41.8, 41.4, 41.0, 34.5, 33.3, 33.1, 29.0, 28.2 (s), 25.7 (s), 19.8 (d), 15.9 (d), 15.7 (d), 11.2 (d) ppm; IR (film) 2975, 2925, 2875, 1720, 1660, 1620, 1455, 1380, 1340, 1310, 1260, 1185, 1160, 1140, 1040, 1020, 1000 cm^{-1}; mass spectrum, m/z 234 (M$^+$). These data represent a mixture of C(8) diastereomers.

Preparation of 39 via the Upjohn Osmylation Procedure.[46] To a solution of 394 mg (1.7 mmol) of dienone **27** in 20 mL of freshly distilled acetone at room temperature was added 21 mL of a stock osmylation solution [prepared by dissolving 6.73 g [57.5 mmol] of 4-methylmorpholine *N*-oxide and 165 mg (0.65 mmol) osmium tetraoxide in 50 mL distilled water]. The resulting mixture was stirred at room temperature for 14 h. The reaction mixture was diluted with 100 mL of reagent grade ether and washed with 20 mL of a saturated aqueous solution of sodium bisulfite. The ethereal phase was washed with brine, dried over anhydrous magnesium sulfate, and filtered and the solvent removed in vacuo to afford 411 mg of crude diol, which was used without further purification or characterization [TLC analysis: hexanes/ether, 1:1; R_f(**27**) 0.88, R_f(diol) 0.15, 0.22].

To a solution of 441 mg of crude diol in 7 mL of *p*-dioxane and 2.1 mL of water was added 363 mg (1.7 mmol) of freshly ground sodium periodate in four equal portions over a 30-min period. The resulting solution was stirred at room temperature for 30 min. Standard ethereal workup furnished 489 mg of crude dione. Purification by chromatography on silica gel (elution with hexanes/ether, 2:1) afforded 328 mg (83%) of a diastereomeric mixture of enedione **39** (hexanes/ether, 1:1; R_f(diol) 0.15, 0.22, R_f(**39**) 0.53). **39** was identical with that characterized from the Lemieux–Johnson procedure.

[4*R,4a*S**]-3,4,4a,5,6,7,8,9-Octahydro-6-methylene-1,4,4a,7-tetramethyl-2*H*-benzocyclohepten-2-ol (40).** To a solution of 75.3 mg (0.33 mmol) of dienone **27** in 1 mL of dry toluene at −78 °C was added dropwise 121 μL of DIBAL-H (1.5 M in toluene). The reaction mixture was allowed to warm to room temperature over a 2-h period. The reaction mixture was then diluted with 20 mL of wet ether, washed with 5 mL of brine, dried over anhydrous magnesium sulfate, filtered, and concentrated. The crude residue was chromatographed on silica gel (elution with hexanes/ether, 3:1) to afford 36 mg of unreacted dienone **27** (56%).

Continued elution (hexanes/ether, 2:1) provided 31.3 mg (41%) of allylic alcohol **40**, which was homogeneous by TLC analysis (hexanes/ether, 1:2; R_f(**27**) 0.87, R_f(**40**) 0.74): ^{1}H NMR (CCl_4) δ 0.75–1.08 (m, 9 H), 1.1–1.5 (m, 3 H), 1.57 (br s, 3 H), 1.6–2.4 (m, 8 H), 3.72–3.92 (m, 1 H), 4.34 (m, 2 H); IR (film) 3500–3200, 3095, 2950–2850, 1640, 1460, 1410, 1380, 1300, 1260, 1200, 1150, 1120, 1050, 1000, 950, 900, 840 cm^{-1}; mass spectrum, *m*/*z* 216 (M − 18).

Preparation of Alcohol 40 Using $LiAlH_4$. To a solution of 47.1 mg (0.20 mmol) of dienone **27** in dry ether at −60 °C was added 6.2 mg (0.16 mmol) of $LiAlH_4$. The reaction mixture was warmed to room temperature over a 45-min period. Standard ethereal workup provided 53 mg of crude residue, which was purified via chromatography on silica gel (elution with hexanes/ether, 3:1) to afford 38 mg (80%) of allylic alcohol **40**, which was identical with that prepared using DIBAL-H.

Osmylation of Dienol 40. To a solution of 79.1 mg (0.40 mmol) of dienol **40** in 1.5 mL of *p*-dioxane and 0.5 mL of water was added 4 mg of osmium tetraoxide. The reaction mixture was stirred for a 15-min period, and 160 mg (0.75 mmol) of freshly ground sodium periodate was added in four equal portions over a 30-min period. The reaction mixture was stirred an additional 1 h. Standard ethereal workup furnished 54 mg of a brown oil, which was chromatographed on silica gel (elution with hexanes/ether, 3:1) to afford 44 mg (56%) of enedione **39**, which was identical with that previously characterized [hexanes/ether, 1:2; R_f(**40**) 0.68, R_f(**39**) 0.55].

[1*R,4a*R**,8*S**,9a*S**]-Octahydro-1,4,7,9a-tetramethyl-4a,8-epoxy-4a*H*-benzocyclohepten-3(4*H*)-one (43).** To a solution of 75 mg (0.32 mmol) of enedione **39** in 2.1 mL of absolute ethanol at −20 °C was added 12.3 mg (0.32 mmol) of sodium borohydride. The reaction mixture was stirred for 20 min and was then quenched with water. Standard ethereal workup provided 50 mg of crude residue, which was chromatographed on silica gel (elution with hexanes/ether, 1:1) to afford 62 mg (89%) of tetrahydrofuran **43**, which was homogeneous by TLC analysis (ether; R_f(**39**) 0.88, R_f(**43**) 0.77): ^{1}H NMR (CCl_4) δ 0.85–1.4 (m, 20 H), 1.85–2.2 (m, 3 H), 3.8–4.0 (m, 1 H); IR (film) 2990–2875, 1720, 1680, 1480, 1460, 1380, 1360, 1335, 1280, 1255, 1230, 1180, 1120, 1075, 1000, 980, 890, 850, 800 cm^{-1}. Anal. Calcd for $C_{15}H_{24}O$: C, 81.76; H, 10.98. Found: C, 81.85; H, 11.04.

[4*R,4a*S**]-3,4,4a,5,6,7,8,9-Octahydro-1,4,4a,7-tetramethyl-6-(trimethylsiloxy)-2*H*-benzocycloheptene-2-one (42).** To a solution of 48 mg (0.2 mmol) of enedione **39** in 1.2 mL of absolute ethanol at −20 °C was added 7.8 mg (0.2 mmol) of sodium borohydride. After being stirred for 20 min, the reaction was quenched with saturated ammonium chloride solution. Standard ethereal workup afforded a crude residue, which was used directly in the next reaction without further purification or characterization.

The crude alcohol was diluted with 1 mL of dry THF and treated with 25 μL (0.3 mmol) of dry pyridine and 307 mg (0.3 mmol) of 4-(dimethylamino)pyridine [DMAP]. After the mixture was stirred for 5 min, 52 μL (0.4 mmol) of freshly distilled chlorotrimethylsilane was added. The resulting mixture was stirred for 20 h at room temperature. Standard ethereal workup provided 97 mg of a crude residue. Purification on silica gel (elution with hexanes/ether, 3:1) gave 15 mg (25%) of silyl ether **42**, which was homogeneous by TLC analysis (hexanes/ether, 1:2; R_f(**39**) 0.55, R_f(**42**) 0.69): ^{1}H NMR ($CDCl_3$) δ 0.00 (s, 9 H), 0.75–1.2 (m, 9 H), 1.65 (s, 3 H), 1.7–2.2 (m, 10 H), 3.65 (m, 1 H); IR (film) 2990–2850, 1720, 1640, 1620, 1460, 1380, 1360, 1340, 1255, 1180, 1130, 1075, 1020, 960, 880 cm^{-1}.

Continued elution gave 13.5 mg (27%, hexanes/ether, 3:1; R_f(**43**) 0.81) of tetrahydrofuran **43**, which was identical with that previously characterized.

Attempted Preparation of (±)-Perforenone (24) via Martin's Dehydrating Agent.[50] To a solution of 21.6 mg (0.09 mmol) of **43** in 0.5 mL of $CHCl_3$ was added 86 mg (0.13 mmol) of bis[α,α′-bis(trifluoromethyl)benzenemethanolate]diphenylsulfur in 0.5 mL of $CHCl_3$. The reaction mixture was stirred for 2 h at room temperature. TLC analysis revealed that no reaction had taken place. An additional 46 mg (0.07 mmol) of the dehydrating agent was then added, and the resulting mixture was refluxed for 13 h. Standard ethereal workup afforded a crude residue, which TLC analysis indicated was predominantly unreacted tetrahydrofuran **43** with a trace amount of perforenone.

***cis*-3,4,4a,5,6,7,8,9-Octahydro-6-oxo-1,4,4a,7-tetramethylspiro[2*H*-benzocycloheptene-2,2′-[1,3]dithiolane] (45).** To a solution of 111 mg (0.47 mmol) of enedione **39** in 1.2 mL dry ether was added 3 mg of zinc iodide at room temperature. After the mixture was stirred for 5 min, 135 μL (0.52 mmol) of (1,2-ethylenedithio)bis(trimethylsilane) (**44**) was added dropwise. The resulting mixture was stirred at room temperature for 20 h. The reaction was quenched with 1 mL of water and extracted with two 60-mL portions of ether. The combined ethereal extracts were washed with brine, dried over anhydrous magnesium sulfate, filtered, and concentrated to a residue. Chromatography on silica gel (elution with hexanes/ether, 3:1) afforded 33 mg (18%) of bis(dithioketal) **46** which was homogeneous by TLC analysis (hexanes/ether, 2:1; R_f(**39**) 0.21, R_f(**46**) 0.82): ^{1}H NMR (CCl_4) δ 0.75–1.0 (m, 9 H), 1.0–2.25 (m, 10 H), 1.80 (br s, 3 H), 2.6–2.95 (m, 4 H), 3.0–3.35 (m, 4 H); IR (film) 2960–2850, 2550, 2325, 1720, 1700, 1640, 1460, 1420, 1375, 1260, 1190, 800 cm^{-1}; mass spectrum, *m*/*z* 386 (M$^+$).

Continued elution (hexanes/ether, 3:1) gave 78 mg (53%) of **45** which was homogeneous by TLC analysis (hexanes/ether, 2:1; R_f(**39**) 0.21, R_f(**45**) 0.63): ^{1}H NMR (CCl_4) δ 0.8–1.18 (m, 12 H), 1.72 (s, 2 H), 1.78 (s, 1 H), 1.9–2.55 (m, 7 H), 2.92–3.33 (m, 4 H); ^{13}C NMR ($CDCl_3$) 211.6 (s), 142 (s), 130 (s), 71 (s), 48.9, 48.2, 47.7, 43.6, 41.2, 39.6, 35, 33.6, 29.4, 27.4, 21, 16, 15.6 ppm; IR (film) 2960–2900, 2850, 1710, 1620, 1450, 1370, 1310, 1275, 1245, 1180, 1150, 1100, 1035, 980, 960, 940, 900, 880, 840 cm^{-1}; mass spectrum, *m*/*z* 310 (M$^+$). Anal. Calcd for $C_{17}H_{26}S_2O$: C, 65.75; H, 8.43. Found: C, 65.63; H, 8.18. These data represent a mixture of C(8) diastereomers.

Dedithioketalization of bis(dithioketal) (46). To a stirred suspension of 126 mg (0.46 mmol) of mercuric chloride in 3 mL of 80% acetonitrile was added 40 mg (0.1 mmol) of bis(dithioketal) **46** in 3 mL of 80% acetonitrile. The reaction mixture was refluxed for 5 h and then cooled to room temperature. The reaction mixture was diluted with reagent grade ether, washed with 5 N ammonium acetate, and dried over anhydrous magnesium sulfate. Filtration and removal of the solvent in vacuo gave 30 mg of a crude residue, which was purified by chromatography on silica gel (with hexanes/ether, 1:1) to afford 11 mg (45%) of dione **39**, which was identical with that previously characterized.

[4*R,4a*S**,6*S**]-3,4,4a,5,6,7,8,9-Octahydro-6-hydroxy-1,4,4a,7-tetramethylspiro[2*H*-benzocycloheptene-2,2′-[1,3]-dithiolane] (47).** To a solution of 65 mg (0.21 mmol) of ketone **45** in 1.5 mL of absolute ethanol at −15 °C was added 8 mg (0.21 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 hexanes/ether, 3:1) to afford 19.5 mg (30%) of alcohol **47**, which was homogeneous by TLC analysis (hexanes/ether, 2:1; R_f(**45**) 0.64, R_f(**47**) 0.64): ^{1}H NMR (CCl_4) δ 0.75–0.99 (m, 9 H), 1.0–1.75 (m, 5 H), 1.76 (s, 3 H), 1.8–2.5 (m, 6 H), 3.1–3.4 (m, 4 H), 3.5–3.7 (m, 1 H); IR (film) 3550–3400, 2950–2850, 2375, 1720, 1640, 1560, 1440, 1380, 1370, 1260, 1210, 1180, 1140, 1080, 1050, 1000, 890, 840, 820, 800 cm^{-1}; mass spectrum, *m*/*z* 312 (M^+).

Continued elution afforded 4 mg (6%) of a diastereomeric alcohol **48**, which was homogeneous by TLC analysis (hexanes/ether, 2:1; R_f 0.45): ^{1}H NMR (CCl_4) δ 0.75 (m, 5 H), 1.78 (s, 3 H), 1.8–2.5 (m, 6 H), 3.1–3.4 (m, 5 H); IR (film) 3550–3300, 2950–2850, 2350, 1710, 1680, 1530, 1440, 1380, 1280, 1260, 1220, 1160, 1100, 1050, 1000, 960, 840 cm^{-1}; mass spectrum, *m*/*z* 312 (M^+).

Alcohol 47 via Lithium Aluminum Hydride Reduction. To a solution of 38.1 mg (0.13 mmol) of ketone **45** in 0.7 mL of dry THF at 0 °C was added 4.7 mg (0.12 mmol) of $LiAlH_4$. After being stirred at 0 °C for 1 h, the reaction mixture was quenched with 20 mL of wet ether and dried over anhydrous magnesium sulfate. Filtration and concentration of the ethereal phase provided a crude residue, which was purified via chromatography on silica gel (elution hexanes/ether, 3:1) to provide 24 mg (60%) of alcohol **47**, which was identical with the major product of the $NaBH_4$ reduction.

Continued elution (hexanes/ether, 3:1) gave 4.7 mg (12%) of a diastereomeric alcohol **48** (R_f 0.45), which was identical with that characterized via the $NaBH_4$ reduction.

Alcohol 47 via DIBAL-H Reduction. To a solution of 38 mg (0.12 mmol) of ketone **45** in 1 mL of toluene at −20 °C was added dropwise 98 μL (0.14 mmol) of a 1.5 M solution of DIBAL-H in toluene (Aldrich). The reaction mixture was stirred at −20 °C for 40 min, and then cautiously quenched with 20 mL of wet ether. Standard ethereal workup provided a crude residue, which was purified via chromatography on silica gel (elution with hexanes/ether, 3:1) to afford 24 mg (64%) of alcohol **47**, which was homogeneous by TLC analysis (hexanes/ether, 2:1; R_f(**45**) 0.64, R_f(**47**) 0.64) and identical with that characterized via the $NaBH_4$ reduction. No diastereomeric alcohol was obtained.

Alcohol 47 via Lithium Tri-*tert*-butoxyaluminohydride Reduction. To a solution of 160 mg (0.51 mmol) of ketone **45** in dry THF at −15 °C was added 116 mg (0.65 mmol) of lithium tri-*tert*-butoxyaluminohydride in four equal portions over a 45-min period. The reaction mixture was stirred an additional 30 min at −15 °C. The reaction mixture was quenched with water and extracted with three 25-mL portions of ether. The combined ethereal extracts were washed with brine, dried over anhydrous magnesium sulfate, and filtered, and the solvent was removed in vacuo. The crude residue obtained was purified via chromatography on silica gel (elution with hexanes/ether, 3:1) to afford 125 mg (78%) of alcohol **47**, which was identical with that obtained via the $NaBH_4$ reduction.

Continued elution afforded 27 mg (16%) of a diastereomeric alcohol (hexanes/ether, 3:1; R_f(**48**) 0.45), which was identical with that characterized via the $NaBH_4$ reduction.

***cis*-3,4,4a,5,8,9-Hexahydro-1,4,4a,7-tetramethylspiro[2*H*-benzocycloheptene-2,2′-[1,3]dithiolane] (49).** To a solution of 21.5 mg (0.07 mmol) of alcohol **47** in 1 mL of dry pyridine was rapidly added 84 μL (0.89 mmol) of freshly distilled $POCl_3$. The reaction mixture was refluxed at 105 °C for a 40-min period and then cooled to room temperature. The reaction mixture was diluted with 100 mL of ether and then carefully quenched with 1 mL of water. The ethereal phase was first washed with 5% HCl, 5% Na_2CO_3, and 10% $CuSO_4$ solutions, and then dried over anhydrous magnesium sulfate. Filtration and concentration of the solvent afforded 61 mg of an oil. Purification by chromatography on silica gel (elution with hexanes/ether, 2:1) gave 18 mg (89%) of olefin **49**, which was homogeneous by TLC analysis (hexanes/ether, 2:1; R_f(**47**) 0.64, R_f(**49**) 0.93): ^{1}H NMR (CCl_4) δ 0.75 (s, 3 H), 0.78 (d, 3 H, *J* = 6 H), 1.5 (br s, 3 H), 1.78 (s, 3 H), 1.8–2.4 (m, 9 H), 2.9–3.3 (m, 4 H), 4.95–5.25 (m, 1 H); ^{13}C NMR ($CDCl_3$) 143.3 (s), 137 (s), 128 (s), 119.6 (d), 72 (s), 48.6 (2 overlapping t), 45 (s), 41.4 (t), 39.4 (t), 34 (q), 33.2 (t), 32.7 (t), 29.5 (d), 25.4 (q), 20 (q), 16.2 (q) ppm; IR (film) 2950–2820, 1660, 1630, 1480, 1440, 1420, 1365, 1275, 1240, 1220, 1140, 1120, 1100, 1050, 1020, 970, 890, 840 cm^{-1}; mass spectrum, *m*/*z* 294 (M^+). Anal. Calcd for $C_{17}H_{26}S_2$: C, 69.32; H, 8.98. Found: C, 69.51; H, 8.78.

[4*R,4a*S**,6*S**]-3,4,4a,7,8,9-Hexahydro-1,4,4a,7-tetramethylspiro[2*H*-benzocycloheptene-2,2′-[1,3]dithiolane] (50).** To a solution of 111.5 mg (0.36 mmol) of alcohol **48** in 5.3 mL of dry pyridine was rapidly added 433 μL (4.65 mmol) of freshly distilled $POCl_3$. The reaction mixture was refluxed at 105 °C for a 40 min period and then cooled to room temperature. The reaction mixture was diluted with 200 mL of ether and then carefully quenched with 10 mL of water. The ethereal phase was first washed with 5% HCl, 5% Na_2CO_3, and 10% $CuSO_4$ solutions and then dried over anhydrous magnesium sulfate. Filtration and concentration provided an oil, which was chromatographed on silica gel (elution with hexanes) to afford 30 mg (29%) of olefin **50**, which was homogeneous by TLC analysis (hexanes; R_f(**50**) 0.25): ^{1}H NMR (CCl_4) δ 0.76–1.0 (m, 9 H), 1.05–1.4 (m, 3 H), 1.77 (s, 3 H), 1.85–2.5 (m, 5 H), 2.95–3.3 (m, 4 H), 4.8–5.2 (m, 2 H); IR (film) 3000–2850, 1630, 1460, 1420, 1375, 1280, 1260, 1130, 1080, 1020, 980, 960, 880, 790, 740 cm^{-1}.

Continued elution afforded 42 mg (40%) of olefin **49** (hexanes; R_f(**49**) 0.17), which was identical with that previously characterized.

(±)-Perforenone (24) via Dedithioketalization Using Mercury (II) Chloride.[52a] To a stirred solution of 93 mg (0.34 mmol) of dithioketal **49** in 14 mL 80% acetonitrile at room temperature was added 205 mg (0.7 mmol) of mercuric chloride. The reaction mixture was refluxed for 5 h. The reaction mixture was cooled to room temperature and filtered. The crystalline residue was washed two times with 50-mL portions of a solution of hexanes/methylene chloride (1:1). The combined filtrates were concentrated to a residue, which was then diluted with wet ether and washed with 5 N ammonium acetate. Standard ethereal workup provided 71 mg of crude residue, which was chromatographed on silica gel (elution with hexanes/ether, 4:1) to afford 25 mg (46%) of crystalline (±)-perforenone [mp 66–68 °C], which was homogeneous by TLC analysis (hexanes/ether, 2:1; R_f(**49**) 0.93, R_f(**24**) 0.58): ^{1}H NMR (CCl_4) δ 0.90 (d, 3 H), 0.92 (s, 3 H), 1.58 (s, 3 H), 1.70 (s, 3 H), 2.0–2.8 (m, 9 H), 5.0–5.3 (m, 1 H); ^{13}C NMR ($CDCl_3$) 199, 167, 137, 131, 120, 47, 42, 34, 33.5, 33, 27, 25, 19, 16, 11 ppm; IR (film) 2960–2860, 1650, 1620, 1450, 1370, 1340, 1310, 1270, 1220, 1200, 1160, 1140, 1100, 1020, 900, 880, 840, 800 cm^{-1}; mass spectrum, *m*/*z* 218 (M^+).

(±)-Perforenone (24) via Dedithioketalization Using Mercuric Oxide.[52b] To a vigorously stirred solution of 144 mg (0.66 mmol) of mercuric oxide and 82.1 μL (0.66 mmol) of freshly distilled boron trifluoride etherate in 1.5 mL of 15% aqueous THF at room temperature was slowly added a solution of 98 mg (0.33 mmol) of dithioketal **49** in 1.5 mL of 15% aqueous THF. The resulting mixture was stirred for 2 h and then diluted with 10 mL of wet ether. Standard ethereal workup afforded 53 mg of a crude residue, which was purified via chromatography on silica gel (elution with hexanes/ether, 3:1) to furnish 65.5 mg (90%) of perforenone.

(±)-Epiguadalupol (25). To a solution of 61 mg (0.28 mmol) of (±)-perforenone in 1.5 mL of THF at −15 °C was added 13 mg (0.33 mmol) of LAH. After being stirred for 1 h at −15 °C, the reaction mixture was quenched by the careful addition of 5 mL of wet ether followed by the addition of 2 drops of water. The resulting solution was diluted with 20 mL of ether, washed with 5 mL of brine, dried over anhydrous magnesium sulfate, filtered, and concentrated. The crude residue was chromatographed (elution with hexanes/ether, 3:1) to afford 52.1 mg (85%) of epiguadalupol, which was homogeneous by TLC analysis (hexanes/ether, 2:1; R_f(**24**) 0.58, R_f(**25**) 0.30): ^{1}H NMR (CCl_4) δ 0.75 (s, 3 H), 0.85 (d, 3 H, *J* = 7 Hz), 1.55 (s, 3 H), 1.65 (s, 3 H), 1.75–2.5 (m, 10 H), 4.0 (dd, 1 H, *J* = 7, 7 Hz), 5.2 (m, 1 H); ^{13}C NMR ($CDCl_3$) 141.7 (s), 137 (s), 129 (s), 120 (d), 71 (d), 45 (s), 38 (t), 33 (t), 33 (t), 32.9 (d), 25.5 (q), 24.5 (t), 20.6 (q), 16 (q), 14.5 (q) ppm; IR (film) 3500–3200, 2950–2850, 1700, 1660, 1650, 1480, 1470, 1450, 1440, 1370, 1280, 1260, 1200, 1180, 1140, 1060, 1040, 1020, 1000, 900, 880 cm^{-1}; mass spectrum, *m*/*z* 202 (M − 18).

Reduction of Perforenone Using L-Selectride. To a solution of 22 mg (0.10 mmol) of (±)-perforenone in 2 mL of THF at −78 °C was added dropwise 110 μL (0.11 mmol) of a 1.0 M solution of L-Selectride in THF (Aldrich). After being stirred for 30 min at −78 °C, the reaction mixture was warmed to −50 °C, stirred at −50 °C for 3 h, and then quenched by the addition of 10 mL of wet ether with 1 drop of water. Standard ethereal workup provided 25 mg of an oily residue. Purification on silica gel (elution with hexanes/ether, 4:1) afforded 5.1 mg of unreacted perforenone and 6.8 mg (31%) of pure (±)-guadalupol **26** (R_f(**26**) 0.40; hexanes/ether, 2:1), which was homogeneous by TLC analysis: ^{1}H NMR (CCl_4) δ 0.72 (s, 3 H), 0.84 (d, 3 H, J = 8 Hz), 1.55 (s, 3 H), 1.70 (s, 3 H), 1.80–2.5 (m, 10 H), 3.65 (br s, 1 H), 5.0–5.32 (m, 1 H); IR (film) 3500–3200, 2950, 2850, 1450, 1380, 1260, 1215, 1150, 1110, 1070, 1030, 1000, 870, 850, 800 cm^{-1}; ^{13}C ($CDCl_3$) 154.7, 128, 122.7, 119.9, 69.7, 45.3, 36.5, 33.7, 33.0, 29.7, 28.6, 28.5, 24.1, 19.2, 16.3; mass spectrum, m/z 202 (M − 18).

Continued elution provide 7.0 mg (31.5%) of pure (±)-epiguadalupol (**25**), which was identical with that previously characterized. A sample of a 1:1 mixture of the above alcohols (3 mg) was not separated further.

Reduction of Perforenone Using DIBAL-H. To a solution of 11.3 mg (0.05 mmol) of (±)-perforenone in 1 mL of dry toluene at −15 °C was added dropwise 41 μL of a 1.5 M solution of DIBAL-H in toluene (Aldrich). After being stirred for 1 h at −15 °C, the reaction mixture was quenched by the addition of 5 mL of wet ether followed by the addition of 2 drops of water. Standard ethereal workup provided a crude residue, which was chromatographed (elution with hexanes/ether, 1:1) on silica gel to yield 9.1 mg of a 1:4 mixture of (±)-guadalupol (**26**) and (±)-epiguadalupol (**25**) based on NMR integration.

Reduction of (±)-Perforenone Using Lithium Tri-*tert*-butoxyaluminohydride. To a solution of 12 mg (0.05 mmol) of (±)-perforenone in 1 mL of dry THF at −15 °C was added 15.5 mg (0.06 mmol) of lithium tri-*tert*-butoxyaluminohydride in four equal portions over a 15-min period. The reaction mixture was stirred an additional 1 h at −15 °C and then quenched with water and extracted with two 25-mL portions of ether. The combined ethereal extracts were washed with brine, dried over anhydrous magnesium sulfate, and filtered and the solvent removed in vacuo. The crude residue obtained was purified via chromatography on silica gel (elution with hexanes/ether, 3:1) to afford 1 mg of **26** and 10 mg of **25**, which were identical with material previously characterized.

Preparation of (±)-Guadalupol Benzoate (51).[57] To a solution of 53 mg (0.24 mmol) of (±)-epiguadalupol **25** and 192 mg (0.73 mmol) of triphenylphosphine, in 1 mL of dry THF, was added dropwise at room temperature over a 1-h period a solution of 45 mg (0.36 mmol) of benzoic acid and 58 μL (0.36 mmol) of diethyl azodicarboxylate in 1 mL of dry THF. The resulting mixture was stirred at room temperature for 5 h. Standard ethereal workup provided an oily residue, which was chromatographed on silica gel (elution with hexanes/ether, 4:1) to provided 51 mg (66%) of benzoate **51**, which was homogeneous by TLC analysis (hexanes/ether, 2:1; R_f(**25**) 0.30, R_f(**51**) 0.95): ^{1}H NMR (CCl_4) δ 0.90 (m, 6 H), 1.40 (s, 3 H), 1.67 (s, 3 H), 1.8–2.6 (m, 10 H), 3.51–3.53 (m, 1 H), 7.25–8.15 (m, 5 H); IR (film) 2950–2850, 1680, 1460, 1380, 1260, 1100, 1040, 1000, 800 cm^{-1}; mass spectrum, m/z 323 (M$^+$).

Guadalupol (26) via $LiAlH_4$ Reduction. To a solution of 51 mg (0.16 mmol) of benzoate **51** in 1 mL of dry ether was added 9.6 mg (0.25 mmol) $LiAlH_4$ at 0 °C. The reaction mixture was stirred for 30 min and then quenched with water. Standard ethereal workup provided a crude residue, which was chromatographed on silica gel (elution with hexanes ether, 4:1) to afford 13 mg (38%) of pure (±)-guadalupol (hexanes/ether, 2:1; R_f(**51**) 0.95, R_f(**26**) 0.40) which was identical with that previously characterized.

A mixture of guadalupol and benzyl alcohol (27 mg) was also obtained. No further purification of this mixture was attempted.

(±)-Guadalupol (26) via Sodium Methylate Transesterification. To a stirred solution of 6 mg (0.11 mmol) of sodium methylate [Aldrich] in 0.5 mL dry MeOH was added 17 mg (0.05 mmol) of benzoate **51** in 0.5 mL dry MeOH. The reaction mixture was stirred at 0 °C for 4 h and then quenched with water. Standard ethereal workup provided a crude residue, which was chromatographed on silica gel (elution with hexanes/ether, 4:1) to afford 71 mg (61%) of pure (±)-guadalupol, which was identical with that previously characterized.

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