Cyclobutenone-Based Syntheses of Polyquinanes and Bicyclo[6.3.0]undecanes by Tandem Anionic Oxy-Cope Reactions. Total Synthesis of (±)-Precapnelladiene

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The addition of ethenyllithium derivatives to the carbonyl of dialkyl squarate-derived bicycloheptenones, e.g., **1a** and **6a**, initiates a low-temperature anion-accelerated oxy-Cope rearrangement to provide polyquinanes by a transannular aldol reaction of the intermediate bicyclo[6.3.0]-undecadienone **4**. Additional functionality is introduced by alkylation of the enolate **3** resulting from the oxy-Cope rearrangement. Phosphorylation or triflation of enolate **3** provides an entry into the bicyclo[6.3.0]undecane ring system. An application of this new methodology is demonstrated by the total synthesis of the sesquiterpene natural product (±)-precapnelladiene from diisopropyl squarate (10 steps, 12%).

Introduction

Over 30 years have passed since the first structure determination of a polyquinane natural product,[3] and yet the development of synthetic methods for this class of often disparately functionalized compounds continues unabated.[4] Several of these methods provide rapid and efficient access to polyquinanes but often lack generality and, in some cases, lead to products having an undesirable oxidation level.[5] Many of these problems are now circumvented by the results of the study reported herein. Specifically, a general, regiospecific, tandem reaction sequence leading to highly substituted linearly-fused polyquinanes from readily available dialkyl squarates and various organometallic reagents is now presented.[6,7] Its primary advantage is that it allows the strategic placement of functionality at nearly every position of the polyquinane skeleton by a judicious choice of the starting organometallic reagents. A further compliment is the observation that the linear analogues available by this route have recently been shown to function as precursors to angularly fused isomers, a transformation of some significance since both ring systems are commonly found in nature[8]

A variant of the new tandem sequence also provides access to bicyclo[6.3.0]undecadienones, still another ring system found in nature. The utility of this modification will be illustrated by its employment as the key reaction sequence in a total synthesis of the naturally occurring sesquiterpene (±)-precapnelladiene (**47**).

Results and Discussion

The new methodology relies on a charge and strain accelerated, low-temperature,[9] oxy-Cope[10] rearrangement which converts readily available bicyclo[3.2.0]heptenones, such as **1a**, into bicyclo[6.3.0]undecadienones **4** via the intermediate alkoxide **2** and ring-expanded enolate **3** upon treatment with vinyllithium at −78 °C (Scheme 1).[11] Hydrolysis of the resulting silyl enol ether moiety in **4** during the workup procedure initiates a transannular ring closure to provide the triquinane **5** (69%). In a complementary study, bicycloheptanones bearing an exocyclic silyl enol ether moiety, e.g., **6a**, were observed to undergo a similar transformation to give **7** and subsequently the triquinane **8** (48%).

The required bicycloheptenones precursors, **1a**−**c**, and bicycloheptanones, **6a**−**c**, were prepared as outlined in Schemes 2 and 3, respectively. The bicycloheptenone series arises from dimethyl squarate **9** which gave the ketal **10**[12] (75%) upon treatment with, for example, methyllithium followed by addition of trifluoroacetic

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(3) For reviews of the synthesis of polyquinanes, see: Mehta, G.; Srikrishna, A. *Chem. Rev.* **1997**, *97*, 671. Paquette, L. A.; Doherty. A. M. *Polyquinane Chemistry*. In *Reactivity and Structure Concepts in Organic Chemistry*; Springer-Verlag: New York, 1987; Vol. 26. Trost, B. M. *Chem. Soc. Rev.* **1982**, *11*, 141−170. Paquette, L. A. *Top. Curr. Chem.* **1979**, *79*, 43−152. Hudlicky, T.; Rulin, F.; Lovelace, T. C.; Reed, J. W. In *Studies in Natural Products Chemistry*; Atta-ur-Rahman, Ed.; Elsevier: Amsterdam, 1989; Vol. 3, pp 3−72.

(4) For examples see the following and references cited therein: Santora, V. S.; Moore, H. W. *J. Org. Chem.* **1996**, *61*, 7976. Jung, M. E.; Rayle, H. L. *J. Org. Chem.* **1997**, *62*, 4601. Enholm, E. J.; Zia, Z. Z. J. *J. Org. Chem.* **1997**, *62*, 174.

(5) Paquette, L. A.; Doyon, J. *J. Org. Chem.* **1997**, *62*, 1723 and references therein.

(6) For a preliminary account of this work see: Santora, V. S.; Moore, H. W. *J. Am. Chem. Soc.* **1995**, *117*, 8486.

(7) For recent examples of other tandem reactions involving oxy-Cope reactions, see: Jacobi, P. A.; Armacost, L. M.; Brielmann, H. L.; Cann, R. O.; Kravitz, J. I.; Martinelli, M. J. *J. Org. Chem.* **1994**, *59*, 5292−5304. Balakumar, A.; Janardhanam, S.; Rajagopalan, K. *J. Org. Chem.* **1993**, *58*, 5482−5486. Paquette, L. A.; Shi, Y.-J. *J. Org. Chem.* **1989**, *54*, 5205−5207. Jisheng, L.; Gallardo, T.; White, J. B. *J. Org. Chem.* **1990**, *55*, 5426−5428.

(8) MacDougall, J. M.; Moore, H. W. *J. Org. Chem.* **1997**, *62*, 4554.

(9) The presence of the bicyclo[3.2.0]heptenol could not be detected by analysis of the crude reaction mixture that was obtained upon quenching the oxy-Cope reaction at −78 °C.

(10) For reviews of the oxy-Cope rearrangement, see: (a) Paquette, L. A. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 609−626. (b) Lutz, R. P. *Chem. Rev.* **1984**, *84*, 206−290.

(11) For an elegant example of this rearrangement on similar bicyclo[3.2.0] systems, see: Gadwood, R. C.; Lett, R. M.; Wissinger, J. E. *J. Am. Chem. Soc.* **1986**, *108*, 6343.

(12) Moore, H. W.; Liu, H.; Gayo, L. M.; Sullivan, R. W.; Choi, A. Y. H. *J. Org. Chem.* **1994**, *59*, 3284.

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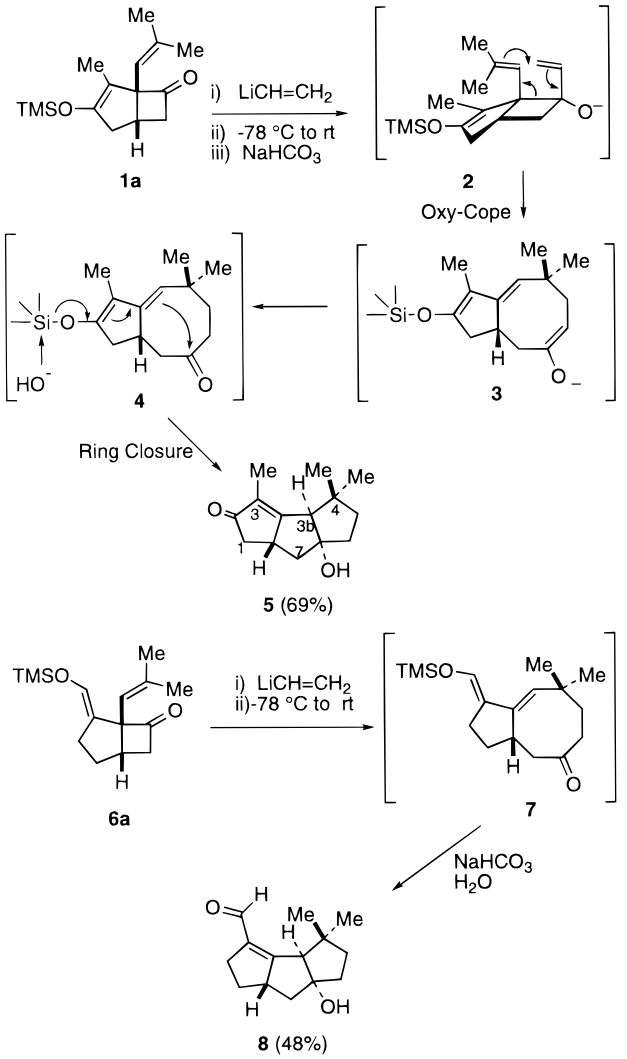
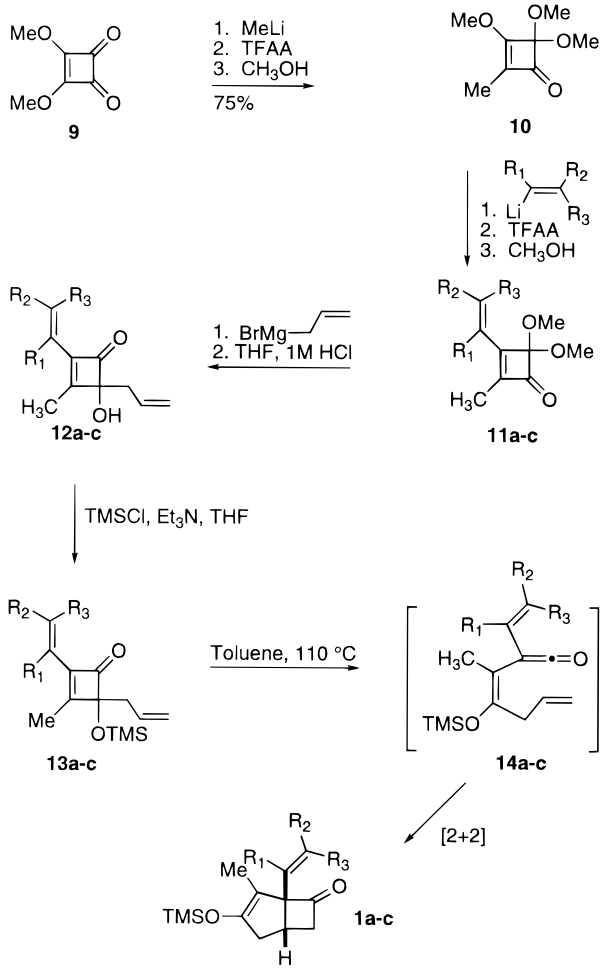
Scheme 1



anhydride (TFAA) and an anhydrous methanol quench (Scheme 2).[13] Subsequent addition of, respectively, 1-lithio-2-methylpropene, vinyllithium, and 1-lithiocyclopentene to **10** followed by trifluoroacetylation of the β-alkoxy enol ether and then workup under mildly basic conditions gave the corresponding cyclobutenedione monoketals **11a**−**c** in yields ranging from 70 to 77%. Treatment of these with allylmagnesium bromide followed by hydrolysis of the dimethyl ketal provided the 4-allyl-4-hydroxycyclobutenones **12a** (93%), **12b** (75%), and **12c** (86%).[14] Trimethylsilylation of the 4-hydroxy group (TMSCl) gave **13a**−**c** which upon thermolysis (toluene, 110 °C) resulted in a torquoselective[15] electrocyclic ring opening to the vinylketene intermediates **14a**−**c**. The ketene then undergoes an intramolecular [2 + 2] cycloaddition to the allyl double bond to give bicyclo[3.2.0]-heptenones **1a**−**c** in nearly quantitative yield.[16−18]

Scheme 2



	R_1	R_2	R_3	%11	%12	%13	%1
a	H	CH_3	CH_3	77	93	94	98
b	H	H	H	74	75	81	98
c	$-CH_2CH_2CH_2-$		H	70	86	70	98

The bicyclo[3.2.0]heptanones series **6a**−**c** was prepared in a related manner (Scheme 3). For example, treatment of diisopropyl squarate **15** with 1-lithio-2-methylpropene or vinyllithium followed by TFAA and an aqueous workup gave **16a** (94%) and **16b** (94%), respectively. Selective reduction of the more electrophilic carbonyl group in **16a** gave **18** in high yield (93%). Addition of 4-lithio-1-butene to the vinylogous ester in **18** and then acid hydrolysis of the resulting β-hydroxyl enol ether was accomplished in a one-pot operation to give **19** (80%). Trimethylsilyation and thermal rearrangement as described above then gave **6a** in 76% isolated yield (53% overall from **15**). In an analogous fashion, **16a** was converted to **17a** (75%) upon sequential treatment with methyllithium, trimethylsilyl chloride, and 4-lithio-1-butene followed by acid hydrolysis. Hydroxyl group protection (67%) and rearrangement gave **6b** in quantitative yield (47% overall from **15**). Finally, employing this same sequence of reactions allowed the conversion of **16b** to **6c** in 46% overall yield from **15**.

(13) For the preparation of dialkyl squarates from squaric acid, see: Lui, H.; Tamooka, C. S.; Moore, H. W. *Synth. Commun.* **1997**, *27*, 2177.

(14) This is an excellent procedure for the regiospecific preparation of substituted cyclobutenones. For more details see: Gayo, L.; Winters, M. P.; Moore, H. W. *J. Org. Chem.* **1992**, *57*, 6896.

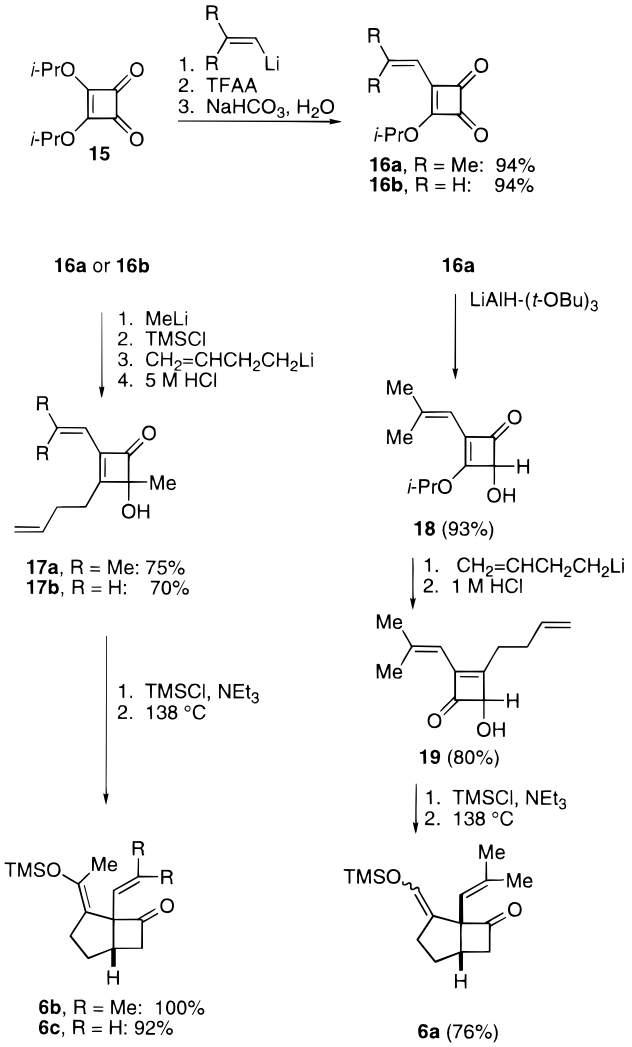
(15) For references to the torquoselective ring opening of cyclobutenes and cyclobutenones see: Kirmse, W.; Rondan, N. G.; Houk, K. N. *J. Am. Chem. Soc.* **1984**, *108*, 7989. Niwayama, S.; Kallel, E. A.; Houk, K. N. *J. Org. Chem.* **1996**, *61*, 2517.

(16) Moore, H. W.; Xu, S. L. *J. Org. Chem.* **1989**, *54*, 6018. Moore, H. W.; Xia, H.; Xu, S. L. *J. Org. Chem.* **1991**, *56*, 6094.

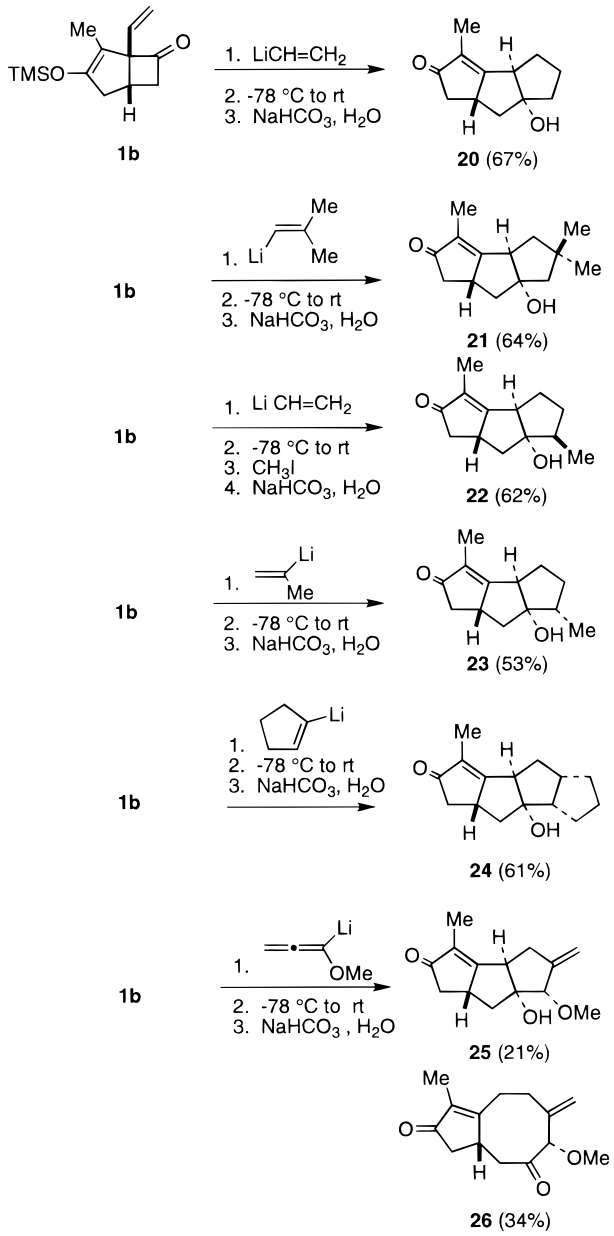
(17) For reviews on intramolecular ketene cycloadditions see: Snider, B. *Chemtracts* **1991**, 403. Snider, B. *Chem. Rev.* **1988**, *88*, 793.

(18) For a review concerning the synthetic applications of cyclobutenones, see: Moore, H. W.; Yerxa, B. R. *Advances in Strain in Organic Chemistry*; JAI Press: Greenwich, CT, 1995; Vol. 4.

Scheme 3



Scheme 4

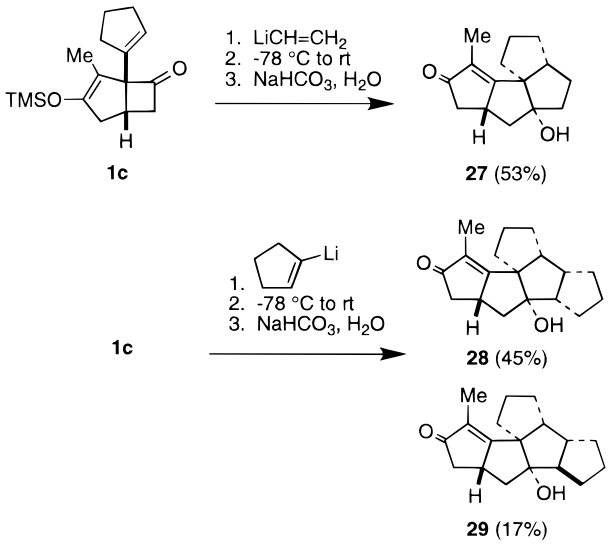


The bicyclo[3.2.0]heptenone derivative **1b** participates comparably in the tandem sequence with a number of different ethenyllithium reagents to afford both tri- and tetraquinanes **20**−**25** in yields ranging from 21 to 67% (Scheme 4). Some noteworthy observations regarding these transformations are the following: (1) The methyl group at position-1 of **22** is introduced stereospecifically by capture of the intermediate bicyclo[6.3.0]undecadienone enolate (convex face methylation) prior to the transannular ring closure. (2) The stereochemistry at position-1 has been inverted in **23** by utilizing 2-propenyllithium as the oxy-Cope-initiating ethenyl anion in place of the vinyllithium/MeI sequence (convex face protonation). (3) As evidenced by the conversion of **1b** to the tetraquinane **24**, cyclic as well as acyclic vinyllithium reagents can be employed in the oxy-Cope reaction. (4) Formation of the bicyclo[6.3.0]undecendione (cyclopentacyclooctenes) **26** as the major product of the reaction of **1b** with 1-lithio-1-methoxyallene is interesting and may suggest a subtle conformational change imparted by the additional sp^2 carbon atom in the eight-membered ring which reduces the facility of the transannular ring closure.

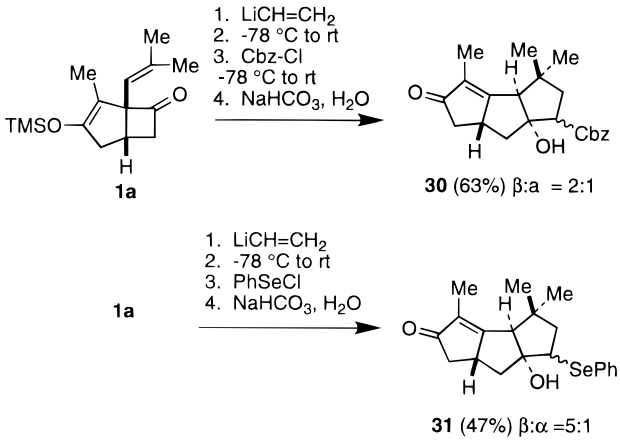
The new reaction sequence can also be used to construct angularly fused polyquinanes when the starting bicyclo[3.2.0]heptenone bears a cyclic alkene at the bridgehead position (Scheme 5). For example, bicyclo[3.2.0]heptenone **1c**, possessing a cyclopentene ring at the bridgehead position, leads to the tetraquinane **27** (53%) when treated with vinyllithium. Analogously, the pentaquinanes **28** (45%) and **29** (17%) resulted when **1c** was treated with 1-lithiocyclopentene.

A useful aspect of the tandem sequences outlined herein is that the anionic oxy-Cope reaction gives an enolate anion intermediate (e.g., **3**) that can be trapped with various electrophiles prior to the transannular ring closure, thus providing a convenient route for further functionalization of the polyquinane skeleton. An example of this has already been illustrated in the conversion of **1b** to the triquinane **22**, where the enolate was trapped by methyliodide. Additional examples are provided in Scheme 6. For example, treatment of **1a** with vinylithium followed by carbobenzoxy chloride (Cbz-Cl) and basic workup gave the triquinane **30** as a 2:1 mixture of the β- and α-diastereomers, respectively. In an analogous manner, **1a** gave **31** in 47% isolated yield as a 5:1 mixture of the β- and α-isomers. The enhanced diastereoselectivity ($\beta/\alpha = 5{:}1$) observed in the formation of selenides **31** is not surprising since, unlike the Cbz

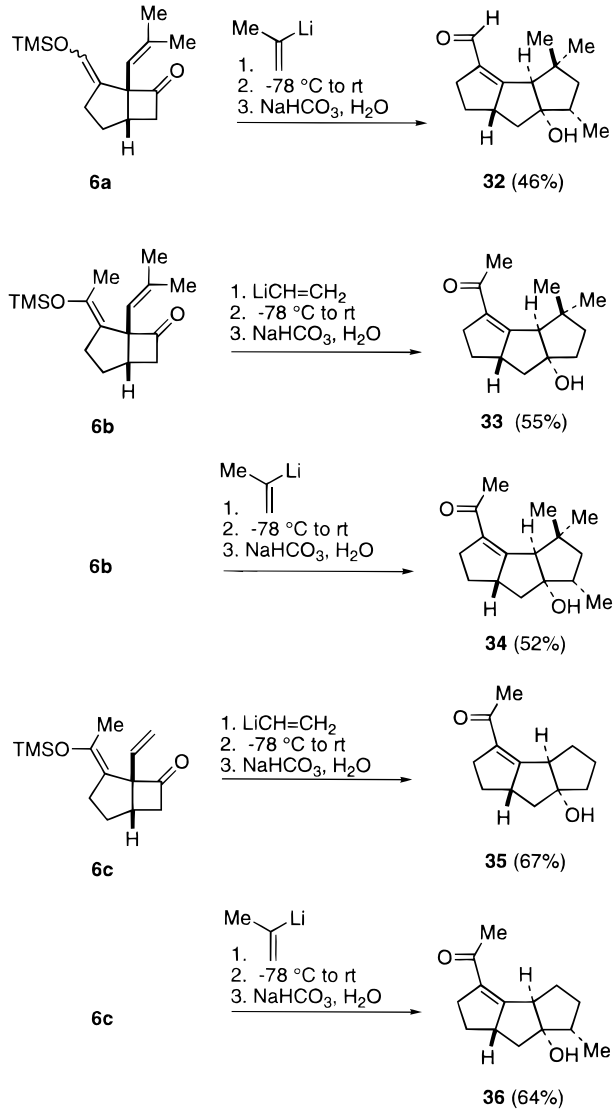
Scheme 5



Scheme 6



Scheme 7



analogues, the selenides would by less likely to undergo facile equilibration at the stereogenic center.

The scope of the polyquinane synthesis was extended to include the conversion of **6a**−**c** to the triquinanes **8** and **32**−**36**. These transformations allow placement of synthetically versatile aldehyde or methyl ketone moieties at position-4 of the linear triquinane (Scheme 7).

Still another advantage of the methodology outlined here is the ability to direct the product distribution to favor bicyclo[6.3.0]undecane formation by *O*-alkylation of the enolate resulting from the initial anionic oxy-Cope rearrangement (Scheme 8). This is noteworthy since the latter ring system is found in a number of natural products.[19] It was reasoned that the more robust *tert*-butyldimethylsilyl group (TBS) in **39** as compared to the TMS group in **4** would allow isolation of the bicyclic system.[20] This was successfully accomplished as outlined below. Treatment of the tertiary alcohols **12a**,**b** with TBSOTf in the presence of 2,6-lutidine gave **37a**,**b**. Subsequent thermal rearrangement (toluene, 110 °C) of these gave **38a** (99%) and **38b** (98%), respectively. Treatment of these with vinyllithium initiated the oxy-Cope rearrangement to **39a**,**b**, which were both isolated in 62% yield. Conversion of these enol ethers to the linear triquinanes **5** and **20** upon treatment with aqueous TBAF occurs in excellent yield and underscores the facility in which the transannular ring closure portion of the tandem route occurs.

In comparison, when the lithium enolate **3** was quenched with *N*-phenyl trifluoromethanesulfonimide or diphenyl chlorophosphate prior to aqueous workup, the enol triflate **40a** (72%) or the diphenyl chlorophosphate[21] **40b** (71%) were obtained. Termination of the transannular ring closure portion of the tandem sequence was extended to the bicyclo[3.2.0]heptanones **42** which was prepared by ring expansion of the TBS-protected cyclobutenone **41**. Oxy-Cope ring expansion upon treatment of **42** with vinyllithium then gave **43** in 64% isolated yield as a 4:1 mixture of diastereomers.

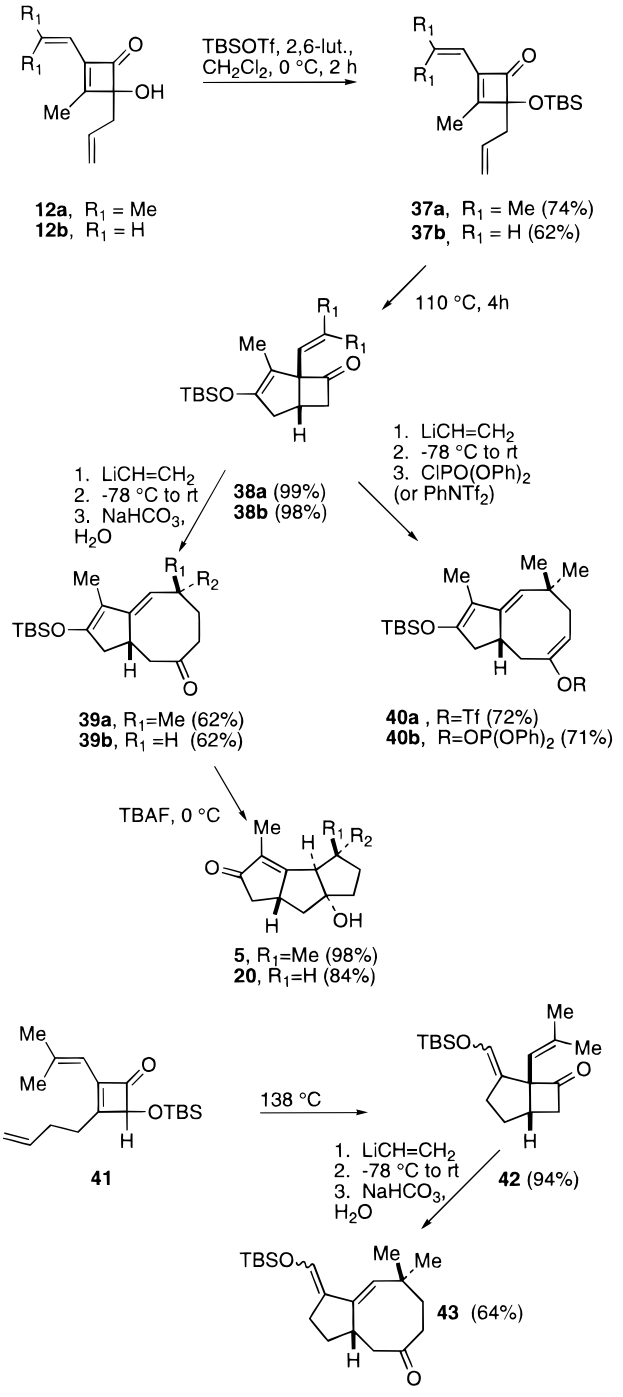
An application of the 3-homoallylcyclobutenone rearrangement to bicyclo[3.2.0]heptanones and the subse-

(19) For an excellent review on the synthesis of eight-membered rings see: Petasis, N. S.; Patane, M. A. *Tetrahedron* **1992**, 5757.

(20) For selected other methods of constructing the bicyclo[6.3.0]-undecane ring system, see: (a) Wender, P. A.; Nuss, J. M.; Smith, D. B.; SuarezSobrino, A. *J. Org. Chem.* **1997**, *62*, 2, 4908. (b) Snapper, M. L.; Tallarico, J. A.; Randall, M. L. *J. Am. Chem. Soc.* **1997**, *119*, 1478.

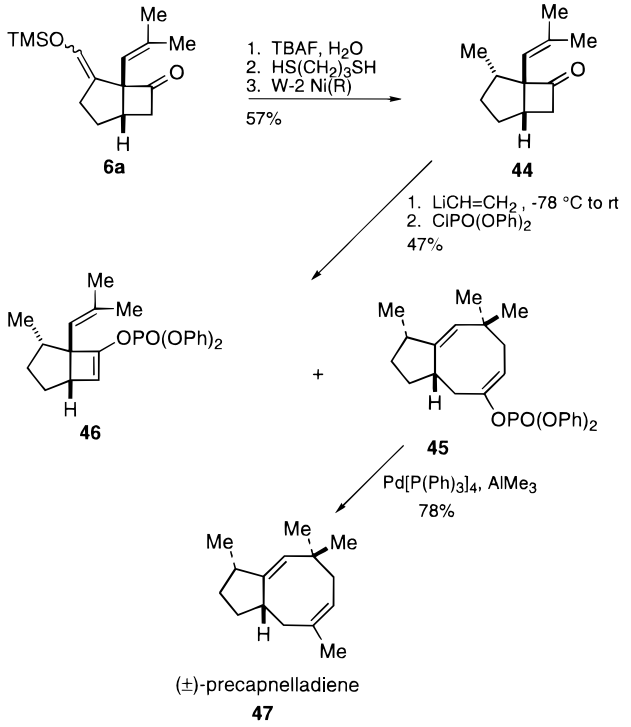
(21) For a recent example of the use of diphenyl phosphates, see: Nicolaou, K. C.; Shi, G.-Q.; Gunzner, J. L.; Gartner, P.; Yang, Z. *J. Am. Chem. Soc.* **1997**, *119*, 5467.

Scheme 8



quent utility of these as precursors to bicyclo[6.3.0]-undecadienes is shown in Scheme 9, in which the total synthesis of the sesquiterpene natural product (±)-precapnelladiene (**47**) is outlined. Highlights of the synthesis include establishment of the stereochemistry of the cyclopentyl methyl group at the bicyclo[3.2.0]-heptanone stage and control of the 1,5-cyclooctadiene regiochemistry through the oxy-Cope ring expansion. Treatment of **6a** with aqueous acid resulted in the formation of a 10:1 mixture of diastereomeric aldehydes, which favored the desired α-epimer as established by a single-crystal X-ray analysis of the major isomer. Chemoselective thioacetalization of the aldehyde carbonyl followed by desulfurization with W-2 Raney nickel afforded **44** (53% from **41**). Addition of vinyllithium induced the

Scheme 9



oxy-Cope ring expansion, and the resulting enolate was trapped as its diphenyl phosphate derivative to afford a mixture of **45** (47%) and **46** (12%). Exposure of **45** to $AlMe_3$ in the presence of catalytic $Pd[PPh_3]_4$ provided **47** (44−78%). Spectral data for this compound were identical in all respects to those of the natural product.[22,23]

Unsuccessful attempts were also made to prepare (±)-precapnelladiene from the C-5 methyl derivatives of **40a**,**b**. Unfortunately, desilyation of these gave the corresponding cyclopentenone analogues thus destroying the required 1,5-cyclooctadiene regiochemistry needed for the natural product.

Structure Assignments

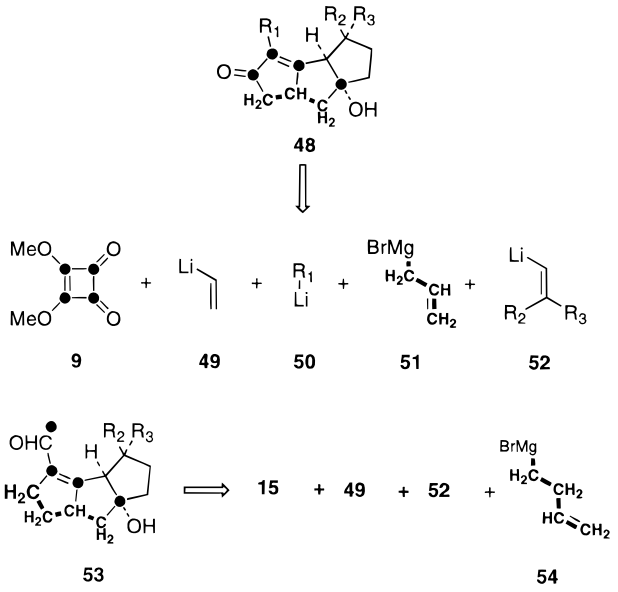
The structure assignments of the new compounds reported here are in agreement with their observed spectral data (Experimental Section). Also, with respect to the polyquinanes, they are either directly or indirectly assigned on the basis of single-crystal X-ray structure determination. Specifically, the structures of **5**, **23**, **27**, and **29** were determined by single-crystal X-ray crystallography. Having the structure of **23** allows an unambiguous assignment of its epimer **22**. Similarly, the structure of **29** allows the assignment of **28** and the structure of **5** accounts for the assignment of **30** and **31**. Thus, having the structures of **5**, **22**, **23**, and **27**−**31** provides the foundation for the assignments of the related polyquinanes **20**, **21**, **24**, **25, 8**, and **32**−**36**.

The stereochemistry at position-6 (Scheme 1, structure **5**) in each linear triquinane would be expected to be controlled by convex face attack of the electrophile (H^+, CH_3I, CbzCl, PhSeCl) on the enolate generated in the oxy-Cope rearrangement prior to transannular ring

(22) For a preliminary account of the precapnelladiene synthesis see: MacDougall, J. M.; Turnbull, P.; Verma, S. K.; Moore, H. W. *J. Org. Chem.* **1997**, *62*, 3792.

(23) The authors are grateful to Professor Leo Paquette for providing an ^1H NMR spectrum of an authentic sample of (±)-precapnelladiene.

Scheme 10



closure. In the case of the diastereomers of **31**, the relative stereochemistry was confirmed by comparative NOE studies. Irradiation of the methine proton on the selenium-bonded carbon in the major diastereomer [δ 3.44 (ddd, J = 13.8, 7.0, 1.2 Hz)] resulted in an enhancement of the signal for the C-3 methyl protons on the α-face [δ 1.31 (s)].[24] Irradiation of the corresponding proton [δ 2.98 (d, J = 12.2 Hz)] in the minor diasteriomer resulted in a weaker effect. The deshielding effect in the major diasteriomer may result from the proximity of this hydrogen to nonbonding electrons on the vicinal hydoxyl on the same face. The same effect is observed in the ^{1}H NMR spectra of the carbobenzyloxy analogues **30**.

Conclusions

In conclusion, the following significant points are noted: (1) The tandem oxy-Cope/transannular ring closure sequence represents an important advance in the preparation of highly functionalized polyquinanes and contributes to the already considerable synthetic utility of cyclobutenone derivatives.[18] (2) Syntheses of the bicyclo[3.2.0]heptenones as outlined in Schemes 2 and 3 are noteworthy not only because they provide an efficient route to these versatile synthetic intermediates but also because they present a general and selective route to vinylketenes of the appropriate geometry and substitution pattern to allow facile intramolecular ketene/alkene [2 + 2] cycloadditions. (3) Although the tandem sequence is particularly important for the synthesis of polyquinanes, it can be terminated after the oxy-Cope step, thus providing a useful synthetic route to bicyclo[6.3.0]-undecenones. (4) It is particularly noteworthy that the oxy-Cope/transannular methodology presented here translates to readily available and simple starting materials. In this regard, it is noted that the generalized triquinane **48** comes from dimethyl squarate **9** and the organometallic reagents, **49**−**52** (Scheme 10). Analogously, the triquinane **53** stems from **9**, **49**, **52**, and the homoallyl Grignard reagent, **53**.

Experimental Section

General Information. All reactions were conducted under a positive pressure of nitrogen or argon at ambient temperature using flame-dried glassware unless otherwise indicated. Temperatures designated to be 0 or −78 °C are approximate and refer to bath temperatures. Air- and moisture-sensitive liquids were transferred via syringe at ambient temperature or via cannula at −78 °C through rubber septa. Silica gel (230−400 mesh) was used for column chromatography (chromatography) unless otherwise specified.[25] Tetrahydrofuran and diethyl ether (ether) were purged with nitrogen and then passed through two 4 × 36 in. columns of anhydrous neutral A-2 alumina (8 × 14 mesh; LaRoche Chemicals; activated under a flow of nitrogen at 350 °C for 3.5 h) to remove water. Toluene, *p*-xylene, 1,2-dichloroethane and CH_2Cl_2 were distilled from CaH_2 immediately before use. Triethylamine and 2,6-lutidine were distilled from CaH_2 and stored over KOH pellets. *n*-Butyllithium and *tert*-butyllithium were used as solutions in hydrocarbon solvents. Methyllithium and vinyllithium were used as solutions in ether. Methyliodide was filtered through a pipet of basic alumina under N_2 before use. All other solvents and reagents were used as received. ^{1}H NMR and ^{13}C NMR spectra were recorded at 500 and 125 MHz, respectively, in $CDCl_3$ unless specified otherwise. Melting points are uncorrected.

General Procedure for the Thermolytic Rearrangement of 4-Allylcyclobutenones. (±)-2-Methyl-1-(2-methyl-1-propenyl)-3-[(trimethylsilyl)oxy]bicyclo[3.2.0]hept-2-ene-7-one (1a). A toluene (75 mL) solution of **13a** (220 mg, 0.83 mmol) was heated at reflux for 4 h, cooled to room temperature, and concentrated. The resulting oil was dissolved in a minimum amount of dry $CHCl_3$ and filtered ($CHCl_3$) through a pipet column of basic alumina (1 in.). Concentration gave **1a** (216 mg, 98%) as a pale yellow oil: ^{1}H NMR δ 5.37 (s, 1H), 3.30 (dd, J = 9.0, 18.0 Hz, 1H), 2.90−2.85 (m, 1H), 2.77 (dd, J = 18.0, 5.0 Hz, 1H), 2.58−2.50 (m, 1H), 2.27 (d, J = 16.0, 1H), 1.72 (d, J = 1.0, 3H), 1.53 (s, 3H), 1.46 (m, 3H), 0.21 (s, 9H); ^{13}C NMR δ 209.0, 147.3, 136.6, 120.5, 114.0, 80.3, 50.9, 40.2, 30.7, 26.0, 18.9, 9.1, 0.6 (3C); IR (film, cm^{-1}) 1772, 1670; HRMS (CI) calcd for $C_{15}H_{25}O_2Si$ (MH^+) *m/e* 265.1624, obsd *m/e* 265.1613.

General Method for the Tandem Oxy-Cope/Aldol Sequence. (±)-1,3bα,4,5,6,6a,7,7a*β*-Octahydro-6aα-hydroxy-3,4,4-trimethyl-1*H*-cyclopenta[*a*]pentalen-2-one (5). To a −78 °C THF (40 mL) solution of **1a** (180 mg, 0.681 mmol) was added vinyllithium (0.45 mL, 0.81 mmol), and after 10 min the cooling bath was removed. After 1 h, saturated aqueous $NaHCO_3$ was added, and after an additional 10 min, the mixture was extracted with ether. The combined organic layers were washed with brine, dried ($MgSO_4$), filtered, and concentrated. Chromatography (3:1 hexanes/EtOAc) gave **5** (103 mg, 69%) as a colorless oil that formed a white solid upon standing. Recrystallization (EtOAc/pentane) gave white crystals: mp, 93−94 °C; ^{1}H NMR δ 2.85 (bs, 1H), 2.65−2.59 (m, 2H), 2.38 (dd, J = 12.0, 7.5 Hz, 1H), 2.11−1.95 (m, 4H), 1.85−1.78 (m, 1H), 1.70 (s, 3H), 1.58−1.53 (m, 1H), 1.32−1.27 (m, 1H), 1.30 (s, 3H), 0.88 (s, 3H); ^{13}C NMR δ 209.6, 181.6, 134.2, 93.4, 63.5, 46.8, 44.2, 43.0, 41.6, 41.3, 41.1, 30.8, 25.5, 8.8; IR (film, cm^{-1}) 3425, 1694, 1658; HRMS (EI) calcd for $C_{14}H_{20}O_2$ (M^+) *m/e* 220.1463, obsd *m/e* 220.1458.

General Procedure for the Thermolytic Rearrangement of 3-Homoallylcyclobutenones. (±)-(*E,Z*)-2-[(Trimethylsilyl)oxy]methylene-1-(2-methyl-1-propenyl)-2-bicyclo[3.2.0]heptan-7-one (6a). A *p*-xylene (23 mL) solution of 3-(3-butenyl)-2-(2-methyl-1-propenyl)-4-[(trimethylsilyl)oxy]-2-cyclobuten-1-one (120 mg, 0.45 mmol) was heated at reflux for 1.5 h. Concentration and filtration through a plug of Florisil (10:1 hexanes/EtOAc) gave **6a** (120 mg, 100%) as yellow oil that consisted of a mixture of *E*- and *Z*-diastereomers in the ratio of 4.5:1, respectively: ^{1}H NMR (mixture) δ 6.10 (s, 1H), 5.98 (s, 1H), 5.40 (s, 1H), 5.35 (s, 1H), 3.15 (dd, J = 18.4, 9.1 Hz, 2H), 2.93−2.83 (m, 3H), 2.65 (dd, J = 18.4, 5.7

(24) The C-3 methyl on the α-face is deshielded relative to the C-3 methyl group on the *β*-face, which is above the plane of the C-3b/C-4 carbon double bond (Scheme 6). See, for example: Romo De Vivar, A.; Nieto, D. A.; Gavino, R.; Ana-Lidia Perez, C. *Phytochemistry* **1995**, *40*, 167.

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

Hz, 1H), 2.38−2.18 (m, 4H), 2.05−1.96 (m, 2H), 1.86−1.82 (m, 2H), 1.74 (s, 3H), 1.72 (s, 3H), 1.60 (s, 3H),1.57 (s, 3H), 0.15 (s, 9H), 0.14 (s, 9H); ^{13}C (major diastereomer) NMR δ 210.7, 136.4, 135.1, 125.8, 122.9, 76.8, 48.5, 39.7, 30.6, 26.1, 25.7, 20.1, −0.47 (3C); IR (film, cm^{-1}, mixture) 1778, 1669; HRMS (CI, mixture) calcd for $C_{15}H_{24}SiO_2$ (M^+) *m/e* 264.1546, found *m/e* 264.1539.

4,4-Dimethoxy-2-methyl-3-(2-methyl-1-propenyl)-2-cyclobuten-1-one (11a). 1-Bromo-2-methylpropene (0.65 mL, 6.3 mmol) was added to a −78 °C THF (50 mL) solution of *tert*-butylithium (9.0 mL, 12.6 mmol), and after 30 min the colorless solution was transferred to a −78 °C THF (120 mL) solution of ketal **10**[12] (0.78 g, 4.53 mmol) over 20 min. Trifluoroacetic anhydride (1.4 mL, 9.9 mmol) was added after 10 min, followed by saturated aqueous $NaHCO_3$ after an additional 10 min. The mixture was warmed to room temperature and extracted with ether. The combined organic layers were washed with brine, dried ($MgSO_4$), filtered, and concentrated. Chromatography (4:1 hexanes/EtOAc) gave **11** (684 mg, 77%) as a yellow-green oil: ^{1}H NMR δ 6.20 (s, 1H), 3.44 (s, 6H), 2.06 (s, 3H), 2.01 (s, 3H), 1.81 (s, 3H); ^{13}C NMR δ 196.6, 173.9, 152.4, 149.6, 116.8, 115.4, 53.4 (2C), 27.9, 21.5, 7.3; IR (film, cm^{-1}) 1746, 1632, 1586; HRMS (EI) calcd for $C_{11}H_{16}O_3$ (M^+) *m/e* 196.1099, *m/e* obsd 196.1092.

4-Hydroxy-3-methyl-2-(2-methyl-1-propenyl)-4-(3-propenyl)-2-cyclobuten-1-one (12a). To a −78 °C THF (200 mL) solution of **11** (1.41 g, 7.19 mmol) was added allylmagnesium bromide (8.6 mL, 8.6 mmol) over 5 min. This caused the green color of the solution to fade to cloudy gray upon consumption of the dienone. Water was added after 15 min, and the mixture was warmed to room temperature and extracted with ether. The combined organic layers were washed with brine, dried (Na_2SO_4), filtered, and concentrated to provide the crude ketal−alcohol intermediate. To a 0 °C THF (200 mL) solution of the crude ketal−alcohol was added HCl (1 M, aqueous, 0.5 mL). After 40 min, saturated aqueous $NaHCO_3$ was added and the product was isolated in the same manner as the ketal−alcohol intermediate. Chromatography (3:1 hexanes/EtOAc) gave **12a** (1.29 g, 93%) as a pale yellow oil: ^{1}H NMR δ 5.82−5.70 (m, 1H), 5.50 (s, 1H), 5.15−5.10 (m, 2H), 3.04 (bs, 1H), 2.58−2.55 (m, 2H), 2.11 (s, 3H), 1.97 (s, 3H), 1.83 (s, 3H); ^{13}C NMR δ 192.6, 174.4, 147.7, 144.3, 132.3, 119.1, 111.9, 91.6, 38.2, 26.3, 21.3, 11.2; IR (film, cm^{-1}) 3395, 1746, 1663, 1591; HRMS (CI) calcd for $C_{12}H_{16}O_2$ *m/e* 192.1150, obsd *m/e* 192.1153.

3-Methyl-2-(2-methyl-1-propenyl)-4-[(trimethylsilyl)-oxy]-4-(3-propenyl)-2-cyclobuten-1-one (13a). To a THF (50 mL) solution of **12a** (1.29 g, 6.72 mmol) was added NEt_3 (6.4 mL, 45.9 mmol) followed by TMSCl (5.7 mL, 44.9 mmol). A white precipitate of NEt_3·HCl formed immediately. After 5 d the yellow-white mixture was poured onto CH_2Cl_2 (80 mL) and $NaHCO_3$ (saturated, 40 mL). The aqueous layer was extracted with additional CH_2Cl_2, and the combined organic layers were washed with brine, dried (Na_2SO_4), filtered, and concentrated. The residue was immediately chromatographed (Florisil, 4:1 hexanes/EtOAc) to provide **13a** (1.68 g, 94%) as a yellow oil: ^{1}H NMR δ 5.71−5.61 (m, 1H), 5.52 (s, 1H), 5.03 (d, J = 17.0 Hz, 1H), 4.99 (d, J = 10.0 Hz, 1H), 2.55−2.45 (m, 1H), 2.06 (s, 3H), 1.97 (s, 3H), 1.81 (s, 3H) 0.08 (s, 9H); ^{13}C NMR δ 192.5, 175.8, 147.2, 143.7, 133.0, 117.7, 112.0, 93.7, 39.5, 26.2, 21.2, 11.4, 1.2 (3C); IR (film, cm^{-1}) 1754, 1663, 1595; HRMS (EI) calcd for $C_{15}H_{24}O_3Si$ (MH^+) *m/e* 264.1545, obsd *m/e* 264.1554.

3-(4-Butenyl)-4-hydroxy-4-methyl-2-(2-methyl-1-propenyl)-2-cyclobuten-1-one (17a). To a −78 °C THF (100 mL) solution of **16a** (1.0 g, 5.2 mmol) was added MeLi (5.6 mL, 5.7 mmol). After 5 min, TMSCl (0.85 mL, 6.7 mmol) was added and the solution was warmed to 0 °C and then cooled to −78 °C. A THF (100 mL) solution of 4-lithio-1-butene, which was generated from 4-bromo-1-butene (1.32 mL, 12.9 mmol) and *tert*-butyllithium (16.2 mL, 27.5 mmol), was added. HCl (5 M aqueous, 6 mL) was added, and the solution was warmed to room temperature. Saturated aqueous $NaHCO_3$ was added, the mixture was extracted with ether, and the combined organic layers were washed with brine, dried ($MgSO_4$), filtered, and concentrated. Chromatography (3:1 hexanes/EtOAc) provided **17a** (798 mg, 75%) as a pale yellow oil: ^{1}H NMR δ 5.89−5.81(m, 1H), 5.58 (s, 1H), 5.08 (dd, J = 17.1, 1.5 Hz, 1H), 5.04 (dd, J = 10.1, 1.1 Hz, 1H), 2.73−2.61 (m, 2H), 2.46−2.41 (m, 2H), 2.02 (s, 3H), 1.85 (s, 3H), 1.82 (broad s, 1H), 1.49 (s, 3H); ^{13}C NMR δ 194.1, 178.4, 146.7, 144.3, 137.2, 115.6, 112.4, 89.9, 30.8, 26.3, 25.9, 21.2, 19.9; IR (film, cm^{-1}) 3403, 3077, 1751, 1660, 1636; HRMS (EI) calcd for $C_{13}H_{18}O_2$ (M^+) *m/e* 206.1307, obsd *m/e* 206.1299.

4-Hydroxy-3-isopropoxy-2-(2-methylpropenyl)-2-cyclobuten-1-one (18). To a 0 °C THF (100 mL) solution of **16a** (1.59 g, 8.18 mmol) was added lithium tri-*tert*-butoxyaluminohydride (2.30 g, 9.00 mmol) in several portions. After 15 min, HCl (10% aqueous, 20 mL) was added. After an additional 10 min, the mixture was extracted with ether and the combined organic layers were washed with brine, dried ($MgSO_4$), filtered, and concentrated to a pale yellow oil. Chromatography (7:3 hexanes/EtOAc) gave **18** (1.45 g, 93%) as a white crystalline solid: mp, 42−44 °C; ^{1}H NMR δ 5.45 (s, 1H), 5.23 (d, J = 6.0 Hz, 1H), 4.98 (septet, J = 6.0 Hz, 1H), 4.81 (d, J = 6.5 Hz, 1H), 1.92 (s, 3H), 1.79 (s, 3H), 1.44 (d, J = 6.0 Hz, 3H), 1.41 (d, J = 6.0 Hz, 3H); ^{13}C NMR δ 188.5, 178.5, 142.0, 124.6, 110.2, 81.1, 77.8, 26.0, 23.2, 22.5, 21.1, IR (film, cm^{-1}) 3349,1743, 1660, 1587; HRMS (CI) calcd for $C_{11}H_{17}O_3$ (MH^+) *m/e* 197.1177, obsd *m/e* 197.1180.

3-(4-Butenyl)-4-hydroxy-2-(2-methylpropenyl)-2-cyclobuten-1-one (19). To a −78 °C THF (60 mL) solution of **18** (1.15 g, 5.87 mmol) was added a −78 °C THF (50 mL) solution of 4-lithio-1-butene, prepared from *tert*-BuLi (23.6 mL, 40.1 mmol) and 4-bromo-1-butene (1.95 mL, 19.2 mmol) over 30 min. The solution was warmed to room temperature, and HCl (5 M aqueous, 10 mL) was added. $NaHCO_3$ (saturated aqueous, 40 mL) was added after 1 h. The mixture was extracted with ether, and the combined organic layers were washed with brine, dried ($MgSO_4$), filtered, and concentrated. Chromatography (7:3 hexanes/EtOAc) gave **19** (870 mg, 80%) as a colorless oil: ^{1}H NMR δ 5.88−5.80 (m, 1H), 5.58 (d, J = 0.5 Hz, 1H), 5.11−5.01 (m, 3H), 3.34 (s, 1H), 2.71 (t, J = 7.5 Hz, 2H), 2.48−2.37 (m, 2H), 2.00 (s, 3H), 1.84 (s, 3H); ^{13}C NMR δ 190.4, 174.6, 147.8, 144.9, 137.0, 115.8, 112.0, 83.5, 30.1, 26.6, 26.4, 21.3; IR (film, cm^{-1}) 3391, 3078, 1748, 1660, 1581; HRMS (EI) calcd for $C_{12}H_{17}O$ (MH^+) *m/e* 193.1228, obsd *m/e* 193.1225.

General Method for the Tandem Oxy-Cope/Enolate Alkylation Sequence. (±)-1,3bα,4,5,6,6a,7,7a*β*-Octahydro-6aα-hydroxy-3,5,5-trimethyl-1*H*-cyclopenta[*a*]pentalen-2-one (21). To a −78 °C THF (25 mL) of 1-bromo-2-methylpropene (0.15 mL, 1.46 mmol) was added *tert*-butyllithium (1.7 mL, 2.90 mmol). After 30 min, the colorless solution was transferred into a −78 °C THF (30 mL) solution of **1b** (235 mg, 0.995 mmol). The cooling bath was removed after 10 min. After 1 h, workup in the manner analogous to the synthesis of **5** and chromatography (1:1.5 hexanes/EtOAc) gave **21** (140 mg, 64%) as colorless oil: ^{1}H NMR δ 3.18 (t, J = 9.0 Hz, 1H), 2.94 (bs, 1H), 2.60 (dd, J = 18.0, 6.5 Hz, 1H), 2.37 (dd, J = 12.0, 7.5 Hz, 1H), 2.09 (dd, J = 18.0, 2.5 Hz, 1H), 2.05−2.02 (m, 1H), 1.88 (dd, J = 13.5, 2.5 Hz, 1H), 1.86 (bs, 1H), 1.68 (d, J = 2.0 Hz, overlapping m, 4H), 1.27−1.17 (m, 2H), 1.23 (s, 3H), 1.08 (s, 3H); ^{13}C NMR δ 209.9, 182.7, 131.1, 93.6, 56.2, 51.9, 47.5, 47.0, 41.7, 40.8, 40.1, 29.0, 27.2, 8.3; IR (film, cm^{-1}) 3427, 1703, 1659; HRMS (CI) calcd for $C_{14}H_{21}O_2$ (MH^+) *m/e* 221.1533, obsd *m/e* 221.1537.

General Method for the Tandem Oxy-Cope/Enolate Alkylation Sequence. (±)-1,3bα,4,5,6,6a,7,7a*β*-Octahydro-6aα-hydroxy-3,6*β*-dimethyl-1*H*-cyclopenta[*a*]pentalen-2-one (22). To a −78 °C THF (30 mL) solution of **1b** (145 mg, 0.614 mmol) was added vinyllithium (0.50 mL, 0.75 mmol). After 10 min the reaction was warmed to room temperature, and after 1 h MeI (0.80 mL, 1.30 mmol) was added. After an additional 30 min, workup in the manner used to prepare **5** and chromatography (1:1 hexanes/EtOAc) gave **22** (78 mg, 62%) as a white solid: mp, 98−99 °C; ^{1}H NMR δ 3.01 (d, J = 10.0 Hz, 1H), 2.77 (bm, 1H), 2.64−2.56 (m, 2H), 2.23−2.11 (m, 2H), 2.03 (dd, J = 17.5, 2.5 Hz, 1H), 1.96−1.91(m, 1H), 1.70 (d, J = 2.0 Hz, 3H), 1.62 (bs, 1H), 1.61−1.58 (m, 1H), 1.34−1.23 (m, 1H), 1.16 (t, J = 12.5 Hz, 1H), 1.10 (d, J = 7.0 Hz,

3H); ^{13}C NMR δ 210.4, 185.0, 131.2, 93.7, 51.5, 46.6, 42.8, 42.3, 41.1, 34.1, 28.9, 13.8, 8.2; IR (film, cm^{-1}) 3413, 1694, 1651; HRMS (CI) calcd for $C_{13}H_{18}O_2$ (M^+) *m/e* 206.1306, obsd *m/e* 206.1392.

(±)-6α-(Benzyloxycarbonyl)-1,3bα,4,5,6,6a,7,7a*β*-octahydro-6aα-hydroxy-3,4,4-trimethyl-1*H*-cyclopenta[*a*]pentalen-2-one (30α) and (±)-6*β*-(Benzyloxycarbonyl)-1,3bα,4,5,6,6a,7,7a*β*-octahydro-6aα-hydroxy-3,4,4-trimethyl-1*H*-cyclopenta[*a*]pentalen-2-one (30*β*). A −78 °C solution of **1a** (207 mg, 0.782 mmol) was treated with vinyllithium (0.61 mL, 0.86 mmol) and after 40 min warmed to room temperature. The solution was recooled to −78 °C, and benzylchloroformate (0.120 mL, 0.84 mmol) was added. The solution was then warmed to 0 °C. Workup in the manner analogous to the synthesis of **5** and chromatography (3:1 followed by 1:1 hexanes/EtOAc) provided **30**α (63 mg, 23%) followed by **30*β*** (112 mg, 40%) as colorless oils. Spectral data for **30**α: ^{1}H NMR δ 7.39−7.35 (m, 5H), 5.19 (m, 2H), 3.55 (s, 1H), 2.94 (dd, J = 13.5, 6.0 Hz, 1H), 2.88 (m, 1H), 2.85 (bs, 1H), 2.64 (dd, J = 18.0, 6.0 Hz, 1H), 2.52 (dd, J = 12.5, 7.5 Hz, 1H), 2.31 (t, J = 13.0 Hz, 1H), 2.11 (dd, J = 18.0, 2.5 Hz, 1H), 1.91 (dd, J = 12.5, 6.0 Hz, 1H) 1.71 (d, J = 1.0 Hz, 3H), 1.35 (s, 3H), 1.29 (t, J = 12.0 Hz, 1H), 0.85 (s 3H); ^{13}C NMR δ 209.1, 179.6, 173.2, 135.4, 134.4, 128.7 (2C), 128.5, 128.3 (2C), 93.3, 66.8, 63.5, 51.6, 44.4, 43.25, 43.15, 41.5, 41.0, 31.8, 25.1, 8.9; IR (film, cm^{-1}) 3431, 1737, 1704, 1657; HRMS calcd for $C_{22}H_{26}O_4$ *m/e* 354.1831 (M^+), obsd *m/e* 354.1825. Spectral data for **30*β***: ^{1}H NMR δ 7.38−7.35 (m, 5H), 5.25 (d, J = 12.0 Hz, 1H), 5.17 (d, J = 12.0 Hz, 1H), 3.44 (dd, J = 13.5, 7.0 Hz, 1H), 2.82 (m, 1H), 2.79 (s, 1H), 2.67 (s, 1H), 2.56 (dd, J = 18.0, 6.0 Hz, 1H), 2.24 (dd, J = 12.5, 7.5 Hz, 1H), 1.96−1.88 (m, 2H), 1.77 (dd, J = 13.0, 7.0 Hz, 1H), 1.70 (d, J = 1.5 Hz, 3H), 1.31 (s, 3H), 1.23 (t, J = 12.5 Hz, 1H), 0.96 (s, 3H); ^{13}C NMR δ 209.5, 180.5, 172.6, 135.5, 134.6, 128.6, 128.4, 93.5, 66.6, 62.5, 56.2, 45.1, 42.9, 42.4, 41.8, 41.5, 30.2, 26.0, 8.9; IR (film, cm^{-1}) 3430, 1728, 1702, 1654; HRMS (CI) calcd for $C_{22}H_{26}O_4$ (M^+) *m/e* 354.1831, obsd *m/e* 354.1823.

3-Methyl-2-(2-methyl-1-propenyl)-4-(2-propenyl)-4-[(*tert*-butyldimethylsilyl)oxy]-2-cyclobuten-1-one (37a). To a 0 °C dichloromethane (18 mL) solution of **12a** (500 mg, 2.60 mmol) was added 2,6-lutidine (0.60 mL, 5.14 mmol) followed by TBDMSOTf (0.89 mL, 3.9 mmol). After 5 min the ice bath was removed. The solution was poured onto saturated aqueous $NaHCO_3$ after 2 h. The aqueous layer was extracted with dichloromethane, and the combined organic layers were washed with brine, dried (Na_2SO_4), filtered, and concentrated. Workup and chromatography (25:1 hexanes/EtOAc) provided **37a** (590 mg, 74%) as a pale yellow oil: ^{1}H NMR δ 5.76−5.71 (m, 1H), 5.54 (s, 1H), 5.08−5.01 (m, 2H), 2.50−2.49 (m, 2H), 2.08 (s, 3H), 1.98 (s, 3H), 1.84 (s, 3H), 0.86 (s, 9H), 0.12 (s, 3H), −0.02 (s, 3H); IR (film, cm^{-1}) 1756, 1663, 1596; HRMS (CI) calcd for $C_{18}H_{30}SiO_2$ (M^+) *m/e* 306.2015, obsd *m/e* 306.2001.

Conversion of 39a to 5. To a 0 °C THF (5 mL) solution of **39a** (66 mg, 0.20 mmol) was added TBAF (0.24 mL, 0.26 mmol) with yellowing. After 50 min, water (2 mL) and EtOAc (10 mL) were added. The separated aqueous layer was extracted with EtOAc, and the combined organic layers were washed with brine, dried (Na_2SO_4), filtered, and concentrated. Chromatography (1:1 hexanes/EtOAc) gave a yellow-green oil (43 mg, 98%). The ^{1}H NMR spectrum of this oil was identical to that of **5** prepared directly from **1b**.

3-(4-Butenyl)-4-[(*tert*-butyldimethylsilyl)oxy]-2-(2-methyl-1-propenyl)-2-cyclobuten-1-one (41). To a DMF (6 mL) solution of **12a** (550 mg, 2.9 mmol) was added imidazole (584 mg, 8.6 mmol) followed by TBDMSCl (864 mg, 5.7 mmol). After 1 h the solution was concentrated and filtered through a plug of Florisil (EtOAc) to give **41** (684 mg, 78%) as a pale yellow oil: ^{1}H NMR δ 5.89−5.81 (m, 1H), 5.58 (s, 1H), 5.12−5.06 (m, overlapping with s, 2H), 5.05−5.02 (m, 1H), 2.68−2.63 (m, 2H), 2.45−2.33 (m, 2H), 2.03 (s, 3H), 1.84 (s, 3H), 0.92 (s, 9H), 0.15 (s, 6H); ^{13}C NMR δ 189.0, 174.0, 147.0, 144.2, 137.0, 115.6, 112.3, 84.0, 30.3, 26.6, 26.4, 25.7 (3C), 21.3, 18.2, −4.6, −5.1; IR (film, cm^{-1}) 1755, 1661, 1589; HRMS (CI) calcd for $C_{18}H_{31}O_2Si$ (MH^+) *m/e* 307.2093, found *m/e* 307.2088.

(±)-*endo*-2-Formyl-1-(2-methyl-1-propenyl)bicyclo[3.2.0]heptan-7-one and (±)-*exo*-2-formyl-1-(2-methyl-1-propenyl)-bicyclo[3.2.0]heptan-7-one. To −78 °C THF (60 mL) solution of **6a** (672 mg, 2.54 mmol) was added water (1 mL) followed by TBAF (0.6 mL, 0.66 mmol, 1.1 M solution in THF). Water (50 mL) was added after 2 h, and the solution was extracted with ether. The combined organic layers were washed with brine, dried (Na_2SO_4), filtered, and concentrated. Chromatography (8:1 hexanes/EtOAc) provided the *exo*-aldehyde (34 mg, 7%) as a colorless oil, followed by the *endo*-aldehyde (305 mg, 63%) as a white solid (mp = 47−48 °C). Spectral data for the *exo*-isomer: ^{1}H NMR δ 9.57 (d, J = 2.5 Hz, 1H), 5.34 (s, 1H), 3.37 (dd, J = 18.5, 9.5 Hz, 1H), 3.23−3.21 (m, 1H), 2.88−2.85 (m, 1H), 2.57 (dd, J = 18.5, 4.5 Hz, 1H), 2.30 (dd, J = 13.5, 7.5 Hz, 1H), 2.11−2.06 (m, 1H), 1.88−1.75 (m overlapping with d, J = 1.5 Hz, 5H), 1.72 (d, J = 1.5 Hz, 3H); ^{13}C NMR δ 210.2, 202.0, 139.4, 118.3, 77.19, 56.2, 50.3, 38.1, 31.4, 26.2, 26.1, 20.5; IR (film, cm^{-1}) 1771, 1720; HRMS (EI) calcd for $C_{12}H_{16}O_2$ *m/e* 192.1150, found *m/e* 192.1152. Spectral data for the *endo*-isomer: ^{1}H NMR δ 9.74 (d, J = 2.0 Hz, 1H), 5.36 (s, 1H), 3.30 (dd, J = 19.0, 9.5 Hz, 1H), 2.98−2.94 (m, 1H), 2.78−2.74 (m, 1H), 2.56 (dd, J = 19.0, 4.5 Hz, 1H), 2.14−2.09 (m, 1H), 2.04−1.94 (m, 3H), 1.73 (d, J = 1.5 Hz, 3H), 1.67 (s, 3H); ^{13}C NMR δ 211.3, 201.6, 137.4, 121.3, 77.04, 63.1, 49.6, 37.4, 32.0, 26.4, 25.6, 19.6; IR (film, cm^{-1}) 1772, 1720; HRMS (CI) calcd for $C_{12}H_{16}O_2$ (M^+) *m/e* 192.1150, found *m/e* 192.1148.

(±)-1-(2-Methyl-1-propenyl)-*endo*-2-methyl-(1,1-propylenedithio)bicyclo[3.2.0]heptan-7-one. To a 0 °C CH_2Cl_2 (8 mL) solution of *endo*-2-formyl-1-(2-methyl-1-propenyl)-bicyclo[3.2.0]heptan-7-one (159 mg, 0.83 mmol) was added 1,3-propanedithiol (0.091 mL, 0.91 mmol) followed by $BF_3{\cdot}OEt_2$ (0.112 mL, 0.91 mmol). CH_2Cl_2 (10 mL) and water (4 mL) were added after 10 min, and the separated aqueous layer was extracted with CH_2Cl_2. The combined organic layer was washed with brine, dried ($MgSO_4$), filtered, and concentrated. Chromatography (10:1 hexanes/EtOAc) gave the title compound (218 mg, 93%) as a white solid: mp, 80−82 °C; ^{1}H NMR δ 5.46 (s, 1H), 4.06 (d, J = 10.0 Hz, 1H), 3.20 (dd, J = 18.5, 10.0 Hz, 1H), 2.93−2.85 (m, 3H), 2.81−2.74 (m, 2H), 2.54 (dd, J = 18.5, 5.0 Hz, 1H), 2.36−2.29 (m, 2H), 2.09−2.04 (m, 2H), 1.89−1.62 (m, 3H), 1.69 (d, J = 1.0 Hz, 3H), 1.61 (d, J = 1.0 Hz, 3H); ^{13}C NMR δ 211.9, 134.1, 124.3, 78.0, 55.6, 49.8, 49.5, 38.6, 31.8, 30.8, 30.6 (2C), 26.3, 25.8, 19.4; IR (film, cm^{-1}) 2929, 1768, 1101; HRMS (CI) calcd for $C_{15}H_{23}OS_2$ (MH^+) *m/e* 283.1190, obsd *m/e* 283.1178.

(±)-*endo*-2-Methyl-1-(2-methyl-1-propenyl)bicyclo[3.2.0]heptan-7-one (44). An EtOH (anhydrous, 50 mL) heterogeneous mixture of 1-(2-methyl-1-propenyl)-*endo*-2-methyl-(1,1-propylenedithio)bicyclo[3.2.0]heptan-7-one (94 mg, 0.33 mmol) and deactivated W-2 Raney Nickel (four spatula tips) was heated at reflux for 12 h with vigorous stirring. Filtration, concentration at 20 mmHg, and chromatography (4:1 hexanes/CH_2Cl_2) provided **44** (57 mg, 97%) as a colorless oil with a camphor-like odor: ^{1}H NMR δ 5.27 (s, 1H), 3.15 (dd, J = 18.5, 9.0 Hz, 1H), 2.87 (dt, J = 9.0, 5.0 Hz, 1H), 2.43 (dd, J = 18.5, 4.5 Hz, 1H), 2.04−1.92 (m, 3H), 1.82 (dd, J = 12.5, 6.5 Hz, 1H), 1.71 (s, 3H), 1.64 (s, 3H), 1.46−1.41 (m, 1H), 1.03 (d, J = 6.5 Hz, 3H); ^{13}C NMR δ 214.6, 135.0, 123.4, 49.5, 47.4, 37.5, 33.1, 32.3, 26.4, 19.4, 14.5 (the signal for the quaternary carbon was not observed); IR (neat, cm^{-1}) 1770; HRMS (CI) calcd for $C_{12}H_{18}O$ (M^+) *m/e* 178.1358, obsd *m/e* 178.1352.

(±)-Precapnelladiene (47). To a 1,2-dichloroethane (0.35 mL) solution of **45** (13 mg, 0.029 mmol) was added $Pd[PPh_3]_4$ (7 mg, 0.006 mmol) followed by $AlMe_3$ (0.03 mL, 0.057 mmol, 2.0 M in hexanes), which caused the heterogeneous mixture to turn deep red in color. After 6 h, the mixture was diluted with ether (10 mL) and washed with 1 M HCl, saturated aqueous $NaHCO_3$ and brine, dried (Na_2SO_4), filtered, and concentrated. Chromatography (pentane followed by 15:1 pentane/EtOAc) and careful concentration at 20 mmHg provided **47** (4.5 mg, 78%) as a colorless oil with a camphor-like odor: ^{1}H NMR δ 5.33 (t, J = 9.5 Hz, 1H), 5.02 (d, J = 1.0 Hz, 1H); 3.51 (dt, J = 12.0, 6.5 Hz, 1H), 2.90 (dd, J = 13.5, 9.5 Hz, 1H) 2.41−2.34 (m, 2H), 1.76−1.54 (m, 4H), 1.63 (s, 3H), 1.43−

1.39 (m, 1H), 1.26−1.20 (m, 1H), 1.04 (d, $J = 7.0$ Hz, 3H), 0.98 (s, 3H), 0.97 (s, 3H); ^{13}C NMR δ 145.5, 136.3, 130.2, 121.8, 42.3, 40.5, 39.6, 38.9, 38.7, 33.7, 31.5, 31.3, 29.8, 26.7, 22.0; IR (neat, cm^{-1}) 2952, 2866, 1470, 1459, 1374, 1358, 854; HRMS (EI) calcd for $C_{15}H_{24}$ (M^+) *m/e* 204.1878, obsd *m/e* 204.1869. Comparison of the ^{1}H NMR spectrum of the product to the spectrum of an authentic sample of (±)-precapnelladiene, provided by Professor Leo Paquette showed them to be identical.

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Supporting Information Available: Characterization data for **1b**,**c**, **6b**,**c**, **8**, **11b**,**c**, **12b**,**c**, **13b**,**c**, 3-(3-butenyl)-2-(2-methyl-1-propenyl)-4-[(trimethylsilyl)oxy]-2-cyclobuten-1-one, **16a**,**b**, **17b**, 3-(4-butenyl)-4-methyl-2-(2-methylpropenyl)-4-[(trimethylsilyl)oxy]-2-cyclobuten-1-one, 3-(4-butenyl)-2-ethenyl-4-methyl-4-[(trimethylsilyl)oxy]-2-cyclobuten-1-one, **20**, **23**−**29**, **31**α,β, **32**−**36**, **37b**, **38a**,**b**, **39a**,**b**, **40a**,**b**, **42**, **43**, **45**, and **46** not included in the text and ^{13}C NMR spectral data for all new compounds (13 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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