The Squarate Ester−Polyquinane Connection. An Analysis of the Capacity of Achiral Divinyl Adducts To Rearrange Spontaneously to Polycyclic Networks Housing Multiple Stereogenic Centers

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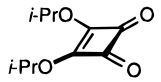
Abstract: The condensation of diisopropyl squarate and related cyclobutene-1,2-diones with 2 equiv of the same alkenyl anion or 1 equiv each of two different alkenyl anions can be a very effective method for the highly stereocontrolled synthesis of di-, tri-, and tetraquinanes. Two reaction cascades have been identified. The most prevalent and often exclusive reaction course is triggered by trans 1,2-addition of the two nucleophiles. Two consecutive conrotatory processes subsequently arise to deliver a doubly charged eight-membered ring intermediate, protonation of which leads to transannular adolization. The second option begins with cis 1,2-addition, this event triggering structural reorganization via a dianionic oxy-Cope rearrangement. When the alkenyl anions are sufficiently substituted, the two pathways are distinguishable on stereochemical grounds. A minor pathway consisting of trans 1,4-addition is seen to operate in certain contexts, especially when the alkenyllithium is "soft". Acetylide anions can also be utilized successfully; in such cases, the benefit of regiocontrolled protonation surfaces and gives rise to a single product. Other aspects of these complex tandem reactions have been investigated and are discussed.

The latent potential of tandem or cascade reactions for rapid molecular construction has recently been highlighted by the issuance of a textbook on the subject[2] and the convening of an international conference by the Royal Society of Chemistry.[3] Accordingly, the discovery of any new multistage process that lends itself conveniently to dramatic increases in structural intricacy warrants detailed follow-up investigation. Recently, we made the observation that twofold addition of the same or different alkenyl anions to a squarate ester triggers a cascade of chemical events that culminates in the *direct formation* of complex polycyclic products.[4,5] A notably striking feature of these deep-seated transformations is that while both starting reagents are achiral, each product contains several contiguous stereogenic centers. Although in simple cases the total number can reach five, further increases can be realized simply by preincorporating asymmetric carbons in either or both nucleophilic reagents.

In this report, we address the salient features of the fundamental reaction and provide a mechanistic foundation that establishes not only an appreciation of the associated chemical events but also sets the stage for rational development of the successive electrocyclic pathways in various directions.[6−8]

Results and Discussion

Twofold Addition of the Identical Alkenyllithium Reagent. The basis of the initial experiments lies in the utilization of a common alkenyl anion such that symmetry is maintained as long as possible in the several intermediates involved. Recourse was made to diisopropyl squarate (**1**) because of its considerably lessened irritant properties relative to the dimethyl derivative.



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When **1** was treated with >2 equiv each of 2-propenyllithium or cyclopentenyllithium in THF at −78 °C and the reaction mixtures were allowed to warm to room temperature overnight prior to being quenched with saturated NH_4Cl solution, the products shown in Scheme 1 were isolated. For vinyllithium, best results were achieved when the temperature was maintained at −78 °C until workup was initiated. The structural assignment to **2** rests reliably on a combination of 2D, NOE, and semiselective DEPT studies at 300 MHz. The features of the stereochemically more complex di- and tetraquinanes **3**−**5** were elucidated by X-ray crystallographic analysis. Direct comparison of the spectroscopic characteristics of **4** and **5** with those of **6** made possible accurate definition of the trans,trans relationship of the three methine protons in the latter product.

The level of substitution resident in **2** and **3** is inadequate to differentiate between second-stage addition to monoadduct **A** from the anti or syn direction (Scheme 2). The relevance of this stereochemical outcome becomes apparent when it is recognized that dialkoxides **B** and **C** have rather divergent mechanistic options available to them. In **B**, the pendant double bonds are too remote to interact. Instead, the doubly-charged nature of this intermediate can be expected to greatly facilitate conrotatory ring opening to the helical octatetraene **D**. As noted

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(1) National Needs Fellow, 1991−1996.

(2) *Tandem Reactions*; Ho, T. L., Ed.; John Wiley and Sons, Inc.: New York, 1992.

(3) Cascade Reactions in Synthesis; University of Leeds, September 12−14, 1994; Grigg, R., organizing chairman.

(4) Negri, J. T.; Morwick, T.; Doyon, J.; Wilson, P. D.; Hickey, E. R.; Paquette, L. A. *J. Am. Chem. Soc.* **1993**, *115*, 12189.

(5) (a) Paquette, L. A.; Morwick, T. *J. Am. Chem. Soc.* **1995**, *117*, 1451. (b) Paquette, L. A.; Doyon, J. *J. Am. Chem. Soc.* **1995**, *117*, 6799. (c) Paquette, L. A.; Doyon, J.; Kuo, L. H. *Tetrahedron Lett.* **1996**, *37*, 3299.

(6) Paquette, L. A.; Doyon, J. Submitted for publication.

(7) Paquette, L. A.; Hamme, A. T., II; Kuo, L. H.; Doyon, J.; Kreuzholz, R. *J. Am. Chem. Soc.* **1997**, *119*, 1242.

(8) Paquette, L. A.; Kuo, L. H.; Doyon, J. *Tetrahedron* **1996**, *52*, 11625.

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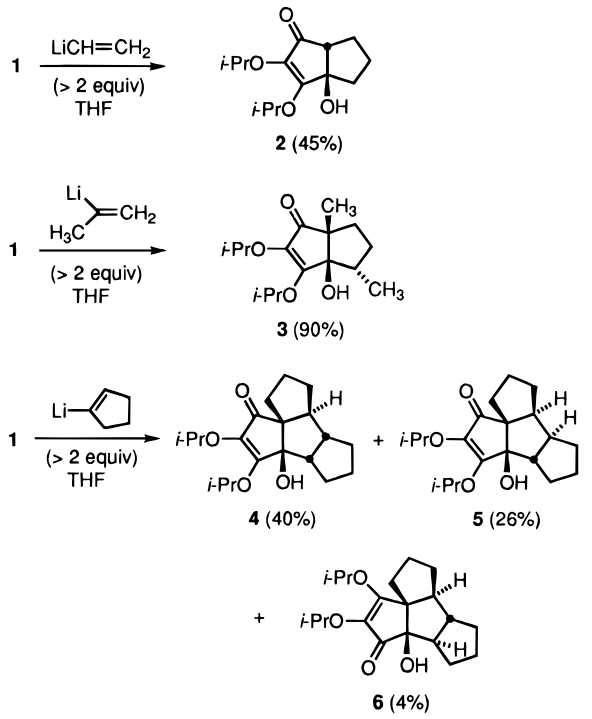
Scheme 1

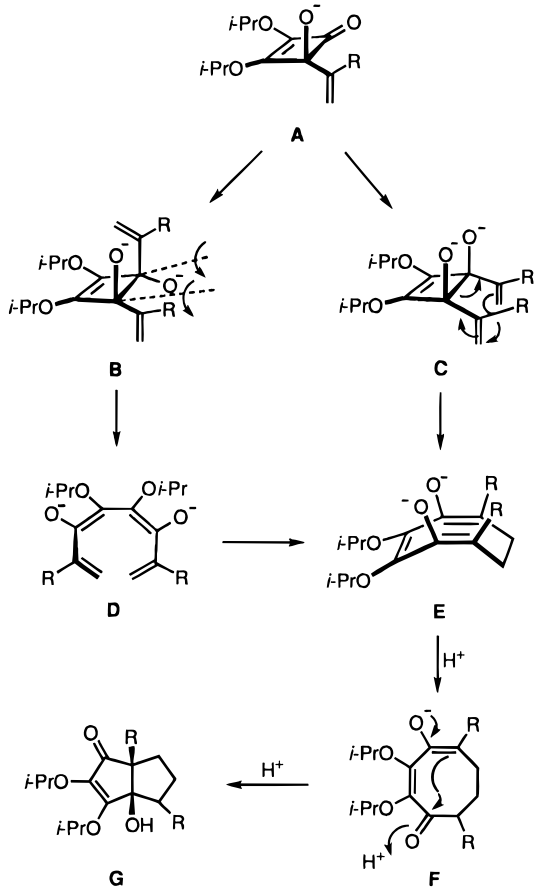


by Houk on theoretical grounds,[9] the donor character of the oxido anions should give rise to a very large kinetic preference for outward rotation of these atoms. Adoption of this course of action provides for the delivery of **D** in a conformation ideally suited to more advanced (also conrotatory[10,11]) electrocyclization. The substantially increased efficiency with which **3** is formed relative to **2** suggests that this reaction channel is indeed operative and that alkyl substitution at R is favorable to maintaining the conformation most conducive to 8π ring closure.

The involvement of **C**, on the other hand, would without doubt result in rapid dianionic oxy-Cope rearrangement[12] from a boat conformation[13] to provide **E** some-what more directly. Were the terminal olefinic carbons in **C** and **D** suitably substituted, the **A** → **B** → **D** → **E** pathway would be distinguishable from the **A** → **C** → **E** route on stereochemical grounds (see Scheme 2). In any event, monoprotonation of **E** at either of its symmetry-related enolate carbons will give rise to **F**, whose intramolecular aldolization leads ultimately to the observable diquinane **G**.

Silylative Trapping of Intermediates. The cyclopentenyl example satisfies the criterion of adequate substitution, such

Scheme 2



that the stereochemistry inherent in **4**−6 and the spatial relationship of the carbonyl and hydroxyl groups therein serve as indicators of mechanistic origin.[14] Thus, the results of trans addition and subsequent 2-fold electrocyclization via intermediates of type **B** and **D** necessarily leads to the generation of bisenolate **7** (Scheme 3). To the extent that the **B** → **D** and **D** → **E** steps are obligatorily conrotatory, as precedent indicates they should be, the relative stereochemistry of the two adjacent stereocenters in **7** is necessarily trans. If cis addition and the dianionic oxy-Cope variant are selected, and [3,3] sigmatropy occurs by way of a boat alignment, the cis-fused bisenolate **10** arises.

In light of these distinctive stereochemical markers, trapping experiments were undertaken. The addition of excess chlorotrimethylsilane after treatment of **1** with 3 equiv of cyclopentenyllithium provided a chromatographically separable mixture of **8** (43%), **11** (24%), and **13** (5%). The two major products were readily distinguished from the third isomer on the basis of their symmetry. X-ray crystallographic analysis of a congener of **8** has earlier been reported.[14] While **11** gave evidence of being a relatively rigid structure, **8** is clearly a conformationally dynamic molecule, the time-averaged symmetry of which reduces its ^{1}H and ^{13}C signal count by 50%. Structural differentiation between **8** and **11** was made possible by chemical correlation. To this end, the three bissilyl enol ethers were individually exposed to excess methyllithium in order to liberate the enolate anions. An ensuing aqueous quench returned **4**, **5**, and **6**/**15**, respectively (Schemes 3 and 4). The obvious loss of stereocontrol during the protonation of **K** may be the result of the dissimilarity in reaction conditions. Alternatively, the very minor amount of **6** produced from the squarate condensation could be cause for the nondetection of its epimer.

(9) (a) Kirmse, W.; Rondan, N. G.; Houk, K. N. *J. Am. Chem. Soc.* **1984**, *106*, 7989. (b) Rondan, N. G.; Houk, K. N. *J. Am. Chem. Soc.* **1985**, *107*, 2099. (c) Niwayama, S.; Kallel, E. A.; Spellmeyer, D. C.; Sheu, C.; Houk, K. N. *J. Org. Chem.* **1996**, *61*, 2813.

(10) (a) Huisgen, R.; Dahmen, A.; Huber, H. *J. Am. Chem. Soc.* **1967**, *89*, 7130. (b) Huisgen, R.; Dahmen, A.; Huber, H. *Tetrahedron Lett.* **1969**, 1461. (c) Dahmen, A.; Husigen, R. *Tetrahedron Lett.* **1969**, 1465. (d) Nicolaou, K. C.; Petasis, N. A.; Zipkin, R. E.; Uenishi, J. *J. Am. Chem. Soc.* **1982**, *104*, 5555. (e) Snider, B. B.; Harvey, T. C. *J. Org. Chem.* **1994**, *59*, 504. (f) Pohnert, G.; Boland, W. *Tetrahedron* **1994**, *50*, 10235.

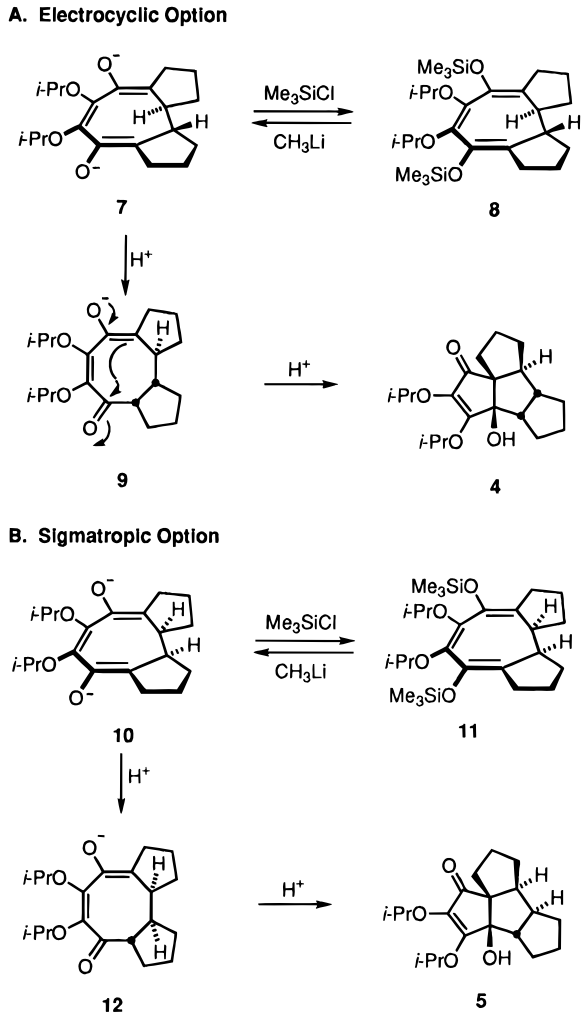
(11) Thomas, B. E., IV; Evanseck, J. D.; Houk, K. N. *J. Am. Chem. Soc.* **1993**, *115*, 4165.

(12) (a) Geetha, P.; Huq, C. A. M. A.; Rajagopalan, K.; Swaminathan, S. *Tetrahedron Lett.* **1982**, *23*, 569. (b) Alder, R. W.; Colclough, D.; Grams, F.; Orpen, A. G. *Tetrahedron* **1990**, *46*, 7933. (c) Saito, S.; Yamamoto, T.; Matsuoka, M.; Moriwake, T. *Synlett* **1992**, 239. (d) Brands, M.; Goddard, R.; Wey, H. G.; Butenschön, H. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 267. (e) Brands, M.; Bruckmann, J.; Krüger, C.; Butenschön, H. *J. Chem. Soc., Chem. Commun.* **1994**, 999. (f) Brands, M.; Wey, H. G.; Brückmann, J.; Krüger, C.; Butenschön, H. *Chem. Eur. J.* **1996**, *2*, 182.

(13) (a) Berson, J. A.; Dervan, P. B. *J. Am. Chem. Soc.* **1972**, *94*, 7597. (b) Paquette, L. A.; Colapret, J. A.; Andrews, D. R. *J. Org. Chem.* **1985**, *50*, 201.

(14) Paquette, L. A.; Morwick, T. M.; Negri, J. T.; Rogers, R. D. *Tetrahedron* **1996**, *52*, 3075.

Scheme 3

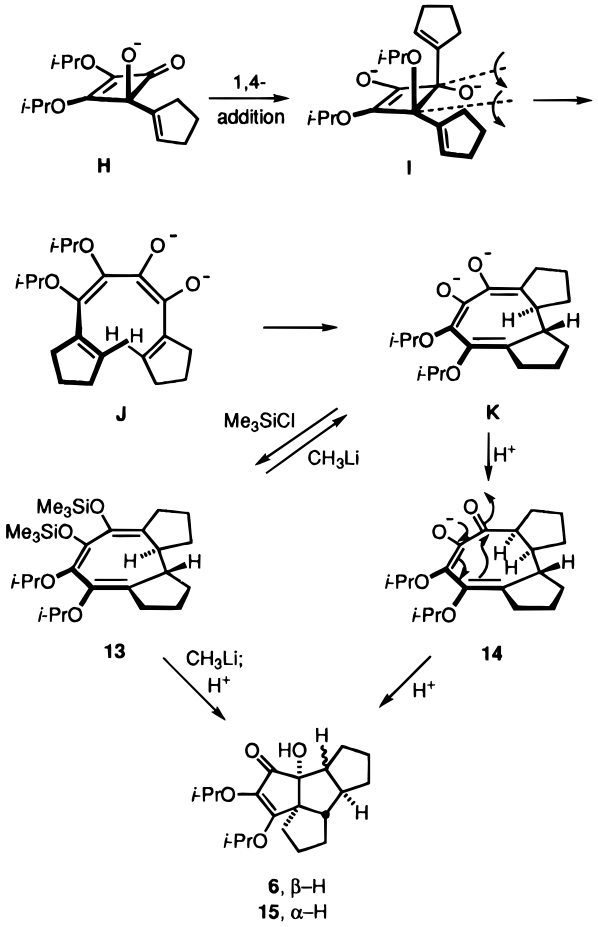


These data show that cyclopentenyllithium exhibits an unusually high propensity for cis 1,2-addition to **H**. Although *trans*-dialkoxide formation is indeed favored by approximately 2:1, this ratio falls considerably below the customarily high kinetic preference for anti addition. The incursion of 1,4-addition to generate **I** is very modest, and in many cases is not observed. When such an event occurs, the trans cyclobutene dialkoxide isomerizes as does **B** and leads via **J** to the doubly-charged cyclooctatriene **K**. It will be noted that advancement along this reaction channel has the incontrovertible consequence of delivering an α-hydroxy-substituted polyquinane as product.

The conformational rigidity imposed by the third vicinal stereogenic carbon in **9** and **12** so limits the conformational freedom of these cyclooctadienones that the final transannular aldolization proceeds in a single, well-defined stereochemical direction. That the initial protonation of doubly-charged intermediate **7** proceeds with installation of a cis ring fusion is anticipated, since considerable torsional deformation of the medium-ring framework would accompany proton delivery from the opposite face. By comparison, the initial protonaton of **10** occurs in trans fashion to afford **12**. In order to provide insight into whether this kinetic preference conforms as well to the thermodynamic bias of the system, the neutral and anionic forms of the two relevant diastereomers were minimized in the MODEL KS 2.96 program.[15] Both forms were examined in order to guarantee reliable parameterization for the enolate. Also,

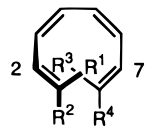
(15) We thank Prof. W. C. Still (Columbia) for making his program available to us and Prof. K. Steliou (Boston University) for providing us with updates of his software package.

Scheme 4



the isopropyl groups were replaced by methyl in order to reduce the number of possible sidechain rotamers. The data reveal a close correlation between the neutral and oxido species. More relevantly, the cis,trans isomer gives evidence of being thermodynamically advantaged, perhaps by as much as 3 kcal/mol.

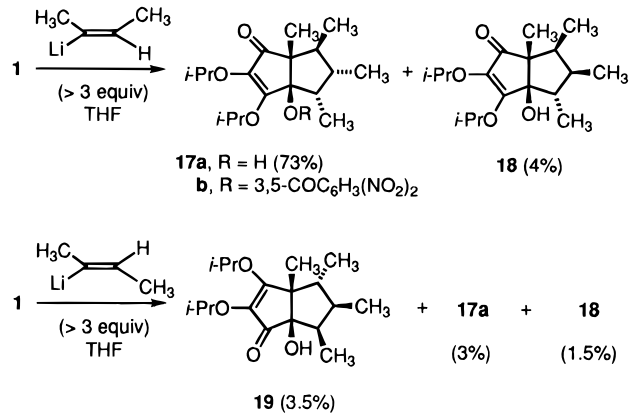
Consequences of Locus of Substitution on Reaction Efficiency. In his classical study of the stereospecific conrotatory valence isomerization of octatetraenes **16a**−**c** to the corresponding 1,3,5-cyclooctatrienes, Huisgen demonstrated that the rate of reaction was highly dependent upon the geometry of the terminal methyl groups.[10a−c] The temperatures given are those required for essentially complete ring closure within 30 h. Trans isomers in general have been calculated to have 0.2−0.4 kcal/mol lower activation energies than the parent hydrocarbon.[11] For the cis isomers, steric crowding is apparently exacerbated when advancing into the transition state.



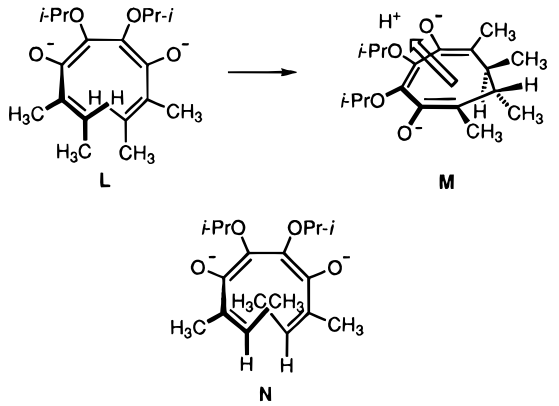
16a, $R^1 = R^3 = H$, $R^2 = R^4 = CH_3$ (-10 °C)
b, $R^1 = R^4 = H$, $R^2 = R^3 = CH_3$ (9 °C)
c, $R^2 = R^4 = H$, $R^1 = R^3 = CH_3$ (65 °C)

While the kinetic consequences of terminal substitution were particularly engaging in the present context, certain observations described above suggested that the presence of methyl groups at C-2 and C-7 were particularly conducive to efficient product formation. The efficiency with which **3** and **4**−**6** can be isolated formed the early basis for this conclusion.

Scheme 5



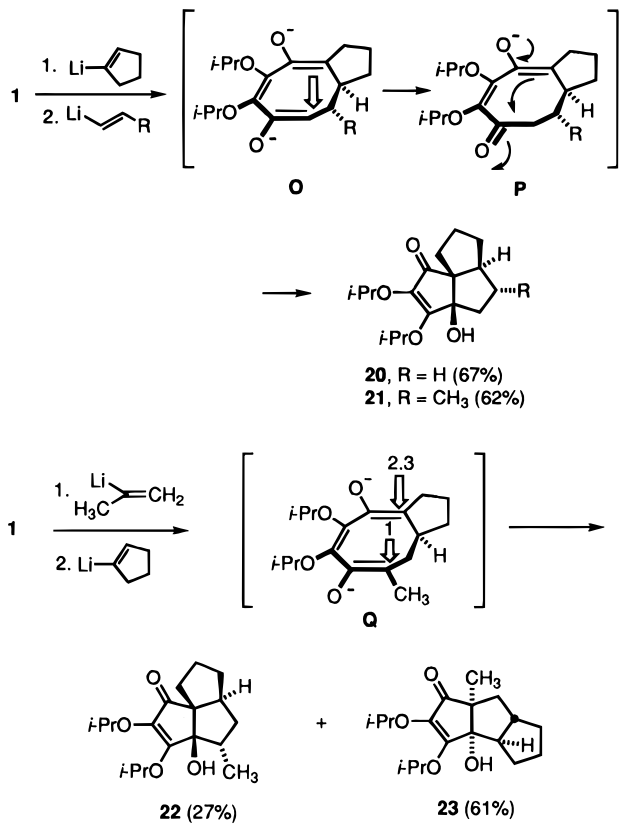
The *cis*- and *trans*-2-butenyllithiums[16] share geometrical and substitutive characteristics that bear directly on these issues. Consequently, these reagents were individually generated and added in excess to **1** (Scheme 5). The cis isomer was found to engage readily in reaction and to generate efficiently (77%) a 19:1 mixture of **17a** and **18**. On the basis of spectroscopic data, **18** was clearly a product of 1,2-addition having four cis-oriented substituents in its saturated ring. In order to derive comparable structural information from the major diquinane, it was necessary to prepare the 3,5-dinitrobenzoate derivative **17b**. The stereochemistry determined for **17** is consistent with the intervention of tetraene **L**, its conrotatory cyclization to **M**, and stereocontrolled monoprotonation of **M** to establish a cis relationship between two adjacent methyl substituents. Significantly, **L** exhibits no obvious major barrier to ring closure. Also, the protonation of **M** parallels exactly the behavior of **7** (Scheme 3).



The inefficiency associated with *trans*-butenyllithium addition to **1** contrasts strikingly with the above. The only product passing through intermediate **N** is **17a**, and it is formed in only 3% yield. Roughly comparable amounts of products derived from *trans*-1,4- (**19**, 3.5%; structure established by X-ray crystallography) and *cis*-1,2-addition (**18**, 1.5%) could be isolated. Although we have yet to appreciate whether the pair of oxido substituents attached to tetraenes such as **L** and **M** provides an electronic driving force for cyclooctatriene formation, the presence of interior methyl groups at the bonding termini clearly act to deter electrocyclization.

Mixed Alkenyl Anion Additions. Site-Selective Protonation. The addition of two different alkenyl anions to **1** provides an opportunity to extend our appreciation of several facets of this cascade reaction. For example, considerable advantage could be gained if the two enolate centers in **O** (Scheme 6) could be engaged separately in subsequent reactions. This intermediate can be readily generated by the sequential introduction of 1 equiv of vinyllithium (or (*E*)-1-propenyllithium[17]) to **1** followed by an excess of cyclopentenyllithium. In both experiments, only the triquinanes **20** and **21**, respectively, were isolated in good yield. These findings show that protonation operates very predominantly at the less sterically hindered carbon and may come under steric control. However, MM2 calculations performed on both **P** and its protonated regioisomer show **P** to be thermodynamically favored as well, and by approximately 2 kcal/mol.

Scheme 6



By comparison, the two reactive sites in **Q** are now comparably substituted. Both protonation options now operate concurrently to provide ultimately a 1:2.3 mixture of **22** and **23** (structure confirmed by X-ray crystallography) in 88% yield.

Protonation at the five-membered ring may be kinetically favored because of underlying thermodynamic reasons, but this entire question warrants additional study. Surprisingly, an issue as fundamental as the competitive reactivity of two enolateanions in comparable structural environments has only been very infrequently examined.[18]

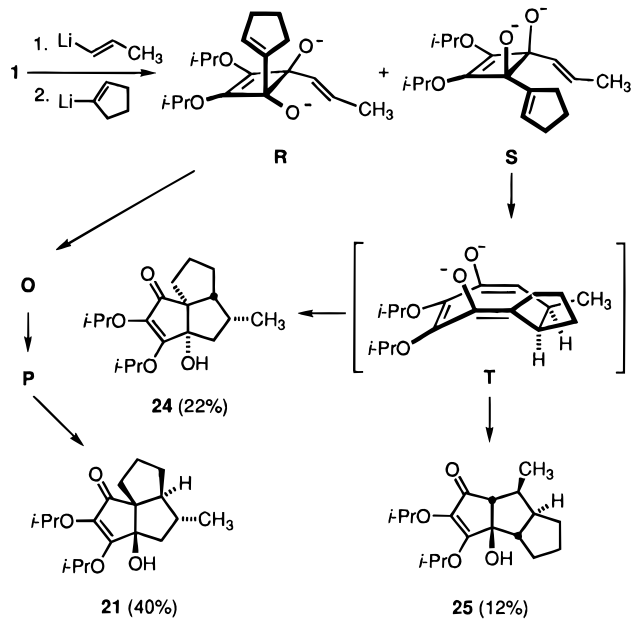
During this phase of the investigation, we became aware of the fact that octatetraenes can continue to experience conrotatory cyclization after such species are protonated. Thus, workup of the first reactions in Scheme 6 immediately after quenching gave **20** and **21** in yields as low as 26% and 20%, respectively. The significantly more enhanced reaction efficiencies given earlier could, however, be achieved simply by storage of the aqueous

(16) Dreiding, A. S.; Pratt, R. J. *J. Am. Chem. Soc.* **1954**, *76*, 1902.

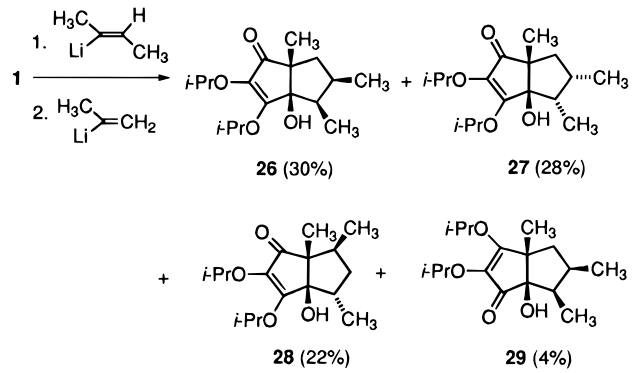
(17) Linstrumelle, G.; Krieger, J. K.; Whitesides, G. M. *Org. Synth.* **1976**, *55*, 103.

(18) (a) Paquette, L. A.; Ternansky, R. J.; Balogh, D. W. *J. Am. Chem. Soc.* **1982**, *104*, 4502. (b) Paquette, L. A.; Ternansky, R. J.; Balogh, D. W.; Taylor, W. J. *J. Am. Chem. Soc.* **1983**, *105*, 5441. (c) Paquette, L. A.; Balogh, D. W.; Ternansky, R. J.; Begley, W. J.; Banwell, M. G. *J. Org. Chem.* **1983**, *48*, 3282.

Scheme 7



Scheme 8

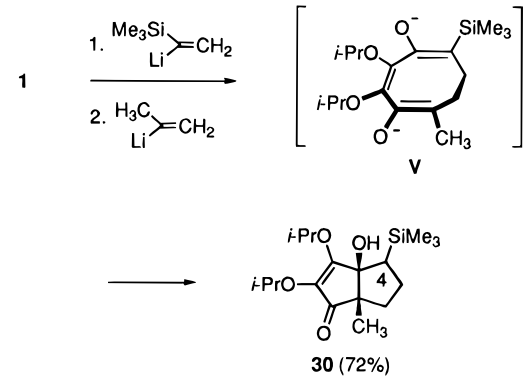


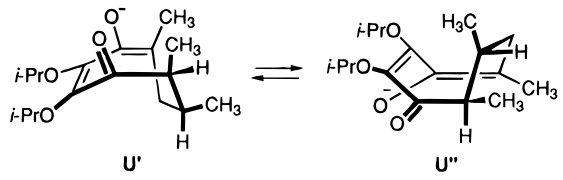
THF solutions overnight under argon prior to product isolation. The physical model most consistent with this behavior is the notion that the neutralized intermediates achieve a reasonable level of enol character.

In certain instances, the sequence in which the alkenyl anions are introduced can have an impact on product formation. A case in point is illustrated in Scheme 7. If cyclopentyllithium is added *subsequent to* 1-propenyllithium, the yield of **21** drops to 40% and the two coproducts **24** (22%) and **25** (12%) now make their appearance in a significant manner. This deviation from the reaction course followed when 1-propenyllithium was the second nucleophile (Scheme 6) has its origins in the previously observed tendency for the cyclopentenyl anion to undergo cis 1,2-addition. While **R** was formed almost exclusively in the original experiment, the second-stage entry of cyclopentenyllithium results in the competitive formation of **S** at an approximately equivalent level! Once **S** is formed, the opportunity for [3,3] sigmatropic rearrangement to **T** materializes. The formation of **24** and **25** from **T** represents a compromise between protonation at the less and more substituted enolate sites, with the first of these options being favored by approximately 2:1.

The example presented in Scheme 8 holds interest for yet other reasons. When direct comparison is made with Scheme 5, it is seen that a significant recouping of Scheme 8 efficiency is possible if the second anion is 2-propenyllithium and recourse is made to the modified reaction conditions (isolation deferred for a number of hours after quenching with saturated NH_4Cl solution). Diquinanes **26** (30%) and **27** (28%) are recognized to arise via the electrocyclic pathway and the common monoprotonated intermediate **U**. In this instance, the conversion to **U** is accompanied with the capa-bility for conformational equilibration represented by **U′** → **U″**. This singular ring inversion, which probably borders on being an isoenergetic process, opens the way for transannular aldolization to occur from diastereotopic π-faces of the carbonyl group.[19] The near-equal distribution of **26** to **27** indicates the cyclization rates for the two species to be closely comparable. Molecular models show that the annealing of a five-membered ring to **U**, as would arise when cyclopentenyllithium is utilized, conveys considerable rigidity to the system, thereby precluding a comparable conformational interconversion.

Scheme 9





Product **28** arises from the second possible pre-aldol regioisomer, formed by protonation of the bisenolate at the second reactive site. In this instance, conformational interconversion, if operative, is of little significance since transannular cyclization proceeds to deliver only that isomer having the vicinal methyl groups both β-oriented.

The minor constituent **29** is the obvious end result of 1,4-addition by the 2-lithiopropene.

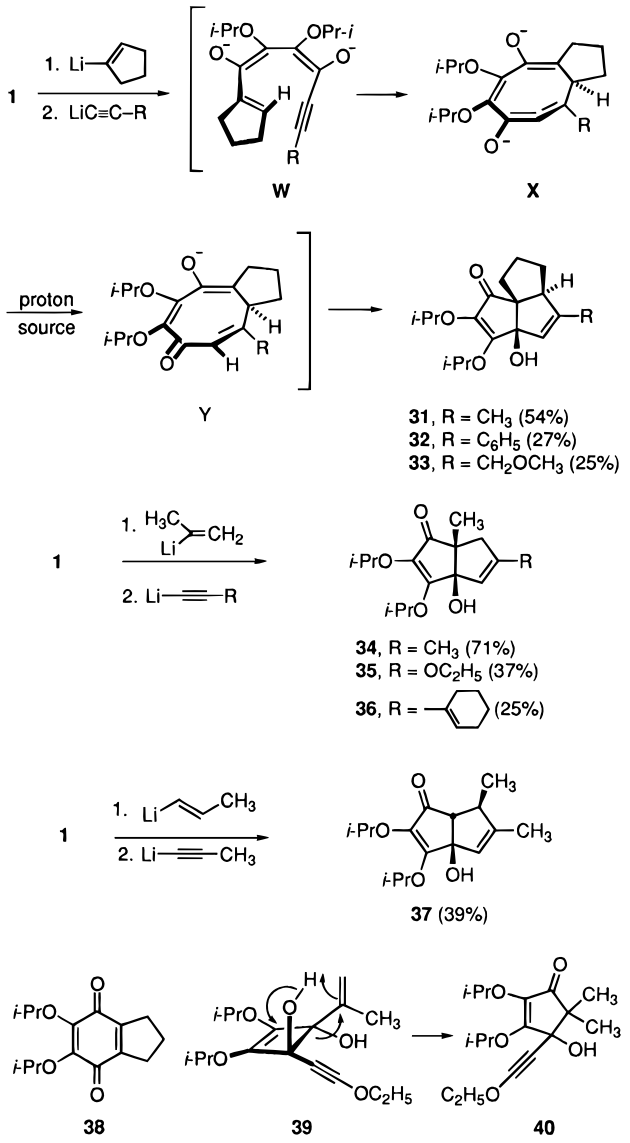
The use of 1-lithiotrimethylsilylethylene[20] as a first-stage reactant ultimately leads to generation of the dianionic intermediate **V** having electronically disparate enolate centers (Scheme 9). In this experiment, **30** was isolated as a single epimer of unknown configuration at C-4 in 72% yield. Consequently, the protonation of **V** is directed predominantly to the silicon-substituted carbon.

Acetylide Anion Additions. A Means for Exerting Complete Control over Aldolization. An obvious alternative ploy for fostering regioselective protonation is to increase the energy content and reactivity of one enolate center significantly over the other. The possibility of achieving reliable regioselectivity in this manner can be productively realized by replacing the second alkenyl anion with a lithium acetylide (Scheme 10).

(19) Strictly speaking, **27** is drawn in an enantiomeric relationship to the formal cyclization product of **U″** for the purpose of showing its structural relationship to **26** more clearly.

(20) (a) Boeckman, R. K., Jr.; Blum, D. M.; Ganem, B.-T.; Halvey, N. *Org. Synth.* **1978**, *58*, 152. (b) Gröbel, B.-T.; Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 83. (c) Zweifel, G.; Lewis, W. *J. Org. Chem.* **1978**, *43*, 2739.

Scheme 10



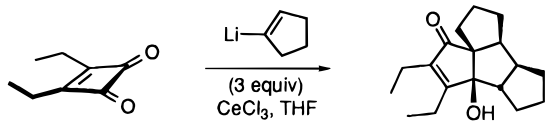
Although the capability of 1,3,5-octatrien-7-ynes, e.g., **W**, to undergo cyclization had not been explored previously, our expectation was that this process would operate and give rise to highly strained intermediates such as **X**. Once **X** is generated, protonation of its cumulenic enolate domain should be kinetically accelerated since relief of strain is maximized while proceeding to **Y**. With arrival at **Y**, only one transannular aldol pathway can operate. In the first three test cases, the exclusive isolation of **31**, **32**, and **33** conformed nicely to the outlined mechanistic proposal and provided the impetus to explore this directed scaffolding process in more depth.

The dropoff in reaction efficiency would appear to be linked to the onset of competitive side reactions. In selected examples, these byproducts have been identified. For example, those experiments that deliver **32** and **33** also lead to the production of small amounts of **38**, a benzoquinone recognized to be the readily formed isomer of the cyclopentenyl monoadduct of **1**.[21] The relative slowness with which the acetylide anions attack the monoadducts could provide adequate opportunity for the unimolecular rearrangement to take place.

In the experiment involving ethoxyacetylene, **40** (36%) is formed as abundantly as **35**. In light of the very general nature of cyclobutenol ring expansions,[22] this hydroxy ketone might well arise by means of the illustrated electronic reorganization.

The one-step conversion to unsaturated polyquinanes proceeds irrespective of whether the alkenyl anion is cyclic or acyclic. The pathway to product likely utilizes two sequential conrotatory processes as before, notwithstanding the need to involve highly strained, doubly charged, and quadruply unsaturated eight-membered rings of a type related to **X**.

Involvement of Other Cyclobutenediones. The isopropoxy groups in **1** are amenable to ready replacement by a variety of substituents either singly or in toto. The electronic character of the resultant cyclobutenedione is often significantly altered during such chemical changes. At issue in the present context is the extent to which these perturbations impact on the operability of the two principal mechanistic pathways. The results of condensing the diethyl derivative **41**[23] with an excess of cyclopentenyllithium proved to be immediately diagnostic of significant differences. In this instance, tetraquinane **42** was



found to be the only isolable product. Its stereochemical features, verified by means of X-ray diffraction, reveal that the dianionic oxy-Cope process continues to operate satisfactorily. Since it is highly unlikely that the second-stage addition occurs exclusively in cis fashion, it would appear that the pendant alkyl substitution interferes with the efficiency of the electrocyclic alternative. Presently, it is not known whether the complication arises during the 4π ring opening or the 8π cyclization.

The results of the condensation reactions of the acetylenic systems **43**,[24] **44**, and **45**[21d,24a] with excess 2-propenyllithium, summarized in Scheme 11, call notice to the prevalence with which 1,4-addition operates without concern for the nature of the R group. Therefore, the direct connection of a triple bond to an isopropoxycyclobutene-1,2-dione plays an unmistakable role in guiding entry of the second nucleophile. In the methyl example **44**, a third product was isolated in low yield, obtained in a pure state by chromatographic means, and tentatively formulated as **54**. Finally, attention is called to the fact that the addition of an excess (≥4 equiv) of 2-propenyllithium to **43** results in concomitant desilylation. This phenomenon is not otherwise apparent at lower concentrations, thereby providing added flexibility.

Finally, it is not only possible but also likely that the lithium counterions play an important role in directing nucleophilic attack and in facilitating both electrocyclic processes. Since **41** and **43**−**45** respond less efficiently to this series of reactions,

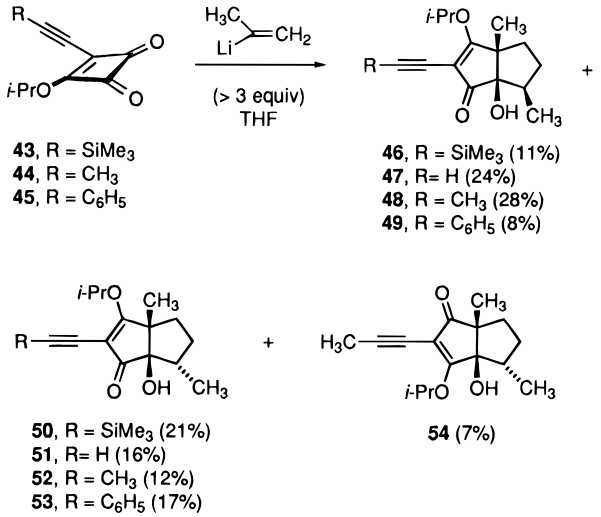
(21) (a) Moore, H. W.; Yerxa, B. R. *Chemtracts: Org. Chem.* **1992**, *5*, 273. (b) Moore, H. W.; Decker, O. H. W. *Chem. Rev.* **1986**, *86*, 821. (c) Liebeskind, L. S.; Wang, J. *J. Org. Chem.* **1993**, *58*, 3550. (d) Liebeskind, L. S. *Tetrahedron* **1989**, *45*, 3053.

(22) See, for example: (a) Stone, G. B.; Liebeskind, L. S. *J. Org. Chem.* **1990**, *55*, 4614. (b) Liebeskind, L. S.; Bombrun, A. *J. Org. Chem.* **1994**, *59*, 1149. (c) Mowick, T.; Doyon, J.; Paquette, L. A. *Tetrahedron Lett.* **1995**, *36*, 2369. (d) Paquette, L. A.; Doussot, P. *Research Chem. Intermed.* **1996**, *22*, 767.

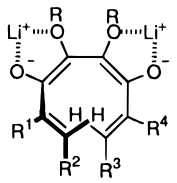
(23) (a) Hambrecht, J.; Henner, S. *Tetrahedron Lett.* **1976**, 1079. (b) Adams, C. M.; Schemenauer, J. E.; Crawford, E. S.; Joslin, S. A. *Synth. Commun.* **1992**, *22*, 1385. (c) Birchler, A. G.; Liu, F.; Liebeskind, L. A. *J. Org. Chem.* **1994**, *59*, 7737.

(24) (a) Liebeskind, L. S.; Fengl, R. W.; Wirtz, K. R.; Shawe, T. T. *J. Org. Chem.* **1988**, *53*, 2482. (b) Liebeskind, L. S.; Wang, J. *Tetrahedron Lett.* **1990**, *31*, 4293.

Scheme 11



the double lithium chelation illustrated in **55** (and their protonated counterparts) may be especially critical in assuring the



55

s-cis configuration required for ring closure. While this formalism was not used herein for reasons of simplification, it is adopted in the following paper.[7]

Experimental Section

General Methods. All reactions were carried out under an inert atmosphere of argon. Glassware was generally oven-dried or flame-dried in vacuo and purged with argon. Tetrahydrofuran was distilled from sodium-benzophenone ketyl immediately prior to use. Reactions were monitored by thin-layer chromatography. Melting points are uncorrected. The column chromatographic separations were performed with Woelm silica gel (230−400 mesh). Solvents were reagent grade and in most cases dried prior to use. The purity of all compounds was shown to be >95% by TLC and high-field ^{1}H (300 MHz) and ^{13}C NMR (75 MHz). The high-resolution and fast-atom-bombardment mass spectra were obtained at The Ohio State University Campus Chemical Instrumentation Center. Elemental analyses were performed at the Scandinavian Microanalytical Laboratory, Herlev, Denmark.

(*E*)- and (*Z*)-2-Bromo-2-butene. Three sequential distillations of a commercial isomeric mixture through a 30-cm glass bead-packed column afforded material containing greater than 97% of the *Z*-isomer, bp 82−83 °C (lit.[25] bp 85.5 °C).

The residue from the first distillation which was now richer in the *E*-isomer (*E*/*Z* = 80:20, VPC analysis) was taken in 4 g lots, combined with 290 mg of NaOH in cyclopentanol (15 mL), and heated to 90 °C. After 10 h, volatile material was distilled from the reaction vessel. Four fractions were collected (total 2 g), the isomeric content of which varied from 1.4% *Z* to 0% *Z*. These were combined and redistilled from CaH_2 through a short Vigreux column to furnish the *E*-isomer containing less than 1% of the *Z*-contaminant, bp 90−91 °C (lit.[26] bp 93.9 °C).

While the pure isomers appear to be stable to heat, they are very prone to equilibration when exposed to light. Therefore, all handling of these materials was performed with the exclusion of light to the maximum extent possible.

Prototypical Procedure for Double Addition of a Single Alkenyl Anion. Method A. All apparatus was either flame-dried under vacuum and purged with argon or flame-dried under argon immediately prior to use. An argon atmosphere was maintained throughout the reaction until quench. An alkenyl halide (2.7−3.25 equiv) was dissolved in dry THF (10−15 mL), cooled to −78 °C, and treated dropwise with *tert*-butyllithium (5.4−6.5 equiv, 1.7 M in hexanes) via syringe. The reaction mixture was stirred at −78 °C for 30 min, treated with a cold (−78 °C) solution of diisopropyl squarate (198 mg, 1.0 mmol) in THF (5 mL) via cannula, and allowed to stir at −78 °C (1 h), 0 °C (0−16 h), and room temperature (16 h). Subsequently, the contents were opened to the atmosphere, quenched with saturated NH_4Cl solution (6 mL), and diluted with ether (25 mL) and water (25 mL). The separated aqueous phase was extracted with ether (2 × 25 mL), and the combined organic phases were washed with water (25 mL) and brine (25 mL), dried, and concentrated. Product separation and purification were customarily accomplished by MPLC on silica gel.

Method B. In glassware, dried as described above, was placed a vinyl halide or tributylvinylstannane (3−3.75 equiv) dissolved in dry THF (10−15 mL). After cooling to −78 °C, *tert*-butyllithium (6−7.5 equiv) or *n*-butyllithium (3−3.75 equiv, 1.6 M in ether) was introduced dropwise. After 30 min, a cold (−78 °C) solution of diisopropyl squarate (198 mg, 1.0 mmol) in dry THF (5 mL) was added via cannula, and the resultant mixture was stirred at −78 °C (1−24 h), 0 °C (0−16 h), and room temperature (0−16 h). The reaction mixture was quenched with saturated NH_4Cl solution (6 mL, previously deoxygenated by bubbling argon through for 20 min prior to use) and stirred at 20 °C for an additional 1−16 h. The remainder of the workup parallels very closely that described under method A.

(3a*R,6a*R**)-4,5,6,6a-Tetrahydro-3a-hydroxy-2,3-diisopropoxy-1(3a*H*)-pentalenone (2).** Method B was utilized with tributylvinylstannane (1.77 mL, 4.0 mmol) and *n*-butyllithium (2.5 mL, 4.0 mmol) for the following time periods: 24, 0, 0, and 16 h. There was isolated 111 mg (44%) of **2** as a colorless oil: IR (neat, cm^{-1}) 3418, 1693, 1608; ^{1}H NMR (300 MHz, C_6D_6) δ 5.32 (heptet, J = 6 Hz, 1 H), 5.20 (heptet, J = 6 Hz, 1 H), 2.91 (br s, 1 H), 2.61 (d, J = 9 Hz, 1 H), 2.04 (dd, J = 13, 6 Hz, 1 H), 1.94−1.87 (m, 1 H), 1.81−1.68 (m, 1 H), 1.64−1.43 (m, 2 H), 1.28−1.14 (m, 1 H), 1.16 (d, J = 6 Hz, 3 H), 1.13 (d, J = 6 Hz, 3 H), 1.11 (d, J = 6 Hz, 6 H); ^{13}C NMR (75 MHz, C_6D_6) pm 199.7, 167.4, 133.2, 82.2, 73.4, 71.6, 55.8, 37.3, 28.3, 25.0, 22.7 (4 C); MS *m*/*z* (M^+) calcd 254.1518, obsd 254.1519.

Anal. Calcd for $C_{14}H_{22}O_4$: C, 66.12; H, 8.72. Found: C, 66.01; H, 8.78.

(3a*R,4*S**,6a*R**)-4,5,6,6a-Tetrahydro-3a-hydroxy-2,3-diisopropoxy-4,6a-dimethyl-1(3a*H*)-pentalenone (3).** Method A was employed with 2-bromopropene (0.33 mL, 3.75 mmol) and *tert*-butyllithium (4.4 mL, 7.5 mmol) for the following time periods: 1, 16, and 16 h. There was isolated 253 mg (90%) of **3** as a white solid, mp 51−52 °C: IR ($CHCl_3$) 3589, 1697, 1616, 1381, 1311; ^{1}H NMR (300 MHz, C_6D_6) δ 5.38−5.24 (m, 2 H), 2.24−2.18 (m, 2 H), 1.94−1.86 (m, 1 H), 1.43−1.23 (m, 2 H), 1.28 (s, 3 H), 1.11 (d, J = 6 Hz, 3 H), 1.10 (d, J = 6 Hz, 3 H), 1.09 (d, J = 6 Hz, 3 H), 1.07 (d, J = 6 Hz, 3 H), 1.01 (d, J = 7 Hz, 3 H), 0.98−0.84 (m, 1 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 202.7, 165.4, 132.5, 83.1, 73.6, 71.2, 56.7, 46.9, 35.0, 31.3, 22.9, 22.6 (2 C), 22.5, 19.6, 15.5; MS *m*/*z* (M^+) calcd 282.1831, obsd 282.1831.

Anal. Calcd for $C_{16}H_{26}O_4$: C, 68.06; H, 9.28. Found: C, 68.35; H, 9.34.

Also isolated was 7 mg (2.5%) of **i** as a white solid, mp 109−110 °C: IR ($CHCl_3$, cm^{-1}) 3560, 1650, 1600, 1385; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.40 (heptet, J = 6 Hz, 1 H), 4.89 (heptet, J = 6 Hz, 1 H), 2.85 (s, 1 H), 2.01−1.91 (m, 2 H), 1.72−1.64 (m, 1 H), 1.45−1.34 (m, 1 H), 1.30 (d, J = 6 Hz, 3 H), 1.29 (d, J = 6 Hz, 3 H), 1.27 (d, J = 6 Hz, 3 H), 1.19 (d, J = 6 Hz, 3 H), 1.13 (s, 3 H), 1.07−0.96 (m, 1 H), 0.97 (d, J = 7 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 199.9, 171.9, 131.4, 83.9, 73.4, 71.1, 52.8, 46.6, 34.3, 30.8, 22.8, 22.6, 22.3 (2 C), 19.9, 15.3; MS *m*/*z* (M^+) calcd 282.1831, obsd 282.1830.

(3a*R,6a*R**,6b*S**,9a*S**,9b*S**)-1,2,3,6a,6b,7,8,9,9a,9b-Decahydro-6a-hydroxy-5,6-diisopropoxy-4*H*-dicyclopenta[*a*,*b*]pentalen-4-one (4),**

(25) Lepingle, M. *Bull. Soc. Chim.* **1926**, *39*, 741.

(26) Dreiding, A. S.; Pratt, R. J. *J. Am. Chem. Soc.* **1954**, *76*, 1902. The isomerically pure bromides are currently available from Aldrich Chemical Company.

(27) This procedure was adapted from Reed, M. W.; Pollart, D. J.; Perri, S. T.; Foland, L. D.; Moore, H. W. *J. Org. Chem.* **1988**, *53*, 2477.

(3a*R,6a*R**,6b*S**,9a*R**,9b*S**)-1,2,3,6a,6b,7,8,9,9a,9b-Decahydro-6a-hydroxy-5,6-diisopropoxy-4*H*-dicyclopenta[*a,b*]pentalen-4-one (5), and (3a*R**,6a*R**,6b*R**,9a*S**,9b*S**)-1,2,3,6a,6b,7,8,9,9a,9b-Decahydro-6a-hydroxy-4,5-diisopropoxy-6*H*-dicyclopenta[*a,b*]pentalen-6-one (6).** From 1.57 g (8.0 mmol) of cyclopentenyl iodide, 9.4 mL (16 mmol) of *tert*-butyllithium, and 594 mg (3.0 mmol) of diisopropyl squarate according to method A for the following time periods 1, 0, and 16 h, there was obtained in the order of elution 37 mg (4%) of **6**, 276 mg (28%) of **4**, and 217 mg (22%) of **5**. In a second run, involving 400 mg (2.04 mmol) of cyclopentenyl iodide, 2.4 mL (4.08 mmol) of *tert*-butyllithium, and 150 mg (0.75 mmol) of diisopropyl squarate and the following time periods 1, 0, and 16 h, there was isolated 100 mg (40%) of **4** and 64 mg (26%) of **5**.

For **4**: colorless crystals, mp 125−126 °C; IR ($CHCl_3$, cm^{-1}) 3575, 1680, 1610, 1375, 1300, 1100; ^1H NMR (250 MHz, $CDCl_3$) δ 5.30 (heptet, J = 6.1 Hz, 1 H), 4.86 (heptet, J = 6.1 Hz, 1 H), 2.37 (m, 2 H), 2.20−2.00 (m, 3 H), 1.80−1.51 (m, 6 H), 1.51−1.38 (m, 5 H), 1.30 (d, J = 6.1 Hz, 6 H), 1.20 (d, J = 6.1 Hz, 3 H), 1.15 (d, J = 6.1 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 204.5, 166.1, 130.1, 85.4, 73.9, 71.7, 68.4, 57.1, 52.9, 52.5, 33.3, 33.2, 30.7, 28.2, 26.6, 24.9, 23.0, 22.8, 22.7, 22.3; MS *m/z* (M^+) calcd 334.2144, obsd 334.2148.

Anal. Calcd for $C_{20}H_{30}O_4$: C, 71.82; H, 9.04. Found: C, 71.75; H, 9.05.

For **5**: colorless crystals, mp 87−89 °C: IR ($CHCl_3$, cm^{-1}) 3580, 1685, 1610, 1380, 1305, 1100; ^1H NMR (250 MHz, $CDCl_3$) δ 5.36 (heptet, J = 6.1 Hz, 1 H), 4.98 (heptet, J = 6.1 Hz, 1 H), 2.19 (m, 1 H), 2.05−1.55 (m, 3 H), 1.55−1.25 (series of m, 4 H), 1.30 (d, J = 6.1 Hz, 6 H), 1.20 (d, J = 6.1 Hz, 3 H), 1.18 (d, J = 6.1 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 203.5, 165.2, 133.3, 78.6, 73.7, 73.0, 71.5, 48.11, 48.09, 30.0, 28.6, 27.6, 26.4, 23.0, 22.7, 22.4, 22.1, 21.9; MS *m/z* (M^+) calcd 334.2144, obsd 334.2149.

Anal. Calcd for $C_{20}H_{30}O_4$: C, 71.82; H, 9.04. Found: C, 71.92; H, 9.08.

For **6**: white solid, mp 171−172 °C: IR ($CHCl_3$, cm^{-1}) 3550, 1690, 1600, 1470, 1315, 1100; ^1H NMR (300 MHz, C_6D_6) δ 5.34 (heptet, J = 6 Hz, 1 H), 5.22 (heptet, J = 6 Hz, 1 H), 2.96 (s, 1 H), 2.26−2.20 (m, 1 H), 2.16−2.10 (m, 1 H), 2.06−1.90 (m, 1 H), 1.88−1.41 (m, 11 H), 1.14−1.07 (m, 12 H), 0.99−0.84 (m, 1 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 200.8, 172.4, 127.0, 79.8, 73.3, 72.0, 71.4, 60.3, 56.3, 49.0, 31.7 (2 C), 28.0, 27.0, 26.0, 22.8, 22.7, 22.6, 22.5, 19.9; MS *m/z* (M^+) calcd 334.2144, obsd 334.2144.

Anal. Calcd for $C_{20}H_{30}O_4$: C, 71.81; H, 9.05. Found: C, 71.40; H, 9.27.

[[(10a*R,10b*R**)-1,2,3,8,9,10,10a,10b-Octahydro-5,6-diisopropoxydicyclopenta[*a,c*]cycloocten-4,7-ylene]dioxy]bis[trimethylsilane] (8), [[(10a*R**,10b*S**)-1,2,3,8,9,10,10a,10b-Octahydro-5,6-diisopropoxydicyclopenta[*a,c*]cycloocten-4,7-ylene]dioxy]bis[trimethylsilane] (11), and [[(10a*R**,10b*R**)-1,2,3,8,9,10,10a,10b-Octahydro-6,7-diisopropoxydicyclopenta[*a,c*]cycloocten-4,5-ylene]dioxy]bis[trimethylsilane] (13).** A vacuum-dried flask was purged with argon, an atmosphere of which was maintained throughout the reaction. A solution of cyclopentenyl iodide (1.17 g, 6.0 mmol) in dry THF (20 mL) was cooled to −78 °C, treated sequentially with *tert*-butyllithium (7.06 mL of 1.7 M in hexanes, 12 mmol) and then 396 mg (2.0 mmol) of diisopropyl squarate according to the general procedure (0.5, 0.75, and 16 h). The reaction mixture was cooled to 0 °C, treated with triethylamine (20 drops) and chlorotrimethylsilane (0.68 mL, 6.0 mmol), and stirred for 1 h. The solvent was evaporated, and the residue was flashed through a short column of silica gel that had been pretreated with 2% triethylamine in petroleum ether. Separation of the isomers was effected with 0.5% triethylamine and 2% ether in petroleum ether as eluant. There was isolated 231 mg (24%) of **11**, 50 mg (5%) of **13**, and 409 mg (43%) of **8**.

For **8**: colorless crystalline solid, mp 88−90 °C; IR ($CHCl_3$, cm^{-1}) 1255, 1110, 880, 850; ^1H NMR (300 MHz, C_6D_6, 400 K) δ 4.32 (heptet, J = 7.5 Hz, 2 H), 2.59−2.49 (m, 4 H), 2.43−2.30 (m, 2 H), 1.83−1.57 (m, 5 H), 1.51−1.32 (m, 3 H), 1.28 (d, J = 7.5 Hz, 6 H), 1.25 (d, J = 7.5 Hz, 6 H), 0.28 (s, 18 H); ^{13}C NMR (75 MHz, C_6D_6, 350 K) ppm 135.7, 70.6, 31.1, 28.5, 23.3, 23.2, 22.4, 0.99 (3 C's not observed due to dynamic conformational equilibration); MS *m/z* (M^+) calcd 478.2934, obsd 478.2964.

For **11**: colorless oil; IR ($CHCl_3$, cm^{-1}) 1250, 1110, 870, 850; ^1H NMR (300 MHz, C_6D_6) δ 4.42 (heptet, J = 6 Hz, 2 H), 3.03 (m, 2 H), 2.67−2.57 (m, 2 H), 2.37−2.25 (m, 2 H), 1.77−1.64 (m, 4 H), 1.51−1.12 (m, 4 H), 1.27 (d, J = 6 Hz, 6 H), 1.19 (d, J = 6 Hz, 6 H), 0.32 (s, 18 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 137.7, 137.6, 130.5, 70.8, 47.6, 31.5, 30.0, 23.9, 23.3, 23.1, 1.1; MS *m/z* (M^+) calcd 478.2934, obsd 478.2934.

For **13**: colorless oil; IR ($CHCl_3$, cm^{-1}) 1255, 1105, 880, 850; ^1H NMR (300 MHz, C_6D_6, 350 K) δ 4.33 (heptet, J = 7 Hz, 1 H), 4.19 (heptet, J = 7 Hz, 1 H), 2.67−2.19 (m, 6 H), 1.81−1.25 (m, 8 H), 1.23−1.19 (m, 12 H), 0.31 (s, 9 H), 0.24 (s, 9 H); ^{13}C NMR (50 MHz, C_6D_6) ppm 70.2, 23.4, 1.4, 0.6 (other peaks are not observed because of conformational interconversion); MS *m/z* (M^+) calcd 478.2934, obsd 478.2939.

General Procedure for Dienolate Generation from 8, 11, and 13. A flame-dried flask was purged with argon, an atmosphere of which was maintained throughout the course of reaction. A solution of **8** (27 mg, 0.057 mmol) in dry THF (2 mL) was cooled to −78 °C, treated dropwise with methyllithium (0.16 mL of 1.4 M in ether, 0.23 mmol), and allowed to warm to room temperature after 15 min. The reaction mixture was quenched with water (3 mL) and extracted with ether (3×). The combined organic phases were dried and evaported to leave 20 mg (100%) of **4**.

Comparable treatment of **11** (22 mg, 0.046 mmol) furnished 14.3 mg (93%) of **5**.

When **13** (12.8 mg, 0.027 mmol) was subjected to analogous treatment, 7.8 mg (87%) of a 1:1 mixture of **6** and **15** was recovered. Alternatively, when **13** (19 mg, 0.04 mmol) was similarly treated with tetrabutylammonium fluoride (0.25 mL of 1 M in THF, 5 equiv) in place of methyllithium, 10 mg (75%) of **15** was isolated as a single diastereomer: colorless oil; IR ($CHCl_3$, cm^{-1}) 3550, 1685, 1590, 1380, 1370, 1310, 1095; ^1H NMR (300 MHz, $CDCl_3$) δ 5.41 (heptet, J = 6 Hz, 1 H), 4.87 (heptet, J = 6 Hz, 1 H), 2.77 (br s, 1 H), 2.43−2.30 (m, 2 H), 2.19−2.15 (m, 1 H), 2.05−1.99 (m, 1 H), 1.79−1.32 (m, 9 H), 1.29 (d, J = 6 Hz, 6 H), 1.23 (d, J = 6 Hz, 3 H), 1.21 (d, J = 6 Hz, 3 H), 0.98−0.83 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 200.9, 175.0, 128.6, 86.0, 73.6, 71.9, 65.0, 57.2, 52.9, 52.5, 33.5, 32.4, 31.2, 28.0, 26.3, 25.5, 22.7 (3 C), 22.5; MS *m/z* (M^+) calcd 334.2144, obsd 334.2144.

Anal. Calcd for $C_{20}H_{30}O_6$: C, 71.81; H, 9.05. Found: 72.04; H, 9.35.

(3a*R,4*S**,5*S**,6*S**,6a*R**)-4,5,6,6a-Tetrahydro-3a-hydroxy-2,3-diisopropoxy-4,5,6,6a-tetramethyl-1(3a*H*)-pentalenone (17a) and (3a*R**,4*S**,5*R**,6*S**,6a*R**)-4,5,6,6a-Tetrahydro-3a-hydroxy-2,3-diisopropoxy-4,5,6,6a-tetramethyl-1(3a*H*)-pentalenone (18).** Method A was employed with *E*-2-bromo-2-butene (506 mg, 3.75 mmol) and *tert*-butyllithium (4.4 mL, 7.5 mmol) for the following time periods: 1, 16, and 16 h. There was isolated 226 mg (73%) of **17a** and 11.5 mg (4%) of **18**.

For **17a**: white solid, mp 53−54 °C; IR (film, cm^{-1}) 3445, 1695, 1615, 1380, 1302; ^1H NMR (300 MHz, $CDCl_3$) δ 5.32 (heptet, J = 6 Hz, 1 H), 4.90 (heptet, J = 6 Hz, 1 H), 2.10 (s, 1 H), 2.10−1.95 (m, 2 H), 1.74−1.68 (m, 1 H), 1.34 (d, J = 6 Hz, 3 H), 1.30 (d, J = 6 Hz, 3 H), 1.20 (d, J = 6 Hz, 3 H), 1.18 (d, J = 6 Hz, 3 H), 1.00 (s, 3 H), 0.95 (d, J = 7 Hz, 3 H), 0.82 (d, J = 6 Hz, 3 H), 0.75 (d, J = 7 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 204.6, 165.6, 129.8, 85.5, 73.9, 71.7, 57.1, 47.9, 43.1, 40.9, 23.0, 22.7 (2 C), 22.4, 15.1, 14.0, 13.5, 10.5; MS *m/z* (M^+) calcd 310.2144, obsd 310.2152.

Anal. Calcd for $C_{18}H_{30}O_4$: C, 69.64; H, 9.74. Found: C, 69.38; H, 9.79.

The 3,5-dinitrobenzoate ester **17b** was prepared conventionally and isolated as a yellowish oil: IR ($CHCl_3$, cm^{-1}) 1730, 1690, 1620, 1540, 1340, 1310; ^1H NMR (300 MHz, $CDCl_3$) δ 9.22 (t, J = 2 Hz, 1 H), 9.08 (d, J = 2 Hz, 2 H), 5.40 (heptet, J = 6 Hz, 1 H), 5.07 (heptet, J = 6 Hz, 1 H), 2.61 (dq, J = 7.5, 7.5 Hz, 1 H), 2.17−2.09 (m, 1 H), 1.90−1.80 (m, 1 H), 1.35 (d, J = 6 Hz, 3 H), 1.31 (d, J = 6 Hz, 3 H), 1.27 (d, J = 6 Hz, 3 H), 1.21 (d, J = 6 Hz, 3 H), 1.09 (s, 3 H), 1.02 (d, J = 6.9 Hz, 3 H), 0.95 (d, J = 6 Hz, 3 H), 0.94 (d, J = 7.6 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 201.5, 163.0, 161.0, 148.7, 134.6, 131.0, 129.2, 122.3, 97.2, 74.6, 72.2, 57.7, 45.7, 43.5, 42.0, 23.1, 22.9, 22.8, 22.6, 13.9, 13.8, 13.6, 9.9; MS *m/z* (M^+) calcd 504.2107, obsd 504.2111.

For **18**: colorless oil; IR ($CHCl_3$, cm^{-1}) 3590, 1690, 1620, 1450, 1380, 1300; ^1H NMR (300 MHz, C_6D_6) δ 5.35 (heptet, J = 6 Hz, 1 H), 5.27 (heptet, J = 6 Hz, 1 H), 2.44 (dq, J = 7.5, 7.5 Hz, 1 H), 2.05 (s, 1 H), 1.77 (dq, J = 12, 7 Hz, 1 H), 1.35−1.27 (m, 1 H), 1.20 (s, 3 H), 1.12 (d, J = 6 Hz, 6 H), 1.10 (d, J = 6 Hz, 3 H), 1.05 (d, J = 6 Hz, 3 H), 0.94 (d, J = 7 Hz, 3 H), 0.82 (d, J = 7 Hz, 3 H), 0.71 (d, J = 7 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 202.9, 164.9, 131.3, 84.0, 73.4, 71.0, 59.1, 49.4, 40.7, 40.2, 22.7, 22.4, 22.3 (2 C), 16.1, 13.7, 13.3, 9.6; MS *m/z* (M^+) calcd 310.2144, obsd 310.2146.

(3a*R,4*R**,5*R**,6*R**,6a*R**)-4,5,6,6a-Tetrahydro-6a-hydroxy-2,3-diisopropoxy-3a,4,5,6-tetramethyl-1(3a*H*)-pentalenone (19).** Method B was utilized with *Z*-2-bromo-2-butene (506 mg, 3.75 mmol) and *tert*-butyllithium (4.4 mL, 7.5 mmol) for the following time periods: 1, 36, 6, and 1 h. There was obtained 25 mg of a mixture of **17a** (3%), **18** (1.5%), and **19** (3.5%) (estimated by NMR integration). A pure sample of **19** was obtained following chromatography of several runs.

For **19**: white solid, mp 105−106 °C; IR ($CHCl_3$, cm^{-1}) 3560, 1690, 1595, 1450, 1370, 1310; ^1H NMR (300 MHz, C_6D_6) δ 5.40 (heptet, J = 6 Hz, 1 H), 5.31 (heptet, J = 6 Hz, 1 H), 2.87 (s, 1 H), 2.42−2.36 (m, 1 H), 1.52−1.36 (m, 2 H), 1.34 (s, 3 H), 1.20 (d, J = 6 Hz, 3 H), 1.15 (d, J = 6 Hz, 3 H), 1.14 (d, J = 6 Hz, 3 H), 1.10 (d, J = 6 Hz, 3 H), 0.95 (d, J = 6 Hz, 3 H), 0.94 (d, J = 6.5 Hz, 3 H), 0.79 (d, J = 6.5 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 202.2, 173.1, 131.0, 82.5, 73.7, 71.1, 52.7, 46.8, 42.2, 39.4, 22.9, 22.7, 22.6, 22.5, 19.3, 14.3, 13.3, 9.1; MS *m/z* (M^+) calcd 310.2144, obsd 310.2143.

Prototypical Procedure for Mixed Alkenyllithium Additions. Method C. All apparatus was flame-dried under argon, an atmosphere of which was maintained until quenching was effected. A solution of the first vinyl halide (1.25 equiv) in dry THF (5−10 mL) was cooled to −78 °C, treated dropwise with *tert*-butyllithium (2.5 equiv), and stirred at −78 °C for 30 min. During this time, the second alkenyllithium was similarly generated from 4 equiv of a second vinyl halide and a proportionate amount of *tert*-butyllithium and THF. A solution of diisopropyl squarate (198 mg, 1.0 mmol) in dry THF (5 mL) was cooled to −78 °C and cannulated into the solution of the first anion. After 30 min, the second anion was similarly introduced, and the temperature of the reaction mixture was maintained at −78 °C for 1 h, at 0 °C for 2 h, and at room temperature for 12 h before being returned to 0 °C for quenching with water (6 mL). After 2 h of stirring, ether (25 mL) and water (25 mL) were added, and the separated aqueous phase was extracted with ether (2 × 10 mL). The combined organic phases were washed with water (25 mL) and brine (25 mL), dried, and evaporated. The residue was purified by flash chromatography on silica gel and by further MPLC and/or recrystallization if necessary.

Method D. This procedure differs from method C in that 1.07−1.5 equiv of the first vinyl halide or tributylvinylstannane was treated with *tert*-butyllithium (2.14−3.0 equiv) or *n*-butyllithium (1.07−1.5 equiv). Also, after addition of the second alkenyllithium (2.0−2.5 equiv of the vinyl halide and a proportionate amount of *tert*-butyllithium in THF), the reaction mixture was stirred at −78 °C for 0.5−1 h, at 0 °C for 0−20 h, and at room temperature for 0−20 h. Finally, the reaction mixture was allowed to warm to room temperature after quenching at 0 °C with deoxygenated saturated NH_4Cl solution with continued stirring for 1−24 h under argon prior to workup.

(3a*R,5a*S*,8a*R**)-4,5,5a,6,7,8-Hexahydro-3a-hydroxy-2,3-diisopropoxycyclopenta[*c*]pentalen-1(3a*H*)-one (20).** Method D was adopted with tributylvinylstannane (0.38 mL, 1.3 mmol), *n*-butyllithium (0.82 mL, 1.3 mmol), cyclopentenyl iodide (408 mg, 2.08 mmol), and *tert*-butyllithium (2.5 mL, 4.25 mmol) for the following time periods: 1, 2, and 10 h. After quenching, stirring was continued for 11 h. There was isolated 198 mg (67%) of **20** as a colorless oil: IR (neat, cm^{-1}) 3417, 1692, 1608; ^1H NMR (300 MHz, C_6D_6) δ 5.34−5.23 (m, 2 H), 2.57 (s, 1 H), 2.43−2.37 (m, 1 H), 2.09−2.03 (m, 3 H), 1.88-1.61 (m, 5 H), 1.47−1.30 (m, 2 H), 1.15 (d, J = 6 Hz, 3 H), 1.14 (d, J = 6 Hz, 3 H), 1.11 (d, J = 6 Hz, 3 H), 1.09 (d, J = 6 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 203.2, 166.3, 132.4, 83.0, 73.3, 71.3, 65.3, 50.0, 34.2, 33.8, 30.6, 28.4, 28.0, 22.8, 22.7 (2 C), 22.6; MS *m/z* (M^+) calcd 294.1831, obsd 294.1830.

Anal. Calcd for $C_{17}H_{26}O_4$: C, 69.36; H, 8.90. Found: C, 68.99; H, 8.84.

(3a*R,5*R**,5a*S*,8a*R**)-4,5,5a,6,7,8-Hexahydro-3a-hydroxy-2,3-diisopropoxy-5-methylcyclopenta[*c*]pentalen-1(3a*H*)-one (21).** Method D was employed with cyclopentenyl iodide (210 mg, 1.07 mmol), *tert*-butyllithium (1.26 mL, 2.14 mmol), *E*-1-bromopropene (0.17 mL, 2.0 mmol), and *tert*-butyllithium (2.35 mL, 4.0 mmol) for the following time periods: 0.5, 20, and 0 h. After quenching, stirring was continued for 16 h. There was isolated 190 mg (62%) of **21** and 12 mg (4%) of **24**.

For **21**: white solid, mp 101−102 °C; IR ($CHCl_3$, cm^{-1}) 3590, 1680, 1620, 1300, 1100; ^1H NMR (300 MHz, $CDCl_3$) δ 5.33 (heptet, J = 6.1 Hz, 1 H), 4.89 (heptet, J = 6.1 Hz, 1 H), 2.04−1.39 (series of m, 11 H), 1.33 (d, J = 6.1 Hz, 3 H), 1.32 (d, J = 6.1 Hz, 3 H), 1.22 (d, J = 6.1 Hz, 3 H), 1.17 (d, J = 6.1 Hz, 3 H), 0.94 (d, J = 6.5 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 204.2, 168.2, 128.8, 82.4, 73.7, 71.8, 67.1, 55.5, 48.0, 40.0, 32.1, 31.9, 26.8, 22.8, 22.7, 22.6, 22.2, 18.8; MS *m/z* (M^+) calcd 308.1987, obsd 308.1988.

Anal. Calcd for $C_{18}H_{28}O_4$: C, 70.10; H, 9.15. Found: C, 70.04; H, 9.12.

(3a*R,4*S**,5a*S**,8a*R**)-4,5,5a,6,7,8-Hexahydro-3a-hydroxy-2,3-diisopropoxy-4-methylcyclopenta[*c*]pentalen-1(3a*H*)-one (22) and (3a*R**,3b*S**,6a*R**,7a*R**)-3a,3b,4,5,6,6a,7,7a-Octahydro-3a-hydroxy-2,3-diisopropoxy-7a-methyl-1*H*-cyclopenta[*a*]pentalen-1-one (23).** Method C was adopted with 2-bromopropene (0.11 mL, 1.25 mmol), *tert*-butyllithium (1.5 mL, 2.5 mmol), cyclopentenyl iodide (784 mg, 4.0 mmol), and *tert*-butyllithium (4.7 mL, 8.0 mmol). There was obtained 83 mg (27%) of **22** and 188 mg (61%) of **23**.

For **22**: colorless oil; IR (neat, cm^{-1}) 3460, 1700, 1620; ^1H NMR (300 MHz, C_6D_6) δ 5.31−5.18 (m, 2 H), 2.67 (s, 1 H), 2.45−2.38 (m, 1 H), 2.12−1.94 (m, 3 H), 1.89−1.71 (m, 3 H), 1.50−1.43 (m, 1 H), 1.34−1.18 (m, 2 H), 1.14 (d, J = 6 Hz, 6 H), 1.12 (d, J = 6 Hz, 3 H), 1.07 (d, J = 6 Hz, 3 H), 1.05 (d, J = 7 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 202.9, 165.5, 132.6, 83.7, 73.5, 71.1, 66.3, 47.4, 42.7, 37.1, 33.9, 31.4, 28.3, 23.0, 22.8, 22.7, 22.4, 15.4; MS *m/z* (M^+) calcd 308.1987, obsd 308.1977.

Anal. Calcd for $C_{18}H_{28}O_4$: C, 70.10; H, 9.15. Found: C, 69.81; H, 9.20.

For **23**: white crystals, mp 127−128 °C; IR ($CHCl_3$, cm^{-1}) 3590, 1694, 1618, 1382, 1310; ^1H NMR (300 MHz, C_6D_6) δ 5.39−5.24 (m, 2 H), 2.24 (dd, J = 11.2, 4.4 Hz, 1 H), 1.99 (s, 1 H), 1.94−1.59 (m, 5 H), 1.45−1.23 (m, 2 H), 1.31 (s, 3 H), 1.20−0.86 (m, 14 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 203.0, 164.5, 133.4, 78.7, 73.4, 71.3, 62.7, 62.0, 46.2, 38.8, 28.0, 25.7, 23.0, 22.9, 22.7, 22.6, 22.5, 19.4; MS *m/z* (M^+) calcd 308.1987, obsd 308.1987.

Anal. Calcd for $C_{18}H_{28}O_4$: C, 70.10; H, 9.15. Found: C, 70.12; H, 9.18.

(3a*R,5*S**,5a*S**,8a*R**)-4,5,5a,6,7,8-Hexahydro-3a-hydroxy-2,3-diisopropoxy-5-methylcyclopenta[*c*]pentalen-1(3a*H*)-one (24) and (3a*R**,3b*S**,6a*R**,7*S**,7a*R**)-3a,3b,4,5,5a,6,6a,7a-Octahydro-3a-hydroxy-2,3-diisopropoxy-7-methyl-1*H*-cyclopenta[*a*]pentalen-1-one (25).** Method D was utilized with *E*-1-bromopropene (0.10 mL, 1.1 mmol), *tert*-butyllithium (1.3 mL, 2.2 mmol), cyclopentenyl iodide (400 mg, 2.04 mmol), and *tert*-butyllithium (2.4 mL, 4.08 mmol) for the following time periods: 0, 8, and 8 h. Stirring was continued for 16 h after quenching. There was produced 124.4 mg (40%) of **21**, 66.8 mg (22%) of **24**, and 38.2 mg (12%) of **25**.

For **24**: colorless oil; IR (neat, cm^{-1}) 3440, 1700, 1640, 1390, 1310; ^1H NMR (300 MHz, C_6D_6) δ 5.36−5.27 (m, 2 H), 2.38−2.30 (m, 2 H), 2.17 (dd, J = 13, 6 Hz, 1 H), 2.12−2.06 (m, 2 H), 1.85−1.72 (m, 3 H), 1.58−1.48 (m, 1 H), 1.41 (dd, J = 13, 13 Hz, 1 H), 1.32−1.19 (m, 1 H), 1.15 (d, J = 6 Hz, 6 H), 1.12 (d, J = 6 Hz, 3 H), 1.11 (d, J = 6 Hz, 3 H), 0.79 (d, J = 6.8 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 203.1, 166.3, 133.1, 81.8, 73.2, 71.3, 65.5, 54.9, 40.8, 31.8, 30.2, 28.2, 27.7, 22.8 (2 C), 22.7 (2 C), 15.2; MS *m/z* (M^+) calcd 308.1987, obsd 308.1984.

Anal. Calcd for $C_{18}H_{28}O_4$: C, 70.10; H, 9.15. Found: C, 70.46; H, 9.35.

For **25**: colorless oil; IR ($CHCl_3$, cm^{-1}) 3600, 1693, 1617, 1382, 1307; ^1H NMR (300 MHz, C_6D_6) δ 5.313 (heptet, J = 6 Hz, 1 H), 5.308 (heptet, J = 6 Hz, 1 H), 2.67 (d, J = 0.6 Hz, 1 H), 2.43 (s, 1 H), 2.42−2.30 (m, 1 H), 2.26 (ddd, J = 12.5, 12, 6 Hz, 1 H), 1.81−1.62 (m, 4 H), 1.24−0.99 (m, 3 H), 1.14 (d, J = 6 Hz, 9 H), 1.13 (d, J = 6 Hz, 3 H), 1.00 (d, J = 7.5 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 199.4, 165.2, 134.1, 78.1, 73.5, 71.5, 70.5, 55.8, 52.2, 33.5, 27.8, 23.0,

22.9, 22.70, 22.67 (2 C), 21.2, 14.9; MS *m/z* (M^+) calcd 308.1986, obsd 308.1987.

(3a*R,4*R**,5*R**,6a*R**)-4,5,6,6a-Tetrahydro-3a-hydroxy-2,3-diisopropoxy-4,5,6a-trimethyl-1(3a*H*)-pentalenone (26), (3a*R**,4*S**,5*S**,6a*R**)-4,5,6,6a-Tetrahydro-3a-hydroxy-2,3-diisopropoxy-4,5,6a-trimethyl-1(3a*H*)pentalenone (27), (3a*R**,4*S**,6*S**,6a*R**)-4,5,6,6a-Tetrahydro-3a-hydroxy-2,3-diisopropoxy-4,6,6a-trimethyl-1(3a*H*)-pentalenone (28), and (3a*R**,5*R**,6*R**,6a*R**)-4,5,6,6a-Tetrahydro-6a-hydroxy-2,3-diisopropoxy-3a,5,6-trimethyl-1(3a*H*)-pentalenone (29).** Method D was utilized with *Z*-2-bromobutene (150 mg, 1.1 mmol), *tert*-butyllithium (1.3 mL, 2.2 mmol), 2-bromopro-pene (0.22 mL, 2.5 mmol), and *tert*-butyllithium (3.0 mL, 5.0 mmol) for the following time periods: 1, 10, and 10 h. Stirring was continued for 16 h after quenching. There was isolated 89 mg (30%) of **26**, 84 mg (28%) of **27**, 64 mg (22%) of **28**, and 11 mg (4%) of **20**.

For **26**: colorless oil; IR (neat, cm^{-1}) 3440, 1694, 1613, 1380, 1304; ^{1}H NMR (300 MHz, C_6D_6) δ 5.32 (heptet, J = 6 Hz, 2 H), 2.23 (dq, J = 7, 7 Hz, 1 H), 2.02 (dd, J = 13, 7 Hz, 1 H), 1.83−1.73 (m, 1 H), 1.29 (s, 3 H), 1.27−1.16 (m, 1 H), 1.14−1.08 (m, 12 H), 0.82 (d, J = 7 Hz, 3 H), 0.73 (d, J = 7 Hz, 3 H) (OH not observed); ^{13}C NMR (75 MHz, C_6D_6) ppm 203.3, 166.8, 132.4, 83.6, 73.3, 71.4, 54.5, 42.7, 42.1, 33.2, 22.8, 22.7, 22.6 (2 C), 19.5, 15.0, 8.6; MS *m/z* (M^+) calcd 296.1987, obsd 296.1985.

Anal. Calcd for $C_{17}H_{28}O_4$: C, 68.89; H, 9.52. Found: C, 68.59; H, 9.57.

For **27**: colorless oil; IR (neat, cm^{-1}) 3437, 1692, 1611, 1380, 1303; ^{1}H NMR (300 MHz, C_6D_6) δ 5.8−5.2 (m, 2 H), 2.31−2.19 (m, 1 H), 2.01 (dq, J = 7.2 Hz, 1 H), 1.89 (dd, J = 13, 8 Hz, 1 H), 1.59 (dd, J = 13, 6.8 Hz, 1 H), 1.32 (s, 3 H), 1.16 (d, J = 6 Hz, 3 H), 1.14 (d, J = 6 Hz, 3 H), 1.11 (d, J = 6 Hz, 3 H), 1.09 (d, J = 6 Hz, 3 H), 0.80 (d, J = 8.0 Hz, 3 H), 0.74 (d, J = 7 Hz, 3 H) (OH not observed); ^{13}C NMR (75 MHz, C_6D_6) ppm 203.6, 165.7, 131.1, 85.3, 73.6, 71.4, 55.9, 48.9, 40.9, 36.0, 23.1, 23.0, 22.6, 22.5, 21.2, 14.9, 10.8; MS *m/z* (M^+) calcd 296.1987, obsd 296.1988.

Anal. Calcd for $C_{19}H_{28}O_4$: C, 68.89; H, 9.52. Found: C, 68.85; H, 9.57.

For **28**: colorless oil; IR (neat, cm^{-1}) 3404, 1693, 1614, 1380, 1306; ^{1}H NMR (300 MHz, C_6D_6) δ 5.29 (heptet, J = 6 Hz, 2 H), 2.50−2.44 (m, 1 H), 2.40−2.30 (br s, 1 H), 2.32−2.20 (m, 1 H), 1.34−1.16 (m, 2 H), 1.19 (s, 3 H), 1.12 (d, J = 6 Hz, 3 H), 1.11 (d, J = 6 Hz, 3 H), 1.10 (d, J =6 Hz, 3 H), 1.07 (d, J = 6 Hz, 3 H), 0.98 (d, J = 7 Hz, 3 H), 0.95 (d, J = 7 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 203.4, 165.0, 131.4, 84.1, 73.7, 71.2, 60.2, 43.9, 39.4, 36.4, 23.0, 22.62 (2 C), 22.59, 16.2 (2 C), 15.9; MS *m/z* (M^+) calcd 296.1987, obsd 296.1985.

Anal. Calcd for $C_{17}H_{28}O_4$: C, 68.89; H, 9.52. Found: C, 68.74; H, 9.62.

For **29**: colorless solid, mp 90−91 °C; IR ($CHCl_3$, cm^{-1}) 3554, 1691, 1597, 1383, 1308; ^{1}H NMR (300 MHz, C_6D_6) δ 5.33 (heptet, J = 6 Hz, 1 H), 5.18 (heptet, J = 6 Hz, 1 H), 2.68 (s, 1 H), 1.97−1.83 (m, 1 H), 1.65 (dd, J = 13, 6.5 Hz, 1 H), 1.44 (dd, J = 13, 13 Hz, 1 H), 1.34 (s, 3 H), 1.42−1.32 (m, 1 H), 1.14 (d, J = 6 Hz, 3 H), 1.09 (d, J = 6 Hz, 9 H), 1.05 (d, J = 6 Hz, 3 H), 0.77 (d, J = 6 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 201.0, 174.3, 126.6, 84.2, 73.4, 71.4, 51.9, 50.3, 45.1, 41.4, 22.7 (2 C), 22.6, 22.4, 21.4, 17.2, 10.7; MS *m/z* (M^+) calcd 296.1987, obsd 296.1985.

Anal. Calcd for $C_{17}H_{28}O_4$: C, 68.89; H, 9.52. Found: C, 68.54; H, 9.86.

(3a*R,6a*R**)-4,5,6,6a-Tetrahydro-3a-hydroxy-2,3-diisopropoxy-6a-methyl-4-(trimethylsilyl)-1(3a*H*)-pentalenone (30). Method D.** From 197 mg (1.1 mmol) of α-bromotrimethylvinylsilane, *tert*-butyllithium (1.29 mL, 2.2 mmol), 2-bromopropene (0.18 mL, 2.0 mmol) and *tert*-butyllithium (2.35 mL, 4.0 mmol), there was isolated 245 mg (72%) of **30** as a colorless solid, mp 73−74 °C: IR ($CHCl_3$, cm^{-1}) 3590, 1690, 1620; ^{1}H NMR (300 MHz, C_6D_6) δ 5.25 (heptet, J = 6 Hz, 1 H), 5.17 (heptet, J = 6 Hz, 1 H), 2.90 (s, 1 H), 2.18 (dd, J = 12, 5 Hz, 1 H), 1.42 (ddd, J = 11, 5, 5 Hz, 1 H), 1.31−0.83 (m, 3 H), 1.22 (s, 3 H), 1.18 (d, J = 6 Hz, 3 H), 1.14 (d, J = 6 Hz, 3 H), 1.12 (d, J = 6 Hz, 3 H), 1.04 (d, J = 6 Hz, 3 H), 0.06 (s, 9 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 203.2, 166.6, 133.0, 84.3, 74.3, 71.3, 57.3, 40.2, 38.0, 25.3, 22.9, 22.8, 22.7, 22.6, 19.6, −1.2; MS *m/z* (M^+) calcd 340.2070, obsd 340.2086.

Anal. Calcd for $C_{18}H_{22}O_4Si$: C, 63.49; H, 9.47. Found: C, 63.65; H, 9.39.

General Procedure for Acetylide Anion Additions. The apparatus was flame-dried under argon, an atmosphere of which was maintained until quench. The vinyl halide (1.07−1.25 equiv) was dissolved in anhydrous THF (10 mL), cooled to −78 °C, treated dropwise with *tert*-butyllithium (2.14−2.50 equiv), and stirred for 30 min. In a separate flask, a monosubstituted acetylene (2−5 equiv) was dissolved in THF at −78 °C, treated with *n*-butyllithium (2−5 equiv), and stirred at −78 °C for 30 min. A solution of diisopropyl squarate (198 mg, 1.0 mmol) in THF (4 mL) was cooled to −78 °C and cannulated into a solution of the first anion. After 30 min, the second anion was similarly introduced. Generally, a chelating agent (TMEDA, [12]crown-4, etc) was premixed with the acetylide. The reaction mixture was stirred at −78 °C for 1 h and at room temperature for 16 h, quenched with deoxygenated saturated NH_4Cl solution at 0 °C (6 mL), stirred for 16 h under argon, and partitioned between water (25 mL) and ether (25 mL). The usual workup followed. The regiochemistry of the oxygenated ring has been confirmed by long-range DEPT in selected examples.

(3a*R,5a*S**,8a*R**)-5a,6,7,8-Tetrahydro-3a-hydroxy-2,3-diisopropoxy-5-methylcyclopenta[*c*]pentalen-1(3a*H*)-one (31):** 165 mg (54%); white solid, mp 106 °C; IR ($CHCl_3$, cm^{-1}) 3580, 1690, 1615, 1380, 1305, 1260, 1100; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.41 (m, 1 H), 5.29 (heptet, J = 6 Hz, 1 H), 4.86 (heptet, J = 6 Hz, 1 H), 2.79 (m, 1 H), 2.29 (s, 1 H), 2.02−1.96 (m, 1 H), 1.80−1.70 (m, 3 H), 1.61 (d, J = 1 Hz, 3 H), 1.59−1.47 (m, 2 H), 1.29 (d, J = 6 Hz, 3 H), 1.25 (d, J = 6 Hz, 3 H), 1.16 (d, J = 6 Hz, 3 H), 1.15 (d, J = 6 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 202.9, 169.1, 146.3, 130.7, 126.3, 85.2, 73.7, 71.8, 63.9, 57.3, 31.0, 30.3, 26.7, 22.6, 22.5 (2 C), 22.4, 15.3; MS *m/z* (M^+) calcd 306.1831, obsd 306.1831.

Anal. Calcd for $C_{18}H_{26}O_4$: C, 70.55; H, 8.56. Found: C, 70.73; H, 8.60.

(3a*R,5a*S**,8a*R**)-5a,6,7,8-Tetrahydro-3a-hydroxy-2,3-diisopropoxy-5-phenylcyclopenta[*c*]pentalen-1(3a*H*)-one (32):** 101 mg (27%); colorless crystals, mp 170−171 °C; IR ($CHCl_3$, cm^{-1}) 3585, 1675, 1605, 1370, 1295, 1085; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43−7.42 (m, 2 H), 7.41−7.25 (m, 3 H), 6.19 (s, 1 H), 5.35 (heptet, J = 6 Hz, 1 H), 4.96 (heptet, J = 6 Hz, 1 H), 3.57−3.54 (m, 1 H), 2.49 (s, 1 H), 2.15−2.11 (m, 1 H), 2.08−2.00 (m, 1 H), 1.98−1.80 (m, 2 H), 1.65−1.59 (m, 2 H), 1.37 (d, J = 6 Hz, 3 H), 1.30 (d, J = 6 Hz, 3 H), 1.22 (d, J = 6 Hz, 3 H), 1.18 (d, J = 6 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 202.1, 168.8, 147.7, 134.6, 131.0, 128.4, 128.1, 126.7, 125.7, 85.0, 74.1, 72.0, 63.7, 53.9, 32.0, 31.4, 27.0, 22.7 (2 C), 22.6, 22.5; MS *m/z* (M^+) calcd 368.1987, obsd, 368.1992.

Anal. Calcd for $C_{23}H_{28}O_4$: C, 74.96; H, 7.66. Found: C, 74.80; H, 7.72.

(3a*R,5a*S**,8a*R**)-5a,6,7,8-Tetrahydro-3a-hydroxy-2,3-diisopropoxy-5-(methoxymethyl)cyclopenta[*c*]pentalen-1(3a*H*)-one (33):** 83 mg (25%); colorless oil; IR (neat, cm^{-1}) 3420, 1690, 1600; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.71 (d, J = 1.2 Hz, 1 H), 5.29 (heptet, J = 6 Hz, 1 H), 4.88 (heptet, J = 6 Hz, 1 H), 3.86 (s, 2 H), 3.27 (s, 3 H), 2.95−2.93 (m, 1 H), 2.41 (s, 1 H), 2.03−1.97 (m, 1 H), 1.78−1.71 (m, 3 H), 1.63−1.51 (m, 2 H), 1.31 (d, J = 6 Hz, 3 H), 1.27 (d, J = 6 Hz, 3 H), 1.17 (d, J = 6 Hz, 3 H), 1.15 (d, J = 6 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 202.6, 168.7, 146.6, 130.8, 127.3, 84.9, 73.9, 71.9, 70.0, 63.8, 58.3, 54.0, 30.9, 30.8, 26.9, 22.6 (2 C), 22.5, 22.4; MS *m/z* (M^+) calcd 336.1937, obsd 336.1937.

Anal. Calcd for $C_{19}H_{28}O_5$: C, 67.83; H, 8.39. Found: C, 67.98; H, 8.42.

(3a*R,6a*R**)-6,6a-Dihydro-3a-hydroxy-2,3-diisopropoxy-5,6a-dimethyl-1(3a*H*)-pentalenone (34):** From 336 mg (1.7 mmol) of diisopropyl squarate and other reagent levels adjusted accordingly: 335 mg (71%); colorless oil; IR (neat, cm^{-1}) 3430, 1690, 1610, 1380, 1110, 1030; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.48 (m, 1 H), 5.33 (heptet, J = 6 Hz, 1 H), 4.86 (heptet, J = 6 Hz, 1 H), 2.56 (dm, J = 18 Hz, 1 H), 2.19 (dm, J = 18 Hz, 1 H), 2.16 (s, 1 H), 1.65 (m, 3 H), 1.33 (d, J = 6 Hz, 3 H), 1.29 (d, J = 6 Hz, 3 H), 1.22 (s, 3 H), 1.19 (d, J = 6 Hz, 3 H), 1.17 (d, J = 6 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 203.1, 168.2, 144.6, 130.4, 126.5, 86.2, 74.0, 71.9, 54.1, 45.4, 22.7 (2 C), 22.3 (2 C), 19.3, 16.7; MS *m/z* (M^+) calcd 280.1674, obsd 280.1679.

Anal. Calcd for $C_{16}H_{24}O_4$: C, 68.55; H, 8.63. Found: C, 68.63; H, 8.56.

(3a*R,6a*R**)-5-Ethoxy-6,6a-dihydro-3a-hydroxy-2,3-diisopropoxy-6a-methyl-1(3a*H*)-pentalenone (35):** 114.5 mg (37%); white solid, mp 116−117 °C; IR ($CHCl_3$, cm^{-1}) 3590, 1695, 1620; ^1H NMR (300 MHz, C_6D_6) δ 5.35 (heptet, $J = 6$ Hz, 1 H), 5.20 (heptet, $J = 6$ Hz, 1 H), 4.71 (s, 1 H), 3.42−3.26 (m, 2 H), 2.97 (dd, $J = 17$, 1.2 Hz, 1 H), 2.35 (dd, $J = 17$, 1.7 Hz, 1 H), 2.13 (s, 1 H), 1.38 (s, 3 H), 1.19 (d, $J = 6$ Hz, 6 H), 1.13 (d, $J = 6$ Hz, 3 H), 1.09 (d, $J = 6$ Hz, 3 H), 0.95 (t, $J = 7$ Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 201.1, 167.8, 160.8, 129.7, 97.7, 83.1, 72.6, 70.6, 64.0, 50.8, 40.2, 21.9, 21.8, 21.7, 21.5, 19.1, 13.3; MS *m/z* (M^+) calcd 310.1780, obsd 310.1791.

Anal. Calcd for $C_{17}H_{26}O_5$: C, 65.78; H, 8.44. Found: C, 65.58; H, 8.44.

(3a*R,6a*R**)-5-(1-Cyclohexen-1-yl)-6,6a-dihydro-3a-hydroxy-2,3-diisopropoxy-6a-methyl-1(3a*H*)-pentalenone (36):** 86 mg (25%); colorless oil; IR (neat, cm^{-1}) 3408, 1693, 1605; ^1H NMR (300 MHz, C_6D_6) δ 5.77 (s, 1 H), 5.57 (dd, $J = 4$, 4 Hz, 1 H), 5.32 (heptet, $J = 6$ Hz, 1 H), 5.23 (heptet, $J = 6$ Hz, 1 H), 3.06 (dd, $J = 17$, 1 Hz, 1 H), 2.38 (s, 1 H), 2.37 (dd, $J = 16$, 1.5 Hz, 1 H), 2.00−1.85 (m, 4 H), 1.45−1.32 (m, 4 H), 1.45 (s, 3 H), 1.18 (d, $J = 6$ Hz, 3 H), 1.14 (d, $J = 6$ Hz, 3 H), 1.11 (d, $J = 6$ Hz, 3 H), 1.10 (d, $J = 6$ Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 202.7, 168.0, 146.0, 133.0, 130.9, 128.1, 124.5, 86.2, 73.7, 71.6, 53.5, 41.5, 25.9, 22.9, 22.8 (2 C), 22.7, 22.5, 22.4, 20.0 (one C overlapped); MS *m/z* (M^+) calcd 346.2144, obsd 346.2142.

(3a*R,6*R**,6a*R**)-6,6a-Dihydro-3a-hydroxy-2,3-diisopropoxy-5,6-dimethyl-1(3a*H*)-pentalenone (37):** 110 mg (39%); colorless oil; IR ($CHCl_3$, cm^{-1}) 3588, 1695, 1615, 1381, 1307, 1098; ^1H NMR (300 MHz, C_6D_6) δ 5.49 (m, 1 H), 5.30 (heptet, $J = 6$ Hz, 1 H), 5.24 (heptet, $J = 6$ Hz, 1 H), 2.69−2.66 (m, 1 H), 2.62 (d, $J = 3$ Hz, 3 H), 2.53 (s, 1 H), 1.34−1.33 (m, 3 H), 1.31−1.27 (m, 1 H), 1.17−1.11 (m, 12 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 198.8, 168.6, 148.9, 128.3, 126.0, 84.9, 73.6, 71.7, 62.6, 44.6, 22.9, 22.8, 22.7, 22.6, 20.9, 14.7; MS *m/z* (M^+) calcd 280.1675, obsd 280.1674.

Anal. Calcd for $C_{16}H_{24}O_4$: C, 68.55; H, 8.63. Found: 68.70; H, 8.69.

4-(Ethoxyethynyl)-4-hydroxy-2,3-diisopropoxy-5,5-dimethyl-2-cyclopenten-1-one (40): colorless oil; IR (neat, cm^{-1}) 3427, 1703, 1626; ^1H NMR (300 MHz, C_6D_6) δ 5.33 (heptet, $J = 6$ Hz, 1 H), 5.22 (heptet, $J = 6$ Hz,1 H), 3.52 (q, $J = 7$ Hz, 2 H), 2.63 (s, 1 H), 1.47 (s, 3 H), 1.40 (s, 3 H), 1.19 (d, $J = 6$ Hz, 3 H), 1.16 (d, $J = 6$ Hz, 3 H), 1.11 (d, $J = 6$ Hz, 3 H), 1.10 (d, $J = 6$ Hz, 3 H), 0.87 (t, $J = 7$ Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 201.4, 164.0, 129.1, 94.8, 73.5, 73.2, 72.9, 70.7, 49.0, 37.5, 22.9, 21.8, 21.7, 21.6, 20.7, 13.0 (one C overlapped); MS *m/z* (M^+) calcd 310.1780, obsd 310.1795.

(3a*R,6a*S**,6b*S**,9a*R**,9b*S**)-5,6-Diethyl-1,2,3,6a,6b,7,8,9,9a,9b-decahydro-6a-hydroxy-4*H*-dicyclopenta[*a,b*]pentalen-4-one (42).** Cyclopentenyllithium was generated from the iodide (588 mg, 3.0 mmol) and *tert*-butyllithium (3.52 mL of 1.7 M, 6.0 mmol) as previously described. This solution was cannulated into a slurry of dried cerium trichloride (from 1.12 of the heptahydrate) in THF (10 mL) at −78 °C. After 2 h, a solution of **41** (138 mg, 1.0 mmol) was added, and the reaction mixture was stirred at −78 °C for 3 h and at room temperature overnight prior to quenching with saturated NH_4Cl solution (6 mL). The usual workup gave 63 mg (23%) of **42** as colorless crystals, mp 123−124 °C: IR ($CHCl_3$, cm^{-1}) 3580, 1690, 1630, 1500, 1350; ^1H NMR (300 MHz, $CDCl_3$) δ 2.55−1.34 (m, 2 H), 2.31−2.14 (m, 3 H), 2.07−1.88 (m, 3 H), 1.83−1.51 (m, 8 H), 1.46−1.36 (m, 2 H), 1.20−1.07 (m, 1 H), 1.17 (t, $J = 8$ Hz, 3 H), 1.01 (t, $J = 8$ Hz, 3 H) (OH signal not seen); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 211.3, 170.6, 145.2, 85.8, 74.9, 56.1, 48.9, 47.8, 31.3, 28.5, 27.7, 26.1, 23.3, 21.9, 21.7, 16.9, 14.2, 13.0; MS *m/z* (M^+) calcd 274.1932, obsd 274.1931.

3-Isopropoxy-4-(1-propynyl)-3-cyclobutene-1,2-dione (44). Propyne (ca. 2 mL) was condensed into a flame-dried flask under argon at −78 °C. THF (25 mL) was slowly introduced by syringe followed by the dropwise addition of *n*-butyllithium (8.0 mL of 1.36 M, 11 mmol). The reaction mixture was stirred at −78 °C for 30 min and treated with a precooled (−78 °C) solution of diisopropyl squarate (2.0 g, 10 mmol) in THF (25 mL) via cannula. Reaction was allowed to proceed for 1 h at −78 °C prior to the addition of trifluoroacetic anhydride (1.9 mL, 13.5 mmol). Stirring was maintained for 15 min, at which point saturated NH_4Cl solution (30 mL) was added, and the temperature was allowed to warm to 20 °C.[27] Brine (50 mL) was added, and the product was extracted into ether (2 × 50 mL). The combined organic layers were washed with brine (50 mL), dried, and evaporated to give 1.75 g (97%) of **44** as yellow crystals, mp 99−100 °C (from ether−petroleum ether): IR ($CHCl_3$, cm^{-1}) 2220, 1800, 1770, 1590, 1400; ^1H NMR (200 MHz, $CDCl_3$) δ 5.38 (heptet, $J = 6$ Hz, 1 H), 2.27 (s, 3 H), 1.50 (d, $J = 6$ Hz, 6 H); ^{13}C NMR (50 MHz, $CDCl_3$) ppm 196.2, 195.4, 191.5, 162.3, 118.6, 80.6, 66.9, 22.5, 6.0; MS *m/z* (M^+) calcd 178.0629, obsd 178.0631.

(3a*R,6*R**,6a*R**)-4,5,6,6a-Tetrahydro-6a-hydroxy-3-isopropoxy-3a,6-dimethyl-2-[(trimethylsilyl)ethynyl]-1(3a*H*)-pentalenone (46) and (3a*R**,6*S**,6a*R**)-4,5,6,6a-Tetrahydro-6a-hydroxy-3-isopropoxy-3a,6-dimethyl-2-[(trimethylsilyl)ethynyl]-1(3a*H*)-pentalenone (50).** From 236 mg (1.0 mmol) of **43**, 0.20 mL (2.25 mmol) of 2-bromopropene, and 2.65 mL (4.5 mmol) of *tert*-butyllithium, there was isolated 35 mg (11%) of **46** and 68 mg (21%) of **50**.

For **46**: white solid, mp 113−115 °C; IR ($CHCl_3$, cm^{-1}) 3570, 2160, 1700, 1580, 1320, 1110; ^1H NMR (300 MHz, C_6D_6) δ 5.70 (heptet, $J = 6$ Hz, 1 H), 2.72 (s, 1 H), 1.95−1.88 (m, 1 H), 1.76−1.72 (m, 1 H), 1.70−1.42 (m, 1 H), 1.37−1.31 (m, 2 H), 1.22 (s, 3 H), 1.10 (d, $J = 6$ Hz, 3 H), 1.07 (d, $J = 6$ Hz, 3 H), 0.94 (d, $J = 7$ Hz, 3 H), 0.16 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 204.2, 190.7, 100.0, 95.9, 95.3, 85.5, 75.3, 55.8, 41.5, 34.6, 32.1, 22.7, 22.5, 20.0, 13.2, −0.2; MS *m/z* (M^+) calcd 320.1808, obsd 320.1810.

For **50**: white crystals, mp 108−109 °C; IR ($CHCl_3$, cm^{-1}) 3560, 2160, 1700, 1685; ^1H NMR (300 MHz, $CDCl_3$) δ 5.72 (heptet, $J = 6$ Hz, 1 H), 3.01 (s, 1 H), 2.02−1.91 (m, 2 H), 1.69−1.60 (m, 1 H), 1.50−1.39 (m, 1 H), 1.35 (d, $J = 6$ Hz, 6 H), 1.11 (s, 3 H), 0.94 (d, $J = 7$ Hz, 3 H), 0.98−0.83 (m, 1 H), 0.16 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 203.2, 189.5, 100.3, 99.2, 94.8, 86.3, 75.2, 56.0, 46.8, 34.8, 30.5, 22.6, 22.3, 19.0, 15.0, −0.2; MS *m/z* (M^+) calcd 320.1808, obsd 320.1813.

(3a*R,6*R**,6a*R**)-2-Ethynyl-4,5,6,6a-tetrahydro-6a-hydroxy-3-isopropoxy-3a,6-dimethyl-1(3a*H*)-pentalenone (47) and (3a*R**,6*S**,6a*R**)-2-Ethynyl-4,5,6,6a-tetrahydro-6a-hydroxy-3-isopropoxy-3a,6-dimethyl-1(3a*H*)-pentalenone (51).** From 236 mg (1.0 mmol) of **43**, 0.33 mL (3.75 mmol) of 2-bromopropene, and 4.4 mL (7.5 mmol) of *tert*-butyllithium, there was obtained 60 mg (24%) of **47** and 40 mg (16%) of **51**.

For **47**: white solid, mp 112−113 °C; IR ($CHCl_3$, cm^{-1}) 3550, 3300, 1690, 1580, 1450, 1380, 1320; ^1H NMR (300 MHz, $CDCl_3$) δ 5.67 (heptet, $J = 6$ Hz, 1 H), 3.18 (s, 1 H), 2.58 (s, 1 H), 2.07−2.00 (m, 1 H), 1.89−1.79 (m, 1 H), 1.68−1.46 (m, 3 H), 1.38 (d, $J = 6$ Hz, 6 H), 1.18 (s, 3 H), 0.99 (d, $J = 7$ Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 204.5, 190.7, 94.7, 85.5, 82.7, 75.5, 74.3, 55.8, 41.4, 34.5, 31.9, 22.5, 22.2, 19.9, 13.2; MS *m/z* (M^+) calcd 248.1412, obsd 248.1414.

For **51**: white crystals, mp 107−108 °C; IR ($CHCl_3$, cm^{-1}) 3550, 3310, 2100, 1700, 1570, 1450, 1380, 1320; ^1H NMR (300 MHz, $CDCl_3$) δ 5.66 (heptet, $J = 6$ Hz, 1 H), 3.20 (s, 1 H), 3.02 (s, 1 H), 2.05−1.96 (m, 2 H), 1.71−1.63 (m, 1 H), 1.52−1.42 (m, 1 H), 1.38 (d, $J = 6$ Hz, 3 H), 1.36 (d, $J = 6$ Hz, 3 H), 1.14 (s, 3 H), 0.94 (d, $J = 7$ Hz, 3 H), 0.98−0.83 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 203.4, 189.5, 97.9, 86.4, 83.1, 75.4, 73.9, 56.1, 46.8, 34.7, 30.5, 22.5, 22.2, 19.0, 15.0; MS *m/z* (M^+) calcd 248.1412, obsd 248.1415.

(3a*R,6*R**,6a*R**)-4,5,6,6a-Tetrahydro-6a-hydroxy-3-isopropoxy-3a,6-dimethyl-2(1-propynyl)-1(3a*H*)-pentalenone (48), (3a*R**,6*S**,6a*R**)-4,5,6,6a-Tetrahydro-6a-hydroxy-3-isopropoxy-3a,6-dimethyl-2(1-propynyl)-1(3a*H*)-pentalenone (52), and (3a*R**,4*S**,6a*R**)-4,5,6,6a-Tetrahydro-4,6a-dimethyl-2(1-propynyl)-1(3a*H*)-pentalenone (54).** From 180 mg (1.0 mmol) of **44**, 0.35 mL (4.0 mmol) of 2-bromopropene, and 4.7 mL (8.0 mmol) of *tert*-butyllithium, there was obtained 72 mg (28%) of **48**, 33 mg (12%) of **52**, and 17 mg (7%) of **54**.

For **48**: colorless oil, IR ($CHCl_3$, cm^{-1}) 3555, 1692, 1586, 1384, 1319; ^1H NMR (300 MHz, C_6D_6) δ 5.58 (heptet, $J = 6$ Hz, 1 H), 3.39 (s, 1 H), 2.03 (dd, $J = 13.5$, 7 Hz, 1 H), 1.81−1.72 (m, 1 H), 1.62 (s, 3 H), 1.56−1.46 (m, 1 H), 1.42-1.34 (m, 2 H), 1.28 (s, 3 H), 1.08 (d, $J = 6$ Hz, 3 H), 1.05 (d, $J = 6$ Hz, 3 H), 1.04 (d, $J = 7$ Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 204.7, 188.2, 91.0, 85.7, 74.4, 71.0, 55.6, 41.8, 34.9, 32.1, 22.3 (2 C), 22.2, 20.4, 13.7, 4.1; MS *m/z* (M^+) calcd 262.1569, obsd 262.1574.

For **52**: colorless oil; IR ($CHCl_3$, cm^{-1}) 3547, 1693, 1588, 1384, 1318; ^1H NMR (300 MHz, C_6D_6) δ 5.57 (hept, $J = 6$ Hz, 1 H), 3.38

(s, 1 H), 2.06−1.99 (m, 1 H), 1.98−1.92 (m, 1 H), 1.60 (s, 3 H), 1.46−1.37 (m, 1 H), 1.33−1.27 (m, 1 H), 1.23 (s, 3 H), 1.10 (d, J = 6 Hz, 3 H), 1.05 (d, J = 6 Hz, 3 H), 1.04 (d, J = 6 Hz, 3 H), 0.94−0.88 (m, 1 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 203.3, 186.8, 91.5, 86.5, 74.3, 70.7, 55.9, 47.2, 35.1, 30.9, 22.3 (2 C), 22.1, 19.4, 15.4, 4.1; MS *m/z* (M^+) calcd 262.1569, obsd 262.1572.

For **54**: colorless oil; IR ($CHCl_3$, cm^{-1}) 3587, 1707, 1606; ^{1}H NMR (300 MHz, C_6D_6) δ 5.46 (heptet, J = 6 Hz, 1 H), 2.12−2.06 (m, 1 H), 1.96−1.89 (m, 1 H), 1.71 (s, 1 H), 1.57 (s, 3 H), 1.37−1.21 (m, 2 H), 1.19 (s, 3 H), 1.18 (s, 3 H), 1.16 (d, J = 6 Hz, 3 H), 1.10 (s, 3 H), 1.02−0.77 (m, 1 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 205.8, 156.5, 130.3, 104.2, 85.2, 75.0, 72.2, 57.7, 46.7, 35.7, 30.9, 22.9, 22.6, 19.5, 15.5, 4.7; MS *m/z* (M^+) calcd 262.1569, obsd 262.1547.

(3a*R,6*R**,6a*R**)-4,5,6,6a-Tetrahydro-6a-hydroxy-3-isopropoxy-3a,6-dimethyl-2-(phenylethynyl)-1(3a*H*)-pentalenone (49) and (3a*R**,6*S**,6a*R**)-4,5,6,6a-Tetrahydro-6a-hydroxy-3-isopropoxy-3a,6-dimethyl-2-(phenylethynyl)-1(3a*H*)-pentalenone (53).** From 240 mg (1.0 mmol) of **45**, 0.35 mL (4.0 mmol) of 2-bromopropene, and 4.7 mL (8.0 mmol) of *tert*-butyllithium, there was isolated 26 mg (8%) of **49** and 55 mg (17%) of **53**.

For **49**: colorless solid, mp 126−128 °C; IR ($CHCl_3$, cm^{-1}) 3557, 1695, 1604, 1579; ^{1}H NMR (300 MHz, C_6D_6) δ 7.45−7.41 (m, 2 H), 7.02−6.95 (m, 3 H), 5.63 (heptet, J = 6 Hz, 1 H), 3.15 (s, 1 H), 2.08−2.01 (m, 1 H), 1.82−1.73 (m, 1 H), 1.57−1.50 (m, 1 H), 1.48−1.35 (m, 2 H), 1.29 (s, 3 H), 1.10 (d, J = 6 Hz, 3 H), 1.07 (d, J = 6 Hz, 3 H), 1.03 (d, J = 7 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 203.7, 189.2, 131.7 (3 C), 128.7 (2 C), 123.9, 96.6, 94.6, 85.9, 81.3, 75.2, 56.0, 41.9, 35.1, 32.2, 22.4, 22.2, 20.4, 13.5; MS *m/z* (M^+) calcd 324.1725, obsd 324.1725.

For **53**: colorless solid, mp 118−119 °C; IR ($CHCl_3$, cm^{-1}) 3550, 1697, 1605, 1582; ^{1}H NMR (300 MHz, C_6D_6) δ 7.44−7.36 (m, 2 H), 7.01−6.92 (m, 3 H), 5.61 (heptet, J = 6 Hz, 1 H), 3.64 (s, 1 H), 2.15−2.00 (m, 1 H), 1.99−1.93 (m, 1 H), 1.50−1.40 (m, 1 H), 1.36−1.32 (m, 1 H), 1.29 (s, 3 H), 1.13 (d, J = 7 Hz, 3 H), 1.07 (d, J = 6 Hz, 3 H), 1.05 (d, J = 6 Hz, 3 H), 1.01−0.85 (m, 1 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 202.8, 188.1, 131.6 (3 C), 128.7 (2 C), 123.9, 99.9, 95.0, 86.8, 80.9, 75.1, 56.2, 47.2, 35.2, 31.0, 22.4, 22.1, 19.5, 15.5; MS *m/z* (M^+) calcd 324.1725, obsd 324.1723.

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Supporting Information Available: Long-range DEPT and NOE data for many products, along with variable temperature 300 MHz ^{1}H NMR spectra of **8** (57 pages). See any current masthead page for ordering and Internet access instructions. The authors have deposited the atomic coordinates for the X-ray structures with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, U.K.

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