Combined Addition of Alkenyl and Allenic Anions to Squarate Esters. Direct Competition between Six-Ring and Eight-Ring Electrocyclization of 1,2,4,6,8-Cumulenic Pentaenes

Tina M. Morwick† and Leo A. Paquette*

Evans Chemical Laboratories, The Ohio State University, Columbus, Ohio 43210

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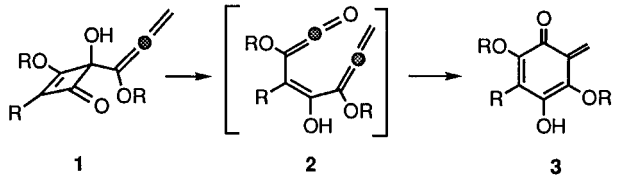
The sequential addition of 1 equiv each of a lithioallene and an alkenyllithium to diisopropyl squarate has been studied. The product compositions resulting from the ensuing reaction cascades were not at all comparable to those resulting from the reverse mode of nucleophile addition. These results require that different intermediates intervene. When the alkenyl anion is the lead reagent, the lithioallene enters predominantly trans and two sequential electrocyclic steps ensue. Initial introduction of methoxyallene causes the second nucleophile to enter preferably from the cis direction, presumably because of oxygen coordination to lithium. The proximal orientation of the unsaturated moieties leads to operation of the dianionic oxy-Cope rearrangement. The second electrocyclic event that transpires following formation of the trans dialkoxide is not of the customary 8π conrotatory type. Rather, a 6π disrotatory process occurs exclusively. This "allene effect" is shown to originate from strain, orbital alignment, and conjugative factors operating at the transition state.

The appearance of the allene unit in organic synthesis has gained enhanced frequency over the past few decades, and a variety of synthetic methods for the preparation and use of these unique substrates have been developed.[1] It was considered that the cumulenic arrangement of the allene nucleophile might extend the utility of the squarate ester cascade[2] and also provide informative insight into the reactivity exhibited by the resulting doubly-charged, ring-opened intermediates.

While the use of nucleophilic allenes is often complicated by their isomerization to propargyl anions,[3] the alkoxyallenes are known to add regioselectively. These versatile building blocks have been used in both chiral and achiral form for natural product synthesis.[4] The parent methoxyallene,[5] which is easily prepared by isomerization of methyl propargyl ether with potassium *tert*-butoxide, can be metalated by *n*-butyllithium at −78 °C and added to a variety of ketones and aldehydes to produce allenic alcohols.

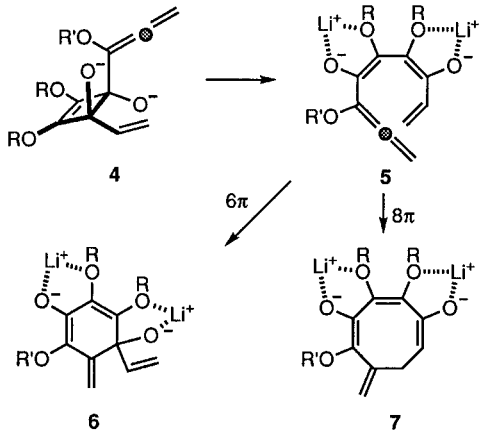
The addition of alkoxyallenes in equimolar amounts to squarate derivatives has been reported by Moore for the synthesis of *o*-quinone methides.[6] These workers found that nucleophilic addition is followed by conventional, thermally-induced ring cleavage to give **2**, which experiences 6π electrocyclization to deliver the observed products **3** (Scheme 1). The sequential addition of an allenic and an alkenyl anion to a squarate ester is, on the other hand, expected to lead predominantly to the trans dialkoxide **4** (Scheme 2). Charge-accelerated conrotatory ring opening[7] will certainly proceed in that

Scheme 1



1 2 3

Scheme 2



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† Present address: Boehringer Ingelheim Pharmaceuticals, Inc., 900 Ridgebury Rd., P.O. Box 368, Ridgefield, CT 06877.

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(1) (a) *The Chemistry of Ketenes, Allenes and Related Compounds*; Patai, S., Ed., John Wiley, New York, 1980. (b) *The Chemistry of the Allenes*; Landor, S. R., Ed., Academic Press: London, 1982. (c) Schuster, H. F.; Coppola, G. M. *Allenes in Organic Synthesis*; John Wiley: New York, 1984.

(2) (a) Negri, J. T.; Morwick, T.; Doyon, J.; Wilson, P. D.; Hickey, E. R.; Paquette, L. A. *J. Am. Chem. Soc.* **1993**, *115*, 12189. (b) Morwick, T.; Doyon, J.; Paquette, L. A. *Tetrahedron Lett.* **1995**, *36*, 2369. (c) Paquette, L. A.; Morwick, T. *J. Am. Chem. Soc.* **1995**, *117*, 1451. (d) Paquette, L. A.; Doyon, J. *J. Am. Chem. Soc.* **1995**, *117*, 6799. (e) Wilson, P. D.; Friedrich, D.; Paquette, L. A. *J. Chem. Soc., Chem. Commun.* **1995**, 1351. (f) Paquette, L. A.; Morwick, T. M.; Negri, J. T.; Rogers, R. D. *Tetrahedron* **1996**, *52*, 3075. (g) Paquette, L. A.; Kuo, L. H.; Doyon, J. *Tetrahedron* **1996**, *52*, 11625. (h) Paquette, L. A.; Doyon, J.; Kuo, L. H. *Tetrahedron Lett.* **1996**, *37*, 3299.

(3) (a) Balme, G.; Doutheau, A.; Goré J.; Malacria, M. *Synthesis* **1979**, 508. (b) Kobayashi, S.; Nishio, K. *J. Am. Chem. Soc.* **1995**, *117*, 6392. (c) Creary, X. *J. Am. Chem. Soc.* **1977**, *93*, 7632.

(4) (a) Zimmer, R. *Synthesis* **1992**, 165. (b) Rochet, P.; Vatéle, J.-M.; Goré, J. *Synlett* **1993**, 105.

(5) (a) *Encyclopedia of Reagents in Organic Synthesis*; Paquette, L. A., Ed.; John Wiley: New York; Volume 5, p 3316. (b) Hoff, S.; Brandsma, L.; Arens, J. F. *Recl. Trav. Chim. Pays-Bas* **1968**, *87*, 916.

(6) (a) Taing, M.; Moore, H. W. *J. Org. Chem.* **1996**, *61*, 329. (b) Ezcurra, J.; Moore, H. W. *Tetrahedron Lett.* **1993**, *34*, 6177.

(7) Wilson, S. R. *Org. React.* **1993**, *43*, 93.

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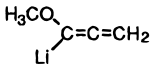
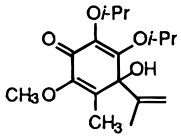
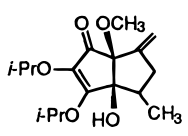
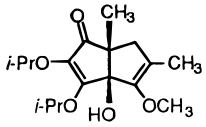
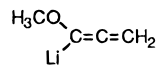
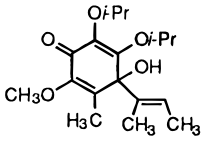
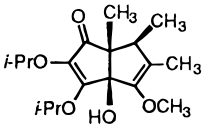
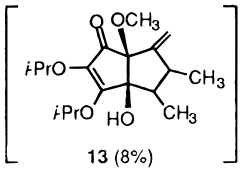
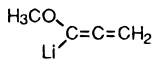
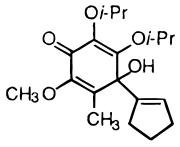
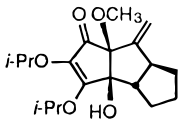
Table 1. Allenic Anion as the Lead Reagent

Expt.	Reactant 1	Reactant 2	Products
1			 **8** (20%)  **9** (17%)  **10** (15%)
2			 **11** (26%)  **12** (38%)  **13** (8%)
3			 **14** (20%)  **15** (22%)

direction which splays the oxido anions to the exterior, in line with theory.[8] With arrival at **5**, two options are contemplated. The first consists of 6π disrotatory ring closure to give **6** in a process directly related to the generation of **3** from **2**. Also likely is 8π conrotatory bonding within this coiled polyolefin in that manner known to be generally favored by 1,3,5,7-octatetraenes.[2,9] The key issue here is whether the presence of the added cumulenic carbon at one terminus of helical intermediate **5** will retard 8π conversion to **7** to a degree such that formation of cyclohexadiene **6** becomes competitive or even kinetically favored.

Results

Two modes of addition were pursued. The consequences of utilizing the allene as the first-stage reactant are summarized in Table 1. Reversal of the addition with the alkenyl anion being introduced first was found to have considerable impact on product distribution (Table 2). While ketones **8**, **11**, and **14** are common to both protocols, the remaining structural entities make their appearance as a direct consequence of the specific follow-up reactant.

The combined product yields ranged from 42% for expt 3 to 74% for the companion reaction 6. Unlike the rearrangements triggered by twofold alkenyllithium addition,[2,10] the allene systems underwent significant decomposition at the dialkoxide stage if the reaction temperature was allowed to proceed above 0 °C. Additionally, maintaining the reaction temperature at −20 °C to 0 °C for an extended length of time was found to reduce efficiency significantly. The yields for runs 2, 5 and 6 were maximized at −10 °C, −15 °C, and −30 °C, respectively, for reaction periods of 1−4 h. Experiments 1 and 3, carried out instead at 0 °C to 20 °C for 9−15 h, afforded a more modest 42−52% combined yield.

In those instances where the allene was introduced first, complications arising from twofold addition of this reagent even at −78 °C sometimes materialized. To minimize operation of this process, the anion was added to a solution of the squarate ester rather than the more typical inverse sequence.

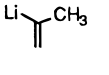
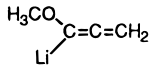
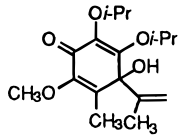
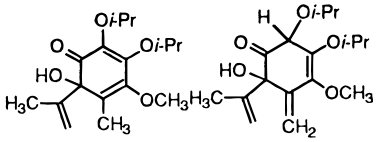
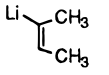
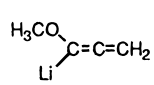
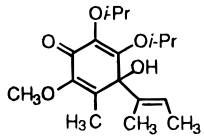
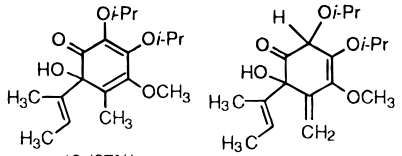
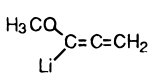
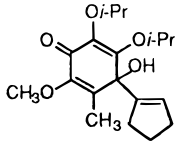
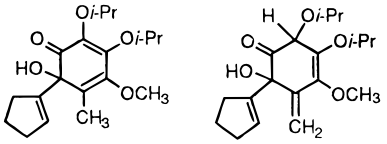
Various spectroscopic methods were employed for structure identification. The generation of ^2J and ^3J

(8) (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.

(9) (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.

(10) (a) Paquette, L. A.; Morwick, T. M. *J. Am. Chem. Soc.* **1997**, *119*, in press. (b) Paquette, L. A.; Doyon, J. *J. Org. Chem.* **1997**, *62*, in press. (c) Paquette, L. A.; Hamme, A. T., II; Kuo, L. H.; Doyon, J.; Kreuzholz, R. *J. Am. Chem. Soc.* **1997**, *119*, in press.

Table 2. Alkenyl Anion as the Lead Reagent

Expt.	Reactant 1	Reactant 2	Products
4			 **8** (36%)  **16** (10%) **17** (15%)
5			 **11** (29%)  **18** (27%) **19** (14%)
6			 **14** (34%)  **20** (34%) **21** (6%)

carbon subspectra by means of semiselective DEPT experiments[11] proved to be particularly informative. Advantage was also taken of the ability to observe weak ^4J coupling for allylic systems when pulsing was carried out for an extended time period. Regioisomers **14** and **20** can be readily differentiated on this basis (Figure 1). Irradiation of H-10 in **14** for at least 24 h provided a spectrum in which C-3 and C-5 were observed (^4J allylic coupling) in addition to C-4, C-9, and two of C-11, -12, and -13 (^2J and ^3J coupling). In a similar vein, irradiation of H-10 for a comparable time period in **20** revealed C-1 (^4J), C-6, C-9, and two of C-11, -12, and -13. The lack of observable polarization transfer to C-5 (^4J) in this instance may result from a nonideal geometric arrangement of the four-bond unit in this molecule.

The regiochemistry of the adducts was additionally substantiated by ultraviolet spectroscopy. Thus, the extended conjugation present in **16**, **18**, and **20** gave rise to absorptions at longer wavelengths than the cross-conjugated network resident, for example, in **8** (see Experimental Section).

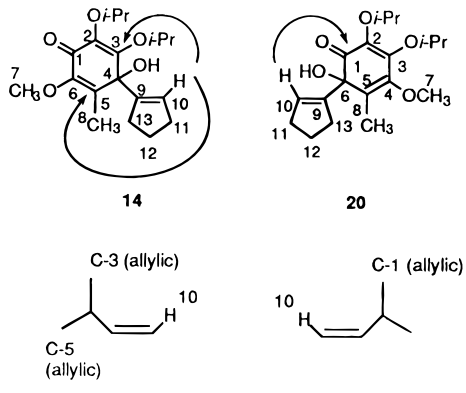


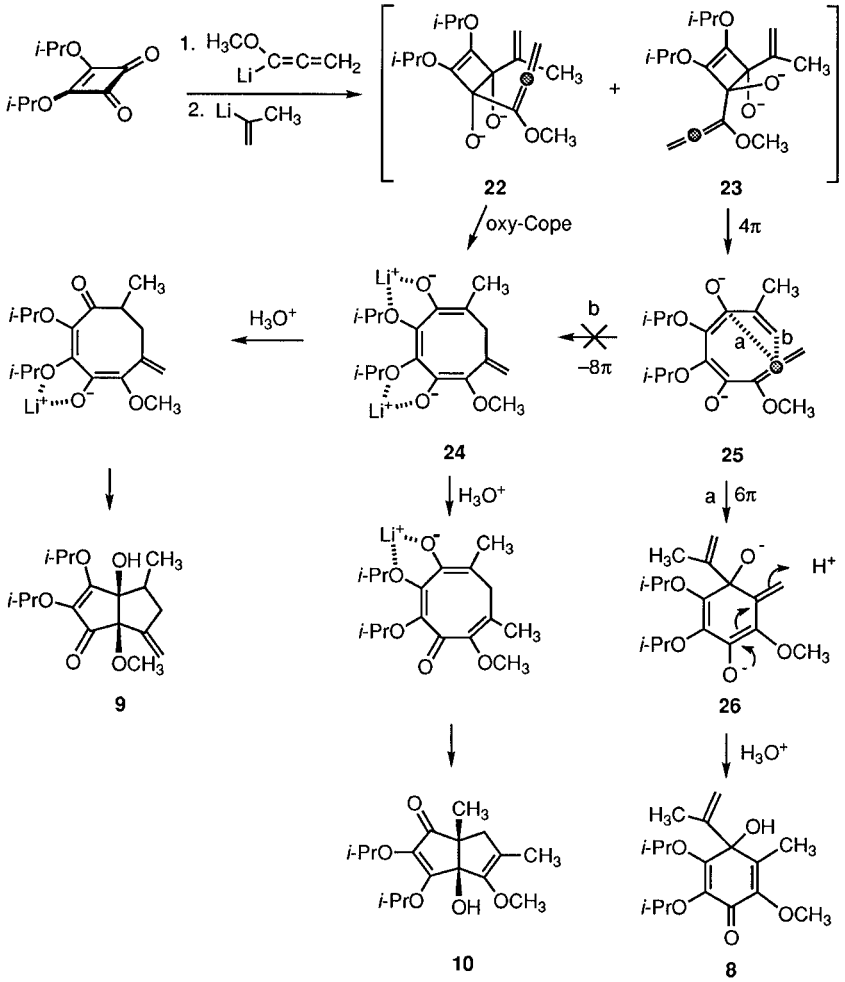
Figure 1. Allylic coupling (^4J) for cyclohexadienones **14** and **20**.

Discussion

With a high degree of assurance, the generation of different product mixtures as a function of the order of

(11) (a) Bax, A. *J. Magn. Reson.* **1984**, *57*, 314. (b) Bax, A.; Nin, C.-H. *J. Am. Chem. Soc.* **1984**, *106*, 1150. (c) Müller, N.; Bauer, A. *J. Magn. Reson.* **1989**, *82*, 400.

Scheme 3



addition is a direct reflection of the fact that adducts of type **4** are not formed exclusively. Rather, the levels of regio- and stereodifferentiation during the second-stage addition must be widely divergent. The mechanistic pathways proposed for formation of the **8**−**10** triad, presented in Scheme 3, encompass as well the cis addition/dianionic oxy-Cope reaction channel.[12,13] In light of the product composition that materializes when 1-lithio-1-methoxyallene is added in advance of the 2-lithiopropene, nucleophilic attack of the latter appears unexpectedly to proceed with formation of both stereoproximal **22** and stereodistal adducts **23**. Once formed, **22** likely experiences rapid [3,3] sigmatropic change to deliver the diquinane products **9** and **10**. Their common origin rests directly on the fact that **24** is a dienolate capable of being protonated at two different sites. Transannular aldolization in two opposite directions ensues.

The 4π electrocyclic opening of **23** produces the acyclic 1,2,4,6,8-pentaene **25**. Although this intermediate holds the capability for advancing along two ring closure pathways, the activation energy for the 6π option (pathway a) is apparently lower than the 8π alternative (pathway b), as the former is the exclusive reaction channel leading via **26** to formation of the cross-conjugated cyclohexadienone **8**.

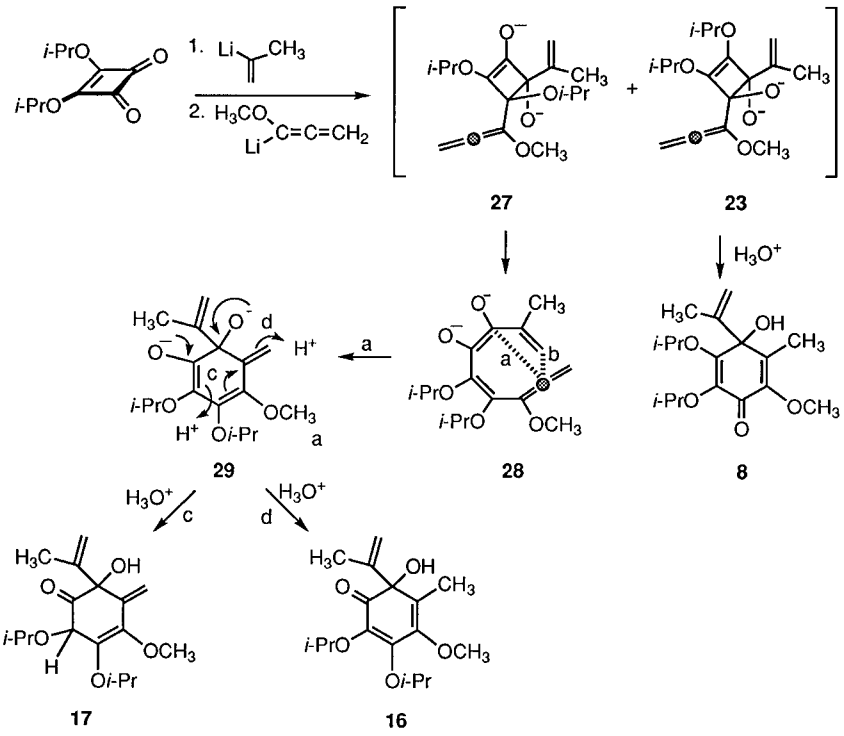
When 2-lithiopropene is made the lead reagent (expt 4), stereoselectivity returns at the customary high level with the result that trans adduct **23** is formed to the exclusion of **22**. However, 1,4-addition is now accommodated by the initially formed monoadduct, and the lithiated allene is found to exercise the 1,4 option in this circumstance leading also to **27** (Scheme 4). Particularly relevant is the absence of diquinane products, which underscores our belief that **25** finds it possible to cyclize only to **26** and not to **24**.

The isomeric ketones **16** and **17** resulting from the conjugate addition mode were isolated as an inseparable mixture. The relative proportion of **16** and **17** was seen to vary from 2:3 at 0 °C to an even greater preference for kinetic product **17** at −40 °C (1:3). Compound **17** and analogs thereof produced in other experiments could, however, be converted into their conjugated regioisomers (e.g. **16**) by treatment with triethylamine. Structural identification of these products was derived in part by their ability to undergo this prototropic shift. In order to distinguish between this functional group array and those compounds resulting from possible protonation of the extended enolate at the γ-position as, for example **30**, recourse was again made to semiselective DEPT studies at 300 MHz. While an upfield shift of the isopropoxy methine heptet (H-14 in **19**) to δ 3.70 was indicative of attachment of the isopropoxy substituent to

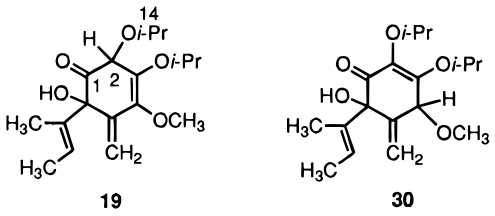
(12) (a) Paquette, L. A. *Synlett* **1990**, 67. (b) Paquette, L. A. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 609.

(13) (a) Wey, H. G.; Butenschön, H. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 880. (b) Brands, M.; Wey, H. G.; Krämer, R.; Krüger, C.; Butenschön, H. *Liebigs Ann.* **1993**, 253. (c) Brands, M.; Wey, H. G.; Bruckmann, J.; Krüger, C.; Butenschön, H. *Chem. Eur. J.* **1996**, *2*, 182.

Scheme 4



a saturated ring position, additional verification was obtained by selective irradiation of H-14 and observation of its ^3J coupling to C-2. Coupling between H-2 and C-1 was noted in a separate experiment.



Allenic oxy-Cope rearrangements have been reported earlier.[14] Recently, Rajagopalan has described an anionic version thereof.[15] Replacement of a vinyl substituent with an allenyl group appears to enhance the reactivity of these systems toward the [3,3] sigmatropic process, a result which is suggestive of potential π bond weakening due to the strain resident in the cumulated diene.

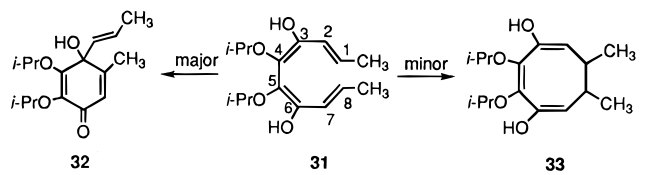
In the current examples, the oxy-Cope rearrangement is evidently also rapid, progressing efficiently at relatively low temperatures. Beyond this, the regioselectivity of protonation of the resulting dienolates holds interest. In the simplest example **24**, the near equal distribution of **9** and **10** stems from an apparent inability to differentiate the relative stabilities of the two enolate sites under the reaction conditions.[10a] The additional strain introduced by the exocyclic double bond may be responsible for increased rates of proton transfer, resulting in a lack of site selectivity.

In expt 2, nearly complete selectivity for protonation of the allenic enolate (γ position) is observed, while the eight-membered intermediate generated in expt 3 experiences protonation at the vinylic site. The temperature at which quenching was conducted may bear some responsibility for the variation in results. The nonselective example (expt 1) was quenched at 0 °C, while water was introduced in expts 2 and 3 at −10 °C and 20 °C, respectively.

The substantive degree to which cis addition occurs when an alkenyllithium is exposed to an allene-substituted monoadduct is attributed to the presence of the methoxy substituent. When ether oxygen atoms reside in close proximity to the cyclobutenone ring after the first-stage addition, complexation of the lithium atom associated with the incoming nucleophile to this oxygen serves to guide the entry of the associated anion. Various facets of this phenomenon are discussed elsewhere.[16]

The "Allene Effect" on Periselection

The inability of the acyclic pentaenes generated in this investigation to undergo 8π pericyclic bond reorganization arises as a direct consequence of the pendant 1,2-diene. In all previous cases, structurally related 1,3,5,7-octatetraenes have been found to undergo 8π electrocyclization, with but one exception. When **31** was maintained at room temperature for 96 h and then refluxed in THF for 8 h, a modest amount (21%) of **32** was isolated in addition to the diquinane resulting from transannular aldolization within **33**.[17] Product **32** derives from 6π electrocyclization followed by air oxidation.



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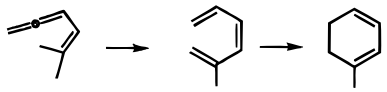
The reduced rate of conversion of **31** to **33** is attributed to the lack of substituents at C-2 and C-7, which are recognized to improve adoption of the helical conformation necessary to 8π ring closure.[10a,c]

To our knowledge, the kinetic effect on 6π electrocyclization associated with substitution of a terminal allene unit into an acyclic hexatriene has not previously been examined. The examples provided by Moore[6] incorporate the 6π event into a tandem squarate reaction without isolation of the acyclic intermediate. However, the associated [1,5] sigmatropic hydrogen shift has been studied kinetically, and Skattebøl has reported the activation energy for the conversion of 5-methyl-1,2,4-hexatriene (**34**) to **36** via **35** to be 24.6 kcal/mol.[18] The magnitude of this value contrasts with conventional activation parameters for closely related processes, which generally range from 30−36 kcal/mol.[19]



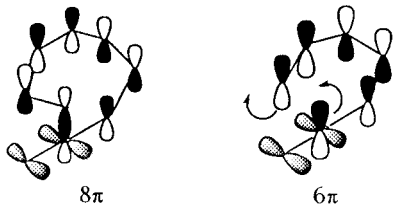
34 **35** **36**

In conjunction with his exhaustive investigation of previtamin D chemistry, Okamura has examined [1,5] as well as [1,7] sigmatropic hydrogen migrations in systems where the terminal vinyl group has been replaced by an allene moiety.[20] This structural change lowers the activation energy for the [1,5] event by 10−12 kcal/mol, but exerts a negligible effect on the [1,7] shift, the activation energies for which are typically already in the 20 kcal/mol range.[19,21]

The transition state structures for [1,7] hydrogen migration and 8π electrocyclization are rather similar in that they both feature a highly-ordered Möbius-like arrangement and exhibit relatively low energies of activation.[22] Schleyer has studied the two systems theoretically and found that both benefit from Möbius aromatic stabilization.[23]

While the similarities between transition state structures for [1,5] hydrogen migration and 6π electrocyclization are not as apparent, both are clearly six-electron processes having similar activation energies and are apparently subject to stabilization by the pendant allene. Conversely, the transition state structure for 8π electrocyclization is not privy to the stabilizing effects of the allene unit, as is the case for [1,7] sigmatropy.

To our knowledge, the allene effect on competitive 6π and 8π electrocyclization has not been examined previously. However, Okamura has scrutinized the pericyclic events associated with an allene system capable of either [1,7] hydrogen migration or 6π electrocyclization.[20e] The discovery was made that while [1,7] shifting is typically



8π 6π

Figure 2. Orbital diagram for 8π conrotatory electrocyclization of a 1,2,4,6,8- pentaene (**37**) and 6π disrotatory electrocyclization of a 1,2,4,6-tetraene (**38**).

the preferred pericyclic channel, substitution by the allene results in bond reorganization via the electrocyclization alternative.

Jensen has recently published the results of a theoretical study of the allene effect in [1,*n*] hydrogen migrations[24] which confirm Okamura's empirical observations. The fact that allene substitution enhances the rate of [1,5] migration but minimally affects the [1,7] variant has been rationalized by considering the electronic structure of the transition states for these conversions as two interacting radical fragments. The geometry of the [1,5] migration is conducive to significant overlap, while in the case of the [1,7] reaction, overlap is poor, strain factors gain importance, and substrate geometry is generally unsuitable to conjugate interaction.

Skattebøl used a similar argument to explain his observations involving **34**. He suggested that if the transition state is productlike, additional conjugation by π electrons from the terminal double bond of the allene should provide a stabilizing contribution.[18]

In the current situation, the lack of planarity in **24** and its congeners and the ring strain necessarily incorporated in the developing medium-sized ring should increase the energy content of a productlike transition state with respect to the planar **26** (Scheme 3). Furthermore, 6π disrotation as depicted in **38** (Figure 2) affords the opportunity for additional conjugative overlap with the terminal π bond of the allene as a result of the necessary rotation of the orbital framework. No comparable orbital twisting operates when the topography of the transition state is Möbius-like as in **37**. As a result, conjugative overlap with the terminal *p* lobes of the allene cannot be a factor.

In conclusion, the ability of a squarate ester to undergo sequential pericyclic events following mixed addition of allenic and alkenyl anions has been investigated. The dianionic oxy-Cope rearrangement ensues when cis-addition operates, and a two-stage electrocyclic rearrangement is triggered following trans addition. Valence isomerization for the second electrocyclic event is, however, diverted from the usual 8π preference to the 6π option as a result of the presence of the allene subunit. The results constitute added independent documentation for the "allene effect" in pericyclic chemistry.

Experimental Section

General. All reactions were carried out under an argon atmosphere. 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

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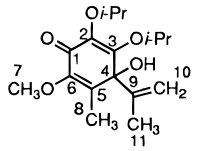
cases dried prior to use. The purity of all compounds was shown to be >95% by TLC and high-field ^{1}H (300 MHz) and ^{13}C NMR (75 MHz). The high-resolution and fast-atom-bombardment mass spectra were obtained at The Ohio State University Campus Chemical Instrumentation Center. Elemental analyses were performed at the Scandinavian Microanalytical Laboratory, Herlev, Denmark.

Prototypical Procedure for Mixed Additions with 1-Lithio-1-methoxyallene and an Alkenyllithium. Method A. All apparatus was flame-dried under argon, an atmosphere of which was maintained until quenching was effected. A solution of methoxyallene (77−158 mg, 1.1−2.25 mmol) in dry THF (5−10 mL) was cooled to −78 °C and treated dropwise with *n*-butyllithium (0.65−1.34 mL of 1.68M in ether, 1.1−2.25 mmol). After 30 min at −78 °C, the anion was cannulated into a solution of diisopropyl squarate (198−396 mg, 1.0−2.0 mmol) in 5−10 mL of THF at −78 °C and stirred at this temperature for 30 min. During this time, the alkenyllithium was generated from 3.0−5.0 mmol of the vinyl halide and 6.0−10.0 mmol of *tert*-butyllithium in 15 mL of THF. After 30 min, the alkenyllithium was similarly introduced, and the temperature of the reaction mixture was maintained at −78 °C for 3−16 h, at −10 °C to 0 °C for 4−15 h, and at rt for 0−5 h, quenched at −10 °C to rt with a solution of deoxygenated NH_4-Cl (argon was bubbled through the solution for 20 min), and stirred at 0 °C to rt for 0−10 h. Subsequently, 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 using 10−30% ethyl acetate and 0.5−1% triethylamine in petroleum ether and by further MPLC and/or recrystallization as necessary.

Method B. All apparatus was flame-dried under argon, an atmosphere of which was maintained until quenching was effected. A solution of diisopropyl squarate (198−396 mg; 1.0−2.0 mmol) in 5−10 mL of THF was cooled to −78 °C, cannulated into a solution of the alkenyllithium generated as above from 1.1−2.2 mmol of the vinyl halide and 2.2−4.4 mmol of *tert*-butyllithium in 10−15 mL of THF, and stirred for 30 min. During this time, a solution of methoxyallene (175−350 mg, 2.5−5.0 mmol) in dry THF (10−15 mL) was cooled to −78 °C and treated dropwise with *n*-butyllithium (1.5−3.1 mL of 1.68M, 2.5−5.0 mmol). After 30 min at −78 °C, the anion was cannulated into the reaction mixture, which was stirred at −78 °C for 1−4 h, −40 °C to 0 °C for 1−3 h, quenched as above at −40 °C to 0 °C, and stirred for an additional 0.5−3 h at 0 °C under argon. Subsequent workup was carried out as in method A.

4-Hydroxy-4-isopropenyl-2,3-diisopropoxy-6-methoxy-5-methyl-2,5-cyclohexadien-1-one (8), (3a*R,6a*R**)-4,5,6,-6a-Tetrahydro-3a-hydroxy-2,3-diisopropoxy-6a-methoxy-4-methyl-6-methylene-1(3a*H*)-pentalenone (9), and *cis*-6,6a-Dihydro-3a-hydroxy-2,3-diisopropoxy-4-methoxy-5,6a-dimethyl-1(3a*H*)-pentalenone (10).** Method A was used with 158 mg (2.25 mmol) of methoxyallene, 1.34 mL (2.25 mmol) of *n*-butyllithium, 396 mg (2.0 mmol) of diisopropyl squarate, 0.45 mL (5.0 mmol) of 2-bromopropene, and 5.9 mL (10 mmol) of *tert*-butyllithium, for 3 h at −78 °C and 15 h at 0 °C. The black reaction mixture was quenched at 0 °C and stirred for 1 h at rt. Typical workup and flash chromatography with 20% ethyl acetate and 1% triethylamine in petroleum ether afforded 230 mg (37%) of a mixture of **8** and **9** (54:46 ratio, estimated by GC) and 94 mg (15%) of **10**. Following several recrystallizations from petroleum ether, **8** was isolated as a white solid: mp 115−116 °C; IR ($CHCl_3$, cm^{-1}) 3565, 1649, 1618; ^{1}H NMR (300 MHz, C_6D_6) δ 5.46 (d, J = 0.4 Hz, 1 H), 5.26 (heptet, J = 6 Hz, 1 H), 5.01 (m, 1 H), 4.66 (heptet, J = 6 Hz, 1 H), 3.65 (s, 3 H), 2.81 (s, 1 H), 1.88 (s, 3 H), 1.42 (d, J = 0.4 Hz, 3 H), 1.19 (d, J = 6 Hz, 3 H), 1.14 (d, J = 6 Hz, 3 H), 1.05 (d, J = 6 Hz, 3 H), 1.03 (d, J = 6 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 180.5, 158.0, 148.8, 144.4, 136.5, 134.6, 113.6, 77.3, 74.7, 73.7, 59.7, 22.6, 22.51, 22.48 (2C), 18.1, 10.3; MS m/z (M^+) calcd 310.1780, obsd 310.1786; $\lambda_{max}^{CH_3OH}$ 320 nm (ϵ 3030).

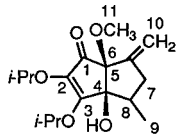
Anal. Calcd for $C_{17}H_{26}O_5$: C, 65.78; H, 8.44. Found: C, 65.88; H, 8.49.



8

Long-range DEPT from H-10 (δ 5.46):
144.3 (C-9, ^2J), 77.3 (C-4, ^3J), and 18.0 ppm (C-11, ^3J).
This experiment was not continued for the extended time period necessary to observe weak ^4J allylic coupling.

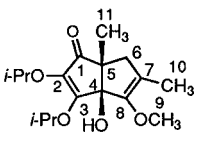
The mother liquors from several recrystallizations were combined, the solvent was evaporated, and the resultant oil was flash chromatographed on silica gel with 25% ether in petroleum ether to provide a pure sample of **9** as a colorless oil: IR (neat, cm^{-1}) 3482, 1706, 1613; ^{1}H NMR (300 MHz, C_6D_6) δ 5.76 (dd, J = 3, 1.5 Hz, 1 H), 5.27 (heptet, J = 6 Hz, 1 H), 5.21 (heptet, J = 6 Hz, 1 H), 5.12 (dd, J = 3, 1.5 Hz, 1 H), 3.53 (s, 3 H), 3.06 (s, 1 H), 2.18−2.03 (m, 3 H), 1.14 (d, J = 6 Hz, 3 H), 1.11 (s, 3 H), 1.09 (d, J = 6 Hz, 3 H), 1.07 (d, J = 6 Hz, 3 H), 1.05 (d, J = 6 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 194.1, 168.8, 144.9, 131.8, 113.8, 82.6, 82.0, 74.0, 71.6, 54.1, 40.1, 39.6, 22.7 (2 C), 22.6 (2 C), 14.5; MS m/z (M^+) calcd 310.1780, obsd 310.1778.



9

Long-range DEPT from H-10 (δ 5.76): 144.8 (C-6, ^2J), 82.6 (C-5, ^3J), and 40.1 ppm (C-7, ^3J)
Long-range DEPT from H-11 (δ 3.53): 82.6 ppm (C-5 ^3J).
Lack of any nOe enhancement to C-9 from C-11 or OH indicates this methyl to be a, which would be expected. However, methine C-8 overlaps with C-7 so that stereochemistry of C-9 is inconclusive.

For **10**: colorless oil; IR (neat, cm^{-1}) 3448, 1685, 1613; ^{1}H NMR (300 MHz, C_6D_6) δ 5.32 (heptet, J = 6 Hz, 1 H), 5.23 (heptet, J = 6 Hz, 1 H), 3.54 (s, 3 H), 2.90 (s, 1H), 2.63 (dd, J = 16.5, 1 Hz, 1 H), 2.00 (dd, J = 16, 1 Hz, 1 H), 1.40 (s, 3 H), 1.38 (s, 3H), 1.17 (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 202.3, 167.7, 152.9, 130.9, 117.5, 83.2, 74.0, 71.6, 59.9, 51.7, 41.9, 22.85, 22.78, 22.6, 22.5, 19.6, 12.5; MS m/z (M^+) calcd 310.1780, obsd 310.1781.



10

Long-range DEPT from H-9 (δ 3.54): 152.9 ppm (C-8, ^3J).
Long-range DEPT from H-6a (δ 2.63): 202.3 (C-1, ^3J), 152.9 (C-8, ^3J), 117.5 (C-7, ^2J), and 51.7 ppm (C-5, ^2J).
Long-range DEPT from H-6b (δ 1.99): 202.3 (C-1, ^3J), 152.9 (C-8, ^3J), 117.5 (C-7, ^2J), 51.7 (C-5, ^2J), and 19.6 ppm (C-11, ^3J).
Long-range DEPT from H-11 (δ 1.40): 202.3 (C-1, ^3J), 83.1 (C-4, ^3J), 51.7 (C-5, ^2J), and 41.9 ppm (C-6, ^3J).
Long-range DEPT from H-10 (δ 1.38): 152.9 (C-8, ^3J), 117.5 (C-7, ^2J), and 41.9 ppm (C-6, ^3J).

6-Hydroxy-6-isopropenyl-2,3-diisopropoxy-4-methoxy-5-methyl-2,4-cyclohexadien-1-one (16) and 6-Hydroxy-6-isopropenyl-2,3-diisopropoxy-4-methoxy-5-methylene-3-cyclohexen-1-one (17). Method B was utilized with 198 mg (1.0 mmol) of diisopropyl squarate, 0.1 mL (1.1 mmol) of 2-bromopropene, 1.3 mL (2.2 mmol) of *tert*-butyllithium, 175 mg (2.5 mmol) of methoxyallene, and 1.5 mL (2.5 mmol) of 1.68 M *n*-butyllithium for 4 h (−78 °C) and 30 min (0 °C). The yellow reaction mixture was quenched at 0 °C and stirred for an additional 20 min at 0 °C. Typical workup provided 77 mg (25%) of a mixture of **16** and **17** (2:3 ratio by ^{1}H NMR) and 111 mg (36%) of **8** as a white solid.

For **17**: ^{1}H NMR (in the mixture) (300 MHz, C_6D_6) δ 5.67−5.63 (m, 2 H), 5.10 (dd, J = 1.5, 0.8 Hz, 1 H) 4.89 (dd, J = 2.6, 1.3 Hz, 1 H), 4.66 (s, 1 H), 4.39 (heptet, J = 6 Hz, 1 H), 4.19 (s, 1 H), 3.69 (heptet, J = 6 Hz, 1 H), 3.50 (s, 3 H), 1.63 (dd, J = 1.3, 0.8 Hz, 3 H), 1.23 (d, J = 6 Hz, 3 H), 1.15 (d, J = 6 Hz, 3 H), 1.13 (d, J = 6 Hz, 3 H), 1.10 (d, J = 6 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 205.1, 145.4, 140.6, 139.0, 115.8, 111.8, 83.6, 76.5, 73.2, 72.8, 59.2, 23.1, 22.9, 22.8, 22.3, 18.9 (one carbon not observed).

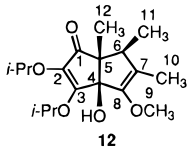
A pure sample of **16** was acquired by treating 54 mg of the mixture of **16** and **17** with 0.024 mL of triethylamine in 5 mL of THF and 1 mL of DMF for a period of 16 h under argon. Following a typical workup, 49 mg (91%) of **16** was isolated as a yellow oil: IR (neat, cm^{-1}) 3466, 1650, 1565; ^{1}H NMR (300 MHz, C_6D_6) δ 5.36 (d, J = 0.7 Hz, 1 H), 5.15 (heptet, J = 6 Hz, 1 H), 4.87 (dd, J = 1.4, x.x Hz, 1 H), 4.58 (heptet, J = 6 Hz, 1 H), 4.00 (s, 1 H), 3.35 (s, 3 H), 1.93 (s, 3 H), 1.66 (dd, J = 1.4, 0.7 Hz, 3 H), 1.18 (d, J = 6 Hz, 3 H), 1.13 (d, J = 6 Hz, 3 H), 1.12 (d, J = 6 Hz, 3 H), 1.07 (d, J = 6 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 198.6, 156.4, 145.6, 144.6, 134.8, 130.2, 112.5, 82.1, 75.7, 73.4, 59.9, 22.7 (3C), 22.5, 17.0, 10.7; MS m/z (M^+) calcd 310.1780, obsd 310.1786; $\lambda_{max}^{CH_3OH}$ 354 nm (ϵ 3075).

In a similar reaction using 2 mmol of diisopropyl squarate and a proportionate amount of the remaining reagents for 2 h (−78 °C) and 3 h (−40 °C), quenching at −40 °C and stirring for an additional 15 h (0 °C) provided, after typical workup, 16% of **16** and **17** (1:3 ratio by ^{1}H NMR) and 46% of **8**.

4-Hydroxy-2,3-diisopropoxy-6-methoxy-5-methyl-4-[(*Z*)-1-methyl-1-propenyl]-2,5-cyclohexadien-1-one (11) and (3a*R,6*S**,6a*R**)-6,6a-Dihydro-3a-hydroxy-2,3-diisopropoxy-4-methoxy-5,6,6a-trimethyl-1(3a*H*)-pentalenone (12).** Method A was used with 158 mg (2.25 mmol) of methoxyallene, 1.34 mL (2.25 mmol) of *n*-butyllithium, 396 mg (2.0 mmol) of diisopropyl squarate, 0.51 mL (5.0 mmol) of (*E*)-2-bromo-2-butene, and 5.9 mL (10 mmol) of *tert*-butyllithium for 3 h (−78 °C) and 4 h (−10 °C). The yellow reaction mixture was quenched at −10 °C and stirred for 10 h at 0 °C. Typical workup and flash chromatography on silica gel with 18−30% ethyl acetate and 0.5% triethylamine in petroleum ether yielded 166 mg (26%) of **11** and 249 mg (38%) of **12**. A portion of **12** was obtained as a mixture with **11** and what is believed to be **13** (relative amounts were estimated by NMR); the remaining **12** was still contaminated with what is believed to be **11** (approximately 8%). This byproduct could not be removed by additional chromatography, nor was it separable by GC.

For **11**: white crystalline solid, mp 133−4 °C; IR ($CHCl_3$, cm^{-1}) 3563, 1649, 1617; ^{1}H NMR (300 MHz, C_6D_6) δ 5.94 (qq, J = 7, 1.0 Hz, 1 H), 5.25 (heptet, J = 6 Hz, 1 H), 4.71 (heptet, J = 6 Hz, 1 H), 3.69 (s, 3 H), 2.52 (m, 1 H), 1.87 (s, 3 H), 1.47 (dd, J = 7, 1 Hz, 3 H), 1.30 (d, J = 1 Hz, 3 H), 1.20 (d, J = 6 Hz, 3 H), 1.17 (d, J = 6 Hz, 3 H), 1.02 (d, J = 6 Hz, 3 H), 0.97 (d, J = 6 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 180.7, 158.3, 148.8, 137.1, 134.8, 134.3, 127.4, 77.5, 74.7, 73.7, 59.7, 22.6 (2C), 22.5 (2C), 13.5, 12.0, 10.4; MS m/z (M^+) calcd 324.1937, obsd 324.1934; $\lambda_{max}^{CH_3OH}$ 320 nm (ϵ 3,050). Anal. Calcd for $C_{18}H_{28}O_5$: C, 66.64; H, 8.70. Found: C, 66.48; H, 8.41.

For **12**: colorless oil; IR (neat, cm^{-1}) 3444, 1683, 1614; ^{1}H NMR (300 MHz, C_6D_6) δ 5.31(heptet, J = 6 Hz, 1 H), 5.17 (heptet, J = 6 Hz, 1 H), 3.57 (s, 3 H), 3.12 (s, 1H), 2.80−2.73 (m, 1 H), 1.40 (d, J = 0.9 Hz, 3 H), 1.30 (s, 3 H), 1.18 (d, J = 6 Hz, 3 H), 1.15 (d, J = 6 Hz, 3 H), 1.11 (d, J = 6 Hz, 3 H), 1.08 (d, J = 6 Hz, 3 H), 1.01 (d, J = 6 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 203.0, 167.3, 153.4, 130.2, 122.6, 83.0, 74.0, 71.5, 59.9, 55.4, 42.4, 22.9, 22.8, 22.6, 22.5, 15.7, 15.0, 11.0; MS m/z (M^+) calcd 324.1937, obsd 324.1940. Anal. Calcd for $C_{18}H_{28}O_5$: C, 66.64; H, 8.70. Found: C, 66.38; H, 8.63.



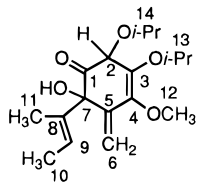
12

Long-range DEPT from H-12 (δ 1.30): 203.0 (C-1, ^3J), 83.0 (C-4, ^3J), 55.4 (C-5, ^2J), and 42.3 ppm (C-6, ^3J).
Long-range DEPT from H-11 (δ .99): 122.6 (C-7, ^3J), 55.4 (C-5, ^3J), and 42.3 ppm (C-6, ^2J).

Irradiate	Observe	% nOe	Irradiate	Observe	% nOe
H-6 (δ 2.76)	H-12	1.0	H-11 (δ 1.01)	OH	1.5
	H-10	3.8		H-6	20
	OH	1.3		H-10	5.7
H-12 (δ 1.30)	H-11	6.2		H-12	5.4
	H-6	3.2			
	OH	5.8			

6-Hydroxy-2,3-diisopropoxy-4-methoxy-5-methyl-6-[(*Z*)-1-methyl-1-propenyl]-2,4-cyclohexadien-1-one (18) and 6-Hydroxy-2,3-diisopropoxy-4-methoxy-5-methylene-6-[(*Z*)-1-methyl-1-propenyl]-3-cyclohexen-1-one (19). Method B was utilized with 396 mg (2 mmol) of diisopropyl squarate, 0.23 mL (2.25 mmol) of (*E*)-2-bromo-2-butene, 2.65 mL (4.5 mmol) of *tert*-butyllithium, 350 mg (5.0 mmol) of methoxyallene, and 3.0 mL (5.0 mmol) of 1.68 M *n*-butyllithium for 3 h (−78 °C) and 1 h (−30 °C). The yellow reaction mixture was quenched at −30 °C and stirred for an additional 3 h at 0 °C. Typical workup provided 265 mg (41%) of a mixture of **18** and **19** (2:1 ratio, by ^{1}H NMR) and 189 mg (29%) of **14** as a white solid.

For **19**: ^{1}H NMR (in the mixture) (300 MHz, C_6D_6) δ 5.73−5.65 (m, 3 H), 4.62 (s, 1H), 4.56 (heptet, J = 6 Hz, 1 H), 3.70 (heptet, J = 6 Hz, 1 H), 3.52 (s, 3 H), 1.53 (d, J = 0.9 Hz, 3 H), 1.35 (dd, J = 7, 0.9 Hz, 3 H), 1.24 (d, J = 6 Hz, 3 H), 1.08 (d, J = 6 Hz, 3 H), (6 protons from isopropoxy methyls overlap



19

Long-range DEPT from H-14 (δ 3.70): 76.7 ppm (C-2, ^3J).
Long-range DEPT from H-2 (δ 4.62): 205.8 (C-1, ^2J), 143.7, 138.6 (C-3,4, 2, ^3J), and 73.0 ppm (C-14, ^3J).

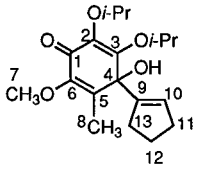
with those of **18**; OH not observed); ^{13}C NMR (75 MHz, C_6D_6) ppm 205.8, 143.7, 140.8, 138.6, 135.9, 125.1, 112.1, 84.6, 76.7, 73.1, 72.4, 59.3, 23.2, 22.6, 22.4, 22.3, 13.6, 11.9.

A pure sample of **18** was acquired by treating 156 mg of the mixture of **18** and **19** with 0.048 mL of triethylamine in 5 mL of THF and 1 mL of DMF for a period of 16 h under argon. Following the typical workup, 143 mg (92%) of **18** was isolated as a yellow oil: IR (neat, cm^{-1}) 3466, 1648, 1567; ^{1}H NMR (300 MHz, C_6D_6) δ 5.36 (qd, J = 7, 1, Hz, 1 H), 5.14 (heptet, J = 6 Hz, 1 H), 4.57 (heptet, J = 6 Hz, 1 H), 3.97 (s, 1 H), 3.38 (s, 3 H), 1.91 (s, 3 H), 1.54 (dd, J = 1, 1 Hz, 3 H), 1.42 (dd, J = 7, 1 Hz, 3 H),1.18 (d, J = 6 Hz, 3 H), 1.15 (d, J = 6 Hz, 3 H), 1.13 (d, J = 6 Hz, 3 H), 1.06 (d, J = 6 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 199.1, 156.0, 145.7, 134.8, 134.6, 130.4, 120.6, 82.2, 75.5, 73.1, 60.0, 22.75 (2C), 22.72, 22.3, 13.5, 10.8, 10.7; MS m/z (M^+) calcd 3324.1937, obsd 324.1936; $\lambda_{max}^{CH_3OH}$ 352 nm (ϵ 3850).

4-(1-Cyclopenten-1-yl)-4-hydroxy-2,3-diisopropoxy-6-methoxy-5-methyl-2,5-cyclohexadien-1-one (14) and (3a*R,3b*R**,6a*R**,7a*R**)-3a,3b,4,5,6,6a,7,7a-Octahydro-3a-**

hydroxy-2,3-diisopropoxy-7a-methoxy-7-methylene-1*H*-cyclopenta[*a*]pentalen-1-one (15). Method A was used with 77 mg (1.1 mmol) of methoxyallene, 0.66 mL (1.1 mmol) of *n*-butyllithium, 198 mg (1.0 mmol) of diisopropyl squarate, 588 mg (3.0 mmol) of 1-iodocyclopentene, and 3.53 mL (6.0 mmol) of *tert*-butyllithium, for 16 h (−78 °C), 4 h (0 °C), and 5 h (rt). The black reaction mixture was quenched at rt. Typical workup, flash chromatography on silica gel with 30% ethyl acetate in petroleum ether, and further purification by MPLC (silica gel, elution with 22% ethyl acetate in methylene chloride) afforded 66 mg (20%) of **14**, 75 mg (22.3%) of **15**, and 37 mg of material resulting from incomplete addition of the first anion.

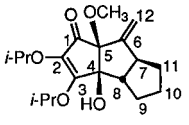
For **14**: white solid, mp 97−98 °C; IR ($CHCl_3$, cm^{-1}) 3569, 1692, 1649, 1614; ^1H NMR (300 MHz, C_6D_6) δ 5.87 (dd, J = 2, 2 Hz, 1 H), 5.27 (heptet, J = 6 Hz, 1 H), 4.66 (heptet, J = 6 Hz, 1 H), 3.67 (s, 3 H), 2.99 (s, 1 H), 2.20−2.15 (m, 2H), 2.06−1.98 (m, 1 H), 1.93 (s, 3 H), 1.93−1.87 (m, 1 H), 1.67−1.59 (m, 2 H), 1.18 (d, J = 6 Hz, 3 H), 1.17 (d, J = 6 Hz, 3 H), 1.07 (d, J = 6 Hz, 3 H), 1.00 (d, J = 6 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 180.5, 158.2, 148.2, 145.2, 136.9, 134.2, 128.6, 75.5, 74.8, 73.6, 59.7, 32.8, 31.9, 24.0, 22.6 (2C), 22.5 (2C) 10.5; MS m/z (M^+) calcd 336.1937, obsd 336.1938; $\lambda_{max}^{CH_3OH}$ 318 nm (ϵ 3000). Anal. Calcd for $C_{19}H_{28}O_5$: C, 67.83; H, 8.39. Found: C, 67.87; H, 8.39.



14

Long-range DEPT from H-10 (δ 5.86): 158.3 (C-3, ^4J, weak allylic coupling), 145.2 (C-9, ^2J), 136.9 (C-5, ^4J, weak allylic coupling), 75.5 (C-4, ^3J), 32.8 and 24.0 ppm (2 of C-11, 12, 13). Allylic coupling to C-3,5 distinguishes this regiochemistry from that of **20**.

For **15**: white solid, mp 67−8 °C; IR (neat, cm^{-1}) 3460, 2990, 1710, 1615; ^1H NMR (300 MHz, C_6D_6) δ 5.53 (dd, J = 0.8, 0.8, Hz, 1 H), 5.51−5.18 (m, 2 H), 4.99 (dd, J = 2.3, 0.8 Hz, 1 H), 3.49 (s, 3 H), 2.90 (s, 1 H), 2.07−1.95 (m, 1 H), 1.89−1.81 (m, 1 H), 1.79−1.69 (m, 3 H), 1.56−1.37 (m, 2 H), 1.06−1.04 (m, 1 H), 1.15 (d, J = 6 Hz, 3 H), 1.14 (d, J = 6 Hz, 3 H), 1.12 (d, J = 6 Hz, 3 H), 1.05 (d, J = 6 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 193.5, 166.0, 146.3, 135.0, 108.0, 92.1, 78.9, 74.4, 71.6, 60.0, 54.2, 49.1, 27.0, 23.4, 23.1 (2C), 22.8, 22.6 (2C); MS m/z (M^+) calcd 336.1937, obsd 336.1934. Anal. Calcd for $C_{19}H_{28}O_5$: C, 67.83; H, 8.39. Found: C, 67.57; H, 8.40.



15

Long-range DEPT from H-8 (δ 1.85): 166.0 (C-3, ^3J), 146.3 (C-6, ^3J), 78.9 (C-4, ^2J), 23.4 and 22.8 ppm (2 of C-9, 10, 11)
Long-range DEPT from H-7 (δ 1.99): 146.3 (^2J), 108.0 (C-12, ^3J), 78.9 (^3J), 23.4 and 22.8 ppm.

Lack of polarization transfer from H-8 to C-5 is indicative of stereochemistry at C-7. For the epimer shown, this dihedral angle is 90°. If the stereochemistry at C-7 were inverted, the angle becomes approximately 180° and should show strong coupling. The lack of NOE enhancement from H-13, OH or H-8 to H-7 is similarly diagnostic.

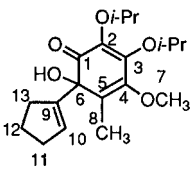
6-(1-Cyclopenten-1-yl)-6-hydroxy-2,3-diisopropoxy-4-methoxy-5-methyl-2,4-cyclohexadien-1-one (20), and 6-(1-Cyclopenten-1-yl)-6-Hydroxy-2,3-diisopropoxy-4-methoxy-5-methylene-3-cyclohexen-1-one (21). Method B was utilized with 198 mg (1.0 mmol) of diisopropyl squarate, 216 mg (1.1 mmol) of 1-iodocyclopentene, 1.3 mL (2.2 mmol) of *tert*-butyllithium, 175 mg (2.5 mmol) of methoxyallene, and 1.5 mL (2.5 mmol) of 1.68 M *n*-butyllithium for 1 h (−78 °C) and 2 h (−15 °C). The yellow reaction mixture was quenched at −15 °C and stirred for an additional 3 h at 0 °C. Typical workup provided 134 mg (40%) of a mixture of **20** and **21** (85:15 ratio, by ^1H NMR) and 114 mg (34%) of **14** as a white solid.

Irradiate	Observe	% nOe
H-13 (δ3.49)	OH	3.5
	H-8	2.2
OH (δ 2.90)	H-8	3.6
	H-13	6.1
H-8 (δ 1.85)	H-13	2.8
H-7 (δ 2.00)	H-11	6.8

For **21**: ^1H NMR (as a mixture: due to low proportion of **21** not all peaks could be designated) (300 MHz, C_6D_6) δ 5.64−5.67 (m, 2 H) H-6, 5.58 (d, J = 1.8 Hz, 1 H) H-9, 5.22 (heptet, J = 6 Hz, 1 H) methine 14, 4.66 (s, 1 H) H-2, 4.42 (heptet, J = 6 Hz, 1 H) methine 15, 3.52 (s, 3 H) H-13. 10, 11, 12, and methyls from 14 and 15 are overlapped. ^{13}C NMR (75 MHz, C_6D_6) ppm 204.7, 145.1, 143.2, 140.9, 138.9, 130.1, 110.6, 80.6, 76.6, 73.1, 73.0, 59.1, 32.8, 31.5, 23.6, 23.0, 22.7, 22.6, 22.5.

A pure sample of **20** was prepared in a reaction using identical quantities as the above for 10 h (−78 °C) and 6 h (0 °C). Quenching at 0 °C and typical workup provided 80 mg (24%) of **20** uncontaminated with its regioisomer **21**. On standing, the unstable **20** decomposes to a mixture of **20** and a new isomer which was separated by chromatography. The ^1H and ^{13}C spectra of this compound indicate it to be of very similar constitution to **20**, possibly resulting from a pinacol-type rearrangement.

For **20**: IR (neat, cm^{-1}) 3460, 2960, 1720, 1640, 1610; ^1H NMR (300 MHz, C_6D_6) δ 5.82 (dd, J = 2, 2 Hz, 1 H), 5.13 (heptet, J = 6 Hz, 1 H), 4.62 (heptet, J = 6 Hz, 1 H), 4.18 (s, 1 H), 3.36 (s, 3 H), 2.39−2.26 (m, 1 H), 2.25−2.09 (m, 3 H), 1.99 (s, 3 H), 1.71−1.61 (m, 2 H), 1.18 (d, J = 6 Hz, 3 H), 1.15 (d, J = 6 Hz, 3 H), 1.14 (d, J = 6 Hz, 3 H), 1.08 (d, J = 6 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 198.5, 156.1, 144.8, 144.7, 134.6, 130.6, 127.7, 80.7, 75.6, 73.2, 60.0, 32.6, 30.5, 23.9, 22.8 (2 C), 22.3 (2 C), 10.9; MS m/z (M^+) calcd 336.1937, obsd 336.1924; $\lambda_{max}^{CH_3OH}$ 350 nm (ϵ 3825).



20

Long-range DEPT from H-10 (δ 5.82): 198.5 (C-1, ^4J, weak allylic coupling), 144.8 (C-9, ^2J), 80.7 (C-6, ^3J), 32.6 and 23.9 ppm (2 of C-11, 12, 13). Allylic coupling to C-1 distinguishes this regioisomer from **14**.

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Supporting Information Available: Copies of the high field ^1H and ^{13}C NMR spectra for those compounds lacking combustion data excluding **17**, **19**, and **21** (10 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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