Evaluation of Amino Substituents as Nucleofugal Controllers of Regioselectivity and as Chelate Modulators of Stereoselectivity in Squarate Ester Cascades

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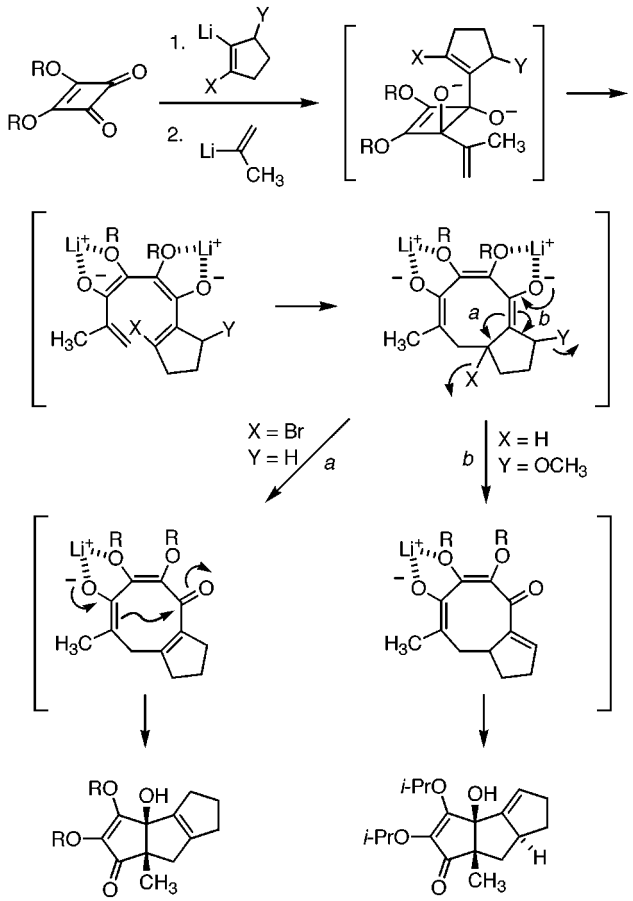
The tandem addition of an alkenyllithium reagent and a 2-lithioallylamine to squarate esters has been systematically examined. The effect of the sequencing of this twofold addition has been investigated. The extent to which the amino group is eliminated was found to be dependent on the structural features of the companion nucleophile. Also assessed was the comparative ease with which the amino and methoxy groups experience competitive β-elimination from the highly reactive, medium-ring dianionic intermediates. Attempts were made to curtail the level of competing 1,4-addition, and success was achieved by increasing the effective size of the *O*-alkyl groups in the squarate ester. The highly stereocontrolled transformations described represent a notably direct means for producing highly fused polycyclic compounds. Mechanistic considerations surrounding these reactions, which are characterized by an impressive enhancement of molecular scaffolding, are discussed.

The sequence of mechanistic events triggered by the twofold addition of alkenyl anions to squarate esters elaborates complex polycyclic products.[1] In those cases where the reactants are minimally functionalized, linear and angular polyquinanes are formed.[2] An effective solution to the control of regioselectivity has been realized by positioning a leaving group β to one of the two enolate anions that develop in an advanced medium-ring intermediate.[3] Halogen atoms and oxygenated substituents have been studied with considerable effectiveness.[4] Upon elimination, irreversible aldol ring closure gives rise to one product (Scheme 1).

Another important facet of these remarkable processes is the directionality of entry of the second nucleophile. While trans stereoselectivity unalterably guides the ensuing reaction into two sequential conrotatory operations capped by equilibration of a helical octatetraenyl intermediate (as **A** ⇆ **A′**),[5] cis addition is followed by concerted dianionic oxy-Cope rearrangement (Scheme 2).[6] Since the consequences of second-stage stereocontrol on product stereochemistry can be profound, the discovery that selected ether and amide groups are capable of augmenting cis delivery, presumably because of their capacity for lithium ion chelation, has ushered in further development of this chemistry.[7,8]

This paper gives attention to the union of these two phenomena in the context of substitution involving amino substituents. The initial question at issue is whether

Scheme 1



tertiary amino groups will exhibit nucleofugal properties[9] under these circumstances. Should elimination be possible, to what extent and under what circumstances would the expulsion of nitrogen-containing residues be competitive with the β-elimination of alkoxide anions? Additionally, can variously substituted amino groups be

(1) Negri, J. T.; Morwick, T.; Doyon, J.; Wilson, P. D.; Hickey, E. R.; Paquette, L. A. *J. Am. Chem. Soc.* **1993**, *115*, 12189.
(2) (a) Paquette, L. A.; Morwick, T. *J. Am. Chem. Soc.* **1995**, *117*, 1451. (b) Paquette, L. A.; Morwick, T. *J. Am. Chem. Soc.* **1997**, *119*, 1230.
(3) Paquette, L. A.; Morwick, T. M.; Negri, J. T.; Rogers, R. D. *Tetrahedron* **1996**, *52*, 3075.
(4) (a) Paquette, L. A.; Doyon, J. *J. Am. Chem. Soc.* **1995**, *117*, 6799. (b) Paquette, L. A.; Doyon, J. *J. Org. Chem.* **1997**, *62*, 1723.
(5) Paquette, L. A.; Hamme, A. T., II.; Kuo, L. H.; Doyon, J.; Kreuzholz, R. *J. Am. Chem. Soc.* **1997**, *119*, 1242.
(6) Review: Paquette, L. A. *Tetrahedron* **1997**, in press.
(7) (a) Paquette, L. A.; Kuo, L. H.; Doyon, J. *Tetrahedron* **1996**, *52*, 11625. (b) Paquette, L. A.; Kuo, L. H.; Doyon, J. *J. Am. Chem. Soc.* **1997**, *119*, 3038.
(8) Paquette, L. A.; Tae, J. *Tetrahedron Lett.* **1997**, *38*, 3151.
(9) Stirling, C. J. M. *Acc. Chem. Res.* **1979**, *12*, 198.

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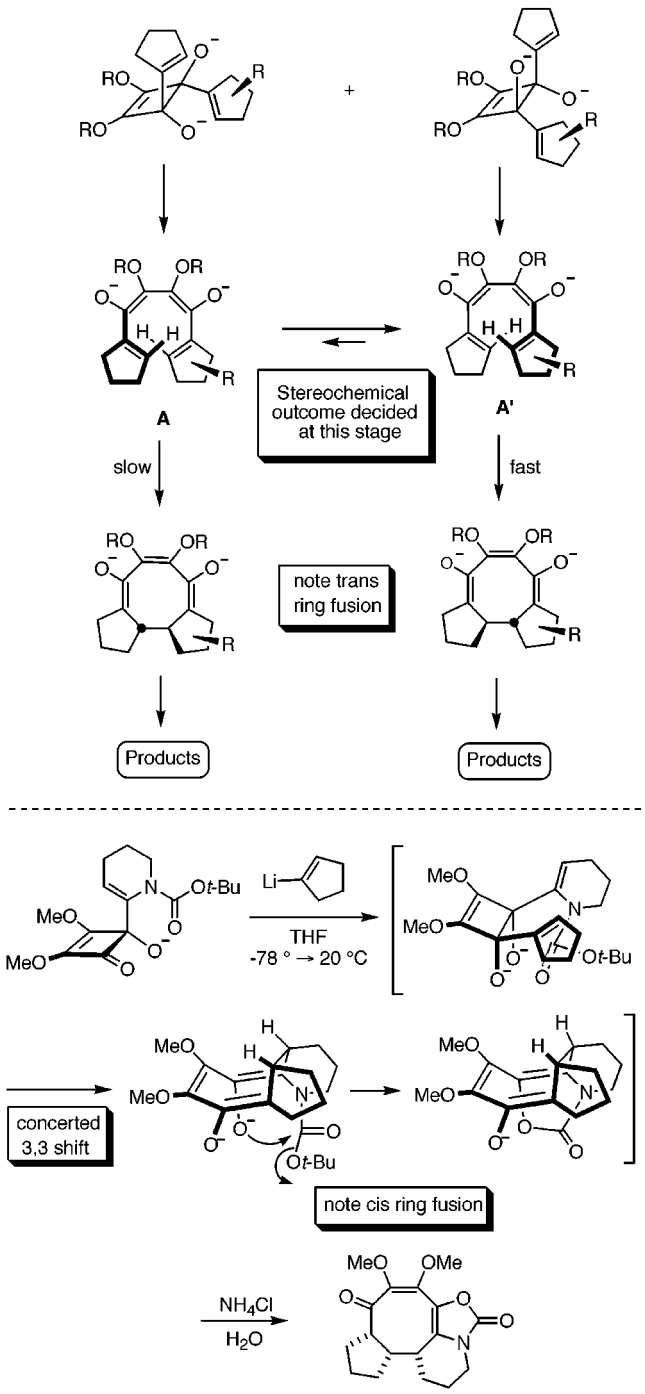
Scheme 2

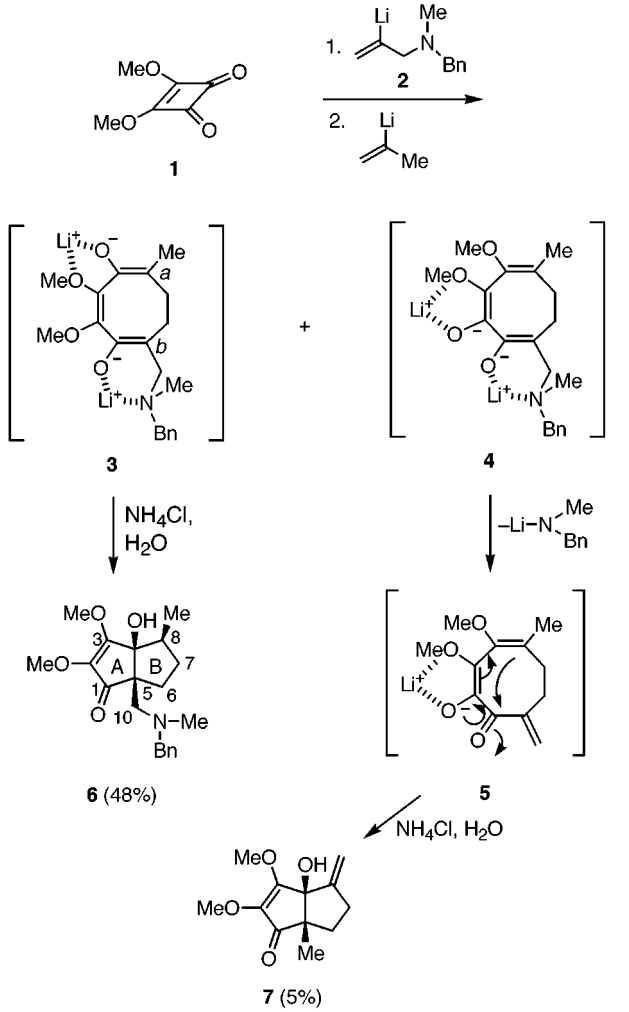


expected to exert a kinetic bias that would eventuate in chaperoning the second anion into the cis 1,2-addition reaction channel? Finally, one may inquire as to the possible relationship of the bulk of the substituents on nitrogen with possible redirection of the second-stage addition into the 1,4-manifold.[3] These issues are herein explored in turn.

Results and Discussion

The Nucleofugality of Amino Substituents. Although Michael reactions are inherently reversible processes, few examples are documented where an amide ion (e.g., R_2N^-, where R is alkyl and/or aryl) serves as the leaving group in a base-promoted retrograde step.[10,11] This is as expected in view of the high basicity of amide species in general. As the "hardness" of the ion is reduced through the introduction of electron-withdrawing groups at R, inductive and resonance stabilization combine to render the β-elimination pathway increasingly feasible kinetically. The first part of the present investigation was undertaken to establish the likelihood of elimination of amino groups during squarate ester cascades in selected cases and to broadly define possible limits to the process.

The first example, which consisted of the sequential addition of 2-lithioallylamine **2**[12] and 2-lithiopropene to dimethyl squarate (**1**), provided initial positive encouragement. In this instance, the diastereomerically homogeneous amino ketone **6** was isolated in 48% yield alongside a lesser amount of **7**. This cis relationship of the methyl and alkylamino substituents in **6** was initially defined by NOE analysis (see Figure 1). The relative orientation of the carbonyl and methoxy functionalities in ring A was established by semiselective DEPT studies at 300 MHz.



The observation of cross-peaks between H-10 (δ 2.59) and C-1 (201.5 ppm), C-4 (84.4 ppm) and C-5 (57.9 ppm), as well as between H-8 (δ 2.25) and C-3 (170.9 ppm) and

(10) (a) Bergmann, E. D.; Ginsburg, D.; Pappo, R. *Org. React.* **1959**, *10*, 179. (b) Little, R. D.; Masjedizadeh, M. R.; Wallquist, O.; McLoughlin, J. I. *Org. React.* **1995**, *47*, 315.

(11) For a leading reference to β-nitrogen elimination involving aluminum or boron enolate derivatives, see: Carlsson, S.; Lawesson, S.-O. *Tetrahedron* **1982**, *38*, 413.

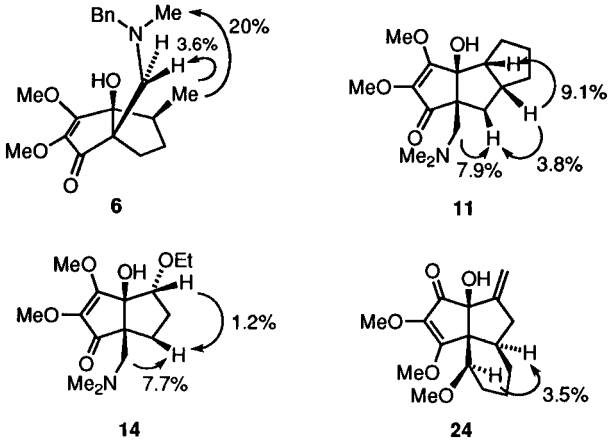


Figure 1. Representative NOE results.

C-4 (84.4 ppm) were particularly diagnostic. This product distribution reveals that the kinetically favored reaction trajectory consists of 1,2-addition of the 2-lithiopropene and transient formation of dienolate **3**. The substitution level in the two alkenyl anions is recognized to be too low to permit a determination of the extent to which **3** was formed by potentially competitive sigmatropic and electrocyclic avenues. At this point, this distinction holds little relevance. It is more significant that **3** experiences protonation regioselectively at the less sterically encumbered position *a* more rapidly than at site *b* (not observed) and at a rate considerably faster than the β-elimination option. The formation of **7** is the result of 1,4-addition, with ensuing conrotatory opening of the four-membered ring, arrival at **4**, and β-elimination of the amino substituent, to give **5** in advance of transannular ring closure.

A relevant consideration is whether the elimination process associated with the conversion of **4** to **5** operates at the dienolate stage or only after quenching with aqueous ammonium chloride solution. Our global experience with the examples given here has been that TLC analysis of reaction mixtures *prior to* workup invariably revealed the products to be already formed. While these observations might be attributed to acceleration of the final stages of the cascade while the intermediates are adsorbed for a brief time on the silica gel, mechanistic analysis of our observations is better served by focusing on the options available to the dienolate intermediates generated in each instance. Relevantly, the energetics associated with the alleviation of the heightened charge repulsion that is resident within any dienolate during the amide elimination process can be expected to contribute to a favorable lowering of the overall enthalpy of the process. Analogies do exist. For example, the aza-Wittig rearrangement consists of the isomerization of an α-lithiated tertiary amine to a lithium amide.[13] The driving force underlying this process has been attributed to transfer of the formal negative charge from the less electronegative α-carbon to the more electronegative heteroatom,[14,15] with accompanying favorable consequences in the HOMO/LUMO gap.[16] In light of these considerations, this mechanistic model is utilized in the ensuing discussion.

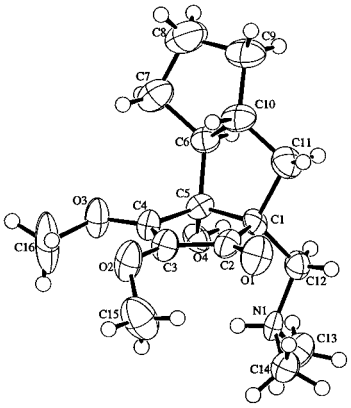
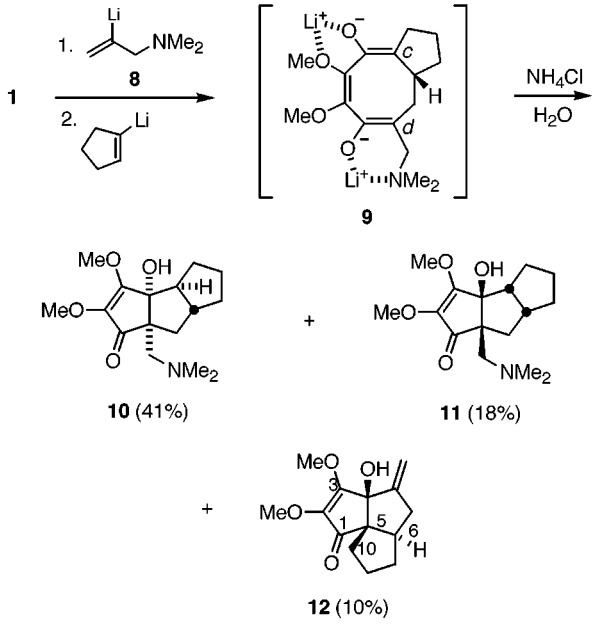


Figure 2. ORTEP diagram of **10**·HCl with the non-hydrogen atoms represented by 50% probability thermal ellipsoids. The hydrogen atoms are drawn with an artificial radius.

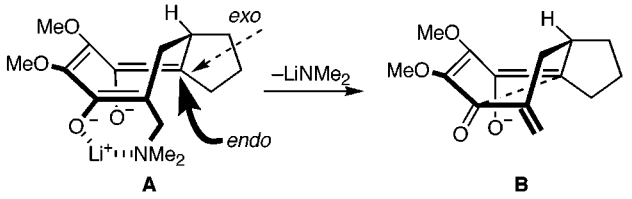
When the steric demands of the second nucleophile were increased somewhat to the cyclopentenyl level and were preceded by the addition of *N,N*-dimethyllithioallylamine **8**,[12] three triquinanes made their appearance



in a combined yield of 69%. Proof of the structure for the major product **10** was secured by single-crystal X-ray analysis of its hydrochloride salt (Figure 2). The stereoisomeric distinction between **10** and **11** was made apparent on the basis of NOE studies (Figure 1). Unequivocal structural definition of **12** was again made possible by semiselective DEPT studies: H-10 (δ 2.06) showed appropriate cross-peaks with C-1 (202.8 ppm), C-4 (81.4 ppm), and C-5 (65.8 ppm), while H-6 (δ 2.35) expectedly interacts strongly with C-1, C-4, C-5, and C-8 (150.7 ppm). The coproduction of **12** is consistent with a somewhat improved capability within **9** (relative to **3**) for the ejection of amide ion. One of the consequences of cyclopentannulation as in **9** is to rigidify one tublike conformation significantly and to deter tub-to-tub conformational interconversion. The thermodynamically

(12) (a) Barluenga, J.; Canteli, R.-M.; Flórez, J. *J. Org. Chem.* **1994**, *59*, 602. (b) Barluenga, J.; Canteli, R.-M.; Flórez, J. *J. Org. Chem.* **1996**, *61*, 3646. (c) Barluenga, J.; Canteli, R.-M.; Flórez, J. *J. Org. Chem.* **1996**, *61*, 3753.
(13) Vogel, C. *Synthesis* **1997**, 497.
(14) Reetz, M. T.; Schinzer, D. *Tetrahedron Lett.* **1975**, *40*, 3485.
(15) Broka, C. A.; Shen, T. *J. Am. Chem. Soc.* **1989**, *111*, 2981.
(16) Murata, Y.; Nakai, T. *Chem. Lett.* **1990**, 2069.

favored conformer is depicted in **A**. The partitioning of

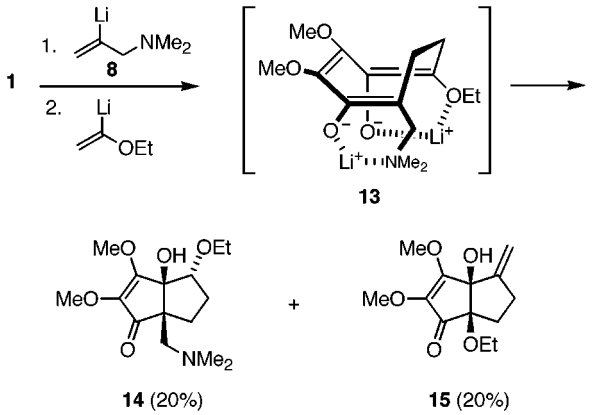


A between progression to **10** or to **11** has its origins in the directionality of protonation at the cyclopentylic enolate site. Note that endo attack is more prevalent by a factor in excess of 2:1. Although postequilibration is possible, this is not viewed as particularly likely since the quenching is accomplished with saturated NH_4Cl solution.

Once again, protonation is seen to operate across the cyclooctatriene ring (position *c*) from the site of the amino substituent (position *d*). These observations raise the interesting prospect that internal chelation of the $O^-\cdots Li^+\cdots NR_3$ type so attenuates the basicity of the associated enolate that its protonation is not competitive.

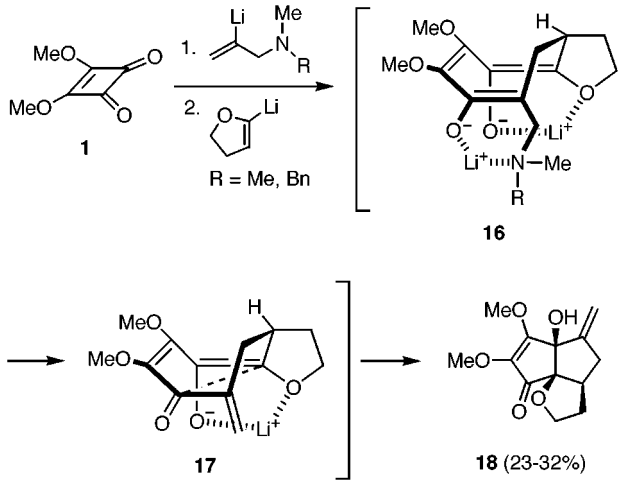
Loss of lithium dimethylamide from **A** leads to **B**, whose topology is highly conducive to transannular aldol cyclization.

An especially informative experiment involved the combined use of **8** and lithiated ethyl vinyl ether. In this

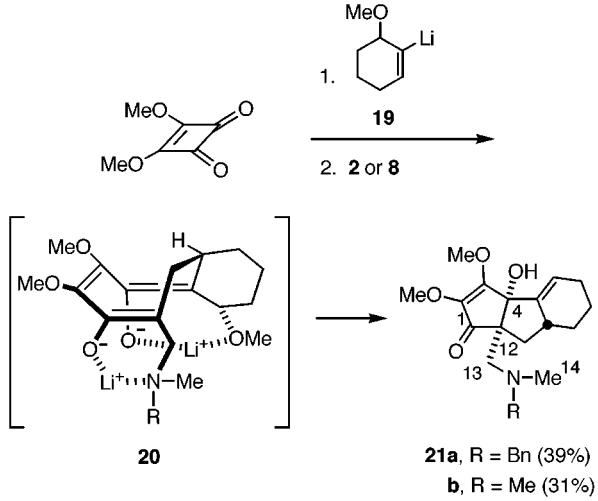


example, a mixture of **14** and **15** was produced in a 1:1 ratio! The reagent combination was intended to lead to a mesocyclic intermediate, viz. **13**, in which a six-centered nitrogen chelate substructure was counterbalanced by an oxygen-centered five-ring complex. It was hoped that the attenuated reactivity intimately associated with the properly positioned ethoxy group would provide added time for amide elimination to take place. The production of comparable levels of diquinanes **14** (Figure 1) and **15** supports this line of reasoning.

The success associated with the above experiment immediately prompted the consideration of 2-lithio-4,5-dihydrofuran as a reaction partner in view of the previously described advantages that accrue to the use of cyclopentenyllithium. Irrespective of whether the initial reactant was **2** or **8**,[12] the exomethylene tricyclic ketone **18** was isolated as the only characterizable product. As before, the promixity of H-6 (δ 2.68) to the carbonyl group (C-1, 197.2 ppm), oxygen-substituted carbons (C-4 and C-5, 90.3 and 78.2 ppm), and the C-8 methylene center (C-8, 147.1 ppm) was confirmed by the same NMR technique. This observation is in accord with the increased basicity of the tetrahydrofuranyl oxygen in **16**, one consequence of which can be construed to be stronger "backside" chelation. With this improved state of affairs, loss of either amide ion has increased opportunity to materialize and does so with reasonable effectiveness.



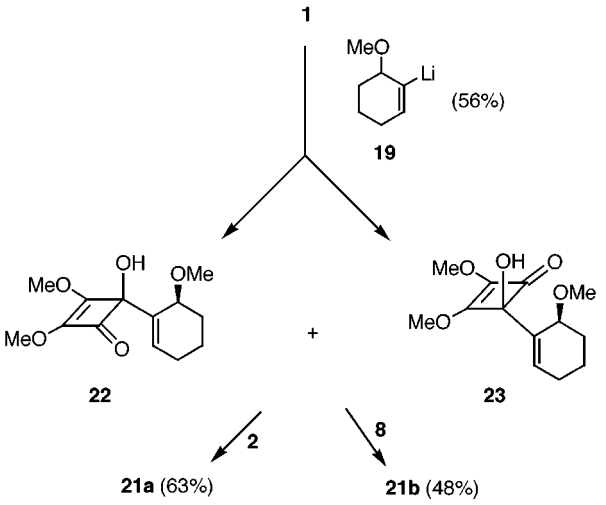
Direct Competition between Disubstituted Amino and Methoxy as the Preferred Leaving Group. The next objective of our research was to develop reaction conditions that allow for the competitive excision of oxygen- and nitrogen-containing substituents. The use of 6-methoxycyclohexenyllithium **19**[17] in advance of either **2** or **8** considerably expands the range of options available to the intermediate dienolate **20**. The 8π conrotatory



event that leads to the generation of **20** can be expected to come under steric control and to lead only to that diastereoisomer having the methoxyl group positioned on the less crowded exterior face of the structure, as shown.[5] The working model that accounts for arrival at the tricyclic amino alcohols parallels that we have previously invoked for self-immolative chirality transfer.[17] Evidently, methoxide ion is the nucleofuge of choice, experiences the more rapid β-elimination, and guides the regioselectivity of the ultimate transannular aldol step. The observation of a 1,4-relationship between the oxygen atoms in **21a** and **21b**, confirmed in the established way

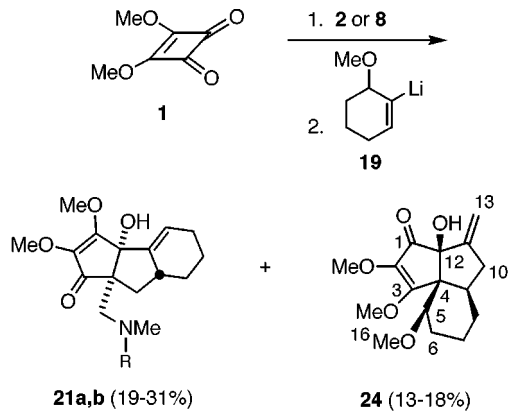
(17) Paquette, L. A., Kuo, L. H.; Hamme, A. T., II.; Kreuzholz, R.; Doyon, J. *J. Org. Chem.* **1997**, *62*, 1730.

by long-range DEPT measurements,[18] signaled the possibility that 1,2-addition was singularly operative. However, because the yields of these products were modest, the initiative was taken to explore this feature in greater depth. Accordingly, **1** was converted by reaction with 1 equiv of **19** into a 2.8:1 mixture of cyclobutenones **22** and **23**, which were purified but not separated. When

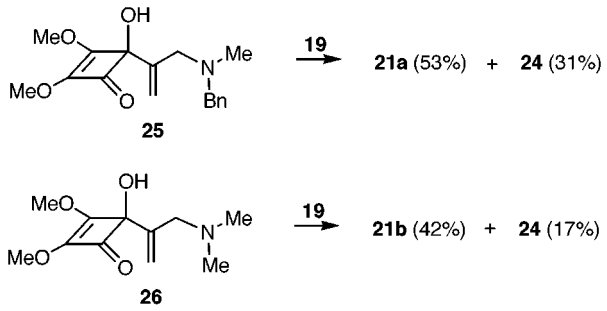


these intermediates were independently treated with **2** and **8**, only **21a** and **21b** were again isolated at significantly improved levels of efficiency. The preponderance of 1,2-addition is obviously very high for these examples.

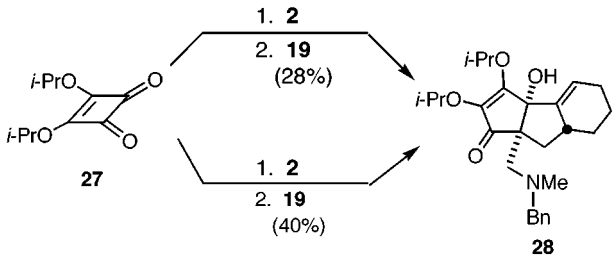
These results are not duplicated when the order of addition of the same reagents is reversed. Although **21a** and **21b** continue to be major products, they are now formed alongside the α-hydroxy ketone **24** (13−18%). Evidence for the regioreversed placement of the oxygenated centers in **24** was derived from long-range DEPT analysis in C_6D_6 solution, which showed H-5 (δ 3.38) to exhibit three-bond coupling to C-3 (166.3 ppm), C-12 (84.4 ppm), and C-16 (57.4 ppm), alongside two-bond coupling to C-4 (60.2 ppm) and C-6 (28.3 ppm). Accordingly, the order of addition holds importance. The energetic difference between the two possible reaction channels cannot be attributed to a diminished ability on the part of secondary amine substituents to direct 1,2-entry of the second nucleophile. Such behavior was encountered earlier to a very modest level (5%) only with **2** and 2-lithiopropene as the reagent twosome. More likely, the combination of subtle effects which are operative as this nucleophile begins to engage in bonding to the monoadduct dictates the relative orientation of **19**.



Independent generation of **25** and **26** for the purpose of capturing **19**[17] independently provided no bias toward an alternative explanation. In both examples, product distributions similar to those determined for the one-pot procedures were observed.



Modulation of the Levels of Competitive 1,4-Addition. It will be recognized that 1,4-addition proceeds by attack of the second nucleophile at an alkoxy-substituted site. Consequently, the expectation is that an effective increase in the steric bulk of the RO groups resident on the squarate ester might well be met with a significant dropoff in conjugate addition. Diisopropyl squarate (**27**) was considered to be appropriately tailored



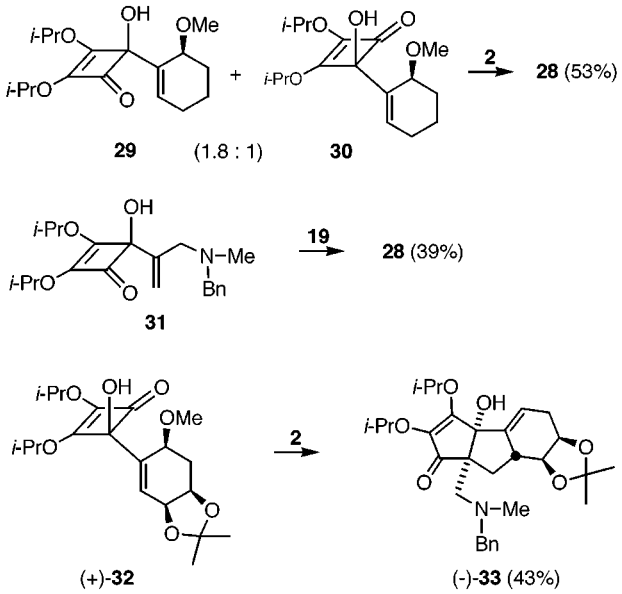
to this purpose. Indeed, the involvement of this substrate with alkenyllithiums **2** and **19** was such that only **28** was formed irrespective of the mode of addition. 1,4-Addition appeared to have been totally suppressed. Confirmation of this conclusion was achieved by means of the two-step variants of these reactions.

The latter exhibited greater overall efficiency and were consequently more convincing of the fact that a product analogous to **24** was not detectable. Comparable addition of **2** to the previously reported dextrorotatory **32**[8] likewise gave evidence of adherence to the 1,2-addition option.

A more detailed appreciation of steric effect analysis prompted consideration of the annulated squarate ester **34**.[19] Examination of molecular models of **34** reveals that conformers having alkyl oxygen substituents projecting well above and below the plane of the four-membered ring can be excluded from consideration. The trimethylene tether interconnecting the pair of oxygen atoms is, of course, not planarized, but it is certainly not free to incur significant angular deformation either. Consequently, our expectation was that **34** would exhibit a return to competitive 1,4-addition. As anticipated, **36** is formed alongside **35**. While the proportion of **36** does not exceed

(18) For **21a**: Long-range DEPT (C_6D_6): irradiate H_a-13 (δ 2.65) and observe cross-peaks for C-1 (200.9 ppm, ^3J), C-4 (82.5 ppm, ^3J), C-12 (56.5 ppm, ^2J), and C-14 (41.7 ppm, ^3J). For **21b**: Long-range DEPT (C_6D_6): irradiate H_a-13 (δ 2.75) and observe cross-peaks for C-1 (200.7 ppm, ^3J), C-4 (82.5 ppm, ^3J), C-12 (56.1 ppm, ^2J), and C-14 (45.7 ppm, ^3J).

(19) Fischer, H.; Bellus, D. U.S. Patent 4,092,146, May 30, 1978.



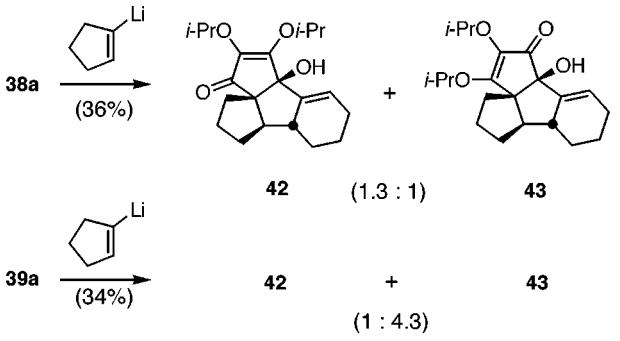
that of **35** under either mode of nucleophilic addition, the initial involvement of **2** is more conducive to its formation (Scheme 3).

Impact of a Cyclohexenylamine on the Regiocontrol of Second-Stage Nucleophilic Addition. Attention was next turned to evaluation of the relative kinetic selectivity of 1,2- vs 1,4-addition of second-stage alkenyl anion addition in monoadducts of the type **38** and **39** (Scheme 4). These representative amino alcohols, readily accessible as a consequence of the ease of generation of lithiated cyclohexenylamines such as **37**, make possible direct comparison with the methoxy derivatives **29** and **30**. There also exists a structural link between **37** and the acyclic lithio amine **2**, although the presence of a six-membered ring in the former has major conformational consequences. When **27** was condensed with **37**[20] in THF at −78 °C, there was produced an inseparable 1:1.8 mixture (^{1}H NMR analysis) of **38a** and **39a**.

Once *O*-silylation had been accomplished with *tert*-butyldimethylsilyl chloride in the presence of imidazole, **38b** and **39b** could be isolated in isomerically pure form. Subsequent individual treatment with TBAF returned samples of **38a** and **39a** not contaminated with each other. To establish the structural identity of these two alcohols, the major diastereomer was hydrogenated under conditions which chemoselectively saturated the cyclohexene double bond and effected *N*-debenzylation. Subsequent direct conversion to carbamate **41** provided a nicely crystalline substance conveniently conducive to X-ray crystallographic analysis. With the structure of **41** established in this manner (Figure 3), it became possible to make proper assignment to **38**−**40**.

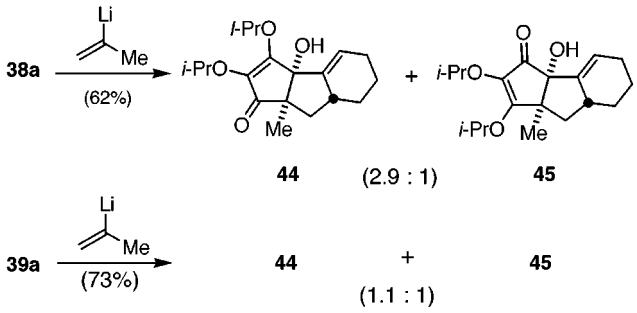
At this point, **38a** and **39a** were subjected to the action of 1-lithiocyclopentene as the second-stage reactant. Both examples led to the isolation of **42** and **43**, but with rather different relative proportions. In the case of **38a**, the distribution of 1,2- and 1,4-addition products is near unity. The major constituent from the second experiment was **43**. This dominance of the α-hydroxy ketone isomer is noteworthy because its magnitude far exceeds that of any comparable methoxycyclohexene analogue.

Proper distinction between **42** and **43** was accomplished by X-ray diffraction analysis of the second isomer (Figure 4). The increased production of **43** from **39a** is



thought to represent a compromise between chelation control and nonbonded steric interactions in the vicinity of the cyclohexenyl substituent, with the first of these options lacking in its ability to direct cis attack of the second anion at the carbonyl site.

A decrease in the bulk of the second-stage nucleophile to the 2-propenyl level results in a significant proportional increase in 1,2-addition. Where **38a** is concerned, the level of **44** is more than double that determined for **42**. For **39a**, **44** and **45** are coproduced in essentially equal amounts, illustrating that the structural features of the alkenyllithium can have a significant impact on product distribution.

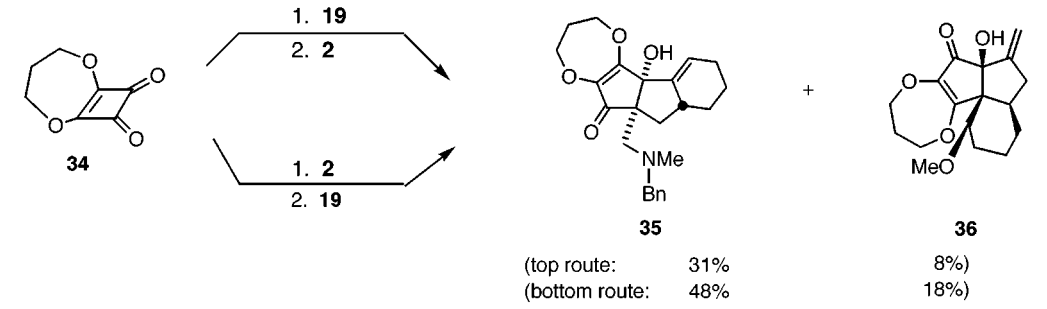


Summary

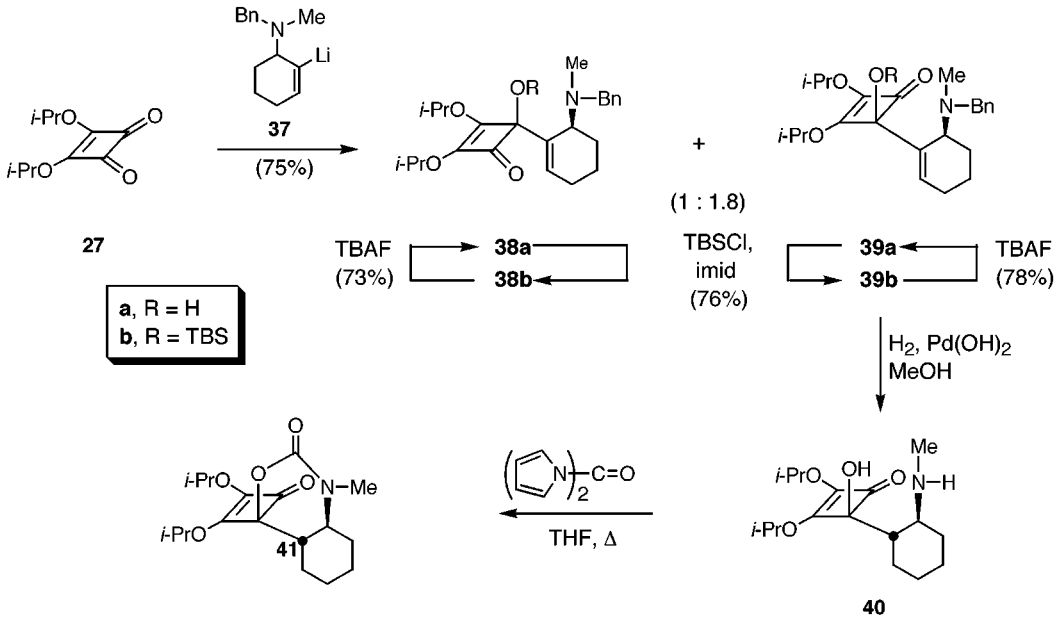
We have demonstrated that cyclic and acyclic 2-lithio allylamines enter effectively into the squarate ester cascade to give highly fused di-, tri-, and tetracyclic compounds. The multiple functionality and stereochemical features in the resultant products, and the one-flask nature of these transformations hold promise for the application of this methodology in a variety of synthetic contexts. The salient features of the overall process include (1) the capacity for ejection of the nitrogen functionality, the extent of which is closely linked to the nature of the companion alkenyl anion, (2) the greater relative ease with which methoxy groups are excised from the dianionic intermediates, and (3) one's ability to attenuate the extent of 1,4-addition simply by increasing the steric bulk of the alkoxy group in the starting squarate ester or the level of *N*-substitution in the lithio allylamine when added first.

Whereas earlier work has shown that steric effects such as those exerted by the R group in Scheme 1 are capable of controlling the stereochemical course of polycycle construction, *the present results reveal that substituent influences resident in the alkenyllithium reactants can be effectively utilized to exert control over the β-elimination and later events*. We are unaware of any prior use of substituent effects in this manner. So far, we have noted no limitation to this general stratagem since

Scheme 3



Scheme 4



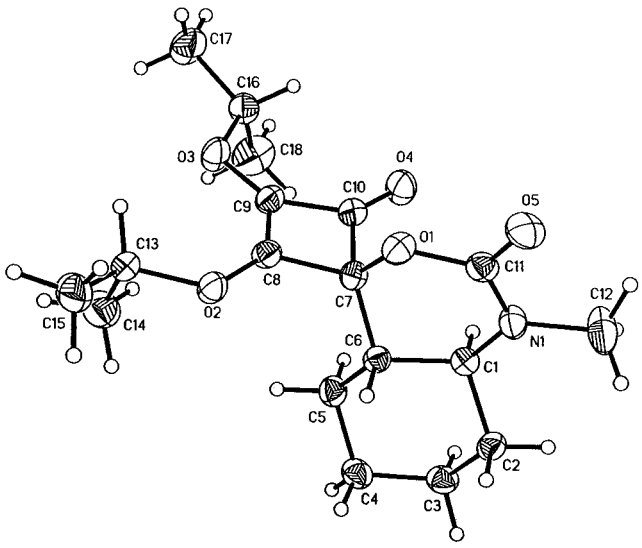


Figure 3. ORTEP diagram of **41** with the non-hydrogen atoms represented by 50% probability thermal ellipsoids. The hydrogen atoms are drawn with an artificial radius.

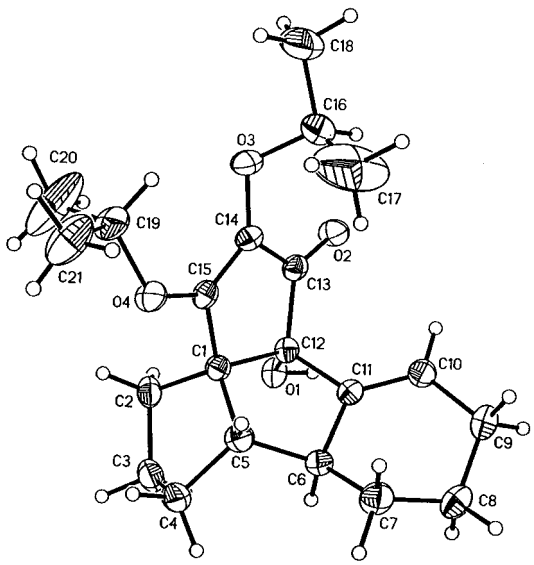


Figure 4. ORTEP diagram of **43** with the non-hydrogen atoms represented by 50% probability thermal ellipsoids. The hydrogen atoms are drawn with an artificial radius.

various readily available 2-bromoallylamines have invariably entered into this reaction cascade. Recourse to chiral nitrogen substituents would set the stage for possible 1,5-asymmetric induction prior to the β-elimination event. The scope of this chirality transfer has been explored and is detailed in the accompanying paper.[21]

Experimental Section

General Methods. All reactions were carried out under an inert atmosphere of argon or nitrogen. Glassware was generally oven-dried or flame-dried in vacuo and purged with argon or nitrogen. 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 (75 MHz) NMR. 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 Atlantic Microlab, Inc., Norcross, GA.

General Procedure for the Use of 2 and 8 as the Lead Anion. A. To a cold (−78 °C), magnetically stirred solution of 2-bromo-*N*-benzyl-*N*-methylallylamine (940 mg, 4.16 mmol) in dry THF (10 mL) was added dropwise 4.9 mL of 1.7 M *tert*-butyllithium in pentane (8.33 mmol). After 30 min at this temperature, a solution of **1** (394 mg, 2.77 mmol) in dry THF (5 mL) was similarly introduced, followed 1 h later with 2-lithiopropene [from 2-bromopropene (0.49 mL, 5.54 mmol) and *tert*-butyllithium (6.5 mL of 1.7 M, 11.1 mmol) in THF (5 mL)] as rapidly as possible. The reaction mixture was kept at −78 °C for 2 h, allowed to warm to room-temperature overnight, recooled to 0 °C, and treated with deoxygenated saturated NH_4Cl solution (10 mL). After 30 min, the two-phase system was stirred at 20 °C for 20 h and diluted with brine (20 mL). The separated aqueous phase was extracted with ether (2 × 30 mL), the combined organic layers were dried and evaporated, and the residue was chromatographed on silica gel (elution with 2:1 hexanes/ethyl acetate). There was isolated 466 mg (48%) of **6** and 31 mg (5%) of **7**.

For **6**: white solid, mp 169−171 °C; IR (film, cm^{-1}) 3250, 1698, 1621, 1462, 1325, 1232; ^{1}H NMR (300 MHz, C_6D_6) δ 7.25−6.90 (m, 5 H), 3.78 (s, 3 H), 3.60 (s, 3 H), 3.45 (d, J = 13.2 Hz, 1 H), 3.06 (d, J = 13.2 Hz, 1 H), 3.01 (d, J = 12.9 Hz, 1 H), 2.59 (d, J = 12.9 Hz, 1 H), 2.25 (m, 1 H), 1.95 (m, 1 H), 1.88 (s, 3 H), 1.45 (m, 1 H), 1.17 (d, J = 7.0 Hz, 3 H), 1.12 (m, 1 H), 1.00 (m, 1 H) (OH not observed); ^{13}C NMR (75 MHz, C_6D_6) 201.5, 170.9, 138.2, 137.8, 129.1, 128.7, 127.5, 84.4, 62.8, 62.4, 59.0, 58.7, 57.8, 46.2, 42.2, 34.9, 31.0, 15.4 ppm; MS m/z (M^+) calcd 345.1939, obsd 345.1938. Anal. Calcd for $C_{20}H_{27}NO_4$: C, 69.54; H, 7.88. Found: C, 69.67; H, 7.91.

For **7**: white solid, mp 111−113 °C; IR (film, cm^{-1}) 3420, 1690, 1610, 1460, 1425, 1340, 1295; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.31 (m, 1 H), 5.11 (m, 1 H), 4.16 (s, 3 H), 3.75 (s, 3 H), 3.19 (s, 1 H), 2.31 (m, 1 H), 2.20 (m, 1 H), 2.05 (m, 1 H), 1.45 (ddd, J = 7.2, 7.6, 12.7 Hz, 1 H), 1.19 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) 198.1, 173.7, 151.7, 132.8, 110.6, 82.2, 59.8, 59.5, 52.8, 32.3, 29.7, 19.5 ppm; MS m/z (M^+) calcd 224.1048, obsd 224.1041. Anal. Calcd for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found: C, 64.35; H, 7.24.

B. Coupling of 2-bromo-*N*,*N*-dimethylallylamine (611 mg, 3.73 mmol) and 1-bromocyclopentene (963 mg, 4.97 mmol) to **1** (353 mg, 2.48 mmol) in the predescribed manner gave after chromatography (elution with 1:1 hexanes/ethyl acetate) 300 mg (41%) of **10**, 133 mg (18%) of **11**, and 59 mg (10%) of **12**.

For **10**: colorless oil; IR (film, cm^{-1}) 3500, 1690, 1625, 1460, 1330, 1230, 1205; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.19 (s, 3 H), 3.84 (s, 3 H), 2.87 (d, J = 12.9 Hz, 1 H), 2.73 (d, J = 12.9 Hz, 1 H), 2.19 (s, 6 H), 2.15−1.80 (series of m, 5 H), 1.65−1.40 (m, 2 H), 1.35−0.90 (series of m, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) 201.9, 169.6, 138.0, 79.6, 63.3, 63.0, 60.8, 59.4, 59.1, 45.9, 45.7, 37.8, 27.7, 25.1, 22.6 ppm; MS m/z (M^+) calcd 295.1783, obsd 295.1776. Anal. Calcd for $C_{16}H_{25}O_4$: C, 65.06; H, 8.53. Found: C, 64.96; H, 8.48.

For **11**: colorless oil; IR (film, cm^{-1}) 3450, 1695, 1625, 1460, 1330, 1200; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.18 (s, 3 H), 3.82 (s, 3 H), 2.90 (m, 1 H), 2.76 (d, J = 12.8 Hz, 2 H), 2.48 (m, 1 H), 2.20 (s, 6 H), 1.90−1.25 (series of m, 8 H) (OH not observed); ^{13}C NMR (75 MHz, $CDCl_3$) 201.9, 170.7, 134.2, 86.1, 63.2, 59.3, 59.0, 58.8, 55.8, 44.9 (2 C), 40.0, 29.4, 27.5, 24.8 ppm; MS m/z (M^+) calcd 295.1783, obsd 295.1776. Anal. Calcd for $C_{16}H_{25}NO_4$: C, 65.06; H, 8.53. Found: C, 64.99; H, 8.59.

For **12**: colorless oil; IR (film, cm^{-1}) 3440, 1700, 1625, 1460 1330, 1210; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.29 (s, 1 H), 5.14 (s, 1 H), 4.15 (s, 3 H), 3.82 (s, 3 H), 2.45−2.35 (m, 2 H), 2.25 (br s, 1 H), 2.20−2.10 (m, 1 H), 1.95−1.85 (m, 3 H), 1.85−1.60 (m, 2 H), 1.20 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) 203.0, 166.2, 150.7, 135.4, 110.1, 81.2, 65.5, 59.7, 59.6, 46.7, 35.2, 33.5, 29.8, 27.2 ppm; MS m/z (M^+) calcd 250.1205, obsd 250.1207. Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25. Found: C, 67.02; H, 7.25.

C. Coupling of 2-bromo-*N*,*N*-dimethylallylamine (513 mg, 3.12 mmol) and ethyl vinyl ether (0.40 mL, 4.17 mmol) to **1** (296 mg, 2.08 mmol) as described above afforded 107 mg (20%) of **14** and 127 mg (20%) of **15**.

For **14**: colorless oil; IR (film, cm^{-1}) 3500, 1698, 1621, 1462, 1326; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.19 (s, 3 H), 3.86 (dd, J = 5.2, 7.8 Hz, 1 H), 3.81 (s, 3 H), 3.71 (m, 1 H), 3.58 (m, 1 H), 2.81 (d, J = 12.8 Hz, 1 H), 2.56 (d, J = 12.8 Hz, 1 H), 2.15 (s, 6 H), 1.83 (m, 1 H), 1.74 (m, 1 H), 1.52 (m, 1 H), 1.25 (m, 1 H), 1.14 (t, J = 7.0 Hz, 3 H) (OH not observed); ^{13}C NMR (75 MHz, $CDCl_3$) 201.0, 170.6, 137.0, 87.1, 85.0, 65.6, 63.5, 59.5, 59.2, 55.4, 45.8 (2 C), 30.7, 28.4, 15.3 ppm; MS m/z (M^+) calcd 299.1732, obsd 299.1735. Anal. Calcd for $C_{15}H_{25}NO_5$: C, 60.18; H, 8.42. Found: C, 60.09; H, 8.47.

For **15**: colorless oil; IR (film, cm^{-1}) 3471, 1704, 1614, 1462, 1425, 1337, 1296; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.41 (d, J = 2.3 Hz, 1 H), 5.16 (d, J = 2.3 Hz, 1 H), 4.18 (s, 3 H), 3.89 (m, 1 H), 3.83 (s, 3 H), 3.70 (m, 1 H), 2.35 (m, 2 H), 1.98 (m, 1 H), 1.62 (m,1 H), 1.16 (t, J = 7.0 Hz, 3 H) (OH not observed); ^{13}C NMR (75 Mz, $CDCl_3$) 196.2, 168.2, 149.2, 136.2, 111.1, 83.2, 78.1, 61.5, 59.8, 59.6, 29.9, 28.3, 15.6 ppm; MS m/z (M^+) calcd 254.1154, obsd 254.1158. Anal. Calcd for $C_{13}H_{18}O_5$: C, 61.41, H, 7.13. Found: C, 61.15, H, 7.17.

D. Coupling of 2-bromo-*N*,*N*-dimethylallylamine (443 mg, 2.70 mmol) and 4,5-dihydrofuran (0.27 mL, 3.60 mmol) to **1** (256 mg, 1.80 mmol) in the predesdribed manner furnished 145 mg (32%) of **18** as a colorless oil: IR (film, cm^{-1}) 3452, 1713, 1621, 1462, 1335; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.48 (s, 1 H), 5.23 (s, 1 H), 4.15 (s, 3 H), 4.06 (m, 2 H), 3.83 (s, 3 H), 3.05 (s, 1 H), 2.70 (m, 1 H), 2.45−2.10 (series of m, 3 H), 1.55 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) 197.3, 167.1, 147.0, 136.8, 113.4, 90.3, 78.2, 71.8, 59.8, 59.4, 43.7, 33.3, 32.1 ppm; MS m/z (M^+) calcd 252.0997, obsd 252.0994. Anal. Calcd for $C_{13}H_{16}O_5$: C, 61.90; H, 6.39. Found: C, 61.81; H, 6.44.

(3a*R,7a*R**,8a*S**)-8a-[(Benzylmethylamino)methyl]-5,6,7,7a,8,8a-hexahydro-3a-hydroxy-2,3-dimethoxycyclopent[*a*]inden-1(3a*H*)-one (21a).** A 100 mL flask charged with 1-bromo-6-methoxycyclohexene (0.46 g, 2.42 mmol) and THF (12 mL) was treated dropwise at −78 °C with *tert*-butyllithium (3.2 mL, 1.7 M in pentane, 5.44 mmol), and the mixture was stirred at this temperature for 1 h. A solution of **1** (0.33, 2.32 mmol) in THF (12 mL) was introduced and the solution was stirred at this temperature for another 2.5 h before **2** [generated from the vinyl bromide (0.90 g, 3.77 mmol) in THF (19 mL) and *tert*-butyllithium (5.0 mL, 1.7 M in pentane, 8.50 mmol) at −78 °C for 1 h] was transferred in via cannula. After 11 h at room temperature, deoxygenated saturated aqueous ammonium chloride solution (10 mL) was added, the mixture was extracted with ether (2 × 20 mL), and the combined organic layers were washed with water (20 mL) and brine (20 mL) prior to drying and solvent evaporation. The residue was purified by flash chromatography on silica gel (elution with hexanes−ethyl acetate 6:1) to give **21a** as a yellow liquid (0.35 g, 39%); IR (film, cm^{-1}) 1698, 1622, 1454, 1327, 1017; ^{1}H NMR (300 MHz, C_6D_6) δ 7.12−6.98 (m, 5 H), 6.43−6.40 (m, 1 H), 3.83 (s, 3 H), 3.64 (s, 3 H), 3.44 (d, J = 13.1 Hz, 1 H), 3.12 (d, J = 13.1 Hz, 1 H), 3.08 (d, J = 12.9 Hz, 1 H), 2.63 (d, J = 12.9 Hz, 1 H), 2.28−2.17 (m, 1 H), 2.16−2.11 (m, 1 H), 2.07−1.90 (m, 2 H), 1.89 (s, 3 H), 1.86−1.65 (m, 1 H), 1.54−1.47 (m, 1 H), 1.28−1.19 (m, 2 H), 0.96−0.84 (m, 2 H); ^{13}C NMR (75 MHz, C_6D_6) 200.9, 170.4, 142.9, 137.8, 136.1, 128.9, 128.4, 127.3, 122.3, 82.5, 62.6, 62.2, 58.6 (2 C), 56.5, 42.0, 41.7, 34.8, 28.8, 25.0, 21.9 ppm; MS m/z (M^+) calcd

(20) He, M. unpublished results from this laboratory.
(21) Paquette, L. A.; Tae, J. *J. Org. Chem.* **1998**, *63*, 2022 (following paper in this issue).

383.2063, obsd 383.2080. Anal. Calcd for $C_{23}H_{29}NO_4$: C, 72.04; H, 7.62. Found: C, 71.75; H, 7.73.

(3a*R,7a*R**,8a*S**)-8a-[(Dimethylamino)methyl]-5,6,7,-7a,8,8a-hexahydro-3a-hydroxy-2,3-dimethoxycyclopent-[*a*]inden-1(3a*H*)-one (21b).** Comparable treatment of **1** (0.32 g, 2.25 mmol) first with **19** and then with **8** afforded a brown liquid whose purification by flash chromatography on silica gel (elution with ethyl acetate/methanol 100:1) afforded **21b** (0.21 g, 31%) as a yellow solid: mp 78−91 °C; IR (film, cm^{-1}) 1698, 1622, 1454, 1312, 1105; ^1H NMR (300 MHz, C_6D_6) δ 6.34 (s, 1 H), 3.82 (s, 3 H), 3.72 (s, 3 H), 2.77 (d, J = 12.7 Hz, 1 H), 2.42 (d, J = 12.7 Hz, 1 H), 2.21−2.03 (m, 2 H), 1.98−1.87 (m, 3 H), 1.85 (s, 6 H), 1.81−1.63 (m, 1 H), 1.51−1.44 (m, 1 H), 1.34−1.14 (m, 1 H), 0.93−0.77 (m, 2 H); ^{13}C NMR (75 MHz, C_6D_6) 200.7, 170.1, 142.7, 136.1, 122.2, 82.5, 63.7, 58.7, 58.5, 56.1, 45.7 (2 C), 41.9, 34.7, 28.9, 25.0, 21.9 ppm; MS m/z (M^+) calcd 307.1777, obsd 307.1780. Anal. Calcd for $C_{17}H_{25}NO_4$: C, 66.41; H, 8.20. Found: C, 66.25; H, 8.23.

(*R)-4-Hydroxy-2,3-dimethoxy-4-[(*S**)-6-methoxy-1-cyclohexen-1-yl]-2-cyclobuten-1-one (22) and (*R**)-4-Hydroxy-2,3-dimethoxy-4-[(*R**)-6-methoxy-1-cyclohexen-1-yl]-2-cyclobuten-1-one (23).** Treatment of **1** (0.37 g, 2.61 mmol) with **19** [from 0.48 g (2.53 mmol) of the bromide] at −78 °C was followed by 1 h of stirring at this temperature, addition of water (10 mL), and extraction with ether (2 × 15 mL). The combined organic phases were dried, concentrated, and subjected to flash chromatography on silica gel (elution with hexanes/ethyl acetate 2.8:1) to give rise to a inseparable 2.8:1 mixture of **22** and **23** in 56% yield as a yellow oil: IR (film, cm^{-1}) 3404, 1775, 1631, 1335, 1044; ^1H NMR (300 MHz, C_6D_6) δ [6.41−6.38 (m, minor isomer), 5.99−5.97 (m, major isomer), total 1 H], 5.23 (br s, 1 H), [4.29 (br s, major isomer), 3.90 (br s, minor isomer), total 1 H], [3.70 (s, minor isomer), 3.63 (s, major isomer), total 3 H], [3.65 (s, minor isomer), 3.58 (s, major isomer), total 3 H], 2.99 (s, 3 H), 1.85−1.73 (m, 1 H), 1.69−1.60 (m, 2 H), 1.58−1.43 (m, 1 H), 1.24−1.13 (m, 2 H); ^{13}C NMR (75 MHz, C_6D_6) [(major isomer: 185.9, 165.3, 134.5, 134.4, 128.9, 89.6, 74.7, 59.1, 51.8, 55.4, 25.3, 25.0, 16.8), (minor isomer: 184.7, 165.3, 134.2, 133.8, 129.4, 88.4, 73.3, 58.9, 57.8, 55.7, 25.9, 25.6, 16.8] ppm; MS m/z (M^+) calcd 254.1145, obsd 254.1149.

Treatment of the 22/23 Mixture with 2. The alcohol mixture (0.24 g, 0.94 mmol) was treated with **2** (from 2.93 mmol of the bromide) in THF (25 mL) at −78 °C, stirred at room temperature for 16 h, and processed as described above to give **21a** (0.23 g, 63%), identical in all respects to the material isolated earlier.

Treatment of the 22/23 Mixture with 8. Reaction of the mixture (0.24 g, 0.94 mmol) with **8** [from 0.50 g (3.05 mmol) of the bromide] under the previously described conditions provided 0.14 g (48%) of **21b**, a yellow solid spectroscopically identical to the sample obtained before.

(3a*R,5a*S**,9*S**,9a*S**)-3a,4,5,5a,6,7,8,9-Octahydro-3a-hydroxy-1,2,9-trimethoxy-4-methylene-3*H*-cyclopent[*c*]-inden-3-one (24). A. Via the Use of 2.** A solution of **2** [prepared from 0.58 g (2.43 mmol) of the bromide] in dry THF (12 mL) cooled to −78 °C was treated sequentially with a solution of **1** (0.34 g, 2.39 mmol) in THF (12 mL) and then **19** [prepared from 0.69 g (3.63 mmol) of the bromide] also dissolved in THF (18 mL) in the manner given above. The standard workup and flash chromatography on silica gel (elution with hexanes/ethyl acetate 8:1) furnished 0.28 g (31%) of **21a** and 0.13 g (18%) of **24** as a yellow solid: mp 64−66 °C; IR (film, cm^{-1}) 3520, 1715, 1633, 1461, 1329; ^1H NMR (300 MHz, $CDCl_3$) δ 5.48 (d, J = 2.6 Hz, 1 H), 5.14 (d, J = 2.6 Hz, 1 H), 4.16 (s, 3 H), 3.77 (s, 3 H), 3.50 (dd, J = 11.7, 5.6 Hz, 1 H), 3.28 (s, 3 H), 2.43 (m, 1 H), 2.15−2.00 (m, 3 H), 1.85−1.55 (m, 3 H), 1.35−1.15 (m, 2 H) (OH not observed); ^{13}C NMR (75 MHz, $CDCl_3$) 198.5, 168.0, 148.8, 134.7, 112.9, 83.8, 79.5, 59.9, 59.8, 59.3, 57.8, 37.5, 36.6, 28.1, 27.5, 22.2 ppm; MS m/z (M^+) calcd 294.1467, obsd 294.1464. Anal. Calcd for $C_{16}H_{22}O_5$: C, 65.29; H, 7.53. Found: C, 65.40; H, 7.54.

B. Via the Use of 8. A solution of **8** [prepared from 0.30 g (1.83 mmol) of the bromide] in dry THF (9 mL) was treated sequentially with a solution of **1** (0.27 g, 1.90 mmol) in THF (9 mL) and then **19** [prepared from 0.53 g (2.79 mmol) of the bromide] also dissolved in THF (14 mL) according to the general procedure. Chromatographic purification gave 70 mg (13%) of **24** and 110 mg (19%) of **21b**.

4-[1-[(Benzylmethylamino)methyl]vinyl]-4-hydroxy-2,3-dimethoxy-2-cyclobuten-1-one (25). A solution of **2** [prepared from 0.59 g (2.47 mmol) of the bromide] in dry THF (12 mL) was added dropwise to **1** (0.35 g, 2.46 mmol) dissolved in THF (12 mL) at −78 °C. The usual workup and flash chromatographic purification (silica gel, elution with hexanes/ethyl acetate 5:1) yielded **25** (0.63 g, 84%) as a yellow liquid: IR (film, cm^{-1}) 1769 1650, 1454, 1348; ^1H NMR (300 MHz, C_6D_6) δ 8.20 (br s, 1 H), 7.23−7.01 (m, 5 H), 5.17 (br s, 1 H), 4.87 (br s, 1 H), 3.64 (s, 3 H), 3.59 (s, 3 H), 3.57 (d, J = 12.5 Hz, 1 H), 3.29 (d, J = 12.7 Hz, 1 H), 3.19 (d, J = 12.7 Hz, 1 H), 2.81 (d, J = 12.5 Hz, 1 H), 1.84 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) 185.7, 165.1, 142.5, 137.3, 134.9, 129.2, 128.4, 127.4, 115.4, 90.3, 62.9, 61.1, 59.0, 57.8, 40.2 ppm; MS m/z (M^+) calcd 303.1504, obsd 303.1487.

Reaction of Anion 19 with 25. A solution of **19** [prepared from 0.91 g (4.79 mmol) of the bromide] in THF (24 mL) was added dropwise at −78 °C to a solution of **25** (0.47 g, 1.55 mmol) in the same solvent (15 mL). Adherence to the usual protocol and subsequent flash chromatography (SiO_2, elution with hexanes/ethyl acetate 6:1) provided 0.31 g (53%) of **21a** and 0.14 g (31%) of **24**.

4-[1-[(Dimethylamino)methyl]vinyl]-4-hydroxy-2,3-dimethoxy-2-cyclobuten-1-one (26). A solution of **8** [prepared from 0.47 g (2.87 mmol) of the bromide] in dry THF (14 mL) was added dropwise to **1** (0.42 g, 2.96 mmol) dissolved in THF (15 mL) at −78 °C. The usual workup and chromatographic purification (silica gel, elution with hexanes/ethyl acetate 1:2) gave **26** (0.25 g, 38%) as a yellow oil: IR (film, cm^{-1}) 1769 1635, 1470, 1336; ^1H NMR (300 MHz, C_6D_6) δ 8.22 (br s, 1 H), 5.09 (br s, 1 H), 4.83 (br s, 1 H), 3.65 (s, 3 H), 3.63 (s, 3 H), 3.39 (d, J = 12.3 Hz, 1 H), 2.59 (d, J = 12.3 Hz, 1 H), 1.85 (s, 6 H); ^{13}C NMR (75 MHz, C_6D_6) 185.7, 165.2, 142.7, 134.7, 114.8, 90.3, 64.2, 59.0, 57.7, 43.8 (2 C) ppm; MS m/z (M^+) calcd 227.1153, obsd 227.1155.

Reaction of Anion 19 with 26. A solution of **19** [prepared from 0.72 g (3.79 mmol) of the bromide] in THF (19 mL) was added dropwise at −78 °C to a solution of **26** (0.28 g, 1.23 mmol) in the same solvent (13 mL). Adherence to the usual protocol and subsequent flash chromatography (elution with ethyl acetate/methanol 100:1) delivered 62 mg (17%) of **24** and 160 mg (42%) of **21b**.

(3a*R,7a*R**,8a*S**)-8a-[(Benzylmethylamino)methyl]-5,6,7,7a,8,8a-hexahydro-3a-hydroxy-2,3-diisopropoxycyclopent[*a*]inden-1(3a*H*)-one (28). A. By Sequential Addition of Anions 2 and 19.** A solution of **2** [prepared from 0.52 g (2.18 mmol) of the bromide] in dry THF (11 mL) cooled to −78 °C was treated sequentially with a solution of **27** (0.43 g, 2.17 mmol) in THF (9 mL) and then **19** [prepared from 0.64 g (3.37 mmol) of the bromide] also dissolved in THF (17 mL) in the manner detailed earlier. After workup and flash chromatography, there was isolated 0.27 g (28%) of **28** as a pale yellow liquid: IR (film, cm^{-1}) 1692, 1613, 1380, 1299, 1107; ^1H NMR (300 MHz, C_6D_6) δ 7.12−6.98 (m, 6 H), 6.36 (s, 1 H), 5.45 (heptet, J = 6.0 Hz, 1H), 5.17 (heptet, J = 6.0 Hz, 1 H), 3.46 (d, J = 13.0 Hz, 1 H), 3.14 (d, J = 13.0 Hz, 1 H), 3.10 (d, J = 12.9 Hz, 1 H), 2.64 (d, J = 12.9 Hz, 1 H), 2.30−2.16 (m, 2 H), 2.15−1.96 (m, 2 H), 1.90 (s, 3 H), 1.76−1.73 (m, 1 H), 1.56−1.51 (m, 1 H), 1.31−1.27 (m, 1 H), 1.21 (d, J = 6.0 Hz, 3 H), 1.17 (d, J = 6.0 Hz, 3 H), 1.15 (d, J = 6.0 Hz, 3 H), 1.05 (d, J = 6.0 Hz, 3 H), 0.98−0.88 (m, 2 H); ^{13}C NMR (75 MHz, C_6D_6) 201.3, 170.1, 143.5, 138.1, 134.2, 129.2, 128.6, 127.5, 121.9, 82.9, 73.4, 71.8, 62.9, 62.5, 56.6, 42.5, 42.0, 35.2, 29.2, 25.3, 22.9, 22.8, 22.7, 22.6, 22.4 ppm; MS m/z (M^+) calcd 439.2766, obsd 439.2744. Anal. Calcd for $C_{27}H_{37}NO_4$: C, 73.77; H, 8.48. Found: C, 73.53; H, 8.55.

B. By Sequential Addition of Anions 19 and 2. Comparable treatment of **27** (0.42 g, 2.12 mmol) first with **19** (2.11 mmol) and then with **2** (3.22 mmol) afforded 0.37 g (40%) of **28**.

(*R)-4-Hydroxy-2,3-diisopropoxy-4-[(*S**)-6-methoxy-1-cyclohexen-1-yl]-2-cyclobuten-1-one (29) and (*R**)-4-Hydroxy-2,3-diisopropoxy-4-[(*R**)-6-methoxy-1-cyclohexen-1-yl]-2-cyclobuten-1-one (30).** Treatment of **27** (0.35 g, 1.77 mmol) with **19** [from 0.34 g (1.79 mmol) of the bromide] at −78 °C in THF (18 mL) in the manner given above followed by flash chromatography (SiO_2, elution with hexanes/ethyl acetate 8:1) gave a mixture of **29** and **30** in a 1.8: 1 ratio (^{1}H NMR analysis) as a yellow liquid in 72% yield: IR (film, cm^{-1}) 3416, 1766, 1613, 1383, 1101; ^{1}H NMR (300 MHz, C_6D_6) δ [6.47−6.44 (m, minor isomer), 6.15−6.12 (m, major isomer), total 1 H], [51.0 (br s, major isomer, 4.65 (br s, minor isomer), total 1 H], 4.92 (heptet, J = 6.1 Hz, 1 H), 4.84−4.72 (m,1 H), [4.25 (br s, major isomer), 3.70 (br s, minor isomer), total 1 H], [3.06 (s, minor isomer), 3.05 (s, major isomer), total 3 H], 1.93−1.43 (m, 4 H), 1.30−1.08 (m, 14 H); ^{13}C NMR (75 MHz, C_6D_6) [(major isomer: 185.9, 164.9, 134.8, 132.4, 128.5, 89.0, 76.0, 74.6, 73.0, 55.4, 25.7, 25.0, 22.5 (2 C), 22.2, 21.8, 16.8 ppm) (minor isomer: 184.6, 167.9, 134.4, 132.3, 129.3, 88.1, 76.3, 73.6, 72.8, 55.6, 26.0, 25.3, 22.6, 22.5, 22.3, 21.9, 16.8 ppm)]; MS m/z (M$^+$) calcd 310.1806, obsd 310.1793.

Reaction of Anion 2 with 29/30. A solution of **2** [prepared from 0.40 g (1.67 mmol) of the bromide] in THF (9 mL) was added dropwise at −78 °C to a solution of the **29/30** mixture (0.17 g, 0.54 mmol) in the same medium (3 mL). After 12 h, the customary workup was applied and 0.12 g (53%) of diquinane **28** was isolated after chromatography.

4-[1-[(Benzylmethylamino)methyl]vinyl]-4-hydroxy-2,3-diisopropoxy-2-cyclobuten-1-one (31). The addition of **2** [from 0.26 g (1.08 mmol) of the bromide] in dry THF (6 mL) to **27** (0.21 g, 1.06 mmol) dissolved in THF (6 mL) at −78 °C followed by chromatography on silica gel (elution with dichloromethane/ ethyl acetate 5:1) provided 0.23 g (61%) of **31** as a yellow oil: IR (film, cm^{-1}) 1769, 1633, 1316, 1099; ^{1}H NMR (300 MHz, C_6D_6) δ 8.02 (br s, 1 H), 7.18−7.10 (m, 2 H), 7.09−6.99 (m, 3 H), 5.30 (br s, 1 H), 4.94 (heptet, J = 6.1 Hz, 1 H), 4.90 (br s, 1 H), 4.74 (heptet, J = 6.1 Hz, 1 H), 3.60 (d, J = 12.3 Hz, 1 H), 3.30 (d, J = 12.7 Hz, 1 H), 3.20 (d, J = 12.7 Hz, 1 H), 2.85 (d, J = 12.3 Hz, 1 H), 1.84 (s, 3 H), 1.19−1.06 (m, 12 H); ^{13}C NMR (75 MHz, C_6D_6) 185.6, 164.9, 142.8, 137.4, 132.8, 129.2, 128.3, 127.2, 115.0, 89.8, 75.9, 73.0, 63.1, 61.1, 40.3, 22.5, 22.4, 22.1, 21.9 ppm; MS m/z (M$^+$) calcd 359.2104, obsd 359.2100.

Reaction of Anion 19 with 31. Dropwise addition at −78 °C of a solution of **19** [from 0.21 g (1.11 mmol) of the bromide] in dry THF (5 mL) to **31** (0.13 g, 0.36 mmol) dissolved in the same medium (4 mL) at −78 °C followed by stirring at 20 °C for 17 h, the usual workup, and chromatography on silica gel delivered 62 mg (39%) of **28**.

(−)-(3a*R*,6*R*,7*S*,7a*R*,8a*S*)-8a-[(Benzylmethylamino)-methyl]-5,6,7,7a,8,8a-hexahydro-3a-hydroxy-2,3-diisopropoxy-6,7-(isopropylidenedioxy)cyclopent[*a*]inden-1(3a*H*)-one (33). The analogous protocol involving **2** [from 0.28 g (1.17 mmol) of the bromide] in dry THF (6 mL) and (+)-**32** (0.15 g, 0.39 mmol) dissolved in THF (2 mL) led to the isolation of 86 mg (43%) of (−)-**33** as a pale yellow oil following chromatography on silica gel (elution with dichloromethane/ ethyl acetate 100:1): IR (film, cm^{-1}) 1693, 1609, 1379, 1301, 1062; ^{1}H NMR (300 MHz, C_6D_6) δ 7.11−6.97 (m, 6 H), 6.29−6.25 (m, 1 H), 5.40 (heptet, J = 6.1 Hz, 1 H), 5.20 (heptet, J = 6.1 Hz, 1 H), 3.99 (q, J = 5.7 Hz, 1 H), 3.77 (t, J = 5.1 Hz, 1 H), 3.45 (d, J = 13.0 Hz, 1 H), 3.13−3.07 (m, 2 H), 2.71−2.56 (m, 3 H) 2.40−2.36 (m, 2 H), 1.90 (s, 3 H), 1.39 (s, 3 H), 1.28 (s, 3 H), 1.22 (d, J = 6.1 Hz, 3 H), 1.17−1.13 (m, 1 H), 1.12 (d, J = 6.1 Hz, 3 H), 1.06 (d, J = 6.1 Hz, 3 H), 1.04 (d, J = 6.1 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) 200.9, 169.6, 142.0, 138.0, 133.7, 129.2, 128.6, 127.6, 119.3, 107.7, 82.5, 79.6, 73.6, 72.6, 71.8, 62.8, 62.6, 56.3, 42.1, 41.6, 39.5, 29.0, 28.5, 26.0, 22.8, 22.7, 22.6, 22.5 ppm; MS m/z (M$^+$) calcd 511.2933, obsd 511.2946; [α] −172.17 (c 0.51, C_6H_6). Anal. Calcd for $C_{30}H_{41}NO_6$: C, 70.42; H, 8.08. Found: C, 70.32; H, 8.04.

(3a*R,7a*R**,8a*S**)-8a-[(Benzylmethylamino)methyl]-5,6,7,7a,8,8a-hexahydro-3a-hydroxy-2,3-(trimethylenedioxy)cyclopent[*a*]inden-1(3a*H*)-one (35) and (3a*R**,-5a*S**,9*S**,9a*S**)-3a,4,5,5a,6,7,8,9-Octahydro-3a-hydroxy-9-methoxy-4-methylene-1,1-(trimethylenedioxy)-3*H*-cyclopent[*c*]inden-3-one (36). A. By Sequential Addition of Anions 19 and 2.** A cold (−78 °C), magnetically stirred solution of **34** (0.20 g, 1.29 mmol) in dry THF (7 mL) was treated sequentially with THF solutions of **19** [from 0.30 g (1.57 mmol) of the bromide] and **2** [from 0.48 g (2.00 mmol) of the bromide]. The reaction mixture was stirred at room temperature for 21 h and processed in the usual way. The dark residue was subjected to flash chromatography on silica gel (elution with hexanes/ethyl acetate 1:1) to give 150 mg (23%) of **35** and 32 mg (8%) of **36**, both as yellow oils.

For **35**: IR (film, cm^{-1}) 1706, 1626, 1268, 1077; ^{1}H NMR (300 MHz, C_6D_6) δ 7.20−7.00 (m, 5 H), 6.42−6.41 (m, 1 H), 3.91−3.76 (m, 2 H), 3.69−3.59 (m, 1 H), 3.55−3.42 (m, 2 H), 3.16 (d, J = 12.6 Hz, 1 H), 3.12 (d, J = 12.9 Hz, 1 H), 2.72 (d, J = 12.9 Hz, 1 H), 2.33−2.26 (m, 1 H), 2.21−2.12 (m, 1 H), 2.08−1.99 (m, 2 H), 1.94 (s, 3 H), 1.89−1.75 (m, 1 H), 1.59−1.55 (m, 1 H), 1.52−1.37 (m, 2 H), 1.36−1.22 (m, 2 H), 1.02−0.90 (m, 2 H); ^{13}C NMR (75 MHz, C_6D_6) 199.4, 164.7, 143.3, 138.0, 136.3, 128.8, 128.4, 127.2, 121.4, 82.5, 73.0, 71.0, 62.9, 61.9, 56.9, 41.9, 41.8, 34.9, 32.2, 28.9, 25.0, 22.0 ppm; MS m/z (M$^+$) 395.2122, obsd 395.2109.

For **36**: IR (film, cm^{-1}) 3498, 1719, 1633, 1273, 1102; ^{1}H NMR (300 MHz, C_6D_6) δ 5.84 (d, J = 2.6 Hz, 1 H), 5.12 (d, J = 2.6 Hz, 1 H), 3.77−3.64 (m, 2 H), 3.61−3.53 (m, 1 H), 3.41−3.35 (m, 2 H), 2.92 (s, 3 H), 2.42−2.33 (m, 1 H), 2.05−1.97 (m, 1 H), 1.94−1.71 (m, 4 H), 1.65−1.58 (m, 1 H), 1.56−1.48 (m, 2 H), 1.46−1.24 (m, 2 H), 1.10−0.95 (m, 1 H); ^{13}C NMR (75 MHz, C_6D_6) 195.6, 161.8, 149.7, 135.6, 112.9, 84.6, 79.5, 72.7, 70.9, 60.0, 57.2, 37.7, 36.7, 32.0, 28.2, 27.2, 22.5 ppm; MS m/z (M$^+$) calcd 306.1475, obsd 306.1471.

B. By Sequential Addition of Anions 2 and 19. Adaptation of the above procedure to 0.45 g (2.92 mmol) of **34**, followed by **2** [from 0.77 g (3.22 mmol) of the bromide] and **19** [from 0.86 g (4.52 mmol) of the bromide] led to the isolation of 0.55 g (48%) of **35** and 0.16 g (18%) of **36**.

(*R)-4-[(*S**)-6-(Benzylmethylamino)-1-cyclohexen-1-yl]-4-(*tert*-butyldimethylsiloxy)-2,3-diisopropoxy-2-cyclobuten-1-one (38b) and (*R**)-4-[(*R**)-6-(Benzylmethylamino)-1-cyclohexen-1-yl]-4-(*tert*-butyldimethyl-siloxy)-2,3-diisopropoxy-2-cyclobuten-1-one (39b).** A cold (−78 °C), magnetically stirred solution of **27** (1.50 g, 7.58 mmol) in dry THF (40 mL) was treated with **37** [prepared from 2.09 g (7.46 mmol) of the bromide], stirred at this temperature for 1 h, quenched with water (20 mL), and extracted with ether (2 × 50 mL). After the usual processing, flash chromatography on silica gel (elution with hexanes/ethyl acetate 10:1) led to the isolation in 75% yield of a 1:1.8 mixture of **38a** and **38b**.

A 2.29 g (5.74 mmol) sample of this mixture was dissolved in DMF (15 mL), treated with *tert*-butyldimethylsilyl chloride (1.73 g, 11.5 mmol) and imidazole (1.56 g, 22.9 mmol), and stirred for 18 h. Water (20 mL) was introduced and the products were extracted into ether (2 × 50 mL), washed with water (50 mL) and brine (50 mL), dried, and evaporated. The residue was subjected to flash chromatography on silica gel (elution with hexanes/ethyl acetate 50:1) to give 0.85 g (29%) of **38b** and 1.38 g (47%) of **39b**, both as yellow oils.

For **38b**: IR (film, cm^{-1}) 1769, 1614, 1383, 1101; ^{1}H NMR (300 MHz,

C_6D_6) δ 7.48−7.46 (m, 2 H), 7.27−7.22 (m, 2 H), 7.14−7.10 (m, 1 H), 6.63 (dt, J = 3.8, 0.9 Hz, 1 H), 5.09 (heptet, J = 6.1 Hz, 1 H), 4.72 (heptet, J = 6.1 Hz, 1 H), 3.67 (d, J = 13.0 Hz, 1 H), 3.57 (d, J = 13.0 Hz, 1 H), 3.37−3.36 (m, 1 H), 2.14 (s, 3 H), 1.97−1.87 (m, 3 H), 1.49−1.29 (m, 3 H), 1.25 (d, J = 6.1 Hz, 3 H), 1.15 (d, J = 6.1 Hz, 3 H), 1.09 (d, J = 6.1 Hz, 3 H), 1.05 (s, 9 H), 1.04 (d, J = 6.1 Hz, 3 H), 0.39 (s, 3 H), 0.32 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) 183.1, 163.4, 139.6, 135.0, 133.7, 130.3, 129.3, 128.0, 126.6, 90.3, 75.1, 72.8, 59.6, 56.6, 36.5, 26.0, 25.2, 22.9, 22.6, 22.3, 22.1, 21.5, 20.4, 18.5, −3.1, −3.4 ppm; MS m/z (M$^+$) calcd 513.3220, obsd 513.3247.

For **39b**: IR (film, cm^{-1}) 1768, 1613, 1321, 1099; ^{1}H NMR (300 MHz, C_6D_6) δ 7.44−7.41 (m, 2 H), 7.24−7.18 (m, 2 H), 7.14−7.09 (m, 1 H), 6.59 (dt, J = 3.8, 1.1 Hz, 1 H), 5.05 (heptet, J = 6.1 Hz, 1 H), 4.93 (heptet, J = 6.1 Hz, 1 H), 3.63 (br s, 1 H), 3.56 (d, J = 12.5 Hz, 1 H), 3.43 (d, J = 12.5 Hz, I H), 2.03

(s, 3 H), 1.99−1.91 (m, 2 H), 1.89−1.81 (m, 1 H), 1.53−1.29 (m, 3 H), 1.25 (d, J = 6.1 Hz, 3 H), 1.18 (d, J = 6.1 Hz, 3 H), 1.13 (d, J = 6.1 Hz, 3 H), 1.03 (s, 9 H), 0.96 (d, J = 6.1 Hz, 3 H), 0.35 (s, 3 H), 0.33 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) 183.8, 167.3, 140.1, 135.2, 132.1, 130.9, 129.6, 127.8, 126.6, 89.2, 75.4, 72.7, 60.0, 58.2, 36.0, 25.9, 25.2, 22.9, 22.7, 22.1, 21.7, 21.6, 20.3, 18.4, −3.2, −3.4 ppm; MS *m*/*z* calcd 513.3220, obsd 513.3262.

(*R)-4-[(*S**)-6-(Benzylmethylamino)-1-cyclohexen-1-yl]-4-hydroxy-2,3-diisopropoxy-2-cyclobuten-1-one (38a).** A 100 mL flask was charged with silyl ether **38b** (0.94 g, 1.83 mmol) and THF (20 mL). Tetrabutylammonium fluoride (3.8 mL, 1 M in THF, 3.80 mmol) was added at 0 °C, and the mixture was stirred at room temperature for 30 min. Water (10 mL) was introduced, the mixture was extracted with ether (2 × 20 mL), and the combined organic layers were washed with water (20 mL) and brine (20 mL) and then concentrated. Purification by flash chromatography on silica gel (elution with hexanes/EtOAc 6:1) gave **38a** as a yellow oil (0.53 g, 73%): IR (film, cm^{-1}) 3452, 1766, 1454, 1103; ^{1}H NMR (300 MHz, C_6D_6) δ 9.06 (br s, 1 H), 7.41−7.39 (m, 2 H), 7.15−7.10 (m, 2 H), 7.07−7.02 (m, 1 H), 6.12 (dt, J = 4.2, 1.6 Hz, 1 H), 5.02 (heptet, J = 6.1 Hz, 1 H), 4.74 (heptet, J = 6.1 Hz, 1 H), 3.74 (br s, 1 H), 3.66 (br s, 1 H), 3.22−3.18 (m, 1 H), 2.08 (s, 3 H), 2.03−1.68 (m, 2 H), 1.58−1.49 (m, 1 H), 1.42−1.20 (m, 3 H), 1.16 (d, J = 6.1 Hz, 3 H), 1.14 (d, J = 6.1 Hz, 3 H), 1.12 (d, J = 6.1 Hz, 3 H), 1.08 (d, J = 6.1 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) 185.4, 165.4, 138.2, 135.1, 134.0, 129.5, 128.5, 128.4, 127.2, 90.2, 75.8, 72.8, 60.1, 57.9, 36.2, 25.1, 22.6, 22.4, 22.1, 22.0, 20.7, 19.8 ppm; MS *m*/*z* (M^+) calcd 399.2441, obsd 399.2405. Anal. Calcd for $C_{24}H_{33}NO_4$: C, 72.15; H, 8.33. Found: C, 72.00; H, 8.21.

(*R)-4-[(*R**)-6-(Benzylmethylamino)-1-cyclohexen-1-yl]-4-hydroxy-2,3-diisopropoxy-2-cyclobuten-1-one (39a).** A 100 mL flask was charged with silyl ether **39b** (1.33 g, 2.59 mmol) and THF (25 mL). Tetrabutylammonium fluoride (5.2 mL, 1 M in THF, 5.20 mmol) was added at 0 °C, and the mixture was stirred at room temperature for 30 min. Water (10 mL) was introduced, the mixture was extracted with ether (2 × 20 mL), and the combined organic layers were washed with water (20 mL) and brine (20 mL), dried, and concentrated. Purification by flash chromatography on silica gel (elution with hexanes/EtOAc 6:1) gave **39a** as a yellow oil (0.80 g, 78%); IR (film, cm^{-1}) 3464, 1766, 1454, 1098; ^{1}H NMR (300 MHz, C_6D_6) δ 9.13 (br s, 1 H), 7.33−7.31 (m, 2 H), 7.14−7.02 (m, 3 H), 6.17 (dt, J = 3.9, 1.5 Hz, 1 H), 5.00 (heptet, J = 6.1 Hz, 1 H), 4.82 (heptet, J = 6.1 Hz, 1 H), 4.07 (br s, 1 H), 3.52 (br s, 1 H), 3.34 (br s, 1 H), 1.90 (s, 3 H), 1.88−1.80 (m, 1 H), 1.73−1.57 (m, 2 H), 1.43−1.20 (m, 3 H), 1.17 (d, J = 6.1 Hz, 3 H), 1.14 (d, J = 6.1 Hz, 3 H), 1.12 (d, J = 6.1 Hz, 3 H), 1.10 (d, J = 6.1 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) 186.9, 164.9, 138.2, 134.2, 132.6, 129.2, 128.4, 127.9, 127.7, 90.7, 75.7, 72.8, 59.8, 57.8, 35.9, 24.7, 22.6, 22.5, 22.2, 21.9, 20.1, 19.9 ppm; MS *m*/*z* (M^+) calcd 399.2441, obsd 399.2425. Anal. Calcd for $C_{24}H_{33}NO_4$: C, 72.15; H, 8.33. Found: C, 72.00; H, 8.27.

(4*R,4a*R**,8a*R**)-4a,5,6,7,8,8a-Hexahydro-2′,3′-diisopropoxy-1-methylspiro[4*H*-3,1-benzoxazine-4,1′-[2]cyclobutene]-2,4′(1*H*)-dione (41).** A mixture of **39a** (0.16 g, 0.40 mmol) and palladium(II) hydroxide (5 mg) in methanol (5 mL) was stirred under 1 atm of hydrogen at room temperature for 12 h, filtered, and concentrated. The residue was dissolved in dry THF (5 mL), treated with 1,1′-carbonyldiimidazole, refluxed for 12 h, and concentrated. Flash chromatography of the residue on silica gel (elution with hexanes/ethyl acetate 1:2) afforded 43 mg (30% overall) of **41** as a white solid: mp 112−114 °C;^{1}H NMR (300 MHz, C_6D_6) δ 4.88 (heptet, J = 6.1 Hz, 1 H), 4.63 (heptet, J = 6.1 Hz, 1 H), 3.37 (dt, J = 11.0, 3.6 Hz, 1 H), 2.72 (s, 3 H), 1.77−1.72 (m, 1 H), 1.70−1.63 (m, I H), 1.59−1.49 (m, 1 H), 1.39−1.25 (m, 2 H), 1.16−1.09 (m, 1 H), 1.07 (d, J = 6.1 Hz, 3 H), 1.05 (d, J = 6.1 Hz, 3 H), 1.04 (d, J = 6.1 Hz, 3 H), 1.01 (d, J = 6.1 Hz, 3 H), 0.92−0.75 (m, 2 H), 0.57−0.48 (m, 1 H); ^{13}C NMR (75 MHz, C_6D_6) 181.2, 161.4, 152.5, 134.7, 92.1, 77.0, 74.0, 56.8, 39.7, 31.6, 30.7, 26.1, 24.7, 24.0, 22.6, 22.5, 22.2, 22.0. Anal. Calcd for $C_{18}H_{17}NO_5$: C, 64.06; H, 8.07. Found: C, 63.98; H, 8.14.

(3a*R,6a*S**,6b*S**,10b*R**)-5,6,6a,6b,7,8,9,10b-Octahydro-10b-hydroxy-1,2-diisopropoxydicyclopent[*a*,*b*]inden-3(4*H*)-one (42) and (3a*R**,6a*S**,6b*S**,10b*R**)-5,6,6a,6b,7,8,9,-10b-Octahydro-10b-hydroxy-2,3-diisopropoxydicyclopent[*a*,*b*]inden-1(4*H*)-one (43). A. From 38a.** *tert*-Butyllithium (3.2 mL of 1.7 M in pentane, 5.44 mmol) was added dropwise at −78 °C to a solution of 1-iodocyclopentene (0.46 g, 2.37 mmol) in dry THF (12 mL), stirred for 1 h in the cold, treated with 0.26 g (0.65 mmol of **38a** dissolved in dry THF (7 mL), and stirred at room temperature for 19 h. The usual workup and chromatographic purification (elution with hexanes/ethyl actate 10:1) furnished 45 mg (20%) of **42** and 36 mg (16%) of **43**, both as white solids.

B. From 39a. *tert*-Butyllithium (7.8 mL of 1.7 M in pentane, 13.3 mmol) was added dropwise at −78 °C to a solution of 1-iodocyclopentene (1.15 g, 5.92 mmol) in dry THF (30 mL), stirred for 1 h in the cold, treated with 0.75 g (1.87 mol) of **39a** dissolved in THF (20 mL), and stirred at room temperature for 16 h. The usual workup and chromatographic purification (elution with hexanes/ethyl acetate 10:1) gave 39 mg (6%) of **42** and 180 mg (28%) of **43**.

For **42**: mp 88−90 °C; IR (film, cm^{-1}) 3428, 1693, 1613, 1380, 1100; ^{1}H NMR (300 MHz, C_6D_6) δ 6.12−6.09 (m, 1 H), 5.33 (heptet, J = 6.0 Hz, 1 H), 5.29 (heptet, J = 6.0 Hz, 1 H), 2.51−2.44 (m, 1 H), 2.30−2.16 (m, 2 H), 2.08 (s, 1 H), 1.99−1.69 (m, 7 H), 1.55−1.46 (m, 2 H), 1.37−1.18 (m, 1 H), 1.16 (d, J = 6.0 Hz, 3 H), 1.13 (d, J = 6.0 Hz, 3 H), 1.11 (d, J = 6.0 Hz, 3 H), 1.08 (d, J = 6.0 Hz, 3 H), 0.93−0.81 (m, 1 H); ^{13}CNMR (75 MHz, C_6D_6) 202.6, 165.6, 147.3, 129.5, 120.0, 80.3, 73.4, 71.1, 66.4, 53.7,46.0, 32.4, 31.8, 28.6, 27.0, 24.7, 22.6 (2 C), 22.3, 22.2, 21.9 ppm; MS *m*/*z* (M^+) calcd 346.2144, obsd 346.2144. Anal. Calcd for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73. Found: C, 72.65; H, 8.83.

For **43**: mp 134−136 °C; IR (film, cm^{-1}) 3363, 1694, 1613, 1380, 1103; ^{1}H NMR (300 MHz, C_6D_6) δ 6.14−6.11 (m, 1 H), 5.29 (heptet, J = 6.1 Hz,1 H), 5.23 (heptet, J = 6.1 Hz, 1 H), 3.96 (s, 1 H), 2.45−2.37 (m, 2 H), 2.09−2.03 (m, 1 H), 1.94−1.81 (m, 3 H), 1.79−1.61 (m, 4 H), 1.54−1.48 (m, 2 H), 1.35−1.14 (m, 1 H), 1.10 (d, J = 6.1 Hz, 3 H), 1.06 (d, J = 6.1 Hz, 3 H), 1.04 (d, J = 6.1 Hz, 3 H), 1.03 (d, J = 6.1 Hz, 3 H), 0.98−0.89 (m, 1 H); ^{13}C NMR (75 MHz, C_6D_6) 198.3, 171.5, 145.3, 128.3, 120.7, 81.9, 73.2, 71.1, 63.1, 54.3, 47.0, 33.0, 31.2, 29.7, 27.3, 24.9, 22.7, 22.6, 22.5, 22.4 (2 C) ppm; MS *mlz* (M^+) calcd 346.2144, obsd 346.2137. Anal. Calcd for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73. Found: C, 72.67; H, 8.65.

(3a*R,7a*R**,8a*R**)-5,6,7,7a,8,8a-Hexahydro-3a-hydroxy-2,3-diisopropoxy-8a-methylcyclopent[*a*]inden-1(3a*H*)-one (44) and (3a*R**,7a*R**,8a*R**)-5,6,6,7,7a,8,8a-Hexahydro-3a-hydroxy-1,2-diisopropoxy-8a-methylcyclopent[*a*]inden-3(3a*H*)-one (45). A. From 38a.** 2-Propenyllithium [prepared from 0.38 g (3.14 mmol) of the bromide] in dry THF (14 mL) was added dropwise at −78 °C to solution of **38a** (0.36, 0.90 mmol) in THF (19 mL). After being stirred at room temperature for 12 h, the predescribed workup led to the isolation of **44** and **45** in a 2.9:1 ratio (^{1}H NMR analysis) in 62% yield: IR (film, cm^{-1}) 3435, 1692, 1613, 1380, 1106; ^{1}H NMR (300 MHz, C_6D_6) δ [6.21−6.19 (m, minor isomer), 5.91−5.89 (m, major isomer), total 1 H], 5.30 (heptet, J = 6.1 Hz, 1 H), 5.23 (heptet, J = 6.1 Hz, I H), [2.77 (br s, major isomer), 2.69 (br s, minor isomer), total 1 H], 2.44−2.38 (m, 1 H), 2.17−1.93 (m, 1 H), 1.91−1.72 (m, 2 H), 1.71−1.64 (m, 1 H), 1.53−1.48 (m, 1 H), [1.41 (s, minor isomer), 1.29 (s, major isomer), total 3 H], 1.26−1.07 (m, 12 H), 1.06−0.78 (m, 3 H); ^{13}C NMR (75 MHz, C_6D_6) [(major isomer **44**: 202.8, 166.0, 145.8, 132.0, 121.3, 81.4, 73.4, 71.8, 55.7, 41.5, 35.9, 28.9, 25.3, 22.9, 22.8, 22.6, 22.5, 22.3, 19.4 ppm) (minor isomer **45**: 202.8, 166.2, 146.3, 129.1, 121.6, 80.7, 73.6, 71.5, 54.4, 43.2, 39.7, 29.1, 25.1, 22.9, 22.8, 22.6, 22.5, 22.1, 18.1 ppm)]; MS *mlz* (M^+) calcd 320.1961, obsd 320.1974.

B. From 39a. Comparable addition of 2-propenyllithium [prepared from 0.56 g (4.62 mmol) of the bromide] to **39a** (0.59 g, 1.47 mmol) furnished a 1.1:1 mixture of **44** and **45** in 73% yield.

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Supporting Information Available: ORTEP drawings for **10**·HCl, **41**, and **43.** Crystallographic experimental details, tables of X-ray crystal data, bond lengths and angles, bond lengths involving the hydrogen atoms, positional parameters and *B*(eq) values, anisotropic displacement parameters, and positional parameters for the hydrogen atoms of **10**•HCl**.** Tables giving the crystal data and structure refinement information, bond lengths and bond angles, atomic and hydrogen coordinates, and isotropic and anisotropic displacement coordinates for **41** and **43** (33 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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