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Reaction Cascades Based on Squarate Esters. 1,3-Dioxolane as a Chaperone Functional Group for Lithium Ions

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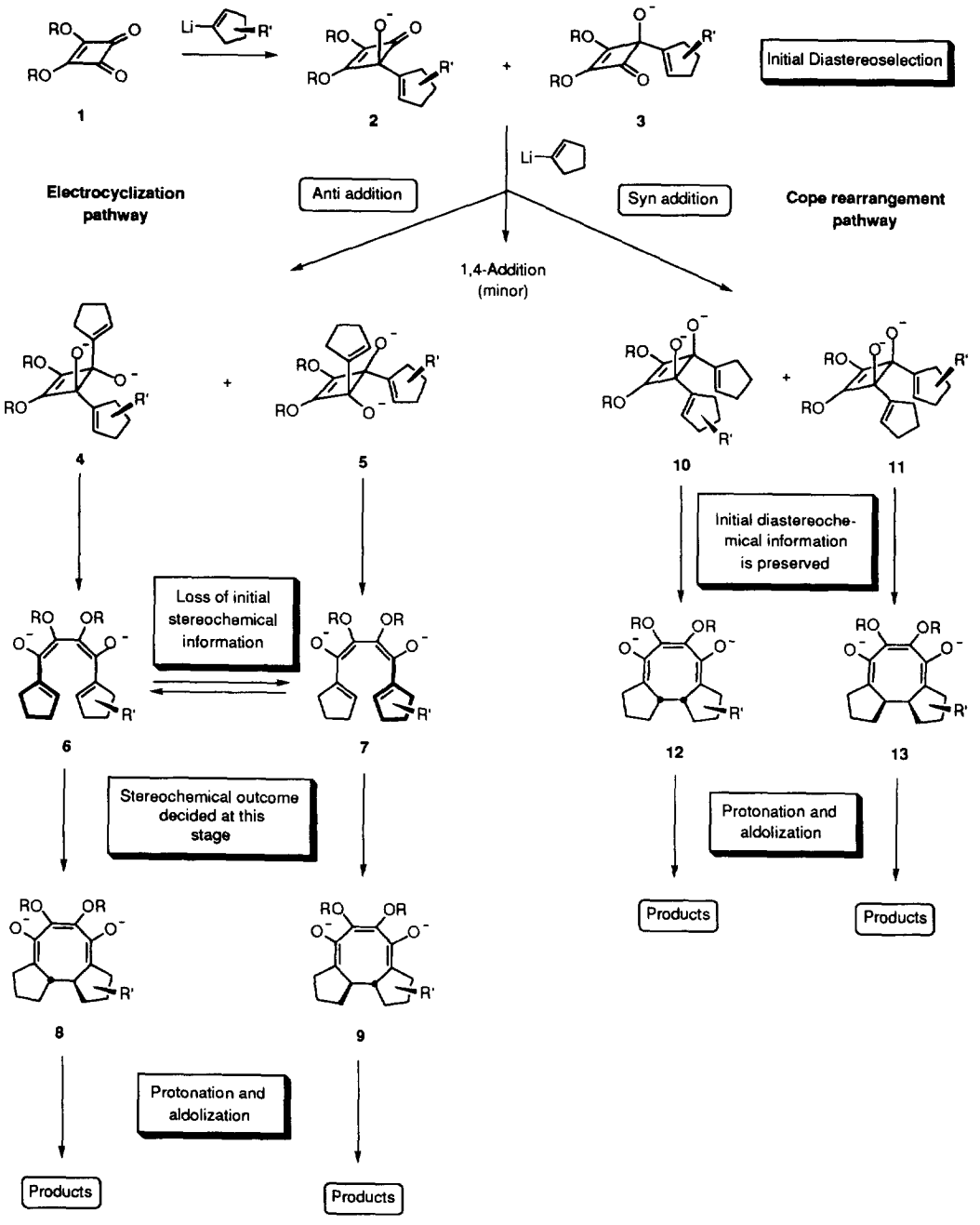
Abstract: The consequences of adding enantiomerically pure 1-lithiocyclohexene-5,6-diol acetonide and 1-cyclopentenyllithium seriatim to diisopropyl squarate has been studied. The first-stage addition leads to a chromatographically separable mixture of diastereomeric keto alcohols, which are formed in a ratio approximating 1:1. Separate reaction of these intermediates with the second cycloalkenyl anion initiates a cascade of chemical steps. The consequences of the second-stage stereoselectivity are profound in dictating the manner in which the polycyclic end products are formed.

From the standpoint of synthetic utility, those cascade reactions initiated by the twofold addition of alkenyllithiums to squarate esters (**1**) constitute exceptionally versatile bond reorganization processes for the single-step elaboration of structurally complex polycyclic systems.[1-4] The permutation consisting of the sequential addition of an alkenyl and an acetylide anion has introduced added versatility.[5] Also, the initially formed products have proven quite amenable to further chemical modification.[6]

Although the second-stage addition to **2** and **3** can in principle occur in both syn and anti fashion, the formation of **4** and **5** is customarily preferred to an overwhelming extent (Scheme 1). This kinetically favored option has been attributed to steric control. An especially salient feature associated with arrival at these trans dialkoxides is that an electrocyclic reaction channel is thereby accessed. Thus, conrotatory opening of **4** and **5** occurs spontaneously at low temperatures to deliver the helical octatetraenes **6** and **7**. The ability of these intermediates to interconvert rapidly removes all of the several stereochemical markers originally introduced except at the stereogenic center substituted by R. As a consequence, product stereochemistry is dictated uniquely by the relative rates at which **6** and **7** undergo ring closure, a process which can strongly favor **7** depending on the exact position of the R substituent.[7] The capacity for controlling the site of protonation and subsequent aldolization within **8** and **9** has been successfully demonstrated.[8]

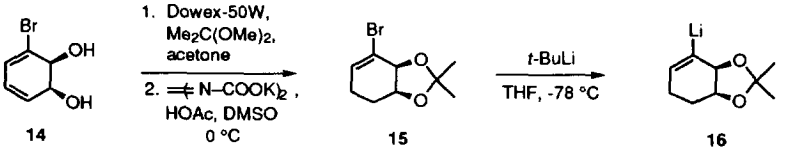
Should the second alkenyl anion add to **2** and **3** from the syn direction, dianionic oxy-Cope rearrangement[9-12] is immediately triggered with relief of charge repulsion and release of ring strain. With anticipated adoption of a boatlike transition state,[13-14] chirality transfer is made highly effective with resultant specific formation of **12** and **13**. The origin of these tricyclooctatrienes is unmistakably revealed by the cis nature of the ring fusion across the bottom. In contrast to the electrocyclization pathway, progress along the oxy-Cope trajectory guarantees that the stereochemical features which distinguish **2** from **3** will be fully translated via **10** and **11** into **12** and **13** without any anticipated loss of fidelity.

Scheme 1


Initial Diastereoselection
Electrocyclization pathway
Anti addition
Syn addition
Cope rearrangement pathway
1,4-Addition (minor)
Initial diastereochemical information is preserved
Loss of initial stereochemical information
Stereochemical outcome decided at this stage
Protonation and aldolization
Protonation and aldolization
Products
Products
Products
Products

In order to realize confirmation of the latter prediction, we initiated a search for means by which syn addition could be fostered by engineered coordination to lithium ions. Reported herein is our first success in this direction. The key reagent is the enantiomerically pure cyclohexenyllithium **16**, which has been previously prepared in these laboratories[15] by short exposure of (+)-*cis*-(2*S*,3*S*)-bromobenzene dihydrodiol[16] to Dowex-50W and 2,2-dimethoxypropane,[17] followed by diimide reduction[18] and lithiation (Scheme 2). The conceptual tactic underlying this selection was an anticipated ability on the part of one or both oxygens derived from **16** to anchor the second alkenyl anion in at least one of the diastereomeric monoadducts.

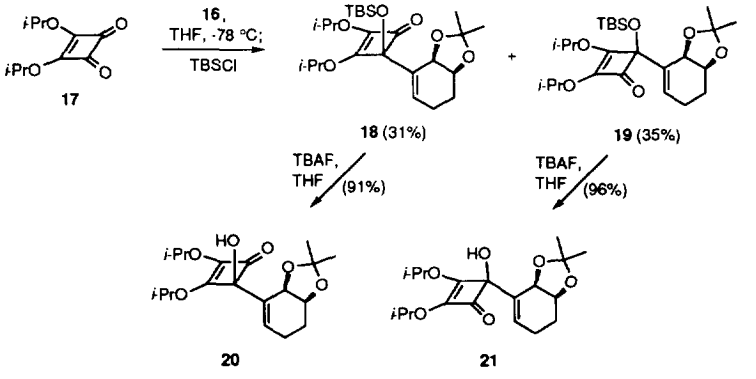
Scheme 2



RESULTS AND DISCUSSION

Following treatment of **15** with two equiv of *tert*-butyllithium in THF at -78 °C to generate **16**, diisopropyl squarate (**17**) was introduced and monoaddition was allowed to proceed at this temperature for 2.5 h. When workup was preceded by exposure of the reaction mixture to *tert*-butyldimethylsilyl chloride, it proved possible to separate diastereomer **18** (35%) cleanly from **19** (31%) by chromatography on silica gel (Scheme 3). The co-production of these oily substances in approximately equal amounts was fully anticipated on the basis of the near-planarity of **17**, its small size, and the many rotational orientations available to the two reactants during nucleophilic addition. Whereas **18** proved to be dextrorotatory, **19** rotated plane-polarized light to about the same level in the levorotatory direction.

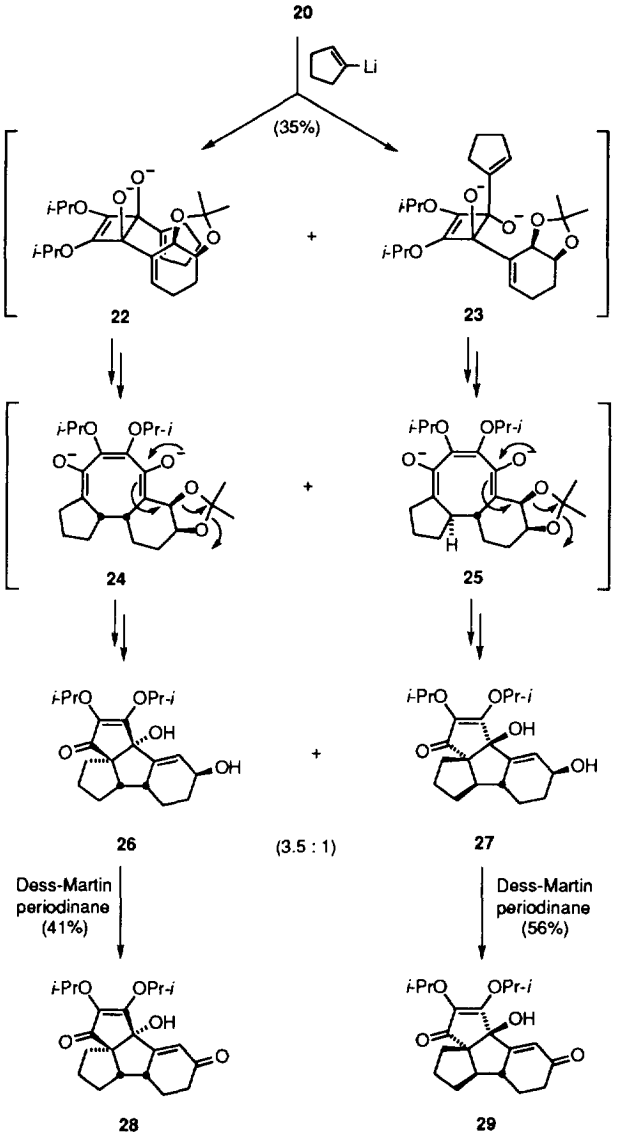
Scheme 3



Unequivocal structural distinction between **18** and **19** was not possible by the usual spectroscopic methods and was therefore deferred to a later stage of the investigation. Both coupling products were readily deprotected to give **20** and **21**, respectively, when treated with tetra-*n*-butylammonium fluoride in THF. Each of the two pure hydroxy ketones was found to be dextrorotatory.

Subjection of **20** to the action of 3 equiv of cyclopentenyllithium in THF initiated both available cascade rearrangements and provided a 3.5:1 mixture of **26** and **27** in a combined yield of 35% (Scheme 4). Diol **26** is a highly crystalline substance and consequently its direct crystallization from the mixture was possible. On the strength of its X-ray crystallographic analysis (Figure 1), this tetracycle clearly emerges as the end product of a dianionic oxy-Cope sequence.

Scheme 4



The specific structural alignment depicted in **22** can be expected to result in highly effective chirality transfer with resultant specific formation of dienolate **24**. Specific attention is drawn to the requirement that

the hydrogen atom positioned on each of the two new stereogenic centers both be fixed syn to the dioxolane ring. At this point, regiocontrolled β-elimination with fragmentation of the acetonide unit delivers a cyclohexenol substructure. Of course, the absolute configuration of its carbinol center continues to have a well defined relationship to the tertiary methine sites. Importantly, the elimination step guarantees that the ensuing transannular aldol cyclization is completely regiocontrolled. Further, the cis relationship of the methine centers sets the conformation of the eight-membered ring such that a single product geometry is feasible on energetic grounds.

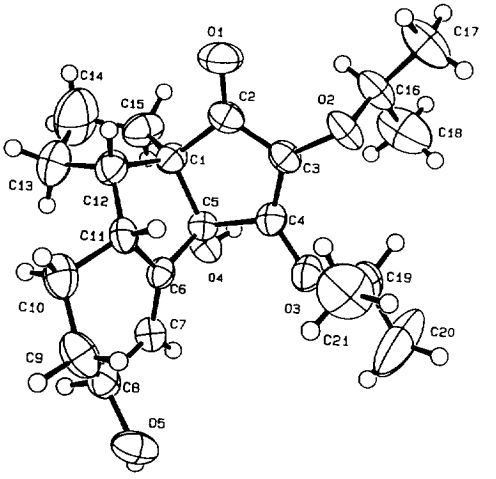
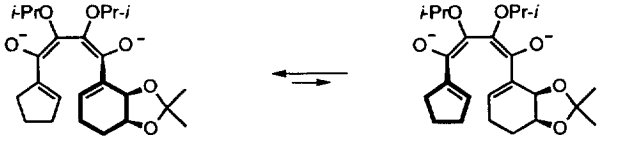


Figure 1. ORTEP drawing of **26**. The non-hydrogen atoms are represented by 50% probability thermal ellipsoids. The hydrogen atoms are drawn with an artificial radius.

Operation of the more customary trans addition to generate **23** initiates electrocyclic ring opening followed by 8π conrotatory cyclization with formation of the trans-fused bis enolate **25**. Since **27** is the only product ultimately produced from this pathway, the implication can be drawn that the helical dialkoxide **30** experiences cyclization appreciably faster than **31**.[7] Obviously, the conversion of **30** to **25** offers less steric congestion than the diastereomeric option where the dioxolane ring is necessarily positioned on the interior of the helix. As before, β-elimination/fragmentation within **25** has two direct consequences: regiocontrolled aldolization and formation of the lone tetracyclic product **27**.



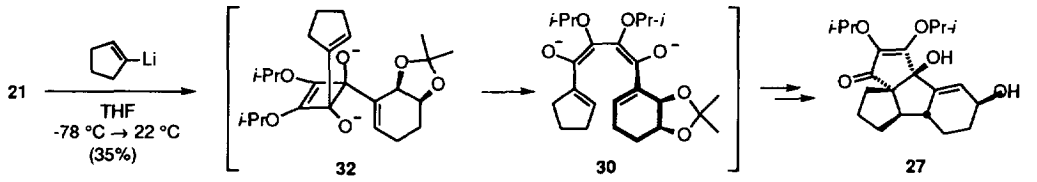
30 **31**

Although the spectral properties of **27** are fully consistent with the assigned structural formula, **26** and **27** were both subjected to oxidation with the Dess-Martin periodinane reagent[19] in order to remove the stereogenicity at the hydroxyl-substituted site and allow direct comparison of the stereochemical

interrelationship of the triquinane networks. As expected, **28** is diastereomerically and not enantiomerically related to **29**.

When **21** was comparably treated with excess cyclopentenyllithium, only **27** was isolated in 35% yield (Scheme 5). These findings indicate that trans addition to deliver **32** operates to the exclusion of cis addition in this instance. Since this is the normal consequence of the double addition of alkenyllithiums to squarate esters,[1-8] the focus of attention necessarily shifts to **20** as the exception.

Scheme 5



Comparison of the potential chelating arrangements available to **20** and **21** reveal subtle but important differences. The geometric attributes of **20** for potential intermolecular coordination to cyclopentenyllithium are depicted in Figure 2. In this system, the unsaturated six-membered ring protrudes well beyond the immediate steric confines of the oxygenated cyclobutenone and offers no contestable nonbonded interactions. More importantly, the lone pair orbitals from the ether oxygen can become comfortably aligned for complexation to cyclopentenyllithium as in **A**. For formal cis addition to occur, the nucleophile need migrate only a short distance across the bottom face of the complex.

The spatial projection of the nonbonded electrons in **21** bear little semblance to that available within **20**. As illustrated in **B**, the carbonyl group is now rotated approximately 90°, such that a suitable binding pocket for lithium ion is generatable only from above. Under these circumstances, the likelihood that anti attack will prevail would appear to be very high, as the cyclohexenyl group also very effectively shields the carbonyl from syn addition.

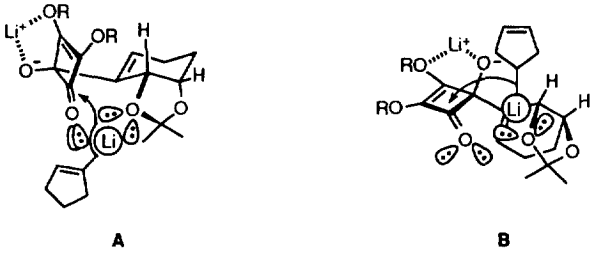


Figure 2. Conformational alignments available to **20** and **21** showing the different nonbonded electron pair alignments of the carbonyl and chaperone acetonide oxygens.

EXPERIMENTAL SECTION

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

(4S)-4-(tert-Butyldimethylsiloxy)-2,3-diisopropoxy-4-[(3aR,7aS)-3a,6,7,7a-tetrahydro-2,2-dimethyl-1, 3-benzodioxol-4-yl]-2-cyclobuten-1-one (18) and (4R)-4-(tert-Butyldimethylsiloxy)-2,3-diisopropoxy-4-[(3aR,7aS)-3a,6,7,7a-tetrahydro-2,2-dimethyl-1,3-benzodioxol-4-yl]-2-cyclobuten-1-one (19). A 100 mL flask was charged with vinyl bromide **15**[15] (0.69 g, 2.98 mmol) and anhydrous THF (15 mL). *tert*-Butyllithium (3.9 mL of 1.7 M in pentane, 6.55 mmol) was added dropwise at -78 °C. After the mixture had stirred at this temperature for 1 h, diisopropyl squarate (**17**, 0.57 g, 2.87 mmol) in anhydrous THF (15 mL) was added, and agitation was maintained at -78 °C for another 2.5 h. *tert*-Butyldimethylsilyl chloride (0.94 g, 6.24 mmol) in THF (30 mL) was introduced and the mixture was stirred at -78 °C for 6 h and at 22 °C for another 12 h prior to the addition of water (10 mL). Following dilution with ether (100 mL), the organic phase was washed with water (50 mL) and brine (50 mL), dried, and concentrated to provide a yellow liquid. Purification of this residue by flash chromatography on silica gel (hexane/EtOAc = 30/1) provided pure samples of **18** (0.47 g, 35%) and **19** (0.42 g, 31%), both as yellow oils.

For **18**: IR (film, cm^{-1}) 2933, 1778, 1633, 1316, 1101; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.22 (t, J = 4.2 Hz, 1 H), 4.94-4.82 (m, 2 H), 4.32 (d, J = 5.6 Hz, 1 H), 4.24-4.19 (m, 1 H), 2.22-2.19 (m, 1 H), 1.94-1.93 (m, 1 H), 1.80-1.68 (m, 2 H), 1.36 (t, J = 6.1 Hz, 6 H), 1.32 (s, 3 H), 1.29-1.26 (m, 9 H), 0.87 (s, 9 H), 0.10 (s, 3 H), 0.07 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 184.6, 164.4, 134.0, 133.1, 129.8, 108.4, 89.0, 76.4, 73.6, 73.4, 71.4, 27.9, 26.5, 25.8, 25.7, 22.9, 22.8, 22.7, 22.4, 21.3, 18.3, -3.4, -3.5; HRMS *m/z* (M^+) calcd for $C_{25}H_{42}O_6Si$ 466.2745, obsd 466.2748; $[\alpha]_D^{22}$ = +47.3 (*c* 2.19, $CHCl_3$).

For **19**: IR (film, cm^{-1}) 2932, 1772, 1621, 1318, 1101; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.27 (t, J = 4.0 Hz, 1 H), 4.83 (hept, J = 6.0 Hz, 2 H), 4.23 (d, J = 5.7 Hz, 1 H), 4.16-4.10 (m, 1 H), 2.20-2.14 (m, 1 H), 1.99-1.95 (m, 1 H), 1.70-1.60 (m, 2 H), 1.35-1.29 (m, 9 H), 1.26-1.18 (m, 9 H), 0.86 (s, 9 H), 0.07 (s, 3 H), 0.06 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 184.9, 168.4, 132.9, 132.5, 130.7, 108.9, 89.2, 76.9, 73.8, 73.1, 70.9, 28.2, 26.2, 26.1, 25.8, 22.9 (2 C), 22.5, 22.4, 22.1, 18.3, -3.4, -3.6; HRMS *m/z* (M^+) calcd for $C_{25}H_{42}O_6Si$ 466.2745, obsd 466.2751; $[\alpha]_D^{22}$ = -46.1 (*c* 2.04, $CHCl_3$).

(4S)-4-Hydroxy-2,3-diisopropoxy-4-[(3aR,7aS)-3a,6,7,7a-tetrahydro-2,2-dimethyl-1,3-benzodioxol-4-yl]-2-cyclobuten-1-one (20). A solution of **18** (0.59 g, 1.26 mmol) in THF (15 mL) was treated with tetra-*n*-butylammonium fluoride (2.6 mL of 1 M in THF, 2.60 mmol) and stirred at 22 °C for 30 min. Water (5 mL) was added and the mixture was diluted with ether (50 mL). The resulting organic phase was washed with water (20 mL) and brine (20 mL), then dried and concentrated. Purification of the residue by flash chromatography on silica gel (hexane/EtOAc = 4/1) gave alcohol **20** as a pale yellow liquid (0.40 g, 91%); IR

(film, cm^{-1}) 3424, 2981, 1773, 1630, 1383; ^1H NMR (300 MHz, C_6D_6) δ 6.26 (t, *J* = 3.0 Hz, 1 H), 5.02 (hept, *J* = 6.1 Hz, 1 H), 4.94 (d, *J* = 5.7 Hz, 1 H), 4.83 (hept, *J* = 6.1 Hz, 1 H), 4.11-4.06 (m, 1 H), 2.83-2.47 (br s, 1 H), 2.23-2.13 (m, 1 H), 1.77-1.60 (m, 2 H), 1.40 (s, 3 H), 1.38-1.32 (m, 1 H), 1.27 (s, 3 H), 1.25-1.08 (m, 12 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 186.0, 164.9, 133.5, 133.2, 128.3 (2 C), 109.0, 88.8, 76.4, 73.3, 73.0, 27.9, 26.4, 25.1, 22.7 (2 C), 22.5, 22.1, 20.5; HRMS *m/z* (M^+) calcd for $C_{19}H_{28}O_6$ 352.1894, obsd 352.1874; $[\alpha]_D^{22}$ = +113.6 (*c* 1.32, C_6H_6).

(4R)-4-Hydroxy-2,3-diisopropoxy-4-[(3aR,7aS)-3a,6,7,7a-tetrahydro-2,2-dimethyl-1,3-benzodioxol-4-yl]-2-cyclobuten-1-one (21). Entirely comparable treatment of **19** (0.90 g, 1.93 mmol) with tetra-*n*-butylammonium fluoride (3.9 mL of 1 M in THF, 3.90 mmol) in THF (15 mL) at rt for 30 min afforded after chromatography 0.65 g (96%) of **21** as a pale yellow oil; IR (film, cm^{-1}) 3402, 2981, 1768, 1614, 1384; ^1H NMR (300 MHz, $CDCl_3$) δ 6.21 (t, *J* = 4.3 Hz, 1 H), 4.86 (hept, *J* = 6.1 Hz, 1 H), 4.83 (hept, *J* = 6.1 Hz, 1 H), 4.52 (d, *J* = 5.7 Hz, 1 H), 4.31-4.26 (m, 1 H), 3.85 (br s, 1 H), 2.27-2.17 (m, 1 H), 1.99-1.84 (m, 1 H), 1.82-1.72 (m, 1 H), 1.70-1.63 (m, 1 H), 1.37 (d, *J* = 6.1 Hz, 6 H), 1.32 (d, *J* = 6.1 Hz, 6 H), 1.24 (2d, *J* = 6.1 Hz, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 184.1, 167.6, 132.5, 131.9, 129.4 (2 C), 108.7, 87.5, 77.0, 73.3, 72.0, 27.9, 26.2, 25.2, 22.7, 22.6, 22.4, 22.2, 20.8; HRMS *m/z* (M^+) calcd for $C_{19}H_{28}O_6$ 352.1894, obsd 351.1890; $[\alpha]_D^{22}$ = +107.7 (*c* 1.51, C_6D_6).

(3aR,6aS,6bR,9S,10bR)-5,6,6a,6b,7,8,9,10b-Octahydro-9,10b-dihydroxy-1,2-diisopropoxydicyclopent[a,b]inden-3(4H)-one (26). A 25 mL flask was charged with cyclopentenyl iodide (0.28 g, 1.44 mmol) and anhydrous THF (7 mL). *tert*-Butyllithium (1.9 mL, 1.7 M in pentane, 3.23 mmol) was added dropwise at -78 °C and the mixture was stirred at -78 °C for 1 h prior to the introduction of **20** (0.17 g, 0.48 mmol) dissolved in THF (3 mL). Agitation was continued at -78 °C for 2.5 h and at 22 °C for 16 h, at which point degassed saturated NH_4Cl solution (5 mL) was added at 0 °C. The mixture was stirred for another 10 min and diluted with water (5 mL) and ether (30 mL). The organic phase was washed with water (10 mL) and brine (10 mL), then dried and concentrated to provide a brown liquid which was purified by flash chromatography on silica gel (hexane/EtOAc = 2/1). A yellow liquid consisting of **26** and **27** in a ratio of 3.5/1 (61.9 mg, 35%) was isolated. Crystallization, effected with hexane/EtOAc, afforded **26** as a white solid, mp 138-140 °C; IR (film, cm^{-1}) 3414, 2936, 1686, 1611, 1100; ^1H NMR (300 MHz, $CDCl_3$) δ 5.87 (br, 1 H), 5.28 (hept, *J* = 6.1 Hz, 1 H), 4.92 (hept, *J* = 6.1 Hz, 1 H), 4.29 (br, 1 H), 2.82-2.41 (br, 1 H), 2.37-2.32 (m, 3 H), 2.12-2.04 (m, 2 H), 1.96-1.86 (m, 1 H), 1.80-1.72 (m, 3 H), 1.69-1.58 (m, 3 H), 1.28 (d, *J* = 6.1 Hz, 3 H), 1.21 (d, *J* = 6.1 Hz, 3 H), 1.16 (t, *J* = 6.1 Hz, 6 H), 1.04-0.98 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 203.4, 166.0, 145.8, 132.8, 126.4, 80.2, 73.9, 71.9, 67.9, 65.1, 51.3, 37.6, 33.0, 29.0, 28.9, 26.6, 24.4, 22.6 (2 C), 22.5, 22.4; HRMS *m/z* (M^+) calcd for $C_{21}H_{30}O_5$ 362.2088, obsd 362.2090; $[\alpha]_D^{22}$ = -249.7 (*c* 1.86, $CHCl_3$).

Crystallographic Analysis of 26. The data collection crystal was a clear, colorless, hexagonal plate which had been cut from the end of a string of crystals. Examination of the diffraction pattern with a Rigaku AFC5S diffractometer indicated a monoclinic crystal system. The space group was uniquely determined as $P2_1/c$. Unit cell constants were obtained by a symmetry-restricted least-squares fit of the diffractometer setting angles for 25 reflections in the 2θ range 19 to 23° with MoKα radiation (λ(Kα1) = 0.70930 Å).

Six standard reflections were measured after every 150 reflections during data collection and indicated that the crystal was stable. Data reduction was done with the TEXSAN package of crystallographic

Table I. X-Ray Crystallographic Details for **26.**

Formula	$C_{21}H_{30}O_5$
Formula weight	362.46
Space group	$P2_1/c$
a, Å	9.245(2)
b, Å	11.358(2)
c, Å	19.536(2)
β, deg	93.54(1)
Volume, Å^3	2047
Z	4
Density (calc), g/cm^3	1.18
Crystal size, mm	0.10 x 0.23 x 0.23
Radiation	MoKα with graphite monochromator
Linear abs. coeff., cm^{-1}	0.77
Temperature	ambient
2θ limits	$4° \leq 2\theta \leq 55°$
Scan speed	4°/min in ω with maximum of 4 scans per reflection
Background time/scan time	0.5
Scan range	1.30° in ω
Data collected	+h, +k, ±l
Scan type	ω
Unique data	4960
Unique data, with $F_o^2 > 1/\sigma^2(F_o^2)$	1490
Final number of variables	243
R(F)[a]	0.088
$R_w(F)$[b]	0.048
Error in observation of unit weight	1.69

[a] $R(F) = \Sigma||F_o|-|F_c||/\Sigma|F_o|$

[b] $R_w(F) = [\Sigma w(|F_o|-|F_c|)^2/\Sigma w|F_o|^2]^{1/2}$ with $w = 1/\sigma^2(F_o)$

programs.[20]

The structure was solved with the direct methods procedure of SHELXS-86.[21] Full-matrix least-squares refinements were performed in TEXSAN;[20] the function minimized was $\Sigma w(|F_o|-|F_c|)^2$ with $w = 1/\sigma^2(F_o)$. The two hydroxyl hydrogen atoms, H(20) bonded to O(4) and H(30) bonded to O(5), were refined isotropically. All the other hydrogen atoms are included in the model as fixed contributions at calculated posi-

tions with C-H = 0.98 Å and B_H = 1.2*Beq (attached carbon atom). Methyl group hydrogen atoms were idealized to sp^3 geometry based on positions located in various difference electron density maps. The final refinement cycle was based on the 1490 intensities with $I > 1\sigma(I)$ and 243 variables and resulted in agreement indices of R = 0.008 and R_w = 0.048. The final difference electron density map contains maximum and minimum peak heights of 0.34 and -0.35 e/Å^3. Scattering factors are from the International Tables for X-ray Crystallography.[22] A structure factor calculation for the model based on the 1078 intensities with $I > 3\sigma(I)$ gives an R factor of 0.051.

There are two intermolecular hydrogen bonding interactions: O(1)----O(5) at 2.863(7)Å andO(4)----O(15) at 2.772(7) Å.

(3aS,6aR,6bR,9S,10bS)-5,6,6a,6b,7,8,9,10b-Octahydro-9,10b-dihydroxy-1,2-diisopropoxydicyclopent[a,b]inden-3(4H)-one (27). Cyclopentenyl iodide (0.45 g, 2.31 mmol) was allowed to react with *tert*-butyllithium (3.0 mL of 1.7 M in pentane, 5.10 mmol) and treated with **21** (0.26 g, 0.73 mmol) in the predescribed manner. Purification of the residue by flash chromatography on silica gel (2:1 hexane/EtOAc) gave **27** as a yellow liquid (93.5 mg, 35%); IR (film, cm^{-1}) 3389, 2935, 1693, 1621, 1108; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.94 (br, 1 H), 5.32 (hept, *J* = 6.1 Hz, 1 H), 4.82 (hept, *J* = 6.1 Hz, 1 H), 4.22-4.17 (m, 1 H), 2.91 (br, 2 H), 2.33-2.17 (m, 1 H), 2.10-1.99 (m, 2 H), 1.98-1.85 (m, 2 H), 1.79-1.43 (m, 6 H), 1.33 (d, *J* = 6.1 Hz, 3 H), 1.30 (d, *J* = 6.1 Hz, 3 H), 1.27-1.19 (m, 1 H), 1.15 (t, *J* = 6.1 Hz, 3 H), 1.11 (t, *J* = 6.1 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 203.8, 166.4, 149.2, 129.1, 123.7, 79.9, 74.2, 71.9, 67.8, 66.2, 53.1, 46.2, 32.5, 31.9, 31.4, 27.9, 26.6, 22.9, 22.7, 22.6, 22.2; HRMS *m/z* (M^+) calcd for $C_{21}H_{30}O_5$ 362.2088, obsd 362.2090; $[\alpha]_D^{22}$ = +87.7 (*c* 2.44, $CHCl_3$).

(3aR,6aS,6bR,10bS)-5,6,6a,6b,7,8-Hexahydro-10b-hydroxy-1,2-diisopropoxydicyclopent[a,b]indene-3,9(4H,10bH)-dione (28). A solution of **26** (64.6 mg, 0.17 mmol) in CH_2Cl_2 (2 mL) was treated with the Dess-Martin periodinane (90.9 mg, 0.21 mmol) and stirred at rt for 2 h. Following the addition of water (5 mL) and CH_2Cl_2 (20 mL), the organic phase was washed with water (10 mL) and brine (10 mL), then dried and concentrated. Purification of the residue by flash chromatography on silica gel (3:1 hexane/EtOAc) furnished **28** as a faintly yellow oil (26.6 mg, 41%); IR (film, cm^{-1}) 3398, 2976, 1672, 1614, 1309; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.22 (d, *J* = 2.4 Hz, 1 H), 5.29 (hept, *J* = 6.1 Hz, 1 H), 5.04 (hept, *J* = 6.1 Hz, 1 H), 2.94 (br, 1 H), 2.75-2.66 (m, 1 H), 2.59-2.32 (m, 2 H), 2.29-2.22 (m, 1 H), 2.12-2.05 (m, 2 H), 1.90-1.65 (m, 6 H), 1.31 (d, *J* = 6.1 Hz, 3 H), 1.21 (d, *J* = 6.1 Hz, 6 H), 1.20 (d, *J* = 6.1 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 202.3, 199.6, 170.2, 164.7, 133.1, 125.2, 80.7, 74.6, 72.2, 65.4, 50.9, 38.7, 37.2, 29.5, 29.2, 26.5, 25.7, 22.8, 22.6, 22.5, 22.4; HRMS *m/z* (M^+) calcd for $C_{21}H_{28}O_5$ 360.1914, obsd 360.1936; $[\alpha]_D^{22}$ = -236.2 (*c* 0.83, $CHCl_3$).

(3aS,6aR,6bR,10bS)-5,6,6a,6b,7,8-Hexahydro-10b-hydroxy-1,2-diisopropoxydicyclopent[a,b]indene-3,9(4H,10bH)-dione (29). Parallel treatment of **27** (83.2 mg, 0.23 mmol) dissolved in CH_2Cl_2 (2 mL) with the Dess-Martin periodinane (0.11 g, 0.25 mmol) at rt for 2 h gave rise to **29** (46.7 mg, 56%) as a pale yellow oil after chromatography on silica gel (3:1 hexane/EtOAc); IR (film, cm^{-1}) 3380, 2977, 1673, 1614, 1307; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.28 (d, *J* = 2.7 Hz, 1 H), 5.35 (hept, *J* = 6.1 Hz, 1 H), 4.93 (hept, *J* = 6.1 Hz, 1 H), 3.00 (br, 1 H), 2.71-2.62 (m, 1 H), 2.46-2.41 (m, 1 H), 2.39-2.10 (m, 3 H), 2.07-2.05 (m, 1 H), 1.91-1.51 (m, 6 H), 1.34 (t, *J* = 6.1 Hz, 6 H), 1.17 (d, *J* = 6.1 Hz, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 202.4, 200.4, 170.7, 164.1, 130.1, 122.3, 80.4, 74.9, 72.1, 66.0, 53.5, 47.0, 37.2, 32.4, 30.7, 29.0,

26.7, 22.9, 22.7 (2 C), 22.4; HRMS *m/z* (M^+) calcd for $C_{21}H_{28}O_5$ 360.1914, obsd 360.1925; $[\alpha]_D^{22}$ = +139.4 (*c* 0.52, $CHCl_3$).

Anal. Calcd for $C_{21}H_{28}O_5$: C, 69.96; H, 7.83. Found: C, 69.63; H, 8.08.

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Supplementary Material Available: Tables of bond lengths and angles, positional and anisotropic displacement parameters, and structure factor data for **26** (20 pages). This information can be obtained on request from The Director, Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, U.K.

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