Reversible Charge-Accelerated Oxy-Cope Rearrangements

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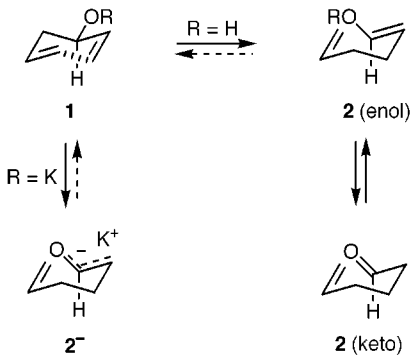
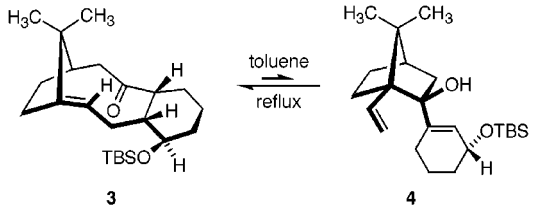
An asymmetric synthesis of the oxetane-containing norbornanone **23** and its coupling to *trans*-1-propenyllithium to give **24** are reported, in tandem with the preparation of the related alcohols **28** and **30**. All three divinyl carbinols undergo anionic oxy-Cope rearrangement very rapidly at low temperature. Quenching of **24**$^-$**K**$^+$ and **28**$^-$**K**$^+$ under these conditions with water or various aqueous salt solutions results in protonation of the alkoxides. If these reaction mixtures are poured instead onto cold (0 °C) silica gel, their sigmatropically related ketones are isolated in very good yield. Whereas the **24**$^-$**K**$^+$ ⇄ **25**$^-$**K**$^+$ equilibrium pair is not reactive to molecular oxygen, **30**$^-$**K**$^+$ is directly converted into an α-hydroperoxy ketone under comparable conditions. These and additional observations are rationalized in the context of atropisomerism involving conversion of oxygen-up enolates, formed reversibly under kinetically controlled conditions, into their thermodynamically favored, more reactive oxygen-down conformers.

[3,3]-Sigmatropic rearrangements have evolved into powerful tools for stereocontrolled chirality transfer.[1,2] As a consequence of the adoption of highly ordered transition states, stereochemical outcomes are often highly predictable, with the result that complex molecular scaffolding can be reliably achieved in rapid fashion.[3] From among the several processes in this category, the oxy-Cope rearrangement holds a special position as a consequence of its capacity for significant anionic acceleration.[4−6] Because its neutral [**1** (R = H) → **2**] and charged variants [**1** (R = K) → **2**$^-$] are so heavily favored thermodynamically, either process has come to be generally viewed as irreversible.[1]



In 1991, we reported the first example of a thermally induced retro-oxy-Cope rearrangement, viz. **3** ⇄ **4**.[7]

Continued investigation of systems related to **3** and **4** as part of our taxusin/taxol synthesis effort[8,9] has provided the forum for discovery of the first remarkable examples of reversibility *under anionic oxy-Cope conditions*. These observations are notable because, as denoted in **1** ⇄ **2**$^-$, the need now exists to overcome the resonance stabilization associated with enolate anion **2**$^-$ which is not present in the potassium alkoxide, **1**. Consequently, although a driving force to proceed in the forward direction is present in the great majority of examples based on the **1** → **2**$^-$ paradigm, this phenomenon should no longer be viewed as all-inclusive.



3 **4**

Results and Discussion

The first system to come under scrutiny was *exo*-norbornanol **24** featuring a completely assembled oxetane ring. The starting material selected for the synthesis of this segment of **24** was D-glucose, which was converted into diacetonide **5**[10] and subsequently transformed into the derived acetate (Scheme 1). Regioselective acid-catalyzed hydrolysis of the C5,C6-acetonide moiety produced diol **6a**, submission of which to a deoxygenation protocol[11,12] gave the vinyl derivative **7**.[13] During this procedure, partial deacetylation was observed and the mixture was therefore directly saponified to hydrolyze

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(3) Review: Paquette, L. A. *Synlett* **1990**, 67.
(4) Review: Paquette, L. A. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 609.
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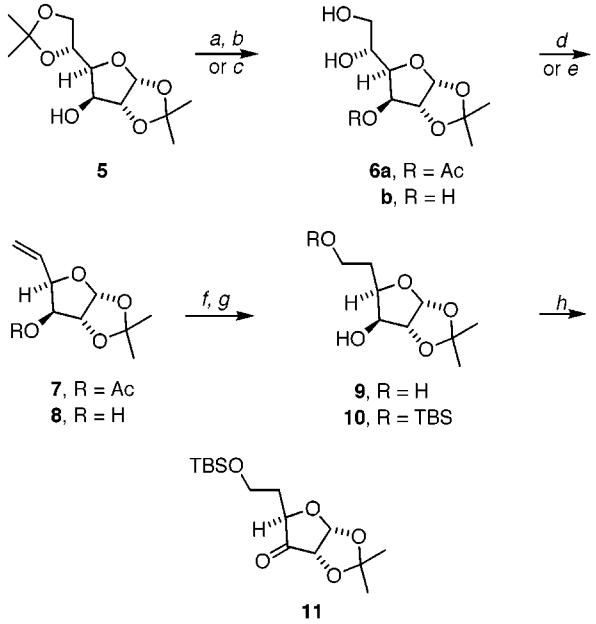
Scheme 1



[a] Ac_2O, Et_3N, (DMAP), CH_2Cl_2, rt (89%). [b] 50% aq HOAc (87%). [c] HCl, H_2O (pH = 2), 40 °C (70%). [d] Ph_3P, imid, I_2, toluene, reflux; NaOH, H_2O (71%). [e] $NaIO_4$, CH_3OH, H_2O, rt; $Ph_3PCH_3^+ I^-$, KHMDS, THF, 0 °C (82%). [f] Disiamylborane, THF, rt; NaOH, H_2O_2 (86%). [g] TBSCl, imid, CH_2Cl_2, 0 °C (90%). [h] Dess-Martin periodinane, CH_2Cl_2, rt (92%).

the remaining **7** and facilitate the purification of **8**. This vinyl tetrahydrofuran could also be prepared by sodium periodate cleavage of triol **6b** followed by Wittig olefination. Hydroboration of **8** with disiamylborane afforded predominantly **9** (86%), the primary hydroxyl group in which was chemoselectively protected as the *tert*-butyldimethylsilyl ether **10**. Oxidation of **10** was accomplished with the Dess−Martin periodinane,[14] providing **11** in 92% yield.

At this juncture, the previously described **12**[15] was transformed into the alkynyl anion by reaction with *n*-butyllithium and added to **11** (Scheme 2). As expected, this 1,2-addition proceeded with excellent π-facial selectivity to provide **13** as the only detectable diastereomer. The stereochemistry at the newly generated stereogenic center is assigned as *R* on the basis of extensive analogy.[16,17]

To guarantee the proper stereodisposition of ring C in our targeted taxane precursors,[18] it was mandatory that the acetylenic linkage in **13** be chemically modified into a trans alkene. When Red-Al[19] was discovered to be ineffective for performing this interconversion, recourse was made instead to lithium aluminum hydride.[20] In the event, refluxing THF was required, these conditions also cleaving the *tert*-butyldimethylsilyl protecting group. Direct resilylation gave rise to **15** in >90% yield. This diol was subsequently oxidized to norbornanone **16** under Dess−Martin conditions prior to benzylation of the tertiary hydroxyl substituent.

The time had now arrived for crafting the oxetane subunit. To this end, it was first necessary to remove the acetonide functionality. This hydrolysis proved to not be trivial. However, success did materialize when **17** was briefly subjected to the action of titanium tetrachloride in CH_2Cl_2 at −78 °C.[21] Under these unoptimized conditions, a mixture of **18** (28%) and **19** (43%) resulted. Following the selective reprotection of **18**, the hemiacetal sector of **19** was cleaved to the aldehydo formate with the Dess−Martin periodinane and subjected in sequence to reduction with sodium borohydride at −40 °C and saponification with sodium hydroxide. The resultant diol **20** proved to be a colorless crystalline solid. Its conversion to oxetane **21** was achieved directly by treatment with potassium hexamethyldisilazide followed by *N*-(5-chloro-2-pyridyl)triflimide.[22] The absolute and relative configurations of **21** follow rigorously from the method of synthesis and from unambiguous spectroscopic features.

The final stages of the route to **24** are depicted in Scheme 3. Ketone **21** was transformed into its silyl enol ether in advance of oxidation with dimethyldioxirane.[23] The exo stereodisposition of the newly introduced hydroxyl group in **22** was based on a similar selectivity observed in related systems[24] and the absence of a vicinal coupling constant to the bridgehead proton.[25] Protection of the hydroxyl group in **22** as the methoxymethyl ether was readily effected, thereby making possible the 1,2-addition of *trans*-1-propenyllithium from the endo direction and arrival at **24**.

The anionic oxy-Cope rearrangement of **24** was induced with potassium hydride and 18-crown-6 in THF solution at 0 °C. After 15 min, the conversion of **24**$^-$**K**$^+$ to **25**$^-$**K**$^+$ was judged to be complete on the basis of the complete disappearance on silica gel thin-layer chromatography (TLC) plates of the spot due to **24** (R_f = 0.42, elution with 4:1 hexanes−ethyl acetate) in favor of a single spot arising from a more polar product (R_f = 0.20) subsequently identified as **25**. *However, all attempts to isolate ketone **25** by quenching of these reaction mixtures in conventional ways (e.g., with saturated NH_4Cl solution) returned **24** quantitatively.* Faced with these observations, we reasoned that silica gel might be somehow mediating a selective protonation of **25**$^-$**K**$^+$ under conditions that did not promote the concomitant formation of **24**. This line of conjecture served to suggest a solution to the preparative isolation of **25**. Indeed, when the cold, basic reaction mixture was poured directly into a beaker of silica gel cooled to 0 °C, and the product was eluted from the adsorbent with ether, **25** was now isolated as the only product. In a typical run, the yield of this bicyclic ketone was 77%. This result removed all impediment to

(14) (a) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4155. (b) Ireland, R. E.; Liu, L. B. *J. Org. Chem.* **1993**, *58*, 2899.
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(17) Schmeichel, M.; Redlich, H. *Synthesis* **1996**, 1002.
(18) Consult, for example: Paquette, L. A.; Huber, S. K.; Thompson, R. C. *J. Org. Chem.* **1993**, *58*, 6874.
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(23) (a) Adam, W.; Chan, Y. Y.; Cremer, D.; Gauss, J.; Scheutzow, D.; Schindler, M. *J. Org. Chem.* **1987**, *52*, 2800. (b) Adam, W.; Prechtl, F. *Chem. Ber.* **1991**, *124*, 2369.
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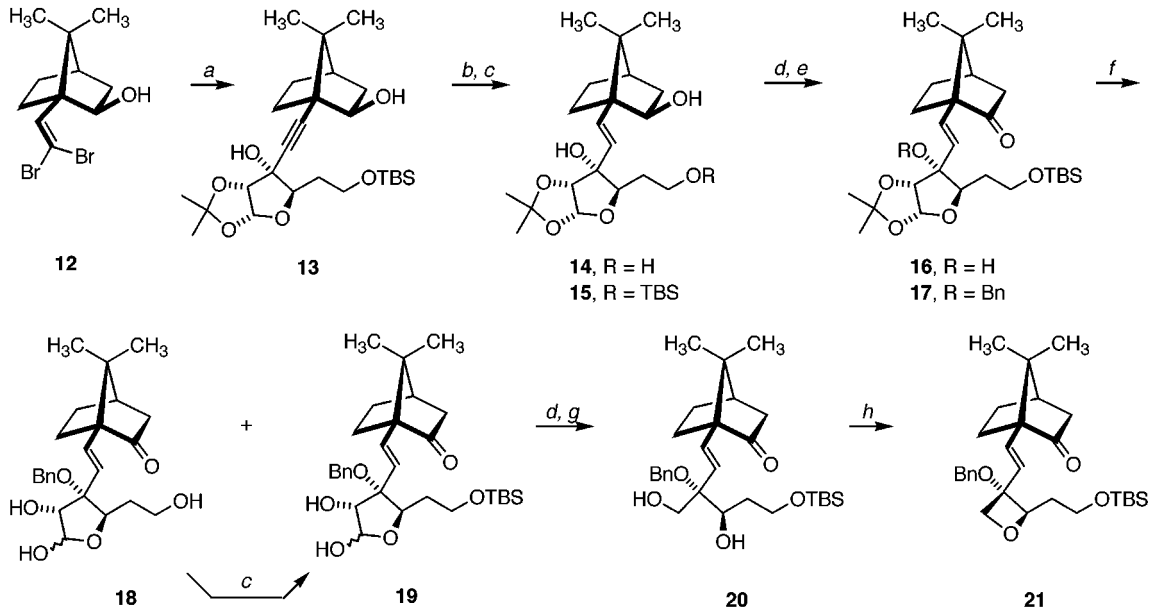
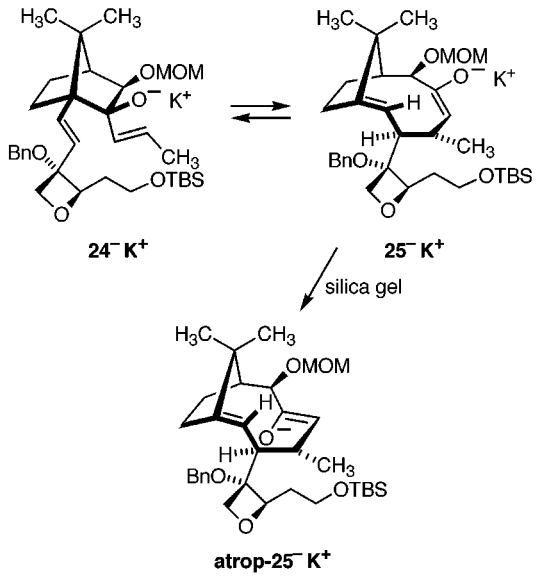
Scheme 2



[a] *n*-BuLi, THF, -78 °C; **11** (50%). [b] $LiAlH_4$, THF, reflux (98%). [c] TBSCl, imid, CH_2Cl_2, 0 °C (92% for **15**; 89% for **19**). [d] Dess-Martin periodinane, CH_2Cl_2, rt (98%). [e] KH, BnBr, THF, 0 °C. [f] $TiCl_4$, CH_2Cl_2, -78 °C (28% of **18**; 43% of **19**). [g] $NaBH_4$, CH_3OH, -40 °C; NaOH (65%). [h] KHMDS, *N*-(5-chloro-2-pyridyl)triflimide, THF, -78 °C (63%).

the flow of synthetic material while providing convincing indication of the reversibility of the **24**$^-$**K**$^+$/**25**$^-$**K**$^+$ equilibrium.



As a direct consequence of the necessary adoption by **24**$^-$**K**$^+$ of the so-called endo-chair transition-state topology[26] for effective sigmatropic realignment, the newly developed carbonyl oxygen in **25** must be initially projected in an upward direction such that it resides in close proximity to the apical syn-methyl substituent. However, this conformation does not persist due to prevailing nonbonded steric interactions, and σ bond rotations occur so as to allow the carbonyl group to be preferably endo-oriented.[26,27] This interconversion was expected to occur with a relatively low energy barrier in **25** because ring C is not yet annealed onto the framework. However, a distinction as to whether realignment would materialize at the enolate anion stage[27a] or only after protonation was not yet apparent. ^{1}H NMR analysis of **25** clearly revealed that its apical syn-methyl substituent is not subject to electronic perturbation by a proximal carbonyl group. Also, reduction of this ketone with lithium aluminum hydride resulted in exclusive formation of the α-carbinol, whose configuration was deduced by NOE analysis of its *p*-methoxybenzyl derivative. Further, should the carbonyl-down conformation of **25** be thermodynamically favored, its regiocontrolled deprotonation should *not* result in reconversion to **24**$^-$**K**$^+$ via **25**$^-$**K**$^+$. At the experimental level, **atrop-25**$^-$**K**$^+$ proved to be indefinitely stable at −78 °C; above this limit, decomposition sets in.

What role does silica gel play in all of this? We propose that the rapidity with which **24** undergoes anionic oxy-Cope rearrangement does not provide adequate opportunity for **25**$^-$**K**$^+$ to undergo slower atropisomerization. The dominant course of protonation at low temperature occurs on the alkoxide **24**$^-$**K**$^+$. Admixing of the reaction mixture with silica gel is accomplished at or above 0 °C, such that resultant binding to the adsorbent in combination with a more elevated temperature greatly facilitates *irreversible* conversion to **atrop-25**$^-$**K**$^+$.

The outcome of two companion experiments allows the relative relationship of **25**$^-$**K**$^+$ and **atrop-25**$^-$**K**$^+$ to be established. Treatment of **24** with KHMDS and 18-crown-6 in THF at −78 °C *in the presence of oxygen*[28] did not result in the formation of α-hydroxy ketone **26** despite TLC evidence for complete isomerization to **25**$^-$**K**$^+$. As before, quenching of the reaction mixture with

(26) Paquette, L. A.; Pegg, N. A.; Toops, D.; Maynard, G. D.; Rogers, R. D. *J. Am. Chem. Soc.* **1990**, *112*, 277.

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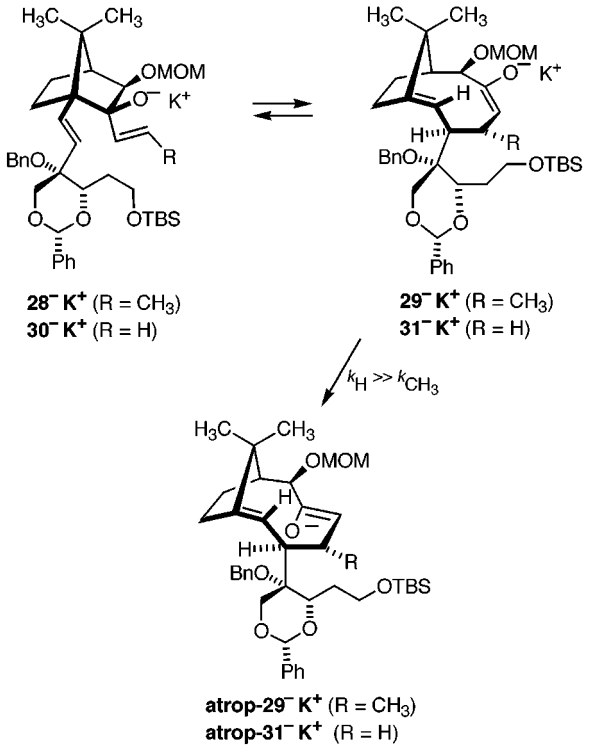
saturated $NaHCO_3$ solution returned only **24**. In contrast, submission of **25** to the identical conditions afforded **26** in 81% yield.[29]

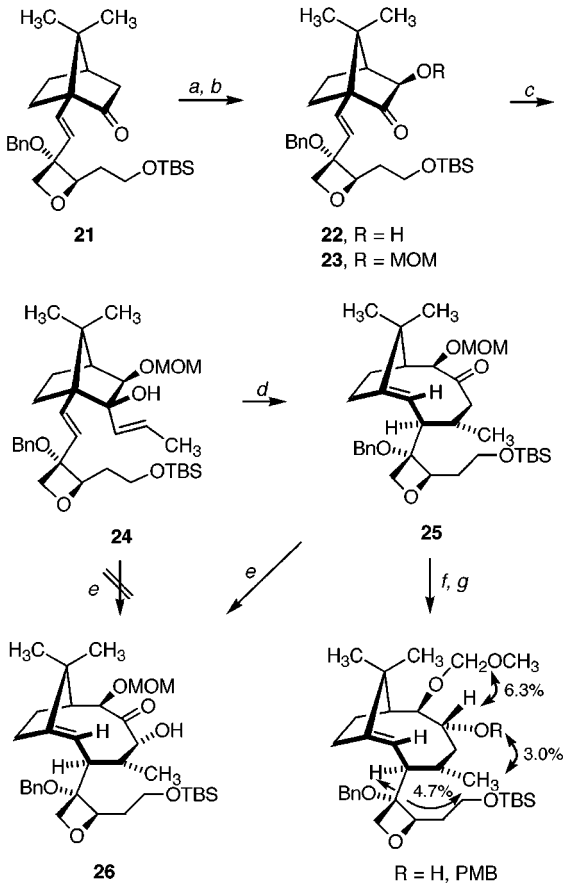
Interestingly, the previously reported 1,3-dioxanyl alcohol **28** responds under anionic conditions in a manner closely paralleling **24** (Scheme 4). Thus, **28**$^-$**K**$^+$ generated at −78 °C is rapidly transformed into **29**$^-$**K**$^+$ (TLC analysis), but this enolate anion is unreactive to oxygen. Only when silica gel becomes involved is α-hydroxylation observed (81% of **29**), presumably because conversion to **atrop-29**$^-$**K**$^+$ has now materialized. Under these circumstances, it is likely that the substantially increased surface area provided by the adsorbent facilitates enolate oxygenation.



It will be recognized that the atropisomerization processes involving **25**$^-$**K**$^+$ and **29**$^-$**K**$^+$ require that the bulky oxygenated side chain and adjacent methyl substituent experience unfavorable $A^{1,3}$ interaction. On this basis, the expectation would be that a desmethyl congener might not be destabilized in this manner and would find it energetically more feasible to undergo irreversible conformational flexing at significantly lower temperatures. To probe this issue, **27** was reacted with the vinylcerate reagent to furnish **32** (Scheme 5). This compound was treated in turn with potassium hexamethyldisilazide and 18-crown-6 in the presence of oxygen at −78 °C. In contrast to **27**, which failed to react until silica gel was introduced, **32** was very efficiently transformed into α-hydroperoxy ketone **33** within 5 min at this temperature. Brief exposure of this product to triphenylphosphine gave **34** in 81% isolated yield as a single epimer.[29]

(29) Although **26** and **33** were isolated as single diastereomers, the stereochemistry of their hydroxyl group was not determined because of pending oxidation to the α-diketone. (Tsui, H.-C. Ph.D. Thesis, The Ohio State University, 1998).

Scheme 3

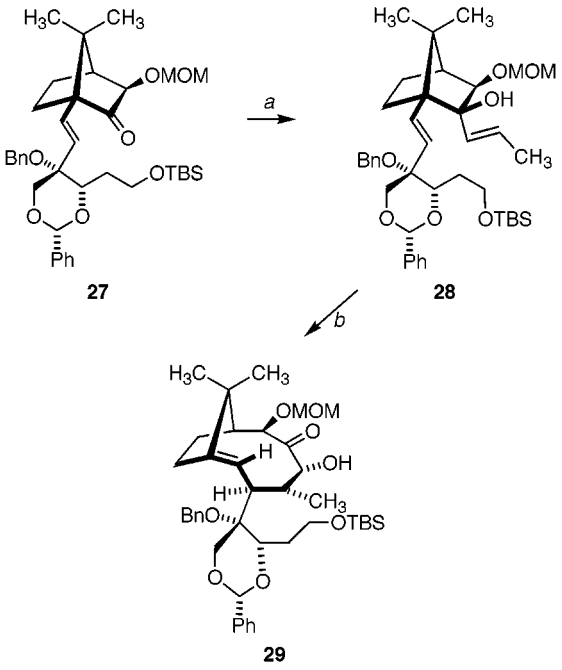


[a] LDA, TMSCl, THF, -78 °C; oxone, acetone; TBAF, THF, 0 °C (73%). [b] MOMCl, *i*-PrNEt$_2$, CH_2Cl_2, rt (83%). [c] *trans*-CH_3CH=CHBr, *t*-BuLi, THF, -78 °C (82%). [d] KH, 18-cr-6, THF, 0 °C; silica gel (77%). [e] KHMDS, 18-cr-6, THF, -78 °C; O_2 (84%). [f] $LiAlH_4$, ether, 0 °C (86%). [g] NaH, $Bu_4N^+ I^-$ (cat), PMBCl, THF-DMF (79%).

Conclusions

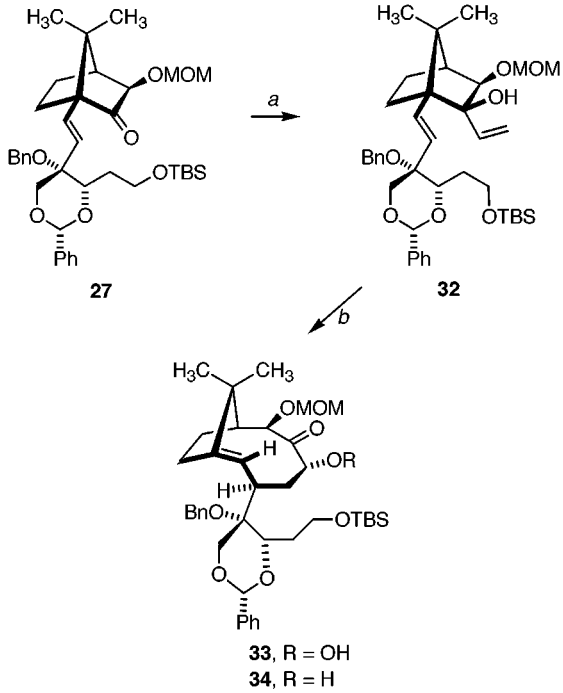
The weight of experimental evidence suggests that the anionically accelerated [3,3] sigmatropic rearrangements of **24** and **28** proceed in a reversible manner at −78 °C. The return to alkoxide can materialize only as long as the enolate anion has its oxygen atom oriented up toward the methano bridge. The geometric demands of the oxy-Cope transition state necessarily generate these enolates in precisely this conformation. However, these structures are thermodynamically unstable relative to their oxygen-down forms. When a methyl group is positioned adjacent to the bulky oxygenated side chain as it is in **25**$^-$**K**$^+$ and **29**$^-$**K**$^+$, the atropisomeric conversion does not operate spontaneously but requires silica gel at more elevated temperatures for its operation. Removal of this steric interference as in **31**$^-$**K**$^+$ lessens the energy barrier significantly. In methylation and oxygenation reactions, the oxygen-down enolates give evidence of being the more reactive of the atropisomeric pair. The greatly diminished nucleophilicity of **25**$^-$**K**$^+$ and **29**$^-$**K**$^+$ could well be matched by a similar decrease in basicity as a consequence of effective steric shielding on both π surfaces. These factors would serve to explain why the alkoxides are preferentially protonated at low temperature. Comparable observations have not previously been reported in any sigmatropic context. It is hoped that the principles delineated

Scheme 4



[a] *trans*-$CH_3CH{=}CHBr$, *t*-BuLi, THF, -78 °C (86%). [b] KHMDS, 18-cr-6, THF, -78 °C; O_2, -78 °C; silica gel; Ph_3P, -78 °C → rt (81%).

Scheme 5



[a] $CH_2{=}CHMgBr$, $CeCl_3$, THF, 0 °C (91%). [b] KHMDS, 18-cr-6, THF, -78 °C; O_2, -78 °C; Ph_3P, -78 °C → rt (81%).

here will translate into a sufficiently large number of systems to justify their broad extrapolation.

Experimental Section

General Methods. 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 NMR. The high-resolution and fast-atom-bombardment spectra were recorded at The Ohio State University Campus Chemical Instrument Center. Elemental analyses were performed at Atlantic Microlab, Inc., Norcross, GA.

3-*O*-Acetyl-1,2,5,6-diisopropylidene-D-glucose. To a solution of **5** (251 mg, 0.964 mmol) in CH_2Cl_2 (5 mL) at 20 °C were added triethylamine (0.40 mL, 2.9 mmol), acetic anhydride (0.14 mL, 1.5 mmol), and a catalytic amount of DMAP. The mixture was stirred for 3 h, quenched with saturated NH_4Cl solution, and diluted with water and ether. The separated aqueous layer was extracted twice with ether. The combined organic extracts were dried, filtered, and evaporated. Ensuing chromatographic purification of the residue on silica gel (elution with 4:1 hexanes−ethyl acetate) gave the acetate of **5** (258 mg, 89%) as a white solid: mp 62−62.5 °C; IR (film, cm^{-1}) 1751; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.86 (d, J = 3.7 Hz, 1 H), 5.24 (d, J = 2.2 Hz, 1 H), 4.48 (d, J = 3.7 Hz, 1 H), 4.24−4.17 (m, 2 H), 4.09−3.98 (m, 2 H), 2.08 (s, 3 H), 1.50 (s, 3 H), 1.39 (s, 3 H), 1.31 (s, 3 H), 1.29 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 169.5, 112.2, 109.3, 105.0, 83.3, 79.7, 76.1, 72.4, 67.1, 26.8, 26.7, 26.2, 25.2, 20.8; MS *m*/*z* (M^+) calcd 302.1365, obsd 302.1327; $[\alpha]^{22}_D$ −27.9 (*c* 1.63, $CHCl_3$).

(1*R*)-1-[(3a*R*,5*R*,6*S*,6a*R*)-Tetrahydro-6-hydroxy-2,2-dimethylfuro[2,3-*d*]-1,3-dioxol-5-yl]-1,2-ethanediol 6-Acetate (6a). The acetate of **5** (150 mg, 0.496 mmol) was dissolved in 50% aqueous acetic acid (2 mL) at 20 °C and stirred for 1 day. Solvents were removed in vacuo. Chromatography of the residue on silica gel (elution with 4:1 hexanes−ethyl acetate) gave **6a** (114 mg, 87%) as white crystals: mp 126−126.5 °C (from hexanes−ether); IR (film, cm^{-1}) 3442, 1746; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.89 (d, J = 3.7 Hz, 1 H), 5.26 (d, J = 2.6 Hz, 1 H), 4.55 (d, J = 3.7 Hz, 1 H), 4.17 (dd, J = 8.8, 2.6 Hz, 1 H), 3.85−3.74 (m, 1 H), 3.72−3.62 (m, 2 H), 3.12 (br s, 1 H), 2.42 (br s, 1 H), 2.14 (s, 3 H), 1.51 (s, 3 H), 1.30 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 171.2, 112.4, 104.8, 83.0, 79.4, 76.7, 68.2, 64.1, 26.6, 26.2, 20.8; MS *m*/*z* (M^+) calcd 263.1131, obsd 263.1110; $[\alpha]^{22}_D$ +18 (*c* 0.93, $CHCl_3$).

(3a*R*,5*R*,6*S*,6a*R*)-Tetrahydro-2,2-dimethyl-5-vinylfuro-[2,3-*d*]-1,3-dioxol-6-ol (8). A. From 6a. To a solution of **6a** (5.00 g, 19.1 mmol) in toluene (200 mL) was added triphenylphosphine (20.0 g, 76.3 mmol) and imidazole (5.19 g, 76.3 mmol). The mixture was heated to 80 °C for 30 min and cooled to room temperature. Iodine (14.6 g, 57.3 mmol) was slowly added in small portions, and the mixture was heated to 80 °C for another 3 h, cooled to room temperature, and treated with zinc dust (2.0 g) until decolorization was complete. The mixture was diluted with ether, and the solid was removed by filtration through a pad of Celite. The filtrate was washed with saturated $NaHCO_3$ solution, dried, and filtered. Removal of solvents left a residue which was dissolved in methanol (100 mL). Sodium hydroxide (5 mL, 2 N in water) was introduced, and the solution was stirred at room temperature for 30 min and diluted with water and ether. The separated aqueous layer was extracted with ether (×2). The combined organic extracts were dried, filtered, and concentrated. Subsequent chromatography on silica gel (elution with 3:1 hexanes−ethyl acetate) gave **8** (2.6 g, 71%) as a white solid: mp 64−65 °C; IR (film, cm^{-1}) 3452, 1647; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.92 (d, J = 3.5 Hz, 1 H), 5.87 (ddd, J = 17.2, 10.7, 5.1 Hz, 1 H), 5.51 (dt, J = 17.4, 1.4 Hz, 1 H), 5.39 (dd, J = 10.7, 1.3 Hz, 1 H), 4.71 (br s, 1 H), 4.55 (d, J = 3.6 Hz, 1 H), 4.07 (br s, 1 H), 1.97 (br s, 1 H), 1.49 (s, 3 H), 1.30 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 131.1, 119.5, 111.6, 104.5, 84.8, 80.8, 75.6, 26.6, 26.1; MS *m*/*z* (M^+) calcd 187.0970, obsd 187.0970; $[\alpha]^{22}_D$ −52.1 (*c* 2.27, $CHCl_3$).

B. Via a Wittig Olefination Sequence. To a mixture of **6b** (2.00 g, 9.08 mmol) in a mixture of methanol (25 mL) and water (25 mL) was added sodium periodate (2.91 g, 13.6 mmol) in small portions. The white suspension was stirred for a additional 30 min, filtered through a pad of Celite, and freed of solvents in vacuo. The white residue was extracted with tetrahydrofuran (×5), and the combined organic extracts were dried, filtered, and evaporated to give a crude aldehyde which was used in the next step without further purification.

To a solution of methyltriphenylphosphonium iodide (8.00 g, 18.0 mmol) in THF (10 mL) at 0 °C was added a solution of potassium hexamethyldisilazide (39.5 mL of 0.5 M in toluene, 18.0 mmol). The yellow suspension was stirred at 0 °C for 1 h, and a solution of the aldehyde from above in THF (5 mL) was added. The resultant brown suspension was allowed to warm to room temperature, stirred for 3 h, and quenched with saturated NH_4Cl solution. Ether was added, and the white solid was removed by filtration through a pad of Celite. The separated aqueous layer was extracted with ether (×2). The combined organic extracts were dried, filtered, and concentrated. Chromatography of the residue on silica gel (elution with 3:1 hexanes−ethyl acetate) gave **8** (831 mg, 67% for 2 steps) as a white solid spectroscopically identical to the original sample.

(3a*R*,5*R*,6*S*,6a*R*)-Tetrahydro-6-hydroxy-2,2-dimethylfuro[2,3-*d*]-1,3-dioxole-5-ethanol (9). To a solution of 2-methyl-2-butene (39 mL of 2.0 M in THF, 0.078 mol) at 0 °C was added borane−tetrahydrofuran complex (39 mL of 1.0 M in THF, 0.078 mol). The mixture was stirred at 0 °C for 1 h, treated with a solution of **8** (2.47 g, 13.1 mmol) in THF (10 mL), and stirred at 0 °C for another hour. Sodium hydroxide solution (2 N, 30 mL) was introduced, followed by 30% hydrogen peroxide (30 mL), and the contents were warmed to room temperature and stirred overnight. Solvents were removed in vacuo, and the solid residue was extracted with tetrahydrofuran (×5). The combined organic solutions were dried and evaporated. The residue was chromatographed on silica gel (elution with 1:5 hexanes−ethyl acetate) to afford **9** (2.3 g, 86%) as a white solid: mp 94−95 °C; IR (film, cm^{-1}) 3354, 3199; ^1H NMR (300 MHz, $CDCl_3$) δ 5.89 (d, J = 3.7 Hz, 1 H), 4.51 (d, J = 3.7 Hz, 1 H), 4.23 (dt, J = 6.9, 2.4 Hz, 1 H), 4.09 (d, J = 2.4 Hz, 1 H), 3.87−3.80 (m, 1 H), 3.73−3.66 (m, 1 H), 3.24 (s, 1 H), 3.25−2.95 (br s, 1 H), 2.02−1.89 (m, 2 H), 1.47 (s, 3 H), 1.29 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 111.3, 104.3, 85.2, 79.6, 75.7, 59.2, 30.3, 26.6, 26.1; MS m/z ($M^+ - CH_3$) calcd 189.0763, obsd 189.0752; $[\alpha]^{23}_D$ −11.9 (*c* 1.70, $CHCl_3$).

(3a*R*,5*R*,6*S*,6a*R*)-5-[2-(*tert*-Butyldimethylsiloxy)ethyl]-tetrahydro-2,2-dimethylfuro[2,3-*d*]-1,3-dioxol-6-ol (10). To a solution of **9** (1.25 g, 6.12 mmol) in CH_2Cl_2 (25 mL) at 0 °C were added imidazole (625 mg, 9.18 mmol) and *tert*-butyldimethylsilyl chloride (1.01 g, 6.73 mmol). The mixture was stirred at 0 °C for 1 h and quenched with saturated $NaHCO_3$ solution. The separated aqueous layer was extracted with CH_2Cl_2 (×2), the combined organic layers were dried, and the filtrate was evaporated. Chromatography of the residue on silica gel (elution with 4:1 hexanes−ethyl acetate) gave **10** (1.75 g, 90%) as a colorless oil: IR (film, cm^{-1}) 3456; ^1H NMR (300 MHz, $CDCl_3$) δ 5.79 (d, J = 3.8 Hz, 1 H), 4.45 (d, J = 3.8 Hz, 1 H), 4.14 (m, 1 H), 3.98 (d, J = 2.5 Hz, 1 H), 3.76−3.70 (m, 1 H), 3.61−3.54 (m, 1 H), 3.44 (br s, 1 H), 1.95−1.80 (m, 2 H), 1.39 (s, 3 H), 1.21 (s, 3 H), 0.81 (s, 9 H), 0.00 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 110.8, 104.2, 85.0, 79.5, 75.3, 59.5, 30.7, 26.5, 25.9, 25.6 (3 C), 17.9, −5.8, −5.9; FAB MS m/z (M^+ + H) calcd 319.19, obsd 319.20; $[\alpha]^{20}_D$ +8.09 (*c* 10.8, $CHCl_3$). Anal. Calcd for $C_{15}H_{30}O_5Si$: C, 56.57; H, 9.49. Found: C, 56.61; H, 9.53.

(3a*R*,5*R*,6a*R*)-5-[2-(*tert*-Butyldimethylsiloxy)ethyl]dihydro-2,2-dimethylfuro[2,3-*d*]-1,3-dioxol-6(5*H*)-one (11). A solution of **10** (3.00 g, 9.42 mmol) in CH_2Cl_2 (20 mL) was treated with the Dess−Martin periodinane (7.99 g, 18.8 mmol), stirred for 2 h, diluted with ether, and washed with NaOH solution (2 N) and brine. The organic phase was dried, freed of solvents, and subjected to chromatography on silica gel (elution with 2:1 hexanes−ether) to furnish **11** (2.8 g, 92%) as a colorless oil: IR (film, cm^{-1}) 1775; ^1H NMR (300 MHz, $CDCl_3$) δ 6.03 (d, J = 4.4 Hz, 1 H), 4.46 (t, J = 4.9 Hz, 1 H), 4.41 (dd, J = 4.4, 1.0 Hz, 1 H), 3.82 (ddd, J = 13.8, 8.0, 5.6 Hz, 1 H), 3.69−3.62 (m, 1 H), 2.00−1.94 (m, 2 H), 1.47 (s, 3 H), 1.40 (s, 3 H), 0.85 (s, 9 H), 0.02 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 210.6, 113.7, 103.1, 76.4, 75.8, 58.0, 34.4, 27.4, 27.2, 25.9 (3 C), 18.4, −5.5, −5.7; FAB MS m/z (M^+ + H) calcd 317.18, obsd 317.11; $[\alpha]^{20}_D$ +91.6 (*c* 1.36, $CHCl_3$).

(3a*R*,5*R*,6*R*,6a*R*)-5-[2-(*tert*-Butyldimethylsiloxy)ethyl]-tetrahydro-6-[[(1*R*,2*R*,4*R*)-2-hydroxy-7,7-dimethylbicyclo-[2.2.1]hept-1-yl]ethynyl]-2,2-dimethylfuro[2,3-*d*]-1,3-dioxol-6-ol (13). To a solution of **12**[15] (5.07 g, 15.6 mmol) in THF (30 mL) at −78 °C was added *n*-butyllithium (29.3 mL of 1.6 M in hexanes, 46.8 mmol). After 1 h of stirring at −78 °C, a solution of **11** (2.75 g, 86.9 mmol) in THF (20 mL) was introduced, and the mixture was stirred at −78 °C for 2 h, quenched with saturated $NaHCO_3$ solution, warmed to room temperature, and diluted with water and ether. The separated aqueous layer was extracted with ether (×2). The combined organic extracts were dried and filtered. Removal of solvents from the filtrate in vacuo followed by chromatography on silica gel (elution with 2:1 hexanes−ethyl acetate) furnished **13** (2.1 g, 50%) as a colorless oil: IR (film, cm^{-1}) 3428; ^1H NMR (300 MHz, $CDCl_3$) δ 5.77 (d, J = 3.5 Hz, 1 H), 4.57 (d, J = 3.5 Hz, 1 H), 4.30 (br s, 1 H), 4.03 (t, J = 6.7 Hz, 1 H), 3.89−3.82 (m, 1 H), 3.78−3.70 (m, 2 H), 2.35 (br s, 1 H), 2.16−2.06 (m, 1 H), 1.97−1.68 (m, 6 H), 1.57 (s, 3 H), 1.35 (s, 3 H), 1.31−1.22 (m, 1 H), 1.13 (s, 3 H), 1.11−1.04 (m, 1 H), 0.94 (s, 3 H), 0.89 (s, 9 H), 0.083 (s, 3 H), 0.077 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 113.2, 103.9, 88.0, 84.6, 83.8. 80.1, 78.2, 76.2, 60.5, 50.8, 49.7, 44.0, 39.4, 32.6, 32.4, 27.2, 26.6, 26.5, 25.9 (3 C), 21.1, 20.4, 18.3, −5.4, −5.5; FAB MS m/z (M^+ + H) calcd 481.30, obsd 481.36; $[\alpha]^{24}_D$ +9.62 (*c* 1.83, $CHCl_3$). Anal. Calcd for $C_{26}H_{44}O_6Si$: C, 64.96; H, 9.23. Found: C, 64.82; H, 9.18.

(3a*R*,5*R*,6*R*,6a*R*)-Tetrahydro-6-hydroxy-6-[(*E*)-2-[(1*S*,2*R*,4*R*)-2-hydroxy-7,7-dimethylbicyclo[2.2.1]hept-1-yl]vinyl]-2,2-dimethylfuro[2,3-*d*]-1,3-dioxole-5-ethanol (14). A solution of **13** (0.85 g, 1.8 mmol) in THF (20 mL) at 0 °C was treated with lithium aluminum hydride (336 mg, 8.84 mmol), heated to reflux for 3 h, cooled to 0 °C, carefully quenched with saturated NH_4Cl solution, and diluted with saturated sodium potassium tartrate solution and ether. The separated aqueous layer was extracted with ether (×4). The combined organic extracts were dried and filtered. Solvent evaporation followed by chromatography on silica gel (elution with 1:5 hexanes−ethyl acetate) gave **14** (638 mg, 98%) as a white foam: IR (film, cm^{-1}) 3408; ^1H NMR (300 MHz, $CDCl_3$) δ 6.08 (d, J = 16.3 Hz, 1 H), 5.79 (d, J = 3.8 Hz, 1 H), 5.36 (d, J = 16.3 Hz, 1 H), 4.25 (d, J = 3.8 Hz, 1 H), 3.99 (t, J = 6.6 Hz, 1 H), 3.78−3.63 (m, 3 H), 3.18 (br s, 3 H), 1.84−1.63 (m, 7 H), 1.59 (s, 3 H), 1.33 (s, 3 H), 1.14 (s, 3 H), 1.10−0.98 (m, 2 H), 0.77 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 130.5, 127.6, 112.6, 103.5, 83.4, 80.4, 80.3, 80.2, 60.1, 54.9, 47.7, 45.6, 40.3, 31.4, 29.9, 26.8, 26.43, 26.39, 20.8, 20.4; MS m/z (M^+) calcd 369.2276, obsd 369.2241; $[\alpha]^{24}_D$ −11.1 (*c* 3.00, CH_2Cl_2). Anal. Calcd for $C_{20}H_{32}O_6$: C, 65.19; H, 8.75. Found: C, 64.99; H, 8.68.

(3a*R*,5*R*,6*R*,6a*R*)-5-[2-(*tert*-Butyldimethylsiloxy)ethyl]-tetrahydro-6-[(*E*)-2-[(1*S*,2*R*,4*R*)-2-hydroxy-7,7-dimethylbicyclo[2.2.1]hept-1yl]vinyl]-2,2-dimethylfuro[2,3-*d*]-1,3-dioxol-6-ol (15). To a solution of **14** (638 mg, 1.73 mmol) in CH_2Cl_2 (10 mL) at 0 °C were added imidazole (181 mg, 2.65 mmol) and *tert*-butyldimethylsilyl chloride (320 mg, 2.12 mmol). The mixture was stirred at 0 °C for 1 h and quenched with saturated $NaHCO_3$ solution. The separated aqueous layer was extracted with CH_2Cl_2 (×2), and the combined organic layers were dried and concentrated. The residue was chromatographed on silica gel (elution with 2:1 hexanes−ethyl acetate) to give **15** (768 mg, 92%) as a colorless oil: IR (film, cm^{-1}) 3442; ^1H NMR (300 MHz, $CDCl_3$) δ 6.13 (d, J = 16.3 Hz, 1 H), 5.79 (d, J = 3.8 Hz, 1 H), 5.38 (d, J = 16.2 Hz, 1 H), 4.25 (d, J = 3.8 Hz, 1 H), 3.99 (dd, J = 8.0, 4.8 Hz, 1 H), 3.78−3.63 (m, 3 H), 1.87−1.61 (m, 7 H), 1.58 (s, 3 H), 1.34 (s, 3 H), 1.15 (s, 3 H), 1.10−0.98 (m, 2 H), 0.87 (s, 9 H), 0.77 (s, 3 H), 0.04 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 130.0, 128.3, 112.4, 103.5, 83.6, 80.4, 80.1, 78.8, 60.1, 55.0, 47.9, 45.5, 40.3, 32.1, 29.9, 27.0, 26.50, 26.45, 25.9 (3 C), 20.7, 20.4, 18.2, −5.4 (2 C); FAB MS m/z (M^+ + H) calcd 483.31, obsd 483.40; $[\alpha]^{24}_D$ −5.90 (*c* 2.93, CH_2Cl_2). Anal. Calcd for $C_{26}H_{46}O_6Si$: C, 64.69; H, 9.60. Found: C, 64.47; H, 9.52.

(1*S*,4*R*)-1-[(*E*)-2-[(3a*R*,5*R*,6*R*,6a*R*)-5-[2-(*tert*-Butyldimethylsiloxy)-ethyl]tetrahydro-6-hydroxy-2,2-dimethylfuro[2,3-*d*]-1,3-dioxol-6-yl]vinyl]-7,7-dimethylbicyclo[2.2.1]-

heptan-2-one (16). A solution of **15** (768 mg, 1.59 mmol) in CH_2Cl_2 (20 mL) was treated with the Dess−Martin periodinane (1.13 g, 2.65 mmol), stirred for 30 min, diluted with ether, filtered, and washed with aqueous NaOH solution (2 N) and brine. The separated organic layer was dried and freed of solvent in advance of chromatography (silica gel, elution with 3:1 hexanes−ethyl acetate). There was obtained 749 mg (98%) of **16** as a colorless oil: IR (film, cm^{-1}) 3466, 1743; ^1H NMR (300 MHz, $CDCl_3$) δ 5.91 (d, J = 16.2 Hz, 1 H), 5.74 (d, J = 3.6 Hz, 1 H), 5.53 (d, J = 16.1 Hz, 1 H), 4.24 (d, J = 3.5 Hz, 1 H), 3.96 (dd, J = 7.6, 5.3 Hz, 1 H), 3.75−3.60 (m, 2 H), 3.01 (br s, 1 H), 2.40 (dd, J = 18.2, 3.8 Hz, 1 H), 2.10 (t, J = 3.7 Hz, 1 H), 1.98−1.91 (m, 2 H), 1.85 (d, J = 18.2 Hz, 1 H), 1.75−1.58 (m, 2 H), 1.54 (s, 3 H), 1.48−1.35 (m, 2 H), 1.30 (s, 3 H), 0.90 (s, 6 H), 0.84 (s, 9 H), 0.01 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 216.4, 130.9, 125.5, 112.3, 103.4, 83.8, 79.9, 78.8, 63.1, 60.0, 48.6, 43.6 43.2, 31.9, 27.0, 26.9, 26.4, 26.3, 25.8 (3 C), 20.1, 19.4, 18.2, −5.46, −5.49; FAB MS m/z (M^+ + H) calcd 481.30, obsd 481.39; $[\alpha]^{24}_D$ +16.0 (c 5.44, CH_2Cl_2). Anal. Calcd for $C_{26}H_{44}O_6Si$: C, 64.96; H, 9.23. Found: C, 64.87; H, 9.22.

(1*S*,4*R*)-1-[(*E*)-2-[(3a*R*,5*R*,6*R*,6a*R*)-6-(Benzyloxy)-5-[2-(*tert*-butyldimethylsiloxy)ethyl]tetrahydro-2,2-dimethylfuro[2,3-*d*]-1,3-dioxol-6-yl]vinyl]-7,7-dimethylbicyclo-[2.2.1]heptan-2-one (17). A solution of **16** (704 mg, 1.56 mmol) in DMF (20 mL) at 0 °C was treated with sodium hydride (75 mg, 0.031 mol), stirred at 0 °C for 15 min before benzyl bromide (0.37 mL, 0.031 mol) and a catalytic amount of tetra-*n*-butylammonium iodide were introduced, warmed to room temperature, stirred for another 4 h, cooled to 0 °C, and quenched with saturated NH_4Cl solution. Water and ether were added, and the separated aqueous layer was extracted with ether (×2). The combined organic extracts were dried and filtered. Removal of solvents from the filtrate in vacuo followed by chromatography (silica gel, elution with 5:1 hexanes−ether) afforded **17** (793 mg, 89%) as a white solid: mp 95−96 °C; IR (film, cm^{-1}) 1743; ^1H NMR (300 MHz, $CDCl_3$) δ 7.42−7.22 (m, 5 H), 5.83 (d, J = 3.7 Hz, 1 H), 5.73 (d, J = 16.6 Hz, 1 H), 5.42 (d, J = 16.6 Hz, 1 H), 4.70 (s, 2 H), 4.61 (d, J = 3.7 Hz, 1 H), 4.26 (dd, J = 9.3, 3.4 Hz, 1 H), 3.79−3.65 (m, 2 H), 2.45 (ddd, J = 18.3, 4.7, 2.0 Hz, 1 H), 2.14 (m, 1 H), 2.08−1.96 (m, 2 H), 1.91 (d, J = 18.3 Hz, 1 H), 1.83−1.72 (m, 1 H), 1.61 (s, 3 H), 1.59−1.40 (m, 3 H), 1.38 (s, 3 H), 0.93 (s, 3 H), 0.90 (s, 3 H), 0.87 (s, 9 H), 0.03 (s, 3 H), 0.02 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 216.3, 138.8, 129.5, 128.1 (2 C), 128.0, 127.5 (2 C), 127.2, 112.5, 104.2, 85.5, 81.6, 78.2, 66.9, 63.4, 60.2, 48.7, 43.6, 44.4, 33.0, 27.0, 26.9, 26.7, 26.6, 25.9 (3 C), 20.2, 19.6, 18.2, −5.4 (2 C); FAB MS m/z (M^+) calcd 571.35, obsd 571.18; $[\alpha]^{24}_D$ +37.7 (c 2.87, CH_2Cl_2). Anal. Calcd for $C_{33}H_{50}O_6Si$: C, 69.44; H, 8.83. Found: C, 69.48; H, 8.84.

(1*S*,4*R*)-1-[(*E*)-2-[(2*R*,3*S*,4*R*)-3-(Benzyloxy)-2-[2-(*tert*-butyldimethylsiloxy)ethyl]tetrahydro-4,5-dihydroxy-3-furyl]vinyl]-7,7-dimethylbicyclo[2.2.1]heptan-2-one (19). Titanium tetrachloride (7.6 mL of 1.0 M in CH_2Cl_2, 7.6 mmol) in CH_2Cl_2 (20 mL) at −78 °C was treated with a solution of **17** (1.08 g, 1.89 mmol) in CH_2Cl_2 (2 mL) in one portion. The red solution was immediately poured into a mixture of saturated $NaHCO_3$ solution (100 mL) and ether (100 mL) at 0 °C. The mixture was stirred at room temperature overnight, and the separated aqueous layer was extracted with ether (×3). The combined organic extracts were dried and evaporated, and the residue was purified chromatographically (silica gel, elution with 2:1 hexanes−ethyl acetate) to give the less polar **19** (430 mg, 43%) as a colorless oil: IR (film, cm^{-1}) 3424, 1741; ^1H NMR (300 MHz, $CDCl_3$) δ 7.39−7.27 (m, 5 H), 5.87 (d, J = 16.6 Hz, 1 H), 5.73 (d, J = 16.6 Hz, 1 H), 5.28 (br s, 1 H), 4.69 (d, J = 11.2 Hz, 1 H), 4.57 (d, J = 11.2 Hz, 1 H), 4.39 (dd, J = 10.3, 2.8 Hz, 1 H), 4.17 (d, J = 4.2 Hz, 1 H), 3.81−3.72 (m, 2 H), 2.47 (ddd, J = 18.3, 4.6, 2.4 Hz, 1 H), 2.17 (m, 1 H), 2.06−2.00 (m, 2 H), 1.93 (d, J = 18.3 Hz, 1 H), 1.84−1.74 (m, 2 H), 1.61−1.42 (m, 4 H), 0.97 (s, 3 H), 0.93 (s, 3 H), 0.89 (s, 9 H), 0.063 (s, 3 H), 0.056 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 215.9, 137.3, 129.8, 128.5 (2 C), 128.3, 127.9, 127.6 (2 C), 96.4, 85.5, 78.2, 73.7, 67.0, 63.3, 60.1, 49.0, 43.7, 43.3, 35.2, 27.5, 27.1 25.9 (3 C), 20.3, 19.7, 18.3, −5.3 (2 C); FAB MS m/z (M^+) calcd 531.31, obsd 531.38; $[\alpha]^{24}_D$ +52.6 (c 1.14, $CHCl_3$).

Continued elution (ethyl acetate) gave **18** (220 mg, 28%), also as a colorless oil: IR (film, cm^{-1}) 3409, 1736; ^1H NMR (300 MHz, $CDCl_3$) δ 7.39−7.27 (m, 5 H), 5.84 (d, J = 16.7 Hz, 1 H), 5.72 (d, J = 16.7 Hz, 1 H), 5.33 (d, J = 4.2 Hz, 1 H), 4.70 (d, J = 11.1 Hz, 1 H), 4.57 (d, J = 11.1 Hz, 1 H), 4.38 (dd, J = 9.7, 3.7 Hz, 1 H), 4.22 (d J = 4.2 Hz, 1H), 3.80−3.76 (m, 2 H), 2.75−2.25 (br s, 3 H), 2.51−2.43 (m, 1 H), 2.18−2.15 (m, 1 H), 2.09−1.98 (m, 2 H), 1.93 (d, J = 18.3 Hz, 1 H), 1.85−1.71 (m, 1 H), 1.69−1.54 (m, 2 H), 1.49−1.42 (m, 1 H), 0.97 (s, 3 H), 0.93 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 216.0, 137.5, 130.1, 128.5 (2 C), 128.3, 128.0, 127.7 (2 C), 96.3, 85.6, 80.7, 73.0, 67.2, 63.4, 60.6, 49.0, 43.6, 43.3, 33.7, 27.5, 27.1, 20.3, 19.7; FAB MS m/z (M^+) calcd 417.23, obsd 417.26; $[\alpha]^{22}_D$ +3.3 (c 0.27, $CHCl_3$).

(1*S*,4*R*)-1-[(1*E*,3*S*,4*R*)-3-(Benzyloxy)-6-(*tert*-butyldimethylsiloxy)-4-hydroxy-3-(hydroxymethyl)-1-hexenyl]-7,7-dimethylbicyclo[2.2.1]heptan-2-one (20). To a solution of **19** (1.22 g, 2.30 mmol) in CH_2Cl_2 (20 mL) at 0 °C was added the Dess−Martin periodinane (1.96 g, 4.60 mmol). The white suspension was stirred at 0 °C for 30 min, diluted with ether, filtered through a pad of Celite, and concentrated. Column chromatography of the residue (silica gel, elution with 6:1 hexanes−ethyl acetate) furnished the formyl ester as a colorless oil. This oil was dissolved in methanol (10 mL) and cooled to −40 °C. Sodium borohydride (104 mg, 2.76 mmol) was added, and the white mixture was stirred at −40 °C for 1 h. Aqueous NaOH solution (2 N, 10 mL) was introduced, and the mixture was warmed to room temperature, diluted with saturated NH_4Cl solution and ether, and extracted with ether (×2). The combined organic phases were dried, freed of solvent, and chromatographed on silica gel (elution with 2:1 hexanes−ethyl acetate). There was obtained 752 mg (65%) of **20** as a white solid: mp 77−78 °C; IR (film, cm^{-1}) 3440, 1742; ^1H NMR (300 MHz, $CDCl_3$) δ 7.42−7.23 (m, 5 H), 5.74 (d, J = 16.7 Hz, 1 H), 5.49 (d, J = 16.7 Hz, 1 H), 4.62 and 4.58 (ABq, J = 10.9 Hz, 2 H), 4.06−4.01 (m, 2 H), 3.95−3.77 (m, 3 H), 3.58 (d, J = 2.5 Hz, 1 H), 3.15 (t, J = 6.0 Hz, 1 H), 2.44 (ddd, J = 18.3, 4.8, 2.2 Hz, 1 H), 2.14 (t, J = 4.3 Hz, 1 H), 2.06−1.84 (m, 3 H), 1.90 (d, J = 18.3 Hz, 1 H), 1.74−1.62 (m, 1 H), 1.59−1.39 (m, 2 H), 0.92 (s, 3 H), 0.91 (s, 3 H), 0.88 (s, 9 H), 0.52 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 216.5, 138.9, 131.1, 128.3 (2 C), 128.1, 127.8 (2 C), 127.4, 80.9, 75.6, 64.7, 63.6, 62.9, 61.9, 48.6, 43.6, 43.3, 33.6, 27.0, 26.7, 25.9 (3 C), 20.2, 19.6, 18.2, −5.49, −5.54; FAB MS m/z (M^+ + H) calcd 503.32, obsd 503.40; $[\alpha]^{23}_D$ +13.4 (c 2.21, $CHCl_3$). Anal. Calcd for $C_{29}H_{46}O_5Si$: C, 69.28; H, 9.22. Found: C, 69.33; H, 9.28.

(1*S*,4*R*)-1-[(*E*)-2-[(2*R*,3*S*)-3-(Benzyloxy)-2-[2-(*tert*-butyldimethyl-siloxy)ethyl]-3-oxetanyl]vinyl]-7,7-dimethylbicyclo[2.2.1]heptan-2-one (21). A cold (−78 °C) solution of **20** (96 mg, 0.19 mmol) in THF was treated with potassium hexamethyldisilazide (0.76 mL of 0.5 M in toluene, 0.38 mmol) and stirred at −78 °C for 15 min before a solution of *N*-(5-chloro-2-pyridyl)triflimide (138 mg, 0.383 mmol) in THF (0.5 mL) was introduced dropwise. The mixture was stirred at −78 °C for another 10 min before being quenched with saturated $NaHCO_3$ solution, diluted with ether, and extracted with ether (×2). The combined organic layers were dried and evaporated prior to purification of the residue by chromatography on silica gel (elution with 6:1 hexanes−ethyl acetate). There was obtained 58 mg (63%) of **21** as a colorless oil: IR (film, cm^{-1}) 1743; ^1H NMR (300 MHz, $CDCl_3$) δ 7.41−7.27 (m, 5 H), 5.84 (s, 2 H), 4.96 (dd, J = 8.7, 5.0 Hz, 1 H), 4.67 (d, J = 6.8 Hz, 1 H), 4.54 (d, J = 7.0 Hz, 1 H), 4.51 (d, J = 11.3 Hz, 1 H), 4.35 (d, J = 11.3 Hz, 1 H), 3.69−3.58 (m, 2 H), 2.48 (ddd, J = 18.3, 4.8, 1.8 Hz, 1 H), 2.19−2.16 (m, 1 H), 2.11−2.00 (m, 2 H), 1.94 (d, J = 18.3 Hz, 1 H), 1.89−1.73 (m, 2 H), 1.60 (t, J = 9.2 Hz, 1 H), 1.46 (t, J = 9.2 Hz, 1 H), 0.98 (s, 3 H), 0.95 (s, 3 H), 0.87 (s, 9 H), 0.03 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 216.2, 138.1, 130.4, 128.5, 128.4 (2 C), 127.7 (2 C), 127.6, 87.7, 81.7, 75.9, 66.4, 63.3, 58.5, 48.7, 43.6, 43.4,

36.0, 27.3, 27.1, 25.9 (3 C), 20.3, 19.6, 18.3, −5.4 (2 C); FAB MS *m*/*z* ($M^+ + H$) calcd 485.31, obsd 485.41; $[\alpha]^{23}_D$ +42 (*c* 0.86, $CHCl_3$).

(1*S*,3*R*,4*S*)-1-[(*E*)-2-[(2*R*,3*S*)-3-(Benzyloxy)-2-[2-(*tert*-butyldimethylsiloxy)ethyl]-3-oxetanyl]vinyl]-3-hydroxy-7,7-dimethylbicyclo[2.2.1]heptan-2-one (22). A solution of **21** (677 mg, 1.40 mmol) in THF (10 mL) at −78 °C was treated with potassium hexamethyldisilazide (5.6 mL of 0.5 M in toluene, 2.8 mmol) and allowed to stir at −78 °C for 1 h. Trimethylsilyl chloride (0.35 mL, 0.028 mol) was added at −78 °C followed by triethylamine (0.52 mL). The mixture was allowed to warm to room temperature and diluted with ether and saturated $NaHCO_3$ solution. The separated aqueous layer was extracted with ether (×2), the combined organic extracts were dried, and the filtrate was concentrated to give the silyl enol ether, which was dissolved in a mixture of water (10 mL), acetone (10 mL), and CH_2Cl_2 (10 mL). A catalytic amount of 18-crown-6 and $NaHCO_3$ (3.50 g) were added followed by oxone (3.50 g) in small portions. The mixture was allowed to stir for another hour, diluted with water and ether, and extracted with ether (×2). The combined organic layers were dried and filtered. Removal of solvents under reduced pressure gave a residue which was dissolved in THF (5 mL) and cooled to 0 °C. Tetra-*n*-butylammonium fluoride (1.40 mL of 1.0 M in THF, 1.40 mmol) was added and the reaction mixture was stirred at 0 °C for 30 min, diluted with ether and water, and extracted with ether (×2). The combined organic extracts were dried, filtered, and freed of solvents in vacuo. Column chromatography of the residue (silica gel, elution with 2:1 hexanes−ethyl acetate) gave **22** (525 mg, 75%) as a colorless oil: IR (film, cm^{-1}) 3415, 1749; ^1H NMR (300 MHz, $CDCl_3$) δ 7.40−7.26 (m, 5 H), 5.90 and 5.86 (ABq, J = 16.6 Hz, 2 H), 4.97 (dd, J = 8.5, 5.1 Hz, 1 H), 4.67 (d, J = 6.8 Hz, 1 H), 4.54 (d, J = 6.7 Hz, 1 H), 4.50 (d, J = 11.2 Hz, 1 H), 4.34 (d, J = 11.2 Hz, 1 H), 3.80 (s, 1 H), 3.67−3.62 (m, 2 H), 3.05 (br s, 1 H), 2.18−1.89 (m, 3 H), 1.86−1.75 (m, 2 H), 1.65−1.58 (m, 1 H), 1.50−1.43 (m, 1 H), 1.11 (s, 3 H), 0.96 (s, 3 H), 0.87 (s, 9 H), 0.03 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 217.0, 138.0, 130.6, 128.4 (2 C), 127.8, 127.7 (2 C), 127.6, 87.7, 81.6, 77.6, 75.8, 66.4, 62.5, 58.5, 49.5, 48.9, 36.0, 26.0, 25.9 (3 C), 25.0, 21.5, 20.6, 18.2, −5.4 (2 C); FAB MS *m*/*z* (M^+) calcd 501.30, obsd 501.33; $[\alpha]^{24}_D$ +46.6 (*c* 3.29, $CHCl_3$).

(1*S*,3*R*,4*S*)-1-[(*E*)-2-[(2*R*,3*S*)-3-(Benzyloxy)-2-[2-(*tert*-butyldimethylsiloxy)ethyl]-3-oxetanyl]vinyl]-3-(methoxymethoxy)-7,7-dimethylbicyclo[2.2.1]heptan-2-one (23). A cold (0 °C) solution of **22** (525 mg, 1.05 mmol) in CH_2Cl_2 (10 mL) at 0 °C was treated with diisopropylethylamine (0.91 mL, 0.052 mol) and methoxymethyl chloride (0.24 mL, 0.031 mmol). The cooling bath was removed, and the mixture was allowed to stir at room temperature for 5 h, quenched with saturated $NaHCO_3$ solution, and diluted with ether. The separated aqueous layer was extracted with ether (×2), and the combined organic layers were dried and evaporated. Chromatography of the residue on silica gel (elution with 4:1 hexanes−ethyl acetate) afforded **23** (474 mg, 83%) as a colorless oil: IR (film, cm^{-1}) 1755; ^1H NMR (300 MHz, $CDCl_3$) δ 7.41−7.25 (m, 5 H), 5.86 (s, 2 H), 4.96 (dd, J = 8.6, 5.1 Hz, 1 H), 4.84 (d, J = 6.6 Hz, 1 H), 4.73 (d, J = 6.6 Hz, 1 H), 4.66 (d, J = 6.8 Hz, 1 H), 4.53 (d, J = 6.6 Hz, 1 H), 4.51 (d, J = 11.2 Hz, 1 H), 4.34 (d, J = 11.2 Hz, 1 H), 3.74 (s, 1 H), 3.66−3.62 (m, 2 H), 3.42 (s, 3 H), 2.19 (d, J = 4.3 Hz, 1 H), 2.15−1.96 (m, 2 H), 1.89−1.75 (m, 2 H), 1.64−1.56 (m, 1 H), 1.51−1.44 (m, 1 H), 1.10 (s, 3 H), 0.96 (s, 3 H), 0.87 (s, 9 H), 0.03 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 214.6, 138.1, 130.7, 128.4 (2 C), 127.9, 127.7 (2 C), 127.6, 96.7, 87.6, 81.6, 81.3, 75.9, 66.4, 62.4, 58.5, 55.5, 48.7, 48.6, 36.0, 26.2, 25.9 (3 C), 25.0, 21.4, 20.4, 18.3, −5.4 (2 C); FAB MS *m*/*z* ($M^+ + H$) calcd 545.35, obsd 545.11; $[\alpha]^{22}_D$ +59.5 (*c* 1.91, $CHCl_3$).

(1*S*,2*S*,3*R*,4*S*)-1-[(*E*)-2-[(2*R*,3*S*)-3-(Benzyloxy)-2-[2-(*tert*-butyldimethylsiloxy)ethyl]-3-oxetanyl]vinyl]-3-(methoxymethoxy)-7,7-dimethyl-2-[(*E*)-1-propenyl]bicyclo[2.2.1]-heptan-2-ol (24). To a solution of *trans*-1-bromo-1-propene (0.37 mL, 0.044 mol) in THF (10 mL) at −78 °C was added *tert*-butyllithium (5.1 mL of 1.7 M in pentane, 8.7 mmol). After 15 min, a solution of **23** (474 mg, 0.870 mmol) in THF (2 mL) was introduced, and the solution was stirred at −78 °C for another 15 min, quenched with saturated $NaHCO_3$ solution, and diluted with ether. The separated aqueous phase was extracted with ether (×2), the combined organic extracts were dried and concentrated, and the residue was chromatographed on silica gel (elution with 4:1 hexanes−ethyl acetate) to furnish **24** (420 mg, 82%) as a colorless oil: IR (film, cm^{-1}) 3529; ^1H NMR (300 MHz, $CDCl_3$) δ 7.40−7.25 (m, 5 H), 6.21 (d, J = 16.6 Hz, 1 H), 5.74 (dq, J = 15.3, 6.2 Hz, 1 H), 5.59 (dd, J = 15.3, 1.1 Hz, 1 H), 5.49 (d, J = 16.6 Hz, 1 H), 4.92 (dd, J = 8.6, 5.0 Hz, 1 H), 4.71 (s, 2 H), 4.63 (s, 2 H), 4.46 (d, J = 11.2 Hz, 1 H), 4.30 (d, J = 11.2 Hz, 1 H), 3.69 (s, 1 H), 3.67−3.59 (m, 2 H), 3.39 (s, 3 H), 3.00 (s, 1 H), 1.97 (d, J = 5.0 Hz, 1 H), 1.90−1.74 (m, 3 H), 1.70 (d, J = 6.3 Hz, 3 H), 1.63 (dd, J = 12.0, 4.7 Hz, 1 H), 1.51−1.42 (m, 1 H), 1.34 (s, 3 H), 1.15−1.03 (m, 1 H), 0.88 (s, 9 H), 0.82 (s, 3 H), 0.03 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 138.4, 135.6, 132.6, 128.3 (2 C), 128.0, 127.8 (2 C), 127.5, 124.4, 97.1, 88.3, 87.8, 82.4, 82.0, 75.7, 66.1, 59.0, 58.7, 55.6, 50.7, 50.6, 36.1, 26.5, 25.9 (3 C), 24.2, 22.6, 22.3, 18.3, 17.9, −5.4 (2 C); FAB MS *m*/*z* (M^+) calcd 587.38, obsd 587.20; $[\alpha]^{24}_D$ +14 (*c* 0.69, $CHCl_3$).

(1*S*,2*R*,5*S*,6*R*,7*R*)-6-[(2*R*,3*S*)-3-(Benzyloxy)-2-[2-(*tert*-butyldimethylsiloxy)ethyl]-3-oxetanyl]-2-(methoxymethoxy)-5,11,11-trimethylbicyclo[6.2.1]undec-7-en-3-one (25). To a mixture of potassium hydride (18 mg, 0.87 mmol) and 18-crown-6 (46 mg, 0.17 mmol) in THF (5 mL) at 0 °C was added a solution of **24** (98 mg, 0.17 mmol) in THF (1 mL). After being stirred at 0 °C for 15 min, the mixture was quenched by slow transfer to a beaker of silica gel cooled to 0 °C. The silica was separated by filtration and washed extensively with ether. Solvent evaporation followed by chromatography (silica gel, elution with 3:1 hexanes−ethyl acetate) afforded **25** (79 mg, 77%) as a colorless oil: IR (film, cm^{-1}) 1704; ^1H NMR (300 MHz, $CDCl_3$) δ 7.45−7.24 (m, 5 H), 5.15 (d, J = 9.7 Hz, 1 H), 5.05 and 5.02 (ABq, J = 12.7 Hz, 2 H), 4.95 (dd, J = 10.3, 3.3 Hz, 1 H), 4.76 and 4.68 (ABq, J = 8.0 Hz, 2 H), 4.61 (d, J = 6.9 Hz, 1 H), 4.43 (d, J = 6.9 Hz, 1 H), 3.89 (d, J = 2.0 Hz, 1 H), 3.73−3.57 (m, 2 H), 3.34 (s, 3 H), 3.13−3.04 (m, 1 H), 2.75 (t, J = 10.6 Hz, 1 H), 2.66−2.57 (m, 1 H), 2.51−2.36 (m, 1 H), 2.32−2.21 (m, 2 H), 2.18 (dd, J = 8.6, 1.5 Hz, 1 H), 2.01−1.83 (m, 2 H), 1.78−1.71 (m, 1 H), 1.67 (dd, J = 15.5, 1.2 Hz, 1 H), 1.15 (s, 3 H), 1.06 (s, 3 H), 0.90 (d, J = 7.0 Hz, 3 H), 0.85 (s, 9 H), 0.01 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 207.6, 146.2, 139.6, 128.4 (2 C), 127.1, 126.5 (2 C), 124.2, 95.1, 87.5, 86.7, 82.6, 78.1, 65.2, 58.9, 55.7, 54.0, 50.4, 48.0, 45.4, 35.2, 34.8, 26.1, 26.0, 25.9 (3 C), 24.4, 20.1, 20.0, 18.2, −5.28, −5.31; FAB MS *m*/*z* ($M^+ + H$) calcd 587.38, obsd 587.38; $[\alpha]^{23}_D$ −68 (*c* 0.95, $CHCl_3$).

Hydride Reduction of 25. To a solution of **25** (61 mg, 0.10 mmol) in ether (0.5 mL) at 0 °C was added lithium aluminum hydride (12 mg, 0.32 mmol). The cooling bath was removed, and the mixture was allowed to stir at room temperature for 3 h, cooled to 0 °C, and quenched with saturated NH_4Cl solution. Water and ether were added, and the separated aqueous layer was extracted with ether (×2). The combined organic extracts were dried, freed of solvents, and chromatographed on silica gel (elution with 2:1 hexanes−ethyl acetate) to provide the α-carbinol as a single diastereomer (53 mg, 86%) as a colorless oil: IR (film, cm^{-1}) 3480; ^1H NMR (300 MHz, $CDCl_3$) δ 7.41−7.28 (m, 5 H), 5.16 (d, J = 11.3 Hz, 1 H), 5.05−4.96 (m, 3 H), 4.81 and 4.77 (ABq, J = 7.8 Hz, 2 H), 4.64 and 4.61 (ABq, J = 6.7 Hz, 2 H), 3.77−3.60 (m, 2 H), 3.47 (d, J = 4.9 Hz, 1 H), 3.39 (s, 3H), 3.33−3.29 (m, 1 H), 2.93 (d, J = 9.8 Hz, 1 H), 2.80 (dd, J = 11.6, 7.7 Hz, 1 H), 2.49−2.41 (m, 1 H), 2.36−2.23 (m, 2 H), 2.22−1.95 (m, 5 H), 1.38−1.30 (m, 1 H), 1.28 (s, 3 H), 1.12 (d, J = 7.0 Hz, 3 H), 1.05 (s, 3 H), 1.03−0.90 (m, 1 H), 0.86 (s, 9 H), 0.02 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 143.4, 139.7, 128.3 (2 C), 127.1, 126.6 (2 C), 121.8, 98.3, 95.0, 86.6, 83.8, 76.8, 68.3, 65.4, 59.0, 55.7, 52.8, 47.7, 46.0, 41.2, 35.2, 30.9, 27.3, 25.9 (3 C), 25.8, 23.0, 22.9, 21.4, 18.3, −5.32, −5.35; FAB MS *m*/*z* ($M^+ + H$) calcd 589.39, obsd 589.18; $[\alpha]^{22}_D$ −121 (*c* 1.29, $CHCl_3$).

To a suspension of sodium hydride (4.0 mg, 0.16 mmol) in THF (1 mL) at 0 °C was added a solution of the α-carbinol (48 mg, 0.082 mmol) in DMF (0.5 mL). The mixture was stirred

at 0 °C for 15 min, and *p*-methoxybenzyl chloride (26 mg, 0.16 mmol) together with a catalytic amount of tetra-*n*-butylammonium iodide in DMF (0.5 mL) was introduced. The mixture was warmed to room temperature, stirred for another 2 h, cooled to 0 °C, and quenched with saturated NH_4Cl solution. Water and ether were added, and the separated aqueous layer was extracted with ether (×2). The combined organic extracts were dried, filtered, and evaporated. Chromatography of the residue on silica gel (elution with 5:1 hexanes−ether) gave the *p*-methoxybenzyl ether (46 mg, 79%) as a colorless oil: IR (film, cm^{-1}) 1613; ^1H NMR (300 MHz, $CDCl_3$) δ 7.41−7.22 (m, 7 H), 6.88−6.83 (m, 2 H), 5.20 (d, J = 11.6 Hz, 1 H), 5.05−4.95 (m, 3 H), 4.78 (s, 2 H), 4.68 and 4.66 (ABq, J = 6.5 Hz, 2 H), 4.49 (d, J = 10.2 Hz, 1 H), 4.19 (d, J = 10.1 Hz, 1 H), 3.91 (d, J = 4.4 Hz, 1 H), 3.79 (s, 3 H), 3.78−3.61 (m, 2 H), 3.35 (s, 3 H), 3.08 (d, J = 3.6 Hz, 1 H), 2.76 (dd, J = 11.6, 8.0 Hz, 1 H), 2.55−2.12 (m, 6 H), 2.03−1.97 (m, 2 H), 1.34 (s, 3 H), 1.34−1.24 (m, 2 H), 1.08 (s, 3 H), 1.02 (d, J = 7.0 Hz, 3 H), 0.87 (s, 9 H), 0.03 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 159.1, 143.3, 139.6, 130.6, 129.5 (2 C), 128.3 (2 C), 127.1, 126.6 (2 C), 122.0, 113.7 (2 C), 95.7, 86.6, 83.7, 82.0, 77.7, 76.9, 69.8, 65.3, 59.0, 55.3, 55.2, 51.3, 48.0, 46.1, 37.6, 35.2, 31.0, 27.4, 26.0, 25.9 (3 C), 23.1, 22.7, 21.5, 18.3, −5.3, −5.4; FAB MS m/z (M^+ + H) calcd 709.45, obsd 709.15; $[\alpha]^{23}_D$ −110 (c 1.09, $CHCl_3$).

(1*S*,2*R*,4*R*,5*R*,6*S*,7*E*)-6-[(2*R*,3*S*)-3-(Benzyloxy)-2-[2-(*tert*-butyldimethylsiloxy)ethyl]-3-oxetanyl]-4-hydroxy-2-(methoxymethoxy)-5,11,11-trimethylbicyclo[6.2.1]undec-7-en-3-one (26). To a solution of **25** (70 mg, 0.12 mmol) and 18-crown-6 (63 mg, 0.24 mmol) in THF (5 mL) at −78 °C was added potassium hexamethyldisilazide (0.48 mL of 0.5 M in toluene, 0.24 mmol). The mixture was stirred at −78 °C for 15 min, and oxygen was bubbled through for another 15 min. A solution of triphenylphosphine (63 mg, 0.24 mmol) in THF (1 mL) was added. After being quenched with saturated $NaHCO_3$ solution, the mixture was warmed to room temperature and diluted with ether. The separated aqueous layer was extracted with ether (×2). The combined organic layers were dried and evaporated, followed by chromatography on silica gel (elution with 2:1 hexanes−ethyl acetate) to give **26** (60 mg, 84%) as a colorless oil: IR (film, cm^{-1}) 3377, 1705; ^1H NMR (300 MHz, $CDCl_3$) δ 7.45−7.24 (m, 5 H), 5.10 (d, J = 8.7 Hz, 1 H), 5.06 and 5.02 (ABq, J = 12.6 Hz, 2 H), 4.93 (dd, J = 8.0, 5.7 Hz, 1 H), 4.77 (s, 2 H), 4.63 (d, J = 6.8 Hz, 1 H), 4.23 (d, J = 6.8 Hz, 1 H), 4.18 (d, J = 1.8 Hz, 1 H), 3.72−3.56 (m, 2 H), 3.48 (t, J = 10.5 Hz, 1 H), 3.35 (s, 3 H), 3.00−2.85 (m, 2 H), 2.56−2.36 (m, 2 H), 2.30−2.20 (m, 2 H), 1.93−1.84 (m, 2 H), 1.80−1.69 (m, 1 H), 1.60 (d, J = 11.5 Hz, 1 H), 1.16 (s, 3 H), 1.05 (s, 3 H), 0.92 (d, J = 6.3 Hz, 3 H), 0.84 (s, 9 H), 0.00 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 208.2, 146.5, 139.5, 128.4 (2 C), 127.1, 126.4 (2 C), 124.1, 95.2, 86.5, 86.3, 82.7, 78.0, 75.5, 65.1, 58.8, 55.7, 53.8, 48.3, 45.5, 36.9, 34.9, 25.8 (3 C), 25.6 (2 C), 24.1, 19.9, 18.2, 15.3, −5.29, −5.33; FAB MS m/z (M^+ + H) calcd 603.37, obsd 603.28; $[\alpha]^{23}_D$ −67 (c 0.54, $CHCl_3$).

Alcohol 28. To a solution of *trans*-1-bromo-1-propene (0.20 mL, 0.024 mol) in dry THF (5 mL) at −78 °C under N_2 was added *tert*-butyllithium (2.70 mL, 4.72 mmol). The mixture was stirred at −78 °C for 15 min, a solution of **27**[15] (428 mg, 0.658 mmol) in THF (5 mL) was introduced, and the reaction mixture was stirred at −78 °C for another 30 min prior to being quenched with saturated $NaHCO_3$ solution and diluted with ether. The separated aqueous layer was extracted with ether (×2). The combined organic layers were dried, filtered, and concentrated. Column chromatography of the residue on silica gel (elution with 5:1 hexanes−ether) gave **28** (393 mg, 86%) as a colorless oil: IR (film, cm^{-1}) 3533; ^1H NMR (300 MHz, $CDCl_3$) δ 7.57−7.22 (m, 10 H), 6.12 (d, J = 16.8 Hz, 1 H), 5.71 (dq, J = 15.3, 6.4 Hz, 1 H), 5.63 (s, 1 H), 5.54 (dd, J = 15.4, 1.2 Hz, 1 H), 5.20 (d, J = 16.7 Hz, 1 H), 4.79 (d, J = 11.3 Hz, 1 H), 4.71 (s, 2 H), 4.65 (d, J = 11.2 Hz, 1 H), 4.48 (d, J = 12.8 Hz, 1 H), 4.00 (d, J = 12.8 Hz, 1 H), 3.98 (dd, J = 9.9, 9.2 Hz, 1 H), 3.82−3.71 (m, 2 H), 3.69 (s, 1 H), 3.39 (s, 3 H), 2.94 (s, 1 H), 2.09−1.91 (m, 2 H), 1.95 (d, J = 5.1 Hz, 1 H), 1.89−1.74 (m, 1 H), 1.71 (dd, J = 6.3, 1.0 Hz, 3 H), 1.60−1.49 (m, 1 H), 1.49−1.35 (m, 1 H), 1.32 (m, 3 H), 1.12−1.03 (m, 1 H), 0.89 (s, 9 H), 0.79 (s, 3 H), 0.03 (s, 3 H), 0.02 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 139.7, 138.6, 135.6, 131.4, 129.4, 128.7, 128.1 (2 C), 128.0 (2 C), 127.5 (2 C), 127.0, 126.3 (2 C), 124.4, 101.5, 97.1, 88.2, 82.3, 80.3, 74.6, 70.6, 65.4, 59.1, 58.8, 55.6, 50.6, 50.5, 31.1, 26.3, 26.0 (3 C), 24.2, 22.6, 22.2, 18.3, 18.0, −5.3, −5.4; FAB MS m/z (M^+ + H) calcd 693.42, obsd 693.44 $[\alpha]^{24}_D$ −11.7 (c 1.54, $CHCl_3$).

Anionic Oxy-Cope Rearrangement of 28. A solution of **28** (48 mg, 0.069 mmol) and 18-crown-6 (38 mg, 0.14 mmol) in THF (5 mL) was cooled to −78 °C under O_2, treated with a solution of potassium hexamethyldisilazide (0.28 mL, 0.14 mmol, 0.5 M in toluene), and stirred at −78 °C for 1 h prior to the addition of a solution of triphenylphosphine (18 mg, 0.069 mmol) in THF (0.2 mL). The reaction mixture was transferred to a beaker of cold (−78 °C) silica. The silica was filtered and washed with ether, the filtrate was concentrated in vacuo, and the residue was subjected to column chromatography on silica gel (elution with 5:1 hexanes−ether). There was recovered 8 mg (17%) of **28**, followed by the more polar **29** (2:1 hexanes−ether) (35 mg, 81%) as a colorless oil: IR (film, cm^{-1}) 3406, 1706; ^1H NMR (300 MHz, $CDCl_3$) δ 7.53−7.20 (m, 10 H), 5.59 (s, 1 H), 5.14 (d, J = 11.7 Hz, 1 H), 5.07 (d, J = 7.1 Hz, 1 H), 5.06 (d, J = 11.7 Hz, 1 H), 4.64 (d, J = 6.7 Hz, 1 H), 4.48 (d, J = 13.1 Hz, 1 H), 4.43 (d, J = 6.7 Hz, 1 H), 4.36 (dd, J = 10.2, 1.6 Hz, 1 H), 4.26 (d, J = 13.1 Hz, 1 H), 4.18 (d, J = 2.0 Hz, 1 H), 3.88 (dt, J = 10.0, 4.1 Hz, 1 H), 3.79−3.73 (m, 1 H), 3.43 (t, J = 10.3 Hz, 1 H), 3.37 (s, 3 H), 2.62 (q, J = 10.2 Hz, 1 H), 2.57−2.26 (m, 4 H), 2.22 (dd, J = 8.2, 1.8 Hz, 1 H), 2.15−2.11 (m, 1 H), 2.06−1.96 (m, 1 H), 1.77−1.68 (m, 1 H), 1.52 (d, J = 11.3 Hz, 1 H), 1.38 (d, J = 6.3 Hz, 3 H), 1.21 (s, 3 H), 1.09 (s, 3 H), 0.90 (s, 9 H), 0.05 (s, 3 H), 0.04 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 208.5, 145.3, 140.0, 138.4, 128.8, 128.2 (2 C), 128.0 (2 C), 127.1 (2 C), 126.9, 126.2, 125.7 (2 C), 101.0, 95.3, 86.2, 79.2, 76.8, 74.3, 70.9, 67.9, 58.8, 5.57, 53.2, 47.5, 45.6, 39.1, 32.1, 26.0 (3 C), 25.9, 25.6, 23.7, 20.3, 19.4, 18.4, −5.3, −5.4; FAB MS m/z (M^+ + H) calcd 709.41, obsd 709.60; $[\alpha]^{23}_D$ −89.7 (c 1.38, $CHCl_3$).

(1*S*,2*S*,3*R*,4*S*)-1-[(*E*)-[2*R*,4*S*,5*S*)-5-(Benzyloxy)-4-[2-(*tert*-butyldimethylsiloxy)ethyl]-2-phenyl-*m*-dioxan-5-yl]vinyl]-3-(methoxymethoxy)-7,7-dimethyl-2-vinylbicyclo[2.2.1]-heptan-2-ol (32). A solution of **27**[15] (112 mg, 0.172 mmol) was stirred with a suspension of anhydrous cerium trichloride [prepared from cerium trichloride heptahydrate (242 mg, 0.650 mmol)] in THF at room temperature for 5 h. The suspension was cooled in an ice−water bath, and a solution of vinylmagnesium bromide (0.83 mL of 0.78 M in THF, 0.65 mmol) was added. After being stirred at 0 °C for 10 min, the reaction mixture was quenched with saturated NH_4Cl solution and diluted with ether. The separated layer was extracted with ether (×2). The combined organic extracts were dried, filtered, and concentrated in vacuo. Chromatography of the residue on silica gel (elution with hexanes−ether 3:1) gave **32** (107 mg, 92%) as a colorless oil: IR (film, cm^{-1}) 3528; ^1H NMR (300 MHz, $CDCl_3$) δ 7.60−7.27 (m, 10 H), 6.17 (d, J = 16.7 H, 1 H), 5.95 (dd, J = 17.1, 10.7 Hz, 1 H), 5.66 (s, 1 H), 5.32 (d, J = 17.1 Hz, 1 H), 5.23 (d, J = 16.7 Hz, 1 H), 5.13 (dd, J = 10.7, 0.7 Hz, 1 H), 4.82 (d, J = 11.3 Hz, 1 H), 4.73 (s, 2 H), 4.68 (d, J = 11.2 Hz, 1 H), 4.51 (d, J = 12.8 Hz, 1 H), 4.05−3.99 (m, 2 H), 3.85−3.72 (m, 3 H), 3.40 (s, 3 H), 3.05 (s, 1 H), 2.12−1.92 (m, 3 H), 1.74−1.87 (m, 1 H), 1.60 (dt, J = 13.0, 4.8 Hz, 1 H), 1.44−1.37 (m, 1 H), 1.37 (s, 3 H), 1.17−1.08 (m, 1 H), 0.93 (s, 9 H), 0.84 (s, 3 H), 0.07 (s, 3 H), 0.06 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 142.4, 139.6, 138.6, 131.1, 129.3, 128.7, 128.1 (2 C), 128.0 (2 C), 127.4 (2 C), 126.9, 126.3 (2 C), 113.5, 101.5, 97.1, 87.7, 82.6, 80.2, 74.5, 70.5, 65.3, 59.1, 58.6, 55.6, 50.8, 50.5, 31.1, 26.1, 25.9 (3 C), 24.1, 22.4, 22.2, 18.3, −5.3, −5.4; FAB MS m/z (M^+ + H) calcd 679.40, obsd 679.32; $[\alpha]^{16}_D$ −24.1 (c 5.06, $CHCl_3$).

(1*S*,2*R*,4*R*,6*R*,7*E*)-6-[(2*R*,4*S*,5*S*)-5-(Benzyloxy)-4-[2-(*tert*-butyldimethylsiloxy)ethyl]-2-phenyl-*m*-dioxan-5-yl]-4-hydroxy-2-(methoxymethoxy)-11,11-dimethylbicyclo[6.2.1]-undec-7-en-3-one (34). To a solution of **32** (85 mg, 0.13 mmol) and 18-crown-6 (66 mg, 0.25 mmol) in THF (8 mL) at −78 °C under oxygen was added a solution of potassium hexameth-

yldisilazide (0.50 mL of 0.50 M in toluene, 0.25 mmol). The mixture was stirred at −78 °C for 5 min, and a solution of triphenylphosphine (33 mg, 0.13 mmol) in THF (0.5 mL) was added. The reaction mixture was quenched with saturated NH_4Cl solution and diluted with ether. The separated aqueous layer was extracted with ether (×2), the combined organic layers were dried, and solvents were removed under reduced pressure. Chromatography of the residue on silica gel (elution with 2:1 hexanes−ethyl acetate) gave **34** (78 mg, 90%) as a colorless oil: IR (film, cm^{-1}) 3417, 1713; ^1H NMR (300 MHz, $CDCl_3$) δ 7.54−7.21 (m, 10 H), 5.57 (s, 1 H), 5.15 (d, J = 10.4 Hz, 1 H), 5.14 (d, J = 12.2 Hz, 1 H), 5.05 (d, J = 12.2 Hz, 1 H), 4.65 (d, J = 6.8 Hz, 1 H), 4.51 (d, J = 12.9 Hz, 1 H), 4.44 (d, J = 6.8 Hz, 1 H), 4.18−4.12 (m, 3 H), 3.83−3.76 (m, 2 H), 3.73−3.67 (m, 1 H), 3.36 (s, 3 H), 2.87 (dt, J = 11.5, 5.7 Hz, 1 H), 2.65−2.37 (m, 3 H), 2.28−2.20 (m, 2 H), 2.15−2.05 (m, 1 H), 1.96−1.85 (m, 3 H), 1.77−1.68 (m, 1 H), 1.18 (s, 3 H), 1.08 (s, 3 H), 0.91 (s, 9 H), 0.04 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 208.4, 145.5, 140.2, 138.4, 128.9, 128.3 (2 C), 128.1 (2 C), 126.8, 126.6 (2 C), 126.2 (2 C), 123.8, 101.1, 95.2, 86.5, 80.0, 72.4, 72.0, 71.2, 67.7, 58.7, 55.7, 53.1, 45.4, 42.2, 34.6, 32.3, 26.1, 26.0 (3 C), 25.8, 23.7, 20.0, 18.3, −5.3, −5.4; FAB MS m/z ($MH^+ - C_7H_6$) calcd 605.35, obsd 605.47; $[\alpha]^{20}_D$ −74 (*c* 0.99, $CHCl_3$).

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Supporting Information Available: High-field ^1H NMR spectra of those compounds lacking elemental analysis (16 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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