Studies Directed toward the Total Synthesis of Cerorubenic Acid-III. 4. Exploration of an Organometallic Approach to Construction of the Eastern Sector

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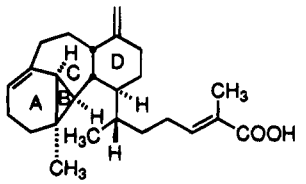
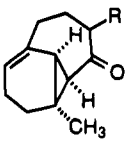
The concept of an intramolecular organometallic approach to the most illustrious member of the cerorubenic acid family is outlined. Alkylation of ketone **2** with the ethyl iodoacetate and conversion of the resultant intermediate into lactone **9** provided a ready means for attaching side chains carrying a vinyl iodide substituent. Arrival at the key iodo ketones was next realized by a three-step sequence involving sodium borohydride reduction, regiocontrolled silylation of the primary hydroxyl group in the diol, and Dess–Martin oxidation. The crucial six-membered cyclization of these intermediates is not favored kinetically, and reductive deiodination was observed, if reaction occurred at all. Attempts to generate vinyl stannanes from these same substrates were also ineffective. The failure of this approach demonstrates the difficulties associated with closure of ring D, a phenomenon that has earlier been observed in the context of other exploratory routes to cerorubenic acid-III.

In three full papers,[2] we have described a retrosynthetic analysis of cerorubenic acid-III (**1**) in which the ABC subunit was rapidly assembled by anionically-accelerated oxy-Cope rearrangement.[3] This approach is characterized by considerable flexibility, with modest structural changes allowing for direct generation of the parent tricyclic ketone **2** (R = H) or derivatives thereof which contain side chains presumed to be adaptable to the assembly of ring D. For a variety of reasons, limitations have surfaced in our attempts to realize subsequent fusion of the fourth ring.



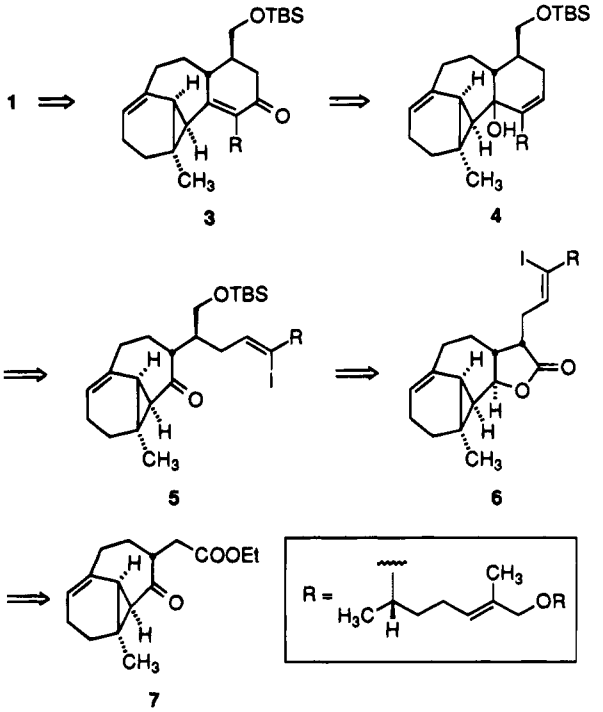
1



2

Since the simple construction of **2** (R = H) in this fashion continues to be viewed by us as a key operation in the *de novo* elaboration of **1**, other avenues for assembly of the eastern sector have more recently been investigated. From the retromanipulative perspective, iodo ketone **5** appeared to be an ideal advanced intermediate, since its intramolecular cyclization to **4** and subsequent oxidation of this allylic alcohol was envisioned as a possible pathway to **3** (Scheme 1). Further disassembly of **5** traced a possible linkup via **6** to the keto ester **7** as shown. An added desirable advantage of this route includes initiation of the sequence with **2** (R = H) of high enantiomeric purity (either antipode),[2c] thereby enabling ultimate construction of this sesterterpenoid in its proper absolute configuration. The latter remains to be established.[4]

Scheme 1



Results and Discussion

The goals set above required that **2** (R = H) be first transformed via keto ester **7** into an appropriately cyclized lactone. Racemic compounds were employed in this phase of the study. Deprotonation of the ketone with LDA proceeded regioselectively and efficiently to deliver an enolate anion that condensed smoothly with ethyl iodoacetate to provide a single alkylation product. Ap-

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(2) (a) Paquette, L. A.; Poupart, M.-A. *J. Org. Chem.* **1993**, *58*, 4245. (b) Paquette, L. A.; Lassalle, G. Y.; Lovely, C. J. *J. Org. Chem.* **1993**, *58*, 4254. (c) Paquette, L. A.; Deaton, D. N.; Endo, Y.; Poupart, M.-A. *J. Org. Chem.* **1993**, *58*, 4262.

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

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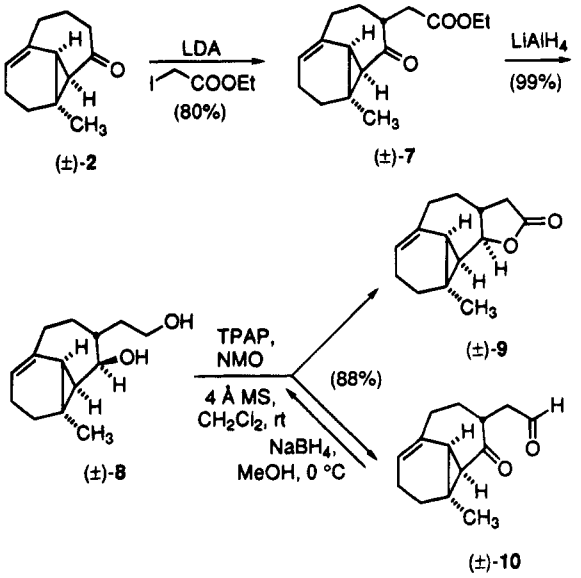
0022-3263/95/1960-4813$09.00/0

Scheme 2



proach of the electrophile to the less sterically hindered surface of this reactive intermediate was expected, and stereochemical formulation of **7** as shown in Scheme 2 was tentatively supported by 2-D COSY and NOE studies performed at the 300-MHz level. Exposure of **7** to lithium aluminum hydride afforded diol **8**, oxidation of which with tetra-*n*-propylammoniumperruthenate (TPAP)[5] gave rise to a 4:1 mixture of **9** and **10** in a combined yield of 88%. In order to facilitate the isolation of **9** (coelutes with **10**), the mixture was routinely stirred briefly with sodium borohydride in methanol at 0 °C. This pretreatment resulted in the return of **10** to **8** and the establishment of a polarity differential sufficiently large to facilitate considerably the chromatographic separation. The recycling of **8** is also well served. The increased structural rigidification present in **9** allowed its stereochemistry to be unequivocally defined by 2-D COSY and NOE methods (Figure 1).

With **9** in hand, a vinyl iodide structurally simpler than that ultimately required was first prepared as an initial probe of workability. To arrive at this lower homologue, methyl butynoate (**11**) was heated with sodium iodide in acetic acid in order to add HI in trans fashion across the triple bond[6] (Scheme 3). DIBAL-H reduction of **12** gave alcohol **13a**, which was best transformed into bromide **13c** via the mesylate. Although the more direct conversion of **13a** into **13c** with carbon tetrabromide and triphenylphosphine[7] proceeded equally well, the bromide could not easily be freed of bromoform either chromatographically or by distillation.

In the convergent step, the lithium enolate of **9** was admixed with **13c**,[8] leading in 72% yield to a >20:1 mixture of diastereomers (Scheme 4). The stereochemistry of the colorless crystalline **14** was once again corroborated by means of tandem 2-D COSY and NOE measurements (Figure 1). Since the reduction of **14** with lithium aluminum hydride proceeded with competitive

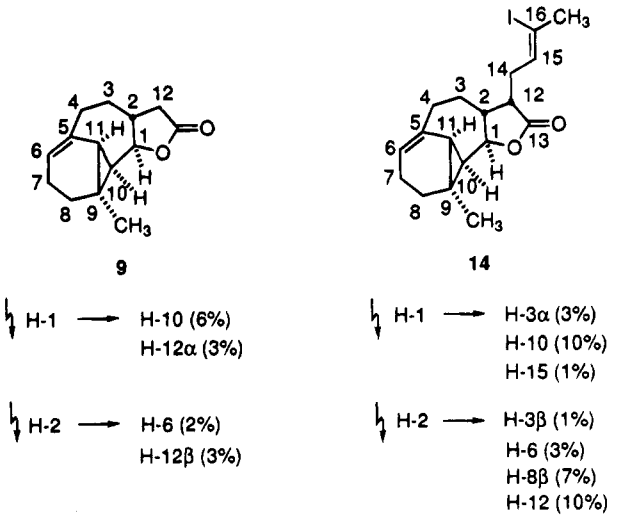
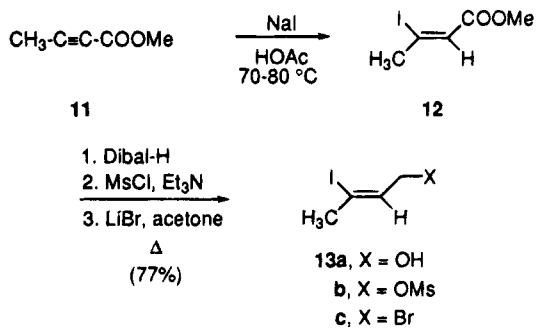
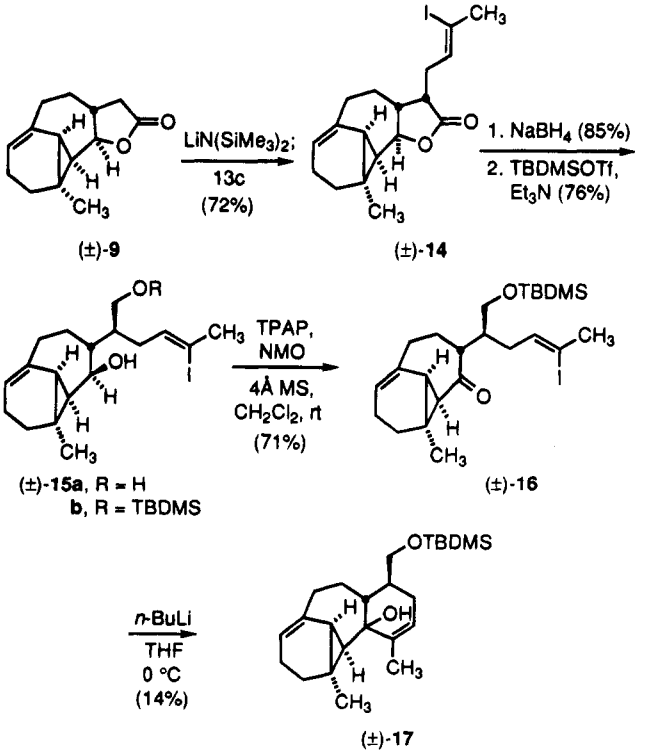


Figure 1. Results of NOE experiments on **9** and **14**. The atomic numbering used is arbitrary.

Scheme 3



Scheme 4



deiodination, recourse was made instead to sodium borohydride. Under these conditions,[9] diol **15a** was produced in 85% yield. Examination of a number of protecting groups led ultimately to selection of the *tert*-

(5) (a) Griffith, W. P.; Ley, S. V.; Whitcombe, G. P.; White, A. D. *J. Chem. Soc., Chem. Commun.* **1987**, 1625. (b) Griffith, W. P.; Ley, S. V. *Aldrichim. Acta* **1990**, *23*, 13. (c) Bloch, R.; Brillet, C. *Synlett* **1991**, 829.

(6) (a) Ma, S.; Lu, X. *Tetrahedron Lett.* **1990**, *31*, 7653. (b) Marek, I.; Alexakis, A.; Normant, J. F. *Tetrahedron Lett.* **1991**, *32*, 5329. (c) Ma, S.; Lu, X.; Li, Z. *J. Org. Chem.* **1992**, *57*, 709.

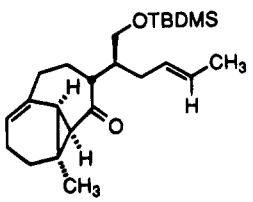
(7) Hooz, J.; Gilani, S. S. H. *Can. J. Chem.* **1968**, *46*, 86.

(8) Alker, D.; Jones, D. N.; Taylor, G. M.; Wood, W. W. *J. Chem. Soc. Perkin Trans. 1* **1992**, 1119.

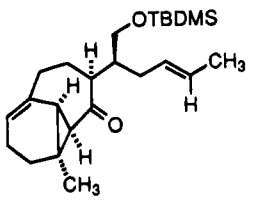
butyldimethylsilyl derivative. The hydroxyl groups in the diol proved to be rather unreactive, and it was necessary to utilize the silyl triflate[10] to achieve a reasonable etherification rate. Despite the heightened reactivity of this reagent, only the primary hydroxyl group was protected as in **15b**.

Confident that the TPAP/NMO reagent combination, utilized to earlier advantage in the formation of **9** (and **10**), could again serve to effect nondestructive oxidation of the sensitive ring system in hand, we proceeded to perform this step in the usual manner.[5] Indeed, the formation of **16** was uneventful and respectably efficient (71%). Since the side chain in **16** is already in the thermodynamically preferred orientation,[2] no loss of stereochemical integrity was anticipated, nor was it observed.

A variety of attempts to achieve the ring closure of **16** by means of halogen–metal exchange met with considerable reductive deiodination. In his recent dolastatrienol synthesis, Piers employed magnesium metal to form an iodo Grignard intermediate as a prelude to intramolecular 1,2-addition to a carbonyl group.[11] When these conditions were applied to **16**, only the loss of iodine was achieved. Epimerization α to the carbonyl occurred as well, giving rise to both **18** and **19**[12] in 22 and 43% isolated yield, respectively. Evidently, the initially-generated vinyl organometallic enters predominantly into



(±)-**18**

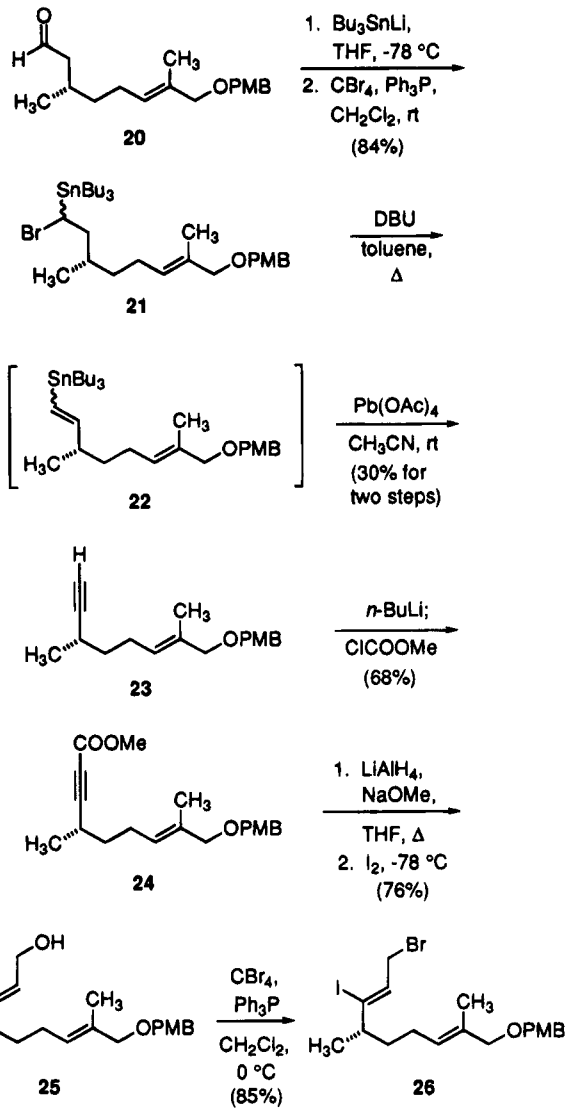


(±)-**19**

deprotonation of the neighboring ketone to generate the enolate anion. Quenching of the reaction mixture eventuates in proton delivery from the less hindered direction[2b] to provide **19**. Diastereomer **18** is the thermodynamic product.

It was reasoned that a transient vinyllithium intermediate might be more nucleophilic and lead instead predominantly to the desired **17**. Both *n*-butyllithium and *tert*-butyllithium have been reported to serve advantageously in the intramolecular cyclization of vinyl halides onto carbonyl groups.[13–15] Modest success was realized when the first of these reagents was reacted with **16** in THF at 0 °C. Following HPLC purification, **17** was isolated in 14% yield alongside comparable quantities of **18** and **19**. Particularly diagnostic NMR characteristics of **17** are its two vinyl proton signals at δ 5.77 and 5.24, as well as the appearance of its tertiary carbinol absorption at 78.9 ppm (in C_6D_6 solution).

Scheme 5



Efforts to improve the **16** → **17** conversion by expanding the range of experimental conditions to include vinyl cuprates[16,17] or chromium(II) chloride[18] were to no avail. These results notwithstanding, attention was directed in turn to ring closure studies of more fully elaborated congeners related to **5**.

In preparation for construction of the appropriate side chain, aldehyde **20** was produced from (*S*)-citronellol as earlier reported.[2c] A salient feature of the conversion of **20** into bromide **26** as outlined in Scheme 5 was the need to transform the acetaldehyde moiety into an alkyne *without chain extension*. Initial plans called for the generation from **20** of a vinyl stannane.[19] When neither the direct approach (LDA; $PhNTf_2$)[20] nor the route via the silyl enol ether (MeLi; $PhNTf_2$) successfully provided the vinyl triflate, we pursued the option of adding (tri-*n*-butylstannyl)lithium in 1,2-fashion to **20** and of derivatizing the resulting hydroxy stannane as the corresponding bromide **21** with carbon tetrabromide and triphenylphosphine.[21] An 84% yield of **21** was reproduc-

(9) Hanessian, S.; Sahoo, S. P.; Botta, M. *Tetrahedron Lett.* **1987**, *28*, 1147.
(10) Corey, E. J.; Cho, H.; Rücker, C.; Hua, D. H. *Tetrahedron Lett.* **1981**, *22*, 3455.
(11) (a) Piers, E.; Friesen, R. W. *J. Org. Chem.* **1986**, *51*, 3405. (b) Piers, E.; Friesen, R. W. *Can. J. Chem.*, **1992**, *70*, 1204.
(12) The side chain double bond has remained trans in both **18** and **19** in light of the vinyl–vinyl coupling constant of ca. 15 Hz. The otherwise near-identity of the two products, e.g., IR (1700 vs 1685 cm^{-1}) and ^{13}C NMR (208.1 and 210.7 ppm), indicates them to be epimerically related and not geometric isomers.
(13) Cooke, M. P., Jr.; Houpis, I. N. *Tetrahedron Lett.* **1985**, *26*, 4987.
(14) Wender, P. A.; Mucciaro, T. P. *J. Am. Chem. Soc.* **1992**, *114*, 5878.
(15) (a) Piers, E.; Marais, P. E. *Tetrahedron Lett.* **1988**, *29*, 4053. (b) Piers, E.; Cook, K. L.; Rogers, C. *Tetrahedron Lett.* **1994**, *35*, 8573.
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(17) Grootaert, W. M.; DeClercq, P. J. *Tetrahedron Lett.* **1982**, *23*, 3291.
(18) Rowley, M.; Tsukamoto, M.; Kishi, Y. *J. Am. Chem. Soc.* **1989**, *111*, 2735.
(19) Ritter, K. *Synthesis* **1993**, 735.
(20) Hendrickson, J. B.; Bergeron, R. *Tetrahedron Lett.* **1973**, 4607.

ibly realized when an approximate 2-fold excess of Bu_3SnLi was employed in order to maximize conversion to the carbinol.

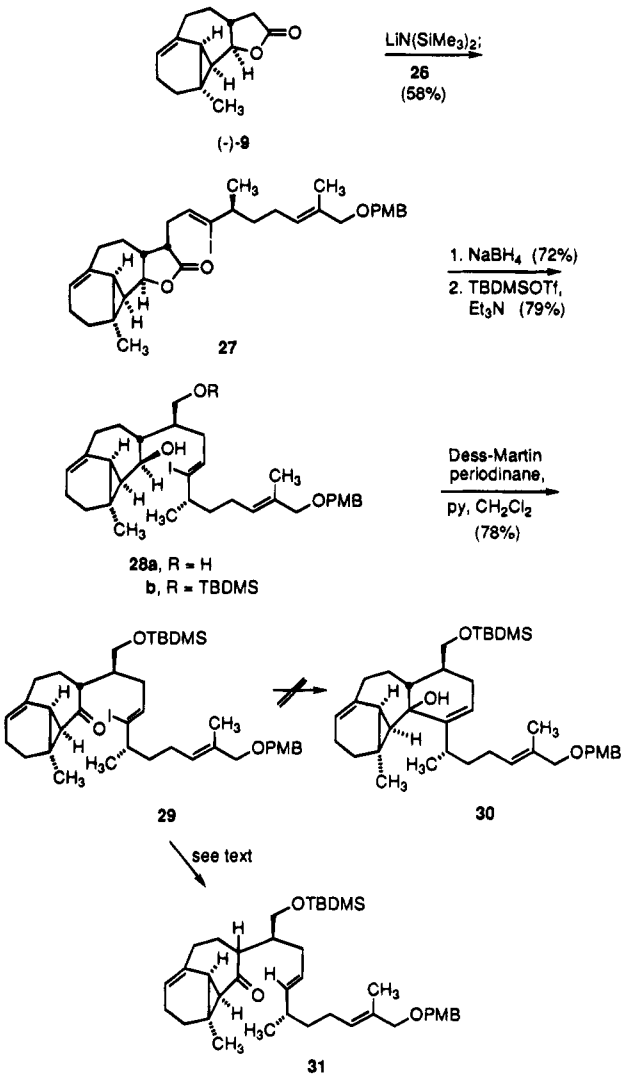
Although **21** is formed as a mixture of diastereomers, both undergo dehydrobromination smoothly in refluxing toluene containing DBU to deliver the vinyl stannane **22** in quantitative yield. Direct exposure of **22** to the action of lead tetraacetate in acetonitrile at rt[22] afforded alkyne **23**, but only with modest efficiency (30%). The reason for the low yield is not clear. Control experiments on precursors to **20** revealed that the protected allylic alcohol subunit is not sensitive to this reagent. The adaptation of lead tetrabenzoate[23] was also examined, but with comparable consequences. When alternative routes involving conversion of **20** into the 1,1-dichloro derivative followed by elimination[24] or trapping of the enolate of **20** with diethyl chlorophosphate and subsequent elimination[25] did not provide **23**, the $Pb(OAc)_4$-based protocol was permanently adopted.

The conversion of **23** into ester **24** followed along conventional lines.[26] Iodinative reduction of **24** according to Corey[27] resulted in the direct formation of *Z*-allyl alcohol **24** (76%) as a consequence of the transient intervention of a five-membered cyclic complex.[28] In contrast to Corey's study, we came to favor in situ reduction of the ester such that this functionality and the triple bond were engaged concurrently in reaction. A secure basis for efficiently performing this tandem sequence resides in the direct addition of a large excess (ca. 8-fold) of iodine without solvent after completion of the reductive phase of the process. Reaction of **25** with triphenylphosphine and carbon tetrabromide[29] afforded **26** (85%).

Condensation of the enolate anion of **9** with **26** under the predescribed conditions gave **27** (58%) with excellent stereoselectivity (>20:1). None of the minor diastereomer could be detected by high-field ^1H NMR. The stereochemical assignment of the newly generated stereogenic center, initially assigned by analogy to **14**, was supported by ^1H NMR data (Scheme 6). The reduction and monoprotection of **27**, performed in line with preestablished conditions, proved serviceable in making **28a** and subsequently **28b** available in good yield. Subjection of **28b** to Dess–Martin oxidation generated **29** (78%) and set the stage for detailed examination of the ring closure of this iodo ketone.

In the first of a myriad of experiments, **29** was treated in dry THF with activated magnesium metal prepared according to Rieke's procedure.[30] The result was a complex mixture consisting of unreacted **29** (30%), the deiodinated ketone **31** (12%), and several minor unidentified constituents whose IR spectrum (as a mixture) also exhibited a ketone carbonyl band. This problem was not resolved by making recourse to samarium(II) iodide in the same reaction medium.[31] In this instance, no cyclized product was again observed and, although 19% of **29** was recovered, the balance of the mixture was devoid of the TBDMS protecting group.

Scheme 6



Attempts to cyclize **29** through the use of mixtures of chromium(II) chloride and nickel(II) chloride, as developed earlier by Kishi,[32] were similarly to no avail. Usually, only unchanged starting material could be identified (ca. 50% recovery). When no evidence was uncovered for the conversion to **30** via these reaction conditions, attention was directed to several alternative cyclization possibilities. Recourse to trimethyl(tri-*n*-butylstannyl)silane in the presence of cesium fluoride as metalating agent[33] led solely to the recovery of unchanged **29** (48%) after 2 h at rt. A modest level of desilylation was effected concurrently. At this juncture, a viable strategy via the vinylstannane was sought. However, the anticipated formation of this intermediate by treatment of **29** with hexamethyldistannane and tetrakis(triphen-

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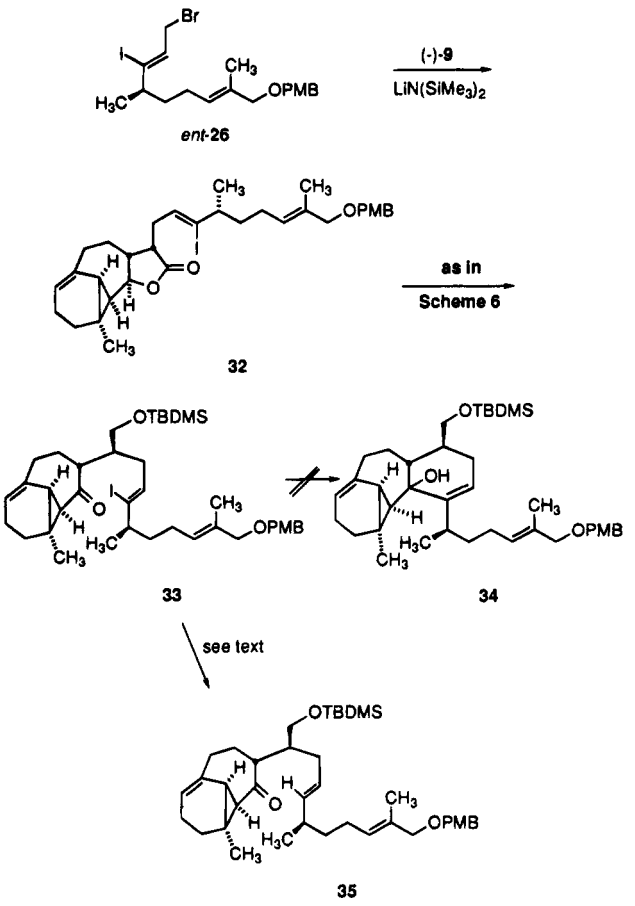
(22) Corey, E. J.; Wollenberg, R. H. *J. Am. Chem. Soc.* **1974**, *96*, 5581.
(23) Criegee, R. *Liebigs Ann. Chem.* **1930**, *481*, 263.
(24) Dehmlow, E. V.; Lissel, M. *Liebigs Ann. Chem.* **1980**, 1.
(25) Negishi, E.; King, A. O.; Klima, W. L. *J. Org. Chem.* **1980**, *45*, 2526.
(26) Earl, R. A.; Townsend, L. B. *Organic Syntheses*; Wiley: New York, 1990; Collect. Vol. VII, p 334.
(27) (a) Corey, E. J.; Katzenellenbogen, J. A.; Posner, G. H. *J. Am. Chem. Soc.* **1967**, *89*, 4245. (b) Corey, E. J.; Katzenellenbogen, J. A.; Gilman, N. W.; Roman, S. A.; Erickson, B. W. *J. Am. Chem. Soc.* **1968**, *90*, 5618.
(28) Corey, E. J.; Katzenellenbogen, J. A.; Roman, S. A.; Gilman, N. W. *Tetrahedron Lett.* **1971**, 1821.
(29) Aoyagi, S.; Wang, T.-C.; Kibayashi, C. *J. Am. Chem. Soc.* **1993**, *115*, 11393 and relevant references cited therein.
(30) Rieke, R. D.; Bales, S. E.; Hudnall, P. M.; Burns, T. P.; Poindexter, G. S. *Organic Syntheses*; Wiley: New York, 1988; Collect. Vol. VI, p 845.
(31) (a) Murakami, M.; Hayashi, M.; Ito, Y. *Synlett* **1994**, 179. (b) Fevig, T. L.; Elliott, R. L.; Curran, D. P. *J. Am. Chem. Soc.* **1988**, *110*, 5064.
(32) Rowley, M.; Tsukamoto, M.; Kishi, Y. *J. Am. Chem.* **1989**, *111*, 2735.
(33) Mori, M; Isono, N.; Kaneta, N.; Shibasaki, M. *J. Org. Chem.* **1993**, *58*, 2972.

Scheme 7



ylphosphine)palladium[34] resulted in decomposition. The use of a stannyl cuprate was also examined,[35] and this reaction provided **31** in 66% yield after chromatography.

The information gained from the predescribed studies raised the possibility that the configuration of the secondary methyl group on the side chain might be contributing to a rate-retarding effect of significant proportions. In order to resolve this question, diastereomer **33** was prepared (Scheme 7) and subjected in turn to a battery of probe cyclization reactions. In this context, it was interesting to observe that while *n*-butyllithium was insufficiently reactive to enter into halogen–metal exchange with **33**,[15a] *tert*-butyllithium did so quite effectively but returned only **35** in modest amounts (35–40%).

In conclusion, the use of organometallic-promoted cyclization of iodo ketone **29** and congeners thereof has not constituted a concise route into the framework of cerorubenic acid-III. This inertness to an otherwise well established process was not entirely unexpected. The carbonyl group in the eastern sector of these molecules was previously recognized to have reduced reactivity toward nucleophiles, although this attenuation did not adversely affect additions involving Grignard reagents.[2b] It would appear nonetheless that no effective matchup of electrophilicity/nucleophilicity can be established to allow smooth formation of the carbocyclic six-membered D ring. Other ineffective attempts to actuate ring D cyclization via Robinson annulation pathways have earlier been documented.[2b,c] To date, the only means uncovered for achieving this key step has involved a high-pressure Diels–Alder cycloaddition.[2a,35] Accordingly, our intention is to return to this expeditious process and to elaborate **1** from that direction. The merits of such a potential ultimate solution are that all adverse stereoelectronic effects are effectively skirted.

(34) Wulff, W. D.; Peterson, G. A.; Bauta, W. E.; Chan, K. S.; Faron, K. L.; Gilbertson, S. R.; Kaessler, R. W.; Yang, D. C.; Murray, C. K. *J. Org. Chem.* **1986**, *51*, 277.
(35) Paquette, L. A.; Poupart, M.-A. *Tetrahedron Lett.* **1988**, *29*, 273.

Experimental Section

See reference 2a for a listing of generic experimental details.

Ethyl (1*R,2*R**,4*R**,11*S**)-11-methyl-3-oxotricyclo-[5.4.0.0^{2,11}]undec-7-en-4-yl Acetate (7).** A solution of **2** (1.20 g, 6.8 mmol) in dry THF (19 mL) was added dropwise to a cold (−78 °C), magnetically stirred solution of LDA [prepared by the addition of *n*-butyllithium (5.3 mL of 1.4 M in hexanes, 7.48 mmol) to a solution of diisopropylamine (1.10 mL, 7.85 mmol) in THF (15 mL) at 0 °C with stirring for 15 min]. After 90 min, ethyl iodoacetate (1.51 mL, 15.3 mmol) was introduced in one portion. The reaction mixture was allowed to warm to rt overnight, quenched with saturated NH_4Cl solution (50 mL), and extracted with ether (4 × 50 mL). The combined organic phases were dried, filtered, and concentrated to afford a yellow oil, which was purified by flash chromatography on silica gel (elution with 0–5% ethyl acetate in petroleum ether). There was isolated 1.43 g (80%) of **7** as a colorless oil: IR (neat, cm^{-1}) 1745, 1700; ^1H NMR (300 MHz, $CDCl_3$) δ 5.56 (br d, J = 8.0 Hz, 1 H), 3.92 (q, J = 7.0 Hz, 2 H), 2.57 (d ABq, J_{AB} = 5.9, 16.4 Hz, $\Delta\nu_{AB}$ = 23.3 Hz, 2 H), 2.35–2.23 (m, 2 H), 2.20–2.10 (m, 1 H), 1.98–1.88 (m, 1 H), 1.88–1.82 (m, 1 H), 1.77 (dd, J = 3.3, 12.8 Hz, 1 H), 1.69 (s, J = 8.8 Hz, 1 H), 1.61–1.45 (m, 2 H), 1.33–1.26 (m, 1 H), 0.94 (t, J = 7.1 Hz, 3 H), 0.92 (s, 3 H), 0.84 (br d, J = 8.8 Hz, 1 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 209.3, 171.9, 137.5, 60.3, 47.7, 40.4, 37.7, 34.7, 28.7, 28.0, 26.5, 24.5, 23.1, 21.4, 14.2; MS m/z (M^+) calcd 262.1569, obsd 262.1550.

(1*R,2*R**,4*R**,11*S**)-3-Hydroxy-11-methyltricyclo-[5.4.0.0^{2,11}]undec-7-ene-4-ethanol (8).** A solution of **7** (390 mg, 1.49 mmol) in dry THF (15 mL) was added dropwise to a cold (−78 °C) stirred suspension of lithium aluminum hydride (340 mg, 8.95 mmol). After 90 min of stirring, the reaction mixture was warmed slowly to rt and quenched with water (0.34 mL), 15% NaOH solution (0.34 mL), and water (1.02 mL) prior to cooling and suction filtration. The solids were washed with ethyl acetate, the aqueous layer was separated, and the organic phase was dried and concentrated. The residue was chromatographed on silica gel (elution with 60% ethyl acetate in petroleum ether) to provide 328 mg (99%) of **8** as a thick colorless syrup which solidified upon standing for several days: white solid, mp 69–71 °C; IR (film, cm^{-1}) 3700–3090; ^1H NMR (300 MHz, C_6D_6) δ 5.69 (br dt, J = 1.3, 7.2 Hz, 1 H), 4.02 (t, J = 8.1 Hz, 1 H), 3.60–3.43 (m, 2 H), 2.31 (dq, J = 4.2, 13.1 Hz, 2 H), 2.25 (br s, 2 H), 2.19–1.95 (m, 2 H), 1.87–1.25 (series of m, 7 H), 1.05 (s, 3 H), 0.86–0.75 (m, 2 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 139.5, 128.3, 76.4, 61.3, 39.3, 37.3, 34.0, 32.3, 29.9, 28.8, 28.3, 25.9, 24.0, 22.2; MS m/z (M^+) calcd 222.1620, obsd 222.1617.

(3a*R,6a*R**,7*S**,7a*R**,7b*R**)-3,3a,4,5,6a,7,7a,7b-Octahydro-7-methyl-2*H*-7,6-[1]propanyl[3]ylidenecyclopropa-[6,7]cyclohepta[1,2-*b*]furan-2-one (9).** A mixture of **8** (1.06 g, 4.77 mmol), *N*-methylmorpholine *N*-oxide (1.87 g,15.0 mmol), and 4 Å molecular sieves (2.41 g) in CH_2Cl_2 (20 mL) was stirred at rt for 10 min and treated portionwise with TPAP (107 mg, 0.30 mmol). After 1 h, the reaction mixture was placed directly atop a silica gel column. Elution with 10–20% ethyl acetate in petroleum ether gave 0.92 g (88%) of a 4:1 mixture of **9** and **10** (^1H NMR analysis). This mixture was dissolved in methanol (40 mL), cooled to 0 °C, and treated portionwise with sodium borohydride (75 mg, 2.03 mmol). After 2 h at 0 °C, saturated NH_4Cl solution (50 mL) was added and the product was extracted into ethyl acetate (4 × 100 mL), dried, and concentrated. Chromatography of the residue (silica gel, elution with 20% ethyl acetate in petroleum ether) afforded **9** (0.47 g, 51%) as a colorless oil that solidified to a waxy solid upon storage in the refrigerator: mp 64–66 °C; IR (film, cm^{-1}) 1770; ^1H NMR (300 MHz, C_6D_6) δ 5.53 (dt, J = 2.2, 7.3 Hz, 1 H), 3.87 (dd, J = 7.5, 11.5 Hz, 1 H), 2.28–2.12 (m, 1 H), 2.05–

1.85 (m, 2 H), 1.87 (dd, J = 6.8, 16.1 Hz, 2 H), 1.67–1.58 (m, 1 H), 1.55 (dd, J = 13.0, 16.1 Hz, 2 H), 1.44 (dq, J = 3.0, 12.6 Hz, 1 H), 1.26–1.15 (m, 1 H), 0.95 (s, 3 H), 0.93 (dd, J = 10.0, 19.0 Hz, 1 H), 0.80 (dd, J = 1.5, 9.5 Hz, 1 H), 0.79–0.71 (m, 1 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 174.7, 136.3, 131.7, 87.8, 36.5, 36.2, 30.1 (2 C), 27.6, 27.3, 27.2, 25.2, 24.5, 22.8; MS m/z (M^+) calcd 218.1307, obsd 218.1305. Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 76.67; H, 8.47.

(*Z*)-4-Bromo-2-iodo-2-butene (13c). To a cold (0 °C), magnetically stirred solution of ester **12**[6] (8.82 g, 39.03 mmol) in anhydrous ether (100 mL) was added 1 M DIBAL-H solution (117 mL in THF, 117 mmol). The reaction mixture was stirred at 0 °C for 30 min and quenched with ethyl acetate (20 mL) followed by sufficient 1 M HCl to dissolve all of the precipitated solid. The separated aqueous phase was extracted with ether (3 × 100 mL), and the combined organic phases were washed with 1 M HCl (3 x 200 mL) and saturated $NaHCO_3$ solution (100 mL), dried, and concentrated to give **13a** (7.13 g, 92%). This colorless oil (4.00 g, 20.2 mmol) and triethylamine (3.1 mL, 22.4 mmol) in CH_2Cl_2 (20 mL) were cooled to −23 °C and treated dropwise with methanesulfonyl chloride (1.73 mL, 22.4 mmol). The mixture was stirred for 2 h at −23 °C and then allowed to warm to rt where it was quenched with 10% citric acid solution (20 mL) and diluted with CH_2Cl_2. The organic phase was washed with 10% citric acid solution (3 × 20 mL), dried, and concentrated to give crude mesylate (5.78 g). A 2.50 g portion (9.06 mmol) of this material was dissolved in acetone (25 mL), LiBr (4.83 g, 54.6 mmol) was added, and the mixture was refluxed for 25 min. After cooling, water (10 mL) was introduced and the product was extracted into ether and purified by chromatography on silica gel. Elution with petroleum ether gave 1.93 g (84%) of **13c** as a colorless oil, which rapidly turned purple and had to be used without delay: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.78 (tq, J = 1.5, 7.8 Hz, 1 H), 3.98 (dq, J = 0.8, 7.8 Hz, 2 H), 2.58 (dt, J = 0.8, 1.6 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 131.1, 107.3, 35.6, 33.7; MS m/z (M^+) calcd 261.8637, obsd 261.8614.

(3*R,3a*S**,6a*S**,7*R**,7a*S**,7b*S**)-3,3a,4,5,6a,7,7a,7b-Octahydro-3[(*Z*)-3-iodo-2-butenyl]-7-methyl-2*H*-7,6-[1]propanyl[3]ylidenecyclopropa[6,7]cyclohepta[1,2-*b*]furan-2-one (14).** A cold (−78 °C), magnetically stirred solution of **9** (103 mg, 0.471 mmol) in dry THF (4 mL) was treated dropwise with lithium hexamethyldisilazide (0.60 mL of 1.0 M in THF, 0.60 mmol) and stirred at this temperature for 1 h. Following the dropwise addition of **13c** (185 mg, 0.707 mmol) dissolved in THF (3 mL), stirring was maintained at −78 °C for 1.5 h prior to quenching with saturated NH_4Cl solution (3 mL), dilution with water, and extraction with ether (4 × 25 mL). The combined organic solutions were dried and concentrated to leave a residue that was purified by chromatography on silica gel (elution with 5–10% ethyl acetate in petroleum ether). There was isolated 135 mg (72%) of **14** as a colorless solid: mp 99–102 °C; IR ($CHCl_3$, cm^{-1}) 1760; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.84 (br d, J = 6.5 Hz, 1 H), 5.56 (tq, J = 1.5, 6.6 Hz, 1 H), 4.72 (dd, J = 7.4, 12.0 Hz, 1 H), 2.78 (ddd, J = 2.6, 7.8, 19.6 Hz, 1 H), 2.51 (q, J = 1.3 Hz, 3 H), 2.48–2.40 (m, 1 H), 2.38–2.28 (m, 4 H), 2.13–2.04 (br m, 1 H), 1.97–1.87 (m, 1 H), 1.82–1.69 (m, 2 H), 1.63–1.46 (m, 2 H), 1.22 (d, J = 12.3 Hz, 1 H), 1.19 (d, J = 16.2 Hz, 1 H), 1.17 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 177.8, 136.1, 132.3, 131.3, 103.5, 86.1, 43.8, 38.5, 33.5, 32.6, 30.01, 29.97, 27.2 (2 C), 26.7, 24.2, 22.7, 21.3; MS m/z (M^+) calcd 398.0743, obsd 398.0753.

(1*R,2*R**,3*R**,4*R**,11*S**)-4-[(1*S**,3*Z*)-1-(Hydroxymethyl)-4-iodo-3-pentenyl]-11-methyltricyclo[5.4.0.0^{2,11}]undec-7-en-3-ol (15a).** Lactone **14** (395 mg, 1.0 mmol) was dissolved in 3:1 THF–water (20 mL), and sodium borohydride (145 mg, 3.8 mmol) was added portionwise. The mixture was stirred for 12 h during which time further portions of sodium borohydride (30 mg lots) were introduced every 2 h. When reduction was complete, saturated NH_4Cl solution (20 mL) was added and the product was extracted into ethyl acetate (4 × 50 mL). The combined organic layers were dried and concentrated, and the residue was purified by silica gel chromatography (gradient elution with 10–60% ethyl acetate in petroleum ether). There was obtained 340 mg (85%) of **15a** as a thick colorless oil: IR (neat, cm^{-1}) 3700–3250; ^{1}H NMR (300 MHz, C_6D_6) δ 5.78 (dd, J = 3.0, 4.8 Hz, 1 H), 5.29 (tq, J = 1.4, 6.1 Hz, 1 H), 4.10 (dd, J = 9.2, 10.2 Hz, 1 H), 3.57 (dd, J = 5.7, 11.1 Hz, 1 H), 3.42 (dd, J = 4.2, 11.1 Hz, 1 H), 2.80 (br s, 1 H), 2.38–2.28 (m, 2 H), 2.26 (q, J = 1.1 Hz, 3 H), 2.28–2.01 (m, 5 H), 2.01–1.82 (m, 2 H), 1.79–1.71 (m, 2 H), 1.65–1.52 (m, 1 H), 1.50–1.30 (m, 2 H), 1.05 (s, 3 H), 0.76 (d, J = 9.0 Hz, 1 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 138.4, 135.0, 130.0, 101.8, 72.9, 63.9, 43.9, 41.9, 35.6, 34.8, 33.5, 33.1, 30.8, 27.9, 25.7, 25.6, 24.2, 20.9; MS m/z (M^+) calcd 402.1056, obsd 402.1011. Anal. Calcd for $C_{18}H_{27}IO_2$: C, 53.74; H, 6.74. Found: C, 53.84; H, 6.96.

(1*R,2*R**,3*R**,4*R**,11*S**)-4-[(1*S**,3*Z*)-1-[(*tert*-Butyldimethylsiloxy)methyl]-4-iodo-3-pentenyl]-11-methyltricyclo[5.4.0.0^{2,11}]undec-7-en-3-ol (15b).** A cold (0 °C), magnetically stirred solution of **15a** (0.94 g, 2.34 mmol) in CH_2Cl_2 (10 mL) was treated with a solution of *tert*-butyldimethylsilyl triflate (0.62 mL, 2.69 mmol) and triethylamine (1.87 mL, 13.5 mmol) in CH_2Cl_2 (5 mL) via cannula and stirred at this temperature for 30 min and at rt for an equal length of time. The reaction mixture was quenched with saturated $NaHCO_3$ solution and extracted with ethyl acetate (4 × 50 mL). The combined organic layers were dried and concentrated to leave a residue whose purification was achieved by silica gel chromatography (elution with 0–5% ethyl acetate in petroleum ether). There was isolated 0.92 g (76%) of **15b** as a thick, colorless oil: IR ($CHCl_3$, cm^{-1}) 3550–3300; ^{1}H NMR (300 MHz, C_6D_6) δ 5.81 (dd, J = 1.3, 6.3 Hz, 1 H), 5.22–5.18 (m, 1 H), 4.25 (t, J = 9.4 Hz, 1 H), 3.63 (dd, J = 5.3, 10.2 Hz, 1 H), 3.49 (dd, J = 5.0, 10.2 Hz, 1 H), 2.45–2.40 (m, 1 H), 2.36–2.31 (m, 1H), 2.25 (d, J = 1.0 Hz, 3 H), 2.25–1.99 (series of m, 5 H), 1.91–1.73 (m, 3 H), 1.63 (ddd, J = 2.4, 3.4, 12.2 Hz, 1 H), 1.52–1.38 (m, 2 H), 1.06 (s, 3 H), 1.01 (t, J = 5.6 Hz, 1 H), 0.97 (s, 9 H), 0.79 (d, J = 9.0 Hz, 1 H), 0.08 (s, 3 H), 0.07 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 138.9, 135.1, 129.8, 101.7, 73.5, 64.1, 41.7, 41.4, 37.2, 34.8, 33.5, 30.7, 28.0, 26.1 (3 C), 25.7, 24.2, 23.8, 21.0, 18.4, −5.3, −5.4; MS m/z (M^+ − t-BuMe$_2$SiOH) calcd 384.0950, obsd 384.0948. Anal. Calcd for $C_{24}H_{41}IO_2Si$: C, 55.80; H, 8.00. Found: C, 56.18; H, 8.15.

(1*R,2*R**,4*R**,11*S**)-4-[(1*S**,3*Z*)-1-[(*tert*-Butyldimethylsiloxy)methyl]-4-iodo-3-pentenyl]-11-methyltricyclo[5.4.0.0^{2,11}]undec-7-en-3-one (16).** A mixture of **15b** (0.92 g, 1.78 mmol), 4 Å molecular sieves (0.92 g), *N*-methylmorpholine *N*-oxide (0.46 g, 3.93 mmol), and CH_2Cl_2 (10 mL) was stirred for 10 min before TPAP (68 mg, 0.19 mmol) was added in one portion. The reaction mixture was stirred at rt for 1 h, placed directly atop a column of silica gel, and eluted with 0–5% ethyl acetate in petroleum ether to give 0.65 g (71%) of **16** as a colorless crystalline solid: mp 83–85 °C; IR ($CHCl_3$, cm^{-1}) 1680; ^{1}H NMR (300 MHz, C_6D_6) δ 5.61 (br d, J = 7.2 Hz, 1 H), 5.13 (tq, J = 1.3, 7.4 Hz, 1 H), 3.58–3.46 (m, 2 H), 2.68–2.59 (m, 1 H), 2.48 (br d, J = 12.7 Hz, 1 H), 2.23 (qd, J = 5.4, 11.9 Hz, 1 H), 2.16 (d, J = 1.2 Hz, 3 H), 1.91 (d, J = 10.0 Hz, 1 H), 2.14–1.85 (series of m, 5 H), 1.79 (d, J = 9.0 Hz, 1 H), 1.64–1.46 (m, 3 H), 1.02 (s, 3 H), 0.96 (s, 9 H), 0.98–0.94 (m, 1 H), 0.084 (s, 3 H), 0.077 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 210.8, 137.7, 134.5, 127.4, 102.6, 64.5, 52.2, 44.5, 41.2, 37.3, 35.6, 33.5, 28.1, 26.8, 26.2 (3 C), 23.6, 23.0, 22.5, 20.1, 18.7, −5.27, −5.33; MS m/z (M^+) calcd 514.1764, obsd 514.1721. Anal. Calcd for $C_{24}H_{39}IO_2Si$: C, 56.02; H, 7.64. Found: C, 56.43; H, 7.68.

(1*R,1a*S**,4a*S**,5*R**,8b*S**)-4-[(1*S**,3*Z*)-1-[(*tert*-Butyldimethylsiloxy)methyl]-1a,4,4a,5,6,7,8,8b-octahydro-1,8-dimethyl-1*H*-1,2-[1]propanyl[3]ylidenebenzo[*a*]cyclopropa[*c*]cyclohepten-8a(3*H*)-ol (17).** A solution of **16** (40 mg, 76.8 μmol) in dry THF (3 mL) was cooled to 0 °C and treated dropwise with *n*-butyllithium (0.17 mL of 1.4 M in hexanes, 231 μmol). After 4 h at 0 °C, water (1 mL) was added and the mixture was allowed to warm to rt. Further dilution with water (4 mL), extraction with ether (4 × 5 mL), and drying of the combined organic layers was followed by concentration and chromatography of the residue on silica gel (elution with 1.5:1:97.5 ethyl acetate/CH_2Cl_2/hexanes). There were isolated (in order of elution) 5.4 mg (18%) of **19**, 3.1 mg (10%) of **18**, and 4.3 mg (14%) of **17**.

For **17**: IR ($CHCl_3$, cm^{-1}) 3690; ^{1}H NMR (300 MHz, C_6D_6) δ 5.57 (br d, J = 7.1 Hz, 1 H), 524 (s, 1 H), 3.60 (dd, J = 3.4, 9.9 Hz, 1 H), 3.53 (dd, J = 5.0, 9.9 Hz, 1 H), 2.88 (ddd, J =

5.0, 12.7, 13.9 Hz, 1 H), 2.26–2.01 (m, 5 H), 1.99 (d, J = 1.9 Hz, 3 H), 1.96–1.86 (m, 2 H), 1.74–1.50 (m, 5 H), 1.04 (s, 3 H), 0.98 (s, 9 H), 0.90 (d, J = 10.2 Hz, 1 H), 0.74 (d, J = 9.5 Hz, 1 H), 0.07 (s, 6 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 143.7, 141.4, 124.2, 119.4, 78.9, 65.7, 49.5, 36.6, 36.0, 33.1, 30.4, 29.3, 28.1, 27.5, 26.3, 26.1 (3 C), 24.6, 23.8, 18.5, 18.3, −5.3, −5.4; MS m/z ($M^+ - H_2O$) calcd 370.2691, obsd 370.2711.

(1*R,2*R**,4*R**,11*S**)-4-[(1*S**,3*E*)-1-[(*tert*-Butyldimethylsiloxy)methyl]-3-pentenyl]-11-methyltricyclo[5.4.0.0^{2,11}]-undec-7-en-3-one and (1*R**,2*R**,4*S**, 11*S**)-4-[(1*S**,3*E*)-1-[(*tert*-Butyldimethylsiloxy)methyl]-3-pentenyl]-11-methyltricyclo[5.4.0.0^{2,11}]undec-7-en-3-one (18 and 19).** A mixture of **16** (33 mg, 63.5 μmol), magnesium (23 mg, 0.96 mmol), 1,2-dibromoethane (1 drop), and THF (9.3 mL) was refluxed overnight, cooled, diluted with wet ether (10 mL), and washed with saturated NH_4Cl solution (5 mL). The organic phase was dried and concentrated to leave a residue, chromatography of which on silica gel (elution with 0–2% ether in petroleum ether) furnished 10.5 mg (43%) of **19** and 5.3 mg (22%) of **18**.

For **18**: colorless oil; IR ($CHCl_3$, cm^{-1}) 1685; ^{1}H NMR (300 MHz, C_6D_6) δ 5.58 (br d, J = 6.3 Hz, 1 H), 5.44–5.30 (m, 2 H), 3.55 (d, J = 6.8 Hz, 2 H), 2.60–2.52 (m, 1 H), 2.51–2.41 (m, 1 H), 2.29–1.82 (m, 6 H), 1.79 (d, J = 9.1 Hz, 1 H), 1.65–1.37 (m, 7 H), 1.03 (s, 3 H), 0.96 (s, 9 H), 1.00–0.95 (m, 1 H), 0.09 (s, 3 H), 0.07 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 210.7, 137.8, 130.0, 127.9, 126.8, 64.3, 52.4, 44.5, 41.1, 35.4, 33.3, 28.1, 26.8, 26.2 (3 C), 23.5, 23.0, 22.8, 20.3, 18.7, 18.0, −5.3, −5.4; MS m/z (M^+) calcd 388.2798, obsd 388.2807.

For **19**: colorless oil; IR ($CHCl_3$, cm^{-1}) 1700; ^{1}H NMR (300 MHz, C_6D_6) δ 5.63 (br d, J = 5.9 Hz, 1 H), 5.48–5.43 (m, 2 H), 3.83 (dd, J = 5.4, 9.9 Hz, 1 H), 3.63 (dd, J = 4.0, 9.9 Hz, 1 H), 2.75–2.67 (m, 1 H), 2.51 (td, J = 4.5, 13.2 Hz, 1 H), 2.11 (m, 3 H), 2.03–1.88 (m, 2 H), 1.83–1.70 (m, 3 H), 1.61 (d, J = 4.6 Hz, 3 H), 1.60–1.57 (m, 1 H), 1.51 (ddd, J = 2.0, 4.5, 13.6 Hz, 1 H), 0.98 (s, 9 H), 0.96 (s, 3 H), 1.05–0.91 (m, 2 H), 0.07 (s, 6 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 208.1, 138.9, 130.1, 126.7, 63.3, 55.0, 43.1, 42.4, 35.2, 32.8, 32.3, 27.8, 26.6, 26.23, 26.18 (3 C), 24.9, 23.6, 18.5, 18.1, −5.3 (2 C); MS m/z (M^+) calcd 388.2798, obsd 388.2789.

[(1*RS*,3*R*,6*E*)-1-Bromo-8-[(*p*-methoxybenzyl)oxy]-3,7-dimethyl-6-octen-1-yl]tributylstannane (21). To a cold (0 °C) solution of diisopropylamine (7.69 mL, 54.8 mmol) in dry THF (110 mL) was added dropwise 1.3 M n-butyllithium in hexanes (38.3 mL, 49.8 mmol). Upon completion of the addition, the mixture was stirred at 0 °C for 15 min prior to the introduction of tri-n-butyltin hydride (13.4 mL, 49.8 mmol) at the same temperature. After 15 additional min at 0 °C, a solution of **20**[2c] (7.22 g, 24.9 mmol) in dry THF (25 mL) was added dropwise at −78 °C, stirred for 2 h at −78 °C, and quenched with a mixture of saturated NH_4Cl solution (25 mL) and water (25 mL). The reaction mixture was partitioned between water (150 mL) and petroleum ether (300 mL), and the separated aqueous phase was extracted once with petroleum ether (300 mL). The combined organic layers were dried and concentrated below 30 °C. The residue was dissolved in dry CH_2Cl_2 (50 mL), cooled to 0 °C, and treated sequentially with carbon tetrabromide (10.7 g, 32.4 mmol) dissolved in dry CH_2Cl_2 (25 mL) and triphenylphosphine (7.19 g, 27.4 mmol). This mixture was stirred at rt for 15 h and freed of solvent in vacuo to leave a residue which was chromatographed on silica gel (elution with 25:1 petroleum ether–ethyl acetate) to give 13.5 g (84%) of **21** as a mixture of two diastereomers: colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.19 (td, J = 2.4, 6.7 Hz, 2 H), 6.80 (td, J = 2.4, 6.7 Hz, 2 H), 5.36–5.32 (m, 1 H), 4.34 (s, 2 H), 3.80 (s, 2 H), 3.72 (s, 3 H), 3.71–3.62 (m, 1 H), 2.07–1.88 (m, 4 H), 1.78–1.65 (m, 2 H), 1.62 (s, 3 H), 1.57–1.41 (m, 8 H), 1.33–1.20 (m, 8 H), 1.11–0.96 (m, 1 H), 0.94–0.88 (m, 2 H), 0.93 (d, J = 7.4 Hz, 3 H), 0.83 (t, J = 7.3 Hz, 9 H); MS m/z ($M^+ - C_4H_9Br$) calcd 506.2358, obsd 506.2387.

This material was subjected directly to dehydrobromination.

α-[[(2*E*,6*S*)-2,6-Dimethyl-2-octen-7-ynyl]oxy]-*p*-methoxytoluene (23). A solution of **21** (13.1 g, 20.3 mmol) in toluene (40 mL) containing 9.27 g (60.9 mmol) of DBU was refluxed for 2 h, allowed to cool to rt, and diluted with ether (100 mL). Hydrolysis with saturated NH_4Cl solution (100 mL) was followed by separation of the phases and extraction of the aqueous layer with ether (100 mL). The combined organic solutions were dried and evaporated to leave the isomeric vinyl stannanes which were dissolved in dry acetonitrile (100 mL, freshly distilled from P_2O_5) and treated with lead tetraacetate (10.8 g, 24.4 mmol, freshly recrystallized from acetic acid). The reaction mixture was stirred for 3 h at rt while a light brown precipitate formed, diluted with petroleum ether (40 mL), and filtered through a short pad of Celite. The filtrate was poured into saturated KF solution (100 mL), well shaken to allow formation of a white precipitate, and again filtered. The phases in the filtrate were separated, and the aqueous layer was extracted with ethyl acetate (3 × 50 mL). The combined organic solutions were dried and evaporated to leave a residue which was purified by Kugelrohr distillation (150–160 °C/2 Torr). There was obtained 1.70 g (30%) of **23** as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 (td, J = 2.4, 8.6 Hz, 2 H), 6.82 (td, J = 2.4, 8.6 Hz, 2 H), 5.41 (dt, J = 1.2, 7.3 Hz, 1 H), 4.39 (s, 2 H), 3.88 (s, 2 H), 3.80 (s, 3 H), 2.48–2.41 (m, 1 H), 2.26–2.17 (m, 2 H), 2.06 (d, J = 2.4 Hz, 1 H), 1.70 (s, 3 H), 1.57–1.46 (m, 2 H), 1.19 (d, J = 6.9 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 159.1, 132.9, 130.7, 129.3 (2 C), 127.4, 113.7 (2 C), 75.9, 71.1, 68.4, 55.3, 36.5, 25.4, 25.3, 20.9, 13.9; MS m/z (M^+) calcd 272.1776, obsd 272.1775; $[\alpha]^{20}_D$ +23.9 (c 1.17, $CHCl_3$).

The (*R*)-enantiomer of **23** exhibited $[\alpha]^{20}_D$ −32.6° (c 1.14, $CHCl_3$).

Methyl (4*S*,7*E*)-9-[(*p*-Methoxybenzyl)oxy]-4,8-dimethyl-7-nonen-2-ynoate (24). To a cold (−30 °C) solution of n-butyllithium (0.55 mL of 1.3 M in hexanes, 0.72 mmol) in dry ether (1 mL) was added dropwise **23** (163 mg, 0.60 mmol) dissolved in ether (0.5 mL). This mixture was stirred at 0 °C for 3 h, recooled to −30 °C, treated with freshly distilled methyl chloroformate (0.70 mL, 0.50 mmol), and allowed to warm to rt. After 40 h of stirring, the reaction mixture was poured into ice–water (5 mL) and the separated aqueous phase was extracted with ether (3 × 5 mL). The combined organic solutions were dried and concentrated, and the residue was subjected to chromatography on silica gel (elution with 10% ethyl acetate in petroleum ether) to provide 134 mg (68%) of **24** as a pale yellow oil: IR ($CHCl_3$, cm^{-1}) 1740; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 (td, J = 2.6, 8.7 Hz, 2 H), 6.87 (td, J = 2.6, 8.7 Hz, 2 H), 5.38 (dt, J = 1.2, 7.3 Hz, 1 H), 4.38 (s, 2 H), 3.86 (s, 2 H), 3.80 (s, 3 H), 3.75 (s, 3 H), 2.64–2.53 (m, 1 H), 2.27–2.14 (m, 2 H), 1.68 (s, 3 H), 1.64–1.43 (m, 2 H), 1.23 (d, J = 6.9 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 159.1, 154.3, 133.4, 130.6, 129.3 (2 C), 126.6, 113.7 (2 C), 93.3, 75.8, 73.2, 71.2, 55.3, 52.6, 35.6, 25.5, 25.4, 19.8, 14.0; MS m/z (M^+) calcd 330.1831, obsd 330.1831; $[\alpha]^{20}_D$ +46.6 (c 1.01, $CHCl_3$).

The (*R*)-enantiomer of **24** exhibited $[\alpha]^{20}_D$ −53.8° (c 1.10, $CHCl_3$).

(2*Z*,4*S*,7*E*)-3-Iodo-9-[(*p*-methoxybenzyl)oxy]-4,8-dimethyl-2,7-nonadien-1-ol (25). A solution of **24** (686 mg, 2.11 mmol) in dry THF (10 mL) was added at rt to a stirred suspension of lithium aluminum hydride (240 mg, 6.33 mmol) and sodium methoxide (686 mg, 12.7 mmol) in dry THF (20 mL), refluxed for 4 h, and cooled to −60 °C prior to the direct addition of iodine (3.21 g, 12.7 mmol). The mixture was allowed to warm to 0 °C overnight, at which point water (2 mL), 10% NaOH solution (2 mL), and water (12 mL) were added in turn, followed by saturated $K_2S_2O_3$ solution until the red-brown color of the solution had completely faded. The solids were removed by filtration, the filtrate was extracted with ether (3 × 20 mL), and the combined organic solutions were dried and evaporated. The residue was subjected to spinning plate chromatography on silica gel. Elution with 20% ethyl acetate in petroleum ether gave 694 mg (76%) of **25** as a colorless oil: IR ($CHCl_3$, cm^{-1}) 3600, 1610; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 (td, J = 2.4, 8.7 Hz, 2 H), 6.88 (td, J = 2.4, 8.7 Hz, 2 H), 5.96 (t, J = 5.7 Hz, 1 H), 5.40 (dt, J = 1.1, 7.2 Hz, 1 H), 4.39 (s, 2 H), 4.22 (d, J = 5.7, 2 H), 3.86 (s, 3 H), 3.81 (s, 3 H), 2.07–1.87 (m, 2 H), 1.72 (br s, 1 H), 1.65 (s, 3 H), 1.58–1.45 (m, 1 H), 1.37–1.24 (m, 1 H), 1.02 (d, J = 6.6 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 159.2, 132.9, 132.6, 130.7, 129.3 (2 C), 127.6, 120.3, 113.8 (2 C), 76.0, 71.3, 67.0, 55.3, 45.6, 35.9, 25.3, 21.7, 14.1; MS m/z (M^+ − I) calcd 303.1960, obsd 303.1965; $[\alpha]^{20}_D$ +19.4 (c 1.15, $CHCl_3$).

α-[[(2*E*,6*S*,7*Z*)-9-Bromo-7-iodo-2,6-dimethyl-2,7-nonadienyl]oxy]-*p*-methoxytoluene (26). To a cold (0 °C) solu-

tion of **25** (35 mg, 0.10 mmol) and triphenylphosphine (55 mg, 0.21 mmol) in dry CH_2Cl_2 (0.5 mL) was added 80 mg (0.24 mmol) of carbon tetrabromide. The reaction mixture was stirred at 0 °C for 15 min, diluted with ether (10 mL), filtered, and concentrated. The residue was purified by chromatography on silica gel (elution with 10% ethyl acetate in petroleum ether) to give 35 mg (85%) of **26** as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 (d, J = 8.5 Hz, 2 H), 6.88 (d, J = 8.5 Hz, 2 H), 5.95 (t, J = 7.7 Hz, 1 H), 5.39 (m, 1 H), 4.39 (s, 2 H), 4.06 (d, J = 7.7 Hz, 2 H), 3.87 (s, 2 H), 3.81 (s, 3 H), 2.09−1.80 (m, 3 H), 1.66 (s, 3 H), 1.53−1.47 (m, 1 H), 1.36−1.33 (m, 1 H), 1.03 (d, J = 6.6 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 159.0, 132.8, 130.7, 129.3, 129.2 (2 C), 127.2, 126.2, 113.8 (2 C), 75.9, 71.2, 55.3, 45.7, 36.2, 35.3, 25.1, 21.6, 14.1; MS m/z (M^+) calcd 494.0120, obsd 494.0110; $[\alpha]^{20}_D$ +21.9 (c 1.24, $CHCl_3$).

(3*S*,3a*R*,6a*R*,7*S*,7a*R*,7b*R*)-3,3a,4,5,6a,7,7a,7b-Octahydro-3-[(2*Z*,4*S*,7*E*)-3-iodo-9-[(*p*-methoxybenzyl)oxy]-4,8-dimethyl-2,7-nonadienyl]-7-methyl-2*H*-7,6-[1]propanyl[3]-ylidenecyclopropa[6,7]cyclohepta[1,2-*b*]furan-2-one (27). A cold (−78 °C) solution of **9** exhibiting $[\alpha]^{20}_D$ −202.8 (c 1.03, $CHCl_3$) (491 mg, 2.25 mmol) in dry THF (50 mL) was treated with lithium bis(trimethylsilyl)amide (4.22 mL of 1 M in THF, 4.22 mmol) and stirred at rt for 1 h prior to the addition of **26** (1.14 g, 2.32 mmol) dissolved in dry THF (25 mL). The reaction mixture was stirred at −78 °C for 4 h, allowed to warm to 0 °C during 13 h, quenched with saturated NH_4Cl solution (25 mL) and water (50 mL), and extracted with ether (5 × 50 mL). The combined organic extracts were dried and evaporated to leave a residue which was purified by chromatography on silica gel. Elution with 10% ethyl acetate in petroleum ether furnished 808 mg (58%) of **27** as a colorless, viscous oil: IR (neat, cm^{-1}) 1760; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 (tt, J = 2.3, 8.6 Hz, 2 H), 6.87 (tt, J = 2.3, 8.6 Hz, 2 H), 5.85−5.83 (m, 1 H), 5.78 (t, J = 6.2 Hz, 1 H), 5.42−5.38 (m, 1 H), 4.73 (dd, J = 7.3, 12.0 Hz, 1 H), 4.38 (s, 2 H), 3.86 (s, 2 H), 3.80 (s, 3 H), 2.81−2.74 (m, 1 H), 2.51−2.30 (m, 5 H), 2.17−1.86 (m, 5 H), 1.82−1.68 (m, 2 H), 1.65 (s, 3 H), 1.62−1.43 (m, 3 H), 1.35−1.19 (m, 3 H), 1.18 (s, 3 H), 1.00 (d, J = 6.6 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 177.5, 159.0, 136.1, 132.5, 132.2, 130.7, 129.8, 129.2 (2 C), 127.6, 122.5, 113.7 (2 C), 86.0, 75.9, 71.1, 55.2, 45.7, 43.8, 38.5, 36.2, 32.0, 30.0, 29.9, 27.2, 26.7, 25.3, 24.2, 22.7, 21.8, 21.3, 14.0; MS m/z (M^+) calcd 630.2165, obsd 630.2202; $[\alpha]^{20}_D$ −118.2 (c 0.75, $CHCl_3$).

(*β*S,1*R*,2*R*,3*R*,4*R*,11*S*)-3-Hydroxy-*β*-[(2*Z*,4*S*,7*E*)-3-iodo-9-[(*p*-methoxybenzyl)oxy]-4,8-dimethyl-2,7-nonadienyl]-11-methyltricyclo[5.4.0.0^{2,11}]undec-7-ene-4-ethanol (28a). To a magnetically stirred solution of **27** (418 mg, 0.86 mmol) in a 3:1 mixture of THF and water (24 mL) was added sodium borohydride (80 mg, 2.11 mmol) at rt. Stirring was maintained for 62 h during which time further portions (20 × 30 mg) of $NaBH_4$ were introduced. Following hydrolysis with saturated NH_4Cl solution (40 mL), the product was extracted with ethyl acetate (4 × 50 mL), and the combined organic phases were dried and evaporated. The residue was subjected to column chromatography on silica gel (elution with 40% ethyl acetate in petroleum ether) to give 392 mg (72%) of **28a** as a colorless oil: IR (neat, cm^{-1}) 3360, 1510, 1460; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 (d, J = 7.3 Hz, 2 H), 6.86 (d, J = 7.3 Hz, 2 H), 5.81−5.79 (m, 1 H), 5.65 (t, J = 6.7 Hz, 1 H), 5.39 (m, 1 H), 4.37 (s, 2 H), 4.24 (t, J = 9.2 Hz, 1 H), 3.85 (s, 2 H), 3.79 (s, 3 H), 3.62 (A part of ABX, J_{AB} = 11.2 Hz, J_{AX} = 5.7 Hz, 1 H), 3.48 (B part of ABX, J_{AB} = 11.2 Hz, J_{BX} = 3.7 Hz, 1 H), 2.76 (br s, 1 H), 2.48−2.42 (m, 1 H), 2.34−2.25 (m, 2 H), 2.05−1.78 (series of m, 7 H), 1.69−1.53 (m, 2 H), 1.64 (s, 3 H), 1.53−1.42 (m, 2 H), 1.35−1.17 (m, 5 H), 1.15 (s, 3 H), 1.00 (dd, J = 1.1, 6.5 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 159.0, 138.0, 132.6, 132.5, 130.6, 129.9, 129.2 (2 C), 127.8, 120.8, 113.7 (2 C), 76.0, 72.9, 71.1, 63.7, 55.2, 45.7, 43.7, 41.7, 36.2, 34.3 (2 C), 32.8, 30.5, 27.7, 25.6, 25.5, 25.4, 23.7, 21.8, 20.8, 14.0; MS m/z ($M^+ - H_2O$) calcd 616.2405, obsd 616.2405; $[\alpha]^{20}_D$ −70.7 (c 1.03, $CHCl_3$).

(1*R*,2*R*,3*R*,4*R*,11*S*)-4-[(1*S*,3*Z*,4*S*,8*E*)-1-[(*tert*-Butyldimethylsiloxy)methyl]-4-iodo-10-[(*p*-methoxybenzyl)oxy]-5,9-dimethyl-3,8-decadienyl]-11-methyltricyclo[5.4.0.0^{2,11}]undec-7-en-3-ol (28b). A solution of **28a** (173 mg, 0.272 mmol) in dry CH_2Cl_2 (5 mL) was cooled to −78 °C, added to an equally cold mixture of *tert*-butyldimethylsilyl triflate (68.3 μL, 0.300 mmol) and triethylamine (164 μL), stirred at this temperature for 30 min, and hydrolyzed with saturated $NaHCO_3$ solution (10 mL). The product was extracted with ethyl acetate (4 × 25 mL), and the combined organic layers were dried and concentrated. The remaining residue was purified by silica gel chromatography (elution with 10% ethyl acetate in petroleum ether) to give 161 mg (79%) of **28b** as a colorless oil: IR (neat, cm^{-1}) 3480, 1510; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 (td, J = 2.3, 8.6 Hz, 2 H), 6.88 (td, J = 2.3, 8.6 Hz, 2 H), 5.78 (d, J = 6.5 Hz, 1 H), 5.60 (t, J = 6.4 Hz, 1 H), 5.43−5.38 (m, 1 H), 4.38 (s, 2 H), 4.28 (m, 1 H), 3.87 (s, 2 H), 3.80 (s, 3 H), 3.62 (A part of ABX, J_{AB} = 10.2 Hz, J_{AX} = 5.9 Hz, 1 H), 3.49 (B part of ABX, J_{AB} = 10.2 Hz, J_{BX} = 4.2 Hz, 1 H), 2.45−2.41 (m, 1 H), 2.27−2.19 (m, 2 H), 2.15−1.89 (series of m, 10 H), 1.87−1.71 (m, 2 H), 1.66 (s, 3 H), 1.53−1.44 (m, 3 H), 1.35−1.21 (m, 2 H), 1.17 (s, 3 H), 1.01 (d, J = 6.6 Hz, 3 H), 0.96 (s, 9 H), 0.06 (s, 3 H), 0.05 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 159.1, 138.7, 131.7, 132.6, 130.7, 129.5, 129.3, 127.7, 120.8, 113.7, 76.0, 73.7, 71.1, 63.6, 55.3, 45.9, 41.6, 41.4 36.3, 36.0, 34.3, 32.2, 30.4, 27.9, 26.0, 25.3, 25.2, 23.8, 23.6, 21.8, 20.9, 18.2, 14.0, −5.4, −5.5; MS m/z ($M^+ - I - H_2O$) calcd 603.4233, obsd 603.4207; $[\alpha]^{20}_D$ −60.6 (c 1.0, $CHCl_3$).

(1*R*,2*R*,4*R*,11*S*)-4-[(1*S*,3*Z*,5*S*,8*E*)-1-[(*tert*-Butyldimethylsiloxy)methyl]-4-iodo-10-[(*p*-methoxybenzyl)oxy]-5,9-dimethyl-3,8-decadienyl]-11-methyltricyclo[5.4.0.0^{2,11}]undec-7-en-3-one (29). A mixture of **28b** (160 mg, 0.214 mmol) and pyridine (143 μL, 0.859 mmol) in dry CH_2Cl_2 (15 mL) was treated with the Dess−Martin periodinane (183 mg, 0.427 mmol) at rt. The reaction mixture was stirred for 5 min, diluted with ether (20 mL), treated with 1 M NaOH solution (5 mL), and agitated for an additional 10 min. The separated organic phase was washed with 1 M NaOH (5 mL) and water (5 mL), dried, and evaporated. Chromatography of the residue on silica gel (elution with 10% ethyl acetate in petrolem ether) afforded **29** (124 mg, 78%) as a colorless oil: IR (neat, cm^{-1}) 1610; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68 (td, J = 2.5, 8.7 Hz, 2 H), 6.83 (td, J = 2.5, 8.7 Hz, 2 H), 5.67−5.60 (m, 2 H), 2.41 (m, 1 H), 4.39 (s, 2 H), 3.88 (s, 2 H), 3.82 (s, 3 H), 3.54−3.51 (m, 2 H), 2.62−2.56 (m, 1 H), 2.50−2.48 (m, 1 H), 2.32 (dq, J = 5.2, 11.8 Hz, 1 H), 2.20−2.01 (m, 3 H), 2.00−1.90 (m, 4 H), 1.87−1.82 (m, 2 H), 1.76−1.69 (m, 1 H), 1.66 (s, 3 H), 1.65−1.61 (m, 3 H), 1.54−1.45 (m, 1), 1.32−1.25 (m, 2 H), 1.13 (s, 3 H), 1.01 (d, J = 6.6 Hz, 3 H), 0.90 (s, 9 H), 0.57 (s, 3 H), 0.49 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 212.7, 159.1, 137.3,-132.6, 132.5, 130.7, 129.2 (2 C), 127.5, 127.2, 121.7, 113.7 (2 C), 75.9, 71.1, 63.8, 55.2, 52.1, 45.7, 43.8, 40.8, 36.4, 36.2, 35.0, 27.7, 26.7, 26.0 (3 C), 25.3, 23.4, 22.6, 22.1, 22.0, 20.1, 18.4, 14.0, −5.4, −5.5; MS m/z ($M^+ - C_4H_9$) calcd 689.2482, obsd 689.2524; $[\alpha]^{20}_D$ −17.6 (c 2.73, $CHCl_3$).

Reductive Deiodination of 29 on Attempted Cyclization. (1*R*,2*R*,4*R*,11*S*)-4-[(1*S*,3*E*,5*S*,8*E*)-1-[(*tert*-Butyldimethylsiloxy)methyl]-10-[(*p*-methoxybenzyl)oxy]-5,9-dimethyl-3,8-decadienyl]-11-methyltricyclo[5.4.0.0^{2,11}]undec-7-en-3-one (31). To a cold (0 °C) solution of 24.5 μL (0.174 mmol) of diisopropylamine in dry THF (1 mL) was added 109 μL (0.174 mmol) of *n*-butyllithium. The resulting solution was stirred at 0 °C for 15 min, treated with tri-*n*-butyltin hydride (39.5 μL, 0.148 mmol), and stirred 15 min longer. The mixture was cooled to −78 °C, copper(I) cyanide (6.6 mg, 0.070 mmol) was introduced, and stirring was maintained at −55 °C for 5 min prior to recooling to −78 °C and addition of **29** (9.8 mg, 0.013 mol) dissolved in dry THF (0.5 mL). The reaction mixture was stirred at −20 °C for 15 h, hydrolyzed with saturated $NaHCO_3$ solution (5 mL), and extracted with ether (3 × 5 mL). The combined organic phases were washed with saturated $NaHCO_3$ solution (5 mL) and brine (5 mL), dried, and concentrated. The residue (51.1 mg) was dissolved in anhydrous ether (2 mL), cooled to −78 °C, treated with *n*-butyllithium (10.9 μL, 0.017 mmol), and allowed to warm to 0 °C during 4 h. Hydrolysis with water (5 mL) was followed by ether extraction (3 × 10 mL), drying of the combined organic phases, and solvent evaporation. Chromatography of the residue on silica gel (elution with 10% ethyl acetate in petroleum ether) gave 5.1 mg (66%) of **31**.

For **31**: colorless oil; IR ($CHCl_3$, cm^{-1}) 1697; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 (td, J = 2.5, 8.7 Hz, 2 H), 6.87 (td, J =

2.5, 8.7 Hz, 2 H), 5.72 (dd, J = 0.8, 6.3 Hz, 1 H), 5.39 (m, 1 H), 5.32–5.28 (m, 2 H), 4.37 (s, 2 H), 3.87 (s, 2 H), 3.80 (s, 3 H), 3.60 (A part of ABX, J_{AB} = 7.4 Hz, J_{AX} = 5.2 Hz, 1 H), 3.52 (B part of ABX, J_{AB} = 7.4 Hz, J_{BX} = 3.9 Hz, 1 H), 2.73 (m, 1 H), 2.35 (m, 1 H), 2.27–1.85 (series of m, 10 H), 1.82–1.74 (m, 2 H), 1.66–1.54 (m, 2 H), 1.43 (s, 3 H), 1.36–1.21 (m, 3 H), 1.13 (s, 3 H), 0.97 (d, J = 6.7 Hz, 3 H), 0.89 (s, 9 H), 0.21 (s, 3 H), 0.11 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 210.2, 159.1, 138.5, 138.1, 137.2, 132.0, 129.3 (2 C), 128.6, 127.7, 126.9, 113.8 (2 C), 76.1, 71.0, 62.6, 55.3, 54.8, 42.8, 41.8, 36.9, 36.6, 34.3, 32.4, 31.8, 27.5, 26.7, 26.2, 26.0, 25.6 (3 C), 24.7, 23.2, 20.5, 18.3, 14.0, −5.4 (2 C); MS m/z (M^+) calcd 620.4261, obsd 620.4245.

(3*S*,3a*R*,6a*R*,7*S*,7a*R*,7b*R*)-3,3a,4,5,6a,7,7a,7b-Octahydro-3-[(2*Z*,4*R*,7*E*)-3-iodo-9-[(*p*-methoxybenzyl)oxy]-4,8-dimethyl-2,7-nonadienyl]-7-methyl-2*H*-7,6-[1]propanyl[3]ylidenecyclopropa[6,7]cyclohepta[1,2-*b*]furan-2-one (32). A 130 mg (0.594 mmol) sample of **9** was alkylated with *ent*-**26** (293 mg, 0.594 mmol) in the presence of lithium hexamethyldisilazide and THF in the manner described above. Spinning plate chromatography on silica gel (elution with 10% ethyl acetate in petroleum ether) returned 21 mg (7%) of unreacted bromide and afforded 205 mg (55%) of **32** as a colorless oil: IR ($CHCl_3$, cm^{-1}) 1762; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 (d, J = 8.5 Hz, 2 H), 6.86 (d, J = 8.5 Hz, 2 H), 5.83 (dd, J = 0.8, 5.5 Hz, 1 H), 5.75 (t, J = 6.3 Hz, 1 H), 5.38 (t, J = 7.0 Hz, 1 H), 4.72 (dd, J = 7.3, 12.0 Hz, 1 H), 4.36 (s, 2 H), 3.85 (s, 2 H), 3.78 (s, 3 H), 2.77 (dq, J = 2.0, 11.5 Hz, 1 H), 2.50–2.39 (m, 2 H), 2.36–2.25 (m, 3 H), 2.12–1.88 (series of m, 5 H), 1.83–1.70 (m, 2 H), 1.64 (s, 3 H), 1.61–1.44 (m, 3 H), 1.37–1.18 (m, 3 H), 1.16 (s, 3 H), 0.99 (d, J = 6.6 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 177.5, 159.0, 136.0, 132.5, 132.2, 130.6, 129.8 (2 C), 129.2, 127.5, 122.4, 113.6 (2 C), 86.0, 75.9, 71.0, 55.2, 45.6, 43.8, 38.5, 36.1, 32.0, 29.9, 27.2 (3 C), 26.7, 25.9, 24.1, 22.6, 21.7, 21.3, 13.9; MS m/z (M^+) calcd 630.2172, obsd 630.2183; $[\alpha]^{20}_D$ −140.2 (c 1.02, $CHCl_3$).

(1*R*,2*R*,4*R*,11*S*)-4-[(1*S*,3*Z*,5*R*,8*E*)-1-[(*tert*-Butyldimethylsiloxy)methyl]-4-iodo-10-[(*p*-methoxybenzyl)oxy]-5,9-dimethyl-3,8-decadienyl]-11-methyltricyclo[5.4.0.0^{2,11}]undec-7-en-3-one (33). Lactone **32** (201 mg, 0.318 mmol) was reduced with sodium borohydride (50 g, 1.32 mmol) as before to give 149 mg (74%) of diol as a colorless oil: IR ($CHCl_3$, cm^{-1}) 3400; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.18 (d, J = 8.5 Hz, 2 H), 6.80 (d, J = 8.5 Hz, 2 H), 5.74 (dd, J = 2.9, 4.5 Hz, 1 H), 5.58 (t, J = 6.7 Hz, 1 H), 5.32 (t, J = 6.3 Hz, 1 H), 4.30 (s, 2 H), 4.18 (t, J = 9.3 Hz, 1 H), 3.78 (s, 2 H), 3.72 (s, 3 H), 3.57 (A part of ABX, J_{AB} = 11.1 Hz, J_{AX} = 5.7 Hz, 1 H), 3.40 (B part of ABX, J_{AB} = 11.1 Hz, J_{BX} = 4.5 Hz, 1 H), 2.50 (br s, 1 H), 2.37 (m, 1 H), 2.27–2.19 (m, 1 H), 2.12–2.03 (m, 1 H), 1.96 (s, 3 H), 1.94–1.78 (m, 6 H), 1.75–1.62 (m, 2 H), 1.58 (s, 3 H), 1.54–1.36 (m, 3 H), 1.26–1.13 (m, 3 H), 1.08 (s, 3 H), 0.93 (d, J = 6.6 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 159.0, 138.0, 132.8, 132.5, 130.6, 129.9, 129.3, 127.7, 120.9, 113.7, 75.9, 73.0, 71.1, 63.7, 55.2, 45.7, 43.3, 41.3, 36.1, 34.5, 34.2, 32.8, 30.5, 27.7, 25.4, 25.3, 25.0, 23.7, 21.9, 20.7, 14.0; MS m/z (M^+ − H_2O) calcd 616.2373, obsd 616.2439; $[\alpha]^{20}_D$ −108.4 (c 1.01, $CHCl_3$).

A solution of the diol (179 mg, 0.282 mmol) in dry CH_2Cl_2 (5 mL) was added at −78 °C to a magnetically stirred solution of *tert*-butyldimethylsilyl triflate (76.9 μL, 0.338 mmol) and triethylamine (185 μL) in CH_2Cl_2 (5 mL). The reaction mixture was stirred at −78 °C for 30 min, hydrolyzed with saturated $NaHCO_3$ solution (10 mL), and extracted with ethyl acetate (4 × 25 mL). The combined organic phases were dried and concentrated, and the residue was purified by chromatography on silica gel (elution with 10% ethyl acetate in petroleum ether) to give 155 mg (73%) of the monosilylated derivative as a colorless oil: IR ($CHCl_3$, cm^{-1}) 3300–3110, 1610, 1590, 1510; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 (td, J = 2.5, 8.7 Hz, 2 H), 6.88 (td, J = 2.5, 8.7 Hz, 2 H), 5.63 (t, J = 7.0 Hz, 1 H), 5.49–5.38 (m, 4 H), 4.38 (s, 2 H), 3.87 (s, 2 H), 3.80 (s, 3 H), 3.61 (A part of ABX, J_{AB} = 10.1 Hz, J_{AX} = 5.7 Hz, 1 H), 3.51 (B part of ABX, J_{AB} = 10.1 Hz, J_{BX} = 6.6 Hz, 1 H), 3.44–3.40 (m, 1 H), 2.63–2.57 (m, 2 H), 2.50–2.41 (m, 2 H), 2.36–2.17 (m, 5 H), 2.06–1.87 (m, 3 H), 1.78 (d, J = 1.6 Hz, 3 H), 1.76–1.67 (m, 2 H), 1.65 (s, 3 H), 1.58–1.46 (m, 2 H), 1.35–1.21 (m, 2 H), 1.02 (d, J = 6.6 Hz, 2 H), 0.89 (s, 9 H), 0.04 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 159.1, 137.6, 134.7, 133.2, 133.0, 132.5, 131.9, 130.8, 129.3, 127.8, 120.7, 119.9, 118.7, 113.8, 76.0, 71.1, 63.5, 55.2, 46.1, 45.8, 42.5, 38.2, 36.2, 35.5, 34.9, 27.7, 27.2, 26.0, 25.8, 22.0, 21.8, 14.0, −5.4; MS m/z (M^+ − H_2O) calcd 730.3284, obsd 730.3284; $[\alpha]^{20}_D$ −100.9 (c 1.0, $CHCl_3$).

The monosilylated derivative (149 mg, 0.200 mmol) and pyridine (133 μL, 0.800 mmol) in dry CH_2Cl_2 (10 mL) were treated with 170 mg (0.400 mmol) of the Dess-Martin periodinane at rt, stirred for 5 min, diluted with ether (20 mL) and 1 M NaOH solution (5 mL), and stirred for an additional 10 min. The separated organic layer was washed with 5 mL of 1 M NaOH and 5 mL of water, dried, and evaporated to leave a residue which was purified by chromatography on silica gel. There was isolated 99 mg (66%) of **33** as a colorless oil: IR ($CHCl_3$, cm^{-1}) 1680, 1610, 1580, 1510; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 (td, J = 2.4, 8.7 Hz, 2 H), 6.87 (td, J = 2.4, 8.7 Hz, 2 H), 5.66 (d, J = 7.1 Hz, 1 H), 5.58 (t, J = 6.5 Hz, 1 H), 5.39 (t, J = 6.8 Hz, 1 H), 4.37 (s, 2 H), 3.86 (s, 2 H), 3.80 (s, 3 H), 3.50–3.44 (m, 2 H), 2.58–2.45 (m, 2 H), 2.35–2.22 (m, 1 H), 2.18–2.02 (m, 3 H), 1.99–1.86 (m, 3 H), 1.83–1.77 (m, 3 H), 1.65–1.60 (m, 3 H), 1.64 (s, 3 H), 1.56–1.42 (m, 1 H), 1.32–1.21 (m, 3 H), 1.18 (s, 3 H), 0.98 (d, J = 6.6 Hz, 3 H), 0.87 (s, 9 H), 0.28 (s, 3 H), 0.20 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 213.0, 159.1, 137.4, 132.5, 132.4, 129.3, 127.7, 127.2, 113.7, 75.9, 71.1, 63.8, 55.2, 52.0, 45.7, 43.7, 40.8, 36.3, 36.2, 35.0, 27.8, 26.7, 26.0, 25.3, 23.4, 22.6, 22.0, 21.9, 20.1, 18.5, 14.0, −5.4, −5.5; MS m/z (M^+) calcd 746.3187, obsd 746.3238; $[\alpha]^{20}_D$ −32.3 (c 1.29, $CHCl_3$).

(1*R*,2*R*,4*R*,11*S*)-4-[(1*S*,3*E*,5*R*,8*E*)-1-[(*tert*-Butyldimethylsiloxy)methyl]-10-[(*p*-methoxybenzyl)oxy]-5,9-dimethyl-3,8-decadienyl]-11-methyltricyclo[5.4.0.0^{2,11}]undec-7-en-3-one (35). A cold (−78 °C) solution of **33** (33 mg, 0.0438 mmol) in anhydrous ether (4 mL) was treated with *tert*-butyllithium (103 μL of 1.6 M in pentane, 0.0268 mmol), stirred at this temperature for 9 h, allowed to warm to −10 °C overnight, hydrolyzed with water (10 mL), and extracted with ether (3 × 15 mL). The combined organic layers were dried and evaporated, and the residue was purified by chromatography on silica gel (elution with 5% ethyl acetate in petroleum ether). There was obtained 10 mg (37%) of **35**, 4 mg of a mixture of unknown compounds, and 5 mg (14%) of unreacted **33**.

For **35**: colorless oil; IR ($CHCl_3$, cm^{-1}) 1697; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 (d, J = 8.5 Hz, 2 H), 6.87 (d, J = 8.5 Hz, 2 H), 5.72 (d, J = 6.7 Hz, 1 H), 5.40 (m, 1 H), 5.35–5.29 (m, 2 H), 4.37 (s, 2 H), 3.87 (s, 2 H), 3.80 (s, 3 H), 3.60 (A part of ABX, J_{AB} = 9.5 Hz, J_{AX} = 5.4 Hz, 1 H), 3.53 (B part of ABX, J_{AB} = 9.5 Hz, J_{BX} = 3.3 Hz, 1 H), 2.73 (m, 1 H), 2.37–2.27 (m, 1 H), 2.15–1.85 (series of m, 10 H), 1.80–1.73 (m, 1 H), 1.66 (s, 3 H), 1.63–1.55 (m, 2 H), 1.36–1.17 (m, 4 H), 1.13 (s, 3 H), 0.97 (d, J = 6.7 Hz, 3 H), 0.89 (s, 9 H), 0.20 (s, 3 H), 0.11 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 210.2, 159.1, 138.1, 132.0, 130.8, 129.3 (2 C), 128.6, 127.3, 126.9, 113.8 (2 C), 76.1, 71.1, 62.8, 55.3, 54.7, 42.8, 41.9, 36.9, 36.0, 34.3, 32.4, 31.8, 27.5, 26.8, 26.2, 26.0 (3 C), 25.6, 24.7, 23.2, 20.9, 18.3, 14.0, −5.4 (2 C); MS m/z (M^+) calcd 620.4261, obsd 620.4245; $[\alpha]^{20}_D$ −15.2 (c 0.51, $CHCl_3$).

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Supporting Information Available: 300-MHz ^{1}H and 75-MHz ^{13}C NMR spectra of those compounds lacking combustion data (39 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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