A Means for Stereocontrolled Introduction of the C-2 Oxygen Substituent in Functionalized *cis*-Tricyclo[9.3.1.0^{3,8}]pentadecanones Related to Taxol

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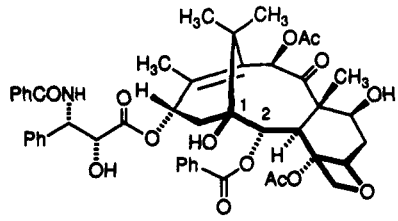
Several optically pure *cis*-tricyclo[9.3.1.0^{3,8}]pentadecanones have been prepared via anionic oxy-Cope rearrangement of *exo*-norbornanol precursors that have been obtained by convergent coupling of two functionalized reaction partners. The sigmatropic rearrangement is shown to proceed with exceptionally good stereochemical transmission because of universal adherence to the same endo-chair transition state. The atropisomeric aspects of this pivotal transformation are addressed. Also investigated was the proclivity of the products to undergo transannular hemiketal formation following osmylation of the bridgehead double bond. As matters turn out, the operation or nonoperation of this intramolecular addition to the C-9 carbonyl group is amenable to control merely by adjusting properly the stereochemistry of a single pendant substituent.

During the past couple of years, we have been concerned with the design[2] and development[3] of a unique strategy for the enantiospecific synthesis of taxane diterpenes. These early studies have established the feasibility of producing in relatively few steps from a common intermediate the core tricyclic frameworks of taxusin (hydrogen atom at C-1)[4] and taxol (hydroxyl group at C-1; see 1).[5]



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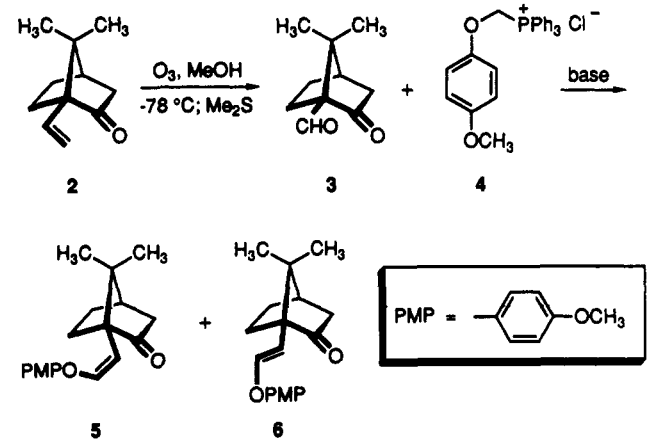
In the present report, we document the ease with which a C-2 oxygen functionality can be introduced directly and with complete stereocontrol into the tricyclo[9.3.1.0^{3,8}]-pentadecane framework by simple extension of the original protocol.

In a two-step sequence, the enantiopure β,γ-unsaturated ketone **2**[6] was first ozonolyzed to produce keto aldehyde **3** (97%, Scheme I).[7] The carbonyl groups in **3** can easily be chemodifferentiated. For our purposes, it was relevant to engage **3** in a Wittig reaction with phosphonium salt **4**. The latter reagent was formed by heating (*p*-methoxyphenoxy)methyl chloride[8] with triphenylphosphine in benzene for 24 h. Subsequent ylide generation, when

Scheme I



2 **3** **4** **5** **6**

effected with *n*-butyllithium in benzene, afforded the *cis*- and *trans*-vinyl ethers **5** and **6** in a ratio of 1:2 (^{1}H NMR analysis) with a combined efficiency of 93%. The individual isomers, which are efficiently separated by means of silica gel chromatography, could be conveniently distinguished on the basis of the chemical shifts and coupling constants of their vinyl protons (see Experimental Section). When the olefination step was performed with potassium hexamethyldisilazide (KHMDS) at 0 °C, a 1:1.5 distribution of **5** and **6** was realized. Substitution of hexane for THF had no measurable impact on the stereochemical outcome. No further evaluation was made of this condensation since both **5** and **6** were important to our projected examination of issues dealing with stereochemical transmission (see below).

Optically active vinyl bromide **7**,[9] prepared by conventional benzylation of (*R*)-1-bromo-3-cyclohexenol (74% ee),[4b] was transformed first into the lithium reagent by halogen–metal exchange with *tert*-butyllithium. As a consequence of the sterically enforced need for nucleophiles to attack the carbonyl carbons of **5** and **6** from the endo direction, the basicity of the reagent must be significantly attenuated in order to offset wholesale

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(1) National Institutes of Health Postdoctoral Fellow, 1990–1992.

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

(3) (a) Paquette, L. A.; Combrink, K. D.; Elmore, S. W.; Rogers, R. D. *J. Am. Chem. Soc.* **1991**, *113*, 1335. (b) Pegg, N. A.; Paquette, L. A. *J. Org. Chem.* **1991**, *56*, 2461.

(4) (a) Elmore, S. W.; Combrink, K. D.; Paquette, L. A. *Tetrahedron Lett.* **1991**, *32*, 6679. (b) Paquette, L. A.; Elmore, S. W.; Combrink, K. D.; Hickey, E. R.; Rogers, R. D. *Helv. Chim. Acta* **1992**, *75*, 1755.

(5) Paquette, L. A.; Combrink, K. D.; Elmore, S. W.; Zhao, M. *Helv. Chim. Acta* **1992**, *75*, 1772.

(6) Fischer, N.; Opitz, G. *Organic Syntheses*; Wiley: New York, 1973; Collect. Vol. V, p 877.

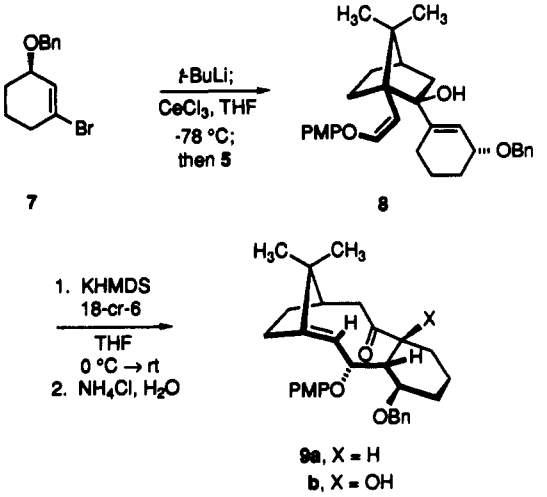
(7) A more lengthy synthesis of **3** has been earlier described: Polonski, T. *J. Chem. Soc. Perkin Trans. 1* **1983**, 305.

(8) Masaki, Y.; Iwata, I.; Mukai, I.; Oda, H.; Nagashima, H. *Chem. Lett.* **1989**, 659.

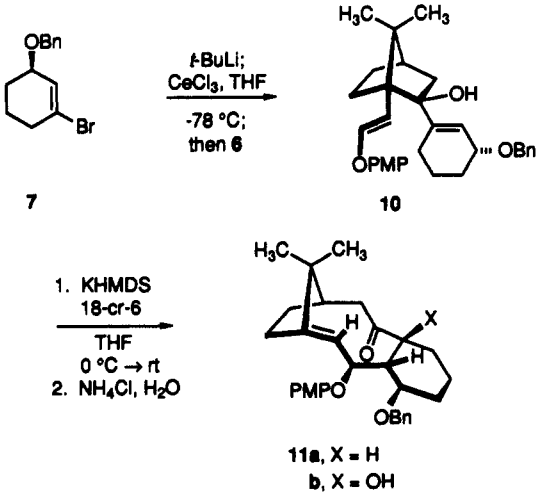
(9) The racemic form of **7** has been previously reported: Denmark, S. E.; Habermas, K. L.; Hite, G. A.; Jones, T. K. *Tetrahedron* **1986**, *42*, 2821.

0022-3263/93/1958-6874$04.00/0

Scheme II



Scheme III

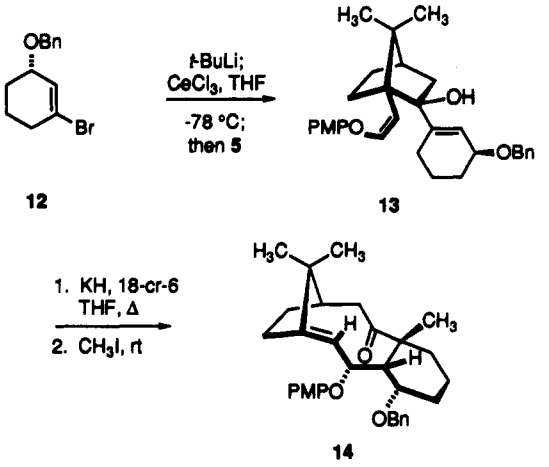


deprotonation.[10] Imamoto's tactic[11] of dichlorocerate formation (based on stoichiometry) was therefore adopted. Individual condensation of this intermediate with **5** (Scheme II) and with **6** (Scheme III) in THF at −78 °C led smoothly to carbinols **8** and **10**, respectively.

Exposure of **8** to KHMDS and 18-crown-6 in THF at 0 °C to room temperature *under conditions where care was taken to rigorously exclude oxygen* resulted in unidirectional anionic oxy-Cope rearrangement to **9a** (71%). When oxygen was present, conversion to **9b** was realized instead because of the high latent oxidizability of the "naked" enolate anion formed following the [3,3] sigmatropic event. Precedent for this extraordinarily facile α-hydroxylation was available from earlier investigations.[12]

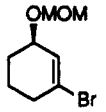
Entirely parallel observations were made when **10** was handled analogously. In this instance, **11a** and **11b** were isolated in 68 and 63% yields, respectively. As expected, therefore, *both carbinols undergo the oxy-Cope rearrangement exclusively via the same endo-chair transition*

Scheme IV



state that is strictly adopted by the parent vinyl systems.[2] The structural assignments to **9a,b**, and **11a,b**, follow from extensive NOE studies. The conformational rigidity[3] of these tricyclic ketones contribute in a very direct way to the convincing assessment of proximity relationships.

Attention was next focused on the concurrent introduction of the angular C-8 methyl group. For this purpose, the enantiomeric bromide **12** was transformed into its cerate as before and condensed with **5** to give **13** (Scheme IV). When the potassium alkoxide of **13** was generated from KH and 18-crown-6 under anaerobic conditions and refluxed in THF for 30 min, the desired sigmatropic event could be clearly observed as being complete by TLC. Further, the regiospecifically generated enolate was found capable of reacting with methyl iodide at rt to deliver **14** in 65% yield. While the unmaximized efficiency of the pivotal step was acceptable, that of the coupling reaction leading to **13** never surpassed 35%. In the light of this observation, the hydroxyl protective group was changed to MOM as in **15** and **16**.[3a]



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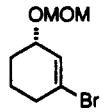

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For the purposes detailed above, it was desirable to carry out the four transformations encompassed in Scheme V. Several qualitative observations are noteworthy. While **19** and **21** undergo rapid anionic oxy-Cope rearrangement at rt, the rates for **17** and **23** are appreciably slower. Heating **17** to approximately 50 °C is needed to reach product in the same time frame. Where **23** is concerned, warming of the reaction mixture proved deleterious to the yield. Therefore, prolonged reaction times at rt were utilized.

The provocative atropisomeric aspects of these rearrangements, which have been delineated earlier,[3a] continue to hold fascination in the present investigation. Thus, **22** and **24** are isolated as conformationally pure isomers having their C-9 carbonyl groups pointed down. Although this structural topography can be confidently inferred from NOE studies (see Experimental Section), **22** was also subjected to X-ray crystallographic analysis for added corroboration. The relevant geometric features of this tricyclic ketone are made clearly apparent in its ORTEP diagram (Figure 1).

(10) (a) Paquette, L. A.; Learn, K. S. *J. Am. Chem. Soc.* **1986**, *108*, 7873. (b) Paquette, L. A.; Learn, K. S.; Romine, J. L.; Lin, H.-S. *J. Am. Chem. Soc.* **1988**, *110*, 879. (c) Paquette, L. A.; Romine, J. L.; Lin, H.-S.; Wright, J. *J. Am. Chem. Soc.* **1990**, *112*, 9284.

(11) (a) Imamoto, T.; Sugiura, Y.; Takiyama, N. *Tetrahedron Lett.* **1984**, *25*, 4233. (b) Imamoto, T.; Takiyama, N.; Nakamura, K. *Tetrahedron Lett.* **1985**, *26*, 4763. (c) Imamoto, T.; Takiyama, N.; Nakamura, K.; Hatajima, T.; Kamiya, Y. *J. Am. Chem. Soc.* **1989**, *111*, 4392.

(12) Paquette, L. A.; DeRussy, D. T.; Pegg, N. A.; Taylor, R. T.; Zydowsky, T. M. *J. Org. Chem.* **1989**, *54*, 4576.

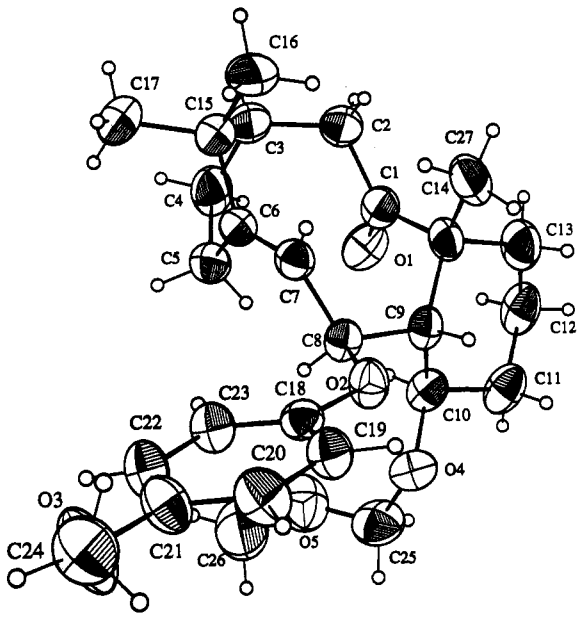
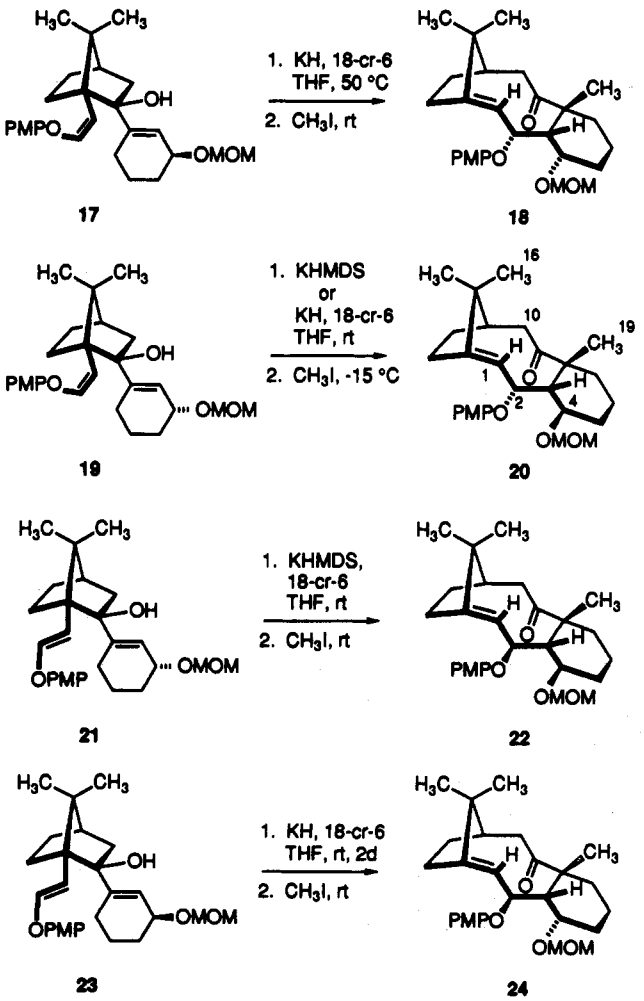


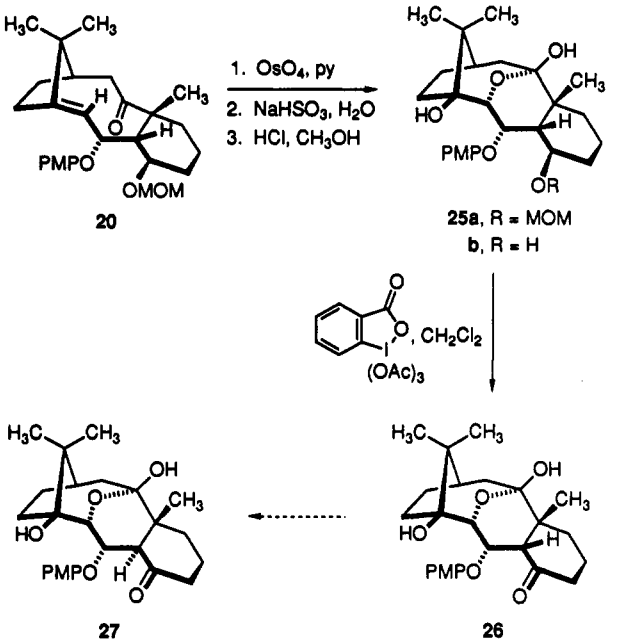
Figure 1. Computer-generated perspective drawing of the final X-ray model of **22**.

Scheme V



In contrast, **20** is initially produced in the carbonyl-up conformation. Although this atropisomeric form is kinetically favored, thermodynamics is evidently better satisfied by the alternative geometry shown in Scheme V, into which the initial product changes irreversibly upon standing at rt. This behavior contrasts with that of ketone

Scheme VI



18, which persists as a 1.5:1 mixture of atropisomers even after being heated for prolonged periods of time.

The dynamic conformational properties of **20** carry over to its product of dihydroxylation with osmium tetroxide (Scheme VI). Following reductive workup, the transannular hemiketal **25a** is formed exclusively. Furthermore, ring closure occurs with sufficient rapidity that the implementation of conditions intended to reduce the C-9 carbonyl prior to hydrolysis of the osmate ester (e.g., exposure to $LiAlH_4$ or DIBAL-H) only gave **25a** as well. This hyperreactivity may be attributed to increased steric strain introduced at C-2 by the neighboring *p*-methoxyphenoxy (PMPO) substituent. In the conformation likely adopted by the osmate ester, the PMPO group is oriented pseudoaxially and thrust well into the crowded concave surface of the molecule. The increased torsional strain that is concentrated principally within ring B is substantially relieved upon rotation of the C-1/C-2 bond. This motion projects the rather large PMPO unit pseudoequatorially while simultaneously placing the C-1 hydroxyl close to the C-9 carbonyl. Understandably, hemiketal formation lessens the level of nonbonded steric interaction still more.

An examination of molecular models suggested that the driving force for transannular hemiketal formation might well be reversed in diastereomeric systems characterized by a *trans*-B/C ring junction. This issue was therefore pursued by chemoselective deprotection of the MOM group to give **25b** and oxidation to **26** with the Dess–Martin periodinane reagent.[13] Somewhat to our dismay, **26** proved resistant to chemical change under a variety of conditions. Under no circumstances was the isomeric ketone **27** observed. β-Elimination of the PMPO group did not operate for stereoelectronic reasons (orthogonal relationship of the C–O bond to the flanking enolate π network). Two causative factors may be responsible for the inertness of **26**. First, the hemiketal may not be at all prone to undergo ring opening,[14] such that small amounts of the hydroxy ketone tautomer may not be present during

(13) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4155.
(14) That **25a** resides completely in the closed form is suggested (but not proven) by its total inertness to hydroxylamine, acidic methanol, and a host of oxidants.

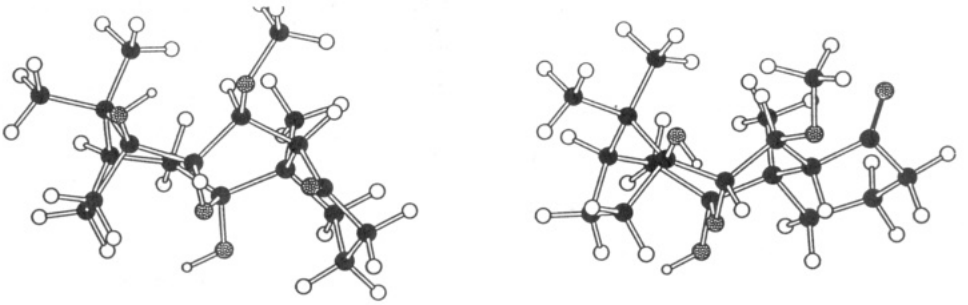
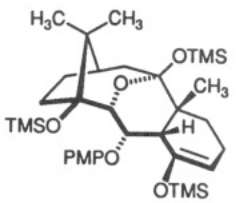


Figure 2. Global minimum energy conformations of **26**-OMe (left) and **27**-OMe (right) as determined by molecular mechanics calculations (Chem-3D output).

equilibration. MM2 calculations[15] performed in simplified derivatives of **26** and **27** (OMe replacing PMPO) show **26**-OMe to be modestly preferred thermodynamically by 0.6 kcal/mol (Figure 2). Consequently, in the absence of a ring-opened tautomer, direct epimerization would seem unlikely. Secondly, the kinetic acidity of the angular proton at C-3 may be significantly abated. The efficient conversion (84%) of **26** into the $\Delta^{4,5}$-silyl enol ether **28** upon treatment with trimethylsilyl iodide indicates that at least under these conditions there is little tendency to generate the more highly substituted enolate.



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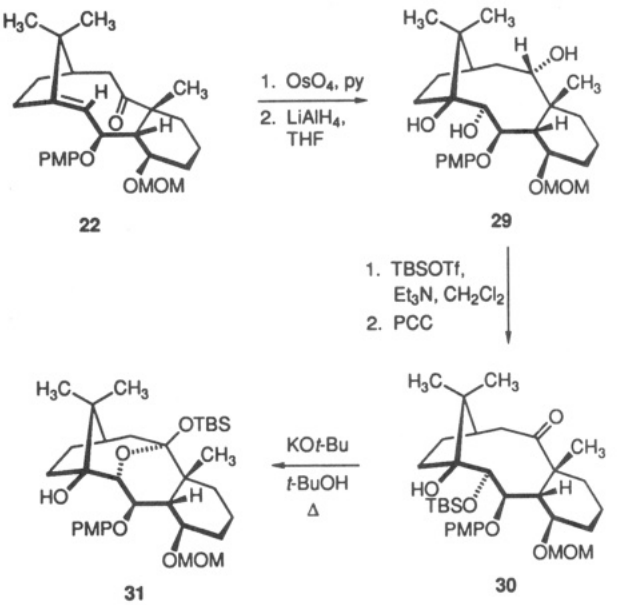
Lastly, it was of interest to inform ourselves of the conditions under which a β-PMPO diastereomer would experience transannular hemiketalization. Differences were already apparent during the osmylation–reduction process since triol **29** was conveniently isolated from this two-step sequence (Scheme VII). The conformational control brought on by the configurational change at C-2 provides the opportunity for ketone reduction to be kinetically feasible. Regioselective protection of the less-hindered secondary hydroxyl at C-2 made possible oxidation at C-9 to give **30**. When **30** was heated with potassium *tert*-butoxide, isomerization to **31** occurred in 80% yield. Consequently, although transannular ketalization is less than ideally accommodated by a β-PMPO substituent, hemiketal formation does operate at somewhat more elevated temperatures.

Summary. The chemistry described herein highlights the fact that the convergent assembly of *cis*-tricyclo[9.3.1.0^{3,8}]pentadecanones typified by **18**, **20**, **22**, **24**, and related ketones is governed by strict adherence to an endo-chair transition state during the anionic oxy-Cope rearrangement process. As a result, chirality transfer occurs with very high fidelity in a totally predictable manner. More specifically, *Z* vinyl ether geometry in the starting 7,7-dimethylnorbornenone translates directly into an α-configuration for the C(2)–O bond, precisely as required for ultimately attaining taxol.

Scheme VII



22 **29** **31** **30**

The limitations associated with transannlar ketalization following dihydroxylation of the bridgehead olefinic bond in the tricyclic enones have also been explored. For steric reasons, an α-PMPO group greatly facilitates addition of the C-1 hydroxyl across the carbonyl double bond. Elevated temperatures are required to achieve the same end result when the PMPO substituent is oriented β. Consequently, operation of this bonding scheme is amenable to control merely by adjusting the stereochemistry of but one pendant group.[16]

Experimental Section

Melting points are uncorrected. ^{1}H NMR spectra were recorded at 300 MHz and ^{13}C NMR spectra at 75 MHz. High resolution and fast atom bombardment mass spectra were

(15) (a) Allinger, N. L. *J. Am. Chem. Soc.* **1977**, *99*, 8127. (b) Burkert, U.; Allinger, N. L. *Molecular Mechanics*; American Chemical Society: Washington, D.C., 1982, Monograph 177. (c) The actual program used was MODEL version KS 2.96 (Steliou, K., private communication).

(16) For simplification purposes, taxol numbering has been utilized in the textual part of this paper. The compounds named in the Experimental Section are based upon the IUPAC system.

obtained at The Ohio State University Campus Chemical Instrumentation Center. Elemental analyses were performed at the Scandinavian Microanalytical Laboratory, Herlev, Denmark. 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 analyses.

(1*R*,4*R*)-1-Formyl-7,7-dimethyl-2-norbornanone (3). Into a dry, nitrogen-blanketed 500-mL round-bottomed flask was placed a solution of **2** (5.25 g, 0.032 mol) in methanol (150 mL). After cooling to −78 °C, ozone was bubbled through the solution until all of the starting material was consumed as judged by TLC analysis. Dimethyl sulfide (7.0 mL, 0.096 mol) was then introduced into the reaction mixture, which after 10 min was allowed to warm to rt and maintained as such for 2 h. Evaporation of the solvent in vacuo and purification of the residual oil by flash chromatography (elution with 5:1 hexane–ethyl acetate) gave **3** as a white solid (5.14 g, 97%), mp 189–194 °C (lit.[7] mp 204–205 °C); $[\alpha]^{20}_D$ +72.3° (*c* 0.68, C_2H_5OH) (lit.[7] $[\alpha]^{20}_D$ +77° (*c* 2, C_2H_5OH). This material was used without further purification.

[(*p*-Methoxyphenoxy)methyl]triphenylphosphonium Chloride (4). To a magnetically stirred solution of PCl_5 (6.96 g, 33.4 mmol) in CCl_4 (50 mL) was added 1,4-dimethoxybenzene (3.10 g, 22.5 mmol) followed by benzoyl peroxide (13.6 mg, 56 mmol). The reaction mixture was refluxed under a drying tube for 26 h, during which time additional benzoyl peroxide (10–15 mg) was introduced at 6–8 h intervals. After the contents had been cooled to rt, diluted with ether (100 mL), washed with 1 N NaOH (100 mL), and dried, the solvent was evaporated and the product purified by flash chromatography (elution with 10:1 hexane–ethyl acetate). There was isolated 2.80 g of a colorless oil that contained 79% of the monochloro derivative[8] (^{1}H NMR analysis). This material, obtained in an effective yield of 57%, was used directly.

The product obtained above was added to a solution of triphenylphosphine (2.53 g, 9.65 mmol) in benzene (10 mL) and heated under N_2 for 24 h, during which time the salt precipitated from solution. This white solid (2.42 g) was separated by filtration and the filtrate was again heated to reflux to give an additional 794 mg of **4**, mp 173–175 °C; ^{1}H NMR (DMSO-d_6) δ 7.96–7.76 (m, 15 H), 7.10 (d, *J* = 9.1 Hz, 2 H), 6.86 (d, *J* = 9.1 Hz, 2 H), 6.42 (d, *J* = 5.8 Hz, 2 H), 3.69 (s, 3 H); ^{13}C NMR (DMSO-d_6) ppm 154.8, 151.6 (d, $^3J_{C,P}$ = 12.7 Hz), 135.32 (d, $^4J_{C,P}$ = 2.7 Hz), 134.0 (d, $^3J_{C,P}$ = 10.1 Hz), 130.2 (d, $^2J_{C,P}$ = 12.6 Hz), 116.4, 116.3 (d, $^1J_{C,P}$ = 86.3 Hz), 114.6, 61.7 (d, $^1J_{C,P}$ = 68.3 Hz), 55.4.

(1*S*,4*R*)-1-[(*Z*)-2-(*p*-Methoxyphenoxy)vinyl]-7,7-dimethyl-2-norbornanone and (1*S*,4*R*)-1-[(*E*)-2-(*p*-Methoxyphenoxy)vinyl]-7,7-dimethyl-2-norbornanone (5 and 6). A solution of **4** (4.77 g, 11.0 mmol) in THF (30 mL) was cooled to −78 °C, treated with *n*-butyllithium (8.0 mL of 1.5 M in hexane, 12.0 mmol), warmed to 0 °C for 5–8 min, and again cooled to −78 °C. A solution of **3** (1.209 g, 7.28 mmol) in THF (7 mL) was introduced via cannula and the reaction mixture was maintained at −78 °C for 10 min, warmed to rt, and quenched with water (5 mL). After dilution with more water (100 mL) and ether extraction (2 × 75 mL), the combined organic phases were dried and concentrated. Flash chromatography (elution with 10:1 petroleum ether–ethyl acetate) of the residual oil gave a 1:2 mixture of **5** and **6** (1.93 g, 93%). MPLC separation (silica gel, elution with 10:1 petroleum ether–ethyl acetate) afforded the pure isomers (**5**, 497 mg, 24%, **6**, 1.08 g, 52%), both as colorless oils.

For **5**: IR (neat, cm^{-1}) 2980, 1750, 1675, 1515, 1235, 1050, 1030, 840; ^{1}H NMR ($CDCl_3$) δ 6.93 (d, *J* = 9.1 Hz, 2 H), 6.83 (d, *J* = 9.1 Hz, 2 H), 6.54 (d, *J* = 6.8 Hz, 1 H), 4.60 (d, *J* = 6.8 Hz, 1 H), 3.77 (s, 3 H), 2.58–2.38 (m, 2 H), 2.10–1.89 (m, 3 H), 1.82–1.73 (m, 1 H), 1.45–1.36 (m, 1 H), 1.06 (s, 3 H), 0.94 (s, 3 H); ^{13}C NMR ($CDCl_3$) 216.4, 155.4, 151.3, 145.5, 117.7, 114.7, 103.7, 62.0, 55.7, 49.3, 43.4, 42.8, 27.4, 27.1, 20.3, 20.2; MS *m/z* (M$^+$) calcd 286.1569, obsd 286.1575; $[\alpha]^{20}_D$ −16.7° (*c* 0.73, $CHCl_3$). Anal. Calcd for $C_{18}H_{22}O_3$: C, 75.50; H, 7.74. Found: C, 75.28; H, 7.77.

For **6**: IR (neat, cm^{-1}) 2970, 1745, 1670, 1505, 1230, 1125, 1040, 835; ^{1}H NMR ($CDCl_3$) δ 6.96 (d, *J* = 9.1 Hz, 2 H), 6.84 (d, *J* = 9.1 Hz, 2 H) 6.61 (d, *J* = 12.5 Hz, 1 H), 5.17 (d, *J* = 12.5 Hz, 1 H), 3.77 (s, 3 H), 2.48–2.39 (m, 1 H), 2.14 (t, *J* = 4.5 Hz, 1 H), 2.08–1.87 (m, 3 H), 1.55 (dt, *J* = 12.8, 3.6 Hz, 1 H), 1.41 (dt, *J* = 11.6, 3.0 Hz, 1 H), 0.97 (s, 3 H), 0.91 (s, 3 H); ^{13}C NMR ($CDCl_3$) ppm 216.7, 155.4, 151.2, 146.6, 117.9, 114.7, 105.2, 60.9, 55.6, 48.6, 43.6, 42.8, 27.9, 27.2, 20.0, 19.4; MS *m/z* (M$^+$) calcd 286.1569, obsd 286.1566; $[\alpha]^{20}_D$ −11.3° (*c* 0.44, $CHCl_3$). Anal. Calcd for $C_{18}H_{22}O_3$: C, 75.50; H, 7.74. Found: C, 75.48; H, 7.75.

(*R*)-Benzyl 3-Bromo-2-cyclohexen-1-yl Ether (7).[9] To a suspension of NaH (201 mg, 50% dispersion in oil, washed with 3 x 5 mL of pentane, 4.21 mmol) in cold (0 °C) DMF (5 mL) under N_2 was introduced benzyl chloride (0.35 mL, 3.04 mmol) via syringe. A solution of (*R*)-1-bromo-3-cyclohexenol (508 mg, 2.87 mmol, 74% ee)[4b] in DMF (5 mL) was added dropwise during 15 min. The reaction mixture was subsequently stirred at rt for 2.5 h, quenched by the dropwise addition of water (2 mL), and acidified with 5% HCl (20 mL). The product was extracted into ether (2 × 25 mL) and the combined organic phases were dried and concentrated prior to flash chromatography (elution with 15:1 hexane–ethyl acetate). There was obtained 707 mg (92%) of **7** as a colorless oil; IR (neat, cm^{-1}) 2920, 2860, 1640, 1080; ^{1}H NMR ($CDCl_3$) δ 7.39–7.27 (m, 5 H), 6.24–6.22 (m, 1 H), 4.57 (s, 2 H), 4.00–3.95 (m, 1H), 2.56–2.33 (m, 2 H), 1.99–1.60 (m, 4 H); ^{13}C NMR ($CDCl_3$) ppm 138.5, 129.4, 128.4, 127.6 (2 C), 127.3, 73.5, 70.3, 35.4, 27.2, 20.8; MS *m/z* (M$^+$) calcd 266.0306, obsd 266.0330; $[\alpha]^{20}_D$ +63.1° (*c* 3.7, $CHCl_3$).

(1*S*,2*S*,4*R*)-2-[(*R*)-3-(Benzyloxy)-1-cyclohexen-1-yl]-1-[(*Z*)-2-(*p*-methoxy-phenoxy)vinyl]-7,7-dimethyl-2-norbornanol (8). Cerium trichloride heptahydrate (426 mg, 1.14 mmol) was placed in a dry 25-mL round-bottomed flask and heated at 140 °C under vacuum (< 0.1 Torr) for 17 h. After a N_2 atmosphere had been established, the dry $CeCl_3$ powder was cooled to rt and suspended in THF (5 mL). The resulting slurry was stirred vigorously under N_2 for 4 h to give a uniform texture. Meanwhile, a THF solution (5 mL) of **7** (109 mg, 0.408 mmol) was cooled to −78 °C under nitrogen and treated with *tert*-butyllithium (0.55 mL of 1.7 M in pentane, 0.94 mmol) to give a greenish-yellow solution. The $CeCl_3$ slurry was next titrated with *tert*-butyllithium until an orange coloration was achieved, cooled to −78 °C, and treated with the vinyllithium solution via cannula. The resulting mixture was maintained at −78 °C for 50 min, at which point a cold (−78 °C) THF solution (3 mL) of **5** (61.4 mg, 0.215 mmol) was added via cannula. After 1 h, the reaction mixture was quenched with saturated NH_4Cl solution (1 mL), warmed to rt, filtered through a pad of Celite, diluted with ether (20 mL), and washed with water (25 mL). The organic phase was dried and concentrated, and the residue was purified by flash chromatography (elution with 5:1 hexane–ethyl acetate) to give enantiomerically pure **8** as a colorless oil (70.7 mg, 70%); IR (neat, cm^{-1}) 3450, 2940, 1655, 1505, 1225, 835; ^{1}H NMR ($CDCl_3$) δ 7.38–7.27 (m, 5H), 6.93–6.81 (m, 4 H), 6.42 (d, *J* = 7.1 Hz, 1 H), 6.02 (br s, 1 H), 4.89 (d, *J* = 7.1 Hz, 1 H), 4.59 (ABq, *J* = 12.1 Hz, Δν = 10.3 Hz, 2 H), 4.03 (br s, 1 H), 3.77 (s, 3 H), 2.30-2.10 (m, 4 H), 2.00–1.96 (m, 2 H), 1.84–1.66 (m, 6 H), 1.53–1.50 (m, 1 H), 1.28 (s, 3 H), 1.12–1.08 (m, 1 H), 0.92 (s, 3 H); ^{13}C NMR ($CDCl_3$) ppm 155.1, 151.4, 146.0, 142.3, 139.2, 128.3, 127.5, 127.3, 122.8, 117.3, 114.7, 109.1, 84.9, 73.5, 69.8, 57.2, 55.6, 52.2, 44.6, 42.2, 28.3, 27.9, 26.8, 26.0, 21.7, 21.6, 20.3; MS *m/z* (M$^+$) calcd 474.2770, obsd 474.2778; $[\alpha]^{20}_D$ +14.3° (*c* 0.69, $CHCl_3$). Anal. Calcd for $C_{31}H_{38}O_4$: C, 78.45; H, 8.07. Found: C, 78.28; H, 8.20.

(1*R*,4a*R*,7*R*,10*E*,12*R*,12a*R*)-1-(Benzyloxy)-2,3,4,4a,6,7,8,9,-12,12a-decahydro-12-(*p*-methoxyphenoxy)-13,13-dimethyl-7,10-methanobenzocyclodecen-5(1*H*)-one (9a). A THF solution (3 mL) of **8** (23.1 mg, 0.049 mmol) and 18-crown-6 (40 mg, 0.15 mmol) was cooled to 0 °C, rigorously deoxygenated with bubbling N_2 for 30 min, treated with KHMDS (0.30 mL of 0.5 M in toluene, 0.15 mmol), stirred at 0 °C for 30 min, and warmed to rt. After an additional 30 min, the reaction mixture was quenched with saturated NH_4Cl solution (1 mL) and diluted with water (2 mL) prior to ether extraction (3 × 5 mL). The combined organic phases were dried and concentrated under reduced pressure. The residue was subjected to flash chromatography (elution with 5:1 hexane–ethyl acetate) and 16.5 mg (71%) of **9a** was isolated as a white solid: mp 143–146 °C; IR ($CHCl_3$, cm^{-1}) 2950, 1690, 1510, 1225; ^{1}H NMR ($CDCl_3$) δ 7.12-7.08 (m, 3 H), 6.93–6.87 (m, 4 H), 6.81–6.77 (m, 2 H), 5.22–5.17 (m, 2 H), 4.55–4.50 (m, 2 H), 4.40 (d, *J* = 10.1 Hz, 1 H), 3.75 (s, 3 H), 3.29–3.26 (br m, 1 H), 2.98–2.88 (m, 1 H), 2.66 (dd, *J* = 11.2, 1.4 Hz, 1 H), 2.39–2.34 (m, 1 H), 2.26–2.18 (m, 1 H), 1.96–1.78

(m, 3 H), 1.70–1.40 (m, 4 H), 1.32–1.16 (m, 5 H), 1.05 (s, 3 H), 0.95–0.88 (m, 1 H); ^{13}C NMR ($CDCl_3$) ppm 212.2, 153.2, 152.3, 147.3, 139.0, 128.2, 128.0, 127.2, 121.8, 115.5, 114.5, 75.3, 75.0, 71.2, 55.7, 51.8, 51.7, 51.3, 46.4, 43.4, 32.0, 27.4, 25.3, 24.9, 22.9, 22.5, 19.3; MS *m/z* (M^+) calcd 474.2770, obsd 474.2780; $[\alpha]^{20}_D$ −167.2° (*c* 0.82, $CHCl_3$). Anal. Calcd for $C_{31}H_{38}O_4$: C, 78.45; H, 8.07. Found: C, 78.31; H, 8.25.

(1*R*,4a*R*,7*R*,10*E*,12*R*,12a*S*)-1-(Benzyloxy)-2,3,4,4a,6,7,8,9,-12,12a-decahydro-12-(*p*-methoxyphenoxy)-13,13-dimethyl-12a-hydroxy-7,10-methanobenzocyclodecen-5(1*H*)-one (9b). A THF solution (1 mL) of **8** (15.1 mg, 0.032 mmol) under nitrogen was cooled to 0 °C and treated with 18-crown-6 (24.7 mg, 0.094 mmol) followed by KHMDS (0.20 mL of 0.5 M in toluene, 0.10 mmol). After 1 h at 0 °C, the reaction mixture was warmed to rt for 1 h, quenched by the addition of saturated NH_4Cl solution (0.5 mL), diluted with water (2 mL), and extracted with ether (2 × 10 mL). The combined organic phases were dried and concentrated to leave a residue that was purified by flash chromatography (elution with 2:1 hexane–ethyl acetate) to give 7.0 mg (45%) of **9b** as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.13–7.08 (m, 5 H), 6.89–6.76 (m, 4 H), 5.68 (br s, 1 H), 5.22 (dd, *J* = 7.6, 2.1 Hz, 1 H), 4.52–4.43 (m, 2 H), 4.37 (d, *J* = 10.1 Hz, 1 H), 3.75 (s, 3 H), 3.14 (dd, *J* = 11.8, 1.1 Hz, 1 H), 2.82–2.72 (m, 1 H), 2.37–2.31 (m, 1 H), 2.06–1.55 (m, 7 H), 1.35 (s, 3 H), 1.32–1.20 (m, 5 H), 1.02 (s, 3 H); MS *m/z* (M^+) calcd 490.2719, obsd 490.2716.

(1*S*,2*S*,4*R*)-2-[(*R*)-3-(Benzyloxy)-1-cyclohexen-1-yl]-1-[(*E*)-2-(*p*-methoxyphenoxy)vinyl]-7,7-dimethyl-2-norbornanol (10). A 413-mg (1.108 mmol) sample of $CeCl_3 \cdot 7H_2O$ was dried at 140 °C under high vacuum for 1.5 h. Bromide **7** (108 mg, 0.403 mmol) was transformed into the dichlorocerate as above and condensed with **6** (58.1 mg, 0.203 mmol) in the predescribed manner. Purification of the product by flash chromatography (elution with 5:1 hexane–ethyl acetate) furnished 74.4 mg (77%) of enantiomerically pure **10** as a colorless oil: IR (neat, cm^{-1}) 3470, 2920, 1660, 1500, 1450, 1225, 1115, 950, 830; ^{1}H NMR ($CDCl_3$) δ 7.38–7.27 (m, 5 H), 6.97–6.83 (m, 4 H), 6.32 (d, *J* = 12.5 Hz, 1H), 5.98 (br s, 1 H), 5.69 (d, *J* = 12.5 Hz, 1 H), 4.60 (ABq, *J* = 12.1 Hz, Δν = 13.2 Hz, 2 H), 4.07 (br s, 1 H), 3.78 (s, 3 H), 2.17–1.61 (m, 12 H), 1.35–1.13 (m, 5 H), 0.87 (s, 3 H); ^{13}C NMR ($CDCl_3$) ppm 155.1, 151.5, 145.6, 143.9, 139.1, 128.3, 127.5, 127.4, 123.3, 117.6, 114.7, 111.0, 84.5, 73.4, 69.9, 55.9, 55.6, 51.4, 45.1, 42.0, 28.3, 27.0, 26.6, 26.4, 21.6, 21.2, 20.4; MS *m/z* (M^+) calcd 474.2770, obsd 474.2776; $[\alpha]^{20}_D$ +47.7° (*c* 3.7, $CHCl_3$). Anal. Calcd for $C_{31}H_{38}O_4$: C, 78.45; H, 8.07. Found: C, 78.23; H, 8.16.

(1*R*,4a*R*,7*R*,10*E*,12*S*,12a*R*)-1-(Benzyloxy)-2,3,4,4a,6,7,8,9,-12,12a-decahydro-12-(*p*-methoxyphenoxy)-13,13-dimethyl-7,10-methanobenzocyclodecen-5(1*H*)-one (11a). A THF solution (5 mL) of **10** (24.4 mg, 0.052 mmol) and 18-crown-6 (41.6 mg, 0.16 mmol) was cooled to 0 °C and deoxygenated by bubbling N_2 through the solution for 30 min. Treatment with KHMDS (0.30 mL of 0.5 M in toluene, 0.15 mmol) and workup in the predescribed manner afforded after flash chromatography (elution with 5:1 hexane–ethyl acetate) 16.5 mg (68%) of **11a** as a white solid: mp 112–117 °C; IR ($CHCl_3$, cm^{-1}) 2990, 2940, 2870, 1685, 1505, 1220; ^{1}H NMR ($CDCl_3$) δ 7.08 (s, 5 H), 6.75 (d, *J* = 1.1 Hz, 4H), 5.22 (d, *J* = 10.8 Hz, 1 H), 4.76 (dd, *J* = 10.8, 5.9 Hz, 1 H), 4.62 (d, *J* = 11.5 Hz, 1 H), 4.40–4.31 (m, 2 H), 3.76 (s, 3 H), 3.42 (br m, 1 H), 2.66 (d, *J* = 11.8 Hz, 1 H), 2.30–1.95 (m, 6 H), 1.80 (dd, *J* = 11.5, 5.3 Hz, 1 H), 1.65–1.28 (m, 4 H), 1.26 (s, 3 H), 1.11 (s, 3 H), 0.98–0.83 (m, 2 H); ^{13}C NMR ($CDCl_3$) ppm 214.5, 153.2, 152.7, 147.4, 138.9, 128.0, 127.8, 127.0, 124.6, 116.2, 114.4, 79.2, 78.3, 70.8, 55.8, 53.6, 51.6, 51.5, 45.5, 42.7, 31.8, 27.1, 24.9, 24.8, 22.5, 22.1, 19.7; MS *m/z* (M^+) calcd 474.2770, obsd 474.2777; $[\alpha]^{20}_D$ −42.3° (*c* 0.83, $CHCl_3$). Anal. Calcd for $C_{31}H_{38}O_4$: C, 78.45; H, 8.07. Found: C, 78.23; H, 8.10.

(1*R*,4a*R*,7*R*,10*E*,12*S*,12a*S*)-1-(Benzyloxy)-2,3,4,4a,6,7,8,9,-12,12a-decahydro-12-(*p*-methoxyphenoxy)-13,13-dimethyl-12a-hydroxy-7,10-methanobenzocyclodecen-5(1*H*)-one (11b). A THF solution (2 mL) of **10** (20.0 mg, 0.042 mmol) under N_2 was cooled to 0 °C and treated sequentially with 18-crown-6 (34.4 mg, 0.13 mmol) and KHMDS (0.25 mL of 0.5 M in toluene, 0.13 mmol). After 1 h at 0 °C and 1 h at rt, the reaction mixture was processed as described to give after flash chromatography (gradient elution with 5:1 to 2:1 hexane–ethyl acetate) 13.1 mg (63%) of **11b** as a colorless oil; IR (neat, cm^{-1}) 3590, 3000, 2920, 1675, 1500, 1220, 1050; ^{1}H NMR ($CDCl_3$) δ 7.16–7.00 (m, 5 H), 6.78-6.70 (m, 4 H), 5.67 (dd, *J* = 10.4, 1.2 Hz, 1 H), 4.74 (dd, *J* = 10.4, 4.8 Hz, 1 H), 4.60 (d, *J* = 11.5 Hz, 1 H), 4.35 (d, *J* = 11.5 Hz, 1 H), 4.16 (dt, *J* = 10.7, 4.4 Hz, 1 H), 3.76 (s, 3 H), 3.18 (d, *J* = 11.7 Hz, 1 H), 2.31–2.09 (m, 4 H), 2.01–1.77 (m, 5 H), 1.65–1.51 (m, 4 H), 1.43–1.27 (m, 4 H), 1.10 (s, 3 H); ^{13}C NMR ($CDCl_3$) ppm 215.1, 153.3, 152.5, 146.2, 138.4, 128.0, 127.9, 127.1, 124.9, 116.3, 114.4, 81.3, 80.7, 78.4, 71.0, 65.0, 55.7, 51.1, 45.0, 39.5, 35.7, 30.6, 25.4, 24.9, 22.5, 20.7, 18.8; MS *m/z* (M^+) calcd 490.2719, obsd 490.2700.

(*S*)-Benzyl 3-Bromo-2-cyclohexen-1-yl Ether (12). Prepared as described above for **7** from sodium hydride (1.93 g, 80.4 mol), (*S*)-1-bromo-3-cyclohexenol (10.16 g, 57.4 mmol) and benzyl bromide (7.5 mL, 63 mmol) in DMF (100 mL). The yield was 98%; $[\alpha]^{23}_D$ −62.0° (*c* 3.78, $CHCl_3$) (71% ee).

(1*S*,2*S*,4*R*)-2-[(*S*)-3-(Benzyloxy)-1-cyclohexen-1-yl]-1-[(*Z*)-2-(*p*-methoxyphenoxy)vinyl]-7,7-dimethyl-2-norbornanol (13). The general procedure described for **8** and **10** was used. From **12** (770 mg, 2.88 mmol), *tert*-butyllithium in pentane (4 mL of 1.7 M, 6.8 mmol), dried cerium trichloride heptahydrate (3.00 g, 8.05 mmol), and **5** (330 mg, 1.15 mmol) in THF (40 mL total) there was obtained 194 mg (35%) of **13** as a colorless oil after flash chromatography on silica gel (elution with 20% ethyl acetate in hexanes); IR (neat, cm^{-1}) 3540, 1502, 1243; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38–7.24 (m, 5 H), 6.89 (d, *J* = 9.2 Hz, 2 H), 6.82 (d, *J* = 9.2 Hz, 2 H), 6.37 (d, *J* = 7.1 Hz, 1 H), 5.94 (t, *J* = 1.7 Hz, 1 H), 4.94 (d, *J* = 7.1 Hz, 1 H), 4.63 (d, *J* = 12.0 Hz, 1 H), 4.55 (d, *J* = 12.0 Hz, 1 H), 4.04 (br s, 1 H), 3.77 (s, 3 H), 2.35–2.25 (m, 3 H), 2.14 (d, *J* = 13.6 Hz, 1 H), 1.95 (dt, *J* = 3.5, 13.6 Hz, 1 H), 1.85–1.50 (m, 8 H), 1.26 (s, 3 H), 1.07–0.98 (m, 1 H), 0.90 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 155.1, 151.5, 146.2, 141.9, 139.1, 128.3, 127.7, 127.4, 122.1, 117.3, 113.7, 109.5, 85.0, 73.3, 70.1, 56.8, 55.7, 52.4, 44.6, 42.5, 28.1, 27.6, 26.7, 25.7, 21.8, 21.7, 20.1; MS *m/z* (M^+) calcd 474.2770, obsd 474.2758. Anal. Calcd for $C_{31}H_{38}O_4$: C, 78.44; H, 8.07. Found: C, 78.44; H, 8.13.

(1*S*,4a*R*,7*R*,10*E*,12*R*,12a*S*)-1-(Benzyloxy)-2,3,4,4a,6,7,8,9,-12,12a-decahydro-12-(*p*-methoxyphenoxy)-12a,13,13-trimethyl-7,10-methanobenzocyclodecan-5(1*H*)-one (14). A solution of **13** (197 mg, 0.453 mmol) and 18-crown-6 (620 mg, 2.35 mmol) in dry THF (10 mL) was deoxygenated by sparging with N_2 for 30 min and then transferred via cannula into a flask containing a suspension of potassium hydride (380 mg of 25% dispersion in oil, 2.37 mmol). This mixture was heated at reflux for 30 min, cooled to rt, and treated with freshly distilled methyl iodide (1 mL). The resulting pale yellow suspension was stirred at rt for 3 days, quenched carefully with water, and extracted with ether (3 × 10 mL). The combined organic extracts were dried, filtered, and concentrated, and the residue was purified by flash chromatography on silica gel (elution with 15% ethyl acetate in hexanes). There was isolated 143 mg (65%) of **14**, a pale yellow oil, as a 70:30 mixture of atropisomers; IR (neat, cm^{-1}) 1690, 1660, 1510, 1235; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34–6.71 (series of m, 9 H), 5.42 (br s, 0.7 H), 5.17 (t, *J* = 4.0 Hz, 0.3 H), 5.89 (br s, 0.7 H), 4.86 (br s, 0.3 H), 4.65 (d, *J* = 12.1 Hz, 0.7 H), 4.59 (d, *J* = 12.2 Hz, 0.3 H), 4.54 (d, *J* = 12.2 Hz, 0.3 H), 4.53 (d, *J* = 12.1 Hz, 0.7 H), 4.06–4.02 (m, 0.3 H), 3.76 (s, 1 H), 3.74 (s, 2 H), 3.75–3.65 (m, 0.7 H), 3.55–3.50 (m, 0.3 H), 3.08 (t, *J* = 5.5 Hz, 0.3 H), 2.60–1.25 (series of m, 13 H), 1.37 (s, 1 H), 1.13 (s, 2 H), 1.10 (s, 1 H), 1.06 (s, 2 H), 1.04 (s, 1 H), 1.02 (s, 2 H); MS *m/z* (M^+) calcd 488.2926, obsd 488.2896; $[\alpha]^{20}_D$ −151.3° (*c* 0.46, $CHCl_3$).

(1*S*,2*S*,4*R*)-2-[(1*S*)-3-(Methoxymethoxy)-1-cyclohexen-1-yl]-1-[(*Z*)-2-(*p*-methoxyphenoxy)vinyl]-7,7-dimethyl-2-norbornanol (17). The general procedure described for **8** and **10** was used. From **16** [510 mg, 2.31 mmol, $[\alpha]^{23}_D$ −74.2° (*c* 1.69, $CHCl_3$)] (86% e.e.), *tert*-butyllithium (3.0 mL of 1.7 M in pentane, 5.1 mmol), dried cerium trichloride heptahydrate (1.05 g, 2.82 mmol), and **5** (290 mg, 1.01 mmol) in THF (18 mL total) there was obtained 232 mg (54%) of **17** after flash chromatography on silica gel (elution with 30% ethyl acetate in hexanes). Also recovered was 130 mg (45%) of unreacted **5**.

For **17**: colorless oil: IR (neat, cm^{-1}) 3482, 1665, 1509, 1250; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.94–6.80 (m, 4 H), 6.36 (d, *J* = 7.1 Hz, 1 H), 5.88 (d, *J* = 1.8 Hz, 1 H), 4.92 (d, *J* = 7.1 Hz, 1 H), 4.72 (d, *J* = 6.8 Hz, 1 H), 4.69 (d, *J* = 6.8 Hz, 1 H), 4.17–4.12 (m, 1 H), 3.77 (s, 3 H), 3.38 (s, 3 H), 2.36–2.03 (m, 4 H), 1.94 (ddd,

J = 3.4, 3.8, 13.6 Hz, 1 H), 1.83–1.51 (m, 8 H), 1.25 (s, 3 H), 1.20–1.00 (m, 1 H), 0.89 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 155.1, 151.4, 146.4, 142.0, 122.0, 117.3, 114.6, 109.3, 95.0, 85.0, 71.7, 56.7, 55.7, 55.2, 52.4, 44.6, 42.4, 28.8, 27.6, 25.5, 21.8, 21.6, 19.9; MS m/z (M^+) calcd 428.2563, obsd 428.2588. Anal. Calcd for $C_{28}H_{36}O_5$: C, 72.87; H, 8.47. Found: C, 72.70; H, 8.91.

(1*S*,4a*R*,7*R*,10*E*,12*R*,12a*S*)-1-(Methoxymethoxy)-2,3,-4,4a,6,7,8,9,12,12a-decahydro-12-(*p*-methoxyphenoxy)-4a,13,-13-trimethyl-7,10-methanobenzocyclodecen-5(1*H*)-one (18). To a suspension of potassium hydride (780 mg of 25% dispersion in oil, 4.87 mmol) in dry THF (5 mL) was added 18-crown-6 (720 mg, 2.72 mmol). This mixture and a solution of **17** (380 mg, 0.89 mmol) in the same solvent (10 mL) were separately deoxygenated by sparging with N_2 for 30 min. The KH/18-crown-6 mixture was cooled to 0 °C and the solution of **17** was introduced via cannula. After the cessation of effervescence, the mixture was allowed to warm to rt, heated at 50 °C for 1 h, returned to rt, and treated with methyl iodide (1 mL). A white precipitate formed immediately. After 30 min of stirring, the reaction mixture was carefully quenched with saturated $NaHCO_3$ solution (15 mL) and extracted with ether (1 × 30 mL; 4 × 10 mL). The combined ethereal phases were dried, filtered, and concentrated to leave a residue that was purified by chromatography on Florisil (gradient elution with 5–10% ethyl acetate in hexane). There was isolated 304 mg (77%) of **18** as a faintly yellow foam; this material consists of a 70:30 mixture of atropisomers; IR (neat, cm^{-1}) 1690, 1665, 1512, 1235, 1090; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.87–6.76 (m, 4 H), 5.36 (br s, 0.7 H), 5.15 (dd, J = 3.9 Hz, 0.3 H), 5.02 (br s, 0.7 H), 4.86 (dd, J = 1.7, 3.3 Hz, 0.3 H), 4.73 (d, J = 6.8 Hz, 0.7 H), 4.68 (d, J = 6.8 Hz, 0.7 H), 4.67 (d, J = 6.7 Hz, 0.3 H), 4.62 (d, J = 6.7 Hz, 0.3 H), 4.20 (ddd, J = 6.0, 12.0, 9.8 Hz, 0.3 H), 3.86 (ddd, J = 4.5, 4.9, 12.0 Hz, 0.7 H), 3.74 (s, 1 H), 3.73 (s, 2 H), 3.34 (s, 2 H), 3.27 (s, 1 H), 2.95 (dd, J = 5.0, 6.0 Hz, 0.3 H), 2.7–1.4 (series of m, 13 H), 1.36 (s, 1 H), 1.33 (br s, 0.3 H), 1.38–1.22 (m, 0.7 H), 1.20 (s, 2 H), 1.13 (s, 2 H), 1.07 (s, 3 H), 1.00 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 221.0, 213.1, 153.5, 153.4, 151.9, 151.8, 146.4, 144.9, 124.4, 122.7, 116.2, 116.0, 114.5, 114.4, 114.2, 95.5, 95.0, 78.0, 77.7, 77.2, 76.8, 75.9, 75.4, 73.9, 55.7, 55.6, 55.5, 55.3, 54.9, 53.7, 52.3 52.2, 48.5, 48.1, 47.6, 46.6, 46.4, 34.6, 29.8, 29.3, 27.6, 26.7, 26.5, 26.2, 25.0, 24.3, 24.2, 23.6, 22.1, 21.6, 20.5, 20.3, 28.9; MS m/z (M^+) calcd 442.2719, obsd 442.2695.

(1*S*,2*S*,4*R*)-2-[(*R*)-3-(Methoxymethoxy)-1-cyclohexen-1-yl]-1-[(*Z*)-2-(-*p*-methoxyphenoxy)vinyl]-7,7-dimethyl-2-norbornanol (19). The general procedure described for **8** and **10** was used. From **15** [2.41 g, 10.90 mmol, $[\alpha]^{23}_D$ +69.1° (c 4.14, $CHCl_3$)] (76% e.e.), *tert*-butyllithium (0.7 mL of 1.7 M), dried cerium trichloride heptahydrate (5.95 g, 15.97 mmol), and **5** (860 mg, 3.00 mmol) in THF (65 mL total) there was isolated 672 mg (52%) of **19** following flash chromatography on silica gel (gradient elution 10–30% ethyl acetate in hexanes). Also recovered was 412 mg (48%) of **5**.

For **19**: colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.91 (d, J = 9.2 Hz, 2 H), 6.83 (d, J = 9.2 Hz, 2 H), 6.39 (d, J = 7.1 Hz, 1 H), 5.94 (d, J = 1.6 Hz, 1 H), 4.87 (d, J = 7.1 Hz, 1 H), 4.72 (d, J = 6.8 Hz, 1 H), 4.68 (d, J = 6.8 Hz, 1 H), 4.16-4.11 (m, 1 H), 3.76 (s, 3 H), 3.37 (s, 3 H), 2.36–1.46 (series of m, 14 H), 1.25 (s, 2 H), 1.20–1.05 (m, 1 H), 0.89 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 155.1, 151.4, 145.9, 142.3, 122.8, 117.3, 114.7, 109.0, 95.1, 85.0, 72.2, 57.1, 55.6, 55.1, 52.3, 44.6, 42.2, 29.0, 27.9, 26.7, 25.8, 21.7, 21.6, 20.1; MS m/z (M^+) calcd 428.2562, obsd 428.2594; $[\alpha]^{20}_D$ +5.5° (c 0.50, $CHCl_3$). Anal. Calcd for $C_{28}H_{36}O_5$: C, 72.87; H, 8.47. Found: C, 72.75; H, 8.58.

(1*R*,4a*R*,7*R*,10*E*,12*R*,12a*S*)-1-(Methoxymethoxy)-2,3,-4,4a,6,7,8,9,12,12a-decahydro-12-(*p*-methoxyphenoxy)-4a,13,-13-trimethyl-7,10-methanobenzocyclodecen-5(1*H*)-one (20). A solution of **19** (500 mg, 1.17 mmol) and 18-crown-6 (1.23 g, 4.65 mmol) in dry THF (25 mL) was deoxygenated by sparging with N_2 at rt, cooled to −78 °C, and treated dropwise with a solution of potassium hexamethyldisilazide in toluene (12.5 mL of 0.5 M, 6.3 mmol). After 1 h at rt, additional base (3 mL) was introduced and stirring was maintained for 30 min. The mixture was cooled to −15 °C and treated with methyl iodide (4 mL). After 30 min at this temperature, saturated NH_4Cl solution (6 mL) was carefully introduced followed by 100 mL of ether. The organic phase was washed with H_2O (2 × 30 mL) and brine (30 mL) and the aqueous washings were back-extracted with ether. The dried ether solutions were concentrated to leave a residue that was purified by chromatography on Florisil (elution with 10% ethyl acetate in hexanes) to give 422 mg (82%) of **20** as a colorless oil: IR (neat, cm^{-1}) 1679, 1512, 1232, 1045; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.83–6.72 (m, 4 H), 5.42 (br s, 1 H), 5.10 (dd, J = 2.9, 7.0 Hz, 1 H), 4.72 (d, J = 6.6 Hz, 1 H), 4.40 (ddd, J = 5.1, 10.2, 10.2 Hz, 1 H), 4.32 (d, J = 6.6 Hz, 1 H), 3.72 (s, 3 H), 3.19 (s, 3 H), 2.7–2.6 (m, 2 H), 2.29–2.17 (m, 1 H), 2.13 (dd, J = 7.2, 9.5 Hz, 1 H), 1.85 (d, J = 5.6 Hz, 1 H), 1.78–1.14 (series of m, 9 H), 1.50 (s, 3 H), 1.23 (s, 3 H), 1.01 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 212.4, 153.1, 151.6, 148.8, 119.8, 115.4, 114.2, 97.6, 78.2, 75.8, 59.7, 55.4, 55.2, 51.6, 51.1, 46.1, 38.6, 36.2, 32.5, 32.1, 25.83, 25.79, 22.5, 21.3, 18.9; MS m/z (M^+) calcd 442.2719, obsd 442.2754; $[\alpha]^{20}_D$ −113° (c 0.34, $CHCl_3$). Anal. Calcd for $C_{27}H_{38}O_5$: C, 73.27; H, 8.65. Found: C, 73.36; H, 8.68.

In NOE experiments performed on **20**, double irradiation of the H-19 signal was seen to enhance the following absorption integrals: H-1, 14.2%; H-2, −1.3%; H-3, 11.4%; H-10β, 8.7%. Similar treatment of the H-16 signal affected the H-1 (9.9%) and H-10β intensities (5.8%). The NOE enhancement between the H-19 protons and H-10β indicates adoption of the "carbonyl down" arrangement. The negative NOE between H-19 and H-2 is due to transfer from H-1 and indicates H-2 to be on the same β-face of the B-ring as H-1.

(1*S*,2*S*,4*R*)-2-[(*R*)-3-(Methoxymethoxy)-1-cyclohexen-1-yl]-1-[(*E*)-2-(*p*-methoxyphenoxy)vinyl]-7,7-dimethyl-2-norbornanol (21). The general procedure described for **8** and **10** was followed. From **15** (3.15 g, 15.25 mmol), *tert*-butyllithium (0.4 mL of 1.7 M), dried cerium trichloride heptahydrate (6.4 g, 17 mmol), and **6** (1.65 g, 5.76 mmol, 4.3:1 E/Z mixture) in dry THF (70 mL total) there was produced 1.89 g (77%) of **21** following flash chromatography on silica gel (elution with 20% ethyl acetate in hexanes). Also recovered was 350 mg (12%) of **6**.

For **21**: viscous, colorless oil; IR ($CHCl_3$, cm^{-1}) 3605, 1665, 1501, 1032; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.93–6.80 (m, 4 H), 6.29 (d, J = 12.5 Hz, 1 H), 5.89 (t, J = 1.6 Hz, 1 H), 5.67 (d, J = 12.5 Hz, 1 H), 4.70 (dd, J = 6.8, 13.2 Hz, 2 H), 4.16–4.06 (m, 1 H), 3.75 (s, 3H), 3.36 (s, 3 H), 2.28–2.06 (m, 3 H), 1.99–1.92 (m, 1 H), 1.87-1.47 (series of m, 8 H), 1.32–1.24 (m, 1 H), 1.22 (s, 3 H), 1.16–1.05 (m, 1 H), 0.84 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 155.1, 151.4, 145.5, 143.8, 123.2, 117.5, 117.2, 114.63, 114.59, 111.0, 95.1, 84.4, 72.1, 55.8, 55.6, 55.1, 51.4, 45.0, 42.0, 29.0, 26.7, 26.5, 26.3, 21.5, 21.2, 20.1; MS m/z (M^+) calcd 428.2563, obsd 428.2559; $[\alpha]^{20}_D$ +41.1° (c 0.72, $CHCl_3$). Anal. Calcd for $C_{28}H_{36}O_5$: C, 72.87; H, 8.47. Found: C, 72.69; H, 8.52.

(1*R*,4a*R*,7*R*,10*E*,12*S*,12a*S*)-1-(Methoxymethoxy)-2,3,-4,4a,6,7,8,9,12,12a-decahydro-12-(*p*-methoxyphenoxy)-4a,13,-13-trimethyl-7,10-methanobenzocyclodecen-5(1*H*)-one (22). A solution of **21** (1.06 g, 2.47 mmol) and 18-crown-6 (3.27 g, 12.4 mmol) in 50 mL of anhydrous THF was reacted with potassium hexamethyldisilazide (25 mL of 0.5 M in toluene, 12.5 mmol) in the manner described for **20** (no heat, 1 h at rt) and followed by stirring with methyl iodide (10 mL) for 30 min at rt. The identical workup furnished 910 mg (83%) of **22** as a colorless solid, mp 110–111 °C (from hexanes); IR ($CHCl_3$, cm^{-1}) 1659, 1508, 1040; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.80–6.72 (m, 4 H), 5.46 (d, J = 10.0 Hz, 1 H), 4.81 (dd, J = 4.2, 10.0 Hz, 1 H), 4.60 (d, J = 6.8 Hz, 1 H), 4.52 (d, J = 6.8 Hz, 1 H), 4.18 (td, J = 4.4, 10.5 Hz, 1 H), 3.73 (s, 3 H), 3.16 (s, 3 H), 2.72 (d, J = 12.7 Hz, 1 H), 2.46–2.36 (m, 1 H), 2.27–2.10 (m, 3 H), 2.08–2.02 (m, 3 H), 1.96–1.86 (m, 3 H), 1.78–1.67 (m, 1 H), 1.64–1.57 (m, 1 H), 1.60 (s, 2 H), 1.53–1.31 (m, 2 H), 1.23 (s, 3 H), 1.12 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 215.2, 153.3, 152.6, 147.1, 124.3, 116.5, 114.3, 95.8, 80.5, 79.5, 63.2, 55.7, 55.6, 51.5, 50.9, 45.4, 39.5, 36.4, 32.1, 30.8, 25.6, 25.4, 22.0, 20.9, 19.8; MS m/z (M^+) calcd 442.2719, obsd 442.2712; $[\alpha]^{20}_D$ −78.3° (c 0.45, $CHCl_3$). Anal. Calcd for $C_{27}H_{38}O_5$: C, 73.27; H, 8.65. Found: C, 73.18; H, 8.67.

NOE experiments performed on **22** gave results comparable to those recorded earlier for **20**. In addition, a COSY experiment revealed the existence of W-coupling between H-10β and H-12β. The combined data are compatible only with the "carbonyl down" atropisomeric formulation.

(1*S*,2*S*,4*R*)-2-[(*S*)-3-(Methoxymethoxy)-1-cyclohexen-1-yl]-1-[(*E*)-2-(*p*-methoxyphenoxy)vinyl]-7,7-dimethyl-2-norbornanol (23). The general procedure described for **8** and **10**

was followed. From **16** (1.41 g, 4.92 mmol), *tert*-butyllithium (13.2 mL of 1.7 M, 22.4 mmol), dried cerium trichloride heptahydrate (5.13 g, 13.8 mmol), and **6** (2.40 g, 10.85 mmol) in dry THF (75 mL total) there was isolated 1.70 g (81%) of **23** after flash chromatography on silica gel (elution with 20% ethyl acetate in hexanes). Also recovered was 300 mg (20%) of **6**.

For **23**: viscous, colorless oil; IR (neat, cm^{-1}) 3470, 1670, 1510, 1230, 1115, 1040; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.87 (d, J = 9.2 Hz, 2 H), 6.79 (d, J = 9.2 Hz, 2 H), 6.25 (d, J = 12.6 Hz, 1 H), 5.85 (dd, J = 1.7, 1.9 Hz, 1 H), 5.64 (d, J = 12.6 Hz, 1 H), 4.67 (d, J = 6.8 Hz, 1 H), 4.63 (d, J = 6.8 Hz, 1 H), 4.12–4.05 (m, 1 H), 3.72 (s, 3 H), 3.32 (s, 3 H), 2.25–2.00 (m, 4 H), 1.90 (ddd, J = 2.4, 4.0, 13.7 Hz, 1 H), 1.78 (t, J = 4.0 Hz, 1 H), 1.77–1.50 (m, 6 H), 1.22–1.12 (m, 1 H), 1.17 (s, 3 H), 1.07–1.01 (m, 1 H), 0.79 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 155.1, 151.5, 146.4, 143.7, 122.7, 117.6, 114.7, 111.1, 95.1, 84.4, 71.3, 55.8, 55.7, 55.2, 51.4, 45.2, 42.0, 28.8, 26.8, 26.6, 26.4, 21.6, 21.2, 19.7; MS m/z (M^+) calcd 428.2563, obsd 428.2596; $[\alpha]^{20}_D$ −25.9° (c 1.0, $CHCl_3$). Anal. Calcd for $C_{26}H_{36}O_5$: C, 72.87; H, 8.47. Found: C, 72.67; H, 8.47.

(1*S*,4a*R*,7*R*,10*E*,12*S*,12a*S*)-1-(Methoxymethoxy)-2,3,-4,4a,6,7,8,9,12,12a-decahydro-12-(*p*-methoxyphenoxy)-4a,13,-13-trimethyl-7,10-methanobenzocyclodecen-5(1*H*)-one (24). Treatment of **23** (740 mg, 1.73 mmol) with potassium hydride (2.0 g of 25% in mineral oil, 12.5 mmol) and 18-crown-6 (3.0 g, 11.3 mmol) in the manner described for **18** (no heat, rt, 2 days) was followed by stirring with methyl iodide (10 mL) for 2 h at rt. The identical workup furnished 520 mg (68%) of **24** as an off-white solid, mp 126–127 °C; IR ($CHCl_3$, cm^{-1}) 1682, 1510, 1215, 1040; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.79–6.72 (m, 4 H), 5.21 (dd, J = 1.4, 10.8 Hz, 1 H), 4.80 (dd, J = 9.0, 10.7 Hz, 1 H), 4.66 (d, J = 6.8 Hz, 1 H), 4.59 (d, J = 6.8 Hz, 1 H), 4.12 (ddd, J = 2.8, 3.1, 6.2 Hz, 1 H), 3.73 (s, 3 H), 3.22 (s, 3 H), 2.82 (d, J = 13.3 Hz, 1 H), 2.48–2.24 (m, 2 H), 2.20–2.05 (m, 3 H), 1.95–1.82 (m, 3 H), 1.78 (dd, J = 3.4, 8.8 Hz, 1 H), 1.64–1.54 (m, 3 H), 1.51 (s, 3 H), 1.24 (s, 3 H), 1.14 (s, 3 H), 1.09–1.07 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 214.6, 153.5, 152.7, 151.7, 120.1, 116.4, 114.4, 96.2, 75.6, 72.5, 59.7, 55.6, 55.4, 51.0, 49.3, 45.7, 36.3, 36.0, 29.6, 26.1, 25.6, 25.2, 21.9, 21.2, 15.6; MS m/z (M^+) calcd 442.2719, obsd 442.2720; $[\alpha]^{20}_D$ −11.5° (c 0.72, $CHCl_3$). Anal. Calcd for $C_{27}H_{38}O_5$: C, 73.27; H, 8.65. Found: C, 72.82; H, 8.59.

Upon double irradiation of the following signals, the indicated enhancements were observed: H-19: H-13 (17.4%), H-10β (16.6%), H-1 (10.2%), H-4 (−0.9%); H-16: H-10β (10.2%), H-1 (19.8%); H-10β: H-19/H-10α (36.7%), H-16 (7.4%); H-4: H-2 (2.3%), H-3 (8.1%), p-anisyl protons; H-2: H-4 (1.9%), p-anisyl protons. The strong NOE effect to H-10β from H-19 indicates the carbonyl group to be down, while that from H-19 to H-3 indicates the B/C ring juncture to be cis. The negative NOE from H-19 to H-4 is transferred from H-3 and indicates a syn relationship between H-3 and H-4. The absence of an NOE effect between H-2 and everything except H-4 shows the substituent at C-2 to be β-oriented.

(1*R*,4a*R*,5*S*,7*R*,10*S*,11*S*,12*S*,12a*R*)-Dodecahydro-1-(methoxymethoxy)-12-(*p*-methoxyphenoxy)-4a,14,14-trimethyl-5,-11-epoxy-7,10-methanobenzocyclodecene-5,10-diol (25a). To a solution of **20** (30 mg, 0.067 mmol) in pyridine (1 mL) was added osmium tetroxide (25 mg, 0.098 mmol). The black mixture was stirred overnight at rt, treated with 10% aqueous $NaHSO_3$ solution, and stirred for 24 h. After the introduction of ethyl acetate (10 mL), the separated organic phase was washed with 1.2 N HCl (2 × 5 mL) and the acidic layers were back-extracted with ethyl acetate (2 × 5 mL). The combined organic solutions were dried, filtered, and evaporated to leave a brown residue, flash chromatography of which on silica gel (elution with 30% ethyl acetate in hexanes) afforded 24 mg (76%) of **25a** as a colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.91 (d, J = 9.2 Hz, 2 H), 6.75 (d, J = 9.1 Hz, 2 H), 4.56 (dd, J = 7.1, 7.5 Hz, 2 H), 4.42 (d, J = 6.1 Hz, 1 H), 3.81 (s, 1 H), 3.74 (br d, J = 4.2 Hz, 1 H), 3.69 (s, 3 H), 3.30 (s, 3 H), 2.60 (d, J = 5.9 Hz, 1 H), 2.50–1.15 (series of m, 15 H), 1.13 (s, 3 H), 1.05 (s, 3 H), 1.00 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 154.2, 150.4, 117.4, 114.7, 101.8, 95.6, 86.9, 84.1, 76.4, 72.1, 55.7, 55.3, 46.7, 43.5, 41.9, 40.1, 38.0, 35.9, 28.7, 27.6, 24.7, 23.0, 19.2, 19.1, 17.2; MS m/z (M^+) calcd 476.2774, obsd 476.2765. Anal. Calcd for $C_{27}H_{40}O_7$: C, 68.04; H, 8.46. Found: C, 67.80; H, 8.42.

(1*R*,4a*R*,5*S*,7*R*,10*S*,11*S*,12*S*,12a*R*)-Dodecahydro-12-(*p*-methoxyphenoxy)-4a,14,14-trimethyl-5,11-epoxy-7,10-methanobenzocyclodecene-1,5,10-triol (25b). A solution of **25a** (208 mg, 0.436 mmol) in methanol (8 mL) was treated with 1 drop of concentrated HCl and heated at reflux for 4 h. The cooled reaction mixture was freed of solvent in vacuo, and the residue was purified by flash chromatography on silica gel (gradient elution with 30–50% ethyl acetate in hexanes) to give 167 mg (89%) of **25b** as colorless crystals, mp 168–169 °C; IR ($CHCl_3$, cm^{-1}) 3565, 1510, 1210; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.96 (d, J = 9.1 Hz, 2 H), 6.81 (d, J = 9.1 Hz, 2 H), 4.50 (d, J = 6.2 Hz, 1 H), 4.07 (t, J = 2.0 Hz, 1 H), 3.88 (s, 3 H), 3.75 (s, 3 H), 2.58 (d, J = 6.0 Hz, 1 H), 2.42–1.01 (series of m, 14 H), 1.23 (s, 3 H), 1.12 (s, 3 H), 1.06 (s, 3 H); ^{13}C NMR (75 MHz, $CHCl_3$) ppm 154.1, 150.5, 117.3, 114.7, 101.7, 87.1, 84.0, 72.0, 70.7, 55.6, 46.7, 45.4, 41.7, 39.9, 37.9, 35.7, 31.1, 27.5, 24.7, 23.0, 19.7, 19.5, 16.6; MS m/z (M^+) calcd 432.2512, obsd 432.2491; $[\alpha]^{20}_D$ −80.0° (c 0.43, $CHCl_3$).

(4a*R*,5*S*,7*R*,10*S*,11*S*,12*S*,12a*S*)-Dodecahydro-5,10-dihydroxy-12-(*p*-methoxy-phenoxy)-4a,14,14-trimethyl-5,11-epoxy-7,10-methanobenzocyclodecen-1(2*H*)-one (26). A solution of **25b** (61 mg, 0.141 mmol) in CH_2Cl_2 (3 mL) was treated with the Dess–Martin periodinane (90 mg, 0.21 mmol), stirred for 30 min, and evaporated to approximately half-volume under reduced pressure. The remaining solution was loaded onto a silica gel column and eluted with 30% ethyl acetate in hexanes to afford 48 mg (78%) of **26** as white crystals, mp 222–224 °C dec (from $CHCl_3$–hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.88 (d, J = 9.1 Hz, 2 H), 6.78 (d, J = 9.1 Hz, 2H), 4.53 (d, J = 6.5 Hz, 1 H), 4.04 (s, 1 H), 3.73 (s, 3 H), 3.07 (d, J = 5.8 Hz, 1 H), 2.72–2.55 (m, 1 H), 2.53–2.36 (m, 3 H), 2.12–1.75 (m, 8 H), 1.73–1.66 (m, 1 H), 1.60 (br d, J = 12.9 Hz, 1 H), 1.29–1.19 (br m, 1 H), 1.08 (s, 3 H), 1.04 (s, 3 H), 0.98 (s, 3 H); ^{13}C NMR (300 MHz, $CDCl_3$) ppm 211.8, 154.8, 149.8, 118.5, 114.7, 100.7, 86.8, 83.9, 72.2, 55.8, 55.6, 46.9, 42.5, 41.6, 39.6, 37.8, 35.8, 27.5, 23.5, 23.1, 19.5, 19.1, 19.0; MS m/z (M^+) calcd 430.2356, obsd 430.2365. Anal. Calcd for $C_{25}H_{34}O_6$: C, 69.74; H, 7.96. Found: C, 69.53; H, 7.91.

[[(4a*R*,5*R*,7*R*,10*S*,11*S*,12a*S*)-3,4,4a,6,7,8,9,11,12,12a-Decahydro-12-(*p*-methoxyphenoxy)-4a,14,14-trimethyl-5,11-epoxy-7,10-methanobenzocyclodecene-1,5,10-triyl]trioxy]tris[trimethylsilane] (28). A solution of **26** (21 mg, 0.050 mmol) in CH_2Cl_2 (1 mL) containing hexamethyldisilazane (0.1 mL) was cooled to 0 °C and treated with trimethylsilyl iodide (0.045 mL, 0.32 mmol). The mixture was stirred at 0 °C for 1 h and at rt for 24 h before being quenched with saturated $NaHCO_3$ solution (1 mL) and diluted with ether (4 mL). The organic layer was separated, dried, and evaporated to leave a yellow oil, purification of which by flash chromatography (silica gel, elution with 5% ethyl acetate in hexanes) gave **28** as a colorless oil (27 mg, 84%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.85 (d, J = 9.1 Hz, 2 H), 6.74 (d, J = 9.1 Hz, 2 H), 4.74 (dd, J = 2.0, 4.2 Hz, 1 H), 4.49 (d, J = 5.7 Hz, 1 H), 4.01 (s, 2 H), 3.74 (s, 3 H), 2.64 (d, J = 5.6 Hz, 1 H), 2.25–1.86 (m, 9 H), 1.76 (dd, J = 7.4, 7.5 Hz, 1 H), 1.36–1.26 (m, 1 H), 1.03 (s, 3 H), 0.96 (s, 3 H), 0.92 (s, 3 H), 0.21 (s, 9 H), 0.07 (s, 9 H), −0.13 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 153.9, 152.9, 147.5, 118.6, 114.5, 103.6, 103.3, 88.1, 86.7, 70.9, 55.9, 47.9, 47.1, 41.7, 40.7, 38.5, 34.9, 28.8, 23.6, 22.9, 21.2, 19.0, 18.2, 2.9, 2.1, 0.2.

(1*R*,4a*R*,5*S*,7*R*,10*S*,12*R*,12a*R*)-Tetradecahydro-1-(methoxymethoxy)-12-(*p*-methoxyphenoxy)-4a,13,13-trimethyl-7,-10-methanobenzocyclodecene-5,10,11-triol (29). A solution of **22** (910 mg, 2.06 mmol) in pyridine (25 mL) was treated with osmium tetraoxide (600 mg, 2.36 mmol), stirred at rt for 3 days, and freed of solvent in vacuo. The brown residue was taken up in THF (25 mL), cooled to −78 °C, and treated via cannula with an equally cold suspension of lithium aluminum hydride (1.5 g, 40 mmol) in THF (15 mL). The cooling bath was removed and the mixture was stirred for 5 h before being cooled to 0 °C, *carefully* diluted with ethyl acetate (50 mL), and *slowly* quenched with 5% NaOH solution (6 mL). The slurry was filtered through a pad of Celite, which was exhaustively rinsed with ethyl acetate and again filtered. The combined filtrates were washed with brine, dried, and concentrated to leave a residue that was purified by flash chromatography (silica gel, elution with 40% ethyl acetate in hexanes). There was obtained 760 mg (77%) of **29** as a colorless crystalline solid, mp 168–169 °C (from CH_2Cl_2–hexanes); IR ($CHCl_3$, cm^{-1}) 3635, 3560, 1510, 1225, 1040; ^{1}H NMR (300 MHz,

$CDCl_3$) δ 7.14 (d, J = 9.2 Hz, 2 H), 6.81 (d, J = 9.1 Hz, 2 H), 5.18 (d, J = 8.2 Hz, 1 H), 4.69 (d, J = 6.8 Hz, 1 H), 4.62 (d, J = 6.8 Hz, 1 H), 4.11 (br s, 1 H), 3.75 (s, 3 H), 3.72–3.66 (m, 2 H), 3.39 (s, 3 H), 2.99–2.80 (m, 1 H), 2.80–2.61 (br m, 1 H), 2.55–2.51 (m, 1 H), 2.36–2.26 (m, 1 H), 2.16–1.99 (m, 5 H), 1.95–1.66 (m, 4 H), 1.64–1.55 (m, 1 H), 1.45–1.41 (m, 1 H), 1.25 (dd, J = 7.1, 7.6 Hz, 1 H), 1.22 (s, 3 H), 1.15 (s, 3 H), 1.10 (s, 3 H), 0.94 (d, J = 14.4 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 154.0, 152.2, 116.6, 114.7, 94.6, 85.9, 85.1, 79.5, 72.3, 71.5, 55.6, 55.4, 48.5, 47.6, 47.1, 39.9, 34.1, 32.4, 30.8, 28.7, 28.5, 25.0, 21.7, 19.9, 16.8; MS m/z (M^+) calcd 478.2930, obsd 478.2938; $[\alpha]^{20}_D$ −40.0° (c 0.77, $CHCl_3$). Anal. Calcd for $C_{27}H_{42}O_7$: C, 67.76; H, 8.85. Found: C, 67.34; H, 8.81.

In NOE experiments performed on **29**, double irradiation of the H-17 signal was seen to enhance the following absorption integrals: H-1, 5%; H-3, 14%; H-10β, 6%, H-11, 2%. Similar treatment of the H-18 signal effected the H-3 (3.7%), H-6β (4.4%), H-9 (9%), and H-10β intensities (3.7%). The strong NOE between H-18 and H-9 indicates the hydroxyl group to be α, while the NOE enhancements between the H-18 and H-10β as well as H-17 and H-3 indicate that a "carbonyl down" type conformation has been adopted. Finally, the W-coupling between H-3 and H-7β reveals both protons to be equatorial.

(1*R*,4a*R*,7*R*,10*S*,11*S*,12*R*,12a*R*)-11-(*tert*-Butyldimethylsiloxy)-dodecahydro-10-hydroxy-1-(methoxymethoxy)-12-(*p*-methoxyphenoxy)-4a,13,13-trimethyl-7,10-methanobenzocyclodecen-5(1*H*)-one (**30**). A solution of **29** (300 mg, 0.63 mmol) and triethylamine (0.5 mL) in CH_2Cl_2 (5 mL) was cooled to 0 °C and treated with *tert*-butyldimethylsilyl triflate (0.1 mL). After 1 h of stirring at rt, saturated $NaHCO_3$ solution (2 mL) was added, followed by ether (20 mL). The separated organic phase was washed with water (5 mL) and brine (5 mL), dried, filtered, and evaporated. Flash chromatography of the residue (silica gel, elution with 4–10% ethyl acetate in hexanes) afforded a pale yellow solid (350 mg, 94%) which was taken up in CH_2Cl_2 (20 mL) and treated in turn with powdered and activated 3-Å molecular sieves (450 mg), sodium acetate (260 mg), and pyridinium chlorochromate (360 mg, 1.67 mmol). After being stirred 24 h, ether (100 mL) and Celite (1 g) were introduced and the mixture was filtered through a plug of silica gel and evaporated. Flash chromatography of the residue on silica gel (elution with 10% ethyl acetate in hexanes) afforded **30** (330 mg, 95%) as a colorless oil; IR (neat, cm^{-1}) 3580, 1700, 1520, 1220, 1050; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.78 (s, 4 H), 4.75 (d, J = 6.9 Hz, 1H), 4.67 (d, J = 6.9 Hz, 1 H), 4.28 (dd, J = 1.8, 1.9 Hz, 1H), 3.81 (d, J = 6.7 Hz, 1 H), 3.75 (s, 3 H), 3.47 (dd, J = 1.1, 6.4 Hz, 1 H), 3.45 (s, 3 H), 3.21 (d, J = 13.6 Hz, 1 H), 2.99 (s, 1 H), 2.52–2.43 (m, 2 H), 2.24–2.15 (m, 2 H), 2.11–1.85 (m, 2 H), 1.75–1.40 (m, 4 H), 1.37 (s, 3 H), 1.27 (s, 4 H), 1.21 (d, J = 7.0 Hz, 1 H), 1.17 (s, 3 H), 0.92–0.82 (m, 1 H), 0.80 (s, 9 H), 0.32 (s, 3 H), 0.20 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 217.0, 153.7, 152.2, 116.9, 114.3, 94.6, 85.6, 80.2, 75.3, 71.6, 65.8, 55.6, 55.3, 51.1, 48.2, 47.2, 45.1, 36.6, 33.4, 32.9, 27.4, 26.1, 22.7, 21.3, 19.8, 18.4, 16.3, 15.2, −3.0, −5.4; MS m/z (M^+) calcd 390.3639, obsd 390.3654; $[\alpha]^{20}_D$ +63.0° (c 2.3, $CHCl_3$).

(1*R*,4a*R*,5*R*,7*R*,10*S*,11*S*,12*R*,12a*S*)-5-(*tert*-Butyldimethylsiloxy)tetradecahydro-12-(*p*-methoxyphenoxy)-4a,14,14-trimethyl-1-(trimethylsiloxy)-5,11-epoxy-7,10-methanobenzocyclodecen-10-ol (31). A solution of **30** (29 mg, 0.049 mmol) in *tert*-butyl alcohol (4 mL) was treated with potassium *tert*-butoxide (18 mg, 0.16 mmol) and refluxed for 15 min. The mixture was cooled to rt, quenched with saturated $NaHCO_3$ solution (2 mL), and partitioned between ether (20 mL) and water (5 mL). The separated organic phase was washed with brine, and the combined aqueous solutions were back-extracted with ether (10 mL). The ethereal phases were dried and evaporated to leave a residue that was purified by flash chromatography on silica gel (elution with 20% ethyl acetate in hexanes) to give **31** (23 mg, 80%) as a colorless oil; IR ($CHCl_3$, cm^{-1}) 3590, 1510, 1230, 1147, 1103, 1079, 1058, 635; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.75 (s, 4 H), 4.72 (dd, J = 9.6, 11.3 Hz, 1 H), 4.55 (d, J = 6.6 Hz, 1 H), 4.51 (d, J = 6.6 Hz, 1 H), 4.38 (d, J = 9.4 Hz, 1 H), 3.83 (br s, 1 H), 3.74 (s, 3 H), 3.31 (s, 3 H), 2.53 (d, J = 11.4 Hz, 1 H), 2.31 (ddd, J = 4.5, 7.6, 14.5 Hz, 1 H), 2.12 (s, 1 H), 2.04–1.67 (m, 8 H), 1.64–1.45 (m, 3 H), 1.37–1.17 (m, 2 H), 1.28 (s, 3 H), 1.14 (s, 3 H), 1.05 (s, 3 H), 0.52 (s, 9 H), 0.05 (s, 3 H), −0.07 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 154.7, 153.7, 116.1, 114.6, 101.3, 95.5, 90.3, 81.7, 72.9, 72.7, 55.7, 55.3, 47.45, 47.38, 42.8, 41.4, 37.2, 35.7, 29.0, 26.1, 25.1, 24.6, 23.2, 21.3, 20.0, 18.4, 16.4, −0.5, −1.5; MS m/z (M^+) calcd 390.3639, obsd 390.3631.

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Supplementary Material Available: Final calculated atomic coordinates for **26**-OMe and **27**-OMe. Copies of ^{1}H and ^{13}C NMR spectra of **9b**, **14**, **18**, **25b**, and **28–31** (15 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.