(d, J = 1 Hz, 5 H total), 3.53 and 3.47 (dq, J = 7.5, 7.1, 8.5, 6.8 Hz, 1 H total), 3.32 and 3.14 (dq, J = 7.5, 7.1, 8.5, 6.8 Hz, 1 H total), 1.42 and 1.01 (d, J = 6.8, 7.5 Hz, 3 H total), 0.89 and 0.51 (d, J = 7.5, 6.8 Hz, 3 H total). Anal. Calcd for $C_{35}H_{33}O_2PFe$: C, 73.43; H, 5.81. Found: C, 73.16; H, 6.17.

In an analogous fashion PhLi was added to the cinnamyl iron complex **22** followed by reaction with MeI to give the product shown in eq 15 in 85% yield (11:1 ratio of diastereomers). Major product: IR (CH_2Cl_2, cm^{-1}) 1910, 1600; ^{1}H NMR ($CDCl_3$) 7.70–6.80 (m, 25 H), 4.35 (d, J = 1 Hz, 5 H), 4.07 (d, J = 5 Hz, 1 H), 3.56 (dq, J = 5, 7.5 Hz, 1 H), 0.89 (t, J = 7.5 Hz, 3 H). Anal. Calcd for $C_{40}H_{35}FeO_2P$: C, 75.71; H, 5.56. Found: C, 75.51; H, 5.87.

Oxidative Cleavage Reaction To Yield Erythro Ester 28 and Hydrolysis To Yield Erythro Acid 29. Diastereomerically pure iron complex **27** (R = Me, Nu = Ph, 100 mg, 0.175 mmol) was dissolved in 4 mL of CS_2:EtOH (degassed with N_2), with enough CH_2Cl_2 added to maintain solubility of this complex at −78 °C. Bromine (0.21 mL of a freshly made 1.0 M solution in CS_2, 0.21 mmol) was added slowly at −78 °C. The solution instantly turned from orange to deep green upon bromine addition. The solution was stirred for 10 min, and analysis by TLC showed no starting material present. A 5% NH_4Cl solution (20 mL) was then added, and this aqueous solution was extracted with CH_2Cl_2 (2 × 30 mL). These CH_2Cl_2 extracts were dried (Na_2SO_4), and the solvent was removed by rotary evaporation to yield a crude green product. This product was chromatographed on a 2-mm silica gel prep plate with 4:1 pentane:ethyl acetate to yield a light yellow oil (R_f 0.8, 32.9 mg, 83%). **28**: IR (CH_2Cl_2, cm^{-1}) 3098, 3070, 3039, 2981, 2941, 2884, 1726, 1608, 1498, 1455, 1380, 1341, 1305, 1229, 1180, 1149, 1099, 1075, 1028, 969, 915, 865, 850; ^{1}H NMR ($CDCl_3$) 7.35–7.15 (m, 5 H), 4.20 (dq, J = 7, 3.5 Hz, 2 H), 2.89 (dq, J = 10, 7 Hz, 1 H), 2.58 (dq, J = 10, 6 Hz, 1 H), 1.29 (t, J = 7 Hz, 3 H), 1.25 (d, J = 7 Hz, 3 H), 0.93 (d, J = 6 Hz, 3 H). This ester (20 mg, 0.097 mmol) was placed into 20 mL of 95:5 ethanol:water, and sodium hydroxide (300 mg, 7.5 mmol) was added. The solution was refluxed for 1.5 h, and then the ethanol was removed by rotary evaporation. This solution was acidified with concentrated HCl and extracted with ether (3 × 20 mL). The ether extracts were dried over $MgSO_4$, and the ether was removed by rotary evaporation and pumping under vacuum to yield 6.0 mg (35%) of a yellow-white solid **29**: mp 132–134 °C (hexane/ether);[54] IR (CH_2Cl_2, cm^{-1}) 3500, 3400–2500 underlying OH, 3096, 3039, 2965, 2939, 2881, 1709, 1604, 1497, 1458, 1381, 1298, 1218, 1156, 1125, 1080, 881, 832; ^{1}H NMR ($CDCl_3$) 12.8 (s, v br, 1 H), 7.34–7.15 (m, 5 H), 2.91 (dq, J = 10, 7 Hz, 1 H), 2.61 (dq, J = 10, 7 Hz, 1 H), 1.32 (d, J = 7 Hz, 3 H), 0.97 (d, J = 7 Hz, 3 H).

General Procedure for Cis Disubstituted β-Lactam Formation. Iron complex **27** (R = Me, Nu = $NHCH_2Ph$, 104 mg, 0.173 mmol) was dissolved in 3 mL of CS_2 with a minimum amount of CH_2Cl_2 added to maintain the solubility of the complex at −78 °C, and the solution was degassed at room temperature with N_2. (In some cases, improved yields of β-lactams were noted when 2 equiv of anhydrous K_2CO_3 was also added to the solution.) .Bromine (0.208 mL of a freshly made 1.0 M solution in CS_2, 0.208 mmol) was added dropwise, and the solution rapidly turned from orange to deep green. The solution was stirred for 15 min at −78 °C and then 20 mL of water was added. The usual CH_2Cl_2 extracting (2 × 30 mL), Na_2SO_4 drying, and removing of solvent by rotary evaporation yielded a crude green product which was chromatographed on a 2-mm silica gel prep plate (10:1, CH_2Cl_2:Et_2O) to yield the desired β-lactam **30** as a light yellow oil (R_f 0.25, 25.6 mg, 78%). β-Lactam **30**:[51] IR (CH_2Cl_2, cm^{-1}) 3098, 3042, 2981, 2938, 2905, 1741, 1501, 1456, 1438, 1409, 1386, 1359, 1239, 1201, 1156, 1143, 1113, 1080, 1031, 969, 912; ^{1}H NMR ($CDCl_3$) 7.38–7.22 (m, 5 H), 4.60 (d, J = 16 Hz, 1 H), 4.10 (d, J = 16 Hz, 1 H), 3.65 (dq, J = 6, 6 Hz, 1 H), 3.25 (dq, J = 7.5, 6 Hz, 1 H), 1.18 (d, J = 7.5 Hz, 3 H), 1.09 (d, J = 6 Hz, 3 H). *cis*-1-Benzyl-3-ethyl-4-methylazetidinone (80%) was synthesized analogously: IR (CH_2Cl_2, cm^{-1}) 3096, 3041, 2974, 2939, 2882, 1740, 1501, 1458, 1437, 1408, 1388, 1359, 1239, 1193, 1152, 1141, 1070, 1031, 1004, 942, 821; ^{1}H NMR ($CDCl_3$) 7.31 (m, 5 H), 4.61 (d, J = 15.5 Hz, 1 H), 4.10 (d, J = 15.5 Hz, 1 H), 3.67 (dq, J = 6.6, 6.1 Hz, 1 H), 3.06 (ddd, J = 8, 8, 6.6 Hz, 1 H), 1.75 (ddq, J = 13.5, 8, 7.7 Hz, 1 H), 1.57 (ddq, J = 13.5, 8, 7.7 Hz, 1 H), 1.12 (d, J = 6.6 Hz, 3 H), 1.04 (t, J = 7.7 Hz, 3 H). Anal. Calcd for $C_{13}H_{17}NO$: C, 76.81; H, 8.43; N, 6.89. Found: C, 76.41; H, 8.29; N, 6.90. *cis*-1-Benzyl-3-benzyl-4-methylazetidinone (63%) was synthesized analogously: IR (CH_2Cl_2, cm^{-1}) 3095, 3039, 2976, 2924, 2861, 1739, 1608, 1499, 1452, 1435, 1405, 1383, 1359, 1238, 1148, 1122, 1078, 1029, 982, 948, 920; ^{1}H NMR ($CDCl_3$) 7.26 (m, 10 H), 4.64 (d, J = 15.7 Hz, 1 H), 4.13 nd, J = 15.7 Hz, 1 H), 3.72 (dq, J = 6.4, 5 Hz, 1 H), 3.57 (ddd, J = 9.3, 5.7, 5 Hz, 1 H), 3.19 (dd, J = 14.8, 5.7 Hz, 1 H), 2.86 (dd, J = 14.8, 9.3 Hz, 1 H), 1.12 (d, J = 6.4 Hz, 3 H). Anal. Calcd for $C_{17}H_{19}NO$: C, 80.60; H, 7.56; N, 5.53. Found: C, 80.69; H, 7.87; N, 5.20. *cis*-1-Benzyl-3-allyl-4-methylazetidinone (22%) was also synthesized analogously: IR (CH_2Cl_2, cm^{-1}) 3051, 2978, 2930, 1740, 1641, 1499, 1453, 1438, 1408, 1384, 1360, 1121, 1095, 1075, 1049, 1030, 921, 880, 848; ^{1}H NMR ($CDCl_3$) 7.39–7.22 (m, 5 H), 5.86 (dddd, J = 17.4, 8.7, 7.5, 5.6 Hz, 1 H), 5.17 (ddd, J = 17.4, 2, 1.5 Hz, 1 H), 5.06 (ddd, J = 8.7, 2, 1.5 Hz, 1 H), 4.61 (d, J = 15.2 Hz, 1 H), 4.10 (d, J = 15.2 Hz, 1 H), 3.71 (dq, J = 6.3, 5.7 Hz, 1 H), 3.26 (ddd, J = 9.6, 5.7, 5.2 Hz, 1 H), 2.53 (dddd, J = 15, 5.6, 5.2, 1.5 Hz, 1 H), 2.33 (dddd, J = 15, 9.6, 7.8, 1.5 Hz, 1 H), 1.13 (d, J = 6.3 Hz, 3 H); exact mass calcd for $C_{14}H_{17}NO$ 215.1310, found 215.1312.

Acknowledgment. This investigation was supported by the National Science Foundation under Grants CHE-8305055 and CHE-8501125. We thank Prof. Virgil Goedken for assistance with the X-ray crystallography.

Supplementary Material Available: Stereoviews, tables of interatomic distances and bond angles, and tables of positional and thermal parameters for compounds **5** and **7** (19 pages); tables of calculated and observed structure factors (42 pages). Ordering information can be found on any current masthead page.

Total Synthesis of (±)-Poitediol and (±)-Dactylol

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Abstract: The unusual cyclooctanoid sesquiterpene, poitediol (**7**), was synthesized in racemic form in 20 steps from 2-methoxy-4-methyl-2-cyclohexen-1-one (**14**). The key step in the synthesis was the oxy-Cope rearrangement of 5-ethenyl-6-ethynyl-2-methylbicyclo[3.2.0]heptan-6-ol (**22**) to afford *cis*-1,2,3,3a,4,8-hexahydro-3-methyl-5*H*-cyclopentacycloocten-5-one (**10**). Racemic dactylol (**8**) was prepared in one step from poitediol by reduction with sodium in liquid ammonia.

The cyclooctanoid terpenes are a structurally diverse and potentially biologically important family of compounds. There are currently over 35 known natural products in this family, all of which are characterized by the presence of a cyclooctane fused to other carbocyclic rings. The first cyclooctanoid natural product to be isolated was the sesterterpene ophiobolin A (**1**), isolated from a plant pathogenic fungus.[1] Interestingly, ophiobolin A was the

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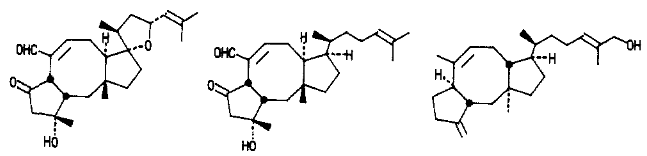
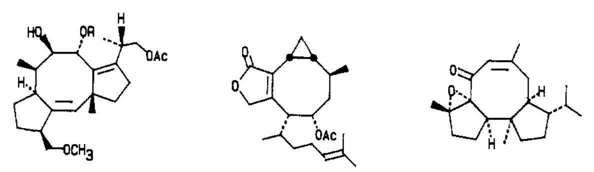
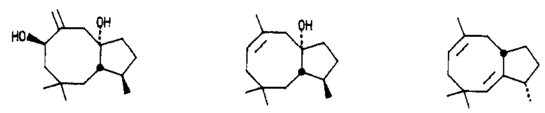


1 2 3



4 (R=sugar) 5 6



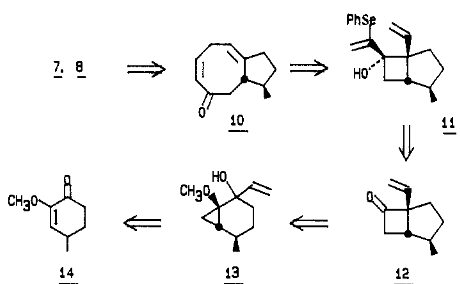
7 8 9

first naturally occurring sesterterpene to have its structure completely elucidated. Other representative examples of cyclooctanoid sesterterpenes are ophiobolin C (**2**), also isolated from a phytopathogenic fungus,[2] and ceroplastol I (**3**), isolated from insect wax.[3] A large group of cyclooctanoid diterpenes is also known, with representative examples being fusicoccin A (**4**), isolated from another phytopathogenic fungus,[4] acetoxycrenulide (**5**), isolated from sea hares,[5] and basmenone (**6**), isolated from tobacco plants.[6] Lastly, several cyclooctanoid sesquiterpenes have been isolated from marine sources, and these are poitediol (**7**),[7] dactylol (**8**),[8] and precapnelladiene (**9**).[9]

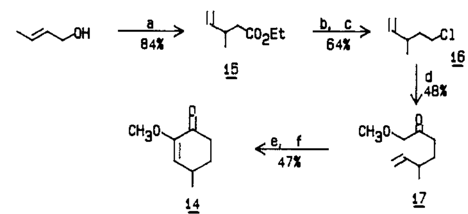
The cyclooctanoid terpenes are challenging targets for total synthesis, presenting several unique synthetic problems due to the presence of the cyclooctane ring. First of all, because of unfavorable entropic and enthalpic factors, cyclooctanes cannot be efficiently prepared by traditional methods of ring formation, and new strategies need to be developed for their synthesis. Secondly, cyclooctanes are very susceptible to transannular reactions, and, therefore, functionality on the cyclooctane must be kept to a minimum, or protected, throughout the synthesis. Lastly, compared to smaller alicyclic rings, cyclooctane reaction stereoselectivity is difficult to predict or control, primarily because of the large number of low-energy conformations available to eight-membered rings. Due in large part to these factors, no complete total synthesis of a cyclooctanoid sesterterpene or diterpene has yet been reported, although a number of groups have made considerable progress in this area.[10] Greater success has been realized with the simpler cyclooctanoid sesquiterpenes, and as part of our ongoing program directed toward the synthesis of cyclooctanoid natural products, we recently completed the first total syntheses of poitediol[11] and dactylol.[12] The synthesis of precapnelladiene[13] and other syntheses of dactylol[14] have been more recently reported. The full account of our syntheses of poitediol and dactylol is reported herein.

Our approach to poitediol and dactylol was based on the oxy-Cope rearrangement of a dialkenylcyclobutanol, a method

Scheme I

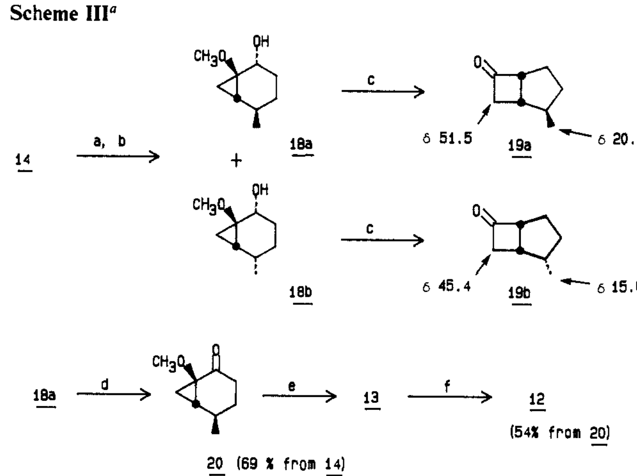


Scheme II[a]



[a](a) $(EtO)_3CCH_3$, $CH_3CH_2CO_2H$; (b) LAH, Et_2O; (c) $SOCl_2$, Bu_3N; (d) 1) Mg°, THF; 2) $MeOCH_2CN$, PhH; (e) 1) O_3, CH_2Cl_2, −78°; 2) Me_2S; (f) NaOH, MeOH.

Scheme III[a]



[a](a) DIBAH, Et_2O, −100 °C; (b) CH_2I_2, Et_2Zn, O_2; (c) aq HBF_4, THF; (d) PCC, CH_2Cl_2; (e) $CH_2{=}CHMgBr$, PhH; (f) BF_3-Et_2O, Et_2O.

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which we had previously reported to be an efficient means of construction of substituted cyclooctenones.[15] As shown in Scheme I, it was anticipated that poitediol and dactylol would be available from cyclooctadienone **10**, which in turn would be produced upon oxy-Cope rearrangement of the dialkenylbicyclo[3.2.0]heptanol **11** and subsequent selenoxide generation and elimination. The synthetic precursor of alcohol **11** can be seen to be the bicyclo[3.2.0]heptanone **12** which in turn might be prepared via acid-catalyzed rearrangement[16] of the bicyclo[4.1.0]heptanol **13**. The logical precursor of **13** was 2-methoxy-4-methyl-2-cyclohexenone (**14**), and our synthesis thus began with the preparation of this cyclohexenone.

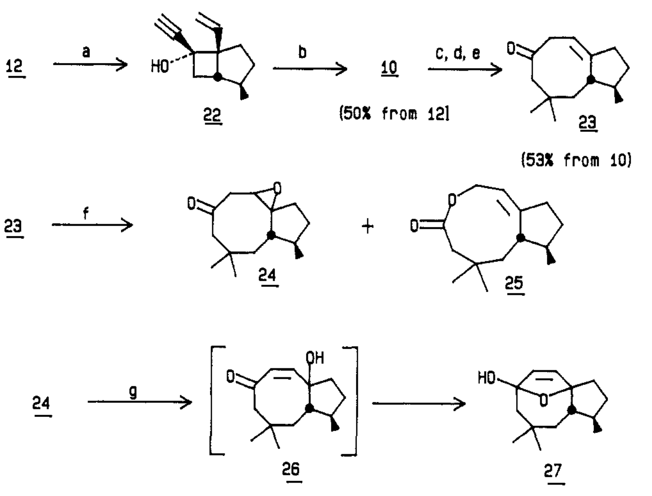
Although **14** appears to be a very simple compound, all of our successful syntheses of this cyclohexenone require a minimum of six steps from commercially available starting materials. The most convenient synthesis of **14** is presented in Scheme II. Reaction of crotyl alcohol with triethyl orthoacetate under modified Claisen conditions[17] led to ester **15** in 84% yield. Reduction of **15** and conversion to the chloride **16** occurred smoothly. Grignard reaction of this chloride with methoxyacetonitrile cleanly gave ketone **17**, although with a maximum yield of only 48% despite considerable effort at optimization.[18] Finally, ozonolysis followed by reductive workup and intramolecular aldol cyclization afforded the desired enone **14**. The conversion of this compound to the key bicyclo[3.2.0]heptanone **12** is shown in Scheme III.

In order to establish the relative stereochemistry needed for poitediol, it was necessary to selectively reduce enone **14** to a *trans*-cyclohexenol. Hydroxyl-directed cyclopropanation[19] would then place the methyl group on the exo face of the norcaranol, and subsequent reactions would maintain the desired cis relationship between this methyl group and the ring fusion hydrogen. In general, only modest stereoselectivity was observed in the reduction of **14** with a variety of hydride reducing agents. The best results were obtained with DIBAH in diethyl ether at −100 °C,[20] affording an inseparable mixture of isomeric alcohols which upon modified Simmons–Smith reaction[19b] led to norcaranols **18a** and **18b** in a 6.8:1 ratio.

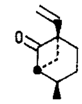
The relative stereochemistry of these norcaranols was proven by individually subjecting each isomer to acid-catalyzed rearrangement[16] to produce bicyclo[3.2.0]heptanones **19a** and **19b**. The rearrangement was stereospecific, with each diastereomeric alcohol producing a single, unique bicyclo[3.2.0]heptanone. The relative stereochemical assignments of **19a** and **19b** could be readily deduced on the basis of ^{13}C NMR data. As shown in Scheme III, there is a clear upfield shift of both the methyl carbon and the C7 carbon in the endo isomer **19b** relative to the exo isomer **19a** due to steric shielding.[21] Since **19a** was produced upon rearrangement of the major norcaranol **18a**, this norcaranol must have the desired stereochemistry (exo methyl group). Reduction of enone **14** with DIBAH must therefore have produced predominantly the *trans*-alcohol as desired.

Oxidation of **18a** give ketone **20**. Addition of vinylmagnesium bromide produced the allylic alcohol **13**, and immediate rearrangement with boron trifluoride etherate led to the target bicyclo[3.2.0]heptanone (**12**) in 54% overall yield from **20**.[22] In this case, attempted rearrangement of the intermediate allylic alcohol with aqueous acid led to an inseparable mixture of **12** and an isomeric ketone presumed to be **21**.[16]

Scheme IV[a]



[a] (a) HC_2Li, THF, −30 °C; (b) 50 °C, 3 h; (c) MeLi, Et_2O, −78 °C; (d) PCC, CH_2Cl_2; (e) Me_2CuLi, Et_2O; (f) MCPBA, CH_2Cl_2; (g) DBU, THF.



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Our original plan had called for reaction of ketone **12** with (1-phenylselenenyl)ethenyllithium[23] and subsequent anionic oxy-Cope rearrangement to an α-phenylselenenylcyclooctenone which could be converted to the desired cyclooctadienone **10**. However, the overall yield of this process was generally quite low (ca. 10%). Comparable results were obtained starting with (1-phenylsulfenyl)ethenyllithium.[24] In contrast, reaction of **12** with lithium acetylide[25] proceeded quite cleanly, and subsequent rearrangement of the adduct **22** at 50 °C under neutral conditions led to the desired cyclooctadienone **10** in 50% overall yield (Scheme IV).[26] The highest yields of **22** were obtained when the addition of lithium acetylide to **12** was carried out at −30 °C for 5 min. At lower temperatures, addition was extremely sluggish, and at higher temperatures or longer reaction times, the adduct began to decompose, presumably via anionic oxy-Cope rearrangement to a very unstable 1,2-cyclooctadienolate. The favorable energetics associated with the oxy-Cope rearrangement of the intermediate alkynylvinylcyclobutanol are underscored by the facile formation of a high-energy 1,2,5-cyclooctatrienol as the initial rearrangement product. Normally, 1,2-cyclooctadienes are unstable at room temperature,[27] and it is presumably only due to rapid keto–enol tautomerization that **10** is isolated in good yield.

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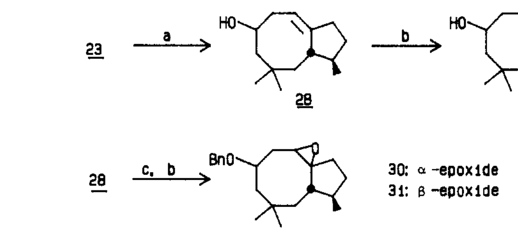
Scheme V[a]



[a] (a) LAH, Et_2O, −78 °C; (b) MCPBA, CH_2Cl_2; (c) KH, $PhCH_2Br$, Bu_4NI, THF.

Once in hand, cyclooctadienone **10** was carried along the path to poitediol and dactylol by sequential treatment with methyllithium, oxidative rearrangement with pyridinium chlorochromate,[28] and reaction with lithium dimethyl cuprate (Scheme IV). This series of steps afforded cyclooctenone **23**, in 53% overall yield from **10**. Although it seemed at this point that the conversion of **23** to poitediol would be quite straightforward, the actual completion of the synthesis ultimately required ten more steps and considerable experimentation due to the interference of transannular reactions.

Our original plan had called for a Markovnikov hydration of **23**, but reaction with mercuric acetate or trifluoroacetate[29] led only to recovery of unreacted **23**. Bromohydration with NBS in aqueous DME[30] produced an intractable mixture of products. Epoxidation with MCPBA led to isolation of the epoxide **24** as a mixture of isomers along with the lactone **25** (Scheme IV). Although reaction of epoxide **25** with DBU presumably produced the desired hydroxy ketone **26** as an intermediate, the only isolable product was the transannular lactol **27** which could not be converted to any useful form of a protected hydroxy ketone.

Since it was apparent that the C3 carbonyl and the C1 hydroxyl could not coexist in unprotected form, a double protection–deprotection strategy was employed to complete the synthesis (Scheme V). Reduction of cyclooctenone **23** with LAH in diethyl ether at −78 °C gave an inseparable mixture of alcohols **28** in a 3.7:1 ratio. Interestingly, DIBAH was less selective in this reaction, producing a 2:1 mixture of isomers. Reduction with lithium in ammonia produced a mixture of alcohols with the same degree of stereoselectivity as the LAH reaction but in the opposite sense (1:3.5). The actual stereochemistry of the major alcohols from these reductions remains to be determined.[31]

Attempted epoxidation of the mixture of homoallylic alcohols from either the LAH or Li/NH3 reduction using *tert*-butylhydroperoxide and a vanadium catalyst[32] was unsuccessful, generally returning only starting material or leading to decomposition under forcing conditions. This result was not unexpected, since it is clear from models that both homoallylic alcohol isomers prefer the hydroxyl group to be in a pseudoequatorial orientation, directed away from the double bond and unable to complex with the vanadium catalyst in the epoxidation transition state.[32] Epoxidation with MCPBA occurred in high yield, but both alcohols gave predominantly the undesired β-epoxide **29**, presumably as a result of attack of the peracid on the less sterically hindered face of the alkene. It was found, however, that prior benzylation reversed the stereoselectivity of the epoxidation of one of the alcohols. Thus benzylation of the mixture of alcohols **28** derived from the LAH reduction of cyclooctenone **23**, followed by epoxidation with MCPBA, led to formation of epoxides **30** and **31** in a ratio of 3.7:1 (Scheme V). Benzylation and epoxidation of the alcohols produced via reduction by lithium in ammonia still afforded predominantly the undesired β-epoxide. The relative stereochemistries of **30** and **31** were confirmed by their eventual conversion to poitediol and 1-epipoitediol, respectively.[31]

Once in hand, the α-epoxide **30** was reductively opened by treatment with lithium triethylborohydride,[33] and the resulting alcohol **32** was subsequently protected as a [(trimethylsilyl)ethoxy]methyl (SEM) ether[34] (Scheme VI). Debenzylation with sodium in liquid ammonia proceeded smoothly, and Swern oxidation[35] then led to the protected hydroxy ketone **33** in 79% overall yield from **32**. Treatment of this ketone with LDA resulted in regiospecific deprotonation at the less hindered position, and subsequent reaction with formaldehyde afforded a mixture of an intermediate α-hydroxymethyl ketone and the α-methylene ketone **34**. Treatment of this mixture with methanesulfonyl chloride and *N,N*-diisopropylethylamine completed the conversion of the α-hydroxymethyl ketone to **34** (Scheme VI).

At this point in the synthesis, all that remained was to reduce enone **34** stereoselectively and to deprotect the C1 hydroxyl. However, both of these steps were initially problematic. Reduction of enone **34** with NaBH4 in the presence of $CeCl_3$[36] gave a 95:5 mixture of alcohols in which the major alcohol was found to be the undesired α-alcohol **35**. As previously observed in the reduction of ketone **23**, DIBAH was found to be relatively nonstereoselective, affording both alcohols in a 1:1 ratio. Triisobutylaluminum was found to be quite stereoselective in the desired sense, producing a 6:1 mixture of the alcohols **36** and **35**.[31] Unfortunately, the yield of this reduction was only 41%.

Attempted deprotection of **36** with fluoride ion from a variety of sources was unsuccessful, generally returning only starting material or resulting in decomposition under forcing conditions. However, it was found that treatment with dilute methanolic HCl (0.1 M) led to rapid and clean deprotection without interference from either dehydration or transannular reactions (Scheme VII). The identity of the material thus obtained as racemic poitediol was secured by the exact correspondence of its IR and 270-MHz ^{1}H NMR spectral data with that of an authentic sample of (−)-poitediol.[37]

Although several direct approaches to dactylol from ketone **32** might be envisioned, we found that treatment of poitediol with sodium in liquid ammonia resulted in clean reduction to dactylol in 91% yield. Once again, the identity of this material as racemic dactylol was established by comparison of IR and high-field NMR spectral data with that of authentic (+)-dactylol.[38] Interestingly, reduction of 4-epipoitediol (derived from the α-alcohol **35**) under the same conditions afforded mostly the E isomer of dactylol. This result is presumably a consequence of both stereoelectronic control in the reduction and the differing conformational preferences of 4-epipoitediol and poitediol.[12]

The successful syntheses of poitediol and dactylol demonstrate the utility of the oxy-Cope rearrangement of dialkenylcyclobutanols for the synthesis of cyclooctanoid natural products. Efforts directed toward the synthesis of other cyclooctanoid natural products are currently underway in our laboratories.

Experimental Section

General Methods. Dry tetrahydrofuran (THF) and diethyl ether (Et_2O) were obtained by distillation from sodium by using benzophenone as an indicator. All reagents and chemicals were obtained from Aldrich Chemical Company and used as received unless otherwise specified.

Organic phases from aqueous extractions were dried over $MgSO_4$, and unless otherwise specified, were concentrated by rotary evaporation at

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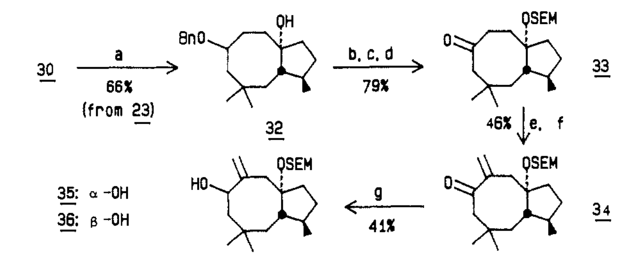
(37) An authentic sample of poitediol was graciously provided by Dr. Valerie Paul from the laboratory of Professor W. Fenical, Scripps Institution of Oceanography.

(38) An authentic sample of dactylol was unavailable. However, spectra of authentic dactylol were kindly provided by Professor F. Schmitz, University of Oklahoma.

Scheme VI[a]



[a](a) $LiEt_3BH$, THF, 50 °C; (b) SEMCl, i-Pr_2NEt, THF, 50 °C; (c) Na, NH_3; (d) 1) ClCOCOCl, DMSO, −78 °C; 2) i-Pr_2NEt; (e) 1) LDA, THF, −78 °C; 2) HCHO; (f) MsCl, i-Pr_2NEt; (g) i-Bu_3Al, hexane, 25 °C.

aspirator vacuum, followed by removal of traces of solvent at 1.0 torr vacuum.

Preparative HPLC separations were carried out by using a 25 cm × 1 cm Alltech column containing 10 μm silica gel. Flash chromatography was carried out in the standard way by using Merck silica gel 60 (230–400 mesh). Thin-layer chromatography was carried out on silica gel plates by using radial elution in inexpensive radial TLC chambers.[39] The purity of all distilled or chromatographed compounds was determined to be ≥95% by ^1H NMR analysis.

^1H NMR spectra were recorded at 270 MHz, unless otherwise specified. ^{13}C NMR spectra were recorded at 67.5 MHz. All shifts are reported downfield from an internal Me_4Si standard.

Elemental analyses were performed by Micro-Tech Laboratories Inc., Skokie, IL.

3-Methyl-4-pentenoic Acid Ethyl Ester (15). Crotyl alcohol (21.3 mL, 13.5 g, 0.188 mol), triethyl orthoacetate (68.4 mL, 60.8 g, 0.375 mol), and propanoic acid (0.559 mL, 0.555 g, 75 mmol) were mixed in a 100-mL, 3-necked, round-bottomed flask equipped with a thermometer, a 10-cm Vigreux column capped by a distillation head, and a glass stopper. The reaction was slowly heated to 135–140 °C with stirring over a 2-h period, during which time the theoretical amount of ethanol distilled over. Care must be taken not to heat the reaction beyond 140 °C, or some of the relatively volatile product will also be lost. After distillation had ceased, the reaction was cooled to room temperature, and water (4.05 mL, 4.05 g, 0.225 mol) was added. The reaction was again heated to 80–100 °C to distill off the ethanol produced. After about 1.5 h distillation of ethanol slowed, and the remaining crude material was purified by distillation under aspirator vacuum to afford 22.5 g (84% yield) of **15**: bp_{17} 59–61 °C (lit. bp_8 44–47 °C[40]); IR (CCl_4) 3090 (m), 2990 (s), 1740 (s), 1640 (m) cm^{-1}; 90-MHz ^1H NMR (CCl_4) δ 5.75 (1 H, m), 5.00 (2 H, m), 4.08 (2 H, q, *J* = 7 Hz), 2.60 (1 H, m), 2.20 (2 H, m), 1.30 (3 H, t, *J* = 7 Hz), 1.10 (3 H, d, *J* = 7 Hz).

3-Methyl-4-penten-1-ol. To a suspension of lithium aluminum hydride (6.03 g, 0.159 mol) in 150 mL of dry Et_2O at 0 °C was added dropwise a solution of **15** (17.4 g, 0.122 mol) in 100 mL of dry Et_2O. After addition was complete, the reaction was allowed to warm to room temperature, stirred for 2 h, and then poured into a 1-L beaker. Water (6.03 mL), 15% NaOH (6.03 mL), and then more water (18.1 mL) were carefully added with good stirring over a 30-min period. The white solids were removed by filtration and were washed well with Et_2O. The combined filtrates were dried and concentrated by distillation at atmospheric pressure. The residue was distilled to afford 9.04 g (74% yield) of the product: bp_{22} 66 °C (lit. bp_{25} 63–64 °C[41]); IR (CCl_4) 3640 (w), 3330 (s), 3080 (m), 2930 (s), 1640 (m), 1050 (s), 990 (s), 910 (s) cm^{-1}; 90-MHz ^1H NMR (CCl_4) δ 5.65 (1 H, m), 4.90 (2 H, m), 3.55 (2 H, m), 3.30 (1 H, m), 2.25 (1 H, m), 1.50 (2 H, q, *J* = 7 Hz), 1.00 (3 H, d, *J* = 7 Hz).

3-Methyl-5-chloro-1-pentene (16). *Caution! This procedure generates a large amount of SO_2 and must be performed in an efficient fume hood!* Tributylamine (18.3 g, 0.099 mol) and 3-methyl-4-penten-1-ol (9.00 g, 0.090 mol) were added to a 100-mL, 3-necked, round-bottomed flask equipped with a mechanical stirrer and an addition funnel. This mixture was chilled to 0 °C, and thionyl chloride (6.90 mL, 11.3 g, 0.0945 mol, distilled from $(PhO)_3P$) was added while the reaction temperature was maintained below 5 °C. After addition was complete, the ice bath was removed, and the reaction was stirred for 1 h. The addition funnel was replaced with a distillation head, and all of the volatile material in the reaction mixture was distilled under aspirator vacuum into a flask chilled to −78 °C. A heating mantle was used to maintain the reaction flask at room temperature during distillation. Distillation was continued until the vacuum had reached 20 torr and no further material was distilling. The distillate (which contains a large amount of SO_2) was carefully allowed to warm to room temperature during which time most of the SO_2 boiled off. The residue was redistilled through a 10-cm Vigreaux column to afford 9.31 g (87% yield) of **16**: bp 118–120 °C (lit. bp 124–126 °C[42]); IR (CCl_4) 3080 (m), 2960 (s), 1640 (m), 990 (s), 920 (s) cm^{-1}; 90-MHz ^1H NMR (CCl_4) δ 5.60 (1 H, m), 5.05 (1 H, m), 3.50 (2 H, t, *J* = 7 Hz), 2.40 (1 H, m), 1.75 (2 H, q, *J* = 7 Hz), 1.05 (3 H, d, *J* = 7 Hz).

1-Methoxy-5-methyl-6-hepten-2-one (17). Approximately one-third of a solution prepared from **16** (9.25 g, 0.0781 mol) and 75 mL of dry THF was added to magnesium turnings (2.09 g, 0.0859 mol) in a flame-dried, 250-mL, round-bottomed flask. A crystal of iodine was added, and the flask was heated under nitrogen until the iodine color discharged (about 15 min). The rest of the THF solution of **16** was then added dropwise to the reaction at a rate sufficient to sustain a gentle reflux. After addition was complete, the reaction was refluxed for 1.5 h, cooled to room temperature, and then added via cannula to methoxyacetonitrile (4.991 g, 0.0703 mol) in 75 mL of dry benzene (distilled from LAH) at 0 °C. After addition was complete, the resulting yellowish suspension was stirred at room temperature for 2 h and then chilled in an ice bath. Saturated, aqueous NH_4Cl (35 mL) was carefully added, followed by 6 M HCl (12 mL), H_2O (10 mL), and then more 6 M HCl (12 mL). After stirring for 1 h at room temperature, the phases were separated, and the aqueous phase was extracted with ether. After washing with saturated, aqueous $NaHCO_3$ (30 mL) and brine (30 mL), the combined organic phases were dried and concentrated, and the residue was distilled to afford 5.27 g (48% yield) of **17**: $bp_{1.25}$ 59 °C; IR (CCl_4) 3080 (m), 2930 (s), 1729 (s), 1640 (m), 1100 (s), 990 (s), 910 (s) cm^{-1}; 90-MHz ^1H NMR (CCl_4) δ 5.65 (1 H, m), 4.95 (1 H, m), 3.80 (2 H, s), 3.38 (3 H, s), 2.41 (2 H, t, *J* = 7 Hz), 2.12 (1 H, m), 1.55 (2 H, m), 1.05 (3 H, d, *J* = 7 Hz).

2-Methoxy-4-methyl-2-cyclohexen-1-one (14). To a 100-mL, 3-necked, round-bottomed flask fitted with gas inlet and outlet tubes and a glass stopper was added **17** (4.72 g, 0.0303 mol) in 50 mL of CH_2Cl_2. This solution was chilled to −78 °C, and ozone was bubbled into the stirred solution at a moderate rate. After 30 min, the solution had turned blue, and the ozone flow was stopped. Nitrogen was bubbled through the solution until it was colorless, and then dimethyl sulfide (22.2 mL, 18.8 g, 0.303 mol) was added. The gas inlet and outlet tubes were replaced with a condensor and a stopper, and the mixture was refluxed for 6 h. Removal of the solvent at atmospheric pressure afforded the crude aldehyde which was not purified but was used immediately in the next reaction.

A solution of NaOH (0.80 g, 0.020 mol) in 50 mL of MeOH was added to the aldehyde, and the resulting orange solution was stirred at room temperature for 20 min. After neutralization with HOAc, the reaction was concentrated, and the residue was dissolved in 20 mL of H_2O and 30 mL of Et_2O. The phases were shaken and separated, and the aqueous phase was extracted with Et_2O. The combined organic phases were washed with saturated, aqueous $NaHCO_3$ (20 mL) and brine (20 mL), then dried, and concentrated. The residue was distilled to afford 1.97 g of **14** (47% yield from **17**): $bp_{0.1}$ 60–62 °C; IR (CCl_4) 2950 (s), 1690 (s), 1620 (s), 1215 (s), 1150 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.68 (1 H, br d, *J* = 2.6 Hz), 3.59 (3 H, s), 2.68 (1 H, m), 2.60 (1 H, dt, *J* = 16.8, 4.6 Hz), 2.46 (1 H, ddd, *J* = 16.8, 12.7, 4.8 Hz), 2.06 (1 H, dqd, *J* = 13.0, 4.7, 1.0 Hz), 1.62 (1 H, tdd, *J* = 12.8, 9.5, 4.7 Hz), 1.18 (3 H, d, *J* = 6.9 Hz); MS (70 eV) *m/e* (rel intensity) 140 (M^+), 125, 97, 69 (base), 67, 55, 41. Anal. Calcd for $C_8H_{12}O_2$: C, 68.55; H, 8.63. Found: C, 68.09; H, 8.70.

2-Methoxy-4-methyl-2-cyclohexen-1-ol (Mixture of Cis and Trans Isomers). A flame-dried, 500-mL, 3-necked flask was fitted with a septum, mechanical stirrer, and nitrogen inlet. Diisobutylaluminum hydride (1 M in hexane, 74.7 mL, 0.0747 mol) and dry Et_2O (200 mL) were added, and this solution was chilled under nitrogen in a liquid nitrogen/Et_2O bath. A solution of enone **14** (8.72 g, 0.0623 mol) in 10 mL of dry Et_2O was added via syringe pump over 1 h, while the temperature of the cold bath was maintained at −105 to −95 °C. After addition was complete, the cold bath was removed, and the reaction was stirred for 30 min. Methanol (10 mL) was cautiously added, and the reaction was transferred to a 1-L beaker. An additional 100 mL of methanol were added, and the reaction was stirred until it turned gelatinous. Hexane (120 mL) was added, and the suspension was filtered through Celite. The solids were transferred to a 600-mL beaker and washed well with 3 100-mL portions of Et_2O. The combined filtrates were concentrated to about 20 mL, diluted with 150 mL of hexane, and

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then filtered again through Celite. The solution was dried by concentration, dilution with 60 mL of benzene, and concentration again. The crude mixture of alcohols thus obtained (ca. 8.8 g) was found to be somewhat unstable at room temperature in concentrated form, on one occasion turning to a crystalline solid after about 4 h. For this reason, the mixture of alcohols was typically not purified but was used immediately in the next reaction. Spectral data for this mixture were the following: IR (CCl_4) 3590 (m), 3460 (w), 2955 (s), 1665 (s), 1450 (m), 1205 (s) cm^{-1}; 90-MHz ^{1}H NMR (CCl_4) δ 4.45 (1 H, d, J = 3 Hz), 3.95 (1 H, m), 3.50 (3 H, s), 2.40 (1 H, br s), 2.0–1.0 (5 H, br m), 0.95 (3 H, d, J = 7 Hz).

(1β,2α,5β,6β)-(±)-1-Methoxy-5-methylbicyclo[4.1.0]heptan-2-ol (18a) and (1β,2α,5α,6β)-(±)-1-Methoxy-5-methylbicyclo[4.1.0]heptan-2-ol (18b). A solution of the above cyclohexenols (8.85 g crude, ca. 0.0623 mol) in 25 mL of toluene was added to diethylzinc (15% solution in toluene, 113 mL, 15.4 g, 0.125 mol) at 0 °C under nitrogen. Vigorous evolution of ethane occurred during the addition. The resulting solution was warmed to room temperature, diiodomethane (10.0 mL, 33.4 g, 0.125 mol) was added rapidly, and air was bubbled through the reaction mixture. The temperature of the reaction rose quickly, reaching a maximum of 76 °C within 5–10 min. After the reaction had cooled, it was poured into 100 mL of 3 M NaOH, and the layers were shaken and separated. The aqueous phase was extracted with Et_2O, and the combined organic phases were washed with 100 mL of brine, dried, and concentrated to afford a mixture of norcaranols (9.64 g, 99% crude yield) in a 6.8:1 ratio (**18a**:**18b**) by HPLC analysis (30% ethyl acetate in hexane; silica gel column). Although separation could be accomplished at this point, the mixture of alcohols was generally used directly in the next reaction.

Spectral data for **18a**: IR (CCl_4) 3590 (m), 3440 (m), 2920 (s), 1465 (m), 1455 (m), 1220 (m), 1040 s) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.34 (1 H, dd, J = 9.1, 6.3 Hz), 3.32 (3 H, s), 2.47 (1 H, br s), 1.86 (1 H, m), 1.51 (2 H, m), 1.08 (3 H, d, J = 6.6 Hz), 0.95 (4 H, m), 0.62 (1 H, t, J = 5.3 Hz); MS (70 ev), m/e (rel intensity) 156 (M$^+$), 138, 123, 100 (base), 82, 67, 55, 41.

Spectral data for **18b**: IR and MS fundamentally similar to that of **18a**; 60-MHz ^{1}H NMR ($CDCl_3$) δ 4.40 (1 H, t, J = 6 Hz), 3.25 (3 H, s), 2.2 (3 H, m), 1.4 (4 H, m), 0.95 (3 H, d, J = 7 Hz), 0.62 (2 H, d, J = 8 Hz).

(1β,2β,5β)-(±)-2-Methylbicyclo[3.2.0]heptan-6-one (19a). To a solution of alcohol **18a** (47.0 mg, 0.301 mmol) in 5 mL of THF was added fluoboric acid (48% aqueous solution, 1 mL), and the resulting reaction mixture was stirred at room temperature for 3 h. The reaction was diluted with 25 mL of Et_2O, washed with two 10-mL portions of saturated, aqueous $NaHCO_3$, dried, and concentrated. Purification by HPLC (10% ethyl acetate in hexane) afforded 27.0 mg of **19a** (73% yield): IR (CCl_4) 2960 (s), 2870 (m), 1775 (s), 1455 (m), 1080 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.57 (1 H, br s), 3.17 (1 H, ddd, J = 19.4, 10.2, 4.6 Hz), 2.52 (2 H, m), 2.16 (1 H, p, J = 6.6 Hz), 2.0–1.8 (3 H, br m), 1.55 (1 H, m), 0.94 (3 H, d, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 214.2 (s), 64.4 (d), 51.5 (t), 39.9 (d), 36.6 (d), 31.9 (t), 27.1 (t), 20.3 (q); MS (70 eV), m/e (rel intensity) 124 (M$^+$), 96, 82, 81, 67 (base).

(1β,2α,5β)-(±)-2-Methylbicyclo[3.2.0]heptan-6-one (19b). Ketone **19b** was prepared in the same way as ketone **19a**: IR and MS fundamentally similar to that of **19a**; ^{1}H NMR ($CDCl_3$) δ 3.52 (1 H, m), 3.0–2.6 (3 H, m), 2.17 (1 H, sextet, J = 5 Hz), 1.96 (1 H, dd, J = 13, 6 Hz), 1.80 (1 H, m), 1.65 (1 H, m), 1.28 (1 H, m), 1.05 (3 H, d, J = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 212.0 (s), 65.0 (d), 45.4 (t), 37.5 (d), 33.6 (d), 32.1 (t), 28.9 (t), 15.0 (q).

(1β,5β,6β)-(±)-1-Methoxy-5-methylbicyclo[4.1.0]heptan-2-one (20). To a rapidly stirring mixture of Celite (20 g), pyridinium chlorochromate (19.9 g, 0.0923 mol), and CH_2Cl_2 (250 mL) was added a solution of alcohol **18a** (9.6 g, 0.062 mol) in 10 mL of CH_2Cl_2. After stirring 1.5 h at room temperature, the reaction mixture was filtered through 80 g of Florisil with 500 mL of CH_2Cl_2. After concentration, the residue was diluted with 100 mL of Et_2O, and the resulting suspension was filtered through Celite with 150 mL more Et_2O. After concentration, the residue was diluted with 50 mL of 20% ethyl acetate in hexane, and the resulting suspension was filtered through 50 g of silica gel with 300 mL more 20% ethyl acetate in hexane. Finally, after concentration, the residue was distilled to afford 6.578 g (69% overall yield from **14**) of **20**: bp$_{0.15}$ 53 °C; IR (CCl_4) 2960 (s), 1695 (s), 1440 (m), 1230 (m), 1125 (m), 1045 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.38 (3 H, s), 2.25 (3 H, m), 1.77 (2 H, m), 1.48 (3 H, m), 1.14 (3 H, d, J = 6.9 Hz); MS (70 eV), m/e (rel intensity) 154 (M$^+$), 139, 111, 98, 97, 83, 55 (base).

2-Ethenyl-1-methoxy-5-methylbicyclo[4.1.0]heptan-2-ol (13). To a flame-dried, 250-mL, 3-necked, round-bottomed flask fitted with a thermometer, a glass stopper, and an addition funnel was added 110 mL of dry benzene and ketone **20** (6.55 g, 0.0425 mol). The flask was chilled in an ice bath, and vinylmagnesium bromide (1.0 M in THF, 55.3 mL, 0.0553 mol) was added while maintaining the reaction temperature below 10 °C. After addition was complete (15 min), the reaction was stirred at room temperature for 2 h, and then chilled in an ice bath while it was cautiously quenched with 40 mL of saturated, aqueous NH_4Cl. The phases were shaken and separated, and the aqueous phase was extracted with Et_2O. The combined organic phases were washed with brine, dried, and concentrated. The crude material thus obtained was not further purified but was used immediately in the next reaction. Spectral data on the crude alcohol were the following: IR (CCl_4) 3550 (m), 2960 (s), 1445 (m), 1070 (m), 1040 (m), 930 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.07 (1 H, dd, J = 10.5, 17.1 Hz), 5.50 (1 H, dd, J = 17.1, 1.8 Hz), 5.11 (1 H, dd, J = 10.5, 1.8 Hz), 3.27 (3 H, s), 2.98 (1 H, d, J = 2.0 Hz), 1.44 (3 H, m), 1.29 (2 H, m), 1.17 (1 H, m), 1.11 (3 H, d, J = 6.6 Hz), 0.96 (1 H, m), 0.33 (1 H, t, J = 6.3 Hz).

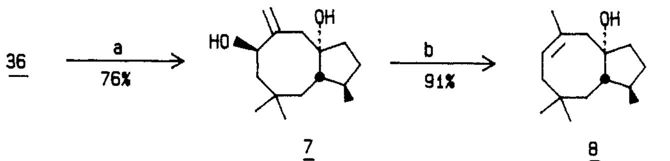
(1β,2β,5β)-(±)-5-Ethenyl-2-methylbicyclo[3.2.0]heptan-6-one (12). To a solution of the crude alcohol prepared as above (7.7 g, 0.042 mol) in 150 mL of dry Et_2O at 0 °C was added boron trifluoride etherate (5.23 mL, 6.04 g, 0.0425 mol) with good stirring under nitrogen. The reaction mixture was stirred for 10 min at 0 °C, and then 50 mL of saturated, aqueous Na_2CO_3 were added. The layers were shaken and separated, and the aqueous layer was extracted with Et_2O. The combined organic phases were washed with 50 mL of brine, dried, and concentrated. The residue could be purified by distillation (bp$_{0.75}$ 48 °C) but a cleaner product was obtained by flash chromatography by using 2.5% ethyl acetate in hexane to afford 3.465 g of **12** (54% yield overall from ketone **20**): IR (CCl_4) 3100 (w), 2950 (s), 1780 (s), 1635 (m), 1070 (m), 990 (m), 910 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.96 (1 H, dd, J = 17.3, 10.5 Hz), 5.16 (1 H, dd, J = 17.3, 1.0 Hz), 5.05 (1 H, dd, J = 10.5, 1.0 Hz), 3.21 (1 H, H_X of ABX, J_{AX} = 18.5 Hz, J_{BX} = −9.55 Hz), 2.51 (1 H, H_A of ABX, J_{AB} = 4.62 Hz, J_{AX} = 18.45 Hz), 2.47 (1 H, H_B of ABX, J_{AB} = 4.62 Hz, J_{BX} = −9.55 Hz), 2.19 (1 H, m), 2.06 (1 H, m), 1.93 (1 H, m), 1.77 (1 H, m), 1.61 (1 H, m), 0.98 (3 H, d, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 212.7 (s), 136.6 (d), 113.3 (t), 78.0 (s), 48.9 (t), 42.5 (d), 39.7 (d), 33.3 (t), 31.7 (t), 20.1 (q); MS (15 eV), m/e (rel intensity) 150 (M$^+$), 108 (base), 93. Anal. Calcd for $C_{10}H_{14}O$: C, 79.96; H, 9.39. Found: C, 79.41; H, 9.20.

***cis*-(±)-1,2,3,3a,4,8-Hexahydro-3-methyl-5*H*-cyclopentacycloocten-5-one (10).** A flame-dried, 250-mL, 3-necked flask was fitted with gas inlet and outlet tubes and a glass stopper. To this flask was added 100 mL of THF, and the flask was chilled to −78 °C under a nitrogen atmosphere. Acetylene which had been first passed through a dry ice/acetone trap and a $CaSO_4$ drying tube was bubbled into the THF with good stirring. The addition of C_2H_2 was continued at a flow rate of 360 mL/min for 20 min (total volume of C_2H_2 was approximately 7.2 L, 0.294 mol) at −78 °C. After addition of the acetylene was complete, *n*-BuLi (1.55 M in hexane, 29.8 mL, 0.0462 mol) was added via syringe pump over 35 min, while keeping the tip of the syringe needle under the surface of the THF solution. After addition of the *n*-BuLi was complete, the reaction flask was placed in a −30 °C cold bath and stirred for 5 min. A solution of ketone **12** in 10 mL of THF was chilled to −78 °C and then quickly added to the lithium acetylide via cannula. The resulting yellow solution was stirred at −30 °C for 7 min and then poured into 25 mL of saturated, aqueous NH_4Cl in a 500-mL Erlenmeyer flask. The resulting phases were allowed to warm to room temperature during which time the excess acetylene boiled off. The phases were separated, and the aqueous phase was extracted with Et_2O. The combined organic phases were washed with 25 mL of brine, dried, and concentrated to a volume of about 100 mL.

This solution of crude **22** was refluxed for 3 h (pot temperature was 50 °C during reflux) and then concentrated. The residue was purified by flash chromatography by using 5% ethyl acetate in hexane as eluent to afford 2.00 g (50% yield from **12**) of the product: bp$_{0.2}$ 60–61 °C; IR (CCl_4) 3030 (w), 2950 (m), 1665 (s), 1455 (m), 1385 (m), 850 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.63 (1 H, ddd, J = 11.6, 9.2, 6.6 Hz), 6.03 (1 H, br d, J = 11.6 Hz), 5.50 (1 H, m), 3.18 (1 H, m), 3.13 (1 H, dd, J = 13.5, 5.9 Hz), 2.88 (1 H, m), 2.70 (1 H, dd, J = 13.4, 4.1 Hz), 2.36 (1 H, d, J = 16.4, 9.0), 2.23 (2 H, m), 1.79 (2 H, m), 1.17 (1 H, m), 1.08 (3 H, d, J = 5.9 Hz); MS (70 eV), m/e (rel intensity) 176 (M$^+$), 91 (base), 79, 77, 53, 51.

(3β,3aβ)-(±)-1,2,3,3a,4,8-Hexahydro-3,5-dimethyl-5*H*-cyclopentacycloocten-5-ol. To a solution of enone **10** (1.908 g, 10.84 mmol) in 50 mL of dry Et_2O at −78 °C under nitrogen was added methyllithium (LiBr complex, 1.4 M in Et_2O, 11.62 mL, 16.26 mmol) via syringe over 2 min. After stirring for 30 min at −78 °C, the reaction was cautiously quenched with 15 mL of saturated, aqueous NH_4Cl and allowed to warm to room temperature. The phases were shaken and separated, and the aqueous phase was extracted with Et_2O. The combined organic phases were washed with brine, dried, and concentrated to give 1.956 g (94% yield) of the product alcohol as a 1:1 mixture of diastereomers. This material was generally of high purity (≥95% by ^{1}H NMR analysis) and

Scheme VII[a]



[a] (a) 0.1 M HCl/MeOH; (b) Na, EtOH, NH_3.

could be used directly in the next reaction: IR (CCl_4) 3600 (w), 3530 (w), 3020 (w), 2950 (s), 1465 (m), 1375 (m), 1105 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.62 (1.5 H, m), 5.40 (1.5 H, m), 3.13 (0.5 H, m), 2.90 (0.5 H, m), 2.72 (0.5 H, m), 2.50 (0.5 H, m), 2.30 (3 H, m), 1.99 (2 H, m), 1.75 (3 H, m), 1.36 (1.5 H, m), 1.35 (1.5 H, m), 1.13 (1 H, m), 1.06 (1.5 H, d, J = 6.3 Hz), 0.99 (1.5 H, d, J = 6.6 Hz).

***cis*-(±)-1,2,3,5,9,9a-Hexahydro-1,8-dimethyl-6*H*-cyclopentacycloocten-6-one.** A 250-mL, round-bottomed flask was charged with Celite (8 g), pyridinium chlorochromate (6.59 g, 30.56 mmol), and CH_2Cl_2 (75 mL). A solution of the above alcohol (1.96 g, 10.2 mmol) was added in 1 portion. The reaction mixture was stirred for 3 h at room temperature and then filtered through 35 g of Florisil with 300 mL of CH_2Cl_2. After concentration, the residue was diluted with 50 mL of Et_2O and then filtered through Celite with 200 mL of Et_2O. After concentration again, the crude product was dissolved in 25 mL of 10% ethyl acetate in hexane and filtered through 10 g of silica gel with 200 mL of 10% ethyl acetate in hexane. The filtrate was concentrated to afford 1.51 g (78% yield) of the ketone which was generally of sufficient purity (≥95% by ^1H NMR analysis) to be used directly in the next reaction: IR (CCl_4) 2950 (s), 1655 (s), 1455 (m), 1375 (m), 1265 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.93 (1 H, br s), 5.38 (1 H, tq, J = 8.4, 2.6 Hz), 3.65 (1 H, dd, J = 13.8, 8.9 Hz), 3.23 (1 H, dd, J = 14.2, 6.3 Hz), 2.90 (1 H, dd, J = 13.8, 7.9 Hz), 2.39 (2 H, m), 2.21 (2 H, m), 1.98 (3 H, d, J = 1.6 Hz), 1.82 (1 H, m), 1.59 (1 H, septet, J = 6.3 Hz), 1.18 (1 H, m), 1.11 (3 H, d, J = 6.3 Hz); MS (70 eV), m/e (rel intensity) 190 (M^+), 108, 93, 82 (base).

***cis*-(±)-1,2,3,5,7,8,9,9a-Octahydro-1,8,8-trimethyl-6*H*-cyclopentacycloocten-6-one (23).** A flame-dried, 100-mL, three-necked flask fitted with a thermometer and two septa was charged with 20 mL of Et_2O, 20 mL of Me_2S, and CuBr–Me_2S complex (3.27 g, 15.88 mmol).[43] The resulting pink solution was chilled under nitrogen to 10 °C in an ice bath, and methyllithium (1.4 M in Et_2O, LiBr complex, 22.7 mL. 31.77 mmol) was added via syringe while keeping the reaction temperature below 25 °C. To the resulting clear solution was added the above dienone (1.51 g, 7.94 mmol) in 10 mL of Et_2O via cannula, again keeping the reaction temperature below 25 °C. After stirring 20 min at room temperature, the resulting yellow suspension was poured into 30 mL of saturated, aqueous NH_4Cl in a 400-mL beaker. The layers were shaken and separated, and the aqueous layer was extracted with Et_2O. The combined organic phases were washed with 25 mL of brine, dried, and concentrated. The residue was diluted with 25 mL of 5% ethyl acetate in hexane, and the resulting suspension was filtered through 5 g of silica gel with 250 mL of 5% ethyl acetate in hexane. The combined eluents were concentrated and purified by Kugelrohr distillation (oven temperature = 70–72 °C at 0.2 torr) to afford 1.188 g (73% yield, 53% overall yield from dienone **10**) of **23**: IR (CCl_4) 2950 (s), 1700 (s), 1455 (m), 1370 (m), 1230 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.37 (1 H, tq, J = 6.0, 2.0 Hz), 3.03 (1 H, br d, J = 5.6 Hz), 2.73 (1 H, d, J = 11.9 Hz), 2.34 (2 H, m), 2.12 (1 H, dd, J = 11.9, 1.0 Hz), 1.87 (2 H, m), 1.70 (1 H, m), 1.55–1.15 (3 H, br m), 1.04 (3 H, s), 0.98 (3 H, s), 0.92 (3 H, d, J = 6.9 Hz); MS (70 eV), m/e (rel intensity) 206 (M^+), 93 (base), 91, 79, 77, 55. Anal. Calcd for $C_{14}H_{22}O$: C, 81.50; H, 10.74. Found: C, 81.15; H, 10.53.

(1α,9aα)-(±)-1,2,3,5,7,8,9,9a-Octahydro-1,8,8-trimethyl-6*H*-cyclopentacycloocten-6-ol (28). To a chilled (−78 °C) solution of lithium aluminum hydride (1.0 M in THF, 3.55 mL, 3.55 mmol) in 25 mL of dry Et_2O was added cyclooctenone **23** (0.732 g, 3.55 mmol) in 10 mL of Et_2O. After stirring for 15 min at −78 °C, the reaction was warmed to 0 °C and quenched with 0.150 mL of H_2O, followed by 8 mL of 2 M HCl. The layers were shaken and separated, and the aqueous layer was saturated with NaCl and extracted with Et_2O. The combined organic phases were washed with saturated, aqueous $NaHCO_3$ (10 mL) and brine (10 mL), dried, and concentrated. The residue was filtered through 3 g of silica gel with 10% ethyl acetate in hexane to afford 0.74 g (100% crude yield) of an inseparable mixture of alcohols **28** (3.7:1 by 400-MHz ^1H NMR analysis) which was used directly in the next reaction. Spectral data for the mixture (NMR data reported for the major diastereomer only) are as follows: IR (CCl_4) 3600 (m), 3400 (m), 2950 (s), 1470 (m), 1370 (m), 1020 (m) cm^{-1}; 400-MHz ^1H NMR ($CDCl_3$) δ 5.29 (1 H, tq, J = 7.6, 2.0 Hz), 3.96 (1 H, m), 2.71 (1 H, m), 2.5–2.1 (4 H, br m), 2.0–1.0 (8 H, br m), 0.98 (3 H, s), 0.97 (3 H, d, J = 6.6 Hz), 0.96 (3 H, s); MS (70 eV), m/e (rel intensity) 208 (M^+), 93 (base), 91, 79, 77.

(1β,9aβ)-(±)-1,2,3,5,7,8,9,9a-Octahydro-6-(phenylmethoxy)-1,8,8-trimethyl-6*H*-cyclopentacyclooctane. The above mixture of alcohols (0.74 g crude, ca. 3.55 mmol) in 5 mL of dry THF was added to potassium hydride (1.014 g of 35% oil suspension, 0.355 g of KH, 8.88 mmol) which had been washed twice with hexane, once with dry THF, and then covered with 10 mL of dry THF. This reaction was stirred for 15 min at room temperature, and then benzyl bromide (0.464 mL, 0.668 g, 3.91 mmol) was added along with a small crystal of tetrabutylammonium iodide. After stirring at room temperature for 4 h, the reaction was poured into 10 mL of saturated, aqueous NH_4Cl. The layers were shaken and separated, and the aqueous layer was extracted with Et_2O. The combined organic phases were washed with brine (10 mL), dried, and concentrated. The residue was filtered through 3 g of silica gel with hexane to afford 1.1 g of the crude benzyl ether. This material was usually contaminated with a small amount of excess benzyl bromide but was of sufficient purity (≥90% by ^1H NMR analysis) to be used directly in the next reaction: IR (CCl_4) 3080 (w), 3030 (m), 2960 (s), 1450 (s), 1090 (s), 1070 (s), 690 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.35 (5 H, m), 5.31 (1 H, m), 4.54 (1 H, H of AB, J = 12.0 Hz), 4.50 (1 H, H of AB, J = 12.0 Hz), 3.65 (1 H, m), 2.7–2.0 (4 H, br m), 1.0–2.0 (8 H, br m), 1.01 (3 H, s), 0.98 (3 H, d, J = 6.6 Hz), 0.95 (3 H, s).

(1α,6aβ,7aβ)-(±)-Decahydro-5,5,7-trimethyl-3-(phenylmethoxy)-cyclopenta[6,7]cyclooct[1,2-*b*]oxirene (30). The crude benzyl ether prepared above (1.06 g, ca. 3.54 mmol) was dissolved in 20 mL of CH_2Cl_2, and this solution was chilled to −30 °C. MCPBA (80% pure, 0.764 g, 3.54 mmol) was added in 15 mL of CH_2Cl_2, and the reaction was stirred for 1 h during which time it was allowed to warm to −10 °C. The reaction was then poured into 10 mL of saturated, aqueous $NaHCO_3$, and the layers were shaken and separated. The aqueous phase was extracted with CH_2Cl_2, and the combined organic phases were washed with brine, dried, and concentrated. The residue was passed through 3 g of silica gel with 5% ethyl acetate in hexane to afford 1.013 g (91% crude yield) of a mixture of diastereomers **30** and **31**. This mixture was inseparable but clearly contained predominantly one isomer. This mixture was used without further purification in the next reaction. Spectral data (NMR shifts reported for predominant α-epoxide diastereomer **30** only): IR (CCl_4) 3030 (w), 2950 (s), 1450 (m), 1370 (m), 1185 (m), 1165 (m), 690 (m) cm^{-1}; 400-MHz ^1H NMR δ 7.33 (5 H, m), 4.49 (1 H, H of AB, J = 11.8 Hz), 4.47 (1 H, H of AB, J = 11.8 Hz), 3.45 (1 H, m), 3.13 (1 H, dd, J = 4.8, 2.8 Hz), 2.40 (1 H, ddd, J = 15.2, 6.4, 2.4 Hz), 2.25 (1 H, ddd, J = 15.2, 8.8, 2.4 Hz), 2.20 (1 H, ddd, J = 13.6, 10.4, 4.0 Hz), 1.90 (2 H, m), 1.65 (2 H, m), 1.50 (5 H, m), 1.07 (3 H, d, J = 6.4 Hz), 0.90 (3 H, s), 0.85 (3 H, s): MS (CI, CH_4), m/e (rel intensities) 315 (M + 1), 207 (base), 189, 163, 91.

(1β,3aα,9aβ)-(±)-Decahydro-1,8,8-trimethyl-6-(phenylmethoxy)-3a*H*-cyclopentacyclooctan-3a-ol (32). The mixture of diastereomeric epoxides **30** and **31** prepared above (1.09 g crude, ca. 3.46 mmol) was dissolved in 10 mL of dry THF, and to this stirred solution was added lithium triethylborohydride (1.0 M in THF, 13.8 mL, 13.8 mmol) at room temperature. The reaction was stirred for 2 h at room temperature and then was heated to 50 °C for 30 min. The reaction was cooled, diluted with 20 mL of Et_2O, and poured into 10 mL of H_2O. The aqueous phase was saturated with NaCl, and the layers were shaken and separated. The aqueous phase was extracted with Et_2O, and the combined organic phases were washed with brine (10 mL), dried, and concentrated. This residue was purified by flash chromatography by using 15% ethyl acetate in hexane to afford 0.615 g of the desired α-alcohol **32** and 0.166 g of the β-alcohol (3.7:1 mixture of alcohols, 66% overall yield from enone **23**). Data for the α-alcohol **32** are as follows: IR (CCl_4) 3610 (w), 3460 (w), 3030 (m), 2950 (s), 1450 (m), 1370 (m), 1090 (m), 1060 (m), 690 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.30 (5 H, m), 4.51 (1 H, H_A of AB, J = 11.9 Hz), 4.45 (1 H, H_B of AB, J = 11.9 Hz), 3.64 (1 H, m), 2.2–1.0 (15 H, br m), 0.97 (3 H, d, J = 6.3 Hz), 0.94 (3 H, s), 0.89 (3 H, s); MS (CI, CH_4), m/e (rel intensity) 317 $(M + 1)^+$, 299, 209, 191 (base). Anal. Calcd for $C_{21}H_{32}O_2$: C, 79.70; H, 10.19. Found: C, 79.49; H, 10.17.

Data for the β-alcohol are as follows: IR and MS fundamentally similar to that of the α-alcohol; ^1H NMR ($CDCl_3$) δ 7.30 (5 H, m), 4.52 (1 H, H_A of AB, J = 12.0 Hz), 4.46 (1 H, H_B of AB, J = 12.0 Hz), 3.25 (1 H, m), 2.0–1.0 (15 H, m), 1.00 (3 H, d, J = 6.6 Hz), 0.93 (3 H, s), 0.89 (3 H, s).

(1β,3aα,9aβ)-(±)-Decahydro-1,8,8-trimethyl-3a-[[2-(trimethylsilyl)-ethoxy]methoxy]-6-(phenylmethoxy)-3a*H*-cyclopentacyclooctane. α-Alcohol **32** (0.615 g, 1.95 mmol) was dissolved in 7 mL of dry THF, and *N*,*N*-diisopropylethylamine (1.77 mL, 1.32 g, 10.2 mmol) and (2-(tri-

(43) House, H. O.; Chu, C. V.; Wilkins, J. M.; Umen, M. J. *J. Org. Chem.* **1975**, *40*, 1460.

methylsilyl)ethoxy)methyl chloride (SEMCl, 0.970 mL, 1.02 g, 6.12 mmol) were added. The reaction was stirred at 50 °C under nitrogen for 24 h, then cooled, and diluted with 35 mL of hexane and 15 mL of saturated, aqueous Na_2CO_3. The layers were shaken and separated, and the aqueous phase was extracted with hexane. The combined organic phases were dried and concentrated, and the residue was filtered through 3 g of silica gel with 2.5% ethyl acetate in hexane to afford 1.1 g of the crude SEM ether. Although this material was generally contaminated with a small amount of unreacted SEMCl, it was used directly in the next reaction. Spectral data for a small sample purified by HPLC (4% ethyl acetate in hexane): IR (CCl_4) 3030 (w), 2950 (s), 1470 (m), 1350 (m), 1130 (s), 860 (m), 840 (m), 695 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.30 (5 H, m), 4.69 (1 H, H of AB, J = 7.1), 4.66 (1 H, H of AB, J = 7.1), 4.48 (1 H, H of AB, J = 11.9), 4.42 (1 H, H of AB, J = 11.9), 3.60 (3 H, m), 2.1–1.0 (16 H, br m), 0.91 (3 H, d, J = 6.6 Hz), 0.89 (3 H, s), 0.84 (3 H, s), 0.00 (9 H, s); MS (CI, CH_4), m/e (rel intensity) 447 $(M + 1)^+$, 417, 299, 191 (base).

(1β,3aα,9aβ)-(±)-Decahydro-1,8,8-trimethyl-3a-[[2-(trimethylsilyl)-ethoxy]methoxy]-3a*H*-cyclopentacyclooctan-6-ol. A solution of the SEM ether prepared above (1.05 g crude, ca. 2.04 mmol) in 10 mL of dry Et_2O was added to 35 mL of liquid NH_3 at reflux (the starting material was only partially soluble). Sodium (0.141 g, 6.11 mmol) was added in small pieces over 5 min, the dark blue reaction was stirred at –33 °C until it decolorized (1 h), and then 0.5 g of solid NH_4Cl and 20 mL of Et_2O were cautiously added. The NH_3 was allowed to boil off, and then 10 mL of saturated, aqueous NH_4Cl and 2 mL of H_2O were added to the residue. The layers were shaken and separated, and the aqueous layer was extracted with Et_2O. The combined organic phases were dried and concentrated to afford 0.75 g of the crude alcohol which was used directly in the next reaction: IR (CCl_4) 3605 (w), 3450 (w), 2960 (s), 1365 (m), 1050 (m), 1025 (s), 860 (m), 835 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.69 (1 H, H_A of AB, J = 7.2 Hz), 4.67 (1 H, H_B of AB, J = 7.2 Hz), 4.00 (1 H, m), 3.62 (2 H, m), 2.2–1.7 (7 H, br m), 1.7–1.0 (10 H, br m), 0.94 (3 H, s), 0.92 (3 H, d, J = 6.6 Hz), 0.85 (3 H, s), 0.00 (9 H, s).

(1β,3aα,9aβ)-(±)-Decahydro-1,8,8-trimethyl-3a-[[2-(trimethylsilyl)-ethoxy]methoxy]-6*H*-cyclopentacyclooctan-6-one (33). Me_2SO (0.536 mL, 0.397 g, 5.10 mmol) was added dropwise to a stirred solution of oxalyl chloride (0.213 mL, 0.311 g, 2.45 mmol) in 20 mL of CH_2Cl_2 at –78 °C. This mixture was stirred for 15 min at –78 °C, and then a solution of the above alcohol (0.74 g crude, ca. 2.04 mmol) in 5 mL of CH_2Cl_2 was added dropwise via syringe. After the reaction had been stirred for an additional 15 min at –78 °C, *N*,*N*-diisopropylethylamine (2.83 mL, 2.10 g, 16.3 mmol) was added, and the reaction was allowed to warm to room temperature. After 1 h, the reaction was poured into 10 mL of saturated, aqueous $NaHCO_3$. The layers were shaken and separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine (10 mL), dried, and concentrated. The residue was diluted with 25 mL of hexane, washed with 5 mL of H_2O, dried, and concentrated. Purification by flash chromatography on 25 g silica gel with 10% ethyl acetate in hexane afforded 0.546 g of **33** (79% overall yield from **32**): IR (CCl_4) 2950 (s), 1700 (s), 1460 (s), 1250 (s), 1020 (s), 860 (s), 835 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.70 (2 H, s), 3.62 (2 H, m), 2.50 (1 H, m), 2.28 (2 H, s), 2.20 (2 H, m), 1.87 (5 H, m), 1.51 (1 H, m), 1.2–0.9 (5 H, br m), 0.99 (3 H, s), 0.93 (3 H, s), 0.92 (3 H, d, J = 6.3 Hz), 0.0 (9 H, s); MS (CI, CH_4), m/e (rel intensity) 355 $(M + 1)^+$, 279, 207, 189 (base). Anal. Calcd for $C_{20}H_{38}O_3Si$: C, 67.74; H, 10.80. Found: C, 67.46; H, 10.67.

(1β,3aα,9aβ)-(±)-Decahydro-1,8,8-trimethyl-5-methylene-3a-[[2-(trimethylsilyl)ethoxy]methoxy]-6*H*-cyclopentacyclooctan-6-one (34). To a solution of diisopropylamine (distilled from CaH, 0.094 mL, 0.067 g, 0.67 mmol) in 5 mL of dry THF was added *n*-BuLi (2.1 M in hexane, 0.283 mL, 0.594 mmol) at –78 °C with stirring. The resulting solution was stirred without an ice bath for 15 min, and then chilled to –78 °C again. Ketone **33** (0.163 g, 0.461 mmol) was added as a cold solution in 3 mL of dry THF, the reaction was stirred for 15 min at –78 °C, and then the dry ice bath was removed. Formaldehyde was added to the reaction by heating paraformaldehyde (0.14 g, 4.67 mmol) in a 25-mL 3-necked, round-bottomed flask and then passing the vapors through $CaSO_4$ and into the reaction with a stream of nitrogen. The reaction was warmed to room temperature and then stirred for 1 h. Saturated, aqueous NH_4Cl (2 mL) and Et_2O (5 mL) were added, and the layers were shaken and separated. The aqueous layer was saturated with NaCl and then extracted with 2 5-mL portions of Et_2O. The organic phases were washed with brine, dried, and concentrated to give a mixture of enone **34** and the intermediate α-hydroxymethyl ketone.

This mixture was dissolved in 5 mL of dry Et_2O and *N*,*N*-diisopropylethylamine (0.34 mL, 0.25 g, 1.94 mmol) was added. Methanesulfonyl chloride (0.030 mL, 0.044 g, 0.388 mmol) was added, and the reaction was stirred at room temperature for 5 h. The reaction was filtered and concentrated, and the residue was passed through 2 g of Al_2O_3 (70–230 mesh, activity I) with 10% ethyl acetate in hexane. After concentration, this process was repeated to afford 0.107 g of crude **34**. This material was purified by HPLC with 10% ethyl acetate in hexane to afford 0.078 g of **34** (46% yield from **33**): mp 67–69 °C; IR (CCl_4) 2950 (s), 1685 (s), 1605 (m), 1460 (m), 1245 (s), 1020 (s), 900 (s), 860 (s), 830 (s) cm^{-1}; 400-MHz ^1H NMR ($CDCl_3$) δ 6.04 (1 H, s), 5.14 (1 H, s), 4.81 (1 H, H_A of AB, J = 7.5 Hz), 4.73 (1 H, H_B of AB, J = 7.5 Hz), 3.61 (2 H, m), 2.90 (1 H, H_A of AB, J = 15.1 Hz), 2.66 (1 H, H_B of AB, J = 15.1 Hz), 2.52 (1 H, H_A of AB, J = 11.3 Hz), 2.31 (1 H, H_B of AB, J = 11.3 Hz), 1.90 (4 H, m), 1.55 (1 H, m), 1.10 (5 H, m), 1.03 (3 H, s), 0.95 (3 H, s), 0.92 (3 H, d, J = 7 Hz), 0.00 (9 H, s).

(1β,3aα,6β,9aβ)-(±)-Decahydro-1,8,8-trimethyl-5-methylene-3a-[[2-(trimethylsilyl)ethoxy]methoxy]-3a*H*-cyclopentacyclooctan-6-ol (36). To a solution of enone **34** in 6 mL of dry pentane at room temperature was added triisobutylaluminum (25% solution in hexane, 0.208 mL, 0.184 mmol) over 1.5 min. The resulting yellow solution was stirred for 1 h at room temperature and then quenched by addition of 1.5 mL of saturated, aqueous NH_4Cl and 2 mL of Et_2O. After extraction with Et_2O, the organic phases were dried and concentrated, and the residue was purified by HPLC by using 20% ethyl acetate in hexane to afford 19 mg of the α-alcohol **36** and 3 mg of the β-alcohol **35** (41% combined yield). Spectral data for **36** are as follows: IR (CCl_4) 3600 (m), 3460 (w), 2960 (s), 1640 (w), 1460 (m), 1250 (m), 1020 (s), 1000 (m), 855 (m), 830 (m) cm^{-1}; 400-MHz ^1H NMR ($CDCl_3$) δ 5.19 (1 H, br s), 4.97 (1 H, d, J = 7.5 Hz), 4.78 (1 H, br s), 4.69 (1 H, d, J = 7.5 Hz), 4.26 (1 H, dd, J = 11.5, 4.0 hZ), 3.82 (1 H, ddd, J = 11.7, 9.3, 4.7 Hz), 3.44 (1 H, ddd, J = 11.7, 9.2, 6.0 Hz), 2.56 (1 H, d, J = 14.1 Hz), 2.20 (1 H, m), 2.08 (1 H, d, J = 14.1 Hz), 1.89 (3 H, m), 1.69 (1 H, m), 1.44 (2 H, m), 1.21 (1 H, m), 0.98 (5 H, m), 0.96 (3 H, d, J = 6.8 Hz), 0.95 (3 H, s), 0.85 (3 H, s), 0.00 (9 H, s).

(1β,3aα,6β,9aβ)-(±)-Decahydro-1,8,8-trimethyl-5-methylene-3a*H*-cyclopentacyclooctane-3a,6-diol [(±)-Poitediol] (7). A 0.1 M solution of methanolic HCl was prepared by adding acetyl chloride (0.014 mL, 0.016 g, 0.20 mmol) to methanol (2 mL). This solution was added to **36** (0.033 g, 0.090 mmol), and the resulting solution was stirred for 30 min at room temperature and then quenched by the addition of 1 mL of saturated, aqueous Na_2CO_3. The methanol was removed on a rotary evaporator, and the aqueous residue was extracted with Et_2O. After drying and concentration, the crude poitediol was purified by HPLC by using 40% ethyl acetate in hexane to afford 16.2 mg (76% yield) of pure (±)-poitediol (**7**): mp 92–94 °C followed by solidification and remelting at 106–108 °C (lit. mp 40 °C for (–)-poitediol **7**); IR (CCl_4) 3610 (m), 3570 (w), 3470 (w), 3070 (w), 2960 (s), 1630 (w), 1470 (m), 1000 (s), 915 (m), 905 (m) cm^{-1}; 400-MHz ^1H NMR ($CDCl_3$) δ 5.20 (1 H, d, J = 2.0 Hz), 5.05 (1 H, d, J = 2.0 Hz), 4.24 (1 H, dd, J = 11.8, 3.7 Hz), 2.33 (2 H, s), 2.04 (2 H, br s), 1.95 (1 H, dtd, J = 13.5, 9.4, 7.4 Hz), 1.71 (4 H, m), 1.42 (1 H, ddd, J = 14.2, 4.2, 2.0 Hz), 1.26 (1 H, dd, J = 15.2, 6.9 Hz), 1.17 (1 H, m), 0.99 (1 H, dd, J = 11.2, 6.8 Hz), 0.94 (3 H, s), 0.92 (3 H, d, J = 6.1 Hz), 0.85 (1 H, d, J = 15.4 Hz), 0.84 (3 H, s). These data are identical with those of an authentic sample of (–)-poitediol.[37]

(1β,3aα,9aβ)-(±)-1,2,3,4,7,8,9,9a-Octahydro-1,5,8,8-tetramethyl-3a*H*-cyclopentacycloocten-3a-ol [(±)-Dactylol] (8). Sodium (5.0 mg, 0.24 mmol) was added to 5 mL of liquid NH_3 at reflux. Poitediol (5.6 mg, 0.024 mmol) and ethanol (0.014 mL, 11 mg, 0.24 mmol) were added as a solution in 1 mL of dry Et_2O. Because the reaction decolorized immediately after addition, 5 mg more of Na were added. The reaction was stirred at –33 °C for 15 min, and then the NH_3 was allowed to evaporate. The residue was dissolved in 1 mL of saturated, aqueous NH_4Cl and 5 mL of Et_2O. Extractive workup with Et_2O, followed by drying and solvent removal, afforded nearly pure dactylol (**8**) (4.8 mg, 91% yield) which crystallized. After filtration through 1 g of silica gel with 15% ethyl acetate in hexane, pure crystalline dactylol was isolated: mp 48–50 °C (lit. mp 50.3–51.5 °C for (+)-dactylol[8]); IR (CCl_4) 3600 (w), 3480 (w), 2950 (s), 1465 (m), 1360 (m), 1250 (m), 1040 (m), 1020 (m), 855 (m) cm^{-1}; 400-MHz ^1H NMR (C_6D_6) δ 5.49 (1 H, complex triplet, J = 8.2 Hz), 2.21 (1 H, H_A of AB, J = 13.3 Hz), 2.07 (1 H, H_B of AB, J = 13.3 Hz), 1.90 (3 H, m), 1.82 (3 H, s), 1.78 (1 H, m), 1.66 (1 H, ddd, J = 13.9, 9.3, 3.8 Hz), 1.53 (2 H, m), 1.45 (1 H, dd, J = 14.9, 8.0 Hz), 1.23 (1 H, m), 1.05 (1 H, m), 0.91 (3 H, d, J = 6.8 Hz), 0.90 (3 H, s), 0.85 (3 H, s), 0.72 (1 H, d, J = 15.0 Hz). These data are identical with those provided for authentic (+)-dactylol (^1H NMR of authentic dactylol recorded at 220 MHz in C_6D_6).[38]

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, to the National Science Foundation (CHE-8310105), and to the National Institutes of Health (GM-33259) for support of this work.