the authentic samples in every respect.

21-Hydroxypregn-4-ene-3,20-dione (2): mp 136–137.5 °C (lit.[13b] mp 135–137 °C); ^{1}H NMR (60 MHz, $CDCl_3$) δ 0.70 (3 H, s, 18-Me), 1.20 (3 H, s, 19-Me), 4.18 (2 H, s, 21-CH_2), 5.77 (1 H, s, 4-H).

Pregn-4-ene-3,20-dione (3): mp 116–119 °C (lit.[13b] mp 117–118 °C); ^{1}H NMR (60 MHz, $CDCl_3$) δ 0.70 (3 H, s, 18-Me), 1.20 (3 H, s, 19-Me), 2.12 (3 H, s, 21-Me), 5.77 (1 H, s, 4-H).

21-Hydroxypregn-4-ene-3,11,20-trione (10): mp 153–157 °C (lit.[13b] mp 153–157 °C); ^{1}H NMR (60 MHz, $CDCl_3$) δ 0.67 (3 H, s, 18-Me), 1.40 (3 H, s, 19-Me), 4.18 (2 H, s, 21-CH_2), 5.73 (1 H, s, 4-H).

Pregn-4-ene-3,11,20-trione (11): mp 167–169 °C (lit.[13b] mp 172–173 °C); ^{1}H NMR (60 MHz, $CDCl_3$) δ 0.65 (3 H, s, 18-Me), 1.42 (3 H, s, 19-Me), 2.12 (3 H, S, 21-Me), 5.73 (1 H, s, 4-H).

Pregna-1,4-diene-3,11,20-trione (14): mp 163–165 °C (lit.[20] mp 167–169 °C); ^{1}H NMR (60 MHz, $CDCl_3$) δ 0.70 (3 H, s, 18-Me), 1.47 (3 H, s, 19-Me), 2.13 (3 H, s, 21-Me), 6.18 (1 H, d, J = 2 Hz, 4-H), 6.20 (1 H, dd, J = 10 and 2 Hz, 2-H), 7.70 (1 H, d, J = 10 Hz, 1-H).

17aβ-Methyl-D-homoandrost-4-ene-3,17-dione (15). To a solution of 17α-hydroxypregn-4-ene-3,20-dione (97 mg, 0.29 mmol) in $CHCl_3$ were added TMSI (118 mg, 5.87 mmol) and MeOH (14 mg, 0.45 mmol), and the mixture was stirred at room temperature for 9 h. The same workup of the mixture as above gave an oily product, which was purified by silica gel column chromatography (hexane/AcOEt) and then recrystallized from AcOEt to give **15** (37 mg, 40%) as colorless prisms: mp 208–209 °C (lit.[14] mp 210–212 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.70 (3 H, s, 18-Me), 0.94 (3 H, d, J = 6.6 Hz, 17aβ-Me), 1.18 (3 H, s, 19-Me), 5.75 (1 H, d, J = 0.7 Hz, 4-H).

Compound **15** was identical with the authentic sample obtained according to the method previously reported by Rakhit et al.[14] in every respect.

Deuterium-Labeling Reaction. (1) TMSI (290 mg, 1.45 mmol) and MeOD (99 atom %, 3.6 mg, 0.109 mmol) were added to a solution of **1** (25 mg, 0.073 mmol) in 1 mL of $CHCl_3$. The mixture was stirred at room temperature for 9 h under N_2 and the crude product obtained as above was purified by silica gel thin-layer chromatography (hexane/AcOEt) and recrystallization from acetone–hexane to give deuterium-labeled **3** (15 mg, 66%): mp 113–116 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.67 (3 H, s, 18-Me), 1.18 (3 H, s, 19-Me), 2.13 (1.85 H, s, 21-Me), 2.30–2.47 (3.28 H, m, 2α, 2β, 6α, and 6β protons), 2.54 (0.29 H, m, 17α-H), 5.74 (0.86 H, s, 4-H); EI-MS m/z 314 (M^+) d_0 20%, d_1 34%, d_2 27%, d_3 15%, and d_4 4%, m/z 43 (CH_3CO^+) d_0 62%, d_1 30%, and d_2 8%. The spectral data show that deuterium was incorporated into the C-2, C-4, C-6, C-17α, and C-21 positions.

(2) A solution of **1** (55 mg, 0.16 mmol) in 2 mL of $CHCl_3$ containing TMSI (48 mg, 0.24 mmol) and MeOD (99 atom %, 11 mg, 0.32 mmol) was stirred at room temperature for 5 h under N_2. The same workup as described above yielded **1** (51 mg, 93%): mp 157–159 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.70 (3 H, s, 18-Me), 1.18 (3 H, s, 19-Me), 2.29–2.46 (4 H, m, 2α, 2β, 6α, and 6β protons), 2.59 (0.8 H, t, J = 9.1 Hz, 17α-H), 3.41 (3 H, s, 21-OMe), 3.96 (1 H, d, J = 17.2 Hz, 21-Ha), 4.03 (1 H, d, J = 17.2 Hz, 21-Hb), 5.73 (0.8 H, s, 4-H).

^{1}H NMR and IR Spectrometric Studies of the Deoxygenation Reaction of the Ether 1. (1) IR Analysis. TMSI (83 μL, 0.581 mmol) was added to a solution of **1** (10 mg, 0.029 mmol) and MeOH (2 μL, 0.048 mmol) in 0.17 mL of $CHCl_3$, the mixture was immediately transferred to an IR cell (NaCl, 0.1 mm), and the spectrum between 5000 and 330 cm^{-1} was first obtained at 1-min reaction time (scan time: 4 min). The spectra were then measured repeatedly at 10-min intervals up to 1-h reaction time.

(2) ^{1}H NMR Analysis. TMSI (206 μL, 1.82 mmol) was added to a solution of **1** (25 mg, 0.072 mmol) and MeOH (4.5 μL, 0.111 mmol) in $CDCl_3$ in an NMR tube, and the spectra (60 MHz) between 0 and 10 ppm were obtained repeatedly at 10-min intervals for the first 1-h reaction time (scan time: 250 s).

Acknowledgment. We thank Prof. T. Nambara of Tohoku University for providing elemental analysis data and Drs. K. Hisamichi and S. Suzuki for 400-MHz ^{1}H NMR and MS analysis.

Registry No. 1, 20380-14-7; 2, 64-85-7; 3, 57-83-0; 4, 19953-77-6; 5, 129786-18-1; 6, 26623-68-7; 7, 68-96-2; 8, 129786-19-2; 9, 129786-20-5; 10, 72-23-1; 11, 516-15-4; 12, 129786-21-6; 13, 67067-81-6; 14, 4368-11-0; 15, 15296-76-1; TMSI, 16029-98-4; MeOH, 67-56-1.

(20) British Drug Houses Ltd., Brit. Patent 854343, 1960; *Chem. Abstr.* **1960**, *55*, 18813i.

Stereocontrolled Synthesis of Functionalized Diquinanes from Pauson–Khand-Derived *exo*-Tricyclo[5.2.1.0^{2,6}]decenones

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A 10-step sequence is described for the conversion of 4-methyl-*exo*-tricyclo[5.2.1.0^{2,6}]deca-4,8-dien-3-one (the Pauson–Khand cycloaddition product of norbornadiene with propyne) into 3,3-dimethyl-2-[(2-methoxyethoxy)methoxy]-8-(1-methyl-2-oxopropyl)bicyclo[3.3.0]octan-6-ol. The latter diquinane, formed with complete stereocontrol and well-differentiated functionality, is appropriately substituted to serve as an entry to highly functionalized linearly fused triquinanes, although attempts to close a third five-membered ring via an enolate–epoxide ring-opening process were unsuccessful.

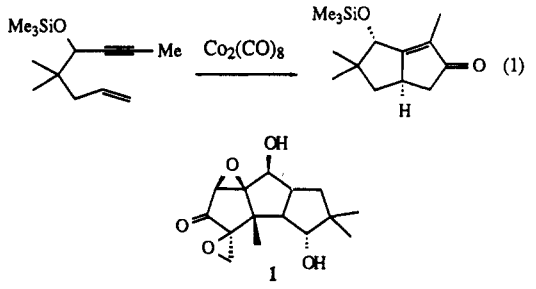
The intramolecular Pauson–Khand cycloaddition reaction has seen considerable recent development in the synthesis of natural products containing the bicyclo[3.3.0]octenone ("diquinane") structural unit.[1-3] In a typical example, Magnus utilized this methodology to convert an appropriately functionalized enyne into a bicyclo[3.3.0]octenone (eq 1) which, in turn became the precursor to the linearly fused triquinane natural product coriolin (1).[4,5]

(1) Schore, N. E.; Croudace, M. C. *J. Org. Chem.* **1981**, *46*, 5436.

(2) General reviews: (a) Pauson, P. L.; Khand, I. U. *Ann. N.Y. Acad. Sci.* **1977**, *295*, 2. (b) Pauson, P. L. *Tetrahedron* **1985**, *41*, 5855. (c) Pauson, P. L. In *Organometallics in Organic Synthesis. Aspects of a Modern Interdisciplinary Field*; de Meijere, A., Dieck, H. T., Eds.; Springer: Berlin, 1988; p 233. See also: (d) Schore, N. E. *Chem. Rev.* **1988**, *88*, 1081.

(3) E.g., (a) hirsutic acid: Magnus, P.; Exon, C.; Albaugh-Robertson, P. *Tetrahedron* **1985**, *41*, 5861. (b) Pentalenene: Hua, D. H. *J. Am. Chem. Soc.* **1986**, *108*, 3835. Also (c) Schore, N. E.; Rowley, E. G. *J. Am. Chem. Soc.* **1988**, *110*, 5224. (d) Quadrone: Magnus, P.; Principe, L. M.; Slater, M. J. *J. Org. Chem.* **1987**, *52*, 1483. (e) Pentalenolactone: Hua, D. H.; Coulter, M. J.; Badejo, I. *Tetrahedron Lett.* **1987**, *28*, 5465.

0022-3263/91/1956-0338$02.50/0



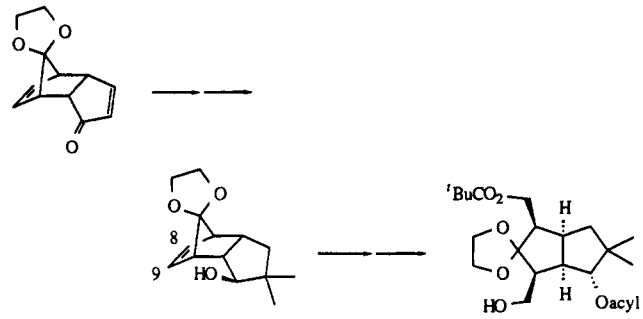
1

A number of elegant procedures for approaching triquinanes such as coriolin have been published.[6] Of the syntheses in this area[7] one that caught our attention was that of Schuda, in which a diquinane that is ultimately incorporated as rings B and C in the final product is derived from the Diels–Alder dimer of cyclopentadienone ketal (Scheme I).[8] The inherent rigidity of this system permitted a number of highly stereoselective reactions, including a highly controlled Li/NH_3 reduction of the C-ring ketone. In cleaving the C(8)–C(9) double bond no differentiation between the resulting carbinol carbons was initially possible, although both Schuda and, later, Matsumoto developed methods to overcome this problem.[9]

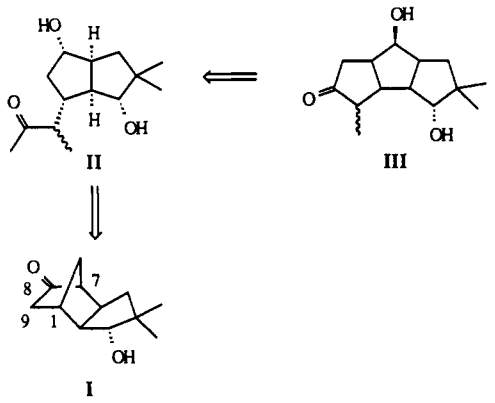
In these approaches the endo ring fusion associated with the Diels–Alder origin of the starting compounds and the symmetrical cleavage of the double bond reduce the utility of the resulting carbons in further construction of the triquinane skeleton with the proper cis-anti-cis stereochemistry. Thus in both cases it was necessary to cleave off a superfluous carbon, and then to build up again with a new carbon fragment.

As an approach to these problems, we devised a plan to incorporate the entire triquinane framework at an early stage, through the use of an *inter*molecular Pauson–Khand cycloaddition, using compound I as a key intermediate.[10] The basic framework of I should be available from Pauson–Khand reaction of an appropriate norbornene derivative and should possess an exo rather than and endo ring fusion. This gives rise to the correct stereochemistry at

Scheme I



C(1) for direct use of carbons 8 and 9 in construction of ring A of the triquinane system, after Baeyer–Villiger cleavage of the C(7)–C(8) bond. Indeed, using coriolin as a target for illustrative purposes, 12 of its 15 carbons are present in I, ring C is complete, and the stereochemistry of all four ultimate ring-fusion sites and five of the eight stereocenters is set. Within this framework an approach to coriolin from I might take the shape shown below.



Syntheses of compounds I and II, and studies aimed toward a novel approach to III, are described in the sections that follow.

Results and Discussion

Ketone I. At first one might reasonably ask whether 4-methyl-5-norbornen-2-one (2) would be a useful starting point. Indeed, were its Pauson–Khand cycloaddition to proceed with the desired regiochemistry, the product (3) would also contain the needed methyl group at C-1. Unfortunately, early in this study it became clear that both steric and electronic considerations would favor the opposite regiochemistry in such a cycloaddition;[11] this alkene is also relatively inaccessible.[12] Our attention turned therefore to norbornadiene as a more practical initial substrate.[13]

Pauson originally reported the cobalt-mediated cycloaddition of norbornadiene with alkynes in 1973.[14] We, like Pauson, found that double cycloaddition could be minimized by carrying out the reaction at 75 °C for 3 h in the presence of a catalytic amount of dicobalt octacarbonyl. One typically obtains ≥40% yields of enone 4,

(4) (a) Magnus, P.; Principe, L. M. *Tetrahedron Lett.* **1985**, *26*, 4851. (b) Exon, C.; Magnus, P. *J. Am. Chem. Soc.* **1983**, *105*, 2477.

(5) Isolation: Takeuchi, T.; Iinuma, H.; Iwanaga, J.; Takahashi, S.; Takita, T.; Umezawa, H. *J. Antibiot.* **1969**, *22*, 215. Structure: (a) Takahashi, S.; Naganawa, H.; Iinuma, H.; Takita, T.; Maeda, K.; Umezawa, H. *Tetrahedron Lett.* **1971**, 1955. (b) Nakamura, H.; Takita, T.; Umezawa, H.; Kunishima, M.; Nakayama, Y.; Iitaka, Y. *J. Antibiot.* **1974**, *27*, 301.

(6) General reviews: Paquette, L. A. *Top. Curr. Chem.* **1979**, *79*, 41; **1984**, *119*, 1.

(7) Selected syntheses of coriolin: (a) Tatsuta, K.; Akimoto, K.; Kinoshita, M. *J. Antibiot.* **1980**, *33*, 100. (b) Danishefsky, S.; Zamboni, R.; Kahn, M.; Etheredge, S. J. *J. Am. Chem. Soc.* **1980**, *102*, 2097; **1981**, *103*, 3460. (c) Trost, B. M.; Curran, D. P. *J. Am. Chem. Soc.* **1980**, *102*, 5699; **1981**, *103*, 7380. (d) Koreeda, M.; Mislankar, S. G. *J. Am. Chem. Soc.* **1983**, *105*, 7203. (e) Wender, P. A.; Howbert, J. J. *Tetrahedron Lett.* **1983**, *24*, 5325. (f) Demuth, M.; Ritterskamp, P.; Schaffner, K. *Helv. Chim. Acta* **1984**, *67*, 2023. (g) Hijfte, L. V.; Little, R. D. *J. Org. Chem.* **1985**, *50*, 3940. (h) Curran, D. P.; Rakiewicz, D. M. *J. Am. Chem. Soc.* **1985**, *107*, 1448. (i) Funk, R. L.; Bolton, G. L.; Daggett, J. U.; Hansen, M. M.; Horcher, L. H. M. *Tetrahedron* **1985**, *41*, 3479.

(8) (a) Schuda, P. F.; Ammon, H. L.; Heimann, M. R.; Bhattacharjee, S. *J. Org. Chem.* **1982**, *47*, 3434. (b) Schuda, P. F.; Heimann, M. R. *Tet. Lett.* **1983**, 4267; (c) Schuda, P. F.; Heimann, M. R. *Tetrahedron* **1984**, *40*, 2365.

(9) (a) Ito, T.; Tomiyoshi, N.; Nakamura, K.; Azuma, S.; Izawa, M.; Maruyama, F.; Yanagiya, M.; Shirahama, H.; Matsumoto, T. *Tetrahedron Lett.* **1982**, 1721. (b) Ito, T.; Tomiyoshi, N.; Nakamura, K.; Azuma, S.; Izawa, M.; Maruyama, F.; Yanagiya, M.; Shirahama, H.; Matsumoto, T. *Tetrahedron* **1984**, *40*, 241.

(10) The intermolecular Pauson–Khand has also been employed in a rather different way to approach related structures: (a) Keyaniyan, S.; Apel, M.; Richmond, J. P.; de Meijere, A. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 770. (b) Liese, T.; de Meijere, A. *Chem. Ber.* **1986**, *119*, 2995. (c) De Meijere, A. *Chem. Br.* **1987**, 865.

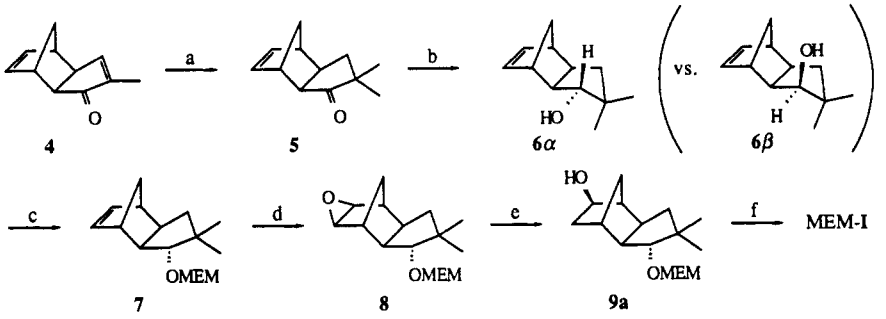
(11) MacWhorter, S. E.; Sampath, V.; Olmstead, M. M.; Schore, N. E. *J. Org. Chem.* **1988**, *53*, 203.

(12) Masar, S. E.; Krieger, H. *Suom. Kemistil.* **1968**, *41B*, 217.

(13) Exploration of 5-norbornen-2-one and 1-methyl-5-norbornen-2-one as initial substrates revealed no advantages over norbornadiene and, in fact, gave rise to several problems due to inseparability of regioisomers: MacWhorter, S. E., unpublished results.

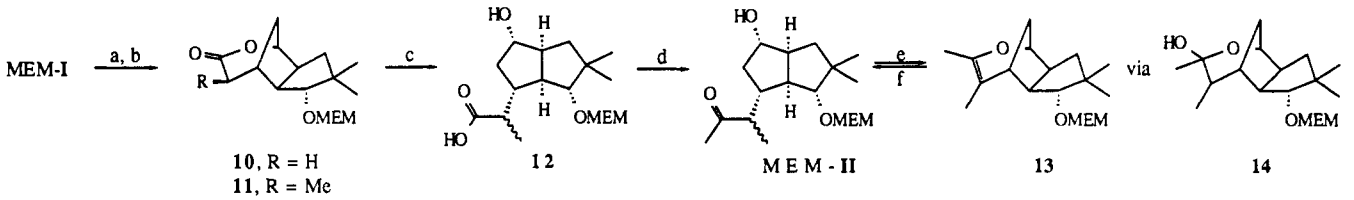
(14) Khand, I. U.; Knox, G. R.; Pauson, P. L.; Watts, W. E.; Foreman, M. I. *J. Chem. Soc. Perkin Trans. 1* **1973**, 997.

Scheme II[a]



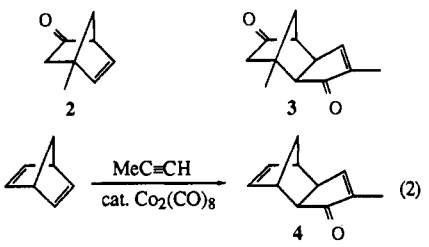
[a] (a) Li, NH_3, MeOH, −33 °C, 5 h, then MeI, Et_2O, 25 °C, 12 h (90%); (b) Li, NH_3, MeOH, −33 °C, 5 h (94%); (c) MEMCl, iPr_2NEt, CH_2Cl_2, 25 °C, 4 h (87%); (d) MCPBA, CH_2Cl_2, 25 °C, 4 h (79%); (e) $LiBHEt_3$, THF, 65 °C, 48 h (53%); (f) PCC, NaOAc, CH_2Cl_2, 25 °C, 7 h (100%).

Scheme III[a]



[a] (a) MCPBA, $NaHCO_3$, $CHCl_3$, 100 °C, 42 h (84%); (b) LDA, THF, −78 °C, 2.5 h, then MeI, HMPA, −78 → 25 °C, 1 h (94%); (c) NaOH, MeOH, 25 °C, 12 h (88%); (d) MeLi, THF, 0 → 25 °C, 6 h, then Me_3SiCl, 0 → 25 °C, then HCl to pH = 4 (86%); (e) HCl to pH = 1; (f) Dilute HCl (pH = 4).

formed with totally regioselective incorporation of the alkyne and virtually totally stereoselective formation of an exo ring fusion (eq 2).



Reductive alkylation of **4** introduced the *gem*-dimethyl moiety to give **5**; very little monomethyl ketone remained (Scheme II). Reduction of **5** with Li/NH_3 gave exclusively the thermodynamically more stable alcohol **6α**. Proton NMR exhibited a broad doublet at δ 3.25 with a coupling constant J = 7.3 Hz for the carbinol proton. Reduction of **5** with $LiAlH_4$ yielded both stereoisomers, with the second displaying the carbinol doublet at δ 3.59. These data were consistent with the Li/NH_3 product possessing the alcohol on the less hindered, α face of the molecule. We have found in these and related bridged/fused tricyclic compounds that protons adjacent to the ring fusion are shielded when they are cis to the fused ring, relative to protons trans to the fused ring.[15] An NOE study supported these isomer assignments. In the expected conformation, the pseudoaxial β carbinol proton in **6α** is much closer to one methyl group than the other, while the pseudoequatorial α carbinol proton in **6β** is nearly equidistant between the two methyl groups. Indeed, an NOE difference experiment on the Li/NH_3 reduction product revealed a very strong interaction between the protons of one of the *gem*-dimethyl groups and the carbinol proton. The other methyl group exhibited only very week NOE enhancement. In the second isomer from the $LiAlH_4$ reduction, the NOE enhancements of the two methyl groups were weak, and of approximately the same intensity.

Introduction of carbonyl functionality at C(8) of the norbornene ring was initially carried out without alcohol protection. In the absence of any obvious way to regiochemically distinguish between C(8) and C(9), we epoxidized the double bond of **6α** with *m*-chloroperoxybenzoic acid (MCPBA), obtaining a single (presumably the exo) stereoisomer in 76% yield.[16] As expected, this epoxide was extremely resistant to hydride reagents giving at best only partial reduction.[17] These reactions unfortunately also gave 2–3:1 regioselectivity in the *wrong* direction. Lithium in ethylenediamine at 50 °C for 1 h yielded a 1:1 mixture of the two diols and no recovered starting material, but only 56% total yield. The structures of the diols were determined by spectroscopic comparison[18] and chemical correlation with the regioisomeric products of Pauson–Khand cycloadditions of norbornenone (see Scheme V).[11] These unsatisfactory results and our lack of success in subsequent experiments aimed at differentiation of the hydroxy groups forced us to consider hydroxyl protection in **6α**.

Use of silyl protecting groups proved troublesome, so we treated **6α** with MEM chloride in the presence of diethylisopropylamine to yield the MEM ether **7**. Epoxidation with MCPBA produced **8** in 79% yield. Reduction of the epoxide using lithium/ethylenediamine produced the alcohols **9a** and its C(9) regioisomer **9s** in a 51:49 ratio, but the yield was only modest (ca. 60%), and the reaction was accompanied by partial loss of the MEM group. Treatment of epoxide **8** with 8 equiv of lithium triethylborohydride in a minimal amount of THF at reflux temperatures gave the best result, a 99% overall yield of

(15) Price, M. E.; Schore, N. E. *J. Org. Chem.* **1989**, *54*, 5662. The same correlation holds for derivatives with the endo ring fusion.[8c]

(16) Brown, H. C.; Ikegami, S.; Kawakami, J. H. *J. Am. Chem. Soc.* **1970**, *92*, 6914.

(17) Brown, H. C.; Ikegami, S.; Kawakami, J. H. *J. Org. Chem.* **1970**, *35*, 3243.

(18) Spectroscopic data are presented in the supplementary materials.

the two alcohols **9a** and **9s** in a ratio of 53:47, which were readily separated by MPLC. The regioisomers were characterized by spectral comparison with, and in the case of **9s**, conversion into ($ZnBr_2/CH_2Cl_2$) the corresponding diols (vide supra).[18] Oxidation of **9a** with pyridinium chlorochromate yielded a protected version of ketone I (MEM-I) in quantitative yield. The synthesis of MEM-I was therefore completed in six fairly straightforward steps, and in 28% overall yield from the cycloaddition product **4**.

Diquinane II. Our plan for synthesizing the BC diquinane II from the bridged tricyclic I involved opening the tricyclo[5.2.1.0]decane to form the required bicyclic system and introducing two methyl groups. Baeyer–Villiger reaction of MEM-I gave exclusively the (desired) product **10** resulting from bridgehead migration.[19] However, the rate of the reaction was extremely slow. Even at reflux and with addition of excess MCPBA at 3-day intervals, lactone formation took 12 days to reach completion, in 77% isolated yield. However, conducting the reaction in a sealed tube with excess MCPBA at 100 °C yielded 84% of lactone **10** as the sole product after only 42 h; IR ν_{CO} = 1741 cm^{-1} (Scheme III). That no unwanted methylene migration occurred during the Baeyer–Villiger reaction was confirmed by high-field proton NMR of the crude product mixture, which showed the broad singlet corresponding to the proton on C(7) shifted downfield to δ 4.42, but no downfield-shifted doublet of doublets that would correspond to protons on C(9) of the product of methylene migration. For comparison, 15% methylene migration occurred in Baeyer–Villiger reaction of an analogue of I containing a ketone instead of a protected alcohol at C(3).

Monomethylation of **10** proceeded in excellent yield. NMR indicated that only one isomer had formed, presumably **11**, from approach of the methyl group from the less hindered exo face of the molecule. The stereochemistry of this center, however, was of no consequence, since at a later stage in the synthesis of any hirsutane natural product this center would become sp^2 hybridized.

Opening the lactone directly to a bicyclo[3.3.0]octane ring system containing the required side-chain ketone proved to be troublesome. Initial attempts involving reaction with MeLi at low temperature failed to yield any ketone. Even with excess MeLi at higher temperatures, no evidence of methyl ketone was obtained. When **11** was warmed in the presence of the $CH_3SOCH_2^-$ anion for 24 h, the NMR data indicated complete consumption of the starting material. A new singlet in the proton NMR spectrum at δ 2.92 suggested that the expected keto sulfoxide had indeed formed.[20] The high polarity of this compound and its consequential solubility in water made isolation difficult. Subsequently aluminum amalgam reduction did provide the desired methyl ketone, but in very poor (≤20%) yield.

Alternatively, hydrolysis of **11** with methanolic NaOH produced carboxylic acid **12** in 88% yield; IR ν_{CO} = 1706 cm^{-1} and ^1H NMR (H-7) δ 3.96. These conditions caused the isomerization of the side chain methyl group to an approximate 50:50 mixture of isomers.

To avoid tertiary alcohol formation in the subsequent addition of MeLi to hydroxy acid[21] **12**, the reaction mixture was quenched with a large excess of chlorotrimethylsilane, thereby destroying excess MeLi prior to workup.[22] Excellent results were obtained by reacting **12** with a 20-fold excess of MeLi, allowing the reaction to stir at room temperature for several hours, and then quenching with a corresponding excess of chlorotrimethylsilane. An aqueous workup of this crude product mixture resulted in loss of the MEM group, due to the HCl liberated by the hydrolysis of the silane. Therefore, prior to workup the excess chlorotrimethylsilane was removed in vacuo. Aqueous workup then yielded the methyl ketone with a silylated alcohol, which could be easily hydrolyzed to MEM-II (IR ν_{CO} = 1715 cm^{-1} and ^1H NMR δ 2.15 for CH_3CO) in 86% yield from **12**.

In carrying out the above reaction sequence, the product MEM-II was invariably contaminated with a side product. Isolation of this material, formed in 11% yield, and spectral studies eventually lead to its identification as the vinyl ether **13**. The IR indicated that no alcohol or carbonyl functionality was present, while the proton NMR proved to be very similar to that of lactone **11**. For example, **11** exhibited two broad singlets at δ 4.37 and 2.29 corresponding to the bridgehead protons on C(7) and C(1), respectively. The side product possessed broad singlets at δ 4.03 and 2.08, slightly upfield from the lactone peaks, consistent with what would be expected for structure **13**. Two sharp methyl singlets appeared at δ 1.58 and 1.60. Finally ^{13}C NMR showed vinyl signals at δ 109.2 and 140.1 ppm. The chemical shift difference between these two peaks was also consistent with a vinyl ether structure.

Interestingly, we found that a diastereomeric mixture of MEM-II was converted to **13** in the presence of strong aqueous acid (pH = 1). Conversely, treatment with weak acid (pH = 3–4) converted **13** back into only one of the diastereomers of MEM-II. In acidic media MEM-II would be expected to be in equilibrium with the hemiacetal **14**. Treatment with strong acid apparently results in elimination of alcohol from the hemiacetal, resulting in the formation of the remarkably stable **13**. In the presence of dilute aqueous acid, water adds across the double bond, reversing the process. Thus, via reconversion of **13** back into MEM-II, the total yield of the latter from carboxylic acid **12** becomes nearly quantitative.

Use of the tricyclo[5.2.1.0]decane as a precursor permits efficient entry to the BC bicyclo[3.3.0]octane ring system of the hirsutanes. This preparation of MEM-II yields a completely functionalized diquinane in an overall yield of 19% after 10 steps from the Pauson–Khand cycloaddition. All necessary stereochemical elements are completely controlled, and the three carbon fragment necessary for construction of the third ring is in place. The following section describes our efforts in this direction.

Approach to Ring A. We chose to focus on a novel approach to closure of ring A which, if successful, would maximize utilization of the existing functionality in II. The hope was to generate from the B-ring alcohol an epoxide that would serve as a site for ring closure via nucleophilic attack by an enolate of the methyl ketone. If the epoxide could be formed on the *more* hindered side of the molecule, attack by the enolate would provide the tricyclic with the desired cis, anti, cis stereochemistry, and in addition, *the alcohol at C(8) would be positioned with the correct stereochemistry* (eq 3). Simultaneous introduction of this alcohol with the closure of ring A would represent a saving of some six steps compared to approaches in which ring-B functionalization is effected on the intact tricyclic.[7b] Continuation in the direction of coriolin would then involve

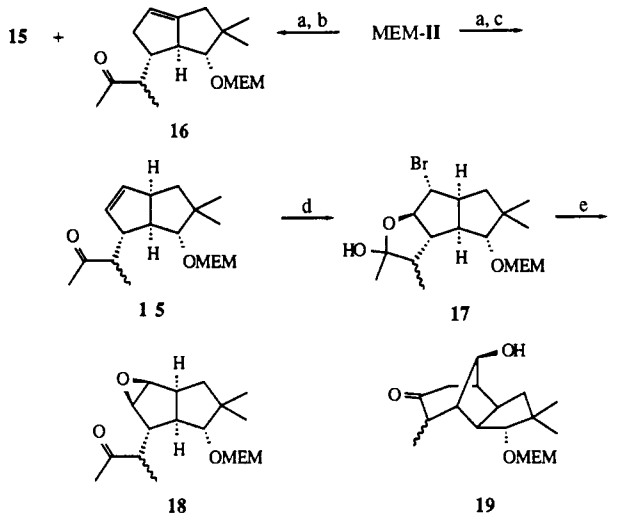
(19) Sauers, R. R.; Ahearn, G. P. *J. Am. Chem. Soc.* **1961**, *83*, 2759. For a review on the Baeyer–Villiger reaction applied to bridged bicyclic ketones see: Krow, G. R. *Tetrahedron* **1981**, *37*, 2697.

(20) Corey, E. J.; Chaykovsky, M. *J. Am. Chem. Soc.* **1964**, *86*, 1639.

(21) Cf. Trost, B. M.; Shuey, C. D.; DiNinno, F., Jr.; McElvain, S. S. *J. Am. Chem. Soc.* **1979**, *101*, 1284.

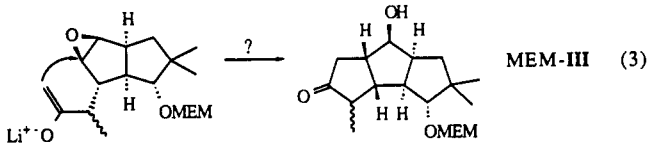
(22) Rubottom, G. M.; Kim, C. *J. Org. Chem.* **1983**, *48*, 1550.

Scheme IV[a]



[a] *p*-TsCl, py, 25 °C, 4 days (83%); (b) NaI, DMF, 45 °C, 4 h, then DBU, DMF, 85 °C, 7 h; (c) DBU, DMF, 85 °C, 7 h (91%); (d) NBA, acetone, 0 °C, 15 min (100%); (e) DBU, C_6H_6, 25 °C, 18 h (84%).

oxidation of the thermodynamic enolate of III to the enone followed by conjugate addition to install the required ring-fusion methyl group.



(3)

Regioselective elimination to form **15** was best achieved by forming the tosylate of MEM-II and then treating with DBU. This result was expected, since work on similar bicyclo[3.3.0]octene systems has demonstrated that the disubstituted alkene is thermodynamically more stable than its more strained regioisomer, **16**.[23] In addition, the stereochemistry of the alcohol in MEM-II was such that anti elimination could give rise only to **15**. As confirmation of these assumptions, when the tosylate of MEM-II was first treated with NaI prior to elimination, a mixture of **15** and **16** was obtained, with **16** the major component and evidently the kinetically favored product of the two anti elimination modes available to the endo iodide.

Preparation of the epoxide from **15** on the more hindered endo face of the bicyclic was achieved via the bromonium ion, following literature precedents (including one involving the parent bicyclo[3.3.0]oct-2-ene system) using *N*-bromoamides as sources of electrophilic bromine.[24] Initial NMR experiments indicated that the reaction of *N*-bromoacetamide with alkene **15** in acetone-d_6–D_2O was extremely fast. After 15 min the alkene peaks at δ 5.38 and 5.68 had completely disappeared. However, the sharp methyl ketone peak at δ 2.17 had also vanished, and new sharp singlets were visible near δ 1.50. The IR of the crude reaction mixture indicated no carbonyl functionality, but a very strong OH absorbance. It was obvious that the expected bromohydrin had not been prepared. We tentatively characterized the product of this reaction as the hemiacetal **17**, Scheme IV, the structure of which was consistent with the spectroscopic data. This assignment suggested that treatment with base should facilitate equilibration with the desired keto-bromohydrin, which should go on to give the epoxide.

Accordingly, what was believed to be **17** was treated with DBU, and after workup the NMR showed the reappearance of the methyl singlet at δ 2.17. New ^{1}H NMR peaks at δ 3.45–3.50 were consistent with the presence of an epoxide on a five-membered ring, as was a strong band in the IR at 1262 cm^{-1}. Two isomers of the product **18** were observed, as expected, due to the stereoisomers at C(15).

The last remaining task involved closing the A ring via attack of the enolate of the methyl ketone on the B ring epoxide, completing a synthesis of the basic *cis,anti,cis*-tricyclo[6.3.0]undecane ring system. Analysis of the feasibility of such a transformation in advance does not lead to a clear-cut answer. There are very few examples in the literature of simple enolates being used as nucleophiles that open epoxides in an intramolecular manner.[25] There are a somewhat larger number of intermolecular examples.[26] As to the question of ring size in the sense of Baldwin's rules, opening of a three-membered ring is considered to be an intermediate situation between a *trig* and a *tet*-targeted process. For both, the 5-*exo* ring closure, which is the reaction desired in the system under consideration, is "allowed", while the other possibility, a 6-*endo* process to give a bridged product, it at least partially disfavored by the degree of *trig* character associated with attack on an epoxide carbon. Using nitrile-stabilized anions, Stork has demonstrated that any of the above modes can take place, but when steric factors are equal, *exo* modes giving the smaller ring size predominate.[27]

In any event, none of our attempts to convert **18** into III succeeded. For example, attempts at closing the ring via simply forming the kinetic enolate with LDA yielded only recovered starting material, regardless of the temperature of the reaction. There was evidence for equilibration at the C(15) center when the reaction was warmed to room temperature, as expected from a system in which formation of the thermodynamic enolate was beginning to occur. Addition of Lewis acids into the system was also explored. Addition of 1 equiv of boron trifluoride etherate to the preformed lithium enolate of **18**, allowing the reaction to stir for several hours at −78 °C, and warming to −20 °C resulted only in the recovery of starting material. When a large excess of the Lewis acid was used under the same reaction conditions the starting material was consumed. From this reaction mixture a single polar compound was isolated by MPLC in approximately 60% yield. High-resolution mass spectrometry displayed a parent ion with the mass of the desired compound, but the IR of this compound, in addition to displaying a hydroxyl absorption at 3473 cm^{-1}, showed a carbonyl peak at 1712 cm^{-1}, not compatible with a cyclopentanone structure. Based on the limited amount of data available from the small amounts of material isolated at the end of this sequence, the bridged structure **19**, resulting from ring closure to C(5) rather than C(6) of the epoxide, is most likely the product that was isolated from reaction under these conditions.

With the failure of epoxide **18** to undergo the desired ring closure, this most direct and efficient use of this bicyclo[3.3.0]octane system in the synthesis of highly func-

(23) E.g., see: Shibasaki, M.; Mase, T.; Ikegami, S. *J. Am. Chem. Soc.* **1986**, *108*, 2090.

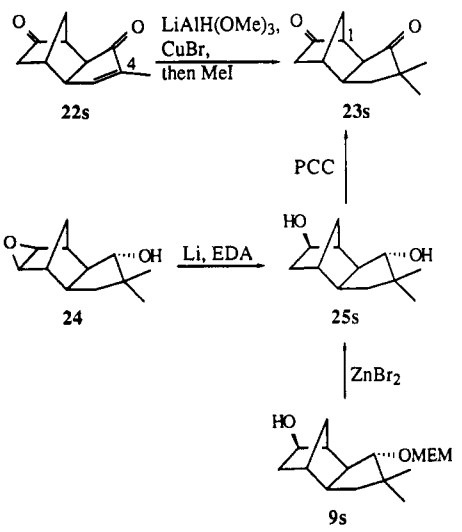
(24) (a) Piers, E.; Jung, G. L.; Moss, N. *Tetrahedron Lett.* **1984**, *25*, 3959. (b) Dimsdale, M. J.; Newton, R. F.; Rainey, D. K.; Webb, C. F.; Lee, T. V.; Roberts, S. M. *J. Chem. Soc., Chem. Commun.* **1977**, 716. (c) Fritsch, W.; Stache, U.; Haede, W.; Radscheit, K.; Ruschig, H. *Justus Liebigs Ann. Chem.* **1969**, *721*, 168. (d) Fritsch, W.; Haede, W.; Radscheit, K.; Stache, U.; Ruschig, H. *Justus Liebigs Ann. Chem.* **1974**, 621.

(25) E.g., McMurry, J. E.; Isser, S. J. *J. Am. Chem. Soc.* **1972**, *94*, 7132.

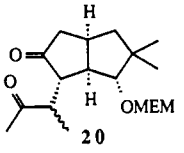
(26) E.g., Hudrlik, P. F.; Wan, C. N. *J. Org. Chem.* **1975**, *40*, 2963.

(27) Stork, G.; Cohen, J. F. *J. Am. Chem. Soc.* **1974**, *96*, 5272.

Scheme V



tionalized tricyclo[6.3.0.0]undecanes went unrealized. However, alkene **15** still possesses other attractive features as a potential precursor to linear triquinanes, e.g. via conversion to the diketone **20**, which possesses the functionality necessary for ring closure via aldol condensation, according to the methodology used in several of hirsutanoid syntheses already cited. As this direction was not one that would explore any new methodological questions, we did not pursue it to any significant extent.[28] Nonetheless, the intermolecular Pauson-Khand cycloaddition of norbornadiene has been shown to be a rapid entry into tricyclo[5.2.1.0]decenones suitable for use as precursors to bicyclo[3.3.0]octanes. The approach permits the stereocontrolled preparation of systems with considerable substitution and functionality, and represents a viable and complementary approach to those using the intramolecular version of the cycloaddition reaction.



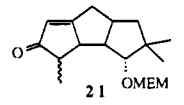
20

Determination of Regioisomeric Structures 9a and 9s. The structures of alcohols **9a** and **9s**, resulting from reduction of epoxide **8** (Scheme II), were determined by chemical correlation with enedione **22s** (Scheme V) and its anti regioisomer **22a** (not shown).

Enones **22a/s** were formed in a 3:1 ratio by Pauson–Khand reaction of 5-norbornen-2-one with propyne, and pure **22s** isolated by crystallization. The regioisomers were characterized by ^1H and ^{13}C NMR correlation with the analogous 4-phenyl enediones, which had been characterized crystallographically.[11] Reductive alkylation of **22s** produces **23s**, which displays a characteristically sharp singlet in the ^1H NMR spectrum for H-1 at δ 2.90. In contrast, the ^1H NMR spectrum of regioisomer **23a** shows the signal for the corresponding bridgehead proton α to the norbornenone carbonyl (H-7, at δ 2.97) as a finely split doublet due to long-range coupling. This syn/anti distinction is consistently found throughout these series.

Scheme V shows the correlation between **9s**, **25s**, and **23s**. Epoxidation of **6**α (Scheme II) gives **24**. Reduction gives a separable mixture of diols **25a/s**, each of which was characterized by oxidation to one of the diones **23a/s**. The NMR of **25s** shows a sharp singlet for H-1 at δ 2.14, while that of **25a** shows a doublet for H-7 at δ 2.22. Spectroscopic correspondence between **25s** and **9s** (H-1 singlet at δ 2.19) and between **25a** and **9a** (H-7 doublet at δ 2.28) was confirmed by deprotection of the presumed **9s** to give exclusively **25s**.

(28) In a brief exploratory investigation alkene **18** was hydroborated with BH_3–THF to give a mixture of diols which was subjected directly to PCC oxidation, forming a mixture of diketones apparently containing about 50% of **20**. Small scale intramolecular aldol condensation with KO^{t}Bu in ^{t}BuOH yielded a mixture of products in quantities too small for separation of individual components, but exhibiting spectroscopic features consistent with the presence of the tricyclic enone **21**.



21

Experimental Section

General. Solvents and Reagents. Tetrahydrofuran (THF) and benzene were vacuum distilled from sodium benzophenone ketyl and stored under N_2 over 4-Å molecular seives. Pyridine, triethylamine, diisopropylamine, and dimethyl sulfoxide were distilled from calcium hydride. Carbon tetrachloride, chloroform, dichloromethane, and dimethylformamide were dried over 4-Å molecular seives. Ethyl ether anhydrous was used as commercially available. Iodomethane was distilled from P_2O_5. The literature procedures were employed for the synthesis of the known 4-methyltricyclo[5.2.1.0^{2,6}]deca-4,8-dien-3-one (**4**)[14] and 4-methyltricyclo[5.2.1.0^{2,6}]dec-4-ene-3,9-dione (**22s**).[11] Unless otherwise noted, all other reagents were used as commercially available. All reactions were carried out under an atmosphere of dried argon or nitrogen.

Separation, Purification, and Analysis. Commercially prepared silica gel columns (EM Reagents) were used for medium-pressure liquid chromatography. Silica gel (Merck) was used for flash column chromatography. Other chromatographic separations were carried out on a Chromatotron (Harrison Research) using silica gel with calcium binder (E. Merck). Iodine was used to visualize non-UV absorbing bands. ^1H NMR were recorded at 60, 90, 300, or 360 MHz. ^{13}C NMR were recorded at 75.4 MHz.

4,4-Dimethyltricyclo[5.2.1.0^{2,6}]dec-8-en-3-one (5). Anhydrous NH_3 (500 mL) was distilled into a 1-L 3-necked flask fitted with a dry ice condenser and overhead stirrer. Lithium wire was added in 2-cm pieces (2.60 g, 371 mmol), and the mixture was stirred for 1 h at −78 °C. A solution of enone **4** (10.65 g, 66.6 mmol) and CH_3OH (2.15 mL, 53.1 mmol) in ether (75 mL) was added via cannula, and the resulting mixture was stirred at −33 °C for 5 h. The reaction was then quenched by the slow addition of CH_3I (150 mL) in ether (175 mL) and stirred at room temperature for 12 h. The mixture was poured into saturated NH_4Cl solution and diluted with ether. Following extraction with ether (3×) the organic layers were combined, washed with brine, and dried (Na_2SO_4). Concentration under reduced pressure yielded **5** as a yellow oil (10.50 g, 59.6 mmol, 90%), which was used without purification in the next step. However, an analytical sample was purified by MPLC (15:85 ether–hexane) to yield a colorless oil: NMR (360 MHz, $CDCl_3$) δ 1.05 (s, 3 H), 1.09 (s, 3 H), 1.11 (br d, J = 9.7 Hz, 1 H), 1.23 (dd, J = 13.4, 7.3 Hz, 1 H), 1.39 (br d, J = 9.7 Hz, 1 H), 2.05 (dd, J = 13.4, 9.2 Hz, 1 H), 2.33 (br q, J = 8.3 Hz, 1 H), 2.42 (br d, J = 8.6 Hz, 1 H), 2.66 (br s, 1 H), 3.10 (br s, 1 H), 6.15 (m, 2 H). IR (CCl_4) 1736 cm^{-1}. Anal. Calcd for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 81.81; H, 9.19.

4,4-Dimethyltricyclo[5.2.1.0^{2,6}]dec-8-en-3α-ol (6α). Reduction of **5** to **6**α was carried out similarly to the above procedure. A solution of **5** (13.03 g, 74.0 mmol) and CH_3OH (2.6 mL, 64.2 mmol) in ether (100 mL) was added to the preformed solution of 3.15 g (450 mmol) of Li in 450 mL of NH_3, and the resulting mixture was allowed to stir for 5 h at −33 °C. Workup as above and concentration under reduced pressure yielded the single isomer **6**α as a white solid (12.40 g, 69.6 mmol, 94%) which was purified by MPLC (1:3 ether–hexane): mp 68–70 °C; NMR (360 MHz, $CDCl_3$) δ 0.91 (dd, J = 13.0, 9.6 Hz, 1 H), 0.93 (s, 3 H), 1.01 (s, 3 H), 1.41 (dqn, J = 9.1, 1.5 Hz, 1 H), 1.46 (br d, J = 9.1 Hz, 1 H), 1.59 (dd, J = 13.0, 8.4 Hz, 1 H), 1.76 (t, J = 8.1 Hz, 1 H), 2.02 (q, J = 8.9 Hz, 1 H), 2.40 (br d, J = 0.8 Hz, 1 H), 2.72 (br

s, 1 H), 3.25 (br d, J = 7.3 Hz, 1 H), 6.07 (t, J = 1.8 Hz, 2 H); IR (CCl_4) 3385 cm^{-1}. Anal. Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18. Found: C, 80.83; H, 10.21.

$LiAlH_4$ reduction of **5** permitted isolation of the stereoisomeric alcohol **6β**. A solution of **5** (10.30 g, 58.5 mmol) in ether (150 mL) was added dropwise to $LiAlH_4$ (4.30 g, 113.1 mmol) in ether (250 mL) at 0 °C under Ar. The resulting mixture was allowed to stir at room temperature for 5 h and then was quenched with H_2O. Filtration through Celite was followed by extraction with ether (3×). The organic layers were combined, dried (Na_2SO_4), and concentrated under reduced pressure to yield the product alcohol (9.36 g, 52.6 mmol, 90%) as a mixture of isomers (3:1 **6α**–**6β**) which could be separated by MPLC (1:3 ether–hexane). For **6β**: NMR (360 MHz, $CDCl_3$) δ 0.92 (s, 3 H), 1.02 (s, 3 H), 1.40 (m, 1 H), 1.79 (br d, J = 8.6 Hz, 1 H), 2.15 (m, 2 H), 2.48 (br s, 1 H), 2.68 (br d, J = 0.7 Hz, 1 H), 3.59 (d, J = 6.1 Hz, 1 H), 6.10–6.16 (m, 2 H).

4,4-Dimethyl-3-[(2-methoxyethoxy)methoxy]tricyclo-[5.2.1.0^{2,6}]dec-8-ene (7). To a solution of alcohol **6α** (5.08 g, 28.5 mmol) in CH_2Cl_2 (150 mL) was added diisopropylethylamine (6.6 mL, 38 mmol) and MEMCl (4.0 mL, 35 mmol). The mixture was stirred at room temperature under Ar for 4 h, after which it was poured into ether (500 mL). The result was washed rapidly with 5% HCl, saturated $NaHCO_3$ solution, and brine. After drying (Na_2SO_4), the solution was concentrated under reduced pressure. Purification by flash column chromatography (2:3 ether–hexane) gave recovered **6α** (1.18 g, 6.63 mmol, 23% recovery) and **7** (5.10 g, 19.2 mmol, 67%, 87% yield based on consumed **6α**) as a clear oil: NMR (360 MHz, $CDCl_3$) δ 0.92 (s, 3 H), 0.99 (s, 3 H), 1.30–1.60 (m, 3 H), 1.83 (t, J = 7.9 Hz, 1 H), 2.03 (br q, J = 8.9 Hz, 1 H), 2.37 (br s, 1 H), 2.73 (br s, 1 H), 3.16 (d, J = 7.1 Hz, 1 H), 3.38 (s, 3 H), 3.56 (t, J = 4.7 Hz, 2 H), 3.70 (m, 2 H), 4.72 (d, J = 6.7 Hz, 1 H), 4.82 (d, J = 6.7 Hz, 1 H), 6.04 (br s, 2 H); IR (CCl_4) 3060 cm^{-1}. Anal. Calcd for $C_{16}H_{26}O_3$: C, 72.14; H, 9.84. Found: C, 71.87; H, 9.90.

4,4-Dimethyl-8,9-*exo*-epoxy-3-[(2-methoxyethoxy)methoxy]tricyclo[5.2.1.0^{2,6}]decane (8). To a solution of alkene **7** (6.05 g, 22.7 mmol) in CH_2Cl_2 (400 mL) was added *m*-chloroperoxybenzoic acid (MCPBA) (6.18 g, 35.9 mmol). The mixture was stirred at room temperature under Ar for 5 h, after which it was washed with saturated Na_2CO_3 (3×) and brine. After drying (Na_2SO_4), the solution was concentrated under reduced pressure. Purification by flash column chromatography (2:3 ether–hexane) yielded epoxide **8** as a clear oil (5.06 g, 17.9 mmol, 79%): NMR (360 MHz, $CDCl_3$) δ 0.80–1.10 (m, 2 H), 0.87 (s, 3 H), 0.95 (s, 3 H), 1.19 (br d, J = 10.7 Hz, 1 H), 1.54 (dd, J = 13.1, 8.5 Hz, 1 H), 1.90 (t, J = 8.7 Hz, 1 H), 2.10 (br q, J = 9.8 Hz, 1 H), 2.11 (br s, 1 H), 2.48 (br s, 1 H), 3.02 (br s, 2 H), 3.14 (d, J = 7.3 Hz, 1 H), 3.37 (s, 3 H), 3.54 (t, J = 4.6 Hz, 2 H), 3.60–3.80 (m, 2 H), 4.67 (d, J = 6.7 Hz, 1 H), 4.76 (d, J = 6.7 Hz, 1 H). Anal. Calcd for $C_{16}H_{26}O_4$: C, 68.06; H, 9.28. Found: C, 67.89; H, 9.33.

4,4-Dimethyl-3-[(2-methoxyethoxy)methoxy]tricyclo-[5.2.1.0^{2,6}]decan-9-ol (9s) and 4,4-Dimethyl-3-[(2-methoxyethoxy)methoxy]tricyclo[5.2.1.0^{2,6}]decan-8-ol (9a). Epoxide **8** (3.50 g, 12.4 mmol) was dissolved in THF (25 mL) and added dropwise to Super-Hydride (87.0 mL, 87.0 mmol) in THF (50 mL) at 0 °C under Ar. The mixture was warmed to reflux and allowed to stir for 48 h. After this time the reaction was quenched by adding sequentially, ethanol (220 mL), 6 N NaOH (75 mL), and 30% H_2O_2 (145 mL). This mixture was stirred for 48 h and was filtered through Celite, washing thoroughly with EtOAc. The filtrate was washed with saturated K_2CO_3 solution (3×) and brine. The organic layer was dried (Na_2SO_4) and concentrated under reduced pressure to yield a 1:1 (**9s**:**9a**) isomer mixture of the product alcohols (3.21 g, 11.3 mmol, 91%) as a clear oil. The isomeric products could be directly separated and purified via MPLC (95:5 ether–hexane). For **9s**: NMR (300 MHz, $CDCl_3$) δ 0.80–0.90 (m, 1 H), 0.85 (s, 3 H), 0.96 (s, 3 H), 1.20–1.70 (series of m, 7 H), 1.82 (br q, J = 8.9 Hz, 1 H), 1.89 (br d, J = 4.0 Hz, 1 H), 2.19 (br s, 1 H), 3.14 (d, J = 7.2 Hz, 1 H), 3.38 (s, 3 H), 3.56 (t, J = 4.5 Hz, 2 H), 3.60–3.80 (m, 3 H), 4.71 (d, J = 6.9 Hz, 1 H), 4.81 (d, J = 6.9 Hz, 1 H); IR (CCl_4) 3456 cm^{-1}. For **9a**: NMR (360 MHz, $CDCl_3$) δ 0.80–1.00 (m, 1 H) 0.87 (s, 3 H), 0.98 (s, 3 H), 1.20–1.70 (series of m, 7 H), 1.81 (br s, 1 H), 1.83 (br q, J = 9.0 Hz, 1 H), 2.28 (br d, J = 4.1 Hz, 1 H), 3.12 (d, J = 7.3 Hz, 1 H), 3.39 (s, 3 H), 3.56 (t, J = 4.6 Hz, 2 H), 3.60–3.80 (m, 3 H), 4.70 (d, J = 7.6 Hz, 1 H), 4.80 (d, J = 7.6 Hz, 1 H); IR (CCl_4) 3468 cm^{-1}. Anal. Calcd for $C_{16}H_{28}O_4$: C, 67.57; H, 9.92. Found: C, 67.27; H, 10.01.

4,4-Dimethyl-3-[(2-methoxyethoxy)methoxy]tricyclo-[5.2.1.0^{2,6}]decan-8-one (MEM-I). To a solution of alcohol **9a** (640 mg, 2.30 mmol), in CH_2Cl_2 (125 mL) was added NaOAc (1.14 g) and PCC (1.18 g, 5.5 mmol). The mixture stirred at room temperature under Ar for 7 h, after which it was diluted with ether and filtered through a short column of silica gel. Concentration under reduced pressure yielded the ketone MEM-I as a light yellow oil (629 mg, 2.20 mmmol) which was used without purification in the next step. An analytical sample was purified by MPLC (85:15 ether–hexane) to yield a colorless oil: NMR (360 MHz, $CDCl_3$) δ 0.90 (s, 3 H), 1.01 (s, 3 H), 1.50–2.10 (series of m, 6 H), 2.26 (br s, 1 H), 2.28 (br q, J = 9.2 Hz, 1 H), 2.69 (br d, J = 2.6 Hz, 1 H), 3.22 (d, J = 7.2 Hz, 1 H), 3.39 (s, 3 H), 3.55 (m, 2 H), 3.60–3.80 (m, 2 H), 4.73 (d, J = 6.7 Hz, 1 H), 4.83 (d, J = 6.7 Hz, 1 H); IR (CCl_4) 1751 cm^{-1}. Anal. Calcd for $C_{16}H_{26}O_4$: C, 68.05; H, 9.28. Found: C, 67.88; H, 9.40.

4,4-Dimethyl-3-[(2-methoxyethoxy)methoxy]-8-oxatricyclo[5.3.1.0^{2,6}]undecan-9-one (10). A solution of MEM-I (1.50 g, 5.32 mmol) in $CHCl_3$ (4 mL), $NaHCO_3$ (1.38 g), and a solution of MCPBA (1.38 g, 7.98 mmol) in $CHCl_3$ (12 mL) was added to a sealable tube. The tube was flushed with Ar and sealed tightly, and the mixture was stirred at 100 °C for 42 h. After this time, the tube was allowed to cool, and the mixture was washed with saturated Na_2CO_3 solution (3×). The organic layer was dried (Na_2SO_4) and concentrated under reduced pressure. Purification by flash column chromatography (3:1 EtOAc–hexane) afforded **10** (1.16 g, 3.89 mmol, 84%) as a white solid: mp 40.5–41.0 °C; NMR (300 MHz, $CDCl_3$) δ 0.79 (dd, J = 12.6, 10.8 Hz, 1 H), 0.90 (s, 3 H), 0.98 (s, 3 H), 1.71 (dd, J = 13.0, 8.9 Hz, 1 H), 1.85 (br s, 2 H), 2.33 (t, J = 8.4 Hz, 1 H), 2.53 (d, J = 17.9 Hz, 1 H), 2.56 (br s, 1 H), 2.74 (dd, J = 17.9, 5.5 Hz, 1 H), 2.87 (br q, J = 9.6 Hz, 1 H), 3.10 (d, J = 8.0 Hz, 1 H), 3.38 (s, 3 H), 3.50–3.85 (m, 4 H), 4.42 (br s, 1 H), 4.71 (d, J = 7.1 Hz, 1 H), 4.80 (d, J = 7.1 Hz, 1 H); IR (CCl_4) 1744 cm^{-1}. Anal. Calcd for $C_{16}H_{26}O_5$: C, 64.41; H, 8.78. Found: C, 64.25; H, 8.83.

4,4,10-Trimethyl-3-[(2-methoxyethoxy)methoxy]-8-oxatricyclo[5.3.1.0^{2,6}]undecan-9-one (11). A solution of lactone **10** (91 mg, 0.31 mmol) in THF (0.2 mL) was added dropwise to LDA (44 mg, 0.41 mmol) in THF (0.4 mL) at −78 °C. The mixture stirred at −78 °C for 2.5 h, after which the reaction was quenched with a solution of CH_3I (0.023 mL, 1.1 mmol) and HMPA (0.06 mL, 0.31 mmol) in THF (0.1 mL). The mixture continued to stir at −78 °C for 1 h and was allowed to warm to room temperature while stirring for an additional 12 h. The crude reaction mixture was treated with saturated NH_4Cl solution and extracted with ether (3×). The organic layers were combined, washed with brine (3×), and dried (Na_2SO_4). Concentration under reduced pressure afforded **11** (88 mg, 0.28 mmol, 94%) as a clear oil which was used without purification in the next step: NMR (360 MHz, $CDCl_3$) δ 0.79 (dd, J = 12.6, 10.8 Hz, 1 H), 0.90 (s, 3 H), 0.98 (s, 3 H), 1.33 (d, J = 7.3 Hz, 3 H), 1.71 (dd, J = 13.0, 8.9 Hz, 1 H), 1.95 (br d, J = 13.5 Hz, 1 H), 2.28 (br s, 1 H), 2.31 (t, J = 8.4 Hz, 1 H), 2.52 (q, J = 7.3 Hz, 1 H), 2.73 (br q, J = 9.6 Hz, 1 H), 3.10 (d, J = 7.5 Hz, 1 H), 3.38 (s, 3 H), 3.5–3.9 (m, 4 H), 4.37 (br s, 1 H), 4.71 (d, J = 7.1 Hz, 1 H), 4.80 (d, J = 7.1 Hz, 1 H); IR (CCl_4) 1740 cm^{-1}. Anal. Calcd for $C_{17}H_{28}O_5$: C, 65.36: H, 9.03. Found: C, 65.18; H, 9.20.

3,3-Dimethyl-8-(1-carboxyethyl)-2-[(2-methoxyethoxy)-methoxy]bicyclo[3.3.0]octan-6-ol (12). Lactone **11** (208 mg, 0.667 mmol) was dissolved in a 1:1 solution of methanol and 1 N NaOH (34 mL). The mixture was allowed to stir at room temperature under Ar for 12 h, after which it was washed with CH_2Cl_2 (3×). The aqueous layer was separated, acidified with dilute HCl to a pH of 4, and extracted with CH_2Cl_2 (3×). The organic layers were combined and dried (Na_2SO_4), and the solvent was removed to yield a 1:1 diastereomeric mixture of **12** (193 mg, 0.585 mmol, 88%) as clear oil. The mixture of diastereomers was carried on to the next step; however, one isomer could be separated from the mixture by MPLC (60:38:2 EtOAc–hexane–MeOH): NMR (300 MHz, $CDCl_3$, one diastereomer) δ 0.89 (s, 3 H), 1.00 (s, 3 H), 1.17 (d, J = 6.9 Hz, 3 H), 1.64 (dt, J = 13.4, 6.3 Hz, 1 H), 1.75 (dd, J = 12.9, 8.8 Hz, 1 H), 1.99 (dt, J = 13.4, 6.2 Hz, 1 H), 2.19 (br d, J = 12.9 Hz, 1 H), 2.41 (br s, 2 H), 2.65 (qn, J = 7.4 Hz, 1 H), 3.35 (d, J = 6.1 Hz, 1 H), 3.40 (s, 3 H), 3.58 (t,

J = 4.4 Hz, 2 H), 3.63–3.83 (m, 2 H), 3.93 (m, 1 H), 4.69 (d, J = 6.7 Hz, 1 H), 4.80 (d, J = 6.7 Hz, 1 H); ^{13}C NMR (75.4 MHz, $CDCl_3$, mixture of diastereomers) δ 15.1 and 16.5, 20.9 and 21.4, 26.9 and 27.2, 37.5 and 37.8, 42.9 and 42.9, 43.5 and 43.8, 46.3 and 47.2, 48.0 and 48.6, 52.3 and 52.6, 67.1 and 67.1, 71.7 and 71.9, 79.4 and 79.9, 92.2 and 92.6, 95.7 and 95.8, 180.4 and 180.5; IR (CCl_4) 3405 (br), 1706 cm^{-1}. Anal. Calcd for $C_{17}H_{30}O_6$: C, 61.80; H, 9.15. Found: C, 61.68; H, 9.02.

3,3-Dimethyl-2-[(2-methoxyethoxy)methoxy]-8-(1-methyl-2-oxopropyl)bicyclo[3.3.0]octan-6-ol (MEM-II). A diastereomeric mixture of the carboxylic acid **12** (45 mg, 0.14 mmol) was dissolved in THF (3 mL), and cooled to 0 °C. MeLi (1.5 M in ether, 2.0 mL, 3.0 mmol) was added rapidly, and the mixture was stirred at room temperature under Ar for 6 h. The mixture was cooled to 0 °C, and chlorotrimethylsilane (1.1 mL, 8.6 mmol) was added. After warming to room temperature, the volatiles were removed on a vacuum line, and the residue was dissolved in ether. Saturated NH_4Cl solution was added, and the mixture was extracted with ether (3×). The organic layers were combined, washed with brine, and dried (Na_2SO_4). Concentration under reduced pressure yielded the trimethylsilyl ether of the desired product (52 mg, 0.14 mmol, 99% crude): NMR (90 MHz, $CDCl_3$) δ 0.01 (s, 9 H), 0.87 (s, 3 H), 0.97 (s, 3 H), 1.03 (d, J = 6 Hz, 3 H) 1.1–2.0 (m, 3 H), 2.07 (s, 3 H), 2.2–3.0 (m, 3 H), 3.33 (s, 3 H), 3.36–3.83 (m, 4 H), 4.70 (s, 2 H).

The trimethylsilyl ether (52 mg, 0.14 mmol) was immediately hydrolyzed by dissolving in MeOH (10 mL), adding a large excess of K_2CO_3, and stirring for 18 h. The mixture was diluted with H_2O and acidified with dilute HCl to pH = 4. The mixture was then extracted with ether (3×), and the organic layers were combined and washed with brine. After drying (Na_2SO_4), concentration under reduced pressure yielded a mixture of the desired target molecule MEM-II as two diastereomers (39 mg, 0.12 mmol, 86% from **12**) and the vinyl ether **13** (5 mg, 0.02 mmol, 11%). The crude mixture was carried on to the next step without further purification; however, a small amount of methyl ketone MEM-II was purified for analysis by MPLC (ether), to yield a mixture of the diastereomers MEM-II as a clear oil. For MEM-II (one diastereomer): NMR (300 MHz, $CDCl_3$) δ 0.86 (s, 3 H), 1.01 (s, 3 H), 1.05 (d, J = 7.0 Hz, 3 H), 1.56 (dt, J = 13.5, 5.6 Hz, 1 H), 1.74 (dd, J = 13.0, 8.8 Hz, 1 H), 1.91 (dt, J = 13.5, 5.7 Hz, 1 H), 2.15 (s, 3 H), 2.21 (br d, J = 7.5 Hz, 1 H), 2.30–2.50 (m, 1 H), 2.82 (qn, J = 7.5 Hz, 1 H), 3.29 (d, J = 7.3 Hz, 1 H), 3.37 (s, 3 H), 3.5–3.8 (m, 4 H), 3.90 (m, 1 H), 4.74 (d, J = 7.0 Hz, 1 H), 4.80 (d, J = 7.0 Hz, 1 H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 13.9, 20.4, 26.3, 28.7, 36.3, 42.7, 44.4, 47.5, 49.9, 52.4, 58.3, 66.5, 71.1, 79.5, 91.9, 95.3, 212.6; IR (CCl_4) 3481, 1715 cm^{-1}. Anal. Calcd for $C_{18}H_{32}O_5$: C, 65.82; H, 9.82. Found: C, 65.54; H, 9.76.

4,4,9,10-Tetramethyl-3-[(2-methoxyethoxy)methoxy]-8-oxatricyclo[5.3.1.0^{2,6}]undec-9-ene (13). Small amounts of vinyl ether **13** could always be isolated from the crude product mixture of MEM-II, as described above. Alternatively, a diastereomeric mixture of MEM-II was dissolved in MeOH and treated with 0.5 N HCl, and the mixture was allowed to stir for 0.5 h. Extraction with ether (3×), drying (Na_2SO_4), and concentration under reduced pressure resulted in the complete conversion to **13**: NMR (300 MHz, $CDCl_3$) δ 0.73 (dd, J = 13.0, 9.6 Hz, 1 H), 0.87 (s, 3 H), 1.58 (s, 3 H), 1.60 (s, 3 H), 1.67 (dd, J = 13.0, 9.4 Hz, 1 H), 1.75 (br s, 2 H), 2.08 (br s, 1 H), 2.4–2.7 (m, 2 H), 3.12 (d, J = 7.4 Hz), 3.39 (s, 3 H), 3.5–3.9 (m, 4 H), 4.03 (br s, 1 H), 4.71 (d, J = 7.0 Hz, 1 H), 4.83 (d, J = 7.0 Hz, 1 H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 15.5, 16.9, 20.8, 26.4, 28.7, 40.6, 41.9, 42.5, 46.5, 57.1, 58.9, 66.8, 71.7, 80.2, 88.8, 95.4, 109.2, 140.1; high resolution (FAB) mass spectrum calculated for $C_{18}H_{31}O_4$ ($[M + H]^+$) 311.2222, found 311.2233.

A single diastereomer of MEM-II could be resynthesized from **13**, by dissolving the vinyl ether in MeOH, adding K_2CO_3, and allowing the mixture to stir for 0.5 h. Dilute HCl was added until the pH was equal to 4. The mixture was extracted with ether (3×), and the organic layers were combined. Drying (Na_2SO_4) and concentration under reduced pressure yielded a single diastereomer of MEM-II.

3,3-Dimethyl-2-[(2-methoxyethoxy)methoxy]-8-(1-methyl-2-oxopropyl)bicyclo[3.3.0]oct-6-ene (15). To a solution of crude methyl ketone MEM-II (125 mg, 0.379 mmol) in pyridine (2.6 mL) was added *p*-toluenesulfonyl chloride (300 mg, 1.6 mmol), and the mixture was stirred under Ar, at room temperature for 4 days. The mixture was diluted with ether and H_2O and extracted with ether (3×). The organic layers were combined and washed with 5% HCl (3×) followed by saturated $NaHCO_3$ solution and brine. The organic layer was dried (Na_2SO_4) and concentrated under reduced pressure to yield the tosylate (152 mg, 0.314 mmol, 83%), which was used without further purification in the next step: NMR (90 MHz, $CDCl_3$) δ 0.77 (s, 3 H), 0.83 (s, 3 H), 2.07 (s, 3 H), 2.40 (s, 3 H), 3.33 (s, 3 H), 3.4–3.8 (m, 4 H), 4.33–4.53 (m, 1 H), 4.57–4.87 (m, 2 H), 7.20–7.87 (m, 4 H).

To a diastereomeric mixture of this tosylate (27 mg, 0.056 mmol) in DMF (1.6 mL) was added diazabicycloundecene (0.26 mL, 1.7 mmol). The mixture stirred at 85 °C for 7 h, after which it was cooled to room temperature, diluted with H_2O, and extracted with ether (3×). The organic layers were combined, washed with saturated NH_4Cl solution, H_2O, saturated $NaHCO_3$ solution, and then brine. After drying (Na_2SO_4), concentration under reduced pressure yielded the desired alkene **15** (15.8 mg, 0.051 mmol, 91%). The crude product was purified by MPLC (60:40 hexane–ether) to give a diastereomeric mixture of **15** as a clear oil. The diastereomers were separated by MPLC for ^1H NMR analysis: NMR (300 MHz, $CDCl_3$, one diastereomer) δ 0.93 (s, 3 H), 1.01 (s, 3 H), 1.09 (d, J = 6.9 Hz, 3 H), 1.75 (dd, J = 12.8, 9.1 Hz, 1 H), 2.14 (s, 3 H), 2.37 (br t, J = 9.0 Hz, 1 H), 2.41 (qn, J = 7.2 Hz, 1 H), 2.83 (br d, J = 7.4 Hz, 1 H), 3.00–3.15 (m, 1 H), 3.32 (d, J = 7.1 Hz, 1 H), 3.40 (s, 3 H), 3.57 (t, J = 4.8 Hz, 2 H), 3.65–3.85 (m, 2 H), 4.79 (br s, 2 H), 5.35–5.45 (m, 1 H), 5.65–5.75 (m, 1 H); NMR (300 MHz, $CDCl_3$, other diastereomer) δ 0.93 (s, 3 H), 0.95 (d, J = 7.0 Hz, 3 H), 1.00 (s, 3 H), 1.75 (dd, J = 12.8, 9.1 Hz, 1 H), 2.18 (s, 3 H), 2.28 (br t, J = 9.0 Hz, 1 H), 2.65 (qn, J = 6.1 Hz, 1 H), 3.00–3.20 (m, 2 H), 3.35 (d, J = 8.1 Hz, 1 H), 3.39 (s, 3 H), 3.57 (t, J = 4.8 Hz, 2 H), 3.65–3.85 (m, 2 H), 4.80 (d, J = 7.0 Hz, 1 H), 4.85 (d, J = 7.0 Hz, 1 H), 5.35–5.45 (m, 1 H), 5.65–5.75 (m, 1 H); ^{13}C NMR (75.4 MHz, $CDCl_3$, mixture of diastereomers) δ 12.1 and 14.2, 21.3 and 21.4, 26.9 and 27.0, 28.7 and 29.1, 42.5 and 42.6, 43.9 and 44.0, 45.0 and 45.4, 52.2 and 53.4, 58.9 and 58.9, 67.3 and 67.3, 71.8 and 71.8, 92.5 and 92.5, 96.1 and 96.2, 128.3 and 129.7, 136.7 and 137.3, 211.4 and 212.0; IR (CCl_4) 1713 cm^{-1}; high-resolution (FAB) mass spectrum calculated for $C_{18}H_{31}O_4$ ($[M + H]^+$) 311.2222, found 311.2227.

3,3-Dimethyl-6,7-*endo*-epoxy-2-[(2-methoxyethoxy)methoxy]-8-(1-methyl-2-oxopropyl)bicyclo[3.3.0]octane (18). Alkene **15** (21 mg, 0.068 mmol) was dissolved in deuterated acetone (0.25 mL) and placed in an NMR tube. D_2O (0.14 mL) was added to the solution, and the tube was cooled to 0 °C. *N*-Bromoacetamide (11 mg, 0.080 mmol) was added all at once, and the tube was allowed to warm to room temperature for 15 min. NMR analysis after this period of time indicated all starting alkene had reacted. The reaction mixture was concentrated under reduced pressure, diluted with H_2O, and extracted with ether (3×). The organic layers were combined and washed with saturated $NaHSO_3$ solution (3×), saturated $KHCO_3$ solution (2×), and brine. The organic layer was dried (Na_2SO_4) and concentrated under reduced pressure to yield a diastereomeric mixture of hemiacetal **17** as a yellow oil (28 mg, 0.068 mmol, 100%), which was used without purification in the next step: NMR (300 MHz, $CDCl_3$) δ 0.90 (s, 3 H), 0.95 (d, J = 7.3 Hz), 1.06 (s, 3 H), 1.07 (s, 3 H), 1.10 (s, 3 H), 1.13 (d, J = 7.1 Hz, 3 H), 1.40 (s, 3 H), 1.46 (s, 3 H), 1.7–3.3 (m, 2 × 5 H), 3.39 (s, 2 × 3 H), 3.5–3.8 (m, 2 × 4 H), 4.08 (t, J = 8.2 Hz, 1 H), 4.16–4.25 (m, 1 H) 4.43 (d, J = 5.6 Hz, 1 H), 4.6–5.0 (m, 2 × 2 H); IR (CCl_4) 3433 cm^{-1}.

To a solution of hemiacetal **17** (78 mg, 0.19 mmol) in benzene (1.6 mL) was added DBU (0.62 mL, 4.1 mmol), and the mixture was allowed to stir at room temperature under Ar for 18 h. After this time, ether and brine were added to the mixture. The organic layer was separated and washed with saturated NH_4Cl solution, H_2O, saturated $KHCO_3$ solution, and brine. After drying (Na_2SO_4), the solution was concentrated under reduced pressure. Purification by MPLC (ether) yielded a diastereomeric mixture of epoxide **18** as a clear oil (52 mg, 0.16 mmol, 84%): NMR (300 MHz, $CDCl_3$) δ 0.92 (s, 3 H), 0.93 (s, 3 H), 1.05 (s, 3 H), 1.07 (s, 3 H), 1.19 (d, J = 7.4 Hz, 3 H), 1.21 (d, J = 7.1 Hz, 3 H), 1.5–1.7 (m, 2 × 1 H), 1.8–1.95 (m, 1 H), 1.95–2.10 (m, 1 H), 2.20 (s, 3 H), 2.23 (s, 3 H), 2.1–2.4 (m, 2 × 1 H), 2.6–2.9 (m, 2 × 2 H), 3.26 (d, J = 6.5 Hz, 1 H), 3.27 (d, J = 6.5 Hz, 1 H), 3.37 (s, 3 H), 3.38 (s, 3 H), 3.45 (d, J = 7.1 Hz, 2 × 1 H), 3.49 (d, J = 7.1 Hz, 2 × 1 H),

3.5–3.9 (m, 2 × 4 H), 4.67 (br s, 2 H), 4.71 (d, J = 7.1 Hz, 1 H), 4.75 (d, J = 7.1 Hz, 1 H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 15.3 and 16.3, 21.4 and 22.0, 27.3 and 27.5, 29.7 and 29.7, 40.2 and 40.5, 42.6 and 43.3, 48.1 and 48.7, 48.4 and 49.2, 53.0 and 53.0, 58.9 and 59.0, 60.3 and 60.6, 61.4, and 62.2, 67.4 and 67.6, 71.7 and 71.8, 95.1 and 96.5, 96.5 and 96.5, 212.0 and 212.0; IR (CCl_4) 1715, 1261 cm^{-1}; high-resolution (electron capture) mass spectrum calculated for $C_{18}H_{39}O_5$ ($[M - H]^-$) 325.2015, found 325.1987; FAB fragmentation for $[M + H]^+$ 297 amu (7% intensity), 267 (3), 251 (55), 221 (100), 203 (27), 161 (8), 149 (28), 89 (11), 59 (8), 43 (3).

Attempted Synthesis of MEM-III via Ring Closure of Epoxide 18. To LDA (20 mg, 0.19 mmol) in THF (0.2 mL) at −78 °C was added a solution of epoxide **18** (19 mg, 0.058 mmol) in THF (0.2 mL). The solution stirred at −78 °C for 2 h, after which time boron trifluoride etherate (0.026 mL, 0.21 mmol) was added. The mixture stirred an additional 3 h at −78 °C and then 1 h at room temperature. The reaction was quenched with saturated NH_4Cl solution and extracted with ether (3×). The organic layers were combined, washed with brine, and dried (Na_2SO_4). Concentration under reduced pressure yielded recovered starting material only.

To LDA (17 mg, 0.16 mmol) in THF (0.2 mL) at −78 °C was added a solution of epoxide **18** (16 mg, 0.049 mmol) in THF (0.2 mL). The solution stirred at −78 °C for 2 h, after which time boron trifluoride etherate (0.13 mL, 1.1 mmol) was added. The mixture stirred for an additional 3 h at −78 °C and 1 h at room temperature. The reaction was quenched with saturated NH_4Cl solution and extracted with ether (3×). The organic layers were combined, washed with brine, and dried (Na_2SO_4). Concentration under reduced pressure yielded 17 mg of a crude product. The crude product was purified by MPLC (55:43:1:1 EtOAc–hexane–acetone–methanol) to yield 6 mg of a compound with the following spectral characteristics: NMR (300 MHz, $CDCl_3$) δ 0.89 (s, 2 × 3 H), 1.07 (s, 3 H), 1.08 (d, J = 7.5 Hz, 3 H), 1.15 (d, J = 7.5 Hz, 3 H), 1.3–1.5 (m, 1 H), 1.5–1.75 (m, 2 H), 1.75–1.9 (m, 2 H), 2.13 (s, 3 H), 2.17 (s, 3 H), 2.0–2.8 (series of m, 5 H), 3.2–3.9 (m, 2 × 9 H), 4.75 (s, 2 H), 4.78 (s, 2 H); IR (CCl_4) 1712 cm^{-1}; high-resolution mass spectrum calculated for $C_{14}H_{21}O_3$ [M^+ − $CH_2OCH_2CH_2OCH_3$] 237.14905, found 237.15049; high-resolution (FAB) mass spectrum calculated for $C_{18}H_{31}O_5$ ($[M + H]^+$) 327.2171, found 327.2179.

4,4-Dimethyltricyclo[5.2.1.0^{2,6}]decane-3,9-dione (23s). To a slurry of 0.22 g (5.8 mmol) of lithium aluminum hydride in 6.7 mL THF cooled to 0 °C was added 0.66 mL (17.0 mmol) of methanol slowly via syringe. After stirring for 45 min this solution was added to a slurry of 1.0 g (7.0 mmol) of dry CuBr in 10 mL of THF at 0 °C, and the mixture was stirred for an additional 45 min. A solution of enone **22s** (0.20 g, 1.1 mmol) in 5 mL of THF was added, and the resulting mixture was stirred at 0 °C for 2 h. The reaction was quenched by addition of CH_3I (40 mL) and stirred at room temperature for 1 h. The mixture was worked up as for **5**. Evaporation and separation by MPLC (8:92 acetone–hexane) afforded 0.086 g of **23s** as a colorless oil. Based on the recovery of 0.032 g **22s**, this corresponds to a 48% yield: NMR (360 MHz, $CDCl_3$) see supplementary material; IR (CCl_4) 1753, 1738 (sh) cm^{-1}.

4,4-Dimethyl-8,9-*exo*-epoxytricyclo[5.2.1.0^{2,6}]decan-3-ol (24). Alkene 6α (0.08 g, 0.45 mmol) in CH_2Cl_2 (20 mL) was epoxidized with MCPBA (0.18 g, 1.04 mmol) using the procedure for preparation of **8**. MPLC (4:1 ether–hexane) yielded **24** as a clear oil (0.065 g, 0.34 mmol, 76%): NMR (360 MHz, $CDCl_3$) see supplementary material; IR (CCl_4) 3471 cm^{-1}.

4,4-Dimethyltricyclo[5.2.1.0^{2,6}]decane-3,9-diol (25s) and 4,4-Dimethyltricyclo[5.2.1.0^{2,6}]decane-3,8-diol (25a). Lithium wire (0.50 g, 71.4 mmol) was added in 1-cm pieces to a solution of epoxide **24** (2.10 g, 10.8 mmol) in ethylenediamine (30 mL). After stirring at 65 °C under Ar for 8 h the reaction was quenched by slow addition of 50 mL water and extracted with ethyl acetate (3×). Workup as for **9a/s** yielded a 1:1 mixture of diols **25a/s** (1.19 g, 6.07 mmol, 56%), which was separated into the individual isomers by MPLC (45:45:5:5 ether–CH_2Cl_2–MeOH–EtOAc, quantitative recovery): NMR (360 MHz, $CDCl_3$) see supplementary material; IR (CCl_4) 3400 cm^{-1}.

Oxidation of the Presumed 25s to 23s. A solution of one of the diols from the procedure above (presumed to be **25s**) (0.06 g, 0.3 mmol) in CH_2Cl_2 (25 mL) was treated with PCC (0.20 g, 0.93 mmol). After stirring at room temperature for 7 h under N_2 the mixture was diluted with ether, filtered through a short column of silica gel, and concentrated to give **23s** (0.054 g, 0.28 mmol, 97%), identical with that prepared from **22s** as above.

Conversion of the Presumed 9s into 25s. A solution of one of the diols from the reduction of epoxide **8** (presumed to be **9s**) (0.017 g, 0.06 mmol) in CH_2Cl_2 (1 mL) was treated with anhydrous $ZnBr_2$ (0.067 g, and an additional 0.080 g after 4 h). After stirring at room temperature for 22 h under N_2 the mixture was partitioned between CH_2Cl_2 (40 mL) and saturated $NaHCO_3$ (40 mL). The organic layer was combined with ether washings of the aqueous layer, washed with brine, and dried (Na_2SO_4). Concentration gave an oil which was found by NMR to consist of a 7:3 mixture of unreacted **9s** and **25s**, the latter identical with that obtained as described above.

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Registry No. (±)-**4**, 85806-42-4; (±)-**5**, 82873-71-0; (±)-**6α**, 130552-47-5; (±)-**6β**, 130552-48-6; (±)-**7**, 130552-49-7; (±)-**8**, 130552-50-0; (±)-**9a**, 130552-51-1; (±)-**9s**, 130552-52-2; (±)-**10**, 130552-53-3; (±)-**11**, 130552-54-4; (±)-**12** (isomer 1), 130552-55-5; (±)-**12** (isomer 2), 130552-56-6; (±)-**13**, 130552-57-7; (±)-**15** (isomer 1), 130552-58-8; (±)-**15** (isomer 2), 130609-57-3; (±)-**16** (isomer 1), 130552-59-9; (±)-**16** (isomer 2), 130609-58-4; **17**, 130552-60-2; (±)-**18** (isomer 1), 130552-61-3; (±)-**18** (isomer 2), 130609-59-5; (±)-**19**, 130552-62-4; (±)-**20** (isomer 1), 130552-63-5; (±)-**20** (isomer 2), 130609-60-8; **20** (keto-alcohol, 130552-64-6; (±)-**21** (isomer 1), 130552-65-7; (±)-**21** (isomer 2), 130609-61-9; (±)-**22s**, 130552-66-8; (±)-**23s**, 130552-67-9; (±)-**24**, 130552-68-0; (±)-**25a**, 130552-70-4; (±)-**25s**, 130552-69-1; (±)-MEM-I, 130552-72-6; (±)-MEM-II (isomer 1), 130552-73-7; (±)-MEM-II (isomer 2), 130552-74-8; (±)-MEM-II (Me_3Si ether, isomer 1), 130573-26-1; (±)-MEM-II (Me_3Si ether, isomer 2), 130552-71-5; (±)-MEM-II (tosylate, isomer 1), 130552-75-9; (±)-MEM-II (tosylate, isomer 2), 130552-76-0.

Supplementary Material Available: High-field NMR spectra for **6α** (^{1}H), **6β** (^{1}H), **13** (^{1}H, ^{13}C), **15** (^{1}H, ^{13}C), **18** (^{1}H, ^{13}C), **9a** (^{1}H), **9s** (^{1}H), **23a** (^{1}H), **23s** (^{1}H), **25a** (^{1}H), and **25s** (^{1}H) (18 pages). Ordering information is given on any current masthead page.