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THE SYNTHESIS OF dl-CORIOLIN

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Abstract: The synthesis of dienone 2, which has previously been converted into the title compound in one step, is described. The methanoindene 7 is transformed into dienone-alcohol 8 in eighteen steps (12% overall yield). This was then hydroxylated at C-8, using the known method, to afford key dienone 2.

A number of projects in our laboratories involve the use of highly functionalized methanoindenes as versatile precursors for the synthesis of polycyclopentanoid natural products. One synthetic target that we have investigated is linearly fused tricyclopentanoid coriolin (1).

Coriolin (1) is one number of a class of sesquiterpenes known as hirsutanes. Since the isolation[1] and structure determination,[2] much attention has been directed to the synthesis of this molecule and others in the hirsutane class. The biological activity,[3] as well as the inherent challenge in assembling the highly functionalized and stereochemically complex and compact coriolin (1) system has given rise to a number of syntheses.[4] Herein, we report the full version of our synthesis of coriolin (1).

SYNTHETIC ANALYSIS

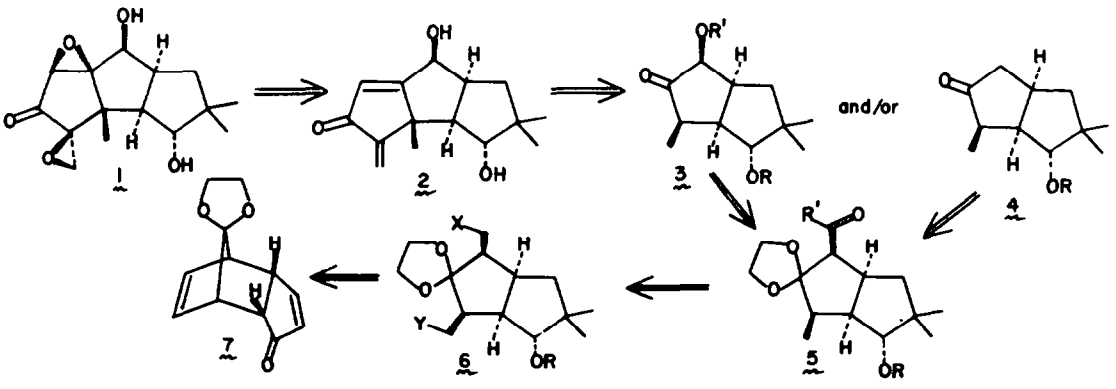
Coriolin (1) has been prepared from dienone 2 by double epoxidation. Therefore, our immediate goal was the preparation of this compound by the A-ring annulation of a suitable BC-ring system. Such a precursor might ideally be 3 with the C-8 β-hydroxyl in place, or a system such as 4 in which this group must be appended at a later time. Either 3 or 4 could be prepared in various ways from a C-8 acylated precursor 5, which would be available from a functionalized and differentiated bicyclo [3.3.0] system 6. We have reported[5] that 6 is easily prepared from enone 7.

RESULTS AND DISCUSSION

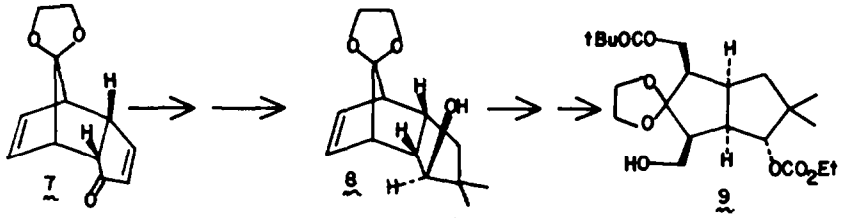
(i) B-RING FUNCTIONALITY

Enone 7[6] was converted to exo alcohol 8 in three steps. This was further transformed into a differentiated derivative 9 in several more steps as previously described[5] (Scheme I). We set about to reduce the C-3 hydroxymethyl to the requisite methyl group. The direct conversion of the primary alcohol of 9 to halide 10 (Scheme II) using standard methods ($SOBr_2$; $POBr_3$; PBr_3, etc.) gave none of the desired product. The conversion of 9 into tosylate 11 or mesylate 12, and subsequent relay attempts at displacement with halide (KI, KBr, NaI, etc.) gave only recovered starting materials. Attempts to directly reduce the sulfonate esters ($LiAlH_4$; $LiEt_3BH$; L or K selectrides; Zn, etc.) gave none of the desired methyl compound.

The two step procedure of Binkley[7] for



SCHEME I

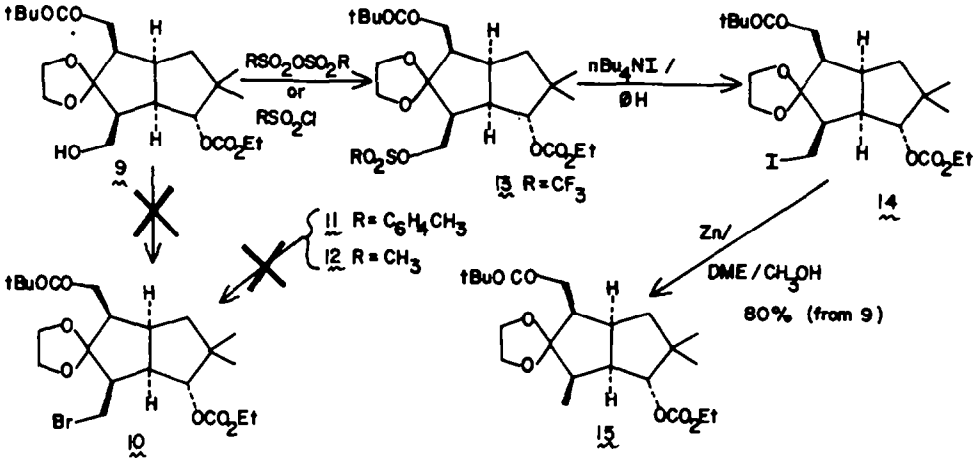


the preparation of hindered secondary halides was successfully applied to 9. Treatment of 9 with trifluoromethanesulfonic anhydride in pyridine gave the unstable triflate 13, which was subjected to halide displacement with tetra-n-butylammonium iodide in refluxing benzene to afford the iodide 14. This intermediate (14) was reduced with zinc in dimethoxyethane/methanol[8] to give the desired C-3 β-methyl compound 15 (80%) over three steps from alcohol 9.

A serious problem was now encountered; that of the selective hydrolysis of the pivalate ester in the presence of the ethyl carbonate in 15. Although numerous precedents existed[9] for the hydrolysis of an ester in the presence of a carbonate, treatment of 15 under either acidic (e.g., HCl/CH_3OH) or basic (e.g., K_2CO_3/CH_3OH; NH_3/CH_3OH) conditions led only to either recovery of starting material or complex product mixtures.

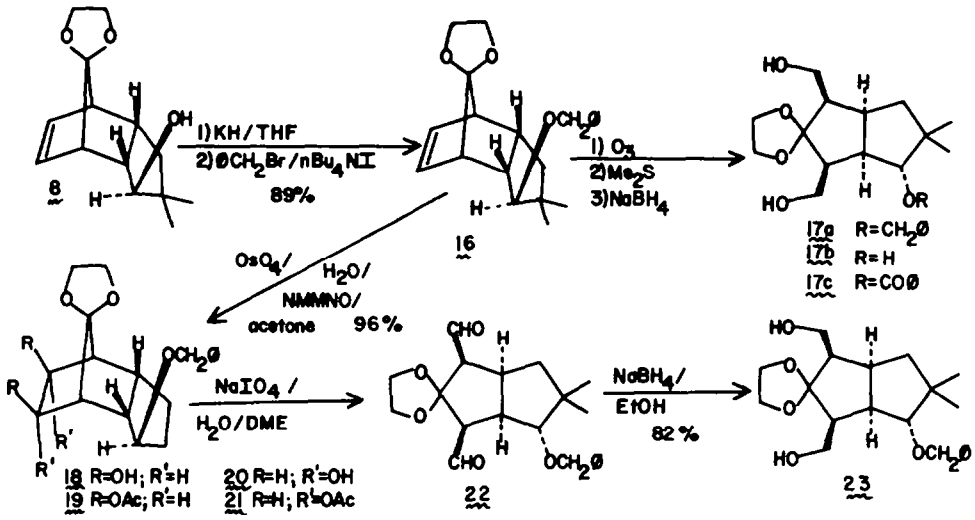
It now became essential to modify the plan so as to replace the C-1 carbonate with a protecting group that would survive the acidic or basic hydrolysis of the pivalate ester. Such a protecting group is the benzyl ether. Treatment of alcohol 8 with potassium hydride followed by addition of benzyl bromide and a catalytic amount of tetra-n-butylammonium iodide gave ether 16 (89%) (Scheme III). The use of NaH[10] or n-BuLi as the base led to longer reaction times and lower yields of 16. The difference in reactivity may be due to tighter binding of the alkoxide to the smaller cations, resulting in greater shielding of the anion and correspondingly lower nucleophilicity of this species.

SCHEME II



Ozonolytic cleavage of the olefin 16 followed by reductive workup ($NaBH_4$)[5] gave compound 17a(18%), as well as 17b(12%) and 17c(31%) which emanate from competitive benzylic oxidation. Fortunately, the reaction of 16 with catalytic osmium tetroxide (1 equiv. of N-methylmorpholine-N-oxide)[11] in aqueous acetone gave diol 18 (96%). The structure of this product is tentatively assigned as β-diol 18 based on the proton nuclear magnetic resonance spectrum of the derived (acetic anhydride/pyridine/4-dimethylaminopyridine)/diacetate 19. The acetate methine proton occur (200 MHz) as a two proton singlet at δ5.32. This is consistent with a 90° dihedral angle between these protons and the adjacent bridgehead protons. (The acetate 21 derived from α-diol (20) would suggest a coupling of 8-10 Hz (dihedral angle of ca. 20°)). The stereochemistry of the

SCHEME III



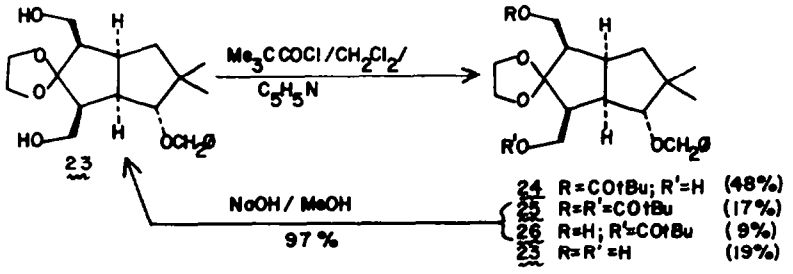
diol is not crucial however, as the next step involves the oxidative cleavage of 18 with sodium metaperiodate to give unstable dialdehyde 22, which was with sodium borohydride to afford bicyclic diol 23 (82% yield over three steps (from 16)).

A selective acylation of 23 was again done with pivaloyl chloride in pyridine/ methylene chloride (Scheme IV), giving a mixture of 24(48%), 25(17%), 26(9%) and 23(19%) (isolated yield after chromatography). Although the regioselectivity of acylation is not as great in the benzyl ether series as it was in the other examples[5], this is offset by the fact that the undesired 25 and 26 are easily recycled to starting diol 23 by saponification (sodium hydroxide/ methanol; 97%). This recycling is precluded in the case where the C-1 substituent is a carbonate because of the lability of this moiety (vide supra). Thus, resubmission of diol 23 to the acylation conditions gave the desired monopivalate 24 (86%)) after two recycles of 23, 25, and 26.

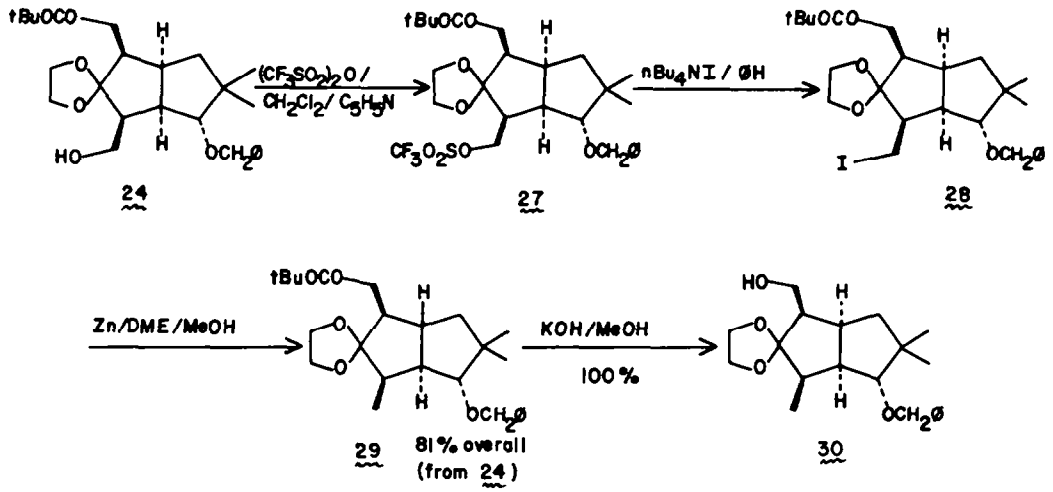
Reduction of the C-3 hydroxymethyl group in 24 was accomplished in the manner previously described. Treatment of alcohol 24 (Scheme V) with trifluoromethanesulfonic anhydride in pyridine/methylene chloride afforded the triflate 27, which was converted to iodide 28 with tetra-n-butylammonium iodide in refluxing benzene.[7] Zinc metal reduction[8] gave the desired 3β-methyl derivative 29 (81% yield over three steps (from 24)). Saponification of ester of 29 with methanolic potassium hydroxide afforded alcohol 30 (100%).

We now faced the conversion of the C-8 β-hydroxymethyl to the C-8 β-hydroxyl necessary for a coriolin (1) synthesis. One approach would involve conversion of the hydroxymethyl group to a methyl ketone and susequent Baeyer-Villiger oxidation (with retention of stereochemistry)[12] to the β-acetate. An alternative method would make use of a C-8 β-carboxylic acid derivative and proceed via a carboxy-inversion reaction sequence.[13] The Baeyer-Villiger sequence was investigated first (Scheme VI). Oxidation of 30 with pyridinium chlorochromate[14] afforded aldehyde 31(94%). Addition of methylmagnesium bromide to 31 gave alcohol 32(81%),

SCHEME IV

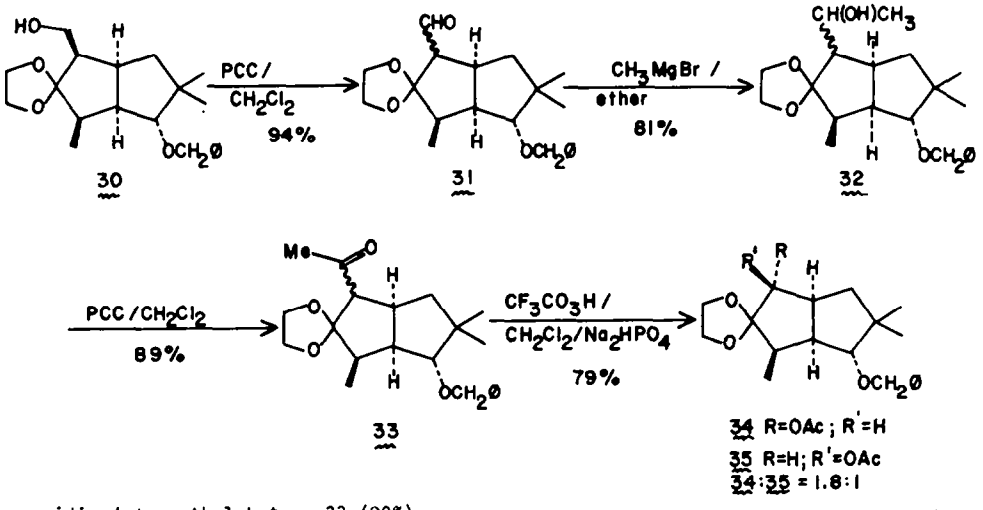


SCHEME V



24 27 28 29 30

SCHEME VI



30 31 32 33

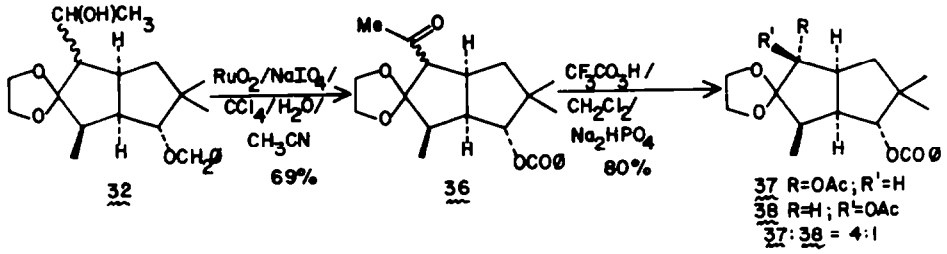
34 R=OAc ; R'=H
35 R=H; R'=OAc
34:35 = 1.8:1

which was oxidized to methyl ketone 33 (89%) with pyridinium chlorochromate.[14] Baeyer-Villiger oxidation[12] of 33 with buffered (Na_2HPO_4) peroxytrifluoroacetic acid[15] resulted in the formation of an acetate (79%). Examination of the proton nuclear magnetic resonance spectrum (200 MHz) revealed two acetyl methyl signals at δ2.06 and 2.07 (ratio ca. 1.8:1) that indicated the presence of two epimeric acetates 34 and 35. The configuration of the major isomer can be assigned to the α-acetoxy configuration based on the presence of the C-8 methine singlet at δ4.58, and the C-8 methine doublet (J=9.3 Hz) at δ4.80 in a ratio of 1.8:1. The δ4.58 singlet is assigned to the undesired C-8 α-acetoxy isomer 34 based on the examination of Dreiding molecular models, which predict a minimal coupling between the C-8 β-hydrogen and the C-9 α-hydrogen (dihedral angle ca. 90°). The δ4.80 doublet (J=9.3 Hz) is in excellent correspondence with the expected coupling between the C-8 α-hydrogen (in 35) and the C-9 α-hydrogen (dihedral angle ca. 10°).

A variation of the Baeyer-Villiger route (Scheme VI) was also pursued, which would convert the C-1 benzyl ether into an ester and allow for the simultaneous deprotection of the C-1 and C-8 alcohols by hydrolysis at a later stage. (Scheme VII). Therefore, alcohol 32 (as prepared in Scheme VI) was oxidized to ketone 36 with ruthenium dioxide and sodium metaperiodate[16] (69%). The ruthenium tetraoxide also oxidize the benzyl ether to a benzoate ester, and thereby gave a two-step oxidative-hydrolytic method of removing the

benzyl ether moiety[16,17] which is commonly removed by reductive methods. Baeyer-Villiger oxidation of 36 with Na_2HPO_4 buffered peroxytrifluoroacetic acid[15] gave an 80% yield of a mixture of C-8 epimeric acetates 37 and 38 (4:1). This ratio was determined by observing the multiplicity and coupling constants for the C-8 methine proton signals of 37 and 38. The undesired 37 showed a singlet at δ4.64 (dihedral angle ca. 90°), while the desired 38 displayed a doublet (J=9.3 Hz; dihedral angle ca. 10°) at δ4.84 in an integrated ratio of ca. 4:1.

SCHEME VII

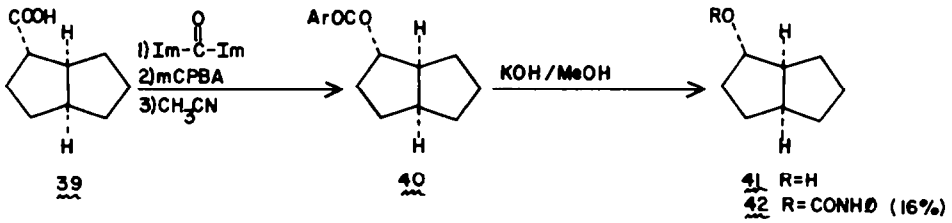


The 200 MHz proton nuclear magnetic resonance spectrum confirmed that epimerization had occurred during the pyridinium chlorochromate oxidation of 30 to 31. The C-8 β-proton signal for the α-aldehyde ($J_{H8\alpha,H9}$=0 Hz) occurs as a singlet at δ2.81 and is superimposed on a multiplet at δ2.73-2.90 corresponding to the C-8 α-proton of the desired β-aldehyde. Attempts to supress this problem by using buffers[14] or alternative oxidizing agents (e.g., CrO_3·2 pyridine[17] or pyridinium dichromate[17]) also resulted in extensive epimerization of the C-8 aldehyde.

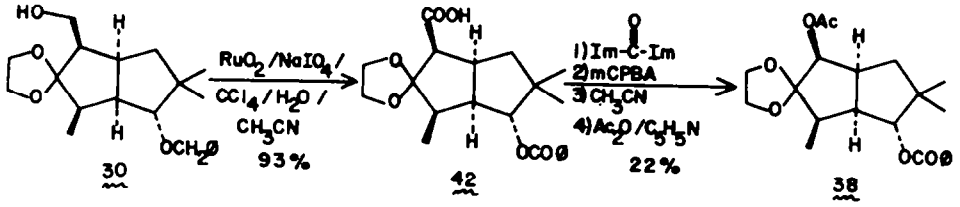
The alternative method for excision of the carbon at C-8 in 30 involved the use of a "carboxy-inversion" sequence.[13] A model study (Scheme VIII) using the bicyclic acid 39[19] was undertaken to optimize the reaction conditions. Treatment of acid 39 with carbonyldiimidazole followed by m-chloroperoxybenzoic acid and acetonitrile gave ester 40.[13f] Saponification with methanolic potassium hydroxide gave a single alcohol 41 (16%) isolated as the known phenylurethane 42.[20]

Application of this sequence to the coriolin (1) pathway was investigated (Scheme IX). Treatment of 30 with ruthenium dioxide and sodium metaperiodate[16,17] gave the acid benzoate 43 (93%). We could find no evidence for the formation of the C-8 epimeric acid. Treatment of 42 under the carboxy-inversion conditions[13f]: (1) carbonyldiimidazole/CH_2Cl_2, (2) m-chloroperoxy-benzoic acid, (3) acetonitrile/heat, (4) acetic anhydride/pyridine afforded a single acetate isomer 38

SCHEME VIII



SCHEME IX



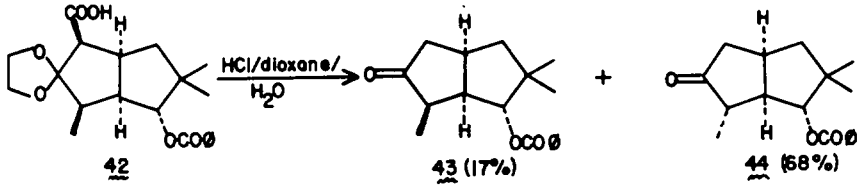
in 22% yield. The proton nuclear magnetic resonance spectrum (200 MHz) of 38 showed the C-8 α-proton as the expected doublet (J=9.3 Hz) at δ4.84 (dihedral angle ca. 10° with the C-9 α-proton).

Thus, two relatively efficient routes (Schemes VII and IX) were developed which gave predominantly the wrong C-8 acetate stereochemistry. The carboxy-inversion sequence gave a low overall yield. The lack of precedents regarding regioselectivity in the annulation of acyloins and derivatives,[21] and the possibility that the C-8 acyloin derivative could epimerize were also problems. This effectively precluded the use of this methodology and forced consideration of the less desirable option of removing the C-8 functionality and introducing the C-8 β-hydroxyl at a later stage.

(ii) A-RING ANNULATION

There have been a number of methods developed for the annulation of a cyclopentane ring.[23] Various approaches have been used in hirsutane syntheses, but the most direct method for a coriolin (1) synthesis is a "chloroolefin annulation" sequence developed by Lansbury.[24] An equivalent of the dipolar species 45 is used in the form of haloallylic alcohol 46. Lansbury reported that the Claisen alkylation[25] of an alkylated bicyclo [3.3.0] system[24a] with 46 (eg. 47) occurred with regio- and stereoselectivity to give the give the tricyclic material 48 in several steps.[26] The four carbon piece 46 is available by displacement (Scheme XI) of chloride ion from 49 by the sodium salt of n-propanethiol.[26] The dichloride 49 is easily prepared by the addition of hydrogen chloride to 1,4-butynediol in acetic acid.[27]

SCHEME X

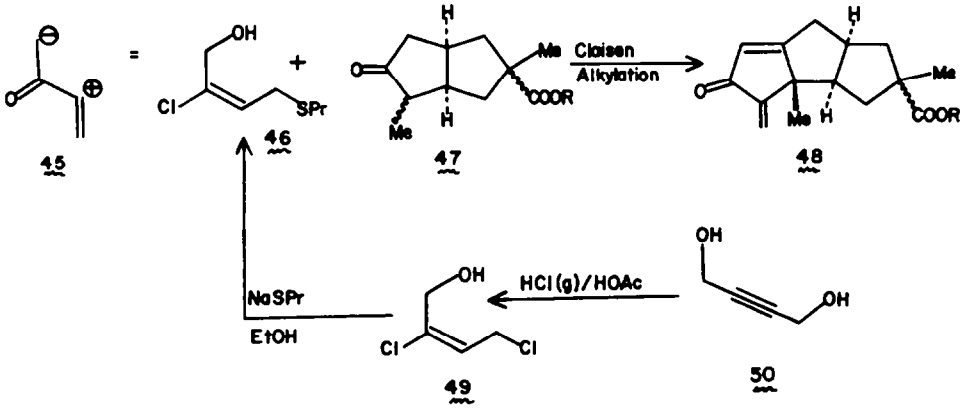


Treatment of acid 42 (Scheme X) with aqueous HCl in dioxane caused hydrolysis-decarboxylation and produced a mixture of epimeric ketones 43 and 44 (85%). The identities of these compounds were secured by comparison of the nuclear magnetic resonance and infrared spectra with spectra of authentic samples.[22] Since ketone 43 has been converted into coriolin (1) by Matsumoto,[4e] preparation of 43 constitutes a formal total synthesis.

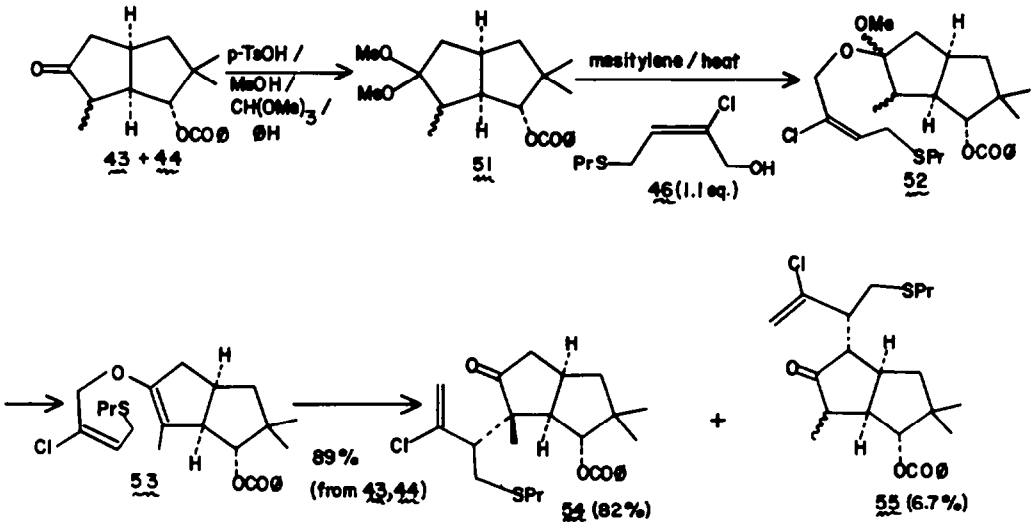
The use of this methodology would append much of the necessary A-ring functionality for a coriolin (1) synthesis. It would also allow us to employ both isomers 43 and 44 since the C-3 carbon becomes sp^2 hybridized prior to the Claisen rearrangement.

Treatment of a mixture of 43 and 44 (Scheme XII) with trimethylorthoformate (1

SCHEME XI



SCHEME XII

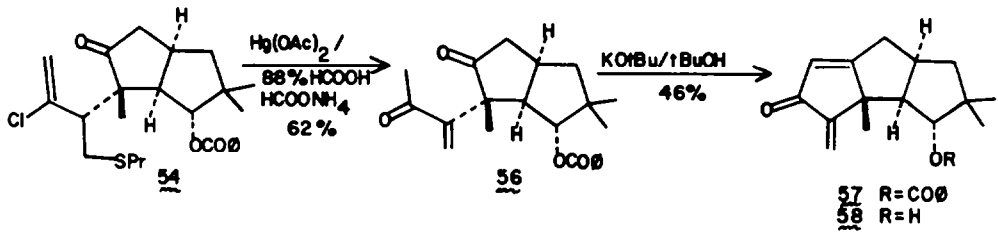


equiv.) and methanol (10 equiv.) in benzene containing p-toluenesulfonic acid and slowly raising the temperature from 25° to 60°C gave a solution of dimethyl ketals 51. The Claisen Alkylation occurs from 51 in one pot (p-TsOH/mesitylene (60° to 160°C)) in three sequential steps: (1) trans-ketalization of 51 (1.1 equiv. 46) to form mixed ketal 52, (2) elimination of methanol to give enol ether 53 and (3) Claisen rearrangement with delivery of the four carbon piece from the sterically less hindered α-face to afford vinyl chloride 54 in 82% yield. A small amount (6.7%) of regioisomer 55 was also isolated. No report of rearrangement in this direction had been reported previously.[24,26] A possible explanation for this may be that the C-1 benzoate, although somewhat distant, could hinder rearrangement of the butenyl side chain (53) to the C-3 position (giving 54). No such interaction present in the C-8 direction (giving 55).

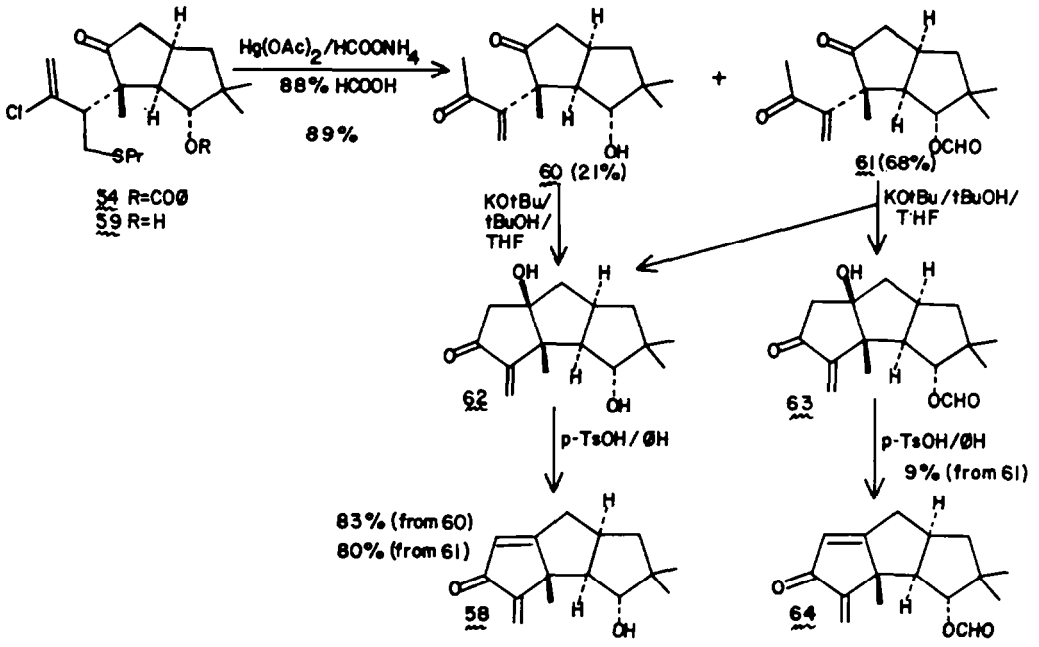
Upon treatment of 54 with mercuric acetate (4 equiv.)[28] in 88% formic acid (Scheme XIII) both hydrolysis of the vinyl chloride and elimination of n-propanethiol occurred to afford enone 56 (62%). Aldol cyclization-dehydration of 56 took place upon treatment with potassium t-butoxide (1 equiv.) in t-butanol to give dienone 57 (46%). However, all attempts to hydrolyze the C-1 benzoate to the known alcohol 58[46] in the presence of the sensitive dienone in the A-ring led to decomposition.

Hydrolysis of the C-1 benzoate at the Claisen alkylation stage (54) (Scheme XIV) with tetra-n-butylammonium hydroxide in aqueous methanol afforded alcohol 59 (100%). Treatment of alcohol 59 with mercuric acetate/ammonium formate/88% formic acid produced a mixture of keto-alcohol 60(21%) and keto-formate 61(68%). Direct aldol-dehydration (potassium t-butoxide/t-butanol) of 60 and 61 gave poor yields (ca. 39%) of the dienone 58. The two-step procedure through the β-ketol[26] led to the product in a more efficient manner. Diketo-alcohol 60 cyclized to the crude β-ketol 62 (potassium t-butoxide/tetrahydrofuran/t-butanol which underwent β-elimination to dienone 58 upon treatment with p-toluenesulfonic acid in benzene (83% over two steps). In a similar manner, formate 61 underwent the aldol con-

SCHEME XIII



SCHEME XIV



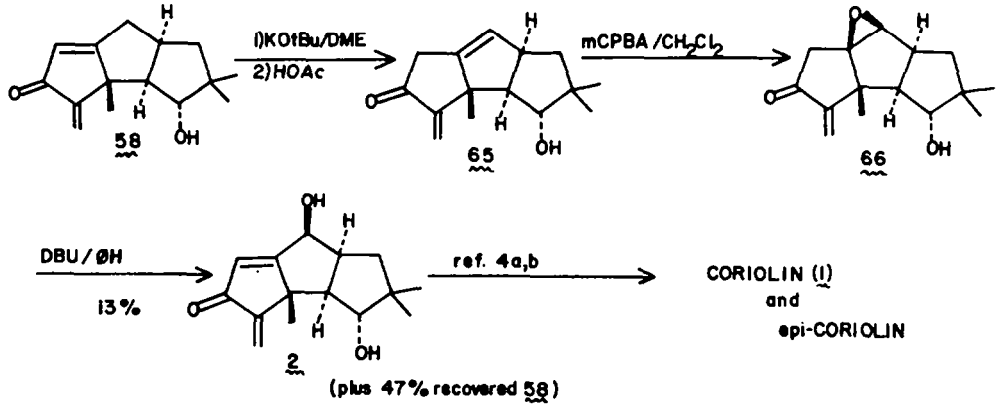
densation to a mixture of alcohol 62 and formate 63, which upon β-elimination afforded a mixture of dienone alcohol 58 (80%) and dienone formate 64 (9%). The spectroscopic properties (^{1}H-NMR;IR;MS) of dienone 58 were identical to those reported by Ikegami.[4c]

For further proof of structure, and for the purpose of introduction of the C-8 β-hydroxyl group, the dienone 58 was converted into the Danishefsky-Tatsuta diol[4a,b] (2) by the Ikegami[4c] procedure (Scheme XV).

Deconjugation of 58[29] (potassium-t-butoxide dimethoxyethane) gave a mixture of β,γ-unsaturated ketone 65 and starting material (58). Epoxidation of the mixture (m-chloroperoxy-benzoic acid/methylene chloride) gave the β,γ-epoxide 66, which underwent β-elimination with diazabicycloundecene (DBU) to afford diol 2 in 13% yield and recovered dienone 58(47%). The spectroscopic data for 2 is also in full accord with the data reported by both Tatsuta[4a] and Danishefsky.[4b] Since 2 has been converted into 1[4a,b], its preparation constitutes a completion of the synthesis of coriolin (1).

The overall yield from methanoindene 7 to the tricyclic alcohol 58, a known coriolin (1) intermediate,[4c] was 12% for eighteen steps. The viability of the strategy of using a readily available and highly funtionalized methanoindene as a source of five-membered rings has been demonstrated by the synthesis of coriolin (1). The application of this strategy to the synthesis of other polycyclopentanoid natural products is in progress.

SCHEME XV



EXPERIMENTAL

Proton spectra were recorded on a Varian EM 360A, Varian XL 100 or IBM WP-200 spectrometer, using Me_4Si as the internal standard. Infrared spectra were recorded on a Perkin-Elmer Model 281 spectrophotometer. Melting points were obtained on a Mel-Temp or Fisher Johns melting point apparatus and are uncorrected. Flash chromatography refers to the method described by Still,[30] using E. Merck silica gel 60 (230-400 mesh). Thin layer chromatography (TLC) was performed on E. Merck glass or aluminum foil supported silica gel 60 (0.25 mm, F-254). Silica gel for column chromatography was Baker reagent grade (60-200 mesh). Analyses for C and H were obtained by Dr. Franz Kasler of the University of Maryland.

Preparation and Zinc Reduction of Bicyclic Iodide. Preparation of 15. Trifluoromethanesulfonic anhydride (0.19 mL, 310mg, 1.1 mmol) was added dropwise to a solution of dry pyridine (0.12 mL, 119mg, 1.5 mmol) in 10 mL of dry CH_2Cl_2 at -10°C. The white suspension was stirred for 5 min followed by dropwise addition of alcohol 9 (228.5mg, 0.53 mmol) in 5 mL of CH_2Cl_2. After stirring for 1.5 h at -10°C, it was poured into 20 mL of saturated aqueous $NaHCO_3$. The aqueous layer was extracted with ether (2 x 15 mL) and the combined organic solutions washed with cold 10% aqueous HCl (2 x 10 mL), saturated aqueous $NaHCO_3$ (2 x 10 mL), and saturated aqueous NaCl (10 mL), dried over Na_2SO_4 and concentrated. The yellow oily residue (13) was treated with nBu_4NI (550mg, 1.5 mmol) in 25 mL of benzene and refluxed for 1 h. The orange solution was diluted with 25 mL of ether, washed with H_2O (2 x 10 mL), saturated aqueous Na_2SO_3 (2 x 10 mL), H_2O (10 mL), and saturated aqueous $NaHCO_3$ (10 mL), dried over Na_2SO_4 and concentrated in vacuo. The yellow oily iodide 14 was refluxed with activated zinc (20 mesh, 1.63g, 2.5 mmol) in 12 mL of DME and 2 mL of methanol for 24 h,[8] diluted with 30 mL of ether and filtered through celite. The filtrate was concentrated in vacuo to a yellow oil which was purified by flash chromatography (10% EtOAc in hexane eluant) to yield 15. (173.1mg, 79%) as a colorless crystalline solid mp 83-84°C (ether-pet.ether). NMR ($CDCl_3$, 200MHz) δ0.92(d, 3H, J=7Hz), 0.92(s, 3H), 1.01(s, 3H), 1.18(s, 9H), 1.28-1.41(m, 1H), 1.31(t, 3H, J=7.1Hz), 1.54-1.80(m, 1H), 2.10-2.30(m, 1H), 2.33-2.84(m, 3H), 3.80-4.05(m, 4H), 4.10-4.30(m, 4H), 4.98(d, 1H, J=6.6Hz); IR ($CHCl_3$) 3030, 2970, 2940, 2900, 1740, 1720, 1270, 1230, 1165, 1010cm^{-1}; m/e 412(M^+).

10,10-Ethylenedioxy-3β-benzyloxy-4,4-dimethyl-1α,2β,6β,7α-tricyclo-[5.2.1.0^{2,6}]dec-8-ene (16). A solution of exo-alcohol 8 (4.81g, 20.3 mmol) in 40 mL of anhydrous THF was added dropwise over 15 min to a suspension of KH (24% in oil, 4.04g, 24 mmol) in 40 mL of THFcooled to 0°C under N_2. The solution was stirred at room temperature for 45 min, then nBu_4NI[10] (72mg, 0.2 mmol) and benzyl bromide (2.9 mL, 4.1g, 24 mmol) added. The mixture was stirred for 75 min, 100 mL of H_2O added and the THF removed in vacuo. The aqueous layer was extracted with ether (4 x 30 mL) and the combined extracts washed with 20 mL of saturated aqueous NaCl, dried over Na_2SO_4 and concentrated to a yellow oil which was purified by flash chromatography (10% EtOAc in hexane eluant) to yield benzyl ether 16 (5.86g, 89%) as a clear viscous oil. NMR($CDCl_3$, 200 MHz) δ0.75-1.05(m, 1H), 0.93(s, 3H), 1.00(s, 3H), 1.30-1.50(m, 1H), 2.44-2.55(m, 1H), 2.58-2.65(m, 1H), 2.65-2.78(m, 1H), 2.81-2.99(m, 1H), 2.92(d, 1H, J=7.7Hz), 3.75-3.85(m, 2H), 3.85-3.96(m, 2H), 4.49(d, 1H, J=12.3Hz), 4.65(d, 1H, J=12.3Hz), 6.02(bd dd, 1H, J=3.3, 6.2Hz), 6.15(bd dd, 1H, J=3.3, 6.2Hz), 7.30(m, 5H); IR ($CHCl_3$) 3060, 3000, 2950, 2880, 2860, 1450, 1280, 1100, 1080cm^{-1}; m/e 326(M^+); Anal. Calcd for $C_{21}H_{26}O_3$: C, 77.27; H, 8.03. Found: C, 77.05; H, 8.18.

Ozonolysis of Benzyl Ether 16. A solution of benzyl ether 16 (816mg, 2.5 mmol) in 30 mL of CH_3OH and 8 mL of CH_2Cl_2 was cooled to -70°C and O_3/O_2 bubbled through for 15 min. Excess ozone was removed by purging with O_2 for 10 min and then dimethyl sulfide (3 mL) was added. The solution was stirred for 10 min, and treated with $NaBH_4$ (760mg, 20 mmol) added in portions over 4 h. The mixture was warmed to 0°C and $NaBH_4$ (380mg, 10 mmol) added. The mixture was stirred at 0°C for 2 h, warmed to room temperature and H_2O (10 mL) added. Methylene chloride and CH_3OH were removed in vacuo, the residue was diluted to 40 mL with H_2O and extracted with CH_2Cl_2 (4 x 30 mL). The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4 and concentrated to 611mg. Flash chromatography (40-100% EtOAc in hexane eluant) of the residue afforded 3 components in order of elution. Diol 17a(159.1mg, 18%). NMR ($CDCl_3$, 200MHz) δ1.01(s, 3H), 1.20-1.40(m, 1H), 1.25(s, 3H), 1.45-1.65(m, 3H), 2.31(dd, 1H, J=7, 15Hz), 2.40-2.58(m, 1H), 2.58-2.80(m, 2H), 3.56-3.98(m, 9H), 4.49(d, 1H, J=10.6Hz), 4.80(d, 1H, J=10.6Hz), 7.23(bd s, 5H); IR ($CHCl_3$) 3600, 3460, 3010, 2960, 2900, 1050, 1030cm^{-1}; Anal. Calcd for $C_{21}H_{30}O_5$: C, 69.59; H, 8.34. Found: C, 69.39; H, 8.55. Benzoate-Diol 17c (288.1mg, 31%). NMR ($CDCl_3$, 60 MHz) δ0.90-1.80(m, 3H), 1.03(s, 6H), 2.00-3.10(m, 5H), 3.40-4.00(m, 8H), 5.30(d, 1H, J=7Hz), 7.05-7.45(m, 3H), 7.75-8.05(m, 2H); IR ($CHCl_3$) 3480, 3030, 2970, 2900, 1715, 1200, 1050, 1025cm^{-1}. Triol 17b(85.8mg, 12%).[5]

10,10-Ethylenedioxy-3β-benzyloxy-8,9-dihydroxy-4,4-dimethyl-1α,2β,6β,7α-tricyclo [5.2.1.0^{2,6}] decane (18). A solution of 16 (979.2mg, 3 mmol) in 12 mL of acetone was added to a solution of N-methylmorpholine-N-oxide monohydrate[11] (426mg, 3.15 mmol) and OsO_4 (10% in THF, 0.15 mL, 0.06 mmol) in 12 mL of H_2O. The two phase system was stirred vigorously for 12 h at 45°C. The light brown mixture was stirred with a slurry of sodium hydrosulfite (300 mg) and 3 g of Florisil in 10 mL of H_2O at room temperature for 1 h. The suspension was filtered through celite and the cake washed with acetone (3 x 10 mL). All volatiles were removed in vacuo and the residue dissolved in 100 mL of 1:1 CH_2Cl_2/EtOAc, washed with H_2O (2 x 10 mL), 10% aqueous HCl (2 x 15 mL), saturated aqueous $NaHCO_3$, and saturated aqueous NaCl, dried over Na_2SO_4 and concentrated to yield diol 18 as a pale yellow oil (1.05 g, 96%) which was used for $NaIO_4$ cleavage (vide infra). For analysis, a small portion of the diol was purified by flash chromatography and acylated (vide infra). NMR ($CDCl_3$, 60 MHz) δ0.90-1.35(m, 2H), 0.99(s, 3H), 1.03(s, 3H), 1.65-2.10(m, 3H), 2.30-3.50(m with d, J=7Hz at 3.23, 7H), 3.75-4.10(m, 4H), 4.47(AB q, 2H, J=11Hz), 7.23(bd s, 5H).

10,10-Ethylenedioxy-8,9-diacetoxy-3β-benzyloxy-4,4-dimethyl-1α,2β,6β,7α-tricyclo[5.2.1.0^{2,6}] decane (19). Diol 18 (257mg, 0.71 mmol) was treated with 1.5 mL of Ac_2O and 4-dimethylamino-pyridine (6mg, 0.05 mmol) in 1.5 mL of pyridine and stirred for 15 h. All volatiles were removed in vacuo and the residue dissolved in CH_2Cl_2 (20 mL), washed with 10% aqueous HCl (2 x 5 mL), saturated aqueous $NaHCO_3$ (5 mL) and saturated aqueous NaCl (5 mL), dried over Na_2SO_4 and concentrated in vacuo to a tan solid (310mg, 98%). Recrystallization from using 95% ethanol gave diacetate 19 (270mg, 85%) as colorless crystals mp 160-161°C. NMR ($CDCl_3$, 200 MHz) δ1.01(s, 3H), 1.07(s, 3H), 1.18-1.58(M, 2H), 1.89(dd, 1H, J=1.5, 4.8Hz), 1.98(dd, 1H, J=1.5, 4.9Hz), 2.08(s, 3H), 2.10(s, 3H), 2.54-2.69(m, 1H), 2.70-2.92(m, 1H), 3.43(d, 1H, J=8.4Hz), 3.78-3.87(m, 2H), 3.92-4.04(m, 2H), 4.54(d, 1H, J=12.2Hz), 4.62(d, 1H, J=12.2), 5.32(s, 2H), 7.27-7.37(m, 5H); IR ($CHCl_3$)3010, 2960, 2880, 1740, 1735, 1260cm^{-1}; m/e 444(M^+), 385(OAc); Anal. Calcd for $C_{25}H_{32}O_7$: C, 67.55; H, 7.26. Found: C, 67.53; H, 7.42.

3,3-(Ethylenedioxy)-2β,4β,-bis-(hydroxymethyl)-6α-benzyloxy-7,7-dimethyl-1α,5α-bicyclo [3.3.0] octane (23). A solution of diol 18 (1.05g, 3 mmol) in 21 mL of DME and 7 mL of H_2O was treated with $NaIO_4$ (674mg, 3.15 mmol) at room temperature for 1.5 h. The salts were filtered and washed with ethyl acetate (3 x 15 mL). The filtrates were concentrated in vacuo to a solid which was dissolved in 30 mL of absolute ethanol and treated with $NaBH_4$ (240mg, 6 mmol). After 2.5 h, 10 mL of H_2O was added, the ethanol removed in vacuo, and the residue diluted to 30 mL with H_2O and extracted with CH_2Cl_2 (4 x 20 mL). The combined extracts were washed with saturated aqueous NaCl (10 mL), dried over Na_2SO_4 and concentrated to a clear oil which crystallized from ether to yield 23 (890mg, 82% over 3 steps from olefin 16) which was identical to a sample prepared by ozonlysis of 16 (vide supra). NMR ($CDCl_3$, 200 MHz) δ1.01(s, 3H), 1.20-1.40(m, 1H), 1.25(s, 3H), 1.45-1.65(m, 3H), 2.31(dd, 1H, J=7, 15Hz), 2.40-2.58(m, 1H), 2.58-2.80(m, 2H), 3.56-3.98(m, 9H), 4.49(d, 1H, J=10.6Hz), 4.80(d, 1H, J=10.6Hz), 7.23(bd s, 5H); IR ($CHCl_3$) 3600, 3460, 3010, 2960, 2900, 1050, 1030cm^{-1}; Anal. Calcd for $C_{21}H_{30}O_5$: C, 69.59; H, 8.34. Found: C, 69.39; H, 8.55.

Reaction of Diol 23 with Pivaloyl Chloride: Preparation of 3,3-(Ethylenedioxy)-2β-(trimethylacetoxymethyl)-4β-(hydroxymethyl)-6α-benzyloxy-7,7-dimethyl-1α,5α-bicyclo [3.3.0] octane (24). A solution of 23 (2.17g, 6.0 mmol) in 10 mL of dry pyridine and 35 mL of dry CH_2Cl_2 was cooled to -20°C and pivaloyl chloride (0.81 mL, 0.80g, 6.6 mmol) in 5 mL of CH_2Cl_2 added dropwise over 30 min. The solution was stirred at -20°C for 20 h, and 3 mL of methanol added to destroy any pivaloyl chloride. The mixture was warmed to room temperature and the volatiles removed in vacuo. The residue was dissolved in 75 mL of CH_2Cl_2 and with 10% aqueous HCl (2 x 15 mL), H_2O (2 x 15 mL), saturated aqueous $NaHCO_3$ (2 x 15 mL), H_2O (15 mL), and saturated aqueous NaCl (15 mL), dried over Na_2SO_4, and concentrated to a yellow oil. The products were separated by flash chromatography (25-100% EtOAc in hexanes eluant) to yield in order of elution:

Dipivalate 25 (532mg, 16.7%). NMR ($CDCl_3$, 200MHz) δ0.98(s, 3H), 1.00-1.34(m, 1H), 1.11(s, 9H), 1.17(s, 3H), 1.19(s, 9H), 1.46-1.66(m, 1H), 2.36-2.53(m, 1H), 2.54-2.74(m, 1H), 3.63(d, 1H, J=7.4Hz), 3.83-4.03(m, 4H), 4.23(dd, 1H, J=11.2, 7.3Hz), 4.38(dd, 1H, J-11.2, 5.6Hz), 4.50(d, 1H, J=10.9Hz), 4.68(d, 1H, J=10.9Hz), 7.20-7.40(m, 5H); IR ($CHCl_3$) 2970, 2940, 2900, 2870, 1720, 1480, 1285, 1165cm^{-1}.

Monopivalate 24 (1.23g, 48.1%) mp. 103.5-104°C (ether). NMR ($CDCl_3$, 200 MHz) δ1.02(s, 3H), 1.14-1.37(m, 1H), 1.19(s, 9H), 1.26(s, 3H), 1.52-1.65(m, 1H), 2.38-2.58(m, 2H), 2.61-2.79(m, 2H), 3.65(bd s, 1H), 3.75-3.95(, 7H), 4.10(d, 2H, J=7.3Hz), 4.49(d, 1H, J=10.6Hz), 4.80(d, 1H, J=10.6Hz), 7.35(m, 5H); IR ($CHCl_3$) 3500, 2970, 2940, 2900, 1720, 1285, 1165cm^{-1}; m/e 430(M^+); Anal. Calcd for $C_{26}H_{38}O_6$: C, 69.93; H, 8.58. Found: C, 70.22; H, 8.87.

Monopivalate 26 (240mg, 9.0%). NMR ($CDCl_3$, 200 MHz) δ0.97(s, 3H), 1.12(s, 9H), 1.15-1.35(m, 1H), 1.16(s, 3H), 1.45-1.70(m, 1H), 1.66(bd s, 1H), 2.24-2.39(m, 1H), 2.40-2.54(m, 1H), 2.55-2.75(m, 2H), 3.62(d, 1H, J=7.6Hz), 3.65(dd, 1H, J=6.5, 10.8Hz), 3.81(dd, 1H, J=7.5, 10.8Hz), 3.88-4.13(m, 4H), 4.21(dd, 1H, J=7.5, 11.3Hz), 4.39 (dd, 1H, J=5.2, 11.3Hz), 4.49(d, 1H, J=11.0Hz), 4.67(d, 1H, J=11.0Hz), 7.20-7.40(m, 5H); IR ($CHCl_3$) 2970, 2940, 2910, 1720, 1485, 1290, 1170cm^{-1}. Diol 23 (411 mg, 18.9%).

Hydrolysis of Dipivalate 25 and Monopivalate 26. A solution of dipivalate 25 (315.7mg, 0.59 mmol), monopivlate 26 (199.1mg, 0.45 mmol), and 5 mL of 5% aqueous NaOH in 15 mL of methanol was refluxed for 28 h. Methanol was removed under reduced pressure, the aqueous residue diluted to 40 mL, with H_2O and extracted with CH_2Cl_2 (4 x 10 mL). The combined extracts were washed with 10 mL of saturated aqueous NaCl, dried over Na_2SO_4, and concentrated to yield pure diol 23 (364mg, 97%).

3,3-(Ethylenedioxy)-2β-(trimethylacetoxymethyl)-6α-benzyl-oxy-4β,7,7-trimethyl-1α,5α-bicyclo [3.3.0] octane (29). A solution of pyridine (0.19 mL, 0.18g, 2.3 mmol) in 3.5 mL of dry CH_2Cl_2 was cooled to -23°C and trifluoromethanesulfonic anhydride (0.37 mL, 0.62g, 2.2 mmol) added slowly. The white suspension was stirred for 10 min followed by addition of alcohol 24 (446.5mg, 1.0 mmol). After stirring at -23°C for 30 min the mixture was partitioned between cold saturated aqueous $NaHCO_3$ (25 mL) and ether (25 mL). The organic layer was washed with cold 10% aqueous HCl (2 x 2 mL), H_2O (2 x 2 mL) and saturated aqueous $NaHCO_3$ (2 x 2 mL), dried over Na_2SO_4 and concentrated to a yellow oil. The triflate 27 was dissolved in 30 mL of benzene, treated with nBu_4NI[7] (1.10g, 3.0 mmol), and heated at reflux for 1.5 h. The solution was diluted with 30 mL of ether, washed with saturated aqueous Na_2SO_3 (4 x 5 mL), saturated aqueous $NaHCO_3$ (2 x 5 mL), H_2O (2 x 5 mL) and saturated aqueous NaCl (5 mL), dried over Na_2SO_4 and concentrated in vacuo to a golden oil. The iodide 28 was treated with activated zinc metal (3.25g, 49.7 mmol) in methanol/DME (3 mL/27mL) and refluxed for 4 d.[8] The suspension was diluted with 30 mL of ether, filtered through celite, and concentrated to afford an oil which was purified by flash

chromatography (5% EtOAc in hexane eluant) to yield 29 (350.1mg, 81%) as a colorless oil. NMR ($CDCl_3$, 200MHz) δ0.98(s, 3H), 1.02(d, 3H, J=6.9Hz), 1.18-1.33(m, 1H), 1.19(s, 12H), 1.49-1.69(s, 1H), 2.15-2.80(m, 4H), 3.65(d, 1H, J=7.9Hz), 3.85-4.22(m, 4H), 4.11(d, 2H, J=7.3Hz), 4.51(d, 1H, J=11.0Hz), 4.71(d, 1H, J=11.0Hz), 7.22-7.44(m, 5H); IR ($CHCl_3$) 2970, 2935, 2890, 1720, 1290, 1165cm^{-1}.

3,3-(Ethylenedioxy)-2β-hydroxymethyl-6α-benzyloxy-4β,7,7-tri-methyl-1α,5α-bicyclo [3.3.0]-octane (30). A solution of pivalate 29 (350.1mg, 0.81 mmol) and KOH (450mg, 8.1 mmol) in 10 mL of methanol and 7 mL of H_2O was refluxed for 6 h. the methanol was removed in vacuo, the aqueous residue diluted to 25 mL with H_2O and extracted with CH_2Cl_2 (4 x 5 mL). The combined extracts were washed with H_2O (5 mL) and saturated aqueous NaCl (5 mL), dried over Na_2SO_4 and concentrated to a solid which was triturated with ether (0°C) to give colorless crystals (271.5mg, 97%) mp 148.5-150°C. NMR ($CDCl_3$, 200MHz) δ0.97(s, 3H), 1.03(d, 3H, J=6.9Hz), 1.18-1.42(m, 1H), 1.18(s, 3H), 1.49-1.70(m, 2H), 2.14-2.37(m, 2H), 2.37-2.77(m, 2H), 3.64(d, 1H, J=7Hz), 3.74-4.16(m, 6H), 4.51(d, 1H, J=10.9Hz), 4.71(d, 1H, J=10.9Hz), 7.19-7.28(m, 5H); IR ($CHCl_3$) 3610, 3550, 3100, 3080, 3040, 3010, 2970, 2940, 2900, 1240, 1125, 1070, 1010cm^{-1}; Anal. Calcd for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73. Found: C, 72.61; H, 8.88.

Pyridinium Chlorochromate (PCC) Oxidation of Alcohol 30. Preparation of 31. Alcohol 30 (346.8mg, 1.0 mmol) was added to a suspension of PCC (430mg, 2.0 mmol) in 12 mL of CH_2Cl_2, stirred at room temperature for 1 hour, then diluted with 25 mL of ether. The supernatant solution was decanted, and the tarry residue triturated with ether (4 x 10 mL). The combined organic solutions were filtered through a short (ca. 6 cm.) column of silica gel. The filtrate was concentrated in vacuo to afford crystals (328.8mg, 94%) of aldehyde 31. NMR ($CDCl_3$, 200MHz, mixture of epimers) δ0.98(s, 3H), 1.05(d, 3H, J=7.0Hz), 1.13-1.30(m, 1H), 1.21(s, 3H), 1.50-1.80(m, 2H), 2.15-2.35(m, 1H), 2.44-2.65(m, 1H), 2.73-2.90(m, s at 2.81, 1H), 3.74(d, 1H, J=8.2Hz), 3.85-4.12(m, 4H), 4.52(d, 1H, J=11.0Hz), 4.73(d, 1H, J=11.0Hz), 7.20-7.40(m, 5H), 9.81(d, 1H, J=1.8Hz); IR ($CHCl_3$) 2970, 2900, 1710, 1450, 1210, 1100cm^{-1}; m/e=344(M^+).

Reaction of Aldehyde 31 with MeMgBr. Preparation of 32. Aldehyde 31 (117.3mg, 0.34 mmol) in 3 mL of anhydrous ether was cooled to 0°C under a N_2 atmosphere and MeMgBr (2.8M in ether, 0.14 mL, 0.39 mmol) added dropwise. The suspension was stirred at 0°C for 30 min, hydrolyzed with 3 mL of 2N aqueous NH_4Cl, and diluted with 15 mL of CH_2Cl_2. The organic layer was washed with H_2O (3 mL) and saturated aqueous NaCl (3 mL), dried over Na_2SO_4 and concentrated to a yellow oil. Flash chromatography (15-30% EtOAc in hexane eluant) yielded alcohol 32 (98.9mg, 81%) as a mixture of epimers. NMR ($CDCl_3$, 60MHz) δ0.95-1.30 (overlapping singlets and doublets, 12H), 1.30-3.15(m, 7H), 3.60(bd d, 1H, J=6Hz), 3.70-4.30(m, 5H), 4.54(AB q, 2H, J=11Hz), 7.10(s, 5H). IR (film) 3400, 2980, 2940, 2890, 1020cm^{-1}.

Pyridinium Chlorochromate (PCC) Oxidation of Alcohol 32. Preparation of 33. Alcohol 32 (98.9mg, 0.27 mmol) in 3 mL of CH_2Cl_2 was added rapidly to a stirred suspension of PCC in 2 mL of CH_2Cl_2 and the mixture stirred for 5 h. Ether (10 mL) was added, the supernatant decanted, and the residue triturated with ether (3 x 10 mL). The combined solutions were filtered through a short column of silica gel and concentrated to an oil which was purified by preparative TLC (20% EtOAc in hexane eluant) to yield an epimeric mixture of ketones 33 (86.5mg, 89%) as a crystalline solid mp 88-90°C (ether-hexane). NMR ($CDCl_3$, 200MHz) δ0.99(s, 3H), 0.95-1.30(m, 1H), 1.01(d, 3H, J=8Hz), 1.35-1.75(m, 1H), 1.18(s, 3H), 2.05-2.35(m, 1H), 2.10(s, 3H), 2.40-2.65(m, 1H), 2.80-3.15(m, s at 2.98, 2H), 3.75(d, 1H, J=8.0Hz), 3.90-4.30(m, 4H), 4.51(d, 1H, J=10.8Hz), 4.71(d, 1H, J=10.8Hz), 7.20-7.50(m, 5H); IR ($CHCl_3$) 3020, 2990, 2940, 2905, 1715, 1470, 1460, 1360, 1210, 1125, 1075, 1060cm^{-1}; Anal. Calcd for $C_{22}H_{30}O_4$: C, 73.71; H, 8.44. Found: C, 73.66; H, 8.64.

Baeyer-Villiger Oxidation of Ketone 33 with Peroxytrifluro-acetic acid.[15] Preparation of 34 and 35. Trifluoroacetic anhydride (38μL, 0.27 mmol) was added to a mixture of 90% H_2O_2 (6μL, 0.25 mmol) in 1 mL of dry CH_2Cl_2 at 0°C. The solution was stirred at 0°C for 5 min, warmed to room temperature for 10 min, then stirred over 100mg anhydrous Na_2SO_4. The peracid solution was decanted and added to a suspension of ketone 33 and Na_2HPO_4 (38mg, 0.27 mmol) in 1 mL of CH_2Cl_2 at 0°C. The reaction mixture was stirred at 0°C for 30 min, then at room temperature for 2 h. Additional portions of Na_2HPO_4 (190mg, 1.35 mmol) and CF_3CO_3H (0.5 mmol, prepared from 80μL $(CF_3CO)_2O$ and 12μL 90% H_2O_2 in 1 mL of CH_2Cl_2) were added and stirring continued at room temperature for 16 h. Ether (20 mL) and the solution was washed with saturated aqueous $NaHSO_3$ (2 x 2 mL), H_2O (2 x 2 mL), saturated aqueous $NaHCO_3$ (2 x 2 mL), H_2O (2 mL), and saturated aqueous NaCl (3 mL), dried over Na_2SO_4 and concentrated in vacuo to an oil which was purified by mplc (15% EtOAc in hexane eluant) to yield 34 and 35 (29.5mg, 79%). NMR ($CDCl_3$, 200MHz) characteristic peaks δ0.96, 0.97(s, s, 3H), 1.02, 1.04(d, d, 3H, J=6.7Hz, J=7.0Hz), 1.18, 1.19(s, s, 3H), 2.06, 2.07(s, s, 3H, ratio 1.8:1 α-OAc:β-OAc), 3.69, 3.74(d, d, 1H, J=7.1Hz, J=8.2Hz, $-CHOCH_2Ph$), 4.58, 4.80(s, d(J=9.3Hz), 1H, ratio 1.8:1 CH-αOAc, CH-βOAc), 4.65(AB q 2H, J=11.0Hz); ($CHCl_3$) 2970, 2950, 2900, 1735, 1250, 1210, 1130cm^{-1}; m/e=374(M^+).

Ruthenium Tetraoxide[16,17] Oxidation of Alcohol 32 to Keto-Benzoate 36. Ruthenium dioxide (0.2mg, 4.4 mol%) was added to a vigorously stirred two-phase mixture of alcohol 32 (108mg, 0.3 mmol) and $NaIO_4$ (385mg, 1.8 mmol) in 3 mL of CCl_4, 3 mL of CH_3CN and 4.5 mL of H_2O. The reaction was stirred for 16 h and an additional portion of $NaIO_4$ (193mg, 0.9 mmol) added. After stirring for an additional 24 h, 25 mL of CH_2Cl_2 was added. The aqueous layer was extracted with CH_2Cl_2 (4 x 20 mL) and the combined organic portions washed with saturated aqueous $NaHSO_3$ (2 x 5 mL), H_2O (2 x 5 mL), saturated aqueous $NaHCO_3$ (2 x 5 mL), and saturated aqueous NaCl (5 mL), dried over $MgSO_4$ and concentrated to an oil (115mg) which was purified by mplc (5% EtOAc in Skelly F eluant) to yield an epimeric mixture of 33 and

38 (77.1mg, 69%) mp. 95-97°C (ether/pentane). NMR ($CDCl_3$, 60MHz) δ0.85(d, 3H, J=7Hz), 1.05(s, 6H), 0.90-3.10(m, 6H), 2.13(s, 3H), 3.90-4.40(m, 4H), 5.48(d, 1H, J=6.5Hz), 7.20-7.60(m, 3H), 7.85-8.15(m, 2H); IR ($CHCl_3$) 3020, 2970, 2940, 2900, 1715, 1320, 1280, 1120cm^{-1}; Anal. Calcd for $C_{22}H_{28}O_5$: C, 70.94; H, 7.58. Found: C, 70.71; H, 7.73.

Baeyer-Villiger Oxidation of Keto-Benzoate 36 with Peroxytrifluoroacetic acid.[15] Preparation of 37 and 38. Trifluoroacetic anhydride (0.16mL, 1.1 mmol) was added to a solution of 90% H_2O_2 (24μL, 1 mmol) in 1 mL of dry CH_2Cl_2 at 0°C. The solution was stirred for 5 min, then warmed to room temperature and stirred for 15 min. Na_2HPO_4 (162mg, 1.1 mmol), and ketone 36 (74.4mg, 0.2 mmol) in 2 mL of CH_2Cl_2 were added and the reaction stirred for 75 min. The mixture was diluted to 30 mL with CH_2Cl_2 and washed with H_2O (5 mL), saturated aqueous $NaHSO_3$ (1 mL) and saturated aqueous $NaHCO_3$ (2 mL), dried over Na_2SO_4 and concentrated to an oil which was purified by mplc (10% EtOAc in hexane eluant) to yield a mixture of acetates 37 and 38. (61.1mg, 79%). NMR ($CDCl_3$, 200MHz) δ0.88(d, 3H, J=7.0Hz), 0.97, 0.99(s, s, 3H), 1.04, 1.05(s, s, 3H), 1.15-1.35(m, 1H), 1.48-1.65(m, 1H), 1.70-1.90(m, 1H), 2.07, 2.10(s, s, 3H, ratio 4:1 α-OAc:βOAc), 2.30-2.85(m, 3H), 3.80-4.20(m, 4H), 4.64, 4.84(s, d(J=9.3Hz), ratio 4:1 CH-αOAc, CH-βOAc), 5.46, 5.54(d, d, 1H, J=8.6Hz, J=8.5Hz), 7.35-7.70(m, 3H), 8.00-8.10(m, 2H); IR ($CHCl_3$) 3030, 2970, 2950, 2900, 1735, 1720, 1280, 1250, 1125, 1030cm^{-1}.

Carboxy-Inversion[13] Reaction on exo-cis-Bicyclo [3.3.0] octane-2-carboxylic acid (39) with m-Chloroperbenzoic acid (mCPBA). Preparation of 42. Carbonyldiimidazole (486.5mg, 3.0 mmol) in 10 mL of CH_2Cl_2 was cooled to 0°C and bicyclic acid 39[19] (457.2mg, 3.0 mmol) in 5 mL of CH_2Cl_2 added dropwise. When evolution of CO_2 had subsided, the solution was stirred for 30 min, mCPBA (517.7mg, 3.0 mmol) added, and the mixture stirred for 1 h at 0°C. The solution was concentrated in vacuo to an oily residue which was dissolved in 30 mL of CH_3CN and stirred for 36 h at room temperature. The solution was concentrated in vacuo and the residue treated with 10 mL of 1N $NaOCH_3$ in CH_3OH. The mixture was refluxed for 8 h, 5 mL of H_2O added, and refluxing continued for 16 h. The mixture was diluted with 30 mL of H_2O and extracted with CH_2Cl_2 (4 x 10 mL). The combined extracts were washed with H_2O (10 mL) and saturated aqueous NaCl (10 mL), dried over Na_2SO_4 and concentrated to an oil. The residue was treated with 0.5 mL of phenyl isocyanate in 1 mL of pyridine at room temperature for 3 h. Excess phenyl isocyanate was quenched by addition of 5 mL of H_2O. The diphenyl urea which formed was removed by filtration. The filtrate was washed with 10% aqueous HCl (2 x 10 mL), saturated aqueous $NaHCO_3$ (10 mL), H_2O (10 mL) and saturated aqueous NaCl (10 mL), dried over Na_2SO_4 and concentrated to an oil which was purified by preparative TLC (eluant 10% ether in hexane) to yield 42 (118.3mg, 16%) mp 71-73°C (lit. 75-75.2°C[6,7]). NMR ($CDCl_3$, 60MHz) δ0.90-2.80(m, 12H), 4.80(m, 1H), 6.65(bd s, 1H), 6.85-7.40(m, 5H).

3,3-(Ethylenedioxy)-6α-benzoyloxy-4β,7,7-trimethyl-1α,5α-bicyclo [3.3.0]octane-2β-carboxylic acid (42). Ruthenium dioxide (6mg, 2 mol%) was added to a vigorously stirred, two-phase mixture of alcohol 30 (519.8mg, 1.5 mmol) and $NaIO_4$ (3.21g, 15 mmol) in 15 mL of CCl_4, 15 mL of CH_3CN and 22.5 mL of H_2O. The reaction was stirred at room temperature for 4 h, diluted with 75 mL of CH_2Cl_2, and filtered. The aqueous layer extracted with CH_2Cl_2 (4 x 50 mL) and the combined organic solutons washed with 5% aqueous $NaHSO_3$ (2 x 10 mL) and saturated aqueous NaCl (10 mL), dried over $MgSO_4$ and concentrated under reduced pressure to a green solid. This was dissolved in ether and filtered through a short (ca. 5 cm) column of silica gel to remove traces of ruthenium salts. Concentration of the filtrate yielded white crystals (521.3mg, 93%). mp 175-176.5°C (ether). NMR ($CDCl_3$, 200MHz) δ0.91(d, 3H, J=7.0Hz), 1.00(s, 3H), 1.05(s, 3H), 1.50-1.85(m containing bd s at 1.59 (CO_2H), 3H), 2.13-2.30(m, 1H), 2.67-2.85(m, 1H), 3.00-3.20(m, 2H), 4.03-4.33(m, 4H), 5.51(d, 1H, J=8.6Hz), 7.40-7.63(m, 3H), 8.00-8.10(m, 2H); IR ($CHCl_3$) 3300-2500 (CO_2H), 3030, 2980, 2950, 2910, 1750, 1720, 1280, 1120cm^{-1}; m/e 374(M^+); Anal. Calcd for $C_{21}H_{26}O_6$: C, 67.36; H, 7.00. Found: C, 66.92; H, 7.08. Analyzed as methyl ester (vide infra).

3,3-(Ethylenedioxy)-6α-benzoyloxy-2β-carbomethoxy-4β,7,7-trimethyl-1α,5α-bicyclo [3.3.0]-octane. Esterification of 42. Acid 42 (152.6mg, 0.41 mmol) in 5 mL of ether was cooled to ca. 0°C and treated with diazomethane in ether (3 mL, ca. 0.95M, 2.7 mmol). After ca. 1 min, excess diazomethane was destroyed by dropwise addition of 5% acetic acid in ether. The solution was washed with saturated aqueous $NaHCO_3$ (2 x 2 mL) and saturated aqueous NaCl (2 mL), dried over $MgSO_4$ and concentrated to 157.8mg (99%). The ester was chromatographed (mplc, 15% EtOAc in hexane eluant) and recrystallized (ether) for analysis. mp 116.5-117.5°C. NMR ($CDCl_3$, 200MHz) δ0.88(d, 3H, J=7.0Hz), 0.99(s, 3H), 1.04(s, 3H), 1.63-1.75(m, 2H), 2.08-2.25(m, 1H), 2.63-2.80(m, 1H), 2.69-2.88(m, 2H), 3.67(s, 3H), 3.93-4.30(m, 4H), 5.52(d, 1H, J=8.4Hz), 7.35-7.63(m, 3H), 8.00-8.10(m, 2H); IR ($CHCl_3$) 3030, 2970, 2910, 1735, 1715, 1610, 1590, 1280, 1245, 1210, 1120cm^{-1}; Anal. Calcd for $C_{22}H_{28}O_6$: C, 68.02; H, 7.27. Found: C, 68.05; H, 7.24.

Carboxy-Inversion[13] Reaction of Bicyclic Acid (42) with mCPBA. Preparation of 43. Acid 42 (37.5mg, 0.1 mmol) in 3 mL of CH_2Cl_2 was treated with carbonyldiimidazole (17.8mg, 0.11 mmol) and stirred at room temperature for 10 min under a N_2 atmosphere, then cooled to -23°C and treated with mCPBA (85%, 41.4mg, 0.24 mmol) added in 2 portions over 3 h. The mixture was diluted with 10 mL of ether and washed with saturated aqueous $NaHCO_3$ (2 x 2 mL), H_2O (2 x 2 mL) and saturated aqueous NaCl (2 mL), dried over $MgSO_4$ and concentrated to a clear oil which was dissolved in 3 mL of CH_3CN, stirred at room temperature for 15 h and heated at reflux for 20 h. After removal of CH_3CN in vacuo, the residue was dissolved in 30 mL of CH_2Cl_2, washed with saturated aqueous $NaHSO_3$ (2 x 3 mL), H_2O (3 mL), 10% aqueous Na_2CO_3 (2 x 3 mL), H_2O (3 mL) and saturated NaCl (3 mL), dried over $MgSO_4$ and concentrated to a dark brown oil which was purified by preparative TLC (eluant; 30% ethyl

acetate in hexane) to yield an alcohol. This was acylated by treatment with 1 mL of acetic anhydride in 1 mL of pyridine at room temperature for 16 h. The volatiles were removed in vacuo and the residue dissolved in ether, washed with saturated aqueous $NaHCO_3$, 10% aqueous HCl, and saturated aqueous NaCl, dried over $MgSO_4$ and concentrated to yield acetate 43 (8.6mg, 22%). NMR ($CDCl_3$, 200MHz), δ0.88(d, 3H, J=7.0Hz), 0.98(s, 3H), 1.05(s, 3H), 1.10-1.40(m, 1H), 1.80(t, 1H, J=11.5Hz), 2.10(s, 3H), 2.18(t, 1H, J=7.5Hz), 2.60-2.80(m, 1H), 2.93-3.15(m, 1H), 3.83-4.40(m, 4H), 4.84(d, 1H, J=9.3Hz), 5.53(d, 1H, J=8.1Hz), 7.40-7.60(m, 3H), 8.00-8.10(m, 2H); IR ($CHCl_3$) 3020, 2970, 2950, 2900, 1735, 1715, 1275, 1260, 1240, 1210, 1120cm^{-1}; m/e 388(M^+).

6α-Benzoyloxy-4β,7,7-trimethyl-1α,5α-bicyclo [3.3.0] octan-3-one (43) and 6α-Benzoyloxy-4α,7,7-trimethyl-1α,5α-bicyclo [3.3.0]octan-3-one (44). Ketal-acid 42 (74.5mg, 0.2 mmol) in 2 mL of 1N aqueous HCl and 2 mL of dioxane heated at reflux for 2 h. The mixture was cooled, diluted with 2 mL of saturated aqueous NaCl and extracted with CH_2Cl_2 (4 x 5 mL). The combined extracts were washed with 2 mL of H_2O, dried over Na_2SO_4 and concentrated to a pale yellow oil. The crude mixture of ketones was separated by mplc (eluant 5% EtOAc in hexane) to yield α-methyl ketone 44 (31.1mg, 68%) and β-methyl ketone 43 (10.0mg, 17%).[4e] 44 NMR ($CDCl_3$, 200 MHz) δ1.13(s, 3H), 1.13(d, 3H, J=6.9Hz), 1.17(s, 3H), 1.43(dd, 1H, J=10.5, 13.3Hz), 1.98-2.23(m, 2H), 2.33-2.66(m, 3H), 2.78-3.02(m, 1H), 5.04(d, 1H, J=6.0Hz), 7.35-7.6(m, 3H), 8.00-8.10(m, 2H); IR ($CHCl_3$) 3030, 2980, 2950, 2880, 1720, 1610, 1590, 1280, 1120cm^{-1}. 43 NMR ($CDCl_3$, 200MHz) δ1.03(d, 3H, J=7.1Hz), 1.05(s, 3H), 1.08(s, 3H), 1.20-1.37(m, 1H), 1.84-2.18(m, 2H), 2.48-3.00(m, 3H), 3.15(q, 1H, J=9Hz), 5.06(d, 1H, J=9.6Hz), 7.40-7.65(m, 3H), 8.00-8.10(m, 2H); IR ($CHCl_3$) 3030, 2980, 2950, 1720, 1280, 1120cm^{-1}. These spectroscopic data were identical with those of authentic materials.[4e,22]

4α-[(2-Chloro-4-propylthio-1-buten)-3-yl]-6α-benzoyloxy-4β,7,7-trimethyl-1α,5α-bicyclo [3.3.0]-octan-3-one (54). A solution of ketones 43 and 44 (312.6mg, 1.09 mmol), trimethylorthoformate (119μL, 116mg, 1.09 mmol), p-TsOH (3.7mg, 0.02 mmol) and methanol (0.9 mL) in 11 mL of dry benzene was stirred at room temperature under N_2 for 16 h. The mixture was distilled through a short-path apparatus until the head temperature reached 55°C. A solution of 2-chloro-4-propylthio-2-bu-ten-1-ol (46)[26] 217mg, 1.2 mol) in 11 mL of mesitylene was added and distillation continued through a 6" distillation column packed with glass helices. The oil bath temperature was gradually increased over a 3 hour period until the head temperature reached 165°C. Distillation was discontinued and the solution stirred at 160°C (oil bath temperature) for 15 min followed by dis-tillation of the mesitylene through a short-path apparatus. The residue was purified by flash chromatography (eluant 2% ethyl acetate in Skelly F) to yield a small amount of the undesired regioisomer 55 (33mg, 6.7%) as a mixture of epimers. NMR ($CDCl_3$, 200MHz) δ0.98(t, 3H, J=7Hz), 1.12(s, 3H), 1.14(d, 3H, J=7Hz), 1.18(s, 3H), 1.23-1.65(m, 4H), 2.15(dd, 1H, J=9, 13Hz), 2.35-2.82(m, 5H), 2.39(d, 2H, J=7.2Hz), 3.37(d of t, 1H, J=3.3, 7.7Hz), 5.11(d, 1H, J=6.8Hz), 5.32(s, 2H), 7.40-7.65(m, 3H), 8.00-8.10(m, 2H); IR ($CHCl_3$) 2970, 2940, 2880, 1740 (shoulder), 1720, 1630, 1280, 1120cm^{-1}. Further elution yielded the desired vinyl chloride 54 (403mg, 82%) as a colorless crystalline solid mp 94-95°C (35-60°C pet. ether). NMR ($CDCl_3$, 200MHz) δ0.97(t, 3H, J=7.3Hz), 1.07(s, 3H), 1.09(s, 3H), 1.10(s, 3H), 1.37(dd, 1H, J=7.1, 13.3Hz), 1.47-1.66(m, 2H), 2.04-2.23(m, 2H), 2.39-2.60(m, 3H), 2.66-2.89(m, 4H), 3.38(t, J=9Hz), 5.21-5.31(m, 3H), 7.40-7.65(m, 3H), 8.00-8.10(m, 2H); IR ($CHCl_3$ 2980, 2950, 2890, 1745, 1720, 1630, 1280, 1120cm^{-1}; m/e 448(M^+), 450 (M + 2); Anal. Calcd for $C_{25}H_{33}ClO_3S$: C, 66.87; H, 7.41; Cl, 7.90. Found: C, 66.86; H, 7.41; Cl, 8.14.

$Hg(OAc)_2$ Hydrolysis[28] of Vinyl Chloride 54. Preparation of 56. Vinyl chloride 54 (89.8mg, 0.2 mmol) and mercuric acetate (255mg, 0.8 mmol) in 12 mL of 88% formic acid was stirred at room temperature for 42 h. Water (6 mL) was added and the mixture stirred an additional 4 h, then diluted with 40 mL of H_2O and extracted with ether (4 x 30 mL). The combined extracts were washed with 10% aqueous Na_2CO_3 and saturated aqueous NaCl, dried over $MgSO_4$ and concentrated in vacuo. The residue was treated with ammonium formate (1g, 16 mmol) and 4 mL of H_2O in 6 mL of 88% formic acid for 16 h to complete hydrolysis of the intermediate mercury salts, then diluted with 25 mL of H_2O and extracted with ether. The ether extracts were washed with 10% aqueous Na_2CO_3 and saturated aqueous NaCl, dried over $MgSO_4$ and concentrated to an oil which was purified by flash chromatography (10% ethyl acetate in hexane eluant) to yield 56 (43.9mg, 62%). NMR ($CDCl_3$, 60MHz) δ1.13(s, 6H), 1.15-1.55(m, 1H), 1.34(s, 3H), 1.85-3.20(m, 5H), 2.30(s, 3H), 5.31(d, 1H, J=8Hz), 5.92(s, 1H), 6.16(s, 1H), 7.35-7.60(m, 3H), 7.90-8.15(m, 2H); IR ($CHCl_3$) 2970, 2940, 2890, 1740, 1720, 1685, 1275, 1120, 720cm^{-1}; m/e 354(M^+).

Cyclization of Diketone 56 with Potassium t-butoxide /t-Butanol. Preparation of 57. Diketone 56 (19.4mg, 0.555 mmol) in 0.5 mL of t-butanol was treated with freshly prepared potassium t-butoxide in t-butanol (0.01M, 1 mL, 0.01 mmol). The solution was stirred under N_2 for 1.5 h and a second portion (0.01M, 1 mL, 0.01 mmol) of potassium t-butoxide added. After one hour, a third portion of potassium t-butoxide (0.01M, 3.5 mL, 0.35 mmol) was added to make the total amount of base 0.55 mmol (1 equiv.). The mixture was stirred for 10 min, quenched with 30 mL of H_2O and extracted with ether (4 x 15 mL). The combined extracts were washed with H_2O (2 x 5 mL) and saturated aqueous NaCl (5 mL), dried over $MgSO_4$ and concentrated to a yellow oil. The crude dienone 57 was purified by preparative TLC (30% ethyl acetate in Skelly F eluant) to yield 8.5mg (46%). NMR ($CDCl_3$, 200MHz) δ1.12(s, 6H), 1.15-1.32(m, 1H), 1.43(s, 3H), 2.00(dd, 1H, J=7.2, 12.4 Hz), 2.28-2.55(m, 2H), 2.78-3.00(m, 2H), 5.07(s, 1H), 5.51(d, 1H, J=7.7Hz), 5.79(s, H), 5.92(d, 1H, J=1.7Hz), 7.40-7.65(m, 3H), 8.00-8.10(m, 2H); IR ($CHCl_3$) 3020, 2970, 2940, 2880, 1720, 1700, 1630, 1280, 1120cm^{-1}; m/e 336(M^+).

4α-[(2-Chloro-4-propylthio-1-buten)-3-yl]-6α-hydroxy-4β,7,7-trimethyl-1α,5α-bicyclo [3.3.0] octan-3-one (59). Benzoate 54 (449mg, 1 mmol) and 40% aqueous tetra-n-butylammonium hydroxide (5.2 mL, 8 mmol) in 25 mL of methanol were refluxed for 7 h. The solution was diluted with 75 mL of H_2O and extracted with ether (4 x 25 mL). The combined extracts were washed with saturated aqueous $NaHCO_3$ (2 x 10 mL) and saturated aqueous NaCl (10 mL), dried over $MgSO_4$, and concentrated in vacuo to 333.2mg (97%) of 59 which was used for $Hg(OAc)_2$ hydrolysis (vide infra). NMR ($CDCl_3$, 60 MHz) δ0.95-3.05(m with s at δ0.99, 1.06, 1.25, 25H), 3.35-3.65(m, 2H), 5.23(s, 1H), 5.32(s, 1H); IR ($CHCl_3$) 3600, 3450, 3010, 2970, 2940, 2880, 1735, 1630, 1460, 900cm^{-1}; m/e 344(M^+), 346(M+2).

$Hg(OAc)_2$ Hydrolysis[28] of Vinyl Chloride 59. 4α-[(3-oxo-1-buten)-2-yl]-4β,7,7-trimethyl-1α,5α-bibicyclo [3.3.0] octan-6α-ol (60). A solution of vinyl halide 59 (333.2mg, ca. 1 mmol), $Hg(OAc)_2$ (1.28g, 4 mmol) and ammonium formate (5.0g, 80 mmol) in 100 mL of 88% aqueous formic acid was stirred at room temperature for 38 h. The mixture was diluted with 400 mL of H_2O and extracted with CH_2Cl_2 (4 x 100 mL). The combined extracts were washed with 10% aqueous Na_2CO_3 and saturated aqueous NaCl, dried over $MgSO_4$ and concentrated to an amorphous solid which was purified by flash chromatography (15-50% ethyl acetate in Skelly-F eluant) to yield formate 61 (colorless oil, 183.2mg, 68%) and alcohol 60 (50.2mg, 21%) mp 108-110°C. 61 NMR ($CDCl_3$, 200MHz) δ0.98(s, 3H), 1.04(s, 3H), 1.22-1.35(m, 1H, H-8β), 1.28(s, 3H), 2.12(dd, 1.H, J=8, 12.5Hz, H-8α), 2.19(dd, 1H, J=8, 19Hz, H-2β), 2.33(s, 3H), 2.63(dd, 1H, J=8, 12Hz, H-1), 2.86(dd, 1H, J=10, 19Hz, H-2α), 2.98-3.17(m, LH, H-5), 5.16(d, 1H, J=8Hz), 5.95(s, 1H), 6.24(s, 1H), 8.05(s, 1H); IR ($CHCl_3$) 3010, 2970, 2940, 2870, 1730, 1675, 1180, 950cm^{-1}; m/e 278(M^+). 60 NMR ($CDCl_3$, 200MHz) δ0.89(s, 3H), 1.04(s, 3H), 1.10-1.23(m, 1H), 1.31(s, 3H), 1.40(bd s, 1H), 2.00(dd, 1H, J=8, 13Hz), 2.11(dd, 1H, J=7, 17Hz), 2.26-2.40(m, 1H), 2.34(s, 3H), 2.74-3.06(m, 2H), 3.73(bd d, 1H, J=10Hz), 6.01(s, 1H), 6.24(s, 1H); IR 3600, 3500, 3020, 2970, 2880, 1730, 1675, 1630, 950cm^{-1}; m/e 250(M^+).

3α-Hydroxy-11-methylene-1α,4,4-trimethyl-2α,6α-tricyclo-[6.3.0.0^{2,6}] undec-8-en-10-one (58). Direct Cyclization of Diketone 60 to Dienone 58. Diketone 60 (74.2mg, 0.27 mmol) in 6 mL of t-butanol was added dropwise to a solution of potassium t-butoxide (30.3mg, 0.27 mmol) in 2 mL of t-butanol at room temperature under N_2. The orange solution was stirred for 45 min, diluted with 30 mL of H_2O, and extracted with ether (4 x 25 mL). The combined extracts were washed with 10 mL of saturated aqueous NaCl, dried over $MgSO_4$ and concentrated to a dark oil. Flash chromatography (eluant 3:1 ether/Skelly F) yielded dienone 58 as an oil (21.5mg, 34%). Further elution yielded 28mg of polar products which were treated with pTsOH (0.5mg) in 15 mL of benzene and refluxed for 2 h. The solution was concentrated in vacuo and the residue purified by preparative TLC (40% EtOAc in hexane eluant) to yield an additional 2.3mg (4%) of 58 (23.8mg, 38% total). NMR ($CDCl_3$, 200MHz) δ0.92(s, 3H), 1.09(s, 3H), 1.28(s, 3H), 1.40-1.60(bd m, 2H), 1.91(dd, 1H, J=8, 13Hz), 2.09-2.40(m, 2H), 2.59-2.86(m, 2H), 3.88(d, 1H, J=8Hz), 5.36(s, 1H), 5.91(d, 1H, J=2Hz), 5.93(s, 1H); IR ($CHCl_3$) 3600, 3450, 3010, 2970, 2940, 2870, 1690, 1645, 1620cm^{-1}; m/e 232(M^+). These spectroscopic data correspond to those reported by Ikegami for dienone 58.[7e]

Indirect Cyclization[26] of Diketoformate 61 via β-Hydroxy-ketone 63. Preparation of Dienones 58 and 64. Diketone 61 (344.4mg, 1.24 mmol) in 20 mL of 4:1 anhydrous THF/anhydrous t-butanol was added dropwise to a solution of potassium t-butoxide (278mg, 2.48 mmol) in 40 mL of 4:1 THF/t-butanol at -20°C under N_2. The reaction mixture was allowed to warm to -10°C and stirred for 1.5 h. The solution was diluted with 200 mL of H_2O and extracted with ether (5 x 100 mL). The combined extracts were washed with saturated aqueous NaCl (2 x 25 mL), dried over $MgSO_4$ and concentrated to a white solid. The crude β-hydroxyketones 62 and 63 were treated with 20mg of p-TsOH in 125 mL of benzene and refluxed for 1 h. The solution was washed with saturated aqueous $NaHCO_3$ (3 x 10 mL), H_2O (10 mL) and saturated aqueous NaCl (10 mL), dried over $MgSO_4$ and concentrated to a yellow oil, which was purified by flash chromatography (30-40% EtOAc in Skelly F eluant) to yield dienone formate 64 (30.6mg, 9%) and dienone alcohol 58 (230.2mg, 80%). 64 NMR ($CDCl_3$, 60MHz) δ1.03(s, 3H), 1.11(s, 3H), 1.39(s, 3H), 1.15-3.10(m, 6H), 5.08(s, 1H), 5.30(d, 1H, J=8Hz), 5.81(bd s, 2H), 8.05(s, 1H); IR ($CHCl_3$) 3010, 2970, 2940, 2870, 1720, 1695, 1630, 1180cm^{-1}; m/e 260(M^+), 231(-CHO). 58 NMR ($CDCl_3$, 200MHz) δ0.92(s, 3H), 1.09(s, 3H), 1.28(s, 3H), 1.40-1.60(bd m, 2H), 1.91(dd, 1H, J=8, 13Hz), 2.09-2.40(m, 2H), 2.59-2.86(m, 2H), 3.88(d, 1H, J=8Hz), 5.36(s, 1H), 5.91(d, 1H, J=2Hz), 5.93(s, 1H); IR ($CHCl_3$) 3600, 3450, 3010, 2970, 2940, 2870, 1690, 1645, 1620cm^{-1}; m/e 232(M^+).

3α,7β-Dihydroxy-11-methylene-1β,4,4-trimethyl-2α,6α-tricyclo-[6.3.0.0^{2,6}]undec-8-en-10-one (2). The method described by Ikegami[4c] was used. Dienone 58 (117.1mg, 0.5 mmol) in 3 mL of anhydrous DME was added dropwise over 10 min to a solution of potassium t-butoxide (673mg, 6mmol) in 3 mL of anhydrous DME at -70°C under N_2. The solution was stirred for 10 min, then warmed to room temperature and stirred for 1.5 h. The mixture was cooled to 0°C and quenched by rapid addition of 25 mL of cold 10% aqueous acetic acid, followed by 125 mL of cold saturated aqueous $NaHCO_3$. The solution was extracted with ether (4 x 50 mL). The combined extracts were washed with saturated aqueous NaCl (20mL), dried over $MgSO_4$, and concentrated in vacuo using an ice-cold water bath. The residue was treated with mCPBA (80%, 108mg, 0.5 mmol) in 15 mL of dry CH_2Cl_2 at 0°C for 1 h. The CH_2Cl_2 solution was diluted with 75 mL of ether, washed with saturated aqueous Na_2SO_3 (2 x 5 mL), and saturated aqueous $NaHCO_3$ (2 x 5 mL), dried over $MgSO_4$ and concentrated in vacuo. The residue was dissolved in 3 mL of dry benzene, cooled in an ice bath and treated with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (228mg, 1.5 mmol) in 2 mL of benzene. The

solution was stirred for 20 min, quenched with 20 mL of saturated aqueous NH_4Cl, and extracted with ether (5 x 10 mL). The combined extracts were washed with saturated aqueous NaCl, dried over $MgSO_4$, and concentrated to an oil which was purified by flash chromatography (40-50% EtOAc in Skelly F eluant) to yield recovered dienone 58 (55.5mg, 47%) and diol 2 (15.9mg, 13%). 2 NMR ($CDCl_3$, 200MHz) δ1.20-1.95(m, 4H), 0.94(s, 3H), 1.13(s, 3H), 1.52(s, 3H), 2.21(dd, 1H, J=9, 12Hz), 2.55-2.80(m, 1H), 3.89(d, 1H, J=9Hz), 5.37(s, 1H), 5.95(s, 1H), 6.06(d, 1H, J=2.1Hz); IR (film) 3400, 2970, 2880, 1690, 1620, 1080cm^{-1}. These data correspond to reported spectroscopic data for diol 2.[4a,b]

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