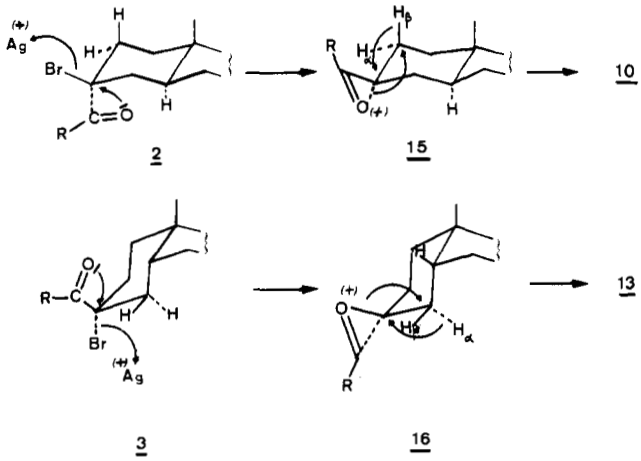
Scheme III



5a: mp 96–100 °C (methanol); IR (CCl_4) 1655 cm^{-1}; ^1H NMR δ 0.67 (s, 3 H, 18-Me), 0.79 (s, 3 H, 19-Me), 6.50 (m, half-with = 8.5 Hz, 1 H, 2-H), 7.3–7.8 (m, 5 H, phenyl); ^{13}C NMR δ 141.2 (2-C), 143.5 (3-C), 198.2 (C=O); mass spectrum, *m/e* 474, 459, 105.

4a: mp 155–160 °C (pentane–ether); IR (CCl_4) 3620, 1685 cm^{-1}; ^1H NMR δ 0.75 (s, 3 H, 18-Me), 1.39 (d, 3 H, 19-Me), 3.67 (tt, J = 12, 2.5 Hz, 1 H, 3-H); ^{13}C NMR δ 74.3 (10-C), 203.6 (C=O); mass spectrum, *m/e* 492, 474, 450, 369, 133, 105; $[\alpha]^{22}_{546}$ +22.7 (*c* 6, CH_2Cl_2).

Pure **1a** (400 mg) gave after reaction, workup, and TLC separation **5a** (109 mg, 32% yield) and **4a** (159 mg, 45% yield).

Pure **2a** (294 mg) gave, by the same procedure, **5a** (62 mg, 25% yield) and **4a** (79 mg, 33% yield). Another hydroxy compound, which remains unidentified, was also obtained (16 mg).

Dehalogenation of 2b. To a solution of **2b** (780 mg) in CH_2Cl_2 (10 mL) at −20 °C was added 900 mg of $AgSbF_6$ (1.5 equiv). The reaction mixture was stirred 40 min, poured into aqueous solution of $NaHCO_3$, extracted (CH_2Cl_2), dried, and concentrated. The crude material was purified by silica gel column chromatography (hexane–ether) to give the following compounds successively. 17-Acetoxyandrost-2-ene: 111 mg (20% yield); mp 97–99 °C (pentane) (lit.[22] mp 96 °C); ^1H NMR δ 0.72 (s, 3 H, 18-Me), 0.80 (s, 3 H, 18-Me), 2.05 (s, 3 H, $OCOCH_3$), 4.58 (t, 1 H, C-17 H), 5.60 (m, 2 H, H–C^2=C^3–H). A mixture of olefinic ketones, 68 mg (11% yield). 3-Acetyl-17-acetoxyandrost-2-ene (**5b**): 37 mg (6% yield); mp 135–140 °C; IR (CCl_4) 1735, 1670 cm^{-1}; ^1H NMR δ 0.70 (s, 3 H, 18-Me), 0.78 (s, 3 H, 19-Me), 2.02 (s, 3 H, $OCOCH_3$), 2.26 (s, 3 H, $COCH_3$), 4.57 (m, 1 H, C-17 H), 6.80 (m, 1 H, H_2C=C). **6**, 30 mg (4.5% yield) vide infra. **4b**: 220 mg (35% yield); mp 158–160 °C; IR (CCl_4) 36208 1730, 1710 cm^{-1}; ^1H NMR δ 0.85 (s, 3 H, 18-Me); 1.28 (d, J = 8 Hz, 3 H, 19-Me), 2.05 (s, 3 H, $OCOCH_3$), 2.16 (s, 3 H, $COCH_3$) 2.41 (t, 1 H, C-3 H), 4.61 (t, 1 H, C-17 H); ^{13}C NMR δ 74.0 (s, C-10) 82.6 (d, C-17), 171.1 ($OCOCH_3$), 212.6 ($COCH_3$); $[\alpha]^{20}_{546}$ −5.4° (*c* 4, CH_2Cl_2).

Dehalogenation of 3. To a solution of **3** (1 g) in CH_2Cl_2 (10 mL) at −40 °C was added 1.3 g of $AgSbF_6$ (1.6 equiv). The temperature was raised to 0 °C progressively in 1 h. After the usual workup, silica gel column chromatography (hexane–CH_2Cl_2–Et_2O) gave hydroxy ketone **6**: 383 mg (45% yield); mp 138–142 °C (petroleum ether–Et_2O); IR (CCl_4) 3630, 1730, 1710 cm^{-1}; ^1H NMR δ 0.76 (s, 3 H, 18-C), 0.89 (s, 3 H, 19-C), 2.03 (s, 3 H, $OCCCH_3$), 2.81 (m, half-width = 16 Hz, C-3 H), 4.58 (t, 1 H, C-17 H); ^{13}C NMR δ 12.0 (18-Me), 16.8 (19-Me), 71.7 (s, C-5), 82.8 (d, C-17), 171.1 ($OCOCH_3$), 214.8 ($COCH_3$); $[\alpha]^{23}_{546}$ −2.3° (*c*, 4.5, CH_2Cl_2).

Elution also gives trace of 17-acetoxy-5β-androstene and a mixture of olefinic ketones (95 mg, 11% yield), among which was 3-acetyl-17β-acetoxy-5β-androst-3-ene [^1H NMR δ 0.78 (s, 3 H, 18-Me) 1.3 (s, 3 H, 19-Me), 4.54 (m, 1 H, C-17 H), 6.58 (s, half-width = 3 Hz, HC=)] and another hydroxy ketone, probably **7**: 35 mg (4% yield); IR (CCl_4) 3620, 1735, 1715 cm^{-1}; ^1H NMR δ 0.77 (s, 3 H, 18-Me), 0.92 (s, 3 H, 19-Me), 2.02 (s, 3 H, $OCOCH_3$), 2.23 (s, 3 H, $COCH_3$), 4.58 (m, 1 H, C-17 H).

Equilibration of 6 and 9. A solution of **6** (130 mg) in 1 N methanolic KOH (20 mL) was refluxed for 60 min. The reaction mixture was then diluted with water, extracted (CH_2Cl_2), dried, and concentrated. Treatment with acetic anhydride in pyridine overnight gave **9**: 102 mg; mp 187–190 °C (hexane-CH_2Cl_2); ^1H NMR δ 0.76 (s, 3 H, 18-Me), 0.92 (s, 3 H, 19-Me), 2.03 (s, 3 H, $OCOCH_3$), 2.15 (s, 3 H, $COCH_3$), 2.84 (m, half-width = 31 Hz), 4.55 (t, 1 H, C-17 H); ^{13}C NMR δ 12.0, 16.8, 73.5 (s, C-5), 82.7 (d, C-17), 170.9 and 212.1; $[\alpha]^{23}_{546}$ +31.1° (*c* 5, CH_2Cl_2).

Baeyer–Villiger Oxidation of 9 to 8. To a solution of **9** (100 mg) in CH_2Cl_2 (5 mL) containing Na_2HPO_4 (1.5 g) was added 2 mL of a trifluoroperoxyacetic acid solution (prepared from 2.5 mL of CH_2Cl_2, 3 mL of trifluoro acetic anhydride and 0.4 mL of 90% H_2O_2). After standing at room temperature for 48 h, the mixture was poured into water, extracted (CH_2Cl_2), washed with water, dried and evaporated to yield the diacetate **8**: 70 mg; mp 221–224 °C (lit.[12] mp 217–219 °C); IR (CCl_4) 3620, 1735 cm^{-1}; ^1H NMR δ 0.77 (s, 3 H, 18-Me), 0.91 (s, 3 H, 19-Me), 2.02 (s, 3 H, $OCOCH_3$), 2.04 (s, 3 H, $OCOCH_3$), 4.58 (t, 1 H, C-17 H), 5.11 (m, 1 H, C-3 H); $[\alpha]^{25}_{546}$ +42° (*c* 1.7, CH_2Cl_2) [lit.[12] $[\alpha]_D$ +45° (*c* 0.5, $CHCl_3$)].

Acknowledgment. We are grateful to Professor S. Wolfe, University of Kingston, for critical suggestions during the preparation of the article. We also thank DGRST (Contract No. 787943) for partial financial support of this work and the Roussel-UCLAF Laboratories for a generous supply of starting materials and for biological tests.

Registry No. 1a, 77825-58-2; **2a**, 77825-59-3; **2b**, 82880-41-9; **3**, 82871-81-6; **4a**, 77825-60-6; **4b**, 82871-82-7; **5a**, 77825-61-7; **5b**, 17006-91-6; **6**, 82871-83-8; **7**, 82871-84-9; **8**, 82871-85-0; **9**, 82871-86-1; 5α-cholestan-3-one, 566-88-1; 2-benzylidene-5α-cholestane, 82871-87-2; 3β-benzoyl-5α-cholestane, 82871-88-3; 17β-acetoxy-5α-androst-2-ene, 2324-10-9; 3-acetyl-17β-acetoxy-5β-androst-3-ene, 82871-89-4.

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An Approach to the BCDE Ring of Quasimarin

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A 10-step route to the BCDE ring system of quasimarin (**1**) is described. Key features of the route include the regioselective protection of diketone **7** by use of intramolecular ketal formation, a two-step lactone to ether reduction, and a regioselective lactonization. The tetracyclic system **15** is produced in 29% overall yield.

Quasimarin (**1**) and bruceantin (**2**) are antitumor agents recently isolated from *Quassia amara*[1] and *Brucea antidysenterica*,[2] respectively. Both have shown in vitro activity against human carcinoma of the nasopharynx (KB)

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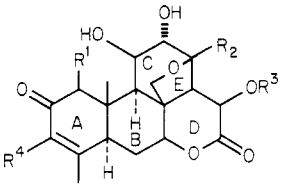
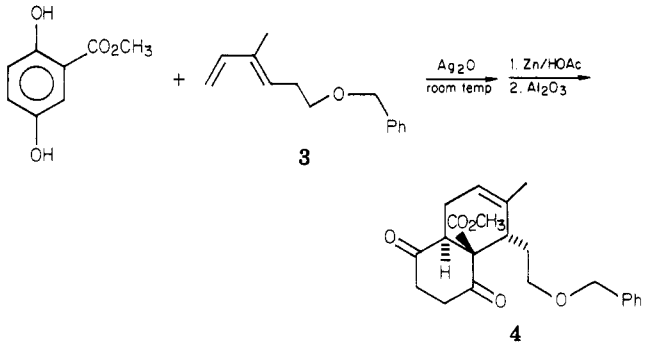
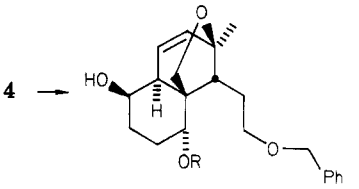


1, R^1 = OH; R^2 = CH_3;
R^3 = COC(OAc)(CH_3)Et; R^4 = H
2, R^1 = H; R^2 = CO_2CH_3;
R^3 = COCH=C(CH_3)(*i*-Pr); R^4 = OH

at the 10^{-3} mg/mL level and inhibitory activity against the P-388 lymphocytic leukemia in the mouse over a broad dosage range. Bruceantin has also shown activity against Walker 256 intramuscular carcinosarcoma and L-1210 lymphoid leukemia. The activity of bruceantin against murine tumors is also of interest.[3] Several approaches to **1** and **2**, which have never been synthesized, have been reported. An approach by Dias involves the degradation of a steroid.[4] Although the A, B, and C rings are present in the starting material, the degradation of the steroidal D ring requires several steps. No progress toward the introduction of the C-ring functionality present in bruceantin or quasimarin has been published by Dias. Watt and co-workers[5] have published an unsuccessful approach to the BC ring system. Fuchs[6] has disclosed model system chemistry directed toward the introduction of the trans-diaxial diol subunit in the C ring. He has solved several difficult problems. Approaches to quassin, a stereochemically less complex quassinoid, have also appeared from the laboratories of Valenta[7] and Grieco.[8] Recently, Grieco has published a direct and elegant total synthesis of quassin.[9]

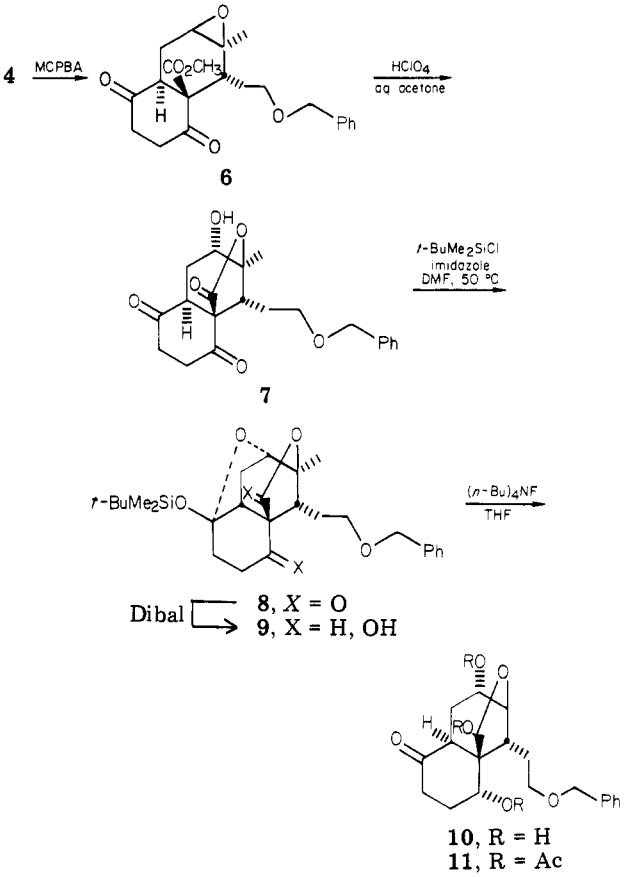
Our initial efforts in this area had focused on the use of Diels–Alder reactions of in situ generated quinones to afford functionalized BC ring precursor **4**.[10] Stereoselective routes were developed that furnished **5a** or **5b**. A variety of oxidants were then employed for the oxidation of alcohol **5b**. We were unable to produce the corresponding ketone. The sensitive axial allylic ether system underwent extensive rearrangement (as evidenced by the complex pattern of singlets in the NMR spectrum around δ 1.5) when chromium-based oxidants[11] were tried. Me_2SO-based oxidations[12] afforded small amounts of the desired β,γ enone that was contaminated with the α,β-unsaturated isomer.





5a, R = H
b, R = THP

In order to circumvent this problem, we converted adduct **4** into epoxide **6** with *m*-chloroperbenzoic acid. Acid-catalyzed epoxide opening[13] afforded lactone **7** in excellent yield. This structure is supported by an IR absorption at 1770 cm^{-1}. Attempted silylation of the hindered secondary alcohol of **7** led unexpectedly to ketal **8**. Presumably the sequence of epimerization, hemiketal formation and silylation was facilitated by the relatively harsh reaction conditions. However, milder conditions afforded only recovered alcohol **7**. Ketal **8** is highly crystalline and shows absorptions at 204 and 105 in the ^{13}C NMR spectrum. The presence of only a single ketone absorption and the signal characteristic of a ketal at 105 strongly support the assigned structure. Reaction of **8** with tetrabutylammonium fluoride[14] regenerates **7**. Importantly, we have *in one step* protected the axial alcohol and



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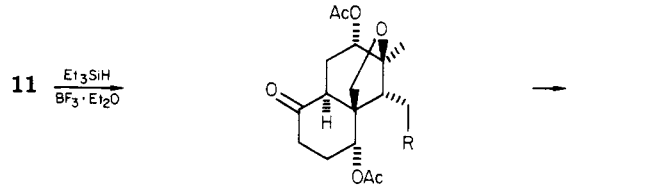
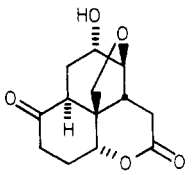
achieved *selective* ketone protection. Because of the ring juncture epimerization, the remaining ketone must now be reduced to an *equatorial* alcohol in order to afford the correct relative stereochemistry. Subsequent deketalization and epimerization will then give the axial C–O bond necessary for **1**. Both reduction of the ketone and lactone can be effected with diisobutylaluminum hydride (Dibal).[15] Lactol alcohol **9** is one isomer as evidenced by thin-layer chromatography in several solvents and the ^{13}C NMR spectrum. The stereochemistry at the lactol carbon was not determined since that center was to be reduced to a methylene group. Reaction of **9** with tetrabutylammonium fluoride provides ketone **10** in 87% yield. Acetylation with acetic anhydride produces triacetate **11**, which is reduced to **12** in 88% yield with triethylsilane and boron trifluoride etherate.[16] Hydrogenolysis of the benzyl group afforded

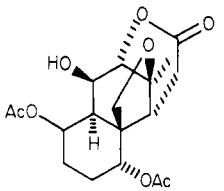


$H_2/Pd/C$ → **12**, R = CH_2OCH_2Ph
Jones oxid → **13**, R = CH_2OH
→ **14**, R = CO_2H



15

13. This alcohol, in contrast to **5b**, was smoothly oxidized to acid **14** with the Jones reagent. Hydrolysis of the acetates and subsequent acidification produces lactone **15**. In principle, two isomeric lactones might be formed. The ^{13}C NMR spectrum indicated that only one lactone was present. The isomeric lactone wherein the carbonyl group was attached to the oxygen atom at C-12 (quassinoid numbering) has not been observed in naturally occurring quassinoids. We had, however, prepared the closely related isomeric lactone **16**.[10] Both ^{13}C NMR and a proton NMR comparisons showed distinct differences. We therefore assign structure **15** to the lactone produced from **14**.



16

The route described above permits a rapid entry (10 steps from **4**) to the BCDE ring system of quasimarin in excellent overall yield (29% from **4**). Our efforts to append the A ring and add the requisite hydroxyl groups at C-11 and C-15 will be described in subsequent publications.

Experimental Section

Infrared spectra were obtained on a Beckman IR 4250 or Acculab 2 spectrometer. The NMR spectra were recorded with a Varian EM-360, A-60, or HA-100 spectrometer or a Hitachi Perkin-Elmer R20-B spectrometer. All chemical shifts are reported in δ relative to tetramethylsilane as an internal standard. The ^{13}C spectra were recorded with a JEOL FX-90Q. The chemical shifts for ^{13}C are reported in parts per million relative to the central peak of $CDCl_3$ (77.06 ppm). An AEI-MS902 mass spectrometer was used for mass spectral data. Ultraviolet spectra were recorded on a Cary-14 spectrometer. Elemental analyses were performed by Galbraith Laboratories, Inc. Tetrahydrofuran was distilled from $LiAlH_4$ prior to use.

Preparation of 4aβ-(Carbomethoxy)-6-methyl-6,7-epoxy-5α-[2-(benzyloxy)ethyl]-2,3,4a,5,8,8aα-hexahydronaphthalene-1,4-dione (6). A 0.30 M CH_2Cl solution containing 2.44 g (6.6 mmol) of **4** was cooled to 0 °C. With stirring, 1.47 g (7.25 mmol) of 85% *m*-chloroperoxybenzoic acid was added. The reaction mixture was allowed to slowly warm to room temperature and stir overnight. The solution was poured into 75 mL of ether and washed with saturated $NaHCO_3$, 10% $NaHSO_3$, saturated $NaHCO_3$, and brine. The ether solution was dried over Na_2SO_4, filtered, and concentrated in vacuo to yield 2.51 g (6.5 mmol) of **6**: NMR ($CDCl_3$) δ 1.46 (s, 3 H), 1.52–2.00 (envelope, 4 H), 2.74 (br s, 4 H), 3.02 (m, 3 H), 3.64 (s, 3 H), 3.68 (m, 2 H), 4.52 (s, 2 H), 7.32 (s, 5 H); 90-MHz ^{13}C NMR ($CDCl_3$) 23.802, 24.647, 27.053, 34.987, 38.564, 38.694, 41.424, 52.675, 59.828, 60.153, 61.844, 67.826, 68.022, 72.639, 127.590, 128.175, 137.995, 169.405, 206.017, 206.667 ppm; IR (film) 3040, 2960, 2880, 1750, 1725, 1440, 1380, 1310, 1250, 1200, 1100, 1030, 740, 700 cm^{-1}.

Preparation of (4α)-10α-[2-(Benzyloxy)ethyl]-1α-methyl-5,8,12-trioxo-11-oxatricyclo[7.2.1.0]dodecan-2α-ol (7). A 0.20 M THF solution containing 5.02 g (13 mmol) of **6** was treated with 4 mL of 3 N $HClO_4$. The reaction mixture was stirred at room temperature for 5 h. The reaction mixture was then poured into 100 mL of ether and washed with saturated $NaHCO_3$ and brine. The ether solution was dried over Na_2SO_4, filtered, and concentrated in vacuo to yield 4.39 g (11.8 mmol) of **7**: NMR ($CDCl_3$) δ 1.56 (s, 3 H), 1.90–2.22 (envelope, 4 H), 2.50 (m, 3 H), 2.72 (m, 2 H), 3.04 (dd, 1 H, J = 4, 11 Hz), 3.46 (m, 2 H), 3.92 (m, 1 H), 4.34 (s, 2 H), 7.32 (s, 5 H); 90-MHz ^{13}C NMR ($CDCl_3$) 20.352, 24.841, 29.523, 35.896, 37.782, 39.853, 49.812, 61.907, 69.321, 70.036, 72.573, 86.749, 127.914, 128.369, 137.538, 173.696, 202.309, 207.309 ppm: IR ($CHCl_3$) 3620, 3460, 3040, 2980, 2880, 1770, 1720, 1450, 1410, 1380, 1360, 1260, 1100, 1050, 980, 905 cm^{-1}; mass spectrum, *m/e* calcd for $C_{21}H_{24}O_6$ (M^+) 373.15730, found 372.15604.

Preparation of (4β)-10α-[2-(Benzyloxy)ethyl]-1α-methyl-2,5α-epoxy-5β-[(*tert*-butyldimethylsilyl)oxy]-8,12-dioxo-11-oxatricyclo[7.2.1.0]dodecane (8). To a 0.50 M DMF solution containing 1.55 g (4.16 mmol) of **7** was added 0.845 g (12.4 mmol) of imidazole and 1.06 g (7.03 mmol) of *tert*-butyldimethylsilyl chloride. The reaction mixture was heated to 40 °C and stirred at this temperature for 24 h. The reaction mixture was poured into 40 mL of H_2O and extracted four times with 75-mL portions of ether. The combined ether extractions were washed with H_2O and brine. The ether solution was dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was recrystallized from ethyl acetate/hexane to yield 1.62 g (3.33 mmol) of **8**; mp 147 °C; NMR ($CDCl_3$) δ 0.14 (s, 3 H), 0.18 (s, 3 H), 1.00 (s, 9 H), 1.56 (s, 3 H), 1.92 (m, 2 H), 2,28 (m, 2 H), 2.40–2.72 (envelope, 3 H), 2.90 (m, 3 H), 3.24 (m, 1 H), 3.44 (m, 1 H), 3.88 (m, 1 H), 4.32 (s, 2 H), 7.30 (s, 5 H); 90-MHz ^{13}C NMR ($CDCl_3$) 18.076, 20.938, 25.752, 25.882, 28.223, 30.239, 38.758, 49.681, 61.063, 69.711, 70.361, 72.833, 86.554, 105.283, 127.719, 128.304, 137.733, 147.163, 173.891, 204.195 ppm; IR ($CHCl_3$) 3020, 2960, 2940, 2900, 2880, 1775, 1725, 1680, 1460, 1415, 1370, 1260–1200, 1100, 1060, 940, 895, 840 cm^{-1}; mass spectrum, *m/e* calcd for $C_{27}H_{38}O_6Si$ (M^+) 486.24378, found 486.24735.

Preparation of (4β)-10α-[2-(Benzyloxy)ethyl]-1α-methyl-2,5α-epoxy-5β-[(*tert*-butyldimethylsilyl)oxy]-11-oxatricyclo[7.2.1.0]dodecane-8α,12-diol (9). A 0.20 M THF solution containing 4.0 g (8.23 mmol) of **8** was cooled to −78 °C. To this was added 33 mL of 1.0 M hexane solution of diisobutylaluminum hydride (33 mmol) over a period of 15 min. The reaction mixture was stirred at −78 °C for 2 h. It was then allowed to slowly warm to room temperature and stir at room temperature for 2 h. The reaction mixture was then poured into a vigorously stirred two-phase system of 50 g of ice, 30 mL of acetic acid, and

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150 mL of $CHCl_3$. The vigorous stirring was continued for 2 h. The layers were separated. The chloroform solution was washed with saturated $NaHCO_3$ and brine. It was then dried over Na_2SO_4, filtered, and concentrated to yield 3.63 g (7.41 mmol) of **9**: mp 157–158 °C; NMR ($CDCl_3$) δ 0.13 (s, 6 H), 0.98 (s, 9 H), 1.47 (s, 3 H), 1.80–2.46 (envelope, 10 H), 3.70 (m, 3 H), 3.92 (m, 2 H), 4.54 (s, 2 H), 4.91 (s, 1 H), 7.32 (s, 5 H); 90-MHz ^{13}C NMR ($CDCl_3$) -3.705, 18.207, 23.144, 25.232, 25.882, 27.313, 29.004, 30.565, 43.504, 54.170, 68.476, 70.557, 73.094, 73.289, 74.264, 83.889, 102.618, 108.861, 127.720, 127.850, 128.370, 145.928 ppm; IR ($CHCl_3$) 3620, 3400, 3010, 2960, 2940, 2860, 1670, 1360, 1250, 1190, 1090, 1045, 920, 870, 830 cm^{-1}.

Preparation of (4α)-10α-[2-(Benzyloxy)ethyl]-1α-methyl-5oxo-11-oxatricyclo[7.2.1.0]dodecane-2α,8β,12-triol (10). A 0.10 M THF solution containing 0.27 g (0.55 mmol) of **9** was treated with 0.55 mL of a 1.0 M THF solution of tetra-*n*-butylammonium fluoride. The reaction mixture was stirred at room temperature for 10 h. It was then poured into 30 mL of ethyl acetate and washed with saturated $NaHCO_3$ and brine. The ethyl acetate was dried over Na_2SO_4, filtered, and concentrated. The residue was chromatographed on silica gel (10/1, w/w), using 60/40 ethyl acetate/hexane as the solvent, to yield 0.182 (0.48 mmol) of **10**: mp 89–90 °C; NMR ($CDCl_3$) δ 1.34 (s, 3 H), 1.68–2.46 (envelope, 7 H), 3.04 (m, 3 H), 3.70 (m, 4 H), 4.58 (s, 2 H), 4.74 (s, 1 H), 7.34 (s, 5 H); 90-MHz ^{13}C NMR ($CDCl_3$) 22.108, 22.433, 25.621, 28.483, 29.845, 36.156, 39.993, 48.316, 56.445, 68.281, 72.247, 73.158, 73.678, 83.237, 98.065, 127.979, 128.564, 137.018, 213.690 ppm; IR ($CHCl_3$) 3400, 3020, 2980, 2880, 1710, 1460, 1240, 1170, 1100, 1050, 910, 850 cm^{-1}.

Preparation of (4α)-10α-[2-(Benzyloxy)ethyl]-1α-methyl-2α,8β,12-triacetoxy-5-oxo-11-oxatricyclo[7.2.1.0]dodecane (11). To a 0.10 M CH_2Cl_2 solution of 0.26 g (0.69 mmol) of **10** were added 0.42 g (4.15 mmol) of triethylamine, 0.352 g (3.45 mmol) of acetic anhydride, and 0.017 g (0.14 mmol) of 4-(dimethylamino)pyridine. The reaction mixture was stirred at room temperature for 10 h. The excess acetic anhydride was destroyed by adding 0.5 mL of CH_3OH and allowing the reaction mixture to stir for an additional 10 min. The reaction mixture was poured into 25 mL of ether and washed with H_2O, 1 N, HCl, saturated $NaHCO_3$, and brine. The ether solution was dried over Na_2SO_4, filtered, and concentrated in vacuo to yield 0.346 g (0.69 mmol) of **11**: NMR ($CDCl_3$) δ 1.30 (s, 3 H), 1.78 (m, 2 H), 2.00 (s, 3 H), 2.08 (s, 3 H), 2.13 (s, 3 H), 2.16–2.78 (envelope, 7 H), 3.08 (dd, 1 H, J = 7, 12 Hz), 3.50 (m, 2 H), 4.52 (s, 2 H), 4.86 (d, 1 H, J = 5 Hz), 5.20 (m, 1 H), 5.74 (s, 1 H), 7.32 (s, 5 H); 90-MHz ^{13}C NMR ($CDCl_3$) 20.807, 22.173, 23.475, 24.711, 26.532, 35.376, 39.928, 46.366, 53.649, 69.451, 70.947, 72.312, 72.703, 83.823, 95.919, 127.394, 128.044, 137.799, 168.948, 169.274, 208.292 ppm; IR ($CHCl_3$) 3020, 2960, 2860, 1750–1720, 1710, 1450, 1370, 1220, 1090, 995, 960 cm^{-1}; mass spectrum, m/e calcd for $C_{25}H_{32}O_7$ (M^+) 444.21481, found 444.21524.

Preparation of (4α)-10α-[2-(Benzyloxy)ethyl]-1α-methyl-2α,8β-triacetoxy-5-oxo-11-oxatricyclo[7.2.1.0]dodecane (12). A 0.05 M CH_2Cl_2 solution of 0.346 g (0.69 mmol) of **11** was treated with 0.088 g (0.76 mmol) of triethylsilane. To this was added dropwise over a period of 1 min 0.11 g (0.76 mmol) of boron trifluoride etherate. The reaction mixture was stirred at room temperature for 3 h. To the reaction mixture was added 5 mL of saturated $NaHCO_3$ solution. The solution was stirred vigorously for 15 min. The reaction was extracted twice with ether. The combined ether extractions were dried over Na_2SO_4, filtered, and concentrated. The residue was chromatographed on silica gel (10/1, w/w), using hexane/ethyl acetate as the solvent, to yield 0.27 g (0.61 mmol) of **12**: NMR ($CDCl_3$) δ 1.24 (s, 3 H), 1.34 (m, 2 H), 1.86 (m, 2 H), 2.02 (s, 3 H), 2.14 (s, 3 H), 2.18–2.66 (envelope, 5 H), 3.02 (dd, 1 H, J = 7, 12 Hz), 3.50 (m, 4 H), 4.52 (s, 2 H), 4.84 (d, 1 H, J = 6 Hz), 5.02 (m, 1 H), 7.34 (s, 5 H); 90-MHz ^{13}C NMR ($CDCl_3$) 21.133, 21.263, 22.108, 24.126, 25.752, 28.418, 35.831, 41.944, 50.723, 51.178, 70.101, 71.987, 73.233, 73.808, 73.938, 82.522, 127.784, 128.434, 138.124, 169.404, 169.794, 209.788 ppm; IR (film) 3040, 2980, 2880, 1735, 1710, 1450, 1370, 1230, 1100, 1040, 1010, 940, 860, 735, 695 cm^{-1}.

Preparation of (4α)-10α-(2-Hydroxyethyl)-1α-methyl-2α,8β-diacetoxy-5-oxo-11-oxatricyclo[7.2.1.0]dodecane (13). To a suspension of 0.552 of 10% Pd/C in 7.5 mL methanol was added 0.035 g (2.1 mmol) of **12**. The suspension was stirred under a hydrogen atmosphere at room temperature for 2 h. After thin-layer chromatography indicated that the starting material had been consumed, the suspension was filtered through Celite and concentrated in vacuo. The yield of crude product (0.747 g) was 100%. **13**: NMR ($CDCl_3$) δ 1.24 (s, 3 H), 2.05 (s, 3 H), 2.19 (s, 3 H), 3.4–3.7 (m, 4 H), 4.79 (br d, J = 6 Hz, 1 H), 5.00 (br t, J = 3 Hz, 1 H).

Preparation of (4α)-1α-Methyl-2α,8β-diacetoxy-5-oxo-11-oxatricyclo[7.2.1.0]dodecane-10α-acetic Acid (14). To a solution of 0.422 g (1.19 mmol) of **13** in 10 mL of acetone at 0 °C was added dropwise over 2 min 0.65 mL (2.6 mmol) of Jones reagent. The solution was stirred 15 min at 0 °C and 30 min at ambient temperature. One milliliter of isopropyl alcohol was then added followed by brine and methylene chloride. The organic layer was extracted again with brine, dried over sodium sulfate, filtered, and concentrated in vacuo. The product was isolated in 97% yield. It was sufficiently pure for the transformation to lactone **15**. The acid was insoluble in several NMR solvents. The NMR data are for the methyl ester derived from reaction with diazomethane: NMR ($CDCl_3$) δ 1.17 (s, 3 H), 2.09 (s, 6 H), 3.68 (s, 3 H), 4.67–5.00 (m, 2 H).

Preparation of Lactone (15). To a solution of 0.284 g (0.772 mmol) of **14** in 7 mL of methanol and three drops of water was added 0.637 g (3.86 mmol) of potassium carbonate. The solution was stirred for 4.5 h at ambient temperature. The solvent was then removed in vacuo, and 7 mL of methylene chloride and 9.5 mL of 1 N HCl were added. The mixture was heated to reflux for 10 h. After the reaction mixture had cooled to ambient temperature, the aqueous layer was extracted with ethyl acetate. The organic layer was wahed with brine, dried over sodium sulfate, filtered, and concentrated in vacuo. Chromatography provided 0.195 g (95%) of lactone **15**: NMR (CD_3COCD_3) δ 1.42 (s, 3 H), 3.92–4.2 (m, 3 H), 4.54 (br d, 1 H); ^{13}C NMR (CD_3COCD_3) 21.5, 33.3, 36.2, 41.4, 47.5, 54.8, 71.8, 73.2, 78.0, 81.5, 169.6, 209.9; IR (film) 3435, 1735, 1730 cm^{-1}.

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