product **2a** was obtained as an air-sensitive, white solid (2–3 mg, ~10% yield) that was pure by TLC and NMR: NMR (D_2O) δ 1.00 (t, 3 H), 1.44 (d, 6 H), 1.56 (m, 2 H), 2.7 (m, 2 H), 3.26 (m, 2 H), 3.54 (m, 1 H), 3.96 (m, 1 H), 6.95 (d, 1 H), 7.03 (d, 1 H).

6-(1-Acetoxyprop-2-enyl)-3,4-bis(benzyloxy)-1-(1,3-dioxolan-2-yl)benzene (19). The allylic alcohol **17** (1.8 g, 4.30 mmol) was dissolved in dry CH_2Cl_2 (40 mL), and dry pyridine (0.4 mL, 5.06 mmol), Ac_2O (0.5 mL, 5.3 mmol), and (dimethylamino)pyridine (5 mg) were added. The mixture was left in the freezer (–20 °C) overnight. Ether was added (100 mL), and the mixture was washed with 2% aqueous KOH (2 × 30 mL), 1% aqueous HCl (2 × 30 mL), and then saturated $NaHCO_3$ (3 × 30 mL). The organic phase was dried over $MgSO_4$ and filtered, and the solvent was removed. The resulting oil of **19** (after high vacuum) was produced in nearly quantitative yield: NMR ($CDCl_3$) δ 2.04 (s, 3 H), 4.04 (s, 4 H), 5.17 (m, 6 H), 5.94 (m, 1 H), 6.02 (s, 1 H), 6.56 (d, 1 H, J = 5 Hz), 6.97 (s, 1 H, 7.20 (s, 1 H), 7.40 (m, 10 H).

6-(3-Acetoxyprop-1-enyl)-3,4-bis(benzyloxy)benzaldehyde (20). The acetate **19** (1.8 g, 3.91 mmol) was dissolved in dry THF (50 mL), and dry CH_3CN (3 drops) was added. To this stirred solution under Ar was added $PdCl_2$ (20 mg). The mixture was stirred overnight at 25 °C. HCl (1 N, 20 mL) was added, and the resulting solution was stirred 1 h at 25 °C and then left overnight at –20 °C. Ether (100 mL) and water (100 mL) were added. The organic phase was separated and washed with saturated aqueous $NaHCO_3$ (3 × 25 mL), dried over $MgSO_4$, and filtered, and the solvent was removed. The oily product was chromatographed on silica gel to give **20** (1.6 g, 89% yield) as an oil: IR (neat) 2750, 1740, 1690, 1600, 1460, 1270 cm^{-1}; NMR ($CDCl_3$) δ 2.12 (s, 3 H), 4.77 (d, 2 H, J = 6 Hz), 5.23 (s, 2 H), 5.27 (s, 2 H), 6.10 (dt, 1 H, $^3J_{MX}$ = 16 Hz, $^3J_{AM}$ = 6 Hz), 7.07 (s, 1 H), 7.44 (m, 11 H), 10.18 (s, 1 H); mass spectrum, m/e 416 (M^+), 374, 373, 357, 356, 344, 343, 325, 322, 318.

Acknowledgment. We are grateful to Hoffmann-La Roche for a grant-in-aid and for support from the National Institutes of Health (Grant No. HL 26340) which enabled us to pursue this research. We thank Dr. Leslie Krasny, Moon Ja Choo, and Dr. Kenneth Melmon of Stanford University for carrying out the biological testing. We also thank Dr. Etienne Sonveaux and Kenneth Jacobson of our laboratories for helpful discussions and suggestions.

Approach to the Total Synthesis of Chlorothricolide: Synthesis of "7-*epi*-Bottom Half" and Its Union with "Top Half" Systems

Robert E. Ireland,* Wayne J. Thompson, Gabriel H. Srouji, and Rolf Etter

The Chemical Laboratories, California Institute of Technology,† Pasadena, California 91125

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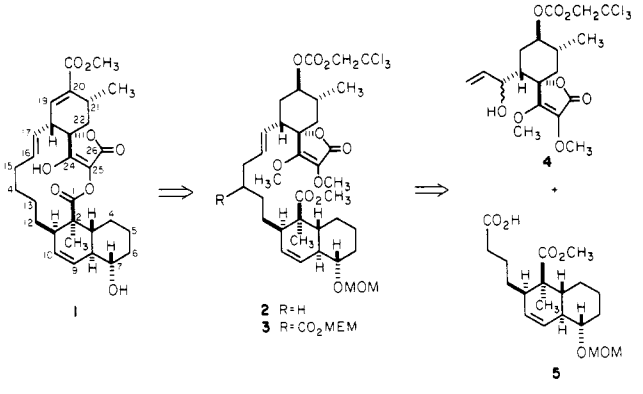
A synthesis of the "bottom half" of the antibiotic aglycon chlorothricolide (1) is described. Compound 1 was prepared in 13 steps from the readily available hydrobenzsuberone system 8; the process entails the stereoselective conjugate addition of [4-(benzyloxy)butyl]magnesium bromide to form the C ring. Union of the "top" and "bottom" halves and decarbonylation of the derived aldehyde are explored.

In a previous report[1] a basic synthetic strategy was presented for the construction of the aglycon chlorothricolide (1) from the macrolide antibiotic chlorothricin[2] (Scheme I). JO11B500##fnt# This plan entails the preparation of the open-chain ester **2** through the application of the ester enolate Claisen rearrangement[3] to the ester formed from "top half" alcohol **4** and "bottom half" acid **5** and then final lactone formation after appropriate deblocking of the ester **2**. In this earlier report[1] an efficient scheme was developed for the synthesis of the "top half" alcohol **4**, and model experiments demonstrated its utility in the proposed ester enolate Claisen rearrangement[3] approach. In the current report the construction of the "7-*epi*-bottom half" is developed, and the union of the two halves to form systems similar to the ester **2** is explored. This successful synthetic scheme stereoselectively generates a system in which the C7-hydroxyl function is epimeric with that in the natural product, but epimerization at this center is possible through oxidation and then reduction of the C7 ketone. Rather than effect this epimerization at this early stage, the "7-*epi*-bottom half" was used in subsequent explorations.

Scheme I



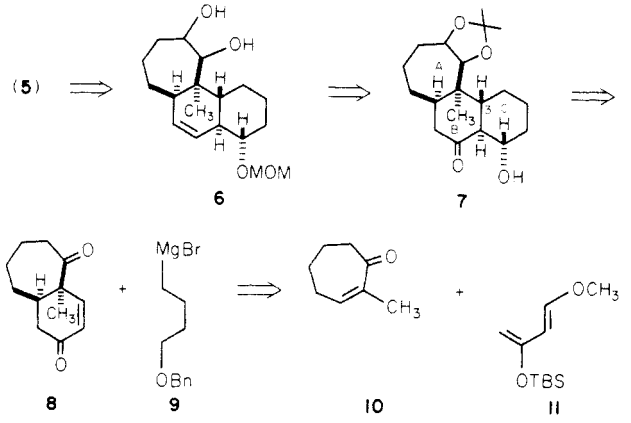
After investigation of several alternate routes, the sequence outlined retrosynthetically in Scheme II was pursued. In order to establish the cis relationship between the butyric acid side chain and the quaternary carboxyl group in the desired diacid **5**, we chose the oxidative cleavage of a cis-fused seven-membered ring system. This decision dictated the cis-anti-trans diol **6** as the penultimate intermediate, which itself was envisaged to arise from the tricyclic aldol-type system **7**. For the construction of this latter cis-anti-trans tricyclic system, advantage was taken of previous experience with the enedione **8**[4] which was available in large quantities by the Diels–Alder condensation of the enone **10** and the diene **11**.[5] The required

† Contribution No. 6435.

(1) Ireland, R. E.; Thompson, W. J. *J. Org. Chem.* **1979**, *44*, 3041–3052.
(2) (a) Keller-Schierlein, W.; Muntwyler, R.; Pache, W.; Zahner, H. *Helv. Chim. Acta* **1969**, *52*, 127–142. (b) Muntwyler, R.; Widmer, J.; Keller-Schierlein, W. *Ibid.* **1970**, *53*, 1544–1547. (c) Muntwyler, R.; Keller-Schierlein, W. *Ibid.* **1972**, *55*, 2071–2094. (d) Brufani, M.; Cerrini, S.; Fedeli, W.; Mazza, F.; Muntwyler, R. *Ibid.* **1972**, *55*, 2094–2102.
(3) Ireland, R. E.; Mueller, R. H.; Willard, A. K. *J. Am. Chem. Soc.* **1976**, *98*, 2868–2877.

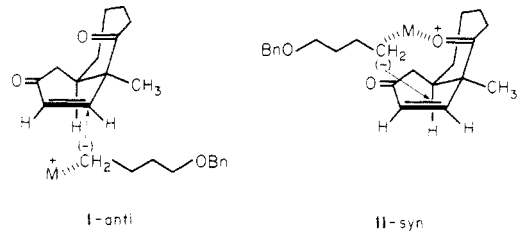
0022-3263/81/1946-4863$01.25/0

Scheme II



anti-trans relationship between this dicyclic ring system and the added C ring was then to be established through conjugative addition of the Grignard reagent **9** and then subsequent aldol-type ring closure. Stereochemically, then, this strategy hinges primarily on the outcome of the organometallic conjugate addition reaction that must establish the required anti relationship at C3 of the tricyclic backbone.

The incoming organometallic nucleophile **9** can approach either side of the α,β-unsaturated ketone system as depicted in the drawings I and II. The cis-fused dicyclic



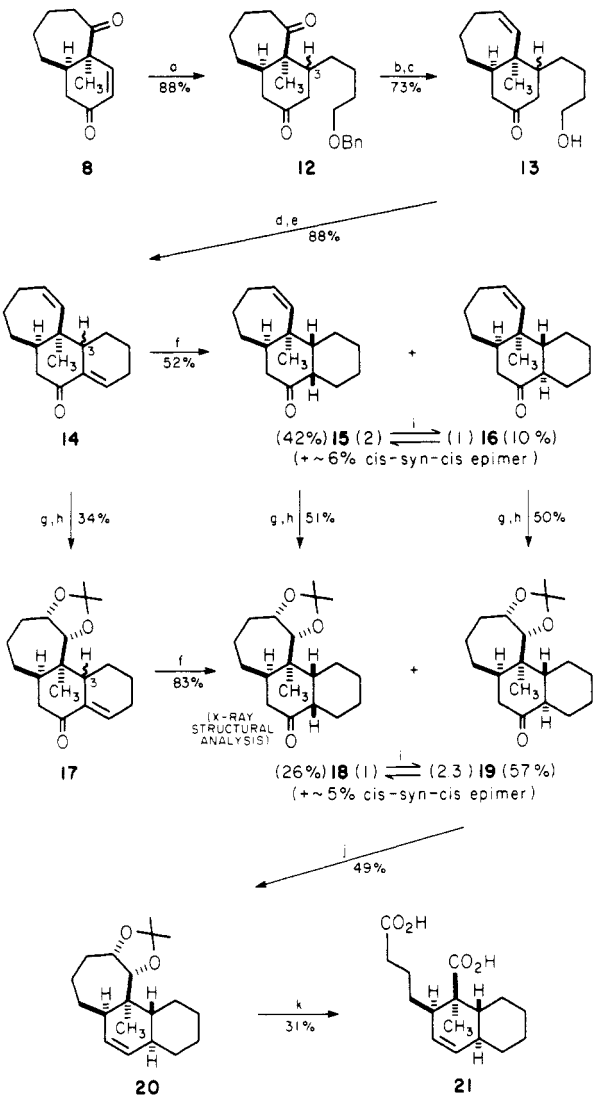
system is cup shaped, and conventional experience suggests that exo attack from the convex face of the dicyclic system should prevail (representation I-anti). The result of addition in this manner is the formation of the required anti relationship between the new substituent and the seven-membered-ring bond. Attack in this pseudoaxial fashion should also be favored on stereoelectronic grounds.

A complicating factor in this analysis is the presence of the seven-membered-ring ketone. It is conceivable that the organometallic reagent **9** will coordinate with the carbonyl oxygen of this ketone and thus promote the delivery of the carbon residue to the enone on the concave face of the dicyclic system (representation II-syn). Should such a situation predominate, the resulting product would have the undesired syn relationship between the newly added carbon substituent and the seven-membered-ring bond. Stereoelectronic control mitigates against this process, for the addition must take place in a pseudoequatorial fashion. Needless to say, gross steric considerations also disfavor such a concave face attack.

This analysis seems to favor the desired convex face approach (I-anti) of the organometallic reagent **9** and offers, as well, an interesting test of the effect of potential oxygen–metal coordination on the outcome of such reactions. As such, the scheme seemed a worthwhile endeavor, and the results are depicted in Schemes III and IV.

In Scheme III the generation of the key intermediate

Scheme III. Synthesis of "7-Deoxy-Bottom Half" (21)[a]



[a] (a) $BnOC_4H_8MgBr$, $Cu(OAc)_2$, THF; (b) $(CH_2OH)_2$, C_6H_6, *p*-TsOH; (c) LDA, THF; $ClPO(NMe_2)_2$; Li, NH_3, THF, *t*-BuOH; (d) $Py_2Cr_2O_7$, CH_2Cl_2; (e) C_6H_6, *p*-TsOH; (f) Li, NH_3, THF, *t*-BuOH; (g) OsO_4, NMO, THF, H_2O, *t*-BuOH; (h) $CH_3C(OCH_3)_2CH_3$, *p*-TsOH; (i) $NaOCH_3$, CH_3OH; (j) LDA, THF; $ClPO(NMe_2)_2$; Li, $EtNH_2$, THF, *t*-BuOH; (k) CH_3OH, H_2O, *p*-TsOH; CH_3OH, H_2O, $NaIO_4$; $Py_2Cr_2O_7$, DMF.

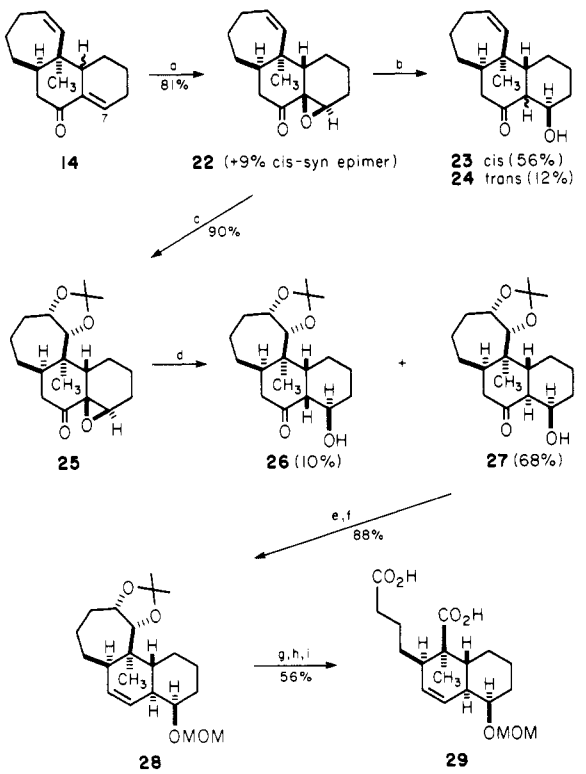
dienone **14** is presented together with its conversion to the "7-deoxy-bottom half" system **21**.

Copper acetate[6] catalyzed conjugate addition of [4-(benzyloxy)butyl]magnesium bromide[7] to the enedione **8**[4] provided what on spectral and chromatographic grounds appeared to be a single adduct **12** in 88% yield. While it was later found that this adduct **12** was an ~9:1 mixture of the C3 epimers in which the desired anti epimer was the preponderant one, it was not possible to detect or separate the isomers at this stage. Rather, it was decided to convert this adduct **12** to the more readily analyzed tricyclic system.

Selective ketalization of the less hindered six-membered-ring ketone, conversion of the seven-membered-ring

(4) Ireland, R. E.; Aristoff, P. A.; Hoyng, C. F. *J. Org. Chem.* **1979**, *44*, 4318–4322.
(5) Danishefsky, S.; Kitahara, T. J. *J. Am. Chem. Soc.* **1974**, *96*, 7807–7808.
(6) Posner, G. H. *Org. React.* **1972**, *19*, 1.
(7) (a) Freedman, H. H.; DuBois, R. A. *Tetrahedron Lett.* **1975**, 3251–3254. (b) Schweizer, E. E.; Creasy, W. S.; Light, K. K.; Shaffer, E. T. *J. Org. Chem.* **1969**, *34*, 212–218.
(8) The structures shown in these schemes depict one enantiomer of a racemic mixture for graphic simplicity, but in all cases only the racemate was obtained. No resolution of these racemates was effected.

Scheme IV.[8] Synthesis of "7-*epi*-Bottom Half" (29)[a]



[a] (a) 30% H_2O_2, 10% aqueous NaOH, CH_3OH; (b) Li, NH_3, THF, NH_4Cl; (c) OsO_4, NMO, THF, H_2O, *t*-BuOH; $CH_3C(OCH_3)_2CH_3$, *p*-TsOH; (d) Na, NH_3, THF; NH_4Cl; (e) CH_3OCH_2Cl, $(i\text{-}C_3H_7)_2C_2H_5N$, CH_2Cl_2; (f) LDA, THF; $ClPO(NMe_2)_2$; Li, $EtNH_2$, THF, *t*-BuOH; (g) CH_3OH, H_2O, PyOTs; (h) $NaIO_4$, CH_3OH, H_2O; (i) $Py_2Cr_2O_7$, DMF.

ketone to an olefin through reductive cleavage of the derived enol phosphorodiamidate,[9] and then ketal hydrolysis afforded the keto alcohol **13** in good yield. Subsequent oxidation of the primary alcohol to an aldehyde and then acid-catalyzed aldol dehydration-condensation completed the formation of the C ring and generated the key dienone **14** in excellent yield. Base-catalyzed ($NaOCH_3/CH_3OH$, 5 °C) aldol condensation conditions were also explored in an effort to generate the C7-hydroxyl substituent directly, but the yield in this process was intolerably low.

For exploration of the final chemical transformations to the "bottom half" diacid system as well as to prepare rapidly a suitably complex intermediate to warrant X-ray structure analysis, the synthetic effort was pushed on toward the "7-deoxy-bottom half" **21**. Reduction of dienone **14** with lithium in liquid ammonia afforded three distinct compounds (TLC analysis). Careful chromatography furnished the cis-anti-cis isomer **15** as the major product. The desired cis-anti-trans isomer **16** was a minor component, and for the first time in the synthetic sequence, it was possible to isolate the cis-syn-cis isomer that resulted from the initial syn addition of the cuprate to the enedione **8**. The stereochemistry of this latter product was established by direct comparison with an authentic sample.[10]

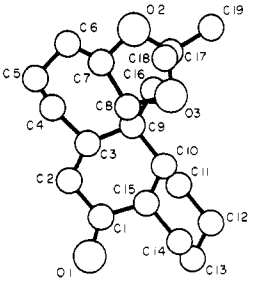


Figure 1. Structure of keto acetonide **18** from X-ray analysis.[11]

Treatment of either the cis-anti-cis isomer **15** or the cis-anti-trans isomer **16** with base produced an equilibrium mixture of the two isomers in a ratio 2:1, respectively. In an effort to modify this unfavorable ratio as well as to continue with the synthesis, we individually converted these isomeric ketones **15** and **16** to the acetonides **18** and **19**, respectively, and base-catalyzed equilibration of the decalone ring system was again explored. In these cases in which the two trigonal carbons in the seven-membered ring were absent, the ratio of the two epimers **18** and **19** was now 1:2.3, and the desired cis-anti-trans isomer **19** was readily available. A more eficient process for the generation of this same isomer mixture then proved to be the initial conversion of the dienone **14** to the acetonide **17**, which was reduced in good yield with lithium in ammonia. After separation of the isomers **18** and **19**, the undesired cis-anti-cis isomer **18** could be reconverted to the equilibrium mixture of isomers, and thus, in theory, the yield of the desired cis-anti-trans isomer approaches the yield of the reduction process.

It was at this juncture that structural and stereochemical conformation was sought, and X-ray structure analysis[11] of the nicely crystalline cis-anti-cis keto acetonide **18** established this arrangement, as shown in Figure 1. By the process of elimination, then, the isomer **19** is the desired cis-anti-trans keto acetonide.

Completion of the synthesis of the "7-deoxy-bottom half" diacid was now readily accomplished through conversion of the keto acetonide **19** to the olefin acetonide **20** by reduction of the derived enol phosphorodiamidate[9] and then periodate cleavage and oxidation of the diol system obtained after acid-catalyzed acetonide cleavage. The information learned in this effort was now applied to the synthesis of the "7-*epi*-bottom half" diacid itself which is shown in Scheme IV.

In order to introduce an oxygen function at C7, advantage was taken of the enone system in the key dienone **14**. Thus oxidation of this dienone **14** with basic hydrogen peroxide readily formed the keto epoxide **22** together with a small amount of the cis-syn epimer derived from material formed during the earlier conjugate addition reaction. The stereochemical result of this oxidation was deferred until completion of the diacid **29** synthesis. Again direct reduction of the keto epoxide **22** with lithium in ammonia led to a mixture of the keto alcohols **23** and **24** in which

(9) Ireland, R. E.; Muchmore, D. C.; Hengartner, U. *J. Am. Chem. Soc.* 1972, *94*, 5098–5100.

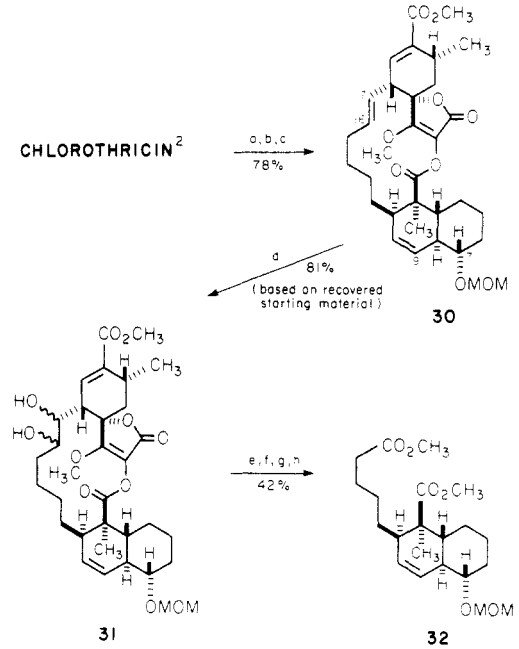
(10) Prepared by an alternate unpublished synthetic scheme by R. C. Anderson in this laboratory (Research Report, 1980) in which the final step was

(11) This X-ray structural analysis was kindly provided by Professor N. Mandel (University of Wisconsin—Milwaukee), and the details will be published independently elsewhere.

(12) The materials prepared in this scheme are derived from the natural product and, as such, are optically active. The structures shown, therefore, represent only the naturally derived enantiomer formed.

(13) Since the allylic alcohol **33** and the acid ester **34** are synthetic materials, and hence racemates, the union of these two compounds produces a diastereosomeric mixture. For the sake of clarity only one diastereoisomeric racemate is shown, but in all cases the materials prepared were indeed inseparable mixtures of diastereoisomeric racemates. Chemical resolution of this mixture is proposed to occur during the final lactonization stage.

Scheme V.[12] Oxidative Cleavage of *O*-Methylchlorothricolide Methyl Ester[a]



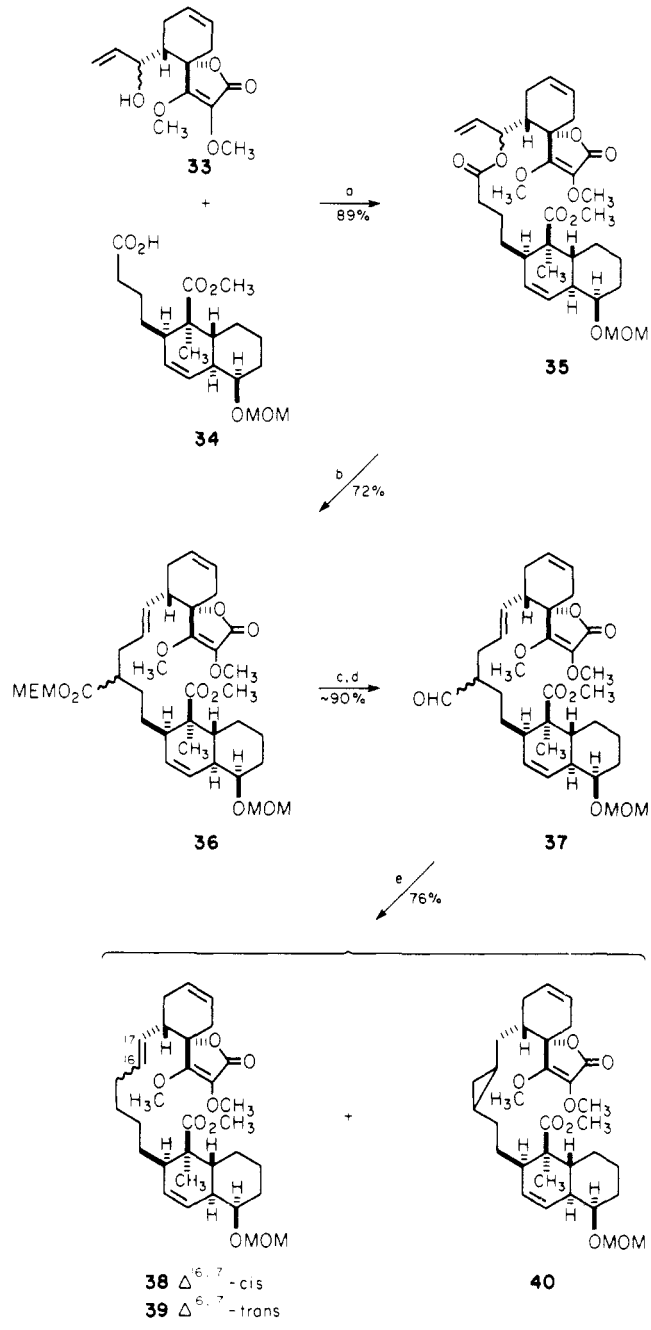
[a] (a) CH_3OH, H_2SO_4, Δ; (b) CH_2N_2, Et_2O; (c) CH_3OCH_2Cl, $(i\text{-}C_3H_7)_2C_2H_5N$, CH_2Cl_2; (d) OsO_4, NMO, THF, H_2O, *t*-BuOH; (e) $NaIO_4$, dioxane, H_2O; (f) $Py_2Cr_2O_7$, DMF; (g) NaOH, EtOH, Δ; (h) CH_2N_2, Et_2O.

the undesired cis-anti-cis epimer predominated. Base-catalyzed equilibration of these isomers was now not possible, as β elimination of the C7-hydroxyl function took precedence. It was gratifying to find, however, that sodium–ammonia reduction of the epoxy keto acetonide **25** formed on epoxidation of the initially formed acetonide gave a mixture of keto alcohols **26** and **27** in which the desired cis-anti-trans isomer **27** greatly predominated. After chromatographic separation of these isomers, the cis-anti-trans isomer **27** was carried on to the diacid **29**, as before, with the additional step necessary to block the C7-hydroxyl function. At this stage it was necessary to establish the stereochemistry of this diacid **29** system, and advantage was taken of the close similarity of this "bottom half" to that derivable from the natural product itself.

A sample of chlorothricin,[2] kindly provided by Professor Keller-Schierlein, was degraded as shown in Scheme V. An interesting feature of this degradation is the selectivity possible in the osmylation reaction to form the diol **31**. The cyclohexenyl C9(10) double bond is significantly more hindered than the side chain C16(17) olefin, and no competitive osmylation of the ring was observed.

Comparison of the ^1H NMR spectrum of the dimethyl ester **32** obtained in this fashion from natural chlorothricin with the corresponding dimethyl ester of the synthetic, lower homologue diacid **29** revealed their close similarity. However, the resonance of the C7-hydrogen of the synthetic diester was a broad singlet (3.87 ppm) which was clearly downfield from the very broad multiplet (3.25 ppm) that represented the corresponding proton in the naturally derived homologue **32**. Even more convincing was the through-space deshielding of the C9 olefinic proton by the equatorial C7-oxygen function in the natural homologue **32**. The resonance of this C9-hydrogen in this diester **32** was a doublet centered at 5.88 ppm while in the synthetic diester this olefinic hydrogen's resonance appeared as a similar doublet centered at 5.40 ppm. Since X-ray analysis and base-catalyzed equilibration studies of the cis-anti-cis ketone ketal **18** have confirmed that the other asymmetric

Scheme VI.[13] Model Studies on the Union of the "Top Half" with "7-*epi*-Bottom Half"[a]



[a] (a) DCC, DMAP, CH_2Cl_2; (b) $KN(Me_3Si)_2$, THF, HMPA; *t*-$BuMe_2SiCl$, THF, $CH_3OC_2H_5OCH_2Cl$, $(i\text{-}C_3H_7)_2C_2H_5N$, CH_2Cl_2; (c) Super Hydride, THF; (d) $Py_2Cr_2O_7$, CH_2Cl_2; (e) $[(C_6H_5)_3P]_3RhCl$, $ClCH_2CH_2Cl$, Δ.

centers compare in chirality with the natural system, these results establish that the synthetic diester is epimeric with the natural material at the C7-oxygen function. After some exploratory efforts to epimerize this center to the natural configuration were only marginally successful, it was decided to postpone this transformation until a later stage, and the "7-*epi*-bottom half" was used in subsequent experiments.

In the previous report[1] on this synthesis, a study of the union of several model "bottom halves" with "top half" systems was undertaken to assure the viability of the ester enolate Claisen rearrangement[3] chemistry for this crucial operation. Now, with "7-*epi*-bottom half" available this union was again pursued. Contrary to the results found with the less hindered model systems,[1] it was not possible

to use the diacid chloride of the diacid **29** in an esterification reaction with "top half" allylic alcohols. While esterification took place, the resulting ester–acid chloride could not be selectively hydrolyzed to the desired ester–acid due to the steric hindrance of the tertiary carboxyl function. In view of this steric congestion it seemed a reasonable assumption that the diester **35** (see Scheme VI) would undergo the ester enolate Claisen rearrangement in contrast to the Dieckmann cyclization that plagued the less hindered model systems studied earlier.[1] Formation of the diester **35** was straightforwardly accomplished when the monoester **34** and the "top half" allylic alcohol **33** were treated with dicyclohexylcarbodiimide in methylene chloride solution. Rearrangement of this diastereoisomeric mixture of diesters **35** and then formation of the (2'-methoxyethoxy)methyl (MEM) ester[14] **36** now proceeded in good yield *without* any Dieckmann cyclization side products. While the mixture was still an unseparable mixture of diastereomers, separation at a later stage (lactonization) was predictable, and diester **36** was carried further to the aldehyde **37**.[15]

The decarbonylation reaction of this aldehyde **37** was studied in some detail, for the reaction product was more complicated than a mere diastereoisomeric mixture would warrant. Separation of this product mixture with the aid of high-pressure liquid chromatography afforded three distinct diastereoisomeric mixtures that were identified as the *cis*-**38** and *trans*-**39** olefins and the cyclopropyl system **40** by analysis of their 500-MHz ^{1}H NMR spectra (see Experimental Section). This product mixture was very difficult to resolve, and while careful spectral reexamination of the previous[1] model system product mixtures now revealed the presence of similar isomeric products, the separation of these latter mixtures was not possible. In both cases modification of the reaction conditions (solvent, temperature, time) in modest ways did not result in much change in the ratio of the three products formed. Thus, while the union of the "top" and "bottom" halves has been efficiently accomplished through the use of the enolate Claisen rearrangement,[3] further methodology must be explored for the subsequent "decarboxylation" stage. The results of this effort and the subsequent lactonization process will be the subject of a future report.

Experimental Section[16]

4-[4-(Benzyloxy)butyl]-4aα-methyl-3,4,4a,7,8,9aα-hexahydro-9*H*-benzocycloheptene-2(1*H*),5(6*H*)-dione (12). To a stirred solution of 14 g (0.07 mol) of enedione **8** and 1.16 g (8 mol %) of copper(II) acetate in 200 mL of dry tetrahydrofuran at −30 °C was added dropwise with stirring 120 mL of 0.73 M [4-(benzyloxy)butyl]magnesium bromide in tetrahydrofuran over a period of 70 min. The deep blue reaction mixture was allowed to warm to room temperature and then stirred for 2.5 h. After 50 mL of 5% hydrochloric acid was added, the reaction mixture was diluted with 400 mL of ether. The organic layer was separated and then washed with water. The aqueous layer was back-extracted with ether, and the combined organic extracts were washed with 10% aqueous sodium bicarbonate solution and brine and then dried ($MgSO_4$). Removal of the solvent at reduced pressure gave a yellow oil which was chromatographed on silica gel. Elution with 50% ether–petroleum ether afforded the diketone **12** as 22.8 g of a pale yellow oil (88%). The analytical sample was prepared by evaporative distillation at >150 °C (0.003 mmHg): IR ($CHCl_3$) 1700 (C=O), 1715 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$) δ 1.15 (s, 3 H, CH_3C), 3.41 (m, 2 H, CH_2OCH_2Ph), 4.42 (s, 2 H, OCH_2Ph), 7.30 (s, 5 H, C_6H_5).

Anal. Calcd for $C_{23}H_{32}O_3$: C, 77.48; H, 9.06. Found: C, 77.56; H, 9.24.

2,2(1*H*)-(Ethylenedioxy)-4-[4-(benzyloxy)butyl]-4aα-methyl-3,4,4a,7,8,9aα-hexahydro-9*H*-benzocyclohepten-5-(6*H*)-one. A solution of 4.48 g (13 mmol) of diketone **12** and 3.5 mL (63 mmol) of ethylene glycol in 120 mL of dry benzene that contained a catalytic amount of *p*-toluenesulfonic acid monohydrate was heated under reflux for 45 min in an argon atmosphere under a Dean–Stark apparatus. After the reaction mixture was cooled to room temperature and then poured into 10% aqueous sodium bicarbonate solution, the organic layer was separated, washed with brine, and then dried ($MgSO_4$). Removal of the solvent at reduced pressure gave 5.09 g of the monoketal as a viscous oil (quantitative). The analytical sample was prepared by evaporative distillation at >150 °C (0.003 mm Hg): IR ($CHCl_3$) 1700 cm^{-1} (C=O); NMR ($CDCl_3$) δ 1.06 (s, 3 H, CH_3C), 3.42 (m, 2 H, CH_2OCH_2Ph), 3.86 (s, 4 H, $(CH_2O)_2$), 4.44 (s, 2 H, OCH_2Ph), 7.30 (s, 5 H, C_6H_5).

Anal. Calcd for $C_{25}H_{36}O_4$: C, 74.96; H, 9.06. Found: C, 75.13; H, 9.10.

4-(4-Hydroxybutyl)-4aα-methyl-3,4,4a,7,8,9aα-hexahydro-9*H*-benzocyclohepten-2(1*H*)-one (13). To a stirred solution of lithium diisopropylamide (47 mmol) in 70 mL of dry tetrahydrofuran at 0 °C was added 9.4 g (23 mmol) of the above monoketal in 50 mL of dry tetrahydrofuran over a period of 30 min. The resulting mixture was stirred with cooling for an additional 30 min. After 8.4 mL of hexamethylphosphoramide was added, 30 mL of bis(dimethylamino)phosphorochloridate was added with stirring in one portion, and the reaction mixture was allowed to warm to room temperature. After being stirred for 1.5 h, the mixture was poured into saturated aqueous sodium bicarbonate solution, and the whole was stirred for 1 h to hydrolyze the excess phosphorochloridate. The aqueous solution was extracted with ether, and the combined organic extracts were washed with brine and then dried ($MgSO_4$). Removal of the solvent at reduced pressure gave the enol phosphorodiamidate as a yellow oil which was used directly without further purification.

A solution of this crude oil in 150 mL of dry tetrahydrofuran was added to a solution of 20 mL of dry *tert*-butyl alcohol in 1 L of dry liquid ammonia. Enough lithium was added to the refluxing solution to keep the dark blue color for 3 h. Excess lithium was destroyed by careful addition of solid ammonium chloride; the ammonia was allowed to evaporate, and then the residue was partitioned between ether and water. The organic layer was separated, and the aqueous layer was extracted with ether. The combined organic extracts were then washed with brine and dried ($MgSO_4$). Removal of the solvent at reduced pressure gave a yellow oil.

Without further purification, this oil was dissolved in 100 mL of acetone; 8 mL of 3 N hydrochloric acid was added, and the reaction mixture was stirred at room temperature for 1.5 h. After removal of the solvent, the residue was dissolved in ether, and the resulting ethereal solution was washed with water, 10% aqueous sodium bicarbonate solution, and brine and then dried ($MgSO_4$). After removal of the ether at reduced pressure, the residual yellow oil was chromatographed on 250 g of silica gel. Elution with 1:1 ethyl acetate–petroleum ether afforded 4.31 g

(14) Corey, E. J.; Gras, L.-L.; Ulrich, P. *Tetrahedron Lett.* **1976**, 809–813.

(15) Ireland, R. E.; Thompson, W. J. *Tetrahedron Lett.* **1979**, 4705–4708.

(16) Melting points were determined by using a Hoover capillary melting point apparatus. All melting points and boiling points are uncorrected. Infrared spectra (IR) were determined on a Perkin-Elmer 727B infrared spectrometer. All proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on a Varian T-60 or EM-390 spectrometer except those for compounds **38–40** which were recorded on a Brucker WM-500 spectrometer.[19] Chemical shifts are reported in parts per million (δ) relative to tetramethylsilane (δ 0.0) as an internal standard. Analytical thin-layer chromatography (TLC) was conducted on 2.5 × 10 cm^{-1} precoated TLC plates (silica gel 60 F-254, layer thickness 0.255 mm, manufactured by E. Merck and Co.). All silica gel used for column chromatography was E. Merck silica gel 60 (70–230 mesh ASTM). Dry solvents were distilled shortly before use from an appropriate drying agent. Ether and tetrahydrofuran (THF) were distilled under argon from sodium metal in the presence of benzophenone. Benzene was distilled from calcium hydride. Dichloromethane was distilled from phosphorus pentoxide. Hexamethylphosphoramide (HMPA) and dimethylformamide (DMF) were distilled from pulverized calcium hydride. Diisopropylamine was distilled before use from calcium hydride. Ammonia and ethylamine were distilled from the tank and then from a blue lithium solution. All other solvents were "reagent grade" unless described otherwise. Elemental combustion analyses were performed by Spang Microanalytical Laboratory.

(17) Corey, E. J.; Schmidt, G. *Tetrahedron Lett.* **1979**, 399–402.

(73%) of a colorless viscous oil. The analytical sample was prepared by evaporative distillation at >150 °C (0.003 mmHg): IR ($CHCl_3$) 3500 (OH) 1700 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 1.20 (s, 3 H, CH_3C), 3.60 (m, 2 H, CH_2O), 5.44 (d, 1 H, J = 12 Hz, vinyl H), 5.80 (m, 1 H, vinyl H).

Anal. Calcd for $C_{16}H_{26}O_2$: C, 76.75; H, 10.47. Found: C, 76.40; H, 10.20.

4-(4-Hydroxybutyl)-4aα-methyl-3,4,4a,7,8,9aα-hexahydro-9*H*-benzocyclohepten-2(1*H*)-one. To a well-stirred suspension of 3.78 g (16 mmol) of pyridinium chlorochromate[18] in 25 mL of dry dichloromethane was added 2.2 g (9 mmol) of keto alcohol **13** in 15 mL of dry dichloromethane. The resulting mixture was allowed to stir at room temperature for 2 h and then diluted with ether. After decantation, the remaining black gum was washed with ether until it became solid. The combined organic extracts were filtered through a column of Florisil and flushed with ether. Removal of the solvent at reduced pressure afforded 2.13 g (97% crude yield) of the corresponding keto aldehyde which was converted to enone **14** without further purification: IR ($CHCl_3$) 1700 (C=O), 1710 (C=O), 2715 cm^{-1} (aldehydic CH); ^1H NMR ($CDCl_3$) δ 1.17, 1.23 (2 s, 3 H, CH_3C), 5.40 (d, 1 H, J = 12 Hz, vinyl H), 5.73 (m, 1 H, vinyl H), 9.70 (t, 1 H, aldehyde); mass measured for molecular ion: calcd for $C_{16}H_{24}O_2$ 248.178, found 248.176.

11aα-Methyl-5aα,9,10,11,11aβ,11b-hexahydronaphtho[*a*]-cyclohept-1-en-7(6*H*)-one (14). A solution of 1.48 g (6 mmol) of the above keto aldehyde in 150 mL of benzene and 25 mg of *p*-toluenesulfonic acid monohydrate was heated at reflux under an argon atmosphere for 2 h in a Dean–Stark apparatus. The reaction mixture was allowed to cool to room temperature and then poured into 10% aqueous sodium bicarbonate solution. The organic layer was separated, washed with brine, and then dried ($MgSO_4$). After removal of the solvent at reduced pressure, the residual yellow oil was chromatographed on silica gel. Elution with 10% ethyl acetate–hexane afforded 1.12 g (88%) of the dienone **14** as a viscous oil: IR ($CHCl_3$) 1680 (C=O), 1610 cm^{-1} (C=C); ^1H NMR ($CDCl_3$) δ 1.13 (s, 3 H, CH_3C), 5.34 (d, 1 H, J = 12 Hz, vinyl H), 5.80 (m, 1 H, vinyl H), 6.88 (m, 1 H, HC=C—C=O); mass measured for molecular ion: calcd for $C_{16}H_{22}O$ 230.167, found 230.165.

11bα-Methyl-5aα,7aβ,8,9,10,11,11aβ,11b-octahydronaphtho[*a*]cyclohepten-7(6*H*)-one (15). 11bα-Methyl-5aα,7aα,8,9,10,11,11aβ,11b-octahydronaphthol[*a*]cyclohepten-7(6*H*)-one (16), and 11bα-Methyl-5aα,7aβ,8,9,10,11,11aα,11b-octahydronaphtho[*a*]cyclohepten-7(6*H*)-one. To a stirred solution of 60 mL of dry ammonia, 320 mg (1.4 mmol) of enone **14** in 9 mL of dry tetrahydrofuran, and 0.14 mL (1.4 mmol) of *tert*-butyl alcohol was added 21 mg (3 mmol) of lithium wire. The blue solution was allowed to reflux under an argon atmosphere for 1.2 h. Excess lithium was destroyed by careful addition of solid ammonium chloride, and the ammonia was then allowed to evaporate. The residue was partitioned between ether and water, and then the organic layer was separated, washed with brine, and dried ($MgSO_4$). Removal of the solvent at reduced pressure afforded 310 mg of a yellow oil. Careful chromatography on 60 g of silica gel with 3% ethyl acetate–hexane gave 140 mg (42%) of the cis isomer **15**. The analytical sample, prepared by recrystallization from hexane, melted at 64–65.5 °C: IR ($CHCl_3$) 1700 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 1.17 (s, 3 H, CH_3C), 5.5 (d, 1 H, J = 12 Hz, vinyl H), 5.82 (m, 1 H, vinyl H).

Anal. Calcd for $C_{16}H_{24}O$: C, 82.70; H, 10.41. Found: C 82.77; H, 10.57.

Further elution with the same solvent mixture afforded 20 mg (6%) of the cis-syn-cis epimer as a waxy solid that was purified for analysis by evaporative distillation at 125 °C (0.003 mmHg): IR ($CHCl_3$) 1700 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 1.20 (s, 3 H, CH_3C), 2.78 (t, 1 H, J = 12 Hz, CH—C=O), 5.63 (d, 1 H, J = 12 Hz, vinyl H), 5.88 (m, 1 H, vinyl H).

Anal. Calcd for $C_{16}H_{24}O$: C, 82.70; H, 10.41. Found: C, 82.68; H, 10.34.

Continued elution with the same solvent mixture gave 30 mg (10%) of the trans isomer **16** as a white solid. The analytical sample, prepared by recrystallization from hexane, melted at 57–59 °C: IR ($CHCl_3$) 1700 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 1.33 (s, 3 H, CH_3C), 2.75 (dd, 1 H, J = 13.5, 6 Hz, CH—C=O), 5.34 (dd, 1 H, J = 2, 12 Hz, vinyl H), 5.70 (ddd, 1 H, J = 6, 7, 12 Hz, vinyl H).

Anal. Calcd for $C_{16}H_{24}O$: C, 82.70; H, 10.41. Found: C, 82.68; H, 10.33.

1α,2α-(Isopropylidenedioxy)-11bα-methyl-5aα,7aβ,8,9,10,11,11aβ,11b-octahydronaphtho[*c*]cyclohepten-7(6*H*)-one (18). To a solution of 150 mg (0.5 mmol) of ketone **15** in 0.5 mL of *tert*-butyl alcohol, 0.17 mL of tetrahydrofuran, and 0.05 mL of water were added 100 mg (0.7 mmol) of *N*-methylmorpholine *N*-oxide monohydrate (NMO) and then 0.13 mL of a 0.1 M solution of osmium tetraoxide in *tert*-butyl alcohol. The reaction mixture was allowed to stir at room temperature for 42 h, after which 30 mL of sodium hydrosulfite, 50 mg of Florisil, and 0.5 mL of water were added. The solid was filtered and then washed with dicholormethane. After acidification of the filtrate with 1 N sulfuric acid, the organic layer was separated, and the aqueous layer was extracted with dichloromethane. The combined dichloromethane extracts were washed with brine and then dried ($MgSO_4$). Removal of the solvent at reduced pressure gave a yellow oil which was chromatographed on 25 g of silica gel. Elution with 1:1 ethyl acetate–hexane provided 90 mg (54%) of a white foam which solidified upon standing at room temperature for several days. This material (mp 111–112 °C) was not further purified but used directly in the following experiment: IR ($CHCl_3$) 3500 (OH), 1700 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 1.13 (s, 3 H, CH_3C), 2.28 (m, 2 H), 4.2 (m, 2 H, $(CHO)_2$).

To a stirred solution of 210 mg (0.80 mmol) of the above diol in 3.5 mL of dimethoxypropane was added 3 mg of *p*-toluenesulfonic acid monohydrate. The reaction mixture was allowed to stir at room temperature for 10 min, and then 0.2 mL of ammonium hydroxide was added. After removal of the solvent at reduced pressure, the residual pale yellow oil was filtered through a short pad of silica gel. Elution with chloroform gave the ketone ketal **18** as a white crystalline solid, 230 mg (95%). The analytical sample, prepared by recrystallization from ether–hexane, melted at 144–146 °C: IR ($CHCl_3$) 1700 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 1.07 (s, 3 H, CH_3C), 1.36, 1.51 (2 s, 6 H, $(CH_3)_2C$), 2.96 (m, 1 H, CHCO).

Anal. Calcd for $C_{19}H_{30}O_3$: C, 74.47; H, 9.87. Found: C, 74.51; H, 9.75.

This material was used for single-crystal X-ray analysis by Professor N. Mandel (University of Wisconsin—Milwaukee).[11]

1α,2α-(Isopropylidenedioxy)-11bα-methyl-5aα,7aα,8,9,10,11,11aβ,11b-octahydronaphtho[*a*]cyclohepten-7(6*H*)-one (19). To a stirred solution of 45 mg (0.15 mmol) of the keto acetonide **18** in 2 mL of dry methanol under an argon atmosphere was added 0.4 mL of a 0.5 M solution of sodium methoxide in methanol, and the resulting mixture was stirred at room temperature for 5 h. The reaction mixture was quenched with 0.1 mL of glacial acetic acid, and then the solvent was removed at reduced pressure. A solution of the residue in dichloromethane was washed with 10% aqueous sodium bicarbonate solution and brine and then dried ($MgSO_4$). After removal of the solvent at reduced pressure, the residual pale yellow solid (44 mg) was chromatographed on silica gel. Elution with 1:1 ether–hexane afforded 33 mg (43%) of the trans isomer **19** and 8 mg (17%) of starting material **18**. The overall yield of the desired product **19** based on recovered starting material was 91%. An analytical sample of the trans isomer **19** was prepared by recrystallization from hexane: mp 127–128 °C: IR ($CHCl_3$) 1700 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 1.33, 1.50 (2 s, 6 H, $(CH_3)_2C$), 1.45 (s, H, CH_3C), 2.75 (dd, 1 H, J = 13.5, 6 Hz, CHCO), 4.32 (br s, 2 H, $(CHO)_2$).

Anal. Calcd for $C_{19}H_{30}O_3$: C, 74.47; H, 9.87. Found: C, 74.32; H, 9.72.

1α,2α-(Isopropylidenedioxy)-11bα-methyl-5aα,9,10,11,11aβ,11b-hexahydronaphtho[*a*]cyclohepten-7(6*H*)-one (17). To a solution of 540 mg (2.3 mmol) of enone **14** in 1.5 mL of *tert*-butyl alcohol, 0.5 mL of tetrahydrofuran, and 0.15 mL of water were added 380 mg (2.8 mmol) of *N*-methylmorpholine *N*-oxide monohydrate and 0.5 mL of a 0.1 M solution of osmium tetraoxide in *tert*-butyl alcohol. The reaction mixture was allowed to stir at room temperature for 6 days, and then 100 mg of sodium hydrosulfite, 100 mg of Florisil, and 0.5 mL of water were added.

(18) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647–2650.
(19) Southern California Regional NMR Facility, NSF Grant No. CHE-7916324.

After the mixture stirred at room temperature for 10 min, the solids were filtered and washed with dichloromethane. The filtrate was acidified with 1 N sulfuric acid and extracted with dichloromethane. The combined organic extracts were washed with 10% aqueous sodium bicarbonate solution and brine and dried ($MgSO_4$). Removal of the solvent at reduced pressure gave a pale brown oil which was chromatographed on silica gel. Elution with 80% ethyl acetate–petroleum ether gave 95 mg of starting material and then 220 mg (27%) of the diol as a white solid. The analytical sample, prepared by recrystallization from chloroform–hexane, melted at 148–149 °C: IR ($CHCl_3$) 3600, 3450 (OH), 1680 (C=O), 1610 cm^{-1} (C=C); ^1H NMR ($CDCl_3$) δ 1.1 (s, 3 H, CH_3C), 4.00 (m, 2 H, $(CHOH)_2$), 6.88 (m, 1 H, HC=C—CO).

Anal. Calcd for $C_{16}H_{24}O_3$: C, 72.69; H, 9.15. Found: C, 72.87; H, 9.19.

To a solution of 180 mg (0.7 mmol) of the above diol in 4 mL of dimethoxypropane was added a catalytic amount of *p*-toluenesulfonic acid monohydrate. The reaction mixture was stirred at room temperature for 5 min, and after the usual workup, the keto acetonide **17** was obtained as a white solid, 180 mg (91%). The analytical sample, prepared by recrystallization from chloroform–hexane, melted at 134–136 °C: IR ($CHCl_3$), 1680 (C=O), 1610 cm^{-1} (C=C); ^1H NMR ($CDCl_3$) δ 1.23 (s, 3 H, CH_3C), 1.33, 1.50 (2 s, 6 H, $(CH_3)_2C$), 4.26 (br s, 2 H, $(CHO)_2$), 6.9 (m, 1 H, HC=C—CO).

Anal. Calcd for $C_{19}H_{28}O_3$: C, 74.96; H, 9.27. Found: C, 74.90; H, 9.10.

Preparation of 18 and 19 by Reduction of Dienone 17. In a manner similar to that described for the reduction of enone **14**, to a blue solution of 4.5 mg (0.6 mmol) of lithium in 25 mL of dry liquid ammonia was added 73 mg (0.24 mmol) of the dienone **17** in 4 mL of dry tetrahydrofuran and 0.025 mL (0.24 mmol) of dry *tert*-butyl alcohol. The blue solution was allowed to reflux for 45 min. After the solution was quenched as described for the reduction of **14**, careful chromatography of the residue on 20 g of silica gel with 30% ether–petroleum ether afforded 42 mg (57%) of the trans isomer **19**. Further elution gave 19 mg (26%) of the cis isomer **18** (isomer ratio 69:31 in 83% overall yield).

1α,2α-(Isopropylidinedioxy)-11bα-methyl-5aα,7aα,8,9,10,11,11aβ,11b-octahydronaphtho[*a*]cycloheptane (20). To a stirred solution of lithium diisopropylamide (0.6 mmol) in 2 mL of dry tetrahydrofuran at −78 °C was added dropwise via syringe 95 mg (0.3 mmol) of the keto acetonide **19** in 1.5 mL of dry tetrahydrofuran. The reaction was stirred at −78° for 30 min. Hexamethylphosphoramide (0.1 mL, 0.6 mmol) was added at 0 °C, and then 15 mL (3.1 mmol) of bis(dimethylamino)-phosphorochloridate was added in one portion. The ice bath was removed, and the reaction mixture stirred at room temperature for 1.5 h and then poured into saturated aqueous sodium bicarbonate solution. The aqueous solution was extracted with ether, and the combined organic extracts were washed with brine and then dried ($MgSO_4$). After removal of the solvent at reduced pressure, the residual yellow oil was dissolved in 3 mL of tetrahydrofuran containing 0.2 mL of *tert*-butyl alcohol, and then this mixture was added to a blue solution of lithium in 20 mL of dry ethylamine. The blue reaction mixture was allowed to reflux for 30 min, and then the excess lithium was destroyed by careful addition of solid ammonium chloride. Ethylamine was allowed to evaporate, and the residue was partitioned between ether and water. The organic layer was separated, washed with brine, and then dried ($MgSO_4$). After removal of the solvent at reduced pressure, the pale yellow oil (83 mg) that remained was chromatographed on 7 g of silica gel. Elution with 25% ether–petroleum ether afforded 70 mg (49%) of the ketal **20** as a colorless oil. An analytical sample was prepared by evaporative distillation [95–98 °C (0.003 mmHg)]: ^1H NMR ($CDCl_3$) δ 1.10 (s, 3 H, CH_3C), 1.33, 1.50 (2 s, 6 H, $(CH_3)_2C$), 4.07 (d, 1 H, J = 6 Hz, OCHC), 4.26 (m, 1H, $OCHCH_2$), 5.21 (d, 1 H, J = 9 Hz, vinyl H), 5.58 (ddd, 1 H, J = 2.8, 5.6, 11.2 Hz, vinyl H).

Anal. Calcd for $C_{19}H_{30}O_2$: C, 78.57; H, 10.41. Found: C, 78.61; H, 10.45.

1α,2α-Dioxo-11bα-methyl-5aα,7aα,8,9,10,11,11aβ,11b-octahydronaphtho[*a*]cycloheptane. To a solution of 35 mg (0.12 mmol) of the acetonide **20** in 1 mL of methanol and 0.2 mL of water was added one crystal of *p*-toluenesulfonic acid monohydrate. The reaction mixture was heated under reflux for 30 min, cooled to room temperature, and diluted with 5 mL of water, and the resulting mixture was extracted with water and then with ether. The combined organic extracts were washed and then dried ($MgSO_4$). After removal of the solvent at reduced pressure, the resulting pale yellow oil was chromatographed on 7 g of silica gel. Elution with 50% ether–petroleum ether provided 29 mg (96%) of the diol as a colorless oil. The analytical sample was prepared by evaporative distillation [135–140 °C (0.003 mmHg)]: ^1H NMR ($CHCl_3$) δ 1.00 (s, 3 H, CH_3C), 3.76 (br s, 1 H, OCHC), 4.05 (m, 1 H, $OCHCH_2$), 5.33 (m, 2 H, CH=CH).

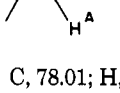
Anal. Calcd for $C_{16}H_{26}O_2$: C, 76.75; H, 10.47. Found: C, 76.63; H, 10.50.

4-[1α-Methyl-1β-carboxy-1,2,4aα,5,6,7,8,8aβ-octahydronaphthyl]butyric Acid (21, "Deoxy Bottom Half"). To a stirred solution of 220 mg (0.87 mmol) of the above diol in 3 mL of methanol was added 250 mg (1.3 mmol) of sodium metaperiodate in 0.5 mL of water. The white suspension was stirred at room temperature for 2.5 h, and then 5 mL of water was added. After extraction of the mixture with ether, the extracts were washed with brine and then dried ($MgSO_4$). Removal of the solvent at reduced pressure gave 204 mg of the desired dialdehyde (93% crude yield) as a colorless oil: IR ($CHCl_3$) 1720 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 1.03 (s, 3 H, CH_3C), 5.52 (m, 2 H, HC=CH), 9.63 (s, 1 H, CCHO), 9.73 (t, 1 H, CH_2CHO).

Without further purification this oil was dissolved in 3 mL of dry dimethylformamide, 1.6 g (5 equiv) of pyridinium dichromate[17] was added, and the brown reaction mixture was stirred at room temperature for 48 h. The reaction mixture was diluted with water and then extracted with ether. The combined ethereal extracts were washed with water and brine and then dried ($MgSO_4$). Removal of the solvents at reduced pressure gave a pale yellow oil which was chromatographed on silica gel. Elution with 1:1 ethyl acetate–petroleum ether afforded 91 mg (31%) of the diacid **21** as a white foam. The analytical sample was prepared by evaporative distillation [170–175 °C (0.003 mmHg)]: IR ($CHCl_3$) 1710 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 1.16 (s, 3 H, CH_3C), 5.51 (m, 2 H, HC=CH), 11.3 (m, 2 H, diacid H).

Anal. Calcd for $C_{16}H_{24}O_4$: C, 68.55; H, 8.63. Found: C, 68.38; H, 8.53.

7aβ,8β-Epoxy-11bα-methyl-5aα,7a,8,9,10,11,11aβ,11b-octahydronaphtho[*a*]cyclohepten-7(6*H*)-one (22) and 7aβ,8β-Epoxy-11bα-methyl-5aα,7a,8,9,10,11,11aα,11b-octahydronaphtho[*a*]cyclohepten-7(6*H*)-one. To a stirred solution of 1.66 g (7.2 mmol) of dienone **14** in 35 mL of methanol was added 8.1 mL (72 mmol) of 30% hydrogen peroxide. After the mixture was cooled to 0 °C, 1 mL of 10% aqueous sodium hydroxide solution was added. After the reaction mixture was stirred for 1 h at room temperature, it was diluted with water, and then the resulting mixture was extracted with ether. The combined organic extracts were washed with 20 mL of water and brine and then dried ($MgSO_4$). After removal of the solvent at reduced pressure, the pale yellow, waxy residue was chromatographed on 100 g of silica gel. Elution with 40% ether–petroleum ether afforded 152 mg (8%) of the cis-syn-cis epoxide as a white solid. The analytical sample, prepared by recrystallization from ether–hexane, melted at 85–86 °C: IR ($CHCl_3$) 1740 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 1.30 (s, 3 H, CH_3C), 3.4 (m, 1 H, H^A), 5.58 (d, 1 H, J = 12.0 Hz, vinyl H), 5.86 (m, 1 H, vinyl H).



Anal. Calcd for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00. Found: C, 78.12; H, 9.03.

Further elution afforded 1.45 g of the epoxide **22** as a white solid (81%). The analytical sample, prepared by recrystallization from ether–hexane, melted at 78–79 °C: IR ($CHCl_3$) 1718 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 1.23 (s, 3 H, CH_3C), 3.16 (br s, 1 H, H^A), 5.37 (d, 1 H, J = 12 Hz, vinyl H), 5.73 (m, 1 H, vinyl H).

Anal. Calcd for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00. Found: C, 77.90; H, 8.84.

8β-Hydroxy-11bα-methyl-5aα,7aβ,8,9,10,11,11aβ,11b-octahydronaphtho[*a*]cyclohepten-7(6*H*)-one (23) and 8β-Hydroxy-11bα-methyl-5aα,7aα,8,9,10,11,11aβ,11b-octahydronaphtho[*a*]cyclohepten-7(6*H*)-one (24). To a solution of 32

mg (4.6 mmol) of lithium in 100 mL of dry liquid ammonia was added 515 mg (2.09 mmol) of the keto epoxide **22** in 20 mL of dry tetrahydrofuran. After 30 min, excess lithium was destroyed by the careful addition of solid ammonium chloride, and the ammonia was allowed to evaporate. The residue was partitioned between ether and water, and then the organic layer was separated, washed with brine, and dried ($MgSO_4$). Removal of the solvent at reduced pressure afforded a pale yellow oil which was chromatographed on silica gel. Elution with 25% ether–petroleum ether afforded 61 mg (12%) of the trans isomer **24**. The analytical sample, prepared by recrystallization from chloroform hexane, melted at 110–112 °C: IR ($CHCl_3$) 3600, 3500 (OH), 1700 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 1.33 (s, 3 H, CH_3C), 4.4 (m, 1 H, CHOH), 5.30 (d, 1 H, J = 12 Hz, vinyl H), 5.72 (m, 1 H, vinyl H).

Anal. Calcd for $C_{16}H_{24}O_2$: C, 77.38; H, 9.74. Found: C, 77.42; H, 9.71.

Further elution afforded 290 mg (56%) of the cis isomer **23**. The analytical sample, prepared by recrystallization from chloroform-hexane, melted at 121–122 °C: IR ($CHCl_3$) 3600 (OH), 1700 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 1.16 (s, 3 H, CH_3C), 4.36 (m, 1 H, CHOH), 5.47 (d, 1 H, J = 12 Hz, vinyl H), 5.80 (m, 1 H, vinyl H).

Anal. Calcd for $C_{16}H_{24}O_2$: C, 77.38; H, 9.74. Found: C, 77.50; H, 9.76.

1α,2α-(Isopropylidenedioxy)-7aβ,8β-epoxy-11bα-methyl-5aα,7a,8,9,10,11,11aβ,11b-octahydronaphtho[a]cyclohept-1-en-7(6*H*)-one (25). To a solution of 5.45 g (21.8 mmol) of keto expoxide **22** in 15 mL of *tert*-butyl alcohol, 5 mL of tetrahydrofuran, and 1.5 mL of water were added 3.22 g (24 mmol) of *N*-methylmorpholine *N*-oxide monohydrate (NMO) and 2.2 mL of a 0.1 M solution of osmium tetraoxide in *tert*-butytl alcohol. After being stirred at room temperature for 4.5 h, the reaction mixture was treated with 1 g of sodium hydrosulfite, 1 g of Florisil, and 3 mL of water. After the dark brown mixture had been stirred for 10 min, the solids were removed by filtration and washed with dichloromethane. The filtrate was acidified with 1 N sulfuric acid and then extracted with dichloromethane. The combined organic extracts were washed with 10% aqueous sodium bicarbonate solution and brine and then dried ($MgSO_4$). Removal of the solvent at reduced pressure afforded 5.82 g (95%) of the diol as a white foam which solidified upon standing for several days: mp 121–122 °C; IR ($CHCl_3$) 3500 (OH), 1710 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 1.26 (s, 3 H, CH_3C), 3.40 (br s, 1 H, H^A), 5.86 (m, 2 H, $(CHOH)_2$).

Without further purification this diol was dissolved in 40 mL of 2,2-dimethoxypropane, 25 mg of *p*-toluenesulfonic acid monohydrate was added, and the mixture was allowed to stir at room temperature for 15 min. After dilution with dicholormethane, the mixture was washed with 10% aqueous sodium bicarbonate solution and brine and then dried ($MgSO_4$). After removal of the solvent at reduced pressure, the residual pale yellow solid was chromatographed on silica gel. Elution with 1:1 ether–petroleum ether gave 6.32 g (90% from **22**) of the keto acetonide **25** as a white foam which solidifed upon standing. The analytical sample, prepared by recrystallization from hexane, melted at 90–91 °C: IR ($CHCl_3$) 1720 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 1.26 (s, 3 H, CH_3C), 1.30, 1.46 (2 s, 6 H, $(CH_3)_2C$), 3.23 (br s, 1 H, H^A), 4.08 (d, 1 H, J = 9 Hz, OCHC), 4.23 (m, 1 H, CH_2CHO).

Anal. Calcd for $C_{19}H_{28}O_4$: C, 71.22; H, 8.81. Found: C, 71.13; H, 8.86.

1α,2α-(Isopropylidenedioxy)-8β-hydroxy-11bα-methyl-5aα,7aα,8,9,10,11,11aβ,11b-octahydronaphtho[a]cyclohepten-7(6*H*)-one (27). A solution of 10.01 g (31 mmol) of the epoxide **25** in 30 mL of dry tetrahydrofuran was added quickly under argon to a refluxing, rapidly stirred solution of 1.43 g of sodium in 200 mL of dry tetrahydrofuran and 733 mL of dry liquid ammonia. The solution decolorized within 5 min, and another 0.08 g of sodium was added (total amount of sodium 1.51 g, 65.3 mol, 1.05 equiv). The blue reaction mixture was quenched with solid ammonium chloride after 15 min, and then the ammonia was evaporated at 0 °C. The mixture was diluted with brine and extracted with ether. The combined organic layers were washed with brine and then dried ($MgSO_4$). After removal of the solvent at reduced pressure and flash chromatography of the residual oil on silica gel, elution with petroleum ether–ether (1:1) gave 8.20 g of the desired keto alcohol **27** and 0.86 g of the cis isomer **26**.

Recrystallization of the main fraction from methylene chloride–ether–petroleum ether gave 7.90 g (78%) of the keto alcohol **27**: mp 142.5–143 °C; IR ($CHCl_3$) 3575 (OH), 1700 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 1.31, 1.43, and 1.50 (3 s, CH_3C and $(CH_3)_2C$), 4.23 (br s, 2 H, 2CHO), 4.43 (m, 1 H, CHOH).

Anal. Calcd for $C_{19}H_{30}O_4$: C, 70.78; H, 9.38. Found: C, 70.59; H, 9.28.

The use of lithium in place of sodium in this reduction gave lower yields and irreproducible results.

1α,2α-(Isopropylidenedioxy)-8β-(methoxymethoxy)-11bα-methyl-5aα,7aα,8,9,10,11,11aβ,11b-octahydronaphtho[a]-cyclohepten-7(6*H*)-one. To a solution of 3.02 g (9.4 mmol) of the keto alcohol **27** in 25 mL of dichloromethane at 0 °C was added 1.41 mL (1.49 g, 18.6 mmol) of chloromethyl methyl ether and 3.6 mL (2.67 g, 20.7 mmol) of ethyldiisopropylamine. After being stirred for 7 h at room temperature, the mixture was treated with saturated aqueous sodium bicarbonate solution and then stirred for another 30 min. This mixture was then partitioned between ether and brine, and the aqueous layer was separated and then extracted with ether. The combined organic layers were washed with brine and then dried ($MgSO_4$). After removal of the solvent at reduced pressure, flash chromatography of the residue on silica gel with ether–petroleum ether (1:1) gave 3.38 g (99%) of the corresponding keto ether as a white solid.

The analytical sample, prepared by recrystallization of a portion of this material from dichloromethane–hexane, melted at 135–135.5 °C: IR ($CHCl_3$) 1700 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 1.34 and 1.60 (2 s, 2 × 3 H, CH_3C and $(CH_3)_2C$), 3.33 (s, 3 H, CH_3OCH_2O), 4.26 (br s, 2 H, 2CHO), 4.43 (m, 1 H, $CHOCH_2OCH_3$), 4.58 and 4.62 (AB system, J = 8 Hz, 2 H, OCH_2OCH).

Anal. Calcd for $C_{21}H_{34}O_5$: C, 68.82; H, 9.35. Found: C, 68.86; H, 9.43.

1α,2α-(Isopropylidenedioxy)-8β-(methoxymethoxy)-11bα-methyl-5aα,7aα,8,9,10,11,11aβ,11b-octahydronaphtho[a]-cycloheptane. A solution of 3.10 g (8.5 mmol) of the above keto ether in 16 mL of dry tetrahydrofuran was added over a period of 45 min to a rapidly stirred solution of 12.3 mmol of lithium diisopropylamide [prepared from 4.4 mL of 2.8 M *n*-butyllithium in hexane and 2.3 mL (16.4 mmol) of diisopropylamine in 15 mL of dry tetrahydrofuran at 0 °C] under argon at −78 °C. The resulting colorless solution was stirred at −78 °C for 30 min and then warmed to 0 °C, and 2.7 mL (15.5 mmol) of hexamethylphosphoramide was added. After being stirred for 20 min at 0 °C, the mixture was treated with 3.2 mL (22.5 mmol) of bis(dimethylamino)phosphorodiloridate over a period of 5 min. The solution was stirred for 15 min at 0 °C and then 5.5 h at room temperature. Excess saturated aqueous sodium bicarbonate solution was then added, and the mixture was stirred for 25 min. After dilution with water, the mixture was extracted with ether, and then the combined organic layers were washed with water and brine and then dried ($MgSO_4$). Removal of the solvent at reduced pressure gave 4.48 g of the crude semisolid phosphorodiamidate.

A solution of this crude material in 25 mL of dry tetrahydrofuran and 3 mL of *tert*-butyl alcohol was added to a rapidly stirred mixture of 180 mL of ethylamine, 1.5 mL of *tert*-butyl alcohol, and 15 cm (635 mg, 91.4 mmol) of lithium wire. After the reaction was quenched by the addition of solid ammonium chloride, the ethylamine was evaporated with gentle warming. The residue was then diluted with water and extracted with ether. The combined organic layers, were washed with brine and then dried ($MgSO_4$). After removal of the solvent at reduced pressure and flash chromatography of the residue on silica gel with ether–petroleum ether (1:3), there was obtained 2.63 g (89%) of the olefin **28**, mp 78–80 °C. The analytical sample, prepared by crystallization of a portion of this material from hexane, melted at 81–82 °C: IR ($CHCl_3$) 3025, 2940, 2880 cm^{-1} (CH); ^1H NMR ($CDCl_3$) δ 1.10, 1.30, and 1.47 (3 s, CH_3C and $(CH_3)_2C$), 3.30 (s, 3 H, CH_3OCH_2O), 3.87 (m, 1 H, $CHOCH_2OCH_3$), 4.07 (d, J = 7 Hz, 1 H) and 4.25 (m, 1 H) both CHO, 4.57 and 4.63 (AB system, J = 8 Hz, 2 H, OCH_2OCH_3), 5.28 (d, J = 10.5 Hz, 14), 5.5–5.8 (m, 1 H, olefinic proteons).

Anal. Calcd for $C_{21}H_{34}O_4$: C, 71.96; H, 9.78. Found: C, 72.03; H, 9.88.

4-[1α-Methyl-1β-carboxy-5β-(methoxymethoxy)-1,2,4aα,5,6,7,8,8aβ-octahydronaphthyl]butyric Acid (29). A solution of 2.82 g (8.05 mmol) of the acetonide **28** in 50 mL of methanol/water (4:1) was heated under reflux in the presence of 203 mg (0.81 mmol) pyridinium *p*-toluenesulfonate for 3 h. Saturated aqueous sodium bicarbonate solution was added, and the mixture was extracted with ether. The organic layer was washed with brine and then dried ($MgSO_4$). After removal of the solvent at reduced pressure and flash chromatography of the residue on silica gel with ethyl acetate–petroleum ether (1:1), there was obtained 2.26 g (91%) of the desired diol as a white foam which crystallized on standing to give 193 mg (7%) of the starting acetonide **28** and 65 mg (2.5%) of the triol (loss of the MOM group). The analytical sample of the diol, prepared by crystallization of a portion of this material from dichloromethane–hexane, melted at 103–105 °C: IR ($CHCl_3$) 3625 cm^{-1} (OH); ^1H NMR ($CDCl_3$) δ 0.99 (s, 3 H, CH_3C), 3.30 (s, 3 H, CH_3OCH_2O), 3.80 (m, 2 H) and 4.10 (m, 1 H), 3CHO, 4.55 and 4.61 (AB system, J = 8 Hz, 2 H, OCH_2OCH_3), 5.25–5.55 (m, 2 H, olefinic protons).

Anal. Calcd for $C_{18}H_{30}O_4$: C, 69.64; H, 9.74. Found: C, 69.61; H, 9.60.

A solution of 2.22 g (7.12 mmol) of the above diol and 1.94 g (9.30 mmol) of sodium metaperiodate in 15 mL of methanol and 4.5 mL of water was stirred for 4 h at room temperature. After dilution with water, the mixture was extracted with ether, and the ethereal extract was washed with brine and then dried ($MgSO_4$). Removal of the solvent at reduced pressure left 2.23 g of the crude dialdehyde, which was oxidized further without additional purification: ^1H NMR ($CDCl_3$) δ 1.00 (s, CH_3C), 3.33 (s, CH_3OCH_2O), 3.92 (m, $CHOCH_2OCH_3$), 4.57 and 4.63 (AB system, J = 8 Hz, OCH_2OCH_3), 5.35–5.85 (m, olefinic protons), 9.70 (s, CHOC), 9.76 (t, J = 3 Hz, $CHOCH_2$).

A solution of 2.23 g (7.23 mmol) of the above crude dialdehyde and 12.3 g (32.7 mmol) pyridinium dichromate[17] in 15.3 mL of dimethylformamide was stirred for 64 h at room temperature. The resulting solution was then carefully added to a mixture of 150 mL of water, 250 mL of ether, and 14 mL of 1 N hydrochloric acid. The aqueous layer was separated and extracted with ether. The combined organic layers were washed with brine and then dried ($MgSO_4$). After removal of the solvent at reduced pressure and then chromatography of the crude product on 150 g of silica gel with ether–petroleum ether (6:4), there was obtained 1.51 g (62% from the diol) of the diacid **29** as a white solid. An analytical sample, prepared by crystallization of a portion of this material from ether, melted at 149–150 °C: IR ($CHCl_3$) 3450–3400 (OH), 1715 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 1.17 (s, CH_3C), 3.33 (s, 3 H, CH_3OCH_2O), 3.93 (br s, 1 H, $CHOCH_2OCH_3$), 4.55 and 4.65 (AB system, J = 8 Hz, 2 H, OCH_2OCH_3), 5.5 (d, J = 10.5 Hz, 1 H), 5.6–5.9 (m, 1 H, olefinic protons), 11.9 (br s, 2 H, CO_2H).

Anal. Calcd for $C_{18}H_{28}O_6$: C, 63.51; H, 8.28. Found: C, 63.61; H, 8.38.

The dimethyl ester of diacid **29** was prepared in 96% yield when 607 mg (1.78 mmol) of the diacid **29** was treated with excess ethereal diazomethane. After chromatography on silica gel with dichloromethane–ether (9:1) and evaporative distillation at ~150 °C (0.003 mmHg), an analytical sample of the diester was obtained as a clear, colorless oil: IR ($CHCl_3$) 1730 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 1.13 (s, CH_3C), 3.35 (s, 3 H, CH_3OCH_2O), 3.60 and 3.61 (2 s, 6 H, CH_3OCO), 3.87 (br s, 1 H, $CHOCH_2OCH_3$), 4.51 and 4.57 (AB system, J = 8 Hz, 2 H, OCH_2OCH_3), 5.40 (d, J = 10.5 Hz, 1 H), 5.65 (ddd, J = 10.5, 5, 2 Hz, 1 H, olefinic protons).

Anal. Calcd for $C_{20}H_{32}O_6$: C, 65.19, H, 8.75. Found: C, 65.19; H, 8.70.

***O*-Methylchlorothricolide Methyl Ester.** The procedure of Muntwyler and Keller-Schierlein[2] was used. To a solution of 5.43 g (5.7 mmol) of chlorothricin in 217 mL of dry methanol was added 2.9 mL of concentrated sulfuric acid, and the resulting mixture was heated at reflux for 3 h. The mixture was then poured into ice–water and extracted with ethyl acetate. The pH of the aqueous layer was adjusted to 4.0 with aqueous ammonium hydroxide and extracted with ethyl acetate. The combined organic layers were washed with brine and then dried (Na_2SO_4). The solvents were removed under reduced pressure, and a small sample was purified by preparative thin-layer chromatography to provide an authentic sample of chlorothricolide methyl ester. The remaining material was treated for 15 min with excess ethereal diazomethane containing methanol. Chromatography of this crude material on 700 g of silica gel with 45% ethyl acetate in cyclohexane afforded 2.6 g (87%) of *O*-methylchlorothricolide methyl ester, 1.66 g of the 3-acetylated methyl 2-deoxyrhamnoside, and 0.580 g (19%) of the *O*-methylketene acetal isomer of chlorothricolide methyl ester. The spectra of these materials were identical with those reported by Keller-Schierlein.[2]

7-*O*-(Methoxymethyl)-24-*O*-methylchlorothricolide Methyl Ester (30). To a stirred solution of 2.2 g (4.3 mmol) of *O*-methylchlorotricolide methyl ester in 14 mL of dry dichloromethane were added 1.5 mL (8.4 mmol) of dry diisopropylamine and 0.63 mL (8.4 mmol) of chloromethyl methyl ether. After 12 h the mixture was partitioned between aqueous sodium bicarbonate solution and dichloromethane. The organic layer was extracted with saturated aqueous copper(II) sulfate solution and brine and then dried ($MgSO_4$). Removal of the solvent at reduced pressure and then chromatography of the residue on 250 g of silica gel with 45% ethyl acetate in cyclohexane afforded 2.5 g (90%) of the protected ester **30**: ^1H NMR ($CDCl_3$) δ 1.27 (d, 3 H, J = 7.5 Hz, CH_3), 1.30 (s, 3 H, CH_3), 3.37 (s, 3 H, OCH_3), 3.72, 3.98 (2 s, 2 × 3 H, $2OCH_3$), 4.42, 4.77 (2 d, 2 × 1 H, J = 13.5 Hz, OCH_2O), 5.0–5.9 (complex multiplets, 4 H, vinyl H's), 6.7 (m, 1 H, $CH{=}CCO_2$).

7-*O*-(Methoxymethyl)-16,17-dihydroxy-24-*O*-methylchlorothricolide Methyl Ester (31). To a stirred solution of 1.0 g (1.8 mmol) of the *O*-(methoxymethyl)-*O*-methylchlorothricolide methyl ester **30** in 1.5 mL of water was added 243 mg (1.8 mmol) of *N*-methylmorpholine *N*-oxide monohydrate (NMO) and 0.07 mL of a 0.1 M osmium tetraoxide in *tert*-butyl alcohol solution. After 24 h at room temperature, 1 mL of water and 200 mg of sodium hydrosulfite were added, and the mixture was stirred for 15 min. The resulting mixture was partitioned between saturated copper(II) sulfate solution and ethyl acetate. The organic layer was separated, washed with water, and dried ($MgSO_4$). After removal of the solvent at reduced pressure and chromatography of the residue on 250 g of silica gel with 75% ethyl acetate in cyclohexane, there was obtained 192 mg (19%) of starting material and 727 mg (68%) of a mixture of two isomeric diols of **31**. The diol with the higher R_f on thin-layer chromatography solidified and after crystallization from ethyl acetate–cyclohexane melted at 217–219 °C: IR ($CHCl_3$) 3600 (OH), 1770 (C=O), 1720 (C=O), 1680 (C=C), 1450, 1350 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.3 (d, 3 H, J = 7.5 Hz, $CHCH_3$), 1.45 (s, 3 H, CH_3), 3.35, 3.72, 4.05 (3 s, 3 × 3 H, OCH_3), 4.42, 4.77 (2 d, 2 × 1 H, J = 13.5 Hz, OCH_2O), 5.66 (dd, 1 H, J = 4.5, 10.5 Hz, vinyl H), 5.8 (d, 1 H, J = 10.5 Hz, vinyl H), 7.25 (s, 1 H, $CH{=}CCO_2$); $[\alpha]^{23}_D$ −50.5° (*c* 1.03, $CHCl_3$).

Anal. Calcd for $C_{33}H_{46}O_{11}$: C, 64.06; H, 7.49. Found: C, 64.10; H, 7.41.

The diol with the lower R_f on thin-layer chromatography was an oil and was dried at high vacuum for analysis: IR ($CHCl_3$) 3600 (OH), 1780 (C=O), 1720 (C=O), 1680 (C=C), 1450, 1350 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.25 (d, 3 H, J = 7.5 Hz, $CHCH_3$), 3.34, 3.75, 4.10 (3 s, 3 × 3 H, $3OCH_3$), 4.42, 4.77 (2 d, 2 × 1 H, J = 13.5 Hz, OCH_2O), 5.55 (dd, 1 H, J = 4.5, 10.5 Hz, vinyl H), 5.85 (d, 1 H, J = 10.5 Hz, vinyl H), 7.25 (m, 1 H, $CH{=}CCO_2$).

7-*O*-(Methoxymethyl)-"homo-bottom half" Dimethyl Ester (32). To a solution of 343 mg (0.58 mmol) of the diols **31** in 5.6 mL of dioxane and 4.0 mL of water was added 770 mg (4 mmol) of sodium metaperiodate, and then the reaction mixture was allowed to stir at room temperature for 48 h. After the mixture was partitioned between dichloromethane and water, the organic layer was separated and then dried ($MgSO_4$). Removal of the solvents at reduced pressure gave a colorless foam. This crude product was taken up in 4–6 mL of dimethylformamide, and this solution was treated with 2.3 g (6 mmol) of pyridinium dichromate.[17] After the mixture had been stirred for 12 h at room temperature, it was partitioned between water and ethyl acetate. The organic layer was separated and then dried ($MgSO_4$). After the solvent was removed under reduced pressure, the resulting crude product was taken up in 10 mL of 0.75 N ethanolic sodium hydroxide solution, and the whole was heated at reflux under argon for 5 h. The mixture was allowed to cool to room temperature, diluted with water, and then acidified with 10% aqueous hydrochloric acid to pH 4.0. This mixture was then extracted with ether, and the combined ethereal extracts were dried (Mg-

SO_4). After treatment of this ethereal solution with excess ethereal diazomethane and then removal of the solvents under reduced pressure, chromatography of the residue on 50 g of silica gel with 15% ethyl acetate in cyclohexane afforded 85 mg (42%) of pure "homo-bottom half" diester **32** as a colorless oil suitable for analysis: IR ($CHCl_3$) 2980, 1725, 1470, 1450, 1150, 1050 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.15 (s, 3 H, CH_3), 2.25 (t, 2 H, J = 7.5 Hz, $CH_2CO_2CH_3$), 3.23 (br m, 1 H, CHOR), 3.35, 3.62 (2 s, 2 × 3 H, $2OCH_3$), 4.65, 4.72 (2 d, 2 × 1 H, J = 13.5 Hz, OCH_2O), 5.65 (dd, 1 H, J = 4.5, 10.5 Hz, vinyl H), 5.88 (d, 1 H, J = 10.5 Hz, vinyl H); $[\alpha]^{23}_D$ −102° (*c* 1.05, $CHCl_3$).

Anal. Calcd for $C_{21}H_{34}O_6$: C, 65.94; H, 8.96. Found: C, 66.19; H, 8.79.

4-[1α-Methyl-1β-(carbomethoxy)-5β-(methoxymethoxy)-1,2,4aα,5,6,7,8,8aβ-octahydronaphthyl]butyric Acid (34). A solution of 480 mg (1.30 mmol) of the dimethyl diester of the diacid **29** in 10 mL of methanol and 5 mL of 1 N aqueous lithium hydroxide was stirred at room temperature for 2.5 h. The solution was then diluted with brine, acidified with hydrochloric acid against methyl orange, and extracted with ether. The organic layer was separated, washed with brine, and dried ($MgSO_4$). Removal of the solvent at reduced pressure gave 472 mg (quantitative yield) of the ester acid **34** as a white solid, which was used in subsequent experiments without further purification. An analytical sample, prepared by crystallization of a portion of this material from ether–petroleum ether, melted at 94–95 °C: IR ($CHCl_3$) 3300–2500 (OH), 1720 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 1.12 (s, CH_3C), 3.29 (s, 3 H, OCH_2OCH_3), 3.60 (s, 3 H, CO_2CH_3), 3.88 (br s, 1 H, $CHOCH_2OCH_3$), 4.51 and 4.59 (AB system, J = 8 Hz, 2 H, OCH_2OCH_3), 5.42 (d, J = 10.5 Hz, 1 H), and 5.66 (ddd, J = 10.5, 5, 2 Hz, 1 H), olefinic protons, 8.8–9.8 (br s, 1 H, CO_2H).

Anal. Calcd for $C_{19}H_{30}O_6$: C, 64.39; H, 8.53. Found: C, 64.38; H, 8.64.

Union of "Top" (33) and "Bottom" (34) Halves and Formation of the Ester 35. To a solution of 113 mg (0.32 mmol) of the ester acid **34**, 84 mg (0.32 mmol) of the allylic alcohol **33**, and 132 mg (0.11 mmol) of 4-(dimethylamino)pyridine in 1.5 mL of dichloromethane at 0 °C was added 86 mg (0.42 mmol) of dicyclohexylcarbodiimide. After being stirred for 5 min, the mixture was allowed to warm to room temperature and then to stir for 5 h. The solution was then filtered from the precipitate, the solvent was removed at reduced pressure, and the resulting oil was chromatographed on silica gel with ether–petroleum ether (75:25). In this manner there was obtained 171 mg (89%) of the ester **35**. An analytical sample was prepared by evaporative distillation of a portion of this material at 200 °C (0.003 mmHg): IR ($CHCl_3$) 1750 (C=O), 1720 (C=O), 1680 cm^{-1}; ^1H NMR ($CDCl_3$, 90 MHz) δ 1.11 (s, C-2 CH_3), 3.28 (s, 3 H, C-7 OCH_2OCH_3), 3.60 (s, 3 H, C-1 OCH_3), 3.75 (s, 3 H, C-25 OCH_3), 3.85 (br s, 1 H, C-7 H), 4.11 (s, 3 H, C-24 OCH_3), 4.50 and 4.56 (AB system, J = 7 Hz, 2 H, C-7 OCH_3OCH_3), 4.9–5.8 (m, 7 H, olefinic protons); ^1H NMR ($CDCl_3$, 500 MHz) δ 1.14 (s, C-2 CH_3), 3.35 (2 s, Δ = 4.5 Hz, 3 H, C-7 OCH_2OCH_3), 3.66 (2 s, Δ = 2.5 Hz, 3 H, C-1 OCH_3), 3.79 (2 s, Δ = 1.8 Hz, 3 H, C-25 OCH_3), 3.92 (br s, 1 H, C-7 H), 4.17 (2 s, Δ = 1.7 Hz, 3 H, C-24 OCH_3), 4.52 (2 d, J = 7.5 Hz, Δ = 3 Hz, 1 H) and 4.66 (2 d, J = 7.5 Hz, Δ = 4 Hz, 1 H) C-7 OCH_2OCH_3, 5.12 (d, J = 17 Hz, 1 H, C-15 H), 5.18 (d, J = 10 Hz, 1 H, C-15 H), 5.36 (m, 1 H, C-17 H), 5.45 (br d, J = 10.5 Hz, 1 H), 5.58 (m, 1 H), 5.70 (m, 2 H), 5.78 (m, 1 H, olefinic protons).

Anal. Calcd for $C_{33}H_{46}O_{10}$: C, 65.76; H, 7.69. Found: C, 65.89; H, 7.61.

Enolate Claisen Rearrangement of the Ester 34 and Formation of the MEM Ester 36. A solution of potassium hexamethyldisilazide was prepared by addition of 0.51 mL (395 mg, 2.45 mmol) of freshly distilled hexamethyldisilazane to a slurry of 75 mg (1.86 mmol) of potassium hydride (obtained from 316 mg of a 23.6% potassium hydride suspension in oil by three washings with pentane) in 9.3 mL of tetrahydrofuran at room temperature. The resulting slightly cloudy mixture was stirred for 45 min. To 4.3 mL of this solution (1.07 mmol of base) was added 1.05 mL of hexamethylphosphoramide at −78 °C, and then 0.65 mL of a 2 M solution of *tert*-butyldimethylsilyl chloride in tetrahydrofuran was added over a period of 12 min. The mixture was stirred at −78 °C for another 30 min, and after warming to room temperature over a period of 75 min, the reaction mixture was stirred for 18 h. Ethanol (2 mL) and 1 N aqueous sodium hydroxide solution (1 mL) were then added, and the mixture was stirred for 50 min at room temperature. After dilution with brine and ether, the mixture was carefully acidified with 1 N aqueous hydrochloric acid against methyl orange. The aqueous layer was separated and then extracted with ether. The combined organic layers were washed with brine and then dried ($MgSO_4$). Removal of the solvent at reduced pressure gave the crude rearranged acid as a slightly brown oil. This acid was dissolved in 1 mL of dichloromethane, and 0.20 mL (1.15 mmol) of ethyldiisopropylamine was added. To this ice-cold solution was added 0.10 mL (0.88 mmol) of chloromethyl 2-methoxyethyl ether, and the resulting mixture was stirred for 30 min at 0 °C and then for 105 min at room temperature. After the addition of 1 mL of saturated aqueous sodium bicarbonate solution, the mixture was stirred for an additional 30 min, diluted with brine, and then extracted with ether. The ethereal layer was washed with brine and then dried ($MgSO_4$). Removal of the solvent at reduced pressure and chromatography of the crude oil on silica gel with ether–dichloromethane (1:3) afforded 106 mg (72%) of the ester **36** as a colorless oil. The analytical sample was obtained after thorough drying of this material under high vacuum: IR ($CHCl_3$) 1750 (C=O), 1720 (C=O), 1680 cm^{-1} (C=C); ^1H NMR ($CDCl_3$, 90 MHz) δ 1.10 (s, C-2 CH_3), 3.27 (s, 3 H, C-7 OCH_2OCH_3), 3.35 (s, 3 H, C-14 $CO_2CH_2OCH_2CH_3$), 3.58 (s, C-1 OCH_3), 3.73 (s, C-25 OCH_3), 3.87 (br s, 1 H, C-7 H), 4.02 (s, 3 H, C-24 OCH_3), 4.47 and 4.55 (AB system, J = 7 Hz, 2 H, C-7 OCH_2OCH_3), 5.1–5.8 (m, olefinic protons); ^1H NMR ($CDCl_3$, 500 MHz) δ 1.12 (2 s, 3 H, C-2 CH_3), 3.34 (2 s, Δ = 2.4 Hz, 3H, C-7 OCH_2OCH_3), 3.39 (2 s, Δ = 0.9 Hz, 3 H, C-14 $CO_2CH_2OCH_2CH_2OCH_3$), 3.57 (m, 2 H, C-14 $CO_2CH_2OCH_2CH_2OCH_3$), 3.65 (2 s, Δ = 0.9 Hz, 3 H, C-1 OCH_3), 3.78 (m, 2 H, C-14 $CO_2CH_2OCH_2OCH_3$), 3.80 (s, 3 H, C-25 OCH_3), 3.93 (br s, 1 H, C-7 H), 4.09 (2 s, Δ = 2.3 Hz, 3 H, C-24 OCH_3), 4.57 (2 d, J = 6.7 Hz, Δ = 5.5 Hz, 1 H), 4.65 (2 d, J = 6.7 Hz, Δ = 5.5 Hz, 1 H, C-7 OCH_2OCH_3), 5.19 (dd, J = 15.3, 8.9 Hz, 1 H, C-16 or C-17 H), 5.26 (2 d, J = 6.1 Hz, Δ = 10.4 Hz, 1 H), 5.36 (2 d, J = 6.1 Hz, Δ = 9.8 Hz, 1 H, C-14 $CO_2CH_2OCH_2CH_2OCH_3$), 5.44 (m, 1 H, C-16 or C-17 H), 5.49 (m, 1 H, C-9 or C-10 H), 5.59 (m, 1 H, C-20 or C-21 H), 5.66 (ddd, J = 10.1, 5.2, 2.4 Hz, 1 H, C-9 or C-10 H), 5.74 (m, 1 H, C-20 or C-21 H). The signal at 5.19 ppm collapses to a doublet (J = 15.3 Hz) upon irradiation at a multiplet at 2.51 ppm. The multiplet at 5.44 ppm is the only signal in the olefinic region which is affected by irradiation at 5.19 ppm.

Anal. Calcd for $C_{37}H_{54}O_{12}$: C, 64.33; H, 7.88. Found: C, 64.56; H, 7.83.

The corresponding methyl ester of this rearrangement product was obtained as follows. The ester enolate Claisen rearrangement of 104 mg (0.17 mmol) of the ester **35** was performed as decribed above. Chromatography of the resulting crude product on 25 g of silica gel with ether–petroleum ether (1:1) gave 76 mg (74%) of the rearranged acid. A sample of this acid (12 mg, 0.02 mmol) was stirred with excess ethereal diazomethane solution for 25 min at room temperature. The solvent was then removed at reduced pressure, and the residue was chromatographed on silica gel with ether–petroleum ether (1:3). In this manner 11 mg (88%) of the methyl ester corresponding to the ester **36** was obtained as a colorless oil: IR ($CHCl_3$) 1760 (C=O), 1730 (C=O), 1690 cm^{-1} (C=C); ^1H NMR ($CDCl_3$) δ 1.11 (s, C-2 CH_3), 3.31 (s, 3 H, C-7 OCH_2OCH_3), 3.65 (s, 6 H, C-1 OCH_3 and C-14 CO_2CH_3), 3.77 (s, 3 H, C-25 OCH_3), 3.90 (br s, 1 H, C-7 H), 4.05 (s, 3 H, C-24 OCH_3), 4.55 and 4.61 (AB system, J = 8 Hz, 2 H, C-7 OCH_2OCH_3), 5.13 (dd, J = 15, 8 Hz) and 5.3–5.8 (m), total 6 H (olefinic protons); ^1H NMR ($CDCl_3$, 500 MHz) δ 1.13 (2 s, C-2 CH_3), 3.34 (s, 3 H, C-7 OCH_2OCH_3), 3.65 (2 s, 6 H, C-1 OCH_3 and C-14 CO_2CH_3), 5.80 (s, 3 H, C-25 OCH_3), 5.92 (br s, 1 H, C-7 H), 4.09 (2 s, 3 H, C-24 OCH_3), 4.57 (2 d, J = 6.7 Hz, Δ = 3 Hz, 1 H), 4.66 (2 d, J = 6.7 Hz, Δ = 3 Hz, 1 H, C-7 OCH_2OCH_3), 5.18 (dd, J = 15.3, 8.9 Hz, 1 H, C-16 or C-17 H), 5.45 and 5.50 (2 m, 2 H), 5.60 (m, 1 H), 5.66 (m, 1 H), 5.73 (m, 1 H, 5 olefinic protons). Irradiation at 2.25 ppm collapses the multiplet at 5.45 ppm into a dd pattern (J = 15.3, 6.4 Hz). The pattern at 5.18 ppm is reduced to virtually a doublet (J = 8.9 Hz) upon irradiation at 5.45 ppm (C-16 or C-17 H). The coupling constant of 15.3 Hz for the protons of the Δ^{16} double bond indicates the *E* configuration.

Formation of the Aldehyde 37. To a solution of 103 mg (0.15

mmol) of the MEM ester 36 in 2.5 mL of tetrahydrofuran at −78 °C was added 0.52 mL (0.49 mmol, 3.3 equiv) of a 0.84 M solution of Super Hydride in tetrahydrofuran. The reaction mixture was stirred for 15 min at −78 °C and then for 1 h at −30 ± 5 °C. The reaction was quenched by addition of 1 mL of saturated aqueous ammonium chloride solution, and the resulting mixture was then partitioned between ether and brine. The aqueous layer was separated and then extracted with ether. The combined organic layers were washed with brine and then dried ($MgSO_4$). Removal of the solvent at reduced pressure and then chromatography of the residue on silica gel with ether–dichloromethane (1:1) afforded 81 mg (93%) of the corresponding monoalcohol as a colorless oil. The analytical sample was prepared by drying a portion of this material under high vacuum: IR ($CHCl_3$) 3650 (OH), 1760 (C=O), 1730 (C=O), 1690 cm^{-1} (C=C); ^1H NMR ($CDCl_3$) δ 1.14 (s, C-2 CH_3), 3.34 (s, 3 H, C-7 OCH_2OCH_3), 3.42 (m, 2 H, C-14 (CH_2OH), 3.65 (s, 3 H, C-1 OCH_3), 3.78 (s, 3 H, C-25 OCH_3), 3.90 (br s, 1 H, C-7 H), 4.10 (s, 1 H, C-24 OCH_3), 4.57 (s, 3 H, C-24 OCH_3), 4.60 and 4.66 (AB system, J = 7 Hz, 2 H, C-7 OCH_2OCH_3), 5.0–5.9 (m, 6 H, olefinic protons).

Anal. Calcd for $C_{33}H_{46}O_{10}$: C, 67.32; H, 8.22. Found: C, 67.47; H, 8.72.

To a well-stirred solution of 87 mg (0.15 mmol) of the above monalcohol in 2 mL of dichloromethane was added 80 mg (0.37 mmol) of pyridinium chlorochromate.[18] The reaction was stirred at room temperature for 1.5 h, and after dilution with ether, the resulting mixture was washed with saturated aqueous ammonium chloride solution and brine. The aqueous layer was then extracted with ether, and the combined organic layers were then dried ($MgSO_4$). The crude aldehyde **37** (88 mg) that resulted from removal of the solvent at reduced pressure was decarbonylated directly without further purification: IR ($CHCl_3$) 1760 (C=O), 1730 (C=O), 1690 cm^{-1} (C=C); ^1H NMR δ 1.13 (s, C-2 CH_3), 3.30 (s, 3 H, C-7 OCH_2OCH_3), 3.61 (s, 3 H, C-1 OCH_3), 3.79 (s, 3 H, C-25 OCH_3), 3.89 (br s, 1 H, C-7 H), 4.07 (s, 3 H, C-24 OCH_3), 4.51 and 4.59 (AB system, J = 7 Hz, 2 H, C-7 OCH_2OCH_3), 5.0–5.8 (m, 6 H, olefinic protons), 5.48 (br s, 1 H, C-14 CHO).

Decarbonylation of the Aldehyde 37. A solution of 68 mg (0.11 mmol) of the aldehyde **37** and 126 mg (0.14 mmol) of tris(triphenylphosphine)rhodium chloride in 4 mL of freshly distilled 1,2-dichloroethane was degassed by three cycles of freeze–thawing. The dark red solution was then heated under reflux for 1 h under argon. After the mixture was cooled to room temperature, the solvent was removed at reduced pressure, and the residue was taken up in ether and filtered through cotton in order to remove the precipitated triphenylphosphine. The residue was washed thoroughly with ether, and then the solvent was removed from the combined filtrates at reduced pressure. Chromatography of the resulting slightly yellow oil on silica gel with dichloromethane–ether (9:1) gave 49 mg (76%) of the decarbonylation product as a colorless oil, which was homogeneous by thin-layer silica gel chromatography. The analytical sample was prepared by drying this material under high vacuum: IR ($CHCl_3$) 1750 (C=O), 1725 (C=O), 1680 cm^{-1} (C=C); ^1H NMR ($CDCl_3$) δ 1.13 (s, C-2 CH_3), 3.32 (s, 3 H, C-7 OCH_2OCH_3), 3.64 (s, 3 H, C-1 OCH_3), 3.82 (s, 3 H, C-25 OCH_3), 3.90 (br s, 1 H, C-7 H), 4.10 and 4.12 (2 s, 3 H, C-24 OCH_3), 4.56 (AB system, J = 7 Hz, 2 H, C-7 OCH_2OCH_3), 5.1–5.8 (m, 6 H, olefinic protons).

Anal. Calcd for $C_{32}H_{46}O_8$: C, 68.79; H, 8.30. Found: C, 68.90; H, 8.41.

The 500-MHz ^1H NMR spectrum showed the presence of at least five different compounds in this product. High-pressure liquid chromatographic separation of a sample of this decarbonylation product with hexane–ethyl acetate (9:1) gave three peaks in a ratio of 38:47:15 which were assigned as the cyclopropane **40**, the cis isomer **38**, and the trans isomer **39**, respectively. Collection of the fractions gave 24 mg of the cyclopropane **40**, 2.0 mg of mixed fractions, 28 mg of cis isomer **38**, 4.5 mg of mixed fractions, and finally 7.5 mg of trans isomer **39**.

^1H NMR of the cyclopropane **40** ($CDCl_3$ 500 MHz): δ −0.43 (dq J = 20, 5 Hz, cyclopropane protons), 0.62 (m, cyclopropane protons), 1.14 (2 s, Δ = 3.3 Hz, C-2 CH_3), 3.35 (2 s, Δ = 4.8 Hz, C-7 OCH_2OCH_3), 3.65 (2 s, Δ = 1.5 Hz, C-1 OCH_3), 3.83 (2 s, Δ = 3.7 Hz, C-25 OCH_3), 3.93 (br s, 1 H, C-7 H), 4.13 (2 s, Δ = 3.7 Hz, 3 H, C-24 OCH_3), 4.58 (2 d, J = 6.6 Hz, Δ = 3.7 Hz, 1 H) and 4.66 (2 d, J = 7 Hz, Δ = 5.9 Hz), C-7 OCH_2OCH_3, 5.47 (dq, J = 10, 2 Hz, 1 H), 5.59 (dm, J = 10 Hz, 1 H), 5.67 (m, 1 H), 5.76 (m, 1 H, 4 olefinic protons). Irradiation at 0.62 ppm collapses the signal at −4.2 ppm to a doublet (J = 20 Hz).

^1H NMR of cis isomer **38** ($CDCl_3$, 500 MHz): δ 1.14 (s, C-2 CH_3), 3.34 (s, 3 H, C-7 OCH_2OCH_3), 3.66 (s, 3 H, C-1 OCH_3), 3.84 (s, 3 H, C-25 OCH_3), 3.94 (br s, 1 H, C-7 H), 4.15 (2 s, Δ = 1.5 Hz, 3 H, C-24 OCH_3), 4.59 (d, J = 7 Hz, 1 H) and 4.67 (d, J = 7 Hz, 1 H), C-7 OCH_2OCH_3, 5.3–5.45 (m, 2 H, C-16 H and C-17 H), 5.50 (dt, J = 10, 2 Hz, 1 H), 5.6 (m, 1 H), 5.7 (ddd, J = 10, 5, 3 Hz, 1 H) and 5.75 (m, 1 H), 4 olefinic protons. Irradiation at 1.95 ppm collapses the signal at 5.3–5.45 ppm into an AB system (J = 10 Hz, Δ = 22 Hz) and the signals at 5.50, 5.6, and 5.7 ppm into doublets (J = 10 Hz each).

^1H NMR of the trans isomer **39** ($CDCl_3$, 500 MHz): δ 1.10 (2 s, Δ = 1.8 Hz, C-2 CH_3), 3.35 (s, 3 H, C-7 OCH_2OCH_3), 3.66 (2 s, Δ = 1.8 Hz, 3 H, C-1 OCH_3), 3.84 (2 s, Δ = 1.1 Hz, 3 H, C-25 OCH_3), 3.90 (br s, 1 H, C-7 H), 4.15 (2 s, Δ = 1.5 Hz, 3 H, C-24 OCH_3), 4.54 (d, J = 7 Hz, 1 H) and 4.62 (d, J = 7 Hz, 1H), C-7 OCH_2OCH_3, 5.28 (m, 2 H, C-16 and C-17 H), 5.45 (dd, J = 10, 2 Hz, 1 H), 5.54 (m, 1 H), 5.64 (m, 1 H) and 5.72 (m, 1 H), 4 olefinic protons. Irradiation at 1.9 ppm changes the multiplet at 5.28 ppm (2 H, Δ^{16} double bond) into two separate patterns: δ 5.25 (dd, J = 16, 2 Hz) and 5.31 (dm, J = 16 Hz).

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Registry No. 1, 39036-76-5; 1 (24-methyl ether), 38992-34-6; 8, 79391-94-9; 12, 79391-95-0; 12 (2-ethylene ketal), 79391-96-1; 12 (2-ethylene ketal, 5-phosphoro enol), 79391-97-2; 13, 79391-98-3; 13 (2-ethylene ketal), 79391-99-4; 14, 79409-39-5; 14 (1,2-diol), 79392-00-0; 15, 79392-01-1; 15 (1,2-diol), 79392-02-2; 16, 79434-53-0; 17, 79392-03-3; 18, 79392-04-4; 19, 79434-54-1; 19 (7-phosphoro enol), 79409-40-8; 20, 79392-05-5; 21, 79392-06-6; 22, 79392-07-7; 22 (1,2-diol), 79392-08-8; 23, 79392-09-9; 24, 79434-55-2; 25, 79392-10-2; 26, 79392-11-3; 27, 79434-56-3; 27 (7-phosphoro enol, 8-MOM ether), 79409-41-9; 28, 79392-12-4; 28 (1,2-diol), 79392-13-5; 28 (1,2,8-triol), 79392-14-6; 29, 79392-15-7; 29 (dimethyl ester), 79392-16-8; 30, 79392-17-9; 31, 79392-18-0; 32, 79392-19-1; 33, 70728-40-4; 34, 79392-20-4; 35, 79392-21-5; 35 (ester enolate), 79409-42-0; 36 (MEM ester), 79392-22-6; 36 (methyl ester), 79409-43-1; 36 (monoalcohol), 79392-23-7; 37, 79392-24-8; 38 (isomer 1), 79392-25-9; 38 (isomer 2), 79434-60-9; 39 (isomer 1), 79434-57-4; 39 (isomer 2), 79434-61-0; 40, 79392-26-0; 4-(benzyloxy)butyl bromide, 60789-54-0; bis(dimethylamino)phosphorochloridate, 1605-65-8; 4-(4-oxobutyl)-4aα-methyl-3,4,4a,7,8,9aα-hexahydro-9*H*-benzocyclohepten-2(1*H*)-one, 79392-27-1; 11bα-methyl-5aα,7aβ,8,9,10,11,11aα,11b-octahydronaphtho[*a*]cyclohepten-7(6*H*)-one, 79434-58-5; 2,2-dimethoxypropane, 77-76-9; 1α,2α-dihydroxy-11bα-methyl-5aα,7aα,8,9,10,11,11aβ,11b-octahydronaphtho[*a*]cycloheptane, 79392-28-2; 4-[1α-methyl-1β-carboxaldehyde-1,2,4aα,5,6,7,8,8aβ,octahydronaphthyl]butyraldehyde, 79392-29-3; 7aβ,8β-epoxy-11bα-methyl-5aα,7a,8,9,10,11,11aα,11b-octahydronaphtho[*a*]cyclohepten-7(6*H*)-one, 79434-59-6; chloromethyl methyl ether, 107-30-2; 1α,2α-(isopropylidenedioxy)-8β-(methoxymethoxy)-11bα-methyl-5aα,7aα,8,9,10,11,11aβ,11b-octahydronaphtho[*a*]cyclohepten-7(6*H*)-one, 79392-30-6; 4-[1α-methyl-1β-carboxaldehyde-5*b*-(methoxymethoxy)-1,2,4aα,5,6,7,8,8aβ-octahydronaphthyl]butyraldehyde, 79409-44-2; chlorothricin, 34707-92-1; 3-acetylated methyl 2-deoxyrhamoside, 79392-31-7; chloromethyl 2-methoxyethyl ether, 3970-21-6.