The First Stereoselective Synthesis of Racemic β-Multistriatin: A Pheromone Component of the European Elm Bark Beetle *Scolytus multistriatus* (Marsh.)

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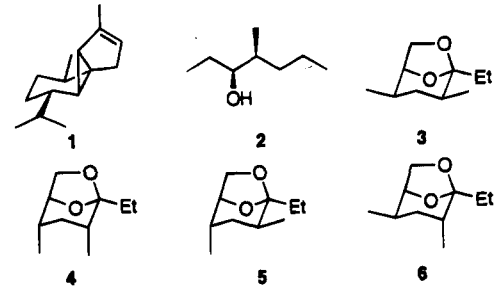
The first stereoselective synthesis of racemic β-multistriatin (**4**), a component of the pheromone of the European elm bark beetle *Scolytus multistriatus* (Marsh.), is described. Potassium glycerate (**23**) is alkylated with 2-bromopentanone (**26**) in the presence of the phase transfer catalyst TDA-1 to form the acyloin ester **29** in 75% yield. After trimethylsilylation of **29**, intramolecular acetalization of the product **30** in the presence of catalytic amounts of trimethylsilyl triflate and perchloric acid affords a mixture of diastereomers of the bicyclic lactone **28** in 65% yield. Reduction of **28** with $LiAlH_4$ gives the cis-disubstituted dioxolane diol **34** in 82% yield. Oxidation of both the primary and secondary hydroxy groups present in **34** by a modified Swern oxidation affords the keto aldehyde **35** in 61% yield. The change of the reagent ratio of oxalyl chloride:DMSO:NEt_3 from 1.1:2.4:5 to 1.2:1.2:3 and a nonaqueous workup procedure are crucial for the success of this oxidation. Intramolecular aldol condensation of **35** catalyzed by triethylammonium chloride affords the aldol **38**. Acetylation of **38** and pyrolytic distillation give the bicyclic enone **37**. Oxidation of **34**, aldol reaction, and formation of the enone **37** can be combined in a one-pot procedure to give an overall yield of 21%. 1,4-Addition of lithium dimethylcuprate to the enone **37** affords ketone **36** with the methyl group exclusively in the axial position. After Wittig methylenation of **36**, the olefin **40** is obtained in 76% yield. Catalytic hydrogenation of **40** with PtO_2 gives a 92:8 mixture of β- and δ-multistriatin in 85% yield. Acid-catalyzed epimerization of **4** affords δ-multistriatin (**5**). Some of the compounds prepared (**28**, **36**, **37**, and **40**) are of interest as multistriatin analogues. Olefin **40** is also a valuable storage form for the unstable β-multistriatin (**4**).

Introduction

In 1921, a formerly unknown disease afflicting elm trees was noted in the Netherlands. The disease, which now is known as Dutch elm disease, has spread rapidly over the northern hemisphere[1] and caused enormous economic damage in the afflicted areas.[2] The most important vector of the disease in the United States is the European elm bark beetle *Scolytus multistriatus* Marsham.[3] The aggregation pheromone of this species has been identified as a combination of the sesquiterpene (−)-α-cubebene (**1**), (−)-4-methyl-3-heptanol (**2**), and the bicyclic acetals (−)-α-multistriatin (**3**) and traces of β-multistriatin (**4**)[3] (Scheme 1).

While numerous syntheses for **3** and the unnatural diastereomer δ-multistriatin (**5**) have been reported,[4] surprisingly, no stereoselective syntheses for the natural **4** or γ-multistriatin (**6**) are known. Instead, the latter compounds were obtained from mixtures of multistriatin

Scheme 1



1 2 3 4 5 6

diastereomers by tedious preparative GC separation procedures.[5] In this paper, we describe the first stereoselective synthesis for the naturally occurring β-multistriatin (**4**) as a racemate. The synthesis of racemic **4** seemed acceptable for the planned field tests since neither the unnatural enantiomer (+)-α-multistriatin[6] nor the "wrong" diastereomers of 4-methyl-3-heptanol[7] cause inhibition of the aggregation.

All[4] but one[4c] of the known multistriatin syntheses use in the final step the intramolecular acetalization of the keto diol **9**. This approach is not applicable for the synthesis of **4** because **4** readily epimerizes to **5** under mild acidic conditions,[8] via the intermediates **7** and **8**. The sensitivity of **4** to acids also led to its confusion with

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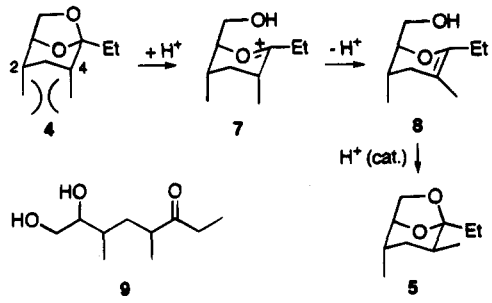
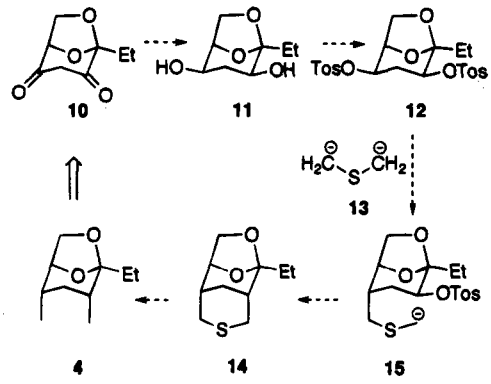
Scheme 2



Scheme 3



5 during the first isolation of 4.[9] The epimerization proceeds through the dihydropyran intermediate 8 which undergoes subsequent cyclization to 5, thus avoiding the strong repulsive interactions between the C-2 and C-4 methyl groups present in 4. In the resulting equilibrium mixture, we found a ratio of 4:5 of 2:98 (Scheme 2).

To avoid epimerization of the labile C-4 methyl group in 4, we planned to establish this labile group in the last synthetic step by reductive desulfurization of the tricycle 14 with Raney nickel under basic conditions. The further retrosynthetic planning was based on the fact that the 6,8-dioxabicyclo[3.2.1]octane system is preferentially attacked from the *exo* side for steric reasons.[10] Thus, our first synthetic goal was the β-diketone **10** which, after reduction with a bulky reagent, should give the diol **11**. Alkylation of the tosylate **12** with a reagent for the difunctional synthon **13** under S_N2 conditions was expected to form **15** in the first step, while the known reluctance of the second alkylation step should be overcome by the intramolecular course of the reaction (Scheme 3).

Two disconnections leading to the 1,3-dicarbonyl unit in **10** by ester condensation are possible. We chose that one leading to glyceric acid because (2*S*)-glyceric acid[11] or (2*R*)-isopropylideneglyceraldehyde[12] as a precursor for (2*R*)-glyceric acid[13] is readily available from the chiral pool. Access to chiral derivatives of glyceric acid is also given by enzymatic hydrolysis of suitable precursors.[14] Starting from chiral derivatives of glyceric acid thus in principle will allow for the synthesis of either enantiomer of **4**. However, to develop our synthesis, we started from racemic calcium glycerate (**22**) which was obtained by a modified literature procedure.[15] To perform the synthesis of **10**, it seemed most simple to start with the condensation of **17** and **18b** and to complete the synthetic sequence by the intramolecular transacetalization of **19b** (Scheme 4).

For test purposes, we wanted to condense **17** with the known ketone **18a**.[16] While it was not possible to obtain **19a** according to the conditions given in the literature for similar substrates,[17] the diketone **19a** was obtained in 26% yield using sodium methoxide in cyclohexane as condensing agent. However, all attempts to perform the intramolecular transacetalization of **19a** to give the bicyclic β-diketone **20** failed.[18] Neither **20** nor the alternative product **21** could be observed. Therefore, an alternative synthetic sequence to prepare **10** was devised. The main problem here is the stereoselective preparation of the *cis*-1,3-dioxolane **33**. The key step in the preparation of **33** is the intramolecular transacetalization of the acyloin ester **27** to form the bicyclic lactone **28**. By this step, not only is the acetalic center of **33** formed with the required stereochemistry, but also the acyloin ester moiety in **28** serves as a precursor for the acetyl group in **33** by a sequence of hydrolysis and subsequent oxidation of the liberated hydroxy group.

Hydrolysis of **17** with KOH in MeOH generated the potassium salt **25** *in situ*, which was readily alkylated with bromopentanone **26** to give the acyloin ester **27**. All attempts to transform **27** into the bicyclic lactone **28** via intramolecular transacetalization by use of moist acetonitrile with *p*-toluenesulfonic acid as catalyst failed. Instead, only products resulting from ester cleavage were observed. An alternative approach was performed by heating **27** in the presence of catalytic amounts of concentrated H_2SO_4 under vacuum in a spinning band distillation apparatus just below the boiling point of **27**. It was expected that the formed **28** would distill from the reaction mixture, thus shifting the equilibrium into the right direction. However, not even traces of **28** were formed, and the distillate obtained by slightly raising the temperature only contained unreacted **27**. To avoid the problem of ester cleavage prior to the removal of the isopropylidene protective group during the transacetalization of **27**, we next started to prepare the unprotected derivative **29** by reaction of an alkali metal glycerate with **26**. The required salts were readily obtained by saponification of methyl glycerate **16** in methanol by the corresponding alkali metal hydroxide. In contrast to the isopropylidene-protected salt **25** which was very soluble in methanol, the salts **23** and **24** were obtained as a syrup which was insoluble in MeOH, DMF, or DMSO. It was not possible to react the salts in this form with **26**,

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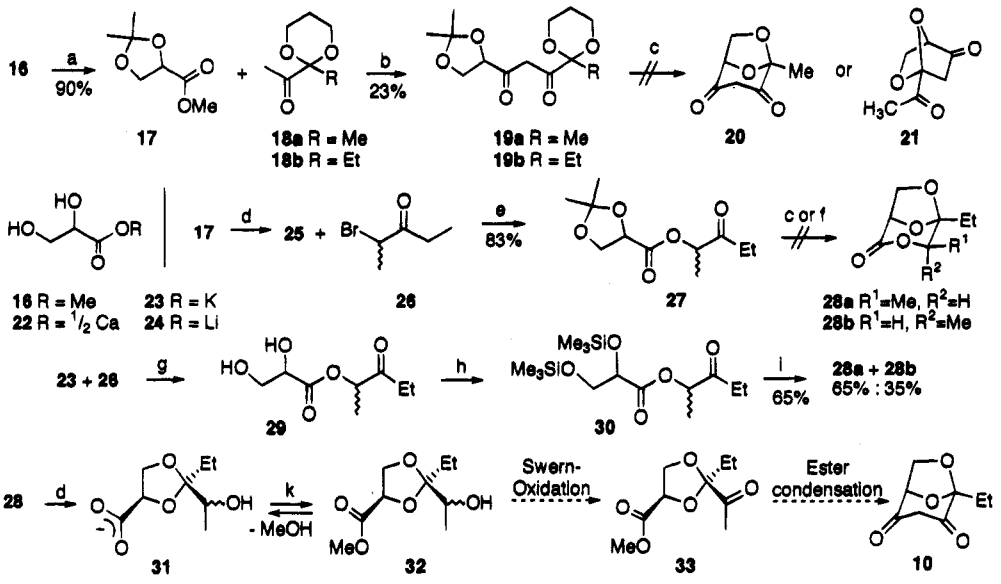
Scheme 4[a]



[a] (a) CH_3COCH_3, 1.2 equiv of $HC(OMe)_3$; (b) NaOMe in cyclohexane, 6 h reflux; (c) 2% H_2O in CH_3CN, catalytic *p*-TsOH, decomposition; (d) KOH (1 equiv) in MeOH, quantitative; (e) 8 h reflux in EtOH; (f) catalytic H_2SO_4, no conversion; (g) $CH_3CN/CHCl_3$, catalytic TDA-1, 2 d reflux; (h) 0.7 equiv of HMDS/Me_3SiCl (1:1), $CHCl_3$; (i) $CHCl_3$, catalytic $Me_3SiOTf/HClO_4$; (k) CH_3I (1.5 equiv), CH_3CN, 1 h, 40 °C.

probably because the required surface was too small. Attempts to obtain the salts by crystallization from water–methanol mixtures failed. However, **23** and **24** could be obtained in crystalline form by heating the syrup to 70 °C for 2 weeks, but it was not possible to obtain crystalline sodium glycerate in an analogous manner. The crystallized salts **23** and **24** were reacted with bromopentanone **26** in acetonitrile as solvent in the presence of catalytic amounts of the podand tris[2-(methoxyethoxy)ethyl]amine TDA-1.[19] The nature of the cation was crucial for the reactivity of the glycerate. With potassium glycerate (**23**), the reaction was completed within 2 days while only traces of **29** were formed by reaction of the lithium glycerate (**24**) under the same conditions. The differing reactivity from carboxylates is known and has been explained by the greater charge separation with voluminous cations, thus leading to enhanced reactivity.[20] Calcium glycerate (**22**) is not suitable for the alkylation because the formed product **29** is hydrolyzed by the crystal water of **22**. The podand TDA-1 proved to be superior compared to 18-crown-6, which also has been recommended as a catalyst for this type of reaction.[21] By use of TDA-1, 2 days were required to react the bromopentanone **26**, resulting in a 75% yield of **29**, while use of 18-crown-6 as catalyst required 3 days for the reaction to give only a 60% yield.

Contrary to our initial expectations, the intramolecular acetalization of **29** proved to be tedious. On heating **29** with trimethyl orthoformate, not even traces of **28** could be detected. Heating a solution of **29** in $CHCl_3$ with a Dean–Stark trap and addition of catalytic amounts of $BF_3{\cdot}OEt_2$ resulted in rapid formation of water accompanied by complete decomposition. Eventually this catalyst led to the elimination of the β-hydroxy group of the glyceric acid ester to form a pyruvate which subsequently polymerized. By use of catalytic amounts of *p*-toluenesulfonic acid, very slow formation of **28** was observed, resulting in a 25% yield after 1 week. The acetalization problem was solved by use of a variant of the Noyori acetalization method.[22] The required bis-silylated diol **30** was obtained in almost quantitative yield from **29** by reaction with a Me_3SiCl:$(Me_3Si)_2NH$ mixture in a 1:1 molar ratio. This method, originally described as a derivatization procedure of sugars for GC–MS analysis,[23] also worked well on a multimolar scale. Addition of pyridine as described in the original procedure proved to be unnecessary. Treatment of **30** with catalytic amounts of Me_3SiOTf in $CHCl_3$ gave **28** in a 10 mmol scale without any problem. However, on scaling up, frequently incomplete conversion of **30** even under prolonged reaction times was observed. While heating the mixture had no significant effect, surprisingly, addition of catalytic amounts of 70% perchloric acid resulted in the rapid conversion of **30** to the desired lactone **28** in 65% yield. The role of the perchloric acid is probably to remove the last traces of NH_4Cl from the reaction mixture which otherwise would react with the catalyst to form the catalytically inactive species MeSiCl and $NH_4^+TfO^-$. The lactone **28** was obtained as a 65:35 mixture of the diastereomers **28a** and **28b**. The structural assignment is based on the X-ray analysis of the di-*p*-chlorobenzoate of the main diastereomer of the diol **34**.[24]

Reaction of the bicyclic lactone **28** with KOH in MeOH resulted in the clean formation of the salt **31** which was subsequently alkylated with methyl iodide to form the methyl ester **32**. However, during chromatographic or distillative workup, **32** underwent intramolecular transesterification to re-form the starting lactone **28**; thus, the synthesis of **10** as depicted in Scheme 4 could not be completed. Since both approaches to obtain **10** had failed, the initial route to β-multistriatin (**4**) was aban-

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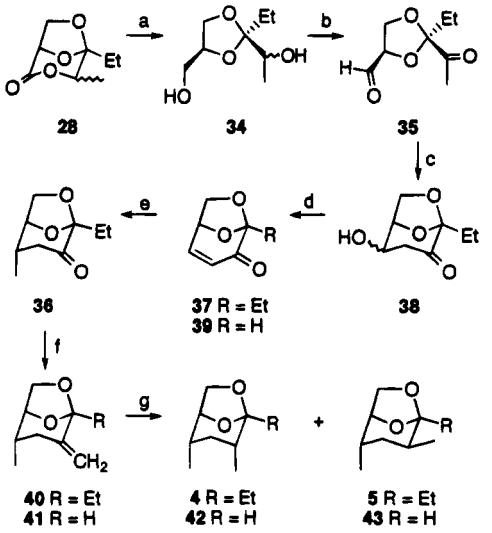
Scheme 5[a]



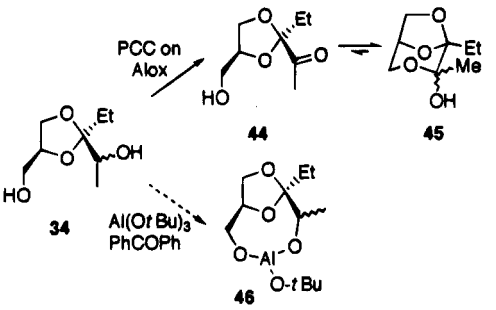
[a] (a) $LiAlH_4$, Et_2O, 82%; (b) modified Swern oxidation, 61%; (c) $HNEt_3^+Cl^-$, 2 d, rt; (d) Ac_2O, NEt_3, catalytic DMAP, ca. 21% from **34**; (e) Me_2CuLi, −30 °C → rt, 83%; (f) $Ph_3PCH_3^+Br^-$, KO-*t*-Bu, 76%; (g) PtO_2, H_2, 85%.

doned. The successful route (Scheme 5) employed lactone **28** as starting material for enone **37**, to which the methyl groups could be appended stereoselectively as in the known conversion of laevoglucosenone (**39**) to the β-multistriatin analogue **42**.[25]

Reduction of lactone **28** with $LiAlH_4$ afforded the diol **34** in high yield. Due to the hydrophilic nature of **34**, however, it was necessary to isolate the diol from the crude reaction mixture by continuous extraction. For the choice of an appropriate oxidation method to prepare the keto aldehyde **35** from **34**, not only the expected sensitivity of **35** to epimerization of the formyl group under basic conditions but also the potential danger of cleavage of the acetal group even under slightly acidic conditions had to be considered. During an attempted oxidation of **34** by PCC on an Alox carrier,[26] instead of the desired keto aldehyde **35**, we only observed the hemiacetal **45** as a mixture of diastereomers. Obviously, the secondary hydroxyl group of **34** is oxidized preferentially, and by formation of **45**, the primary hydroxyl group is effectively protected against further oxidation. Oxidation of **45** to **35** was not possible even by utilization of a great excess of oxidant and prolonged reaction times. An attempt to obtain the enone **37** directly from **34** by Oppenauer oxidation with $Al(O\text{-}t\text{-}Bu)_3$ and benzophenone and consecutive aldol cyclization of **35** catalyzed by the aluminium alcoholates[27] also failed. A possible explanation therefore may be the formation of the cyclic aluminium alcoholate **46**. From observations on oxidations of steroidal cis-diols, it was supposed that alcoholates of this type prevent oxidation of the substrate[28] (Scheme 6).

A method suitable to prepare **35** from **34** was the Swern oxidation.[29] Two modifications of the original

Scheme 6



procedure were crucial for the success of the oxidation step. The acidic aqueous workup procedure as described by Swern was impractical since rapid hydrolysis of **35** took place to give glyceric aldehyde and pentane-2,3-dione; the latter was isolated as the sole product. Even with an acetate buffer solution at pH 5, the hydrolytic cleavage of **35** was complete at 0 °C within 5 min. To avoid the aqueous workup, the triethylammonium chloride formed during the oxidation was precipitated by addition of ether to the reaction mixture at −40 °C and filtered off immediately. However, the large excess of DMSO used in the original procedure still caused problems, since after distillation, the obtained **35** contained considerable amounts of DMSO due to the similar boiling points of both compounds. In a series of test oxidations of the substrate citronellol, it could be demonstrated that the molar ratio of the reagents oxalyl chloride, DMSO, and NEt_3 could be reduced from the original ratio of 1.1:2.4:5 to 1.2:1.2:3, still giving an 85% yield of citronellal even up to a 2 M scale. When both modifications were applied to the original Swern procedure, it was possible to isolate **35** nearly free from DMSO in 61% yield. The distilled keto aldehyde **35** showed no tendency to undergo spontaneous aldol condensation. Treatment of a diluted ethereal solution of **35** with basic catalysts like KOH, NaOH, BaO, or NaOEt at room temperature gave no conversion of **35**, while heating to reflux resulted in slow conversion within 2 days, as monitored by ^{1}H-NMR. However, the desired products **37** or **38** could be obtained only in traces while mostly polymeric products were formed. Application of acidic catalysts also seemed impractical due to the sensitivity of **35** to hydrolytic cleavage. A suitable catalyst was found by serendipity. It was noted that some batches of the Swern oxidation which could be worked up only after prolonged standing gave no **35**, but instead, large amounts of **38** had been formed. Initially, the applied drying agent $MgSO_4$ was suspected to be the catalyst, but closer examination demonstrated that triethylammonium chloride, which remained in traces after the precipitation, was the actual catalyst. The aldol **38** which could be obtained from the reaction mixture by chromatography was subsequently heated with $KHSO_4$ in order to form **37** by elimination of water. Unexpectedly, the starting aldehyde **35** was re-formed while no **37** could be detected. From this observation, it was concluded that elimination of water from **38** to form the 6,8-dioxabicyclo[3.2.1]oct-2-en-4-one system present in **37** is hindered by the developing steric strain. This conclusion is in good accordance with the fact that laevoglucosenone (**39**) is a highly reactive

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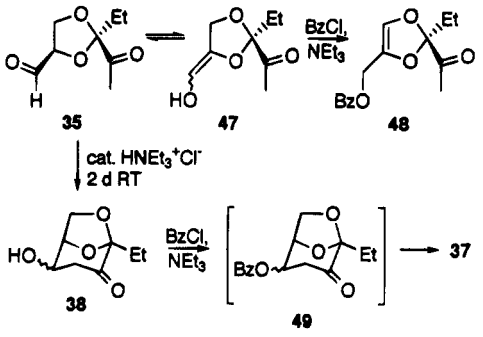
Scheme 7



Michael acceptor which readily adds even the O-nucleophiles water and methanol from the *exo* side.[30]

Since **38** could be obtained only by tedious chromatography and due to the problematic elimination of water, we decided to prepare the benzoate **49** with the expectation that elimination to **37** would be enhanced. Immediately after addition of benzoyl chloride and triethylamine to a freshly prepared solution of **35**, a smooth reaction took place. Interestingly, the isolated product was the 1,3-dioxol **48**, which must have been formed by acylation of the enol **47** and a subsequent shift of the olefinic bond. However, allowing the solution of **35** to stand for 2 days to perform the aldol reaction and adding the same reagents then directly gave the desired enone **37** after chromatographic workup (Scheme 7). By replacing benzoyl chloride with acetyl chloride, we made the isolation of the product more simple, since all byproducts could be removed by distillation. It was possible to combine all steps for the transformation of the diol **34** to the enone **37** in a one-pot procedure to give a reproducible yield of 20% for the enone from **34**.

With the enone **37** in our hands, the further synthesis of β-multistriatin was straightforward. Lithium dimethylcuprate was added to **37** in a completely stereospecific manner from the *exo* side to afford **36**. The high stereoselectivity of this addition step is crucial because the product from the *endo* addition finally would be transformed into α-multistriatin (**3**). Due to its high biological activity, this compound would impair the biological tests of the obtained β-multistriatin (**4**). Wittig olefination of **36** gave the olefin **40** in 76% yield, if care was taken to avoid loss by the high volatility of **40** during the workup. Stereoselective hydrogenation of **40** completed the synthesis of β-multistriatin (**4**). The best results were obtained with PtO_2 as catalyst in ether, to give a product with a ratio of **4**:**5** of 92:8. With Pd on charcoal, the ratio was 76:24. These ratios are in good agreement with the results obtained by Mori on the hydrogenation of **41** to **42** and **43**.[26b] Hydrogenation of **40** with Wilkinson's catalyst proceeded only sluggishly to give after a reaction time of 2 days a product with a ratio of **4**:**5** of 79:21 and 93% conversion of the olefin. The configuration of **4** was secured by high-field NMR spectroscopy. The similar coupling constants of either the 3-*endo* or 3-*exo* proton with the adjacent protons on C-2 and C-4 give proof for the local C_S symmetry at C-3. From the observed coupling constants, it can be concluded that the pyran ring in **4** is flattened while both methyl groups are bend outward. Treatment of **4** with trifluoroacetic acid gave after 2 days a mixture with a ratio of β-multistriatin (**4**): δ-multistriatin (**5**) of 2:98. Analysis of the NMR spectra of **5** gave evidence that the pyran ring in **5** is present in a chair conformation. It should also be noted that the tentative assignment made for the shifts of the methyl groups at C-2 and C-4 in **5**[31] is correct.

With our newly developed synthesis, racemic β-multistriatin (**4**) has become available on a 20 g scale. These amounts are sufficient for field tests to evaluate the biological activity of **4**. Due to the sensitivity of β-multistriatin (**4**), the olefin **40** is an ideal storage form, from which **4** is readily prepared. In the course of our synthesis, a number of analogues of the multistriatins (**28**, **36**, **37**, and **40**) have been obtained. Tests on the biological activity of these compounds are under way.

Experimental Section:

General. DMSO was dried over CaH_2. CH_2Cl_2 was dried over P_4O_{10}. THF was dried with sodium/benzophenone. All other solvents were used without further pretreatment. Microanalyses were performed at the microanalytical laboratory of the Rheinisch Westfälische Universität Aachen. The spinning band distillation column was a Normag SAA-08101 model.

Calcium Glycerate Dihydrate (22). In a well-ventilated hood, charge 400 g of glycerol to a 5 L Erlenmeyer flask, add 640 mL of 42% nitric acid and 3 g of sodium nitrite, and cover with a watch glass. After 3–5 h, an almost instantaneous reaction with vigorous formation of nitrous gases takes place. The reaction calms down within 30 min. After stirring overnight, the reaction mixture is charged to a 2 L beaker and is neutralized with good agitation by careful addition of calcium carbonate. Since toward the end, the neutralization is rather slow, the calcium carbonate should not be added faster than 5 g/min to avoid overcharging, which results in slow filtration. The required amount of calcium carbonate is approximately 120 g. The crystallization of the crude **22** is completed by stirring the mixture overnight. The crystals are isolated by filtration on a Büchner funnel. The filter cake is squeezed out as much as possible, and the filtrate is discarded. The crude product is dissolved in 1 L of boiling water (or mother liquor from previous batches) and the solution filtered to remove the excess calcium carbonate. To avoid the crystallization of the product in the filter paper, the vacuum line on the filter flask is disconnected during most of the filtration time and opened only occasionally to restore sufficient vacuum in the flask. Doing the filtration in small portions has proven to be the most efficient method to prevent cooling and crystallization of **22** on the filter. The residue on the filter is then washed with 300 mL of hot water. From the combined filtrate and water wash, the product crystallizes overnight. The purified product is filtered and squeezed as much as possible. The mother liquor is removed and can be reused up to 20 times for the purification step. The filter cake is finally washed with 50% ethanol until the effluent is almost colorless. After dry squeezing, the product is dried at 70 °C. The batch size should be in the range of 300–400 g of glycerol. At higher amounts, the reaction can get out of control; at lower amounts, the reaction is too slow. Yield: 155 g of calcium glycerate dihydrate (25% of theory, based on glycerol). Mp: 139–140 °C dec. ^{1}H-NMR (D_2O, 300 MHz): δ 3.77 (dd, 1, $|^2J|$ = 11.7 Hz, ^3J = 4.7 Hz, H-3), 3.83 (dd, 1, ^3J = 2.7 Hz, H-3′), 4.20 (br tr, 1, H-2). ^{13}C-NMR (75 MHz, D_2O): δ 66.74 (C-3), 76.21 (C-2), 181.54 (C-1). Elementary analysis: C calcd 25.17, found 25.07; H calcd 4.93, found 4.82.

Potassium Glycerate (23). Dissolve in a 5 L beaker 572 g of **22** (2 mol) in 2 L of boiling water. Add 30 g of charcoal to this solution and stir for 20 min. Then add slowly a boiling

(30) (a) Shafizadeh, F.; Ward, D. D.; Pang, D. *Carbohydr. Res.* **1982**, *102*, 217. (b) Blattner, R.; Furneaux, R. H.; Mason, J. M.; Tyler, P. C. *Pestic. Sci.* **1991**, *31*, 419. (c) Furneaux, R. H.; Mason, J. M.; Tyler, P. C.; Blattner, R.; Lawson, K. R.; Chrystal, E. J. T.; Mitchell, G.; Pilkington, B. L. EP 0 302 599 A2, July 7, 1988.

(31) Pearce, G. T.; Gore, W. E.; Silverstein, R. M. *J. Magn. Res.* **1977**, *27*, 497.

solution of 332 g (2 mol) of potassium oxalate in 1 L of water. The filtration of the precipitated calcium oxalate is very slow, even through a large Büchner funnel. To obtain a good yield, resuspend the filter cake with 1 L of boiling water, filter, and repeat this once more. The water is evaporated from the combined filtrates. Then the highly viscous residue (ca. 560 g) is poured into a porcelain dish which has been lined with polyethylene film. This is accomplished most effectively overnight by installing the flask upside down over the dish. After being placed in an oven at 70 °C, the slightly yellow **23** crystallizes within ca. 2 weeks, or 2–3 days if seeded. The polyethylene film is then easily peeled off, and the cake is cracked to pieces of ca. 1.5 cm and dried for 3 days in vacuo over a little P_4O_{10}, which is replaced daily. Then the product is crushed to 5 mm pieces and dried to constant weight. Finally, a course powder is obtained by milling small portions in a blender. Proper safety precautions should be taken since, in one isolated case, a dust explosion was observed. The product is dried completely in vacuo over P_4O_{10}. Yield: 541 g (94% of theory, based on **22**). Elementary analysis: C calcd 24.99, found 21.51; H calcd 3.50, found 2.96. The low values probably result from incomplete combustion. From the obtained values, a C:H ratio of 3:4.92 was calculated which is in good agreement with the theoretical ratio of 3:5.

2-Bromopentan-3-one (26). Charge to a 2 L round bottom flask with a paddle agitator, a pressure-equalized addition funnel, and a thermometer a solution of 176 g (1.8 mol) of 96% H_2SO_4 in 500 mL of water and 516 g (6 mol) of pentan-3-one. Add to this mixture within 45 min 240 g (0.45 mol) of bromine. Initially, the reaction is somewhat sluggish, but later, the bromine reacts almost instantaneously while the temperature rises to70 °C. After adding the Br_2, cool the flask with a water bath until the temperature has dropped to 30 °C. Then 94.8 g (0.6 mol) of $KMnO_4$ is added in small portions at such a rate that the temperature does not exceed 70 °C. After cooling the mixture to ambient temperature, separate the lachrymatory organic layer and extract the aqueous phase with 50 mL of pentan-3-one. The organic phases are combined, and 20 g $CaCO_3$ is added. This mixture is distilled at normal pressure over a 60 cm Vigreux column with a distillate splitter at a heating bath temperature of 160 °C. The distillate which contains water and pentan-3-one is collected until a temperature of 105 °C is reached. At this time, the heating is stopped until the temperature of the heating bath has dropped to 70 °C, and then the distillation is continued under reduced pressure at 45 mmHg. After the reflux ratio is adjusted to 10:1, the distillate is collected until a temperature of 75 °C is reached. The obtained fraction which contains mostly pentan-3-one is combined with the forerun from the normal pressure distillation and may be used as starting material in another batch. Then the reflux ratio is adjusted to 3:1, and the product is collected in the boiling range from 73–76 °C. Further product is collected at a reflux ratio of 10:1 up to 78 °C. After termination, a solution of 60 g of KOH in 300 mL of methanol is added to the distillation residues and the mixture refluxed for 30 min to decompose higher brominated products. Yield: 352 g (71% of theory, based on Br_2). The product obtained in this way has a purity of 98% and is stable for more than 1 year at ambient temperature. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 1.11 (tr, 3, ^3J = 7.2 Hz, CH_3), 1.73 (d, 3, ^3J = 6.4 Hz, CH_3), 2.61, 2.87 (2 dqu, 1 each, $|^2J|$ = 18.1 Hz, CH_2), 4.47 (q, 1, CHBr). ^{13}C-NMR (75 MHz, $CDCl_3$): δ 8.18 (CH_3), 20.14 (CH_3), 31.97 (CH_2), 47.35 (CHBr), 204.65 (CO).

(±)-Glyceric Acid 1-Methyl-2-oxo-butyl Ester (29). Charge to a 4 L round bottom flask with a Hershberg stirrer and a reflux condenser 605 g of potassium glycerate (**23**) (4.2 mol), 660 g of 2-bromopentan-3-one (**26**) (4 mol), 5 g of TDA-1 (tris[2-(methoxyethoxy)ethyl]amine), 600 mL of $CHCl_3$, and 600 mL of CH_3CN. Reflux for 36 h. After 24 h, the heating source is temporarily removed, and caked up lumps of potassium bromide are scratched from the walls into the mixture. After reaction, the mixture is cooled to room temperature, and the precipitated potassium bromide is filtered off. The filter cake is washed with ca. 500 mL of trichloromethane, and from the filtrate are removed on a rotavapor the solvents. About 780 g of crude **29** remain as a brown oil, which can be used in the following silylation. If desired, the product can be purified by vacuum (0.01 mbar) distillation in small portions of 250 g each, as long as the oil bath temperature does not exceed 180 °C. These conditions are necessary to avoid decomposition. After distillation, the yield is ca. 500 g (ca. 65% of theory, based on **26**). ^{1}H-NMR (300 MHz, $CDCl_3$): δ 1.06 (tr, 3, ^3J = 7.3 Hz, CH_3), 1.45, 1.46 (2 d, 3, ^3J = 7.1 Hz, CH_3), 2.55 (q, 2, CH_2), 3.85–4.02 (m, 2, $HOCH_2$), 4.17 (br s, 2, OH), 4.37 (m, 1, C*H*(OH)), 5.21, 5.26 (2 q, 1, CH_3CH). ^{13}C-NMR (75 MHz, $CDCl_3$): δ 7.21 (CH_3), 16.14, 16.22 (CH_3), 31.39, 31.48 (CH_2), 64.19, 64.57 ($HOCH_2$), 72.04 (*C*H(OH)COO), 75.51, 75.59 ($OCHCH_3$), 172.30, 172.45 (*C*OO), 208.28, 208.69 (*C*O). Elementary analysis: C calcd 50.52, found 49.85; H calcd 7.24, found 7.41.

(±)-1,2-Bis(trimethylsilyl)glyceric Acid 1-Methyl-2-oxo-butyl Ester (30). The crude **29** is redissolved in 500 mL of trichloromethane and transferred back to the apparatus used for its preparation. To this solution is added a mixture of 318.9 g of trimethylchlorosilane (2.57 mol) and 472.5 g of hexamethyldisilazane (2.57 mol) over 8 h while the exothermic reaction is maintained at room temperature with a water bath. After the mixture is stirred overnight, the precipitated ammonium chloride is filtered off quickly through a dried 18 cm Büchner funnel. The filter cake is sucked dry and washed thoroughly with several 300 mL portions of $CHCl_3$ to avoid considerable yield losses. The solvent is removed on a rotavapor, and the residue is distilled under vacuum over a 30 cm Vigreux column. After a small initial fraction, the product is collected at 100 °C/1 mmHg or 143 °C/13 mmHg. Yield: 1000 g (75% of theory, based on **26**). ^{1}H-NMR (300 MHz, $CDCl_3$): δ 0.11–0.17 (5 signals, 18, $SiMe_3$), 1.05, 1.06 (2 tr, 6, ^3J = 7.4 Hz, ^3J = 7.2 Hz, CH_3), 1.41 (d, 3, ^3J = 7.1 Hz, $CHCH_3$), 2.43–2.65 (m, 2, CH_2), 3.77–3.93 (m, 2, $SiOCH_2$), 4.30–4.35 (m, 1, SiOCH), 5.15 (q, 1, CH_3CH). ^{13}C-NMR (75 MHz, $CDCl_3$): δ 0.097–0.615, (11 signals, $SiMe_3$), 7.82, 7.87 (CH_3), 16.95, 16.97 (CH_3CH), 31.92, 31.97 (CH_2), 65.90, 65.93 ($SiOCH_2$), 73.91, 73.95 (SiOCH), 75.65, 75.71 ($CHCH_3$), 171.79 (COO), 208.47, 208.50 (CO). Due to the sensitivity of **30**, no satisfactory elementary analysis could be obtained.

(±)-5-Ethyl-4-methyl-2-oxo-3,6,8-trioxabicyclo[3.2.1]-octane (28). Charge to a 3 L round bottom flask 1.5 of trichloromethane and 3 mL of 70% perchloric acid. The perchloric acid is dissolved almost completely by shaking for ca. 2 min. Add 10 mL of trimethylsilyl triflate and then, at once, 1003 g of **30** (3 mol). Depending on the purity of **30**, the slightly exothermic reaction should start immediately, and the temperature rises to 30–45 °C. Any impurity of NH_4Cl can inhibit the reaction. In this case, more trimethylsilyl triflate is added in portions of 2 mL until the reaction starts. After 0.5–2 h, the reaction is complete when the intermediate peaks in the gas chromatogram disappear and only the product peak remains. The following conditions are recommended: 4 m OV101 packed column, 170 °C isothermic, and a retention time of 4.7 min. Under these conditions, a partial separation of the diastereomers of **28** is observed. At this point, the dark brown reaction mixture poured into a 4 L separatory funnel containing a solution of 30 g of K_2CO_3 in 500 mL of water. The color changes upon neutralization to golden yellow. The organic phase is separated and the solvent removed on a rotavapor. The recovered solvent can be reused for the same reaction after being dried over $CaCl_2$. The residue is transferred into a 1 L round bottom flask and distilled as quickly as possible at ca. 13 mbar by using an oil bath preheated to 200 °C. The fraction boiling at 100–140 °C (ca. 480 g) contains the product. The pure **28** is obtained by distillation over a 1 m spinning band column at 12 mbar and at an oil bath temperature of 160 °C. Beginning with a 100 °C head temperature, the rate of distillate collection is reduced to 1 drop per 3 s until 113 °C is reached. At this temperature, the product is collected, and the distillation rate can be increased. Yield: 332 g (65% of theory, based on **30**). The product **28** is obtained as a mixture of two diastereomers from which the main diastereomer (65%) has the shorter GC retention time. ^{13}C-NMR of major diastereomer (75 MHz, $CDCl_3$): δ 6.13 (CH_3), 16.08 (4-CH_3), 25.34 (CH_2), 69.18 (C-7), 73.57 (C-4), 81.87 (C-1), 107.10 (C-5), 167.65 (C-2). ^{13}C-NMR of minor

diastereomer (75 MHz, $CDCl_3$): δ 6.07 (CH_3), 17.59 (4-CH_3), 25.57 (CH_2), 69.21 (C-7), 74.68 (C-4), 82.64 (C-1), 107.45 (C-5), 167.25 (C-2). Elementary analysis: C calcd 55.80, found 55.68; H calcd 7.03, found 7.10.

(±)-1-[(2Ξ)-2-Ethyl-*c*-4-(hydroxymethyl)[1,3]dioxolan-*r*-2-yl]ethanol (34). Charge to a dry 2 L round bottom flask with a paddle agitator, a pressure-equalized addition funnel, and an efficient reflux condenser 20.9 g of $LiAlH_4$ (0.55 mol), flush with nitrogen, and add 1 L of dry ether through the dropping funnel. To the obtained $LiAlH_4$ slurry is added a solution of 172 g of **28** (1 mol) in 200 mL of ether within 2 h. Then the mixture is kept refluxing overnight. Hydrolysis of the reaction mixture is performed by the slow addition of water. During hydrolysis, the mixture becomes temporarily viscous; at that time, the addition of water has to be done with great care. After completion of the hydrolysis, the reaction mixture is transferred into a continuous extraction apparatus and extracted with ether for 2 days. The extract which is obtained after this time is stored in the refrigerator, and the extraction is continued for a further 6 days. Then the extracts are combined, and the solvents are removed on a rotavapor. The residue is distilled under vacuum over a 30 cm Vigreux column. The fraction boiling at 110 °C/1.5 mmHg is collected to give **34** as a thick colorless oil which slowly crystallizes. Yield: 144 g (82% based on **28**). After several recrystallizations from ethyl acetate, the main diastereomer was obtained as leaflets, mp = 65 °C. ^{1}H-NMR of major diastereomer (500 MHz, $CDCl_3$): δ 0.93 (tr, 3, ^3J = 7.5 Hz, CH_3), 1.21 (d, 3, ^3J = 6.4 Hz, CH_3), 1.57, 1.69 (ddq, 2, $|^2J|$ = 14.4 Hz, CH_2, by NOE measure, 1.57 = *pro-S*-H), 3.50 (br s, 1, OH), 3.60 (dd, 1, $|^2J|$ = 11.9 Hz, ^3J = 1.8 Hz, dioxolane 5-H), 3.75 (br s, OH), 3.86 (q, 1, CH_3CH), 3.94 (dd, 1, ^3J = 2.8 Hz, dioxolane 5-H′), 4.04 (tr, 1, ^3J = 7.6 Hz, CH_2OH), 4.11 (dd, 1, $|^2J|$ = 7.8 Hz, ^3J = 6.9 Hz, CH_2OH), 4.30 (ddtr, dioxolane 4-H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ 7.38 (CH_3), 17.37 (CH_3CH), 27.83 (CH_2), 61.73 (CH_2), 67.20 (CH_2OH), 70.87 (CH_3CH), 77.29 (dioxolane C-4), 113.27 (dioxolane C-2). ^{13}C-NMR of minor diastereomer (75 MHz, $CDCl_3$): δ 7.38 (CH_3), 17.61 (CH_3CH), 27.01 (CH_2), 62.58 (CH_2), 66.89 (CH_2OH), 70.28 (CH_3CH), 77.49 (dioxolane C-4), 113.28 (dioxolane C-2).

(±)-*r*-2-Acetyl-2-ethyl-*c*-4-formyl[1,3]dioxolane (35). Charge to a thoroughly dried 1 L round bottom flask with a paddle agitator, a pressure-equalized addition funnel, a thermometer, and a calcium chloride drying tube a solution of 57.2 g of oxalyl chloride (0.45 mol) in 350 mL of dry CH_2Cl_2. Cool the mixture to −65 °C with dry ice/ethanol. Note: Ethanol is preferred over acetone because of its greater heat capacity. Add a solution of 35.1 g (0.45 mol) of freshly dried DMSO in 100 mL of CH_2Cl_2 as fast as possible, avoiding a temperature increase above −55 °C. The reaction is highly exothermic, and the time required for the addition is about 6−8 min. After the DMSO addition is complete, the addition funnel is rinsed through with 50 mL of dry CH_2Cl_2 and the reaction mixture is stirred for 5 min. When the temperature has dropped back to −65 °C, a solution of 33 g of **34** (0.187 mol) in 150 mL of dry CH_2Cl_2 is added at such a rate that the temperature does not exceed −60 °C. The mixture is stirred for a further 30 min. Finally, the color of the slightly cloudy solution is light yellow-orange. Add 136.3 g of NEt_3 (1.35 mol) at such a rate that a temperature of −40 °C is not exceeded. This usually takes 12 min. The reaction is initially very exothermic. After ca. half of the amine has been added, the mixture turns colorless, and the reaction becomes less exothermic. After the amine addition is completed, the mixture is stirred for a further 5 min, and the triethylammonium chloride is quickly filtered off in a Büchner funnel. Since the filter cake tends to crack, it has to be squeezed carefully. Rinse through with 300 mL of CH_2Cl_2 which has been cooled to −40 °C in the reaction flask during the filtration to wash the filter cake. At this point, **35** can be isolated from the almost colorless filtrate, if the isolation is of interest. In this case, the solvent is evaporated without delay. The residue is dissolved in ether, to separate **35** from last traces of ammonium salts by filtration. After evaporation of the filtrate and distillation of the residue at 105 °C/1.5 mbar, **35** is obtained with 61% yield. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 0.94 (tr, 3, ^3J = 7.5 Hz, CH_3), 1.89 (q, 2, CH_2), 2.23 (s, 3, CH_3), 3.96 (dd, 1, $|^2J|$ = 8.5 Hz, ^3J = 6.0 Hz, dioxolane H-5), 4.28 (dd, 1, ^3J = 7.5 Hz, dioxolane H-5′), 4.55 (ddd, 1, dioxolane H-4), 9.71 (d, 1, ^3J = 1.3 Hz, CHO). ^{13}C-NMR (75 MHz, $CDCl_3$): δ 6.83 (CH_3), 25.01 (CH_3), 27.07 (CH_2), 65.77 (dioxolane C-5), 80.57 (dioxolane C-4), 111.55 (dioxolane C-2), 199.62 (CHO), 204.76 (CO). Due to contamination of **35** with differing amounts of DMSO, satisfying elementary analysis data could not be obtained.

(±)-5-Ethyl-2-hydroxy-4-oxo-6,8-dioxabicyclo[3.2.1]-octane (38). If the keto aldehyde **35** is not isolated, the solution obtained above is left standing at room temperature for 2 days to perform the aldol reaction. A sample of the aldol product **38** was isolated by HPLC (silica gel, cyclohexane:ethyl acetate, 8:2 by volume) as slightly yellow syrup. There was only one diastereomer obtained; however, it was not possible to determine the stereochemistry of the 2-hydroxyl group from the NMR spectra. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 0.95 (tr, 3, ^3J = 7.5 Hz, CH_3), 1.82, 1.84 (ddq, 2, $|^2J|$ = 14.4 Hz, CH_2), 2.57 (ddd, 1, $|^2J|$ = 15.6 Hz, ^3J = 9.9 Hz, J = 0.5 Hz (long range coupling), H-3), 2.75 (ddd, 1, ^3J = 7.0 Hz, J = 1.7 Hz (long range coupling), H-3′), 3.36 (dd, 1, $^3J \approx 4$ Hz, J = 1.0 Hz (long range coupling), OH), 3.92 (ddd, 1, $|^2J|$ = 7.9 Hz, ^3J = 5.0 Hz, *exo* H-7), 4.34 (m, 1, H-2), 4.37 (dd, 1, ^3J = 0.8 Hz, *endo* H-7), 4.55 (br "tr", 1, ^3J (H-1,H-2) ≈ 4.5 Hz, H-1). ^{13}C-NMR (75 MHz, $CDCl_3$): δ 6.24 (CH_3), 22.21 (CH_2), 41.85 (C-3), 64.54 (C-7), 68.21 (C-2), 76.86 (C-1), 105.32 (C-5), 199.69 (C-4).

(±)-5-Ethyl-6,8-dioxabicyclo[3.2.1]oct-2-en-4-one (37). To obtain **37** from **38**, the solution of the aldol **38** is placed in a 2 L round bottom flask, and 94.7 g of triethylamine (0.934 mol) and a catalytic amount of DMAP (0.5 g) are added. After cooling the mixture to −3 °C, add dropwise 58.9 g (0.75 mol) of acetyl chloride while maintaining a temperature of 0−5 °C. After the addition is complete, stir out for 90 min at −5 °C. The precipitated triethylammonium chloride is then filtered off and washed thoroughly with ether. From the combined filtrates is evaporated the solvent at a bath temperature of 70 °C. The residue is mixed thoroughly with 1 L of ether. Usually, the yellow ether phase can be decanted from a tarry residue. Otherwise, the precipitate is filtered off. The filtrate is then concentrated in a rotavapor and transferred to a 100 mL flask, and the last traces of volatiles are removed at 100 °C/12 mbar.

The remaining brown oil is distilled at 1.2 mbar using a preheated oil bath at 180 °C. During the distillation, the temperature is raised to 200 °C. The distillation is interrupted when either the 140 °C head temperature is reached or a solid deposit (dehydroacetic acid) begins to appear in the condenser. The yield of crude **37** which is in the light orange distillate is 25−28% of theory, based on **34** as determined by capillary GC. For purification, six batches were combined and distilled in the presence of 2,6-di-*tert*-butylphenol as polymerization inhibitor over a spinning band column, collecting the fraction at 86−88 °C/1 mbar. Yield: 36.4 g (20.8% of theory, based on **34**). After prolonged cooling to −78 °C, **37** solidifies, mp = −5 °C. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 0.96 (tr, 3, ^3J = 7.4 Hz, CH_3), 1.98 (q, 2, CH_2), 3.70 (d, 1, $|^2J|$ = 6.7 Hz, $^3J \approx 0$ Hz, *endo* H-7), 3.93 (dd, 1, ^3J = 4.7 Hz, *exo* H-7), 5.01 (tr, 1, ^3J (H-1,H-2) ≈ 4.7 Hz, H-1), 6.10 (d, 1, ^3J (H-2,H-3) = 9.7 Hz, H-3), 7.27 (dd, 1, H-2). ^{13}C-NMR (75 MHz, $CDCl_3$): δ 6.22 (CH_3), 22.59 (CH_2), 67.24 (C-7), 72.31 (C-1), 108.23 (C-5), 122.31 (C-3), 148.01 (C-2), 189.75 (C-4). Elementary analysis: C calcd 62.32, found 62.05; H calcd 6.54, found 6.63.

(±)-5-Ethyl-2-*exo*-methyl-4-oxo-6,8-dioxabicyclo[3.2.1]-octane (36). Charge to a 2 L round bottom flask with a magnetic stirring bar, a pressure-equalized addition funnel, a thermometer, and a reflux condenser 80 g of CuBr·Me_2S (0.389 mol) and 250 mL of ether. After cooling the mixture to −60 °C, add slowly 460 mL of a 1.7 M MeLi solution in ether (0.78 mol). During the addition, the mixture first becomes yellow, but later a white suspension is formed. On the solution being warmed to −30 °C, a colorless solution is formed within 20 min. After the obtained solution of Me_2CuLi is recooled to −60 °C, a solution of 36.3 g of **37** (0.236 mol) in 200 mL of ether is added within 10 min. A slightly exothermic reaction occurs, and an intense yellow precipitate is formed during the addition of **37**. The mixture is stirred for a further 15 min

and is then hydrolyzed by cautions addition of water. After warming, the ethereal layer is decanted from the brown precipitate. The latter is extracted overnight with ether in a continuous extraction apparatus. After the combined organic phases are dried ($MgSO_4$), the obtained solution of **36** can be used directly in the preparation of **40** (vide infra). Concentrating the solution and short path chromatography over silica gel with pentane affords after removal of the solvent **36** as colorless crystals, mp = 33 °C. Yield: 30.9 g (83% based on **37**). ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 0.95 (tr, 3, ^3J = 7.6 Hz, CH_3), 1.18 (d, 3, ^3J = 7.1 Hz, CH_3), 1.85 (q, 2, CH_2), 2.05 (br d, 1, $|^2J|$ = 16.1 Hz, *exo* H-3), 2.35 (quint, 1, ^3J (H-1,H-2) ≈ 7.3 Hz, H-2), 2.87 (dd, 1, ^3J = 7.8 Hz, *endo* H-3), 4.03 (m, 2, H-7, H-7′), 4.40 (br s, H-1). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 6.28 (CH_3), 18.64 (CH_3), 22.47 (CH_2), 36.99 (CH2), 39.65 (C-3), 69.18 (C-7), 79.94 (C-1), 107.24 (C-5), 201.40 (C-4). Elementary analysis: C calcd 63.51, found 63.40; H calcd 8.29, found 8.42.

(±)-5-Ethyl-2-*exo*-methyl-4-methylene-6,8-dioxabicyclo-[3.2.1]octane (40). Charge to a dry 2 L round bottom flask with a magnetic stirring bar, a thermometer, and a pressure-equalized addition funnel 100 g of methyltriphenylphosphonium bromide (0.28 mol) and 32 g of KO-*t*-Bu (0.28 mol), flush with nitrogen, and add 800 mL of dry THF. Stir the yellow solution for 6 h to complete the formation of the ylide. Then cool the mixture to −20 °C and add slowly a solution of 30.9 g of **36** (0.182 mol) in 250 mL of ether. A slightly exothermic reaction takes place. To complete the olefination, the mixture is stirred overnight. After the excess ylide is destroyed by addition of 30 mL of acetone, the reaction mixture is concentrated to 150 mL by slowly distilling the solvents over a 1 m packed column. To the residue add slowly under efficient stirring 1 L of petroleum ether (boiling range, 30−50 °C). After 30 min, a coarse precipitate of triphenylphosphine oxide and KBr has separated and is filtered off. The filter cake is then triturated with an ether:petroleum ether mixture (15:85 v:v) and filtered again. The filtrate from the first filtration is passed over a silica gel pad (40 cm length, 5 cm diameter) and eluted with the second filtrate. The combined eluates are concentrated to 200 mL as described above. Further concentration to 70 mL is done by distillation of the solvents over a spinning band column under a low vacuum (250 mmHg). This operation has to be done carefully since the solution tends to bump. The solution of **40** obtained by this way is transferred into a 100 mL flask and fractionated over the spinning band column under vacuum (39 mmHg). The product is collected at 113 °C. Yield: 23.3 g (76% based on **36**). Bp = 85 °C at 13 mmHg. After prolonged cooling to −78 °C and then storing at −24 °C, the product becomes a solid, mp = +1 °C. ^{1}H-NMR (C_6D_6, 300 MHz): δ 0.99 (d, 3, ^3J = 7.1 Hz, CH_3), 1.11 (tr, 3, ^3J = 7.4 Hz, CH_3), 1.34 (quint, 1, H-2), 1.67 (m, 1, $|^2J|$ = 14.4 Hz, *exo* H-3), 1.97, 2.02 (ddq, 2, $|^2J|$ = 14 Hz, CH_2), 2.65 (dddd, 1, ^3J (H-2,*endo* H-3) = 6.7 Hz, $|^4J|$(endo H-3,methylene H) = 2.3 Hz, $|^4J|$ (*endo* H-3,methylene H′) = 2.3 Hz, *endo* H-3), 3.57 (d, 1, $|^2J|$ = 6.9 Hz, *endo* H-7), 3.63 (dd, 1, ^3J = 5.0 Hz, *exo* H-7), 3.84 (m, 1, H-1), 4.62 (m, 1, $|^2J|$ = 2.4 Hz, =CH_2), 4.78 (m, 1, =CH_2). ^{13}C-NMR (C_6D_6, 75 MHz): δ 7.24 (CH_3), 17.42 (CH_3), 25.92 (CH_2), 34.17 (C-3), 34.88 (C-2), 69.62 (C-7), 79.20 (C-1), 106.75 (C=CH_2), 107.79 (C-5), 146.21 (*C*=CH_2). Elementary analysis: C calcd 71.44, found 70.73; H calcd 9.59, found 9.62.

(±)-5-Ethyl-2-*exo*-methyl-4-*exo*-methyl-6,8-dioxabicyclo-[3.2.1]octane (4). Charge to a 100 mL Schlenk flask 350 mg of PtO_2 and 25 mL of ether. Then flush the flask with hydrogen. After stirring the mixture for 10 min, add 5.6 g of **40** (33.3 mmol) via syringe. The hydrogenation starts immediately. After the calculated volume of hydrogen has been taken up (ca. 3 h), add 0.1 g of NEt_3 to the mixture and filter the catalyst off. Then most of the ether is removed without heating on a rotavapor under vacuum (12 mmHg) during 40 min. Distillation of the residue by a Kugelrohr apparatus (oven temperature, 130 °C; cooling with dry ice) gives β-multitriatin (**4**) as a colorless volatile liquid. Yield: 4.45 g (85% based on **40**). The diastereomeric ratio of β-multistriatin (**4**): δ-multistriatin (**5**) is 92:8. ^{1}H-NMR (C_6D_6, 500 MHz): δ 0.930 (d + long range couplings < 1 Hz, 1, $|^2J|$ = 14.0 Hz, *exo* H-3), 1.026 (d, 3, ^3J = 7.3 Hz, 4-CH_3), 1.038 (tr, 3, ^3J = 7.3 Hz, CH_3), 1.120 (m, 3, 2-CH_3), 1.175 (m, 1, *endo* H-2), 1.670, 1.802 (ddq, 1 each, $|^2J|$ = 14.5 Hz, CH_2), 1.722 (quint, 1, ^3J (exo-H-3,endo-H-4) ≈ 0 Hz, *endo* H-4), 2.145 (dtr, 1, ^3J (endo-H-3,endo-H-4) = 6.9 Hz, ^3J (endo-H-2,endo-H-3) = 6.9 Hz, *endo* H-3), 3.527 (d, 1, $|^2J|$ = 6.7 Hz, ^3J ≈ 0 Hz, *endo* H-7), 3.630 (dd, 1, ^3J = 5.2 Hz, *exo* H-7), 3.864 (d, 1, ^3J (H-1,H-2) ≈ 0 Hz, H-1). ^{13}C-NMR (C_6D_6, 125 MHz): δ 7.18 (CH_3), 18.88 (4-CH_3), 20.49 (2-CH_3), 28.23 (CH_2), 31.30 (C-3), 32.18 (C-2), 35.75 (C-4), 69.58 (C-7), 79.82 (C-1), 111.16 (C-5). Elementary analysis: C calcd 70.54, found 70.13; H calcd 10.66, found 11.08.

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Supporting Information Available: Experimental procedures for the preparation of compounds **5**, **16**, **17**, **19a**, **27**, and **48**; MS and IR spectra in tabular form for compounds **4**, **28a,b**, **36**, **37**, and **40**; ^{1}H- and ^{13}C-NMR spectra for compounds **4**, **5**, **19a**, **27**, **36**, **37**, and **40** (30 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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