Asymmetric Dihydroxylation−Haloetherification Strategy for the Synthesis of Tetrahydrofuran-Containing Acetogenins†

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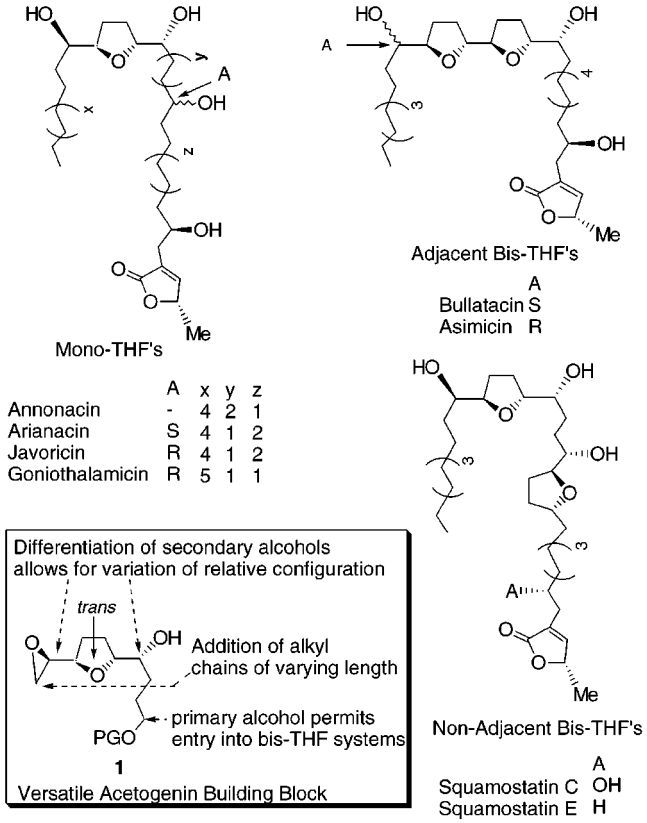
The tetrahydrofuran (THF)-containing acetogenins are a relatively new group of natural products which are known for their potent antitumor and pesticidal activities.[1,2] Over 200 members have been isolated. They are C35−C39 compounds which generally contain one or two 2,5-disubstituted THF's, although structures containing a higher number of THF rings have been found. The 2 and 5 positions of the THF subunits are usually flanked by a secondary carbinol center. In the mono-THF structures these positions are attached to hydrocarbon chains, one of which terminates in a butenolide. The THF residues in the bis-THF derivatives may be adjacently or nonadjacently linked. In addition to the number and connectivity of THF rings, structures vary with respect to the length and degree of oxygenation of the hydrocarbon chains and the relative and absolute stereochemistry of the four stereogenic centers in the 2,5-bis(hydroxyalkyl)-THF subunits. 2,5-trans THF's are much more predominant than the cis derivatives (Figure 1).

There has been considerable interest in the synthesis of analogues for bioactivity studies[3] and in the determination of relative and absolute stereochemistry.[4] A number of different synthetic approaches have been reported, with the majority centering on the cyclization of hydroxy olefin and hydroxy epoxide precursors.[5−8] We envisaged the mono-THF **1** as a versatile building block.



	A	x	y	z
Annonacin	-	4	2	1
Arianacin	S	4	1	2
Javoricin	R	4	1	2
Goniothalamicin	R	5	1	1

Figure 1. Representative trans-2,5-disubstituted THF acetogenins.

The epoxide residue permits entry to derivatives with different chain length, and the differentiation of the secondary alcohol positions facilitates the preparation of analogues in which the configurations at the flanking carbinol centers can be varied. Furthermore, **1** could be elaborated into both adjacently and nonadjacently linked structures.

As part of our studies on the use of conformationally restricted acetals in stereoselective THF synthesis, we recently showed that 5,6-*O*-isopropylidene acetal-alkenes **2** on treatment with iodonium ion gave exclusively the trans-2,5-disubstituted THF **3**.[9] Notable aspects of this methodology are the use of experimentally straightforward procedures, high THF stereoselectivity, and the dual role of the cyclic acetal as a stereocontrolling element as well as a protecting group. Application to the acetogenin synthon **1** calls for a *threo*-*O*-isopropylidene-*E*-alkene precursor **4**, the synthesis of which could benefit from recent advances in Sharpless asymmetric hydroxylation technology (Scheme 1).[10]

The first stage in the synthesis was the design of a suitable diene compound on which an enantioselective mono-dihydroxylation could be performed. Toward this end the diene ester **5-E,E** was prepared from 4-(benzyloxy)butanal[11] in 67% overall yield over three straightforward steps: addition of vinylmagnesium bromide to

† This paper is dedicated to Dr. Erwin Fleissner on his retirement as Dean of Science and Mathematics at Hunter College.

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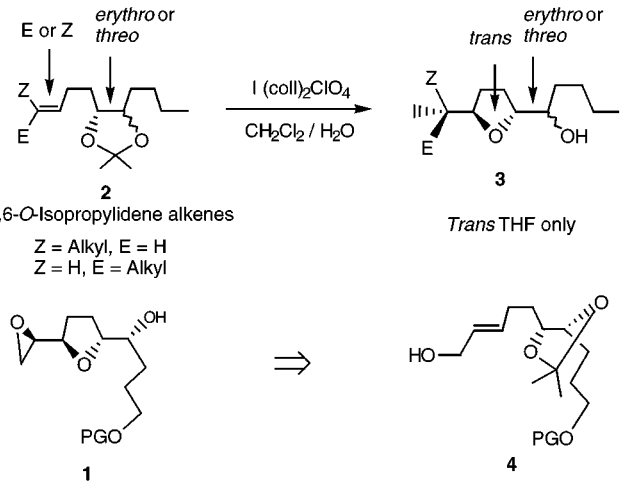
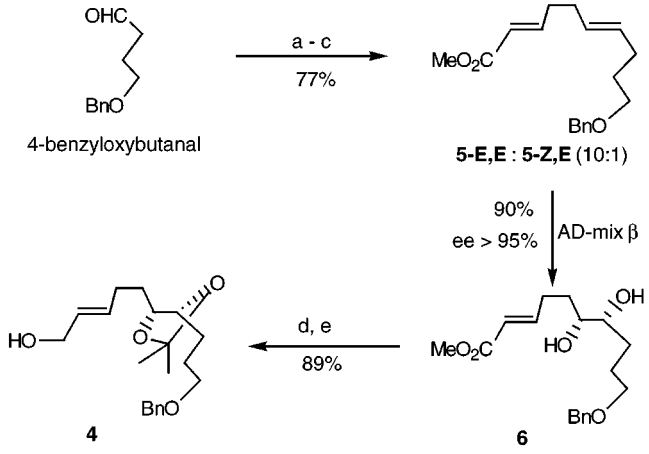
Scheme 1



Scheme 2



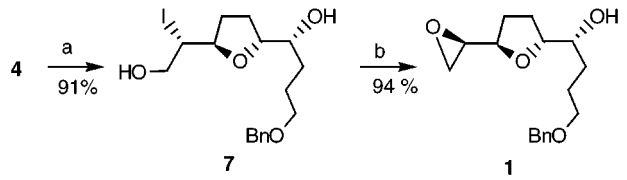
(a) vinyl MgBr; (b) butyl vinyl ether, Δ; (c) $Ph_3P{=}CHCO_2Me$, CH_3CN, Δ; (d) 2,2-dimethoxypropane, CSA; (e) DIBALH

give the allylic alcohol, followed by a "one-pot" vinyl ether exchange−Claisen rearrangement protocol,[12] and reaction of the resulting aldehyde with (carbomethoxymethylene)triphenylphosphorane. Treatment of **5-E,E** with AD-mix β for 3 d at 0 °C gave the diol **6** in 90% yield in greater than 95% ee.[13] Isopropylidenation of the diol residue in **6**, thence reduction of the ester, led to the key isopropylidene *E*-alkene substrate **4** (Scheme 2).

Treatment of **4** with iodonium dicollidine perchlorate (IDCP) in 1% aqueous acetonitrile led to formation of a single trans THF-iodide product **7** in 91% yield. As expected from our previous work the iodocyclization of the triol derivative of **4** was less selective, giving a 1:3 mixture of cis:trans THF's. Accordingly, the trans stereochemistry was tentatively assigned to **7**.[9] Treatment of the THF-iodohydrin **7** with K_2CO_3/MeOH gave the desired epoxy-THF **1** in 94% yield (Scheme 3).

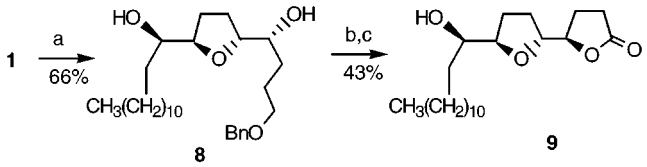
To confirm the stereochemical assignment, and also to illustrate its synthetic utility, **1** was converted to the known THF-lactone **9**. Butyrolactones such as **9** have been used as precursors to mono-THF acetogenins and adjacently connected oligo-THF's.[6b,8d] Thus, treatment

Scheme 3



(a) IDCP, 1% H_2O- CH_3CN; (b) K_2CO_3, MeOH

Scheme 4



(a)$CH_3(CH_2)_{10}MgBr$, CuI (b) H_2, Pd/C, HCOOH, MeOH (c) TEMPO

of **1** with undecylmagnesium bromide in the presence of copper(I) iodide[14] afforded the diol **8**. Hydrogenolysis of **8** followed by TEMPO oxidation[15] of the resulting triol led to **9**, which was essentially identical (nmr, α_D, mp), to the known compound[6b] (Scheme 4). Since **9** is a precursor to solamin and reticulatacin, this sequence constitutes a formal synthesis of these natural products.

In summary, a concise, straightforward, and high-yielding synthesis of a relay compound **1**, whose structure is primed for elaboration into a variety of naturally occurring mono- and bis-THF acetogenins, has been developed. The strategy capitalizes on the enantioselectivity and regioselectivity of the Sharpless asymmetric dihydroxylation and the high trans-THF bias in the iodoetherification of 5,6-*O*-isopropylidene alkenes. The synthon **1** was obtained in 44% yield over eight steps from 4-(benzyloxy)butanal.

Experimental Section

TLC was performed on aluminum sheets precoated with silica gel 60 (HF-254, E. Merck) to a thickness of 0.25 mm. Flash column chromatography was performed using Kieselgel 60 (230−400 mesh, E. Merck) and usually employed a stepwise solvent polarity gradient, correlated with TLC mobility. Unless otherwise stated, ^1H and ^{13}C NMR spectra were recorded at 300 and 75.5 MHz, respectively, in C_6D_6 or $CDCl_3$ solutions, with $CHCl_3$ or C_6H_6, respectively, as internal standard.

Methyl (2*E*,6*E*)-10-(Benzyloxy)-2,6-decadienoate (5-E,E) and Methyl (2*Z*,6*E*)-(Benzyloxy)-2,6-decadienoate (5-Z,E). Vinylmagnesium bromide (12.5 mL of a 1 M solution in THF, 12.5 mmol) was added dropwise, over a period of 20 min, at 0 °C to a solution of 4-(benzyloxy)butanal[11] (1.70 g, 9.60 mmol) in dry THF (30 mL), under an atmosphere of argon. After stirring for an additional 30 min, the reaction mixture was diluted with saturated NH_4Cl (30 mL) and extracted with diethyl ether. The organic phase was dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was purified by flash column chromatography to give 6-(benzyloxy)-1-hexen-3-ol (1.78 g, 90%): $R_f = 0.20$ (20% EtOAc:petroleum ether); ^1H NMR (C_6D_6) δ 1.53−1.69 (m, 4H), 2.60 (bs, 1H), 3.26 (t, 2H, $J = 6.0$ Hz), 3.97 (q, 1 H, $J = 4.5$ Hz), 4.29 (s, 2H), 4.95 (bd, 1H, $J = 10.4$ Hz), 5.21 (bd, 1H, $J = 17.2$ Hz), 5.76 (m, 1H), 7.19 (m, 5H); ^{13}C NMR (C_6D_6) δ 26.2, 34.5, 70.5, 72.6, 72.9, 113.7, 127.6, 127.7, 128.5, 139.2 142.1; MS (NH_3/DCI) *m/z* 207 $(M + H)^+$.

A mixture of the allylic alcohol from the previous step (1.68 g, 8.16 mmol), *n*-butyl vinyl ether (20 mL), and $Hg(OAc)_2$ (2.54

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(13) Enantiomeric excess determined by ^{1}HNMR analysis of the bis-Mosher ester of **6** (ref 4a). The absolute configuration of **6** was confirmed by conversion of **6** to **9** (vide infra).

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g, 7.96 mmol) was heated at reflux for 18 h over an argon atmosphere. The mixture was then cooled to room temperature, diluted with saturated aqueous Na_2CO_3 (20 mL), and extracted with CH_2Cl_2. The organic phase was dried (Na_2SO_4), filtered, and concentrated in vacuo. Flash column chromatography of the residual oil afforded 4(*E*)-8-(benzyloxy)-4-octenal (1.60 g, 85%): $R_f = 0.65$ (20% EtOAc:petroleum ether); ^{1}H NMR (C_6D_6) δ 1.58 (m, 2H), 1.83 (m, 2H), 2.04 (m, 4H), 3.27 (t, 2H, $J = 6.3$ Hz), 4.32 (s, 2H), 5.23 (m, 2H), 7.18 (m, 5H), 9.28 (s, 1H). ^{13}C NMR (C_6D_6) δ 25.3, 29.4, 29.9, 43.4, 69.7, 72.9, 127.5, 127.6, 127.7, 128.4, 131.1, 139.0, 200.2; MS (NH_3/DCI) *m*/*z* 250 $(M + NH_4)^+$, 233 $(M + H)^+$.

To a solution of the aforementioned aldehyde (1.2 g, 5.2 mmol) in CH_3CN (80 mL) was added (carbomethoxymethylene)triphenylphosphorane (3.91 g, 11.7 mmol). The mixture was heated at 60 °C for 40 min and then cooled to room temperature and filtered. The filtrate was concentrated in vacuo and the residue purified by flash column chromatography to afford the 2*E*,6*E*-methyl ester **5-E**,**E** (1.29 g, 87%) and the 2*Z*,6*E* isomer **5-Z,E** (0.11 g, 8%). For **5-E**,**E**: $R_f = 0.55$ (10% EtOAc: petroleum ether); ^{1}H NMR (C_6D_6) δ 1.55 (m, 2H), 1.87 (m, 4H), 2.05 (m, 2H), 3.29 (t, 2H, $J = 6.4$ Hz), 3.42 (s, 3H), 4.34 (s, 2H), 5.23 (m, 2H), 5.82 (d, 1H, $J = 15.6$ Hz), 7.00 (m, 1H), 7.18 (m, 5H); ^{13}C NMR (C_6D_6) δ 29.5, 30.0, 31.2, 32.2, 50.9, 69.7, 72.9, 121.7, 127.5, 127.7, 128.0, 131.2, 139.3, 148.5, 166.4; MS (NH_3/DCI) *m*/*z* 306 $(M + NH_4)^+$; 289 $(M + H)^+$. Anal. Calcd for $C_{18}H_{24}O_3$: C:74.96, H: 8.38. Found: C: 74.83, H: 8.90. For **5-Z**,**E**: $R_f = 0.50$ (10% EtOAc/petroleum ether); ^{1}H NMR (C_6D_6) δ 1.60 (m, 2H), 2.04 (m, 4H), 2.78 (q, 2H, $J = 7.2$ Hz), 3.28 (t, $J = 6.4$ Hz), 3.36 (s, 3H), 4.32 (s, 2H) 5.34 (m, 2H), 5.78 (d, 1H, $J = 11.5$ Hz), 5.87 (m, 1H), 7.18 (m, 5H); ^{13}C NMR (C_6D_6) δ 29.8, 30.2, 30.8, 32.9, 51.2, 70.5, 73.6, 120.6, 127.5, 128.0, 128.7, 130.4, 131.7, 140.3, 150.5, 167.0. MS (NH_3/DCI) *m*/*z* 306 $(M + NH_4)^+$, 289 $(M + H)^+$.

Methyl (2*E*,6*R*,7*R*)-10-(Benzyloxy)-6,7-dihydroxy-2-decenoate (6). AD-mix-β (4.84 g, 1.4 g/mmol alkene) and methanesulfonamide (329 mg, 3.46 mmol) were added to a solution of diene **5-E,E** (1.0 g, 3.46 mmol) in *tert*-butyl alcohol (17.3 mL) and water (17.3 mL). After stirring at 0 °C for 3 d, Na_2SO_3 (300 mg) was added and the solution extracted with CH_2Cl_2. The organic phase was dried (Na_2SO_4), filtered, and concentrated in vacuo. Purification of the residue by flash column chromatography gave ene diol **6** (1.0 g, 90%): $R_f = 0.15$ (30% EtOAc: petroleum ether); $[\alpha]^{25}_D = +15.5°$ (c 1.0, $CHCl_3$); $R_f = 0.15$ (30% EtOAc:petroleum ether); ^{1}H NMR (C_6D_6) δ 1.29−1.80 (m, 6H), 2.05−2.23 (m, 2H), 3.15−3.40 (m, 4H), 3.42 (s, 3H), 4.29 (s, 2H), 5.88 (d, 1H, $J = 15.6$ Hz), 7.03−7.31 (m, 5H); ^{13}C NMR (C_6D_6) δ 26.2, 28.4, 30.8, 31.9, 50.6, 70.3, 72.8, 73.5, 74.0, 121.2, 127.4, 128.5, 127.7, 127.8, 138.2, 149.1, 166.5. Anal. Calcd for $C_{18}H_{26}O_5$: C: 67.05, H: 8.12. Found: C: 66.73, H: 8.38.

The %ee of **6** was determined by preparation of the bis-(*R*)-MTPA ester of **6** and comparison of its ^{1}HNMR spectrum with the bis-(*R*)-MTPA ester mixture of racemic **6** obtained from the OsO_4 reaction on **5-E,E**. The ee was determined to be greater than 95%.[4a]

(2*E*,6*R*,7*R*)-10-(Benzyloxy)-6,7-(isopropylidenedioxy)-2-decene (4). 2,2-Dimethoxypropane (0.30 mL, 2.48 mmol) and (±)-10-camphorsulfonic acid (22 mg, 0.09 mmol) were added to a solution of diol **6** (400 mg, 1.24 mmol) in anhydrous CH_2Cl_2 (20 mL). The reaction mixture was stirred for 30 min and then neutralized by addition of 1 M NaOMe/MeOH. The solvent was removed in vacuo and the residue purified by flash column chromatography to yield the isopropylidene ester (419 mg, 93%): $[\alpha]^{25}_D = +23.3°$ (c 1.9, $CHCl_3$); $R_f = 0.80$ (10% EtOAc: petroleum ether); ^{1}H NMR (C_6D_6) δ 1.26−2.11 (m, 8H), 1.33, 1.34 (both s, 6H), 3.42 (s, 3H), 3.22−3.52 (m, 4H), 4.32 (s, 2H), 5.84 (d, 1H, $J = 15.6$ Hz), 6.97 (dt, 1H, $J = 3.5$, 15.7 Hz), 7.18 (m, 5H); ^{1}H NMR (C_6D_6) δ 26.6, 27.2, 28.7, 29.5, 31.1, 50.6, 69.8, 72.7, 80.1, 80.6, 107.8, 121.4, 127.4, 127.5, 127.7, 128.2, 138.0, 148.2, 166.2; MS (NH_3/DCI) *m*/*z* 380 $(M + NH_4)^+$, 363 $(M + H)^+$.

DIBALH (2.58 mL, 1 M in heptane, 2.58 mmol) was added to a solution of the isopropylidene ester obtained from the previous step (450 mg, 1.29 mmol), in anhydrous CH_2Cl_2 (20 mL) at −40 °C, under an atmosphere of argon. The reaction was stirred at this temperature for 30 min and then quenched by the addition of MeOH and warmed to room temperature. Saturated aqueous potassium sodium tartrate (20 mL) was added, and the mixture stirred for an additional 1 h and then extracted with with CH_2Cl_2. The organic phase was washed with water, saturated aqueous $NaHCO_3$, and brine and then dried (Na_2SO_4), filtered, and concentrated in vacuo. Purification of the residue by flash column chromatography gave the isopropylidene alkene **4** (380 mg, 92%): $[\alpha]^{25}_D = +20.4°$ (c 1.0, $CHCl_3$); $R_f = 0.20$ (30% EtOAc: petroleum ether); ^{1}H NMR (C_6D_6) δ 1.30−2.27 (m, 8H), 1.39 (s, 6H), 3.35 (m, 2H), 3.55 (m, 2H), 3.86 (bs, 2H), 4.31 (s, 2H), 5.53 (m, 2H), 7.20 (m, 5H); ^{13}C NMR (C_6D_6) δ 26.9, 27.6, 29.2, 29.9, 32.8, 63.3, 70.2, 73.0, 80.7, 81.0, 108.1, 127.7, 127.8, 128.3, 128.4, 130.5, 131.1, 138.0. Anal. Calcd for $C_{20}H_{30}O_4$: C:71.81, H: 9.05. Found: C: 71.93, H: 9.05.

(4*R*,5*R*,8*R*,9*S*)-1-(Benzyloxy)-4,10-dihydroxy-5,8-epoxy-9-iododecane (7). IDCP (420 mg, 0.89 mmol) was added to a solution of isopropylidene alkene **4** (120 mg, 0.36 mmol) in 1% aqueous CH_3CN (10 mL). The solution was stirred for 5 min at room temperature and then diluted with 10% aqueous $Na_2S_2O_3$, (5 mL) and extracted with diethyl ether. The combined organic phase was dried (Na_2SO_4), filtered, and concentrated in vacuo. Purification of the residue by flash column chromatography gave trans-THF **7** (138 mg, 91%): $[\alpha]^{25}_D = +11.3°$ (*c* 0.8, $CHCl_3$); $R_f = 0.20$ (30% EtOAc:petroleum ether); ^{1}H NMR (400 MHz, C_6D_6) δ 1.20−1.50 (m, 5H), 1.68 (m, 1H), 1.88 (m, 2H), 2.44 (bs, 1H, D_2O exchange), 2.72 (bs, 1H, D_2O exchange), 3.17 (m, 1H), 3.31 (m, 2H), 3.65 (m, 2H), 3.79 (m, 2H), 3.90 (m, 1H), 4.31 (s, 2H), 7.18 (m, 5H); ^{13}C NMR (C_6D_6) δ 27.1, 28.6, 31.5, 34.6, 41.5, 68.0, 71.0, 73.7, 74.2, 82.6, 84.7, 127.7, 128.0, 128.3, 139.2; MS (NH_3/DCI) *m*/*z* 438 $(M + NH_4)^+$. Anal. Calcd for $C_{17}H_{25}O_4I$: C: 48.56, H: 6.00. Found: C: 48.57, H: 6.29.

(4*R*,5*R*,8*R*,9*R*)-1-(Benzyloxy)-5,8:9,10-diepoxy-4-hydroxydecane (1). K_2CO_3 (100 mg) was added to a solution of compound **7** (50 mg, 0.12 mmol) in MeOH (5 mL). The reaction mixture was stirred for 5 min at room temperature and then diluted with water (5 mL) and extracted with CH_2Cl_2. The organic phase was dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was purified by flash column chromatography to give **1** (33 mg, 94%): $[\alpha]^{25}_D = +13.1°$ (*c* 0.9, $CHCl_3$); $R_f = 0.20$ (30% EtOAc:petroleum ether); ^{1}H NMR (C_6D_6) δ 1.21−1.97 (m, 8H), 2.38 (m, 2H), 2.59 (m, 1H), 3.26 (m, 1H), 3.38 (m, 2H), 3.48 (m, 1H), 3.67 (m, 1H), 4.29 (ABq, 2H, $\Delta\delta = 0.08$ ppm, $J = 13.0$ Hz), 7.21 (m, 5H); ^{13}C NMR (C_6D_6) δ 26.5, 28.1, 29.3, 30.9, 43.3, 53.9, 70.5, 72.9, 73.7, 78.8, 83.6; 127.7, 128.0, 128.3, 139.4; HRCIMS calcd for $C_{17}H_{24}O_4$ $(M + H)^+$ 293.1753. Found 293.1758.

(4*R*,5*R*,8*R*,9*R*)-1-(Benzyloxy)-5,8-epoxy-4,9-dihydroxyhenicosane (8). A solution of undecylmagnesium bromide (5.0 mL of a ca. 0.4 M solution in THF, 6.0 mmol) was added dropwise to a suspension of CuBr (30 mg, 0.21 mmol) in anhydrous THF (2 mL) at 0 °C. A solution of **1** (98 mg, 0.34 mmol) in anhydrous THF (1 mL) was then introduced at 0 °C, and the reaction mixture was stirred for 2 h at this temperature. At this time saturated aqueous NH_4Cl/aqueous ammonia (9/1, 10 mL) was added and the mixture extracted with diethyl ether. The organic phase was dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was purified by flash column chromatography to give **8** (101 mg, 67%): $R_f = 0.75$ (50% EtOAc:petroleum ether); ^{1}H NMR (C_6D_6) δ 0.92 (t, 3H, $J = 7.5$ Hz), 1.18−1.90 (m, 29H), 1.99 (m, 1H), 3.36 (m, 4H), 3.62 (m, 2H), 4.34 (m, 2H), 7.20 (m, 5H). ^{13}C NMR (C_6D_6) 14.6, 23.8, 26.9, 27.3, 29.8, 30.7, 31.1, 31.4, 33.3, 34.8, 71.4, 73.8, 75.0, 75.2, 83.9, 84.2, 127.7, 128.0, 128.2, 139.5. HRCIMS calcd for $C_{28}H_{49}O_4$ $(M + H)^+$ 449.3622. Found 449.3631.

THF-lactone (9). Formic acid (0.05 mL) was added under argon to a mixture of **8** (74 mg, 0.17 mmol) and 10% palladium on carbon (25 mg) in methanol (5 mL). The reaction mixture was stirred over an atmosphere of hydrogen for 18 h and then purged with argon and filtered through a pad of Celite. The filtrate was evaporated and the residue subjected to flash chromatography to give the debenzylated triol product (42 mg, 71%). $R_f = 0.20$ (50% EtOAc:petroleum ether); ^{1}H NMR (C_6D_6) δ 0.92 (t, $J = 7.5$ Hz, 3H), 1.20−1.86 (m, 30H), 3.42 (m, 1H), 3.50−3.80 (m, 3H), 4.30−4.54 (m, 2H); ^{13}C NMR (C_6D_6) δ 14.7, 23.5, 26.5, 29.4, 29.5, 29.9, 30.2, 30.6, 31.1, 32.7, 34.1, 63.1, 74.9, 83.2, 83.6.

A flask was charged with a solution of the triol from the previous step (20.0 mg, 0.056 mmol) in CH_2Cl_2 (1 mL), TEMPO (0.1 mg, 0.001 mmol), saturated aqueous $NaHCO_3$ (0.8 mL), KBr (6.6 mg 0.06 mmol) and $^nBu_4NCl$ (0.8 mg, 0.003 mmol). To this cooled (0 °C) and well-stirred mixture was added a solution made

of NaClO (0.11 mL of a 2.0 M aqueous solution, 0.22 mmol), saturated aqueous $NaHCO_3$ (0.8 mL), and brine (1.5 mL) dropwise over 45 min. The mixture was stirred for 1 h at 0 °C and then for 20 min at 20 °C. The progress of the reaction was carefully monitored by TLC. The aqueous phase was extracted with CH_2Cl_2, and the combined extracts were washed with saturated aqueous $NaHCO_3$ and brine, dried (Na_2SO_4), and filtered. Evaporation of the solvent and flash chromatography of the crude residue gave **9** (12.0 mg, 61%); R_f = 0.50 (50% EtOAc:petroleum ether); mp 94−96 °C; $[\alpha]^{25}_D$ = −7.16° (c 0.72, $CHCl_3$). Literature: 95−96 °C; $[\alpha]^{25}_D$ = −7.36° (*c* 1.44, $CHCl_3$). ^1H NMR ($CDCl_3$) was identical to previously prepared **9**.[6b] HRCIMS calcd for $C_{21}H_{39}O_4$ $(M + H)^+$ 355.2848. Found 355.2848.

Acknowledgment. This investigation was supported in part by a "Research Centers in Minority Institutions" award, RR-03037, from the Division of Research Resources, National Institutes of Health.

Supporting Information Available: ^1H and ^{13}C NMR spectra of (4*E*)-8-(benzyloxy)-4-octenal, **1**, **4**, **5-E,E**, **5-Z,E**, **6**, **6**-bis-MTPA ester, (±)-**6**-bis-MTPA ester, **7**, **8**, and **9** (28 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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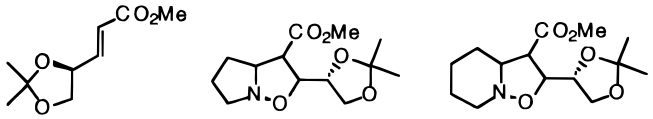
Additions and Corrections

Vol. 61, 1996

Félix Busqué, Pedro de March,* Marta Figueredo, Josep Font,* Montserrat Monsalvatje, Albert Virgili, Ángel Álvarez-Larena, and Juan F. Piniella. Diastereofacial Selectivity in the Cycloaddition of Nitrones to (*E*)-γ-Oxygenated α,β-Unsaturated Esters.

Page 8578. Charts 1 and 3. Formula **6** in Chart 1 and formulae **11a,b** and **17a−d** in Chart 3 should have the opposite absolute configuration at the chiral center. Corrected structures are as follows:



6 **11a, b** **17a-d**

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Nobuya Katagiri,* Masahiro Takebayashi, Hideaki Kokufuda, Chikara Kaneko, Kouichi Kanehira, and Masahiro Torihara. Efficient Synthesis of Carbovir and Its Congener *via* π-Allylpalladium Complex Fomation by Ring Strain-Assisted C−N Bond Cleavage.

Page 1580. Reference 3a should read as follows: Daluge, S. M.; Good, S. S.; Martin, M. T.; Tibbels, S. R.; Miller, W. H.; Averett, D. R.; Clair, M. S. St.; Ayers, K. M. In *Abstracts of the 34th interscience Conference on Antimicrobial Agents and Chemotherapy*; American Society for Microbiology: Washington, DC, 1994; Abstr. I6, p 7.

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Published on Web 02/24/1998

Naoki Asao, Takashi Shimada, Tomoko Sudo, Naofumi Tsukada, Kazuhiko Yazawa, Young Soo Gyoung, Tadao Uyehara, and Yoshinori Yamamoto*. Highly Diastereoselective Conjugate Addition of Lithium Dialkylamides to α,β-Unsaturated Esters Having a Chiral Center at the γ-Position.

Page 6282. The following acknowledgment should be added.

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László Poszávácz and Gyula Simig*. Synthesis of 4-Amino-5*H*-1,2-oxathiole 2,2-Dioxides by Cyclization of Cyanohydrin Mesylates. New Routes to β-Amino and β-Keto Sulfonic Acids.

Page 7021, column 2, 15th line. With respect to the sentence "To the best of our knowledge, compounds **3** are the first 4-amino substituted 1,2-oxathioles, which may find interesting applications in organic synthesis.", we regret our failure to mention the pioneering studies reported by Dr. María-José Camarasa and his co-workers on the cyclization of cyanohydrin mesylates to 4-amino substituted 1,2-oxathioles. References are given below:

(1) Calvo-Mateo, A.; Camarasa, M. J.; Díaz-Ortíz, A.; de las Heras, F. G. *J. Chem. Soc., Chem. Commun.* **1988**, 1114.

(2) Pérez-Pérez, M. J.; Balzarini, J.; Hosoya, M.; De Clercq, E.; Camarasa, M. J. *BioMed. Chem. Lett.* **1992**, *2*, 647.

(3) Camarasa, M. J.; Pérez-Pérez, M. J.; San-Félix, A.; Balzarini, J.; De Clercq, E. *J. Med. Chem.* **1992**, *35*, 2721.

JO974034+

S0022-3263(97)04034-6
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