Stereospecific Synthesis of the C-9—C-16 Segment of Carbonolide B, the Aglycon of Carbomycin B†

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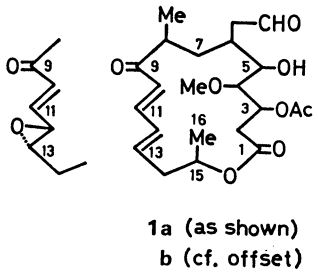
Stereospecific synthetic routes to methyl (*R*)-7-hydroxy-(2*E*,4*E*)-octadienoate (**9**) and its (2*E*,4*Z*)-isomer (**16**), the former which can be a useful chemical precursor to the 16-membered-ring aglycon of carbomycin B (carbonolide B), are discussed. Compound **9**, corresponding to its C-9—C-16 segment, was synthesized starting with methyl 2-deoxy-α-D-*arabino*-hexopyranoside (**2**). The deoxysugar **2** was converted to the masked 2,4,6-trideoxy-D-*threo*-hexopyranose (**6**) *via* the 4,6-dichloro-2,4,6-trideoxy-α-D-*lyxo*-hexopyranoside derivative. Treatment of **6** with *p*-toluenesulfonyl chloride and triethylamine afforded 3-*O*-acetyl-1,5-anhydro-2,4,6-trideoxy-D-*threo*-hex-1-enitol, which by reaction with mercury(II) acetate was converted to (*R*)-5-hydroxy-(2*E*)-hexenal (**8**). Reaction of **8** with Wittig reagent gave the (2*E*,4*E*)-isomer **9**. Compound **16** was prepared by the Wittig reaction with the 2,3-unsaturated deoxysugar, 2,3,4,6-tetradeoxy-D-*glycero*-hex-2-enopyranose, which was derived from methyl 2,3-anhydro-4,6-dideoxy-α-D-*lyxo*-hexopyranoside by treatment with potassium selenocyanate followed by acid hydrolysis.

In the course of studies directed toward the total synthesis of 16-membered macrolide antibiotics, the regio- and stereoselective introduction of an aminodisaccharide onto the 16-membered aglycon has been reported.[1] Carbomycin B[2] is a representative antibiotic of the 16-membered-ring macrolides, and the structure of the aglycon, carbonolide B (**1a**), can be divided into two segments of C-1—C-8 and C-9—C-16. The latter is stereochemically related to methyl (*R*)-7-hydroxy-(2*E*,4*E*)-octadienoate (**9**), where the C-1 and C-8 carbon atoms correspond to the C-9 and C-16 of carbonolide B. This paper reports the stereospecific synthesis of **9** as an intermediate in the synthesis of carbonolide B using carbohydrates. Recently, a variety of carbohydrates have been used as chiral intermediate in the total synthesis[3,4] of and/or in the synthetic approach[5] to natural products.

The key process was the conversion of 3-*O*-acetyl-1,5-anhydro-2,4,6-trideoxy-D-*threo*-hex-1-enitol (**7**) by mercury(II) acetate to (*R*)-5-hydroxy-(2*E*)-hexenal (**8**), which reacted with Wittig reagent to give **9**. Methyl (*R*)-7-hydroxy-(2*E*,4*Z*)-octadienoate (**16**) was prepared by the Wittig reaction with 2,3,4,6-tetradeoxy-D-*glycero*-hex-2-enopyranose (**15**) in order to provide a reference for **9**.



1a (as shown)
b (cf. offset)

Chart 1.

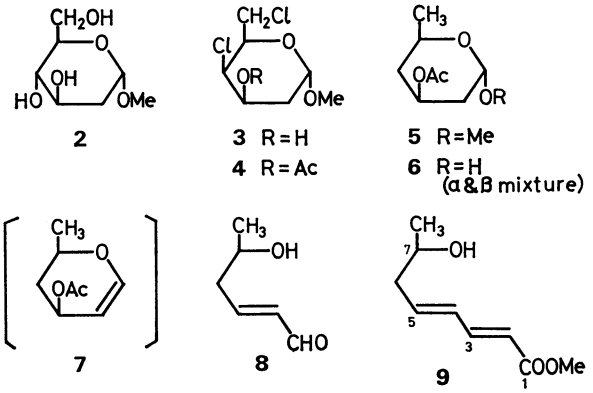


Chart 2.

Results and Discussion

The starting methyl 2-deoxy-α-D-*arabino*-hexopyranoside[6] (**2**) was treated with sulfuryl chloride in pyridine followed by treatment with sodium iodide in aqueous methanol, to give methyl 4,6-dichloro-2,4,6-trideoxy-α-D-*lyxo*-hexopyranoside (**3**). The corresponding 3-*O*-chlorosulfate, which could not be isolated, was considered to be an intermediate.[7] Acetylation of **3** gave a syrupy product **4**, which was dechlorinated with tributylstannane and successively hydrolyzed with dilute hydrochloric acid to give 3-*O*-acetyl-2,4,6-trideoxy-D-*threo*-hexopyranose (**6**). The intermediate methyl 3-*O*-acetyl-2,4,6-trideoxy-α-D-*threo*-hexopyranoside (**5**) was intractable because of its volatility. Conversion of the 2-deoxysugars to the corresponding glycals was achieved by treatment with *p*-toluenesulfonyl chloride in the presence of triethylamine.[1,8] The method was effectively applied to the preparation of 3-*O*-acetyl-1,5-anhydro-2,4,6-trideoxy-D-*threo*-hex-1-enitol (**7**) from **6**. Attempts were unsuccessful to prepare **7** from 2,3-di-*O*-acetyl-4,6-dideoxy-α-D-*xylo*-hexopyranosyl bromide by the usual manner.[9] As **7** was too labile to be purified, it was, without isolation, treated with mercury(II) acetate. This was followed by the addition of dilute sulfuric acid, which gave the syrupy (*R*)-5-hydroxy-(2*E*)-hexenal (**8**)

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in a moderate overall-yield. The structure was supported by the characteristic, intense IR absorption at 1695 cm^{-1} and a weak absorption (shoulder) at 1650 cm^{-1}, complemented by a maximum at 223 nm in the UV spectrum. The NMR spectrum provided independent evidence for the open-chain structure of **8**, namely, the doublet at extremely low field (δ 9.62) for H-1, the well-resolved multiplets (δ 6.19 and 6.93) for H-2 and H-3, and the presence of a hydroxyl group (signal at δ 1.80, that disappeared upon addition of D_2O); the large value for $J_{2,3}$ (15.5 Hz) indicated the *trans* position of the olefinic protons. This transformation agrees with expectations based on the reaction of 3,4,6-tri-*O*-acetyl-D-glucal with acidic mercury(II) sulfate.[10] The Wittig reaction of **8** with methoxycarbonylmethylenetriphenylphosphorane provided an 80% yield of the dienoate **9**. The UV and NMR spectra of **9** were very similar to those of ethyl (2*E*,4*E*)-hexadienoate,[11] showing that **9** was a desired (2*E*,4*E*)-isomer implying not only the stereospecific synthesis of the C-9—C-16 segment of carbonolide B but also the utility of the key intermediate, the *trans*-unsaturated aldehyde **8**.

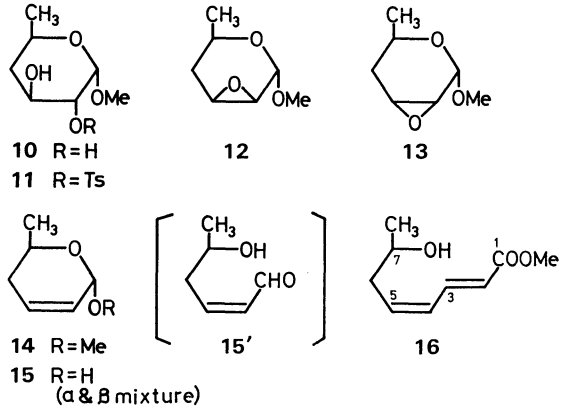

Chart 3.

The (2*E*,4*Z*)-isomer **16** was directly synthesized from the reducing sugar **15** by the Wittig reaction. Selective tosylation of the starting methyl 4,6-dideoxy-α-D-*xylo*-hexopyranoside[12] (**10**) gave predominantly the corresponding 2-*O*-*p*-toluenesulfonate **11** in 72% yield. Treatment of the crude *p*-toluenesulfonate **11**, containing a small amount of the 3-*O*-*p*-toluenesulfonate, with sodium methoxide gave a *ca.* 30: 1 mixture of methyl 2,3-anhydro-4,6-dideoxy-α-D-*lyxo*- and *ribo*-hexopyranosides (**12** and **13**), suggesting that the 3-*O*-*p*-toluenesulfonate was a very minor component. The product **12** could configurationally be a precursor of the C-11—C-16 segment of carbonolide A (**1b**), an aglycon of carbomycin A.[13] Compound **12**, which was isolated as needles, was treated with a boiling solution of potassium selenocyanate[14] in aqueous 2-methoxyethanol for twenty minutes to give methyl 2,3,4,6-tetradeoxy-α-D-*glycero*-hex-2-enopyranoside (**14**). The syrupy product **13**, however, required two hours for the complete reaction to give **14** in the same conditions as described above. Acid hydrolysis of **14** gave a syrupy compound **15**, which was subsequently treated with the Wittig reagent to give the (2*E*,4*Z*)-isomer **16** in 77% overall yield. The structure of **16** was confirmed by UV and NMR spectra in comparison with those of **9** and ethyl (2*E*,4*Z*)-hexadienoate.[11] It appears reasonable on the basis of the above results to suppose that, during the Wittig reaction, the *trans* and *cis* unsaturated aldehydo-forms **8** and **15'**, the latter of which is considered to take part in the reaction of **15** as an intermediate, do not suffer the *trans-cis* and *cis-trans* isomerizations, and the newly produced olefin groups possess the *trans* configuration in both cases.

The utility of the deoxy unsaturated carbohydrates **8** and **15** is thus demonstrated for stereospecific synthesis of α,β: γ,δ-unsaturated esters.

Experimental

Melting points were determined on a micro hot-stage Yanaco MP-S3 and are uncorrected. Specific rotations were measured (0.2-dm tube) with a Carl Zeiss Photoelectric Precision Polarimeter. The NMR spectra were determined with Varian A60, EM-390 or XL100 spectrometers. Unless otherwise stated, chloroform-*d* was used as a solvent and internal tetramethylsilane as a standard. Coupling constants were obtained by measuring spacings of spectra judged to be first-order. TLC and column chromatography were performed on silica gel Wakogel B-5 and Wakogel C-300, respectively. In general, concentration was carried out under reduced pressure below 30 °C.

The starting materials, methyl 2-deoxy-α-D-*arabino*-hexopyranoside[6] [**2**; which was recrystallized from ethyl acetate to give cubics; mp 94—95 °C; $[\alpha]_D^{16}+160°$ (*c* 1.0, CH_3OH)] and methyl 4,6-dideoxy-α-D-*xylo*-hexopyranoside[12] [**10**; which was purified by sublimation at 47 °C at 1 Torr††; mp 108—109 °C, $[\alpha]_D^{24}+179°$ (*c* 1.0, CH_3OH)] were prepared according to the published procedures.

1) Methyl 4,6-Dichloro-2,4,6-trideoxy-α-D-lyxo-hexopyranoside (3). To a stirred solution of **2** (8.91 g) in a dry mixture of pyridine (33 ml) and chloroform (82 ml), cooled in a Dry Ice–acetone bath, was added sulfuryl chloride (21.3 ml) drop by drop over 30 min. Cooling was continued for a further 2 h, after which the reaction mixture was allowed to stand at room temperature overnight. The resulting precipitate, possibly of pyridine salts, was filtered from the chloroform solution. The filtrate was washed successively with 10% sulfuric acid, saturated $NaHCO_3$ solution and water, dried (Na_2SO_4), and evaporated to give an oil. To a methanolic solution (200 ml) of the oil was added a solution of sodium iodide (6.60 g) in 50% aq methanol (16 ml). The mixture was vigorously stirred for 2 h at room temperature and then neutralized with $NaHCO_3$ (11.7 g). The resulting precipitate was removed by filtration, the filtrate evaporated, and the residue chromatographed on a column of silica gel (500 g) with benzene–ethyl acetate (3: 1). The eluate containing the major product (R_f 0.40 by TLC with the same solvent system) was evaporated to give a solid that was further purified by recrystallization from hexane, followed by sublimation at 67 °C under reduced pressure (12 Torr), to give crystals of **3** (4.4 g, 41%): mp 114—115 °C; $[\alpha]_D^{17}+175°$ (*c* 1.0, CH_3OH); NMR δ=1.6—2.6 (3H, m, CH_2-2 and OH-3), 3.39 (3H, s, OCH_3), 3.67 (2H, m, CH_2-5), 3.9—4.3 (2H, m, H-3 and 5), 4.45 (1H, m, H-4) and 4.85 (1H, t, $J_{1,2a}=J_{1,2e}\approx2.5$ Hz, H-1).

Found: C, 39.15; H, 5.44; Cl, 32.72%. Calcd for C_7H_{12}-

†† Throughout this paper 1 Torr≈133.322 Pa.

O_3Cl_2: C, 39.09; H, 5.62; Cl, 32.97%.

*2) Methyl 3-O-Acetyl-4,6-dichloro-2,4,6-trideoxy-α-*D*-lyxo-hexopyranoside (4).* A solution of **3** (121 mg) in a mixture of acetic anhydride (0.11 ml) and pyridine (0.61 ml) was kept overnight at room temperature and, after addition of ethanol (0.11 ml), was concentrated *in vacuo* to give a residue that was chromatographed on a column of silica gel (10 g) with hexane–ethyl acetate (6: 1) to give an oil of **4** (143 mg, 93%). Micro-distillation of **4** at 35 °C at 1 Torr gave an analytically pure oil: $[\alpha]_D^{17}+153°$ (*c* 2.0, CH_3OH); NMR $\delta=1.6$—2.6 (2H, m, CH_2-2), 2.08 (3H, s, OAc), 3.37 (3H, s, OCH_3), 3.64 (2H, d, $J_{5,CH_2}=7$ Hz, CH_2-5), 4.15 (1H, dt, $J_{4,5}=1$ Hz, H-5), 4.59 (1H, m, H-4), 4.87 (1H, dd, $J=1$ and 3 Hz, H-1) and 5.30 (1H, m, H-3).

Found: C, 42.34; H, 5.41; Cl, 27.27%. Calcd for $C_9H_{14}O_4Cl_2$: C, 42.04; H, 5.49; Cl, 27.58%.

*3) 3-O-Acetyl-2,4,6-trideoxy-*D*-threo-hexopyranose (6).* To a solution of **4** (318 mg) in dry toluene (3.2 ml) under an argon atmosphere was added tributylstannane (792 mg) and α,α′-azobisisobutyronitrile (20 mg). The solution was stirred overnight at 100 °C and then concentrated to afford a residue, which was chromatographed on a column of silica gel with benzene–ethyl acetate (7: 1). The eluate containing the product (R_f 0.42 on TLC with the same solvent system) was carefully concentrated with an aspirator to give an oil **5**, which contained a little solvent: NMR $\delta=0.7$—2.4 (4H, m, CH_2-2 and 4), 1.23 (3H, d, $J=6.5$ Hz, CH_3-5), 2.02 (3H, s, OAc), 3.34 (3H, s, OCH_3), ≈3.9 (1H, m, H-5), 4.86 (1H, dd, $J=1$ and 3 Hz, H-1) and ≈5.1 (1H, m, H-3). The oil was kept in a desiccator under reduced pressure, where it was distilled away to disappear. Then, a solution of the oil in 10% aq acetic acid (5 ml) containing 1 M hydrochloric acid (1.7 ml) was kept at 40 °C for 3 h, after which TLC (hexane–ethyl acetate=1: 1) indicated that hydrolysis of the glycoside was complete. The solution was neutralized by addition of solid $NaHCO_3$ and extracted with ethyl acetate (10 ml×2). The extracts were combined, washed with saturated NaCl solution, dried ($MgSO_4$), and evaporated. The residue was chromatographed on a column of silica gel (10 g) with the same solvent system described above to give a solid of **6** (181 mg, 84%): mp 49—51 °C; $[\alpha]_D^{20}+13.8°\rightarrow+50.1°$ (*c* 1.0, CH_3OH, 26 h); NMR ($CDCl_3+D_2O$) $\delta=1.19$ and 1.29 (3H in total, each d, $J=7$ Hz, CH_3-5), 2.06 and 2.08 (3H in total, each s, OAc).

Found: C, 55.22; H, 8.02%. Calcd for $C_8H_{14}O_4$: C, 55.16; H, 8.10%.

*4) (*R*)-5-Hydroxy-(2*E*)-hexenal (8).* *p*-Toluenesulfonyl chloride (100 mg) was added to an ice-cold, stirred solution of **6** (60 mg) in dry acetonitrile (0.6 ml) containing triethylamine (0.15 ml). The mixture was allowed to stand at room temperature for 6 h and, after addition of a few drops of water, was poured into water (5 ml). The product was extracted with dichloromethane (2 ml×3). The combined extracts were washed with saturated NaCl solution, dried (Na_2SO_4), and evaporated to give an oil containing **7**. TLC with hexane–ethyl acetate (5: 1) clearly established the R_f of 0.60. Attempts to isolate pure **7** were unsuccessful. To a stirred solution of the oil in 50% aq acetone (2.4 ml) was added mercury(II) acetate (112 mg). After stirring at room temperature for 1 h, the mixture (pH 4) was acidified to pH 1 with dilute sufuric acid and again stirred overnight. The resulting solution, on TLC with hexane–ethyl acetate (1: 2), showed a major product at R_f 0.48. The solution was adjusted to pH 4 with barium carbonate and the suspension filtered and the filtrate extracted with dichloromethane (2.0 ml×5). The combined extracts were dried (Na_2SO_4) and evaporated to a residue, which was passed through a short column of Sephadex LH-20 with hexane–ethyl acetate (1: 2) to give a crude product of **8**. The crude product was further chromatographed on a column of silica gel (1g) to give an analytically pure oil of **8** (20 mg, 51%): $[\alpha]_D^{18}-23°$ (*c* 1.0, $CHCl_3$); IR (CCl_4) 3450 (OH), 1695 and 1650 cm^{-1} (C=C-CHO); UV_{max} (CH_3OH) 223 nm (ε 11,100); NMR $\delta=1.30$ (3H, d, $J=6.5$ Hz, CH_3-5), 1.80 (1H, OH-5), 2.52 (2H, t with a little long-range coupling, $J=7$ Hz, CH_2-4), ≈4.1 (1H, m, H-5), 6.19 (1H, dd, $J_{1,2}=7.5$ Hz, $J_{2,3}=15.5$ Hz, H-2), 6.93 (1H, dt, $J_{3,4}=7$ Hz, H-3) and 9.62 (1H, d, CHO-1).

Found: C, 62.92; H, 8.74%. Calcd for $C_6H_{10}O_2$: C, 63.13; H, 8.83%.

*5) Methyl (*R*)-7-Hydroxy-(2*E*,4*E*)-octadienoate (9).* To a solution of **8** (16 mg) in dry benzene (1 ml) was added methoxycarbonylmethylenetriphenylphosphorane (52 mg), and the mixture refluxed for 1 h and then evaporated *in vacuo*. The residue was chromatographed on a column of alumina (Woelm neutral, 3.5 g) with chloroform–acetone (5: 1), followed by chromatography on a column of silica gel (2 g) with hexane–ethyl acetate (1: 1) to give an oil of **9** (20 mg, 83%): TLC (hexane–ethyl acetate 1: 1) R_f 0.50; $[\alpha]_D^{20}-17°$ (*c* 2.0, $CHCl_3$); IR ($CHCl_3$) 3460 (OH), 1720, 1705 (C=O), 1645, 1620 cm^{-1} (C=C-C=C); UV_{max} (CH_3OH) 260 nm (ε 27,800); NMR $\delta=1.23$ (3H, d, $J=6.5$ Hz, CH_3-7), 1.97 (1H, broad s, OH-7), 2.34 (2H, m, CH_2-6), 3.74 (3H, s, $COOCH_3$), 3.91 (1H, m, H-7), 5.83 (1H, d, $J_{2,3}=15$ Hz, H-2), 6.0—6.4 (2H, m, H-4 and 5) and 7.27 (1H, m, H-3).

Found: C, 63.46; H, 8.17%. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.29%.

*6) Methyl 4,6-Dideoxy-2-*O*-p-tolylsulfonyl-α-*D*-xylo-hexopyranoside (11).* To an ice-cold, stirred solution of **10** (2.46 g) in pyridine (24 ml) was added *p*-toluenesulfonyl chloride (3.76 g), and the mixture allowed to stand at room temperature for 1 day. The mixture was then poured into agitated ice-water (70 ml), and the product extracted with chloroform (80 ml×2). The extracts were combined, washed successively with an ice-cold, saturated $KHSO_4$ solution, saturated $NaHCO_3$ solution and water, dried (Na_2SO_4), and evaporated. The residue was chromatographed on a column of silica gel (200 mg) with benzene–ethyl acetate (3: 1) to give an oil of **11** (3.46 g, 72%): $[\alpha]_D^{20}+99°$ (*c* 2.0, CH_3OH); NMR $\delta=1.18$ (3H, d, $J=6.5$ Hz, CH_3-5), 1.3—2.5 (3H, m, CH_2-4 and OH-3), 2.46 (3H, s, Ts-CH_3), 3.28 (3H, s, OCH_3), 3.5—4.3 (2H, m, H-3 and 5), 4.21 (1H, dd, $J_{1,2}=3$ Hz and $J_{2,3}=1.5$ Hz, H-2), 4.67 (1H, d, H-1), 7.37 and 7.87 (each 2H, AB quartet, $J=8.5$ Hz, Ts).

Found: C, 52.91; H, 6.38%. Calcd for $C_{14}H_{20}O_6S$: C, 53.15; H, 6.37%.

*7) Methyl 2,3-Anhydro-4,6-dideoxy-α-*D*-lyxo- and* ribo-*Hexopyranosides (12 and 13).* To a methanolic solution (2.8 ml) of a crude sample of **11** (817 mg) was added a 28% methanolic sodium methoxide solution (0.70 ml), and the solution refluxed for 1 h. After cooling, the solution was poured into ice-water (30 ml) and the product extracted with dichloromethane (35 ml×3). The combined extracts were washed with water, dried (Na_2SO_4), and evaporated. The residue was chromatographed on a column of silica gel (40 g) with benzene–ethyl acetate (7: 1) to give **12** (286 mg) and **13** (8 mg), which on TLC with the same solvent system gave R_f 0.48 and 0.31 respectively, in 79% total yield. Micro-distillation of **12** at 45—80 °C at 16 Torr gave analytically pure needles: mp 28—30 °C; $[\alpha]_D^{20}+70°$ (*c* 1.0, CH_3OH); NMR $\delta=1.15$ (3H, d, $J=6.5$ Hz, CH_3-5), 1.5—2.1 (2H, m, CH_2-4), 2.98 (1H, d, $J_{2,3}=4$ Hz, H-2), 3.40 (1H, m, H-3), 3.48 (3H, s, OCH_3), 3.88 (1H, m, H-5) and 4.91 (1H, s, H-1).

Found: C, 58.35; H, 8.31%. Calcd for $C_7H_{12}O_3$: C, 58.31; H, 8.39%. Compound **13** was an oil: NMR δ=1.15 (3H, d, J=6.5 Hz, CH_3-5), 1.4—2.3 (2H, m, CH_2-4), 3.2—3.5 (2H, m, H-2 and 3), 3.46 (3H, s, OCH_3), 3.85 (1H, m, H-5) and 4.92 (1H, d, $J_{1,2}$=3 Hz, H-1).

*8) Methyl 2,3,4,6-Tetradeoxy-α-*D*-glycero-hex-2-enopyranoside (14).* To a solution of **12** (57 mg) in 90% aq 2-methoxyethanol (1.1 ml) was added 80% potassium selenocyanate (150 mg), and the mixture refluxed for 20 min. After cooling, the mixture was poured into water (5 ml) and the product extracted with dichloromethane (6 ml×3). The combined extracts were washed with water, dried ($MgSO_4$), and evaporated. The residue was chromatographed on a column of silica gel (3 g) with dichloromethane–chloroform (4: 1) to give an oil of **14** (21 mg, 42%): $[\alpha]_D^{16}$−48° (*c* 2.0, $CHCl_3$); NMR δ=1.25 (3H, d, J=6.5 Hz, CH_3-5), 1.7—2.2 (2H, m, CH_2-4), 3.45 (3H, s, OCH_3), 4.00 (1H, m, H-5), 4.87 (1H, dd, J=1 and 3 Hz, H-1), 5.74 (1H, m, H-2) and 6.01 (1H, dt, $J_{2,3}$=10 Hz, $J_{3,4}$=4 Hz, H-3).

Found: C, 65.42; H, 9.25%. Calcd for $C_7H_{12}O_2$: C, 65.59; H, 9.44%. Compound **13** was treated with potassium selenocyanate in a similar manner as above, except for a 2-h reaction time, to give **14** in 23% yield.

*9) Methyl (*R*)-7-Hydroxy-(2*E*, 4*Z*)-octadienoate (16).* A suspension of **14** (69 mg) in a mixture of 1 M hydrochloric acid (0.38 ml) and 50% aq acetone (3.4 ml) was stirred at room temperature for 2 min. The resulting solution was then neutralized with $NaHCO_3$ (90 mg) and extracted with dichloromethane (2 ml×6). The combined extracts were dried (Na_2SO_4) and evaporated to give a crude oil of **15** (56 mg), which on TLC with chloroform–acetone (9: 1) gave an R_f of 0.54: NMR δ=1.23 and 1.24 (3H in total, d, J=6.5 Hz, CH_3-5), 1.58 (1H, sharp m, OH), 1.6—2.3 (2H, m, CH_2-4), 3.7—4.3 (1H, m, H-5), ≈5.4 (1H, m, H-1) and 5.5—6.2 (2H, m, H-2 and 3).

To a solution of the oil (56 mg) in benzene (1.0 mg) was added methoxycarbonylmethylenetriphenylphosphorane (180 mg), and the mixture was refluxed for 3 h, after which time TLC (chloroform–acetone=9: 1) indicated that the Wittig reaction was complete to give a single product (R_f 0.46). The solvent was evaporated, and the residue extracted with pentane (5 ml) under reflux for 30 min. After cooling, the pentane solution was decanted and evaporated. The residue was chromatographed on a column of silica gel (5 g) with chloroform–acetone (9: 1), followed by chromatography on a column of alumina (Woelm neutral, 10 g) with chloroform, to give an oil of **16** (71 mg, 77%): $[\alpha]_D^{15}$+5.2° (*c* 2.0, $CHCl_3$); IR ($CHCl_3$) 3420 (OH), 1720, 1710 (C=O), 1640, 1605 cm^{-1} (C=C–C=C); UV_{max} (CH_3OH) 265 nm (ε 20,600); NMR δ= 1.24 (3H, d, J=6.5 Hz, CH_3-7), 1.84 (1H, s, OH), 2.50 (2H, t with a little long-range coupling, J=6.5 Hz, CH_2-6), 3.79 (3H, s, $COOCH_3$), 3.95 (1H, sextet, H-7), 5.7—6.2 (1H, m, H-5), 5.95 (1H, d, $J_{2,3}$=15 Hz, H-2), 6.32 (1H, t, $J_{3,4}$= $J_{4,5}$=10.5 Hz, H-4) and 7.65 (1H, dd, H-3).

Found: C, 63.39; H, 8.10%. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.29%.

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