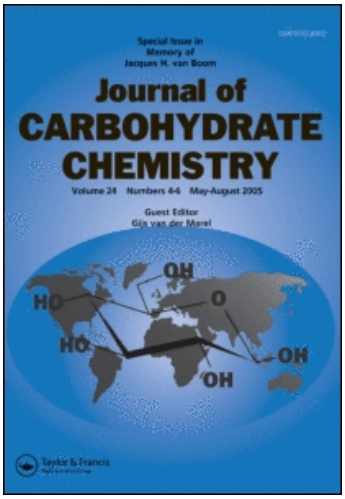

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Tartraldehydes 5:[1] Syntheses of Chiral Synthetic Building Blocks for Some Intermediates of the Arachidonic Acid Cascade

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TARTRALDEHYDES 5:[1] SYNTHESES OF CHIRAL SYNTHETIC BUILDING BLOCKS FOR SOME INTERMEDIATES OF THE ARACHIDONIC ACID CASCADE

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ABSTRACT

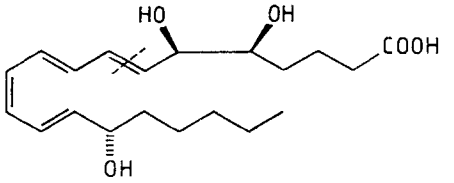
Two enantiomeric 5,6-dihydroxy-7-oxoheptanoates (**4ba, 4bb**) and three stereoisomeric 2,3-dihydroxyoctanal (**5ba, 5bb, 5bc**) derivatives have been synthesized in three steps from tartraldehydes **6**, **7** and **8**.

INTRODUCTION

Eicosanoic acid derivatives lipoxins A_4 (**1**),[2,3] B_4 (**2**)[2,3] and 5,6-dihydroxyeicosatetraenoic acid (5,6-diHETE, **3**)[4] are natural products derived from

arachidonic acid in a metabolic cascade. Since these compounds exhibit various biological effects,[5,6] great efforts have been made by several groups[7-14] towards the synthesis of **1**, **2** and **3**, as well as their stereoisomers. The latter derivatives served for structure-biological activity studies.

The general synthetic routes to the diastereoisomers of **1-3** elaborated by Nicolaou et al.[7,12-14] apply the chiral oxo compounds of the type **4a** and **5a** as starting materials.



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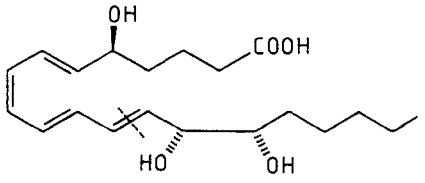

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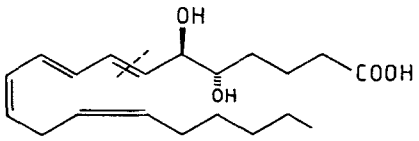

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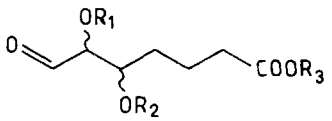
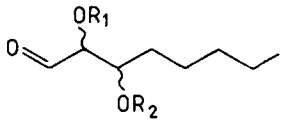




4a $R_1 = R_2 = Si^tBuMe_2$ $R_3 = Me$

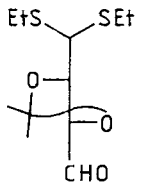
4b $R_1 + R_2 =$  $R_3 = Et$

5a $R_1 = R_2 = Si^tBuMe_2$

5b $R_1 + R_2 =$ 

Diastereoisomers of **4a**, precursors of the epimers of **1** and **3**, have been prepared from 5-hexyn-1-ol in 14 steps.[7]

Recently we have found that tartraldehyde mercaptal stereoisomers **6**, **7** and **8** could be used as versatile, chiral building blocks for the synthesis of various deoxy



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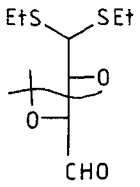

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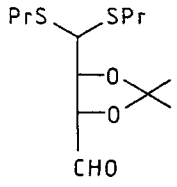
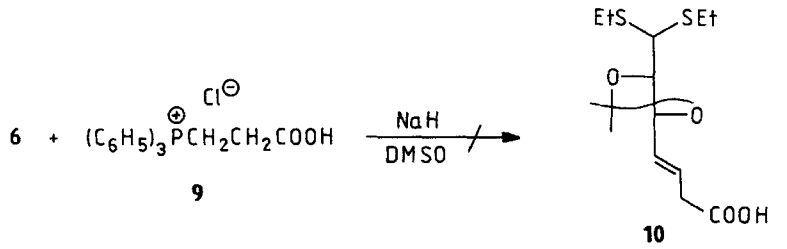


8

sugars.[15,16] Since chiral fragments of molecules of the type **4a** and **5a** can be deduced from **6-8** it was obvious to extend our work to the synthesis of those important intermediates.

RESULTS AND DISCUSSION

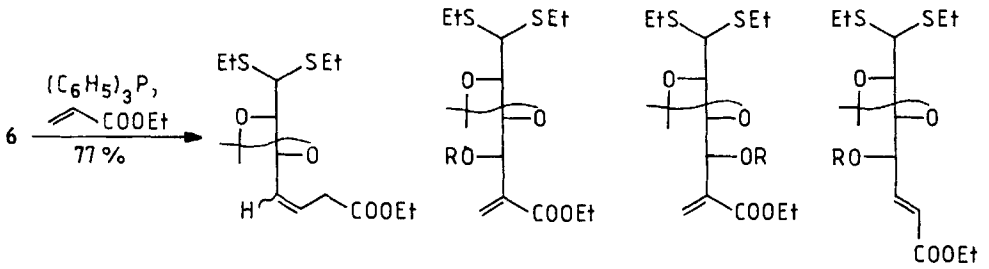
To prepare **4ba**, Wittig-type chain extension of **6** was attempted using phosphonium salt **9**[17] and dimsyl sodium but the desired **10** was not formed.



9 **10**

Oda et al.[18] reported on Wittig reactions using *in situ* generated ylides obtained by conjugate addition of triphenylphosphine on acrylic derivatives.

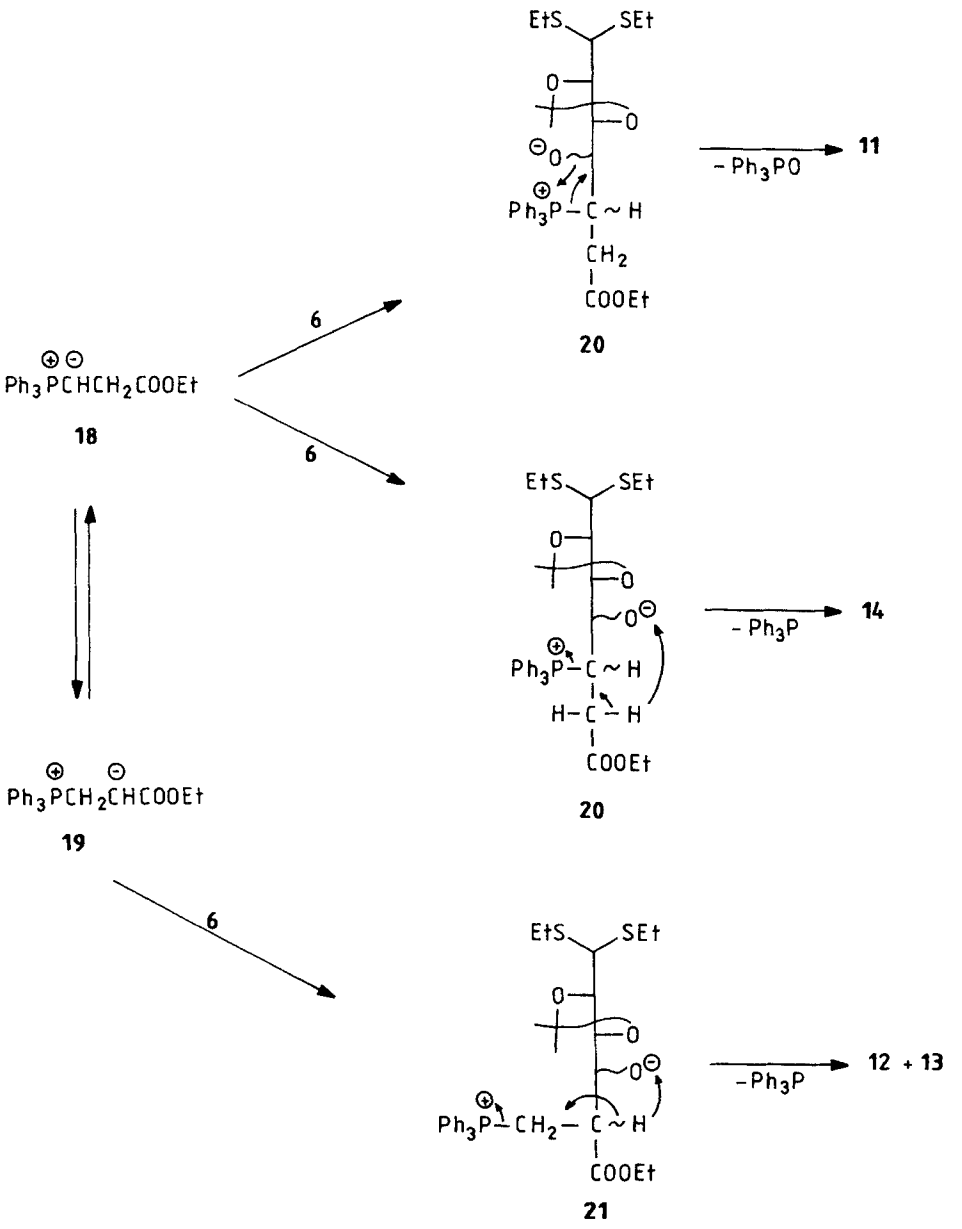
Applying the aforementioned method, **6** was treated with triphenylphosphine in ethyl acrylate at 100 °C for 22 hours. The mixture of products formed was separated by column chromatography. The major product was the expected β,γ-unsaturated ester **11a** with *Z* configuration contaminated with 20% of the *E* isomer **11b**. In addition, α-methylenecarboxylate diastereomers **12** and **13** as well as the α,β-unsaturated ester **14** were isolated.



11 **12** R = H, **15** R = Ac; **13** R = H, **16** R = Ac; **14** R = H, **17** R = Ac

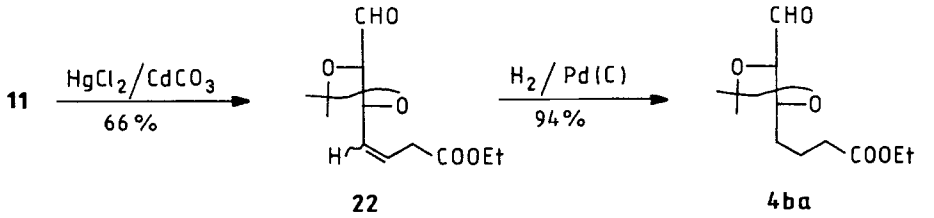
Structures of **11a,b-17** were established by ^{1}H and ^{13}C NMR techniques. On the basis of those data the configurations of the newly formed chiral centers in **12-14** could not be determined.

For the formation of **11a,b-14** the following mechanism can be postulated:



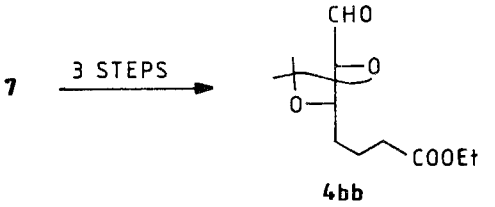
Phosphonium ylide **18** exists in equilibrium with its counterpart **19** bearing the negative charge on the α-carbon atom. After the addition of the nucleophile **18** to the aldehyde **6**, triphenylphosphine oxide eliminates from the intermediate **20** affording the "normal" Wittig products **11a,b**. By a parallel route, triphenylphosphine splits out from **20** together with simultaneous proton migration from the α-CH_2 to the oxygen giving rise to **14**. Addition of the other species **19** to the carbonyl of **6** leads to the formation of the intermediate **21** which releases triphenylphosphine with concomitant proton migration to give **12** and **13**. The latter process has been observed by Morita et al.[19] in the reaction of aldehydes with acrylates in the presence of tricyclohexylphosphine.

The mercaptal protecting group of **11a,b** was removed by mercury salt promoted hydrolysis to aldehydes **22a,b** and the double bond was finally saturated by catalytic hydrogenation giving rise to the 5*R*,6*S* derivative **4ba**.



22 **4ba**

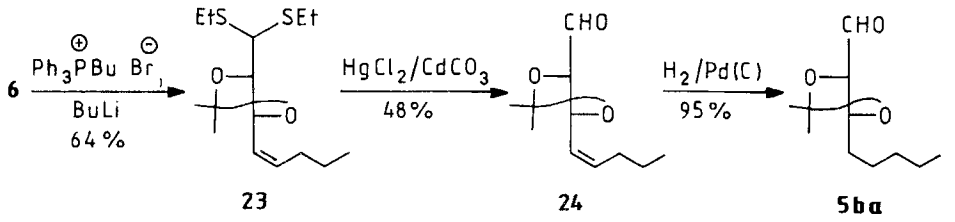
The 5*S*,6*R* enantiomer **4bb** has been prepared from **7** following the same route:



4bb

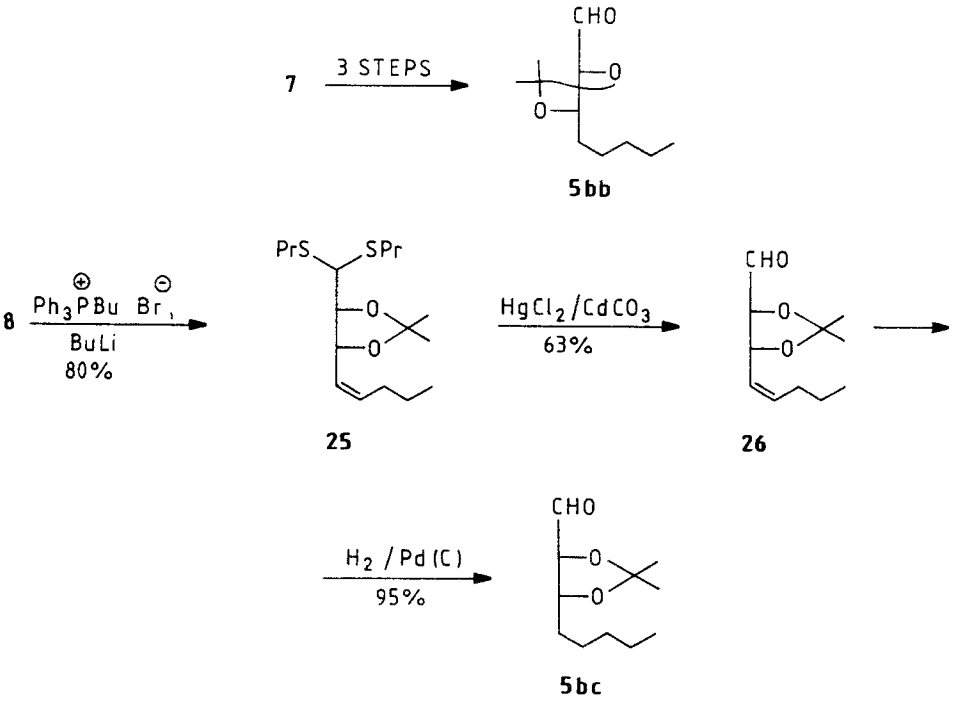
4ba and **4bb** have been characterized in the form of their 4-nitrophenylhydrazones.

2,3-Dihydroxyoctanal derivatives of the type **5b**, potential precursors of **2**, were synthesized in a similar way. The 2*S*,3*R*-aldehyde **5ba** was prepared from **6**. The latter was allowed to react with butylidenetriphenylphosphorane to give the *Z*-isomer **23**. The mercaptal was hydrolyzed using mercury(II) chloride resulting in **24**. The double bond was saturated by catalytic hydrogenation affording **5ba**.



23 24 **5ba**

The 2*R*,3*S* (**5bb**) and the 2*R*,3*R* (**5bc**) aldehydes were prepared from **7** and **8**, respectively, by the same reaction sequences. The end products were converted into their 4-nitrophenylhydrazones.



Using tartraldehyde derivatives **6-8**, two enantiomeric 5,6-dihydroxy-7-oxoheptanoates and three stereoisomeric protected 2,3-dihydroxyoctanals could be synthesized in 7 steps from easily available, inexpensive monosaccharides like D-glucose, D-arabinose, L-arabinose or D-ribose. Because of its simplicity and brevity our method seems to be a good alternative for the synthesis of chiral precursors of lipoxins A and B and of diHETE diastereomers.

EXPERIMENTAL

General Procedures. Solvents were distilled before use. Organic extracts were dried over magnesium sulfate. Solutions were concentrated at 40 °C (bath) at ca. 17 Torr. Melting points were determined on a Kofler melting point apparatus and are reported uncorrected. Analytical thin-layer chromatography (TLC): precoated aluminium-backed plates (Silica gel $60F_{254}$, Merck), layer thickness: 0.2 mm. Compounds were visualized by charring with 5% sulfuric acid in ethanol. Column chromatography: Merck silica gel 60, 0.063 to 0.200 mm, solvents: *n*-hexane/ethyl acetate (mixture A), dichloromethane/methanol (mixture B), dichloromethane/acetone (mixture C). ^{1}H NMR (200 MHz) and ^{13}C NMR (50.3 MHz): Bruker WP-200SY instrument, tetramethylsilane (TMS) as internal standard, $CDCl_3$ as solvent. Specific rotations were measured in chloroform at room temperature on a Perkin-Elmer 141 MC polarimeter. Mass spectra were obtained with a VG TRIO-2 (VG Masslab, England) instrument connected with a Waters 501 HPLC pump in an isocratic mode. Samples were dissolved in a 0.1 M NH_4OAc buffer/methanol mixture (1:1) and injected into the same solvent system at a flow rate of 1 mL/min; PSP interface tip temperature 210 °C. Electron ionisation mass spectra have been obtained using a VG-7035 instrument.

Reaction of triphenylphosphine and ethyl acrylate with 6. Compound **6**[15] (2.81 g, 10.6 mmol) and triphenylphosphine (3.07 g, 11.7 mmol) in ethyl acrylate (30 mL) were heated at 100 °C (bath) for 22 h. Removal of the solvent under vacuum gave an oily residue which was a mixture of four main compounds separable by column chromatography using mixture A of increasing polarity (15:1 10:1). The first eluted product was a mixture of **ethyl (3*Z*,5*R*,6*S* and 3*E*,5*R*,6*S*)-7,7-bis(ethylthio)-5,6-dihydroxy-5,6-*O*-isopropylidene-hept-3-enoates (11a,b):** 1.27 g oil (34%), R_f = 0.43 [mixture A, (8:2)]. ^{1}H NMR δ 1.19-1.32 (3t, 9 H, SCH_2CH_3, OCH_2CH_3), 1.43 and 1.48 [2s, 6 H, $C(CH_3)_2$], 2.62-2.83 (m, 4 H, SCH_2CH_3), 3.12 [dd, 0.35 H, H-2, (3*E* isomer)], 3.28 [dd, 1.65 H, H-2, (3*Z* isomer)], 3.89 (d, 1 H, H-7), 3.96-4.25 (m, 3 H, OCH_2CH_3, H-6), 4.51-4.61 [m, 0.35 H, H-5, (3*E* isomer)], 4.76-4.88 [m, 1.65 H, H-5, (3*Z* isomer)], 5.50-5.73 (m, $J_{3,4}$ = 9 Hz, 1 H, H-4), 5.81-6.07 (m, 1 H, H-3). Ratio of *Z*/*E* isomers: 5:1. ^{13}C NMR δ 14.0, 14.1, 14.2 (SCH_2CH_3, OCH_2CH_3); 24.9, 25.0 [SCH_2CH_3, (3*Z* isomer)]; 25.1, 25.2 [SCH_2CH_3, (3*E* isomer)]; 26.7, 27.0 [$C(CH_3)_2$, (3*Z* isomer)]; 26.8, 26.9 [$C(CH_3)_2$, (3*E* isomer)]; 33.5 (C-2); 51.5 (C-7); 60.5 (OCH_2CH_3); 74.8 (C-5); 84.1 [C-6, (3*E* isomer)]; 84.2 [C-6, (3*Z* isomer)]; 109.4 [$C(CH_3)_2$, (3*E* isomer)]; 109.5 [$C(CH_3)_2$, (3*Z* isomer)]; 127.0 [C-

3, (3*E* isomer)]; 127.1 [C-3, (3*Z* isomer)], 129.3 (C-4); 170.8 (C-1). MS: *m/z* (%) 366 (100) [M + NH_4^+], 349 (10) [M^+ + 1].

Anal. Calcd for $C_{16}H_{28}O_4S_2$: C, 55.14; H, 8.10; S, 18.40. Found: C, 54.78; H, 7.96; S, 18.11.

The next two compounds eluted were diastereoisomers: **ethyl (3*S*,4*R*,5*S* and 3*R*,4*R*,5*S*)-6,6-bis(ethylthio)-4,5-*O*-isopropylidene-2-*C*-methylene-3,4,5-trihydroxy-hexanoate (12 and 13). 12**: 0.65 g oil (17%), R_f = 0.37 [mixture A, (8:2)], $[\alpha]_D$ = +66° (*c* = 1.09). ^1H NMR δ 1.19-1.40 (m, 9 H, SCH_2CH_3, OCH_2CH_3), 1.42 and 1.47 [2s, 6 H, $C(CH_3)_2$], 2.58-2.85 (m, 4 H, SCH_2CH_3), 3.25 (d, 1 H, OH), 3.86 (d, 1 H, H-6), 4.25 (q, 2 H, OCH_2CH_3), 4.28-4.47 (m, 2 H, H-4, H-5), 4.54-4.64 (m, 1 H, H-3), 5.97 (t, $J_{a,b}$ = 1 Hz, 1 H, $=CH^a$), 6.37 (t, 1 H, $=CH^b$). ^{13}C NMR δ 14.1, 14.3, 14.4 (SCH_2CH_3, OCH_2CH_3); 25.1, 25.4 (SCH_2CH_3); 27.2 [$C(CH_3)_2$]; 53.3 (C-6); 61.1 (OCH_2CH_3); 71.6 (C-3); 79.6 (C-5); 87.7 (C-4); 110.2 [$C(CH_3)_2$]; 127.3 (H_2C=C); 138.6 (C-2); 166.1 (C-1). MS: *m/z* (%) 365 (100) [M^+].

Anal. Calcd for $C_{16}H_{28}O_5S_2$: C, 57.72; H, 7.74; S, 17.59. Found: C, 57.02; H, 7.39; S, 17.35.

Compound **12** was acetylated with acetic anhydride in pyridine to give **15**: R_f = 0.43 [mixture A, (8:2)], $[\alpha]_D$ = +65° (*c* = 1.13). ^1H NMR δ 2.13 (s, 3 H, $COCH_3$). MS: *m/z* (%) 424 (100) [M + NH_4^+], 407 (7) [M^+].

13: 0.31 g oil (8%), R_f = 0.35 [mixture A, (8:2)], $[\alpha]_D$ = +63° (*c* = 0.85). ^1H NMR: δ = 1.21-1.38 (2t, 9 H, SCH_2CH_3, OCH_2CH_3), 1.45 [2s, 6 H, $C(CH_3)_2$], 2.62-2.84 (m, 4 H, SCH_2CH_3), 2.97 (d, 1 H, OH), 3.89 (d, $J_{5,6}$ = 5 Hz, 1 H H-6), 4.25 (q, 2 H, OCH_2CH_3), 4.30 (d, $J_{4,5}$= 7.7 Hz, 1 H, H-4), 4.39 (dd, 1 H, H-5), 4.65-4.75 (m, 1 H, H-3), 5.95 (t, $J_{a,b}$ = 1 Hz, 1 H, $=CH^a$), 6.37 (t, 1 H, $=CH^b$). ^{13}C NMR δ 14.1, 14.3, 14.4 (SCH_2CH_3, OCH_2CH_3); 25.1, 25.5 (SCH_2CH_3); 27.3 [$C(CH_3)_2$]; 53.1 (C-6); 60.9 (OCH_2CH_3); 69.8 (C-3); 80.7 (C-5); 81.3 (C-4); 110.1 [$C(CH_3)_2$]; 126.1 (H_2C=C); 140.4 (C-2); 166.1 (C-1). MS: *m/z* (%) 365 (100) [M^+].

Anal. Calcd for $C_{16}H_{28}O_5S_2$: C, 57.72; H, 7.74; S, 17.59. Found: C, 57.38; H, 7.57; S, 17.40.

Compound **13** was acetylated to **16** in a similar way: R_f = 0.40 [mixture A, (8:2)], $[\alpha]_D$ = +71° (*c* = 1.20). ^1H NMR δ 2.13 (s, 3 H, $COCH_3$). MS: *m/z* (%) 424 (100) [M + NH_4^+], 407 (7) [M^+].

The fourth eluted compound was **ethyl (2*E*,4*?*,5*R*,6*S*)-7,7-bis(ethylthio)-5,6-*O*-isopropylidene-4,5,6-trihydroxyhept-2-enoate (14)**: 0.70 g oil (18%), R_f = 0.31 [mixture A, (8:2)], $[\alpha]_D$ = +50° (*c* = 1.19). ^1H NMR δ 1.19-1.36 (m, 9 H, SCH_2CH_3, OCH_2CH_3), 1.44 and 1.48 [2s, 6 H, $C(CH_3)$], 2.58 (d, 1 H, OH), 2.61-2.83

(m, 4 H, SCH_2CH_3), 3.84 (d, 1 H, H-7), 4.22 (q, 2 H, OCH_2CH_3), 4.20-4.35 (m, 2 H, H-5, H-6), 4.50-4.60 (m, 1 H, H-4), 6.19 (dd, $J_{2,3}$ = 16 Hz, $J_{2,4}$ = 2 Hz, 1 H H-2), 7.00 (dd, $J_{3,4}$ = 4.5 Hz, 1 H, H-3). ^{13}C NMR δ 14.1, 14.2 (SCH_2CH_3, OCH_2CH_3); 25.0, 25.3 (SCH_2CH_3); 27.1, 27.2 [$C(CH_3)_2$]; 52.9 (C-7); 60.4 (OCH_2CH_3); 71.1 (C-4); 80.7 (C-5); 81.1 (C-6); 110.2 [$C(CH_3)_2$]; 122.1 (C-2); 145.3 (C-3); 166.0 (C-1). MS: *m/z* (%) 382 (100) [M + NH_4^+], 365 (14) [M^+].

Anal. Calcd for $C_{16}H_{28}O_5S_2$: C, 57.72; H, 7.74; S, 17.59. Found: C, 57.32; H, 7.52; S, 17.31.

14 was acetylated to **17** as above: R_f = 0.38 [mixture A (8:2)], $[\alpha]_D$ = +53° (*c* = 1.35). ^1H NMR δ 2.15 (s, 3 H, $COCH_3$). MS: *m/z* (%) 424 (100) [M + NH_4^+], 407 (9) [M^+].

Reaction of triphenylphosphine and ethyl acrylate with 7:[15]

Enantiomer of	$[\alpha]_D^o$ (*c* = 1)	Anal. Found:		
		C	H	S
11a,b	-	54.52	7.83	17.98
12	-67	57.15	7.41	17.25
13	-64	57.25	7.45	17.35
14	-48	57.48	7.53	17.44

Ethyl (3*E*,5*R*,6*S*)- and (3*Z*,5*R*,6*S*)-5,6-Dihydroxy-5,6-*O*-isopropylidene-7-oxo-hept-3-enoates (22a,b). Mercury(II) chloride (1.18 g, 4.3 mmol) and cadmium carbonate (1.2 g) were added to a solution of **11a,b** (504 mg, 1.45 mmol) in acetone (20 mL) and water (4 mL). After stirring overnight at room temperature the suspension was filtered into a saturated $NaHCO_3$ solution (10 mL) and washed with acetone (3x10 mL). The mixture was concentrated, the residue was taken up in dichloromethane (100 mL) and washed with brine (15 mL) and 10% potassium iodide solutions (2x10 mL). The organic layer was concentrated and the residue was purified by chromatography using mixture B (200:3) as eluent to give 232 mg (66%) of **22a,b** as an oil. R_f = 0.15 [mixture B, (100:1)]. **22a,b** was characterized as its 4-nitrophenylhydrazone: R_f = 0.22 [mixture C, (100:2)]. ^1H NMR δ 1.09-1.32 (m, 3 H, OCH_2CH_3), 1.40-1.65 [m, 6 H, $C(CH_3)_2$], 2.54-2.66 and 3.08-3.21 (m, 2 H, H-2), 3.93-4.81 (m, 4 H, OCH_2CH_3, H-5, H-6), 5.57-5.75 (m, 1 H, H-4), 5.84-6.03 (m, 1 H, H-3), 6.95-7.15 (m, 3 H, aromatic H, H-7), 7.94-8.20 (m, 3 H, aromatic H, NH). MS: *m/z* (%) 377 (13) [M^+], 362 (4) [$M^+ - CH_3$].

Anal. Calcd for $C_{18}H_{23}N_3O_6$: C, 57.28; H, 6.14; N, 11.13. Found: C, 56.84; H, 5.97; N, 10.89.

The enantiomer of the 4-nitrophenylhydrazone of 22a,b.

Anal. Found: C, 56.57; H, 5.95; N, 10.78.

Ethyl (5*R*,6*S*)-5,6-Dihydroxy-5,6-*O*-isopropylidene-7-oxoheptanoate (4ba). A methanolic (10 mL) solution of **22a,b** (145 mg, 0.60 mmol) was hydrogenated at atmospheric pressure over palladium on charcoal (10%) (55 mg) for a night. The catalyst was filtered off and washed with methanol (6x5 mL), and the solution was concentrated under reduced pressure. The residue was chromatographed with mixture B (100:1) as eluent to give 137 mg (94%) of **4ba.** R_f = 0.29 [mixture B, (100:2)]. **4ba** was characterized as its 4-nitrophenylhydrazone: mp 62-63 °C, R_f = 0.26 [mixture C, (100:2)], $[\alpha]_D$ = -31° (*c* = 1.63). ^{1}H NMR δ 1.24 (t, 3 H, OCH_2CH_3), 1.43 and 1.46 [2s, 6 H, $C(CH_3)_2$], 1.61-1.89 (m, 4 H, H-3, H-4), 2.31-2.45 (m, 2 H, H-2), 3.90-4.34 (m, 2 H, H-5, H-6), 4.12 (q, 2 H, OCH_2CH_3), 7.03 (d, 2 H, aromatic H), 7.10 (d, 1 H, H-7), 8.12 (s, 1 H, NH), 8.15 (d, 2 H, aromatic H). MS: *m/z* (%) 379 (11) [M^+], 364 (11) [$M^+ - CH_3$].

Anal. Calcd for $C_{18}H_{25}N_3O_6$: C, 56.98; H, 6.64; N, 11.07. Found: C, 56.52; H, 6.69; N, 10.48.

4-Nitrophenylhydrazone of 4bb: mp 62-63 °C, $[\alpha]_D$ = +33° (*c* = 1.33).

Anal. Found: C, 56.73; H, 6.58; N, 10.59.

(4*Z*,2*S*,3*R*)-1,1-Bis(ethylthio)-2,3-dihydroxy-2,3-*O*-isopropylideneoct-4-ene (23). 2.5 M *n*-Butyllithium in hexanes (14.3 mmol) was added to a stirred suspension of butyltriphenyl-phosphonium bromide (5.92 g, 14.8 mmol) in toluene (85 mL) under nitrogen. After 30 min **6**[15] (2.31 g, 8.7 mmol) was added to toluene (10 mL). The mixture was stirred for 1 h at room temperature, filtered through a Celite layer, washed with water and dried. After chromatography using mixture A (30:1) 1.70 g (64%) **23** was obtained: R_f = 0.59 [mixture A, (9:1)], $[\alpha]_D$ = +35° (*c* = 0.96). ^{1}H NMR δ 0.94 (t, 3 H, H-8), 1.25 and 1.27 (2t, 6 H, SCH_2CH_3), 1.44 and 1.48 [2s, 6 H, $C(CH_3)_2$], 1.42-1.58 (m, 2 H, H-7), 1.97-2.35 (m, 2 H, H-6), 2.58-2.88 (m, 4 H, SCH_2CH_3), 3.83 (d, $J_{1,2}$ = 4 Hz, 1 H, H-1), 4.02 (dd, $J_{2,3}$ = 8 Hz, 1 H, H-2), 4.91 (ddd, $J_{3,4}$ = 9 Hz, $J_{3,5}$ = 1 Hz, 1 H, H-3), 5.30-5.57 (m, $J_{4,5}$ = 10 Hz, 1 H, H-4), 5.63-5.91 (m, 1 H, H-5). MS: *m/z* (%) 305 (2) [M^+], 229 (15) [$M^+ - SCH_2CH_3 - CH_3$].

Anal. Calcd for $C_{15}H_{28}S_2O_2$: C, 59.16; H, 9.27; S, 21.06. Found: C, 59.43; H, 9.47; S, 20.86.

The enantiomer of 23: $[\alpha]_D$ = -29° (*c* = 1.16).

Anal. Found: C, 58.98; H, 9.38; S, 20.83.

(4*Z*,2*S*,3*R*)-2,3-Dihydroxy-2,3-*O*-isopropylideneoct-4-enal (24). Starting from **23** (1.47 g, 4.8 mmol) following the same procedure [column chromatography: mixture A (85:15)] as described for **22a,b**, **24** (461 mg, 48%) was prepared. R_f = 0.30 [mixture A, (7:3)]. **24** was characterized as a 4-nitrophenylhydrazone: mp 81-82 °C, R_f = 0.31 [mixture A, (7:3)], $[\alpha]_D$ = -219° (*c* = 2.05). ^{1}H NMR δ 0.84 (t, 3 H, H-8), 1.48 [s, 6 H, $C(CH_3)_2$], 1.15-1.65 (m, 2 H, H-7), 1.91-2.20 (m, 2 H, H-6), 4.33 (dd, $J_{3,4}$ = 9 Hz, 1 H, H-3), 5.38-5.57 (m, $J_{4,5}$ = 10 Hz, 1 H, H-4), 5.63-5.90 (m, 1 H, H-5), 7.03 (d, 2 H, aromatic H), 7.11 (d, 1 H, H-1), 7.99 (s, 1 H, NH), 8.15 (d, 2 H, aromatic H). MS: *m/z* (%) 333 (7) [M^+], 318 (6) [M^+ - CH_3], 303 (5) [M^+ - NO].

Anal. Calcd for $C_{17}H_{23}N_3O_4$: C, 61.24; H, 6.95; N, 12.60. Found: C, 61.25; H, 6.80; N, 12.24.

The enantiomer of the 4-nitrophenylhydrazone of 24: mp 78-79 °C, $[\alpha]_D$ = +215° (*c* = 1.82).

Anal. Found: C, 60.88; H, 6.73; N, 12.35.

(2*S*,3*R*)-2,3-Dihydroxy-2,3-*O*-isopropylideneoctanal (5ba). Prepared from **24** (210 mg, 1.06 mmol) following the procedure used for the heptanoate derivative **4ba**. The crude product was purified using mixture A (8:2) to give **5ba** (201 mg, 95%). R_f = 0.35 [mixture A, (7:3)]. **5ba** was characterized in the form of its 4-nitrophenylhydrazone: mp 53-55 °C, R_f = 0.27 [mixture A, (7:3)], $[\alpha]_D$ = -50° (*c* = 1.45). ^{1}H NMR δ 0.88 (t, 3 H, H-8), 1.44 and 1.47 [2s, 6 H, $C(CH_3)_2$], 1.21-1.77 (m, 8 H, H-7, H-6, H-5, H-4), 3.90-4.19 (m, $J_{2,3}$ = 8 Hz, 1 H, H-3), 4.27 (dd, $J_{1,2}$ = 6 Hz, 1 H, H-2), 7.03 (d, 2 H, aromatic H), 7.09 (d, 1 H, H-1), 7.98 (br, 1 H, NH), 8.16 (d, 2 H, aromatic H). MS: *m/z* (%) 335 (3) [M^+], 320 (3) [M^+ - CH_3].

Anal. Calcd for $C_{17}H_{25}N_3O_4$: C, 60.88; H, 7.51; N, 12.53. Found: C, 60.63; H, 7.29; N, 12.42.

The 4-nitrophenylhydrazone of 5bb: mp 57-59 °C, $[\alpha]_D$ = +49° (*c* = 1.32).

Anal. Found: C, 60.78; H, 7.40; N, 12.36.

(4*Z*,2*R*,3*R*)-1,1-Bis(propylthio)-2,3-dihydroxy-2,3-*O*-isopropylideneoct-4-ene (25). The chain elongation of **8**[16] (1.70 g, 5.8 mmol) was performed using the procedure described for **23** to give **25** (1.54 g, 80%) as a light yellow oil: R_f = 0.39 [mixture A, (9:1)], $[\alpha]_D$ = -71° (*c* = 1.29). ^{1}H NMR δ 0.87-1.07 (m, 9 H, H-8, $SCH_2CH_2CH_3$), 1.38 and 1.53 [2s, 6 H, $C(CH_3)_2$], 1.22-1.74 (m, 6 H, H-7,

$SCH_2CH_2CH_3$), 2.52-2.78 (m, 4 H, $SCH_2CH_2CH_3$), 3.74 (d, $J_{1,2}$ = 8 Hz, 1 H, H-1), 4.30 (dd, $J_{2,3}$ = 6 Hz, 1 H, H-2), 4.92 (dd, $J_{3,4}$ = 9 Hz, 1 H, H-3), 5.49-5.78 (m, 2 H, H-4, H-5). MS: *m/z* (%) 332 (20) [M^+].

Anal. Calcd for $C_{17}H_{32}O_2S_2$: C, 61.39; H, 9.70; S, 19.28. Found: C, 61.94; H, 9.77; S, 19.78.

(4*Z*,2*R*,3*R*)-2,3-Dihydroxy-2,3-*O*-isopropylideneoct-4-enal (26). Compound **25** (900 mg, 2.71 mmol) was demercaptalized as described for **22a,b**. The crude product was purified by adsorption chromatography [mixture A, (15:1)] affording **26** (336 mg, 63%). R_f = 0.37 [mixture A, (8:2)]. It was converted to its 4-nitrophenylhydrazone: mp 78-80 °C, R_f = 0.37 [mixture A, (7:3)], $[\alpha]_D$ = -94° (*c* = 1.54). ^1H NMR δ 0.88 (t, 3 H, H-8), 1.21-1.48 (m, 2 H, H-7), 1.45 and 1.56 [2s, 6 H, $C(CH_3)_2$], 1.93-2.18 (m, 2 H, H-6), 4.78 (dd, $J_{1,2}$ = 7 Hz, $J_{2,3}$ = 6.5 Hz, 1 H, H-2), 5.13 (ddd, $J_{3,4}$ = 7.5 Hz, $J_{3,5}$ = 1 Hz, 1 H, H-3), 5.30-5.50 (m, $J_{4,5}$ = 10 Hz, 1 H, H-4), 5.52-5.85 (m, 1 H, H-5), 7.01 (d, 2 H, aromatic H), 7.03 (d, 1 H, H-1), 7.91 (br, 1 H, NH), 8.15 (d, 2 H, aromatic H). MS: *m/z* (%) 333 (6) [M^+], 303 (7) [M^+ - NO].

Anal. Calcd for $C_{17}H_{33}N_3O_4$: C, 61.24; H, 6.95; N, 12.60. Found: C, 61.02; H, 6.87; N, 12.38.

(2*R*,3*R*)-2,3-Dihydroxy-2,3-*O*-isopropylideneoctanal (5bc). Compound **26** (168 mg, 0.85 mmol) was catalytically reduced in the same manner as described for **4ba**, to yield **5bc** (161.6 mg, 95%). R_f = 0.50 [mixture A, (7:3)]. Its 4-nitrophenylhydrazone: R_f = 0.33 [mixture A, (7:3)], $[\alpha]_D$ = +13° (*c* = 1.50). ^1H NMR δ 0.86 (t, 3 H, H-8), 1.41 and 1.53 [2s, 6 H, $C(CH_3)_2$], 1.18-1.65 (m, 8 H, H-7, H-6, H-5, H-4), 4.20-4.39 (m, 1 H, H-3), 4.69 (t, 1 H, H-2), 7.02 (d, 2 H, aromatic H), 7.08 (d, 1 H, H-1), 7.95 (br, 1 H, NH), 8.16 (d, 2 H, aromatic H). MS: *m/z* (%) 335 (18) [M^+], 320 (10) [M^+ - CH_3], 305 (3) [M^+ - NO].

Anal. Calcd for $C_{17}H_{25}N_3O_4$: C, 60.88; H, 7.51; N, 12.53. Found: C, 60.99; H, 7.59; N, 12.36.

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