An Efficient Stereoselective Synthesis of Sphingosine

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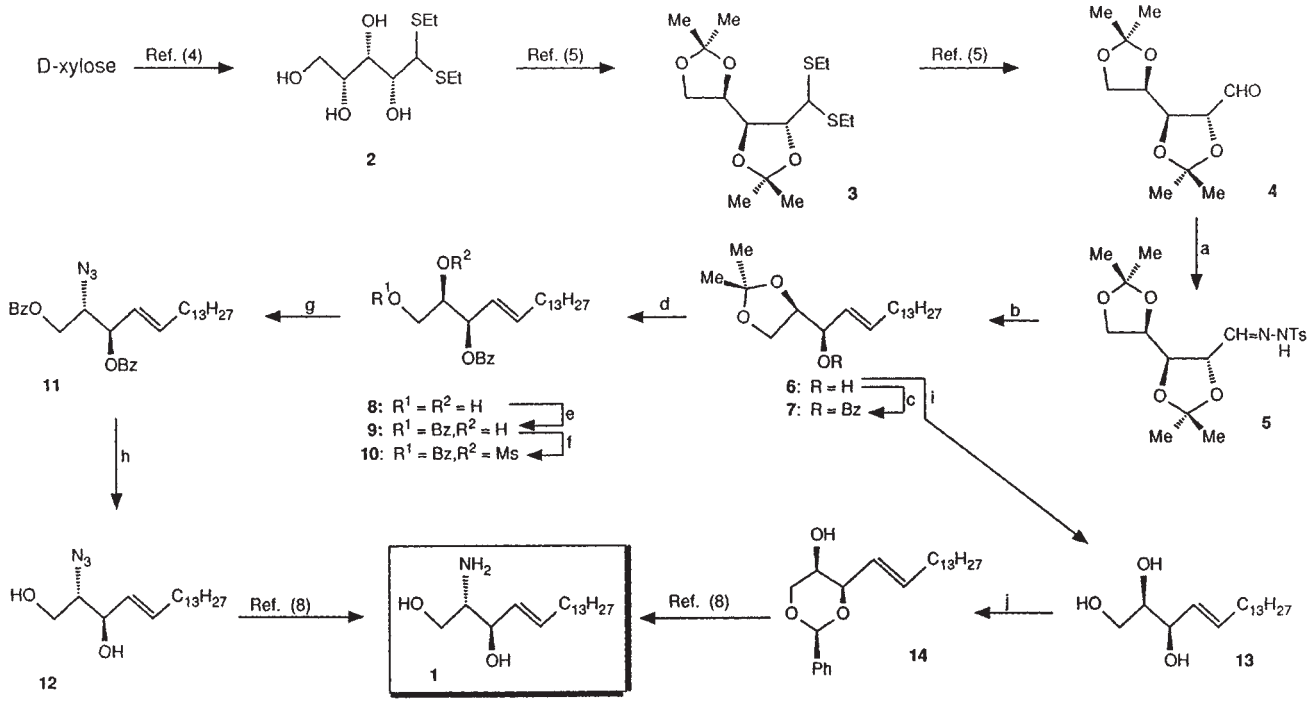
Received 5 May 1997; revised 18 July 1997

A stereocontrolled synthesis of D-(+)-*erythro*-sphingosine (**1**), starting from Dxylose as chiral pool material and employing the addition–fragmentation reaction of tosyl hydrazone of 2,3:4,5-di-*O*-isopropylidene-D-xylose as a key step for the chain extension with concomitant *trans*-selective C=C bond formation, is described.

Sphingosine (**1**), phytosphingosine and the biosynthetic precursor of both, sphinganine, are most abundant long-chain amino alcohols possessing generally 18 or 20 carbon atoms. The occurrence of various structural modifications of the sphingosine moiety in nature and the requirement of structurally varied derivatives for biological testing led us to investigate sphingosine syntheses based on tosyl hydrazones of sugars (Scheme). Various methods for the synthesis of sphingosine and its analogues have been documented in the literature.[1] Recently, we have reported an oxa-Cope rearrangement route as a competitive alternative to the previously published sphingosine syntheses.[2] However, a simple and efficient large scale synthesis is still desirable. Thus, it was envisaged to plan a stereoselective synthesis from readily available carbohydrate precursors. The addition–fragmentation reaction of tosyl hydrazone of sugar was employed as a key step[3] in order to construct the required *trans* C=C bond with concomitant chain extension in one step.

As shown in the Scheme, 2,3:4,5-di-*O*-isopropylidene-aldehydo-D-xylose **4** was prepared following literature procedures in three steps. Thus, D-xylose was converted into D-xylose diethyl dithioacetal **2** by treatment with ethanethiol in quantitative yield.[4] Reaction of **2** with acetone in the presence of catalytic amounts of sulfuric acid gave **3** (73%) which on deprotection of the thiol group with $HgO/HgC1_2$ furnished **4** in good yield.[5] The subsequent treatment of the aldehyde **4** with tosyl hydrazide afforded the corresponding hydrazone **5** (76%) which was subjected to the key addition–fragmentation reaction. The reaction of tosyl hydrazone **5** with 3 equivalents of preformed Grignard reagent prepared from 1-bromotridecane afforded only the desired *trans*-allylic alcohol **6**, yet in moderate yield. Thus, the generally required *trans* C=C bond was constructed with concomitant chain elongation in one step. The stereoselective formation of (*E*)-alkene was determined by ^{1}H NMR and decoupling experiments. Further, the synthesis of sphingosine (**1**) from **6** was achieved employing a series of high-yielding functional



a) $TsNHNH_2$, MeOH, RT, 4 h, 76%. b) $C_{13}H_{27}MgBr$, Et_2O, 0°C for 0.5 h, then RT overnight, 48%. c) PhCOCN, NEt_3, CH_2Cl_2, 0°C for 2 h, then RT for 4 h, 85%. d) 1N HCl, THF, 60°C, 12 h, 77%. e) PhCOCN, NEt_3, THF, -70°C, 3 h, 80%. f) $MeSO_2Cl$, pyridine 70-80°C, 12 h, 75%. g) NaN_3, DMF, 100°C, 36 h, 90%. h) NaOMe, MeOH, RT, 2 h, 98%. i) p-TSA, MeOH, RT, 24 h, 70%. j) $PhCH(OMe)_2$, p-TSA, CH_2Cl_2, RT, 5 h, 60%

group transformations (Scheme). The choice of introducing a readily removable benzoyl protective group seemed to be more appropriate. Indeed, the hydroxyl group protection of **6** with benzoyl cyanide/triethylamine (→ **7**) proceeded smoothly in high yield. Subsequent removal of the isopropylidene group under acid catalysis furnished the diol **8**, Selective 1-*O*-protection was carried out at –70°C using benzoyl cyanide/triethylamine to afford the 1,3-di-*O*-benzoylated compound **9**. However, our attempt to obtain **9** by direct regioselective 1,3-*O*-protection from **13** was unsuccessful. Compound **9** was then converted into 2-*O*-mesylate derivative **10** which on reaction with sodium azide in DMF afforded the corresponding 1,3-di-*O*-benzoylated sphingosine **11**. Removal of the benzoyl group with sodium methoxide in methanol (Zemplén conditions)[6] furnished the azido sphingosine **12** which was in all aspects identical with the reported compound.[7] Transformation into **1** could be readily performed as previously described.[8]

Furthermore, in an alternative approach for the formal synthesis of sphingosine, the cleavage of the isopropylidene group of **6** was carried out under acid catalysis to furnish the triol **13**. The benzylidene protection of **13** was effected with benzaldehyde dimethylacetal in the presence of a catalytic amount of *p*-TSA to afford a mixture of 1,3- and 1,2-benzylidene compound in 9:1 ratio, The desired major 1,3-benzylidene compound **14** was separated by silica gel column chromatography. As the synthesis of sphingosine from **14** has already been reported,[7,8] the formal synthesis of sphingosine **1** was completed.

In summary, a highly stereocontrolled synthesis of D (+)-*erythro*-sphingosine from a sugar precursor by a simple and operationally feasible procedure was achieved. The merits of this synthesis are high-yielding reaction steps, ready access to the required *trans* C=C bond and the various possibilities available for structural modifications.

Solvents were purified and dried by standard procedures before use; petroleum ether of boiling range 35–70°C was used. Melting points are uncorrected.^{1}H NMR spectra: Bruker AC 250, internal standard tetramethylsilane (TMS): *J* values in Hz. Mass spectra: Varian MAT 312 (70eV), Varian MAT 312/AMD 5000 FAB. Flash chromatography: silica gel 60 (Baker, 0.03–0.06 mm) at a pressure of 0.3 bar. Thin layer chromatography (TLC): Foil plates, silica gel 60 F_{254} (Merck; layer thickness 0.2 mm); detection by treatment with a solution of 20 g of ammonium molybdate and 0.4 g of cerium(IV) sulfate in 400 mL of 10% sulfuric acid and heating at 150°C. Elemental analyses: Heraeus CHN-O-Rapid. Optical rotations: Perkin-Elmer polarimeter 241/MS, 1 dm cell.

2,3:4,5-Di-*O*-isopropylidene-D-xylose Tosylhydrazone (5):
A mixture of 4 (5.17 g, 22.47 mmol) and *p*-toluenesulfonyl hydrazide (4.18 g, 22.47 mmol) in anhyd MeOH (37.5 mL) was stirred for 4 h at r.t. under N_2. The hydrazone **5** thus separated as white solid was filtered, washed with anhyd Et_2O (20 mL), dried and used for further reaction without purification. Yield (7.16 g, 76%). TLC (silica gel, petroleum ether/EtOAc, 1:1): R_f = 0.52; mp 126°C; $[\alpha]_D^{20}$ –3.6 (*c* = l .0, $CHCl_3$).
^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.32 (s, 3 H, CH_3), 1.33 (s, 3 H, CH_3), 1.34 (s, 3 H, CH_3), 1.39 (s, 3 H, CH_3), 2.40 (s, 3 H, $SO_2C_6H_4CH_3$), 3.45 (dd, 1 H, *J* = 7.2, 8.5 Hz, H-3), 3.82 (m, 2 H, OCH_2, H-5), 4.02 (m, 1 H, OCH_2CHO, H-4), 4.28 (dd, 1 H, *J* = 6, 7.8 Hz, H-2), 7.08 (d, 1 H, CH=N, *J* = 5.9 Hz), 7.28–7.31 (m, 2 H, Ph), 7.78–7.83 (m, 2 H, Ph), 8.08 (s, 1 H, NH).
MS: *m/z*(%) = (M^+-1) 397(24.11), 383(48.23), 325(9.41), 283(8.82), 268(10), 243(15.88), 185(13.52), 155(13.52), 139(17.64), 113(27.64), 101(48.23), 91(61.17), 59(72.35).
Anal. calcd for $C_{18}H_{26}N_2O_6S$ (398.45): C, 54.26; H, 6.58; N, 7.03; S, 8.05, Found: C, 54.02; H, 6.47; N, 7.28; S, 8.26.

(2*R*,3*R*,4*E*)-1,2-*O*-Isopropylideneoctadec-4-ene-1,2,3-triol (6):
To a stirred suspension of **5** (1.4 g, 3.51 mmol) in anhyd Et_2O (25 mL), maintained at 0°C under N_2 was added dropwise preformed tridecylmagnesium bromide (10.55 mL, 10.53 mmol, 1 M solution in Et_2O). The mixture was stirred at 0°C for 0.5 h, slowly warmed to r.t. and stirred overnight at this temperature. Subsequently, the mixture was hydrolyzed by the addition of ice-cold 1 M NH_4Cl (10 mL) solution. The organic phase was separated and the aqueous phase was saturated with brine and subsequently extracted with Et_2O (2 × 50 mL). The combined organic phases were dried (Na_2SO_4), filtered and concentrated. Column chromatography using petroleum ether/EtOAc (10:1) afforded **6** (0.57 g, 48%) as a colorless oil. TLC (silica gel, petroleum ether/EtOAc, 8:2): R_f = 0.37; $[\alpha]_D^{20}$ –1.3 (*c* = 1.0, $CHCl_3$).
^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.85 (t, 3 H, CH_3, *J* = 6.6 Hz), 1 .15–1.30 (m, 22 H, 11 CH_2), 1.34 (s, 3 H, CH_3CCH_3), 1.42 (s, 3 H, CH_3CCH_3), 2.0 (dt, 2 H, CH=CHC*H2*, *J* = 6.9, 7.5 Hz), 2.3 (br s, 1 H, CHO*H*), 3,69 (m, 1 H, OCH_2), 3.94 (m, 3 H, OCH_2, $OCHCH_2$, C*H*OH), 5.36 (dd, 1 H, C*H*=$CHCH_2$, *J* = 6.9, 15.4 Hz), 5.77 (dt, CH=C*H*CH_2, *J* = 6.7, 15.3 Hz).
MS: *m/z*(%) = M^+-OH 323(8.82), 297(3.52), 239(30.58), 201(6.47), 101(100).
FAB-MAS = $[2M]Na^+$ 703(5), $[M]Na^+$ 363(94.28), 323(50), 265(7.85), 176(15), 154(14.28), 101(100).
Anal. calcd for $C_{21}H_{40}O_3$ (340.53): C, 74.06; H, 11.84. Found: C, 74.10; H, 11.73.

(2*R*,3*R*,4*E*)-1,2-*O*-Isopropylidene-3-*O*-benzoyloctadec-4-ene-1,2,3-triol (7):
To a solution of **6** (100 mg, 0.29 mmol) in anhyd CH_2Cl_2 (4 mL) containing anhyd Et_3N (0.5 mL), maintained at 0°C under N_2 was added dropwise a solution of benzoyl cyanide (42.48 mg, 0.32 mmol) dissolved in anhyd CH_2Cl_2 (1 mL) and the mixture was stirred for 2 h at 0°C and then 4 h at r.t. The excess of benzoyl cyanide was destroyed by adding MeOH (1 mL), the solvent was concentrated in vacuo. The residue was taken up in EtOAc (5 mL) and washed with sat. aq $NaHCO_3$ (2 × 5 mL). The organic phase was dried (Na_2SO_4), filtered and concentrated; column chromatography over silica gel with petroleum ether/EtOAc, (9.5:0.5) gave 7 (111 mg, 85%) as a colorless oil. TLC (silica gel, petroleum ether/EtOAc, 8:2): R_f = 0.75; $[\alpha]_D^{20}$ +17.5 (*c* = 1.0, $CHCl_3$).
^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.88 (t, 3 H, CH_3, *J* = 6.6 Hz), 1.23–l.33 (m, 22 H, 11 CH_2), 1.37 (s, 3 H, CH_3CCH_3), 1.45 (s, 3 H, CH_3CCH_3), 2.04 (dt, 2 H, CH=CHC*H2*, *J* = 6.9,7.3 Hz), 3.83 (m,1 H, OCH_2), 4.04 (m, 1 H, OCH_2), 4.34 (m, 1 H, $OCHCH_2O$), 5.49 (m, 2 H, C*H*=$CHCH_2$, C*H*OCOPh), 5.94 (dt, 1 H, CH=C*H*CH_2, *J* = 6.7, 14.3 Hz), 7.40–7.46 (m, 2 H, Ph), 7.52–7.58 (m, 1 H, Ph), 8.05–8.08 (m, 2 H, Ph).
MS: *m/z*(%) = M^+ 444(20), 429(100), 412(2.85), 397(7.85), 386(7. 14), 356(3.57), 343(5), 322(22.14), 281(6.42), 264(68.57), 237(14.28), 211(10.71), 201(62.14).
Anal. calcd for $C_{28}H_{44}O_4$ (444.63): C, 75.63; H, 9.97. Found: C, 75.34; H, 10.01.

(2*R*,3*R*,4*E*)-3-*O*-Benzoyloctadec-4-ene-1,2,3-triol (8):
To a solution of 7 (330 mg, 0.74 mmol) in THF (25 mL) was added 1N HCl (3 mL), and the mixture was heated under stirring for 12 h at 60°C. Subsequently the solvent was concentrated in vacuo and the residue was taken up in Et_2O and the solution was neutralized with sat. aq $NaHCO_3$ (15 mL). The organic layer was washed with H_2O, dried (Na_2SO_4) and concentrated; column chromatography over silica gel using petroleum ether/acetone (9:1) gave **8** (230 mg, 77%) as a colorless oil. TLC (silica gel, petroleum ether/acetone, 8:2): R_f = 0.32; $[\alpha]_D^{20}$ +l3.1 (*c* = 1.0, $CHCl_3$).
^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.88 (t, 3 H, CH_3, *J* = 6.6 Hz), 1.23–l.36 (m, 22 H, 11 CH_2), 2.05 (dt, 2 H, CH=CHC*H2*, *J* = 6.9, 6.9 Hz), 2.36 (br s, 2 H, OH), 3.67 (m, 2 H, OCH_2), 3.92 (m, 1 H, C*H*OH), 5.55

(m, 2 H, C*H*=CHCH$_2$, C*H*OCOPh), 5.93 (dt, 1 H, CH=C*H*CH$_2$, *J* = 6.7, 14.5 Hz), 7.4l–7.47 (m, 2 H, Ph), 7.54–7.61 (m, 1 H, Ph), 8.02–8.08 (m, 2 H, Ph).
MS: *m/z*(%) = M$^+$ 404(2.35), 373(5.29), 344(80), 264(15.29), 252(85.29), 239(62.35), 222(36.47), 194(23.52), 165(30.58), 105(100).
Anal. calcd for $C_{25}H_{40}O_4$ (404.57): C, 74.21; H, 9.97. Found: C, 73.76; H, 9.80.

(2*R*,3*R*,4*E*)-1,3-Di-*O*-benzoyloctadec-4-ene-1,2,3-trio1 (9):
To a solution of **8** (230 mg, 0.57 mmol) in anhyd THF (23 mL) containing anhyd Et_3N (1.15 mL), maintained at –70°C under an N_2 atmosphere, was added dropwise a solution of benzoyl cyanide (80 mg, 0.61 mmol) in anhyd THF (2 mL) and the mixture was stirred for 3 h at –70°C. The excess of benzoyl cyanide was destroyed by adding MeOH (1 mL), the solvent was concentrated in vacuo. The residue was taken up in EtOAc (15 mL) and washed with sat. aq $NaHCO_3$ (2x15 mL). The organic phase was dried (Na_2SO_4), and concentrated; column chromatography over silica gel with petroleum ether/acetone (9:1) gave **9** (231 mg, 80%) as a colorless oil. TLC (silica gel, petroleum ether/acetone, 7:3): R_f = 0.76; $[\alpha]_D^{20}$ + 9.5 (*c* = 1.0, $CHCl_3$).
^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.88 (t, 3 H, CH_3, *J* = 6.6 Hz), 1.22–1.42 (m, 22 H, 11 CH_2), 2.09 (dt, 2 H, CH=CHC*H*$_2$, *J* = 6.7, 6.9 Hz), 2.55 (br s, 1 H, OH), 4.19 (m, 1 H, C*H*OH). 4.48 (m, 2 H, OCH_2), 5.64 (m, 2 H, C*H*=CHCH$_2$, C*H*OCOPh), 5.97 (dt, 1 H, CH=C*H*CH$_2$, *J* = l4.5, 6.7 Hz), 7.38–7.47 (m, 4 H, Ph), 7,54–7.60 (m, 2 H, Ph), 7.97–8.08 (m, 4 H, Ph).
MS: *m/z*(%) = M$^+$ 508(8.23), M$^+$-H_2O 490(5.88), 386(31.47), 356(27.60), 343(12.35), 264(8.82), 251(5.29), 165(78.82), 105(100), 77(32.35).
Anal. calcd for $C_{32}H_{44}O_5$ (508.67): C, 75.55; H, 8.72. Found: C, 75.67; H, 8.68.

(2*R*,3*R*,4*E*)-1,3-Di-*O*-benzoyl-2-*O*-methylsulfonyloctadec-4-ene-1,2,3-triol (10):
Methanesulfonyl chloride (0.06 g, 0.52 mmol) was added under N_2 to a solution of **9** (0.175 g, 0,34 mmol) in anhyd pyridine (2 mL). The mixture was heated under stirring for 12 h at 70–80°C. The excess of mesyl chloride was destroyed by adding a small amount of MeOH. The above mixture was cooled to r.t. and pyridine was removed by co-evaporation with toluene. Purification of the residue by chromatography over silica gel with petroleum ether/EtOAc (9:1) gave **10** (149 mg, 75%) as a colorless oil. TLC (silica gel, petroleum ether/EtOAc, 8:2): R_f = 0.52; $[\alpha]_D^{20}$ + 5.2 (*c* = 1, $CHCl_3$).
^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.85 (t, 3 H, CH_3, *J* = 6.6 Hz), 1.20–l.40 (m, 22 H, 11 CH_2), 2.04 (dt, 2 H, CH=CHC*H2*, *J* = 6.7, 6.7 Hz), 2.97 (s, 3 H, SCH_3), 4.45 (m, 1 H, OCH_2), 4.67 (m, 1 H, OCH_2), 5.20 (m, 1 H, C*H*OMs), 5.51 (dd, 1 H, C*H*=CHCH$_2$, *J* = 7.7, 15.4 Hz), 5.78 (dd, 1 H, C*H*OCOPh, *J* = 7.4, 7.4 Hz), 6.02 (dt, 1 H, CH=C*H*CH$_2$, *J* = 6.7, 15.3 Hz), 7.40–7.60 (m, 6 H, Ph), 8.04–8.08 (m, 4 H, Ph).
MS: *m/z*(%) = M$^+$ 586(2.85), M$^+$-OSO_2CH_3 491(21.42), 465(2.85), 385(22.14), 368(40.71), 343(11.42), 305(3.57), 264(26.42), 246(18.57), 200(6.42), 122(30), 105(100), 91(25), 77(98.57), 67(20), 55(28.57), 43(53.57).
Anal. calcd for $C_{33}H_{46}O_7S$ (586.76): C, 67.55; H, 7.90; S, 5.46. Found: C, 67.16; H, 8.06; S, 5.74.

(2*S*,3*R*,4*E*)-2-Azido-1,3-di-*O*-benzoyloctadec-4-ene-1,3-diol (11):
To a solution of **10** (110 mg, 0.19 mmol) in anhyd DMF (5 mL) was added NaN_3 (70 mg, 1.09 mmol), and the mixture was heated under stirring at 100°C for 36 h. The mixture was cooled, diluted with Et_2O, washed with H_2O and brine, The organic phase was separated, dried (Na_2SO_4) and concentrated. Purification of the residue over silica gel column with petroleum ether/EtOAc (9.5:0.5) gave **11** (90 mg, 90%) as a colorless oil. TLC (silica gel, petroleum ether/EtOAc, 9:1): R_f = 0.77; $[\alpha]_D^{20}$ – 28.9 (*c* = 1, $CHCl_3$),
^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.85 (t, 3 H, CH_3, *J* = 6.6 Hz), 1.21–1 .40 (m, 22 H, 11 CH_2), 2.06 (dt, 2 H, CH=CHC*H2*, *J* = 7, 7 Hz), 4.12 (m, 1 H, CHN_3), 4.34 (m, 1 H, OCH_2), 4,5 (m, 1 H, OCH_2), 5.62 (m, 2 H, C*H*=CHCH$_2$, C*H*OCOPh), 5.96 (dt, 1 H, CH=C*H*CH$_2$, *J* = 6.7, 14.7 Hz), 7.40–7.60 (m, 6 H, Ph), 8.02–8,07 (m, 4 H, Ph).
MS: *m/z*(%) = M$^+$ 533(5), M$^+$-N_2 505(20), M$^+$-N_3 491(100), 343 (42.85), 262(17.14), 190(83.57), 105(100), 77(81.42), 43(32.85).
Anal. calcd for $C_{32}H_{43}N_3O_4$ (533.66): C, 72,02; H, 8. 12; N, 7.87. Found: C, 71.87; H, 8.16; N, 7.55.

(2*S*,3*R*,4*E*)-2-Azidooctadec-4-ene-1,3-diol (12):
A solution of NaOMe in MeOH (1 mL, 0.2 M) was added to **11** (58 mg, 0.11 mmol) in anhyd MeOH (2 mL) and the mixture was stirred for 2 h at r.t. Subsequently, it was neutralized with ion-exchange resin Amberlite IR 120, H^+-form (20 mg). The resin was filtered off and the filtrate concentrated in vacuo; column chromatographic purification of the residue using CH_2Cl_2/MeOH (9.75:0.25) gave **12** (35 mg, 98%) as a white solid. TLC (silica gel, CH_2Cl_2/MeOH, 9.5:0.5): R_f = 0.45; mp 49 °C; $[\alpha]_D^{20}$ –29.1 (*c* = 1, $CHCl_3$); ref. 7: mp. 49–50°C; $[\alpha]_D^{20}$ –32.9 (*c* = 4. $CHCl_3$). Spectroscopic properties (^{1}H NMR, Mass) were in accord with those described.[7]

(2*S*,3*R*,4*E*)-Octadec-4-ene-1,2,3-triol (13):
To a solution of **6** (300 mg, 0.88 mmol) in anhyd MeOH (10 mL) was added *p*-toluenesulfonic acid (10 mg), and the mixture was stirred at r.t. for 24 h. Subsequently the solvent was concentrated in vacuo and the residue was taken up in $CHCl_3$ and the solution was neutralized with sat. aq $NaHCO_3$ (10 mL); the organic phase was separated, washed with H_2O, dried (Na_2SO_4) and concentrated. Column chromatography using petroleum ether/acetone (7:3) afforded **13** (185 mg, 70%) as a white solid. TLC (silica gel, petroleum ether/acetone, 7:3): R_f = 0.49; mp 59–60°C; $[[\alpha]_D^{20}$ –0.3 (*c* = 1, $CHCl_3$).
^{1}H NMR (250 MHz): 0.85 (t, 3 H, CH_3, *J* = 6.6 Hz), 1.16–1.40 (m, 22 H, 11 CH_2), 2.02 (dt, CH=CHC*H2*, *J* = 6.7, 6.7 Hz), 2.96 (br s, 2 H, 2 OH), 3.53–3.70 (m, 3 H, OCH_2, CH=CHC*H*OH), 4.07 (m, 1 H, CH_2C*H*OH), 5.44 (dd, 1 H, C*H*=CHCH$_2$, *J* = 7.3, 15.6 Hz), 5.74 (dt, 1 H, CH=C*H*CH$_2$, *J* = 6.7. 15.4 Hz),
FAB:MS = [2M]Na$^+$ 623(2.14), 473(4.28), 345(17.14), [M]Na$^+$ 323(100), 200(10.7), 173(20),
Anal. calcd for $C_{18}H_{36}O_3$ (300.47); C, 71.95; H, 12.08. Found: C, 72.17; H, 12.10.

(2*S*,3*R*,4*E*)-1,3-*O*-Benzylideneoctadec-4-ene-1,2,3-trio1 (14):
To a solution of **13** (71 mg, 0.24 mmol) in CH_2Cl_2 (5 mL) was added *p*-toluenesulfonic acid (5 mg) and benzaldehyde dimethylacetal (0.043 g, 0.0425 mL, 0.28 mmol); the mixture was stirred at r.t. for 5 h. Subsequently it was neutralized with sat. aq $NaHCO_3$ (5 mL) and washed with aq $NaHSO_3$ to remove traces of benzaldehyde. The organic phase was separated, washed with H_2O, dried (Na_2SO_4) and concentrated. Column chromatography over silica gel using petroleum ether/acetone (9:1) furnished **14** as major product (55 mg, 60%). TLC (silica gel, petroleum ether/acetone, 9:1): R_f = 0.42; mp 56–57 °C; ref. 7: mp 54–55 °C. Spectroscopic properties (^{1}H NMR, Mass) were in accord with those described.[7]

This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. P. K. is grateful to the Alexander von Humboldtfoundation for a research fellowship.

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