Pergamon

Tetrahedron: *Asymmetry* 11 (2000) 1585–1592

TETRAHEDRON: *ASYMMETRY*

Enantioselective synthesis of *lyxo*-(2*R*,3*R*,4*R*)-C_{18}-phytosphingosine using double stereodifferentiation[1]

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Received 8 February 2000; accepted 17 March 2000

Abstract

lyxo-C_{18}-Phytosphingosine can be synthesized by the *cis*-dihydroxylation of an (*E*)-allylic trichloroacetamide obtained by an Overman rearrangement. A double stereodifferentiation using AD-mix-β and an enantiomerically enriched (*S*)-allylic trichloroacetamide allowed the first synthesis of *lyxo*-(2*R*,3*R*,4*R*)-C_{18}-phytosphingosine with high diastereoselectivity (de = 94%) and excellent enantioselectivity (ee = 93%). This sphingosine was fully characterized by the physical and spectral data of the corresponding tetraacetate.

1. Introduction

Sphingolipids constitute a class of widely ranging natural products in the membranes of eukaryotic cells and in all plasma membranes. These compounds, as well as some of their metabolites, are involved in a number of cellular events including cell growth, differentiation, adhesion and neuronal repair. They have also been shown to play critical roles as secondary messengers in cell signalling.[2] Many physiological processes can be affected by these molecules; however in many cases little is known about the precise function of individual sphingolipids in vivo and furthermore several sphingolipids seem to have not only one but several functions.

Structurally, sphingolipids are formed from two different units: a polar head group (carbohydrates) and a ceramide. The ceramide moiety consists of a sphingoid base (aminoalcohol) linked through an amide bond to a fatty acid. D-*erythro*-Sphingosine **1** is the most common sphingoid base found in the structure of sphingolipids of eukaryotic cells.[3] In addition to **1**, more than 60 other sphingoid base structures have been found in natural sphingolipids. Among them C_{18}-phytosphingosines **2**–**5** and their C_{16}–C_{22} homologues have been isolated from plants, fungi,

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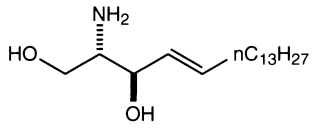
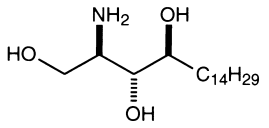
PII: S0957-4166(00)00106-3

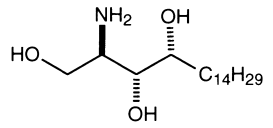
human tissues[4] and marine natural sources.[5] Due to the variety of their biological activities, a great deal of effort has been devoted recently towards the synthesis of sphingolipids and various methods have been developed for their preparation.



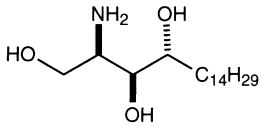
1 D-*erythro*-sphingosine



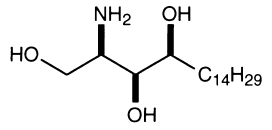
2 (*ribo*)



3 (*lyxo*)



4 (*arabino*)



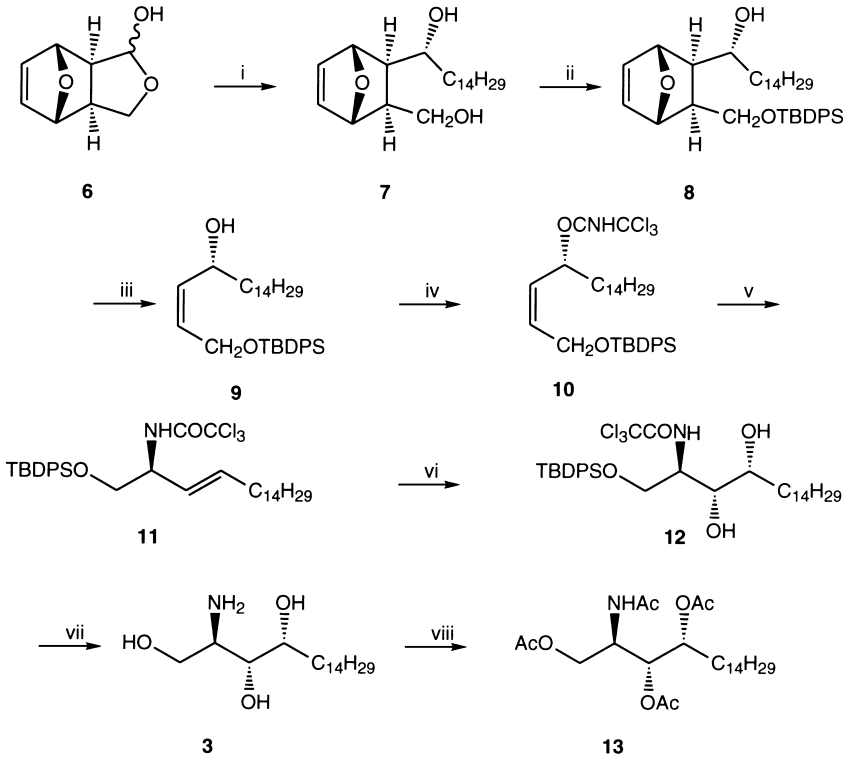
5 (*xylo*)

C_{18}-Phytosphingosines

2. Results and discussion

Previous synthetic studies have focused primarily on the preparation of *ribo*- or *arabino*-phytospingosins, the stereochemistry of the C_2 position being either derived from compounds of the chiral pool[6] or established by asymmetric synthesis.[7] To our knowledge, only six syntheses of *lyxo*- or *xylo*-phytosphingosines either racemic[8] or enantiomerically enriched[9] have been described to date. We have recently reported the synthesis and the rearrangement of (*Z*)-allylic trichloroacetimidates[10] starting from the lactol **6**, easily available in both enantiomeric forms, from the corresponding lactones.[11] The potential of this reaction is illustrated here by the enantioselective synthesis of *lyxo*-(2*R*,3*R*,4*R*)-C_{18}-phytosphingosine. The success of this synthesis depends on the excellent transfer of chirality observed during the rearrangement of allylic trichloroacetimidates to (*E*)-allylic amides[10] and on the diastereoselectivity of the *cis*-dihydroxylation of these (*E*)-allylic amides.[12] Our synthesis is depicted in Scheme 1.

Addition of tetradecylmagnesium bromide to enantiomerically enriched lactol **6** afforded the diol **7** with excellent diastereoselectivity (de = 90% as shown by ^{1}H NMR).[13] After protection of the primary hydroxy group as a *t*-butyldiphenylsilyl ether **8**, a retro Diels–Alder reaction, initiated by microwaves,[14] led quantitatively to the (*Z*)-allylic alcohol **9**. Microwaves were particularly useful for this cycloreversion since a quantitative yield was obtained within a few minutes (150°C, 30 min) while under heating (150°C, oil bath) the reaction proceeded to only 15% conversion after 30 minutes.



Scheme 1. Reagents and conditions: (i) $C_{14}H_{29}MgBr$, THF, 80%; (ii) TBDPSiCl, imidazole, DMF, 70%; (iii) microwaves, 100%; (iv) CCl_3CN, DBU, CH_2Cl_2; (v) xylenes, 140°C, 7 h, 81% for the two steps; (vi) AD-mix-β, 1% $K_2OsO_2(OH)_4$, $CH_3SO_2NH_2$, H_2O/*t*BuOH 1/1, 4 h, 80%; (vii) (a) nBu_4NF, THF, 4 h; (b) NaOH, H_2O/C_2H_5OH 1/1, 100°C, 16 h, 67% for the two steps; (viii) $(CH_3CO)_2O$, pyridine, DMAP (10 mol%), CH_2Cl_2, 6 h, 74%

Alcohol **9** was then reacted with trichloroacetonitrile in the presence of DBU to give the unstable trichloroacetimidate **10** which, without any purification, was thermally rearranged (refluxing xylenes)[15] into the (*E*)-allylic trichloroacetamide **11**. The enantiomeric purity of compound **11** (ee = 93%), determined by chiral HPLC (chiralcel OD-H column, hexane/*i*PrOH 99.5/0.5, 0.5 mL min^{-1}), suggests that the thermal transposition occurred with a total transfer of chirality. The next critical step was the diastereoselective dihydroxylation of the (*E*)-allylic amide **11**. Two main factors are likely to influence the stereochemical outcome of the osmium tetroxide dihydroxylation of the (*E*)-olefin **11**: (a) the configuration and the substitution of the olefinic double bond; and (b) the conformation of the stereogenic centre next to this double bond. Sharpless[16] and Kishi[17] have rationalized the stereochemical results arising from these two factors using empirical models which, in our case, can be represented by Fig. 1 and Fig. 2. Our experimental results are shown in Table 1.

The relative and absolute configurations of the major stereomer **12** have been established after its total deprotection to the (2*R*,3*R*,4*R*)-enantiomer of the known *lyxo*-(2*S*,3*S*,4*S*)-C_{18}-phytosphingosine and its chemical transformation to the corresponding tetraacetate **13**.[18] As shown in Table 1, the (*S*)-configuration of the stereogenic centre has only a small effect on the diastereoselectivity of the dihydroxylation (entries 1 and 2). However the stereochemical outcome of the dihydroxylation of (*S*)-**11** using OsO_4, NMO is in agreement with Kishi's empirical model

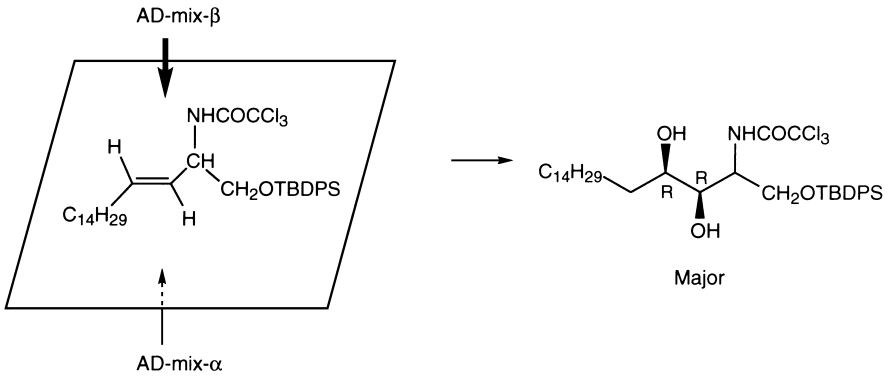


Figure 1. Empirical mnemonic device according to Sharpless[16]

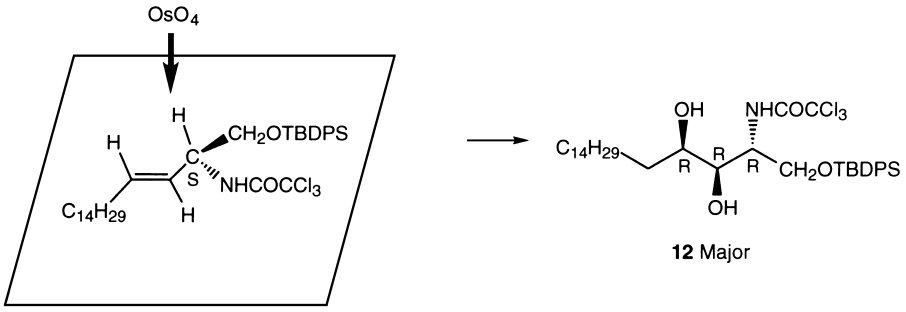
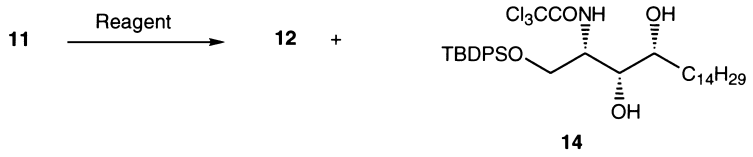


Figure 2. Reactant like empirical model according to Kishi[17]

Table 1
Dihydroxylation of olefin **11**



Entry	Substrate	Reagent	Ratio **12** / **14** [a]
1	rac-**11**	OsO_4, NMO	51 / 49
2	(*S*)-**11**	OsO_4, NMO	62 / 38
3	(*S*)-**11**	AD-mix-β 0.4 mol % Os	82 / 18
4	(*S*)-**11**	AD-mix-β 1.0 mol % Os	97 / 3

a) Ratio determined by ^{1}H NMR spectroscopy

(Fig. 2) so that the reagent approaches the face of the substrate which is also predicted by Sharpless's model for the reaction of (*S*)-**11** with AD-mix-β (Fig. 1). Thus, a double stereodifferentiation should occur for the reaction between (*S*)-**11** and AD-mix-β (matched pair). Effectively, in this case, a good diastereomeric excess was observed (entry 3), which could be further increased (de = 94%) by the use of a larger quantity of catalyst (entry 4).

Direct basic hydrolysis of the trichloroacetamide **12** gave only poor yields of the deprotected aminotriol, and the phytosphingosine **3** was best obtained by basic hydrolysis (KOH, H_2O/C_2H_5OH 1/1, 100°C, 15 h) of the oxazolidinone formed by the reaction of the silylated alcohol **12** with tetrabutylammonium fluoride in THF.[19] The aminotriol **3** was then easily peracylated to afford the tetraacetate **13**.

The absolute (2*R*,3*R*,4*R*)-configuration of **3**, arising from its mode of formation, was confirmed by the sign of its specific rotation which was opposite to the sign of rotation of the known (2*S*,3*S*,4*S*)-enantiomer.[9] The relative configuration of the three asymmetric carbons was established by comparison of the ^1H and ^{13}C NMR spectra of the corresponding tetraacetate **13** with the spectra of the known C_{16} analogue[6h] and of the very recently reported C_{18} enantiomer.[9c]

In conclusion, we have described in this paper an alternative route to enantiomerically enriched *lyxo*-phytosphingosines which could also be adapted to the synthesis of the *xylo*-enantiomers and which compares favourably with the existing methods.

3. Experimental

3.1. General

NMR spectra were recorded on a Bruker AM250 or AC200 spectrometer with tetramethylsilane as an internal standard. Optical rotations were measured on a Perkin–Elmer 241 polarimeter. Mass spectra were obtained with a GC–MS R.10-10 or a Finnigan MAT 95S spectrometer. Microwaves experiments were performed using a single mode reactor Prolabo Synthewave 402. Melting points are reported without correction. Elemental analyses were performed by the analytical centre of Gif/Yvette. All reactions were carried out under an inert atmosphere of argon and monitored by thin-layer chromatography (TLC). TLC was performed on Merck silica gel 60F-254 precoated on glass.

3.2. (1S,2S,3R,4R,1′R)-2-Hydroxymethyl-3-(1′-hydroxypentadecyl)-7-oxabicyclo[2.2.1]hept-5-ene 7

To a stirred solution of tetradecylmagnesium bromide (40 mmol) in THF (50 mL) was added at 0°C 1.54 g (10 mmol) of lactol **6**. The reaction mixture was allowed to reach room temperature and stirred for 4 h. After addition of a saturated ammonium chloride solution (50 mL), the organic layer was separated and the aqueous phase was extracted with dichloromethane (3×40 mL). The combined organic layers were dried ($MgSO_4$), concentrated and the residue purified by flash chromatography on silica gel (eluent: ether) to afford 2.82 g (80%) of a mixture of **7** (95%) and its (1*S*,2*S*,3*R*,4*R*,1′*S*)-diastereomer (5%). The spectral data for **7** follow. ^1H NMR (250 MHz, $CDCl_3$) δ: 0.94 (t, J = 7.0 Hz, 3H), 1.20–1.60 (m, 26H), 1.92 (m, 1H), 1.80 (dd, J = 8.6, 1.7 Hz, 1H), 3.80–4.10 (m, 5H), 5.0 (s, 1H), 5.11 (s, 1H), 6.49 (m, 2H).

3.3. (1S,2S,3R,4R,1′R)-2-(t-Butyldiphenylsilyloxymethyl)-3-(1′-hydroxypentadecyl)-7-oxabicyclo-[2.2.1]hept-5-ene **8**

To a stirred solution of *t*-butyldiphenylsilyl chloride (2.45 g, 8.9 mmol) and imidazole (1.26 g, 18.6 mmol) in dimethylformamide (5 mL) was added slowly at room temperature a solution of diol **7** (2.62 g, 7.44 mmol) in dimethylformamide (10 mL). The mixture was stirred for 1.5 h and diethyl ether (100 mL) was added. The organic phase was washed with water (3×20 mL) and dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica gel (pentane/ether, 50/40) to give 3.08 g (70%) of **8** as a colourless oil. $[\alpha]_D^{20}$+20.8 (c 1.0, CH_3OH); ^1H NMR (200 MHz, $CDCl_3$) δ: 0.89 (t, J = 7.0 Hz, 3H), 1.08 (s, 9H), 1.10–1.45 (m, 26H), 1.69 (dd, J = 8.6, 1.7 Hz, 1H), 1.87 (m, 1H), 2.93 (d, J = 3.2 Hz, 1H), 3.65 (m, 1H), 3.92 (m, 2H), 4.95 (s, 1H), 5.04 (s, 1H), 6.39 (m, 2H), 7.40 (m, 6H), 7.70 (m, 4H); ^{13}C NMR (63 MHz, $CDCl_3$) δ: 14.1, 19.2, 22.6, 26.5, 29.3, 29.6, 31.9, 37.9, 43.1, 43.5, 63.7, 68.7, 79.1, 79.9, 127.7, 129.7, 133.3, 134.8, 134.9, 135.5, 136.9; CIMS (NH_3) *m*/*z* (relative intensity) 608 (MNH_4^+, 48), 591 (MH^+, 100). Anal. calcd for $C_{38}H_{58}O_3Si$: C, 77.23; H, 9.90. Found: C, 77.16; H, 9.93.

3.4. (4R,2Z)-1-(t-Butyldiphenylsilyloxy-2-octadecen-4-ol **9**

Compound **8** (3 g, 5.1 mmol) was placed in a Pyrex open tube allowing the evaporation of furan and was irradiated for 30 minutes in a microwave oven at 150°C. After cooling to room temperature, 2.65 g (100%) of pure unsaturated alcohol **9** was obtained. $[\alpha]_D^{20}$+7.8 (c 1.05, CH_3OH); ^1H NMR (250 MHz, $CDCl_3$) δ: 0.92 (t, J = 6.8 Hz, 3H), 1.10 (s, 9H), 1.20–1.40 (m, 24H), 1.40–1.60 (m, 2H), 4.10–4.40 (m, 3H), 5.46 (dd, J = 11.1, 11.1 Hz, 1H), 5.70 (dt, J = 11.1, 5.5 Hz, 1H), 7.45 (m, 6H), 7.70 (m, 4H); ^{13}C NMR (63 MHz, $CDCl_3$) δ: 14.6, 19.5, 23.1, 25.7, 27.2, 29.8, 30.0, 37.5, 60.7, 68.1, 128.1, 130.2, 130.6, 134.6, 135.9, 136.0; CIMS (NH_3) *m*/*z* (relative intensity) 540 (MNH_4^+, 3), 523 (MH^+, 17), 522 (M^+, 28), 506 (54), 505 (100). Anal. calcd for $C_{34}H_{54}O_2Si$: C, 78.10; H, 10.41. Found: C, 78.32; H, 10.23.

3.5. (2S,3E)-1-t-Butyldiphenylsilyloxy-2-trichloroacetylamino-3-octadecene **11**

To a stirred solution of alcohol **9** (2.30 g, 4.4 mmol) in dichloromethane (70 mL) were added successively at –5°C diazabicycloundecene (1 g, 6.6 mmol) and trichloroacetonitrile (1.14 g, 7.9 mmol). The solution was stirred at –5°C for an additional 1 h and the reaction mixture was quenched by addition of saturated aqueous solution of ammonium chloride (30 mL). After decantation, the organic phase was filtered on sodium sulfate and silica gel. The solvent was removed under reduced pressure to give crude acetimidate **10** which without any purification was dissolved in xylenes (100 mL). The solution was refluxed for 7 h and the solvents were removed under reduced pressure. The residue was purified by flash chromatography on silica gel (pentane/ether, 90/10) to give 2.38 g (81% from **9**) of the trichloroacetamide **11** as a colourless oil. $[\alpha]_D^{20}$+4.2 (c 1.7, MeOH); ^1H NMR (250 MHz, $CDCl_3$) δ: 0.89 (t, J = 6.8 Hz, 3H), 1.07 (s, 9H), 1.10–1.45 (m, 24H), 2.05 (m, 2H), 3.72 (dd, J = 10.2, 3.7 Hz, 1H), 3.83 (dd, J = 10.2, 3.7 Hz, 1H), 4.46 (m, 1H), 5.47 (dd, J = 15.5, 6.2 Hz, 1H), 5.73 (dt, J = 15.5, 5.7 Hz, 1H), 7.40 (m, 6H), 7.70 (m, 4H); ^{13}C NMR (63 MHz, $CDCl_3$) δ: 14.1, 19.2, 22.7, 26.7, 28.9, 29.1, 29.3, 29.5, 29.6, 29.7, 31.9, 32.3, 54.2, 65.5, 92.9, 125.5, 127.8, 129.9, 132.6, 134.3, 135.5, 161.0; CIMS (NH_3) *m*/*z* (relative intensity) 683, 685, 687, 689 (MNH_4^+, 98, 100, 37, 9), 666, 668, 670, 672 (MH^+, 74, 93, 34, 6). Anal. calcd for $C_{36}H_{54}Cl_3NO_2Si$: C, 64.93; H, 8.18; N, 2.10. Found: C, 65.07; H, 8.31; N, 2.14.

3.6. (2R,3R,4R)-1-t-Butyldiphenylsilyloxy-2-trichloroacetylamino-3,4-octadecanediol **12**

To a mixture of *tert*-butylalcohol (5 mL) and water (5 mL) was added AD-mix-β (1.4 g), $K_2OsO_2(OH)_4$ (3.6 mg, 0.01 mmol) and $MeSO_2NH_2$ (95 mg, 1 mmol). The solution was cooled to 0°C, olefin **11** (665 mg, 1 mmol) was added and the reaction mixture was stirred at room temperature for 4 h, quenched with sodium sulfite (1.5 g) and extracted with dichloromethane (6×20 mL). The organic phase was dried over magnesium sulfate and the solvents were removed under reduced pressure. The residue was purified by flash chromatography on silica gel (ether) to afford 560 mg (80%) of **12** as a colourless oil. $[\alpha]_D^{20}$ –3.7 (c 0.83, CH_3OH); ^{1}H NMR (250 MHz, $CDCl_3$) δ: 0.89 (t, J = 6.8 Hz, 3H), 1.09 (s, 9H), 1.15–1.50 (m, 26H), 2.35 (d, J = 14 Hz, 1H), 3.12 (d, J = 5 Hz, 1H), 3.65 (m, 2H), 3.82 (m, 2H), 4.24 (d, J = 13 Hz, 1H), 7.40 (m, 6H), 7.70 (m, 4H); ^{13}C NMR (63 MHz, $CDCl_3$) δ: 14.1, 19.2, 22.7, 26.8, 28.9, 29.3, 29.4, 31.9, 32.8, 54.3, 61.8, 69.7, 71.6, 92.9, 127.9, 130.1, 132.0, 132.3, 135.4, 135.5, 163.2; CIMS (NH_3) *m*/*z* (relative intensity) 717, 719, 721, 723 (MNH_4^+, 46, 48, 37, 15), 700, 702, 704, 706 (MH^+, 49, 51, 31, 15). Anal. calcd for $C_{36}H_{56}Cl_3NO_4Si$: C, 61.78; H, 8.07; H, 2.0. Found: C, 61.67; H, 8.12; N, 1.91.

3.7. (2R,3R,4R)-2-Aminooctadecane-1,3,4-triol **3**

To a solution of compound **12** (140 mg, 0.2 mmol) in dry THF (5 mL) was added 400 μl (0.4 mmol) of a 1 M solution of tetrabutylammonium fluoride in THF. The solution was stirred for 4 h at room temperature. The solvent was removed under reduced pressure and to the residue was added a solution of NaOH (400 mg) in a mixture of water (2.5 mL) and ethanol (2.5 mL). The reaction mixture was stirred at 100°C for 16 h, cooled to room temperature and poured into water (15 mL). The aqueous phase was extracted with ether (10×15 mL). The organic phase was dried over magnesium sulfate and the solvent was removed under reduced pressure. Chromatography of the residue on silica gel (CH_2Cl_2/MeOH/NH_4OH, 4/1/0.1) gave 43 mg (67%) of triol **3** as a white powder. $[\alpha]_D^{20}$+7.7, (c 1.4, pyridine) [lit.,[9c] $[\alpha]_D^{20}$–7.8 (c 0.46, pyridine), lit.,[6a] $[\alpha]_D^{20}$–7.1 (c 0.4, pyridine) for enantiomer]; mp 95–96°C [lit.,[6a] mp 96–98°C for enantiomer].

3.8. (2R,3R,4R)-2-Acetamino-1,3,4-triacetoxyoctadecane **13**

To a solution of 32 mg (0.1 mmol) of triol **3** in dichloromethane (10 mL) were added acetic anhydride (1 mL), pyridine (1 mL) and DMAP (5 mg). The reaction mixture was stirred for 6 h and water (15 mL) was added. After decantation, the aqueous phase was extracted with dichloromethane (3×10 mL). The organic phase was washed with 20 mL of water and dried over magnesium sulfate. The solvent and excess of reagents were removed under reduced pressure (10^{-2} torr) and the residue was purified by chromatography on silica gel (CH_3CO_2Et/pentane, 65/35) to afford 36 mg (74%) of the tetraacetate **13** as a colourless solid. $[\alpha]_D^{20}$+4.3 (c 0.5, $CHCl_3$) [lit.,[9c] $[\alpha]_D^{20}$–3.1 (c 1.1, $CHCl_3$) for the enantiomer]; mp 74°C; IR 3430, 3372, 1740, 1685 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ: 0.88 (t, J = 6.7 Hz, 3H), 1.25 (m, 24H), 1.50 (m, 2H), 1.98 (s, 3H), 2.07 (s, 3H), 2.10 (s, 3H), 2.13 (s, 3H), 3.96 (dd, J = 11.7, 3.2 Hz, 1H), 4.24 (dd, J = 11.7, 4.5 Hz, 1H), 4.54 (m, 1H), 5.09 (m, 2H), 5.71 (d, J = 9.7 Hz, 1H); ^{13}C NMR (63 MHz, $CDCl_3$) δ: 14.1, 20.7, 20.8, 21.0, 22.7, 23.3, 25.2, 29.4, 29.5, 29.7, 30.9, 31.9, 47.4, 63.1, 71.2, 71.9, 169.6, 170.3, 170.6, 170.8; CIMS (NH_3) *m*/*z* (relative intensity) 486 (MH^+, 100), 485 (M^+, 8), 426 (7), 144 (12). Anal. calcd for $C_{26}H_{47}O_7N$: C, 64.30; H, 9.75; N, 2.88. Found: C, 64.19; H, 9.71; N, 2.55.

References

1. This work is part of the PhD thesis of C. Martin, Orsay, December 1998.
2. Reviews: (a) Merrill Jr., A. H.; Sweeley, C. C. In *Biochemistry of Lipids, Lipoproteins and Membranes*; Vance, D. E.; Vance, J. E., Eds.; Elsevier Science: Amsterdam, 1996; Chapter 12, pp. 309–339; (b) Koskinen, P. M.; Koskinen, A. M. P. *Synthesis* **1998**, 1075–1091; (c) Kolter, T.; Sandhoff, K. *Angew. Chem., Int. Ed.* **1999**, *38*, 1532–1568.
3. For D-*erythro*-sphingosine synthesis, see: (a) Ref. 2b; (b) Nugent, T. C.; Hudlicky, T. *J. Org. Chem.* **1998**, *63*, 510–520; (c) Hoffman, R. V.; Tao, J. *Tetrahedron Lett.* **1998**, *39*, 3953–3956; (d) Hoffman, R. V.; Tao, J. *J. Org. Chem.* **1998**, *63*, 3979–3985; (e) Khiar, N.; Singh, K.; Garcia, M.; Martin-Lomas, M. *Tetrahedron Lett.* **1999**, *40*, 5779–5782; (f) Hertweck, C.; Boland, W. *J. Org. Chem.* **1999**, *64*, 4426–4430 and references cited therein.
4. Murakami, T.; Taguchi, K. *Tetrahedron* **1999**, *55*, 989–1004 and references cited therein.
5. Higuchi, R.; Kagoshima, M.; Komori, T. *Liebigs Ann. Chem.* **1988**, 19–24.
6. (a) Prostenik, M.; Majhofer-Orescanin, B.; Ries-Lesic, B.; Stanacev, N. Z. *Tetrahedron* **1965**, *21*, 651–655; (b) Gigg, J.; Gigg, R.; Warren, C. D. *J. Chem. Soc. (C)* **1966**, 1872–1876; (c) Gigg, J.; Gigg, R. *J. Chem. Soc. (C)* **1966**, 1876–1878; (d) Mulzer, J.; Brand, C. *Tetrahedron* **1986**, *42*, 5961–5968; (e) Sugiyama, S.; Honda, M.; Komori, T. *Liebigs Ann. Chem.* **1988**, 619–625; (f) Schmidt, R. R.; Maier, T. *Carbohydr. Res.* **1988**, *174*, 169–179; (g) Guanti, G.; Banfi, L.; Narisano, E. *Tetrahedron Lett.* **1989**, *30*, 5507–5510; (h) Sugiyama, S.; Honda, M.; Komori, T. *Liebigs Ann. Chem.* **1990**, 1069–1078; (i) Dondoni, A.; Fantin, G.; Fogagnolo, M.; Pedrini, P. *J. Org. Chem.* **1990**, *55*, 1439–1446; (j) Wild, R.; Schmidt, R. R. *Tetrahedron: Asymmetry* **1994**, *5*, 2195–2208; (k) Murakami, T.; Minamikawa, H.; Hato, M. *Tetrahedron Lett.* **1994**, *35*, 745–748; (l) Nakashima, H.; Hirata, N.; Iwamura, T.; Yamagiwa, Y.; Kamikawa, T. *J. Chem. Soc., Perkin Trans. 1* **1994**, 2849–2857; (m) Matsumoto, K.; Ebatu, T.; Matsushita, H. *Carbohydr. Res.* **1995**, *279*, 93–106; (n) Wild, R.; Schmidt, R. R. *Liebigs Ann. Chem.* **1995**, 755–764; (o) Li, Y. L.; Mao, X. H.; Wu, Y. L. *J. Chem. Soc., Perkin Trans. 1* **1995**, 1559–1563; (p) Kemp, S. J.; Bao, J.; Pedersen, S. F. *J. Org. Chem.* **1996**, *61*, 7162–7167; (q) Yoda, H.; Oguchi, T.; Takabe, K. *Tetrahedron: Asymmetry* **1996**, *7*, 2113–2116; (r) Shimizu, M.; Wakioka, I.; Fujisawa, T. *Tetrahedron Lett.* **1997**, *38*, 6027–6030; (s) Imashiro, R.; Sakurai, O.; Yamashita, T.; Horikawa, H. *Tetrahedron* **1998**, *54*, 10657–10670; (t) Takikawa, H.; Muto, S.; Mori, K. *Tetrahedron* **1998**, *54*, 3141–3150; (u) Li, S.; Pang, J.; Wilson; W. K.; Schroepfer Jr., J. *Tetrahedron: Asymmetry* **1999**, *10*, 1697–1707; (v) Murakami, T.; Toguchi, K. *Tetrahedron* **1999**, *55*, 989–1004.
7. (a) Kobayashi, S.; Hayashi, T.; Kawasuji, T. *Tetrahedron Lett.* **1994**, *35*, 9573–9576; (b) Lin, G. Q.; Shi, Z. C. *Tetrahedron* **1996**, *52*, 2187–2192; (c) Murakami, M.; Ito, H.; Ito, Y. *Chem. Lett.* **1996**, 185–186; (d) Wee, A. G. H.; Tang, F. *Tetrahedron Lett.* **1996**, *37*, 6677–6680.
8. Sisido, K.; Tamura, H.; Kobata, H.; Takagisi, M.; Isida, T. *J. Org. Chem.* **1970**, *35*, 350–353.
9. (a) See Ref. 6(f), (h), (o); (b) Nakamura, T.; Shiozaki, M. *Tetrahedron Lett.* **1999**, *40*, 9063–9064; (c) Shirota, O.; Nakanishi, K.; Berova, N. *Tetrahedron* **1999**, *55*, 13643–13658.
10. Martin, C.; Bortolussi, M.; Bloch, R. *Tetrahedron Lett.* **1999**, *40*, 3735–3736.
11. Bloch, R.; Guibé-Jampel, E.; Girard, C. *Tetrahedron Lett.* **1985**, *26*, 4086–4090.
12. As this work was in progress, a similar dihydroxylation of (*Z*)-allylic amides leading to *ribo*- and *arabino*-phytosphingosins has been reported, see Ref. 6(s). Our method giving access to the *lyxo*- or the *xylo*-diastereomers appears to be complementary with the one described in this reference.
13. Bloch, R.; Mandville G. In *Recent Research Developments in Organic Chemistry*; Pandalai, S. G., Ed.; Transworld Research Network, Trivandrum: India, 1998; Tome 2, pp. 441–452.
14. Bortolussi, M.; Bloch, R.; Loupy, A. *J. Chem. Research (S)* **1998**, *50*, 34–35.
15. (a) Overman, L. E. *J. Am. Chem. Soc.* **1976**, *98*, 2901–2910; (b) Imogaï, H.; Petit, Y.; Larchevêque, M. *Synlett* **1997**, 615–617.
16. Kolb, H. C.; VanNieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, *94*, 2483–2547.
17. Cha, J. K.; Christ, N. J.; Kishi, Y. *Tetrahedron* **1984**, *40*, 2247–2255. See also: Vedejs, E.; Mc Clure, C. K. *J. Am. Chem. Soc.* **1986**, *108*, 1094–1096.
18. The relative configuration of the minor isomer **14** (racemic) has also been determined after its transformation to the tetraacetate of the C_{18}-*xylo*-phytosphingosine (±)-**5** and comparison of its ^{1}H and ^{13}C NMR spectra with the spectra of the known C_{16} analogue, Ref. 6(h).
19. Mehmandoust, M.; Petit, Y.; Larchevêque, M. *Tetrahedron Lett.* **1992**, *33*, 4313–4316.