Tetrahedron: *Asymmetry* 20 (2009) 1164–1167

Contents lists available at ScienceDirect

Tetrahedron: *Asymmetry*

journal homepage: www.elsevier.com/locate/tetasy

# A chemoenzymatic asymmetric synthesis of methyl (6*S*,13*R*)-6,13-dihydroxy-tetradeca-(2*E*,4*E*,8*E*)-trienoate, a component of *Mycosphaerella rubella*

Anubha Sharma *, Sunita Gamre, Subrata Chattopadhyay

*Bio-Organic Division, Bhabha Atomic Research Centre, Mumbai 400 085, India*

ARTICLE INFO

*Article history:*
Received 26 February 2009
Accepted 17 April 2009
Available online 22 May 2009

ABSTRACT

The first asymmetric synthesis of (6*S*,13*R*)-6,13-dihydroxytetradeca-(2*E*,4*E*,8*E*)-trienoate has been developed. The key steps of the synthesis were the use of an efficient lipase-catalyzed acylation, a chiral template-driven enantiocontrolled allylation for introducing the stereogenic centers, and a cross-metathesis for controlling the C-8 olefin geometry.



## 1. Introduction

Hydroxy acids and the macrolides derived from them are of wide occurrence in various natural sources; several of these show impressive biological activity. For example, the $C_{18}$-hydroxy acids with diverse oxygenation patterns have been reported to be cytotoxic against HeLa cells,[1a] and P388 mouse leukemic cells.[1b] Earlier, the encouraging anti-cancer activity of a ketohydroxy acid, obtained[1c] from corn, prompted us to develop its enantioselective synthesis.[2] Likewise, the isolation of a new hydroxytetradecatrienoic acid growth inhibitor from *Valsa ambiens*,[3a] and that of other antiviral hydroxylated unsaturated fatty acids from the Basidiomycete, *Filoboletus*, have been described.[3b] The fungi in the genus *Mycosphaerella* includes many phytopathogenic species which are sources of interesting metabolites; some of these compounds exhibit interesting pharmacological activities.[4] For example, the novel anthraquinone metabolites of rubellins A–D,[5a,b] and a phenanthrenequinone, biruloquinone[5c] have been isolated from *Mycosphaerella rubella* (the causal agent of a disease of *Angelica sih, estris*). More recently, methyl (6*S*,13*R*)-6,13-dihydroxytetradeca-(2*E*,4*E*,8*E*)-trienoate **14**, and the corresponding hydroxy acid **15**, along with some other derivatives, have been isolated from the ethyl acetate extracts of the same fungus.[5d] Compound **15** showed weak antibacterial activity (100 μg per disc) against *Sarcina lutea, Bacillus cereus*, and *Bacillus subtilis*, but not against *Escherichia coli* and *Saccharomyces cerevisiae*. For the past few years we have extensively used the easily available (*R*)-cyclohexylideneglyceraldehyde for the syntheses of a diverse array of bioactive compounds. Herein, we report the first synthesis of (6*S*,13*R*)-**14** using the same chiral pool material and invoking a lipase-catalyzed asymmetric strategy for the generation of the C-13 stereogenic center.

## 2. Results and discussion

For the synthesis, acetaldehyde was reacted with the Grignard reagent prepared from 5-bromopentene to furnish (±)-**2**. For its resolution, a lipase-catalyzed *trans*-acetylation appeared promising. Lipases are currently widely used in asymmetric organic synthesis, since they do not require any cofactor, operate on a wide range of substrates, retain good catalytic activity in different media, display good stereoselectivity, and are commercially available in free form as well as in immobilized form.[6a–c] We were particularly interested in the lipase preparation, Novozyme 435® which is inexpensive, robust, and effective in resolving racemic carbinols and amines.[6d] Although the above lipase is generally effective in resolving linear secondary alcohols, the enantioselectivity is known to be governed by reaction conditions such as solvent used and/or acyl donor.[7a–c]

For our studies, we used the inexpensive acyl donor, vinyl acetate and carried out the resolution in diisopropyl ether. True to our expectation, alcohol **2** could be efficiently resolved under these conditions to obtain (*R*)-acetate **3** (96% ee) and (*S*)-**2** (87% ee) after 44% conversion (cf. GC, 1 h). Alkaline hydrolysis of acetate (*R*)-**3** with KOH/MeOH furnished alcohol (*R*)-**2**. The resolved alcohol (*S*)-**2** could be enantiomerically enriched to 98% ee by a second Novozyme 435®-catalyzed acetylation (10% conversion) as described above. This was subsequently converted to its antipode under Mitsunobu conditions (*p*-nitrobenzoic acid/$Ph_3P$/DEAD/THF, 92%).[8] The enantiomeric excesses of the enantiomeric alcohols (*R*)-**2** and (*S*)-**2** were determined from the relative intensities of the methoxyl resonances of the corresponding α-methoxytrifluoromethyl phenyl acetates (MTPAs), prepared using with (*R*)-MTPA chloride.[9] The configurations of the alcohols were assigned by converting a small aliquot of the respective alkenol enantiomers into heptan-2-ol enantiomers and by comparing their specific rotations with those reported for the authentic samples.[10]

* Corresponding author. Tel.: +91 22 25590267; fax: + 91 22 25505151.
*E-mail address:* anubhas@barc.gov.in (A. Sharma).

0957-4166/$ - see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetasy.2009.04.004

Alcohol (*R*)-**2** was silylated with *tert*-butyldiphenylsilyl chloride (TBDPSCl) in the presence of 4-dimethylaminopyridine (DMAP) to furnish **4**. This was subjected to a cross-metathesis reaction with the known[11] homoallylic alcohol **5**, obtained by an enantioselective Zn-mediated Barbier type allylation of (*R*)-cyclohexylideneglyceraldehyde. The reaction proceeded smoothly in the presence of Grubbs–Hoveyda second generation catalyst to furnish the desired alcohol **6** (63%) along with the homo-coupled products of the starting olefins (together 24%). However, the Grubbs' first and second generation catalysts did not produce any product. The *E*-geometry of the olefin **6** was ascertained from its $^1$H NMR spectrum. Generally, increasing steric bulk through the addition of a hydroxyl protection reduces the cross-metathesis reactivity of the alkenols.[12a] Given that substrate **5** already contained a bulky cyclohexylidene group adjacent to the carbinol functionality, we preferred to use free alcohol **5** for the cross-metathesis reaction. Also, higher *E*-selectivity has been reported when the cross-metathesis is carried with olefinic alcohols.[12b]

Silylation of **6** with TBDPSCl/DMAP produced compound **7**, which on treatment with aqueous trifluoroacetic acid (TFA) furnished diol **8**. Cleavage of the diol function of **8** with $NaIO_4$ afforded aldehyde **9**. The other required achiral unit **12** was prepared as follows. Bromination of *E*-crotonic acid **10** with *N*-bromosuccinimide (NBS) followed by esterification gave the bromoester **11**, which on heating with triethyl phosphite furnished phosphonate **12**. Its base-catalyzed reaction with the aldehyde **9** produced the conjugated ester **13**. This on desilylation with $Bu_4NF$ afforded the target natural ester **14** (Scheme 1).

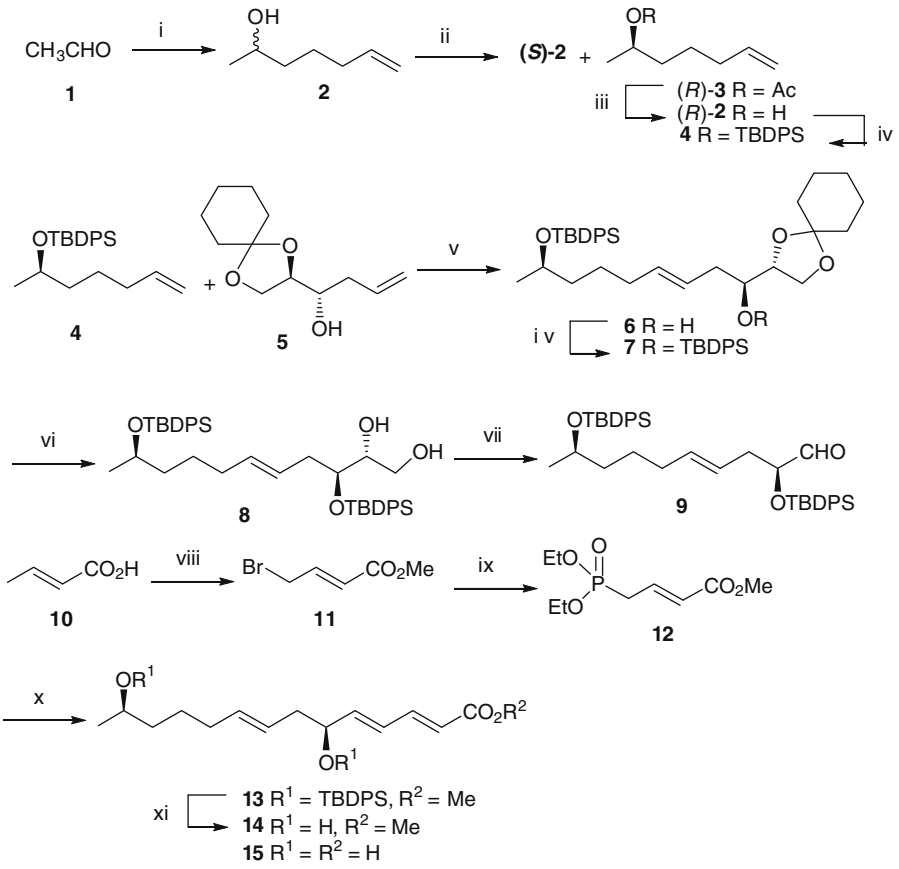
## 3. Experimental

### 3.1. General experimental details

All chemicals (Fluka and Lancaster) were used as received. Other reagents were of AR grade. All anhydrous reactions were carried out under an Ar atmosphere using freshly dried solvents. Unless otherwise mentioned, the organic extracts were dried over anhydrous $Na_2SO_4$. The IR spectra as thin films were scanned with a Jasco model A-202 FT-IR spectrophotometer. The $^1$H NMR (200 MHz) and $^{13}$C NMR (50 MHz) spectra were recorded with a Bruker AC-200 spectrometer. The optical rotations were recorded with a Jasco DIP 360 digital polarimeter.

### 3.2. (±)-6-Hepten-2-ol 2

To a stirred solution of the Grignard reagent prepared from 5-bromo-1-pentene (15.92 g, 0.107 mol) and Mg (3.09 g, 0.128 mol) in THF (80 mL), was added acetaldehyde (4.7 g, 0.107 mmol) in THF (20 mL). After stirring for 3 h, the mixture was treated with saturated aqueous $NH_4Cl$, and the organic layer was separated and the aqueous portion was extracted with $Et_2O$. The combined organic extracts were washed with water and brine, dried, and concentrated in vacuo. The residue was purified by column chromatography (silica gel, 0–10% $Et_2O$/hexane) to afford pure **2**. Yield: 9.15 g (75%); IR: 3373, 1642 cm$^{-1}$; $^1$H NMR: $\delta$ 1.18 (d, $J$ = 6.4 Hz, 3H), 1.43–1.46 (m, 4H), 1.83 (br s, 1H), 2.04–2.07 (m, 2H), 3.75–3.81 (m, 1H), 4.91–5.03 (m, 2H), 5.69–5.90 (m, 1H); $^{13}$C NMR: $\delta$




**Scheme 1.** Reagents and conditions: (i) $CH_2$=$CH(CH_2)_3MgBr$/THF/25 °C/3 h (75%); (ii) vinyl acetate/Novozyme 435/diisopropyl ether/25 °C/1 h (40%); (iii) KOH/MeOH/25 °C/6 h (88%); (iv) TBDPSCl/imidazole/DMAP/$CH_2Cl_2$/25 °C (**4**: 83%; **7**: 88%); (v) Grubbs–Hoveyda second generation catalyst/$CH_2Cl_2$/25 °C/4 h (63%); (vi) aqueous TFA/0 °C/3 h (88%); (vii) $NaIO_4$/$CH_3CN$–$H_2O$/2 h/2 h (91%); (viii) NBS/$CCl_4$; MeOH/$H_2SO_4$/Δ; (ix) $P(OEt)_3$/Δ; (x) NaH/THF/**9**/25 °C/18 h (79%); (xi) $Bu_4NF$/THF/0 °C/12 h (87%).

23.2, 24.9, 33.5, 38.5, 67.6, 114.3, 138.5. Anal. Calcd for $C_7H_{14}O$: C, 73.63; H, 12.36. Found: C, 73.59; H, 12.24.

### 3.3. (*R*)-2-Acetoxyhept-6-ene (*R*)-3

A mixture of (±)-**2** (0.912 g, 8.0 mmol), vinyl acetate (0.90 mL, 9.6 mmol), and Novozyme 435® (0.05 g) in diisopropyl ether (20 mL) was agitated on an orbital shaker at 110 rpm for 1 h. The reaction mixture was filtered, and the solution was concentrated in vacuo to get a residue, which on chromatography (silica gel, 0–10% EtOAc/hexane) gave pure (*S*)-**2** and (*R*)-**3**. Compound (*S*)-**2**: Yield: 0.401 g (44%); colorless oil; $[\alpha]_D^{22} = +6.2$ (*c* 1.0, $CHCl_3$). Compound (*R*)-**3**: Yield: 0.500 g (40%); colorless oil; $[\alpha]_D^{22} = -1.5$ (*c* 1.58, $CHCl_3$); IR: 1736, 1243 $cm^{-1}$; $^1H$ NMR: $\delta$ 1.22 (d, *J* = 7.0 Hz, 3H), 1.40–1.46 (m, 4H), 1.98–2.10 (m containing a s at $\delta$ 2.0, 5H), 4.84–4.97 (m, 3H), 5.71–5.84 (m, 1H); $^{13}C$ NMR: $\delta$ 21.0, 37.8, 39.8, 73.6, 117.8, 138.8, 170.3. Anal. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 69.05; H, 10.40.

### 3.4. (*R*)-6-Hepten-2-ol (*R*)-2

A mixture of (*R*)-**3** (2.34 g, 15 mmol) and KOH (1.68 g, 30 mmol) in MeOH (25 mL) was stirred at room temperature for 6 h. The mixture was filtered, and concentrated in vacuo, after which water was added to it, and extracted with EtOAc. The organic layer was washed with water and brine, and dried. Removal of the solvent in vacuo followed by column chromatography of the residue (silica gel, 0–10% EtOAc/hexane) afforded pure (*R*)-**2**. Yield: 1.50 g (88%); colorless oil; $[\alpha]_D^{22} = -6.8$ (*c* 1.22, $CHCl_3$).

### 3.5. (*R*)-2-(*tert*)-Butyldiphenylsilyloxy-6-heptene (*R*)-4

To a stirred and cooled (−30 °C) solution of a mixture of (*R*)-**2** (1.20 g, 10.52 mmol), imidazole (0.857 g, 12.60 mmol), and DMAP (catalytic) in $CH_2Cl_2$ (20 mL) was dropwise added TBDPSCl (3.47 g, 12.60 mmol) in $CH_2Cl_2$ (15 mL). After stirring the mixture for 7 h at room temperature, it was poured into ice-cold water. The organic layer was separated and the aqueous portion was extracted with $CHCl_3$. The combined organic extracts were washed with water and brine, and dried. Removal of solvent in vacuo followed by purification of the residue by column chromatography (silica gel, 0–5% EtOAc/hexane) afforded pure **4**. Yield: 3.07 g (83%); colorless oil; $[\alpha]_D^{22} = +13.2$ (*c* 1.14, $CHCl_3$); IR: 3050, 1642 $cm^{-1}$; $^1H$ NMR: $\delta$ 1.17 (merged s and d, *J* = 6.8 Hz, 12H), 1.26–1.49 (m, 4H), 1.93–1.96 (m, 2H), 3.81–3.86 (m, 1H), 4.87–4.98 (m, 2H), 5.65–5.85 (m, 1H), 7.36–7.46 (m, 6H), 7.66–7.70 (m, 4H); $^{13}C$ NMR: $\delta$ 19.3, 23.2, 24.5, 27.1, 33.7, 38.9, 69.4, 114.3, 127.4, 127.5, 129.4, 134.4, 135.9, 138.9. Anal. Calcd for $C_{23}H_{32}OSi$: C, 78.35; H, 9.15. Found: C, 78.51; H, 9.32.

### 3.6. (2*R*,3*S*,10*R*)-10-(*tert*)-Butyldiphenylsilyloxy-1, 2-cyclohexanedioxyundec-5*E*-en-3-ol (2*R*,3*S*,10*R*)-6

A mixture of **4** (0.680 g, 1.93 mmol), alcohol **5** (0.409 g, 1.93 mmol), and Grubbs–Hoveyda second generation catalyst (5 mol %) in $CH_2Cl_2$ (10 mL) was stirred for 4 h. After concentrating the mixture in vacuo, the residue was subjected to column chromatography (silica gel, 0–15% EtOAc/hexane) to give pure **6**. Yield: 0.651 g (63%); colorless oil; $[\alpha]_D^{22} = +18.8$ (*c* 1.04, $CHCl_3$); IR: 3307, 1642, 967 $cm^{-1}$; $^1H$ NMR: $\delta$ 1.15 (merged s and d, *J* = 6.8 Hz, 12H), 1.38–1.48 (m, 6H), 1.58–1.61 (m, 8H), 1.99–1.95 (m, 2H), 2.14–2.22 (m, 2H), 3.68–3.71 (m, 1H), 3.80–3.88 (m, 2H), 3.93–4.00 (m, 2H), 5.33–5.51 (m, 2H), 7.25–7.44 (m, 6H), 7.64–7.73 (m, 4H); $^{13}C$ NMR: $\delta$ 19.2, 23.2, 23.8, 24.0., 24.9, 27.0, 32.5, 34.8, 36.2, 38.9, 64.9, 69.3, 70.7, 78.1, 109.8, 125.0, 127.3, 127.4, 129.4, 134.0, 134.3, 135.5, 135.8. Anal. Calcd for $C_{33}H_{48}O_4Si$: C, 73.83; H, 9.01. Found: C, 73.62; H, 8.78.

### 3.7. (2*R*,3*S*,10*R*)-3,10-Di-(*tert*-butyldiphenylsilyloxy)-1, 2-cyclohexanedioxyundec-5*E*-ene (2*R*,3*S*,10*R*)-7

As described earlier, the silylation of **6** (0.780 g, 1.46 mmol) with TBDPSCl (0.44 mL, 1.96 mmol) in the presence of imidazole (0.118 g, 1.04 mmol) and DMAP (catalytic) in $CH_2Cl_2$ (20 mL) followed by purification (column chromatography, silica gel, 0–10% EtOAc/hexane) furnished pure **7**. Yield: 1.0 g (88%); colorless oil; $[\alpha]_D^{22} = +24.6$ (*c* 1.12, $CHCl_3$); IR: 1660, 1461, 970 $cm^{-1}$; $^1H$ NMR: $\delta$ 1.12 (merged s and d, *J* = 6.4 Hz, 21H), 1.24–1.43 (m, 6H), 1.53–1.57 (m, 8H), 1.76–1.78 (m, 2H), 2.03–2.06 (m, 2H) 3.72–3.78 (m, 2H), 3.83–3.89 (m, 2H), 3.93–4.02 (m, 1H), 5.16–5.22 (m, 2H), 7.25–7.44 (m, 12H), 7.64–7.67 (m, 8H); $^{13}C$ NMR: $\delta$ 19.3, 19.5, 23.4, 24.0, 24.1, 25.4, 27.2, 33.2, 35.0, 36.3, 39.1, 65.9, 69.5, 73.5, 77.8, 109.3, 125.0, 127.6, 129.6, 129.8, 134.3, 134.6, 134.9, 135.9, 136.1. Anal. Calcd for $C_{49}H_{66}O_4Si_2$: C, 75.92; H, 8.58. Found: C, 75.71; H, 8.39.

### 3.8. (2*R*,3*S*,10*R*)-3,10-Di-(*tert*-butyldiphenylsilyloxy)undec-5*E*-ene-1,2-diol (2*R*,3*S*,10*R*)-8

Compound **7** (1.0 g, 1.29 mmol) was mixed with 80% aqueous TFA (10 mL), stirred for 3 h at 0 °C, and diluted with $CHCl_3$ and water. The organic layer was separated, the aqueous layer was extracted with $CHCl_3$, and the combined organic layers were washed successively with aqueous 2% $NaHCO_3$, water, and brine, and dried. Solvent removal in vacuo followed by column chromatography of the residue (silica gel, 0–5% MeOH/$CHCl_3$) furnished pure **8**. Yield: 0.790 g (88%); thick liquid; $[\alpha]_D^{22} = +13.1$ (*c* 3.12, $CHCl_3$); IR: 3438, 971 $cm^{-1}$; $^1H$ NMR: $\delta$ 1.14 (merged s and d, *J* = 6.8 Hz, 21H), 1.26–1.44 (m, 4H), 1.75 (br s, 2H), 2.14–2.27 (m, 4H), 3.62–3.81 (m, 4H), 4.05–4.15 (m, 1H), 5.15–5.25 (m, 2H), 7.25–7.40 (m, 12H), 7.66–7.74 (m, 8H); $^{13}C$ NMR: $\delta$ 19.3, 23.1, 24.7, 27.0, 32.4, 36.6, 38.8, 62.9, 69.3, 73.4, 75.4, 127.3, 128.3, 129.4, 129.9, 133.0, 133.6, 134.8, 135.3. Anal. Calcd for $C_{43}H_{58}O_4Si_2$: C, 74.30; H, 8.41. Found: C, 74.14; H, 8.56.

### 3.9. (2*S*,9*R*)-2,9-Di-(*tert*-butyldiphenylsilyloxy)dec-4*E*-enal (2*S*,9*R*)-9

To a cooled (10 °C) and stirred solution of **8** (0.350 g, 0.50 mmol) in 60% aqueous acetonitrile (20 mL) was added $NaIO_4$ (0.212 g, 1.0 mmol) in portions. After stirring for 2 h, the mixture was filtered, and the filtrate was treated with 10% aqueous $NaHSO_3$ and was extracted with $CHCl_3$. The organic layer was washed with water and brine, and was concentrated in vacuo to get a residue, which on column chromatography (silica gel, 0–10% EtOAc/hexane) furnished pure **9**. Yield: 0.304 g (91%); thick liquid; $[\alpha]_D^{22} = +16.0$ (*c* 0.861, $CHCl_3$); IR: 1712, 989, 961 $cm^{-1}$; $^1H$ NMR: $\delta$ 1.06 (s, 18H), 1.12 (d, *J* = 6.4 Hz, 3H), 1.65–1.84 (m, 4H), 2.21–2.32 (m, 4H), 3.79–3.89 (m, 1H), 3.99–4.02 (m, 1H), 5.28–5.32 (m, 2H), 7.19–7.36 (m, 12H), 7.63–7.67 (m, 8H), 9.52 (d, *J* = 1.4 Hz, 1H); $^{13}C$ NMR: $\delta$ 19.1, 19.4, 24.5, 27.8, 36.2, 63.1, 75.7, 127.2, 128.4, 129.8, 129.5, 132.7, 133.7, 135.2, 135.7, 198.1. Anal. Calcd for $C_{42}H_{54}O_3Si_2$: C, 76.08; H, 8.21. Found: C, 75.91; H, 8.09.

### 3.10. Methyl (6*S*,13*R*)-6,13-di-(*tert*-butyldiphenylsilyloxy) tetradeca-(2*E*,4*E*,8*E*)-trienoate 13

To a stirred suspension of pentane-washed NaH (33 mg, 0.68 mmol, 50% suspension in oil) in THF (5 mL) was added phosphonate **12** (0.160 g, 0.68 mmol) in THF (5 mL). After 15 min, when the solution became clear, the mixture was cooled to 0 °C, and aldehyde **9** (0.300 g, 0.46 mmol) in THF (5 mL) was dropwise added to it. After stirring at room temperature for 18 h, the mixture was poured into ice-cold water and extracted with $Et_2O$. The ether layer was washed with water and brine, dried, and concentrated in vacuo to give a residue, which on column chromatography (silica

gel, 0–10% $Et_2O$/hexane) furnished pure **13**. Yield: 0.265 g (79%); colorless oil; $[\alpha]_D^{22} = +8.9$ (*c* 0.842, $CHCl_3$); IR: 1742 $cm^{-1}$; $^1H$ NMR: $\delta$ 1.08 (s, 18H), 1.25–1.42 (m containing a d at $\delta$ 1.21, *J* = 6.4 Hz, 7H), 2.04–2.17 (m, 4H), 3.69–3.81 (m containing a s at $\delta$ 3.73, 4H), 4.18–4.21 (m, 1H), 5.21–5.23 (m, 2H), 5.75 (d, *J* = 15.4 Hz, 1H), 6.05–6.09 (m, 2H), 7.18–7.22 (m, 1H), 7.25–7.41 (m, 12H), 7.61–7.76 (m, 8H); $^{13}C$ NMR: $\delta$ 19.3, 26.6, 27.1, 29.7, 38.5, 40.8, 51.2, 64.2, 67.0, 120.5, 124.7, 127.7, 129.5, 129.7, 134.8, 135.2, 135.9, 144.2, 144.4, 168.2. Anal. Calcd for $C_{47}H_{60}O_4Si_2$: C, 75.76; H, 8.12. Found: C, 75.63; H, 8.36.

### 3.11. Methyl (6*S*,13*R*)-6,13-dihydroxytetradeca-(2*E*,4*E*,8*E*)-trienoate 14

To a cooled (0 °C) and stirred solution of **13** (0.265 g, 0.36 mmol) in THF (5 mL) was added $Bu_4NF$ (1.1 mL, 1.10 mmol, 1.0 M in THF). The reaction mixture was brought to room temperature and was stirred until the reaction was complete (cf. TLC, 12 h). The mixture was poured into ice-cold water and was extracted with EtOAc. The organic extract was washed with water and brine, and dried. Removal of the solvent followed by column chromatography of the residue (silica gel, 0–15% EtOAc/hexane) furnished **14**. Yield: 0.083 g (87%); colorless oil; $[\alpha]_D^{22} = +14.8$ (*c* 0.618, MeOH) (lit.[5d] $[\alpha]_D = +15.2$ (*c* 0.2, MeOH)); IR: 3412, 1724 $cm^{-1}$; $^1H$ NMR: $\delta$ 1.16 (t, *J* = 6.2 Hz, 3H), 1.29–1.58 (m, 4H), 2.03–2.08 (m, 2H), 2.21–2.33 (m, 2H), 3.72–3.98 (m containing a s at $\delta$ 3.73, 4H), 4.18–4.27 (m, 1H), 5.41–5.57 (m, 2H), 5.87 (d, *J* = 15.8 Hz, 1H), 6.08–6.14 (m, 2H), 7.21–7.28 (m, 1H); $^{13}C$ NMR: $\delta$ 24.2, 26.2, 30.7, 38.5, 40.7, 51.4, 67.7, 69.8, 120.5, 124.4, 127.4, 129.7, 134.9, 135.7, 144.2, 144.5, 168.3.

## References


1. (a) Kawagishi, H.; Ando, M.; Micno, T.; Yokota, H.; Konishi, S. *Agric. Biol. Chem.* **1990**, *54*, 1329–1331; (b) Kuga, H.; Ejima, A.; Mitui, I.; Sato, K.; Ishihara, N.; Fukunda, K.; Saito, F.; Uenaki, K. *Biosci., Biotechnol., Biochem.* **1993**, *57*, 1020–1021; (c) Gardner, H. W. *J. Lipid Res.* **1970**, *11*, 311–321.
2. Sharma, A.; Chattopadhyay, S. *Enantiomer* **1998**, *3*, 225–229.
3. (a) Jiao, Y.; Yoshihara, T.; Akimoto, M.; Ichihara, A. *Phytochemistry* **1995**, *38*, 419–422; (b) Simon, B.; Anke, T.; Sterner, O. *Phytochemistry* **1994**, *36*, 815–816.
4. Turner, W. B.; Aldridge, D. C. In *Fungal Metabolites II*; Academic Press: London, 1983.
5. (a) Arnone, A.; Camarda, L.; Nasini, G.; Assante, G. *J. Chem. Soc., Perkin Trans. 1* **1986**, 255; (b) Arnone, A.; Assante, G.; Nasini, G.; Camarda, L. *Gazz. Chim. Ital.* **1989**, *119*, 35. and references cited therein; (c) Arnone, A.; Nasini, G.; Vajna de Pava, O. *Phytochemistry* **1991**, *30*, 2729–2731; (d) Arnone, A.; Nasini, G.; De Pava, O. V. *Phytochemsitry* **1998**, *48*, 507–510.
6. (a) Reetz, M. T. *Curr. Opin. Chem. Biol.* **2002**, *6*, 145–150; (b) Faber, K. *Biotransformations in Organic Chemistry*, 5th ed.; Springer: Heidelberg, Germany, 2004; (c) Bornscheuer, U. T.; Kazlauskas, R. J. *Hydrolases in Organic Synthesis*, 2nd ed.; Wiley-VCH: Weinheim, Germany, 2005; (d) Gotor-Fernández, V.; Busto, E.; Gotor, V. *Adv. Synth. Catal.* **2006**, 797–812.
7. (a) Ohtani, T.; Nakatsukasa, H.; Kamezawa, M.; Tachibana, H.; Naoshima, Y. *J. Mol. Catal. B: Enzym.* **1998**, *4*, 53–60; (b) Fuji, M.; Fukumura, M.; Hory, Y.; Hirai, Y.; Akita, H.; Nakamura, K.; Toriizuka, K.; Ida, Y. *Tetrahedron: Asymmetry* **2006**, *17*, 2292–2298; (c) Felluga, F.; Forzato, C.; Ghelfi, F.; Nitti, P.; Pitacco, G.; Pagnoni, U. M.; Roncaglia, F. *Tetrahedron: Asymmetry* **2007**, *18*, 527–536.
8. (a) Mitsunobu, O. *Synthesis* **1981**, 1–28; (b) Dembinski, R. *Eur. J. Org. Chem.* **2004**, 2763–2772.
9. Dale, J. A.; Mosher, S. H. *J. Am. Chem. Soc.* **1973**, *95*, 512–519.
10. Hirata, H.; Ikushima, M.; Watanabe, M.; Kawauchi, K.; Miyagishi, M.; Chen, Y.-G.; Yanagishita, H. *J. Oleo Sci.* **2003**, *52*, 375–386.
11. (a) Salaskar, A.; Sharma, A.; Chattopadhyay, S. *Tetrahedron: Asymmetry* **2006**, *17*, 325–329; (b) Roy, S.; Sharma, A.; Dhotare, B.; Vichare, P.; Chattopadhyay, A.; Chattopadhyay, S. *Synthesis* **2007**, 1082–1090; (c) Mula, S.; Chattopadhyay, S. *Lett. Org. Chem.* **2006**, *3*, 54–55.
12. (a) Chatterjee, A. K.; Choi, T.-L.; Sanders, D. P.; Grubbs, R. H. *J. Am. Chem. Soc.* **2003**, *125*, 11360–11370; (b) Blackwell, H. E.; O'Leary, D. J.; Chatterjee, A. K.; Washenfelder, R. A.; Bussmann, D. A.; Grubbs, R. H. *J. Am. Chem. Soc.* **2000**, *122*, 58–71.