Pergamon

Tetrahedron: *Asymmetry* 9 (1998) 2627–2633

TETRAHEDRON: *ASYMMETRY*

Enantiospecific synthesis of 6-methylheptadec-(9*E*)-enoic acid enantiomers, the antimicrobial principles of *Sporothrix* species

Sivaraman Sankaranarayanan and Subrata Chattopadhyay *

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

Received 19 May 1998; accepted 6 July 1998

Abstract

An efficient synthesis of the title compound **I** in both its enantiomeric forms has been developed starting from (*R*)-citronellol. This involved the introduction of the required alkyl chain and the acidic component at the termini of the starting chiron via judicious derivatization of its bifunctionality to provide the enantiomers of **I**. The other key features of the synthesis were: (i) use of easily accessible and inexpensive materials/reagents; (ii) operational simplicity; and (iii) brevity.

1. Introduction

The role of antifungal molecules in disease suppression is of considerable importance and the screening of mycelial cultures of some biocontrol agents has led to the discovery of a great number of metabolites with antimicrobial activity.[1] In this context, the isolation of several compounds with antibiotic activity from the *Sporothrix* species is revealing. One of the members of the family viz. *S. flocculosa* is known to be a potential antagonist[2a,b] against powdery mildew fungi and thus promises to be an efficient biocontrol device. Very recently, Hajlaoui et al.[3] suggested the involvement of extracellular diffusible molecules for the disintegration of the host *S. flocculosa* cytoplasm by *Sphaerotheca pannosa*. Earlier, several such organic compounds possessing wide spectrum anti-fungal and anti-bacterial activities were isolated[4] from the liquid culture of *S. flocculosa* and other *Sporothrix* species. Very recently, a structurally similar but new compound viz. 6-methylheptadec-(9*E*)-enoic acid **I** was isolated,[5] which exhibited potent anti-fungal activity against *Cladosporium cucumerinum*. Until now, no information is available about its absolute configuration nor about the dependence of its bioactivity on the stereochemistry. This can be attributed to its low natural abundance and can be resolved by synthesizing its enantiomers, correlating their chiroptical data with those of the natural product and carrying out bioassays of the individual isomers.

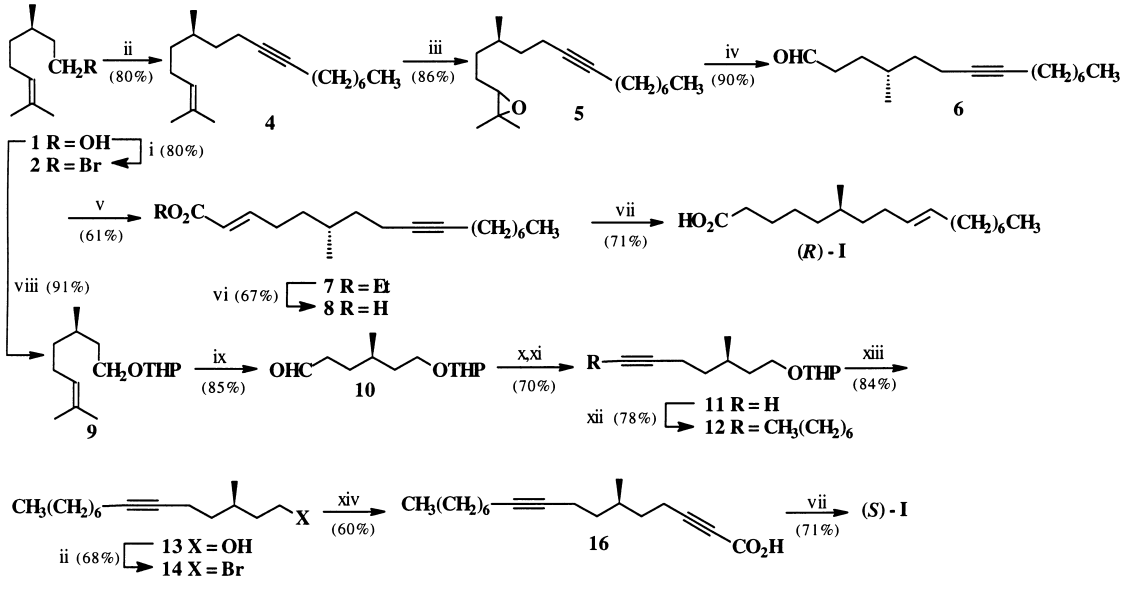
* Corresponding author. Fax: 91-22-5560750; e-mail: bod@magnum.barct1.ernet.in

0957-4166/98/$ - see front matter
PII: S0957-4166(98)00265-1

Against the above background, it was imperative to formulate an efficient enantiospecific synthesis of the antipodes of **I**. Consequently, we developed an enantiospecific route for both (*R*)- and (*S*)-**I** starting from (*R*)-citronellol **1** as described below. To the best of our knowledge, so far no synthesis of **I** has been reported in the literature.

2. Results and discussion

*Synthesis of (*R*)-**I***: For this, the alcohol **1** was converted[6] to the bromide **2** and used for the alkylation[7] of 1-nonyne **3** to give the hydrocarbon **4**. Its reaction with 1.0 equiv. of *m*-CPBA (*meta*-chloroperbenzoic acid) at −78°C proceeded regioselectively at the olefinic site furnishing **5**. This, on H_5IO_6 cleavage, gave the aldehyde **6** which was converted to the ester **7** via Wittig–Horner olefination with triethyl phosphonoacetate. Its alkaline hydrolysis furnished the acid **8** which, on Na/NH_3 reduction[8] in the presence of a proton donor, directly afforded the desired (*R*)-acid **I** (Scheme 1).



i) $Ph_3P.Br_2/CH_2Cl_2$/pyridine, ii) $LiC{\equiv}C(CH_2)_6CH_3$ (**3**)/THF/HMPA/-78 °C, iii) *m*-CPBA/CH_2Cl_2/-78 °C, iv) H_5IO_6/THF/ether, v) $NaH/(EtO)_2P(O)CH_2CO_2Et$, vi) Alcoholic KOH, vii) Na/NH_3/EtOH/ether, viii) DHP/CH_2Cl_2/PPTS, ix) O_3/CH_2Cl_2; Ph_3P/-40 °C, x) Ph_3P/CBr_4/TEA/CH_2Cl_2, xi) EtMgBr/THF, xii) *n*-BuLi/THF/HMPA/$CH_3(CH_2)_6Br$/-78 °C, xiii) MeOH/PTS/Δ, xiv) *n*-BuLi/ $HC{\equiv}CCO_2H$ (**15**)/THF/HMPA/-78 °C.

Scheme 1.

*Synthesis of (*S*)-**I***: The same alcohol (*R*)-**1** was pyranylated[9] to **9** which was converted to the ozonide and subsequently reduced[10] with triphenylphosphine (TPP) to give the aldehyde **10**. This, on reaction with CBr_4–TPP[11] and subsequent treatment with EtMgBr, gave the alkynol derivative **11**. Its alkylation with 1-bromoheptane gave **12**, which on acid catalyzed deprotection[9] to **13** followed by bromination[6] afforded **14**. Alkylation of propiolic acid **15** with **14** furnished the acid **16** which was converted to (*S*)-**I** as in the case of the (*R*)-antipode.

The spectral data of both the enantiomers of **I** were commensurate with the reported[5] values. For the estimation of the enantiomeric purity of the starting chiron (*R*)-**1**, it was oxidized with PDC (pyridinum dichromate)/DMF and the resultant acid was subsequently reacted with (*R*)-phenylethylamine in the

presence of DCC (1,3-dicyclohexyl carbodiimide) to give the corresponding diastereomeric amide. Its GLC analysis[12] (3% OV-17 column, 40 ml/min N_2) revealed its ee to be 94.3%. Since the subsequent reactions were carried out under non-racemizing conditions and retain the chiral integrity of (*R*)-**1**, the ee of both (*R*)- and (*S*)-**I** should also be same. This was further confirmed by capillary GLC analysis (β-Dex 120, 30 m×0.25 mm, split ratio 100:1, temp. prog. 100–200°C @ 4°C/min, 1 ml/min He) of the methyl esters of **I**, the t_Rs being 16.8 and 15.7 mins, respectively, for (*R*)- and (*S*)-**I**. However, due to a lack of available specific rotation data, the configuration for the natural **I** could not be established.

3. Experimental

All the boiling points are uncorrected. The IR spectra were scanned as thin films with a Perkin–Elmer spectrophotometer model 837. The ^{1}H NMR spectra were recorded in $CDCl_3$ with a Bruker AC-200 (200 MHz) instrument. The optical rotations were measured with a Jasco DIP 360 polarimeter. Anhydrous reactions were carried out under Ar using freshly dried solvents. All the reactions except depyranylation were carried out using dry solvents (THF, ether and HMPA dried over Na and CH_2Cl_2 over P_2O_5). The organic extracts were dried over anhydrous Na_2SO_4.

*3.1. (*R*)-Citronellyl bromide **2***

To a stirred and cooled (0°C) solution of Ph_3P (15.74 g, 0.06 mol) in CH_2Cl_2 (80 ml) was dropwise added Br_2 (10.0 ml, 0.055 mol, 5.5 M in CCl_4). After 0.5 h, a mixture of the alcohol (*R*)-**1** (7.8 g, 0.05 mol) and pyridine (4.45 ml, 0.055 mol) in CH_2Cl_2 (20 ml) was added to the resulting white solid and stirring continued at room temperature for 3 h. Most of the solvent was removed in vacuo and the residue dissolved in hexane. The hexane extract was passed through a small pad (2 in.) of silica gel and the eluent concentrated to furnish pure **2**. Yield: 8.75 g (80%); bp: 108–110°C/10 mmHg, $[\alpha]_D^{22}$ −6.27 (c 4.5, $CHCl_3$); IR: 1480, 1380 cm^{-1}; ^{1}H NMR: δ 0.93 (d, *J*=7 Hz, 3H), 1.0–1.4 (m, 4H), 1.58 (s, 3H), 1.62 (s, 3H), 1.8–2.2 (m, 3H), 3.54 (t, *J*=7 Hz, 2H), 5.06 (t, *J*=6 Hz, 1H).

*3.2. (6*R*)-2,6-Dimethylheptadec-2-en-9-yne **4***

To a stirred and cooled (−25°C) solution of **3** (2.5 g, 20.16 mmol) in THF (40 ml) was slowly injected *n*-BuLi (12.5 ml, 20.06 mmol, 1.6 M in hexane). After 0.5 h, the mixture was cooled to −78°C, HMPA (hexamethylphosphoramide) (5.0 ml) was added and stirring continued for a further 15 min. The bromide **2** (4.0 g, 18.26 mmol) in THF (20 ml) was added and the mixture stirred for 3 h at the same temperature and for 18 h at room temperature. It was poured into ice-cold water, the organic layer separated and the aqueous portion was extracted with ether. The combined organic extract was thoroughly washed with water and brine, and finally dried. The crude product was purified by column chromatography (silica gel, hexane) to give **4**. Yield: 3.8 g (80%); $[\alpha]_D^{22}$ −1.23 (c 0.9, $CHCl_3$); IR: 2210, 1460, 1380 cm^{-1}; ^{1}H NMR: δ 0.9 (merged d and t, 6H), 1.29 (br. s, 14H), 1.62 (s, 3H), 1.68 (s, 3H), 1.8–2.2 (m, 7H), 5.06 (t, *J*=6 Hz, 1H). Anal. calcd for $C_{19}H_{34}$: C 86.94, H 13.06; found: C 86.78, H 13.22.

*3.3. (2*RS*,6*S*)-2,6-Dimethyl-2-epoxyheptadec-9-yne **5***

To a cooled (−78°C) and stirred solution of **4** (1.1 g, 4.2 mmol) in CH_2Cl_2 (30 ml) was added *m*-CPBA (1.6 g, 4.64 mmol, 50%) in portions. After stirring for 3 h at the same temperature, when there was no

starting material left, the mixture was filtered and the precipitate washed with cold $CHCl_3$. The combined organic layer was washed successively with 10% aqueous Na_2SO_3, water, 10% aqueous $Na_2S_2O_3$, water and brine, and dried. Removal of the solvent followed by chromatography of the product (silica gel, 0–5% ether:hexane) furnished pure **5**. Yield: 1.0 g (86%); $[\alpha]_D^{22}$ −4.1 (c 1.1, $CHCl_3$); IR: 2210, 1480, 1380, 1200, 1120 cm^{-1}; ^1H NMR: δ 0.9–1.0 (d and t merged, 6H), 1.3 (br. s, 14H), 1.54 (s, 3H), 1.60 (s, 3H), 1.8–2.0 (m, 3H), 2.1–2.3 (m, 4H), 2.62 (t, *J*=4.8 Hz, 1H).

*3.4. (4S)-4-Methylpentadec-7-ynal **6***

To a cooled (0°C) and stirred solution of **5** (1.0 g, 3.6 mmol) in THF:H_2O (2:1, 20 ml) was added H_5IO_6 (1.23 g, 5.39 mmol). After 3 h, ether was added to the mixture, the organic layer separated and was worked up as detailed for **5** to give pure **6** after isolation and column chromatography (silica gel, 0–10% ether:hexane). Yield: 0.764 g (90%); $[\alpha]_D^{22}$ +5.31 (c 0.78, $CHCl_3$); IR: 2715, 2370, 1730 cm^{-1}; ^1H NMR: δ 0.9–1.0 (d and t merged, 6H), 1.32 (br. s, 14H), 1.8–2.1 (m, 5H), 2.2–2.3 (m, 2H), 9.78 (t, *J*=1.5 Hz, 1H). Anal. calcd for $C_{16}H_{28}O$: C 81.29, H 11.94; found: C 81.48, H 12.15.

*3.5. Ethyl (6R)-6-Methylheptadec-(2E)-en-9-ynoate **7***

To a cooled (0°C) and stirred suspension of pentane-washed NaH (0.192 g, 4.0 mmol, 50% suspension in oil) in THF (20 ml) was added triethyl phosphonoacetate (0.896 g, 4.0 mmol) in THF (10 ml). After stirring for 0.5 h at the same temperature, compound **6** (0.75 g, 3.18 mmol) in THF (10 ml) was added to the reaction mixture and stirring was continued for 3 h at 0°C and at room temperature for 12 h. The mixture was poured into ice-cold water, the organic layer separated and the aqueous portion was extracted with ether. The combined organic extract was washed with water and brine, and dried. Removal of the solvent followed by column chromatography (silica gel, 0–10% ether:hexane) of the crude product furnished pure **7**. Yield: 0.593 g (61%); $[\alpha]_D^{22}$ −6.12 (c 2.94, $CHCl_3$); IR: 1720, 1650, 985 cm^{-1}; ^1H NMR: δ 0.9–1.0 (d and t merged, 6H), 1.16 (t, *J*=6 Hz, 3H), 1.3 (br. s, 14H), 1.9–2.3 (m, 7H), 4.14 (q, *J*=7 Hz, 2H), 5.89 (d, *J*=15.6 Hz, 1H), 6.91 (dt, *J*=15.6, 6 Hz, 1H). Anal. calcd for $C_{20}H_{34}O_2$: C 78.38, H 11.18; found: C 78.68, H 11.06.

*3.6. (6R)-6-Methylheptadec-(2E)-en-9-ynoic acid **8***

A mixture of **7** (0.5 g, 1.6 mmol) and alcoholic KOH (2 N, 10 ml) was stirred at room temperature for 4 h. Most of the solvent was removed in vacuo, the residue extracted with EtOAc, the organic extract washed with water and brine, and dried. Concentration of the extract and preparative TLC and chromatography (silica gel, 5% MeOH:$CHCl_3$) of the product gave pure **8**. Yield: 0.304 g (67%); $[\alpha]_D^{22}$ −8.92 (c 1.3, $CHCl_3$); IR: 3700–3500, 1710, 980 cm^{-1}; ^1H NMR: δ 0.9–1.0 (d and t merged, 6H), 1.3–1.6 (m containing a br. s at δ 1.32, 14H), 1.9–2.3 (m, 7H), 5.90 (d, *J*=15.6 Hz, 1H), 6.91 (dt, *J*=15.6, 6 Hz, 1H), 9.7 (br. s, D_2O exchangeable, 1H). Anal. calcd for $C_{18}H_{30}O_2$: C 77.65, H 10.86; found: C 77.88, H 11.17.

*3.7. (6R)-6-Methylheptadec-(9E)-enoic acid **I***

To a stirred solution of **8** (0.28 g, 1.01 mmol) in a mixture of liquid NH_3 (20 ml), EtOH (10 ml) and ether (20 ml) was added Na metal (0.244 g, 10.6 mmol) in pieces at −78°C. After 3 h, NH_3 was allowed to evaporate, and ice-cold water was added to the flask followed by ether. The organic layer was

separated and discarded, the aqueous portion acidified with aqueous HCl (2 N) and extracted with ether. The ether layer was washed with water and brine, and dried. Removal of the solvent and preparative chromatography (silica gel, 5% MeOH:$CHCl_3$) gave pure (*R*)-**I**. Yield: 0.202 g (71%); $[\alpha]_D^{22}$ −5.0 (c 0.88, $CHCl_3$); IR: 3700–2500, 1720, 980 cm^{-1}; ^1H NMR: δ 0.9–1.0 (d and t merged, 6H), 1.32 (br. s, 19H), 1.9–2.2 (m, 4H), 2.34 (t, *J*=6 Hz, 2H), 5.3–5.6 (m, 2H), 8.6 (br. s, D_2O exchangeable, 1H). Anal. calcd for $C_{18}H_{34}O_2$: C 76.54, H 12.13; found: C 76.81, H 12.37.

*3.8. (3*R*)-1-Tetrahydropyranyloxycitronellol **9***

A mixture of **1** (2.0 g, 12.82 mmol), DHP (1.29 g, 15.36 mmol) and PPTS (pyridinium *p*-toluenesulphonate) (0.1 g) in CH_2Cl_2 (50 ml) was stirred at room temperature for 12 h. The reaction was quenched with 10% aqueous $NaHCO_3$, the organic layer separated and the aqueous portion was extracted with $CHCl_3$. The combined organic extract was washed with water and brine, and dried. Removal of solvent followed by column chromatography of the residue furnished pure **9**. Yield: 2.8 g (91%); $[\alpha]_D^{22}$ +1.1 (c 2.0, $CHCl_3$); IR: 1480, 1380, 880, 810 cm^{-1}; ^1H NMR: δ 0.9 (d, *J*=7 Hz, 3H), 1.0–1.4 (m, 4H), 1.5–1.7 (m, containing two s at δ 1.58 and 1.62, 12H), 1.8–2.2 (m, 3H), 3.6–3.7 (m, 4H), 4.48 (br. s, 0.5H), 4.57 (br. s, 0.5H), 5.06 (t, *J*=6 Hz, 1H). Anal. calcd for $C_{15}H_{28}O_2$: C 74.95, H 11.74; found: C 75.18, H 11.88.

*3.9. (4*R*)-6-Tetrahydropyranyloxy-4-methylhexanal **10***

Ozone was bubbled through a cooled (−78°C) solution of **9** (2.7 g, 11.25 mmol) in CH_2Cl_2 (50 ml) until saturation. The mixture was warmed to 0°C and excess ozone was removed by purging with N_2. Ph_3P (4.43 g, 16.88 mmol) was added to the mixture and stirring was continued for 60 h. Most of the solvent was removed in vacuo, the residue dissolved in hexane and the hexane solution cooled to 0°C. The solution was filtered, the precipitated solid was washed with cold hexane and the organic extract was concentrated. The residue obtained was given the same treatment thrice before purification by column chromatography (silica gel, 0–15% EtOAc:hexane) to afford **10**. Yield: 2.05 g (85%); $[\alpha]_D^{22}$ +3.4 (c 0.6, $CHCl_3$); IR: 2710, 1720, 880, 810 cm^{-1}; ^1H NMR: δ 0.9 (d, *J*=7 Hz, 3H), 1.4–1.8 (m, 11H), 2.1–2.3 (m, 2H), 3.6–3.8 (m, 4H), 4.51 (br. s, 0.5H), 4.55 (br. s, 0.5H), 9.78 (t, *J*=1.5 Hz, 1H).

*3.10. (3*R*)-1-Tetrahydropyranyloxy-3-methylhept-6-yne **11***

To a cooled (0°C) and stirred solution of Ph_3P (6.36 g, 24.26 mmol) in CH_2Cl_2 (15 ml) was added CBr_4 (4.10 g, 12.39 mmol). The aldehyde **10** (2.0 g, 9.35 mmol) in CH_2Cl_2 (10 ml) was then introduced into it at such a rate as to maintain the reaction temperature <15°C. The mixture was again cooled to 0°C and triethylamine (TEA) (1.3 ml, 9.35 mmol) was added. It was stirred at the same temperature for 0.5 h, brought to room temperature and stirred for another hour. The mixture was poured into hexane (50 ml) and passed through a pad of Celite (2 in.), eluting with ether. The organic layer was concentrated in vacuo, taken up in cold hexane and filtered. The filtrate on concentration gave the crude product which was used as such for the next step.

To the ice-cooled and stirred solution of the above compound in THF (20 ml) was added EtMgBr (18.7 mmol) [prepared from EtBr (2.04 g, 18.72 mmol) and Mg (0.545 g, 22.44 mmol) in THF (30 ml)]. The mixture was brought to room temperature and stirred for 12 h. It was poured into water, extracted with ether and the organic extract was washed with water and brine, and dried. Removal of the solvent and subsequent column chromatography (silica gel, 0–10% ether:hexane) gave **11**. Yield: 1.37 g (70%);

$[\alpha]_D^{22}$ −5.09 (c 0.51, $CHCl_3$); IR: 3340, 2230, 880, 810 cm^{-1}; ^1H NMR: δ 0.88 (d, *J*=7 Hz, 3H), 1.2–1.6 (m, 4H), 1.7–2.1 (m, 10H), 3.55–3.72 (m, 4H), 4.55 (br. s, 0.5H), 4.65 (br. s, 0.5H). Anal. calcd for $C_{13}H_{22}O_2$: C 74.24, H 10.54; found: C 74.14, H 10.68.

*3.11. (3*R*)-3-Methyltetradec-6-yn-1-ol **13***

To a cooled (−30°C) and stirred solution of **11** (1.3 g, 6.19 mmol) in THF (30 ml) was added *n*-BuLi (4.1 ml, 6.56 mmol, 1.6 M in hexane). After stirring for 0.5 h, HMPA (2 ml) was added followed by 1-bromoheptane (1.33 g, 7.43 mmol) in THF (10 ml). The mixture was stirred at the same temperature for 4 h and at room temperature overnight. It was poured into water, extracted with ether and the organic extract was washed with water and brine, and dried. Removal of the solvent and subsequent column chromatography (silica gel, 0–10% ether:hexane) gave **12**. Yield: 1.49 g (78%); $[\alpha]_D^{22}$ +6.0 (c 1.18, $CHCl_3$); IR: 1470, 1380, 880, 810 cm^{-1}; ^1H NMR: δ 0.88 (t, *J*=7 Hz, 3H), 0.93 (d, *J*=7 Hz, 3H), 1.32 (br. s, 14H), 1.7–1.9 (m, 7H), 2.0–2.19 (m, 4H), 3.55–3.68 (m, 4H), 4.5 (br. s, 0.5H), 4.55 (br. s, 0.5H). Anal. calcd for $C_{20}H_{36}O_2$: C 77.86, H 11.76; found: C 78.12, H 12.02.

A solution of **12** (1.49 g, 4.84 mmol) and PTS (*p*-toluenesulphonic acid) (0.05 g) in MeOH (30 ml) was refluxed for 4 h, at which time there was no starting material left. Most of the solvent was removed in vacuo, the residue was taken up in ether and the ether layer was washed successively with aqueous 10% $NaHCO_3$, water and brine, and dried. Solvent removal followed by column chromatography of the product (silica gel, 0–15% EtOAc:hexane) furnished **13**. Yield: 0.91 g (84%); $[\alpha]_D^{22}$ +3.0 (c 0.8, $CHCl_3$); IR: 3440, 1480, 1380 cm^{-1}; ^1H NMR: δ 0.88 (t, *J*=7 Hz, 3H), 0.95 (d, *J*=7 Hz, 3H), 1.29 (br. s, 14H), 1.9–2.2 (m, 5H), 2.84 (br. s, D_2O exchangeable, 1H), 3.68 (t, *J*=7 Hz, 2H). Anal. calcd for $C_{15}H_{28}O$: C 80.29, H 12.58; found: C 80.48, H 12.65.

*3.12. (3*R*)-1-Bromo-3-methyltetradec-6-yne **14***

As described for **2**, bromination of **13** (0.91 g, 4.06 mmol) with Ph_3P (1.28 g, 4.88 mmol), Br_2 (0.82 ml, 4.51 mmol, 5.5 M solution in CCl_4) and pyridine (0.36 ml, 4.47 mmol) gave **14**. Yield: 0.793 g (68%); $[\alpha]_D^{22}$ +4.62 (c 0.78, $CHCl_3$); IR: 1480, 1380 cm^{-1}; ^1H NMR: δ 0.93 (d and t merged, 6H), 1.32 (br. s, 14H), 1.8–2.1 (m, 5H), 3.59 (t, *J*=7 Hz, 2H).

*3.13. (6*R*)-6-Methylheptadeca-2,9-diynoic acid **16***

As described for **12**, alkylation of **15** (0.29 g, 4.14 mmol) with **14** (0.79 g, 2.75 mmol) was carried out at −78°C using *n*-BuLi (5.16 ml, 8.26 mmol, 1.6 M in hexane) as the base in a mixture of THF (10 ml) and HMPA (10 ml). The product obtained after work-up was purified by column chromatography (silica gel, 0–5% MeOH:$CHCl_3$) to give pure (*R*)-**16**. Yield: 0.456 g (60%); $[\alpha]_D^{22}$ +5.3 (c 1.24, $CHCl_3$); IR: 3700–3500, 1720, 1480 cm^{-1}; ^1H NMR: δ 0.9–1.0 (d and t merged, 6H), 1.32 (br. s, 14H), 1.9–2.2 (m, 5H), 2.34 (t, *J*=6 Hz, 2H), 8.6 (br. s, D_2O exchangeable, 1H). Anal. calcd for $C_{18}H_{28}O_2$: C 78.21, H 10.21; found: C 78.48, H 10.39.

*3.14. (6*S*)-6-Methylheptadec-(9*E*)-enoic acid **I***

Reduction of **16** (0.41 g, 1.45 mmol) with Na metal (0.667 g, 29.0 mol) in a mixture of NH_3 (50 ml), EtOH (15 ml) and ether (35 ml) gave (*S*)-**I** after purification by preparative TLC (silica gel, 5%

MeOH:$CHCl_3$). Yield: 0.289 g (71%); $[\alpha]_D^{22}$ +4.8 (c 0.95, $CHCl_3$). The spectral data of (*S*)-**I** were identical with those for its antipode.

References

1. Fravel, D. R. *Ann. Rev. Phytopathol*., **1988**, *26*, 75.
2. (a) Jarvis, W. R.; Shaw, L. A.; Traquair, J. A. *Mycol. Res*., **1989**, *92*, 162. (b) Belanger, R. R.; Labbe, C.; Jarvis, W. R. *Plant. Dis*., **1994**, *78*, 420 and references cited therein.
3. Hajlaoui, M. R.; Benhamou, N.; Belanger, R. R. *Phytopathology*, **1992**, *82*, 583.
4. Chowdhury, S. R.; Traquair, J. A.; Jarvis, W. R. *J. Nat. Prod*., **1994**, *57*, 700.
5. Benyagoub, M.; Rhlid, R. B.; Belanger, R. R. *J. Chem. Ecol*., **1996**, *22*, 405.
6. Wiley, G. A.; Hershkowitz, R. L.; Rein, B. M.; Chung, B. C. *J. Am. Chem. Soc*., **1964**, *86*, 964.
7. Brandsma, L. In *Preparative Acetylenic Chemistry*, Elsevier: Amsterdam, 1971.
8. Ghosh, S. K.; Satpathi, T. K.; Subba Rao, P. S. V.; Sarkar, T. K. *Synth. Commun*., **1988**, *18*, 1883.
9. Miyashita, M.; Yoshikoshi, A.; Grieco, P. A. *J. Org. Chem*., **1977**, *42*, 3772.
10. Fieser, L.; Fieser, M. In *Reagents in Organic Synthesis*, John Wiley & Sons: New York, 1980; Vol. 1, p. 1238.
11. Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett*., **1972**, 3769.
12. Chattopadhyay, S.; Mamdapur, V. R.; Chadha, M. S. *Synth. Commun*., **1990**, *20*, 825.