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Note

Synthesis of the (17*R*)- and (17*S*)-Isomers of Volicitin, an Elicitor of Plant Volatiles Contained in the Oral Secretion of the Beet Armyworm

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Both the (17*R*)- and (17*S*)-isomers of volicitin, which is contained in the oral secretion of the beet armyworm and induces corn seedlings to emit a blend of volatile compounds to attract the natural enemy of the herbivore, were synthesized *via* the semi-hydrogenation of an intermediary diyne and (*Z*)-selective olefination as the key steps. They were both obtained as crystalline compounds.

Key words: volicitin; elicitor; *Spodoptera exigua*; 17-hydroxylinolenic acid

Volicitin (**1a**) was isolated by Alborn *et al.* in 1997 from the oral secretion of beet armyworm caterpillars (*Spodoptera exigua* Hüber) as an elicitor which induces corn seedlings (*Zea may* L.) to release a mixture of volatile terpenoids and indole when the plant is damaged by the insect herbivore (Figure).[1,2] The mixture plays the role of attracting the parasitic wasp (*Cotesia marginiventris*), a natural enemy of the caterpillar, resulting in the indirect protection of the plant from attack by the herbivore. Alborn *et al.* also accomplished the synthesis of a mixture of (17*R*)- and (17*S*)-**1a** *via* coupling racemic 17-hydroxylinolenic acid (**7d**) with either a protected or unprotected L-glutamine, which resulted in the confirmation of the proposed structure, excluding the stereochemistry of its 17-hydroxyl group.[1,2] Since then, two research groups have reported synthetic works on volicitin. One group made use of a highly efficient one-pot double-Wittig approach for the preparation of both (*R*)- and (*S*)-**7a**.[3,4] Each of the esters was hydrolyzed to give (*R*)- or (*S*)-**7b**, which was then converted into (17*R*)- or (17*S*)-volicitin (**1a**), respectively, by coupling with L-glutamine and subsequent removal of the TBS-protecting group. The absolute configuration of the C-17 stereogenic center of volicitin as depicted in the Figure was determined quite recently by transforming (*R*)- and (*S*)-**7c** into the corresponding cabamates with a treatment by (*R*)-1-phenyethyl isocyanate. The GLC-retention times of the resulting diastereomeric carbamates were then compared with that of a carbamate sample derived in the same manner from the methanolysis product of natural volicitin.[5] The other group reported later a formal synthesis of (17*RS*)-**1a** by preparing (±)-**7d**, a synthetic precursor of (17*RS*)-**1a** described by Alborn *et al.*, in which semi-hydrogenation of a triene intermediate was employed as the key step to obtain (±)-**7d**.[6] Although the absolute configuration of

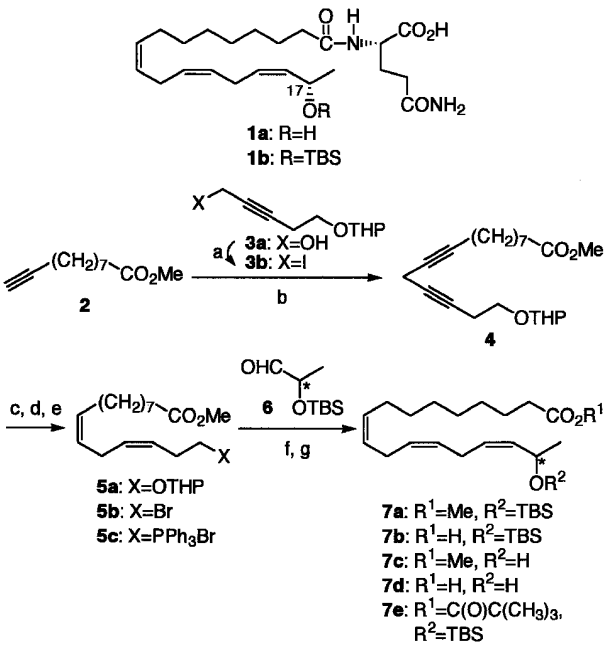

Figure. *Reagents*: a) I_2, Ph_3P, imidazole, THF; b) CuI, $(n\text{-}Bu)_4NI$, Na_2CO_3, DMF; c) H_2, Lindlar catalyst, hexane; d) $C_6H_2Br_4O$, Ph_3P, CH_2Cl_2; e) Ph_3P, CH_3CN; f) $KN(TMS)_2$, THF-HMPA; g) LiOH, H_2O-THF

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Abbreviations: MTPA, α-methoxy-α-trifluorophenylacetyl; TBS, *tert*-butyldimethylsilyl

volicitin has already been established to be 17*S*, we describe here our synthesis of both (17*R*)- and (17*S*)-volicitin, together with the experimental details.

Known acetylenic ester **2**[6] was coupled with iodide **3b**, which had been obtained by treating the corresponding alcohol (**3a**)[7] with iodine, imidazole, and triphenylphosphine in tetrahydrofuran, to give **4** in an 85% yield. Catalytic semi-hydrogenation of the diyne in the presence of the Lindlar catalyst gave **5a**, the (tetrahydropyran-2-yl)oxy group of which was then substituted with bromine by Tanaka's method[8] to directly give bromide **5b**. Repeated chromatographic purification of this crude bromide enabled us to obtain geometrically pure (9*Z*,12*Z*)-**5b**, as judged by ^{13}C-NMR. The bromide (**5b**) was converted into the corresponding phosphonium salt (**5c**), which was then subjected to (*Z*)-selective Wittig olefination[9] with both enantiomers of aldehyde **6**.[10,11] The resulting triene products were repeatedly chromatographed over silica gel to give ^{13}C-NMR spectroscopically pure (*R*)- and (*S*)-**7a**. In order to determine their enantiomeric excess, the TBS ethers were separately treated with tetrabutylammonium fluoride and then with (*S*)-MTPACl to give the corresponding diastereomeric MTPA-esters. A ^{1}H-NMR analysis revealed both of them to be optically pure. The enantiomeric esters, (*R*)-**7a** and (*S*)-**7a**, were hydrolyzed with lithium hydroxide in THF to respectively afford (*R*)-**7b** and (*S*)-**7b**, which were condensed with L-glutamine *via* the corresponding mixed anhydrides (**7e**). Finally, the TBS protecting group of the resulting amides (**1b**) was removed to afford (17*R*)-volicitin {mp 86.5–88.0°; $[\alpha]_D^{21}$ −3.9° (*c* = 0.90, CH_3OH), lit.[3] $[\alpha]_D^{22}$ −4.0° (*c* = 0.82, CH_2Cl_2)} and (17*S*)-volicitin {mp 54–61°C; $[\alpha]_D^{21}$ +6.6° (*c* = 0.80, CH_3OH), lit.[3] $[\alpha]_D^{22}$ +3° (*c* = 0.82, CH_2Cl_2)} as crystals in both cases. Probably due to their crystalline nature, our synthetic samples did not dissolve very well in dichloromethane which had been used for measuring the specific rotation values of volicitins synthesized by Pohnert *et al.* Therefore, methanol was used for this measurement instead of dichloromethane in our case. Unfortunately, the melting point of our synthetic (17*S*)-**1a** does not seem to be accurate, because of the presence of a small amount of impurities which could not be removed, even by reverse-phase chromatography and recrystallization. The ^{1}H- and ^{13}C-NMR spectra of (17*R*)-volicitin were indistinguishable from those of (17*S*)-volicitin, and were identical with authentic spectra kindly supplied by Dr. Pohnert.

Experimental

IR spectra were measured as films by a Jasco FT/IR-5000 spectrometer. ^{1}H-NMR (500 MHz) and ^{13}C-NMR (125 MHz) spectra were recorded with TMS as an internal standard in $CDCl_3$ by a JEOL JNM-A500 spectrometer, unless otherwise stated. Optical rotation values were measured with a Jasco DIP-370 polarimeter. Tetrahydrofuran was purified by distilling from sodium benzophenone ketyl, and dichloromethane was purified by drying with P_2O_5 and then by distillation from CaH_2. Merck silica gel 60 (70–230 mesh) was used for silica gel column chromatography.

Methyl 9-decynoate (2). This acetylenic ester was prepared by modifying the literature procedure.[6] Potassium hydride (35% in mineral oil, 0.970 g, 8.46 mmol) was washed three times with pentane under a nitrogen atmosphere. It was then mixed with trimethylene diamine (8 ml) in a reaction vessel cooled with a water bath, and the mixture was stirred at room temperature for 1 h. To the solution was added dropwise 3-decyn-1-ol (0.500 ml, 2.84 mmol) while cooling with the water bath. After being stirred for 2 h, the reaction mixture was quenched by adding ethanol (0.98 ml). The mixture was poured into sat. NH_4Cl aq. and extracted with ether. The ethereal solution was successively washed with water and brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was chromatographed over silica gel (16 g, hexane-ethyl acetate, 6:1) to give 0.393 g (79%) of 9-decyn-1-ol. To a stirred solution of this alcohol (3.46 g, 22.4 mmol) in acetone (70 ml) was added dropwise the Jones reagent (2.67 M, 12.3 ml, 32.8 mmol) at 0°C. After 2 h, the reaction mixture was quenched with 2-propanol (2 ml), diluted with water (70 ml) and concentrated *in vacuo*. The residue was diluted with water and extracted with ether. The ethereal solution was successively washed with water and brine, and then concentrated again *in vacuo*. The residue was dissolved in ether and extracted with KOH aq. (2 M, 18 ml). After acidification with HCl aq. (12 M), the water layer was extracted with ether. The ethereal solution was successively washed with water and brine, dried ($MgSO_4$), and concentrated *in vacuo* to give 3.15 g (83%) of crude 9-decynoic acid. A mixture of this carboxylic acid (3.45 g, 20.5 mmol) and conc. H_2SO_4 (0.1 ml) in anhydrous methanol (10 ml) was stirred for 1 h at room temperature. The reaction mixture was then quenched with $NaHCO_3$ powder (0.82 g) and concentrated *in vacuo*. The residue was diluted water and extracted with ether. The ethereal solution was successively washed with water and brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was distilled under reduced pressure to give 3.28 g (87.6%) of **2**, bp 86–87°C (2 Torr). The IR and ^{1}H-NMR spectral data were identical with those reported in the literature.[6]

1-Iodo-5-[(tetrahydropyran-2-yl)oxy]-2-pentyne (3b). To a solution of **3a** (1.07 g, 5.80 mmol) in THF (21 ml) was successively added imidazole (905 mg, 13.3 mmol), triphenylphosphine (1.82 g, 6.90 mmol)

and iodine (1.69 g, 6.60 mmol). After being stirred for 30 min, the mixture was poured into water and extracted with hexane. The organic layer was successively washed with water, 5% H_2O_2, water, 5% $Na_2S_2O_3$ aq., water and brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was triturated with hexane-ether (1:1) and chromatographed over silica gel (30 g, hexane-ethyl acetate, 3:1, containing 1% triethylamine) to give 1.46 g (85%) of **3b**. IR ν_{max} cm^{-1}: 2940 (s), 1175 (m), 1135 (s), 1120 (s), 1070 (s), 1030 (s), 965 (m), 870 (m), 815 (m). ^{1}H-NMR δ: 1.48–1.56 (2H, m, 4′-H_2), 1.56–1.64 (2H, m, 5′-H_2), 1.69–1.75 (1H, m, 3′-H), 1.80–1.88 (1H, m, 3′-H), 2.50 (2H, tt, J=7.0, 2.5 Hz, 4-H_2), 3.49–3.54 (1H, m, 6′-H), 3.54 (1H, dt, J=9.5, 7.0 Hz, 5-H), 3.69 (2H, t, J=2.5 Hz, 1-H_2), 3.80 (1H, dt, J=9.5, 7.0 Hz, 5-H), 3.89 (1H, ddd, J=11.2, 8.1, 3.4 Hz, 6′-H), 4.65 (1H, br t, J=3.6 Hz, 2′-H). *Anal.* Found: C, 41.13; H, 5.14%. Calcd. for $C_{10}H_{15}O_2I$: C, 41.16; H, 5.14%.

Methyl 15-[(tetrahydropyran-2-yl)oxy]-9,12-pentadecadiynoate (4). Cuprous iodide (0.291 g, 1.53 mmol), tetrabutylammonium iodide (0.414 g, 1.12 mmol) and sodium carbonate (0.205 g, 1.93 mmol) were placed in a reaction vessel under a nitrogen atmosphere. To the mixture were successively added a solution of **3b** (0.300 g, 1.02 mmol) in DMF (2 ml), a solution of **2** (0.204 g, 1.12 mmol) in DMF (2 ml), and DMF (0.5 ml). After being stirred for 17 h at room temperature, the mixture was poured into water and extracted with ether. The ethereal solution was successively washed with water (3 times) and brine (4 times), dried (K_2CO_3), and concentrated *in vacuo*. The residue was chromatographed over silica gel (40 g, hexane-ethyl acetate, 10:1, containing 1% triethylamine) to give 0.291 g (82%) of **4**. IR ν_{max} cm^{-1}: 2940 (s), 2855 (m), 2210 (w), 1735 (vs), 1200 (s), 1035 (s). ^{1}H-NMR δ: 1.29–1.40 (6H, m, 4-H_2, 5-H_2, 6-H_2), 1.45–1.55 (4H, m, 7-H_2, 4′-H_2), 1.55–1.65 (4H, m, 3-H_2, 5′-H_2), 1.68–1.74 (1H, m, 3′-H), 1.80–1.87 (1H, m, 3′-H), 2.14 (2H, tt, J=7.1, 2.4 Hz, 8-H_2), 2.30 (2H, t, J=7.5 Hz, 2-H_2), 2.47 (2H, tt, J=7.0, 2.4 Hz, 14-H_2), 3.11 (2H, qui, J=2.4 Hz, 11-H_2), 3.48–3.53 (1H, m, 6′-H), 3.54 (1H, dt, J=9.5, 7.0 Hz, 15-H), 3.67 (3H, s, OCH_3), 3.80 (1H, dt, J=9.5, 7.0 Hz, 15-H), 3.88 (1H, ddd, J=11.2, 8.1, 3.4 Hz, 6′-H), 4.64 (1H, br t, J=3.6 Hz, 2′-H). *Anal.* Found: C, 72.31; H, 9.13%. Calcd. for $C_{21}H_{32}O_4$: C, 72.37; H, 9.26%.

Methyl (9Z,12Z)-15-[(tetrahydropyran-2-yl)oxy]-9,12-pentadecadienoate (5a). A mixture of **4** (150 mg, 0.431 mmol) and the Lindlar catalyst (22.4 mg) in hexane (3 ml) was stirred for 10 min in an atmosphere of hydrogen. The mixture was filtered through a Celite pad, and the filtrate was concentrated *in vacuo*. The residue was repeatedly chromatographed over silica gel to give 133 mg (88%) of **5a**. IR ν_{max} cm^{-1}: 3014 (m), 2932 (vs), 2860 (s), 1742 (vs), 1201 (s), 1172 (s), 1139 (s), 1122 (s), 1079 (s), 1035 (s), 984 (m), 870 (m), 725 (m). ^{1}H-NMR δ: 1.27–1.37 (6H, m, 4-H_2, 5-H_2, 6-H_2), 1.47–1.55 (4H, m, 7-H_2, 4′-H_2), 1.55–1.65 (4H, m, 3-H_2, 5′-H_2), 1.68–1.74 (1H, m, 3′-H), 1.79–1.87 (1H, m, 3′-H), 2.04 (2H, br q, J=7.0 Hz, 8-H_2), 2.30 (2H, t, J=7.5 Hz, 2-H_2), 2.38 (2H, br q, J=7.0 Hz, 14-H_2), 2.80 (2H, br t, J=7.0 Hz, 11-H_2), 3.42 (1H, dt, J=9.5, 7.0 Hz, 15-H), 3.47–3.53 (1H, m, 6′-H), 3.66 (3H, s, OCH_3), 3.74 (1H, dt, J=9.5, 7.0 Hz, 15-H), 3.88 (1H, ddd, J=11.2, 8.1, 3.4 Hz, 6′-H), 4.60 (1H, dd, J=4.2, 3.0 Hz, 2′-H), 5.33 (1H, br dt, J=10.5, 7.0 Hz, 9-H), 5.38 (1H, br dt, J=10.5, 7.0 Hz, 10-H), 5.39–5.46 (2H, m, 12-H, 13-H). ^{13}C-NMR δ: 19.59, 24.93, 25.49, 25.74, 27.21, 27.99, 29.09, 29.11, 29.15, 29.55, 30.73, 34.10, 51.43, 62.30, 66.99, 98.76, 125.86, 127.74, 130.09, 130.29, 174.30. *Anal.* Found: C, 71.55; H, 10.04%. Calcd. for $C_{21}H_{36}O_4$: C, 71.55; H, 10.29%.

Methyl (9Z,12Z)-15-bromo-1,12-pentadecadienoate (5b). To a stirred solution of triphenylphosphine (214 mg, 0.816 mmol) in dichloromethane (2 ml) was added 2,4,4,6-tetrabromo-2,5-cyclohexadienone (0.314 g, 0.766 mmol) at 0°C. After 2 h, a solution of **5a** (100 mg, 0.284 mmol) in dichloromethane (1 ml) was added, and the resulting mixture was stirred for 5 h at room temperature. The mixture was poured into water and extracted with ether. The ethereal solution was successively washed with water and brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was chromatographed over silica gel (hexane-ether, 2:1) to give 93.0 mg (99%) of **5b**. IR ν_{max} cm^{-1}: 3016 (m), 2930 (s), 2858 (s), 1742 (vs), 1199 (s), 1174 (s), 725 (m). ^{1}H-NMR δ: 1.27–1.38 (6H, m, 4-H_2, 5-H_2, 6-H_2), 1.51–1.57 (2H, m, 7-H_2), 1.57–1.66 (2H, m, 3-H_2), 2.05 (2H, br q, J=7.0 Hz, 8-H_2), 2.30 (2H, t, J=7.5 Hz, 2-H_2), 2.65 (2H, br q, J=7.2 Hz, 14-H_2), 2.79 (2H, br t, J=7.2 Hz, 11-H_2), 3.38 (2H, t, J=7.2 Hz, 15-H_2), 3.67 (3H, s, OCH_3), 5.32 (1H, ddt, J=11.0, 7.0, 1.5 Hz, 10-H or 12-H), 5.36–5.43 (2H, m, 9-H, 13-H), 5.52 (1H, dtt, J=11.0, 7.5, 1.5 Hz, 10-H or 12-H). *Anal.* Found: C, 58.07; H, 8.00%. Calcd. for $C_{16}H_{27}O_2Br$: C, 58.01; H, 8.21%.

[(3Z,6Z)-14-Methoxycarbonyl-3,6-tetradecadienyl] triphenylphosphonium bromide (5c). A mixture of **5b** (1.03 g, 3.11 mmol) and triphenylphosphine (0.817 g, 3.11 mmol) in acetonitrile (11 ml) was stirred at reflux for 120 h under a nitrogen atmosphere and then concentrated *in vacuo*. The residue was dissolved in acetonitrile (2 ml), before dry ether (10 ml) was added to the solution while stirring to give a two-phase mixture. The supernatant solution containing unreacted triphenylphosphine was

removed. This treatment was repeated 3 times, and the residue was concentrated *in vauo* to give 1.75 g (95%) of **5c** as a sticky oil. IR ν_{max} cm^{-1}: 3056 (m), 3012 (m), 2930 (s), 2858 (s), 1734 (s), 1589 (m), 1485 (m), 1195 (s), 1114 (s), 748 (s), 721 (s), 694 (s). ^{1}H-NMR δ: 1.17–1.34 (6H, m, 4-H_2, 5-H_2, 6-H_2), 1.48–1.64 (4H, m, 3-H_2, 7-H_2), 1.87 (2H, br q, J= 7.0 Hz, 8-H_2), 2.30 (2H, t, J=7.5 Hz, 2-H_2), 2.48 (2H, br q, J=7.0 Hz, 14-H_2), 2.53 (2H, br t, J=7.5, 11-H_2), 3.66 (3H, s, OCH_3), 4.01 (2H dt, J=12.5, 7.5 Hz, 15-H_2), 5.15 (1H, br dt, J=10.5, 7.0 Hz, 10-H), 5.31 (1H, br dt, J=10.5, 8.0 Hz, 9-H), 5.37 (1H, br dt, J=10.5, 8.0 Hz, 12-H), 5.60 (1H, br dt, J=10.5, 7.0 Hz, 13-H), 7.70 (6H, td, J=7.5, 3.4 Hz, *m*-H_6), 7.78 (3H, tm, J=7.5 Hz, *p*-H_3), 7.89 (6H, br dd, J=12.5, 7.5 Hz, *o*-H_6). This phosphonium salt was employed for the next step without further purification.

Methyl (9Z,12Z,15Z,17R)-17-[(tert-butyldimethylsilyl)oxy]-9,12,15-octadecatrienoate [(R)-7a]. To a stirred solution of **5c** (389 mg, 0.656 mmol) in THF-HMPA (4:1, 4 ml) was added a solution of potassium hexamethyldisilazide (0.5 M in toluene, 1.32 ml, 0.660 mmol) at 0°C. After 1 h, the mixture was cooled to −78°C, and a solution of (*R*)-**6** (160 mg, 0.851 mmol) in THF (1.6 ml) was added. The mixture was stirred at −78°C for 10 min and then gradually warmed to 0°C over 2 h. The mixture was poured into sat. NH_4Cl aq. and extracted with ether. The ethereal solution was successively washed with water and brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was repeatedly chromatoraphed over silica gel (30 g, benzene-hexane, 2:1) to give 169 mg (61%) of (*R*)-**7a**, $[\alpha]_D^{24}$ −20.7° (c=1.01, $CHCl_3$). IR ν_{max} cm^{-1}: 3018 (m), 2930 (vs), 2860 (s), 1744 (s), 1087 (s), 835 (s), 777 (s). ^{1}H-NMR δ: 0.05 (3H, s, $SiCH_3$), 0.06 (3H, s, $SiCH_3$), 0.88 (9H, s, *t*-Bu), 1.19 (3H, d, J=6.2 Hz, 18-H_3), 1.27–1.38 (8H, m, 4-H_2, 5-H_2, 6-H_2, 7-H_2), 1.62 (2H, qui, J= 7.5 Hz, 3-H_2), 2.05 (2H, br q, J=7.0 Hz, 8-H_2), 2.30 (2H, t, J=7.5 Hz, 2-H_2), 2.80 (2H, br t, J=7.0 Hz, 11-H_2), 2.81 (2H, br t, J=7.0 Hz, 14-H_2), 3.67 (3H, s, OCH_3), 4.63 (1H, dqd, J=8.2, 6.2, 1.3 Hz, 17-H), 5.25 (1H, dtd, J=11.0, 7.5, 1.3 Hz, 15-H), 5.30–5.46 (5H, m, 9-H, 10-H, 12-H, 13-H, 16-H). ^{13}C-NMR δ: −4.70, −4.48, 18.25, 24.83, 25.00, 25.68, 25.93, 25.97, 27.29, 29.18, 29.22, 29.62, 34.17, 51.53, 65.19, 126.13, 127.76, 127.88, 128.90, 130.65, 135.91, 174.56. *Anal.* Found: C, 71.23; H, 10.81%. Calcd. for $C_{25}H_{46}O_3Si$: C, 71.03; H, 10.97%.

Methyl (9Z,12Z,15Z,17S)-17-(tert-butyldimethylsilyloxy)-9,12,15-octadecatrienoate [(S)-7a]. In the same manner as that described for the preparation of (*R*)-**7a**, **5c** (396 mg, 0.668 mmol) was allowed to react with aldehyde (*S*)-**6** (147 mg, 0.781 mmol) to give 144 mg (51%) of (*S*)-**7a**, $[\alpha]_D^{24}$ +18.1° (c=1.01, $CHCl_3$). *Anal.* Found: C, 71.20; H, 10.80%. Calcd. for $C_{25}H_{46}O_3Si$: C, 71.03; H, 10.97%. The IR, ^{1}H- and ^{13}C-NMR spectra were identical with those of (*R*)-**7a**.

Determination of the enantiomeric excesses of (R)-7a and (S)-7a. Two milligrams (6.4 μmol) of (*R*)-**7c**, easily obtainable by treating (*R*)-**7a** with a 1 M solution of tetrabutylammonium fluoride in THF, was dissolved in pyridine (25 μl), and (*S*)-MTPACl (5.0 μl, 27 μmol) was added. The mixture was stirred for 12 h at room temperature, and then diluted with ether. The ethereal solution was successively washed with sat. $CuSO_4$ aq., water and brine, dried ($MgSO_4$), and concentrated *in vacuo* to give the (*R*)-MTPA-ester of (*R*)-**7c**. In the same manner, (*S*)-**7c** was treated with (*S*)-MTPACl to give the (*R*)-MTPA-ester of (*S*)-**7c**. These MTPA-esters were analyzed by ^{1}H-NMR (500 MHz, $CDCl_3$) without any purification. A doublet signal due to the terminal methyl of the MTPA-ester derived from (*R*)-**7c** appeared at 1.33 ppm (J=6.5 Hz), while in the NMR spectrum of the MTPA-ester derived from (*S*)-**7c**, the doublet was observed at 1.40 ppm (J=6.5 Hz). In each spectrum, no doublet signal due to the terminal methyl group of the diastereomer of the MTPA-ester was observed. Therefore, both (*R*)-**7a** and (*S*)-**7a** were evaluated to be optically pure.

(9Z,12Z,15Z,17R)-17-[(tert-Butyldimethylsilyl) oxy]-9,12,15-octadecatienoic acid [(R)-7b]. To a stirred mixture of (*R*)-**7a** (159 mg, 0.377 mmol) in THF-water (9:7, 3.2 ml) was added lithium hydroxide monohydrate (66.0 mg, 1.57 mmol). After 12 h, the reaction mixture was neutralized with a solution of oxalic acid dihydrate (199 mg, 1.57 mmol) in water (6 ml), and extracted with ether. The ethereal solution was successively washed with water and brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was chromatographed over silica gel (10 g, hexane-ethyl acetate, 1:1) to give 151 mg (98%) of (*R*)-**7b**, $[\alpha]_D^{24}$ −21.0° (c=1.01, $CHCl_3$) IR ν_{max} cm^{-1}: 3018 (m), ~3000 (br), 2930 (vs), 2860 (s), 2660 (w), 1713 (vs), 1464 (m), 1367 (w), 1253 (m), 1129 (m), 1087 (s), 1006 (m), 872 (m), 835 (s), 777 (m). ^{1}H-NMR δ: 0.05 (3H, s, $SiCH_3$), 0.06 (3H, s, $SiCH_3$), 0.88 (9H, s, *t*-Bu), 1.19 (3H, d, J=6.2 Hz, 18-H_3), 1.28–1.39 (8H, m, 4-H_2, 5-H_2, 6-H_2, 7-H_2), 1.64 (2H, qui, J=7.5 Hz, 3-H_2), 2.05 (2H, br q, J=7.0 Hz, 8-H_2), 2.34 (2H, t, J=7.5 Hz, 2-H_2), 2.80 (2H, br t, J=7.0 Hz, 11-H_2), 2.81 (2H, br t, J=7.0 Hz, 14-H_2), 4.63 (1H, br qui, J=7.0 Hz, 17-H), 5.25 (1H, br dt, J=11.0, 7.5 Hz, 15-H), 5.30–5.46 (5H, m, 9-H, 10-H, 12-H, 13-H, 16-H). *Anal.* Found: C, 70.58; H, 10.60%. Calcd. for $C_{24}H_{44}O_3Si$: C, 70.53; H, 10.85%.

(9Z,12Z,15Z,17S)-17-(tert-Butyldimethylsilyl)oxy-

9,12,15-octadecatienoic acid [(S)-7b]. In the same manner as that described for the preparation of (*R*)-**7b**, (*S*)-**7a** (136 mg, 0.320 mmol) was converted into 0.131 mg (quantitative) of (*S*)-**7b**, $[\alpha]_D^{24}$ +18.6° (*c* = 1.07, $CHCl_3$) Its IR and ^{1}H-NMR spectra were identical with those of (*R*)-**7b**. *Anal.* Found: C, 70.56; H, 10.62%. Calcd. for $C_{24}H_{44}O_3Si$: C, 70.53; H, 10.85%.

N - [(R) - 17 - Hydroxylinolenoyl] - L - glutamine [(17R)-1a]. To a stirred solution of (*R*)-**7b** (139 mg, 0.341 mmol) and triethylamine (57.0 μl, 0.409 mmol) in THF (2.4 ml) was added pivaloyl chloride (45.6 μl, 0.370 mmol) at 0°C. After being stirred for 2 h at the same temperature, the mixture was quickly filtered and the filter cake was washed with THF (2.5 ml). The combined filtrate and washings containing mixed anhydride **7e** were diluted with 1,4-dioxane (2.2 ml) and used as the acylating agent in the next operation. Meanwhile, to a stirred solution of L-glutamine (99.4 mg, 0.680 mmol) in water (0.8 ml) was added triethylamine (95.0 μl, 0.682 mmol) at room temperature, and the mixture was stirred for 2 h. To the resulting solution was added the solution of (*R*)-**7e** prepared as already described at room temperature. After 20 min, triethylamine (48.0 μl, 0.344 mmol) was added again to the mixture, and stirring was continued for 4 h at room temperature. The mixture was adjusted to pH 3 with dil. HCl aq., poured into water and extracted with dichloromethane. The organic layer was washed with brine, dried ($MgSO_4$), and concentrated *in vacuo* to give 161 mg of crude (17*R*)-**1b**. To a stirred solution of this crude (17*R*)-**1b** (80.0 mg, 0.149 mmol) in acetonitrile-THF (1:1, 1 ml) was added a 46% aqueous solution of HF (0.1 ml), and the mixture was stirred for 30 min at room temperature. The mixture was poured into water and extracted with dichloromethane. The organic layer was washed with brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was chromatographed over silica gel [12 g, successively eluting with dichloromethane, dichloromethane-methanol (4:1) and finally dichloromethane-methanol (2:1)] to give 38.2 mg (53% in 2 steps) of (17*R*)-**1a** as a microcrystalline solid, which was further purified by recrystallization from acetonitrile to give 23.9 mg of pure (17*R*)-**1a**, mp 86.5–88.0°C, $[\alpha]_D^{21}$ −3.9° (*c* = 0.90, methanol). ^{1}H-NMR (in CD_3OD, TMS as an internal standard) δ: 1.20 (3H, d, J = 6.4 Hz, 18′-H_3), 1.24–1.43 (8H, m, 4′-H_2–7′-H_2), 1.57–1.62 (2H, m, 3′-H_2), 1.90–1.99 (1H, m, 3-H), 2.08 (2H, q, J = 7.0 Hz, 8′-H_2), 2.12–2.20 (1H, m, 3-H), 2.24 (2H, t, J = 7.3 Hz, 2′-H_2), 2.27–2.35 (2H, m, 4-H_2), 2.82 (2H, t, J = 6.0 Hz, 11′-H_2), 2.85–2.90 (2H, m, 14′-H_2), 4.38 (1H, dd, J = 9.0, 5.0 Hz, 2-H), 4.62 (1H, dq, J = 7.0, 6.4 Hz, 17′-H), 5.30–5.43 (6H, olefinic protons). ^{13}C-NMR [in CD_3OD, CD_3OD (δ = 49.00 ppm) as an internal standard] δ: 24.05, 26.52, 26.79, 26.86, 28.18, 28.71, 30.23, 30.28, 30.34, 30.71, 32.82, 36.89, 53.51, 64.39, 128.69 (probably two overlapping peaks), 129.18, 129.66, 131.23, 135.43, 175.36, 176.35, 177.80.

N-[(S)-17-Hydroxylinolenoyl]-L-glutamine [(17S)-1a, volicitin]. In the same manner as that described for the preparation of (17*R*)-**1a**, (*S*)-**7b** (68.0 mg, 0.160 mmol) was converted into 99.4 mg of crude (17*S*)-**1b**, a portion (97.0 mg) of which was then transformed into 31.7 mg (46% in two steps) of (17*S*)-**1a**, mp 54–61°C, $[\alpha]_D^{21}$ +6.6° (*c* = 0.80, methanol). The IR, ^{1}H- and ^{13}C-NMR spectra of (17*S*)-**1a** were indistinguishable from those of (17*R*)-**1a**.

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