Resin Glycosides. XVIII.[1] Determination by Mosher's Method of the Absolute Configurations of Mono- and Dihydroxyfatty Acids Originated from Resin Glycosides

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The absolute configurations of four hydroxyfatty acids, jalapinolic acid, convolvulinolic acid, ipurolic acid and 3,11-dihydroxyhexadecanoic acid, obtained by acid hydrolysis of various resin glycosides, have been determined to be 11*S*,11*S*,3*S*,11*S*, and 3*S*,11*S*, respectively, by Mosher's method. The *R*-configuration of jalapinolic acid previously defined by Horeau's method was therefore revised to *S*.

Keywords absolute configuration; hydroxyfatty acid; Mosher's method; (11*S*)-jalapinolic acid; (11*S*)-convolvulinolic acid; (3*S*,11*S*)-ipurolic acid

The so-called resin glycosides, which are characteristic components of Convolvulaceae plants, contain a variety of hydroxyfatty acids such as jalapinolic acid (11-hydroxyhexadecanoic acid), convolvulinolic acid (11-hydroxytetradecanoic acid), ipurolic acid (3,11-dihydroxytetradecanoic acid), and 3,11-dihydroxyhexadecanoic acid, *etc.*[2] as the aglycones of their glycosidic acid moieties.

In the course of our structural study on the resin glycosides of *Ipomoea orizabensis*, the absolute configuration at 11-C of (+)-jalapinolic acid (**1**) has been taken as *R*[3] according to Horeau's method.[4] But, the result was suspected to be possibly erroneous, because the specific optical rotation of the enantiomeric mixture of (+)- and (−)-2-phenylbutyric acids obtained from the excess amounts of their anhydride used in esterification was very small ($[\alpha]_D$ +0.46°).

We have now conducted a reexamination by the more reliable Mosher's method[5] based on another principle, and, as reported preliminarily, it has been concluded that the configuration should be not *R*, but *S*.[6] At the same time, Kitagawa *et al.* have synthesized *S*- and *R*-jalapinolic acids *via* Sharpless asymmetric epoxidation and also determined the configuration of (+)-jalapinolic acid ($[\alpha]_D$ +0.5°), which they obtained from the resin glycosides of the tuber of *Merremia mammosa*, to be *S* by direct comparison.[7]

Further, convolvulinolic acid (**2**), ipurolic acid (**3**) and 3,11-dihydroxyhexadecanoic acid (**4**) have been examined by Mosher's method, and they were assigned the configurations 11*S*,3*S*,11*S* and 3*S*,11*S*, respectively. This paper deals with the details of the determinations.

As the first step, in order to establish whether Mosher's method is applicable to a hydroxyfatty acid such as **1**, having one chiral center located in the middle of a straight and rather long methylene chain, methyl (+)-jalapinolate (**5**) was oxidized followed by reduction to give the racemate (**6**), and the ^{1}H-NMR spectrum (400 MHz, in $CDCl_3$) of its (*R*)-(+)-2-methoxy-2-trifluoromethylphenylacetate (MTPA ester) (**7**) was taken. The spectrum showed, along with a sharp triple triplet due to 11-H (δ 5.088) and a triplet due to 2-H_2 (δ 2.298), a pair of triplets assignable to the terminal 16-H_3 at δ 0.840 and 0.876. However, none of 12—15-H_2 could be assigned. Therefore, commercial 2*S*-pentanol (**8**), $[\alpha]_D$ +13.2° (neat), 2*S*-hexanol (**9**), $[\alpha]_D$ +10.6° (neat) and 2*S*-heptanol (**10**), $[\alpha]_D$ +9.5° (neat),[8] were converted into the corresponding (−)- and (+)-MTPA esters (**11**, **12**; **13**, **14**; **15**, **16**) and their ^{1}H-NMR spectra were recorded. All the pairs of compounds showed in their spectra a pair of triplets due to the terminal H_3, and the magnitudes of the chemical shift differences ($\Delta\delta$), [δ(−)-MTPA ester − δ(+)-MTPA ester], all having a positive value, decreased with increasing number of methylene groups from the chiral centers (Fig. 1). It is considered that the chemical shift difference at the terminal methyl signals of **7** arises substantially from the difference of configurations at 11-C and that Mosher's method is applicable to determine the configuration of a chiral center by use of the signals of the terminal methyl group, which is separated by as much as four methylene groups from the asymmetric carbon.

The ^{1}H-NMR spectra of the (−)- and (+)-MTPA esters (**17** and **18**) of methyl (+)-jalapinolate (**5**), $[\alpha]_D$ +1.0°, exhibited the 16-H_3 signal at δ 0.840 and 0.878, respectively. The $\Delta\delta$ value, −0.038 ppm, indicates the configuration at 11-C of **1** to be *S* (Fig. 1). All the specimens of methyl jalapinolate (**5**), obtained from glycosidic acids of the ether-soluble resin glycosides (jalapins), such as orizabins,[3] muricatins,[9] merremosides,[10] mammosides,[10] operculins,[11] scammonins[12] and simonins,[13] also showed + $[\alpha]_D$ values and were considered to have 11*S* configuration.

The (−)- and (+)-MTPA esters (**19** and **20**) of methyl convolvulinolate (**21**), $[\alpha]_D$ +1.0°, obtained either from quamoclins of the seeds of *Quamoclit pennata*[14] or rhamnoconvolvulin[15] of Mexican Jalap, exhibited 14-H_3 signals at δ 0.850 and 0.918, respectively. The $\Delta\delta$ value, −0.068 ppm, shows **2** to have 11*S*-configuration.

Ipurolic acid (**3**), the common aglycone of pharbitic acids C and D[16] from pharbitin, an ether-insoluble resin glycoside (convolvulin) of Pharbitidis Semen, is 3,11-dihydroxytetradecanoic acid, that is, 3-hydroxyconvolvulinolic acid.

Application of Mosher's method (or its modification using a lanthanide shift reagent) to several 3-hydroxycarboxylic acids has been reported,[17] and we attempted to apply the method to **3**. As a model experiment, commercial methyl 3*S*-hydroxybutyrate (**22**),[8] $[\alpha]_D$ +18.0° (neat), was esterified to afford diastereomeric (−)- and

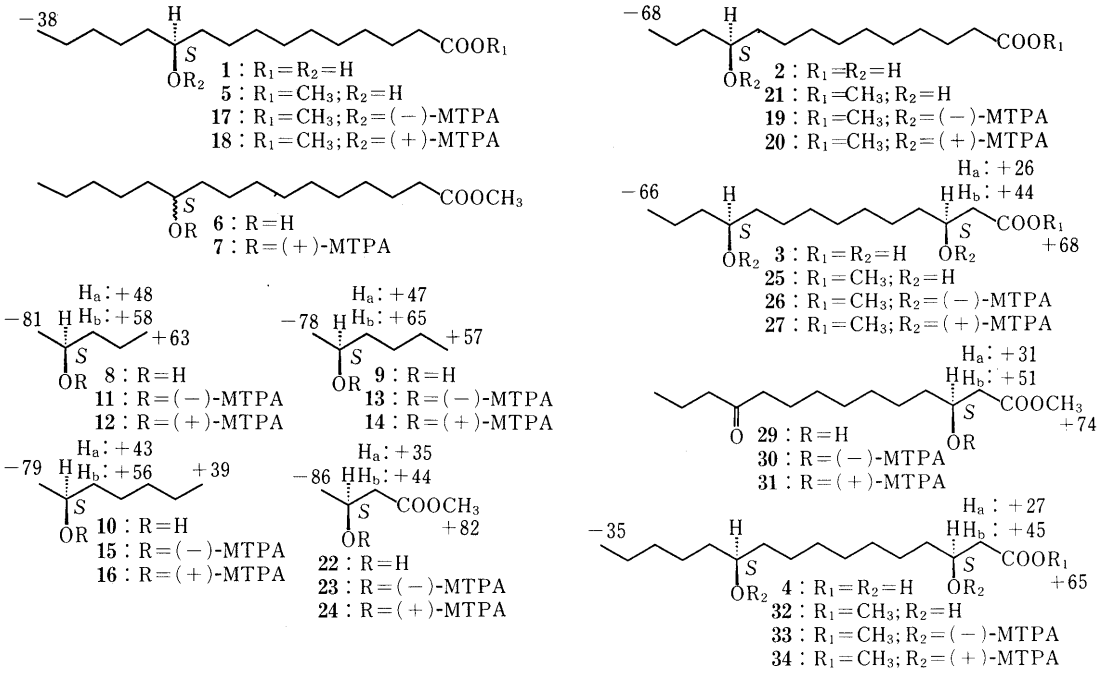

Fig. 1. Values of ^{1}H-NMR Chemical Shift Difference (ppm) [$\Delta\delta$: δ(−)-MTPA−δ(+)-MTPA Ester ($\times 10^{-3}$)] for MTPA Esters (400 MHz)

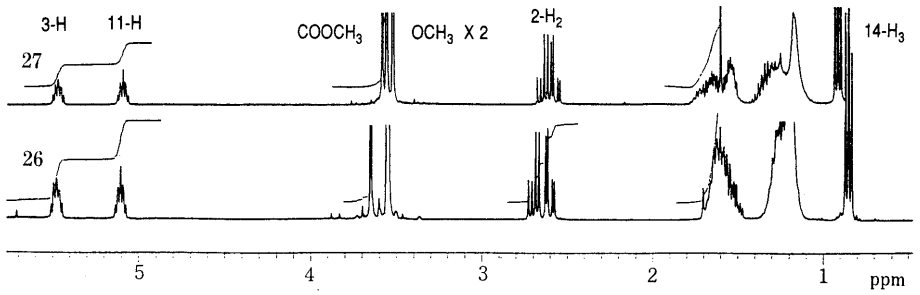

Fig. 2. ^{1}H-NMR Spectra of **26** snd **27** (in $CDCl_3$, 400 MHz)

(+)-MTPA esters (**23** and **24**). Their ^{1}H-NMR spectra showed signals due to the 4-H_3, 2-H_a, 2-H_b and ester methyl protons, and the $\Delta\delta$ values in regard to the respective proton(s) were −0.086, +0.035, +0.044 and +0.082 ppm. These data are consistent with those predicted for 3*S*-configuration of **22**. Therefore, the configuration at 3-C of **3** could be determined by use of the 2-methylene and ester methyl signals.

Ipurolic acid methyl ester (**25**), $[\alpha]_D$ +1.2°, was completely acylated by (−)- and (+)-MTPACl to give (−)- and (+)-MTPA diesters (**26** and **27**). Comparison of the ^{1}H-NMR spectrum of **26** with that of **27** showed, similarly to the case of **19** and **20**, as well as **23** and **24**, the $\Delta\delta$ values −0.066, +0.026, +0.044 and +0.068 ppm in regard to 14-H_3, 2-H_a, 2-H_b and ester methyl proton signals, respectively (Fig. 2), suggesting that the configurations at 3- and 11-C of **3** are both *S*. However, the possibility can not necessarily be excluded that the $\Delta\delta$ values might be affected by interaction between the two MTPA residues at 3- and 11-C in **26** and **27**. This possibility was ruled out as follows.

Methyl 11-hydroxytetradec-2-enoate (**28**), which was prepared from crude pharbitic acid by successive dehydration with AcONa–Ac_2O, and alkaline and acidic hydrolyses according to Okabe *et al.*,[18] was hydrogenated to afford methyl 11-hydroxytetradecanoate (**21′**). Its $[\alpha]_D$ value, melting point and ^{13}C-NMR spectrum were identical with those of methyl convolvulinolate (**21**). Compound **25** was partially oxidized to give methyl 3-hydroxy-11-oxotetradecanoate (**29**), and the ^{1}H-NMR spectra of its (−)- and (+)-MTPA esters (**30** and **31**) showed $\Delta\delta$ values of +0.031, +0.051 and +0.074 ppm for the 2-H_a, 2-H_b and ester methyl proton signals, respectively, in parallel with those between **23** and **24**.

Thus, the configurations at both 3- and 11-C of **3** are properly regarded as *S*.

The methyl ester (**32**) of 3,11-dihydroxyhexadecanoic acid (**4**), the aglycone of pharbitic acid B,[16] was converted into the (−)- and (+)-MTPA esters (**33** and **34**). Comparison of their ^{1}H-NMR spectra revealed the $\Delta\delta$ values of −0.035, +0.027, +0.045 and +0.065 ppm for 16-H_3, 2-H_a, 2-H_b and ester methyl proton signals, respectively. By analogy with the case of **3**, **4** is also considered to have the 3*S*,11*S*-configurations.

The ^{1}H-NMR spectra of the MTPA esters of **5**, **21**, **25** and **32** exhibited no signals due to their counterpart

diastereomers, and hence compounds **1**, **2**, **3** and **4** obtained from the resin glycosides were considered to be optically pure.

Mosher's method was thus found to be useful for determination of the absolute configuration and optical purity of a minute amount of hydroxyfatty acid, whose specific rotation is small (less than 2°).

Experimental

^{1}H-NMR spectra were recorded on a JEOL JNM GSX-400 spectrometer (400 MHz) at 25 °C using tetramethylsilane as an internal reference. Optical rotations were determined on a JASCO DIP-140 polarimeter at 16—22 °C.

Preparation of 6 A mixture of 1% CrO_3–pyridine (3 ml) was added to a solution of **5** (300 mg) in pyridine (1 ml), and the mixture was left to stand at room temperature overnight. The reaction mixture was poured into ice water (20 ml) and extracted with ether (20 ml × 3). The extractive was purified by silica gel chromatography (*n*-hexane–AcOEt, 1 : 1) to give methyl 11-oxohexadecanoate (**35**) (224 mg), colorless needles (petroleum ether), mp 38—39 °C, electron impact (EI)-MS *m/z*: 284 $[M]^+$. $NaBH_4$ (30 mg) was added in portions to a solution of **35** (163 mg) in MeOH (2.5 ml) for 5 min under stirring. The mixture was worked up in the usual manner to furnish **6** (145 mg), colorless needles (petroleum ether), mp 44—45 °C; field desorption (FD)-MS *m/z*: 287 $[M+H]^+$, 269 $[M+H-H_2O]^+$, 215 $[M-CH_3(CH_2)_4]^+$, 186, 135, 101, $[CH_3(CH_2)_4$-$CH(OH)]^+$.

Preparation of 21′ A solution of crude pharbitic acid (3.0 g) and AcONa (6.0 g) in Ac_2O (60 ml) was heated at 95 °C for 5 h and poured into ice-water to afford yellowish precipitates (3.6 g). They were refluxed with 3.5% KOH–EtOH (60 ml), and the mixture was neutralized with 2 N HCl then evaporated *in vacuo*. The residue was hydrolyzed with 2 N HCl (50 ml) at 90 °C for 2 h. The mixture was extracted with ether (50 ml × 3) and the ether layer was washed with H_2O (30 ml × 2) then evaporated. The residue was methylated with ethereal diazomethane and the product was subjected successively to silica gel chromatography (*n*-hexane : AcOEt = 5 : 1), preparative HPLC (Kusano CIG prepacked Si, 2.2 cm i.d. × 10 cm, *n*-hexane : AcOEt = 5 : 1) and vacuum distillation to give **28** (115 mg), a colorless oil, bp 166—167 °C (4 mmHg). ^{1}H-NMR (in $CDCl_3$, 400 MHz) δ: 0.928 (3H, t, J = 7.0 Hz, 14-H_3), 2.196 (2H, ddt, J = 1.2, 7.0, 7.0 Hz, 4-H_2), 3.597 (1H, m, 11-H), 3.726 (3H, s, OCH_3), 5.818 (1H, dt, J = 15.6, 1.2 Hz, 2-H), 6.972 (1H, dt, J = 15.6, 7.0 Hz, 3-H). ^{13}C-NMR (in $CDCl_3$) δ: 14.1 (14-C), 18.8, 15.6, 28.0, 29.1, 29.4, 29.6, 32.2, 37.5, 39.7, 51.4 (OCH_3), 71.7 (11-C), 120.8 (2-C), 149.8 (3-C), 167.2 (1-C).

A suspension of **28** (115 mg) and 10% palladium on charcoal (50 mg) in 1,4-dioxane (5 ml) was stirred under a hydrogen atmosphere for 5 h. The catalyst was filtered off and the filtrate was concentrated *in vacuo* to give **21′** (77 mg), colorless needles (petroleum ether), mp 34 °C, $[\alpha]_D$ +0.9° (c = 4.6, $CHCl_3$). This product was identical with an authentic sample of methyl convolvulinolate[13] as judged from a comparison of their ^{13}C-NMR spectra.

Preparation of 29 A mixture of CrO_3–pyridine (8%, 10 ml) was added to a solution of **25** (100 mg) in CH_2Cl_2–pyridine (1 : 1, 6 ml). The mixture was stirred at room temperature for 4.5 h, diluted with water (150 ml), then extracted with ether (50 ml × 5). The ether layer was dried over $MgSO_4$ and concentrated *in vacuo* to give a residue. It was subjected to silica gel column chromatography (*n*-hexane : AcOEt = 4 : 1 → 3 : 1 → 2 : 1 → AcOEt) to give **29** (46 mg), colorless needles (*n*-hexane–AcOEt), mp 42—43 °C, ^{1}H-NMR (in $CDCl_3$) δ: 0.910 (3H, t, J = 7.3 Hz, 14-H_3), 1.595 (2H, tq, J = 7.3, 7.3 Hz, 13-H_2), 2.372 (2H, t, J = 7.3 Hz, 12-H_2), 2.379 (2H, t, J = 7.3 Hz, 10-H_2), 2.409 (1H, dd, J = 9.2, 16.5 Hz, 2-H_a), 2.515 (1H, dd, J = 3.1, 16.5 Hz, 2-H_b), 2.874 (1H, d, J = 4.0 Hz, 3-OH), 3.717 (3H, s, $OC\underline{H}_3$), 3.997 (1H, m, 3-H). ^{1}H-NMR (in pyridine-d_5) δ: 0.853 (3H, t, J = 7.3 Hz, 14-H_3), 2.314 (2H, t, J = 7.0 Hz, 12-H_2 or 10-H_2), 2.328 (2H, t, J = 7.0 Hz, 10-H_2 or 12-H_2), 2.700 (1H, dd, J = 4.5, 15.0 Hz, 2-H_a), 2.766 (1H, dd, J = 8.0, 15.0 Hz, 2-H_b), 3.647 (3H, s, OCH_3), 4.438 (1H, m, 3-H). ^{13}C-NMR (in pyridine-d_5) δ: 13.9 (14-C), 17.5, 24.1, 26.1, 29.5, 29.8, 38.1, 42.7, 43.5, 44.5, 51.3 (OCH_3), 68.1 (3-C), 172.8 (1-C), 210.3 (11-C). EI-MS *m/z*: 272 $[M]^+$, 254 $[M-H_2O]^+$, 187 $[(CH_2)_7CH(OH)CH_2COOH]^+$, 71 $[C_3H_7CO]^+$ and methyl 3,11-dioxotetradecanoate (36 mg), colorless needles (*n*-hexane–AcOEt), mp 44—45 °C. ^{1}H-NMR (in $CDCl_3$) δ: 0.909 (3H, t, J = 7.3 Hz, 14-H_3), 2.368 (3H, t, J = 7.3 Hz, 12-H_2 or 10-H_2), 2.376 (3H, t, J = 7.6 Hz, 10-H_2 or 12-H_2), 2.526 (2H, t, J = 7.3 Hz, 4-H_2), 3.441 (2H, s, 2-H_2), 3.734 (3H, s, OCH_3). ^{13}C-NMR (in $CDCl_3$) δ: 13.8 (14-C), 17.3, 23.3, 23.7, 28.8, 29.0, 29.1, 42.7, 43.0, 44.7, 49.0, 52.3 (OCH_3), 167.7 (1-C), 202.8 (3-C), 211.5 (11-C). EI-MS *m/z*: 270 $[M]^+$, 185 $[(CH_2)_7COCH_2COOH)]^+$, 71 $[C_3H_7CO]^+$.

Preparation of (−)- and (+)-MTPA Esters, 7, 17, 18, 19, 20, 26, 27, 30, 31, 33 and 34 Freshly prepared (−)- or (+)-MTPA chloride (10—120 mg) was added to a solution of a starting hydroxy compound (1—45 mg) in pyridine (2 ml) and CCl_4 (5 drops), and the mixture was left to stand at room temperature overnight. The solvent was removed under an N_2 stream to give a residue. The residue was purified by chromatography over silica gel (benzene : AcOEt = 10 : 1 → 8 : 1 → 5 : 1 → AcOEt) to furnish the corresponding MTPA ester in a yield of 50—98%.

7: 47 mg, a colorless oil. ^{1}H-NMR (in $CDCl_3$) δ: 0.840, 0.876 (each 3/2H, t, J = 7.0 Hz, 16-H_3), 2.298 (2H, t, J = 7.6 Hz, 2-H_2), 3.557 (3H, q, J = 1.2 Hz, OCH_3), 3.658, 3.660 (each 3/2H, s, $COOCH_3$), 5.088 (1H, tt, J = 5.5, 7.0 Hz, 11-H).

17: 31 mg, a colorless oil. ^{1}H-NMR (in $CDCl_3$) δ: 0.840 (3H, t, J = 6.9 Hz, 16-H_3), 2.298 (2H, t, J = 7.5 Hz, 2-H_2), 3.556 (3H, q, J = 1.2 Hz, OCH_3), 3.663 (3H, s, $COOCH_3$), 5.083 (1H, tt, J = 5.5, 6.7 Hz, 11-H).

18: 28 mg, a colorless oil. ^{1}H-NMR (in $CDCl_3$) δ: 0.878 (3H, t, J = 6.9 Hz, 16-H_3), 2.299 (2H, t, J = 7.5 Hz, 2-H_2), 3.557 (3H, q, J = 1.2 Hz, OCH_3), 3.664 (3H, s, $COOCH_3$), 5.083 (1H, tt, J = 5.5, 6.7 Hz, 11-H).

19: 23 mg, a colorless oil. ^{1}H-NMR (in $CDCl_3$) δ: 0.850 (3H, t, J = 7.3 Hz, 14-H_3), 2.298 (2H, t, J = 7.5 Hz, 2-H_2), 3.552 (3H, q, J = 1.2 Hz, OCH_3), 3.662 (3H, s, $COOCH_3$), 5.098 (1H, tt, J = 5.3, 7.0 Hz, 11-H).

20: 23 mg, a colorless oil. ^{1}H-NMR (in $CDCl_3$) δ: 0.918 (3H, t, J = 7.3 Hz, 14-H_3), 2.299 (2H, t, J = 7.6 Hz, 2-H_2), 3.560 (3H, q, J = 1.2 Hz, OCH_3), 3.664 (3H, s, $COOCH_3$), 5.096 (1H, tt, J = 5.5, 7.0 Hz, 11-H).

26: 110 mg, a colorless oil. ^{1}H-NMR (in $CDCl_3$) δ: 0.853 (3H, t, J = 7.3 Hz, 14-H_3), 2.600 (1H, dd, J = 4.6, 15.9 Hz, 2-H_a), 2.694 (1H, dd, J = 7.9, 15.9 Hz, 2-H_b), 3.539 (3H, br s, OCH_3), 3.548 (3H, q, br s, OCH_3), 3.656 (3H, s, $COOCH_3$), 5.094 (1H, ddt, J = 5.2, 6.5, 6.5 Hz, 11-H), 5.467 (1H, ddt, J = 5.0, 6.8, 6.8 Hz, 3-H).

27: 70 mg, a colorless oil. ^{1}H-NMR (in $CDCl_3$) δ: 0.919 (3H, t, J = 7.3 Hz, 14-H_3), 2.574 (1H, dd, J = 4.9, 15.9 Hz, 2-H_a), 2.650 (1H, dd, J = 7.9, 15.9 Hz, 2-H_b), 3.527 (3H, q, J = 1.2 Hz, OCH_3), 3.563 (3H, q, J = 1.2 Hz, OCH_3), 3.588 (3H, s, $COOCH_3$), 5.095 (1H, tt, J = 5.7, 7.0 Hz, 11-H), 5.474 (1H, ddt, J = 4.9, 7.9, 6.0 Hz, 3-H).

30: 1 mg, a colorless oil. ^{1}H-NMR (in $CDCl_3$) δ: 0.913 (3H, t, J = 7.5 Hz, 14-H_3), 2.369 (2H, t, J = 7.4 Hz, 12-H_2), 2.373 (2H, t, J = 7.3 Hz, 10-H_2), 2.604 (1H, dd, J = 4.6, 16.2 Hz, 2-H_a), 2.699 (1H, dd, J = 8.1, 16.2 Hz, 2-H_b), 3.543 (3H, q, J = 1.2 Hz, OCH_3), 3.663 (3H, s, $COOCH_3$), 5.473 (1H, ddt, J = 4.6, 8.1, 5.5 Hz, 3-H).

31: 1 mg, a colorless oil. ^{1}H-NMR (in $CDCl_3$) δ: 0.911 (3H, t, J = 7.5 Hz, 14-H_3), 2.372 (2H, t, J = 7.4 Hz, 12-H_2), 2.376 (2H, t, J = 7.3 Hz, 10-H_2), 2.573 (1H, dd, J = 4.9, 16.2 Hz, 2-H_a), 2.648 (1H, dd, J = 7.9, 16.2 Hz, 2-H_b), 3.527 (3H, d, J = 0.7 Hz, OCH_3), 3.589 (3H, s, $COOCH_3$), 5.473 (1H, ddt, J = 4.9, 7.9, 6.0 Hz, 3-H).

33: 45 mg, a colorless oil. ^{1}H-NMR (in $CDCl_3$) δ: 0.842 (3H, t, J = 6.8 Hz, 16-H_3), 2.600 (1H, dd, J = 4.8, 16.0 Hz, 2-H_a), 2.695 (1H, dd, J = 8.0, 16.0 Hz, 2-H_b), 3.541 (3H, q, J = 0.9 Hz, OCH_3), 3.555 (3H, q, J = 0.9 Hz, OCH_3), 3.655 (3H, s, $COOCH_3$), 5.082 (1H, tt, J = 5.5, 7.0 Hz, 11-H), 5.469 (1H, ddt, J = 4.8, 8.0, 6.3 Hz, 3-H).

34: 31 mg, a colorless oil. ^{1}H-NMR (in $CDCl_3$) δ: 0.877 (3H, t, J = 7.0 Hz, 16-H_3), 2.573 (1H, dd, J = 4.9, 15.9 Hz, 2-H_a), 2.650 (1H, dd, J = 8.0, 15.9 Hz, 2-H_b), 3.527 (3H, q, J = 1.2 Hz, OCH_3), 3.558 (3H, q, J = 1.2 Hz, OCH_3), 3.590 (3H, s, $COOCH_3$), 5.081 (1H, tt, J = 5.5, 7.0 Hz, 11-H), 5.470 (1H, ddt, J = 4.9, 8.0, 6.0 Hz, 3-H).

Preparation of (−)- and (+)-MTPA Esters, 11, 12, 13, 14, 15, 16, 23 and 24 Freshly prepared (−)- or (+)-MTPA chloride (45 mg) was added to a solution of starting material (10 mg) in pyridine (0.5 ml) and CCl_4 (10 drops), and the mixture was left to stand at room temperature overnight. It was then diluted with H_2O (5 ml) and extracted with ether (5 ml × 3). The organic layer was washed with 0.2 N HCl (10 ml), 0.3% aqueous Na_2CO_3 (10 ml) and H_2O (10 ml × 2), successively. The ether layer was dried over $MgSO_4$ and concentrated under reduced pressure to afford a colorless oil (yield 67—86%).

11: 24 mg, a colorless oil. ^{1}H-NMR (in $CDCl_3$) δ: 0.921 (3H, t, J = 7.3 Hz, 5-H_3), 1.251 (3H, d, J = 6.1 Hz, 1-H_3), 1.527 (1H, m, 3-H_a), 1.690 (1H, m, 3-H_b), 3.549 (3H, q, J = 1.2 Hz, OCH_3), 5.153 (1H, ddq, J = 5.1, 7.5, 6.1 Hz, 2-H).

12: 22 mg, a colorless oil. ^{1}H-NMR (in $CDCl_3$) δ: 0.858 (3H, t, J = 7.3 Hz, 5-H_3), 1.332 (3H, d, J = 6.3 Hz, 1-H_3), 1.479 (1H, m, 3-H_a), 1.632 (1H, m, 3-H_b), 3.562 (3H, q, J = 1.2 Hz, OCH_3), 5.167 (1H, ddq, J = 5.0, 7.6, 6.3 Hz, 2-H).

13: 21 mg, a colorless oil. ^{1}H-NMR (in $CDCl_3$) δ: 0.888 (3H, t, J = 7.0 Hz, 6-H_3), 1.252 (3H, d, J = 6.1 Hz, 1-H_3), 1.558 (1H, m, 3-H_a), 1.688 (1H, m, 3-H_b), 3.548 (3H, q, J = 1.2 Hz, OCH_3), 5.139 (1H, ddq, J = 5.1, 7.0, 6.1 Hz,

2-H).

14: 22 mg, a colorless oil. ^{1}H-NMR (in $CDCl_3$) δ: 0.831 (3H, t, J=7.0 Hz, 6-H_3), 1.330 (3H, d, J=6.3 Hz, 1-H_3), 1.511 (1H, m, 3-H_a), 1.623 (1H, m, 3-H_b), 3.567 (3H, q, J=1.2 Hz, OCH_3), 5.153 (1H, ddq, J=5.1, 7.0, 6.3 Hz, 2-H).

15: 19 mg, a colorless oil. ^{1}H-NMR (in $CDCl_3$) δ: 0.878 (3H, t, J=6.9 Hz, 7-H_3), 1.251 (3H, d, J=6.1 Hz, 1-H_3), 1.546 (1H, m, 3-H_a), 1.676 (1H, m, 3-H_b), 3.547 (3H, q, J=1.2 Hz, OCH_3), 5.140 (1H, ddq, J=5.0, 7.0, 6.1 Hz, 2-H).

16: 20 mg, a colorless oil. ^{1}H-NMR (in $CDCl_3$) δ: 0.839 (3H, t, J=7.0 Hz, 7-H_3), 1.330 (3H, d, J=6.3 Hz, 1-H_3), 1.503 (1H, m, 3-H_a), 1.620 (1H, m, 3-H_b), 3.569 (3H, q, J=1.2 Hz, OCH_3), 5.157 (1H, ddq, J=5.0, 7.3, 6.3 Hz, 2-H).

23: 21 mg, a colorless oil. ^{1}H-NMR (in $CDCl_3$) δ: 1.336 (3H, d, J=6.4 Hz, 4-H_3), 2.573 (1H, dd, J=4.7, 16.2 Hz, 2-H_a), 2.727 (1H, dd, J=8.5, 16.2 Hz, 2-H_b), 3.526 (3H, q, J=1.2 Hz, OCH_3), 3.663 (3H, s, $COOCH_3$), 5.543 (1H, ddq, J=4.7, 8.5, 6.4 Hz, 3-H).

24: 20 mg, a colorless oil. ^{1}H-NMR (in $CDCl_3$) δ: 1.422 (3H, d, J=6.4 Hz, 4-H_3), 2.538 (1H, dd, J=5.1, 16.0 Hz, 2-H_a), 2.683 (1H, dd, J=8.2, 16.0 Hz, 2-H_b), 3.535 (3H, q, J=1.2 Hz, OCH_3), 3.581 (3H, s, $COOCH_3$), 5.550 (1H, ddq, J=5.1, 8.2, 6.4 Hz, 3-H).

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References and Notes

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