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Pheromone synthesis. Part 253: Synthesis of the racemates and enantiomers of triglycerides of male *Drosophila* fruit flies with special emphasis on the preparation of enantiomerically pure 1-monoglycerides☆

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In memory of Professor Masanao Matsui, my Dr. thesis advisor, who deceased on 12 March 2012 at the age of 94

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ABSTRACT

The racemates and enantiomers of triglycerides **1a**–**e** (2,3-ditigloyloxypropyl esters of palmitic, palmitoleic, stearic, oleic, and linoleic acids) of male *Drosophila* fruit flies were synthesized in three steps from the racemate and enantiomers of 2,3-acetoneglycerol (**2**) via 1-monoglycerides **4a**–**e** derived from the above fatty acids. Appropriate conditions were established for the preparation of enantiomerically pure 1-monoglycerides **4a**–**e**, and their enantiomeric purities were determined by NMR analysis of the corresponding bis-(*R*)-MTPA esters.

1. Introduction

Triglycerides are naturally occurring and abundant tricarboxylic esters of glycerol (**A**, Fig. 1). Triglycerides **B** with the same three acyl groups as well as glycerol (**A**) itself are symmetrical and therefore achiral. However, triglycerides with different acyl groups, such as **C** and **D** are dissymmetric and chiral. Naturally occurring triglycerides are believed to be biosynthesized in a stereoselective fashion, although their specific rotations are almost zero; for example, $[\alpha]_D$ 0.00 to +0.09 in the case of **C**, R^1=*n*-$C_{11}H_{23}$ and R^2=*n*-$C_{15}H_{31}$.[2,3] Two exceptions were reported in 1930 with $[\alpha]_D$ values −0.149 for peanut oil and +1.970 for castor bean oil.[4] Extremely facile ester exchange of the three acyl groups causes randomization and racemization. Accordingly, synthesis of enantiomerically pure triglycerides of type **C** is not at all a trivial work even at present.

Recently, Yew (2011)[5] and Ruther (2012)[6] found triglycerides as components of insect cuticular lipids. Yew demonstrated the presence of triglycerides in epicuticle of two *Drosophila* fruit flies, *Drosophila arizonae* and *Drosophila mojavensis*.[5] The triglycerides of *D. mojavensis* are male-specific, transferred from male to females during copulation, and therefore may serve as a class of courtship-

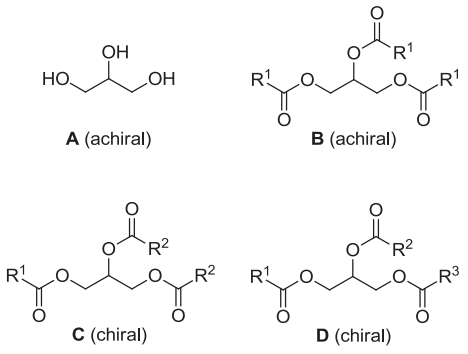

Fig. 1. Structures of glycerol (**A**) and triglycerides (**B**–**D**).

☆ For Part 252, see Ref. 1.

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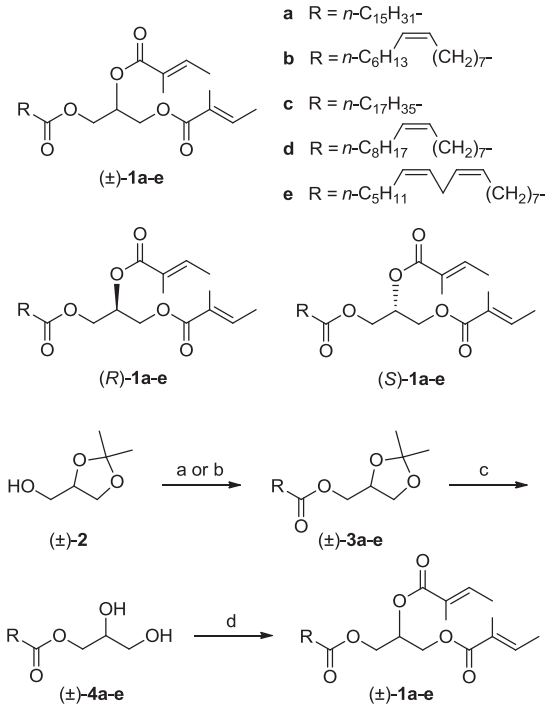
related semiochemicals in *Drosophila* species.[5] In Ruther's case, triglycerides with common fatty acids of 16 and 18 carbon atoms occur in the cuticle of a parasitic wasp *Lariophagus distinguendus*, and they are essential for a full pheromone response of the wasp.[6]

In January 2012, Jacqueline Chin of Yew's group at National University of Singapore announced the identification of triglycerides in epicuticular lipids of male *Drosophila* fruit flies as **1a**–**e** (Scheme 1).[7] These structures were tentatively proposed entirely on the basis of mass spectroscopic analysis, and nothing was known about their absolute configuration. In order to verify the unique structures **1a**–**e** with two tiglic acids for each triglyceride, Dr. Joanne Y. Yew requested me to synthesize **1a**–**e** in amounts sufficient for their biological studies.



Scheme 1. Structures of triglycerides **1a**–**e** of male *Drosophila* fruit flies and their synthesis as racemates. Reagents: (a) RCOCl, DMAP, C_5H_5N (80–93%); (b) RCO_2H, DCC, DMAP, CH_2Cl_2 (95%-quant.); (c) 80% AcOH, 130 °C, 30 min (68%-quant.); (d) MeCH=C(Me)COCl, DMAP, C_5H_5N, C_6H_6 (72–93%).

I decided to synthesize not only the racemates but also the enantiomers of **1a**–**e** with a hope to determine the absolute configuration of the naturally occurring triglycerides. This paper reports the synthetic results of my endeavor in that direction.

2. Results and discussion

2.1. Synthesis of the racemates of triglycerides 1a–e

The racemates of triglycerides **1a**–**e** were synthesized as shown in Scheme 1. Commercially available (±)-2,2-dimethyl-1,3-dioxolane-4-methanol (**2**, 2,3-acetoneglycerol) was esterified to give (±)-esters **3a**–**e**. Since palmitoyl chloride (n-$C_{15}H_{31}COCl$), stearoyl chloride (n-$C_{17}H_{35}COCl$), and oleoyl chloride [(*Z*)-n-$C_8H_{17}CH{=}CH(CH_2)_7COCl$] were commercially available, (±)-**3a**, (±)-**3c**, and (±)-**3d** were prepared by acylation of (±)-**2** with each acyl chloride in the presence of 4-dimethylaminopyridine (DMAP) in pyridine in 80–93% yield (cf. Ref. 8). In the cases of the preparation of (±)-**3b** and (±)-**3e**, (±)-**2** was esterified with palmitoleic acid [(*Z*)-n-$C_6H_{13}CH{=}CH(CH_2)_7CO_2H$] and linoleic acid [(9*Z*,12*Z*)-n-$C_5H_{11}CH{=}CHCH_2CH{=}CH(CH_2)_7CO_2H$], respectively, in the presence of *N*,*N*-dicyclohexylcarbodiimide (DCC) and DMAP in CH_2Cl_2 to give them in almost quantitative yield.[9,10] Small amounts of DCC and *N*,*N*′-dicyclohexylurea were the contaminants in the esters (±)-**3b** and (±)-**3e**.

Removal of the acetonide protective group of (±)-**3a**–**e** was achieved by treatment with 80% acetic acid [AcOH/H_2O=4:1 (v/v)] at 130 °C for 30 min to give (±)-**4a**–**e** in 68% to quantitative yield.[11] Rather harsh conditions such as these were not problematic for the synthesis of (±)-**4a**–**e**, because possible ester exchange or 1,3-acyl migration gave the same (±)-**4a**–**e**. Finally, acylation of diol (±)-**4a**–**e** with tigloyl chloride and DMAP in pyridine gave the desired triglycerides (±)-**1a**–**e** in 72–93% yield. Comparison of the mass spectra of (±)-**1a**–**e** with those of the natural triglycerides proved them to be nearly identical, supporting the structural assignment.[12]

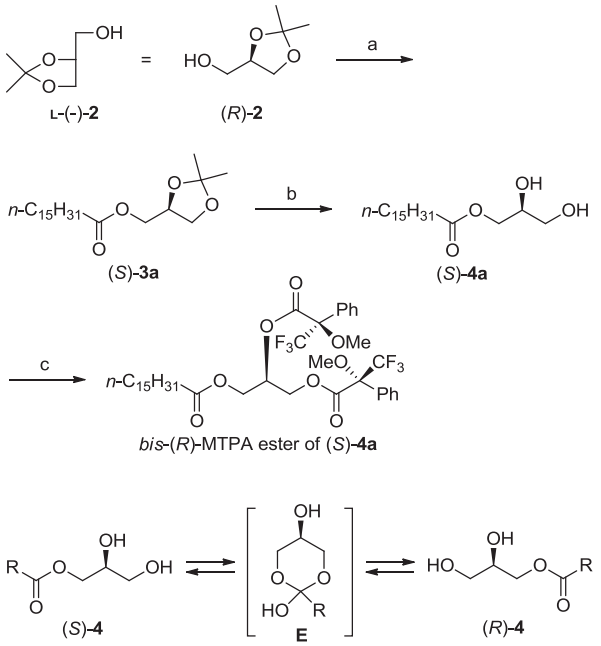
2.2. Preparation of the enantiomers of 1-monoglyceride 4a by removal of the acetonide protective group of 3a

*2.2.1. Determination of the enantiomeric purity of **4a** by NMR analysis of its bis-(R)-MTPA ester.* Preparation of the pure enantiomers of 1-monoglycerides **4a**–**e** was the prerequisite to the synthesis of the enantiomers of **1a**–**e**. Baer and Fischer were the first to prepare (*R*)-**4a** with high enantiomeric purity, although there was no reliable method available in 1945 to determine its enantiomeric purity.[8] They treated enantiomerically pure (*R*)-**3a**, $[\alpha]_D^{50}$ +4.95 (neat), with concd HCl and Et_2O at 0 °C for 30 min to give (*R*)-**4a**, $[\alpha]_D$ −4.37 (*c* 7.8, pyridine). The product (*R*)-**4a** gave back (*R*)-**3a**, $[\alpha]_D^{50}$ +4.86 (neat), upon acetonide formation. Since the loss in the specific rotation of (*R*)-**3a** was only 1.8%, their (*R*)-**4a** was thought to be almost enantiomerically pure (98% optical purity).

In the present task, it was necessary to prepare unsaturated 1-monoglycerides, such as **4b**, **4d**, and **4e**. Use of concd HCl must be avoided due to its possible interaction with the olefinic double bond(s) of palmitoleic, oleic, and linoleic acids. An attempt was therefore made to prepare (*S*)-**4a** by treatment of (*S*)-**3a** with aqueous acetic acid.[11,13] Treatment of commercially available (*R*)-**2** [=L-(−)-2,3-acetoneglycerol] with palmitoyl chloride gave (*S*)-**3a** (Scheme 2). The acetonide protective group of (*S*)-**3a** was then removed quantitatively by heating it with 80% acetic acid at 130 °C for 30 min. The specific rotation of the crystalline (*S*)-**4a** thus obtained was $[\alpha]_D$ +1.89 (*c* 1.54, pyridine), while Baer and Fischer reported their (*R*)-**4a** to show $[\alpha]_D$ −4.37 (*c* 7.8, pyridine). Apparently heating at 130 °C in 80% acetic acid caused racemization of (*S*)-**4a** as shown in Scheme 2.

In order to determine the enantiomeric purity of the present (*S*)-**4a** more rigorously, Mosher's α-methoxy-α-trifluoromethylphenylacetate (MTPA) derivatives of (±)-**4a** and the present sample of (*S*)-**4a** were prepared by acylation with (*S*)-(+)-MTPACl and DMAP in pyridine,[14,15] and their ^{1}H NMR spectra were measured at 400 MHz in $CDCl_3$. As shown in Fig. 2(a), bis-(*R*)-MTPA ester of (±)-**4a** shows several pairs of signals owing to the presence of the two diastereomeric esters. The triplet due to CH_2CO appears as a pair of triplets (*J* 7.5) at δ 2.22 and 2.27. Although not shown in Fig. 2(a), a pair of singlets due to OMe groups is observed at δ 3.40, 3.42 and 3.48, one at δ 3.42 being an overlapping signal. A pair of doubled doublets (*J* 6,12) due to one of the protons of $CH_2OCOC_{15}H_{31}$ appears at δ 4.05 and 4.14, a pair of doubled doublets (*J* 4,12) due to one of the protons of CH_2OMTPA is observed at δ 4.32 and 4.39, a pair of doubled doublets (*J* 6,12) due to one of the protons of $CH_2OCOC_{15}H_{31}$ appears at δ 4.34 and 4.41, and a pair of doubled doublets (*J* 4,12) due to one of the protons of CH_2OMTPA is observed at δ 4.62 and 4.71. A pair of slightly overlapping multiplets due to CHOMTPA appears at δ 5.51 and 5.56.

The ^{1}H NMR spectrum of bis-(*R*)-MTPA ester of the partially racemized (*R*)-**4a** {$[\alpha]_D^{24}$ −2.01 (*c* 1.09, pyridine)} prepared by treatment of (*R*)-**3a** with hot 80% acetic acid (130 °C, 30 min) is



Scheme 2. Preparation of bis-(*R*)-MTPA ester of (*S*)-**4a** and racemization of (*S*)-**4** and (*R*)-**4** to give (±)-**4**. Reagents: (a) *n*-$C_{15}H_{31}COCl$, DMAP, C_5H_5N (93%); (b) 80% AcOH, 50 °C, 2 h (quant.)*; (c) (*S*)-MTPACl, DMAP, C_5H_5N, CH_2Cl_2, room temp, 3 days (quant.). *For other conditions, see Table 1.

shown in Fig. 2(b). It is clear that the signals at δ 4.0–4.8 due to one of the protons of $CH_2OCOC_{15}H_{31}$ and one of the protons of CH_2OMTPA can be used for the determination of the diastereomeric ratio of the NMR sample and hence the enantiomeric purity of the original (*R*)-**4a**. The analyzed sample of (*R*)-**4a** was enantiomerically quite impure (52% ee).

The next thing to do was to find out the best conditions for the removal of the acetonide protective group, employing the above described MTPA/NMR method of analysis as a tool.

*2.2.2. Searching the best conditions for the removal of the acetonide protective group of (S)-**4a** with minimal racemization.* A number of deprotection methods are known for an acetonide protective group. Several of them were carefully examined, which were believed to be mild enough to cause no racemization of 1-monoglyceride due to the ester exchange. Treatment of (*S*)-**3c** with Amberlyst 15 (H^+ form) in $MeOH/CH_2Cl_2$ was believed to give (*S*)-**4c** (1-stearoylglycerol) without any racemization.[9,10] In my hands, however, this method resulted in extensive racemization, (*S*)-**3a** giving (*S*)-**4a** of only 12% ee [see Table 1 (1)]. Kim et al. recommended the use of $FeCl_3$ adsorbed on SiO_2 for the cleavage of acetals.[16] This method yielded (*S*)-**4a** of 65% ee [Table 1 (2)]. Although there was a similar method to employ $CuCl_2\cdot 2H_2O$ in EtOH,[17] it was not examined due to the use of the toxic copper salt in an excessive amount.

A method was proposed by Vijayasaradhi et al. to effect selective hydrolysis of a terminal acetonide with $Zn(NO_3)_2\cdot 6H_2O$ in MeCN.[18] This procedure was mild enough to give (*S*)-**4a** of 90% ee [Table 1 (3)]. The drawback of $Zn(NO_3)_2\cdot 6H_2O$ method was the use of a large amount of the zinc salt and use of MeCN as the solvent. The latter caused a slightly brown coloration of the resulting (*S*)-**4a**. Accordingly, deprotection with 80% acetic acid was reexamined at a lower temperature, although heating at 130 °C for 30 min as before caused extensive racemization to give (*S*)-**4a** of only 48% ee [Table 1 (4)]. After 2 h at 50 °C, (*S*)-**3a** disappeared as checked by TLC to give (*S*)-**4a** as a colorless solid, which was of 92% ee.

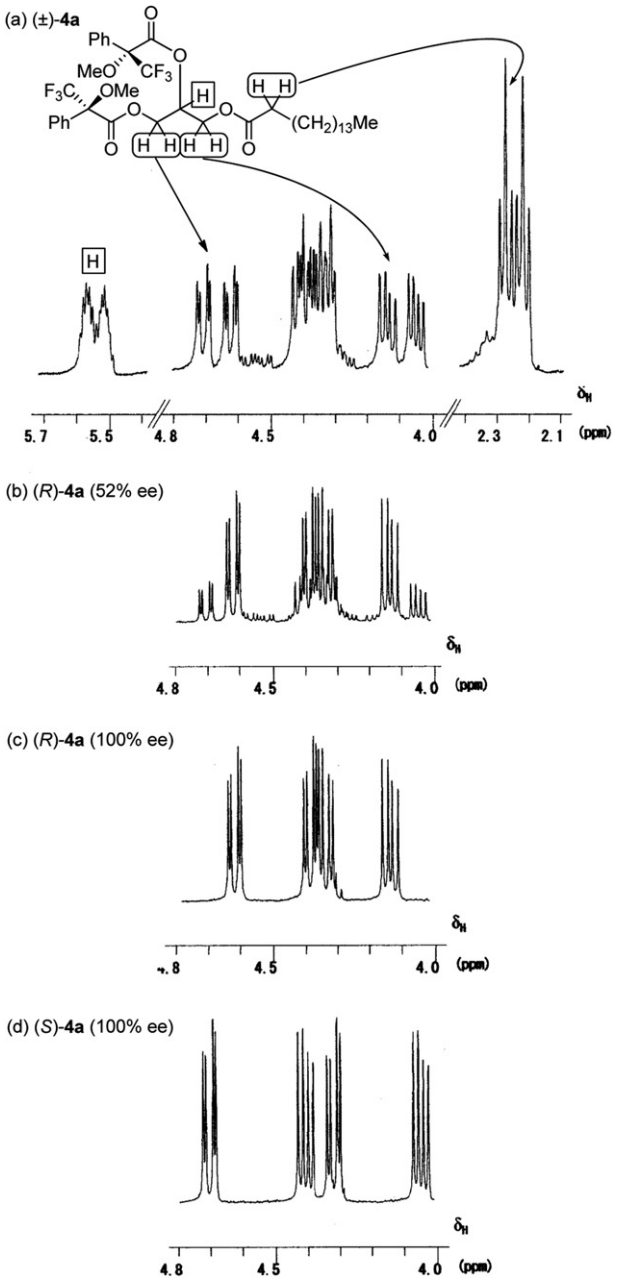


Fig. 2. ^1H NMR spectra of bis-(*R*)-MTPA esters of diol **4a** (400 MHz, $CDCl_3$). (a) Bis-(*R*)-MTPA ester of (±)-diol **4a**; (b) that of (*R*)-diol **4a** of 52% ee; (c) that of (*R*)-**4a**; (d) that of (*S*)-**4a**.

Recrystallization of the crude (*S*)-**4a** from EtOAc/pentane gave enantiomerically pure (*S*)-**4a** [Table 1 (5)]. Similarly, under the same conditions at 50 °C for 2 h, enantiomerically pure (*R*)-**4a** could also be obtained. The ^1H NMR spectra of their bis-(*R*)-MTPA esters are shown in Fig. 2(c) for (*R*)-**4a** and Fig. 2(d) for (*S*)-**4a**. The present MTPA/NMR method of analysis was extremely useful for determining the enantiomeric purity of optically active 1-monoglycerides, such as **4a**–**e**.

2.3. Synthesis of the enantiomers of triglycerides 1a–e

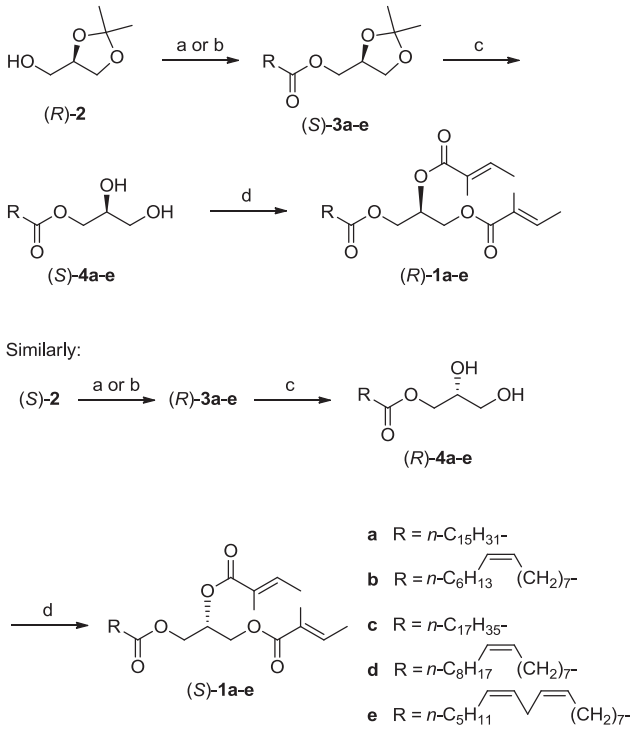
With the reliable analytical method in hands for the determination of the enantiomeric purity of the enantiomers of **4a**–**e**, the target triglycerides **1a**–**e** were synthesized from the enantiomers of 2,3-acetoneglycerol (**2**) as shown in Scheme 3. Acylation of

Table 1
Specific rotation and enantiomeric purity of 1-monoglyceride (*S*)-**4a** resulting from deprotection of the corresponding acetonide (*S*)-**3a**

Method of deprotection	Specific rotation of (*S*)-**4a** in pyridine[a]	Enantiomeric purity (% ee) of (*S*)-**4a**[b]
(1) Amberlyst 15 (H^+ form), MeOH/CH_2Cl_2, reflux, 2 h[9,10]	$[\alpha]_D^{21}$ +0.21 (*c* 2.06)	12
(2) $FeCl_3/SiO_2$, $CHCl_3$, room temp, 6 h[16]	$[\alpha]_D^{23}$ +1.40 (*c* 0.47)	65
(3) $Zn(N0_3)_2{\cdot}6H_2O$, MeCN, 50 °C, 4 h[18]	$[\alpha]_D^{26}$ +3.51 (*c* 0.34)	90
(4) AcOH/H_2O (4:1, v/v), 130 °C, 30 min[11]	$[\alpha]_D^{21}$ +1.89 (*c* 1.54)	48
(5) AcOH/H_20 (4:1, v/v), 50 °C, 2 h	$[\alpha]_D^{26}$ +4.14 (*c* 2.53)[c]	92 (100[c])

[a] Reported value of pure (*R*)-**4a**: $[\alpha]_D$ −4.37 (*c* 7.8).[8]
[b] Determined by MTPA/NMR analysis.
[c] After recrystallization from EtOAc/pentane.

(*R*)-**2** with either acyl chlorides or acids afforded acetonide esters (*S*)-**3a**–**e**. Removal of the acetonide protective groups of (*S*)-**3a**–**e** furnished (*S*)-**4a**–**e**. The crystalline (*S*)-**4a** and (*S*)-**4c** could be purified by recrystallization at this stage to give enantiomerically pure diols. The remaining oily diols (*S*)-**4b**, **4d**, and **4e** (90–100% ee as analyzed by the MTPA/NMR method) were employed in the final step without further purification.



Scheme 3. Synthesis of the enantiomers of **1a**–**e**, the triglycerides of male *Drosophila* fruit flies. Reagents: (a) RCOCl, DMAP, C_5H_5N (85–99%); (b) RCO_2H, DCC, DMAP, CH_2Cl_2 (94%-quant.); (c) 80% AcOH, 50 °C, 2 h (66%-quant.); (d) (*E*)-MeCH=C(Me)COCl, DMAP, C_5H_5N, C_6H_6 (72%-quant.).

Esterification of (*S*)-**4a**–**e** with an excess amount of tigloyl chloride and DMAP in pyridine gave (*R*)-**1a**–**e** after chromatographic purification over SiO_2. Their IR, ^1H and ^{13}C NMR, and mass spectra supported the expected structures. The values of specific rotation (at 25 or 26 °C) of (*R*)-**1a**–**e** (+4.66∼+5.40 in hexane) were not so small in contrast to those reported (0.00∼+0.09) for the ordinary triglycerides of natural origin.[2,3] Similarly, (*S*)-**2** yielded triglycerides (*S*)-**1a**–**e** with $[\alpha]_D^{23-26}$ value of −4.71 to −5.45. The enantiomeric purity of these final products (*R*)- and (*S*)-**1a**–**e** was regarded to be same as that of (*S*)- and (*R*)-**4a**–**e**, because no racemization was observed when the enantiomers of **4a**–**e** were treated with excess amounts of (*S*)-(+)-MTPACl to give their bis-(*R*)-MTPA esters. The overall yield of the enantiomers of **1a**–**e** was 54–96% (average 73%) over three steps based on (*R*)- or (*S*)-**2**.

3. Conclusion

The racemates and enantiomers of triglycerides **1a**–**e** of male *Drosophila* fruit flies were synthesized in amounts sufficient for further biological studies. Synthesis of the enantiomers of **1a**–**e** was made possible by developing reliable methods for preparation and determination of their enantiomeric purities of the enantiomers of 1-monoglycerides **4a**–**e**. Biological studies on the role of **1a**–**e** in the courtship behavior of *Drosophila* fruit flies will be reported in due course by Dr. J.Y. Yew at National University of Singapore.

4. Experimental

4.1. General

Melting points are uncorrected values. Refractive indices (n_D) were measured on an Atago DMT-1 refractometer. Optical rotations were measured on a Jasco P-1020 polarimeter. IR spectra were measured on a Jasco FT/IR-410 spectrometer. ^1H NMR spectra (400 MHz, TMS at δ=0.00 as internal standard) and ^{13}C NMR spectra (100 MHz, $CDCl_3$ at δ=77.0 as internal standard) were recorded on a Jeol JNM-AL 400 spectrometer. GC–MS were measured on Agilent Technologies 5975 inert XL. HRMS were recorded on Jeol JMS-SX102A or Waters Synapt G2 HDMS. Column chromatography was carried out on Merck Kieselgel 60 Art 1.07734.

4.2. General procedure for the preparation of 2,2-dimethyl-1,3-dioxolane-4-methyl carboxylate (3)

*4.2.1. Acylation of 2,2-dimethyl-1,3-dioxolane-4-methanol (**2**) with acyl chloride.* A solution of RCOCl [2.75 g (10 mmol) in the case of *n*-$C_{15}H_{31}COCl$] in dry C_6H_6 (10 mL) was added dropwise to a stirred and ice-cooled solution of (±)-**2** (1.00 g, 7.6 mmol) and DMAP (50 mg, 0.4 mmol) in dry pyridine (5 mL) at 5–10 °C. Stirring was continued for 1 h at 0–5 °C, and the mixture was left to stand overnight in a refrigerator. After dilution with ice and water, the mixture was extracted with Et_2O. The extract was washed successively with dil HCl, $NaHCO_3$ solution and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was chromatographed over SiO_2 (35 g). Elution with hexane/EtOAc (20:1) gave 2.60 g (93%) of (±)-**3a**. Preparation of **3a**, **3c**, and **3d** was executed by the above procedure.

*4.2.2. Acylation of **2** with acid and DCC.* A solution of DCC (824 mg, 4 mmol) in dry CH_2Cl_2 (7 mL) was added dropwise to a stirred and ice-cooled solution of (9*Z*,12*Z*)-*n*-$C_5H_{11}CH{=}CHCH_2CH{=}CH(CH_2)_7CO_2H$ (linoleic acid, 560 mg, 2 mmol), (±)-**2** (264 mg, 2 mmol), and DMAP (15 mg, 0.12 mmol) in dry CH_2Cl_2 (10 mL) over 30 min at 0–5 °C. Stirring was continued for 1 h at 0–5 °C, and the mixture was left to stand overnight at room temperature. It was then diluted with hexane and filtered through Celite. The Celite layer was washed with hexane. The combined filtrate and washings

were concentrated in vacuo. The residue was chromatographed over SiO_2 (15 g). Elution with hexane/EtOAc (20:1) gave 836.5 mg (quant.) of (±)-**3e** contaminated with DCC, which could be removed in the next step. Preparation of **3b** and **3e** was executed by the above procedure.

4.3. 2,2-Dimethyl-1,3-dioxolane-4-methyl hexadecanoate (3a)

4.3.1. Racemate. Colorless prisms, mp 29–30 °C; ν_{max} (Nujol): 1742 (s), 1220 (s), 849 (m); δ_H ($CDCl_3$): 0.88 (3H, t, *J* 6.8), 1.25 (24H, br), 1.37 (3H, s), 1.44 (3H, s), 1.62 (2H, m), 2.34 (2H, t, *J* 7.2), 3.70–3.76 (1H, m), 4.05–4.11 (2H, m), 4.15–4.19 (1H, m), 4.30–4.33 (1H, m); GC–MS [Column: HP-5MS 5% phenylmethylsiloxane, 30 m×0.25 mm i.d.; carrier gas, He; press: 52.7 kPa, temp: 50–160 °C (+10 °C/min), then 160–220 °C (+4 °C/min)]: t_R17.56 min (96.7%); MS of (±)-**3a** (70 eV, EI): *m*/*z* 355 (100) [$(M-CH_3)^+$], 312 (10), 269 (7), 239 (6), 185 (6), 171 (10), 129 (16), 116 (16), 101 (28), 57 (8), 43 (18). HRMS calcd for $C_{21}H_{39}O_4$ [$(M-CH_3)^+$]: 355.2848, found: 355. 2847.

4.3.2. (R)-Isomer. Hexadecanoyl chloride (3.02 g) and (*S*)-**2** (Tokyo Kasei, 1.00 g) gave 2.60 g (93%) of (*R*)-**3a** as rhombs, mp 31.0–31.5 °C [Ref. 8 mp 33.0–34.5 °C]; $[\alpha]_D^{23}$ +8.32 (*c* 3.41, hexane) {Ref. 8 $[\alpha]_D$ +4.95 (neat at 50 °C)}. Its IR, ^{1}H NMR, and mass spectra were identical with those of (±)-**3a**. GC–MS [same conditions as those for (±)-**3a**]: t_R 17.53 min (99.7%). HRMS calcd for $C_{21}H_{39}O_4$ [$(M-CH_3)^+$]: 355.2848, found: 355.2833.

4.3.3. (S)-Isomer. Hexadecanoyl chloride (3.02 g) and (*R*)-**2** (Tokyo Kasei, 1.00 g) gave 2.37 g (85%) of (*S*)-**3a** as rhombs, mp 32.0–32.5 °C; $[\alpha]_D^{20}$ −7.91 (*c* 3.14, hexane); Its IR, ^{1}H NMR, and mass spectra were identical with those of (±)-**3a**. GC–MS [same conditions as those for (±)-**3a**]: t_R 17.52 min (99.7%). HRMS calcd for $C_{21}H_{39}O_4$ [$(M-CH_3)^+$]: 355.2848, found: 355.2854.

4.4. 2,2-Dimethyl-1,3-dioxolane-4-methyl (*Z*)-9-hexadecenoate (3b)

4.4.1. Racemate. (*Z*)-9-Hexadecenoic acid (520 mg) and (±)-**2** (264 mg) gave 717 mg (95%) of (±)-**3b** as a colorless oil, n_D^{21}=1.4632; ν_{max} (film): 2929 (s), 2855 (s), 2120 (contaminating DCC), 1742 (s), 1657 (w),1456 (m), 1370 (s), 1214 (s), 1161 (s), 1057 (s), 843 (m), 725 (m); δ_H ($CDCl_3$): 0.88 (3H, t, *J* 7.2), 1.22–1.40 (16H, br), 1.37 (3H, s), 1.43 (3H, s), 1.58–1.70 (2H, m), 1.96–2.08 (4H, m), 2.34 (2H, t, *J* 7.6), 3.71–3.76 (1H, m), 4.05–4.12 (2H, m), 4.14–4.19 (1H, m), 4.29–4.34 (1H, m), 5.30–5.40 (2H, m); GC–MS [same conditions as those for (±)-**3a**]: t_R 17.46 min (76.9%), 12.93 min (11.3%, DCC); MS of (±)-**3b** (70 eV, EI): *m*/*z* 368 (<1) [M^+], 353 (100) [$(M-CH_3)^+$], 310 (23), 267 (6), 253 (7), 239 (6), 185 (20), 171 (11), 129 (54), 116 (16), 101 (24), 83 (9), 69 (13), 55 (21), 43 (22). HRMS calcd for $C_{22}H_{40}O_4$: 368.2927, found: 368.2924.

4.4.2. (R)-Isomer. (*Z*)-9-Hexadecenoic acid (690 mg) and (*S*)-**2** (356 mg) gave 990.6 mg (99%) of (*R*)-**3b** as a colorless oil, n_D^{24}=1.4572; $[\alpha]_D^{24}$ +7.80 (*c* 3.57, hexane); Its IR, ^{1}H NMR, and mass spectra were identical with those of (±)-**3b**. GC–MS [same conditions as those for (±)-**3a**]: t_R 17.45 min (98.2%). HRMS calcd for $C_{22}H_{40}O_4Na$: 391.2824, found: 391.2820.

4.4.3. (S)-Isomer. (*Z*)-9-Hexadecenoic acid (690 mg) and (*R*)-**2** (360 mg) gave 940.3 mg (94%) of (*S*)-**3b** as a colorless oil, n_D^{24}=1.4568; $[\alpha]_D^{23}$ −7.76 (*c* 3.62, hexane); Its IR, ^{1}H NMR, and mass spectra were identical with those of (±)-**3b**. GC–MS [same conditions as those for (±)-**3a**]: t_R 17.45 min (98.3%). HRMS calcd for $C_{22}H_{40}O_4Na$: 391.2824, found: 391.2820.

4.5. 2,2-Dimethyl-1,3-dioxolane-4-methyl octadecanoate (3c)

4.5.1. Racemate. Octadecanoyl chloride (3.03 g) and (±)-**2** (1.58 g) gave 3.55 g (89%) of (±)-**3c** as colorless rods, mp 38.0–38.5 °C: ν_{max} (Nujol): 1733 (s), 1163 (s), 851 (m); δ_H ($CDCl_3$): 0.88 (3H, t, *J* 6.8), 1.25 (28H, br), 1.37 (3H, s), 1.44 (3H, s), 1.63 (2H, m), 2.34 (2H, t, *J* 7.6), 3.72–3.74 (1H, m), 4.06–4.17 (3H, m), 4.29–4.33 (1H, m); GC–MS [same conditions as those for (±)-**3a**]: t_R 18.56 min (99.5%); MS of (±)-**3c** (70 eV, EI): *m*/*z* 398 (<1)[M^+], 383 (100) [$(M-CH_3)^+$], 340 (8), 297 (4), 185 (5), 171 (9), 129 (14), 116 (13), 101 (21), 57 (11), 43 (18). HRMS calcd for $C_{23}H_{43}O_4$ [$(M-CH_3)^+$]: 383.3161, found: 383.3156.

4.5.2. (R)-Isomer. Octadecanoyl chloride (3.02 g) and (*S*)-**2** (1.00 g) gave 2.60 g (93%) of (*R*)-**3c** as colorless rhombs, mp 40–41 °C (Ref. 8 mp 41–42 °C); $[\alpha]_D^{20}$ +7.00 (*c* 3.35, hexane) {Ref. 8 $[\alpha]_D$ +4.94 (neat at 50–55 °C)}; Its IR, ^{1}H NMR, and mass spectra were identical with those of (±)-**3c**. GC–MS [same conditions as those for (±)-**3a**]: t_R 18.56 min (99.5%). HRMS calcd for $C_{24}H_{46}O_4Na$: 421.3294, found: 421.3293.

4.5.3. (S)-Isomer. Octadecanoyl chloride (3.02 g) and (*R*)-**2** (1.00 g) gave 2.37 g (85%) of (*S*)-**3c** as colorless rhombs, mp 41–42 °C; $[\alpha]_D^{23}$ −7.38 (*c* 3.95, hexane); Its IR, ^{1}H NMR, and mass spectra were identical with those of (±)-**3c**. GC–MS [same conditions as those for (±)-**3a**]: t_R 18.55 min (99.8%). HRMS calcd for $C_{24}H_{46}O_4Na$: 421.3294, found: 421.3295.

4.6. 2,2-Dimethyl-1,3-dioxolane-4-methyl (*Z*)-9-octadecenoate (3d)

4.6.1. Racemate. (*Z*)-9-Octadecenoyl chloride (3.00 g) and (±)-**2** (1.58 g) gave 3.17 g (80%) of (±)-**3d** as a colorless oil, n_D^{21}=1.4582; ν_{max} (film): 2926 (s), 2855 (s), 1742 (s), 1161 (s), 844 (m); δ_H ($CDCl_3$): 0.86 (3H, t, *J* 6.8), 1.24–1.35 (18H, br, two peaks at 1.27 and 1.30), 1.37 (3H, s), 1.44 (3H, s), 1.60–1.68 (2H, m), 1.96–2.10 (2H, m), 2.34 (2H, t, *J* 6.8), 3.70–3.76 (1H, m), 4.05–4.18 (3H, m), 4.28–4.40 (1H, m), 5.30–5.42 (2H, m); GC–MS [same conditions as those for (±)-**3a**]: t_R 18.48 min (89.4%); MS of (±)-**3d** (70 eV, EI): *m*/*z* 396 (<1)[M^+], 381 (100) [$(M-CH_3)^+$], 338 (28), 295 (6), 253 (6), 239 (6), 185 (21), 171 (11), 129 (53), 116 (16), 101 (22), 83 (9), 69 (13), 55 (19), 43 (19). HRMS calcd for $C_{24}H_{44}O_4$: 396.3240, found: 396.3232.

4.6.2. (R)-Isomer. (*Z*)-9-Octadecenoyl chloride (3.01 g) and (*S*)-**2** (1.00 g) gave 3.01 g (99%) of (*R*)-**3d** as a colorless oil, n_D^{26}=1.4566; $[\alpha]_D^{21}$ +7.14 (*c* 3.71, hexane); Its IR, ^{1}H NMR, and mass spectra were identical with those of (±)-**3d**. GC–MS [same conditions as those for (±)-**3a**]: t_R 18.45 min (92.1%). HRMS calcd for $C_{24}H_{44}ONa$: 419.3137, found: 419.3139.

4.6.3. (S)-Isomer. (*Z*)-9-Octadecenoyl chloride (3.01 g) and (*R*)-**2** (1.00 g) gave 2.91 g (96%) of (*S*)-**3d** as a colorless oil, n_D^{20}=1.4564; $[\alpha]_D^{22}$ −7.07 (*c* 3.82, hexane); Its IR, ^{1}H NMR, and mass spectra were identical with those of (±)-**3d**. GC–MS [same conditions as those for (±)-**3a**]: t_R 18.45 min (90.2%). HRMS calcd for $C_{24}H_{44}O_4Na$: 419.3137, found: 419.3130.

4.7. 2,2-Dimethyl-1,3-dioxolane-4-methyl (9*Z*,12*Z*)-9,12-octadecadienoate (3e)

4.7.1. Racemate. A colorless oil, n_D^{21}=1.4720; ν_{max} (film): 3008 (m), 2929 (s),2856 (s), 2120 (contaminating DCC), 1742 (s), 1656 (w), 1453 (m), 1371 (s), 1215 (s), 1161 (s), 1087 (m), 1057 (m), 843 (m), 724 (m); δ_H ($CDCl_3$): 0.89 (3H, t, *J* 6.8), 1.15–1.40 (14H, br), 1.37 (3H, s), 1.43 (3H, s), 1.55–1.70 (2H, m), 2.00–2.10 (4H, m), 2.34 (2H, t, *J* 7.6), 2.77 (2H, t, *J* 6.8), 3.70–3.76 (1H, m), 4.05–4.10 (2H, m),

4.12–4.18 (1H, m), 4.28–4.36 (1H, m), 5.30–5.42 (4H, m); GC–MS [same conditions as those for (±)-**3a**]: t_R 12.93 min (19.2%, DCC), 18.44 min (80.7%); MS of (±)-**3e** (70 eV, EI): *m*/*z* 394 (<1) [M^+], 379 (100) [$(M-CH_3)^+$], 336 (38), 171 (9), 129 (22), 101 (25), 81 (20), 67 (25), 55 (20), 43 (21). HRMS calcd for $C_{24}H_{42}O_4$: 394.3083, found: 394.3091.

4.7.2. (R)-Isomer. (9*Z*,12*Z*)-9,12-Octadecadienoic acid (581 mg) and (*S*)-**2** (283 mg) gave 820 mg (quant.) of (*R*)-**3e** as a colorless oil, n_D^{24}=1.4680; $[\alpha]_D^{25}$ +6.76 (*c* 3.57, hexane); Its IR, ^{1}H NMR, and mass spectra were identical with those of (±)-**3e**. GC–MS [same conditions as those for (±)-**3a**]: t_R 12.93 min (3.32%, DCC), 18.44 min (95.1%). HRMS calcd for $C_{24}H_{42}O_4Na$: 417.2981, found: 417.2979.

4.7.3. (S)-Isomer. (9*Z*,12*Z*)-9,12-Octadecadienoic acid (570.5 mg) and (*R*)-**2** (283 mg) gave 793 mg (99%) of (*S*)-**3e** as a colorless oil, n_D^{24}=1.4682; $[\alpha]_D^{23}$ −6.84 (*c* 3.58, hexane); Its IR, ^{1}H NMR, and mass spectra were identical with those of (±)-**3e**. GC–MS [same conditions as those for (±)-**3a**]: t_R 12.93 min (5.46%, DCC), 18.44 min (92.5%). HRMS calcd for $C_{24}H_{42}O_4Na$: 417.2981, found: 417.2975.

4.8. Scrutiny of the conditions to convert (*S*)-3a to (*S*)-4a with minimal racemization

4.8.1. With Amberlyst 15 (H^+ form). Amberlyst 15 (H^+ form, 1.0 g) was added to a solution of (*S*)-**3a** (600 mg) in MeOH (6 mL) and CH_2Cl_2 (3 mL), and the mixture was stirred for 2 h at 50 °C. It was then filtered, and the resin particles were washed with EtOAc. The combined filtrate and washings were concentrated in vacuo. The residue was recrystallized from EtOAc/pentane to give 322 mg (61%) of crystalline (*S*)-**4a**, $[\alpha]_D^{21}$ +0.21 (*c* 2.06, pyridine); whose enantiomeric purity was 12% ee as determined by MTPA/NMR analysis (see Section 4.8.6). The hydrolysis of (*S*)-**3a** could be followed by SiO_2-TLC developed with hexane/EtOAc=4:1 (R_f of **3a**=0.82, R_f of **4a**=0.11).

4.8.2. With $FeCl_3/SiO_2$. $FeCl_3/SiO_2$ was prepared from $FeCl_3\cdot 6H_2O$ (1.2 g) and Merck silica gel 60 (10.0 g) in acetone (16 mL) according to Kim.[16] Yellow-colored $FeCl_3/SiO_2$ (100 mg) was added to a solution of (*S*)-**3a** (199 mg) in $CHCl_3$ (10 mL), and the mixture was stirred for 5 h at room temperature. It was then filtered, and the solid was washed with EtOAc. The combined filtrate and washings were concentrated in vacuo, and the residue was recrystallized from EtOAc/pentane to give 112 mg (64%) of crystalline (*S*)-**4a**, $[\alpha]_D^{23}$ +1.40 (*c* 0.47, pyridine), whose enantiomeric purity was 65% ee.

4.8.3. With $Zn(NO_3)_2\cdot 6H_2O$ in MeCN. $Zn(NO_3)_2\cdot 6H_2O$ (742 mg, 2.5 mmol) was added to a solution of (*S*)-**3a** (199 mg, 0.53 mmol) in MeCN (2.0 mL). The solution was stirred and heated at 50 °C for 4 h, and concentrated in vacuo. The residue was dissolved in EtOAc and H_2O. The organic layer was washed with water and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was recrystallized from EtOAc/pentane to give 105 mg (60%) of slightly tan and crystalline (*S*)-**4a**, $[\alpha]_D^{26}$ +3.51 (*c* 0.34, pyridine), whose enantiomeric purity was 90% ee. Use of MeCN as solvent seemed to make crystals slightly tan-colored.

4.8.4. With 80% AcOH at 130 °C, for 30 min. The procedure detailed in Section 4.9.1 furnished a sample of (*S*)-**4a**, $[\alpha]_D^{21}$ +1.89 (*c* 1.54, pyridine); whose enantiomeric purity was 52% ee.

4.8.5. With 80% AcOH at 50 °C for 2 h. The procedure detailed in Section 4.9.2 was first tested with a small amount (187 mg) of (*S*)-**3a** in 80% AcOH (2 mL) at 50 °C. At first the mixture was turbid, and it became homogeneous after 30 min. After 1 h, TLC check showed that a small amount of (*S*)-**3a** was still present in the solution. After 2 h, there was no (*S*)-**3a** in the solution. The crude crystalline (*S*)-**4a** was of 92% ee. Recrystallized (*S*)-**4a** was enantiomerically pure (100% ee). In this case, crystals were colorless. This procedure was therefore adopted for the preparative works.

*4.8.6. Derivatization of **4a** with (S)-(+)-MTPACl.* (S)-(+)-MTPACl (Aldrich or Tokyo Kasei, 12.6 mg, 0.05 mmol) was added to a solution of (±)-, (*R*)- or (*S*)-**4a** (5.5 mg, 0.017 mmol) and DMAP (2 mg, 0.02 mmol) in dry CH_2Cl_2 (3 drops) and dry pyridine (3 drops) in a vial. The vial was sealed with a stopper, shaken vigorously, and left to stand for 3 d at room temperature. The mixture was diluted with water, and extracted with Et_2O. The Et_2O extract was washed with dil HCl, $NaHCO_3$ solution and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was dissolved in $CHCl_3$. The solution was transferred to a small flask, and concentrated in vacuo. The residue in $CDCl_3$ was analyzed by NMR spectroscopy (see Fig. 2). Signals at δ 4.0–4.8 were carefully analyzed to determine the diastereomeric ratio of the bis-MTPA ester, which allowed the calculation of the enantiomeric purity of **4a**.

4.9. General procedure for the preparation of 2,3-dihydroxypropyl carboxylate (1-monoglyceride 4)

4.9.1. Heating with 80% AcOH at 130 °C. Aqueous acetic acid [AcOH/H_2O=80:20 (v/v), 20 mL] was added to solid (±)-**3a** (3.20 g, 8.6 mmol), and the mixture was stirred and heated at 130 °C (bath temperature) for 30 min. After cooling, the mixture was diluted with Et_2O. The Et_2O solution was washed with water, $NaHCO_3$ solution and brine, dried ($MgSO_4$), and concentrated in vacuo to give crude (±)-**4a** as a solid. This was recrystallized from EtOAc/pentane to give 2.76 g (97%) of (±)-**4a** as colorless plates. All the racemates were prepared by the present procedure.

4.9.2. Heating with 80% AcOH at 50 °C. Aqueous acetic acid [AcOH/H_2O=80:20 (v/v), 12 mL] was added to solid (*S*)-**3a** (1.12 g, 3 mmol), and the mixture was stirred and warmed at 50 °C (bath temperature) for 2 h. TLC check at this point confirmed the disappearance of **3a**. Work-up of the mixture yielded 792 mg (80%) of (*S*)-**4a** as needles. All the optically active diols were prepared by the present method.

4.10. 2,3-Dihydroxypropyl hexadecanoate (1-monopalmitin, 4a)

4.10.1. Racemate. Colorless plates from EtOAc/pentane, mp 72 °C (sinter at 66 °C); ν_{max} (Nujol): 1731 (s), 1180 (m), 1047 (m), 720 (m); δ_H ($CDCl_3$): 0.88 (3H, t, *J* 6.8), 1.25 (24H, br), 1.62 (2H, m), 2.11 (1H, m), 2.35 (2H, t, *J* 7.6), 2.55 (1H, d, *J* 4.8), 3.58–3.63 (1H, m), 3.67–3.72 (1H, m), 3.90–3.98 (1H, m), 4.12–4.24 (2H, m). For the NMR spectrum of the corresponding bis-MTPA ester, see Fig. 2. HRMS calcd for $C_{19}H_{38}O_4$: 330.2770, found: 330.2755.

4.10.2. (R)-Isomer. Acetonide (*R*)-**3a** (1.119 g) gave 819 mg (83%) of (*R*)-**4a** as colorless needles from EtOAc/pentane, mp 68–69 °C (Ref. 8 mp 71–72 °C); $[\alpha]_D^{24}$ −4.16 (*c* 2.54, pyridine); 100% ee (by MTPA/NMR analysis; see Fig. 2). Its IR and ^{1}H NMR spectra were identical with those of (±)-**4a**. HRMS calcd for $C_{19}H_{38}O_4$: 330.2770, found: 330.2768.

4.10.3. (S)-Isomer. Acetonide (*S*)-**3a** (1.120 g) gave 792 mg (80%) of (*S*)-**4a** as colorless needles from EtOAc/pentane, mp 68.5–69.5 °C; $[\alpha]_D^{24}$ +4.14 (*c* 2.53, pyridine), 100% ee (by MTPA/NMR analysis; see

Fig. 2) Its IR and ^{1}H NMR spectra were identical with those of (±)-**4a**. HRMS calcd for $C_{19}H_{38}O_4$: 330.2770, found: 330.2755.

4.11. 2,3-Dihydroxypropyl (*Z*)-9-hexadecenoate (1-monopalmitolein, 4b)

4.11.1. Racemate. Acetonide (±)-**3b** (634 mg) gave 444 mg (79%) of (±)-**4b** as a colorless and viscous oil, n_D^{22}=1.4696. This oil solidifies in a deep freezer. ν_{max} (Nujol): 3408 (s), 3005 (m), 2925 (s), 2855 (s), 1740 (s), 1653 (w), 1464 (m), 1379 (m), 1241 (m), 1177 (s), 1119 (m), 1052 (m), 724 (m); δ_H ($CDCl_3$): 0.88 (3H, t, *J* 7.2), 1.22–1.48 (18H, br), 1.60–1.68 (2H, m), 1.98–2.05 (4H, m), 2.35 (2H, t, *J* 7.2), 3.57–3.62 (1H, m), 3.66–3.72 (1H, m), 3.82–3.96 (1H, m), 4.12–4.22 (2H, m), 5.30–5.39 (2H, m). HRMS calcd for $C_{19}H_{36}O_4$: 328.2614, found: 328.2603.

4.11.2. (R)-Isomer. Acetonide (*R*)-**3b** (454 mg) gave 390 mg (97%) of (*R*)-**4b** as a colorless oil, n_D^{22}=1.4672; $[\alpha]_D^{25}$ −3.60 (*c* 1.12, pyridine); 95% ee (by MTPA/NMR analysis). Its IR and ^{1}H NMR spectra were identical with those of (±)-**4b**. HRMS calcd for $C_{19}H_{36}O_4Na$: 351.2511, found: 351.2504.

4.11.3. (S)-Isomer. Acetonide (*S*)-**3b** (450 mg) gave 399 mg (99%) of (*S*)-**4b** as a colorless oil, n_D^{26} 1.4673; $[\alpha]_D^{25}$ +3.67 (*c* 2.61, pyridine); 95% ee (by MTPA/NMR analysis). Its IR and ^{1}H NMR spectra were identical with those of (±)-**4b**. HRMS calcd for $C_{19}H_{36}O_4Na$: 351.2511, found: 351.2504.

4.12. 2,3-Dihydroxypropyl octadecanoate (1-monostearin, 4c)

4.12.1. Racemate. Acetonide (±)-**3c** (3.50 g) gave 3.20 g (quant.) of (±)-**4c** as a colorless solid, which was recrystallized from EtOAc/pentane to give 1.95 g (62%) of pure (±)-**4c** as plates, mp 76–78 °C (sinter at 44 °C); ν_{max} (Nujol): 1731 (s), 1179 (m), 1047 (m), 720 (m); δ_H ($CDCl_3$): 0.88 (3H, t, *J* 6.8), 1.25 (28H, br), 1.60–1.63 (2H, m), 2.08 (1H, br), 2.35 (2H, t, *J* 7.6), 2.51 (1H, br), 3.56–3.62 (1H, m), 3.66–3.74 (1H, m), 3.90–3.96 (1H, m), 4.15 (1H, dd, *J* 4.8, 7.8), 4.21 (1H, dd, *J* 4.8, 7.8). HRMS calcd for $C_{21}H_{42}O_4$: 358.3083, found: 358.3077.

4.12.2. (R)-Isomer. Acetonide (*R*)-**3c** (1.203 g) gave 1.18 g (quant.) of (*R*)-**4c** as a colorless solid, which was recrystallized from EtOAc/pentane to give 842 mg (78%) of pure (*R*)-**4c** as leaflets, mp 73–74 °C (Ref. 8 mp 76–77 °C); $[\alpha]_D^{23}$ −3.83 (*c* 2.63, pyridine) {Ref. 8 $[\alpha]_D$ −3.58 (*c* 12.3, pyridine)}; 95% ee (by MTPA/NMR analysis). Its IR and ^{1}H NMR spectra were identical with those of (±)-**4c**. HRMS calcd for $C_{21}H_{42}O_4Na$: 381.2981, found: 381.2976.

4.12.3. (S)-Isomer. Acetonide (*S*)-**3c** (1.234 g) gave 1.20 g (quant.) of (*S*)-**4c** as a colorless solid, which was recrystallized from EtOAc/pentane to give 785 mg (71%) of pure (*S*)-**4c** as leaflets, mp 73–74 °C; $[\alpha]_D^{23}$ +4.10 (*c* 2.58, pyridine); 96% ee (by MTPA/NMR analysis). Its IR and ^{1}H NMR spectra were identical with those of (±)-**4c**. HRMS calcd for $C_{21}H_{42}O_4Na$: 381.2981, found: 381.2975.

4.13. 2,3-Dihydroxypropyl (*Z*)-9-octadecenoate (1-monoolein 4d)

4.13.1. Racemate. Acetonide (±)-**3d** (3.57 g) gave 3.04 g (95%) of (±)-**4d** as a colorless oil, which solidified in a deep freezer as prisms, mp 26–28 °C. ν_{max} (Nujol): 1731 (s), 1466 (m), 1183 (m), 1062 (m), 721 (m); δ_H ($CDCl_3$): 0.88 (3H, t, *J* 6.8), 1.20–1.40 (22H, br, peaks at 1.26, 1.27, and 1.30), 1.58–1.68 (2H, m), 1.82–1.88 (1H), 1.95–2.08 (3H, m), 2.30–2.40 (2H, m), 3.56–3.62 (1H, m), 3.66–3.73 (1H, m), 3.90–4.00 (1H, m), 4.12–4.22 (2H, m), 5.30–5.40 (2H, m). HRMS calcd for $C_{21}H_{40}O_4$: 356.2927, found: 356.2927.

4.13.2. (R)-Isomer. Acetonide (*R*)-**3d** (1.188 g) gave 974 mg (91%) of (*R*)-**4d** as a colorless oil, which solidified in a deep freezer. Its mp could not be determined. n_D^{24} 1.4660; $[\alpha]_D^{27}$ −2.98 (*c* 4.38, pyridine); 96% ee (by MTPA/NMR analysis). Its IR and ^{1}H NMR spectra were identical with those of (±)-**4d**. HRMS calcd for $C_{21}H_{40}O_4Na$: 379.2824, found: 379.2824.

4.13.3. (S)-Isomer. Acetonide (*S*)-**3d** (1.190 g) gave 1.070 g (quant.) of (*S*)-**4d** as a colorless oil, which solidified in a deep freezer. Its mp could not be determined. n_D^{24} 1.4686; $[\alpha]_D^{27}$ +3.21 (*c* 4.09, pyridine); 95% ee (by MTPA/NMR analysis). Its IR and ^{1}H NMR spectra were identical with those of (±)**4d**. HRMS calcd for $C_{21}H_{40}O_4Na$: 379.2824, found: 379.2827.

4.14. 2,3-Dihydroxypropyl (9*Z*,12*Z*)-9,12-octadecadienoate (monolinolein 4e)

4.14.1. Racemate. Acetonide (±)-**3e** (758 mg) gave 467 mg (68%) of (±)-**4e** as a colorless and viscous oil, n_D^{21} 1.4774, which solidified in a deep freezer. ν_{max} (film): 3414 (s), 3009 (m), 2927 (s), 2855 (s), 1740 (s), 1654 (w), 1464 (m), 1241 (s), 1177 (s), 1051 (m), 723 (m); δ_H ($CDCl_3$): 0.89 (3H, t, *J* 7.2), 1.22–1.40 (16H, br), 1.48–1.70 (2H, m), 2.05 (4H, q-like, *J* 6.8), 2.35 (2H, t, *J* 6.8), 2.77 (2H, t, *J* 6.4), 3.56–3.62 (1H, m), 3.67–3.72 (1H, m), 3.80–3.97 (1H, m), 4.10–4.22 (2H, m), 5.28–5.42 (4H, m). HRMS calcd for $C_{21}H_{38}O_4$: 354.2770, found: 354.2764.

4.14.2. (R)-Isomer. Acetonide (*R*)-**3e** (630 mg) gave 540 mg (95%) of (*R*)-**4e** as a colorless and viscous oil, n_D^{24}=1.4750; $[\alpha]_D^{24}$ −2.99 (*c* 3.52, pyridine); 90% ee (by MTPA/NMR analysis). Its IR and ^{1}H NMR spectra were identical with those of (±)-**4e**. HRMS calcd for $C_{21}H_{38}O_4Na$: 377.2668, found: 377.2665.

4.14.3. (S)-Isomer. Acetonide (*S*)-**3e** (1.182 g) gave 701.5 mg (66%) of (*S*)-**4e** as a colorless and viscous oil, n_D^{24}=1.4775; $[\alpha]_D^{24}$ +3.23 (*c* 3.63, pyridine); ca. 100% ee (by MTPA/NMR analysis). Its IR and ^{1}H NMR spectra were identical with those of (±)-**4e**. HRMS calcd for $C_{21}H_{38}O_4Na$: 377.2668, found: 377.2664.

4.15. General procedure for the preparation of 2,3-di[(*E*)-2-methyl-2-butenoyloxy]propyl carboxylate (triglyceride 1)

A solution of (*E*)-2-methyl-2-butenoyl chloride (tigloyl chloride, Tokyo Kasei, 700 mg, 5.8 mmol) in dry C_6H_6 (3 mL) was added dropwise over 15 min to a stirred and ice-cooled solution of (±)-**4a** (739 mg, 2.2 mmol) and DMAP (10 mg, 0.08 mmol) in dry C_5H_5N (5 mL) at 0–5 °C. Stirring was continued for 30 min at 0–5 °C, and 1 h at room temperature. The mixture was then diluted with ice and water, and extracted with Et_2O. The Et_2O solution was washed with dil HCl, $NaHCO_3$ solution and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was chromatographed over SiO_2 (20 g). Elution with hexane/EtOAc (20:1) gave 837 mg (72%) of (±)-**1a** as an oil. The product was further purified by rechromatography on SiO_2, if necessary, after checking its purity by GC–MS.

4.16. 2,3-Di[(*E*)-2-methyl-2-butenoyloxy]propyl hexadecanoate (1a)

4.16.1. Racemate. A pale yellow oil, n_D^{20}=1.4704; ν_{max} (film): 2925 (vs), 2854 (s), 1740 (s), 1718 (vs), 1652 (m), 1250 (vs), 1133 (s), 1076 (m), 733 (m); δ_H ($CDCl_3$): 0.88 (3H, t, *J* 6.8), 1.26 (24H, br), 1.60 (2H, br), 1.80 (6H, d, *J* 7.2), 1.82 (6H, s), 2.31 (2H, t, *J* 7.2), 4.22–4.29 (2H, m), 4.32–4.38 (2H, m), 5.38 (1H, m), 6.87 (2H, m); δ_C ($CDCl_3$): 11.95,

11.97, 14.08, 14.38, 14.40, 22.62, 22.66, 24.87, 29.09, 29.24, 29.33, 29.43, 29.60, 29.63, 29.67, 31.56, 31.90, 34.08, 62.24, 62.35, 69.14, 128.08, 128.14, 138.09, 138.24, 166.95, 167.42, 173.34; GC–MS [column: HP-5MS. 5% phenylmethylsiloxane, 30 m×0.25 mm i.d.; carrier gas He; press: 52.8 kPa, temp 50 °C (2 min), then +15 °C/min, 300 °C (60 min): t_R 10.28 min (4.25%, unknown impurity M^+=154), 22.55 min (95.75%); MS (70 eV, EI): *m*/z 494 (<1) [M^+], 395 (26) [$(M-C_5H_7O_2)^+$], 238 (25), 83 (100), 55 (18). HRMS calcd for $C_{29}H_{50}O_6$: 494.3607, found: 494.3604. The unidentified impurity showed the following IR spectral properties: ν_{max} (film): 1771 (vs), 1713 (s), 1649 (m), 1223 (s), 1014 (vs).

4.16.2. (R)-Isomer. Diol (*S*)-**4a** (501.5 mg) gave 737.2 mg (98%) of (*R*)-**1a**, which was further purified by SiO_2 chromatography to give 202 mg of pure (*R*)-**1a** as a colorless oil, n_D^{25}=1.4690. This oil solidifies in a deep freezer. $[\alpha]_D^{25}$ +5.40 (*c* 1.84, hexane). Its IR, NMR, and mass spectra were identical with those of (±)-**1a**. GC–MS [same conditions as those for (±)-**1a**]: t_R 22.55 min (100%). HRMS calcd for $C_{29}H_{50}O_6$: 494.3607, found: 494.3608.

4.16.3. (S)-Isomer. Diol (*R*)-**4a** (497.8 mg) gave 637.6 mg (80%) of (*S*)-**1a**, which was further purified by SiO_2 chromatography to give 412 mg of pure (*S*)-**1a** as a colorless oil, n_D^{25}=1.4680. This oil solidifies in a deep freezer. $[\alpha]_D^{25}$ −5.45 (*c* 2.85, hexane). Its IR, NMR, and mass spectra were identical with those of (±)-**1a**. GC–MS [same conditions as those for (±)-**1a**]: t_R 22.55 min (96.26%). HRMS calcd for $C_{29}H_{50}O_6$: 494.3607, found: 494.3602.

4.17. 2,3-Di[(*E*)-2-methyl-2-butenoyloxy]propyl (*Z*)-9-hexadecenoate (1b)

4.17.1. Racemate. Diol (±)-**4b** (351 mg) gave 404 mg (82%) of (±)-**1b** as a colorless oil, n_D^{21}=1.4744; ν_{max} (film): 3002 (m), 2929 (s), 2855 (s), 1744 (s), 1718 (vs), 1652 (m), 1458 (m), 1381 (m), 1250 (vs), 1133 (s), 1077 (s), 733 (s); δ_H ($CDCl_3$): 0.88 (3H, t, *J* 6.8), 1.20–1.40 (16H, br), 1.56–1.65 (2H, m), 1.80 (6H, d, *J* 7.6), 1.82 (6H, s), 1.95–2.10 (4H, m), 2.31 (2H, t, *J* 7.6), 4.22–4.37 (4H, m), 5.30–5.40 (3H, m), 6.82–6.92 (2H, m); δ_C ($CDCl_3$): 11.77, 11.85, 13.97, 14.28, 14.70, 22.54, 24.74, 27.04, 27.09, 28.86, 28.91, 28.96, 29.05, 29.57, 29.61, 31.66, 33.94, 62.13, 62.23, 69.03, 127.98, 128.03, 129.59, 129.85, 137.95, 138.10, 166.79, 167.26, 173.15; GC–MS [same conditions as those for (±)-**1a**]: 22.51 min (95.21%); MS (70 eV, EI) *m*/*z*: 492 (<1) [M^+] 392 (7), 239 (20), 157 (6), 83 (100), 55 (45). HRMS calcd for $C_{29}H_{48}O_6$: 492.3451, found: 492.3446.

4.17.2. (R)-Isomer. Diol (*S*)-**4b** (313 mg) gave 446 mg (quant.) of (*R*)-**1b**, which was further purified by SiO_2 chromatography to give 121 mg of pure (*R*)-**1b** as a colorless oil, n_D^{23}=1.4758, $[\alpha]_D^{26}$ +4.96 (*c* 1.02, hexane). Its IR, NMR, and mass spectra were identical with those of (±)-**1b**. GC–MS [same conditions as those for (±)-**1a**]: t_R 22.54 min (100.00%). HRMS calcd for $C_{29}H_{48}O_6Na$: 515.3349, found: 515.3338.

4.17.3. (S)-Isomer. Diol (*R*)-**4b** (289 mg) gave 413 mg (quant.) of (*S*)-**1b**, which was further purified by SiO_2 chromatography to give 84 mg of pure (*S*)-**1b** as a colorless oil, n_D^{23}=1.4754, $[\alpha]_D^{23}$ −5.15 (*c* 0.66, hexane). Its IR, NMR, and mass spectra were identical with those of (±)-**1b**. GC–MS [same conditions as those for (±)-**1a**]: t_R 22.43 min (99.70%). HRMS calcd for $C_{29}H_{48}O_6Na$: 515.3349, found: 515.3350.

4.18. 2,3-Di[(*E*)-2-methyl-2-butenoyloxy]propyl octadecanoate (1c)

4.18.1. Racemate. Diol (±)-**4c** (796 mg) gave 903 mg (83%) of (±)-**1c** as a colorless oil, n_D^{20}=1.4698; ν_{max} (film): 2925 (vs), 2854 (s), 1740 (s), 1719 (vs), 1652 (m), 1250 (vs), 1133 (s), 1076 (s), 733 (m); δ_H ($CDCl_3$): 0.88 (3H, t, *J* 6.8), 1.26 (28H, br), 1.56–1.65 (2H, m), 1.79 (6H, d, *J* 6.8), 1.82 (6H, s), 2.31 (2H, t, *J* 3.2), 4.23–4.38 (4H, m), 5.32–5.40 (1H, m), 6.82–6.90 (2H, m); δ_C ($CDCl_3$): 11.96, 11.98, 14.09, 14.40, 22.63, 22.67, 24.87, 29.09, 29.25, 29.34, 29.44, 29.60, 29.64, 29.68, 31.57, 31.91, 34.08, 62.24, 62.35, 69.13, 128.08, 128.13, 138.09, 138.25, 166.95, 167.42, 173.35; GC–MS [same conditions as those for (±)-**1a**]: t_R 25.01 min (93.93%); MS (70 eV, EI) *m*/*z*: 522 (<1) [M^+], 423 (22), 238 (23), 83 (100), 55 (18). HRMS calcd for $C_{31}H_{54}O_6$: 522.3920, found: 522.3928.

4.18.2. (R)-Isomer. Diol (*S*)-**4c** (501.3 mg) gave 704 mg (96%) of (*R*)-**1c**, which was further purified by SiO_2 chromatography to give 183 mg of pure (*R*)-**1c** as a colorless oil, n_D^{26}=1.4702; $[\alpha]_D^{26}$ +4.91 (*c* 1.63, hexane). Its IR, NMR, and mass spectra were identical with those of (±)-**1c**. GC–MS [same conditions as those for (±)-**1a**]: t_R 25.04 min (97.64%). HRMS calcd for $C_{31}H_{59}O_6Na$: 545.3818, found: 545.3810.

4.18.3. (S)-Isomer. Diol (*R*)-**4c** (530.5 mg) gave 732 mg (95%) of (*S*)-**1c**, which was further purified by SiO_2 chromatography to give 161 mg of pure (*S*)-**1c** as a colorless oil, n_D^{26}=1.4701; $[\alpha]_D^{25}$ −4.88 (*c* 1.40, hexane). Its IR, NMR, and mass spectra were identical with those of (±)-**1c**. GC–MS [same conditions as those for (±)-**1a**]: t_R 25.01 min (96.14%). HRMS calcd for $C_{31}H_{59}O_6NaNa$: 545.3818, found: 545.3810.

4.19. 2,3-Di[(*E*)-2-methyl-2-butenoyloxy]propyl (*Z*)-9-octadecenoate (1d)

4.19.1. Racemate. Diol (±)-**4d** (429 mg) gave 546 mg (93%) of (±)-**1d** as a colorless oil, n_D^{21}=1.4752; ν_{max} (film): 2925 (s), 2855 (s), 1740 (s), 1718 (vs), 1653 (m), 1250 (s), 1133 (s), 1076 (s), 733 (m); δ_H ($CDCl_3$): 0.88 (3H, t, *J* 6.8), 1.20–1.40 (20H, br, peaks at 1.27 and 1.29), 1.55–1.64 (2H, m), 1.79 (6H, d, *J* 7.2), 1.82 (6H, s), 1.95–2.08 (4H, m), 2.31 (2H, t, *J* 7.2), 4.23–4.37 (4H, m), 5.30–5.40 (3H, m), 6.80–6.90 (2H, m); δ_C ($CDCl_3$): 12.00, 12.02, 14.13, 14.43, 14.45, 22.71, 24.90, 25.64, 27.19, 27.24, 29.09, 29.12, 29.20, 29.34, 29.55, 29.73, 29.79, 31.55, 31.93, 62.27, 62.38, 69.17, 128.12, 128.17, 129.74, 130.01, 138.11, 138.27, 166.95, 167.42, 173.35; GC–MS [same conditions as those for (±)-**1a**]: t_R 24.71 min (93.20%); MS (70 eV, EI) *m*/*z*: 520 (<1) [M^+] 420 (8), 239 (27), 83 (100), 55 (20). HRMS calcd for $C_{31}H_{52}O_6$: 520.3764, found: 520.3757.

4.19.2. (R)-Isomer. Diol (*S*)-**4d** (934 mg) gave 1.254 g (92%) of (*R*)-**1d**, which was further purified by SiO_2 chromatography to give 347 mg of pure (*R*)-**1d** as a colorless oil, n_D^{24}=1.4752; $[\alpha]_D^{25}$ +4.66 (*c* 3.30, hexane). Its IR, NMR, and mass spectra were identical with those of (±)-**1d**. GC–MS [same conditions as those for (±)-**1a**]: t_R 24.77 min (96.08%). HRMS calcd for $C_{31}H_{52}O_6Na$: 543.3662, found: 543.3653.

4.19.3. (S)-Isomer. Diol (*R*)-**4d** (992 mg) gave 1.421 g (98%) of (*S*)-**1d**, which was further purified by SiO_2 chromatography to give 511 mg of pure (*S*)-**1d** as a colorless oil, n_D^{24}=1.4754; $[\alpha]_D^{26}$ −4.71 (*c* 2.12, hexane). Its IR, NMR, and mass spectra were identical with those of (±)-**1d**. GC–MS [same conditions as those for (±)-**1a**]: t_R 24.74 min (96.96%). HRMS calcd for $C_{31}H_{52}O_6Na$: 543.3662, found: 543.3671.

4.20. 2,3-Di[(*E*)-2-methyl-2-butenoyloxy]propyl (9*Z*,12*Z*)-9,12-octadecadienoate (1e)

4.20.1. Racemate. Diol (±)-**4e** (372 mg) gave 410 mg (80%) of (±)-**1e** as a pale yellow oil, n_D^{21}=1.4804; ν_{max} (film): 3008 (m), 2928 (s), 2856 (s), 1745 (s), 1714 (vs), 1651 (m), 1457 (m), 1381 (m), 1251 (s), 1133 (s), 1077 (m), 733 (m); δ_H ($CDCl_3$): 0.89 (3H, t, *J* 6.8), 1.22–1.40 (14H, br) 1.55–1.66 (2H, m), 1.79 (6H, d, *J* 7.2), 1.82 (6H, s), 2.01–2.10 (4H, m), 2.32 (2H, t, *J* 7.6), 2.77 (4H, t, *J* 6.4) 4.22–4.30 (2H,

m), 4.32–4.37 (2H, m), 5.28–5.42 (5H, m), 6.83–6.91 (2H,m); δ_C ($CDCl_3$): 11.87, 11.89, 13.98, 14.32, 14.34, 22.48, 24.77, 25.54, 27.11, 28.98, 29.01, 29.09, 29.26, 29.52, 31.43, 33.98, 62.16, 62.27, 69.06, 127.81, 127.96, 128.00, 128.05, 129.91, 130.10, 138.02, 138.17, 166.85, 167.32, 173.20; GC–MS [same conditions as those for (±)-**1a**]: t_R 24.74 min (92.06%); MS (70 eV, EI) *m*/*z*: 518 (<1) [M^+], 418 (7), 239 (23), 157 (7), 83 (100), 55 (21). HRMS calcd for $C_{31}H_{50}O_6$: 518.3607, found: 518.3605.

4.20.2. (R)-Isomer. Diol (*S*)-**4e** (400 mg) gave 449 mg (77%) of (*R*)-**1e**, which was further purified by SiO_2 chromatography to give 250 mg of pure (*R*)-**1e** as a colorless oil, n_D^{24}=1.4792; $[\alpha]_D^{26}$ +4.88 (*c* 1.21, hexane). Its IR, NMR, and mass spectra were identical with those for (±)-**1e**. GC–MS [same conditions as those for (±)-**1a**]: t_R 24.73 min (100.00%). HRMS calcd for $C_{31}H_{50}O_6Na$: 541.3505, found: 541.3506.

4.20.3. (S)-Isomer. Diol (*R*)-**4e** (388 mg) gave 479 mg (84%) of (*S*)-**1e**, which was further purified by SiO_2 chromatography to give 203 mg of pure (*S*)-**1e** as a colorless oil, n_D^{24}=1.4793; $[\alpha]_D^{25}$ −4.95 (*c* 1.81, hexane). Its IR, NMR, and mass spectra were identical with those of (±)-**1e**. GC–MS [same conditions as those for (±)-**1a**]: t_R 24.76 min (99.57%). HRMS calcd for $C_{31}H_{50}O_6Na$: 541.3505, found: 541.3504.

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