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Synthesis of (+)-Disparlure from Diethyl (–)-Malate via Opening and Fragmentation of the Three-Membered Ring in Tertiary Cyclopropanols

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Abstract— (+)-Disparlure [(7*R*,8*S*)-7,8-epoxy-2-methyloctadecane, pheromone of the gypsy moth *Lymantria dispar* L.] was synthesized starting from diethyl (–)-malate via cyclopropanation of the ester groups, selective protection of the 1,3-diol functionality, and successive opening and fragmentation of the three-membered rings in the corresponding tertiary cyclopropanols as key stages.

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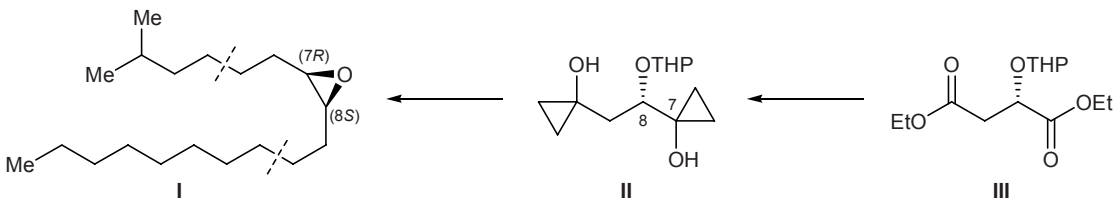
Cyclopropanols and their derivatives undergo opening of the three-membered ring with formation of aldehydes, ketones, carboxylic acids, allyl halides, and some other compounds [1]. These transformations often occur under mild conditions and with high selectivity, so that substituted cyclopropanols attract considerable interest as intermediate products in organic synthesis. A convenient synthetic approach to cyclopropanols having chiral substituents is based on titanium(IV) alkoxide-catalyzed reactions of natural hydroxy- and aminocarboxylic acid esters with alkylmagnesium halides [2, 3]. The key step in the stereoselective syntheses of branched carbon skeletons of pheromones of the pine sawfly (*Diprion pini* L.) [4], alkaloid Heliotridane [5], and C^{13}–C^{21} fragments of Epothilones [6] was cleavage of the three-membered carbon ring in chiral cyclopropanols.

In the present work we used the cyclopropanol strategy to synthesize (+)-disparlure [**I**, (7*R*,8*S*)-7,8-epoxy-2-methyloctadecane] which is sex attractant of the gypsy moth *Lymantria dispar* L., The stereogenic structural fragment in molecule **I** is oxirane ring [7, 8]. The key intermediate was THP-protected bis-cyclopropanol **II**; it was synthesized by titanium(IV) isopropoxide-catalyzed reaction of ethylmagnesium bromide with *O*-tetrahydropyranyl derivative of diethyl (*S*)-malate (**III**) [6], and the necessary carbon chain was built up via alkylation of products of successive oxidative cleavage and fragmentation of the three-membered rings (Scheme 1; for other synthetic approaches to (+)-disparlure (**I**) based on natural hydroxy carboxylic acids, see [9]).

Differentiation of the cyclopropanol fragments in molecule **II** is readily attained via its selective transformation into 1,3-dioxane derivative **IV** [6] as shown in Scheme 2. Treatment of acetonide **IV** with sodium hypobromite in water–diethyl ether gave vinyl ketone **V** whose concentration in the products was more than 90% (according to the ^{1}H NMR data). The use of other brominating agents, such as Br_2–MeOH, *N*-bromosuc-

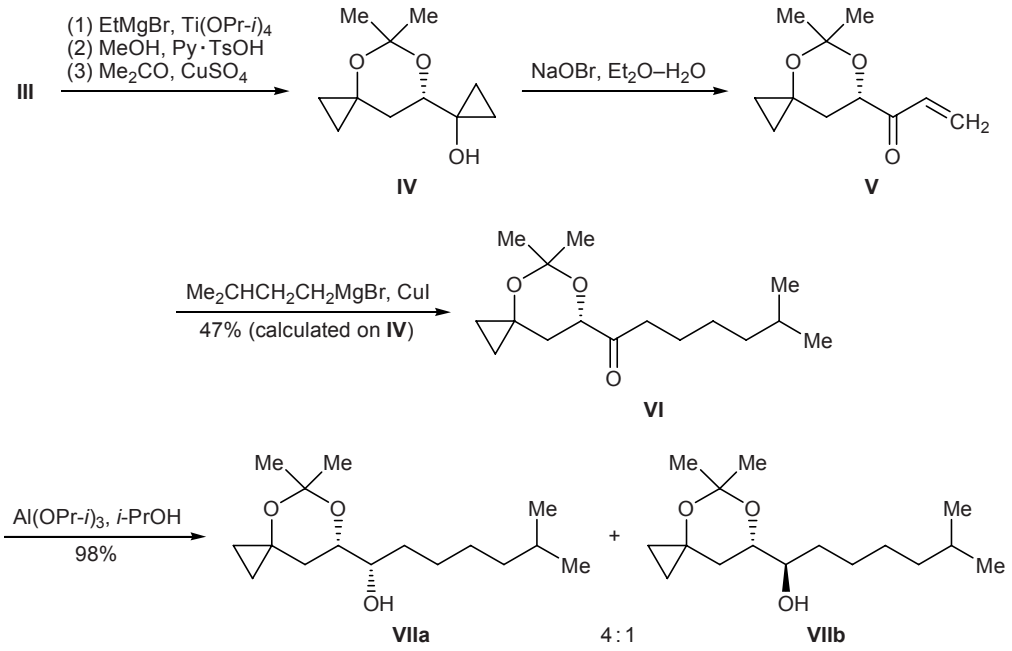
Scheme 1.



I **II** **III**

THP is tetrahydropyran-2-yl.

Scheme 2.

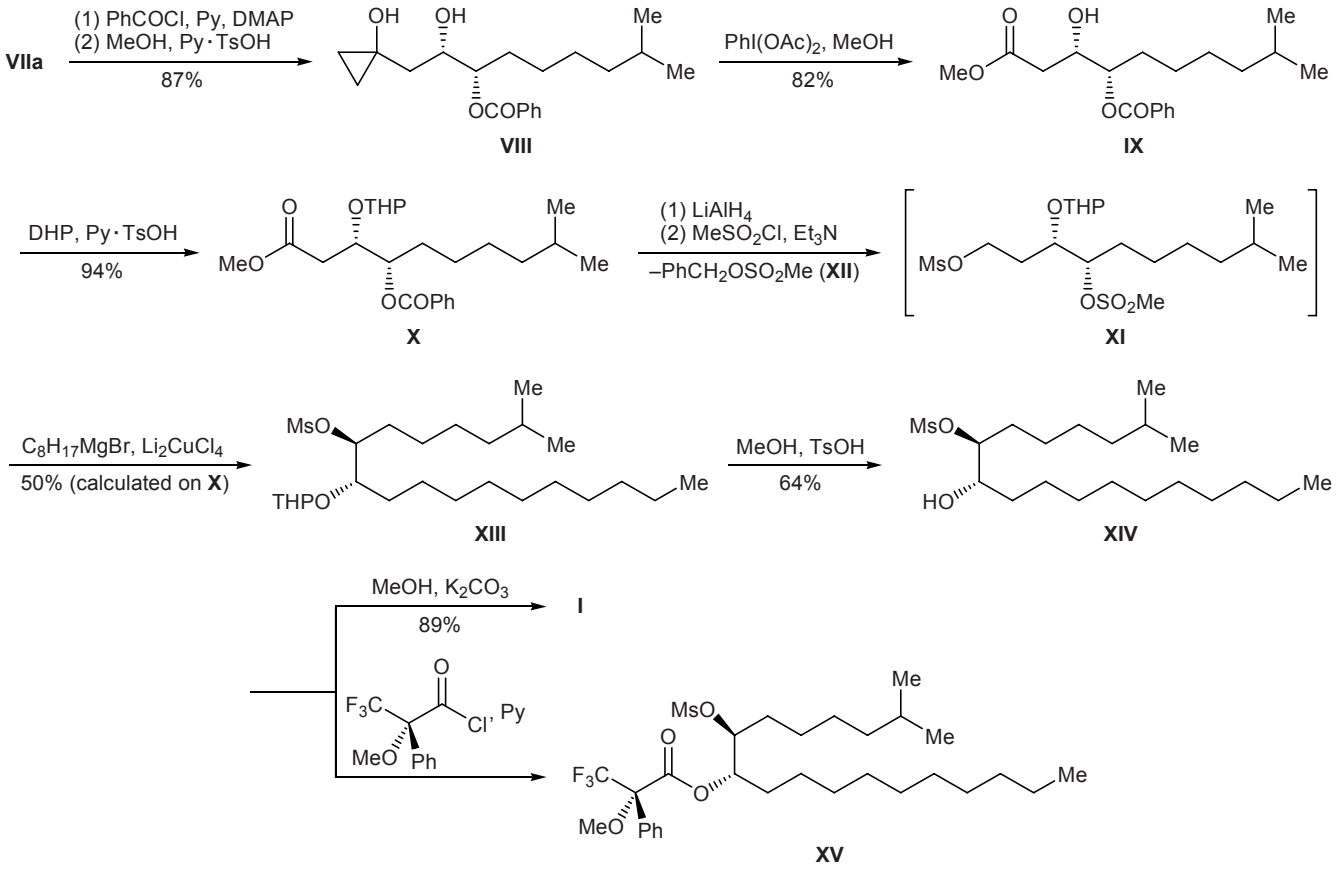


cinimide, and pyridine–bromine complex, resulted in the formation of intractable mixtures of products. Taking into account low stability of vinyl ketone **V**, it was brought (without additional purification) into the copper(I) iodide-catalyzed reaction with isopentylmagnesium bromide. The reduction of the carbonyl group in compound **VI** with lithium tetrahydridoaluminate or diisobutylaluminum hydride at room temperature was characterized by low stereoselectivity, and diastereoisomeric alcohols **VIIa** and **VIIb** were obtained at a ratio close to equimolar. When compound **VI** was treated with $LiAlH_4$ in diethyl ether at –78°C, *anti* isomer **VIIb** was formed as the major product (**VIIa**:**VIIb** = 1:4), while aluminum(III) isopropoxide as reducing agent in a mixture of benzene with isopropyl alcohol ensured the reverse isomer ratio; pure stereoisomers **VIIa** and **VIIb** were separated by column chromatography on silica gel.

Benzoylation of the hydroxy group in alcohol **VIIa**, subsequent removal of the acetonide protection, and fragmentation of the three-membered ring in cyclopropanol **VIII** by the action of (diacetoxy-λ^3-iodanyl)-benzene [10] gave methyl 4-benzoyloxy-3-hydroxy-9-methyldecanoate (**IX**) in a good yield (Scheme 3). Compound **IX** was converted into 3-*O*-tetrahydropyranyl derivative **X** which was reduced with lithium tetrahydridoaluminate to the corresponding triol with one protected hydroxy group and benzyl alcohol formed as a result of reduction of the benzoate fragment. The reduction products were characterized by similar chromatographic mobilities. They were treated with methanesulfonyl chloride, and a mixture of sulfonates **XI** and **XII** thus obtained was brought into reaction with octylmagnesium bromide in the presence of dilithium tetrachlorocuprate(II). Selective replacement of sulfonate groups at primary carbon atoms afforded *syn*-diol derivative **XIII** and nonylbenzene, which were readily separated by chromatography. The best yield of **XIII** was obtained when Li_2CuCl_4 was added to the reaction mixture in several portions. The overall yield of key intermediate **XIII** was not improved by carrying out the reaction with preliminarily isolated (by chromatography) bis-sulfonate **XI**. Removal of the THP protection from compound **XIII** gave monosulfonate **XIV** with an *ee* (enantiomeric excess) value of 90%. The optical purity was determined from the intensity ratio of signals from protons in the methoxy and methylsulfonyl groups in the ^1H NMR spectrum of its acylation product with (*S*)-Mosher acid chloride [(*S*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoyl chloride] [11]. The assignment of proton signals to the minor diastereoisomer was confirmed by comparison of chemical shifts with those in the spectrum of the corresponding ester obtained from racemic Mosher acid. Treatment of **XIV** with anhydrous potassium carbonate in methanol smoothly afforded (+)-disparlure (**I**) as a result of closure of oxirane ring.

To conclude, it should be noted that the proposed scheme of synthesis of (+)-disparlure (**I**) from natural

Scheme 3.



DHP is dihydropyran.

(*S*)-malic acid [12] is experimentally simple. It demonstrates synthetic utility of cyclopropanols as equivalents of vinyl ketone and ester moieties.

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra were recorded from solutions in $CDCl_3$ on a Bruker AC-400 instrument at 400 and 100 MHz, respectively. The IR spectra were recorded on a Bruker Vertex 70 spectrometer from thin films. Individual compounds were isolated by column chromatography on silica gel (70–230 mesh). All solvents were dried according to standard procedures and distilled before use.

1-{(7*S*)-5,5-Dimethyl-4,6-dioxaspiro[2.5]oct-7-yl}prop-2-en-1-one (V). An aqueous solution of sodium hypobromite prepared from 0.27 ml (5.30 mmol) of bromine and 0.25 g (6.30 mmol) of sodium hydroxide in 20 ml of water was added dropwise under vigorous stirring to a solution of 0.70 g (3.53 mmol) of acetonide **IV** [6] in 30 ml of diethyl ether. The mixture was stirred for 5–10 min at room temperature, a solution of 0.15 g (3.75 mmol) of sodium hydroxide in 5 ml of water was added, and the mixture was stirred for 5 min more. The organic phase was separated, the aqueous phase was extracted with diethyl ether (3×10 ml), the extracts were combined with the organic phase, washed with a saturated aqueous solution of Na_2SO_3, and dried over Na_2SO_4, and the solvent was distilled off under reduced pressure to isolate 0.55 g (2.80 mmol) of crude vinyl ketone **V** which was brought into the next step without additional purification. IR spectrum, ν, cm^{-1}: 3088 (C–H, cyclopropane), 1701 (C=O), 1613 (C=C). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.45 d.d.d (1H, CH_2CH_2, J = 10.3, 6.4, 5.5 Hz), 0.66 d.d.d (1H, CH_2CH_2, J = 10.3, 6.4, 4.8 Hz), 0.73–0.79 m (1H, CH_2CH_2), 0.82–0.88 m (1H, CH_2CH_2), 1.25 d.d (1H, 8′-H, J = 13.3, 3.0 Hz), 1.44 s and 1.56 s (3H each, CH_3), 2.18–2.24 m (1H, 8′-H), 4.64 d.d (1H, 7′-H, J = 11.9, 3.0 Hz), 5.79 d.d (1H, C**H**=CH_2, J = 10.6, 1.7 Hz), 6.43 d.d (1H, CH=C**H**$_2$, J = 17.5, 1.7 Hz), 6.86 d.d (1H, CH=C**H**$_2$, J = 17.5, 10.6 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C,

ppm: 10.0 (CH_2), 13.4 (CH_2), 21.0 (CH_3), 29.6 (CH_3), 33.2 (CH_2), 53.4 (C), 73.5 (CH), 100.5 (C), 129.9 (CH_2), 130.8 (CH), 198.1 (C).

1-{(7*S*)-5,5-Dimethyl-4,6-dioxaspiro[2.5]oct-7-yl}-6-methylheptan-1-one (VI). A solution of isopentylmagnesium bromide, prepared from 0.32 g (13.3 mmol) of magnesium and 2.10 g (14.0 mmol) of isopentyl bromide in 12 ml of THF, was added with stirring under argon to a suspension of 0.90 g (4.7 mmol) of CuI in 15 ml of THF, cooled to –25°C. The mixture was stirred for 30 min at –20 to –25°C and cooled to –70°C, and a solution of 0.55 g (2.80 mmol) of crude vinyl ketone **V** in 15 ml of THF was added dropwise under stirring over a period of 1 h. The mixture was treated with 10 ml of a saturated aqueous solution of sodium carbonate and diluted with 25 ml of petroleum ether, and the precipitate was filtered off and washed with petroleum ether (2×10 ml). The organic phase was washed with a saturated aqueous solution of Na_2CO_3 and dried over Na_2SO_4. The solvent was distilled off under reduced pressure, and the residue was subjected to chromatography on silica gel using petroleum ether–ethyl acetate (50:1) as eluent. Yield 0.45 g (47%, calculated on acetonide **IV**), $[\alpha]_D$ = 5.5° (*c* = 7.3, Et_2O). IR spectrum, ν, cm^{-1}: 3084 (C–H, cyclopropane), 1719 (C=O). ^1H NMR spectrum, δ, ppm: 0.41 d.d.d (1H, 2′-H or 3′-H, *J* = 10.2, 6.4, 5.4 Hz), 0.62 d.d.d (1H, 2′-H or 3′-H, *J* = 10.2, 6.1, 5.0 Hz), 0.73 d.d.d (1H, 2′-H or 3′-H, *J* = 10.8, 6.1, 5.6 Hz), 0.70–0.76 m (1H, 2′-H or 3′-H), 0.83 d [6H, $CH(CH_3)_2$, *J* = 6.7 Hz], 1.12–1.31 m (5H, CH_2, 8′-H), 1.41 s and 1.51 s [3H each, $C(CH_3)_2$], 1.47–1.56 m (3H, 6-H, CH_2), 2.07–2.14 m (1H, 8′-H), 2.51–2.66 m (2H, CH_2), 4.42 d.d (1H, 7′-H, *J* = 12.0, 2.8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 10.0 (CH_2), 14.4 (CH_2), 20.9 (CH_3), 22.50 (CH_3), 22.51 (CH_3), 23.2 (CH_2), 26.9 (CH_2), 27.8 (CH), 29.6 (CH_3), 33.4 (CH_2), 37.6 (CH_2), 38.7 (CH_2), 53.5 (C), 74.2 (CH), 100.3 (C), 210.9 (C). Found, %: C 71.46; H 10.59. $C_{16}H_{28}O_3$. Calculated, %: C 71.60; H 10.52.

(1*S*)-1-{(7*S*)-5,5-Dimethyl-4,6-dioxaspiro[2.5]oct-7-yl}-6-methylheptan-1-ol (VIIa). A 1.3 M solution of aluminum(III) isopropoxide in benzene, 12.9 ml (16.8 mmol), was added to a solution of 1.50 g (5.60 mmol) of ketone **VI** in 45 ml of isopropyl alcohol, and the mixture was kept for 36 h at room temperature. The mixture was evaporated under reduced pressure to 1/3 of the initial volume, 80 ml of water and 50 ml of ethyl acetate were added to the residue, the organic phase was separated, and the aqueous phase was extracted with ethyl acetate (3×10 ml). The extracts were combined with the organic phase and filtered through a thin layer of silica gel, the solvent was distilled off under reduced pressure, and the residue was subjected to chromatography on silica gel using petroleum ether–ethyl acetate (40:1 to 30:1) as eluent. Yield 0.75g (50%), $[\alpha]_D$ = 25.3° (*c* = 3.8, Et_2O). IR spectrum, ν, cm^{-1}: 3485 (OH), 3086 (C–H, cyclopropane). ^1H NMR spectrum, δ, ppm: 0.40 d.d.d (1H, 2′-H or 3′-H, *J* = 10.2, 6.3, 5.7 Hz), 0.59 d.d.d (1H, 2′-H or 3′-H, *J* = 10.2, 6.0, 4.9 Hz), 0.72–0.78 m (1H, 2′-H or 3′-H), 0.80–0.85 m (1H, 2′-H or 3′-H), 0.85 d [6H, $CH(CH_3)_2$, *J* = 6.7 Hz], 0.90 d.d (1H, 8′-H, *J* = 12.9, 2.5 Hz), 1.14–1.55 m (9H, 6-H, CH_2), 1.40 s and 1.52 s [3H each, $C(CH_3)_2$], 2.06–2.14 m (1H, 8′-H), 2.50 d (1H, OH, *J* = 3.7 Hz), 3.43 m (1H, C**H**OH), 3.87 d.d.d (1H, 7′-H, *J* = 11.6, 6.3, 2.5 Hz). ^{13}C NMR spectrum, δ_C, ppm: 9.8 (CH_2), 14.7 (CH_2), 21.3 (CH_3), 22.5 (CH_3), 22.6 (CH_3), 25.6 (CH_2), 27.4 (CH_2), 27.9 (CH), 29.7 (CH_3), 32.1 (CH_2), 33.4 (CH_2), 38.9 (CH_2), 53.1 (C), 71.7 (CH), 73.9 (CH), 100.2 (C). Found, %: C 70.91; H 11.25. $C_{16}H_{30}O_3$. Calculated, %: C 71.07; H 11.18.

(1*S*)-1-{(7*S*)-5,5-Dimethyl-4,6-dioxaspiro[2.5]oct-7-yl}-6-methylhept-1-yl benzoate. Alcohol **VIIa**, 1.16 g (4.30 mmol), was dissolved in a mixture of 20 ml of methylene chloride and 3 ml (37.2 mmol) of pyridine, 0.74 ml (6.37 mmol) of benzoyl chloride and 0.03 g (0.24 mmol) of 4-dimethylaminopyridine (DMAP) were added, and the mixture was kept for 12 h at room temperature. The solvent was distilled off under reduced pressure, the residue was dissolved in 20 ml of methanol, 1 ml (7.2 mmol) of triethylamine was added, and the mixture was kept for 10 h. The mixture was then diluted with water and extracted with diethyl ether (3×20 ml), the extracts were combined and dried over Na_2SO_4, the solvent was distilled off under reduced pressure, and the residue was subjected to chromatography on silica gel using petroleum ether–ethyl acetate (25:1) as eluent. Yield 1.58 g (98%), $[\alpha]_D$ = 12.4° (*c* = 7.6, Et_2O). IR spectrum, ν, cm^{-1}: 3087 (C–H, cyclopropane), 1720 (C=O). ^1H NMR spectrum, δ, ppm: 0.38 d.d.d (1H, 2′-H or 3′-H, *J* = 10.2, 6.3, 5.6 Hz), 0.56–0.61 m (1H, 2′-H or 3′-H), 0.70–0.75 m (1H, 2′-H or 3′-H), 0.80–0.85 m (1H, 2′-H or 3′-H), 0.84 d [6H, $CH(CH_3)_2$, *J* = 6.7 Hz], 0.90 d.d (1H, 8′-H, *J* = 12.8, 2.3 Hz), 1.10–1.17 m (2H, CH_2), 1.25–1.42 m (4H, CH_2), 1.46–1.55 m [1H, C**H**$(CH_3)_2$], 1.39 s and 1.52 s [3H each, $C(CH_3)_2$], 1.71–1.79 m (2H, CH_2), 2.25 d.d.d (1H, 8′-H, *J* = 12.8, 12.0, 1.3 Hz), 4.27 d.d.d (1H, 7′-H, *J* = 12.0, 3.7, 2.3 Hz),

5.16 d.d.d (1H, 1-H, J = 6.9, 6.5, 3.7 Hz), 7.42–7.48 m (2H, H_{arom}), 7.56–7.60 m (1H, H_{arom}), 8.04–8.08 m (2H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 9.8 (CH_2), 14.4 (CH_2), 21.0 (CH_3), 22.5 (CH_3), 22.6 (CH_3), 25.7 (CH_2), 27.3 (CH_2), 27.8 (CH), 29.6 (CH_2), 29.8 (CH_3), 32.8 (CH_2), 38.8 (CH_2), 53.4 (C), 69.0 (CH), 75.5 (CH), 100.3 (C), 128.3 (2CH), 129.5 (2CH), 130.4 (C), 132.8 (CH), 166.3 (C). Found, %: C 73.90; H 9.07. $C_{23}H_{34}O_4$. Calculated, %: C 73.76; H 9.15.

(2*S*,3*S*)-2-Hydroxy-1-(1-hydroxycyclopropyl)-8-methylnonan-3-yl benzoate (VIII). A solution of 1.06 g (2.83 mmol) of (1*S*)-1-{(7*S*)-5,5-dimethyl-4,6-dioxaspiro[2.5]oct-7-yl}-6-methylhept-1-yl benzoate and 0.10 g (0.39 mmol) of pyridinium *p*-toluenesulfonate in 30 ml of methanol was heated for 30 min under reflux. The solvent was distilled off under reduced pressure, and the residue was subjected to chromatography on silica gel using petroleum ether–ethyl acetate (5:1) as eluent. Yield 0.84 g (89%), $[\alpha]_D$ = –20.0° (c = 4.3, MeOH). IR spectrum, ν, cm^{-1}: 3418 (OH), 3086 (C–H, cyclopropane), 1717 (C=O). ^1H NMR spectrum, δ, ppm: 0.35–0.52 m and 0.75–0.84 m (2H each, 2′-H, 3′-H), 0.83 d [6H, CH(CH_3)$_2$, J = 6.5Hz], 1.10–1.16 m (2H, CH_2), 1.25–1.38 m (5H, CH_2, 1-H), 1.42–1.53 m (1H, 8-H), 1.71–1.79 m (2H, CH_2), 2.10 d.d (1H, 1-H, J = 14.5, 10.5 Hz), 3.15 d (1H, OH, J = 5.2 Hz), 3.61 br.s (1H, OH), 4.16–4.20 m (1H, 2-H), 5.11 d.t (1H, 3-H, J = 6.6, 4.2 Hz), 7.41–7.46 m (2H, H_{arom}), 7.55–7.60 m (1H, H_{arom}), 8.04–8.08 m (2H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 12.5 (CH_2), 14.0 (CH_2), 22.5 (CH_3), 22.6 (CH_3), 25.7 (CH_2), 27.2 (CH_2), 27.8 (CH), 30.4 (CH_2), 38.7 (CH_2), 40.4 (CH_2), 55.3 (C), 73.1 (CH), 77.3 (CH), 128.4 (CH), 129.7 (CH), 130.0 (C), 133.1 (CH), 166.6 (C). Found, %: C 71.67; H 9.11. $C_{20}H_{30}O_4$. Calculated, %: C 71.82; H 9.04.

(3*S*,4*S*)-3-Hydroxy-1-methoxy-9-methyl-1-oxodecan-4-yl benzoate (IX). Diacetoxy(phenyl)-λ^3-iodane, 0.38 g (1.20 mmol), was added to a solution of 0.40 g (1.20 mmol) of diol **VIII** in 10 ml of methanol, the mixture was kept for 10 min at room temperature, the solvent was distilled off under reduced pressure, and the residue was subjected to chromatography on silica gel using petroleum ether–ethyl acetate (10:1) as eluent. Yield 0.33 g (82%), $[\alpha]_D$ = –20.0° (c = 3.5, $CHCl_3$). IR spectrum, ν, cm^{-1}: 3494 (OH), 1730 (C=O), 1717 (C=O). ^1H NMR spectrum, δ, ppm: 0.83 d (6H, CH_3, J = 6.6 Hz), 1.11–1.17 m (2H, CH_2), 1.25–1.40 m (4H, CH_2), 1.44–1.54 m (1H, 9-H), 1.77–1.83 m (2H, CH_2), 2.50–2.61 m (2H, 2-H), 3.22 br.s (1H, OH), 3.63 s (3H, OCH_3), 4.22–4.28 m (1H, 3-H), 5.15 d.t (1H, 4-H, J = 6.7, 3.5 Hz), 7.42–7.50 m (2H, H_{arom}), 7.54–7.60 m (1H, H_{arom}), 8.02–8.08 m (2H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 22.50 (CH_3), 22.54 (CH_3), 25.7 (CH_2), 27.2 (CH_2), 27.8 (CH), 30.2 (CH_2), 37.8 (CH_2), 38.7 (CH_2), 51.8 (CH_3), 68.8 (CH), 76.2 (CH), 128.3 (2CH), 129.7 (2CH), 129.9 (C), 133.1 (CH), 166.2 (C), 172.8 (C). Found, %: C 67.98; H 8.32. $C_{19}H_{28}O_5$. Calculated, %: C 67.83; H 8.39.

(3*S*,4*S*)-1-Methoxy-9-methyl-1-oxo-3-(tetrahydro-2*H*-pyran-2-yloxy)decan-4-yl benzoate (X). A solution of 0.50 g (1.48 mmol) of ester **IX**, 0.19 g (2.26 mmol) of dihydropyran, and 0.02 g (0.079 mmol) of pyridinium *p*-toluenesulfonate in 6 ml of methylene chloride was heated for 2–4 h under reflux. The mixture was washed with a saturated aqueous solution of $NaHCO_3$, the organic phase was dried over Na_2SO_4, the solvent was distilled off under reduced pressure, and the residue was subjected to chromatography on silica gel using petroleum ether–ethyl acetate (10:1) as eluent. Yield 0.59 g (94%), 1:1 mixture of diastereoisomers. IR spectrum, ν, cm^{-1}: 1745 (C=O), 1722 (C=O). ^1H NMR spectrum, δ, ppm: 0.83 d (6H, CH_3, J = 6.7 Hz), 1.12–1.85 m (15H), 2.58–2.75 m (2H, 2-H), 3.43–3.57 m (1H), 3.61 s (3H, OCH_3), 3.79–3.91 m (1H), 4.31–4.38 m (1H), 4.71–4.75 m (1H), 5.24 d.t (0.5H, 4-H, J = 8.7, 3.9 Hz), 5.36 d.t (0.5H, 4-H, J = 9.5, 3.9 Hz), 7.44 m (2H, H_{arom}), 7.56 m (1H, H_{arom}), 8.03 m (2H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 19.8 (CH_2), 22.5 (CH_3), 22.6 (CH_3), 25.3 (CH_2), 25.8 (CH_2), 26.0 (CH_2), 27.1 (CH_2), 27.8 (CH), 28.9 (CH_2), 29.3 (CH_2), 30.9 (CH_2), 35.5 (CH_2), 37.2 (CH_2), 38.6 (CH_2), 38.7 (CH_2), 51.5 (CH_3), 51.6 (CH_3), 62.9 (CH_2), 63.0 (CH_2), 74.3 (CH), 74.8 (CH), 75.0 (CH), 75.4 (CH), 99.4 (CH), 100.4 (CH), 128.3 (CH), 129.6 (CH), 130.1 (C), 130.3 (C), 132.8 (CH), 132.9 (CH), 165.9 (C), 166.0 (C), 171.6 (C), 171.8 (C). Found, %: C 68.41; H 8.69. $C_{24}H_{36}O_6$. Calculated, %: C 68.54; H 8.63.

(7*S*,8*S*)-2-Methyl-8-(tetrahydro-2*H*-pyran-2-yloxy)octadecan-7-yl methanesulfonate (XIII). Lithium tetrahydridoaluminate, 0.095 g (2.5 mmol), was added at room temperature to a solution of 0.40 g (0.97 mmol) of ester **X** in 8 ml of anhydrous diethyl ether. The mixture was stirred for 30 min at room temperature and treated in succession with 5 ml of ethyl acetate and 0.5 ml of water. The precipitate was filtered off and washed with ethyl acetate (3×5 ml), and the solvent was distilled off from the filtrate under reduced pressure. The residue was dissolved in 8 ml of anhydrous diethyl ether, 1 ml (7.2 mmol) of triethylamine was added, the mixture was cooled to 0°C, and

0.39 ml (5.0 mmol) of methanesulfonyl chloride was added dropwise. The mixture was stirred for 30 min at 0°C and poured into water, the organic phase was separated, and the aqueous phase was extracted with ethyl acetate (2×10 ml). The extracts were combined with the organic phase, washed with a saturated aqueous solution of $NaHCO_3$, and dried over Na_2SO_4, the solvent was distilled off under reduced pressure, the residue was passed through a thin layer of silica gel, and the sorbent was washed with petroleum ether–ethyl acetate (5:1). The solvent was distilled off to isolate 0.52 g of a mixture of methanesulfonates **XI** and **XII**. The product mixture was dissolved in a mixture of 6 ml of THF and 2 ml of benzene, the solution was cooled to 0°C, and 8 ml of a solution of octylmagnesium bromide, prepared from 1.38 ml (8.0 mmol) of *n*-octyl bromide and 0.30 g (12.5 mmol) of magnesium in a mixture of 5.5 ml of THF and 1.5 ml of benzene, was added under argon. A solution of Li_2CuCl_4 prepared from 0.032 g (0.76 mmol) of LiCl and 0.051 g (0.38 mmol) of $CuCl_2$ in 1.8 ml of THF was added in 0.3-ml portions over a period of 40 min under stirring at 0°C. After addition of the catalyst, the mixture was stirred for 20 min and treated with water and 10 ml of petroleum ether. The organic phase was separated, the aqueous phase was extracted with petroleum ether (2×10 ml), the extracts were combined with the organic phase, washed with a saturated aqueous solution of Na_2CO_3, and dried over Na_2SO_4. The solvent was distilled off under reduced pressure, and the residue was subjected to chromatography on silica gel using petroleum ether–ethyl acetate (20:1) as eluent. Yield 0.22 g (50%), 1.5:1 mixture of diastereoisomers. IR spectrum, ν, cm^{-1}: 1354, 1176 (SO_2). ^1H NMR spectrum, δ, ppm: 0.85 d [6H, $CH(CH_3)_2$, J = 6.4 Hz], 0.86 t (3H, CH_3, J = 6.7 Hz), 1.13–1.80 m (33H), 3.00 s (1.2H, CH_3SO_2), 3.03 s (1.8H, CH_3SO_2), 3.46–3.51 m (1H), 3.77–3.82 m (1H), 3.84–3.90 m (1H), 4.55–4.57 m (0.6H), 4.62–4.66 m (0.8H), 4.76–4.81 m (0.6H). ^{13}C NMR spectrum, δ_C, ppm: 14.1 (CH_3), 20.0 (CH_2), 20.5 (CH_2), 22.5 (CH_3), 22.6 (CH_3), 25.0 (CH_2), 25.2 (CH_2), 25.3 (CH_2), 25.7 (CH_2), 27.1 (CH_2), 27.9 (CH), 28.9 (CH_2), 29.3 (CH_2), 29.4 (CH_2), 29.5 (CH_2), 29.6 (CH_2), 29.7 (CH_2), 29.8 (CH_2), 30.4 (CH_2), 31.0 (CH_2), 31.8 (CH_2), 38.3 (CH_3), 38.6 (CH_2), 38.7 (CH_2), 63.2 (CH_2), 63.7 (CH_2), 77.1 (CH), 78.3 (CH), 83.4 (CH), 84.1 (CH), 99.4 (CH), 100.3 (CH). Found, %: C 65.03; H 10.81. $C_{25}H_{50}O_5S$. Calculated, %: C 64.89; H 10.89.

(7*S*,8*S*)-8-Hydroxy-2-methyloctadecan-7-yl methanesulfonate (XIV). A solution of 0.22 g (0.48 mmol) of compound **XIII** and 0.02 g (0.11 mmol) of *p*-toluenesulfonic acid in 5 ml of methanol was kept for 2 h at room temperature. The mixture was diluted with water and extracted with diethyl ether (5×5 ml), the extracts were combined and dried over Na_2SO_4, the solvent was distilled under reduced pressure, and the residue was subjected to chromatography on silica gel using petroleum ether–ethyl acetate (10:1) as eluent. Yield 0.17 g (94%), $[\alpha]_D$ = –12.3° (c = 2.5, $CHCl_3$). IR spectrum, ν, cm^{-1}: 3532 (OH); 1342, 1174 (SO_2). ^1H NMR spectrum, δ, ppm: 0.85 d [6H, $CH(CH_3)_2$, J = 6.6 Hz], 0.86 t (3H, CH_3, J = 6.7 Hz), 1.38–1.80 m (27H), 2.03 d (1H, OH, J = 6.3 Hz), 3.07 s (3H, CH_3SO_2), 3.64–3.70 m (1H, 8-H), 4.57 d.t (1H, 7-H, J = 5.2, 7.4 Hz). ^{13}C NMR spectrum, δ_C, ppm: 14.1 (CH_3), 22.5 ($2CH_3$), 22.6 (CH_2), 25.2 (CH_2), 25.3 (CH_2), 27.1 (CH_2), 27.8 (CH), 29.3 (CH_2), 29.4 (CH_2), 29.5 (CH_2), 29.6 (CH_2), 31.1 (CH_2), 31.9 (CH_2), 33.1 (CH_2), 38.7 (CH_3), 72.1 (CH), 86.6 (CH). Found, %: C 63.60; H 11.24. $C_{20}H_{42}O_4S$. Calculated, %: C 63.45; H 11.18.

(7*S*,8*S*)-2-Methyl-7-methylsulfonyloctadecan-8-yl (2*S*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (XV). Compound **XIV**, 17 mg (0.045 mmol), was dissolved in 0.5 ml of carbon tetrachloride, 50 mg (0.62 mmol) of pyridine and 23 mg (0.090 mmol) of (2*S*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoyl chloride were added, and the mixture was kept for 24 h at room temperature, diluted with 2 ml of petroleum ether, treated with 10% sulfuric acid, washed with water and a saturated aqueous solution of $NaHCO_3$, and dried over Na_2SO_4. The solvent was distilled off under reduced pressure, and the residue was subjected to chromatography on silica gel using petroleum ether–ethyl acetate (20:1) as eluent. Yield quantitative; the product contained 5% of minor diastereoisomer. ^1H NMR spectrum, δ, ppm: 0.85 m (9H, CH_3), 1.15–1.70 m (27H), 2.93 s (0.15H, CH_3SO_2), 3.00 s (2.85H, CH_3SO_2), 3.52 s (2.85H, CH_3O), 3.56 s (0.15H, CH_3O), 4.71–4.75 m (1H, 7-H), 5.20–5.25 m (1H, 8-H), 7.40–7.43 m (3H, H_{arom}), 7.53–7.55 m (2H, H_{arom}).

(7*R*,8*S*)-7,8-Epoxy-2-methyloctadecane (I). Potassium carbonate, 0.55 g (4.0 mmol), was added at room temperature to a solution of 0.43 g (1.14 mmol) of compound **XIV** in 10 ml of methanol. The mixture was stirred for 10 min, diluted with water, and extracted with diethyl ether (3×10 ml), the extracts were combined and dried over Na_2SO_4, the solvent was distilled off under reduced pressure, and the residue was subjected to chromatography on silica gel using petroleum ether–ethyl acetate (30:1) as eluent. Yield

0.29 g (89%). The spectral parameters and optical rotation value of compound **I** coincided with the data given in [9].

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