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Influence of Some Factors on the Progress of a New Reaction in the Chemistry of Organoaluminum Compounds

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Abstract—We earlier discovered a new reaction in the chemistry of organoaluminum compounds (OACs), specifically, the formation of *O*-isobutyl acetals on low-temperature (–70°C) treatment of seven-membered lactones with a double (or more) molar amount of diisobutylaluminum hydride (DIBAH) in methylene chloride. To assess the boundaries for the formation of isobutyl acetals depending on the ring size, we involved in the low-temperature hydride reduction six-, eight-, and thirteen-membered lactones. To determine how the scope of the new reaction depends on the nature of the organoaluminum reagent, we tested triisobutylaluminum (TIBA). To determine how the formation of isobutyl acetals on low-temperature (–70°C) reduction with excess DIBAH in CH_2Cl_2 depends on whether the starting ester is cyclic or acyclic and, if the former is the case, on the ring size in the ester, we used the acyclic methyl octadecanoate as the starting compound. It was found that the new reaction in the chemistry of AOC with DIBAH as the reducer is characteristic only of seven-membered lactones and atypical of acyclic methyl octadecanoate and ricinoleate (i.e. acids with the carbon chain length more than 6).

Keywords: lactones, oxepan-2-ones, acyclic esters, low-temperature reduction, diisobutylaluminum hydride, methylene chloride

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Earlier [1–9] we discovered a new reaction in the chemistry of organoaluminum compounds (OACs): the formation of O-isobutyl acetals **1–9** on low-temperature (–70°C) treatment of seven-membered lactones 7*S*-**10**, 7*R*-**10**, and **11–18** with a double (or more) molar amount of diisobutylaluminum hydride (DIBAH) in methylene chloride (Scheme 1).

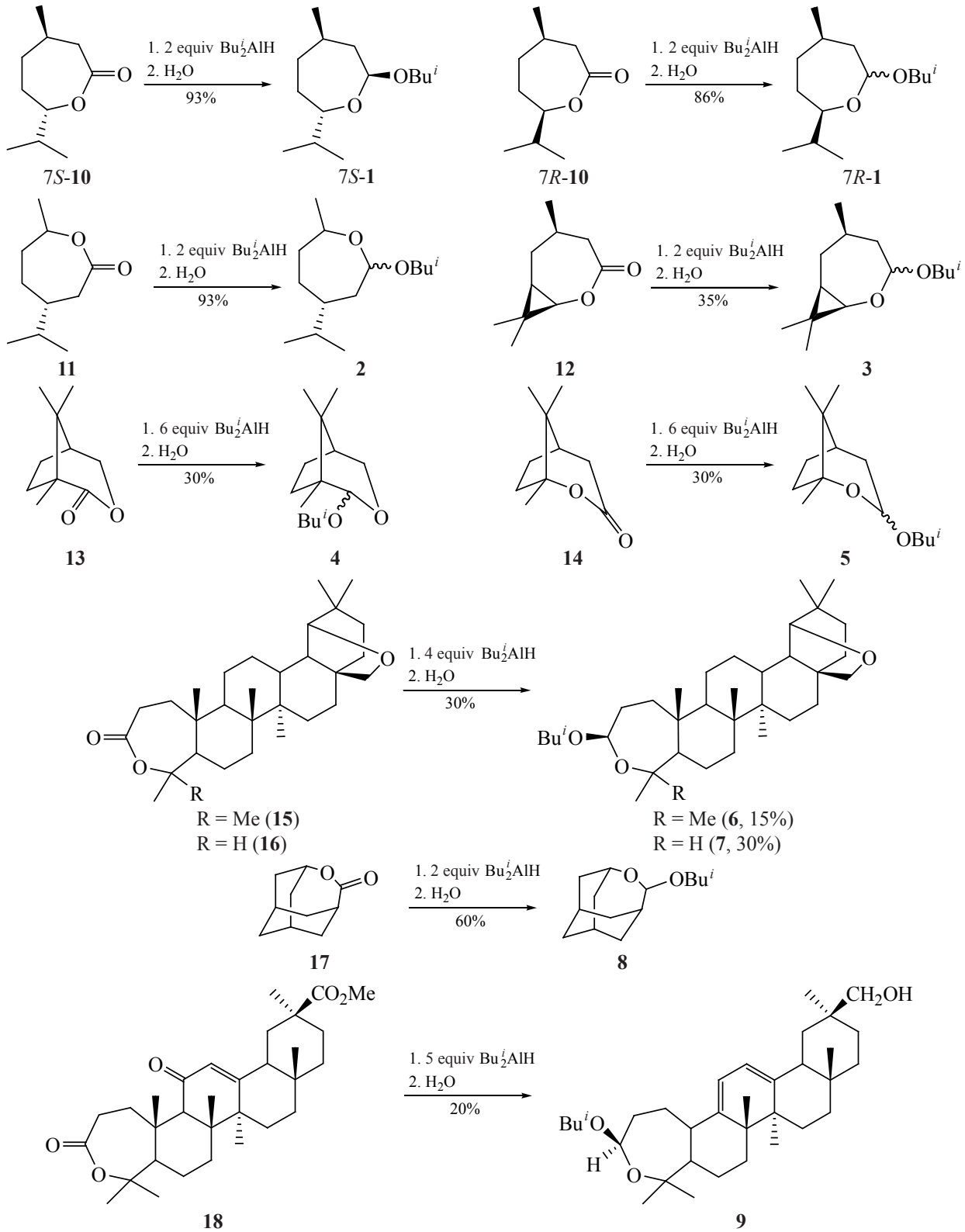
Analysis of the resulting data raised a number of questions. Whether the reaction forming isobutyl acetals is characteristic exclusively of oxepan-2-ones or successful reaction may also take place with other types of lactones? Whether the reaction may not occur without DIBAH or isobutyl acetals will also form with other OACs, for example, triisobutylaluminum (TIBA)? Whether isobutyl acetals will form on the reduction of acyclic carboxylic esters? The present work was undertaken to address these questions.

To assess the boundaries for the formation of isobutyl acetals depending on the ring size in the starting lactone, we involved in the low-temperature hydride reduction six-, eight-, and thirteen-membered lactones **19–21**, respectively. Their reduction with a double molar amount of DIBAH in methylene chloride at–70°C gave mixtures of the corresponding alcohols **22** and **23** and hydroxyaldehydes **24–26**. With a large excess (6 equiv) of DIBAH, no isobutyl acetals formed (Scheme 2).

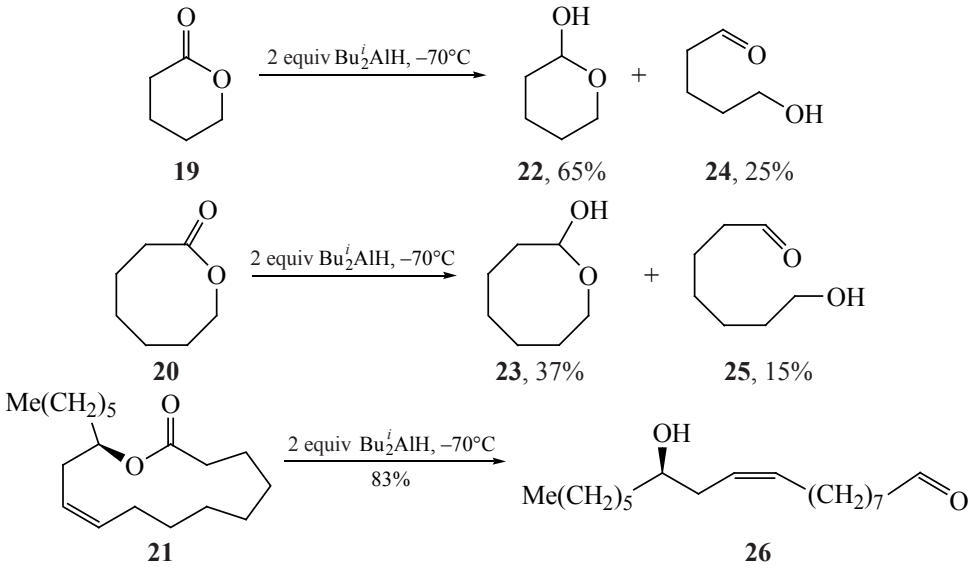
To determine how the scope of the new reaction depends on the nature of the organoaluminum reagent, we employed triisobutylaluminum (TIBA). However, attempted reaction of TIBA with (–)-mentolactone 7*S*-**10** at different temperatures (from –70°C to ambient) failed and resulted in the recovery of the starting oxepan-2-one 7*S*-**10**. The reaction in CH_2Cl_2 under refluxed gave a complete reduction product diol 6*S*-**27** (conversion 50%). This result is likely to be explained by the fact that TIBA transforms, according to [10], into DIBAH at 40°C, and the latter, in its turn, acts as the hydride reagent (Scheme 3).

To find out whether the formation of isobutyl acetals on low-temperature (–70°C) reduction with excess DIBAH in CH_2Cl_2 depends on whether the starting ester

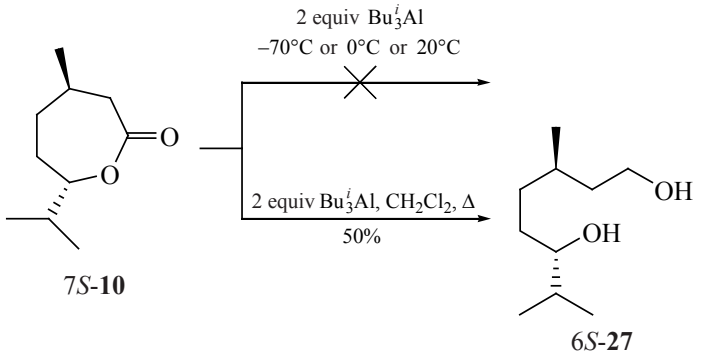
Scheme 1.


1. 2 equiv Bu$_2^i$AlH
2. H$_2$O
93%
7*S*-**10**
7*S*-**1**
1. 2 equiv Bu$_2^i$AlH
2. H$_2$O
86%
7*R*-**10**
7*R*-**1**
1. 2 equiv Bu$_2^i$AlH
2. H$_2$O
93%
11
2
1. 2 equiv Bu$_2^i$AlH
2. H$_2$O
35%
12
3
1. 6 equiv Bu$_2^i$AlH
2. H$_2$O
30%
13
4
1. 6 equiv Bu$_2^i$AlH
2. H$_2$O
30%
14
5
1. 4 equiv Bu$_2^i$AlH
2. H$_2$O
30%
R = Me (**15**)
R = H (**16**)
R = Me (**6**, 15%)
R = H (**7**, 30%)
1. 2 equiv Bu$_2^i$AlH
2. H$_2$O
60%
17
8
1. 5 equiv Bu$_2^i$AlH
2. H$_2$O
20%
18
9

Scheme 2.



Scheme 3.

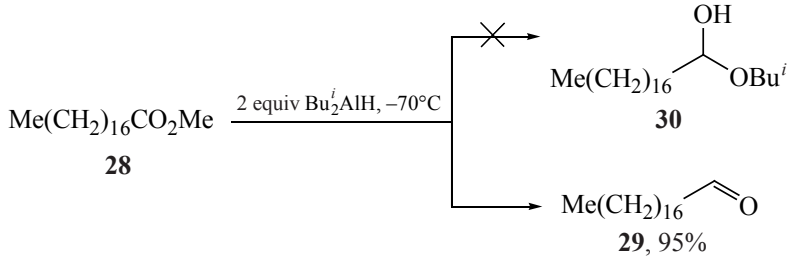


is cyclic or acyclic, we employed the acyclic methyl octadecanoate **28** as the substrate. The reaction resulted in the quantitative isolation of its partial reduction product aldehyde **29**, whereas the expected hemiacetal **30** was not detected (Scheme 4).

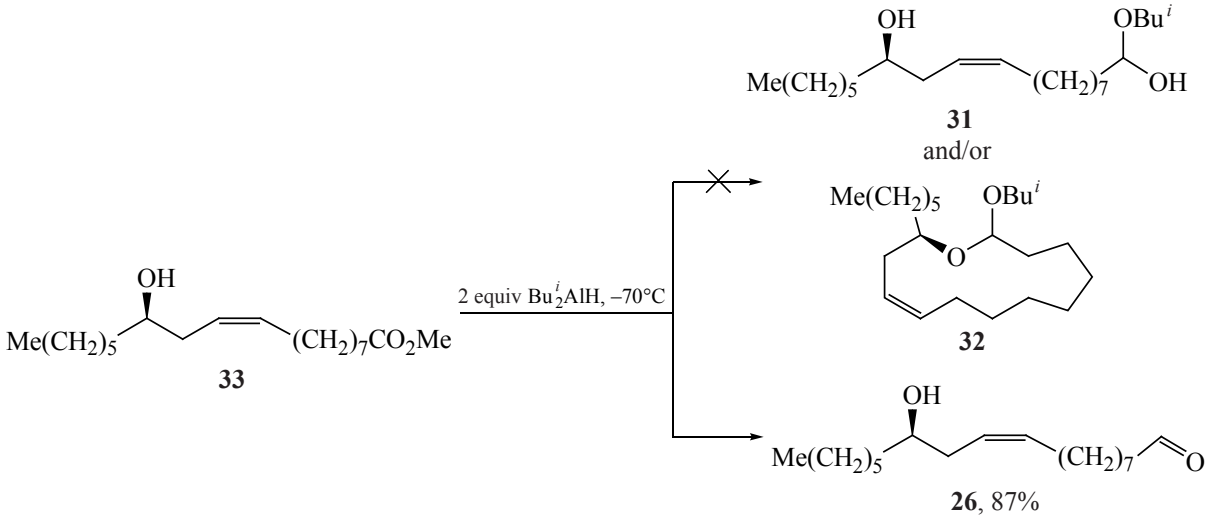
Hemiacetal **31** and acetal **32** were also not detected after the reduction under the above conditions of the methyl ester of (9*Z*,12*R*)-12-hydroxyoctadec-9-enoic (ricinoleic) acid **33**. Hydroxyaldehyde **26** isolated in a high yield was the only reaction product (Scheme 5).

Note that, like with methyl (3*R*,6*S*)-6-hydroxy-3,7-dimethyloctanoate (**34**) from (–)-mentolactone 7*S*-**10** [8], the reduction of hydroxyester **35** forms, along with hydroxyaldehyde **36**, acetal **37**, enen though in small amounts (3%, by ^1H and ^{13}C NMR) (Scheme 6).

Scheme 4.



Scheme 5.



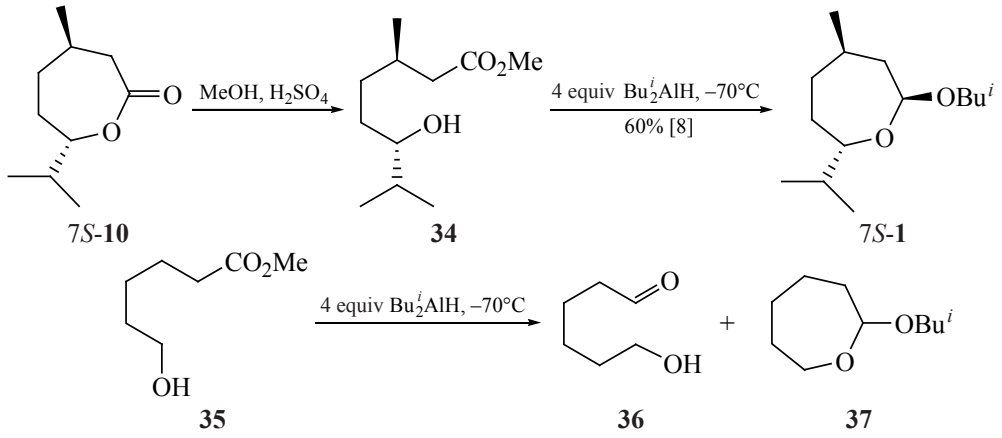
Thus, the new reaction in the chemistry of AOC is characteristic exclusively of seven-membered lactones, occurs with DIBAH as the reducer, and uncharacteristic of the acyclic methyl octadecanoate and ricinoleate (with the carbon chain length more than 6).

EXPERIMENTAL

The IR spectra were recorded on a Shimadzu IR Prestige21 FTIR spectrophotometer in thin films. The NMR spectra were measured on a Bruker AM-500 spectrometer at 500.13 (^{1}H NMR) and 125.76 (^{13}C NMR) MHz in $CDCl_3$ solutions and calibrated using residual $CHCl_3$ signal (δ 7.27 ppm) as internal reference for ^{1}H NMR and $CDCl_3$ signal (δ_C 77.00 ppm) as internal reference for ^{13}C NMR. This-layer chromatography was performed on Sorbfil SiO_2 plates. Gas chromatography was performed on Chrom-5 [column length 1.2 m, packing SE-30 (5%) on Chromaton N-AW-DMCS (0.16–0.20 mm), temperature ramp 50–300°C) and Shimadzu GC-9A chromatographs (quartz capillary column, length 25 m, stationary phase OV-101, temperature ramp 80–280°C); carrier gas helium. Column chromatography was performed on a Lancaster silica gel. The elemental analyses of the synthesized compounds were consistent with calculation. Chemical grade THF, petroleum ether 40–70°C (PE), and *tert*-butyl methyl ether (TBME) purchased from EKOS-1 (Russia) and chemical grade methylene chloride purchased from Reakhim (Russia) were purified and dried according to [11].

Reduction of lactones and esters (*general procedure*). A solution of 7.7 mmol {0.77 g of tetrahydropyran-2-one (**19**) [12] or 0.99 g of oxocan-2-one (**20**) [13] or 2.15 g of (9*Z*,12*R*)-12-hexyloctadec-9-en-12-olide (**21**) [14] or 1.12 g of methyl 6-hydroxyhexanoate (**35**) [15]

Scheme 6.



or 2.29 g of methyl octadecanoate (**28**) [16] or 2.40 g of methyl (9*Z*,12*R*)-12-hydroxyoctadec-9-enoate (**33**) [17]} in 12 mL of anhydrous CH_2Cl_2 was added dropwise to a solution of 4.0 mL (16.0 mmol) of a 73% solution of DIBAH in toluene and 15 mL of anhydrous CH_2Cl_2 (Ar, –70°C). After standing for 3 h at –70°C and addition of 20 mL of a 1 : 1 mixture of THF and water, the reaction mixture was allowed to warm up to room temperature, diluted with 50 mL of CH_2Cl_2, filtered through a bed of Al_2O_3 (5 cm), dried over Na_2SO_4, and evaporated.

The reduction of tetrahydropyran-2-one (**19**) gave 0.71 g of a mixture of alcohol **22** and hydroxyaldehyde **24** in a 2.6 : 1.0 ratio (by ^{1}H NMR).

Tetrahydropyran-2-ol (22). R_f 0.28 (PE–TBME, 2 : 1). ^{1}H NMR spectrum, δ, ppm: 1.30–1.90 m (6H, H^4, H^5, H^3), 3.93 br.s (1H, OH), 3.30–3.95 m (2H, H^6), 4.80 m (1H, H^2). ^{13}C NMR spectrum, δ, ppm: 19.51 (C^4), 25.36 (C^5), 30.97 (C^3), 62.30 (C^6), 98.84 (C^2). Cf. [12].

5-Hydroxyhexanal (24). R_f 0.43 (PE–TBME, 2 : 1). ^{1}H NMR spectrum, δ, ppm: 1.35–1.85 m (4H, H^4, H^3), 2.40 m (2H, H^2), 3.00 br.s (1H, OH), 3.40–3.75 m (2H, H^5), 9.81 t (1H, H^1, *J* 2.0 Hz). ^{13}C NMR spectrum, δ, ppm: 29.26 (C^3), 32.02 (C^4), 43.64 (C^2), 63.78 (C^5), 202.50 (C^1). Cf. [12].

The reduction of oxocan-2-one (**20**) gave 0.60 g of a mixture of alcohol **23** and hydroxyaldehyde **25** in a 2.5 : 1.0 ratio.

Oxocan-2-ol (23). R_f 0.30 (PE–TBME, 2 : 1). ^{1}H NMR spectrum, δ, ppm: 1.40 m (8H, H^3–H^6), 1.81–1.91 m (2H, H^7), 3.24–3.28 m (2H, H^8), 3.92 br.s (1H, OH), 4.81–4.86 m (1H, H^2). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 24.88 (C^4), 26.91 (C^5), 30.15 (C^6), 34.22 (C^3), 65.48 (C^7), 103.12 (C^2).

7-Hydroxyheptanal (25). R_f 0.45 (PE–TBME, 2 : 1). ^{1}H NMR spectrum, δ, ppm: 1.41–1.60 m (4H, H^4, H^5), 1.64–1.71 m (2H, H^3), 2.38–2.41 m (2H, H^2), 2.57 t (1H, OH), 3.58–3.61 m (2H, H^6), 9.72 t (1H, HC=O, *J* 2.1 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 24.76 (C^3), 26.94 (C^5), 28.93 (C^4), 32.25 (C^6), 43.75 (C^2), 62.73 (C^7), 202.89 (C^1). Cf. [18].

The reduction of (9*Z*,12*R*)-12-hexyloctadec-9-en-12-olide (**21**) gave 1.84 g (85%) of **(9*Z*,12*R*)-12-hydroxyoctadec-9-enal** (**26**). IR spectrum (KBr), ν, cm^{-1}: 1711 (C=O). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 14.70 (C^{18}), 22.07 (C^3), 22.75 (C^{17}), 25.26 (C^8), 26.90 (C^{14}), 28.76 (C^4), 28.81 (C^5), 29.21 (C^{15}), 29.35 (C^6), 29.91 (C^7), 31.47 (C^{16}), 33.06 (C^{11}), 36.54 (C^{13}), 43.80 (C^2), 71.38 (C^{12}), 127.34 (C^{10}), 129.63 (C^9), 202.74 (C^1). Mass spectrum, *m/z* (I_{rel}, %), (Scan C+): 246 [$M^+ - 2H_2O$], 217 (93.0), 189 (100.0), 161 (61.0). Cf. [19].

Reaction of (–)-mentolactone 7*S*-10 with triisobutylaluminum. A solution of 2.00 g (12 mmol) mentolactone 7*S*-**10** in 17 mL of anhydrous CH_2Cl_2 was added dropwise to a solution of of 6 mL (21.0 mmol) of TIBA in 20 mL of anhydrous CH_2Cl_2 (Ar, 20°C). The mixture was heated under reflux for 3 h, cooled to 0°C and, after addition of 54 mL of a 1 : 1 mixture of THF and water, diluted with 60 mL of CH_2Cl_2, filtered through a bed of Al_2O_3 (5 cm), dried over Na_2SO_4, and evaporated to isolate 2.00 g of a 1 : 1 mixture of the starting lactone 7*S*-**10** and diol 6*S*-**27**. Column chromatography on SiO_2 [PE–ethyl acetate (EA), 5 : 1] gave 0.80 g (40%) of diol 6*S*-**27**.

(3*R*,6*S*)-3,7-Dimethyloctane-1,6-diol (6*S*-27). R_f 0.10 (PE–EA, 7 : 3), $[\alpha]_D^{20}$ –10.3 (*c* 2.43, $CHCl_3$). IR spectrum (KBr), ν, cm^{-1}: 3400, 1100, 1055 (OH). ^{1}H NMR spectrum, δ, ppm: 0.80 d (3H, CH_3C^3, *J* 6.7 Hz), 0.88 d (3H, CH_3C^7, *J* 6.7 Hz), 0.92 d (3H, H^8, *J* 6.7 Hz), 1.10–1.70 m (9H, H^2–H^7), 2.50 br.s (2H, OH), 3.50–3.75 m (2H, H^1). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 16.99 and 18.81 (CH_3C^7, C^8), 19.74 (CH_3C^3), 29.54 (C^3), 31.20 (C^5), 32.77 (C^4), 33.37 (C^7), 39.58 (C^2), 60.13 (C^1), 76.67 (C^6). Cf. [1].

The reduction of methyl octadecanoate (**28**) gave 1.96 g (95%) of **octadecanal (29)**. ^{1}H NMR spectrum, δ, ppm: 0.88–0.92 m (3H, H^{18}), 1.08–1.14 m (2H, H^{16}), 1.23–1.38 m (26H, H^4–H^{15}, H^{17}), 1.56–1.63 m (2H, H^3), 2.40–2.44 m (2H, H^2), 9.74 t (1H, HC=O, *J* 1.6 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 14.35 (C^{18}), 22.05 (C^3), 22.52 (C^{17}), 28.86 (C^4), 29.08 (C^5), 29.38 (C^{15}), 29.52 (C^7–C^{11}, C^{13}), 29.56 (C^{14}), 29.37 (C^{15}), 32.06 (C^{16}), 43.71 (C^2), 202.60 (C^1).

The reduction of methyl (9*Z*,12*R*)-12-hydroxyoctadec-9-enoate (**33**) gave 1.89 g (87%) of aldehyde **26**.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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