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Synthesis of the Deuterated Sex Pheromone Components of the Grape Borer, *Xylotrechus pyrrhoderus*

Ryutaro KIYOTA,[1] Rei YAMAKAWA,[1] Kikuo IWABUCHI,[2] Keita HOSHINO,[2] and Tetsu ANDO[1,†]

[1]*Graduate School of Bio-Applications and Systems Engineering, Tokyo University of Agriculture and Technology, Koganei, Tokyo 184-8588, Japan*
[2]*Department of Applied Biological Science, Faculty of Agriculture, Tokyo University of Agriculture and Technology, Fuchu, Tokyo 183-8509, Japan*

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Adult males of the grape borer, *Xylotrechus pyrrhoderus*, secrete (*S*)-2-hydroxy-3-octanone [(*S*)-1] and (2*S*,3*S*)-2,3-octanediol [(2*S*,3*S*)-2] from their nota of prothoraces as sex pheromone components. Their structural similarity suggests that one of them is the biosynthetic precursor of the other component. In order to confirm the biochemical conversion, deuterated derivatives of both components were synthesized by starting from a Wittig reaction between hexanal and an ylide derived from D_5-iodoethane and ending with enantiomeric resolution by chiral HPLC. The molecular ions of 1 and 2 could scarcely be detected by using a GC-MS analysis, and the labeled compounds showed similar mass spectra to the unlabeled pheromone components. However, several fragment ions, including four deuterium atoms, were observed in the mass spectra of their acetate derivatives, indicating that the conversion could be confirmed by examining a compound with the diagnostic ions after acetylation of the volatiles collected from insects treated with the labeled precursors.

Key words: sex pheromone; Cerambycidae; deuterated precursor; pheromone biosynthesis; long-horned beetle

The grape borer, *Xylotrechus pyrrhoderus* Bates (Coleoptera: Cerambycidae), is a harmful pest of grapevines in Japan. The mating behavior of this long-horned beetle is mediated by sex pheromones secreted by both the male and female adults.[1)] During the first phase, the female is attracted over a long range by the male pheromone which is composed of (*S*)-2-hydroxy-3-octanone [(*S*)-**1**] and (2*S*,3*S*)-2,3-octanediol [(2*S*,3*S*)-**2**] (Fig. 1).[2)] It has been reported that these compounds are secreted from glands on the prothorax surface, although their biosynthetic pathways are still unknown. The structural similarity of **1** and **2** suggests that one of them is the biosynthetic precursor of the other component. In order to confirm the biosynthetic conversion, deuterated derivatives of both components were synthesized by using deuterated iodoethane.

Results and Discussion

Before preparing deuterated pheromone components, [1,1,1,2]-D_4-(*S*)-**1** and [1,1,1,2]-D_4-(2*S*,3*S*)-**2**, each synthetic step in Scheme 1 was examined by using unlabeled iodoethane. Namely, a Wittig reaction between hexanal and an ylide derived from iodoethane produced (*Z*)-2-octene (**3**) which included about 30% of the undesired (*E*)-isomer. To prevent the volatile products from being lost, the mixture was treated with MCPBA without any purification, and *cis*-2,3-epoxyoctane (**4**) contaminated with the *trans*-isomer was obtained. The epoxides were transformed to a 3:1:3:1 mixture of *threo*-2-acetoxy-3-octanol (**5**), its *erythro*-isomer, *threo*-3-acetoxy-2-octanol (**6**), and its *erythro*-isomer by heating in acetic acid. While separation of the *threo*- and *erythro*-isomers was not accomplished, the positional isomers were separable by MPLC with a Lobar column. The former two 3-octanols, which eluted faster than the latter two 2-octanols, were oxidized to 2-acetoxy-3-octanone (**7**) by PCC after MPLC separation. The acetate was hydrolyzed by K_2CO_3 to yield racemic 2-hydroxy-3-octanone (**1**). On the other hand, the acetoxy groups of **6** and the *erythro*-isomer were methanolysed to yield a 3:1 mixture of *threo*-2,3-octanediol (**2**) and its *erythro*-isomer, which were separable by HPLC with a silica gel column functionalized with the 3-(4-nitrophenyl)propyl group (an NO_2 column). The *threo*-diol (**2**), which eluted faster than the minor *erythro*-isomer, was isolated by HPLC. Unlabeled **1** and **2** showed identical spectroscopic data with those of previous publications.[2,3)]

Resolution of the stereoisomers of **1**, **2**, and their related compounds was examined by chiral HPLC conducted under normal-phase conditions with a Chiralpak AS-H or AD-H column and under reversed-phase condition with a Chiralcel OJ-R column (Table 1). While no enatiomeric separation was achieved by the OJ-R column, the AS-H column accomplished resolution of **1** and **2**, and the AD-H column, that of **1** and the *erythro*-isomer of **2**. Dextrorotatory (*S*)-**1** was eluted faster than levorotatory (*R*)-**1** from both normal-phase chiral columns, and levorotatory (2*S*,3*S*)-**2** eluted faster than dextrorotatory (2*R*,3*R*)-**2**.

By applying this established method, [1,1,1,2]-D_4-(*S*)-**1** and [1,1,1,2]-D_4-(2*S*,3*S*)-**2** were synthesized by starting from D_5-iodoethane (Scheme 1). In addition to the final products, the structures of the synthetic intermediates, including four D atoms, were confirmed by NMR. The ^{1}H signals of a methyl at the 1-position and methine

† To whom correspondence should be addressed. Tel/Fax: +81-42-388-7278; E-mail: antetsu@cc.tuat.ac.jp

at the 2-position disappeared in each spectrum, and the ^{13}C signals at the 1- and 2-positions were also undetected in the spectra measured with a usual scanning number. These signals are indicated with asterisks in the data given in the Experimental section. Several synthetic methods have been published for (*S*)-**1**,[2–5] but they do not seem to be adaptable for labeling with deuterium. Our strategy to resolve the racemic mixture by chiral HPLC was simple, and both stereoisomers could be easily obtained with a high enantiomeric excess. Although the unselective ring opening of epoxide **4** produced two acetoxy alcohols (**5** and **6**), they could be used for the syntheses of **1** and **2** after MPLC separation.

On the other hand, a GC-MS analysis showed that all D_4-compounds flowed out slightly faster than the corresponding unlabeled compounds (see the Experimental section). In the deuterated compounds with an acetoxy group, **5**–**7**, $[M\text{-}60]^+$ ions were detected at m/z positions 4 mass units larger than those of the corresponding unlabeled compounds. However, the mass spectra of D_4-**1** and D_4-**2** were almost the same as those of the unlabeled compounds, as shown in Fig. 2A–D, indicating that fragment ions had mainly been produced from the part including no D atoms. The M^+ ions of **1** and **2** could scarcely be detected by using the analysis in the EI mode, and it was difficult to clearly observe the biochemical conversion of the labeled precursors at the pheromone gland, including the endogenous natural pheromone components. This problem was overcome by comparing the mass spectra of the

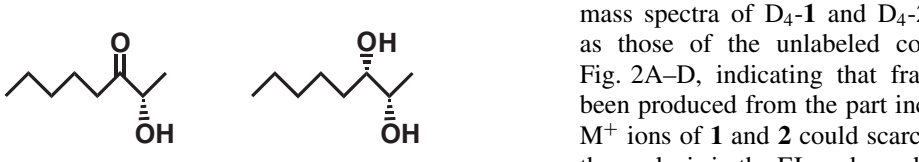
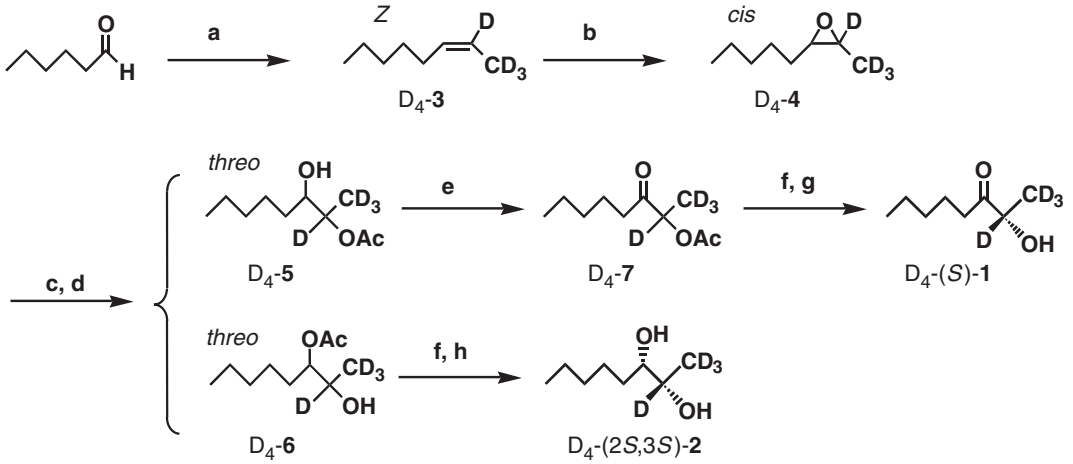


Fig. 1. Male Sex Pheromone Components of the Grape Borer, (*S*)-2-Hydroxy-3-octanone [(*S*)-**1**] and (2*S*,3*S*)-2,3-Octanediol [(2*S*,3*S*)-**2**].



Scheme 1. Synthetic Routes for Deuterated Derivatives of the Pheromone Components of the Grape Borer, D_4-(*S*)-**1** and D_4-(2*S*,3*S*)-**2**.
a, $CD_3CD{=}PPh_3$/THF; b, 3-chloroperbenzoic acid (MCPBA)/CH_2Cl_2; c, AcOH; d, MPLC; e, pyridinium chlorochromate (PCC)/CH_2Cl_2; f, K_2CO_3/MeOH; g, chiral HPLC; h, 1) achiral HPLC, 2) chiral HPLC

Table 1. Enantiomeric Separation of 2-Hydroxy-3-octanone (**1**), 3-Hydroxy-2-octanone, *threo*-2,3-Octanediol (**2**), and the *erythro*-Isomer in Chiral HPLC Columns [a]

Compound		Normal-phase				Reversed-phase Chiralcel OJ-R[d] t_R (min)
		Chiralpak AS-H[b]		Chiralpak AD-H[c]		
		t_R (min)	Separation factor (α)	t_R (min)	Separation factor (α)	
2-Hydroxy-3-octanone (**1**)						
	(+)-(*S*)-Isomer	19.88	1.07	18.79	1.33	16.67
	(−)-(*R*)-Isomer	20.79		22.46		∼[e]
3-Hydroxy-2-octanone[f]						
	(−)-Isomer	22.00	1.16	18.50	1.08	16.46
	(+)-Isomer	24.50		19.33		∼[e]
2,3-Octanediol						
threo (**2**)	(−)-(*S*,*S*)-Isomer	16.75	1.12	25.21	1.00	19.17
	(+)-(*R*,*R*)-Isomer	18.08		∼[e]		∼[e]
erythro	(−)-Isomer	19.04	1.00	26.63	1.04	15.96
	(+)-Isomer	∼[e]		27.46		∼[e]

[a]Each deuterated derivative showed almost the same chromatographic behavior as that of the corresponding unlabeled compound.
[b]Eluent: 2% and 5% 2-propanol in hexane for ketols and diols, respectively. Flow rate: 0.50 ml/min.
[c]Eluent: 2% and 4% 2-propanol in hexane for ketols and diols, respectively. Flow rate: 0.50 ml/min.
[d]Eluent: 20% and 10% CH_3CN in water for ketols and diols, respectively. Flow rate: 0.50 ml/min.
[e]The racemic compound showed one peak.
[f]The racemic compound was synthesized from a mixture of **6** and the *erythro*-isomer.

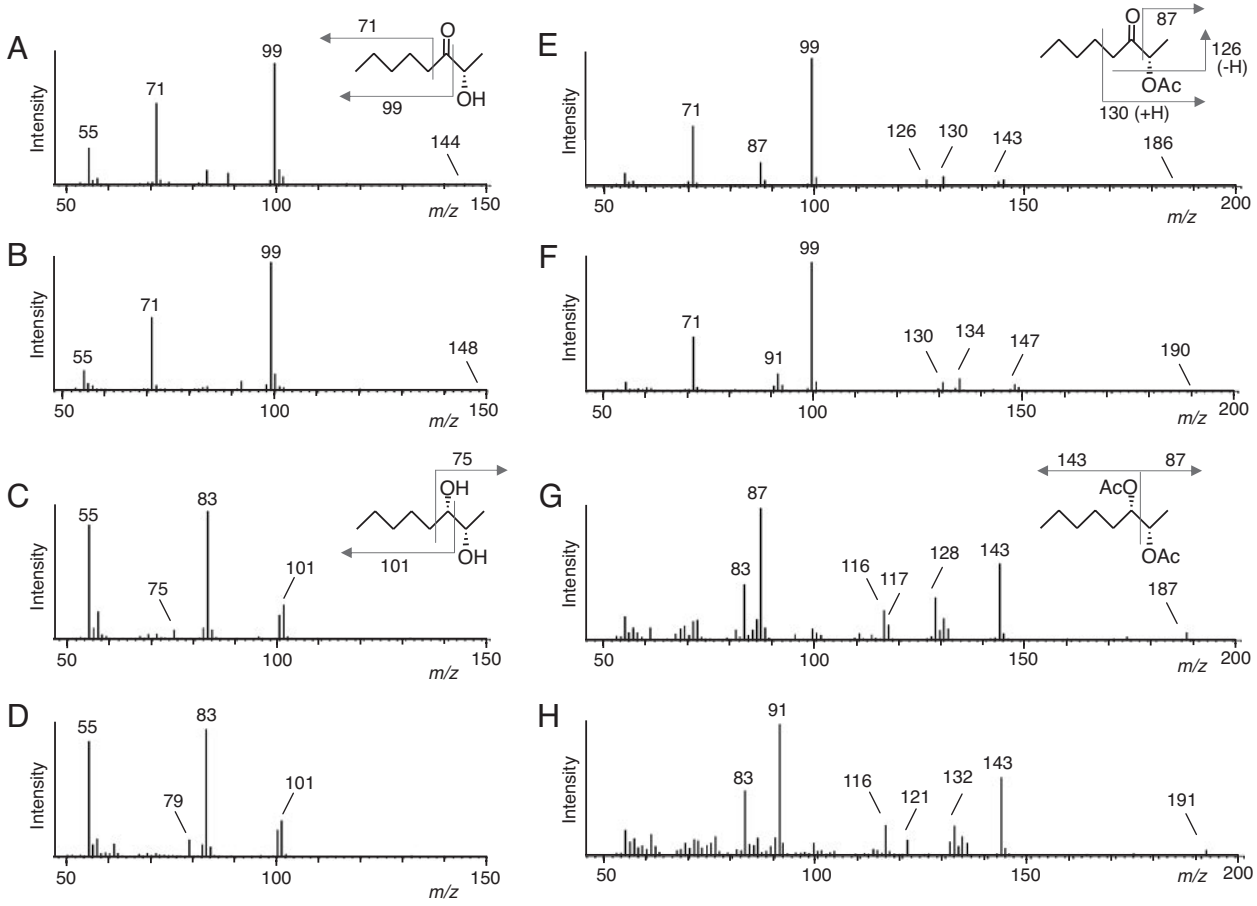


Fig. 2. Mass Spectra of Unlabeled and Labeled Pheromone Components of the Grape Borer and Their Acetate Derivatives.
A, 2-hydroxy-3-octanone (**1**); B, [1,1,1,2]-D_4-**1**; C, *threo*-2,3-octanediol (**2**); D, [1,1,1,2]-D_4-**2**; E, acetate of **1** (= **7**); F, acetate of [1,1,1,2]-D_4-**1** (= D_4-**7**); G, diacetate of **2**; H, diacetate of [1,1,1,2]-D_4-**2**

labeled and unlabeled pheromone components after acetylation. Fragment ions at m/z 130 and 87 in the acetate of **1** (= **7**) were shifted to m/z 134 and 91 in the acetate of D_4-**1** (= D_4-**7**), respectively, and ions at m/z 187, 128, and 87 in the diacetate of **2** were shifted to m/z 191, 132, and 91 in the diacetate of D_4-**2**, respectively (Fig. 2E–H). Since **1** was easily isomerized to 3-hydroxy-2-ketone by heat, it is known that differentiation between naturally occurring components and by-products by GC-MS is difficult.[2,5,6] Fortunately, no isomerization of **7** was apparent with the GC-MS analysis.

The adults of *X. pyrrhoderus* appear once a year, and preliminary experiments with D_4-(*S*)-**1** and D_4-(2*S*,3*S*)-**2** were carried out in the summer of 2008. Each compound was topically applied to the prothoraces of adult males, and the collected volatiles were analyzed by GC-MS with reference to the foregoing diagnostic ions after acetylation. While no conversion of the diol into the ketol could be detected, the ketol was reproducibly converted into the diol, indicating biosynthesis of (2*S*,3*S*)-**2** *via* (*S*)-**1**. When the male was treated with 10 µg of D_4-(*S*)-**1**, the exogenous deuterated diol represented about 10% of the diol recovered as a volatile. In the summer of 2009, we will examine this biochemical conversion again in detail, also using their antipodes and some other related compounds in order to examined the substrate specificity of the enzyme that is expected to occur in the pheromone gland. These results will be reported elsewhere. In addition to the C_8 compounds, C_6 and C_{10} homologous pheromones have been identified from some long-horned beetles in *Xylotrechus* and other genera.[6–8] Their biosynthetic pathways, however, have never been investigated.[9] Elucidation of the steps for the construction of the 2-hydroxy-3-one structure that is universally present in the pheromones of long-horned beetles is an interesting future subject for a better understanding of the mating communication systems of these beetles.

Experimental

Spectroscopy and chromatography. ^{1}H- and ^{13}C-NMR spectra were recorded by a Delta 2 Fourier transform spectrometer (Jeol, Tokyo, Japan) at 399.8 and 100.5 MHz, respectively, for $CDCl_3$ solutions containing TMS as an internal standard. GC-MS was conducted in the EI mode (70 eV) with an HP5973 mass spectrometer (Hewlett-Packard) equipped with a split/splitless injector and a DB-23 column (0.25 mm ID × 30 m, 0.25 µm film; J & W Scientific, Folsom, CA, USA). The column temperature program was 50 °C for 2 min, 4 °C/min to 150 °C, 10 °C/min to 220 °C, and 220 °C for 10 min. The carrier gas was He. A high-resolution MS (HR-MS) analysis was performed with a JMS-MS700V mass spectrometer (Jeol). IR spectra were recorded as a thin film (neat liquid) with a FT/IR-350 (Jasco, Tokyo, Japan). The specific rotation of each $CHCl_3$ solution was measured with a Jasco DIP-4 polarimeter. All LC analyses employed the same system composed of a pump (PU-980, Jasco), an RI detector (RI-98SCOPE, Labo System, Tokyo, Japan), and an integrator (807-IT, Jasco). MPLC separation of 2-acetoxy-3-octanol from 3-acetoxy-2-octanol was accomplished with a Lobar column (Merck Lichroprep Si 60, 10 mm ID × 24 cm, 40–63 µm) which was eluted with 20% THF in hexane at a flow rate of 2.0 ml/min. Separation of *threo*-octanediol from the *erythro*-isomer used achiral HPLC equipped with a functionalized

silica column (Senshu-pak NO_2-3151-N, 8 mm ID × 15 cm) which was eluted with 30% EtOAc in hexane at a flow rate of 1.0 ml/min. Resolution of the enantiomers by chiral HPLC was examined with the following three columns (see Table 1 for the eluent and flow rate): Chiralpak AD-H (4.6 mm ID × 25 cm; Daicel Chemical Industry, Osaka, Japan), Chiralpak AS-H (4.6 mm ID × 25 cm; Daicel Chemical Industry), and Chiralcel OJ-R (4.6 mm ID × 15 cm; Daicel Chemical Industry).

cis-*2,3-Epoxyoctane (**4**).* A mixture of iodoethane (2.03 g, 13 mmol), triphenylphosphine (3.93 g, 15 mmol), and benzene (30 ml) was heated overnight at 100 °C while refluxing and stirring. The crystals formed were collected by filtration and dried in vacuum to give a phosphonium salt (4.77 g, 80%). To a suspension of this salt (2.09 g, 5 mmol) in dry THF (15 ml) in a three-necked flask cooled in an ice bath, butyllithium (1.6 M solution in hexane, 3.1 ml, 5 mmol) was added dropwise under N_2 to form an ylide. After 30 min, hexanal (0.50 g, 5.5 mmol) dissolved in dry THF (0.5 ml) was added to the ylide solution. The reaction mixture was stirred for 1 h at room temperature (rt) and poured into water, and the produced 2-octene [a mixture of **3** and its (*E*)-isomer] was extracted with pentane (3 × 15 ml). After most of the solvent had carefully been removed by evaporation, the concentrated products were successively mixed with CH_2Cl_2 (20 ml) and MCPBA (77%, 0.67 g, 3.0 mmol) while stirring in an ice bath. The mixture was stirred at 0 °C for 1 h and at rt for 2 h, poured into water, and extracted with pentane. Column chromatography with silica gel (1 g, eluent of pentane) gave 2,3-epoxyoctane, a mixture of *cis*-2,3-epoxyoctane (**4**) and its *trans*-isomer in an approximate 3:1 ratio (0.29 g, 45% from the phosphonium salt). Starting from D_5-iodoethane (99.5 atom% D, Aldrich), a mixture of [1,1,1,2]-D_4-**4** and its *trans*-isomer (0.26 g, 39%) was synthesized in the similar manner and yield. **4**: ^{1}H-NMR δ: 0.91 (3H, t, J = 7 Hz), 1.26* (3H, d, J = 5.5 Hz), 1.3–1.55 (8H, m), 2.89 [1H, dt J = 4.5, 6 Hz (t, J = 6 Hz in D_4-**4**)], 3.04* (1H, dq, J = 4.5, 5.5 Hz); ^{13}C-NMR δ: 13.2*, 14.0, 22.6, 26.2, 27.5, 31.72, 52.7*, 57.2; GC-MS m/z (relative intensity): t_R 6.95 min, 113 (4%, $[M-15]^+$), 85 (36%), 56 (100%) [D_4-**4**: t_R 6.88 min, 114 (3%, $[M-18]^+$), 89 (32%), 56 (100%)]. *trans*-Isomer of **4**: ^{1}H-NMR δ: 0.90 (3H, t, J = 7 Hz), 1.29* (3H, d, J = 5 Hz), 1.3–1.55 (8H, m), 2.62 [1H, td, J = 5.5, 2 Hz (t, J = 5.5 Hz in D_4-compound)], 2.74* (1H, dq, J = 2, 5 Hz); ^{13}C-NMR δ: 14.0, 17.7*, 22.6, 25.7, 31.68, 32.0, 54.7*, 59.9; GC-MS m/z: t_R 6.09 min, 113 (4%, $[M-15]^+$), 85 (36%), 56 (100%) [D_4-compound: t_R 6.01 min, 114 (4%, $[M-18]^+$), 89 (30%), 56 (100%)]. The NMR signals indicated with an asterisk were not detected in the corresponding deuterated compound.

threo-*2-Acetoxy-3-octanol (**5**) and* threo-*3-acetoxy-2-octanol (**6**).* *cis*-Epoxide **4** mixed with the *trans*-isomer (200 mg) was dissolved in AcOH (1.0 ml). After stirring at 55 °C for 6 h, the mixture was poured into water and extracted with Et_2O. While the exact mixing ratio of produced alcohols could not be obtained with a GC-MS analysis because of thermal isomerization, an NMR analysis indicated that the crude product included **5**, the *erythro*-isomer of **5**, **6**, and the *erythro*-isomer of **6** in a ratio of 3:1:3:1. The former two 3-octanols and the latter two 2-octanols showed a signal split to a double quartet at δ ~4.8 ppm and ~3.8 ppm, respectively. Two adjacent spots were detected by TLC of the mixture (benzene/EtOAc 5:1, Rf 0.32 and 0.24), and the 3-octanols (74 mg, 37%, t_R 20.3 min) were completely separated from the 2-octanols (67 mg, 34%, t_R 30.3 min) by MPLC. From the deuterated epoxides, a mixture of the corresponding deuterated alcohols was obtained in a similar manner and yield. **5**: ^{1}H-NMR δ: 0.89 (3H, t, J = 7 Hz), 1.24* (3H, d, J = 6.5 Hz), 1.25–1.5 (8H, m), 2.08 (3H, s), 3.53 [1H, m, (dd, J = 7.5, 4 Hz, in D_4-**5**)], 4.83* (1H, dq, J = 5, 6.5 Hz); ^{13}C-NMR δ: 14.0, 16.4*, 21.26, 22.6, 25.2, 31.8, 33.1, 73.6*, 73.8, 170.8; IR ν_{max} cm^{-1}: 3451, 2933, 2860, 1736, 1373, 1244, 1053; GC-MS m/z: t_R 23.17 min, 128 (3%, $[M-60]^+$), 61 (100%) [D_4-**5**: t_R 23.08 min, 132 (3%, $[M-60]^+$), 61 (100%)]. *erythro*-Isomer of **5**: ^{1}H-NMR δ: 0.89 (3H, t, J = 7 Hz), 1.21* (3H, d, J = 6.5 Hz), 1.25–1.5 (8H, m), 2.07 (3H, s), 3.69 [1H, m (dd, J = 6, 6 Hz, in D_4-compound)], 4.88* (1H, dq, J = 3, 6.5 Hz); ^{13}C-NMR δ: 13.6*, 14.0, 21.34, 22.6, 25.5, 31.8, 32.3, 73.3*, 73.9, 170.6; GC-MS m/z: t_R 23.34 min, 128 (3%, $[M-60]^+$), 61 (100%) [D_4-compound: t_R 23.24 min, 132 (3%, $[M-60]^+$), 61 (100%)]. **6**: ^{1}H-NMR δ: 0.88 (3H, t, J = 7 Hz), 1.17* (3H, d, J = 6.5 Hz), 1.25–1.5 (8H, m), 2.10 (3H, s), 3.80* (1H, dq, J = 5, 6.5 Hz), 4.77 [1H, ddd, J = 7.5, 5, 5 Hz (dd, J = 7.5, 5 Hz in D_4-**6**)]; ^{13}C-NMR δ: 14.0, 19.5*, 21.10, 22.5, 25.0, 30.4, 31.70, 68.6*, 77.9, 171.2; IR ν_{max} cm^{-1}: 3456, 2931, 2862, 1738, 1373, 1244, 1026, GC-MS m/z: t_R 23.27 min, 128 (1%, $[M-60]^+$), 88 (100%) [D_4-**6**: t_R 23.17 min, 132 (1%, $[M-60]^+$), 92 (100%)]. *erythro*-Isomer of **6**: ^{1}H-NMR δ: 0.88 (3H, t, J = 7 Hz), 1.16* (3H, d, J = 6.5 Hz), 1.25–1.5 (8H, m), 2.10 (3H, s), 3.88* (1H, dq, J = 3, 6.5 Hz), 4.87 [1H, m (dd, J = 9, 4.5 Hz in D_4-compound)]; ^{13}C-NMR δ: 14.0, 17.7*, 21.15, 22.5, 25.3, 29.3, 31.66, 69.2*, 78.1, 171.5; GC-MS m/z: t_R 23.50 min, 128 (1%, $[M-60]^+$), 88 (100%) [D_4-compound: t_R 23.40 min, 132 (1%, $[M-60]^+$), 92 (100%)].

*2-Acetoxy-3-octanone (**7**).* PCC (100 mg) was added by bits to a stirred CH_2Cl_2 solution (40 ml) of *threo*-2-acetoxy-3-octanol (**5**) mixed with the *erythro*-isomer (74 mg, 0.39 mmol) at rt. After stirring for 4 h, the reaction mixture was poured into hexane (100 ml), and the dark precipitate was removed by filtration. The solvent was evaporated, and residual materials were purified by column chromatography with silica gel (5 g, eluent of benzene/EtOAc 10:0 to 8:2) to give **7** (56 mg, 0.30 mmol, 77%). In a similar manner and yield, D_4-**7** was synthesized. ^{1}H-NMR δ: 0.89 (3H, t, J = 7 Hz), ~1.3 (4H, m), 1.39* (3H, d, J = 7 Hz), 1.59 (2H, ddt, J = 7.5, 7.5, 7.5 Hz), 2.14 (3H, s), 2.41 (1H, dt, J = 17.5, 7.5 Hz), 2.52 (1H, dt, J = 17.5, 7.5 Hz), 5.09* (1H, q, J = 7Hz); ^{13}C-NMR δ: 13.9, 16.2*, 20.8, 22.5, 22.9, 31.3, 38.2, 74.6*, 170.4, 207.9; IR ν_{max} cm^{-1}: 2935, 2873, 1745, 1730, 1373, 1236, 1047; GC-MS m/z: t_R 20.31 min, 186 (0.5%, M^+), 126 (6%, $[M-60]^+$), 99 (100%) [D_4-**7**: t_R 20.23 min, 130 (7%, $[M-60]^+$), 99 (100%)]. HR-MS m/z ($[M-43]^+$) of **7**: calcd. for $C_8H_{15}O_2$, 143.1072; found, 143.1049. HR-MS m/z ($[M-43]^+$) of D_4-**7**: calcd. for $C_8H_{11}D_4O_2$, 147.1319; found, 147.1342.

*2-Hydroxy-3-octanone (**1**).* A mixture of **7** (56 mg), K_2CO_3 (10 mg), and MeOH (3 ml) was stirred at rt for 2 h. After the reaction mixture had been poured into water (10 ml), the product was extracted with hexane and purified by column chromatography with silica gel (3 g, eluent of benzene/EtOAc 10:0 to 7:3) to give **1** (37 mg, 0.27 mmol, 90%). In a similar manner and yield, D_4-**1** was synthesized. ^{1}H-NMR δ: 0.90 (3H, t, J = 7 Hz), ~1.3 (4H, m), 1.38* (3H, d, J = 7 Hz), 1.63 (2H, ddt, J = 7.5, 7.5, 7.5 Hz), 2.43 (1H, dt, J = 17, 7.5 Hz), 2.52 (1H, dt, J = 17, 7.5 Hz), 4.24* (1H, q, J = 7Hz); ^{13}C-NMR δ: 14.0, 19.9*, 22.4, 23.3, 31.4, 37.5, 72.6*, 212.8; IR ν_{max} cm^{-1}: 3454, 2931, 2871, 1714, 1373, 1122, 1053; GC-MS m/z: t_R 16.86 min, 144 (0.5%, M^+), 99 (100%) [D_4-**1**: t_R 16.77 min, 148 (0.5%, M^+), 99 (100%)]. With a GC-MS analysis, thermally isomerized products, 3-hydroxy-2-octanone [t_R 16.98 min, 144 (0.2%, M^+), 101 (24%), 83 (63%), 55 (100%)] derived from **1** and D_4-3-hydroxy-2-octanone [t_R 16.88 min, 147 (0.1%, M^+), 101 (30%), 83 (70%), 55 (100%)] derived from D_4-**1**, were detected.[2,5,6] The resolution of these racemic mixtures by chiral HPLC equipped with an AD-H column gave (*S*)-**1**, D_4-(*S*)-**1**, and their enantiomers. $[\alpha]_D^{23}$: (*S*)-**1**, 65.8° (c = 0.75, $CHCl_3$); (*R*)-**1**, −68.0° (c = 0.74, $CHCl_3$); D_4-(*S*)-**1**, 57.5° (c = 0.63, $CHCl_3$); D_4-(*R*)-**1**, −57.6° (c = 0.58, $CHCl_3$).

threo-*2,3-Octanediol (**2**).* A mixture of *threo*-3-acetoxy-2-octanol (**6**) associated with the *erythro*-isomer (67 mg, 0.36 mmol), K_2CO_3 (10 mg), and MeOH (3 ml) was stirred at rt for 2 h. After the reaction mixture had been poured into water (10 ml), the product was extracted with Et_2O and purified by column chromatography with silica gel (3 g, eluent of benzene/EtOAc 10:0 to 4:6) to give a *threo*-diol (**2**) associated with the *erythro*-isomer (44 mg, 0.30 mmol, 83%). Achiral HPLC separation gave **2** (t_R 18.58 min, 28 mg) and the *erythro*-isomer (t_R 22.00 min, 9 mg). In a similar manner and yield, D_4-**2** was synthesized. **2**: ^{1}H-NMR δ: 0.90 (3H, t, J = 7 Hz), 1.17* (3H, d, J = 6.5 Hz), 1.25–1.5 (8H, m), 3.31* (1H, m), 3.57 (1H, m); ^{13}C-NMR δ: 14.1, 19.5*, 22.6, 25.3, 31.9, 33.3, 70.9*, 76.3; IR ν_{max} cm^{-1}: 3388, 2931, 2860, 1460, 1379, 1065; GC-MS m/z: t_R 21.79 min, 101 (22%, $[M-45]^+$), 83 (93%), 55 (100%) [D_4-**2**: t_R 21.72 min, 101 (30%, $[M-49]^+$), 83 (100%), 55 (92%)]. *erythro*-Isomer of **2**: ^{1}H-NMR δ: 0.90 (3H, t, J = 7 Hz), 1.13* (3H, d, J = 6.5 Hz), 1.25–1.4 (7H, m), 1.51 (1H, m), 3.57* (1H, m), 3.77 (1H, m); ^{13}C-NMR δ: 14.1, 16.5*, 22.6, 25.8, 31.8, 31.9, 70.5*, 75.0; GC-MS m/z: t_R 22.63 min, 101 (24%, $[M-45]^+$), 83 (90%), 55 (100%) [D_4-compound: t_R 22.57 min, 101 (30%, $[M-49]^+$), 83 (100%), 55 (92%)]. HR-MS m/z ($[M-43]^+$) of diacetate

of **2**: calcd. for $C_{10}H_{19}O_3$, 187.1334; found, 187.1338. HR-MS m/z ($[M\text{-}43]^+$) of diacetate of D_4-**2**: calcd. for $C_{10}H_{15}D_4O_3$, 191.1581; found, 191.1513. The resolution of racemic **2** and D_4-**2** by chiral HPLC equipped with an AS-H column gave (2*S*,3*S*)-**2**, D_4-(2*S*,3*S*)-**2**, and their enantiomers. $[\alpha]_D^{23}$: (2*S*,3*S*)-**2**, -18.0° (c = 0.31, $CHCl_3$); (2*R*,3*R*)-**2**, 18.7° (c = 0.32, $CHCl_3$); D_4-(2*S*,3*S*)-**2**, -32.4° (c = 0.28, $CHCl_3$); D_4-(2*R*,3*R*)-**2**, 25.7° (c = 0.20, $CHCl_3$).

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