Original Article

Synthesis of Both Enantiomers of Altholactone, Isoaltholactone and 5-Hydroxygoniothalamin from Tri-*O*-acetyl-D-glucal, and Their Biological Activities¹

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Both enantiomers of altholactone, isoaltholactone and 5-hydroxygoniothalamin were synthesized from tri-*O*-acetyl-D-glucal, and biological activities of altholactones were examined. For brine shrimp, the configuration of 3-hydroxy group at convex site was important for lethal activity, while (2*S*,3*S*)-configuration was inhibitory to lettuce germination.

Key words: altholactone, isoaltholactone, 5-hydroxygoniothalamin, total synthesis, tri-*O*-acetyl-D-glucal.

INTRODUCTION

In the preceding paper,¹⁾ we described the synthesis of (–)-*ent*-altholactone [(–)-**1**], (–)-*ent*-isoaltholactone [(–)-**2**], and their *trans*-fused diastereomers from 2, 3-*O*-cyclohexylidene-D-glyceraldehyde. However, the total yield of each compound was not satisfactory. To improve the synthesis and to compare their biological activities with natural enantiomers, we reinvestigated the synthesis of **1** and **2**. Recently, we reported the improved method of phenolic Ferrier rearrangement reaction to prepare aryl *O*- Δ^2 -glycosides,^{2,3)} so we adopted this method to synthesize altholactones through a biomimetic route postulated by Sam *et al.*⁴⁾ via 5-hydroxygoniothalamin (**3**), which was isolated from the stem bark of *Goniothalamus dolichocarpus*.⁵⁾ In this paper, we report the synthesis of these compounds.

MATERIALS AND METHODS

1. General

Mp values are uncorrected. Optical rotation (in CHCl₃, unless otherwise noted); Jasco DIP-4. IR spectra; Jasco IR-810. ¹H NMR; Jeol JNM GSX-270 ($\delta_{\text{TMS}}^{\text{CDCl}_3}$ ppm), *J* values are given in Hertz (Hz). Mass spectra (FAB); JEOL DX-303HF. CC; SiO₂.

2. Synthesis of Compounds

2.1 (2*R*,5*S*,6*R*)-6-(Benzoyloxy)methyl-5,6-dihydro-2-(4'-methoxyphenoxy)-2*H*-pyran-5-ol. (**6**)

In the same manner as described in lit.,¹⁾ **5**⁶⁾ (9.00 g, 35.7 mmol) was converted to **6** (11.7 g, 32.8 mmol, 92%) as colorless needles, mp 97°C, $[\alpha]_{\text{D}}^{20} +61.4^\circ$ (*c*=0.360), IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{–1}: 3480 (O–H), 1690 (C=O), 1490, ¹H NMR δ : 2.42 (1H, br. s, OH), 3.74 (3H, s, Me), 4.13 (1H, ddd, *J*=3.0, 5.2, 9.3, 6-H), 4.19 (1H, dddd, *J*=1.5, 2.7, 6.6, 9.3, 5-H), 4.53 (1H, dd, *J*=2.0, 12.0, CHHO), 4.71 (1H, dd, *J*=5.2, 12.0, CHHO), 5.58 (1H, d, *J*=2.2, 2-H), 5.94 (1H, ddd, *J*=2.2, 2.7, 10.3, 4-H), 6.11 (1H, pseudo d, *J*=10.3, 3-H), 6.7–8.0 (9H, m, Ar). Found: C, 67.23; H, 5.59, Calcd. for C₂₀H₂₀O₆: C, 67.40; H, 5.66%.

2.2 (2*R*,5*S*,6*R*)-6-(Benzoyloxy)methyl-5,6-dihydro-2-(4'-methoxyphenoxy)-5-(tetrahydropyran-2''-yl)oxy-2*H*-pyran. (**7**)

A solution of **6** (4.20 g, 11.7 mmol), 3,4-dihydro-2*H*-pyran (1.5 g) and PPTS (10 mg) in CH₂Cl₂ (30 ml) was stirred at 0°C for 6 hr. This was poured into aq.

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¹ This work was carried out under a proposal and supervision of the late Dr. Takeyoshi Sugiyama, who passed away on September 5, 1999 at 53 years of age. This paper is dedicated to his memory.

Abbreviations: DEAD, diethyl azodicarboxylate; PPTS, pyridinium *p*-toluenesulfonate; THP, tetrahydropyranyl; PTLC, preparative thin layer chromatography; NOBA, *m*-nitrobenzyl alcohol; Ag(DPAH)₂, silver dipicolinate; CC, column chromatography; THF, tetrahydrofuran; MP, *p*-methoxyphenyl

NaHCO₃, extracted with CH₂Cl₂, washed with brine, dried (MgSO₄) and concentrated *in vacuo*. CC (hexane/EtOAc) gave **7** (5.00 g, 11.3 mmol, 97%) as a colorless oil. IR $\nu_{\text{max}}^{\text{film}}$ cm⁻¹: 1720 (C=O), 1500. ¹H NMR δ : 1.48–1.88 [6H, m, (CH₂)₃], 3.46–3.57 (2H, m), 3.72 and 3.74 (total 3H, each s, Me), 3.75–4.02 (2H, m), 4.21–4.56 (2H, m), 4.88 (1H, dd, *J* = 3.7, 5.6), 5.59 (1H, br. s, 2-H), 5.93 and 5.99 (total 1H, each ddd, *J* = 2.0, 3.9, 10.3, 4-H), 6.19 and 6.29 (total 1H, each dd, *J* = 1.0, 10.3, 3-H), 6.7–7.1 (4H, m, Ar), 7.3–8.1 (5H, m, Ar). HRMS (PEG+NOBA) *m/z*: 463.1734; Calcd. for (C₂₅H₂₈O₇+Na)⁺, 463.1733.

2.3 (2*R*,5*S*,6*R*)-5,6-Dihydro-6-hydroxymethyl-2-(4'-methoxyphenoxy)-5-(tetrahydropyran-2''-yl)oxy-2*H*-pyran. (8)

Similarly to **5**, **7** (5.00 g, 11.3 mmol) gave **8** (3.80 g, 11.3 mmol, quant.) as a colorless oil. IR $\nu_{\text{max}}^{\text{film}}$ cm⁻¹: 3460 (O–H), 1505. ¹H NMR δ : 1.5–1.9 [6H, m, (CH₂)₃], 1.65 (0.5 H, br. s, OH), 2.58 (0.5H, dd, *J* = 6.1, 7.3, OH), 3.55 (1H, m), 3.67–4.01 (4H, m), 3.78 (3H, s, Me), 4.30 and 4.42 (total 1H, each ddd, *J* = 1.5, 4.9, 9.4, 5-H), 4.72–4.77 (1H, m), 5.56 (1H, br. s, 2-H), 5.87 and 5.91 (total 1H, each ddd, *J* = 2.2, 4.9, 10.4, 4-H), 6.14 and 6.27 (total 1H, each d, *J* = 10.4, 3-H), 6.8–7.4 (4H, m, Ar). Found: C, 63.75; H, 7.04, Calcd. for C₁₈H₂₄O₆: C, 64.27; H, 7.19%.

2.4 (2*R*,5*S*,6*R*,3*E*)-5,6-Dihydro-2-(4'-methoxyphenoxy)-6-(2''-phenylethenyl)-5-(tetrahydropyran-2'''-yl)oxy-2*H*-pyran [(5*S*,6*R*)-9]

In the same manner as described in lit.,¹⁾ **8** (3.80 g, 11.3 mmol) gave aldehyde, which was coupled with Ph₃P=CHPh to give (5*S*,6*R*)-**9** (2.9 g, 7.1 mmol, 63%) as a colorless oil. IR $\nu_{\text{max}}^{\text{film}}$ cm⁻¹: 1505. ¹H NMR δ : 1.4–1.9 [6H, m, (CH₂)₃], 3.50 (1H, m), 3.76 and 3.77 (total 3H, each s, Me), 3.90 (1H, m), 4.12 and 4.26 (total 1H, each ddd, *J* = 1.7, 3.0, 9.4, 5-H), 4.56 and 4.59 (total 1H, each dd, *J* = 6.2, 9.4, 6-H), 4.70 (0.5H, dd, *J* = 3.9, 4.4), 4.96 (0.5H, t, *J* = 3.1), 5.57 (1H, br. s, 2-H), 5.92 and 5.97 (total 1H, each ddd, *J* = 1.9, 3.1, 10.2, 4-H), 6.19 and 6.24 (total 1H, each dd, *J* = 1.5, 10.2, 3-H), 6.25 and 6.39 (total 1H, each dd, *J* = 6.2, 16.1, 1''-H), 6.70 (1H, d, *J* = 16.1, 2''-H), 6.8–7.4 (9H, m, Ar). HRMS (PEG+NOBA) *m/z*: 431.1836; Calcd. for (C₂₅H₂₈O₅+Na)⁺, 431.1834.

2.5 (5*S*,6*R*,3*E*)-5,6-Dihydro-6-(2'-phenylethenyl)-5-(tetrahydropyran-2''-yl)oxy-2*H*-pyran-2-one [(5*S*,6*R*)-10]

A solution of (5*S*,6*R*)-**9** (2.9 g, 7.1 mmol), Ag (DPAH)₂ (10.0 g, 21.8 mmol) in MeCN/H₂O (4:1, 50 ml) was stirred at 20°C for 0.5 hr. The mixture was filtered, and the filtrate was poured into aq. Na₂S₂O₃ and extracted with ether. The extract was washed with brine, dried (MgSO₄) and concentrated *in vacuo*. CC (benzene/EtOAc) gave hemiacetal (2.0 g, 6.6 mmol, 93%) as a colorless oil, IR $\nu_{\text{max}}^{\text{film}}$ cm⁻¹: 3400 (O–H). This crude hemiacetal was used in the next step without further

purification.

A suspension of the oil (1.5 g, 5.0 mmol) and activated MnO₂ (30 g) in CH₂Cl₂ (30 ml) was shaken at 20°C for 2 hr. The mixture was filtered through a Celite pad and the filtrate was concentrated *in vacuo* to give (5*S*,6*R*)-**10** (1.4 g, 4.7 mol, 94%) as a colorless oil. IR $\nu_{\text{max}}^{\text{film}}$ cm⁻¹: 1730 (C=O). ¹H NMR δ : 1.5–1.9 [6H, m, (CH₂)₃], 3.5–3.6 (1H, m, 6''-H), 3.8–3.95 (1H, m, 6''-H), 4.37 (0.5H, ddd, *J* = 1.7, 2.7, 8.0, 5-H), 4.45 (0.5H, ddd, *J* = 1.2, 3.2, 6.8, 5-H), 4.73 (0.5H, dd, *J* = 2.9, 4.2, 2''-H), 4.89 (0.5H, dd, *J* = 2.9, 2.9, 2''-H), 4.99 and 5.13 (total 1H, each ddd, *J* = 1.4, 6.7, 7.4, 6-H), 6.04 and 6.11 (total 1H, each dd, *J* = 1.5, 10.0, 3-H), 6.22 and 6.26 (total 1H, each dd, *J* = 6.7, 16.1, 1'-H), 6.78 and 6.79 (total 1H, each dd, *J* = 1.5, 16.1, 2'-H), 6.90 and 6.98 (total 1H, each dd, *J* = 3.0, 10.0, 4-H), 7.2–7.4 (5H, m, Ar).

2.6 (5*S*,6*S*)-10

A solution of (5*S*,6*R*)-**10** (1.4 g, 4.7 mmol), 1 N NaOH (4.8 ml) in 1,4-dioxane/H₂O (1:1, 20 ml) was stirred at 0°C for 0.5 hr. The mixture was acidified with dil. HCl and extracted with EtOAc. The extract was washed with brine, dried (MgSO₄) and concentrated *in vacuo*. To the residual oil and Ph₃P (1.3 g, 5.0 mmol) in THF (30 ml) was added DEAD (0.80 ml, 5.0 mmol) at –20°C under N₂ and the mixture was stirred at this temp. for 10 hr. The reaction mixture was concentrated *in vacuo* and CC (CH₂Cl₂/EtOAc) gave (5*S*,6*S*)-**10** (0.59 g, 42.0 mol, 42%) as a colorless oil. IR $\nu_{\text{max}}^{\text{film}}$ cm⁻¹: 1725 (C=O). ¹H NMR δ : 1.5–1.9 [6H, m, (CH₂)₃], 3.5 (1H, m, 6''-H), 3.8 (1H, m, 6''-H), 4.25 and 4.46 (total 1H, each dd, *J* = 3.7, 5.1, 5-H), 4.74 (0.5H, t, *J* = 3.3, 2''-H), 4.82 (0.5H, t, *J* = 2.9, 2''-H), 5.06 and 5.14 (total 1H, each ddd, *J* = 1.2, 3.7, 7.0, 6-H), 6.14 and 6.18 (total 1H, each d, *J* = 9.8, 3-H), 6.38 and 6.51 (total 1H, each dd, *J* = 7.0, 16.1, 1'-H), 6.78 (1H, dd, *J* = 1.2, 16.1, 2'-H), 7.02 (1H, dd, *J* = 5.1, 9.8, 4-H), 7.25–7.45 (5H, m, Ar).

2.7 (5*S*,6*S*,3*E*)-5,6-Dihydro-5-hydroxy-6-(2'-phenylethenyl)-2*H*-pyran-2-one [(5-hydroxygoniothalamine, (+)-3]

A suspension of (5*S*,6*S*)-**10** (0.50 g, 1.7 mmol) and Amberlyst-15 in dry MeOH (20 ml) was stirred at 20°C for 4 hr. The mixture was filtered and the filtrate was concentrated *in vacuo*. CC (hexane/ether) gave (+)-**3** (0.35 g, 1.6 mol, 89%) as colorless plates, mp 113–114°C, [α]_D²⁰ +252° (*c* = 0.50) {natural; lit.,⁵⁾ mp 98°C, [α]_D²⁰ +79° (*c* = 0.2). synthetic; lit.,⁷⁾ oil, [α]_D²¹ +62.4° (*c* = 0.12, CH₂Cl₂)}. Spectral data were identical with those reported. Found: C, 71.97; H, 5.48, Calcd. for C₁₃H₁₂O₃: C, 72.21; H, 5.55%.

2.8 (2*R*,3*R*,3*aS*,7*aS*)-3-Hydroxy-2-phenyl-2,3,3*a*,7*a*-tetrahydro-5*H*-furo[3,2*b*]pyran-5-one [(+)-altholactone, (+)-1] and its (2*S*,3*S*,3*aS*,7*aS*)-isomer [(+)-isoaltholactone, (+)-2]

To a solution of (+)-**3** (0.10 g, 0.46 mmol) and vanadyl acetylacetonate (10 mg) in dry benzene (25 ml)

was added dropwise 5 M *t*-BuOOH in toluene (0.12 ml, 0.60 mmol) under N₂ and the mixture was stirred for 1 day at 40°C. After being cooled to 20°C, the mixture was poured into aq. Na₂S₂O₃ and extracted with ether. The extract was washed with brine, dried (MgSO₄) and concentrated *in vacuo*. The crude oil was treated with Amberlyst-15 in CH₂Cl₂ (20 ml) for 2 hr. Then the mixture was filtered and the filtrate was concentrated *in vacuo*. PTLC (hexane/ether=1:2) and recrystallization (hexane/ether) gave (+)-**1** (23 mg, 0.10 mmol, 22%) as an oil and (+)-**2** (46 mg, 0.20 mmol, 44%) as colorless needles. (+)-**1**, [α]_D²⁰ +182° (*c*=0.550) (see lit.¹⁾). (+)-**2**, mp 107°C, [α]_D²⁰ +55° (*c*=0.50) (see lit.¹⁾).

2.9 (2*R*,5*S*,6*R*,3*E*)-5,6-Dihydro-2-(4'-methoxyphenoxy)-6-(2''-phenylethenyl)-2*H*-pyran-5-ol [(5*S*,6*R*)-**11**]

In the similar manner as the conversion of (5*S*,6*S*)-**10** to (+)-**3**, (5*S*,6*R*)-**9** (1.7 g, 4.1 mmol) gave (5*S*,6*R*)-**11** (0.83 g, 2.5 mmol, 63%) as colorless needles, mp 142°C, [α]_D²⁰ +130° (*c*=1.00). IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 3440 (O-H). ¹H NMR δ : 1.71 (1H, d, *J*=6.1, OH), 3.76 (3H, s, Me), 4.15 (1H, ddd, *J*=2.2, 6.1, 9.0, 5-H), 4.42 (1H, dd, *J*=6.8, 9.0, 6-H), 5.58 (1H, d, *J*=1.2, 2-H), 5.96 (1H, dd, *J*=2.2, 10.3, 4-H), 6.15 (1H, dd, *J*=1.2, 10.3, 3-H), 6.30 (1H, dd, *J*=6.8, 16.1, 1''-H), 6.75 (1H, d, *J*=16.1, 2''-H), 6.8–7.5 (9H, m, Ar). Found: C, 73.90; H, 6.22, Calcd. for C₂₀H₂₀O₄: C, 74.05; H, 6.22%.

2.10 (2*R*,5*S*,6*R*,3*E*)-5,6-Dihydro-2-(4'-methoxyphenoxy)-5-(4''-nitrobenzoyloxy)-6-(2'''-phenylethenyl)-2*H*-pyran (**12**)

To a solution of (5*S*,6*R*)-**11** (0.83 g, 2.5 mmol), Ph₃P (2.0 g, 7.6 mmol) and *p*-nitrobenzoic acid (0.43 g, 2.5 mmol) in dry THF (20 ml) was added DEAD (0.40 ml, 2.5 mmol) at 0°C under N₂. The mixture was stirred at 20°C for 3 hr and concentrated *in vacuo*. CC (CH₂Cl₂/EtOAc) and recrystallization (ether) gave **12** (1.0 g, 2.1 mol, 84%) as yellow plates, mp 138°C, [α]_D²⁰ –340° (*c*=1.00). IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 1750 (C=O), 1520, 1500. ¹H NMR δ : 3.78 (3H, s, Me), 5.10 (1H, ddd, *J*=1.5, 2.5, 5.6, 6-H), 5.42 (1H, dd, *J*=2.5, 5.4, 5-H), 5.77 (1H, d, *J*=2.9, 2-H), 6.26 (1H, dd, *J*=5.6, 16.1, 1'''-H), 6.31 (1H, dd, *J*=2.9, 10.1, 3-H), 6.40 (1H, dd, *J*=5.4, 10.1, 4-H), 6.77 (1H, dd, *J*=1.5, 16.1, 2'''-H), 6.8–8.3 (13H, m, Ar). HRMS (NOBA) *m/z*: 496.1372; Calcd. for (C₂₇H₂₃O₇+Na)⁺, 496.1372.

2.11 (5*R*,6*R*)-**11**

In the similar manner as the conversion of **5** to **6**, **12** (1.0 g, 2.1 mmol) gave (5*R*,6*R*)-**11** (0.57 g, 1.7 mmol, 81%) as colorless needles, mp 82°C, [α]_D²⁰ –73.9° (*c*=1.00).

2.12 (5*R*,6*R*)-**9**

In the similar manner as the conversion of **6** to **7**, (5*R*,6*R*)-**11** (0.57 g, 1.7 mmol) gave (5*R*,6*R*)-**9** (0.57 g, 1.4 mmol, 87%) as a colorless oil.

2.13 (5*R*,6*R*)-**10**

Similarly to (5*S*,6*R*)-**10**, (5*R*,6*R*)-**9** (0.57 g, 1.4 mmol) gave (5*R*,6*R*)-**10** (0.37 g, 1.2 mmol, 85%) as a colorless oil.

2.14 *ent*-5-Hydroxygoniothalamin [(–)-*ent*-**3**]

Similarly to (+)-**3**, (5*R*,6*R*)-**10** (0.37 g, 1.2 mmol) gave (–)-*ent*-**3** (0.22 g, 1.0 mmol, 83%) as colorless plates, mp 113–114°C, [α]_D²⁰ –250° (*c*=0.50).

2.15 *ent*-Altholactone [(–)-*ent*-**1**] and *ent*-isoaltholactone [(–)-*ent*-**2**]

Similarly to (+)-**1** and (+)-**2**, (–)-*ent*-**3** (0.10 g, 0.46 mmol) gave (–)-*ent*-**1** (21 mg, 0.090 mmol, 20%), mp 72°C, [α]_D²⁰ –190° (*c*=0.50, EtOH) [lit.⁸⁾ [α]_D –166° (*c*=0.5, EtOH); lit.⁹⁾ [α]_D²² –180.5° (*c*=0.2, EtOH)]; and (–)-*ent*-**2** (44 mg, 0.19 mmol, 41%), mp 107°C, [α]_D²⁰ –54° (*c*=0.50, EtOH) [lit.¹⁾ mp 106.5–107.5°C, [α]_D –54.4° (*c*=0.500, EtOH)]. These were separated by PTLC.

3. Bioassays

3.1 Brine shrimp test

Eggs of brine shrimp (*Artemia salina*) were incubated to hatch in 200 ml of artificial sea water at 26°C for 2 days. About twenty larvae were transferred to sample tube. To this was added a solution of each test compound in aq. Tween 80 (5%), and the total concentration was adjusted to 250 ppm. This mixture was incubated for 1.5 days at 22°C and the ratio of lethality was counted.

3.2 Lettuce germination test

This test was done according to the method reported by us.¹⁰⁾

RESULTS AND DISCUSSION

1. Synthesis

As shown in Scheme 1, tri-*O*-acetyl-D-glucal (**4**) was converted to **5**^{2,3,6)} and the primary hydroxymethyl group was selectively benzoylated to give **6**. The remaining secondary hydroxy group was protected as THP ether (**7**) and the benzoyl group was removed to afford **8**. The hydroxy group of **8** was oxidized to aldehyde and elongated with benzylidene(triphenyl)phosphorane to give **9**. The geometry of the double bond was exclusively *E*. Then the MP group was removed with Ag(DPAH)₂^{2,3)} and the formed hemiacetal was oxidized to lactone (5*S*,6*R*)-**10**. Next the 6*S*-configuration was inverted as follows: hydrolysis of the lactone ring gave hydroxy acid, which cyclized *via* intramolecular Mitsunobu reaction to afford (5*S*,6*S*)-**10**. Removal of the THP group afforded 5-hydroxygoniothalamin (**3**), which was submitted to epoxidation followed by acid treatment to give the desired natural altholactone (+)-**1** and isoaltholactone (+)-**2**. These isomers were separated by PTLC and the total yields was 4.0% and 8.0%, respectively in 7 steps.

We also synthesized the antipodes of altholactones. The key intermediate (5*S*,6*R*)-**9** was deprotected to give (5*S*,6*R*)-**11**. Inversion of 5-position was achieved by

Scheme 1 Synthesis of compounds. a) benzoyl chloride, pyridine. b) DHP, PPTS. c) K_2CO_3 , MeOH. d) i. Swern oxi. ii. $PhCH=PPh_3$. e) i. $Ag(DPAH)_2$, H_2O ii. MnO_2 . f) i. aq. NaOH. ii. DEAD, Ph_3P . g) H^+ , MeOH. h) i. vanadyl acetylacetonate, *t*-BuOOH. ii. H^+ . i) $p\text{-NO}_2C_6H_4COOH$, DEAD, PPh_3 .

Mitsunobu reaction by using *p*-nitrobenzoic acid. (–)-*Ent*-**3**, (–)-*ent*-**1** and (–)-*ent*-**2** were prepared from (5*S*, 6*S*)-**11** by the method similar to that for the natural isomers. The total yields of (–)-*ent*-**1** and (–)-*ent*-**2** were 3.0% and 6.1%, respectively.

2. Bioassays

Since (+)-altholactone was isolated by monitoring the bioactivity with brine shrimp lethality, this test was applied for the synthetic altholactones. Inhibition of lettuce germination was also investigated. The 7a-epimers with *trans*-fused ring were also tested.¹⁾ Table 1 shows the results of the brine shrimp test. Compounds (+)-7a-*epi*-1, (+)-1, (–)-*ent*-1 and (–)-7a-*epi*-2 showed strong activity, while the activity of (+)-2 and (–)-*ent*-2 was low. This could be due to the difference in the orientation of the 3-hydroxy groups. Each 3-hydroxy group of the former four active compounds was situated at the convex (sterically non-hindered) site of the

Table 1 Biological activities of the synthetic compounds.

Entry	Compounds	Death rate (brine shimp)	Germination rate (lettuce)
1	none	5%	75%
2	(+)- 1	40	50
3	(-)- <i>ent</i> - 1	31	5 ^b
4	(+)- 2	13	25 ^b
5	(-)- <i>ent</i> - 2	8	69
6	(+)-7a- <i>epi</i> - 1 ^a	48	63
7	(-)-7a- <i>epi</i> - 2 ^a	31	56 ^b

a) Synthesis of these compounds are described in lit.¹⁾

b) Elongation of the roots were strongly inhibited for the germinating seeds (<10% compared with the control length).

bicyclo[4.3.0]nonane ring. On the other hand, that of the latter was situated at the concave site and shielded by the ring. Consequently, this lethal activity was affected by the 3-hydroxy group and the configuration of other positions would not be important.

For the test of lettuce, the rates of germination were low for (–)-**ent-1** and (+)-**2**. In addition, elongation of roots of the lettuce was strongly inhibited by (–)-**7a-epi-2**. As a result, the compounds with (2*S*,3*S*)-configuration showed the inhibitory activity for lettuce germination.

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要 約

**トリ-O-アセチル-D-グルカールを出発物質とする
アルトラクトン、イソアルトラクトンおよび5-ヒド
ロキシゴニオタラーン両鏡像体の合成と生物活性**

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前報に続き, アルトラクトン, イソアルトラクトン, 5-ヒ
ドロキシゴニオタラミンの両鏡像体の合成を行った. トリ-
O-アセチル-D-グルカールから得られたアセタールに必

要な側鎖を延長後, アセタールをラクトンに導き, 立体化
学を修飾することにより, 5-ヒドロキシゴニオタラーンの
両鏡像体を得た. 更にエポキシ化・酸処理によってアルト
ラクトンとイソアルトラクトンの両鏡像体を合成した. ア
ルトラクトンの6種の異性体の生物活性を測定した結果,
殺ブラインシュリンプテストでは, 3位の水酸基がconvex
面にある(立体的に空いている)化合物の活性が強かった.
レタス発芽においては(2*S*, 3*S*)の立体を有する化合物が
発芽, 特に根の伸長に強い阻害効果を示した.