Inhibitory activity of 6-O-decyl-D-allose and 6-(decanoylamino)-6-deoxy-D-allose against plant growth

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Abstract

6-O-Decyl-D-allose (1) and 6-(decanoylamino)-6-deoxy-D-allose (2) were synthesized and evaluated the inhibitory activity on plant growth. The ether derivative 1 exhibited the activity comparable to 6-O-decanoyl-D-allose, suggesting that the carbonyl group of the acyl group is not necessary for the activity. On the other hand, the amide derivative 2 showed significantly weak inhibitory activity, implying that the oxygen atom at C-6 might be important for the activity.

Keyword: rare sugar, D-allose, inhibitory activity, plant growth

Introduction

D-Allose, a C-3 epimer of D-glucose, is one of rare sugars that has been extensively studied and found to exhibit various biological activities such as antioxidant effect, antiproliferative effect against cancer cells, and immunosuppressive effect. Recently, D-allose has attracted much attention as a lead compound for the development of novel plant growth-regulator because it significantly inhibited the growth of lettuce (Lactuca sativa), rice (Oryza sativa), and Arabidopsis thaliana. In Arabidopsis and rice, the inhibitory activity was not alleviated by co-addition of gibberellin, suggesting that D-allose could inhibit the gibberellin-signalling pathway. We recently found that an acylation at C-6 of D-allose increased its inhibitory effect on the growth of lettuce and rice. In addition, we described that the effect of length of the acyl group on rice growth-retarding activity. Furthermore, the inhibitory effect of 6-O-acyl-D-allose was reversed by co-addition of gibberellin, implying that 6-O-acyl-D-allose might inhibit gibberellin biosynthesis as the known plant growth regulators.

In this study, to examine the importance of the ester bond at C-6 of the D-allose, we synthesized two different analogs of 6-O-decanoyl-D-allose (All-C10): 6-O-decyl-D-allose (1) and 6-(decanoylamino)-6-deoxy-D-allose (2) having the ether and amide bond at C-6, respectively. Then, we evaluated their biological activities on plant growth using lettuce seedlings. They are considered to be chemically and biologically stable as compared with All-C10 having the ester bond.

Materials and Methods

General

The following spectroscopic and analytical instruments were used: Digital Polarimeter, Jasco P-1010 (Jasco, Tokyo, Japan); H and 13C, JOEL JNM-ECA 600 (Jeol, Japan, reference TMS); HPLC, JASCO PU-980 Intelligent HPLC pump with a JASCO PV-970 Intelligent UV/VIS Detector (JASCO, Tokyo, Japan); MPLC, EPCLC-AI-580S; FAB-MS, JEOL JMS-600. HPLC column was carried out on a YMC-ODS AM

Figure 1 The structures of 6-O-decanoyl-D-allose, 6-O-decyl-D-allose, and 6-(decanoylamino)-6-deoxy-D-allose.

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The synthesis of 6-O-decyl-d-allose (1) was carried out using an alcohol 3 as a starting material as shown in Scheme 1. The alcohol 3 was prepared from commercially available d-allose in five steps. Alkylaion of 3 with decyl bromide followed by deprotection of benzyl group and acetonide gave the ether derivative (1) with 65% overall yield in three steps. 

**Synthetic Procedures**

The synthesis of 6-O-decyl-d-allose (1) was carried out using an alcohol 3 as a starting material as shown in Scheme 1. The alcohol 3 was prepared from commercially available d-allose in five steps. Alkylaion of 3 with decyl bromide followed by deprotection of benzyl group and acetonide gave the ether derivative (1) with 65% overall yield in three steps. NMR (600 MHz, CD,OD) δ for β-pyranose: 0.90 (3H, t, J = 7.0 Hz), 1.30-1.40 (14H, m), 3.50-3.53 (3H, m), 3.65 (1H, dd, J = 10.8, 5.1 Hz), 3.71 (1H, dd, J = 10.8, 2.2 Hz), 3.92 (1H, ddd, J = 10.1, 5.1, 2.2 Hz), 4.04 (1H, m), 5.01 (1H, br-d, J = 3.2 Hz); for α-furanose: 5.10 (1H, d, J = 1.8 Hz); β-furanose: 5.20 (1H, d, J = 4.3 Hz); Other peaks for the β- and α-furanose had weak intensities. β-pyranose/α-pyranose/β-furanose/α-furanose = 20 : 7.3 : 2.7 : 1; 13C NMR (150MHz, CD,OD) δ for β-pyranose: 14.48, 23.39, 27.25, 30.51, 30.68, 30.76, 30.77, 30.80, 33.11, 69.28, 72.03, 72.81, 72.95, 73.54, 74.38, 95.44; for α-pyranose: 14.48, 23.79, 27.25, 30.51, 30.68, 30.76, 30.77, 30.80, 33.11, 67.73, 68.44, 69.11, 71.48, 72.83, 74.29, 95.31;  [α]D 20 +88.2° (c 0.145, EtOH) 

The synthesis of 6-(decanoylamino)-6-deoxy-d-allose (2) was also carried out using the alcohol 3 as a starting material as shown in Scheme 2. Tosylaion of 3 and azidation with sodium azide afforded the azide (6). Reduction of 6 with NaBH₄-NiCl₂ acylation with decanoyl chloride, and deprotection of benzyl group and acetonide gave the amide derivative 2 with 63% overall yield in five steps. NMR (600 MHz, CD,OD) δ for β-pyranose: 0.90 (3H, t, J = 7.0 Hz), 1.25-1.35 (12H, m), 1.60 (2H, m), 2.21 (2H, m), 3.22 (1H, dd, J = 7.9, 2.9 Hz), 3.29 (1H, dd, J = 9.3, 2.9 Hz), 3.33 (1H, dd, J = 14.1, 6.7 Hz), 3.55 (1H, dd, J = 14.1, 2.9 Hz), 3.74 (1H, ddd, J = 9.6, 6.7, 2.9 Hz), 4.04 (1H, t, J = 2.9 Hz), 4.80 (1H, d, J = 7.9 Hz); for α-pyranose: 0.90 (3H, t, J = 7.0 Hz), 1.25-1.35 (12H, m), 1.60 (2H, m), 2.21 (2H, m), 3.28 (1H, dd, J = 9.3, 2.9 Hz), 3.40 (1H, dd, J = 14.0, 6.5 Hz), 3.50 (1H, m), 3.57 (1H, dd, J = 14.0, 2.8 Hz), 3.92 (1H, ddd, J = 9.3, 6.5, 2.6 Hz), 4.06 (1H, brs), 4.99 (1H, br-d, J = 3.6 Hz); for β-furanose: 5.11 (1H, d, J = 1.6 Hz); α-furanose: 5.21 (1H, d, J = 4.2 Hz); Other peaks for the β- and α-furanose had weak intensities. β-pyranose/α-pyranose/β-furanose/α-furanose = 29 : 91 : 25 : 1; 13C NMR (150MHz, CD,OD) δ for β-pyranose: 14.49, 23.78, 27.11, 30.40, 30.52, 30.66, 33.10, 37.05, 42.00, 70.42, 72.83, 73.55, 73.64, 95.61, 167.98; for α-pyranose: 14.49, 23.78, 27.11, 30.40, 30.52, 30.66, 33.10, 37.05, 41.66, 67.06, 69.20, 69.74, 74.11, 95.28, 177.04; [α]D 20 +94° (c 0.318, MeOH) ; HR-FAB-MS m/z: 334.2242 (MH⁺, calcd. For C₁₆H₁₄NO₆ 334.2230).

**Bioassay**

6-O-Decyl-d-allose (1) and 6-(decanoylamino)-6-deoxy-d-allose (2) were dissolved in a small volume of methanol, were added to a sheet of filter paper (Toyo No.2) in a 3.5 cm

![Scheme 1. Synthesis of 6-O-decyl-d-allose (1).](image)

![Scheme 2. Synthesis of 6-(decanoylamino)-6-deoxy-d-allose (2).](image)
Petri dish and then dried. The filter paper in the Petri dish was then moistened with 0.8 mL of a 0.05% (v/v) aqueous solution of Tween 20. Ten lettuce seeds were arranged on the filter paper and grown in the dark at 25 °C. The control seedlings were treated with only a solution of Tween 20. The lengths of the hypocotyls and roots of the lettuce seedlings were measured after 48 h in the dark and the percentage of hypocotyl lengths and root lengths were calculated with reference to the length of the control group.

Results and Discussion

The biological activities of the two derivatives (1 and 2) were evaluated using lettuce seedlings (Figure 2). The ether derivative (1) showed the inhibitory activity similar to that of All-C10 in a concentration dependent manner at concentrations from 0.03 to 1 mM, and completely inhibited the root growth at 3 mM. On the other hand, the amide derivative (2) showed little inhibitory activity (60%, at even 3 mM). It is interesting that the amide derivative (2) exhibited the promoting activity on the root growth (160% at 1 mM).

The concentrations required for 50% inhibition (IC₅₀) of lettuce hypocotyl and root were listed in Table 1. The ether derivative (1) showed the plant growth-inhibitory activity comparable to All-C10 (IC₅₀ = 0.54 and 0.50 mM; hypocotyl, 0.37 and 0.47 mM; root, respectively). On the other hand, the amide derivative (2) exhibited considerably weak inhibitory activity against the growth of hypocotyl and root at even 3 mM. These results suggest that the carbonyl group of the acyl group is not necessary for the inhibitory activity and that the oxygen atom at C-6 might be important for the activity.

In summary, to clarify the role of the ester bond of All-C10, we synthesized the ether derivative 1 and the amide derivative 2, and evaluated their inhibitory activities on plant growth. The ether derivative 1 exhibited the similar activity to All-C10, suggesting that the carbonyl group of the acyl is not necessary for the activity. On the other hand, the amide derivative 2 showed considerably weak inhibitory activities, implying that the oxygen atom at C-6 might be important for the activity.

Table 1. IC₅₀ values of 6-O-decyl-D-allose (1), 6-O-(decanoylamino)-D-allose (2), and All-C10 against lettuce growth.

<table>
<thead>
<tr>
<th>compound</th>
<th>IC₅₀ (mM)</th>
<th>hypocotyl</th>
<th>root</th>
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<tbody>
<tr>
<td>All-C10</td>
<td>0.50</td>
<td>0.47</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>0.54</td>
<td>0.37</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>&gt;3</td>
<td>&gt;3</td>
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Figure 2. Biological activities of 1 and 2 on A) hypocotyl and B) root of lettuce seedlings. Values are mean ± SE from three independent experiments.

References


6-O-デシル-D-アロースおよび6-デカノイルアミノ-6-デオキシ-D-アロースの
植物生長抑制活性

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要 約

6-O-デシル-D-アロース1および6-デカノイルアミノ-6-デオキシ-D-アロース2を合成し、その植物生長抑制活性を評価した。エーテル誘導体1は6-O-デカノイル-D-アロースと同じ活性を示し、これはアシル基のカルボニル基が必要ではないことを示唆している。一方、アミド誘導体2はかなり弱い抑制活性を示し、これはC-6位の酸素原子が活性には重要であることを示唆している。