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Note

A synthesis of diastereomeric isofloridoside*

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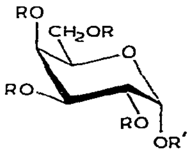
Isofloridoside (2,3-dihydroxypropyl α-D-galactopyranoside, **1a**), was first isolated from the red alga *Porphyra umbilicalis*[1]. It has since been obtained from other natural sources[2] and has been implicated as playing an active role in maintaining osmotic balance in algae[3]. As part of a comprehensive program on isolation and preparation of phytotoxic sugar derivatives[4], we had to prepare a small quantity of **1a**.

Synthesis of **1a** through benzylated glycerol intermediates in modifications of the Koenigs–Knorr reaction have been reported[5]; however, the β anomer was a major contaminant**. These methodologies also require use of appropriately protected galactosyl bromides, and removal of the protecting groups may decrease yields substantially. This problem, coupled with the formation of unwanted β anomer, indicated the need for a new approach to isofloridoside.

Initial efforts focused on the allyl glycoside (**1c**), which was prepared from D-galactose (**1b**) and allyl alcohol saturated with dry hydrogen chloride gas[6]. Acetyla-



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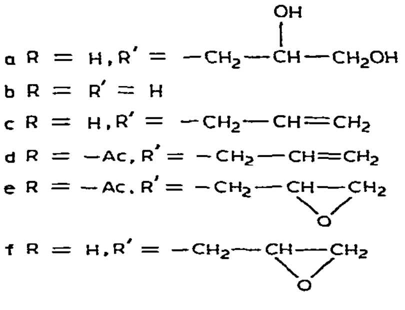

$\mathbf{a}\ R = H, R' = -CH_2-CH(OH)-CH_2OH$

$\mathbf{b}\ R = R' = H$

$\mathbf{c}\ R = H, R' = -CH_2-CH{=}CH_2$

$\mathbf{d}\ R = -Ac, R' = -CH_2-CH{=}CH_2$

$\mathbf{e}\ R = -Ac, R' = -CH_2-\overset{O}{CH-CH_2}$

$\mathbf{f}\ R = H, R' = -CH_2-\overset{O}{CH-CH_2}$

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**In this method, generally specific for the α anomer, the penultimate reaction-product, 3-*O*-(2,3,4-tri-*O*-benzyl-α-D-galactopyranosyl)-L-glycerol contains ~10% of the β anomer.

tion of the free hydroxyl groups with acetic anhydride gave **1d**, which was converted into **1e** with *m*-chloroperoxybenzoic acid. Sodium methoxide-mediated deacetylation of **1e** gave the epoxy galactoside, (**1f**). Treatment of **1f** with dilute perchloric acid produced isofloridoside. The synthetic material exhibited chromatographic behavior identical to that of an authentic sample of the natural product (ethyl acetate–water–methanol, 84:18:28 v/v; R_F 0.25 on silica gel). Proton-n.m.r. spectra for the synthetic and natural product were identical[7].

EXPERIMENTAL

Preparation of allyl α-D-galactopyranoside (**1c**). — Prepared according to the published procedure[6], **1c** had acceptable physical data.

Preparation of allyl 2,3,4,6-tetra-O-acetyl-α-D-galactopyranoside (**1d**). — The allyl glycoside **1c** (0.32 g) was dissolved in a solution containing 1.4 mL of dry acetic anhydride (from 4-Å molecular sieves) and 1.9 mL of dry pyridine (from barium oxide) at 0°. After 19 h at room temperature, the mixture was poured into 6.5 mL of ice–water and extracted with dichloromethane. The pooled extract was successively washed with M hydrochloric acid, saturated sodium hydrogencarbonate, and water and was then dried over magnesium sulfate. Removal of solvent left a crude product (0.5 g, 97%), which was crystallized from hot 95% ethanol, m.p. 82–83°, $[\alpha]_D^{27.5}$ +146.9° (*c* 4.7, chloroform).

Anal. Calc. for $C_{17}H_{24}O_{10}$: C, 52.57; H, 6.23. Found: C, 52.35; H, 6.14.

Preparation of 2,3-epoxypropyl 2,3,4,6-tetra-O-acetyl-α-D-galactopyranoside (**1e**). — To a solution of *m*-chloroperoxybenzoic acid (0.783 g, 4.5 mmol) in chloroform (10 mL) was added 0.5 g of **1d**. During a 47-h reaction at room temperature, the mixture was monitored by t.l.c. [silica gel; 2:3 ethyl acetate–petroleum ether (30–60°) (solvent *1*); R_F 0.33]. After this time, the mixture was washed twice with 0.5M potassium hydrogencarbonate, dried (magnesium sulfate), and evaporated. The resulting syrup was chromatographed on a column (17 × 2.3 cm) of silica gel using the same solvent system. The product from this purification crystallized during solvent concentration (0.4 g, 77%), and was recrystallized from abs. ethanol, m.p. 91.5–92.5°, $[\alpha]_D^{27.1}$ +126.5° (*c* 1.8, chloroform).

Anal. Calc. for $C_{17}H_{24}O_{11}$: C, 50.50; H, 5.98. Found: C, 50.32; H, 5.77.

Preparation of 2,3-epoxypropyl α-D-galactopyranoside (**1f**). — Methanolic sodium methoxide (0.08 mL of M solution) was added to a solution of the epoxide **1e** (127 mg, 0.31 mmol), suspended in 1.27 mL of dry methanol. The mixture was shaken until the solid dissolved. After 15 min, Dry Ice was added and the solvent was removed under vacuum. The resulting product exhibited R_F 0.46 by t.l.c. [silica gel; 84:18:28 ethyl acetate–water–methanol (solvent *2*)]. The product was purified on a column (17 × 2.3 cm) of silica gel using solvent *2*, resulting in a syrup (58 mg, 78%), which was taken directly to the next step.

Preparation of isofloridoside (**1a**). — Perchloric acid (1 drop) was added to a solution of **1f** (2 mg) in 1 mL of water. The mixture was kept overnight at ~25, whereupon t.l.c. (solvent *2*) indicated reaction to be complete. The synthetic and natural products exhibited identical R_F values (R_F 0.25, solvent *2*). Proton-n.m.r. spectra for the two samples were identical.

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