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Preliminary communication

Synthetic studies on rhynchosporoside: Stereoselective synthesis of 1-*O*- and 2-*O*-α-cellotriosyl-3-deoxy-2(*R*)- and -2(*S*)-glycerol*

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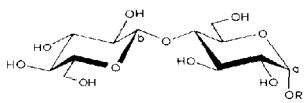
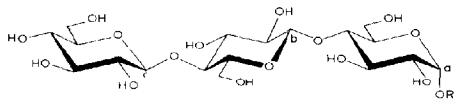
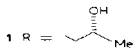
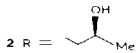
In 1980, it was proposed[2] that the structure of rhynchosporoside, a phytotoxic compound, is 1-*O*-α-cellobiosyl- or 1-*O*-α-cellotriosyl-3-deoxyglycerol and in 1982, we reported[1] that 1-*O*-α-cellobiosyl-3-deoxy-2(*R*)-glycerol (**1**) is more toxic towards *Hordeum sativum* Jessen than the 2(*S*) isomer **2**.

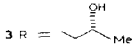
We now describe a stereoselective synthesis of the α-cellotriosyl derivatives **3**–**6**. A preliminary biological test† showed that **3** is more toxic, and **5** and **6** are less toxic, than **1**, whereas **4** is not toxic at all as in the case of **2**. These results indicated that both the 2(*R*) configuration of the diol residue and the α-D configuration of the cellotriosyl group on the primary hydroxyl group of the diol are required for production of the phytotoxicity.

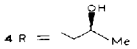


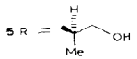


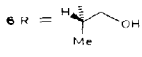
1 R = 

2 R = 

3 R = 

4 R = 

5 R = 

6 R = 

*Synthetic Studies on Glycosidic Phytotoxins, Part II. Fort Part I, see ref. 1.

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†Phytotoxicity of compounds **3**–**6** towards *Hordeum sativum* Jessen was examined by us. Prof. Strobel performed biological testing of **1**–**4** towards *Hordeum vulgare* L., and observed the same trend for the toxicity of the synthetic samples as did we. We are grateful to Prof. Strobel for his kind co-operation.

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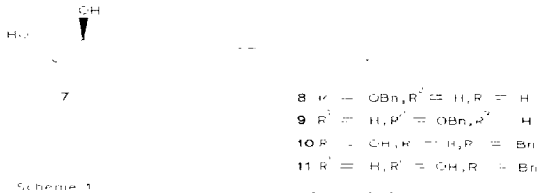
In planning the synthesis of **3**, **4**, **5**, and **6**, the target structures were retrosynthesized into the glycosyl acceptors **8**, **9**, **10**, or **11**, the D-glucosyl donors **13** or **14**, and the cellobiosyl donor **19**. The chiral glycosyl acceptors **8**–**11** were prepared by starting from 3-deoxy-2(*S*)-glycerol (**7**), readily available from L-(+)-lactic acid by $LiAlH_4$ reduction. Compound **7** was converted into **8** in 5 steps (44%); namely (*i*) TrCl, (*ii*) Ph_3P–$PhCO_2H$–DEAD[3] in THF, (*iii*) NaOMe–MeOH, (*iv*) BnBr–NaH in DMF, and (*v*) camphorsulfonic acid (CSA) in MeOH; the 3,5-dinitrobenzoate (DNB) of **8** had $[\alpha]_D$ −18.3°†. Compound **9** was prepared in 3 steps (65%) from **7**: (*i*) TrCl, (*ii*) BnBr–NaH in DMF, and (*iii*) CSA in MeOH; 3,5-DNB of **9**, $[\alpha]_D$ +17.8°. Compound **11** was prepared from **7** in 70% yield: (*i*) $(Bu_3Sn)_2O$[4], and (*ii*) BnBr–Bu_4NBr[5]; 3,5-DNB of **11**, $[\alpha]_D$ +29.0°. Compound **10** was prepared from **11** in 87% yield: (*i*) Ph_3P–$PhCO_2H$–DEAD and (*ii*) NaOMe–MeOH; 3,5-DNB of **10**, $[\alpha]_D$ −29.1°.



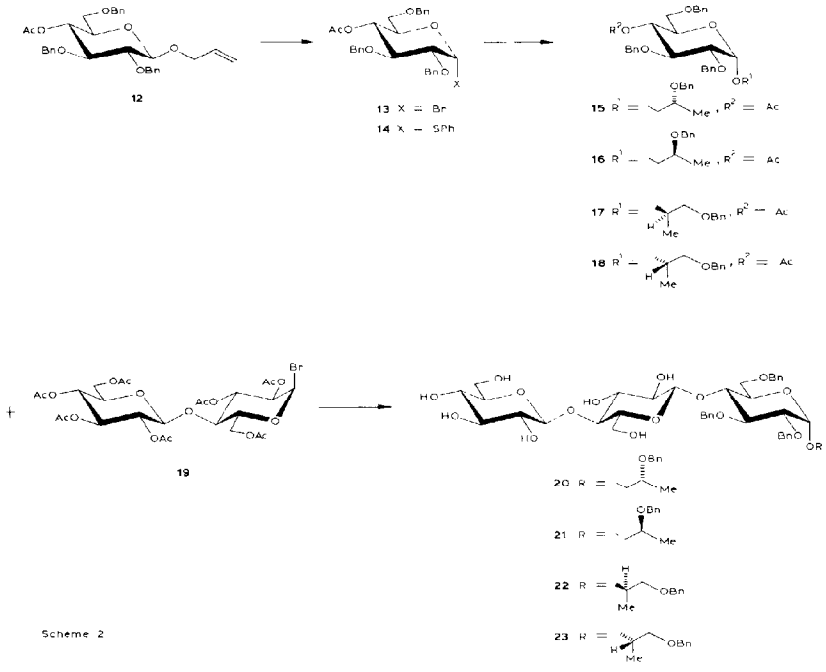
Scheme 1

By using these chiral propanediol derivatives as the glycosyl acceptors, the target molecules **3** and **4** were synthesized in the following way. Allyl β-D-glucopyranoside **12**[1] was treated with (*i*) $PdCl_2$–AcONa–aq. AcOH[6] and (*ii*) Ph_3P–CBr_4[7], to give **13**, which was respectively treated with the glycosyl acceptors **8** and **9** in the presence of Et_4NBr–powdered molecular sieves[8] 4A in $Cl(CH_2)_2Cl$ for 3 days at 70°, to give **15**, $[\alpha]_D$ +29.2°, and **16**, $[\alpha]_D$ +41.0°, in 47 and 32% yield, respectively. Compound **15** was then converted into **20**, $[\alpha]_D$ +39.1° (R_F 0.45 in 9:1 $CHCl_3$–MeOH), in 3 steps (55%). (*i*) NaOMe–MeOH, (*ii*) **19**–$AgOSO_2CF_3$–powdered molecular sieves 4A in $Cl(CH_2)_2Cl$, and (*iii*) NaOMe–MeOH. The same reaction-sequence with **16** afforded a 63% yield of **21**, $[\alpha]_D$ +25.0°; R_F 0.45 in 9:1 $CHCl_3$–MeOH. Catalytic hydrogenolysis of **20** and **21** in the presence of 10% Pd–C in MeOH at 50° respectively afforded **3**, $[\alpha]_D$ +58.0° (H_2O); R_F 0.30 in 20:20:1 $CHCl_3$–MeOH–AcOH; δ_C (D_2O): 103.25 and 103.08 (C-1b and C-1c, $^1J_{CH}$ 162.1 Hz), 99.10 (C-1a, $^1J_{CH}$ 170.9 Hz), 79.33 and 79.17 (C-4a and C-4b), and 18.81 (CH_3), and **4**, $[\alpha]_D$ +65.0° (H_2O); R_F 0.30 in 20:20:1 $CHCl_3$–MeOH–AcOH; δ_C§ (D_2O): 103.35 and 103.08 (C-1b and C-1c, $^1J_{CH}$ 163.1 Hz), 98.55 (C-1a, $^1J_{CH}$ 169.9 Hz), 79.33 and 79.17 (C-4a and C-4b), and 18.82 (CH_3).

Next, the target molecules **5** and **6**, the regio-isomers of **3** and **4**, were synthesized as follows. Allyl β-D-glucopyranoside (**12**) was converted into a mixture of **14**,

† Values of $[\alpha]_D$ were measured for $CHCl_3$ solutions at 25°, unless noted otherwise. Compounds having $[\alpha]_D$ recorded gave satisfactory data for elemental analyses.

§ The values of δ_C are expressed in p.p.m. downward from tetramethylsilane, referenced indirectly with an internal standard of 1,4-dioxane (δ_C 67.10).



Scheme 2

δ_C ($CDCl_3$): 87.1 (C-1), δ_H ($CDCl_3$): 1.88 (Ac), and its β anomer, δ_C ($CDCl_3$): 87.7 (C-1), δ_H ($CDCl_3$): 1.86 (Ac), in the ratio of 3:4, in 3 steps (72% yield): (*i*) $PdCl_2$–AcONa– aq.AcOH, (*ii*) Ac_2O–pyridine, and (*iii*) Bu_3SnSPh–$Me_3SiOSO_2CF_3$ in CH_2Cl_2[9]. The glycosylation of **10** with a mixture of **14** and its β anomer in the presence of NBS and powdered molecular sieves 4A[10], and deacetylation of the product, afforded a 43% yield of **17**, $[\alpha]_D$ +52.4°; R_F 0.36 in 5:1 toluene EtOAc, and a 44% yield of the β anomer of **17**, $[\alpha]_D$ −15.3°; R_F 0.30 in 5:1 toluene–EtOAc. In the same way, **11** was converted into **18**, $[\alpha]_D$ +39.1°; R_F 0.36 in 5:1 toluene–EtOAc, and the β anomer of **18**, $[\alpha]_D$ −11.4°, R_F 0.30 in 5:1 toluene–EtOAc, in 25 and 31% yield respectively. Further transformation of **17** and **18** into **5** and **6**, respectively, was achieved *via* **22**, $[\alpha]_D$ +50.0° (R_F 0.45 in 9:1 $CHCl_3$–MeOH) and **23**, $[\alpha]_D$ +37.5° (R_F 0.45), in 31 and 30% yield, respectively, as in the case of **15** and **16**; **5**, $[\alpha]_D$ +44.3° (H_2O), R_F 0.30, **6**, $[\alpha]_D$ +62.0° (H_2O), R_F 0.30 in 20:20:1 $CHCl_3$–MeOH–AcOH.

Comparison of the ^{1}H-n.m.r. data for the samples of synthetic **3**, **4**, **5**, and **6** (see Table I) with those reported[2] for rhynchosporoside did not definitely identify the structure of the natural product, owing to the presence, in the spectrum of the natural

TABLE I

400-MHz, ^{1}H-N.M.R. DATA FOR SYNTHETIC COMPOUNDS[a]

Compound	*H-1c*		*H-1b*		*H-1a*		CH_3	
1			4.521	(7.81)	4.936	(3.91)	1.181	(6.35)
2			4.523	(7.81)	4.939	(3.90)	1.202	(6.35)
3	4.517	(7.81)	4.545	(8.30)	4.935	(3.42)	1.180	(6.35)
4	4.517	(7.81)	4.546	(8.30)	4.938	(3.42)	1.202	(6.84)
5	4.517	(7.81)	4.547	(7.81)	5.097	(3.91)	1.234	(6.35)
6	4.516	(7.81)	4.546	(8.06)	5.063	(3.91)	1.166	(6.35)

[a] The values of δ_H are expressed in p.p.m. downward from the internal standard, sodium 2,2,3,3-tetradeuterio-4,4-dimethyl-4 silapentanoate, in D_2O. The values in parentheses are $^3J_{HH}$ values expressed in Hz.

sample, of a broad DOH signal at δ 4.7–5.0 which was overlapped by the signals of H-1a of the proposed structures **3** and **4**.

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