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Preliminary communication

Stereoselective synthesis of 1-α-cellobiosyloxy-2(*R*)- and -2(*S*)-propanol*

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Rhynchosporium secalis Davis is the causal organism of scald disease in barley and many other grasses. In 1978, Strobel *et al.*[1] isolated rhynchosporoside, a phytotoxic compound, from cultures of *R. secalis*, and in 1980, it was proposed[2] that the structure was 1-α-cellobiosyloxy- or 1-α-cellotriosyloxy-2-propanol.

In order to clarify the relationship between the stereochemistry at the 2-hydroxyl group of 1,2-propanediol and the biological activity of rhynchosporoside, we report here a stereoselective synthesis of 1-α-cellobiosyloxy-2(*R*)-propanol (**1**) and its 2(*S*) isomer (**2**). A preliminary biological test using synthetic compounds **1** and **2** showed that compound **1** [having the 2 (*R*) configuration] is more toxic towards *Hordeum sativum* JESSEN than the 2(*S*) isomer **2**.

In planning the unambiguous synthesis of **1** and **2**, the epoxides **3** and **4** were designed as the versatile, key intermediates, as ring opening of these epoxides with nucleophiles should lead to formation, not only of rhynchosporosides **1** and **2** (R^3 = H), but also of a variety of such synthetic analogs as **1** and **2** ($R^3 \neq$ H).The epoxides **3** and **4** might be constructed from the two glucopyranosyl donors **5** and **6**, and the glycosyl acceptor **7**, as envisaged in Scheme 1.

Even though the preparation of the glucopyranosyl donor **6** from *O*-benzylamylose had been reported by Anderson *et al.*[3], we developed an alternative approach to **6**, starting from allyl β-D-glucopyranoside[4], in 7 steps with a 48.3% overall yield. Thus, treatment of allyl β-D-glucopyranoside with $PhCH(OMe)_2$–TsOH–DMF gave a 91.1% yield of **8**; m.p. 144–145° (i-Pr_2O), $[\alpha]_D$ −53.3° (*c* 0.21)***.

Benzylation of **8** with NaH–BnBr gave **9** (71%), $[\alpha]_D$ −34.6° (*c* 0.280), and hydrolysis of **9** with 5:3 AcOH–H_2O at 100° gave a 97.6% yield of diol **10**; m.p. 63–64° (pet. ether), $[\alpha]_D$ −24.2° (*c* 0.260). Selective monobenzylation of **10** was achieved by the stannylation-alkylation method[5] in the presence[6] of $Bu_4N^+Br^-$, to give a 97% yield of **11**; m.p. 36–37°, $[\alpha]_D$ −10.5°; δ_C ($CDCl_3$): 70.28 (C-6a). Acetylation of **11** gave **12**

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***Optical rotations were determined for solutions in $CHCl_3$ at 25°, unless noted otherwise. Compounds with $[\alpha]_D$ provided gave satisfactory elemental analyses.

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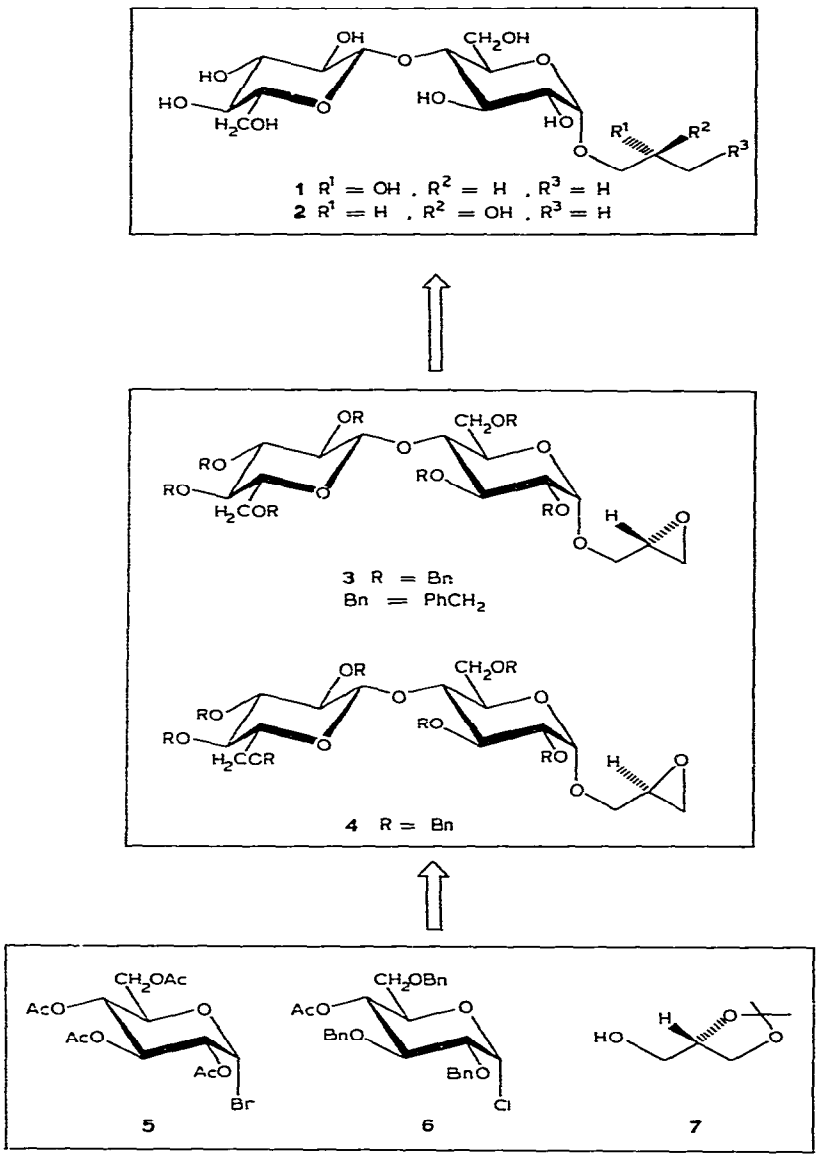
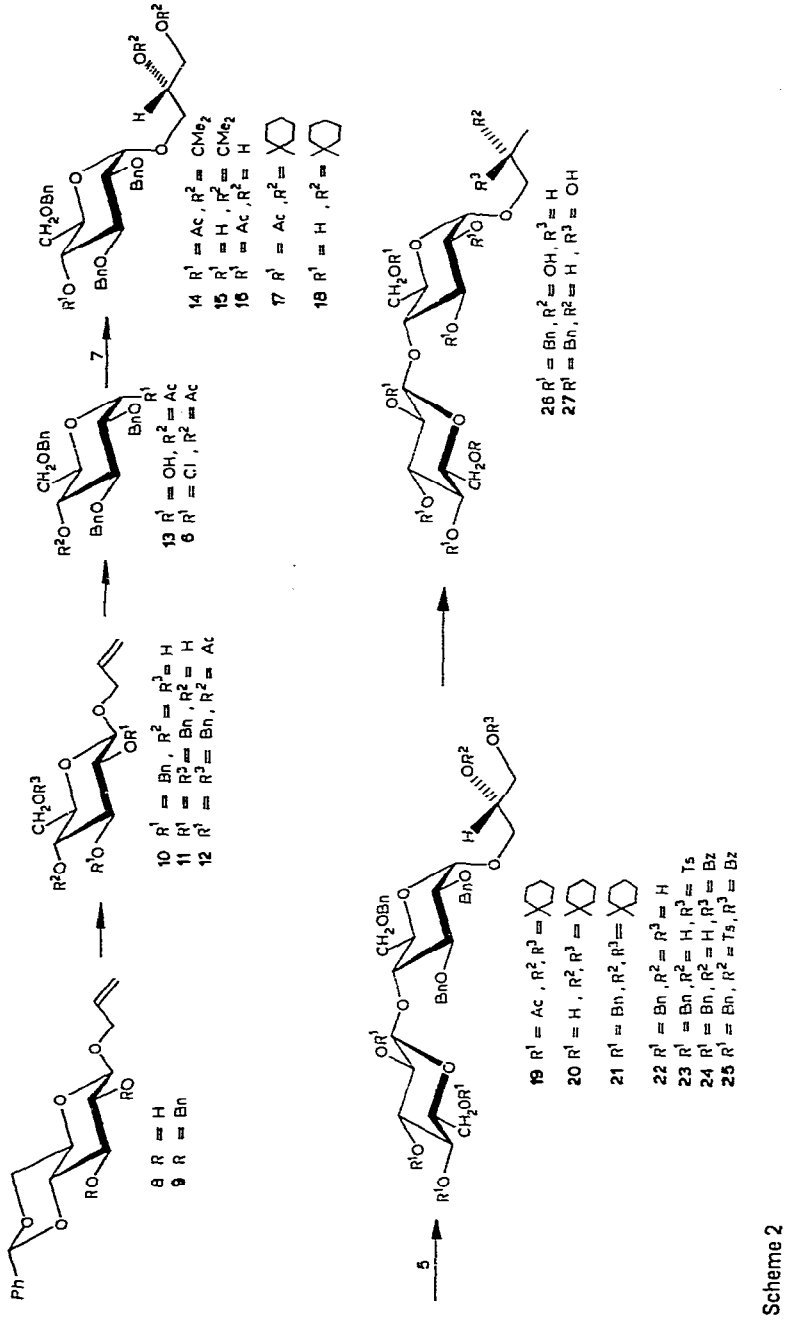


Scheme 1

(94.0%), $[\alpha]_D$ +10.8° (*c* 0.185), and deallylation of **12** with $PdCl_2$–aq.AcOH–NaOAc[7] afforded an 84.2% yield of **13**; m.p. 111–112° (i-Pr_2O), $[\alpha]_D$ +9.4°. Treatment of **13** with $SOCl_2$ in $Cl(CH_2)_2Cl$ in the presence of a catalytic amount of DMF* afforded a quantitative yield of **6**, $[\alpha]_D$ +61.9° (*c* 0.210), which reacted with glycosyl acceptor[9] **7**

*The reactive species in this transformation should be $[Me_2N^+{=}CH\text{-}OSOCl]\ Cl^-$; see ref. 8.


8 R = H
9 R = Bn
10 R¹ = Bn, R² = R³ = H
11 R¹ = R³ = Bn, R² = H
12 R¹ = R³ = Bn, R² = Ac
13 R¹ = OH, R² = Ac
6 R¹ = Cl, R² = Ac
14 R¹ = Ac, R² = CMe₂
15 R¹ = H, R² = CMe₂
16 R¹ = Ac, R² = H
17 R¹ = Ac, R² =
18 R¹ = H, R² =
19 R¹ = Ac, R², R³ =
20 R¹ = H, R², R³ =
21 R¹ = Bn, R², R³ =
22 R¹ = Bn, R² = R³ = H
23 R¹ = Bn, R² = H, R³ = Ts
24 R¹ = Bn, R² = H, R³ = Bz
25 R¹ = Bn, R² = Ts, R³ = Bz
26 R¹ = Bn, R² = OH, R³ = H
27 R¹ = Bn, R² = H, R³ = OH

Scheme 2

in the presence of $Bu_4N^+Br^-$ and i-Pr_2NEt, according to the procedure of Lemieux *et al.*[10], to give a 68.1% yield of α-D-glucopyranoside **14**, $[\alpha]_D$ +25.3° (*c* 0.320). Deacetylation of **14** gave **15**, $[\alpha]_D$ +29.7°; δ_C ($CDCl_3$): 97.41 (C-1a, $^1J_{CH}$ 168.5 Hz), but attempted glycosidation of **15** with **5** under various conditions did not afford a reproducible result, most probably due to facile cleavage of the isopropylidene group. However, the β-(1→4) linkage desired could be achieved by using a cyclohexylidene group instead of the isopropylidene group of **15**, as follows.

Cleavage of the isopropylidene group of **14** with camphorsulfonic acid in MeOH afforded a 65.5% yield of diol **16**, $[\alpha]_D$ +23.5° (*c* 0.395), and treatment of **16** with cyclohexanone dimethyl acetal–TsOH gave a 98.3% yield of **17**, $[\alpha]_D$ +40.6° (*c* 0.320). Deacetylation of **17** gave **18**, $[\alpha]_D$ +34.8° (*c* 0.310), and glycosidation of **18** with **5** in the presence of $AgOSO_2CF_3$–powdered molecular sieves 4A in $Cl(CH_2)_2Cl$ afforded a 92.5% yield of **19**; $[\alpha]_D$ +15.7° (*c* 0.325); R_F 0.40 in 2:1 toluene–EtOAc; δ_C ($CDCl_3$): 100.12 (C-1b, $^1J_{CH}$ 164.8 Hz), 97.43 (C-1a, $^1J_{CH}$ 166.0 Hz). Deacetylation of **19** gave **20**, $[\alpha]_D$ +51.7° (*c* 0.290), and benzylation of **20** afforded **21**, $[\alpha]_D$ +37.3° (*c* 0.220); treatment of **21** with TsOH in MeOH afforded a 52.9% overall yield of **22**; m.p. 110–114°, $[\alpha]_D$ +29.6° (*c* 0.125). Selective tosylation of diol **22** at the primary hydroxyl group with TsCl in pyridine afforded a 72.2% yield of monotosylate **23**, $[\alpha]_D$ +28.7° (*c* 0.230); R_F 0.24 in 5:1 toluene–EtOAc. Treatment of **23** with MeONa–MeOH gave a quantitative yield of **3**; $[\alpha]_D$ +26.4° (*c* 0.125); R_F 0.36 in 5:1 toluene–EtOAc. Inversion of the stereochemistry at C-2 could be achieved in the conventional way. Monobenzoylation of **22** with benzoyl chloride in pyridine gave **24**, $[\alpha]_D$ +29.6° (*c* 0.125); tosylation of **24** afforded **25**, $[\alpha]_D$ +38.7° (*c* 0.225), and treatment of **25** with MeONa–MeOH afforded a 49.5% overall yield of **4**. The key intermediates **3** and **4** were separately treated with $LiAlH_4$ and the product hydrogenolyzed in the presence of 10% Pd–C, to give **1**, $[\alpha]_D$ +65.8° (*c* 0.190, MeOH), and **2**, $[\alpha]_D$ +72.1° (*c* 0.190, MeOH).

Compounds **1** and **2** had the same R_F value (0.40 in 10:10:1 $CHCl_3$–MeOH–AcOH), and gave the following n.m.r. data; **1**, δ_C (D_2O): 102.77 (C-1b, $^1J_{CH}$ 162.4 Hz), 98.63 (C-1a, $^1J_{CH}$ 169.7 Hz), 78.94 (C-4a), and 18.31 (CH_3); δ_H (D_2O): 4.94 (H-1a, $J_{1,2}$ 3.9 Hz), 4.52 (H-1b, $J_{1,2}$ 7.8 Hz), and 1.18 (CH_3, *J* 6.8 Hz); **2**, δ_C (D_2O): 102.82 (C-1b, $^1J_{CH}$ 163.5), 98.09 (C-1a, $^1J_{CH}$ 170.9 Hz), 78.99 (C-4a), and 18.31 (CH_3); δ_H (D_2O): 4.94 (H-1a, $J_{1,2}$ 3.9 Hz), 4.52 (H-1b, $J_{1,2}$ 7.8 Hz), and 1.20 (CH_3, *J* 8.4 Hz).

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