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Preliminary communication

A new synthesis of Prumycin

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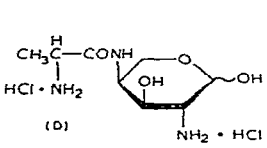
Prumycin, isolated by Hata *et al.*[1] in 1971, is a new antibiotic exhibiting a selective, inhibitory effect against phytopathogenic fungi such as *Sclerotinia sclerotiorum*. The structure was elucidated to be that of 4-(D-alanylamino)-2-amino-2,4-dideoxy-L-arabinopyranose by Ohmura *et al.*[2] in 1974. Recently, Kuzuhara *et al.*[3] and Yoshimura *et al.*[4] independently confirmed this structure by chemical synthesis.

We report here a facile synthesis of Prumycin dihydrochloride from 2-amino-2-deoxy-D-glucose. Compound **2**, prepared from 2-(benzyloxycarbonyl)amino-2-deoxy-D-glucose in one step[5], was benzoylated by the usual method, to give **3** in quantitative yield. Without purification, hydrolytic removal of the isopropylidene group of **3** under mild conditions gave benzyl 3-*O*-benzoyl-2-(benzyloxycarbonyl)amino-2-deoxy-β-D-glucofuranoside (**4**) in good yield; m.p. 131°, $[\alpha]_D^{25}$ −15° (*c* 0.3 chloroform). Oxidative cleavage between C-5 and C-6 in compound **4** with sodium metaperiodate gave a syrupy aldehyde which was converted into benzyl 3-*O*-benzoyl-2-(benzyloxycarbonyl)amino-2-deoxy-β-D-xylofuranoside (**5**) {m.p. 118°, $[\alpha]_D^{25}$ −33° (*c* 0.4, methanol); n.m.r. data (90 MHz, $CDCl_3$): τ 4.47 (1 H, q, $J_{2,3}$ 3.4 Hz, $J_{3,4}$ 6.0 Hz, H-3) and 4.84 (1 H, d, $J_{1,2}$ 2.0 Hz, H-1)} by reduction with sodium borohydride for 10 min at 0° (in 95% yield). Hydrolytic removal of the 1-*O*-benzyl group of **5** with 20 : 1 (v/v) acetic acid–2M hydrochloric acid at 55° afforded 3-*O*-benzoyl-2-(benzyloxycarbonyl)amino-2-deoxy-D-xylopyranose (**6**) in good yield; m.p. 168°, $[\alpha]_D^{21}$ +52.5° (*c* 0.5, equil., methanol). Treatment of **6** with benzyl alcohol in the presence of Amberlite IR-120 (H^+) resin at 85° gave benzyl 3-*O*-benzoyl-2-(benzyloxycarbonyl)amino-2-deoxy-β-D-xylopyranoside (**7**) {m.p. 143°, $[\alpha]_D^{25}$ −3.3° (*c* 0.3, chloroform); n.m.r. data (90 MHz, $CDCl_3$): τ 4.88 (1 H, t, $J_{2,3} = J_{3,4}$ 6.2 Hz, H-3) and 5.27 (1 H, d, $J_{1,2}$ 4.2 Hz, H-1)} in 44% yield, and the corresponding benzyl α-D-xylopyranoside {m.p. 154°, $[\alpha]_D^{25}$ +179° (*c* 0.3, chloroform), n.m.r. data ($CDCl_3$): τ 4.82 (1 H, q, $J_{2,3}$ 10.0 Hz, $J_{3,4}$ 8.0 Hz, H-3) and 5.08 (1 H, d, $J_{1,2}$ 3.5 Hz, H-1) in 35% yield. Mesylation of **7** gave benzyl 3-*O*-benzoyl-2-(benzyloxycarbonyl)amino-2-deoxy-4-*O*-mesyl-β-D-xylopyranoside (**8**), m.p. 149°, $[\alpha]_D^{25}$ −36.5° (*c* 0.3, chloroform); n.m.r. data ($CDCl_3$): τ 4.66 (1 H, t, $J_{2,3} = J_{3,4}$ 6.4 Hz, H-3), 5.25 (1 H, d, $J_{1,2}$ 5.0 Hz, H-1), and 7.06 (3 H, s, Ms). Displacement of the mesyloxy group in **8** with sodium azide in *N,N*-dimethylformamide for 10 h at 120° gave

the expected benzyl 4-azido-3-*O*-benzoyl-2-(benzyloxycarbonyl)amino-2,4-dideoxy-α-L-arabinopyranoside (**9**) in 85% yield; m.p. 114°, $[\alpha]_D^{25}$ −25.5° (*c* 0.5, chloroform); n.m.r. data ($CDCl_3$): τ 4.50 (1 H, q, $J_{2,3}$ 8.2 Hz, $J_{3,4}$ 3.0 Hz, H-3) and 5.35 (1 H, d, $J_{1,2}$ 6.0 Hz, H-1).

Saponification of **9** with sodium methoxide in methanol afforded benzyl 4-azido-2-(benzyloxycarbonyl)amino-2,4-dideoxy-α-L-arabinopyranoside (**10**) in quantitative yield; m.p. 185°, $[\alpha]_D^{25}$ −110° (*c* 0.3, methanol). Selective reduction of the azide function in compound **10** in 1:1 (v/v) 1,4-dioxane–triethylamine with hydrogen in the presence of Pd/C catalyst (10%) gave the desired benzyl 4-amino-2-(benzyloxycarbonyl)amino-2,4-dideoxy-α-L-arabinopyranoside, which was used without purification for the next reaction. The amino compound obtained was treated in 1,4-dioxane with an equivalent amount of *N*-[*N*-benzyloxycarbonyl)-D-alaninoyloxy]succinimide, affording benzyl *N,N'*-bis(benzyloxycarbonyl)-α-prumycinide (**11**) {m.p. 125°, $[\alpha]_D^{25}$ −44° (*c* 0.3 chloroform); n.m.r. data



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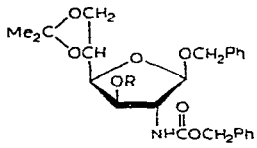
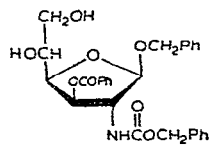


2 R = H
3 R = PhCO



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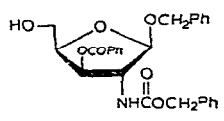
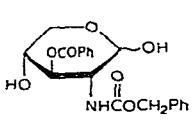


5



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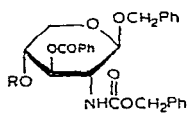
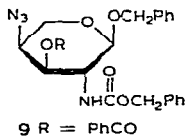
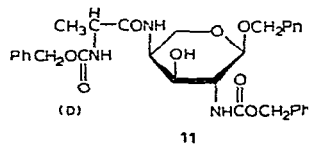


7 R = H
8 R = Ms



9 R = PhCO
10 R = H



11

(90 MHz, $CDCl_3$): τ 2.71 (15 H, 3 Ph), 3.38, 4.38, and 4.50 (3 H, 3 NH), 4.93 (4 H, s, 2 CO_2CH_2Ph), 5.27 (1 H, d, $J_{1,2}$ 2.0 Hz, H-1) and 8.71 (3 H, d, $J_{Me,H}$ 6.0 Hz, CH_3)} in 82% yield (on the basis of compound **10**), after purification by chromatography on a column of silicic acid. Compound **11** was catalytically reduced in 10:1 (v/v) methanol–water with Pd/C (10%) in the presence of acetic acid. After evaporation of the methanol, the amount of 0.1M hydrochloric acid calculated equivalent to the base was added to the residual solution, and the mixture was evaporated *in vacuo* at 30° to give prumycin dihydrochloride (**1**) in quantitative yield. The i.r. and n.m.r. spectra, and R_F values of the thin-layer chromatograms were all identical with those of an authentic sample of prumycin dihydrochloride. The synthetic prumycin dihydrochloride was crystallized from methanol to give the β anomer, m.p. 195–199° (dec.), $[\alpha]_D^{25}$ +95° (*c* 0.5, methanol); lit.[2] m.p. 198–200° (dec.), $[\alpha]_D^{20}$ +115° (*c* 0.5, methanol); lit.[3] m.p. 196–200°, $[\alpha]_D^{20}$ +93° (*c* 0.7, methanol).

New compounds gave elemental analyses and i.r. data compatible with the structures assigned.

ACKNOWLEDGMENT

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