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A FACILE SYNTHESIS OF ANOMERIC DL-TOLYPOSAMINE[1)]

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Anomeric mixture (α:β = 4:3 by NMR integration) of 4-nitro-2,3,4,6-tetradeoxyhexopyranose (1) could be synthesized from acrolein and 1-nitro-2-propanol in a reasonable yield. When α- and β-anomer of 2 were hydrogenated in the presence of Raney Nickel, the respective methyl DL-tolyposaminides were obtained; α- and β-anomer of N-benzoyl derivatives (4) of 3 were identical with the authentic samples.

The structure of tolypomycin Y[2)] was established in 1969 by Kishi et al.[3)]. This structure consists of deoxyaminosugar, tolyposamine (4-amino-2,3,4,6-tetradeoxy-L-erythrohexopyranose (5), which is not only important in the studies directed towards a total synthesis of tolypomycin, but also aroused our interest particularly in fields of aminosugars synthesis.

In 1973, Brimacombe et al.[4)] reported the synthesis of L-tolyposamine derivatives by way of an azide displacement on methyl 2,3,4,6-tetradeoxy-4-iodo-α-L-erythrohex-2-enopyranoside, in which the steps employed are rather complicated.

The authors wish to report on a facile synthesis of DL-tolyposamine, by an addition reaction of nitropropanol to acrolein in an initial step, followed by cyclization to give 4-nitro-2,3,4,6-tetradeoxyhexopyranose (1). After reduction, 2 was converted to 4, as shown in Scheme 1.

A typical procedure is as follows: a mixture of 2.00 g (35.7 mmol) of acrolein and 11.28 g (107.1 mmol) of 1-nitro-2-propanol was heated at 60 ± 5°C for about 20 hrs in the presence of diethylamine and formic acid (1:1.75 mole; employed 0.5% of total weight). After removal of excess nitropropanol in vacuo, the oily product was chromatographed on silica gel using ethyl acetate-chloroform (1:2) as solvent. Anomeric mixture (α:β = 4:3 by NMR integration) of 1; mp 64.5-68.5°C (recrystallized from n-hexane-diethyl ether), Found: C, 44.96; H, 6.93; N, 8.91 %, Calcd for $C_6H_{11}NO_4$: C, 44.72; H, 6.83; N, 8.69 %, ν_{max}^{KBr} (cm^{-1}): 3280 (OH), 1550, 1350 (C-NO_2)., was thus obtained in 33 % yield.

Hydrochloric acid (0.03 ml) in methanol (3 ml) was added to 300 mg of 1, and the solution was heated at 50°C for 0.5 hr to give two products, α- and β-anomer of methyl hexopyranoside (2)[5)]; α-anomer as colorless oil, 180 mg in 55 % yield, ν_{max}^{film} (cm^{-1}): 1550, 1375 (C-NO_2), δ ($CDCl_3$): 4.70 (d-d, $J_{1,2a}$ = 2 Hz, $J_{1,2b}$ = 3.5 Hz, anomeric H), β-anomer as colorless crystals, 65 mg in 20 % yield, mp 31.5-32°C (from ethanol-water) ν_{max}^{KBr} (cm^{-1}): 1550, 1390 (C-NO_2); δ ($CDCl_3$): 4.47 (d-d, $J_{1,2a}$ = 3 Hz, $J_{1,2b}$ = 9 Hz, anomeric H), Found: C, 47.89; H, 7.52; N, 7.83 %, Calcd for $C_7H_{13}NO_4$: C, 47.99; H, 7.48; N, 8.00 %.

A 450 mg (2.57 mmol) portion of α-anomer in methanol was hydrogenated using Raney

Nickel T-1[6] catalyst under 3.5 kg/cm^2 (initial)[7] in about one hour. Benzoylation of crude, reduced product with benzoic anhydride gave methyl N-benzoyltolyposaminide (α-anomer of 4) in 79 % yield, mp 148-149°C (from ethyl acetate-petroleum ether); ν_{max}^{KBr} (cm^{-1}): 3220 (NH), 1625 (amide-I), 1560 (amide-II); δ ($CDCl_3$): 1.25 (3H, d, $J_{5,6}$ = 6 Hz, CH_3), 3.36 (3H, s, OCH_3), 4.70 (1H, s, fine splitting, anomeric H), 6.05 (1H, d, NH); Found: C, 67.52; H, 7.74; N, 5.51 %; Calcd for $C_{14}H_{19}NO_3$: C, 67.44; H, 7.68; N, 5.62 %.

ß-Anomer of 2 was reduced and subsequently benzoylated in a similar procedure; ß-anomer of 4, mp 171-172.5°C (ethyl acetate-petroleum ether), in 84 % yield, ν_{max}^{KBr} (cm^{-1}): 3210 (NH), 1630 (amide-I), 1570 (amide-II); δ ($CDCl_3$): 1.31 (3H, d, $J_{5,6}$ = 6 Hz, CH_3), 3.47 (3H, s, OCH_3), 4.37 (1H, d-d, $J_{1,2a}$ = 3 Hz, $J_{1,2b}$ = 8 Hz, anomeric H), 6.20 (1H, d, NH); Found: C, 67.78; H, 7.66; N, 5.91 %; Calcd for $C_{14}H_{19}NO_3$: C, 67.44; H, 7.68; N, 5.62 %.

The identities of these α- and ß-N-benzoyltolyposaminide (4) in this series were confirmed by a comparison of their melting points, IR and NMR spectra with those of the authentic samples[8].

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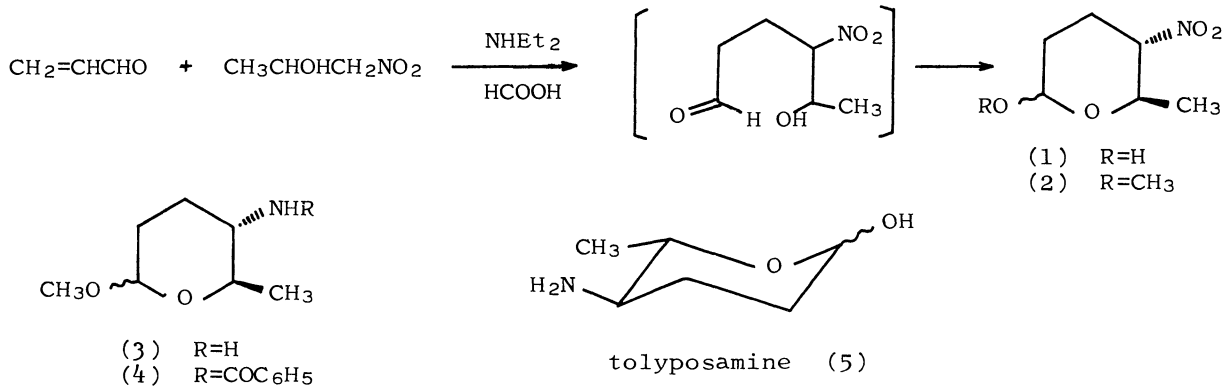
Scheme 1



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