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Note

A convenient new route to methyl *N*,*O*-diacetyl-α-L-ristosaminide

ISTVÁN PELYVÁS, FERENC SZTARICSKAI, AND REZSŐ BOGNÁR
Research Group for Antibiotics, Hungarian Academy of Sciences, H-4010 Debrecen (Hungary)
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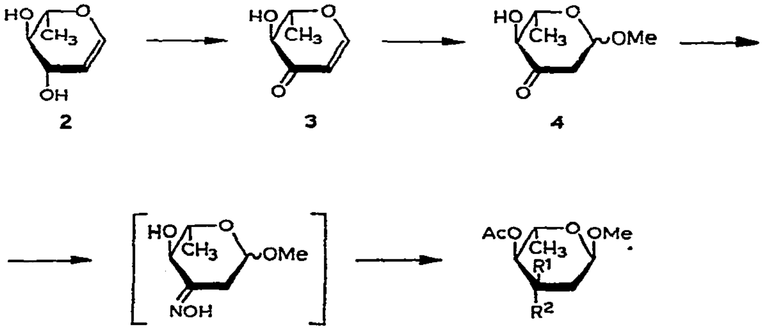
Methyl 3-acetamido-4-*O*-acetyl-2,3,6-trideoxy-α-L-*ribo*-hexopyranoside (**1**), the *N*,*O*-diacetyl derivative of methyl α-L-ristosaminide[1–3] derived from the antibiotic ristomycin-A[4], should serve as a suitable starting-material for glycosylation of the aglycons of anthracycline-type antibiotics[5].

The title compound (**1**) was first obtained[1] by the methanolysis of ristomycin-A followed by acetylation; later, it was synthesized[3,6] in several steps* from 1,5-anhydro-2,6-dideoxy-L-*arabino*-hex-1-enitol (L-rhamnal).

We now describe a rapid and convenient route to **1**, with an overall yield of 18.6% calculated for the starting L-rhamnal (**2**).

Oxidation of **2** in dry benzene with the silver carbonate-on-Celite reagent (Fetizon reagent[7]) gave crystalline 1,5-anhydro-2,6-dideoxy-L-*erythro*-hex-1-en-3-ulose (**3**) in 59% yield. Compound **3** has been recently prepared by Paulsen and Bünsch[8] by the oxidation of **2** with manganese dioxide.

Addition of methanol to **3** in the presence of sodium methoxide, according to



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1 R¹ = NHAc, R² = H
6 R¹ = H, R² = NHAc

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*Both methods were reported without experimental details.

the procedure of Thiem and Elvers[9], resulted in a *ca.* 15:1 mixture (**4**) of methyl 2,6-dideoxy-α-L-*erythro*-hexopyranosid-3-ulose and the corresponding β anomer. Oximation of the mixture **4** at room temperature with methanolic hydroxylamine gave **5**, contaminated with two minor components. This product was hydrogenated without purification in the presence of Raney nickel under atmospheric pressure, and then acetylated in pyridine. According to g.l.c. investigation, the product consisted of 79.2% of methyl 3-acetamido-4-*O*-acetyl-2,3,6-trideoxy-α-L-*ribo*-hexopyranoside (**1**), 14.4% of methyl 3-acetamido-4-*O*-acetyl-2,3,6-trideoxy-α-L-*arabino*-hexopyranoside (**6**, methyl *N,O*-diacetyl-α-L-acosaminide[10]), and three unidentified, minor components (4.5, 0.94, and 0.95%). For comparison of the *T* values, authentic samples of **1**[1] and **6**[11] were used.

The main components **1** (37.7%) and **6** (3.4%) were isolated crystalline after column chromatography, and their physical constants were in good agreement with those reported in the literature.

EXPERIMENTAL

General. — Melting points were determined on a Kofler hot-stage and are uncorrected. Optical rotations were measured with Schmidt–Haensch and Perkin–Elmer 241 polarimeters. ^{1}H-N.m.r. spectra were recorded with a JEOL MH-100 instrument. G.l.c. was performed with a Hewlett–Packard HP 5830 A instrument and a column of 3% ECNSS-M at 150° (5°/min). T.l.c. and column chromatography were performed on Kieselgel G (Merck) with 85:15 benzene–methanol. Concentrations were performed under diminished pressure at 40°.

*1,5-Anhydro-2,6-dideoxy-*L-erythro-*hex-1-en-3-ulose* (**3**). — To a solution of 1,5-anhydro-2,6-dideoxy-L-*arabino*-hex-1-enitol (**2**, 6 g) in abs. benzene (450 ml) was added the Fetizon reagent[7] (95 g). The mixture was concentrated on a rotary evaporator to half volume and, after the addition of 150 ml of abs. benzene, boiled under reflux for 3 h and then filtered. The filtrate was evaporated to give colourless, crystalline **3** (3.5 g, 59.3%), m.p. 92–93° (in a closed capillary-tube), $[\alpha]_D^{25}$ −194° (*c* 1.0, chloroform); lit.[8] m.p. 86° (subl.), $[\alpha]_D^{28}$ −227° (*c* 1.5, methanol). ^{1}H-N.m.r. data ($CDCl_3$): δ 1.58 (d, 3 H, $J_{5,6}$ 6 Hz, CH_3-5), 3.82 (s, 1 H, HO-4), 3.98 (d, 1 H, $J_{4,5}$ 12.5 Hz, H-4), 4.18 (qd, 1 H, H-5), 5.45 (d, 1 H, $J_{1,2}$ 6 Hz, H-1), and 7.39 (d, 1 H, H-2).

Anal. Calc. for $C_6H_8O_3$: C, 56.24; H, 6.29. Found: C, 56.43; H, 6.28.

*Methyl 2,6-dideoxy-α,β-*L-erythro-*hexopyranosid-3-ulose* (**4**). — A solution of **3** (900 mg) in 0.01M methanolic sodium methoxide (120 ml) was kept at room temperature for 10 min, and then neutralized with AG 50W-X12(H^+) cation-exchange resin and evaporated to dryness to give colourless, syrupy **4** (940 mg, 83%; α,β ratio ~15:1), $[\alpha]_D^{25}$ −139° (*c* 0.31, methanol); lit.[9] $[\alpha]_D^{20}$ −177.8° (*c* 1.7, methanol) for the pure α anomer. ^{1}H-N.m.r. data ($CDCl_3$): δ 1.42 (d, 3 H, $J_{5,6}$ 5 Hz, CH_3-5), 2.60 (dd, 1 H, $J_{1e,2e}$ ~1.5, $J_{2e,2a}$ 13.5 Hz, H-2e), 2.84 (dd, 1 H, $J_{1e,2a}$

~4 Hz, H-2a), 3.6–4.1 (m, 2 H, H-4 and H-5), 5.10 (dd, 1 H, H-1e); for the contaminating (~6–6.5%) β anomer: δ 4.61 (dd, 1 H, $J_{1a,2a}$ ~8, $J_{1a,2e}$ ~4 Hz, H-1a).

Anal. Calc. for $C_7H_{12}O_4$: C, 52.49; H, 7.55. Found: C, 52.31; H, 7.53.

*Methyl 3-acetamido-4-*O*-acetyl-2,3,6-trideoxy-α-*L*-*ribo*-hexopyranoside* (**1**; *methyl* N,O*-diacetyl-α-*L*-ristosaminide*). — To a solution of **4** (450 mg) in abs. methanol (5 ml) was added a solution of hydroxylamine in abs. methanol [10 ml; prepared from hydroxylamine hydrochloride (1.17 g) and potassium hydroxide (975 mg)]. After storage at room temperature for 4 h, **4** had disappeared (t.l.c.). The reaction mixture was evaporated to dryness to give a syrupy residue (400 mg) consisting of **5** (R_F 0.44) and two minor components (less than 5%, R_F 0.2 and 0.15).

This mixture was dissolved in abs. methanol (20 ml) and, after the addition of Raney nickel (1 g), it was hydrogenated at atmospheric pressure for 5 h. The catalyst was filtered off, the filtrate was evaporated, and the residue was acetylated in dry pyridine (2.5 ml) with acetic anhydride (2.5 ml) for 16 h. The reaction mixture was poured onto ice–water and extracted with chloroform, and the organic layer was washed with water, dried ($MgSO_4$), and concentrated to yield a syrupy mixture of **1** (79.2%, T 2.62 min), **6** (14.4%, T 4.15 min), and three unidentified components with T 1.80, 3.91, and 6.33 min (4.5, 0.94, and 0.95%, respectively). The T values of the authentic samples of **1**[1] and **6**[11] were 2.64 and 4.13 min, respectively.

Column chromatography of this mixture gave methyl *N,O*-diacetyl-α-L-ristosaminide (**1**), which was recrystallized from light petroleum containing one drop of water; yield, 260 mg (37.7%), m.p. 49–51°, $[\alpha]_D^{25}$ −132° (*c* 0.62, chloroform), R_F 0.57; lit.[1] m.p. 51–52°, $[\alpha]_D^{25}$ −134° (*c* 0.5, chloroform). The crystalline sample of **1** did not give correct elemental analyses; however, after storage over $CaCl_2$ and paraffin for several days, the resulting syrupy material gave correct microanalytical data.

Anal. Calc. for $C_{11}H_{19}NO_5$: C, 53.87; H, 7.81; N, 5.71. Found: C, 54.13; H, 7.78; N, 5.66.

Eluted second was the product with R_F 0.43, which gave methyl 3-acetamido-4-*O*-acetyl-2,3,6-trideoxy-α-L-*arabino*-hexopyranoside (**6**) as colourless crystals, m.p. 162–163°, $[\alpha]_D^{25}$ −189° (*c* 0.23, methanol); lit.[10] m.p. 163–164°, $[\alpha]_D^{22}$ −191° (*c* 0.52, methanol).

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