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Note

A convenient synthesis of *N*-acetyllactosamine

JOCELYNE ALAIS AND ALAIN VEYRIÈRES
Laboratoire de Chimie Organique Multifonctionelle, Bât. 420, Université de Paris-Sud, 91405 Orsay (France)

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Lee and Lee[1] have recently reported a simple preparation of 2-acetamido-2-deoxy-4-*O*-β-D-galactopyranosyl-D-glucose (*N*-acetyllactosamine), wherein the key step is an addition of hydrogen cyanide, generated *in situ*, to 1-*N*-benzyl-3-*O*-β-D-galactopyranosyl-D-arabinosylamine, a compound easily obtained from 3-*O*-β-D-galactopyranosyl-D-arabinose. Although this procedure avoids the handling of anhydrous hydrogen cyanide, it requires a tedious separation of the *gluco* and *manno* epimers, at the last stage, by repeated chromatographies on Bio-Gel.

Owing to the growing need for substantial amounts of *N*-acetyllactosamine for synthetic purposes, we now report a very similar procedure that allows the preparation of 10–20-g amounts of this disaccharide without any chromatographic purification. The addition of hydrogen cyanide was performed in a way similar to that described originally by Walker and Barker[2], and allowed the preponderant 2-benzylamino-2-deoxy-D-gluconononitrile derivative to crystallize spontaneously from the reaction mixture in 79% yield. This product could not be recrystallized, as, according to Kuhn and Jochims[3], it epimerizes easily in boiling hydroxylic solvents. When dried, it could be stored for several days at −20° without noticeable modification.

Simultaneous hydrogenolysis of the benzylamino and nitrile groups, followed by *N*-acetylation of the amino group, as described by Kuhn and Kirschenlohr[4], afforded, after one crystallization from methanol, *N*-acetyllactosamine, sufficiently pure for synthetic purposes, in 59% yield. Thus, starting from 100 g of lactose, we were able to prepare 13 g of *N*-acetyllactosamine. However, when these last two steps of the synthesis were applied to the impure mixture of the 2-benzylamino-2-deoxy-nitriles obtained either by evaporation of the reaction mixture or by precipitation with ether, crystallization of pure *N*-acetyllactosamine in good yield was impossible.

EXPERIMENTAL

General methods. — Melting points are uncorrected. Optical rotations were determined with a Roussel–Jouan electronic, digital micropolarimeter. I.r. spectra

were recorded with a Unicam model SP 1100 spectrometer. T.l.c. was performed on plates of silica gel (with fluorescence indicator; layer thickness 0.25 mm; E. Merck, Darmstadt, Germany). The compounds were detected by spraying the plates with 1:19 (v/v) conc. sulfuric acid–ethanol.

*2-Benzylamino-2-deoxy-4-*O*-β-*D*-galactopyranosyl-*D*-glucononitrile.* — To a stirred suspension of 1-*N*-benzyl-3-*O*-β-D-galactopyranosyl-D-arabinosylamine[4] (32 g, 80 mmol) and sodium cyanide (4.32 g, 88 mol) in absolute ethanol (320 mL), cooled to 0–5°, was added dropwise a solution of glacial acetic acid (5.28 g, 88 mmol) in absolute ethanol (80 mL). The mixture was stirred at room temperature until complete dissolution (~5 h). Storage overnight in the cold yielded a precipitate that was filtered off, washed successively with cold absolute ethanol and dry ether, and dried (27 g, 79%); m.p. 99–102° (dec.), $[\alpha]_D^{20}$ +19 (5 min)→+2 (18 h)→−2° (48 h; *c* 1.01, water); ν_{max}^{Nujol} 2250 (C≡N) and 702 cm^{-1} (phenyl); t.l.c. in 3:3:2 (v/v) ethyl acetate–2-propanol–water showed the product (R_F 0.54) to contain a minor impurity (R_F 0.25).

*2-Acetamido-2-deoxy-4-*O*-β-*D*-galactopyranosyl-*D*-glucopyranose.* — The crude nitrile (18.4 g, 43 mmol) was dissolved in cold 0.5M hydrochloric acid (200 mL, 2.3 equiv.). To this solution was added 10% palladium-on-barium sulfate (6.4 g), and the mixture was hydrogenated at room temperature and atmospheric pressure until absorption of hydrogen stopped (~19 h, 1750 mL, 85%). The catalyst was filtered off with the aid of Celite and washed with water. The pH of the slightly acidic filtrate was brought to 6 by addition of solid sodium hydrogencarbonate, and the solution concentrated to 30 mL. Sodium acetate (7.3 g) and methanol (30 mL) were added, followed by acetic anhydride (10.3 mL). After 18 h at room temperature, methanol was evaporated. The cations were removed by passage through a column of Amberlite IR-120 (H^+) ion-exchange resin (200 mL). The pH of the eluate was brought to 4–5 by addition of Amberlite IR-45 (OH^-) ion-exchange resin. After filtration, the solution was evaporated to dryness. The residue was dissolved in methanol (60 mL) and stored overnight at 0–5°. The crystalline precipitate was filtered off, washed successively with cold methanol, ethanol, and ether, and dried (10.6 g, 59%), m.p. 163–165° (lit.[4] m.p. 168–170°). Concentration of the mother liquors afforded a less pure product (0.86 g, 5%).

O-Acetylation of the material having m.p. 163–165° according to Zilliken *et al.*[5] yielded the crystalline α-heptaacetate of *N*-acetyllactosamine in 83% yield, m.p. 220–221°; lit.[5] m.p. 220°.

REFERENCES

1 R. T. Lee and Y. C. Lee, *Carbohydr. Res.*, 77 (1979) 270–274.
2 T. E. Walker and R. Barker, *Carbohydr. Res.*, 64 (1978) 266–270.
3 R. Kuhn and J. C. Jochims, *Chem. Ber.*, 96 (1963) 983.
4 R. Kuhn and W. Kirschenlohr, *Justus Liebigs Ann. Chem.*, 600 (1956) 135–143.
5 F. Zilliken, P. N. Smith, R. M. Tomarelli, and P. György, *Arch. Biochem. Biophys.*, 54 (1955) 398–405.