Note

The synthesis of 2-acetamido-3,4,6-tri-*O*-acetyl-*N*-[*N*-(benzyloxycarbonyl)-L-aspart-1-and 4-oyl]-2-deoxy-β-D-glucopyranosylamine*

HARI G. GARG AND ROGER W. JEANLOZ†

Laboratory for Carbohydrate Research, Departments of Biological Chemistry and Medicine, Harvard Medical School and Massachusetts General Hospital, Boston, Massachusetts 02114 (U. S. A.)

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2-Acetamido-3,4,6-tri-*O*-acetyl-*N*-[*N*-(benzyloxycarbonyl)-L-aspart-4-oyl]-2-deoxy-β-D-glucopyranosylamine (**4**) was needed as an intermediate in our program of synthesis of glycopeptides containing a 2-acetamido-2-deoxy-D-glucose–L-asparagine residue. A multistep route starting from the known 1-benzyl *N*-(benzyloxycarbonyl)-L-aspart-4-oyl derivative **3**, obtained either *via* the dicyclohexylcarbodiimide[1] or the chloride[2] methods, and involving removal of the protective benzyl and *N*-(benzyloxycarbonyl) groups and re-introduction of the latter group, appeared unattractive in view of the large quantity of 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl azide (**1**) that this would require. Instead, 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosylamine[1,2] (**2**), obtained by catalytic hydrogenation of the azide **1**, was, without further purification, directly condensed with *N*-(benzyloxycarbonyl)-L-aspartic anhydride[4], to give a mixture of the desired compound **4** and its 1-oyl isomer **6**. The mixture of **4** and **6** could readily be resolved by fractional recrystallization from methanol, and, for identification, the resulting pure compounds were hydrogenolyzed to the known[5] compounds **5** and **7**, respectively. Although the total yield of **4** was only 24% (instead of a theoretical yield of 50%), this synthesis was accomplished in one step from **2**, as compared with the four steps necessary when 1-benzyl *N*-(benzyloxycarbonyl)-L-aspartate is used.

EXPERIMENTAL

General methods. — Melting points were determined with a Mettler FP-2 apparatus and correspond to "corrected melting point". Rotations were determined, for solutions in 1-dm, semimicro tubes, with a Perkin–Elmer No. 141 polarimeter.

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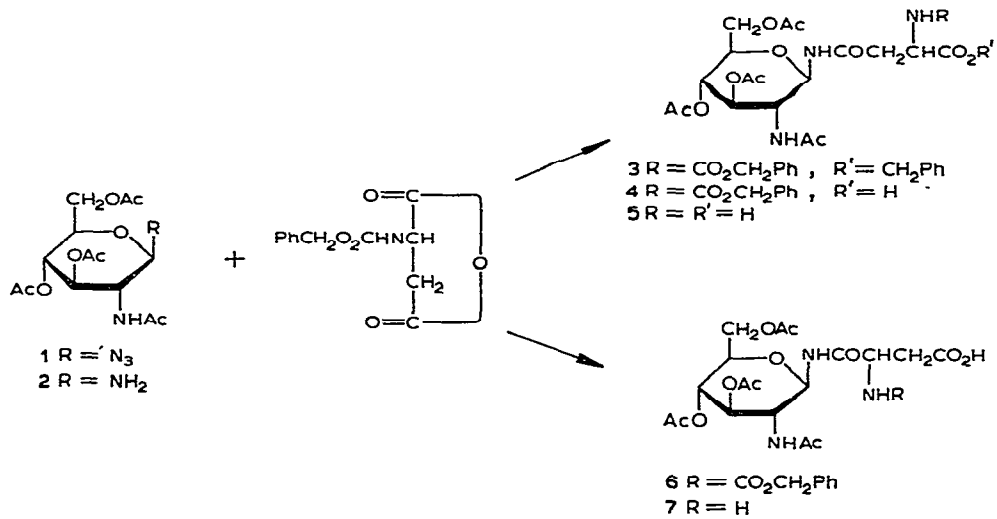
†To whom inquiries should be addressed.



I.r. spectra were recorded with a Perkin–Elmer spectrophotometer Model 237. Evaporations were performed *in vacuo*, the bath temperature being kept below 45°. The homogeneity of nonpolar compounds was verified by ascending t.l.c. on precoated plates of Silica Gel G (Merck); the spots were detected by spraying with 20% sulfuric acid and heating at 300–400° for a few min. The microanalyses were performed by Dr. M. Manser, Zürich, Switzerland.

*2-Acetamido-3,4,6-tri-*O*-acetyl-*N*-[N-(benzyloxycarbonyl)-*L*-aspart-4-oyl]-2-deoxy-β-*D*-glucopyranosylamine* (**4**). — A solution of *N*-(benzyloxycarbonyl)-L-aspartic anhydride[4] (1.26 g) in ethyl acetate (20 ml) was added to a solution of 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosylamine [**2**, obtained from 2.0 g of 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl azide[1–3] (**1**)] in ethyl acetate (30 ml). The mixture was warmed for a few min until it became clear, and then kept overnight at room temperature. The resulting precipitate was filtered off, to give 1.6 g (50% yield, based on **1**) showing, on t.l.c. in 7:3 (v/v) chloroform–methanol, two spots (R_F 0.4 and 0.6). Crystallization from methanol gave the slower-moving product (**4**, 0.70 g, 22%) as long needles, m.p. 235–237° (dec); $[\alpha]_D^{20}$ +10.1° (*c* 1.1, *N*,*N*-dimethylformamide); i.r. data: ν_{max}^{KBr} 1655 (CONH), 1745 (OAc), 1705 (benzyloxycarbonyl C=O), and 1530 cm^{-1} (peptide Amide I). The mother liquor was saved for the isolation of **6**.

Anal. Calc. for $C_{26}H_{33}N_3O_{13}$: C, 52.45; H, 5.58; N, 7.22; O, 34.90. Found: C, 52.33; H, 5.57; N, 7.04; O, 35.05.

A solution of **4** (0.40 g) in 9:1 (v/v) acetic acid–water (50 ml) was hydrogenated in the presence of 10% palladium-on-charcoal (50 mg) for 3.5 h at room temperature. The catalyst was filtered off, and the filtrate was evaporated to dryness. Recrystallization from acetone gave 2-acetamido-3,4,6-tri-*O*-acetyl-*N*-(L-aspart-4-oyl)-2-deoxy-β-D-glucopyranosylamine (**5**) (0.24 g, 79%), m.p. 225–227° (dec.); $[\alpha]_D^{20}$ +7.8° (*c*, 1.16, water); lit.[5] m.p. 212–214°, $[\alpha]_D^{21}$ +11° (water).

Compound **5** gave only one spot in t.l.c. on silica gel in 4:1:5 (v/v) butyl alcohol–acetic acid–water, and a brown color with the ninhydrin reagent.

2-Acetamido-3,4,6-tri-O-acetyl-N-[N-(benzyloxycarbonyl)-L-aspart-1-oyl]-2-deoxy-β-D-glucopyranosylamine (**6**). — The mother liquor of the preparation of **4** gave, after slow concentration followed by recrystallization from abs. ethanol, compound **6** (0.40 g, 12.5%), m.p. 197–198°; $[\alpha]_D^{20}$ −13.5° (*c* 1.0, *N,N*-dimethylformamide); i.r. data: ν_{max}^{KBr} 1655 (CONH), 1750 (OAc), 1680 (benzyloxycarbonyl CO), and 1530 cm^{-1} (peptide Amide I).

Anal. Calc. for $C_{26}H_{33}N_3O_{13}$: C, 52.45; H, 5.58; N, 7.22; O, 34.90. Found: C, 52.34; H, 5.60; N, 7.04; O, 34.90.

Hydrogenolysis of **6** (0.15 g), as described for the preparation of **5** from **4**, gave 2-acetamido-3,4,6-tri-*O*-acetyl-*N*-(L-aspart-1-oyl)-2-deoxy-β-D-glucopyranosylamine (**7**) (98 mg, 70%), m.p. 226–227° (dec.), $[\alpha]_D^{20}$ −1.7° (*c* 1.15, water); lit.[5] m.p. 207–209°; $[\alpha]_D^{21.5}$ +5° (water). Compound **7** gave only one spot in t.l.c. on silica gel in 4:1:5 (v/v) butyl alcohol–acetic acid–water, and gave a purple color with the ninhydrin reagent.

Of the total material (1.5 g) obtained by evaporation of the mother liquors of **4** and **6**, 1.0 g was applied to a column (40 × 2 cm) of silica gel. Successive elution with a linear gradient (15:1 to 3:2) of ethyl acetate–acetone, followed by acetone and then methanol, gave **6** (0.50 g; containing some contamination that trailed to the origin on t.l.c.) that was eluted with acetone, and **4** (375 mg, showing a behavior on t.l.c. similar to that of **6**) that was eluted with methanol. Repeated recrystallization gave pure **4** (0.60 g, total yield 24%) and pure **6** (0.24 g, total yield 19%).

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